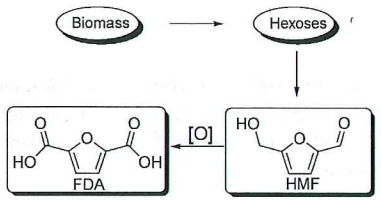
The aerobic oxidation of 5-hydroxymethylfurfural, a versatile biomass-derived chemical, is examined in water with a titania-supported gold-nanoparticle catalyst at ambient temperature (30 °C). The selectivity of the reaction towards 2,5-furandicarboxylic acid and the intermediate oxidation product 5-hydroxymethyl-2-furancarboxylic acid is found to depend on the amount of added base and the oxygen pressure, suggesting that the reaction proceeds via initial oxidation of the aldehyde moiety followed by oxidation of the hydroxymethyl group of 5-hydroxymethylfurfural. Under optimized reaction conditions, a 71% yield of 2,5-furandicarboxylic acid is obtained at full 5-hydroxymethylfurfural conversion in the presence of excess base.

Introduction

The focus on technologies that facilitate conversion of biorenewables into transportation fuels and chemicals has increased markedly in recent years.[1,2] Today's economic growth requires industrial processes to be sustainable, thus making biomass a fundamental feedstock for chemical production,[3] and a shift from conventional petrochemical feedstocks towards biomass-based feedstocks is of both environmental and economical importance for the future production of commodity chemicals.[4]

Sugars, in the form of mono- and disaccharides, are readily available from various biomass sources by, for example, enzymatic hydrolysis[5] and form a useful feedstock for the production of versatile chemicals. For example, hexose monosaccharides such as glucose and fructose can be catalytically dehydrated into 5-hydroxymethylfurfural (HMF). HMF is a chemical precursor for the production of 2,5-furandicarboxylic acid (FDA) by oxidation (Scheme 1) using various oxygen sources, process



Scheme 1. Biomass-based feedstocks can be converted to versatile molecules such as, for example, 5-hydroxymethylfurfural (HMF), which can be oxidized to the polymer building block 2,5-furandicarboxylic acid (FDA).

designs, and catalyst types.[6–8] The US Department of Energy biomass program has identified FDA as one of the twelve chemicals obtained from biomass in biorefineries that can be used as chemical building blocks in the future.[9] In particular the presence of two carboxylic groups in FDA makes it a valuable polymer building block and, thus, a possible alternative to presently used terephthalic, isophthalic, and adipic acids produced from fossil-based resources.

In order to comply with the need for the clean production of value-added chemicals such as FDA from HMF, there is a demand for aerobic catalytic systems that use dioxygen as oxidant and produce only water as a byproduct. Heterogeneous metal catalysts are of particular interest in this context because HMF, being both an aromatic aldehyde and an alcohol, may be oxidized using such catalysts, although there are limited reports on this reaction. However, Vinke et al. have demonstrated the oxidation of aqueous HMF to FDA in near-quantitative yield under basic reaction conditions with a Pt/Al_2O_3 catalyst at 60 °C.[10]

Instead of the fully oxidized product FDA the partially oxidized intermediate 2,5-diformylfuran (DFF) is in fact more frequently obtained. For example, Halliday et al. have reported the oxidation of HMF to DFF with oxygen by using ion-exchange resins and vanadyl phosphate (VPO) catalysts as part of a direct in situ transformation of fructose to DFF (with yields up to 45%) without isolation of the intermediate.[11] Similarly, Carlini et al. have oxidized HMF, both as a starting reagent and after producing it in a one-pot conversion from fructose, to the corresponding dialdehyde in a biphasic water/methyliso-

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butylketone (MIBK) medium as well as in pure organic solvent with metal-doped unsupported/TiO_2-supported VPO catalysts under an oxygen pressure of 1 MPa.[12] For the mixed solvent system the yield remained lower than 10% (3 10% HMF conversion; 60 100% selectivity) whereas better conversion rates and selectivities were obtained in MIBK alone (98% conversion; 50% selectivity) or in other low-polarity organic solvents (e.g., benzene, toluene). Yields of up to 81% (conversion 84%; selectivity 97%) were obtained in the polar solvent dimethylformamide.

The above-described compound DFF is often used as an intermediate for the production of FDA. However, catalytic routes that lead to the formation of FDA without isolating DFF as an intermediate have also been reported.[13] Ribeiro and Schuchardt obtained FDA from fructose in 71% yield via HMF formation (72% conversion from fructose; 99% selectivity) using silica-encapsulated cobalt acetylacetonate as a bifunctional acid-redox catalyst at 160 °C and an air pressure of 2 MPa.[14] Furthermore, Lilga et al. have recently patented an industrially promising method to oxidize HMF to FDA in up to 98% yield (100% conversion; up to 98% selectivity) at 100 °C and 1 MPa oxygen pressure using a Pt/ZrO_2 catalyst.[15]

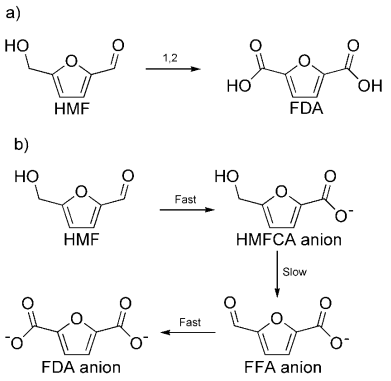
In addition to the catalyst systems described above, gold has also been found to be an excellent catalyst for the oxidation of both aromatic and aliphatic alcohols to their corresponding acids or esters with oxygen as the oxidant under benign conditions.[16 25] Recently, aerobic oxidation of HMF in methanol with titanium dioxide-supported gold nanoparticles was reported by Taarning et al. to give 2,5-furandimethylcarboxylate in 98% selectivity and 60% isolated yield at 130 °C using an oxygen pressure of 4 bar (1 bar 10^5 Pa) and added base (sodium methoxide) as the promoter.[23] In contrast, while the promoting effect of base on the aqueous-phase oxidation of glycerol and CO has been described,[17] no report to date has described the base-promoted oxidation of aqueous HMF by gold catalysts.

Accordingly, we have in this work examined the aerobic oxidation of HMF in basic aqueous solution at ambient temperature using a commercial heterogeneous Au/TiO_2 catalyst. More specifically, the influences of the oxidant (dioxygen) pressure and the amount of hydroxide base on the selectivity and yield of the reaction are reported, along with a hypothesis on the oxidation pathway.

Results and Discussion

Initially, the oxidation of HMF was performed with 20 equivalents of sodium hydroxide at 20 bar oxygen pressure (ca. 8 mmol) at 30 °C (Scheme 2a). The oxidation reaction was followed by using HPLC to measure the concentration of the reaction products (with acidic eluent to obtain the FDA).

The measured yields of all observed reaction products are plotted against the reaction time (HMF was fully converted) in Figure 1. HMF initially underwent relatively fast oxidation to 5-hydroxymethyl-2-furancarboxylic acid (HMFCA) before being further oxidized to FDA (Scheme 2b), as also previously found in methanol solution.[23] Thus, no indication supporting a reaction route involving initial oxidation of the HMF alcohol group due to stabilizing electron effects of the furan ring and formyl group, as claimed by Vinke et al.,[10] was found under these reaction conditions.



Scheme 2. a) Oxidation of HMF to FDA. 1) Au/TiO_2, OH^-/H_2O, $P(O_2) = 20$ bar, 30 °C; 2) H^+. b) Possible route for the HMF oxidation reaction via initial oxidation of the formyl group.

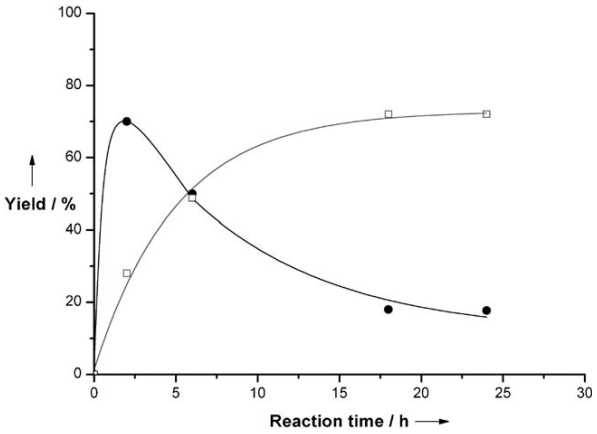


Figure 1. Product formation as a function of reaction time in the oxidation of HMF by dioxygen in aqueous solution using 1 wt% Au/TiO_2 catalyst (20 equiv NaOH, 20 bar O_2, 30 °C; FDA: □, HMFCA: ●). Lines were added to guide the eye.

An 18 h control reaction conducted under an inert nitrogen atmosphere in the absence of dioxygen (but with all other reaction conditions unchanged) also resulted in full HMF conversion, but with product yields of 51% HMFCA, 38% 2,5-dihydroxymethylfuran (DHMF), and 11% levulinic acid (LA). This result suggests that under the generally applied reaction conditions byproducts form partly by the Cannizzaro reaction (disproportionation of HMF into HMFCA and DHMF[15]) and partly by HMF degradation, thereby limiting the available FDA yield. Hence, under optimized conditions a maximum FDA yield of 71% was obtained after 18 h of reaction. Interestingly, HMF degradation apparently resulted in LA formation in the ab-

sence of oxidant while traces of formic acid (FA) were exclusively formed in the presence of dioxygen (vide infra).

HMF was also oxidized in the presence of various amounts of NaOH in the reaction mixture, as shown in Figure 2. The use of aqueous KOH gave identical results.

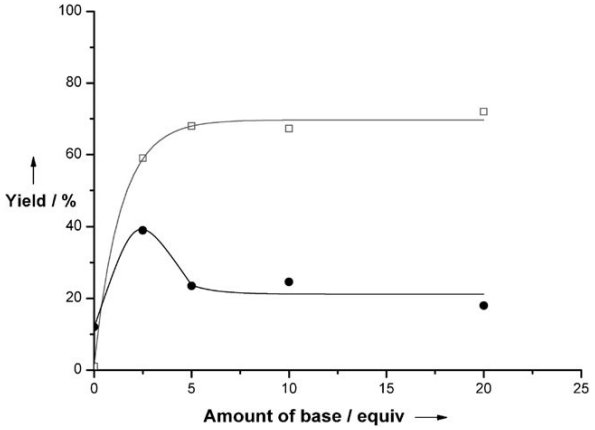


Figure 2. Product formation as a function of the introduced amount of base (NaOH) in the oxidation HMF by dioxygen in aqueous solution using 1 wt% Au/TiO_2 catalyst (20 bar O_2, 30 °C, 18 h; FDA: □, HMFCA: ●). Lines were added to guide the eye.

In reactions with low amounts of added NaOH base (2.5 equiv.) the yield of the intermediate oxidation product (HMFCA) was high relative to FDA, resulting only in a moderate yield of FDA at full HMF conversion. In contrast, the conversion of HMF was only 13% without added base (12% and 1% yields of HMFCA and FDA, respectively), suggesting deactivation of the gold catalyst by the initially formed acids as also previously reported for alcohol oxidation in a methanol solution.[25] Additionally, precipitation of the formed FDA onto the catalyst surface may also have hampered the reaction significantly in the absence of base, where the solubility of FDA is quite low.[15]

The formation of byproducts was largely avoided at all examined base concentrations (for both NaOH and KOH), with only traces of up to 3% FA being observed at the higher base concentrations examined along with FDA and HMFCA yields of about 70% and 25%, respectively. Unexpectedly, LA was not observed, in contrast to what is usually found when HMF is degraded by rehydration in aqueous acidic medium.[2,6] Moreover, no conversion was observed under the applied reaction conditions when LA was introduced as a substrate in place of HMF. This suggests that the trace of FA generated from HMF degradation was formed by a route that does not involve LA formation. A possible route could involve peroxides generated in situ from oxygen, which have also been found to induce byproduct formation by C–C bond cleavage in the gold-catalyzed aerobic oxidation of aqueous glycerol.[16,17] This would also explain why FA was not formed in the absence of dioxygen (vide supra).

In addition to the reactions described at 20 bar oxygen pressure (vide supra), reactions with added NaOH were also examined at both lower and higher oxygen pressures (10 and 30 bar, respectively; Figure 3).

As shown in Figure 3, an initial increase in the oxygen pressure from 10 to 20 bar (or 30 bar) markedly increased the formation of FDA relative to HMFCA (from 43% to 71%), whereas

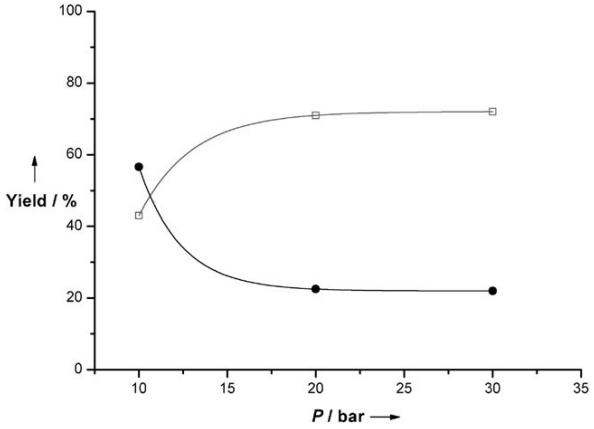


Figure 3. Product formation in as a function of the oxidant pressure in the aerobic oxidation of HMF in aqueous solution using 1 wt% Au/TiO_2 catalyst (20 equiv NaOH, 30 °C, 18 h; FDA: □, HMFCA: ●). Lines were added to guide the eye.

full HMF conversion was achieved at all pressures. This indicates that an insufficient amount of oxygen was dissolved to facilitate the full reaction at 10 bar. Furthermore, it confirms that the aldehyde moiety of HMF is more easily oxidized than the hydroxymethyl group (thereby leading to initial formation of HMFCA), in accordance with previous findings for analogous oxidations performed in methanol.[24] As no intermediate DFF product was observed during the reaction, it further implies that the final aldehyde oxidation step from DFF to FDA is faster than the initial aldehyde oxidation, as shown in Scheme 2b.

Upon reuse (after filtration and drying) the catalyst used in the reaction at 20 bar with 20 equiv. of added base yielded a lower activity towards the oxidation, resulting in a 5 10% lower HMFCA conversion at comparable reaction times. Analysis of the post-reaction mixture by inductively coupled plasma (ICP) spectrometry confirmed that this correlated well with gold leaching (corresponding to <4% of the original metal inventory).

Conclusions

In the present work the oxidation of aqueous HMF to FDA by a heterogeneous supported gold catalyst and oxygen has been investigated. Under optimized basic reaction conditions, a 1 wt% Au/TiO_2 catalyst was found to oxidize HMF into FDA in 71% yield at 30 °C in 18 h with 20 bar oxygen. Lower pressures or low concentrations of base (i.e., corresponding to less than five equivalents) afforded relatively more of the intermediate oxidation product HMFCA compared to FDA. Ob-

served traces of FA were proposed to originate, in part, from peroxide degradation of the initially formed LA produced by HMF rehydration, while base prevented deactivation of the gold catalyst and possibly also stabilized the FDA product in its anionic form.

The reaction procedure introduced in this work involves HMF oxidation at ambient temperature using an abundant and environmentally friendly oxidant and solvent. When combined, these features make the protocol an interesting alternative to oxidation reactions based on stoichiometric amounts of heavy metal oxidants (e.g., chromium and manganese oxygenates) that have traditionally been applied to the oxidation of substrates with similar functionalities.[26] Further development of the catalyst system to circumvent the significant metal leaching and thus improve catalyst durability is in progress.

Experimental Section

Materials: 5 hydroxymethylfurfural (>99%), levulinic acid (98%), formic acid (98%), sodium hydroxide (>98%), and potassium hydroxide (>98%) were acquired from Sigma Aldrich. 2,5 furandicarboxylic acid (>99%) and 5 hydroxymethyl 2 furancarboxylic acid (>99%) were purchased from Toronto Research Chemicals Inc. and dioxygen (99,5%) was obtained from Air Liquide Denmark. All chemicals were used as received. For the oxidation reactions a commercial 1 wt% Au/TiO_2 catalyst was used (Mintek, Brunauer Emmett Teller (BET) surface area 49 $m^2 g^{-1}$), which by high resolution transmission electron microscopy analysis (JEM 2000FX microscope, 300 kV; sample mounted on a 300 mesh copper grid coated with holey carbon film) was found to contain gold particles with an average size of 4 8 nm.

Oxidation reactions: Oxidations were carried out in a stirred Parr minireactor autoclave equipped with internal thermocontrol (T316 steel, Teflon beaker insert, 25 mL). In each reaction the autoclave was charged with 126 mg of HMF (1 mmol) and a solution of alkali hydroxide (0.1 0.8 g, 2.5 20 mmol) in 10 mL water. Subsequently, 1 wt% Au/TiO_2 catalyst was added (0.197 g, 0.01 mmol Au) and the autoclave was flushed and then pressurized with dioxygen (10 30 bar, ca. 4 12 mmol) and maintained at 30 °C for a given period under stirring (800 rpm). After the reaction, the autoclave was cooled to room temperature (i.e., 20 °C) and after filtering off the catalyst a sample was taken out for HPLC analysis (Agilent Technologies 1200 series, Aminex HPX 87H column from Bio Rad, 300 mm × 7.8 mm × 9 µm, flow 0.6 mL min^{-1}, solvent 5 mM H_2SO_4, temperature 60 °C). Reference samples were used to quantify the products. Reported results are averaged data (<7% absolute error) obtained from 2 3 separate reactions with an apparent carbon mass balance of >90% (no CO_2 product observed by TCD GC analysis). ICP analysis (Perkin Elmer ELAN 6000 with cross flow nebulizer and argon plasma) was performed on the diluted post reaction mixture and quantified with an ICP standard solution (1.000 g L^{-1}, Fluka).

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Keywords: biomass · gold · oxygen · supported catalysts · titania

[1] P. Gallezot, *Green Chem.* **2007**, *9*, 295 302.
[2] A. Corma, S. Iborra, A. Velty, *Chem. Rev.* **2007**, *107*, 2411 2502.
[3] B. Kamm, M. Kamm, *Adv. Biochem. Eng./Biotechnol.* **2007**, *105*, 175 204.
[4] C. H. Christensen, J. Rass Hansen, C. C. Marsden, E. Taarning, K. Egeblad, *ChemSusChem* **2008**, *1*, 283 289.
[5] T. Schäfer, T. W. Borchert, V. S. Nielsen, P. Skagerlind, K. Gibson, K. Wenger, F. Hatzack, L. B. Nilsson, S. Salmon, S. Pedersen, H. P. Heldt Hansen, P. B. Poulsen, H. Lund, K. M. Oxenbøll, G. F. Wu, H. H. Pedersen, H. Xu, *Adv. Biochem. Eng./Biotechnol.* **2007**, *105*, 59 131.
[6] J. Lewkowski, ARKIVOC **2001**, *I*, 17 54.
[7] E. Taarning, C. H. Christensen, *Chim. Oggi* **2007**, *25*, 70 73.
[8] C. Moreau, M. N. Belgacemb, A. Gandinib, *Top. Catal.* **2004**, *27*, 11 30.
[9] T. Werpy, G. Petersen, *Top Value Added Chemicals from Biomass Vol.1* **2004**, 26 28; available at: http://www.osti.gov/bridge (accessed May 2009).
[10] P. Vinke, W. van der Poel, H. van Bekkum, *Stud. Surf. Sci. Catal.* **1991**, *59*, 385 394.
[11] G. A. Halliday, R. J. Young, Jr., V. V. Grushin, *Org. Lett.* **2003**, *5*, 2003 2005.
[12] C. Carlini, P. Patrono, A. M. R. Galletti, G. Sbrana, V. Zima, *Appl. Catal. A* **2005**, *289*, 197 204.
[13] W. Partenheimer, V. V. Grushin, *Adv. Synth. Catal.* **2001**, *343*, 102 111.
[14] M. L. Ribeiro, U. Schuchardt, *Catal. Commun.* **2003**, *4*, 83 86.
[15] M. A. Lilga, R. T. Hallen, J. Hu, J. F. White, M. J. Gray, US Patent 20080103318, **2008**.
[16] W. C. Ketchie, M. Murayama, R. J. Davis, *J. Catal.* **2007**, *250*, 264 273.
[17] W. C. Ketchie, M. Murayama, R. J. Davis, *Top. Catal.* **2007**, *44*, 307 317.
[18] W. C. Ketchie, Y. L. Fang, M. S. Wong, M. Murayama, R. J. Davis, *J. Catal.* **2007**, *250*, 94 101.
[19] C. H. Christensen, B. Jørgensen, J. Rass Hansen, K. Egeblad, R. Madsen, S. K. Klitgaard, S. M. Hansen, M. R. Hansen, H. C. Andersen, A. Riisager, *Angew. Chem.* **2006**, *118*, 4764 4767; *Angew. Chem. Int. Ed.* **2006**, *45*, 4648 4651.
[20] S. K. Klitgaard, K. Egeblad, U. V. Mentzel, A. G. Popov, T. Jensen, E. Taarning, I. S. Nielsen, C. H. Christensen, *Green Chem.* **2008**, *10*, 419 423.
[21] C. Marsden, E. Taarning, D. Hansen, L. Johansen, S. K. Klitgaard, K. Egeblad, C. H. Christensen, *Green Chem.* **2008**, *10*, 168 170.
[22] E. Taarning, A. T. Madsen, J. M. Marchetti, K. Egeblad, C. H. Christensen, *Green Chem.* **2008**, *10*, 408 414.
[23] E. Taarning, I. S. Nielsen, K. Egeblad, R. Madsen, C. H. Christensen, *Chem SusChem* **2008**, *1*, 75 78.
[24] B. Jørgensen, S. E. Christiansen, M. L. D. Thomsen, C. H. Christensen, *J. Catal.* **2007**, *251*, 332 337.
[25] S. K. Klitggard, A. T. DeLa Riva, S. Helveg, R. M. Werchmeister, C. H. Christensen, *Catal. Lett.* **2008**, *126*, 213 217.
[26] T. J. Donohoe, *Oxidation and Reduction in Organic Synthesis*, Oxford University Press, Oxford, **1994**.

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