

Subject _____



Filed in Book Number/Title _____

	L224715 Tartrate	1. EtOAc - NaOH		
		2. H ₃ PO ₄ EtOH/H ₂ O		
Reagents:		For	cont	mol
	L224715 Tartrate	557	2.00g	3.60
	EtOAc		20 ml	1.
	NaOH		10 ml	10

Procedure: Stirred material in EtOAc Added NaOH. cont
 layers washed w/ 20 ml, 20% NaCl. Assayed EtOAc
 layer to contain 1.45g of 715 ~ 99%. Concentrated base
 Redissolved in 6ml Ethanol & filtered into 3ml RBF
 Added 1.5 ml H₂O (20% water); Dissolved ^{430g} 445 mg of Phosphoric
 acid in 1.5 ml EtOH Heat soln to 70°C. Added H₃PO₄ soln - it
 was clear - no xhals. Removed heat & cooled to 40°C slurry form
 Reheated to 72°C but still solids added 0.75 ml H₂O & most of all of
 solids dissolved. Cooled to RT @ 5°C/hr & then aged over weekend
 11 Feb 2002 - slurry present dark material in it from probe
 rubbing up against stir shaft. Added 48 ml Ethanol filter
 isolated 1.20g white solids (71). Recovery
 Dissolved in hot water until saturated w/ solid - material is 90g/g solubility
 in H₂O
 12 Feb 2002 4. NMR of salt (10g/ml in D₂O) & a saturated
 soln of Freebase
 Methine & to amine is clear shifted downfield in salt sample
 relative to Freebase. ~~12 Feb 2002~~

Countersigned by _____



DO NOT BEGIN NEW EXPERIMENTS ON THIS PAGE.

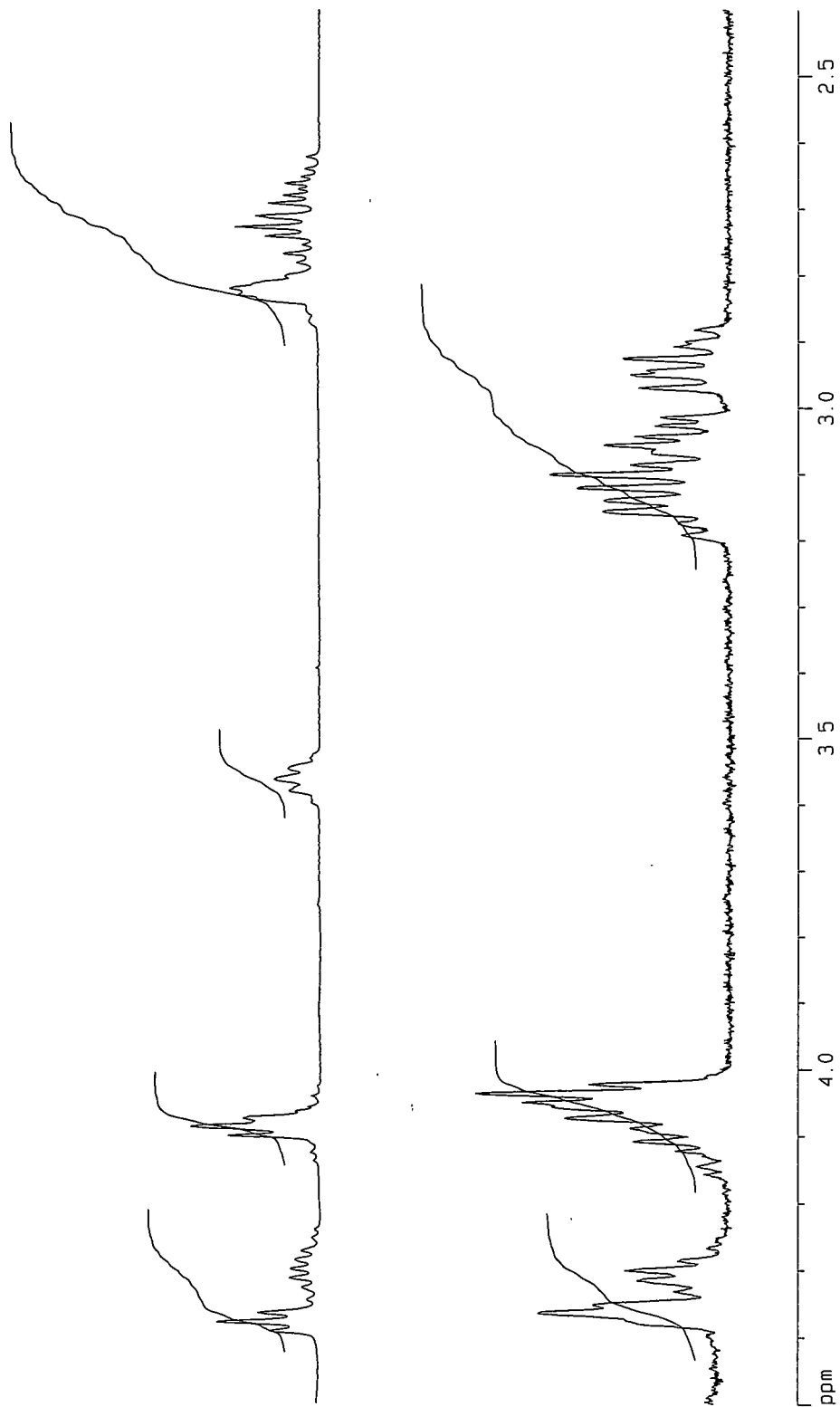
12 Feb 2002 - This supports the salt not dissociating
in water. ~~RBR~~ 12 Feb 2002



Countersigned by _____

Date _____

Top: L224,715 free base sat in d2o
Bottom: L224715 phosphate salt 10mg/ml



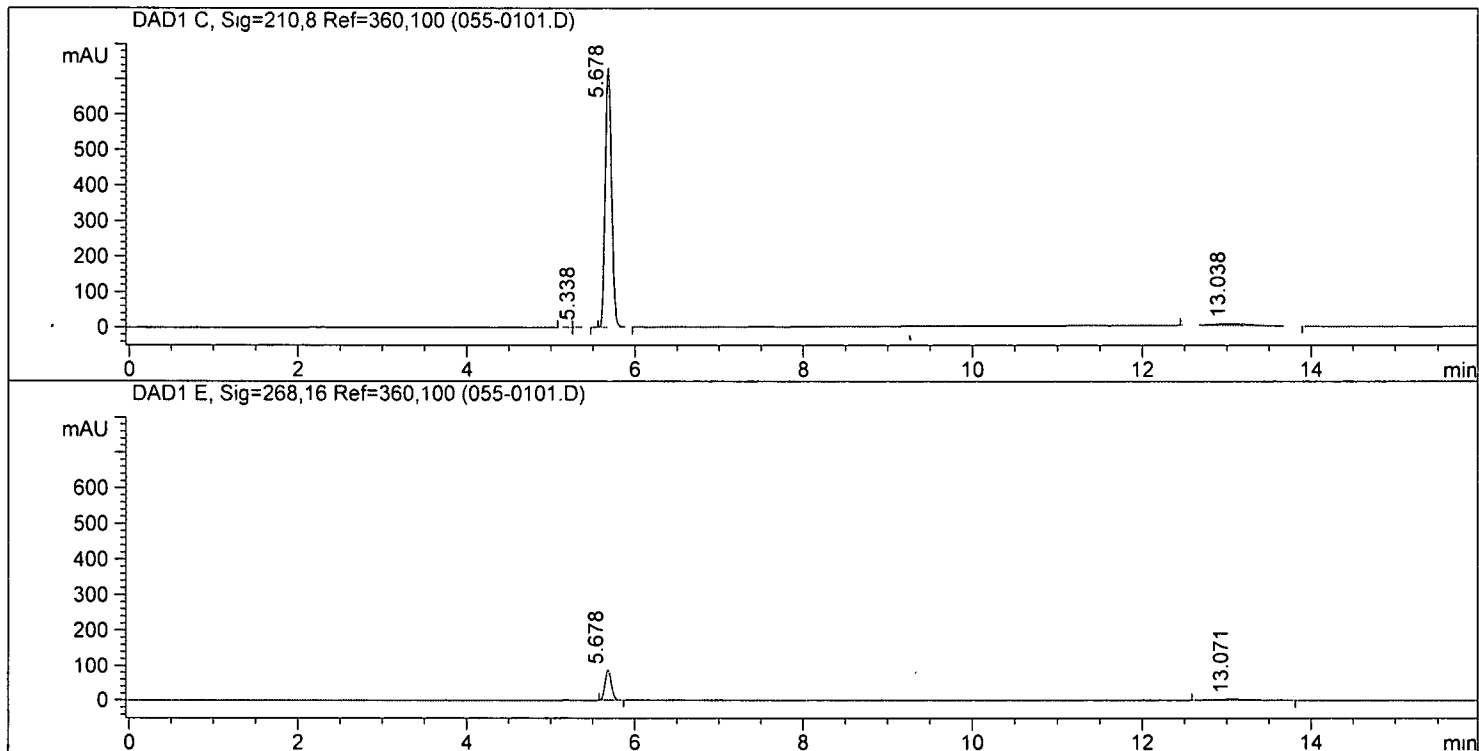
0.5610g/50ml of saturated aq soln

->

```

=====
Injection Date : 02/11/2002  9:14:02 AM      Seq Line   : 1
Sample Name    : 70316-037                    Vial No    : 55
Acq Operator   : hansen                       Inj. No.   : 1
                                           Inj. Vol.  : 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 01/14/2002  1:00:57 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 01/14/2002  1:00:30 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	5.17	BV	0.077	1.11	5.463	0.14	0.000000	
2	5.34	VP	0.078	1.34	6.661	0.16	0.000000	
3	5.68	BB	0.081	734.72	3843.763	95.16	1.017704	L-224,715
4	13.04	BP	0.430	5.66	183.469	4.54	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	5.68	BB	0.080	86.51	448.537	84.16	1.017704	L-224,715
2	13.07	BP	0.404	2.76	84.451	15.84	0.000000	

*** End of Report ***

L224,715 free base
 sat in d2o
 nmr400a h-1

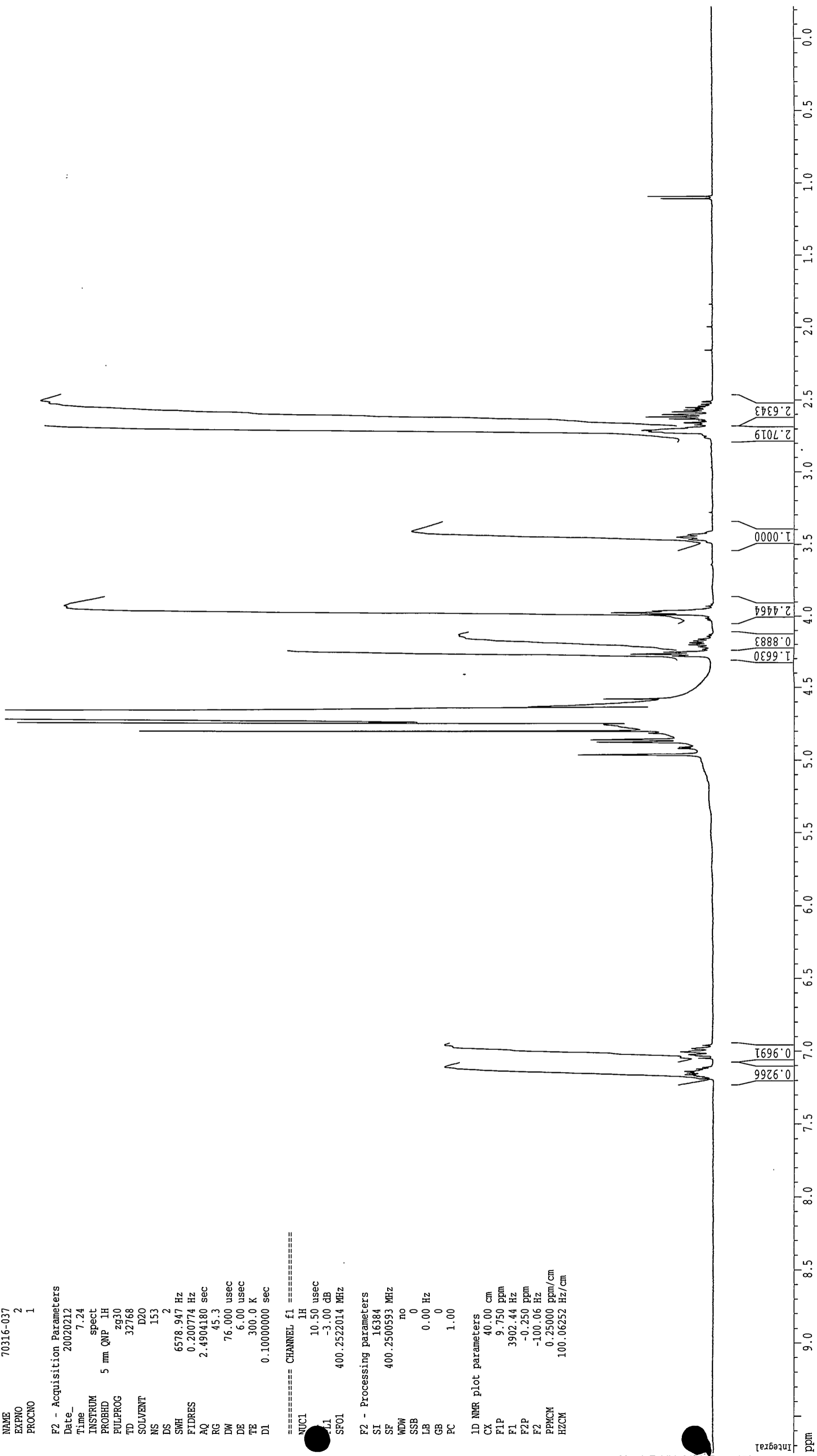
Current Data Parameters
 NAME 70316-037
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20020212
 Time 7.24
 INSTRUM spect
 PROBHD 5 mm QNP 1H
 PULPROG zg30
 TD 32768
 SOLVENT D2O
 NS 153
 DS 2
 SWH 6578.947 Hz
 FIDRES 0.200774 Hz
 AQ 2.4904180 sec
 RG 45.3
 DW 76.000 usec
 DE 6.00 usec
 TE 300.0 K
 D1 0.10000000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 400.2522014 MHz

F2 - Processing parameters
 SI 16384
 SF 400.2500593 MHz
 WDW no
 SSB 0
 LB 0.00 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 40.00 cm
 F1P 9.750 ppm
 F1 3902.44 Hz
 F2P -0.250 ppm
 F2 -100.06 Hz
 PPMCM 0.25000 ppm/cm
 HZCM 100.06252 Hz/cm



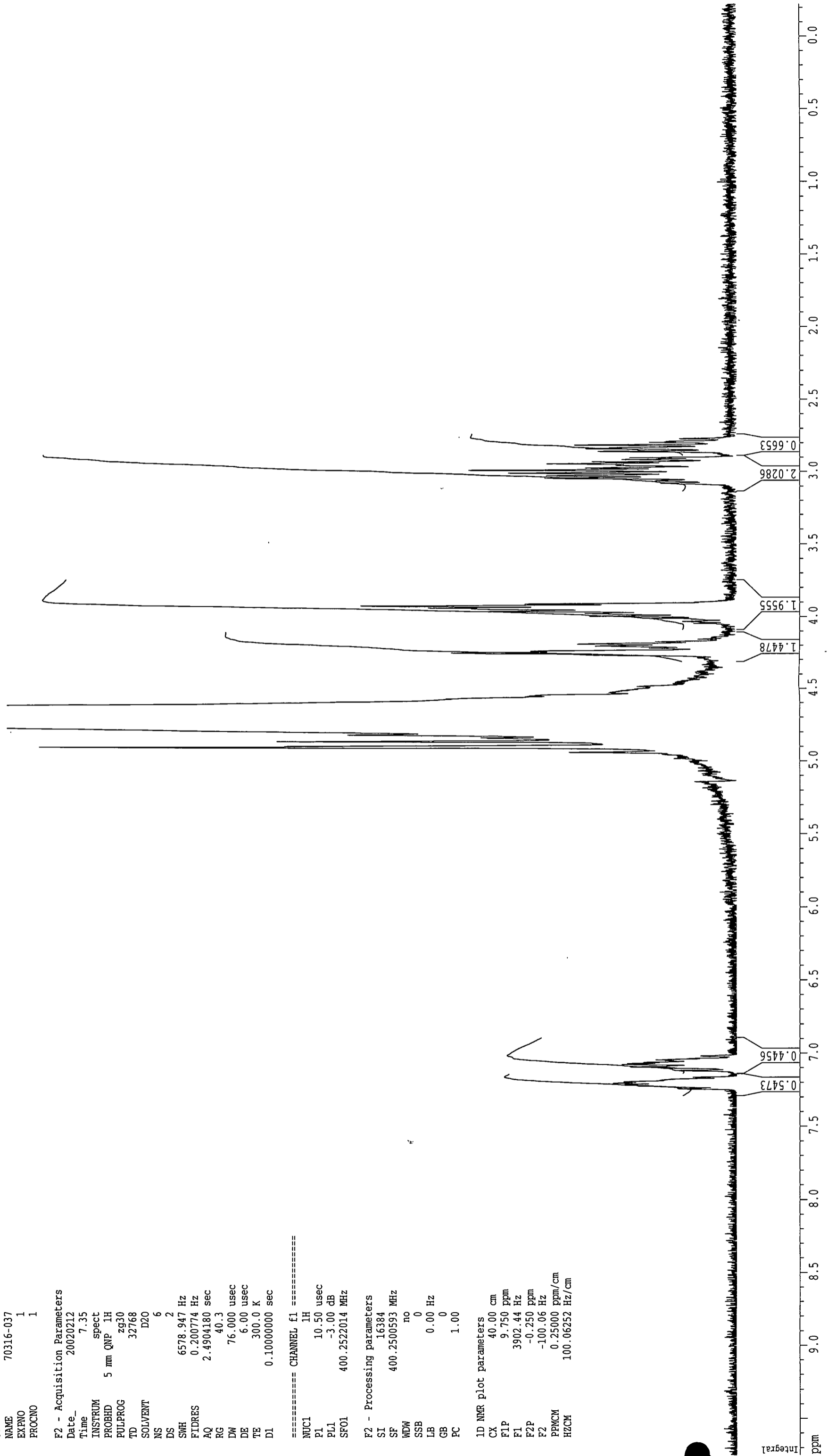
Current Data Parameters
 NAME 70316-037
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20020212
 Time 7.35
 INSTRUM spect
 PROBHD 5 mm QNP 1H
 PULPROG zg30
 TD 32768
 SOLVENT D2O
 NS 6
 DS 2
 SWH 6578.947 Hz
 FIDRES 0.200774 Hz
 AQ 2.4904180 sec
 RG 40.3
 DW 76.000 usec
 DE 6.00 usec
 TE 300.0 K
 DI 0.10000000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 400.2522014 MHz

F2 - Processing parameters
 SI 16384
 SF 400.2500593 MHz
 WDW no
 SSB 0
 LB 0.00 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 40.00 cm
 F1P 9.750 ppm
 F1 3902.44 Hz
 F2P -0.250 ppm
 F2 -100.06 Hz
 PPMCM 0.25000 ppm/cm
 HZCM 100.06252 Hz/cm



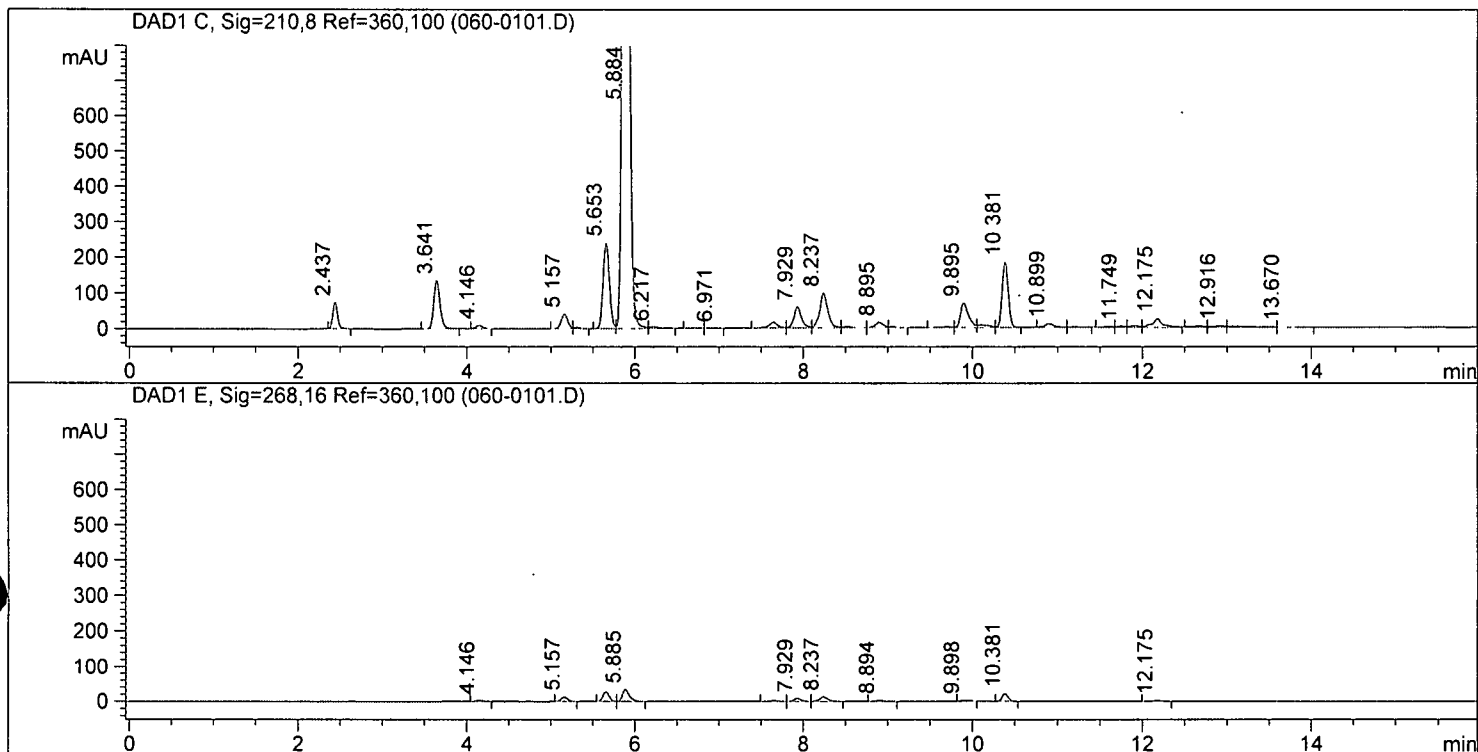
6.37g/50ml of 146.86 ML and wash

->

```

=====
Injection Date : 02/12/2002  3:04:29 PM      Seq Line : 1
Sample Name    : 70316-035                Vial No  : 60
Acq Operator   : hansen                    Inj. No. : 1
                                           Inj. Vol.: 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 01/14/2002  1:00:57 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

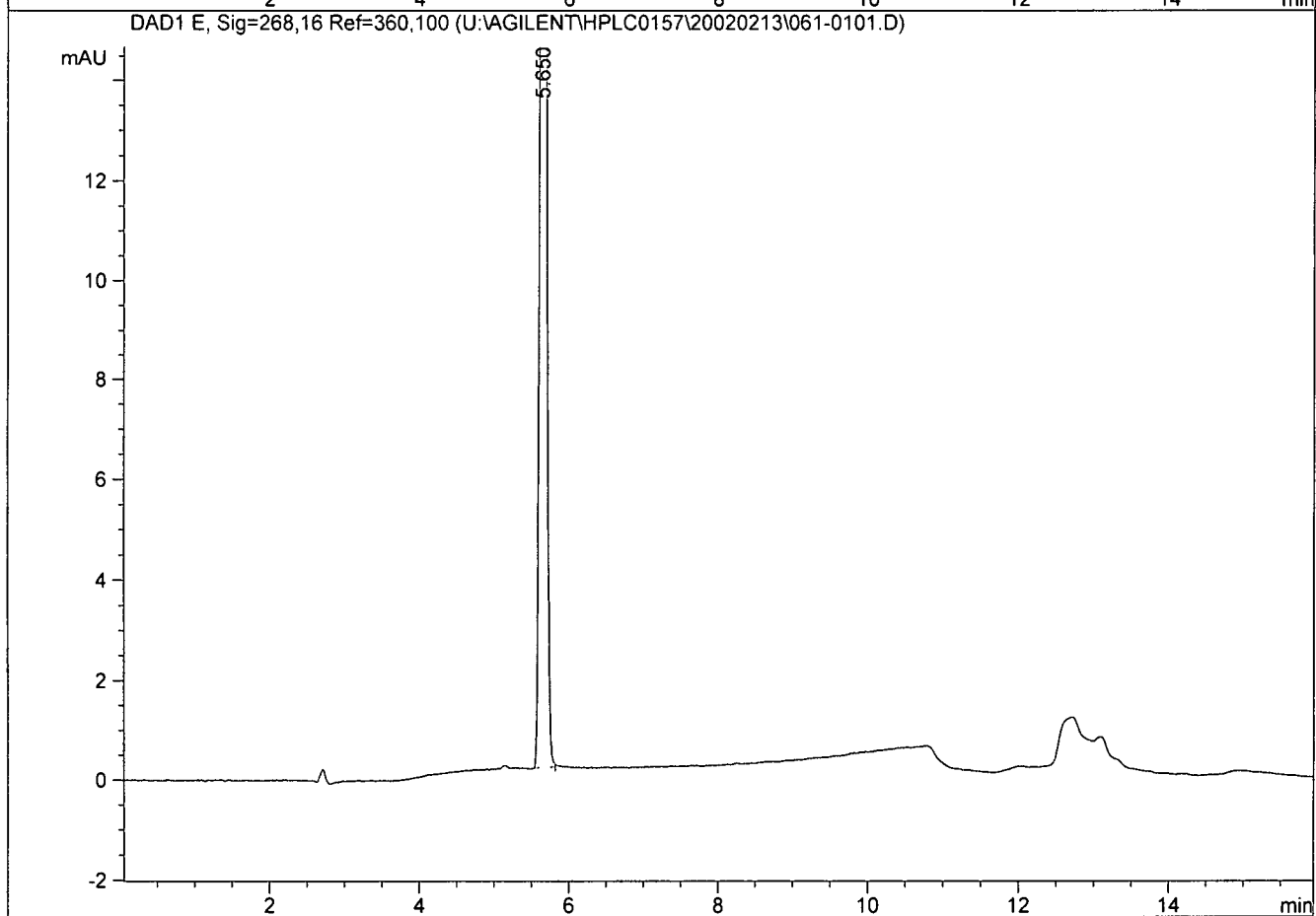
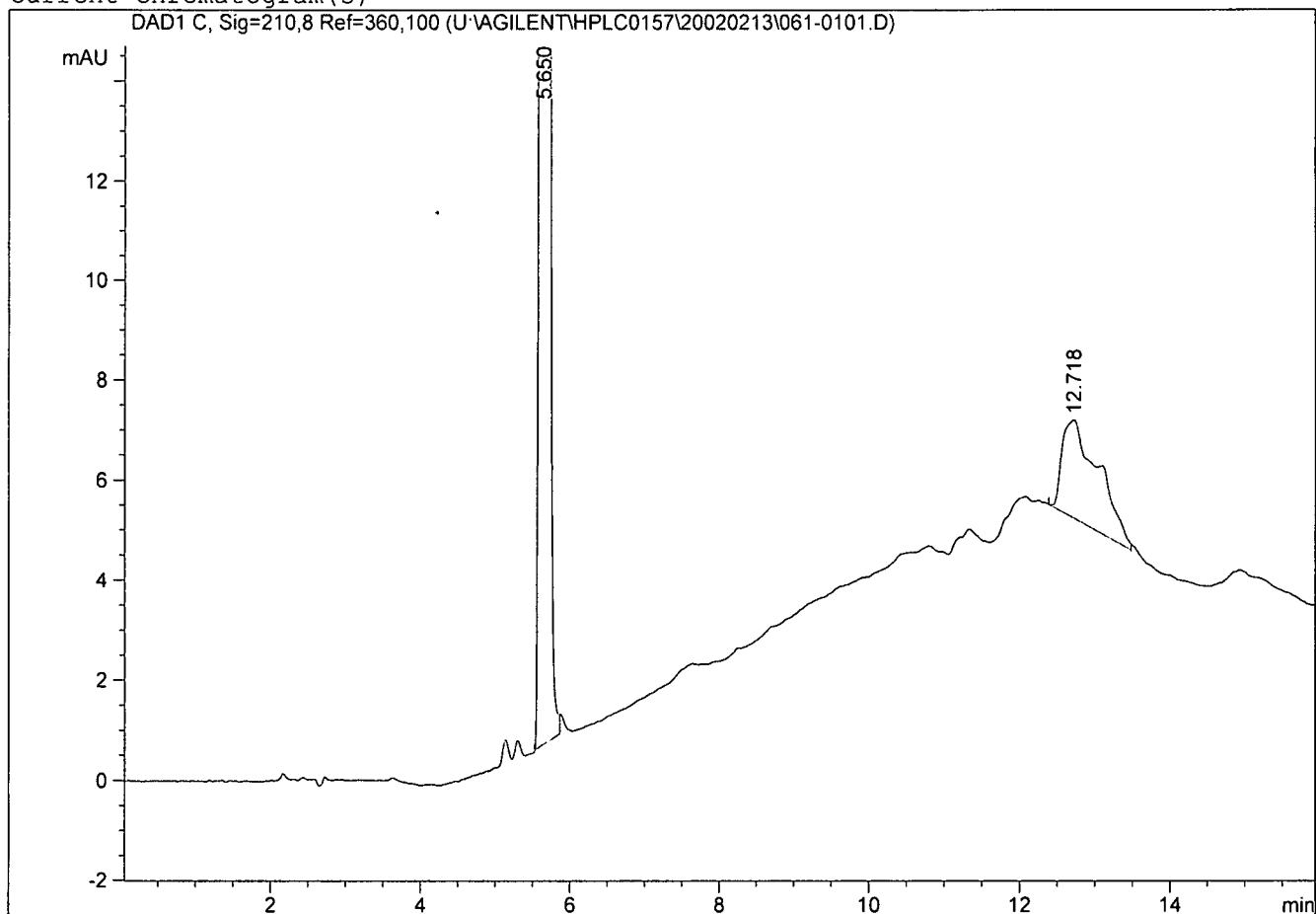
```

Sorted By      : Signal
Calib. Data Modified : 01/14/2002  1:00:30 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.44	VB	0.060	73.72	289.753	1.64	0.000000	
2	3.64	VB	0.082	135.35	713.782	4.04	0.000000	
3	4.15	BV	0.090	9.93	59.210	0.33	0.000000	
4	5.16	BV	0.086	41.08	226.496	1.28	0.000000	
5	5.30	VB	0.075	4.00	19.388	0.11	0.000000	
6	5.65	BV	0.081	240.31	1259.296	7.12	0.331258	L-224,715
7	5.88	VV	0.092	2.06e3	1.170e4	66.19	0.000000	0.3825
8	6.22	VB	0.122	4.59	40.838	0.23	0.000000	
9	6.69	BV	0.127	1.17	10.716	0.06	0.000000	
10	6.97	VV	0.122	1.00	8.968	0.05	0.000000	
11	7.64	VV	0.105	16.41	122.782	0.69	0.000000	
12	7.93	VV	0.091	59.85	373.427	2.11	0.000000	
13	8.24	VV	0.096	97.68	655.861	3.71	0.000000	
14	8.52	VV	0.106	4.07	30.668	0.17	0.000000	
15	8.89	VV	0.097	15.34	103.325	0.58	0.000000	

Current Chromatogram(s)

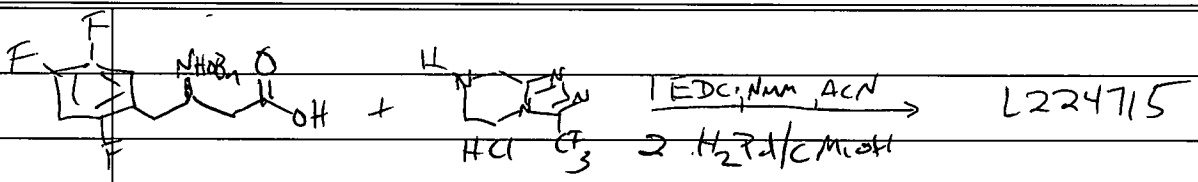


Investigator _____ Date 13 Feb 2002

Subject Coupling ~ 90% ee Amino acid



Filed in Book Number/Title _____



Reagents:		FW	amt	mmol	eq
Amino acid	72324-102 90% ee	339.11	4.07g	~12.0	1.0
Heterocycle-HCl	72176-100	228.04	4.10g	18.0	1.5
EDC		191.71	3.45g	18.0	1.5
NMM	N-methylmorpholine 0.920	101.15	1.2g (1.31ml)	12.0	1.0
ACN			40ml		

Dissolved acid in ACN added HCl Triazole salt cooled to 0°C. Added EDC & NMM sequentially 7:30 AM.

Reaction complete after 2.75h. Added 40ml H₂O 4ml EtOAc. Cut washed 20ml 5% NaHCO₃ & 20ml 5% NaCl.

Concentrated for oil. Redissolved in 40ml Methanol & submitted to hydrolysis 40PSI, 150°C, 1.2g, 10% Pd/C O/N.

14 Feb 2002. Fil Rxn complete. Filtered soln through 5.5Kri-Floc w/ methanol. Assayed @ 3.48% ⁽¹¹¹⁰³³⁰⁷⁾ 7/5. Concentrated & flushed w/ Ethanol twice. Redissolved in 8ml Ethanol.

Filtered into 100ml 3neck. Washed w/ 4.5ml EtOH. Dissolved 1.00g H₃PO₄ (85%) in 5.25ml H₂O. Added to soln @ 65°C & cloudiness occurred. Seeded w/ 35mg of 70316-005. Continued addn. After addn a slurry of crystals are present. These look smaller w/ a lo scoop but still pretty nice. heated to 75°C to achieve complete soln. Cooled @ 5°C/WO/N.

Countersigned by _____



DO NOT BEGIN NEW EXPERIMENTS ON THIS PAGE.

15 Feb 2002 - Flask is a thick slurry of xhals these are not the normal plates under scope! very thin needles.
Filter ~2-3ml of slurry & gave to c. Lehmann
to check Form. 70316-039A

heated to 60°C seed w/ 35 mg of 70316-035 - content
waiting to 65°C

After 1.5 hrs solids seemed to turnover Filtered

Small sample - Filtered fast. gave to Phys Mems 70316-039B

Cooled to RT @ 5°C/hr

18 Feb 2002 - Added 52.5 ml Ethanol to slurry.

Aged 45 minutes then filtered washed w/ Ethanol
isolated 3.02g white solids

Assayed ML's to contain 90% of product.

Solids & ML's were given to Analytical for analysis

21 Feb 2002 Analytical Result 99.6% pure by LC typical

Solids 96.02% major, 3.98% minor

ML's 94.22% major, 5.78% minor.

High level ML's suggest upgrade may be difficult at this speed

Samples given to Phys Mems show presence of new Form but mostly
desired Form - all solids ~~18~~ 21 Feb 2002



Countersigned by _____

REQUEST FOR ANALYSIS

DATE Feb 19, 2002	PPCL # 0213055 / 0213056	NOTEBOOK OR BATCH # 70316-039	PROJECT #	EXT
SUBMITTED BY	SAMPLE DISPOSITION [] RETAIN [] RETURN [] DISCARD	MOLECULAR WEIGHT	SEND REPORT TO	AREA
COMPLETE STRUCTURE	CHEMICAL NAME L-224715 phosphate salt 0213055 L-224715 m.c.s 0213056			
OTHER TESTS AND COMMENTS				
EMPIRICAL FORMULA				

<input checked="" type="checkbox"/>	TEST	KARL FISCHER	TOTAL SOLIDS	LOSS ON DRYING	UV	MELTING POINT	SPECIFIC ROTATION	RESIDUE ON IGNITION	IR
<input type="checkbox"/>	TITRATION	COLOR OF SOLUTION	HEAVY METALS	IRON	DISC	pH	VPC	<input checked="" type="checkbox"/> LC <i>area % chiral</i>	NMR
<input type="checkbox"/>	MICRO ANALYSIS	PSA	DSC	TG	X-RAY	TLC	BULK	MESH ANALYSIS	ALL CONTROLS
<input type="checkbox"/>	CHN								

DO NOT WRITE BELOW THIS LINE

RESULTS

~~0213055~~ 0213055

<u>RET</u>	<u>Area %</u>
0.95	0.17%
0.97	0.11%
1.00	99.67%

Chiral
(0213055)
L-224715 major = 96.02%
minor = 3.98%

0213056

<u>RET</u>	<u>Area %</u>
0.86	0.47%
1.00	83.72%
1.10	6.98%
1.12	0.16%
1.13	0.30%
1.31	0.12%
1.40	0.32%
1.42	0.65%
1.47	1.32%
1.52	0.13%
1.53	0.25%
1.69	0.30%
1.71	0.60%
1.73	0.23%
1.74	0.13%
1.76	2.40%
2.01	0.67%
2.04	0.28%

10 others
0.10% > 10 imp > 0.05%

(0213056)
L-224715 major = 94.22%
minor = 5.78%

NB# 25878-115

PP LAB PROC #	ANALYST J.G.D.	DATE Feb 26, 2002
---------------	--------------------------	-----------------------------

Hansen, Karl

From: Dorwart, Jason G.
Sent: Thursday, February 21, 2002 11:13 AM
To: Hansen, Karl
Subject: RE:

<u>RRT</u>	<u>Area%</u>
0.95	0.17%
0.97	0.11%
1.00	99.67%

Jason

-----Original Message-----

From: Hansen, Karl
Sent: Thursday, February 21, 2002 9:34 AM
To: Dorwart, Jason G.
Subject: RE:

How was the chemical purity?

-----Original Message-----

From: Dorwart, Jason G.
Sent: Thursday, February 21, 2002 9:30 AM
To: Hansen, Karl
Subject:

Here are the chiral purity results for the Phosphate salt and ML's from NB#70316-039

Solids = 96.02% major 3.98% minor
ML's = 94.22% major 5.78% minor

Jason

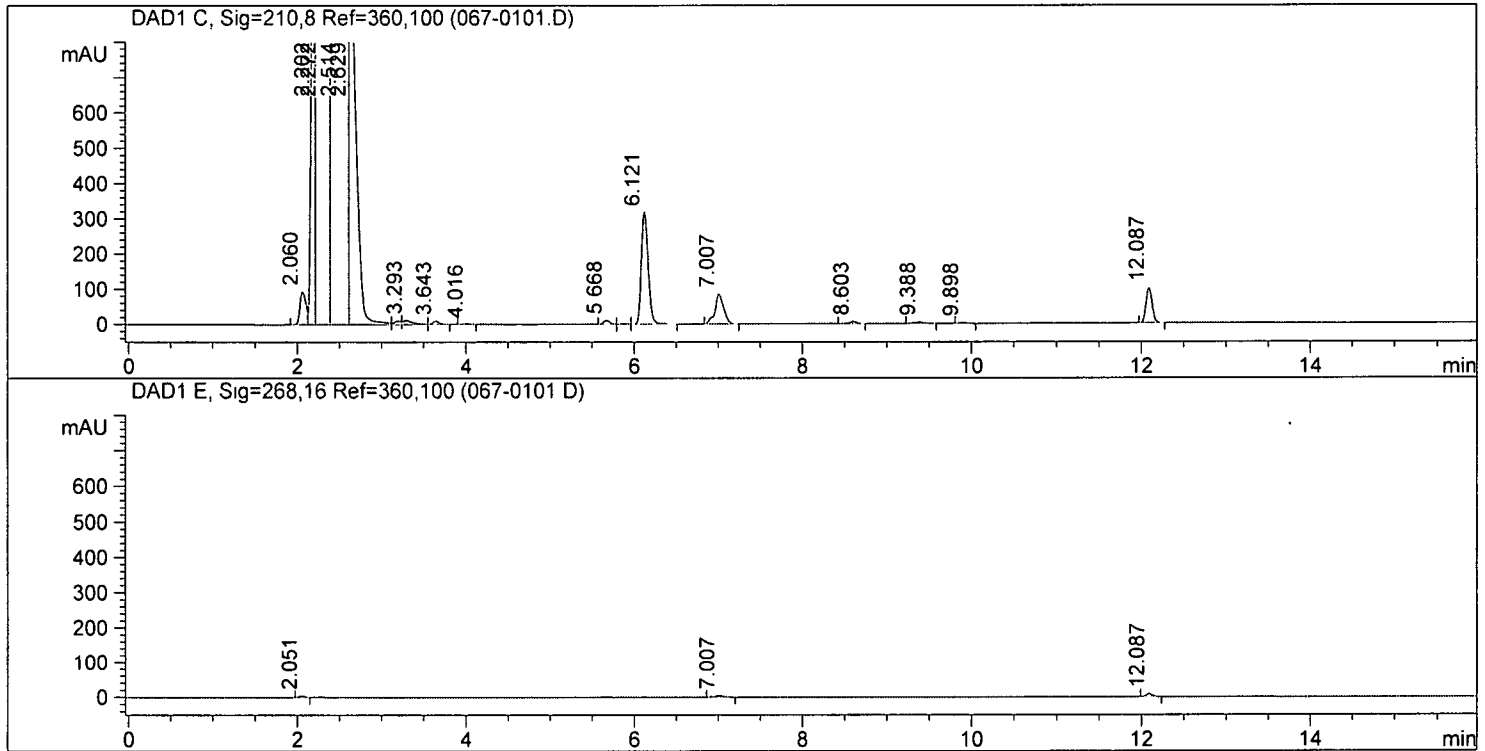
aqueous washes

->

```

=====
Injection Date : 02/14/2002 12:42:50 PM      Seq Line : 1
Sample Name    : 70316-039                   Vial No   : 67
Acq Operator   : hansen                       Inj. No.  : 1
                                           Inj. Vol. : 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 01/14/2002 1:00:57 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



=====
 Customized Report:karlo
 =====

```

Sorted By           : Signal
Calib. Data Modified : 01/14/2002 1:00:30 PM
Multiplier          : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.06	BV	0.081	94.62	463.151	0.77	0.000000	
2	2.20	VV	0.046	1.77e3	5194.654	8.63	0.000000	
3	2.27	VV	0.120	2.34e3	2.129e4	35.39	0.000000	
4	2.51	VV	0.176	2.09e3	2.414e4	40.12	0.000000	
5	2.63	VV	0.095	1.02e3	5797.346	9.64	0.000000	
6	3.19	VV	0.079	10.37	56.353	0.09	0.000000	
7	3.29	VV	0.115	12.32	102.662	0.17	0.000000	
8	3.64	VB	0.086	9.89	57.430	0.10	0.000000	
9	4.02	BV	0.111	1.45	11.322	0.02	0.000000	
10	5.67	BV	0.076	10.94	54.555	0.09	0.011273	L-224,715
11	5.87	VV	0.076	2.17	10.401	0.02	0.000000	
12	6.12	VB	0.088	318.25	1791.939	2.98	0.000000	
13	7.01	BP	0.104	85.48	613.774	1.02	0.000000	
14	8.60	VB	0.084	6.19	33.679	0.06	0.000000	
15	9.39	BB	0.105	4.35	33.252	0.06	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
16	9.90	PP	0.082	2.83	14.608	0.02	0.000000	
17	12.09	VB	0.078	99.20	496.372	0.83	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.05	BV	0.072	4.51	21.712	22.52	0.000000	
2	0.00		0.000	0.00	0.000	0.00	0.011273	L-224,715
3	7.01	BB	0.104	4.85	34.697	35.98	0.000000	
4	12.09	BB	0.078	8.01	40.019	41.50	0.000000	

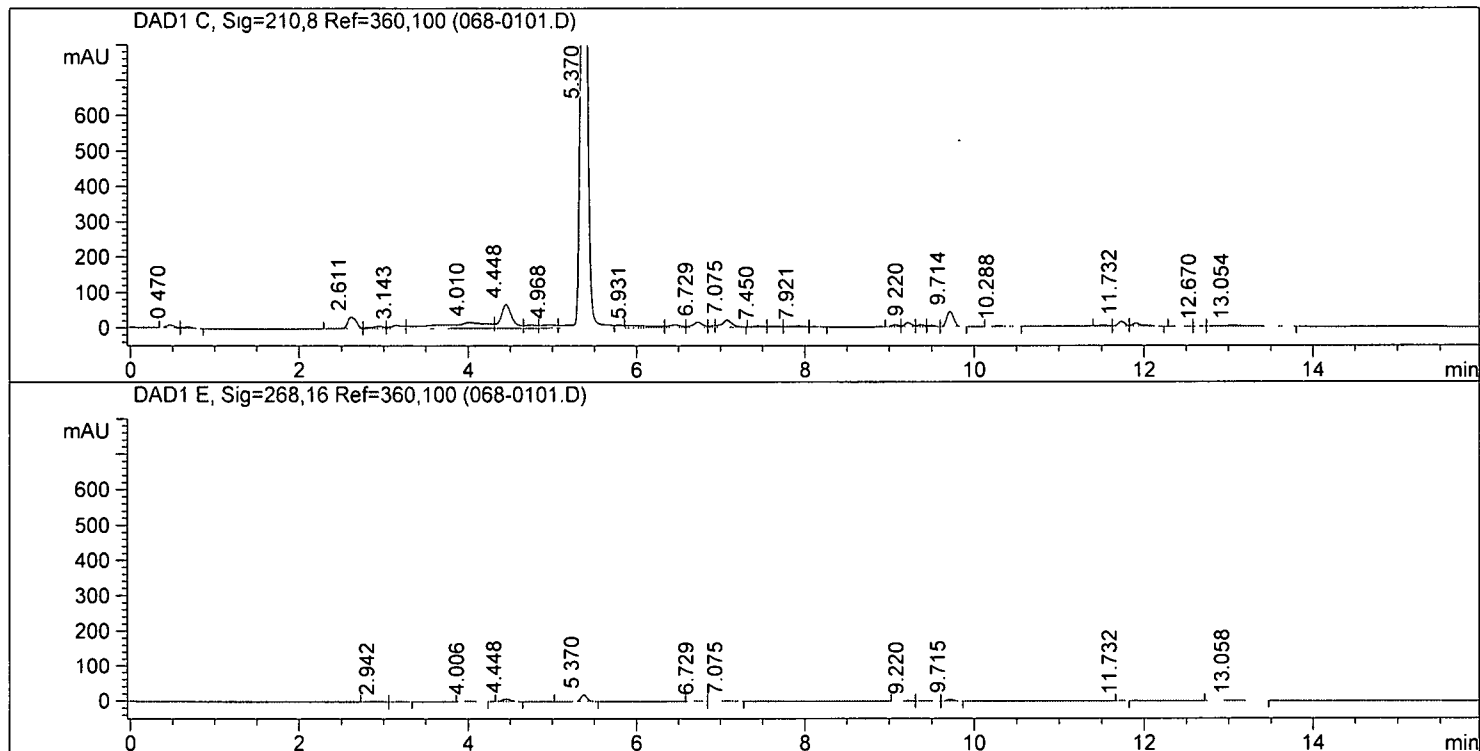
=====
*** End of Report ***

5.07g/50ml of 50.00g ml and wash

->

Injection Date : 02/19/2002 10:46:47 AM Seq Line : 1
 Sample Name : 70316-039 Vial No : 68
 Acq Operator : hansen Inj. No. : 1
 Inj. Vol. : 2 µl

Method : C:\HPCHEM\HPLC0157\METHODS\715.M
 Last Changed : 01/14/2002 1:00:57 PM
 75/25 0.1% HClO4/Acetonitrile, 1ml/min
 10min 25/75 water/acn; 75/25 from 10 to 14 min
 waters c18 symmetry, 250 nm



Customized Report:karlo

Sorted By : Signal
 Calib. Data Modified : 01/14/2002 1:00:30 PM
 Multiplier : 1.000000

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.47	BV	0.106	8.68	60.632	0.50	0.000000	
2	0.68	VP	0.107	4.08	28.938	0.24	0.000000	
3	2.61	BV	0.123	33.82	256.923	2.13	0.000000	
4	2.94	VV	0.149	7.44	82.116	0.68	0.000000	
5	3.14	VV	0.132	9.65	97.780	0.81	0.000000	
6	4.01	VV	0.496	17.12	683.647	5.66	0.000000	
7	4.45	VV	0.131	67.86	608.926	5.04	0.000000	
8	4.75	VV	0.133	9.61	89.556	0.74	0.000000	
9	4.97	VV	0.163	9.37	115.106	0.95	0.000000	
10	5.37	VB	0.089	1.54e3	8643.102	71.60	0.000000	
11	0.00		0.000	0.00	0.000	0.00	0.000000	L-224, 715
12	5.93	BV	0.282	6.93	154.725	1.28	0.000000	
13	6.45	VV	0.144	8.21	85.602	0.71	0.000000	
14	6.73	VV	0.116	15.35	128.594	1.07	0.000000	
15	6.90	VV	0.070	4.66	22.367	0.19	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
16	9.66	PV	0.161	1.00	12.317	0.12	0.000000	
17	9.96	VV	0.100	15.46	108.147	1.05	0.000000	
18	10.09	VV	0.077	7.07	36.859	0.36	0.000000	
19	10.18	VV	0.075	4.37	21.152	0.20	0.000000	
20	10.37	VB	0.079	51.84	260.206	2.52	0.000000	
21	10.89	BB	0.095	1.22	7.651	0.07	0.000000	
22	11.89	VV	0.118	2.30	19.265	0.19	0.000000	
23	12.07	VV	0.077	12.96	66.009	0.64	0.000000	
24	12.16	VV	0.097	10.05	70.204	0.68	0.000000	
25	12.44	VV	0.121	1.62	13.435	0.13	0.000000	
26	12.67	VV	0.121	2.41	20.793	0.20	0.000000	
27	12.91	VV	0.127	2.32	21.691	0.21	0.000000	
28	13.12	VB	0.145	6.01	58.331	0.56	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	4.12	BB	0.088	1.62	9.190	3.00	0.000000	
2	5.13	BB	0.085	3.33	17.950	5.87	0.000000	
3	5.63	BV	0.080	15.60	80.034	26.16	0.182926	L-224,715
4	5.87	VP	0.078	21.00	107.740	35.21	0.000000	
5	7.91	BP	0.086	1.75	10.195	3.33	0.000000	
6	8.22	BB	0.084	2.60	15.164	4.96	0.000000	
7	9.96	BV	0.085	2.21	12.245	4.00	0.000000	
8	10.37	VB	0.079	6.18	31.036	10.14	0.000000	
9	13.12	BB	0.127	2.76	22.397	7.32	0.000000	

*** End of Report ***

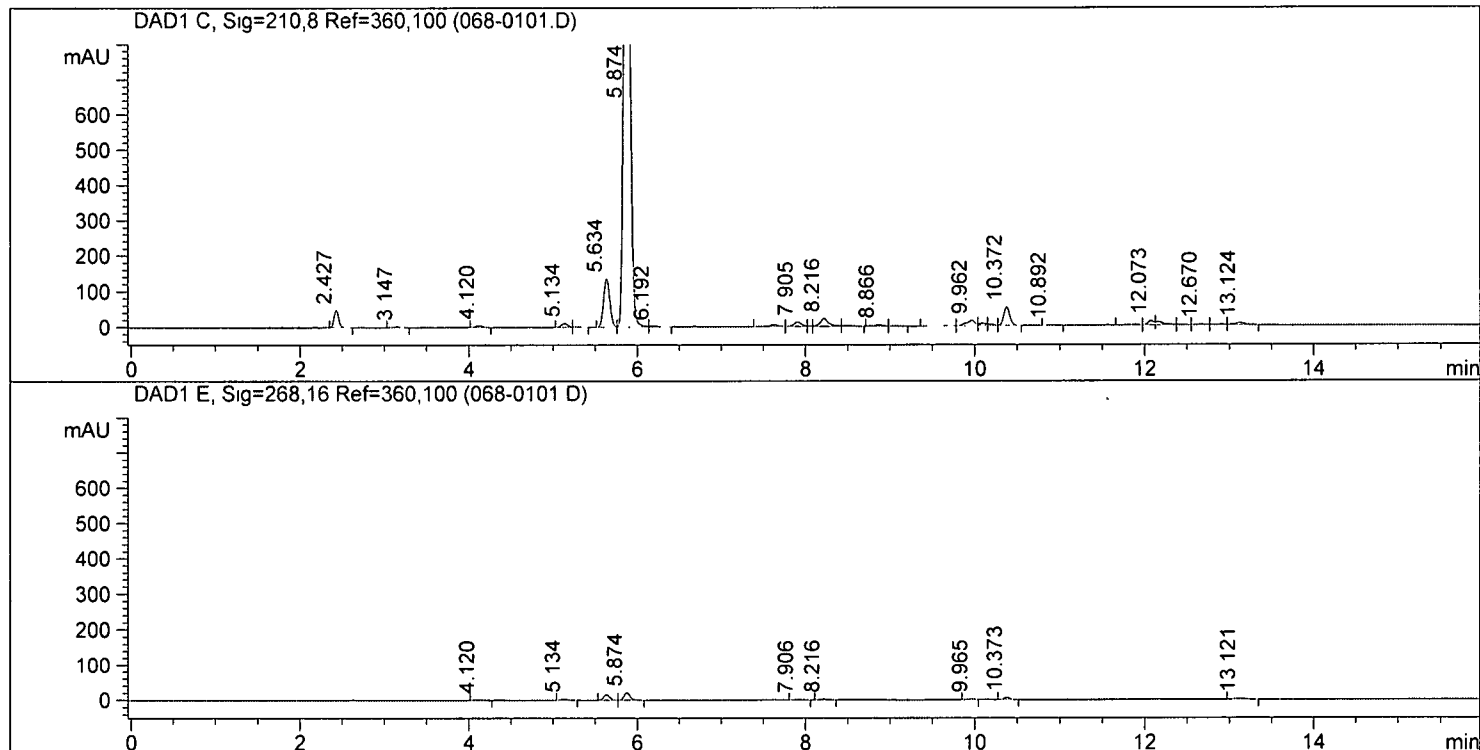
5.07g/50ml of 50.00g ml and wash

->

```

=====
Injection Date : 02/19/2002  11:22:57 AM      Seq Line : 1
Sample Name    : 70316-039                    Vial No  : 68
Acq Operator   : hansen                       Inj. No. : 1
                                           Inj. Vol.: 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 01/14/2002  1:00:57 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

=====
Sorted By      : Signal
Calib. Data Modified : 01/14/2002  1:00:30 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.43	VP	0.058	48.45	184.439	1.78	0.000000	
2	3.15	BV	0.091	2.32	13.726	0.13	0.000000	
3	4.12	BP	0.088	5.26	29.849	0.29	0.000000	
4	5.13	BV	0.085	10.91	58.757	0.57	0.000000	
5	5.28	VP	0.077	1.68	8.590	0.08	0.000000	
6	5.63	BV	0.080	136.26	700.828	6.78	0.182926	L-224,715
7	5.87	VV	0.082	1.62e3	8255.455	79.81	0.000000	
8	6.19	VB	0.109	2.77	21.703	0.21	0.000000	
9	7.62	BV	0.110	5.79	45.499	0.44	0.000000	
10	7.90	VV	0.094	12.82	83.163	0.80	0.000000	
11	8.06	VV	0.053	1.56	5.439	0.05	0.000000	
12	8.22	VV	0.101	22.52	159.956	1.55	0.000000	
13	8.50	VB	0.101	3.56	25.411	0.25	0.000000	
14	8.87	BV	0.102	4.00	28.711	0.28	0.000000	
15	9.05	VB	0.073	1.26	5.976	0.06	0.000000	

90~

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
16	7.07	VB	0.123	20.84	183.348	1.52	0.000000	
17	7.45	BV	0.138	4.07	39.146	0.32	0.000000	
18	7.63	VV	0.133	3.48	31.944	0.26	0.000000	
19	7.92	VV	0.150	3.86	42.976	0.36	0.000000	
20	8.11	VB	0.108	1.57	11.531	0.10	0.000000	
21	9.07	BV	0.093	5.73	34.086	0.28	0.000000	
22	9.22	VV	0.091	11.81	70.083	0.58	0.000000	
23	9.37	VV	0.089	5.84	34.695	0.29	0.000000	
24	9.49	VV	0.086	4.01	22.802	0.19	0.000000	
25	9.71	VB	0.090	43.41	247.354	2.05	0.000000	
26	10.29	PB	0.131	1.46	12.139	0.10	0.000000	
27	11.51	BV	0.114	3.48	26.805	0.22	0.000000	
28	11.73	VV	0.092	13.42	80.036	0.66	0.000000	
29	11.90	VP	0.118	9.35	78.452	0.65	0.000000	
30	12.40	BV	0.111	1.16	8.880	0.07	0.000000	
31	12.67	VV	0.095	1.50	9.658	0.08	0.000000	
32	13.05	VB	0.365	2.72	78.748	0.65	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.94	BP	0.122	1.65	14.471	4.53	0.000000	
2	3.18	VB	0.104	1.38	9.700	3.03	0.000000	
3	4.01	BB	0.163	1.83	21.120	6.61	0.000000	
4	4.45	BP	0.114	6.97	52.463	16.41	0.000000	
5	5.37	VB	0.086	19.02	104.015	32.54	0.000000	
6	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
7	6.73	VV	0.096	1.78	11.865	3.71	0.000000	
8	7.07	VB	0.119	2.57	21.869	6.84	0.000000	
9	9.22	BV	0.110	1.88	14.103	4.41	0.000000	
10	9.38	VP	0.163	1.11	13.691	4.28	0.000000	
11	9.71	VB	0.087	5.08	28.500	8.92	0.000000	
12	11.73	BV	0.079	1.02	5.164	1.62	0.000000	
13	13.06	PB	0.256	1.23	22.646	7.09	0.000000	

*** End of Report ***

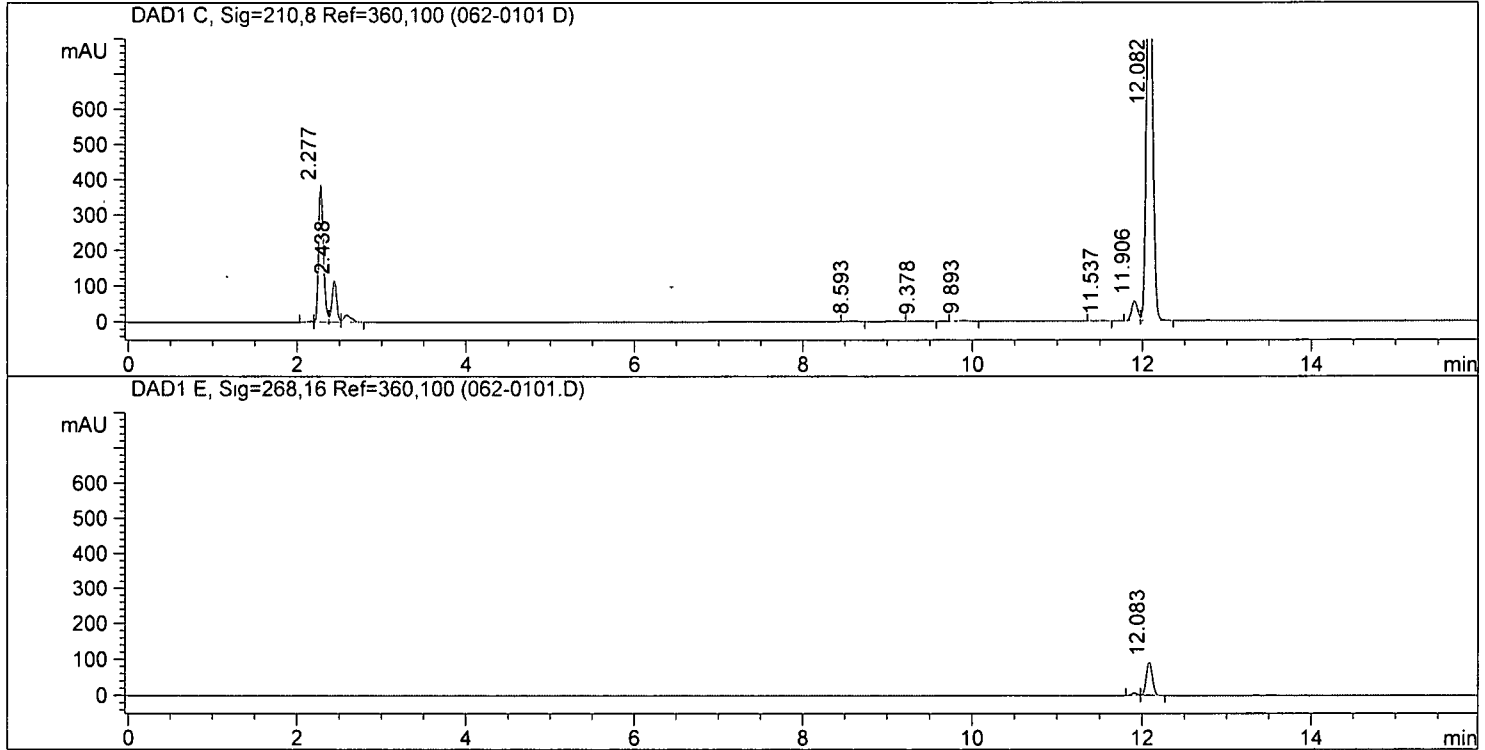
EDC coupling 1h at 0 C

->

```

=====
Injection Date : 02/13/2002  8:29:32 AM      Seq Line   : 1
Sample Name    : 70316-035                    Vial No    : 62
Acq Operator   : hansen                       Inj. No.   : 1
                                           Inj. Vol.  : 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 01/14/2002  1:00:57 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By           : Signal
Calib. Data Modified : 01/14/2002  1:00:30 PM
Multiplier          : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.16	BV	0.062	3.18	13.010	0.16	0.000000	
2	2.28	VV	0.060	382.63	1520.607	18.91	0.000000	
3	2.44	VV	0.061	116.66	449.003	5.59	0.000000	
4	2.58	VB	0.088	20.46	125.811	1.56	0.000000	
5	0.00		0.000	0.00	0.000	0.00	0.000000	L-224, 715
6	8.59	BP	0.080	2.81	14.814	0.18	0.000000	
7	9.38	PP	0.104	1.14	8.628	0.11	0.000000	
8	9.89	BP	0.093	2.61	15.884	0.20	0.000000	
9	11.54	BV	0.110	1.03	7.976	0.10	0.000000	
10	11.91	VV	0.077	55.68	273.914	3.41	0.000000	
11	12.08	VB	0.081	1.10e3	5609.710	69.78	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
2	11.91	BV	0.077	7.27	35.742	7.14	0.000000	
3	12.08	VB	0.079	92.24	465.031	92.86	0.000000	

=====
*** End of Report ***

EDC coupling 2.75h at 0 C

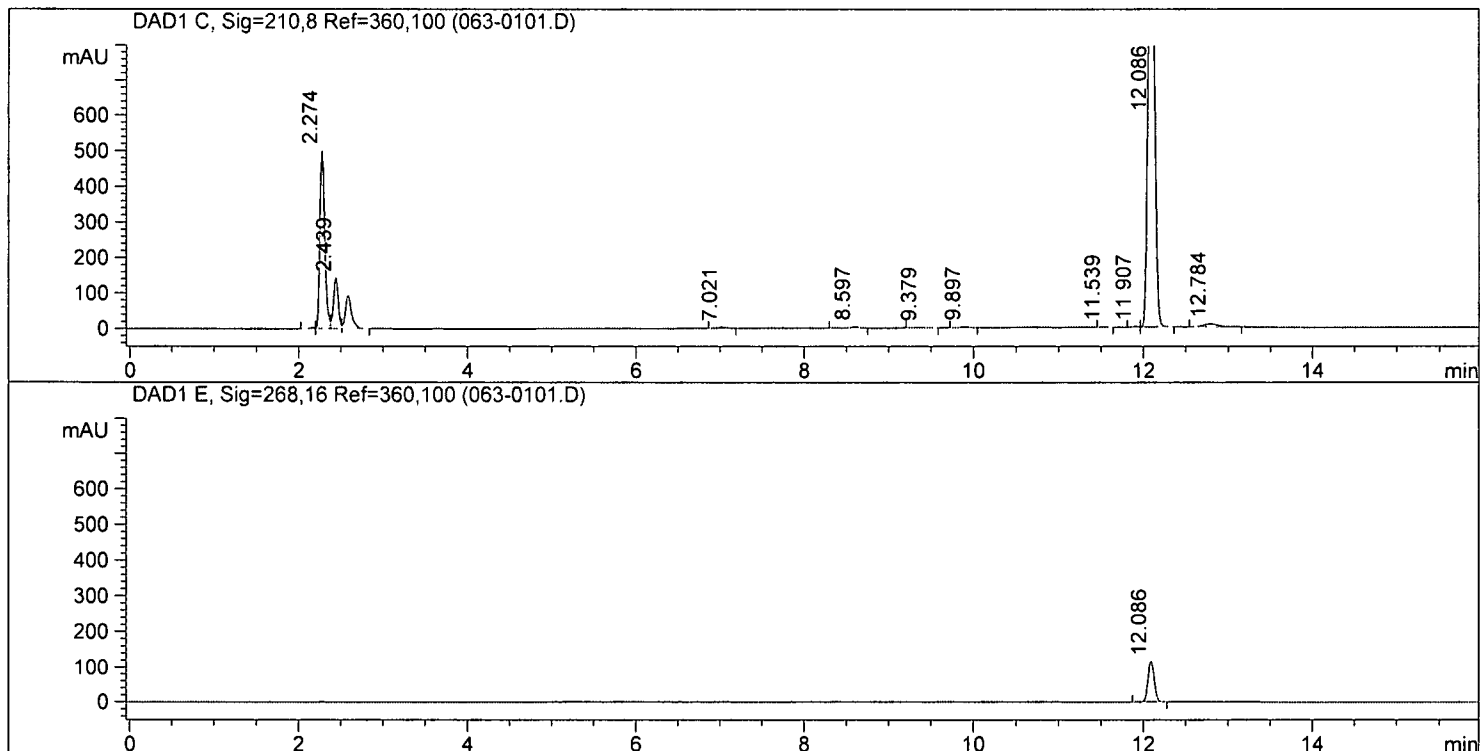
->

```

=====
Injection Date : 02/13/2002 10:16:15 AM      Seq Line : 1
Sample Name    : 70316-035                    Vial No  : 63
Acq Operator   : hansen                       Inj. No. : 1
                                           Inj. Vol.: 2 µl
    
```

```

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 01/14/2002 1:00:57 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



=====
 Customized Report:karlo
 =====

```

Sorted By      : Signal
Calib. Data Modified : 01/14/2002 1:00:30 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.16	BV	0.067	2.98	13.452	0.13	0.000000	
2	2.27	VV	0.063	502.58	2004.184	19.60	0.000000	
3	2.44	VV	0.061	144.18	561.382	5.49	0.000000	
4	2.58	VB	0.075	94.13	473.539	4.63	0.000000	
5	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
6	7.02	BB	0.093	3.42	22.671	0.22	0.000000	
7	8.60	BP	0.086	3.72	21.564	0.21	0.000000	
8	9.38	BB	0.117	1.57	13.351	0.13	0.000000	
9	9.90	BP	0.089	3.17	18.353	0.18	0.000000	
10	11.54	BV	0.086	1.16	6.516	0.06	0.000000	
11	11.91	VV	0.074	2.36	10.846	0.11	0.000000	
12	12.09	VB	0.080	1.36e3	6971.021	68.16	0.000000	
13	12.78	PB	0.204	8.22	111.157	1.09	0.000000	

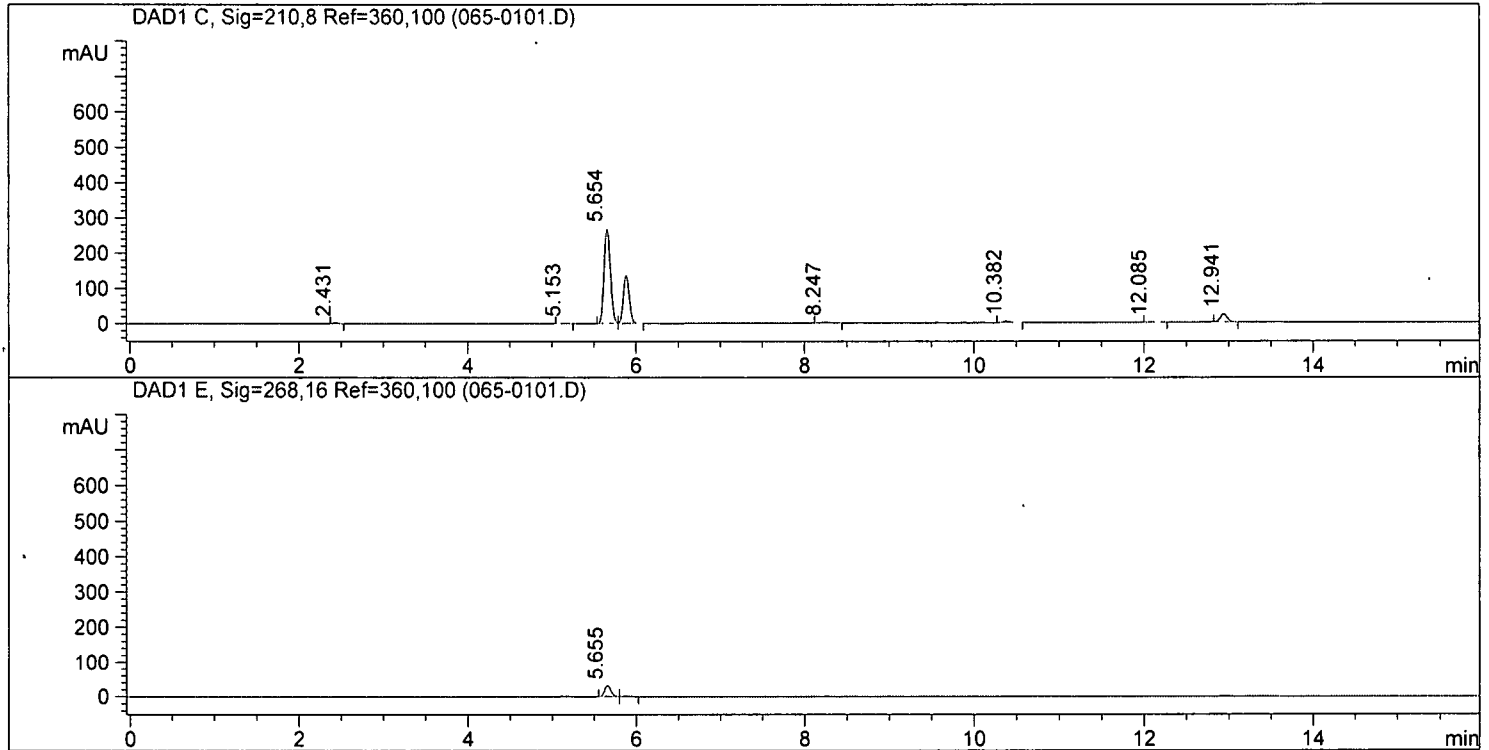
0.3990gt/50ml of 74.83g methanol filtrate

->

```

=====
Injection Date : 02/14/2002  9:58:33 AM      Seq Line : 1
Sample Name    : 70316-039                Vial No  : 65
Acq Operator   : hansen                   Inj. No. : 1
                                           Inj. Vol.: 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 01/14/2002  1:00:57 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

=====
Sorted By      : Signal
Calib. Data Modified : 01/14/2002  1:00:30 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.43	BB	0.058	3.25	12.246	0.54	0.000000	
2	5.15	BV	0.089	1.41	8.051	0.35	0.000000	
3	5.65	BV	0.081	269.11	1411.016	61.92	0.371556	L-224,715
4	5.88	VB	0.078	136.67	676.410	29.68	0.000000	
5	8.25	BP	0.090	2.33	14.869	0.65	0.000000	
6	10.38	BB	0.083	3.87	20.999	0.92	0.000000	
7	12.08	PB	0.101	1.09	7.926	0.35	0.000000	
8	12.94	BB	0.089	22.77	127.373	5.59	0.000000	

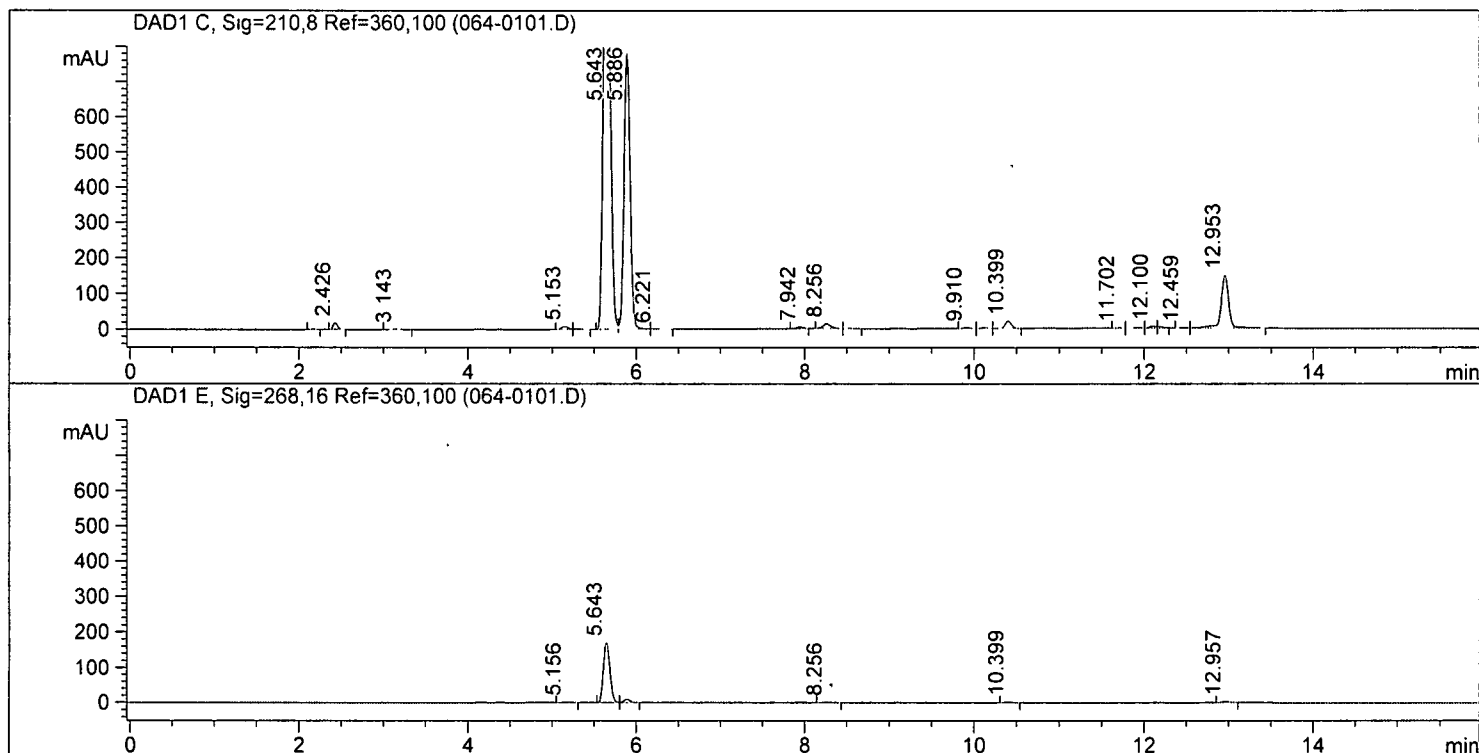
hydrog after 18h 50C, 40PSI

->

```

=====
Injection Date : 02/14/2002  9:33:56 AM      Seq Line : 1
Sample Name    : 70316-039                Vial No  : 64
Acq Operator   : hansen                   Inj. No. : 1
                                           Inj. Vol.: 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 01/14/2002  1:00:57 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 01/14/2002  1:00:30 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.17	BV	0.060	1.33	5.278	0.04	0.000000	
2	2.43	VB	0.055	19.89	70.466	0.55	0.000000	
3	3.14	BB	0.111	1.27	9.055	0.07	0.000000	
4	5.15	BV	0.088	8.07	45.540	0.36	0.000000	
5	5.31	VP	0.079	2.18	11.385	0.09	0.000000	
6	5.64	BV	0.088	1.36e3	7478.898	58.36	1.983213	L-224, 715
7	5.89	VB	0.078	779.93	3891.804	30.37	0.000000	
8	6.22	BB	0.113	1.21	9.728	0.08	0.000000	
9	7.94	PV	0.088	5.18	31.008	0.24	0.000000	
10	8.26	VV	0.099	14.25	99.158	0.77	0.000000	
11	8.52	VB	0.086	1.35	7.644	0.06	0.000000	
12	9.91	PV	0.081	2.68	14.072	0.11	0.000000	
13	10.11	VV	0.079	1.91	9.602	0.07	0.000000	
14	10.40	VP	0.079	20.55	104.739	0.82	0.000000	
15	11.70	BV	0.091	1.16	7.237	0.06	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
16	11.93	VV	0.118	1.74	14.323	0.11	0.000000	
17	12.10	VV	0.080	5.87	31.169	0.24	0.000000	
18	12.18	VB	0.074	4.10	21.077	0.16	0.000000	
19	12.46	BV	0.106	1.40	10.325	0.08	0.000000	
20	12.95	VB	0.096	148.23	942.241	7.35	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	5.16	BB	0.088	2.07	11.680	1.15	0.000000	
2	5.64	BV	0.082	171.21	913.134	89.54	1.983213	L-224,715
3	5.89	VB	0.080	9.45	48.453	4.75	0.000000	
4	8.26	BB	0.099	1.83	12.758	1.25	0.000000	
5	10.40	PP	0.077	2.42	11.930	1.17	0.000000	
6	12.96	BB	0.098	3.36	21.860	2.14	0.000000	

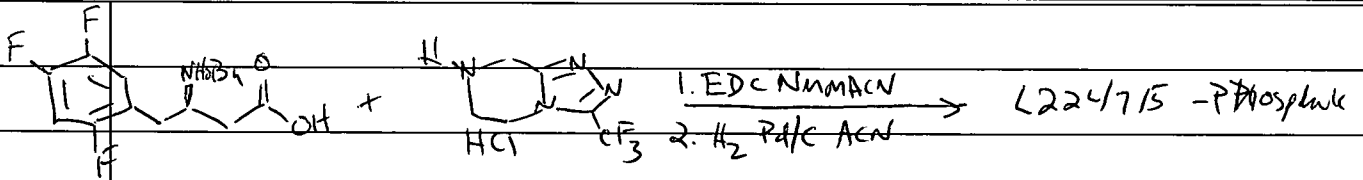
=====
*** End of Report ***

Investigator _____ Date 18 Feb 2002

Subject Coupling w/ Racemik



Filed in Book Number/Title _____



Reagents		Fw	amt	mmol	eq
Amino Acid	72324- ¹²⁴ 102 Racemik	339.11	4.22g	12.45	1.0
Triazole	72176-100	228.04	4.2g	18.7	1.5
EDCI		191.71	3.60g	18.7	1.5
NMM	0.920	101.15	1.26g	13.4ml	12.45
ACN			42ml		

Procedure Dissolved Acid in ACN & Racemik at twice
 Added 42ml ACN then 4.26g of Triazole HCl. Cooled slurry
 to 0°C. Added EDC then NMM sequentially aged.
 After 1.5 hr 598% conv of Acid observed

Added 20ml H₂O, 20ml EtOAc. Cut w/ 5% NaHCO₃
 w/ small amt salt (20ml). Then sat NaCl. Concentrated to oil
 Submitted for Hydroly 40ml methanol, 1.2g 10% Pd/C, 40 PSI 50°C

21 Feb 2002 - Assayed - all w/ B₂O cleaved. Filtered off
 catalyst & washed w/ methanol. Assayed filtrate to contain
 4.54g (89% yield) of L224715. Concentrated to oil.
 & Re-dissolved in methanol & concentrated 2x.

Redissolved in 13.5ml Ethanol filtered into 3neck RBF.
 washed flask, filter w/ 4.5ml Ethanol total 18ml Ethanol yield 1/5.

Dissolved 1.34g H₃PO₄ (1.05 equiv) in 6.75ml H₂O.
 & charged to addl funnel. Heated to 60°C & seeded w/ 45mg

Ala 21 Feb 2002

Countersigned by _____



Date _____

S.25

DO NOT BEGIN NEW EXPERIMENTS ON THIS PAGE.

21 Feb 2002

of 70316-035 Added H_2PO_4 soly slowly. Slurry formed
Solids looked like thin plates under Microscope
Added 65ml Ethanol to slurry @ $60^\circ C$. Cooled to RT. Aged
 $1/2$ hr then filtered w/ wash of 20ml Ethanol.

1H -NMR of Solids show no ethanol.

$[715]_{DMLs} = 0.934 \text{ g/g}$ $62\% \text{ present } 1.4\%$

Xray of Solids show that it is entirely new form present
in 70316-039 supporting the fact that this new
form may be exclusively racemic.

5.25g of Solids isolated 83.5% yield.

Countersigned by _____

Date _____

REQUEST FOR ANALYSIS

DATE Feb 21, 2002		PPCL # 0213061		NOTEBOOK OR BATCH # 70316-041		PROJECT #		EXT 2345	
SUBMITTED BY David Hansen			SAMPLE DISPOSITION [] RETAIN [] RETURN [] DISCARD			MOLECULAR WEIGHT		SEND REPORT TO AREA David Hansen	
COMPLETE STRUCTURE					CHEMICAL NAME C-224,715 H₃PO₄ Racemate				
EMPIRICAL FORMULA					OTHER TESTS AND COMMENTS				

<input checked="" type="checkbox"/>	TEST	<input type="checkbox"/>	KARL FISCHER	<input type="checkbox"/>	TOTAL SOLIDS	<input type="checkbox"/>	LOSS ON DRYING	<input type="checkbox"/>	UV	<input type="checkbox"/>	MELTING POINT	<input type="checkbox"/>	SPECIFIC ROTATION	<input type="checkbox"/>	RESIDUE ON IGNITION	<input type="checkbox"/>	IR
<input type="checkbox"/>	TITRATION	<input type="checkbox"/>	COLOR OF SOLUTION	<input type="checkbox"/>	HEAVY METALS	<input type="checkbox"/>	IRON	<input type="checkbox"/>	DISC	<input type="checkbox"/>	pH	<input type="checkbox"/>	VPC	<input checked="" type="checkbox"/>	LC LCAD	<input type="checkbox"/>	NMR
<input type="checkbox"/>	MICRO ANALYSIS	<input type="checkbox"/>	PSA	<input type="checkbox"/>	DSC	<input type="checkbox"/>	TG	<input type="checkbox"/>	X-RAY	<input type="checkbox"/>	TLC	<input type="checkbox"/>	BULK	<input type="checkbox"/>	MESH ANALYSIS	<input type="checkbox"/>	ALL CONTROLS
<input type="checkbox"/>	CHN																

DO NOT WRITE BELOW THIS LINE

RESULTS

LCAD

<u>Rt</u>	<u>Area%</u>
0.91	0.18%
0.95	0.05%
0.97	0.11%
1.00	99.66%

0.34%

Chiral

C-400,224 - 49.92%

C-224,715 - 50.08%

NB # 25878-117

PP LAB PROC. #	ANALYST J.G.D.	DATE Feb 22, 2002
----------------	--------------------------	-----------------------------

HYDROGENATION OR HIGH PRESSURE REACTION

2002022054.001
DO NOT WRITE IN THIS SPACE

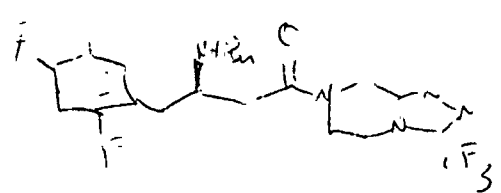
REQUESTED BY Hansen BLDG/RM 70 B269 EXT. 1 DATE Feb 20 2002

PROJECT NO. 224715 PROJECT M... 2-1 NOTEBOOK - PAGE NO. 216-11

CHECK HERE IF REACTION IS GMP/GLP **STARTING MATERIAL**

NO. 1 _____	NO. 2 _____
M.W. _____ AMOUNT <u>1</u> G. MOLES <u>1.5mmol</u>	M.W. _____ AMOUNT _____ G. MOLES _____

STRUCTURAL FORMULA:



CATALYST 2 G. OF 10% Pd/C

SOLVENT _____ ML. OF 1

MOLES OF HYDROGEN REQUIRED 5

OTHER MATERIALS 1.5mmol AlCl3

REACTION CONDITIONS, ETC. 40 psi, r.t.

PRECAUTIONS: _____

EMPIRICAL FORMULA: _____

TO BE FILLED IN BY HYDROGENATION LABORATORY

NO. 1: 64 G. MOLES 0.0124 NO. 2: _____ G. MOLES _____

CATALYST 1.2 G. OF 10% Pd/C lot # CDC 98025

SOLVENT 411 ML. OF meOH

OTHER MATERIALS _____

CELL NO. _____ HEATER NO. _____ REC. POINT INTERNAL _____ EXTERNAL _____ BOMB NO. _____ VESSEL SIZE 250 ML.

SHAKER NO. 54 LINER _____ SHAKER TANK 176 AUX. TANK _____ SYSTEM VOLUME 79 ML.

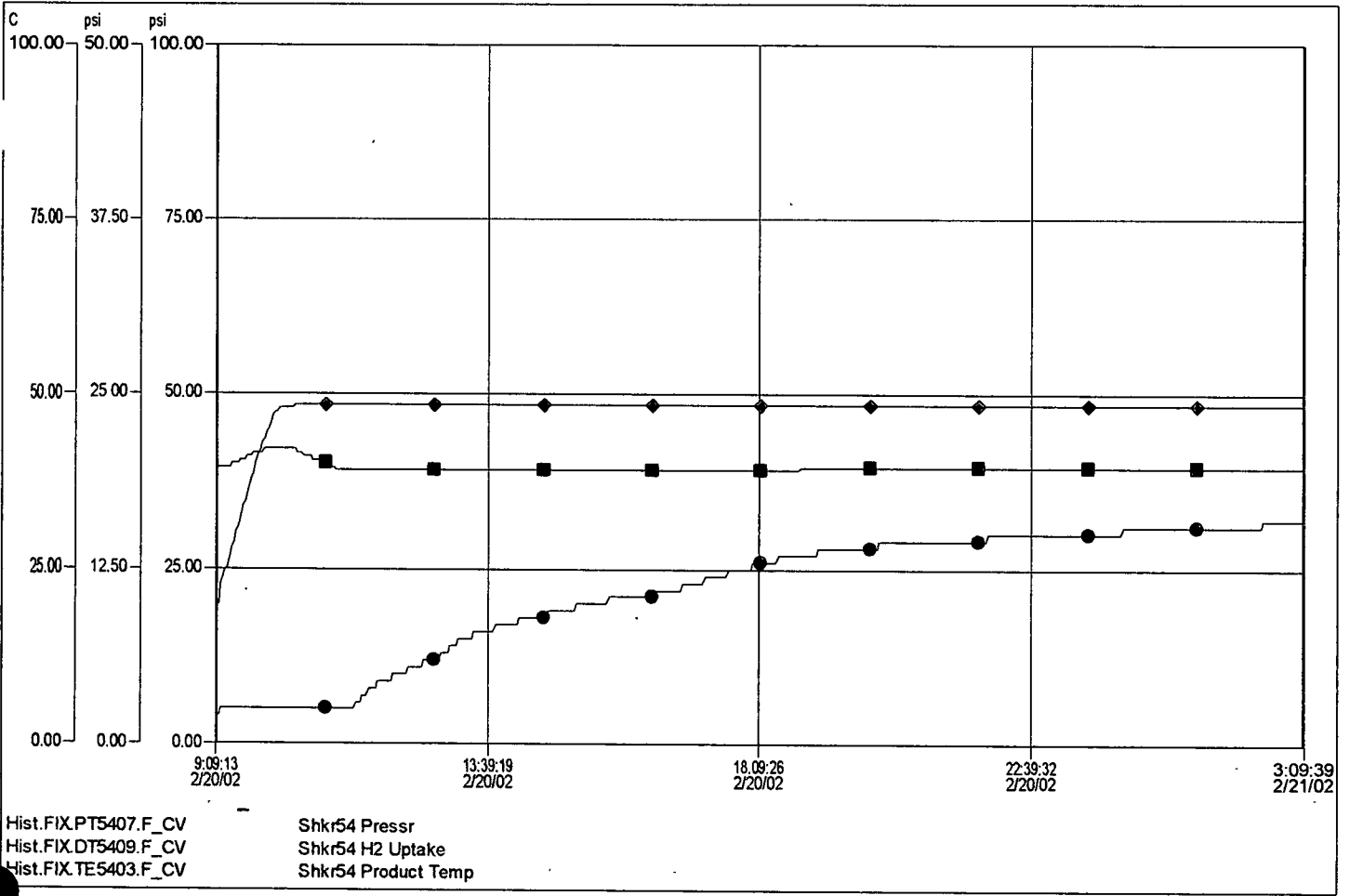
CL₂H₂ PRESSURE DROP = _____ LBS./MOLE 0.0124 MOLES = 17.4 LBS.

CONDITIONS _____ HRS. AT 50 C. MISC. DATA: 40 psi, H₂

TIME	TEMP.	PRESSURE		TIME	TEMP.	PRESSURE		TIME	TEMP.	PRESSURE	
		OBS.	DROP			OBS.	DROP			OBS.	DROP
09:10	17.2	40	2	15:34	48.5	39	10	21:58	48.5	40	15
09:22	26.9	40	2	15:46	48.5	39	10	22:10	48.5	40	15
09:34	33.4	41	2	15:58	48.5	39	10	22:22	48.5	40	15
09:46	38.8	42	2	16:10	48.5	39	10	22:34	48.5	40	15
09:58	44.3	42	2	16:22	48.5	39	10	22:46	48.5	40	15
10:10	48.0	42	2	16:34	48.5	39	11	22:58	48.5	40	15
10:22	48.0	42	2	16:46	48.5	39	11	23:10	48.5	40	15
10:34	48.5	42	2	16:58	48.5	39	12	23:22	48.5	40	15
10:46	48.5	41	2	17:10	48.5	39	12	23:34	48.5	40	15
10:58	48.5	40	2	17:22	48.5	39	12	23:46	48.5	40	15
11:10	48.5	39	2	17:34	48.5	39	12	23:58	48.5	40	15
11:22	48.5	39	2	17:46	48.5	39	12	00:10	48.5	40	16
11:34	48.5	39	4	17:58	48.5	39	12	00:22	48.5	40	16
11:46	48.5	39	4	18:10	48.5	39	13	00:34	48.5	40	16
11:58	48.5	39	4	18:22	48.5	39	13	00:46	48.5	40	16
12:10	48.5	39	5	18:34	48.5	39	14	00:58	48.5	40	16
12:22	48.5	39	6	18:46	48.5	39	14	01:10	48.5	40	16
12:34	48.5	39	6	18:58	48.5	40	14	01:22	48.5	40	16
12:46	48.5	39	6	19:10	48.5	40	14	01:34	48.5	40	16
12:58	48.5	39	6	19:22	48.5	40	14	01:46	48.5	40	16
13:10	48.5	39	8	19:34	48.5	40	14	01:58	48.5	40	16
13:22	48.5	39	8	19:46	48.5	40	14	02:10	48.5	40	16
13:34	48.5	39	8	19:58	48.5	40	14	02:22	48.5	40	16
13:46	48.5	39	8	20:10	48.5	40	14	02:34	48.5	40	16
13:58	48.5	39	8	20:22	48.5	40	14	02:46	48.5	40	16
14:10	48.5	39	9	20:34	48.5	40	14	02:58	48.5	40	16
14:22	48.5	39	9	20:46	48.5	40	14				
14:34	48.5	39	9	20:58	48.5	40	14				
14:46	48.5	39	10	21:10	48.5	40	14				
14:58	48.5	39	10	21:22	48.5	40	14				
15:10	48.5	39	10	21:34	48.5	40	14				
15:22	48.5	39	10	21:46	48.5	40	14				

RUN BY D. Hansen DATE Feb 20, 2002

RUN BY _____ DATE _____



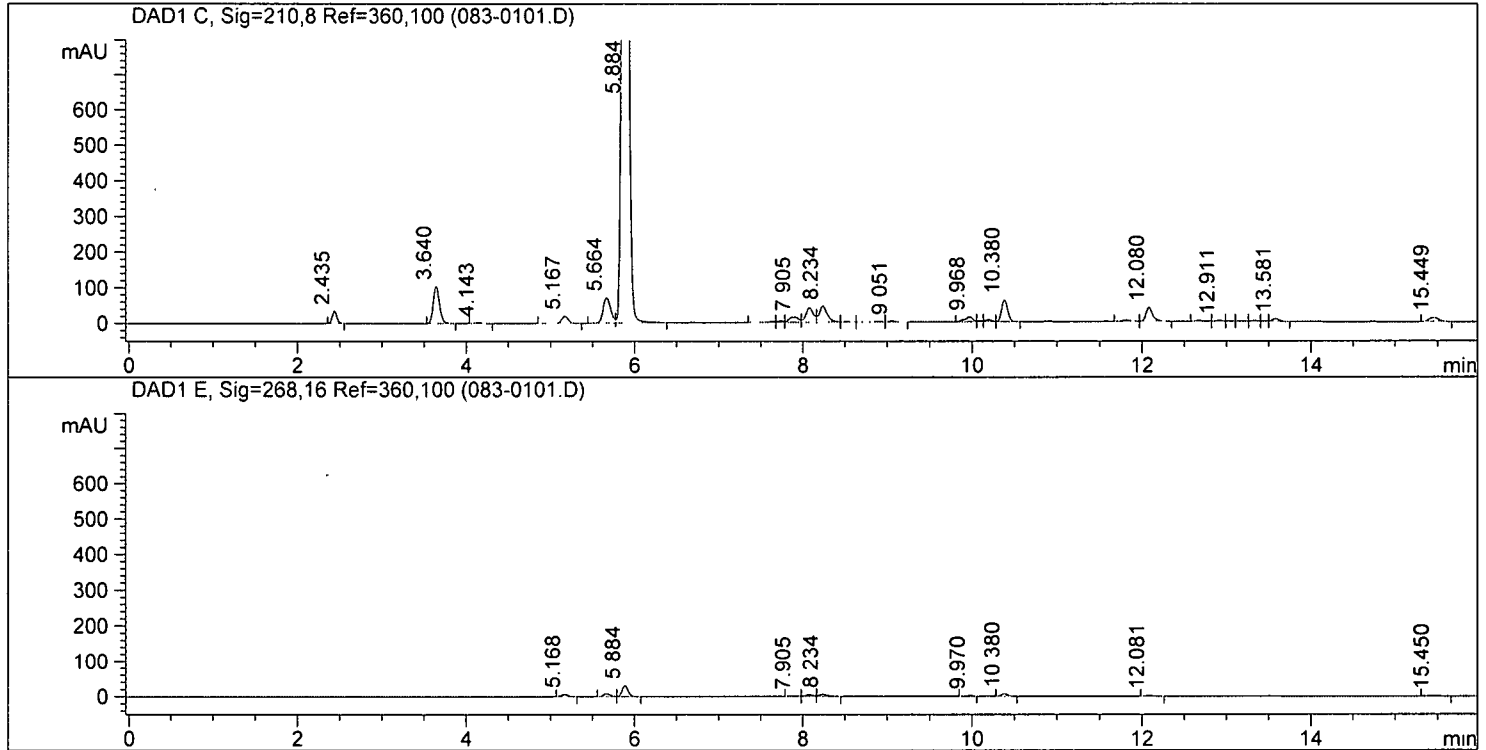
12.50g/100ml of 66.25 g ML's

->

```

=====
Injection Date : 02/21/2002  2:00:19 PM      Seq Line : 1
Sample Name   : 70316-041                Vial No  : 83
Acq Operator  : hansen                    Inj. No. : 1
                                           Inj. Vol.: 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed  : 02/21/2002  7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

=====
Sorted By      : Signal
Calib. Data Modified : 02/20/2002  3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.43	VB	0.059	35.38	135.757	0.97	0.000000	
2	3.64	PB	0.080	105.11	540.202	3.86	0.000000	
3	4.14	PP	0.085	2.19	11.908	0.09	0.000000	
4	5.17	VP	0.084	20.69	113.330	0.81	0.000000	
5	5.66	BV	0.097	71.88	451.690	3.23	0.116754	
6	5.88	VB	0.088	2.02e3	1.106e4	79.07	0.000000	
7	7.64	BV	0.117	2.46	20.081	0.14	0.000000	
8	7.74	VV	0.072	4.15	20.054	0.14	0.000000	
9	7.90	VV	0.111	14.58	118.122	0.84	0.000000	
10	8.08	VV	0.091	41.70	259.979	1.86	0.000000	
11	8.23	VV	0.095	46.06	305.568	2.18	0.000000	
12	8.51	VV	0.102	1.49	10.709	0.08	0.000000	
13	8.89	VV	0.148	1.65	18.654	0.13	0.000000	
14	9.05	VB	0.095	2.94	18.810	0.13	0.000000	
15	9.97	PV	0.097	14.34	94.398	0.67	0.000000	

L-224, 715
 0.9344 mg/s
 62.0mg

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
16	10.10	VV	0.062	3.13	12.846	0.09	0.000000	
17	10.20	VV	0.082	5.72	30.532	0.22	0.000000	
18	10.38	VB	0.078	61.39	305.114	2.18	0.000000	
19	11.81	VV	0.090	4.32	26.748	0.19	0.000000	
20	12.08	VB	0.085	38.72	215.145	1.54	0.040783	benzyloxy amide
21	12.67	BB	0.097	2.54	16.712	0.12	0.000000	
22	12.91	BV	0.092	2.81	17.402	0.12	0.000000	
23	13.05	VV	0.088	1.53	9.184	0.07	0.000000	
24	13.15	VV	0.117	1.47	11.522	0.08	0.000000	
25	13.34	VV	0.086	2.54	14.823	0.11	0.000000	
26	13.46	VV	0.071	2.01	9.566	0.07	0.000000	
27	13.58	VB	0.090	7.88	46.094	0.33	0.000000	
28	15.45	BB	0.120	11.96	92.362	0.66	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	5.17	BP	0.084	6.35	33.503	8.40	0.000000	
2	5.66	BV	0.094	7.93	47.519	11.91	0.116754	L-224,715
3	5.88	VB	0.078	30.86	153.100	38.37	0.000000	
4	7.91	VV	0.108	2.03	16.102	4.04	0.000000	
5	8.08	VV	0.089	5.28	32.237	8.08	0.000000	
6	8.23	VB	0.095	6.00	40.393	10.12	0.000000	
7	9.97	BV	0.084	2.06	11.407	2.86	0.000000	
8	10.38	VB	0.078	7.27	36.250	9.08	0.000000	
9	12.08	BB	0.086	3.12	17.737	4.44	0.040783	benzyloxy amide
10	15.45	BB	0.121	1.39	10.807	2.71	0.000000	

=====
*** End of Report ***

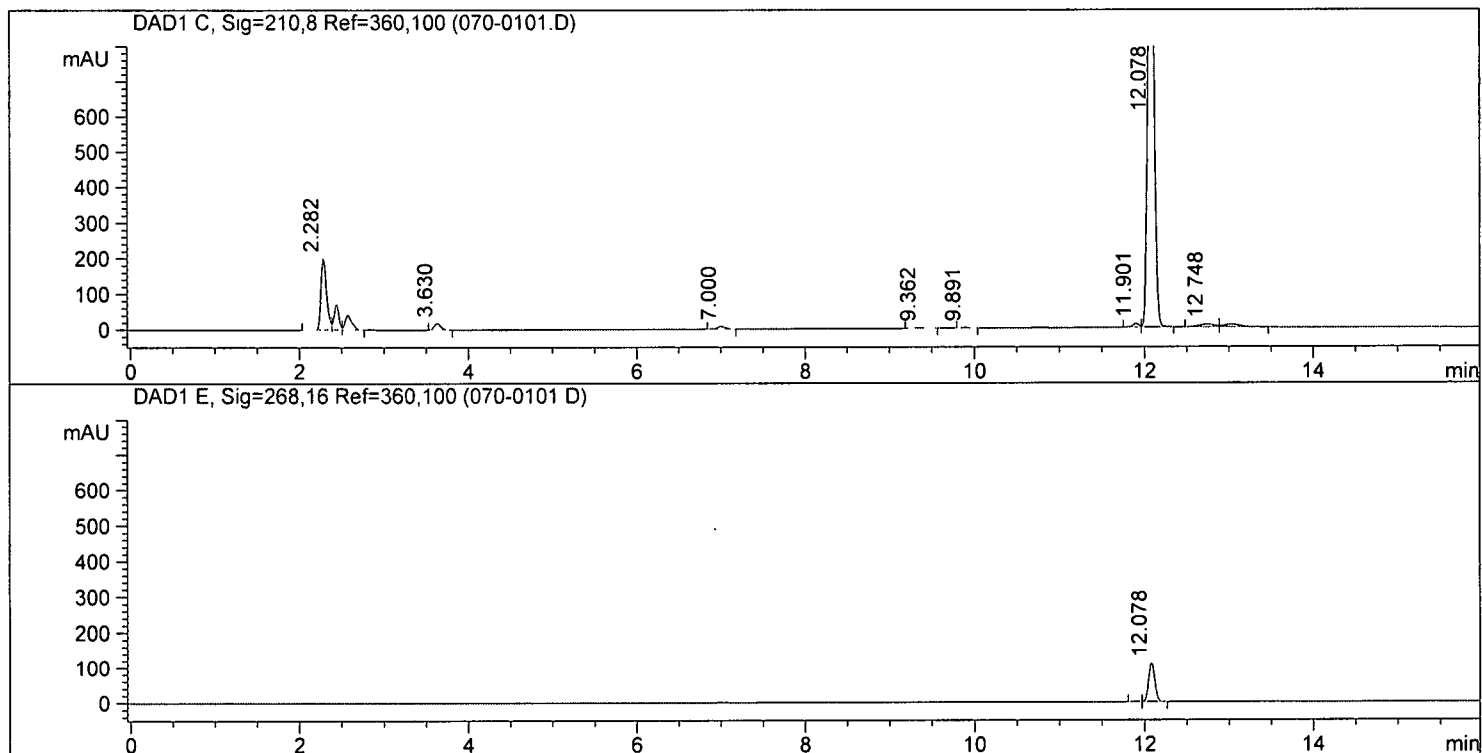
coupling after 1.5 h

->

```

=====
Injection Date : 02/19/2002  1:13:25 PM      Seq Line : 1
Sample Name    : 70316-041                Vial No  : 70
Acq Operator   : hansen                    Inj. No. : 1
                                           Inj. Vol.: 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 01/14/2002  1:00:57 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 01/14/2002  1:00:30 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.28	BV	0.070	202.28	933.038	10.87	0.000000	
2	2.44	VV	0.059	72.72	280.741	3.27	0.000000	
3	2.57	VB	0.081	42.70	237.644	2.77	0.000000	
4	3.63	BB	0.083	18.74	101.496	1.18	0.000000	
5	0.00		0.000	0.00	0.000	0.00	0.000000	L-224, 715
6	7.00	BP	0.095	8.00	52.590	0.61	0.000000	
7	9.36	BB	0.107	1.65	12.585	0.15	0.000000	
8	9.89	PP	0.082	1.56	8.025	0.09	0.000000	
9	11.90	PV	0.081	10.91	56.839	0.66	0.000000	
10	12.08	VB	0.082	1.30e3	6678.729	77.83	0.000000	
11	12.75	BV	0.177	8.63	109.855	1.28	0.000000	
12	13.03	VB	0.199	8.10	110.137	1.28	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
2	11.90	BV	0.077	1.40	6.766	1.20	0.000000	
3	12.08	VB	0.079	111.20	559.139	98.80	0.000000	

=====
*** End of Report ***

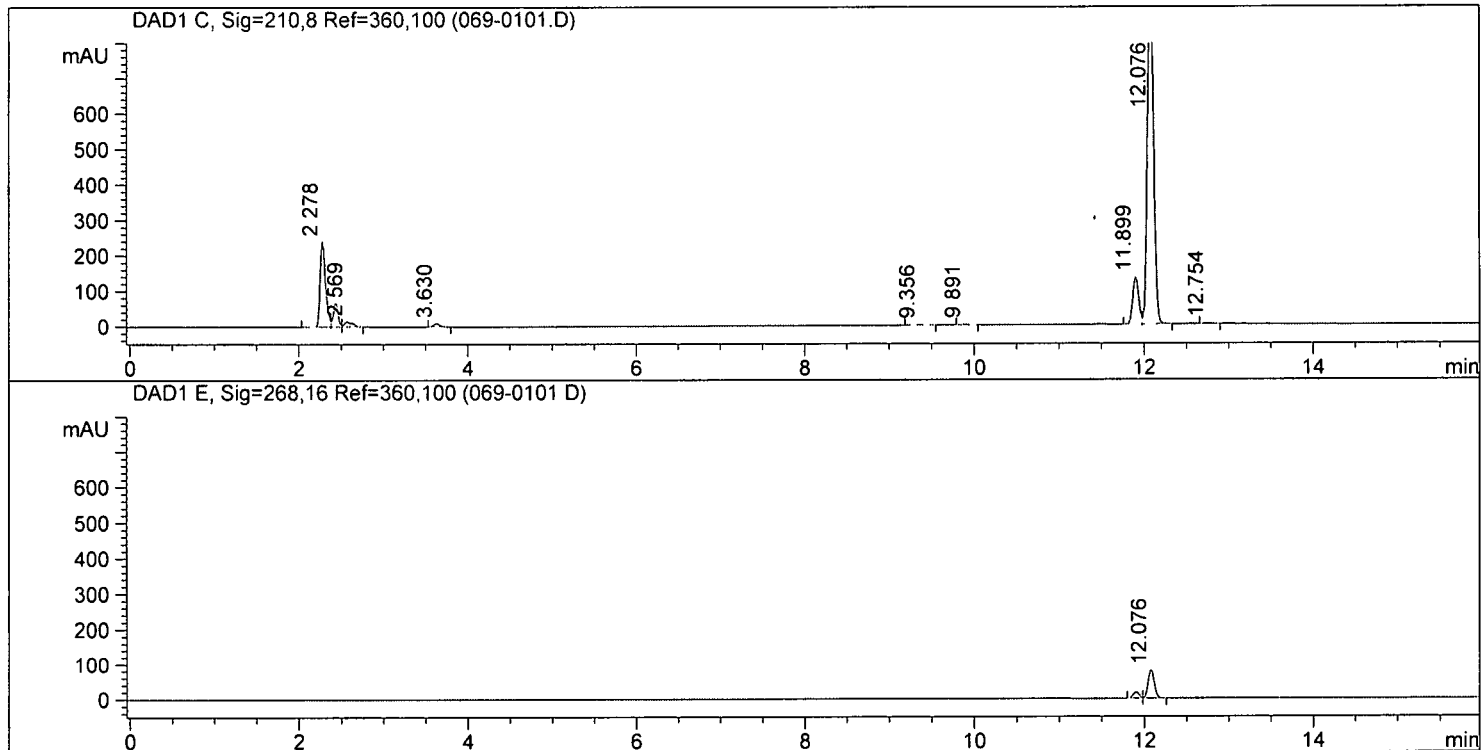
coupling after 0.5 h

->

```

=====
Injection Date : 02/19/2002 12:17:24 PM      Seq Line : 1
Sample Name    : 70316-041                   Vial No  : 69
Acq Operator   : hansen                       Inj. No. : 1
                                           Inj. Vol.: 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 01/14/2002 1:00:57 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 01/14/2002 1:00:30 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.28	BV	0.068	239.06	1065.164	15.07	0.000000	
2	2.43	VV	0.061	67.64	262.453	3.71	0.000000	
3	2.57	VB	0.095	14.23	98.965	1.40	0.000000	
4	3.63	BB	0.083	8.92	48.279	0.68	0.000000	
5	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
6	9.36	BB	0.108	1.32	10.144	0.14	0.000000	
7	9.89	PP	0.083	1.34	6.998	0.10	0.000000	
8	11.90	PV	0.078	131.70	654.250	9.26	0.000000	
9	12.08	VB	0.079	968.34	4912.232	69.52	0.000000	
10	12.75	BB	0.085	1.41	7.865	0.11	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
2	11.90	BV	0.078	17.39	86.368	17.56	0.000000	
3	12.08	VB	0.079	80.51	405.441	82.44	0.000000	

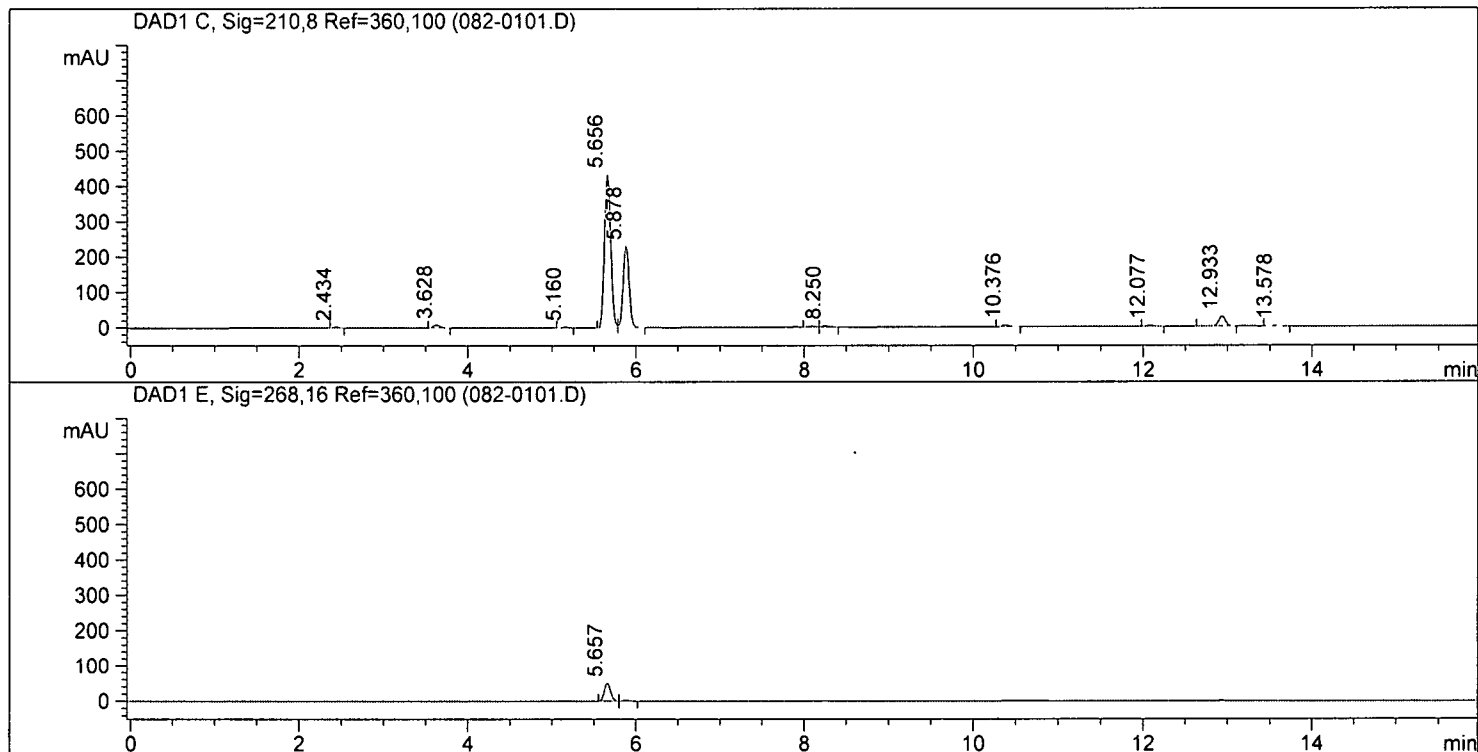
=====
*** End of Report ***

0.4506g/50ml of 68.30g of methanol filtrate

->

Injection Date : 02/21/2002 9:45:19 AM Seq Line : 1
 Sample Name : 70316-041 Vial No : 82
 Acq Operator : hansen Inj. No. : 1
 Inj. Vol. : 2 µl

Method : C:\HPCHEM\HPLC0157\METHODS\715.M
 Last Changed : 02/21/2002 7:13:49 AM
 75/25 0.1% HClO4/Acetonitrile, 1ml/min
 10min 25/75 water/acn; 75/25 from 10 to 14 min
 waters c18 symmetry, 250 nm



Customized Report:karlo

Sorted By : Signal
 Calib. Data Modified : 02/20/2002 3:33:04 PM
 Multiplier : 1.000000

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.43	BB	0.057	2.95	10.963	0.29	0.000000	
2	3.63	BB	0.083	8.33	45.204	1.21	0.000000	
3	5.16	BV	0.086	1.92	10.511	0.28	0.000000	
4	5.66	BV	0.081	434.68	2269.569	60.74	0.599591	4.54 ₅ L-224,715
5	5.88	VB	0.076	230.45	1141.925	30.56	0.000000	
6	8.09	VV	0.086	3.21	19.348	0.52	0.000000	
7	8.25	VB	0.090	3.73	23.083	0.62	0.000000	
8	10.38	PB	0.081	5.21	27.294	0.73	0.000000	
9	12.08	PP	0.083	3.18	17.037	0.46	0.000000	benzyloxy amide
10	12.93	BB	0.089	27.88	160.147	4.29	0.000000	
11	13.58	BP	0.094	1.91	11.748	0.31	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	5.66	BV	0.081	50.44	262.624	94.93	0.599591	L-224,715
2	5.88	VB	0.078	2.72	14.039	5.07	0.000000	
3	0.00		0.000	0.00	0.000	0.00	0.000000	benzyloxy amide

=====
*** End of Report ***

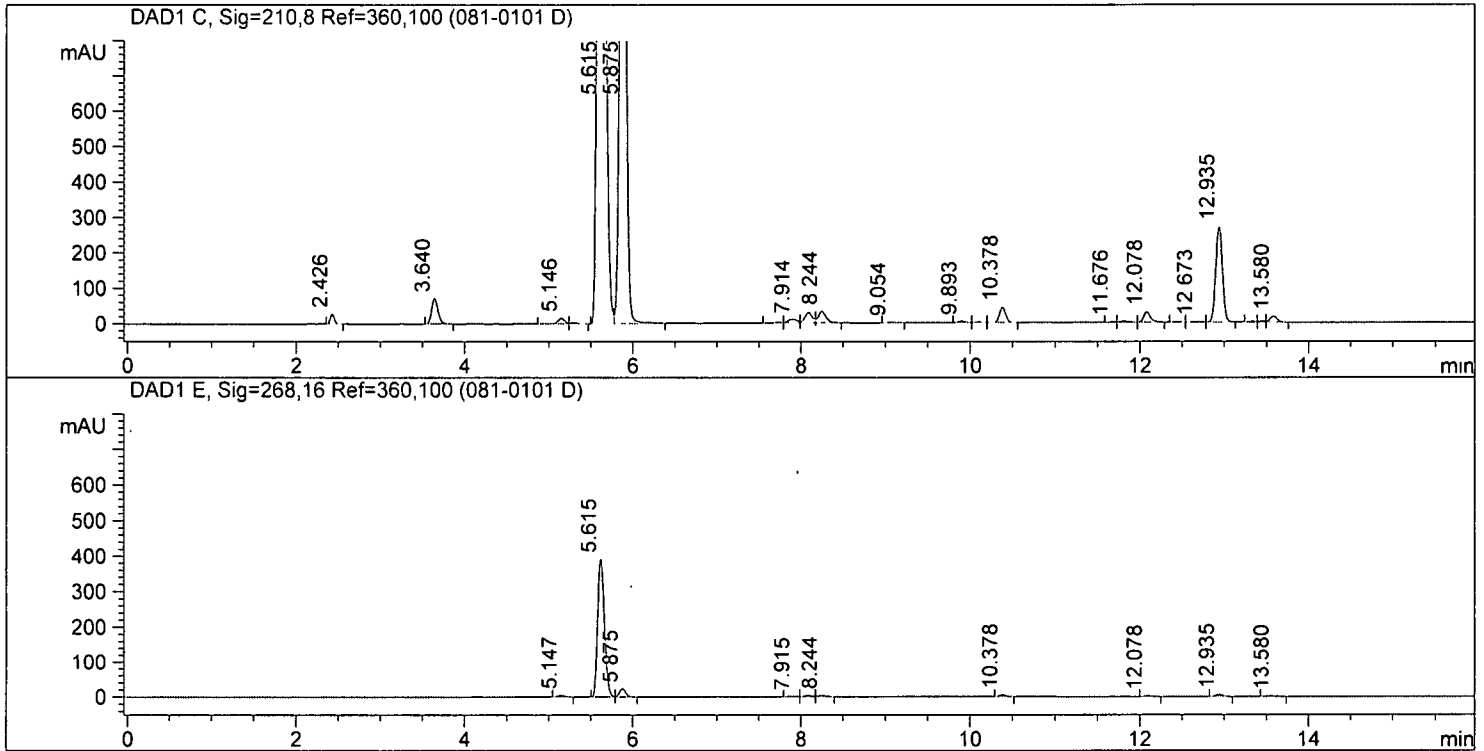
hydrog on racemate

->

```

=====
Injection Date : 02/21/2002  9:21:28 AM      Seq Line : 1
Sample Name    : 70316-041                    Vial No   : 81
Acq Operator   : hansen                       Inj. No.  : 1
                                           Inj. Vol. : 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002  7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 02/20/2002  3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.43	VB	0.053	28.36	95.220	0.36	0.000000	
2	3.64	BB	0.081	72.37	381.358	1.44	0.000000	
3	5.15	VV	0.088	16.12	91.591	0.35	0.000000	
4	5.29	VP	0.078	3.67	18.855	0.07	0.000000	
5	5.62	BV	0.110	2.10e3	1.409e4	53.34	3.738111	L-224,715
6	5.87	VB	0.083	1.74e3	9085.580	34.40	0.000000	
7	7.74	BV	0.099	2.88	20.088	0.08	0.000000	
8	7.91	VV	0.108	9.92	78.003	0.30	0.000000	
9	8.09	VV	0.091	29.76	186.235	0.71	0.000000	
10	8.24	VB	0.093	33.32	215.009	0.81	0.000000	
11	9.05	PB	0.097	1.66	11.296	0.04	0.000000	
12	9.89	PV	0.084	4.22	23.219	0.09	0.000000	
13	10.10	VV	0.084	1.69	9.284	0.04	0.000000	
14	10.38	VB	0.079	43.09	219.777	0.83	0.000000	
15	11.68	BV	0.083	1.60	8.868	0.03	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
16	11.81	VV	0.107	3.81	28.506	0.11	0.000000	.
17	12.08	VB	0.086	30.21	175.365	0.66	0.032219	benzyloxy amide
18	12.44	BV	0.117	1.71	14.520	0.05	0.000000	
19	12.67	VV	0.122	2.63	22.953	0.09	0.000000	
20	12.93	VB	0.089	270.87	1503.265	5.69	0.000000	
21	13.33	BV	0.093	2.28	14.770	0.06	0.000000	
22	13.47	VV	0.067	3.63	16.643	0.06	0.000000	
23	13.58	VB	0.089	17.33	101.970	0.39	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	5.15	BB	0.084	4.65	25.595	1.03	0.000000	
2	5.62	BV	0.087	392.31	2192.617	88.52	3.738111	L-224,715
3	5.87	VB	0.080	23.08	118.492	4.78	0.000000	
4	7.92	VV	0.105	1.41	11.020	0.44	0.000000	
5	8.09	VV	0.090	3.79	23.358	0.94	0.000000	
6	8.24	VB	0.092	4.36	27.529	1.11	0.000000	
7	10.38	BB	0.077	5.05	24.679	1.00	0.000000	
8	12.08	BP	0.081	2.33	12.660	0.51	0.032219	benzyloxy amide
9	12.93	PP	0.087	5.61	30.491	1.23	0.000000	
10	13.58	BP	0.093	1.73	10.563	0.43	0.000000	

=====
*** End of Report ***

HYDROGENATION OR HIGH PRESSURE REACTION

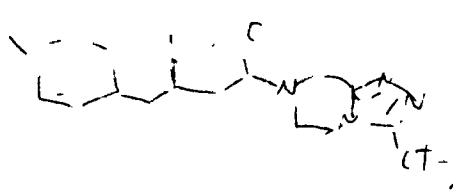
2002021354.001
DO NOT WRITE IN THIS SPACE

REQUESTED BY Hansen BLDG/RM 503 B269 EXT. 0552 DATE 2.13.02

PROJECT NO. 1175 PROJECT 1175 NOTEBOOK - PAGE NO. 1175

CHECK HERE IF REACTION IS GMP/GLP **STARTING MATERIAL**

NO. 1 _____ M.W. <u>513</u> AMOUNT <u>6.15</u> G. MOLES <u>2</u>	NO. 2 _____ M.W. _____ AMOUNT _____ G. MOLES _____
---	---

STRUCTURAL FORMULA: 

CATALYST 1.2 G. OF 10% Pt
 SOLVENT 41 ML. OF MeOH
 MOLES OF HYDROGEN REQUIRED _____
 OTHER MATERIALS _____
 REACTION CONDITIONS, ETC. _____
 PRECAUTIONS: _____

EMPIRICAL FORMULA: _____

TO BE FILLED IN BY HYDROGENATION LABORATORY

NO. 1: 6.15 G. MOLES 0.012 NO. 2: _____ G. MOLES _____

CATALYST 1.2 G. OF 10% Pt lot # SA 98025

SOLVENT 41 ML. OF MeOH

OTHER MATERIALS _____

CELL NO. _____ HEATER NO. _____ REC. POINT INTERNAL _____ EXTERNAL _____ BOMB NO. _____ VESSEL SIZE 250 ML.

SHAKER NO. 54 LINER _____ SHAKER TANK 176 AUX. TANK _____ SYSTEM VOLUME 79 ML.

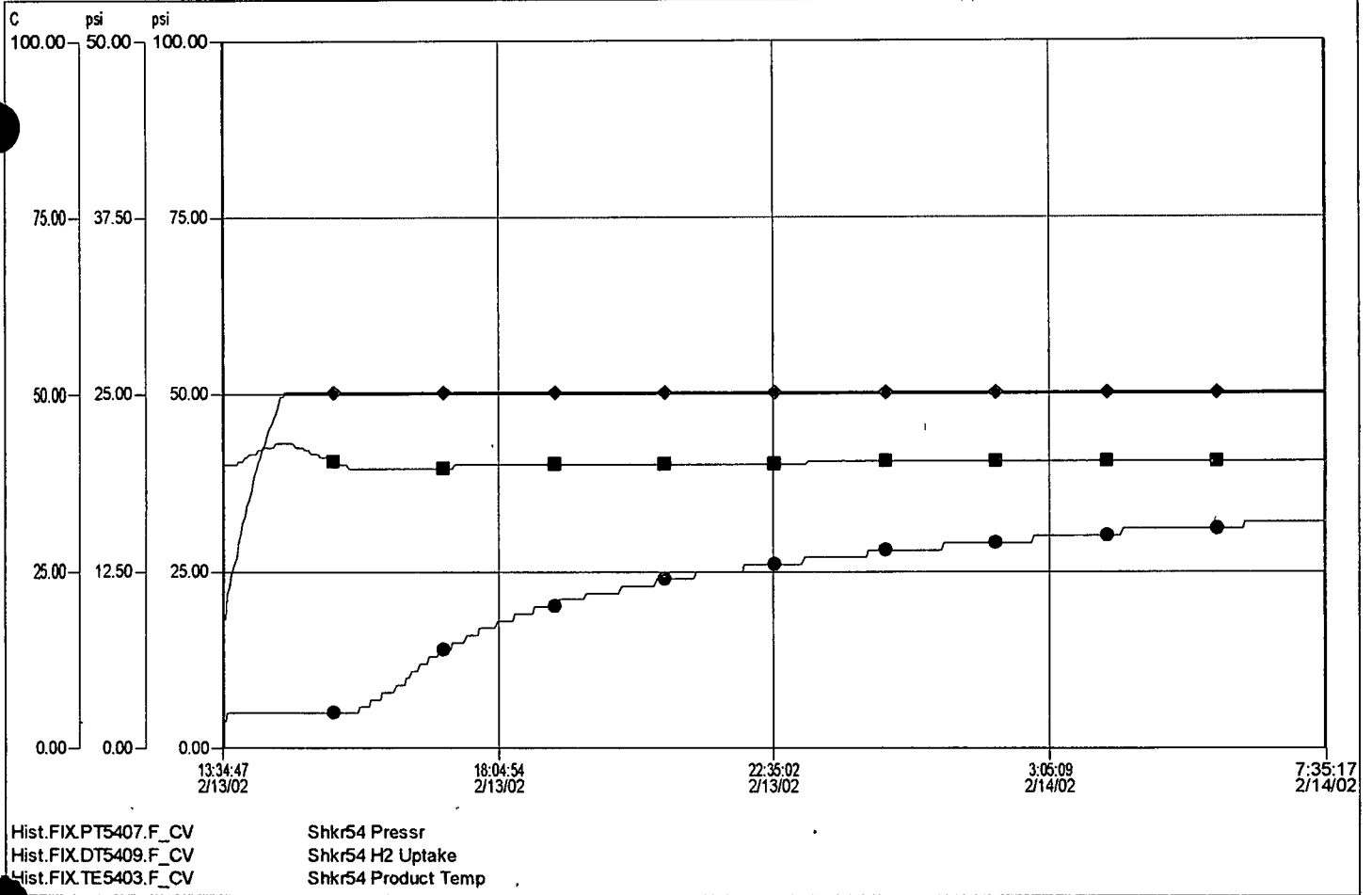
C'D H₂ PRESSURE DROP = 1107.5 LBS./MOLE 0.012 MOLES = 16.8 LBS.

CONDITIONS 18 HRS. AT 50 C. MISC. DATA: 1175

TIME	TEMP.	PRESSURE		TIME	TEMP.	PRESSURE		TIME	TEMP.	PRESSURE	
		OBS.	DROP			OBS.	DROP			OBS.	DROP
13:35	18.9	40	0	21:35	50.2	40	12	05:35	50.2	41	16
13:50	29.3	41	2	21:50	50.2	40	12	05:50	50.2	41	16
14:05	38.4	42	2	22:05	50.2	40	12	06:05	50.2	41	16
14:20	45.1	43	2	22:20	50.2	40	13	06:20	50.2	41	16
14:35	50.2	43	2	22:35	50.2	40	13	06:35	50.2	41	16
14:50	50.2	43	2	22:50	50.2	40	13	06:50	50.2	41	16
15:05	50.2	42	2	23:05	50.2	40	14	07:05	50.2	41	16
15:20	50.2	41	2	23:20	50.2	41	14	07:20	50.2	41	16
15:35	50.2	40	2	23:35	50.2	41	14				
15:50	50.2	39	3	23:50	50.2	41	14				
16:05	50.2	39	4	00:05	50.2	41	14				
16:20	50.2	39	4	00:20	50.2	41	14				
16:35	50.2	39	5	00:35	50.2	41	14				
16:50	50.2	39	6	00:50	50.2	41	14				
17:05	50.2	39	6	01:05	50.2	41	14				
17:20	50.2	39	8	01:20	50.2	41	14				
17:35	50.2	40	8	01:35	50.2	41	14				
17:50	50.2	40	8	01:50	50.2	41	14				
18:05	50.2	40	9	02:05	50.2	41	14				
18:20	50.2	40	10	02:20	50.2	41	14				
18:35	50.2	40	10	02:35	50.2	41	14				
18:50	50.2	40	10	02:50	50.2	41	15				
19:05	50.2	40	10	03:05	50.2	41	15				
19:20	50.2	40	10	03:20	50.2	41	15				
19:35	50.2	40	11	03:35	50.2	41	15				
19:50	50.2	40	11	03:50	50.2	41	15				
20:05	50.2	40	12	04:05	50.2	41	15				
20:20	50.2	40	12	04:20	50.2	41	16				
20:35	50.2	40	12	04:35	50.2	41	16				
20:50	50.2	40	12	04:50	50.2	41	16				
21:05	50.2	40	12	05:05	50.2	41	16				
21:20	50.2	40	12	05:20	50.2	41	16				

RUN BY: A. Newman DATE: Feb 13 2002

RUN BY: _____ DATE: _____



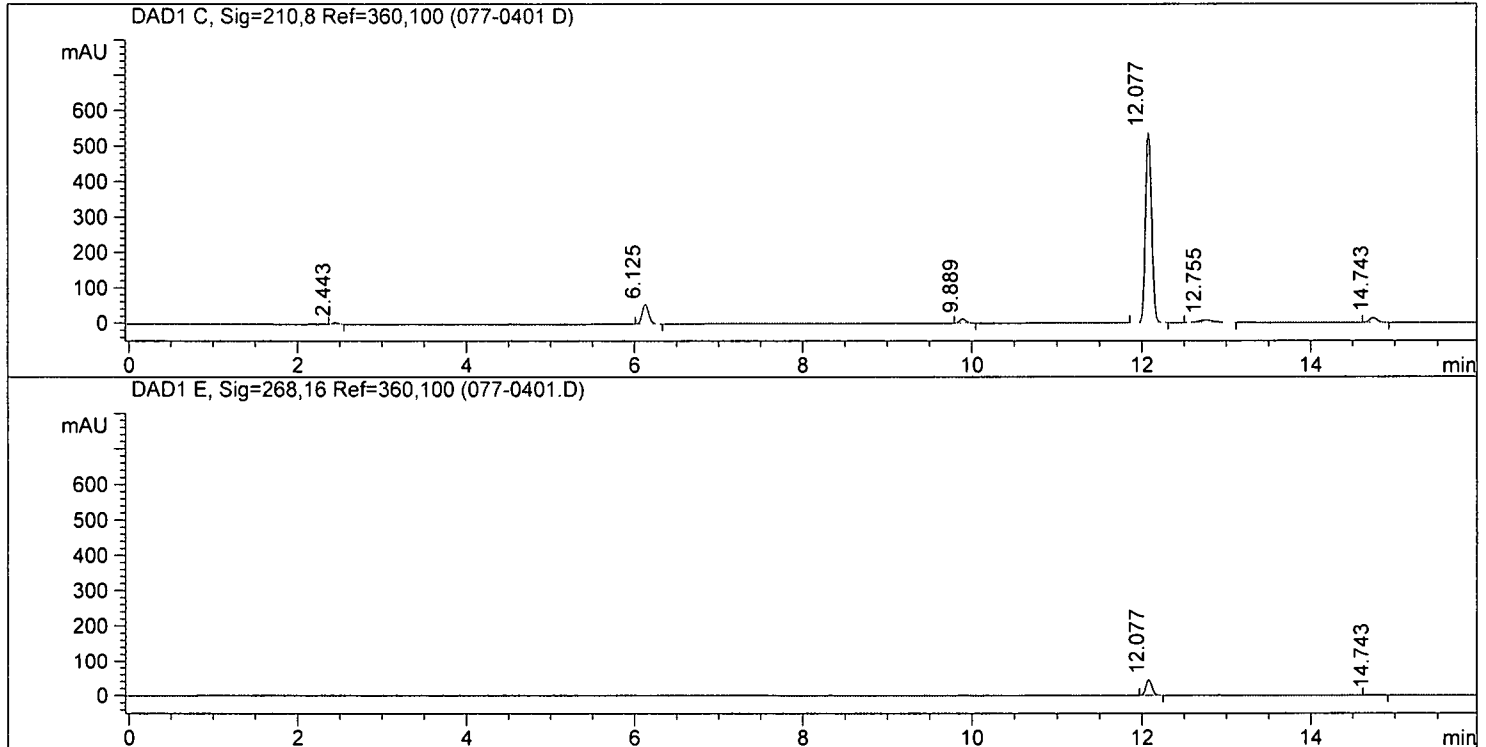
0.3914g/50ml of 72.29g ethylacetate extractions

->

```

=====
Injection Date : 02/20/2002  3:35:32 PM      Seq Line : 4
Sample Name    : 70316-043                Vial No   : 77
Acq Operator   : hansen                    Inj. No.  : 1
                                           Inj. Vol. : 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/20/2002  3:33:04 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

=====
Sorted By      : Signal
Calib. Data Modified : 02/20/2002  3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.44	VB	0.062	5.04	20.045	0.62	0.000000	
2	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
3	6.13	PB	0.085	55.19	297.730	9.14	0.000000	
4	9.89	BP	0.083	11.55	60.718	1.86	0.000000	
5	12.08	BB	0.081	534.91	2701.141	82.95	0.575947	benzyloxy amide
6	12.75	PB	0.192	7.05	89.539	2.75	0.000000	
7	14.74	BB	0.102	13.40	87.158	2.68	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
2	12.08	BB	0.079	43.72	220.113	95.09	0.575947	benzyloxy amide

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
3	14.74	BB	0.102	1.75	11.361	4.91	0.000000	

=====
*** End of Report ***

isolated solids
nmr400a h-1

Current Data Parameters
NAME 70316-041
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters

Date_ 20020221
Time 15.14
INSTRUM spect
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 32768
SOLVENT D2O
NS 32
DS 2
SWH 6578.947 Hz
FIDRES 0.200774 Hz
AQ 2.4904180 sec
RG 45.3
DW 76.000 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec

===== CHANNEL f1 =====

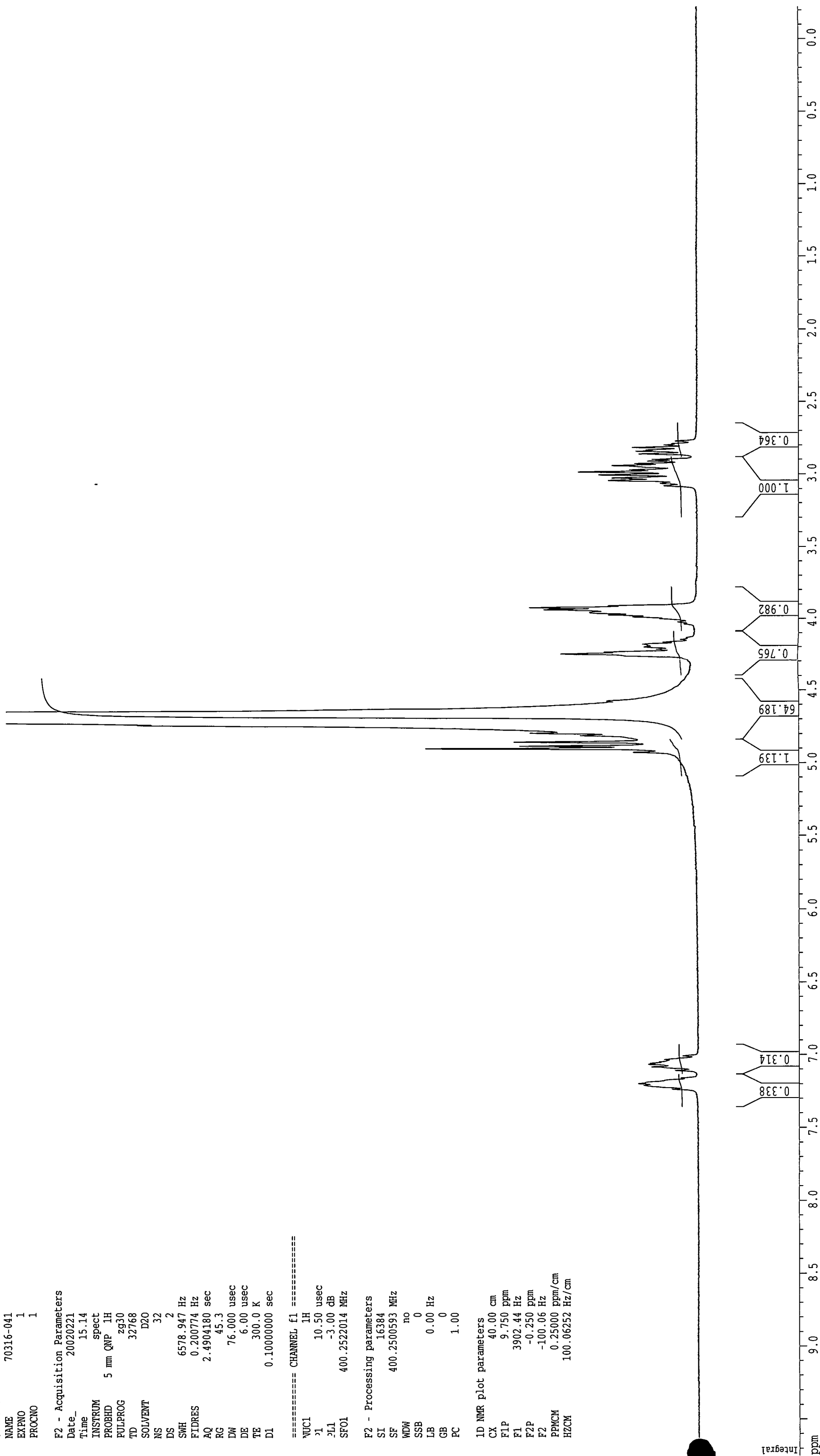
NUC1 1H
P1 10.50 usec
PL1 -3.00 dB
SFO1 400.2522014 MHz

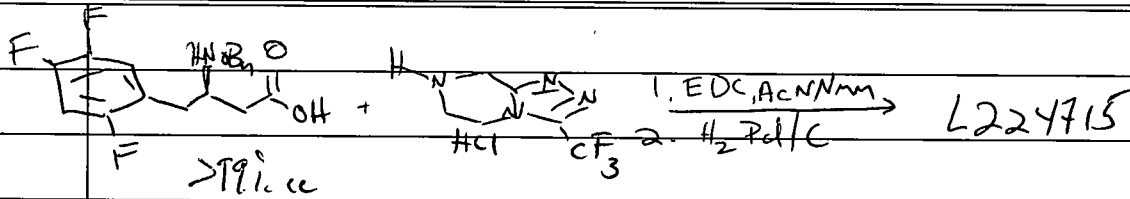
F2 - Processing parameters

SI 16384
SF 400.2500593 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

1D NMR plot parameters

CX 40.00 cm
F1P 9.750 ppm
F1 3902.44 Hz
F2P -0.250 ppm
F2 -100.06 Hz
PPMCM 0.25000 ppm/cm
HZCM 100.06252 Hz/cm





Reagents:	FW	Am't	mmol	eq
Amide acid 72324-107	339.11	4.10g	12.1	1.0
triethyl HCl 72176-100	228.04	4.14g	18.15	1.5
EDC	191.71	3.47g	18.15	1.5
ACN N-methylmorpholine 0.920	101.15	1.22g (1.2ml)	12.1	1.0
NMM ACN		40-1		1.0

Procedure: Dissolved acid in ACN concentrate. Then re-dissolve in 40-1 ACN KF=262 PPM. Added HCl salt cooled to 0°C. Added EDC, NMM sequentially. After 2.5 hrs @ 0°C Rxn complete by LC. Quenched w/ 20-1 H₂O 40-1 EtOAc wash to RT - cut layers washed w/ 5% NaHCO₃ 20-1 + 5-1 sat NaCl, then washed 20-1 sat NaCl.

Assay of amine at Ag

72.29g organic	73.57mg/s	5.32g product	86% assay yield.
22.34g Ag-1	0.219g/s	4.9mg product	
28.75g Ag-2	0.010g/s	< 1mg product	
26.6g Ag-3	no product		

Very low Ag solubility.

Concentrated into Methanol. Added 35-1 Methanol final volume & gave to Hydroxy.

Hydroxy.

-25 Feb 2002 Hydroxy product on 22nd aged over weekend

Countersigned by



Date

1.07

DO NOT BEGIN NEW EXPERIMENTS ON THIS PAGE.

25 Feb 2002. Complete conversion to L224715 observed
 Filtered solids through Silka Floc & washed w/ MeOH
 Assayed filtrate to contain 3.60g of L224715 (73% yield)
 yield is ~10% lower than usual & 10% lost from
 first assay point. This could be due to prolonged sitting
 of B₂O₃ H₂O dry substance. Concentrated tail
 Dissolved oil in EtOH & re-concentrated. Re-solved in 10ml
 EtOH & filtered w/ white solids. Washed filter w/ 4ml
 EtOH 14ml total. Dissolved 1.07g 85% A₂PO₄ in
 5.25ml H₂O. Seeded w/ 35mg of 70316-035
 Added H₃PO₄ silica dropwise over 0.5hr. Sat. @ 60°C. Solids
 were plates under scope. Cooled to RT. Added 50ml
 Ethanol dropwise. Aged 1hr. Filtered & washed
 w/ 30ml EtOH. Isolated 4.16g white solids. Assayed
 ML's to contain 1.72g, 715 0.11g, total
 95.5% mass balance.

26 Feb 2002 - assayed solids to be 80.0 wt% by HPLC. theoretical
 80.6 wt%. ~~PR~~ 26 Feb 2002

26 Feb 2002 Phys measurements indicate that these solids are anew
 form (identical to 70316-039 90% ee form B).
 0.500g sent to Leigh Shultz PR&D.

1 March 2002 Analytical RRT Acc.?

0.95	0.12	0.06% minor impurities
0.97	0.09	Phys. Mss indicates same Form as 70316-035 By SS-NMR
1.00	99.74	



Countersigned by _____

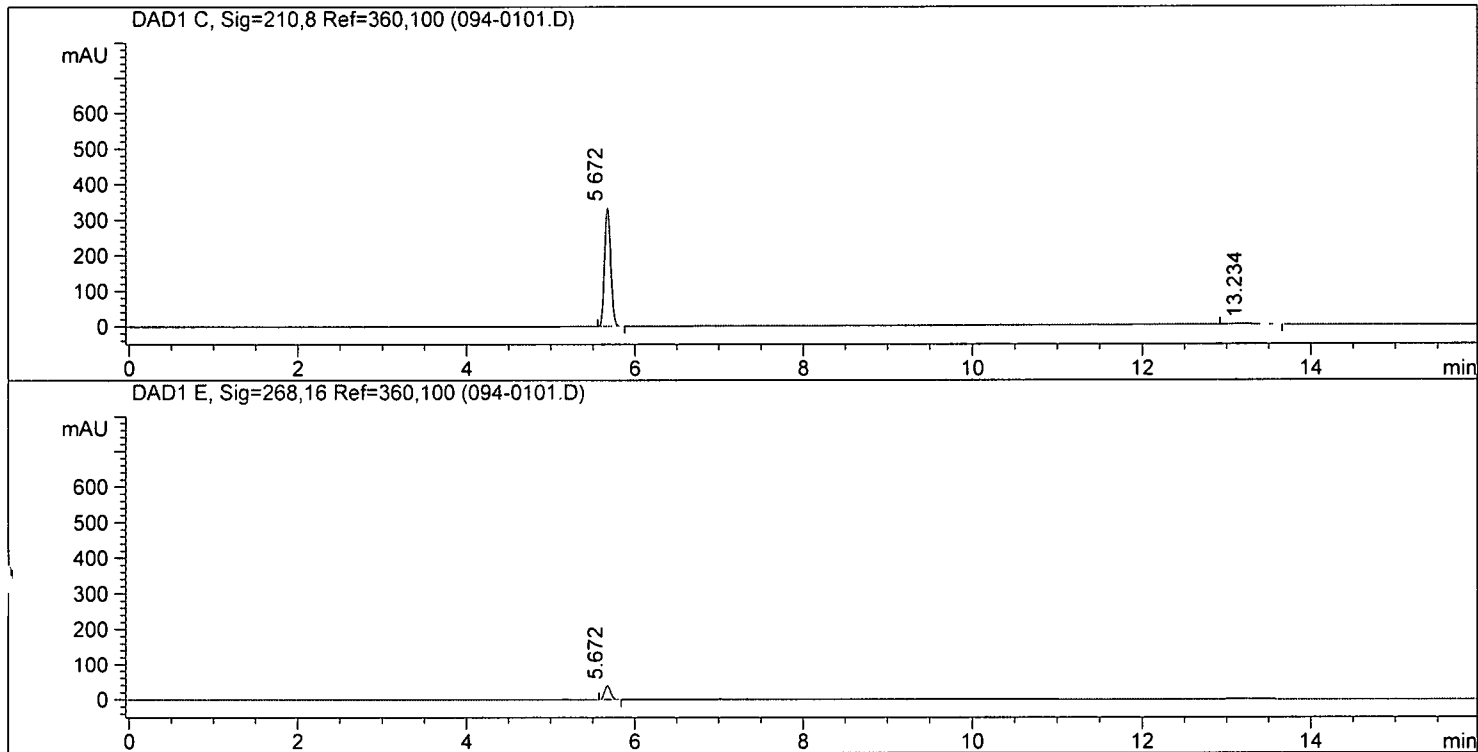
28.0mg/50ml of isolated solids

->

```

=====
Injection Date : 02/26/2002  8:20:46 AM      Seq Line : 1
Sample Name    : 70316-043                 Vial No  : 94
Acq Operator   : hansen                     Inj. No. : 1
                                           Inj. Vol.: 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002  7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 02/20/2002  3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	5.67	PB	0.079	334.10	1698.536	98.28	0.447922	L-224,715
2	0.00		0.000	0.00	0.000	0.00	0.000000	benzyloxy amide
3	13.23	BP	0.241	1.73	29.746	1.72	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	5.67	BB	0.077	38.65	195.850	100.00	0.447922	L-224,715
2	0.00		0.000	0.00	0.000	0.00	0.000000	benzyloxy amide

*** End of Report ***

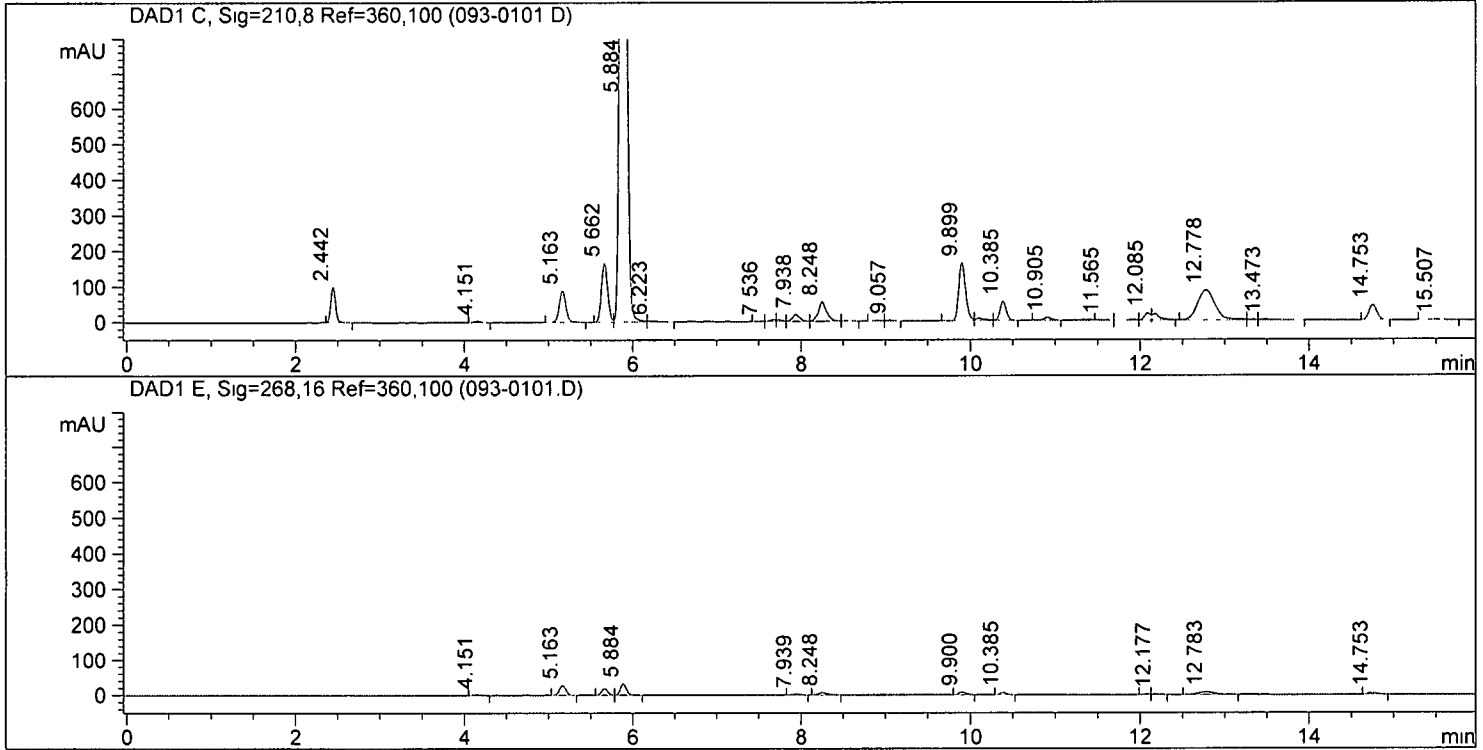
6.54g/50ml of 64.0g ML's

->

```

=====
Injection Date : 02/25/2002  3:30:29 PM      Seq Line : 1
Sample Name    : 70316-043                Vial No  : 93
Acq Operator   : hansen                    Inj. No.  : 1
                                           Inj. Vol. : 2 µl

Method         : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002  7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

=====
Sorted By      : Signal
Calib. Data Modified : 02/20/2002  3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.44	VP	0.062	100.35	399.745	2.37	0.000000	
2	4.15	BP	0.088	3.78	21.346	0.13	0.000000	
3	5.16	BP	0.085	89.17	494.252	2.93	0.000000	
4	5.66	BV	0.080	165.85	859.408	5.09	0.225046	L-224, 715
5	5.88	VV	0.091	2.04e3	1.131e4	66.98	0.000000	
6	6.22	VB	0.123	3.40	30.151	0.18	0.000000	
7	7.54	BV	0.070	1.10	5.238	0.03	0.000000	
8	7.67	VV	0.075	4.89	25.506	0.15	0.000000	
9	7.74	VV	0.074	4.70	23.529	0.14	0.000000	
10	7.94	VV	0.090	20.18	124.658	0.74	0.000000	
11	8.25	VV	0.099	54.88	380.229	2.25	0.000000	
12	8.53	VB	0.099	1.37	9.805	0.06	0.000000	
13	8.90	BV	0.097	1.98	13.309	0.08	0.000000	
14	9.06	VB	0.080	2.74	14.594	0.09	0.000000	
15	9.90	BV	0.087	163.33	914.935	5.42	0.000000	

1.72 mg/s
0.1103

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
16	10.10	VV	0.108	7.02	55.271	0.33	0.000000	
17	10.38	VB	0.081	54.56	286.981	1.70	0.000000	
18	10.90	BB	0.113	8.67	67.731	0.40	0.000000	
19	11.57	BV	0.142	1.79	18.071	0.11	0.000000	
20	11.91	VV	0.136	2.06	20.573	0.12	0.000000	
21	12.09	VV	0.076	20.89	103.631	0.61	0.016777	benzyloxy amide
22	12.18	VB	0.092	18.75	122.682	0.73	0.000000	
23	12.78	BV	0.227	85.14	1251.309	7.41	0.000000	
24	13.31	VV	0.096	2.36	15.820	0.09	0.000000	
25	13.47	VB	0.162	2.40	28.458	0.17	0.000000	
26	14.75	BB	0.102	42.57	279.042	1.65	0.000000	
27	15.51	BB	0.140	1.38	13.025	0.08	0.000000	

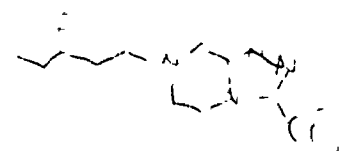
Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	4.15	BP	0.086	1.16	6.528	0.90	0.000000	
2	5.16	BB	0.083	27.76	149.995	20.78	0.000000	
3	5.66	BV	0.080	18.97	97.838	13.55	0.225046	L-224,715
4	5.88	VP	0.079	32.06	163.229	22.61	0.000000	
5	7.94	VB	0.088	2.94	17.512	2.43	0.000000	
6	8.25	BB	0.101	7.16	51.024	7.07	0.000000	
7	9.90	BV	0.092	7.35	45.228	6.27	0.000000	
8	10.38	BB	0.078	6.34	31.447	4.36	0.000000	
9	12.09	PV	0.069	1.61	7.265	1.01	0.016777	benzyloxy amide
10	12.18	VB	0.085	2.00	11.552	1.60	0.000000	
11	12.78	PB	0.215	7.50	103.610	14.35	0.000000	
12	14.75	BB	0.102	5.59	36.648	5.08	0.000000	

*** End of Report ***

HYDROGENATION OR HIGH PRESSURE REACTION

2002022260 001
DO NOT WRITE IN THIS SPACE

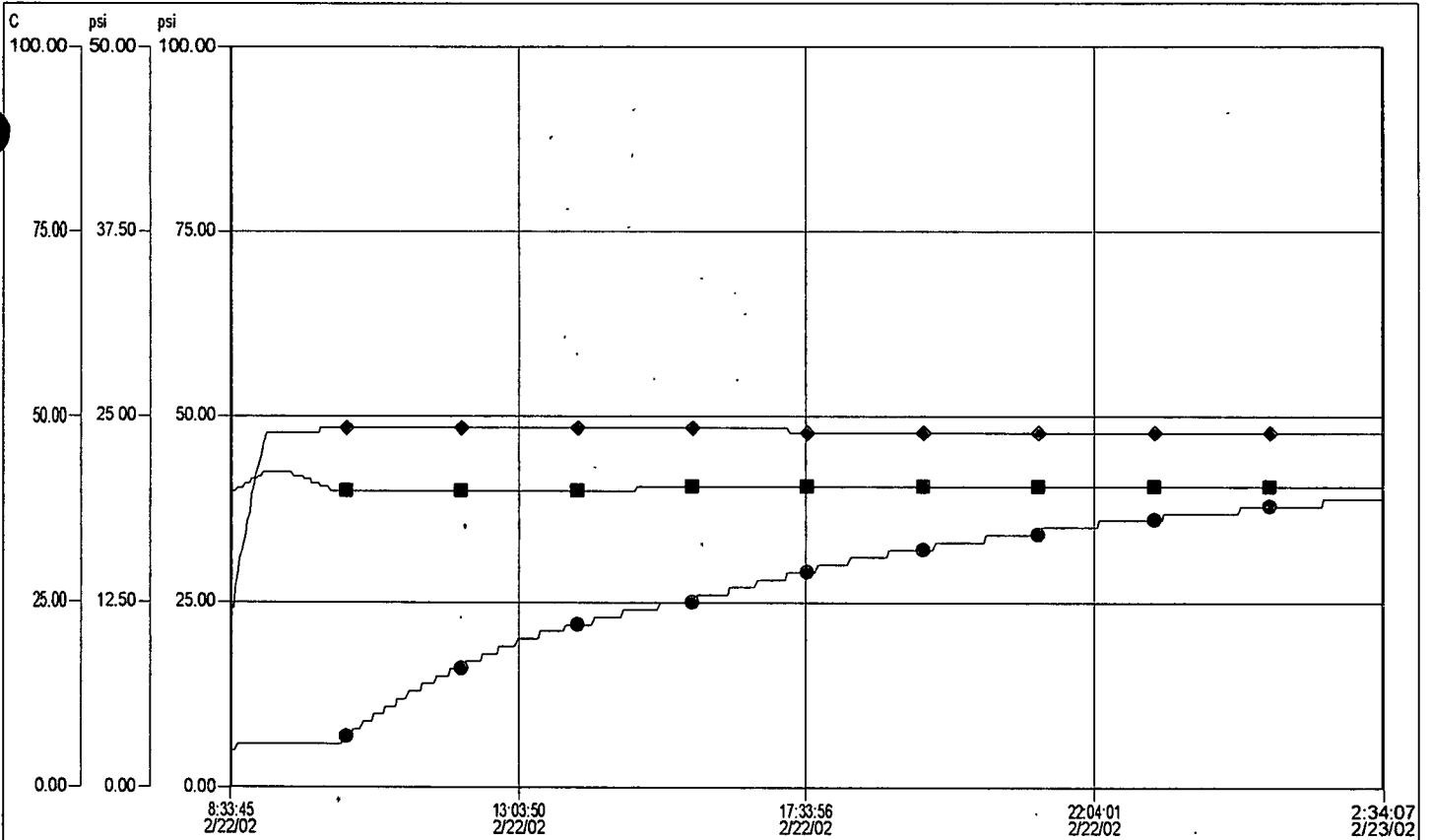
REQUESTED BY Hansen BLDG/RM 69 EXT. 257 DATE 22 Feb 2002
 PROJECT NO. 2215 PROJECT 227 NOTEBOOK - PAGE NO. 70-16-41
 CHECK HERE IF REACTION IS GMP/GLP **STARTING MATERIAL**
 NO. 1 _____ NO. 2 _____
 M.W. _____ AMOUNT _____ G. MOLES _____ M.W. _____ AMOUNT _____ G. MOLES _____
 STRUCTURAL FORMULA:  CATALYST _____ G. OF _____
 SOLVENT _____ ML. OF _____
 MOLES OF HYDROGEN REQUIRED _____
 OTHER MATERIALS _____
 REACTION CONDITIONS, ETC. _____
 PRECAUTIONS: _____
 EMPIRICAL FORMULA: _____

TO BE FILLED IN BY HYDROGENATION LABORATORY

NO. 1: 5.32 G. MOLES 0.1003 NO. 2: _____ G. MOLES _____
 CATALYST 1.2 G. OF 11% Pd/C 1st # SDC 48025
 SOLVENT 1/4 ML. OF 11:1 MeOH
 OTHER MATERIALS _____
 CELL NO. _____ HEATER NO. _____ REC. POINT INTERNAL _____ EXTERNAL _____ BOMB NO. _____ VESSEL SIZE 750 ML.
 SHAKER NO. 60 LINER _____ SHAKER TANK 172.7 AUX. TANK _____ SYSTEM VOLUME 717 ML.
 CLD H₂ PRESSURE DROP = _____ LBS./MOLE 0.103 MOLES = 15 LBS.
 CONDITIONS _____ HRS. AT 50 C. MISC. DATA: 1/10, 2002 H₂

TIME	TEMP.	PRESSURE		TIME	TEMP.	PRESSURE		TIME	TEMP.	PRESSURE	
		OBS.	DROP			OBS.	DROP			OBS.	DROP
08:34	20.5	39	1	16:34	48.4	40	14	00:34	47.9	40	19
08:49	36.5	41	3	16:49	48.4	40	14	00:49	47.9	40	19
09:04	46.8	42	3	17:04	48.4	40	14	01:04	47.9	40	19
09:19	47.9	42	3	17:19	47.9	40	14	01:19	47.9	40	19
09:34	47.9	42	3	17:34	47.9	40	14	01:34	47.9	40	19
09:49	47.9	41	3	17:49	47.9	40	15	01:49	47.9	40	20
10:04	48.4	40	3	18:04	47.9	40	15	02:04	47.9	40	20
10:19	48.4	40	4	18:19	47.9	40	16	02:19	47.9	40	20
10:34	48.4	40	4	18:34	47.9	40	16				
10:49	48.4	40	5	18:49	47.9	40	16				
11:04	48.4	40	6	19:04	47.9	40	16				
11:19	48.4	40	6	19:19	47.9	40	16				
11:34	48.4	40	7	19:34	47.9	40	16				
11:49	48.4	40	8	19:49	47.9	40	16				
12:04	48.4	40	8	20:04	47.9	40	16				
12:19	48.4	40	8	20:19	47.9	40	16				
12:34	48.4	40	9	20:34	47.9	40	17				
12:49	48.4	40	10	20:49	47.9	40	17				
13:04	48.4	40	10	21:04	47.9	40	17				
13:19	48.4	40	10	21:19	47.9	40	18				
13:34	48.4	40	10	21:34	47.9	40	18				
13:49	48.4	40	11	21:49	47.9	40	18				
14:04	48.4	40	11	22:04	47.9	40	18				
14:19	48.4	40	12	22:19	47.9	40	18				
14:34	48.4	40	12	22:34	47.9	40	18				
14:49	48.4	40	12	22:49	47.9	40	18				
15:04	48.4	40	12	23:04	47.9	40	18				
15:19	48.4	40	12	23:19	47.9	40	18				
15:34	48.4	40	12	23:34	47.9	40	18				
15:49	48.4	40	12	23:49	47.9	40	18				
16:04	48.4	40	13	00:04	47.9	40	18				
16:19	48.4	40	13	00:19	47.9	40	18				

RUN BY D. Nelson DATE Feb 27, 2002
 RUN BY _____ DATE _____



Hist.FIX.PT6007.F_CV Shkr60 Pressr
Hist.FIX.DT6009.F_CV Shkr60 H2 Uptake
Hist.FIX.TE6003.F_CV Shkr60 Product Temp

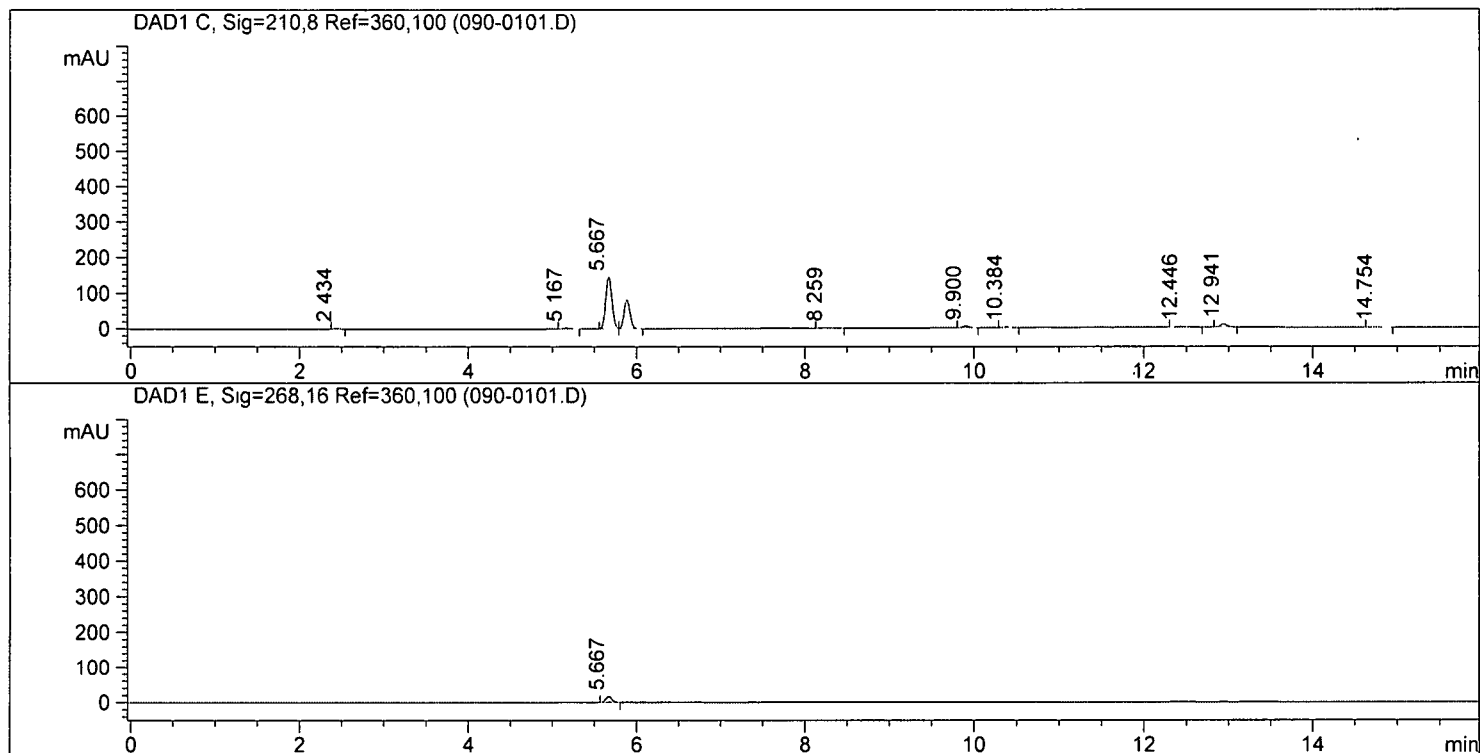
0.1744g/50ml of 64.14g methanol filtrate

->

```

=====
Injection Date : 02/25/2002 10:12:22 AM      Seq Line : 1
Sample Name    : 70316-043                    Vial No   : 90
Acq Operator   : hansen                       Inj. No.  : 1
                                           Inj. Vol. : 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002 7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

=====
Sorted By      : Signal
Calib. Data Modified : 02/20/2002 3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.43	BB	0.057	2.90	10.762	0.83	0.000000	
2	5.17	BB	0.088	2.76	15.633	1.21	0.000000	
3	5.67	BV	0.082	144.63	749.983	58.09	0.195982	L-224,715
4	5.88	VB	0.078	81.24	400.525	31.02	0.000000	3.605
5	8.26	PB	0.092	1.55	9.788	0.76	0.000000	
6	9.90	BP	0.084	4.63	24.548	1.90	0.000000	
7	10.38	BP	0.078	1.49	7.378	0.57	0.000000	
8	0.00		0.000	0.00	0.000	0.00	0.000000	benzyloxy amide
9	12.45	BB	0.140	1.79	17.502	1.36	0.000000	
10	12.94	BB	0.088	8.13	45.777	3.55	0.000000	
11	14.75	BP	0.107	1.34	9.136	0.71	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	5.67	BV	0.083	16.60	86.143	100.00	0.195982	L-224,715
2	0.00		0.000	0.00	0.000	0.00	0.000000	benzyloxy amide

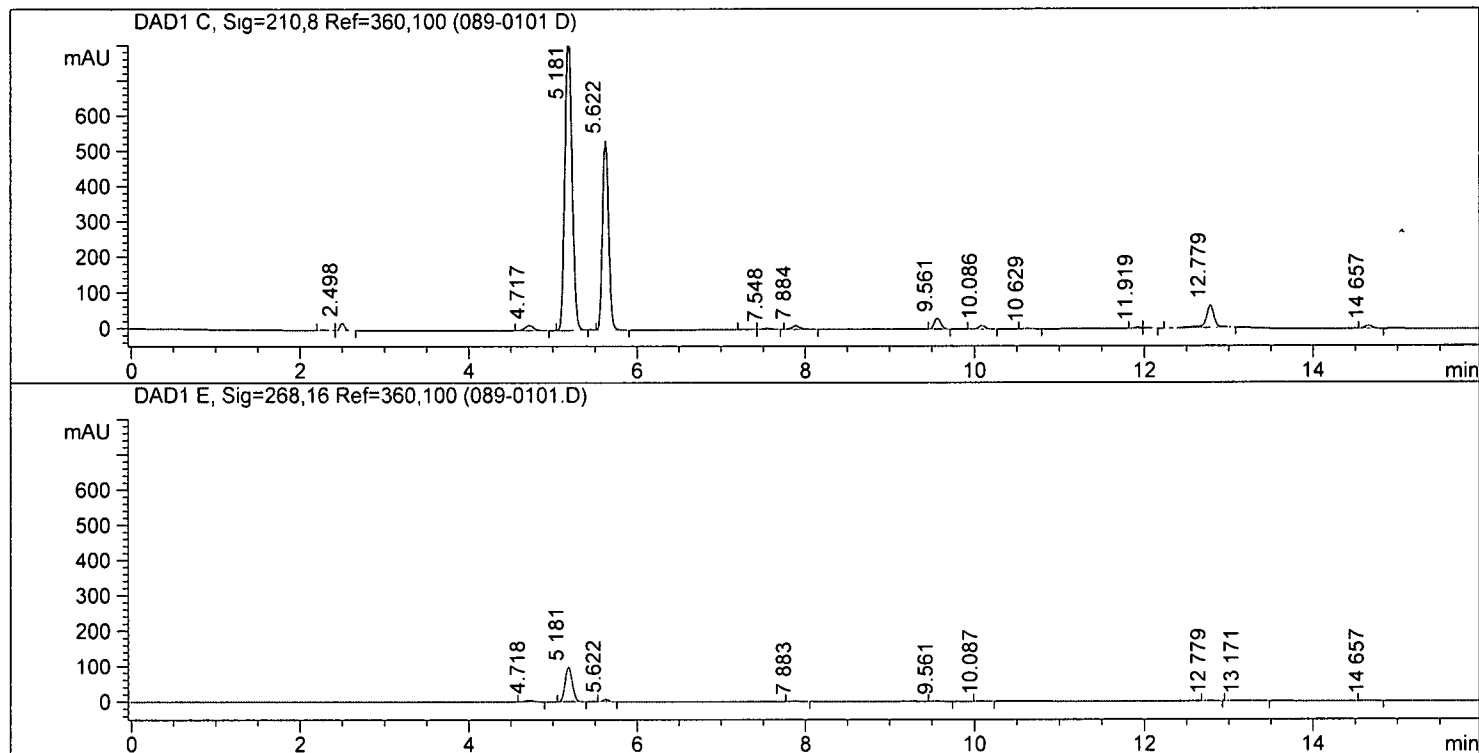
=====
*** End of Report ***

hydrog

->

Injection Date : 02/25/2002 8:42:59 AM Seq Line : 1
 Sample Name : 70316-043 Vial No : 89
 Acq Operator : hansen Inj. No. : 1
 Inj. Vol. : 2 µl

Method : C:\HPCHEM\HPLC0157\METHODS\715.M
 Last Changed : 02/21/2002 7:13:49 AM
 75/25 0.1% HClO4/Acetonitrile, 1ml/min
 10min 25/75 water/acn; 75/25 from 10 to 14 min
 waters c18 symmetry, 250 nm



Customized Report:karlo

Sorted By : Signal
 Calib. Data Modified : 02/20/2002 3:33:04 PM
 Multiplier : 1.000000

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.28	PV	0.086	1.76	9.927	0.11	0.000000	
2	2.50	VB	0.058	21.32	81.013	0.93	0.000000	
3	4.72	BP	0.111	14.65	106.944	1.22	0.000000	
4	5.18	BB	0.093	831.88	4938.364	56.51	0.000000	
5	5.62	BB	0.079	537.14	2722.693	31.16	0.719943	L-224, 715
6	7.35	BV	0.109	1.09	8.329	0.10	0.000000	
7	7.55	VB	0.094	3.89	26.057	0.30	0.000000	
8	7.88	BB	0.099	10.52	74.879	0.86	0.000000	
9	9.56	PV	0.085	30.55	165.244	1.89	0.000000	
10	10.09	VP	0.085	9.73	52.162	0.60	0.000000	
11	10.63	BP	0.098	1.51	9.630	0.11	0.000000	
12	11.92	VV	0.078	4.14	20.502	0.23	0.000000	
13	12.04	VB	0.075	3.05	14.919	0.17	0.000000	benzyloxy amide
14	12.78	PB	0.106	62.85	451.544	5.17	0.000000	
15	14.66	BP	0.102	8.77	56.785	0.65	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	4.72	BB	0.106	4.52	31.146	4.40	0.000000	
2	5.18	BB	0.091	98.83	580.864	82.03	0.000000	
3	5.62	BB	0.080	6.19	31.558	4.46	0.719943	L-224,715
4	7.88	BB	0.096	1.36	9.316	1.32	0.000000	
5	9.56	PP	0.082	1.33	6.833	0.97	0.000000	
6	10.09	PB	0.079	1.14	5.754	0.81	0.000000	
7	0.00		0.000	0.00	0.000	0.00	0.000000	benzyloxy amide
8	12.78	BB	0.104	1.38	9.697	1.37	0.000000	
9	13.17	BB	0.224	1.61	25.462	3.60	0.000000	
10	14.66	BP	0.102	1.15	7.487	1.06	0.000000	

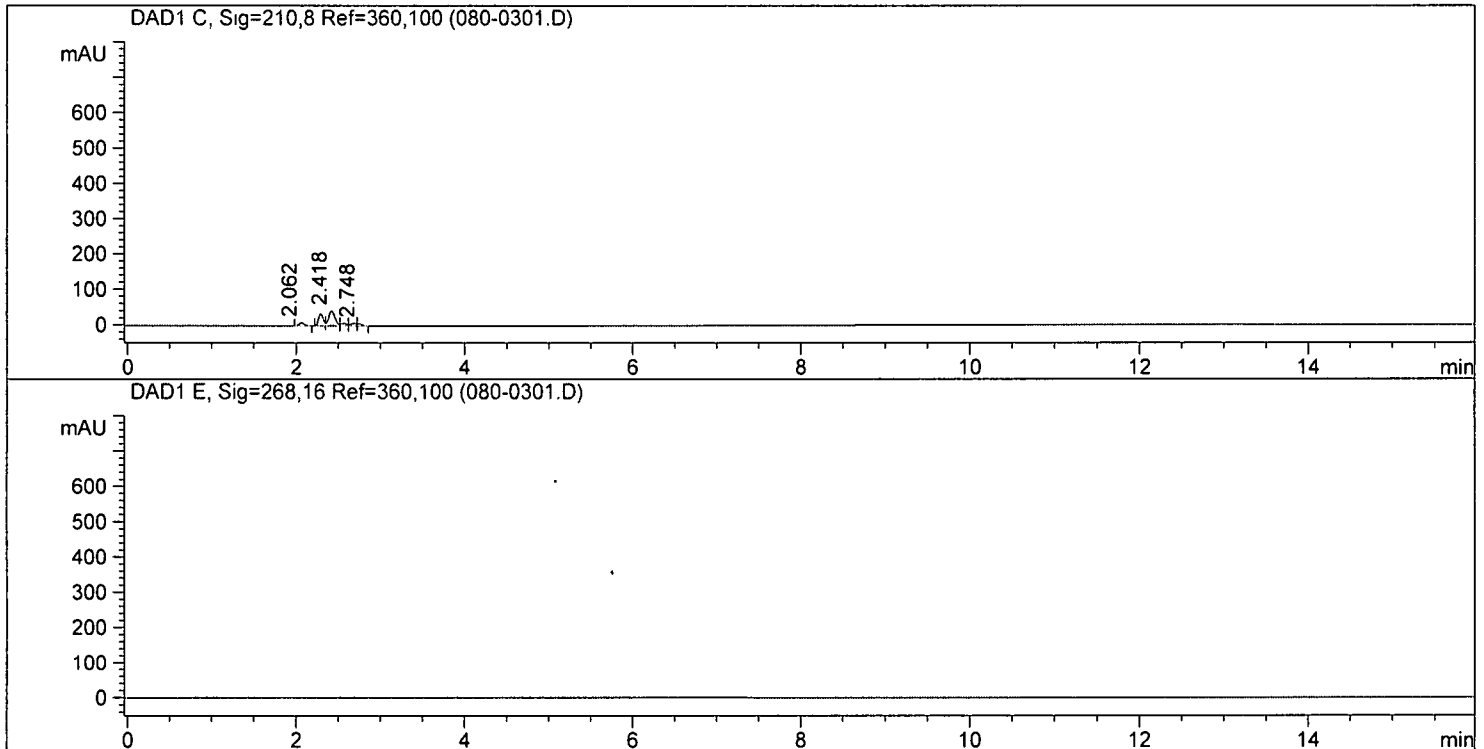
=====
*** End of Report ***

5.00g/50ml of 26.6g aq-3

->

```

=====
Injection Date : 02/21/2002  7:58:18 AM      Seq Line : 3
Sample Name    : 70316-043                  Vial No   : 80
Acq Operator   : hansen                      Inj. No.  : 1
                                           Inj. Vol. : 2 µl
Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002  7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
=====
    
```



=====
 Customized Report:karlo
 =====

```

Sorted By      : Signal
Calib. Data Modified : 02/20/2002  3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.06	BB	0.071	8.68	39.545	8.03	0.000000	
2	2.29	BV	0.061	34.53	134.026	27.20	0.000000	
3	2.42	VV	0.084	41.81	223.706	45.40	0.000000	
4	2.57	VV	0.073	7.42	35.957	7.30	0.000000	
5	2.68	VV	0.071	7.35	36.103	7.33	0.000000	
6	2.75	VB	0.056	6.26	23.382	4.75	0.000000	
7	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
8	0.00		0.000	0.00	0.000	0.00	0.000000	benzyloxy amide

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
2	0.00		0.000	0.00	0.000	0.00	0.000000	benzyloxy amide

=====
*** End of Report ***

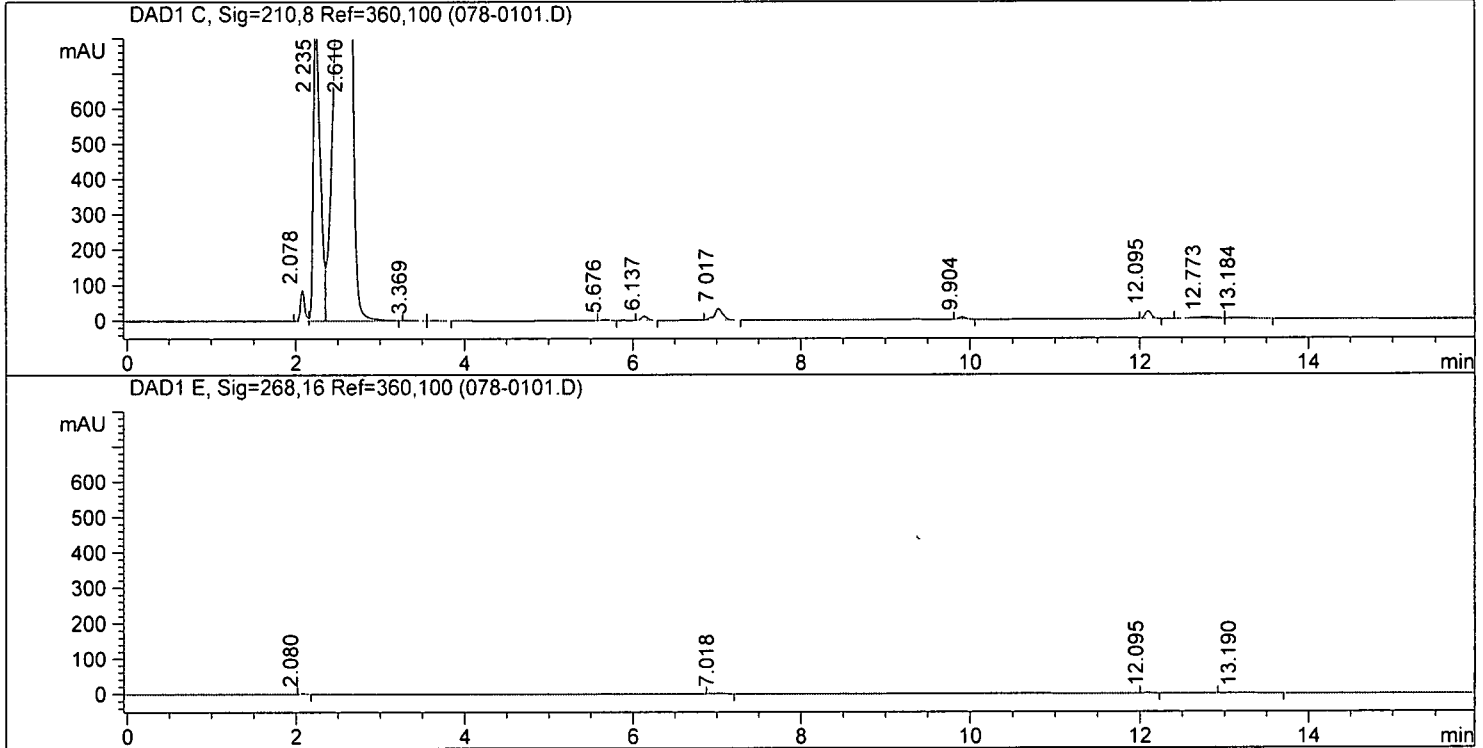
4.174g/50ml of 22.34g aq-1

->

```

=====
Injection Date : 02/21/2002  7:21:08 AM      Seq Line : 1
Sample Name    : 70316-043                Vial No   : 78
Acq Operator   : hansen                    Inj. No.  : 1
                                           Inj. Vol. : 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002  7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 02/20/2002  3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.08	BV	0.055	86.77	301.853	0.93	0.000000	
2	2.24	VV	0.081	854.52	4797.196	14.77	0.000000	
3	2.61	VB	0.186	2.27e3	2.677e4	82.44	0.000000	
4	3.37	BV	0.168	1.67	21.506	0.07	0.000000	
5	3.64	VB	0.122	1.54	13.788	0.04	0.000000	
6	5.68	BB	0.075	3.29	16.163	0.05	0.001076	L-224,715
7	6.14	BB	0.085	11.30	60.641	0.19	0.000000	
8	7.02	BB	0.099	32.89	229.618	0.71	0.000000	
9	9.90	BP	0.084	6.42	33.853	0.10	0.000000	
10	12.09	BP	0.079	22.02	110.462	0.34	0.018247	benzyloxy amide
11	12.77	BV	0.290	3.92	74.723	0.23	0.000000	
12	13.18	VB	0.252	2.28	41.770	0.13	0.000000	4.9mg

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.08	BB	0.051	2.79	9.329	19.58	0.000000	
2	0.00		0.000	0.00	0.000	0.00	0.001076	L-224,715
3	7.02	BB	0.099	1.86	12.905	27.09	0.000000	
4	12.09	BP	0.079	1.78	8.962	18.81	0.018247	benzyloxy amide
5	13.19	PP	0.266	1.01	16.445	34.52	0.000000	

=====
*** End of Report ***

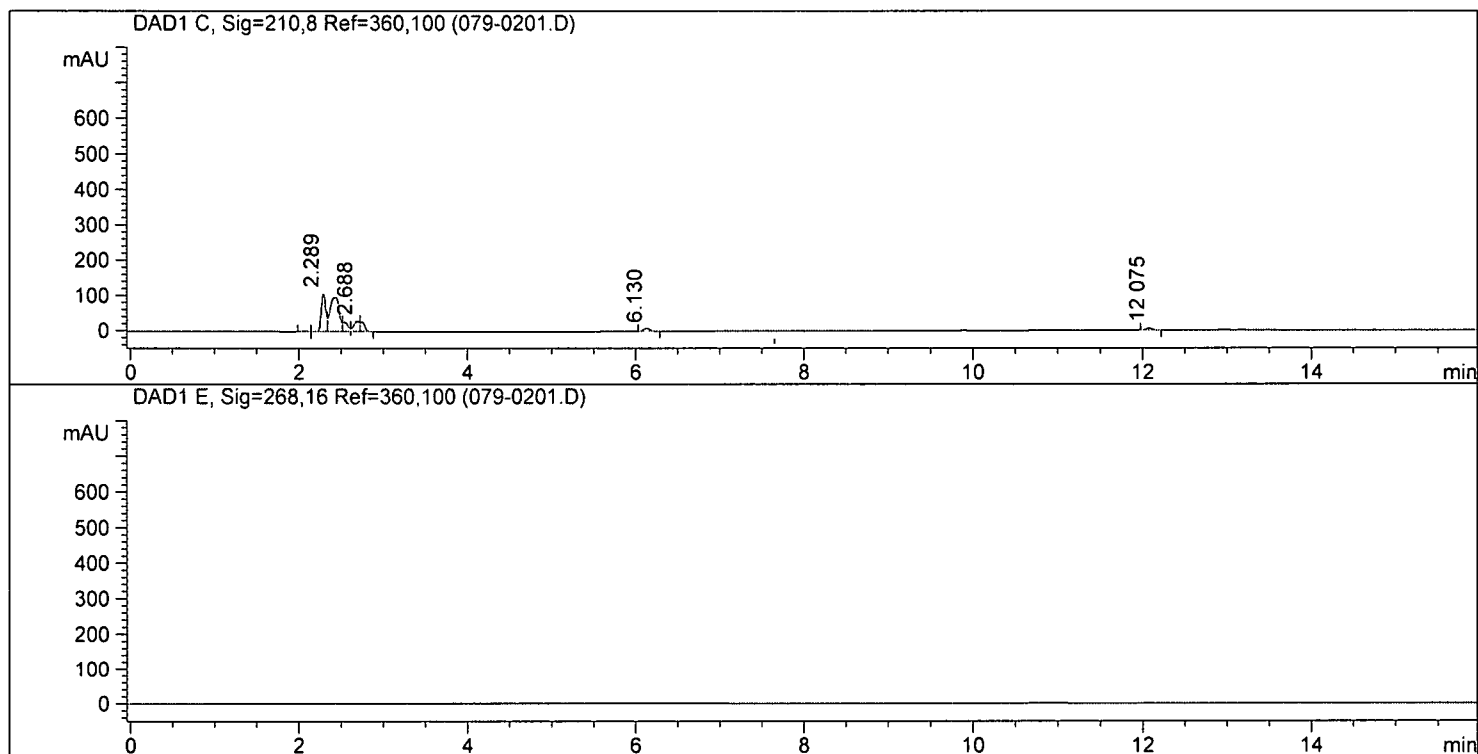
4.364g/50ml of 28.75g aq-2

->

```

=====
Injection Date : 02/21/2002  7:39:41 AM      Seq Line   : 2
Sample Name    : 70316-043                    Vial No    : 79
Acq Operator   : hansen                       Inj. No.   : 1
                                           Inj. Vol.  : 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002  7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

=====
Sorted By      : Signal
Calib. Data Modified : 02/20/2002  3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.06	PV	0.064	1.83	7.524	0.48	0.000000	
2	2.29	VV	0.057	108.42	398.594	25.37	0.000000	
3	2.44	VV	0.102	97.73	735.912	46.85	0.000000	
4	2.54	VV	0.064	26.57	113.909	7.25	0.000000	
5	2.69	VV	0.072	29.52	142.506	9.07	0.000000	
6	2.75	VB	0.057	26.93	98.471	6.27	0.000000	
7	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
8	6.13	PB	0.082	8.30	44.053	2.80	0.000000	
9	12.07	VB	0.079	5.94	29.912	1.90	0.000907	benzyloxy amide

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
2	0.00		0.000	0.00	0.000	0.00	0.000907	benzyloxy amide

=====
*** End of Report ***

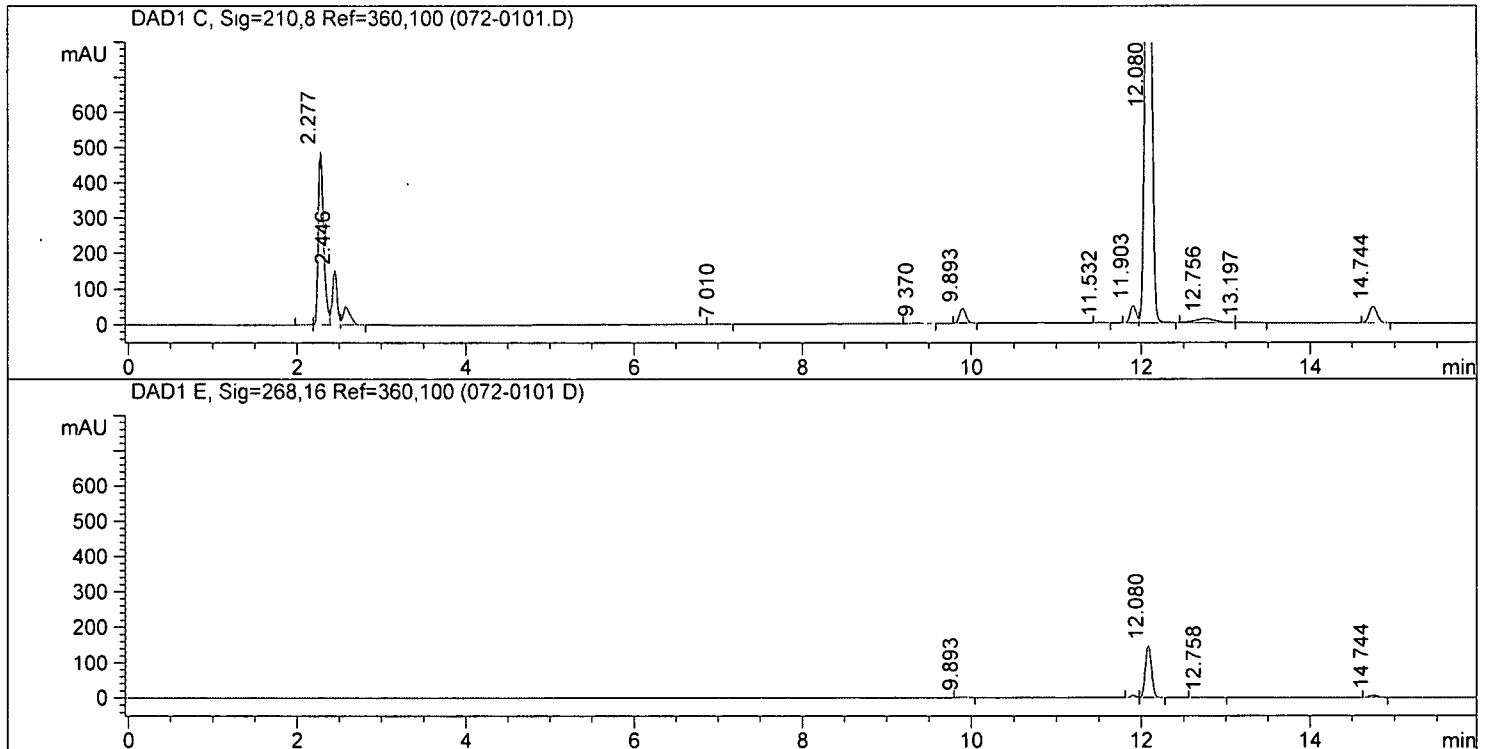
coupling after 1.5h

->

```

=====
Injection Date : 02/20/2002 10:55:16 AM      Seq Line : 1
Sample Name    : 70316-043                   Vial No   : 72
Acq Operator   : hansen                       Inj. No.  : 1
                                           Inj. Vol. : 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 01/14/2002 1:00:57 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

=====
Sorted By      : Signal
Calib. Data Modified : 01/14/2002 1:00:30 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.17	BV	0.080	2.12	12.378	0.10	0.000000	
2	2.28	VV	0.067	493.08	2139.813	16.89	0.000000	
3	2.45	VV	0.060	152.36	595.936	4.70	0.000000	
4	2.58	VB	0.084	51.15	298.751	2.36	0.000000	
5	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
6	7.01	BB	0.093	1.76	11.615	0.09	0.000000	
7	9.37	PB	0.109	2.02	15.761	0.12	0.000000	
8	9.89	BB	0.084	41.45	219.022	1.73	0.000000	
9	11.53	BV	0.090	1.07	6.194	0.05	0.000000	
10	11.90	VV	0.077	48.72	238.873	1.89	0.000000	
11	12.08	VB	0.083	1.64e3	8593.731	67.82	0.000000	
12	12.76	BV	0.225	12.63	215.780	1.70	0.000000	
13	13.20	VB	0.167	1.46	17.628	0.14	0.000000	
14	14.74	BB	0.102	47.02	305.960	2.41	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
2	9.89	BB	0.084	1.85	9.894	1.18	0.000000	
3	11.90	PV	0.077	6.34	30.915	3.70	0.000000	
4	12.08	VB	0.081	147.52	742.571	88.82	0.000000	
5	12.76	BB	0.169	1.02	12.595	1.51	0.000000	
6	14.74	BB	0.102	6.17	40.098	4.80	0.000000	

=====
*** End of Report ***

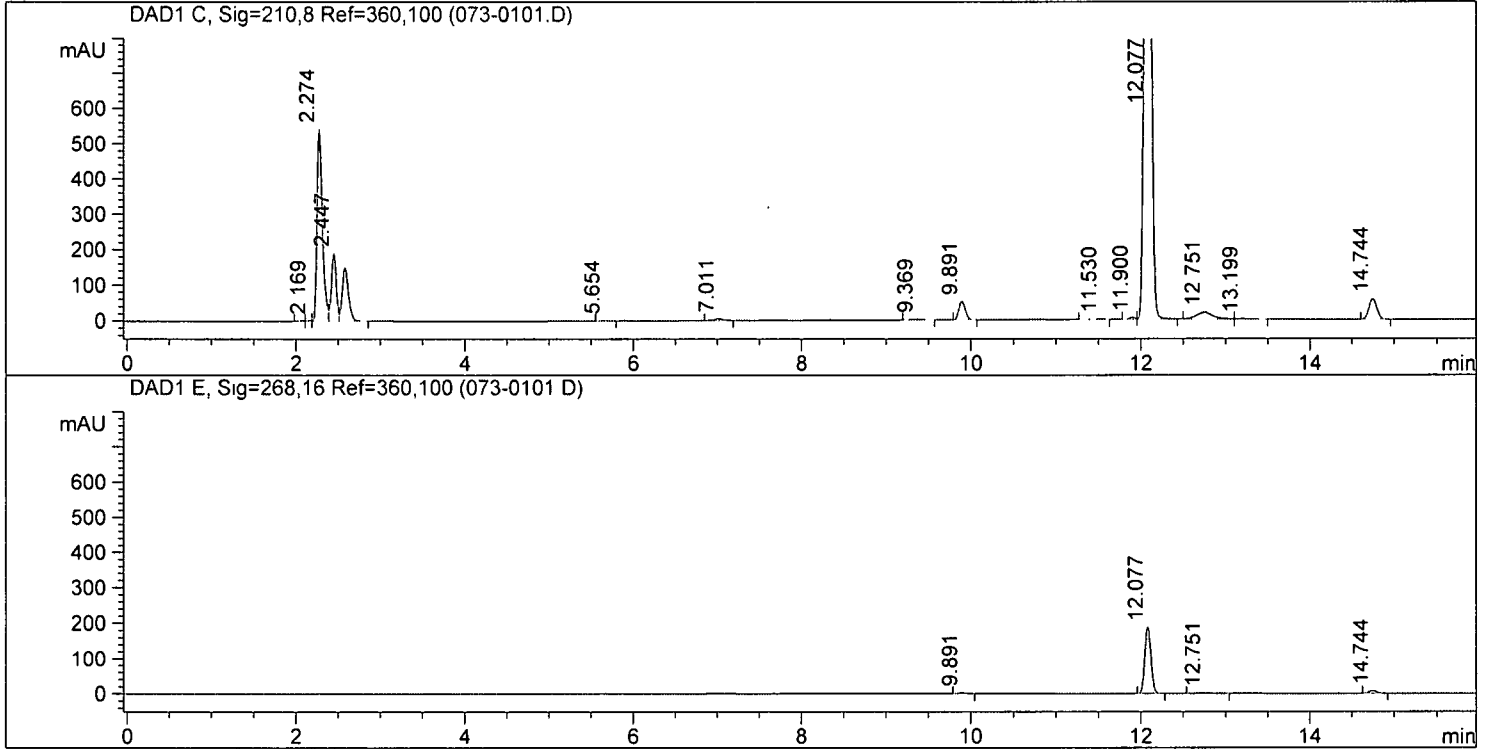
coupling after 2.5h

->

```

=====
Injection Date : 02/20/2002 12:19:34 PM      Seq Line : 1
Sample Name    : 70316-043                  Vial No  : 73
Acq Operator   : hansen                     Inj. No. : 1
                                           Inj. Vol.: 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 01/14/2002 1:00:57 PM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 01/14/2002 1:00:30 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.08	BV	0.063	1.39	5.813	0.04	0.000000	
2	2.17	VV	0.056	2.30	8.618	0.06	0.000000	
3	2.27	VV	0.067	544.27	2378.625	15.47	0.000000	
4	2.45	VV	0.062	191.69	753.968	4.90	0.000000	
5	2.58	VB	0.077	151.21	768.366	5.00	0.000000	
6	5.65	PB	0.080	1.07	5.540	0.04	0.000000	L-224,715
7	7.01	BB	0.096	5.92	39.536	0.26	0.000000	
8	9.37	BB	0.111	2.57	20.348	0.13	0.000000	
9	9.89	BB	0.083	51.06	269.063	1.75	0.000000	
10	11.53	BV	0.136	1.62	15.797	0.10	0.000000	
11	11.90	VV	0.080	5.68	29.136	0.19	0.000000	
12	12.08	VB	0.087	1.92e3	1.040e4	67.64	0.000000	
13	12.75	BV	0.194	20.13	278.900	1.81	0.000000	
14	13.20	VB	0.185	1.79	24.781	0.16	0.000000	
15	14.74	BP	0.102	57.88	376.318	2.45	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
2	9.89	BP	0.084	2.28	12.040	1.17	0.000000	
3	12.08	VB	0.079	188.11	947.726	92.09	0.000000	
4	12.75	BP	0.164	1.71	20.023	1.95	0.000000	
5	14.74	BB	0.102	7.60	49.333	4.79	0.000000	

=====
*** End of Report ***

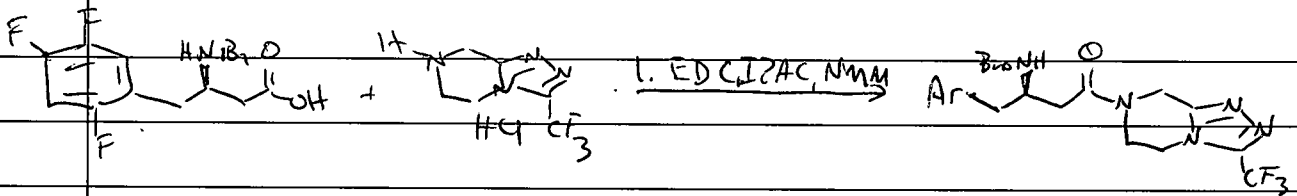
Investigator _____

Date 22 Feb 2002

Subject _____



Filed in Book Number/Title _____



Reagents:	FW	Am't	mol	eq
B-Amino acid 72324-125	339.11	0.500g	1.47	1.0
Triazolopyrazine 72176-100	228.04	0.500g	2.21	1.5
EDCN	191.71	0.424g	2.21	1.5
N-methylmorpholine 0.920	101.15	0.161ml	1.47	1.0
EtOAc		5ml		

Procedure: Acid, was dissolved in 5ml EtOAc. Added Pyrazines cooled to 0°C. Charged EDC & NMM. After 45 min @ 0°C ~ 20% conversion of Amino acid was observed. Slurry was warmed to RT & a lot of solids gelled up.

Agitated with 4
25 Feb 2002 - ~ 95% conversion to the Desired product.

Solids are a problem - did not work up.

[Signature] 25 Feb 2002

Countersigned by _____



Date _____

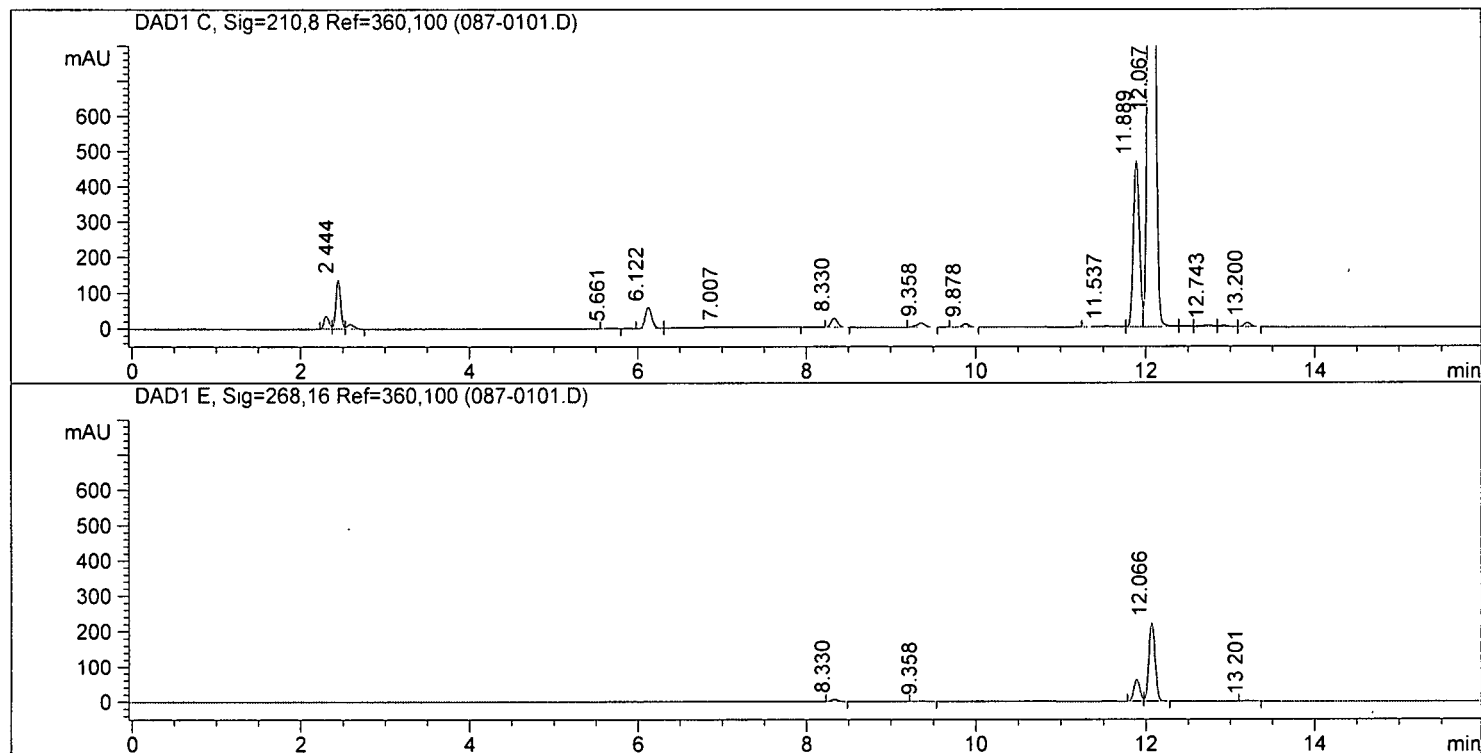
coupling after 4h in etoac

->

```

=====
Injection Date : 02/22/2002  2:48:18 PM      Seq Line : 1
Sample Name    : 70316-045                    Vial No  : 87
Acq Operator   : hansen                       Inj. No. : 1
                                           Inj. Vol.: 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002  7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 02/20/2002  3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.30	BV	0.062	37.12	153.019	0.96	0.000000	
2	2.44	VV	0.061	138.68	537.543	3.39	0.000000	
3	2.58	VB	0.086	13.54	79.231	0.50	0.000000	
4	5.66	PV	0.097	2.58	17.000	0.11	0.001298	L-224,715
5	6.12	VB	0.086	59.89	329.918	2.08	0.000000	
6	7.01	BB	0.754	3.10	195.944	1.24	0.000000	
7	8.33	PB	0.085	25.37	137.690	0.87	0.000000	
8	9.36	BB	0.099	12.45	86.794	0.55	0.000000	
9	9.88	BP	0.086	9.84	56.023	0.35	0.000000	
10	11.54	BV	0.247	2.85	51.619	0.33	0.000000	
11	11.89	VV	0.080	466.76	2339.157	14.75	0.000000	
12	12.07	VB	0.092	2.06e3	1.169e4	73.68	2.510658	benzyloxy amide
13	12.46	BV	0.118	3.43	29.866	0.19	0.000000	
14	12.74	VV	0.156	4.93	56.704	0.36	0.000000	
15	12.92	VV	0.114	4.31	34.073	0.21	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
16	13.20	VB	0.088	12.19	71.015	0.45	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.001298	L-224,715
2	8.33	BB	0.085	6.37	34.641	2.33	0.000000	
3	9.36	BP	0.099	1.09	7.517	0.50	0.000000	
4	11.89	PV	0.080	61.78	308.323	20.70	0.000000	
5	12.07	VB	0.079	223.44	1130.782	75.91	2.510658	benzyloxy amide
6	13.20	BB	0.090	1.38	8.354	0.56	0.000000	

=====
*** End of Report ***

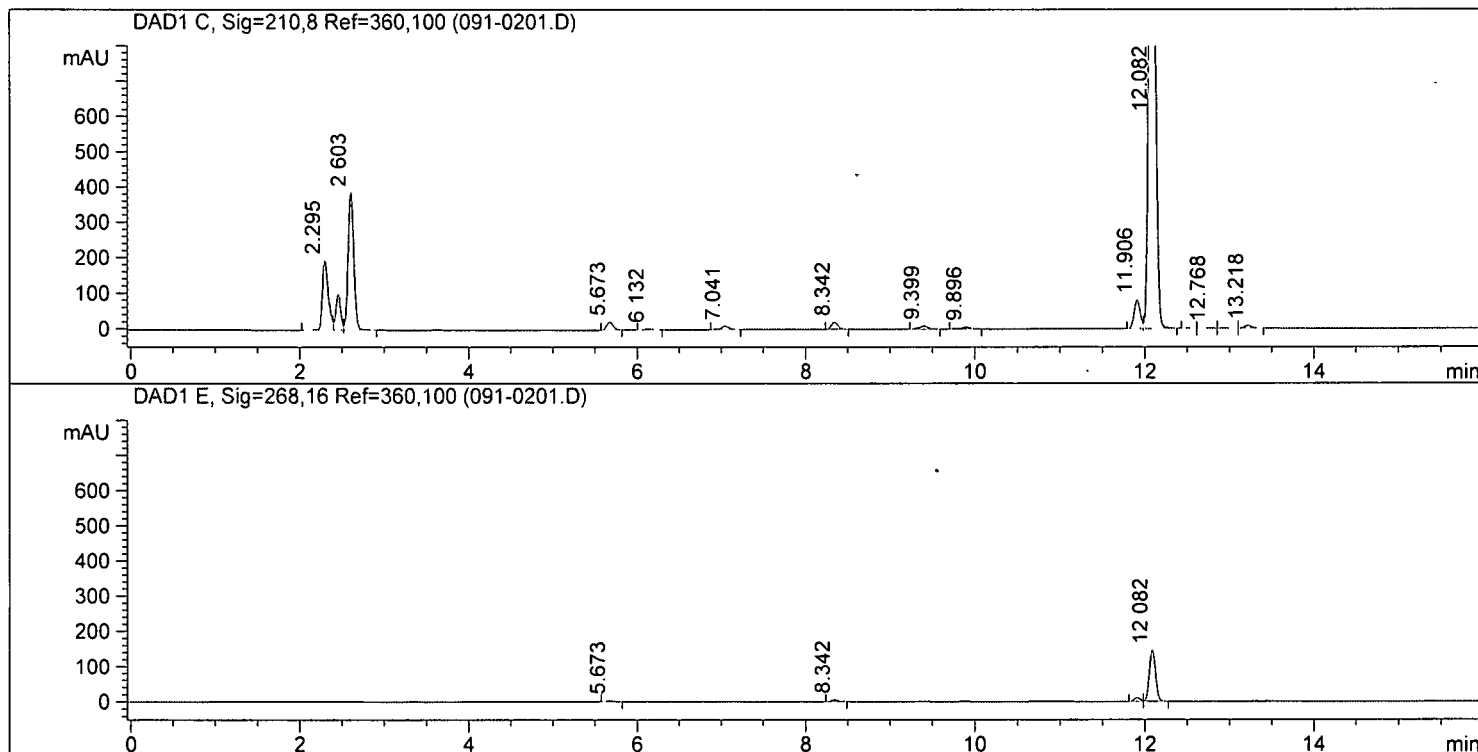
ethyl acetate coupling

->

```

=====
Injection Date : 02/25/2002 10:30:56 AM      Seq Line : 2
Sample Name    : 70316-045                    Vial No  : 91
Acq Operator   : hansen                       Inj. No. : 1
                                           Inj. Vol.: 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002 7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

=====
Sorted By      : Signal
Calib. Data Modified : 02/20/2002 3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.30	BV	0.073	195.40	950.818	7.58	0.000000	
2	2.45	VV	0.062	100.34	394.214	3.14	0.000000	
3	2.60	VB	0.073	387.11	1812.854	14.45	0.000000	
4	5.67	BV	0.084	21.78	119.197	0.95	0.028443	L-224,715
5	6.13	VB	0.082	3.23	17.278	0.14	0.000000	
6	7.04	BP	0.094	9.64	64.835	0.52	0.000000	
7	8.34	BB	0.085	19.50	105.895	0.84	0.000000	
8	9.40	BB	0.101	8.65	61.667	0.49	0.000000	
9	9.90	BB	0.098	5.72	38.179	0.30	0.000000	
10	11.91	VV	0.078	80.32	397.029	3.16	0.000000	
11	12.08	VB	0.083	1.62e3	8509.132	67.83	1.826243	benzyloxy amide
12	12.51	BV	0.101	1.26	8.967	0.07	0.000000	
13	12.77	VV	0.112	1.47	11.767	0.09	0.000000	
14	12.94	VV	0.124	1.26	11.040	0.09	0.000000	
15	13.22	VB	0.086	7.48	42.338	0.34	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	5.67	BB	0.084	2.47	13.473	1.63	0.028443	L-224,715
2	8.34	BB	0.085	4.88	26.532	3.21	0.000000	
3	11.91	BV	0.078	10.54	52.106	6.30	0.000000	
4	12.08	VB	0.079	145.35	734.345	88.85	1.826243	benzyloxy amide

=====
*** End of Report ***

coupling after 45 min in etoac

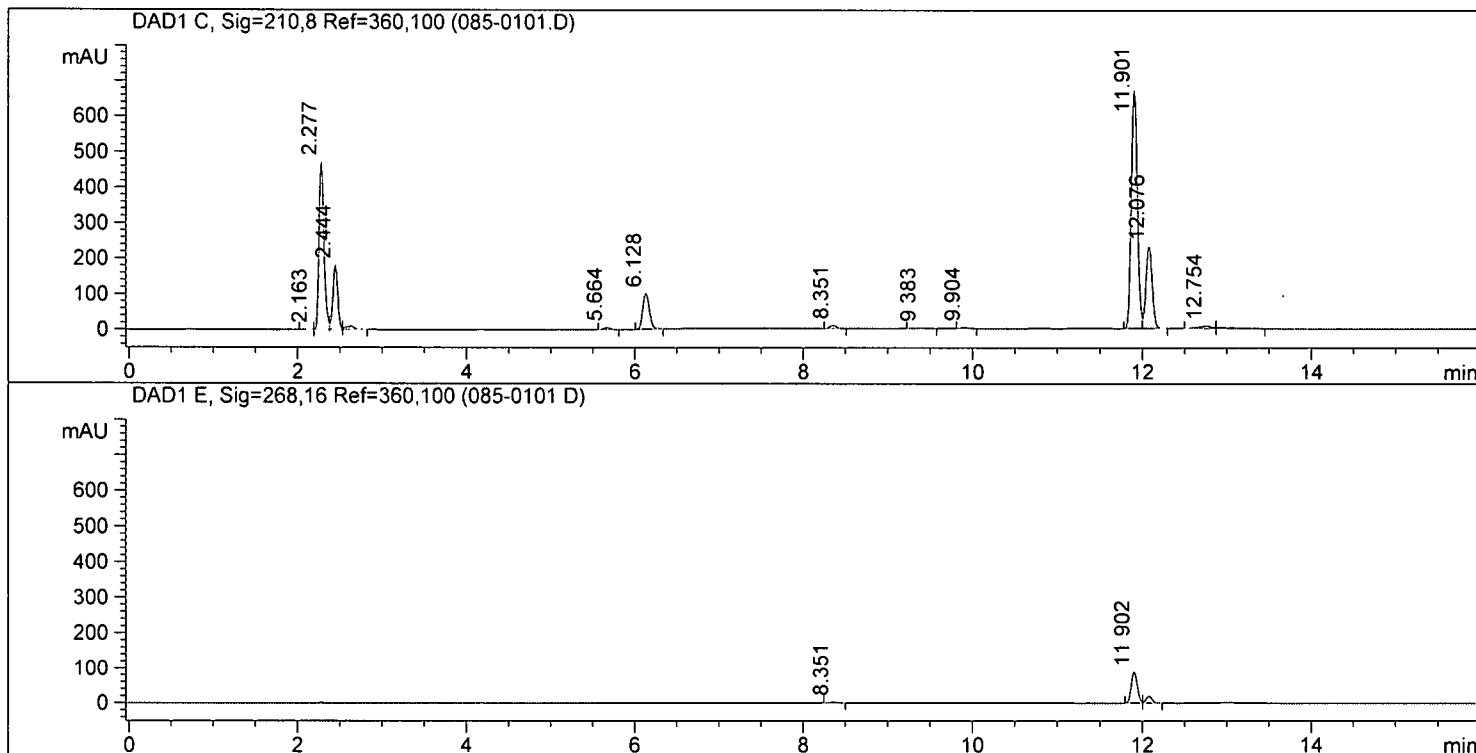
->

```

=====
Injection Date : 02/22/2002  9:58:50 AM      Seq Line   : 1
Sample Name    : 70316-045                    Vial No    : 85
Acq Operator   : hansen                       Inj. No.   : 1
                                           Inj. Vol.  : 2 µl
    
```

```

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002  7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 02/20/2002  3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.16	BV	0.071	1.32	6.709	0.08	0.000000	
2	2.28	VV	0.061	472.07	1910.312	23.89	0.000000	
3	2.44	VV	0.062	182.15	718.248	8.98	0.000000	
4	2.63	VB	0.097	9.40	65.652	0.82	0.000000	
5	5.66	BP	0.081	5.59	29.326	0.37	0.004572	L-224,715
6	6.13	PB	0.086	101.69	555.724	6.95	0.000000	
7	8.35	BP	0.086	8.41	45.821	0.57	0.000000	
8	9.38	BB	0.111	1.45	11.775	0.15	0.000000	
9	9.90	BP	0.081	3.38	17.705	0.22	0.000000	
10	11.90	PV	0.080	665.47	3333.534	41.69	0.000000	
11	12.08	VB	0.079	230.83	1168.709	14.62	0.246058	benzyloxy amide
12	12.75	BV	0.147	6.80	73.801	0.92	0.000000	
13	12.93	VB	0.257	2.84	57.753	0.72	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.004572	L-224,715
2	8.35	BP	0.086	2.12	11.631	2.11	0.000000	
3	11.90	BV	0.080	88.88	444.325	80.58	0.000000	
4	12.08	VB	0.079	18.82	95.472	17.31	0.246058	benzyloxy amide

=====
*** End of Report ***

Investigator

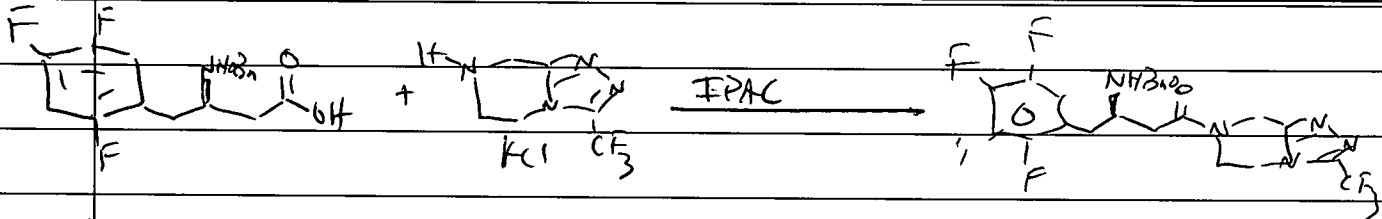
Date

22 Feb 2002

Subject



Filed in Book Number/Title



Reagents:		FW	Ant	mmol	eq
B-Amino acid	72324-125	339.11	0.528	1.56	1.0
Triazolopyrazine	72176-100	228.04	0.532g	2.34	1.0
EDC		191.71	448g	2.34	1.5
N-methyl morpholine		101.15	158g, 172ml	1.56	1.0
IPAC			5ml		

Procedure set up side by side w/ 70316-45. Same conversion after the solid ground up after warming to RT

Agitated over water
 25 Feb 2002 - complete conv observed lots of gummy solids
 not - the way to go

[Signature] 22 Feb 2002

Countersigned by



Date

coupling after 4h in IPAC

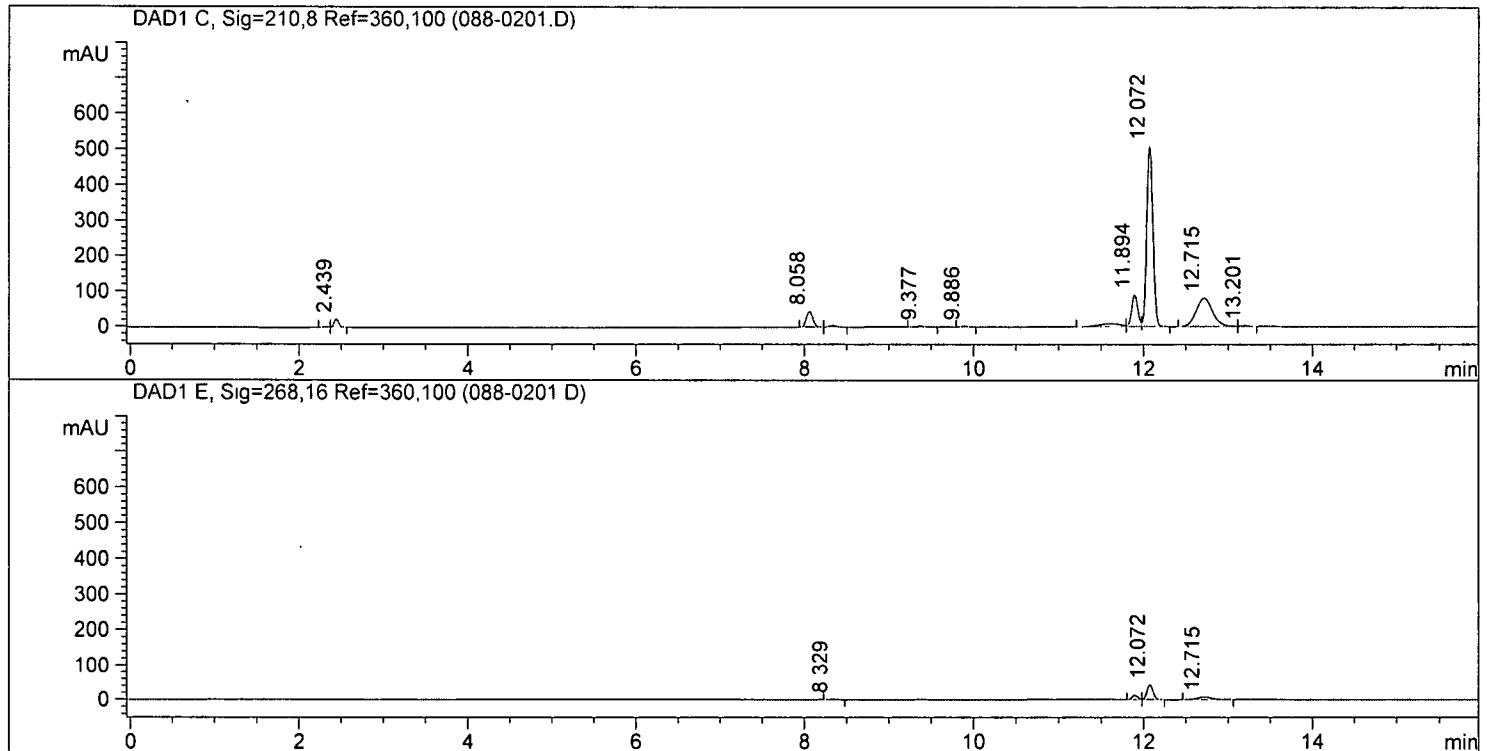
->

```

=====
Injection Date : 02/22/2002  3:06:48 PM      Seq Line   : 2
Sample Name    : 70316-047                    Vial No    : 88
Acq Operator   : hansen                       Inj. No.   : 1
                                           Inj. Vol.  : 2 µl
    
```

```

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002  7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 02/20/2002  3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.31	VV	0.069	2.77	12.113	0.26	0.000000	
2	2.44	VB	0.061	24.44	95.093	2.02	0.000000	
3	0.00		0.000	0.00	0.000	0.00	0.000000	L-224, 715
4	8.06	PV	0.085	45.01	243.129	5.15	0.000000	
5	8.33	VB	0.089	5.01	28.698	0.61	0.000000	
6	9.38	BB	0.096	2.61	17.372	0.37	0.000000	
7	9.89	BP	0.081	1.85	9.612	0.20	0.000000	
8	11.61	BV	0.290	8.75	161.938	3.43	0.000000	
9	11.89	VV	0.079	90.78	461.469	9.78	0.000000	
10	12.07	VB	0.079	508.99	2573.583	54.56	0.548488	benzyloxy amide
11	12.71	BV	0.210	80.76	1096.948	23.25	0.000000	
12	13.20	VB	0.091	2.86	17.433	0.37	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
2	8.33	BB	0.084	1.20	6.400	1.76	0.000000	
3	11.89	PV	0.077	11.60	56.616	15.55	0.000000	
4	12.07	VP	0.078	41.38	207.166	56.90	0.548488	benzyloxy amide
5	12.72	BP	0.206	7.13	93.933	25.80	0.000000	

=====
*** End of Report ***

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.000103	L-224,715
2	8.33	BB	0.086	1.41	7.717	2.16	0.000000	
3	11.89	BV	0.078	56.43	282.570	78.98	0.000000	
4	12.07	VP	0.079	13.40	67.481	18.86	0.176014	benzyloxy amide

=====
*** End of Report ***

IPAC coupling

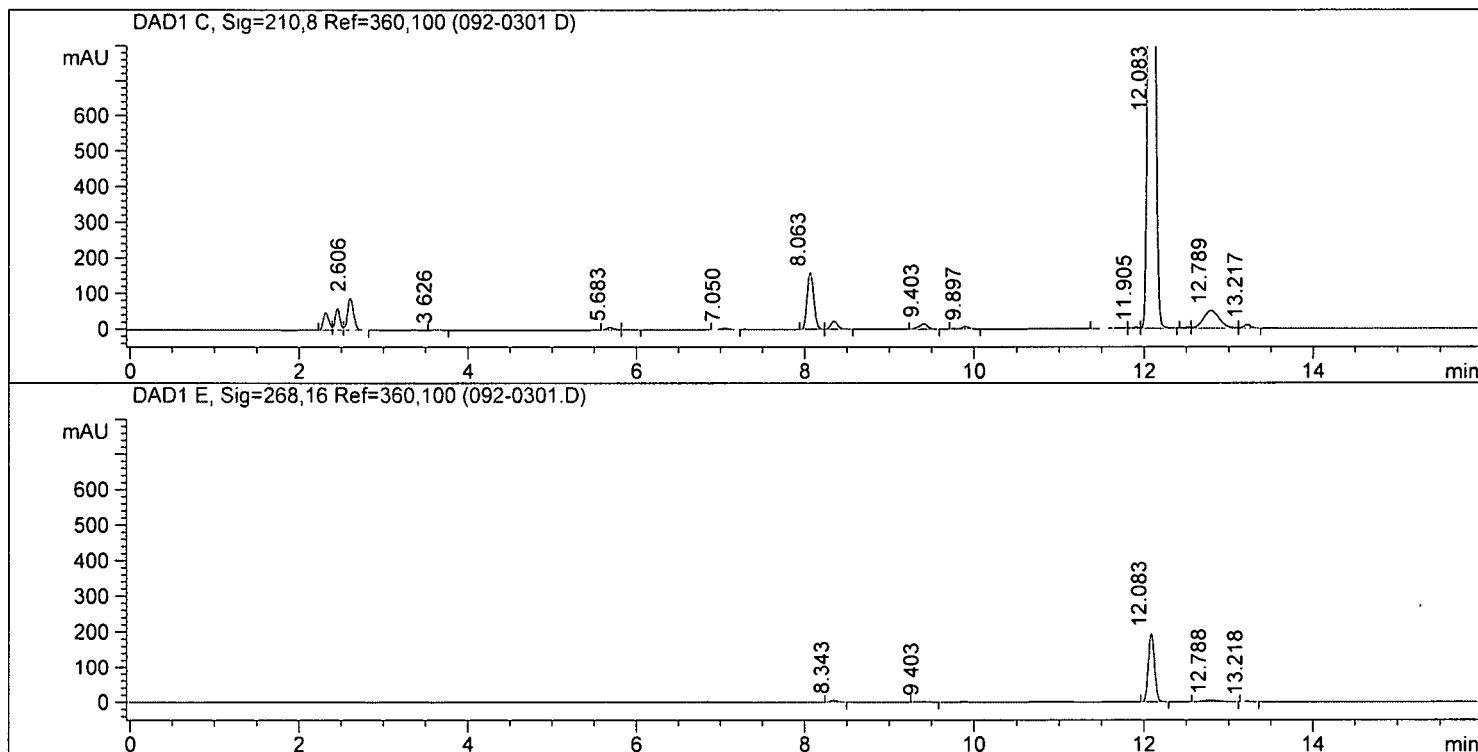
->

```

=====
Injection Date : 02/25/2002 10:49:27 AM      Seq Line : 3
Sample Name    : 70316-047                  Vial No  : 92
Acq Operator   : hansen                     Inj. No. : 1
                                           Inj. Vol.: 2 µl
    
```

```

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002 7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

=====
Sorted By      : Signal
Calib. Data Modified : 02/20/2002 3:33:04 PM
Multiplier    : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

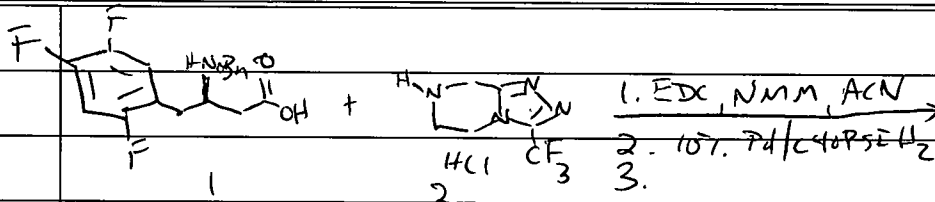
Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.31	BV	0.069	49.38	226.104	1.66	0.000000	
2	2.45	VV	0.062	61.51	240.386	1.76	0.000000	
3	2.61	VB	0.078	90.08	447.595	3.29	0.000000	
4	3.63	BB	0.084	1.10	6.041	0.04	0.000000	
5	5.68	PV	0.095	6.81	44.043	0.32	0.008481	L-224,715
6	5.87	VB	0.093	1.41	9.077	0.07	0.000000	
7	7.05	BP	0.097	4.06	27.405	0.20	0.000000	
8	8.06	BV	0.086	159.70	878.847	6.45	0.000000	
9	8.34	VB	0.091	22.96	135.377	0.99	0.000000	
10	9.40	BB	0.099	15.39	106.218	0.78	0.000000	
11	9.90	BP	0.093	7.20	45.320	0.33	0.000000	
12	11.71	BV	0.210	1.58	25.655	0.19	0.000000	
13	11.90	VV	0.087	3.72	21.349	0.16	0.000000	
14	12.08	VB	0.088	1.95e3	1.066e4	78.27	2.289882	benzyloxy amide
15	12.51	BV	0.088	3.06	19.461	0.14	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
16	12.79	VV	0.203	50.11	664.839	4.88	0.000000	
17	13.22	VB	0.088	10.65	61.862	0.45	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.008481	L-224,715
2	8.34	PB	0.087	5.53	30.753	2.83	0.000000	
3	9.40	BP	0.099	1.35	9.370	0.86	0.000000	
4	12.08	VB	0.081	195.32	984.664	90.77	2.289882	benzyloxy amide
5	12.79	BP	0.194	4.33	53.989	4.98	0.000000	
6	13.22	BB	0.082	1.13	5.983	0.55	0.000000	

=====
*** End of Report ***



Reagents	FW	Am't	mmol	eq
Amnoacid 72324-148 KF2007PM in 50 ml ACN	339.11	5.10g	15.0	1.0
Triazole 72176-100	228.04	4.29g	18.8	1.25
EDC	191.71	4.31g	22.5	1.50
NMM methylmorpholine 6920	101.15	15.2g 1.65ml	15.0	1.00
ACN		50 ml		

Procedure: To soln of Amnoacid in 50 ml ACN added HCl salt of triazole cooled to 0°C Added EDC, NMM. Aged 2.25h at which point ~99% of acid had converted to amide. Quenched w/ 25 ml H₂O 50 ml EtOH. Rmt washed w/ 5% NaHCO₃, sat NaCl. Co Assayed organics to contain 7.66g of Product 98% yield. Concentrated & dissolved-reconcentrated twice w/ MeOH. Redissolved in 45 ml MeOH submitted to Hydrog 40% EtOH, 55°C 1.50g 10% Pd/C. 27 Feb 2002 Reaction complete by HPLC.

Filtered through 5.00g pad of silica Floe washed pad w/ 40 ml Methanol. Assayed Methanol filtrate to contain 5.14g of 715 84% Assay yield. Concentrated & flushed 2x w/ EtOH Redissolved in 30 ml EtOH & filtered into 3-neck washed filter flask w/ 10 ml EtOH (4 ml/g total). Dissolved 1.50g H₂PO₄ (85%).

Countersigned by _____



DO NOT BEGIN NEW EXPERIMENTS ON THIS PAGE.

27 Feb 2002.

in 75 ml H₂O. Heated EtOH soln to 60°C
 & added 50g of 70316-043 as seed. Added
 1/3 PO₄ soln dropwise @ 60°C to slurry^(15min) solids
 took a while to form. Rinsed all funnel w/ 1-2-1 EtOH.
 Aged @ 60°C for 1/2 hrs then cooled to RT @
 20°C/hr. Once cooled Ethanol was added to the batch
 (73ml) dropwise - Aged O/N @ RT.

28 Feb 2002 - Filtered solids & washed w/ 25 ml Ethanol
 for 0.6g isolated as white solids

1 March 2002 - Impurity profile from Analytical Research

#PLC	RRT	Acct.	
	0.95	0.07	No minor impurities detected
	0.97	0.08	
	1.00	99.83	

impurities are lower probably due to O/N age of slurry.

Phys Mens indicates that solid state NMR of 70316-035,43
 & this batch is identical despite small d.i.F. Feasible xray powder pattern

[Signature] 1 March 2002



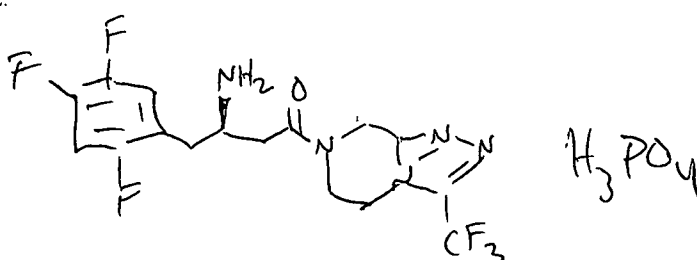
Countersigned by _____

DELIVERY SHEET (A): CHEMICAL FOR NON-CLINICAL USE

L224715-006F

MOLECULAR FORMULA: <i>C₁₆H₁₈F₆N₅O</i>	MOLECULAR WT.: <i>505</i>	DATE: <i>7M_N2002</i>	ASSIGNED BY:
--	------------------------------	------------------------------------	--------------

CHEMICAL/TRIVIAL NAME:

STRUCTURE: 	LABELING INSTRUCTIONS (FOR OUTSIDE DELIVERIES) <input type="checkbox"/> L NUMBER <input type="checkbox"/> NAME AS SHOWN ABOVE <input type="checkbox"/> QUANTITY <input type="checkbox"/> OTHER (Specify Under "Remarks") <input type="checkbox"/> HAZARDOUS <input type="checkbox"/> NON-HAZARDOUS
	PROJECT NUMBER: <i>L224715</i>

Prepared by/Commercial Source:	Notebook Ref./Lot No.: <i>70316-049</i>	Criteria of Purity, Safety or Potency: <input type="checkbox"/> TLC <input checked="" type="checkbox"/> HPLC <input type="checkbox"/> GC
		<input type="checkbox"/> IR <input type="checkbox"/> UV <input type="checkbox"/> NMR <input type="checkbox"/> MS

CHARACTERIZATION DATA

COMPOUND IS PUBLISHED YES NO UNDETERMINED

OTHER ASSAY RESULTS OR PHYSICAL CONSTANTS*:
 data generated by Analytical Research

PERMISSION TO RELEASE TO CAS FOR NOMENCLATURE DEVELOPMENT
 YES NO

LIT. REF./CAS REG. NO.

REMARKS
2.00g to Leigh Shultz for Formulation Development.

PB ECL-
 Storage Conditions (check one)
 "controlled room temperature" (25°C)
 "refrigeration" (4°C)
 "freezer" (-20°C)
 -70°C freezer.
 other _____

*If GMP Compliance has not signed below, data has *not* been audited. For safety information and special handling precautions, access CHIS.

SEND TO: (NAME, LOCATION, QUANTITY, TEST NO. OR ACRONYM AND INDICATE IF DELIVERED)

Material is (select one) ___ GMP ; ___ non-GMP and will be used in (select one): ___ GMP/GLP study; ___ non-GMP study.

CC: NAMES AND LOCATIONS:

Transfer Requested By Name: Location:	Delivery Sheet By. Name/ Location:	APPROVED FOR DELIVERY BY MRL GMP COMPLIANCE		Transfer Completed By:
		Dept Approval	Quality Approval	

4.61g/50ml of 76.08g ML's

->

```

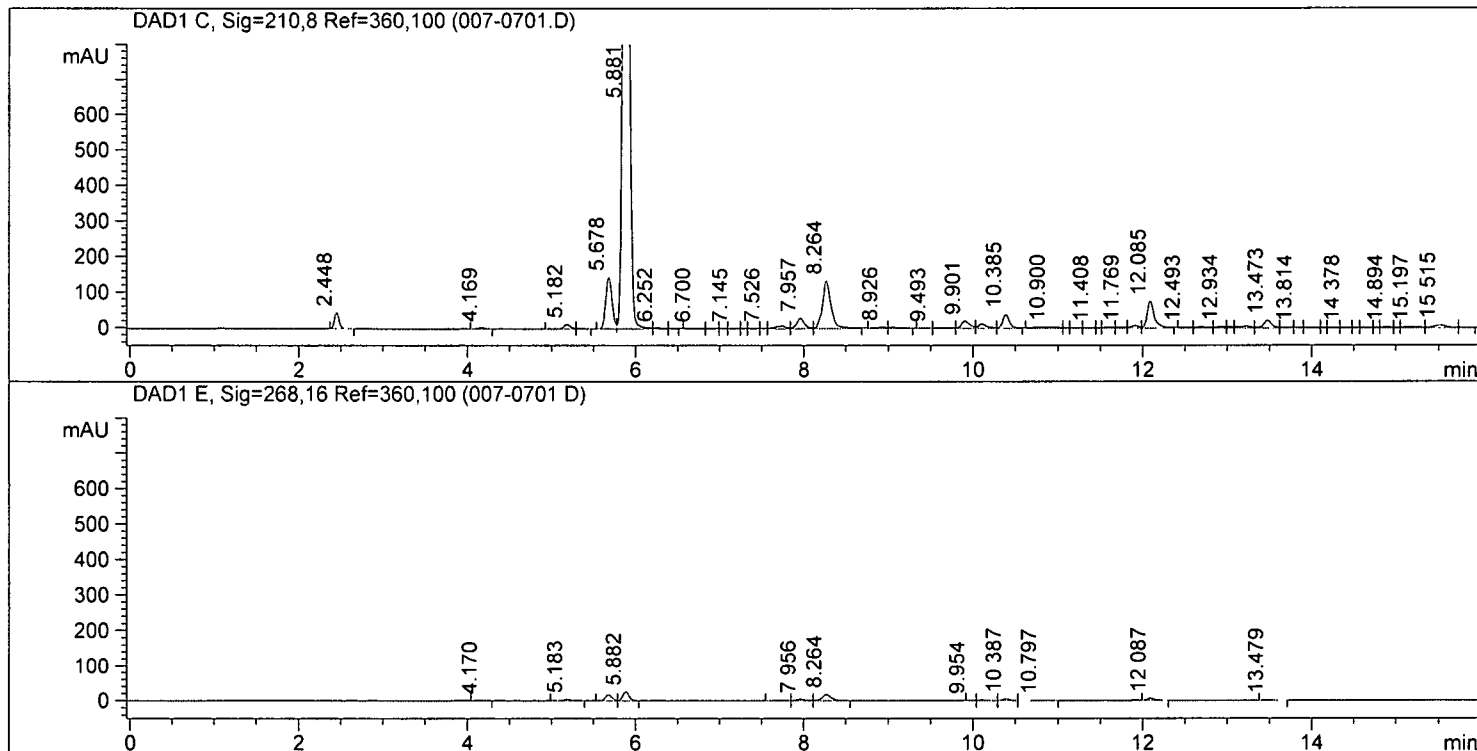
=====
Injection Date : 02/28/2002  10:07:18 AM      Seq Line : 7
Sample Name    : 70316-049                    Vial No   : 7
Acq Operator   : hansen                       Inj. No.  : 1
                                           Inj. Vol. : 2 µl

```

```

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/28/2002  10:06:27 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm

```



```

=====
Customized Report:karlo
=====

```

```

Sorted By      : Signal
Calib. Data Modified : 02/28/2002  9:43:53 AM
Multiplier     : 1.000000

```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.45	VP	0.059	45.09	174.918	1.21	0.000000	
2	4.17	BV	0.100	3.21	21.518	0.15	0.000000	
3	5.18	VV	0.087	12.41	71.604	0.50	0.000000	
4	5.33	VV	0.086	1.78	10.400	0.07	0.000000	
5	5.68	VV	0.081	145.17	761.632	5.28	0.199076	L-224,715
6	5.88	VB	0.084	1.84e3	9782.957	67.80	0.000000	
7	6.25	BV	0.117	3.22	27.237	0.19	0.000000	
8	6.42	VB	0.095	1.68	12.190	0.08	0.000000	
9	6.70	BV	0.159	2.30	27.744	0.19	0.000000	
10	6.95	VV	0.114	1.71	15.267	0.11	0.000000	
11	7.03	VB	0.079	1.55	8.826	0.06	0.000000	
12	7.14	BB	0.112	1.58	13.786	0.10	0.000000	
13	7.29	BV	0.067	1.63	7.671	0.05	0.000000	
14	7.45	VV	0.103	1.82	14.479	0.10	0.000000	
15	7.53	VV	0.070	2.06	10.265	0.07	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
16	7.74	VV	0.126	8.02	75.636	0.52	0.000000	
17	7.96	VV	0.092	29.91	195.048	1.35	0.000000	
18	8.26	VB	0.103	135.21	984.369	6.82	0.000000	
19	8.93	BV	0.139	4.86	48.017	0.33	0.000000	
20	9.05	VB	0.150	4.35	49.336	0.34	0.000000	
21	9.49	BV	0.134	2.21	24.259	0.17	0.000000	
22	9.72	VV	0.166	3.24	42.302	0.29	0.000000	
23	9.90	VV	0.105	21.63	154.736	1.07	0.000000	
24	10.10	VV	0.109	13.54	103.450	0.72	0.000000	
25	10.38	VB	0.089	39.93	236.877	1.64	0.000000	
26	10.90	BV	0.258	4.83	95.319	0.66	0.000000	
27	11.10	VV	0.063	2.86	12.999	0.09	0.000000	
28	11.18	VB	0.113	2.81	24.435	0.17	0.000000	
29	11.41	BV	0.113	2.85	25.630	0.18	0.000000	
30	11.49	VV	0.056	2.91	11.474	0.08	0.000000	
31	11.57	VV	0.118	3.43	31.172	0.22	0.000000	
32	11.77	VV	0.110	3.65	28.745	0.20	0.000000	
33	11.91	VV	0.106	7.67	55.507	0.38	0.000000	
34	12.09	VB	0.094	76.01	479.292	3.32	0.097646	benzyloxy amide
35	12.49	BV	0.135	2.94	31.101	0.22	0.000000	
36	12.68	VV	0.162	4.13	49.521	0.34	0.000000	
37	12.93	VV	0.126	4.72	39.504	0.27	0.000000	
38	13.04	VV	0.074	4.34	22.901	0.16	0.000000	
39	13.21	VV	0.143	6.13	65.657	0.46	0.000000	
40	13.47	VV	0.108	22.51	164.959	1.14	0.000000	
41	13.66	VV	0.120	3.37	31.278	0.22	0.000000	
42	13.81	VB	0.090	3.03	20.206	0.14	0.000000	
43	13.99	BV	0.148	2.80	32.099	0.22	0.000000	
44	14.14	VV	0.066	2.74	12.591	0.09	0.000000	
45	14.22	VV	0.118	2.74	24.848	0.17	0.000000	
46	14.38	VB	0.109	2.73	22.807	0.16	0.000000	
47	14.53	BV	0.073	2.69	14.134	0.10	0.000000	
48	14.62	VV	0.119	2.78	25.429	0.18	0.000000	
49	14.77	VV	0.069	2.77	12.969	0.09	0.000000	
50	14.89	VV	0.114	2.89	26.799	0.19	0.000000	
51	15.01	VV	0.067	2.62	11.778	0.08	0.000000	
52	15.20	VV	0.191	3.31	50.773	0.35	0.000000	
53	15.51	VV	0.162	8.75	103.219	0.72	0.000000	
54	15.77	VV	0.142	2.49	27.831	0.19	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	4.17	BV	0.131	1.48	13.831	2.33	0.000000	
2	5.18	VB	0.113	4.32	34.543	5.82	0.000000	
3	5.68	VV	0.085	17.16	95.348	16.06	0.199076	L-224,715
4	5.88	VB	0.080	25.55	136.411	22.97	0.000000	
5	7.75	VV	0.124	1.69	16.219	2.73	0.000000	
6	7.96	VV	0.097	4.61	31.904	5.37	0.000000	
7	8.26	VV	0.106	18.09	136.200	22.94	0.000000	
8	9.95	VV	0.075	1.28	7.600	1.28	0.000000	
9	10.11	VV	0.100	1.80	13.483	2.27	0.000000	
10	10.39	VV	0.090	4.75	28.488	4.80	0.000000	
11	10.80	VV	0.200	1.27	21.208	3.57	0.000000	
12	12.09	VV	0.096	6.24	40.792	6.87	0.097646	benzyloxy amide
13	13.48	VV	0.120	2.26	17.791	3.00	0.000000	

*** End of Report ***

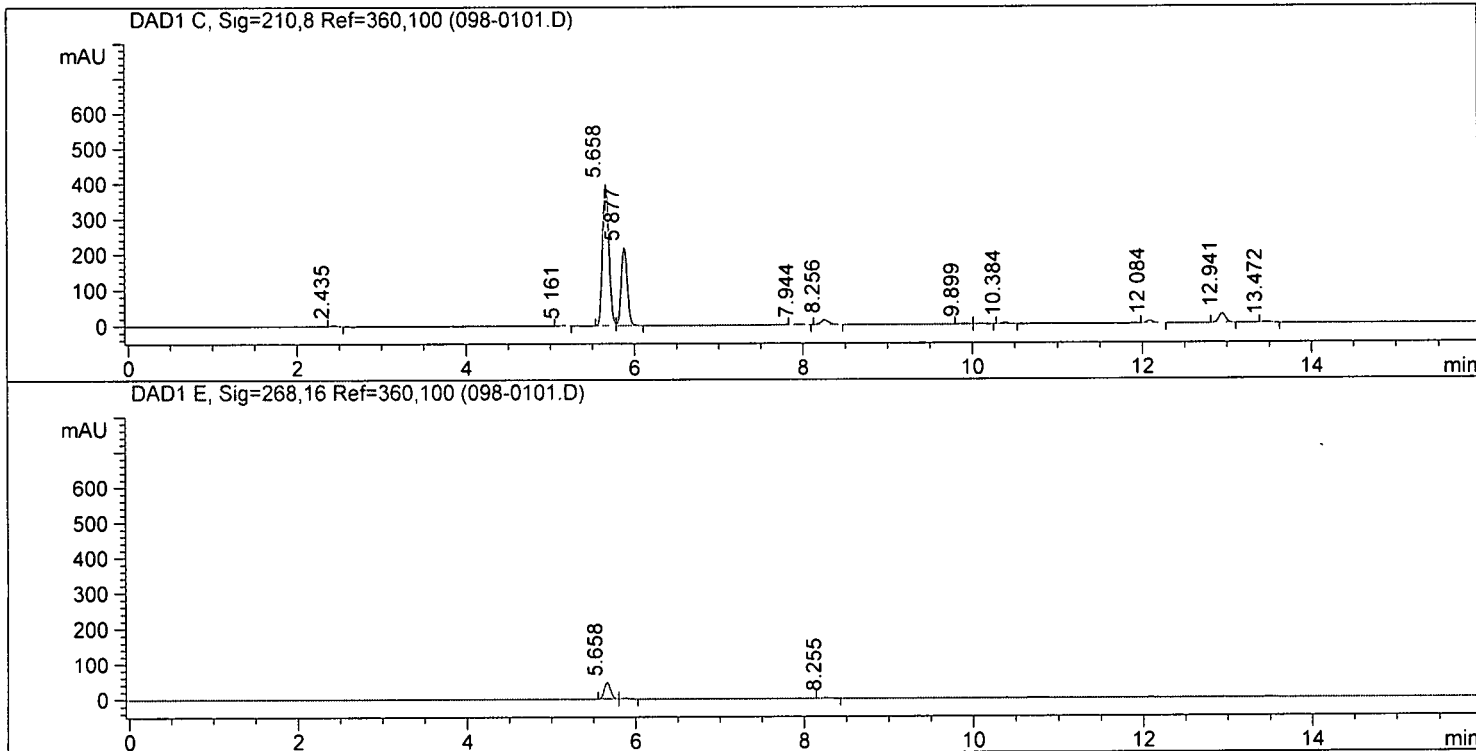
0.3589g/50ml of 66.47g methanol filtrate

->

```

=====
Injection Date : 02/27/2002 9:33:49 AM      Seq Line : 1
Sample Name    : 70316-049                  Vial No  : 98
Acq Operator   : hansen                     Inj. No. : 1
                                           Inj. Vol.: 2 µl

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002 7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 02/20/2002 3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

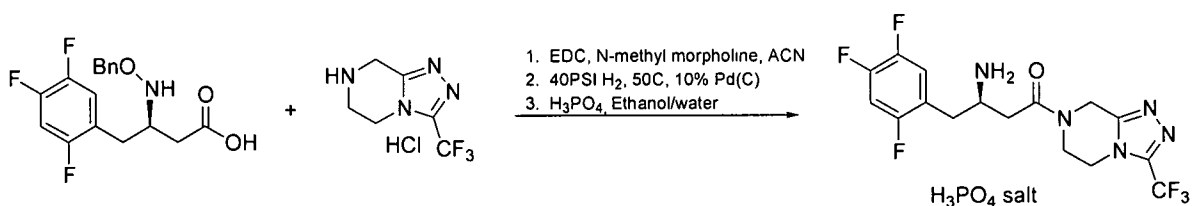
Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.43	BB	0.060	4.31	16.335	0.46	0.000000	
2	5.16	BV	0.087	1.47	8.222	0.23	0.000000	
3	5.66	BV	0.083	399.09	2102.453	59.08	0.555205	L-224,715
4	5.88	VB	0.078	219.10	1091.532	30.67	0.000000	
5	7.94	VP	0.084	2.70	15.392	0.43	0.000000	
6	8.26	BB	0.094	13.77	91.574	2.57	0.000000	
7	9.90	PV	0.083	1.87	9.777	0.27	0.000000	
8	10.10	VB	0.080	1.06	5.432	0.15	0.000000	
9	10.38	BP	0.076	3.63	17.957	0.50	0.000000	
10	12.08	VB	0.084	7.24	39.887	1.12	0.003055	benzyloxy amide
11	12.94	BB	0.087	25.97	144.038	4.05	0.000000	
12	13.47	BB	0.087	2.86	15.842	0.45	0.000000	

5.145

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	5.66	BV	0.083	46.28	243.425	90.53	0.555205	L-224,715
2	5.88	VB	0.081	2.60	13.575	5.05	0.000000	
3	8.26	BB	0.093	1.79	11.894	4.42	0.000000	
4	0.00		0.000	0.00	0.000	0.00	0.003055	benzyloxy amide

*** End of Report ***

L224,715- Coupling, reduction and salt formation



Reagent	Source	dens	FW	Amt	Mole	eq
Benzyloxy aminoacid		-	339.1			1.0
Triazolepyrazine-HCl			228.0			1.25
EDC			191.71			1.5
N-Methylmorpholine		0.920	101.15			1.0
Acetonitrile		0.786	41.05		82	10ml/g
Water		1	18			5ml/g
Ethyl Acetate		0.902	88.1		77	10ml/g
NaHCO ₃			84			5ml/g
NaCl _{aq} (Sat.)			58.44			5ml/g
MeOH		0.791	32.04		65	10ml/g
10% Pd/C						20wt%
Ethanol		0.790	46.07		78	4+14 5ml/g
H ₃ PO ₄			98			1.05
Water		1	18			1.5ml/g

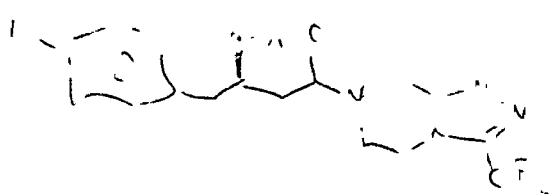
Benzyloxyamino acid was dissolved in 10 ml/g CH₃CN. The solution is charged with 1.25 equiv. of triazolepyrazine HCl salt and then cooled to 0°C. EDC (1.5 equiv.) and N-methyl morpholine (1.0 equiv.) are added sequentially to the heterogeneous mixture. The reaction is aged at 0°C for 2h at which point 99% of the acid had converted to the amide. The slurry was diluted with 5ml/g water water and 10ml/g EtOAc. The layers are cut and the organic was washed with 5ml/g saturated NaHCO₃ (some sat NaCl may be needed to obtain a clear cut), then 5ml/g saturated NaCl. The organics were concentrated to an oil, flushed twice with methanol and finally re-dissolved in 10ml/g MeOH. 10% Pd/C was charged and the mixture was subjected to 40PSI H₂ at 50C for 18h at which point the benzyloxy group had been cleaved. The mixture was filtered though silkafloc, which was washed with 2ml/g methanol. The filtrate assayed to contain a91 % assay yield of 715.

The methanol was removed in vacuo and the oil flushed twice with ethanol. The oil after flushing was re-dissolved in 3.0 ml/gof ethanol and then filtered into a RBF. The filter was washed with 1ml/g ethanol (total 40ml, ~4ml/g). 2.91g (1.0 equiv.) of phosphoric acid was dissolved in 1.5ml/g water. This solution was added to the ethanol solution of 715 at 60°C, which had been seeded with 1% of the phosphate salt. Solids formed immediately and the slurry was cooled to RT after complete addition of the acid solution. The slurry was then diluted with 14.5ml/g ethanol dropwise. The concentration of 715 was 2.22 mg/g after 0.5 h and 2.34 mg/g after 3h. The slurry was filtered and washed with 5ml/g EtOH.

11.81g of white crystalline solids were recovered (75% overall yield). A 96% mass-balance was observed for crystallization. Solids are 80.6 wt% by HPLC (theoretical 80.6%).

HYDROGENATION OR HIGH PRESSURE REACTION

2002022660.001
DO NOT WRITE IN THIS SPACE

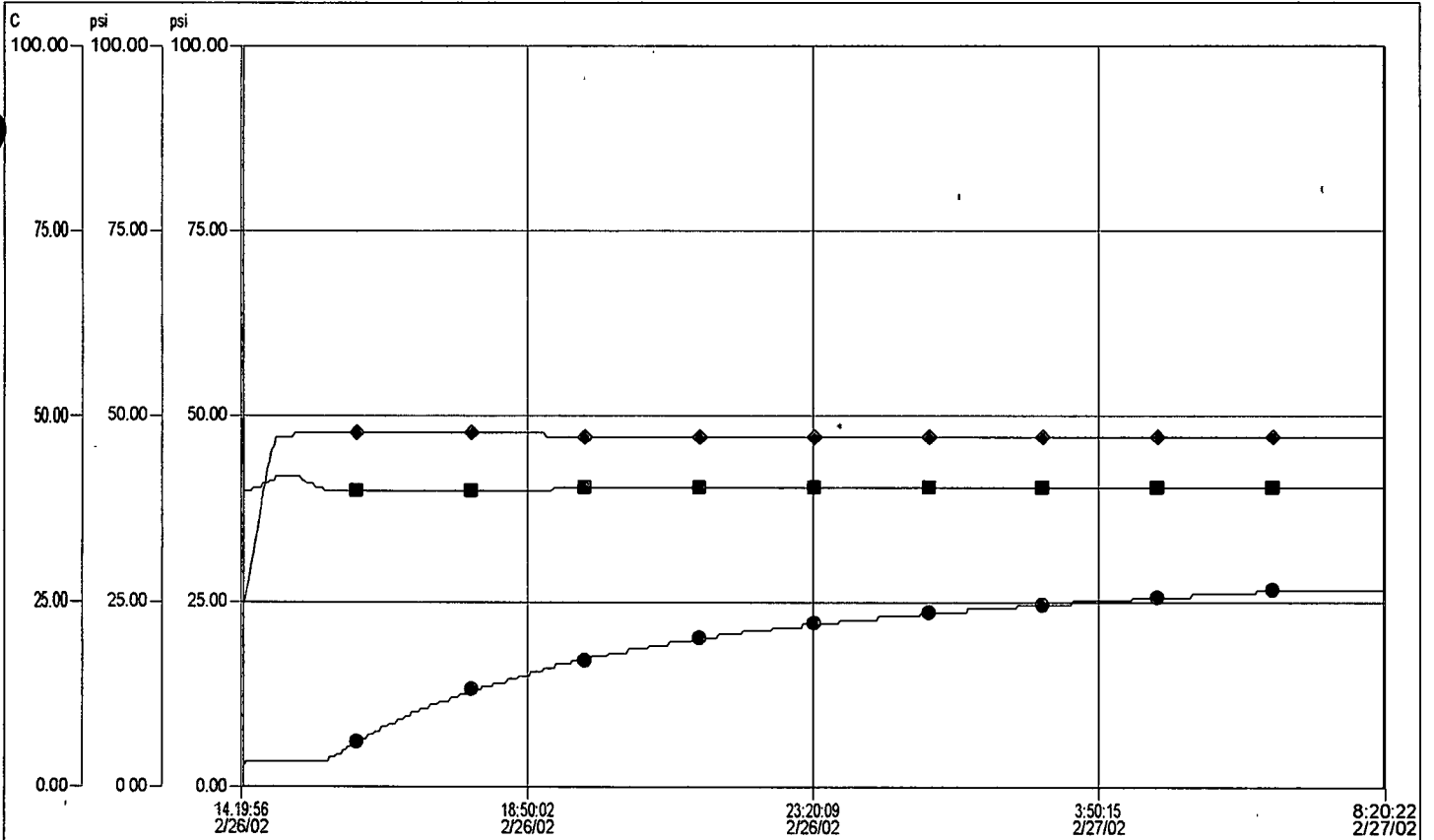
REQUESTED BY Hansen BLDG/RM 203269 EXT. 0 DATE 2/26/02
 PROJECT NO. 120115 PROJECT 02237 NOTEBOOK - PAGE NO. 36
 CHECK HERE IF REACTION IS GMP/GLP **STARTING MATERIAL**
 NO. 1 _____ NO. 2 _____
 M.W. _____ AMOUNT 1.5 G. MOLES _____ M.W. _____ AMOUNT _____ G. MOLES _____
 STRUCTURAL FORMULA: 
 CATALYST _____ G. OF _____
 SOLVENT _____ ML. OF _____
 MOLES OF HYDROGEN REQUIRED _____
 OTHER MATERIALS _____
 REACTION CONDITIONS, ETC. _____
 PRECAUTIONS: _____
 EMPIRICAL FORMULA: _____

TO BE FILLED IN BY HYDROGENATION LABORATORY

NO. 1: 7.50 G. MOLES 0.0111 NO. 2: _____ G. MOLES _____
 CATALYST 1.5 G. OF 10% Pd/C lot # 50895025
 SOLVENT 50 ML. OF meoh
 OTHER MATERIALS _____
 CELL NO. _____ HEATER NO. _____ REC. POINT INTERNAL _____ EXTERNAL _____ BOMB NO. _____ VESSEL SIZE 750 ML.
 SHAKER NO. 60 LINER _____ SHAKER TANK 197 AUX. TANK _____ SYSTEM VOLUME 77 ML.
 CALC'D H₂ PRESSURE DROP = _____ LBS./MOLE 16.044 MOLES = 21.3 LBS.
 CONDITIONS _____ HRS. AT 50 C. MISC. DATA: 160 psi

TIME	TEMP.	PRESSURE		TIME	TEMP.	PRESSURE		TIME	TEMP.	PRESSURE	
		OBS.	DROP			OBS.	DROP			OBS.	DROP
14:20	24.4	40	2	22:20	47.3	40	21	06:20	47.3	40	27
14:35	36.0	40	4	22:35	47.3	40	21	06:35	47.3	40	27
14:50	46.0	41	4	22:50	47.3	40	22	06:50	47.3	40	27
15:05	47.3	42	4	23:05	47.3	40	22	07:05	47.3	40	27
15:20	47.8	41	4	23:20	47.3	40	22	07:20	47.3	40	27
15:35	47.8	40	4	23:35	47.3	40	22	07:35	47.3	40	27
15:50	47.8	40	4	23:50	47.3	40	23	07:50	47.3	40	27
16:05	47.8	40	5	00:05	47.3	40	23	08:05	47.3	40	27
16:20	47.8	40	7	00:20	47.3	40	23				
16:35	47.8	40	8	00:35	47.3	40	23				
16:50	47.8	40	9	00:50	47.3	40	23				
17:05	47.8	40	10	01:05	47.3	40	24				
17:20	47.8	40	11	01:20	47.3	40	24				
17:35	47.8	40	12	01:35	47.3	40	24				
17:50	47.8	40	13	01:50	47.3	40	24				
18:05	47.8	40	13	02:05	47.3	40	24				
18:20	47.8	40	14	02:20	47.3	40	24				
18:35	47.8	40	15	02:35	47.3	40	25				
18:50	47.8	40	15	02:50	47.3	40	25				
19:05	47.8	40	16	03:05	47.3	40	25				
19:20	47.3	40	17	03:20	47.3	40	25				
19:35	47.3	40	17	03:35	47.3	40	25				
19:50	47.3	40	18	03:50	47.3	40	25				
20:05	47.3	40	18	04:05	47.3	40	25				
20:20	47.3	40	18	04:20	47.3	40	25				
20:35	47.3	40	19	04:35	47.3	40	26				
20:50	47.3	40	19	04:50	47.3	40	26				
21:05	47.3	40	20	05:05	47.3	40	26				
21:20	47.3	40	20	05:20	47.3	40	26				
21:35	47.3	40	20	05:35	47.3	40	26				
21:50	47.3	40	21	05:50	47.3	40	26				
22:05	47.3	40	21	06:05	47.3	40	26				

RUN BY J. Nunez DATE Feb. 26, 2002
 RUN BY _____ DATE _____



Hist.FIX.PT6007.F_CV Shkr60 Pressr
Hist.FIX.DT6009.F_CV Shkr60 H2 Uptake
Hist.FIX.TE6003.F_CV Shkr60 Product Temp

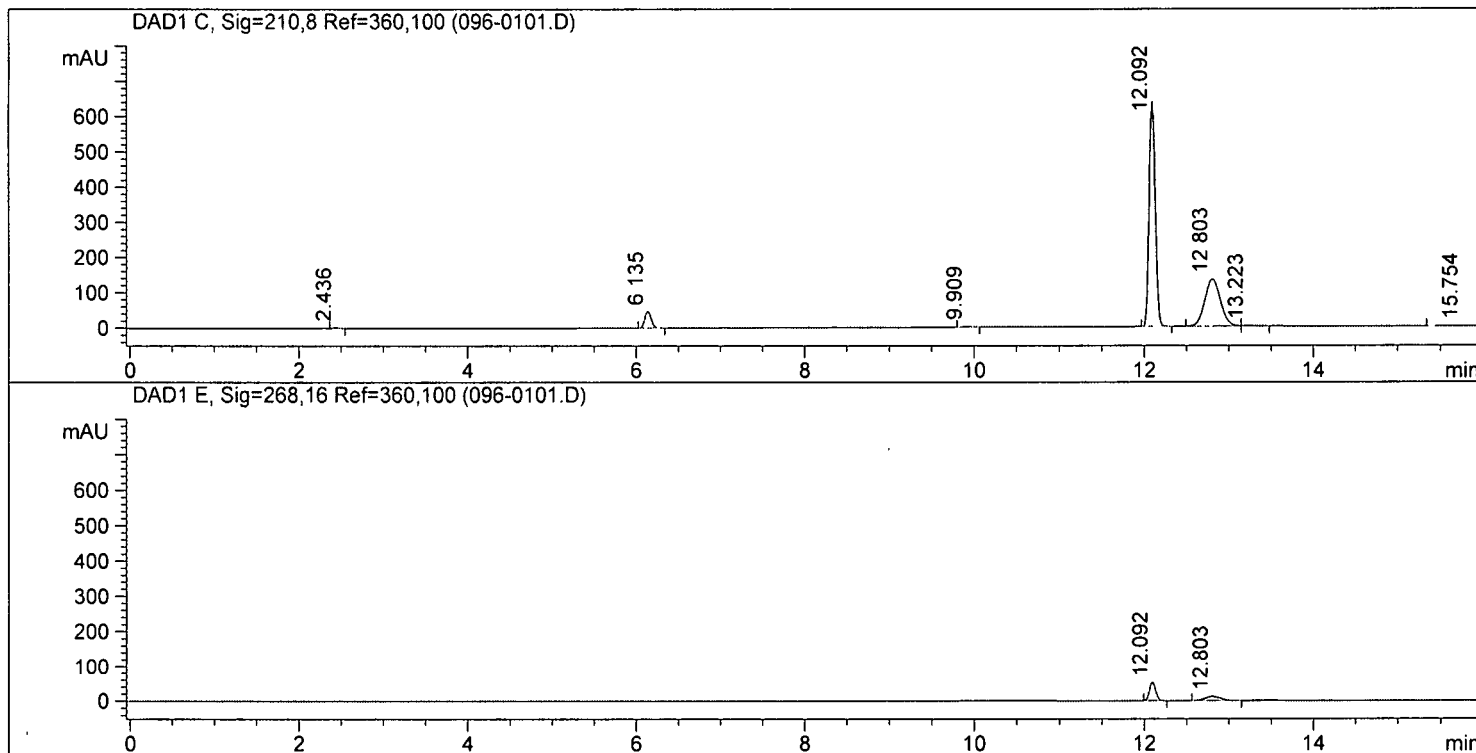
0.3591g/50ml of 79.84g etoac extratcs

->

Injection Date : 02/26/2002 1:31:53 PM Seq Line : 1
 Sample Name : 70316-049 Vial No : 96
 Acq Operator : hansen Inj. No. : 1
 Inj. Vol. : 2 µl

Method : C:\HPCHEM\HPLC0157\METHODS\715.M
 Last Changed : 02/21/2002 7:13:49 AM
 75/25 0.1% HClO4/Acetonitrile, 1ml/min
 10min 25/75 water/acn; 75/25 from 10 to 14 min
 waters c18 symmetry, 250 nm

7.612g
 99% yield?



Customized Report:karlo

Sorted By : Signal
 Calib. Data Modified : 02/20/2002 3:33:04 PM
 Multiplier : 1.000000

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.44	VB	0.061	2.91	11.225	0.21	0.000000	
2	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
3	6.14	BB	0.083	47.24	253.280	4.79	0.000000	
4	9.91	BB	0.089	2.88	16.496	0.31	0.000000	
5	12.09	VB	0.079	635.52	3206.216	60.66	0.684675	benzyloxy amide
6	12.80	BV	0.201	133.77	1729.025	32.71	0.000000	
7	13.22	VB	0.139	1.81	18.425	0.35	0.000000	
8	15.75	BBA	0.340	2.12	50.901	0.96	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.000000	L-224,715
2	12.09	BB	0.079	52.03	260.971	63.47	0.684675	benzyloxy amide
3	12.80	BP	0.198	11.84	150.173	36.53	0.000000	

=====
*** End of Report ***

2.25 h coupling

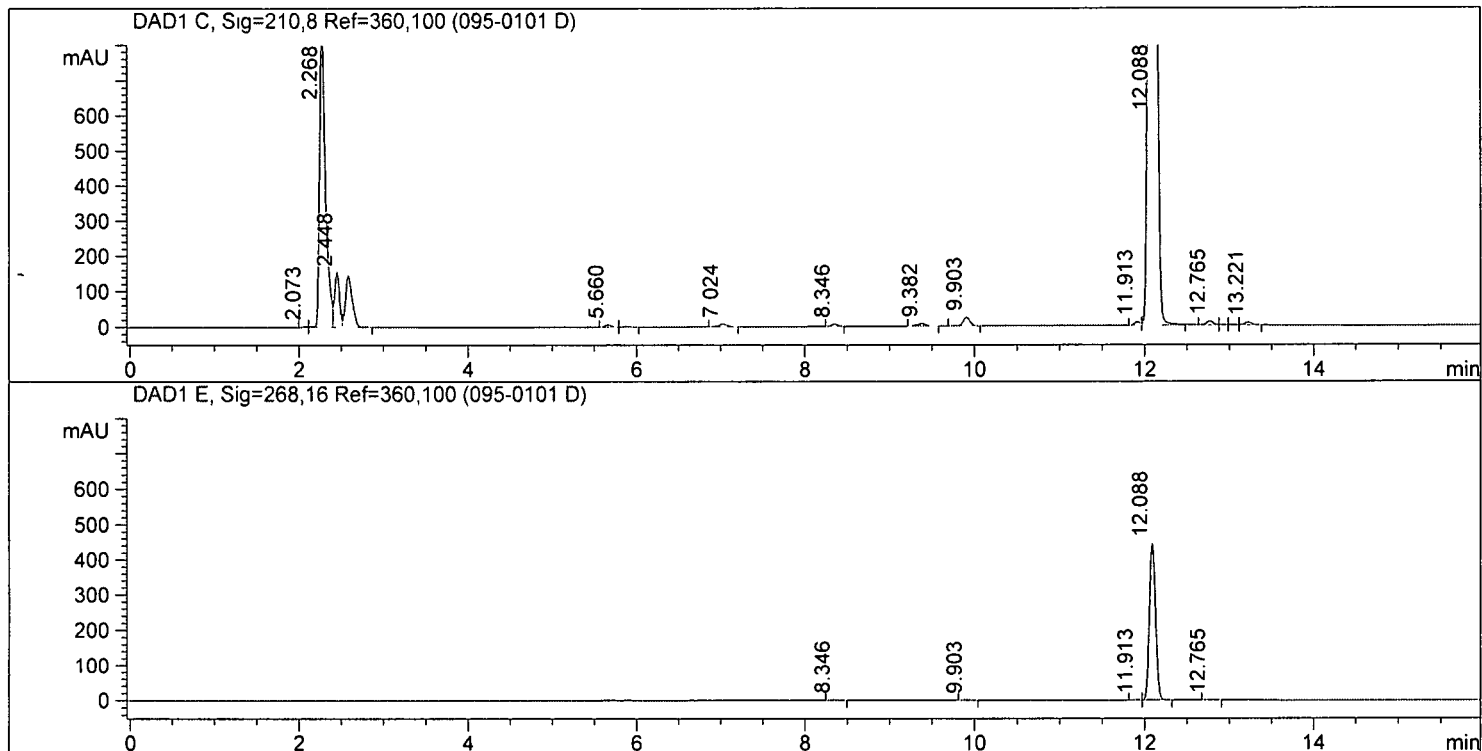
->

```

=====
Injection Date : 02/26/2002 12:59:23 PM      Seq Line : 1
Sample Name    : 70316-049                    Vial No   : 95
Acq Operator   : hansen                       Inj. No.  : 1
                                           Inj. Vol. : 2 µl
    
```

```

Method        : C:\HPCHEM\HPLC0157\METHODS\715.M
Last Changed   : 02/21/2002 7:13:49 AM
75/25 0.1% HClO4/Acetonitrile, 1ml/min
10min 25/75 water/acn; 75/25 from 10 to 14 min
waters c18 symmetry, 250 nm
    
```



Customized Report:karlo

```

Sorted By      : Signal
Calib. Data Modified : 02/20/2002 3:33:04 PM
Multiplier     : 1.000000
    
```

Signal: 1 DAD1 C, Sig=210,8 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	2.07	BV	0.058	3.17	12.046	0.06	0.000000	
2	2.27	VV	0.071	838.67	4062.625	18.62	0.000000	
3	2.45	VV	0.062	155.00	611.290	2.80	0.000000	
4	2.58	VB	0.083	144.77	800.680	3.67	0.000000	
5	5.66	BV	0.083	6.38	33.342	0.15	0.005639	L-224,715
6	5.88	VB	0.078	2.20	11.023	0.05	0.000000	
7	7.02	BB	0.094	8.17	54.257	0.25	0.000000	
8	8.35	BV	0.084	6.51	34.570	0.16	0.000000	
9	9.38	BB	0.103	6.89	50.258	0.23	0.000000	
10	9.90	BP	0.084	24.01	132.439	0.61	0.000000	
11	11.91	BV	0.074	9.53	44.426	0.20	0.000000	
12	12.09	VB	0.112	2.31e3	1.583e4	72.54	3.401939	benzyloxy amide
13	12.77	BV	0.093	11.81	73.679	0.34	0.000000	
14	12.93	VV	0.086	1.66	9.963	0.05	0.000000	
15	13.04	VV	0.092	1.75	11.096	0.05	0.000000	

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
16	13.22	VB	0.091	8.31	50.288	0.23	0.000000	

Signal: 2 DAD1 E, Sig=268,16 Ref=360,100

Peak #	RT [min]	Type	Width [min]	Height	Area [mAU*s]	Area %	Amount mg/ml	Name
1	0.00		0.000	0.00	0.000	0.00	0.005639	L-224,715
2	8.35	BB	0.084	1.61	8.501	0.37	0.000000	
3	9.90	BP	0.083	1.09	5.874	0.26	0.000000	
4	11.91	PV	0.074	1.19	5.498	0.24	0.000000	
5	12.09	VB	0.079	446.26	2252.005	98.89	3.401939	benzyloxy amide
6	12.77	BP	0.076	1.12	5.385	0.24	0.000000	

=====
*** End of Report ***