US Patent & Trademark Office

US 8,865,921

USPTO Transaction Information*

SEQ.[δ]	DATE	DESCRIPTION
1	21 Oct 2014	Recordation of Patent Grant Mailed
2	01 Oct 2014	Issue Notification Mailed
3	21 Oct 2014	Patent Issue Date Used in PTA Calculation
4	19 Sep 2014	Dispatch to FDC
5	19 Sep 2014	Application Is Considered Ready for Issue
6	18 Sep 2014	Issue Fee Payment Verified
7	18 Sep 2014	Issue Fee Payment Received
8	20 Jun 2014	Mail Notice of Allowance
9	18 Jun 2014	Document Verification
10	18 Jun 2014	Notice of Allowance Data Verification Completed
11	17 Jun 2014	Information Disclosure Statement considered
12	17 Jun 2014	Date Forwarded to Examiner
13	13 Jun 2014	Response after Final Action
14	23 May 2014	Electronic Information Disclosure Statement
15	23 May 2014	Information Disclosure Statement (IDS) Filed
16	31 Mar 2014	Mail Final Rejection (PTOL - 326)
17	25 Mar 2014	Final Rejection
18	13 Mar 2014	Information Disclosure Statement considered
19	13 Mar 2014	Date Forwarded to Examiner
20	07 Mar 2014	Response after Non-Final Action
21	10 Jan 2014	Electronic Information Disclosure Statement
22	10 Jan 2014	Information Disclosure Statement (IDS) Filed
23	11 Dec 2013	Mail Non-Final Rejection
24	09 Dec 2013	Non-Final Rejection
25	22 Mar 2012	Information Disclosure Statement considered
26	20 Nov 2012	Case Docketed to Examiner in GAU
27	08 Nov 2012	Transfer Inquiry to GAU
28	25 Oct 2012	PG-Pub Issue Notification
29	22 Mar 2012	Substitute Specification Filed
30	22 Mar 2012	Preliminary Amendment
31	22 Mar 2012	Request for Foreign Priority (Priority Papers May Be Included)
32	22 Mar 2012	Electronic Information Disclosure Statement

US Patent & Trademark Office

US 8,865,921

USPTO Transaction Information*

SEQ.[δ]	DATE	DESCRIPTION
33	13 Aug 2012	Application Dispatched from OIPE
34	09 Jul 2012	371 Completion Date
35	18 Jul 2012	Sent to Classification Contractor
36	18 Jul 2012	Filing Receipt
37	18 Jul 2012	Notice of DO/EO Acceptance Mailed
38	09 Jul 2012	Additional Application Filing Fees
39	09 Jul 2012	A statement by one or more inventors satisfying the requirement under 35 USC 115, Oath of the Applic
40	17 May 2012	Notice of DO/EO Missing Requirements Mailed
41	22 Mar 2012	Information Disclosure Statement (IDS) Filed
42	22 Mar 2012	Cleared by OIPE CSR
43	22 Mar 2012	Initial Exam Team nn

Patent Assignment Abstract of Title

Total Assignments: 1

Application #: 13497690 **Filing Dt:** 07/09/2012 **Patent #:** 8865921 **Issue Dt:** 10/21/2014

PCT #: NONE **Intl Reg #:** **Publication #:** US20120271060 **Pub Dt:** 25-OCT-12

Inventors: Cesar Muñoz de Diego, Gerardus Johannes Maria Gruter, Matheus Adrianus Dam

Title: METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

Assignment: 1

Reel/Frame: 028514 / 0284 **Received:** 07/09/2012 **Recorded:** 07/09/2012 **Mailed:** 07/10/2012 **Pages:** 2

Conveyance: ASSIGNMENT OF ASSIGNORS INTEREST (SEE DOCUMENT FOR DETAILS).

Assignors:

MUNOZ DE DIEGO, CESAR	**Exec Dt:** 03/26/2012
DAM, MATHEUS ADRIANUS	**Exec Dt:** 03/26/2012
GRUTER, GERARDUS JOHANNES MARIA	**Exec Dt:** 03/26/2012

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AMSTERDAM, NETHERLANDS 1014 BV

Correspondent: HOFFMANN & BARON, LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

US Patent & Trademark Office

US 8,865,921

Maintenance Fee Statement*

	Fee Description	Amount	Surcharge	Small Entity	Attorney Docket No.	Status
1	Due at 3.5 years	0.00	0.00			NONE
2	Due at 7.5 years	0.00	0.00			NONE
3	Due at 11.5 years	0.00	0.00			NONE

MISSING PAGE(S) FROM THE U.S. PATENT OFFICE OFFICIAL FILE WRAPPER

File Wrapper Cover

PTO-1390 (09-11)
Approved for use through 4/30/2013. OMB 0651-0021
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A SUBMISSION UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	U.S. APPLICATION NO. (If known, see 37 CFR 1.5)
903-457 PCT/US	

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/NL2010/050654	6 October 2010	7 October 2009

TITLE OF INVENTION
METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE

APPLICANT(S) FOR DO/EO/US
Cesar Munoz de Diego; Matheus Adrianus Dam; Gerardus Johanes Maria Gruter

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☑ This is a **FIRS**T submission of items concerning a submission under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUEN**T submission of items concerning a submission under 35 U.S.C. 371.
3. ☑ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. ☐ The US has been elected (Article 31).
5. ☑ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☐ is attached hereto (required only if not communicated by the International Bureau).
   b. ☑ has been communicated by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. ☐ is attached hereto.
   b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☑ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are attached hereto (required only if not communicated by the International Bureau).
   b. ☐ have been communicated by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☑ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. ☑ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☑ A preliminary amendment.
14. ☑ An Application Data Sheet under 37 CFR 1.76.
15. ☑ A substitute specification.
16. ☑ A power of attorney and/or change of address letter.
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13*ter*.3 and 37 CFR 1.821- 1.825.
18. ☑ A second copy of the published International Application under 35 U.S.C. 154(d)(4).
19. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).

PTO-1390 (09-11)
Approved for use through 4/30/2013. OMB 0651-0021
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
	PCT/NL2010/050654	903-457 PCT/US

20. Other items or information:
IDS Certification; General Authorization for Extension of Time; PCT International Search Report; NL Search Report; Copy of Priority Document; Statement for Submission of Priority Document; Statement for Submission of Substitute Specfications

The following fees have been submitted	CALCULATIONS	PTO USE ONLY
21. ☑ Basic national fee (37 CFR 1.492(a)) **$380**	$ 380.00	
22. ☑ Examination fee (37 CFR 1.492(c)) If the written opinion prepared by ISA/US or the international preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4)..... **$0** All other situations..... **$250**	$250.00	
23. ☑ Search fee (37 CFR 1.492(b)) If the written opinion of the ISA/US or the International preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4)..... **$0** Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority..... **$120** International Search Report prepared by an ISA other than the US and provided to the Office or previously communicated to the US by the IB..... **$490** All other situations..... **$620**	$ 490.00	
TOTAL OF 21, 22 and 23 =	1,120.00	
☐ Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing in compliance with 37 CFR 1.821(c) or (e) in an electronic medium or computer program listing in an electronic medium) (37 CFR 1.492(j)). The fee is **$310** for each additional 50 sheets of paper or fraction thereof.		

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof (round **up** to a whole number)	RATE	
- 100 =	/50 =		x $**310**	$

Surcharge of **$130.00** for furnishing any of the search fee, examination fee, or the oath or declaration after the date of commencement of the national stage (37 CFR 1.492(h)).	$	

CLAIMS	NUMBER FILED		NUMBER EXTRA	RATE	$	
Total claims	15	- 20 =	0	x $ **60**	$	
Independent claims	3	- 3 =	0	x **$250**	$	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)				+ **$450**	$	
				TOTAL OF ABOVE CALCULATIONS =	$1,120.00	
☑ Applicant claims small entity status. See 37 CFR 1.27. Fees above are reduced by ½.						
				SUBTOTAL =	$ 560.00	
Processing fee of **$130.00** for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(i)). +					$	
				TOTAL NATIONAL FEE =	$ 560.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +					$	
				TOTAL FEES ENCLOSED =	$ 560.00	
				Amount to be refunded:	$	
				Amount to be charged	$560.00	

a. ☐ A check in the amount of $ _____ to cover the above fees is enclosed.

b. ☑ Please charge my Deposit Account No. 08-2461 in the amount of $ 560.00 to cover the above fees.

c. ☑ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. -8-2461.

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038. The PTO-2038 should only be mailed or faxed to the USPTO. However, when paying the basic national fee, the PTO-2038 may NOT be faxed to the USPTO.

ADVISORY: If filing by EFS-Web, do **NOT** attach the PTO-2038 form as a PDF along with your EFS-Web submission. Please be advised that this is **not** recommended and by doing so your **credit card information may be displayed via PAIR**. To protect your information, it is recommended paying fees online by using the electronic payment method.

NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the International Application to pending status.

SEND ALL CORRESPONDENCE TO:

Salvatore J. Abbruzzese, Esq.
Hoffmann & Baron, LLP
6900 Jericho Turnpike
Syosset, New York 11791-4407

Phone: 973-331-1700

/John S. SOPKO, Reg. #41321/
SIGNATURE

John S. Sopko
NAME

41,321
REGISTRATION NUMBER

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

PTO/SB/14 (11-08)
Approved for use through 09/30/2010. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	903-457 PCT/US
	Application Number	
Title of Invention	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Applicant Information:

Applicant 1 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Cesar		Muñoz de Diego	

Residence Information (Select One) ○ US Residency ◉ Non US Residency ○ Active US Military Service

City	Amsterdam	Country Of Residence[i]	NL
Citizenship under 37 CFR 1.41(b)[i]	ES		

Mailing Address of Applicant:

Address 1	c/o Furanix Technologies B.V.		
Address 2	29, Zekeringstraat		
City	Amsterdam	State/Province	
Postal Code	1014 BV	Country[i]	NL

Applicant 2 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Matheus	Adrianus	Dam	

Residence Information (Select One) ○ US Residency ◉ Non US Residency ○ Active US Military Service

City	Amsterdam	Country Of Residence[i]	NL
Citizenship under 37 CFR 1.41(b)[i]	NL		

Mailing Address of Applicant:

Address 1	c/o Furanix Technologies B.V.		
Address 2	29, Zekeringstraat		
City	Amsterdam	State/Province	
Postal Code	1014 BV	Country[i]	NL

Applicant 3 Remove

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Gerardus	Johannes Maria	Gruter	

Residence Information (Select One) ○ US Residency ◉ Non US Residency ○ Active US Military Service

City	Amsterdam	Country Of Residence[i]	NL

PTO/SB/14 (11-08)
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	Application Number	
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Citizenship under 37 CFR 1.41(b) [i]	NL		
Mailing Address of Applicant:			
Address 1	c/o Furanix Technologies B.V.		
Address 2	29, Zekeringstraat		
City	Amsterdam	**State/Province**	
Postal Code	1014 BV	**Country**[i]	NL

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below.
For further information see 37 CFR 1.33(a).

☐ **An Address is being provided for the correspondence Information of this application.**

Customer Number	23869		
Email Address	JSOPKO@HBIPLAW.COM	Add Email	Remove Email

Application Information:

Title of the Invention	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID		
Attorney Docket Number	903-457 PCT/US	**Small Entity Status Claimed**	☒
Application Type	Nonprovisional		
Subject Matter	Utility		
Suggested Class (if any)		**Sub Class (if any)**	
Suggested Technology Center (if any)			
Total Number of Drawing Sheets (if any)		**Suggested Figure for Publication (if any)**	

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S. C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32).
Enter either Customer Number or complete the Representative Name section below. If both sections are completed the Customer Number will be used for the Representative Information during processing.

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)

PTO/SB/14 (11-08)
Approved for use through 09/30/2010. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	903-457 PCT/US
	Application Number	
Title of Invention	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID	
Customer Number	23869	

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, or 365(c) or indicate National Stage entry from a PCT application. Providing this information in the application data sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78(a)(2) or CFR 1.78(a)(4), and need not otherwise be made part of the specification.

Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
	a 371 of international	PCT/NL2010/050654	2010-10-06
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
PCT/NL2010/050654	non provisional of	61249395	2009-10-07

Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button. Add

Foreign Priority Information:

This section allows for the applicant to claim benefit of foreign priority and to identify any prior foreign application for which priority is not claimed. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55(a).

Remove

Application Number	Country [i]	Parent Filing Date (YYYY-MM-DD)	Priority Claimed
2003606	NL	2009-10-07	(•) Yes ( ) No

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button. Add

Assignee Information:

Providing this information in the application data sheet does not substitute for compliance with any requirement of part 3 of Title 37 of the CFR to have an assignment recorded in the Office.

Assignee 1 Remove

If the Assignee is an Organization check here. [X]

Organization Name	Furanix Technologies B.V.		
Mailing Address Information:			
Address 1	29, Zekeringstraat		
Address 2			
City	Amsterdam	**State/Province**	
Country [i]	NL	Postal Code	1014 BV
Phone Number		Fax Number	
Email Address			

Additional Assignee Data may be generated within this form by selecting the **Add** button. Add

PTO/SB/14 (11-08)
Approved for use through 09/30/2010. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	903-457 PCT/US
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Title of Invention	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID	

Signature:

A signature of the applicant or representative is required in accordance with 37 CFR 1.33 and 10.18. Please see 37 CFR 1.4(d) for the form of the signature.

Signature	/John S. SOPKO, Reg. # 41321/			Date (YYYY-MM-DD)	2012-03-22
First Name	John	Last Name	Sopko	Registration Number	41321

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

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Confirmation No:	Unassigned	Docket:	903-457 PCT/US
Filed:	Herewith	Dated:	March 22, 2012

For: METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

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Respectfully submitted,

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(54) **Title**: METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

(57) **Abstract**: The application describes a method for the preparation of 2,5-furan dicarboxylic acid comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5- methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C.

Title: Method for the preparation of 2,5-furandicarboxylic acid and for the preparation of the dialkyl ester of 2,5-furandicarboxylic acid

The present invention relates to a method for the preparation of 2,5-furandicarboxylic acid ("FDCA") from 5-hydroxymethylfurfural ("HMF") and/or derivatives thereof. FDCA can be produced in particular from esters of HMF, such as for example 5-acetoxymethylfurfural (AMF) or a mixture of one or more of these compounds with HMF, such as for example from a mixture of AMF and HMF. The invention further relates to a process for the preparation of the dialkyl ester of 2,5-furandicarboxylic acid.

2,5-Furandicarboxylic acid, also known as dehydromucic acid is a furan derivative. This organic compound was first obtained by Fittig and Heinzelmann in 1876. The first review, by Henry Hill was published in 1901 (Am. Chem. Journ. 25, 439). FDCA was more than 125 years later identified by the US Department of Energy as one of 12 priority chemicals for establishing the "green" chemistry industry of the future. However, to date, no commercial process exists for its production. On laboratory scale it is often synthesized from 5-hydroxymethylfurfural (HMF), which in turn can be obtained from carbohydrate containing sources such as glucose, fructose, sucrose and starch. From fructose and glucose HMF is obtained by acidic elimination of three moles of water.

The derivatives of HMF are identified as potential and versatile fuel components and precursors for the production of plastics. The polyester from FDCA dimethyl diester and ethylene glycol was first reported in 1946 (GB 621,971).

WO 01/72732 describes the oxidation of HMF to FDCA. The maximum FDCA yield reported is 59%, obtained at 105 °C. The oxidation of HMF in an aqueous medium with oxygen using a catalyst from the Pt-group is described in US 4977283. Taarning et al. described the oxidation of HMF over gold based catalysts (ChemSusChem, 2008, 1, 1-4).

Partenheimer et al (Adv. Synth. Catal. **2001**, *343*, pp 102-11) describe the synthesis of 2,5-furandicarboxylic acid by catalytic air-oxidation of 5-hydroxymethylfurfural with metal/bromide catalysts such as Co/Mn/Br in acetic acid at temperatures ranging from 50 to 125 °C. With the Co/Mn/Br catalyst the highest FDCA yield obtained is 35.2% (Table 3, experiment 4). On page 103 of the same paper, under the header "products formed" it is stated: "A side reaction is the esterification of the alcohols to form the more oxidatively stable acetate ...." As apparently 5-hydroxymethylfurfural reacts with acetic acid a loss of the starting material takes place. Further, in the reaction scheme given in Figure 1 on page 103, it is indicated that 5-(acetoxymethyl)furfural is an end-point. There is no further reaction of this compound indicated to FDCA (in contrast to the ester of the intermediate product 5-

(acetoxymethyl)furan-2-carboxylic acid). In other words, the 5-(acetoxymethyl)furfural (AMF) formed through reaction of HMF with acetic acid solvent, is not oxidized to FDCA and its formation leads therefore to yield loss.

This result was confirmed in US 2009/0156841. Although the intention of the process according to US 2009/0156841 was to obtain FDCA, the product isolated and erroneously characterized as being FDCA was in fact the starting material acetoxymethyl furfural (AMF). Under the low temperature conditions deployed (100 °C), AMF is quite stable, as was already reported by Partenheimer (see above).

In US 2009/0156841 a ^{1}H NMR spectrum is shown in Figure 8 and suggested that it is the spectrum of the product that was identified as FDCA. However, this is not the case. The ^{1}H NMR spectrum of the product shown in Figure 8 is the same as that in Figure 6 and represents the starting material AMF. The 1H NMR spectrum of FDCA shows a singlet at a shift of about 7.26 ppm. Moreover, the product is described as a tan solid. In the experience of the present inventors, AMF is a tan solid, while FDCA is a white solid. It would seem that no FDCA was obtained in the experiments according to US 2009/0156841.

The experiments executed under the conditions of US 2009/0156841 were repeated. These comparative experiments confirm the low reactivity of AMF under conditions given in US 2009/0156841. Thus, a person skilled in the art would therefore have concluded that FDCA cannot be obtained in interesting yields from AMF using the conditions that are reported in US 2009/0156841, i.e., using a Co/Mn/Br catalyst in acetic acid at between 85 and 110 °C within a time frame of from 100 and 150 minutes. In Example 7 of US 2009/0156841, slightly more than 50% of the starting material was the only product isolated from the reaction.

The present inventors have now surprisingly found that when using an oxidation catalyst, e.g., based on both cobalt and manganese and containing a bromide, at temperatures higher than 140 °C, derivatives of HMF, and in particular esters of HMF optionally in combination with HMF, such as for example 5-(acetoxymethyl)furfural (AMF) can be oxidized to FDCA in high yields.

Thus, in a first aspect the invention provides a method for the preparation of 2,5-furan dicarboxylic acid comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C. The feed may optionally comprise 5-hydroxymethylfurfural as a further compound.

The invention described hereinafter may use any of the compounds described above in the feed. A preferred ester of HMF contains an ester moiety of an alkyl carboxylic acid

wherein the alkyl group contains up to 6 carbon atoms, preferably from 1 to 5 carbon atoms, i.e. methyl, ethyl, propyl, isopropyl, butyl, 2-butyl, tert-butyl, pentyl, 2-pentyl, neopentyl and 3-pentyl. Particularly preferred are alkyl groups with 1 to 4 carbon atoms. There is a preference for methyl, giving (5-acetoxymethyl)furfural. Hence, 5-acetoxymethylfurfural is the preferred feedstock, by itself or in combination with HMF.

In another aspect of the invention, we have also investigated the oxidation of other furan-based substrates under the process conditions according to the current invention. We have been able to convert 5-(chloromethyl)furfural, 5-(chloromethyl)furoic acid, 5-methylfurfural, 5-methylfuroic acid and 2,5-dimethylfuran all to FDCA in very interesting yields.

In WO 2007/104515 and WO 2009/030512, the synthesis of esters of HMF such as 5-acetoxymethylfurfural (AMF) from biomass sources is described. Given the higher stability of the HMF esters than HMF and hence improved production pathways and given the fact that upon oxidation in acetic acid the acetoxy functionality that was obtained from acetic acid is now liberated as acetic acid and given the green reputation of these esters, they were considered by the present inventors as interesting starting point in the preparation of furan-based monomers that could be used for the production of furandicarboxylic acid-based polyesters, for instance as an alternative for PET or FDCA-based polyamids (nylons). The most important conventional, oil-based, polyester monomer to produce PET is Purified Terephthalic acid (PTA) and its dialkyl ester DiMethyl Terephthalate (DMT).

AMF can be obtained from biomass sources as described in WO 2007/104515 and WO 2009/030512. Depending on the process conditions the product obtained in accordance with the process of these references may also contain HMF.

FDCA, the product of the reaction can be used in the preparation of a polyester, by reaction of FDCA or its dialkyl ester with a suitable diol. Such polyester preparations are preferably performed by transesterification, whereby the di-methyl ester or di-ethyl ester of FDCA is used and wherein the methyl or ethyl groups are exchanged in the form of a volatile alcohol during the transesterification with the diol.

The oxidation catalyst can be selected from a variety of oxidation catalysts, but is preferably a catalyst based on both cobalt and manganese and suitably containing a source of bromine, preferably a bromide.

The bromine source can be any compound that produces bromide ions in the reaction mixture. These compounds include hydrogen bromide, sodium bromide, elemental bromine, benzyl bromide and tetrabromoethane. Also other bromine salts, such as an alkali or alkaline earth metal bromide or another metal bromide such as $ZnBr_2$ can be used. There is a preference for hydrobromic acid or sodium bromide. The amount of bromine mentioned in here relates to the amount measured as Br relative to cobalt.

Suitable metal bromide catalysts employed in all of the processes of this invention comprise a cobalt compound and a manganese compound and a bromine-containing compound. Preferably these compounds are soluble in the reaction mixture.

Preferably, the catalyst comprises both Co and Mn. The metal and bromide catalyst contains, in addition to bromide, Co and Mn and optionally may contain one or more additional metals, in particular Zr and/or Ce. Alternative and suitable catalysts are described in W. Partenheimer, Catalysis Today 23(2), 69-158 (1995) in particular on pages 89-99, included herein by reference.

Each of the metal components can be provided in any of their known ionic forms. Preferably the metal or metals are in a form that is soluble in the reaction solvent. Examples of suitable counterions for cobalt and manganese include, but are not limited to, carbonate, acetate, acetate tetrahydrate and halide, with bromide being the preferred halide.

As described in Partenheimer, ibid, pages 86-88, suitable solvents for use in the processes of the present invention, described above, preferably have at least one component that contains a monocarboxylic acid functional group. The solvent may also function as one of the reagents. The processes may be run in a solvent or solvent mixture that does not contain an acid group. In that case, preferably one of the reagents does contain a monocarboxylic acid functional group. Suitable solvents can also be aromatic acids such as benzoic acid and derivatives thereof. A preferred solvent is an aliphatic C_2-C_6 monocarboxylic acid, such as but not limited to acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, trimethylacetic acid, and caproic acid and mixtures thereof. Said mixtures may also include benzene, acetonitrile, heptane, acetic anhydride, chlorobenzene, o-dichlorobenzene, and water. The most preferred solvent is acetic acid ("AcOH").

The oxidant in the processes of the present invention is preferably an oxygen-containing gas or gas mixture, such as, but not limited to air and oxygen-enriched air. Oxygen by itself is also a preferred oxidant.

The processes of the instant invention described above can be conducted in a batch, semi-continuous or continuous mode. Especially for the manufacture of FDCA, operation in the batch mode with increasing temperature at specific times, increasing pressure at specific times, variation of the catalyst concentration at the beginning of the reaction, and variation of the catalyst composition during the reaction is desirable. For example, variation of the catalyst composition during the reaction can be accomplished by addition of cobalt and/or manganese and/or zirconium, and/or cerium, and/or bromide at specified times.

The pressure in a commercial oxidation process may vary within wide ranges. When a diluent is present, and in particular with acetic acid as diluent, the temperature and the pressure in such a process are not independent. The pressure is determined by the solvent

(e.g., acetic acid) pressure at a certain temperature. The pressure of the reaction mixture is preferably selected such that the solvent is mainly in the liquid phase. In practice this means that pressures between 5 and 100 bar can be used with a preference for pressures between 10 and 80 bar. In case the oxidant is an oxygen-containing gas, such as air, the gas can be continuously fed to and removed from the reactor, or the gas can be supplied all at the start of the reaction. In the latter case, the pressure of the system will depend on the headspace volume and the amount of gas required to convert the starting material. It is clear that in the latter case, the pressure of the system may be significantly higher than the pressure in a process wherein an oxygen containing gas is continuously fed and removed. In the case of continuously feeding and removing the oxidant gas to and from the reactor, the oxygen partial pressure will suitably be between 1 and 30 bar or more preferably between 1 and 10 bar.

The temperature of the reaction mixture is at least 140 °C, preferably from 140 and 200 °C, most preferably between 160 and 190 °C. Temperatures higher than 180 °C may lead to decarboxylation and to other degradation products. Good results to FDCA have been achieved at a temperature of about 180 °C.

Molar ratios of cobalt to manganese (Co/Mn) are typically 1/1000 - 100/1, preferably 1/100 - 10/1 and more preferably 1/10 - 4/1.

Molar ratios of bromine to metals (e.g. Br/(Co+Mn)) are typically 0.001-5.00, preferably 0.01 - 2.00 and more preferably 0.1 - 0.9.

Catalyst concentration (Co + Mn) is typically from 0.1 to 10 mol %, relative to the substrate, with a preference for concentrations from 2 to 6 mol %. Good results were obtained in general with catalyst concentrations of around 4 mol %.

The starting materials for the production of FDCA may originate from a carbohydrate source as described above. Examples of such disclosures are WO 2007/104515 and WO 2009/030512. Accordingly, the invention also provides a method for the preparation of 2,5-furandicarboxylic acid wherein a carbohydrate source is converted in the presence of an alkyl carboxylic acid into products comprising an HMF ester and optionally 5-hydroxymethyl furfural, from which is isolated a feed comprising the ester of HMF and optionally 5-hydroxymethyl furfural, and which method further comprises the subsequent step of contacting the feed with an oxidant in the presence of an oxidation catalyst, in particular a cobalt and manganese and bromide-containing catalyst, under appropriate reaction conditions, in particular at temperatures higher than 140 °C

In another aspect, the FDCA obtained according to the process of the present invention can be transformed using common esterification reactions to a diester by contacting the starting material under appropriate conditions with the relevant alcohol. Thus, in one aspect, the invention also relates to the use of FDCA obtained according to the

process of the current invention in the preparation of a dialkylester of 2,5-dicarboxylic acid by reaction of the FDCA with a C_1-C_5 alkyl alcohol, preferably methanol to prepare the dimethyl ester of FDCA.

Accordingly, the present invention also provides a process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C, and esterifying the thus obtained product. Preferably, the product is esterified with an alkyl alcohol, suitably having 1 to 5 carbon atoms.

The esterification of 2,5-furan dicarboxylic acid is known. As a specific example for the manufacture of these esters, reference is made to US 2673860 wherein the diester is obtained by transesterification of another dicarboxylic acid ester in the presence of sulphuric acid. A more general description for the esterification of dicarboxylic acids is presented in US 2628249.

In a further aspect of the invention, the di-methylester can be used in the preparation of polyester polymers by reaction with a diol. Reacting the di-methylester with a diol will result in the formation of methanol that quickly vaporises. In 1946 the polymerization of FDCA dimethyl ester with ethylene glycol was described as a first example of such a polymerization in GB 621,971.

Indeed, polyesters are generally made by a combined esterification/polycondenzation reaction between monomer units of a diol (e.g., ethylene glycol (EG)) and a dicarboxylic acid. Additives such as catalysts and stabilizers may be added to facilitate the process and stabilize the polyester towards degradation.

Examples:

Experiments were carried out in parallel 8 ml magnetically stirred stainless steel batch reactors. The reactors are grouped in blocks containing 12 batch reactors. The standard procedure for all the reactions was as follows:

0.5 ml of starting material stock solution in acetic acid (0.78 mmol/ml) were added into a reactor lined with a Teflon insert. To the reactor 1 ml of a catalyst stock solution in acetic acid was subsequently added. In a typical experiment, a catalyst composition Co/Mn/Br with a relative 1-x-y ratio, the concentration of $Co(OAc)_2*4H_2O$ was varied. As a Mn source, $Mn(OAc)_2*4H_2O$ was used and as a bromine source NaBr was used. The reactors were closed with a rubber septum, after which the reactors were sealed and pressurized to the desired air pressure, ranging from 20-60 bars. After pressurization, the block with 12 reactors was placed in the test unit which was preheated at the desired temperature, ranging from

ranging from 100 to 220 °C. After the desired reaction time, ranging from 0.5 hr to 24 hrs, the block is placed into an ice bath for 20 minutes. When the block had cooled down, it was depressurized. After opening, HPLC samples were prepared. First 5 ml of a saccharine solution in DMSO (11.04 mg/ml) was added to each reactor and the mixture was stirred for 5 minutes. Then 10 µl of this mixture was diluted to 1000 µl with water in a HPLC vial. The samples were analyzed using HPLC.

Example 1

Example 1 shows the selectivity of FDCA in the oxidation of HMF, of a HMF/AMF 3/2 mixture, of a HMF/AMF 2/3 mixture and of AMF, respectively, with 2.7 mol% Co catalyst (relative to substrate), and Co/Mn molar ratio of 1/1, so that the catalyst concentration (Co + Mn) amounted to 5.4 mol%. The Br/(Co+Mn) molar ratio was 1.0; 0.7; 0.4 and 0.1 at 0.26 M substrate concentration in acetic acid at 180 °C for 1 hr with 20 bar air. The amount of oxygen was 2.69 mol oxygen per mol substrate. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn) > 1, corrosion will be a problem on commercial scale. HMF gives slightly higher yields than AMF at one hour reaction time. The results of these experiments are given in Table 1.

Example 2

Example 2 shows the selectivity to FDCA for the AMF oxidation of Example 1, together with the comparative examples based on the experimental conditions described in US 2009/0156841. In those comparative experiments (2a and 2b) 10 wt/wt% AMF in acetic acid was oxidized with 1.75 and 2.65 mol % Co catalyst and a fixed Br/(Co + Mn) molar ratio of 1.0 and a Co/Mn molar ratio of 1.0 at 100 °C and 30 bar for 2 hours. The amount of oxygen was 2.88 mol oxygen per mol substrate. Under these conditions, the yield of FDCA was lower than the result suggested in US 2009/0156841 and also lower than the results obtained at higher temperature. The results of these experiments are given in Table 2.

Example 3

Example 3 shows the yield of FDCA in the oxidation of 5-methylfurfural (5MF) and 2,5-dimethylfurfural (DMF) at 180 °C with 2.7 mol% Co catalyst (relative to substrate), and Co/Mn ratio of 1/1, so that the catalyst concentration (Co + Mn) amounted to 5.4 mol%. The Br/(Co+Mn) molar ratio was 1.0, 0.7, 0.4 and 0.1. The substrate concentration was 0.26 M in acetic acid. The reaction temperature was at 180 °C and the reaction was conducted with 50 bars air. The amount of oxygen was 6.7 mol oxygen per mol substrate. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn) > 1, corrosion will be a problem on commercial scale. Reactions with 5-MF give higher yields than reactions with DMF. The results of these experiments are also given in Table 3.

Table 1

Experiment No.	Substrate HMF/AMF molar ratio		Br/ (Co+Mn)	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
	HMF	AMF				
1a	1	0	1	3.3	100.00	76.66
1b	3	2	1	3.8	100.00	71.19
1c	2	3	1	4.0	100.00	77.66
1d	0	1	1	4.4	100.00	64.82
1e	1	0	0.7	3.3	100.00	78.08
1f	3	2	0.7	3.8	100.00	66.96
1g	2	3	0.7	4.0	100.00	75.14
1h	0	1	0.7	4.4	100.00	60.64
1i	1	0	0.4	3.3	100.00	73.27
1j	3	2	0.4	3.8	100.00	65.67
1k	2	3	0.4	4.0	100.00	73.21
1l	0	1	0.4	4.4	100.00	57.36
1m	1	0	0.1	3.3	100.00	67.92
1n	3	2	0.1	3.8	100.00	60.92
1o	2	3	0.1	4.0	100.00	69.64
1p	0	1	0.1	4.4	100.00	46.85

Table 2

Experiment No.	Temp [° C]	Reaction time [Hours]	Catalyst concentration [(Co + Mn) mol %]	Mn/Co	Br/ (Co+Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
1d	180	1	5.4	1	1	2.69	4.4	100.00	64.82
1h	180	1	5.4	1	0.7	2.69	4.4	100.00	60.64
1l	180	1	5.4	1	0.4	2.69	4.4	100.00	57.36
1p	180	1	5.4	1	0.1	2.69	4.4	100.00	46.85
2a	100	2	3.5	1	1	2.88	10.0	100.00	23.48
2b	100	2	5.3	1	1	2.88	10.0	100.00	29.05

Table 3

Experiment No.	Substrate	Reaction time [Hours]	Br/ (Co+Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
3a	5-MF	1	1	6.7	2.9	100.00	42.62
3b	5-MF	1	0.7	6.7	2.9	100.00	39.94
3c	DMF	1	1	6.7	2.5	100.00	16.17
3d	DMF	1	0.7	6.7	2.5	100.00	14.09
3e	DMF	1	0.4	6.7	2.5	100.00	11.30
3f	DMF	1	0.1	6.7	2.5	100.00	7.19

Claims

1. Method for the preparation of 2,5-furan dicarboxylic acid comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethylfurfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C.

2. Method according to claim 1, wherein the feed comprises a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), esters of HMF and a mixture thereof.

3. Method according to claim 1 or 2, wherein the oxidation catalyst comprises at least one metal selected from the group consisting of Co and Mn.

4. Method according to claim 1 or 2 or 3, wherein the oxidation catalyst comprises a source of bromine.

5. Method according to claim 4, wherein the oxidation catalyst contains both Co and Mn.

6. Method according to claim 5, wherein the oxidation catalyst comprises at least one additional metal.

7. Method according to claim 6, wherein the additional metal is Zr and/or Ce.

8. Method according to claims 1-6, wherein the oxidant is selected from oxygen, air or other oxygen-containing gases.

9. Method according to any of the previous claims wherein the temperature is between 140 and 200 °C, most preferably between 160 and 190 °C.

10. Method according to any one of the previous claims, wherein a solvent or solvent mixture is present, preferably comprising a solvent containing a monocarboxylic acid functional group, more preferably acetic acid or acetic acid and water mixtures.

11. Method according to any of the previous claims, wherein the feed comprises an ester of HMF containing an ester moiety of an alkyl carboxylic acid wherein the alkyl group contains up to 6 carbon atoms, preferably from 1 to 5 carbon atoms.

12. Process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C, and esterifying the thus obtained product.

13. Process according to claim 12, wherein the product is esterified with a C_1-C_5 alkyl alcohol.

14. Process according to claim 13, wherein the C_1-C_5 alkyl alcohol is methanol and the dialkyl ester is the dimethylester of 2,5-furan dicarboxylic acid.

15. Method for the preparation of 2,5-furandicarboxylic acid wherein a carbohydrate source is converted in the presence of an alkyl carboxylic acid into products comprising an HMF ester and optionally 5-hydroxymethyl furfural, from which is isolated a feed comprising the ester of HMF and optionally 5-hydroxymethyl furfural, and which method comprises further the subsequent step of contacting the feed with an oxidant in the presence of an oxidation catalyst, preferably a cobalt and manganese and bromide-containing catalyst, under appropriate reaction conditions.

INTERNATIONAL SEARCH REPORT

International application No
PCT/NL2010/050654

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D307/68
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WALT PARTENHEIMER ET AL.: "Synthesis of 2,5-diformylfuran and furan-2,5-dicarboxylic acid by catalytic air oxidation of 5-hydroxymethylfurfural. Unexpectedly selective aerobic oxidation of benzyl alcohol to benzaldehyde with metal/bromide catalysts", ADV. SYNTH. CATAL., vol. 343, no. 1, 2001, pages 102-111, XP002584717, cited in the application the whole document in particular figure 1, tables 1 and 3. ----- -/--	1-11,15

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 December 2010	05/01/2011

Name and mailing address of the ISA/	Authorized officer
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X,P	JP 2009 242312 A (AIR WATER INC) 22 October 2009 (2009-10-22) the whole document in particular paragraphs 31 and 43-46.	1-11,15
X	HAWORTH W N ET AL: "The conversion of sucrose into furan compounds. Part II. Some 2 : 5-disubstituted tetrahydrofurans and their products of ring scission", JOURNAL OF THE CHEMICAL SOCIETY, CHEMICAL SOCIETY, LETCHWORTH; GB, no. 1, 1 January 1945 (1945-01-01), pages 1-4, XP008122626, ISSN: 0368-1769, DOI: DOI:10.1039/JR9450000001 the whole document in particular 1st paragraph on page 1 and last before paragraph on page 3.	12-15
X	WO 2006/063220 A2 (ARCHER DANIELS MIDLAND CO [US]; SANBORN ALEXANDRA J [US]) 15 June 2006 (2006-06-15) claims 1-26; examples 1-24	15
X,P	TONG X ET AL: "Biomass into chemicals: Conversion of sugars to furan derivatives by catalytic processes", APPLIED CATALYSIS A: GENERAL, ELSEVIER SCIENCE, AMSTERDAM, NL, vol. 385, no. 1-2, 15 September 2010 (2010-09-15), pages 1-13, XP027230510, ISSN: 0926-860X [retrieved on 2010-07-30] the whole document in particular pages 9-10.	1-11,15

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BOISEN A ET AL: "Process integration for the conversion of glucose to 2,5-furandicarboxylic acid", CHEMICAL ENGINEERING RESEARCH AND DESIGN, PART A, INSTITUTION OF CHEMICAL ENGINEERS, XX, vol. 87, no. 9, 1 September 2009 (2009-09-01), pages 1318-1327, XP026613647, ISSN: 0263-8762, DOI: DOI:10.1016/J.CHERD.2009.06.010 [retrieved on 2009-07-25] the whole document in particular paragraph 4.2.2	1-11,15
X	WO 01/72732 A2 (DU PONT [US]; GRUSHIN VLADIMIR [US]; PARTENHEIMER WALTER [US]; MANZER) 4 October 2001 (2001-10-04) page 7, line 2 - line 7; claims 11-21; examples 16-40	1-11,15
X	WO 2008/054804 A2 (BATTELLE MEMORIAL INSTITUTE [US]; LILGA MICHAEL A [US]; HALLEN RICHARD) 8 May 2008 (2008-05-08) * abstract; claims 1-28 paragraphs [0049], [0050], [0058]; claims 5,10; figure 31; example 1	1-11,15
X	JP 2009 001519 A (CANON KK) 8 January 2009 (2009-01-08) * abstract paragraph [0025]	1-11
X	SU 636 233 A1 (INST ORGANICHESKOGO SINTEZA AK [SU]; INST KHIM FIZ AN SSSR [SU]) 5 December 1978 (1978-12-05) the whole document in particular column 2, lines 9-10, examples 1, 2 and 4 and claim 1	1-11
E	WO 2010/132740 A2 (ARCHER DANIELS MIDLAND CO [US]; SANBORN ALEXANDRA [US]) 18 November 2010 (2010-11-18) claims 1-18; examples 8,12	1-11,15
A	EP 0 356 703 A2 (HOECHST AG [DE]) 7 March 1990 (1990-03-07) the whole document	1-11,15

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GRABOWSKI G ET AL: "The electrochemical oxidation of 5-hydroxymethylfurfural with the nickel oxide/hydroxide electrode", ELECTROCHIMICA ACTA, ELSEVIER SCIENCE PUBLISHERS, BARKING, GB, vol. 36, no. 13, 1 January 1991 (1991-01-01), page 1995, XP026726025, ISSN: 0013-4686, DOI: DOI:10.1016/0013-4686(91)85084-K [retrieved on 1991-01-01] the whole document	1-11

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/NL2010/050654

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2009156841 A1	18-06-2009	CA 2708232 A1	18-06-2009
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Cesar Muñoz de Diego et al.	Examiner:	Unassigned
Application No.:	Unassigned	Group Art Unit:	Unassigned
Confirmation No:	Unassigned	Docket:	903-457 PCT/US
Filed:	Herewith	Dated:	March 22, 2012

For: METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Certificate of EFS-Web Transmission
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Dated: March 22, 2012

Signature: K.J. Goodhand */K.J. Goodhand/*

SUBMISSION OF PRIORITY DOCUMENT(S)

Sir:

As a courtesy to the Office, please find enclosed a copy of the priority document, i.e., Application No. NL 2003606, which has been previously submitted or transmitted to the International Bureau in compliance with PCT Rule 17.1 (a) or (b) during the PCT phase of PCT Application No. PCT/NL2010/050654.

Respectfully submitted,

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Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a),(b) or (b-*bis*)

Agentschap NL
Ministerie van Economische Zaken

Hierbij wordt verklaard, dat in Nederland op 7 oktober 2009 onder nummer 2003606,
ten name van:
FURANIX TECHNOLOGIES B.V.
te Amsterdam
een aanvrage om octrooi werd ingediend voor:
"Method for preparation of 2,5-furandicarboxylic acid from 5-hydroxymethylfurfural and/or derivatives thereof, and the use thereof",
en dat de hieraan gehechte stukken overeenstemmen met de oorspronkelijk ingediende stukken.

Rijswijk, 15 oktober 2010

De Directeur van NL Octrooicentrum,
voor deze,

Mw.C.M.A. Streng

Abstract

The application describes a method for the preparation of 2,5-furandicarboxylic acid comprising the step of contacting a feed comprising 5-hydroxymethylfurfural (HMF), one or more derivatives of HMF or a mixture of HMF with one or more derivatives of HMF as starting material, with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140°C.

P30061NL00/MKO

Title: Method for the preparation of 2,5-furandicarboxylic acid from 5-hydroxymethylfurfural and/or derivatives thereof, and the use thereof

The present invention relates to a method for the preparation of 2,5-furandicarboxylic acid ("FDCA") from 5-hydroxymethylfurfural ("HMF") and/or derivatives thereof, in particular from esters of HMF such as for example 5-acetoxymethylfurfural (AMF), from 5-(chloromethyl)furfural, 5-(chloromethyl)furoic acid, 5-methylfurfural, 5-methylfuroic acid or 2,5-dimethylfuran, or from a mixture of two or more of these HMF derivatives or a mixture of one or more of these derivatives with HMF, such as for example from a mixture of AMF + HMF.

2,5-Furandicarboxylic acid, also known as dehydromucic acid is a furan derivative. This organic compound was first obtained by Fittig and Heinzelmann in 1876. The first review, by Henry Hill was published in 1901 (Am. Chem. Journ. 25, 439). FDCA was more than 125 years later identified by the US Department of Energy as one of 12 priority chemicals for establishing the "green" chemistry industry of the future. However, to date, no commercial process exists for its production. On the laboratory scale it is often synthesized from 5-hydroxymethylfurfural (HMF), which in turn can be obtained from carbohydrate containing sources such as glucose, fructose, sucrose and starch. From fructose and glucose HMF is obtained by acidic elimination of three mols of water.

The derivatives of HMF are identified as potential and versatile fuel components and precursors for the production of plastics. The polyester from FDCA dimethyl diester and ethylene glycol was first reported in 1946 (GB 621,971).

WO0172732 describes the oxidation of HMF to FDCA. The maximum FDCA yield reported is 59%, obtained at 105 °C. The oxidation of HMF in an aqueous medium with oxygen using a catalyst from the Pt-group is described in US4977283. Taarning et al. described the oxidation of HMF over gold based catalysts (ChemSusChem, 2008, 1, 1-4).

Partenheimer et al describes the synthesis of furan-2,5-dicarboxylic acid by catalytic air-oxidation of 5-hydroxymethylfurfural with metal/bromide catalysts such as Co/Mn/Br in Adv. Synth. Catal. **2001**, *343*, pp 102-11. With the Co/Mn/Br catalyst the highest FDCA yield obtained is 35.2% (Table 3, experiment 4).On page 103 of the same paper, under the header "products formed" it is stated: "A side reaction is the esterification of the alcohols [HMF and 5-(hydroxymethyl)furan-2-carboxylic acid] to form the more oxidatively stable acetate [respectively 5-(acetoxymethyl)furfural (from HMF) and 5-(acetoxymethyl)furan-2-carboxylic acid from the intermediate 5-(hydroxymethyl)-2-furan carboxylic acid]." And further

on page 106 under the header "general considerations" it is stated: "Although acetoxylation of the alcohols with the acetic acid solvent does occur, this side reaction results in only a 5-8% yield loss". Also, in the reaction scheme given in Figure 1 on page 103, it is indicated that 5-(acetoxymethyl)furfural is an end-point. There is no further reaction of this compound indicated to FDCA (in contrast to the ester of the intermediate product 5-(acetoxymethyl)furan-2-carboxylic acid). In other words, the 5-(acetoxymethyl)furfural (AMF) formed through reaction of HMF with acetic acid solvent, is not oxidized to FDCA and its formation leads therefore to yield loss.

Unknowingly to the authors, this result was confirmed recently in US2009/0156841 (ADM). On page 6, in paragraph [0060] it is stated:

"A mixture of HMF ester such as ...5-acetoxymethylfurfural (AcHMF), ...acetic acid, along with cobalt acetate, manganese acetate and sodium bromide is placed in a reactor and subjected to between about 400 to about 1000 psi oxygen.....at between about 85 °C to about 110 °C,....for between about 100 to about 150 minutes. The solution is filtered and the solvent evaporated to obtain 2,5-Furandicarboxylic acid (FDCA)."

This general recipe is illustrated in Example 7 on page 10 of this reference:

"A reaction mixture containing AcHMF (5.0 g), acetic acid (50 mL), cobalt acetate (0.132 g), manganese acetate (0.135 g), and sodium bromide (0.114 g) is placed in a 100 mL reactor and subjected to 500-800 psi oxygen at 100 °C for 2 hours. Upon filtration and evaporation of the solvent, 2.53 g of tan solid is isolated. ^{1}H NMR indicates substantially pure FDCA. The overall yield of FDCA from AcHMF is 54%.."

Although the intention of the authors was to obtain FDCA, the product they isolated and erroneously characterized as being FDCA was in fact the starting material AcHMF. Under the low temperature conditions deployed (100 °C), AcHMF is quite stable, as was already reported by Partenheimer (see above). FDCA has an extremely low solubility in acetic acid, even at 100 °C. Taking into account that water is formed during the oxidation we can note the following two observations by Partenheimer in Adv. Synth. Catal. 2001, 343:

On page 105, right column we can read that FDCA precipitates during the reaction, even at 100-125 °C.

On page 110 (right column) it is stated: "*The solubility of 2,5-Furandicarboxylic acid is 6.6 x 10-4 g/g in 3% H2O/HOAc at room temperature. Hence 99% of the 2,5-furandicarboxylic acid precipitates.*"

The authors wrote that the FDCA product was obtained from the solution after filtration and evaporation. Thus, taking into account the Partenheimer statements, which were independently confirmed by us, this isolated product cannot be FDCA.

The authors showed an ^{1}H NMR spectrum of their product in Figure 8 and concluded that it is FDCA. However, this is not the case. The ^{1}H NMR spectrum of the product shown in Figure 8 is without doubt the starting material AcHMF. Finally, the authors refer to the product as a tan solid. In our experience, AcHMF is a tan solid, while FDCA is a white solid.

We have repeated the results of experiments executed under the US2009/0156841 conditions. These comparative experiments confirm the low reactivity of AMF under conditions given in US2009/0156841 (cf. the results reported in the experimental section). Thus, a person skilled in the art would therefore have concluded that FDCA cannot be obtained in interesting yields from AMF (AcHMF) using the conditions reported in US2009/0156841 using a Co/Mn/Br catalyst in acetic acid at between 85 and 110 °C within a time frame of from 100 and 150 minutes. In Example 7 of this prior art reference, 2.53 g or slightly more than 50% of the starting material was the only product isolated from the reaction.

The present inventors have now surprisingly found that when using a catalyst based on both Cobalt and Manganese and containing a bromide, at temperatures higher than 140 °C the derivatives of HMF, and in particular esters of HMF optionally in combination with HMF, such as for example 5-(acetoxymethyl)furfural (AMF) can be oxidized within 1 hour to FDCA in high yields.

Thus, in a first aspect the invention relates to a method for the preparation of 2,5-furandicarboxylic acid comprising the step of contacting a feed comprising 5-hydroxymethylfurfural (HMF), one or more derivatives of HMF or a mixture of HMF with one or more derivatives of HMF, e.g., 5-acetoxymethylfurfural (AMF) or 5-hydroxymethylfurfural (HMF) or mixtures thereof (AMF+HMF) as starting material with an oxidant in the presence of a catalyst based on both Cobalt and Manganese and containing a bromide at a temperature higher than 140 °C.

The invention is described hereinafter with 5-acetoxymethylfurfural as the preferred feedstock, by itself or in combination with HMF. 5-(Chloromethyl)furfural, or 5-(chloromethyl)furoic acid, or 5-methylfurfural, or 5-methylfuroic acid, or 2,5-dimethylfuran, or an ester of 5-(hydroxymethyl)furfural may be used instead, as well as combinations of two or more of these HMF derivatives, or combinations of one or more of these HMF derivatives together with 5-(hydroxymethyl)furfural.

In WO2007104515 and WO2009030512, the synthesis of esters of HMF such as 5-acetoxymethylfurfural (AMF) from biomass sources is described. Given the higher stability of the HMF esters than HMF and hence improved production pathways and given the fact that upon oxidation in acetic acid the acetoxy functionality that was obtained from acetic acid is now liberated as acetic acid and given the green reputation of these esters, they were considered by the present inventors as interesting starting point in the preparation of furan-

based monomers that could be used for the production of furandicarboxylic acid -based polyesters, for instance as an alternative for PET or FDCA-based polyamids (nylons). The most important conventional, oil-based, polyester monomer to produce PET is Purified Terephthalic acid (PTA) and its dialkyl ester dimethyl Terephthalate (DMT).

AMF can be obtained from biomass sources as described in WO2007104515 and WO2009030512. Depending on the process conditions the product obtained in accordance with the process of these references may also contain HMF.

The alkyl of the ester functionality of the HMF ester can be C1-C5 alkyl, i.e. methyl, ethyl, propyl, isopropyl, butyl, 2-butyl, tert-butyl, pentyl, 2-pentyl, neopentyl and 3-pentyl. There is a preference for methyl, giving (5-acetylmethyl)furfural

FDCA, the product of the reaction can be used in the preparation of a polyester, by reaction of FDCA or its dialkyl ester with a suitable diol. Such polyester preparations are preferably performed by transesterification, whereby the di-methyl ester or di-ethyl ester of FDCA is used and wherein the methyl or ethyl groups are exchanged in the form of a volatile alcohol during the transesterification with the diol.

The bromine source can be any compound that produces bromide ions in the reaction mixture. These compounds include hydrogen bromide, sodium bromide, elemental bromine, benzyl bromide, tetrabromoethane. Also other bromine salts, such as an alkali or earth alkali metal bromine or another metal bromide such as $ZnBr_2$ can be used. There is a preference for hydrobromic acid or sodium bromide. The amount of bromine mentioned in here relates to the amount measured as Br relative to cobalt.

Metal bromide catalysts employed in all of the processes of this invention comprise a preferably soluble cobalt compound and a preferably soluble manganese compound and a preferably soluble bromine-containing compound.

The metal and bromide catalyst contains next to bromide Co and Mn and optionally can contain Zr and/or Ce or other metals. Alternative and suitable catalysts are described in W. Partenheimer, Catalysis Today 23(2), 69-158 (1995) in particular on pages 89-99, included herein by reference.

Each of the metal components can be provided in any of their known ionic forms. Preferably the metal or metals are in a form that is soluble in the reaction solvent. Examples of suitable counterions for cobalt and manganese include, but are not limited to, carbonate, acetate, acetate tetrahydrate and halide with bromide being the preferred halide.

As described in Partenheimer, ibid, pages 86-88, suitable solvents for use in the processes of the present invention, described above, preferably have at least one component that contains a monocarboxylic acid functional group. The solvent may also function as one of the reagents. The processes may be run in a solvent or solvent mixture that does not contain an acid group. In that case, preferably one of the reagents does

contain a monocarboxylic acid functional group. Suitable solvents can also be aromatic acids such as benzoic acid and derivatives thereof. A preferred solvent is an aliphatic C_2-C_6 monocarboxylic acid, such as but not limited to acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, trimethylacetic acid, and caproic acid and mixtures thereof. Components of said mixtures can include benzene, acetonitrile, heptane, acetic anhydride, chlorobenzene, o-dichlorobenzene, and water. Most preferred as solvent is acetic acid ("AcOH").

The oxidant in the processes of the present invention is preferably an oxygen-containing gas or gas mixture, such as, but not limited to air. Oxygen by itself is also a preferred oxidant.

The processes of the instant invention described above can be conducted in the batch, semi-continuous or continuous mode. Especially for the manufacture of FDCA, operation in the batch mode with increasing temperature at specific times, increasing pressure at specific times, variation of the catalyst concentration at the beginning of the reaction, and variation of the catalyst composition during the reaction is desirable. For example, variation of the catalyst composition during reaction can be accomplished by addition of cobalt and/or manganese and/or zirconium, and/or cerium, and/or bromide at specified times.

The temperature and pressure in a commercial oxidation process with acetic acid as diluent are not independent. The pressure is determined by the solvent (e.g., acetic acid) pressure at a certain temperature. The pressure of the reaction mixture is preferably selected such that the solvent is mainly in the liquid phase. In practice this means that pressures between 5 and 100 bar can be used with a preference for pressures between 10 and 80 bars. In case the oxidant is an oxygen containing gas, such as air, the gas can be continuously fed to and removed from the reactor, or the gas can be supplied all at the start of the reaction. In the latter case, the pressure of the system will depend on the headspace volume and the amount of gas required to convert the starting material. It is clear that in the latter case, the pressure of the system will be significantly higher than when continuously feeding and removing an oxygen containing gas. In the case of continuously adding and removing the oxidant gas to and from the reactor, the oxygen partial pressure will be between 1 and 30 bars or more preferably between 1 and 10 bars.

The temperature of the reaction mixture is between 140 and 200 degrees Celsius, most preferably between 160 and 190 degrees Celsius. Temperatures higher than 180 degrees Celcius tend to lead to decarboxylation and to other degradation products. Good results to FDCA have been achieved at a temperature of about 180 °C.

Ratio's of Cobalt to Manganese (Co/Mn) are typically 1/1000 - 100/1, preferably 1/100 - 10/1 and more preferably 1/10 - 4/1.

Ratio's of bromine to metals (e.g. Br/(Co+Mn)) are typically 0.001-5.00, preferably 0.01 - 2.00 and more preferably 0.1 - 0.9.

Catalyst concentration (Co + Mn) is typically between 0.1 - 10 mol % relative to the substrate, with a preference for loads between 2 and 6 mol %. Good results were obtained in general with catalyst loads of around 4 mol %.

In another aspect of the invention, we have also investigated the oxidation of other furan-based substrates under the process conditions according to the current invention. We have been able to convert 5-(chloromethyl)furfural, 5-(chloromethyl)furoic acid, 5-methylfurfural, 5-methylfuroic acid and 2,5-dimethylfuran all to FDCA in very interesting yields.

In another aspect, the FDCA obtained according to the process of the present invention can be transformed using common esterification reactions to a diester by contacting the starting material under appropriate conditions with the relevant alcohol. Thus, in one aspect, the invention also relates to the use of FDCA obtained according to the process of the current invention in the preparation of a dialkylester of 2,5-dicarboxylic acid by reaction of the FDCA with a C_1-C_5 alkyl alcohol, preferably methanol to prepare the dimethyl ester of FDCA.

In a further aspect of the invention, the di-methylester can be used in the preparation of polyester polymers by reaction with a diol. Reacting the di-methylester with a diol will result in the formation of methanol that quickly vaporises. In 1946 the polymerization of FDCA dimethyl ester with ethylene glycol was described as a first example of such a polymerization (GB 621,971).

Indeed, polyesters are generally made by a combined esterification/polycondenzation reaction between monomer units of a diol (e.g., ethylene glycol (EG)) and a dicarboxylic acid. Additives such as catalysts and stabilizers may be added to facilitate the process and stabilize the polyester towards degradation.

Description of the figures:

Figure 1 shows the yield of FDCA in the oxidation of HMF, of a HMF/AMF 3/2 mixture, of a HMF/AMF 2/3 mixture and of AMF, respectively with 2.7 mol% Co catalyst (relative to substrate), 0.26 M substrate concentration in acetic acid and Co/Mn ratio of 1/1 and Br/(Co+Mn): 1.0; 0.7; 0.4 and 0.1 at 180 °C for 1 hr with 20 bar air. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn) > 1, corrosion will be a problem on commercial scale. HMF gives slightly higher yields than AMF at one hour reaction time. The data of these experiments is also given in Table 1.

Figure 2 shows the selectivity to FDCA for the AMF oxidation of Figure 1 together with the comparative examples based on the experimental conditions described in

US/20090156841; according to the text 10 wt/wt% AMF was oxidized with 1.75 and 2.65 mol % Co catalyst and a fixed Br/(Co/Mn) of 1.0 and a Co/Mn of 1.0 at 100 °C and 30 bar for 2 hours Under these conditions, the yield of FDCA was lower than the result described in US/20090156841 and than the results obtained at high temperature. The data of these experiments is also given in Table 2.

Figure 3 shows the yield of FDCA in the oxidation of 5-methylfurfural (5MF) and 2,5-dimethylfurfural (DMF) at 180 °C with 2.7 mol% Co catalyst (relative to substrate), 0.26 M substrate concentration in acetic acid and Co/Mn ratio of 1/1 and a Br/(Co+Mn) of 1.0, 0.7, 0.4 and 0.1 at 180 °C for 2 hrs with 50 bars air. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn) > 1, corrosion will be a problem on commercial scale. Reactions with 5MF give higher yields than reactions with DMF. The data of these experiments is also given in Table 3.

Examples:

Experiments were carried out in parallel 8 mL magnetically stirred stainless steel batch reactors. The reactors are grouped in blocks containing 12 batch reactors. The standard procedure for all the reactions was as follows:

0.5 ML of starting material stock solution in acetic acid (0.78 mmol/ml) were added into a reactor lined with a Teflon insert. 1 ML of a catalyst stock solution in acetic acid was subsequently added to the reactor. In a typical experiment, a catalyst composition Co/Mn/Br with a relative 1-x-y ratio, the concentration of $Co(OAc)_2{}^*4H_2O$ was varied. As a Mn source, $Mn(OAc)_2{}^*4H_2O$ was used and as a bromine source NaBr was used. The reactors were closed with a rubber septum, after which the reactors were sealed and pressurized to the desired air pressure, ranging from 20-60 bars. After pressurization, the block with 12 reactors was placed in the test unit which was preheated at the desired temperature, ranging from 100 to 220 °C. After the desired reaction time, ranging from 0.5 hr to 24 hrs, the block is placed into an ice bath for 20 minutes. When the block had cooled down, it was depressurized. After opening, HPLC samples were prepared. First 5 ml of a saccharine solution in DMSO (11.04 mg/mL) was added to the each reactor and the mixture was stirred for 5 minutes. Then 10 µL of this mixture was diluted to 1000 µL with water in a HPLC vial. The samples were analyzed using HPLC.

Illustrative but not limiting results are presented in the figures 1-3 and Tables 1-3.

Table 1

Substrate HMF/AMF molar ratio		Temp [° C]	Reaction time [Hours]	Catalyst concentration [(Co + Mn) mol %]	Mn/Co	Br/ (Co+Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
HMF	AMF									
1	0	180	1	5.4	1	1	2.69	3.3	100.00	76.11
1	0	180	1	5.4	1	1	2.69	3.3	100.00	76.66
3	2	180	1	5.4	1	1	2.69	3.8	100.00	71.19
3	2	180	1	5.4	1	1	2.69	3.8	100.00	70.91
2	3	180	1	5.4	1	1	2.69	4.0	100.00	77.66
2	3	180	1	5.4	1	1	2.69	4.0	100.00	76.84
0	1	180	1	5.4	1	1	2.69	4.4	100.00	64.82
0	1	180	1	5.4	1	1	2.69	4.4	100.00	63.76
1	0	180	1	5.4	1	0.7	2.69	3.3	100.00	77.69
1	0	180	1	5.4	1	0.7	2.69	3.3	100.00	78.08
3	2	180	1	5.4	1	0.7	2.69	3.8	100.00	66.53
3	2	180	1	5.4	1	0.7	2.69	3.8	100.00	66.96

Table 2

Substrate	Temp [° C]	Reaction time [Hours]	Catalyst concentration [(Co + Mn) mol %]	Mn/Co	Br/ (Co+Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
AMF	180	1	5.4	1	1	2.69	3.3	100.00	64.82
AMF	180	1	5.4	1	1	2.69	3.3	100.00	63.76
AMF	180	1	5.4	1	0.7	2.69	3.8	100.00	60.64
AMF	180	1	5.4	1	0.7	2.69	3.8	100.00	59.83
AMF	180	1	5.4	1	0.4	2.69	4.0	100.00	57.11
AMF	180	1	5.4	1	0.4	2.69	4.0	100.00	57.36
AMF	180	1	5.4	1	0.1	2.69	4.4	100.00	46.85
AMF	180	1	5.4	1	0.1	2.69	4.4	100.00	46.53
AMF	100	2	3.5	1	1	2.88	10.0	100.00	23.48
AMF	100	2	3.5	1	1	2.88	10.0	100.00	23.96
AMF	100	2	5.25	1	1	2.88	10.0	100.00	29.05
AMF	100	2	5.25	1	1	2.88	10.0	100.00	29.87

Table 3

Substrate	Temp [° C]	Reaction time [Hours]	Catalyst concentration [(Co + Mn) mol %]	Mn/Co	Br/ (Co+Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
5-MF	180	1	5.4	1	1	6.7	2.9	100.00	42.62
5-MF	180	1	5.4	1	1	6.7	2.9	100.00	42.04
5-MF	180	1	5.4	1	0.7	6.7	2.9	100.00	39.47
5-MF	180	1	5.4	1	0.7	6.7	2.9	100.00	39.94
DMF	180	1	5.4	1	1	6.7	2.5	100.00	16.13
DMF	180	1	5.4	1	1	6.7	2.5	100.00	16.17
DMF	180	1	5.4	1	0.7	6.7	2.5	100.00	13.68
DMF	180	1	5.4	1	0.7	6.7	2.5	100.00	14.09
DMF	180	1	5.4	1	0.4	6.7	2.5	100.00	11.30
DMF	180	1	5.4	1	0.4	6.7	2.5	100.00	10.89
DMF	180	1	5.4	1	0.1	6.7	2.5	100.00	7.19
AMF	180	1	5.4	1	0.1	6.7	2.5	100.00	7.12

Claims

1. Method for the preparation of 2,5-furandicarboxylic acid comprising the step of contacting a feed comprising 5-hydroxymethylfurfural (HMF), one or more derivatives of HMF or a mixture of HMF with one or more derivatives of HMF as starting material, with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140°C.

2. Method according to claim 1 comprising the step of contacting an ester of 5-(hydroxymethyl)furfural or 5-(hydroxymethyl)furfural or a mixture of these components with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C.

3 Method according to claim 1 or 2, wherein the oxidation catalyst comprises at least one metal selected from the group consisting of Co and Mn.

4 Method according to claim 1 or 2 or 3, wherein the oxidation catalyst comprises a source of bromine.

5 Method according to claim 4, wherein the oxidation catalyst contains both Co and Mn.

6 Method according to claim 5, wherein the oxidation catalyst comprises at least one additional metal.

7. Method according to claim 6, wherein the additional metal is Zr and or Ce.

8. Method according to claims 1-6, wherein the oxidant is selected from oxygen, air or other oxygen-containing gases.

9. Method according to any of the previous claims wherein the temperature is between 140 and 200 degrees Celsius, most preferably between 160 and 190 degrees Celsius.

10. Method according to any one of the previous claims, wherein a solvent or solvent mixture is present, preferably comprising a solvent containing a monocarboxylic acid functional group, more preferably acetic acid or acetic acid and water mixtures.

11. Method according to any of the previous claims wherein the alkyl of the ester group of the HMF ester is C_1-C_5 alkyl, preferably methyl.

12 Use of the reaction product obtained via the method of any of the claims 1-11 in the preparation of a dialkylester of 2,5-furan dicarboxylic acid via an esterification reaction with a C_1-C_5 alkyl alcohol.

13. Use according to claim 12 wherein the C_1-C_5 alkylalcohol is methanol and the diester is the dimethylester of 2,5-furan dicarboxylic acid.

14. Method for the preparation of 2,5-furandicarboxylic acid wherein a carbohydrate source is converted in the presence of an alkyl carboxylic acid into products comprising an HMF ester and optionally 5-hydroxymethyl furfural, from which is isolated a feed comprising the ester of HMF and optionally 5-hydroxymethyl furfural, comprising the subsequent step of contacting the feed with an oxidant in the presence of a cobalt and manganese and bromide containing catalyst under appropriate reaction conditions.

Fig 1

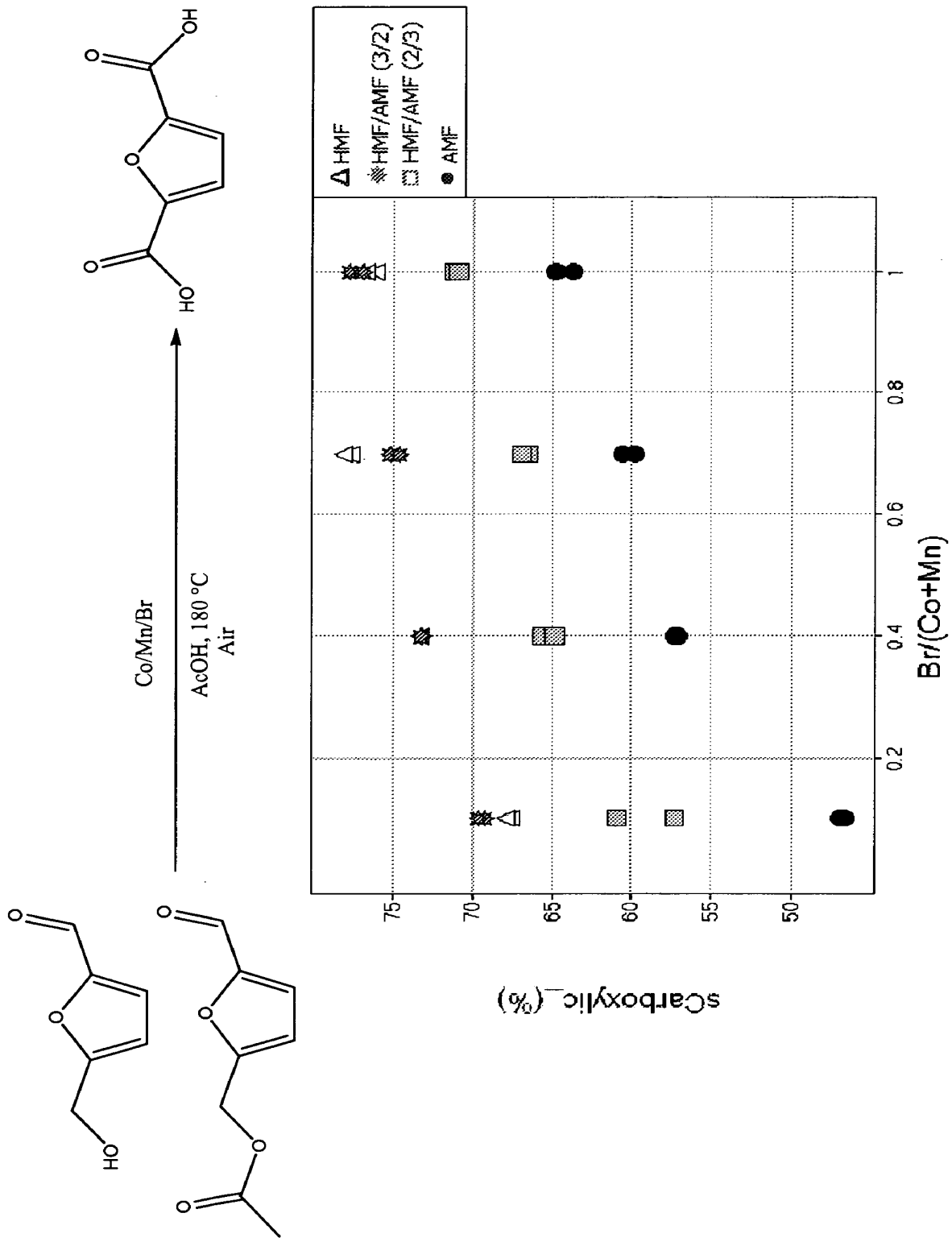

Co/Mn/Br
AcOH, 180 °C
Air
HO
OH
O
HMF
HMF/AMF (3/2)
HMF/AMF (2/3)
AMF
Carboxylic (%)
Br/(Co+Mn)
50
55
60
65
70
75
0.2
0.4
0.6
0.8
1

Fig 2

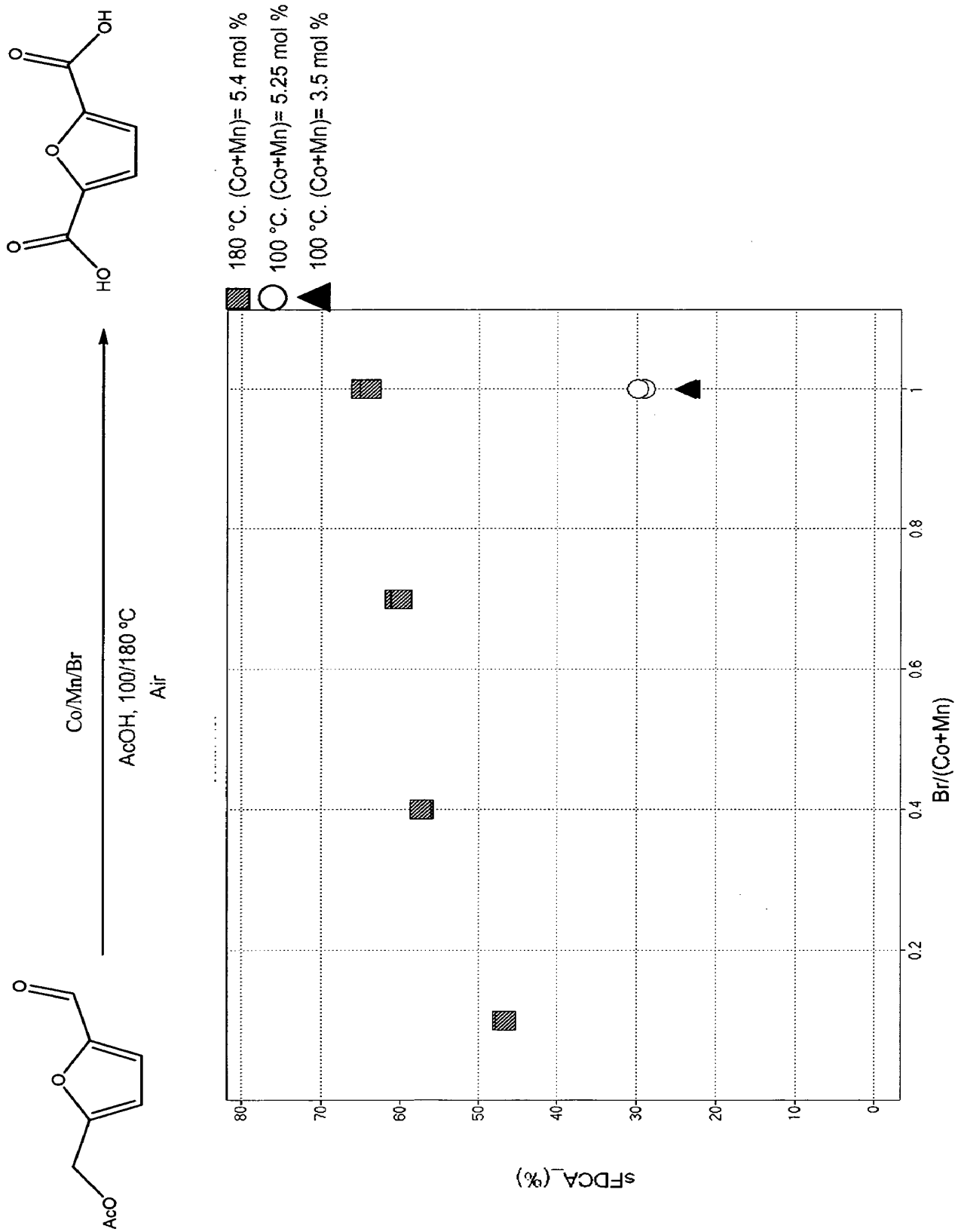
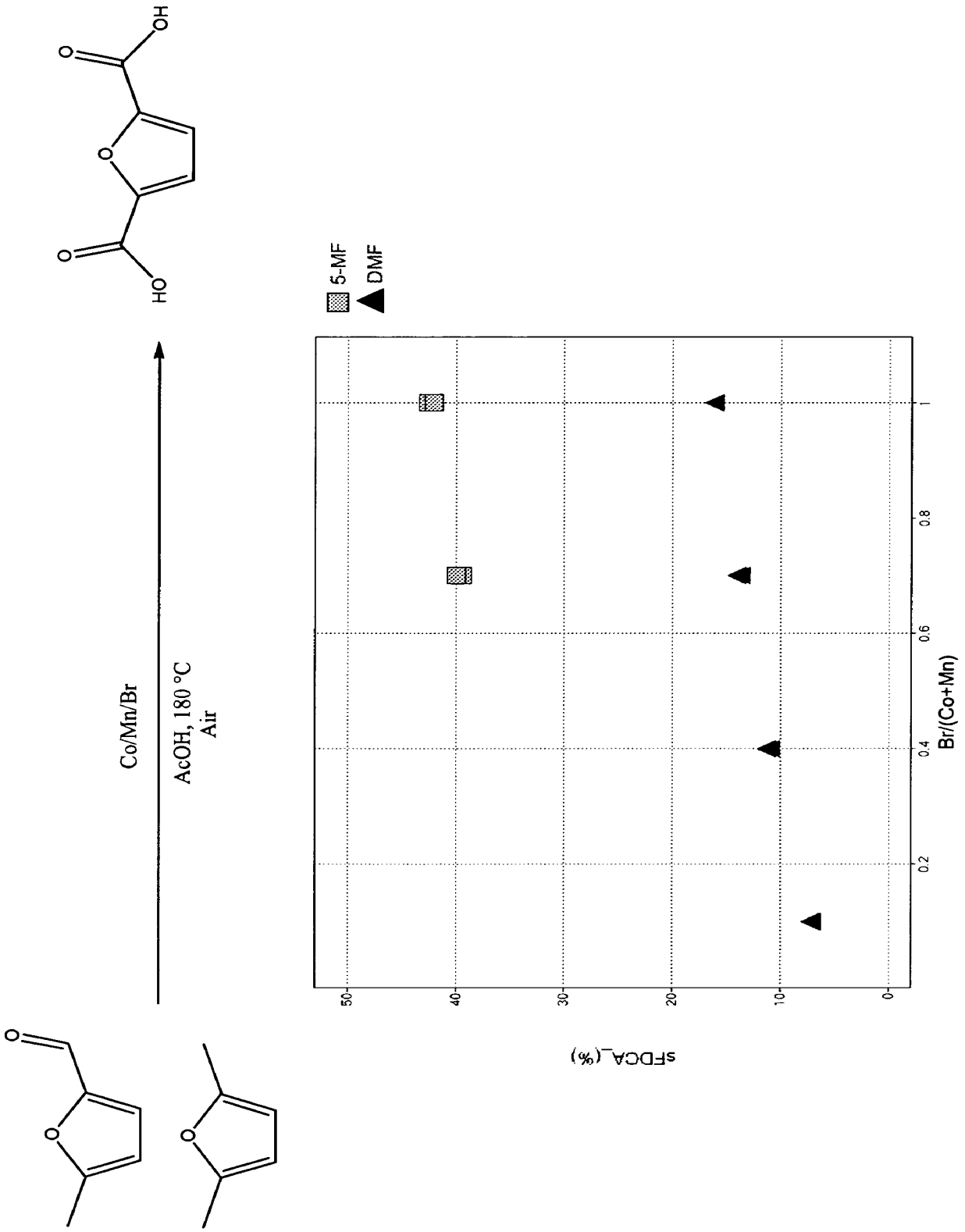

Co/Mn/Br
AcOH, 100/180 °C
Air
AcO
HO
180 °C. (Co+Mn)= 5.4 mol %
100 °C. (Co+Mn)= 5.25 mol %
100 °C. (Co+Mn)= 3.5 mol %
sFDCA (%)
Br/(Co+Mn)
0
10
20
30
40
50
60
70
80
0.2
0.4
0.6
0.8
1

Fig 3


Co/Mn/Br
AcOH, 180 °C
Air
5-MF
DMF
sFDCA_(%)
Br/(Co+Mn)
0
10
20
30
40
50
0.2
0.4
0.6
0.8
1

SAMENWERKINGSVERDRAG (PCT)

RAPPORT BETREFFENDE NIEUWHEIDSONDERZOEK VAN INTERNATIONAAL TYPE

IDENTIFICATIE VAN DE NATIONALE AANVRAGE	KENMERK VAN DE AANVRAGER OF VAN DE GEMACHTIGDE
	P30061NL00/MKO
Nederlands aanvraag nr. **2003606**	Indieningsdatum **07-10-2009**
	Ingeroepen voorrangsdatum
Aanvrager (Naam) **Furanix Technologies B.V.**	
Datum van het verzoek voor een onderzoek van internationaal type **27-01-2010**	Door de Instantie voor Internationaal Onderzoek aan het verzoek voor een onderzoek van internationaal type toegekend nr. **SN 53579**

I. CLASSIFICATIE VAN HET ONDERWERP (bij toepassing van verschillende classificaties, alle classificatiesymbolen opgeven)

Volgens de internationale classificatie (IPC)

C07D307/68

II. ONDERZOCHTE GEBIEDEN VAN DE TECHNIEK

Onderzochte minimumdocumentatie

Classificatiesysteem	Classificatiesymbolen
IPC8	**C07D**

Onderzochte andere documentatie dan de minimum documentatie, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen

III. ☐ **GEEN ONDERZOEK MOGELIJK VOOR BEPAALDE CONCLUSIES** (opmerkingen op aanvullingsblad)

IV. ☐ **GEBREK AAN EENHEID VAN UITVINDING** (opmerkingen op aanvullingsblad)

Form PCT/ISA 201 A (11/2000)

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Nummer van het verzoek om een onderzoek naar de stand van de techniek
NL 2003606

A. CLASSIFICATIE VAN HET ONDERWERP
INV. C07D307/68
ADD.

Volgens de Internationale Classificatie van octrooien (IPC) of zowel volgens de nationale classificatie als volgens de IPC.

B. ONDERZOCHTE GEBIEDEN VAN DE TECHNIEK

Onderzochte minimum documentatie (classificatie gevolgd door classificatiesymbolen)
C07D

Onderzochte andere documentatie dan de minimum documentatie voor dergelijke documenten voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen

Tijdens het onderzoek geraadpleegde elektronische gegevensbestanden (naam van de gegevensbestanden en waar uitvoerbaar gebruikte trefwoorden)
EPO-Internal, CHEM ABS Data, WPI Data

C. VAN BELANG GEACHTE DOCUMENTEN

Categorie °	Geciteerde documenten, eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
X	W.N. HAWORTH ET AL.: "1. The conversion of sucrose into furan compounds. Part II. Some 2:5-disubstituted tetrahydrofurans and their products of ring scission" J. CHEM. SOC., 1945, bladzijden 1-4, XP8122626 * Esterification of furan-2,5-dicarboxylic acid with methanol in hte presence of hydrogen chloride, page 3 (Methyl Furan-2:5-dicarboxylate) *	12,13
A,D	US 2009/156841 A1 (SANBORN ALEXANDRA J [US] ET AL) 18 juni 2009 (2009-06-18) in de aanvraag genoemd * voorbeeld 7 * * figuur 8 *	1-11,14

-/--

[X] Verdere documenten worden vermeld in het vervolg van vak C.

[X] Leden van dezelfde octrooifamilie zijn vermeld in een bijlage

° Speciale categorieën van aangehaalde documenten

'A' niet tot de categorie X of Y behorende literatuur die de stand van de techniek beschrijft

'D' in de octrooiaanvrage vermeld

'E' eerdere octrooi(aanvrage), gepubliceerd op of na de indieningsdatum waarin dezelfde uitvinding wordt beschreven

'L' om andere redenen vermelde literatuur

'O' niet-schriftelijke stand van de techniek

'P' tussen de voorrangsdatum en de indieningsdatum gepubliceerde literatuur

'T' na de indieningsdatum of de voorrangsdatum gepubliceerde literatuur die niet bezwarend is voor de octrooiaanvrage, maar wordt vermeld ter verheldering van de theorie of het principe dat ten grondslag ligt aan de uitvinding

"X" de conclusie wordt als niet nieuw of niet inventief beschouwd ten opzichte van deze literatuur

'Y' de conclusie wordt als niet inventief beschouwd ten opzichte van de combinatie van deze literatuur met andere geciteerde literatuur van dezelfde categorie, waarbij de combinatie voor de vakman voor de hand liggend wordt geacht

'&' lid van dezelfde octrooifamilie of overeenkomstige octrooipublicatie

Datum waarop het onderzoek naar de stand van de techniek van internationaal type werd voltooid	Verzenddatum van het rapport van het onderzoek naar de stand van de techniek van internationaal type
28 mei 2010	

Naam en adres van de instantie	De bevoegde ambtenaar
European Patent Office P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Diederen, Jeroen

1

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Nummer van het verzoek om een onderzoek naar de stand van de techniek
NL 2003606

C (Vervolg) VAN BELANG GEACHTE DOCUMENTEN

Categorie *	Geciteerde documenten eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
A,D	WALT PARTENHEIMER ET AL.: "Synthesis of 2,5-diformylfuran and furan-2,5-dicarboxylic acid by catalytic air oxidation of 5-hydroxymethylfurfural. Unexpectedly selective aerobic oxidation of benzyl alcohol to benzaldehyde with metal/bromide catalysts" ADV. SYNTH. CATAL., deel 343, nr. 1, 2001, bladzijden 102-111, XP002584717 in de aanvraag genoemd * het gehele document *	1-11,14
E	JP 2009 242312 A (AIR WATER INC) 22 oktober 2009 (2009-10-22) * Working example *	1,3-5, 8-10

1

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Informatie over leden van dezelfde octrooifamilie

Nummer van het verzoek om een onderzoek naar de stand van de techniek
NL 2003606

In het rapport genoemd octrooigeschrift	Datum van publicatie	Overeenkomend(e) geschrift(en)	Datum van publicatie
US 2009156841	A1 18-06-2009	WO 2009076627 A2	18-06-2009
JP 2009242312	A 22-10-2009	GEEN	

OCTROOICENTRUM NEDERLAND

WRITTEN OPINION

File No.	Filing date *(day/month/year)*	Priority date *(day/month/year)*	Application No.
SN53579	07.10.2009		NL2003606

International Patent Classification (IPC)
INV. C07D307/68

Applicant
Furanix Technologies B.V. te Amsterdam

This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the application
- ☒ Box No VIII Certain observations on the application

	Examiner
	Diederen, Jeroen

WRITTEN OPINION

Box No. I Basis of this opinion

1. This opinion has been established on the basis of the latest set of claims filed before the start of the search.

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ on paper

   ☐ in electronic form

   c. time of filing/furnishing:

   ☐ contained in the application as filed.

   ☐ filed together with the application in electronic form.

   ☐ furnished subsequently for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box II Priority

This opinion has been established as if the claimed priority date were valid, unless indicated otherwise on the **separate sheet**

WRITTEN OPINION

Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty	Yes:	Claims	1-11, 14
	No:	Claims	12, 13
Inventive step	Yes:	Claims	1-11, 14
	No:	Claims	12, 13
Industrial applicability	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

☒ Certain published documents

see the Search Report

☐ Non-written disclosures

Box No. VIII Certain observations on the application

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1 W.N. HAWORTH ET AL.: "1. The conversion of sucrose into furan compounds. Part II. Some 2:5-disubstituted tetrahydrofurans and their products of ring scission" J. CHEM. SOC., 1945 , bladzijden 1-4, XP8122626

D2 US 2009/156841 A1 (SANBORN ALEXANDRA J [US] ET AL) 18 juni 2009 (2009-06-18) in de aanvraag genoemd

D3 WALT PARTENHEIMER ET AL.: "Synthesis of 2,5-diformylfuran and furan-2,5-dicarboxylic acid by catalytic air oxidation of 5-hydroxymethylfurfural. Unexpectedly selective aerobic oxidation of benzyl alcohol to benzaldehyde with metal/bromide catalysts" ADV. SYNTH. CATAL., deel 343, nr. 1, 2001 , bladzijden 102-111, XP002584717 in de aanvraag genoemd

1. Novelty

The present application does not meet the criteria of patentability, because the subject-matter of claims 12,13 is not new.

Document D1 discloses the conversion of furan-2,5-dicarboxylic acid into the dimethyl ester by reaction with methanol/hydrogen chloride at reflux for 6 hours. The fact that furan-2,5-dicarboxylic acid was made in a new way, does not render the known use of such a compound in the preparation of a known compound novel. Claims 12,13 are therefore not considered novel over the prior art.

2. Inventive Step (Article 56 EPC)

The present application does not meet the criteria of patentability, because the subject-matter of claim 12,13 does not involve an inventive step.

Claims 12,13 which are not novel, cannot be considered inventive.

The closest prior art for the subject-matter of claims 1-11,14 is found in documents D1 and D2. In both documents furan-2,5-dicarboxylic acid is (allegedly) produced by oxidation of 5-hydroxymethylfurfural (D3) or by oxidation of 5-acetoxymethylfurfural (D2). In both cases an oxidation catalyst and an oxidant is used at a temperature lower than 140°C. The present application claims such a process at a temperature of at least 140°C. Therefore is the subject-matter of claims 1-11,14 novel over the prior art.

It was shown by the applicant that the conversion of 5-acetoxymethylfurfural to furan-2,5-dicarboxylic acid under the conditions as disclosed in D2 and at reaction temperatures below 140°C cannot take place. The desired product could not have been produced. This was also shown by the provided 1H-NMR, which shows the starting material 5-acetoxymethylfurfural (figure 8). It was also shown in D3 that oxidation of 5-hydroxymethylfurfural under similar conditions leads to the formation of the desired furan-2,5-dicarboxylic acid in a low yield. This can be attributed to the fact that acetic acid reacts with 5-hydroxymethylfurfural to form 5-acetoxymethylfurfural, which is stable under 140°C.

The problem to be solved by the application was to provide an improved process for the preparation of furan-2,5-dicarboxylic acid. At the time of writing the application, a skilled person would not increase the temperature and come to the solution of the present application. He would not have expected that by increasing the temperature, higher yields of furan-2,5-dicarboxylic acid were feasible. There is no indication in the prior art to expect this.

It is therefore considered that the subject-matter of claims 1-11,14 is novel and inventive over the prior art.

Re Item VIII

Clarity

Claim 1 is not clear. The wording "derivatives of HMF" is not a well defined term in the art, rendering the scope of claim 1 unclear.

INTERNATIONAL SEARCH REPORT

International application No
PCT/NL2010/050654

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D307/68
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WALT PARTENHEIMER ET AL.: "Synthesis of 2,5-diformylfuran and furan-2,5-dicarboxylic acid by catalytic air oxidation of 5-hydroxymethylfurfural. Unexpectedly selective aerobic oxidation of benzyl alcohol to benzaldehyde with metal/bromide catalysts", ADV. SYNTH. CATAL., vol. 343, no. 1, 2001, pages 102-111, XP002584717, cited in the application the whole document in particular figure 1, tables 1 and 3. ----- -/--	1-11,15

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 December 2010	05/01/2011

Name and mailing address of the ISA/	Authorized officer
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Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2009/156841 A1 (SANBORN ALEXANDRA J [US] ET AL) 18 June 2009 (2009-06-18) cited in the application the whole document in particular paragraph 60, example 7 and figure 8	1-11,15
X,P	JP 2009 242312 A (AIR WATER INC) 22 October 2009 (2009-10-22) the whole document in particular paragraphs 31 and 43-46.	1-11,15
X	HAWORTH W N ET AL: "The conversion of sucrose into furan compounds. Part II. Some 2 : 5-disubstituted tetrahydrofurans and their products of ring scission", JOURNAL OF THE CHEMICAL SOCIETY, CHEMICAL SOCIETY, LETCHWORTH; GB, no. 1, 1 January 1945 (1945-01-01), pages 1-4, XP008122626, ISSN: 0368-1769, DOI: DOI:10.1039/JR9450000001 the whole document in particular 1st paragraph on page 1 and last before paragraph on page 3.	12-15
X	WO 2006/063220 A2 (ARCHER DANIELS MIDLAND CO [US]; SANBORN ALEXANDRA J [US]) 15 June 2006 (2006-06-15) claims 1-26; examples 1-24	15
X,P	TONG X ET AL: "Biomass into chemicals: Conversion of sugars to furan derivatives by catalytic processes", APPLIED CATALYSIS A: GENERAL, ELSEVIER SCIENCE, AMSTERDAM, NL, vol. 385, no. 1-2, 15 September 2010 (2010-09-15), pages 1-13, XP027230510, ISSN: 0926-860X [retrieved on 2010-07-30] the whole document in particular pages 9-10.	1-11,15

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BOISEN A ET AL: "Process integration for the conversion of glucose to 2,5-furandicarboxylic acid", CHEMICAL ENGINEERING RESEARCH AND DESIGN, PART A, INSTITUTION OF CHEMICAL ENGINEERS, XX, vol. 87, no. 9, 1 September 2009 (2009-09-01), pages 1318-1327, XP026613647, ISSN: 0263-8762, DOI: DOI:10.1016/J.CHERD.2009.06.010 [retrieved on 2009-07-25] the whole document in particular paragraph 4.2.2	1-11,15
X	WO 01/72732 A2 (DU PONT [US]; GRUSHIN VLADIMIR [US]; PARTENHEIMER WALTER [US]; MANZER) 4 October 2001 (2001-10-04) page 7, line 2 - line 7; claims 11-21; examples 16-40	1-11,15
X	WO 2008/054804 A2 (BATTELLE MEMORIAL INSTITUTE [US]; LILGA MICHAEL A [US]; HALLEN RICHARD) 8 May 2008 (2008-05-08) * abstract; claims 1-28 paragraphs [0049], [0050], [0058]; claims 5,10; figure 31; example 1	1-11,15
X	JP 2009 001519 A (CANON KK) 8 January 2009 (2009-01-08) * abstract paragraph [0025]	1-11
X	SU 636 233 A1 (INST ORGANICHESKOGO SINTEZA AK [SU]; INST KHIM FIZ AN SSSR [SU]) 5 December 1978 (1978-12-05) the whole document in particular column 2, lines 9-10, examples 1, 2 and 4 and claim 1	1-11
E	WO 2010/132740 A2 (ARCHER DANIELS MIDLAND CO [US]; SANBORN ALEXANDRA [US]) 18 November 2010 (2010-11-18) claims 1-18; examples 8,12	1-11,15
A	EP 0 356 703 A2 (HOECHST AG [DE]) 7 March 1990 (1990-03-07) the whole document	1-11,15

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GRABOWSKI G ET AL: "The electrochemical oxidation of 5-hydroxymethylfurfural with the nickel oxide/hydroxide electrode", ELECTROCHIMICA ACTA, ELSEVIER SCIENCE PUBLISHERS, BARKING, GB, vol. 36, no. 13, 1 January 1991 (1991-01-01), page 1995, XP026726025, ISSN: 0013-4686, DOI: DOI:10.1016/0013-4686(91)85084-K [retrieved on 1991-01-01] the whole document	1-11

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		EP 2217584 A2	18-08-2010
		KR 20100092054 A	19-08-2010
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JP 2009242312 A	22-10-2009	NONE	
WO 2006063220 A2	15-06-2006	AT 443059 T	15-10-2009
		AU 2005313945 A1	15-06-2006
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		CA 2590082 A1	15-06-2006
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		EP 1838688 A2	03-10-2007
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		EP 2233476 A1	29-09-2010
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		EP 2233478 A1	29-09-2010
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Cesar Muñoz de Diego et al.	Examiner:	Unassigned
Application No.:	Unassigned	Group Art Unit:	Unassigned
Confirmation No:	Unassigned	Docket:	903-457 PCT/US
Filed:	Herewith	Dated:	March 22, 2012
For:	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID		

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Dated: March 22, 2012

Signature: K.J. Goodhand /*K.J. Goodhand*/

STATEMENT UNDER 37 C.F.R. § 1.125(b)

Sir:

The substitute specifications, which do not include claim listings, filed concurrently herewith include no new matter.

Respectfully submitted,

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~~Title: Method for the preparation of 2,5-furandicarboxylic acid and for the preparation of the dialkyl ester of 2,5-furandicarboxylic acid~~ METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

CROSS-REFERENCE TO RELATED APPLICATIONS:

[0001] This application is the National Stage of International Application No. PCT/NL2010/050654, filed October 6, 2010, which claims the benefit of Netherlands Application No. 2003606, filed October 7, 2009, and U.S. Provisional Application No. 61/249,395, filed October 7, 2009, the contents of all of which are incorporated by reference herein.

FIELD OF THE INVENTION:

[0002] The present invention relates to a method for the preparation of 2,5-furandicarboxylic acid ("FDCA") from 5-hydroxymethylfurfural ("HMF") and/or derivatives thereof. FDCA can be produced in particular from esters of HMF, such as for example 5-acetoxymethylfurfural (AMF) or a mixture of one or more of these compounds with HMF, such as for example from a mixture of AMF and HMF. The invention further relates to a process for the preparation of the dialkyl ester of 2,5-furandicarboxylic acid.

BACKGROUND OF THE INVENTION:

[0003] 2,5-Furandicarboxylic acid, also known as dehydromucic acid is a furan derivative. This organic compound was first obtained by Fittig and Heinzelmann in 1876. The first review, by Henry Hill was published in 1901 (Am. Chem. Journ. 25, 439). FDCA was more than 125 years later identified by the US Department of Energy as one of 12 priority chemicals for establishing the "green" chemistry industry of the future. However, to date, no commercial process exists for its production. On laboratory scale it is often synthesized from 5-hydroxymethylfurfural (HMF), which in turn can be obtained from carbohydrate containing sources such as glucose, fructose, sucrose and starch. From fructose and glucose HMF is obtained by acidic elimination of three moles of water.

[0004] The derivatives of HMF are identified as potential and versatile fuel components and precursors for the production of plastics. The polyester from FDCA dimethyl diester and ethylene glycol was first reported in 1946 (GB 621,971).

[0005] WO 01/72732 describes the oxidation of HMF to FDCA. The maximum FDCA yield reported is 59%, obtained at 105 °C. The oxidation of HMF in an aqueous medium with oxygen using a catalyst from the Pt-group is described in US 4977283. Taarning et al. described the oxidation of HMF over gold based catalysts (ChemSusChem, 2008, 1, 1-4).

[0006] Partenheimer et al (Adv. Synth. Catal. **2001**, *343*, pp 102-11) describe the synthesis of 2,5-furandicarboxylic acid by catalytic air-oxidation of 5-hydroxymethylfurfural with metal/bromide catalysts such as Co/Mn/Br in acetic acid at temperatures ranging from 50 to 125 °C. With the Co/Mn/Br catalyst the highest FDCA yield obtained is 35.2% (Table 3, experiment 4). On page 103 of the same paper, under the header "products formed" it is stated: "A side reaction is the esterification of the alcohols to form the more oxidatively stable acetate …." As apparently 5-hydroxymethylfurfural reacts with acetic acid a loss of the starting material takes place. Further, in the reaction scheme given in Figure 1 on page 103, it is indicated that 5-(acetoxymethyl)furfural is an end-point. There is no further reaction of this compound indicated to FDCA (in contrast to the ester of the intermediate product 5-(acetoxymethyl)furan-2-carboxylic acid). In other words, the 5-(acetoxymethyl)furfural (AMF) formed through reaction of HMF with acetic acid solvent, is not oxidized to FDCA and its formation leads therefore to yield loss.

[0007] This result was confirmed in US 2009/0156841. Although the intention of the process according to US 2009/0156841 was to obtain FDCA, the product isolated and erroneously characterized as being FDCA was in fact the starting material acetoxymethyl furfural (AMF). Under the low temperature conditions deployed (100 °C), AMF is quite stable, as was already reported by Partenheimer (see above).

[0008] In US 2009/0156841 a ^{1}H NMR spectrum is shown in Figure 8 and suggested that it is the spectrum of the product that was identified as FDCA. However, this is not the case. The ^{1}H NMR spectrum of the product shown in Figure 8 is the same as that in Figure 6 and represents the starting material AMF. The 1H NMR spectrum of FDCA shows a singlet at a shift of about 7.26 ppm. Moreover, the product is described as a tan solid. In the experience of the present inventors, AMF is a tan solid, while FDCA is a white solid. It would seem that no FDCA was obtained in the experiments according to US 2009/0156841.

[0009] The experiments executed under the conditions of US 2009/0156841 were repeated. These comparative experiments confirm the low reactivity of AMF under conditions

given in US 2009/0156841. Thus, a person skilled in the art would therefore have concluded that FDCA cannot be obtained in interesting yields from AMF using the conditions that are reported in US 2009/0156841, i.e., using a Co/Mn/Br catalyst in acetic acid at between 85 and 110 °C within a time frame of from 100 and 150 minutes. In Example 7 of US 2009/0156841, slightly more than 50% of the starting material was the only product isolated from the reaction.

SUMMARY OF THE INVENTION:

[0010] The present inventors have now surprisingly found that when using an oxidation catalyst, e.g., based on both cobalt and manganese and containing a bromide, at temperatures higher than 140 °C, derivatives of HMF, and in particular esters of HMF optionally in combination with HMF, such as for example 5-(acetoxymethyl)furfural (AMF) can be oxidized to FDCA in high yields.

DETAILED DESCRIPTION OF THE INVENTION:

[0011] Thus, in a first aspect the invention provides a method for the preparation of 2,5-furan dicarboxylic acid comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C. The feed may optionally comprise 5-hydroxymethylfurfural as a further compound.

[0012] The invention described hereinafter may use any of the compounds described above in the feed. A preferred ester of HMF contains an ester moiety of an alkyl carboxylic acid wherein the alkyl group contains up to 6 carbon atoms, preferably from 1 to 5 carbon atoms, i.e. methyl, ethyl, propyl, isopropyl, butyl, 2-butyl, tert-butyl, pentyl, 2-pentyl, neopentyl and 3-pentyl. Particularly preferred are alkyl groups with 1 to 4 carbon atoms. There is a preference for methyl, giving (5-acetoxymethyl)furfural. Hence, 5-acetoxymethylfurfural is the preferred feedstock, by itself or in combination with HMF.

[0013] In another aspect of the invention, we have also investigated the oxidation of other furan-based substrates under the process conditions according to the current invention. We have been able to convert 5-(chloromethyl)furfural, 5-(chloromethyl)furoic acid, 5-methylfurfural, 5-methylfuroic acid and 2,5-dimethylfuran all to FDCA in very interesting yields.

[0014] In WO 2007/104515 and WO 2009/030512, the synthesis of esters of HMF such as 5-acetoxymethylfurfural (AMF) from biomass sources is described. Given the higher stability of the HMF esters than HMF and hence improved production pathways and given the fact that upon oxidation in acetic acid the acetoxy functionality that was obtained from acetic acid is now liberated as acetic acid and given the green reputation of these esters, they were considered by the present inventors as interesting starting point in the preparation of furan-based monomers that could be used for the production of furandicarboxylic acid-based polyesters, for instance as an alternative for PET or FDCA-based polyamids (nylons). The most important conventional, oil-based, polyester monomer to produce PET is Purified Terephthalic acid (PTA) and its dialkyl ester DiMethyl Terephthalate (DMT).

[0015] AMF can be obtained from biomass sources as described in WO 2007/104515 and WO 2009/030512. Depending on the process conditions the product obtained in accordance with the process of these references may also contain HMF.

[0016] FDCA, the product of the reaction can be used in the preparation of a polyester, by reaction of FDCA or its dialkyl ester with a suitable diol. Such polyester preparations are preferably performed by transesterification, whereby the di-methyl ester or di-ethyl ester of FDCA is used and wherein the methyl or ethyl groups are exchanged in the form of a volatile alcohol during the transesterification with the diol.

[0017] The oxidation catalyst can be selected from a variety of oxidation catalysts, but is preferably a catalyst based on both cobalt and manganese and suitably containing a source of bromine, preferably a bromide.

[0018] The bromine source can be any compound that produces bromide ions in the reaction mixture. These compounds include hydrogen bromide, sodium bromide, elemental bromine, benzyl bromide and tetrabromoethane. Also other bromine salts, such as an alkali or alkaline earth metal bromide or another metal bromide such as $ZnBr_2$ can be used. There is a preference for hydrobromic acid or sodium bromide. The amount of bromine mentioned in here relates to the amount measured as Br relative to cobalt.

[0019] Suitable metal bromide catalysts employed in all of the processes of this invention comprise a cobalt compound and a manganese compound and a bromine-containing compound. Preferably these compounds are soluble in the reaction mixture.

[0020] Preferably, the catalyst comprises both Co and Mn. The metal and bromide catalyst contains, in addition to bromide, Co and Mn and optionally may contain one or more additional metals, in particular Zr and/or Ce. Alternative and suitable catalysts are described in W. Partenheimer, Catalysis Today 23(2), 69-158 (1995) in particular on pages 89-99, included herein by reference.

[0021] Each of the metal components can be provided in any of their known ionic forms. Preferably the metal or metals are in a form that is soluble in the reaction solvent. Examples of suitable counterions for cobalt and manganese include, but are not limited to, carbonate, acetate, acetate tetrahydrate and halide, with bromide being the preferred halide.

[0022] As described in Partenheimer, ibid, pages 86-88, suitable solvents for use in the processes of the present invention, described above, preferably have at least one component that contains a monocarboxylic acid functional group. The solvent may also function as one of the reagents. The processes may be run in a solvent or solvent mixture that does not contain an acid group. In that case, preferably one of the reagents does contain a monocarboxylic acid functional group. Suitable solvents can also be aromatic acids such as benzoic acid and derivatives thereof. A preferred solvent is an aliphatic C_2-C_6 monocarboxylic acid, such as but not limited to acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, trimethylacetic acid, and caproic acid and mixtures thereof. Said mixtures may also include benzene, acetonitrile, heptane, acetic anhydride, chlorobenzene, o-dichlorobenzene, and water. The most preferred solvent is acetic acid ("AcOH").

[0023] The oxidant in the processes of the present invention is preferably an oxygen-containing gas or gas mixture, such as, but not limited to air and oxygen-enriched air. Oxygen by itself is also a preferred oxidant.

[0024] The processes of the instant invention described above can be conducted in a batch, semi-continuous or continuous mode. Especially for the manufacture of FDCA, operation in the batch mode with increasing temperature at specific times, increasing pressure at specific times, variation of the catalyst concentration at the beginning of the reaction, and variation of the catalyst composition during the reaction is desirable. For example, variation of the catalyst composition during the reaction can be accomplished by addition of cobalt and/or manganese and/or zirconium, and/or cerium, and/or bromide at specified times.

[0025] The pressure in a commercial oxidation process may vary within wide ranges. When a diluent is present, and in particular with acetic acid as diluent, the temperature and the pressure in such a process are not independent. The pressure is determined by the solvent (e.g., acetic acid) pressure at a certain temperature. The pressure of the reaction mixture is preferably selected such that the solvent is mainly in the liquid phase. In practice this means that pressures between 5 and 100 bar can be used with a preference for pressures between 10 and 80 bar. In case the oxidant is an oxygen-containing gas, such as air, the gas can be continuously fed to and removed from the reactor, or the gas can be supplied all at the start of the reaction. In the latter case, the pressure of the system will depend on the headspace volume and the amount of gas required to convert the starting material. It is clear that in the latter case, the pressure of the system may be significantly higher than the pressure in a process wherein an oxygen containing gas is continuously fed and removed. In the case of continuously feeding and removing the oxidant gas to and from the reactor, the oxygen partial pressure will suitably be between 1 and 30 bar or more preferably between 1 and 10 bar.

[0026] The temperature of the reaction mixture is at least 140 ºC, preferably from 140 and 200 ºC, most preferably between 160 and 190 ºC. Temperatures higher than 180 ºC may lead to decarboxylation and to other degradation products. Good results to FDCA have been achieved at a temperature of about 180 °C.

[0027] Molar ratios of cobalt to manganese (Co/Mn) are typically 1/1000 - 100/1, preferably 1/100 - 10/1 and more preferably 1/10 - 4/1.

[0028] Molar ratios of bromine to metals (e.g. Br/(Co+Mn)) are typically 0.001-5.00, preferably 0.01 - 2.00 and more preferably 0.1 - 0.9.

[0029] Catalyst concentration (Co + Mn) is typically from 0.1 to 10 mol %, relative to the substrate, with a preference for concentrations from 2 to 6 mol %. Good results were obtained in general with catalyst concentrations of around 4 mol %.

[0030] The starting materials for the production of FDCA may originate from a carbohydrate source as described above. Examples of such disclosures are WO 2007/104515 and WO 2009/030512. Accordingly, the invention also provides a method for the preparation of 2,5-furandicarboxylic acid wherein a carbohydrate source is converted in the presence of an alkyl carboxylic acid into products comprising an HMF ester and optionally 5-hydroxymethyl furfural, from which is isolated a feed comprising the ester of HMF and optionally 5-

hydroxymethyl furfural, and which method further comprises the subsequent step of contacting the feed with an oxidant in the presence of an oxidation catalyst, in particular a cobalt and manganese and bromide-containing catalyst, under appropriate reaction conditions, in particular at temperatures higher than 140 °C

[0031] In another aspect, the FDCA obtained according to the process of the present invention can be transformed using common esterification reactions to a diester by contacting the starting material under appropriate conditions with the relevant alcohol. Thus, in one aspect, the invention also relates to the use of FDCA obtained according to the process of the current invention in the preparation of a dialkylester of 2,5-dicarboxylic acid by reaction of the FDCA with a C_1-C_5 alkyl alcohol, preferably methanol to prepare the dimethyl ester of FDCA.

[0032] Accordingly, the present invention also provides a process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C, and esterifying the thus obtained product. Preferably, the product is esterified with an alkyl alcohol, suitably having 1 to 5 carbon atoms.

[0033] The esterification of 2,5-furan dicarboxylic acid is known. As a specific example for the manufacture of these esters, reference is made to US 2673860 wherein the diester is obtained by transesterification of another dicarboxylic acid ester in the presence of sulphuric acid. A more general description for the esterification of dicarboxylic acids is presented in US 2628249.

[0034] In a further aspect of the invention, the di-methylester can be used in the preparation of polyester polymers by reaction with a diol. Reacting the di-methylester with a diol will result in the formation of methanol that quickly vaporises. In 1946 the polymerization of FDCA dimethyl ester with ethylene glycol was described as a first example of such a polymerization in GB 621,971.

[0035] Indeed, polyesters are generally made by a combined esterification/polycondenzation reaction between monomer units of a diol (e.g., ethylene glycol

(EG)) and a dicarboxylic acid. Additives such as catalysts and stabilizers may be added to facilitate the process and stabilize the polyester towards degradation.

[0036] Examples:

[0037] Experiments were carried out in parallel 8 ml magnetically stirred stainless steel batch reactors. The reactors are grouped in blocks containing 12 batch reactors. The standard procedure for all the reactions was as follows:

[0038] 0.5 ml of starting material stock solution in acetic acid (0.78 mmol/ml) were added into a reactor lined with a Teflon insert. To the reactor 1 ml of a catalyst stock solution in acetic acid was subsequently added. In a typical experiment, a catalyst composition Co/Mn/Br with a relative 1-x-y ratio, the concentration of $Co(OAc)_2*4H_2O$ was varied. As a Mn source, $Mn(OAc)_2*4H_2O$ was used and as a bromine source NaBr was used. The reactors were closed with a rubber septum, after which the reactors were sealed and pressurized to the desired air pressure, ranging from 20-60 bars. After pressurization, the block with 12 reactors was placed in the test unit which was preheated at the desired temperature, ranging from 100 to 220 °C. After the desired reaction time, ranging from 0.5 hr to 24 hrs, the block is placed into an ice bath for 20 minutes. When the block had cooled down, it was depressurized. After opening, HPLC samples were prepared. First 5 ml of a saccharine solution in DMSO (11.04 mg/ml) was added to each reactor and the mixture was stirred for 5 minutes. Then 10 µl of this mixture was diluted to 1000 µl with water in a HPLC vial. The samples were analyzed using HPLC.

[0039] Example 1

[0040] Example 1 shows the selectivity of FDCA in the oxidation of HMF, of a HMF/AMF 3/2 mixture, of a HMF/AMF 2/3 mixture and of AMF, respectively, with 2.7 mol% Co catalyst (relative to substrate), and Co/Mn molar ratio of 1/1, so that the catalyst concentration (Co + Mn) amounted to 5.4 mol%. The Br/(Co+Mn) molar ratio was 1.0; 0.7; 0.4 and 0.1 at 0.26 M substrate concentration in acetic acid at 180 ºC for 1 hr with 20 bar air. The amount of oxygen was 2.69 mol oxygen per mol substrate. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn) > 1, corrosion will be a problem on commercial scale. HMF gives slightly higher yields than AMF at one hour reaction time. The results of these experiments are given in Table 1.

[0041] Example 2

[0042] Example 2 shows the selectivity to FDCA for the AMF oxidation of Example 1, together with the comparative examples based on the experimental conditions described in US 2009/0156841. In those comparative experiments (2a and 2b) 10 wt/wt% AMF in acetic acid was oxidized with 1.75 and 2.65 mol % Co catalyst and a fixed Br/(Co + Mn) molar ratio of 1.0 and a Co/Mn molar ratio of 1.0 at 100 °C and 30 bar for 2 hours. The amount of oxygen was 2.88 mol oxygen per mol substrate. Under these conditions, the yield of FDCA was lower than the result suggested in US 2009/0156841 and also lower than the results obtained at higher temperature. The results of these experiments are given in Table 2.

[0043] Example 3

[0044] Example 3 shows the yield of FDCA in the oxidation of 5-methylfurfural (5MF) and 2,5-dimethylfurfural (DMF) at 180 ºC with 2.7 mol% Co catalyst (relative to substrate), and Co/Mn ratio of 1/1, so that the catalyst concentration (Co + Mn) amounted to 5.4 mol%. The Br/(Co+Mn) molar ratio was 1.0, 0.7, 0.4 and 0.1. The substrate concentration was 0.26 M in acetic acid. The reaction temperature was at 180 ºC and the reaction was conducted with 50 bars air. The amount of oxygen was 6.7 mol oxygen per mol substrate. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn) > 1, corrosion will be a problem on commercial scale. Reactions with 5-MF give higher yields than reactions with DMF. The results of these experiments are also given in Table 3.

Table 1

Experiment No.	Substrate HMF/AMF molar ratio		Br/ (Co+Mn)	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
	HMF	AMF				
1a	1	0	1	3.3	100.00	76.66
1b	3	2	1	3.8	100.00	71.19
1c	2	3	1	4.0	100.00	77.66
1d	0	1	1	4.4	100.00	64.82
1e	1	0	0.7	3.3	100.00	78.08
1f	3	2	0.7	3.8	100.00	66.96
1g	2	3	0.7	4.0	100.00	75.14
1h	0	1	0.7	4.4	100.00	60.64
1i	1	0	0.4	3.3	100.00	73.27
1j	3	2	0.4	3.8	100.00	65.67
1k	2	3	0.4	4.0	100.00	73.21
1l	0	1	0.4	4.4	100.00	57.36
1m	1	0	0.1	3.3	100.00	67.92
1n	3	2	0.1	3.8	100.00	60.92
1o	2	3	0.1	4.0	100.00	69.64
1p	0	1	0.1	4.4	100.00	46.85

Table 2

Experiment No.	Temp [° C]	Reaction time [Hours]	Catalyst concentration [(Co + Mn) mol %]	Mn/Co	Br/ (Co+Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
1d	180	1	5.4	1	1	2.69	4.4	100.00	64.82
1h	180	1	5.4	1	0.7	2.69	4.4	100.00	60.64
1l	180	1	5.4	1	0.4	2.69	4.4	100.00	57.36
1p	180	1	5.4	1	0.1	2.69	4.4	100.00	46.85
2a	100	2	3.5	1	1	2.88	10.0	100.00	23.48
2b	100	2	5.3	1	1	2.88	10.0	100.00	29.05

Table 3

Experiment No.	Substrate	Reaction time [Hours]	Br/ (Co+Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
3a	5-MF	1	1	6.7	2.9	100.00	42.62
3b	5-MF	1	0.7	6.7	2.9	100.00	39.94
3c	DMF	1	1	6.7	2.5	100.00	16.17
3d	DMF	1	0.7	6.7	2.5	100.00	14.09
3e	DMF	1	0.4	6.7	2.5	100.00	11.30
3f	DMF	1	0.1	6.7	2.5	100.00	7.19

ABSTRACT

A ~~The application describes a~~ method for the preparation of 2,5-furan dicarboxylic acid includes ~~comprising~~ the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5- methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5- dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C.

METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

CROSS-REFERENCE TO RELATED APPLICATIONS:

[0001] This application is the National Stage of International Application No. PCT/NL2010/050654, filed October 6, 2010, which claims the benefit of Netherlands Application No. 2003606, filed October 7, 2009, and U.S. Provisional Application No. 61/249,395, filed October 7, 2009, the contents of all of which are incorporated by reference herein.

FIELD OF THE INVENTION:

[0002] The present invention relates to a method for the preparation of 2,5-furandicarboxylic acid ("FDCA") from 5-hydroxymethylfurfural ("HMF") and/or derivatives thereof. FDCA can be produced in particular from esters of HMF, such as for example 5-acetoxymethylfurfural (AMF) or a mixture of one or more of these compounds with HMF, such as for example from a mixture of AMF and HMF. The invention further relates to a process for the preparation of the dialkyl ester of 2,5-furandicarboxylic acid.

BACKGROUND OF THE INVENTION:

[0003] 2,5-Furandicarboxylic acid, also known as dehydromucic acid is a furan derivative. This organic compound was first obtained by Fittig and Heinzelmann in 1876. The first review, by Henry Hill was published in 1901 (Am. Chem. Journ. 25, 439). FDCA was more than 125 years later identified by the US Department of Energy as one of 12 priority chemicals for establishing the "green" chemistry industry of the future. However, to date, no commercial process exists for its production. On laboratory scale it is often synthesized from 5-hydroxymethylfurfural (HMF), which in turn can be obtained from carbohydrate containing sources such as glucose, fructose, sucrose and starch. From fructose and glucose HMF is obtained by acidic elimination of three moles of water.

[0004] The derivatives of HMF are identified as potential and versatile fuel components and precursors for the production of plastics. The polyester from FDCA dimethyl diester and ethylene glycol was first reported in 1946 (GB 621,971).

[0005] WO 01/72732 describes the oxidation of HMF to FDCA. The maximum FDCA yield reported is 59%, obtained at 105 ºC. The oxidation of HMF in an aqueous medium with

oxygen using a catalyst from the Pt-group is described in US 4977283. Taarning et al. described the oxidation of HMF over gold based catalysts (ChemSusChem, 2008, 1, 1-4).

[0006] Partenheimer et al (Adv. Synth. Catal. **2001**, *343*, pp 102-11) describe the synthesis of 2,5-furandicarboxylic acid by catalytic air-oxidation of 5-hydroxymethylfurfural with metal/bromide catalysts such as Co/Mn/Br in acetic acid at temperatures ranging from 50 to 125 °C. With the Co/Mn/Br catalyst the highest FDCA yield obtained is 35.2% (Table 3, experiment 4). On page 103 of the same paper, under the header "products formed" it is stated: "A side reaction is the esterification of the alcohols to form the more oxidatively stable acetate …." As apparently 5-hydroxymethylfurfural reacts with acetic acid a loss of the starting material takes place. Further, in the reaction scheme given in Figure 1 on page 103, it is indicated that 5-(acetoxymethyl)furfural is an end-point. There is no further reaction of this compound indicated to FDCA (in contrast to the ester of the intermediate product 5-(acetoxymethyl)furan-2-carboxylic acid). In other words, the 5-(acetoxymethyl)furfural (AMF) formed through reaction of HMF with acetic acid solvent, is not oxidized to FDCA and its formation leads therefore to yield loss.

[0007] This result was confirmed in US 2009/0156841. Although the intention of the process according to US 2009/0156841 was to obtain FDCA, the product isolated and erroneously characterized as being FDCA was in fact the starting material acetoxymethyl furfural (AMF). Under the low temperature conditions deployed (100 °C), AMF is quite stable, as was already reported by Partenheimer (see above).

[0008] In US 2009/0156841 a ^{1}H NMR spectrum is shown in Figure 8 and suggested that it is the spectrum of the product that was identified as FDCA. However, this is not the case. The ^{1}H NMR spectrum of the product shown in Figure 8 is the same as that in Figure 6 and represents the starting material AMF. The 1H NMR spectrum of FDCA shows a singlet at a shift of about 7.26 ppm. Moreover, the product is described as a tan solid. In the experience of the present inventors, AMF is a tan solid, while FDCA is a white solid. It would seem that no FDCA was obtained in the experiments according to US 2009/0156841.

[0009] The experiments executed under the conditions of US 2009/0156841 were repeated. These comparative experiments confirm the low reactivity of AMF under conditions given in US 2009/0156841. Thus, a person skilled in the art would therefore have concluded that FDCA cannot be obtained in interesting yields from AMF using the conditions that are

reported in US 2009/0156841, i.e., using a Co/Mn/Br catalyst in acetic acid at between 85 and 110 °C within a time frame of from 100 and 150 minutes. In Example 7 of US 2009/0156841, slightly more than 50% of the starting material was the only product isolated from the reaction.

SUMMARY OF THE INVENTION:

[0010] The present inventors have now surprisingly found that when using an oxidation catalyst, e.g., based on both cobalt and manganese and containing a bromide, at temperatures higher than 140 °C, derivatives of HMF, and in particular esters of HMF optionally in combination with HMF, such as for example 5-(acetoxymethyl)furfural (AMF) can be oxidized to FDCA in high yields.

DETAILED DESCRIPTION OF THE INVENTION:

[0011] Thus, in a first aspect the invention provides a method for the preparation of 2,5-furan dicarboxylic acid comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C. The feed may optionally comprise 5-hydroxymethylfurfural as a further compound.

[0012] The invention described hereinafter may use any of the compounds described above in the feed. A preferred ester of HMF contains an ester moiety of an alkyl carboxylic acid wherein the alkyl group contains up to 6 carbon atoms, preferably from 1 to 5 carbon atoms, i.e. methyl, ethyl, propyl, isopropyl, butyl, 2-butyl, tert-butyl, pentyl, 2-pentyl, neopentyl and 3-pentyl. Particularly preferred are alkyl groups with 1 to 4 carbon atoms. There is a preference for methyl, giving (5-acetoxymethyl)furfural. Hence, 5-acetoxymethylfurfural is the preferred feedstock, by itself or in combination with HMF.

[0013] In another aspect of the invention, we have also investigated the oxidation of other furan-based substrates under the process conditions according to the current invention. We have been able to convert 5-(chloromethyl)furfural, 5-(chloromethyl)furoic acid, 5-methylfurfural, 5-methylfuroic acid and 2,5-dimethylfuran all to FDCA in very interesting yields.

[0014] In WO 2007/104515 and WO 2009/030512, the synthesis of esters of HMF such as 5-acetoxymethylfurfural (AMF) from biomass sources is described. Given the higher stability of the HMF esters than HMF and hence improved production pathways and given the fact that

upon oxidation in acetic acid the acetoxy functionality that was obtained from acetic acid is now liberated as acetic acid and given the green reputation of these esters, they were considered by the present inventors as interesting starting point in the preparation of furan-based monomers that could be used for the production of furandicarboxylic acid-based polyesters, for instance as an alternative for PET or FDCA-based polyamids (nylons). The most important conventional, oil-based, polyester monomer to produce PET is Purified Terephthalic acid (PTA) and its dialkyl ester DiMethyl Terephthalate (DMT).

[0015] AMF can be obtained from biomass sources as described in WO 2007/104515 and WO 2009/030512. Depending on the process conditions the product obtained in accordance with the process of these references may also contain HMF.

[0016] FDCA, the product of the reaction can be used in the preparation of a polyester, by reaction of FDCA or its dialkyl ester with a suitable diol. Such polyester preparations are preferably performed by transesterification, whereby the di-methyl ester or di-ethyl ester of FDCA is used and wherein the methyl or ethyl groups are exchanged in the form of a volatile alcohol during the transesterification with the diol.

[0017] The oxidation catalyst can be selected from a variety of oxidation catalysts, but is preferably a catalyst based on both cobalt and manganese and suitably containing a source of bromine, preferably a bromide.

[0018] The bromine source can be any compound that produces bromide ions in the reaction mixture. These compounds include hydrogen bromide, sodium bromide, elemental bromine, benzyl bromide and tetrabromoethane. Also other bromine salts, such as an alkali or alkaline earth metal bromide or another metal bromide such as $ZnBr_2$ can be used. There is a preference for hydrobromic acid or sodium bromide. The amount of bromine mentioned in here relates to the amount measured as Br relative to cobalt.

[0019] Suitable metal bromide catalysts employed in all of the processes of this invention comprise a cobalt compound and a manganese compound and a bromine-containing compound. Preferably these compounds are soluble in the reaction mixture.

[0020] Preferably, the catalyst comprises both Co and Mn. The metal and bromide catalyst contains, in addition to bromide, Co and Mn and optionally may contain one or more additional metals, in particular Zr and/or Ce. Alternative and suitable catalysts are described in

W. Partenheimer, Catalysis Today 23(2), 69-158 (1995) in particular on pages 89-99, included herein by reference.

[0021] Each of the metal components can be provided in any of their known ionic forms. Preferably the metal or metals are in a form that is soluble in the reaction solvent. Examples of suitable counterions for cobalt and manganese include, but are not limited to, carbonate, acetate, acetate tetrahydrate and halide, with bromide being the preferred halide.

[0022] As described in Partenheimer, ibid, pages 86-88, suitable solvents for use in the processes of the present invention, described above, preferably have at least one component that contains a monocarboxylic acid functional group. The solvent may also function as one of the reagents. The processes may be run in a solvent or solvent mixture that does not contain an acid group. In that case, preferably one of the reagents does contain a monocarboxylic acid functional group. Suitable solvents can also be aromatic acids such as benzoic acid and derivatives thereof. A preferred solvent is an aliphatic C_2-C_6 monocarboxylic acid, such as but not limited to acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, trimethylacetic acid, and caproic acid and mixtures thereof. Said mixtures may also include benzene, acetonitrile, heptane, acetic anhydride, chlorobenzene, o-dichlorobenzene, and water. The most preferred solvent is acetic acid ("AcOH").

[0023] The oxidant in the processes of the present invention is preferably an oxygen-containing gas or gas mixture, such as, but not limited to air and oxygen-enriched air. Oxygen by itself is also a preferred oxidant.

[0024] The processes of the instant invention described above can be conducted in a batch, semi-continuous or continuous mode. Especially for the manufacture of FDCA, operation in the batch mode with increasing temperature at specific times, increasing pressure at specific times, variation of the catalyst concentration at the beginning of the reaction, and variation of the catalyst composition during the reaction is desirable. For example, variation of the catalyst composition during the reaction can be accomplished by addition of cobalt and/or manganese and/or zirconium, and/or cerium, and/or bromide at specified times.

[0025] The pressure in a commercial oxidation process may vary within wide ranges. When a diluent is present, and in particular with acetic acid as diluent, the temperature and the pressure in such a process are not independent. The pressure is determined by the solvent (e.g., acetic acid) pressure at a certain temperature. The pressure of the reaction mixture is

preferably selected such that the solvent is mainly in the liquid phase. In practice this means that pressures between 5 and 100 bar can be used with a preference for pressures between 10 and 80 bar. In case the oxidant is an oxygen-containing gas, such as air, the gas can be continuously fed to and removed from the reactor, or the gas can be supplied all at the start of the reaction. In the latter case, the pressure of the system will depend on the headspace volume and the amount of gas required to convert the starting material. It is clear that in the latter case, the pressure of the system may be significantly higher than the pressure in a process wherein an oxygen containing gas is continuously fed and removed. In the case of continuously feeding and removing the oxidant gas to and from the reactor, the oxygen partial pressure will suitably be between 1 and 30 bar or more preferably between 1 and 10 bar.

[0026] The temperature of the reaction mixture is at least 140 ºC, preferably from 140 and 200 ºC, most preferably between 160 and 190 ºC. Temperatures higher than 180 ºC may lead to decarboxylation and to other degradation products. Good results to FDCA have been achieved at a temperature of about 180 °C.

[0027] Molar ratios of cobalt to manganese (Co/Mn) are typically 1/1000 - 100/1, preferably 1/100 - 10/1 and more preferably 1/10 - 4/1.

[0028] Molar ratios of bromine to metals (e.g. Br/(Co+Mn)) are typically 0.001-5.00, preferably 0.01 - 2.00 and more preferably 0.1 - 0.9.

[0029] Catalyst concentration (Co + Mn) is typically from 0.1 to 10 mol %, relative to the substrate, with a preference for concentrations from 2 to 6 mol %. Good results were obtained in general with catalyst concentrations of around 4 mol %.

[0030] The starting materials for the production of FDCA may originate from a carbohydrate source as described above. Examples of such disclosures are WO 2007/104515 and WO 2009/030512. Accordingly, the invention also provides a method for the preparation of 2,5-furandicarboxylic acid wherein a carbohydrate source is converted in the presence of an alkyl carboxylic acid into products comprising an HMF ester and optionally 5-hydroxymethyl furfural, from which is isolated a feed comprising the ester of HMF and optionally 5-hydroxymethyl furfural, and which method further comprises the subsequent step of contacting the feed with an oxidant in the presence of an oxidation catalyst, in particular a cobalt and manganese and bromide-containing catalyst, under appropriate reaction conditions, in particular at temperatures higher than 140 ºC

[0031] In another aspect, the FDCA obtained according to the process of the present invention can be transformed using common esterification reactions to a diester by contacting the starting material under appropriate conditions with the relevant alcohol. Thus, in one aspect, the invention also relates to the use of FDCA obtained according to the process of the current invention in the preparation of a dialkylester of 2,5-dicarboxylic acid by reaction of the FDCA with a C_1-C_5 alkyl alcohol, preferably methanol to prepare the dimethyl ester of FDCA.

[0032] Accordingly, the present invention also provides a process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C, and esterifying the thus obtained product. Preferably, the product is esterified with an alkyl alcohol, suitably having 1 to 5 carbon atoms.

[0033] The esterification of 2,5-furan dicarboxylic acid is known. As a specific example for the manufacture of these esters, reference is made to US 2673860 wherein the diester is obtained by transesterification of another dicarboxylic acid ester in the presence of sulphuric acid. A more general description for the esterification of dicarboxylic acids is presented in US 2628249.

[0034] In a further aspect of the invention, the di-methylester can be used in the preparation of polyester polymers by reaction with a diol. Reacting the di-methylester with a diol will result in the formation of methanol that quickly vaporises. In 1946 the polymerization of FDCA dimethyl ester with ethylene glycol was described as a first example of such a polymerization in GB 621,971.

[0035] Indeed, polyesters are generally made by a combined esterification/polycondenzation reaction between monomer units of a diol (e.g., ethylene glycol (EG)) and a dicarboxylic acid. Additives such as catalysts and stabilizers may be added to facilitate the process and stabilize the polyester towards degradation.

[0036] Examples:

[0037] Experiments were carried out in parallel 8 ml magnetically stirred stainless steel batch reactors. The reactors are grouped in blocks containing 12 batch reactors. The standard procedure for all the reactions was as follows:

[0038] 0.5 ml of starting material stock solution in acetic acid (0.78 mmol/ml) were added into a reactor lined with a Teflon insert. To the reactor 1 ml of a catalyst stock solution in acetic acid was subsequently added. In a typical experiment, a catalyst composition Co/Mn/Br with a relative 1-x-y ratio, the concentration of $Co(OAc)_2*4H_2O$ was varied. As a Mn source, $Mn(OAc)_2*4H_2O$ was used and as a bromine source NaBr was used. The reactors were closed with a rubber septum, after which the reactors were sealed and pressurized to the desired air pressure, ranging from 20-60 bars. After pressurization, the block with 12 reactors was placed in the test unit which was preheated at the desired temperature, ranging from 100 to 220 °C. After the desired reaction time, ranging from 0.5 hr to 24 hrs, the block is placed into an ice bath for 20 minutes. When the block had cooled down, it was depressurized. After opening, HPLC samples were prepared. First 5 ml of a saccharine solution in DMSO (11.04 mg/ml) was added to each reactor and the mixture was stirred for 5 minutes. Then 10 µl of this mixture was diluted to 1000 µl with water in a HPLC vial. The samples were analyzed using HPLC.

[0039] Example 1

[0040] Example 1 shows the selectivity of FDCA in the oxidation of HMF, of a HMF/AMF 3/2 mixture, of a HMF/AMF 2/3 mixture and of AMF, respectively, with 2.7 mol% Co catalyst (relative to substrate), and Co/Mn molar ratio of 1/1, so that the catalyst concentration (Co + Mn) amounted to 5.4 mol%. The Br/(Co+Mn) molar ratio was 1.0; 0.7; 0.4 and 0.1 at 0.26 M substrate concentration in acetic acid at 180 ºC for 1 hr with 20 bar air. The amount of oxygen was 2.69 mol oxygen per mol substrate. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn) > 1, corrosion will be a problem on commercial scale. HMF gives slightly higher yields than AMF at one hour reaction time. The results of these experiments are given in Table 1.

[0041] Example 2

[0042] Example 2 shows the selectivity to FDCA for the AMF oxidation of Example 1, together with the comparative examples based on the experimental conditions described in US 2009/0156841. In those comparative experiments (2a and 2b) 10 wt/wt% AMF in acetic acid was oxidized with 1.75 and 2.65 mol % Co catalyst and a fixed Br/(Co + Mn) molar ratio of

1.0 and a Co/Mn molar ratio of 1.0 at 100 °C and 30 bar for 2 hours. The amount of oxygen was 2.88 mol oxygen per mol substrate. Under these conditions, the yield of FDCA was lower than the result suggested in US 2009/0156841 and also lower than the results obtained at higher temperature. The results of these experiments are given in Table 2.

[0043] Example 3

[0044] Example 3 shows the yield of FDCA in the oxidation of 5-methylfurfural (5MF) and 2,5-dimethylfurfural (DMF) at 180 ºC with 2.7 mol% Co catalyst (relative to substrate), and Co/Mn ratio of 1/1, so that the catalyst concentration (Co + Mn) amounted to 5.4 mol%. The Br/(Co+Mn) molar ratio was 1.0, 0.7, 0.4 and 0.1. The substrate concentration was 0.26 M in acetic acid. The reaction temperature was at 180 ºC and the reaction was conducted with 50 bars air. The amount of oxygen was 6.7 mol oxygen per mol substrate. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn) > 1, corrosion will be a problem on commercial scale. Reactions with 5-MF give higher yields than reactions with DMF. The results of these experiments are also given in Table 3.

Table 1

Experiment No.	Substrate HMF/AMF molar ratio		Br/ (Co+Mn)	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
	HMF	AMF				
1a	1	0	1	3.3	100.00	76.66
1b	3	2	1	3.8	100.00	71.19
1c	2	3	1	4.0	100.00	77.66
1d	0	1	1	4.4	100.00	64.82
1e	1	0	0.7	3.3	100.00	78.08
1f	3	2	0.7	3.8	100.00	66.96
1g	2	3	0.7	4.0	100.00	75.14
1h	0	1	0.7	4.4	100.00	60.64
1i	1	0	0.4	3.3	100.00	73.27
1j	3	2	0.4	3.8	100.00	65.67
1k	2	3	0.4	4.0	100.00	73.21
1l	0	1	0.4	4.4	100.00	57.36
1m	1	0	0.1	3.3	100.00	67.92
1n	3	2	0.1	3.8	100.00	60.92
1o	2	3	0.1	4.0	100.00	69.64
1p	0	1	0.1	4.4	100.00	46.85

Table 2

Experiment No.	Temp [° C]	Reaction time [Hours]	Catalyst concentration [(Co + Mn) mol %]	Mn/Co	Br/ (Co+Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
1d	180	1	5.4	1	1	2.69	4.4	100.00	64.82
1h	180	1	5.4	1	0.7	2.69	4.4	100.00	60.64
1l	180	1	5.4	1	0.4	2.69	4.4	100.00	57.36
1p	180	1	5.4	1	0.1	2.69	4.4	100.00	46.85
2a	100	2	3.5	1	1	2.88	10.0	100.00	23.48
2b	100	2	5.3	1	1	2.88	10.0	100.00	29.05

Table 3

Experiment No.	Substrate	Reaction time [Hours]	Br/ (Co+Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
3a	5-MF	1	1	6.7	2.9	100.00	42.62
3b	5-MF	1	0.7	6.7	2.9	100.00	39.94
3c	DMF	1	1	6.7	2.5	100.00	16.17
3d	DMF	1	0.7	6.7	2.5	100.00	14.09
3e	DMF	1	0.4	6.7	2.5	100.00	11.30
3f	DMF	1	0.1	6.7	2.5	100.00	7.19

ABSTRACT

A method for the preparation of 2,5-furan dicarboxylic acid includes the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural (“HMF”), an ester of 5-hydroxymethyl-furfural, 5- methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5- dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Cesar Muñoz de Diego et al	Examiner:	Unassigned
Application No.:	Unassigned	Group Art Unit:	Unassigned
Confirmation No:	Unassigned	Docket:	903-457 PCT/US
Filed:	Herewith	Dated:	March 22, 2012

For: METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

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Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Certificate of EFS-Web Transmission
I hereby certify that this correspondence is being transmitted to the U.S. Patent and Trademark Office via the Office's electronic filing system
Dated: March 22, 2012

Signature: K.J. Goodhand */K.J. Goodhand/*

PRELIMINARY AMENDMENT ACCOMPANYING NATIONAL PHASE FILING UNDER 35 U.S.C. §371

Sir:

Please amend the above-identified application as follows:

Amendments to the Specification begin on page 2 of this submission.

Amendments to the Abstract begin on page 4 of this submission.

Amendments to the Claims begin on page 5 of this submission.

Remarks begin on page 8 of this submission.

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A. Amendments to the Specification:

Please amend the title of the invention at the top of page 1, as follows:

~~Title: Method for the preparation of 2,5-furandicarboxylic acid and for the preparation of the dialkyl ester of 2,5-furandicarboxylic acid~~ METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

Please add the following immediately after the title of the invention:

CROSS-REFERENCE TO RELATED APPLICATIONS:

This application is the National Stage of International Application No. PCT/NL2010/050654, filed October 6, 2010, which claims the benefit of Netherlands Application No. 2003606, filed October 7, 2009, and U.S. Provisional Application No. 61/249,395, filed October 7, 2009, the contents of all of which are incorporated by reference herein.

Please add the following new paragraph immediately prior to the paragraph beginning at page 1, line 1 and after the Cross Reference to Related Applications, as follows:

FIELD OF THE INVENTION:

Please add the following new paragraph immediately prior to the paragraph beginning at page 1, line 7, as follows:

BACKGROUND OF THE INVENTION:

Please add the following new paragraph immediately prior to the paragraph beginning at page 2, line 24, as follows:

SUMMARY OF THE INVENTION:

Please add the following new paragraph immediately prior to the paragraph beginning at page 2, line 29, as follows:

DETAILED DESCRIPTION OF THE INVENTION:

Please amend the Abstract, as follows:

A ~~The application describes a~~ method for the preparation of 2,5-furan dicarboxylic acid includes ~~comprising~~ the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C.

B. Amendments to the Claims:

Please amend the claims as follows:

1. (Currently amended): ~~Method~~ A method for the preparation of 2,5-furan dicarboxylic acid comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethylfurfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 ºC.

2. (Currently amended): ~~Method~~ The method according to claim 1, wherein the feed comprises a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), esters of HMF and a mixture thereof.

3. (Currently amended): ~~Method~~ The method according to claim 1 ~~or 2~~, wherein the oxidation catalyst comprises at least one metal selected from the group consisting of Co and Mn.

4. (Currently amended): ~~Method~~ The method according to claim 1 ~~or 2 or 3~~, wherein the oxidation catalyst comprises a source of bromine.

5. (Currently amended): ~~Method~~ The method according to claim 4, wherein the oxidation catalyst contains both Co and Mn.

6. (Currently amended): ~~Method~~ The method according to claim 5, wherein the oxidation catalyst comprises at least one additional metal.

7. (Currently amended): ~~Method~~ The method according to claim 6, wherein the additional metal is Zr and/or Ce.

8. (Currently amended): ~~Method~~ The method according to claim 1 ~~claims 1-6~~, wherein the oxidant is selected from oxygen, air or other oxygen-containing gases.

9. (Currently amended): ~~Method~~ The method according to claim 1, ~~any of the previous claims~~ wherein the temperature is between 140 and 200 ºC, most preferably between 160 and 190 ºC.

10. (Currently amended): ~~Method~~ The method according to claim 1 ~~any one of the previous claims~~, wherein a solvent or solvent mixture is present, preferably comprising a solvent containing a monocarboxylic acid functional group, more preferably acetic acid or acetic acid and water mixtures.

11. (Currently amended): ~~Method~~ The method according to claim 1 ~~any of the previous claims~~, wherein the feed comprises an ester of HMF containing an ester moiety of an alkyl carboxylic acid wherein the alkyl group contains up to 6 carbon atoms, preferably from 1 to 5 carbon atoms.

12. (Currently amended): ~~Process~~ A process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 ºC, and esterifying the thus obtained product.

13. (Currently amended): ~~Process~~ The process according to claim 12, wherein the product is esterified with a C_1-C_5 alkyl alcohol.

14. (Currently amended): ~~Process~~ The process according to claim 13, wherein the C_1-C_5 alkyl alcohol is methanol and the dialkyl ester is the dimethylester of 2,5-furan dicarboxylic acid.

15. (Currently amended): ~~Method~~ A method for the preparation of 2,5-furandicarboxylic acid wherein a carbohydrate source is converted in the presence of an alkyl carboxylic acid into products comprising an HMF ester and optionally 5-hydroxymethyl furfural, from which is isolated a feed comprising the ester of HMF and optionally 5-hydroxymethyl furfural, and which method comprises further the subsequent step of contacting the feed with an oxidant in the presence of an oxidation catalyst, preferably a cobalt and manganese and bromide-containing catalyst, under appropriate reaction conditions.

C. Remarks/Arguments:

The claims have been non-narrowingly amended to remove multiple dependencies and to conform with standard U.S. practice. No new matter is introduced with the amendments to the claim. Further, no new matter is introduced with the amendments to the Specification. Moreover, pursuant 37 C.F.R. §1.125(b), the Substitute Specifications filed herewith do not include new matter.

This application is believed to be in condition for examination on the merits. Favorable action thereon is therefore respectfully solicited.

Should the Examiner have any questions or comments concerning the above, the Examiner is respectfully invited to contact the undersigned attorney at the telephone number given below.

The Commissioner is hereby authorized to charge payment of any additional fees associated with this communication, or credit any overpayment, to Deposit Account No. 08-2461. Such authorization includes authorization to charge fees for extensions of time, if any, under 37 C.F.R. § 1.17 and also should be treated as a constructive petition for an extension of time in this reply or any future reply pursuant to 37 C.F.R. § 1.136.

Respectfully submitted,

/John S. SOPKO, Reg. # 41321/
John S. Sopko
Registration No.: 41,321
Attorney for Applicants

HOFFMANN & BARON, LLP
6900 Jericho Turnpike
Syosset, New York 11791
(973) 331-1700

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	
Filing Date	
First Named Inventor	Cesar Munoz de Diego
Art Unit	
Examiner Name	Unassigned
Attorney Docket Number	903-457 PCT/US

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	2673860		1954-03-30	Kuhn et al.	
	2	2628249		1953-02-10	Bruno	
	3	4977283		1990-12-11	Leupold et al.	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20090156841	A1	2009-06-18	Sanborn et al.	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	0356703	EP	A2	1990-03-07	Hoeshst Aktiengesellschaft		☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	
	Filing Date	
	First Named Inventor	Cesar Munoz de Diego
	Art Unit	
	Examiner Name	Unassigned
	Attorney Docket Number	903-457 PCT/US

	2	621971	GB		1947-10-27	Drewitt et al.		☐
	3	2009001519	JP		2007-06-21	Canon Inc.		☐
	4	2009242312	JP		2009-10-22	Air Water Inc.		☐
	5	636233	RU		1976-06-24			☐
	6	01/72732	WO	A2	2001-10-04	E.I. DuPont de Nemours and Company		☐
	7	2006/063220	WO	A2	2006-06-15	Archer-Daniels-Midland Company		☐
	8	2007/104515	WO	A1	2007-09-20	Avantium International B.V.		☐
	9	2008/054804	WO	A2	2008-05-08	Battelle Memorial Institute		☐
	10	2009/030512	WO	A2	2009-03-12	Furanix Technologies B.V.		☐
	11	2010/132740	WO	A2	2010-11-18	Archer-Daniels-Midland Company		☐

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NON-PATENT LITERATURE DOCUMENTS Remove

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	
	Filing Date	
	First Named Inventor	Cesar Munoz de Diego
	Art Unit	
	Examiner Name	Unassigned
	Attorney Docket Number	903-457 PCT/US

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Boisen et al., "Process integration for the conversion of glucose to 2,5-furandicarboxylic acid", Chemical Engineering Research and Design, Part A, Institution of Chemical Engineers, vol. 87, no. 9, pp 1318-1327, 2009	☐
	2	Grabowski et al., "The Electrochemical Oxidation of 5-Hydroxymethyfurfural With the Nickel Oxide/Hydroxide Electrode", Electrochimica ACTA, vol. 36, no. 13, pg. 1995, 1991	☐
	3	Haworth et al., "The Conversion of Sucrose into Furan Compounds. Part II. Some 2: 5-disubstituted tetrahydrofurans and their products of ring scission", Journal of the Chemical Society, pp 1-4, 1945	☐
	4	Partenheimer et al., "Synthesis of 2,5-Diformylfuran and Furan-2,5-Dicarboxylic Acid by Catalytic Air-Oxidation of 5-Hydroxymethylfurfural. Unexpectedly Selective Aerobic Oxidation of Benzyl Alcohol to Benzaldehyde with Metal/ Bromide Catalysts", Adv. Synth. Catal., vol. 343, no. 1, pp 102-111, 2001	☐
	5	Tong et al., "Biomass into chemicals: Conversion of sugars to furan derivatives by catalytic processes", Applied Catalysis A: General, vol. 385, no. 1-2, pp 1-13, 2010	☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	
	Filing Date	
	First Named Inventor	Cesar Munoz de Diego
	Art Unit	
	Examiner Name	Unassigned
	Attorney Docket Number	903-457 PCT/US

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/John S. SOPKO, Reg. #41321/	Date (YYYY-MM-DD)	2012-03-22
Name/Print	John S. Sopko	Registration Number	41321

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

EUROPEAN PATENT OFFICE

Patent Abstracts of Japan

PUBLICATION NUMBER : 2009001519
PUBLICATION DATE : 08-01-09

APPLICATION DATE : 21-06-07
APPLICATION NUMBER : 2007163711

APPLICANT : CANON INC;

INVENTOR : KONO TAKENOBU;

INT.CL. : C07D 307/68 (2006.01), C07B 61/00 (2006.01)

TITLE : METHOD FOR PRODUCING 2,5-FURANDICARBOXYLIC ACID

ABSTRACT : PROBLEM TO BE SOLVED: To provide a method for easily producing 2,5-furandicarboxylic acid from 5-hydroxymethylfurfural in high efficiency and yield and to provide a production method enabling the reuse of a catalyst to effectively utilize resources.

SOLUTION: The method for producing 2,5-furandicarboxylic acid comprises the oxidation of 5-hydroxymethylfurfural, (A) in the presence of a catalyst composed mainly of ruthenium, cobalt and cerium, (B) under heating, (C) under pressure, (D) in an aqueous solution, (E) with molecular oxygen.

EUROPEAN PATENT OFFICE

Patent Abstracts of Japan

PUBLICATION NUMBER : 2009242312
PUBLICATION DATE : 22-10-09

APPLICATION DATE : 31-03-08
APPLICATION NUMBER : 2008091762

APPLICANT : AIR WATER INC;

INVENTOR : FUJIBAYASHI RYOICHI;

INT.CL. : C07D 307/68 (2006.01), C07B 61/00 (2006.01)

TITLE : PROCESS FOR PRODUCING 2,5-FURANDICARBOXYLIC ACID

ABSTRACT : PROBLEM TO BE SOLVED: To provide a method for producing 2,5-furandicarboxylic acid (FDCA) by oxidizing 5-hydroxymethylfurfural (5HMF) of a starting material in the presence of a catalyst comprising Co, Mn, and Br with a molecular oxygen in an industrially employable high yield and preferably in high purity.

SOLUTION: The atomic ratio of Co in terms of metal to Mn in terms of metal in the catalyst is 2:1 to 4:1, and the oxygen concentration in an exhaust gas is measured while supplying an oxidizing gas containing a molecular oxygen into a reaction fluid, and after determining that the molecular oxygen has reached to a point of completing absorption in the reaction fluid, the oxidizing gas is further supplied to continue the oxidation reaction. Suitably, the obtained FDCA is dissolved in an aqueous solution of an alkali metal hydroxide, thereafter treated with sodium hypochlorite and/or hydrogen peroxide, then subjected to acid deposition, and is recovered.

BNSDOCID: <JP_____2009242312A_AJ_>

Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/NL2010/050654

International filing date: 06 October 2010 (06.10.2010)

Document type: Certified copy of priority document

Document details: Country/Office: US
Number: 61/249,395
Filing date: 07 October 2009 (07.10.2009)

Date of receipt at the International Bureau: 26 November 2010 (26.11.2010)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a),(b) or (b-*bis*)

PA 7253991

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

August 18, 2010

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE UNDER 35 USC 111.

APPLICATION NUMBER: ***61/249,395***
FILING DATE: ***October 07, 2009***

THE COUNTRY CODE AND NUMBER OF YOUR PRIORITY APPLICATION, TO BE USED FOR FILING ABROAD UNDER THE PARIS CONVENTION, IS ***US61/249,395***

By Authority of the
Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office

W. Montgomery

W. MONTGOMERY
Certifying Officer

Electronic Acknowledgement Receipt

EFS ID:	6219460
Application Number:	61249395
International Application Number:	
Confirmation Number:	9251
Title of Invention:	*METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID FROM 5-HYDROXYMETHYLFURFURAL AND/OR DERIVATIVES THEREOF, AND THE USE THEREOF*
First Named Inventor/Applicant Name:	Cesar MUNOZ DE DIEGO
Customer Number:	01444
Filer:	Roger Lowen Browdy/Katrina Brooks
Filer Authorized By:	Roger Lowen Browdy
Attorney Docket Number:	MUNOZ=1
Receipt Date:	07-OCT-2009
Filing Date:	
Time Stamp:	15:19:38
Application Type:	Provisional

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$220
RAM confirmation Number	1624
Deposit Account	
Authorized User	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)

1	Provisional Cover Sheet (SB16)	2009-10-07transmittal.pdf	42445 dbc9f12528b9515c247daab86371014aac4 25b20	no	1
Warnings:					
This is not a USPTO supplied Provisional Cover Sheet SB16 form.					
Information:					
2		2009-10-07application.pdf	147549 bf21c7cfd63b90afadcbd3639c70a707f2ffe 2ea	yes	15
	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Specification		1	10	
	Claims		11	11	
	Abstract		12	12	
	Drawings-only black and white line drawings		13	15	
Warnings:					
Information:					
3	Fee Worksheet (PTO-875)	fee-info.pdf	29661 9086e2a28180dfbeee53f8a1fc0010b1e168 241b	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	219655		

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

U.S. PATENT AND TRADEMARK OFFICE
PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT
under 37 C.F.R. §1.53(b)(2)

Atty. Docket: MUNOZ=1

INVENTOR(S)/APPLICANT(S)		
LAST NAME	GIVEN NAME	RESIDENCE (CITY AND EITHER STATE OR FOREIGN COUNTRY)
MUÑOZ DE DIEGO	Cesar	Amsterdam, Netherlands

☐ Additional inventors are being named on separately numbered sheets attached hereto

TITLE OF THE INVENTION (500 characters max)

METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID FROM 5-HYDROXYMETHYLFURFURAL AND/OR DERIVATIVES THEREOF, AND THE USE THEREOF

CORRESPONDENCE ADDRESS

Direct all correspondence to the address associated with **Customer Number 001444,** *which is presently:*

BROWDY AND NEIMARK, P.L.L.C.
624 Ninth Street, N.W., Suite 300
Washington, D.C. 20001-5303

ENCLOSED APPLICATION PARTS (check all that apply)

☒ Specification	Number of Pages 12	☐ Other	
☒ Drawings	Number of Pages 3		

FEES AND METHOD OF PAYMENT OF FILING FEES (check all that apply)

☒ Basic Filing fee				$ 220.00
☐ Additional Fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is $260.00 for each additional 50 sheets of paper or fraction thereof.				
Total Sheets	Extra Sheets	# of each additional 50 (round up to a whole number)	RATE	
15- 100 =	/ 50 =		× 260.00	$
			SUB-TOTAL	$220.00
☐ Applicant claims small entity status. See 37 CFR 1.27.				<$>
			TOTAL FILING FEES	$220.00

☒ Credit Card Payment authorization submitted herewith to cover the total filing fees.

☒ The Commissioner is hereby authorized to charge any underpayment of filing fees and credit any overpayments to Deposit Account Number 02-4035.

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☒ No ☐ Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,
BROWDY AND NEIMARK, P.L.L.C.

Date: October 7, 2009

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RSJ:klb

P30061US00/MKO

Title: Method for the preparation of 2,5-furandicarboxylic acid from 5-hydroxymethylfurfural and/or derivatives thereof, and the use thereof

The present invention relates to a method for the preparation of 2,5-furandicarboxylic acid ("FDCA") from 5-hydroxymethylfurfural ("HMF") and/or derivatives thereof, in particular from esters of HMF such as for example 5-acetoxymethylfurfural (AMF), from 5-(chloromethyl)furfural, 5-(chloromethyl)furoic acid, 5-methylfurfural, 5-methylfuroic acid or 2,5-dimethylfuran, or from a mixture of two or more of these HMF derivatives or a mixture of one or more of these derivatives with HMF, such as for example from a mixture of AMF + HMF.

2,5-Furandicarboxylic acid, also known as dehydromucic acid is a furan derivative. This organic compound was first obtained by Fittig and Heinzelmann in 1876. The first review, by Henry Hill was published in 1901 (Am. Chem. Journ. 25, 439). FDCA was more than 125 years later identified by the US Department of Energy as one of 12 priority chemicals for establishing the "green" chemistry industry of the future. However, to date, no commercial process exists for its production. On the laboratory scale it is often synthesized from 5-hydroxymethylfurfural (HMF), which in turn can be obtained from carbohydrate containing sources such as glucose, fructose, sucrose and starch. From fructose and glucose HMF is obtained by acidic elimination of three mols of water.

The derivatives of HMF are identified as potential and versatile fuel components and precursors for the production of plastics. The polyester from FDCA dimethyl diester and ethylene glycol was first reported in 1946 (GB 621,971).

WO0172732 describes the oxidation of HMF to FDCA. The maximum FDCA yield reported is 59%, obtained at 105 ºC. The oxidation of HMF in an aqueous medium with oxygen using a catalyst from the Pt-group is described in US4977283. Taarning et al. described the oxidation of HMF over gold based catalysts (ChemSusChem, 2008, 1, 1-4).

Partenheimer et al describes the synthesis of furan-2,5-dicarboxylic acid by catalytic air-oxidation of 5-hydroxymethylfurfural with metal/bromide catalysts such as Co/Mn/Br in Adv. Synth. Catal. **2001**, *343*, pp 102-11. With the Co/Mn/Br catalyst the highest FDCA yield obtained is 35.2% (Table 3, experiment 4).On page 103 of the same paper, under the header "products formed" it is stated: "A side reaction is the esterification of the alcohols [HMF and 5-(hydroxymethyl)furan-2-carboxylic acid] to form the more oxidatively stable acetate [respectively 5-(acetoxymethyl)furfural (from HMF) and 5-(acetoxymethyl)furan-2-carboxylic acid from the intermediate 5-(hydroxymethyl)-2-furan carboxylic acid]." And further on page 106 under the header "general considerations" it is stated: "Although acetoxylation of the

alcohols with the acetic acid solvent does occur, this side reaction results in only a 5-8% yield loss". Also, in the reaction scheme given in Figure 1 on page 103, it is indicated that 5-(acetoxymethyl)furfural is an end-point. There is no further reaction of this compound indicated to FDCA (in contrast to the ester of the intermediate product 5-(acetoxymethyl)furan-2-carboxylic acid). In other words, the 5-(acetoxymethyl)furfural (AMF) formed through reaction of HMF with acetic acid solvent, is not oxidized to FDCA and its formation leads therefore to yield loss.

Unknowingly to the authors, this result was confirmed recently in US2009/0156841 (ADM). On page 6, in paragraph [0060] it is stated:

"A mixture of HMF ester such as ...5-acetoxymethylfurfural (AcHMF), ...acetic acid, along with cobalt acetate, manganese acetate and sodium bromide is placed in a reactor and subjected to between about 400 to about 1000 psi oxygen.....at between about 85 ºC to about 110 ºC,....for between about 100 to about 150 minutes. The solution is filtered and the solvent evaporated to obtain 2,5-Furandicarboxylic acid (FDCA)."

This general recipe is illustrated in Example 7 on page 10 of this reference:

"A reaction mixture containing AcHMF (5.0 g), acetic acid (50 mL), cobalt acetate (0.132 g), manganese acetate (0.135 g), and sodium bromide (0.114 g) is placed in a 100 mL reactor and subjected to 500-800 psi oxygen at 100 ºC for 2 hours. Upon filtration and evaporation of the solvent, 2.53 g of tan solid is isolated. ^{1}H NMR indicates substantially pure FDCA. The overall yield of FDCA from AcHMF is 54%.."

Although the intention of the authors was to obtain FDCA, the product they isolated and erroneously characterized as being FDCA was in fact the starting material AcHMF. Under the low temperature conditions deployed (100 ºC), AcHMF is quite stable, as was already reported by Partenheimer (see above). FDCA has an extremely low solubility in acetic acid, even at 100 ºC. Taking into account that water is formed during the oxidation we can note the following two observations by Partenheimer in Adv. Synth. Catal. 2001, 343:

On page 105, right column we can read that FDCA precipitates during the reaction, even at 100-125 ºC.

On page 110 (right column) it is stated: "*The solubility of 2,5-Furandicarboxylic acid is 6.6 x 10-4 g/g in 3% H2O/HOAc at room temperature. Hence 99% of the 2,5-furandicarboxylic acid precipitates.*"

The authors wrote that the FDCA product was obtained from the solution after filtration and evaporation. Thus, taking into account the Partenheimer statements, which were independently confirmed by us, this isolated product cannot be FDCA.

The authors showed an ^{1}H NMR spectrum of their product in Figure 8 and concluded that it is FDCA. However, this is not the case. The ^{1}H NMR spectrum of the product shown in

Figure 8 is without doubt the starting material AcHMF. Finally, the authors refer to the product as a tan solid. In our experience, AcHMF is a tan solid, while FDCA is a white solid.

We have repeated the results of experiments executed under the US2009/0156841 conditions. These comparative experiments confirm the low reactivity of AMF under conditions given in US2009/0156841 (cf. the results reported in the experimental section). Thus, a person skilled in the art would therefore have concluded that FDCA cannot be obtained in interesting yields from AMF (AcHMF) using the conditions reported in US2009/0156841 using a Co/Mn/Br catalyst in acetic acid at between 85 and 110 ºC within a time frame of from 100 and 150 minutes. In Example 7 of this prior art reference, 2.53 g or slightly more than 50% of the starting material was the only product isolated from the reaction.

The present inventors have now surprisingly found that when using a catalyst based on both Cobalt and Manganese and containing a bromide, at temperatures higher than 140 ºC the derivatives of HMF, and in particular esters of HMF optionally in combination with HMF, such as for example 5-(acetoxymethyl)furfural (AMF) can be oxidized within 1 hour to FDCA in high yields.

Thus, in a first aspect the invention relates to a method for the preparation of 2,5-furandicarboxylic acid comprising the step of contacting a feed comprising 5-hydroxymethylfurfural (HMF), one or more derivatives of HMF or a mixture of HMF with one or more derivatives of HMF, e.g., 5-acetoxymethylfurfural (AMF) or 5-hydroxymethylfurfural (HMF) or mixtures thereof (AMF+HMF) as starting material with an oxidant in the presence of a catalyst based on both Cobalt and Manganese and containing a bromide at a temperature higher than 140 ºC.

The invention is described hereinafter with 5-acetoxymethylfurfural as the preferred feedstock, by itself or in combination with HMF. 5-(Chloromethyl)furfural, or 5-(chloromethyl)furoic acid, or 5-methylfurfural, or 5-methylfuroic acid, or 2,5-dimethylfuran, or an ester of 5-(hydroxymethyl)furfural may be used instead, as well as combinations of two or more of these HMF derivatives, or combinations of one or more of these HMF derivatives together with 5-(hydroxymethyl)furfural.

In WO2007104515 and WO2009030512, the synthesis of esters of HMF such as 5-acetoxymethylfurfural (AMF) from biomass sources is described. Given the higher stability of the HMF esters than HMF and hence improved production pathways and given the fact that upon oxidation in acetic acid the acetoxy functionality that was obtained from acetic acid is now liberated as acetic acid and given the green reputation of these esters, they were considered by the present inventors as interesting starting point in the preparation of furan-based monomers that could be used for the production of furandicarboxylic acid -based polyesters, for instance as an alternative for PET or FDCA-based polyamids (nylons). The

most important conventional, oil-based, polyester monomer to produce PET is Purified Terephthalic acid (PTA) and its dialkyl ester dimethyl Terephthalate (DMT).

AMF can be obtained from biomass sources as described in WO2007104515 and WO2009030512. Depending on the process conditions the product obtained in accordance with the process of these references may also contain HMF.

The alkyl of the ester functionality of the HMF ester can be C1-C5 alkyl, i.e. methyl, ethyl, propyl, isopropyl, butyl, 2-butyl, tert-butyl, pentyl, 2-pentyl, neopentyl and 3-pentyl. There is a preference for methyl, giving (5-acetylmethyl)furfural

FDCA, the product of the reaction can be used in the preparation of a polyester, by reaction of FDCA or its dialkyl ester with a suitable diol. Such polyester preparations are preferably performed by transesterification, whereby the di-methyl ester or di-ethyl ester of FDCA is used and wherein the methyl or ethyl groups are exchanged in the form of a volatile alcohol during the transesterification with the diol.

The bromine source can be any compound that produces bromide ions in the reaction mixture. These compounds include hydrogen bromide, sodium bromide, elemental bromine, benzyl bromide, tetrabromoethane. Also other bromine salts, such as an alkali or earth alkali metal bromine or another metal bromide such as $ZnBr_2$ can be used. There is a preference for hydrobromic acid or sodium bromide. The amount of bromine mentioned in here relates to the amount measured as Br relative to cobalt.

Metal bromide catalysts employed in all of the processes of this invention comprise a preferably soluble cobalt compound and a preferably soluble manganese compound and a preferably soluble bromine-containing compound.

The metal and bromide catalyst contains next to bromide Co and Mn and optionally can contain Zr and/or Ce or other metals. Alternative and suitable catalysts are described in W. Partenheimer, Catalysis Today 23(2), 69-158 (1995) in particular on pages 89-99, included herein by reference.

Each of the metal components can be provided in any of their known ionic forms. Preferably the metal or metals are in a form that is soluble in the reaction solvent. Examples of suitable counterions for cobalt and manganese include, but are not limited to, carbonate, acetate, acetate tetrahydrate and halide with bromide being the preferred halide.

As described in Partenheimer, ibid, pages 86-88, suitable solvents for use in the processes of the present invention, described above, preferably have at least one component that contains a monocarboxylic acid functional group. The solvent may also function as one of the reagents. The processes may be run in a solvent or solvent mixture that does not contain an acid group. In that case, preferably one of the reagents does contain a monocarboxylic acid functional group. Suitable solvents can also be aromatic acids such as benzoic acid and derivatives thereof. A preferred solvent is an aliphatic C_2-C_6 monocarboxylic

acid, such as but not limited to acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, trimethylacetic acid, and caproic acid and mixtures thereof. Components of said mixtures can include benzene, acetonitrile, heptane, acetic anhydride, chlorobenzene, o-dichlorobenzene, and water. Most preferred as solvent is acetic acid ("AcOH").

The oxidant in the processes of the present invention is preferably an oxygen-containing gas or gas mixture, such as, but not limited to air. Oxygen by itself is also a preferred oxidant.

The processes of the instant invention described above can be conducted in the batch, semi-continuous or continuous mode. Especially for the manufacture of FDCA, operation in the batch mode with increasing temperature at specific times, increasing pressure at specific times, variation of the catalyst concentration at the beginning of the reaction, and variation of the catalyst composition during the reaction is desirable. For example, variation of the catalyst composition during reaction can be accomplished by addition of cobalt and/or manganese and/or zirconium, and/or cerium, and/or bromide at specified times.

The temperature and pressure in a commercial oxidation process with acetic acid as diluent are not independent. The pressure is determined by the solvent (e.g., acetic acid) pressure at a certain temperature. The pressure of the reaction mixture is preferably selected such that the solvent is mainly in the liquid phase. In practice this means that pressures between 5 and 100 bar can be used with a preference for pressures between 10 and 80 bars. In case the oxidant is an oxygen containing gas, such as air, the gas can be continuously fed to and removed from the reactor, or the gas can be supplied all at the start of the reaction. In the latter case, the pressure of the system will depend on the headspace volume and the amount of gas required to convert the starting material. It is clear that in the latter case, the pressure of the system will be significantly higher than when continuously feeding and removing an oxygen containing gas. In the case of continuously adding and removing the oxidant gas to and from the reactor, the oxygen partial pressure will be between 1 and 30 bars or more preferably between 1 and 10 bars.

The temperature of the reaction mixture is between 140 and 200 degrees Celsius, most preferably between 160 and 190 degrees Celsius. Temperatures higher than 180 degrees Celcius tend to lead to decarboxylation and to other degradation products. Good results to FDCA have been achieved at a temperature of about 180 °C.

Ratio's of Cobalt to Manganese (Co/Mn) are typically 1/1000 - 100/1, preferably 1/100 - 10/1 and more preferably 1/10 - 4/1.

Ratio's of bromine to metals (e.g. Br/(Co+Mn)) are typically 0.001-5.00, preferably 0.01 - 2.00 and more preferably 0.1 - 0.9.

Catalyst concentration (Co + Mn) is typically between 0.1 - 10 mol % relative to the substrate, with a preference for loads between 2 and 6 mol %. Good results were obtained in general with catalyst loads of around 4 mol %.

In another aspect of the invention, we have also investigated the oxidation of other furan-based substrates under the process conditions according to the current invention. We have been able to convert 5-(chloromethyl)furfural, 5-(chloromethyl)furoic acid, 5-methylfurfural, 5-methylfuroic acid and 2,5-dimethylfuran all to FDCA in very interesting yields.

In another aspect, the FDCA obtained according to the process of the present invention can be transformed using common esterification reactions to a diester by contacting the starting material under appropriate conditions with the relevant alcohol. Thus, in one aspect, the invention also relates to the use of FDCA obtained according to the process of the current invention in the preparation of a dialkylester of 2,5-dicarboxylic acid by reaction of the FDCA with a C_1-C_5 alkyl alcohol, preferably methanol to prepare the dimethyl ester of FDCA.

In a further aspect of the invention, the di-methylester can be used in the preparation of polyester polymers by reaction with a diol. Reacting the di-methylester with a diol will result in the formation of methanol that quickly vaporises. In 1946 the polymerization of FDCA dimethyl ester with ethylene glycol was described as a first example of such a polymerization (GB 621,971).

Indeed, polyesters are generally made by a combined esterification/polycondenzation reaction between monomer units of a diol (e.g., ethylene glycol (EG)) and a dicarboxylic acid. Additives such as catalysts and stabilizers may be added to facilitate the process and stabilize the polyester towards degradation.

Description of the figures:

Figure 1 shows the yield of FDCA in the oxidation of HMF, of a HMF/AMF 3/2 mixture, of a HMF/AMF 2/3 mixture and of AMF, respectively with 2.7 mol% Co catalyst (relative to substrate), 0.26 M substrate concentration in acetic acid and Co/Mn ratio of 1/1 and Br/(Co+Mn): 1.0; 0.7; 0.4 and 0.1 at 180 ºC for 1 hr with 20 bar air. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn) > 1, corrosion will be a problem on commercial scale. HMF gives slightly higher yields than AMF at one hour reaction time. The data of these experiments is also given in Table 1.

Figure 2 shows the selectivity to FDCA for the AMF oxidation of Figure 1 together with the comparative examples based on the experimental conditions described in US/20090156841; according to the text 10 wt/wt% AMF was oxidized with 1.75 and 2.65 mol % Co catalyst and a fixed Br/(Co/Mn) of 1.0 and a Co/Mn of 1.0 at 100 °C and 30 bar for 2 hours Under these conditions, the yield of FDCA was lower than the result described in

US/20090156841 and than the results obtained at high temperature. The data of these experiments is also given in Table 2.

Figure 3 shows the yield of FDCA in the oxidation of 5-methylfurfural (5MF) and 2,5-dimethylfurfural (DMF) at 180 ºC with 2.7 mol% Co catalyst (relative to substrate), 0.26 M substrate concentration in acetic acid and Co/Mn ratio of 1/1 and a Br/(Co+Mn) of 1.0, 0.7, 0.4 and 0.1 at 180 ºC for 2 hrs with 50 bars air. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn) > 1, corrosion will be a problem on commercial scale. Reactions with 5MF give higher yields than reactions with DMF. The data of these experiments is also given in Table 3.

Examples:

Experiments were carried out in parallel 8 mL magnetically stirred stainless steel batch reactors. The reactors are grouped in blocks containing 12 batch reactors. The standard procedure for all the reactions was as follows:

0.5 ML of starting material stock solution in acetic acid (0.78 mmol/ml) were added into a reactor lined with a Teflon insert. 1 ML of a catalyst stock solution in acetic acid was subsequently added to the reactor. In a typical experiment, a catalyst composition Co/Mn/Br with a relative 1-x-y ratio, the concentration of $Co(OAc)_2*4H_2O$ was varied. As a Mn source, $Mn(OAc)_2*4H_2O$ was used and as a bromine source NaBr was used. The reactors were closed with a rubber septum, after which the reactors were sealed and pressurized to the desired air pressure, ranging from 20-60 bars. After pressurization, the block with 12 reactors was placed in the test unit which was preheated at the desired temperature, ranging from 100 to 220 ºC. After the desired reaction time, ranging from 0.5 hr to 24 hrs, the block is placed into an ice bath for 20 minutes. When the block had cooled down, it was depressurized. After opening, HPLC samples were prepared. First 5 ml of a saccharine solution in DMSO (11.04 mg/mL) was added to the each reactor and the mixture was stirred for 5 minutes. Then 10 µL of this mixture was diluted to 1000 µL with water in a HPLC vial. The samples were analyzed using HPLC.

Illustrative but not limiting results are presented in the figures 1-3 and Tables 1-3.

Table 1

Substrate HMF/AMF molar ratio		Temp [° C]	Reaction time [Hours]	Catalyst concentration [(Co + Mn) mol %]	Mn/Co	Br/ (Co+Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
HMF	AMF									
1	0	180	1	5.4	1	1	2.69	3.3	100.00	76.11
1	0	180	1	5.4	1	1	2.69	3.3	100.00	76.66
3	2	180	1	5.4	1	1	2.69	3.8	100.00	71.19
3	2	180	1	5.4	1	1	2.69	3.8	100.00	70.91
2	3	180	1	5.4	1	1	2.69	4.0	100.00	77.66
2	3	180	1	5.4	1	1	2.69	4.0	100.00	76.84
0	1	180	1	5.4	1	1	2.69	4.4	100.00	64.82
0	1	180	1	5.4	1	1	2.69	4.4	100.00	63.76
1	0	180	1	5.4	1	0.7	2.69	3.3	100.00	77.69
1	0	180	1	5.4	1	0.7	2.69	3.3	100.00	78.08
3	2	180	1	5.4	1	0.7	2.69	3.8	100.00	66.53
3	2	180	1	5.4	1	0.7	2.69	3.8	100.00	66.96
2	3	180	1	5.4	1	0.7	2.69	4.0	100.00	75.14
2	3	180	1	5.4	1	0.7	2.69	4.0	100.00	74.55
0	1	180	1	5.4	1	0.7	2.69	4.4	100.00	60.64
0	1	180	1	5.4	1	0.7	2.69	4.4	100.00	59.83
1	0	180	1	5.4	1	0.4	2.69	3.3	100.00	73.27
1	0	180	1	5.4	1	0.4	2.69	3.3	100.00	73.23
3	2	180	1	5.4	1	0.4	2.69	3.8	100.00	65.67
3	2	180	1	5.4	1	0.4	2.69	3.8	100.00	64.89
2	3	180	1	5.4	1	0.4	2.69	4.0	100.00	73.15
2	3	180	1	5.4	1	0.4	2.69	4.0	100.00	73.21
0	1	180	1	5.4	1	0.4	2.69	4.4	100.00	57.11
0	1	180	1	5.4	1	0.4	2.69	4.4	100.00	57.36
1	0	180	1	5.4	1	0.1	2.69	3.3	100.00	67.57
1	0	180	1	5.4	1	0.1	2.69	3.3	100.00	67.92
3	2	180	1	5.4	1	0.1	2.69	3.8	100.00	60.92
3	2	180	1	5.4	1	0.1	2.69	3.8	100.00	57.38
2	3	180	1	5.4	1	0.1	2.69	4.0	100.00	69.18
2	3	180	1	5.4	1	0.1	2.69	4.0	100.00	69.64

Table 2

Substrate	Temp [° C]	Reaction time [Hours]	Catalyst concentration [(Co + Mn) mol %]	Mn/Co	Br/ (Co+Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
AMF	180	1	5.4	1	1	2.69	3.3	100.00	64.82
AMF	180	1	5.4	1	1	2.69	3.3	100.00	63.76
AMF	180	1	5.4	1	0.7	2.69	3.8	100.00	60.64
AMF	180	1	5.4	1	0.7	2.69	3.8	100.00	59.83
AMF	180	1	5.4	1	0.4	2.69	4.0	100.00	57.11
AMF	180	1	5.4	1	0.4	2.69	4.0	100.00	57.36
AMF	180	1	5.4	1	0.1	2.69	4.4	100.00	46.85
AMF	180	1	5.4	1	0.1	2.69	4.4	100.00	46.53
AMF	100	2	3.5	1	1	2.88	10.0	100.00	23.48
AMF	100	2	3.5	1	1	2.88	10.0	100.00	23.96
AMF	100	2	5.25	1	1	2.88	10.0	100.00	29.05
AMF	100	2	5.25	1	1	2.88	10.0	100.00	29.87

Table 3

Substrate	Temp [° C]	Reaction time [Hours]	Catalyst concentration [(Co + Mn) mol %]	Mn/Co	Br/ (Co+Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
5-MF	180	1	5.4	1	1	6.7	2.9	100.00	42.62
5-MF	180	1	5.4	1	1	6.7	2.9	100.00	42.04
5-MF	180	1	5.4	1	0.7	6.7	2.9	100.00	39.47
5-MF	180	1	5.4	1	0.7	6.7	2.9	100.00	39.94
DMF	180	1	5.4	1	1	6.7	2.5	100.00	16.13
DMF	180	1	5.4	1	1	6.7	2.5	100.00	16.17
DMF	180	1	5.4	1	0.7	6.7	2.5	100.00	13.68
DMF	180	1	5.4	1	0.7	6.7	2.5	100.00	14.09
DMF	180	1	5.4	1	0.4	6.7	2.5	100.00	11.30
DMF	180	1	5.4	1	0.4	6.7	2.5	100.00	10.89
DMF	180	1	5.4	1	0.1	6.7	2.5	100.00	7.19
AMF	180	1	5.4	1	0.1	6.7	2.5	100.00	7.12

Claims

1. Method for the preparation of 2,5-furandicarboxylic acid comprising the step of contacting a feed comprising 5-hydroxymethylfurfural (HMF), one or more derivatives of HMF or a mixture of HMF with one or more derivatives of HMF as starting material, with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140ºC.

2. Method according to claim 1 comprising the step of contacting an ester of 5-(hydroxymethyl)furfural or 5-(hydroxymethyl)furfural or a mixture of these components with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 ºC.

3 Method according to claim 1, wherein the oxidation catalyst comprises at least one metal selected from the group consisting of Co and Mn.

4 Method according to claim 1, wherein the oxidation catalyst comprises a source of bromine.

5 Method according to claim 4, wherein the oxidation catalyst contains both Co and Mn.

6 Method according to claim 5, wherein the oxidation catalyst comprises at least one additional metal.

7. Method according to claim 6, wherein the additional metal is Zr and or Ce.

8. Method according to claims 1, wherein the oxidant is selected from oxygen, air or other oxygen-containing gases.

9. Method according to claim 1, wherein the temperature is between 140 and 200 degrees Celsius, most preferably between 160 and 190 degrees Celsius.

10. Method according to claim 1, wherein a solvent or solvent mixture is present, preferably comprising a solvent containing a monocarboxylic acid functional group, more preferably acetic acid or acetic acid and water mixtures.

11. Method according to claim 1 wherein the alkyl of the ester group of the HMF ester is C_1-C_5 alkyl, preferably methyl.

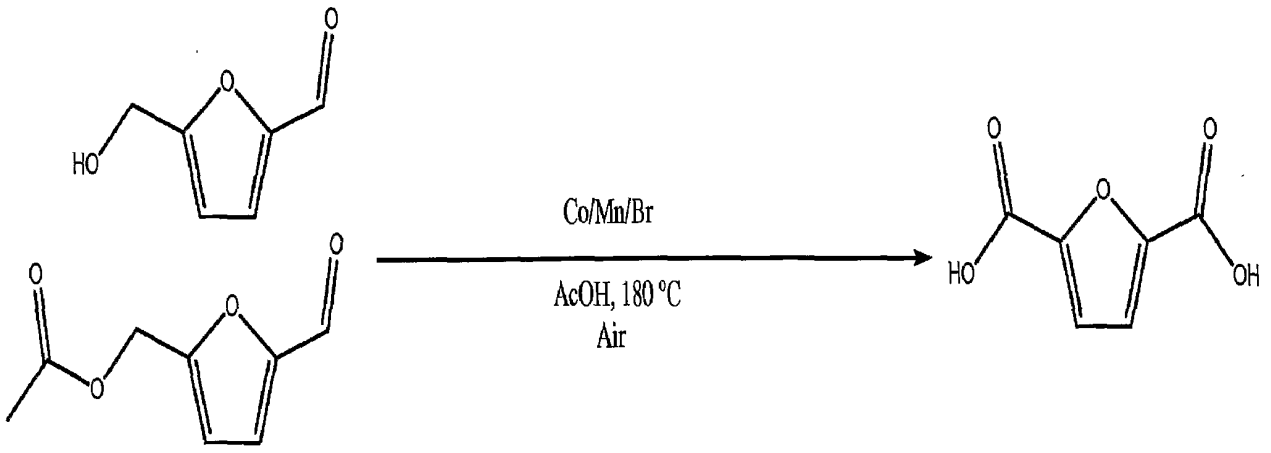
12 Use of the reaction product obtained via the method claim 1 in the preparation of a dialkylester of 2,5-furan dicarboxylic acid via an esterification reaction with a C_1-C_5 alkyl alcohol.

13. Use according to claim 12 wherein the C_1-C_5 alkylalcohol is methanol and the diester is the dimethylester of 2,5-furan dicarboxylic acid.

14. Method for the preparation of 2,5-furandicarboxylic acid wherein a carbohydrate source is converted in the presence of an alkyl carboxylic acid into products comprising an HMF ester and optionally 5-hydroxymethyl furfural, from which is isolated a feed comprising the ester of HMF and optionally 5-hydroxymethyl furfural, comprising the subsequent step of contacting the feed with an oxidant in the presence of a cobalt and manganese and bromide containing catalyst under appropriate reaction conditions.

Abstract

The application describes a method for the preparation of 2,5-furandicarboxylic acid comprising the step of contacting a feed comprising 5-hydroxymethylfurfural (HMF), one or more derivatives of HMF or a mixture of HMF with one or more derivatives of HMF as starting material, with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140ºC.



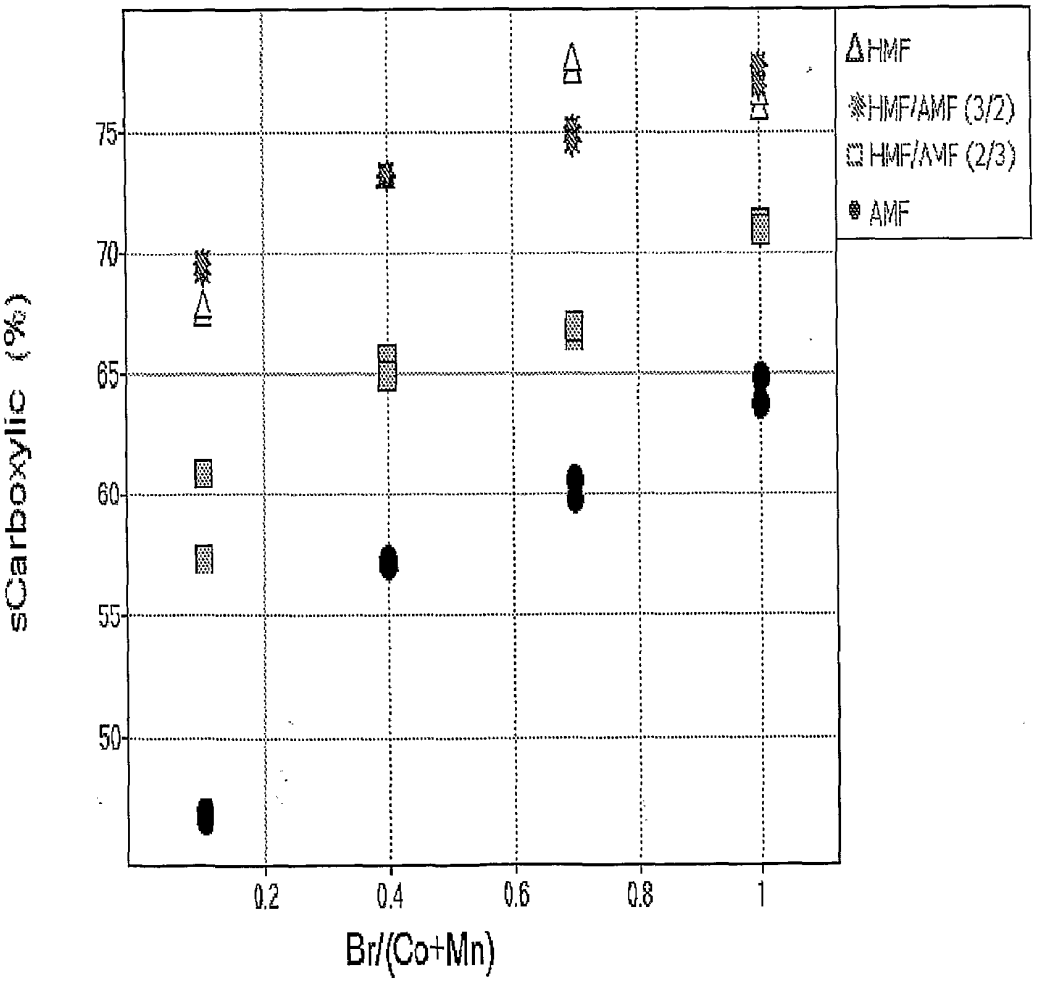


Fig 1

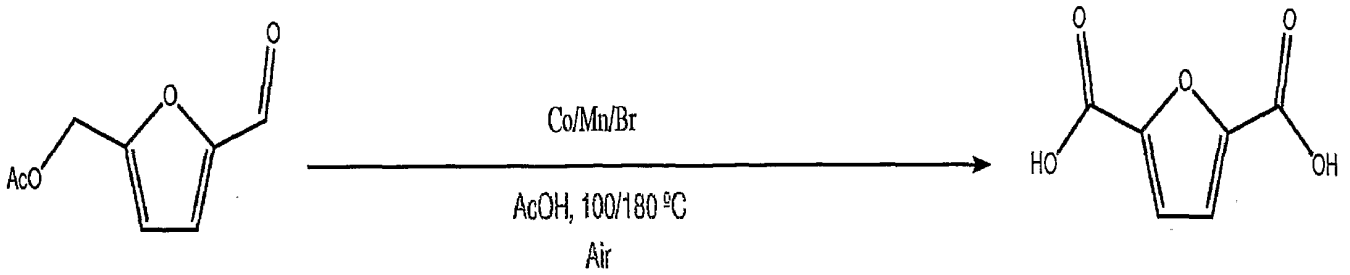
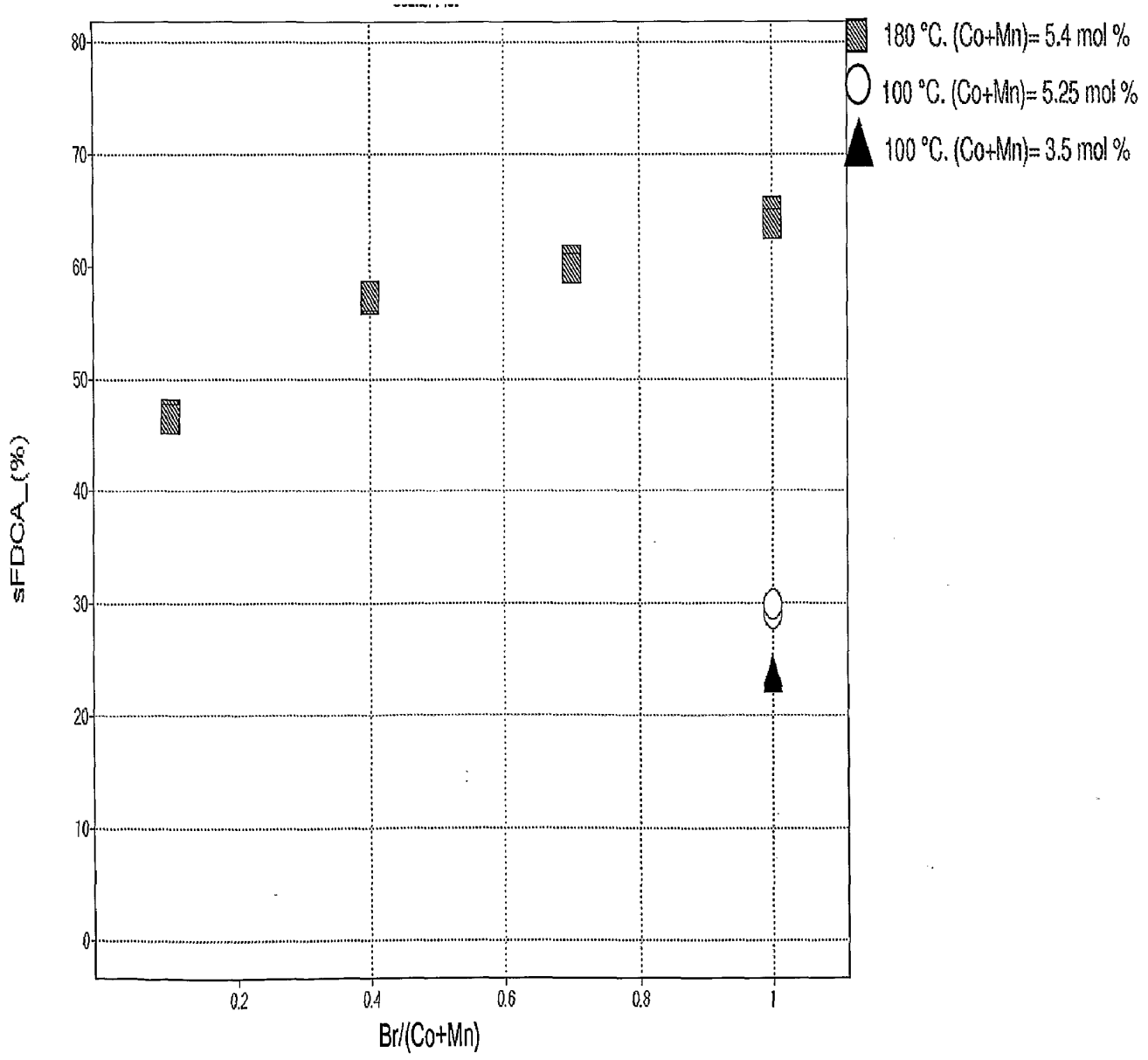
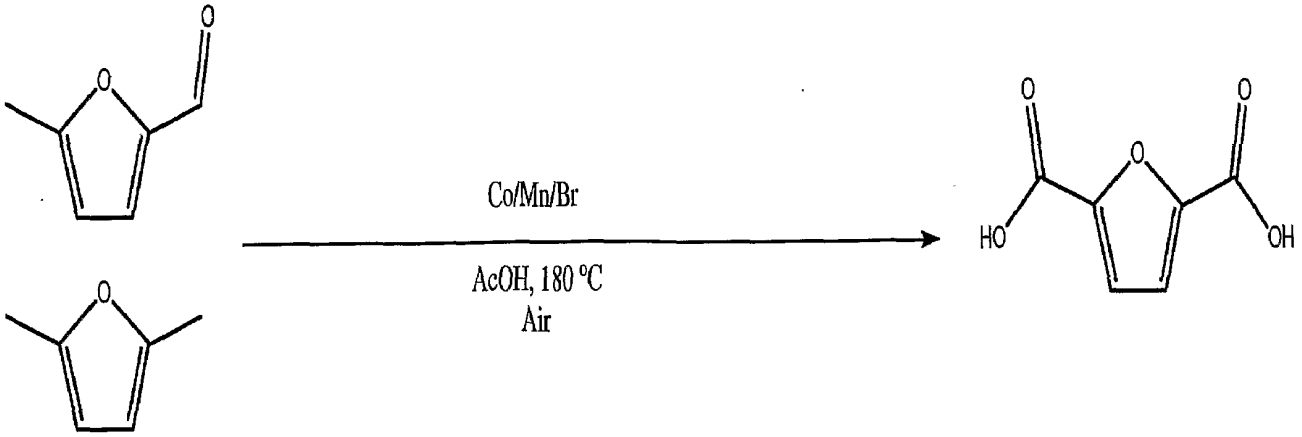


Fig 2





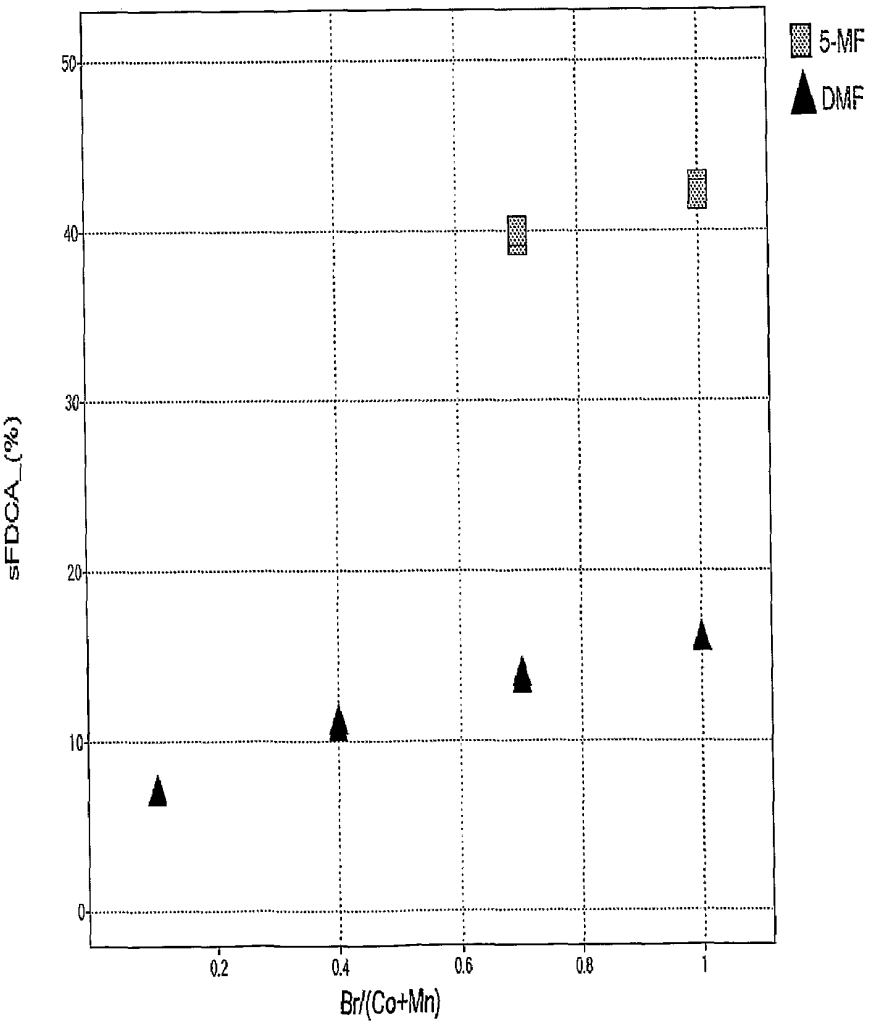


Fig 3

PCT REQUEST

Print Out (Original in Electronic Form)

0	**For receiving Office use only**	
0-1	International Application No.	**PCT/NL2010/050654**
0-2	International Filing Date	**06 October 2010 (06.10.2010)**
0-3	Name of receiving Office and "PCT International Application"	**RO/NL**

0-4	**Form PCT/RO/101 PCT Request**	
0-4-1	Prepared Using	**PCT Online Filing Version 3.5.000.221 MT/FOP 20020701/0.20.5.9**
0-5	**Petition** The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	**Receiving Office (specified by the applicant)**	**Netherlands Patent Office (RO/NL)**
0-7	**Applicant's or agent's file reference**	**P30061PC00**
I	**Title of Invention**	**Method for the preparation of 2,5-furandicarboxylic acid and for the preparation of the dialkyl ester of 2,5-furandicarboxylic acid**
II	**Applicant**	
II-1	This person is	**Applicant only**
II-2	Applicant for	**All designated States except US**
II-4	Name	**Furanix Technologies B.V.**
II-5	Address	**29, Zekeringstraat 1014 BV Amsterdam Netherlands**
II-6	State of nationality	**NL**
II-7	State of residence	**NL**
III-1	**Applicant and/or inventor**	
III-1-1	This person is	**Applicant and inventor**
III-1-2	Applicant for	**US only**
III-1-4	Name (LAST, First)	**MUÑOZ DE DIEGO, Cesar**
III-1-5	Address	**c/o 29, Zekeringstraat 1014 BV AMSTERDAM Netherlands**
III-1-6	State of nationality	**ES**
III-1-7	State of residence	**NL**

PCT REQUEST

Print Out (Original in Electronic Form)

III-2	**Applicant and/or inventor**	
III-2-1	This person is	Applicant and inventor
III-2-2	Applicant for	US only
III-2-4	Name (LAST, First)	DAM, Matheus Adrianus
III-2-5	Address	c/o 29, Zekeringstraat 1014 BV AMSTERDAM Netherlands
III-2-6	State of nationality	NL
III-2-7	State of residence	NL
III-3	**Applicant and/or inventor**	
III-3-1	This person is	Applicant and inventor
III-3-2	Applicant for	US only
III-3-4	Name (LAST, First)	GRUTER, Gerardus Johannes Maria
III-3-5	Address	co/ 29, Zekeringstraat 1014 BV AMSTERDAM Netherlands
III-3-6	State of nationality	NL
III-3-7	State of residence	NL
IV-1	**Agent or common representative; or address for correspondence**	
	The person identified below is hereby/ has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:	Agent
IV-1-1	Name (LAST, First)	VOLMER, J.C.
IV-1-2	Address	P.O. Box 3241 2280 GE RIJSWIJK Netherlands
V	**DESIGNATIONS**	
V-1	**The filing of this request constitutes under Rule 4.9(a), the designation of all Contracting States bound by the PCT on the international filing date, for the grant of every kind of protection available and, where applicable, for the grant of both regional and national patents.**	
VI-1	**Priority claim of earlier national application**	
VI-1-1	Filing date	09 October 2009 (09.10.2009)
VI-1-2	Number	61/248,395
VI-1-3	Country	US
VI-2	**Priority claim of earlier national application**	
VI-2-1	Filing date	09 October 2009 (09.10.2009)
VI-2-2	Number	2003606
VI-2-3	Country	NL

PCT REQUEST

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VI-3	**Priority document request** The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s):	VI-2	
VI-4	**Incorporation by reference :** where an element of the international application referred to in Article 11(1)(iii)(d) or (e) or a part of the description, claims or drawings referred to in Rule 20.5(a) is not otherwise contained in this international application but is completely contained in an earlier application whose priority is claimed on the date on which one or more elements referred to in Article 11(1)(iii) were first received by the receiving Office, that element or part is, subject to confirmation under Rule 20.6, incorporated by reference in this international application for the purposes of Rule 20.6.		
VII-1	**International Searching Authority Chosen**	European Patent Office (EPO) (ISA/EP)	
VII-2	**Request to use results of earlier search; reference to that search**		
VII-2-1	Filing date	09 October 2009 (09.10.2009)	
VII-2-2	Application Number	2003606	
VII-2-3	Country (or regional Office)	NL	
VII-2-5	Documents are available to the ISA in a form and manner acceptable to it and therefore do not need to be submitted by the applicant to the ISA (Rule 12bis.1(f)):	A copy of the results of the earlier search	
VIII	**Declarations**	Number of declarations	
VIII-1	Declaration as to the identity of the inventor	-	
VIII-2	Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent	-	
VIII-3	Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application	-	
VIII-4	Declaration of inventorship (only for the purposes of the designation of the United States of America)	-	
VIII-5	Declaration as to non-prejudicial disclosures or exceptions to lack of novelty	-	

PCT REQUEST

Print Out (Original in Electronic Form)

IX	Check list	Number of sheets	Electronic file(s) attached
IX-1	Request (including declaration sheets)	4	✓
IX-2	Description	9	✓
IX-3	Claims	2	✓
IX-4	Abstract	1	✓
IX-5	Drawings	0	–
IX-7	TOTAL	16	
	Accompanying Items	Paper document(s) attached	Electronic file(s) attached
IX-8	Fee calculation sheet	–	✓
IX-18	PCT-SAFE physical media	–	–
IX-20	**Figure of the drawings which should accompany the abstract**		
IX-21	**Language of filing of the international application**	English	
X-1	**Signature of applicant, agent or common representative**	(PKCS7 Digital Signature)	
X-1-1	Name	EP&C	
X-1-2	Name of signatory	NL, Exter Polak & Charlouis B.V., A. Zeestraten 22141	
X-1-3	Capacity	(Representative)	

FOR RECEIVING OFFICE USE ONLY

10-1	**Date of actual receipt of the purported international application**	06 October 2010 (06.10.2010)
10-2	**Drawings:**	
10-2-1	Received	
10-2-2	Not received	
10-3	**Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application**	
10-4	**Date of timely receipt of the required corrections under PCT Article 11(2)**	
10-5	**International Searching Authority**	ISA/EP
10-6	**Transmittal of search copy delayed until search fee is paid**	

FOR INTERNATIONAL BUREAU USE ONLY

11-1	**Date of receipt of the record copy by the International Bureau**	

Electronic Patent Application Fee Transmittal

Application Number:	
Filing Date:	
Title of Invention:	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID
First Named Inventor/Applicant Name:	Cesar Munoz de Diego
Filer:	John S. Sopko/Kathleen Goodhand
Attorney Docket Number:	903-457 PCT/US

Filed as Small Entity

U.S. National Stage under 35 USC 371 Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Basic National Stage Fee	2631	1	190	190
Natl Stage Search Fee - Report provided	2642	1	245	245
Natl Stage Exam Fee - all other cases	2633	1	125	125
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**560**

Electronic Acknowledgement Receipt

EFS ID:	12368674
Application Number:	13497690
International Application Number:	PCT/NL10/50654
Confirmation Number:	1013
Title of Invention:	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID
First Named Inventor/Applicant Name:	Cesar Munoz de Diego
Customer Number:	23869
Filer:	John S. Sopko/Kathleen Goodhand
Filer Authorized By:	John S. Sopko
Attorney Docket Number:	903-457 PCT/US
Receipt Date:	22-MAR-2012
Filing Date:	
Time Stamp:	15:48:58
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$560
RAM confirmation Number	2648
Deposit Account	082461
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. 1.492 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal of New Application	Transmittal_Letter.pdf	268404 4415303a5da7fc976c3a48c64b54229d6277848d	no	4
Warnings:					
Information:					
2	Application Data Sheet	903-457_PCT-US_Application_Data_Sheet_sb0014.pdf	1432011 5055844c51430bb3edd49ab0304c2e6156484f1a	no	5
Warnings:					
Information:					
3	Authorization for Extension of Time all replies	General_Authorization_EOT.pdf	91461 78a2755cca9e6d4cb52a0a3c6974c7068d7e1f1e	no	1
Warnings:					
Information:					
4	Change of Address	Change_Correspondence_Address.pdf	304065 8e09c88e9f3e79953efe479343a9dad91ee1778d	no	2
Warnings:					
Information:					
5	Documents submitted with 371 Applications	WO_2011-043661_A1.pdf	787960 b7c538f33dd36091192f8952e57e6c69647ac642	no	17
Warnings:					
Information:					
6	Documents submitted with 371 Applications	Submission_Priority_Documents.pdf	89590 689ee99ea04dd659ad89c03611f7f27735115ef2	no	1
Warnings:					
Information:					
7	Documents submitted with 371 Applications	NL_2003606.pdf	678187 046184398cf40b747ce69b9070a122edfb54c6e7	no	17
Warnings:					
Information:					
8	Documents submitted with 371 Applications	NL_Search_Report.pdf	412572 803ca8802f394d745b07648d8406d1ac7f58559b	no	9

Warnings:					
Information:					
9	Documents submitted with 371 Applications	PCT_Search_Report.pdf	183902 de8fdc979a37949c78b8b5d6bb9ec5cc32f9629d	no	5
Warnings:					
Information:					
10	Documents submitted with 371 Applications	Statement_Substitute_Specifications.pdf	90946 6d6ed0fed84cdae3f4be0babb2a442e35b2e8952	no	1
Warnings:					
Information:					
11		Substitute_Specification_Version_Showing_Changes.pdf	119801 34b0e5d9d37690b106da6e21a61a87f9a8189272	yes	12

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Specification	1	11
	Abstract	12	12

Warnings:					
Information:					
12		Substitute_Spectification_Clean_Version.pdf	118023 57db3211f72f075a7f58b44e78e22cb9084e791d	yes	12

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Specification	1	11
	Abstract	12	12

Warnings:					
Information:					
13		Preliminary_Amendment.pdf	110685 cdc74b7ba6224c88ecc04a802c50a0817505402b	yes	8

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Preliminary Amendment	1	1

	Specification		2		3
	Abstract		4		4
	Claims		5		7
	Applicant Arguments/Remarks Made in an Amendment		8		8
Warnings:					
Information:					
14	Information Disclosure Statement (IDS) Form (SB08)	PTO_SB_08a.pdf	1719080 4db9d0603c333da767689b6bd9472f50d7db1e4a	no	5
Warnings:					
Information:					
15	Foreign Reference	EP_0356703_A2.pdf	399679 d5d15c1c8aadf057dce7d81eca76a5133b30f9f1	no	6
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Information:					
16	Foreign Reference	GB_621971_A.pdf	512293 a71627eed741eff830be0c4026aa29f9c689c77f	no	5
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17	Foreign Reference	JP_2009-1519_A.pdf	390057 1d7c89f79046633eddf13ac9988b2422f8670b61	no	10
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Information:					
18	Foreign Reference	JP_2009-242312_A.pdf	673541 452606016d3bf1d3cbb50a7a8dfa590168c8442f	no	11
Warnings:					
Information:					
19	Foreign Reference	SU_636233_A1.pdf	162696 17ad33c370223191bcff27284111f358a1499cc4	no	2
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Information:					
20	Foreign Reference	WO_01-72732_A2.pdf	1278500 5e29904d36184380f64129be2d75d5b16037820b	no	23
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Information:					
21	Foreign Reference	WO_2006-063220_A2.pdf	1709869 6bb42742dbedaf505715aeb37596dd51dd44ecb0	no	39
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22	Foreign Reference	WO_2007-104515_A1.pdf	681833 bd368799525d6d0387726d4106b09ee763003e88	no	17
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23	Foreign Reference	WO_2008-054804_A2.pdf	1585925 7caf15a55885ca3c90b5ac92093fce2db885a7e1	no	57
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Information:					
24	Foreign Reference	WO_2009-030512_A2.pdf	535527 7ef5fbd558d42bfc26b4ba0e4a095be28d789a08	no	12
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Information:					
25	Foreign Reference	WO_2010-132740_A2.pdf	1025152 a543457f4e264bb3ccc336ec8adce611c646ba19	no	21
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Information:					
26	Non Patent Literature	NPL_Boison_et_al.pdf	1199431 174543146e6e088a0ade14d16ecdc094ce0c3dc6	no	10
Warnings:					
Information:					
27	Non Patent Literature	NPL_Grabowski_et_al.pdf	74343 c0d3b62e43f83bc12d08015f73bf036ce408f5e8	no	1
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28	Non Patent Literature	NPL_Haworth_et_al.pdf	419325 9a2f269f5d011b29471ae8fdfeb8ef81d4eaa787	no	4
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Information:					
29	Non Patent Literature	NPL_Partenheimer_et_al.pdf	861853 29381bc37dbb0df980d161e4b3fac43edc335b08	no	10
Warnings:					

Information:					
30	Non Patent Literature	NPL_Tong_et_al.pdf	1335135 0adaf726b47276f16030a4cbffbe4e3efda34f75	no	13
Warnings:					
Information:					
31	Fee Worksheet (SB06)	fee-info.pdf	35388 07f21a7e3101166613edf11f08fd0f4a3d1bbb3b	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	19287234	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (07-06)
Approved for use through 1/31/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
13/497,690	07/09/2012	

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY ☒ RATE ($)	SMALL ENTITY ☒ FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	03/22/2012	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 15	Minus	** 20	= 0	X $30 =	0	OR	X $ =	
	Independent (37 CFR 1.16(h))	* 3	Minus	***3	= 0	X $125 =	0	OR	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE	0	OR	TOTAL ADD'L FEE	

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)	OR	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =		OR	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Legal Instrument Examiner:
/DAWN BREWER/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

U.S. APPLICATION NUMBER NO.	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
13/497,690	Cesar Munoz de Diego	903-457 PCT/US

23869
HOFFMANN & BARON, LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

INTERNATIONAL APPLICATION NO.	
PCT/NL10/50654	
I.A. FILING DATE	PRIORITY DATE
10/06/2010	10/07/2009

CONFIRMATION NO. 1013
371 FORMALITIES LETTER

OC000000054348219

Date Mailed: 05/17/2012

NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C. 371 IN THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as a Designated Office (37 CFR 1.494):

- Indication of Small Entity Status
- Priority Document
- Copy of the International Application filed on 03/22/2012
- Copy of the International Search Report filed on 03/22/2012
- Preliminary Amendments filed on 03/22/2012
- Information Disclosure Statements filed on 03/22/2012
- Request for Immediate Examination filed on 03/22/2012
- U.S. Basic National Fees filed on 03/22/2012
- Assignee Statement for PGPUB filed on 03/22/2012
- Priority Documents filed on 03/22/2012

The applicant needs to satisfy supplemental fees problems indicated below.

The following items **MUST** be furnished within the period set forth below in order to complete the requirements for acceptance under 35 U.S.C. 371:

- Oath or declaration of the inventors, in compliance with 37 CFR 1.497(a) and (b), identifying the application by the International application number and international filing date.
- To avoid abandonment, a surcharge (for late submission of filing fee, search fee, examination fee or oath or declaration) as set forth in 37 CFR 1.492(h) of $65 for a small entity in compliance with 37 CFR 1.27, must be submitted with the missing items identified in this letter.

SUMMARY OF FEES DUE:

Total additional fees required for this application is $**65** for a Small Entity:

- $**65** Surcharge.

ALL OF THE ITEMS SET FORTH ABOVE MUST BE SUBMITTED WITHIN TWO (2) MONTHS FROM THE DATE OF THIS NOTICE OR BY 32 MONTHS FROM THE PRIORITY DATE FOR THE APPLICATION, WHICHEVER IS LATER. FAILURE TO PROPERLY RESPOND WILL RESULT IN ABANDONMENT.

The time period set above may be extended by filing a petition and fee for extension of time under the provisions of 37 CFR 1.136(a).

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web.
https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html

For more information about EFS-Web please call the USPTO Electronic Business Center at **1-866-217-9197** or visit our website at http://www.uspto.gov/ebc.

If you are not using EFS-Web to submit your reply, you must include a copy of this notice.

JOHN L ANDERSON

Telephone: (571) 272-0385

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 13/497,690

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	190		N/A	
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	245		N/A	
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	125		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	15 minus 20 =	*	x 30 =	0.00	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	3 minus 3 =	*	x 125 =	0.00			
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			0.00			
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				0.00			
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	560		TOTAL	

APPLICATION AS AMENDED - PART II

AMENDMENT A

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
Application Size Fee (37 CFR 1.16(s))									
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)		RATE($)	ADDITIONAL FEE($)
Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
Application Size Fee (37 CFR 1.16(s))									
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

MULTIPLE DEPENDENT CLAIM FEE CALCULATION SHEET

Substitute for Form PTO-1360
(For use with Form PTO/SB/06)

Application Number	Filing Date
13497690	

Applicant(s) Cesar Munoz de Diego

* May be used for additional claims or amendments

CLAIMS	AS FILED		AFTER FIRST AMENDMENT		AFTER SECOND AMENDMENT	
	Indep	Depend	Indep	Depend	Indep	Depend
1	1		1			
2		1		1		
3		2		1		
4		(1)		1		
5		(1)		1		
6		(1)		1		
7		(1)		1		
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9		(1)		1		
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Total Indep	3		3		0	
Total Depend	13	↵	12	↵	0	↵
Total Claims	16		15		0	

	*		*		*	
	Indep	Depend	Indep	Depend	Indep	Depend
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Cesar Muñoz de Diego et al.	Examiner:	Unassigned
Application No.:	13/497,690	Group Art Unit:	Unassigned
Confirmation No:	1013	Docket:	903-457 PCT/US
Filed:	March 22, 2012	Dated:	July 9, 2012

For: METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

Mail Stop PCT
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Certificate of EFS-Web Transmission
I hereby certify that this correspondence is being transmitted to the U.S. Patent and Trademark Office via the Office's electronic filing system
Dated: July 9, 2012

Signature: K.J. Goodhand */K.J. Goodhand/*

RESPONSE TO NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C. §371 IN THE UNITED STATES DESIGNATED/ELECTED OFFICE

Sir:

In response to the Notification of Missing Requirements dated May 17, 2012, a response to which is due July 17, 2012, for the above-identified case, Applicants submit the following:

1. A Combined Declaration and Power of Attorney signed by the inventors of the above-identified invention, such Declaration identifying the application by the afforded U.S. Application Number and Filing Date and by the International PCT Application Number and International PCT Filing Date.

2. A fee in the amount of $65.00, which is due for payment of the surcharge fee for the missing requirements, may be charged to Deposit Account No. 08-2461.

The Commissioner is hereby authorized to charge payment of any additional fees associated with this communication, or credit any overpayment, to Deposit Account

No. 08-2461. Such authorization includes authorization to charge fees for extensions of time, if any, under 37 C.F.R § 1.17 and also should be treated as a constructive petition for an extension of time in this reply or any future reply pursuant to 37 C.F.R. § 1.136.

Should the Examiner have any questions regarding this submission, please contact the undersigned counsel at the telephone number below.

Respectfully submitted,

/John S. SOPKO, Reg. # 41,321/
John S. Sopko
Registration No.: 41,321
Attorney for Applicant(s)

HOFFMANN & BARON, LLP
6900 Jericho Turnpike
Syosset, New York 11791
(973) 331-1700

Combined Declaration for Patent Application and Power of Attorney

As a below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name; and that I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

Method for the preparation of 2,5-furandicarboxylic acid and for the preparation of the dialkyl ester of 2,5-furandicarboxylic acid

the specification of which (check one)

[ ] is attached hereto;
[ ] was filed in the United States under 35 U.S.C. §111 on _____, as U.S. Appln. No. _____*; or
[X] was/will be filed in the U.S. under 35 U.S.C. §371 by entry into the U.S. national stage of an international (PCT) application, PCT/NL2010/050654; filed October 6, 2010, entry requested on March 12, 2012*; national stage application received U.S. Appln. No. 13/497,690*; §371/§102(e) date March 22, 2012* (* if known)

and was amended on _____ (if applicable).
(include dates of amendments under PCT Art. 19 and 34 if PCT)

I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above; and I acknowledge the duty to disclose to the Patent and Trademark Office (PTO) all information known by me to be material to patentability as defined in 37 C.F.R. §1.56.

I hereby claim foreign priority benefits under 35 U.S.C. §§ 119 (a)-(d) and 365 (b) of any prior foreign application(s) for patent or inventor's certificate, or §365(a) of any prior PCT application(s) designating a country other than the U.S., listed below with the "Yes" box checked, and have also identified below, by checking the "No" box, any foreign application for patent or inventor's certificate or PCT international application having a filing date before that of the application on which priority is claimed:

61/249,395 (Number)	United States (Country)	October 7, 2009 (Day Month Year Filed)	[X] YES	[ ] NO
2003606 (Number)	the Netherlands (Country)	October 7, 2009 (Day Month Year Filed)	[X] YES	[ ] NO

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional applications listed below:

(Application No.)	(Day Month Year Filed)
(Application No.)	(Day Month Year Filed)

I hereby claim the benefit under 35 U.S.C. §120 of any prior U.S. non-provisional application(s) or under §365(c) of any prior PCT international application(s) designating the U.S., listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in such U.S. or PCT international application in the manner provided by the first paragraph of 35 U.S.C. §112, I acknowledge the duty to disclose to the PTO all information which is material to patentability as defined in 37 C.F.R. §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

(Application No.)	(Day Month Year Filed)	(Status: patented, pending, abandoned)
(Application No.)	(Day Month Year Filed)	(Status: patented, pending, abandoned)

As a named inventor, I hereby appoint the following registered practitioners to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

All of the practitioners associated with Customer Number 23869. Direct all correspondence to the address associated with **Customer Number 23869**, which is presently:

Hoffmann & Baron, LLP
6 Campus Drive
PARSIPPANY, NJ 07054
United States

The undersigned hereby authorizes the U.S. Attorneys or Agents appointed herein to accept and follow instructions from Exter Polak & Charlouis B.V., P.O. Box 3241, 2280 GE RIJSWIJK, The Netherlands as to any action to be taken in the U.S. Patent and Trademark Office regarding this application without direct communication between the U.S. Attorneys or Agents and the undersigned. In the event of a change of the persons from whom instructions may be taken, the U.S. Attorneys or Agents appointed herein will be so notified by the undersigned.

 Atty. Docket:

Title: Method for the preparation of 2,5-furandicarboxylic acid and for the preparation of the dialkyl ester of 2,5-furandicarboxylic acid

U.S. Application filed March 22, 2012, Serial No. 13/497,690

PCT Application filed October 6, 2010, Serial No. PCT/NL2010/050654

I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

FULL NAME OF FIRST INVENTOR	INVENTOR'S SIGNATURE	DATE
Cesar MUÑOZ DE DIEGO		15-Feb-2012
RESIDENCE		CITIZENSHIP
1014 BV AMSTERDAM, Netherlands		ES
POST OFFICE ADDRESS		
c/o 29, Zekeringstraat, 1014 BV AMSTERDAM, Netherlands		
FULL NAME OF SECOND JOINT INVENTOR	INVENTOR'S SIGNATURE	DATE
Matheus Adrianus Dam		15-FEB-2012
RESIDENCE		CITIZENSHIP
1014 BV AMSTERDAM, Netherlands		NL
POST OFFICE ADDRESS		
c/o 29, Zekeringstraat, 1014 BV AMSTERDAM, Netherlands		
FULL NAME OF THIRD JOINT INVENTOR	INVENTOR'S SIGNATURE	DATE
Gerardus Johannes Maria GRUTER		15-FEB-2012
RESIDENCE		CITIZENSHIP
1014 BV AMSTERDAM, Netherlands		Nl
POST OFFICE ADDRESS		
c/o 29, Zekeringstraat, 1014 BV AMSTERDAM, Netherlands		
FULL NAME OF FOURTH JOINT INVENTOR	INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP
POST OFFICE ADDRESS		
FULL NAME OF FIFTH JOINT INVENTOR	INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP
POST OFFICE ADDRESS		
FULL NAME OF SIXTH JOINT INVENTOR	INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP
POST OFFICE ADDRESS		
FULL NAME OF SEVENTH JOINT INVENTOR	INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP
POST OFFICE ADDRESS		

ALL INVENTORS MUST REVIEW APPLICATION AND DECLARATION BEFORE SIGNING. ALL ALTERATIONS MUST BE INITIALED AND DATED BY ALL INVENTORS PRIOR TO EXECUTION. NO ALTERATIONS CAN BE MADE AFTER THE DECLARATION IS SIGNED. ALL PAGES OF DECLARATION MUST BE SEEN BY ALL INVENTORS.

Electronic Patent Application Fee Transmittal

Application Number:	13497690
Filing Date:	
Title of Invention:	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID
First Named Inventor/Applicant Name:	Cesar Munoz de Diego
Filer:	John S. Sopko/Kathleen Goodhand
Attorney Docket Number:	903-457 PCT/US

Filed as Small Entity

U.S. National Stage under 35 USC 371 Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Oath/decl > 30 mo. from priority date	2617	1	65	65
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**65**

Electronic Acknowledgement Receipt

EFS ID:	13199255
Application Number:	13497690
International Application Number:	
Confirmation Number:	1013
Title of Invention:	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID
First Named Inventor/Applicant Name:	Cesar Munoz de Diego
Customer Number:	23869
Filer:	John S. Sopko/Kathleen Goodhand
Filer Authorized By:	John S. Sopko
Attorney Docket Number:	903-457 PCT/US
Receipt Date:	09-JUL-2012
Filing Date:	
Time Stamp:	13:10:10
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$65
RAM confirmation Number	10159
Deposit Account	082461
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. 1.492 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Applicant Response to Pre-Exam Formalities Notice	Response_Missing_Requirements.pdf	95147 48b5803b98a7e24eac795783297aabac077b2d3b	no	2
Warnings:					
Information:					
2	Oath or Declaration filed	Declaration.pdf	296799 2ea59d1423e7c4ef97605179b69d31e1989a1227	no	2
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30587 ef2fedc3fdfe5f265defb32bf7326573227f174a	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	422533		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

<u>New Applications Under 35 U.S.C. 111</u>
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

<u>National Stage of an International Application under 35 U.S.C. 371</u>
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

<u>New International Application Filed with the USPTO as a Receiving Office</u>
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

U.S. APPLICATION NUMBER NO.	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
13/497,690	Cesar Muñoz de Diego	903-457 PCT/US

23869
Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

INTERNATIONAL APPLICATION NO.	
PCT/NL10/50654	
I.A. FILING DATE	PRIORITY DATE
10/06/2010	10/07/2009

CONFIRMATION NO. 1013
371 ACCEPTANCE LETTER

OC000000055391226

Date Mailed: 07/18/2012

NOTICE OF ACCEPTANCE OF APPLICATION UNDER 35 U.S.C 371 AND 37 CFR 1.495

The applicant is hereby advised that the United States Patent and Trademark Office in its capacity as a Designated / Elected Office (37 CFR 1.495), has determined that the above identified international application has met the requirements of 35 U.S.C. 371, and is ACCEPTED for national patentability examination in the United States Patent and Trademark Office.

The United States Application Number assigned to the application is shown above and the relevant dates are:

07/09/2012	07/09/2012
DATE OF RECEIPT OF 35 U.S.C. 371(c)(1), (c)(2) and (c)(4) REQUIREMENTS	DATE OF COMPLETION OF ALL 35 U.S.C. 371 REQUIREMENTS

A Filing Receipt (PTO-103X) will be issued for the present application in due course. **THE DATE APPEARING ON THE FILING RECEIPT AS THE " FILING DATE" IS THE DATE ON WHICH THE LAST OF THE 35 U.S.C. 371 (c)(1), (c)(2) and (c)(4) REQUIREMENTS HAS BEEN RECEIVED IN THE OFFICE. THIS DATE IS SHOWN ABOVE.** *The filing date of the above identified application is the international filing date of the international application (Article 11(3) and 35 U.S.C. 363).* Once the Filing Receipt has been received, send all correspondence to the Group Art Unit designated thereon.

The following items have been received:

- Indication of Small Entity Status
- Copy of the International Application filed on 03/22/2012
- Copy of the International Search Report filed on 03/22/2012
- Preliminary Amendments filed on 03/22/2012
- Information Disclosure Statements filed on 03/22/2012
- Oath or Declaration filed on 07/09/2012
- Request for Immediate Examination filed on 03/22/2012
- U.S. Basic National Fees filed on 03/22/2012
- Assignee Statement for PGPUB filed on 03/22/2012
- Priority Documents filed on 03/22/2012

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

JOHN L ANDERSON

Telephone: (571) 272-0385

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
13/497,690	07/09/2012		625	903-457 PCT/US	15	3

CONFIRMATION NO. 1013

23869
Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

FILING RECEIPT

OC000000055391225

Date Mailed: 07/18/2012

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Applicant(s)

Cesar Muñoz de Diego, Amsterdam, NETHERLANDS;
Matheus Adrianus Dam, Amsterdam, NETHERLANDS;
Gerardus Johannes Maria Gruter, Amsterdam, NETHERLANDS;

Assignment For Published Patent Application

FURANIX TECHNOLOGIES B.V., Amsterdam, NL

Power of Attorney: The patent practitioners associated with Customer Number 23869

Domestic Priority data as claimed by applicant

This application is a 371 of PCT/NL10/50654 10/06/2010
which claims benefit of 61/249,395 10/07/2009

Foreign Applications (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.)
NETHERLANDS 2003606 10/07/2009

If Required, Foreign Filing License Granted: 07/16/2012

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 13/497,690**

Projected Publication Date: 10/25/2012

Non-Publication Request: No

Early Publication Request: No
**** SMALL ENTITY ****

Title

METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

Preliminary Class

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4158).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as

set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 13/497,690

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	190		N/A	
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	245		N/A	
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	125		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	15 minus 20 =	*	x 30 =	0.00	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	3 minus 3 =	*	x 125 =	0.00			
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			0.00			
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				0.00			
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	560		TOTAL	

APPLICATION AS AMENDED - PART II

AMENDMENT A

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
Application Size Fee (37 CFR 1.16(s))									
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
Application Size Fee (37 CFR 1.16(s))									
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/497,690	07/09/2012	Cesar Mu?oz de Diego	903-457 PCT/US

CONFIRMATION NO. 1013

23869
Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

PUBLICATION NOTICE

OC00000057297675

Title:METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

Publication No.US-2012-0271060-A1
Publication Date:10/25/2012

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently http://www.uspto.gov/patft/.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Office of Public Records. The Office of Public Records can be reached by telephone at (703) 308-9726 or (800) 972-6382, by facsimile at (703) 305-8759, by mail addressed to the United States Patent and Trademark Office, Office of Public Records, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently http://pair.uspto.gov/. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/497,690	07/09/2012	Cesar Muñoz de Diego	903-457 PCT/US	1013

23869 7590 12/11/2013

Hoffmann & Baron LLP
6900 Jericho Turnpike
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EXAMINER	
SOLOLA, TAOFIQ A	
ART UNIT	PAPER NUMBER
1622	
MAIL DATE	DELIVERY MODE
12/11/2013	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 13/497,690	Applicant(s) MUÑOZ DE DIEGO ET AL.	
	Examiner Taofiq A. Solola	Art Unit 1622	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) 1-15 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) 1-15 is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☒ All b)☐ Some * c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

The present application is being examined under the pre-AIA first to invent provisions. Claims 1-15, are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims lack adequate support in the specification. There is no conclusive evidence that all known catalysts and oxidizing gases are applicable in the invention. Only known specific catalysts and oxidizing gases and solvents are applicable in this type of reaction, and there is no evidence in the specification contrary to this well-known principle. One must read the specification into the claims, contrary to several precedent decisions by the US courts and official practice, to ascertain the applicable catalyst and oxidizing gas. Even then, the entire scope of the claims cannot be ascertained from the specification because, the claims are broader in scope than the enabling disclosure in the specification. Determination of suitable catalyst and oxidizing gas would require trial by error experimentations, starting from the beginning of organic textbooks to the end, trying each known oxidizing gas. Such experimentations if successful would make the user the inventor of the process.

There is no conclusive evidence in the specification that the instant process can be performed without a solvent (claims 1-9, 11-15). All the examples (pp. 10-11, tables 1-3) in the

specification are performed in a solvent, and in the presence of Br/Co/Mn as catalyst. Therefore, there is no support in the specification for using partial catalyst as in claims 3-4. All the examples relate to claims 1-11. No examples are disclosed for 12-15. Therefore, there is no evidence applicant was in possession of the claims at the time this application was filed.

A claim must stand alone to define the invention, and incorporation into the claims by reference to the specification or an external source is not permitted. *Ex parte Fressola,* 27 USPQ 2d 1608, BdPatApp & Inter. (1993).

In patent examination, it is essential for claims to be precise, clear, correct, and unambiguous. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). Applicant should note that the requirement of 35 USC 112, is not what is obvious to one of ordinary skill in the art but a "full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same", *Lookwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed Cir. 1997. Appropriate correction is required.

Claims 1-15, are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. For the reasons set forth above the scope of the invention is not enabled without reference to an external source.

"All questions of enablement are evaluated against the claimed subject matter. The focus of the examination inquiry is whether everything within the scope of the claim is enabled. Accordingly, the first analytical step requires that the examiner determine exactly what subject

matter is encompassed by the claims." See, e.g., *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244, 68 USPQ2d 1280, 1287 (Fed. Cir. 2003).

The scope of the claims is beyond the specification disclosure because applicable catalyst and gas are defined explicitly in the specification. Therefore, there is no conclusive evidence that applicant was in possession of the invention as claimed at the time the application was filed.

"While it is appropriate to use the specification to determine what applicant intends a term to mean, a positive limitation from the specification cannot be read into a claim that does not itself impose that limitation. In the instant there is no indication applicant intends to limit the bases to the examples in the specification. Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified." MPEP 2106. *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969). The court explained that "reading a claim in light of the specification, to thereby interpret limitations explicitly recited in the claim, is a quite different thing from reading limitations of the specification into a claim, to thereby narrow the scope of the claim." See also *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. *In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999).

"Though understanding the claim language may be aided by explanations contained in the

written description, it is important not to import into a claim limitations that are not part of the claim." *Superguide Corp. v. DirecTV Enterprises, Inc.,* 358 F.3d 870, 875, 69 USPQ2d

1865, 1868 (Fed. Cir. 2004). See also *Liebel-Flarsheim Co. v. Medrad Inc.,* 358 F.3d 898, 906, 69 USPQ2d 1801, 1807 (Fed. Cir. 2004).

> The following is a quotation of 35 U.S.C. 112(b):
> (b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.
>
> The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-11, 15, are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

In claim 10, solvent or solvent mixture lacks proper antecedent basis in claim 1, while claim 11 is confusing as written. It is not clear what applicant is claiming in lines 2-4.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claims [9-10, 15] do not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as", [“preferably”, “in particular”] and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 9-10, recite broad ranges, the claims also recites “preferably”, which is followed

by narrower statements of the ranges/limitations. By deleting "preferably" in every occurrence and the narrower statements the rejection would be overcome.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of pre-AIA 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-11, 15, are rejected under pre-AIA 35 U.S.C. 102(a) as being anticipated by Sanborn et al., US 2009/0156841 A1 (published 6/18/09).

Sanborn et al., a process of making 2,5-furandicarboxylic acid comprising making HMF and derivatives thereof from carbohydrates (hexose sugars) and oxidizing the HMF or derivatives in the presence of Br/Mn/Co catalyst to obtain 2,5-furandicarboxylic acid. The process was performed at 110 to 150°C. See [0016] to [0021] and [0040] to [0044], particularly [0018] to [0019]. See also examples 1, 3-6 and claims 1-13.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-15, are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanborn et al., US 2009/0156841 A1 (published 6/18/09), in view of Gruter et al., WO/2009/030521 (published 3/12/09).

Applicant claims a process of making furan-2,5-dicarboxylic acid (FDCA), comprising oxidation of HMA or derivatives thereof with oxidation gas in the presence of a catalyst. In preferred embodiments the catalyst comprises cobalt, manganese and bromine, the reaction temperature is greater than 140°C and the HMF is made from carbohydrates in the presence of alkyl carboxylic acid (claim 15). The FDCA is esterified to its dialkyl ester (claims 12-14).

Determination of the scope and content of the prior art (MPEP ∋2141.01)

Sanborn et al., teach a similar process of making 2,5-furandicarboxylic acid comprising making HMF and derivatives thereof from carbohydrates (hexose sugars) and oxidizing the HMF or derivatives in the presence of Br/Mn/Co catalyst to obtain 2,5-furandicarboxylic acid. The process was performed at 110 to 150°C. See [0016] to [0021] and [0040] to [0044], particularly [0018] to [0019]. See also examples 1, 3-6 and claims 1-13.

Ascertainment of the difference between the prior art and the claims (MPEP ∋2141.02)

The difference between the instant invention and that of Sanborn is that applicant claims a temperature greater than 140°C instead of 110 to 150°C by Sanborn et al. The FADC is further esterified to its dialkyl ester and the HMF is made from carbohydrates in the presence of alkyl carboxylic acid in the instant invention but not by Sanborn et al.

Finding of prima facie obviousness---rational and motivation (MPEP ∋2142.2413)

However, Gruter et al., teach esterification of HMF to its alkyl ester. See pp. 3, lines 13-15; page 4line 26 to page 5, line 7. A temperature of 150°C is greater than 140°C. The processes by the prior arts must necessarily be performed in the presence of alkyl carboxylic acid because such is a by-product of oxidation of HMF, and well-known in the art. For example, see Sanborn et al., *supra.* In claims 7-8, applicant claims optional presence of metal in the reaction mixture, and therefore, such is not a critical element of the process.

Claims 12-14 are selective combination of the processes by the prior arts done in a manner obvious to one of ordinary skill in the art. There is no indication that such combination would lead one of ordinary skill in the art to doubt that the combination could not be made [because the prior arts and the invention are in the same area of endeavor]. *In re Mostovych,* 144 USPQ 38 (CCPA, 1964). Therefore, the instant invention is prima facie obvious from the teachings of the prior arts absent a showing of unexpected result.

It would have been obvious for one of ordinary skill in the art to try the selective combination of the prior arts' processes at the time this invention was made, because such is a finite and predictable modification. *KSR Int. Co. v. Teleflex Inc*, 550 U.S. 398, 82 USPQ2d 1385 (2007). It has a reasonable expectation of success because the instant invention and that of the prior arts are in the same field of endeavor, and each procedure was successfully performed by the prior arts.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD. JD., whose telephone number is (571) 272-0709.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Kosar, can be reached on (571) 272-0913. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

/Taofiq A. Solola/

Primary Examiner, Art Unit 1622

November 7, 2013

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99**)		
	Application Number	
	Filing Date	
	First Named Inventor	Cesar Munoz de Diego
	Art Unit	
	Examiner Name	Unassigned
	Attorney Docket Number	903-457 PCT/US

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	2673860		1954-03-30	Kuhn et al.	
	2	2628249		1953-02-10	Bruno	
	3	4977283		1990-12-11	Leupold et al.	

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20090156841	A1	2009-06-18	Sanborn et al.	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	0356703	EP	A2	1990-03-07	Hoeshst Aktiengesellschaft		☐

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.S./

Receipt date: 03/22/2012	Application Number	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	Filing Date	
(Not for submission under 37 CFR 1.99)	First Named Inventor	Cesar Munoz de Diego
	Art Unit	
	Examiner Name	Unassigned
	Attorney Docket Number	903-457 PCT/US

	2	621971	GB		1947-10-27	Drewitt et al.		☐
	3	2009001519	JP		2007-06-21	Canon Inc.		☐
	4	2009242312	JP		2009-10-22	Air Water Inc.		☐
	5	636233	RU		1976-06-24			☐
	6	01/72732	WO	A2	2001-10-04	E.I. DuPont de Nemours and Company		☐
	7	2006/063220	WO	A2	2006-06-15	Archer-Daniels-Midland Company		☐
	8	2007/104515	WO	A1	2007-09-20	Avantium International B.V.		☐
	9	2008/054804	WO	A2	2008-05-08	Battelle Memorial Institute		☐
	10	2009/030512	WO	A2	2009-03-12	Furanix Technologies B.V.		☐
	11	2010/132740	WO	A2	2010-11-18	Archer-Daniels-Midland Company		☐

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Receipt date: 03/22/2012	Application Number	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	Filing Date	
(Not for submission under 37 CFR 1.99)	First Named Inventor	Cesar Munoz de Diego
	Art Unit	
	Examiner Name	Unassigned
	Attorney Docket Number	903-457 PCT/US

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Boisen et al., "Process integration for the conversion of glucose to 2,5-furandicarboxylic acid", Chemical Engineering Research and Design, Part A, Institution of Chemical Engineers, vol. 87, no. 9, pp 1318-1327, 2009	☐
	2	Grabowski et al., "The Electrochemical Oxidation of 5-Hydroxymethyfurfural With the Nickel Oxide/Hydroxide Electrode", Electrochimica ACTA, vol. 36, no. 13, pg. 1995, 1991	☐
	3	Haworth et al., "The Conversion of Sucrose into Furan Compounds. Part II. Some 2: 5-disubstituted tetrahydrofurans and their products of ring scission", Journal of the Chemical Society, pp 1-4, 1945	☐
	4	Partenheimer et al., "Synthesis of 2,5-Diformylfuran and Furan-2,5-Dicarboxylic Acid by Catalytic Air-Oxidation of 5-Hydroxymethylfurfural. Unexpectedly Selective Aerobic Oxidation of Benzyl Alcohol to Benzaldehyde with Metal/ Bromide Catalysts", Adv. Synth. Catal., vol. 343, no. 1, pp 102-111, 2001	☐
	5	Tong et al., "Biomass into chemicals: Conversion of sugars to furan derivatives by catalytic processes", Applied Catalysis A: General, vol. 385, no. 1-2, pp 1-13, 2010	☐

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Examiner Signature	/Taofiq Solola/	Date Considered	11/07/2013

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Receipt date: 03/22/2012

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	
Filing Date	
First Named Inventor	Cesar Munoz de Diego
Art Unit	
Examiner Name	Unassigned
Attorney Docket Number	903-457 PCT/US

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

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☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/John S. SOPKO, Reg. #41321/	Date (YYYY-MM-DD)	2012-03-22
Name/Print	John S. Sopko	Registration Number	41321

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

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CONFIRMATION NO. 1013

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
13/497,690	07/09/2012	549	1622	903-457 PCT/US

APPLICANTS

Cesar Muñoz de Diego, Amsterdam, NETHERLANDS;
Matheus Adrianus Dam, Amsterdam, NETHERLANDS;
Gerardus Johannes Maria Gruter, Amsterdam, NETHERLANDS;

**** CONTINUING DATA ***************************

This application is a 371 of PCT/NL10/50654 10/06/2010
which claims benefit of 61/249,395 10/07/2009

**** FOREIGN APPLICATIONS ***************************

NETHERLANDS 2003606 10/07/2009

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED **** ** SMALL ENTITY **
07/16/2012

Foreign Priority claimed ☑ Yes ☐ No 35 USC 119(a-d) conditions met ☑ Yes ☐ No Verified and Acknowledged /TAOFIQ A SOLOLA/ Examiner's Signature	☐ Met after Allowance Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		NETHERLANDS	0	15	3

ADDRESS

Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791
UNITED STATES

TITLE

METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

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Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13497690	MUÑOZ DE DIEGO ET AL.
	Examiner	Art Unit
	TAOFIQ A SOLOLA	1622

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
549	485	11/7/2013	yo

SEARCH NOTES		
Search Notes	Date	Examiner
ISR of pct/NL1050654, inventor/	11/7/201	yo

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(Not for submission under 37 CFR 1.99)

Application Number	13497690
Filing Date	2012-07-09
First Named Inventor	Cesar Munoz de Diego
Art Unit	1622
Examiner Name	SOLOLA, Taofiq A.
Attorney Docket Number	903-457 PCT/US

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	1	WO 2009/076627	WO	A2	2009-06-18	Archer Daniels Midland Co.		☐

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13497690
	Filing Date	2012-07-09
	First Named Inventor	Cesar Munoz de Diego
	Art Unit	1622
	Examiner Name	SOLOLA, Taofiq A.
	Attorney Docket Number	903-457 PCT/US

	1	English translation of a Chinese Office Action dated December 4, 2013 for a *counterpart foreign application*	☐

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Filing Date	2012-07-09
	First Named Inventor	Cesar Munoz de Diego
	Art Unit	1622
	Examiner Name	SOLOLA, Taofiq A.
	Attorney Docket Number	903-457 PCT/US

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☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/John S. SOPKO, Reg. No. 41,321/	Date (YYYY-MM-DD)	2014-01-10
Name/Print	John S. Sopko	Registration Number	41321

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Electronic Acknowledgement Receipt

EFS ID:	17879069
Application Number:	13497690
International Application Number:	
Confirmation Number:	1013
Title of Invention:	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID
First Named Inventor/Applicant Name:	Cesar Muñoz de Diego
Customer Number:	23869
Filer:	John S. Sopko/Kathleen Goodhand
Filer Authorized By:	John S. Sopko
Attorney Docket Number:	903-457 PCT/US
Receipt Date:	10-JAN-2014
Filing Date:	09-JUL-2012
Time Stamp:	13:46:54
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	903-457_PCT_US_IDS_PTO_SB_082.PDF	612293 ebb4feeca0d5451ba144beb78beb98126bb58d94	no	4

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Cesar Muñoz de Diego	Examiner:	Solola, Taofiq A.
Application No.:	13/497,690	Group Art Unit:	1622
Confirmation No:	1013	Docket:	903-457 PCT/US
Filing or § 371 (c) Date:	July 9, 2012	Dated:	March 7, 2014

For: METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

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Dated: March 7, 2014

Signature Jane Callahan / Jane Callahan /

AMENDMENT AND RESPONSE TO NON-FINAL OFFICE ACTION PURSUANT TO 37 C.F.R. §1.111

Sir:

In response to the Non-Final Office Action dated December 11, 2013, a reply to which is due March 11, 2014, please amend the above-identified application as follows:

Amendments to the Specification begin on page 2 of this submission.

Amendments to the Claims begin on page 3 of this submission.

Remarks/Arguments begin on page 6 of this submission.

Amendments to the Specification:

Please amend the paragraph beginning at page 6, line 12, as follows:

The esterification of 2,5-furan dicarboxylic acid is known. As a specific example for the manufacture of these esters, reference is made to US 2673860 wherein the diester is obtained by transesterification of another dicarboxylic acid ester in the presence of sulphuric acid. A more general description for the esterification of dicarboxylic acids is presented in US 2628249. Accordingly, the invention provides a process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C, and esterifying the thus obtained product.

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the subject application, and please amend the claims as follows:

1. (Currently amended): A method for the preparation of 2,5-furan dicarboxylic acid comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethylfurfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an ~~oxidant~~ oxygen-containing gas, in the presence of an oxidation catalyst comprising at least one metal selected from Co and Mn, at a temperature ~~higher than~~ between 140 ºC and 200 ºC at an oxygen partial pressure of 1 to 10 bar, wherein a solvent or solvent mixture comprising acetic acid or acetic acid and water mixtures is present.

2. (Previously presented): The method according to claim 1, wherein the feed comprises a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), esters of HMF and a mixture thereof.

3. (Canceled)

4. (Currently amended): The method according to claim 1, wherein the oxidation catalyst further comprises a source of bromine.

5. (Previously presented): The method according to claim 4, wherein the oxidation catalyst contains both Co and Mn.

6. (Previously presented): The method according to claim 5, wherein the oxidation catalyst comprises at least one additional metal.

7. (Previously presented): The method according to claim 6, wherein the additional metal is Zr and/or Ce.

8. (Canceled)

9. (Currently amended): The method according to claim 1, wherein the temperature is ~~between 140 and 200 ºC, most preferably~~ between 160 and 190 ºC.

10. (Canceled)

11. (Currently amended): The method according to claim 1, wherein the feed comprises an ester of HMF containing an ester moiety of an alkyl carboxylic acid wherein the alkyl group contains up to 6 carbon atoms~~, preferably from 1 to 5 carbon atoms~~.

12. (Currently amended): A process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an ~~oxidant~~ oxygen-containing gas in the presence of an oxidation catalyst comprising at least one metal selected from Co and Mn, at a temperature ~~higher than~~ between 140 ºC and 200 ºC at an oxygen partial pressure of 1 to 10 bar, wherein a solvent or solvent mixture comprising acetic acid or acetic acid and water mixtures is present, and esterifying the thus obtained product.

13. (Previously presented): The process according to claim 12, wherein the product is esterified with a C_1-C_5 alkyl alcohol.

14. (Previously presented): The process according to claim 13, wherein the C_1-C_5 alkyl alcohol is methanol and the dialkyl ester is the dimethylester of 2,5-furan dicarboxylic acid.

15. (Canceled)

16. (New): A method according to claim 2, wherein the feed comprises an HMF ester and optionally 5-hydroxymethyl furfural, which has been obtained by converting a carbohydrate source in the presence of an alkyl carboxylic acid.

Remarks/Arguments:

Introduction

Amended claim 1 has been limited to oxidation catalysts that contain at least one of the metals Co and Mn, to a range of reaction temperatures, including an upper limit, to the presence of a specific acetic acid-containing solvent or solvent mixture, to the use of an oxygen-containing gas as oxidant and to a specific range of oxygen partial pressures. Support for these amendments can be found, *inter alia*, in originally filed claims 3, 8, 9 and 10. The range for the oxygen partial pressure is disclosed on page 5, lines 11-12 of the PCT application.

Claims 3, 8 and 10 have been canceled.

The Specification at page 6 at the paragraph beginning with line 12 has been amended to include the description of originally filed claim 12.

No new matter is introduced with these amendments. Entry of the amendments is respectfully requested.

Section 112 Rejections

Claims 1-15 are rejected as allegedly failing to comply with the written description requirement. Claims 9-11 and 15 are rejected as allegedly being indefinite. Applicants respectfully submit that with the claim amendments presented herewith the concerns raised by the Examiner are obviated. In particular, the amended paragraph beginning at page 6, line 12, fully supports claim 12, and the Specification at page 5, lines 26-33, fully support claim 15. Furthermore, it is respectfully submitted that examples of each feature of the invention are not required for enablement. Therefore, reconsideration and withdrawal of the Section 112 rejections are respectfully requested.

Section 102 Rejections

Claims 1-11 and 15 were rejected under 35 U.S.C. §102(b) (pre-AIA) as allegedly being anticipated by US 2009/0156841 (Sanborn). Applicants respectfully traverse.

The present invention now provides the preparation of 2,5-furandicarboxylic acid from a selected group of furfural derivatives with an oxygen-containing gas, in which preparation a Co- and/or Mn-containing catalyst is used in a solvent that comprises acetic acid or an acetic acid/water mixture. The reaction temperature is in the range of 140 to 200 °C and the oxygen partial pressure is in the range of 1 to 10 bar.

Sanborn describes a number of reactions, some of which are as follows:

A first reaction is the conversion of a carbohydrate source to 5-hydroxymethyl furfural ("HMF") and esters of HMF. HMF esters can be produced by heating a carbohydrate source with a solvent in a column and by making it continuously flow through a solid phase catalyst in the presence of an organic solvent (cf. Sanborn paragraph [0016]). Alternatively, HMF esters are formed by heating the carbohydrate source with an organic acid and a solid catalyst in a solvent (cf. Sanborn paragraph [0017]).

A second reaction concerns an oxidation reaction. The HMF ester or a mixture of HMF and HMF ester may be oxidized to 2,5-furan-dicarboxylic acid (FDCA) over a catalyst that contains Co, Mn and Br (cf. Sanborn paragraphs [0018] and [0019]).

A third reaction is a reduction reaction. An HMF ester may be reduced by the addition of an alcohol and a reducing agent under pressure (cf. Sanborn paragraph [0020]).

For the production of HMF esters a reaction temperature of up to 125 °C can be applied in the embodiment wherein a column is being used (cf. Sanborn paragraph [0054]). In the alternative embodiment, the temperature may be between 100 and 140 °C (cf. Sanborn paragraph

[0059]). The reduction of HMF esters may be conducted at temperatures up to 195 °C (cf. Sanborn paragraph [0061]).

It is emphasized that these reaction temperatures have absolutely no relation to the conditions that are taught by Sanborn for the oxidation of HMF esters to FDCA.

Sanborn teaches that the oxidation of HMF esters to FDCA is conducted at a temperature in the range of 85 to 110 °C and an oxygen pressure of 400 to 1000 psi (cf. Sanborn paragraph [0060]).

As the present invention provides for an oxidation method that is conducted at 140 to 200 °C and an oxygen partial pressure of 1 to 10 bar (i.e. 14.5 to 145 psi), it is submitted that differences between Sanborn and the presently claimed invention include a different temperature range and a different pressure range. Therefore, the present invention is novel over Sanborn.

Reconsideration and withdrawal of the rejections under 35 USC §102 (pre-AIA) is withdrawn.

Section 103 Rejections

Claims 1-15 were rejected under 35 U.S.C. §103(a) (pre-AIA) as allegedly being obvious over Sanborn in view of WO 2009030521 (Gruter). Applicant respectfully traverses.

The present invention is also non-obvious or patentably distinct over Sanborn. The examples 7 and 9 in Sanborn show the oxidation of HMF ester to FDCA. The reaction of example 7 is conducted at a temperature of 100 °C and an oxygen pressure of 500-800 psi (i.e. about 34 -55 bar). The reaction lasted two hours. A selectivity of 54% has been reported (cf. Sanborn paragraph [0075]).

In contradistinction therewith, Table 1 of the present application shows the results of experiments wherein at an air pressure of 20 bar, i.e. an oxygen partial pressure of about 4 bar,

and a temperature of 180 ºC, higher selectivities for the conversion of the same HMF ester can be obtained, viz. in the range of 57 to about 65% (cf. present application Table 1, experiments 1d, 1h and 1l). These higher selectivities were obtained in a reaction period of 1 hour which is considerably shorter than the experiments of Example 7 of Sanborn.

It is therefore, submitted that the present invention is non-obvious over Sanborn alone.

Gruter discloses the preparation of HMF esters from a hexose-containing starting material with an alcohol in an ionic liquid, using a metal chloride as catalyst. It is observed that Gruter does not relate to the oxidation of the HMF esters. Therefore, Gruter fails to disclose, teach or suggest the oxidation of the HMF esters with an oxygen-containing gas over a Co and/or Mn-containing catalyst at a temperature of 140 to 200 ºC and an oxygen partial pressure of 1 to 10 bar.

Even if a person having ordinary skill in the art would combine the teachings of Sanborn and Gruter he would not arrive at the features of the present invention. Therefore, the present invention is held non-obvious.

Reconsideration and withdrawal of the Section 103 rejections are respectfully requested.

Summary

Therefore, Applicants respectfully submit that claims 1, 2, 4-7, 9, 11-14 and 16 are patentably distinct. This application is believed to be in condition for allowance. Favorable action thereon is therefore respectfully solicited.

It is believed that all outstanding rejections have been addressed. The absence of a reply to a specific issue or comment presented by the Office Action does not signify that Applicant agree with or concede to that issue or comment. Because arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims, or other claims

(including the cancelled claims, if any), that have not been expressed. Nothing in this submission should be construed as a concession of or an intent to concede any issue with regard to any claim, except as specifically stated herein.

Should the Examiner have any questions or comments concerning the above, the Examiner is respectfully invited to contact the undersigned attorney at the telephone number given below.

The Commissioner is hereby authorized to charge payment of any additional fees associated with this communication, or credit any overpayment, to Deposit Account No. 08-2461. Such authorization includes authorization to charge fees for extensions of time, if any, under 37 C.F.R § 1.17 and also should be treated as a constructive petition for an extension of time in this reply or any future reply pursuant to 37 C.F.R. § 1.136.

Respectfully submitted,

/John S. SOPKO, Reg. # 41,321/
John S. Sopko
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Attorney of Record and/or for Applicant

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Electronic Acknowledgement Receipt

EFS ID:	18398407
Application Number:	13497690
International Application Number:	
Confirmation Number:	1013
Title of Invention:	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID
First Named Inventor/Applicant Name:	Cesar Muñoz de Diego
Customer Number:	23869
Filer:	John S. Sopko/Jane Callahan
Filer Authorized By:	John S. Sopko
Attorney Docket Number:	903-457 PCT/US
Receipt Date:	07-MAR-2014
Filing Date:	09-JUL-2012
Time Stamp:	10:49:22
Application Type:	U.S. National Stage under 35 USC 371

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		903-457_PCT-US_Amendment_to_Office_Action_of_12-11-13.PDF	37089 ddb8176373ed227a758170e21efe274008a7124a	yes	10

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Amendment/Req. Reconsideration-After Non-Final Reject	1	1
	Specification	2	2
	Claims	3	5
	Applicant Arguments/Remarks Made in an Amendment	6	10
Warnings:			
Information:			
	Total Files Size (in bytes):	37089	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (09-11)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 13/497,690	Filing Date 07/09/2012	☐ To be Mailed

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)		
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)
☒ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	**190**
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	**190**

APPLICATION AS AMENDED – PART II

AMENDMENT	03/07/2014	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 12	Minus	** 20	= 0	X $40 =	0
	Independent (37 CFR 1.16(h))	* 2	Minus	***3	= 0	X $210 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	**0**

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/FELICIA JENKINS/

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/497,690	07/09/2012	Cesar Muñoz de Diego	903-457 PCT/US	1013

23869 7590 03/31/2014

Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

EXAMINER	
SOLOLA, TAOFIQ A	
ART UNIT	PAPER NUMBER
1622	
MAIL DATE	DELIVERY MODE
03/31/2014	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 13/497,690	Applicant(s) MUÑOZ DE DIEGO ET AL.	
	Examiner Taofiq A. Solola	Art Unit 1622	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/7/14*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *1,2,4-7,9,11-14 and 16* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,2,4-7,9,11-14 and 16* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

The present application is being examined under the pre-AIA first to invent provisions.

Claims 1-2, 4-7, 9, 11-14, 16, are pending in this application.

Claims 3, 8, 10, 15, are deleted.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-7, 9, 11-14, 16, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims lack adequate support in the specification. The examples (pp. 10-11, tables 1-3) in the specification are performed in the presence of Br/Co/Mn as catalyst. Therefore, there is no support in the specification for using partial catalyst as in claims 3-4. All the examples relate to claims 1-2, 4-7, 9, 11, 16. No examples are disclosed for 12-14. Therefore, there is no evidence applicant was in possession of the inventions at the time this application was filed.

A claim must stand alone to define the invention, and incorporation into the claims by reference to the specification or an external source is not permitted. *Ex parte Fressola,* 27 USPQ 2d 1608, BdPatApp & Inter. (1993).

In patent examination, it is essential for claims to be precise, clear, correct, and unambiguous. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). Applicant should note that the requirement of 35 USC 112, is not what is obvious to one of ordinary skill in the art

but a “full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same”, *Lookwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed Cir. 1997.

Appropriate correction is required.

> The following is a quotation of 35 U.S.C. 112(b):
> (b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.
>
> The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

In claim 11, ‘containing” and “contain”, lines 2 and 3 respectively render the claim indefinite. By replacing the terms with “having” and “have” respectively the rejection would be overcome.

Response to Argument

Applicant's arguments filed 3/7/14, have been fully considered but they are not persuasive. Applicant contends the amendment to the specification obviates above rejections, and that not every element of the invention is required to be exemplified. This is not persuasive because the examples are not commensurate in scope with the claims. In addition, US 2,673,860, and 2,628,249, are not incorporated by reference in accordance with the MPEP. See MPEP 608.01(p) and 37 CFR 1.57(b)(1). See 37 CFR 1.57(c), 1.57(c)(1) to (3). See the MPEP 608.01(p), which states:

A mere reference to another application, publication or patent is not an incorporation of anything therein into the application containing such reference for the purpose of satisfying the requirement of 35 USC 112, first paragraph. *In re de Seversky,* 474 F.2d 671, 177 USPQ 144 (CCPA 1973). Particular attention should be directed to the subject matter and the specific portions of the referenced document where the subject matter being incorporated may be found.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 4-7, 9, 11-14, 16, are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanborn et al., US 2009/0156841 A1 (published 6/18/09), in view of Gruter et al., WO/2009/030521 (published 3/12/09).

Applicant claims a process of making furan-2,5-dicarboxylic acid (FDCA), comprising oxidation of HMA or derivatives thereof with oxidation gas in the presence of a catalyst comprising at least one metal selected from Co and MN. The reaction temperature is between 140 and 200°C and the solvents are the same as in the prior art by Sanborn. In preferred embodiments the catalyst comprises cobalt, manganese and bromine, and the HMF is made from carbohydrates in the presence of alkyl carboxylic acid (claim 16). The FDCA is esterified to its dialkyl ester (claims 12-14).

Determination of the scope and content of the prior art (MPEP ∋2141.01)

Sanborn et al., teach a similar process of making 2,5-furandicarboxylic acid comprising making HMF and derivatives thereof from carbohydrates (hexose sugars) and oxidizing the HMF or derivatives in the presence of Br/Mn/Co catalyst to obtain 2,5-furandicarboxylic acid.

The process was performed at 110 to 150°C See [0016] to [0021] and [0040] to [0044], particularly [0018] to [0019]. See also examples 1, 3-6 and claims 1-13.

Ascertainment of the difference between the prior art and the claims (MPEP ∋2141.02)

The difference between the instant invention and that of Sanborn is that applicant claims a temperature is from 140-200°C instead of 110 to 150°C by Sanborn et al. The FADC is further esterified to its dialkyl ester and the HMF is made from carbohydrates in the presence of alkyl carboxylic acid in the instant invention but not by Sanborn et al. Applicant also changed the pressure.

Finding of prima facie obviousness---rational and motivation (MPEP ∋2142.2413)

However, Gruter et al., teach esterification of HMF to its alkyl ester. See pp. 3, lines 13-15; page 4, line 26 to page 5, line 7. A temperature of 150°C is embraced by 140-200°C. The processes by the prior arts must necessarily be performed in the presence of alkyl carboxylic acid because such is a by-product of oxidation of HMF, and well-known in the art. For example, see Sanborn et al., *supra.* In claims 7-8, applicant claims optional presence of metal in the reaction mixture, and therefore, such is not a critical element of the process.

Changing the pressure, temperature, amount of catalyst and/or of reagents is a mere optimization of a variable, which is not patentable absent unexpected result due to the variable, which is different in kind and not merely in degree from that of the prior art. This is routinely done by chemists in order to increase the yield of the product. See also, *In re Aller,* 22 F.2d 454,105 USPG 233 (CCPA, 1955), *In re Boesch and Slaney,* 205 USPQ 215 (CCPA, 1980).

Therefore, the instant invention is prima facie obvious from the teachings of the prior art. It would have been obvious for one of ordinary skill in the art to change the amounts/ratios of the catalyst and/or the pressure at the time this invention was made because such is routinely done by organic chemists. The motivation is to increase the yield of the product.

Claims 12-14 are selective combination of the processes by the prior arts done in a manner obvious to one of ordinary skill in the art. There is no indication that such combination would lead one of ordinary skill in the art to doubt that the combination could not be made [because the prior arts and the invention are in the same area of endeavor]. *In re Mostovych,* 144 USPQ 38 (CCPA, 1964). Therefore, the instant invention is prima facie obvious from the teachings of the prior arts absent a showing of unexpected result.

It would have been obvious for one of ordinary skill in the art to try the selective combination of the prior arts' processes at the time this invention was made, because such is a finite and predictable modification. *KSR Int. Co. v. Teleflex Inc*, 550 U.S. 398, 82 USPQ2d 1385 (2007). It has a reasonable expectation of success because the instant invention and that of the prior arts are in the same field of endeavor, and each procedure was successfully performed by the prior arts.

Response to Argument

Applicant's arguments filed 3/7/14, have been fully considered but they are not persuasive. Applicant contends the pressure and temperature of the invention are different from the prior art's, and consequently the yield of the product is higher than prior art's. This is not persuasive because changing the pressure, temperature, amount of catalyst and/or of reagents is a mere optimization of a variable, which is not patentable absent unexpected result due to the variable, which is different in kind and not merely in degree from that of the prior art. This is routinely done by chemists in order to increase the yield of the product. See also, *In re Aller,* 22 F.2d 454,105 USPG 233 (CCPA, 1955), *In re Boesch and Slaney,* 205 USPQ 215 (CCPA, 1980). Therefore, the results in table 1 are not unexpected. Also, the assays wherein the combination of all the metals is used as catalyst are not valid representatives of the claims wherein one or any combination of two thereof is used as catalyst.

Applicant further argues that Gruter et al., did not teach oxidation of HMF with oxygen gas in the presence of the instant catalyst, at the temperature range and pressure. Applicant cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD. JD., whose telephone number is (571) 272-0709.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Kosar, can be reached on (571) 272-0913. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

/Taofiq A. Solola/

Primary Examiner, Art Unit 1622

March 14, 2014

Receipt date: 01/10/2014
Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13497690
Filing Date	2012-07-09
First Named Inventor	Cesar Munoz de Diego
Art Unit	1622
Examiner Name	SOLOLA, Taofiq A.
Attorney Docket Number	903-457 PCT/US

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	WO 2009/076627	WO	A2	2009-06-18	Archer Daniels Midland Co.		☐

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.S./

Receipt date: 01/10/2014		
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Application Number	13497690
	Filing Date	2012-07-09
	First Named Inventor	Cesar Munoz de Diego
	Art Unit	1622
	Examiner Name	SOLOLA, Taofiq A.
	Attorney Docket Number	903-457 PCT/US

	1	English translation of a Chinese Office Action dated December 4, 2013 for a counterpart foreign application	☐

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Examiner Signature	/Taofiq Solola/	Date Considered	03/13/2014

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Receipt date: 01/10/2014

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CERTIFICATION STATEMENT

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☐ See attached certification statement.

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☒ A certification statement is not submitted herewith.

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Signature	/John S. SOPKO, Reg. No. 41,321/	Date (YYYY-MM-DD)	2014-01-10
Name/Print	John S. Sopko	Registration Number	41321

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3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13497690	MUÑOZ DE DIEGO ET AL.
	Examiner	Art Unit
	TAOFIQ A SOLOLA	1622

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
549	485	11/7/2013	yo
updated		3/14/2014	yo

SEARCH NOTES		
Search Notes	Date	Examiner
ISR of pct/NL1050654, inventor/	11/7/201	yo
updated	3/14/2014	yo

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Application Number	13497690
Filing Date	2012-07-09
First Named Inventor	Cesar Muñoz de Diego
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Examiner Name	Solola, Taofiq A.
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	1	2009/076627	WO	A2	2009-06-18	ARCHER DANIELS MIDLAND CO		☐

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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Signature	/John S. SOPKO, Reg. #41,321/	Date (YYYY-MM-DD)	2014-05-23
Name/Print	John S. Sopko	Registration Number	41,321

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Electronic Patent Application Fee Transmittal

Application Number:	13497690
Filing Date:	09-Jul-2012
Title of Invention:	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID
First Named Inventor/Applicant Name:	Cesar Muñoz de Diego
Filer:	John S. Sopko/Jane Callahan
Attorney Docket Number:	903-457 PCT/US

Filed as Large Entity

U.S. National Stage under 35 USC 371 Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
		Total in USD ($)		**180**

Electronic Acknowledgement Receipt

EFS ID:	19112694
Application Number:	13497690
International Application Number:	
Confirmation Number:	1013
Title of Invention:	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID
First Named Inventor/Applicant Name:	Cesar Muñoz de Diego
Customer Number:	23869
Filer:	John S. Sopko/Jane Callahan
Filer Authorized By:	John S. Sopko
Attorney Docket Number:	903-457 PCT/US
Receipt Date:	23-MAY-2014
Filing Date:	09-JUL-2012
Time Stamp:	13:23:37
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$180
RAM confirmation Number	9402
Deposit Account	082461
Authorized User	SOPKO, JOHN S

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Foreign Reference	WO2009-076627A2.PDF	4497751 ee1567c441394d324b683382de45b481fc633315	no	41
Warnings:					
Information:					
2	Non Patent Literature	NPL-Communication_dated_12-4-13.PDF	178148 f4fb478e2e5d9db33f7e6b50b455812cffeb105d	no	9
Warnings:					
Information:					
3	Information Disclosure Statement (IDS) Form (SB08)	903-457_PCT-US_-_IDS.PDF	612260 f373863059af91e57a996bfce8ee1fd85e5f9e8d	no	4
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4	Fee Worksheet (SB06)	fee-info.pdf	31020 547721478ae89ba6912e14b905d5df98921da9e3	no	2
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		Total Files Size (in bytes):	5319179		

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Cesar Muñoz de Diego	Examiner:	Solola, Taofiq A.
Application No.:	13/497,690	Group Art Unit:	1622
Confirmation No:	1013	Docket:	903-457 PCT/US
Filing or § 371 (c) Date:	July 9, 2012	Dated:	June 13, 2014

For: METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

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Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

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Dated: June 13, 2014

Signature John S. Sopko /John S. Sopko/

AMENDMENT AND RESPONSE TO FINAL OFFICE ACTION PURSUANT TO 37 C.F.R. §1.116

Sir:

In response to the Final Office Action dated March 31, 2014, a reply to which is due June 30, 2014, please amend the above-identified application as follows:

Amendments to the Claims begin on page 2 of this submission.

Remarks/Arguments begin on page 5 of this submission.

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the subject application, and please amend the claims as follows:

1. (Currently amended): A method for the preparation of 2,5-furan dicarboxylic acid comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethylfurfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxygen-containing gas, in the presence of an oxidation catalyst comprising ~~at least one metal selected from~~ both Co and Mn, and further a source of bromine, at a temperature between 140 °C and 200 °C at an oxygen partial pressure of 1 to 10 bar, wherein a solvent or solvent mixture comprising acetic acid or acetic acid and water mixtures is present.

2. (Previously presented): The method according to claim 1, wherein the feed comprises a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), esters of HMF and a mixture thereof.

3. – 5. (Canceled)

6. (Currently amended): The method according to claim 1 [[5]], wherein the oxidation catalyst comprises at least one additional metal.

7. (Previously presented): The method according to claim 6, wherein the additional metal is Zr and/or Ce.

8. (Canceled)

9. (Previously presented): The method according to claim 1, wherein the temperature is between 160 and 190 °C.

10. (Canceled)

11. (Currently amended): The method according to claim 1, wherein the feed comprises an ester of HMF ~~containing~~ having an ester moiety of an alkyl carboxylic acid wherein the alkyl group ~~contains~~ has up to 6 carbon atoms.

12. (Currently amended): A process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxygen-containing gas in the presence of an oxidation catalyst comprising ~~at least one metal selected from~~ both Co and Mn, and further a source of bromine, at a temperature between 140 °C and 200 °C at an oxygen partial pressure of 1 to 10 bar, wherein a solvent or solvent mixture comprising acetic acid or acetic acid and water mixtures is present, and esterifying the thus obtained product.

13. (Previously presented): The process according to claim 12, wherein the product is esterified with a C1-C5 alkyl alcohol.

14. (Previously presented): The process according to claim 13, wherein the C1-C5 alkyl alcohol is methanol and the dialkyl ester is the dimethylester of 2,5-furan dicarboxylic acid.

15. (Canceled)

16. (Previously presented): A method according to claim 2, wherein the feed comprises an HMF ester and optionally 5-hydroxymethyl furfural, which has been obtained by converting a carbohydrate source in the presence of an alkyl carboxylic acid.

Remarks/Arguments:

Introduction

Claims 1 and 12 have been amended to include the limitations of claims 4 and 5. Claims 4 and 5 have been canceled. Claim 6 has been amended to depend from claim 1. Claim 11 has been amended as suggested by the Examiner.

No new matter is introduced with these amendments. Entry of the amendments is respectfully requested.

Section 112 Rejections

Claims 1, 2, 4-7, 9, 11-14 and 16 were rejected as allegedly failing to comply with the written description requirement; claim 11 was rejected as allegedly being indefinite. Applicants respectfully submit that with the claim amendments presented herewith all concerns raised by the Examiner are obviated. Therefore, reconsideration and withdrawal of the Section 112 rejections are respectfully requested.

Section 103 Rejections

Claims 1-15 were rejected under 35 U.S.C. §103(a) (pre-AIA) as allegedly being obvious over US 2009/0156841 (Sanborn) in view of WO 2009030521 (Gruter). Applicants respectfully traverse.

In connection therewith the Examiner has determined the scope and content of the prior art. The Examiner alleges that:

> *"Sanborn et al., teach a similar process of making 2,5-furandicarboxylic acid comprising making HMF and derivatives thereof from carbohydrates (hexose sugars) and oxidizing the HMF or derivatives in the presence of Br/Mn/Co catalyst to obtain*

2,5-furandicarboxylic acid. The process was performed at 110 to 150°C See [0016] to [0021] and [0040] to [0044], particularly [0018] to [0019]. See also examples 1, 3-6 and claims 1-13."

It is respectfully submitted that paragraphs [0016], [0017], [0020] and [0021], and [0040] to [0044] of Sanborn do not relate to the oxidation of HMF or HMF esters to FDCA (2,5-furandicarboxylic acid). Only paragraphs [0018] and [0019] describe the oxidation of an HMF ester or a mixture of HMF and an HMF ester to FDCA. However, the latter paragraphs do not disclose any temperature range. In fact, none of the paragraphs cited by the Examiner mention a temperature range.

The examples of Sanborn that were cited by the Examiner have no relation to the oxidation of HMF or and HMF ester to FDCA. They relate to the synthesis of HMF and the acetyl ester of HMF (acetoxymethylfurfural, or AcHMF) (cf. examples 1 to 4). Example 5 relates to the purification of AcHMF and example 6 relates to the synthesis of propionoxymethyl furfural from fructose. Hence, these specific examples of Sanborn do not disclose the oxidation of an HMF ester to FDCA. As to temperatures it would seem that the Examiner has derived the cited range of 110 - 150 °C from Example 1, wherein three temperatures for the synthesis of AcHMF were tested: 110°C, 125°C and 150°C.

Only claims 10 and 11 of Sanborn relate to the forming of FDCA from an HMF ester. Claim 10 of Sanborn indicates the catalyst and refers to "elevated temperature and pressure", and claim 11 of Sanborn specifies the elevated pressure as a range of about 400 to 1000 psi.

In Applicants' previous Amendment and Response, Applicants have already submitted that Sanborn specifically teaches that the formation of FDCA from an HMF ester is conducted at a pressure of about 400 to 1000 psi oxygen and a temperature of about 85 to 110°C (cf. paragraph [0060]). This is confirmed by Example 7 in Sanborn showing the oxidation of AcHMF to FDCA at 100°C, 500-800 psi oxygen for 2 hours.

In view thereof, a correct determination of the scope and content of the prior art would be that:

> *Sanborn et al., teach a process of making 2,5-furandicarboxylic acid by oxidizing HMF or HMF derivatives in the presence of Br/Mn/Co catalyst to obtain 2,5-furandicarboxylic acid. The oxidation process is performed at 85 to 110 °C. See [0018] to [0019] and [0060]. See also examples 7 and 9 and claims 10 and 11.*

The differences between the prior art and the presently claimed invention would therefore include a different temperature range, *viz.* 140 to 200°C instead of 85 to 110°C, and a different pressure range, *viz.* an oxygen pressure of 1 to 10 bar, instead of 400 to 1000 psi (corresponding with 27.6 to 68.9 bar).

The Examiner alleges these differences *prima facie* obvious. The Examiner appears to base such an assertion on the statement that *"[c]hanging the pressure, temperature, amount of catalyst and/or of reagents is a mere optimization of a variable, which is not patentable absent unexpected result due to the variable, which is different in kind and not merely in degree from that of the prior art."* In that respect reference is made to *In re Aller and In re Boesch.*

It is observed that *In re Aller* the pressure was not mentioned. Also, the MPEP only refers to differences in concentration or temperature (*cf.* MPEP 2144.05 II.A). Hence, the Examiner has gone beyond the scope of *In re Aller* by asserting that differences in pressure are within the scope of *In re Aller.*

Moreover, the combination of higher temperature and lower oxygen pressure leads to unexpected results with the present invention.

In Example 7 of Sanborn FDCA is prepared from the oxidation of AcHMF over a Co/Mn/Br catalyst at an oxygen pressure of about 500 to 800 psi (about 34 to 55 bar) and at a

temperature of about 100°C. The reaction lasted two hours. The overall yield of FDCA was 54%.

In Experiments 2a and 2b of the Subject Application, FDCA was prepared from the oxidation of AcHMF over a Co/Mn/Br catalyst at 100 °C and at an air pressure of 30 bar, corresponding to an oxygen pressure of about 6 bar. The reaction lasted two hours.

The overall yield of FDCA was between 23 and 30%. It is observed that the conversion of AcHMF was 100%, but the selectivity to FDCA was only between 23 and 30 %.

Hence, the selectivity to FDCA was found to be lower than in Example 7 of Sanborn, when only the oxygen pressure was reduced from about 34 to about 6 bar.

It could not be expected by a person having ordinary skill in the art that the selectivity at these low pressures would be increased to above the level of Sanborn when the temperature would be elevated to a value within the range of 140 to 200 °C. That is precisely what is shown by the results of the experiments of Example 1 of the Subject Application. Table 2 in the Present Application shows that when the oxygen pressure is low and the reaction temperature is increased to 180 °C, the selectivity to FDCA is increased to levels above the selectivity of Sanborn.

It is submitted that this is a difference in kind, rather than a difference in degree. In this respect it is respectfully submitted that the results provide the evidence in the form of indirect comparison with the closest prior art in accordance with the provisions of *In re Boesch* (cf. MPEP 716.02(b) III).

In view of the above arguments Applicants submit that the currently presented claim 1 contains matter that is clearly patentably distinct over Sanborn.

It is submitted that the disclosure of Gruter does not add any relevant information to the disclosure of Sanborn in relation to presently presented claim 1.

The Examiner seems to accept this and refers to Gruter in relation to the rejection of claims 12-14. It is assumed that Gruter is also cited in connection with claim 16.

Gruter merely discloses a process for producing an HMF ester from a carbohydrate in the presence of an alkyl carboxylic acid. In that respect Gruter discloses a process that is similar to the method for producing HMF esters from a carbohydrate source as described in paragraph [0017] of Sanborn.

It is observed that the end-product of both the process according to Gruter and the above-mentioned method according to paragraph [0017] of Sanborn is an HMF ester. Examples thereof include acetoxymethylfurfural and propionoxymethylfurfural.

In contradistinction therewith, the process according to claim 12 of the subject application concerns a two-step process; a first step wherein HMF or an HMF ester is oxidized via a method as claimed in the presently presented claim 1; and a second step wherein the product of this first step, *i.e.* comprising FDCA, is esterified to yield a dialkyl ester of FDCA.

It is respectfully submitted that neither Sanborn nor Gruter disclose, teach or suggest the sequence of the above-described two steps. That is already an indication of the non-obviousness of the process according to claim 12.

In addition, it is observed that the first step is non-obvious, as shown *supra*. For that reason alone, the two-step process according to claim 12 is to be held non-obvious, too.

As to the dependent claims it is observed that since the independent claims, on which they are dependent, are non-obvious, the dependent claims derive their non-obviousness at least from the patentably distinct limitations of these independent claims.

Therefore, reconsideration and withdrawal of the Section 103 rejections are respectfully requested.

Summary

Thus, Applicants respectfully submit that independent claims 1 and 12, and all claims dependent therefrom, are patentably distinct. This application is believed to be in condition for allowance. Favorable action thereon is therefore respectfully solicited.

It is believed that all outstanding rejections have been addressed. The absence of a reply to a specific issue or comment presented by the Office Action does not signify that Applicant agree with or concede to that issue or comment. Because arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims, or other claims (including the cancelled claims, if any), that have not been expressed. Nothing in this submission should be construed as a concession of or an intent to concede any issue with regard to any claim, except as specifically stated herein.

Should the Examiner have any questions or comments concerning the above, the Examiner is respectfully invited to contact the undersigned attorney at the telephone number given below.

The Commissioner is hereby authorized to charge payment of any additional fees associated with this communication, or credit any overpayment, to Deposit Account No. 08-2461. Such authorization includes authorization to charge fees for extensions of time, if any, under 37 C.F.R § 1.17 and also should be treated as a constructive petition for an extension of time in this reply or any future reply pursuant to 37 C.F.R. § 1.136.

Respectfully submitted,

/John S. SOPKO, Reg. # 41,321/
John S. Sopko
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Attorney of Record and/or for Applicants

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Electronic Acknowledgement Receipt

EFS ID:	19296043
Application Number:	13497690
International Application Number:	
Confirmation Number:	1013
Title of Invention:	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID
First Named Inventor/Applicant Name:	Cesar Muñoz de Diego
Customer Number:	23869
Filer:	John S. Sopko
Filer Authorized By:	
Attorney Docket Number:	903-457 PCT/US
Receipt Date:	13-JUN-2014
Filing Date:	09-JUL-2012
Time Stamp:	11:13:08
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		903-457_PCT-US_Amendment_and_Response_filed_06-13-14.PDF	39647 760dd98424c368f665618330ca725d09dcb b4d89	yes	11

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Response After Final Action	1	1
	Claims	2	4
	Applicant Arguments/Remarks Made in an Amendment	5	11
Warnings:			
Information:			
	Total Files Size (in bytes):	39647	

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (09-11)
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 13/497,690	Filing Date 07/09/2012	☐ To be Mailed

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☒ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	**190**
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	**190**

APPLICATION AS AMENDED – PART II

AMENDMENT **06/13/2014**

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 12	Minus	** 20	= 0	X $40 =	0
Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0	X $210 =	0
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	**0**

AMENDMENT

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/GLORIA TRAMMELL/

Notice of Allowability	Application No. 13/497,690	Applicant(s) MUÑOZ DE DIEGO ET AL.	
	Examiner Taofiq A. Solola	Art Unit 1622	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment filed 6/13/14*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *1-2,6-7,9,11-14,16*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/Taofiq A. Solola/
Primary Examiner, Art Unit 1622

Receipt date: 05/23/2014
Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-10)
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13497690
Filing Date	2012-07-09
First Named Inventor	Cesar Muñoz de Diego
Art Unit	1622
Examiner Name	Solola, Taofiq A.
Attorney Docket Number	903-457 PCT/US

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	1	2009/076627	WO	A2	2009-06-18	ARCHER DANIELS MIDLAND CO		☐

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Receipt date: 05/23/2014		
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Application Number	13497690
	Filing Date	2012-07-09
	First Named Inventor	Cesar Muñoz de Diego
	Art Unit	1622
	Examiner Name	Solola, Taofiq A.
	Attorney Docket Number	903-457 PCT/US

	1	English translation of communication dated December 4, 2013 from a counterpart foreign (Chinese) application	☐

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EXAMINER SIGNATURE

Examiner Signature	/Taofiq Solola/	Date Considered	06/17/2014

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

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Receipt date: 05/23/2014

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13497690
Filing Date	2012-07-09
First Named Inventor	Cesar Muñoz de Diego
Art Unit	1622
Examiner Name	Solola, Taofiq A.
Attorney Docket Number	903-457 PCT/US

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/John S. SOPKO, Reg. #41,321/	Date (YYYY-MM-DD)	2014-05-23
Name/Print	John S. Sopko	Registration Number	41,321

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.S./

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

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2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.S./

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13497690	MUÑOZ DE DIEGO ET AL.
	Examiner	**Art Unit**
	TAOFIQ A SOLOLA	1622

CPC				
Symbol			**Type**	**Version**
C07D	307 /	68	F	2013-01-01
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CPC Combination Sets						
Symbol			**Type**	**Set**	**Ranking**	**Version**
	/					
	/					

NONE (Assistant Examiner) (Date)	**Total Claims Allowed:** 10	
/TAOFIQ A SOLOLA/ Primary Examiner.Art Unit 1622 6/17/14 (Primary Examiner) (Date)	O.G. Print Claim(s) 1	O.G. Print Figure --

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13497690	MUÑOZ DE DIEGO ET AL.
	Examiner	**Art Unit**
	TAOFIQ A SOLOLA	1622

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION	
CLASS	SUBCLASS	CLAIMED	NON-CLAIMED
549	485	C 0 7 D 307 / 68 (2006.01.01)	

CROSS REFERENCE(S)					
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)				

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	10	
/TAOFIQ A SOLOLA/ Primary Examiner.Art Unit 1622	6/17/14	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	--

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13497690	MUÑOZ DE DIEGO ET AL.
	Examiner	**Art Unit**
	TAOFIQ A SOLOLA	1622

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 10	
/TAOFIQ A SOLOLA/ Primary Examiner.Art Unit 1622 (Primary Examiner)	6/17/14 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure --

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13497690	MUÑOZ DE DIEGO ET AL.
	Examiner	Art Unit
	TAOFIQ A SOLOLA	1622

CPC- SEARCHED		
Symbol	Date	Examiner
C07D 307/68	6/17/2014	yo

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
549	485	11/7/2013	yo
updated		3/14/2014	yo
updated		6/17/2014	yo

SEARCH NOTES		
Search Notes	Date	Examiner
ISR of pct/NL10/50654; inventor	11/7/201	yo
updated	3/14/2014	yo
updated	6/17/2014	yo

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
549/ C07D	485/ 307/68	6/17/2014	yo

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Cesar Muñoz de Diego	Examiner:	Solola, Taofiq A.
Application No.:	13/497,690	Group Art Unit:	1622
Confirmation No:	1013	Docket:	903-457 PCT/US
Filing or § 371 (c) Date:	July 9, 2012	Dated:	June 13, 2014

For: METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

pls enter amdt 6/17/14 YD.

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Certificate of EFS-Web Transmission
I hereby certify that this correspondence is being transmitted to the U.S. Patent and Trademark Office via the Office's electronic filing system.

Dated: June 13, 2014

Signature /John S. Sopko/

AMENDMENT AND RESPONSE TO FINAL OFFICE ACTION PURSUANT TO 37 C.F.R. §1.116

Sir:

In response to the Final Office Action dated March 31, 2014, a reply to which is due June 30, 2014, please amend the above-identified application as follows:

Amendments to the Claims begin on page 2 of this submission.

Remarks/Arguments begin on page 5 of this submission.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

23869 7590 06/20/2014

Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

EXAMINER
SOLOLA, TAOFIQ A

ART UNIT	PAPER NUMBER
1622	

DATE MAILED: 06/20/2014

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/497,690	07/09/2012	Cesar Muñoz de Diego	903-457 PCT/US	1013

TITLE OF INVENTION: METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	09/22/2014

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

23869 7590 06/20/2014
Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/497,690	07/09/2012	Cesar Muñoz de Diego	903-457 PCT/US	1013

TITLE OF INVENTION: METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	09/22/2014

EXAMINER	ART UNIT	CLASS-SUBCLASS
SOLOLA, TAOFIQ A	1622	549-485000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ❑ Applicant certifying micro entity status. See 37 CFR 1.29 — NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ❑ Applicant asserting small entity status. See 37 CFR 1.27 — NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
- ❑ Applicant changing to regular undiscounted fee status. — NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
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Alexandria, Virginia 22313-1450
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/497,690	07/09/2012	Cesar Muñoz de Diego	903-457 PCT/US	1013

23869 7590 06/20/2014

Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

EXAMINER	
SOLOLA, TAOFIQ A	

ART UNIT	PAPER NUMBER
1622	

DATE MAILED: 06/20/2014

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

PART B - FEE(S) TRANSMITTAL

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Commissioner for Patents
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CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

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Hoffmann & Baron LLP
6900 Jericho Turnpike
Syosset, NY 11791

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

Thea Bachman VIA EFS	(Depositor's name)
/Thea Bachman/	(Signature)
September 18, 2014	(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/497,690	07/09/2012	Cesar Muñoz de Diego	903-457 PCT/US	1013

TITLE OF INVENTION: METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	09/22/2014

EXAMINER	ART UNIT	CLASS-SUBCLASS
SOLOLA, TAOFIQ A	1622	549-485000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 John S. Sopko
2 Hoffman & Baron, LLP
3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: FURANIX TECHNOLOGIES B.V.
(B) RESIDENCE: (CITY and STATE OR COUNTRY): AMSTERDAM, NETHERLANDS

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
☒ Issue Fee
☐ Publication Fee (No small entity discount permitted)
☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
☐ A check is enclosed.
☒ Payment by credit card. Form PTO-2038 is attached.
☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number 082461 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
☐ Applicant certifying micro entity status. See 37 CFR 1.29
NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
☐ Applicant asserting small entity status. See 37 CFR 1.27
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
☐ Applicant changing to regular undiscounted fee status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /John S. Sopko/ Date September 18, 2014
Typed or printed name John S. Sopko Registration No. 41321

Electronic Patent Application Fee Transmittal

Application Number:	13497690
Filing Date:	09-Jul-2012
Title of Invention:	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID
First Named Inventor/Applicant Name:	Cesar Muñoz de Diego
Filer:	John S. Sopko/Thea Bachman
Attorney Docket Number:	903-457 PCT/US

Filed as Small Entity

U.S. National Stage under 35 USC 371 Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Utility Appl Issue Fee	2501	1	480	480
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**480**

Electronic Acknowledgement Receipt

EFS ID:	20172764
Application Number:	13497690
International Application Number:	
Confirmation Number:	1013
Title of Invention:	METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID
First Named Inventor/Applicant Name:	Cesar Muñoz de Diego
Customer Number:	23869
Filer:	John S. Sopko/Thea Bachman
Filer Authorized By:	John S. Sopko
Attorney Docket Number:	903-457 PCT/US
Receipt Date:	18-SEP-2014
Filing Date:	09-JUL-2012
Time Stamp:	10:18:11
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$480
RAM confirmation Number	7731
Deposit Account	082461
Authorized User	SOPKO, JOHN S

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. 1.492 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Issue Fee Payment (PTO-85B)	903_457_ISSUE_FEE.PDF	100520 3dc8a96983a3374a6f6774487830d206a835a759	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30897 a351560b408d90b733bc2d80a47995e1dd33bb1b	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	131417		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Change(s) applied to document, /M.K./ 7/22/2014

Amendments to the Specification:

Please amend the paragraph beginning at page ~~6~~ 7, line ~~12~~ 15, as follows:

The esterification of 2,5-furan dicarboxylic acid is known. As a specific example for the manufacture of these esters, reference is made to US 2673860 wherein the diester is obtained by transesterification of another dicarboxylic acid ester in the presence of sulphuric acid. A more general description for the esterification of dicarboxylic acids is presented in US 2628249. Accordingly, the invention provides a process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140 °C, and esterifying the thus obtained product.

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ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 185 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

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Process integration for the conversion of glucose to 2,5-furandicarboxylic acid

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ABSTRACT

The development of biorefineries means that a key feedstock for many new processes will be sugars in various forms, such as glucose or fructose. From these feedstocks a range of chemicals can be synthesized using heterogeneous catalysis, immobilized enzymes, homogeneous catalysts, soluble enzymes, fermentations or combinations thereof. This presents a particularly interesting process integration challenge since the optimal conditions for each conversion step will be considerably different from each other. Furthermore, compared to oil-based refineries the feedstock represents a relatively high proportion of the final product value and therefore yield and selectivity in these steps are of crucial importance. In this paper using the conversion of glucose to 2,5-furandicarboxylic acid and associated products as an example, alternative routes will be compared with respect to achievable selectivity, and achievable yield.

Keywords: Biorefineries; Glucose isomerase; 5-Hydroxymethylfurfural; 2,5-Furandicarboxylic acid

1. Introduction

While the increasing cost of oil is driving particular interest in the production of new fuels from biomass there is little doubt that today of equal importance is the production of chemicals from biomass. Indeed for the supply of fuels in the future there are many potential sources aside from biomass. In a world with limited (or very expensive) oil it is less clear where the chemicals of the future will originate. There is currently an existing infrastructure based on the use of the seven established platform chemicals (toluene; benzene; xylene; 1,3-butadiene; propylene; ethene; methane). In the short term one could consider if we can use the same infrastructure and just create the seven chemicals from alternative sources. However in the longer term it will be necessary to devise new processes based on a different set of platform chemicals. One group will be based around glucose (the hydrolytic product of starch and therefore readily available from biomass). In a biorefinery it will be necessary to develop a structure which can manage a range of feedstocks, a range of technologies and a range of products. This presents a considerable challenge for design and optimization as well as process integration. In order to illustrate the complexity and the challenge that lies ahead we have studied one specific example with a defined starting and endpoint: the production of 5-hydroxymethylfurfural (HMF) or 2,5-furandicarboxylic acid (FDA) from glucose or fructose. Greatest value is obtained by going the whole way from glucose to FDA. However even in this small reaction pathway there are many alternative technologies. Some can be integrated together, some give the required yield and selectivity, some are difficult to implement and others are untested at scale. This illustrates very well the challenge that design engineers face. To date glucose finds its major use in food applications (as a feedstock for sorbitol and high fructose corn syrup). The possibility of non-food products like HMF or FDA implies the use of other technologies not governed by the strict

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food regulations. Nevertheless all the potential technologies (whether approved for food or non-food production) need to be able to overcome the pH and temperature instability and limited solubility in organic solvents. It is because of the nature of glucose therefore that one obvious starting point is to use enzymatic catalysis (water based and under mild conditions). In this paper we will review the alternative technologies and routes from glucose to FDA, and discuss some of the limitations and challenges.

2. Biomass as a raw material for biorefineries

Nature is producing vast amounts of biomass driven by sunlight via photosynthesis:

$$nCO_2 + nH_2O \rightarrow (CH_2O)_n + nO_2$$

However, utilization of biomass for producing chemicals and fuels is still in its infancy with only 3.5% being used for food or non-food purposes. Plant biomass consists mainly of carbohydrates, lignin, protein and fats. Out of an estimated 170 billion metric tons of biomass produced every year roughly 75% are in the form of carbohydrates which makes biomass carbohydrates the most abundant renewable resource (Röper, 2002). Together with their amenability towards enzymatic processes this makes carbohydrates the center of attention when looking for new and greener feedstocks to replace petroleum for producing commodity chemicals as well as fuels. In plant biomass most of the carbohydrates are stored as sugar polymers such as starch, cellulose or hemicellulose.

Starch is the second largest biomass produced on earth and commonly found in vegetables, such as corn, wheat, rice, potatoes and beans. The total world production in 2004 was 60 million tons of which more than 70% came from corn. Starch consists of chains of glucose molecules, which are linked together by α-1,4 and α-1,6 glycosidic bonds. The two major parts of starch are amylose (20–30%), essentially linear α-1,4 glucan chains and amylopectin (70–80%), a branched molecule containing 4–5% α-1,6 linkages.

Starch is industrially hydrolyzed to glucose by the three enzymes: α-amylase, glucoamylase, and pullulanase (Schäfer et al., 2007). Bacterial α-amylases (EC 3.2.1.1) catalyze the hydrolysis of internal α-1,4 glycosidic bonds. This reduces the viscosity, which is necessary for further processing. Glucoamylase (EC 3.2.1.3) is an exo-amylase that is added to the partly hydrolyzed starch after liquefaction. Glucose units are removed in a stepwise manner from the non-reducing end of the molecule. The third enzyme is pullulanase (EC 3.2.1.41). Industrially used pullulanases are heat stable enzymes, which act simultaneously with glucoamaylase during saccharification. Pullulanases catalyze the hydrolysis of the α-1,6 linkages in amylopectin, and especially in partially hydrolysed amylopectin. Typical process conditions for production of glucose from starch are given in Table 1.

Cellulose is a glucose polymer consisting of linear chains of glucopyranose units linked together via β-1,4 glucosidic bonds. Unlike starch, cellulose is a crystalline material where inter- and intra-molecular hydrogen bonding gives rise to the very stable cellulose fiber. Hemicellulose is a polysaccharide consisting of short highly branched chains of different carbohydrate units, including five- as well as six-carbon units (e.g. xyloses, galactose, glucose, mannose and arabinose). Hemicelluloses are much easier to hydrolyze than cellulose. The structured portion of biomass, such as straw, corn stover, grasses and wood, is made of lignocellulose composed mainly of cellulose (30–60%), hemicellulose (20–40%) and lignin (10–30%). Both cellulose and hemicellulose consist of carbohydrate components whereas lignin is a highly branched aromatic polymer.

Currently, there is intensive research on the use of lignocellulosic raw material as a biomass source for producing chemicals and fuels (as exemplified by many of the other articles in this special edition). However this research still faces considerable challenges due to lignocellulose being remarkably resistant towards hydrolysis and enzymatic attack (Peters, 2007). Energy demanding thermal pre-treatment of lignocellulose is necessary in order to break up the extremely stable cellulose–hemicellulose–lignin composites prior to adding cellulose-hydrolyzing enzymes and the current situation does not allow the efficient use of lignocellulosic materials. Nevertheless, there is little doubt given the great abundance of lignocellulose that in the future this will become an attractive option. It is therefore important to continue to develop processes that can economically convert lignocellulose into chemicals. Moreover, glucose is one of the most abundant monosaccharides in biomass, accessible by enzymatic or chemical hydrolysis from starch, sugar or cellulose. Furthermore, a range of chemical products can be obtained from glucose which gives it a key position as a basic raw material/building block.

3. Glucose – a biorefinery building block

Fermentation of polymer building blocks is already under commercial introduction. For example, Cargill produces lactic acid by fermentation and products based on polylactic acid are being introduced to the market. Several companies focus on succinic acid as a polymer building block, but also as a potential raw material for chemicals (e.g. butanediol). 1,3-propandiol is marketed by DuPont Tate & Lyle BioProducts for Sorona™ polytrimethylene terephthalate (PTT) polyester. Likewise Cargill is working on developing 3-hydroxypropionic acid (3-HP). 3-HP is a potential raw material for existing chemicals such as propanediol and acrylic acid. Polyhydroxyalkanoate (PHA) is marketed by Telles, a J/V between ADM and Metabolix. Roquette, the French starch producer, has commercialized isosorbide, a derivative of sorbitol. Isosorbide is used as a co-monomer for high temperature polyethylene terephthalate. However, even if commercialization of polymer building blocks made by fermentation is commercially underway, the technology has certain drawbacks such as loss of carbon as CO_2, low yields and difficult recovery of the products

Table 1 – Process conditions for production of glucose from starch.

Process	Temperature (°C)	Dry substance content (%)	pH	Process time (h)
Jet cooking/dextrinization	105/95	30–35	5.2–5.6	0.1/1–2
Saccharification	60	30–35	4.3–4.5	25–50

from the fermentation broth. The technology presented here (combined chemical and enzymatic catalysis from glucose) has the potential to overcome these problems and represents a promising next generation technology.

One chemical transformation (besides fermentations) of carbohydrate monomers for the degradation of functionality is the dehydration reaction. This facilitates the removal of some of the functional groups in carbohydrates and allows the formation of defined building blocks. Triple dehydration of glucose yields HMF—a building block molecule that subsequently can be transformed into a multitude of bio-based chemicals. By a subsequent hydration reaction or an oxidation, HMF can be converted into levulininc acid or FDA, respectively Both of these molecules are on the list of the 12 bio-based platform chemicals identified as being of highest potential to be converted into new families of useful molecules (Werpy and Petersen, 2004). In the following we will focus on the dehydration of glucose to HMF as an example of the need to efficiently combine enzymatic aqueous processes with inorganic heterogeneous catalytic processes that have so far mainly been developed for running reactions within the petrochemical industry.

HMF is in itself a rather unstable molecule. It can be found in natural products such as honey and a variety of heat processed food products formed in the thermal decomposition of carbohydrates. Interestingly, HMF can be chemically converted into a range of other valuable chemicals. The oxidation of HMF is of particular interest. Here, the ultimate objective is to obtain FDA as suggested by Schiwek et al. (1991). The diacid can be used as a replacement for terephthalic acid in the production of polyethylene terephthalate and polybutylene terephthalate (Gandini and Belgacem, 1997; Kunz, 1993) which was recently reviewed by Moreau et al. (2004). The partially oxidized compounds can also be used as polymer building blocks although these are more difficult to produce selectively. FDA is a chemically very stable compound. Its only current uses are in small amounts in fire foams and in medicine where it can be used to remove kidney stones.

Several extensive reviews describing the chemistry of HMF and its derivatives have been reported (see Fig. 1). The most recent review focuses on chemical transformation of biomass to a variety of chemicals with particular emphasis on the dehydration of monosaccharides giving either furfural (from pentoses) or HMF from hexoses, respectively (Corma et al., 2007). Moreau et al. (2004) described the recent catalytic advances in substituted furans from biomass and focused especially on the ensuing polymers and their properties. A review by Lewkowski (2001) on the chemistry of HMF and its derivatives also appeared recently. Two other relevant reviews are from Cottier and Descotes (1991) and Kuster (1990).

The mechanism for the dehydration of fructose to HMF has been interpreted to proceed via two different routes; either via acyclic compounds or cyclic compounds (Haworth and Jones, 1944; Kuster, 1990; Van Dam et al., 1986; Antal et al., 1990). Besides HMF, the acid-catalyzed dehydration can lead to several other by-products such as insoluble polymers, called humins or humic acids. In an industrial process it is very important to find the right process conditions that avoid the formation of humins as these, besides lowering the selectivity of the reaction, potentially can clog up your reactor or deactivate the heterogeneous catalysts.

In spite of all the research carried out within this area an efficient way of producing HMF or its corresponding dicarboxylic acid, FDA, still remains to be found. Traditionally, chemists have been struggling with finding an inexpensive way of producing pure HMF. Given the immense field of its application, it is interesting that relatively few of the listed reviews have described the challenges that might be faced in

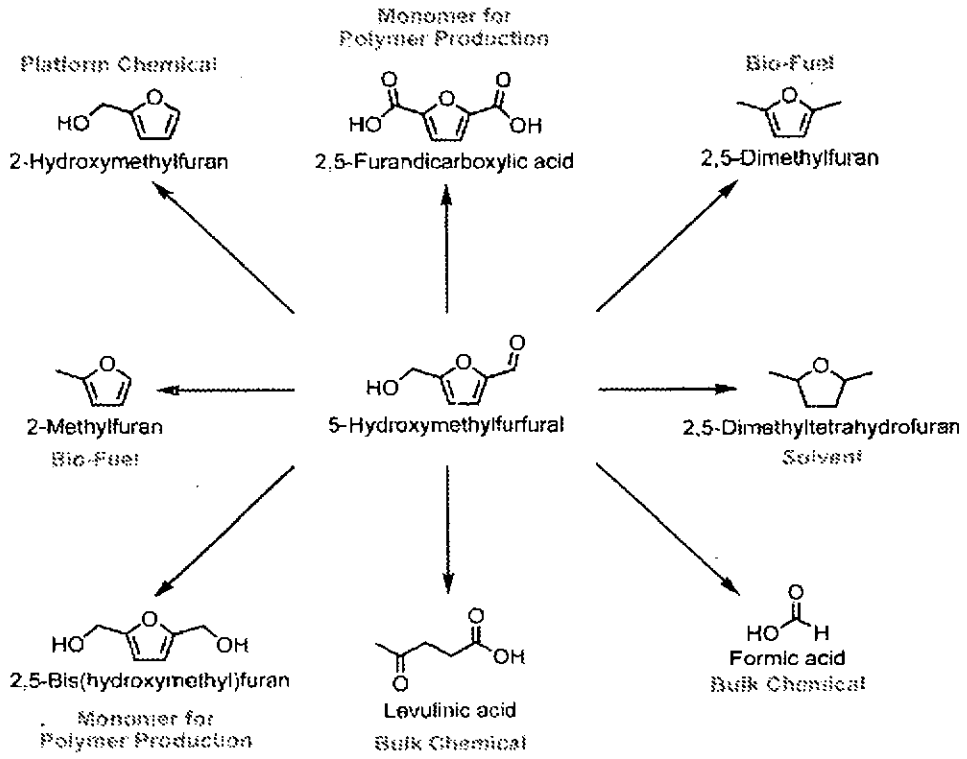

Fig. 1 – HMF as a precursor for a range of commercial chemicals.

Table 2 – Typical reaction conditions for immobilized glucose isomerase.

Process	Temperature (°C)	Dry substance content (%)	pH	Process time (h)
Isomerization	50–60	40–50	7–8	0.3–3

a biorefinery manufacturing HMF or its derivatives. The most likely biorefinery scenario will not be restricted to one product but make a series of high and low value products (including fuel). This allows the biorefinery to shift focus from one product to another if the market changes. In the case of HMF or FDA production this means that producing purely HMF or FDA is not the ultimate target and side-streams producing other valuable products besides HMF or FDA can actually be of benefit. One potential by-product of value is levulinic acid. This is formed via a rehydration of HMF to give levulininc acid along with formic acid. Both of these molecules are valuable products that are potentially worth isolating as side streams. In this respect the goal of completely selective dehydration may in the future be misplaced.

The synthesis of HMF is based on the acid-catalyzed triple dehydration of C6-sugar monomers, mainly glucose and fructose. However, various polysaccharides have also been reported as HMF sources (Rapp, 1987). The most convenient method for the preparation of HMF is by dehydration of fructose. When starting from ketohexoses (such as fructose) the dehydration reaction proceeds more efficiently and selectively. This can be explained by aldohexoses (such as glucose) only being able to enolyze to a low degree which is considered the limiting step in the production of HMF from glucose. However, glucose is the favored source of HMF due to the lower cost of glucose compared to fructose. Fructose may be obtained by enzyme or acid-catalyzed hydrolysis of sucrose and inulin or by the isomerization of glucose to fructose. Inulin is a linear β-2,1 linked fructose polymer which is terminated by a single glucose unit. It is found as a food reserve in a number of plants including Jerusalem artichoke and chicory. Industrially fructose is produced from glucose by the enzyme glucose isomerase (EC 5.3.1.5). The equilibrium conversion under industrial conditions is 50% making chromatographic separation necessary in order to obtain the industrial product of 55% fructose, which has sweetness similar to sucrose. Glucose isomerase is used industrially as an immobilized enzyme with typical reaction conditions as shown in Table 2.

Commercial immobilized glucose isomerase preparations used in a packed column have half-lives between 100 and 200 days. Most columns therefore last for more than 1 year and productivities are typically around 15 tons of syrup dry substance/kg immobilized enzyme

4. Case studies

4.1. Case 1: conversion of glucose/fructose to HMF

To date most of the work regarding the acid-catalyzed conversion of fructose, and to a less extent glucose, into HMF has been carried out in aqueous reaction media. Obviously water being very abundant and non-hazardous is the preferred solvent of choice when exploring green and sustainable chemistry. Furthermore water is a good solvent for dissolving the monosaccharide substrates (fructose and glucose) as well as the product, HMF. However the dehydration of fructose to yield HMF in aqueous media is hampered by a competitive rehydration process resulting in the by-products levulinic acid and formic acid. In addition soluble and insoluble polymerization products (humins), that are thought to arise from the self- and cross-polymerization of HMF, fructose and other by-products seem to be more pronounced in an aqueous reaction medium than an organic one (Van Dam et al., 1986). Nevertheless, several interesting papers have been published on the dehydration of fructose into HMF. The conversion of glucose into HMF is more difficult and as a result there are only a few publications on this process.

4.1.1. *Aqueous media*

Several mineral acids such as HCl, H_2SO_4 and H_3PO_4 have been employed in the homogeneous catalyzed dehydration of fructose to yield HMF (Newth, 1951; Mednick, 1962; Román-Leshkov et al., 2006). So far, however, the yield and selectivity of reactions carried out in aqueous reaction media are not comparable to those observed in aprotic high-boiling organic solvents such as DMSO where the solvent also serves as the catalyst (Musau and Munavu, 1987). Despite high yields and selectivity, the cost of removing high-boiling solvents makes these solvents unsuitable for industrial and large-scale processes. Heterogeneous catalysts have, due to separation and recycling considerations, drawn more attention than homogenous catalysts. The use of various acidic heterogeneous catalysts such as niobic acid ($Nb_2O_5 \cdot nH_2O$) and niobium phosphate ($NbOPO_4$) have been reported to have an intermediate selectivity of about 30% for the production of HMF at about 80% conversion of fructose (Carniti et al., 2006). Zirconium and titanium phosphates/pyrophosphates have been shown to have a very high selectivity of up to 100% at 100 °C in a period of 18 min for the formation of HMF in water. However as the reaction time increases, the selectivity drops fast which is thought to be due to the formation of polymeric by-products. Additionally, titanium oxides (TiO_2), zirconium oxides (ZrO_2) and H-form zeolites catalyze the dehydration reaction (Moreau et al., 1996). Especially interesting is the direct conversion of glucose to HMF which can be enhanced up to 5-fold compared to the hydrothermal dehydration, by employing an α-TiO_2 at 200 °C (Watanabe et al., 2005a,b). The main disadvantage with these catalysts seems to be the high temperature needed in order for the reaction to proceed without limited selectivity and conversion rates. Highly acidic cation-exchange resins such as those derivatized with sulfonic acid groups are also effective catalysts, providing the acidity of mineral acids together with the advantages of the heterogeneous catalysts (Rigal et al., 1981). These, often polystyrene based resins, can only tolerate temperatures up to around 130 °C, which reduces the range of their application. However this temperature range seems to be sufficient to overcome the activation energy barrier, when simultaneously applying the effect of microwave heating (Qi et al., 2008).

4.1.2. *Modified aqueous media and two-phase systems*

Phase modifiers have within the last couple of years proved very effective in promoting the conversion of fructose to HMF. Polar organic solvents that are miscible with water are added in order to increase the rate of the reaction to HMF and reduce the rate of the rehydration process forming by-products (Van

Dam et al., 1986). Commonly employed aqueous phase modifiers are acetone, DMSO and polyethylene glycol (PEG) (Qi et al., 2008; Chheda et al., 2007; Van Dam et al., 1986). A further modification of the aqueous phase system is the introduction of a second immiscible phase to create a two-phase reaction system. An organic phase extracts the HMF from the aqueous phase as it is produced and consequently reduces the formation of rehydration and polymeric by-products. Even with an initial concentration of fructose as high as 50 wt%, remarkable results with selectivity of 77% and a conversion of 90% at 180 °C with HCl as the catalyst have been reported. In comparison similar conditions in water resulted only in a selectivity of 28% and a conversion of 51% (Román-Leshkov et al., 2006).

4.1.3. *Non-aqueous organic solvents*

Until now, the best results for the dehydration of fructose to HMF have been made in high-boiling organic solvents. The low concentration of water prevents the rehydration of HMF to levulinic acid and formic acid. Iodine catalyzes the dehydration of the fructose part of sucrose in anhydrous DMF at 100 °C. Glucose is unaffected under the same conditions (Bonner et al., 1960). High selectivity has also been obtained when using PEG-600 as a solvent together with catalytic HCl. With the acid present a 1:1 solution of fructose and PEG-600 can be obtained at 85 °C (Kuster and Laurens, 1977). The first really high yields were reported by Nakamura and Morikawa (1980) using a strongly acidic ion-exchange resin as the catalyst in DMSO at 80 °C. These conditions gave a yield of 90% after 8 h. The rate of the reaction was strongly affected by the type of resin used (Nakamura and Morikawa, 1980). Quantitative yields, without the use of a catalyst, were reported soon after in DMSO at 100 °C for 16 h (Brown et al., 1982). Good results were also obtained during an investigation of the optimum fructose concentration in DMSO. With 8.5 molar equivalents of DMSO with respect to fructose, a yield of 92% was obtained at 150 °C without any catalyst after 2 h (Musau and Munavu, 1987).

None of the above examples are suitable for production on a large-scale. High-boiling aprotic solvents such as DMSO, DMF and NMP are all miscible with water as well as many other common organic solvents. This makes separation of the desired products very difficult. Furthermore, both DMF and NMP are considered to be teratogenic.

4.1.4. *Supercritical/subcritical solvents*

Since the best results for the dehydration of hexoses to HMF have been in high-boiling organic solvents, the use of low-boiling solvents in their sub- or supercritical state would be an interesting alternative. Subcritical water has emerged in recent years as a feasible alternative to organic solvents at larger scale. Its unique intrinsic acidic and basic properties, makes it particularly interesting as a reaction medium for the dehydration of carbohydrates. When glucose is dehydrated in pure subcritical water, HMF is formed with greater selectivity than when using sulfuric acid or sodium hydroxide as catalysts under the same pressures and temperatures (Simkovic et al., 1987). Watanabe et al. (2005a) explored the use of different TiO_2 and ZrO_2 catalysts in highly compressed water. The anatase-TiO_2 catalyst showed both basic and acidic properties and catalyzed the conversion of glucose to HMF. Yields were only about 20%, but the selectivity was more than 90%. The basic properties of the catalyst were thought to catalyze the isomerization of glucose to fructose, whereas the acidic properties were thought to catalyze the dehydration (Watanabe et al., 2005b). Yields of up to 50% were obtained when using fructose as the starting sugar and different zirconium phosphates as catalysts in subcritical water. No rehydration products were observed, yet the highest selectivity was not more than 61%. By-products were humins and furaldehyde (Asghari and Yoshida, 2006). Interesting results have recently been reported on the catalytic effect of H_3PO_4, H_2SO_4 and HCl in the direct conversion of glucose to HMF in water at 523 K. It was concluded that the weakest acid, H_3PO_4, was the best catalyst for the conversion of glucose into HMF and the strongest acid, HCl, was the best catalyst for the conversion of HMF to levulinic acid. The best yield for HMF was 40% (Takeuchi et al., 2008). More extensive studies on the kinetics of the dehydration of D-glucose and D-fructose in sub- and supercritical water have been made as well as the behavior of HMF under similar conditions (Kabyemela et al., 1999; Asghari and Yoshida, 2007; Chuntanapum et al., 2008).

Nevertheless, the overall results from sub- and supercritical water have so far been unsatisfactory in terms of yields. Bicker et al. (2003) explored other low-boiling solvents such as acetone, methanol and acetic acid. An acetone/water mixture at 180 °C and 20 MPa gave 99% conversion of fructose and a selectivity of 77% to HMF. This excellent result was explained by the structural similarities between acetone and DMSO, which would promote the furanoid form of fructose and hence favor the formation of HMF. The authors also propose a continuous process for the reaction (Bicker et al., 2003, 2005).

4.1.5. *Ionic liquids*

Another attractive alternative to high-boiling organic solvents is the use of ionic liquids. Their unique physical properties such as negligible vapor pressure and non-flammability make them particularly suitable as solvents for large-scale production. There is a possibility to design and functionalize the ions of the ionic liquid, giving them ability to work both as solvent and reagent for certain reactions. There are several examples of ionic liquids that have the ability to solubilize natural polymers such as cellulose, starch and chitin. This opens an excellent opportunity to convert crude biomass into fine chemicals (Liu et al., 2005; El Seoud et al., 2007).

The first dehydrations of fructose and glucose with the help of ionic liquids date back 25 years. Fructose was dehydrated in the presence of pyridinium chloride to HMF in high purity with 70% yield. The corresponding result for glucose was only 5% (Fayet and Gelas, 1983). In 1-butyl-3-methylimidazolium tetrafluoroborate and 1-butyl-3-methylimidazolium hexafluorophosphate, yields up to 80% from fructose were obtained using DMSO as a co-solvent and Amberlyst-15 resin as the catalyst. The DMSO helped to solubilize the starting fructose and the reaction was faster than in DMSO alone. Performing the reaction in 1-butyl-3-methylimidazolium tetrafluoroborate alone gave a yield of 50% within 3 h (Lansalot-Matras and Moreau, 2003). The best results so far from fructose were made by using the acidic 1-H-3-methylimidazolium chloride as reaction medium. This acted both as solvent and catalyst giving a yield of 92% after 15–45 min at 90 °C. There was no sign of HMF decomposition and glucose remained completely unreacted (Moreau et al., 2006). Recently remarkably good results were found using the ionic liquid 1-ethyl-3-methylimidazolium chloride together with $CrCl_2$, giving a total yield of 70% HMF directly from glucose and virtually no levulinic acid. The authors propose that the actual catalytic specie is the $CrCl_3^-$ ion formed together with the solvent

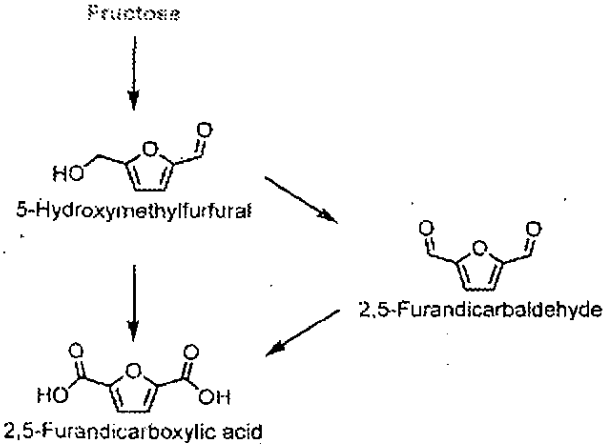

Fig. 2 – Oxidation of HMF to DFF and FDA.

and that it catalyzes the isomerization of β-glucopyranose to fructofuranose, which is subsequently dehydrated to HMF (Zhao et al., 2007). Bao et al. (2008) concluded that ionic liquids with a Lewis acid moiety were more efficient than those with a Brønsted acid counterpart when dehydrating fructose. These ionic liquids were also successfully immobilized on silica, giving a yield of up to 70% from fructose to HMF and completely retained their catalytic activity after five reaction cycles (Bao et al., 2008)

4.2. *Case 2: HMF oxidation to 2,5-diformylfuran and FDA*

FDA has been identified by the U.S. Department of Energy (DOE) biomass program as one of the 12 chemicals that in the future can be used as a feedstock from biomass in biorefineries (Werpy and Petersen, 2004). Due to the presence of the two carboxylic acid groups, FDA is considered to be a biorenewable building block to form polymers from biomass and therefore become an alternative to terephthalic, isophthalic and adipic acids, which are all produced from fossil fuels. Sugars in the form of mono- and disaccharides are easily available from biomass. The hexose type monosaccharides such as glucose and fructose can be catalytically dehydrated into HMF (Corma et al., 2007; Gallezot, 2007; Moreau et al., 2004). HMF can then be oxidized into FDA using a variety of routes and reaction types with stochiometric amount of oxidants. Most of them are described in a review by Lewkowski (2001), including electrochemical oxidation, use of barium and potassium permanganates, nitric acid and chromium trioxide. In this section we will focus on the recently reported catalytic routes for the oxidation of HMF into FDA.

4.2.1. *Oxidation of HMF to DFF*

Though production of FDA from HMF has been of great interest recently, there are few papers on catalytic aerobic oxidation of HMF. In the catalytic route to form FDA the partially oxidized intermediate 2,5-diformylfuran (DFF) is often observed (Fig. 2).

The dialdehyde is a useful product to form other derivatives, and a number of studies have reported on the selective formation of DFF. Thus, Halliday et al. (2003) reported oxidation of HMF to DFF using an in situ reaction protocol where HMF was directly generated from fructose and not isolated. Hence, using ion-exchange resins and, then, VOP-type catalysts the authors obtained DFF with a maximum yield of 45% based on fructose (Halliday et al., 2003). Carlini et al. (2005) reported that HMF, as a starting reagent or produced one pot from fructose, was oxidized to the corresponding dialdehyde in water with methylisobutylketone (MIBK), as well as pure organic solvents, with vanadyl phosphate (VPO) based catalysts (Zr, Nb, Cr, Fe modified) as such or using a TiO_2 support at 75–200 °C and 1 MPa. However, the reported yields were low (H_2O:MIBK = 0:30–5:30, HMF conversion 3–10%, selectivity to DFF 100–60%, respectively). Considering the oxidation as a stand-alone reaction and changing the solvents to less polar ones (benzene, toluene) better conversion rates and selectivity were obtained, and using MIBK as a solvent lead to 98% conversion with 50% selectivity. However, in DMF the results are even better (at 150 °C) giving 84% conversion and 97% selectivity.

4.2.2. *Oxidation of HMF to FDA*

The above-described DFF may either be used as a valuable by-product or as an intermediate for obtaining FDA. On the other hand, catalytic reactions leading to the formation of FDA are also reported

Partenheimer and Grushin (2000) obtained DFF from HMF using metal bromide catalysts (Co/Mn/Zr/Br). The reactions were carried out in acetic acid at atmospheric pressure and also at 70 bar; the yields were 57% and 63% with the conversion of HMF 98% and 92%, respectively. Cobalt as a catalyst was also used by Ribeiro and Schuchardt (2003). Using cobalt acetylacetonate as a bi-functional acidic and redox catalyst encapsulated in silica in an autoclave at 160 °C, they obtained FDA, from fructose via HMF formation, with 99% selectivity to FDA at 72% conversion of fructose. By in situ oxidation of HMF to FDA starting from fructose, Kröger et al. (2000) described a way of producing FDA via acid-catalyzed formation and subsequent oxidation of HMF in a MIBK/water mixture using solid acids for fructose transformation and PtBi-catalyst encapsulated in silicone and swollen in MIBK. The reaction was carried out in a reactor divided with a PTFE-membrane in order to prevent the oxidation of fructose. However, though in principle the integration process has been described, the yields remain quite low. The resulting yield of FDA was 25% based on fructose. In the oxidation of HMF to FDA the use of noble metals was first studied by Vinke et al. (1991). Here, mainly Pd, Pt, Ru supported on different carriers were used as the aerobic oxidation catalysts. Although all the noble metals revealed catalytic activities, only Pt supported on Al_2O_3 remained stable and active and gave quantitative yields of FDA. The reactions were carried out in water at pH 9 using a reaction temperature of 60 °C and a partial oxygen pressure of 0.2.

4.2.3. *Oxidation of HMF to FDA derivatives*

A new approach to the oxidation of HMF has been reported recently by Taarning et al. (2008) using methanol as both solvent and reagent. They performed a reaction with a gold nanoparticle catalyst in an autoclave at 130 °C and 4 bars of dioxygen, and obtaining FDA with 98% yield (according to GC analysis) and 60% isolated yield after sublimation.

5. Process technology

Table 3 indicates some of the key features of possible routes for the conversion of fructose to HMF. A number of observations can be made:

Table 3 – Key features of possible routes for the conversion of fructose to HMF.

Mode of operation[a]	Catalyst[b]	Temp.	Fructose concentration	Solvent media[c]	Highest yield	Reference
B	Hetero.	80 °C	3–4% (w/w)	Water, MIBK	41%	Carlini et al. (2005)
B	Homo.	170 °C	10% (w/w)	Water, DMSO, MIBK, 2-butanol, DCM	87%	Chheda et al. (2007)
B	Homo.	90 °C	3–50% (w/w)	$HMIM^+Cl^-$	92%	Moreau et al. (2006)
B	Hetero.	165 °C	10% (w/w)	Water, MIBK	69%	Moreau et al. (1996)
B	Hetero.	80 °C	6% (w/w)	Water	42%	Carlini et al. (2004)
			3% (w/w)		59%	
B	Homo.	180 °C	30% (w/w)	Water, DMSO, PVP, MIBK, 2-butanol	76%	Román-Leshkov et al. (2006)
			50% (w/w)		71%	
B	Hetero.	90 °C	10% (w/w)	Water, DMSO, PVP, MIBK, 2-butanol	59%	Román-Leshkov et al. (2006)
			30% (w/w)		54%	
B	Hetero.	110 °C	6–10% (w/w)	Water	31%	Carlini et al. (1999)
B		100 °C	6–10% (w/w)	Water, MIBK	74%	
C		85 °C	10–20% (w/w)	Water	26%	
B	Hetero.	100 °C	6% (w/w)	Water	85%	Benvenuti et al. (2000)
C	Hetero.	165 °C	0.5–3.5% (w/w)	Water, MIBK	–	Rivalier et al. (1995)

[a] Process is continuous (C) or batch (B).
[b] Catalyst is homogenous (homo.) or heterogenous (hetero.).
[c] Solent media are: methylisobutylketone (MIBK), dimethyl sulfoxide (DMSO), poly(1-vinyl-2-pyrrolidinone) (PVP), dicholormethane (DCM), and 1-H-3-methyl imidazolium chloride ($HMIM^+Cl^-$).

- Catalyst type
  A variety of catalysts like mineral and organic acids, salts, and solid acid catalysts such as ion-exchange resins and zeolites have been used in the dehydration reaction. The homogeneous acid-catalyzed processes are frequently associated with low selectivity (30–50%) for HMF at a relatively high conversion (50–70%) (Carlini et al., 1999). Moreover, problems related to separation and recycling of the mineral acid as well as of plant corrosion are expected. Thus, recent research has been based on heterogeneous acid catalysts which have considerable potential for industrial application (Carlini et al., 1999).
- Mode of operation
  The dehydration process has mostly been studied in batch operated reactors. Few researchers have examined a continuous process. One exception is the work reported by Kuster and Laurens (1977), who developed a continuous homogeneous catalyzed process for dehydration of fructose to HMF by using a tube reactor with polyethyleneglycol-600 as the solvent. Dehydration of fructose in a continuous stirred tank reactor with phosphoric acid and MIBK as a solvent was also reported by Kuster and van der Steen (1977).
- Media
  The dehydration of hexoses and pentoses has been studied in water, organic solvents, biphasic systems, ionic liquids, and near- and supercritical water. The most convenient solvent for dehydration of fructose to HMF is water. However, water is the reactant in the reverse reaction. Moreover, with the presence of water, HMF decomposes to levulinic acid, formic acid and humins. Organic solvents are thus introduced to improve the dehydration reaction by shifting the equilibrium and suppressing HMF hydrolysis. Relatively high yields were reported for the use of DMSO with ion-exchange catalysts (Nakamura and Morikawa, 1980; Rigal and Gaset, 1985) and quantitative yields of HMF were also reported by heating fructose in the absence of catalyst (Brown et al., 1982; Musau and Munavu, 1987). In spite of the advantages of using DMSO, the difficulties of separation limit its application. Moreover, possible toxic sulfur containing by-products from decomposition of DMSO may cause a risk to health and the environment (Moreau et al., 2004). A biphasic reactor system has been developed to suppress HMF degradation by using organic solvent to separate HMF immediately from the reaction medium as it forms. Consequently some work has been carried out to find the proper extraction solvent. Amongst the solvents reported, MIBK is the most commonly used solvent for extraction of HMF. Due to its relatively low-boiling point, it is relatively easy to separate HMF from MIBK. In general, poor HMF partitioning in the organic solvents leads to the use of large amounts of solvent. Purification of the diluted HMF product thus causes large energy expenditure in the subsequent process (Chheda et al., 2007).

5.1. *New technology*

Román-Leshkov et al. (2006) developed a cost-effective method to produce HMF using a biphasic batch reactor system with phase modifiers. They obtained D-fructose to HMF in high yields (>80%) at high fructose concentrations (10–50 wt%) and delivered the product in a separation-friendly solvent. In the biphasic reactor system, DMSO and/or poly(1-vinyl-2-pyrrolidinone) (PVP) were added as modifiers to suppress the formation of dehydration by-products in the aqueous phase with HCl as the acid catalyst. The product was continuously extracted into an organic phase MIBK modified with 2-butanol to enhance partitioning from the reactive aqueous solution. In this study, they reported an improvement in selectivity from 60 to 75% by adding small amounts of aqueous phase modifiers (such as DMSO and PVP) in the biphasic reactor system. Additionally, by optimizing the partitioning of HMF product into the organic phase, the process not only minimized the degradation of HMF in the aqueous phase, but also achieved efficient product recovery.

Zhao et al. (2007) used a metal chloride catalyst in an ionic liquid for the dehydration of HMF. In this reaction, the only water present in the system was from the dehydration of fructose to HMF reaction, which indicated that the conditions for HMF degradation to levulinic and formic acids were not met. By using this metal chloride in ionic liquid, the reaction could take place at reduced temperature, 80 °C for fructose dehy-

dration, and 100 °C for glucose. 90% yield was achieved from fructose and 70% yield from glucose.

Bicker et al. (2003) reported the use of benign solvents such as acetone, methanol or acetic acid in a sustainable process outline. They reported the dehydration of D-fructose to HMF in sub- and supercritical acetone/water mixtures. The use of this reaction media resulted in higher yields of HMF (77% selectivity, 99% conversion). No solid impurities (humins) were formed. The authors also claimed the potential for a technical process based on this low-boiling point solvent, whereby a price for HMF of about 2 Euro/kg could be achieved if fructose was available at a price of around 0.5 Euro/kg.

However all these new technology approaches for making HMF from fructose have been carried out at a small scale. On a larger scale Rapp has reported yields of ~2.5 kg HMF from aqueous dehydration of fructose (Rapp, 1987). The production of HMF, close to a kg scale, has also been reported using DMSO as the reaction media (M'Bazoa et al., 1990). Nevertheless since high selectivity is crucial for implementing this reaction on an industrial scale, the recent research has been highly focused on alternative routes for improving the selectivity of the dehydration reaction.

5.2. *Process implementation, integration and scale-up*

In order to comply with the demands of efficient and specific conversions of the chemical reactants in a biorefinery with a minimum of economic cost, a special focus on process implementation, integration and scale-up must be paid. The development of combined biological and chemical catalytic reactions without intermediate recovery steps has the potential to become an important future direction for carrying out sustainable organic syntheses (Hailes et al., 2007).

The synthesis of a variety of important chemical building blocks involves multistep reactions often catalyzed by a chemical or biological catalyst. In many cases, the optimal operating conditions are rather different for the individual steps of such synthesis reactions. However, it could prove favorable if such reaction steps are combined or integrated, allowing them to occur concurrently, in proximity to one another, and at or close to their respective optimal operating conditions. Also from an engineering point of view, integration of unit operations could contribute to among other things simpler design, less equipment and less piping (Koolen, 1998). Furthermore, integration could reduce operating time and costs as well as consumption of chemicals and use of energy (Bruggink et al., 2003). An important aspect of process integration is the different working condition for the individual reactions. When the aim is to match different reactions involving enzymes, important factors such as enzyme stabilities, reaction rates, reaction media (e.g. pH, temperature, pressure) and reactor design must be considered. Tools to aid integration of different processes include reactor compartmentalization (Fournier et al., 1996; Byers et al., 1993; de Jong et al., 2008; Chen et al., 1997), medium engineering (Bao et al., 2008; Zhao et al., 2007), ISPR (Freeman et al., 1993; Woodley et al., 2008), optimized reactor designs (Stankiewicz and Moulijn, 2003) and multifunctional catalysts (Bruggink et al., 2003).

The conversion of glucose to FDA involves three steps, each with different optimal physical and chemical parameters like pH, temperature and pressure. Furthermore, the catalysts are of different nature with a bio-catalyst (enzyme) in the isomerization of glucose to fructose and a number of potential chemical catalysts of both heterogeneous and homogeneous nature in the following dehydration and oxidation reactions. While the potential for integration exists, it is only via an economic evaluation that such options can be further considered. A valuable process implementation tool to achieve both qualitative and quantitative understanding of the reaction processes and their potential for improvement is mathematical modeling. A good model should facilitate knowledge and understanding of the chemical reactions and include in a quantitative manner the most important physical and chemical governing parameters. As more is understood about the alternative synthetic routes to FDA, the appropriate modeling tools will also need to be developed.

6. Future outlook

With the implementation of biorefineries and increased interest in biofuel it is clear that the associated sugar-based chemistry will provide a rich variety of chemical products as building blocks for higher value molecules. The extent to which this happens depends on two factors. First the economics of the biorefinery will act as a driver in many cases to provide a means to develop higher value products alongside fuel. Ultimately the value of each product tree will need to be evaluated alongside the associated cost of implementing additional technology. Secondly it is clear that new technology and improved catalytic methods are required to produce high value building blocks such as FDA. Some of the more promising routes lie in new media such as ionic liquids but it is also clear that far higher selectivities are required. In this respect enzyme based catalysis will have a particular and likely expanding role in the future development of biorefinery technology. Finally, the implementation of new technology for biorefineries must be evaluated within the context of green chemistry and the necessary environmental requirements. For example the selection of organic solvents and catalysts must adhere to the criteria for sustainable processing. This is essential in order to ensure that new processes use sustainable processing methods as well as making use of sustainable resources.

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THE ELECTROCHEMICAL OXIDATION OF 5-HYDROXYMETHYLFURFURAL WITH THE NICKEL OXIDE/HYDROXIDE ELECTRODE

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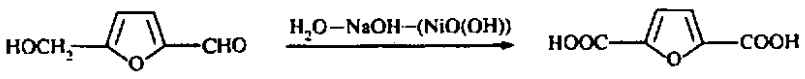
Abstract—The electrochemical oxidation of 5-hydroxymethylfurfural with nickel oxide/hydroxide anode gave 2,5-furandicarboxylic acid in 71% yield.

Although 5-hydroxymethylfurfural is known as an important intermediate in organic syntheses, its electrochemical properties are scarcely examined; the only study is that of electrolysis in methanol with platinum anode[1].

We oxidized electrochemically 5-hydroxymethylfurfural (I) with a nickel oxide/hydroxide anode, in aqueous basic solution. The substrate converted into 2,5-furandicarboxylic acid (II). This acid has been previously prepared by the oxidation of 5-hydroxymethylfurfural (HMF): with potassium hypermanganate in aqueous sodium hydroxide[2], with oxygen, catalysed by palladium or platinum in a basic solution[3], or with dinitrogen tetraoxide in dimethylsulphoxide[4]. The former method gave the product in a poor yield, the two latter methods are difficult for laboratory use. Thus, our reaction seems to be an effective synthetic method to obtain the compound (II).



(I) (II)

The *dc* electrolysis was carried out in a divided, H-shaped cell, at a current density of 0.016 A cm^{-2}. 0.005 M (0.63 g) of the substrate (I), was electrolysed for 4 h, in 100 ml of 1 M aqueous sodium hydroxide, with nickel oxide/hydroxide anode and stainless steel cathode at room temperature. The geometric area of the anode was 12.5 cm^2. The nickel oxide/hydroxide anode was prepared following the described procedure[5].

The previous constant potential coulometry was carried out at 0.600 V *vs sce* with 0.005 M of the substrate. We have investigated the reaction with the use of *uv* spectroscopy. Analysis of spectra showed that the molar concentration of HMF ($\lambda_{max} = 292$ nm) decreases proportionally to the increasing molar concentration of 2,5-furandicarboxylic dianion ($\lambda_{max} = 265$ nm) and there was no evidence of any other product. So, together with *uv* spectroscopy, constant potential coulometry showed 6 F mol^{-1} passed electricity in 84% current efficiency (CE).

After electrolysis the anodic mixture was acidified with hydrochloric acid up to pH 3; the product isolated in 71% yield, as dark yellow crystals not melting below 330°C and partly sublimating over 250°C. 2,5-Furandicarboxylic acid can be purified by recrystallization from water.

The identity of compound (II) has been confirmed by both *ir* and ^1H NMR spectra. Similar electrolysis has been carried out under the same conditions, but in an undivided cell. The product was obtained in 57% yield.

Thus, the electrolysis of HMF with the nickel oxide/hydroxide anode should be carried out in a divided cell to achieve a better yield.

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1. *The Conversion of Sucrose into Furan Compounds. Part II. Some 2 : 5-Disubstituted Tetrahydrofurans and their Products of Ring Scission.*

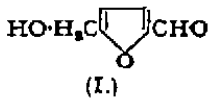
By W. N. Haworth, W. G. M. Jones, and L. F. Wiggins.

5-Hydroxymethylfurfuraldehyde is converted into 2 : 5-*bishydroxymethyltetrahydrofuran* and 5-hydroxymethylfuran-2-carboxylic acid into the corresponding tetrahydrofuran derivative by catalytic hydrogenation. Some derivatives of these compounds are described together with the products obtained by their ring fission. A new synthesis of adipic acid is recorded.

The preparation from sucrose of 5-hydroxymethylfurfuraldehyde has been described (J., 1944, 667) and it is envisaged that this compound might be an intermediate in the conversion of sucrose into useful compounds. We have now investigated the conversion of 5-hydroxymethylfurfuraldehyde into open-chain compounds. This may be accomplished in two ways : (i) by cleavage of the furan ring with hydrolytic agents, and (ii) by cleavage of the reduced furan ring. As examples of the first method may be considered the conversion of furfurylacrylic acid into 4-ketopimelic acid by treatment with ethyl-alcoholic hydrogen chloride (Marckwald, *Ber.*, 1887, **20**, 2811) and the conversion of 5-furfurylidenelævulic acid into 4 : 7-diketosebacic acid (Kehrer and Hofacker, *Annalen*, 1896, **294**, 165). An example of the second method is the cleavage of the tetrahydrofuran ring in 2 : 5-dimethyltetrahydrofuran by hydrogen halides (Freid and Kleene, *J. Amer. Chem. Soc.*, 1941, **63**, 2691) with the formation of 2 : 5-dihalogenohexanes. Ring fission of the tetrahydrofuran ring can also be brought about by acetyl chloride or acetic anhydride. Thus Paul obtained methyl 5-chloro-2-acetoxyvalerate from methyl tetrahydrofuran-2-carboxylate and acetyl chloride (*Compt. rend.*, 1941, **212**, 401) and 1 : 2 : 5-triacetoxypentane from acetoxymethyltetrahydrofuran and acetic anhydride in the presence of zinc chloride (*Bull. Soc. chim.*, 1941, **8**, 369). We have used method (ii) in the work described in this paper in obtaining open-chain compounds from 5-hydroxymethylfurfuraldehyde.

Relatively few 2 : 5-disubstituted derivatives of tetrahydrofuran have so far been described in the literature. Amongst these are 2 : 5-dimethyltetrahydrofuran obtained from the corresponding furan derivative by catalytic hydrogenation over palladised asbestos (Shuikin, Nikiforov, and Stolyarova, *J. Gen. Chem., U.S.S.R.*, 1937, **7**, 1501) and *cis*-tetrahydrofuran-2 : 5-dicarboxylic acid, which can be prepared, amongst other ways, by the action of alcoholic potassium hydroxide on *meso*-2 : 5-dibromoadipic acid. The preparation of this acid by the catalytic hydrogenation of furan-2 : 5-dicarboxylic acid (dehydromucic acid) has apparently not been described. On the other hand, many monosubstituted derivatives of tetrahydrofuran derived from the commercially available furfuraldehyde are known, *e.g.*, tetrahydrofuran-2-carboxylic acid and the corresponding 2-hydroxymethyl and 2-methyl derivatives.

5-Hydroxymethylfurfuraldehyde (I), readily prepared from sucrose (see J., 1944, 667), has been subjected to hydrogenation over Raney nickel and converted into 2 : 5-*bishydroxymethyltetrahydrofuran* (II) in excellent yield. This formed a liquid *bisacetoxy*-derivative and was characterised by the formation of a *bis*- 3 : 5-*dinitrobenzoate*.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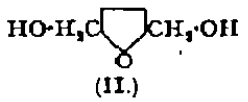
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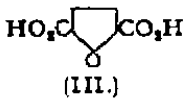
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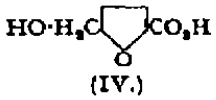
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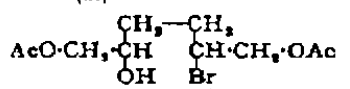
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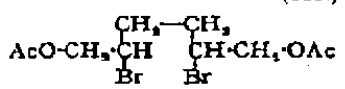
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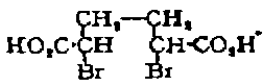

(VII.)

Unsuccessful attempts were made to oxidise it to the corresponding 2 : 5-dicarboxylic acid (III), degradation products only being formed. Thus oxidation with chromic anhydride led to complete degradation, and with nitric acid, succinic and oxalic acids were obtained.

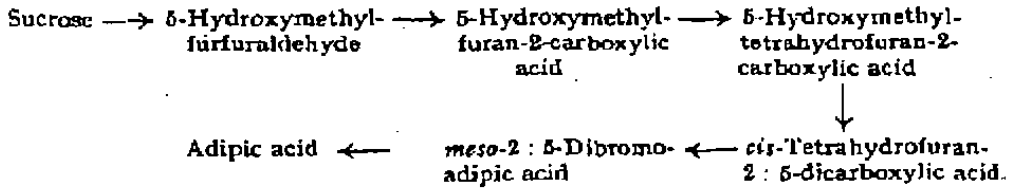
Experiments on the ring fission of 2 : 5-bisacetoxymethyltetrahydrofuran were carried out and the following results obtained. On treatment at room temperature with a mixture of acetic anhydride, acetic acid and sulphuric acid, reagents used successfully in the acetolysis of benzylidene derivatives of the hexahydric alcohols (see, for example, Hann, Hudson, and Wolff, *J. Amer. Chem. Soc.*, 1942, **64**, 1493), the compound underwent ring fission to a small extent (10%) and crystalline 1 : 2 : 5 : 6-*tetra-acetoxyhexane* was isolated. Deacetylation

by the Zemplén catalytic method gave crystalline 1 : 2 : 5 : 6-tetrahydroxyhexane (m. p. 98°), probably identical with one of the products (m. p. 95·5°) obtained by Wagner (*Ber.*, 1888, 21, 3343) by the oxidation of diallyl with potassium permanganate. 2 : 5-Bisacetoxymethyltetrahydrofuran on treatment with hydrogen bromide in glacial acetic acid gave 2 : 5-*dibromo*-1 : 6-*diacetoxyhexane* (VI). 2-Bromo-5-hydroxy-1 : 6-diacetoxyhexane (V) is probably the first product of the reaction and in fact 2-*bromo*-1 : 5 : 6-*triacetoxyhexane* was produced as a by-product.

5-Hydroxymethylfurfuraldehyde can easily be converted into the corresponding carboxylic acid by oxidation with alkaline silver oxide (Reichstein, *Helv. Chim. Acta*, 1926, 9, 1066). Hydrogenation of the carboxylic acid over Raney nickel led to the formation of a resinous material, probably a polymer of the polyester type, which, however, was readily broken down on treatment with ethyl-alcoholic hydrogen chloride; the product isolated was *ethyl 5-hydroxymethyltetrahydrofuran-2-carboxylate* and was characterised by the formation of a crystalline *amide*. The compound was better prepared by the hydrogenation of ethyl 5-hydroxymethylfuran-2-carboxylate. The free carboxylic acid was obtained by hydrolysis of the ethyl ester. The hydroxyl group in ethyl 5-hydroxymethyltetrahydrofuran-2-carboxylate was acetylated, and *ethyl 5-acetoxymethyltetrahydrofuran-2-carboxylate* was prepared from the corresponding hydroxy-compound by treatment with thionyl chloride and pyridine. Ring fission of ethyl 5-acetoxymethyltetrahydrofuran-2-carboxylate was effected by the use of the acetolysing reagent (acetic anhydride, acetic acid and sulphuric acid) and took place to a greater extent than in the case of 2 : 5-bis-acetoxymethyltetrahydrofuran. Thus *ethyl* 2 : 5 : 6-*triacetoxyhexoate* was obtained in 55% of the theoretical yield.

5-Hydroxymethyltetrahydrofuran-2-carboxylic acid (IV) was oxidised with nitric acid, and *cis*-tetrahydrofuran-2 : 5-dicarboxylic acid (III) isolated in 60% yield. Attempts to prepare this dibasic acid by the catalytic hydrogenation of furan-2 : 5-dicarboxylic acid led only to poor yields of the desired product and the reduction was only accomplished by the use of high temperatures and pressures with Raney nickel as the catalyst. The catalytic hydrogenation of methyl furan-2 : 5-dicarboxylate was not accomplished.

The investigation of the ring fission of *cis*-tetrahydrofuran-2 : 5-dicarboxylic acid (III) led to a synthesis of adipic acid as below described. The dibasic acid was heated with hydrogen bromide in glacial acetic acid at 125° under pressure, and *meso*-2 : 5-dibromoadipic acid (VII) obtained in 60% yield. Catalytic hydrogenation of the latter over Raney nickel in the presence of calcium carbonate gave adipic acid in good yield. The series of reactions which constitute a synthesis of adipic acid from sucrose is as follows:



Tetrahydrofuran-2 : 5-dicarboxylic acid proved to be a very stable compound. It was recovered unchanged after treatment with nitric acid at 95° and after treatment with fuming hydrochloric acid under pressure. The comparative stability of this compound is further exemplified by the fact that *methyltetrahydrofuran-2 : 5-dicarboxylate*, obtained by boiling the corresponding dicarboxylic acid with methyl-alcoholic hydrogen chloride and characterised as its crystalline *diamide*, did not undergo ring cleavage on treatment with the acetolysing reagent.

Experimental.

2 : 5-*Bishydroxymethyltetrahydrofuran*.—5-Hydroxymethylfurfuraldehyde (10 g.), dissolved in ether (600 c.c.), was hydrogenated over Raney nickel at 130°/75 atms. for 6 hours. After filtration and evaporation of the filtrate the product, 2 : 5-*bishydroxymethyltetrahydrofuran*, distilled at 120° (bath temp.)/0·07 mm. as a fairly mobile, colourless liquid, $n_D^{25°}$ 1·4700. It was soluble in alcohol, acetone and water, slightly soluble in ether, and insoluble in light petroleum (Found: C, 54·7; H, 9·5. $C_6H_{12}O_3$ requires C, 54·6; H, 9·1%). A crystalline 3 : 5-*dinitrobenzoate* was obtained and had m. p. 178° (Found: C, 46·5; H, 3·4; N, 10·9. $C_{20}H_{16}O_{12}N_4$ requires C, 46·2; H, 3·1; N, 10·8%).

2 : 5-*Bisacetoxymethyltetrahydrofuran*.—2 : 5-Bishydroxymethyltetrahydrofuran (6 g.) was refluxed for 15 minutes with acetic anhydride (50 c.c.) and sodium acetate (6 g.), the product poured on ice, the acetic acid neutralised with sodium bicarbonate, and the solution extracted with chloroform. After the extract had been dried over anhydrous magnesium sulphate, it was evaporated to dryness, and a liquid obtained which distilled at 115° (bath temp.)/0·015 mm. The product was a colourless mobile liquid, $n_D^{18°}$ 1·4515. Yield, almost quantitative (Found: C, 55·5; H, 7·7. $C_{10}H_{16}O_5$ requires C, 55·5; H, 7·4%).

Acetolysis of 2 : 5-*Bisacetoxymethyltetrahydrofuran*.—The material (4·2 g.) was dissolved at 0° in the acetolysing reagent, prepared by mixing at 0° acetic anhydride (35 c.c.), acetic acid (15 c.c.), and concentrated sulphuric acid (1 c.c.) (see, for example, Hann, Hudson, and Wolff, *loc. cit.*), and was kept at room temperature for 24 hours. Thereafter it was poured on ice, neutralised with sodium bicarbonate, and extracted with ether. After the extract had been dried over anhydrous magnesium sulphate, it was evaporated to a syrup, which was distilled and collected in two fractions: Fraction 1 (2·6 g.), b. p. 140°/0·03 mm., $n_D^{18°}$ 1·4517; fraction 2 (1·2 g.), b. p. 170°/0·03 mm., $n_D^{18°}$ 1·4480. Both fractions were partly crystalline and after drying on porous tile the crystalline material in each was separately collected and recrystallised from ether–light petroleum. Each sample had m. p. 78°, either separately or in admixture. Yield, 0·21 g. (Found: C, 53·3; H, 6·6. $C_{14}H_{22}O_8$ requires C, 52·9; H, 6·9%). The material was 1 : 2 : 5 : 6-*tetra-acetoxyhexane*. Fraction 1 had *O*-acetyl, 42·4%, and fraction 2 had *O*-acetyl, 45·4%. The presence of only tetra-acetoxyhexane and

bisacetoxymethyltetrahydrofuran being assumed, fraction 1 contains 0·26 g. of the former and fraction 2, 0·4 g. Thus the calculated yield of tetra-acetoxyhexane is 10·3% of the theoretical.

The crystalline tetra-acetoxyhexane was deacetylated by treatment with a trace of sodium in dry methyl-alcoholic solution in the usual way. A crystalline compound resulted, which, on being twice recrystallised from ethyl acetate–alcohol, had m. p. 98° and was 1 : 2 : 5 : 6-tetrahydroxyhexane. It was probably identical with one of the products of the action of potassium permanganate on diallyl (Wagner, *loc. cit.*) (Found : C, 48·5; H, 9·3. Calc. for $C_6H_{14}O_4$: C, 48·0; H, 9·3%).

Treatment of 2 : 5-*Bisacetoxymethyltetrahydrofuran with Hydrogen Bromide in Glacial Acetic Acid.*—The substance (4·4 g.) was dissolved in glacial acetic acid (4 c.c.), and the solution saturated at room temperature with dry hydrogen bromide, heated in a sealed tube at 125° for 2 hours, poured on ice, and extracted with ether. The extract was washed with sodium bicarbonate solution and with water, dried over anhydrous magnesium sulphate, and evaporated. A syrup (6 g.) was obtained which distilled in two fractions : Fraction 1, b. p. 105° (bath temp.)/0·008 mm., a very mobile, colourless liquid (1·2 g.), $n_D^{23°}$ 1·4806, was 2-*bromo*-1 : 5 : 6-*triacetoxyhexane* (Found : C, 42·7; H, 5·65; Ac, 36·8. $C_{12}H_{19}O_8Br$ requires C, 42·8; H, 5·6; Ac, 38·1%). Fraction 2, b. p. 145° (bath temp.)/0·08 mm., a fairly viscid, yellow liquid (3·8 g.), $n_D^{23°}$ 1·4957, was mainly 2 : 5-*dibromo*-1 : 6-*diacetoxyhexane* (Found : C, 33·2; H, 4·5; Ac, 26·8. $C_{10}H_{16}O_4Br_2$ requires C, 33·3; H, 4·4; Ac, 24·0%).

Oxidation of 2 : 5-*Bishydroxymethyltetrahydrofuran.*—A solution of the material (0·5 g.) in nitric acid (*d* 1·15) (30 c.c.) was slowly warmed to 100° and kept thereat for 1 hour, vigorous evolution of nitrous fumes occurring. The solution was diluted with water and evaporated at constant volume until most of the excess of nitric acid had disappeared. On evaporation to dryness a solid residue was left which after recrystallisation from ether gave (*a*) oxalic acid dihydrate (m. p. 101°) and (*b*) succinic acid (m. p. 186°).

Ethyl 5-*Hydroxymethyltetrahydrofuran-2-carboxylate.*—(*a*) 5-Hydroxymethylfuran-2-carboxylic acid (5 g.) was dissolved in water (500 c.c.) and hydrogenated over Raney nickel at 165°/60 atms. for 10 hours. On evaporation a red-brown resinous material remained, which was refluxed with ethyl alcohol (150 c.c.) containing 2% of hydrogen chloride for 7 hours. After neutralisation with silver carbonate, filtration and evaporation, a mobile liquid was obtained which distilled at 85° (bath temp.)/0·02 mm. and showed $n_D^{17°}$ 1·4540. Yield, 3·58 g. The distillate was a colourless mobile liquid, soluble in alcohol, ether, acetone and chloroform and slightly soluble in light petroleum.

(*b*) Ethyl 5-hydroxymethylfuran-2-carboxylate (35 g.) in ethyl acetate (600 c.c.) was hydrogenated over Raney nickel (1 g.) at 140°/130 atm. for 7 hours. Filtration of the resulting solution and evaporation of the solvent gave a mobile liquid, b. p. 85° (bath temp.)/0·02 mm., identical in properties with the material obtained in (*a*); this was *ethyl* 5-*hydroxymethyltetrahydrofuran-2-carboxylate*. Yield, 29 g. (Found : OEt, 25·3. $C_8H_{14}O_4$ requires OEt, 25·9%).

Ethyl 5-*Chloromethyltetrahydrofuran-2-carboxylate.*—Ethyl 5-hydroxymethyltetrahydrofuran-2-carboxylate (2 g.) was dissolved in dry pyridine (0·93 c.c.), and thionyl chloride (1·14 c.c.) carefully added at 0°. The mixture was heated at 100° for 1 hour, ether added, and the mixture washed successively with water, sodium bicarbonate solution, and water. After being dried over anhydrous magnesium sulphate, the ether was removed; the resulting liquid distilled at 82° (bath temp.)/0·023 mm. The product had $n_D^{23°}$ 1·4585 and was a colourless mobile oil. Yield, 0·75 g. The *chloromethyl* derivative was insoluble in water, very slightly soluble in light petroleum, and soluble in alcohol, ether, acetone, and chloroform (Found : C, 50·3; H, 6·5; OEt, 22·0. $C_8H_{13}O_3Cl$ requires C, 49·9; H, 6·7; OEt, 23·2%).

Ethyl 5-*Acetoxymethyltetrahydrofuran-2-carboxylate.*—The 5-hydroxymethyl ester (3 g.) was refluxed for 1 hour with acetic anhydride (10 c.c.) and fused sodium acetate (1·5 g.), and the solution poured into water and neutralised with sodium bicarbonate. The mixture was then extracted with ether, and the extract dried over anhydrous magnesium sulphate. Distillation of the solvent gave a liquid which distilled as a colourless mobile oil at 115° (bath temp.)/0·03 mm., $n_D^{21°}$ 1·4453. Yield, 80% of the theoretical (Found : Ac, 23·0. $C_{10}H_{16}O$ requires Ac, 20·0%).

5-*Hydroxymethyltetrahydrofuran-2-carboxyamide.*—A solution of the ethyl ester (0·2 g.) in ethyl alcohol (3 c.c.) was saturated with ammonia at 0°, kept at 0° for 24 hours, the solvent and ammonia then evaporated, and the residue recrystallised from acetone; m. p. 99°. Yield, 0·12 g. (Found : C, 49·7; H, 7·8; N, 10·3. $C_6H_{11}O_3N$ requires C, 49·7; H, 7·6; N, 9·7%).

5-*Hydroxymethyltetrahydrofuran-2-carboxylic Acid.*—The ethyl ester (0 g.) was heated at 70° with a slight excess of hydrated barium hydroxide (6·3 g.) for 1 hour, N-sulphuric acid added exactly to precipitate the barium as sulphate, which was removed by centrifuging, the supernatant liquid evaporated, and the residue extracted with chloroform. Evaporation of this extract gave a moderately viscid liquid which did not crystallise (Found : equiv., 150. $C_6H_{10}O_4$ requires equiv., 146).

Acetolysis of Ethyl 5-*Hydroxymethyltetrahydrofuran-2-carboxylate.*—The ester (0·5 g.) was added to a mixture of acetic anhydride (9 c.c.), acetic acid (4 c.c.), and concentrated sulphuric acid (0·25 c.c.) at 0°, the whole kept at room temperature for 40 hours and poured on ice, and the resulting solution extracted with chloroform. The extract was washed free from acid with dilute sodium bicarbonate solution, dried over anhydrous magnesium sulphate, and evaporated to dryness. The resulting syrup was distilled in two fractions : (*a*) Ethyl 5-acetoxymethyltetrahydrofuran-2-carboxylate (0·12 g.), b. p. 115° (bath temp.)/0·03 mm., $n_D^{21°}$ 1·4453 (Found : Ac, 21·8; OEt, 19·7. Calc. for $C_{10}H_{16}O_5$: Ac, 20·0; OEt, 20·8%). (*b*) *Ethyl* 2 : 5 : 6-*triacetoxyhexoate* (0·4 g.), b. p. 150° (bath temp.)/0·05 mm., $n_D^{21°}$ 1·4434 (Found : Ac, 36·7; OEt, 13·5. $C_{14}H_{22}O_8$ requires Ac, 38·1; OEt, 14·1%).

Oxidation of 5-*Hydroxymethyltetrahydrofuran-2-carboxylic Acid with Nitric Acid.*—The acid (5·6 g.) was dissolved in nitric acid (70 c.c., *d* 1·42) and heated at 80° until oxidation was complete. The solution, after dilution with water, was evaporated several times until the nitric acid had gone. The product was a crystalline solid, m. p. 126—127° after recrystallisation from ether–petrol and was *cis*-tetrahydrofuran-2 : 5-dicarboxylic acid (yield, 60% of the theoretical); the m. p. was not depressed by an authentic specimen prepared from *meso*-2 : 5-dibromoadipic acid by the method of Le Sueur and Haas (J., 1910, **97**, 173). The mother-liquors on evaporation gave a crystalline residue of indefinite m. p., probably a mixture of the *cis*- and the *trans*-isomer of the dicarboxylic acid.

Furan-2 : 5-*dicarboxylic Acid.*—*Potassium hydrogen saccharate* was boiled with 60% hydrobromic acid for 36 hours, and the required acid, m. p. 342°, isolated by Phelps and Hale's method (*J. Amer. Chem. Soc.*, 1901, **23**, 446). Yield, 56% of the theoretical. The substance was obtained in colourless plates after being treated with animal charcoal, but even the purest specimens reduced Fehling's solution.

Methyl Furan-2 : 5-*dicarboxylate.*—The dicarboxylic acid (20 g.) was boiled with 2% methyl-alcoholic hydrogen chloride for 6 hours. The main bulk of the ester crystallised on cooling and the remainder was obtained by neutralising the filtrate with silver carbonate, evaporating the solution, and recrystallising the residue from methyl alcohol. Yield, 90% of the theoretical, m. p. 110°.

Hydrogenation of Furan-2 : 5-*dicarboxylic Acid.*—The acid (10 g.), dissolved in 600 c.c. of water, was heated at 235° for 8 hours with Raney nickel (0·7 g.) at 135 atms. of hydrogen. On evaporation the solution gave a thick resinous mass, which appeared to be a polymer. The product was boiled for 5 hours with 2% methyl-alcoholic hydrogen chloride (100 c.c.), the acid neutralised with silver carbonate, and the solution filtered and evaporated. The residue was a mobile liquid (2·6 g.), b. p. 110—130°/0·04 mm., $n_D^{20°}$ 1·4505, which contained methyl tetrahydrofuran-2 : 5-dicarboxylate. A

sample of the distillate (1 g.) was hydrolysed by heating with a solution of hydrated barium hydroxide (1·8 g.) for 2 hours at 80°. After exact neutralisation with N-sulphuric acid, removal of barium sulphate, and evaporation of the filtrate to dryness, the residue obtained was extracted with acetone, and the extract evaporated to give a crystalline residue from which *cis*-tetrahydrofuran-2 : 5-dicarboxylic acid, m. p. 128°, was obtained in small yield.

Methyl cis-*Tetrahydrofuran-2 : 5-dicarboxylate.*—The dicarboxylic acid (1 g.) was dissolved in 1% methyl-alcoholic hydrogen chloride and boiled for 5 hours. The acid was neutralised with silver carbonate, the solution filtered, and the filtrate evaporated to give a liquid (1·1 g.), b. p. 90° (bath temp.)/0·03 mm., $n_D^{18°}$ 1·4550 (Found: OMe, 32·4. $C_8H_{12}O_4$ requires OMe, 33·0%).

cis-*Tetrahydrofuran-2 : 5-dicarboxyamide.*—A solution of the methyl ester (0·3 g.) in dry methyl alcohol (10 c.c.) was saturated with ammonia at 0° and kept overnight at this temperature, the solvent and ammonia then removed in a vacuum, and the residue recrystallised from acetone–methyl alcohol. Yield, 0·21 g., m. p. 189° (Found: C, 45·9; H, 6·0; N, 17·8. $C_6H_{10}O_2N_2$ requires C, 45·6; H, 6·3; N, 17·7%).

Attempted Acetolysis of Methyl Tetrahydrofuran-2 : 5-dicarboxylate.—The ester (0·8 g.) was dissolved in 20 c.c. of the acetolysing reagent (acetic anhydride 15 c.c., acetic acid 4·6 c.c., concentrated sulphuric acid 0·4 c.c.) at 0°, kept at room temperature for 10 days, and poured into ice-water; after being neutralised with sodium bicarbonate, the solution was extracted with chloroform. The extract on evaporation gave a liquid (0·6 g.), b. p. 90—100° (bath temp.)/0·03 mm., $n_D^{18°}$ 1·4505 (Found: OMe, 32·5. Calc. for $C_8H_{12}O_4$: OMe, 33·0%), which was unchanged starting material.

Ring Fission of cis-*Tetrahydrofuran-2 : 5-dicarboxylic Acid with Hydrogen Bromide in Glacial Acetic Acid.*—The dicarboxylic acid (0·65 g.) was dissolved in glacial acetic acid (7 c.c.). A solution, saturated at 0°, of hydrogen bromide in glacial acetic acid (3·5 c.c.) was added, and the mixture heated in a sealed tube at 125° for 12 hours. The solution was poured into ice-water and extracted with ether, the extract dried (anhydrous magnesium sulphate), filtered, and evaporated, and the residue recrystallised from formic acid. The product was *meso*-2 : 5-dibromoadipic acid identical with the product obtained by Le Sueur and Haas (*loc. cit.*) by the bromination of adipyl chloride. Yield, 0·7 g., 60% of the theoretical, m. p. 192—194°.

Conversion of meso-2 : 5-*Dibromoadipic Acid into Adipic Acid.*—The dibromo-acid (2 g.) (m. p. 191°) was reduced with hydrogen over Raney nickel at 90 atms. for 4 hours at 125° in water in the presence of excess of calcium carbonate. The solution was filtered, evaporated to small bulk, acidified with dilute sulphuric acid, and extracted with ether. The extract, after being dried over magnesium sulphate, was distilled; the residue, on recrystallisation from nitric acid (*d*, 1·47), formed long needles (1 g.), m. p. 151—152°, not depressed by authentic adipic acid.

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Synthesis of 2,5-Diformylfuran and Furan-2,5-Dicarboxylic Acid by Catalytic Air-Oxidation of 5-Hydroxymethylfurfural. Unexpectedly Selective Aerobic Oxidation of Benzyl Alcohol to Benzaldehyde with Metal/Bromide Catalysts**

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Abstract: The alcohol group of hydroxymethylfurfural (compound 1, HMF) is preferentially oxidized by dioxygen and metal/bromide catalysts [Co/Mn/Br, Co/Mn/Zr/Br; Co/Mn=Br/(Co+Mn) = 1.0 mol/mol] to form the dialdehyde, 2,5-diformylfuran (compound 2, DFF) in 57% isolated yield. HMF can be also oxidized, via a network of identified intermediates, to the highly insoluble 2,5-furandicarboxylic acid (compound 5, FDA) in 60% yield. For comparison, benzyl alcohol gives benzaldehyde in 80% using the same catalyst system. Over-oxidation (to CO_2) of HMF is much higher than that of the benzyl alcohol but can be greatly reduced by increasing catalyst concentration.

Keywords: cobalt; dioxygen; green chemistry; homogeneous catalysis; hydroxymethylfurfural; oxidation

Introduction

At the current rate of consumption, proven crude oil reserves are estimated to last for less than four decades.[1] Therefore, in recent years serious consideration has been given, in both academia and industry, to alternative feedstocks for the chemical industry of the future. The use of renewable resources, i.e., naturally occurring carbohydrates and oils produced by various plants, would result in the development of benign, environmentally friendly processes, the so-called green chemistry.[2]

5-Hydroxymethylfurfural (HMF; compound 1) is one of the few individual organic compounds that can be prepared directly from various carbohydrates in up to 98% yield. While the best yields of HMF have been obtained from fructose, other abundant, low-cost mono-, di-, and polysaccharides can be used, such as glucose, sucrose, and starch.[3]

Selective oxidation reactions of HMF are presently viewed as attractive routes to 2,5-furandicarboxylic acid (FDA) and/or 2,5-diformylfuran (DFF; compound 2), monomers for furan-containing polymers and materials with special properties.[4] While a variety of oxidants have been used for oxidation of HMF to 2,5-furandicarboxylic acid and DFF, only few reports describe catalytic oxidations of HMF with oxygen or air, the most economical oxidants. Thus, HMF has been oxidized with O_2 to 2,5-furandicarboxylic acid in the presence of heterogeneous Pt catalysts with stoichiometric amounts of alkali[5,6] and to DFF with TEMPO radicals[7,8] or supported vanadium catalysts.[9,10] Although homogeneously catalyzed oxidation reactions of alcohols have received much attention in recent years,[11-18] no reports have appeared in the literature, describing the oxidation of HMF with O_2 and soluble metal complex catalysts.

In this paper, we report the first examples of aerobic HMF oxidation reactions, catalyzed with homogeneous metal/bromide systems. The easily prepared, low-cost metal/bromide catalysts, the most common being a mixture of Co/Mn/Br, are widely used for the selective and efficient autoxidation reactions of hydrocarbons,[19] e.g., the large scale industrial synthesis of terephthalic, isophthalic, and trimellitic acids

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from *p*-xylene, *m*-xylene, and pseudocumene respectively.[11,19] Surprisingly little is known, however, *about oxidation of alcohols using the metal/bromide* catalysts.[19] In this work, we found that, depending on reaction conditions, hydromethylfurfural can be oxidized to DFF or 2,5-furandicarboxylic acid with unexpectedly high selectivity. Furthermore, the selective formation of DFF in the metal bromide-catalyzed oxidation of HMF prompted us to study the oxidation of benzyl alcohol under similar conditions. Remarkably, it was found that under controlled conditions this oxidation can afford benzaldehyde in high yield.

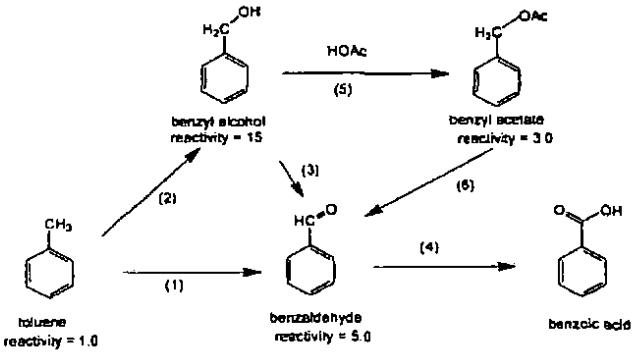

Figure 2. Products during autoxidation of benzyl alcohol

Results

Products Formed

GC/MS studies were performed on two selected samples during HMF autoxidation at 70 bar, which are consistent with the products and pathways given on Figure 1. In addition, the usual products from the autoxidation of acetic acid were observed, i. e., formic acid, acetoxyacetic acid, glycolic acid, maleic acid, fumaric acid, succinic acid, and bromosuccinic acid in trace amounts. A side reaction is the esterification of the alcohols to form the more oxidatively stable acetate, see compounds 6 and 7 in Figure 1 and benzyl acetate in Figure 2. DFF and FDA have been isolated and characterized by elemental analysis and NMR spectra. The 2-carboxy-5-formylfuran was identified and quantified by ^{1}H NMR spectroscopy of isolated solid samples that were either 2,5-furandicarboxylic acid or 2,5-furandicarboxylic acid/2-carboxy-5-formylfuran mixtures. The oxidation of benzyl alcohol gives the expected benzaldehyde, benzyl acetate, and benzoic acid products (see Figure 2).

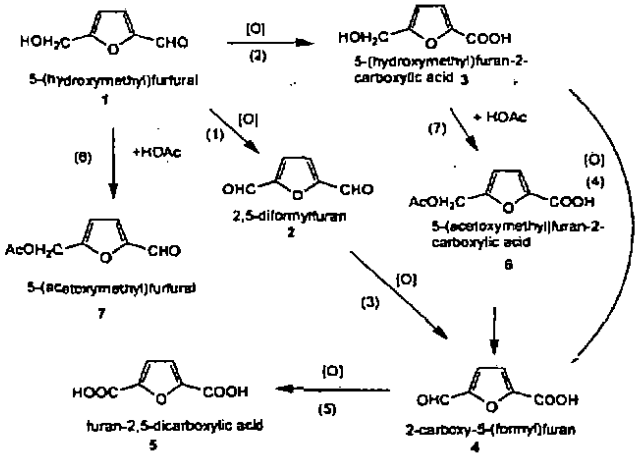

Figure 1. Products from the autoxidation of hydroxymethylfurfural

Formation of Diformylfuran from Hydromethylfurfural and Benzaldehyde from Benzyl Alcohol at Atmospheric Pressure (Table 1)

In experiments 1 and 5, the attempt to initiate the reaction at the lower temperature failed, hence the temperature was raised to the higher given value. The formation of the reaction products, as determined by GC and LC, from HMF and benzyl alcohol is illustrated in Figures 3 and 4. Maximum observed yield of the aldehydes is 57% for DFF and 80% for benzaldehyde. Maximum aldehyde yields occur as the conversion of the alcohol approaches 100%. The selectivity decreases as the conversion of the alcohol increases with the values for HMF (51–90%) being lower than for benzyl alcohol (80–93%), see Figure 5. Doubling the catalyst concentration during the oxygenation of HMF (i) increases the reaction rate by a factor of 2.1, (ii) increases the yield and selectivity to DFF by 5 and 10%, respectively, and (iii) decreases the 'overoxidation' to CO and CO_2 by a factor of 4 (see experiments 2, 3, and 4 in Table 1 and Figure 6). Further increase in catalyst concentration does not further improve DFF yield (see experiments 4, 5, and 6). For benzyl alcohol, the maximum benzaldehyde yield of 80% occurs at a conversion of 85% with only 4.6% benzoic acid and 3.8% benzyl acetate formed (Table 1, experiment 7). Based on their rates of disappearance, benzyl alcohol is 2.0 times more reactive than HMF (see examples 4, 7, and 8 in Table 8).

The rate of disappearance of the alcohol and the rate of disappearance of the aromatic aldehyde are consistent with first order kinetics and the rate constants are given on Table 1. The rate of disappearance of HMF is 8.1 times faster than the rate of disappearance of 2-carboxy-5-formylfuran, suggesting that the dialdehyde is quite stable, as seen from the kinetic data on Table 1. This is consistent with the subsequent work-up of the reaction mixture and isolation of DFF in a yield close to that previously determined by GC. The benzyl alcohol, however, reacts to form benzaldehyde faster by only a factor of 1.1 than benzaldehyde reacting to benzoic acid (Table 1). Re-

Table 1. Oxygenation of hydroxymethylfurfural and benzyl alcohol at ambient atmospheric pressure

Exp.	1	2	3	4	5	6	7
	HMF	HMF	HMF	HMF	HMF	HMF	benzyl alcohol
Temp, °C	50 then 95	75	75	75	50 then 75	75	75
Reagent, M	0.725	0.794	0.804	0.797	0.796	0.806	0.793
Co, mM	2.6	6.6	6.6	13.5	26.8	27.3	13.4
Zr, mM	0.0	0.15	0.15	0.15	0.15	0.15	0.15
Rate, s^{-1} [a]	–	9.68(0.18) [0.997]	8.12(0.61) [0.972]	16.6(1.4) [0.999]	10.8(0.5) [0.992]	15.1(0.5) [0.994]	40.4(3.9) [0.988]
Alcohol, half-life, min	–	119	142	69	108	76.5	28.5
Rate, s^{-1} [b]	–	1.22(0.34) [0.862]	–	–	–	–	30(3) [0.945]
Time,min [c]	414	450	642	310	550	430	100
Yield [c]	41	51	50	57	51	52	80
Conv.,% [c]	98	92	95	91	95	97	85
Select.,% [c]	42	55	53	65	54	54	93
Acetate,%[c]	8.4	5.9	7.5	7.2	6.1	5.7	5.6
Alcohol to CO_x [d]	–	7.4	8.5	2.1	1.8	2.6	0.05

[a] Rate of disappearance of aromatic alcohol $\times 10^5$. Standard deviation in parenthesis ( ), correlation coefficient in brackets [ ].
[b] Rate of disappearance of aromatic aldehyde.
[c] When maximum alkylaromatic aldehyde is observed.
[d] Loss of alcohol due to carbon monoxide and carbon dioxide formation. Assumes no CO_x formation from the solvent.

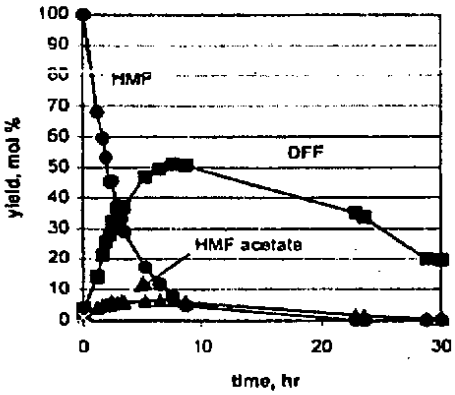

Figure 3. Autoxidation of hydroxymethylfurfural at 75 °C

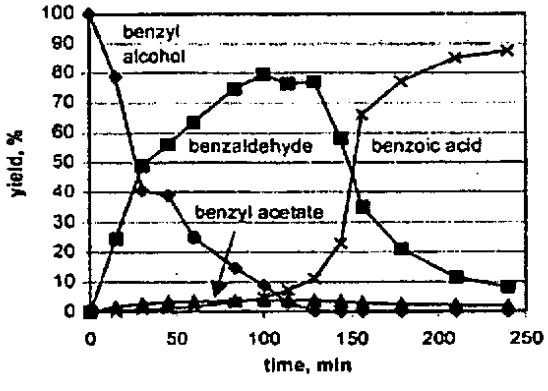

Figure 4. Autoxidation of benzyl alcohol at 75 °C

markably, the oxidation is catalyzed in such a way that essentially all the benzyl alcohol reacts *first*. The benzaldehyde formed starts to undergo further oxidation to benzoic acid only after the oxidation of the

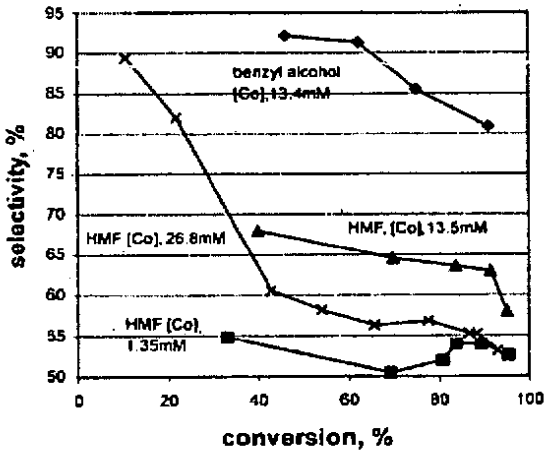

Figure 5. Benzaldehyde selectivity as function of catalyst concentration and type of alkylaromatic alcohol

benzyl alcohol is close to completion, despite the fact that $PhCH_2OH$ and PhCHO exhibit very similar measured reactivities in the same experiment.

Formation of DFF from HMF at 70 Bar Air (Table 2) Experimental error, as determined by 5 replicate experiments, is given in entry 7 of Table 2. As can be seen, 50 and 75 °C for 2 h are sufficient conditions for obtaining good yields of DFF, up to 63%. By comparing experiments 1 and 2, 3 and 4, 5 and 6, and 8 and 9, one finds that increasing catalyst concentration leads to (i) increased activity as evidenced by higher conversions, (ii) higher selectivity for DFF (except for experiments 5 and 6), and (iii) higher yield. Comparing experiments 1 and 3, 2 and 4, 5 and 8, and 6 and 9, one finds that the Co/Mn/Zr/Br catalyst is

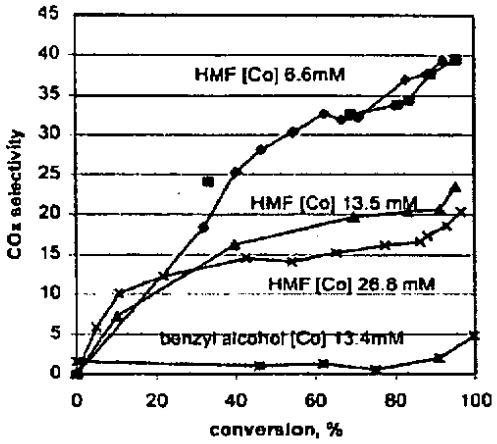

Figure 6. Carbon oxide selectivity as function of catalyst concentration and type of alkylaromatic alcohol

more active, giving higher conversion, than Co/Mn/Br, with the only exception being experiments 2 and 3 where the conversions are similar. The addition of zirconium not only affects conversion, but can also profoundly increase the selectivity (Table 2). This point is illustrated by experiments 1 and 3 where the addition of Zr results in a much higher yield of DFF (67 vs. 38%) at the same conversion of ca. 60%. Experiments 6 and 8, for which the conversions vary significantly, represent the only exception. Under comparable conditions, the conversion increases with temperature, as expected.

Formation of 2-Carboxy-5-formylfuran and 2,5-Furandicarboxylic Acid at 70 Bar (Table 3)

The initial amount of HMF used was only 0.2–0.75 g and the yields are based on isolated and washed solids which were analyzed by NMR. When the temperature is increased from 75 to 100–125 °C, precipitation of poorly soluble 2,5-furandicarboxylic acid commences. 2-Carboxy-5-formylfuran is also either fairly insoluble or is prone to co-crystallization with 2,5-furandicarboxlic acid, which results in their co-precipitation. The yield increases with catalyst concentration (Figure 7), with temperature (entries 1 and 2 and 3 and 4 of Table 3), but not with the addition of Zr to the Co/Mn/Br catalyst (entries 1 and 3 and 2 and 4). Extrapolation from Figure 7 suggests that the maximum obtainable 2,5-furandicarboxylic acid yield is about 70% using the Co/Mn/Zr/Br catalyst at the specified molar ratios of these elements. It is believed that variation of the molar amounts of the Co, Mn, Zr, and Br could well improve the yield of 2,5-furandicarboxylic acid. Since the oxidation proceeds through three steps from HMF to 2,5-furandicarboxylic acid (steps 1, 3, and 5 in Figure 1) and the reactivity of the HMF is probably higher than 2-carboxy-5-formylfuran one would expect that staging the temperature would increase yield.[19] This was not observed however, since staging the temperature from an initial value of 50 °C for 1 h and then 125 °C for 2 h gave no better results than the oxygenation at 125 °C for 3 h (Figure 7).

Table 2. Oxidation of hydroxymethylfurfural (HMF) to diformylfuran (DFF) at 70 bar air

Exp.	Catalyst	[Co], mM	HMF, M	Temp, °C	Time, h	HMF, conv. %	DFF select. %	DFF, yield %
1	Co/Mn/Br/Zr	3.44	0.375	50	2	60.4	66.6	40.2
2	Co/Mn/Br/Zr	6.82	0.372	50	2	69.2	65.5	45.2
3	Co/Mn/Br	3.44	0.375	50	2	60.6	38.4	23.3
4	Co/Mn/Br	6.82	0.377	50	2	61.7	54.6	33.7
5	Co/Mn/Br/Zr	3.44	0.375	75	2	82.5	73.2	60.4
6	Co/Mn/Br/Zr	6.82	0.375	75	2	99.7	61.6	61.4
7	Co/Mn/Br/Zr	6.82	1.12	75	2	74.1(1.0)	67.5(1.4)	49.9(0.6)
8	Co/Mn/Br	3.44	0.377	75	2	71	54.5	38.6
9	Co/Mn/Br	6.82	0.377	75	2	92.2	68.3	63.0

Table 3. Oxidation of hydromethylfurfural to 2-carboxy-4-formylfuran (CFF) and furan-2,5-dicarboxyfuran (FDA) at 70 bar air

Exp.	catalyst	[Co], mM	[HMF], M	temp, C	time, h	CFF, mol %	FDA, mol %
1	Co/Mn/Br/Zr	3.44	0.377	100	2	5.1	18.7
2	Co/Mn/Br/Zr	3.44	0.371	125	2	2.1	36.5
3	Co/Mn/Br	3.44	0.377	100	2	4.1	29.7
4	Co/Mn/Br	3.44	0.374	125	2	1.8	35.2
5	Co/Mn/Br/Zr	3.44	0.758	50, 125	1, 2	1.6	28.3
6	Co/Mn/Br/Zr	6.82	0.753	50, 125	1, 2	2.5	28.1
7	Co/Mn/Br/Zr	13.7	0.749	50, 125	1, 2	0.0	55.4
8	Co/Mn/Br/Zr	20.5	0.755	50, 125	1, 2	0.0, 0.0	58.4, 63.1
9	Co/Mn/Br/Zr	3.41	0.781	125	3	1.7	27.7
10	Co/Mn/Br/Zr	6.82	0.774	125	3	0.0	41.6
11	Co/Mn/Br/Zr	13.7	0.0755	125	3	0.0	54.6
12	Co/Mn/Br/Zr	20.5	0.768	125	3	0.0, 0.0	60.9, 58.6

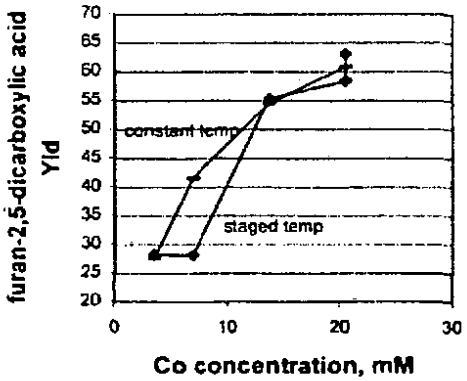

Figure 7. Effect of catalyst concentration and temperature staging on FDA yield. See details in Table 3.

Discussion

General Considerations

The reaction network in Figure 1 is consistent with the detailed studies of the oxidation reactions of many substituted methylaromatic species, aromatic alcohols, and benzaldehydes using metal/bromide catalysts.[19] The latter is thought to operate via a modified free radical chain mechanism (see below). The free radical chain mechanism gives the oxidizability of toluene, benzyl alcohol, and benzaldehyde as 0.05, 0.85, and 290 respectively.[22] It is clear from these values that the steady state concentration of benzaldehyde is *expected* to remain low in metal/bromide catalyzed systems. We find however that the oxygenation of HMF gives preferentially DFF rather than 5-(hydroxymethyl)furan-2-carboxylic acid (compare steps 1 and 2 on Figure 1). Extending this work to benzyl alcohol gave even higher yields and selectivity to aldehydes. The kinetics of the Co/Br catalyzed oxygenation of benzyl alcohol has been reported[23] albeit without a comment on potentially high selectivities and yields of benzaldehyde.

The advantages of the catalytic oxidation described herein is that the catalyst is composed of inexpensive, simple metal acetate salts and a source of ionic bromide (NaBr, HBr, etc.). The reaction times are within a few hours at easily accessible temperatures. The acetic acid solvent is inexpensive and nearly all alcohols are highly soluble in it. Although acetoxylation of the alcohols with the acetic acid solvent does occur, this side-reaction results in only a 5–8% yield loss. It is noteworthy that there are other solvents available for metal/bromide catalyzed systems, which could potentially eliminate this problem.[19] Due to the high activity of the metal/bromide catalysts the aldehyde formed in high yield can undergo further oxidation. To obtain high yields of aromatic benzaldehydes from the corresponding aromatic alcohols the catalytic process should be carefully monitored, so that subsequent oxidation of the aldehyde formed can be avoided.

Structure of the Catalyst

Addition of the simple acetate salts into acetic acid results in a complex mixture which is only partially understood. A brief synopsis based on available information follows. The structures of Co(II) and Mn(II) in acetic acid/water mixtures can be summarized by the equation:

$$\{M(HOAc)_4(OAc)_2\}_n \xrightleftharpoons{+\ HOAc} \{\{M(HOAc)_5(OAc)\}(OAc)\}_n \qquad n = 1, 2$$

where the square brackets indicate the ligands in the inner coordination sphere. In acetic acid, the cationic metal species are largely associated, with the small quantities of the dissociated species existing as ion pairs[24] in both monomeric and dimeric forms (n = 1, 2).[25–27] Upon addition of water, equilibrium is established between various metal aquo acetic acid complexes. Using reported equilibrium constants[28] one can calculate the distribution of these complexes and demonstrate that these aquo/acetic acid metal species exist in 10% water/acetic acid mixtures.[29] The weakly bound AcOH ligand (5.9 kcal/mol) is labile, exchanging with water and acetic acid instantaneously at room temperature.[30] The addition of peracids, peroxy radicals, oxygenated intermediates, etc. to a mixture of Co(II)/Mn(II) in acetic acid may therefore result in fast ligand exchange to form the transient catalytic species. Addition of hydrogen bromide to Co(II) or Mn(II) or a Co(II)/Mn(II) mixture in anhydrous acetic acid results in the majority of the bromide being coordinated to the metal. However, addition of water (5% or greater) results in almost complete ionization of the M–Br bond.[29] In the presence of water the addition of bromide results in outer-sphere ligand exchange processes, as shown in the equation below.

$$\{\{M(HOAc)_m(H_2O)_{m-5}(OAc)\}_n(OAc)\} + \{H^+\ Br^-\} \longrightarrow \{\{M(HOAc)_m(H_2O)_{m-5}(OAc)\}_n(Br)\} + HOAc$$

It is possible that the ion-paired bromide forms hydrogen bonds to the aquo ligands (Figure 8, structure b). The lability of the ligands, the known dimeric structure of Co(II) acetate, and polynuclearity of Zr(IV) in water suggests that polynuclear Co(II)–Mn(II) and Co(II)–Zr(IV)–Mn(II) may exist (Figure 8). Such mixed-metal polymeric species have been isolated from acetic acid.[31] Recent observations[32] suggest that acetic acid/water solutions may be more complex, containing water-rich microphases. It is proposed that Co(III) aquo

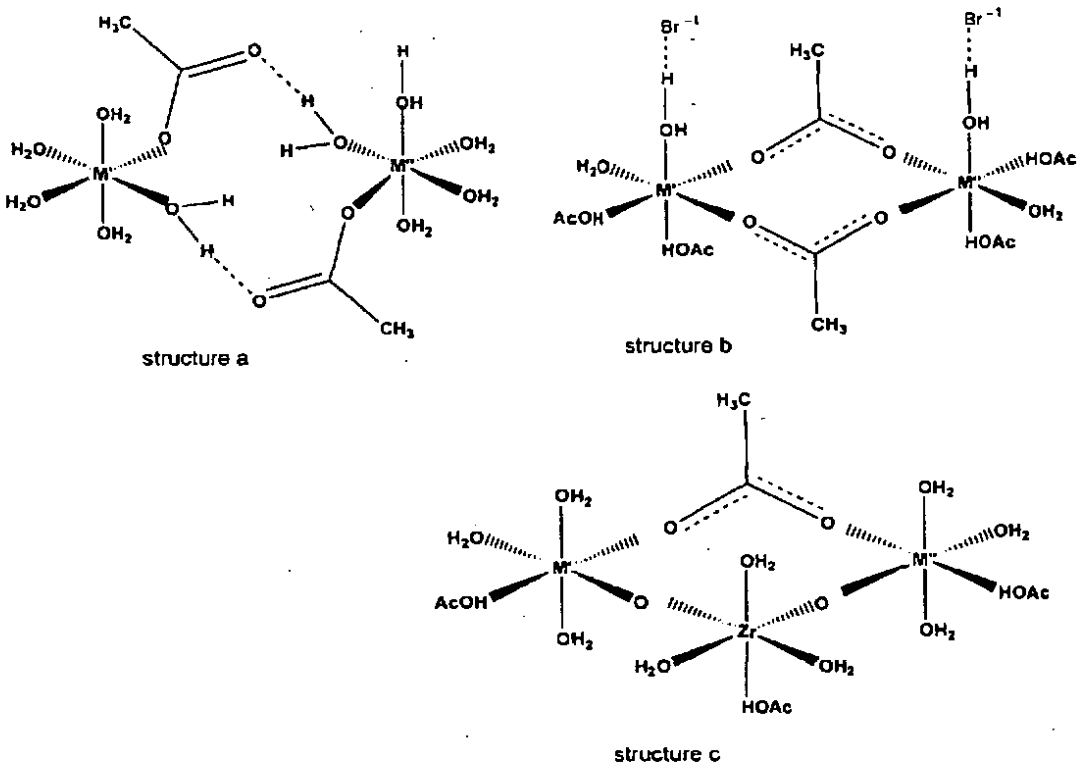

Figure 8. Suggested structures for Co,Mn,Br mixtures in 5% H_2O/HOAc. M'=M''=Co(II), Co(III), Mn(II), Mn(III)

acetate and Co(III) aquo acetate bromide have structures similar to those shown in Figure 8 (a and b, respectively).

Theory and Models of Metal/Bromide Catalysis

Different aspects of metal/bromide catalysis have been discussed with emphasis on high reactivity,[19,27,33–36] superior selectivity over a broad temperature range,[19,54] and the synergy and antagonism of the metals.[34,36,37] Important new observations in this field have been recently reported.[38] Kinetic studies suggest that oxidation of Co(II) by peracids (to give carboxylic acids)[27,37] and peroxy radicals (to give peroxides)[33] initiates the series of reactions shown in Figure 9. The rapidity of the peroxide reactions with Co, followed by the subsequent redox cascade leading to the generation of the selective bromide atom or the dibromide radical[38] accounts for the properties of these catalysts. Initiation of the hydrocarbon RH to the radical R· via the Co/Mn/Br redox cascade is faster than Co/Br, which in turn is faster than Co. Co(III)^a, Co(III)^a, Co(III)^c are different Co(III) compounds, with structures suggested in Figure 8 possessing different reactivity.[26]

Rationale for High Yields of Aromatic Benzaldehydes from Aromatic Alcohols

High yields of benzaldehydes are observed despite the fact that benzyl alcohol and benzaldehyde react at nearly the same rate in the metal/bromide catalyzed system. In particular, for benzyl alcohol oxidation the benzoic acid yield remains under 1% at 60% conversion and is only 4.6% when the maximum yield of benzaldehyde is obtained (80%) at 85% conversion. These observations are certainly unexpected and hence merit a comment. There are at least three factors which would account for the clean and selective formation of benzaldehyde under the conditions employed.

There may be a rapid, preferential bonding of the aromatic alcohol with either or both Co(II) and Mn(II), which initiates their oxidation in preference to the benzaldehyde. The formation of benzyl alcohol metal species might occur via replacement of the labile, weak acetic acid or aquo ligands or hydrogen bonding to the *coordinated* AcOH or water molecules (similar to the bromide in Fig. 9). Once all of the aromatic alcohol has been oxidized the catalyst initiates the benzaldehyde oxidation.

There is experimental evidence that acetic acid retards autoxidation by hydrogen bonding to the peroxy

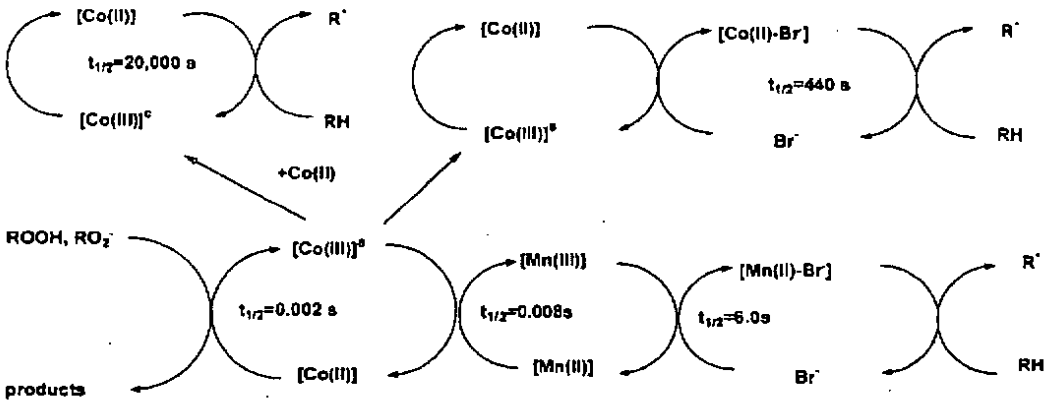

Figure 9. Summary of chemistry of Co, Co/Br, and Co/Mn/Br autoxidation catalysts. Half-lifes are at 60°C in 10% water/acetic acid

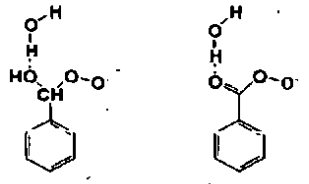

Figure 10. Suggested structure of hydrogen bonded acetic acid to benzyl alcohol intermediates

radicals at the α-position (Figure 10).[39] It is conceivable that the acetic acid is more effective at inhibiting the carbonyl functionality than the benzylic hydroxy group. This explanation seems less likely because the oxidation of the aromatic alcohol and benzaldehyde would have been already initiated, and even if they proceed further at different rates, significant amounts of aromatic acids should be formed from the benzaldehyde. However, the actual amount of benzoic acid formed from benzaldehyde does not exceed 1–5% (see above).

It is possible that one or more coordination compounds in the reaction mixture specifically inhibits the benzaldehyde oxidation or promotes the aromatic alcohol reaction. We have found that sodium bromide strongly inhibits the oxidation of benzaldehyde, whereas Co enhances this reaction. The rate of oxygen uptake is 12.0 mL/min without catalyst, 0.3 mL/min with sodium bromide and 13.2 mL/min with Co(II) acetate at 80°C in acetic acid.[40]

Obviously, further experimentation is required to confirm these conjectures.

Effect of Zirconium on Selectivity

In the high pressure experiments, we found that the selectivity to DFF increased in the presence of Zr in the Co/Mn/Br catalyst. The effect of Zr on cobalt metal/bromide catalysts is generally thought to increase its activity[19,35,41] and Zr does *not* affect the rate determining step because the ρ values in a Hammett plot of Co/Mn/Zr/Br and Co/Mn/Br are the same within experimental error.[35] However, there is a brief report that addition of Zr to a Co/Br catalyst decreases the rate of benzyl alcohol formation and increases the rate of benzaldehyde formation.[42] We have duplicated this effect with a Co/Mn/Zr/Br catalyst in 10% water/acetic acid at 95°C with the oxygenation of *p*-xylene. The increase in the rate of reaction is proportional to the Zr concentration which in turn is directly proportional to the observed reduction of the benzyl alcohol/benzaldehyde ratio.[40] One possibility is that the rate of alcohol oxidation (Figure 2, step 3) is increasing relative to step 2. It is also possible that step 1 is becoming more important than step 2. We suggest that the new catalytic species form when Zr is added to Co/Mn/Br (see Figure 8), which goes through similar redox cascades as shown in Figure 9, changing some of the relative rates presented in Figure 2. More details on the function of Zr are available.[19]

Overoxidation to CO_x

A weakness of most published work on oxygenations using air as the primary oxidant is the lack of measurement of CO_x formation during the reaction. The potential for the formation of the highly reactive peroxides and consequently peroxy, hydroxyl, etc. radicals always exists when mixtures of transition metals, dioxygen, hydrocarbons, and organic solvents are present and hence 'overoxidation' to CO_x nearly always occurs.

Much higher amounts of carbon monoxide and carbon dioxide (CO_x; x = 1, 2) form during HMF oxygenations as compared with the benzyl alcohol oxidation under similar conditions (Table 1, Figure 6). Tracer studies indicate that the origin of CO_x is from both the aromatic substrates and the acetic acid solvent.[43] The formation of CO_x in the HMF reaction is

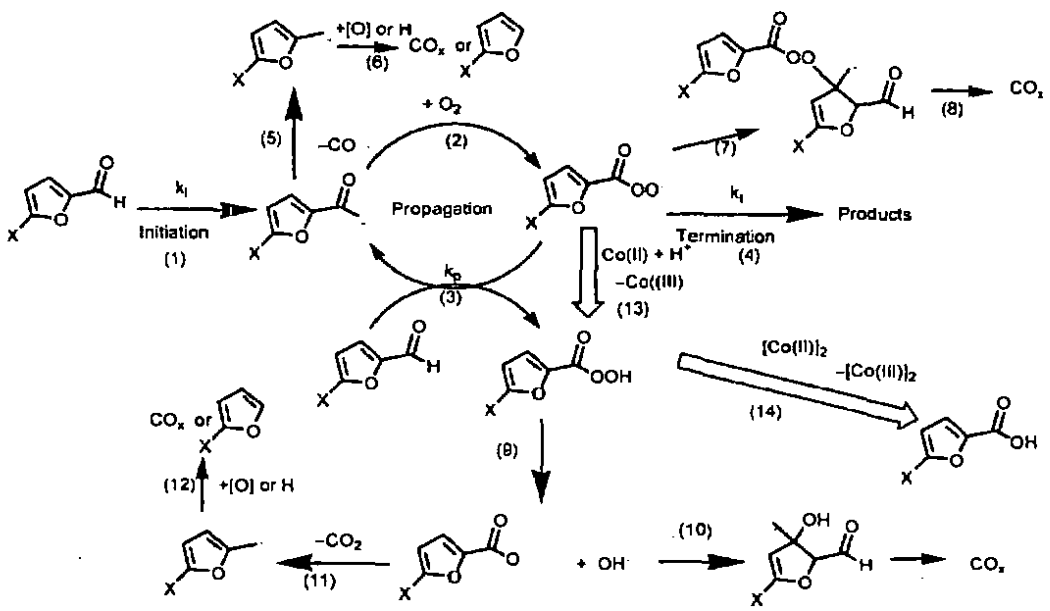

Figure 11. Important pathways in hydroxymethylfurfural oxidation

apparently *not* predominately from the solvent because only trace amounts of acetoxyacetic acid, an oxidatively stable by-product formed from the acetic acid, is observed by GC. We determined the amount of CO_x formed by numerical integration and then assumed that 100% came from the total destruction of HMF. A significant yield loss of 1.8 to 8.5% is calculated. This significant loss, as compared to the benzyl alcohol oxidation (ca. 0.05% lost to CO_x) is accounted for by at least two reasons.

Decarbonylation. By-product formation during *p*-xylene[44] and alkylnaphthalene oxidation[19] is consistent with hydrogen atom abstraction from the aldehyde followed by decarbonylation and eventual aromatic ring loss via the formation of phenol (Figure 11). HMF is initially a di-functional molecule already containing a formyl functionality in contrast to benzyl alcohol. Hence higher HMF loss via this mechanism is anticipated.

Enhanced ring attack due to reduced resonance energy. The resonance energy values for benzene, naphthalene, and furan are 36, 31, and 17 kcal/mol.[45] The difference between metal/bromide catalyzed alkylbenzene and alkylnaphthalene oxygenations has been discussed[19, 46] and is largely due to the enhanced ring bromination and enhanced peroxy radical ring attack that occurs in the naphthalene derivatives. This forms intermediates (e.g., phenols) which quickly undergo exhaustive oxidation to CO_x. Since the resonance energy of furan is even lower than naphthalene (31 vs. 17 kcal/mol), the higher rate of CO_x formation is not surprising.

Effect of Catalyst Concentration on Activity and Overoxidation to CO_x

We find that increasing catalyst concentration increases activity at the early stages, but then remains constant or decreases slightly (Table 1), consistent with previous observations.[19] Kinetic studies show a second order dependence of cobalt concentration for a Co/Br catalyst.[55]

Remarkably, overoxidation to CO_x is suppressed at higher catalyst concentrations. This has been observed in metal/bromide catalyzed systems previously.[47] The *non-selective, thermal* pathways are (i) decarbonylation in step 5 and subsequent by-product formation in step 6, (ii) peroxy radical attack on the furan ring in step 7, and (iii) thermal dissociation of the peroxide (step 9), leading to the carboxylate radical and the highly reactive OH radical. Step 9 is followed by ring addition of the hydroxyl radical to furan (step 10), which will eventually lead to by-products including CO_x. The carboxylate radical can decarboxylate (step 11), leading to the same products as in the decarbonylation process (step 12). As the catalyst concentration increases at least two *selective, metal catalyzed pathways* become increasingly important. At [Co] > 0.01 M, kinetic and chemiluminescence data provide evidence that the direct oxidation of Co(II) by peroxy radicals becomes important[53] (step 13). This reaction will increasingly supplant step 7 as the catalyst concentration increases, hence reducing ring attack and deaccelerating the CO_x formation. Because step 14 is 400,000 times faster than step 9, displaying a 18 kcal/mol lower activation energy barrier,[27] hydroxyl radical formation and decarboxylation are

greatly diminished as the cobalt concentration increases. The reason *both* selectivity and activity are often enhanced in metal/bromide systems is that reactions 13 and 14 produce Co(III) which quickly goes through the redox cascade shown in Figure 9 to continue to initiate the reaction.

In the future, it is planned to extend the methodology described herein to substituted benzylic alcohols, aliphatic alcohols, and a variety of other alkylaromatic systems such as naphthalene, pyrrole, and thiophene derivatives.

Experimental Section

Aldrich cobalt(II) and Fluka manganese(II) acetate tetrahydrates, Alfa cerium(III) acetate hydrate, EM Science sodium bromide, benzyl alcohol and acetic acid, Baker hydrobromic acid, Aldrich zirconium(IV) acetate and biphenyl, and Lancaster hydromethylfurfural were used as received. Catalysts were prepared by dissolving the above compounds into acetic acid in the amounts specified on Table 1–3.

Autoxidation at Ambient Atmospheric Pressure

A glass cylindrical reactor, as previously described,[20] was used. Initial weight of acetic acid was 100 g, with Co/Mn = 1.0 mol/mol, Br/(Co+Mn) = 1.0 mol/mol in all cases. We found that HMF, but not benzylic alcohol, required addition of 0.5–1.0 g of acetaldehyde to initiate the reaction at 75 °C. The rate of oxygen uptake was continually monitored by measuring the flow rate into the reactor and the concentration of dioxygen in the vent gases. The vent gases (O_2, N_2, CO, CO_2) were measured using an automated GC system. Liquid samples were removed during the reaction and analyzed via GC as soon as possible.

Autoxidation at 70 Bar in Air

These reactions were performed in a 20-mL cylindrical glass reactor. The samples were analyzed after removal from the reactor. *Caution: The use of high pressures and the use of dioxygen/nitrogen mixtures is potentially explosive and dangerous. They should be performed only with adequate barriers for protection.*

The rate of dioxygen uptake, in mL/min, is given by the equation: $R(O_2) = F(20.9 - [O_2])$ where F = flow rate of air into the reactor, $[O_2]$ = concentration of oxygen in the exit gas stream and 20.9 is the concentration of dioxygen in air (in %). The carbon dioxide (x = 2) and carbon monoxide (x = 1) selectivity is defined by:

S_{COx} = rate of formation of CO_x/rate of dioxygen reacted.

$S_{COx} = R_{COx}/Ro = F[CO_x]/(F(20.9 - Vo)) = [CO_x]/(20.9 - Vo)$

where $[CO_x]$ is the vent carbon oxide concentration, expressed as percent.

DFF from example 5, Table 1, was isolated by evaporation of the solvent and vacuum sublimation of the residual solid (90 °C at 10–50 millitorr). The sublimed material (5.2 g; 51% in agreement with the GLC yield) was 95% pure DFF containing ca. 3–5% 5-acetoxymethylfurfural (NMR). The crude DFF was further purified by filtration of its dichloromethane solution through silica, followed by partial evaporation of the filtrate and precipitation with hexanes. ^{1}H NMR ($CDCl_3$, 20 °C): δ = 7.4 (s, 2H, furan H), 9.8 (s, 2H, CHO); ^{13}C NMR (CD_2Cl_2, 20 °C): δ = 120.4 (s, CH), 154.8 (s, qC), 179.7 (s, CHO); Mass spectrum: *m/z* = 124.

2,5-Furandicarboxylic acid was isolated in the following manner. The solubility of 2,5-furandicarboxylic acid is 6.6×10^{-4} g/g in 5% H_2O/HOAc at room temperature. Hence when the reaction solutions are cooled to room temperature 99% of the 2,5-furandicarboxylic acid precipitates. The solids after reaction were filtered, washed with acetic acid, then water, and air-dried. If insufficiently oxidized, the solids contained both 2-carboxy-5-formylfuran and 2,5-furandicarboxylic acid in varying amounts. *All of the reported 2-carboxy-5-formylfuran and 2,5-furandicarboxylic acid yields are based on the precipitated solids only.* The composition of the isolated solids containing 2-carboxy-5-formylfuran and 2,5-furandicarboxylic acid in the solids were determined from their NMR spectra in DMSO.

For 2-carboxy-5-formylfuran; ^{1}H NMR (DMSO): δ = 7.4 (s, 1H, furan CH), 7.7 (s, 1H, furan CH), 9.8 (s, 1H, CHO); ^{13}C NMR (DMSO): δ = 122.3 (s, CH), 153.2 (s, CH), 172.0 (s, COOH), 179.7 (s, CHO).

For 2,5-furandicarboxylic acid; ^{1}H NMR (DMSO): δ = 7.3 (s, 2H, furan CH); ^{13}C NMR (DMSO): δ = 118.5 (s, CH), 148.1 (s, C), 158.8 (s, COOH); anal. calcd. for $C_8H_4O_5$, %: C, 46.16; H, 2.59; found for solids obtained in experiments 6, 7, 11, 12 in Table 5, %: C, 45.95; 45.95; 45.45; 45.79; H, 2.57; 2.45; 2.44; 2.43.

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Review

Biomass into chemicals: Conversion of sugars to furan derivatives by catalytic processes

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ABSTRACT

Recently, the production of furan derivatives from sugars has become exciting in chemistry and in catalysis studies, because it aids one of the major routes for achieving sustainable energy supply and chemicals production. 5-Hydroxymethylfurfural (5-HMF), 2,5-furan-dicarboxylic acid (2,5-FDCA) and 2,5-dimethylfuran (2,5-DMF) have been called the "sleeping giants" of renewable intermediate chemicals. 5-HMF is a dehydration product of hexoses and a potential substitute of petroleum-based building blocks of various polymers. 2,5-FDCA is derived from oxidative dehydration of hexoses and is considered as one of the top 12 compounds made from a sugar into a value-added chemical [T. Werpy, G. Petersen, Top Value Added Chemicals From Biomass, 2004. Available electronically at http://www.osti.gov/bridge]. 2,5-DMF is produced through hydrogenation of HMF and is less volatile and of 40% higher energy density than ethanol. This review discusses mainly the catalytic routes for the synthesis of 5-HMF, 2,5-FDCA, 2,5-DMF and other furanic derivatives from sugars. Meanwhile, the possible reaction mechanism for the conversion of hexoses is discussed, and furthermore, some promising research orientations and advantageous catalysts are suggested based on the major problems encountered in the recent research.

Contents

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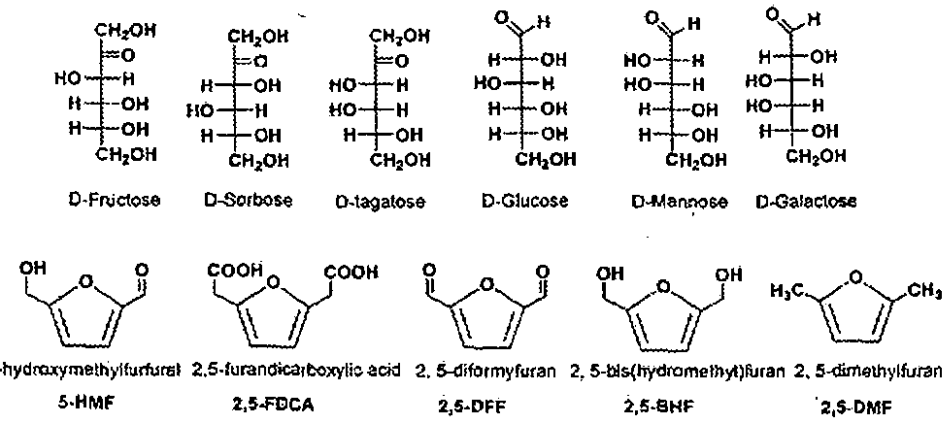


Fig. 1. The structures of the representative hexoses and furans.

1. Introduction

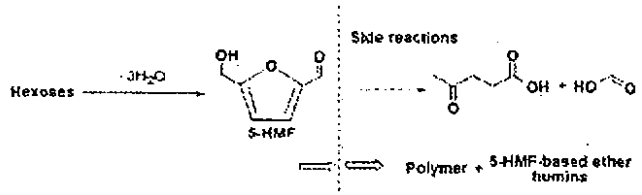
In recent years, an increasing effort has been devoted to find ways to utilize biomass as feedstocks for the production of organic chemicals because of its abundance, renewability and worldwide distribution [1–8]. If one considers the possible downstream chemical processing technologies, the conversion of sugars to value-added chemicals is very important [9,10]. Hexoses are the six-carboned carbohydrates and are the most abundant monosaccharide existing in nature (Fig. 1). Among them D-fructose and glucose are economical and suitable to be used as the chemical feedstocks [11–16]. Nowadays, the catalytic transformation of hexoses into furans is very interesting in the point of chemistry because it involves several steps as dehydration, hydrolysis, isomerization, reforming, aldol condensation, hydrogenation and oxidation, etc., which are of general interest. The furanic products involved in this strategy include 5-hydroxymethylfurfural (5-HMF), 2,5-diformylfuran (2,5-DFF), 2,5-furandicarboxylic acid (2,5-FDCA), 2,5-bis(hydroxymethyl)-furan (2,5-BHF) and 2,5-dimethylfuran (2,5-DMF) (structures are shown in Fig. 1). These can be used as the starting materials for new products as well as for the replacement of oil-derived chemicals [17–20]. As a dehydration product of hexoses, 5-HMF has been considered to be an important and renewable platform chemical in the bio-based renaissance. Its derivatives including 2,5-furfuryldiamine, 2,5-furfuryldiisocyanate and 5-hydroxymethyl furfurylidenester are particularly suitable starting materials for the preparation of polymeric materials such as polyesters, polyamides and polyurethane [21–24]. The obtained furan-based polymers display very good properties. The polyurethane shows very high resistance to thermal treatment. The kevlar-like polyamides produced from furan diamines and diacids exhibit liquid crystal behavior. The photoreactive polyesters have been used for printing ink formulation. Furthermore, the furan-based polyconjugated polymers possess good electrical conductivity [24]. Thus, 5-HMF has been called a 'sleeping giant' in the field of intermediate chemicals from re-growing resources [17].

In the chemical conversion processes, the compounds like 5-HMF, 2,5-FDCA, 2,5-DFF, 2,5-BHF or 2,5-DMF are interrelated by the reaction network. For instance, 2,5-FDCA or 2,5-DFF is formed from the complete or partial oxidation of 5-HMF, and is the co-product in the one-pot dehydration and oxidation reaction of hexoses [25]. Indeed, 2,5-FDCA has been found useful as a fungicide, corrosion inhibitor and melting agent for foundry sands as well as an intermediate in pharmaceutical and photography fields [26–29]. Moreover, 2,5-FDCA has also gained a great interest as a monomer of new polymeric materials for special applications [30–33]. In fact, 2,5-FDCA has also a large potential as a replacement of terephthalic acid, a widely used component in various polyesters such as polyethylene terephthalate (PET) and polybutyleneterephthalate (PBT) [34,35]. 2,5-FDCA can also serve as a starting material for the production of succinic acid, which is consumed at present in a fairly large scale. Thus, 2,5-FDCA has been identified as one of the 12 building block compounds that can be produced from sugars *via* biological or chemical processes [36]. Meanwhile, 2,5-DFF has also numerous applications, including those as monomers in the synthesis of special polymers [37–39], as intermediates of pharmaceuticals [40] and as antifungal agents [41]. It is also used in the preparation of macrocyclic ligands [42,43] and as a cross-linking agent for poly(vinyl alcohol) [44]. Furthermore, 2,5-BHF and 2,5-DMF are produced from the partial or deep hydrogenation of HMF, respectively, and can also be generated in the one-pot dehydration and hydrogenation of hexoses. 2,5-DMF is a very promising liquid fuel in the future, with a high energy density, 31.5 MJ/L, which is similar to that of gasoline (35.0 MJ/L), and is 40% higher than that of ethanol (23.0 MJ/L) [45,46]. Moreover, 2,5-DMF (bp 92–94 °C) is less volatile than ethanol (bp 78 °C) and is immiscible with water, so that it is especially suitable to be used as a transportation fuel.

In 2007, Corma et al. [15] and Dumesic and coworkers [16] have reviewed the chemical routes for the transformation of biomass into chemicals and fuels, respectively. Considering the rapid progress on the catalytic conversion of biomass, this review concentrates mainly on describing the state-of-the-art and the works reported within the recent few years. In this review, the synthesis methods of 5-HMF, 2,5-FDCA, 2,5-DFF, 2,5-BHF and 2,5-DMF from carbohydrates with suitable catalyst systems are discussed in detail. For the production of 5-HMF, various acids, sometimes with the presence of metal ions, are used as catalysts. For the manufacture of 2,5-FDCA, there are two routes. One is the direct oxidation of 5-HMF by a suitable oxidant. The other is the one-pot dehydration and oxidation of hexoses, requiring a multi-functional catalyst. 2,5-DFF has been prepared through a partial oxidation of 5-HMF with the function of a catalyst such as Pd/C, V_2O_5/TiO_2 or metal/bromine. 2,5-BHF and 2,5-DMF have been synthesized from selective hydrogenation of 5-HMF, which is originally formed from hexoses in a special media or a biphasic reactor.

2. Synthesis of 5-hydroxymethylfurfural

From the commercial point of view, 5-HMF is a versatile and multi-functional compound. It is a good starting point for the synthesis of precursors of pharmaceuticals, thermoresistant polymers, and macrocyclic compounds, and particularly for the synthesis of dialdehydes, ethers, amino alcohols, and other organic intermediates. These may lead to the possibility of numerous chemical



Scheme 1. The production of 5-HMF and the corresponding side reactions.

products such as solvents, surface-active agents, phytosanitary products, resins, and the like [14–16].

Since the last decade of the 19th century, 5-HMF had been of great interest [47]. It was first separated with 20% yield from the reaction mixture of fructose and sucrose in the presence of oxalic acid [48]. Then, Fenton and coworkers [49–51] performed extensive investigations on 5-HMF. In 1909, the correct structure of 5-HMF was assigned [52]. After an intensive examination, Middendorp [53] presented detailed results concerning the synthesis, physical properties and chemical behaviors of 5-HMF. In the following years, Reichstein and Zschokke [54,55] and Haworth and Jones [56] contribute to immense progress in 5-HMF chemistry. They proposed the synthesis method of 5-HMF which is used still in the modern time, and they discussed the mechanism of fructose dehydration. Besides, 5-HMF can also be produced by heating a 30% aqueous solution of sucrose at 170 °C under H_2 pressure, with a 22% yield of 5-HMF attained [57].

Thirty years ago, van Dam et al. [58] and Cottier et al. [59] showed that both an aqueous and a non-aqueous process lead to around 37% yield of 5-HMF; they found that the reactions performed in the aqueous solution provoke the degradation of 5-HMF and that its polymerization occurs in both aqueous and non-aqueous media. In the following work, Antal et al. proved that 5-HMF was formed from hexoses through removing three water molecules in the acid-catalyzed dehydration reaction [60]. Scheme 1 presents a general dehydration route of hexoses and the most representative by-products found in the process. In the aqueous system, 5-HMF enters into a consecutive reaction sequence taking up two molecules of water, and forms levulinic and formic acid as semifinal products. In the non-aqueous system, the hydrolysis of 5-HMF can be suppressed. However, the cross-polymerization reactions occur under all circumstances, which lead to the production of colored soluble polymers and insoluble brown humins [12]. In order to prevent the side reactions and obtain a high yield of 5-HMF, one can design and employ a suitable catalyst tuned to the formation of 5-HMF, while not promoting the consecutive reactions or alternatively the continuous removal of 5-HMF from the reaction mixture.

The production of 5-HMF and the kinetic studies of the dehydration reaction had been reviewed by Kuster in 1990 [11] and Lewkowski in 2001 [12]. The following sections emphasize the recent research developments and summarize the efficient catalyst system for the synthesis of 5-HMF. The catalysts used are generally classified as mineral acid, organic acid and solid acid catalysts, and metal-containing catalysts.

2.1. Mineral and organic acid catalysts

2.1.1. Production of 5-hydroxymethylfurfural from fructose

The dehydration of D-fructose can generally be catalyzed by a protonic acid as well as by a Lewis acid [61,62]. From the first oxalic acid-catalyzed synthesis of 5-HMF, nearly one hundred inorganic and organic acidic compounds have been positively identified as catalysts for the synthesis of 5-HMF. The most commonly used inexpensive acids have been H_2SO_4, H_3PO_4 and hydrochloric acid (HCl) [63–65]. Moreover, hydroiodic acid (HI) has also been found to exhibit catalytic action in the iodine-catalyzed dehydration of hexoses [66]. The reported organic acids also include the oxalic acid, levulinic acid, and p-toluenesulfonic acid [56,67–70].

Antal et al. [60,71] reported the dehydration of D-fructose with H_2SO_4 as a catalyst in sub-critical water at 250 °C, and gained a yield of 5-HMF as high as 53%. Bicker et al. [17] investigated the synthesis of 5-HMF in the presence of H_2SO_4 when sub-critical or supercritical acetone–water mixture was employed as a reaction medium. It was found that the carbon atom efficiency is quite good and that no solid impurities are formed. In the supercritical acetone–water mixture, the maximum yield of 5-HMF reached 78% at 180 °C. Recently, a two-phase reactor system with HCl as the catalyst was reported by Roman-Leshkov et al. [18]. As shown in Fig. 2, D-fructose is dehydrated to 5-HMF in the aqueous phase with HCl as a catalyst. In this process, dimethylsulfoxide (DMSO)

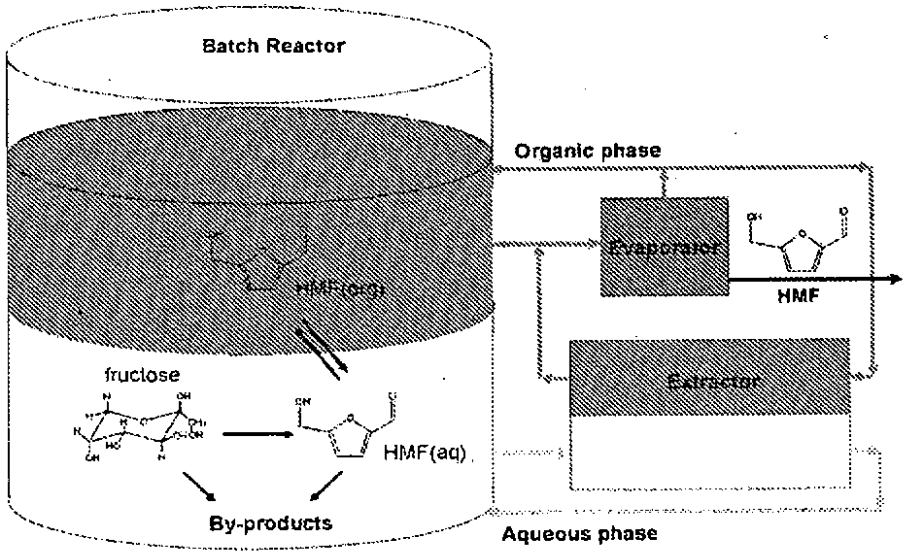


Fig. 2. The production of 5-HMF from D-fructose with simulated countercurrent extraction and evaporation steps (The aqueous phase contains fructose, DMSO, PVP, and catalyst; the organic phase contains MIBK and 2-butanol; this figure is modified and taken from Ref. [18] with permission of the American Association for the Advancement of Science. 2006 Copyright Science Publishing).

Table 1
The catalytic reaction results for the fructose dehydration with typical solid acid catalysts.

Catalyst	Solvent	T (°C)	Time (min)	Conv. (%)	5-HMF yield (%)	Ref.
H-form mordenite	H_2O-MIBK	165	60	76.0	69.2	[80]
Vanadyl phosphate	H_2O	50	60	50.2	41.9	[81]
$NbOPO_4$	H_2O	100	120	61.4	21.6	[82]
C-ZrP_2O_7	H_2O	100	30	44.4	44.3	[85]
Amberlyst-15	$[BMIM]^+BF_4^-$	80	180	–	52	[99]
Dowex 50wx8-100	Acetone/H_2O	150	15	95.1	73.4	[101]
Dowex 50wx8-100	Acetone/DMSO	150	10	96.4	82.1	[102]
Anatase TiO_2	H_2O	200	5	83.6	38.1	[103]
Amberlyst-15	DMF	100	180	>99	73	[106]
SO_4/ZrO_2	DMF	100	180	57	21	[106]

and poly(1-vinyl-2-pyrrolidinone) (PVP) were added to suppress the undesired side reactions. The product 5-HMF was continuously extracted into an organic methylisobutylketone (MIBK) phase modified with 2-butanol to enhance the partitioning from the reactive aqueous solution. It was reported that an 80% 5-HMF selectivity at a 90% conversion was achieved for 10 wt.% D-fructose solution. Moreover, Román-Leshkov and Dumesic [72] investigated the solvent effect on the dehydration of fructose in biphasic system with saturated inorganic salt, in which tetrahydrofuran demonstrates a high extracting ability as a reaction medium for the reaction and an 83% selectivity of 5-HMF is achieved. Furthermore, a continuous process using a microreactor has been proposed based on the HCl-catalyzed dehydration of fructose in pure aqueous solution in order to improve the "green" synthesis of 5-HMF [73]. The process conditions were deliberately shifted to high temperature and pressure (185 °C, 17 bar) in only 1 min and the product 5-HMF was obtained with a 54% yield at 71% D-fructose conversion.

2.1.2. Production of 5-hydroxymethylfurfural from glucose

The dehydration of glucose has been reported to have lower reaction rate and lower selectivity to 5-HMF compared to these of fructose [11], even though glucose is the most inexpensive and abundantly available feedstock. A yield of only 15.5% was obtained during the dehydration of glucose in the presence of H_3PO_4 at 190 °C [74]. The low yield of 5-HMF from glucose is attributed to its stable ring structure. A low fraction of open-chain molecules exists in the solution and as a consequence a low speed of enolization develops which determines the rate of 5-HMF generation. Nonetheless, a strong incentive exists for developing a process utilizing cheaply and abundantly available glucose to produce directly the value-added 5-HMF for useful chemicals.

Different solvents have been tested in glucose dehydration with mineral acid as catalyst [68]. It was found that the dehydration of glucose to 5-HMF was nonselective (about 6%) in pure water. Meanwhile, the yield of 5-HMF in an aprotic polar solvent (e.g. DMSO) was also low (no more than 42%) even for a 3 wt.% glucose solution. Recently, a valuable breakthrough appeared [75]. It was found that the yield of 5-HMF can be improved with a specially designed biphasic reactor system and with a 10 wt.% glucose feed solution. The biphasic reaction system was composed of DMSO, water, and a mixture of MIBK/2-butanol (70:30, w/w) as the extraction solvent. As a result, the selectivity of 5-HMF increased from 11% in pure water to 53% with the presence of DMSO and the extraction solvent.

Recently, Huang et al. [76] proposed an efficient method for the selective conversion of glucose to 5-HMF, in which a combination of glucose isomerase and HCl was employed as the catalyst and the reaction was performed in a water–butanol biphasic reactor. As a result, a 63.3% yield of 5-HMF was obtained from glucose.

2.1.3. Production of 5-hydroxymethylfurfural from polysaccharides and biomass feedstocks

Employing polysaccharides, cellulose and lignocellulose directly as feedstocks for the production of 5-HMF is more promising commercially. Recently, Chheda et al. [75] got good selectivities for 5-HMF at high conversions from polysaccharides such as sucrose, starch, cellobiose and xylan using a mineral acid (HCl, H_2SO_4 or H_3PO_4) as a catalyst in a biphasic reactor. The reactor system composed of a reactive aqueous phase modified with DMSO and an organic extracting phase consisting of a 7:3 (w/w) MIBK–2-butanol mixture. Moreover, Ilgen et al. [77] reported that 25 and 57% yields of 5-HMF are obtained respectively from inulin and sucrose using p-toluenesulfonic acid as catalyst in a melt system consisting of choline chloride (ChCl) and up to 50 wt.% of carbohydrates. Remarkably, Binder and Raines [78] found that *N,N*-dimethylacetamide (DMAc) containing alkali metal halide is a privileged solvent that enables the synthesis of 5-HMF from lignocellulosic biomass, as well as from cellulose, glucose, and fructose, with the mineral acid as the catalyst. For instance, a 92% yield of 5-HMF was obtained from lignocellulosic biomass using 6.0 mol% H_2SO_4 as the catalyst in DMAc-KI solvent at 100 °C for 5 h.

2.2. Solid acid catalysts

Solid acid catalysts have several advantages over liquid acid catalysts: (a) they facilitate the separation of product and can be recycled; (b) they can work at high temperatures, thus shortening the reaction time and favoring the formation of 5-HMF instead of its decomposition during a prolonged reaction period; (c) they are capable of adjusting the surface acidity to improve the selectivity of 5-HMF, which will be very useful to the conversion of polysaccharides and biomass feedstocks. In the dehydration of carbohydrates, the reported solid acid catalysts generally included H-form zeolites, ion-exchange resins, vanadyl phosphate, and ZrO_2.

2.2.1. Production of 5-hydroxymethylfurfural from fructose

The reaction results of D-fructose dehydration are summarized in Table 1.

Moreau et al. [79,80] studied the dehydration of D-fructose in the presence of the dealuminated H-form mordenite at 165 °C in a solvent consisting of water and MIBK. A D-fructose conversion of 76% and a 5-HMF selectivity of 92% were achieved at the same time. In addition, the conversion of D-fructose and the selectivity of 5-HMF are found to be related to the kind of acid and the structural properties of the acid, as well as to its micropore vs. mesopore volume distribution. The maximum reaction rate of D-fructose was observed on the H-mordenite with a Si/Al ratio of 11, and a significant increase (*ca.* 10%) of the selectivity of 5-HMF was obtained by the simultaneous extraction of 5-HMF with MIBK circulating

in a countercurrent manner in a continuous heterogeneous pulsed column reactor [80].

Carlini et al. [81] reported the catalytic properties of vanadyl phosphate (VOP) for the dehydration of D-fructose to 5-HMF in aqueous solution. A 40.2 or 32.9% yield of 5-HMF was obtained for 6.0 and 30 wt.% aqueous solution of fructose using VOP as the catalyst within 0.5 h, respectively. Moreover, other VOP-based catalysts which contain different trivalent metal ions (Fe^{3+}, Cr^{3+}, Ga^{3+}, Mn^{3+} or Al^{3+}) were also investigated. When Fe-containing VOP catalyst was employed with 40 wt.% fructose solution, the yield and selectivity of 5-HMF went up to 50.4 and 87.3% within 0.5 h, respectively. Furthermore, Nb-based catalysts were also used in the reaction and showed a high catalytic efficiency [82–84]. Niobium phosphate ($NbOPO_4$) and phosphoric acid-treated niobium oxide exhibited high catalytic activity. As a result, 70–80% selectivity of 5-HMF at a D-fructose conversion of 30–50% was reported at 100 °C in pure water and without any extraction solvent [85,86]. Moreover, further investigations showed that the initial catalytic performance of $NbOPO_4$ is superior to that of niobate acid in the dehydration of fructose in aqueous phase, which was related to the more effective surface acidity of $NbOPO_4$ in polar liquids [84]. In addition, a similar approach was carried out in the presence of Zr- and Ti-based catalysts with different structures [85]. When cubic zirconium pyrophosphate (C-ZrP_2O_4) was employed in the dehydration of 6 wt.% aqueous solution of fructose, a 44.3% yield of 5-HMF in a 99.8% selectivity was obtained at 100 °C within 0.5 h. Meanwhile, γ-titanium phosphate also exhibited promising performance (a 35.3% yield of 5-HMF in 96.1% selectivity) under similar conditions.

There have been numerous works on the application of ion-exchange resins for the synthesis of 5-HMF from sugars. Nakamura [86] investigated a strongly acidic ion-exchange resin in D-fructose dehydration and obtained an 80% yield of 5-HMF. Gaset and coworkers [87,88] produced 5-HMF with 39–80% yield using the Levatit® SPC-108 as a catalyst. Moreover, Diaion® PK-216 resin was also found to be an efficient catalyst for D-fructose dehydration and a 90% yield of 5-HMF was obtained on it [89]. Compared to that with a mineral acid as catalyst, some improvements are achieved in terms of process facility when an acidic ion-exchange resin is used in aqueous medium, but the selectivity of 5-HMF has been a significant challenge [90–92]. Further investigations by Chheda and Dumesic [93] showed that very good yields of 5-HMF from fructose were achieved with the Diaion® PK216 resin as catalyst in the water–MIBK biphasic system by employing DMSO or NMP as an aqueous-phase modifier.

Cottier et al. [94] found that an ion-exchange resin in water media allowed the conversion of D-fructose with a satisfactory result. However, 5-HMF was obtained with only a 28% yield with a chosen mode of separation. Moreover, they also observed no effect of the high dilution ratio on the efficiency. It was suspected that the low selectivity to 5-HMF in water resulted from the presence of hydronium species within the macropores of resins, which would lead to the further evolvement of 5-HMF [95]. On the other hand, numerous investigations showed that a high selectivity of 5-HMF can be obtained with DMSO as the solvent under moderate operating conditions [89,96–98]. D-Fructose was selectively and almost quantitatively converted into 5-HMF in the presence of ion-exchange resins. The advantage of DMSO as solvent is that it is a dipolar aprotic solvent and prevents the formation of levulinic acid and humins. Its disadvantage is the concern about the separation of DMSO, 5-HMF and water formed, and about the toxic by-products arising from the decomposition of the solvent. Lansalot-Matras and Moreau [99] examined the dehydration of D-fructose with Amberlyst-15 as a catalyst in ionic liquids. The reaction was performed in a micro-batch reactor at 80 °C using two commercially available ionic liquids, a hydrophilic 1-butyl-3-methyl imidazolium tetrafluoroborate ([BMIM]BF_4) and a hydrophobic 1-butyl-3-methyl imidazolium hexafluorophosphate ([BMIM]PF_6). The yield of 5-HMF was 52% after 3 h reaction with [BMIM]BF_4 as solvent. Moreover, the ionic liquid allows the reaction to proceed more rapidly than in DMSO and the reaction achieves a yield of 5-HMF close to 80% in [BMIM]PF_6 solvent. Ilgen et al. [77] reported that a 40% yield of 5-HMF was obtained using Amberlyst-15 as catalyst in the choline chloride (ChCl)/D-fructose system. Furthermore, the effect of co-solvents such as acetone, DMSO, ethanol, methanol, ethyl acetate, and supercritical CO_2 in the Amberlyst-15 resin/ionic liquid system was investigated in detail at room temperature [100]. Recently, Qi et al. [101] used an acetone–water reaction medium and got a yield of 5-HMF as high as 73.4% with a 94.0% D-fructose conversion by microwave heating at 150 °C with the presence of a cationic exchange resin (Dowex 50wx8-100) catalyst. Moreover, the catalytic activity and selectivity after reuse of the resin five times remained nearly unchanged. They also found that the addition of acetone to DMSO solvent further improved the formation of 5-HMF from D-fructose [102].

Watanabe and coworkers [103,104] examined the production of 5-HMF from D-fructose catalyzed by TiO_2 and ZrO_2 under microwave irradiation. In the case of TiO_2, the yield of 5-HMF reached 38.1% with a D-fructose conversion of 83.6% at 200 °C after 5 min. Moreover, a 30.5% 5-HMF yield and 65% D-fructose conversion were obtained in the presence of ZrO_2 after 5 min. Furthermore, Shimizu et al. [105] found that water removal from the reaction mixture by a mild evacuation at 0.97×10^5 Pa increases the yield of 5-HMF for the system with several solid catalysts (heteropoly acid, zeolite, and acidic resin). Also, it was interesting to note that the crushed and sieved Amberlyst-15 powder in a size of 0.15–0.053 mm shows 100% 5-HMF yield at high fructose concentration (50 wt.% in DMSO), which may be due to an improved removal of adsorbed water in the small-sized resin particles.

2.2.2. Production of 5-hydroxymethylfurfural from glucose, polysaccharides and biomass feedstocks

Based on the isomerization of glucose and the successive dehydration of fructose into 5-HMF over solid acid catalyst, Takagaki et al. [106] found that 42–54% yield of 5-HMF can be produced from glucose and sucrose by a simple one-pot synthesis using a combination of Amberlyst-15 and Mg–Al hydrotalcite (HT) as catalyst in *N,N*-dimethylformamide at 100 °C. Moreover, in the TiO_2 and ZrO_2 catalyzed conversion of glucose to 5-HMF, TPD measurement results and experimental data showed that the amount of the basic sites was the key factor for the isomerization, while the strength of the acidity and basicity was important for the 5-HMF formation from glucose [103,104]. Lourvanij and Rorrer [107] found that the molecular sieves, *i.e.* HY zeolite, aluminum-pillared montmorillonite, MCM-20 and MCM-41, also promote the dehydration of glucose; however, formic acid or 4-oxopentanoic acid is easily formed in those processes. Very recently, Hu and coworkers [108] reported that a 47.6% yield of 5-HMF was obtained within 4 h at 403 K over a SO_4^{2-}/ZrO_2–Al_2O_3 catalyst with a Zr–Al mole ratio of 1:1. It was also found that the solid acid catalyst with higher acidity and moderate basicity was more favorable for the formation of 5-HMF from glucose.

Carlini et al. [82] found that a 27 or 31% yield of 5-HMF was obtained from 12.7 wt.% sucrose or 6.0 wt.% inulin with niobium phosphate as catalyst in aqueous medium. Chheda and Dumesic [93] investigated the conversion of inulin and sucrose to 5-HMF in the presence of the Diaion® PK-216 resin; and 69 and 43% yields of HMF were respectively obtained in the biphasic system by adding a certain amount of NMP into aqueous phase (H_2O:NMP = 4:6, w/w). Moreover, with highly concentrated melt systems consisting of ChCl and up to 50 wt.% of carbohydrates, 9, 27 and 54% yields

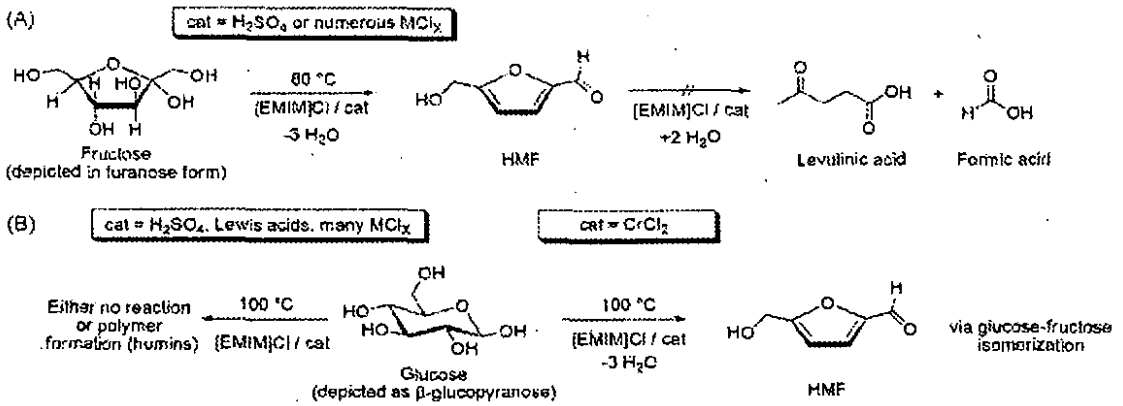


Fig. 3. The synthesis of HMF from D-fructose (A) or glucose (B) in [EMIM]$^+Cl^-$ with the presence of MClx catalyst (Reprinted from Ref. [114] with permission of the American Association for the Advancement of Science. 2007 Copyright Science Publishing).

of 5-HMF were obtained from glucose, sucrose and inulin with Amberlyst-15 resin as catalyst, respectively [77].

2.3. Metal-containing catalysts

The dehydration of D-fructose using transition metal elements began in the 1960s [109]. Trapmann and Sethi [110] found that thorium- and zirconium metals catalyze the formation of 5-HMF in a monosaccharide solution. Ishida and Seri [111] found that lanthanoide (III) ions catalyze the dehydration of D-glucose to 5-HMF and that 5-HMF decomposes further in the reaction. Meanwhile, it was found that a correlation between the catalytic activities and the atomic number of the lanthanoide (III) ions follows a double arc-shaped pattern with a break point at Sm^{3+}, which is very helpful for the design of an active catalyst. Further research revealed that all of the lanthanide (III) ions (La^{3+}–Lu^{3+}) catalyze efficiently the dehydration of hexoses in the aqueous media at 140 °C to produce 5-HMF without levulinic acid formation [112,113]. Kinetic analysis revealed that the rate-determining step is not the complex formation of lanthanide (III) ion with the hexose molecule, but is the subsequent reaction of the substrate–catalyst complex.

Recently, some significant progress for the metal-catalyzed dehydration of hexoses has been reported [114–116]. Zhao et al. [114] reported that metal halides in 1-ethyl-3-methylimidazolium chloride ([EMIM]$^+Cl^-$) are very efficient dehydration catalysts, among which $CrCl_2$ was uniquely effective, leading to about 70% yield of 5-HMF from D-fructose and glucose (Fig. 3). In the dehydration of glucose, $CrCl_3^-$ anion plays a role in proton transfer, and promotes the isomerization of glucose to fructose in [EMIM]$^+Cl^-$ solvent.

In the following work, Yong et al. [115] employed *N*-heterocyclic carbene-Cr/ionic liquid as a catalyst system for the dehydration of hexoses. As a result, 5-HMF was obtained as the only product separated after extraction with diethyl ether, and the yield is as high as 96 or 81% for D-fructose or glucose, respectively. Moreover, this catalyst system also allows high substrate loading, and the catalyst can be recycled. Furthermore, the same group found that WCl_6 can also efficiently promote the dehydration of fructose in a 1-butyl-3-methylimidazolium chloride-tetrahydrofuran ([BMIM]Cl–THF) biphasic system, in which a 72% yield of 5-HMF was obtained at 50 °C for 4 h [116]. Besides, Hu et al. [117] found that $SnCl_4$ can efficiently convert glucose to 5-HMF in 1-ethyl-3-methylimidazolium tetrafluoroborate ([EMIM]BF_4); they proposed that the formation of the five-membered ring chelate complex of the Sn atom and glucose plays a key role for the 5-HMF formation. Ståhlberg et al. [118] reported that $YbCl_3$ and $Yb(OTf)_3$ were good catalysts for the conversion of glucose to 5-HMF in alkylimidazolium chlorides. They postulated that the reaction mechanism on the lanthanides is different from that on the chromium catalysts.

Recently, Ilgen et al. [77] obtained 60, 31, 43 and 46% yields of 5-HMF respectively from fructose, glucose, sucrose and inulin using $CrCl_3$ as catalyst in a system consisting of ChCl and up to 50 wt.% of carbohydrates. Moreover, a single-step conversion of cellulose to 5-HMF has successfully been performed with a pair of metal chlorides ($CuCl_2$ and $CrCl_2$) as the catalyst in [EMIM]Cl solvent, and a 55.4 ± 4.0% yield of 5-HMF was obtained [119]. Especially, Zhang et al. [120] achieved an 89% conversion of cellulose for the production of 5-HMF in the presence of $CrCl_2$ in the [EMIM]Cl–water mixture.

2.4. Other catalytic systems

Mednick [121,122] used ammonium phosphate, triethylamine phosphate and pyridinium phosphate for the synthesis of 5-HMF. The highest 5-HMF yield reached 44% in the presence of pyridinium phosphate. Fayet and Gelas [123] employed pyridinium trifluoroacetate, hydrochloride, hydrobromide, perbromate and p-toluenesulfonate as catalysts for D-fructose dehydration, and a yield close to 70% for 5-HMF was obtained after 30 min at 120 °C. Moreover, Smith [124] patented the use of ammonium sulfate or sulfite as the catalyst in D-fructose dehydration. A 50% high yield of 5-HMF was obtained at 170 °C and after 12 s with $NH_4Al(SO_4)_2$ as a catalyst [125]. In addition, it was also reported that the yield and selectivity of 5-HMF can be improved with activated carbon as adsorbent in acid-catalyzed dehydration of D-fructose [126].

Nowadays, green chemistry is getting more and more associated with catalytic processes [127,128]. The ionic liquids as solvents or catalysts have received great attention due to their stability, low vapor pressure and recyclability [129–133]. The merit of ionic liquids as solvents has been mentioned in the dehydration of sugars in the presence of acidic resin and metal chlorides [99,114–117]. Herein, we mainly discuss the reaction systems for the dehydration of hexoses with ionic liquids as catalysts. The pyridinium-based ionic liquids were firstly proved to be efficient for the dehydration of D-fructose [123]. Moreau et al. [134] investigated the dehydration of D-fructose at 90 °C using 1-H-3-methyl imidazolium chloride ([HMIM]$^+Cl^-$) acting as solvent and catalyst. As a result, a 92% yield of 5-HMF was obtained after 15–45 min. Furthermore, Bao et al. [135] reported the preparation of 5-HMF by the dehydration of D-fructose in the presence of the ionic liquids, 3-allyl-1-(4-sulfobutyl)imidazolium trifluoromethanesulfonate ([ASBI][Tf]), as well as its Lewis acid derivative, 3-allyl-1-(4-sulfurylchloride butyl)imidazolium triflu-

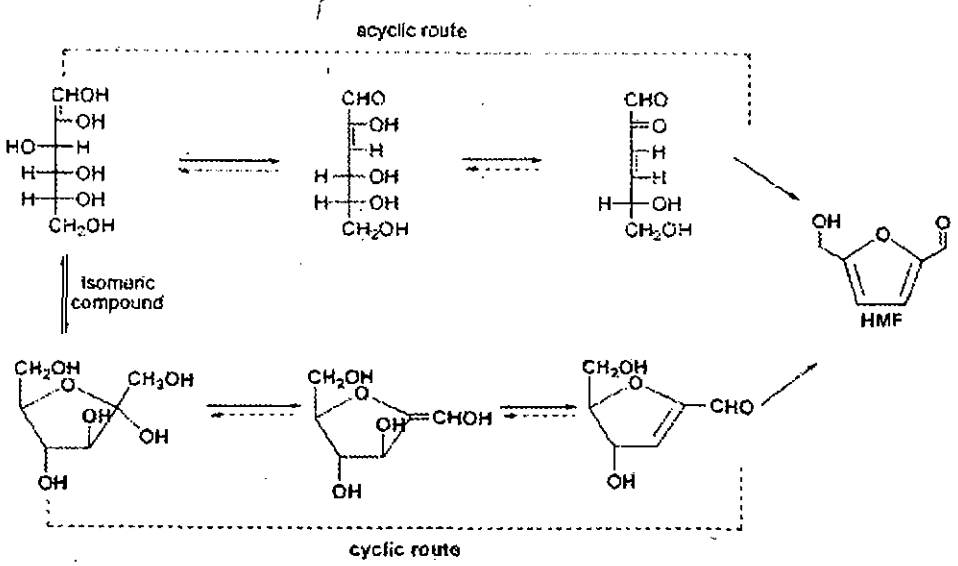


Fig. 4. The possible mechanism for the dehydration of hexoses.

oromethanesulfonate ([ASCB][Tf]). It was concluded that the type of acidic ionic liquid used played a significant role in the reaction, and the Lewis acidic ionic liquid acts more effectively than its Brøsted acidic counterpart. Recently, our group has studied the dehydration of sugar with acidic ionic liquid [136,137]. We found that *N*-methyl-2-pyrrolidonium([NMP]$^+$)-based and *N*-methyl-morpholinium-based ionic liquids showed high catalytic activity for the dehydration of fructose or sucrose under mild conditions. For example, in the presence of 7.5 mol% *N*-methyl-2-pyrrolidonium methyl sulfonate $[NMP]^+[CH_3SO_3]^-$, a 72.3% yield of HMF with 87.2% selectivity were obtained from D-fructose at 90 °C for 2 h in DMSO [136]. When *N*-methylmorpholinium methyl sulfonate ($[NMM]^+[CH_3SO_3]^-$) was used as catalyst in *N*,*N*-dimethylformimide containing a lithium bromide (DMF–LiBr) system, 74.8 or 47.5% yield of HMF was obtained from fructose or sucrose at 90 °C for 2 h under nitrogen atmosphere, respectively [137]. Moreover, it was also reported that 1-ethyl-3-methylimidazolium hydrogen sulfate ($[EMIM]^+[HSO_4]^-$) is effective in converting fructose into 5-HMF. An 88% yield was obtained at 30 min with MIBK as a co-solvent [138]. In a biphasic system composed of ChoCl/citric acid ionic liquid and ethyl acetate, the yield of 5-HMF from fructose reached 91.4% with a 93.6% 5-HMF selectivity at 80 °C for 1 h [139].

Microwave irradiation has been also employed in the synthesis of 5-HMF from sugars. Hansen et al. [140] have studied the microwave-assisted dehydration of highly concentrated aqueous fructose solution (27 wt.%) to 5-HMF in the presence of HCl. These results revealed a significant increase in the fructose conversion rate over the conventional heated systems and a 52% conversion of fructose with 63% selectivity of 5-HMF was obtained with a short reaction time of only 1 s. Moreover, Li et al. [141] reported an efficient strategy for $CrCl_3$-mediated production of 5-HMF with *ca.* 90% yields from glucose in ionic liquid under microwave irradiation. In the following work, Zhang and Zhao [142] also found the microwave-assisted conversion of lignocellulosic biomass to 5-HMF with yields of 45–52% after 3 min, where corn stalk, rice straw and pine wood were used. Besides, under microwave heating, sulfated zirconia also showed good catalytic performance for the fructose dehydration [143], in which 93.6% conversion of fructose and 72.8% yield of 5-HMF were obtained at 180 °C for 20 min reaction time in acetone–DMSO mixtures.

2.5. Mechanism of hexoses dehydration

Haworth and Jones [56] proposed the first mechanism for the dehydration of fructose to 5-HMF. In the following works, van Dam et al. [58], Kuster [11] and Antal et al. [60] assumed that the dehydration of hexoses goes through one of the two possible pathways: one includes the transformation of ring structures, while the other path is based on the acyclic compounds (Fig. 4). In general, the reaction pathways for the production of 5-HMF from hexoses are composed of isomerization, dehydration, fragmentation, reversion, and condensation steps. Several works have suggested that 5-HMF formation takes place through an open-chain 1, 2-enediol mechanism or through a fructofuranosyl intermediate [80,144,145]. However, Antal et al. [146] and Newth [147] proposed that the formation of 5-HMF from D-fructose proceeds *via* cyclic intermediates. They gave the evidence as: (1) facile conversion of 2,5-anhydro-D-mannose (an intermediate enol in cyclic mechanism) to HMF; (2) facile formation of 5-HMF from D-fructose but difficult from glucose, which could be concluded from the dehydration of sucrose; (3) lack of carbon–deuterium bond formation in 5-HMF due to keto-enol tautomerism in the open-chain mechanism when the reaction was carried out in D_2O solvent. Furthermore, Amarasekara et al. [148] identified two key intermediates as (4R, 5R)-4-hydroxy-5-hydroxymethyl-4,5-dihydrofuran-2-carbaldehyde in the reaction based on the data of ^1H and ^{13}C NMR spectra.

In the dehydration of glucose catalyzed by metal halide, the mutarotation and isomerization steps are necessary [114,117]. Fig. 5 presents the mutarotation leading to interconversion of α- and β-glucopyranose anomers and the isomerization of glucopyranose to fructofuranose, in which the mutarotation leading to an equilibrium mixture of anomers is rapid in the presence of a catalytic amount of $CrCl_2$. It promotes the isomerization of glucopyranose to fructofuranose, and the further dehydration to 5-HMF. Similarly, the results from theoretical simulations solidified the conclusion that cyclic reaction pathways are dominant during the formation of 5-HMF from glucose [144]. Very recently, the research of Pidko et al. [149] showed that, in the presence of $CrCl_2$, the facile reactions of sugar ring opening and closure involve coordination to a single Cr center. The rate-controlling H-shift reaction can be facilitated by the transient self-organization of the Lewis acidic Cr^{2+} centers into a binuclear complex with the open form of glu-

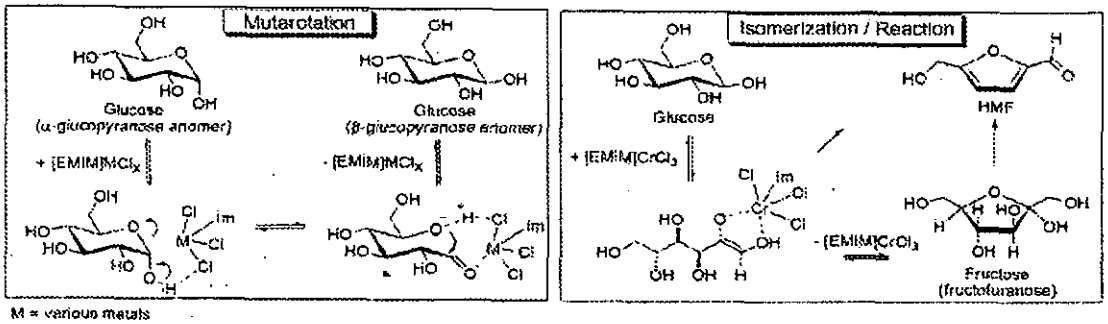


Fig. 5. Possible interactions between metal halide and glucose in [EMIM]Cl (Reprinted from Ref. [114] with permission of the American Association for the Advancement of Science. 2007 Copyright Science Publishing).

cose, which is possibly a result of the dynamic nature of the Cr complexes and the presence of moderately basic sites in the ionic liquid.

3. Synthesis of 5-hydroxymethylfurfural-based furan derivatives

Numerous furan derivatives have been synthesized from sugar based on the further catalytic transformation of 5-HMF. Fig. 6 presents the catalytic oxidation and hydrogenation process using 5-HMF as a platform chemical. Recently, thermodynamic analysis for the synthesis of 5-HMF-based furan derivatives has also been performed according to hydrogenation and oxidation pathways; results revealed a very high feasibility of these processes [150]. In the following part, we will review mainly the synthesis methods of very useful 2,5-DFF, 2,5-FDCA, 2,5-BHF and 2,5-DMF from 5-HMF or directly from hexoses by catalytic processes.

3.1. Synthesis of 2,5-diformylfuran

It is well-known that selective and partial oxidation of 5-HMF leads to the formation of 2,5-DFF, which has potential applications in the synthesis of drugs, fungicides, and new polymeric materials [25,151,152]. Commercially, high yields of 2,5-DFF are only attained under non-catalytic conditions, with the presence of stoichiometric quantities of classical oxidants [153,154] or with the presence of electrophilic agents [155]. However, from the viewpoints of economy and sustainability, the catalytic routes for 2,5-DFF production are promising in the future.

In the early works, hydrogen peroxide was used as the oxidant and the synthetic titanium silicalite (TS1) was used as a recyclable catalyst [156]. However, the oxidation of 5-HMF over TS1 catalyst with 30 wt.% aqueous hydrogen peroxide solution in methanol or water was unsatisfactory because the maximum yield for 2,5-DFF obtained was only 25%. Moreover, chloroperoxidase-catalyzed oxidation of 5-HMF with hydrogen peroxide as the oxidant was also investigated [157], and it was found that the reaction proceeded with 60–74% selectivity for 2,5-DFF. Moreau and coworkers [158,159] investigated the oxidation of 5-HMF into 2,5-DFF with a supported V_2O_5/TiO_2 catalyst using air as the oxidant and toluene or MIBK as solvent and found that the catalyst can be regenerated *in situ*. The complete transformation of 5-HMF and a yield of 2,5-DFF as high as 90% are achieved with a monolayered V_2O_5/TiO_2 at 90 °C under 1.6 MPa within 4 h. It was found also that, when a Pt/C catalyst was used in the reaction, the product distribution showed dependence on the type of the solvent, pH value, partial pressure of oxygen, temperature, and the nature of the catalyst [160]. As a result, the oxidation of 5-HMF prevails to give 2,5-DFF as the major product under a high temperature and neutral pH, where 19% yield of DFF is obtained. Besides, a homogeneous metal/bromide catalyst was also used in the air oxidation of 5-HMF [161], in which the yield of 2,5-DFF was 57%. However, a prominent disadvantage is the corrosion problem of this reaction system. Recently, Amarasekara et al. [162] found that 5-HMF was efficiently oxidized to 2,5-DFF in

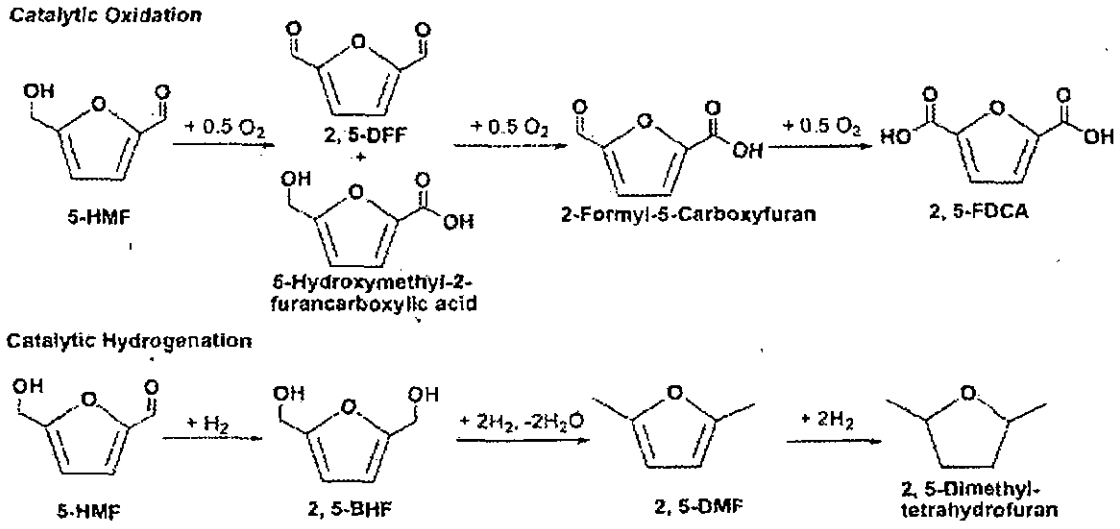


Fig. 6. Catalytic oxidation and hydrogenation route of 5-HMF.

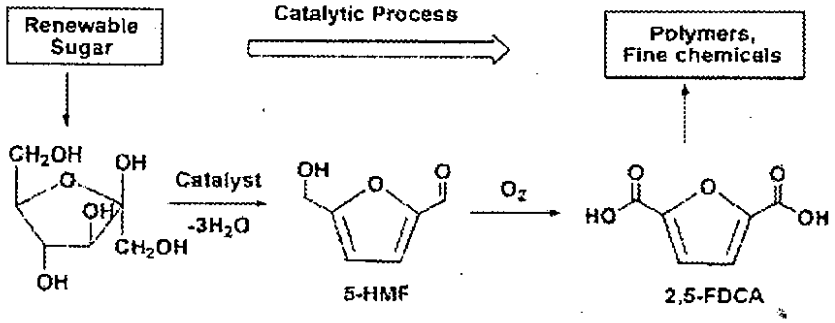


Fig. 7. Pathways from renewable resources to chemical products.

63–89% yield using Mn(III)–salen catalyst and sodium hypochlorite, in a phosphate buffer–CH_2Cl_2 biphasic system at room temperature. Moreover, Navarro et al. [163] studied the aerobic oxidation of 5-HMF to 2,5-DFF catalyzed by immobilized vanadyl complexes on PVP and organofunctionalized SBA-15 supports. With pyridine as additive, an 82% conversion and 99% selectivity of 2,5-DFF were obtained with vanadyl-acetylacetonate/PVP as catalyst; however, only a 50% conversion and 98% selectivity of 2,5-DFF were obtained over vanadyl complexes supported on SBA-15.

Halliday and coworkers [28,164] first reported the oxidation of 5-HMF to 2,5-DFF using an *in situ* reaction strategy where 5-HMF was directly generated from D-fructose and converted consequently to 2,5-DFF. D-Fructose is firstly dehydrated to 5-HMF on the acidic ion-exchange resin catalyst in the DMSO phase, and consequently the 5-HMF is oxidized in the same phase to 2,5-DFF on the vanadium oxide catalysts. A maximum yield of 45% was obtained based on D-fructose at 1 bar air pressure and 150 °C. Carlini et al. [165] also tested the one-pot process directly from D-fructose and found that the reaction cannot be accomplished either in water or in a mixed water/MIBK medium with VOP catalysts. Then, they studied the oxidation of 5-HMF to 2,5-DFF with VOP as catalyst and with air as oxidant at 150 °C. An 84% conversion with 97% selectivity of 2,5-DFF was obtained within 6 h. In addition, the catalyst modification by partial substitution of VO^{3+} with other metal cations did not improve the catalytic performance.

3.2. Synthesis of 2,5-furandicarboxylic acid

As we know, the ultimate objective of 5-HMF oxidation is to obtain 2,5-FDCA which has properties and applications similar to those of both terephthalic and isophthalic acids used in the production of polymers and fine chemicals [21,166,167]. The products obtained from 2,5-FDCA have been considered as important alternatives for their petroleum-based counterparts in the chemical industry [24] (as shown in Fig. 7).

The noble metal catalysts, e.g. carbon or alumina-supported platinum have been found to be efficient for the oxidation of 5-HMF to 2,5-FDCA [168,169]. In these reaction systems, the oxidation of 5-HMF favorably proceeds to the deep oxidation to diacid when the reaction was performed under oxygen pressure and a controlled pH value. The oxidation of 5-HMF in aqueous phase to 2,5-FDCA was demonstrated with a near-quantitative yield on a Pt/Al_2O_3 catalyst in basic reaction conditions at 60 °C [170]. In addition, it was found that a high yield of 2,5-FDCA was also obtained when a Pt/Pb bimetallic catalyst is used [29]. However, when Pt-based catalysts were used for the HMF to 2,5-FDCA reaction with oxygen as oxidant in water, a high catalyst-to-substrate weight ratio could be required [171]. Furthermore, a Co/Mn/Br catalyst was applied in the air oxidation of 5-HMF to 2,5-FDCA, and a 60% yield was obtained when the reaction was performed at 125 °C under 7.0 MPa air pressure for 3 h [160]. This catalyst system has been used in commercial oxidation reactions.

Kröger et al. [27] studied the production of 2,5-FDCA from fructose *via* acid-catalyzed formation and subsequent oxidation of 5-HMF. As shown in Fig. 8, an effective separation of the oxidation catalyst and the formed 5-HMF and its derivatives into the MIBK phase with the automatic extraction facilitates the efficient formation of 2,5-FDCA *via* the consequent oxidation in the MIBK phase. The maximum selectivity of 50% with a yield of 25% for 2,5-FDCA were achieved. Ribeiro and Schuchardt [172] investigated the one-pot dehydration and oxidation of D-fructose over a bifunctional redox catalyst, *i.e.* cobalt acetylacetonate encapsulated in sol–gel silica. The synergic effect of the two catalyst functions was impressive, and a 99% selectivity of 2,5-FDCA with 72% conversion of D-fructose was obtained at 160 °C under 2.0 MPa air.

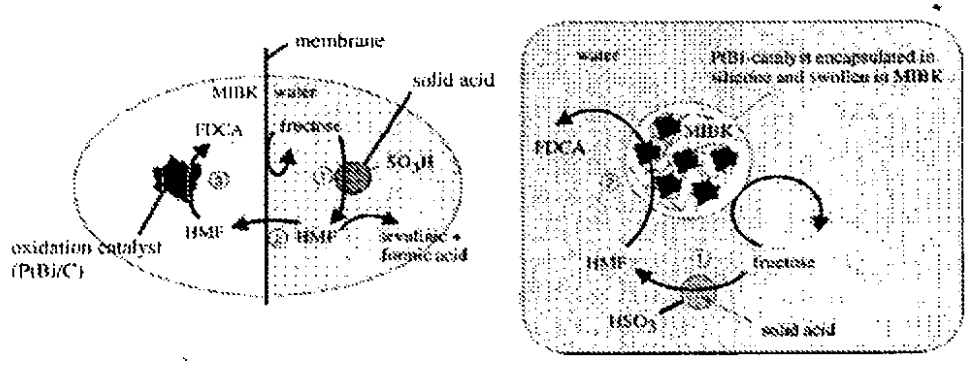


Fig. 8. The catalytic processes for synthesis of 2,5-FDCA in membrane reactor and batch reactor ((a) Membrane reactor, (1) 5-HMF formation in water phase; (2) diffusion of 5-HMF in MIBK phase through the membrane and (3) oxidation of 5-HMF. (b) Batch reactor, (1) dehydration of fructose in batch reactor; (2) diffusion and oxidation of 5-HMF into 2,5-FDCA. Reprinted from Ref. [27] with permission of Plenum Publishing Corporation. 2000 Copyright Springerlink publishing).

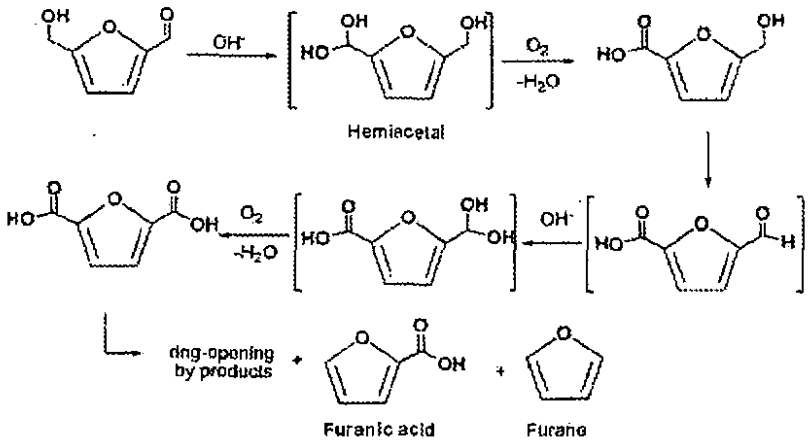


Fig. 9. The possible pathway for aqueous 5-HMF aerobic oxidation with gold catalysts.

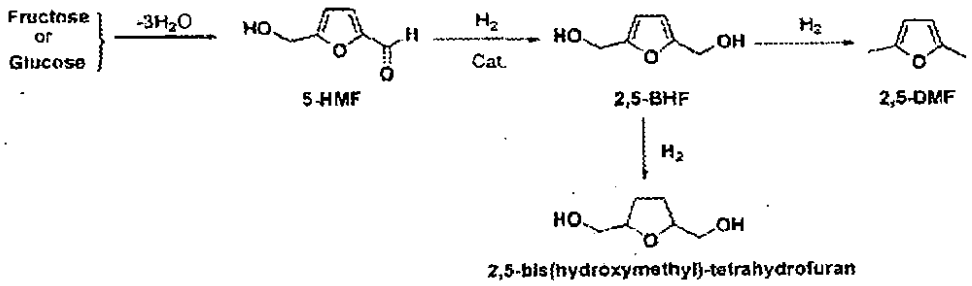
In recent years, gold has proved itself as an excellent catalyst for selective oxidation with molecular oxygen when dispersed as nanoparticles [173–176]. Casanova et al. [177] found that 5-HMF was selectively converted into 2,5-FDCA (99 mol% yield) in water, under mild conditions (65–130 °C, 1.0 MPa air) with gold nanoparticles supported on ceria ($Au–CeO_2$) catalyst. A reaction mechanism was proposed and the rate-limiting step of the reaction was the hydroxyl oxidation of 5-hydroxymethyl-2-furancarboxylic acid into 2,5-FDCA (shown in Fig. 9). Gorbanev et al. [178] studied the oxidation of 5-HMF to 2,5-FDCA on an Au/TiO_2 catalyst and with NaOH as an additive at ambient temperature. A 71% yield of 2,5-FDCA at total 5-HMF conversion was obtained after 18 h at 30 °C under 2.0 MPa oxygen.

Taarning et al. [179] reported the oxidative esterification of 5-HMF to furan-2,5-dimethyldicarboxylate, a 2,5-FDCA-based derivative, over Au/TiO_2 catalyst with oxygen as the oxidant using sodium methoxide as a promoter at 130 °C under 4 bar pressure. They obtained 98% selectivity and 60% yield of furan-2,5-dimethyldicarboxylate. Furthermore, Casanova et al. [180] reported a conversion of 5-HMF into furan-2,5 dimethyldicarboxylate with 99 mol% yield with Au/CeO_2 catalyst in methanol. They proposed also that, after the reaction, the furan-2,5-dimethyldicarboxylate can be converted directly to 2,5-FDCA through a simple hydrolysis reaction.

3.3. Synthesis of 2,5-bis(hydroxymethyl)furan and 2,5-dimethylfuran

The hydrogenation products of 5-HMF, 2,5-BHF and 2,5-DMF are very important fine chemicals that can be applied in the manufacture of polyurethane foams or polyesters [14–16,150]. The efficient production of these compounds starting from hexoses with dehydration and catalytic hydrogenation reactions is therefore extremely demanding [181] (as shown in Scheme 2). Herein, the catalytic hydrogenation of aldehyde group (–CHO) and furan ring take place and a careful control of the conditions allows to improve the selectivity of 2,5-BHF. Nearly quantitative yields in 2,5-BHF or 2,5-bis(hydroxymethyl)-tetrahydrofuran were obtained over conventional hydrogenation catalysts, such as Raney nickel and different supported metal catalysts (copper, platinum, palladium, cobalt, chromium, molybdenum) with H_2O as solvent at high temperature and under high hydrogen pressure [182–185].

2,5-DMF, produced from the selective removal of five oxygen atoms from hexoses molecules, has a boiling point suitable for a liquid transportation fuel, and has the lowest water solubility and the highest research octane number (RON) among all the mono-oxygenated C6 compounds. Moreover, compared to bioethanol, it has also a energy density, *ca.* 30 kJ cm^{-3} higher, by 40% and a boiling point higher by 20 °C [46,78]. Recently, Roman-Leshkov et al. [46] developed a catalytic route for the production of 2,5-DMF from D-fructose, *via* a two-step process. The first step is the acid-catalyzed dehydration of D-fructose to produce 5-HMF in a bipbasic reactor. Then, 5-HMF is extracted in the organic phase of the reactor and is subsequently converted to 2,5-DMF by hydrogenolysis of C–O bonds over a copper–ruthenium (CuRu) catalyst (Fig. 10). Binder and Raines [78] also reported the preparation of 2,5-DMF from D-fructose with a two-step method. Firstly, based on production of 5-HMF from D-fructose with H_2SO_4 as catalyst, they studied the separation of 5-HMF with a flow-chromatograph method with loading the mixture into a column of ion-exchange resin and eluting with deionized water. In the following step, the 5-HMF was taken up in 1-butanol and hydrogenated with a Cu–Ru/C catalyst. As a result, a 32.5% yield of 2,5-DMF based on D-fructose was obtained. Very recently, Luijkx et al. [186] reported the production of 2,5-DMF by the hydrogenation of 5-HMF over a palladium catalyst in 1-propanol. During the reaction the main intermediate is



Scheme 2. The synthesis route of 2,5-BHF and 2,5-DMF from hexoses.

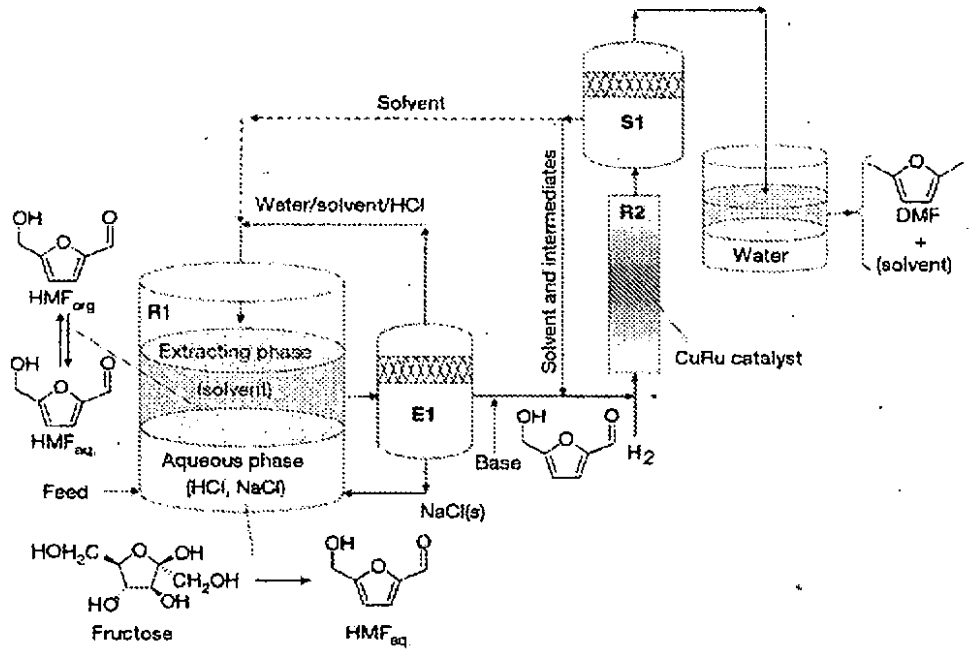


Fig. 10. The preparation of 2,5-DMF from fructose in the biphasic reactor (Diagram includes selective dehydration of fructose to form 5-HMF in the reactor (R1); evaporation of water and HCl from the liquid solvent containing 5-HMF, leading to precipitation of NaCl (E1); hydrogenolysis of 5-HMF to 2,5-DMF over a CuRu catalyst (R2); and separation of 2,5-DMF from the extracting solvent and unreacted intermediates (S1). Reprinted from Ref. [46] with permission of Macmillan Publishers Limited, 2007 Copyright Nature Publishing Group).

5-hydroxymethyl-2-(propyloxymethyl)furan. However, when 1,4-dioxane was employed as solvent in the reaction, 2,5-BHF are formed as a major product.

4. Conclusion and perspectives

The use of sugars for the production of furan chemicals is a vital alternative to fossil-based energy resource, such use is of real significance in the sustainable chemistry. In this review, we focus on the efficient catalytic methods for the synthesis of 5-HMF, 2,5-DFF, 2,5-FDCA, 2,5-BHF, 2,5-DMF and other furanic derivatives. In summary: (1) 5-HMF have been obtained with high efficiency from the dehydration of sugar catalyzed by mineral acids, organic acids, solid acids and metal-containing catalysts; (2) for 2,5-DFF and 2,5-FDCA, the major routes include a direct oxidation of 5-HMF by suitable oxidant and one-pot dehydration and oxidation of hexoses with multi-functional catalysts; (3) in particular, 2,5-BHF and 2,5-DMF are effectively produced from the selective hydrogenation of 5-HMF or one-pot catalytic process with a specially designed biphasic reactor.

Although great progress has been achieved recently for the catalytic transformation of sugar to furan chemicals, further improvement of conversion and selectivity are still necessary in many cases for achieving the goal of commercial application of those processes. Moreover, with the introduction of the concept of green chemistry, efforts in catalysis should be devoted to the economic, rapid and environmentally benign production of furan chemicals. Furthermore, multi-functional catalysts, which originate from incorporating transition metals with solid acid/base catalysts, deserve the priority in catalytic chemistry. It is expected that the multi-functional catalysts will allow several reaction steps to be finished in one reactor and will avoid the costly intermediate separation process. The last but not the least, the recycling of the catalyst and the efficient separation of the target product are always the active topics for catalytic process research.

The near term challenges can be listed as:

(a) Mechanism of the transformation reactions, and the structure–property relationships of catalysts.
(b) Catalyst development and optimization.
(c) Multi-functional catalyst and the suitable solvent systems.
(d) Process composition and large-scale production.

Acknowledgements

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The State Intellectual Property Office of the People's Republic of China

Postcode: 100097 11/F, Block B, KingSound International Center, 116 Zizhuyuan Road, Haidian District, Beijing, PRC **KINGSOUND & PARTNERS** ZHU Mei, CHEN Guojun	Date of Issuing: December 4, 2013
Application No: 201080044421.4	Issuance No.: 20131129012107 70
Applicant:	**FURANIX TECHNOLOGIES B.V.**
Title of Invention:	**METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID**

NOTIFICATION OF THE FIRST OFFICE ACTION

(National Phase of PCT Application)

1. ☑ Upon the request for substantive examination, in accordance with Article 35.1 of the Patent Law of China, the examination is made by SIPO as to substance of the above-identified patent application for invention.

   ☐ In accordance with Article 35.2 of the Patent Law of China, the SIPO, on its own initiative, decided to proceed with the examination as to substance of the above-identified patent application for invention.

2. ☑ The applicant claims the filing date:

   October 7, 2009 when the previous application was filed with the US Patent Office as the priority date,

   October 7, 2009 when the previous application was filed with the NL Patent Office as the priority date.

3. ☐ Upon examination, the amended documents submitted on _____ are not in conformity with Rule 51.1 of the Implementing Regulations of the Patent Law of China.

4. ☑ The examination is conducted based on the initially filed Chinese international application documents or Chinese translation of initially filed international application documents.

   ☐ The examination is conducted on the basis of the following application documents:

5. ☑ The present notification cites the following documents (of which the serial numbers continue to be used in the examination hereafter):

Code	Reference No. or Title	Publication Date (or Filing Date of Conflict Application)
1	SU 636233A1	December 5, 1978
2	WO 2009076627A2	June 18, 2009
3	"The Conversion of Sucrose into Furan Compounds. Part I. 5-hydroxymethylfuraldehyde and some derivatives", W. N. HAWOR, etc., Journal of The Chemical Society, Vol.1, p667-670, January 1945.	January 1, 1945

6. Conclusive opinion:

   Regarding the Description:

   ☐ The contents of the application belong to the unpatentable scope set forth by Article 5 of the Patent Law of China.

   ☐ The Description is not in conformity with Article 26.3 of the Patent Law of China.

   ☐ The Description is not in conformity with Article 33 of the Patent Law of China.

☐ The presentation manner of the Description is not in conformity with Rule 17 of the Implementing Regulations of the Patent Law of China.

☐_____

Regarding the Claims:

☐Claims_____do not conform to Article 2.2 of the Patent Law of China.

☐Claims_____do not conform to Article 9.1 of the Patent Law of China.

☑Claim 1 does not possess novelty under Article 22.2 of the Patent Law of China.

☑Claims 1-15 do not involve an inventive step under Article 22.3 of the Patent Law of China.

☐Claims_____do not possess utility under Article 22.4 of the Patent Law of China.

☐Claims_____fall in the unpatentable scope set forth by Article 25 of the Patent Law of China

☑Claims 9-11 do not conform to Article 26.4 of the Patent Law of China.

☐Claims_____do not conform to Article 31.1 of the Patent Law of China.

☐Claims_____do not conform to Article 33 of the Patent Law of China.

☐Claims_____do not conform to Rule 19 of the Implementing Regulations of the Patent Law of China.

☐Claims_____do not conform to Rule 20 of the Implementing Regulations of the Patent Law of China.

☐Claims_____do not conform to Rule 21 of the Implementing Regulations of the Patent Law of China.

☑Claims 4 and 8-11 do not conform to Rule 22 of the Implementing Regulations of the Patent Law of China.

☐_____

☐ The application does not conform to Article 26.5 of the Patent Law of China or Rule 26 of the Implementing Regulations of the Patent Law of China.

☐ The application does not conform to Article 20.1 of the Patent Law of China

☐ Divisional application does not conform to Rule 43.1 of the Implementing Regulations of the Patent Law of China.

Please refer to the text of the notification in detail for the above.

7. Based on the above conclusive opinion, the examiner holds that

☐ the applicant should amend the application documents according to the requirements stated in the text of the notification.

☐ the applicant should state the reason in his observation why the application may be granted a patent right and make amendments to contents in inconformity with the laws as pointed out in the text of the notification, or no patent right for the application shall be granted.

☑ No patentable substantive contents are presented in the application. If the applicant does not submit his observation or his observation is not convincing, the application shall be rejected.

☐_____

8. The applicant shall pay an attention to the following:

(1) According to Article 37 of the Patent Law of China, the applicant should submit his observation within **FOUR** months from the date of receiving the notification. Failure to make a response without any justified reason within the time limit will result in the application being deemed withdrawn.

(2) The amendments to the application documents should meet the requirement of Article 33 of the Patent Law of China and shall not go beyond the scope recorded in the original description and claims. The amendments to the application documents should meet the requirement of Rule 51.3 of the Implementing Regulations of the Patent Law of China and should be made according to the requirement of this notification.

(3) The observation and/or amended documents should be mailed to or submitted directly to the Receiving Section of the Patent Office of the SIPO of China, and the documents which were not mailed or directly submitted to the Receiving Section are of no legal effect.

(4) Without an appointment, the applicant and/or attorney may not interview with the examiner.

9. The text of this notification consists of 3 pages, including the following annexes:

☑ 7 pages of 2 copies of the cited references.

Examiner: YUAN Jing

Department of Examination:
Chemistry Examination Department of
Patent Examination Assistance Center in Jiangsu

Text of the Notification of the First Office Action

(National Phase of PCT Application)

Application No.: 201080044421.4

The present application relates to a method for the preparation of 2,5-furandicarboxylic acid and for the preparation of the dialkyl ester of 2,5-furandicarboxylic acid. After examination, specific comments are made as follows.

I. Claim 1 does not conform to Article 22.2 of the Patent Law of China.

1.1 Claim 1 claims a method for the preparation of 2,5-furandicarboxylic acid. Reference 1 (SU636233A1) discloses the following content (see the abstract of Reference 1): 5-methylfuran is oxidized by the air or oxygen to produce a furan-2,5-dicarboxylic acid (i.e., 2,5-furandicarboxylic acid in claim 1); the reaction is conducted in the presence of the catalyst $CuO.Ag_2O.Ce_2O_3$ at 110-150℃ (partially overlapping with the temperature higher than 140℃ in claim 1). Hence, Reference 1 discloses all the technical features of claim 1, and both claim 1 and Reference 1 have the same technical solution, belong to the same technical field of preparing 2,5-furandicarboxylic acid from 5-methylfurfurol, and solve the same technical problem and achieve the same technical effects. Therefore, claim 1 does not possess novelty, thereby being in inconformity with Article 22.2 of the Patent Law of China.

As for the claims possessing novelty, they still have the following defects:

II. Claims 1-15 do not conform to Article 22.3 of the Patent Law of China.

2.1 Claim 1 claims a method for the preparation of 2,5-furandicarboxylic acid. Reference 2 (WO2009076627A2, published on June 18, 2009) is the closest prior art, and it also discloses a method for preparation of 2,5-furandicarboxylic acid and specifically discloses the following content (see Example 9 in paragraph 76 of the description of Reference 2): a product mixture composed of predominantly HMF ester with residual HMF in acetic acid is subjected to oxidation with the addition of cobalt acetate, manganese acetate, and sodium bromide. This mixture is pressurized with oxygen and heated to over 100℃ for over an hour. Finally, a product of FDCA (i.e. 2,5-furandicarboxylic acid) is obtained. The distinguishing technical features between claim 1 and Reference 2 lie in that: 1) claim 1 defines that the reaction is carried out at the temperature higher than 140℃; and 2) in addition to HMF, the starting material in claim 1 also includes an ester of 5-hydroxymethylfurfural, 5-(chloromethyl)furfural, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds. Thus, the technical problem actually to be solved by the invention is to provide more

alternative solutions for preparing 2,5-furandicarboxylic acid. As for the above distinguishing technical feature 1), it is known in the art that appropriate increase of the reaction temperature may accelerate the reaction rate, and may also improve the reaction yield for endothermic reaction, so under the condition of over 100℃ disclosed by Reference 2, a person skilled in the art has the motive to properly raise the reaction temperature. As for the above distinguishing technical feature 2), it is known that 5-(chloromethyl)furfural, 5-(chloromethyl)furoic acid, and 2,5-dimethylfuran are all HMF derivatives, and the oxidization reaction occurred in Reference 1 is to oxidize the carbon-containing group at Sites 2 and 5 of the furfural into carboxylic groups. Under such technical hint, a person skilled in the art has the motive to select more HMF derivatives as the starting material of the reaction based on Reference 2, so as to provide more alternative solutions for preparing 2,5-furandicarboxylic acid. It can be seen that, it is obvious for a person skilled in the art to obtain the technical solution of claim 1 based on Reference 2, and the technical solution of claim 1 does not produce any unforeseeable technical effects. Therefore, claim 1 does not possess any prominent substantive features or notable progress, thereby being in inconformity with Article 22.3 of the Patent Law of China.

2.2 Claims 2-11 further define the reaction method of claim 1. Reference 2 also discloses the following content (see paragraphs 55 and 56 of the description of Reference 2): the oxidation catalyst is selected from the group consisting of cobalt acetate, manganese acetate, and sodium bromide; the oxidant is oxygen; the reaction temperature is 85-110℃; the reaction solvent is an organic acid but is not limited to acetic acid. As for the selection of the starting material and the temperature of the reaction, please see the corresponding comments in 2.1. As for the selection of other metals, a person skilled in the art has the motive to select other metals such as the transitional metal zirconium and the rare earth metal cerium. It can be seen that, it is obvious for a person skilled in the art to obtain the technical solutions of claims 2-11 based on Reference 2 when combined with the customary selections in the art, and there is no unexpected technical effects generated by the technical solutions of claims 2-11. Therefore, claims 2-11 do not possess any prominent substantive features or notable progress, thereby being in inconformity with Article 22.3 of the Patent Law of China.

2.3 Claim 15 claims a method for the preparation of 2,5-furandicarboxylic acid wherein carbohydrate source is the starting material. Reference 2 discloses that the fructose is subjected to dehydration in the presence of an organic acid and a catalyst, and is then isolated and purified with resin to obtain HMF ester; the HMF ester thus obtained is pressurized with oxygen with addition of cobalt acetate, manganese acetate, and sodium bromide and is heated to 85-110℃ for

100-150mins, to obtain FDCA (see paragraphs 55 and 56, and Example 9 in paragraph 76 of the description of Reference 2). The distinguishing technical feature between claim 15 and Reference 2 lies in that: claim 15 defines that the fructose reacts in the presence of alkyl carboxylic acid, while that disclosed in Reference 2 is an organic acid. Therefore, the technical problem actually to be solved by the invention is to provide a method of preparing FDCA from carbohydrate source. As for the above distinguishing technical feature, it is known in the art that alkyl carboxylic acid is a specific term of organic acid, so a person skilled in the art can make customary selections when Reference 2 discloses that an organic acid may be used. Hence, it is obvious for a person skilled in the art to obtain the technical solution of claim 15 based on Reference 2 when combined with the customary selections in the art, and the technical solution of claim 15 does not produce any unforeseeable technical effects. Therefore, claim 15 does not possess any prominent substantive features or notable progress, thereby being in inconformity with Article 22.3 of the Patent Law of China.

2.4 Claim 12 claims a process for the preparation of a dialkyl ester of 2,5-furandicarboxylic acid. Reference 2 discloses that a product mixture composed of HMF ester and HMF contacts with oxygen in the presence of oxidation catalyst to obtain FDCA (see paragraphs 55 and 56 of the description of Reference 2). The distinguishing technical feature between claim 12 and Reference 2 lies in that: claim 12 defines that FDCA is esterified to produce a dialkyl ester of 2,5-furandicarboxylic acid. Thus, the technical problem actually to be solved by the invention is to provide a method for preparation of an dialkyl ester of 2,5-furandicarboxylic acid. Regarding the above distinguishing technical feature, Reference 3 ("The Conversion of Sucrose into Furan Compounds. Part 1. 5-hydroxymethylfuraldehyde and some derivatives", W. N. HAWOR, etc., *Journal of The Chemical Society*, Vol.1, p667-670, January 1, 1945) relates to a method for the preparation of ethyl 5-hydroxymethylfuraldehyde-2-acetate, and specifically discloses that an esterification reaction occurs between 5-hydroxymethylfuraldehyde-2-acetic acid and ethyl-alcoholic hydrogen chloride (see paragraph 3 on page 670 of Reference 3). Reference 3 and claim 12 have the same type of reaction, and both belong to the reaction of esterifying the carboxylic group of the furan formic acid. In order to provide a method for the preparation of an dialkyl ester of 2,5-furandicarboxylic acid, a person skilled in the art has the motive to obtain the technical solution of claim 12 based on Reference 2 when combined with the method of Reference 3. Therefore, claim 12 does not possess any prominent substantive features or notable progress, thereby being in inconformity with Article 22.3 of the Patent Law of China.

2.5 Claims 13-14 further define the esterification of claim 12. As mentioned above, Reference 3 discloses the esterification between 5-hydroxymethylfuraldehyde-2-acetic acid and

ethanol. A person skilled in the art can absolutely select corresponding starting materials according to the product to be prepared, which is also a common technical knowledge in the art. It can be seen that, it is obvious for a person skilled in the art to obtain the technical solutions of claims 13-14 based on Reference 2 when combined with Reference 3 and the common knowledge in the art, and the technical solutions of claims 13-14 do not produce any unforeseeable technical effects. Therefore, claims 13-14 do not possess any prominent substantive features or notable progress, thereby being in inconformity with Article 22.3 of the Patent Law of China.

III. Claims 9-11 are not clear, thereby being in inconformity with Article 26.4 of the Patent Law of China.

3.1 Claims 9-11 present the expressions of "preferably" and "more preferably" in many places, which make claims 9-11 define different protection scopes. As a result, the protection scopes of claims 9-11 are not clear, which does not conform to Article 26.4 of the Patent Law of China.

IV. Claims 4 and 8-11 do not conform to Rule 22 of the Implementing Regulations of the Patent Law of China.

4.1 Claim 4 refers to any one of claims 1 to 3, but the cited claim 3 is a multiple dependent claim and thus cannot serve as a reference basis of another multiple dependent claim; similarly, claim 8 has similar defect. The above problems make claims 4 and 8 in inconformity with Rule 22.2 of the Implementing Regulations of the Patent Law of China.

4.2 Claims 9-11 refer to any one of the preceding claims. According to Rule 22.1 of the Implementing Regulations of the Patent Law of China, a dependent claim shall be clearly written with the sequence number of the claims it refer to. Hence, claims 9-11 do not conform to Rule 22.1 of the Implementing Regulations of the Patent Law of China.

Based on the above reasons, the present application does not have a prospect of being patentable. If the applicant cannot provide convincing reasons within the time limit set in the notification, the application shall be rejected.

Examiner: YUAN Jing

Code: 699802

RELEVANT PROVISIONS

PATENT LAW OF THE PEOPLE'S REPUBLIC OF CHINA

Article 22. Any invention or utility model for which patent right may be granted must possess novelty, inventiveness and practical applicability.

Novelty means that, the invention or utility model does not belong to the prior arts; and an application for the identical invention or utility model has not been filed with the Patent Administration Department under the State Council by any entity or individual before the filing date and is not recorded in the published or announced patent documents after the filing date.

Inventiveness means that, as compared with the prior arts, the invention possesses prominent substantive features and represents a notable progress and that the utility model possesses substantive features and represents progress.

Practical applicability means that the invention or utility model can be made or used and can produce effective results.

"Prior arts" in the Patent Law means the arts known at home and abroad before the filing date.

Article 26. Where an application for a patent for invention or utility model is filed, a request, a description and its abstract, and claims shall be submitted.

The request shall state the title of the invention or utility model, the name of the inventor or creator, the name and the address of the applicant and other related matters.

The description shall set forth the invention or utility model in a manner sufficiently clear and complete so as to enable a person skilled in the relevant field of technology to carry it out; where necessary, drawings are required. The abstract shall state briefly the main technical points of the invention or utility model.

The claims shall be supported by the description and shall define the extent of the patent protection sought for in a clear and concise manner.

Where an invention-creation is developed relying on the genetic resources, the applicant shall indicate, in the application documents, the direct and original source of such genetic

resources; where the applicant fails to indicate the original source, he or it shall state the reasons thereof.

Article 33. An applicant may amend his or its application for a patent, but the amendment to the application for a patent for invention or utility model may not go beyond the scope of the disclosure contained in the initial description and claims, and the amendment to the application for a patent for design may not go beyond the scope of the disclosure as shown in the initial drawings or photographs.

IMPLEMENTING REGULATIONS OF THE PATENT LAW OF THE PEOPLE'S REPUBLIC OF CHINA

Rule 22. Any dependent claim of an invention or utility model shall contain a reference portion and a characterizing portion, and be presented in the following manner:

(l) a reference portion: indicating the serial number(s) of the claim(s) referred to, and the title of the subject matter;

(2) a characterizing portion: stating the additional technical features of the invention or utility model.

Any dependent claim shall only refer to the preceding claim or claims. Any multiple dependent claim, which refers to two or more claims, shall refer to the preceding one in the alternative only, and shall not serve as a basis for any other multiple dependent claims.

Patented Feb. 10, 1953

2,628,249

UNITED STATES PATENT OFFICE

2,628,249

ESTERIFICATION PROCESS

Anthony J. Bruno, Jr., Pittsburgh, Pa., assignor to Pittsburgh Coke & Chemical Company, Pittsburgh, Pa., a corporation of Pennsylvania

No Drawing. Application January 3, 1951, Serial No. 204,285

12 Claims. (Cl. 260—475)

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This invention relates to new improvements in esterification processes and is particularly concerned with the production of discoloration-free esters of high molecular weight and low vapor pressure from the corresponding alcohol and acid.

FIELD OF INVENTION

Large quantities of esters are consumed each year as plasticizers in the formation of plastic compositions, coating compositions, films, filaments, and the like. One of the prime considerations given to any ester for use in such manner is the purity of the product, i. e., the lack of contaminating materials giving the product undesirable color characteristics or acidic or similar properties, which may cause the ester or the materials with which they are mixed to be unstable or cause the products to be unusable for many purposes. Accordingly, an extensive amount of work has been carried out in an effort to devise improvements in the existing procedures for ester production, so as to produce products having the highest possible degree of purity and freedom from discoloration.

In this regard, it has been known that certain materials, such as mineral acids, sulfonic acids, ion exchange resins, or the like, can be used as catalysts in esterifications. However, such materials, as the ion exchange resins, are costly and difficulty of recovery from the reaction mixture and bulkiness make them generally unattractive. On the other hand, the mineral acids and aryl sulfonic acids possess the disadvantage that they discolor the resulting esters. Although the such discolored ester can be rendered colorfree, the treatments required are most involved and quite costly. Consequently, the trade has been attempting for some time to find new and better esterification catalysts and methods which do not possess the detracting disadvantages referred to.

OBJECTS

A principal object of this invention is the provision of new improvements in esterification procedures, particularly, the methods used to form high molecular weight esters. Further objects include:

(1) The provision of new methods for forming plasticizer-type esters in very high yields, which are substantially free of discoloration and which possess an extremely high degree of purity.

(2) The provision of new catalysts for use in esterification reactions which may be employed in place of prior known esterification catalysts without causing discoloration of desired products, and

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(3) The provision of new esterification catalysts which increase the speed of reaction to such an extent that the tendency to produce color-forming bodies is greatly reduced.

Still further objects and the entire scope of applicability of the present invention will become apparent from the detailed description given hereinafter; it should be understood, however, that the detailed description and specific examples, while indicating preferred embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description.

GENERAL DESCRIPTION

These objects are accomplished according to the present invention by the production of esters through the condensation of a carboxylic acid with an alcohol in liquid phase contact with a catalyst comprising a mixture of (1) a sulfur-containing acid from the group consisting of sulfuric and sulfonic acids, and (2) activated carbon. Sufficient of the catalytic mixture is used to have a catalytic effect upon the condensation of the alcohol and the acid.

The success of the present invention is due primarily to the unique discovery that a mixture of activated carbon with sulfuric acid or an aryl sulfonic acid can serve as a catalyst in esterification procedures and that, when this catalytic mixture is employed, the resulting esters possess unpredictably high degrees of purity and lack of discoloration and are obtained in surprisingly high yields. This is in contrast to the results obtained when the aryl sulfonic acids, sulfuric acid, or activated carbon per se are used as esterification catalysts which, in the case of the acids, result in the formation of discolored esters and which generally require longer periods of time for completion.

EXAMPLES

A more complete understanding of the procedures of this invention may be had by reference to the following illustrative examples of actual operations in accordance with the invention, wherein all parts are by weight.

Example I

This example illustrates the preparation of dibutyl phthalate.

200 parts of phthalic anhydride, 200 parts of butyl alcohol, one part of 95% sulfuric acid and 2.5 parts of activated carbon are charged into a

suitable reaction vessel fitted with a reflux condenser, a reflux water separator, and an efficient stirrer. With the contents of the vessel thoroughly agitated, they are heated up to a controlled reflux temperature of 145° to 150° C. and retained there for five hours. During this period, water of reaction is removed and 90 parts of butyl alcohol are added in 10 part portions to compensate for loss of alcohol dissolved in the removed water.

At the end of five hours, the reflux condenser is shut off and the excess alcohol is allowed to distill off from the reaction vessel. The dibutyl phthalate contained in the reaction vessel is withdrawn and passed to a mixing vessel where sufficient caustic soda is added to just neutralize the free mineral acid. The ester is then washed with an excess of water, after which it is passed through filters and collected. It is then blown with steam to insure complete removal of volatiles, dried and filtered.

354 parts of dibutyl phthalate having the following specifications are obtained:

Percent ester	99.5%
Percent acid (as phthalic acid)	0.003%
Color APHA scale	10 to 15
Specific gravity 20°/20°	1.0474
Percent water	0.05
Refractive index n_D^{25}	1.4910

Example II

The reaction of Example I is carried out in an identical manner, except that 50 parts of benzene are added to the reaction mixture as an azeotropic agent in order to effect a controlled temperature of 145° to 150° C. and obtain an efficient separation of water. The resulting product has the same specifications as the product of Example I.

Example III

The reaction of Example I is carried out in an identical manner, except that the activated carbon is omitted. The resulting ester has an APHA color of about 200.

Example IV

This example illustrates the preparation of di-2-ethylhexyl sebacate.

The following ingredients are charged into a reaction vessel equipped with stirrer, reflux condenser, and reflux water separator:

606 parts sebacic acid
859 parts 2-ethylhexanol
200 parts benzene
1.5 parts sulfuric acid (95%)
15 parts activated carbon

The materials are heated to 125° to 130° C. with controlled reflux and simultaneous removal of condensed water. The reaction is carried out for six hours when refluxing is discontinued and the excess alcohol and benzene are allowed to distill off. Sufficient caustic soda is then added to neutralize free acid and the resulting ester is washed with water. The product is then blown with steam to completely remove volatiles, dryed and filtered. Without further treatment, 1190 parts of 2-ethylhexyl sebacate, having the following properties, are obtained:

Percent ester	99.3%
Percent acid (as sebacic acid)	0.016%
Color APHA scale	50 to 60
Specific gravity 25°/25°	0.9119
Percent water	0.083%
Refractive index n_D^{25}	1.4496

DETAILED DESCRIPTION

One of the important reactants for use in these new procedures is activated carbon which may be derived from a number of different sources. The exact form in which the activated carbon is used in the reaction is not critical, but most effective results are obtained when the carbon is used in an extremely finely divided form, e. g., a size where 85 to 95% will pass a 325 mesh standard sieve. Most activated carbons appear to be more or less generally useful for this purpose, but equally desirable results are not obtained with all activated carbons. It has been discovered that activated decolorizing carbons are most desirable.

The other component of the catalytic mixture for use with these new procedures is a sulfur-containing acid, which may be either sulfuric acid or a sulfonic acid. Examples of suitable aryl sulfonic acids include benzene, toluene, naphthalene, or para-butylphenol sulfonic acids. Also alkane sulfonic acids, such as petroleum oil sulfonic acids, may be used. Sulfuric acid is the preferred material, and it is desirable to employ a substantially concentrated sulfuric acid, such as the commercial 95% acid. However, less concentrated acid may be used.

The relative proportions of carbon to acid in the catalytic mixture may be varied. However, for best results, it has been found that mixtures containing about one part of the sulfur-containing acid for each one to 20 parts of activated carbon give the best esters with the greatest speed.

The quantity of the catalytic mixture of activated carbon and acid relative to the amounts of acid and alcohol used in the esterification reaction can be varied and will be dependent to some extent upon the particular acid and alcohol used in the process. Broadly, sufficient of the catalytic mixture is employed to produce a catalytic effect upon the condensation on the alcohol and acid to form the ester. However, best results have been obtained using between 0.1 and 5% by weight of the catalytic mixture in the esterification, i. e., between about 0.05 and 2.5% H_2SO_4 and about 0.05 and 4.5% activated carbon.

The ability of the new catalytic mixtures of this invention to form esters of high purity and freedom from discoloration seems to be general for all esterification procedures, which form impure or discolored esters when mineral acids, such as sulfuric or aryl sulfonic acids, are used as the catalysts. However, the invention is most usefully applied in the formation of high molecular weight esters, such as those formed from polycarboxylic acids, of molecular weight greater than 105 to give esters having a molecular weight between 120 and 400.

A large variety of different types of alcohols may be successfully used in carrying out the procedures of this invention. Examples of useful alcohols include:

(a) Monohydric alkyl alcohols, e. g., methanol; ethanol; n- or sec.-propanol; n-, sec.-, or tertiary butanol; n-, sec.-, or isoamyl alcohol; isooctyl alcohol; 2-ethylhexyl alcohol; nonyl alcohol; lauryl alcohol; stearyl alcohol and dodecanol;

(b) Dihydric alkyl alcohols, e. g., glycol; 1-3-propylene glycol; 1,4-butylene glycol; 1,6-hexamethylene glycol, and 1,8-octandiol;

(c) Higher polyhydric alkyl alcohols, e. g., glycerol; 1,3,4-butantriol; 1,2,6-hexantriol; pentaerythritol; pentaglycerol and sucrose;

(d) Phenols, e. g., phenol; cresols; chloro-

phenol; amylphenol; polychlorophenol; p-hydroxy biphenyl; betahydroxy naphthalene; 2-chloro-3-methyl phenyl; paranitrophenol and salicyl alcohol;

(e) Alicyclic alcohols, e. g., cyclohexanol, inositol; hydroxy benzene hexachloride; 2-methylcyclohexanol; cycloheptanol, and benzyl alcohol;

(f) Heterocyclic alcohols, e. g., furfuryl alcohol; tetrahydrofurfuryl alcohol; alpha, beta, or gamma-pyridone and carbostyril;

(g) Ether alcohols, e. g., diethylene glycol; diethylene glycol monomethyl ether; ethylene glycol monoethyl ether; tetraethylene glycol; butoxyethanol; pentanoxymethanol and butylene glycol monobutyl ether.

A large variety of carboxylic acids may be used in the esterification procedures of this invention. Examples of usable acids include:

(a) Aliphatic monocarboxylic acids, e. g., acetic; propionic; butyric; caproic; lauric; myristic; palmitic; stearic; pelargonic; ethyl butyric; ethyl hexanoic; and oleic acids.

(b) Aliphatic dicarboxylic acids, e. g., succinic; oxalic; suberic; azelaic; adipic; sebacic; maleic; glutaric and fumaric acids;

(c) Higher aliphatic polycarboxylic acids, e. g., citric; aconitic and tricarballylic;

(d) Aryl carboxylic acids; e. g., benzoic; phenylacetic; salicylate; 4-chlorobenzoic; O-, m-, or p-toluic; phthalic; naphthoic; 2-nitrobenzoic and pyromellitic acids;

(e) Alicyclic carboxylic acids, e. g., cyclohexanoic; 2-methyl cyclohexanoic; α-cyclohexyl butyric; 2-methyl cyclohexyl acetic; cyclohexyl succinic and benzene hexachloride acetic acids;

(f) Heterocyclic carboxylic acids, e. g., furoic; picolinic; nicotinic; lutidinic; cinchomeronic; and 2-methyl furoic acids;

(g) Miscellaneous acids, e. g., chloroacetic; abietic; tartaric; glycolic; levalinic and ricinoleic acids.

Where it is desired, the anhydride, if available, of any of these acids may be employed in place of the acid per se.

Using the above acids and alcohols in this invention, examples of esters of high molecular weight with substantial freedom from discoloration or presence of impurities which can be prepared include:

(a) Aliphatic monocarboxylic acid esters, e. g., butyl laurate; amyl laurate; glycerol monolaurate; butyl oleate; ethylhexyl oleate; benzyl stearate; cyclohexyl stearate; lauryl butyrate; glycerol tributyrate; dodecyl acetate; nonyl ethylhexanoate; sucrose octoacetate and tetrahydrofurfuryl oleate;

(b) Aliphatic dicarboxylic acid esters, e. g., diisooctyl adipate; dinonyl adipate; dinonyl azelate; diisooctyl sebacate; diethyl adipate; dimethoxymethyl adipate; bis-(methylcyclohexyl) adipate; dibenzyl sebacate; dibutyl succinate and dilauryl oxalate;

(c) Higher aliphatic polycarboxylic acid esters, e. g., triethyl citrate; tributyl tricarballylate; triamyl aconitate; and triphenyl citrate;

(d) Aryl carboxylic acid esters, e. g., lauryl benzoate; nonyl phenylacetate; octyl naphthoate; diethyl phthalate; tetraethyl pyromellitate and diamyl phthalate;

(e) Alicyclic carboxylic acid derivatives, e. g., lauryl 2-methylcyclohexanoate; tetrahydrofurfuryl cyclohexanoate; diamyl cyclohexylsuccinate and naphthyl cyclohexanoate;

(f) Heterocyclic carboxylic acid esters, e. g., lauryl furoate; phenyl nicotinate; myristyl picolinate; ethylhexyl picolinate and biphenyl furoate;

(g) Glycol derivative esters, e. g., ethylene glycol dipropionate; diethylene glycol diacetate; triethylene glycol di-2-ethylbutyrate; polyethylene glycol sebacate; tetraethylene glycol di-ethylhexoate; diethylene glycol ricinoleate; polyethylene glycol dilevulinate; ethylene glycol adipate; tetraethylene glycol azelate; tri-(ethylene glycol monoethyl ether) citrate; and ethylene glycol monoamyl ether ricinoleate.

The reaction conditions used in carrying out esterifications with my new catalytic mixtures can be varied and are primarily dependent upon the particular esters being formed. Thus, the temperatures will vary and depend primarily upon the alcohols used, but in any case, a temperature sufficient to cause the esterification to proceed in the presence of the catalytic mixtures should be used. Generally, temperatures between 50 and 200° C. will be employed.

No specific type of apparatus is required, and the general type of equipment normally used in esterification reactions can be utilized. Likewise, general information and knowledge regarding esterification reactions can be applied by those skilled in the art in carrying out the operations in accordance with this invention.

CONCLUSIONS

This present invention provides new catalytic mixtures for use in the liquid phase esterification of carboxylic acids with alcohols to form esters. The new catalysts which are used in the liquid phase with the reactants are generally applicable to the formation of all esters, but they are most effectively employed in the formation of esters of high molecular weight which generally produce discolored products when formed using mineral acids or sulfonic acids as the esterification catalysts. The usefulness of the new catalytic mixtures of this invention is primarily due to their ability to form esters at relatively high reaction rates, which are of very high purity and do not contain discolorizing ingredients.

I claim:

1. In the process for the production of esters, the step which comprises condensing a material from the group consisting of carboxylic acids and anhydrides thereof with an alcohol in the presence of between 0.1 and 5% by weight of a mixture of (1) a sulfur-containing acid from the group consisting of sulfuric and sulfonic acids, and (2) activated carbon.

2. A process for the production of substantially colorless low vapor pressure esters of carboxylic acids, which comprises adding between 0.05 and 2.5% by weight of H_2SO_4 and between 0.05 and 4.5% by weight of activated carbon to an esterification mixture, subjecting the mixture to a temperature sufficient to cause esterification and recovering an ester from the reaction mixture.

3. In the process for the production of high molecular weight esters having very good color characteristics, the improvement comprising carrying out the esterification using a mixture of sulfuric acid and activated carbon as the esterification catalyst.

4. A process as claimed in claim 3, wherein said mixture comprises one to 20 parts of activated carbon for each part of sulfuric acid.

5. A process as claimed in claim 1 wherein the condensation is carried out at a temperature between 50 and 200° C.

6. A process as claimed in claim 1, wherein said

material is a dicarboxylic acid of the general formula:

$$HOOC(CH_2)_xCOOH$$

wherein x is an integer from 2 to 10.

7. A process as claimed in claim 1, wherein said alcohol is a saturated monohydric alkyl alcohol having between one and 18 carbon atoms.

8. A process as claimed in claim 1, wherein said material is an aryl dicarboxylic acid.

9. A process as claimed in claim 8, wherein said material is phthalic anhydride.

10. A process as claimed in claim 1, wherein said carbon is of such fineness that at least 85 to 95% will pass a 325 mesh standard sieve.

11. A process as claimed in claim 1, wherein a mixture of alcohols is used.

12. In the process for the production of esters, the step which comprises condensing a material from the group consisting of carboxylic acids and anhydrides thereof with an alcohol in the presence of a catalyst comprising a mixture of (1) a sulfur-containing acid from the group consisting of sulfuric and sulfonic acids, and (2) activated carbon.

ANTHONY J. BRUNO, JR.

No references cited.

Patented Mar. 30, 1954

2,673,860

UNITED STATES PATENT OFFICE

2,673,860

PREPARATION OF FURAN-α,α'-DICARBOXYLIC ACID ESTERS

Richard Kuhn and Karl Dury, Heidelberg, Germany

No Drawing. Application July 16, 1951, Serial No. 237,078

1 Claim. (Cl. 260—347.5)

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This invention relates to the preparation of furan-α,α'-dicarboxylic acid esters.

If an α,α'-diketoadipic acid ester or an α,α'-dihydroxymuconic acid ester or an acyl derivative of the latter, is treated with a dehydrating agent, e. g. concentrated sulfuric acid, ring closure occurs, even in the cold, without saponification, to give a furan-α,α'-dicarboxylic acid ester in practically quantitative yield. These esters are compounds of potential value as intermediates in chemical syntheses and have valuable pharmacological properties. Thus furan-α,α'-dicarboxylic acid diethyl ester has strong anesthetic action which is similar to that of cocaine with respect to speed of initiation and duration of total anesthesia (measured on the cornea of the rabbit's eye).

Examples

In the following examples parts by weight and volume are to be taken in metric units.

One part by weight of α,α'-dihydroxymuconic acid diethyl ester is dissolved in 5 volumes of concentrated sulfuric acid and allowed to stand for 2 hours at approximately 20° C. The mixture is then poured on ice and crystallized from petroleum ether. The yield is 95% of the theory of furan-α,α'-dicarboxylic acid diethyl ester as white needles having a melting point of 47° C.

From α,α'-diacetoxymuconic acid diethyl ester under the same conditions 98% of the theory of

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pure furan-α,α'-dicarboxylic acid diethyl ester is obtained.

In a corresponding manner from the dimethyl, dipropyl and di-n-butyl esters of α,α'-dihydroxymuconic acid are obtained the dimethyl ester (M. P. 107° C.), di-n-propyl ester (boiling point/12 mm., 164° C.) and the di-n-butyl ester (M. P. 40° C.) of furan-α,α'-dicarboxylic acid.

The dehydration can also be effected by other agents, e. g. by heating with silver sulfate.

We claim:

The method of preparing a furan-α,α'-dicarboxylic acid lower alkyl ester which comprises dissolving a lower alkyl diester of a dicarboxylic acid selected from the group consisting of α,α'-diketoadipic acid, α,α'-dihydroxymuconic acid and acyl derivatives of α,α'-dihydroxymuconic acid in concentrated sulfuric acid at room temperature, allowing the solution to stand until ring closure has been effected, and precipitating the desired ester by diluting the reaction mixture with water while cooling to absorb the heat of dilution.

RICHARD KUHN.
KARL DURY.

References Cited in the file of this patent

Fieser and Fieser, "Organic Chemistry," pp. 54–56 (1944).
Beilstein, vol. 18, pp. 328–330.
Chem. Abs., vol. 38, col. 1230.

United States Patent [19]

Leupold et al.

[11] **Patent Number: 4,977,283**

[45] **Date of Patent: Dec. 11, 1990**

[54] **PROCESS FOR THE OXIDATION OF 5-HYDROXYMETHYLFURFURAL**

[75] Inventors: **Ernst I. Leupold,** Neu-Anspach; **Matthias Wiesner,** Mainz; **Merten Schlingmann,** Königstein; **Knut Rapp,** Offstein, all of Fed. Rep. of Germany

[73] Assignee: **Hoechst Aktiengesellschaft,** Frankfurt am Main, Fed. Rep. of Germany

[21] Appl. No.: **387,086**

[22] Filed: **Jul. 27, 1989**

[30] **Foreign Application Priority Data**

Jul. 30, 1988 [DE] Fed. Rep. of Germany 3826073

[51] **Int. Cl.**[5] **C07D 307/48;** C07D 307/68

[52] **U.S. Cl.** **549/484;** 549/485; 549/488

[58] **Field of Search** 549/484, 485, 488

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,326,944 6/1967 Lew 549/485

OTHER PUBLICATIONS

J. J. Blanksma, *Chemisches Zentralblatt:*(1910)T, 539.

S. Morikawa, Chem. Abstr. 92:198181a, (1980).

Primary Examiner—Howard L. Raymond

[57] **ABSTRACT**

A process for the oxidation of 5-hydroxymethylfurfural which comprises oxidizing 5-hydroxymethylfurfural in an aqueous medium with oxygen in the presence of a catalyst which contains at least one metal of the platinum group.

23 Claims, No Drawings

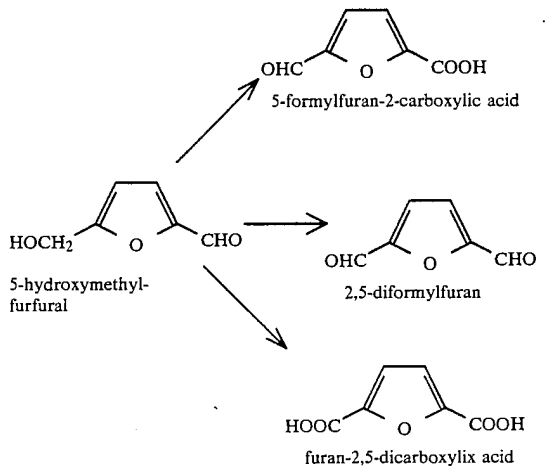
PROCESS FOR THE OXIDATION OF 5-HYDROXYMETHYLFURFURAL

DESCRIPTION

The present invention relates to the catalytic oxidation of 5-hydroxymethylfurfural to form products which can be put to a multiplicity of uses and which in particular can be used as intermediates for the preparation of surfactants, plastics and resins.

It is known to oxidise 5-hydroxymethylfurfural without the co-use of catalysts, using various oxidizing agents, such as concentrated nitric acid (J. J. Blanksma, Chemisches Zentralblatt 1910 I, 539) or a mixture of dimethyl sulfoxide on the one hand and acetic anhydride, dinitrogen tetroxide or nitric acid on the other hand (Morikawa, Chem. Abstr. Vol. 92 (1980), 198181a).

Essentially, three reaction products are found on the oxidation:



However, the methods hitherto known for the preparation of oxidation products of 5-hydroxymethylfurfural are associated with considerable disadvantages. When using the conventional reagents nitric acid, dinitrogen tetroxide and dimethyl sulfoxide, large amounts of undesired products, such as nitrous gases or sulfur compounds, depending on the particular reagents, inevitably form the disposal of which requires considerable expenditure. Likewise, it is very expensive to separate off excess oxidizing agent during working-up. There is thus a need for a process for the oxidation of 5-hydroxymethylfurfural which can be carried out without the said disadvantages in a technically simple manner.

The invention relates to a process for the oxidation of 5-hydroxymethylfurfural, which comprises oxidizing 5-hydroxymethylfurfural in an aqueous medium using oxygen as the oxidizing agent in the presence of a catalyst which contains at least one metal from the platinum group.

Suitable catalysts are those which contain metals of the platinum group, such as iridium, rhodium, ruthenium, but advantageously palladium and/or platinum. Catalysts which contain only platinum as the metal from the platinum group are very particularly preferred. The metals of the platinum group are preferably used on a support, particularly on activated charcoal. The metal, particularly platinum, content of the catalyst is preferably 1 to 10 by weight. Examples of suitable catalysts are commercially available catalysts having 5 to 10% by weight of platinum on activated charcoal.

The concentration of 5-hydroxymethylfurfural in the aqueous medium may vary within wide limits. It is preferably used in an amount from 5 to 30, particularly 10 to 20% by weight relative to the amount of water and solubilizer.

In order to avoid the precipitation of reaction products during the oxidation, it has proved advantageous, particularly at relatively high concentrations, to use a solubilizer which is inert toward the reactants under the reaction conditions, preferably in a concentration of 10 to 75% by weight, particularly 30 to 50% by weight, relative to the amount of water and solubilizer. Solubilizers used are expediently those which have relatively low volatility when oxygen is passed through the aqueous solution, so that a risk of explosion in the vapor space is substantially avoided; on the other hand, those solubilizers which are easily separated off, for example by distillation, after the oxidation are preferred.

Examples of suitable solubilizers are glycol ethers without free OH groups, such as glycol ethers of the formula $R^1O[CH_2CH(CH_3)O]_nR^2$, in which n is an integer from 1 to 4 and R^1 and R^2 in each case independently of one another denote C_1–C_4-alkyl. The dimethyl, diethyl or methyl ethyl ethers and the corresponding propylene glycol ethers of the said general formula with boiling points in the range from 100° to about 250° C., for example triethylene glycol dimethyl ether and particularly diethylene glycol dimethyl ether, are particularly suitable. Other ethers also, such as crown ethers, are suitable as solubilizers, it being necessary in each individual case to take particular account in the economics of the process of the expenditure for the separation and the costs of using the solubilizer.

Pure oxygen is the preferred oxidizing agent. However, it is also possible to use mixtures of oxygen with gases which are inert under the reaction conditions, for example in the form of air, for example mixtures of oxygen with inert gases or with air.

Generally, the operation is carried out at a total pressure of between 0.5 and 100 bar. The reaction velocity increases significantly with increasing partial pressure of oxygen; however, with regard to the economics of the process, the advantage of the higher reaction velocity may be over compensated by the higher expenditure on apparatus required due to the application of a higher pressure. A pressure range from atmospheric pressure up to 10 bar (absolute) is preferred, operation at atmospheric pressure being particularly simple to carry out.

As a rule, the process according to the invention is carried out at a temperature from 30° C. up to the boiling point of the aqueous medium, preferably from 50° to 95° C., particularly 60° to 90° C.

The reaction can be carried out in various ways with respect to the pH value, and the pH control may have an influence on the proportions of the individual products in the end product. Thus, for example, the reaction may be carried out in a medium which becomes acid due to the reaction products, i.e. in a pH range of below pH 7. Likewise, it is possible to control the pH value during the oxidation by the addition of bases, acids or buffer mixtures, a pH value of less than 8 as a rule being maintained. The oxidation may, however, also still be carried out at higher pH values.

It is possible, for example, by continuous addition of a base such as sodium hydroxide, potassium hydroxide or corresponding aqueous solutions of these bases, to establish a substantially constant pH value in the range from 6.5 to 8, preferably 7 to 7.5. In the latter mode of operation, the oxidation product furan-2,5-dicarboxylic acid is preferentially formed in the form of the di-salt. According to another embodiment, the oxidation is started at about pH 7 and continued without the addition of acids or bases. In the acid medium, 2,5-diformylfuran and 5-formylfuran-2-carboxylic acid preferentially form.

The process according to the invention takes place in a three-phase system comprising solid catalyst, aqueous medium and gaseous oxygen. It may be carried out in all apparatuses which are suitable for carrying out reactions in the liquid phase with or without the application of excess pressure. Examples of this are operating in a stirred vessel or in a bubble column with suspended catalyst. However, the oxidation may also be carried out as a fixed-bed reaction with a granular catalyst in a trickle-bed reactor.

The reaction time required for the formation of the desired reaction product in each case is expediently determined by withdrawing samples of the reaction solution at certain time intervals and analyzing them. For example, the yield of the reaction products can continually determined in a simple manner by analysis of a sample with the aid of high pressure liquid chromatography in comparison with standard solutions. It is advisable to optimize the reaction time, since if the passage of oxygen is unnecessarily prolonged this can lead increasingly to excessive oxidations, followed for example by decarboxylations, and thus to a loss in yield of the desired reaction products.

The reaction mixture can be worked up by known methods. In a suitable process, the solubilizer and the water are first removed by distillation and a subsequent purification by crystallization or extraction is carried out.

Compared with the conventional oxidation processes mentioned initially, the process according to the invention has the advantage that the formation of undesired products, such as nitrous gases or sulfur compounds, is avoided and the separation of excess oxidizing agent is also eliminated. In the catalytic oxidation according to the invention, apart from the desired products, only water is inevitably produced, which in any case is used as the solvent.

The oxidation products of 5-hydroxymethylfurfural are valuable intermediates for the preparation of plastics, surfactants and resins. For example, furan-2,5-dicarboxylic acid can be used as a component of polyesters, and the aldehydes 2,5-diformylfuran and 5-formylfuran-2-carboxylic acid can be used after reaction with long chain amines as surfactants, or in polymerization and copolymerization reactions for the preparation of novel plastics and resins.

EXAMPLES

(1) 80 liters (STP) per hour of oxygen are introduced at a temperature of 70° C. from below through a glass frit into an externally heated, vertically arranged glass tube (diameter: 50 mm, length: 1200 mm), which is filled with a mixture of 162 g of 5-hydroxymethylfurfural, 1460 g of water and 81 g of a commercially available catalyst (5% by weight of platinum on activated charcoal). The pH value is kept at 7 to 7.5 by the continuous addition of 30% aqueous sodium hydroxide solution. After a reaction time of 2.5 hours the reaction solution contains 234 g of furan-2,5-dicarboxylic acid in the form of the disodium salt, corresponding to a yield of 91% of theory.

(2) In the apparatus described in Example 1, 1500 g of a 20% aqueous solution of 5-hydroxymethylfurfural are oxidized in the presence of 50 g of the catalyst used in Example 1 at a temperature of 85° C. with 80 (STP) liters per hour of oxygen. After a reaction time of 11 hours, during which the pH value was maintained at 7 to 7.5 by the addition of 30% aqueous sodium hydroxide solution, the reaction mixture contains 376 g of furan-2,5-dicarboxylic acid in the form of the disodium salt, corresponding to a yield of 79% of theory.

(3) In the apparatus described in Example 1, a mixture of 180 g of 5-hydroxymethylfurfural, 700 g of water, 700 g of diethylene glycol dimethyl ether and 75 g of a commercially available catalyst (5% by weight of platinum on activated charcoal) is reacted with oxygen at a temperature of 60° C. In contrast to Examples 1 and 2, no sodium hydroxide is added, so that the pH value falls, due to the formation of carboxyl groups, from an initial value of about 7 to below 7. After a reaction time of 8 hours the reaction mixture contains 122 g (61% of theory) of 5-formylfuran-2-carboxylic acid, 43 g (24% of theory) of 2,5-diformylfuran and 18 g (8% of theory) of furan-2,5dicarboxylic acid.

(4) The reaction described in Example 1 is carried out for 4 hours at 60° C. under otherwise identical conditions. The reaction solution contains 252 g of furan-2,5-dicarboxylic acid in the form of the disodium salt, corresponding to a yield of 98% of theory.

We claim:

1. A process for the oxidation of 5-hydroxymethylfurfural which comprises oxidizing 5-hydroxymethylfurfural in an aqueous medium at a pH value of at most 8 with oxygen in the presence of a catalyst which contains at least one metal of the platinum group.

2. A process as claimed in claim 1, wherein the platinum metal is palladium, platinum or a combination of palladium and platinum.

3. A process as claimed in claim 2, wherein the platinum metal is platinum.

4. A process as claimed in claim 3, wherein the catalyst consists of 1 to 10% by weight of platinum on a carrier.

5. A process as claimed in claim 4, wherein the carrier is active carbon.

6. A process as claimed in claim 1, wherein the oxidation is carried out at a pressure in the range from 0.5 to 100 bar.

7. A process as claimed in claim 6, wherein the oxidation is carried out at a pressure in the range of from atmospheric pressure to 10 bar.

8. A process as claimed in claim 7, wherein the oxidation is carried out at atmospheric pressure.

9. A process as claimed in claim 1, wherein the aqueous medium also contains a solubilizer inert towards the reactants under the reaction conditions.

10. A process as claimed in claim 9, wherein the solubilizer is present in an amount of from 10 to 75% by weight, referred to the amount of water and solubilizer.

11. A process as claimed in claim 10, wherein the solubilizer is present in an amount of from 30 to 50% by weight, referred to the amount of water and solubilizer.

12. A process as claimed in claim 9, wherein the solubilizer is a glycol ether having no free hydroxy groups.

13. A process as claimed in claim 12, wherein the glycol ether has the formula $R^1O[CH_2CH(CH_3)O]_nR^2$, wherein n is an integer from 1 to 4 and R^1 and R^2 are equal or different alkyl groups having from 1 to 4 carbon atoms.

14. A process as claimed in claim 13, wherein the solubilizer is diethyleneglycol dimethylether.

15. A process as claimed in claim 1, wherein the oxidation is carried out at a temperature in the range of from 30° C. to the boiling point of the aqueous medium.

16. A process as claimed in claim 15, wherein the oxidation is carried out at a temperature in the range of from 50° to 95° C.

17. A process as claimed in claim 15, wherein the oxidation is carried out at a temperature in the range of from 60° to 90° C.

18. A process as claimed in claim 1, wherein the aqueous medium contains, at the beginning of the oxidation, 5 to 30% by weight of 5-hydroxymethylfurfural, referred to the amount of aqueous medium.

19. A process as claimed in claim 1, wherein the pH-value is adjusted to a range of from 6.5 to 8 during the oxidation by the addition of a base.

20. A process as claimed in claim 19, wherein the pH-value is adjusted to a range of from 7 to 7.5 during the oxidation by the addition of a base.

21. A process as claimed in claim 1, wherein the oxidation is started at a pH-value of about 7 and is carried out without addition of an acid or a base.

22. A process for the oxidation of 5-hydroxymethylfurfural which comprises oxidizing at a pH of at most 8 5-hydroxymethylfurfural in an aqueous medium with oxygen in the presence of a catalyst which contains a metal of the platinum group, selected from the group consisting of platinum, palladium and a combination thereof on active carbon at a pressure in the range of from atmospheric pressure to 10 bar at a temperature in the range of from 50° C. to the boiling point of the aqueous medium, the aqueous medium containing from 5 to 30% by weight of 5-hydroxymethylfurfural, referred to the aqueous medium.

23. A process for the oxidation of 5-hydroxymethylfurfural which comprises oxidizing 5-hydroxymethylfurfural in an aqueous medium at a pH value of at most 8 with oxygen in the presence of a catalyst which contains at least one metal of the platinum group, the aqueous medium also containing a solubilizer inert towards the reactants under the reaction conditions in an amount of from 10 to 75% by weight, referred to the amount of water and solibilizer, the reaction being started at a pH value of about 7 and carried out without addition of an acid or a base and also carried out at a temperature in the range of from 50° C. to the boiling point of the aqueous medium.

* * * * *

US 20090156841A1

(19) United States

(12) Patent Application Publication

(10) Pub. No.: US 2009/0156841 A1

(43) Pub. Date: Jun. 18, 2009

SANBORN et al.

(54) **CONVERSION OF CARBOHYDRATES TO HYDROXYMETHYLFURFURAL (HMF) AND DERIVATIVES**

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WASHINGTON, DC 20005-3096 (US)

(21) Appl. No.: **12/334,038**

(22) Filed: **Dec. 12, 2008**

Related U.S. Application Data

(60) Provisional application No. 61/006,012, filed on Dec. 14, 2007, provisional application No. 60/996,946, filed on Dec. 12, 2007.

Publication Classification

(51) **Int. Cl.**

C07D 307/50	(2006.01)
C07C 51/00	(2006.01)
C07C 69/704	(2006.01)

(52) **U.S. Cl.** **549/488**; 562/515; 560/180

(57) **ABSTRACT**

A method of producing substantially pure HMF, HMF esters and other derivatives from a carbohydrate source by contacting the carbohydrate source with a solid phase catalyst. A carbohydrate starting material is heated in a solvent in a column and continuously flowed through a solid phase catalyst in the presence of an organic acid, or heated with the organic acid and a solid catalyst in solution to form a HMF ester. Heating without organic acid forms HMF. The resulting product is purified by filtration to remove the unreacted starting materials and catalyst. The HMF ester or a mixture of HMF and HMF ester may then be oxidized to 2,5-furandicarboxylic acid (FDCA) by combining the HMF ester with an organic acid, cobalt acetate, manganese acetate and sodium bromide under pressure. Alternatively, the HMF ester may be reduced to form a furan or tetrahydrofuran diol.

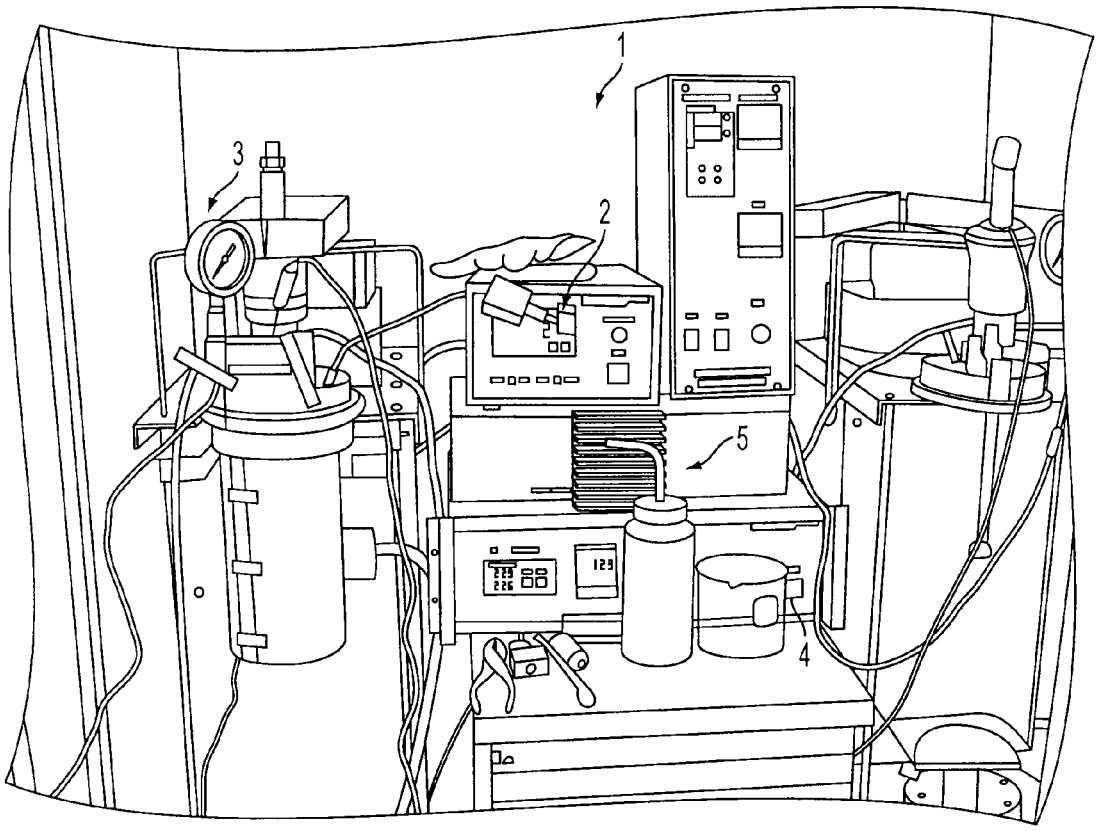


FIG. 1
PRIOR ART

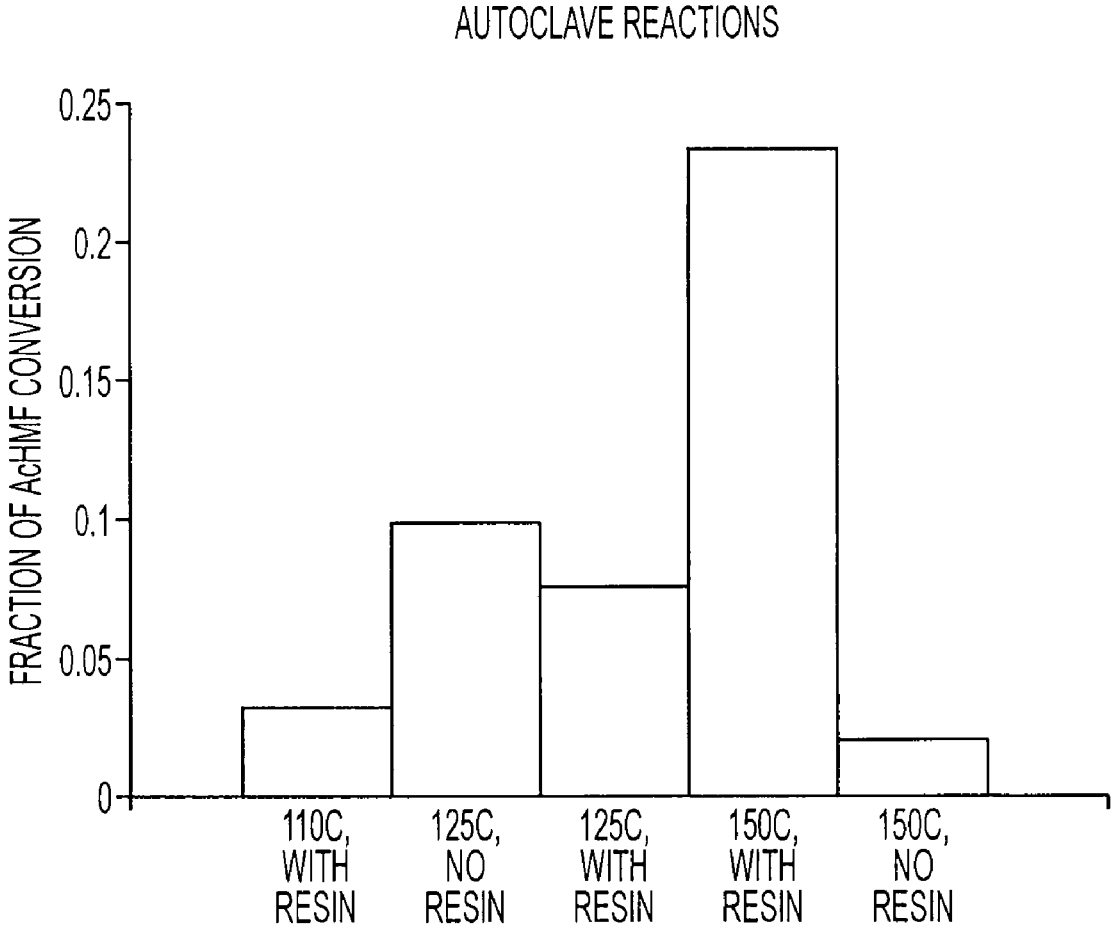


FIG. 2
PRIOR ART

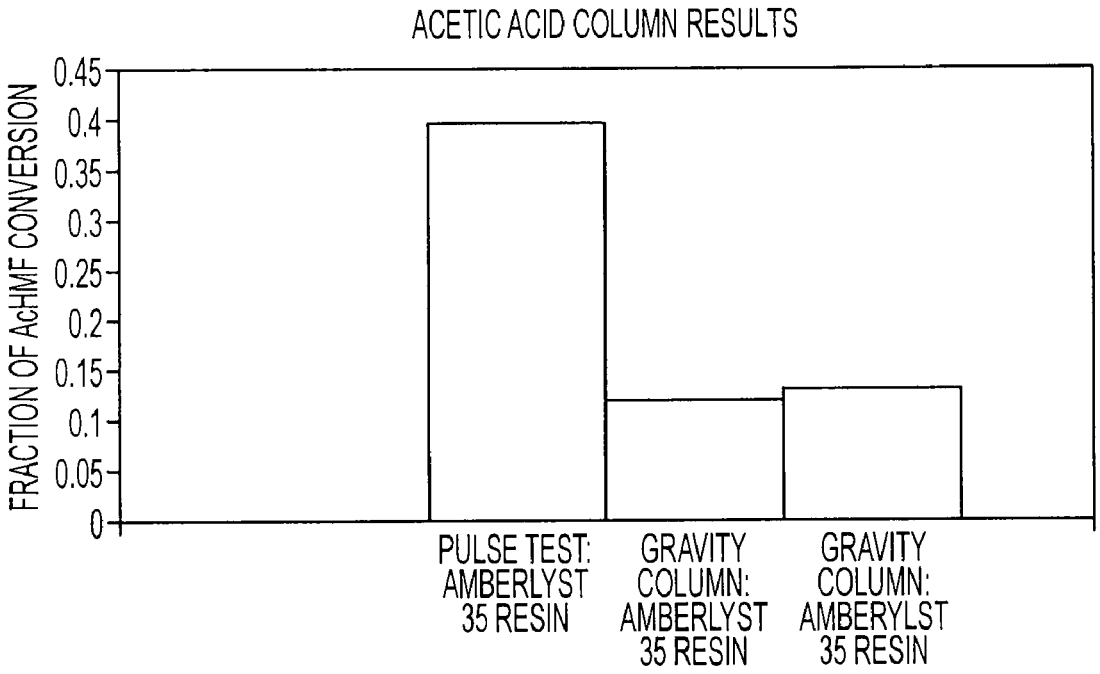

ACETIC ACID COLUMN RESULTS
FRACTION OF AcHMF CONVERSION
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
PULSE TEST: AMBERLYST 35 RESIN
GRAVITY COLUMN: AMBERLYST 35 RESIN
GRAVITY COLUMN: AMBERYLST 35 RESIN

FIG. 3

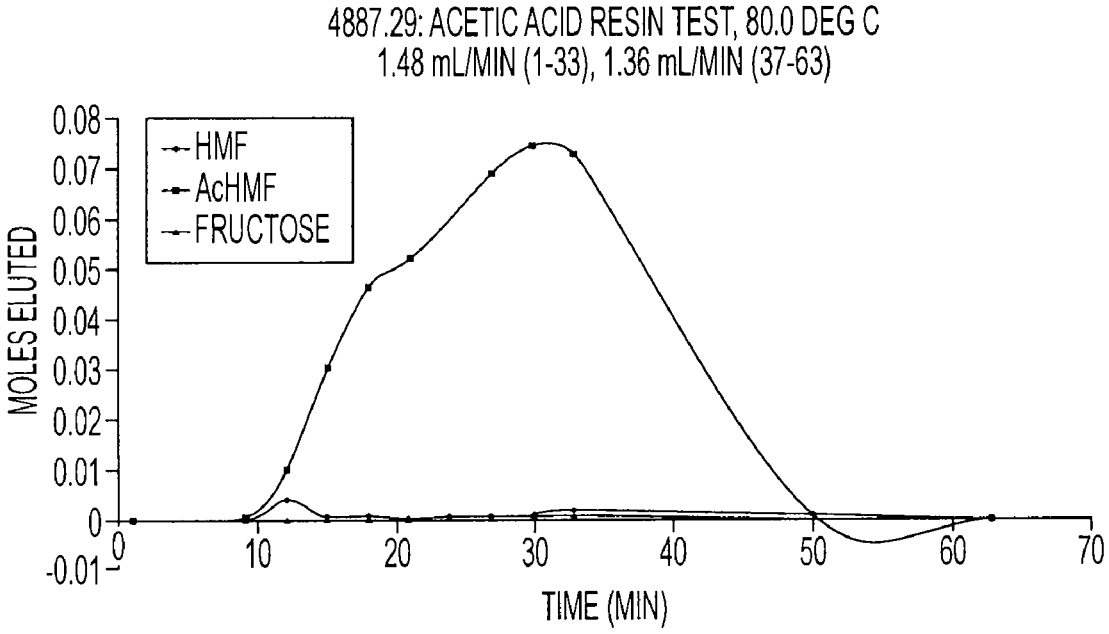

4887.29: ACETIC ACID RESIN TEST, 80.0 DEG C
1.48 mL/MIN (1-33), 1.36 mL/MIN (37-63)
HMF
AcHMF
FRUCTOSE
MOLES ELUTED
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
-0.01
0
10
20
30
40
50
60
70
TIME (MIN)

FIG. 4

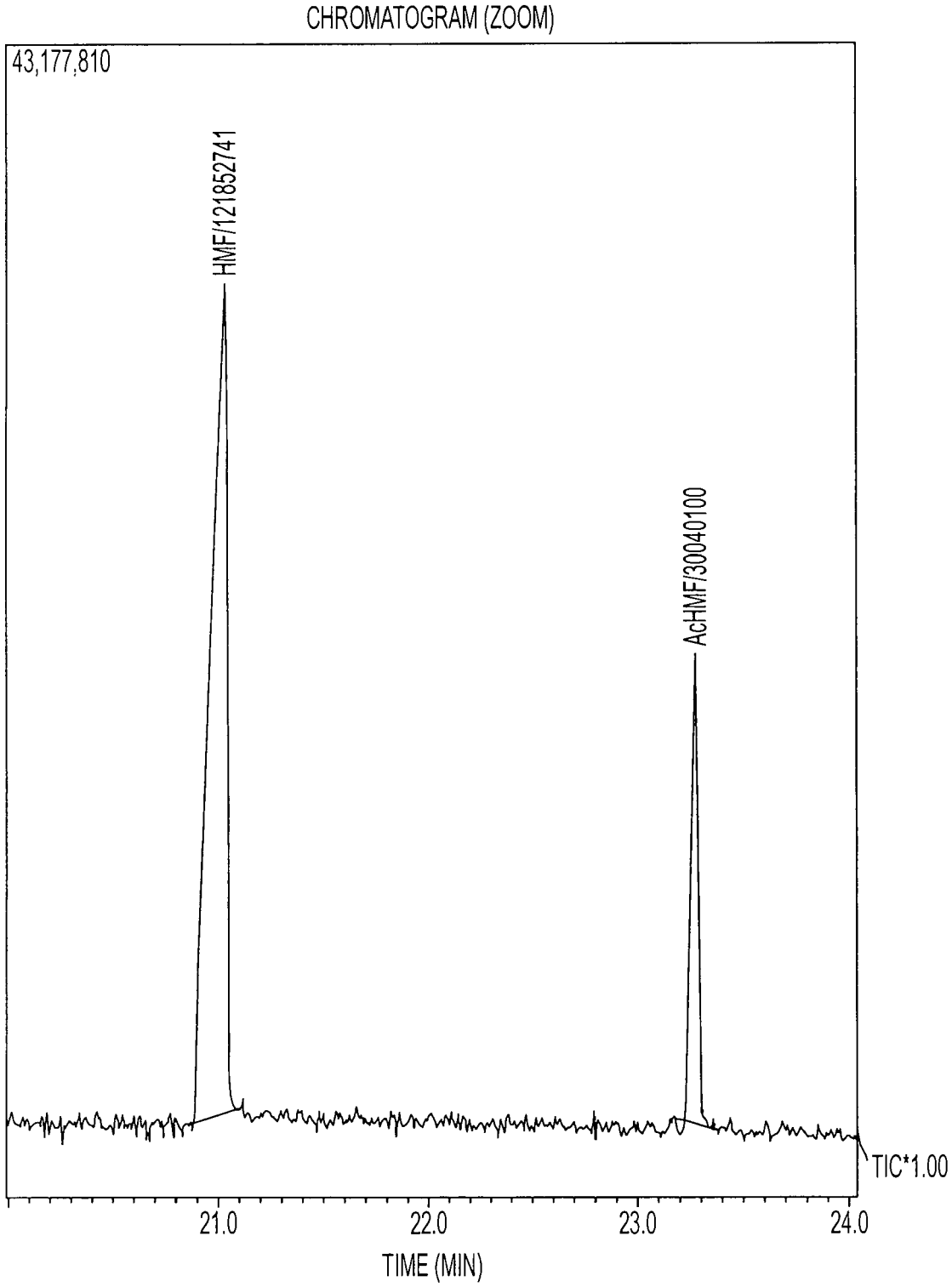

CHROMATOGRAM (ZOOM)
43,177,810
HMF/121852741
AcHMF/30040100
TIC*1.00
21.0
22.0
23.0
24.0
TIME (MIN)

FIG. 5

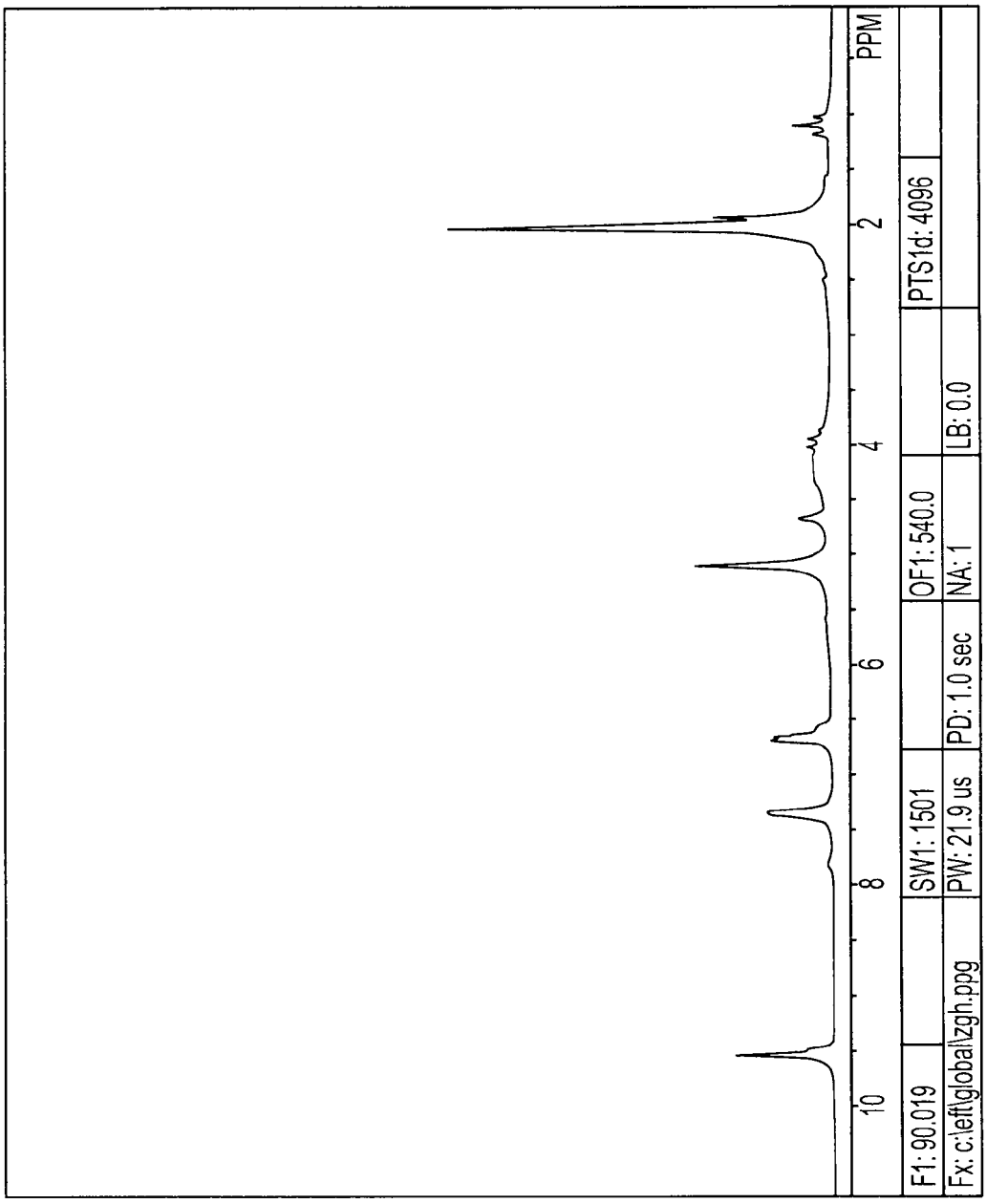

10
8
6
4
2
PPM
F1: 90.019
SW1: 1501
OF1: 540.0
PTS1d: 4096
Fx: c:\leftlglobal\zgh.ppg
PW: 21.9 us
PD: 1.0 sec
NA: 1
LB: 0.0

FIG. 6

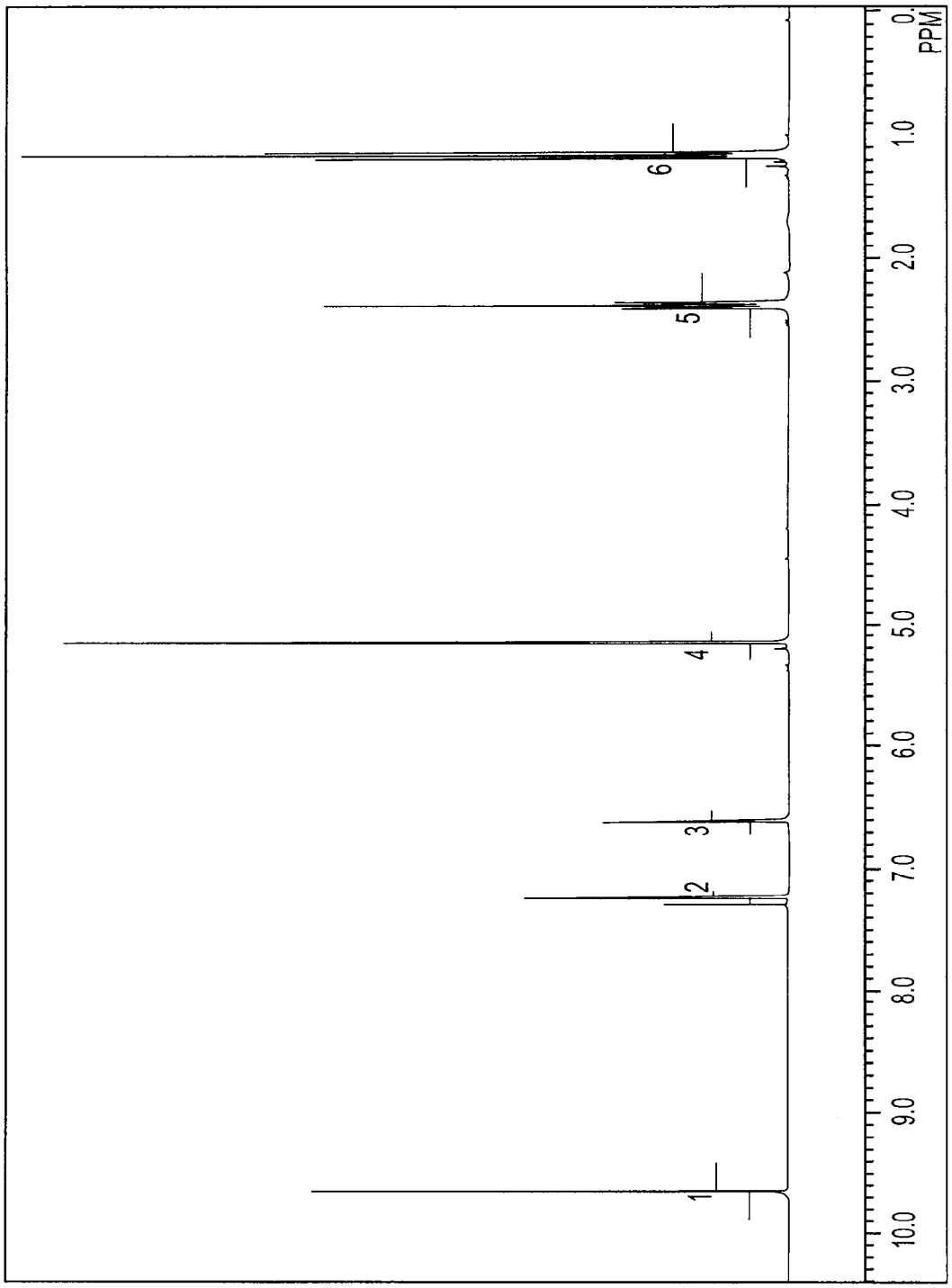


FIG. 7

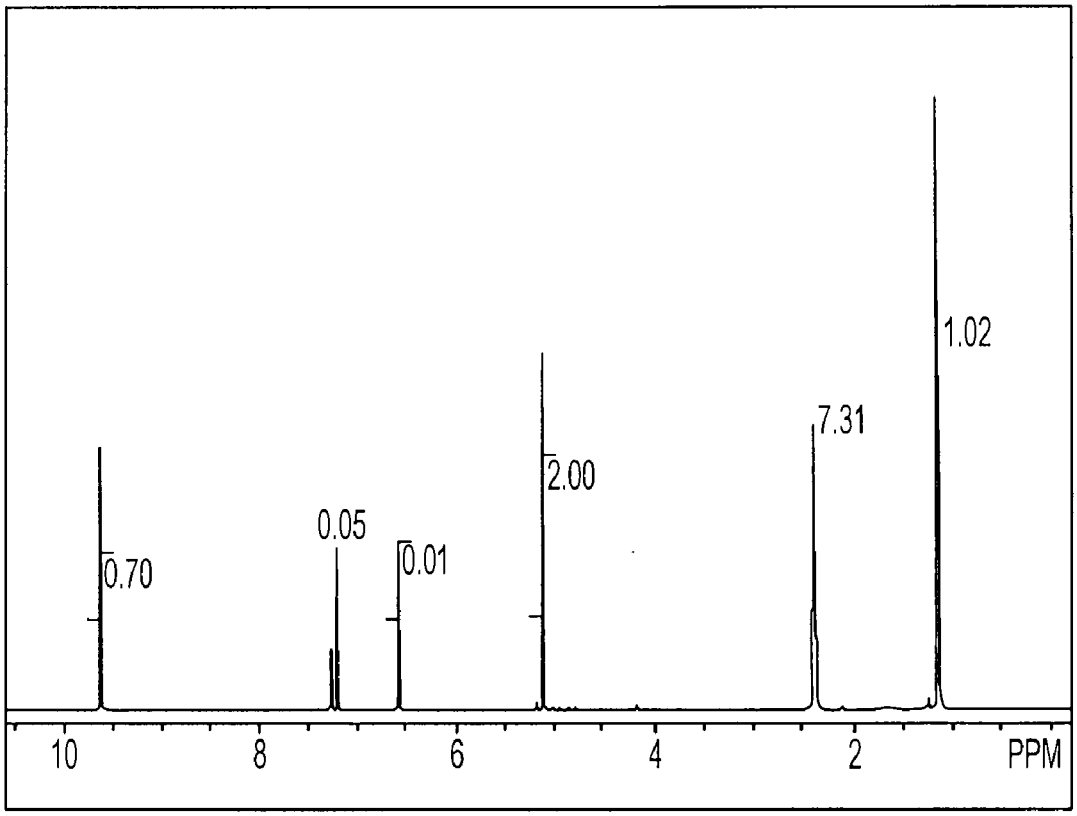


FIG. 8

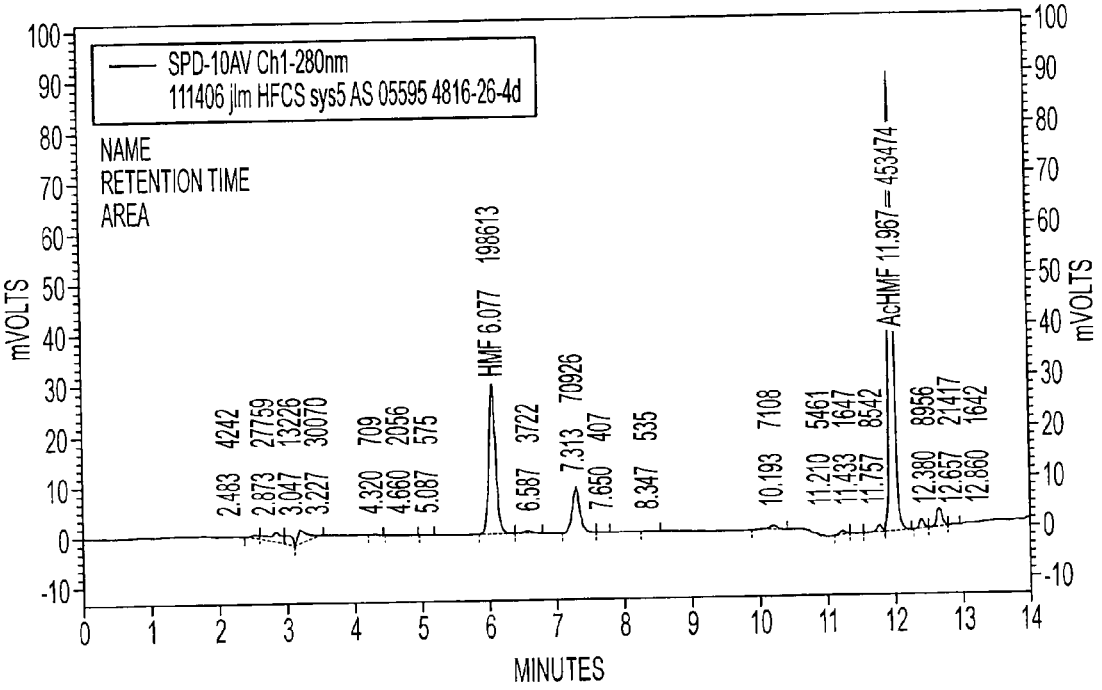

SPD-10AV Ch1-280nm
111406 jlm HFCS sys5 AS 05595 4816-26-4d
NAME
RETENTION TIME
AREA
2.483 4242
2.873 27759
3.047 13226
3.227 30070
4.320 709
4.660 2056
5.087 575
HMF 6.077 198613
6.587 3722
7.313 70926
7.650 407
8.347 535
10.193 7108
11.210 5461
11.433 1647
11.757 8542
AcHMF 11.987 = 453474
12.380 8956
12.657 21417
12.860 1642
mVOLTS
MINUTES

FIG. 9

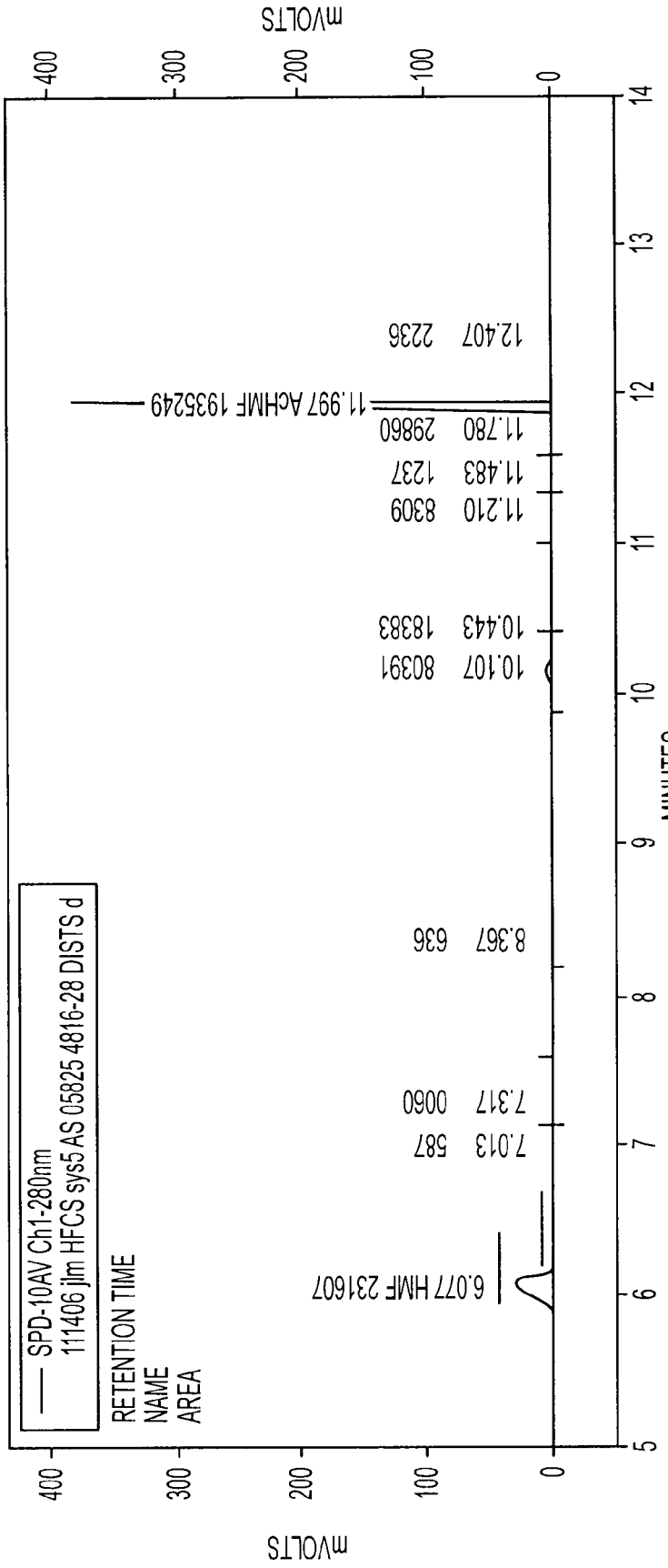

mVOLTS
400
300
200
100
0
SPD-10AV Ch1-280nm
111406 jlm HFCS sys5 AS 05825 4816-28 DISTS d
RETENTION TIME
NAME
AREA
6.077 HMF 231607
7.013 587
7.317 0060
8.367 636
10.107 80391
10.443 18383
11.210 8309
11.483 1237
11.780 29860
11.997 AcHMF 1935249
12.407 2236
5
6
7
8
9
10
11
12
13
14
MINUTES

FIG. 10

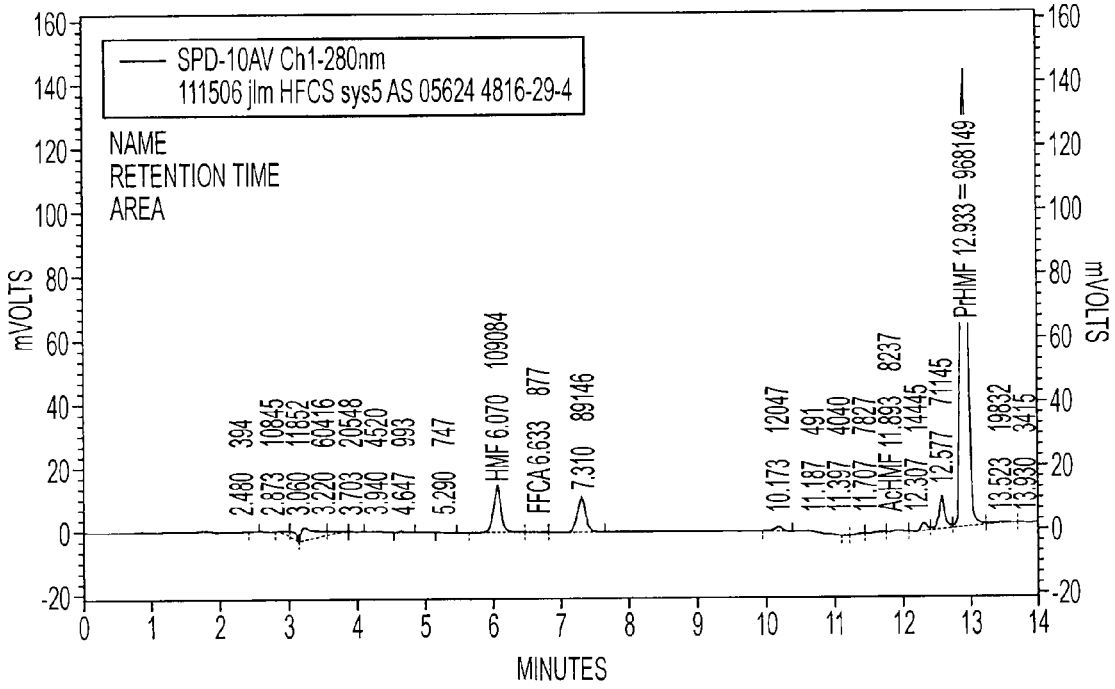

SPD-10AV Ch1-280nm
111506 jlm HFCS sys5 AS 05624 4816-29-4
NAME
RETENTION TIME
AREA
mVOLTS
MINUTES
2.480 394
2.873 10845
3.060 11852
3.220 60416
3.703 20548
3.940 4520
4.647 993
5.290 747
HMF 6.070 109084
FFCA 6.633 877
7.310 89146
10.173 12047
11.187 491
11.397 4040
11.707 7827
AcHMF 11.893 8237
12.307 14445
12.577 71145
PrHMF 12.933 = 968149
13.523 19832
13.930 3415

FIG. 11

CONVERSION OF CARBOHYDRATES TO HYDROXYMETHYLFURFURAL (HMF) AND DERIVATIVES

CROSS REFERENCE TO PROVISIONAL APPLICATION

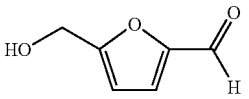
[0001] This application is based upon and claims the benefit of priority from Provisional U.S. Patent Application 61/006,012 (Attorney Docket No. 010253-0020) filed on Dec. 14, 2007, and from Provisional U.S. Patent Application 60/996,946 (Attorney Docket No. 010253-0021) filed on Dec. 12, 2007, the entire contents of which are incorporated by reference herein.

TECHNICAL FIELD

[0002] The present invention relates to a process for the synthesis and recovery of substantially pure HMF and derivatives thereof from hexose carbohydrate feedstocks such as fructose or high fructose corn syrup (HFCS). More particularly, HMF and its derivatives are synthesized, separated, and recovered via contact of the carbohydrate with strong acid cation exchange resins, such as a solid phase catalyst.

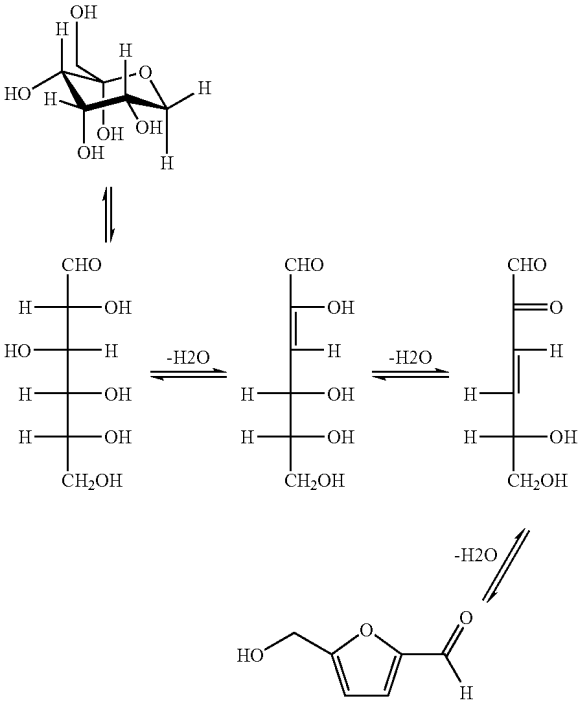
BACKGROUND

[0003] A major product in the acid-catalyzed dehydration of fructose is 2-hydroxymethyl-5-furfuraldehyde, also known as hydroxymethylfurfural (HMF). The structure of HMF is shown below:



[0004] Hydroxymethylfurfural

[0005] HMF represents one key intermediate substance readily accessible from renewable resources like carbohydrates and is a suitable starting source for the formation of various furan monomers which are used for the preparation of non-petroleum-derived polymeric materials. While not being bound by theory, it is generally believed that fructose is converted to HMF via an acyclic pathway, although evidence also exists for the conversion to HMF via cyclic fructofuransyl intermediate pathways. Regardless of the mechanism of HMF formation, the intermediate species formed during the reaction may in turn undergo further reactions such as condensation, rehydration, reversion and other rearrangements, resulting in a plethora of unwanted side products. Below is one proposed pathway for the conversion of fructose to HMF:



[0006] HMF and 2,5-disubstituted furanic derivatives have great potential in the field of intermediate chemicals from regrowing resources. Due to its various functionalities, it has been proposed that HMF could be utilized to produce a wide range of products such as polymers, solvents, surfactants, pharmaceuticals, and plant protection agents, and has been reported to have antibacterial and anticorrosive properties. HMF is also a key component, as either a starting material or intermediate, in the synthesis of a wide variety of compounds, such as furfuryl dialcohols, dialdehydes, esters, ethers, halides and carboxylic acids.

[0007] In addition, HMF has great potential as a biofuel, which are fuels derived from biomass and are considered promising alternatives to fossil fuels. HMF is also currently under investigation as a treatment for sickle cell anemia. In short, HMF is an important chemical compound and a method of synthesis on a large scale to produce HMF absent significant amounts of impurities, side products and remaining starting material has been sought for nearly a century.

[0008] HMF is a suitable starting source for the formation of various furan monomers used in the preparation of non-petroleum-derived polymeric materials. A furan is a 5-membered heterocyclic organic compound. HMF and 2,5-disubstituted furanic derivatives have great potential in the field of intermediate chemicals from growing resources. Due to its various functionalities, it has been proposed that HMF may be utilized to produce a wide range of products such as polymers, solvents, surfactants, pharmaceuticals, and plant protection agents, and HMF has been reported to have antibacterial and anticorrosive properties.

[0009] Although preparation of HMF has been known for many years, a method which provides HMF with good selectivity and in high yields has yet to be found. Complications arise from the rehydration of HMF, which yields by-products, such as, levulinic and formic acids. Another unwanted side

reaction includes the polymerization of HMF and/or fructose resulting in humin polymers, which are solid waste products. Further complications may arise as a result of solvent selection. Water is easy to dispose of and dissolves fructose, but unfortunately, low selectivity and increased formation of polymers and humin increases under aqueous conditions.

[0010] Agricultural raw materials such as starch, cellulose, sucrose or inulin are inexpensive starting materials for the manufacture of hexoses, such as glucose and fructose. As shown above, these hexoses can in turn, be converted to HMF. The dehydration of sugars to produce HMF is well known. HMF was initially prepared in 1895 from levulose by Dull (*Chem. Ztg.,* 19, 216) and from sucrose by Kiermayer (*Chem. Ztg.,* 19, 1003). However, these initial syntheses were not practical methods for producing HMF due to low conversion of the starting material to product.

[0011] Commonly used catalysts for the preparation of HMF includes cheap inorganic acids such as H_2SO_4, H_3PO_4, and HCl. These acid catalysts are used in solution and are difficult to regenerate. In order to avoid the regeneration and disposal problems, solid sulfonic acid catalysts have been used. Unfortunately, the usefulness of solid acid resins is limited because of the formation of deactivating humin polymers on the surface of the resins.

[0012] The purification of HMF has also proved to be a troublesome operation. On long exposure to temperatures at which the desired product can be distilled, HMF and impurities associated with the synthetic mixture tend to form tarry degradation products. Because of this heat instability, a falling film vacuum still must be used. Even in such an apparatus, resinous solids form on the heating surface causing a stalling in the rotor and frequent shut down time making the operation inefficient. Prior work has been performed with distillation and the addition of a non-volatile solvent like PEG-600 to prevent the buildup of solid humin polymers (Cope, U.S. Pat. No. 2,917,520). Unfortunately, the use of polyglycols leads to the formation of HMF-PEG ethers.

[0013] The prior art processes also fail to provide a method for producing HMF that can be performed economically. For example, Besemer et al *Netherlands Organ. Appl. Sci. Res. Nutr. Food Res.,* describes the enzymatic synthesis of HMF esters. This process requires the use of expensive enzymes and therefore does not provide an economically feasible route to synthesizing HMF esters.

[0014] Garber et al., Canadian Patent 6 54240, describe the synthesis of the 2,5-tetrahydrofurandimethanol monoesters from HMF using excess amounts of anhydride and pyridine solvent. Reduction is performed using Raney Ni catalyst in diethyl ether. However the reference does not disclose the synthesis of HMF esters from fructose or using a carboxylic acid. Furthermore, the removal of Raney Ni catalyst is dangerous and the costs of disposing the catalyst may be burdensome.

[0015] The present disclosure, which is directed, in-part, to chromatographic processes for the synthesis and recovery of HMF from natural resources addresses and eliminates these problems and provides high purity products. In addition to HMF, studies have broadened to include the synthesis and purification of a variety of HMF derivatives. Derivatives of particular interest include the esters of HMF, and oxidized forms (2,5-diformylfuran, 2,5-furandicarboxylic acid and acid ester), and the reduced forms (furan-2,5-dimethanol and tetrahydrofuran diol) of HMF. The esters are more stable and can be readily separated, potentially making them even more useful than HMF itself.

SUMMARY OF THE DISCLOSURE

[0016] In order to address the above mentioned problems, the disclosure provides a method of producing substantially pure HMF, HMF esters or HMF ethers from a carbohydrate source by contacting the carbohydrate source with a solid phase catalyst. In the present disclosure substantially pure means a purity of HMF of about 70% or greater, optionally about 80% or greater, or about 90% or greater.

[0017] The disclosure also provides a method of producing HMF esters from a carbohydrate source and organic acids. In one embodiment, a carbohydrate starting material is heated with an solvent in a column and continuously flowed through a solid phase catalyst in the presence of an organic acid to form a HMF ester. The solvent is removed by rotary evaporation to provide a substantially pure HMF ester. In another embodiment, a carbohydrate is heated with the organic acid and a solid catalyst in a solution to form an HMF ester. The resulting HMF ester may then be purified by filtration, evaporation, extraction, and distillation or any combination thereof.

[0018] In another embodiment, there is provided a method for oxidizing an HMF ester to 2,5-furandicarboxylic acid (FDCA) by combining the HMF ester with an organic acid, cobalt acetate, manganese acetate and sodium bromide under pressure and to obtain substantially pure FDCA after filtration and evaporation.

[0019] In another embodiment, there is provided a method of oxidizing a reaction mixture of HMF and HMF ester to FDCA by the addition of cobalt acetate, manganese acetate, and sodium bromide under pressure and heat and isolating FDCA following filtration and evaporation.

[0020] In an alternative embodiment, there is provided a method of reducing an HMF ester by the addition of an alcohol, such as ethanol, a reducing agent, under pressure, heat, filtration and evaporation.

[0021] Advantages of the methods as described herein are the high rate of conversion of carbohydrates into HMF-esters and derivatives. This results in a more stable form for HMF, and a lower cost in materials.

[0022] In another embodiment, there is provided a method for producing citrate esters from a citric acid source and an alcohol. Citric acid is esterified with an alcohol in the presence of a catalyst on a chromatography column to produce trialkyl citrate or mono- and di-esters of the citric acid. In an alternative embodiment, a fermentation broth containing primarily citric acid and residual microorganisms and fermentation side products is used to produce trialkyl citrate or mono- and di-esters of the citric acid. In another embodiment, the mono- and di-esters are recycled through the catalyst and column to generate the triester.

[0023] In yet an another embodiment, there is provided a method of preparing HMF via deacylation of an intermediate HMF ester. In one embodiment of this method, fructose is dehydrated in the presence of an organic acid and a catalyst, and separated via a chromatography column to produce the HMF ester. In an alternative embodiment, the HMF ester is deacylated with a solid phase catalyst in a chromatography column. Alternatively, the deacylation and separation of the HMF ester is performed using a metal alkoxide.

[0024] In another embodiment, there is provided a method for the synthesis of levulinic acid or levulinic ester by con-

tacting a carbohydrate mixture with or without an organic acid present, with a solid phase catalyst under elevated temperature. HMF ethers and/or levulinate esters, which are more stable than HMF may be synthesized and purified by this process using an alcohol solvent. Advantages of the methods as described herein are the high rate of conversion of carbohydrates into substantially pure HMF, HMF esters and other HMF derivatives.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] FIG. **1** illustrates a conventional autoclave reactor;

[0026] FIG. **2** illustrates the fraction of AcHMF conversion in a conventional method using an autoclave reactor;

[0027] FIG. **3** illustrates the fraction of AcHMF conversion according to an embodiment of the present application;

[0028] FIG. **4** illustrates a graph of the products using the pulse resin test according to an embodiment of the present application; and

[0029] FIG. **5** illustrates a chromatogram according to an embodiment of the present application.

[0030] FIG. **6** is a ^{1}H NMR analysis graph showing substantially pure 4-acetoxymethylfurfural (AcHMF).

[0031] FIG. **7** is a ^{1}H NMR analysis graph showing substantially pure 5-propionoxymethylfurfual.

[0032] FIG. **8** is a ^{1}H NMR analysis graph showing substantially pure 2,5-diformylfuran, 2,5-furandicarboxylic acid (FDCA).

[0033] FIG. **9** is a HPLC trace showing the formation of 5-acetoxymethylfurfual (AcHMF) from fructose according to Example 1.

[0034] FIG. **10** is a HPLC trace showing the formation of 5-acetoxymethylfurfual (AcHMF) from fructose according to Example 2.

[0035] FIG. **11** is a HPLC trace showing the formation of showing substantially pure 5-propionoxymethylfurfual (PrHMF) from fructose.

DETAILED DESCRIPTION

[0036] The present application provides methods for synthesizing and separating hydroxymethylfurfural (HMF) and hydroxymethylfurfural esters from a carbohydrate source by contacting the carbohydrate with a solid phase catalyst.

[0037] The use of solid phase catalysts in a chromatography column to synthesize and purify HMF limits exposure time to heat and acid catalysts and enables synthesis at a lower temperature. Lower temperatures result in reduced energy costs and reduced time for heating and cooling the reaction. Non-limiting examples of solid phase catalysts that may be used in the process include acidic resins such as Amberlyst 35, Amberlyst 15, Amberlyst 36, Amberlyst 70, Amberlyst 131 (Rohm and Haas); Lewatit S2328, Lewatit K2431, Lewatit S2568, Lewatit K2629 (Bayer Company); and Dianion SK104, PK228, RCP160, Relite RAD/F (Mitsubishi Chemical America, Inc.). Other solid phase catalysts such as clays and zeolites such as CBV 3024 and CBV 5534G (Zeolyst International), T-2665, T-4480 (United Catalysis, Inc), LZY 64 (Union Carbide), H-ZSM-5 (PQ Corporation) can also be used. Acidic resins such as Amberlyst 35 are cationic, while catalysts such as zeolite, alumina, and clay are porous particles that trap small molecules. Soluble catalysts including inorganic acids, such as H_2SO_4, H_3PO_4, HCl, and organic acids such as p-toluene sulfonic acid may also be used.

[0038] An advantage of solid phase catalysts is that they do not dissolve in solvent and remain in the column. Depending on the column size and type of solvent used, about 30-50 g of resin is packed into the column. For example, the solvent dimethylformamide (DMF) causes Amberlyst 35 resin to expand in the column, and thus only about 30 g of resin is preferably used in a 300 mm length column. Approximately 50 g of Amberlyst 35 resin is used when acetic acid is the solvent because acetic acid does not cause the resin to swell.

[0039] Because the synthesis of HMF is a dehydration reaction, a cation exchange resin having reduced water content is preferred. The presence of water in the reaction increases formation of byproducts, such as, polymers and humin. Therefore, the maximum water content of the solid phase catalyst in a column experiment is typically less than about 20%, optionally less than about 15%, or less than about 10%. Many commercially available solid phase catalysts, such as, dry Amberlyst 35 have approximately 3% water content. However, solid phase catalysts with greater than 20% may be used under certain conditions. Solid phase catalysts having a water content greater than about 20% are considered "wet resins" due to their excess water content and ability to generate water during the reaction. If the water content of the wet resin is greater than about 20%, a solvent that is miscible with water may be selected as the solvent for the reaction in order to remove water from the wet resin.

[0040] Solvents including aprotic polar solvents are preferred because they are miscible with water, which helps with the solubility of fructose and with removing water. An example of an polar aprotic solvent is acetone, which is used to wash the wet resin and dehydrate the wet resin before the reaction on the column. The resulting dehydrated resin is then dried under a vacuum prior to the reaction on the column. In addition, DMF is miscible with water and may be used as a solvent to dehydrate the wet resin on the column. The dehydration of the wet resin may include raising the temperature of the reaction or any suitable method for dehydrating the wet resin or a combination thereof.

[0041] An additional advantage of using a column in the conversion of a carbohydrate source to HMF, HMF esters or other HMF derivatives is the ability for the reaction to proceed and separate the product from the unreacted starting material or other unwanted side products that may form all in one step. As the reactants pass through the column, differences in the retention of the products from the starting materials will allow for these to separate after the reaction occurs in the column. As a result, the product will elute from the column in a substantially pure form.

[0042] Any carbohydrate source can be used, although fructose is the preferred source. Suitable carbohydrate sources that can be used for preparing HMF derivatives include, but are not limited to, hexose, fructose syrup, crystalline fructose, and process streams from the crystallization of fructose. Suitable mixed carbohydrate sources may comprise any industrially convenient carbohydrate source, such as corn syrup. Other mixed carbohydrate sources include, but are not limited to, hexoses, fructose syrup, crystalline fructose, high fructose corn syrup, crude fructose, purified fructose, high fructose corn syrup refinery intermediates and by-products, process streams from crystallizing fructose or glucose or xylose, and molasses, such as soy molasses resulting from production of soy protein concentrate, or a mixture thereof.

[0043] Synthesis of HMF esters from a carbohydrate source and organic acids or acid salts provides a direct pathway for a series of useful molecules. Aliphatic and aromatic esters of HMF are commercially available and have a variety of uses. The present process has many advantages in the production of HMF esters. Suitable carbohydrate sources that can be used for preparing HMF esters include, but are not limited to hexose, fructose syrup, crystalline fructose, and process streams from the crystallization of fructose. Suitable mixed carbohydrate sources may comprise any industrially convenient carbohydrate sources, such as corn syrup. The mixed carbohydrate sources include, but are not limited to, hexoses, fructose syrup, crystalline fructose, high fructose corn syrup, crude fructose, purified fructose, high fructose corn syrup refinery intermediates and by-products, process streams from crystallizing fructose or glucose or xylose, and molasses, such as soy molasses resulting from production of soy protein concentrate. In addition to the wide variety of starting sources, the process can be performed with various organic acids including, but not limited to acetic, propionic, butyric, citric or diacids.

[0044] The disclosed process minimizes and/or eliminates the formation of humins and polymeric by-products. If the reaction is not complete and HMF and or unreacted carbohydrate is observed in the reaction mixture, these components may be separated into the aqueous phase and recycled. In addition, the solvents can be recovered and recycled. This method is more beneficial than other methods as it eliminates the difficult task of isolating substantially pure HMF for use as a starting source. It is a simple process, leading to a substantially pure product, which can be used as a feeding source in the transformation of HMF esters to a variety of useful derivatives and end products. The purity of the product will vary according to the particular reagents and conditions used.

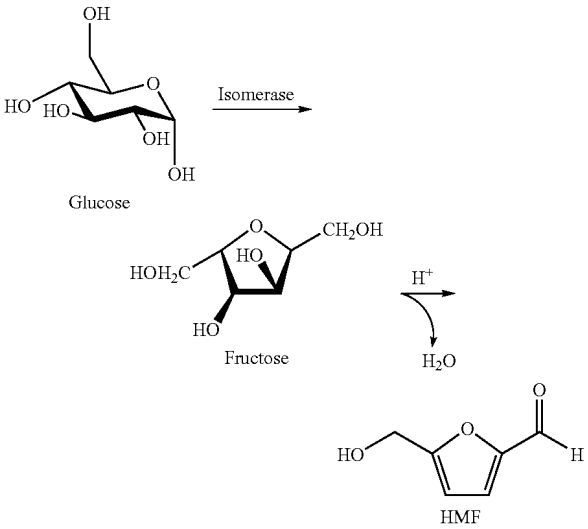
[0045] Additionally, the present application provides methods for synthesizing citrate esters, and methods of synthesizing levulinic acid or levulinic esters using a heated solid phase catalyst in a column, and subsequent purification of the resulting products in a column. In an example of levulinate ester synthesis, a carbohydrate mixture in solution (e.g. 25% fructose in Acetic acid) is passed through a heated column that is packed with a strong acid cationic resin (e.g. Amberlyst 35). The temperature of the column is maintained at 75 C and the flow rate is set to 5 mL/min. Upon the initial pass both Ac-HMF and Ac-levulinate acid are formed. Subsequent passes generate a higher ratio of Ac-levulinate to Ac-HMF. The concentration of acetic acid may range from >99% reagent grade acetic acid to 1% acetic acid in aqueous solution.

[0046] For the synthesis of a levulinic acid, an example synthesis involves a carbohydrate mixture in solution (e.g. 25% fructose in aqueous or DMF solution) is passed through a heated column that is packed with a strong acid cationic resin (e.g. Amberlyst 35). The temperature of the column is maintained at 100° C. and the flow rate is set to 5 mL/min. Upon the initial pass both HMF and levulinic acid are formed. Subsequent passes generate a higher ratio of levulinic acid to HMF.

[0047] Various HMF esters are selectively prepared by modifying the choice of solvent used in the processes of the invention. The amount of purification and fractionation of the end product depends on the type of solvent used. For example, a continuous flow of a solution of fructose dissolved in acetic acid through a solid phase catalyst results in the formation of substantially pure acetylated HMF (AcHMF), which is a desired end product. HMF ethers and/or levulinate esters, which are more stable than HMF may be synthesized and purified by this process using an alcohol solvent.

[0048] AcHMF has a lower boiling point than HMF, and is isolated by vacuum distillation. AcHMF is also more stable than HMF. AcHMF is not appreciably soluble in water making extraction in a nonpolar organic solvents an effective method of purification. AcHMF crystallizes in nonpolar solvents at low temperatures (e.g., hexanes around 0-25° C.). Moreover, HMF decomposes upon heating and produces by-products that are not easily isolated or removed.

Synthesis of HMF from glucose and fructose



[0049] For one embodiment of the present disclosure, the set up of the chromatography column including a column packed with solid phase catalysts may be a continuous separation where the fructose, HMF, and solvent are fed through the packed column multiple times and/or the speed of additional reactants is varied. This purification technique can include Simulated Moving Bed chromatography, which is a chromatographic technique based on a flow of liquid (mobile phase) moving countercurrent to a constant flow of solid (stationary phase). Countercurrent flow enhances the potential for separation and, hence, makes the process more efficient. It also allows a continuous flow of feed material to be separated, and utilizes less solvent and improves the throughput of the equipment compared to traditional batch chromatography. Alternatively, the system may include, but is not limited to, a simulated moving bed, continuous set up (CSEP), or a continuous flow pipe system.

[0050] For example, in Simulated Moving Bed chromatography, the solutes move faster than the bed and are eluted at the top of the column, whereas those moving slower than the bed are brought down by the moving bed below the feed point. A section of the bed below the feed point is then heated to increase the elution rate of the solutes and any solute moving faster than the bed can be eluted through a side tube by a second flow of gas while those solutes still moving at a slower rate than the bed continue to move down the column in the stationary phase. The higher fractions can be removed in the same way by a section of the column heated to an even higher

temperature. In order to heat the column in Simulated Moving Bed chromatography, a jacketed column allows the mixture to pass heating fluid, such as, propylene glycol, around the resin bed.

[0051] In most of the reactions carried out by the methods described herein, the catalyst provides the necessary acidity for the reaction to occur. Ion exchange resins are synthetic polymers capable of combining or exchanging ions in a surrounding solution and are used primarily for chromatography of organic molecules. Advantages of ion exchange resins include long lifetime, reusable, high selectivity and catalytic ability, stability, and can be used in both aqueous and non-aqueous conditions (Rohm and Haas).

[0052] A first type of column that may be used in the disclosed methods is a gravity flow column. The reaction mixture is loaded onto the top of the column, which is heated by a jacket, then allowed to slowly flow through the resin, allowing maximum retention time on the column. The flow rate in a gravity flow column is generally less than 1.0 mL/min, or typically 0.1-1.0 mL/min. Once the product is fed through the column, it may be reloaded for a second pass, to produce a higher yield of the desired product and increased purity by allowing more time on the resin. The samples of the gravity column are collected in a large fraction or multiple fractions and analyzed for yield.

[0053] Another column that may be used is a pulse column. The starting material is loaded on top of the resin and a mechanical pump is used to pump solvent onto the column to maintain a constant flow rate. The product is collected from the bottom of the column in timed fractions, and, therefore, may be analyzed for retention time, separation of products and reactants, as well as total yield.

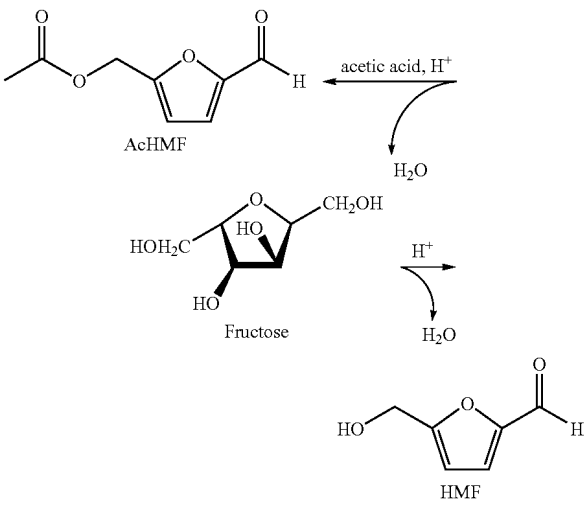
[0054] For the column experiments, depending on the type of column used and the stability of the solvent, the temperature may be varied from about 70° C. to about 125° C., optionally from about 75° C. to about 95° C., or optionally from about 80° C. to about 90° C. The flow rate is typically kept at about 1.0 ml/minute to allow maximum retention time on the column and flow through to the top of the column. However, for gravity columns, the flow rate may be kept lower, since it is not dependent on a mechanical source. Higher temperatures may be used.

[0055] In one embodiment of the present application, Amberlyst 35 is packed in a heated glass jacketed column with fructose solubilized with acetic acid. The use of a continuous moving bed minimizes exposure time of the product to resin since it passes through the column by stream, rather than batch. The resulting product is highly purified acetyl HMF.

[0056] In another embodiment of the invention, a continuous flow process enables the formation of citrate esters. The starting material, citric acid may be in solution with the solvent or in a fermentation broth containing solvent. An alcohol solvent is used to obtain either substantially pure trialkyl citrate or the mono- and di-esters of citric acid. Factors such as type of solvent, type of resin, time on column, and/or temperature determine whether mono- and di-esters are formed or whether substantially pure trialkyl citrate is formed. If mono- and di-esters are obtained, the mixture can be recycled in the column to generate the substantially pure triester.

[0057] Another aspect of this invention allows for the chromatographic synthesis, separation, and purification of an anhydrosugar alcohol from a selected sugar alcohol or monoanhydrosugar alcohol starting material using a solid phase catalyst. More specifically, isosorbide is synthesized, separated, and purified from a sorbitol source and a solid phase catalyst in a chromatography column. The intermediate compound, sorbitan, or mixtures of sorbitan/isosorbide/sorbitol can be recovered and recycled until substantially pure isosorbide is obtained.

Synthesis of HMF from AcHMF and Fructose

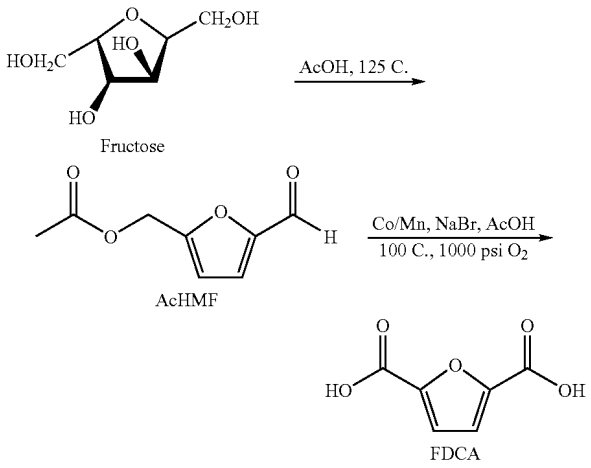


[0058] In another aspect of the invention, there is provided a process for preparing HMF via an intermediate HMF ester. Fructose is preferably used as a carbohydrate source and is subjected to dehydration in the presence of an organic acid and catalyst in a chromatography column to provide a HMF ester. The HMF ester is then subjected to deacylation upon treatment with a base. The basic material may include, but is not limited to, a solid phase catalyst such as resins, clays, aluminas, and zeolites. The saponification of the ester can be carried out in any manner, so long as it can bring the starting material and basic catalyst are brought into mutual contact. For example, this reaction can be carried out batchwise or continuously in a fluidized bed, tubular reactor, coil, column, or pipe. Deacylation of AcHMF to HMF can also be achieved using a metal alkoxide. This method may be preferable due to the fact that HMF esters are generally more stable than HMF.

[0059] In another embodiment of forming a HMF ester, a carbohydrate is combined with an organic acid and solid phase catalyst in solution. The solution is heated to a temperature between about 100 to about 140° C., for between about 90 to about 150 minutes, resulting in the formation of an HMF ester. The HMF ester can be further purified via column chromatography, precipitation and recrystallization or combinations thereof. The synthesized HMF ester is filtered and/or evaporated, e.g., via rotary evaporation to remove the catalyst and organic acid. HMF ester can be collected by extraction with methyl t-butyl ether. The crude material can be subjected to simple distillation (115° C., 3 torr) to provide the HMF ester as crystals. Alternatively, the filtered HMF ester may then be extracted with a suitable solvent, such as hot hexane, after the evaporation of the solvent.

[0060] In one embodiment for the forming of FDCA, a reaction mixture containing a HMF ester such as, but not

limited to, 5-acetoxymethylfurfural (AcHMF), or organic acid such as, but not limited to, acetic acid, along with cobalt acetate, manganese acetate and sodium bromide is placed in a reactor and subjected to between about 400 to about 1000 psi, or between about 500 to about 800 psi oxygen at between about 85° C. to about 110° C., or between at about 100° C. for between about 100 to about 150 minutes. The solution is then filtered and the solvent evaporated to obtain 2,5-Furandicarboxylic acid (FDCA).



[0061] In an embodiment for reducing an HMF ester, a reaction mixture containing AcHMF and ethanol is charged in a reaction vessel. The G-69B catalyst obtained from Sud Chemie, Louisville, Ky. is added to the vessel and the vessel is purged with hydrogen, preferably at 4×500 psi with stirring, preferably at 1000 rpm. The vessel is then pressurized, preferably to 600 psi and heated to a temperature above 150° C., preferably to 170° C. with continual stirring. After about an hour the reaction is heated to 195° C. for about an hour and then allowed to cool to room temperature. The catalyst is then removed via vacuum filtration. The solvent is preferably removed, for example, by rotary evaporation. Products of reduction include but are not limited to 2,5-furandimethanol (FDM) and tetrahydrofuran diol (THF-diol).

[0062] As an example of the versatility of the HMF-esters, a reaction mixture containing a combination of HMF and an HMF-ester can be oxidized to the single product, FDCA. 2,5-Furandicarboxylic acid (FDCA) is formed from a mixture of predominantly HMF ester with residual HMF in an organic acid. The mixture is reacted in an organic acid, for example acetic acid along with cobalt acetate, manganese acetate and sodium bromide. The entire mixture can be pressurized with oxygen or air and heated to at least 100° C. for over an hour. The resulting solution is filtered and evaporated and the FDCA is isolated.

[0063] HMF can be synthesized from a fructose source through and HMF ester intermediate. For example, fructose is subjected to dehydration in the presence of an organic acid and catalyst to provide an HMF ester. The HMF ester is subjected to deacylation upon treatment with a base. The basic material may include, but is not limited to, a solid phase catalyst such as resins, clays, aluminas, and zeolites. The saponification of the ester can be carried out in any manner, so long as it can bring the material and basic catalyst into mutual contact. For example, this reaction can be carried out batchwise or continuously in a fluidized bed, tubular reactor, coil, column, or pipe. Deacylation of AcHMF to HMF can also be achieved using a metal alkoxide.

EXAMPLES

Example 1

[0064] The conventional method for synthesizing HMF and AcHMF from fructose includes a batch reaction on an autoclave (Parr) reactor followed by a separate step for purification. As shown in FIG. **1**, the temperature control **2** controls both the temperature of the reaction mixture and the heating jacket in the autoclave reactor **1**. A heating jacket (not shown) is used to heat the reaction. The pressure gauge **3** shows if the reaction is creating gas, or monitors the pressure on the vessel if it was applied. The speed control **4** is for the stirring mechanism. Stirring is necessary to keep the reaction mixture in contact with all necessary materials. The sample port **5** allows the scientist to retrieve samples and specific points during the reaction to monitor for progress. Reactants must be in solution before being put into a reactor vessel.

[0065] The reaction conditions for the autoclave reactions were varied to test the effect of different reaction conditions. The reactions were performed in the 100 mL capacity Parr reactor. About 20 grams of High fructose corn syrup (HFCS) is added to each reaction. Three different temperatures: 110°, 125°, and 150° Celsius were tested with and without an ion exchange resin. The resin of choice was Amberlyst 35 exchange. Results are shown in Table 1.

TABLE 1

	Comparative Example				
	#1	#2	#3	#4	#5
Temperature (° C.)	110	125	125	150	150
Resin	yes	no	Yes	yes	No
Fructose added (g)	5.6998	5.7995	6.7799	6.7799	6.7799
Moles	.03164	0.0322	0.0376	0.0376	0.0376
Fructose out (g)	0.62	0.64	1.34	0.55	2.07
Moles	0.0034	0.00354	0.0074	0.0030	0.0115
HMF out (g)	2.13	1.22	1.60	1.48	0.79
Moles	0.0169	0.0097	0.0127	0.0118	0.0063
AcHMF out (g)	0.18	0.54	0.49	1.48	0.13
Moles	0.001053	0.0033	0.0029	0.0088	0.0007
HFCS added (g)	20	20.35	23.79	23.79	23.79
Fructose added (g)	5.6998	5.7995	6.7799	6.7799	6.7800
AcHMF yield	0.0332	0.1000	0.0764	0.2331	0.0197
HMF yield	0.5348	0.3005	0.3378	0.3125	0.1663
Fructose yield	0.1080	0.1101	0.1974	0.0812	0.3048

[0066] As can be seen in Table 1 above, AcHMF was formed in the largest amount in Comparative Example #4 at 150° C. using a resin in an autoclave reactor as shown in FIG. **2**. In a 100 mL capacity Parr reactor, 6.7799 g of fructose and 23.79 g of HFCS in solution was heated to 150° C. The AcHMF yield was 0.2331 in Comparative Example #4.

[0067] In these examples of Example 1, a first method of production of substantially pure HMF uses packed columns. Two different types of columns were used to produce and purify HMF. Each column, however, was packed with a cation exchange resin, which had been soaked in the desired solvent, then loaded to a heated column once the resin had appropriately expanded. A cation exchange resin is an ion exchange resin that adds protons to the reaction. The water content of the resin used ranged from less than about 20%, to less than about 10% in order to prevent the rehydration of HMF. The results of the columns are shown in FIG. **3**. The major product was HMF with the remainder being unreacted fructose. In this example, the Amberlyst 35 exchange resin performed best of all columns tested, including the gravity flow columns.

[0068] Maximal reaction conditions included 80° C. in a column packed with the Amberlyst 35 ion exchange resin and acetic acid, providing a yield of AcHMF is approximately 0.395 moles. Columns performed more consistently than the conventional batch reactions, which may be due to a number of reasons. Product stays longer on the resin in a chromatography column, and a larger amount of the resin remains in the column than in the batch reactions. There is also better control of the temperature in the column due to the heated jacketed column.

[0069] Samples marked with (*) in Table 2 are comparative examples. The comparative examples include batch reactions. The temperatures in the autoclave varied from approximately 105° C.-155° C. in the course of the reaction. The reaction mixture from the columns could also be fed back through for another pass, which will further increase the yield of the desired product. The yield is lower during a batch reaction when it is run at a higher temperature, such as 125° C., compared to a pulse reaction at 80° C. and a gravity column reaction at 90° C. The yield in the batch reaction using Amberlyst 35 having a temperature of 150° C. is increased due to the high temperature.

TABLE 2

Type of Reaction	Temperature (° C.)	Type of Resin (if used)	AcHMF yield
Pulse	80	Amberlyst 35	0.394914426
Gravity Column	90	Amberlyst 35	0.117696633
Gravity Column	90	Amberlyst 35	0.130347712
Batch Reaction*	110	Amberlyst 35	0.033283962
Batch Reaction*	125	No resin	0.100020489
Batch Reaction*	125	Amberlyst 35	0.076392506
Batch Reaction*	150	Amberlyst 35	0.233076043
Batch Reaction*	150	No resin	0.019697

Example 2

[0070] The graph shown in FIG. **4** illustrates the results of the pulse resin test at 80° C. where the flow rate was set at about 1.48 mL/min. for the first 33 minutes and about 1.36 mL/min. after the 33rd minute until completion of the reaction at about 63 minutes. After approximately 30 minutes, 0.07 moles of AcHMF was eluted, compared to a mole fraction of approximately 0.0006 for the starting material, fructose. The byproducts, levulinic and formic acids, are also measured. No measurable levulinic acid was found during the synthesis of AcHMF.

TABLE 3

Time (min.)	Sample weight (g)	Percent water in sample	Fraction of water in sample	Weight of water in sample (g)	moles of water in sample
1	0.5060	2.28	0.0228	0.0115368	0.000640364
9	0.5189	1.39	0.0139	0.00721271	0.00040035
12	0.5059	1.44	0.0144	0.00728496	0.000404361
15	0.4982	1.30	0.0130	0.0064766	0.000359492
18	0.5071	1.26	0.0126	0.00638946	0.000354655
21	0.5062	1.24	0.0124	0.00627688	0.000348406
24	0.4122	1.40	0.0140	0.0057708	0.000320315
27	0.4782	1.46	0.0146	0.00698172	0.000387529
30	0.5051	1.37	0.0137	0.00691987	0.000384096
33	0.5005	1.34	0.0134	0.0067067	0.000372264
50	0.5065	1.16	0.0116	0.0058754	0.000326121
63	0.5105	1.95	0.0195	0.00995475	0.000552551

Time (min.)	Sample weight (g)	HMF in sample (g/kg)	Fraction of HMF in sample	Weight of HMF in sample (g)	moles of HMF in sample
1	0.5060	0.00	0.00000	0	0
9	0.5189	0.00	0.00000	0	0
12	0.5059	1.49	0.00149	0.000752273	5.96514E−06
15	0.4982	0.23	0.00023	0.000116081	9.20459E−07
18	0.5071	0.28	0.00028	0.000143002	1.13393E−06
21	0.5062	0.12	0.00012	5.87192E−05	4.65613E−07
24	0.4122	0.27	0.00027	0.000109233	8.66161E−07
27	0.4782	0.25	0.00025	0.000117159	9.2901E−07
30	0.5051	0.28	0.00028	0.000141933	1.12546E−06
33	0.5005	0.36	0.00036	0.000181682	1.44064E−06
50	0.5065	0.00	0.00000	0	0
63	0.5105	0.00	0.00000	0	0

TABLE 3-continued

Time (min.)	Sample weight (g)	Acetic Acid in sample (g/kg)	Fraction of Acetic Acid in sample	Weight of Acetic Acid in sample (g)	moles of Acetic Acid in sample
1	0.5060	960.17	0.9602	0.48584349	0.008090326
9	0.5189	967.75	0.9678	0.502167551	0.008362156
12	0.5059	896.88	0.8969	0.453733616	0.007555628
15	0.4982	924.96	0.9250	0.460815072	0.00767355
18	0.5071	907.85	0.9078	0.460369214	0.007666125
21	0.5062	846.98	0.8470	0.428742288	0.00713947
24	0.4122	871.93	0.8719	0.359409958	0.005984939
27	0.4782	880.87	0.8809	0.421230121	0.007014376
30	0.5051	876.47	0.8765	0.442705502	0.007371987
33	0.5005	857.03	0.8570	0.428941013	0.007142779
50	0.5065	903.94	0.9039	0.45784713	0.007624127
63	0.5105	980.54	0.9805	0.50056567	0.008335482

Time (min.)	Sample weight (g)	Fructose in sample (g/kg)	Fraction of Fructose in sample	Weight of Fructose in sample (g)	moles of Fructose in sample
1	0.5060	0.00	0.0000	0	0
9	0.5189	0.04	0.0000	1.91993E−05	1.0657E−07
12	0.5059	0.17	0.0002	8.54971E−05	4.74569E−07
15	0.4982	0.12	0.0001	6.02822E−05	3.34609E−07
18	0.5071	0.00	0.0000	1.5213E−06	8.44429E−09
21	0.5062	0.18	0.0002	9.26346E−05	5.14188E−07
24	0.4122	0.45	0.0004	0.000184666	1.02502E−06
27	0.4782	0.28	0.0003	0.000132461	7.35255E−07
30	0.5051	0.64	0.0006	0.000323264	1.79434E−06
33	0.5005	1.03	0.0010	0.000513513	2.85036E−06
50	0.5065	0.30	0.0003	0.00015195	8.4343E−07
63	0.5105	0.00	0.0000	0	0

Time (min.)	Sample weight (g)	Formic in sample (g/kg)	Fraction of Formic in ample	Weight of Formic in sample (g)	moles of Formic in sample
1	0.5060	0.69	0.0007	0.000351164	7.62975E−06
9	0.5189	0.64	0.0006	0.000331577	7.20419E−06
12	0.5059	0.75	0.0007	0.000377401	8.19981E−06
15	0.4982	1.28	0.0013	0.0006367	1.38336E−05
18	0.5071	4.05	0.0040	0.00205122	4.45669E−05
21	0.5062	2.56	0.0026	0.001296884	2.81775E−05
24	0.4122	3.16	0.0032	0.001301728	2.82827E−05
27	0.4782	3.39	0.0034	0.001621098	3.52217E−05
30	0.5051	6.29	0.0063	0.003175564	6.89956E−05
33	0.5005	6.45	0.0065	0.003229727	7.01724E−05
50	0.5065	1.74	0.0017	0.00088283	1.91813E−05
63	0.5105	0.70	0.0007	0.000354798	7.7087E−06

Time (min.)	Sample weight (g)	Levulinic in sample (g/kg)	Fraction of Levulinic in sample	Weight of Levulinic in sample (g)	moles of Levulinic in sample
1	0.5060	0.00	0.0000000	0	0
9	0.5189	0.00	0.0000000	0	0
12	0.5059	0.00	0.0000000	0	0
15	0.4982	0.00	0.0000000	0	0
18	0.5071	0.00	0.0000000	0	0
21	0.5062	0.00	0.0000000	0	0
24	0.4122	0.00	0.0000000	0	0
27	0.4782	0.00	0.0000000	0	0
30	0.5051	0.00	0.0000000	0	0
33	0.5005	0.00	0.0000000	0	0
50	0.5065	0.00	0.0000000	0	0
63	0.5105	0.00	0.0000000	0	0

Time (min.)	Sample weight (g)	AcHMF in sample (g/kg)	Fraction of AcHMF in sample	Weight of AcHMF in sample (g)	moles of AcHMF in sample
1	0.5060	0.00	0.0000000	0	0
9	0.5189	0.22	0.0002200	0.000114158	6.75092E−07
12	0.5059	5.01	0.0050070	0.002533041	1.49795E−05
15	0.4982	15.21	0.0152050	0.007575131	4.47968E−05
18	0.5071	22.98	0.0229820	0.011654172	6.89188E−05
21	0.5062	27.97	0.0279720	0.014159426	8.3734E−05
24	0.4122	31.95	0.0319470	0.013168553	7.78744E−05
27	0.4782	36.23	0.0362280	0.01732423	0.00010245
30	0.5051	37.00	0.0370010	0.018689205	0.000110522

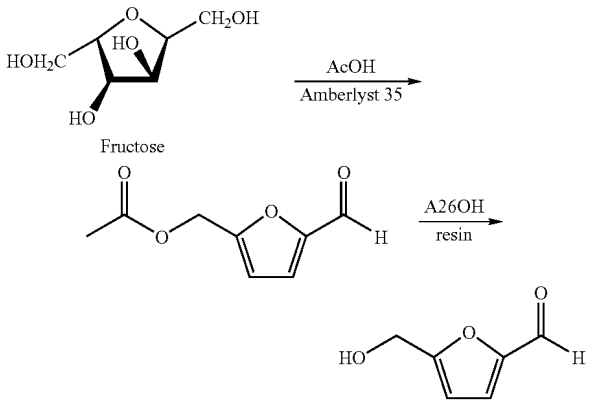
TABLE 3-continued

33	0.5005	36.52	0.0365190	0.01827776	0.000108088
50	0.5065	0.35	0.0003540	0.000179301	1.06033E-06
63	0.5105	0.00	0.0000000	0	0

Example 3

Preparation of HMF from Fructose Using a HMF Ester Intermediate

[0071] This example illustrates the use of the present methods to deprotect HMF ester to provide substantially pure HMF. The feed material was prepared and placed in a vial of methanol and Amberlyst A26OH resin obtained from Rohm and Haas Company (Woodridge, Ill.). Amberlyst A26OH resin is a strong base, type 1, anionic, macroreticular polymeric resin based on crosslinked styrene divinylbenzene copolymer containing quaternary ammonium groups. After sitting at room temperature for about 5 minutes, the material was analyzed by thin layer chromatography (tlc) to show deacylation. The solid yield was about 85% HMF with about 8% AcHMF determined by a Shimadzu QP-2010 GC Mass spectrometer. The chromatogram is shown in FIG. **5**. The remaining material was residual methanol. Heating the methanol solution with a heat gun to 60° C. for less than 5 minutes converted the remaining AcHMF to HMF. Alternatively, passing the product through the chromatography column with a solid phase catalyst would convert the remaining AcHMF to HMF.



Example 4

Preparation of 5-Acetoxymethylfurfural (ACHMF) from Fructose

[0072] Crystalline fructose (18 g) is placed in a 100 mL reaction vessel with acetic acid (50 g) and Amberlyst 15 resin (4 g). The solution is heated to 110° C. for 3 hours with samples collected regularly. Analytical results and HPLC trace confirm the formation of AcHMF. Analysis of the product mixture indicated a solution of 9.89% AcHMF and 5.14% HMF for a 41% yield of AcHMF and 28% yield of HMF. The yields disclosed herein are exemplary only and do not necessarily reflect the optimal yields possible when reaction conditions are optimized. HPLC trace confirmed formation of AcHMF, (see FIG. **4**).

Example 5

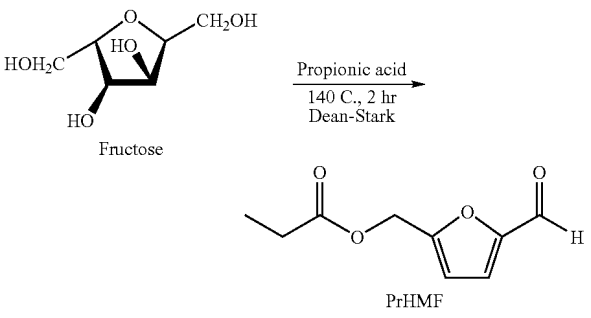
Synthesis and Purification of AcHMF from Fructose

[0073] Crystalline fructose (180 g) is placed in a 1 L reaction vessel with acetic acid (500 g) and Amberlyst 15 resin (40 g). The solution is heated to 125° C. for 2 hours. NMR and analytical results indicates the formation of AcHMF. The solution is filtered to remove the resin catalyst and acetic acid is removed by rotary evaporation. AcHMF is collected by extraction with methyl t-butyl ether. The crude material is subjected to simple distillation (115° C., 3 torr) to provide AcHMF as orange crystals. HPLC trace confirms AcHMF formation, (see FIG. **5**), and ^{1}H NMR analysis indicates substantially pure AcHMF. NMR (δ, 1 H): 9.70 (s, 1.0 H); 7.40 (s, 1.0 H); 6.80 (s, 1.0 H); 5.10 (s, 2.0 H); 2.10 (s, 3.0H). See FIG. **1**.

Example 6

Synthesis of Propionoxymethylfurfural (PrHMF) from Fructose

[0074] Crystalline fructose (40 g), propionic acid (100 mL), and dry Amberlyst 15 resin is placed in a 500 mL three neck round bottom flask equipped with a Dean-Stark trap, magnetic stir bar, and temperature probe. The reaction mixture is allowed to heat to 130° C. for 30 minutes. HPLC trace indicates rapid conversion to the HMF ester. Resin is removed by filtration, the solvent evaporated and the crude oil is extracted with hot hexane. Evaporation of the hexane extract provides yellow oil which ^{1}H NMR identified as substantially pure 5-propionoxymethylfurfural. Calculations indicate the overall yield of PrHMF from fructose is 28%. Reaction conditions have not been optimized. HPLC trace confirms PrHMF formation, (see FIG. **6**) and ^{1}H NMR analysis indicates PrHMF formation (δ, 1 H): 9.70 (s, 1.0 H); 7.20 (s, 1.0 H); 6.60 (s, 1.0 H); 5.06 (s, 2.0 H); 2.47 (t, 2.0 H); 1.05 (d, 3.0H). See FIG. **2**.



Example 7

Oxidation of 5-Acetoxymethylfurfural (AcHMF) to 2,5-Furandicarboxylic Acid (FDCA)

[0075] A reaction mixture containing AcHMF (5.0 g), acetic acid (50 mL), cobalt acetate (0.132 g), manganese acetate (0.135 g), and sodium bromide (0.114 g) is placed in a 100 mL reactor and subjected to 500-800 psi oxygen at 100° C. for 2 hours. Upon filtration and evaporation of the solvent, 2.53 g of tan solid is isolated. ^{1}H NMR indicates substantially pure FDCA. The overall yield of FDCA from AcHMF is 54%. See FIG. **3**.

Example 8

Reduction of 5-Acetoxymethylfurfural (AcHMF)

[0076] A reaction mixture containing AcHMF (5.0 g) and ethanol (50 mL) is charged into a 100 mL reaction vessel. The G-69B catalyst may be obtained from Sub Chemie, Louisville, Ky. (0.50 g) is added to the vessel. The vessel is purged with hydrogen (4×500 psi) with stirring (1000 rpm). The vessel is then pressurized to 600 psi and heated to 170° C. with continual stirring. After 1 hour, the reaction is allowed to heat to 195° C. for an additional hour. The reaction is then allowed to cool to room temperature and the catalyst removed by vacuum filtration. Most of the solvent is removed by rotary evaporation to provide yellow oil (16.97 g). The UV analysis (λ=284 nm) does not show the presence of AcHMF, indicating complete conversion of AcHMF to 2,5-dihydroxymethyltetrahydrofuran.

Example 9

Oxidation of a Mixture of HMF and HMF Ester to FDCA

[0077] A product mixture composed of predominantly HMF ester with residual HMF in acetic acid is subjected to oxidation with the addition of cobalt acetate, manganese acetate, and sodium bromide. This mixture is pressurized with oxygen and heated to over 100° C. for over an hour. Upon filtration and evaporation, a product of FDCA is isolated.

Example 10

Preparation of HMF from Fructose

[0078] To a jacketed column was added a slurry of Amberlyst 35 dry resin (40 g) in DMF. The column was heated by an oil circulating bath at 95° C. The resin was washed with anhydrous DMF. The level of DMF was then lowered to the top of the resin. The column was then loaded with 150 g of 30% fructose in DMF. The fructose solution was passed slowly through the resin over a period of about 1 hour two times. Tlc and NMR analysis indicate 68% yield of HMF.

[0079] It will be understood that certain of the above-described structures, functions and operations of the above-described preferred embodiments are not necessary to practice the present disclosure and are included in the description simply for completeness of an exemplary embodiment or embodiments. In addition, it will be understood that specifically described structures, functions, and operations set forth in the above-referenced patents can be practiced in conjunction with the present disclosure, but they are not essential to its practice.

[0080] The embodiments of the disclosure may be practiced otherwise than as specifically described without actually departing from the spirit and scope of the present disclosure. The yields disclosed herein are exemplary only and do not necessarily reflect the optimal yields possible when reaction conditions are optimized.

What is claimed is:

1. A method for synthesizing HMF by contacting a carbohydrate source with a solid phase catalyst.

2. The method of claim **1**, wherein the step of contacting the carbohydrate source further includes the steps of:

forming a solution of the carbohydrate source in an solvent;

passing the solution through a solid phase catalyst in a column; and

eluting said HMF from the column.

3. The method of claim **2**, wherein said solvent is DMF.

4. A method of preparing HMF esters comprising:

combining materials comprising a carbohydrate source, a carboxylic acid, with or without an added catalyst to provide a reaction mixture;

heating said reaction mixture to a temperature and for a time sufficient to promote an acid-catalyzed reaction of said carbohydrate source to form a product mixture; and

isolating an HMF ester from said product mixture.

5. The method of claim **4**, wherein the step of heating said reaction mixture further includes the steps of:

passing the solution through a solid phase catalyst in a column, and

eluting said HMF ester.

6. The method of claim **4**, wherein said HMF ester is isolated from the product mixture by a process selected from the group consisting of filtration, evaporation, extraction, and distillation.

7. The method of claim **4**, wherein said solvent is a polar, aprotic solvent.

8. The method of claim **2**, wherein the column is heated to a temperature of from about 70° C. to about 125° C.

9. The method of claim **4**, wherein temperature at which the reaction mixture is heated is from about 100° C. to about 140° C.

10. A method of forming FDCA by reacting the HMF ester formed in claim **4** with an organic acid, cobalt acetate, manganese acetate and sodium bromide under elevated pressure and temperature for a period of time sufficient to convert substantially all of the HMF ester to FDCA.

11. The method of claim **10**, wherein the pressure of the reaction is from about 400 psi to about 1000 psi.

12. A method of reducing the HMF ester formed in claim **4** comprising the step of heating a solution of the ester in a solvent, with catalyst, under elevated pressure and temperature, for a time sufficient to reduce the ester.

13. The method of claim **12**, wherein the pressure is about 600 psi and the temperature is about 170° C.

14. A method for synthesizing HMF by contacting an HMF ester with an anionic solid phase catalyst.

15. A method for synthesizing citrate esters by contacting a solution having a citrate source and an alcohol with a solid phase catalyst by eluting the solution through a column packed with the solid phase catalyst to obtain an eluant.

16. The method of claim **15** further comprising the steps of:

collecting the eluant from the column; and

passing the eluant through the column a second time to generate a tri-substituted citrate ester.

17. A method for synthesizing a levulinic acid comprising the steps of:

dissolving a carbohydrate source in a solution,

passing the solution containing the carbohydrate through a column containing a solid phase catalyst, and

eluting said levulinic acid from the column to obtain an eluant.

18. The method of claim **17**, further comprising the steps of:

after passing the solution containing the carbohydrate through the column,

collecting the eluant containing the reaction product, and

after collecting the eluant, passing the eluant through the column.

19. A method for synthesizing a levulinate ester comprising the steps of:

dissolving a carbohydrate source in a solution containing acetic acid,

passing the solution containing the carbohydrate through a column containing a solid phase catalyst,

and eluting said levulinate ester from the column to obtain an eluant.

20. The method of claim **19**, further comprising the steps of:

after passing the solution containing the carbohydrate through the column,

collecting the eluant containing the reaction product,

after collecting the eluant, passing the eluant through the column.

21. The method of claim **19**, wherein the concentration of acetic acid in the solution is greater than about 75%

22. A method for synthesizing HMF by contacting a fructose source with an organic acid and solid phase catalyst in a column to produce HMF ester, and

deacylating the HMF ester.

23. The method of claim **22**, wherein the HMF ester is deacylated with a metal oxide.

24. The method of claim **2**, wherein the HMF is purified during the reaction by passing the solution through the column.

25. The method of claim **5**, wherein the HMF ester is purified during the reaction by passing the solution through the column.

26. The method of claim **17**, wherein the citrate ester is purified during the reaction by passing the solution through the column.

27. The method of claim **19**, wherein the levulinic acid is purified during the reaction by passing the solution through the column.

28. The method of claim **21**, wherein the levulinic ester is purified during the reaction by passing the solution through the column.

29. A method for synthesizing a levulinate ester comprising the steps of:

dissolving a carbohydrate source in a solution containing an alcohol,

passing the solution containing the carbohydrate through a column containing a solid phase catalyst,

and eluting said levulinate ester from the column to obtain an eluant containing a reaction product.

30. The method of claim **29**, further comprising the steps of:

after obtaining the eluant containing the reaction product, passing the eluant through the column.

* * * * *

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Muñoz de Diego et al.

(54) **METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID**

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(57) **ABSTRACT**

A method for the preparation of 2,5-furan dicarboxylic acid includes the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140° C.

METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is the National Stage of International Application No. PCT/NL2010/050654, filed Oct. 6, 2010, which claims the benefit of Netherlands Application No. 2003606, filed Oct. 7, 2009, and U.S. Provisional Application No. 61/249,395, filed Oct. 7, 2009, the contents of all of which are incorporated by reference herein.

FIELD OF THE INVENTION

[0002] The present invention relates to a method for the preparation of 2,5-furandicarboxylic acid ("FDCA") from 5-hydroxymethylfurfural ("HMF") and/or derivatives thereof. FDCA can be produced in particular from esters of HMF, such as for example 5-acetoxymethylfurfural (AMF) or a mixture of one or more of these compounds with HMF, such as for example from a mixture of AMF and HMF. The invention further relates to a process for the preparation of the dialkyl ester of 2,5-furandicarboxylic acid.

BACKGROUND OF THE INVENTION

[0003] 2,5-Furandicarboxylic acid, also known as dehydromucic acid is a furan derivative. This organic compound was first obtained by Fittig and Heinzelmann in 1876. The first review, by Henry Hill was published in 1901 (Am. Chem. Journ. 25, 439). FDCA was more than 125 years later identified by the US Department of Energy as one of 12 priority chemicals for establishing the "green" chemistry industry of the future. However, to date, no commercial process exists for its production. On laboratory scale it is often synthesized from 5-hydroxymethylfurfural (HMF), which in turn can be obtained from carbohydrate containing sources such as glucose, fructose, sucrose and starch. From fructose and glucose HMF is obtained by acidic elimination of three moles of water.

[0004] The derivatives of HMF are identified as potential and versatile fuel components and precursors for the production of plastics. The polyester from FDCA dimethyl diester and ethylene glycol was first reported in 1946 (GB 621,971).

[0005] WO 01/72732 describes the oxidation of HMF to FDCA. The maximum FDCA yield reported is 59%, obtained at 105° C. The oxidation of HMF in an aqueous medium with oxygen using a catalyst from the Pt-group is described in U.S. Pat. No. 4,977,283. Taarning et al. described the oxidation of HMF over gold based catalysts (ChemSusChem, 2008, 1, 1-4).

[0006] Partenheimer et al (Adv. Synth. Catal. 2001, 343, pp 102-11) describe the synthesis of 2,5-furandicarboxylic acid by catalytic air-oxidation of 5-hydroxymethylfurfural with metal/bromide catalysts such as Co/Mn/Br in acetic acid at temperatures ranging from 50 to 125° C. With the Co/Mn/Br catalyst the highest FDCA yield obtained is 35.2% (Table 3, experiment 4). On page 103 of the same paper, under the header "products formed" it is stated: "A side reaction is the esterification of the alcohols to form the more oxidatively stable acetate . . . " As apparently 5-hydroxymethylfurfural reacts with acetic acid a loss of the starting material takes place. Further, in the reaction scheme given in FIG. 1 on page 103, it is indicated that 5-(acetoxymethyl)furfural is an endpoint. There is no further reaction of this compound indicated to FDCA (in contrast to the ester of the intermediate product 5-(acetoxymethyl)furan-2-carboxylic acid). In other words, the 5-(acetoxymethyl)furfural (AMF) formed through reaction of HMF with acetic acid solvent, is not oxidized to FDCA and its formation leads therefore to yield loss.

[0007] This result was confirmed in U.S. 2009/0156841. Although the intention of the process according to U.S. 2009/0156841 was to obtain FDCA, the product isolated and erroneously characterized as being FDCA was in fact the starting material acetoxymethyl furfural (AMF). Under the low temperature conditions deployed (100° C.), AMF is quite stable, as was already reported by Partenheimer (see above).

[0008] In U.S. 2009/0156841 a ^{1}H NMR spectrum is shown in FIG. 8 and suggested that it is the spectrum of the product that was identified as FDCA. However, this is not the case. The ^{1}H NMR spectrum of the product shown in FIG. 8 is the same as that in FIG. 6 and represents the starting material AMF. The 1H NMR spectrum of FDCA shows a singlet at a shift of about 7.26 ppm. Moreover, the product is described as a tan solid. In the experience of the present inventors, AMF is a tan solid, while FDCA is a white solid. It would seem that no FDCA was obtained in the experiments according to U.S. 2009/0156841.

[0009] The experiments executed under the conditions of U.S. 2009/0156841 were repeated. These comparative experiments confirm the low reactivity of AMF under conditions given in U.S. 2009/0156841. Thus, a person skilled in the art would therefore have concluded that FDCA cannot be obtained in interesting yields from AMF using the conditions that are reported in U.S. 2009/0156841, i.e., using a Co/Mn/Br catalyst in acetic acid at between 85 and 110° C. within a time frame of from 100 and 150 minutes. In Example 7 of U.S. 2009/0156841, slightly more than 50% of the starting material was the only product isolated from the reaction.

SUMMARY OF THE INVENTION

[0010] The present inventors have now surprisingly found that when using an oxidation catalyst, e.g., based on both cobalt and manganese and containing a bromide, at temperatures higher than 140° C., derivatives of HMF, and in particular esters of HMF optionally in combination with HMF, such as for example 5-(acetoxymethyl)furfural (AMF) can be oxidized to FDCA in high yields.

DETAILED DESCRIPTION OF THE INVENTION

[0011] Thus, in a first aspect the invention provides a method for the preparation of 2,5-furan dicarboxylic acid comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140° C. The feed may optionally comprise 5-hydroxymethylfurfural as a further compound.

[0012] The invention described hereinafter may use any of the compounds described above in the feed. A preferred ester of HMF contains an ester moiety of an alkyl carboxylic acid wherein the alkyl group contains up to 6 carbon atoms, preferably from 1 to 5 carbon atoms, i.e. methyl, ethyl, propyl,

isopropyl, butyl, 2-butyl, tert-butyl, pentyl, 2-pentyl, neopentyl and 3-pentyl. Particularly preferred are alkyl groups with 1 to 4 carbon atoms. There is a preference for methyl, giving (5-acetoxymethyl)furfural. Hence, 5-acetoxymethylfurfural is the preferred feedstock, by itself or in combination with HMF.

[0013] In another aspect of the invention, we have also investigated the oxidation of other furan-based substrates under the process conditions according to the current invention. We have been able to convert 5-(chloromethyl)furfural, 5-(chloromethyl)furoic acid, 5-methylfurfural, 5-methylfuroic acid and 2,5-dimethylfuran all to FDCA in very interesting yields.

[0014] In WO 2007/104515 and WO 2009/030512, the synthesis of esters of HMF such as 5-acetoxymethylfurfural (AMF) from biomass sources is described. Given the higher stability of the HMF esters than HMF and hence improved production pathways and given the fact that upon oxidation in acetic acid the acetoxy functionality that was obtained from acetic acid is now liberated as acetic acid and given the green reputation of these esters, they were considered by the present inventors as interesting starting point in the preparation of furan-based monomers that could be used for the production of furandicarboxylic acid-based polyesters, for instance as an alternative for PET or FDCA-based polyamids (nylons). The most important conventional, oil-based, polyester monomer to produce PET is Purified Terephthalic acid (PTA) and its dialkyl ester DiMethyl Terephthalate (DMT).

[0015] AMF can be obtained from biomass sources as described in WO 2007/104515 and WO 2009/030512. Depending on the process conditions the product obtained in accordance with the process of these references may also contain HMF.

[0016] FDCA, the product of the reaction can be used in the preparation of a polyester, by reaction of FDCA or its dialkyl ester with a suitable diol. Such polyester preparations are preferably performed by transesterification, whereby the dimethyl ester or di-ethyl ester of FDCA is used and wherein the methyl or ethyl groups are exchanged in the form of a volatile alcohol during the transesterification with the diol.

[0017] The oxidation catalyst can be selected from a variety of oxidation catalysts, but is preferably a catalyst based on both cobalt and manganese and suitably containing a source of bromine, preferably a bromide.

[0018] The bromine source can be any compound that produces bromide ions in the reaction mixture. These compounds include hydrogen bromide, sodium bromide, elemental bromine, benzyl bromide and tetrabromoethane. Also other bromine salts, such as an alkali or alkaline earth metal bromide or another metal bromide such as $ZnBr_2$ can be used. There is a preference for hydrobromic acid or sodium bromide. The amount of bromine mentioned in here relates to the amount measured as Br relative to cobalt.

[0019] Suitable metal bromide catalysts employed in all of the processes of this invention comprise a cobalt compound and a manganese compound and a bromine-containing compound. Preferably these compounds are soluble in the reaction mixture.

[0020] Preferably, the catalyst comprises both Co and Mn. The metal and bromide catalyst contains, in addition to bromide, Co and Mn and optionally may contain one or more additional metals, in particular Zr and/or Ce. Alternative and suitable catalysts are described in W. Partenheimer, Catalysis Today 23 (2), 69-158 (1995) in particular on pages 89-99, included herein by reference.

[0021] Each of the metal components can be provided in any of their known ionic forms. Preferably the metal or metals are in a form that is soluble in the reaction solvent. Examples of suitable counterions for cobalt and manganese include, but are not limited to, carbonate, acetate, acetate tetrahydrate and halide, with bromide being the preferred halide.

[0022] As described in Partenheimer, ibid, pages 86-88, suitable solvents for use in the processes of the present invention, described above, preferably have at least one component that contains a monocarboxylic acid functional group. The solvent may also function as one of the reagents. The processes may be run in a solvent or solvent mixture that does not contain an acid group. In that case, preferably one of the reagents does contain a monocarboxylic acid functional group. Suitable solvents can also be aromatic acids such as benzoic acid and derivatives thereof. A preferred solvent is an aliphatic C_2-C_6 monocarboxylic acid, such as but not limited to acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, trimethylacetic acid, and caproic acid and mixtures thereof. Said mixtures may also include benzene, acetonitrile, heptane, acetic anhydride, chlorobenzene, o-dichlorobenzene, and water. The most preferred solvent is acetic acid ("AcOH").

[0023] The oxidant in the processes of the present invention is preferably an oxygen-containing gas or gas mixture, such as, but not limited to air and oxygen-enriched air. Oxygen by itself is also a preferred oxidant.

[0024] The processes of the instant invention described above can be conducted in a batch, semi-continuous or continuous mode. Especially for the manufacture of FDCA, operation in the batch mode with increasing temperature at specific times, increasing pressure at specific times, variation of the catalyst concentration at the beginning of the reaction, and variation of the catalyst composition during the reaction is desirable. For example, variation of the catalyst composition during the reaction can be accomplished by addition of cobalt and/or manganese and/or zirconium, and/or cerium, and/or bromide at specified times.

[0025] The pressure in a commercial oxidation process may vary within wide ranges. When a diluent is present, and in particular with acetic acid as diluent, the temperature and the pressure in such a process are not independent. The pressure is determined by the solvent (e.g., acetic acid) pressure at a certain temperature. The pressure of the reaction mixture is preferably selected such that the solvent is mainly in the liquid phase. In practice this means that pressures between 5 and 100 bar can be used with a preference for pressures between 10 and 80 bar. In case the oxidant is an oxygen-containing gas, such as air, the gas can be continuously fed to and removed from the reactor, or the gas can be supplied all at the start of the reaction. In the latter case, the pressure of the system will depend on the headspace volume and the amount of gas required to convert the starting material. It is clear that in the latter case, the pressure of the system may be significantly higher than the pressure in a process wherein an oxygen containing gas is continuously fed and removed. In the case of continuously feeding and removing the oxidant gas to and from the reactor, the oxygen partial pressure will suitably be between 1 and 30 bar or more preferably between 1 and 10 bar.

[0026] The temperature of the reaction mixture is at least 140° C., preferably from 140 and 200° C., most preferably between 160 and 190° C. Temperatures higher than 180° C. may lead to decarboxylation and to other degradation products. Good results to FDCA have been achieved at a temperature of about 180° C.

[0027] Molar ratios of cobalt to manganese (Co/Mn) are typically 1/1000-100/1, preferably 1/100-10/1 and more preferably 1/10-4/1.

[0028] Molar ratios of bromine to metals (e.g. Br/(Co+Mn)) are typically 0.001-5.00, preferably 0.01-2.00 and more preferably 0.1-0.9.

[0029] Catalyst concentration (Co+Mn) is typically from 0.1 to 10 mol %, relative to the substrate, with a preference for concentrations from 2 to 6 mol %. Good results were obtained in general with catalyst concentrations of around 4 mol %.

[0030] The starting materials for the production of FDCA may originate from a carbohydrate source as described above. Examples of such disclosures are WO 2007/104515 and WO 2009/030512. Accordingly, the invention also provides a method for the preparation of 2,5-furandicarboxylic acid wherein a carbohydrate source is converted in the presence of an alkyl carboxylic acid into products comprising an HMF ester and optionally 5-hydroxymethyl furfural, from which is isolated a feed comprising the ester of HMF and optionally 5-hydroxymethyl furfural, and which method further comprises the subsequent step of contacting the feed with an oxidant in the presence of an oxidation catalyst, in particular a cobalt and manganese and bromide-containing catalyst, under appropriate reaction conditions, in particular at temperatures higher than 140° C.

[0031] In another aspect, the FDCA obtained according to the process of the present invention can be transformed using common esterification reactions to a diester by contacting the starting material under appropriate conditions with the relevant alcohol. Thus, in one aspect, the invention also relates to the use of FDCA obtained according to the process of the current invention in the preparation of a dialkylester of 2,5-dicarboxylic acid by reaction of the FDCA with a C_1-C_5 alkyl alcohol, preferably methanol to prepare the dimethyl ester of FDCA.

[0032] Accordingly, the present invention also provides a process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140° C., and esterifying the thus obtained product. Preferably, the product is esterified with an alkyl alcohol, suitably having 1 to 5 carbon atoms.

[0033] The esterification of 2,5-furan dicarboxylic acid is known. As a specific example for the manufacture of these esters, reference is made to U.S. Pat. No. 2,673,860 wherein the diester is obtained by transesterification of another dicarboxylic acid ester in the presence of sulphuric acid. A more general description for the esterification of dicarboxylic acids is presented in U.S. Pat. No. 2,628,249.

[0034] In a further aspect of the invention, the di-methylester can be used in the preparation of polyester polymers by reaction with a diol. Reacting the di-methylester with a diol will result in the formation of methanol that quickly vaporises. In 1946 the polymerization of FDCA dimethyl ester with ethylene glycol was described as a first example of such a polymerization in GB 621,971.

[0035] Indeed, polyesters are generally made by a combined esterification/polycondenzation reaction between monomer units of a diol (e.g., ethylene glycol (EG)) and a dicarboxylic acid. Additives such as catalysts and stabilizers may be added to facilitate the process and stabilize the polyester towards degradation.

EXAMPLES

[0036] Experiments were carried out in parallel 8 ml magnetically stirred stainless steel batch reactors. The reactors are grouped in blocks containing 12 batch reactors. The standard procedure for all the reactions was as follows:

[0037] 0.5 ml of starting material stock solution in acetic acid (0.78 mmol/ml) were added into a reactor lined with a Teflon insert. To the reactor 1 ml of a catalyst stock solution in acetic acid was subsequently added. In a typical experiment, a catalyst composition Co/Mn/Br with a relative 1-x-y ratio, the concentration of $Co(OAc)_2$* $4H_2O$ was varied. As a Mn source, $Mn(OAc)_2$*$4H_2O$ was used and as a bromine source NaBr was used. The reactors were closed with a rubber septum, after which the reactors were sealed and pressurized to the desired air pressure, ranging from 20-60 bars. After pressurization, the block with 12 reactors was placed in the test unit which was preheated at the desired temperature, ranging from 100 to 220° C. After the desired reaction time, ranging from 0.5 hr to 24 hrs, the block is placed into an ice bath for 20 minutes. When the block had cooled down, it was depressurized. After opening, HPLC samples were prepared. First 5 ml of a saccharine solution in DMSO (11.04 mg/ml) was added to each reactor and the mixture was stirred for 5 minutes. Then 10 μl of this mixture was diluted to 1000 μl with water in a HPLC vial. The samples were analyzed using HPLC.

Example 1

[0038] Example 1 shows the selectivity of FDCA in the oxidation of HMF, of a HMF/AMF 3/2 mixture, of a HMF/AMF 2/3 mixture and of AMF, respectively, with 2.7 mol % Co catalyst (relative to substrate), and Co/Mn molar ratio of 1/1, so that the catalyst concentration (Co+Mn) amounted to 5.4 mol %. The Br/(Co+Mn) molar ratio was 1.0; 0.7; 0.4 and 0.1 at 0.26 M substrate concentration in acetic acid at 180° C. for 1 hr with 20 bar air. The amount of oxygen was 2.69 mol oxygen per mol substrate. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn)>1, corrosion will be a problem on commercial scale. HMF gives slightly higher yields than AMF at one hour reaction time. The results of these experiments are given in Table 1.

Example 2

[0039] Example 2 shows the selectivity to FDCA for the AMF oxidation of Example 1, together with the comparative examples based on the experimental conditions described in U.S. 2009/0156841. In those comparative experiments (2a and 2b) 10 wt/wt % AMF in acetic acid was oxidized with 1.75 and 2.65 mol % Co catalyst and a fixed Br/(Co+Mn) molar ratio of 1.0 and a Co/Mn molar ratio of 1.0 at 100° C. and 30 bar for 2 hours. The amount of oxygen was 2.88 mol oxygen per mol substrate. Under these conditions, the yield of FDCA was lower than the result suggested in U.S. 2009/

0156841 and also lower than the results obtained at higher temperature. The results of these experiments are given in Table 2.

Example 3

[0040] Example 3 shows the yield of FDCA in the oxidation of 5-methylfurfural (5MF) and 2,5-dimethylfurfural (DMF) at 180° C. with 2.7 mol % Co catalyst (relative to substrate), and Co/Mn ratio of 1/1, so that the catalyst concentration (Co+Mn) amounted to 5.4 mol %. The Br/(Co+Mn) molar ratio was 1.0, 0.7, 0.4 and 0.1. The substrate concentration was 0.26 M in acetic acid. The reaction temperature was at 180° C. and the reaction was conducted with 50 bars air. The amount of oxygen was 6.7 mol oxygen per mol substrate. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn)>1, corrosion will be a problem on commercial scale. Reactions with 5-MF give higher yields than reactions with DMF. The results of these experiments are also given in Table 3.

TABLE 1

Experiment	Substrate HMF/AMF molar ratio			Substrate concentration	Conversion	s FDCA
No.	HMF	AMF	Br/(Co + Mn)	[wt %]	[%]	[%]
1a	1	0	1	3.3	100.00	76.66
1b	3	2	1	3.8	100.00	71.19
1c	2	3	1	4.0	100.00	77.66
1d	0	1	1	4.4	100.00	64.82
1e	1	0	0.7	3.3	100.00	78.08
1f	3	2	0.7	3.8	100.00	66.96
1g	2	3	0.7	4.0	100.00	75.14
1h	0	1	0.7	4.4	100.00	60.64
1i	1	0	0.4	3.3	100.00	73.27
1j	3	2	0.4	3.8	100.00	65.67
1k	2	3	0.4	4.0	100.00	73.21
1l	0	1	0.4	4.4	100.00	57.36
1m	1	0	0.1	3.3	100.00	67.92
1n	3	2	0.1	3.8	100.00	60.92
1o	2	3	0.1	4.0	100.00	69.64
1p	0	1	0.1	4.4	100.00	46.85

TABLE 2

Experiment No.	Temp [° C.]	Reaction time [Hours]	Catalyst concentration [(Co + Mn) mol %]	Mn/Co	Br/(Co + Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
1d	180	1	5.4	1	1	2.69	4.4	100.00	64.82
1h	180	1	5.4	1	0.7	2.69	4.4	100.00	60.64
1l	180	1	5.4	1	0.4	2.69	4.4	100.00	57.36
1p	180	1	5.4	1	0.1	2.69	4.4	100.00	46.85
2a	100	2	3.5	1	1	2.88	10.0	100.00	23.48
2b	100	2	5.3	1	1	2.88	10.0	100.00	29.05

TABLE 3

Experiment No.	Substrate	Reaction time [Hours]	Br/(Co + Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
3a	5-MF	1	1	6.7	2.9	100.00	42.62
3b	5-MF	1	0.7	6.7	2.9	100.00	39.94
3c	DMF	1	1	6.7	2.5	100.00	16.17
3d	DMF	1	0.7	6.7	2.5	100.00	14.09
3e	DMF	1	0.4	6.7	2.5	100.00	11.30
3f	DMF	1	0.1	6.7	2.5	100.00	7.19

1. A method for the preparation of 2,5-furan dicarboxylic acid comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140° C.

2. The method according to claim **1**, wherein the feed comprises a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), esters of HMF and a mixture thereof.

3. The method according to claim **1**, wherein the oxidation catalyst comprises at least one metal selected from the group consisting of Co and Mn.

4. The method according to claim **1**, wherein the oxidation catalyst comprises a source of bromine.

5. The method according to claim **4**, wherein the oxidation catalyst contains both Co and Mn.

6. The method according to claim **5**, wherein the oxidation catalyst comprises at least one additional metal.

7. The method according to claim **6**, wherein the additional metal is Zr and/or Ce.

8. The method according to claim **1**, wherein the oxidant is selected from oxygen, air or other oxygen-containing gases.

9. The method according to claim **1**, wherein the temperature is between 140 and 200° C., most preferably between 160 and 190° C.

10. The method according to claim **1**, wherein a solvent or solvent mixture is present, preferably comprising a solvent containing a monocarboxylic acid functional group, more preferably acetic acid or acetic acid and water mixtures.

11. The method according to claim **1**, wherein the feed comprises an ester of HMF containing an ester moiety of an alkyl carboxylic acid wherein the alkyl group contains up to 6 carbon atoms, preferably from 1 to 5 carbon atoms.

12. A process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140° C., and esterifying the thus obtained product.

13. The process according to claim **12**, wherein the product is esterified with a C_1-C_5 alkyl alcohol.

14. The process according to claim **13**, wherein the C_1-C_5 alkyl alcohol is methanol and the dialkyl ester is the dimethylester of 2,5-furan dicarboxylic acid.

15. A method for the preparation of 2,5-furandicarboxylic acid wherein a carbohydrate source is converted in the presence of an alkyl carboxylic acid into products comprising an HMF ester and optionally 5-hydroxymethyl furfural, from which is isolated a feed comprising the ester of HMF and optionally 5-hydroxymethyl furfural, and which method comprises further the subsequent step of contacting the feed with an oxidant in the presence of an oxidation catalyst, preferably a cobalt and manganese and bromide-containing catalyst, under appropriate reaction conditions.

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(12) **United States Patent**
Muñoz De Diego et al.

(10) **Patent No.: US 8,865,921 B2**
(45) **Date of Patent: Oct. 21, 2014**

(54) **METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID**

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(58) **Field of Classification Search**
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See application file for complete search history.

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(57) **ABSTRACT**

A method for the preparation of 2,5-furan dicarboxylic acid includes the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140° C.

10 Claims, No Drawings

METHOD FOR THE PREPARATION OF 2,5-FURANDICARBOXYLIC ACID AND FOR THE PREPARATION OF THE DIALKYL ESTER OF 2,5-FURANDICARBOXYLIC ACID

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is the National Stage of International Application No. PCT/NL2010/050654, filed Oct. 6, 2010, which claims the benefit of Netherlands Application No. 2003606, filed Oct. 7, 2009, and U.S. Provisional Application No. 61/249,395, filed Oct. 7, 2009, the contents of all of which are incorporated by reference herein.

FIELD OF THE INVENTION

The present invention relates to a method for the preparation of 2,5-furandicarboxylic acid ("FDCA") from 5-hydroxymethylfurfural ("HMF") and/or derivatives thereof. FDCA can be produced in particular from esters of HMF, such as for example 5-acetoxymethylfurfural (AMF) or a mixture of one or more of these compounds with HMF, such as for example from a mixture of AMF and HMF. The invention further relates to a process for the preparation of the dialkyl ester of 2,5-furandicarboxylic acid.

BACKGROUND OF THE INVENTION

2,5-Furandicarboxylic acid, also known as dehydromucic acid is a furan derivative. This organic compound was first obtained by Fittig and Heinzelmann in 1876. The first review, by Henry Hill was published in 1901 (Am. Chem. Journ. 25, 439). FDCA was more than 125 years later identified by the US Department of Energy as one of 12 priority chemicals for establishing the "green" chemistry industry of the future. However, to date, no commercial process exists for its production. On laboratory scale it is often synthesized from 5-hydroxymethylfurfural (HMF), which in turn can be obtained from carbohydrate containing sources such as glucose, fructose, sucrose and starch. From fructose and glucose HMF is obtained by acidic elimination of three moles of water.

The derivatives of HMF are identified as potential and versatile fuel components and precursors for the production of plastics. The polyester from FDCA dimethyl diester and ethylene glycol was first reported in 1946 (GB 621,971).

WO 01/72732 describes the oxidation of HMF to FDCA. The maximum FDCA yield reported is 59%, obtained at 105° C. The oxidation of HMF in an aqueous medium with oxygen using a catalyst from the Pt-group is described in U.S. Pat. No. 4,977,283. Taarning et al. described the oxidation of HMF over gold based catalysts (ChemSusChem, 2008, 1, 1-4).

Partenheimer et al (Adv. Synth. Catal. 2001, 343, pp 102-11) describe the synthesis of 2,5-furandicarboxylic acid by catalytic air-oxidation of 5-hydroxymethylfurfural with metal/bromide catalysts such as Co/Mn/Br in acetic acid at temperatures ranging from 50 to 125° C. With the Co/Mn/Br catalyst the highest FDCA yield obtained is 35.2% (Table 3, experiment 4). On page 103 of the same paper, under the header "products formed" it is stated: "A side reaction is the esterification of the alcohols to form the more oxidatively stable acetate . . . " As apparently 5-hydroxymethylfurfural reacts with acetic acid a loss of the starting material takes place. Further, in the reaction scheme given in FIG. 1 on page 103, it is indicated that 5-(acetoxymethyl)furfural is an end-point. There is no further reaction of this compound indicated to FDCA (in contrast to the ester of the intermediate product 5-(acetoxymethyl)furan-2-carboxylic acid). In other words, the 5-(acetoxymethyl)furfural (AMF) formed through reaction of HMF with acetic acid solvent, is not oxidized to FDCA and its formation leads therefore to yield loss.

This result was confirmed in U.S. 2009/0156841. Although the intention of the process according to U.S. 2009/0156841 was to obtain FDCA, the product isolated and erroneously characterized as being FDCA was in fact the starting material acetoxymethyl furfural (AMF). Under the low temperature conditions deployed (100° C.), AMF is quite stable, as was already reported by Partenheimer (see above).

In U.S. 2009/0156841 a ^{1}H NMR spectrum is shown in FIG. 8 and suggested that it is the spectrum of the product that was identified as FDCA. However, this is not the case. The ^{1}H NMR spectrum of the product shown in FIG. 8 is the same as that in FIG. 6 and represents the starting material AMF. The 1H NMR spectrum of FDCA shows a singlet at a shift of about 7.26 ppm. Moreover, the product is described as a tan solid. In the experience of the present inventors, AMF is a tan solid, while FDCA is a white solid. It would seem that no FDCA was obtained in the experiments according to U.S. 2009/0156841.

The experiments executed under the conditions of U.S. 2009/0156841 were repeated. These comparative experiments confirm the low reactivity of AMF under conditions given in U.S. 2009/0156841. Thus, a person skilled in the art would therefore have concluded that FDCA cannot be obtained in interesting yields from AMF using the conditions that are reported in U.S. 2009/0156841, i.e., using a Co/Mn/Br catalyst in acetic acid at between 85 and 110° C. within a time frame of from 100 and 150 minutes. In Example 7 of U.S. 2009/0156841, slightly more than 50% of the starting material was the only product isolated from the reaction.

SUMMARY OF THE INVENTION

The present inventors have now surprisingly found that when using an oxidation catalyst, e.g., based on both cobalt and manganese and containing a bromide, at temperatures higher than 140° C., derivatives of HMF, and in particular esters of HMF optionally in combination with HMF, such as for example 5-(acetoxymethyl)furfural (AMF) can be oxidized to FDCA in high yields.

DETAILED DESCRIPTION OF THE INVENTION

Thus, in a first aspect the invention provides a method for the preparation of 2,5-furan dicarboxylic acid comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140° C. The feed may optionally comprise 5-hydroxymethylfurfural as a further compound.

The invention described hereinafter may use any of the compounds described above in the feed. A preferred ester of HMF contains an ester moiety of an alkyl carboxylic acid wherein the alkyl group contains up to 6 carbon atoms, preferably from 1 to 5 carbon atoms, i.e. methyl, ethyl, propyl, isopropyl, butyl, 2-butyl, tert-butyl, pentyl, 2-pentyl, neopentyl and 3-pentyl. Particularly preferred are alkyl groups with 1 to 4 carbon atoms. There is a preference for methyl, giving

(5-acetoxymethyl)furfural. Hence, 5-acetoxymethylfurfural is the preferred feedstock, by itself or in combination with HMF.

In another aspect of the invention, we have also investigated the oxidation of other furan-based substrates under the process conditions according to the current invention. We have been able to convert 5-(chloromethyl)furfural, 5-(chloromethyl)furoic acid, 5-methylfurfural, 5-methylfuroic acid and 2,5-dimethylfuran all to FDCA in very interesting yields.

In WO 2007/104515 and WO 2009/030512, the synthesis of esters of HMF such as 5-acetoxymethylfurfural (AMF) from biomass sources is described. Given the higher stability of the HMF esters than HMF and hence improved production pathways and given the fact that upon oxidation in acetic acid the acetoxy functionality that was obtained from acetic acid is now liberated as acetic acid and given the green reputation of these esters, they were considered by the present inventors as interesting starting point in the preparation of furan-based monomers that could be used for the production of furandicarboxylic acid-based polyesters, for instance as an alternative for PET or FDCA-based polyamids (nylons). The most important conventional, oil-based, polyester monomer to produce PET is Purified Terephthalic acid (PTA) and its dialkyl ester DiMethyl Terephthalate (DMT).

AMF can be obtained from biomass sources as described in WO 2007/104515 and WO 2009/030512. Depending on the process conditions the product obtained in accordance with the process of these references may also contain HMF.

FDCA, the product of the reaction can be used in the preparation of a polyester, by reaction of FDCA or its dialkyl ester with a suitable diol. Such polyester preparations are preferably performed by transesterification, whereby the dimethyl ester or di-ethyl ester of FDCA is used and wherein the methyl or ethyl groups are exchanged in the form of a volatile alcohol during the transesterification with the diol.

The oxidation catalyst can be selected from a variety of oxidation catalysts, but is preferably a catalyst based on both cobalt and manganese and suitably containing a source of bromine, preferably a bromide.

The bromine source can be any compound that produces bromide ions in the reaction mixture. These compounds include hydrogen bromide, sodium bromide, elemental bromine, benzyl bromide and tetrabromoethane. Also other bromine salts, such as an alkali or alkaline earth metal bromide or another metal bromide such as $ZnBr_2$ can be used. There is a preference for hydrobromic acid or sodium bromide. The amount of bromine mentioned in here relates to the amount measured as Br relative to cobalt.

Suitable metal bromide catalysts employed in all of the processes of this invention comprise a cobalt compound and a manganese compound and a bromine-containing compound. Preferably these compounds are soluble in the reaction mixture.

Preferably, the catalyst comprises both Co and Mn. The metal and bromide catalyst contains, in addition to bromide, Co and Mn and optionally may contain one or more additional metals, in particular Zr and/or Ce. Alternative and suitable catalysts are described in W. Partenheimer, Catalysis Today 23 (2), 69-158 (1995) in particular on pages 89-99, included herein by reference.

Each of the metal components can be provided in any of their known ionic forms. Preferably the metal or metals are in a form that is soluble in the reaction solvent. Examples of suitable counterions for cobalt and manganese include, but are not limited to, carbonate, acetate, acetate tetrahydrate and halide, with bromide being the preferred halide.

As described in Partenheimer, ibid, pages 86-88, suitable solvents for use in the processes of the present invention, described above, preferably have at least one component that contains a monocarboxylic acid functional group. The solvent may also function as one of the reagents. The processes may be run in a solvent or solvent mixture that does not contain an acid group. In that case, preferably one of the reagents does contain a monocarboxylic acid functional group. Suitable solvents can also be aromatic acids such as benzoic acid and derivatives thereof. A preferred solvent is an aliphatic C_2-C_6 monocarboxylic acid, such as but not limited to acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, trimethylacetic acid, and caproic acid and mixtures thereof. Said mixtures may also include benzene, acetonitrile, heptane, acetic anhydride, chlorobenzene, o-dichlorobenzene, and water. The most preferred solvent is acetic acid ("AcOH").

The oxidant in the processes of the present invention is preferably an oxygen-containing gas or gas mixture, such as, but not limited to air and oxygen-enriched air. Oxygen by itself is also a preferred oxidant.

The processes of the instant invention described above can be conducted in a batch, semi-continuous or continuous mode. Especially for the manufacture of FDCA, operation in the batch mode with increasing temperature at specific times, increasing pressure at specific times, variation of the catalyst concentration at the beginning of the reaction, and variation of the catalyst composition during the reaction is desirable. For example, variation of the catalyst composition during the reaction can be accomplished by addition of cobalt and/or manganese and/or zirconium, and/or cerium, and/or bromide at specified times.

The pressure in a commercial oxidation process may vary within wide ranges. When a diluent is present, and in particular with acetic acid as diluent, the temperature and the pressure in such a process are not independent. The pressure is determined by the solvent (e.g., acetic acid) pressure at a certain temperature. The pressure of the reaction mixture is preferably selected such that the solvent is mainly in the liquid phase. In practice this means that pressures between 5 and 100 bar can be used with a preference for pressures between 10 and 80 bar. In case the oxidant is an oxygen-containing gas, such as air, the gas can be continuously fed to and removed from the reactor, or the gas can be supplied all at the start of the reaction. In the latter case, the pressure of the system will depend on the headspace volume and the amount of gas required to convert the starting material. It is clear that in the latter case, the pressure of the system may be significantly higher than the pressure in a process wherein an oxygen containing gas is continuously fed and removed. In the case of continuously feeding and removing the oxidant gas to and from the reactor, the oxygen partial pressure will suitably be between 1 and 30 bar or more preferably between 1 and 10 bar.

The temperature of the reaction mixture is at least 140° C., preferably from 140 and 200° C., most preferably between 160 and 190° C. Temperatures higher than 180° C. may lead to decarboxylation and to other degradation products. Good results to FDCA have been achieved at a temperature of about 180° C.

Molar ratios of cobalt to manganese (Co/Mn) are typically 1/1000-100/1, preferably 1/100-10/1 and more preferably 1/10-4/1.

Molar ratios of bromine to metals (e.g. Br/(Co+Mn)) are typically 0.001-5.00, preferably 0.01-2.00 and more preferably 0.1-0.9.

Catalyst concentration (Co+Mn) is typically from 0.1 to 10 mol %, relative to the substrate, with a preference for concentrations from 2 to 6 mol %. Good results were obtained in general with catalyst concentrations of around 4 mol %.

The starting materials for the production of FDCA may originate from a carbohydrate source as described above. Examples of such disclosures are WO 2007/104515 and WO 2009/030512. Accordingly, the invention also provides a method for the preparation of 2,5-furandicarboxylic acid wherein a carbohydrate source is converted in the presence of an alkyl carboxylic acid into products comprising an HMF ester and optionally 5-hydroxymethyl furfural, from which is isolated a feed comprising the ester of HMF and optionally 5-hydroxymethyl furfural, and which method further comprises the subsequent step of contacting the feed with an oxidant in the presence of an oxidation catalyst, in particular a cobalt and manganese and bromide-containing catalyst, under appropriate reaction conditions, in particular at temperatures higher than 140° C.

In another aspect, the FDCA obtained according to the process of the present invention can be transformed using common esterification reactions to a diester by contacting the starting material under appropriate conditions with the relevant alcohol. Thus, in one aspect, the invention also relates to the use of FDCA obtained according to the process of the current invention in the preparation of a dialkylester of 2,5-dicarboxylic acid by reaction of the FDCA with a C_1-C_5 alkyl alcohol, preferably methanol to prepare the dimethyl ester of FDCA.

Accordingly, the present invention also provides a process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140° C., and esterifying the thus obtained product. Preferably, the product is esterified with an alkyl alcohol, suitably having 1 to 5 carbon atoms.

The esterification of 2,5-furan dicarboxylic acid is known. As a specific example for the manufacture of these esters, reference is made to U.S. Pat. No. 2,673,860 wherein the diester is obtained by transesterification of another dicarboxylic acid ester in the presence of sulphuric acid. A more general description for the esterification of dicarboxylic acids is presented in U.S. Pat. No. 2,628,249. Accordingly, the invention provides a process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxidant in the presence of an oxidation catalyst at a temperature higher than 140° C., and esterifying the thus obtained product.

In a further aspect of the invention, the di-methylester can be used in the preparation of polyester polymers by reaction with a diol. Reacting the di-methylester with a diol will result in the formation of methanol that quickly vaporises. In 1946 the polymerization of FDCA dimethyl ester with ethylene glycol was described as a first example of such a polymerization in GB 621,971.

Indeed, polyesters are generally made by a combined esterification/polycondenzation reaction between monomer units of a diol (e.g., ethylene glycol (EG)) and a dicarboxylic acid. Additives such as catalysts and stabilizers may be added to facilitate the process and stabilize the polyester towards degradation.

EXAMPLES

Experiments were carried out in parallel 8 ml magnetically stirred stainless steel batch reactors. The reactors are grouped in blocks containing 12 batch reactors. The standard procedure for all the reactions was as follows:

0.5 ml of starting material stock solution in acetic acid (0.78 mmol/ml) were added into a reactor lined with a Teflon insert. To the reactor 1 ml of a catalyst stock solution in acetic acid was subsequently added. In a typical experiment, a catalyst composition Co/Mn/Br with a relative 1-x-y ratio, the concentration of $Co(OAc)_2$* $4H_2O$ was varied. As a Mn source, $Mn(OAc)_2$*$4H_2O$ was used and as a bromine source NaBr was used. The reactors were closed with a rubber septum, after which the reactors were sealed and pressurized to the desired air pressure, ranging from 20-60 bars. After pressurization, the block with 12 reactors was placed in the test unit which was preheated at the desired temperature, ranging from 100 to 220° C. After the desired reaction time, ranging from 0.5 hr to 24 hrs, the block is placed into an ice bath for 20 minutes. When the block had cooled down, it was depressurized. After opening, HPLC samples were prepared. First 5 ml of a saccharine solution in DMSO (11.04 mg/ml) was added to each reactor and the mixture was stirred for 5 minutes. Then 10 μl of this mixture was diluted to 1000 μl with water in a HPLC vial. The samples were analyzed using HPLC.

Example 1

Example 1 shows the selectivity of FDCA in the oxidation of HMF, of a HMF/AMF 3/2 mixture, of a HMF/AMF 2/3 mixture and of AMF, respectively, with 2.7 mol % Co catalyst (relative to substrate), and Co/Mn molar ratio of 1/1, so that the catalyst concentration (Co+Mn) amounted to 5.4 mol %. The Br/(Co+Mn) molar ratio was 1.0; 0.7; 0.4 and 0.1 at 0.26 M substrate concentration in acetic acid at 180° C. for 1 hr with 20 bar air. The amount of oxygen was 2.69 mol oxygen per mol substrate. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn)>1, corrosion will be a problem on commercial scale. HMF gives slightly higher yields than AMF at one hour reaction time. The results of these experiments are given in Table 1.

Example 2

Example 2 shows the selectivity to FDCA for the AMF oxidation of Example 1, together with the comparative examples based on the experimental conditions described in U.S. 2009/0156841. In those comparative experiments (2a and 2b) 10 wt/wt % AMF in acetic acid was oxidized with 1.75 and 2.65 mol % Co catalyst and a fixed Br/(Co+Mn) molar ratio of 1.0 and a Co/Mn molar ratio of 1.0 at 100° C. and 30 bar for 2 hours. The amount of oxygen was 2.88 mol oxygen per mol substrate. Under these conditions, the yield of FDCA was lower than the result suggested in U.S. 2009/0156841 and also lower than the results obtained at higher temperature. The results of these experiments are given in Table 2.

Example 3

Example 3 shows the yield of FDCA in the oxidation of 5-methylfurfural (5MF) and 2,5-dimethylfurfural (DMF) at

180° C. with 2.7 mol % Co catalyst (relative to substrate), and Co/Mn ratio of 1/1, so that the catalyst concentration (Co+Mn) amounted to 5.4 mol %. The Br/(Co+Mn) molar ratio was 1.0, 0.7, 0.4 and 0.1. The substrate concentration was 0.26 M in acetic acid. The reaction temperature was at 180° C. and the reaction was conducted with 50 bars air. The amount of oxygen was 6.7 mol oxygen per mol substrate. Under these conditions, higher Br amounts give higher yields but when Br/(Co+Mn)>1, corrosion will be a problem on commercial scale. Reactions with 5-MF give higher yields than reactions with DMF. The results of these experiments are also given in Table 3.

TABLE 1

Experiment	Substrate HMF/AMF molar ratio			Substrate concentration	Conversion	s FDCA
No.	HMF	AMF	Br/(Co + Mn)	[wt %]	[%]	[%]
1a	1	0	1	3.3	100.00	76.66
1b	3	2	1	3.8	100.00	71.19
1c	2	3	1	4.0	100.00	77.66
1d	0	1	1	4.4	100.00	64.82
1e	1	0	0.7	3.3	100.00	78.08
1f	3	2	0.7	3.8	100.00	66.96
1g	2	3	0.7	4.0	100.00	75.14
1h	0	1	0.7	4.4	100.00	60.64
1i	1	0	0.4	3.3	100.00	73.27
1j	3	2	0.4	3.8	100.00	65.67
1k	2	3	0.4	4.0	100.00	73.21
1l	0	1	0.4	4.4	100.00	57.36
1m	1	0	0.1	3.3	100.00	67.92
1n	3	2	0.1	3.8	100.00	60.92
1o	2	3	0.1	4.0	100.00	69.64
1p	0	1	0.1	4.4	100.00	46.85

TABLE 2

Experiment No.	Temp [° C.]	Reaction time [Hours]	Catalyst concentration [(Co + Mn) mol %]	Mn/Co	Br/ (Co + Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
1d	180	1	5.4	1	1	2.69	4.4	100.00	64.82
1h	180	1	5.4	1	0.7	2.69	4.4	100.00	60.64
1l	180	1	5.4	1	0.4	2.69	4.4	100.00	57.36
1p	180	1	5.4	1	0.1	2.69	4.4	100.00	46.85
2a	100	2	3.5	1	1	2.88	10.0	100.00	23.48
2b	100	2	5.3	1	1	2.88	10.0	100.00	29.05

TABLE 3

Experiment No.	Substrate	Reaction time [Hours]	Br/ (Co + Mn)	O_2/Subs [mol/mol]	Substrate concentration [wt %]	Conversion [%]	s FDCA [%]
3a	5-MF	1	1	6.7	2.9	100.00	42.62
3b	5-MF	1	0.7	6.7	2.9	100.00	39.94
3c	DMF	1	1	6.7	2.5	100.00	16.17
3d	DMF	1	0.7	6.7	2.5	100.00	14.09
3e	DMF	1	0.4	6.7	2.5	100.00	11.30
3f	DMF	1	0.1	6.7	2.5	100.00	7.19

The invention claimed is:

1. A method for the preparation of 2,5-furan dicarboxylic acid comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethylfurfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxygen-containing gas, in the presence of an oxidation catalyst comprising both Co and Mn, and further a source of bromine, at a temperature between 140° C. and 200° C. at an oxygen partial pressure of 1 to 10 bar, wherein a solvent or solvent mixture comprising acetic acid or acetic acid and water mixtures is present.

2. The method according to claim **1**, wherein the feed comprises a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), esters of HMF and a mixture thereof.

3. The method according to claim **1**, wherein the oxidation catalyst comprises at least one additional metal.

4. The method according to claim **3**, wherein the additional metal is Zr and/or Ce.

5. The method according to claim **1**, wherein the temperature is between 160 and 190° C.

6. The method according to claim **1**, wherein the feed comprises an ester of HMF having an ester moiety of an alkyl carboxylic acid wherein the alkyl group has up to 6 carbon atoms.

7. A process for the preparation of a dialkyl ester of 2,5,-furan dicarboxylic acid, comprising the step of contacting a feed comprising a compound selected from the group consisting of 5-hydroxymethylfurfural ("HMF"), an ester of 5-hydroxymethyl-furfural, 5-methylfurfural, 5-(chloromethyl)furfural, 5-methylfuroic acid, 5-(chloromethyl)furoic acid, 2,5-dimethylfuran and a mixture of two or more of these compounds with an oxygen-containing gas in the presence of an oxidation catalyst comprising both Co and Mn, and further a source of bromine, at a temperature between 140° C. and 200° C. at an oxygen partial pressure of 1 to 10 bar, wherein a solvent or solvent mixture comprising acetic acid or acetic acid and water mixtures is present, and esterifying the thus obtained product.

8. The process according to claim 7, wherein the product is esterified with a C1-C5 alkyl alcohol.

9. The process according to claim 8, wherein the C1-C5 alkyl alcohol is methanol and the dialkyl ester is the dimethylester of 2,5-furan dicarboxylic acid.

10. A method according to claim 2, wherein the feed comprises an HMF ester and optionally 5-hydroxymethyl furfural, which has been obtained by converting a carbohydrate source in the presence of an alkyl carboxylic acid.

* * * * *

PROCESS FOR THE OXIDATION OF 5-HYDROXYMETHYLFURFURAL

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Abstract of EP 0356703 A2

Verfahren zur Oxidation von 5-Hydroxymethylfurfural, dadurch gekennzeichnet, dar 5-Hydroxymethylfurfural in wässrigem Medium mit Sauerstoff als Oxidationsmittel in Gegenwart eines Katalysators, der mindestens ein Platinmetall enthält, oxidiert wird.

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(54) Verfahren zur Oxidation von 5-Hydroxymethylfurfural.

(57) Verfahren zur Oxidation von 5-Hydroxymethylfurfural, dadurch gekennzeichnet, dar 5-Hydroxymethylfurfural in wäßrigem Medium mit Sauerstoff als Oxidationsmittel in Gegenwart eines Katalysators, der mindestens ein Platinmetall enthält, oxidiert wird.

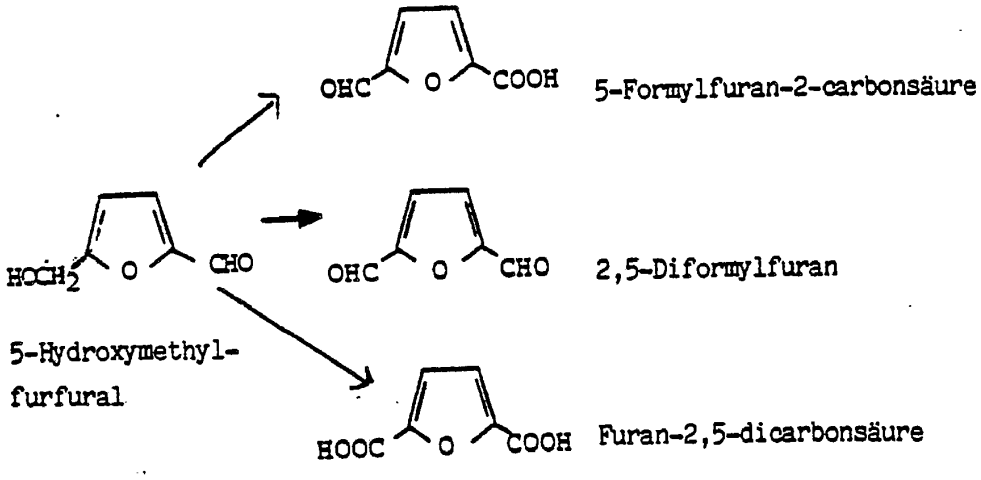
EP 0 356 703 A2

Verfahren zur Oxidation von 5-Hydroxymethylfurfural

Die vorliegende Erfindung betrifft die katalytische Oxidation von 5-Hydroxymethylfurfural zu vielseitig verwendbaren Produkten, die insbesondere als Zwischenprodukte zur Herstellung von Tensiden, Kunststoffen und Harzen eingesetzt werden können.

Es ist bekannt, 5-Hydroxymethylfurfural ohne Mitverwendung von Katalysatoren mit verschiedenen Oxidationsmitteln, wie konzentrierter Salpetersäure (J.J. Blanksma, Chemisches Zentralblatt 1910 I, 539) oder einer Mischung aus Dimethylsulfoxid einerseits und Essigsäureanhydrid Distickstofftetroxid oder Salpetersäure andererseits zu oxidieren (Morikawa, Chem. Abstr. Vol. 92 (1980), 198181a).

Bei der Oxidation werden im wesentlichen drei Reaktionsprodukte gefunden:



Die bisher bekannten Methoden zur Herstellung von Oxidationsprodukten des 5-Hydroxymethylfurfurals sind jedoch mit erheblichen Nachteilen behaftet. Bei Verwendung der herkömmlichen Reagenzien Salpetersäure, Distickstofftetroxid und Dimethylsulfoxid entstehen in Abhängigkeit von den jeweiligen Reagenzien zwangsläufig große Mengen an unerwünschten Produkten, wie nitrose Gase oder Schwefel-Verbindungen, deren Entsorgung einen beträchtlichen Aufwand erfordert. Ebenso ist es sehr aufwendig, bei der Aufarbeitung überschüssiges Oxidationsmittel abzutrennen. Es besteht somit ein Bedarf an einem Verfahren zur Oxidation von 5-Hydroxymethylfurfural, das ohne die genannten Nachteile in technisch einfacher Weise durchgeführt werden kann.

Gegenstand der Erfindung ist ein Verfahren zur Oxidation von 5-Hydroxymethylfurfural, das dadurch gekennzeichnet ist, daß 5-Hydroxymethylfurfural in wäßrigem Medium mit Sauerstoff als Oxidationsmittel in Gegenwart eines Katalysators, der mindestens ein Platinmetall enthält, oxidiert wird.

Als Katalysatoren eignen sich solche, die Metalle der Platingruppe, wie Iridium, Rhodium, Ruthenium, vorteilhaft aber Palladium und/oder Platin, enthalten. Ganz besonders bevorzugt sind Katalysatoren, die als Platinmetall nur Platin enthalten. Vorzugsweise sind die Platinmetalle auf einem Träger, insbesondere auf Aktivkohle aufgebracht. Der Gehalt des Katalysators an dem Metall, insbesondere Platin, liegt vorzugsweise bei 1 bis 10 Gew.-%. Geeignete Katalysatoren sind beispielsweise handelsübliche Katalysatoren mit 5 bis 10 Gew.-% Platin auf Aktivkohle.

Die Konzentration des 5-Hydroxymethylfurfurals in dem wäßrigen Medium kann in weiten Grenzen schwanken. Vorzugsweise wird es in einer Menge von 5 bis 30, insbesondere 10 bis 20 Gew.-%, bezogen auf die Menge von Wasser und Losungsvermittler, eingesetzt.

Um das Ausfallen von Reaktionsprodukten während der Oxidation zu vermeiden, hat es sich insbesondere bei höheren Konzentrationen als vorteilhaft erwiesen, einen unter den Reaktionsbedingungen gegenüber den Reaktionsteilnehmern inerten Lösungsvermittler, vorzugsweise in einer Konzentration von 10 bis 75 Gew.-%, insbesondere 30 bis 50 Gew.-%, bezogen auf die Menge an Wasser und Lösungsvermittler, einzusetzen. Zweckmäßig werden solche Lösungsvermittler verwendet, die beim Durchleiten von Sauerstoff durch die wäßrige Lösung relativ wenig flüchtig sind, so daß eine Explosionsgefahr im Dampfraum weitgehend vermieden wird; auf der anderen Seite werden solche Lösungsvermittler bevorzugt, die nach der Oxidation leicht abtrennbar sind, beispielsweise durch Destillation.

Geeignete Lösungsvermittler sind beispielsweise Glykoläther ohne freie OH-Gruppen, wie Glykoläther der Formel $R^1O[CH_2CH(CH_3)O]_nR^2$, wobei n eine ganze Zahl von 1 bis 4 ist und R^1 und R^2 jeweils unabhängig voneinander C_1-C_4-Alkyl bedeuten. Besonders geeignet sind die Dimethyl-, Diäthyl- oder Methyl-äthyl-äther und die entsprechenden Propylenglykoläther der genannten allgemeinen Formel mit Siedepunkten im Bereich von 100 bis etwa 250 °C, beispielsweise Triäthylenglykoldimethyläther und insbesondere Diäthylenglykoldimethyläther. Auch andere Äther, wie Kronenäther, sind als Lösungsvermittler geeignet, wobei im Einzelfall der Aufwand für die Abtrennung und die Kosten für den Einsatz der Lösungsvermittler bei der Wirtschaftlichkeit des Verfahrens besonders berücksichtigt werden müssen.

Bevorzugtes Oxidationsmittel ist reiner Sauerstoff. Es können jedoch auch Mischungen von Sauerstoff mit unter den Reaktionsbedingungen inerten Gasen, z.B. in Form von Luft, beispielsweise Mischungen von Sauerstoff mit Inertgasen oder mit Luft, verwendet werden.

Im allgemeinen arbeitet man bei einem Gesamtdruck zwischen 0,5 und 100 bar. Bei steigendem Sauerstoffpartialdruck steigt die Reaktionsgeschwindigkeit deutlich an; jedoch kann hinsichtlich der Wirtschaftlichkeit des Verfahrens der Vorteil der höheren Reaktionsgeschwindigkeit durch den bei Anwendung von höherem Druck erforderlichen höheren apparativen Aufwand überkompensiert werden. Bevorzugt ist ein Druckbereich von Atmosphärendruck bis 10 bar (absolut), wobei das Arbeiten bei Atmosphärendruck besonders einfach auszuführen ist.

Das erfindungsgemäße Verfahren wird in der Regel bei einer Temperatur von 30 °C bis zum Siedepunkt des wäßrigen Mediums, vorzugsweise von 50 bis 5 °C, insbesondere 60 bis 90 °C, durchgeführt.

Die Reaktion kann bezüglich des pH-Wertes unterschiedlich durchgeführt werden, wobei die pH-Führung einen Einfluß auf die Anteile der einzelnen Produkte im Endprodukt haben kann. So kann die Reaktion beispielsweise im durch die Reaktionsprodukte sauer werdenden Milieu, d.h. in einem pH-Bereich von unter pH 7 durchgeführt werden. Ebenso ist es möglich, während der Oxidation den pH-Wert durch Zugabe von Basen, Säuren oder Puffergemischen zu steuern, wobei in der Regel ein pH-Wert von weniger als 8 eingehalten wird. Aber auch bei höheren pH-Werten kann die Oxidation noch durchgeführt werden.

Beispielsweise ist es möglich, durch kontinuierliche Zugabe einer Base wie Natriumhydroxyd, Kaliumhydroxyd oder entsprechender wäßriger Lösungen dieser Basen den pH-Wert weitgehend konstant im Bereich von 6,5 bis 8, vorzugsweise 7 bis 7,5 einzustellen. Bei letzterer Verfahrensweise wird das Oxidationsprodukt Furan-2,5-dicarbonsäure in Form des Disalzes bevorzugt gebildet. Nach einer anderen Ausführungsform beginnt man die Oxidation bei etwa pH 7 und führt sie ohne Zusatz von Säuren oder Basen fort. Im sauren Milieu bilden sich bevorzugt 2,5-Diformylfuran und 5- Formylfuran-2-carbonsäure.

Das erfindungsgemäße Verfahren verläuft in einem Dreiphasensystem aus festem Katalysator, wäßrigem Medium und gasförmigem Sauerstoff. Es kann in allen Apparaturen, die sich für die Durchführung von Reaktionen in der Flüssigphase mit oder ohne Anwendung von Überdruck eignen, durchgeführt werden. Beispiele dafür sind die Durchführung in einem Rührkessel oder in einer Blasensäule mit suspendiertem Katalysator. Die Oxidation kann aber auch als Festbettreaktion mit gekörntem Katalysator in einem Rieselphasenreaktor durchgeführt werden.

Die für die Bildung des jeweils gewünschten Reaktionsproduktes erforderliche Reaktionszeit wird zweckmäßig dadurch bestimmt, daß man in gewissen Zeitabständen Proben der Reaktionslösung entnimmt und analysiert. Beispielsweise kann die Ausbeute der Reaktionsprodukte auf einfache Weise durch Analyse einer Probe mit Hilfe der Hochdruckflüssigkeits-Chromatographie im Vergleich zu Standardlösungen laufend bestimmt werden. Die Optimierung der Reaktionszeit ist zu empfehlen, da eine unnötig verlängerte Einleitung von Sauerstoff verstärkt zu Überoxidationen, in der Folge beispielsweise zu Decarboxylierungen, und damit zum Verlust an Ausbeute bei den gewünschten Reaktionsprodukten führen kann.

Das Reaktionsgemisch kann nach bekannten Methoden aufgearbeitet werden. In einem geeigneten Verfahren werden zunächst der Lösungsvermittler und das Wasser destillativ entfernt und eine anschließende Reinigung durch Kristallisation oder Extraktion vorgenommen.

Das erfindungsgemäße Verfahren besitzt gegenüber den anfangs genannten herkömmlichen Oxidationsverfahren den Vorteil, daß die Bildung unerwünschter Produkte, wie nitrose Gase oder Schwefelverbindungen, vermieden wird und auch die Abtrennung von überschüssigem Oxidationsmittel entfällt. Bei der erfindungsgemäßen katalytischen Oxidation entsteht neben den gewünschten Produkten zwangsweise nur noch Wasser, das ohnehin als Lösungsmittel verwendet wird.

Die Oxidationsprodukte des 5-Hydroxymethylfurfurals sind wertvolle Zwischenprodukte für die Herstellung von Kunststoffen, Tensiden und Harzen. Beispielsweise können die Furan-2,5-dicarbonsäure als Polyesterkomponente und die Aldehyde 2,5-Diformylfuran und 5-Formylfuran-2-carbonsäure nach Umsetzung mit langkettigen Aminen als Tenside oder in Polymerisations- und Copolymerisationsreaktionen zur Herstellung neuer Kunststoffe und Harze eingesetzt werden.

Beispiele

1) In ein von außen beheiztes senkrecht angeordnetes Glasrohr (Durchmesser: 50 mm, Länge: 1200 mm), das mit einer Mischung aus 162 g 5-Hydroxymethylfurfural, 1460 g Wasser und 81 g eines handelsüblichen Katalysators (5 Gew.-% Platin auf Aktivkohle) gefüllt ist, leitet man von unten durch eine Glasfritte 80 Normal-Liter pro Stunde Sauerstoff bei einer Temperatur von 70 °C ein. Durch kontinuierliche Zugabe von 30 %iger wäßriger Natronlauge wird der pH-Wert bei 7 bis 7,5 gehalten. Nach einer Reaktionszeit von 2,5 Stunden enthält die Reaktionslösung 234 g Furan-2,5-dicarbonsäure in Form des Dinatriumsalzes, entsprechend einer Ausbeute von 91 % der Theorie.

2) In der im Beispiel 1 beschriebenen Apparatur werden 1500 g einer 20 %igen wäßrigen Lösung von 5-Hydroxymethylfurfural in Gegenwart von 50 g des in Beispiel 1 verwendeten Katalysators bei einer Temperatur von 85 °C mit 80 Normal-Liter pro Stunde Sauerstoff oxidiert. Nach einer Reaktionszeit von 11 Stunden, während der der pH-Wert durch Zugabe von 30 %iger wäßriger Natronlauge bei 7 bis 7,5 gehalten wurde, enthält das Reaktionsgemisch 376 g Furan-2,5-dicarbonsäure in Form des Dinatriumsalzes, entsprechend einer Ausbeute von 79 % der Theorie.

3) In der in Beispiel 1 beschriebenen Apparatur wird ein Gemisch aus 180 g 5-Hydroxymethylfurfural, 700 g Wasser, 700 g Diäthylenglykoldimethyläther und 75 g eines handelsüblichen Katalysators (5 Gew.-% Platin auf Aktivkohle) bei einer Temperatur von 60 °C mit Sauerstoff umgesetzt. Im Gegensatz zu den Beispielen 1 und 2 wird keine Natronlauge zugesetzt, so daß der pH-Wert durch Bildung von Carboxylgruppen von anfangs etwa 7 auf unter 7 sinkt. Nach einer Reaktionszeit von 8 Stunden enthält das Reaktionsgemisch 122 g (61 % der Theorie) 5-Formylfuran-2-carbonsäure, 43 g (24 % der Theorie) 2,5-Diformylfuran und 18 g (8 % der Theorie) Furan-2,5-dicarbonsäure.

4) Die in Beispiel 1 beschriebene Umsetzung wird 4 Stunden bei 60 °C unter sonst gleichen Bedingungen durchgeführt. Die Reaktionslösung enthält 252 g Furan-2,5-dicarbonsäure in Form des Dinatriumsalzes, entsprechend einer Ausbeute von 98 % der Theorie.

Ansprüche

1. Verfahren zur Oxidation von 5-Hydroxymethylfurfural, dadurch gekennzeichnet, daß 5-Hydroxymethylfurfural in wäßrigem Medium mit Sauerstoff als Oxidationsmittel in Gegenwart eines Katalysators, der mindestens ein Platinmetall enthält, oxidiert wird.

2. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß der Katalysator als Platinmetall Palladium, Platin oder ein Gemisch von Palladium und Platin, insbesondere nur Platin, enthält.

3. Verfahren nach Anspruch 1 oder 2, dadurch gekennzeichnet, daß der Katalysator aus 1 bis 10 Gew.-% Platinmetall und einem Träger, vorzugsweise Aktivkohle besteht.

4. Verfahren nach einem oder mehreren der Ansprüche 1 bis 3, dadurch gekennzeichnet, daß die Oxidation in einem Druckbereich von 0,5 bis 100 bar, vorzugsweise von Atmosphärendruck bis 10 bar und insbesondere bei Atmosphärendruck, durchgeführt wird.

5. Verfahren nach einem oder mehreren der Ansprüche 1 bis 4, dadurch gekennzeichnet, daß das wäßrige Medium einen unter den Reaktionsbedingungen gegenüber den Reaktionsteilnehmern inerten Lösungsvermittler, vorzugsweise in einer Menge von 10 bis 75 Gew.-%, insbesondere 30 bis 50 Gew.-%, enthält, bezogen auf die Menge an Wasser und Lösungsvermittler.

6. Verfahren nach Anspruch 5, dadurch gekennzeichnet, daß der Lösungsvermittler ein Glykoläther ohne Hydroxygruppen ist, vorzugsweise der Formel $R^1O[CH_2CH(CH_3)O]_nR^2$, wobei n eine ganze Zahl von 1 bis 4 ist und R^1 und R^2 jeweils unabhängig voneinander C_1-C_4-Alkyl bedeuten, insbesondere Diäthylenglykoldimethyläther ist.

7. Verfahren nach einem oder mehreren der Ansprüche 1 bis 6, dadurch gekennzeichnet, daß die Oxidation bei einer Temperatur von 30 °C bis zum Siedepunkt des wäßrigen Mediums, vorzugsweise von 50 bis 95 °C, insbesondere von 60 bis 90 °C, durchgeführt wird.

8. Verfahren nach einem oder mehreren der Ansprüche 1 bis 7, dadurch gekennzeichnet, daß das wäßrige Medium am Beginn der Oxidation 5 bis 30 Gew.-% bezogen auf die Menge von Wasser und Lösungsvermittler, 5-Hydroxymethylfurfural enthält.

9. Verfahren nach einem oder mehreren der Ansprüche 1 bis 8, dadurch gekennzeichnet, daß die Oxidation bei einem pH-Wert von höchstens 8 durchgeführt wird, wobei vorteilhaft der pH-Wert bei der Oxidation durch Zusatz einer Base im pH-Bereich von 6,5 bis 8, vorzugsweise 7 bis 7,5 gehalten wird.

10. Verfahren nach einem oder mehreren der Ansprüche 1 bis 9, dadurch gekennzeichnet, daß die Oxidation bei etwa pH 7 beginnt und ohne Zusatz von Säuren oder Basen durchgeführt wird.

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(54) **Verfahren zur Oxidation von 5-Hydroxymethylfurfural.**

(57) Verfahren zur Oxidation von 5-Hydroxymethylfurfural, dadurch gekennzeichnet, dar 5-Hydroxymethylfurfural in wäßrigem Medium mit Sauerstoff als Oxidationsmittel in Gegenwart eines Katalysators, der mindestens ein Platinmetall enthält, oxidiert wird.

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Nummer der Anmeldung

EP 89 11 3659

EINSCHLÄGIGE DOKUMENTE

Kategorie	Kennzeichnung des Dokuments mit Angabe, soweit erforderlich, der maßgeblichen Teile	Betrifft Anspruch	KLASSIFIKATION DER ANMELDUNG (Int. Cl.5)
A	GB-A-2 188 927 (INTEROX CHEMICALS LTD.) * Seite 5, Anspruch 1 * ---	1	C 07 D 307/68
A	US-A-3 890 381 (K. TADAMITSU et al.) * Spalte 7, Anspruch 1 * ---	1	
A	EP-A-0 048 974 (KAO SOAP CO.) * Seite 17, Anspruch * ---	1	
A	EP-A-0 073 545 (STAMICARBON) * Seite 5, Anspruch 1 * -----	1	

RECHERCHIERTE SACHGEBIETE (Int. Cl.5)

C 07 D 307/00
C 07 C 51/00
C 07 B 33/00

Der vorliegende Recherchenbericht wurde für alle Patentansprüche erstellt

Recherchenort	Abschlußdatum der Recherche	Prüfer
BERLIN	28-11-1989	KYRIAKAKOU G

KATEGORIE DER GENANNTEN DOKUMENTE

X : von besonderer Bedeutung allein betrachtet
Y : von besonderer Bedeutung in Verbindung mit einer anderen Veröffentlichung derselben Kategorie
A : technologischer Hintergrund
O : nichtschriftliche Offenbarung
P : Zwischenliteratur

T : der Erfindung zugrunde liegende Theorien oder Grundsätze
E : älteres Patentdokument, das jedoch erst am oder nach dem Anmeldedatum veröffentlicht worden ist
D : in der Anmeldung angeführtes Dokument
L : aus andern Gründen angeführtes Dokument

& : Mitglied der gleichen Patentfamilie, übereinstimmendes Dokument

EPO FORM 1503 03.82 (P0403)

IMPROVEMENTS IN POLYMERS

Patent Number:	GB 621971 A	
Inventor(s):		
Applicant(s):	JAMES GORDON NAPIER DREWITT; JAMES LINCOLN	
Classification:	**- international:**	C08G63/42; C08G63/672; C08G63/688; C08G63/82
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Application number:	GB19460033600 19461112	
Priority number(s):	GBX2551731 19461112; GB19460033600 19461112	
Also published as:	US2551731 (A)	

Abstract of GB 621971 A

Polyesters are prepared by reacting glycols with dicarboxylic acids of which at least one contains a heterocyclic ring and is such that its di-methyl ester melts above 100 DEG C. (preferably at 120 DEG C. or above). The carboxyl groups are preferably attached to the ring directly and as far apart as possible. Specified ingredients are: di-acids-thiophene-2 : 4- and 2 : 5-, furane-2 : 5-, 1 : 4 - pyrane - 2 : 6-, pyridine - 2 : 5- and 2 : 6-, pyrrole-2 : 5-, pyrazole-3 : 5-, 4-methyl-pyrazole-3 : 5-, 2 : 4 : 6 - trimethyl - 1 : 4 - dihydropyridine - 3 : 5-, 3 : 5 - dimethylpyrrole - 2 : 4-dicarboxylic acids; furane-2 : 5-diacrylic acid; 5 : 51-benzal-bis-(2 : 4 - dimethyl - pyrrole - 3 - carboxylic acid); glycols-ethylene, tri-, tetra-, hexa- and decamethylene, propylene, b -chlor-trimethylene and p-xylylene glycols. The reagents may be replaced by their ester-forming derivatives, e.g. acids, by their dialkyl and diaryl esters, half-esters, acid chlorides, half-ester-half-acid chlorides, mixed anhydrides (e.g. with acetic acid), polyanhydrides or half-ester-anhydrides, and glycols by e.g. mono- or di-formates or -acetates. The products may be used in coating and moulding compositions or as films, filaments, or softening agents. They may be mixed with plasticizers, e.g. sulphonamide, phenolic, urea and thiourea plasticizers; cellulose derivatives, e.g. cellulose acetate, aceto-butyrate, butyrate, aceto-stearate, ethyl, oxyethyl and benzyl cellulose, oxyethyl cellulose acetate; dyestuffs; and pigments. In examples: furane-2 : 5-thiophene-2 : 5- or pyrazole-3 : 5-dicarboxylic acid dimethyl ester was heated with ethylene glycol in the presence of sodium methylate and magnesium ribbon, first under reflux, then open to the atmosphere, and finally under high vacuum. The use of N : N1 - diphenyl - piperazine-, N : N1 - diphenyl - tetrahydroglyoxaline- and N : N1 - diphenyl - ethylenetrimethylenediamine-4 : 41-dicarboxylic acids is disclaimed.

PATENT SPECIFICATION

621,971

Application Date: Nov. 12, 1946. No. 33600/46.

Complete Specification Left: Oct. 27, 1947.

Complete Specification Accepted: April 25, 1949.

Index at acceptance:—**Class 2(v)**, R3c8, R3d(1: 2: 5: 6).

PROVISIONAL SPECIFICATION

Improvements in Polymers

We, JAMES GORDON NAPIER DREWITT and JAMES LINCOLN, both British subjects, of Celanese House, 22 and 23, Hanover Square, London, W.1, do hereby declare the nature of this invention to be as follows:—

This invention relates to the production of polymers, and is especially concerned with polyesters.

According to the invention, valuable polyesters are obtained by reacting a glycol with a dicarboxylic acid containing a heterocyclic ring. In particular we use dicarboxylic acids in which two carboxylic groups are attached directly or through one or more atoms to a heterocyclic ring, the acids being such that their dimethyl esters melt at a temperature in the range 100—120° C. or higher. By this means, high melting polyesters may be obtained, the melting point in many cases being above 200° C.

The reagents may be used in such proportions and the reaction continued for such a time that a product of molecular weight sufficient to form films is obtained. Preferably the reaction conditions are such that a polymer is obtained capable of forming films and/or of forming filaments orientable by cold-drawing.

Among the heterocyclic compounds which may be used according to the present invention are thiophene-2.4- and 2.5-dicarboxylic acids, furane-2.5-dicarboxylic acid, pyrane-2.6-dicarboxylic acid, pyridine-2.5- and 2.6-dicarboxylic acids, and furane-2.5-diacrylic acid. The most suitable reagents are those in which the two carboxylic groups are attached directly to an unsaturated heterocyclic 5- or 6-membered ring in positions as remote as possible from each other. If the direct bond in such compounds is attached to a ring atom which is itself attached only to two other atoms, then the carboxylic group is substantially co-planar with the ring. Such is the case, for example in the 2.5-positions of thiophene, furane, or pyridine, and this type of compound appears to be the best.

All the above reagents are free from functional groups other than the desired carboxylic groups, and such reagents are the preferred ones according to the present invention. However, other reagents can be used, as for example pyrrole-2.5-dicarboxylic acid, pyrazole-3.5-dicarboxylic acid, 4-methyl-pyrazole-3.5-dicarboxylic acid, 2.4.6-trimethyl-1.4-dihydro-pyridne - 3.5 - dicarboxylic acid, 3.5-dimethyl pyrrole-2.4-dicarboxylic acid and 5.5¹-benzal-bis-(2.4-dimethyl-pyrrol-3-carboxylic acid). Such compounds as the pyrrole-2.5-dicarboxylic acid and the 3.5-dimethyl pyrrole-2.4-dicarboxylic acid may, prior to the condensation according to the present invention, be subjected alone to a preliminary condensation to form the cyclic amide, the product being then condensed with a glycol in accordance with the invention.

The above heterocyclic acids may be condensed with any suitable glycol, as for example ethylene glycol, trimethylene glycol, tetramethylene glycol, hexamethylene glycol, decamethylene glycol, propylene glycol, β-chlor-trimethylene glycol and paraxylylene glycol. Of these, the glycols of the general formula $HO(CH_2)_nOH$, n being an integer at least 2, are the most suitable.

In carrying out polyester formation with relatively volatile glycols, the diacid can be heated, preferably in an inert atmosphere or stream of inert gas, with at least an equimolecular proportion of the glycol, and preferably with an excess, e.g. 1.25—2.5 molecular proportions of the glycol. The inital heating can be in the neighbourhood of 200° C., and subsequent heating at a temperature above the melting point of the polymer, say 220—280° C. The final heating may advantageously be carried out in a high vacuum, i.e. at an absolute pressure of less than 5 mms., and better still, less than 0.1 mm., of

[Price 2/-

Price 4s 6d.

mercury. Similar considerations apply to the reaction of di-acids with non-volatile glycols but in this case it is preferred to use approximately equimoles of the two components, e.g. within 5%, or better within 2%, of the equimolar proportions.

In some cases a smoother reaction can be obtained by using a solvent, for example meta-cresol, for the ingredients and the resulting polymers. In place of the di-acid, there can be used the equivalent ester-forming derivatives of the acids, for example the dialkyl or diaryl esters, the corresponding half esters, the acid chlorides, the half-ester half-acid-chlorides or mixed anhydrides, e.g. with acetic acid, or a polyanhydride or a half-ester-anhydride. It is particularly desirable to use the esters where acids are used which tend to be unstable and to develop carbon dioxide under the conditions of the reaction. When using di-esters, it is of advantage to include in the reaction mixture an ester-interchange catalyst, as for example an alkali metal, magnesium or tin. Reactions with acid chlorides can be effected even at room temperature, and if desired a basic substance can be present, e.g. pyridine, to neutralise the hydrogen chloride evolved.

In a similar way the free glycol may be replaced in the process of the invention by an equivalent ester-forming reagent. Thus, for example, instead of the glycol, we may employ its mono- or di-formate or mono- or di-acetate.

If desired, mixtures of di-acids can be condensed with mixtures of glycols, or a single di-acid can be condensed with a mixture of glycols and *vice versa*, at least one of the di-acids being of the heterocyclic character described above.

The polymers of the invention are of value in coating compositions and in moulding, and, when of sufficiently high molecular weight, can be spun into filaments. In forming filaments, the choice of the method of spinning depends in part on the properties of the polymers. Where solutions in organic solvents can readily be produced, dry spinning methods may be employed with solutions in volatile solvents, and wet spinning methods with solutions in volatile or even comparatively non-volatile solvents. The polymers can be spun by melt spinning methods, i.e. by extruding a melt of the polymer through suitable orifices. In general, the temperature of the polymer to be extruded should be some 10—30° above the melting point of the polymer. This melting temperature may be modified to some extent by mixing the polymer with suitable proportions of plasticisers, for example sulphonamide plasticisers, phenolic plasticisers, urea and thiourea plasticisers. Such plasticisers may either be left in the products or may be partly or completely extracted therefrom.

The filaments so formed may be drawn out at comparatively low temperatures, or even at atmospheric temperature, to very fine filaments having high tenacity and good elasticity. The resulting filaments may then be used for any of the purposes to which artificial silks have in the past been applied.

While the invention is especially directed to the manufacture and application of fibre-forming polymers, it is not limited thereto and embraces the production of polymers suitable, for example, for use as softening agents, coatings and film-forming substances. Moreover, for these applications the polymers of the present invention may be mixed with other compatible fibre-forming, film-forming or lacquer substances or other ingredients, for example cellulose acetate, aceto-butyrate, butyrate and aceto-stearate, ethyl cellulose, oxyethyl cellulose, oxyethyl cellulose acetate, benzyl cellulose and other cellulose derivatives, plasticisers or softening agents, dyestuffs and pigments. Further, the invention includes the preparation of higher polymers by further condensation of low polymers obtainable from the above described components.

Dated this 11th day of November, 1946.
STEPHENS & ALLEN,
Chartered Patent Agents,
Wykeham House, Gordon Avenue,
Stanmore, Middlesex.

COMPLETE SPECIFICATION

Improvements in Polymers

We, JAMES GORDON NAPIER DREWITT, a British subject, of the Works of British Celanese Limited, Spondon, near Derby, (formerly of Celanese House, 22/23, Hanover Square, London, W.1), and JAMES LINCOLN, a British subject, of Celanese House, 22/23, Hanover Square, London, W.1, do hereby declare the nature of this invention, and in what manner the same is to be performed, to be

particularly described and ascertained in and by the following statement:—

This invention relates to the production of polymers, and is especially concerned with polyesters.

According to the invention, valuable polyesters are obtained by reacting a glycol with a dicarboxylic acid containing a heterocyclic ring in which the two carboxylic acid groups are attached directly or through one or more atoms to the heterocyclic ring, the acid being such that its dimethyl ester melts above 100° C. and preferably at 120° C. or higher.

The reagents may be used in such proportions and the reaction continued for such a time that a product of molecular weight sufficient to form films is obtained. Preferably the reaction conditions are such that a polymer is obtained capable of forming films and/or of forming filaments orientable by cold-drawing.

Among the heterocyclic dicarboxylic acids which may be used according to the present invention are thiophene-2.4- and 2.5-dicarboxylic acids, furane-2.5-dicarboxylic acid, 1.4-pyrane-2.6-dicarboxylic acid, pyridine-2.5- and 2.6-dicarboxylic acids and furane-2.5-diacrylic acid. The most suitable reagents are those in which the two reactive groups are attached directly to an unsaturated heterocyclic ring in positions as remote as possible from each other. If the direct bond in such compounds is attached to a ring atom which is itself attached only to two other atoms, then the carboxylic group is substantially co-planar with the ring. Such is the case, for example in the 2.5-positions of thiophene, furane, or pyridine, and this type of compound appears to be the best.

All the above reagents are free from functional groups other than the desired carboxylic groups, and such reagents are the preferred ones according to the present invention. However, other reagents can be used, as for example pyrrole-2.5-dicarboxylic acid, pyrazole-3.5-dicarboxylic acid, 4-methyl-pyrazole-3.5-dicarboxylic acid, 2.4.6-trimethyl-1.4-dihydro-pyridine-3.5-dicarboxylic acid, 3.5-dimethyl pyrrole-2.4-dicarboxylic acid and 5.5¹-benzal-bis-(2.4-dimethyl-pyrrole-3-carboxylic acid). Such compounds as the pyrrole-2.5-dicarboxylic acid and the 3.5-dimethyl-pyrrole-2.4-dicarboxylic acid may, prior to the condensation according to the present invention, be subjected alone to a preliminary condensation to form the cyclic amide, the product being then condensed with a glycol in accordance with the invention.

The above heterocyclic acids may be condensed with any suitable glycol, as for example ethylene glycol, trimethylene glycol, tetramethylene glycol, hexamethylene glycol, decamethylene glycol, propylene glycol, β-chlor-trimethylene glycol and para-xylene glycol. Of these, the glycols of the general formula $HO(CH_2)_nOH$, n being an integer at least 2, are the most suitable.

In carrying out polyester formation with relatively volatile glycols the di-acid can be heated, preferably in an inert atmosphere or stream of inert gas, with at least an equimolecular proportion of the glycol, and preferably with an excess, e.g. 1.25—2.5 molecular proportions of the glycol. The initial heating can be in the neighbourhood of 200° C., and subsequent heating at a temperature above the melting point of the polymer, say 220—280° C. The final heating may advantageously be carried out in a high vacuum. i.e. at an absolute pressure of less than 5 mms., and better still, less than 1 mm., of mercury. Similar considerations apply to the reaction of di-acids with non-volatile glycols, but in this case it is preferred to use approximately equimoles of the two components, e.g. within 5%, or better within 2%, of the equimolar proportions.

In some cases a smoother reaction can be obtained by using a solvent, for example meta-cresol, for the ingredients and the resulting polymers. In place of the di-acid, there can be used the equivalent ester-forming derivatives of the acids, for example the dialkyl or diaryl esters, the corresponding half esters, the acid chlorides, the half-ester half-acid-chlorides or mixed anhydrides, e.g. with acetic acid, or a poly-anhydride or a half-esteranhydride. It is particularly desirable to use the esters where acids are used which tend to be unstable and to develop carbon dioxide under the conditions of the reaction. When using di-esters, it is of advantage to include in the reaction mixture an ester interchange catalyst, as for example an alkali metal, magnesium or tin. Reactions with acid chlorides can be effected even at room temperature, and if desired a basic substance can be present, e.g. pyridine, to neutralise the hydrogen chloride evolved.

In a similar way the free glycol may be replaced in the process of the invention by an equivalent ester-forming reagent. Thus, for example, instead of the glycol, we may employ its mono- or di-formate or mono- or di-acetate.

If desired, mixtures of di-acids can be condensed with mixtures of glycols, or a single di-acid can be condensed with a mixture of glycols and *vice versa*, at least one of the di-acids being of the heterocyclic character described above.

The polymers of the invention are of value in coating compositions and in moulding, and, when of sufficiently high molecular weight, can be spun into filaments. In forming filaments, the choice of the method of spinning depends in part on the properties of the polymers. Where solutions in organic solvents can readily be produced, dry spinning methods may be employed with solutions in volatile solvents, and wet spinning methods with solutions in volatile or even comparatively non-volatile solvents. The polymers can be spun by melt spinning methods, i.e. by extruding a melt of the polymer through suitable orifices. In general, the temperature of the polymer to be extruded should be some 10—30° above the melting point of the polymer. This melting temperature may be modified to some extent by mixing the polymer with plasticisers, for example sulphonamide plasticisers, phenolic plasticisers, urea and thiourea plasticisers. Such plasticisers may either be left in the products or may be partly or completely extracted therefrom.

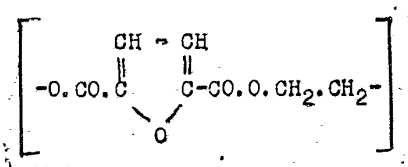
The filaments so formed may be drawn out at comparatively low temperatures, or even at atmospheric temperature, to very fine filaments having high tenacity and good elasticity. The resulting filaments may then be used for any of the purposes to which artificial silks have in the past been applied.

While the invention is especially directed to the manufacture and application of fibre-forming polymers, it is not limited thereto and embraces the production of polymers suitable, for example, for use as softening agents, coatings and film-forming substances. Moreover, for these applications the polymers of the present invention may be mixed with other compatible fibre-forming, film-forming or lacquer substances or other ingredients, for example cellulose acetate, aceto-butyrate, butyrate and aceto-stearate, ethyl cellulose, oxyethyl cellulose, oxyethyl cellulose acetate, benzyl cellulose and other cellulose derivatives, plasticisers or softening agents, dyestuffs and pigments. Further, the invention includes the preparation of higher polymers by further condensation of low polymers obtainable from the above described components.

The following examples illustrate the invention, all parts being by weight:—

EXAMPLE 1.

18.4 parts (1 mole) of furane-2.5-dicarboxylic acid dimethyl ester (M.P. 109—110° C.) were mixed with 10 parts (about 1.6 moles) of ethylene glycol, and 0.025 parts of sodium dissolved in 8 parts of methanol and a small quantity of magnesium ribbon added. The mixture was first heated at 160° C. for half an hour using a water-cooled reflux condenser and then for a further hour with an air-cooled reflux. At this stage the product was a crystalline mass with a melting point of under 120° C. The condenser was removed and the mass heated for 2 hours at 220° C. with the polymerising vessel open to the atmosphere. The vessel was then connected to a high vacuum pump and a hydrogen bubbling apparatus was fitted and the heating was continued with a stream of hydrogen bubbling through the molten mass and under an absolute pressure of 3 mms. of mercury, first at 190° C. for 2 hours and finally at 220° C. for 3 hours. The product had a melting point of 205—210° C. and readily yielded filaments from a melt. It showed on analysis a carbon content, on an ash-free basis, of 52.83%. The theoretical value for the infinite polymer



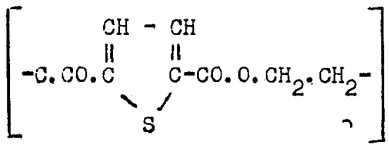
is 52.75%.

EXAMPLE 2.

Equal parts of furane-2.5-dicarboxylic acid and ethylene glycol (molar ratio 1:2.52) were refluxed for 3 hours at 180° C., the reflux condenser removed and heating continued for a further 4 hours at 210° C. A vacuum pump was then connected and heating continued for a further 7 hours at the same temperature and under an absolute pressure of 2 mms. of mercury. The resulting polymer had properties very similar to those of the product produced according to Example 1.

EXAMPLE 3.

15 parts (1 mole) of thiophene-2.5-dicarboxylic acid dimethyl ester (recrystallised from methanol, M.P. 152° C.), 7.5 parts (about 1.6 moles) of ethylene glycol, a solution of 0.025 parts of sodium in 8 parts of methanol and a small quantity of magnesium ribbon were heated for 40 minutes at 160° C. under a water-cooled reflux in an atmosphere of hydrogen and then for 3 hours under an air-cooled reflux. The condenser was then removed and heating continued at 230° C. for 3 hours and then for a further 7 hours under an absolute pressure of 2—3 mms. of mercury with a temperature rising from 170° C. to 200° C. The product, melting point 180—190° C., readily gave fibres and had a carbon content, on an ash-free basis, of 49.14%. Theory for the infinite polymer



is 48.49%.

EXAMPLE 4.

15 parts (1 mole) of pyrazole-3.5-dicarboxylic acid dimethyl ester (recrystallised from benzene, M.P. 155° C.), 10 parts (about 2 moles) of ethylene glycol, a solution of 0.01 parts of sodium in 8 parts of methanol and a small quantity of magnesium ribbon were heated in hydrogen first for 45 minutes at 160° C. under a water-cooled reflux and then for 2 hours at 180° C. under an air-cooled condenser. The condenser was then removed and heating continued for 1 hour at 200° C. and 2 hours at 225° C. Finally the polymer was heated for 5 hours at 200—210° C. under an absolute pressure of 2—3 mms. The resulting polymer, which was translucent, melted at 200—210° C.

We do not claim the production of polyesters using N.N^1-diphenyl-piperazine-4.4^1-dicarboxylic acid, N.N^1-diphenyl-tetrahydroglyoxaline - 4.4^1 - dicarboxylic acid or N.N^1 - diphenyl-ethylene-trimethylene-diamine-4.4^1-dicarboxylic acid, nor do we claim polymers produced with the aid of these acids.

Having now particularly described and ascertained the nature of our said invention, and in what manner the same is to be performed, we declare that, subject to the foregoing disclaimer, what we claim is:—

1. Process for the production of polymers which comprises heating a glycol with a heterocyclic dicarboxylic acid whose dimethyl ester melts at above 100° C.

2. Process according to Claim 1, wherein the glycol is ethylene glycol.

3. Process according to Claim 1 or 2, wherein the heterocyclic dicarboxylic acid is one whose dimethyl ester melts at above 120° C.

4. Process according to any of Claims 1—3, wherein the dicarboxylic acid or glycol is replaced by an ester-forming derivative thereof.

5. Process according to any of the preceding claims, wherein the later stages of the condensation are carried out under high vacuum.

6. Process according to any of the preceding claims, wherein the condensation is continued until a filament-forming polymer is produced.

7. Process for the production of polymers, substantially as hereinbefore described.

8. Polymers whenever obtained by any of the processes hereinbefore particularly described and ascertained or by their obvious chemical equivalents.

9. Filaments and films having a basis of a polymer obtainable according to any of Claims 1—7.

Dated this 25th day of October, 1947.

STEPHENS & ALLEN,
Chartered Patent Agents,
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METHOD FOR PRODUCING 2,5-FURANDICARBOXYLIC ACID

Patent Number:	JP 2009-001519 A
Inventor(s):	MIURA TOSHINARI; SHINAGAWA HIROSHI; HORIE HITOSHI; KONO TAKENOBU
Applicant(s):	CANON KK
Classification:	**- international:** C07D307/68; C07B61/00 **- cooperative:**
Application number:	JP20070163711 20070621
Priority number(s):	JP20070163711 20070621
Also published as:	JP5147309 (B2)

Abstract of JP 2009-001519 A

PROBLEM TO BE SOLVED: To provide a method for easily producing 2,5-furandicarboxylic acid from 5-hydroxymethylfurfural in high efficiency and yield and to provide a production method enabling the reuse of a catalyst to effectively utilize resources.

SOLUTION: The method for producing 2,5-furandicarboxylic acid comprises the oxidation of 5-hydroxymethylfurfural, (A) in the presence of a catalyst composed mainly of ruthenium, cobalt and cerium, (B) under heating, (C) under pressure, (D) in an aqueous solution, (E) with molecular oxygen.

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最終頁に続く

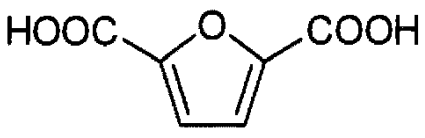
(54)【発明の名称】２，５－フランジカルボン酸の製造方法

(57)【要約】
【課題】本発明の課題は、簡単に効率よく高収率で５－ヒドロキシメチルフルフラールから２，５－フランジカルボン酸を製造する方法を提供することにある。また、触媒の再利用が可能で、資源を有効に利用することが可能な製造方法を提供することにある。
【解決手段】そこで、本発明に係る２，５－フランジカルボン酸の製造方法は、５－ヒドロキシメチルフルフラールを、（Ａ）ルテニウム、コバルト及びセリウムを主成分とする触媒の存在下、（Ｂ）加熱条件下、（Ｃ）加圧条件下、（Ｄ）水溶液中、（Ｅ）分子状酸素により、酸化することを特徴とする。
【選択図】なし

【特許請求の範囲】
【請求項1】
５－ヒドロキシメチルフルフラールを、（Ａ）ルテニウム、コバルト及びセリウムを主成分とする触媒の存在下、（Ｂ）加熱条件下、（Ｃ）加圧条件下、（Ｄ）水溶液中、（Ｅ）分子状酸素により、酸化することを特徴とする２，５－フランジカルボン酸の製造方法。
【請求項2】
前記触媒が、硝酸コバルト（II）６水和物、硝酸セリウム（III）６水和物及び塩化ルテニウム（III）ｎ水和物より調製した触媒であることを特徴とする請求項１に記載の２，５－フランジカルボン酸の製造方法。
【請求項3】
前記加熱条件が、温度を７０℃～１００℃とする条件であることを特徴とする請求項１又は２に記載の２，５－フランジカルボン酸の製造方法。
【請求項4】
前記加圧条件が、反応雰囲気の圧力を１ＭＰａ～４０ＭＰａとする条件であることを特徴とする請求項１乃至３のいずれかの請求項に記載の２，５－フランジカルボン酸の製造方法。
【請求項5】
前記加圧条件が、分子状酸素を用いて反応雰囲気の圧力を１ＭＰａ～４０ＭＰａとする条件であることを特徴とする請求項１乃至３のいずれかの請求項に記載の２，５－フランジカルボン酸の製造方法。

【発明の詳細な説明】
【技術分野】
【0001】
本発明は、穏やかな条件で、５－ヒドロキシメチルフルフラール（以下、５－ＨＭＦと略す）から効率よく、高収率で２，５－フランジカルボン酸（以下、ＦＤＣＡと略す）を製造する方法に関する。
【背景技術】
【0002】
ＦＤＣＡは医薬、農薬、殺虫剤、抗菌剤、香料、高分子材料、その他各種の分野の中間体として利用価値が高く、様々な製造方法について検討されている。
【0003】
そのうちの一つとして、５－ＨＭＦを触媒存在下における酸化によりＦＤＣＡを得る製造方法が検討されている。例えば、５－ＨＭＦから、アルカリ性水溶液中で活性炭担持白金触媒および酸化銀酸化銅触媒存在下、常温で酸素バブリングを行い選択的に酸化してＦＤＣＡを得る方法が報告されている（特許文献１）。しかしながら、上記特許文献１に記載の方法は、白金がアルカリ水溶液中で徐々に溶解するため、白金の回収においてロスが避けられない欠点や触媒活性が低下する欠点等があった。また、白金は埋蔵量が少ない貴金属であるため、工業的生産への適用には問題があった。
【0004】
一方、不均一触媒のルテニウム（Ｒｕ）、コバルト（Ｃｏ）及びセリウム（Ｃｅ）を主成分とする触媒を利用し、アルコールを対応するカルボニル化合物に酸化する方法が報告されている（非特許文献１）。この方法では、ベンゾトリフルオリドを溶媒として使用し、６０℃で空気バブリングを行うことにより収率良く酸化する方法である。非特許文献１では、触媒の再利用についても記載されている。しかしながら、非特許文献１の製造方法では、ベンゾトリフルオリドに溶解しない基質は酸化不可能である。５－ＨＭＦはベンゾトリフルオリドに溶解しないので、非特許文献１に記載の方法でＦＤＣＡを製造するのは困難であった。
【特許文献1】米国特許３，３２６，９４４
【非特許文献1】Ｔｅｔｒａｈｅｄｒｏｎ　Ｌｅｔｔｅｒｓ　４３巻　（２００２年）

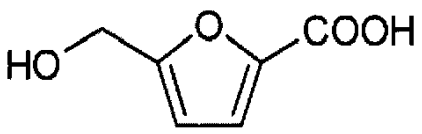
７１７９ページ－７１８３ページ
【発明の開示】
【発明が解決しようとする課題】
【0005】
本発明の課題は、簡単に効率よく高収率で５－ＨＭＦからＦＤＣＡを製造する方法を提供することにある。また、再利用が可能で資源を有効に利用することができる触媒を用いたＦＤＣＡの製造方法を提供することにある。
【課題を解決するための手段】
【0006】
本発明者らは、５－ＨＭＦからＦＤＣＡを製造できる方法について鋭意研究した。その結果、水中でルテニウム、コバルト及びセリウムを主成分とする触媒を用い、加熱条件及び加圧条件下で、５－ＨＭＦからＦＤＣＡを高収率で得ることが出来る事を見出した。
【0007】
そこで、本発明に係るＦＤＣＡの製造方法は、
５－ＨＭＦを、
（Ａ）ルテニウム、コバルト及びセリウムを主成分とする触媒の存在下、
（Ｂ）加熱条件下、
（Ｃ）加圧条件下、
（Ｄ）水溶液中、
（Ｅ）分子状酸素により、
酸化することを特徴とする。
【発明の効果】
【0008】
本発明に係るＦＤＣＡの製造方法は、簡単で効率よく高収率でＦＤＣＡを製造することができる。また、本発明に使用する触媒は再利用が可能であり、資源を有効に利用したＦＤＣＡの製造ができる。
【発明を実施するための最良の形態】
【0009】
本発明に係るＦＤＣＡの製造方法は、
５－ＨＭＦを、
（Ａ）ルテニウム、コバルト及びセリウムを主成分とする触媒の存在下、
（Ｂ）加熱条件下、
（Ｃ）加圧条件下、
（Ｄ）水溶液中、
（Ｅ）分子状酸素により、
酸化することを特徴とする。
【0010】
ここで、ＦＤＣＡは以下の化学式で表されるものである。
【0011】
【化1】



ＦＤＣＡ

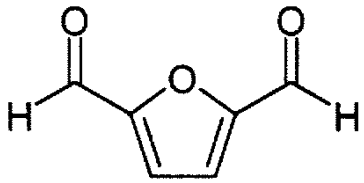
【0012】
また、本発明に係る反応により得られるＦＤＣＡ以外のフラン環化合物としては、ヒドロキシメチルフロ酸、２，５－ジホルミルフラン（ＤＦＦ）、５－ホルミルフラン－２－カルボン酸（ＣＦＦ）等が挙げられ、以下にその化学式を示す。

【0013】
【化2】



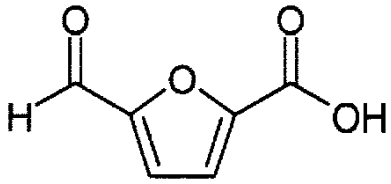
ヒドロキシメチルフロ酸

【0014】
【化3】



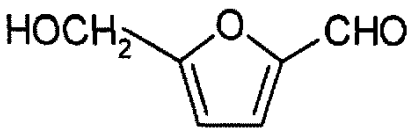
ＤＦＦ

【0015】
【化4】



ＣＦＦ

【0016】
５－ＨＭＦは、フルクトースやグルコースを構成単位に持つ糖類を酸性触媒の存在下で加熱脱水反応させることにより得られるフラン化合物であり、例えば、フルクトース、イヌリン、キクイモ、とうもろこし、サトウキビ、キャッサバ等農作物や、木材、ナフサ由来のもの等を使用することができる。なお、本発明のフラン環化合物の製造方法に用いる５－ＨＭＦは、以下の化学式で表されるものである。
【0017】
【化5】



５－ＨＭＦ

【0018】
本発明に用いる非特許文献１に記載のルテニウム、コバルト及びセリウムを主成分とする触媒は、大気圧酸素下で効果的に各種アルコールをカルボニル化合物に酸化する不均一触媒として知られている。特に一級脂肪族アルコールをカルボン酸に変換する高い活性を有することが知られている。
【0019】
上記ルテニウムは、例えば、塩化ルテニウム（ＩＩＩ）ｎ水和物を材料とすることができる。上記コバルトは、例えば、硝酸コバルト（ＩＩ）６水和物を材料とすることができる。

上記セリウムは、例えば、硝酸セリウム（III）６水和物を材料とすることができる。上記触媒の調製は、例えば、非特許文献１に記載の方法で調製することができる。

【0020】

上記触媒の使用量は、例えば、５－ＨＭＦに対して、質量で０．１倍から１０倍が好ましく、１倍から５倍がより好ましい。

【0021】

本発明に用いる水の使用量は、例えば、５－ＨＭＦ対して質量で１倍から１００倍が好ましく、１０倍から５０倍がより好ましい。

【0022】

本発明に用いる分子状酸素は、酸素ガスや酸素を含んだガス、例えば、空気として、反応に供することができる。

【0023】

本発明における加圧条件としては、反応温度により適宜選択されるが、反応雰囲気の圧力を１ＭＰａ～４０ＭＰａとすることが好ましく、５ＭＰａ～２０ＭＰａとすることがより好ましく、１０ＭＰａ～１５ＭＰａとすることがさらに好ましい。１ＭＰａ未満では実用的な反応速度が得られない場合がある。一方、４０ＭＰａを越える圧力では副反応が促進されるので、ＦＤＣＡの選択率が低下してしまう場合がある。また、加圧条件は、酸素ガスを容器に封入して圧力を調整することで行うこともできる。

【0024】

本発明では、このような加圧条件を達成するため、反応装置としてオートクレーブ等の加圧可能な装置内で反応を行うことができる。

【0025】

本発明における加熱条件としては、例えば、温度を５０℃～２００℃とすることが好ましく、６０℃～１２０℃とすることがより好ましく、７０℃～１００℃とすることがさらに好ましい。５０℃以上とすることで、５－ＨＭＦをＦＤＣＡに酸化することができ、２００℃以下とすることで、原料の分解を抑えることができる。

【0026】

なお、上記５－ＨＭＦ、触媒及び水の混合の順番は、いずれの順番であってもよい。

【実施例】

【0027】

以下に、本発明のＦＤＣＡの製造方法を具体的に詳細に説明するが、本発明の技術的範囲はこれらに限定されるものではない。

【0028】

（触媒の調製）

本実施例で用いた触媒は非特許文献１に記載された方法と同様に調整した。

【0029】

まず、炭酸ナトリウム１．４２ｇ（キシダ化学特級、純度９９．５％）と水酸化ナトリウム１．９３ｇ（キシダ化学特級、純度９６％）を蒸留水に溶解し、３０ｍｌとした。その溶液に、硝酸コバルト（II）６水和物３．０３ｇ（キシダ化学特級、純度９８％）、硝酸セリウム（III）６水和物２．２６ｇ（キシダ化学特級、純度９８％）および塩化ルテニウム（III）ｎ水和物０．３５ｇ（Ｒｕ含有量４３．４質量％、キシダ化学化学用）を蒸留水に溶解して２０ｍｌとした水溶液をゆっくり加えた。その後、６５℃で１８時間激しく撹拌した。得られた暗褐色の泥状物をろ過し蒸留水で洗い、１１０℃で１２時間乾燥し、黒色粉末のルテニウム、コバルト及びセリウムを主成分とする触媒を得た。

【0030】

（分析方法）

高速液体クロマトグラフィー（ＨＰＬＣ）

（ＨＰＬＣの測定条件）

装置：日本分光株式会社高速液体クロマトグラフ

カラム：Ｓｈｏｄｅｘ　ＳＵＧＡＲ　ＳＨ１０１１（１本使用）

カラム温度：８０℃
移動相：３ｍＭ　過塩素酸（キシダ化学製の過塩素酸をイオン交換水で希釈したもの）
流量：０．６ｍｌ／ｍｉｎ（０～２０ｍｉｎ）、１．４ｍｌ／ｍｉｎ（２０～３５ｍｉｎ）
検出器：ＲＩ
リテンションタイム：５－ＨＭＦ（２４．０ｍｉｎ）、ＤＦＦ（２６．０ｍｉｎ）、ＣＦＦ（１８．０ｍｉｎ）、ＦＤＣＡ（１４．３ｍｉｎ）
（試薬）
７０％過塩素酸：キシダ化学製、特級、５００ｇ入り、比重１．６７
５－ＨＭＦ：アルドリッチ製
（票品）
ＤＦＦ：東京化成工業製
ＣＦＦ：東京化成工業製
ＦＤＣＡ：自社製（水で再結晶した物）（^{1}Ｈ－ＭＮＲ。カルボン酸のＨ：δ＝３．３７ｐｐｍ、シングレット。フラン環のＨ：δ＝３．７０、トリプレット。溶媒：ＤＭＳＯ－ｄ６）

【0031】
（実施例１）
容量１００ｍｌの加熱撹拌装置付オートクレーブに５－ＨＭＦ１ｇ（７．９３ｍＭ）、イオン交換水５０ｇ及び触媒２ｇを入れて密閉し、１３ＭＰａの酸素ガスを封入した。加熱温度は、７０℃、８０℃、９０℃及び１００℃とし、それぞれの温度について反応を行った。

【0032】
反応後、得られた生成物をＨＰＬＣで分析した結果について、表１に示す。結果として、７０℃で６７Ｈｒ反応させた場合のＦＤＣＡの生成率が９０．９％となり、良好であった。７０℃程度の低温の方が、ＦＤＣＡの生成率が良好であった。

【0033】
【表1】

反応温度	反応時間	FDCA	CFF	HMFA	5-HMF	合計
70℃	67.0	90.9	2.8	0.0	0.0	93.8
80℃	39.0	89.0	0.8	2.4	0.0	92.3
90℃	20.0	79.3	2.5	0.6	0.0	82.4
100℃	20.0	78.2	0.0	0.0	0.0	78.2
	Hr	(mol%)	(mol%)	(mol%)	(mol%)	(mol%)

【0034】
（実施例２）
実施例１と同条件９０℃・２０時間の反応を繰り返し、触媒のリサイクル回数に対するＦＤＣＡの生成率を調査した。触媒の回収は、反応後の液をろ過し、固形分を精製水で洗浄し乾燥することにより行い、回収した触媒を次の実験に供した。なお、反応に用いる５－ＨＭＦ及びイオン交換水の量は、回収された触媒の質量に応じて調製することとし、それぞれ回収した触媒の質量の０．５倍及び２５倍とした。

【0035】
実験はリサイクル回数４回目まで行った。ＦＤＣＡの生成率は１回目（新品）＝７９．３％、２回目（再利用１回目）＝７７．５％、３回目（再利用２回目）＝７６．７％、４回目（再利用３回目）＝７５．１％、５回目（再利用４回目）＝７４．９％となり、リサイクル性能は良好であった。

【0036】
使用前及び使用後の触媒の元素分析結果を表２に示す。使用後ではＣｅ及びＲｕ成分が

増加していた。この理由としては、ＯまたはＯＨが酸化反応により減少したため、Ｃｅ及びＲｕ成分が相対的に増加したものと考えられる。結果より、特に著しい元素組成の変化は認められなかった。

【0037】

【表2】

ルテニウム、コバルト及びセリウムを主成分とする触媒の元素分析結果							
		Co	Ce	Ru	C	NO3	合計
使用前	wt%	26.4	31.7	6.27	0.63	1.27	66.3
	元素モル比	7.2	3.6	1.0			
1回使用後	wt%	26.1	35.4	7.00	0.43	0.15	69.1
	元素モル比	6.4	3.6	1.0			
分析方法		ICP	ICP	ICP	燃焼	溶出+滴定	
		wt(%)	wt(%)	wt(%)	wt(%)	wt(%)	wt(%)

【0038】

（比較例１）

１００ｍｌ丸底フラスコに実施例１と同様の５－ＨＭＦ、触媒、水を入れた。さらに、その溶液を水酸化ナトリウムを用いてｐＨ＝１２に調整し、空気を毎分２リットルでバブリングし、室温で１６時間反応を行った。結果は、表３に示すように、ＦＤＣＡの生成率は低く、原料、中間体の残存が多かった。つまり、加圧をしなければ反応が効率的に進まないことがわかった。なお、本比較例では水酸化ナトリウムを添加しているが、水酸化ナトリウムを添加しなければ全く反応は進行しないことが確認されている。

【0039】

【表3】

時間	ＦＤＣＡ	ＤＦＦ	ＣＦＦ	ＨＭＦＡ	ギ酸	5-ＨＭＦ
Ｈｒ	（ｍｏｌ％）	（ｍｏｌ％）	（ｍｏｌ％）	（ｍｏｌ％）	（ｍｏｌ％）	（ｍｏｌ％）
1	０．０	０．０	０．２	５．５	０．０	８５．４
4	１．６	０．０	０．８	３３．２	０．５	５４．８
２６	３．１	０．０	２．９	４４．４	０．８	３２．２
５１	３．３	０．０	３．３	４７．８	０．７	２８．２

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Ｆターム(参考) 4C037 MA01
4H039 CA65

PROCESS FOR PRODUCING 2,5-FURANDICARBOXYLIC ACID

Patent Number:	JP 2009-242312 A
Inventor(s):	EBIHARA YOSUKE; FUJIBAYASHI RYOICHI
Applicant(s):	AIR WATER INC
Classification:	**- international:** C07D307/68; C07B61/00 **- cooperative:**
Application number:	JP20080091762 20080331
Priority number(s):	JP20080091762 20080331
Also published as:	JP5252969 (B2)

Abstract of JP 2009-242312 A

PROBLEM TO BE SOLVED: To provide a method for producing 2,5-furandicarboxylic acid (FDCA) by oxidizing 5-hydroxymethylfurfural (5HMF) of a starting material in the presence of a catalyst comprising Co, Mn, and Br with a molecular oxygen in an industrially employable high yield and preferably in high purity.

SOLUTION: The atomic ratio of Co in terms of metal to Mn in terms of metal in the catalyst is 2:1 to 4:1, and the oxygen concentration in an exhaust gas is measured while supplying an oxidizing gas containing a molecular oxygen into a reaction fluid, and after determining that the molecular oxygen has reached to a point of completing absorption in the reaction fluid, the oxidizing gas is further supplied to continue the oxidation reaction. Suitably, the obtained FDCA is dissolved in an aqueous solution of an alkali metal hydroxide, thereafter treated with sodium hypochlorite and/or hydrogen peroxide, then subjected to acid deposition, and is recovered.

(19)日本国特許庁(JP)　(12)公開特許公報(A)　(11)特許出願公開番号
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Fターム(参考)　4C037 MA01
4H039 CA65　CC20　CC30

(54)【発明の名称】２，５－フランジカルボン酸の製造方法

(57)【要約】
【課題】Co,Mn,およびBrを含む触媒の存在下で、出発物質の5-ヒドロキシメチルフルフラール(5HMF)を分子状酸素により酸化して2，5-フランジカルボン酸(FDCA)を製造する方法について、工業的に採用しうる高い収率、および好ましくは高い純度で製造する方法を提供する。
【解決手段】触媒における金属換算Coおよび金属換算Mnの原子比が2:1～4:1であって、分子状酸素を含む酸化性気体を反応液に供給しつつ、排気ガスの酸素濃度を計測し、反応液に対する分子状酸素の吸収終了点に達したと判定した後に、さらに酸化性気体の供給を行って酸化反応を継続させる。好適には、得られたFDCAをアルカル金属水酸化物の水溶液に溶解後、次亜塩素酸ナトリウムおよび／または過酸化水素で処理した後、酸析して回収する。
【選択図】なし

【特許請求の範囲】
【請求項1】
コバルト、マンガン、および臭素を含む触媒を含む反応液中で、５－ヒドロキシメチルフルフラールを分子状酸素により酸化する２，５－フランジカルボン酸の製造方法において、
前記触媒における金属換算コバルトおよび金属換算マンガンの原子比が２：１～４：１であって、
分子状酸素を含む酸化性気体を前記反応液に供給しつつ計測した排気ガスの酸素濃度に基づいて、前記反応液に対する分子状酸素の吸収終了点に達したと判定した後に、さらに酸化性気体の供給を行って酸化反応を継続させること
を特徴とする２，５－フランジカルボン酸の製造方法。
【請求項2】
前記反応液に添加される触媒が、
５－ヒドロキシメチルフルフラール１ｍｏｌに対する金属換算コバルトの比率が０．０１～０．３グラム原子、かつコバルトおよびマンガンの金属換算総和１グラム原子に対する臭素イオンの比率が０．０５～２０ｍｏｌである、請求項１記載の２，５－フランジカルボン酸の製造方法。
【請求項3】
請求項１または２に記載される製造方法により製造された２，５－フランジカルボン酸をアルカル金属水酸化物の水溶液に溶解後、次亜塩素酸ナトリウムおよび過酸化水素から選ばれる一種または二種で処理した後、酸析して回収することを特徴とする２，５－フランジカルボン酸の製造方法。

【発明の詳細な説明】
【技術分野】
【0001】
本発明は、植物由来プラスチックの原料、あるいは医薬、農薬の原料として利用価値の高い２，５－フランジカルボン酸の製造方法に関する。
【背景技術】
【0002】
２，５－フランジカルボン酸（ＦＤＣＡ）は、植物に多く含まれるフルクトース（果糖）から合成可能でありながら、ＰＥＴなどプラスチックの原料物質として使用されるテレフタル酸の代替物質となりうるものであり、また、その誘導体は医薬品や農薬としても使用しうる。このため、ＦＤＣＡは、米国エネルギー省（Ｄｅｐａｒｔｍｅｎｔ　ｏｆ　Ｅｎｅｒｇｙ）が選定したバイオリファイナリーのビルディングブロック材料の１つに選定されている。
【0003】
このＦＤＣＡのフルクトースからの合成は、フルクトースを脱水環化し、５－ヒドロキシメチルフルフラール（５ＨＭＦ）とした後に、５ＨＭＦを酸化することによってＦＤＣＡに誘導する方法が一般的である。
【0004】
５ＨＭＦの酸化方法としては、$KMnO_4$、硝酸、酸化銀などの酸化性固体や、酸素、空気等の酸化性気体など酸化剤を使用した例が報告されている（たとえば非特許文献１参照。）が、経済性、及び環境への影響の点から、空気を酸化剤として使用する方法が優れている。
【0005】
空気を酸化剤として使用する例としては特許文献１や非特許文献２に、金属臭素化物、Ｃｏ，Ｍｎ触媒の存在下、酢酸溶媒中７ＭＰａの空気により酸化する例が記載されている。
【特許文献1】国際公開ＷＯ０１／０７２７３２パンフレット
【非特許文献1】Ｒｅａｃｔ　Ｋｉｎｅｔ．Ｃａｔａｌ．Ｌｅｔｔ．，　１９７９．

１１．　２１５
【非特許文献2】Ａｄｖ．　Ｓｙｎｔｈ．　Ｃａｔａｌ．　２００１．　３４５．　１０２
【発明の開示】
【発明が解決しようとする課題】
【0006】
特許文献１および非特許文献２に記載される方法は、空気を酸化剤として使用する点で他の酸化剤を使用する方法より優れているが、収率は７０ｍｏｌ％に達しておらず、工業的に採用しうる方法とはいえない。また酸化中間体である５－ホルミル－２－フランカルボン酸（ＦＦＣＡ）が残留しており、収率、品質共に満足できる方法ではない。
【0007】
そこで、本発明は、５ＨＭＦを酸化してＦＤＣＡを製造する方法について、工業的に採用しうる高い収率、および好ましくは高い純度で製造する方法を提供することを目的とする。
【課題を解決するための手段】
【0008】
上記課題を解決すべく、本発明者が鋭意研究した結果、酢酸等を溶媒として５ＨＭＦおよびコバルト－マンガン－臭素系の触媒を含む反応液に、分子状酸素を含む酸化性気体（典型的には空気）を供給して酸化するにあたって、その触媒における金属換算コバルトおよび金属換算マンガンの原子比が特定の範囲（２：１～４：１）である場合には、反応液に対する酸化性気体の吸収がなくなった、すなわち分子状酸素の吸収終了点に到達した後に、酸化性気体の供給をさらに行って反応液における酸化反応を継続させることにより、収率を工業的に採用しうる７０ｍｏｌ％以上にまで高めることが可能であることを見出した。
【0009】
本発明は係る知見に基づくものであり、コバルト、マンガン、および臭素を含む触媒を含む反応液中で、５－ヒドロキシメチルフルフラールを分子状酸素により酸化する２，５－フランジカルボン酸の製造方法において、触媒における金属換算コバルトおよび金属換算マンガンの原子比が２：１～４：１であって、分子状酸素を含む酸化性気体を前記反応液に供給しつつ計測した排気ガス（反応器から排出される気体）の酸素濃度（分子状酸素の濃度）に基づいて、反応液に対する分子状酸素の吸収終了点に達したと判定した後に、さらに酸化性気体の供給を行って酸化反応を継続させることを特徴とする２，５－フランジカルボン酸の製造方法である。
【0010】
ここで、反応液に添加される触媒が、５－ヒドロキシメチルフルフラール１ｍｏｌに対する金属換算コバルトの比率が０．０１～０．３グラム原子、かつコバルトおよびマンガンの金属換算総和１グラム原子に対する臭素イオンの比率が０．０５～２０ｍｏｌであるようにすることが好ましい。
【0011】
また、酸化性気体の酸化により得られた粗ＦＤＣＡをアルカリ金属水酸化物の水溶液に溶解し、次亜塩素酸ナトリウムおよび過酸化水素から選ばれる一種または二種で処理した後、酸析することによって、さらに高純度のＦＤＣＡを得ることが可能である。
【発明の効果】
【0012】
本発明によれば、酸化反応の収率を、工業的に採用可能なレベルである７０ｍｏｌ％以上に高めることが可能である。また、酸化反応による生成した粗ＦＤＣＡを効率的に高純度化することも可能である。
【発明を実施するための最良の形態】
【0013】
以下、本発明のＦＤＣＡの製造方法について詳細に説明する。

１．反応液

（１）５ＨＭＦ

出発原料として使用する５ＨＭＦの製法には制限は無い。セルロース、デンプンなどの六糖類、ショ糖、マルトース、セロビオース、ラクトースなどの少糖類、フルクトース、グルコースなどの単糖類の脱水反応によって得られる植物由来品を使用してもよい。

【0014】

（２）溶媒

本発明に係る酸化反応のための反応液の溶媒としては、従来技術に係る酸化反応の場合と同様に、酢酸、プロピオン酸または酢酸/無水酢酸の混合溶媒を使用する。この溶媒は少量の水を含有していてもよい。溶媒の使用量は重量比で出発原料（５ＨＭＦ）の３～２０倍とするのが好ましい。

【0015】

（３）触媒

本発明では、酸化触媒としてコバルト触媒、マンガン触媒および臭素化合物からなる触媒系を用いる。コバルトおよびマンガン触媒としては、反応温度において反応溶媒に溶解可能なものであれば特に制限されない。

【0016】

例えば、コバルトでは、その無機酸（例えば、臭素化物、炭酸塩等）および有機酸塩（例えば、酢酸塩、プロピオン酸塩等）からなる群から選ばれる一種または二種以上を使用すればよい。同様にマンガンも、その無機酸（例えば、臭素化物、炭酸塩等）および有機酸塩（例えば、酢酸塩、プロピオン酸塩等）からなる群から選ばれる一種または二種以上を使用すればよい。

【0017】

臭素化合物としては、反応温度において反応溶媒に溶解して臭素イオンを供給できるものであればよく、具体例としては、臭素、臭化水素、アルカリ金属およびアンモニウムの臭化物(例、臭化カリウム、臭化アンモニウム)、臭化コバルトなどの無機化合物、ならびに臭化ベンジル、ブロモエタンなどの有機臭化物が挙げられる。なお、臭化コバルトはコバルト触媒と臭化化合物の両方を兼ねる。

【0018】

触媒を構成する各物質の含有量に関し、本発明では、コバルト触媒およびマンガン触媒におけるコバルト金属およびマンガン金属の原子比を２：１～４：１とする。コバルト金属のグラム原子数がマンガン金属のグラム原子数に対して２倍未満となると、収率が低下する傾向を示すようになる。一方、コバルトがマンガンに対して多くなっても収率には影響しないものの、コバルトは比較的高価であるから、経済的観点での不利益が大きくなる。

【0019】

さらに、次の範囲とすると、ＦＤＣＡを高い収率で得ることが安定的に実現される。

まず、原料物質（５ＨＭＦ）１ｍｏｌに対するコバルト触媒（コバルト金属換算）の比率を０．０１～０．３グラム原子とすることが好ましく、０．０３～０．２グラム原子とすれば特に好ましい。この範囲から過剰に小さくなると、収率が低下する傾向を示す。なお、コバルト触媒の使用量を酸化反応の溶媒に対して規定すれば、コバルト金属換算で０．０８重量%以上とすることが好ましい。より好ましくは０．１４～０．５４重量%である。

【0020】

また、コバルト触媒およびマンガン触媒（いずれも金属換算）の総和の１グラム原子に対する臭素イオンの比率を、０．０５～２０ｍｏｌとすることが好ましく、０．１～５ｍｏｌとすれば特に好ましい。なお、臭素イオン量をコバルト触媒量に対して規定すれば、コバルト金属１グラム原子に対して臭素イオン量は０．２～２．０ｍｏｌとすることが好ましい。

【0021】

２．酸化反応

（１）概要

本発明に係る製造方法では、上記の反応液に酸化性気体を供給して、原料物質である５ＨＭＦを酸化することによりＦＤＣＡを製造する。この液相での空気酸化反応により５ＨＭＦのアルコール部位（ＡｒＣＨ$_2$ＯＨ）がアルデヒド（ＡｒＣＨＯ）を経緯してカルボン酸（ＡｒＣＯＯＨ）に変換され、アルデヒド部位もカルボン酸に変換されたＦＤＣＡが生成する。

【0022】

本発明に係る製造方法では、分子状酸素を含む酸化性気体を供給しつつ、排気ガスの酸素濃度を計測し反応液に対する分子状酸素の吸収終了点に達したと判定した後に、さらに酸化性気体の供給を行って酸化反応を継続させることで収率を工業的に採用しうる７０ｍｏｌ％以上にまで高めることを安定的に実現する。

【0023】

（２）酸化性気体

酸化性気体とは、原料物質である５ＨＭＦを酸化することができる分子状酸素を含む気体であり、最も典型的には空気が例示される。

【0024】

ここで、酸化性気体に含まれる分子状酸素の濃度（酸素濃度）は、たとえば実験室レベルなどにおいて、オートクレーブを用いて爆発の危険性を低下させた状態で酸化する場合には、約２１体積％の酸素を含む空気をそのまま用いてもよいし、純酸素のように酸素濃度をさらに高めて酸化させてもよい。一方、工業的には、排気ガスの酸素濃度が爆発限界を超えない、すなわち１１体積％未満となるように、窒素などいわゆる不活性気体によって空気を希釈して酸化性気体としてもよい。

【0025】

（３）酸化性気体の供給方法、圧力、流量

酸化性気体の供給方法は、所定の圧力・流量で供給されることが実現されれば、特に制限されない。典型的には、空気と希釈用不活性ガス（窒素、アルゴンなど）とを公知の混合器により混合し、酸素濃度が制御された混合ガスとして所定圧力および／または所定流量で反応器に供給する。

【0026】

酸化性気体の圧力は、反応溶媒が反応温度において液相を保つことができるのであれば、高ければ高いほど反応性が高まるため好ましい。しかしながら、圧力が過剰に高い場合には、機密性確保のための設備投資が大きくなってしまう。また、反応前後の準備時間が長くなる場合が多いため、生産性の低下を招く可能性が高まる。これらの観点から、酸化性気体の圧力は、１～４０ｋｇ／ｃｍ^{2}とすることが好ましく、１０～３０ｋｇ／ｃｍ^2(いずれもゲージ圧)程度とすれば特に好ましい。

【0027】

酸化性気体の流量は、大きければ大きいほど反応性は高まるものの、流量が過剰に大きい場合には供給のための設備投資が大きくなる上に、排気ガス量も多くなるため、生産性の低下を招く。したがって、酸化性気体の流量は、仕込みの５ＨＭＦ１ｍｏｌ当たり１～２０Ｌ／分とすることが好ましく、２～１０Ｌ／分とすれば特に好ましい。

【0028】

（４）反応形式

酸化反応は、回分式、半連続式、および連続式のいずれの方式で実施してもよい。回分式は、原料物質（５ＨＭＦ）および触媒の全量を反応器に予め装入しておき、酸化性気体を反応液に通気して酸化反応を行い、反応終了後に反応液を一度に回収する方法である。

【0029】

半連続式は、例えば、触媒の全量を反応器に装入し、原料物質と酸化性気体を連続的に反応器に供給しながら酸化反応を行い、反応終了後に反応液を一度に回収する方法である。

【0030】
連続式は、原料物質、触媒および酸化性気体のすべてを連続的に反応器に供給しながら酸化反応を行い、反応液を連続的に回収する方法である。
工業的実施においては、連続式または半連続式が操業効率の点から好ましい。
【0031】
（５）反応温度、時間
本発明に係る酸化反応は９０～１５０℃の範囲の温度で実施することが好ましく、９０～１３０℃とすれば特に好ましい。また、反応開始の１時間または１時間半を９０℃に保ち、その後１３０℃に昇温するといった具合に反応温度を多段とする制御を行ってもよい。
【0032】
酸化反応時間は温度、圧力、触媒組成等の条件により適宜設定され、通常は３～６時間程度である。
（６）排気ガスの酸素濃度計測
本発明に係る酸化反応では、上記のように酸化性気体が所定の流量で反応器に供給されるため、反応器から排出されるガス（排気ガス）の酸素濃度は、反応器内での酸化反応の進行状況を図るためにもっとも適切なパラメータの一つである。本発明に係る酸化反応は、液相にある原料物質（５ＨＭＦ）が液相にある触媒を用いて気相にある分子状酸素と反応するものであるから、分子状酸素の溶媒への溶解度が反応の進みやすさに大きく影響する。しかしながら、この酸素の溶解度は反応溶媒、温度、圧力、触媒などの影響を受けやすいため、必ずしも制御が容易でない。そこで、本発明に係る製造方法では、排気ガスの酸素濃度を計測し、その結果から供給された分子状酸素がどの程度吸収されたかの情報を得て、反応の進行程度を把握することとしている。この酸素濃度の計測は公知の方法により行うことができ、たとえば自動酸素濃度分析装置を用いて、連続的または定期的に計測すればよい。
【0033】
さらに、本発明に係る製造方法では、この計測の結果に基づいて、分子状酸素が反応液に吸収されなくなった吸収終了点に達したか否かを判定する。
吸収終了点とは分子状酸素が反応液に吸収されなくなったときである。分子状酸素が反応液に吸収されている場合には、供給された酸化性気体の酸素濃度（供給酸素濃度）よりも排気ガスの酸素濃度（排気酸素濃度）の方が低くなっているが、分子状酸素が吸収されなくなると究極的には供給酸素濃度と排気酸素濃度とは同一の値となるため、この同一となったときが原理的な吸収終了点である。ただし、実務上は、計測誤差や計測時間遅れなどを考慮して、供給酸素濃度と排気酸素濃度との差が所定の数値以内になったときに吸収終了点に到達したと判定してもよい。この場合の例として、供給する空気（酸素濃度が２１体積％）であるときに差を１％に設定して、吸収終了点の排気酸素濃度を２０体積％とすることが挙げられる。
【0034】
（７）ポストオキシデーション
本発明に係る製造方法は、反応液に対する酸化性気体の吸収がなくなった吸収終了点に到達したと判定した後に、酸化性気体の供給をさらに行って、反応液における酸化反応を継続させる（ポストオキシデーション）。
【0035】
このポストオキシデーションにおいて供給する酸化性気体の条件（酸素濃度、流量など）は、吸収終了点到達前の供給条件と同一でもよいし、異なっていてもよい。その他の条件（温度、圧力など）も吸収終了点到達前の供給条件と同一でもよいし、異なっていてもよい。ポストオキシデーションの時間はその条件により適宜設定されるべきものであるが、０．５～２時間程度が一般的であり、最も典型的には１時間である。
【0036】
なお、上記の回分式および半連続式ではこのポストオキシデーションを追加することは

容易である。連続式においても、原料物質および触媒の供給を一時的に停止し、酸化性気体の供給のみを継続することによってポストオキシデーションを行うようにすればよい。

【0037】

３．酸化剤による処理

本発明に係る製造方法は、好適態様として、上記のポストオキシデーションを含む５ＨＭＦの液相での酸化反応により得られたＦＤＣＡ（以下「粗ＦＤＣＡ」という。）を、酸化剤によって処理することにより、粗ＦＤＣＡの純度を高める。

【0038】

前述のように、本発明に係る酸化反応では、原料の５ＨＭＦはそのヒドロキシメチル基およびアルデヒド基のそれぞれが酸化されてＦＤＣＡとなるが、その反応中間体の一つとして、ヒドロキシメチル基だけがカルボン酸基まで酸化された５－ホルミル－２－フランカルボン酸（ＦＦＣＡ）が形成される。上記の酸化反応により得られたＦＤＣＡを固液分離法(例、沪過、遠心分離、沈降)により溶媒から単離すると、得られた粗ＦＤＣＡには０．１～２０重量％のＦＦＣＡが含まれている。

【0039】

そこで、酸化剤、典型的には次亜塩素酸ナトリウムおよび／または過酸化水素を粗ＦＤＣＡと次のような方法で反応させることにより、残留するＦＦＣＡがＦＤＣＡに変換し、粗ＦＤＣＡの純度を高めることが実現される。

【0040】

まず、空気酸化で得られたＦＦＣＡを含有する粗ＦＤＣＡを、アルカリ金属水酸化物の水溶液に溶解させる。使用するアルカリ金属水酸化物としては経済性の観点で水酸化ナトリウムが好ましい。アルカリ金属水酸化物の量は溶解させるＦＦＣＡに対して２倍以上のモル数であればよい。アルカリ金属水酸化物の水溶液濃度は操作性の面から２～１０重量％とすることが好ましい。

【0041】

なお、アルカリ金属水酸化物の水溶液に溶解した時点で不溶分がある場合には沪過して除いても良い。

次に、この粗ＦＤＣＡを含むアルカリ金属水酸化物の水溶液に次亜塩素酸ナトリウムおよび／または過酸化水素を添加する。添加する次亜塩素酸ナトリウムおよび／または過酸化水素の濃度に制限は無い。市販品をそのまま使用でき、場合によっては希釈して使用することも可能である。次亜塩素酸ナトリウムおよび／または過酸化水素水の添加量は、粗ＦＤＣＡ中に残留するＦＦＣＡに対してモル数換算で等量以上とすればよい。好ましくはモル数換算で２～１０倍である。反応温度は２０～８０℃の範囲で実施できる。

反応時間は反応温度や使用する酸化剤の量により変わるが通常０．５～１０時間である。

【0042】

残存するＦＦＣＡをＦＤＣＡに酸化した後、酸析を行う。使用する酸の種類やその濃度には制限は無く、公知の方法にしたがって行えばよい。こうして着色の少ない高純度のＦＤＣＡが得られるが、必要に応じて水で再結晶を行えば、アルカリ金属の除去も可能である。

【実施例】

【0043】

以下に実施例、比較例によって本発明をより具体的に説明をするが、これらの例により本発明は何ら制限されるものではない。

（比較例１）

撹拌機、ガス吹込み管、還流冷却器付き排ガス抜出し管、原料導入管、および温度計を取り付けた内容積５００ｍｌのチタン製オートクレーブに、純度９８．０重量％の５－ヒドロキシメチルフルフラール２５ｇ、酢酸２２５ｇ、酢酸コバルト４水和物１．４６ｇ、酢酸マンガン４水和物１．３９ｇ、および臭化カリウム０．６７ｇを仕込んだ。このときの、コバルト化合物のコバルト金属換算グラム原子数：マンガン化合物のマンガン金属換

算グラム原子数：臭素イオンモル数（以下「触媒モル比」という。）は１：１：１であった。

【0044】

オートクレーブ内雰囲気を窒素で置換した後、撹拌下に加熱して１２０℃まで昇温させてから、排ガス流量が１．０Ｌ／分となるようにガス吹込み管を通じて空気を導入し始め、反応系を温度１２０℃、圧力３．０ＭＰａに保ちながら空気の供給を継続した。こうして反応させながら排気ガスの酸素濃度を計測したところ、排気ガスの酸素濃度は約１体積％であった。

【0045】

１時間経過後、排気ガスの酸素濃度が５体積％となったため、空気の供給は維持しつつ、オートクレーブ内の温度を１５０℃に昇温し２時間反応を継続すると排気ガスの酸素濃度が２０体積％に達した。この時点から更に１時間空気の供給を行い、その後、空気の導入を停止し、オートクレーブを冷却した。

【0046】

オートクレーブの冷却後、内容物を取り出して結晶を沪別し、２，５－フランジカルボン酸を含むケーキと沪液とを得た。得られたケーキを同体積の酢酸で洗浄した後、真空乾燥し、淡褐色の２，５－フランジカルボン酸２２．４ｇを得た。以下に示す装置および測定条件で高速液体クロマトグラフィー（ＨＰＬＣ）により分析したところ、ＬＣ純度は８７．５重量％であり、収率は６４．８ｍｏｌ％であった。また、５－ホルミル－２－フランカルボン酸が２．９９重量％ケーキ内に残留した。

【0047】

分析機器：高速液体クロマトグラフィー
カラム：昭和電工（株）製　Ｓｈｏｄｅｘ　ＳｕｇａｒＳＨ１００１１
検出器：ＵＶ（２８４ｎｍ）
溶離液：３ｍＭ過塩素酸水溶液
流量：０．６ｍＬ／分　（０～２０分）、１．４ｍＬ／分　（２０～３５分）
内部標準物質：フタル酸

【0048】

（実施例１）

比較例１において酢酸コバルト４水和物の仕込量を２．９２ｇにし、触媒モル比を２：１：１にした以外は同様の操作を行い、淡紫色の２，５－フランジカルボン酸２６．２ｇを得た。そのＬＣ純度は８９．１重量％であり、収率は７７．１ｍｏｌ％であった。また、５－ホルミル－２－フランカルボン酸が４．０１重量％ケーキ内に残留した。

【0049】

（実施例２）

実施例１において酢酸コバルト４水和物の仕込み量を５．８４ｇにし、触媒モル比を４：１：１にした以外は同様の操作を行い、淡紫色の２，５－フランジカルボン酸２７．５ｇを得た。そのＬＣ純度は８５．８重量％であり、収率は７７．７ｍｏｌ％であった。また、５－ホルミル－２－フランカルボン酸が３．６６重量％ケーキ内に残留した。

【0050】

（実施例３）

実施例１において反応温度を９０℃として１．５時間反応させた後に、１３０℃で反応を２時間継続し酸素の吸収がほぼ無くなった時点から更に１時間反応を継続した以外は同様の操作を行い、淡紫色の２，５－フランジカルボン酸２６．２ｇを得た。そのＬＣ純度は９０．２重量％であり、収率は７６．７ｍｏｌ％であった。また、５－ホルミル－２－フランカルボン酸が６．５４重量％ケーキ内に残留した。

【0051】

（実施例４）

撹拌機、温度計を取り付けた内容積５００ｍＬのガラス製３つ口フラスコに、純度９７重量％の水酸化ナトリウム１１．５ｇおよび水３００ｇを仕込んだ。

【0052】
実施例２で得られた２，５－フランジカルボン酸２０ｇをその３つ口フラスコに添加し、撹拌下、反応系を温度２５℃の状態で約１時間反応を継続した。
得られたフラスコ内容物についてパーライトを用いて沪過を行い、固体および沪液を得た。得られた沪液を撹拌機、還流冷却器、滴下ロート、および温度計を取り付けた内容積５００ｍＬのガラス製４つ口フラスコに仕込んだ。
【0053】
撹拌下に加熱して６０℃まで昇温させ、１０重量％の次亜塩素酸ナトリウム水溶液を２８．５ｇ添加して、反応系を温度６０℃の状態で約７時間反応を継続した。
その後、加熱を停止し、フラスコを冷却した。冷却後、過剰量の次亜塩素酸ナトリウムを失活するために１０重量％の亜硫酸水素ナトリウム水溶液を１．０２ｇ添加して、撹拌下、反応系を温度２５℃の状態で３０分間還元反応を行った。
【0054】
３０分間経過後、３５%塩酸３２．４ｇを滴下して、撹拌下、反応系を温度２５℃の状態で約1時間反応を継続した。
内容物を取り出して結晶を沪別し、２，５－フランジカルボン酸を含むケーキと沪液とを得た。得られたケーキを水１００ｇで洗浄した後、撹拌機、温度計を取り付けた内容量３００ｍＬの3つ口フラスコにケーキを加え、水１０７ｇを仕込んだ。
【0055】
撹拌下に加熱して温度を３０℃に昇温して、反応系を温度３０℃に保ち約1時間撹拌を継続した。その後、加熱を停止し、フラスコを冷却した。
内容物を取り出して結晶を沪別し、２，５－フランジカルボン酸を含むケーキと沪液とを得た。３０℃にあらかじめ加熱しておいた水１００ｇで得られたケーキを洗浄した。この３０℃での水洗工程を３回繰り返した後、得られたケーキを真空乾燥し、白色の２，５－フランジカルボン酸１５．０ｇを得た。ＬＣ純度は９９．９重量％であり、収率は８７．６ｍｏｌ％であった。
【0056】
（実施例５）
撹拌機、温度計を取り付けた内容積５００ｍＬのガラス製3つ口フラスコに、純度９７重量％の水酸化ナトリウム１１．５ｇおよび水３００ｇを仕込んだ。
【0057】
実施例３で得られた２，５－フランジカルボン酸２０ｇをフラスコ内に添加し、撹拌下、反応系を温度２５℃の状態で約１時間反応を継続した。
得られたフラスコ内容物についてパーライトを用いて沪過を行い、固体および沪液を得た。得られた沪液を撹拌機、還流冷却器、滴下ロート、および温度計を取り付けた内容積５００ｍＬのガラス製４つ口フラスコに仕込んだ。
【0058】
撹拌下に加熱して３０℃まで昇温させ、３０重量％の過酸化水素水溶液を８．６８ｇ添加して、反応系を温度３０℃の状態で約６時間反応を継続した。
その後、ｔ－ブチルメチルケトンを１８．２ｇ添加し、加熱して６０℃まで昇温した。昇温後、３５％塩酸３１．５ｇを滴下し、４つ口フラスコをオイルバスから外し、撹拌下で１時間保持した。
【0059】
１時間経過後、フラスコ内の内容物を取り出して結晶を沪別して得られたケーキの真空乾燥を行い。白色の２，５－フランジカルボン酸を１７．０ｇ、収率９３．６ｍｏｌ％で回収した。回収した１７．０ｇ中、５ｇを水で再結晶を行うと収率９１．８ｍｏｌ％で白色の２，５－フランジカルボン酸が回収され、そのＬＣ純度は９９．９重量％であった。

METHOD OF OBTAINING 2,5-FURANDICARBOXYLIC ACID

Patent Number:	SU 636233 A1
Inventor(s):	NORIKOV YURIJ D; SLAVINSKAYA VALENTINA A; KREJLE DZIDRA R; EGLITE DZIDRA YA; KRUMINYA LIYA YA
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Classification:	**- international:** C07D307/68; (IPC1-7): C07D307/68 **- cooperative:**
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Abstract not available for SU 636233 A1

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Государственный комитет Совета Министров СССР по делам изобретений и открытий

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(54) СПОСОБ ПОЛУЧЕНИЯ 2,5-ФУРАНДИКАРБОНОВОЙ КИСЛОТЫ

1

Изобретение относится к усовершенствованному способу получения 2,5-фурандикарбоновой кислоты, которая может найти применение в синтезе высокомолекулярных соединений.

Известен способ получения 2,5-фурандикарбоновой кислоты жидкофазным каталитическим окислением кислородом или кислородом воздуха 5-метилфурфурола на кобальтмарганецбромидном катализаторе при температуре 115–140°С и давлении 10–20 атм в среде карбоновых кислот [1].

К недостаткам способа относятся использование дорогостоящего титанового оборудования из-за сильной коррозии в среде соединений брома и уксусной кислоты, необходимость регенерации растворителя и сложный метод регенерации катализатора.

Целью изобретения является упрощение технологии процесса.

Сущность изобретения состоит в том, что 5-метилфурфурол подвергают жидкофазному каталитическому окислению кислородом или кислородом воздуха на катализаторе $CuO \cdot Ag_2O \cdot Ce_2O_3$, нанесенном на Al_2O_3, при температуре 110–150°С и давлении 25–30 атм в среде водной щелочи.

2

Отличие этого способа от известного состоит в том, что в качестве катализатора используют $CuO \cdot Ag_2O \cdot Ce_2O_3$, нанесенный на Al_2O_3, и процесс проводят при температуре 110–150°С и давлении 25–30 атм в среде водной щелочи.

В качестве водной щелочи обычно используют водный раствор NaOH или Na_2CO_3. В качестве катализатора предпочтительно используют смесь $CuO \cdot Ag_2O \cdot Ce_2O_3$ в молярном отношении 1:0,07:0,05, нанесенную на Al_2O_3 (активные компоненты 32% от веса носителя). Гетерогенные катализаторы легко отделяют фильтрацией от оксидата, они не загрязняют целевые продукты. Использование Al_2O_3 как носителя обеспечивает трехкратное уменьшение количества активных

компонентов по сравнению с использованием суспензии окислов активных компонентов как катализатора.

Катализатор выделяют из оксидата фильтрованием. Его можно использовать повторно. При этом его активность несколько уменьшается. Серебро может быть утилизировано из дезактивированных образцов катализатора растворением катализатора в азотной кислоте и осаждением серебра ионом хлора.

К преимуществам предлагаемого способа относятся проведение процесса в проточном автоклаве из нержавеющей стали (реакционная среда мало коррозийна) и отсутствие регенерации растворителя.

Пример 1. В реактор загружают 5,5 г (0,05 моль) 5-метилфурфурола, 4,0 г (0,1 моль) NaOH, 5,5 г $CuO \times Ag_2O \cdot Ce_2O_3$, нанесенного на Al_2O_3, и 75 мл воды. Реакцию проводят при температуре 150°С, давлении кислорода 30 атм, расходе кислорода 0,9 л/мин в течение 3 ч. Оксидат охлаждают, отфильтровывают гетерогенный катализатор, упаривают до 1/2 первоначального объема, раствор подкисляют концентрированной HCl до pH 2. Выпавший осадок отфильтровывают и сушат при 100°С. Оксидат содержит 2,72 г ($1,7 \cdot 10^{-2}$ моль) 2,5-фурандикарбоновой кислоты (выход 33 мол.%) при полной конверсии сырья.

В примерах 2 и 3 те же загрузки, что и в примере 1.

Пример 2. Реакцию проводят при температуре 150°С, давлении воздуха 30 атм, расходе воздуха 0,9 л/мин в течение 3 ч. Оксидат охлаждают, отфильтровывают гетерогенный катализатор, раствор подкисляют концентрированной HCl до pH 2. Оксидат содержит 1,21 г ($0,77 \times 10^{-2}$ моль) 2,5-фурандикарбоновой кислоты (выход 15,5 мол.%) при полной конверсии сырья.

Пример 3. Проводят реакцию при температуре 110°С, давлении кислорода 30 атм, расходе кислорода 0,9 л/мин в течение 5 ч. Оксидат обрабатывают, как в примере 2. Он содержит 1,46 г ($0,94 \times 10^{-2}$ моль) 2,5-фурандикарбоновой кислоты (выход 19 мол.%) при общей конверсии сырья 98,7%.

Пример 4. В реактор загружают 5,5 г (0,05 моль) 5-метилфурфурола, 4,0 г (0,01 моль) NaOH и отработанный катализатор (пример 1). Реакцию проводят при температуре 150°С, давлении кислорода 30 атм, расходе кислорода 0,9 л/мин в течение 5 ч. Оксидат обрабатывают, как в примере 2.

Оксидат содержит 2,22 г ($1,42 \cdot 10^{-2}$ моль) 2,5-фурандикарбоновой кислоты (выход 28,4 мол.%).

Формула изобретения

1. Способ получения 2,5-фурандикарбоновой кислоты жидкофазным каталитическим окислением 5-метилфурфурола кислородом или кислородом воздуха при нагревании и повышенном давлении, отличающийся тем, что, с целью упрощения технологии процесса, в качестве катализатора используют $CuO \cdot Ag_2O \cdot Ce_2O_3$, нанесенный на Al_2O_3, и процесс проводят при температуре 110–150°С и давлении 25–30 атм в среде водной щелочи.

2. Способ по п. 1, отличающийся тем, что используют катализатор $CuO \cdot Ag_2O \cdot Ce_2O_3$ с активными компонентами в молярном отношении 1:0,07:0,05.

Источники информации, принятые во внимание при экспертизе:

1. Авторское свидетельство СССР № 448177, кл. С 07 D 307/68, 30.10.72.

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OXIDATION OF 5-(HYDROXYMETHYL) FURFURAL TO 2,5-DIFORMYLFURAN AND SUBSEQUENT DECARBONYLATION TO UNSUBSTITUTED FURAN

Patent Number:	WO 01/72732 A2	
Inventor(s):	GRUSHIN VLADIMIR [US]; PARTENHEIMER WALTER [US]; MANZER LEO E [US]	
Applicant(s):	DU PONT [US]; GRUSHIN VLADIMIR [US]; PARTENHEIMER WALTER [US]; MANZER LEO E [US]	
Classification:	**- international:**	C07B61/00; C07C45/38; C07C47/54; C07C51/235; C07C55/02; C07D307/36; C07D307/46; C07D307/48; C07D307/68; C08G63/00; C08G63/84; (IPC1-7): C07D307/36; C07D307/46; C07D307/48
	- cooperative:	C07C45/298; C07D307/36; C07D307/46; C07D307/48; C07D307/68; C08G6/00; C08G65/002
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Abstract of WO 01/72732 A2

Alcohols are catalytically oxidized to aldehydes, in particular to benzaldehyde and diformylfuran, which are useful as intermediates for a multiplicity of purposes. The invention also relates to the polymerization of the dialdehyde and to the decarbonylation of the dialdehyde to furan.

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(54) Title: OXIDATION OF 5-(HYDROXYMETHYL) FURFURAL TO 2,5-DIFORMYLFURAN AND SUBSEQUENT DECARBONYLATION TO UNSUBSTITUTED FURAN

(57) Abstract: Alcohols are catalytically oxidized to aldehydes, in particular to benzaldehyde and diformylfuran, which are useful as intermediates for a multiplicity of purposes. The invention also relates to the polymerization of the dialdehyde and to the decarbonylation of the dialdehyde to furan.

TITLE

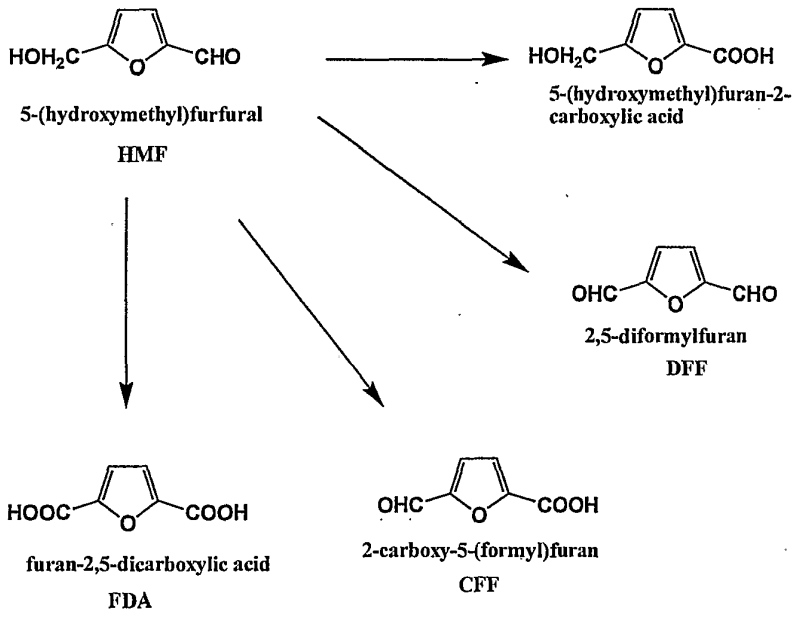
OXIDATION OF 5-(HYDROXYMETHYL) FURFURAL TO 2,5-DIFORMYLFURAN AND SUBSEQUENT DECARBONYLATION TO UNSUBSTITUTED FURAN

FIELD OF INVENTION

The invention relates to the catalytic oxidation of alcohols to aldehydes, in particular the formation of benzaldehyde and diformylfuran, which are useful as intermediates for a multiplicity of purposes. The invention also relates to the polymerization and the decarbonylation of a dialdehyde.

BACKGROUND

5-(Hydroxymethyl)furfural (HMF) is a versatile intermediate that can be obtained in high yield from biomass sources such as naturally occurring carbohydrates, including fructose, glucose, sucrose, and starch. Specifically, HMF is a conversion product of hexoses with 6 carbon atoms. It is known that HMF can be oxidized using a variety of reagents to form any of four different products, which can themselves be converted to one or more of the others:



The selective oxidation of an alcohol functionality in the presence of an aldehyde functionality on the same compound is difficult because of the high reactivity of the aldehyde group. Furthermore, if HMF is reacted with molecular oxygen (O_2), the aldehyde functionality would be expected to oxidize more rapidly than the alcohol and the expected product would be predominantly 5-(hydroxymethyl)furan-2-carboxylic acid (Sheldon, R. A. and Kochi, J. K.

"Metal Catalyzed Oxidations of Organic Compounds", Academic Press, New York, NY 1981, p 19).

Diformylfuran (DFF) has been prepared from HMF using CrO_3 and $K_2Cr_2O_7$ (L. Cottier et al., *Org. Prep. Proced. Int.* (1995), 27(5), 564; JP 54009260) but these methods are expensive and results in large amounts of inorganic salts as waste. Heterogeneous catalysis using vanadium compounds has also been used, but the catalysts have shown low turnover numbers (DE 19615878, Moreau, C. et al., *Stud. Surf. Sci. Catal.* (1997), 108, 399-406). Catalytic oxidation has been demonstrated using hydrogen peroxide (M. P. J. Van Deurzen, *Carbohydrate Chem.* (1997), 16(3), 299) and dinitrogen tetraoxide (JP 55049368) which are expensive. The relatively inexpensive molecular oxygen (O_2) has been used with a Pt/C catalyst (U.S. Patent No. 4,977,283) to form both DFF and furan-2,5-dicarboxlic acid (FDA), but yielded low amounts of DFF. Good yields were found for FDA, but only as the disodium salt which resulted in wasteful salt formation during conversion to the acid form.

Metal bromide catalysts have been used to oxidize substituted alkylbenzenes to various products including the oxidation of alkyl to aldehydes, alkyl to alcohols, alkyl to acids, alcohol to acid, and aldehydes to acids (W. Partenheimer, *Catalysis Today*, 23(2), 69-158, (1995)). However, in such cases, the aldehyde product is either a minor component or is quickly oxidized further. FDA has also been prepared using a Co/Mn/Br catalyst from 5-methylfurfural with DFF seen as a minor byproduct (V. A. Slavinskaya, et al., *React. Kinet. Catal. Lett.* (1979), 11(3), 215-20).

DFF has been polymerized to form polypinacols and polyvinyls (Cooke, et al., *Macromolecules* 1991, 24, 1404). However, preparation of polyesters prepared from diformylfuran is not known in the literature.

DFF can also be used to produce unsubstituted furan. Unsubstituted furan is an important commodity in the chemical industry used in the production of tetrahydrofuran. Supported metal catalysts have been used in the decarbonylation of the monoaldehyde furfural to furan, but a basic promoter is required, adding expense and complexity to the process (U.S. Patent No. 3,007,941, U.S. Patent No. 4,780,552).

Considering the aforementioned discussion, there is a need for an inexpensive, high yield process for the preparation of both DFF and FDA that does not produce large amounts of waste products and which lends itself to easy separation and purification. Additionally, there is a need for a high yielding process to prepare unsubstituted furan from relatively inexpensive, renewable sources.

SUMMARY OF THE INVENTION

The invention is directed to a first process for the preparation of a dialdehyde comprising a) contacting a compound containing an alcohol functionality and an aldehyde functionality with an oxidant in the presence of a metal bromide catalyst; and b) optionally isolating the dialdehyde product. A preferred metal bromide catalyst comprises a source of bromine and at least one metal selected from the group consisting of Co and Mn, and optionally containing Zr. More preferably the metal bromide catalyst contains Co.

Preferably the dialdehyde is of the formula H(C=O)-R-(C=O)H and the compound is of the formula HOH_2C-R-(C=O)H, wherein R is selected from the group consisting of an optionally substituted C_1-C_{20} alkyl or aryl group. The R groups can be linear or cyclic, or a heterocyclic group. More preferably, R is furan, and most preferably the dialdehyde is 2,5-di(formyl)furan. The process of the present invention can be run in a solvent mixture comprising at least one aliphatic C_2-C_6 monocarboxylic acid compound, preferably acetic acid.

The invention is further directed to a second process for the preparation of a diacid of the formula HOOC-R'-COOH from an alcohol/aldehyde of the formula HOH_2C-R'-(C=O)H, wherein R' is an optionally substituted furan ring, comprising the steps:

(a) contacting the alcohol/aldehyde with an oxidant in the presence of a metal bromide catalyst forming an alcohol/acid having the formula HOH_2C-R'-COOH, and optionally isolating the alcohol/acid;

(b) contacting the alcohol/acid with an oxidant in the presence of a metal bromide catalyst forming an acid/aldehyde having the formula HOOC-R'-(C=O)H, and optionally isolating the acid/aldehyde;

(c) contacting the acid/dialdehyde with an oxidant in the presence of a metal bromide catalyst forming the diacid, optionally isolating the diacid.

The invention is further directed to a third process for the preparation of a diacid of the formula HOOC-R'-COOH from an alcohol/aldehyde of the formula HOH_2C-R'-(C=O)H, wherein R' is an optionally substituted furan ring, comprising the steps:

(a') contacting the alcohol/aldehyde with an oxidant in the presence of a metal bromide catalyst forming a dialdehyde having the formula H(C=O)-R'-(C=O)H, and optionally isolating the dialdehyde;

(b') contacting the dialdehyde with an oxidant in the presence of a metal bromide catalyst forming an acid/aldehyde having the formula HOOC-R'-(C=O)H, and optionally isolating the acid/aldehyde; and

(c') contacting the acid/dialdehyde with an oxidant in the presence of a metal bromide catalyst forming the diacid, and optionally isolating the diacid.

The process further comprises the steps of a', b', and c' and wherein before step c' the acid/aldehyde is converted to an acetate ester of the formula $CH_3(C=O)OCH_2$-R'-(C=O)H.

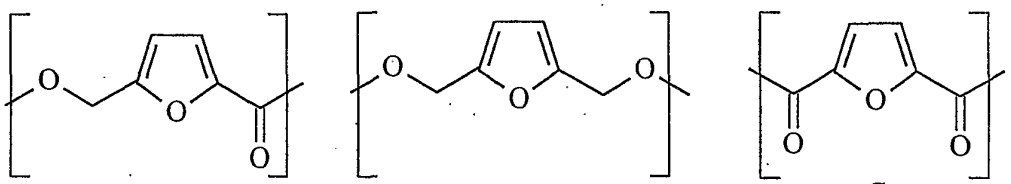
Preferably, in the above process the diacid is furan-2,5-dicarboxlic acid and the alcohol/aldehyde is 5-(hydroxymethyl)furfural.

The process can optionally be run in a solvent or solvent mixture comprising at least one aliphatic C_2-C_6 monocarboxylic acid compound, preferably acetic acid.

The invention is also directed to a fourth process for the preparation of an aldehyde comprising a) contacting a compound of the formula AR-CH_2-OH wherein AR is an optionally substituted aryl with an oxidant in the presence of a metal bromide catalyst; and b) optionally isolating the aldehyde product. Preferably, AR an optionally substituted phenyl group. Most preferably, AR is an unsubstituted phenyl group. A preferred metal bromide catalyst is comprised of a source of bromine and at least one metal selected from the group consisting of Co and Mn. More preferably the metal bromide catalyst contains Co.

The process can be run in a solvent or solvent mixture comprising at least one aliphatic C_2-C_6 monocarboxylic acid compound, preferably acetic acid.

The invention is also directed to a fifth process to form a polyester polymer and the polyester polymer so produced from 2,5-diformylfuran comprising the repeat units A and B and C.



A B C

wherein said process comprises polymerization of di(formyl)furan. The process can be performed in the presence of a catalyst of the formula $M^{+n}(O\text{-}Q)_n$ wherein M is a metal, n is the positive charge on the metal, and Q is an alkyl

group of 1-4 carbons. Preferably, M is aluminum and n is three. Preferably the polyester polymer formed from the process is a homopolymer.

An embodiment of the invention is a polyester polymer comprising repeating units A, B and C. Preferably, the polyester polymer is a homopolymer.

Another aspect of the invention is a sixth process for the preparation of furan comprising converting 2,5-diformylfuran into furan and furfural via decarbonylation in the presence of a catalytic amount of a compound consisting essentially of a optionally supported metal selected from Periodic Group VIII. The furan and furfural product may further be converted via decarbonylation into unsubstituted furan in the presence of a catalytic amount of a compound consisting of an optionally supported metal selected from Periodic Group VIII.

Preferably the catalyst is supported on a catalyst support member, more preferably the metal is palladium and the catalyst support member is carbon.

Another aspect of the invention is to convert the dialdehyde prepared using the above processes, wherein the dialdehyde is 2,5-di(formyl)furan, into furan via decarbonylation in the presence of a catalytic amount of a compound consisting of a optionally supported metal selected from Periodic Group VIII.

DETAILED DESCRIPTION OF THE INVENTION

The present invention concerns a first process for the preparation of a dialdehyde comprising contacting a first compound containing an alcohol functionality and an aldehyde functionality with an oxidant in the presence of a metal bromide catalyst. More specifically, the alcohol can be HMF, the dialdehyde can be DFF, and the catalyst can be comprised of Co and/or Mn, and Br, and optionally Zr.

In addition to the alcohol and the aldehyde, other functional groups may be attached to the first compound as long as the other functional groups are substantially inert under reaction conditions. In a preferred process the first compound is of the formula HOH_2C-R-(C=O)H, and the resulting dialdehyde product that is prepared is of the formula H(C=O)-R-(C=O)H. In the above formula for the first compound and the dialdehyde product of this invention, R is selected from the group consisting of an optionally substituted C_1-C_{20} alkyl and optionally substituted C_1-C_{20} aryl group. The R groups are either linear, cyclic, or heterocyclic. More preferred is where R is selected from the group consisting of an optionally substituted C_1-C_{20} alkyl group, linear or cyclic, and a heterocyclic group. Most preferred is where R is a furan. By optionally substituted herein is meant a group that may be substituted and may contain one or more substituent groups that do not cause the compound to be unstable or unsuitable for the use or reaction intended. Substituent groups which are

generally useful include nitrile, ether, alkyl, ester, halo, amino (including primary, secondary and tertiary amino), hydroxy, silyl or substituted silyl, nitro, and thioether.

The term "aryl" refers to an aromatic carbo-cyclic group having a single ring (e.g., phenyl), multiple rings (e.g., biphenyl), or multiple condensed rings of which at least one is aromatic (e.g., 1,2,3,4-tetrahydronaphthyl, naphthyl, anthryl, or phenanthryl), and which is optionally mono-, di-, or tri- substituted with a functional group such as halogen, lower alkyl, lower alkoxy, lower alkylthio, trifluoromethyl, lower acyloxy, aryl , heteroaryl, and hydroxy. The term "aryl" also refers to heteroaryl groups where heteroaryl is defined as 5-, 6-, or 7-membered aromatic ring systems having at least one hetero-atom selected from the group consisting of nitrogen, oxygen and sulfur. Examples of heteroaryl groups are pyridyl, pyrimidinyl, pyrrolyl, pyrazolyl, pyrazinyl, pyridazinyl, oxazolyl, furanyl, quinolinyl, isoquinolinyl, thiazolyl, and thienyl, which can optionally be substituted with, e.g., halogen, lower alkyl, lower alkoxy, lower alkylthio, trifluoromethyl, lower acyloxy, aryl, heteroaryl, and hydroxy.

A particularly preferred process is where R is 2,5-disubstituted furan, i.e., where the first compound is HMF and the dialdehyde is DFF.

DFF may be further converted via loss of CO to furan, which can be hydrogenated to tetrahydrofuran using standard techniques familiar to those skilled in the art.

The second process concerns preparation of a diacid of the formula HOOC-R'-COOH from an alcohol/aldehyde of the formula HOH_2C-R'-(C=O)H.

The third process concerns preparation of a diacid of the formula HOOC-R'-COOH from an alcohol/aldehyde of the formula HOH_2C-R'-(C=O)H.

In the second and third processes, R' is preferably an optionally substituted furan ring. More preferably, R' is a 2,5-disubstituted furan ring. A preferred metal bromide catalyst is comprised of a source of bromine and at least one metal selected from the group consisting of Co and Mn, and optionally containing Zr. More preferably the metal bromide catalyst contains Co.

Any of the intermediates, the alcohol/acid, acid/aldehyde, or the dialdehyde, may be isolated at any step, or the reaction may proceed without any purification. It is contemplated that the processes of the invention in which DFF and/or FDA is prepared can be run using a biomass feedstock containing HMF, such that only the final product need be isolated and purified.

For the preparation of the dialdehyde, the preferred temperatures are about 20° to 200°C, most preferably about 40° to 130°C. The corresponding pressure is such to keep the solvent mostly in the liquid phase. The preferred time of the

reaction is determined by the temperature, pressure, and catalyst concentration such that maximum yield of dialdehyde is obtained. For preparation of diacid, the preferred temperatures are about 50° to 250°C, most preferentially about 50° to 160°C. The corresponding pressure is such to keep the solvent mostly in the liquid phase. The preferred time of the reaction is determined by the temperature, pressure and catalyst concentration such that a maximum yield of diacid is obtained.

The fourth process concerns preparation of an aldehyde comprising contacting a compound of the formula AR-CH_2-OH, wherein AR is an optionally substituted aryl group, with an oxidant in the presence of a metal bromide catalyst. Preferably, AR an optionally substituted phenyl group. Most preferably, AR is an unsubstituted phenyl group. In addition to the alcohol, other functional groups may be attached to the compound as long as the other functional groups are substantially inert under reaction conditions.

A preferred metal bromide catalyst is comprised of a source of bromine and at least one metal selected from the group consisting of Co and Mn, and optionally containing Zr. More preferably the metal bromide catalyst contains Co.

The process can be run in a solvent or solvent mixture comprising at least one aliphatic C_2-C_6 monocarboxylic acid compound, preferably acetic acid.

Metal bromide catalysts employed in all of the processes of this invention comprise a soluble transition metal compound and soluble bromine-containing compound. One metal or a combination of two or more metals may be present. Many such combinations are known and may be used in the processes of the instant invention. These metal bromide catalysts are described further in W. Partenheimer, *Catalysis Today*, 23(2), 69-158, (1995), in particular pages 89-99, herein incorporated by reference. Preferably the metal is cobalt and/or manganese, optionally containing zirconium. More preferably, the catalyst is comprised of Co/Mn/Zr/Br in the molar ratios of 1.0/1.0/0.1/2.0. The amount of catalyst in the reaction mixture can be 59/55/203/4 ppm to 5900/5500/20000/390 ppm Co/Mn/Br/Zr, preferably 150/140/510/10 ppm to 2400/2200/8100/160 ppm (g of metal/g of solvent). As used herein, the molar ratio is the ratio of moles of the metals alone, not the metals as in their compound forms.

Each of the metal components can be provided in any of their known ionic or combined forms. Preferably the metal or metals are in a form that is soluble in the reaction solvent. Examples of suitable forms include, but are not limited to, metal carbonate, metal acetate, metal acetate tetrahydrate, and metal bromide. Preferably metal acetate tetrahydrates are used.

The source of bromide can be any compound that produces bromide ions in the reaction mixture. These compounds include, but are not limited to, hydrogen bromide, hydrobromic acid, sodium bromide, elemental bromine, benzyl bromide, and tetrabromoethane. Preferred is sodium bromide or hydrobromic acid. As used herein, the amount of bromine means the amount measured as Br. Thus, the molar ratio of bromine to total of the metals used in the catalyst is the moles of Br divided by the sum of the moles of the metal.

As described in Partenheimer, *ibid*, pages 86-88, suitable solvents for use in the processes of the present invention, described above, must have at least one component that contains a monocarboxylic acid functional group. The solvent may also function as one of the reagents. The processes may be run in a solvent or solvent mixture that does not contain an acid group, provided that one of the reagents does contain such a group. Suitable solvents can also be aromatic acids such as benzoic acid and derivatives thereof. A preferred solvent is an aliphatic C_2-C_6 monocarboxylic acid, such as but not limited to acetic acid, propionic acid, n-butyric acid, isobutyric acid, n-valeric acid, trimethylacetic acid, and caproic acid and mixtures thereof. Components of said mixtures can include benzene, acetonitrile, heptane, acetic anhydride, chlorobenzene, o-dichlorobenzene, and water. Most preferred as solvent is acetic acid. One advantage of using a solvent such as acetic acid is that furan-2,5-dicarboxylic acid is insoluble, facilitating purification of the insoluble product.

The oxidant in the processes of the present invention is preferably an oxygen-containing gas or gas mixture, such as, but not limited to air. Oxygen by itself is also a preferred oxidant.

The processes of the instant invention described above can be conducted in the batch, semi-continuous or continuous mode. Especially for the manufacture of FDA, operation in the batch mode with increasing temperature at specific times, increasing pressure at specific times, variation of the catalyst concentration at the beginning of the reaction, and variation of the catalyst composition during the reaction is desirable. For example, variation of the catalyst composition during reaction can be accomplished by addition of cobalt and/or manganese and/or zirconium, and/or bromide at specified times.

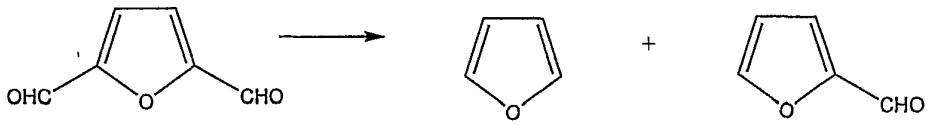
The fifth process concerns the polymerization of di(formyl)furan to form a novel polyester polymer comprising the repeat units A, B and C, as shown in the summary above. The catalysts employed in the polymerization of di(formyl)furan can be selected from any catalyst used for the esterification of a dialdehyde or two separate aldehydes. This esterification is commonly known as the "Tishchenko reaction". A partial list of catalysts used for this reaction are

those listed in Mascarenhas, et al., *Org. Letters*, 1999, Vol. 1, 9, pg. 1427; U.S. Patent No. 3,852,335; and *Reagents for Organic Synthesis*, Fieser (ed.), 1969, Vol. 5, pg. 48, and are herein incorporated by reference. An alternate catalyst is the Shvo catalyst, $[(Ph_4C_5OHOC_5Ph_4)Ru_2(CO)_4(\mu\text{–}H)]$, as described in Menashe, et al., *Organometallics* 1991, 10, 3885. This discussion concerning the Shvo catalyst is also incorporated herein by reference. Preferred catalysts are metal alkoxides of the formula $M^{+n}(O\text{-}Q)_n$ where M is a metal, n is the positive charge on the metal, and Q is an alkyl group of 1-4 carbons. Most preferred is where M is aluminum and n is three. The catalysts of the invention can be obtained already prepared from manufacturers, or they can be prepared from suitable starting materials using methods known in the art.

The repeat units A, B, and C can all be present in the polyester polymer product but are present in varying ratios, in any order in which an ester linkage is present and a polyester is formed. The term polymer is herein defined to include oligomers of 3 or more repeating units as well as higher polymers. This polymer would be useful as a molding resin or may be spun into a fiber.

The polyester polymer produced by the present process may include other repeat units in addition to those shown above. Other polyesters having the above repeat units include, but are not limited to, polyesteramides, polyesterimides, and polyesterethers. A preferred version of the polymer is a homopolymer.

A preferred embodiment of the present invention is the catalytic decarbonylation of DFF to form a mixture of unsubstituted furan and furfural.



DFF Furan Furfural

in the presence of a catalytic amount of a metal selected from Periodic Group VIII, herein defined as Fe, Ru, Os, Co, Rh, Ir, Ni, Pd, and Pt. Preferably, the catalyst consists essentially of one or more of the Periodic Group VIII metals. A particularly preferred catalyst consists essentially of Pd.

The metals may be in any form including Raney catalysts as known to those skilled in the art. The catalysts are preferably supported on a catalyst solid support. The catalyst solid support, which includes but not limited to SiO_2, Al_2O_3, carbon, MgO, zirconia, or TiO_2, can be amorphous or crystalline, or a mixture of amorphous and crystalline forms. Selection of an optimal average particle size for the catalyst supports will depend upon such process parameters as

reactor residence time and desired reactor flow rates. The amount of metal on the support is preferably about 0.5-10% and most preferably 1-5%. The catalysts of the invention can be obtained already prepared from manufacturers, or they can be prepared from suitable starting materials using methods known in the art. One typical procedure is by impregnation of the support by incipient wetness using a soluble metal salt precursor, such as the chloride, acetate, nitrate salt, following by reduction under hydrogen gas.

A preferred embodiment of the fifth process is a liquid phase reaction in which the DFF is dissolved in a suitable, inert solvent. The catalysts are placed in the solvent in a pressure vessel, and pressured to about 200-1000 psi, (1.4-6.9 MPa), more preferably about 500 psi (3.4 MPa) with an inert gas, preferably nitrogen. The reaction temperature is about 150°C-250°C, more preferably about 200°C. The reaction product containing furan and furfural can be recycled through the process one or more times, to eventually form a reaction product consisting essentially of furan.

The above process can also be combined with the process to prepare DFF described above, to create a single integrated process wherein DFF is prepared using the metal bromide catalysts described above, then decarbonylated to furan or furfural.

Materials and Methods

HMF was obtained from Lancaster Synthesis, Windham, NH. Unless otherwise stated, all materials were used as received without further purification. All percentages are by mole percent unless otherwise specified.

EXAMPLES 1-6

Reaction of HMF to DFF at ambient air Pressure

In a cylindrical glass fitted with a stirrer and baffles, 0.165 g of cobalt(II) acetate tetrahydrate, 0.169 g of manganese(II) acetate tetrahydrate, 0.142 g of sodium bromide, 0.220 g biphenyl (GC internal standard), and 10.02 g of 5-hydroxymethyl(furfural) were admixed with 100 g of acetic. The solution was purged with nitrogen gas and the temperature raised to 75°C using an external oil bath. The nitrogen was replaced with air at a flow rate of 100 ml/min at ambient atmospheric pressure. The vent oxygen was constantly monitored and occasionally liquid and vent gas samples for GC analysis were taken at the times shown in Table 2. After 30 hrs the reaction was terminated. The results from the liquid samples taken from the reactor during reaction of Example 1 are given in Table 1. The DFF yield increased with time to a maximum yield of 51% and then decreases thereafter. The mini-reactor data is summarized in Table 3. The rate of reaction, as given by the rate of disappearance of HMF, was dependent upon the

concentration of the catalyst, see especially Examples 3, 4. The maximum yields and chemical species selectivities were also dependent on the concentration of the catalyst, see Examples 1, 3-6. The dependence of the selectivity on the concentration of catalyst is given in detail for Examples 3, 4, and 6 in Table 2. The formation of carbon dioxide and carbon monoxide are undesirable because they are caused by the decomposition of HMF and its products, as well as from the solvent, acetic acid. As can be seen in Table 2, increasing the catalyst concentration greatly decreases the formation of these carbon oxides. Example 4 combines the best yield, shortest reaction time, and one of the lowest rates of carbon oxide formation.

2,5-Diformylfuran was isolated from the reaction mass as follows. The liquid from the reaction mixture was allowed to evaporate. The residue after evaporation of the reaction mixture was (a) sublimed under vacuum, followed by recrystallization of the sublimate from toluene or cyclohexane; or (b) mixed with silica gel and extracted with hexanes or cyclohexane in a Soxhlet extractor; or (c) extracted with hot toluene, with subsequent filtration of the hot toluene solution through silica, evaporation of the filtrate, and recrystallization of the product from toluene or cyclohexane.

One specific example of isolation of DFF is as follows. The dark reaction mixture that was obtained from Example 5, was evaporated to dryness on a vacuum line. The resulting waxy green-tan material was transferred to a sublimation apparatus and sublimed under vacuum (10-50 millitorr) at 90°C (oil bath) to produce 5.2 g (51 mol % based on initial HMF used) of DFF. The resulting DFF (95% pure; ^{1}H NMR and GC-MS analysis) contained 3-5% of 5-acetoxymethylfurfural. DFF that was pure to the limits of spectroscopic detection was obtained by recrystallization of the sublimate from cyclohexane or toluene/hexanes. ^{1}H NMR ($CDCl_3$, 25°C), ppm: 7.4 (s; 2H; furane CH), 9.8 (s; 2H; CHO). ^{13}C NMR (CD_2Cl_2, 25°C), ppm: 120.4 (s; CH), 154.8 (s; q C), 179.7 (s, CHO). m/z = 124. Alternatively, crude DFF can be purified by filtration of its concentrated dichloromethane solution through a short silica plug, followed by precipitation from the filtrate with hexanes.

TABLE 1

Formation of Diformylfuran in Example 1

Time, min	Conversion, %	Selectivity, %	Yield, molar, %
66	31.9	44.5	14.2
96	40.3	52.6	21.2
111	46.6	54.9	25.6
130	54.7	51.2	28.0
144	54.5	59.4	32.4
171	62.5	55.4	34.6
190	66.9	55.5	37.1
204	71.0	52.7	37.4
310	82.9	56.6	46.9
384	88.3	56.1	49.5
450	92.1	55.5	51.1
516	95.2	53.3	50.7
1368	100	35.1	35.1
1410	100	35.7	35.7
1728	100	19.8	19.8
1800	100	19.5	19.5

TABLE 2

Summary of Mini-reactor Oxygenations of Hydroxymethyl(furfural)

	Ex. 1	Ex. 2	Ex. 3	Ex. 4	Ex. 5	Ex. 6
Temp, °C	75	50 then 95(5)	75	75	50 then 75(6)	75
HMF, g	10.015	9.143	10.139	10.051	10.04	10.158
HOAc, g	100	100	100	100	100	100.1
Co, M	0.066	0.026	0.066	0.135	0.268	0.273
Mn, M	0.069	0.025	0.069	0.139	0.274	0.278
Br, M	0.137	0.050	0.137	0.279	0.557	0.580
Zr, M	0.005	0.000	0.005	0.005	0.005	0.005
HMF rate, s^{-1} (1)	$9.68E^{-05}$	$9.28E^{-05}$	$8.13E^{-05}$	$1.64E^{-04}$	-	$1.37E^{-04}$
HMF half-life	119	124	142	70	-	84
R2	0.998	0.878	0.972	0.999	-	0.994
DFF Y, max (2)	51	41	50	57	51	52
Time, max	450	414	642	310	550	430
C, max	92	98	95	91	95	97
S, max	55	42	53	63	54	54

	Ex. 1	Ex. 2	Ex. 3	Ex. 4	Ex. 5	Ex. 6
time, min (3)	1800	564	640	366	550	430
C,%	100	99	95	95	95	97
S,%	19	41	53	58	54	54
Y,%	19	40	50	55	51	52
HMF acet, %	0.4	8.4	7.5	6.1	4.5	5.7
CO_X, ml	878	-	1022	257	219	318
HMF to CO_X (4)	7.4	-	8.5	2.1	1.8	2.6

Footnotes

1 Determined by rate of disappearance of hydroxymethyl(furfural).

2 Abbreviations used: C = % conversion, S = % selectivity, Y= % molar yield, as determined by GC. Max is the highest observed during experiment.

3 Time when experiment was terminated

4 Loss of HMF due to carbon monoxide and carbon dioxide formation. Assumes no CO_X formation from the solvent.

5 Reaction performed at 50°C for 105 min, then 95°C for 459 min. Additional Co/Mn/Br catalyst was add at 115 and 210 min

6 Reaction performed at 50°C for 180 min, then 75°C for 370 min

EXAMPLES 7-15

Reaction of HMF to DFF

Table 3 further illustrates that placing HMF with acetic acid and catalyst metals and then subjecting them to 1000 psi air pressure (7 MPa), can produce high yields of DFF. Molar yields up to 63% were obtained. The yield varied with temperature and type of catalyst used.

TABLE 3

Initial Conditions for the Oxidation of HMF in Shaker Tubes

Ex.	Catalyst	HMF, g	Co, ppm	Mn, ppm	HBr, ppm	Zr, ppm	Temp, °C	Time, hr	HMF, conv., %	HMF, select. %	DFF yld, %
7	Co/Mn/Br/Zr	0.2504	203	189	551	20	50	2	60.4	66.6	40.2
8	Co/Mn/Br/Zr	0.2481	406	378	1102	20	50	2	69.2	65.3	45.2
9	Co/Mn/Br	0.2519	203	189	551	0	50	2	60.6	38.4	23.3
10	Co/Mn/Br	0.252	406	378	1102	0	50	2	61.7	54.6	33.7
11	Co	0.2516	7000	0	0	0	50	2	48.3	22.8	11.0
12	Co/Mn/Br/Zr	0.25	203	189	551	20	75	2	82.5	73.2	60.4
13	Co/Mn/Br/Zr	0.2517	406	378	1102	20	75	2	99.7	61.6	61.4
14	Co/Mn/Br	0.2529	203	189	551	0	75	2	71	54.3	38.6
15	Co/Mn/Br	0.2514	406	378	1102	0	75	2	92.2	68.3	63.0

EXAMPLES 16-40

The Reaction of HMF to CFF and FDA

Placing HMF in reactors with acetic acid and catalyst metals and having them react with air at 1000 psi (7 MPa) gave good yields of FDA. A particular advantage of this method is that the majority of FDA precipitates from solution upon cooling to room temperature. The yields to CFF and FDA , reported on Table 4, are those which were obtained from the solids only. Table 4 illustrates that different catalysts such as those using cobalt, or a mixture such as Co/Mn/Br and Co/Mn/Zr/Br all produced good yields of FDA. It also illustrates that increasing catalyst concentrations at a given temperature and time, nearly always increased the FDA yield.

Examples 35 through 37 are to be compared to Examples 38 through 40. In the latter series the temperature was staged – initially it was held at 75°C for 2 hrs and then raised to 150°C for two hrs. This staging of the temperature gave higher yields.

TABLE 4

Reaction of HMF to CFF and FDA All reactions at 1000 psi air (7 MPa)

Ex.	Catalyst	HMF, g	Co, ppm	Mn, ppm	HBr, Ppm	Zr, ppm	Temp, C	Time, hr	CFF, yld	FDA, yld
16	Co/Mn/Br/Zr	0.2517	203	189	551	20	100	2	3.1	18.7
17	Co/Mn/Br/Zr	0.2533	406	378	1102	20	100	2	6.8	42.3
18	Co/Mn/Br	0.2522	203	189	551	0	100	2	4.1	29.7
19	Co/Mn/Br	0.2505	406	378	1102	0	100	2	3.3	44.8
20	Co	0.2589	7000	0	0	0	100	2	5.1	31.0
21	Co/Mn/Br/Zr	0.2483	203	189	551	20	125	2	2.1	36.5
22	Co/Mn/Br/Zr	0.249	406	378	1102	20	125	2	2.3	45.6
23	Co/Mn/Br	0.2503	203	189	551	0	125	2	1.8	35.2
24	Co/Mn/Br	0.2526	406	378	1102	0	125	2	2.2	44.7
25	Co	0.2616	7000	0	0	0	125	2	4.3	16.8
26	Co/Mn/Br/Zr	0.7535	406	378	1102	20	105	12	3.1	26.4
27	Co/Mn/Br/Zr	0.7568	812	756	2204	20	105	12	4.2	50.6
28	Co/Mn/Br/Zr	0.7498	1218	1134	3306	20	105	12	2.5	58.8
29	Co/Mn/Br/Zr	0.5057	406	378	1102	20	105	12	2.4	24.1
30	Co/Mn/Br/Zr	0.501	812	756	2204	20	105	12	5.1	44.0
31	Co/Mn/Br/Zr	0.4994	1218	1134	3306	20	105	12	5.6	47.4
32	Co/Mn/Br/Zr	0.499	406	378	1102	20	105	8	3.3	32.9

Ex.	Catalyst	HMF, g	Co, ppm	Mn, ppm	HBr, Ppm	Zr, ppm	Temp, C	Time, hr	CFF, yld	FDA, yld
33	Co/Mn/Br/Zr	0.5046	812	756	2204	20	105	8	4.8	41.0
34	Co/Mn/Br/Zr	0.5	1218	1134	3306	20	105	8	7.3	50.6
35	Co/Mn/Br/Zr	0.2498	406	378	1102	20	105	2	3.7	36.9
36	Co/Mn/Br/Zr	0.254	812	756	2204	20	105	2	4.8	40.9
37	Co/Mn/Br/Zr	0.4988	406	378	1102	20	105	2	1.7	14.0
38	Co/Mn/Br/Zr	0.2517	406	378	1102	20	75,150	2,2	5.2	51.4
39	Co/Mn/Br/Zr	0.5077	812	756	2204	20	75,150	2,2	6.2	52.9
40	Co/Mn/Br/Zr	0.5105	406	378	1102	20	75,150	2,2	6.5	54.6

EXAMPLES 41-59

Oxidation of Benzyl Alcohol

0.247 g of cobalt(II) acetate tetrahydrate, 0.242 g of manganese(II) acetate tetrahydrate, 0.337 g of hydrogen bromide, 0.198 g biphenyl (GC internal standard), and 9.72 g of benzyl alcohol were placed in 95 g of acetic acid and 5% water in a cylindrical glass flask fitted with a stirrer and baffles. The solution was purged with nitrogen gas and the temperature raised to 95°C using an external oil bath. The nitrogen was replaced with air at a flow rate of 100 ml/min at ambient atmospheric pressure. Samples were withdrawn from the reactor and analyzed giving the results in Table 5. A yield of 55 mol percent benzaldehyde is observed. (Values of benzaldehyde, benzyl acetate, benzoic acid in mol % based on benzyl alcohol charged).

TABLE 5

Oxidation of Benzyl Alcohol

Ex.	Time, hr.	Conv., %	Benzaldehyde, mol%	Benzyl acetate, mol%	Benzoic acid, mol%
41	0	10.4	0.36	10.9	0
42	0.1	15	1.8	11.3	0
43	0.2	21	5.5	12.9	0
44	0.33	28	10.4	15.1	0
45	0.5	35	15	16.8	0
46	0.6	41	19.2	18.2	0
47	0.67	44	21.1	18.9	0.27
48	0.75	48	24.3	19.6	0.35
49	0.87	52	27.3	20.4	0.45

Ex.	Time, hr.	Conv., %	Benzaldehyde, mol%	Benzyl acetate, mol%	Benzoic acid, mol%
50	1	57	31.5	21.5	0.61
51	1.17	62	34.1	22	0.8
52	1.3	67	37.8	22.8	1.02
53	1.4	69	39.7	23.1	1.21
54	1.53	73	42	23.5	1.55
55	1.75	78	45.4	24.1	1.75
56	1.92	81	47.6	24.3	2.45
57	2.1	83	49.3	24.5	2.69
58	2.33	88	52.4	24.6	3.43
59	2.83	93	54.6	24.2	6.23

EXAMPLE 60

Polymerization of DFF of 5-(hydroxymethyl)-furan-2-carboxylic acid ('Tishchenko polymerization')

The reaction was conducted under rigorously dry conditions. The products were isolated in air. To a mixture of DFF (0.265 g) and dry toluene (6 mL) was added aluminum isopropoxide (Aldrich; 45 mg), and the reaction mixture was vigorously stirred at 95°C (oil bath) for 3 hours. The greenish-brown precipitate was filtered off, washed with toluene, and dried under vacuum to give 0.190 g of a tan powder that appeared to be amorphous (fraction A). The combined mother liquor and the washings were evaporated and dried under vacuum to yield 0.105 g of fraction B as a viscous yellowish oil. ^{1}H NMR spectra of both fractions A and B ($CDCl_3$, 25°C) revealed a number of singlets at 5.2-5.4 ppm (-CH_2-O(O)C-), indicative of polyester formation. A sample of the solid product (0.7460 mg) was studied by TGA in the temperature range of 40-600°C. The onset of decomposition was observed around 100-120°C. The total weight loss measured was about 10% at 147°C, and about 34% at 294°C.

EXAMPLE 61

The reaction was carried out under nitrogen. The Shvo catalyst ([$(Ph_4C_5OHOC_5Ph_4)Ru_2(CO)_4(\mu$–H)]; as described in Menashe, N.; Shvo, Y. Organometallics 1991, 10, 3885; 5 mg) was added to a mixture of DFF (200 mg), toluene (5 mL), and formic acid (cocatalyst; 5 μL). The clear solution was stirred at 100°C (oil bath) for 3 hours. ^{1}H NMR analysis of the reaction mixture indicated 50% conversion to polymeric material. More Shvo catalyst (3 mg) was

added and the mixture was stirred at 100°C (oil bath) for 2 days, 90% conversion was reached (^{1}H NMR).

EXAMPLES 62-69

The catalysts were prepared by taking a carbon support (Englehard Corp., 12 Thompson Rd., E. Windsor, CT) and impregnating by incipient wetness a metal salt. The precursors used were $NiCl_2 \cdot 6H_2O$ (Alfa), Re_2O_7 (Alfa), $PdCl_2$ (Alfa), $RuCl_3 \cdot xH_2O$ (Aldrich), H_2PtCl_6 (Johnson Matthey), $CrCl_3 \cdot 6H_2O$ (Baker), and 5% Rh using $RhCl_3 \cdot xH_2O$ (Alfa). The samples were dried and reduced at 400°C in H_2 for 2 hours. The decarbonylation reactions were performed by dissolving 50 mg of DFF in 1 ml of dioxane, and which was then placed with 50 mg of catalyst in a 5 ml pressure vessel. The vessel was charged to 500 psi with N_2 and heated to 200°C for 2 hours. The sample was then cooled, vented and the product analyzed by GC-MS. Results are shown in Table 6 below.

TABLE 6

Decarbonylation of DFF

			Selectivity (%)			
Ex.	Catalyst	Conv. (%)	Furan	THF	Furfural	Others
62	5%Re/carbon	15.6	2.8	0.0	2.1	95.1
63	5%Pt/carbon	46.1	2.2	0.0	42.7	55.0
64	5%Cr/carbon	27.3	1.3	0.0	0.0	98.7
65	5%Rh/carbon	33.8	1.7	0.0	29.7	68.6
66	5%Ni/carbon	10.3	5.1	0.0	1.7	93.2
67	5%Pd/carbon	98.6	49.8	1.0	48.1	1.1
68	5%Ru/carbon	25.0	3.5	0.0	62.9	33.6

CLAIMS

What is claimed is:

1. A process for the preparation of a dialdehyde comprising:
contacting a compound containing an alcohol functionality and an aldehyde functionality with an oxidant in the presence of a metal bromide catalyst under conditions promoting formation of dialdehyde product to form a reaction mixture.

2. The process of Claim 1 wherein the metal bromide catalyst is comprised of a source of bromine and at least one metal selected from the group consisting of Co and Mn.

3. The process of Claim 3 wherein the metal bromide catalyst comprises Co and Mn.

4. The process of Claim 3 further comprising Zr.

5. The process of Claim 3 wherein the oxidant is selected from the group consisting of air and oxygen.

6. The process of Claim 3 wherein the process is run in a solvent or solvent mixture comprised of at least one aliphatic C_2-C_6 monocarboxylic acid compound.

7. The process of Claim 6 wherein the process is run in acetic acid.

8. The process of Claim 1 wherein the dialdehyde is of the formula H(C=O)-R-(C=O)H and the compound is of the formula HOH_2C-R-(C=O)H, wherein R is selected from the group consisting of a heterocyclic group and a C_1-C_{20} linear or cyclic optionally substituted alkyl or aryl group.

9. The process of Claim 8 wherein R is an optionally substituted furan ring.

10. The process of Claim 8 wherein the dialdehyde is 2,5-di(formyl)furan.

11. A process for the preparation of a diacid of the formula HOOC-R'-COOH from an alcohol/aldehyde of the formula HOH_2C-R'-(C=O)H, wherein R' is an optionally substituted furan ring, comprising the steps:

(a) contacting the alcohol/aldehyde with an oxidant in the presence of a metal bromide catalyst forming an alcohol/acid having the formula HOH_2C-R'-COOH, and optionally isolating the alcohol/acid;

(b) contacting the alcohol/acid with an oxidant in the presence of a metal bromide catalyst forming an acid/aldehyde having the formula HOOC-R'-(C=O)H, and optionally isolating the acid/aldehyde;

(c) contacting the acid/aldehyde with an oxidant in the presence of a metal bromide catalyst forming the diacid, optionally isolating the diacid.

12. The process of Claim 11 wherein the product of the reaction is isolated following steps a, b or c.

13. A process for the preparation of a diacid of the formula HOOC-R'-COOH from an alcohol/aldehyde of the formula HOH_2C-R'-(C=O)H, wherein R' is an optionally substituted furan ring, comprising the steps:

(a) contacting the alcohol/aldehyde with an oxidant in the presence of a metal bromide catalyst forming a dialdehyde having the formula H(C=O)-R'-(C=O)H, and optionally isolating the dialdehyde;

(b) contacting the dialdehyde with an oxidant in the presence of a metal bromide catalyst forming an acid/aldehyde having the formula HOOC-R'-(C=O)H, and optionally isolating the acid/aldehyde; and

(c) contacting the acid/dialdehyde with an oxidant in the presence of a metal bromide catalyst forming the diacid, and optionally isolating the diacid.

14. The process of Claim 13 wherein the product of the reaction is isolated following steps a, b or c.

15. The process of Claim 11 or 13 wherein the process is run in a solvent or solvent mixture comprised of at least one aliphatic C_2-C_6 monocarboxylic acid solvent compound.

16. The process of Claim 15 wherein the process is run in acetic acid.

17. The process of Claim 15 wherein the metal bromide catalyst comprises a source of bromine and at least one metal selected from the group consisting of Co and Mn.

18. The process of Claim 17 further comprising Zr.

19. The process of Claim 18 wherein the catalyst comprises Co and Mn.

20. The process of Claim 16 wherein the process further comprises before step c converting the acid/aldehyde to an acetate ester of the formula $CH_3(C=O)OCH_2$-R'-(C=O)H.

21. The process of Claim 20 wherein the diacid is furan-2,5-dicarboxlic acid and the alcohol/aldehyde is 5-(hydroxymethyl)furfural.

22. A process for the preparation of an aldehyde comprising:
contacting a compound of the formula AR-CH_2-OH wherein AR is an optionally substituted aryl with an oxidant in the presence of a metal bromide catalyst.

23. The process of Claim 22 wherein the metal bromide catalyst is comprised of a source of bromine at least one metal selected from the group consisting of Co and Mn.

24. The process of Claim 22 wherein the metal bromide catalyst comprises Mn and Co.

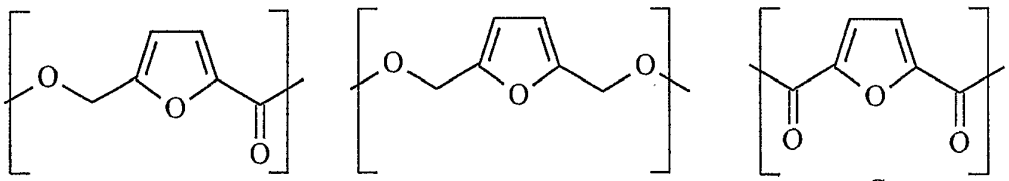
25. The process of Claim 22 wherein the oxidant is selected from the group consisting of air and oxygen.

26. The process of Claim 23 wherein the process is run in a solvent or solvent mixture comprised of at least one aliphatic C_2-C_6 monocarboxylic acid compound.

27. The process of Claim 23 wherein the process is run in acetic acid.

28. The process of Claim 27 wherein AR is an optionally substituted phenyl ring.

29. A process to form a polyester polymer comprising the repeat units A, B and C



A B C

wherein said process comprises polymerization of diformylfuran.

30. The process of Claim 29 wherein the polyester polymer product is a homopolymer.

31. The process of Claim 30 wherein the process is performed in the presence of a catalyst of the formula $M^{+n}(O\text{-}Q)_n$ wherein M is a metal, n is the positive charge on the metal, and Q is an alkyl group of 1-4 carbons.

32. The process of Claim 31 wherein M is aluminum and n is three.

33. A polyester polymer comprising repeating units A and B and C.

34. The polymer of Claim 33 wherein the polyester polymer is a homopolymer.

35. A process for the preparation of furan comprising converting 2,5-diformylfuran into a furan and furfural product mix via decarbonylation in the presence of a catalytic amount of a compound consisting essentially of a optionally supported metal selected from Periodic Group VIII.

36. The process of Claim 35 wherein the process further comprises converting the furan and furfural product mix via decarbonylation into furan in the

presence of a catalytic amount of a compound consisting of a optionally supported metal selected from Periodic Group VIII.

37. The process of Claim 35 wherein the catalyst is supported on a catalyst support member.

38. The process according to Claim 37 wherein the metal is palladium and the catalyst support member is carbon.

39. The process according to Claim 8 further comprising converting the dialdehyde into a furan and furfural product mix via decarbonylation in the presence of a catalytic amount of a compound consisting of a optionally supported metal selected from Periodic Group VIII.

40. The process of Claim 39 wherein the process further comprises converting the furan and furfural product mix via decarbonylation into furan in the presence of a catalytic amount of a compound consisting of a optionally supported metal selected from Periodic Group VIII.

41. The process of Claim 39 wherein the catalyst is supported on a catalyst support member.

42. The process according to Claim 41 wherein the metal is palladium and the catalyst support member is carbon.

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(54) Title: OXIDATION OF 5-(HYDROXYMETHYL) FURFURAL TO 2,5-DIFORMYLFURAN AND SUBSEQUENT DECARBONYLATION TO UNSUBSTITUTED FURAN

(57) Abstract: Alcohols are catalytically oxidized to aldehydes, in particular to benzaldehyde and diformylfuran, which are useful as intermediates for a multiplicity of purposes. The invention also relates to the polymerization of the dialdehyde and to the decarbonylation of the dialdehyde to furan.

INTERNATIONAL SEARCH REPORT

Ir onal Application No
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A. CLASSIFICATION OF SUBJECT MATTER
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, WPI Data, EPO-Internal, BEILSTEIN Data, INSPEC, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GERBER T I A ET AL: "THE PARTIAL AIR OXIDATION OF ALKYL AROMATIC COMPOUNDS CATALYSED BY COBALT/BROMIDE IN CARBOXYLIC ACIDS: MECHANISTIC CONSIDERATIONS" SOUTH-AFRICAN JOURNAL OF CHEMISTRY/ SUID-AFRIKAANSE TIDSKRIF VIR CHEMIE, FOUNDATION FOR EDUCATION, SCIENCE AND TECHNOLOGY,, SA, vol. 51, no. 4, December 1998 (1998-12), pages 178-185, XP000882018 ISSN: 0379-4350 abstract page 181; figure 4; table 1 ---	1-21
Y	EP 0 356 703 A (HOECHST A.-G., FED. REP. GER.) 7 March 1990 (1990-03-07) the whole document ---	1-21
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
29 January 2002	19. 04. 2002

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 96 17836 A (AGRICHIMIE SA ;DURAND GERMAIN (FR); FAUGERAS PIERRE (FR); LAPORTE) 13 June 1996 (1996-06-13) abstract; claims page 2 -page 7 ---	1-21
Y	PARTENHEIMER W: "METHODOLOGY AND SCOPE OF METAL/BROMIDE AUTOXIDATION OF HYDROCARBONS" CATALYSIS TODAY, AMSTERDAM, NL, vol. 23, 1995, pages 69-158, XP001041910 cited in the application page 100 -page 104; tables 4.1-4.3 ---	1-21
A	FR 2 669 634 A (FURCHIM) 29 May 1992 (1992-05-29) abstract; claims ---	1-21
A	OKADA T ET AL: "THE LIQUID-PHASE OXIDATION OF METHYLBENZENES BY THE COBALT-COPPER- BROMIDE SYSTEM" BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, JAPAN PUBLICATIONS TRADING CO. TOKYO, JP, vol. 54, no. 9, September 1981 (1981-09), pages 2724-2727, XP000882017 ISSN: 0009-2673 abstract page 2726 ---	1-21
A	PATENT ABSTRACTS OF JAPAN vol. 015, no. 285 (C-0851), 19 July 1991 (1991-07-19) -& JP 03 101672 A (KAO CORP), 26 April 1991 (1991-04-26) abstract -----	1-21

INTERNATIONAL SEARCH REPORT

national application No.
PCT/US 01/09701

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-21

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-8, and 11-20 relate to processes for the preparation of an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the processes claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the process of independent claims 1 and 11 as far as the subject-matter of claims 9, 10, and 21 are concerned.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-21

   Process for the preparation of dialdehydes and/or diacids starting from compounds containing an alcohol and an aldehyde functionality with an oxidant in the presence of a metal bromide catalyst

2. Claims: 22-28

   Process for the preparation of an aryl aldehyde starting from aryl methyl alcohols with an oxidant in the presence of a metal bromide catalyst

3. Claims: 29-34

   Process for the polymerisation of diformylfuran

4. Claims: 35-42

   Process for the preparation of furan comprising decarbonylation of 2,5-diformylfuran

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/09701

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0356703 A	07-03-1990	DE 3826073 A	01-02-1990
		AT 67994 T	15-10-1991
		CA 1339569 A	02-12-1997
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PROCESSES FOR THE PREPARATION AND PURIFICATION OF HYDROXYMETHYL FURALDEHYDE AND DERIVATIVES

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Inventor(s):	SANBORN ALEXANDRA J [US]		
Applicant(s):	ARCHER DANIELS MIDLAND CO [US]; SANBORN ALEXANDRA J [US]		
Classification:	**- international:**	C07D307/42; C07D307/46	
	- cooperative:	**default**	C07C51/245; C07D307/42; C07D307/46
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Abstract of WO 2006/063220 A2

A method for utilizing an industrially convenient fructose source for a dehydration reaction converting a carbohydrate to a furan derivative is provided. Recovery methods also are provided. Embodiments of the methods improve upon the known methods of producing furan derivatives.

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Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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— *without international search report and to be republished upon receipt of that report*

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(54) Title: PROCESSES FOR THE PREPARATION AND PURIFICATION OF HYDROXYMETHYL FURALDEHYDE AND DERIVATIVES

(57) Abstract: A method for utilizing an industrially convenient fructose source for a dehydration reaction converting a carbohydrate to a furan derivative is provided. Recovery methods also are provided. Embodiments of the methods improve upon the known methods of producing furan derivatives.

WO 2006/063220 A2

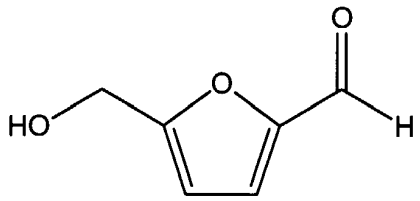
PROCESSES FOR THE PREPARATION AND PURIFICATION OF HYDROXYMETHYLFURALDEHYDE AND DERIVATIVES

Field Of The Invention

Improved methods of producing chemical compounds are included herein. The dehydration reaction of common carbohydrates to form commercially important compounds, furan derivatives, and methods of optimizing the reactions to efficiently synthesize the products, as well as improved methods of purification are included herein. The present application claims priority to and incorporates by reference U.S. Provisional Application No. 60/635,406, filed December 10, 2004 and U.S. Patent Application No. 11/070,063, filed March 2, 2005.

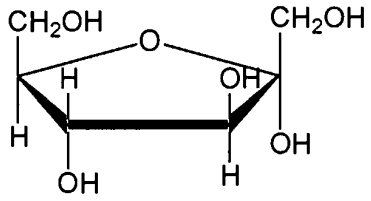
Background Of The Invention

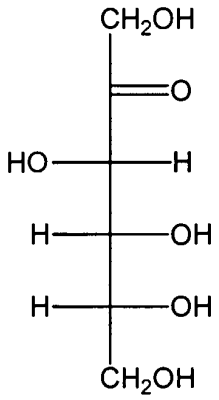
2,5-(Hydroxymethyl)furaldehyde, also known as 2,5-(hydroxymethyl)furfural (HMF), has many important industrial and commercial applications, largely due to its many functional groups and ability to serve as a precursor in many polymerization reactions. HMF, for example, is a suitable starting source for the formation of various furan monomers required for the preparation of non-petroleum-derived polymeric materials. HMF, as well as other 2,5-disubstituted furanic derivatives, also has great potential for use in the field of intermediate chemicals from regrowing resources. Also due to its various functionalities, HMF may be used to produce a wide range of products, including, but not limited to, polymers, solvents, surfactants, pharmaceuticals, and plant protecting agents. HMF is shown in the structure below:



The use of HMF and other furfural derivatives may be compared with the use of corresponding benzene-based macromolecular compounds. In order to be cost-effective and compete in this market, HMF must be able to be produced at competitive prices. The production of HMF has been studied for years, but an efficient and cost-effective method of producing HMF in high yields has yet to be found. HMF is primarily produced from the dehydration reaction of a carbohydrate compound, particularly monosaccharides, including glucose and fructose. Complications arise from the rehydration of HMF after the dehydration occurs, which often yields the by-products of levulinic acid, and formic acid. Another competing side reaction is the polymerization of HMF and/or fructose to form humin polymers.

Hexoses are the preferred carbohydrate source from which HMF is formed. Fructose is the preferred hexose used for the dehydration reaction to form HMF. This is in part because fructose has been shown to be more amendable to the dehydration reaction to a form HMF. Fructose is shown by the structures below:





Fructose however, is more expensive than other hexoses, such as glucose (dextrose), and maltose, for example. Early processes and procedures for the production of HMF concentrated on the use of crystalline fructose, but its widespread use is prevented by its high cost. Other sources of fructose, including

high-fructose corn syrup (HFCS), have been used to produce HMF and other furan derivatives. Szmant and Chundury used high fructose corn syrup as a starting material in forming HMF, as disclosed in a 1981 article in *J. Chem. Tech. Biotechnol., 31*, (pgs. 135-145). Szmant uses a variety of carbohydrates as starting material, but designs reaction conditions specific to each fructose source. Szmant, for example, uses a boron trifluoride catalyst (BF_3 Et_2O) with DMSO as a solvent in the conversion of HFCS to HMF, but utilizes different catalyst/solvent combinations with different starting materials. Use of BF_3 Et_2O as a catalyst is not economically practical since it cannot be recovered and re-used. Furthermore, Szmant requires the use of a Pluronic emulsifier to suppress foaming. Szmant also requires bubbling of nitrogen to suppress oxidation. Still further, Szmant requires the use of DMSO as a solvent, which is not easily separable from the HMF product, and therefore creates difficulties with product recovery. It is very desirable, therefore, to develop an industrially practicable process for producing HMF in high purity.

U.S. Patent No. 6,706,900 to Grushin et al. (Grushin '900) also discloses the dehydration of fructose in the form of high-fructose corn syrup, to form HMF as an intermediate; but this process is performed in the context of forming diformylfuran, also known as 2,5-dicarboxaldehyde (DFF). The reaction proceeds in an aqueous environment, and the HMF that is formed is not isolated from the reaction mixture, but rather is directly converted to DFF without an isolation step. The reaction conditions of Grushin '900 are therefore not constrained by considerations of product yields of HMF, as it is formed as an intermediate that is not isolated as a product. More importantly from a practical commercial standpoint, Grushin '900 is not constrained by considerations of isolating HMF from the product mixture. An efficient method for producing HMF in desirable yields and sufficiently high purity from a natural and industrially convenient fructose source that may include other mixed carbohydrates has yet to be found.

Water has in the past been used as a solvent of choice in dehydration reactions forming HMF because of the solubility of fructose in water. Aqueous conditions, however, have proven to deleteriously affect the dehydration reaction of fructose to HMF in a variety of ways. Aqueous conditions have led to decreased yield of HMF as low selectivity for the dehydration reaction has been demonstrated. Furthermore, solvation of protons in water highly reduces the catalytic activity for the dehydration reaction. Low selectivity of the dehydration reaction simultaneously

leads to increased polymerization reactions and humin formation, which also interfere with the synthesis of HMF.

In an attempt to solve such problems associated with aqueous systems, one proposed solution involves an improvement by simultaneously extracting HMF after the dehydration reaction. A similar attempt to improve yields involves the adsorption of HMF on activated carbon. The key factor in these processes is a rapid removal of HMF from the acidic medium in which it is formed. However, these systems generally suffer from high dilution or partially irreversible adsorption of HMF.

In another attempt to solve the problems of aqueous systems, an organic solvent may be added to the aqueous solution, such as, for example, butanol or dioxane. Such systems, however, present a difficulty in that rehydration of HMF is common and ether formation of HMF occurs with the solvent if alcohols are employed. High yields of HMF, therefore, were not found with the addition of these organic solvents. In a further attempt to provide an adequate solvent system, aqueous solvent mixtures and anhydrous organic solvents have also been employed to ensure favorable reaction conditions. Examples of anhydrous organic solvents used include dimethylformamide, acetonitrile, dimethylsulfoxide, and polyethylene glycol.

Dimethylsulfoxide (DMSO), for example, has been extensively studied and employed as a solvent in the dehydration reaction to form HMF. Improved yields of HMF have been reached with ion exchangers or boron trifluoride etherate as a catalyst, and even without any catalyst. DMSO presents a problem, however, in that recovery of HMF from the solvent is difficult.

Furthermore, although dehydration reactions performed in solvents with high boiling points, such as dimethylsulfoxide and dimethylformamide, have produced improved yields, the use of such solvents is cost-prohibitive, and additionally poses significant health and environmental risks in their use. Still further, purification of the product via distillation has not proven effective for a variety of reasons. First of all, on long exposure to temperatures at which the desired product can be distilled, HMF and impurities associated with the synthetic mixture tend to be unstable and form tarry degradation products. Because of this heat instability, a falling film vacuum still must be used. Even in use with such an apparatus however,

resinous solids form on the heating surface causing a stalling in the rotor, and the frequent shutdown resulting therefrom makes the operation inefficient.

Catalysts may also be used to promote the dehydration reaction. Some commonly used catalysts include cheap inorganic acids, such as H_2SO_4, H_3PO_4, HCl, and organic acids such as oxalic acid, levulinic acid, and p-toluene sulfonic acid. These acid catalysts are utilized in dissolved form, and as a result pose significant difficulties in their regeneration and reuse, and in their disposal. In order to avoid these problems, solid sulfonic acid catalysts have also been used. Solid acid resins, however, are limited in use by the formation of deactivating humin polymers on their surfaces under conditions taught by others. Other catalysts, such as boron trifluoride etherate, can also be used. Metals, such as Zn, Al, Cr, Ti, Th, Zr, and V can be used as ions, salts, or complexes as catalysts. Such use has not brought improved results, however, as yields of HMF have continued to be low. Ion exchange catalysts have also been used, but have also delivered low HMF yields under conditions taught by others, and further limit the reaction temperature to under 130°C.

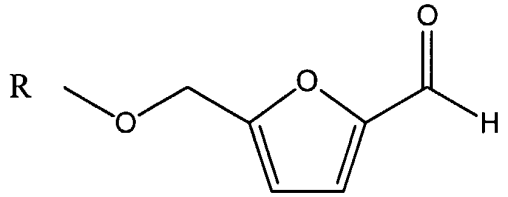
Summary of the Invention

Provided herein is an improved method of preparing 2,5 – (hydroxymethyl)furaldehyde comprising: i) combining a fructose source, a solvent selected from the group consisting of 1-methyl-2-pyrrolidinone, dimethylacetamide, dimethylformamide and combinations of thereof, with a catalyst to provide a reaction mixture; ii) heating said reaction mixture to a temperature and for a time sufficient to promote an acid-catalyzed dehydration reaction of fructose in said fructose source to form a product mixture; and iii) isolating 2,5-(hydroxymethyl)furaldehyde from said product mixture.

In another embodiment, there is provided a method of preparing 2,5 – (hydroxymethyl)furaldehyde comprising: i) combining a fructose source, an organic solvent, and an acid catalyst to provide a reaction mixture; ii) heating said reaction mixture to a temperature and for a time sufficient to promote a dehydration reaction of fructose in said fructose source to form a first product mixture; iii) neutralizing the pH of the first product mixture to a pH of about 7 to 9; iv) distilling the first product mixture after neutralizing the pH to remove said organic solvent remaining in the first product mixture; and v) purifying said product mixture to provide a second product mixture comprising greater than 60% by weight of 2,5 – (hydroxymethyl)furaldehyde.

Also provided also herein is a method of preparing 2,5-(hydroxymethyl)furaldehyde comprising the steps of: i) combining a fructose source, an acid catalyst, a first organic solvent, and a second organic solvent that is non miscible with the first organic solvent to provide a reaction mixture, the first and second organic solvents being selected so that the second organic solvent preferentially dissolves 2,5-(hydroxymethyl)furaldehyde relative to the first organic solvent; ii) heating said reaction mixture to a temperature and for a time sufficient to promote a dehydration reaction of fructose in said fructose source to form a product mixture with a first immiscible phase and a second immiscible phase; and iii) isolating 2,5-(hydroxymethyl)furaldehyde from said second immiscible phase of said product mixture.

In another embodiment, provided herein is a method of preparing an R-oxymethylfurfural ether of hydroxylmethylfurfural of the formula:



where R is selected from the group consisting of alkyl, cycloalkyl, allyl and aryl, comprising: (i) combining a fructose source, an R-OH solvent, and an acid catalyst to form a reaction mixture; (ii) heating said reaction mixture to a temperature and for a time sufficient to promote an acid-catalyzed dehydration reaction fructose in the fructose source and to form R-oxymethylfurfural in a product mixture; and (iii) Isolating the R-oxymethylfurfural from said product mixture.

Also provided herein is a method of preparing levulinic acid comprising: (i) combining a fructose source, at least one of polyethylene glycol and end capped polyethylene glycol, and an acid catalyst to form a reaction mixture; (ii) heating said reaction mixture to a temperature and for a time sufficient to promote an acid-catalyzed dehydration reaction of fructose in the fructose source and to form levulinic acid in a product mixture; and (iii) isolating levulinic acid from said product mixture.

In another embodiment, provided herein is a method of preparing 2,5-bis-(hydroxymethyl)furan comprising: heating a reaction mixture comprising 2,5-(hydroxymethyl)furaldehyde, a solvent, and a catalyst system comprising nickel and zirconium at a temperature, for a time, and at a pressure sufficient to promote

reduction of the 2,5-(hydroxymethyl)furaldehyde to 2,5-bis-(hydroxymethyl)furan to produce a product mixture comprising 2,5-bis-(hydroxymethyl)furan.

Provided herein is an improved method of preparing 2,5 – (hydroxymethyl)furaldehyde. The method includes the steps of: i) combining materials comprising a fructose source, a solvent, and a catalyst to form a reaction mixture; ii) heating said reaction mixture to a temperature and for a time sufficient to promote an acid-catalyzed dehydration reaction of fructose in said fructose source to form a product mixture; and iii) isolating 2,5-(hydroxymethyl)furaldehyde from said product mixture. Preferably the catalyst is a heterogeneous, re-usable, or recyclable catalyst.

In one embodiment the fructose source is high fructose corn syrup, and the method is performed under vacuum conditions. In a further embodiment the carbohydrate source is added gradually in a stepwise fashion once the reaction has been initiated, this entails the addition of two or more discrete aliquots over a specified period of time. In an additional embodiment, the mixed carbohydrate source comprises a first carbohydrate source in a first physical state, and a second carbohydrate source in a second physical state, wherein the first and second physical states are not the same, that is to say they are in different physical states. Suitable carbohydrate sources include, but are not limited to, a hexose, a pentose, fructose syrup, crystalline fructose, and, process streams from the crystallization of fructose.

Suitable mixed carbohydrate source may comprise any industrially convenient carbohydrate sources, such as corn syrup. The mixed carbohydrate sources include, but are not limited to, hexoses, fructose syrup, crystalline fructose, high fructose corn syrup, crude fructose, purified fructose, high fructose corn syrup refinery intermediates and by-products, process streams from crystallizing fructose or glucose, and molasses, such as soy molasses resulting from production of soy protein concentrate.

Provided also herein is a further method of preparing 2,5 – (hydroxymethyl)furaldehyde that includes the steps of: i) combining materials comprising a carbohydrate source, an organic solvent, and an ion-exchange resin catalyst to form a non-aqueous reaction mixture; ii) heating said non-aqueous reaction mixture to a temperature and for a time sufficient to promote a dehydration reaction of said carbohydrate source to form a first product mixture; iii) removing the

ion-exchange resin catalyst from the first product mixture to provide a product isolate; iv) distilling the product isolate to remove said solvent remaining in said product isolate; and v) purifying said product isolate to provide a second product mixture comprising greater than 60% by weight of 2,5 – (hydroxymethyl)furaldehyde. In one embodiment, the product isolate is adjusted to a neutral pH after removing the ion-exchange resin from said product mixture, and before being subjected to a distillation to remove the organic solvent.

In one embodiment, the product mixture may be further isolated by such methods which are well known in the art, such as, but not limited to, filtration, vacuum or suction filtration, or gravity filtration. Purification of the product isolate may be carried out by a solvent extraction process to provide the second product mixture . Examples of solvent extraction processes that may be used include, but are not limited to, a column chromatography process and liquid-liquid extraction. A liquid-liquid extraction process comprises adding a mixture of a water-immiscible organic solvent and water to the product isolate to form an organic phase and an aqueous phase. This is followed by recovering the organic phase, and removing the water-immiscible solvent to yield purified 2,5-(hydroxymethyl) furaldehyde.

The possible extracting solvents include, but are not limited to, ethyl acetate, methyl isobutylketone, methyl ethyl ketone, methyl t-butyl ether, ethyl lactate, octanol, pentanol, and butyl acetate and combinations thereof. In a certain embodiment, the second product mixture comprises greater than 75% by weight of 2,5-(hydroxymethyl)furaldehyde. Yet another embodiment, the second product mixture comprises greater than 95% by weight of 2,5-(hydroxymethyl)furaldehyde.

In one embodiment, after product isolation the ion-exchange resin catalyst may be rinsed with the organic solvent used to carry out the reaction to recover product contained within the resin. After the rinse, the ion-exchange resin catalyst may be reused in a subsequent reaction. In a further embodiment, after product isolation the ion-exchange resin may be rinsed with a second organic solvent to recover product contained with in the resin. After the rinse, the ion-exchange resin catalyst may be reused in a subsequent reaction.

Provided also herein is a further method of preparing 2,5 – (hydroxymethyl)furaldehyde. The method includes: i) combining materials comprising a carbohydrate source, a solvent and an ion-exchange resin catalyst to form a reaction mixture; ii) heating the reaction mixture to a temperature and for a

time sufficient to promote a dehydration reaction of said carbohydrate source to form a first product mixture; iii) isolating the first product mixture to provide a product isolate. The method optionally comprises one or more of the following steps: iv) adjusting the product isolate to a neutral pH; v) adding a non-volatile flowing agent to the product isolate; vi) distilling the non-volatile flowing agent and the product isolate to remove the solvent from the product isolate; and vii) purifying the product isolate to provide a second product mixture comprising greater than 75% by weight of 2,5 – (hydroxymethyl)furaldehyde.

In an embodiment, the purification of the product isolate may be performed by a process selected from the group consisting of short path distillation, thin film evaporation, wiped film evaporation, crystallization, and adsorption to an inert adsorbent. Adsorbents include, but are not limited to, silica, carbon, alumina, and other resins. A non-volatile flowing agent may be added to the product isolate to enhance separation. The non-volatile flowing agent may be chosen from the group consisting of polyethylene glycol, polyethylene glycol monoether, polyethylene glycol diether, and combinations thereof. In a further embodiment, the non-volatile flowing agent may be purified to a re-usable form after it has performed its role in the purification process. Such purification process may take place with the use of carbon as disclosed herein.

Provided also herein is a further method of preparing 2,5-(hydroxymethyl)furaldehyde. The method includes: i) combining materials comprising a carbohydrate source, a catalyst, a first organic solvent, and a second organic solvent to form a non-aqueous reaction mixture wherein said first organic solvent and said second organic solvent are immiscible in each other; ii) heating the non-aqueous reaction mixture to a temperature and for a time sufficient to promote a dehydration reaction of the carbohydrate source in said first organic solvent to form a product mixture with a first immiscible phase and a second immiscible phase; and iii) isolating 2,5-(hydroxymethyl)furaldehyde from said second immiscible phase of said product mixture.

In one embodiment of the above method, the second organic solvent is characterized by an ability to solubilize HMF in the presence of the first organic solvent, which is immiscible with regard to the second organic solvent and HMF. The second organic solvent may be selected from the group including, but not limited to, methyl isobutyl ketone, ethyl acetate, and chloroform. The first organic solvent is

characterized as being less able to solubilize HMF than the second organic solvent when in contact with the second organic solvent; the result of which is a two-phase system. HMF is less soluble in said first immiscible organic phase than in said second immiscible organic phase. In one embodiment, the first organic solvent is dimethyl formamide.

Provided also herein is a method of preparing 2,5-bis-(hydroxymethyl)furan. The method includes heating a reaction mixture comprising 2,5-(hydroxymethyl)furaldehyde, a solvent, and a catalyst system comprising nickel and zirconium at a temperature, for a time, and at a pressure sufficient to promote reduction of the 2,5-(hydroxymethyl)furaldehyde to 2,5-bis-(hydroxymethyl)furan to produce a product mixture comprising 2,5-bis-(hydroxymethyl)furan.

In one embodiment, the method provides that greater than 90% of the 2,5-(hydroxymethylfuraldehyde) is converted to 2,5-bis-(hydroxymethyl)furan. In another embodiment, greater than 95% of the 2,5-(hydroxymethylfuraldehyde) is converted to 2,5-bis-(hydroxymethyl)furan, and in yet a further embodiment, greater than 99% of the 2,5-(hydroxymethylfuraldehyde) is converted to 2,5-bis-(hydroxymethyl)furan.

In an embodiment, the method takes place with a temperature which is between about 125° C and about 175° C. In another embodiment, the method takes place with a temperature which is between about 140° C and about 160° C. In an embodiment, the pressure is between about 1,000 pounds per square inch and about 1,400 pounds per square inch. In another embodiment, the pressure is between about 1050 pounds per square inch and about 1,250 pounds per square inch.

In an embodiment, the time sufficient to promote reduction of the 2,5-(hydroxymethyl)furaldehyde to 2,5-bis-(hydroxymethyl)furan is less than about three hours. In another embodiment, the time sufficient to promote reduction of the 2,5-(hydroxymethyl)furaldehyde to 2,5-bis-(hydroxymethyl)furan is less than about two hours. In a further embodiment, the time sufficient to promote reduction of the 2,5-(hydroxymethyl)furaldehyde to 2,5-bis-(hydroxymethyl)furan is about one hour.

In an embodiment, the method of preparing 2,5-bis-(hydroxymethyl)furan further includes isolating 2,5-bis-(hydroxymethyl)furan from the product mixture by filtration to remove the catalyst and rotary evaporation to remove the solvent. In an embodiment, the solvent is one of ethyl acetate, acetate, methyl

acetate, butyl acetate, isopropanol, and butanol. In another embodiment, the reaction mixture comprising 2,5-(hydroxymethyl)furaldehyde is a crude reaction mixture.

Detailed Description of the Invention

Reusable or recyclable catalysts are preferred for use in the reaction, as they provide for increased efficiency, and economic and industrial feasibility. As used herein, the term "recyclable catalyst" refers to a catalyst which is not irreversibly expended as a result of the reaction. In other words, the catalyst may be used again. Examples of recyclable or reusable catalysts include, but are not limited to, solid acid catalysts, ion-exchange resins, zeolites, Lewis acids, clays, and molecular sieves. Solid acid catalysts often comprise a solid material which has been functionalize to impart acid groups that are catalytically active. Solid acid catalysts may have a broad range of composition, porosity, density, type of acid groups and distribution of acid groups. Solid acid catalysts may be recovered and reused, optionally with a treatment to regenerate any activity that may have been lost in use. Some solid acid catalysts that may be used in the disclosed process include, but are not limited to Amberlyst 35, Amberlyst 36, Amberlyst 15, Amberlyst 131 (Rohm and Haas, Woodridge, IL), Lewatit S2328, Lewatit K2431, Lewatit S2568, Lewatit K2629 (Sybron Corp, Birmingham, NJ), Dianion SK104, Dianion PK228, Dianion RCP160, RCP21H, Relite RAD/F (Mitsubishi Chemical, White Plains, NY), and Dowex 50WX4 (Dow Chemical).

One example of a solvent that may be used is a polar solvent. The polar solvent maybe a polar aprotic solvent. Examples of possible solvents include, but are not limited to, 1-methyl-2-pyrrolidinone, dimethylacetamide, dimethylformamide, dimethyl sulfoxide, methyl ethyl ketone, methyl isobutylketone, acetonitrile, propionitrile, and combinations thereof.

In certain embodiments of the method, over 40% of hexoses present in the starting reactants are converted to HMF, the percent conversion being calculated by molar yield as described below. Yield may be increased by altering any of the variables, such as solvent type, concentration, catalyst, time and/or temperature of the reaction conditions, etc. It has been further found that the gradual removal of water from the dehydration reaction increases the yield of HMF. The dehydration of fructose to HMF occurs with the loss of three water molecules, and the formation of

three points of non-saturation, or double bonds (two alkene bonds, and the carbonyl group). By removing water as it is formed, side-reactions are thereby minimized, and an increased yield has been observed. Water removal may take place via evaporation. A rotary evaporation machine may be employed to promote water removal. The use of a rotary evaporator, or "rotovap," is well-known in the art. Water removal may also be carried out by evaporation from the reaction mixture and condensation as ice or water on a cold finger or reflux condenser. Water may also be removed by distillation, including azeotropic distillation with a water-entraining solvent which may optionally be stripped of water and the water depleted solvent returned to the reaction vessel. A suitable distillation apparatus, such as a Barrett type receiver may also be employed. A water-absorbing material may also be used to remove water. Such materials are well-known in the art, and include, but are not limited to, molecular sieves.

In one embodiment, the reactions disclosed herein are performed at moderately high temperatures, typically in a range of from about 95° to about 125°C. In a further embodiment, the temperature range is from about 105° C to about 115° C. It is preferable to use temperatures below 200 degrees Celsius. The reactions disclosed herein typically occur in a time frame of from about one to about six hours. More typically, the reactions take from about two hours to about five and a half hours. If additional steps regarding the isolation and purification of HMF are preformed, additional time may be required.

As used herein, the term "zeolite" refers to a hydrated silicate of aluminum and one or both of sodium and calcium. Examples include, but are not limited to, analcite, chabazite, heulandite, natrolite, stilbite, thomsonite, in either powder or pellet form. Commercial zeolites products include, but are not limited to, CBV 3024 and CBV 5534G (Zeolyst International), T-2665, T-4480 (United Catalysis, Inc), LZY 64 (Union Carbide), and H-ZSM-5 (PQ Corporation).

As used herein, Cornsweet 90 refers to a high fructose corn syrup product of commerce nominally containing 60% to 70% fructose. High fructose corn syrup refinery intermediate and by-product is a fructose-rich stream generated in a fractionation system positioned after an isomerization column in the production of high fructose corn syrup. A suitable process stream from crystallizing fructose is called "mother liquor" and comprises a solution of fructose in ethanol. Typically this process stream is about 24% solids, almost all of the solids being fructose, and

contains about 60% ethanol. For use in HMF production, the ethanol can be removed from the mother liquor. A similar mother liquor from glucose crystallization contains about 50% solids. Mixed carbohydrate sources can be obtained by blending carbohydrates, such as by adding crystalline fructose to high fructose corn syrup.

As used herein, "reaction yield" is calculated using the equation (moles of product/moles of starting material)*100. Product purity is reported on a weight percent basis.

As used in this equation, "starting material" refers to the fructose present in the carbohydrate source, mixed carbohydrate source, or other reactant for the particular dehydration reaction.

As used herein, the term "fructose source" refers to a material that comprises sucrose. Typical embodiments are solutions having at least 25% sucrose by solute weight, and which may include other materials such as other carbohydrate compounds. Preferably, the carbohydrate compounds are hexoses. The versatility of the reaction conditions provided herein allow an industrially convenient source to be used as the starting material, that is to say, the reaction is not limited to a particular carbohydrate source or to fructose of high purity.

Suitable fructose sources typically include high fructose corn syrup (HFCS) or any HFCS refining process stream that includes at least 25% sucrose. HFCS is typically commercially available in products comprising solutions having 42% to 95% fructose by solute weight which are typically sold for use as industrial scale sweeteners. The most economical embodiments of the invention use HFCS having about 90% sucrose by solute weight. However, less economical embodiment's invention can be practiced with sources having less sucrose by weight. To improve economic efficiencies, less pure sucrose sources can be conveniently blended with higher purity sucrose sources or even crystalline sucrose to achieve a solution having at least 25% sucrose by solute weight.

Optional neutralization of the product isolate is carried out by addition of a suitable alkali substance, such as a basic ion exchange resin, potassium hydroxide, or sodium hydroxide. This neutralization step allows for subsequent product recovery by distillation without heat-catalyzed degradation or polymerization, resulting in the elimination of tarry degradation products and resinous solids being formed in distillation. This neutralization step also allows for subsequent product

recovery with a flowing agent without heat-catalyzed degradation or polymerization, resulting in the elimination of tarry degradation products and resinous solids being formed in distillation.

HMF can be purified from reaction mixtures by removal of catalyst resin and forming a product isolate, neutralizing the product isolate, removing solvent from product isolate by distillation, and treating the resulting distillant with water and an organic solvent. HMF partitions to the organic solvent and can be recovered with purity in excess of 95% by weight. This level of purity has not been obtained by other processes.

After HMF has been purified from reaction mixtures by removal of the solid acid catalyst and forming a product isolate, the solid acid catalyst may be rinsed with the organic solvent used to carry out the reaction to recover product contained within the catalyst. After the rinse, the solid acid catalyst may be reused in a subsequent reaction. In a preferred embodiment, after HMF has been purified from reaction mixtures by removal of the solid acid catalyst forming a product isolate, the solid acid catalyst may be rinsed with a second organic solvent to recover product contained with in the catalyst. After the rinse, the solid acid catalyst may be reused in a subsequent reaction.

Purity was determined by ^{13}C NMR and Proton NMR, in some cases by capillary GC, and in some cases by UV adsorption.

As used herein, the term "non-aqueous mixture" refers to a mixture comprising a non-aqueous solvent and at least one other component, wherein the content of the solvent is greater than the content of the at least one other component, as measured by volume. The at least one other component may comprise, without limitation, a water-containing substrate, such as HFCS, or an organic solvent. Non-aqueous solvents are usually measured by volume, and other components are usually measured by weight.

As used herein, the term "isolate" refers to the process of preservation of a material originally present in a product mixture after the product mixture has been subjected to a step to remove other material from the product mixture, as well as the isolated material resulting from the process. Examples of "other material" that is removed includes without limitation, solid material, such as catalyst by methods including, but not limited to, the processes of filtration, decantation, centrifugation, and washing. Filtration may be performed by one of the processes selected from the

group comprising but not limited to gravity filtration, vacuum filtration, and suction filtration.

The term "non-volatile flowing agent" as used herein refers to an inert material which, when added to a product mixture, aids in the recovery of the desired compound by distillation. In certain embodiments, the fugacity of the flowing agent is sufficiently low so that it will not volatilize as the target product is removed by evaporation.

The formation of two immiscible solvent phases in the reaction mixture facilitates purification of an HMF product. Solvents can be easily classified on the basis of polarity. One such measure of polarity is the Log P value. Log P is defined as the partition coefficient of a given compound in a two-phase system of water and octanol. Log P can be determined experimentally or calculated from hydrophobic fragmental constants according to standard procedures (Hansch, C. & Leo, A (1979) *Substituent constants for correlation analysis in chemistry and biology*. John Wiley & Sons, New York NY; Leo, A., Hansch, C. & Elkins, D. (1971) Chem. Rev. **71**, 525;Rekker, R. F. (1977) *The hydrophobic fragmental constant*, Elsevier, Amsterdam; Rekker, R. F. & de Kort, H. M. (1979) Eur. J. Med. Chim. **14**, 479).

Preferred two-phase organic solvent systems include a first solvent having a log P value of less then zero and a second solvent having a log P value in the range of about 0.4 to about 3.4; a further two-phase organic solvent systems include a first solvent having a log P value in the range of about -0.75 to about -1.95. In a further embodiment the second solvent has a log P value in the range of from about 0.6 to about 2.7, and in an additional embodiment, the two-phase organic solvent systems include a first solvent having a log P value of about -1.04 and a second solvent having a log P value of about 1.32. A suitable two-phase organic solvent system comprises a first phase of dimethylformamide and a second phase of methyl isobutyl ketone. Table 1 provides Log P data for certain solvents.

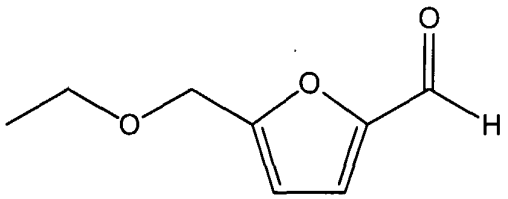
Methyl isobutyl ketone is generally miscible with a broad range of solvents (J. S. Drury (1952) *Miscibility of solvent pairs*, Industrial and Engineering Chemistry **44**:11, page C-684). Solvents immiscible with methyl isobuyl ketone include diethanolamine, ethylene glycol, glycerol and trimethylene glycol. None of these solvents are suitable for the intended reaction because of their reactivity.

Table 1. Log P data for some solvents

Solvent	**Log P ***
1, 2-Dichlorobenzene	3.38
Carbon tetrachloride	2.83
Toluene	2.69
Chloroform	2.24
Benzene	2.03
2-Heptanone	1.83
Butyl acetate	1.71
1,2-Dichloroethane	1.48
Methyl isobutyl ketone	1.32
Dichloromethane	1.25
Ethyl propionate	1.21
2-Pentanone	0.91
Diethyl ether	0.89
t-Amyl alcohol	0.89
Butanol	0.88
Cyclohexanone	0.81
Ethyl acetate	0.66
Pyridine	0.64
Tetrahydrofuran	0.46
2-Butanone	0.29
2-Propanol	0.05
Acetone	-0.24
Dioxane	-0.27
Ethanol	-0.32
Acetonitrile	-0.34
Methanol	-0.77
N, N-Dimethylformamide	-1.04
Dimethyl sulfoxide	-1.35
Formamide	-1.51
Ethylene glycol	-1.93

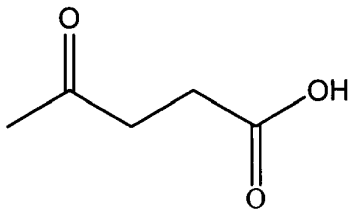
* Log P values were taken from Hansch, C. & Leo, A (1979) *Substituent constants for correlation analysis in chemistry and biology*. John Wiley & Sons, New York NY; Leo, A., Hansch, C. & Elkins, D. (1971) Chem. Rev. **71**, 525.

It has also been surprisingly found that other furan derivatives, particularly HMF ethers may be synthesized using the methods of the present invention with slight variations. Generally, ethers may be formed from any R group, such as alkyl, cycloalkyl, allyl, aryl and the like. Such variations include but are not limited to the introduction of alcohol having the appropriate constituent R group, such as, for example, ethanol (EtOH) where R is C_2H_5, as a polar solvent in either batch reactions or via column elution. This method would therefore comprise: i) combining materials comprising a fructose source, an alcohol solvent, and a catalyst to form a reaction mixture; ii) heating said reaction mixture to a temperature and for a time sufficient to promote an acid-catalyzed dehydration reaction of the fructose in the fructose source to form a product mixture; and iii) isolating an ether derivative from said product mixture. HMF ethers, such as ethoxymethylfurfural (EMF), are more stable than HMF because they lack the exposed hydroxyl group of HMF. EMF is shown in the structure below:

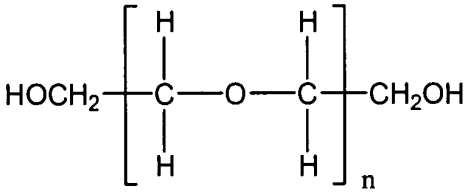


In an embodiment the fructose source is a HFCS. The use of a column in the synthetic process enables a continuous flow of heated fructose solution, thereby decreasing the amount of polymerization and by-product formation. Further distillation may also be performed to purify EMF from the product mixture. The use of column elution creates a continuous flow and is a fairly simple process that efficiently leads to a more stable product. The subsequent purification via distillation is also a simple process that is economically feasible. Furthermore, yields have been surprisingly high, in the range of 85-100%. Purification may also be used in the form of liquid or gas chromatography.

It has also been surprisingly found that levulinic acid may be efficiently synthesized from a carbohydrate source primarily including fructose. Levulinic acid is shown in the structure below:



The method comprises combining a fructose source, such as high-fructose corn syrup, with a polyethylene glycol and an acidic resin to form a reaction mixture. The reaction mixture is then heated with constant, or continuous stirring to a temperature and for a time necessary to promote the reaction and form a product mixture. Levulinic acid is then isolated from the product mixture. A polyethylene glycol block can be seen in the structure below:



The use of end-capped polyethylene glycol material has been surprisingly efficient as it eliminates the formation of undesirable PEG-HMF ethers. As recognized by one of ordinary skill in the art, an end-capped glycol has the forgoing structure except that the terminal hydroxyl groups are substituted with an alkyl or ether group.

Another method of making levulinic acid from a fructose source involves heating a mixture of high-fructose corn syrup and water with an acidic ion exchange resin catalyst. This reaction normally proceeds in a temperature range of 100 -150° C, and has surprisingly been found to produce levulinic acid in high yields. This method provides substantial improvement over the known method of using zeolites as catalysts in synthesizing levulinic acids.

In another embodiment, a method of preparing 2,5-bis-(hydroxymethyl)furan is disclosed. The method includes heating a reaction mixture

comprising 2,5-(hydroxymethyl)furaldehyde, a solvent, and a catalyst system comprising nickel and zirconium at a temperature, for a time, and at a pressure sufficient to promote reduction of the 2,5-(hydroxymethyl)furaldehyde to 2,5-bis-(hydroxymethyl)furan to produce a product mixture comprising 2,5-bis-(hydroxymethyl)furan. In an embodiment, the reaction mixture comprising 2,5-(hydroxymethyl)furaldehyde is a crude reaction mixture.

As used herein, the term "crude reaction mixture" refers to an unrefined or unpurified composition.

Examples

The following are examples of the dehydration of a fructose source to a furan derivative or organic acid, as well as isolation and/or purification techniques to optimize product recovery of increased product yield. The examples are not meant to limit the scope of the invention, as defined by the claims.

EXAMPLE 1

PREPARATION OF HMF FROM HIGH FRUCTOSE CORN SYRUP AT 115°C in N-Methylpyrrolidinone (NMP)

A 250 mL 3-neck round bottom flask was fitted with a magnetic stir bar, heating mantle, reflux condenser, and temperature probe. To this flask was charged 100 mL of NMP (Aldrich) and 20 g of Amberlyst 35 resin (Rohm and Haas, Woodridge, IL). Amberlyst 35 is a macroreticular, strongly acidic, polymeric catalyst. The mixture was heated to 115°C, and 50 g of Cornsweet 90 (HFCS, ADM, Clinton IA) was added. Heating continued in this manner at 115°C over a 5 hour period. Water condensed on the reflux condenser. After 5 hours, the contents of the flask were cooled to about 70°C, and the resin removed by vacuum filtration to provide a product isolate. The product isolate was analyzed to provide a solution of 14.2% HMF by weight and 4.7% fructose. Calculations indicate an 80.6% molar yield of HMF from fructose and 94.1% conversion.

EXAMPLE 2

PREPARATION OF HMF FROM HIGH FRUCTOSE CORN SYRUP AT 105°C in NMP

This example illustrates the effect of temperature on the dehydration of fructose to HMF. A 250 mL 3-neck round bottom flask was fitted with a magnetic stir bar, heating mantle, reflux condenser, and temperature probe. To this flask was charged 100 mL of NMP (Aldrich) and 20 g of Amberlyst 35 resin (Rohm and Haas, Woodridge, IL). The mixture was allowed to heat to 105°C, and 50 g of Cornsweet 90 (HFCS, ADM, Clinton, IA) was added. Heating continued in this manner at 105°C over a 5 hour period. Water condensed on the reflux condenser. After 5 hours, the contents of the flask were cooled to about 70°C, and the resin removed by vacuum filtration to provide a product isolate. The product isolate was analyzed to provide a solution of 12.9% HMF and 3.9% fructose. Calculations indicate a 71.6% molar yield of HMF from fructose and 85.4% conversion.

EXAMPLE 3

PREPARATION OF HMF FROM HIGH FRUCTOSE CORN SYRUP AT 105°C in NMP UNDER VACUUM CONDITIONS

This example illustrates the effect of distillation on the dehydration of fructose to HMF. A 250 mL 3-neck round bottom flask was fitted with a magnetic stir bar, heating mantle, condenser, temperature probe, and receiving flask. To this flask was charged 100 mL of NMP (Aldrich), 20 g of Amberlyst 35 resin (Rohm and Haas, Woodridge, IL), and 50 g of Cornsweet 90 syrup. The mixture was heated to 105°C under house vacuum. The distillate was collected. After 2 hours, the contents of the flask were cooled to about 80°C, and the resin removed by vacuum filtration to provide a product isolate. The product isolate was analyzed to provide a solution of 14.2% HMF and 1.1% fructose. Calculations indicate a 75.7% molar yield of HMF from fructose and 79.5% conversion.

EXAMPLE 4

PREPARATION OF HMF FROM HIGH FRUCTOSE CORN SYRUP AT 115°C IN NMP

This example illustrates the effect of distillation on the dehydration of fructose to HMF. A 2L 3-neck round bottom flask was fitted with a magnetic stir bar,

heating mantle, condenser, temperature probe, and receiving flask. To this flask was added 500 mL of NMP (Aldrich), 200 g of Amberlyst 35 wet resin (Rohm and Haas, Woodridge, IL), and 500 g of Cornsweet 90. The mixture was heated to 115°C and subjected to vacuum distillation under house vacuum. After 4 hours, the resin was removed by filtration to provide a product isolate of 729.68 g of 20.4% HMF. Calculations indicate a 68.6% yield of HMF.

EXAMPLE 5

PREPARATION OF HMF FROM HIGH FRUCTOSE CORN SYRUP AT 105°C in DMAc

This example illustrates the effect of solvent on the dehydration of fructose to HMF. A 250 mL 3-neck round bottom flask was fitted with a magnetic stir bar, heating mantle, reflux condenser, and temperature probe. To this flask was charged 100 mL of DMAc (Aldrich) and 20 g of Amberlyst 35 resin (Rohm and Haas, Woodridge, IL). The mixture was heated to 105°C, and 50 g of Cornsweet 90 (HFCS, ADM, Clinton, IA) was added. Heating was continued in this manner at 105°C over a 5 hour period. Water was condensed on the reflux condenser. After 5 hours, the contents of the flask were cooled to about 90°C, and the resin was removed by vacuum filtration to provide a product isolate. The product isolate was analyzed to provide a solution of 13.5% HMF and 6.0% fructose. Calculations indicate 62.1% molar yield of HMF from fructose and 74.6% conversion.

EXAMPLE 6

PREPARATION OF EMF FROM FRUCTOSE IN BATCH MODE

A 500 mL round bottom flask equipped with a reflux condenser, temperature probe, and magnetic stir bar was charged with a solution of 30 g fructose (Aldrich), 225 mL HPLC grade ethanol (Aldrich), and 30 g of Amberlyst 131 resin (Rohm and Haas). Amberlyst 131 is a strongly acidic polymeric catalyst with a particle size of 0.7-0.8 mm and water content of 65%. The stirred mixture was heated to reflux for 24 hours. At this time, the slurry was filtered and the resin washed with ethanol to provide 174 mL of product isolate containing 5.4 g/L HMF and 61.6 g/L EMF.

EXAMPLE 7

PREPARATION OF EMF FROM FRUCTOSE VIA COLUMN ELUTION

A 100 mL glass liquid-chromatography column (2.54 cm I.D) was slurry packed in HPLC grade ethanol (EtOH) with Amberlyst 131 resin obtained from Rohm and Haas Company (Woodridge, IL). The resin was washed with 500 mL of EtOH. The final packed volume was 100 ml. The feed material consisted of 5 mL of a 20% solution of fructose in EtOH. The feed was then loaded on the resin column by gravity flow and fractions were eluted. The column was maintained at 60°C and elution at 0.6 mL/min. Table 2 summarizes the results of this study. A complete conversion of fructose to a mixture of HMF/EMF was achieved, with the major product being EMF.

Table 2. Column Synthesis of EMF from Fructose using Amberlyst 131 Resin.[1]

Fraction #	Volume (mL)	Fructose (ppm)	HMF (ppm)	EMF (ppm)
2	8	0	0	0
5	13.6	0	0	0
7	21.6	0	0	294
9	32.1	262	370	1,862
11	40.1	79	420	2,613
13	48.1	134	364	4,451
15	57.1	119	794	6,008
17	65.6	120	615	6,385
19	73.6	0	308	4,293
21	82.1	0	0	1,488
24	94.1	0	0	276
26	102.1	0	0	60

[1]Column was maintained at 60° C with a steady flow rate of 0.6 mL/min.

EXAMPLE 8

PREPARATION OF EMF FROM FRUCTOSE VIA COLUMN ELUTION

This example illustrates the effect of change in resin to Amberlyst 35 obtained from Rohm and Haas Company (Woodridge, IL). Amberlyst 35 is a macroreticular, strongly acidic, polymeric catalyst. The feed material was prepared and loaded on to the column by gravity flow as described in Example 7. The column was maintained at 60°C and the elution was carried out at 0.6 mL/min. A summary of this is provided in table 3. Nearly 85% of the starting fructose was converted into a mixture of HMF/EMF with the major product being EMF.

Table 3. Column Synthesis of EMF from Fructose using Amberlyst 35 Resin.[1]

Fraction #	Volume (mL)	Fructose (ppm)	Ethyl Levulinate (ppm)	HMF (ppm)	EMF (ppm)
1	2.0	263	242	263	263
3	13.0	271	249	271	271
5	25.0	230	212	230	230
7	34.5	253	233	253	253
8	37.5	227	209	227	579
10	46.5	2,737	948	1,180	5,687
12	58.0	2,507	203	1,157	7,844
14	67.0	1,970	1,526	1,186	9,526
16	76.0	520	246	325	2,023
18	85.0	282	260	282	282
19	89.5	256	236	256	256
20	96.5	269	248	269	269

[1]Column was maintained at 60° C with a steady flow rate of 0.6 mL/min.

EXAMPLE 9

PROCESS FOR THE SYNTHESIS AND PURIFICATION OF EMF

Dehydration: Amberlyst 131 Wet (145 g) was dried in vacuum at 85°C for three days. This catalyst was combined with 117 g crystalline fructose and 468 g of

100% ethanol in a steel reactor. With stirring at 600 rpm, the reaction mixture was gradually heated to 110° C over 30 minutes. The temperature was maintained for 45 minutes, and then the reaction mixture was cooled to ambient temperature over 7 minutes. The catalyst was filtered from the red-black reaction mixture, and the reaction mixture was treated with a rotary evaporator under house vacuum to remove ethanol.

Distillation of EMF on Wiped-Film Evaporator: Poly(ethylene glycol)-400 (47 g) was added to the dark residue (89 g). EMF was distilled from this mixture on a wiped-film evaporator at 110°C, 4.7 mm Hg, and 400 rpm, yielding a yellow distillate (68 g) containing EMF (44 g, 44% molar yield from fructose), ethyl levulinate (20 g, ELA), and ethanol (5 g). NMR (δ, 1H): 9.54, (s, 0.8 H) EMF; 7.16, (d, 1.0 H), EMF; 6.46, (s, 1.0 H), EMF; 4.46, (s, 2.0 H), EMF; 4.05, (quartet, 1.0 H) ELA; 3.63, (quartet, 0.7 H), EtOH; 3.52, (quartet, 2.0 H), EMF; 2.68, (t, 1.1 H), ELA; 2.49, (t, 1.2 H), ELA; 2.12, (s, 1.6 H), ELA; 1.17, (m, 5.6 H), ELA, EMF, EtOH.

EXAMPLE 10

PREPARATION OF HMF FROM FRUCTOSE USING A TWO-PHASE ORGANIC SOLVENT SYSTEM

A 500 mL round bottom three neck flask was equipped with a reflux-condenser, temperature probe, and a magnetic stir bar. To this flask was added 5 g of fructose, 5 g of Amberlyst 35 resin, and a first organic solvent comprising 50 mL of dimethylformamide (DMF) and a second organic solvent comprising 200 mL of methyl isobutyl ketone (MIBK). The reaction was heated to 85°C for 7h. The mixture was cooled and filtered. The resin was washed with small quantities of MIBK. The two layers were separated and the product isolate (155 mL) in the MIBK phase contained 17.9 g/L HMF to provide an overall yield of 89.3%.

EXAMPLE 11

REPARATION OF LEVULINIC ACID FROM HIGH FRUCTOSE CORN SYRUP USING ACIDIC RESIN CATALYSTS

A 250 mL round bottom three neck flask was equipped with a reflux-condenser, temperature probe, and a magnetic stir bar. To this flask was added 50

g of Cornsweet 90 syrup, 20 g of Amberlyst 35 resin, and 100 mL of poly(ethyleneglycol) dimethyl ether-500. The mixture was heated to 100°C for 4h. The mixture was cooled and filtered to provide an overall yield of 45.3% levulinic acid.

EXAMPLE 12

PREPARATION OF LEVULINIC ACID FROM FRUCTOSE USING ACIDIC RESIN CATALYSTS

A solution of crystalline fructose (30 g, 90%) in water (500 mL) was placed in a 1L autoclave reactor. To this reactor was added 60 g of Amberlyst 35 Wet resin. The solution was stirred (500 rpm) and heated to 150°C. After 4.5 hours, the reactor was cooled and the solution was filtered to remove the catalyst to provide a product isolate. The dark brown product isolate (72.04 g) contained 149.83 g/kg levulinic acid to provide an overall yield of 62% levulinic acid from fructose.

EXAMPLE 13

PREPARATION OF LEVULINIC ACID FROM HIGH FRUCTOSE CORN SYRUP USING ACIDIC RESIN CATALYSTS

A solution of Cornsweet 90 (45.24 g) in water (500 mL) was placed in a 1L autoclave reactor. Amberlyst 35 Wet resin (60 g) was added and the mixture stirred (500 rpm). After 18 hours, the reactor was cooled and the solution filtered to provide a product isolate. The product isolate was treated with a rotary evaporation machine to remove the solvent, and provided 17.98 g of dark brown oil containing 467.22 g/kg levulinic acid for a yield of 41.2%.

EXAMPLE 14

PROCESS FOR THE PREPARATION AND PURIFICATION OF HMF FROM HFCS

Step 14a. Neutralization: A 202.7 g sample of product isolate prepared as described in Example 4 was placed in a 500 mL Erlenmeyer flask, and 25.0 g of poly(ethylene glycol)-600 was added to serve as a flowing agent in later purification. The mixture was stirred continuously for 30 minutes at ambient temperature and neutralized with the gradual addition of Amberlyst A26OH resin (Rohm and Haas) before being subjected to distillation to remove solvent. Amberlyst A26OH is a strong base, type 1, anionic, macroreticular polymeric resin. The pH of the crude

product mixture was increased to 7.5-8.0 by the application of Amberlyst A26OH resin. The Amberlyst A26OH resin was then removed by filtration.

Step 14b. Distillation of DMAc: The solvent (DMAc) was distilled from the neutralized product mixture under vacuum (4-6 torr) at 100°C using a 4" Vigreaux column with six tiers. A brown residue containing HMF and poly(ethylene) glycol (64.5 g, 28.8% HMF) remained in the distillation vessel and 150 g of distilled DMAc were isolated.

Step 14c. Short Path Distillation of HMF: The brown residue containing HMF (145.5 g, 28.8% HMF) obtained from fractional distillation in step 14b was subjected to short path distillation at 150°C and 0.014-0.021 torr. A yellow distillate (96% purity-HMF, 47.4 g) and brown residue (79.6 g) were isolated. The distillate crystallized upon cooling. NMR (δ, 1H): 9.49, (s, 1 H); 7.16, (d, 1.0 H); 6.46, (s, 1.0 H); 4.62, (s, 2.0 H).

Regeneration of PEG for re-use: A 12.5 g portion of the dark brown PEG residue obtained from the short path distillation was treated with 50 mL of hot water and 24 g of carbon (Calgon, CPG-LF 12X40). NMR indicated that the dark brown PEG residue was composed of greater than 95% PEG. The mixture was allowed to stir for three days. The mixture was vacuum filtered to remove the carbon and 8.4 g of a clear yellow oil resembling the starting PEG in appearance was isolated. NMR indicated that the purity of the recovered PEG was 100%.

EXAMPLE 14a

PROCESS FOR THE PURIFICATION OF HMF FROM HFCS

A 180 g sample of material prepared and neutralized as described in Example 4 was added to 20 g poly(ethylene glycol) dimethyl ether-500 flowing agent. This material was subjected to short path distillation at 150°C and 5 mbar. A yellow distillate (67.4% purity HMF, 11.92 g) and brown residue (191 g) were isolated.

EXAMPLE 15

PROCESS FOR THE PURIFICATION OF HMF FROM HFCS

Step 15a. Neutralization: An HMF product isolate as prepared in example 4 was neutralized with the gradual addition of aqueous sodium hydroxide (pH 7.5) before being subjected to distillation to remove solvent.

Step 15b. Fractional Distillation to remove NMP: The neutralized product isolate was subjected to distillation under reduced pressure (4-6 torr) at 115°C using a 4" Vigreaux column with six tiers to remove solvent (NMP). A purified product isolate comprising a brown residue (264.6 g) and 490 g of distilled NMP were obtained.

Step 15c. Solvent Extraction: A 30.25 g sample of purified product isolate (brown residue prepared in step 15b), 45 mL of ethyl acetate, and 15 mL of water were placed in a 125 mL Erlenmeyer flask and allowed to stir at ambient temperature. After 20 min, the mixture was transferred to a separatory funnel and the two layers separated. The ethyl acetate layer was removed and the aqueous layer was washed with 20 mL of ethyl acetate, the organic layers were combined and dried over $MgSO_4$. The dried combined organic layer was filtered and the solvent evaporated to provide 15.91 g of bright red oil which was 84.2% purity HMF.

EXAMPLE 16

PROCESS FOR THE PURIFICATION OF HMF FROM HFCS

Solvent Extraction: A 37.4 g sample of the solvent stripped material prepared as described in Example 15, 47 mL of methyl isobutylketone (MIBK), and 9.6 mL of water were placed in a 125 mL Erlenmeyer flask and allowed to stir at ambient temperature. After 20 min, the solution was transferred to a separatory funnel and the two layers separated. The aqueous phase was washed with 20 mL of MIBK and the organic phases combined and dried over $MgSO_4$. The solution was filtered and the solvent evaporated to provide 24.33 g of bright red oil which was 88% purity HMF in 97% yield.

EXAMPLE 17

PROCESS FOR THE PREPARATION AND PURIFICATION OF HMF FROM FRUCTOSE

Step 17a. Dehydration: Amberlyst 35 Dry (20 g) was combined with 40 g crystalline fructose and 200 mL of acetonitrile (ACN) in a three neck flask equipped with a reflux condenser, temperature probe, and magnetic stir bar. The reaction mixture was heated to reflux (80° C). The temperature was maintained for 5 hours, and then the reaction mixture was cooled. The catalyst was filtered and washed with

acetonitrile to provide a product isolate. The product isolate was subjected to rotary evaporation to provide for evaporation of the solvent and 17.6 g of brown oil containing 33.9% HMF.

Step 17b. Chromatographic Purification of HMF from ACN Reaction Mixture: A glass-liquid chromatography column (2.54 cm I.D) was packed in heptane with C-Gel 560, 60-200 μ silica (Uetikon, Switzerland). The feed material for chromatographic separation using silica gel was prepared by dissolving the dehydration product (2.95 g) in 10 mL of 80:20 heptane:acetone solution. The feed material was loaded on the silica column by gravity flow and fractions were eluted including those shown in Table 3.

Table 4. Chromatographic Purification of HMF from Crude ACN Reaction Mixture.[1]

Fraction #	Fructose	Fructose (ppm)	HMF (ppm)	Formic Acid (g/kg)	Levulinic Acid (g/kg)
1	10	967	23,239	0.70	0.00
5	4	384	476,872	1.53	5.38
7	0	0	826,108	0.00	0.00
8	0	0	814,378	0.00	11.59
9	0	0	622,706	0.00	17.62
10	22	2215	101,450	0.00	43.26
11	14	1386	70,241	0.00	15.22
12	13	1264	90,195	0.00	11.93
13	23	2252	40,207	4.03	12.14
14	28	2782	20,817	7.30	8.84
15	25	2521	30,723	9.20	1.05
16	35	3457	23,024	0.00	0.00
17	58	5847	26,892	20.66	0.00
18	88	8799	38,819	12.46	0.00
19	128	12837	32,050	8.66	0.00
20	116	11590	33,163	22.43	0.00

[1]Samples were eluted from C-Gel 560, 60-200 microns using heptane:acetone gradient system.

Hence, by gradient elution of the column, isolated fractions with HMF content of >81% were obtained.

EXAMPLE 18

PROCESS FOR THE PURIFICATION OF HMF

A 2.0 g sample of HMF (21%) was prepared in as in the dehydration Step 17a. of Example 17 using HFCS, treated with MIBK (2 mL) and water (1 mL), and the layers were separated. The organic layer was dried over $MgSO_4$, filtered, and the solvent evaporated to provide a bright red extract of 78.9% HMF purity with 93.9% recovery of HMF from the crude material.

EXAMPLE 19

PREPARATION OF HMF FROM HFCS USING ACIDIC RESIN CATALYSTS AT 115°C

This example illustrates the effect of resin on the dehydration of fructose to HMF. A summary of data is shown in Table 5. A 250 mL 3-neck round bottom flask was fitted with a magnetic stir bar, heating mantle, reflux condenser, and temperature probe. To this flask was charged 50 mL of NMP (Aldrich), 50 g of polyethylene glycol dimethyl ether-600, and 50 g of HFCS. The mixture was allowed to heat to 65°C, and 20 g of Dianion RCP160M resin (Mitsubishi Chemical America, Inc.) was added. Dianion RCP160M resin is a strongly acidic polymeric catalyst with a particle size distribution of 250 – 710 µm and a water retention of 45-55%. Heating continued in this manner at 115°C over a 4 hour period. Water condensed on the reflux condenser. After 4 hours, the contents of the flask were cooled to about 90°C, and the resin removed by vacuum filtration to provide a product isolate. The product isolate was analyzed and found to be a solution of 17.5% HMF and 0.2% fructose. Calculations indicate 74.5% molar yield of HMF from fructose and 77.1% conversion.

Table 5. Comparison of HMF Conversion with Various Resins.[1]

Reference #	Time (h)	Resin	HMF Yield (%)	Conversion (%)
4474-58	1	RAD/F	54.1	60.1
	2	RAD/F	63.5	67.3
4474-59	1	RCP160M	61.2	63.9
	2	RCP160M	74.5	77.1
4474-29	1	Amberlyst 35	34.6	46.9
	2	Amberlyst 35	57.1	70.2

[1]Reactions were performed with HFCS, in NMP/PEGE at 115° C.

EXAMPLE 20

PROCESS FOR THE PREPARATION AND PURIFICATION OF HMF FROM HFCS

A 10 g sample of solvent stripped material as prepared in Example 15, step 15b (42% HMF purity) was placed in 50 mL of distilled water and 10 g of an inert adsorbent (Calgon CPG 12X40 carbon) was placed in a beaker and allowed to stir at room temperature for 12 hours. HMF adsorbs light at 284 nm. UV analysis (λ = 284 nm) after 12 hours of stirring indicated HMF had been adsorbed from the mixture. The carbon was collected by filtration, washed with water, and then allowed to stir at room temperature in 50 mL of acetone to desorb HMF. After 12 hours, the carbon was removed by filtration and the filtrate evaporated to provide 3.31 g of material with 80.1% HMF purity.

EXAMPLE 21

PROCESS FOR THE PREPARATION AND PURIFICATION OF HMF FROM HFCS

A 33.0 g sample of solvent stripped material as prepared in Example 15 (42% HMF purity) was treated with 35 g of an inert adsorbent (Calgon CPG 12X40 carbon) in 165 mL of distilled water. The mixture was allowed to stir at room temperature for 12 hours. The carbon was removed by Buchner filtration, rinsed with water, and dried under vacuum. The dried carbon was subjected to Soxhlet extraction using 600 mL of acetone for 18 hours to desorb HMF. The solvent was

evaporated to provide 18.41 g of deep red oil having an HMF purity of 67.1%. The total recovery of HMF was 90.1%.

EXAMPLE 22

PREPARATION OF HMF FROM HFCS USING ROTARY EVAPORATION

This example illustrates the effect of rotary evaporation on the dehydration of fructose to HMF. To a 500 mL round bottom flask was charged 100 mL of NMP (Aldrich), 25 g of high-fructose corn syrup, and 15 g of wet Amberlyst 35 resin. An oil bath was heated to 120°C, and the flask rotated in the bath, under vacuum of 200 mm Hg. Rotary evaporation continued in this manner at 120°C over a 1 hour period. Distillate was collected. After 1 hour, the contents of the flask were subjected to Buchner filtration to remove the resin to provide a product isolate. The product isolate was analyzed to show 7.1% HMF, 91.5% NMP, and 1.9% water. Calculations indicate 88.6% molar yield of HMF from HFCS and 90.7% conversion.

EXAMPLE 23

PREPARATION OF HMF FROM HFCS WITH MOLECULAR SIEVES

This example illustrates the usefulness of molecular sieves as drying agents in the production of HMF from HFCS. To a 3-neck 500 round bottom flask equipped with a condenser, temperature probe, and stirring bar, was added 100 mL of NMP, 50 g of HFCS, 20 g of wet Amberlyst 35 resin, and 20 g of UOP 3A molecular sieves. The reaction was heated to 105°C and let stir under these conditions for 1 hour. Results indicate a 10.6% HMF solution providing an overall yield of 60.6%. The addition of sieves to promote the removal of water during the reaction allows for a faster conversion of HFCS to HMF.

EXAMPLE 24

PREPARATION OF HMF WITH GRADUAL ADDITION OF HFCS TO REACTION MIXTURE

This example illustrates the effect of gradual addition of HFCS to a heated reaction mixture. A 3-neck 500 mL round bottom flask was fitted with a dropping funnel, temperature probe, and a jacketed condenser with distilling head. To this flask was added 100 mL of NMP and 40 g of wet Amberlyst 35 resin. The flask was heated to 130°C with vacuum and the feed material (100 g of HFCS in 50 mL of

NMP) was added dropwise over 1.5 hours. Upon complete addition of the feed, the reaction continued with vigorous stirring for 3 hours. At this time, the reaction was cooled to 90°C, and the resin removed via Buchner filtration (#415 VWR paper) to provide a product isolate. Results indicate a product isolate of 10.4% HMF, 85.4% NMP, and 2.76% water. Thus, a 77.8% molar yield of HMF was obtained.

EXAMPLE 25

PREPARATION OF 2,5-BIS-(HYDROXYMETHYL)FURAN (FDM) FROM CRUDE HMF REACTION MIXTURE

The sample of HMF material (30.01 g, 66% HMF) was placed in a 1L Parr reactor vessel with ethyl acetate (350 mL) and 2.0 g of G-69B. G-69B is a powdered catalyst obtained from Sud-Chemie, Louisville, Kentucky, containing nominally 62% Nickel on Kieselguhr, with a Zirconium promoter, and has an average particle size of 10-14 microns. The vessel was purged 3 X 500 psi hydrogen with vigorous stirring (1000 rpm). The pressure was then maintained at 1250-1050 psi with heating to 150°C for 1 hour. The reaction was allowed to cool and the catalyst removed by filtration. The solvent was removed by rotary evaporation to provide 27.32 g of brown liquid that solidified on cooling. TLC analysis indicated the complete conversion of HMF to FDM. ^{1}H NMR data reveal a high purity product (>90%). The overall yield of FDM from HMF is 100%. GC/MS data revealed complete conversion of HMF to FDM m/z = 128, 111, 97.

EXAMPLE 26

PREPARATION OF 2,5-BIS-(HYDROXYMETHYL)FURAN (FDM) FROM CRUDE HMF REACTION MIXTURE

The sample of HMF material (46.09 g, 45% HMF) was placed in a 1L Parr reactor vessel with ethyl acetate (350 mL) and 6.15 g of G-69B. The vessel was purged 3 x 500 psi hydrogen with vigorous stirring (1000 rpm). The pressure was then maintained at 1350 psi with heating to 150°C for 1 hour. The reaction was allowed to cool and the catalyst removed by filtration. The solvent was removed by rotary evaporation to provide 18.48 g of brown solid. ^{1}H NMR and gc/ms data reveal a high purity product (>95%). The overall yield of FDM from HMF is 90%. NMR (δ, 1H): 4.54 (s, 2.0 H); 6.20 (s, 1.0 H).

WHAT IS CLAIMED IS:

1. A method of preparing 2,5 –(hydroxymethyl)furaldehyde comprising:

i) combining a fructose source, a solvent selected from the group consisting of 1-methyl-2-pyrrolidinone, dimethylacetamide, dimethylformamide and combinations of thereof, with a catalyst to provide a reaction mixture;

ii) heating said reaction mixture to a temperature and for a time sufficient to promote an acid-catalyzed dehydration reaction of fructose in said fructose source to form a product mixture; and

iii) isolating 2,5-(hydroxymethyl)furaldehyde from said product mixture.

2. The method of claim 1 wherein said fructose source is comprised of high fructose corn syrup.

3. The method of claim 1 wherein said acid-catalyzed dehydration reaction is carried out under vacuum and temperature conditions sufficient to remove water from the reaction mixture.

4. The method of claim 1 wherein said reaction mixture further includes a water absorbing molecular sieve material.

5. The method of claim 1 wherein said catalyst is selected from the group consisting of a mineral acid, an acidic ion-exchange resin, and a zeolite.

6. The method of claim 1 wherein said catalyst is a solid catalyst comprised of a strong acid ion exchange resin.

7. The method of claim 6 wherein said strong acid ion-exchange resin catalyst is selected from the group consisting of Amberlyst 35, Amberlyst 36, Amberlyst 15, Amberlyst 131, Lewatit S2328, Lewatit K2431, Lewatit S2568, Lewatit K2629, Dianion SK104, Dianion PK228, Dianion RCP160, and Relite RAD/F.

8. The method of claim 1 wherein said reaction mixture is heated to a temperature of from about 95° C to about 125° C.

9. The method of claim 1 wherein said reaction mixture is heated to a temperature of from about 105° C to about 115° C.

10. The method of claim 1 wherein said reaction mixture is heated for a time period of about one to about six hours.

11. A method of preparing 2,5 – (hydroxymethyl)furaldehyde comprising:

i) combining a fructose source, an organic solvent, and an acid catalyst to provide a reaction mixture;

ii) heating said reaction mixture to a temperature and for a time sufficient to promote a dehydration reaction of fructose in said fructose source to form a first product mixture;

iii) neutralizing the pH of the first product mixture to a pH of about 7 to 9;

iv) distilling the first product mixture after neutralizing the pH to remove said organic solvent remaining in the first product mixture; and

v) purifying said product mixture to provide a second product mixture comprising greater than 60% by weight of 2,5 – (hydroxymethyl)furaldehyde.

12. The method of claim 11 wherein said fructose source is comprised of high fructose corn syrup.

13. The method of claim 11 wherein said second product mixture comprises greater than 75% by weight of 2,5 – (hydroxymethyl)furaldehyde.

14. The method of claim 11 wherein purifying said product isolate comprises a solvent extraction process.

15. The method of claim 14 wherein said solvent extraction process comprises:

(i) adding a mixture comprising a water-immiscible organic solvent and water to said product isolate to provide an organic phase and an aqueous phase;

(ii) recovering said organic phase; and

(iii) removing said water-immiscible organic solvent from the recovered organic phase to yield purified HMF.

16. The method of claim 15 wherein said water-immiscible organic solvent is selected from the group consisting of ethyl acetate, methyl isobutylketone, methyl ethyl ketone, methyl t-butyl ether, octanol, pentanol, butyl acetate, and combinations thereof.

17. The method of claim 11 wherein the acid catalyst is an acidic ion exchange resin and the acidic ion exchange resin is removed from the first reaction mixture prior to the act of distilling.

18. The method of claim 11 further comprising adding a non-volatile flowing agent to first product mixture prior to the act of distilling

19. The method according to claim 18 wherein said non-volatile flowing agent is selected from the group consisting of polyethylene glycol, polyethylene glycol monoether, polyethylene glycol diether, end blocked derivates of polyethylene glycol, polyethylene glycol monoether, polyethylene glycol diether, and combinations thereof.

20. The method of claim 11 wherein purifying comprises a process selected from the group consisting of short path distillation, thin film evaporation, wiped film evaporation, and adsorption to an inert adsorbent.

21. A method of preparing 2,5-(hydroxymethyl)furaldehyde comprising the steps of:

i) combining a fructose source, an acid catalyst, a first organic solvent, and a second organic solvent that is non miscible with the first organic solvent to provide a reaction mixture, the first and second organic solvents being selected so that the second organic solvent preferentially dissolves 2,5-(hydroxymethyl)furaldehyde relative to the first organic solvent;

ii) heating said reaction mixture to a temperature and for a time sufficient to promote a dehydration reaction of fructose in said fructose source to form a product mixture with a first immiscible phase and a second immiscible phase; and

iii) isolating 2,5-(hydroxymethyl)furaldehyde from said second immiscible phase of said product mixture.

22. The method of claim 21 wherein said second organic solvent is selected from the group consisting of methyl isobutyl ketone, ethyl acetate and chloroform.

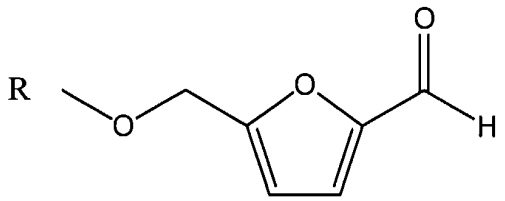
23. The method of claim 21 wherein said first organic solvent is dimethyl formamide.

24. The method of claim 42 wherein said second organic solvent has a Log P value of from about 0.4 to about 3.4, and said first organic solvent has a Log P value of less than zero.

25. The method of claim 47 wherein said second organic solvent has a Log P value of from about 0.6 to about 2.7.

26. The method of claim 47 wherein said first organic solvent has a Log P value of from about -.075 to about –1.95.

27. A method of preparing an R-oxymethylfurfural ether of hydroxylmethylfurfural of the formula:



where R is selected from the group consisting of alkyl, cycloalkyl, allyl and aryl, comprising:

(i) combining a fructose source, an R-OH solvent, and an acid catalyst to form a reaction mixture;

(ii) heating said reaction mixture to a temperature and for a time sufficient to promote an acid-catalyzed dehydration reaction fructose in the fructose source and to form R-oxymethylfurfural in a product mixture; and

(iii) Isolating the R-oxymethylfurfural from said product mixture.

28. The method of claim 27 wherein the R-OH solvent is ethanol and the R-oxymethylfurfural is ethoxymethylfurfural.

29. The method of claim 27 wherein the acid catalyst is an acidic ion exchange resin.

30. A method of preparing levulinic acid comprising:

(i) combining a fructose source, at least one of polyethylene glycol and end capped polyethylene glycol, and an acid catalyst to form a reaction mixture;

(ii) heating said reaction mixture to a temperature and for a time sufficient to promote an acid-catalyzed dehydration reaction of fructose in the fructose source and to form levulinic acid in a product mixture; and

(iii) isolating levulinic acid from said product mixture.

31. The method of claim 30 wherein the acid catalyst is an acidic ion exchange resin.

32. A method of preparing 2,5-bis-(hydroxymethyl)furan comprising:
heating a reaction mixture comprising 2,5-(hydroxymethyl)furaldehyde, a solvent, and a catalyst system comprising nickel and zirconium at a temperature, for a time, and at a pressure sufficient to promote reduction of the 2,5-(hydroxymethyl)furaldehyde to 2,5-bis-(hydroxymethyl)furan to produce a product mixture comprising 2,5-bis-(hydroxymethyl)furan.

33. The method of claim 32 wherein greater than 90% of the 2,5-(hydroxymethylfuraldehyde) is converted to 2,5-bis-(hydroxymethyl)furan.

34. The method of claim 32 wherein the temperature is between about 125° C and about 175° C.

35. The method of claim 32 wherein the pressure is between about 1000 and about 1500 pounds per square inch.

36. The method of claim 32 wherein the time sufficient to promote reduction of the 2,5-(hydroxymethyl)furaldehyde to 2,5-bis-(hydroxymethyl)furan is less than about three hours.

37. The method of claim 32 wherein the solvent is one of ethyl acetate, acetate, methyl acetate, butyl acetate, isopropanol, and butanol.

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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*

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(54) Title: PREPARATION OF 2,5-(HYDR0XYMETHYL)FURALDEHYDE (HMF) , DERIVATIVES THEREOF AND LEVULINIC ACID FROM FRUCTOSE AS WELL AS PREPARATION OF 2 , 5-BIS- (HYDROXYMETHYL) FURAN FROM 2 , 5-(HYDROXYMETHYL) FURALDEHYDE

(57) Abstract: The present application discloses: A method for the preparation of 2,5-(hydroxymethyl)furaldehyde from fructose with specific organic solvents. A method for the preparation of 2,5-(hydroxymethyl)furaldehyde from fructose with an acid catalyst. A method for the preparation of 2,5-(hydroxymethyl)furaldehyde from fructose with a with a two-phase organic solvent system. A method for the preparation of a 2,5-(hydroxymethyl)furaldehyde derivative from fructose. A method for the preparation of levulinic acid from fructose. A method for the preparation of 2,5-bis-(hydroxymethyl)furan from 2,5-(hydroxymethyl)furaldehyde.

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Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, BEILSTEIN Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/024947 A (E.I. DU PONT DE NEMOURS) 27 March 2003 (2003-03-27) page 3, line 29 - line 32 examples 20,23; table 3 claim 4	1-10
X	FR 2 669 635 A (FURCHIM) 29 May 1992 (1992-05-29) the whole document	1-10, 21-23
X	US 2 929 823 A (MERCK & CO INC) 22 March 1960 (1960-03-22) the whole document	1-10, 21-23

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 September 2006	07/11/2006

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Cortés, José

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 2003, BICKER, M. ET AL: "Dehydration of fructose to 5-hydroxymethylfurfural in sub- and supercritical acetone" XP002381410 retrieved from STN Database accession no. 2003:274299 abstract & GREEN CHEMISTRY , 5(2), 280-284 CODEN: GRCHFJ; ISSN: 1463-9262, 2003, -----	1-10
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X	FR 2 664 273 A (BEGHIN SAY SA) 10 January 1992 (1992-01-10) page 2, line 8 claim 6 -----	11-20
X	FR 2 663 933 A (BEGHIN SAY SA) 3 January 1992 (1992-01-03) page 1, line 38 - page 2, line 13 claims 1,5 -----	11-20
X	JP 55 053280 A (NOGUCHI KENKYUSHO) 18 April 1980 (1980-04-18) abstract -----	11-20
X	US 3 483 228 A (JOHN D. GARBER ET AL) 9 December 1969 (1969-12-09) claim 6 -----	11-20
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 28 April 2004 (2004-04-28), YADAV, GANAPATI D. ET AL: "Selectivity engineering in conversion of sugars into 5-hydroxymethylfurfuraldehyde" XP002398123 retrieved from STN Database accession no. 2004:222109 abstract -/--	11-20

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	& ABSTRACTS OF PAPERS, 227TH ACS NATIONAL MEETING, ANAHEIM, CA, UNITED STATES, MARCH 28-APRIL 1, 2004 , CELL-063 PUBLISHER: AMERICAN CHEMICAL SOCIETY, WASHINGTON, D. C. CODEN: 69FGKM, 2004,	
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X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 2000, KROGER, MARTIN ET AL: "A new approach for the production of 2,5-furandicarboxylic acid by in situ oxidation of 5-hydroxymethylfurfural starting from fructose" XP002398125 retrieved from STN Database accession no. 2000:763008 abstract & TOPICS IN CATALYSIS , 13(3), 237-242 CODEN: TOCAFI; ISSN: 1022-5528, 2000,	11-20
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 2000, BENVENUTI, F. ET AL: "Heterogeneous zirconium and titanium catalysts for the selective synthesis of 5-hydroxymethyl-2-furaldehyde from carbohydrates" XP002398126 retrieved from STN Database accession no. 2000:83722 abstract & APPLIED CATALYSIS, A: GENERAL , 193(1,2), 147-153 CODEN: ACAGE4; ISSN: 0926-860X, 2000,	11-20

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Form PCT/ISA/210 (continuation of second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 1995, GRIN, S. A. ET AL: "Character of acid catalysis in the dehydration of fructose with formation of 5-(hydroxymethyl) furfural" XP002398127 retrieved from STN Database accession no. 1995:173907 abstract & KHIMICHESKAYA FIZIKA , 13(5), 113-18 CODEN: KHFID9; ISSN: 0207-401X, 1994, -----	11-20
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X	MUSAU ET AL: "The Preparation of 5-Hydroxymethyl-2-Furaldehyde (HMF) from D-Fructose in the Presence of DMSO" BIOMASS, vol. 13, 1987, pages 67-74, XP002398112 the whole document -----	11-20
X	FAYET ET AL: "Nouvelle méthode de préparation du 5-hydroxyméthyl-2-furaldéhyde par action de sels d'ammonium ou d'immonium sur öles mono-, oligo- et poly-saccharides, accés direct aux 5-halogénométthyl-2-furaldéhydes" CARBOHYDRATE RESEARCH, vol. 122, 1983, pages 59-68, XP002398113 the whole document -----	11-20
X	FR 2 670 209 A (COMMISSARIAT ENERGIE ATOMIQUE) 12 June 1992 (1992-06-12) the whole document -----	21-23
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/044598

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

1-23

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☒ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-10

   a method for the preparation of 2,5-(hydroxymethyl)furaldehyde from fructose with specific organic solvents

   ---

2. claims: 11-20

   a method for the preparation of 2,5-(hydroxymethyl)furaldehyde from fructose with an acid catalyst

   ---

3. claims: 21-23

   a method for the preparation of 2,5-(hydroxymethyl)furaldehyde from fructose with a two-phase organic solvent system

   ---

4. claims: 27-29

   a method for the preparation of an oxy-substituted 2,5-(hydroxymethyl)furaldehyde derivative from fructose

   ---

5. claims: 30-31

   a method for the preparation of levulinic acid from fructose

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6. claims: 32-37

   a method for the preparation of 2,5-bis-(hydroxymethyl)furan from 2,5-(hydroxymethyl)furaldehyde

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2005/044598

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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METHOD FOR THE SYNTHESIS OF ORGANIC ACID ESTERS OF 5-HYDROXYMETHYLFURFURAL AND THEIR USE

Patent Number:	WO 2007/104515 A1
Inventor(s):	GRUTER GERARDUS JOHANNES MARIA [NL]; DAUTZENBERG F [US]
Applicant(s):	AVANTIUM INT BV [NL]; GRUTER GERARDUS JOHANNES MARIA [NL]; DAUTZENBERG F [US]
Classification:	**- international:** C07D307/46; C07D307/50 **- cooperative:** C07D307/46; C07D307/50; C10L1/02
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Priority number(s):	EP20060075565 20060310
Also published as:	EP1834951 (A1) ZA200807984 (A) US2009306415 (A1) US2009306415 (A1) US8242293 (B2) US8242293 (B2) UA98615 (C2) MY145760 (A) JP2009529551 (A) EP2105439 (A1) EP2105439 (B1) EP2050742 (A1) EP2050742 (B1) EP2053047 (A1) EP2001859 (A1) EP2001859 (B1) CN101421259 (A) CA2645060 (A1) BRPI0707099 (A2) AU2007224708 (A1) AU2007224708 (A1) AU2007224708 (B2) AU2007224708 (B2) AT529416 (T) AT473218 (T) AT468330 (T)

Abstract of WO 2007/104515 A1

Method for the manufacture of organic acid esters of 5-hydroxymethylfurfural by reacting a fructose or glucose-containing starting material with an organic acid or its anhydride in the presence of a catalytic or sub-stoechiometric amount of solid acid catalyst. The catalysts are heterogeneous and may be employed in a continuous flow fixed bed reactor. The esters can be applied as a fuel or fuel additive.

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(71) Applicant *(for all designated States except US)*: **AVANTIUM INTERNATIONAL B.V.** [NL/NL]; 29, Zekeringstraat, NL-1014 BV Amsterdam (NL).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **GRUTER, Gerardus, Johannes, Maria** [NL/NL]; 14, Asterkade, NL-2106 BA Heemstede (NL). **DAUTZENBERG, F.** [NL/US]; 5008 Chelterham Ter, San Diego, CA 92130 (US).

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2007/104515 A1

(54) Title: METHOD FOR THE SYNTHESIS OF ORGANIC ACID ESTERS OF 5-HYDROXYMETHYLFURFURAL AND THEIR USE

(57) Abstract: Method for the manufacture of organic acid esters of 5-hydroxymethylfurfural by reacting a fructose or glucose-containing starting material with an organic acid or its anhydride in the presence of a catalytic or sub-stoechiometric amount of solid acid catalyst. The catalysts are heterogeneous and may be employed in a continuous flow fixed bed reactor. The esters can be applied as a fuel or fuel additive.

Title: Method for the synthesis of organic acid esters of 5-hydroxymethylfurfural and their use.

The present invention relates to a method for the preparation of derivatives of 5-hydroxymethylfurfural (HMF), in particular ester derivatives of HMF, such as the condensation product of formic acid or its anhydride with HMF (formioxymethylfurfural), acetic acid or its anhydride with HMF (5-acetoxymethylfurfural), or of propionic acid or its anhydride with HMF(5-propionoxymethylfurfural) and to their application as a fuel or fuel additive.

The conversion of sugars or sugar (hexoses) containing biomass into more economically useful compounds is of increasing interest. Current fuel activities are mainly directed towards ethanol from sugar/glucose. Typically, sucrose and glucose are fermented into ethanol. One glucose molecule is converted into two molecules of ethanol and two molecules of CO2. This conversion has drawbacks especially in view of atom economy, the low energy density of ethanol (7.7 kWh/kg or 6.1 kWh/L) and its relative low boiling point (78,4 degrees Celsius).

Another application area involves the conversion of sugars such as fructose into HMF in the presence of an acid catalyst has been reported (for example in EP0230250 to Suedzucker or EP0561928 to CEA)). In this case, HMF is obtained as a highly potential starting material for obtaining bio-based monomer such as furandicarboxylic acid which can *inter alia* be used as an alternative to terephthalic acid as a monomer for polyethylene terephthalate type polyesters (Moreau et. al. in Topics in Catalysis Vol 27, Nos. 1-4, 2004, 11 - 30 and references cited therein). When under these conditions sucrose or glucose was used as a feed, no conversion to HMF is observed (Moreau et. al. in Topics in Catalysis Vol 27, Nos. 1-4, 2004, p13, col 2. line 2-3), which is a distinct disadvantage given the low price and abundant availability of sucrose and glucose. Only in the presence of DMSO, DMF and DMA (low HMF yields from glucose: Ishida et. al. Bull. Chem. Soc. Jpn 74 2001, 1145) or in a sub- and supercritical mixture of acetone and water (fructose, glucose, sucrose and inulin conversion to HMF in 77%, 48%, 56% and 78% yields respectively: Vogel et. al. Green Chemistry 5, 2003, 280) reasonable HMF yields from starting materials other than fructose were obtained.

In the current market situation, fructose as feed is undesirable given the high price thereof, compared to glucose and/or sucrose. Therefore, so far, no process for the synthesis of HMF has been developed on an industrial scale.

The synthesis chemistry and applications of HMF are reviewed extensively in Lewkowski, ARKIVOC 2001, (i) 17-54; in Gandini, Prog. Polym. Sci. 22, 1997, 1203; in Lichtenthaler, C.R. Chimie, 7, 2004, 65 and Acc. Chem. Res. 35, 2002, 728; and Moreau, Topics in Catalysis, 27, 2004, 11.

Concluding, the current methods for the synthesis of HMF mostly start from fructose and typically do not give high yield, partly attributable to the instability of HMF under the acidic reaction conditions. In most acid-catalysed water-based reactions, the further reaction to levulinic acid and humins has been reported, making this a less attractive alternative.

The present inventors have set out to overcome these disadvantages.

Surprisingly, the inventors have found that the conversion of hexose-containing starting material, in particular fructose and/or glucose -containing starting material and more particular glucose-containing material that may be derived from biomass in the presence of a catalytic or sub-stoechiometric amount of acid in the presence of an organic acid or its anhydride with or without the presence of one or more additional diluents leads to the formation of the corresponding organic acid ester of HMF in good yield and selectivity.

Thus, the invention pertains to a method for the manufacture of organic acid esters of 5-hydroxymethylfurfural by reacting a fructose and/or glucose-containing starting material with an organic acid or its anhydride in the presence of a catalytic or sub-stoechiometric amount of acid catalyst.

It was found that this in situ formation and derivatisation of HMF prevents the occurrence of the onward and undesired reaction towards the above-mentioned levulinic acid and humins, thus leading to an efficient procedure for the conversion of glucose-containing material into HMF derivatives.

In certain embodiments, the organic acid is a mono-carboxylic acid, preferably selected from the group consisting of (un)branched aliphatic acids, (un)branched unsaturated acids, preferably (un)branched aliphatic acids, more preferably C1-C5 (un)branched aliphatic acids, most preferable formic acid, acetic acid, propionic

acid, (iso)-butyric acid, particularly preferable formic acid, acetic acid, more particularly preferable acetic acid or the anhydrides thereof, in particular formic anhydride, acetic anhydride, propionic anhydride and (iso)butyric anhydride. Acetic acid or its anhydride is the most preferred acid/anhydride in the method of the present invention as acetic acid or its anhydride can also be derived from biomass.

As these HMF derivatives can now be obtained in high yields, in one step, from very cheap hexose or hexose containing starting materials such as sucrose and glucose, and as furthermore, the acetyl ester (acetoxymethylfurfural) has a high energy content (typically about 8.7 kWh/L, vs 8.8 kWh/L for gasoline and only 6.1 kWh/L for ethanol) and in contrast to HMF is a liquid at room temperature, they can directly be used as a fuel additive as an alternative for MTBE or as a fuel itself. Mixtures of acids and/or anhydrides may also be employed.

The acid catalyst in the method of the present invention can be selected from amongst (halogenated) organic acids, inorganic acids, salts, Lewis acids, ion exchange resins and zeolites or combinations and/or mixtures thereof. In certain embodiments, the pKa of (halogenated) organic acid catalyst is equal or smaller than the pKa of the organic acid or the anhydride. It is thought that typically the stronger acid functions as the catalyst. In certain preferred embodiments, the acid catalyst is a heterogeneous catalyst. In certain embodiments, the acid catalyst is a homogenous catalyst. The acid may be a protonic, Brønsted or, alternatively, a Lewis acid. In certain embodiment, the acid may be a (halogenated) organic or inorganic acid. In certain embodiments, the organic acid can be selected from amongst formic acid, acetic acid, tri(chloro or fluoro)acetic acid, oxalic acid, levulinic acid, maleic acid or para-toluenesulphonic acid. In certain embodiments, the inorganic acid can be selected from amongst phosphoric acid, sulphuric acid, hydrochloric acid, hydrobromic acid, nitric acid, hydroiodic acid, optionally generated in situ. In certain embodiments, the inorganic acid is selected form the group of sulphuric acid, phosphoric acid, hydrochloric acid, nitric acid.

In certain embodiments, the salt can be one of (NH4)2SO4/SO3, ammonium phosphate, triethylamine phosphate, pyridinium salts, pyridinium phosphate, pyridinium hydrochloride/hydrobromide/perbromate, DMAP, aluminium salts, Th and

Zr ions, zirconium phosphate, Cr-, Al-, Ti-, Ca-, In-ions, ZrOCl2, VO(SO4)2, TiO2, V-porphyrine, Zr-, Cr-, Ti-porphyrine. In certain embodiments, the Lewis acid can be one of ZnCL2, AlCl3, BF3. In certain embodiments, the ion exchange resins can be one of Amberlite, Diaion, levatit. In certain embodiments, it is preferred that the acid catalyst is a solid catalyst that may be selected form the group consisting of acid resins, natural clay mineral, zeolites, supported acids such as silica impregnated with mineral acids, heat treated charcoal, metal oxides, metal sulfides, metal salts and mixed oxides and mixtures thereof. In certain embodiments, mixtures or combinations of acid catalysts can be used.

The temperature at which the reaction is performed may vary, but in general it is preferred that the reaction is carried out at a temperature from 50 to 300 degrees Celsius, preferably from 100 to 250, more preferably from 150 to 200 degrees Celsius. In general, temperatures higher than 300 are less preferred as the selectivity of the reaction as many by-products occur, *inter alia* caramelisation of the sugar. Performing the reaction below the lowest temperature is also less preferable because of the slow reaction speed.

The fructose and/or glucose-containing starting material can be selected from a wide variety of feeds. In general any feed with a sufficient high fructose or glucose content can be used. It is preferred that the glucose-containing starting material is selected from the group of starch, amylose, galactose, cellulose, hemi-cellulose, glucose-containing disaccharides such as sucrose, maltose, cellobiose, lactose, preferably glucose-containing disaccharides, more preferably sucrose or glucose.

The catalyst can be added to the reaction mixture in an amount varying from 0.01 to 40 mole % drawn on the fructose or glucose content of the fructose and/or glucose -containing starting material preferably from 0.1 to 30 mole %, more preferably from 1 to 20 mole %.

In certain embodiments, one or more solvents may be added, in general to aid the dissolution of the glucose containing material or as a diluent. The solvent may be selected form the group consisting of water, sulfoxides, preferably DMSO, ketones, preferably methyl ethylketone, methylisobutylketone, acetone or mixtures of two or more of the above solvents.

In certain embodiments, the ratio of organic acid or anhydride/solvent is from 50 to 0.1, preferably from 20 to 1, more preferably from 10 to 2.

Higher amounts of organic acid or anhydride may have the result that the reaction is too slow due to the limited solubility (hence availability of the glucose containing material), whereas too much solvent in the system may lead to a too high dilution, which in both cases are less preferred results. One of the preferred solvents is water.

In certain embodiments, the method can be performed in a continuous flow process. In such method, homogenous catalysts may be used and the residence time of the reactants in the flow process is between 0.1 second and 10 hours, preferably from 1 second to 5 hours, more preferably from 1 minute to 1 hour.

In certain embodiments, the continuous flow process is a fixed bed continuous flow process or a reactive (catalytic) distillation process with preferably a heterogeneous acid catalyst. To initiate or regenerate the heterogeneous acid catalyst or to improve performance, an inorganic or organic acid may be added to the feed of the fixed bed or reactive distillation continuous flow process. In a fixed bed process, the liquid hourly space velocity (LHSV) can be from 1 to 1000, preferably from 5 to 500, more preferably from 10 to 250 and most preferably from 25 to 100.

As explained above, the application of the products of the method of the present invention, i.e. the esters, is in the use as a fuel or fuel additive and as precursor for the manufacture of 2,5-di(hydroxymethyl)furan, furan-2,5-dicarboxylic acid, 2-hydroxymethylfuran-5-carboxylic acid, 2,5-(dihydroxymethyl)tetrahydrofuran, which can be used as monomers in a polymerisation process, optionally after conversion of the diol to a diamine. See for a review Moreau, Topics in catalysis, 2004, 27, 11-30

Example 1: sucrose feed, mineral acid catalyst

In a continuous flow reactor, sucrose 10 mmol/l, dissolved in water/acetic acid/10% H_2SO_4, was reacted at a temperature of 195 degrees Celsius with a residence time between 6 and 60 seconds and a flow rate of 10 ml/min, i.e. 3.33 ml/min/reactor. At 6 seconds, mainly conversion into fructose and glucose was observed, but at prolonged residence times, 2 main furan peaks were observed in the UV spectrum. Mass spectrometry identified these products as HMF and AMF (5-acetoxymethylfurfural) with a selectivity of >90 % at a conversion of 25%.

Example 2: glucose feed, mineral acid catalyst

In a continuous flow reactor, glucose 10 mmol/l, dissolved in water/acetic acid/10% H_2SO_4, was reacted at a temperature of 195 degrees Celsius with a residence time between 6 and 60 seconds and a flow rate of 10 ml/min, i.e. 3.33 ml/min/reactor. At 30 seconds, 2 main furan peaks were observed in the UV spectrum. Mass spectrometry identified these products as HMF and AMF (5-acetoxymethylfurfural) with a selectivity of >90 % at a conversion of 10%.

Apparatus

Continuous parallel flow reactor system consisting of four quartz reactors inserted in a silver heating block; temperature and flow regulators and three HPLC pumps. Two of the pumps deliver the liquid to the reactors and third one is employed to dilute the reaction products prior to collection.

Analytical Method

The reaction products were quantified with the aid of HPLC-analysis with an internal standard (saccharine, Sigma Aldrich). A Merck-Hitachi L7000 chromatograph, equipped UV and RI detectors, was used. Stationary phase were reverse phase C18 (Sunfire 3.5 µm, 4.6x100mm, Waters) and cation exchange (SupelcogelH, 4.6x300mm, SigmaAldrich) columns connected in series. A gradient elution at a constant flow 0.6 ml/min and temperature 60 °C was used according to the following scheme.

Time (min)	0.2% TFA (aq)	Methanol	Acetonitrile
0	90.0	7.0	3.0
10	90.0	7.0	3.0
11	80.0	0.0	20.0
15	80.0	0.0	20.0
16	90.0	7.0	3.0
21	90.0	7.0	3.0

General Procedure

A 1.25 wt% solution of glucose (99.7 % Sigma Aldrich) in 50% or 90% aqueous acetic acid was flowed through a fixed bed (200 µl) of a

heterogeneous catalyst at 180 °C. Flow rates were chosen such to achieve a space velocity 0.25 or 0.5 min^{-1}, *i.e.* contact time 2 or 4 min. Liquid coming out of the reactors was diluted by a mixture of water and ethanol (50:50) to prevent tubing blockages.

Catalysts tested:
Catalyst 1 Zeolite beta SAR25 (CBV Zeolyst)
Catalyst 2 Zeolite Y high SAR (CBV Zeolyst)
Catalyst 5 Mordenite H SAR 90 (CBV Zeolyst)
Catalyst 7 Zeolite Y SAR 5.17 (CBV Zeolyst)

Contact time and space velocity were calculated as follows:

$$\mathbf{Sv = Fr_{feed} / V_{cat}}$$

Sv space velocity (min^{-1})
Fr_{feed} flow rate feed (ml/min)/
V_{cat} catalyst volume (ml)

$$\mathbf{t_c = 1/ Sv}$$

t_c contact time (min)

Conversion of substrate, selectivity and yield of furan derivatives were calculated according to the following formulae:

$$\mathbf{X = 100 * m_{r\ substrate} / m_{0\ substrate}}$$

X conversion (%)
$m_{r\ substrate}$ amount of reacted substrate (mg)
$m_{0\ substrate}$ amount of substrate in feed (mg)

$$\mathbf{S_{compound} = 100 * n_{r\ substrate} / n_{0\ substrate}}$$

$S_{compound}$ selectivity to compound (%)
$n_{r\ substrate}$ moles of substrate reacted
$n_{0\ substrate}$ moles of substrate in feed

$$\mathbf{Yield = 100 * n_{product} / n_{0\ substrate}}$$

Yield yield (%)
$n_{product}$ moles of product formed

DATA Fructose + acetic acid with solid acid catalyst 1
fructose conc 55.5 mmol/L; 90% AcOH

Res	fructose	Y (HMF)	Y (AMF)	*S* (HMF)	*S* (AMF)

time	conversion				
/ s	%	%	%	%	%
10	25	2	5	8	20
30	50	4	15	8	30
60	75	7	17	9	23
120	98	6	20	6	20

DATA Glucose + acetic acid with solid acid catalyst 1
glucose conc 55.5 mmol/L; 90% AcOH

Res time	glucose conversion	Y (HMF)	Y (AMF)	*S* (HMF)	*S* (AMF)
/ s	%	%	%	%	%
60	73	2	5	3	7
180	92	1	6	1	7
300	97	1	6	1	6
600	98	1	7	1	7

DATA Sucrose + Acetic acid with solid acid catalyst 2
sucrose conc 27.8 mmol/L (55.5 mmol/L C6H12O6); 90% AcOH

Res time	glu + fru conversion	Y (HMF)	Y (AMF)	*S* (HMF)	*S* (AMF)
/ s	%	%	%	%	%
60	86	4	13	5	15
180	96	3	15	3	16
300	98	3	17	3	17
600	99	2	16	2	16

Engine test

In a small-scale model diesel engine, comparative testing is performed with normal commercial diesel as a fuel and the same commercial diesel to which samples of 1 wt.%, 2 wt.%, 3 wt.%, 5 wt%, and 10 wt.% HMF or AMF are added, respectively. The diesel samples with HMF are less homogenous on visual inspection (solid particles remain visible, flocculation) and above 5 wt.% HMF, a solid deposit is sometimes observed. AMF is added as a liquid and does not yield any mixing or flocculation problems. The engine is run stationary with a set volume (100 mL) of fuel until empty. HMF containing fuels run less regular, whereas AMF containing fuels run at a regular pace and for a longer period (up to 15%). On visual inspection of the engine, AMF provides less visual contamination.

Claims

1. Method for the manufacture of organic acid esters of 5-hydroxymethylfurfural by reacting a fructose and/or glucose-containing starting material with an organic acid or its anhydride in the presence of a catalytic or sub-stoechiometric amount of heterogenous acid catalyst.

2. Method according to claim 1, wherein the organic acid is a mono-carboxylic acid, preferably selected from the group consisting of (un)branched aliphatic acids, (un)branched unsaturated acids, preferably (un)branched aliphatic acids, more preferably C1-C5 (un)branched aliphatic acids, most preferable formic acid, acetic acid, propionic acid, (iso)-butyric acid, particularly preferable formic acid, acetic acid, more particularly preferable acetic acid or the anhydrides thereof, in particular formic anhydride, acetic anhydride, propionic anhydride and (iso)butyric anhydride or mixtures and combinations thereof.

3. Method according to claim 1 or 2, wherein the acid catalyst is selected from the group consisting of solid (halogenated)organic acids, inorganic acids, salts, Lewis acids, ion exchange resins, zeolites or mixtures and/or combinations thereof.

4. Method according to claim 3, wherein the pKa of solid (halogenated) organic acid catalyst is equal or smaller than the pKa of the organic acid.

5. Method according to claim 1, wherein the acid is a solid Brønsted acid.

6. Method according to claim 1, wherein the acid is a solid Lewis acid.

7. Method according to claim 1, wherein the heterogeneous acid catalyst is selected form the group consisting of acid resins, natural clay mineral, zeolites, supported acids such as silica impregnated with mineral acids, heat treated charcoal, metal oxides, metal sulfides, metal salts and mixed oxides.

8. Method according to any one of the claims 1 to 7, wherein the reaction is performed at a temperature from 50 to 300 degrees Celsius, preferably from 100 to 250, more preferably from 150 to 200 degrees Celsius.

9. Method according to any one of the claims 1 to 8, wherein the fructose and/or glucose-containing starting material is selected from the group of starch, amylose, galactose, cellulose, hemi-cellulose, glucose-containing disaccharides such as sucrose, maltose, cellobiose, lactose, preferably glucose-containing disaccharides, more preferably sucrose or glucose.

10. Method according to any one of the claims 1 to 9, wherein one or more solvents or diluents are present in addition to the organic acid or the anhydride.

11. Method according to claim 10, wherein the solvent or solvents are is selected form the group consisting of water, sulfoxides, preferably DMSO, ketones, preferably methyl ethylketone, methylisobutylketone and/or acetone and mixtures thereof.

12. Method according to claim 16, wherein the ratio of organic acid/solvent is from 50 to 0.1, preferably from 20 to 1, more preferably from 10 to 2.

13. Method according to any one of the claims 1 to 12, wherein the method is performed in a continuous flow process.

14. Method according to claim 13, wherein the residence time in the flow process is between 0.1 second and 10 hours, preferably from 1 second to 5 hours, more preferably from 1 minute to 1 hour.

15. Method according to claim 13, wherein the continuous flow process is a fixed bed continuous flow process.

16. Method according to claim 15, wherein the fixed bed comprises a heterogeneous acid catalyst.

17. Method according to claim 13, wherein the continuous flow process is a reactive distillation or a catalytic distillation process.

18. Method according to claim 15 or 17, wherein in addition to a heterogeneous acid catalyst, an inorganic or (halogenated) organic acid catalyst is added to the feed of the fixed bed or catalytic distillation continuous flow process.

19. Method according to any one of the claims 18 to 24, wherein the LHSV is from 1 to 1000, preferably from 5 to 500, more preferably from 10 to 250 and most preferably from 25 to 100.

20. Use of the organic acid esters of 5-hydroxymethylfurfural, preferably 5-acetoxymethylfurfural, as a fuel or as a fuel additive.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2007/002146

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D307/46 C07D307/50

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 925 812 A (MERCK & CO., INC) 8 May 1963 (1963-05-08) page 1, left-hand column, line 10 - page 1, right-hand column, line 28	1-19
Y	page 1, left-hand column, line 49 - page 1, left-hand column, line 55; example II	1-19
X,Y	GARVES K: "Acid catalyzed degradation of cellulose in alcohols" JOURNAL OF WOOD CHEMISTRY AND TECHNOLOGY, MARCEL DEKKER, NEW YORK, NY, US, vol. 8, no. 1, 1988, pages 121-134, XP009067962 ISSN: 0277-3813 the whole document	1-19

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 May 2007	12/06/2007

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Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TYRLIK S S K ET AL: "Selective dehydration of glucose to hydroxymethylfurfural and a one-pot synthesis of a 4-acetylbutyrolactone from glucose and trioxane in solutions of aluminium salts" CARBOHYDRATE RESEARCH, ELSEVIER SCIENTIFIC PUBLISHING COMPANY. AMSTERDAM, NL, vol. 315, no. 3-4, 28 February 1999 (1999-02-28), pages 268-272, XP004174265 ISSN: 0008-6215 Introduction: reactivity of glucose the whole document	1-19
Y	DE 36 21 517 A1 (GARVES,KLAUS,DIPL.-CHEM.DR) 7 January 1988 (1988-01-07) claims 1-9	1-19
X	US 2003/032819 A1 (LIGHTNER GENE E [US]) 13 February 2003 (2003-02-13) claims 7,19	20

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2007/002146

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-19

Claims 1-19 relate to a method for the manufacture of esters of 5-hydroxymethylfurfural from glucose-containing material in the presence of an organic acid and an acidic catalyst.

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2. claim: 20

Claim 20 is directed towards the use of the organic acid ester of 5-hydroxymethylfurfural as a fuel or a fuel additive.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2007/002146

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 925812 A	08-05-1963	NONE	
DE 3621517 A1	07-01-1988	NONE	
US 2003032819 A1	13-02-2003	NONE	

HYDROXYMETHYL FURFURAL OXIDATION METHODS

Patent Number:	WO 2008/054804 A2
Inventor(s):	LILGA MICHAEL A [US]; HALLEN RICHARD T [US]; HU JIANLI [US]; WHITE JAMES F [US]; GARY MICHEL J [US]
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Classification:	**- international:** B01J23/00; C07D307/44; C07D307/48 **- cooperative:** C07D307/44; C07D307/48
Application number:	WO2007US23063 20071031
Priority number(s):	US20060863704P 20061031
Also published as:	WO2008054804 (A3) US2008103318 (A1) US7700788 (B2) US2010152470 (A1) US8193382 (B2) US2010152469 (A1) US2010152469 (A1) US8193381 (B2) US8193381 (B2)

Abstract of WO 2008/054804 A2

A method of oxidizing hydroxymethyl furfural (HMF) includes providing a starting material which includes HMF in a solvent comprising water into a reactor. At least one of air and O2 is provided into the reactor. The starting material is contacted with the catalyst comprising Pt on a support material where the contacting is conducted at a reactor temperature of from about 50 DEG C to about 200 DEG C A method of produc ing an oxidation catalyst where ZrO2 is provided and is calcined. The ZrO2 is mixed with platinum (II) acetylacetonate to form a mixture. The mixture is subjected to rotary evaporation to form a product. The product is calcined and reduced under hydrogen to form an activated product. The activated product is passivated under a flow of 2% O2.

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C07D 307/48 (2006.01)

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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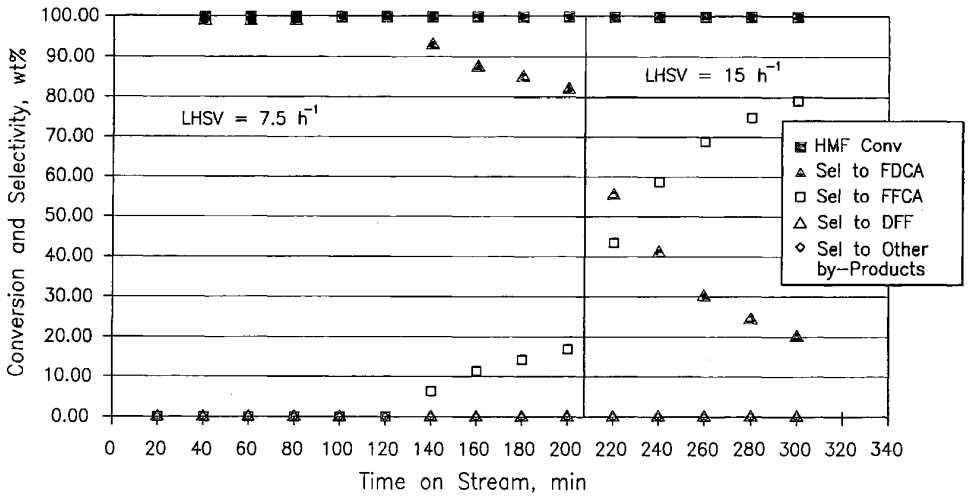
Declaration under Rule 4.17:
— *of inventorship (Rule 4.17(iv))*

Published:
— *without international search report and to be republished upon receipt of that report*

(54) Title: HYDROXYMETHYL FURFURAL OXIDATION METHODS



(57) Abstract: A method of oxidizing hydroxymethylfurfural (HMF) includes providing a starting material which includes HMF in a solvent comprising water into a reactor. At least one of air and O_2 is provided into the reactor. The starting material is contacted with the catalyst comprising Pt on a support material where the contacting is conducted at a reactor temperature of from about 50°C to about 200°C A method of producing an oxidation catalyst where ZrO_2 is provided and is calcined. The ZrO_2 is mixed with platinum (II) acetylacetonate to form a mixture. The mixture is subjected to rotary evaporation to form a product. The product is calcined and reduced under hydrogen to form an activated product. The activated product is passivated under a flow of 2% O_2.

WO 2008/054804 A2

HYDROXYMETHYL FURFURAL OXIDATION METHODS

RELATED PATENT DATA

[0001] This patent claims priority under 35 U.S.C. § 119 to U.S. Provisional Application No. 60/863,704, which was filed October 31, 2006.

TECHNICAL FIELD

[0002] The invention pertains to hydroxymethylfurfural oxidation methods, methods of producing diformyl furan and methods of producing an oxidation catalyst.

BACKGROUND OF THE INVENTION

[0003] Hydroxymethylfurfural (HMF) is a compound which can be produced from various hexoses or hexose-comprising materials. HMF can in turn be converted into a variety of derivatives, many of which are currently or are quickly becoming commercially valuable. Oxidation of HMF can produce oxidation products including diformyl furan (DFF), hydroxymethyl furan carboxylic acid (HMFCA), formylfuran carboxylic acid (FFCA), and furandicarboxylic acid (FDCA). Uses for these oxidation products include but are not limited to adhesives, sealants, composites, coatings, binders, foams, curatives, monomers and resins.

[0004] Although numerous routes and reactions have been utilized for preparing one or more of the oxidation products set forth above, conventional methodology typically results in low HMF conversion, low product selectivity and/or low product yield. It is desirable to develop alternative methodologies for oxidation of HMF and production of HMF oxidation products.

SUMMARY OF THE INVENTION

[0005] In one aspect the invention pertains to a method of oxidizing hydroxymethylfurfural (HMF). The method includes providing a starting material which includes HMF in a solvent comprising water into a reactor. At least one of air and O_2 is provided into the reactor. The starting material is contacted with the catalyst comprising Pt on a support material where the contacting is conducted at a reactor temperature of from about 50°C to about 200°C.

[0006] In one aspect the invention pertains to a method of producing diformylfuran. The method includes providing a mixture comprising HMF and an organic solvent. The

mixture is contacted with a catalyst comprising active γ-MnO_2. The mixture is subjected to reflux temperature for a time of from about 6 hours to about 12 hours.

[0007] In one aspect the invention includes a method of producing an oxidation catalyst. ZrO_2 is provided and is calcined. The ZrO_2 is mixed with platinum (II) acetylacetonate to form a mixture. The mixture is subjected to rotary evaporation to form a product. The product is calcined and reduced under hydrogen to form an activated product. The activated product is passivated under a flow of 2% O_2.

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] Preferred embodiments of the invention are described below with reference to the following accompanying drawings.

[0009] Fig. 1 shows conversion of HMF and selective production of furan dicarboxylic acid and formylfuran carboxylic acid as a function of time on stream utilizing a continuous flow reactor with a 5% platinum supported on carbon catalyst and a base set of parameters in accordance with one aspect of the invention. The parameters included P=150psig, T=100°C, 0.828% Na_2CO_3 added to 1% HMF, liquid hourly space velocity (LHSV)=7.5-15 h^{-1}, air gas hourly space velocity (GHSV)=300 h^{-1}, catalyst reduced at 30°C wet.

[0010] Fig. 2 shows HMF conversion and product selectivity as a function of time on stream using the catalyst of Fig. 1 at a decreased temperature (T=70°C), LHSV=4.5-7.5 h^{-1} and air GHSV=300-600 h^{-1} (all other parameters and conditions being as set forth above with respect to Fig. 1).

[0011] Fig. 3 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 1 and the parameters as set forth for Fig. 2 except for temperature (T=50°C).

[0012] Fig. 4 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 1 and the conditions as set forth at Fig. 2 with the exception of the temperature which was T=30°C.

[0013] Fig. 5 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 1 and the conditions of Fig. 2 with a decreased concentration of Na_2CO_3 of 0.414% and T=100°C.

[0014] Fig. 6 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 1 and the conditions of Fig. 1 except with an increased Na_2CO_3 concentration of 1.66%.

[0015] Fig. 7 shows HMF conversion and product selectivity as a function of temperature using the catalyst of Fig. 1. P=150psig, 0.828% Na_2CO_3 added to 1% HMF, LHSV=7.5 h^{-1} air, GHSV=300 h^{-1}, data taken at time on stream=140min.

[0016] Fig. 8 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 1 at the specified temperature and GHSV (either air or O_2). P=150psig, T=100-115°C, 2.486% Na_2CO_3 added to 3% HMF LHSV=4.5 h^{-1}, air GHSV=300-600 h^{-1} or O_2 GHSV=600 h^{-1}, catalyst reduced at 30°C wet.

[0017] Fig. 9 shows HMF conversion and product selectivity as a function of time on steam utilizing the catalyst of Fig. 1 under air or O_2 at varied LHSV and/or GHSV. P=150psig, T=130°C, 0.828% Na_2CO_3 added to 1% HMF, LHSV=7.5-15 h^{-1}, air GHSV=300-600 h^{-1} or O_2 GHSV=600 h^{-1}, catalyst reduced at 30°C wet.

[0018] Fig. 10 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 1 at P=150psig air, T=100°C, 1% HMF, LHSV=7.5-15 h^{-1}, GHSV=300 h^{-1}.

[0019] Fig. 11 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 1 and the conditions of Fig. 10 with the exception of 0.8% added Na_2CO_3.

[0020] Fig. 12 shows conversion of HMF and selective production of the indicated products as a function of time on stream utilizing a continuous flow reactor with a 5% Pt supported on SiO_2 catalyst and a base set of parameters in accordance with one aspect of the invention; 1% HMF, 150psig air, 60-100°C, LHSV=13-19.6 h^{-1}, GHSV=261 h^{-1}.

[0021] Fig. 13 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 12 in the presence of 0.8% Na_2CO_3. (1% HMF, 0.8% Na_2CO_3, 150psig air, 100°C, LHSV=13-6.5 h^{-1}, GHSV=261 h^{-1}.)

[0022] Fig. 14 shows HMF conversion and product selectivity utilizing a 9.65% Pt supported on carbon catalyst. The conditions utilized were P=150psig, T=100°C, 0.828% Na_2CO_3 added to 1% HMF LHSV=7.5-15 h^{-1}, air GHSV=300 h^{-1}, catalyst reduced at 30°C wet.

[0023] Fig. 15 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 14. P=150psig, T=100°C, 2.414% Na_2CO_3 added to 3% HMF LHSV=4.5 h^{-1}, air GHSV=600 h^{-1}, catalyst reduced at 30°C wet.

[0024] Fig. 16 shows HMF conversion and product selectivity as a function of time on stream for various air GHSV and LHSV. P=150psig, T=100°C, 1% HMF LHSV=7.5-15 h^{1}, air GHSV=75-300 h^{-1}, catalyst reduced at 30°C wet.

[0025] Fig. 17 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 14 at varied temperature and LHSV. P=150psig, T=60-100°C, 1% HMF LHSV=3-7.5 h^1, 1% O_2 diluted air GHSV=300h^1, catalyst reduced at 30°C wet.

[0026] Fig. 18 shows HMF conversion and selective product production utilizing a 5% Pt on an Al_2O_3 support catalyst as a function on time on stream at varied LHSV. P=150psig, T=100°C, 1% HMF LHSV=15-7.5 h^{-1}, air GHSV=300 h^{-1}, catalyst reduced at 30°C wet.

[0027] Fig. 19 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst Fig. 18 at an increased temperature (130°C) relative to Fig. 18. P=150psig, 1% HMF LHSV=7.5 h^{-1}, air GHSV=300 h^{-1}, catalyst reduced at 30°C wet.

[0028] Fig. 20 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 18 in the presence of O_2. P=150psig, T=100°C, 1% HMF LHSV=7.5 h^{-1}, 100% O_2 GHSV=300 h^{-1}, catalyst reduced at 30°C wet.

[0029] Fig. 21 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 18 and the conditions of Fig. 20 with the exception that P=300psig.

[0030] Fig. 22 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 18 and the conditions of Fig. 20 with the exception that 100% O_2 GHSV=600 h^{-1}.

[0031] Fig. 23 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 18 at varied LHSV. P=150 psig, T=100°C, 1% HMF LHSV=7.5-4.5 h^{-1}, air GHSV=600 h^{-1}, catalyst reduced at 30°C wet.

[0032] Fig. 24 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 18 at varied LHSV in the presence of O_2. P=150psig, T=100°C, 0.828 weight % Na_2CO_3 added to 1% HMF LHSV=7.5-4.5 h^{-1}, O_2 GHSV=300 h^{-1}, catalyst reduced at 30°C wet.

[0033] Fig. 25 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 18 at varied LHSV and GHSV. P=150psig, T=100°C, 0.828 % Na_2CO_3 added to 1% HMF LHSV=4.5-7.5 h^{-1}, air GHSV=300-600 h^{-1}, catalyst reduced at 30°C wet.

[0034] Fig. 26 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 18 at varied LHSV and GHSV. P=150psig,

T=70°C, 0.828%Na_2CO_3 added to 1% HMF LHSV=4.5-7.5 h^{-1}, air GHSV=300-600 h^{-1}, catalyst reduced at 30°C wet.

[0035] Fig. 27 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 18 in an 8mL catalyst bed in the presence of air and then O_2. P=150psig, T=100°C, 0.5% HMF LSHV=3.75 h^{-1}, air then O_2 GHSV=150-263 h^{-1}, catalyst reduced at 30°C wet.

[0036] Fig. 28 shows HMF conversion and selective product production as a function of time on stream utilizing a 5% Pt on a ZrO_2 support catalyst at varied LHSV in a continuous flow reactor. P=150psig air, T=100°C 0.5% HMF LHSV=7.5-3 h^{-1}, GHSV=300 h^{-1}.

[0037] Fig. 29 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 28 at varied LHSV and HMF concentration. HMF=0.5-1%, P=150psig air, T=120°C, LHSV=7.5-4.5 h^{-1}, GHSV=300 h^{-1}.

[0038] Fig. 30 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 28 at varied temperature. P=150psig air, T=140-160°C, 0.5% HMF LHSV=7.5 h^{-1}, GHSV=300 h^{-1}.

[0039] Fig. 31 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 28 at varied LHSV at varied temperature and at varied psi air. P=150-300 psig air, T=100-160°C, 0.5% HMF LHSV=7.5-15 h^{-1}, GHSV = 300 h^{-1}.

[0040] Fig. 32 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 28. P=150 psig air, T=140°C, 0.5% HMF LHSV = 7.5 h^{-1}, GHSV = 300 h^{-1}.

[0041] Fig. 33 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 28 and the condition of Fig. 32 with the exception of decreased GHSV (GHSV=150 h^{-1}).

[0042] Fig. 34 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 28 and the condition of Fig. 32 with the exception that P=500 psig air.

[0043] Fig. 35 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 28 and the condition of Fig. 32 with the exception that GHSV=150 h^{-1} and P=150 psig O_2.

[0044] Fig. 36 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 28 after Na_2CO_3 wash; 0.5% HMF, P=150 psig air, T=100°C, LHSV=7.5 h^{-1}, GHSV = 300 h^{-1}.

[0045] Fig. 37 shows the concentration in weight % versus time on stream of the indicated starting material, products and by-products utilizing the catalyst of Fig. 28 after a carbonate wash. 0.5% HMF, P=150 psig air, T=100°C, LHSV=7.5 h^{-1}, GHSV=300 h^{-1}.

[0046] Fig. 38 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 28 at varied temperature in the presence of either air or O_2. 1% HMF in 40% HOAc, 150 psig air/O_2, T=100-140°C, LHSV=7.5 h^{-1}, GHSV=300 h^{-1}.

[0047] Fig. 39 shows HMF conversion and product selectivity as a function of time on stream utilizing the catalyst of Fig. 28 in the presence of either air or O_2 at varied GHSV. 0.5% HMF in 40% HOAc, P=150 psig air/O_2, T=140°C, LHSV = 7.5 h^{-1}, GHSV=150-300 h^{-1}.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0048] This disclosure of the invention is submitted in furtherance of the constitutional purposes of the U.S. Patent Laws "to promote the progress of science and useful arts" (Article 1, Section 8).

[0049] In general, the invention pertains to methods of oxidizing hydroxymethyl furfural (HMF) in an aqueous solution. The oxidation process can be performed as a batch reaction or as a continuous flow process. A starting material is provided comprising HMF in water. Depending on the desired product, the mixture can be basic, neutral or acidic. Where an acidic aqueous solution solvent system is utilized, an appropriate acid can be added such as, for example, acetic acid. Due to the relatively low solubility of HMF oxidation products in neutral and acidic water, appropriate reactor designs can be utilized to accommodate solids formation. Feeds having up to 10% HMF have been successfully used in a batch reactor, and higher HMF concentrations are feasible. In a packed bed up-flow reactor the HMF concentration can preferably be less than or equal to about 3% by weight. Under mildly basic conditions, such as those created by providing Na_2CO_3 into the reaction mixture, products having carboxylic acid groups are present as the sodium salt and have increased solubilities. Solids formation and feed concentration are typically not problematic under these conditions. The

addition of a strong base, such as NaOH, can lead to undesirable side reactions such as the Cannizzaro reaction.

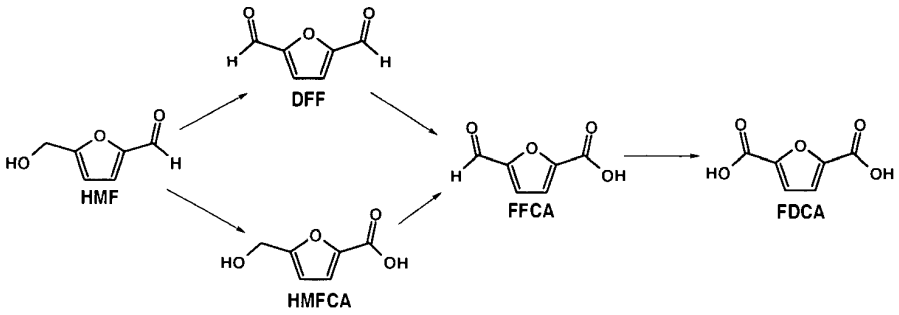
[0050] The starting material comprising HMF is provided into a reactor and at least one of air or O_2 is provided as oxidant. A pressure of from atmospheric to the pressure rating of the equipment can be utilized depending upon the desired reaction rate. A preferred pressure can typically be in the range of 150-500 psi. Similarly an appropriate reaction temperature can be from about 50°C to about 200°C, with a preferred range of from 100°C through about 160°C.

[0051] The starting material is contacted with a catalyst within the reactor. The catalyst typically comprises a metal on a support material. Preferably the metal comprises Pt. The support material can comprise, for example, C, ZrO_2, Al_2O_3, SiO_2, or TiO_2. The particular support material utilized can depend upon, for example, the desired oxidation product(s) (discussed below).

[0052] In particular instances, the reaction mixture can contain Na_2CO_3, or comparable weak base. Where Na_2CO_3 is utilized, such can be present in the mixture at a molar ratio of from 0.25 to 2.0 moles Na_2CO_3 to HMF, preferably at a molar ratio of from 0.5 to about 1.0 relative to HMF. The use of Na_2CO_3 or alternative carbonate bases is advantageous relative to conventional methodology. Other relatively weak bases (relative to NaOH) are contemplated such as those weaker than NaOH and stronger than the furan carboxylate product such that the furan carboxylate (FDCA, FFCA) remains in the soluble salt form. Possible alternative bases include metal carbonates, metal bicarbonates, metal phosphates, and metal hydrogen phosphates. These relatively weak bases can be present in the feed and do not need to be added slowly over the course of the reaction to prevent side reactions that tend to occur with strong bases such as NaOH.

[0053] Where continuous reaction is utilized in an up-flow packed bed reactor with a feed of about 1-3 wt% HMF, the liquid hourly space velocity (LHSV) can be, for example, from about 3 h^{-1} to about 15 h^{-1}, and gas hourly space velocity (GHSV) can be for example from about 75 h^{-1} to about 600 h^{-1}. These parameters can vary depending on the feed concentration and the reactor design and are presented for reference only.

[0054] The oxidation of HMF to fully oxidized product FDCA can occur with involvement of partially oxidized species DFF, HMFCA, and FFCA via the routes shown in the following diagram.



[0055] As shown in the accompanying figures and as discussed further below, particular catalysts and sets of reaction conditions and parameters can favor selective production of one or more reaction products or intermediates. For example, under particular reaction conditions, HMF conversions of 100% were achieved with selectivity to FDCA as high as 98% relative to all other reaction products, intermediates and byproducts.

[0056] Studies utilizing various catalysts including those described herein for neutral and acidic feed solutions indicate that catalysts such as those described having high metal loading on low surface area (conditions that typically gives low dispersion of metal) produce the highest HMF conversion and FDCA selectivity. These results run counter to conventional wisdom that generally indicates best catalytic performance utilizing catalysts having high dispersion and high surface area.

[0057] Inorganic support materials can also be preferred for the present catalysts. Catalysts supported on carbon can result in product holdup and inhibition. Holdup can also increase generally with surface area even for those inorganic support materials, which tend to sorb less than carbon supports.

[0058] As indicated above, the fully oxidized product FDCA is relatively insoluble in water. Higher solubility can be attained in carboxylic acid solvent such as, for example, acetic acid/water mixtures. Table 1 shows the solubility of FDCA in various acetic acid/water mixtures. As indicated, the solubility in a 40/60 ratio HOAc/H_2O is about twice the solubility in pure water. The oxidation of 0.5 weight % HMF in 40/60 HOAc/H_2O with 150 psi O_2 over a 5% Pt/ZrO_2 catalyst at 140°C achieves 100% HMF conversion with up to about 80% selectivity to FDCA.

TABLE 1: Solubility of FDCA in acetic acid/water mixtures

Vol% HOAc	Vol % H_2O	wt% 70°C	wt% 25°C
0	100	0.327	0.086
40	60	0.779	0.153
50	50	0.746	0.173
60	40	0.596	0.171
70	30	0.592	0.143
90	10	0.458	0.138
100	0	0.193	0.080

[0059] As illustrated in Figs. 1-11, HMF oxidation reactions performed utilizing 5% Pt supported on granular carbon can be utilized to selectively produce FFCA relative to individual alternative intermediates and oxidation products. In particular instances, such reactions under appropriate conditions can selectively produce FFCA relative to all other oxidation products, intermediates and byproducts.

[0060] Referring to Figs. 12-13 studies were performed utilizing a 5% Pt/SiO_2 catalyst. Under appropriate reaction conditions the 5% Pt/SiO_2 catalyst can be utilized to selectively produce DFF relative to individual alternative oxidation products, intermediates and byproducts. In particular instances, DFF can be produced selectively relative to all other oxidation products, intermediates and by products (see Fig. 12). In the presence of Na_2CO_3, the 5% Pt/SiO_2 catalyst can be utilized to selectively produce FFCA as its Na salt (see Fig 13).

[0061] The results of studies utilizing an alternative Pt/C catalyst are presented in Figs. 14-17. As shown, an appropriate Pt/C catalyst can be utilized under the indicated reaction parameters to selectively produce FDCA relative to all other oxidation products, intermediates and byproducts.

[0062] Studies were performed utilizing a 5% Pt supported on Al_2O_3 catalyst, the results of which are presented in Figs. 18-27. The 5% Pt supported on Al_2O_3 can be utilized to selectively produce FDCA and FFCA relative to alternative oxidation products and byproducts. Under alternative conditions the Pt/Al_2O_3 catalyst can also be utilized to selectively produce FDCA relative to all other oxidation products, intermediates and byproducts.

[0063] A 5% Pt supported on ZrO_2 catalyst was also utilized to perform HMF oxidation studies. The results of these studies are presented in Figs. 28-39. The data indicates that the 5% Pt supported on ZrO_2 can produce 100% HMF conversion with selective production of FDCA relative to all other oxidation products intermediates and byproducts. Utilizing the same catalyst, an adjustment of reaction conditions can be utilized to produce, selectively, a product mixture of FDCA and FFCA.

[0064] Product isolation, separation and purification can be achieved based upon solubility differences between the compounds (HMF, individual intermediates, byproducts and FDCA) in aqueous and organic solvents.

[0065] In another aspect, the invention pertains to preparation of DFF from HMF. A mixture is provided containing HMF in an organic solvent. The mixture is contacted with the catalyst containing active γ-MnO_2 and is subjected to reflux temperature for a time of from about 6 hours to about 12 hours. The organic solvent can preferably be a chlorinated solvent such as methylene chloride. MnO_2 is removed by filtration followed by solvent removal. The resulting solids are dissolved in hot water and DFF is precipitated. HMF conversion is approximately 80% with DFF product selectivity nearly 100%. This methodology is advantageous relative to conventional methodology which utilizies MnO_2 to oxidize furandimethanol (FDM) as the starting material, where the yield of product DFF is reported as only 40%.

[0066] In yet another aspect the invention pertains to a method of producing an oxidation catalyst. Extrudated ZrO_2 is provided and the extrudated ZrO_2 is calcined. The calcined ZrO_2 is crushed and sieved and is subsequently mixed with platinum(II) acetylacetonate to form a mixture. The mixture is subjected to rotary evaporation to form a product which is subsequently calcined. The product is activated by reducing under hydrogen and passivated under a flow of 2% O_2.

EXAMPLE 1: Oxidation of HMF to FDCA in a Fixed-Bed Continuous Flow Reactor

[0067] A 3/8-inch stainless-steel thick-walled tube (0.065 inch wall thickness) was utilized as a tubular reactor. 4 mL (4.7254 g) of dry 5% Pt/ZrO_2 catalyst was placed in the reaction tube with 60-80 mesh glass beads at the inlet and outlet of the catalyst bed. The reactor tube was attached to a liquid-gas feed system and placed within a tube furnace. The catalyst was wetted with deionized water and reduced prior to testing at

150 psi pressure and ambient temperature with a hydrogen flow. After 30 minutes the hydrogen was shut off and the system was vented and purged with nitrogen.

[0068] Airflow of approximately 100 mL/min was established until the system pressure increased to 150 psig. Water was introduced at a flow rate of 0.5 mL/min with a high-pressure liquid pump and the airflow was then decreased to a flow rate of 20 mL/min (GHSV=300 h^{-1}). The temperature operating set point of the system was increased to 100°C. Upon achieving 100°C a 0.5 weight % feed solution of HMF was fed into the catalyst bed at a rate of 0.2 mL/min (LHSV=3h^{-1}). At 40-60 minute reaction time intervals (measured from the time feed was initiated) liquid samples of the product exiting the reactor were collected for liquid chromatography analysis. Liquid chromatography results for each sample taken showed 100% conversion of HMF with selectivity to FDCA attaining 98% within 40 minutes under these conditions. Conversion and selectivity remained constant for another 220 minutes of testing.

EXAMPLE 2: Oxidation of HMF in a batch reactor

[0069] Batch oxidation of HMF was conducted in a 40 mL autoclave with a glass liner. 0.50 grams of 5% Pt on ZrO_2, 10 mL of deionized water and a magnetic stir bar were added into the glass liner. The vial and contents were sealed in the autoclave and were purged with nitrogen. The contents were then activated by reducing with hydrogen at room temperature. After 10 minutes the hydrogen was purged from the reactor with nitrogen. The nitrogen line was subsequently removed and no attempt was made to exclude air.

[0070] An oxygen line was attached to the reactor and the reactor was filled with oxygen. 0.51 grams of HMF in 5 mL of water was added to the autoclave with a syringe through a valve placed at the top of the autoclave cap. A magnetic stir plate was turned on and the reactor was pressurized to 150 psi with oxygen. The autoclave was heated to 100°C. After 6 hours reaction time a sample was removed from the reactor by cooling to 40°C, venting the oxygen to atmospheric pressure and withdrawing the sample through the top valve using a syringe and an 18 gauge needle. The sample was analyzed utilizing liquid chromatography and indicated that 80% of original HMF had reacted with approximately 68% conversion to DFF and 32% conversion to FFCA. The autoclave was charged to 150 psi with oxygen and was again heated to 100°C for an additional 17 hours. The reactor was then cooled and vented and another sample removed. After a total of 23 hours reaction the HMF was completely depleted. Liquid

chromatography revealed an absence of detectable DFF and FFCA. The primary product revealed utilizing liquid chromatography analysis was FDCA indicating complete oxidation of HMF. The only other product detected was levulinic acid, which resulted from the hydrolysis of HMF.

EXAMPLE 3: Preparation of DFF from HMF

[0071] 1.155 grams of HMF was dissolved in 50 mL of methylene chloride. 7.0606 grams of activated MnO_2 was added to the solution and the mixture was heated to reflux for 8 hours. The MnO_2 was removed from the reaction mixture by filtration and the solids were washed with additional solvent. The solvent was removed to produce and off-white solid. Liquid chromatography analysis of the solid indicated 80% DFF and 20% un-reacted HMF. A trace amount of FDCA was observed utilizing UV detection. The solid was dissolved in hot water and was subsequently cooled to precipitate DFF having a 98.5% purity. Selectivity of the oxidation reaction to DFF was substantially 100%.

EXAMPLE 4: Preparation of 5% Pt on a ZrO_2 Support

[0072] Extrudated ZrO_2 received from Engelhard was calcined at 700°C for 2 hours. The calcined ZrO_2 was crushed and sieved to 40-80 mesh size. 10.6318 grams of the crushed ZrO_2 was mixed at room temperature with 0.7593 grams of platinum(II) acetylacetonate in 50 mL flask. The flask was then mounted on a rotary evaporator and evacuated by a vacuum pump to reach 10 mmHg. The flask was rotated at 60 rpm for 10 minutes. After a thorough mixing the flask was heated to about 180°C utilizing a heat gun. During the process the color of the catalyst changed from a light brown color to black. The temperature was then increased to about 240°C. Heating was stopped after approximately 20 minutes. The catalyst was then calcined in air for about 3 hours at 350°C with a temperature ramp rate of 5°C per minute.

[0073] Activation was carried out by reducing the catalyst in a fixed-bed reactor at 330°C for 3 hours. The hydrogen flow rate was 40 mL/min. After reduction the reactor was cooled to room temperature under hydrogen and was then purged with helium for 30 minutes. Passivation was conducted by flowing 2% O_2 into the reactor at 40 mL/min overnight. The catalyst was unloaded from the reactor and was transferred to a storage container until use.

[0074] In compliance with the statute, the invention has been described in language more or less specific as to structural and methodical features. It is to be understood, however, that the invention is not limited to the specific features shown and described, since the means herein disclosed comprise preferred forms of putting the invention into effect. The invention is, therefore, claimed in any of its forms or modifications within the proper scope of the appended claims appropriately interpreted.

CLAIMS

The invention claimed is:

1. A method of oxidizing hydroxymethyl furfural (HMF), comprising:

providing a starting material comprising HMF in a solvent comprising water into a reactor;

providing at least one of air and O_2 into the reactor; and

contacting the starting material with a catalyst comprising Pt, on a support material, the contacting being conducted at a reactor temperature of from about 50°C to about 200°C.

2. The method of claim 1 wherein the starting material has a pH of less than or equal to about 7, and wherein the method selectively produces at least one of furandicarboxylic acid and formylfuran carboxylic acid, relative to all other intermediates, products and byproducts.

3. The method of claim 1 wherein the starting material has a pH of less than or equal to about 7, and wherein the method selectively produces furandicarboxylic acid relative to all other intermediates, products and byproducts.

4. The method of claim 1 further comprising providing a base selected from the group consisting of metal carbonates, metal bicarbonates, metal phosphates, and metal hydrogen phosphates into the reactor.

5. The method of claim 1 wherein the solvent comprises acetic acid.

6. The method of claim 5 wherein the acetic acid is present at a ratio of 40:60 relative to water.

7. The method of claim 1 wherein the support material comprises at least one of ZrO_2, Al_2O_3, SiO_2, TiO_2 and carbon.

8. The method of claim 1 wherein the catalyst comprises 5%Pt on a ZrO_2 support material.

9. The method of claim 8 wherein the method selectively produces a mixture of furandicarboxylic acid and formylfuran carboxylic acid relative individually to all other products, byproducts and intermediates.

10. The method of claim 8 wherein the method selectively produces furandicarboxylic acid relative individually to all other products, byproducts and intermediates.

11. The method of claim 1 wherein the catalyst comprises 5%Pt on a carbon support material.

12. The method of claim 11 wherein the method selectively produces furandicarboxylic acid relative individually to all other products, byproducts and intermediates.

13. The method of claim 11 wherein the method selectively produces formylfuran carboxylic acid relative individually to all other products, byproducts and intermediates.

14. The method of claim 1 wherein the catalyst comprises 5%Pt on a SiO_2 support material.

15. The method of claim 14 wherein the method selectively produces diformyl furan relative individually to all alternative products, byproducts and intermediates.

16. The method of claim 1 wherein the catalyst comprises 5%Pt on a SiO_2 support material, wherein the method further comprises providing a base selected from the group consisting of metal carbonates, metal bicarbonates, metal phosphates, and metal hydrogen phosphates into the reactor.

17. The method of claim 16 wherein the method selectively produces formylfuran carboxylic acid relative individually to all alternative products, byproducts and intermediates.

18. The method of claim 1 wherein the catalyst comprises 5%Pt on a Al_2O_3 support material.

19. The method of claim 18 wherein the method selectively produces a mixture of furandicarboxylic acid and formylfuran carboxylic acid relative individually to all alternative products, byproducts and intermediates.

20. The method of claim 18 wherein the method selectively produces furandicarboxylic acid relative individually to all alternative products, byproducts and intermediates.

21. A method of producing diformyl furan, comprising:

providing a mixture comprising hydroxymethyl furfural and an organic solvent;

contacting the mixture with a catalyst comprising active γ-MnO_2; and

subjecting the mixture to reflux temperature for a time of from about 6 hours to about 12 hours.

22. The method of claim 21 wherein the organic solvent comprises methylene chloride.

23. The method of claim 21 wherein the production of diformyl furan occurs selectively relative to all other products, byproducts and intermediates.

24. A method of producing an oxidation catalyst, comprising:

providing ZrO_2;

calcining the ZrO_2;

mixing the ZrO_2 with platinum(II) acetylacetonate to form a mixture;

subjecting the mixture to rotary evaporation to form a product;

calcining the product;

reducing the product under hydrogen to form an activated product; and

passivating the activated product under a flow of 2% O_2.

25. The method of claim 24 wherein the ZrO_2 is calcined at a temperature of about 700°C.

26. The method of claim 24 wherein the rotary evaporation is conducted at first temperature of about 180°C until the mixture undergoes a color change from light brown to black, and wherein the temperature is subsequently increased to a second temperature of about 240°C.

27. The method of claim 24 wherein the product calcining is conducted at a temperature of about 350°C.

28. A method of producing an oxidation catalyst comprising:

providing a support material comprising at least one of TiO_2, Al_2O_3, and SiO_2;

calcining the support material;

mixing the calcined support material with platinum(II) acetylacetonate to form a mixture;

subjecting the mixture to rotary evaporation to form a product;

calcining the product;

reducing the product under hydrogen to form an activated product; and

passivating the activated product under a flow of 2% O_2.

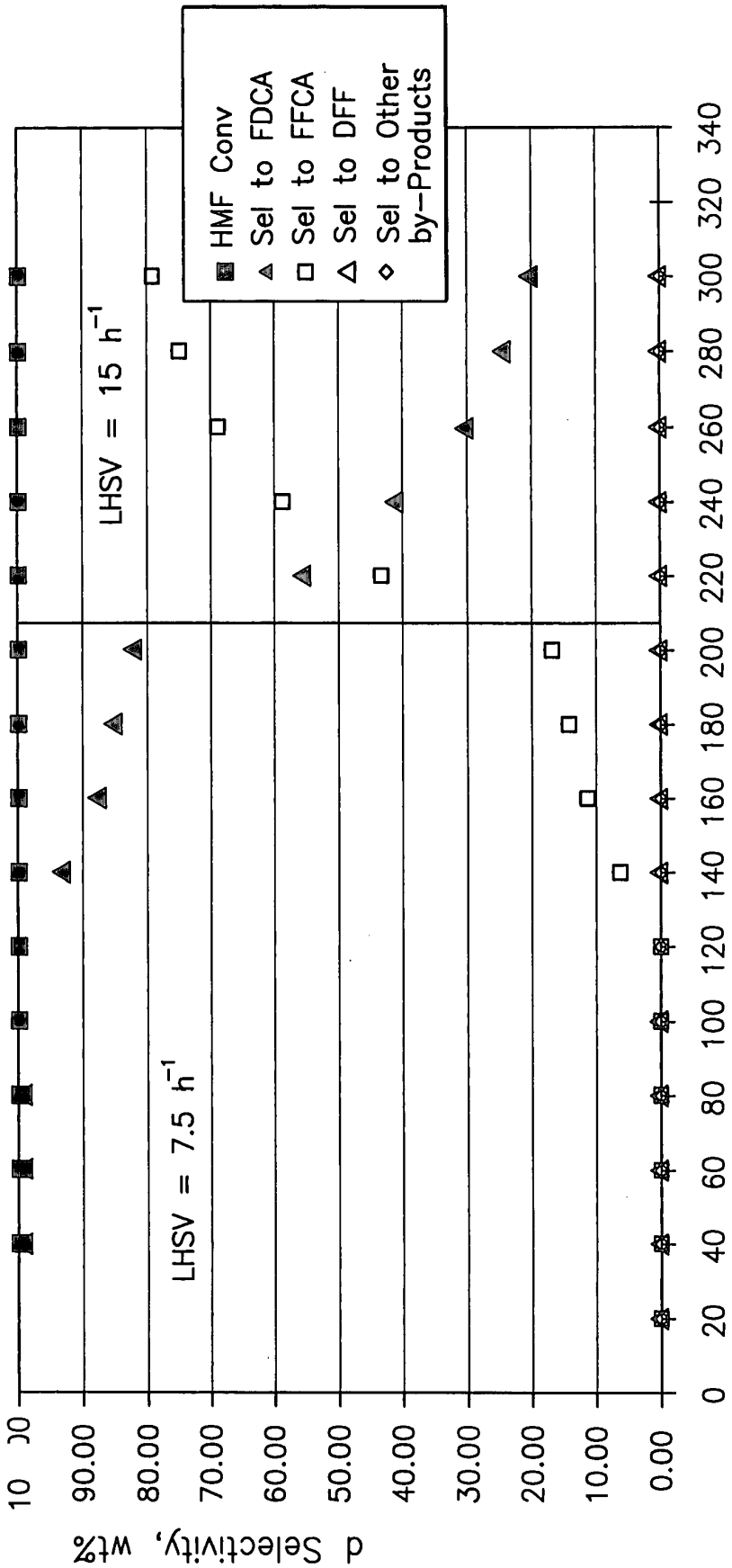

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
LHSV = 15 h-1
LHSV = 7.5 h-1
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
90.00
100.00
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340
Time on Stream, min
d Selectivity, wt%

FIG. 11

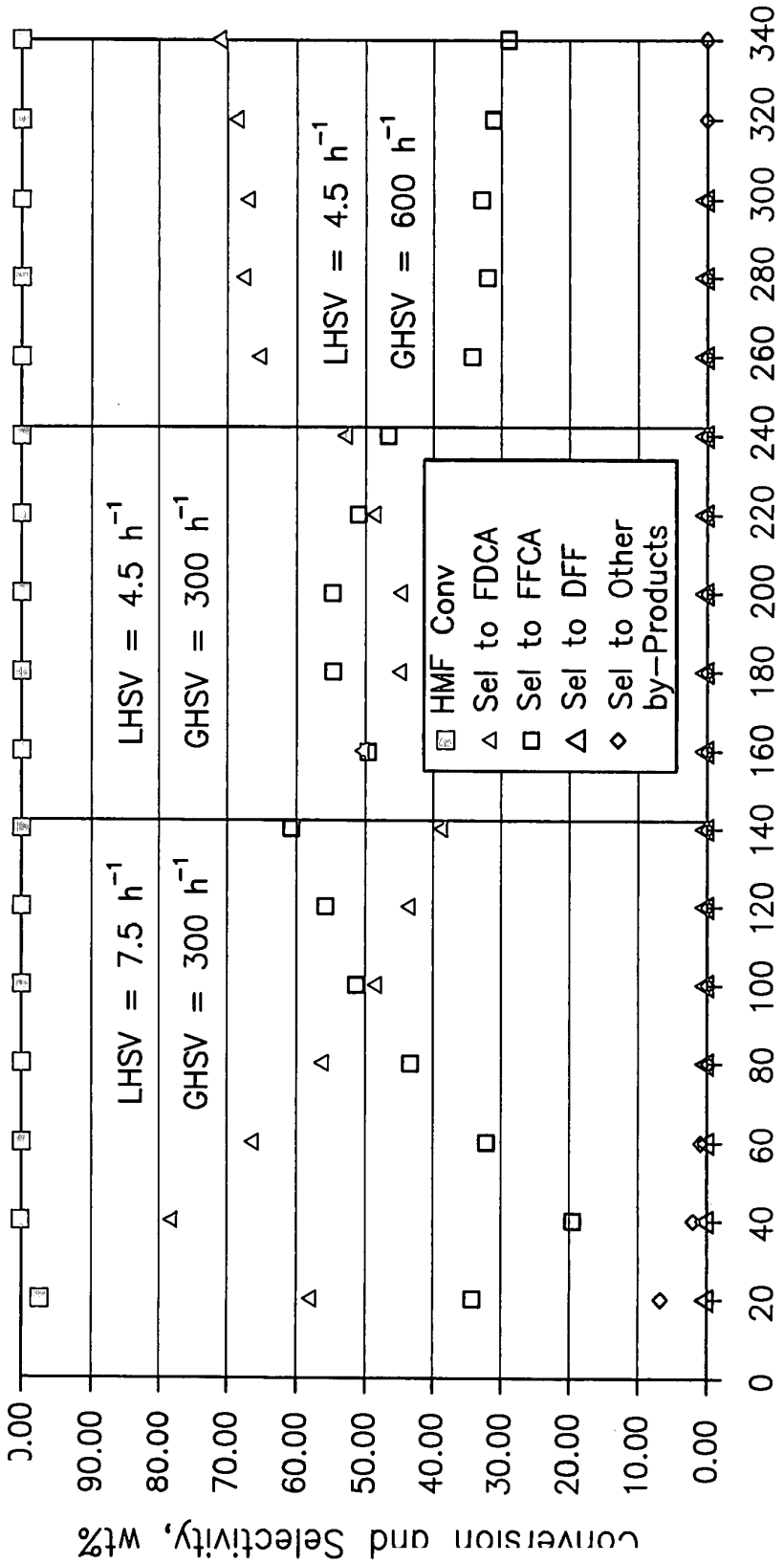

Conversion and Selectivity, wt%
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
90.00
100.00
0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340
Time on Stream, min
LHSV = 7.5 h-1
GHSV = 300 h-1
LHSV = 4.5 h-1
GHSV = 300 h-1
LHSV = 4.5 h-1
GHSV = 600 h-1
HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products

Fig 2

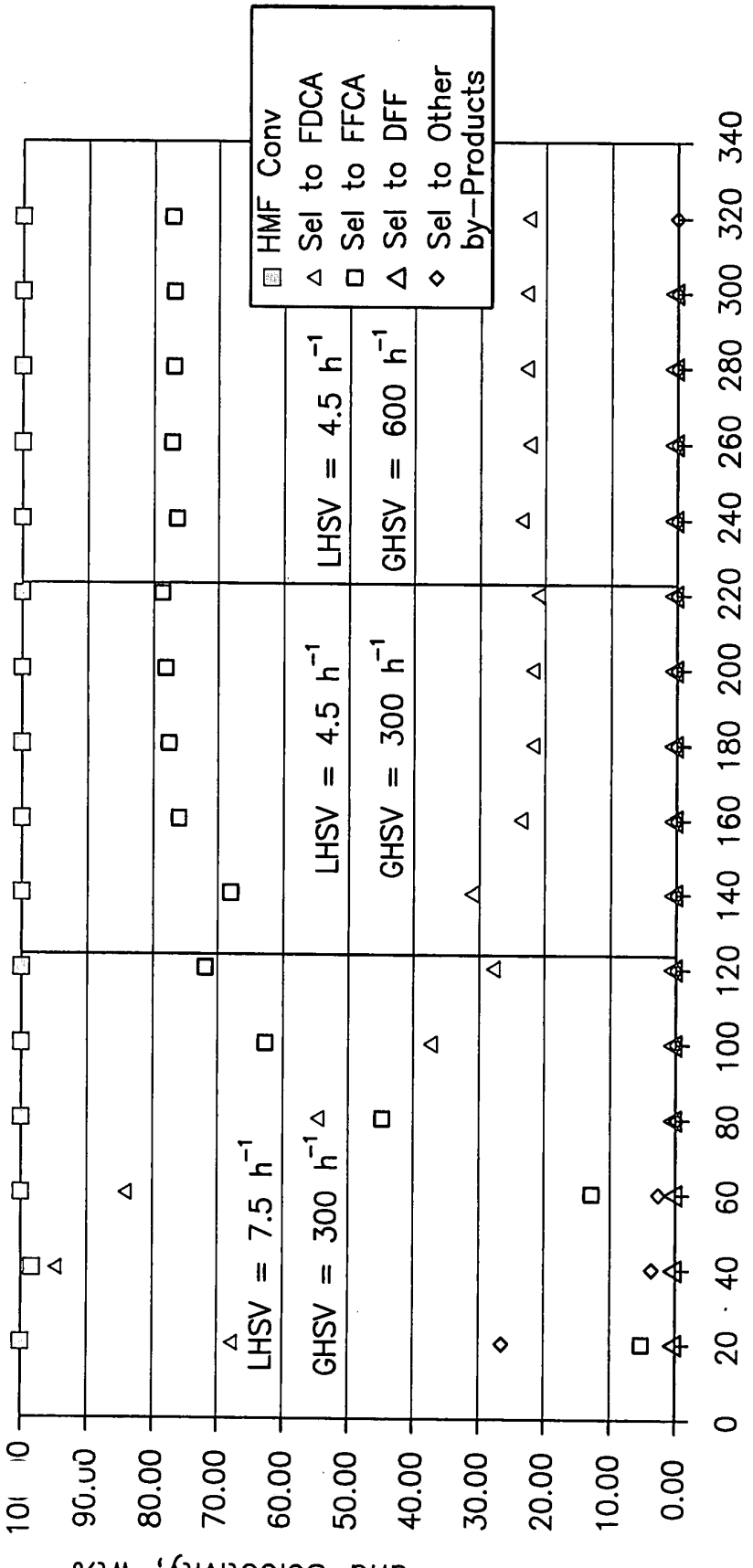

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
LHSV = 7.5 h-1
GHSV = 300 h-1
LHSV = 4.5 h-1
GHSV = 300 h-1
LHSV = 4.5 h-1
GHSV = 600 h-1
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
90.00
100
0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340
Time on Stream, min
and Selectivity, wt%

FIG 3

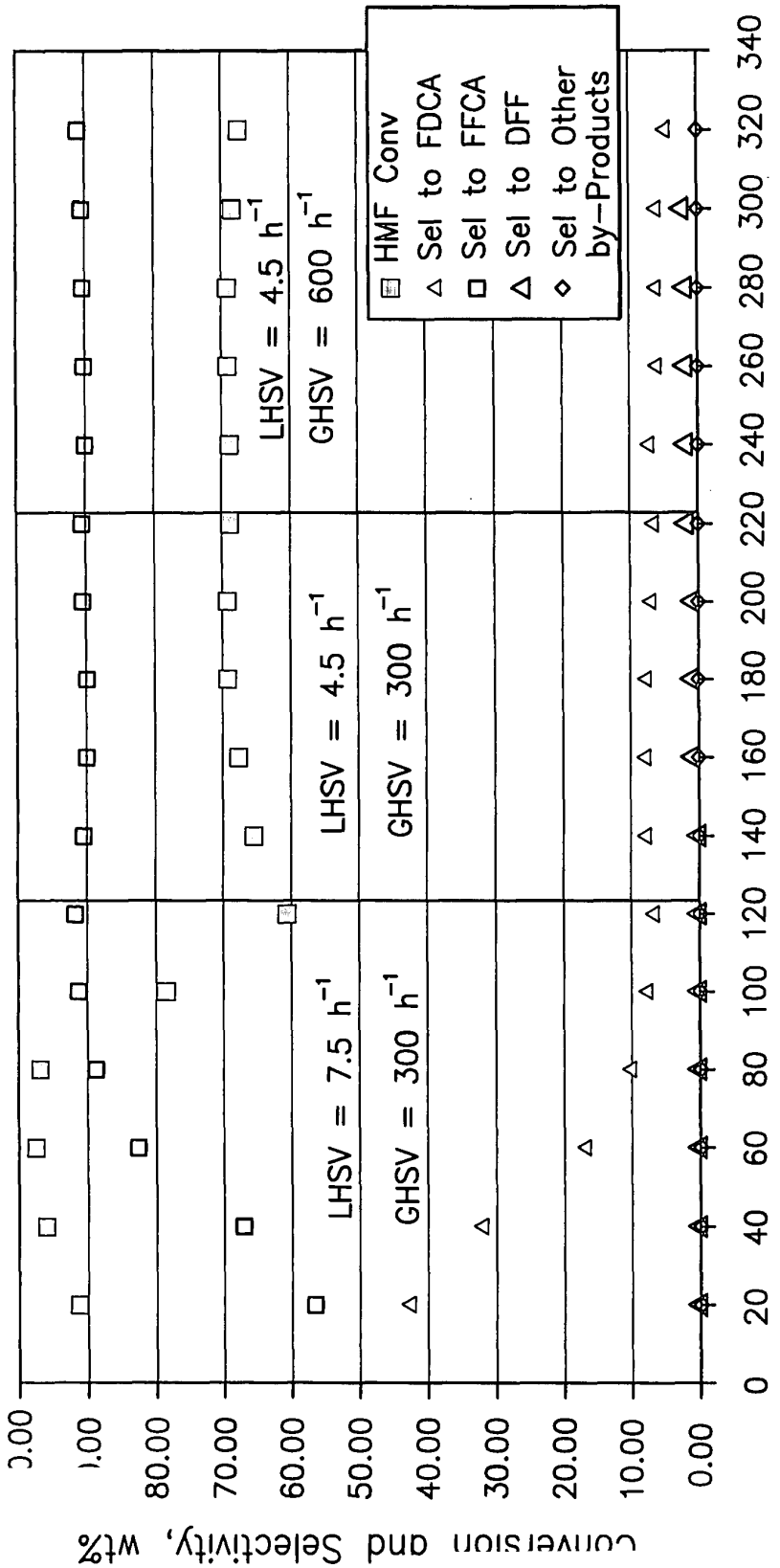

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
LHSV = 7.5 h-1
GHSV = 300 h-1
LHSV = 4.5 h-1
GHSV = 300 h-1
LHSV = 4.5 h-1
GHSV = 600 h-1
Conversion and Selectivity, wt%
Time on Stream, min
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340

Fig 11

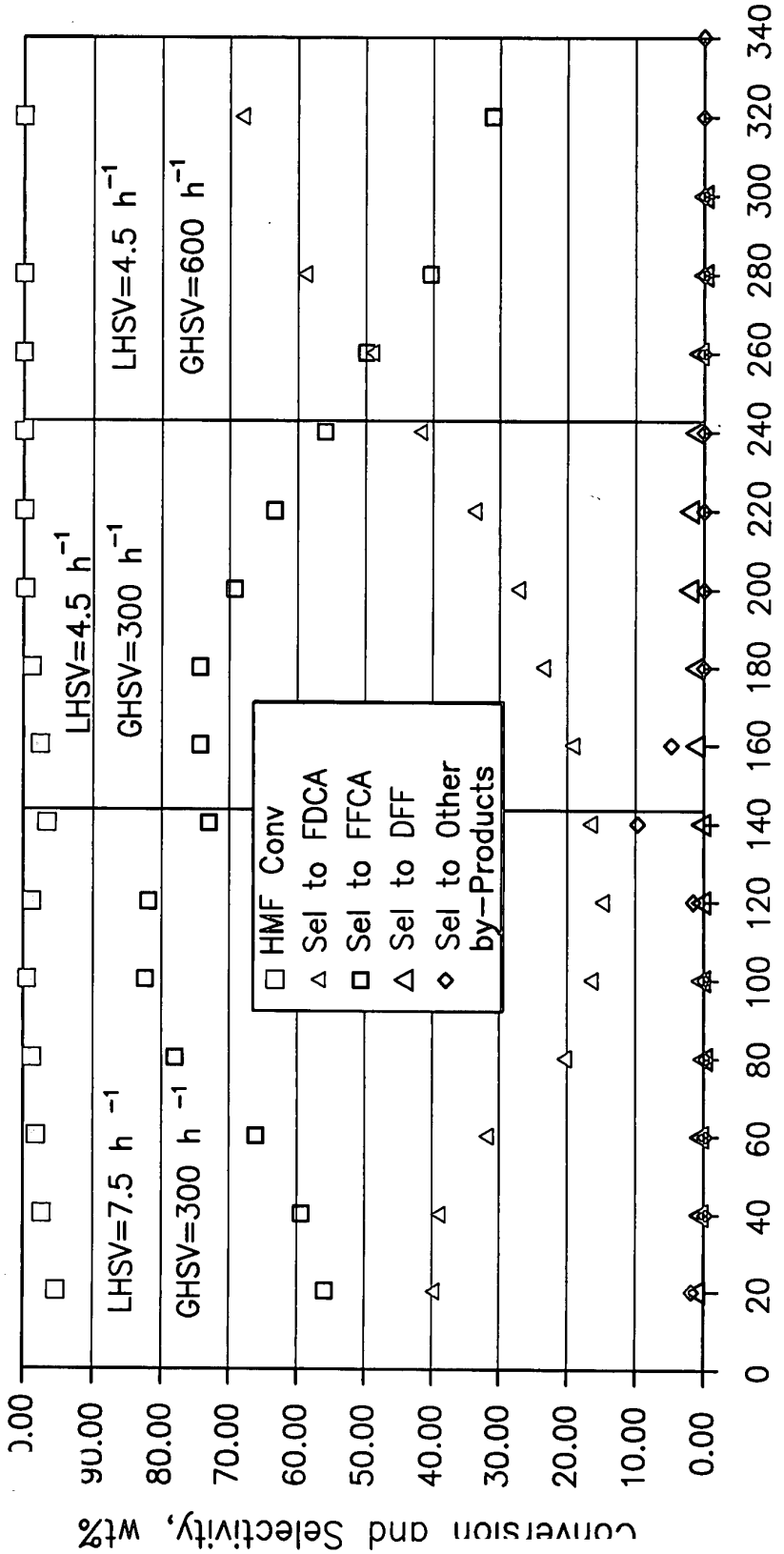

Conversion and Selectivity, wt%
Time on Stream, min
LHSV=7.5 h -1
GHSV=300 h -1
LHSV=4.5 h -1
GHSV=300 h -1
LHSV=4.5 h -1
GHSV=600 h -1
HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
90.00
100.00
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340

Fig 5

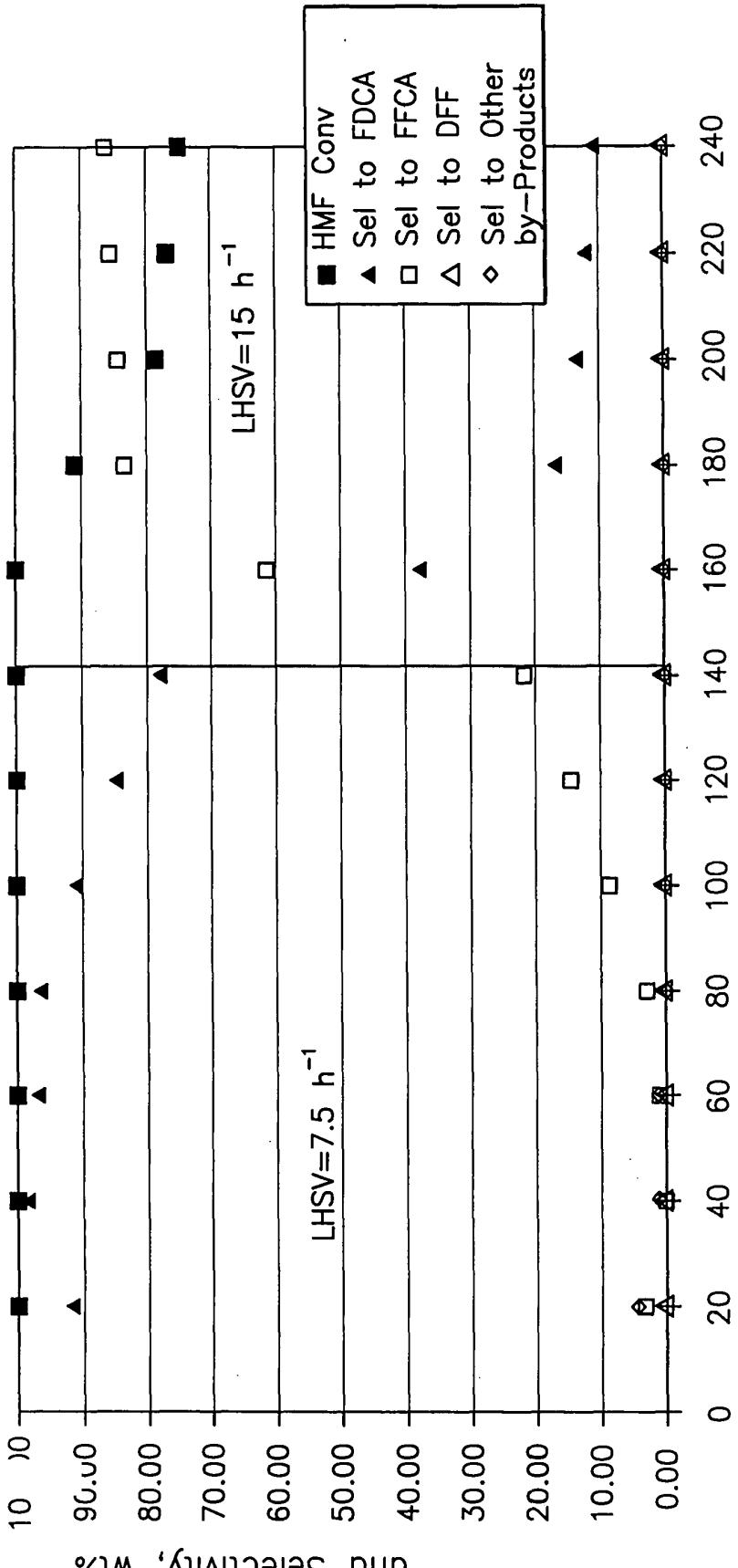

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
LHSV=15 h-1
LHSV=7.5 h-1
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
90.00
100
0
20
40
60
80
100
120
140
160
180
200
220
240
Time on Stream, min
and Selectivity, wt%

FIG 5

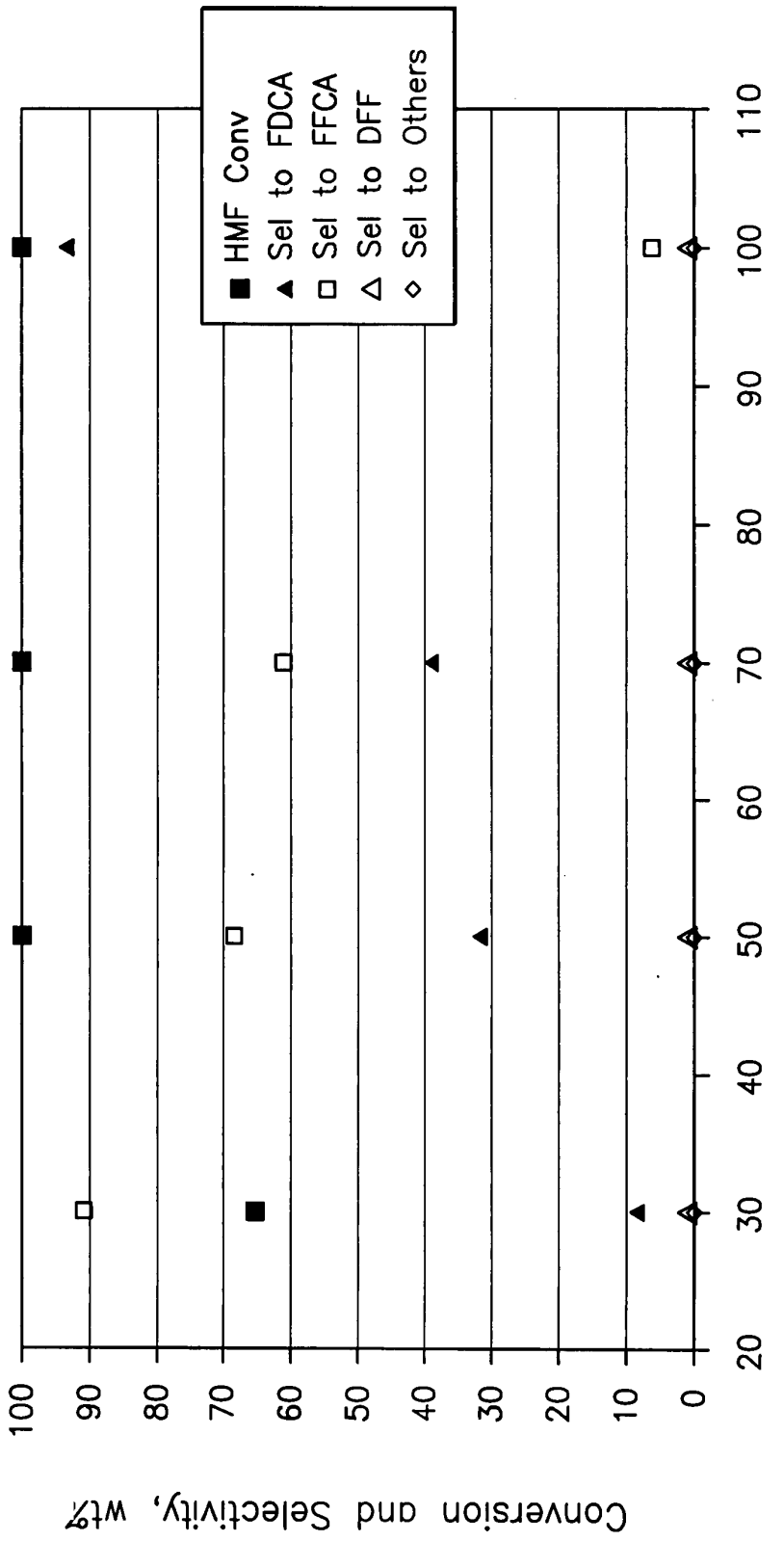

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Others
Conversion and Selectivity, wt%
Temperature, C°
100
90
80
70
60
50
40
30
20
10
0
20
30
40
50
60
70
80
90
100
110

Fig. 11

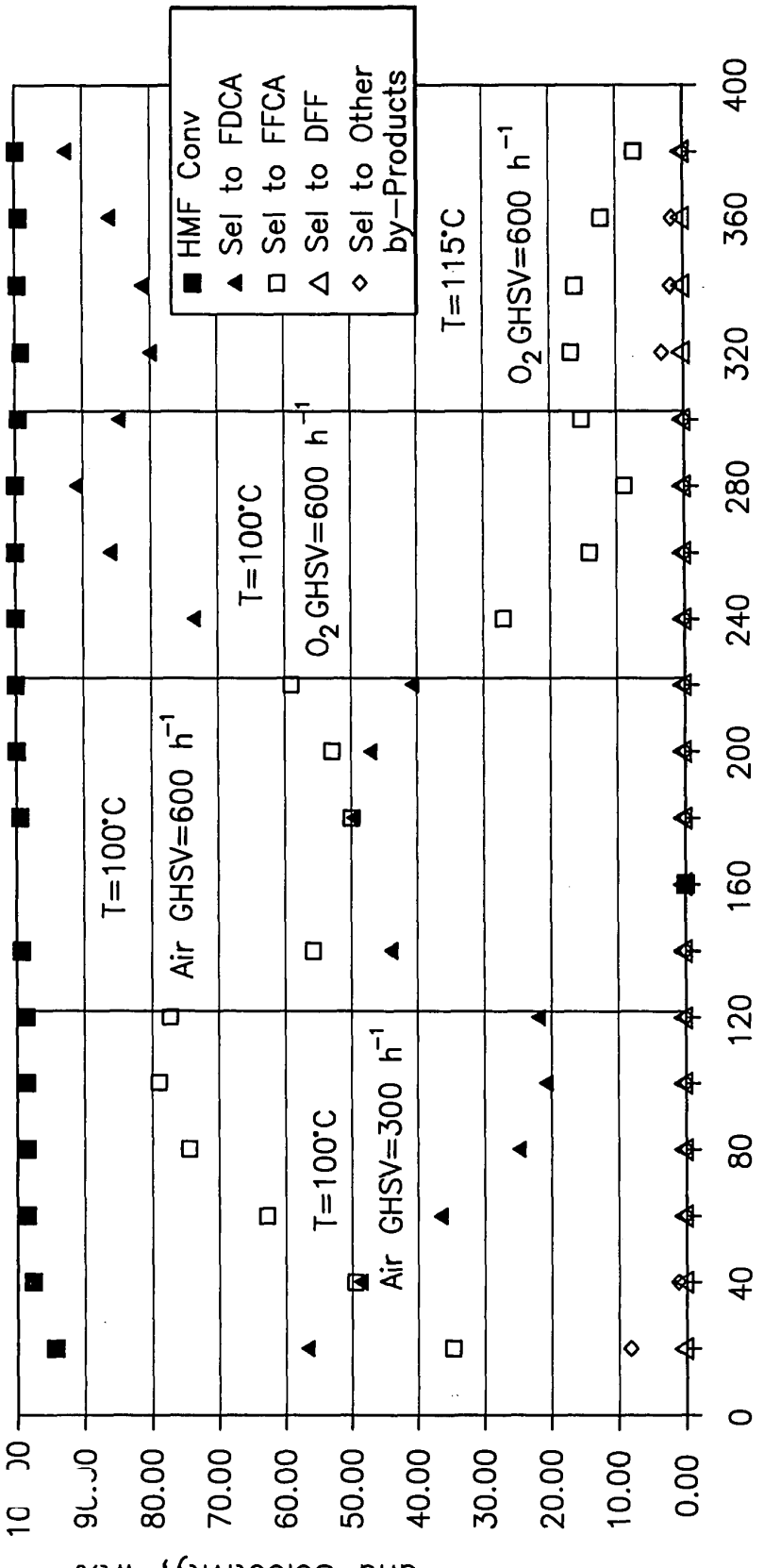
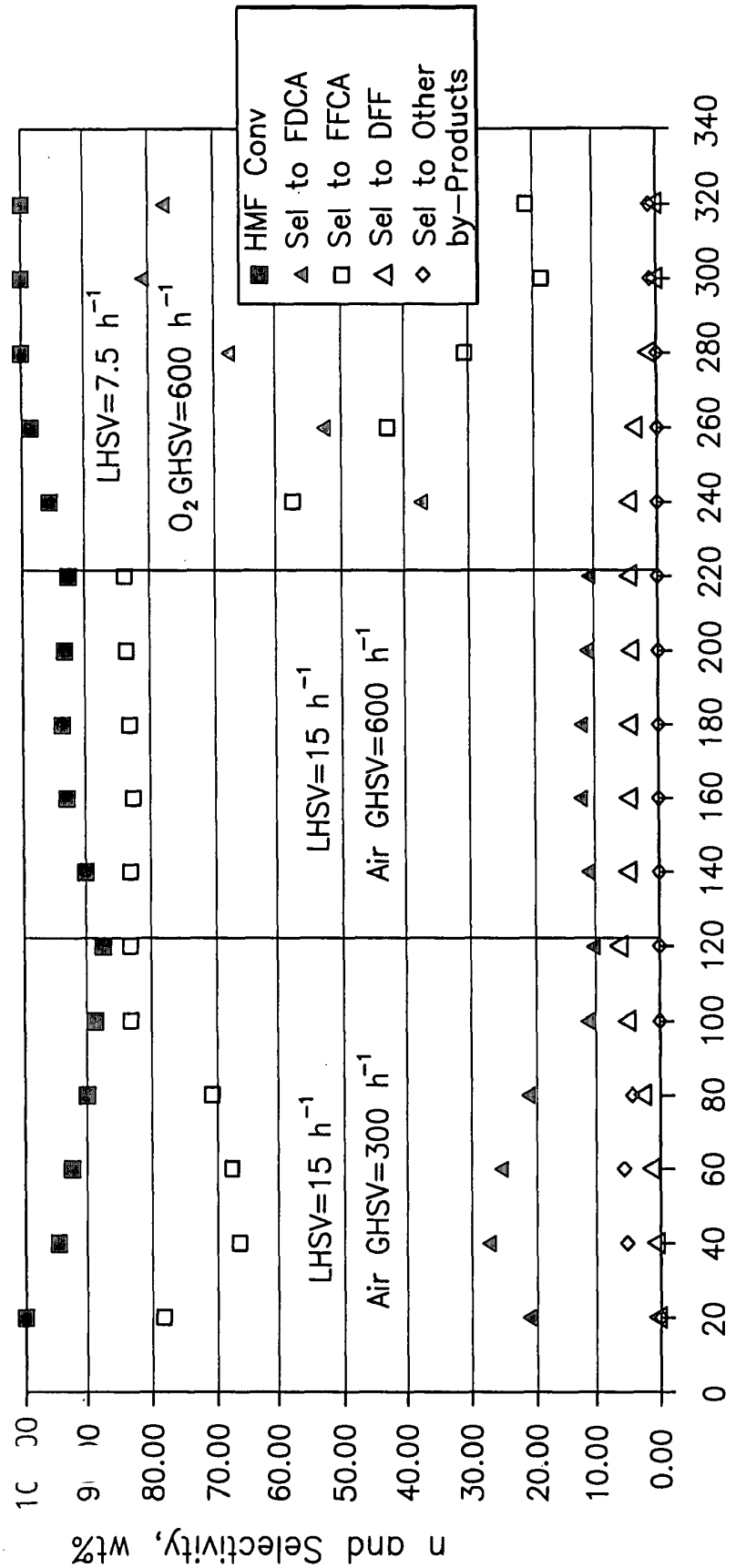

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
T=100°C
Air GHSV=600 h-1
T=100°C
O2 GHSV=600 h-1
T=100°C
Air GHSV=300 h-1
T=115°C
O2 GHSV=600 h-1
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
0
40
80
120
160
200
240
280
320
360
400
Time on Stream, min
and Selectivity, wt%

FIG 8


HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
LHSV=7.5 h-1
O2 GHSV=600 h-1
LHSV=15 h-1
Air GHSV=600 h-1
LHSV=15 h-1
Air GHSV=300 h-1
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340
Time on Stream, min
n and Selectivity, wt%

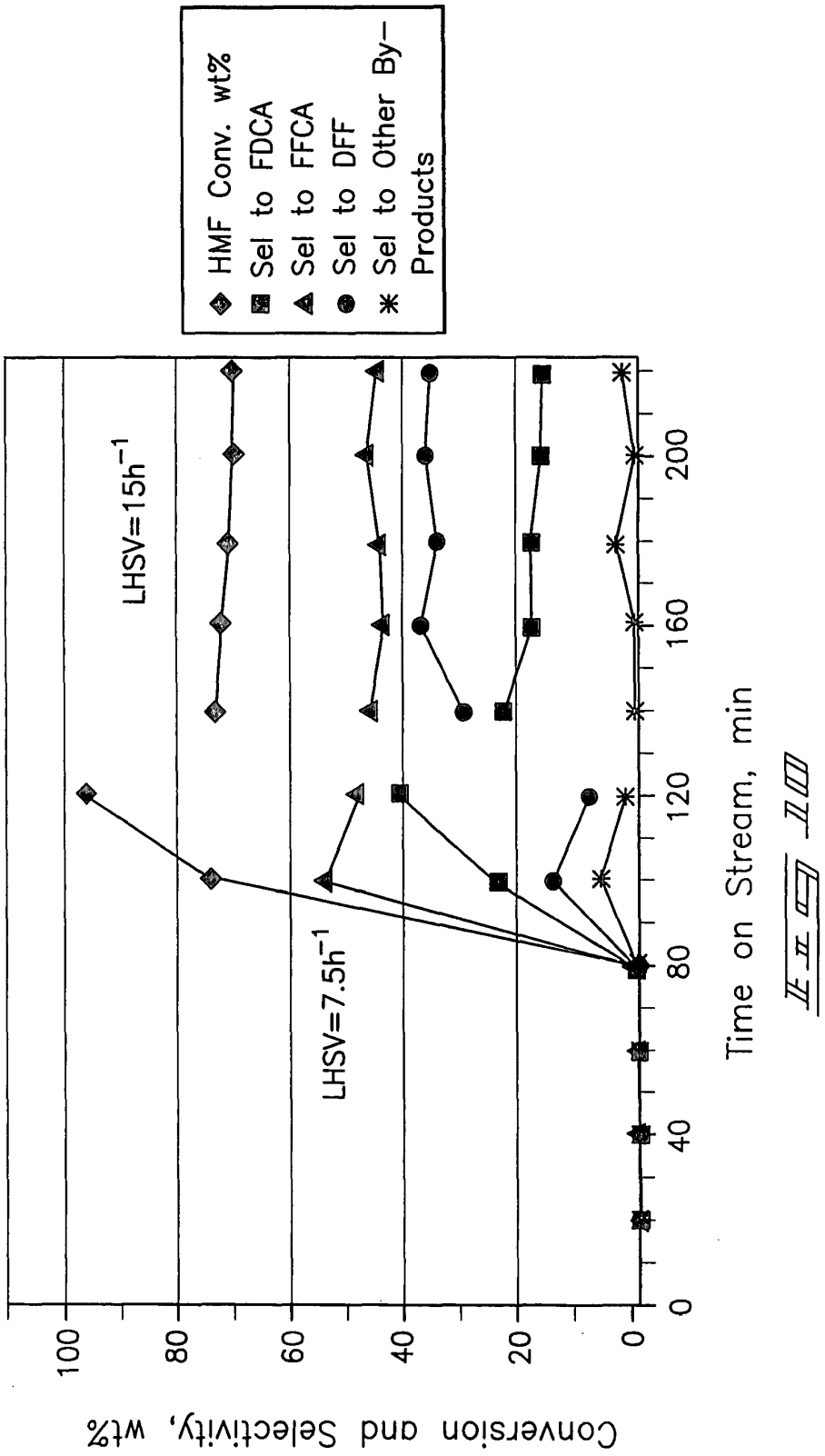

HMF Conv. wt%
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other By-Products
LHSV=15h^{-1}
LHSV=7.5h^{-1}
Conversion and Selectivity, wt%
Time on Stream, min
0
20
40
60
80
100
0
40
80
120
160
200

FIG 10

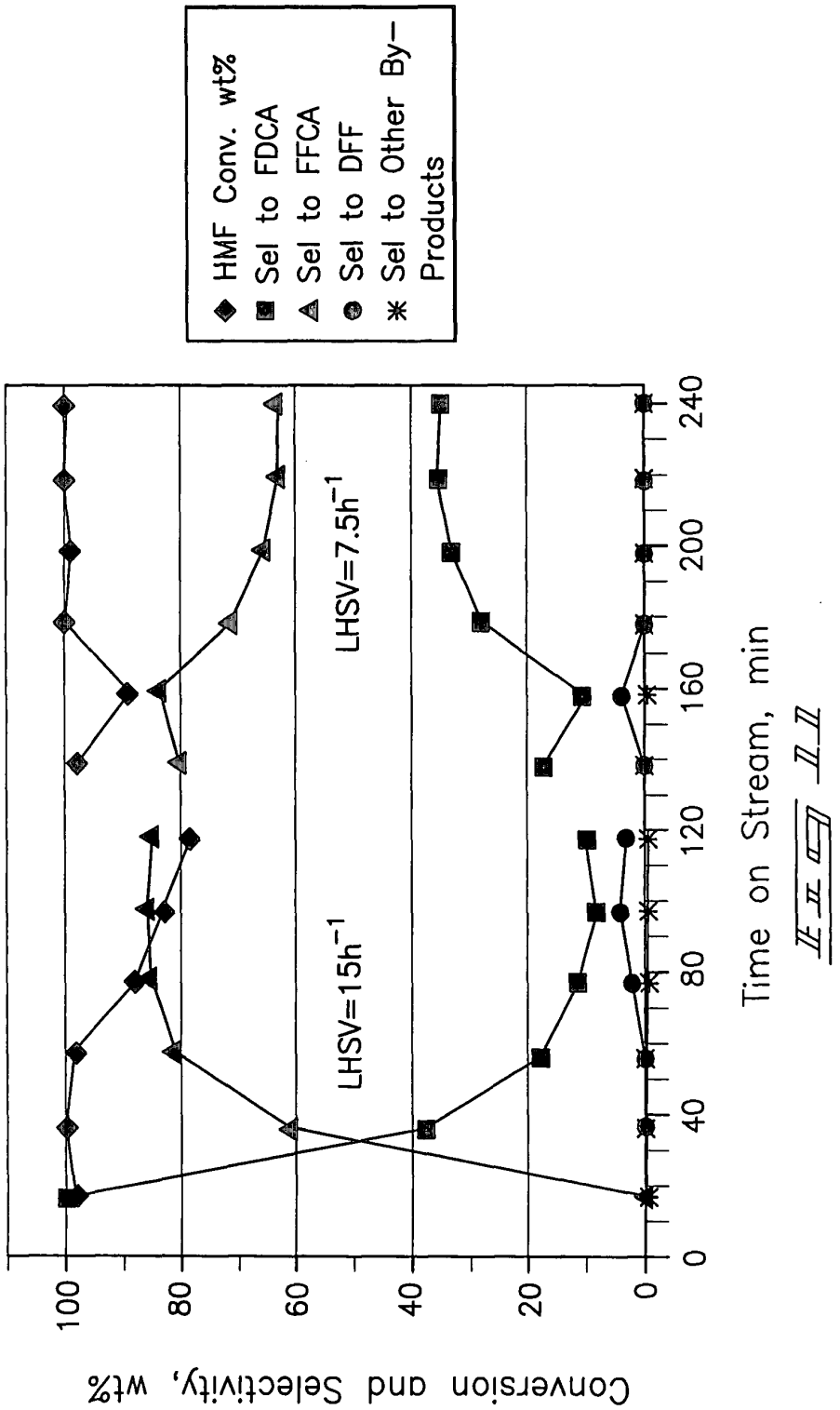

HMF Conv. wt%
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other By-Products
LHSV=7.5h-1
LHSV=15h-1
Conversion and Selectivity, wt%
Time on Stream, min
0
20
40
60
80
100
0
40
80
120
160
200
240

FIG 11

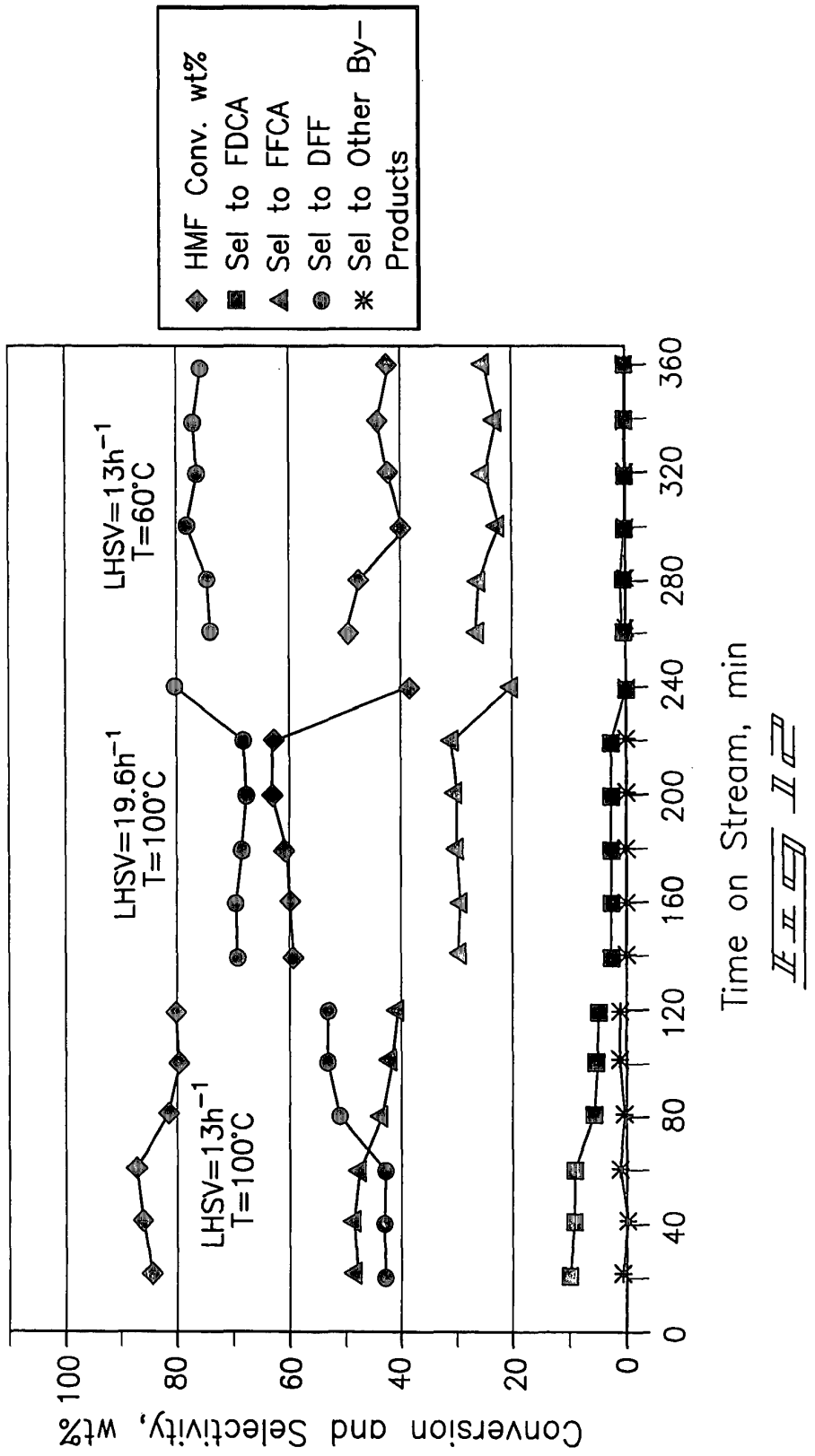

HMF Conv. wt%
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other By-Products
LHSV=13h-1 T=100°C
LHSV=19.6h-1 T=100°C
LHSV=13h-1 T=60°C
Conversion and Selectivity, wt%
Time on Stream, min
0
20
40
60
80
100
0
40
80
120
160
200
240
280
320
360

FIG. 11

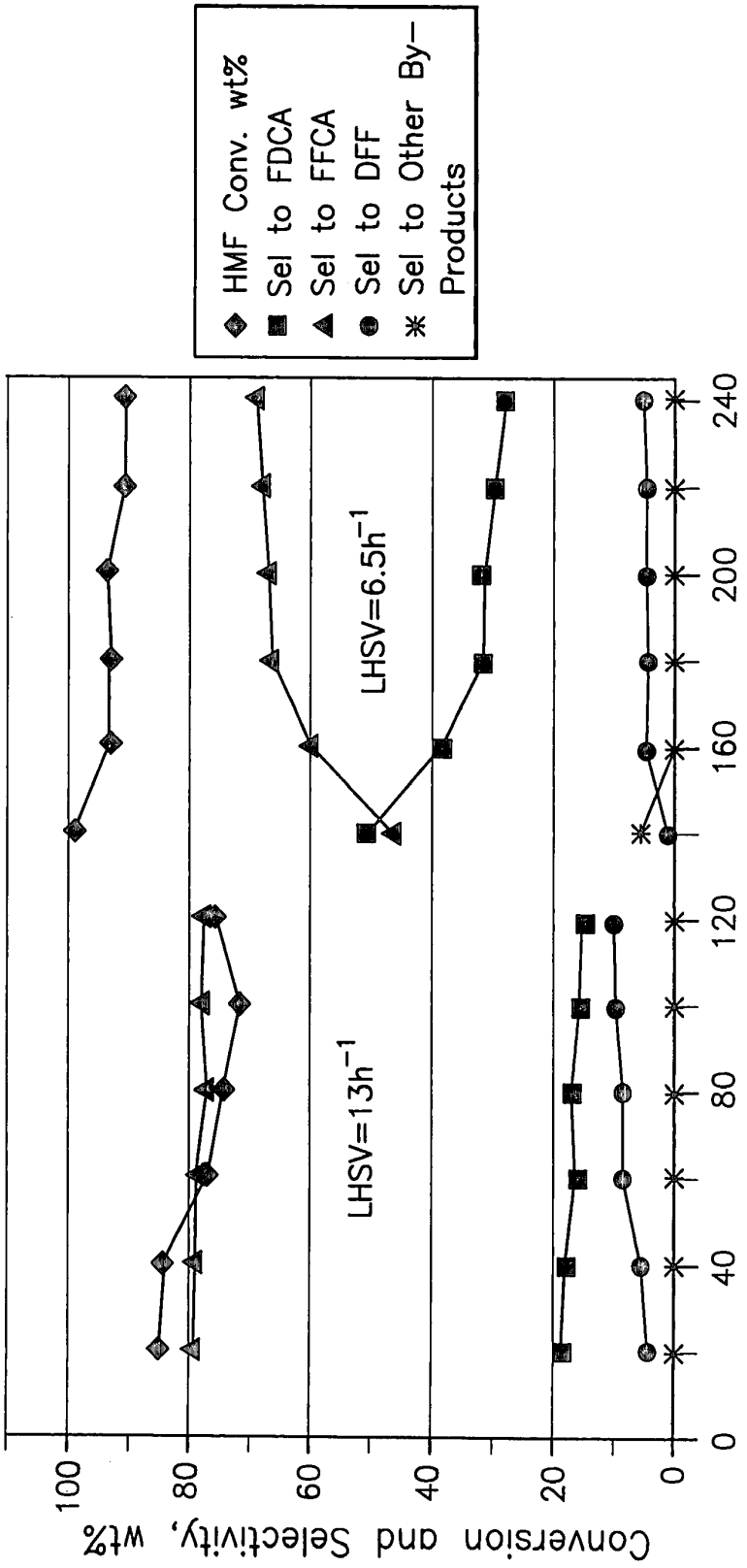

HMF Conv. wt%
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other By-Products
LHSV=13h-1
LHSV=6.5h-1
Conversion and Selectivity, wt%
Time on Stream, min
0
20
40
60
80
100
0
40
80
120
160
200
240

FIG. 11

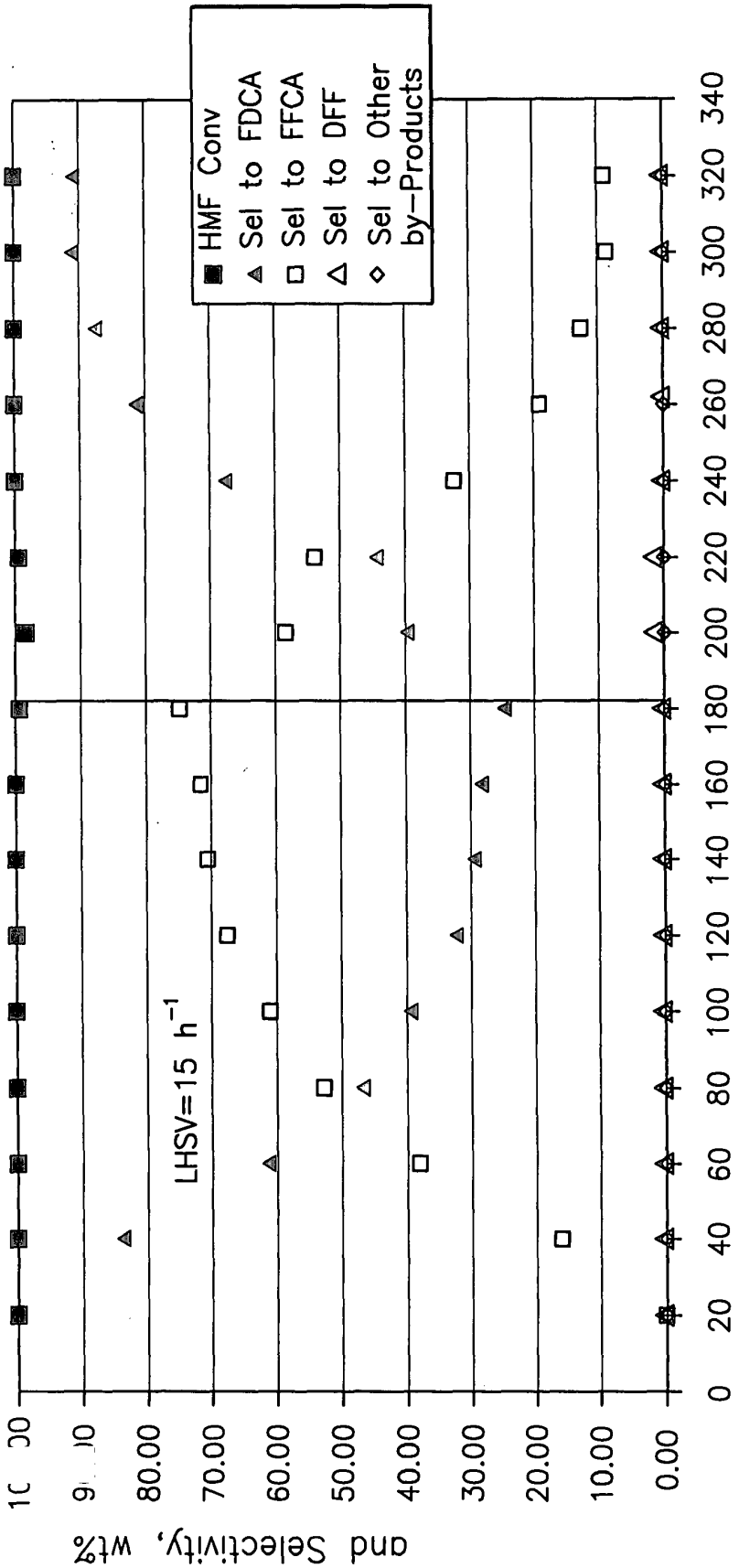

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
LHSV=15 h^{-1}
Time on Stream, min
and Selectivity, wt%
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340

Fig. 11

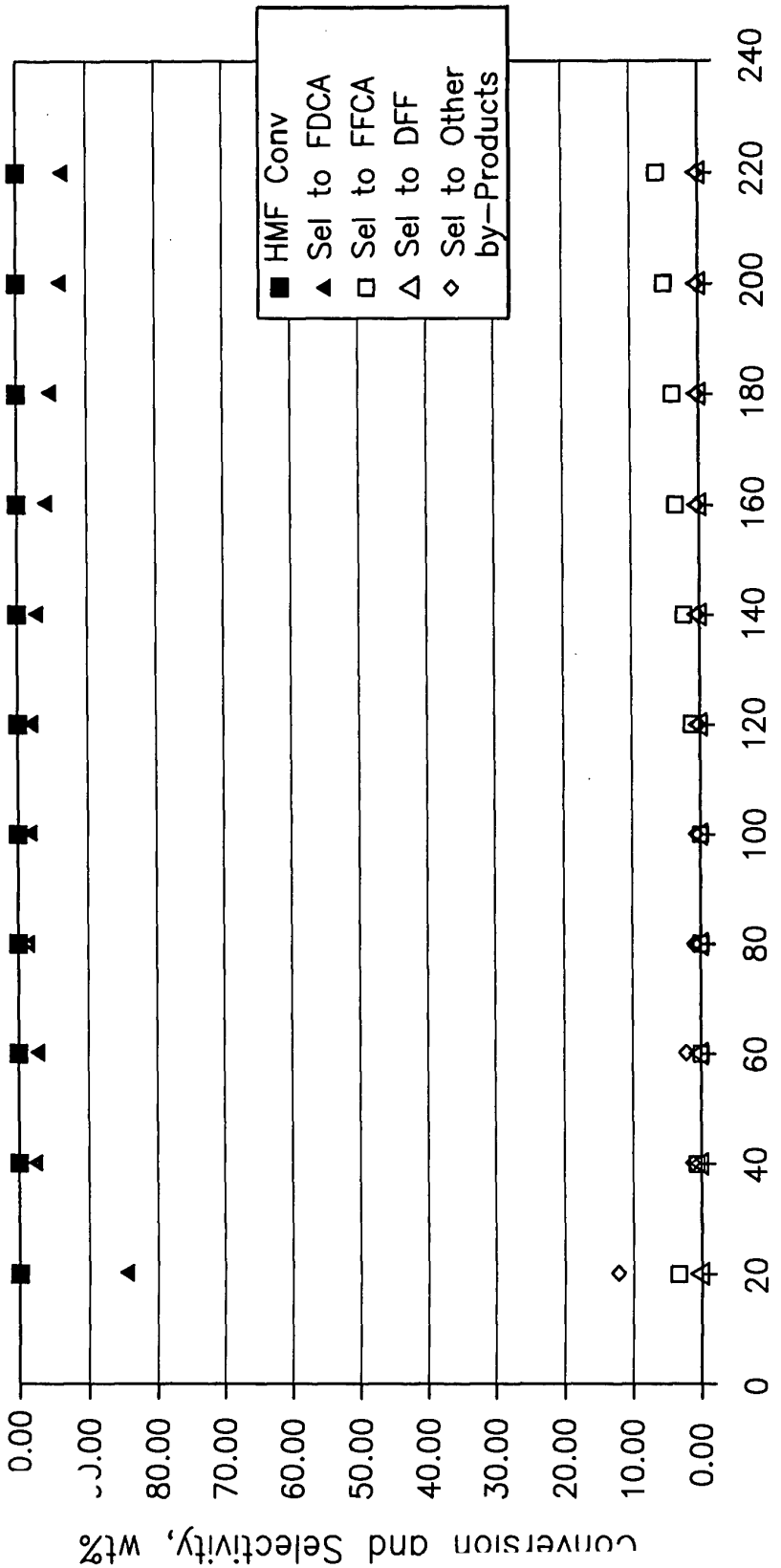

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
Conversion and Selectivity, wt%
Time on Stream, min
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
90.00
0
20
40
60
80
100
120
140
160
180
200
220
240

FIG 15

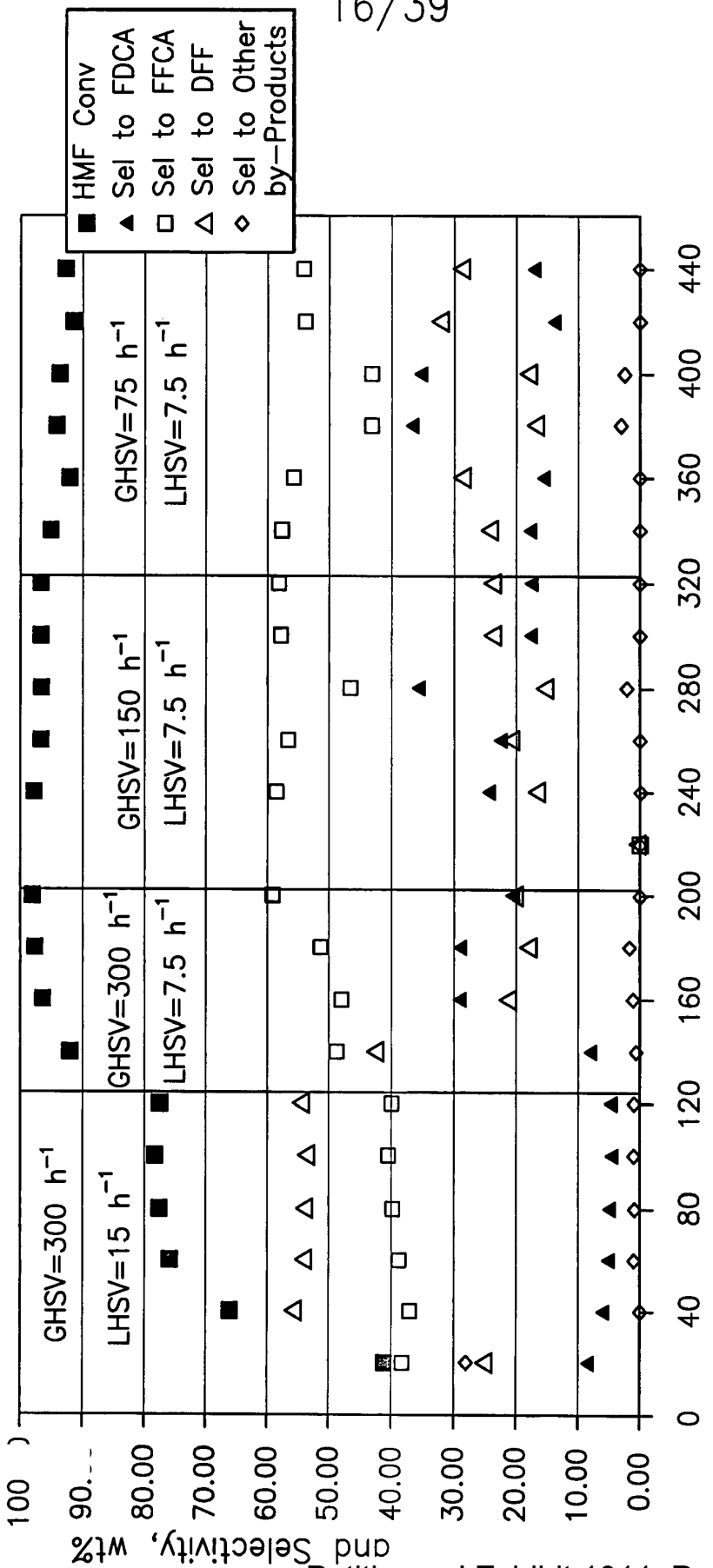

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
GHSV=300 h-1
LHSV=15 h-1
GHSV=300 h-1
LHSV=7.5 h-1
GHSV=150 h-1
LHSV=7.5 h-1
GHSV=75 h-1
LHSV=7.5 h-1
100
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
and Selectivity, wt%
0
40
80
120
160
200
240
280
320
360
400
440
Time on Stream, min

Fig. 11

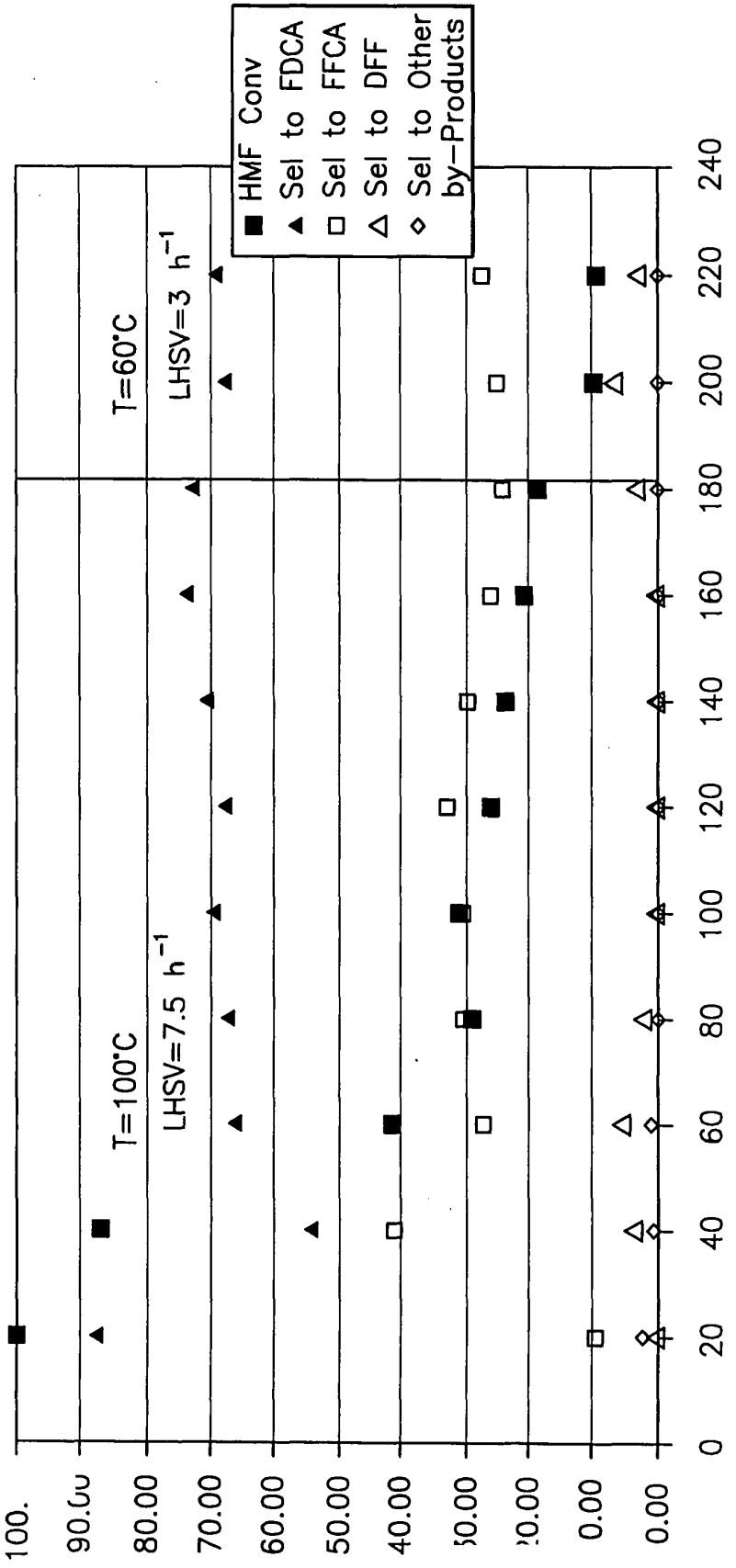

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
T=100°C
LHSV=7.5 h-1
T=60°C
LHSV=3 h-1
Time on Stream, min
and Selectivity, wt%
0
20
40
60
80
100
120
140
160
180
200
220
240
0.00
20.00
40.00
60.00
80.00
100.

FIG. 11

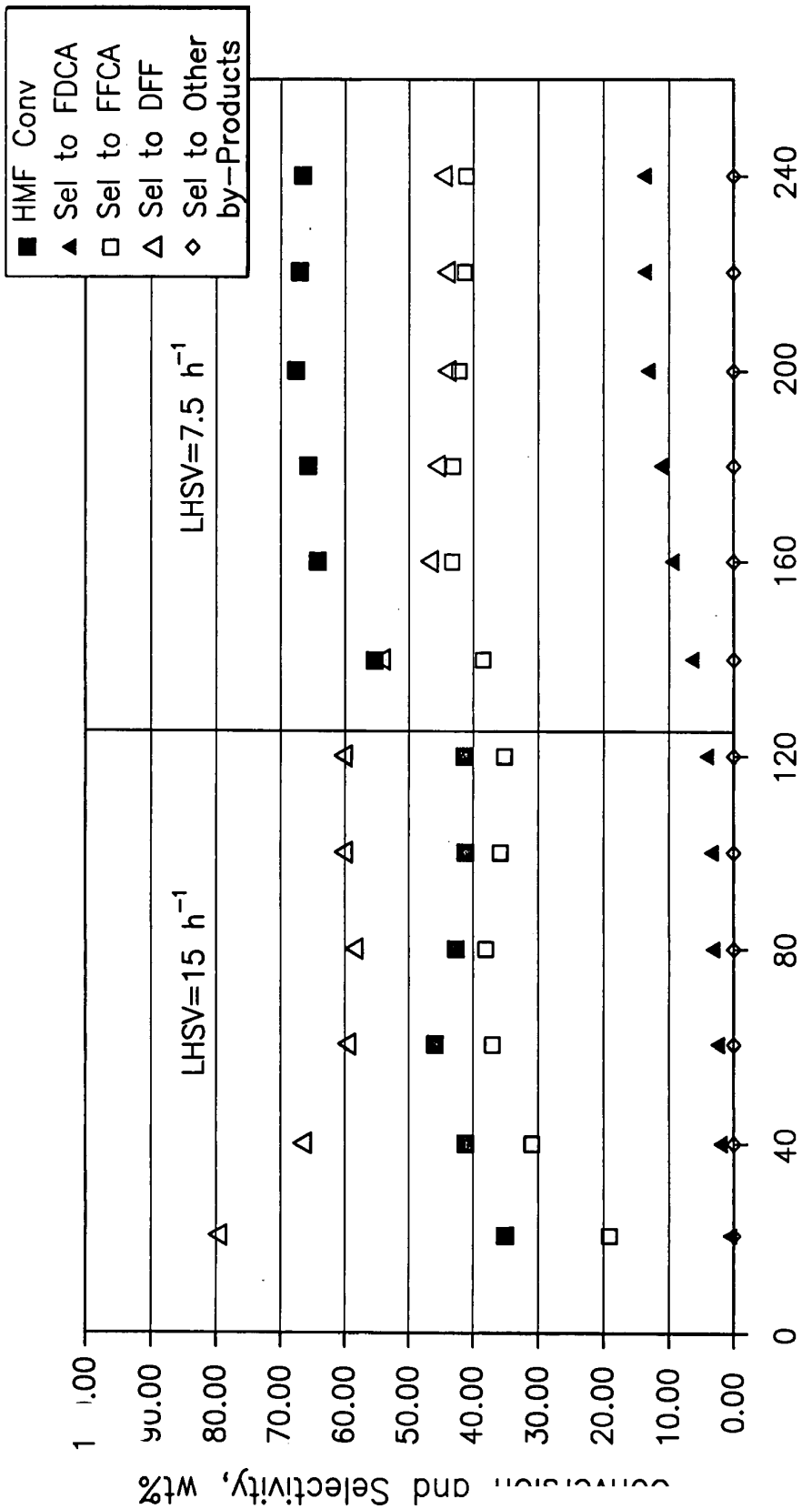

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
LHSV=15 h-1
LHSV=7.5 h-1
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
0
40
80
120
160
200
240
Time on Stream, min

Fig. 11

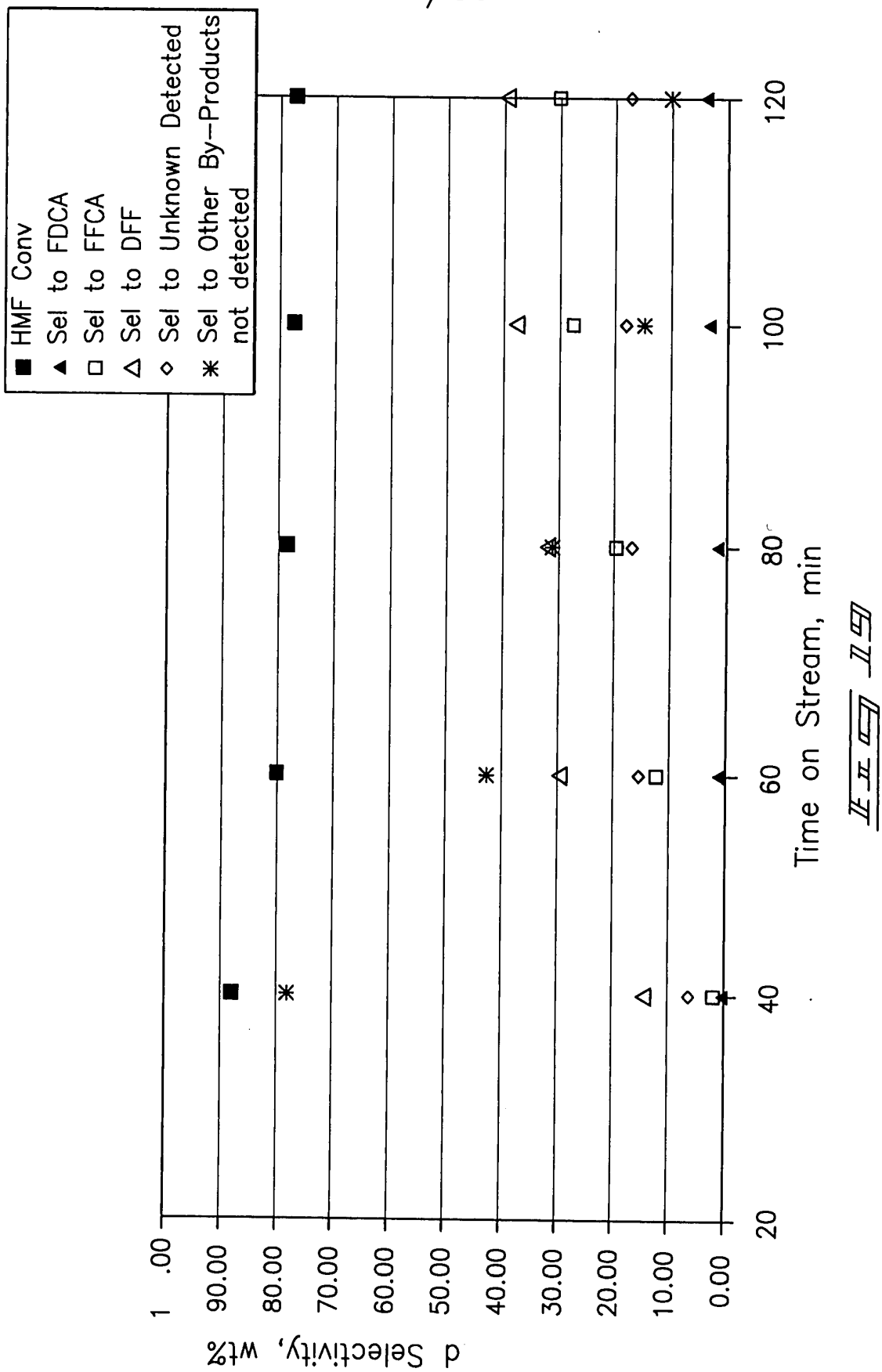

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Unknown Detected
Sel to Other By--Products not detected
d Selectivity, wt%
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
20
40
60
80
100
120
Time on Stream, min

FIG 11

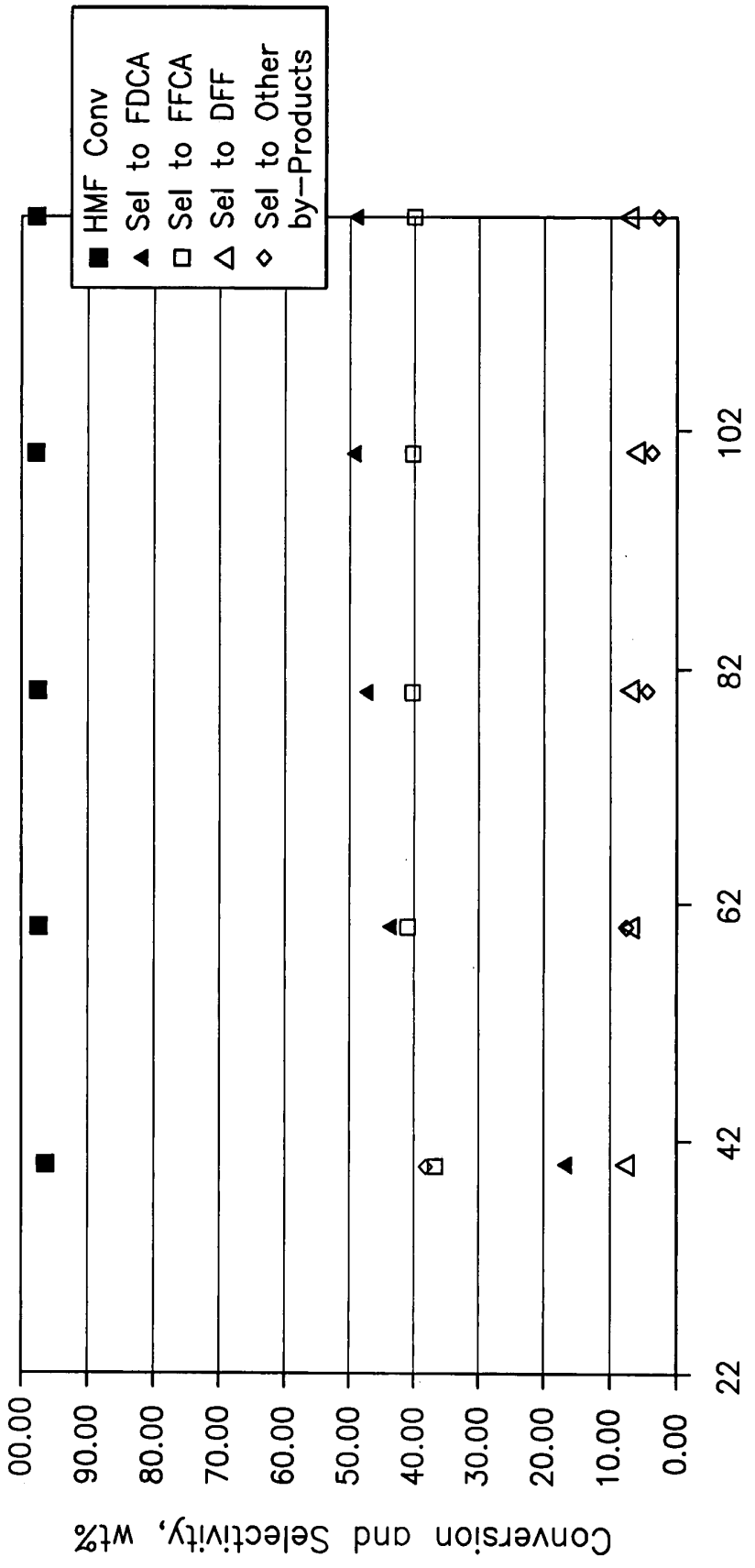

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
Conversion and Selectivity, wt%
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
22
42
62
82
102
Time on Stream, min

FIG 2D

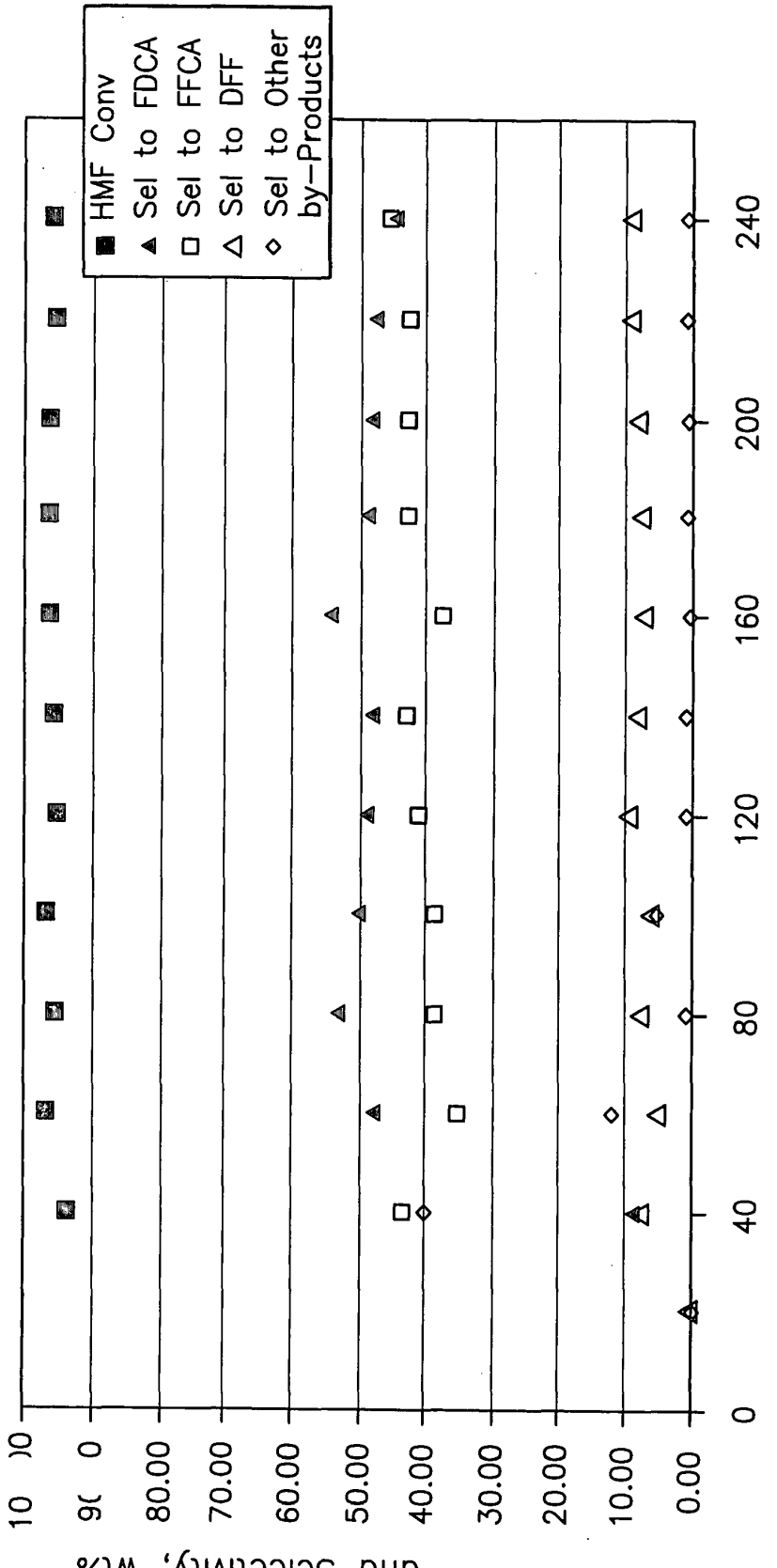

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
90.00
100.00
0
40
80
120
160
200
240
Time on Stream, min
and Selectivity, wt%

FIG. 11

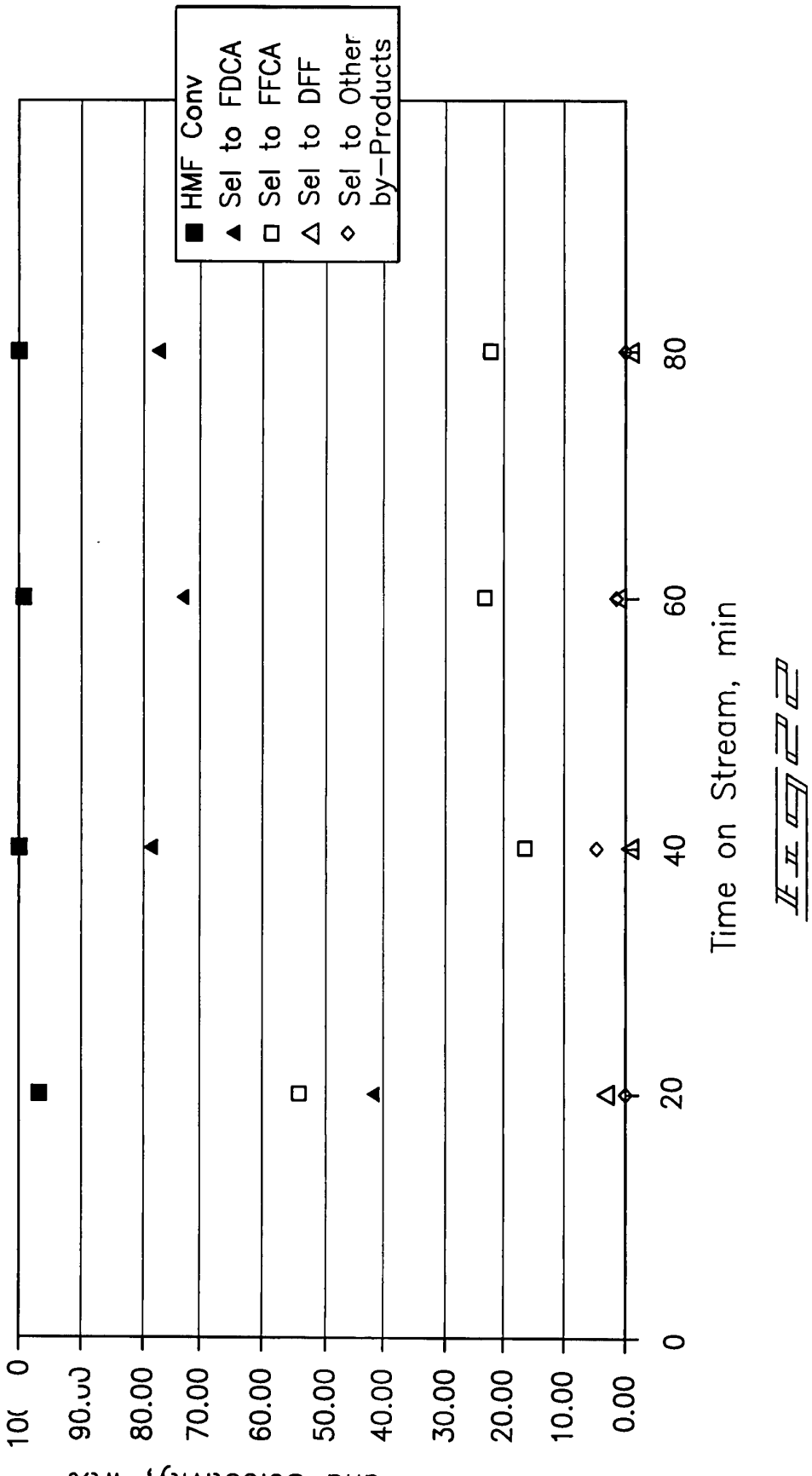

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
90.00
100
0
20
40
60
80
Time on Stream, min
and Selectivity, wt%

FIG 22

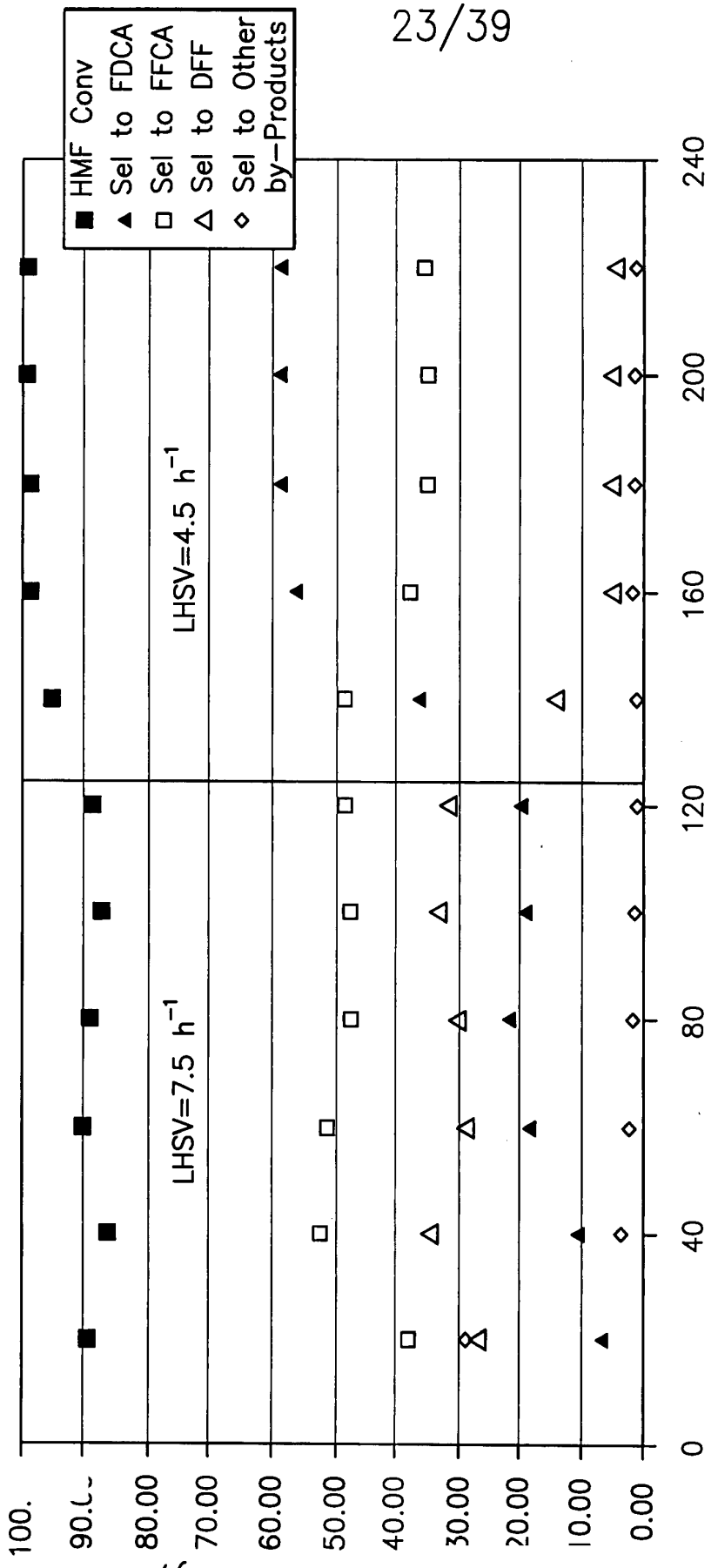

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
LHSV=7.5 h-1
LHSV=4.5 h-1
100.
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
0
40
80
120
160
200
240
Time on Stream, min
and Selectivity, wt%

FIG 3

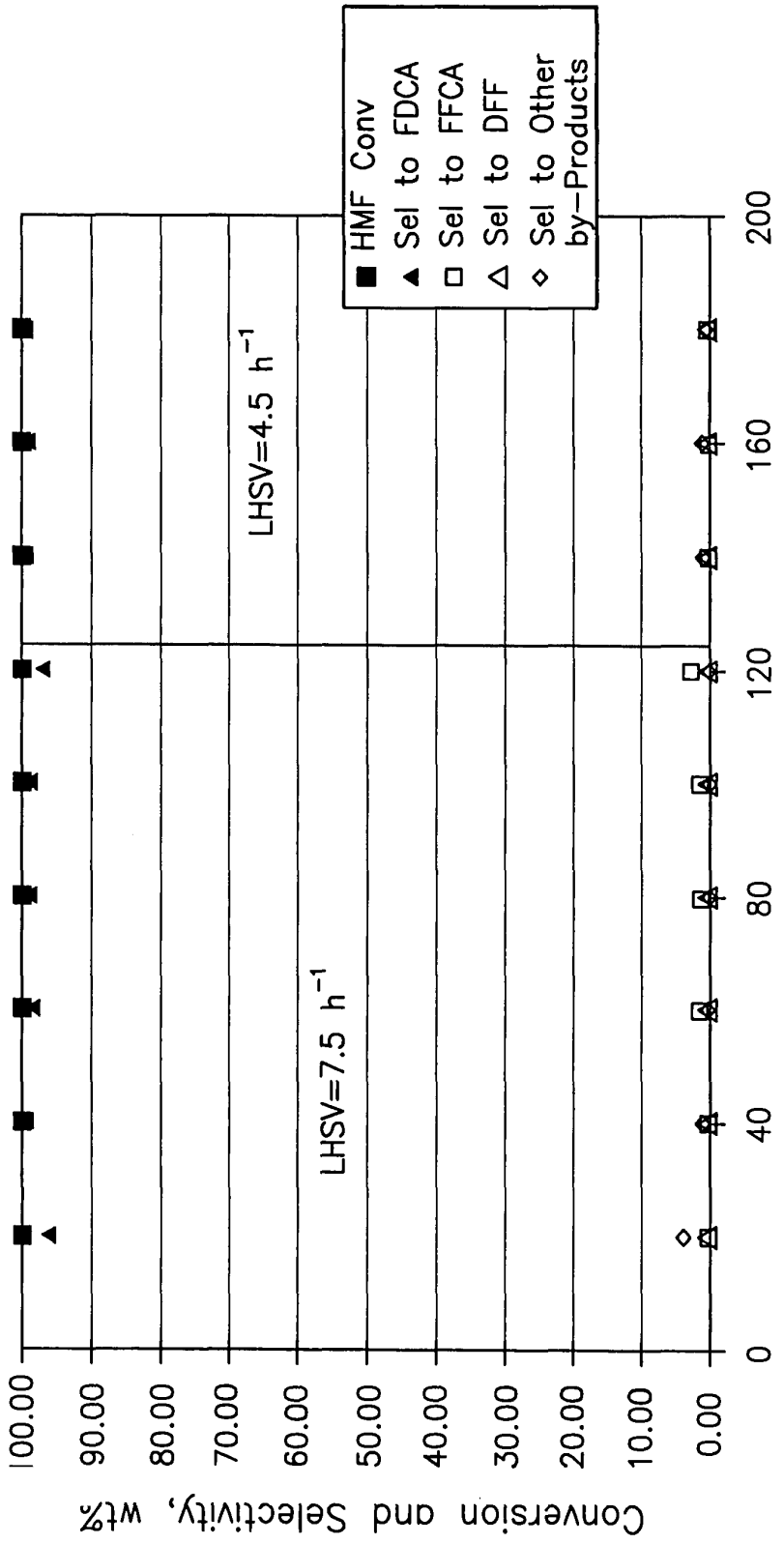

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
LHSV=4.5 h-1
LHSV=7.5 h-1
Conversion and Selectivity, wt%
Time on Stream, min
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
90.00
100.00
0
40
80
120
160
200

Fig 24

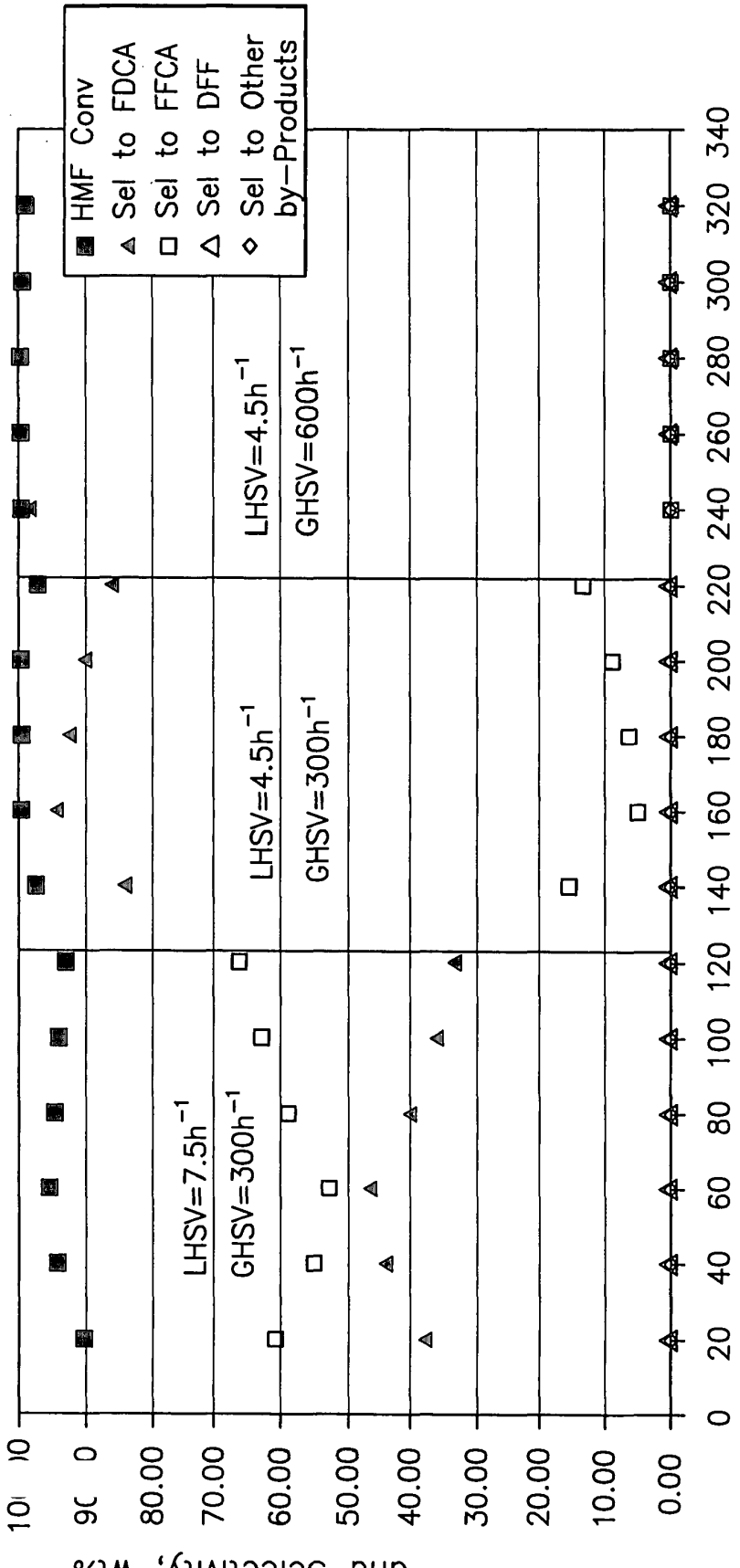

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
LHSV=7.5h-1
GHSV=300h-1
LHSV=4.5h-1
GHSV=300h-1
LHSV=4.5h-1
GHSV=600h-1
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340
Time on Stream, min
and Selectivity, wt%

FIG 23

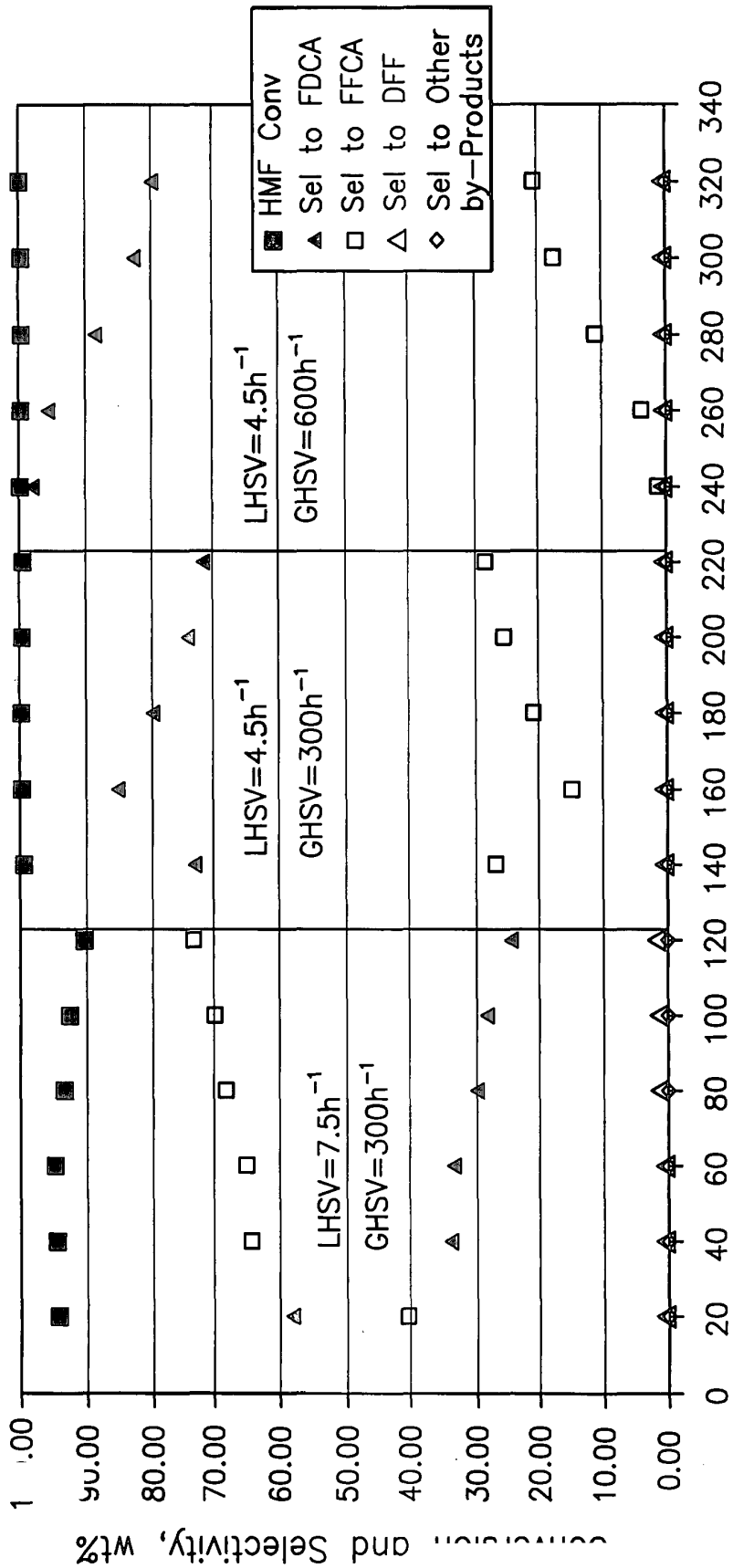

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
LHSV=7.5h^{-1}
GHSV=300h^{-1}
LHSV=4.5h^{-1}
GHSV=300h^{-1}
LHSV=4.5h^{-1}
GHSV=600h^{-1}
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340
Time on Stream, min
Selectivity, wt%

FIG 2

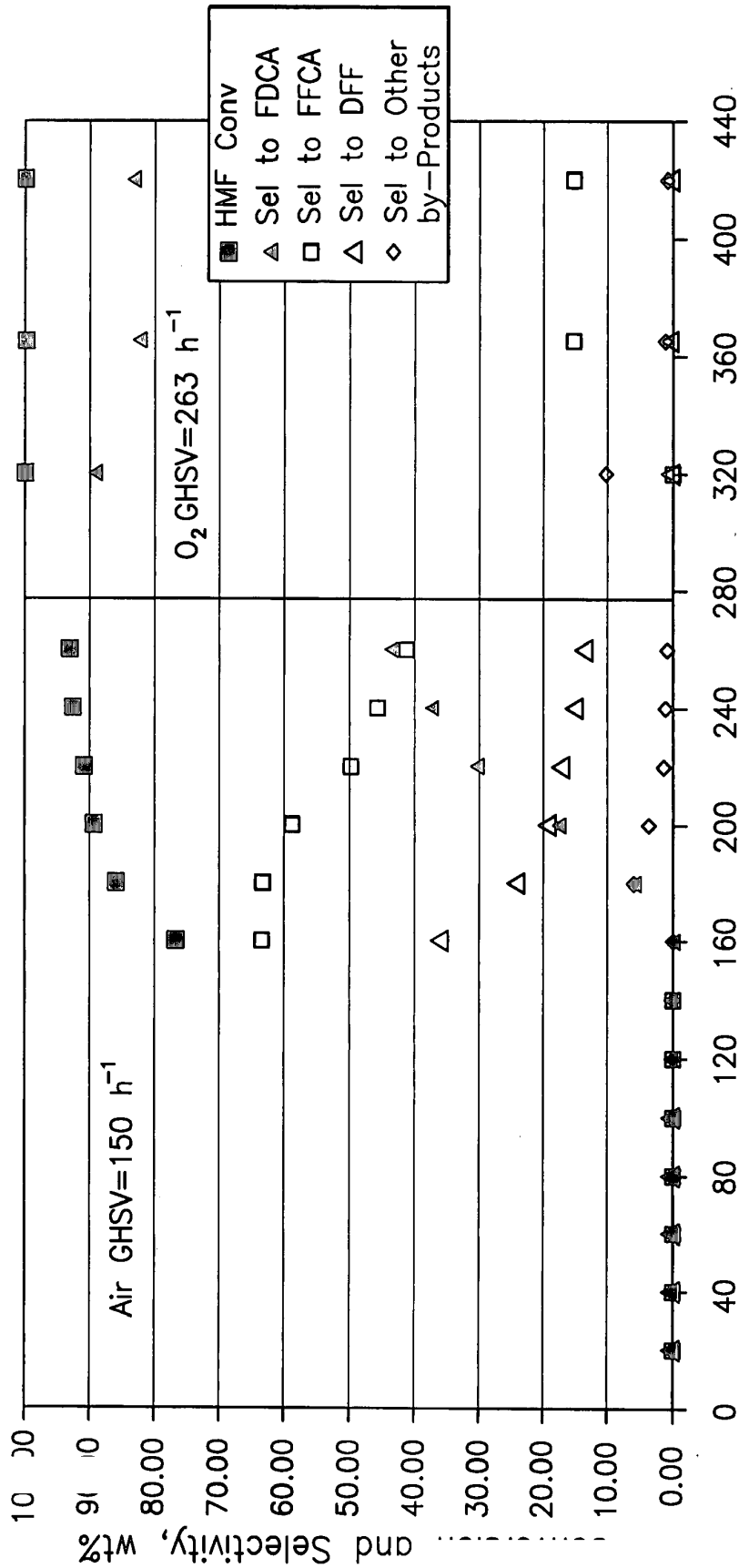

HMF Conv
Sel to FDCA
Sel to FFCA
Sel to DFF
Sel to Other by-Products
Air GHSV=150 h-1
O2 GHSV=263 h-1
Time on Stream, min
and Selectivity, wt%
0.00
10.00
20.00
30.00
40.00
50.00
60.00
70.00
80.00
0
40
80
120
160
200
240
280
320
360
400
440

FIG 27

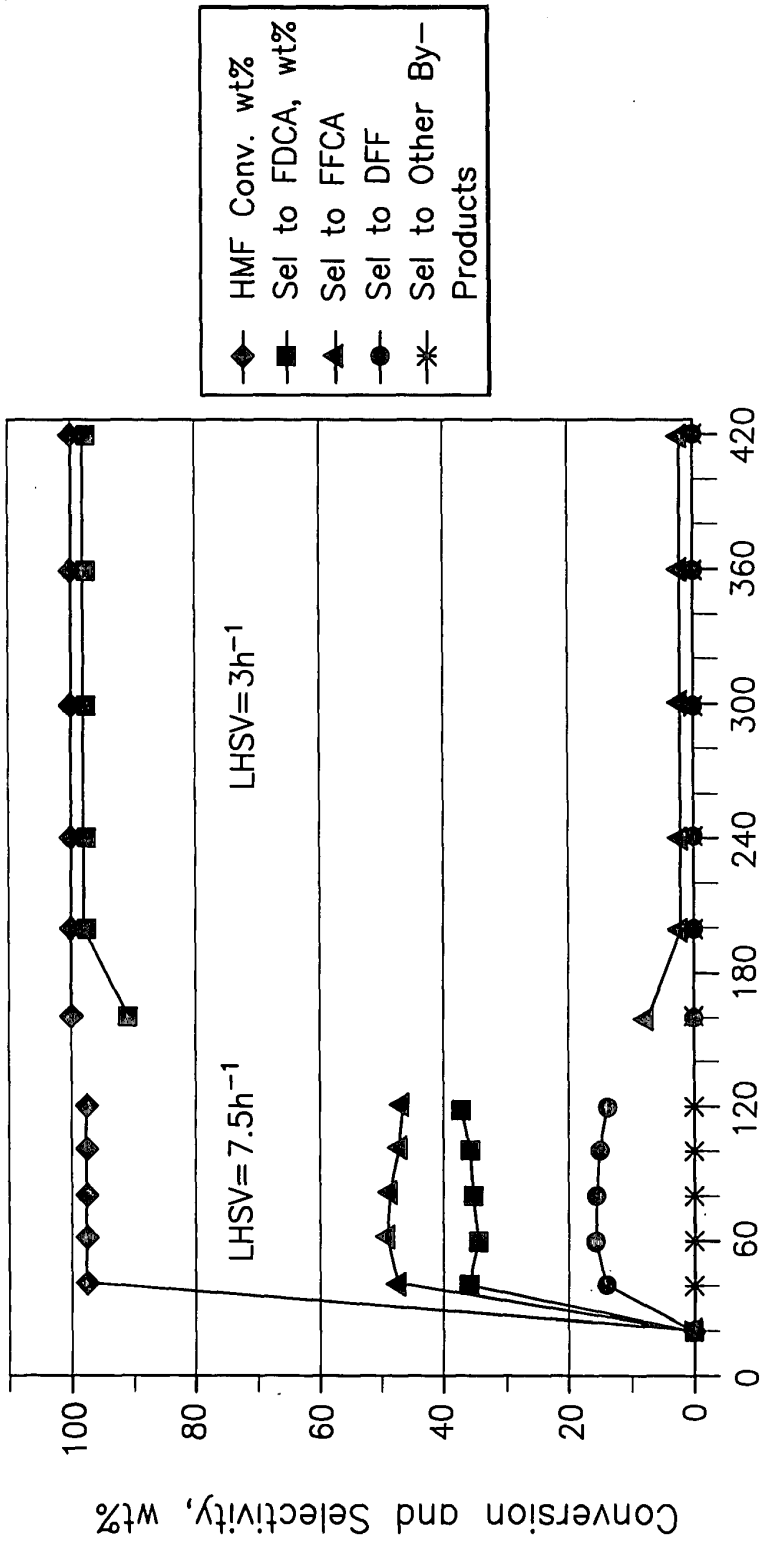

HMF Conv. wt%
Sel to FDCA, wt%
Sel to FFCA
Sel to DFF
Sel to Other By-Products
LHSV=3h-1
LHSV=7.5h-1
Conversion and Selectivity, wt%
Time on Stream, min
0
20
40
60
80
100
0
60
120
180
240
300
360
420

FIG 28

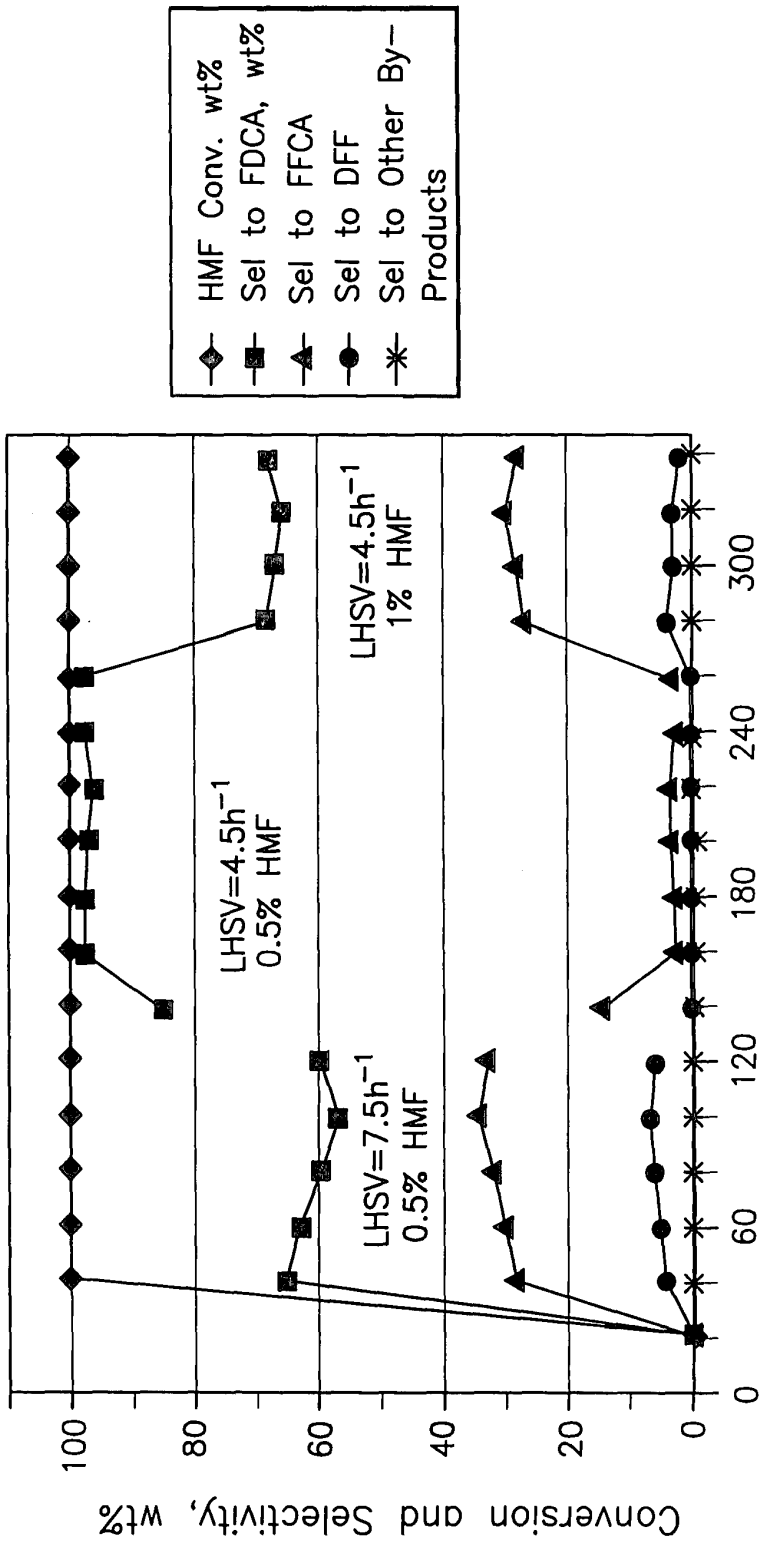

HMF Conv. wt%
Sel to FDCA, wt%
Sel to FFCA
Sel to DFF
Sel to Other By-Products
LHSV=4.5h^{-1} 0.5% HMF
LHSV=7.5h^{-1} 0.5% HMF
LHSV=4.5h^{-1} 1% HMF
Conversion and Selectivity, wt%
Time on Stream, min
0
20
40
60
80
100
0
60
120
180
240
300

Fig 29

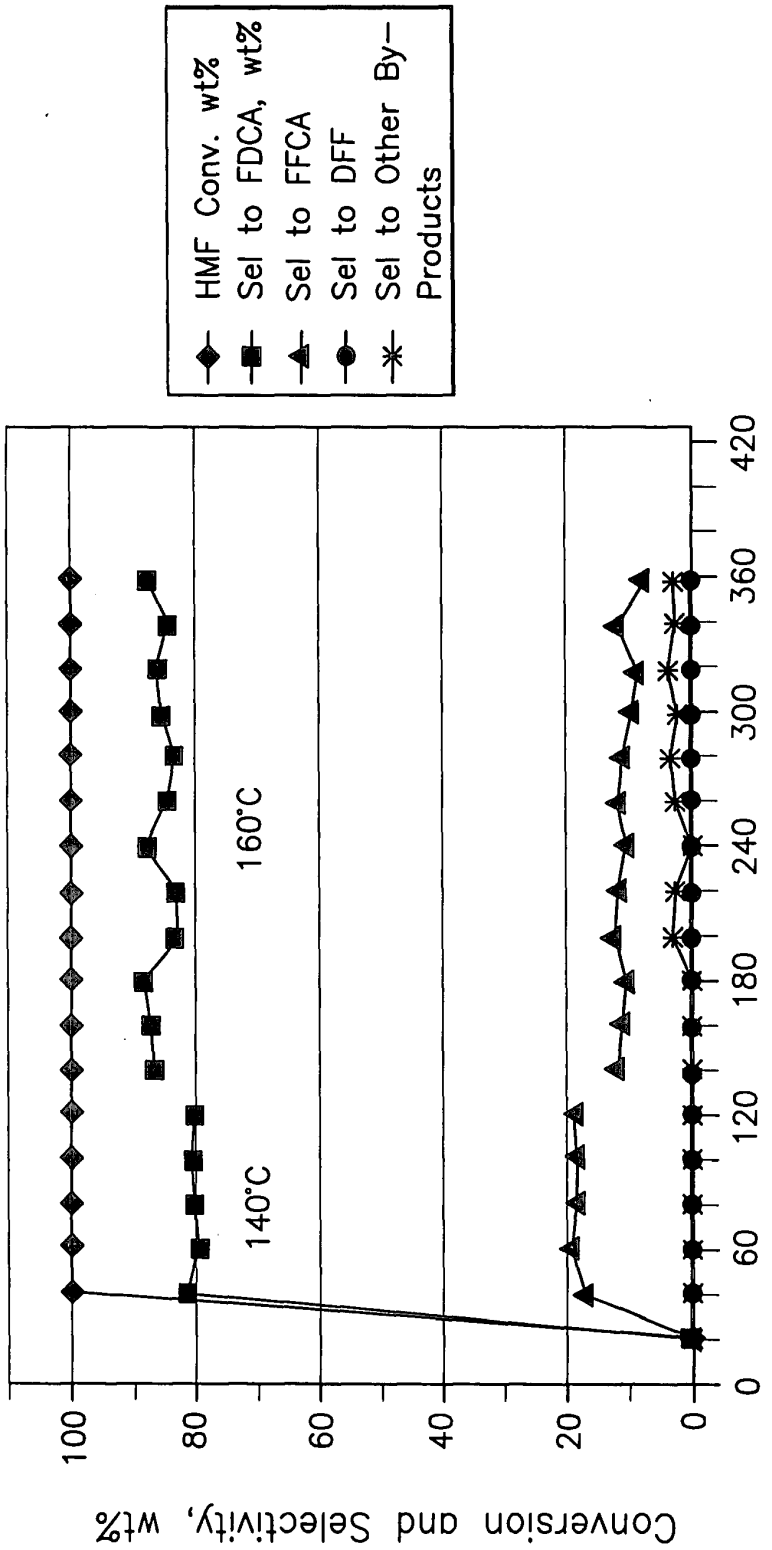

HMF Conv. wt%
Sel to FDCA, wt%
Sel to FFCA
Sel to DFF
Sel to Other By-Products
160°C
140°C
Conversion and Selectivity, wt%
Time on Stream, min
0
20
40
60
80
100
0
60
120
180
240
300
360
420

FIG 3III

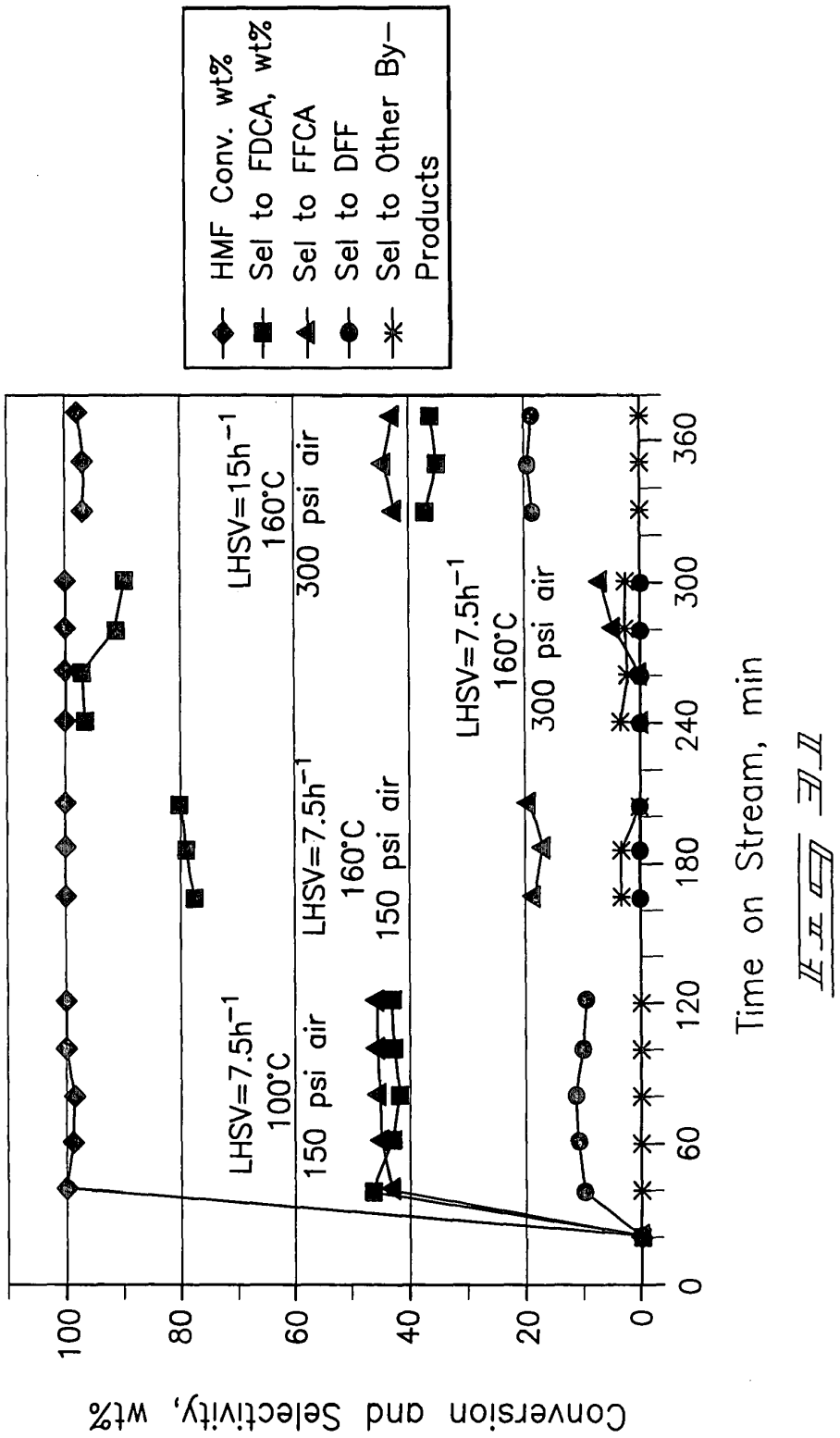

HMF Conv. wt%
Sel to FDCA, wt%
Sel to FFCA
Sel to DFF
Sel to Other By-Products
LHSV=7.5h^{-1}
100°C
150 psi air
LHSV=7.5h^{-1}
160°C
150 psi air
LHSV=15h^{-1}
160°C
300 psi air
LHSV=7.5h^{-1}
160°C
300 psi air
Conversion and Selectivity, wt%
Time on Stream, min
0
20
40
60
80
100
0
60
120
180
240
300
360

FIG 3II

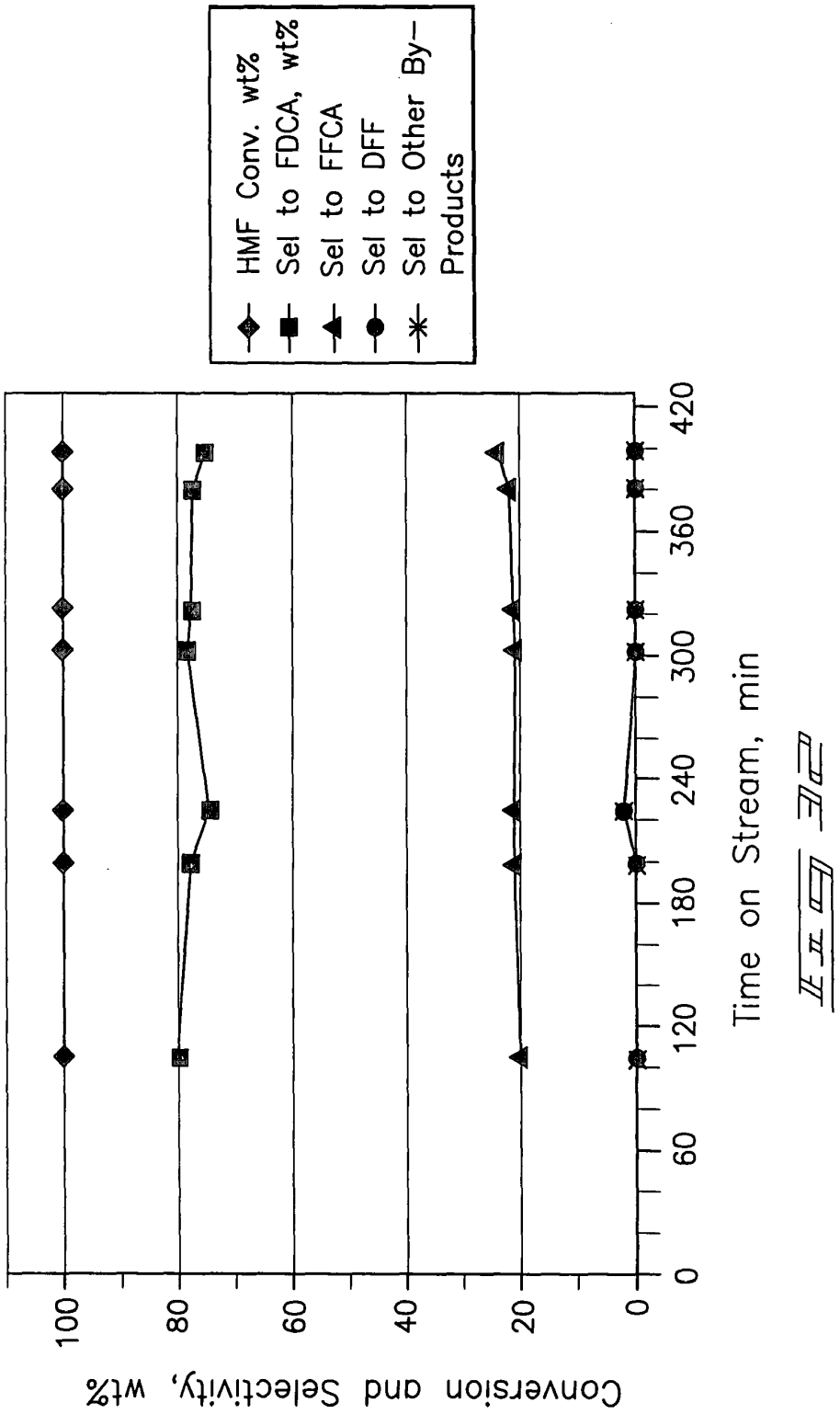

HMF Conv. wt%
Sel to FDCA, wt%
Sel to FFCA
Sel to DFF
Sel to Other By-Products
Conversion and Selectivity, wt%
0
20
40
60
80
100
0
60
120
180
240
300
360
420
Time on Stream, min

FIG 32

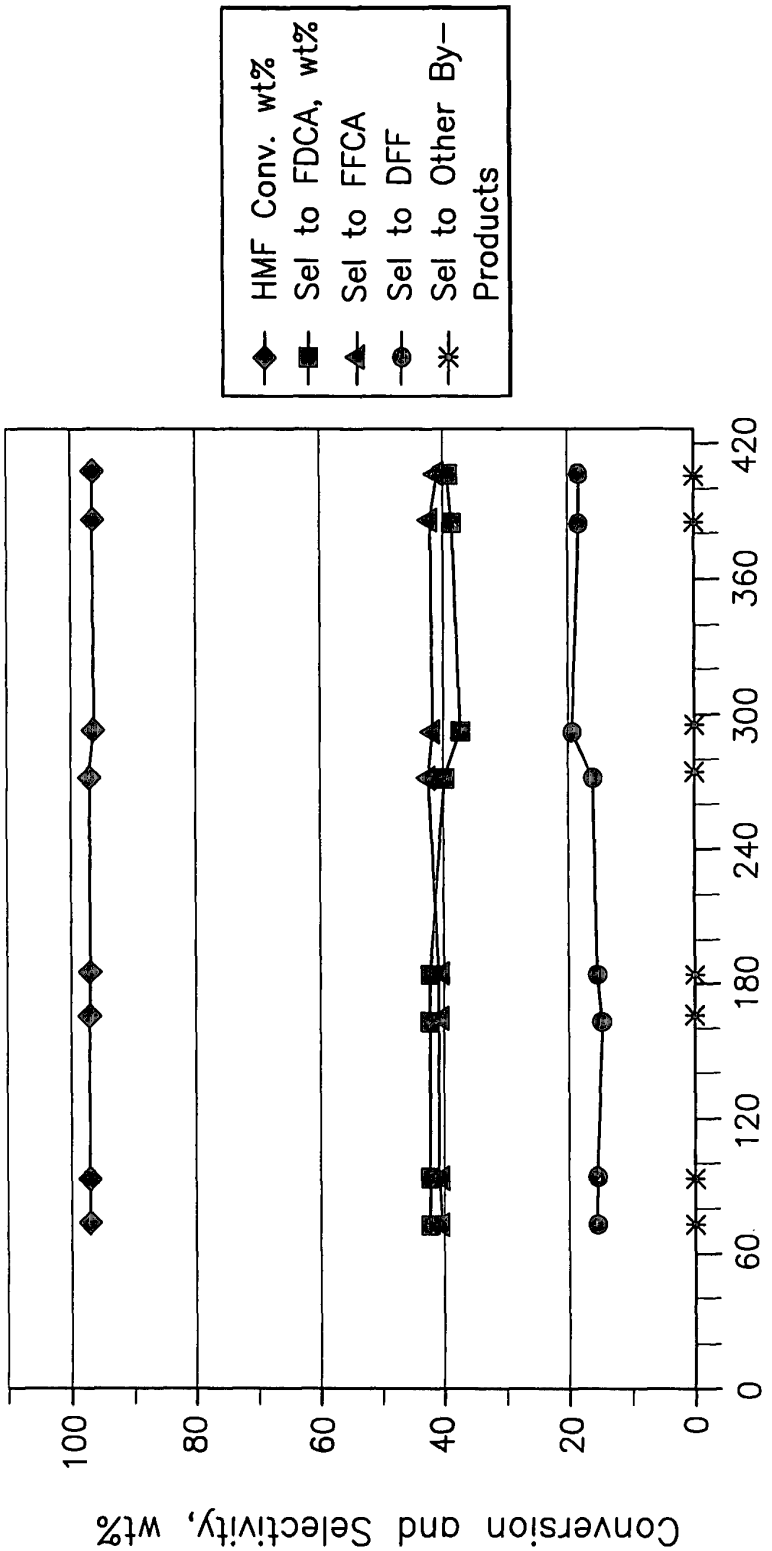

HMF Conv. wt%
Sel to FDCA, wt%
Sel to FFCA
Sel to DFF
Sel to Other By-Products
Conversion and Selectivity, wt%
100
80
60
40
20
0
0
60
120
180
240
300
360
420
Time on Stream, min

FIG 33

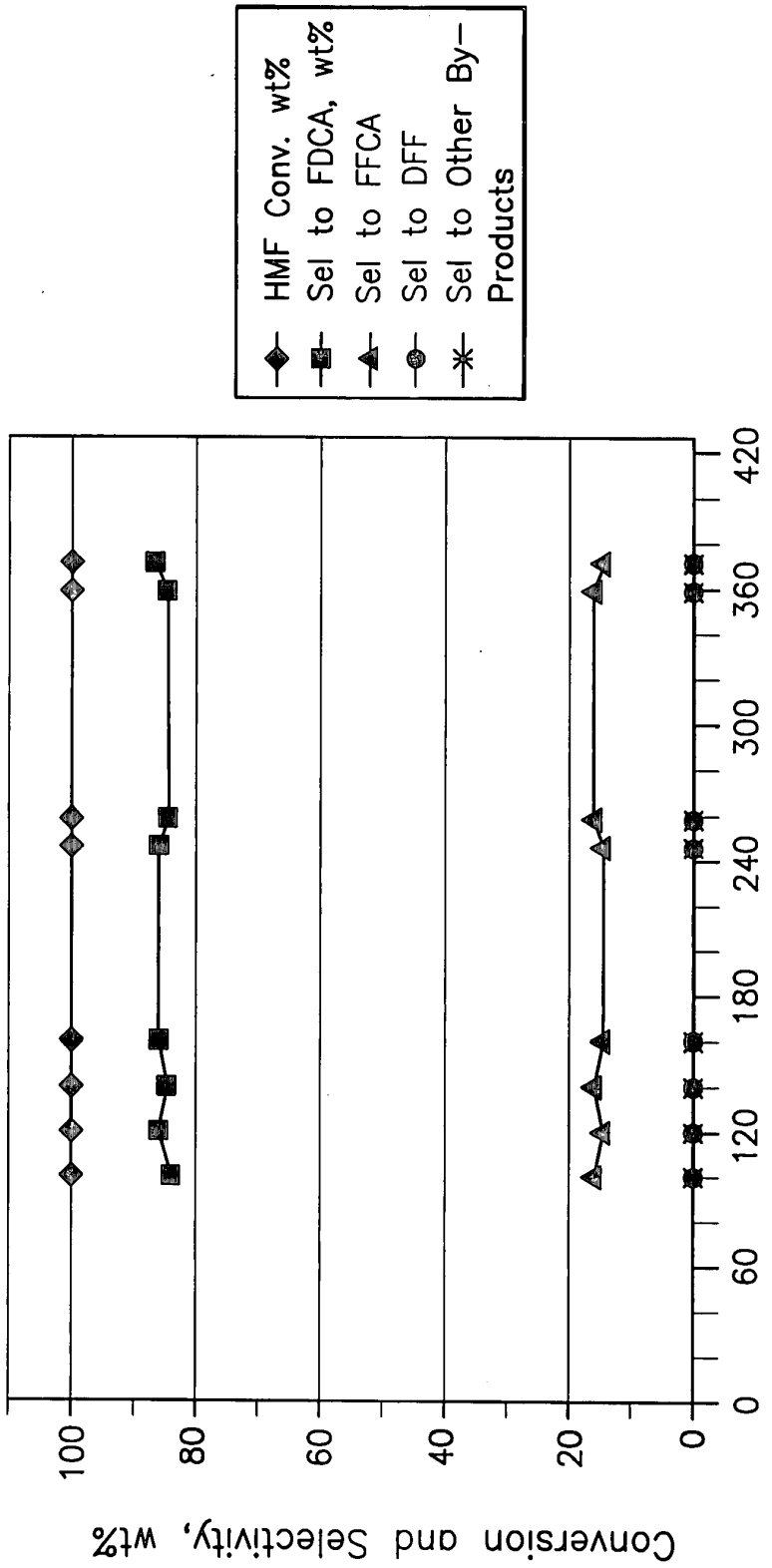

HMF Conv. wt%
Sel to FDCA, wt%
Sel to FFCA
Sel to DFF
Sel to Other By-Products
Conversion and Selectivity, wt%
0
20
40
60
80
100
0
60
120
180
240
300
360
420
Time on Stream, min

Fig. 3

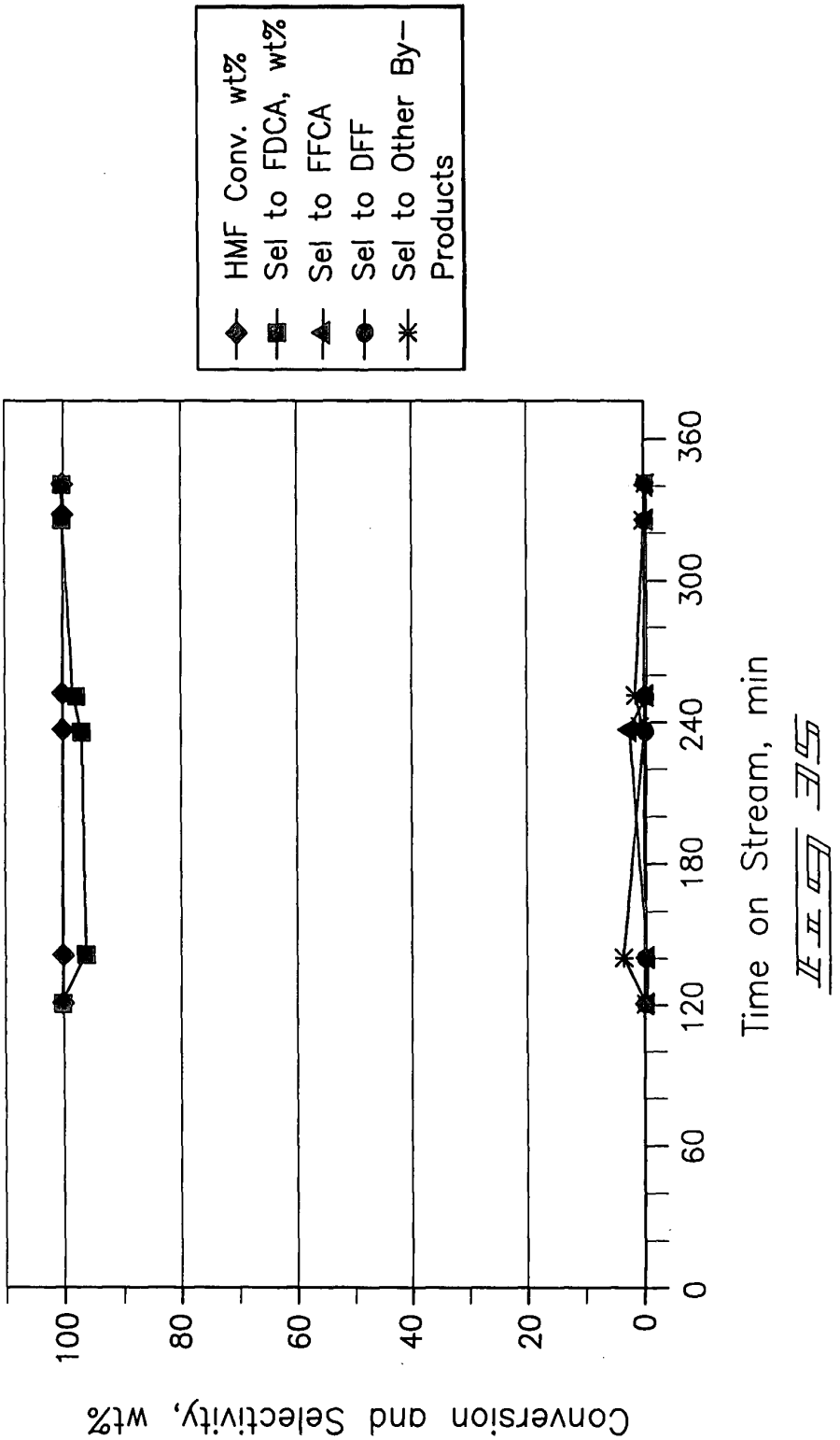

HMF Conv. wt%
Sel to FDCA, wt%
Sel to FFCA
Sel to DFF
Sel to Other By-Products
Conversion and Selectivity, wt%
0
20
40
60
80
100
0
60
120
180
240
300
360
Time on Stream, min

FIG 35

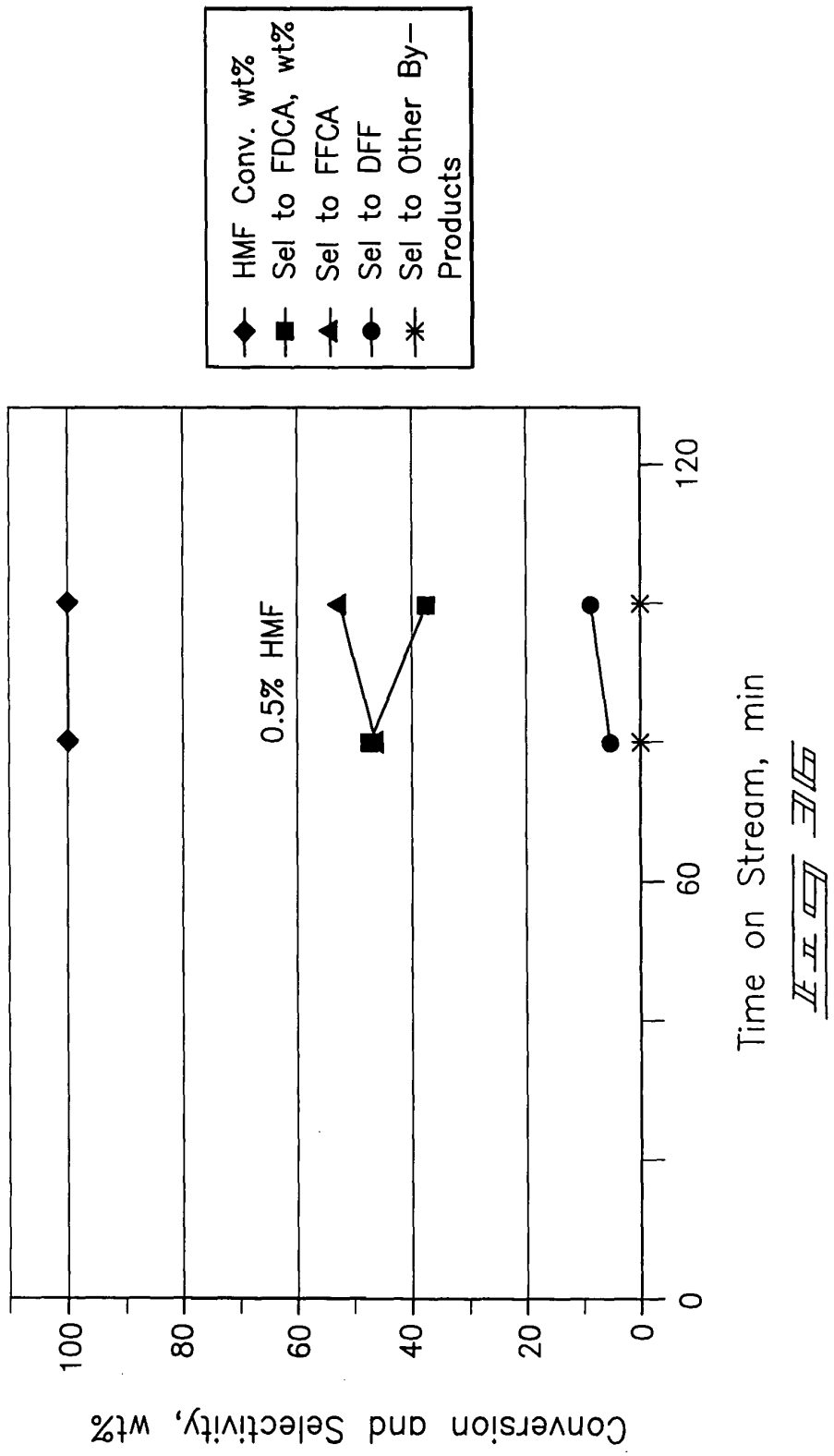

HMF Conv. wt%
Sel to FDCA, wt%
Sel to FFCA
Sel to DFF
Sel to Other By-Products
0.5% HMF
Conversion and Selectivity, wt%
0
20
40
60
80
100
0
60
120
Time on Stream, min

FIG 36

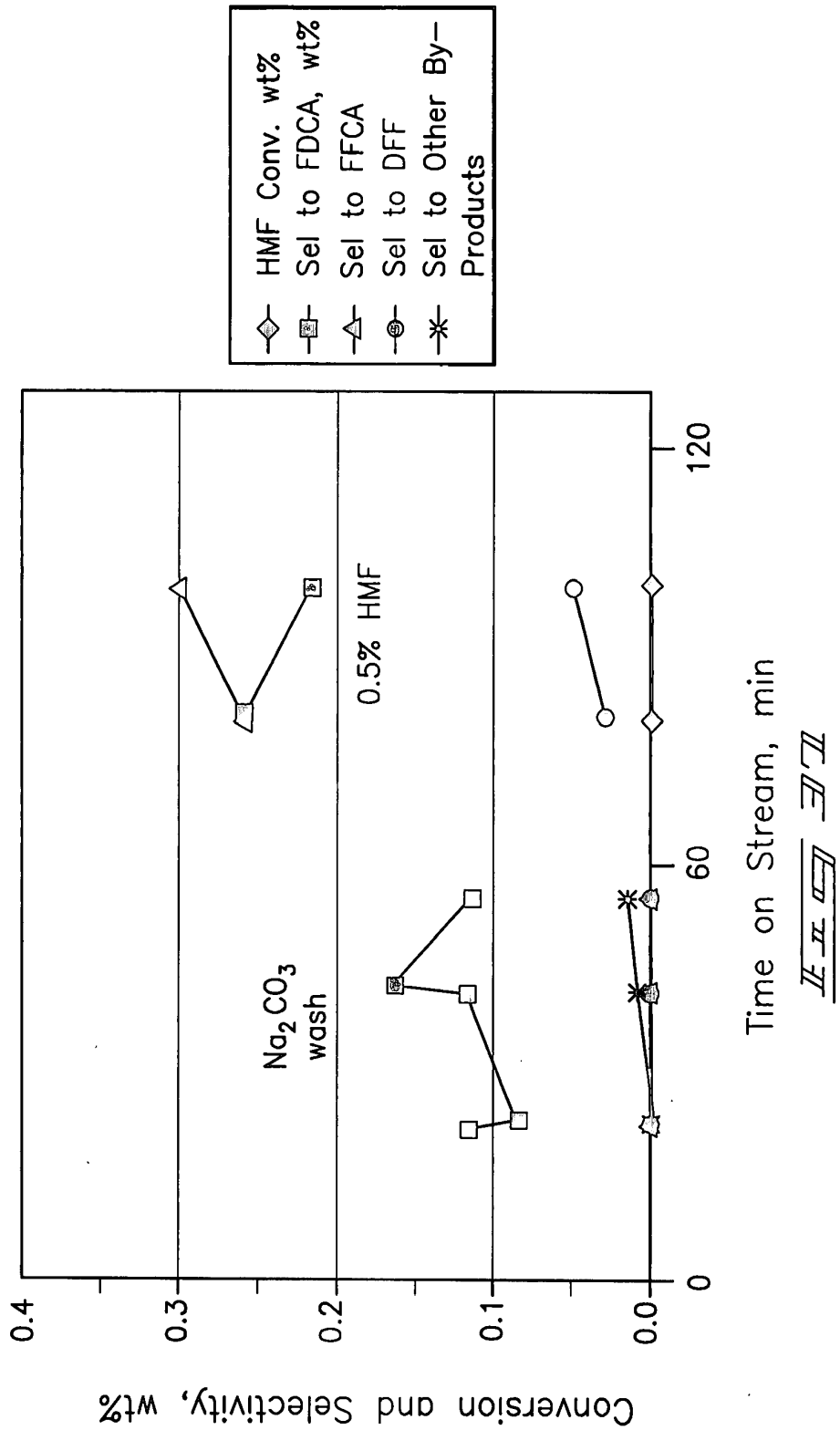

HMF Conv. wt%
Sel to FDCA, wt%
Sel to FFCA
Sel to DFF
Sel to Other By-Products
0.5% HMF
Na_2CO_3 wash
Conversion and Selectivity, wt%
Time on Stream, min
0.0
0.1
0.2
0.3
0.4
0
60
120

FIG 3E

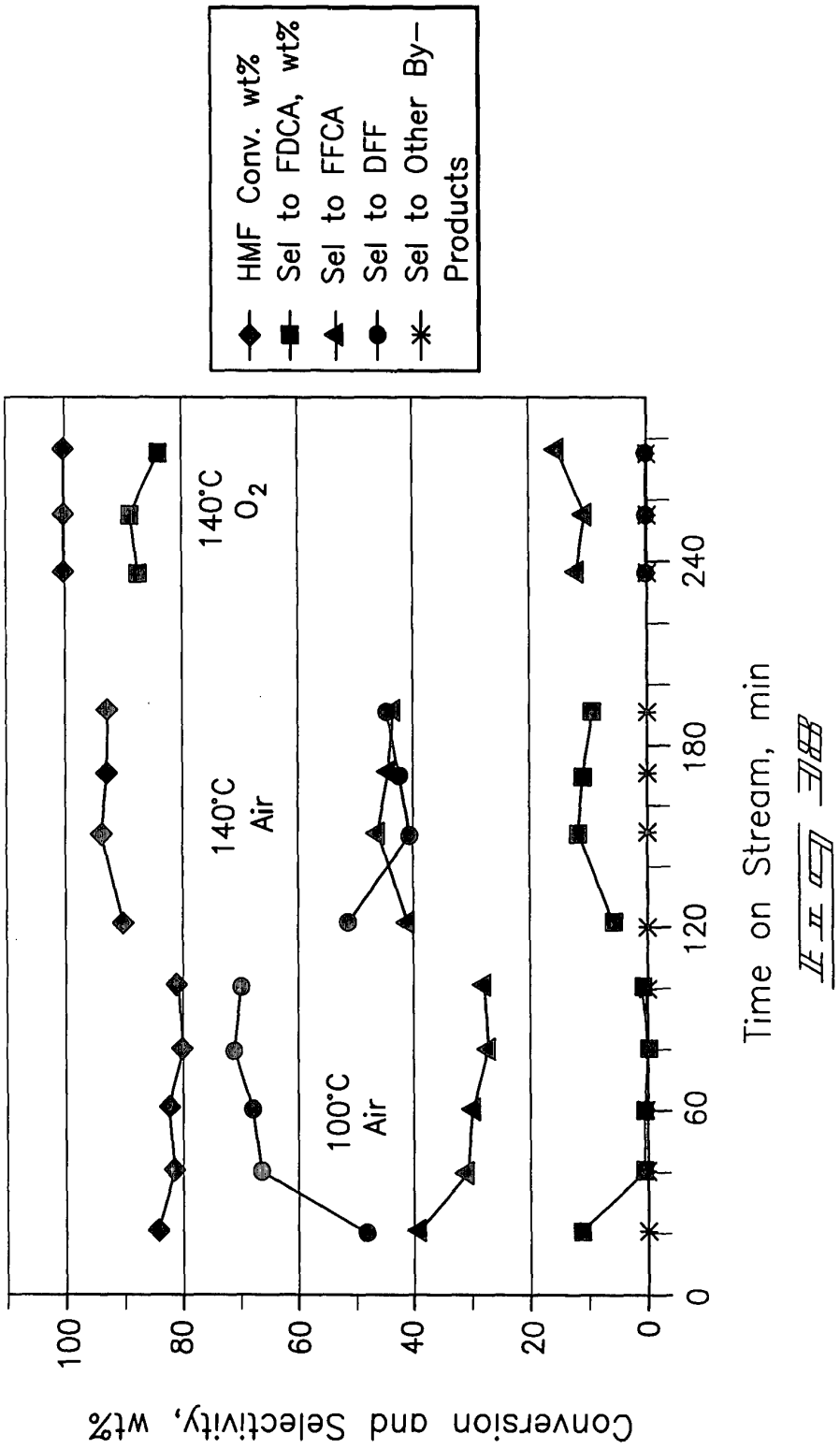

HMF Conv. wt%
Sel to FDCA, wt%
Sel to FFCA
Sel to DFF
Sel to Other By-Products
140°C O2
140°C Air
100°C Air
Conversion and Selectivity, wt%
Time on Stream, min
0
20
40
60
80
100
0
60
120
180
240

FIG 38

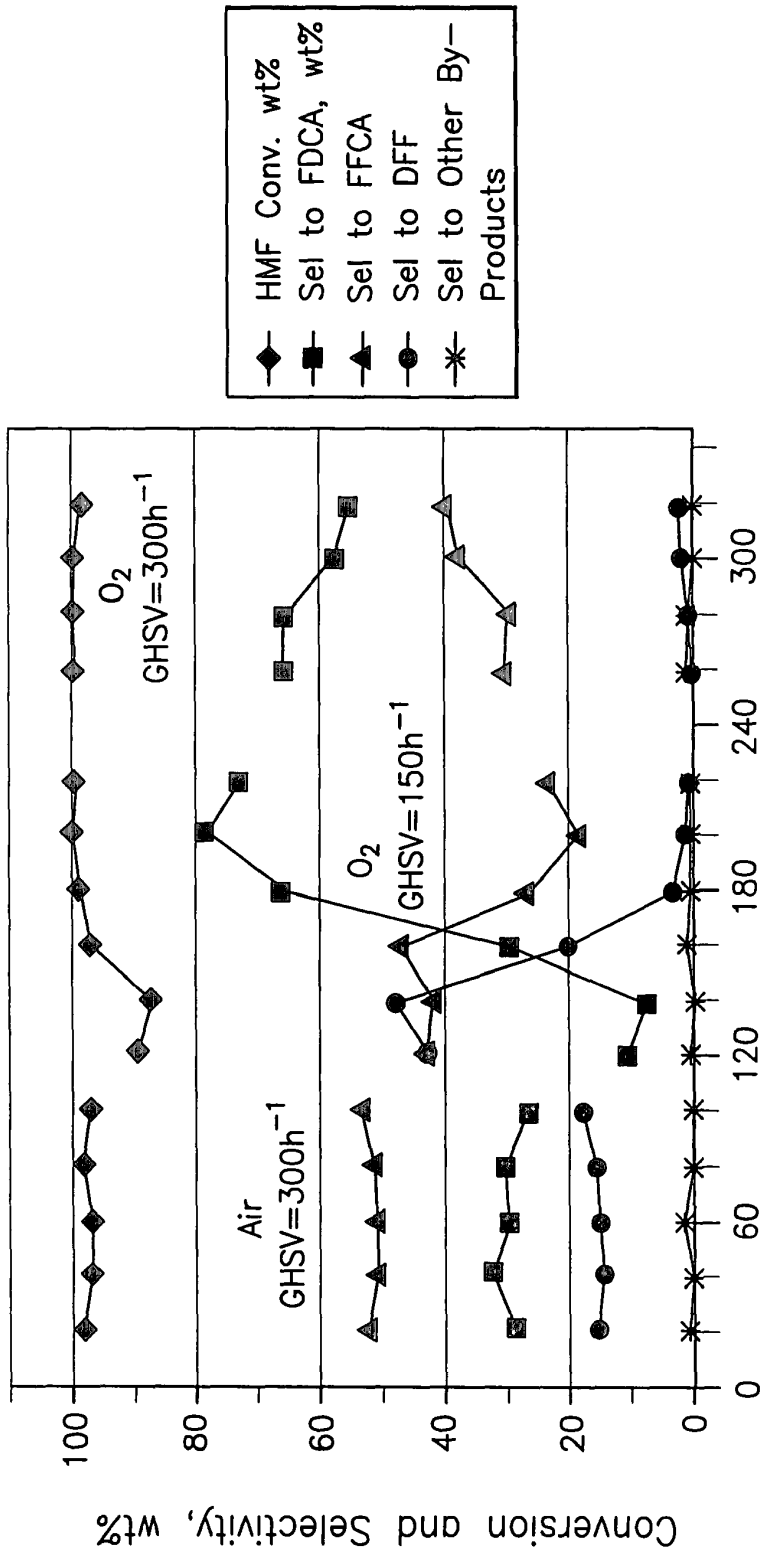

HMF Conv. wt%
Sel to FDCA, wt%
Sel to FFCA
Sel to DFF
Sel to Other By-Products
O2 GHSV=300h-1
O2 GHSV=150h-1
Air GHSV=300h-1
Conversion and Selectivity, wt%
Time on Stream, min
0
20
40
60
80
100
0
60
120
180
240
300

FIG 39

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
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8 May 2008 (08.05.2008)

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WO 2008/054804 A3

(51) International Patent Classification:
C07D 307/44 (2006.01) *B01J 23/00* (2006.01)
C07D 307/48 (2006.01)

(21) International Application Number:
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(26) Publication Language: English

(30) Priority Data:
60/863,704 31 October 2006 (31.10.2006) US

(71) Applicant *(for all designated States except US)*: **BATTELLE MEMORIAL INSTITUTE** [US/US]; Pacific Northwest Division, Intellectual Property Division, 902 Batelle Boulevard, P.o. Box 999, Richland, WA 99352 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **LILGA, Michael, A.** [US/US]; 902 Battelle Boulevard, P.o. Box 9099, Richland, WA 99352 (US). **HALLEN, Richard, T.** [US/US]; 902 Battelle Boulevard, P.o. Box 9099, Richland, WA 99352 (US). **HU, Jianli** [US/US]; 902 Battelle Boulevard, P.o. Box 9099, Richland, WA 99352 (US). **WHITE, James, F.** [US/US]; 902 Battelle Boulevard, P.o. Box 9099, Richland, WA 99352 (US). **GARY, Michel, J.** [US/US]; 902 Battelle Boulevard, P.O. Box 9099, Richland, WA 99352 (US).

(74) Agents: **TAYLOR, Jennifer, J.** et al.; 601 West 1st Avenue, Suite 1300, Spokane, WA 99201-3828 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:
— *of inventorship (Rule 4.17(iv))*

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
18 September 2008

(54) Title: HYDROXYMETHYL FURFURAL OXIDATION METHODS

(57) Abstract: A method of oxidizing hydroxymethylfurfural (HMF) includes providing a starting material which includes HMF in a solvent comprising water into a reactor. At least one of air and O_2 is provided into the reactor. The starting material is contacted with the catalyst comprising Pt on a support material where the contacting is conducted at a reactor temperature of from about 50°C to about 200°C A method of producing an oxidation catalyst where ZrO_2 is provided and is calcined. The ZrO_2 is mixed with platinum (II) acetylacetonate to form a mixture. The mixture is subjected to rotary evaporation to form a product. The product is calcined and reduced under hydrogen to form an activated product. The activated product is passivated under a flow of 2% O_2.

WO 2008/054804 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/023063

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D307/44 C07D307/48 B01J23/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D B01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 356 703 A (HOECHST AG [DE]) 7 March 1990 (1990-03-07)	1-20
A	examples 1-4	21-28
X	VERDEGUER P ET AL: "Oxydation catalytique du HMF en acide 2,5-furane dicarboxylique" JOURNAL OF MOLECULAR CATALYSIS, vol. 85, 1993, pages 327-344, XP002471376	1-20
A	table 8	21-28
X	KRÖGER ET AL: "A new approach for the production of 2,5-furandicarboxylic acid by in situ oxidation of 5-hydroxymethylfurfural starting from fructose" TOPICS IN CATALYSIS, vol. 13, 2000, pages 237-242, XP002471377	1-20
A	paragraph [02.1]	21-28

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 June 2008	23/07/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Usuelli, Ambrogio

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DEEBA ET AL: "Stabilization of platinum on silica promoted with lanthanum oxide and zirconium oxide" APPLIED CATALYSIS A: GENERAL, ELSEVIER SCIENCE, AMSTERDAM, NL, vol. 124, no. 2, 13 April 1995 (1995-04-13), pages 339-344, XP022249836 ISSN: 0926-860X the whole document	24-28
X	DATABASE CAPLUS CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002485191 retrieved from STN accession no. 1971:87814 Database accession no. 74:87814 abstract & SU 282 331 A 1970	21-23
Y	REYES P ET AL: "The nature of the support and the metal precursor on the resistance to sulphur poisoning of Pt supported catalysts" APPLIED CATALYSIS A: GENERAL, ELSEVIER SCIENCE, AMSTERDAM, NL, vol. 163, no. 1-2, 5 December 1997 (1997-12-05), pages 145-152, XP004338256 ISSN: 0926-860X paragraph [0002]	24-28
Y	FLORIAN HUBER ET AL: "Remarks on the passivation of reduced Cu-, Ni-, Fe-, Co-based catalysts" CATALYSIS LETTERS, KLUWER ACADEMIC PUBLISHERS-PLENUM PUBLISHERS, NE, vol. 110, no. 3-4, 1 September 2006 (2006-09-01), pages 211-220, XP019392844 ISSN: 1572-879X the whole document	24-28
A	REYES P ET AL: "The effect of Mo on the catalytic and surface properties of Rh-Mo/ZrO2 catalysts" CATALYSIS LETTERS, vol. 34, 1995, pages 331-341, XP002485204 page 332, line 16 - page 332, line 21	24-28

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/023063

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-20

Method of oxydizing HMF

---

2. claims: 21-23

Method of producing diformyl furane

---

3. claims: 24-28

Method of producing oxydation catalysts

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2007/023063

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0356703 A	07-03-1990	CA 1339569 C	02-12-1997
		DE 3826073 A1	01-02-1990
		ES 2027056 T3	16-05-1992
		JP 2088569 A	28-03-1990
		US 4977283 A	11-12-1990
SU 282331 A		NONE	

HYDROXYMETHYLFURFURAL ETHERS AND ESTERS PREPARED IN IONIC LIQUIDS

Patent Number:	WO 2009/030512 A2
Inventor(s):	GRUTER GERARDUS JOHANNES MARIA [NL]; MANZER LEO ERNEST [US]; DE SOUSA DIAS ANO SOFIA VAGUEIRO [NL]; DAUTZENBERG FRITS [US]; PURMOVA JINDRA [NL]
Applicant(s):	FURANIX TECHNOLOGIES BV [NL]; GRUTER GERARDUS JOHANNES MARIA [NL]; MANZER LEO ERNEST [US]; DE SOUSA DIAS ANO SOFIA VAGUEI [NL]; DAUTZENBERG FRITS [US]; PURMOVA JINDRA [NL]
Classification:	**- international:** C07D307/46 **- cooperative:** C07D307/46; C10L1/1857
Application number:	WO2008EP07429 20080905
Priority number(s):	EP20070017571 20070907
Also published as:	WO2009030512 (A3) AT498616 (T) EP2183236 (A2) EP2183236 (B1) US2010081833 (A1) US2010081833 (A1) US8314260 (B2) US8314260 (B2)

Abstract of WO 2009/030512 A2

Accordingly, the current invention provides a method for the manufacture of an ether or ester of 5-hydroxymethylfurfural by reacting a hexose-containing starting material or HMF with an alcohol or an organic acid dissolved into an ionic liquid, using a metal chloride as catalyst.

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International Bureau

(43) International Publication Date
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PCT

(10) International Publication Number
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(51) International Patent Classification:
C07D 307/46 (2006.01)

(21) International Application Number:
PCT/EP2008/007429

(22) International Filing Date:
5 September 2008 (05.09.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
07017571.6 7 September 2007 (07.09.2007) EP

(71) Applicant *(for all designated States except US)*: **FURANIX TECHNOLOGIES B.V.** [NL/NL]; Zeeringstraat 29, NL-1014 BV Amsterdam (NL).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **GRUTER, Gerardus, Johannes, Maria** [NL/NL]; 14 Asterkade, NL-2106 BA Heemstede (NL). **MANZER, Leo Ernest** [US/US]; 714 Burnley Road, Wilmington, DE 19803 (US). **DE SOUSA DIAS, Ano Sofia Vagueiro** [PT/NL]; 23, Gedempte Voldersgracht, 2011 WB Haarlem (NL). **DAUTZENBERG, Frits** [NL/US]; 5008 Chelterham Ter, San Diego, CA 92130 (US). **PURMOVA, Jindra** [CZ/NL]; 82, Oktoberstraat, 1335 EV Almere (NL).

(74) Agent: **KORTEKAAS, M.C.J.A.**; Exter Polak & Charlouis B.V., P.O. Box 3241, NL-2280 GE Rijswijk (NL).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

WO 2009/030512 A2

(54) Title: HYDROXYMETHYLFURFURAL ETHERS AND ESTERS PREPARED IN IONIC LIQUIDS

(57) Abstract: Accordingly, the current invention provides a method for the manufacture of an ether or ester of 5-hydroxymethylfurfural by reacting a hexose-containing starting material or HMF with an alcohol or an organic acid dissolved into an ionic liquid, using a metal chloride as catalyst.

Title: Hydroxymethylfurfural ethers and esters prepared in ionic liquids

Technical Field

The present invention concerns a method for the manufacture of an ether or an ester of 5-hydroxymethylfurfural (5-(hydroxymethyl)-2-furaldehyde, or HMF) from biomass. More in particular, the present invention concerns a method wherein ionic liquids are used in the manufacture of the ether or ester (jointly referred to as RMF).

Background Art

Fuel, fuel additives and various chemicals used in the petrochemical industry are derived from oil, gas and coal, all finite sources. Biomass, on the other hand, is considered a renewable source. Biomass is biological material (including biodegradable wastes) which can be used for the production of fuels or for industrial production of e.g. fibres, chemicals or heat. It excludes organic material which has been transformed by geological processes into substances such as coal or petroleum.

Production of biomass derived products for non-food applications is a growing industry. Bio-based fuels are an example of an application with strong growing interest..

Biomass contains sugars (hexoses and pentoses) that may be converted into value added products. Current biofuel activities from sugars are mainly directed towards the fermentation of sucrose or glucose into ethanol or via complete breakdown via Syngas to synthetic liquid fuels. EP 0641 854 describes the use of fuel compositions comprising of hydrocarbons and/or vegetable oil derivatives containing at least one glycerol ether to reduce particulate matter emissions.

More recently, the acid catalysed reaction of fructose has been re-visited, creating HMF as an intermediate of great interest. Most processes investigated have the disadvantage that HMF is not very stable at the reaction conditions required for its formation. Fast removal from the water-phase containing the sugar starting material and the acid catalyst has been viewed as a solution for this problem. Researchers at the University of Wisconsin-Madison have developed a process to make HMF from fructose. HMF can be converted into monomers for plastics, petroleum or fuel extenders, or even into fuel itself. The process by prof. James Dumesic and co-workers first dehydrates the fructose in an aqueous phase with the use of

an acid catalyst (hydrochloric acid or an acidic ion-exchange resin). Salt is added to salt-out the HMF into the extracting phase. The extracting phase uses an inert organic solvent that favors extraction of HMF from the aqueous phase. The two-phase process operates at high fructose concentrations (10 to 50 wt %), achieves high yields (80% HMF selectivity at 90% fructose conversion), and delivers HMF in a separation-friendly solvent (DUMESIC, James A, et al. "Phase modifiers promote efficient production of Hydroxymethylfurfural from fructose" . Science. 30 juni 2006, vol.312, no.5782, p.1933-1937). Although the HMF yields from this process are interesting, the multi-solvent process has cost-disadvantages due to the relatively complex plant design and because of the less than ideal yields when cheaper and less reactive hexoses than fructose, such as glucose or sucrose, are used as a starting material. HMF is a solid at room temperature which has to be converted in subsequent steps to useful products. Dumesic has reported an integrated hydrogenolysis process step to convert HMF into dimethylfuran (DMF), which is assumed to be an interesting gasoline additive.

In WO 2006/063220 a method is provided for converting fructose into 5- ethoxymethylfurfural (EMF) at 60 °C, using an acid catalyst either in batch during 24 hours or continuously via column elution during 17 hours. Applications of EMF were not discussed.

Also in copending patent application PCT/EP2007/002145 the manufacture of HMF ethers are described, including the use of such ethers as fuel or fuel additive. Indeed, both the methyl ether and the ethyl ether (methoxymethylfurfural, or MMF; ethoxyethylfurfural or EMF) were prepared and tested. PCT/EP2007/002146 is a similar copending aptent application, but now in respect of the manufacture of HMF esters.

Claude Moreau et all. found that the acid-catalyzed dehydration of fructose may be performed in a microbatch reactor at using 1-H-3-methyl imidazolium chloride ("Dehydration of fructose and sucrose into 5-hydroxymethylfurfural in the presence of 1-H-3-methyl imidazolium chloride acting both as solvent and catalyst", by Claude Moreau et al, Journal of Molecular Catalysis A: Chemical 253 (2006) 165-169).The ionic liquid is a very suitable solvent, there is no decomposition of the produced 5-hydroxymethylfurfural and the fructose is nearly quantitatively transformed into HMF. When sucrose is used (a disaccharide of glucose and fructose) the sugar is nearly quantitatively transformed into HMF and unreacted glucose. It would thus appear that the method of Moreau et al is of no use in the preparation of fuel components based on glucose.

Zhao et al found that the catalytic conversion of sugars into HMF may be improved, using an ionic liquid and certain metal halids dissolved in 1-alkyl-3-methylimidazolium chloride as catalyst. Small amounts of levulinic aced are formed in these reactions ("Metal Chlorides in Ionic Liquid Solvents Converts Sugars to 5-Hydroxymethylfurfural", by Haibo Zhao et al, *Science*. **316**, 1597(15 June 2007).

The current inventors set out to prepare a fuel or fuel component that is not contaminated by levulinic acid and that may be made from various biomass derived sugars, including glucose. Surprisingly, it has been found that such can be achieved by performing the reaction in the presence of an organic acid or alcohol as co-reactant, converting the sugar into an ether or ester of HMF.

Disclosure of Invention

Accordingly, the current invention provides a method for the manufacture of an ether or ester of 5-hydroxymethylfurfural by reacting a hexose-containing starting material or HMF with an alcohol or an organic acid, dissolved into an ionic liquid, using a metal chloride as catalyst.

When the reaction product of the above method is used as such or when it is used as an intermediate for a subsequent conversion, the selectivity of the reaction is preferably high as the product is preferably pure. However, when the reaction product of the above method is used as a fuel, a fuel additive or as a fuel or a fuel additive intermediate, the reaction product does not necessarily need to be pure. Indeed, in the preparation of fuel and fuel additives from biomass, which in itself is a mixture of various monosaccharides, disaccharides and polysaccharides, the reaction product may contain non-interfering components such as levulinic acid derivatives and/or derivatives of pentoses and the like. For ease of reference, however, the method and the reaction product are described in terms of the reaction of a hexose-containing starting material, resulting in an ether or ester of HMF. Also within the scope of the invention is the reaction of HMF with the alcohol or acid, since HMF is believed to be produced as intermediate from the hexose-containing starting material.

The current invention also provides for the use of the reaction product made according to the present invention as fuel or as fuel additive. Fuels for blending with the product of the present invention include but are not limited to gasoline and gasoline-ethanol blends, kerosene, diesel, biodiesel (refers to a non-petroleum-based diesel fuel consisting of short chain alkyl (methyl or ethyl) esters, made by transesterification of vegetable oil, which can be used (alone, or blended with conventional petrodiesel), Fischer-Tropsch liquids (for example obtained from GTL, CTL or BTL gas-to-liquids/coal-to-liquids/biomass to liquids processes), diesel-biodiesel blends and green diesel and blends of diesel and/or biodiesel with green

diesel (green diesel is a hydrocarbon obtained by hydrotreating biomass derived oils, fats, greases or pyrolysis oil; see for example the UOP report OPPORTUNITIES FOR BIORENEWABLES IN OIL REFINERIES FINAL TECHNICAL REPORT, SUBMITTED TO: U.S. DEPARTMENT OF ENERGY (DOE Award Number: DE-FG36-05GO15085). The product is a premium diesel fuel containing no sulfur and having a cetane number of 90 to 100). Fuels for blending with the product of the present invention may also include one or more other furanics, wherein the expression furanics is used to include all derivatives of furan and tetrahydrofuran. The invention also provides a fuel composition comprising a fuel element as described above and the reaction product made according to the present invention.

Mode(s) for Carrying Out the Invention

Biomass resources are well known. The components of interest in biomass are the mono-, di- or polysaccharides (hereinafter referred to as hexose-containing starting material). Suitable 6-carbon monosaccharides include but are not limited to fructose, glucose, galactose, mannose and their oxidized, reduced, etherified, esterified and amidated derivatives, e.g. aldonic acid or alditol, with glucose being the most abundant, the most economic and therefore the most preferred monosaccharide, albeit less reactive than fructose. On the other hand, the current inventors have also succeeded to convert sucrose, which is also available in great abundance. Other disaccharides that may be used include maltose, cellobiose and lactose. The polysaccharides that may be used include cellulose, inulin (a polyfructan), starch (a polyglucan) and hemi-cellulose. The polysaccharides and disaccharides are converted into their monosaccharide component(s) and dehydrated during the manufacture of the 5-HMF ether.

The alcohol used in the method of the current invention should bear at least one hydroxyl group, which may be in a primary, secondary or even tertiary position. Diols and polyhydric compounds may be used as well. The alcohol may comprise from 3 to 20 carbon atoms, preferably from 3 to 8 carbon atoms. Examples include methanol, ethanol, 1-propanol, 2-propanol, 2-butanol, 2-methyl-1-propanol (isobutanol), 2-methyl-2-propanol (*tert*-butanol), 2-pentanol (s-amyl alcohol); 2-methyl-1-butanol (p-amyl alcohol); 2-methyl-2-butanol (t-amyl alcohol); 3-methyl-1-butanol (isoamyl alcohol); 2,2-dimethyl-1-propanol (neopentyl alcohol); 2-hexanol; 2-ethyl-1-hexanol (isooctyl alcohol). Also higher alcohols my be used, which includes natural alcohols such as caproic alcohol and caproyl alcohol the like, and which includes synthetic alcohols made by Fisher-Tropsch or by the Guerbet reaction (e.g., 2-ethylhexanol, prepared from butanol; "Selective synthesis of 2-ethyl-1-hexanol from n-butanol through the Guerbet reaction by using bifunctional catalysts based on copper or palladium

precursors and sodium butoxide", by Carlo Carlini, Journal of Molecular Catalysis A: Chemical 212 (2004) 65–70). Preferred alcohols used in the method of the current invention include isobutanol, *tert*-butanol, isoamyl alcohol, isooctyl alcohol. Also blends of alcohols may be used, e.g., of isobutanol and *tert*-butanol. Also blends of alcohols may be used, e.g., the aforementioned Guerbet alcohols made from a mixed alcohol feed or natural alcohols found as a blend in nature. The current method thus provides an excellent high value outlet for "contaminated" alcohols.

The amount of alcohol used during the manufacture of the HMF ether is preferably at least equimolar on the monosaccharide, but typically is used in much greater excess. Indeed, the alcohol may be used as co-solvent. In such a case, a sufficient amount of alcohol is present to form the HMF ether.

Instead of an alcohol, also an organic acid may be used. Suitably, the organic acid is a mono-carboxylic acid. Preferably the acid is selected from the group consisting of (un)branched aliphatic acids and (un)branched unsaturated acids, more preferably (un)branched aliphatic acids. Still more preferably the organic acid is a C1-C5 (un)branched aliphatic acids, most preferable formic acid, acetic acid, propionic acid, and/or (iso)-butyric acid. In addition to the acid, also the anhydride thereof may be used. Mixtures of acids and/or anhydrides may also be employed..

In view of the good results, the use of an organic acid, and hence the preparation of an ester of 5-hydroxymethylfurfural, is preferred.

The catalyst in the method of the present invention can be selected from amongst any of the metal halides mentioned in by Zhao et al. Examples include $CrCl_2$, $CrCl_3$, $FeCl_2$, $FeCl_3$, CuCl, $CuCl_2$, VCl_3, $MoCl_3$, $PdCl_2$, $PtCl_2$, $PtCl_4$, $RuCl_3$, or $RhCl_3$. $CrCl_2$ is particularly useful.
The amount of catalyst may vary, depending on the selection of catalyst or catalyst mixture. For instance, the catalyst can be added to the reaction mixture in an amount varying from 0.01 to 40 mole % drawn on the hexose content of the biomass resource, preferably from 0.1 to 30 mole %, more preferably from 1 to 20 mole %.

The temperature at which the reaction is performed may vary, but in general it is preferred that the reaction is carried out at a temperature from 50 to 300 degrees Celsius, preferably from 125 to 250 degrees Celsius, more preferably from 150 to 225 degrees Celsius. In general, temperatures higher than 300 are less preferred as the selectivity of the reaction

reduces and as many by-products occur, inter alia caramelisation of the sugar. Performing the reaction below the lowest temperature is also less preferable because of the low reaction rate. If the reactions are carried out above the boiling temperature of water, then the reactions are preferably carried out under pressure, e.g., 10 bar nitrogen or higher.

The hexose-containing starting material is typically dissolved or suspended in a solvent which can be the mixed alcohol reactant, in order to facilitate the reaction. The solvent is a so-called ionic liquid. The latter refers to a class of inert ionic compounds with a low melting point, which may therefore be used as solvent. Examples thereof include 1-alkyl-3-methylimidazolium, 1-alkylpyridinium, N-methyl-N-alkylpyrrolidinium and ammonium ions, whereas a wide range of anions may be employed, from simple halides, which generally inflect high melting points, to inorganic anions such as tetrafluoroborate and hexafluorophosphate and to large organic anions like bis-trifluorsulfonimide, triflate or tosylate. There is no specific limitation to the ionic liquid used in the current invention, albeit that 1-H-3-methyl imidazolium chloride has shown to be a suitable solvent for the biomass-derived sugars. This is therefore a preferred solvent. Use of 1-H-3-methyl imidazolium chloride, is discussed in "Dehydration of fructose and sucrose into 5-hydroxymethylfurfural in the presence of 1-H-3-methyl imidazolium chloride acting both as solvent and catalyst", by Claude Moreau et al, Journal of Molecular Catalysis A: Chemical 253 (2006) 165-169. Also preferred solvents are 1-Ethyl-3-methylimidazolium chloride (EMIM) and H-3-methylimidazolium bis(trifluoromethanesulfonyl)imide (HMIM), and/or mixtures of these solvents.

A sufficient amount of solvent is preferably present to dissolve or suspend the starting material and to limit undesired side-reactions.

The method of the current invention may be carried out in a batch process or in a continuous process, with or without recycle of (part of) the product stream to control the reaction temperature (recycle via a heat exchanger). For instance, the method of the invention can be performed in a continuous flow process. In such method, homogenous catalysts may be used and the residence time of the reactants in the flow process is between 0.1 second and 10 hours, preferably from 1 second to 1 hours, more preferably from 5 seconds to 20 minutes.

Alternatively, the continuous flow process may be a fixed bed continuous flow process or a reactive (catalytic) distillation process with a heterogeneous acid catalyst (meaning a solid catalyst). To initiate or regenerate the heterogeneous acid catalyst or to improve performance, an inorganic or organic acid may be added to the feed of the fixed bed or

reactive distillation continuous flow process. In a fixed bed process, the liquid hourly space velocity (LHSV) can be from 1 to 1000, preferably from 5 to 500, more preferably from 10 to 250 and most preferably from 25 to 100 min^{-1}.

The above process results in a stable HMF ether or ester, which can then be used as such or be converted into a further derivative before being used as fuel and/or as fuel additive.

Examples are enclosed to illustrate the method of the current invention and the suitability of the products prepared therefrom as fuel. The examples are not meant to limit the scope of the invention.

Example 1

In a batch experiment, 50 mg of substrate (glucose or fructose) and 250 mg of 1-Ethyl-3-methylimidazolium chloride (EMIM) or 500 mg of a mixture of EMIM and H-3-methylimidazolium bis(trifluoromethanesulfonyl)imide (HMIM) were loaded in a Teflon lined reactor with 7.5 ml volume. 1 ml of acetic acid was added and the mixture reacted under nitrogen (12.5 bar) in the presence of $CrCl_2$ as catalyst for 3 h at 100 °C. Two products were observed in the UV spectra and identified as HMF and 5-acetoxy methyl furfural (AMF). Selectivities and conversions for catalysts used in this example can be found in table below.

The substrate conversions and the selectivities and yields were calculated according to the formulas:

Conversion = 100* [n_0 (substrate) - n_t (substrate)] / n_0 substrate

Selectivity = 100 * n_t (product) / [n_0 (substrate) - n_t (substrate)]

Yield = 100 * n_t (product) / n_0 substrate,

Where:

n_0- the initial number of moles

n_t- the number the moles of a compound at time "t".

Substrate	Solvent	Amount of catalyst [mg]	Y HMF (%)	Y AMF (%)
Glucose	EMIM	2.0	1.3	5.1
Glucose	EMIM + HMIM	2.0	1.8	6.9
Glucose	EMIM + HMIM	3.5	1.9	9.2
Fructose	EMIM	2.0	22.3	71.5
Fructose	EMIM + HMIM	2.0	29.2	59.4
Fructose	EMIM + HMIM	3.5	19.6	74.8

Example 2

In a batch experiment, 50 mg of substrate (glucose or fructose) and 250 mg of 1-Ethyl-3-methylimidazolium chloride (EMIM) or 500 mg of a mixture of EMIM and H-3-methylimidazolium bis(trifluoromethanesulfonyl)imide (HMIM) were loaded in a Teflon lined reactor with 7.5 ml volume. 1 ml of propionic acid was added and the mixture reacted under nitrogen (12.5 bar) in the presence of $CrCl_2$ as catalyst for 3 h at 100 °C. Two products were observed in the UV spectra and identified as HMF and 5-(propionyloxy)methyl furfural (PMF).

Substrate	Solvent	Amount of catalyst [mg]	Y HMF (%)	Y PMF (%)
Glucose	EMIM	2.0	2.0	3.2
Glucose	EMIM + HMIM	2.0	2.2	3.2
Glucose	EMIM + HMIM	3.5	1.9	3.4
Fructose	EMIM	2.0	33.2	52.0
Fructose	EMIM + HMIM	2.0	39.6	24.3
Fructose	EMIM + HMIM	3.5	33.0	48.7

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Claims

1. Method for the manufacture of an ether or ester of 5-hydroxymethylfurfural by reacting a hexose-containing starting material or HMF with an alcohol or an organic acid dissolved into an ionic liquid, using a metal chloride as catalyst.

2. Method according to claim 1, wherein the ionic liquid used as solvent is selected from the group comprising 1-alkyl-3-methylimidazolium, 1-alkylpyridinium, N-methyl-N-alkylpyrrolidinium and ammonium ions as cation, and halides, or inorganic anions such as tetrafluoroborate and hexafluorophosphate or large organic anions like bis-trifluorsulfonimide, triflate or tosylate as anion, preferably 1-H-3-methyl imidazolium chloride, 1-ethyl-3-methylimidazolium chloride (EMIM) or H-3-methylimidazolium bis(trifluoromethanesulfonyl)imide (HMIM), and/or mixtures of these solvent.

3. Method according to claim 1 or 2, wherein the acid catalyst is selected from the group consisting of homogeneous or heterogeneous catalysts selected from $CrCl_2$, $CrCl_3$, $FeCl_2$, $FeCl_3$, CuCl, $CuCl_2$, VCl_3, $MoCl_3$, $PdCl_2$, $PtCl_2$, $PtCl_4$, $RuCl_3$, or $RhCl_3$. .

4. Method according to claim 3, wherein the acid is $CrCl_2$.

5. Method according to any one of the claims 1 to 4, wherein the reaction is performed at a temperature from 50 to 300 degrees Celsius, preferably from 125 to 250 degrees Celsius, more preferably from 150 to 225 degrees Celsius.

6. Method according to any one of the claims 1 to 5, wherein the hexose-containing starting material is used and wherein the hexose starting material is selected from the group of

- starch, amylose, galactose, cellulose, hemi-cellulose,
- glucose-containing disaccharides such as sucrose, maltose, cellobiose, lactose, preferably glucose-containing disaccharides, more preferably sucrose,
- glucose or fructose.

7. Method according to any one of the claims 1 to 6, wherein an ester of 5-hydroxymethylfurfural is prepared by reacting a hexose-containing starting material or HMF with an organic acid.

8. Method according to claim 7, wherein a mono-carboxylic acid or anhydride or a mixture of acids and/or anhydrides is used, selected from the group consisting of (un)branched aliphatic acids and (un)branched unsaturated acids, and the anhydrides thereof.

9. Method according to claim 8, wherein a C1-C5 (un)branched aliphatic acid or anhydride or a mixture of C1-C5 (un)branched aliphatic acids and/or anhydrides is used.

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(54) Title: HYDROXYMETHYLFURFURAL ETHERS AND ESTERS PREPARED IN IONIC LIQUIDS

(57) Abstract: Accordingly, the current invention provides a method for the manufacture of an ether or ester of 5-hydroxymethylfurfural by reacting a hexose-containing starting material or HMF with an alcohol or an organic acid dissolved into an ionic liquid, using a metal chloride as catalyst.

INTERNATIONAL SEARCH REPORT

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Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data, BEILSTEIN Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HAIBO ZHAO ET AL: "Metal Chlorides in Ionic Liquid Solvents Convert Sugars to 5-Hydroxymethylfurfural" SCIENCE, vol. 316, 15 June 2007 (2007-06-15), pages 1597-1600, XP002468488 cited in the application the whole document ----- -/--	1-9

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MOREAU ET AL: "Dehydration of fructose and sucrose into 5-hydroxymethylfurfural in the presence of 1-H-3-methyl imidazolium chloride acting both as solvent and catalyst" JOURNAL OF MOLECULAR CATALYSIS. A, CHEMICAL, ELSEVIER, AMSTERDAM, NL, vol. 253, no. 1-2, 1 July 2006 (2006-07-01), pages 165-169, XP005466119 ISSN: 1381-1169 cited in the application the whole document	1-9
A	WO 2006/063220 A (ARCHER DANIELS MIDLAND CO [US]; SANBORN ALEXANDRA J [US]) 15 June 2006 (2006-06-15) cited in the application pages 6,11,17; claims 27-29; examples 6,7	1-9

INTERNATIONAL SEARCH REPORT

Information on patent family members

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		WO 2006063287 A2	15-06-2006

CONVERSION OF CARBOHYDRATES TO HYDROXY-METHYLFURFURAL (HMF) AND DERIVATIVES

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Inventor(s):	SANBORN ALEXANDRA [US]; HOWARD STEPHEN [US]	
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Abstract of WO 2009/076627 A2

A method of producing substantially pure HMF, HMF esters and other derivatives from a carbohydrate source by contacting the carbohydrate source with a solid phase catalyst. A carbohydrate starting material is heated in a solvent in a column and continuously flowed through a solid phase catalyst in the presence of an organic acid, or heated with the organic acid and a solid catalyst in solution to form a HMF ester. Heating without organic acid forms HMF. The resulting product is purified by filtration to remove the unreacted starting materials and catalyst. The HMF ester or a mixture of HMF and HMF ester may then be oxidized to 2,5- furandicarboxylic acid (FDCA) by combining the HMF ester with an organic acid, cobalt acetate, manganese acetate and sodium bromide under pressure. Alternatively, the HMF ester may be reduced to form a furan or tetrahydrofuran diol.

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(54) **Title:** CONVERSION OF CARBOHYDRATES TO HYDROXY-METHYLFURFURAL (HMF) AND DERIVATIVES

(57) **Abstract:** A method of producing substantially pure HMF, HMF esters and other derivatives from a carbohydrate source by contacting the carbohydrate source with a solid phase catalyst. A carbohydrate starting material is heated in a solvent in a column and continuously flowed through a solid phase catalyst in the presence of an organic acid, or heated with the organic acid and a solid catalyst in solution to form a HMF ester. Heating without organic acid forms HMF. The resulting product is purified by filtration to remove the unreacted starting materials and catalyst. The HMF ester or a mixture of HMF and HMF ester may then be oxidized to 2,5- furandicarboxylic acid (FDCA) by combining the HMF ester with an organic acid, cobalt acetate, manganese acetate and sodium bromide under pressure. Alternatively, the HMF ester may be reduced to form a furan or tetrahydrofuran diol.

CONVERSION OF CARBOHYDRATES TO HYDROXYMETHYLFURFURAL (HMF) AND DERIVATIVES

CROSS REFERENCE TO PROVISIONAL APPLICATION

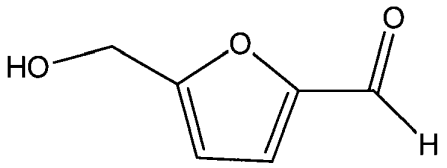
[0001] This application is based upon and claims the benefit of priority from Provisional US Patent Application 61/006,012 (Attorney Docket No. 010253-0020) filed on December 14, 2007, and from Provisional US Patent Application 60/996,946 (Attorney Docket No. 010253-0021) filed on December 12, 2007, the entire contents of which are incorporated by reference herein.

TECHNICAL FIELD

[0002] The present invention relates to a process for the synthesis and recovery of substantially pure HMF and derivatives thereof from hexose carbohydrate feedstocks such as fructose or high fructose corn syrup (HFCS). More particularly, HMF and its derivatives are synthesized, separated, and recovered via contact of the carbohydrate with strong acid cation exchange resins, such as a solid phase catalyst.

BACKGROUND

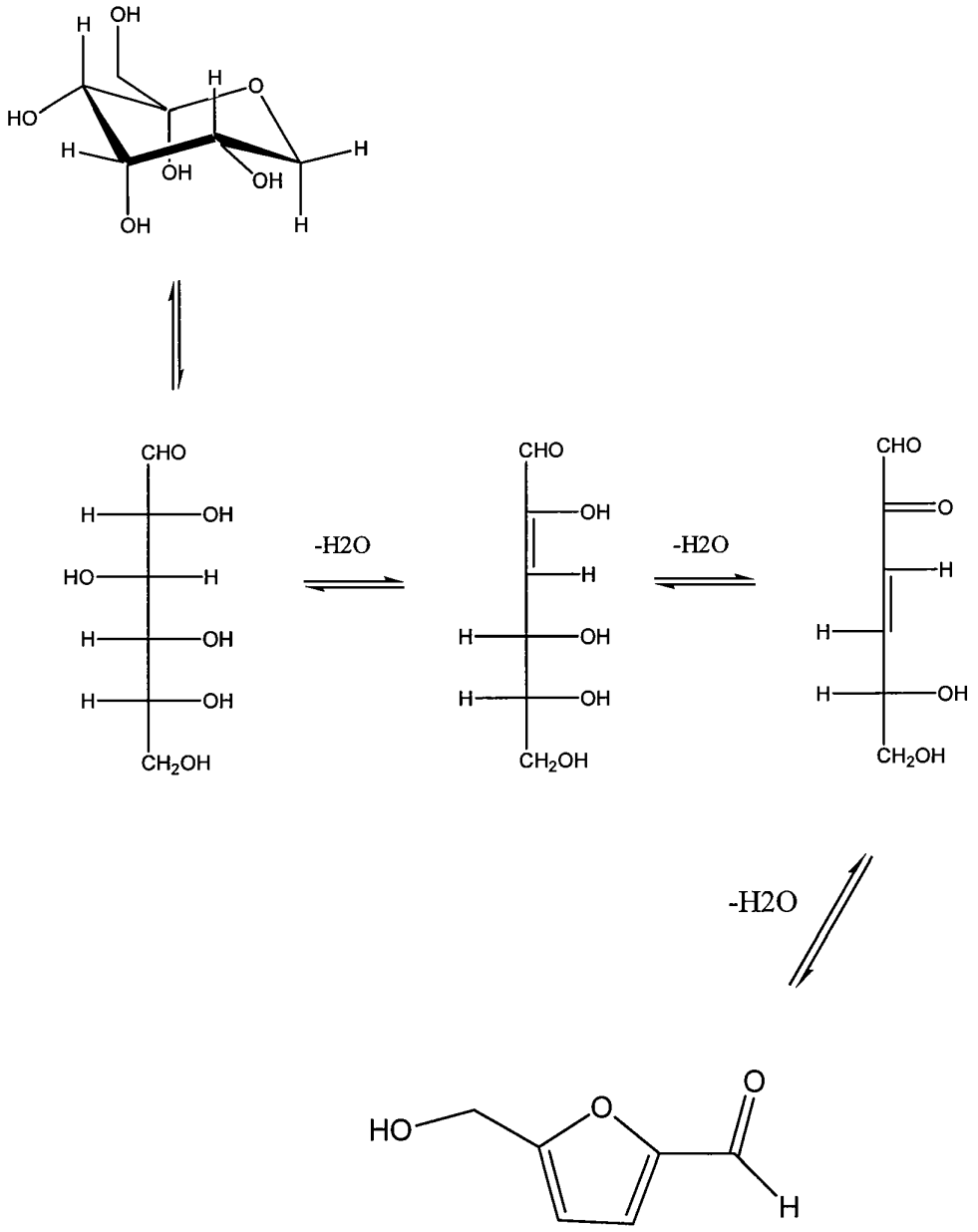
[0003] A major product in the acid-catalyzed dehydration of fructose is 2-hydroxymethyl-5-furfuraldehyde, also known as hydroxymethylfurfural (HMF). The structure of HMF is shown below:



Hydroxymethylfurfural

[0004] HMF represents one key intermediate substance readily accessible from renewable resources like carbohydrates and is a suitable starting source for the formation of various furan monomers which are used for the preparation of non-petroleum-derived polymeric materials. While not being bound by theory, it is generally believed that fructose is converted to

HMF via an acyclic pathway, although evidence also exists for the conversion to HMF via cyclic fructofuransyl intermediate pathways. Regardless of the mechanism of HMF formation, the intermediate species formed during the reaction may in turn undergo further reactions such as condensation, rehydration, reversion and other rearrangements, resulting in a plethora of unwanted side products. Below is one proposed pathway for the conversion of fructose to HMF:



[0005] HMF and 2,5-disubstituted furanic derivatives have great potential in the field of intermediate chemicals from regrowing resources. Due to its various functionalities, it has been proposed that HMF could be utilized to produce a wide range of products such as polymers, solvents, surfactants, pharmaceuticals, and plant protection agents, and has been reported to have antibacterial and anticorrosive properties. HMF is also a key component, as either a starting material or intermediate, in the synthesis of a wide variety of compounds, such as furfuryl dialcohols, dialdehydes, esters, ethers, halides and carboxylic acids.

[0006] In addition, HMF has great potential as a biofuel, which are fuels derived from biomass and are considered promising alternatives to fossil fuels. HMF is also currently under investigation as a treatment for sickle cell anemia. In short, HMF is an important chemical compound and a method of synthesis on a large scale to produce HMF absent significant amounts of impurities, side products and remaining starting material has been sought for nearly a century.

[0007] HMF is a suitable starting source for the formation of various furan monomers used in the preparation of non-petroleum-derived polymeric materials. A furan is a 5-membered heterocyclic organic compound. HMF and 2,5-disubstituted furanic derivatives have great potential in the field of intermediate chemicals from growing resources. Due to its various functionalities, it has been proposed that HMF may be utilized to produce a wide range of products such as polymers, solvents, surfactants, pharmaceuticals, and plant protection agents, and HMF has been reported to have antibacterial and anticorrosive properties.

[0008] Although preparation of HMF has been known for many years, a method which provides HMF with good selectivity and in high yields has yet to be found. Complications arise from the rehydration of HMF, which yields by-products, such as, levulinic and formic acids. Another unwanted side reaction includes the polymerization of HMF and/or fructose resulting in humin polymers, which are solid waste products. Further complications may arise as a result of solvent selection. Water is easy to dispose of and dissolves fructose, but unfortunately, low selectivity and increased formation of polymers and humin increases under aqueous conditions.

[0009] Agricultural raw materials such as starch, cellulose, sucrose or inulin are inexpensive starting materials for the manufacture of hexoses, such as glucose and fructose. As shown above, these hexoses can in turn, be converted to HMF. The dehydration of sugars to produce HMF is well known. HMF was initially prepared in 1895 from levulose by Dull (*Chem.*

Ztg., 19, 216) and from sucrose by Kiermayer (*Chem. Ztg.*, 19, 1003). However, these initial syntheses were not practical methods for producing HMF due to low conversion of the starting material to product.

[0010] Commonly used catalysts for the preparation of HMF includes cheap inorganic acids such as H_2SO_4, H_3PO_4, and HCl. These acid catalysts are used in solution and are difficult to regenerate. In order to avoid the regeneration and disposal problems, solid sulfonic acid catalysts have been used. Unfortunately, the usefulness of solid acid resins is limited because of the formation of deactivating humin polymers on the surface of the resins.

[0011] The purification of HMF has also proved to be a troublesome operation. On long exposure to temperatures at which the desired product can be distilled, HMF and impurities associated with the synthetic mixture tend to form tarry degradation products. Because of this heat instability, a falling film vacuum still must be used. Even in such an apparatus, resinous solids form on the heating surface causing a stalling in the rotor and frequent shut down time making the operation inefficient. Prior work has been performed with distillation and the addition of a non-volatile solvent like PEG-600 to prevent the buildup of solid humin polymers (Cope, U.S. Patent No. 2,917,520). Unfortunately, the use of polyglycols leads to the formation of HMF-PEG ethers.

[0012] The prior art processes also fail to provide a method for producing HMF that can be performed economically. For example, Besemer et al *Netherlands Organ. Appl. Sci. Res. Nutr. Food Res.*, describes the enzymatic synthesis of HMF esters. This process requires the use of expensive enzymes and therefore does not provide an economically feasible route to synthesizing HMF esters.

[0013] Garber et al., Canadian Patent 6 54240, describe the synthesis of the 2,5-tetrahydrofurandimethanol monoesters from HMF using excess amounts of anhydride and pyridine solvent. Reduction is performed using Raney Ni catalyst in diethyl ether. However the reference does not disclose the synthesis of HMF esters from fructose or using a carboxylic acid. Furthermore, the removal of Raney Ni catalyst is dangerous and the costs of disposing the catalyst may be burdensome.

[0014] The present disclosure, which is directed, in-part, to chromatographic processes for the synthesis and recovery of HMF from natural resources addresses and eliminates these problems and provides high purity products. In addition to HMF, studies have broadened to

include the synthesis and purification of a variety of HMF derivatives. Derivatives of particular interest include the esters of HMF, and oxidized forms (2,5-diformylfuran, 2,5-furandicarboxylic acid and acid ester), and the reduced forms (furan-2,5-dimethanol and tetrahydrofuran diol) of HMF. The esters are more stable and can be readily separated, potentially making them even more useful than HMF itself.

SUMMARY OF THE DISCLOSURE

[0015] In order to address the above mentioned problems, the disclosure provides a method of producing substantially pure HMF, HMF esters or HMF ethers from a carbohydrate source by contacting the carbohydrate source with a solid phase catalyst. In the present disclosure substantially pure means a purity of HMF of about 70% or greater, optionally about 80% or greater, or about 90% or greater.

[0016] The disclosure also provides a method of producing HMF esters from a carbohydrate source and organic acids. In one embodiment, a carbohydrate starting material is heated with an solvent in a column and continuously flowed through a solid phase catalyst in the presence of an organic acid to form a HMF ester. The solvent is removed by rotary evaporation to provide a substantially pure HMF ester. In another embodiment, a carbohydrate is heated with the organic acid and a solid catalyst in a solution to form an HMF ester. The resulting HMF ester may then be purified by filtration, evaporation, extraction, and distillation or any combination thereof.

[0017] In another embodiment, there is provided a method for oxidizing an HMF ester to 2,5-furandicarboxylic acid (FDCA) by combining the HMF ester with an organic acid, cobalt acetate, manganese acetate and sodium bromide under pressure and to obtain substantially pure FDCA after filtration and evaporation.

[0018] In another embodiment, there is provided a method of oxidizing a reaction mixture of HMF and HMF ester to FDCA by the addition of cobalt acetate, manganese acetate, and sodium bromide under pressure and heat and isolating FDCA following filtration and evaporation.

[0019] In an alternative embodiment, there is provided a method of reducing an HMF ester by the addition of an alcohol, such as ethanol, a reducing agent, under pressure, heat, filtration and evaporation.

[0020] Advantages of the methods as described herein are the high rate of conversion of carbohydrates into HMF-esters and derivatives. This results in a more stable form for HMF, and a lower cost in materials.

[0021] In another embodiment, there is provided a method for producing citrate esters from a citric acid source and an alcohol. Citric acid is esterified with an alcohol in the presence of a catalyst on a chromatography column to produce trialkyl citrate or mono- and di-esters of the citric acid. In an alternative embodiment, a fermentation broth containing primarily citric acid and residual microorganisms and fermentation side products is used to produce trialkyl citrate or mono- and di-esters of the citric acid. In another embodiment, the mono- and di-esters are recycled through the catalyst and column to generate the triester.

[0022] In yet an another embodiment, there is provided a method of preparing HMF via deacylation of an intermediate HMF ester. In one embodiment of this method, fructose is dehydrated in the presence of an organic acid and a catalyst, and separated via a chromatography column to produce the HMF ester. In an alternative embodiment, the HMF ester is deacylated with a solid phase catalyst in a chromatography column. Alternatively, the deacylation and separation of the HMF ester is performed using a metal alkoxide.

[0023] In another embodiment, there is provided a method for the synthesis of levulinic acid or levulinic ester by contacting a carbohydrate mixture with or without an organic acid present, with a solid phase catalyst under elevated temperature. HMF ethers and/or levulinate esters, which are more stable than HMF may be synthesized and purified by this process using an alcohol solvent. Advantages of the methods as described herein are the high rate of conversion of carbohydrates into substantially pure HMF, HMF esters and other HMF derivatives.

BRIEF DESCRIPTION OF THE DRAWINGS

[0024] Fig. 1 illustrates a conventional autoclave reactor;

[0025] Fig. 2 illustrates the fraction of AcHMF conversion in a conventional method using an autoclave reactor;

[0026] Fig. 3 illustrates the fraction of AcHMF conversion according to an embodiment of the present application;

[0027] Fig. 4 illustrates a graph of the products using the pulse resin test according to an embodiment of the present application; and

[0028] Fig. 5 illustrates a chromatogram according to an embodiment of the present application.

[0029] Fig. 6 is a ^{1}H NMR analysis graph showing substantially pure 4-acetoxymethylfurfural (AcHMF).

[0030] Fig. 7 is a ^{1}H NMR analysis graph showing substantially pure 5-propionoxymethylfurfual.

[0031] Fig. 8 is a ^{1}H NMR analysis graph showing substantially pure 2,5-diformylfuran, 2,5-furandicarboxylic acid (FDCA).

[0032] Fig. 9 is a HPLC trace showing the formation of 5-acetoxymethylfurfual (AcHMF) from fructose according to Example 1.

[0033] Fig. 10 is a HPLC trace showing the formation of 5-acetoxymethylfurfual (AcHMF) from fructose according to Example 2.

[0034] Fig. 11 is a HPLC trace showing the formation of showing substantially pure 5-propionoxymethylfurfual (PrHMF) from fructose.

DETAILED DESCRIPTION

[0035] The present application provides methods for synthesizing and separating hydroxymethylfurfural (HMF) and hydroxymethylfurfural esters from a carbohydrate source by contacting the carbohydrate with a solid phase catalyst.

[0036] The use of solid phase catalysts in a chromatography column to synthesize and purify HMF limits exposure time to heat and acid catalysts and enables synthesis at a lower temperature. Lower temperatures result in reduced energy costs and reduced time for heating and cooling the reaction. Non-limiting examples of solid phase catalysts that may be used in the process include acidic resins such as Amberlyst 35, Amberlyst 15, Amberlyst 36, Amberlyst 70, Amberlyst 131 (Rohm and Haas); Lewatit S2328, Lewatit K2431, Lewatit S2568, Lewatit K2629 (Bayer Company); and Dianion SK104, PK228, RCP160, Relite RAD/F (Mitsubishi Chemical America, Inc.). Other solid phase catalysts such as clays and zeolites such as CBV 3024 and CBV 5534G (Zeolyst International), T-2665, T-4480 (United Catalysis, Inc), LZY 64 (Union Carbide), H-ZSM-5 (PQ Corporation) can also be used. Acidic resins such as Amberlyst 35 are cationic, while catalysts such as zeolite, alumina, and clay are porous particles that trap

small molecules. Soluble catalysts including inorganic acids, such as H_2SO_4, H_3PO_4, HCl, and organic acids such as p-toluene sulfonic acid may also be used.

[0037] An advantage of solid phase catalysts is that they do not dissolve in solvent and remain in the column. Depending on the column size and type of solvent used, about 30-50 g of resin is packed into the column. For example, the solvent dimethylformamide (DMF) causes Amberlyst 35 resin to expand in the column, and thus only about 30 g of resin is preferably used in a 300 mm length column. Approximately 50 g of Amberlyst 35 resin is used when acetic acid is the solvent because acetic acid does not cause the resin to swell.

[0038] Because the synthesis of HMF is a dehydration reaction, a cation exchange resin having reduced water content is preferred. The presence of water in the reaction increases formation of byproducts, such as, polymers and humin. Therefore, the maximum water content of the solid phase catalyst in a column experiment is typically less than about 20%, optionally less than about 15%, or less than about 10%. Many commercially available solid phase catalysts, such as, dry Amberlyst 35 have approximately 3% water content. However, solid phase catalysts with greater than 20% may be used under certain conditions. Solid phase catalysts having a water content greater than about 20% are considered "wet resins" due to their excess water content and ability to generate water during the reaction. If the water content of the wet resin is greater than about 20%, a solvent that is miscible with water may be selected as the solvent for the reaction in order to remove water from the wet resin.

[0039] Solvents including aprotic polar solvents are preferred because they are miscible with water, which helps with the solubility of fructose and with removing water. An example of an polar aprotic solvent is acetone, which is used to wash the wet resin and dehydrate the wet resin before the reaction on the column. The resulting dehydrated resin is then dried under a vacuum prior to the reaction on the column. In addition, DMF is miscible with water and may be used as a solvent to dehydrate the wet resin on the column. The dehydration of the wet resin may include raising the temperature of the reaction or any suitable method for dehydrating the wet resin or a combination thereof.

[0040] An additional advantage of using a column in the conversion of a carbohydrate source to HMF, HMF esters or other HMF derivatives is the ability for the reaction to proceed and separate the product from the unreacted starting material or other unwanted side products that may form all in one step. As the reactants pass through the column, differences in the

retention of the products from the starting materials will allow for these to separate after the reaction occurs in the column. As a result, the product will elute from the column in a substantially pure form.

[0041] Any carbohydrate source can be used, although fructose is the preferred source. Suitable carbohydrate sources that can be used for preparing HMF derivatives include, but are not limited to, hexose, fructose syrup, crystalline fructose, and process streams from the crystallization of fructose. Suitable mixed carbohydrate sources may comprise any industrially convenient carbohydrate source, such as corn syrup. Other mixed carbohydrate sources include, but are not limited to, hexoses, fructose syrup, crystalline fructose, high fructose corn syrup, crude fructose, purified fructose, high fructose corn syrup refinery intermediates and by-products, process streams from crystallizing fructose or glucose or xylose, and molasses, such as soy molasses resulting from production of soy protein concentrate, or a mixture thereof.

[0042] Synthesis of HMF esters from a carbohydrate source and organic acids or acid salts provides a direct pathway for a series of useful molecules. Aliphatic and aromatic esters of HMF are commercially available and have a variety of uses. The present process has many advantages in the production of HMF esters. Suitable carbohydrate sources that can be used for preparing HMF esters include, but are not limited to hexose, fructose syrup, crystalline fructose, and process streams from the crystallization of fructose. Suitable mixed carbohydrate sources may comprise any industrially convenient carbohydrate sources, such as corn syrup. The mixed carbohydrate sources include, but are not limited to, hexoses, fructose syrup, crystalline fructose, high fructose corn syrup, crude fructose, purified fructose, high fructose corn syrup refinery intermediates and by-products, process streams from crystallizing fructose or glucose or xylose, and molasses, such as soy molasses resulting from production of soy protein concentrate. In addition to the wide variety of starting sources, the process can be performed with various organic acids including, but not limited to acetic, propionic, butyric, citric or diacids.

[0043] The disclosed process minimizes and/or eliminates the formation of humins and polymeric by-products. If the reaction is not complete and HMF and or unreacted carbohydrate is observed in the reaction mixture, these components may be separated into the aqueous phase and recycled. In addition, the solvents can be recovered and recycled. This method is more beneficial than other methods as it eliminates the difficult task of isolating substantially pure HMF for use as a starting source. It is a simple process, leading to a substantially pure product,

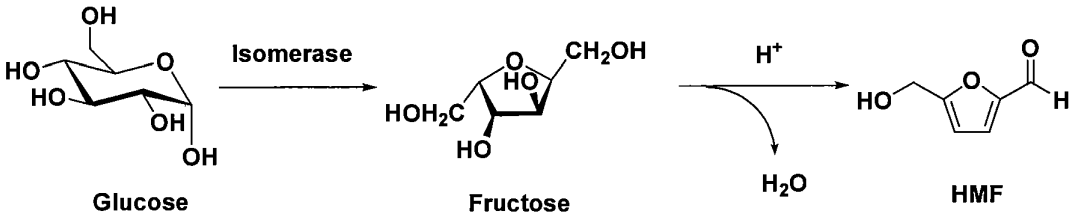
which can be used as a feeding source in the transformation of HMF esters to a variety of useful derivatives and end products. The purity of the product will vary according to the particular reagents and conditions used.

[0044] Additionally, the present application provides methods for synthesizing citrate esters, and methods of synthesizing levulinic acid or levulinic esters using a heated solid phase catalyst in a column, and subsequent purification of the resulting products in a column. In an example of levulinate ester synthesis, a carbohydrate mixture in solution (e.g. 25% fructose in Acetic acid) is passed through a heated column that is packed with a strong acid cationic resin (e.g. Amberlyst 35). The temperature of the column is maintained at 75C and the flow rate is set to 5mL/min. Upon the initial pass both Ac-HMF and Ac-levulinate acid are formed. Subsequent passes generate a higher ratio of Ac-levulinate to Ac-HMF. The concentration of acetic acid may range from >99% reagent grade acetic acid to 1% acetic acid in aqueous solution.

[0045] For the synthesis of a levulinic acid, an example synthesis involves a carbohydrate mixture in solution (e.g. 25% fructose in aqueous or DMF solution) is passed through a heated column that is packed with a strong acid cationic resin (e.g. Amberlyst 35). The temperature of the column is maintained at 100 °C and the flow rate is set to 5mL/min. Upon the initial pass both HMF and levulinic acid are formed. Subsequent passes generate a higher ratio of levulinic acid to HMF.

[0046] Various HMF esters are selectively prepared by modifying the choice of solvent used in the processes of the invention. The amount of purification and fractionation of the end product depends on the type of solvent used. For example, a continuous flow of a solution of fructose dissolved in acetic acid through a solid phase catalyst results in the formation of substantially pure acetylated HMF (AcHMF), which is a desired end product. HMF ethers and/or levulinate esters, which are more stable than HMF may be synthesized and purified by this process using an alcohol solvent.

[0047] AcHMF has a lower boiling point than HMF, and is isolated by vacuum distillation. AcHMF is also more stable than HMF. AcHMF is not appreciably soluble in water making extraction in a nonpolar organic solvents an effective method of purification. AcHMF crystallizes in nonpolar solvents at low temperatures (*e.g.*, hexanes around 0-25°C). Moreover, HMF decomposes upon heating and produces by-products that are not easily isolated or removed.



Synthesis of HMF from glucose and fructose

[0048] For one embodiment of the present disclosure, the set up of the chromatography column including a column packed with solid phase catalysts may be a continuous separation where the fructose, HMF, and solvent are fed through the packed column multiple times and/or the speed of additional reactants is varied. This purification technique can include Simulated Moving Bed chromatography, which is a chromatographic technique based on a flow of liquid (mobile phase) moving countercurrent to a constant flow of solid (stationary phase). Countercurrent flow enhances the potential for separation and, hence, makes the process more efficient. It also allows a continuous flow of feed material to be separated, and utilizes less solvent and improves the throughput of the equipment compared to traditional batch chromatography. Alternatively, the system may include, but is not limited to, a simulated moving bed, continuous set up (CSEP), or a continuous flow pipe system.

[0049] For example, in Simulated Moving Bed chromatography, the solutes move faster than the bed and are eluted at the top of the column, whereas those moving slower than the bed are brought down by the moving bed below the feed point. A section of the bed below the feed point is then heated to increase the elution rate of the solutes and any solute moving faster than the bed can be eluted through a side tube by a second flow of gas while those solutes still moving at a slower rate than the bed continue to move down the column in the stationary phase. The higher fractions can be removed in the same way by a section of the column heated to an even higher temperature. In order to heat the column in Simulated Moving Bed chromatography, a jacketed column allows the mixture to pass heating fluid, such as, propylene glycol, around the resin bed.

[0050] In most of the reactions carried out by the methods described herein, the catalyst provides the necessary acidity for the reaction to occur. Ion exchange resins are synthetic polymers capable of combining or exchanging ions in a surrounding solution and are used

primarily for chromatography of organic molecules. Advantages of ion exchange resins include long lifetime, reusable, high selectivity and catalytic ability, stability, and can be used in both aqueous and non-aqueous conditions (Rohm and Haas).

[0051] A first type of column that may be used in the disclosed methods is a gravity flow column. The reaction mixture is loaded onto the top of the column, which is heated by a jacket, then allowed to slowly flow through the resin, allowing maximum retention time on the column. The flow rate in a gravity flow column is generally less than 1.0 mL/min, or typically 0.1 – 1.0 mL/min. Once the product is fed through the column, it may be reloaded for a second pass, to produce a higher yield of the desired product and increased purity by allowing more time on the resin. The samples of the gravity column are collected in a large fraction or multiple fractions and analyzed for yield.

[0052] Another column that may be used is a pulse column. The starting material is loaded on top of the resin and a mechanical pump is used to pump solvent onto the column to maintain a constant flow rate. The product is collected from the bottom of the column in timed fractions, and, therefore, may be analyzed for retention time, separation of products and reactants, as well as total yield.

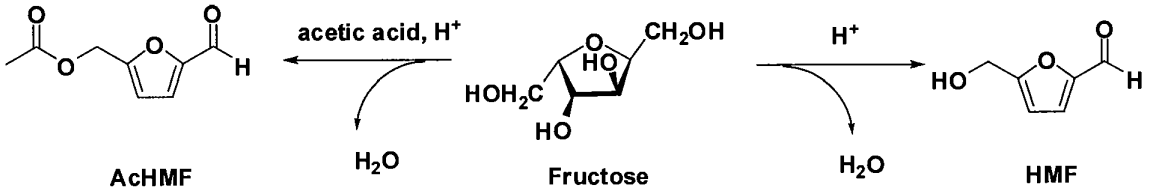
[0053] For the column experiments, depending on the type of column used and the stability of the solvent, the temperature may be varied from about 70°C to about 125°C, optionally from about 75°C to about 95°C, or optionally from about 80° C to about 90°C. The flow rate is typically kept at about 1.0 ml/minute to allow maximum retention time on the column and flow through to the top of the column. However, for gravity columns, the flow rate may be kept lower, since it is not dependent on a mechanical source. Higher temperatures may be used.

[0054] In one embodiment of the present application, Amberlyst 35 is packed in a heated glass jacketed column with fructose solubilized with acetic acid. The use of a continuous moving bed minimizes exposure time of the product to resin since it passes through the column by stream, rather than batch. The resulting product is highly purified acetyl HMF.

[0055] In another embodiment of the invention, a continuous flow process enables the formation of citrate esters. The starting material, citric acid may be in solution with the solvent or in a fermentation broth containing solvent. An alcohol solvent is used to obtain either substantially pure trialkyl citrate or the mono- and di-esters of citric acid. Factors such as type of

solvent, type of resin, time on column, and/or temperature determine whether mono- and di-esters are formed or whether substantially pure trialkyl citrate is formed. If mono- and di-esters are obtained, the mixture can be recycled in the column to generate the substantially pure triester.

[0056] Another aspect of this invention allows for the chromatographic synthesis, separation, and purification of an anhydrosugar alcohol from a selected sugar alcohol or monoanhydrosugar alcohol starting material using a solid phase catalyst. More specifically, isosorbide is synthesized, separated, and purified from a sorbitol source and a solid phase catalyst in a chromatography column. The intermediate compound, sorbitan, or mixtures of sorbitan/isosorbide/sorbitol can be recovered and recycled until substantially pure isosorbide is obtained.



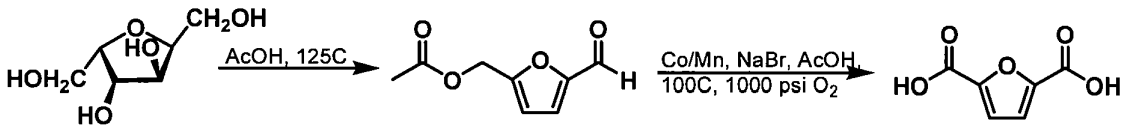
Synthesis of HMF from AcHMF and Fructose

[0057] In another aspect of the invention, there is provided a process for preparing HMF via an intermediate HMF ester. Fructose is preferably used as a carbohydrate source and is subjected to dehydration in the presence of an organic acid and catalyst in a chromatography column to provide a HMF ester. The HMF ester is then subjected to deacylation upon treatment with a base. The basic material may include, but is not limited to, a solid phase catalyst such as resins, clays, aluminas, and zeolites. The saponification of the ester can be carried out in any manner, so long as it can bring the starting material and basic catalyst are brought into mutual contact. For example, this reaction can be carried out batchwise or continuously in a fluidized bed, tubular reactor, coil, column, or pipe. Deacylation of AcHMF to HMF can also be achieved using a metal alkoxide. This method may be preferable due to the fact that HMF esters are generally more stable than HMF.

[0058] In another embodiment of forming a HMF ester, a carbohydrate is combined with an organic acid and solid phase catalyst in solution. The solution is heated to a temperature

between about 100 to about 140°C, for between about 90 to about 150 minutes, resulting in the formation of an HMF ester. The HMF ester can be further purified via column chromatography, precipitation and recrystallization or combinations thereof. The synthesized HMF ester is filtered and/or evaporated, e.g.,. via rotary evaporation to remove the catalyst and organic acid. HMF ester can be collected by extraction with methyl t-butyl ether. The crude material can be subjected to simple distillation (115°C, 3 torr) to provide the HMF ester as crystals. Alternatively, the filtered HMF ester may then be extracted with a suitable solvent, such as hot hexane, after the evaporation of the solvent.

[0059] In one embodiment for the forming of FDCA, a reaction mixture containing a HMF ester such as, but not limited to, 5-acetoxymethylfurfural (AcHMF), or organic acid such as, but not limited to, acetic acid, along with cobalt acetate, manganese acetate and sodium bromide is placed in a reactor and subjected to between about 400 to about 1000 psi, or between about 500 to about 800 psi oxygen at between about 85 °C to about 110 °C, or between at about 100°C for between about 100 to about 150 minutes. The solution is then filtered and the solvent evaporated to obtain 2,5-Furandicarboxylic acid (FDCA).



Fructose AcHMF FDCA

[0060] In an embodiment for reducing an HMF ester, a reaction mixture containing AcHMF and ethanol is charged in a reaction vessel. The G-69B catalyst obtained from Sud Chemie, Louisville, KY is added to the vessel and the vessel is purged with hydrogen, preferably at 4X500 psi with stirring, preferably at 1000 rpm. The vessel is then pressurized, preferably to 600 psi and heated to a temperature above 150°C, preferably to 170°C with continual stirring. After about an hour the reaction is heated to 195°C for about an hour and then allowed to cool to room temperature. The catalyst is then removed via vacuum filtration. The solvent is preferably removed, for example, by rotary evaporation. Products of reduction include but are not limited to 2,5-furandimethanol (FDM) and tetrahydrofuran diol (THF-diol).

[0061] As an example of the versatility of the HMF-esters, a reaction mixture containing a combination of HMF and an HMF-ester can be oxidized to the single product, FDCA. 2,5-

Furandicarboxylic acid (FDCA) is formed from a mixture of predominantly HMF ester with residual HMF in an organic acid. The mixture is reacted in an organic acid, for example acetic acid along with cobalt acetate, manganese acetate and sodium bromide. The entire mixture can be pressurized with oxygen or air and heated to at least 100°C for over an hour. The resulting solution is filtered and evaporated and the FDCA is isolated.

[0062] HMF can be synthesized from a fructose source through and HMF ester intermediate. For example, fructose is subjected to dehydration in the presence of an organic acid and catalyst to provide an HMF ester. The HMF ester is subjected to deacylation upon treatment with a base. The basic material may include, but is not limited to, a solid phase catalyst such as resins, clays, aluminas, and zeolites. The saponification of the ester can be carried out in any manner, so long as it can bring the material and basic catalyst into mutual contact. For example, this reaction can be carried out batchwise or continuously in a fluidized bed, tubular reactor, coil, column, or pipe. Deacylation of AcHMF to HMF can also be achieved using a metal alkoxide.

EXAMPLES

EXAMPLE 1

[0063] The conventional method for synthesizing HMF and AcHMF from fructose includes a batch reaction on an autoclave (Parr) reactor followed by a separate step for purification. As shown in Fig. 1, the temperature control 2 controls both the temperature of the reaction mixture and the heating jacket in the autoclave reactor 1. A heating jacket (not shown) is used to heat the reaction. The pressure gauge 3 shows if the reaction is creating gas, or monitors the pressure on the vessel if it was applied. The speed control 4 is for the stirring mechanism. Stirring is necessary to keep the reaction mixture in contact with all necessary materials. The sample port 5 allows the scientist to retrieve samples and specific points during the reaction to monitor for progress. Reactants must be in solution before being put into a reactor vessel.

[0064] The reaction conditions for the autoclave reactions were varied to test the effect of different reaction conditions. The reactions were performed in the 100 mL capacity Parr reactor. About 20 grams of High fructose corn syrup (HFCS) is added to each reaction. Three different temperatures: 110°, 125°, and 150° Celsius were tested with and without an ion exchange resin. The resin of choice was Amberlyst 35 exchange. Results are shown in Table 1.

Table 1

Comparative Example	**#1**	**#2**	**#3**	**#4**	**#5**
Temperature (°C)	110	125	125	150	150
Resin	yes	no	Yes	yes	No
Fructose added (g)	5.6998	5.7995	6.7799	6.7799	6.7799
Moles	.03164	0.0322	0.0376	0.0376	0.0376
Fructose out (g)	0.62	0.64	1.34	0.55	2.07
Moles	0.0034	0.00354	0.0074	0.0030	0.0115
HMF out (g)	2.13	1.22	1.60	1.48	0.79
Moles	0.0169	0.0097	0.0127	0.0118	0.0063
AcHMF out (g)	0.18	0.54	0.49	1.48	0.13
Moles	0.001053	0.0033	0.0029	0.0088	0.0007
HFCS added (g)	20	20.35	23.79	23.79	23.79
Fructose added (g)	5.6998	5.7995	6.7799	6.7799	6.7800
AcHMF yield	0.0332	0.1000	0.0764	0.2331	0.0197
HMF yield	0.5348	0.3005	0.3378	0.3125	0.1663
Fructose yield	0.1080	0.1101	0.1974	0.0812	0.3048

[0065] As can be seen in Table 1 above, AcHMF was formed in the largest amount in Comparative Example #4 at 150°C using a resin in an autoclave reactor as shown in Fig. 2. In a

100 mL capacity Parr reactor, 6.7799 g of fructose and 23.79 g of HFCS in solution was heated to 150°C. The AcHMF yield was 0.2331 in Comparative Example #4.

[0066] In these examples of Example 1, a first method of production of substantially pure HMF uses packed columns. Two different types of columns were used to produce and purify HMF. Each column, however, was packed with a cation exchange resin, which had been soaked in the desired solvent, then loaded to a heated column once the resin had appropriately expanded. A cation exchange resin is an ion exchange resin that adds protons to the reaction. The water content of the resin used ranged from less than about 20%, to less than about 10% in order to prevent the rehydration of HMF. The results of the columns are shown in Fig. 3. The major product was HMF with the remainder being unreacted fructose. In this example, the Amberlyst 35 exchange resin performed best of all columns tested, including the gravity flow columns.

[0067] Maximal reaction conditions included 80° C in a column packed with the Amberlyst 35 ion exchange resin and acetic acid, providing a yield of AcHMF is approximately 0.395 moles. Columns performed more consistently than the conventional batch reactions, which may be due to a number of reasons. Product stays longer on the resin in a chromatography column, and a larger amount of the resin remains in the column than in the batch reactions. There is also better control of the temperature in the column due to the heated jacketed column.

[0068] Samples marked with (*) in Table 2 are comparative examples. The comparative examples include batch reactions. The temperatures in the autoclave varied from approximately 105°C – 155° C in the course of the reaction. The reaction mixture from the columns could also be fed back through for another pass, which will further increase the yield of the desired product. The yield is lower during a batch reaction when it is run at a higher temperature, such as 125° C, compared to a pulse reaction at 80° C and a gravity column reaction at 90° C. The yield in the batch reaction using Amberlyst 35 having a temperature of 150° C is increased due to the high temperature.

Table 2

Type of Reaction	Temperature (°C)	Type of Resin (if used)	AcHMF yield
Pulse	80	Amberlyst 35	0.394914426
Gravity Column	90	Amberlyst 35	0.117696633
Gravity Column	90	Amberlyst 35	0.130347712
Batch Reaction*	110	Amberlyst 35	0.033283962
Batch Reaction*	125	No resin	0.100020489
Batch Reaction*	125	Amberlyst 35	0.076392506
Batch Reaction*	150	Amberlyst 35	0.233076043
Batch Reaction*	150	No resin	0.019697

EXAMPLE 2

[0069] The graph shown in Fig. 4 illustrates the results of the pulse resin test at 80°C where the flow rate was set at about 1.48 mL/min. for the first 33 minutes and about 1.36 mL/min. after the 33rd minute until completion of the reaction at about 63 minutes. After approximately 30 minutes, 0.07 moles of AcHMF was eluted, compared to a mole fraction of approximately 0.0006 for the starting material, fructose. The byproducts, levulinic and formic acids, are also measured. No measurable levulinic acid was found during the synthesis of AcHMF.

Table 3

Time (min.)	Sample weight (g)	Percent water in sample	Fraction of water in sample	Weight of water in sample (g)	moles of water in sample
1	0.5060	2.28	0.0228	0.0115368	0.000640364
9	0.5189	1.39	0.0139	0.00721271	0.00040035
12	0.5059	1.44	0.0144	0.00728496	0.000404361
15	0.4982	1.30	0.0130	0.0064766	0.000359492
18	0.5071	1.26	0.0126	0.00638946	0.000354655
21	0.5062	1.24	0.0124	0.00627688	0.000348406
24	0.4122	1.40	0.0140	0.0057708	0.000320315
27	0.4782	1.46	0.0146	0.00698172	0.000387529
30	0.5051	1.37	0.0137	0.00691987	0.000384096
33	0.5005	1.34	0.0134	0.0067067	0.000372264
50	0.5065	1.16	0.0116	0.0058754	0.000326121
63	0.5105	1.95	0.0195	0.00995475	0.000552551
Time (min.)	**Sample weight (g)**	**HMF in sample (g/kg)**	**Fraction of HMF in sample**	**Weight of HMF in sample (g)**	**moles of HMF in sample**
1	0.5060	0.00	0.00000	0	0
9	0.5189	0.00	0.00000	0	0
12	0.5059	1.49	0.00149	0.000752273	5.96514E-06
15	0.4982	0.23	0.00023	0.000116081	9.20459E-07
18	0.5071	0.28	0.00028	0.000143002	1.13393E-06
21	0.5062	0.12	0.00012	5.87192E-05	4.65613E-07
24	0.4122	0.27	0.00027	0.000109233	8.66161E-07
27	0.4782	0.25	0.00025	0.000117159	9.2901E-07
30	0.5051	0.28	0.00028	0.000141933	1.12546E-06
33	0.5005	0.36	0.00036	0.000181682	1.44064E-06
50	0.5065	0.00	0.00000	0	0
63	0.5105	0.00	0.00000	0	0

Time (min.)	Sample weight (g)	Acetic Acid in sample (g/kg)	Fraction of Acetic Acid in sample	Weight of Acetic Acid in sample (g)	moles of Acetic Acid in sample
1	0.5060	960.17	0.9602	0.48584349	0.008090326
9	0.5189	967.75	0.9678	0.502167551	0.008362156
12	0.5059	896.88	0.8969	0.453733616	0.007555628
15	0.4982	924.96	0.9250	0.460815072	0.00767355
18	0.5071	907.85	0.9078	0.460369214	0.007666125
21	0.5062	846.98	0.8470	0.428742288	0.00713947
24	0.4122	871.93	0.8719	0.359409958	0.005984939
27	0.4782	880.87	0.8809	0.421230121	0.007014376
30	0.5051	876.47	0.8765	0.442705502	0.007371987
33	0.5005	857.03	0.8570	0.428941013	0.007142779
50	0.5065	903.94	0.9039	0.45784713	0.007624127
63	0.5105	980.54	0.9805	0.50056567	0.008335482
Time (min.)	Sample weight (g)	Fructose in sample (g/kg)	Fraction of Fructose in sample	Weight of Fructose in sample (g)	moles of Fructose in sample
1	0.5060	0.00	0.0000	0	0
9	0.5189	0.04	0.0000	1.91993E-05	1.0657E-07
12	0.5059	0.17	0.0002	8.54971E-05	4.74569E-07
15	0.4982	0.12	0.0001	6.02822E-05	3.34609E-07
18	0.5071	0.00	0.0000	1.5213E-06	8.44429E-09
21	0.5062	0.18	0.0002	9.26346E-05	5.14188E-07
24	0.4122	0.45	0.0004	0.000184666	1.02502E-06
27	0.4782	0.28	0.0003	0.000132461	7.35255E-07
30	0.5051	0.64	0.0006	0.000323264	1.79434E-06
33	0.5005	1.03	0.0010	0.000513513	2.85036E-06
50	0.5065	0.30	0.0003	0.00015195	8.4343E-07
63	0.5105	0.00	0.0000	0	0

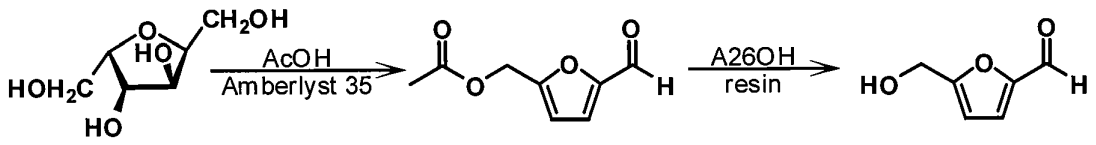
Time (min.)	Sample weight (g)	Formic in sample (g/kg)	Fraction of Formic in sample	Weight of Formic in sample (g)	moles of Formic in sample
1	0.5060	0.69	0.0007	0.000351164	7.62975E-06
9	0.5189	0.64	0.0006	0.000331577	7.20419E-06
12	0.5059	0.75	0.0007	0.000377401	8.19981E-06
15	0.4982	1.28	0.0013	0.0006367	1.38336E-05
18	0.5071	4.05	0.0040	0.00205122	4.45669E-05
21	0.5062	2.56	0.0026	0.001296884	2.81775E-05
24	0.4122	3.16	0.0032	0.001301728	2.82827E-05
27	0.4782	3.39	0.0034	0.001621098	3.52217E-05
30	0.5051	6.29	0.0063	0.003175564	6.89956E-05
33	0.5005	6.45	0.0065	0.003229727	7.01724E-05
50	0.5065	1.74	0.0017	0.00088283	1.91813E-05
63	0.5105	0.70	0.0007	0.000354798	7.7087E-06
Time (min.)	Sample weight (g)	Levulinic in sample (g/kg)	Fraction of Levulinic in sample	Weight of Levulinic in sample (g)	moles of Levulinic in sample
1	0.5060	0.00	0.0000000	0	0
9	0.5189	0.00	0.0000000	0	0
12	0.5059	0.00	0.0000000	0	0
15	0.4982	0.00	0.0000000	0	0
18	0.5071	0.00	0.0000000	0	0
21	0.5062	0.00	0.0000000	0	0
24	0.4122	0.00	0.0000000	0	0
27	0.4782	0.00	0.0000000	0	0
30	0.5051	0.00	0.0000000	0	0
33	0.5005	0.00	0.0000000	0	0
50	0.5065	0.00	0.0000000	0	0
63	0.5105	0.00	0.0000000	0	0

Time (min.)	Sample weight (g)	AcHMF in sample (g/kg)	Fraction of AcHMF in sample	Weight of AcHMF in sample (g)	moles of AcHMF in sample
1	0.5060	0.00	0.0000000	0	0
9	0.5189	0.22	0.0002200	0.000114158	6.75092E-07
12	0.5059	5.01	0.0050070	0.002533041	1.49795E-05
15	0.4982	15.21	0.0152050	0.007575131	4.47968E-05
18	0.5071	22.98	0.0229820	0.011654172	6.89188E-05
21	0.5062	27.97	0.0279720	0.014159426	8.3734E-05
24	0.4122	31.95	0.0319470	0.013168553	7.78744E-05
27	0.4782	36.23	0.0362280	0.01732423	0.00010245
30	0.5051	37.00	0.0370010	0.018689205	0.000110522
33	0.5005	36.52	0.0365190	0.01827776	0.000108088
50	0.5065	0.35	0.0003540	0.000179301	1.06033E-06
63	0.5105	0.00	0.0000000	0	0

EXAMPLE 3

PREPARATION OF HMF FROM FRUCTOSE USING A HMF ESTER INTERMEDIATE

[0070] This example illustrates the use of the present methods to deprotect HMF ester to provide substantially pure HMF. The feed material was prepared and placed in a vial of methanol and Amberlyst A26OH resin obtained from Rohm and Haas Company (Woodridge, IL). Amberlyst A26OH resin is a strong base, type 1, anionic, macroreticular polymeric resin based on crosslinked styrene divinylbenzene copolymer containing quaternary ammonium groups. After sitting at room temperature for about 5 minutes, the material was analyzed by thin layer chromatography (tlc) to show deacylation. The solid yield was about 85% HMF with about 8% AcHMF determined by a Shimadzu QP-2010 GC Mass spectrometer. The chromatogram is shown in Fig. 5. The remaining material was residual methanol. Heating the methanol solution with a heat gun to 60 °C for less than 5 minutes converted the remaining AcHMF to HMF. Alternatively, passing the product through the chromatography column with a solid phase catalyst would convert the remaining AcHMF to HMF.



EXAMPLE 4

PREPARATION OF 5-ACETOXYMETHYLFURFURAL (AcHMF) FROM FRUCTOSE

[0071] Crystalline fructose (18g) is placed in a 100 mL reaction vessel with acetic acid (50 g) and Amberlyst 15 resin (4 g). The solution is heated to 110°C for 3 hours with samples collected regularly. Analytical results and HPLC trace confirm the formation of AcHMF. Analysis of the product mixture indicated a solution of 9.89% AcHMF and 5.14% HMF for a 41% yield of AcHMF and 28% yield of HMF. The yields disclosed herein are exemplary only and do not necessarily reflect the optimal yields possible when reaction conditions are optimized. HPLC trace confirmed formation of AcHMF, (see Fig. 4).

EXAMPLE 5

SYNTHESIS AND PURIFICATION OF AcHMF FROM FRUCTOSE

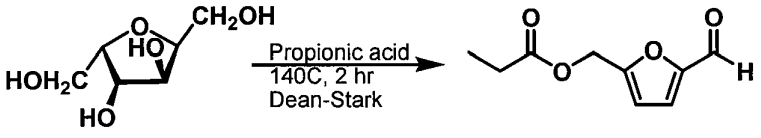
[0072] Crystalline fructose (180 g) is placed in a 1 L reaction vessel with acetic acid (500 g) and Amberlyst 15 resin (40 g). The solution is heated to 125 °C for 2 hours. NMR and analytical results indicates the formation of AcHMF. The solution is filtered to remove the resin catalyst and acetic acid is removed by rotary evaporation. AcHMF is collected by extraction with methyl t-butyl ether. The crude material is subjected to simple distillation (115°C, 3 torr) to provide AcHMF as orange crystals. HPLC trace confirms AcHMF formation, (see Fig. 5), and ^{1}H NMR analysis indicates substantially pure AcHMF. NMR (δ, 1 H): 9.70 (s, 1.0 H); 7.40 (s, 1.0 H); 6.80 (s, 1.0 H); 5.10 (s, 2.0 H); 2.10 (s, 3.0H). See Fig. 1.

EXAMPLE 6

SYNTHESIS OF PROPIONOXYMETHYLFURFURAL (PrHMF) FROM FRUCTOSE

[0073] Crystalline fructose (40 g), propionic acid (100 mL), and dry Amberlyst 15 resin is placed in a 500 mL three neck round bottom flask equipped with a Dean-Stark trap, magnetic stir bar, and temperature probe. The reaction mixture is allowed to heat to 130°C for 30 minutes.

HPLC trace indicates rapid conversion to the HMF ester. Resin is removed by filtration, the solvent evaporated and the crude oil is extracted with hot hexane. Evaporation of the hexane extract provides yellow oil which ^{1}H NMR identified as substantially pure 5-propionoxymethylfurfural. Calculations indicate the overall yield of PrHMF from fructose is 28%. Reaction conditions have not been optimized. HPLC trace confirms PrHMF formation , (see Fig. 6) and ^{1}H NMR analysis indicates PrHMF formation (δ, 1 H): 9.70 (s, 1.0 H); 7.20 (s, 1.0 H); 6.60 (s, 1.0 H); 5.06 (s, 2.0H); 2.47 (t, 2.0 H); 1.05 (d, 3.0H). See Fig. 2.



Fructose **PrHMF**

EXAMPLE 7

OXIDATION OF 5-ACETOXYMETHYLFURFURAL (AcHMF) TO 2,5-FURANDICARBOXYLIC ACID (FDCA)

[0074] A reaction mixture containing AcHMF (5.0 g), acetic acid (50 mL), cobalt acetate (0.132 g), manganese acetate (0.135 g), and sodium bromide (0.114 g) is placed in a 100 mL reactor and subjected to 500-800 psi oxygen at 100°C for 2 hours. Upon filtration and evaporation of the solvent, 2.53 g of tan solid is isolated. ^{1}H NMR indicates substantially pure FDCA. The overall yield of FDCA from AcHMF is 54%. See Fig. 3.

EXAMPLE 8

REDUCTION OF 5-ACETOXYMETHYLFURFURAL (AcHMF)

[0075] A reaction mixture containing AcHMF (5.0 g) and ethanol (50 mL) is charged into a 100 mL reaction vessel. The G-69B catalyst may be obtained from Sub Chemie, Louisville, KY (0.50 g) is added to the vessel. The vessel is purged with hydrogen (4X500 psi) with stirring (1000 rpm). The vessel is then pressurized to 600 psi and heated to 170°C with continual stirring. After 1 hour, the reaction is allowed to heat to 195°C for an additional hour. The reaction is then allowed to cool to room temperature and the catalyst removed by vacuum filtration. Most of the solvent is removed by rotary evaporation to provide yellow oil (16.97 g).

The UV analysis (λ=284 nm) does not show the presence of AcHMF, indicating complete conversion of AcHMF to 2,5-dihydroxymethyltetrahydrofuran.

EXAMPLE 9

OXIDATION OF A MIXTURE OF HMF AND HMF ESTER TO FDCA

[0076] A product mixture composed of predominantly HMF ester with residual HMF in acetic acid is subjected to oxidation with the addition of cobalt acetate, manganese acetate, and sodium bromide. This mixture is pressurized with oxygen and heated to over 100°C for over an hour. Upon filtration and evaporation, a product of FDCA is isolated.

EXAMPLE 10

PREPARATION OF HMF FROM FRUCTOSE

[0077] To a jacketed column was added a slurry of Amberlyst 35 dry resin (40 g) in DMF. The column was heated by an oil circulating bath at 95 °C. The resin was washed with anhydrous DMF. The level of DMF was then lowered to the top of the resin. The column was then loaded with 150 g of 30% fructose in DMF. The fructose solution was passed slowly through the resin over a period of about 1 hour two times. Tlc and NMR analysis indicate 68% yield of HMF.

[0078] It will be understood that certain of the above-described structures, functions and operations of the above-described preferred embodiments are not necessary to practice the present disclosure and are included in the description simply for completeness of an exemplary embodiment or embodiments. In addition, it will be understood that specifically described structures, functions, and operations set forth in the above-referenced patents can be practiced in conjunction with the present disclosure, but they are not essential to its practice.

[0079] The embodiments of the disclosure may be practiced otherwise than as specifically described without actually departing from the spirit and scope of the present disclosure. The yields disclosed herein are exemplary only and do not necessarily reflect the optimal yields possible when reaction conditions are optimized.

CLAIMS

What is claimed is:

1. A method for synthesizing HMF by contacting a carbohydrate source with a solid phase catalyst.

2. The method of claim 1, wherein the step of contacting the carbohydrate source further includes the steps of:

forming a solution of the carbohydrate source in an solvent;

passing the solution through a solid phase catalyst in a column; and

eluting said HMF from the column.

3. The method of claim 2, wherein said solvent is DMF.

4. A method of preparing HMF esters comprising:

combining materials comprising a carbohydrate source, a carboxylic acid, with or without an added catalyst to provide a reaction mixture;

heating said reaction mixture to a temperature and for a time sufficient to promote an acid-catalyzed reaction of said carbohydrate source to form a product mixture; and

isolating an HMF ester from said product mixture.

5. The method of claim 4, wherein the step of heating said reaction mixture further includes the steps of:

passing the solution through a solid phase catalyst in a column, and

eluting said HMF ester.

6. The method of claim 4, wherein said HMF ester is isolated from the product mixture by a process selected from the group consisting of filtration, evaporation, extraction, and distillation.

7. The method of claim 4, wherein said solvent is a polar, aprotic solvent.

8. The method of claim 2, wherein the column is heated to a temperature of from about 70 °C to about 125 °C.

9. The method of claim 4, wherein temperature at which the reaction mixture is heated is from about 100 °C to about 140 °C.

10. A method of forming FDCA by reacting the HMF ester formed in claim 4 with an organic acid, cobalt acetate, manganese acetate and sodium bromide under elevated pressure and temperature for a period of time sufficient to convert substantially all of the HMF ester to FDCA.

11. The method of claim 10, wherein the pressure of the reaction is from about 400 psi to about 1000 psi.

12. A method of reducing the HMF ester formed in claim 4 comprising the step of heating a solution of the ester in a solvent, with catalyst, under elevated pressure and temperature, for a time sufficient to reduce the ester.

13. The method of claim 12, wherein the pressure is about 600 psi and the temperature is about 170 °C.

14. A method for synthesizing HMF by contacting an HMF ester with an anionic solid phase catalyst.

15. A method for synthesizing citrate esters by contacting a solution having a citrate source and an alcohol with a solid phase catalyst by eluting the solution through a column packed with the solid phase catalyst to obtain an eluant.

16. The method of claim 15 further comprising the steps of:

collecting the eluant from the column; and

passing the eluant through the column a second time to generate a tri-substituted citrate ester.

17. A method for synthesizing a levulinic acid comprising the steps of:

dissolving a carbohydrate source in a solution,

passing the solution containing the carbohydrate through a column containing a solid phase catalyst, and

eluting said levulinic acid from the column to obtain an eluant.

18. The method of claim 17, further comprising the steps of:

after passing the solution containing the carbohydrate through the column,

collecting the eluant containing the reaction product, and

after collecting the eluant, passing the eluant through the column.

19. A method for synthesizing a levulinate ester comprising the steps of:

dissolving a carbohydrate source in a solution containing acetic acid,

passing the solution containing the carbohydrate through a column containing a solid phase catalyst,

and eluting said levulinate ester from the column to obtain an eluant.

20. The method of claim 19, further comprising the steps of:

after passing the solution containing the carbohydrate through the column,

collecting the eluant containing the reaction product,

after collecting the eluant, passing the eluant through the column.

21. The method of claim 19, wherein the concentration of acetic acid in the solution is greater than about 75%

22. A method for synthesizing HMF by contacting a fructose source with an organic acid and solid phase catalyst in a column to produce HMF ester, and

deacylating the HMF ester.

23. The method of claim 22, wherein the HMF ester is deacylated with a metal oxide.

24. The method of claim 2, wherein the HMF is purified during the reaction by passing the solution through the column.

25. The method of claim 5, wherein the HMF ester is purified during the reaction by passing the solution through the column.

26. The method of claim 17, wherein the citrate ester is purified during the reaction by passing the solution through the column.

27. The method of claim 19, wherein the levulinic acid is purified during the reaction by passing the solution through the column.

28. The method of claim 21, wherein the levulinic ester is purified during the reaction by passing the solution through the column.

29. A method for synthesizing a levulinate ester comprising the steps of:

dissolving a carbohydrate source in a solution containing an alcohol,

passing the solution containing the carbohydrate through a column containing a solid phase catalyst,

and eluting said levulinate ester from the column to obtain an eluant containing a reaction product.

30. The method of claim 29, further comprising the steps of:

after obtaining the eluant containing the reaction product, passing the eluant through the column.

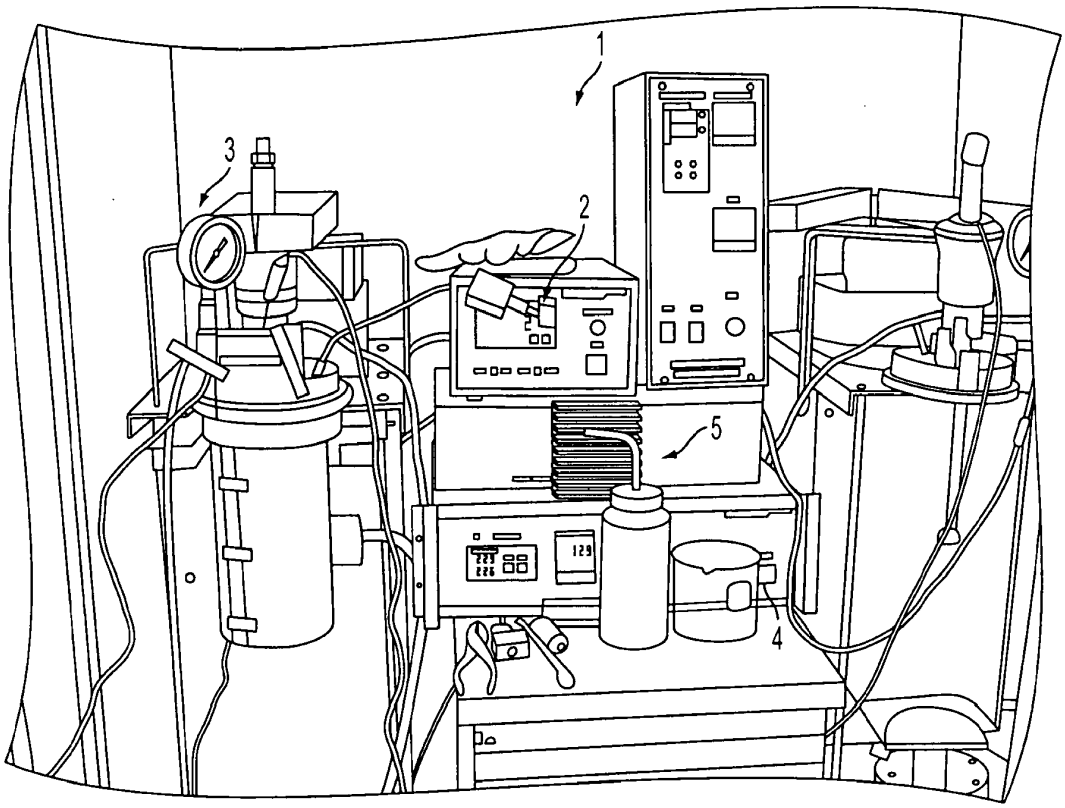


FIG. 1
PRIOR ART

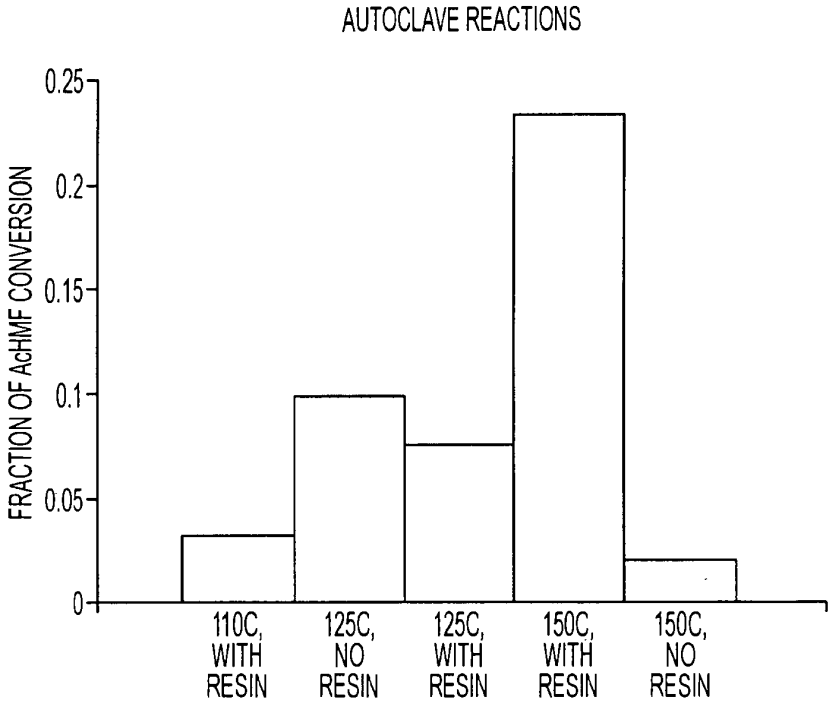


FIG. 2
PRIOR ART

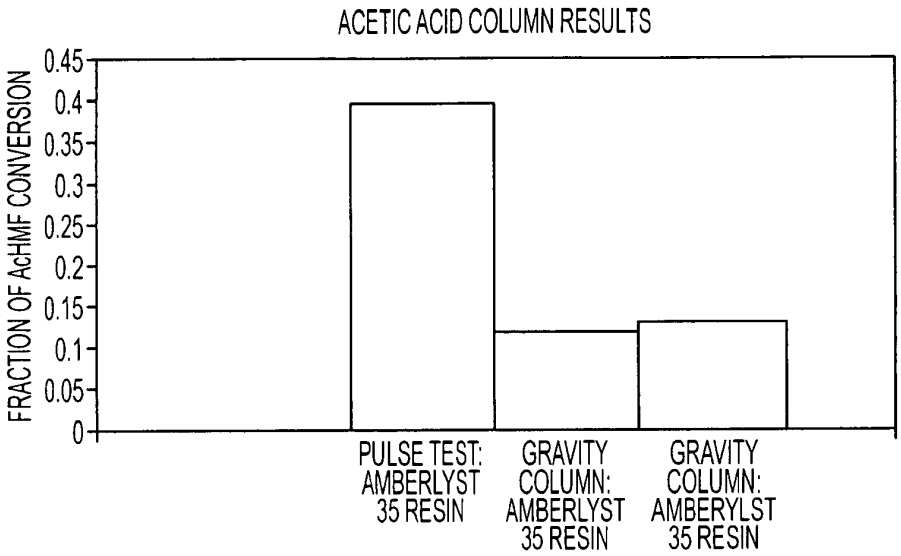

ACETIC ACID COLUMN RESULTS
FRACTION OF AcHMF CONVERSION
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
PULSE TEST: AMBERLYST 35 RESIN
GRAVITY COLUMN: AMBERLYST 35 RESIN
GRAVITY COLUMN: AMBERYLST 35 RESIN

FIG. 3

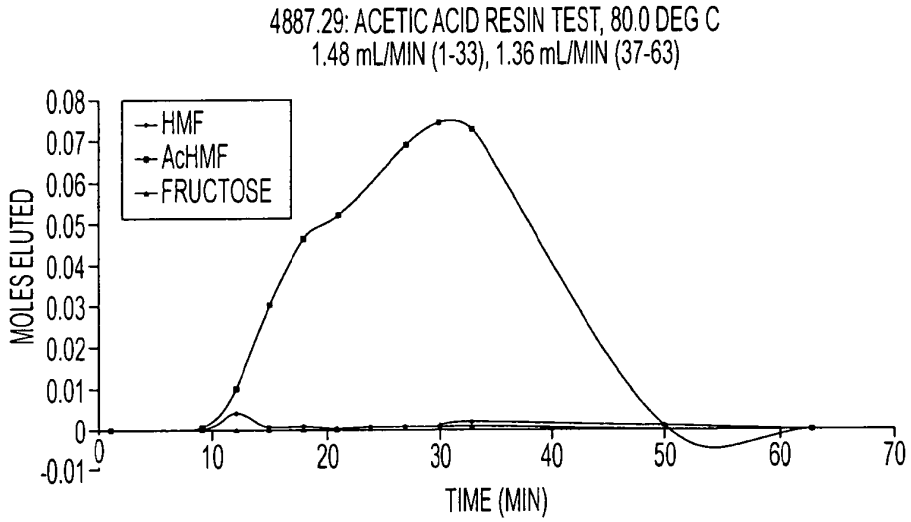

4887.29: ACETIC ACID RESIN TEST, 80.0 DEG C
1.48 mL/MIN (1-33), 1.36 mL/MIN (37-63)
HMF
AcHMF
FRUCTOSE
MOLES ELUTED
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
-0.01
0
10
20
30
40
50
60
70
TIME (MIN)

FIG. 4

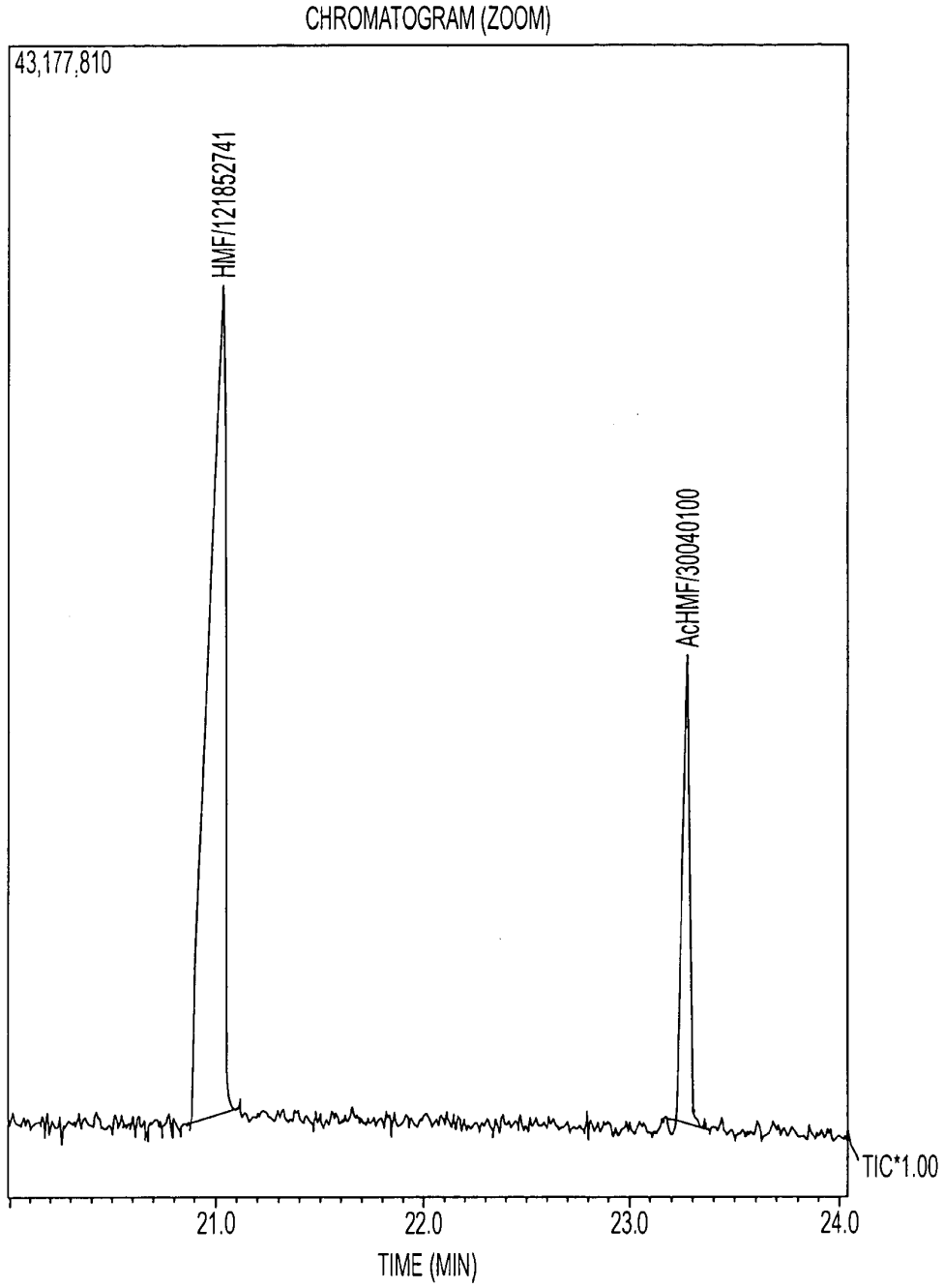

CHROMATOGRAM (ZOOM)
43,177,810
HMF/121852741
AcHMF/30040100
TIC*1.00
21.0
22.0
23.0
24.0
TIME (MIN)

FIG. 5

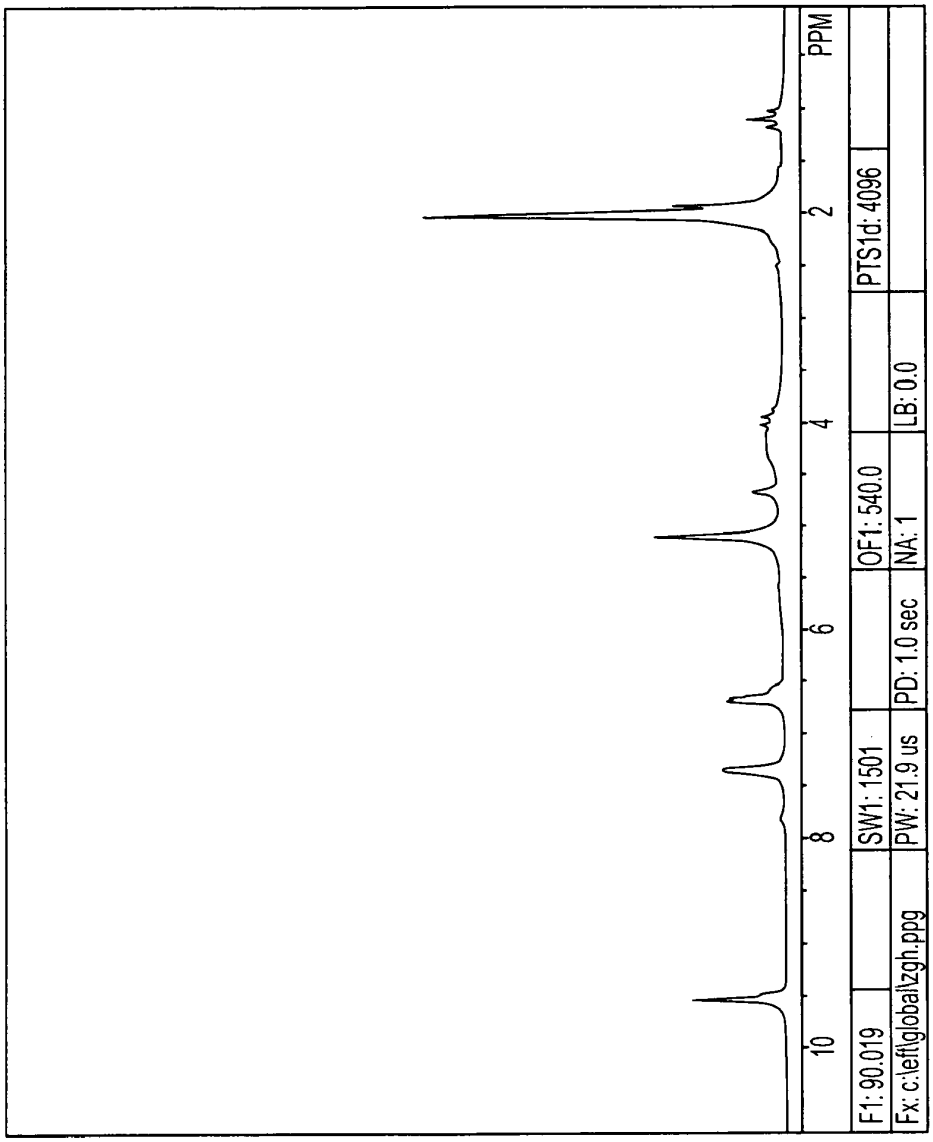

PPM
10
8
6
4
2
F1: 90.019
SW1: 1501
OF1: 540.0
PTS1d: 4096
Fx: c:\efflglobal\zgh.ppg
PW: 21.9 us
PD: 1.0 sec
NA: 1
LB: 0.0

FIG. 6

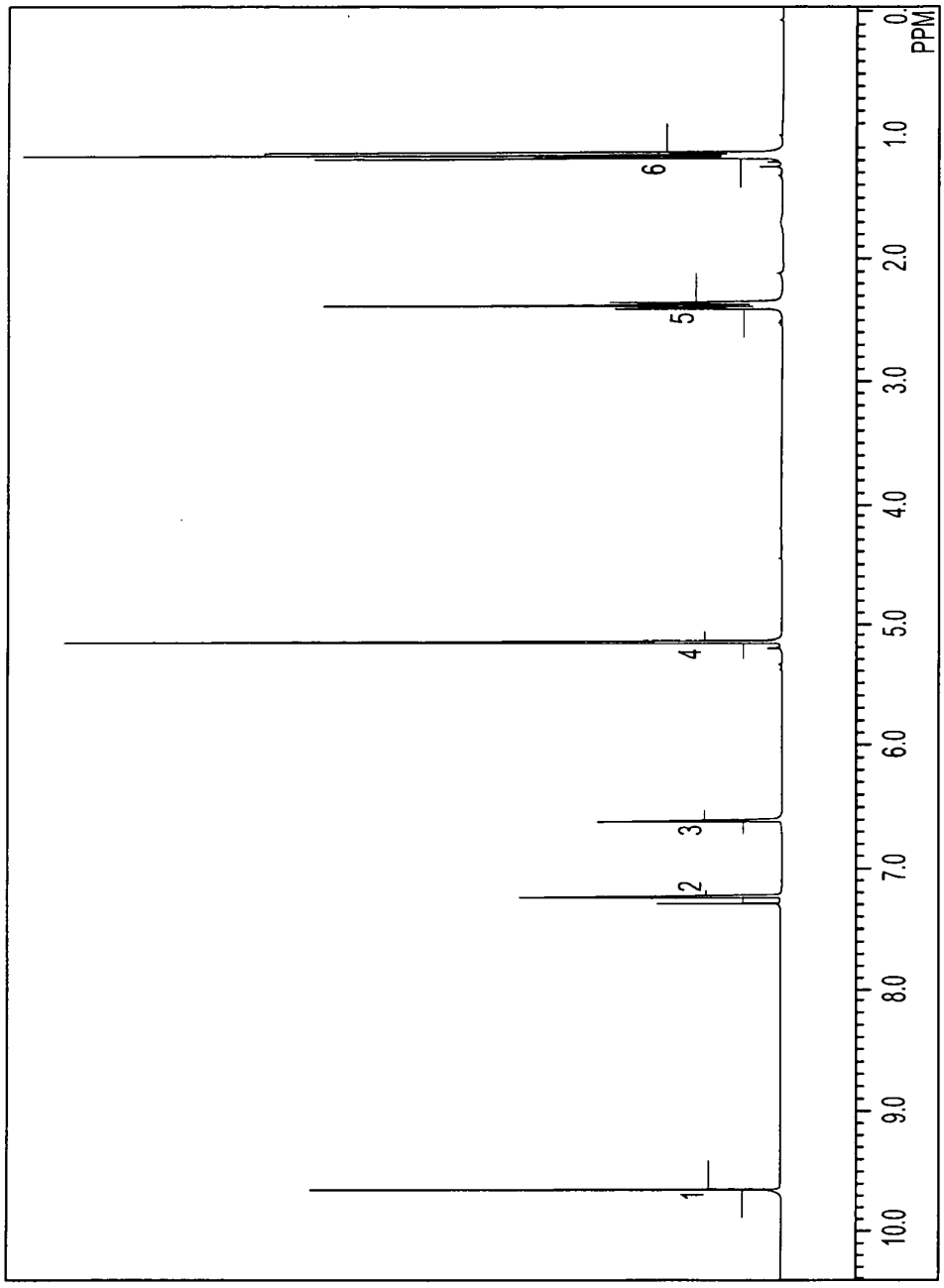


FIG. 7

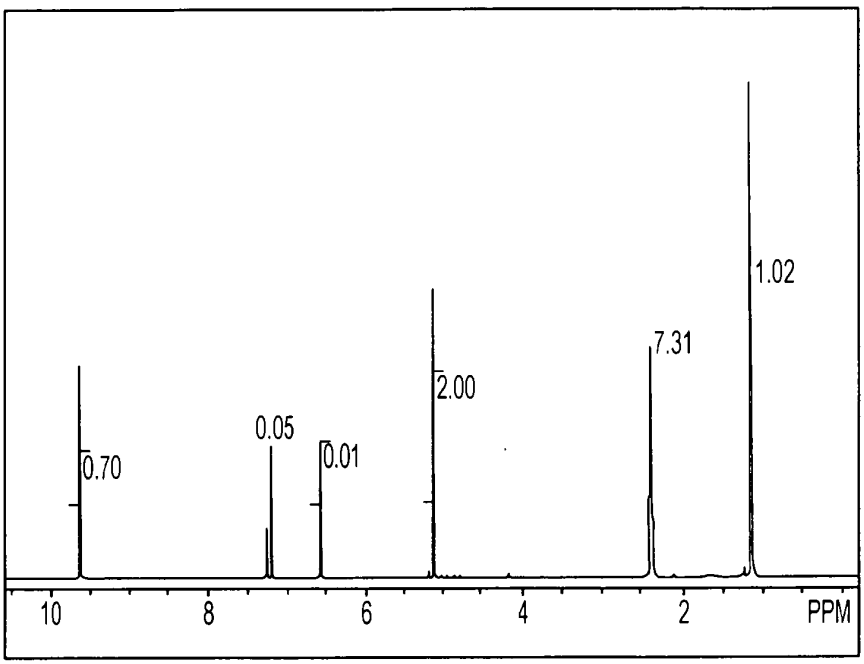


FIG. 8

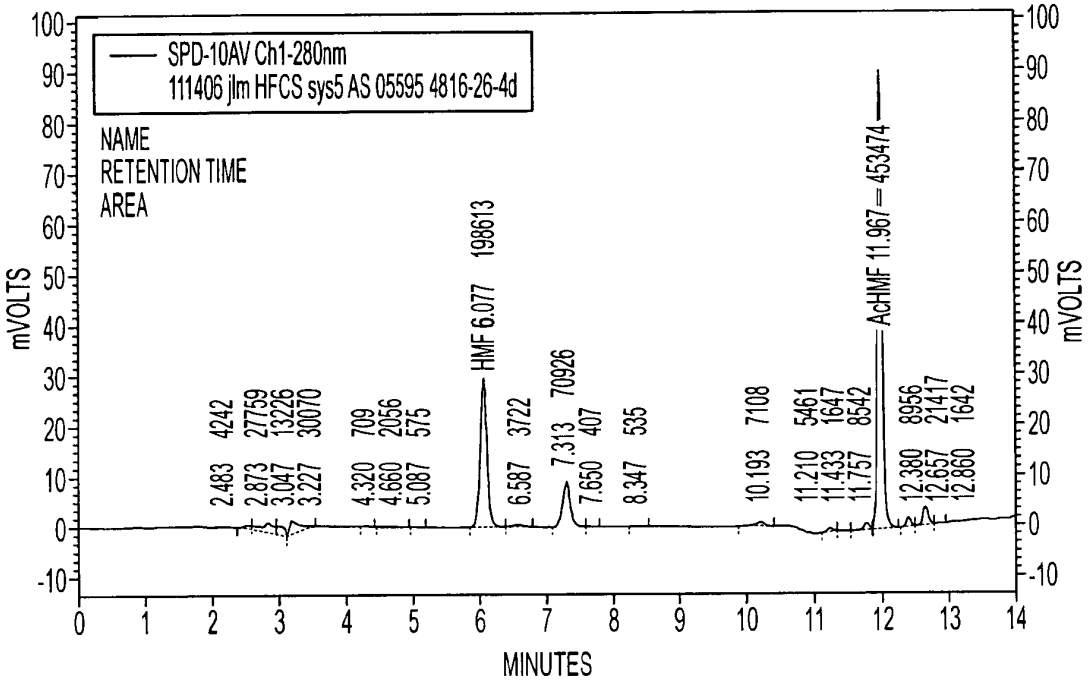

SPD-10AV Ch1-280nm
111406 jlm HFCS sys5 AS 05595 4816-26-4d
NAME
RETENTION TIME
AREA
HMF 6.077 198613
AcHMF 11.967 = 453474
2.483 4242
2.873 27759
3.047 13226
3.227 30070
4.320 709
4.660 2056
5.087 575
6.587 3722
7.313 70926
7.650 407
8.347 535
10.193 7108
11.210 5461
11.433 1647
11.757 8542
12.380 8956
12.657 21417
12.860 1642
mVOLTS
MINUTES

FIG. 9

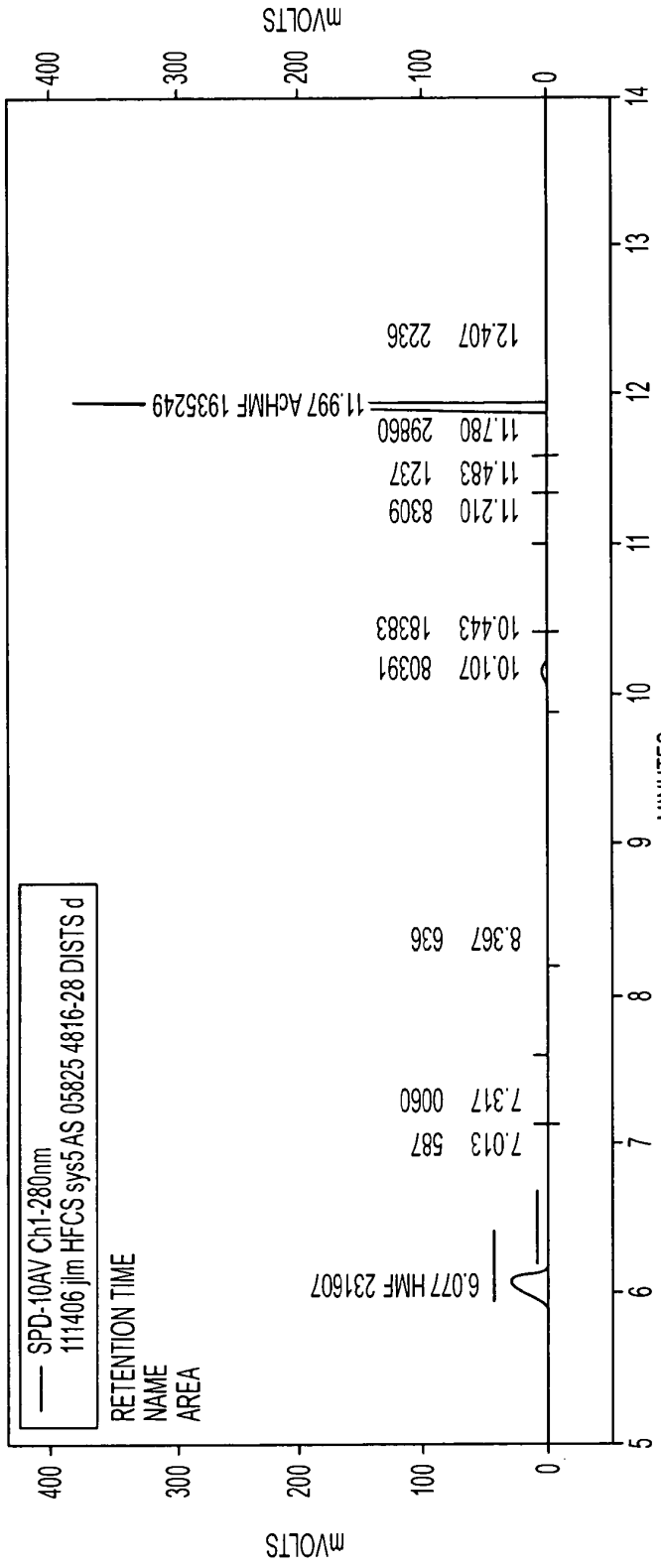

mVOLTS
400
300
200
100
0
SPD-10AV Ch1-280nm
111406 jlm HFCS sys5 AS 05825 4816-28 DISTS d
RETENTION TIME
NAME
AREA
6.077 HME 231607
7.013 587
7.317 0060
8.367 636
10.107 80391
10.443 18383
11.210 8309
11.483 1237
11.780 29860
11.997 AcHMF 1935249
12.407 2236
5
6
7
8
9
10
11
12
13
14
MINUTES

FIG. 10

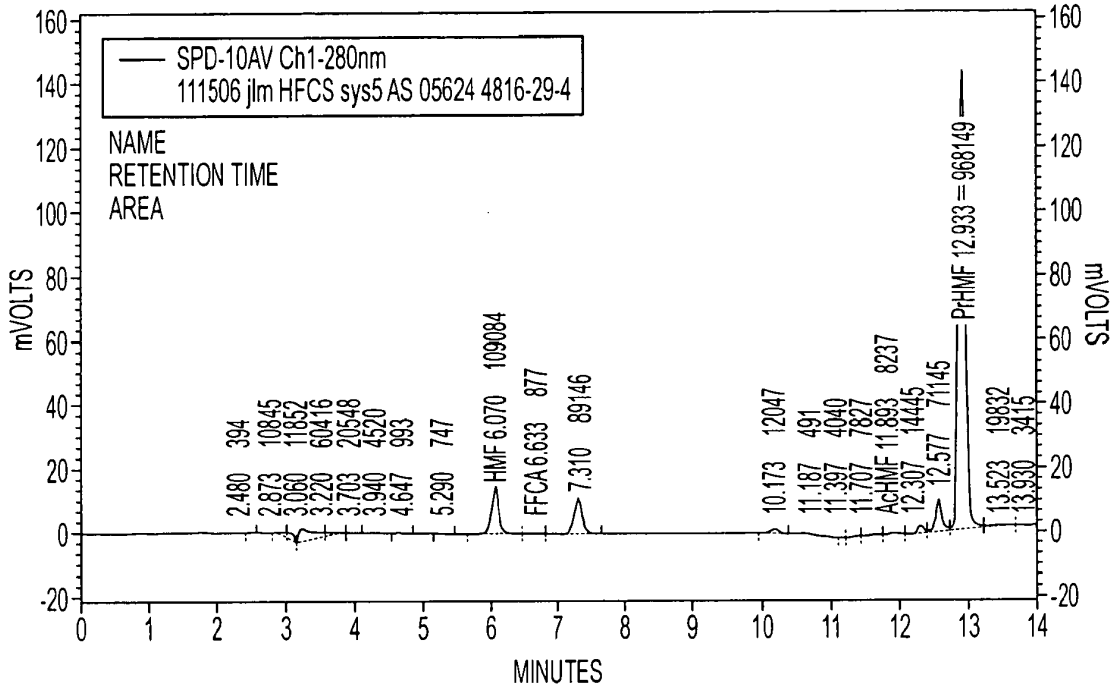

SPD-10AV Ch1-280nm
111506 jlm HFCS sys5 AS 05624 4816-29-4
NAME
RETENTION TIME
AREA
mVOLTS
MINUTES
HMF 6.070 109084
FFCA 6.633 877
7.310 89146
PrHMF 12.933 = 968149
AcHMF 11.883 14445
12.577 71145
12.307 8237
11.707 7827
11.397 4040
11.187 491
10.173 12047
13.523 19832
13.930 3415
2.480 394
2.873 10845
3.060 11852
3.220 60416
3.703 20548
3.940 4520
4.647 993
5.290 747

FIG. 11

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
18 June 2009 (18.06.2009)

PCT

(10) International Publication Number
WO 2009/076627 A3

(51) **International Patent Classification**:
C07D 307/50 (2006.01) *C07D 307/54* (2006.01)

(21) **International Application Number**:
PCT/US2008/086659

(22) **International Filing Date**:
12 December 2008 (12.12.2008)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
60/996,946 12 December 2007 (12.12.2007) US
61/006,012 14 December 2007 (14.12.2007) US

(71) **Applicant** *(for all designated States except US)*: **ARCHER DANIELS MIDLAND CO** [US/US]; 4666 Faires Parkway, Decatur, IL 62525 (US).

(72) **Inventors; and**
(75) **Inventors/Applicants** *(for US only)*: **SANBORN, Alexandra** [US/US]; 1865 Tiffany Avenue, Lincoln, IL 62656 (US). **HOWARD, Stephen** [US/US]; 1649 E Barber Road, Sherman, IL 62684 (US).

(74) **Agent**: **MCQUEEN, Nathaniel, D.**; McDermott Will & Emery, 600 Thirteenth Street, NW, Washington, DC 20005 (US).

(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(88) **Date of publication of the international search report**:
15 October 2009

WO 2009/076627 A3

(54) **Title**: CONVERSION OF CARBOHYDRATES TO HYDROXY-METHYLFURFURAL (HMF) AND DERIVATIVES

(57) **Abstract**: A method of producing substantially pure HMF, HMF esters and other derivatives from a carbohydrate source by contacting the carbohydrate source with a solid phase catalyst. A carbohydrate starting material is heated in a solvent in a column and continuously flowed through a solid phase catalyst in the presence of an organic acid, or heated with the organic acid and a solid catalyst in solution to form a HMF ester. Heating without organic acid forms HMF. The resulting product is purified by filtration to remove the unreacted starting materials and catalyst. The HMF ester or a mixture of HMF and HMF ester may then be oxidized to 2,5- furandicarboxylic acid (FDCA) by combining the HMF ester with an organic acid, cobalt acetate, manganese acetate and sodium bromide under pressure. Alternatively, the HMF ester may be reduced to form a furan or tetrahydrofuran diol.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/086659

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D307/50 C07D307/54

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2006/063220 A (ARCHER DANIELS MIDLAND CO [US]; SANBORN ALEXANDRA J [US]) 15 June 2006 (2006-06-15) page 17, lines 22-30; page 11, lines 6-27; claims 1-17; examples 1-8	1-3,8,24
X	TONI EL HAJJ ET AL: "Synthèse de l'hydroxyméthyl-5 furanne carboxaldéhyde-2 et de ses dérivés par traitement acide de sucres sur résines échangeuses d'ions" BULLETIN DE LA SOCIETE CHIMIQUE DE FRANCE, vol. 5, 1987, pages 855-860, XP009002108 ISSN: 0037-8968 pages 855-857 up to "2. RÉACTIONS D'OXYDATION ..."; pages 858-859, "PRÉPARATION DE L'HYDROMÉTHYL-5 FURANNE CARBOXALDÉHYDE-2".	1-3,8,24

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 August 2009	02/09/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Ladenburger, Claude

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GARY A. HALLIDAY ET AL: "One-pot, two-step, practical catalytic synthesis of 2,5-diformylfuran from fructose" ORGANIC LETTERS, vol. 5, no. 11, 2003, pages 2003-2005, XP002528380 pages 2004-2005, "Step 1: Fructose to HMF"; Scheme 1	1-3,8,24
X	FEDERICA BENVENUTI ET AL: "Heterogeneous zirconium and titanium catalysts for the selective synthesis of 5-hydroxymethyl-2-furaldehyde from carbohydrates" APPLIED CATALYSIS A: GENERAL, vol. 193, no. 1-2, 2000, pages 147-153, XP004272187 ISSN: 0926-860X the whole document	1-3,8,24
X	WO 2007/104515 A (AVANTIUM INT BV [NL]; GRUTER GERARDUS JOHANNES MARIA [NL]; DAUTZENBERG) 20 September 2007 (2007-09-20) page 2, line 18 - page 4, line 27; claims 1-3,7-9,15,16 page 6, line 30 - page 8, line 2	4-7,9,25
X	GB 925 812 A (MERCK & CO INC) 8 May 1963 (1963-05-08) claim 3; example II	4-7,9,25
P,X	EP 1 958 944 A (EVONIK DEGUSSA GMBH [DE]) 20 August 2008 (2008-08-20) page 5, paragraph 23; claims 1-7; example 1A -& US 2008/200698 A1 (REICHERT DIETMAR [DE] ET AL) 21 August 2008 (2008-08-21)	4-7,9,25

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/086659

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

1-9,24,25

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-3,8,24

   one-step synthesis of HMF with a carbohydrate source and a solid phase catalyst

   ---

2. claims: 4-7,9,25

   preparation of HMF esters with a carbohydrate source, a carboxylic acid and optionally a catalyst

   ---

3. claims: 10,11

   preparation of FDCA from HMF esters

   ---

4. claims: 12,13

   reduction of HMF esters

   ---

5. claim: 14

   synthesis of HMF with an HMF ester and an anionic solid phase catalyst

   ---

6. claims: 15,16,26

   synthesis of citrate esters with a citrate source, an alcohol and a solid phase catalyst packed in a column

   ---

7. claims: 17,18,27

   synthesis of levulinic acid with a carbohydrate source and a solid phase catalyst contained in a column

   ---

8. claims: 19-21,28

   synthesis of levulinate esters with a carbohydrate source, acetic acid and a solid phase catalyst contained in a column

   ---

9. claims: 22,23

   two-step synthesis of HMF with a fructose source, an organic acid and a solid phase catalyst in a column

   ---

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

10. claims: 29,30

synthesis of levulinate esters with a carbohydrate source, an alcohol and a solid phase catalyst contained in a column

---

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/086659

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006063220 A	15-06-2006	AU 2005313945 A1	15-06-2006
		AU 2005314681 A1	15-06-2006
		CA 2590082 A1	15-06-2006
		CA 2590123 A1	15-06-2006
		EP 1838688 A2	03-10-2007
		EP 1838689 A2	03-10-2007
		US 2006128843 A1	15-06-2006
		US 2006128977 A1	15-06-2006
		US 2006128844 A1	15-06-2006
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		CN 101421259 A	29-04-2009
		EP 1834951 A1	19-09-2007
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		EP 2053047 A1	29-04-2009
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GB 925812 A	08-05-1963	NONE	
EP 1958944 A	20-08-2008	CA 2620992 A1	16-08-2008
		CN 101245055 A	20-08-2008
		DE 102007007629 A1	21-08-2008
		US 2008200698 A1	21-08-2008
US 2008200698 A1	21-08-2008	CA 2620992 A1	16-08-2008
		CN 101245055 A	20-08-2008
		DE 102007007629 A1	21-08-2008
		EP 1958944 A1	20-08-2008

OXIDATION OF FURFURAL COMPOUNDS

Patent Number:	WO 2010/132740 A2
Inventor(s):	SANBORN ALEXANDRA [US]
Applicant(s):	ARCHER DANIELS MIDLAND CO [US]; SANBORN ALEXANDRA [US]
Classification:	**- international:** C07D307/46; C07D307/48 **- cooperative:** C07D307/68
Application number:	WO2010US34856 20100514
Priority number(s):	US20090178301P 20090514
Also published as:	WO2010132740 (A3) US2012059178 (A1) US2012059178 (A1) US8558018 (B2) US8558018 (B2) EP2862858 (A1) EP2784069 (A1) EP2430010 (A2) EP2430010 (A4) EP2430010 (B1) CN102459214 (A) CN102459214 (A) CN102459214 (B) CN102459214 (B)

Abstract of WO 2010/132740 A2

The disclosure pertains to a process for oxidation of furan aldehydes such as 5-hydroxymethyl)furfural (HMF) and derivatives thereof such as 5-(alkoxymethyl)furfural (AMF), 5-(aryloxymethyl)furfural, 5-(cycloalkoxy-methyl)furfural and 5-(alkoxycarbonyl)furfural compounds in the presence of dissolved oxygen and a Co(II), Mn(II), Ce(III) salt catalyst or mixtures thereof. The products from HMF can be selectively chosen to be predominantly 2,5- diformylfuran (DFF), particularly by inclusion of an aliphatic ketone, like methyl ethyl ketone, or can be further oxidized to 2,5-furandicarboxylic acid (FDCA) by the omission of methyl ethyl ketone and inclusion of bromide..; When the reactant is an ether derivative of HMF the products are surprisingly ester derivatives where either both the ether and aldehyde functional groups have been oxidized or just the ether function group thereby producing one or both of 5-ester-furan-2- acids (i.e., 5-alkoxycarbonylfurancarboxylic acids) or 5-ester-furan aldehydes, (i.e.,- alkoxycarbonylfurfurals a. k. a, 5 -(alkoxycarbonyl)furfural). (I)

(I)

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
18 November 2010 (18.11.2010)

PCT

(10) International Publication Number
WO 2010/132740 A2

(51) International Patent Classification:
C07D 307/48 (2006.01) *C07D 307/46* (2006.01)

(21) International Application Number:
PCT/US2010/034856

(22) International Filing Date:
14 May 2010 (14.05.2010)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/178,301 14 May 2009 (14.05.2009) US

(71) Applicant *(for all designated States except US)*: **ARCHER DANIELS MIDLAND COMPANY** [US/US]; 4666 Faries Parkway, Decatur, IL 62526 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **SANBORN, Alexandra** [US/US].

(74) Agent: **ROBERTS, Mark W.**; ARCHER DANIELS MIDLAND COMPANY, 4666 Faries Parkway, Decatur, Illinois 62526 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

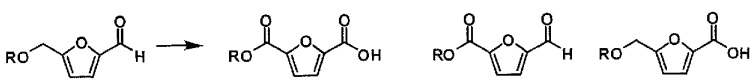
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

— *of inventorship (Rule 4.17(iv))*

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

(54) **Title**: OXIDATION OF FURFURAL COMPOUNDS



(I)

(57) **Abstract**: The disclosure pertains to a process for oxidation of furan aldehydes such as 5- hydroxymethyl)furfural (HMF) and derivatives thereof such as 5-(alkoxymethyl)furfural (AMF), 5-(aryloxymethyl)furfural, 5-(cycloalkoxy-methyl)furfural and 5-(alkoxycarbonyl)furfural compounds in the presence of dissolved oxygen and a Co(II), Mn(II), Ce(III) salt catalyst or mixtures thereof. The products from HMF can be selectively chosen to be predominantly 2,5- diformylfuran (DFF), particularly by inclusion of an aliphatic ketone, like methyl ethyl ketone, or can be further oxidized to 2,5-furandicarboxylic acid (FDCA) by the omission of methyl ethyl ketone and inclusion of bromide.. When the reactant is an ether derivative of HMF the products are surprisingly ester derivatives where either both the ether and aldehyde functional groups have been oxidized or just the ether function group thereby producing one or both of 5-ester-furan-2- acids (i.e., 5-alkoxycarbonylfurancarboxylic acids) or 5-ester-furan aldehydes, (i.e.,- alkoxycarbonylfurfurals *a. k. a*, 5 -(alkoxycarbonyl)furfural. (I)

WO 2010/132740 A2

OXIDATION OF FURFURAL COMPOUNDS

Priority

[0001] This application claims priority to US provisional application No. 61/178,301 filed May 14, 2009, which is incorporated herein by reference in its entirety.

Field of Invention

[0002] The invention pertains to processes for oxidation of furan aldehydes such as 5-(hydroxymethyl)furfural (HMF) to selectively form 2,5-diformylfuran (DFF) and to oxidation of ether derivatives of HMF such as 5-(alkoxymethyl)furfural (AMF), 5-(aryloxymethyl)furfural, 5-(cycloalkoxymethyl)furfural and 5-(acyloxymethyl)furfural compounds to form ester-acid derivatives of HMF, particularly 5-(alkoxycarbonyl)furan-2-carboxylic acids. The oxidations are done or in the presence of dissolved oxygen and a Co(II), Mn(II), Ce(III) salt catalyst or mixtures thereof with or without bromide and with or without an aliphatic ketone to selectively form the desired compounds. The products can be further oxidized for form 2,5 furandicarboxylic acid (FDCA).

Background

[0003] HMF is an important compound with many industrial applications such as use in polymers, solvents, surfactants, pharmaceuticals, and plant protection agents. However, the oxidation derivatives of HMF also have important commercial value. For example, 2,5 diformylfuran (DFF) has various useful applications such as a monomer; as a starting material for the synthesis of drugs, antifungal agents, nematocides and ligands; in photography; and as a cross-linking agent for polyvinyl alcohol. 2,5 furandicarboxylic acid *a.k.a.* furandiacid (FDCA *a.k.a* FDA) represents one key intermediate substance and is a suitable starting source for the formation of various furan monomers required for the preparation of non-petroleum-derived polymeric materials.

[0004] Many methods have been proposed for making DFF and FDCA. However, these reactions provide low yields, poor selectivity and are not environmentally friendly. For example, it is known that the synthesis of DFF from fructose can be done in a two step process, namely, by dehydration of fructose in a high boiling solvent such as dimethylsulfoxide (DMSO) to form HMF, followed by in situ catalytic air oxidation also in the presence of DMSO to form a mixture of DFF, FDCA and various other reaction side products.

[0005] Also, it has been shown that DFF or FDCA could be made from HMF by oxidation in the presence of dissolved oxygen at about 1000 psi, and a catalyst system containing Co(II), Mn(II), and a Br salt preferentially also including Zi (W. Partenhemier & V Grushin: *Adv. Synth. Catal.* (2001) 343, 102-111). However the selectivity for DFF was at most 69% in a catalyst system of Co/Mn/Br, and at most 73%. in a catalyst system of Co/Mn/Br/Zr. The best selectivity for FDCA was 73% in a catalyst system of Co/Mn/Br/Zr and at most about 35% with the same catalyst system but without the Zr. The ability to convert HMF into one predominant oxidation product is difficult due to the reactivity of the aldehyde and alcohol moieties of the HMF molecule. In the above mentioned reference, selectivity between DFF and FDCA as the predominant product was affected by using lower reaction temperatures (50-75°C) for making DFF, and higher reaction temperatures for making FDCA (typically 100-125°C).

[0006] FDCA is a difficult product to handle. It tends to precipitate in solvents used for oxidation when the temperature is raised and tends to co-precipitate with side products. It would be beneficial if an FDCA precursor could be made that is easy to separate and which could subsequently be converted to FDCA in a different reaction. Also it would be beneficial to find other routes to selective preparation of DFF versus FDCA by oxidative methods. The present invention provides for these and other needs that will be apparent from the description that follows.

Summary of the Invention

[0007] The present invention is based at least in-part, on the surprising discovery that 5-ethers of HMF can be simultaneously oxidized at the ether linkage and at aldehyde to form 5-ester furanic acids, (i.e., 5-alkoxycarbonylfurancarboxylic acids, furan-2,5-dicarboxylic acid

monoesters, a.k.a. 5-alkoxycarbonylfuran 2-carboxylic acids) using a catalyst system comprised of Co(II), Mn(II) and Ce(III) salts. These ester compounds are easy to separate by conventional solvent extraction or distillation and can be subsequently converted to FDCA under mild hydrolysis conditions.

[0008] It also has been surprisingly found that under similar reaction conditions, HMF can be selectively converted to DFF by the inclusion of a aliphatic ketone, exemplified by methyl ethyl ketone (MEK). The omission of bromide from the reaction mixture also favors selective production of DFF. Conversely, it also has been found that FDCA can be selectively made from HMF at greater than 40% by the inclusion of bromide in the reaction mixture. It also has been found that selective production of FDCA can occur without need for a zirconium co-catalyst in the reaction mixture. It also has been found that HMF can be converted to FDCA using only cobalt, or only cerium salts in the presence of bromide, without the need for manganese or zirconium co-catalyst.

[0009] More specifically, the present invention provides methods of oxidizing furan aldehydes that includes heating the furan aldehyde in a reaction mixture comprising a solvent containing dissolved oxygen and at least one catalyst selected from the group consisting of Co(II), Mn(II) and Ce(III) salts. If the furan aldehyde is -5-(hydroxymethyl)furfural., the reaction mixture includes a aliphatic ketone which helps make the predominant reaction product of diformylfuran. If the furan aldehyde is a 5- ether of the furan aldehyde, the predominant reaction product is at least one of a 5- ester furan 2-acid and a 5-(alkoxycarbonyl)furfural.. Moreover, if the furan aldehyde is a 5-(alkoxycarbonyl)furfural the predominant reaction product is the 5- ester furan 2-carboxylic acid, meaning that under prolonged reaction conditions, even if 5-(alkoxycarbonyl)furfural or 5-(alkoxymethyl)furoic acid is made from the furan ether aldehyde, intermediate furan can further be oxidized to the ester – acid derivative. The 5-ether of the furan aldehyde can be any ether, especially including a 5-(alkoxymethyl)furfural, a 5-(aryloxymethyl)furfural, and a 5-(cycloalkoxymethyl)furfural. Examples are provided when the furan aldehyde is HMF, and where the 5-ether of the furan aldehyde is 5-(acetoxymethyl)furfural and 5-(butoxymethyl)furfural.

[0010] Under typical conditions the reaction mixture is heated to a temperature of between 80°C and 130°C at a pressure of oxygen or air of about 600-to about 1000 psi for a time sufficient to

form the predominant reaction product. Preferably the temperature is between 100°C and 125°C, and most typically is about 120°C. Air or oxygen can be used under the pressure conditions to supply oxygen to the reaction mixture. In exemplary embodiments, the reaction mixture contains acetic acid as a principle solvent.

[0011] In most desirable embodiments, at least 90% of the furan aldehyde is oxidized into reaction products, and the predominant reaction product is at least 80% of the reaction products. When ester furan aldehydes are used, the predominant reaction product is a 5- ester furan 2-carboxylic acid which can be collected by precipitation from, or evaporation of the reaction mixture in a first purification step. In a second purification step, the precipitate is dissolved in a solvent in which the predominant product has higher solubility than FDCA. in a second purification step. Suitable solvents include, but are not limited to: ethyl acetate, dimethylformamide, dimethylacetate, tetrahydrofuran, dioxane, methyl ethyl ketone, methyl isobutyl ketone, acetonitrile, methyltetrahydrofuran, and C1-C6 alcohols.

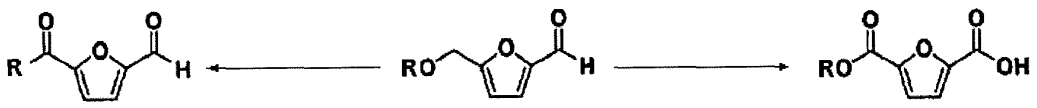
[0012] The catalyst salt can have any typical anion partner, such as acetate, acetate hydrate, bromide, chloride, fluoride, iodide, alkoxide, azide, oxalate, carbonate, carboxylate, hydroxide, nitrate, *borate, oxide, acetylacetonate and mixtures thereof.*

[0013] In certain practices the reaction mixture can include CO_2 expanded in the principle solvent of the reactions mixture, for example, CO_2 expanded acetic acid. The CO_2 should be expanded in the solvent at a pressure of at least 100 psi.. Under typical conditions, the oxygen is provided by oxygen gas or air dissolved in the solvent at a pressure of at least 200 psi and CO_2 is expanded in the solvent at a pressure of at 100 psi, typically 100-200 psi.

[0014] The reaction mixture may also include bromide when it is desirable to form FDCA as .a co-product of the oxidizing in which case, under prolonged conditions, FDCA can become the predominant product when HMF, or even the ether derivative of HMF is the reactant. Conversely, and the reaction mixture omits bromide, contains methyl ethyl ketone with HMF as the reactant, the predominant reaction product is DFF.

Detailed Description of the Invention

[0015] The invention is directed to a low cost and environmentally friendly method for oxidation of a furfural compounds in the presence of oxygen in a reaction mixture containing at least one of Co(II), Mn(II), Ce(III) salt catalysts according to the following reaction scheme:

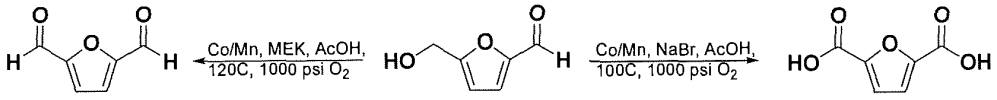


(I)

wherein R represents H, alkyl, aryl, acyl, cycloalkyl or alkylcarbonyl.

[0016] The purification of HMF has proved to be a troublesome operation. On long exposure to temperatures at which the desired product can be distilled, HMF and impurities associated with the synthetic mixture, tend to form tarry degradation products. Because of this heat instability, a falling film vacuum still must be used. Even in such an apparatus, resinous solids form on the heating surface causing a stalling in the rotor. As a result, there is frequent shut down time making the operation inefficient. Prior work has been performed with distillation and the addition of a non-volatile solvent like PEG-600 to prevent the buildup of solid humin polymers. Unfortunately, the use of polyglycols leads to the formation of HMF-PEG ethers.

[0017] Due to the instability and limited applications of HMF, the inventor's studies have broadened to include the synthesis and purification of a variety of HMF derivatives. In a first embodiment, derivatives of particular interest are the oxidized forms of HMF, in which HMF is selectively oxidized to form 2,5-diformylfuran (DFF) or 2,5-furandicarboxylic acid (FDCA).

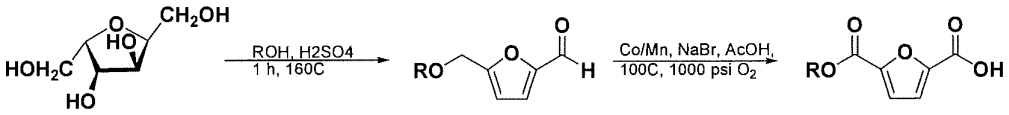


(II) DFF HMF FDCA

[0018] Other embodiments of particular interest are oxidation of ethers of HMF *a.k.a,* 5-alkoxymethylfurfurals.(AMF). In past work, the inventor has been able to obtain overall high yields of AMF by acid dehydration of fructose using crystalline fructose and even high

fructose corn syrup (HFCS) in the first step shown in the reaction below. The ether derivatives can be easily formed, are more stable, and can be separated making them even more useful than HMF itself.

[0019] With the present invention, however, oxidation of AMF can also readily be achieved using the same catalyst as used for oxidizing HMF. The major resulting product is surprisingly found to be ester derivative a 5—(alkoxycarbonyl)furancarboxcylic acid (AcMF) where the alkoxymethyl ether linkage has been oxidized to an ester and while the furan aldehyde is oxidized to the acid shown at the right of the reaction below.



(III) Fructose AMF AcMFA

[0020] The benefit of the ester derivative is that unlike FDCA, the ester derivative is readily soluble in a variety of organic compounds while FDCA is highly insoluble. The ester derivatives, however, can readily be hydrolyzed in the presence of acid or base catalysts, or further oxidized to provide FDCA when FDCA is ultimately the desired product. Because the differential solubility and ease of handling, formation of the ester acid derivative can improve upstream purification processes and yields when it is desired to ultimately obtain FDCA.

[0021] In one embodiment of the invention, HMF (crude or pure) is heated in a solvent in the presence of Co(II) and/or Mn(II) salt catalysts with dissolved oxygen or air. The reaction can proceed to selectively form 2,5-diformylfuran (DFF) by inclusion of an aliphatic ketone, like methyl ethyl ketone and omission of a bromide promoter in the reaction mixture. The reaction will selectively go to or 2,5-furandicarboxylic acid (FDCA) by inclusion of the bromide and omission of the aliphatic ketone in accordance with reaction scheme (II) above. Higher reaction temperatures will drive the reaction to carboxylic acids.

[0022] In certain embodiments :it is preferred to use a CO_2 expanded liquid (CXL) as the solvent for the reaction mixture. A CXL, is generated by mixing nontoxic, nonflammable carbon dioxide with either a conventional organic solvent or a binary mixture of the organic solvent and water

to form a single-phase liquid. The resulting CXL greatly reduces the potential for forming explosive vapors and possesses properties desirable as a medium for performing catalytic reactions. CXLs improve the solubility of liquid and gaseous reactants, as well as catalysts salts, and improve mass transfer compared to traditional pure liquid-phase reactions. Additionally, CXLs reduce the usage of organic solvents and thereby the emissions of organic vapors into the atmosphere. For these reasons, CXL solvents are attractive for many reactions.

[0023] Most solvents are miscible and can be expanded with CO_2. Preferred solvents for the reactions of the present invention are polar organic solvents, which include, but are not limited to, carboxylic acids such as acetic acid and alcohols such as ethanol and methanol, and organic solvents such as acetonitrile, acetone, n-methylpyrrolidinone, methylene chloride, methyl ethyl ketone, methyl isobutyl ketone or combinations thereof. Aqueous mixtures of these solvents may also be included. .

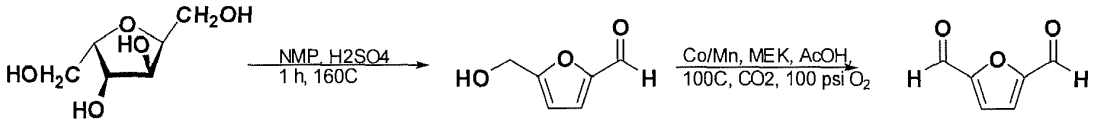
[0024] The reaction includes one or more Co(II), Mn(II), Ce(III) salt catalysts. The anion of salts can be in many forms, typically those selected from the group consisting of an acetate, acetate hydrate, bromide, chloride, fluoride, iodide, alkoxide, azide, oxalate, carbonate, carboxylate, hydroxide, nitrate, borate, oxide, acetylacetonate salts of cobalt, cerium and manganese. The acetate salt of Co(II) in combination with Mn(II) are used in most of the exemplary embodiments disclosed herein, however, Co(II) alone or Ce(III) are also shown to work, and other slats of one or more of these metals in various combinations should also catalyze the oxidation reactions.

[0025] For each reaction, the mixture is heated under mild pressure (Exemplified at 600-1000 psi), and the reactions proceed rapidly. Bromide is favored for the production of FDCA, however FDCA will also be made in the absence of the bromide promoter. The elimination of the bromide promoter in the formation of FDCA makes the reaction system less corrosive and more economical. It also has been surprisingly found, that unlike the sytem described by W. Partenhemier & V Grushin: *Adv. Synth. Catal.* (2001) 343, 102-111), zirconium is not required for selective oxidation to FDCA at high molar yields, Catalyst systems containing only cobalt and bromide or only cerinium and bromide, or the combination of cobalt, manganese and bromide salts can all make FDCA at high molar yields.

[0026] For each reaction, the mixture is heated, typically to between 100-130°C, more typically between 110-125°C, and most typically to about 120°C under mild pressure (typically 800-1000 psi), and the reactions proceed rapidly. Also, the oxidization to FDCA can be advantageously achieved by using dense CXLs. Dense CXLs refers to the production of CO_2 expanded liquids by condensing relatively large amounts of CO_2 into fixed amounts of a polar organic solvent. Typically the CO_2 is expanded into the principle solvent of the reaction mixture at 100-200 psi. The advantage is that a large amount of CO_2 favors oxygen solubility while polar organic solvents favor catalyst solubility. The combination of dense CO_2 and polar organic solvents enables mild conditions and reasonable reaction times. Thus, the method of present invention allows for a cost effective approach towards the synthesis of FDCA from HMF.

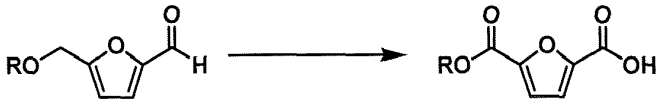
[0027] By using CO_2 expanded acetic acid solvent, the reaction should occur under milder conditions. For example, conditions to form DFF from HMF without the use of CO_2 expanded acetic acid solvent uses pressures of at least about 800-1000 psi oxygen as shown in Examples 1-4. However, when CO_2 expanded acetic acid solvent is used, the pressure can be lowered to 100-200 psi oxygen and 100-200 psi CO_2. Also, the amount of organic solvent is reduced leading to an environmentally friendly and efficient process. In addition, the solubility of oxygen in the CO_2-expanded liquid is improved by the presence of CO_2 resulting in shorter reaction times.

[0028] In one practice of the invention, a sugar can be converted directly to DFF. HMF can be obtained from sugar sources including crystalline fructose and high fructose corn syrup. HMF is prepared by dehydrating a sugar in the presence of an sulfuric acid and a organic solvents such as acetonitrile, acetone, N-methylpyrrolidinone (NMP), methylene chloride, dimethylacetamide, and dimethylformamide for 1 to 3 hours at a temperature from about 170 to about 250 °C and then oxidized to DFF in the presence of oxygen, methyl ethyl ketone and the Co/Mn catalysts as set forth in the reaction scheme (III) below:



(III)

[0029] In still more advantageous embodiments, the starting material can be ethers of HMF including any of 5-(aryloxymethyl)furfural, 5-(cycloalkoxy-methyl)furfural and 5-(alkoxycarbonyl)furfural. These starting materials can be in a pure or crude form. The reaction conditions are substantially the same as those for the oxidation of HMF to FDCA and surprisingly proceeds to an ester acid derivative in accordance with the following reaction scheme.



(IV)

Where R represents H, alkyl, aryl, cycloalkyl or alkylcarbonyl.

[0030] The resulting ester acids can be easily purified from the reaction mixture by precipitation from, or evaporation of the reaction mixture. The precipitation can be conducted by lowering the reaction mixture to room temperature or below for a time sufficient to precipitate the ester furan acid derivative in a first purification step. Any FDCA formed in the reaction mixture will tend to co precipitate with the ester furan acid derivative, however, FDCA is not as soluble in many solvents as the ester furan acid. Accordingly, a second purification step is to redissolve the precipitate in a solvent in which FDCA is less soluble than the ester furan acid derivative. Suitable solvents include, but are not limited to, ethyl acetate, dimethylformamide, dimethylacetate, tetrahydrofuran, dioxane, methyl ethyl ketone, methyl isobutyl ketone, acetonitrile, methyltetrahydrofuran, and C1-C6 alcohols. The recovered ester furan acid derivative can be subsequently hydrolyzed in the presence of a heterogenous or homogenous acid or base catalyst , or subsequently further oxidized to yield FDCA and the R-alcohol co-product, which can be recovered for reuse..

EXAMPLES

[0031] Only a few examples of the present disclosure are shown herein, it is to be understood that the disclosure is capable of practice in various combinations and with any of the materials described in the specification. Thus, while the Examples illustrate use of a cobalt acetate catalyst in combination with manganese acetate, the catalyst could just as well be cobalt alone, manganese or cerium alone, or in other combinations, and the anion of the salt could be any of

those previously mentioned herein. Similarly, the solvent system in the examples is always, acetic acid and includes methyl ethyl ketone. This is for consistency of comparison, and the invention can just well be practices with any of the solvents previously described. Accordingly, the examples are provided for illustrative purposes and no limitation of the invention is implied by the materials and conditions of the examples.

SELECTIVE OXIDATION OF HMF TO DFF USING Co/Mn CATALYSTS IN THE PRESENCE OF METHYL ETHYL KETONE

Example 1

[0032] A reaction mixture containing 97% purity HMF (5.0 g), acetic acid (50 mL), cobalt acetate (0.97 g), manganese acetate (0.98 g), and methyl ethyl ketone (1.90 mL) was placed in a 100 mL reactor and subjected to 1000 psi oxygen at 120°C for 3.5 hours. The sample was spotted on TLC plates (K5F Whatman) and developed in 1:1 EtOAc/hexane and visualized under UV light. Visual analysis indicated that after 3.5 hours, substantially all of the HMF was converted. The reaction mixture (58.58 g) was found to contain 46,356g/kg DFF (86%), 2,908 g/kg FFCA (5%), 4,201 g/kg HMF (8%) and 62 g/kg FDCA (1%) for a DFF selectivity of 86%. Subsequent GC/MS data revealed the conversion of HMF to DFF m/z = 124. Thus, after 3.5 hours, the conversion of HMF to DFF was essentially complete..

Example 2

[0033] A reaction mixture containing 97% purity HMF (5.08 g), acetic acid (50 mL), cobalt acetate (0.973 g), manganese acetate (0.982 g), and methyl ethyl ketone (0.89 mL) was placed in a 100 mL reactor and subjected to 1000 psi oxygen at 120°C for 4.5 hours. The reaction mixture (49.76 g) contained 41,368 mg/kg DFF (87%), 3,344 mg/kg FFCA, 2,671 mg/kg HMF and 32 mg/kg FDCA. Product selectivity of DFF was 87%. GC/MS data revealed complete conversion to DFF m/z = 124. Acetic acid was removed and the product extracted with methyl isobutyl ketone. Substantially pure DFF (92% purity) was recovered.

Example 3

[0034] A reaction mixture containing 97% purity HMF (10.04 g), acetic acid (50 mL), cobalt acetate (1.94 g), manganese acetate (1.94 g), and methyl ethyl ketone (1.78 mL) was placed in a 100 mL reactor and subjected to 1000 psi oxygen at 120°C for 4 hours. Samples were taken at 2 and 4 hours and analyzed by LCMS.

Time (h)	FDCA (mg/kg)	FFCA (mg/kg)	HMF (mg/kg)	DFF (mg/kg)
2	3,939	2,221	14,729	39,179
4	1,021	7,544	7,729	73,737

[0035] As is shown, after 4 hours, the reaction mixture (64.17 g) was found to contain 73,737 mg/kg DFF (82%), 7,544 mg/kg (8.3%) FFCA, 1,021 mg/kg FDCA (1.1%) and 7,729 mg/kg HMF (8.6%). GC/MS analysis revealed the essentially complete conversion to DFF with a parent ion at m/z = 124.

OXIDATION OF HMF TO FDCA

Example 4

[0036] A reaction mixture containing 97% purity HMF (5.02 g), acetic acid (70 mL), cobalt acetate (0.165 g), manganese acetate (0.169 g), and sodium bromide (0.142 g) was placed in a 100 mL reactor and subjected to 800 psi oxygen at 100°C for 5 hours. Analysis (GC/MS and 1H NMR) of the solid precipitate (2.40 g) revealed substantially pure FDCA. The yield of FDCA based on the amount of precipitated solid was 49% (mol/mol) of the HMF, however, no analysis was done on material that remained in the filtrate solution.

Example 5

[0037] A reaction mixture containing 97% purity HMF (10 g), acetic acid (50 mL), cobalt acetate (0.248 g), manganese acetate (0.248 g), and sodium bromide (0.208 g) was placed in a 100 mL reactor and subjected to 800 psi oxygen at 100°C for 4 hours. The solid precipitate was removed by filtration. Analysis (GC/MS and 1H NMR) of the solid precipitate (5.21 g) again revealed substantially pure FDCA. The yield of FDCA based on the amount of precipitated solid was 48% (mol/mol) of the HMF. The filtrate (59.18 g) contained 44142 mg/kg FDCA, 4385 mg/kg FFCA and 193 mg/kg DFF.

OXIDATION OF HMF TO FDCA USING ONLY Co CATALYST

Example 6

[0038] A reaction mixture containing 97% purity HMF (5.0 g), acetic acid (50 mL), cobalt acetate (0.97 g) and methyl ethyl ketone (0.89 mL) was placed in a 100 mL reactor and subjected to 1000 psi oxygen at about 120°C for 4 hours.

Time (h)	FDCA (mg/kg)	FFCA (mg/kg)	HMF (mg/kg)	DFF (mg/kg)
2	4969	5247	3109	1883
4	8555	5946	257	1178

[0039] After 4 hours, substantially all of the HMF was converted. The selectivity of FDCA was 54%. In this system, cobalt was the only catalyst, suggesting that the oxidation can be driven to FDCA without the need for a metal co-catalyst or bromide promoter.

NON SELECTIVE OXIDATION OF HMF TO CARBOXYLIC ACIDS

Example 7

[0040] A reaction mixture containing 97% purity HMF (5.02 g), acetic acid (50 mL), cobalt acetate (0.97 g), manganese acetate (0.98 g), and methyl ethyl ketone (1.90 mL) was placed in a 100 mL reactor and subjected to 1000 psi oxygen at a temperature that varied between 120 - 140°C for 3 hours.

Time (h)	FDCA (mg/kg)	FFCA (mg/kg)	HMF (mg/kg)	DFF (mg/kg)
1	7153	7573	4182	5254
2	10688	14804	3528	9041
3	24619	13241	826	4928

[0041] After 3 hours, essentially complete conversion of HMF had occurred with the reaction mixture containing 24619 mg/kg FDCA (56%), 13241 mg/kg FFCA (30%), 826 mg/kg HMF (2%), and 4928 mg/kg DFF (11%). As is shown, product selectivity is less predictable and favors the formation of carboxylic acids when the temperature was not maintained at 120°C or less.

Example 8

[0042] A reaction mixture containing 97% purity HMF (5.02 g), acetic acid (50 mL), cobalt acetate (0.97 g), manganese acetate (0.98 g), and methyl ethyl ketone (0.85 mL) was placed in a 100 mL reactor and subjected to 1000 psi oxygen that varied between 120 - 140°C for 6 hours.

Time (h)	FDCA (mg/kg)	FFCA (mg/kg)	HMF (mg/kg)	DFF (mg/kg)

1.5	1198	3659	14324	26642
2.5	1920	14744	3692	21126
4.5	1979	17496	1399	18434
6	5486	20882	974	19261

[0043] After 6 hours, essentially complete conversion of HMF has occurred with the reaction mixture containing 5486 mg/kg FDCA (11%), 20882 mg/kg FFCA (45%), 974 mg/kg HMF (2%), and 19261 mg/kg DFF (41%). As is shown, product selectivity decreases significantly when the temperature was not maintained to 120°C or less.

SELECTIVE OXIDATION OF HMF TO FDCA USING Co/Ce CATALYSTS

Example 9

[0044] A reaction mixture containing 97% purity HMF (5 g), acetic acid (50 mL), cobalt acetate (0.165 g), cerium acetate (0.162 g), and sodium bromide (0.142 g) was placed in a 100 mL reactor and subjected to 400 psi oxygen at 100°C for 1.5 hours. A precipitate was formed. Samples of the liquid were taken every 30 minutes and subjected to LCMS analysis.

Time (h)	FDCA (mg/kg)	FFCA (mg/kg)	HMF (mg/kg)	DFF (mg/kg)
0.5	373	768	18547	4027
1.0	9031	694	2731	1025
1.5	7924	438	532	406

[0045] As is shown, after 1.5 hours, the conversion of HMF to FDCA was essentially complete. The solid precipitate (2.37 g) was substantially pure FDCA as characterized by ^{1}H NMR.

SYNTHESIS OF DFF FROM HMF USING AIR

Example 10

[0046] A reaction mixture containing 97% purity HMF (5.00 g), acetic acid (50 mL), cobalt acetate (0.97 g), manganese acetate (0.97 g), and methyl ethyl ketone (0.89 mL) was placed in a 100 mL reactor and subjected to 1000 psi air at 115C for 4 hours. A sample taken at 4 hours was subjected to TLC analysis as described in example 1. Visual analysis indicated partial conversion of HMF to DFF and the AcHMF ether. The temperature was then increased to 125C for an additional 2 hours. The catalysts were removed by filtration and the solvent evaporated. The product was washed with water to give a cream colored solid. ^{1}H NMR analysis of the isolated solid indicated a 1:1 mixture of DFF and 5-acetoxymethylfurfural with essentially complete conversion of HMF.. NMR (δ, 1H): 10.2 (s, 2.0 H) DFF; 7.82 (s, 2.0 H) DFF; 9.84 (s, 1.0H) AcHMF; 7.86 (d, 1H) AcHMF; 6.98 (d, 1H) AcHMF; 5.42 (s, 2H) AcHMF; 2.42 (s, 3H) AcHMF.

PURIFICATION OF DFF FROM REACTION MIXTURE

Example 11

[0047] This example illustrates a simple method of DFF purification. A reaction mixture that was obtained from example 1, was allowed to evaporate. The resulting material was dissolved in diethyl ether with heating and the liquid was decanted from the black waxy material. The ether solution was cooled and a precipitate formed. The precipitate was removed by filtration and dried under vacuum. ^{1}H NMR analysis indicates substantially pure DFF. NMR (δ, 1H): 7.40 (s, 2.0 H); 9.80 (s, 2.0 H). GC/MS: m/z = 124..

EFFECT of HIGH TEMPERATURE ON OXIDATION OF HMF TO FFCA AND DFF

Example 12

[0048] A reaction mixture containing 97% purity HMF (10 g), acetic acid (50 mL), cobalt acetate (1.94 g), manganese acetate (1.94 g), and methyl ethyl ketone (1.78 mL) was placed in a 100 mL reactor and subjected to 1000 psi oxygen at about 130°C for 5 hours. Samples were taken at 2, 4 and 5 hours.

Time (h)	FDCA (mg/kg)	FFCA (mg/kg)	HMF (mg/kg)	DFF (mg/kg)
2	854	4951	30779	19849
4	1579	16731	3694	44072
5	2292	27035	4151	64251

[0049] As is shown, after 5 hours, the reaction mixture contained 2292 mg/kg FDCA (2%), 27035 mg/kg FFCA (28%), 4151 mg/kg HMF (4%), and 64251 mg/kg DFF (66%). Thus, temperature was found to effect product selectivity.

OXIDATION OF BMF to ESTER ACID DERIVATIVE

Example 13

[0050] A reaction mixture containing 82% butoxymethylfurfural (6.12 g), acetic acid (70 mL), cobalt acetate (0.165 g), manganese acetate (0.169 g), and sodium bromide (0.142 g) was placed in a 100 mL reactor and subjected to 1000 psi oxygen at 100°C for 5 hours. GC/MS data revealed complete conversion of BMF, with the predominant product being the ester/acid 5-(butoxycarbonyl)furan-2-carboxylic acidm/z = 157, 139, 56.

Example 14

[0051] A reaction mixture containing 80% butoxymethylfurfural (12.19 g), acetic acid (50 mL), cobalt acetate (0.165 g), manganese acetate (0.165 g), and sodium bromide (0.142 g) was placed in a 100 mL reactor and subjected to 600 psi oxygen at 100°C for 5 hours. Samples

were taken at 0.5 and 1 h and analyzed by TLC as described in example 1. Visual analysis of TLC plate with UV light indicated that after 1 h, essentially all of the BMF was converted to 5-(butoxycarbonyl)furan-2-carboxylic acid. GC/MS analysis confirmed these results (m/z 157, 139, 56. After the reaction was completed, the precipitated solid was removed by filtration and analyzed by ^{1}H NMR. Substantially pure 5-(butoxycarbonyl)furan-2-carboxylic acid (1.88 g) was recovered.

OXIDATION OF AcHMF to FDCA

Example 15

[0052] A reaction mixture containing acetoxymethylfurfural (5.0 g), acetic acid (50 mL), cobalt acetate (0.13 g), manganese acetate (0.13 g), and sodium bromide (0.11 g) was placed in a 100 mL reactor and subjected to 500 psi oxygen at 100C for 2 hours. The solid (2.53 g) was removed by filtration to give a 54% molar yield of FDCA from AcHMF and a 5-(xcetoxymethyl)furan-2-carboxylic acid (AcMFCA) by-product.

PURIFICATION OF OXIDIZED BMF FROM REACTION MIXTURE

Example 16

[0053] A reaction mixture that was obtained from example 5, was allowed to evaporate. The resulting material was placed in a mixture of water (25 mL) and ethyl acetate (25mL). A solution of 4.0M HCl in dioxane was added dropwise to lower the pH to <2. The two layers were allowed to separate. The aqueous layer was washed with ethyl acetate and the organic layers combined and dried over $MgSO_4$. Following filtration of the $MgSO_4$, the solvent was removed by rotary evaporation. ^{1}H NMR and GC/MS data revealed conversion of BMF to the ester/acid m/z = 157, 139, 56 in high purity (>90%).

[0054] While this invention has been described with reference to several preferred embodiments, it is contemplated that various alterations and modifications thereof will become apparent to those skilled in the art upon a reading of the preceding detailed description. It is therefore intended that the following appended claims be interpreted as including all such alterations and modifications

We claim:

1. A method of oxidizing furan aldehydes comprising heating the furan aldehyde in a reaction mixture comprising a solvent containing dissolved oxygen and at least one catalyst selected from the group consisting of Co(II), Mn(II) and Ce(III) salts, wherein:

(i) if the furan aldehyde is -5-(hydroxymethyl)furfural., the reaction mixture includes an aliphatic ketone and a predominant reaction product of the oxidizing is diformylfuran; OR

(ii) if the furan aldehyde is a 5- ether of the furan aldehyde, the predominant reaction product is at least one of a 5- ester furan 2-acid and a 5-(alkoxycarbonyl)furfural.; OR

(iii) if the furan aldehyde is a 5-(alkoxycarbonyl)furfural the predominant reaction product is a 5- ester furan 2-carboxyylic acid; OR -

(iv) if the furan is a 5-(alkoxymethyl)furoic acid the product is a 5-ester furan 2-carboxylic acid.

2. The method of claim 1, wherein the 5-ether of the furan aldehyde is selected from the group consisting of: a 5-(alkoxymethyl)furfural, a 5-(aryloxymethyl)furfural, and a 5-(cycloalkoxy-methyl)furfural.

3. The method of claim 1, wherein the furan aldehyde is 5-(hydroxymethyl)furfural.

4. The method of claim 1, wherein the 5-ether of the furan aldehyde is selected from the group consisting of 5-(acetoxymethyl)furfural and 5-(butoxymethyl)furfural.

5. The method of claim 1, wherein the reaction mixture is heated to a temperature of between 80°C and 130°C at a pressure of oxygen or air of about 800-to about 1000 psi for a time sufficient to form the predominant reaction product.

6. The method of claim 5, wherein the temperature is between 100°C and 125°C.

7. The method of claim 5, wherein the pressure is the pressure of oxygen.

8. The method of claim 1 wherein the reaction mixture contains acetic acid as a principle solvent.

9. The method of claim 1 wherein at least 90% of the furan aldehyde is oxidized into reaction products, and the predominant reaction product is at least 80% of the reaction products.

10. The method of claim 1 wherein the predominant reaction product is a 5- ester furan 2-carboxcylic acid and is collected as a precipitate from the reaction mixture in a first purification step.

11. The method of claim 10 wherein the precipitate is dissolved in a solvent in which the predominant product has higher solubility than FDCA in a second purification step

12. The method of claim 11 wherein the solvent is selected from the group consisting of ethyl acetate, dimethylformamide, dimethylacetamide, tetrahydrofuran, dioxane, methyl ethyl ketone, acetonitrile, methyltetrahydrofuran, methyl isobutyl ketone, and C1-C6 alcohols.

13. The method claim 1 wherein the at least one catalyst salt has an anion selected from the group consisting of an acetate, acetate hydrate, bromide, chloride, fluoride, iodide, alkoxide, azide, oxalate, carbonate, carboxylate, hydroxide, nitrate, borate, oxide, acetylacetonate and mixtures thereof.

14. The method of claim 1, wherein the reaction mixture includes CO_2 expanded in a principle solvent of the reactions mixture.

15. The method of claim 14 wherein the principle solvent is acetic acid.

16 The method of claim 14 wherein the CO_2 is expanded in the solvent at a pressure of at least 100 psi.

17. The method of claim 14 wherein the oxygen is provided by oxygen gas or air dissolved in the solvent at a pressure of at least 200 psi and CO_2 is expanded in the solvent at a pressure of at least 100 psi.

18. The method of claim 1 wherein the reaction mixture also includes bromide and FDCA is formed as .co product of the oxidizing.

19. The method of claim 1 wherein the furan aldehyde is -5-(hydroxymethyl)furfural, the predominant reaction product is diformyl furan, and the reaction mixture does not contain bromide.

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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

— *of inventorship (Rule 4.17(iv))*

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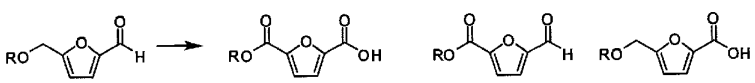

(I)

(57) Abstract: The disclosure pertains to a process for oxidation of furan aldehydes such as 5- hydroxymethyl)furfural (HMF) and derivatives thereof such as 5-(alkoxymethyl)furfural (AMF), 5-(aryloxymethyl)furfural, 5-(cycloalkoxy-methyl)furfural and 5-(alkoxycarbonyl)furfural compounds in the presence of dissolved oxygen and a Co(II), Mn(II), Ce(III) salt catalyst or mixtures thereof. The products from HMF can be selectively chosen to be predominantly 2,5- diformylfuran (DFF), particularly by inclusion of an aliphatic ketone, like methyl ethyl ketone, or can be further oxidized to 2,5-furandicarboxylic acid (FDCA) by the omission of methyl ethyl ketone and inclusion of bromide.. When the reactant is an ether derivative of HMF the products are surprisingly ester derivatives where either both the ether and aldehyde functional groups have been oxidized or just the ether function group thereby producing one or both of 5-ester-furan-2- acids (i.e., 5-alkoxycarbonylfurancarboxylic acids) or 5-ester-furan aldehydes, (i.e.,- alkoxycarbonylfurfurals *a. k. a*, 5 -(alkoxycarbonyl)furfural). (I)

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A. CLASSIFICATION OF SUBJECT MATTER

C07D 307/48(2006.01)i, C07D 307/46(2006.01)i

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D 307/48; C07D 307/02; C07C 45/28; C07D 307/34; C10L 1/185

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal) & Keywords: furan, aldehyde, 5-hydroxymethyl<PHRASE>furfural, cobalt, manganes, cerinium

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003-0055271 A1 (VLADIMIR GRUSHIN et al.) 20 March 2003 See background, example 2, 9-11, 14, 15, 18-20, 23-25, claims 1,2, 5-17, 20-28	1-4,8,9,13,18,19
A	See whole document	5-7,10-12,14-17
T	US 2010-0218415 A1 (GRUTER GERARDUS JOHANNES MARIA et al.) 02 September 2010 See whole document	1-19

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
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