Supplementary Data

Synthesis of structurally diverse benzosuberene analogues and their biological evaluation as anti-cancer agents

Rajendra P. Tanpure[a], Clinton S. George[a], Tracy E. Strecker[a], Laxman Devkota[a], Justin K. Tidmore[a], Chen-Ming Lin[a], Christine Herdman[a], Matthew T. MacDonough[a], Madhavi Sriram[a], David J. Chaplin[b], Mary Lynn Trawick[a], and Kevin G. Pinney[a]*

[a]Department of Chemistry and Biochemistry, Baylor University, One Bear Place #97348, Waco, Texas 76798-7348, United States

[b]OXiGENE Inc., 701 Gateway Boulevard, Suite 210, South San Francisco, California 94080, United States

*Corresponding author: Kevin G. Pinney

Tel.: +1 254 710 4117

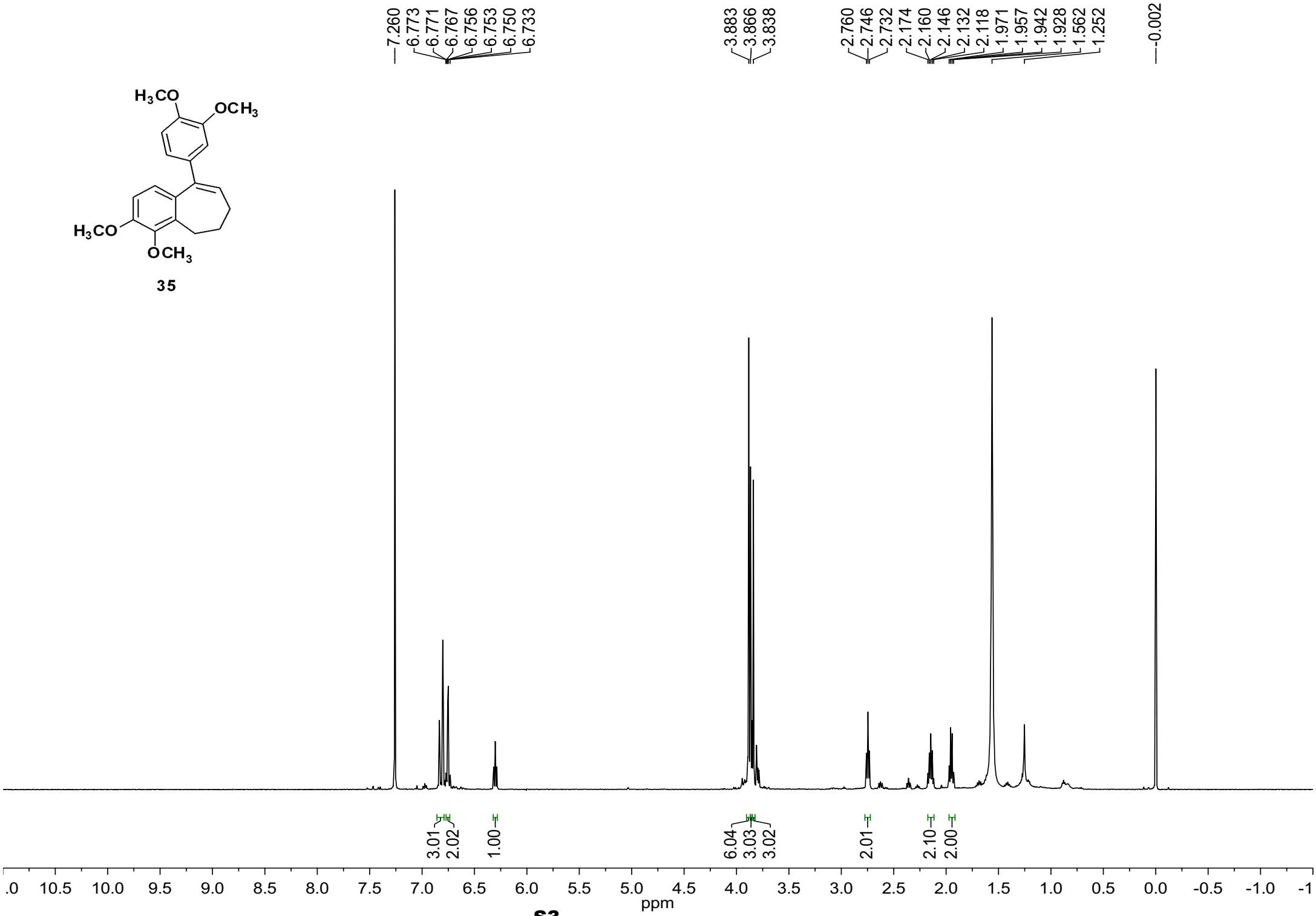
fax: +1 254 710 4272.

E-mail address: Kevin_Pinney@baylor.edu

Table of Contents

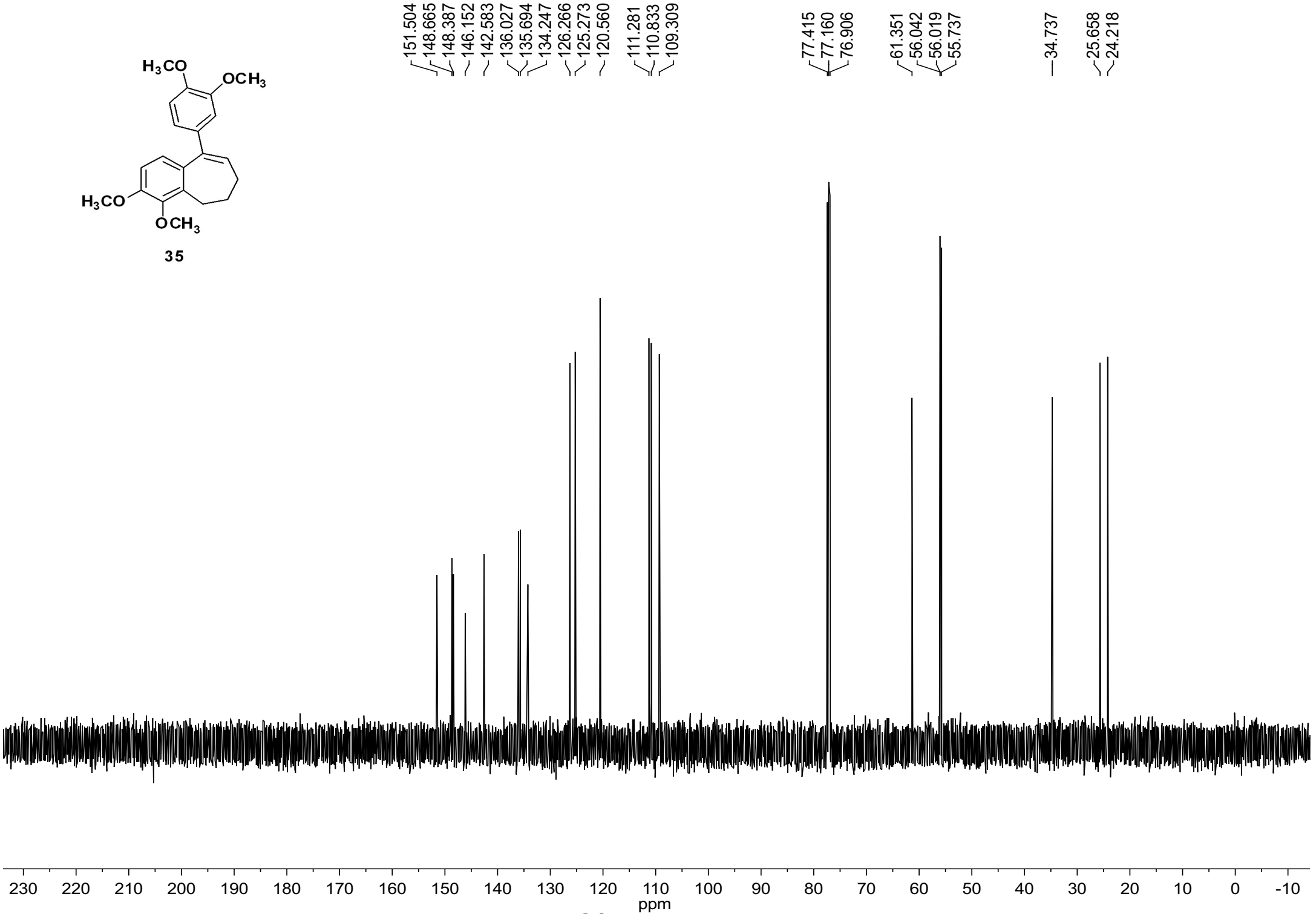
H3CO
OCH3
H3CO
OCH3

35


7.260
6.773
6.771
6.767
6.756
6.753
6.750
6.733
3.883
3.866
3.838
2.760
2.746
2.732
2.174
2.160
2.146
2.132
2.118
1.971
1.957
1.942
1.928
1.562
1.252
-0.002
3.01
2.02
1.00
6.04
3.03
3.02
2.01
2.10
2.00
ppm

H3CO
OCH3
H3CO
OCH3

35

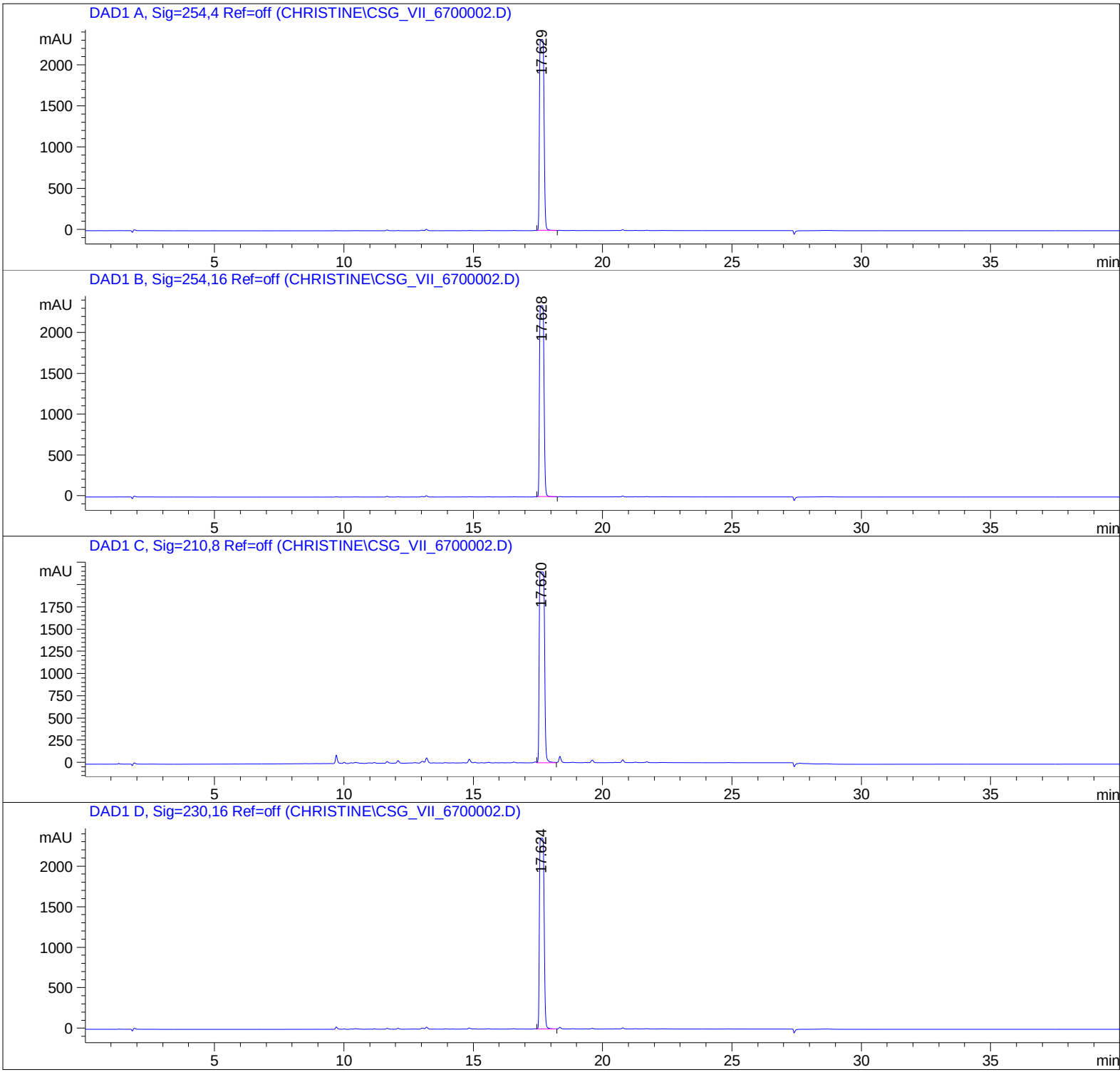

151.504
148.665
148.387
146.152
142.583
136.027
135.694
134.247
126.266
125.273
120.560
111.281
110.833
109.309
77.415
77.160
76.906
61.351
56.042
56.019
55.737
34.737
25.658
24.218
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

Data File C:\CHEM32\1\DATA\CHRISTINE\CSG_VII_6700002.D
Sample Name: run1

HPLC Traces of Compound 35

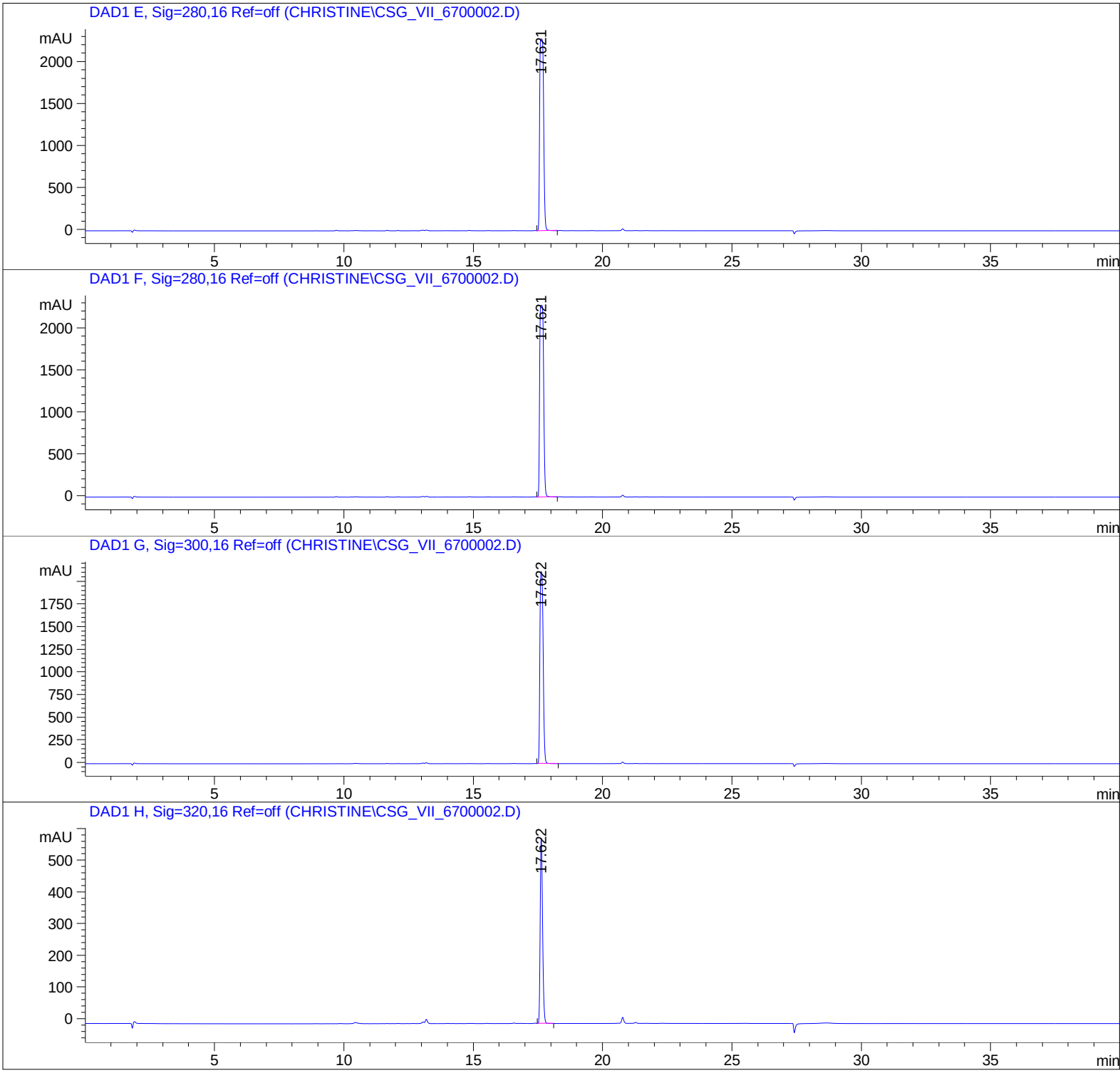
==========

Acq. Operator : Christine
Acq. Instrument : Instrument 1 Location : -
Injection Date : 3/20/2013 3:51:01 PM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 3/20/2013 3:31:29 PM by Christine
Analysis Method : C:\CHEM32\1\DATA\CHRISTINE\CSG_VII_6700002.D\DA.M (MASTERMETHOD.M)
Last changed : 3/20/2013 5:03:40 PM by Christine



Data File C:\CHEM32\1\DATA\CHRISTINE\CSG_VII_6700002.D
Sample Name: run1

HPLC Traces of Compound 35



==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

S6

Data File C:\CHEM32\1\DATA\CHRISTINE\CSG_VII_6700002.D
Sample Name: run1

HPLC Traces of Compound 35

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.629	VV	0.1688	2.76452e4	2323.77466	100.0000
Totals :				2.76452e4	2323.77466	

Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.628	VV	0.1908	2.75209e4	2346.52759	100.0000
Totals :				2.75209e4	2346.52759	

Signal 3: DAD1 C, Sig=210,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.620	VV	0.1899	2.94289e4	2146.80054	100.0000
Totals :				2.94289e4	2146.80054	

Signal 4: DAD1 D, Sig=230,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.624	VV	0.1993	2.85074e4	2354.49072	100.0000
Totals :				2.85074e4	2354.49072	

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.621	VV	0.1705	2.39891e4	2285.56982	100.0000
Totals :				2.39891e4	2285.56982	

HPLC Traces of Compound 35

Signal 6: DAD1 F, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.621	VV	0.1705	2.39891e4	2285.56982	100.0000
Totals :				2.39891e4	2285.56982	

Signal 7: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.622	VB	0.1412	1.84173e4	2122.89526	100.0000
Totals :				1.84173e4	2122.89526	

Signal 8: DAD1 H, Sig=320,16 Ref=off

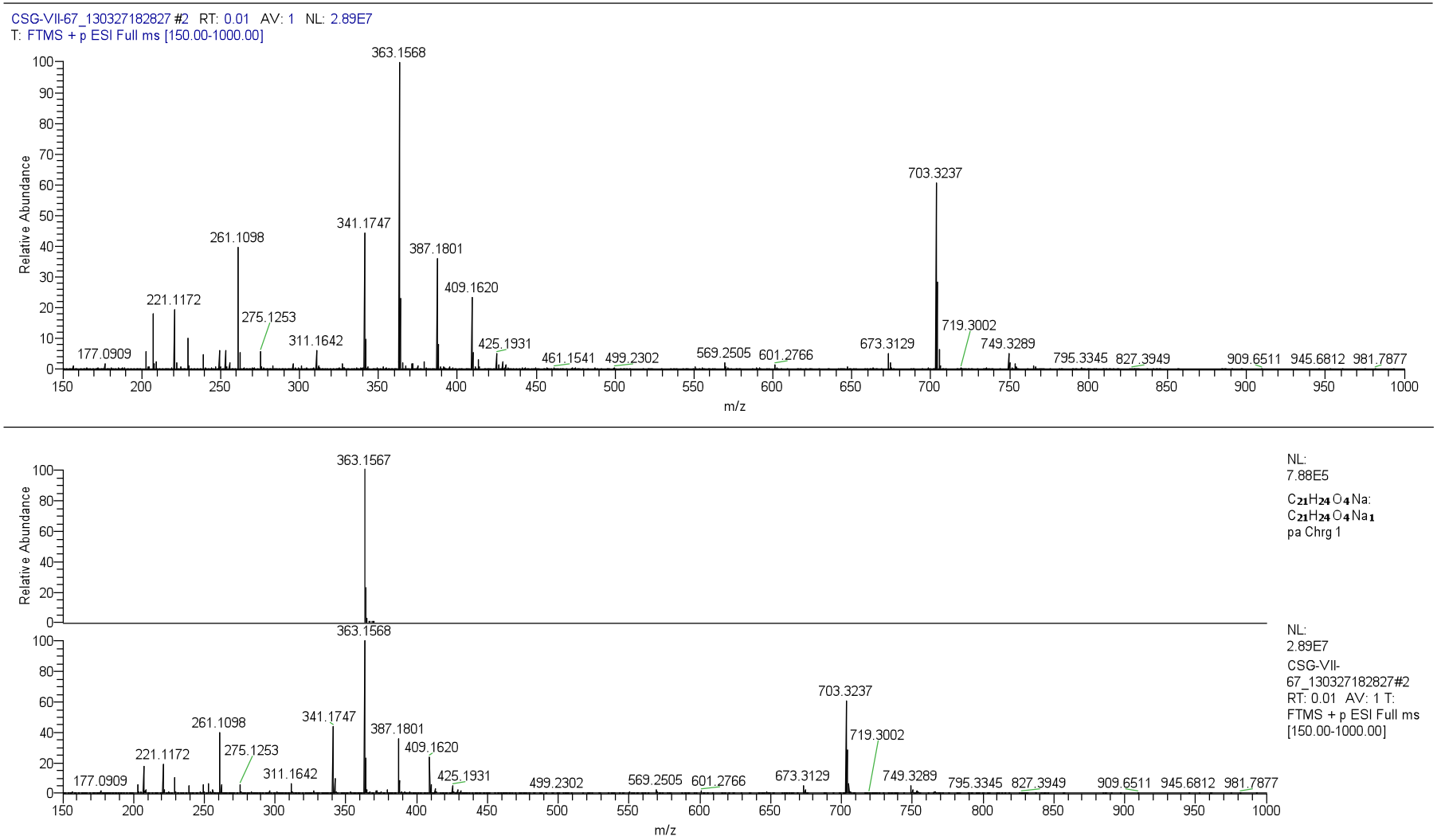
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.622	VB	0.0987	3754.10571	586.34613	100.0000
Totals :				3754.10571	586.34613	

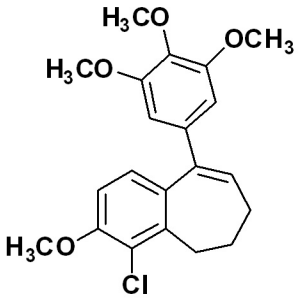
==========

*** End of Report ***

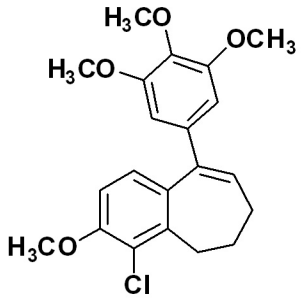
HRMS of Compound 35

C:\Xcalibur\...\CSG-VII-67_130327182827 3/27/2013 6:37:10 PM CSG-VII-67





36



36

154.02
153.06
142.68
141.18
138.04
137.55
134.24
128.28
127.80
121.49
109.13
105.22
77.41
77.16
76.91
61.07
56.31
56.28
33.82
28.73
25.55

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

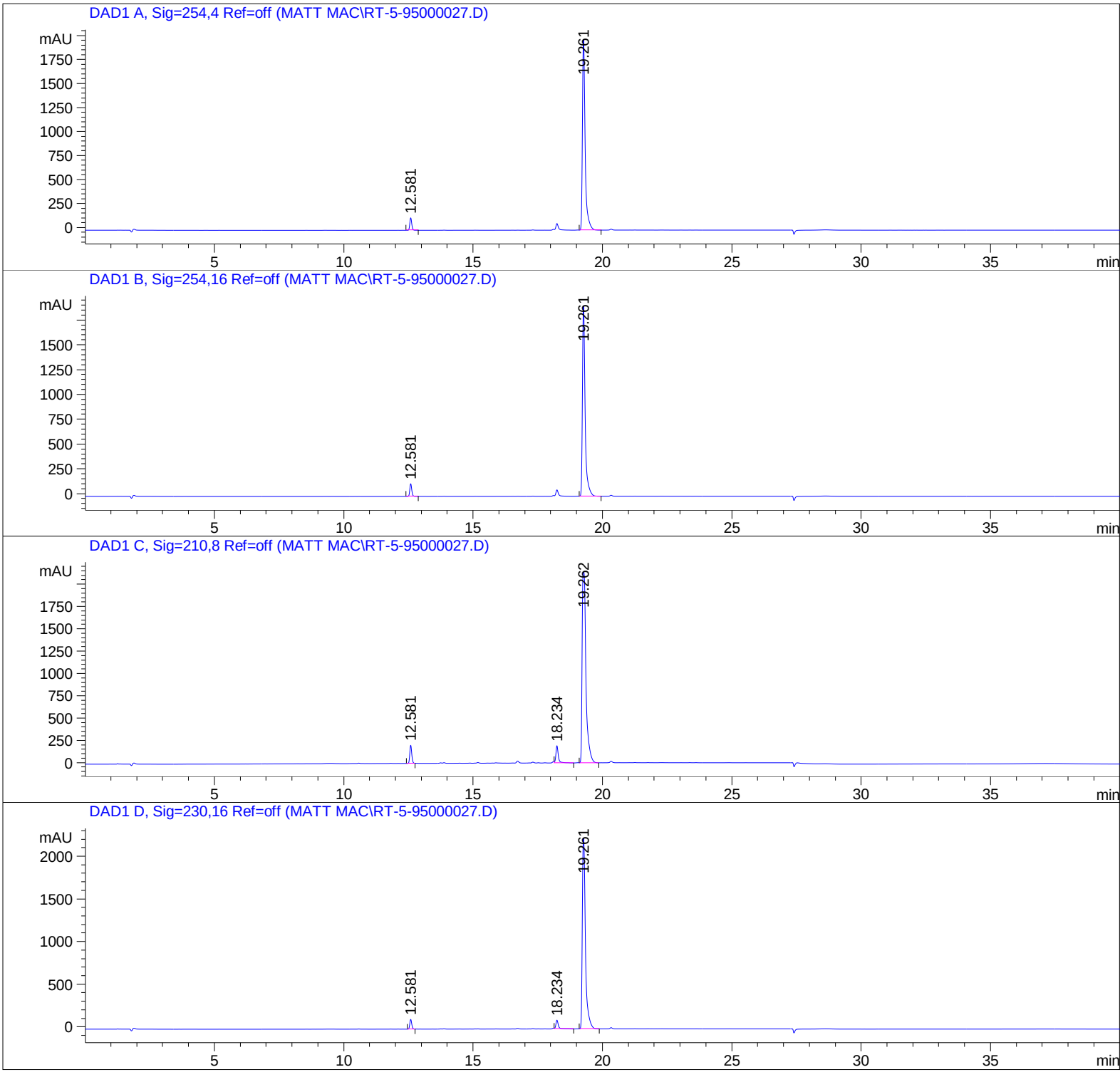
ppm

Data File C:\CHEM32\1\DATA\MATT MAC\RT-5-95000027.D
Sample Name: run1

HPLC Traces of Compound 36

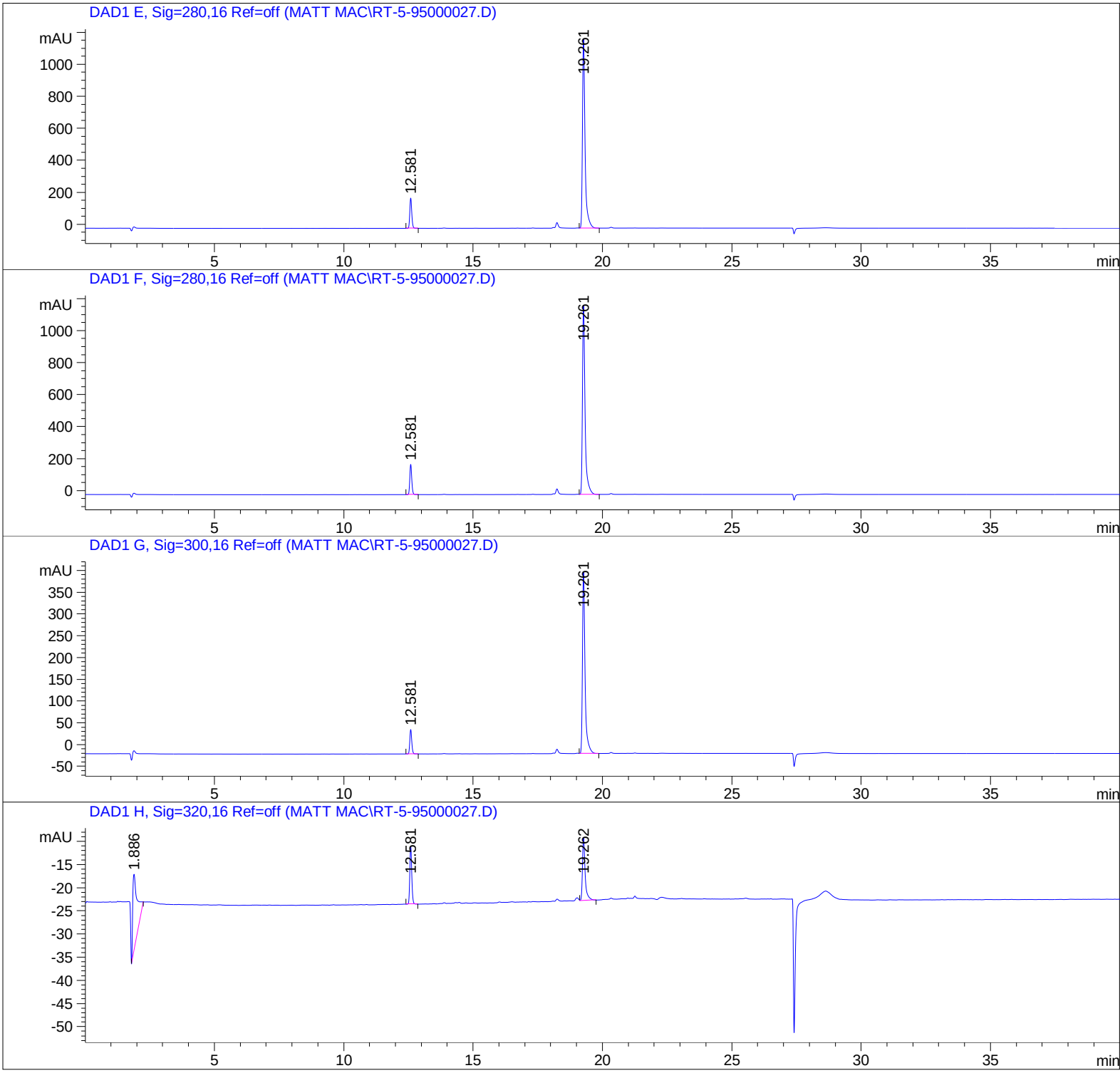
==========

Acq. Operator : Matt Mac
Acq. Instrument : Instrument 1 Location : -
Injection Date : 3/18/2013 11:39:53 AM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 3/18/2013 11:33:23 AM by Matt Mac
Analysis Method : C:\CHEM32\1\DATA\MATT MAC\RT-5-95000027.D\DA.M (MASTERMETHOD.M)
Last changed : 3/25/2013 7:45:37 PM by Christine



Data File C:\CHEM32\1\DATA\MATT MAC\RT-5-95000027.D
Sample Name: run1

HPLC Traces of Compound 36



==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

S13

HPLC Traces of Compound 36

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.581	BB	0.0815	681.45850	129.36571	4.4386
2	19.261	VB	0.1121	1.46717e4	1989.12549	95.5614
Totals :				1.53531e4	2118.49120	

Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.581	BB	0.0815	671.32812	127.42695	4.5695
2	19.261	VB	0.1090	1.40203e4	1924.28955	95.4305
Totals :				1.46917e4	2051.71650	

Signal 3: DAD1 C, Sig=210,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.581	BV	0.0815	1069.45410	202.71822	4.3974
2	18.234	VB	0.0988	1267.77356	192.65639	5.2128
3	19.262	VV	0.1598	2.19831e4	2140.38672	90.3898
Totals :				2.43203e4	2535.76132	

Signal 4: DAD1 D, Sig=230,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.581	BB	0.0811	596.29034	113.85712	2.9539
2	18.234	VB	0.1015	707.17499	103.75703	3.5032
3	19.261	VB	0.1304	1.88831e4	2238.41504	93.5429
Totals :				2.01866e4	2456.02918	

HPLC Traces of Compound 36

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.581	BB	0.0813	991.66333	188.65477	10.6786
2	19.261	VB	0.1037	8294.79199	1184.30872	89.3214
Totals :				9286.45532	1372.96349	

Signal 6: DAD1 F, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.581	BB	0.0813	991.66333	188.65477	10.6786
2	19.261	VB	0.1037	8294.79199	1184.30872	89.3214
Totals :				9286.45532	1372.96349	

Signal 7: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.581	BB	0.0814	294.68988	55.99483	9.1683
2	19.261	VB	0.1033	2919.53296	419.03241	90.8317
Totals :				3214.22284	475.02724	

Signal 8: DAD1 H, Sig=320,16 Ref=off

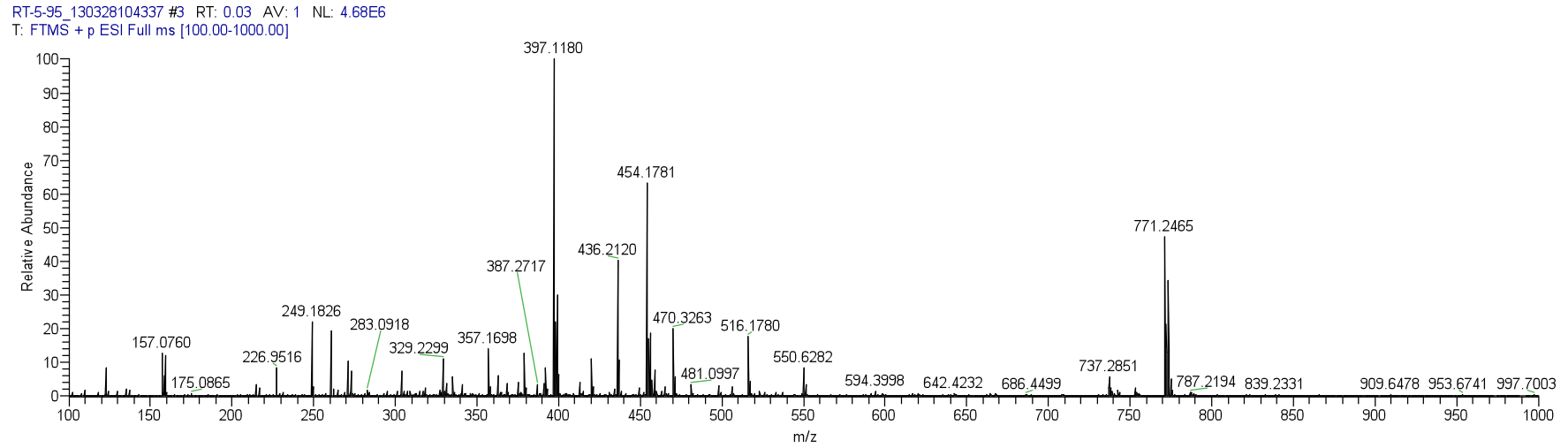
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.886	BB	0.1714	198.32713	16.60401	54.6452
2	12.581	BB	0.0816	65.78312	12.45629	18.1253
3	19.262	VB	0.1069	98.82568	13.57811	27.2295
Totals :				362.93594	42.63841	

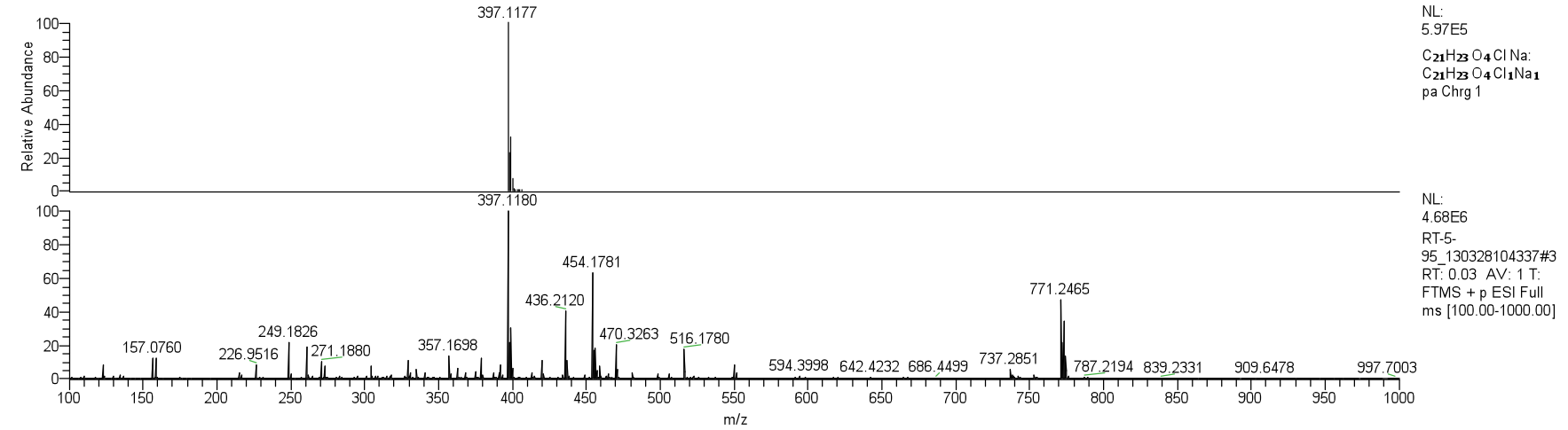
==========

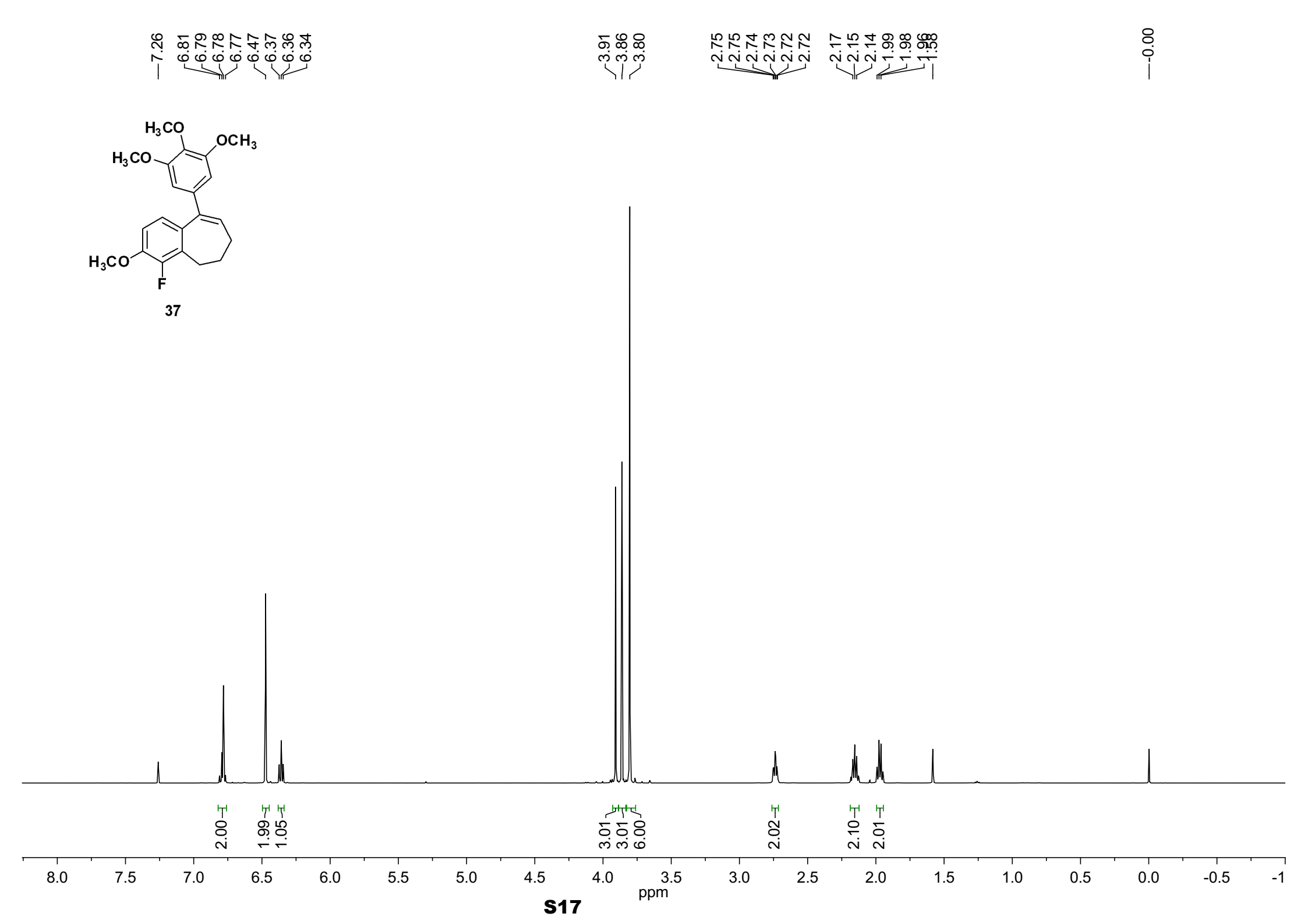
*** End of Report ***

HRMS of Compound 36

C:\Xcalibur\...\RT-5-95_130328104337 3/28/2013 10:43:38 AM RT-5-95

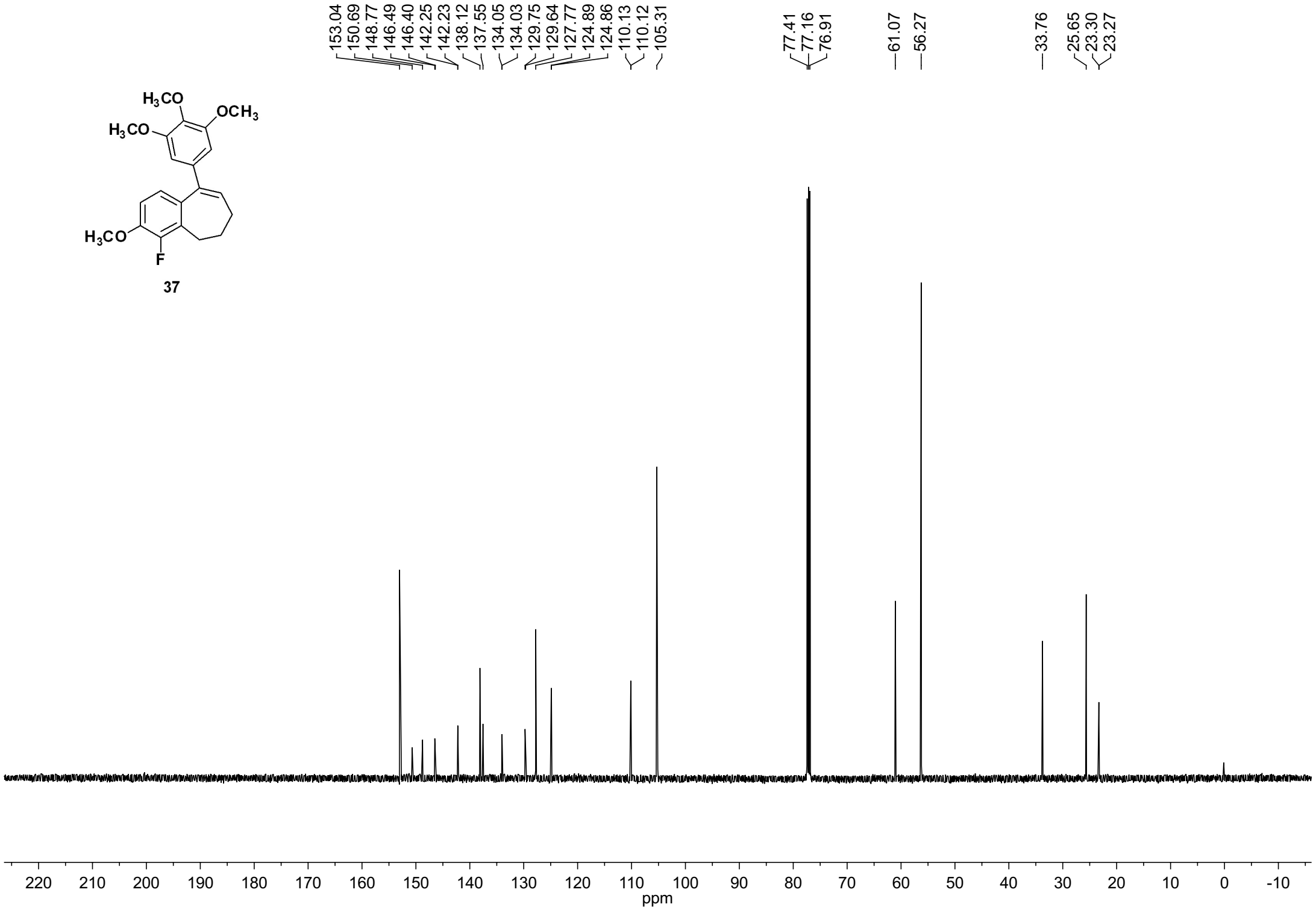





7.26
6.81
6.79
6.78
6.77
6.47
6.37
6.36
6.34
3.91
3.86
3.80
2.75
2.75
2.74
2.73
2.72
2.72
2.17
2.15
2.14
1.99
1.98
1.96
1.58
-0.00
H3CO
OCH3
H3CO
H3CO
F
37
2.00
1.99
1.05
3.01
3.01
6.00
2.02
2.10
2.01
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
ppm

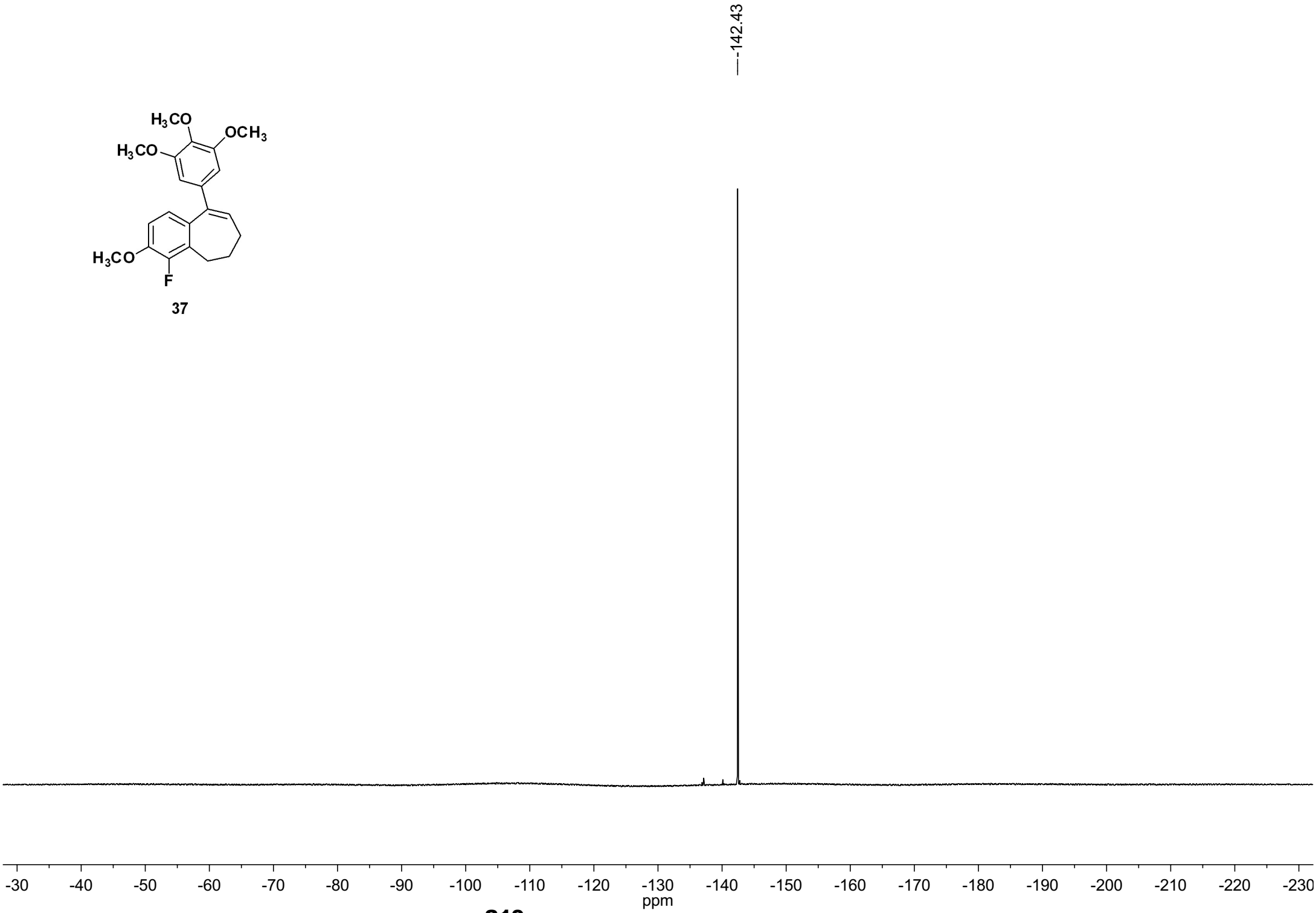
H3CO
OCH3
H3CO
H3CO
F

37


153.04
150.69
148.77
146.49
146.40
142.25
142.23
138.12
137.55
134.05
134.03
129.75
129.64
127.77
124.89
124.86
110.13
110.12
105.31
77.41
77.16
76.91
61.07
56.27
33.76
25.65
23.30
23.27
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

H3CO
OCH3
H3CO
H3CO
F

37

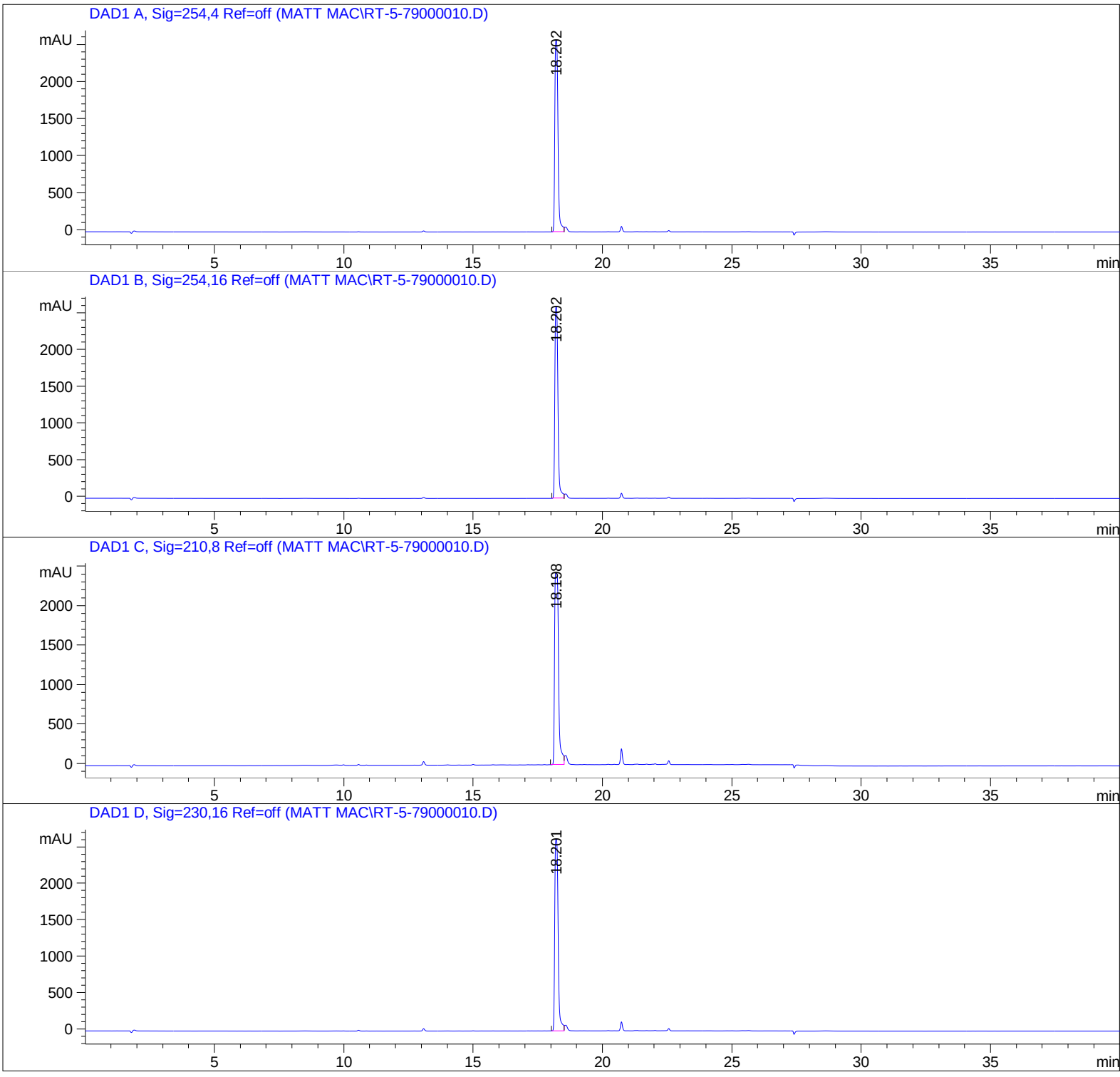

-142.43
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
ppm

Data File C:\CHEM32\1\DATA\MATT MAC\RT-5-79000010.D
Sample Name: run1

HPLC Traces of Compound 37

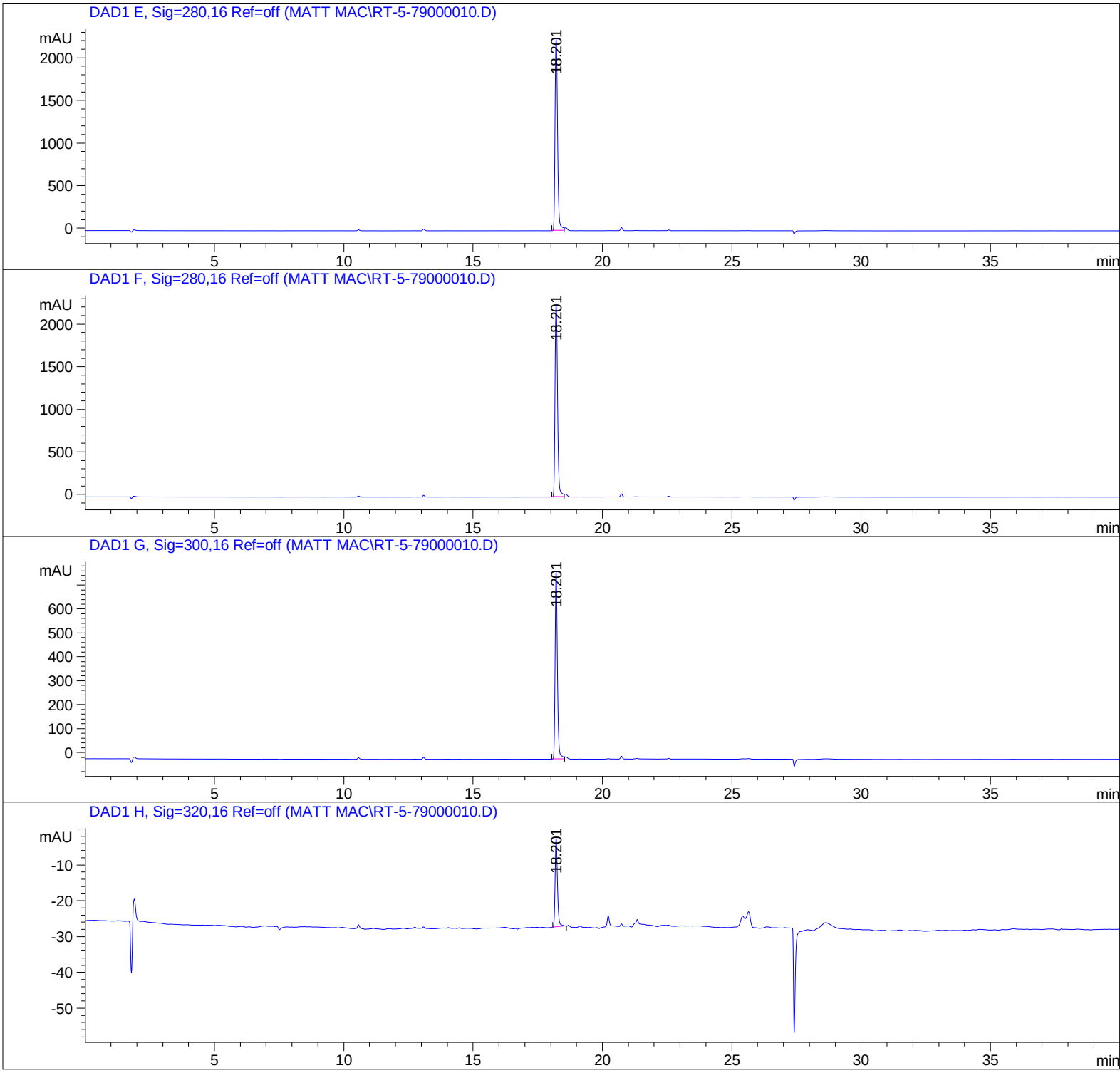
==========

Acq. Operator : Matt Mac
Acq. Instrument : Instrument 1 Location : -
Injection Date : 3/12/2013 2:19:35 PM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 3/12/2013 1:52:29 PM by Matt Mac
Analysis Method : C:\CHEM32\1\DATA\MATT MAC\RT-5-79000010.D\DA.M (MASTERMETHOD.M)
Last changed : 3/12/2013 3:11:18 PM by Matt Mac



Data File C:\CHEM32\1\DATA\MATT MAC\RT-5-79000010.D
Sample Name: run1

HPLC Traces of Compound 37



==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

S21

Data File C:\CHEM32\1\DATA\MATT MAC\RT-5-79000010.D
Sample Name: run1

HPLC Traces of Compound 37

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.202	BV	0.1363	2.22192e4	2585.70190	100.0000
Totals :				2.22192e4	2585.70190	

Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.202	BV	0.1335	2.18342e4	2612.74072	100.0000
Totals :				2.18342e4	2612.74072	

Signal 3: DAD1 C, Sig=210,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.198	VV	0.1708	2.60022e4	2429.85010	100.0000
Totals :				2.60022e4	2429.85010	

Signal 4: DAD1 D, Sig=230,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.201	VV	0.1463	2.39506e4	2628.60571	100.0000
Totals :				2.39506e4	2628.60571	

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.201	BV	0.1087	1.55833e4	2253.99902	100.0000
Totals :				1.55833e4	2253.99902	

HPLC Traces of Compound 37

Signal 6: DAD1 F, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.201	BV	0.1087	1.55833e4	2253.99902	100.0000
Totals :				1.55833e4	2253.99902	

Signal 7: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.201	BV	0.0966	4897.43213	786.51733	100.0000
Totals :				4897.43213	786.51733	

Signal 8: DAD1 H, Sig=320,16 Ref=off

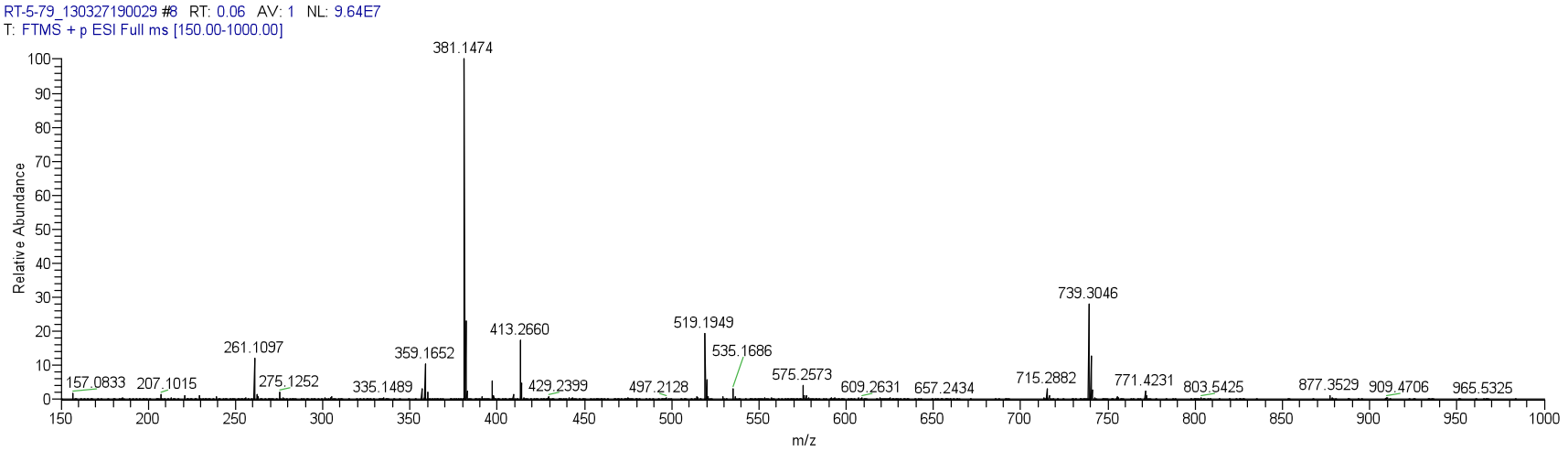
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.201	BB	0.0987	159.84872	24.96538	100.0000
Totals :				159.84872	24.96538	

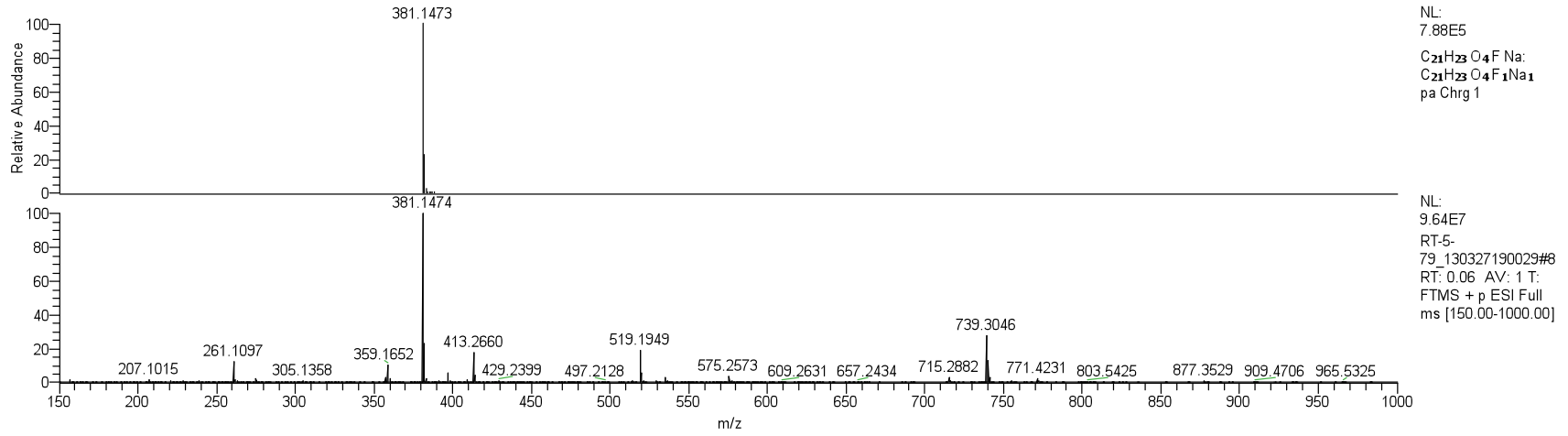
==========

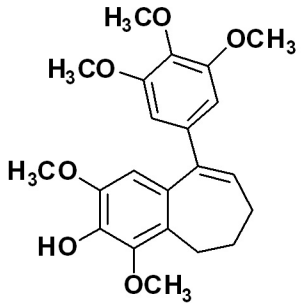
*** End of Report ***

HRMS of Compound 37

C:\Xcalibur\...\RT-5-79_130327190029 3/27/2013 7:00:29 PM RT-5-79



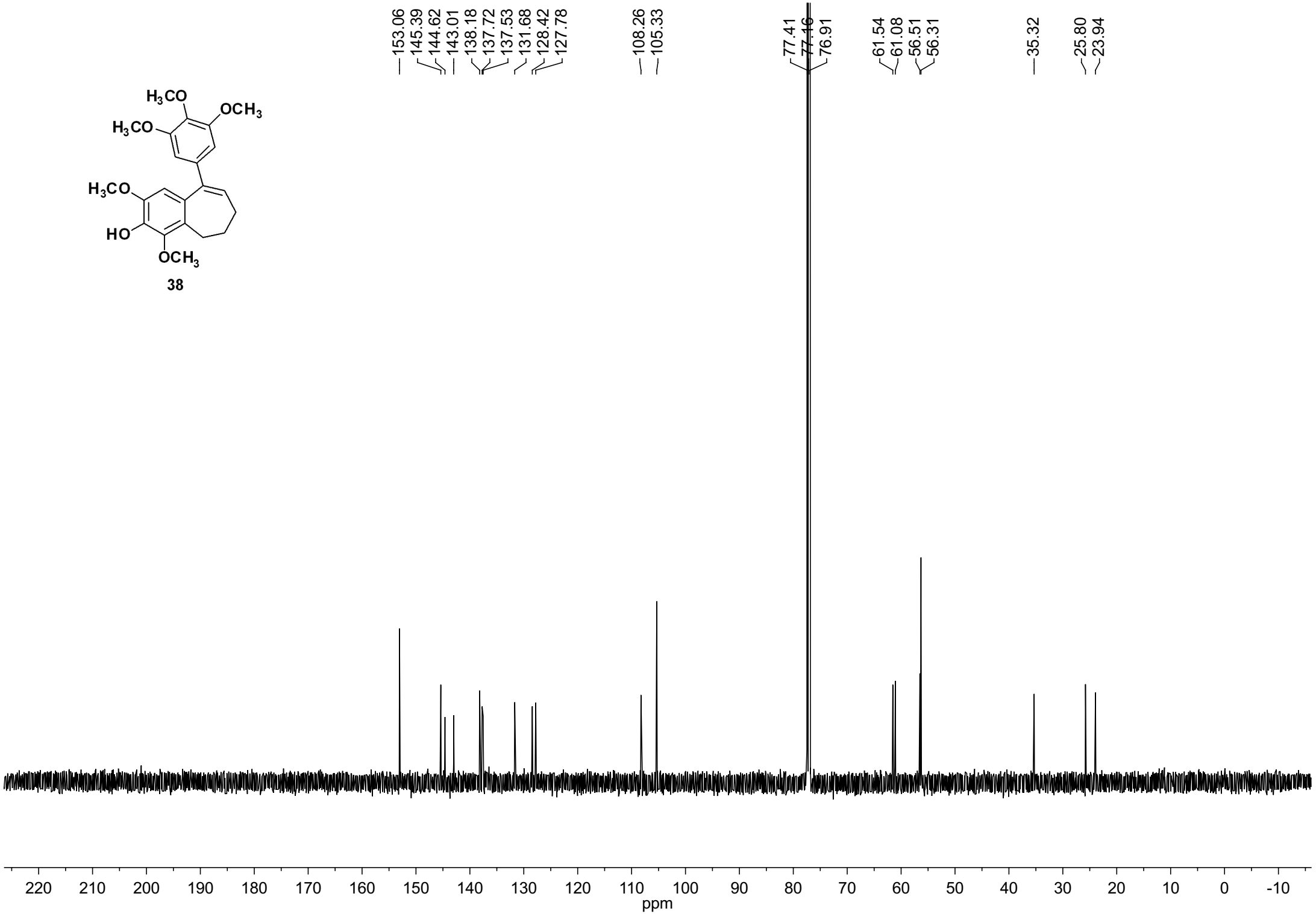




38

H3CO
OCH3
H3CO
H3CO
HO
OCH3

38

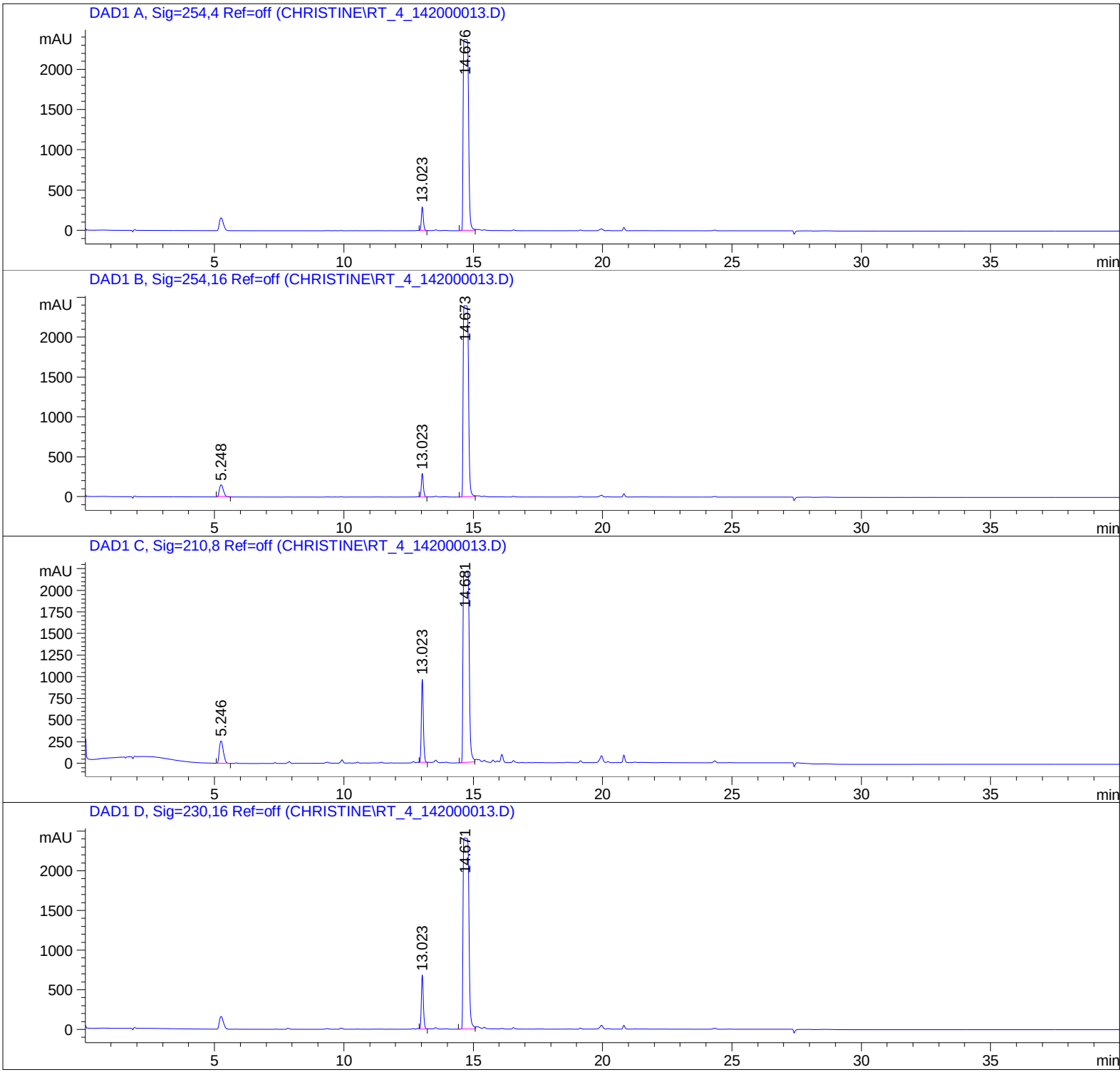

153.06
145.39
144.62
143.01
138.18
137.72
137.53
131.68
128.42
127.78
108.26
105.33
77.41
77.16
76.91
61.54
61.08
56.51
56.31
35.32
25.80
23.94
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

Data File C:\CHEM32\1\DATA\CHRISTINE\RT_4_142000013.D
Sample Name: run1

HPLC Traces of Compound 38

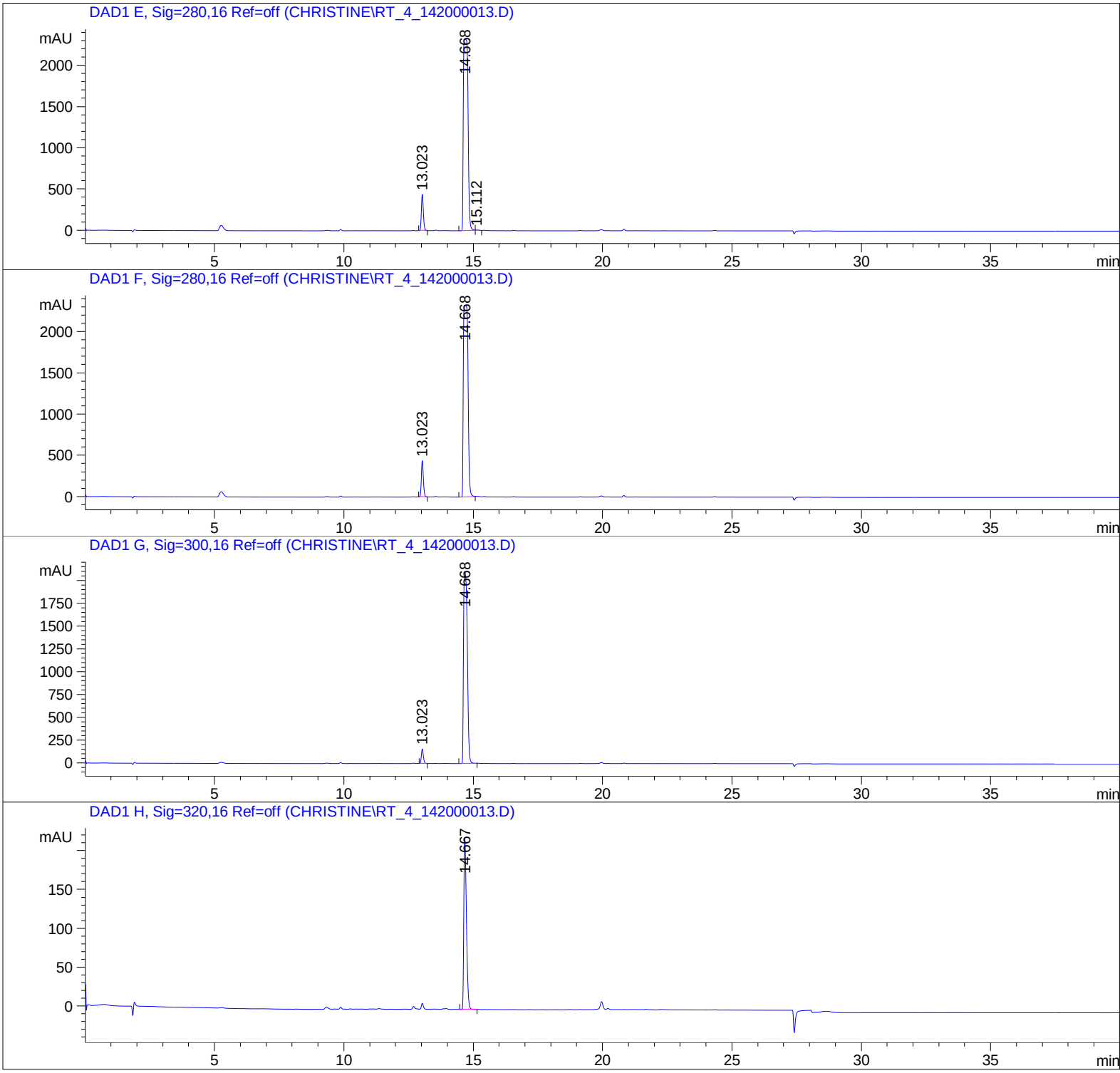
==========

Acq. Operator : Christine
Acq. Instrument : Instrument 1 Location : -
Injection Date : 3/26/2013 11:12:23 AM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 3/26/2013 11:10:20 AM by Christine
Analysis Method : C:\CHEM32\1\DATA\CHRISTINE\RT_4_142000013.D\DA.M (MASTERMETHOD.M)
Last changed : 3/28/2013 10:58:21 AM by Christine



Data File C:\CHEM32\1\DATA\CHRISTINE\RT_4_142000013.D
Sample Name: run1

HPLC Traces of Compound 38



==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Data File C:\CHEM32\1\DATA\CHRISTINE\RT_4_142000013.D
Sample Name: run1

HPLC Traces of Compound 38

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.023	VV	0.0826	1588.48059	295.92328	4.6146
2	14.676	BV	0.1873	3.28346e4	2374.24194	95.3854
Totals :				3.44231e4	2670.16522	

Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.248	BB	0.1724	1645.22827	151.87173	4.5733
2	13.023	VV	0.0826	1585.70972	295.34805	4.4079
3	14.673	BV	0.1853	3.27437e4	2397.76465	91.0189
Totals :				3.59747e4	2844.98444	

Signal 3: DAD1 C, Sig=210,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.246	BB	0.1716	2778.12891	257.99753	6.5013
2	13.023	VV	0.0830	5218.32080	965.62964	12.2118
3	14.681	BV	0.2001	3.47355e4	2201.03906	81.2870
Totals :				4.27320e4	3424.66623	

Signal 4: DAD1 D, Sig=230,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.023	VV	0.0832	3700.61694	683.55157	9.3330
2	14.671	BV	0.2042	3.59502e4	2407.02783	90.6670
Totals :				3.96508e4	3090.57941	

HPLC Traces of Compound 38

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.023	VV	0.0826	2372.75391	441.98782	7.5918
2	14.668	BV	0.2024	2.87855e4	2326.19653	92.1016
3	15.112	VV	0.1450	95.81713	8.66321	0.3066
Totals :				3.12541e4	2776.84757	

Signal 6: DAD1 F, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.023	VV	0.0826	2372.75391	441.98782	7.6152
2	14.668	BV	0.2024	2.87855e4	2326.19653	92.3848
Totals :				3.11583e4	2768.18436	

Signal 7: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.023	VB	0.0826	854.14435	159.29744	3.8653
2	14.668	BV	0.1678	2.12436e4	2104.45508	96.1347
Totals :				2.20978e4	2263.75252	

Signal 8: DAD1 H, Sig=320,16 Ref=off

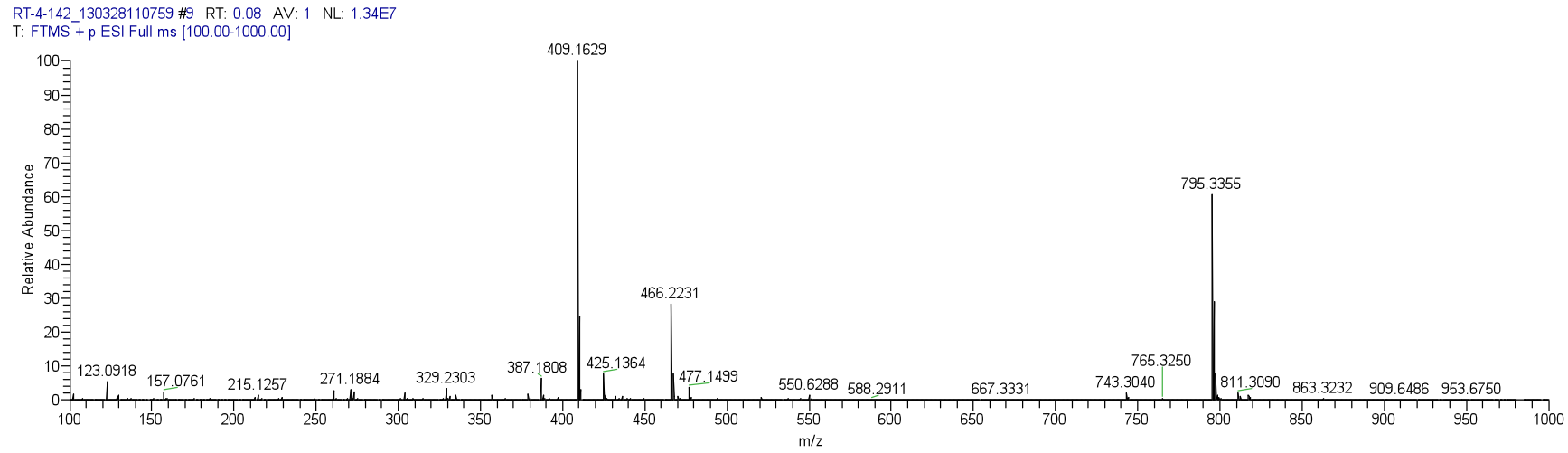
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.667	BB	0.1103	1556.79431	220.70790	100.0000
Totals :				1556.79431	220.70790	

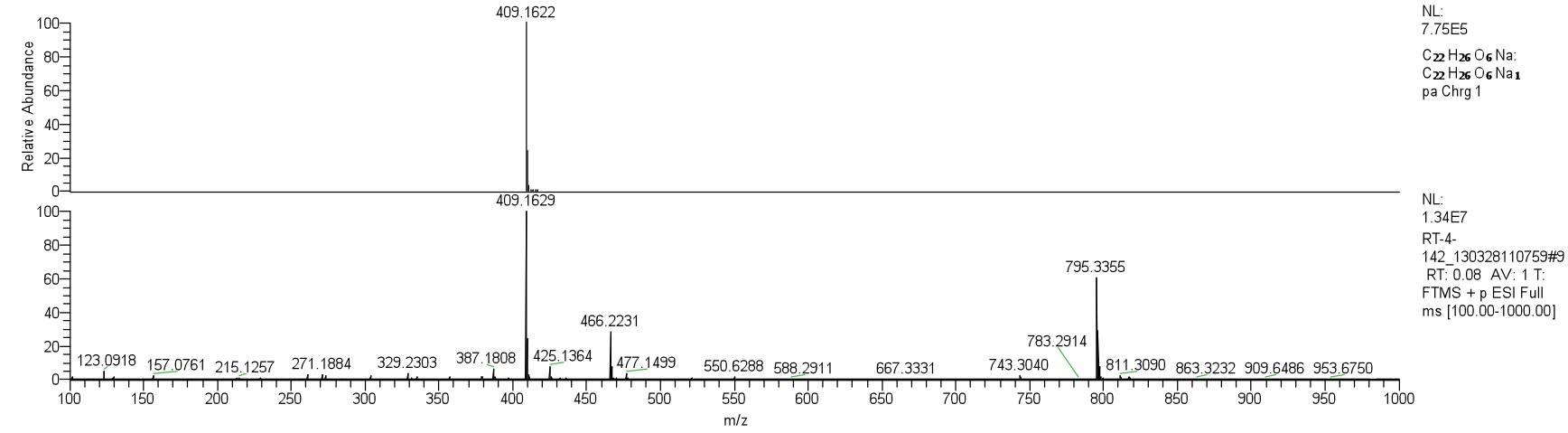
==========

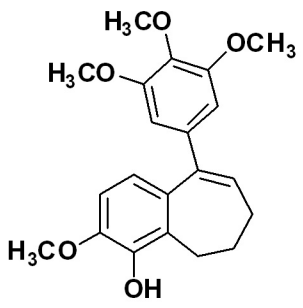
*** End of Report ***

HRMS of Compound 38

C:\Xcalibur\...\RT-4-142_130328110759 3/28/2013 11:08:00 AM RT-4-142



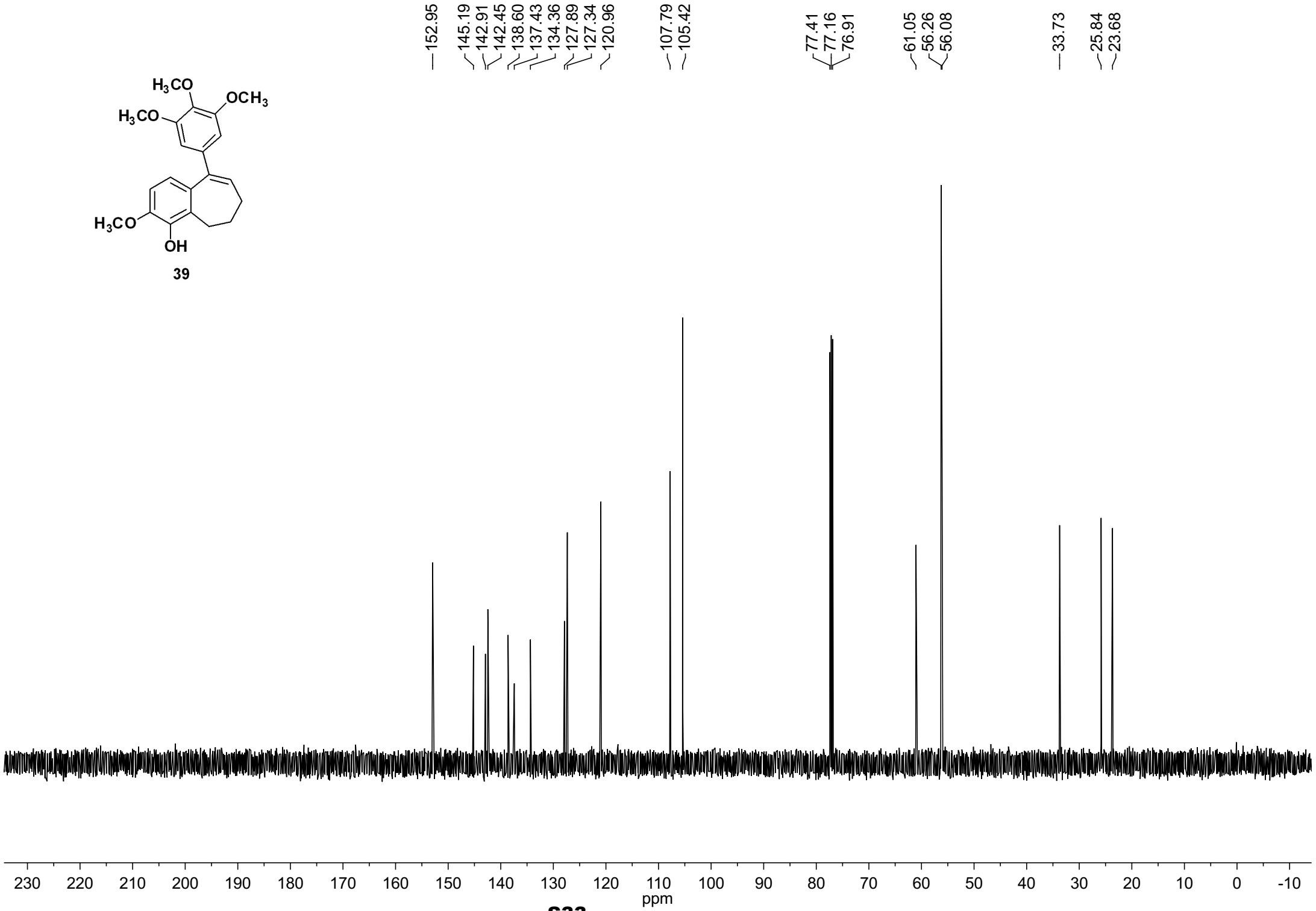




39

H3CO
OCH3
H3CO
H3CO
OH

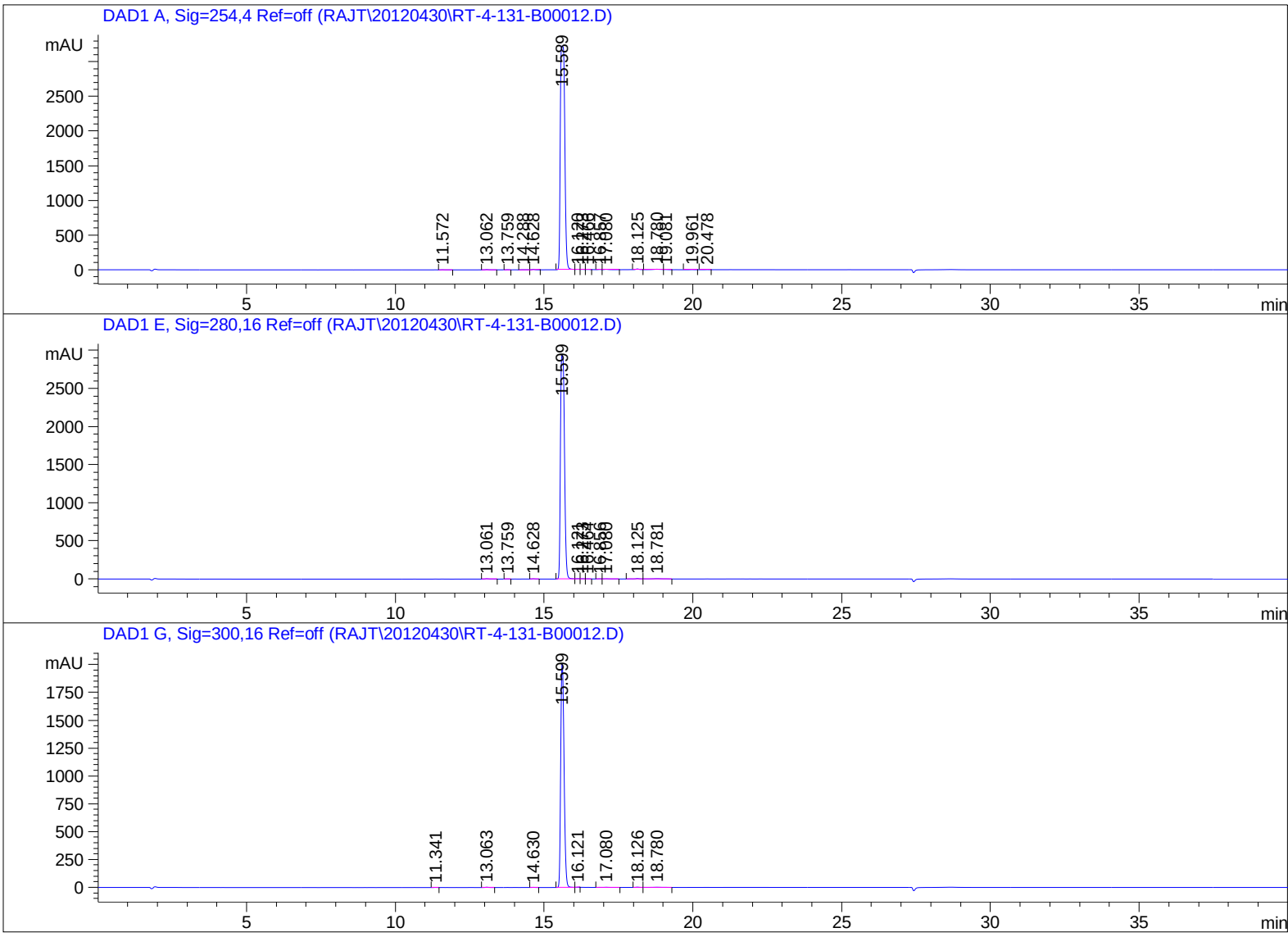
39


152.95
145.19
142.91
142.45
138.60
137.43
134.36
127.89
127.34
120.96
107.79
105.42
77.41
77.16
76.91
61.05
56.26
56.08
33.73
25.84
23.68
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

Data File C:\CHEM32\1\DATA\RAJT\20120430\RT-4-131-B00012.D
Sample Name: RT-4-131-B

HPLC Traces of Compound 39

```
==========================================================================
Acq. Operator   : RajT.
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 5/1/2012 3:16:53 AM
Method          : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed    : 3/28/2012 11:50:33 AM by Erica P
Sample Info     : RT-4-131-B
                  10 uL
```




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs
```

HPLC Traces of Compound 39

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.572	VB	0.1054	8.86056	1.23943	0.0261
2	13.062	BB	0.1102	27.20675	3.68311	0.0803
3	13.759	BB	0.0874	10.59208	1.89063	0.0313
4	14.288	BV	0.2203	18.97442	1.17531	0.0560
5	14.628	VB	0.1016	38.37364	5.62389	0.1132
6	15.589	BV	0.1429	3.34502e4	3228.04907	98.6956
7	16.120	VV	0.1071	31.60700	4.33520	0.0933
8	16.273	VB	0.1064	17.84558	2.58799	0.0527
9	16.466	BB	0.0856	11.81588	2.16696	0.0349
10	16.857	BV	0.1017	16.46457	2.47145	0.0486
11	17.080	VB	0.1409	41.37674	4.27482	0.1221
12	18.125	VB	0.1104	71.28476	9.85255	0.2103
13	18.780	BV	0.2670	108.13129	6.09411	0.3190
14	19.081	VB	0.1237	19.76235	2.35965	0.0583
15	19.961	BB	0.1135	10.75092	1.43386	0.0317
16	20.478	BB	0.1287	9.04683	1.00768	0.0267
Totals :				3.38923e4	3278.24572	

Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.061	BB	0.1090	31.49128	4.31984	0.1143
2	13.759	BB	0.0833	6.19469	1.14234	0.0225
3	14.628	BB	0.0934	17.87844	2.92045	0.0649
4	15.599	BV	0.1484	2.73023e4	2939.58716	99.0950
5	16.121	VV	0.1074	23.29576	3.18086	0.0846
6	16.273	VB	0.1079	13.74622	1.95867	0.0499
7	16.464	BB	0.0837	5.76066	1.08907	0.0209
8	16.856	BV	0.1011	8.87318	1.34317	0.0322
9	17.080	VB	0.1391	21.14997	2.22139	0.0768
10	18.125	BB	0.1151	41.07819	5.37657	0.1491
11	18.781	BB	0.2910	79.88758	3.83501	0.2900
Totals :				2.75517e4	2966.97454	

Data File C:\CHEM32\1\DATA\RAJT\20120430\RT-4-131-B00012.D
Sample Name: RT-4-131-B

HPLC Traces of Compound 39

Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.341	BB	0.0847	5.57106	1.00514	0.0353
2	13.063	BB	0.1015	20.03703	2.94152	0.1270
3	14.630	BB	0.0927	6.82812	1.12611	0.0433
4	15.599	BV	0.1251	1.56773e4	2007.88953	99.3510
5	16.121	VB	0.0906	7.19840	1.22402	0.0456
6	17.080	BB	0.1687	15.58590	1.29198	0.0988
7	18.126	BB	0.1077	15.89127	2.26856	0.1007
8	18.780	BB	0.2950	31.30398	1.50286	0.1984
Totals :				1.57797e4	2019.24970	

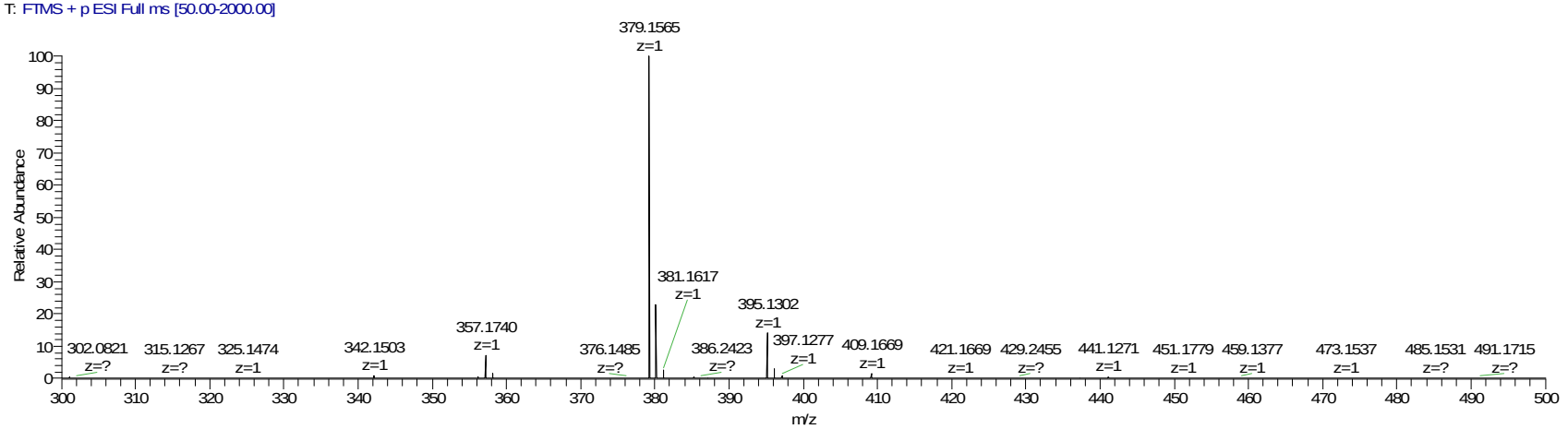
==========

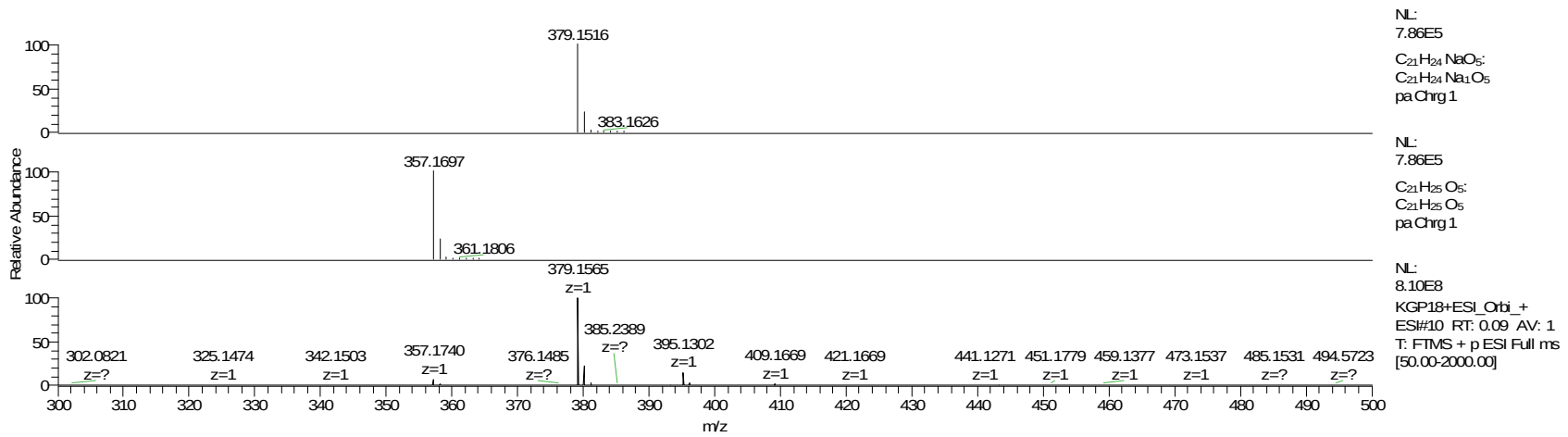
*** End of Report ***

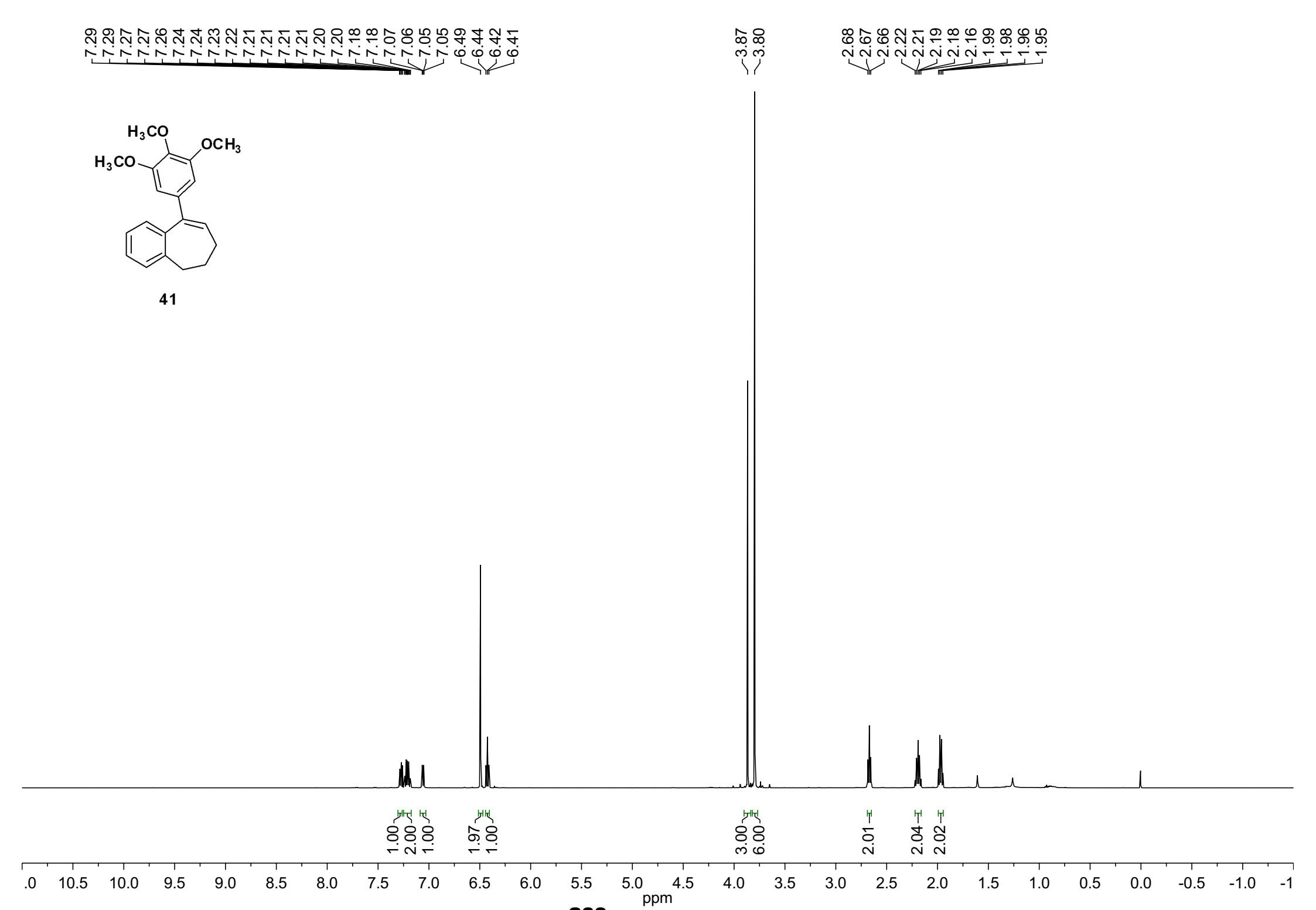
HRMS of Compound 39

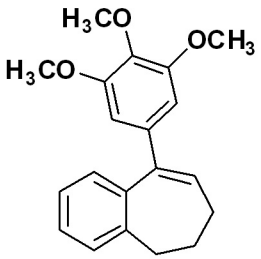
C:\Xcalibur\...\KGP18+ESI_Orbi_+ESI 6/6/2013 10:42:04 PM

KGP18+ESI_Orbi_+ESI #10 RT: 0.09 AV: 1 NL: 8.10E8
T: FTMS + p ESI Full ms [50.00-2000.00]






7.29
7.29
7.27
7.27
7.26
7.24
7.24
7.23
7.22
7.21
7.21
7.21
7.21
7.20
7.20
7.18
7.18
7.07
7.06
7.05
7.05
6.49
6.44
6.42
6.41
3.87
3.80
2.68
2.67
2.66
2.22
2.21
2.19
2.18
2.16
1.99
1.98
1.96
1.95
H3CO
OCH3
H3CO
41
1.00
2.00
1.00
1.97
1.00
3.00
6.00
2.01
2.04
2.02
.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1
ppm



41

153.03
143.10
142.31
140.14
138.31
137.54
129.49
128.72
128.20
127.25
125.92
105.41
77.41
77.16
76.91
61.04
56.26
35.43
32.55
25.49

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

Data File C:\CHEM32\1\DATA\MATT MAC\CSG_VII_1700031.D
Sample Name: run1

HPLC Traces of Compound 41

==========

Acq. Operator : Christine

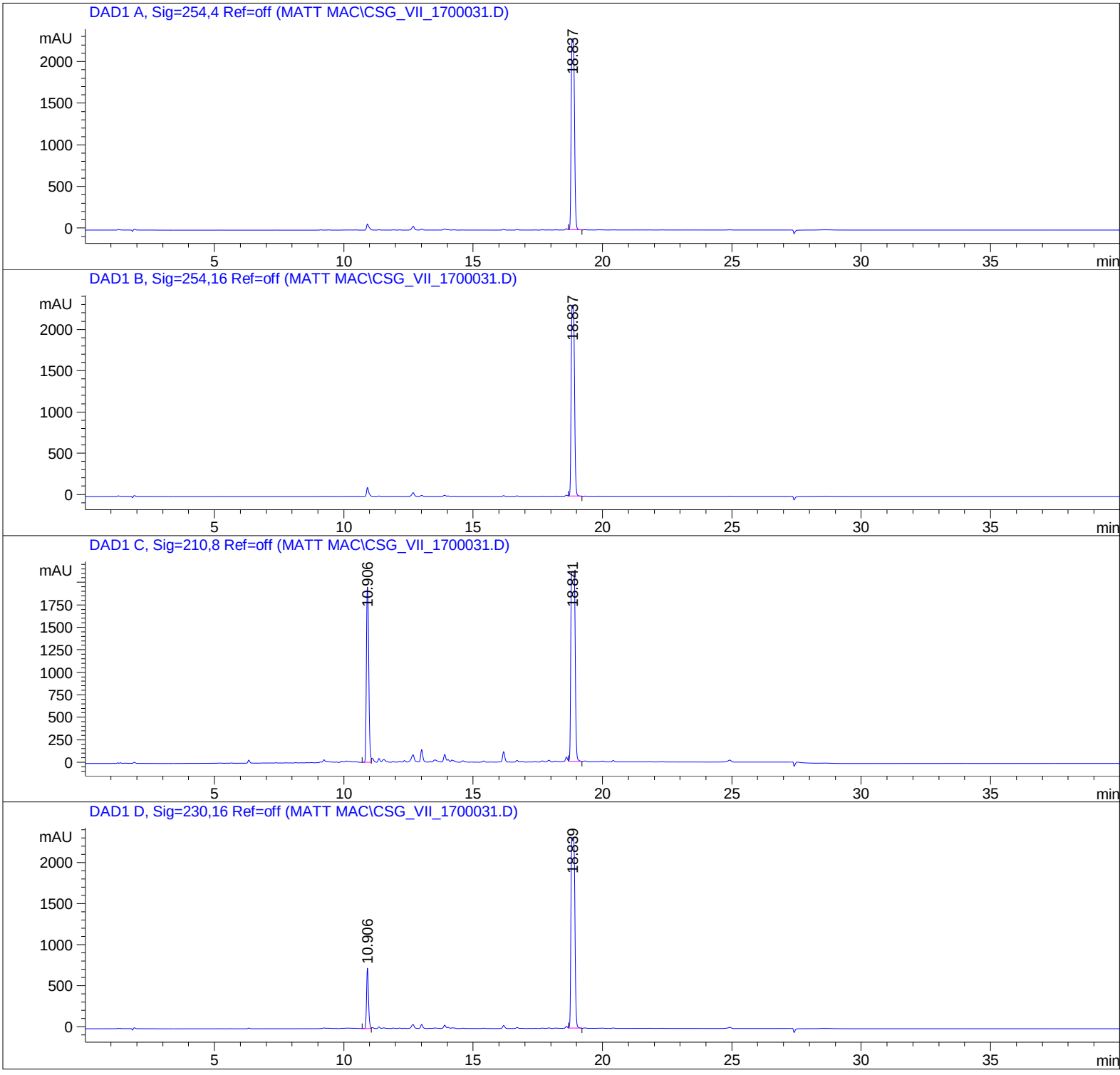
Location : -

Injection Date : 18-Mar-13, 18:39:39

Acq. Method : MASTERMETHOD.M

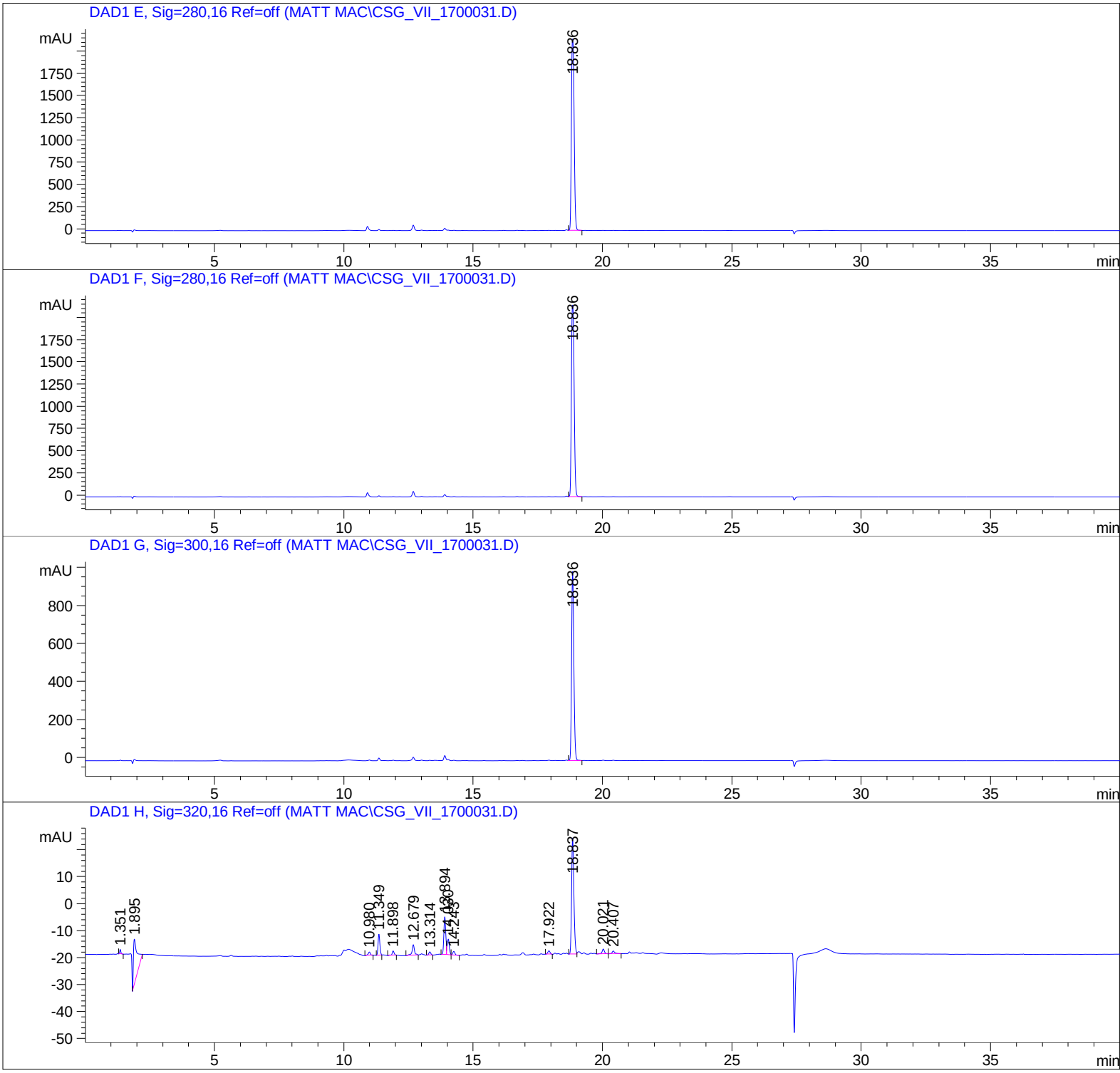
Analysis Method : C:\CHEM32\1\DATA\MATT MAC\CSG_VII_1700030.D\DA.M (MASTERMETHOD.M)

Last changed : 3/18/2013 5:03:32 PM by Christine



Data File C:\CHEM32\1\DATA\MATT MAC\CSG_VII_1700031.D
Sample Name: run1

HPLC of Compound 41



==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

s41

Data File C:\CHEM32\1\DATA\MATT MAC\CSG_VII_1700031.D
Sample Name: run1

HPLC Traces of Compound 41

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.837	VV	0.1428	2.02356e4	2296.00977	100.0000
Totals :				2.02356e4	2296.00977	

Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.837	VV	0.1430	2.04492e4	2317.27686	100.0000
Totals :				2.04492e4	2317.27686	

Signal 3: DAD1 C, Sig=210,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.906	BV	0.1018	1.23464e4	1950.91223	33.9416
2	18.841	VV	0.1865	2.40290e4	2115.81152	66.0584
Totals :				3.63754e4	4066.72375	

Signal 4: DAD1 D, Sig=230,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.906	BV	0.0812	3872.71118	738.14893	14.0531
2	18.839	VB	0.1669	2.36850e4	2323.09839	85.9469
Totals :				2.75577e4	3061.24731	

Signal 5: DAD1 E, Sig=280,16 Ref=off

HPLC Traces of Compound 41

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.836	VB	0.1199	1.58865e4	2157.62085	100.0000
Totals :				1.58865e4	2157.62085	

Signal 6: DAD1 F, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.836	VB	0.1199	1.58865e4	2157.62085	100.0000
Totals :				1.58865e4	2157.62085	

Signal 7: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.836	VV	0.0949	6054.54590	995.95148	100.0000
Totals :				6054.54590	995.95148	

Signal 8: DAD1 H, Sig=320,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.351	BB	0.0473	5.07612	1.67797	0.7572
2	1.895	BB	0.1439	172.15982	17.03720	25.6803
3	10.980	BB	0.0885	7.75652	1.28375	1.1570
4	11.349	BB	0.0739	37.24184	7.77304	5.5552
5	11.898	BB	0.0860	9.72162	1.66915	1.4501
6	12.679	BB	0.0971	25.70506	3.89024	3.8343
7	13.314	BB	0.0821	6.45013	1.21096	0.9621
8	13.894	BV	0.0813	73.76592	14.04108	11.0033
9	14.030	VV	0.0809	31.19659	5.78939	4.6534
10	14.243	VB	0.0903	7.98895	1.36431	1.1917
11	17.922	BB	0.1000	8.20751	1.29417	1.2243
12	18.837	BV	0.0959	266.21088	43.17391	39.7094
13	20.021	BB	0.0967	11.49719	1.79475	1.7150
14	20.407	BB	0.1047	7.41931	1.02215	1.1067
Totals :				670.39748	103.02209	

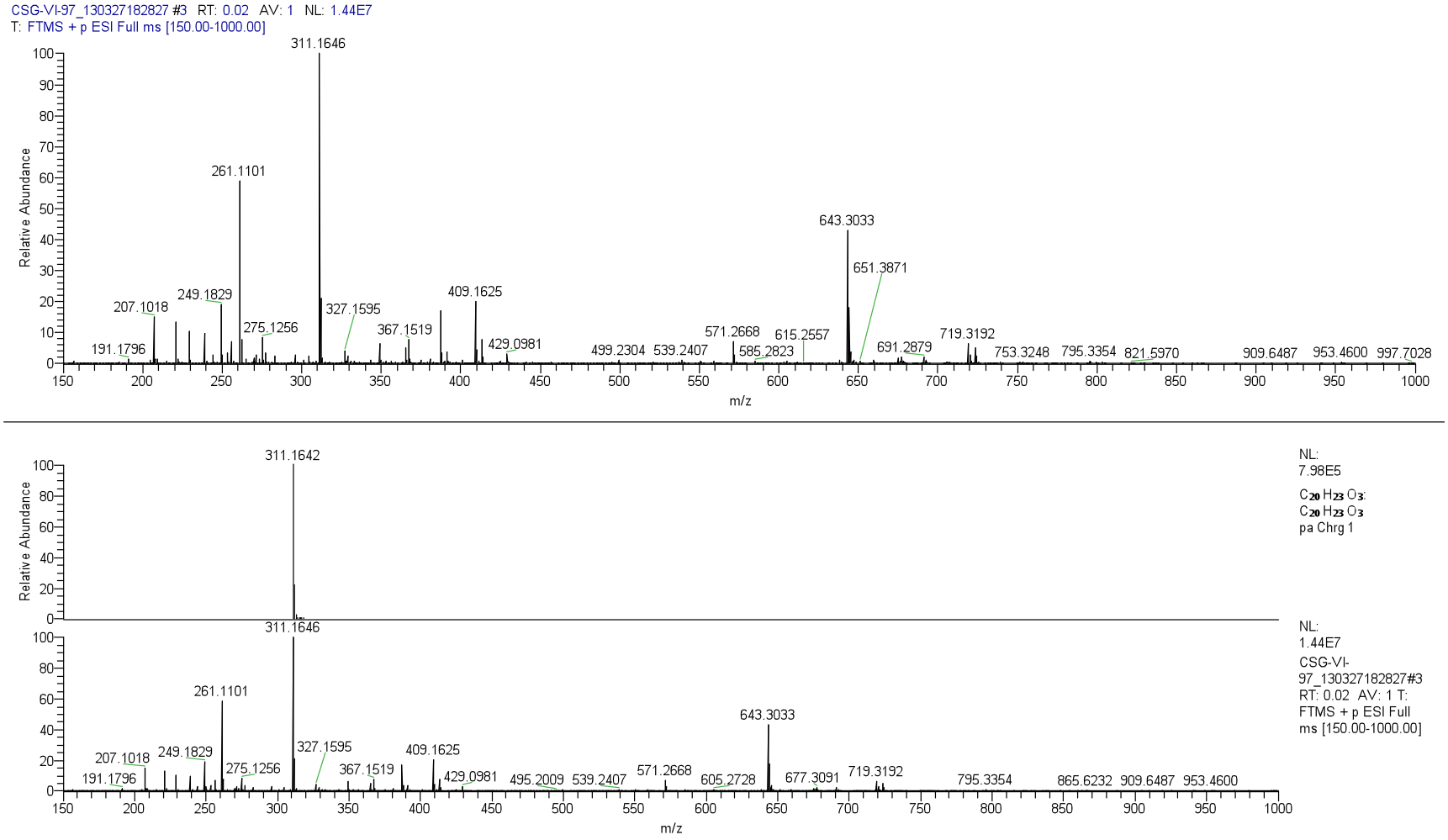
HPLC Traces of Compound 41

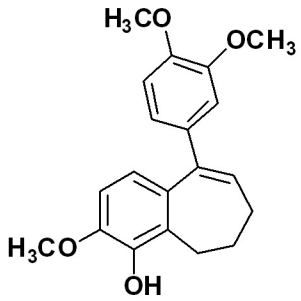
==========

*** End of Report ***

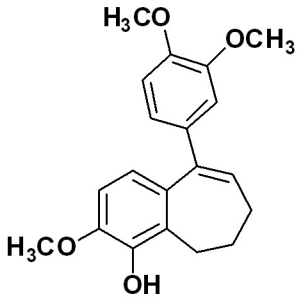
HRMS of Compound 41

C:\Xcalibur\...\CSG-VI-97_130327182827 3/27/2013 6:28:28 PM CSG-VI-97





42



42

148.610
148.331
145.086
142.515
142.422
135.797
134.691
127.901
126.419
120.803
120.553
111.341
110.810
107.722
77.414
77.160
76.905
56.056
56.032
55.985
33.805
25.768
23.635

230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -10

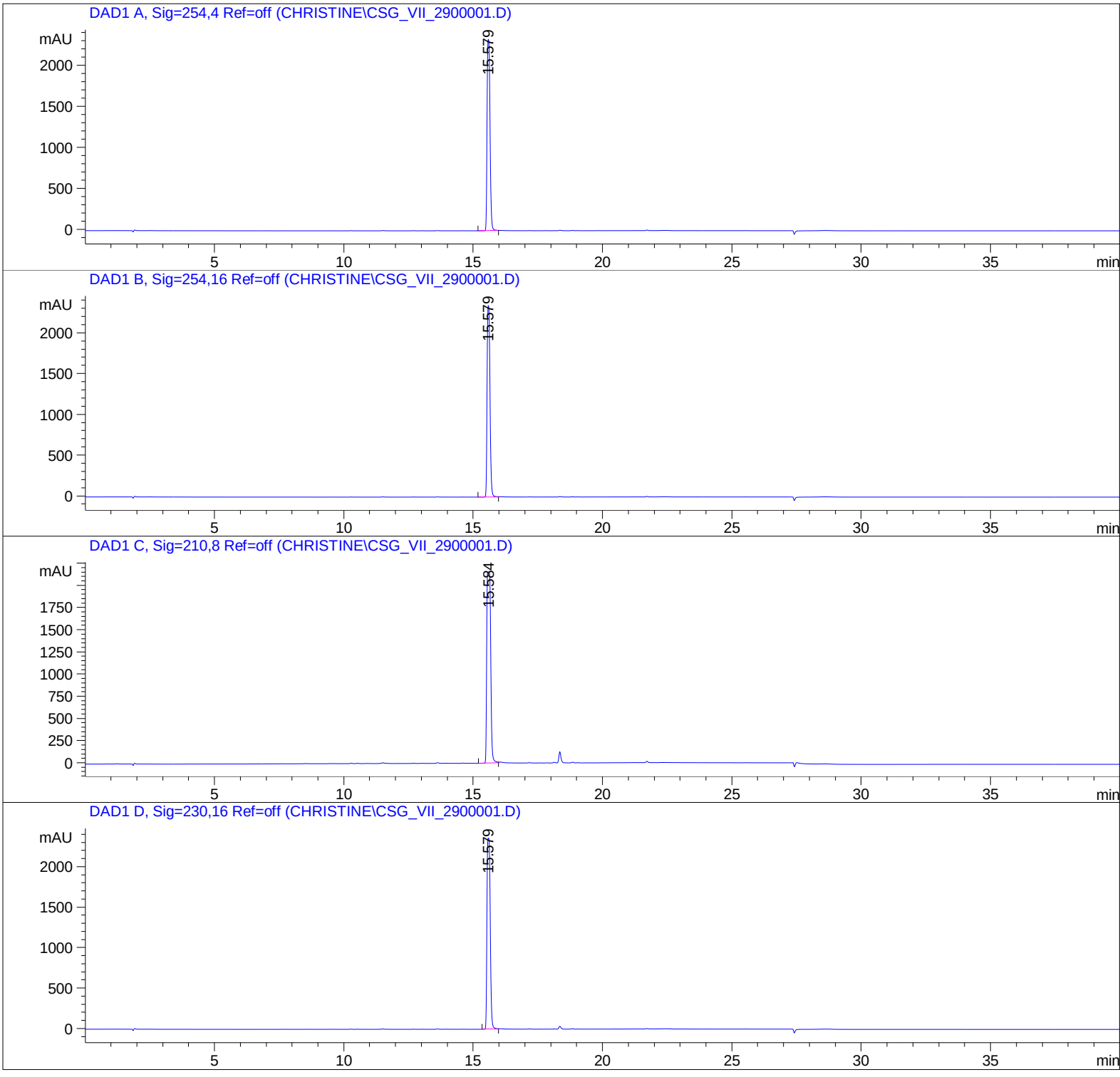
f1 (ppm)

Data File C:\CHEM32\1\DATA\CHRISTINE\CSG_VII_2900001.D
Sample Name: run1

HPLC Traces of Compound 42

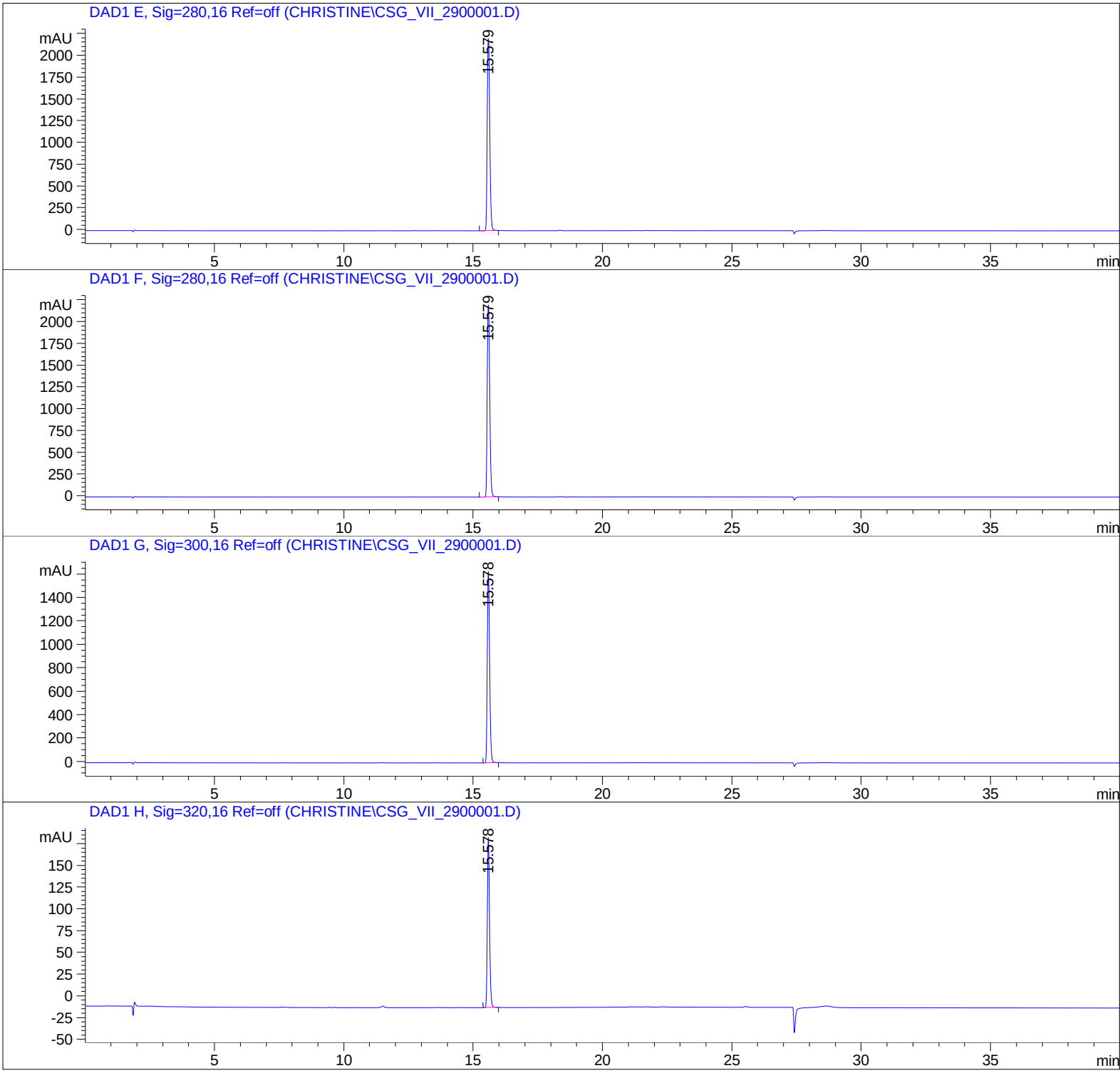
==========

Acq. Operator : Christine
Acq. Instrument : Instrument 1 Location : -
Injection Date : 3/20/2013 1:42:30 PM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 3/20/2013 1:02:27 PM by Christine
Analysis Method : C:\CHEM32\1\DATA\CHRISTINE\CSG_VII_2900001.D\DA.M (MASTERMETHOD.M)
Last changed : 3/20/2013 2:41:46 PM by Christine



Data File C:\CHEM32\1\DATA\CHRISTINE\CSG_VII_2900001.D
Sample Name: run1

HPLC Traces of Compound 42



==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Data File C:\CHEM32\1\DATA\CHRISTINE\CSG_VII_2900001.D
Sample Name: run1

HPLC Traces of Compound 42

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.579	BV	0.1254	1.82404e4	2327.57520	100.0000
Totals :				1.82404e4	2327.57520	

Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.579	BV	0.1238	1.80768e4	2347.87866	100.0000
Totals :				1.80768e4	2347.87866	

Signal 3: DAD1 C, Sig=210,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.584	BV	0.1707	2.26748e4	2156.35889	100.0000
Totals :				2.26748e4	2156.35889	

Signal 4: DAD1 D, Sig=230,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.579	BV	0.1420	2.06525e4	2361.59888	100.0000
Totals :				2.06525e4	2361.59888	

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.579	BV	0.1096	1.50498e4	2206.14380	100.0000
Totals :				1.50498e4	2206.14380	

Data File C:\CHEM32\1\DATA\CHRISTINE\CSG_VII_2900001.D
Sample Name: run1

HPLC Traces of Compound 42

Signal 6: DAD1 F, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.579	BV	0.1096	1.50498e4	2206.14380	100.0000
Totals :				1.50498e4	2206.14380	

Signal 7: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.578	BB	0.0994	1.03041e4	1637.69092	100.0000
Totals :				1.03041e4	1637.69092	

Signal 8: DAD1 H, Sig=320,16 Ref=off

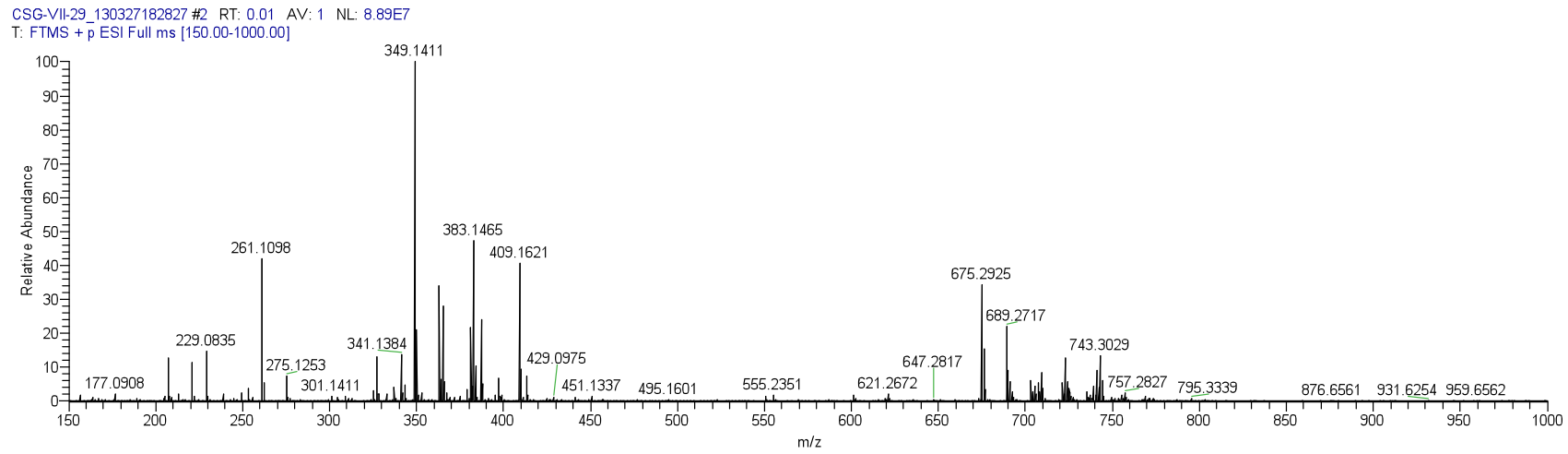
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.578	BB	0.0888	1155.64270	195.93292	100.0000
Totals :				1155.64270	195.93292	

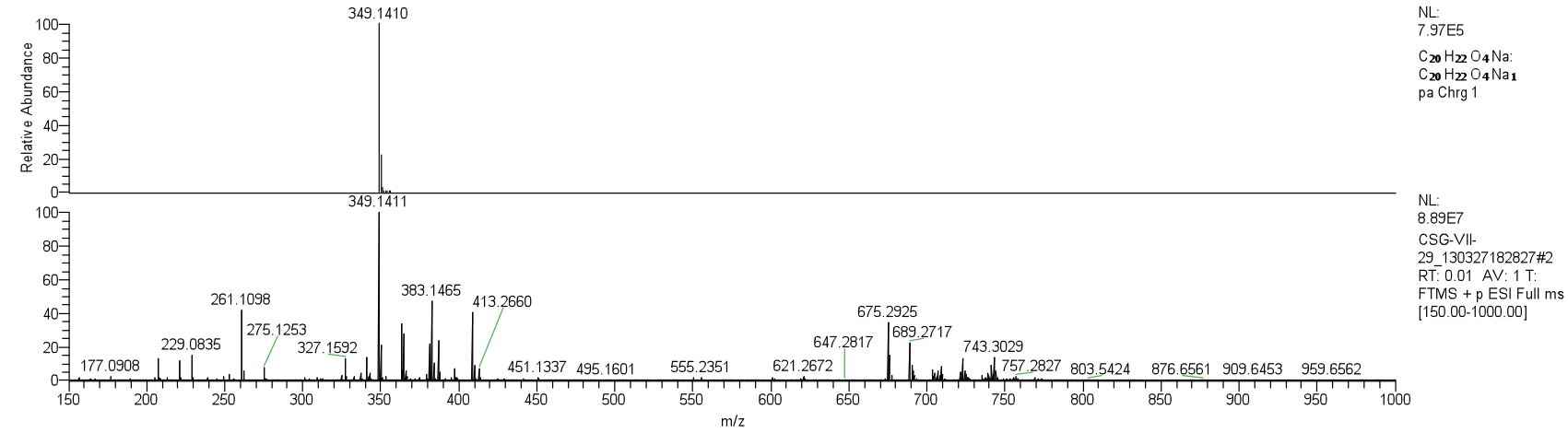
==========

*** End of Report ***

HRMS of Compound 42

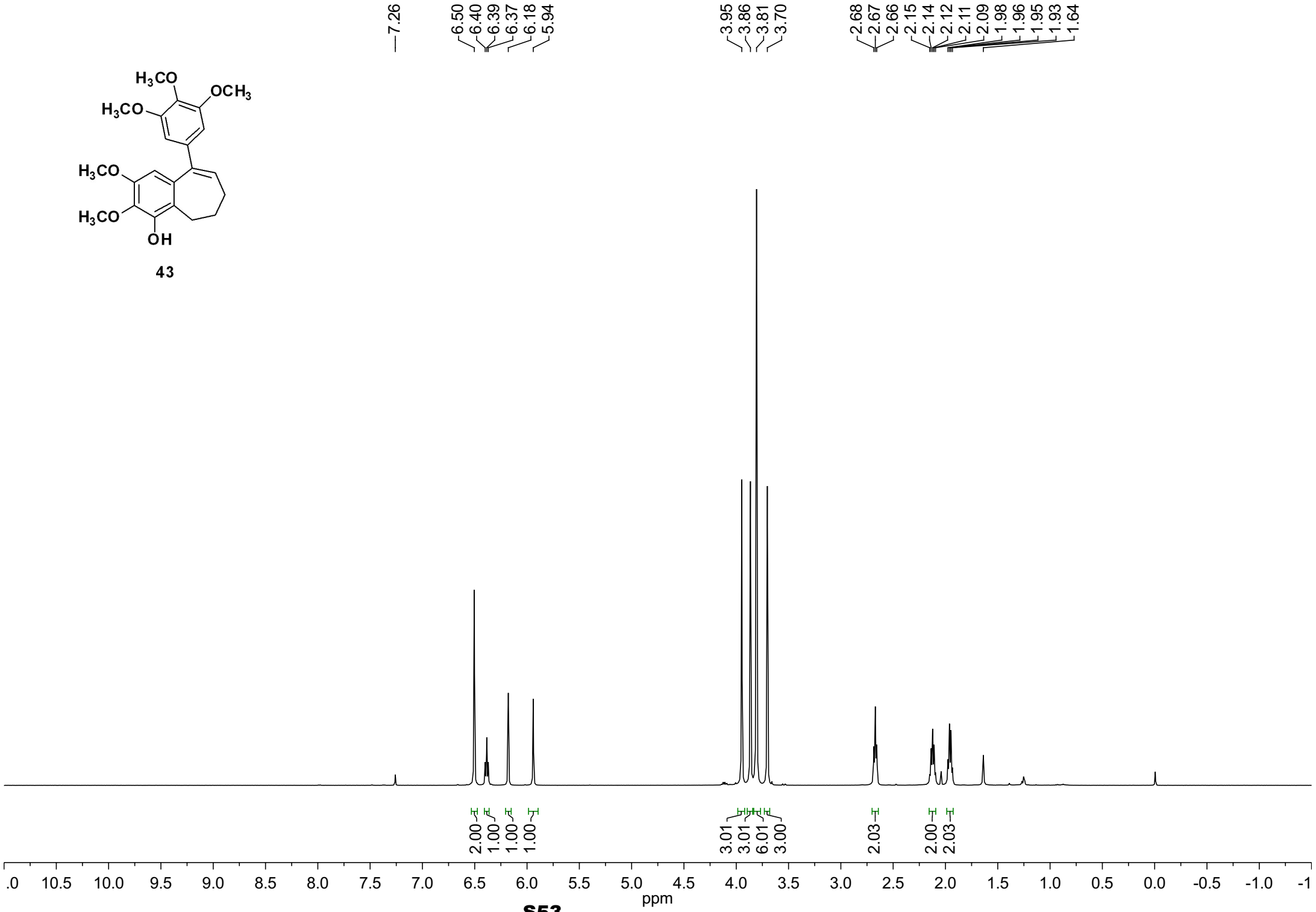
C:\Xcalibur\...\CSG-VII-29_130327182827 3/27/2013 6:54:00 PM CSG-VII-29

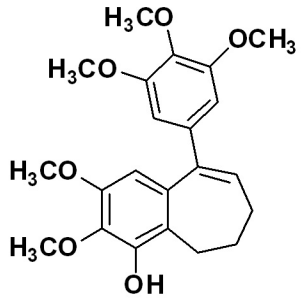




H3CO
OCH3
H3CO
H3CO
H3CO
OH

43


7.26
6.50
6.40
6.39
6.37
6.18
5.94
3.95
3.86
3.81
3.70
2.68
2.67
2.66
2.15
2.14
2.12
2.11
2.09
1.98
1.96
1.95
1.93
1.64
2.00
1.00
1.00
1.00
3.01
3.01
6.01
3.00
2.03
2.00
2.03
ppm



43

153.00
149.82
146.33
142.80
138.06
137.46
136.25
134.31
128.46
121.39
105.32
105.06
77.41
77.16
76.91
61.08
61.06
56.29
56.06
34.29
25.81
23.38

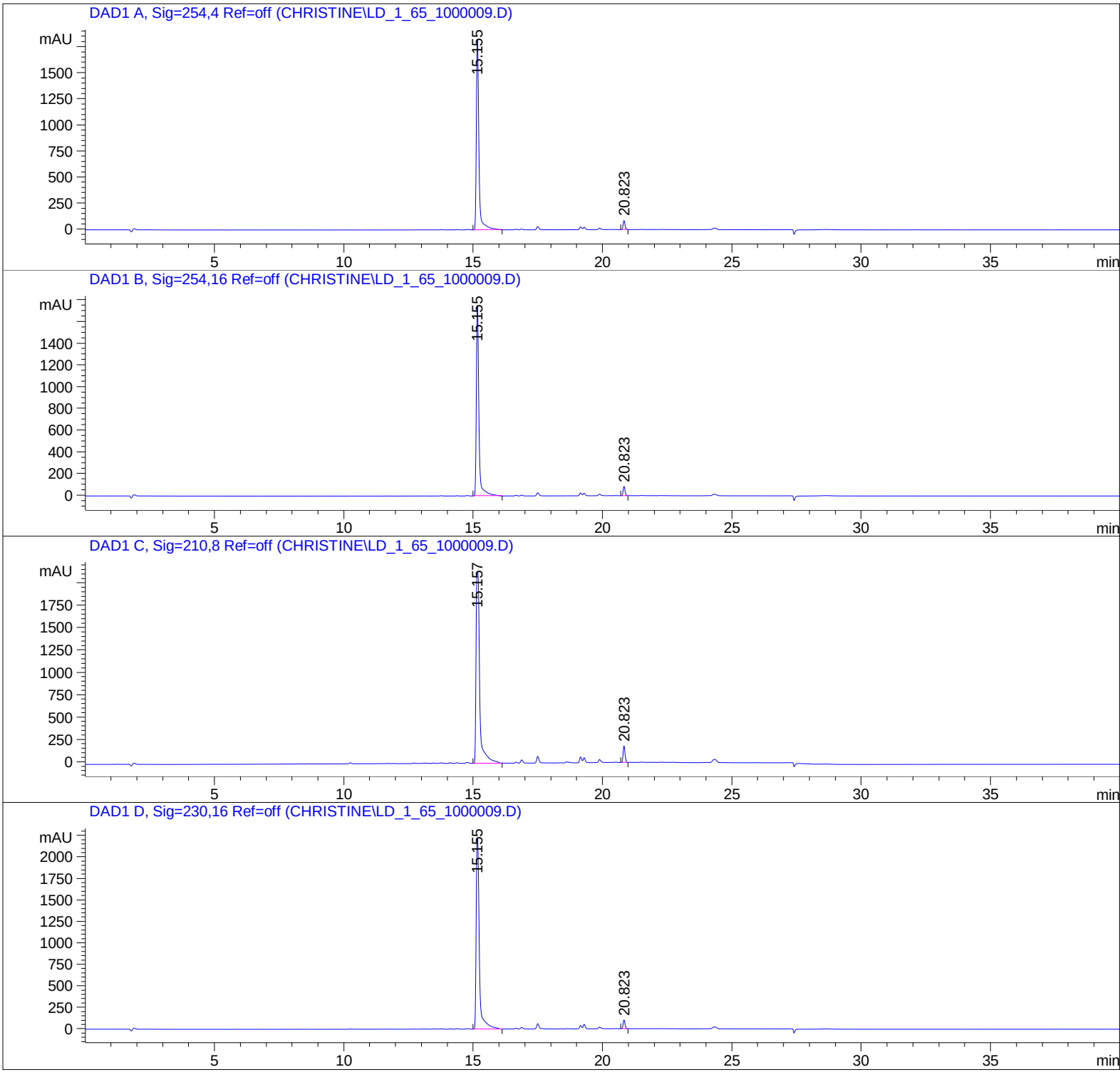
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

Data File C:\CHEM32\1\DATA\CHRISTINE\LD_1_65_1000009.D
Sample Name: run1

HPLC Traces of Compound 43

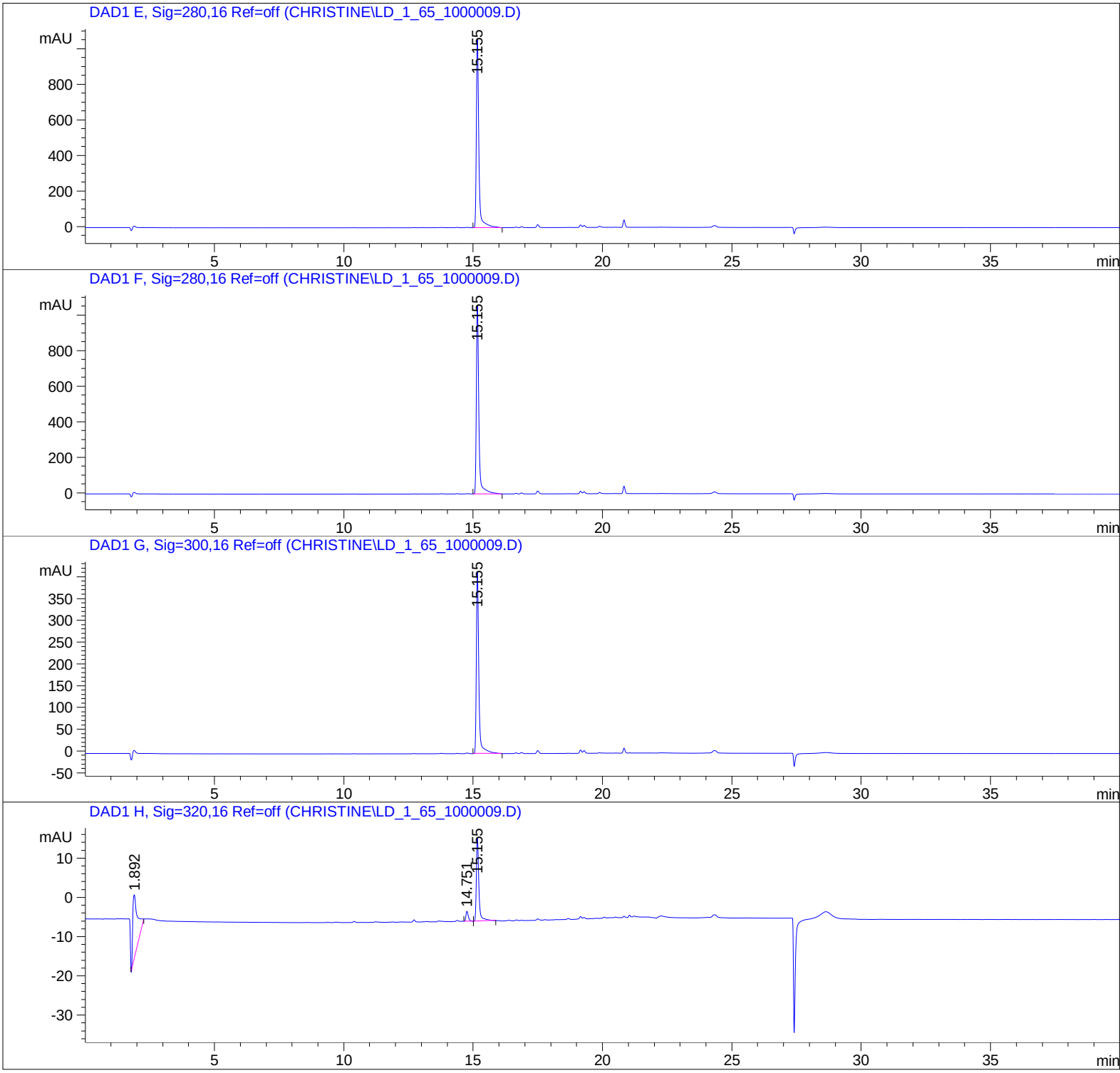
==========

Acq. Operator : Christine
Acq. Instrument : Instrument 1 Location : -
Injection Date : 3/25/2013 6:42:00 PM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 3/25/2013 5:31:33 PM by Christine
Analysis Method : C:\CHEM32\1\DATA\CHRISTINE\LD_1_65_1000009.D\DA.M (MASTERMETHOD.M)
Last changed : 3/25/2013 7:42:29 PM by Christine



Data File C:\CHEM32\1\DATA\CHRISTINE\LD_1_65_1000009.D
Sample Name: run1

HPLC Traces of Compound 43



==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

S56

Data File C:\CHEM32\1\DATA\CHRISTINE\LD_1_65_1000009.D
Sample Name: run1

HPLC Traces of Compound 43

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.155	BB	0.1035	1.27558e4	1826.01721	96.6533
2	20.823	BB	0.0802	441.68518	85.54213	3.3467
Totals :				1.31975e4	1911.55934	

Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.155	BB	0.1029	1.21415e4	1751.75439	96.5072
2	20.823	BB	0.0782	439.43024	85.11578	3.4928
Totals :				1.25809e4	1836.87017	

Signal 3: DAD1 C, Sig=210,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.157	BV	0.1538	2.12365e4	2140.21191	95.6725
2	20.823	BV	0.0805	960.57239	185.28012	4.3275
Totals :				2.21971e4	2325.49203	

Signal 4: DAD1 D, Sig=230,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.155	BV	0.1315	1.89474e4	2221.88965	97.3141
2	20.823	BB	0.0802	522.95447	101.36359	2.6859
Totals :				1.94703e4	2323.25323	

Data File C:\CHEM32\1\DATA\CHRISTINE\LD_1_65_1000009.D
Sample Name: run1

HPLC Traces of Compound 43

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.155	BB	0.1009	7177.51318	1061.98120	100.0000
Totals :				7177.51318	1061.98120	

Signal 6: DAD1 F, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.155	BB	0.1009	7177.51318	1061.98120	100.0000
Totals :				7177.51318	1061.98120	

Signal 7: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.155	BB	0.1006	2817.50952	418.16830	100.0000
Totals :				2817.50952	418.16830	

Signal 8: DAD1 H, Sig=320,16 Ref=off

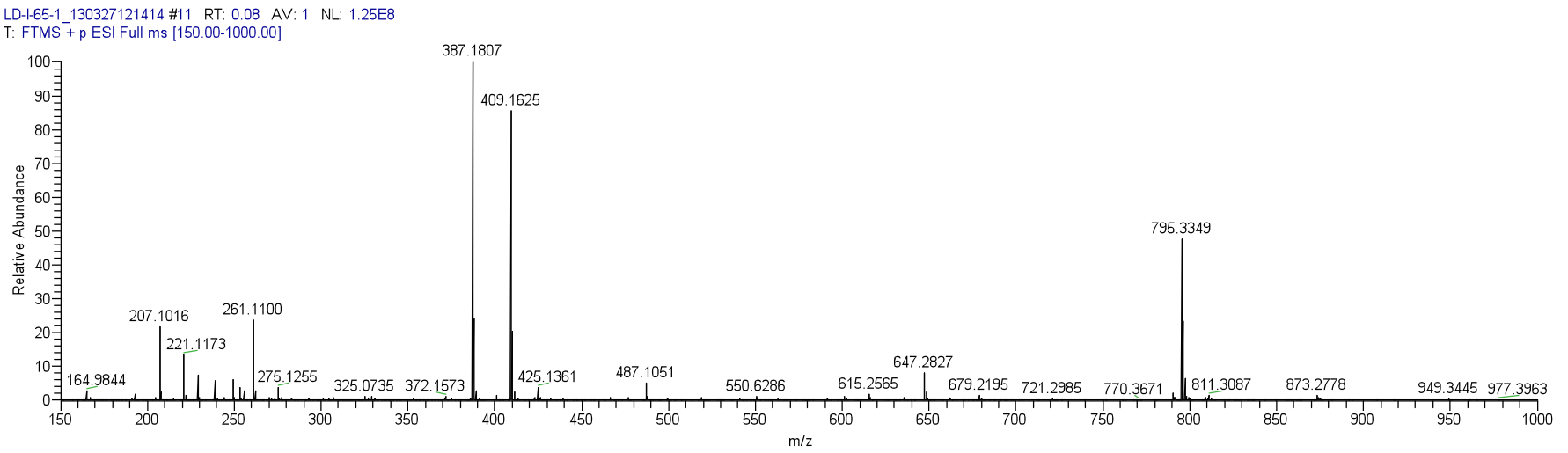
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.892	BB	0.1832	212.84036	16.64317	57.0213
2	14.751	BB	0.0976	16.61544	2.56333	4.4514
3	15.155	BB	0.1010	143.80884	21.22739	38.5273
Totals :				373.26464	40.43389	

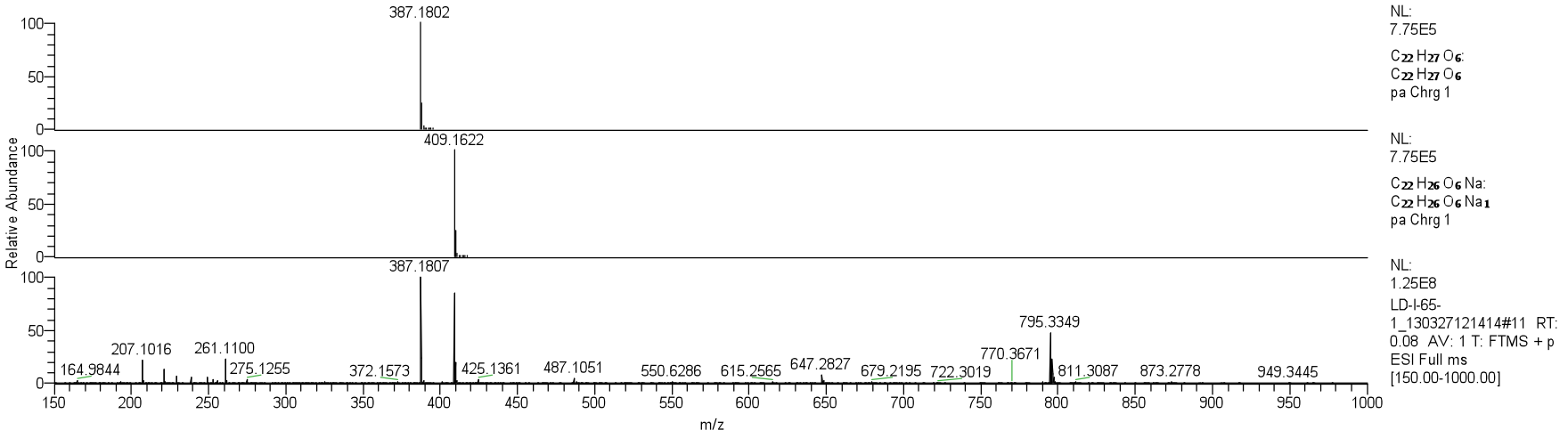
==========

*** End of Report ***

HRMS of Compound 43

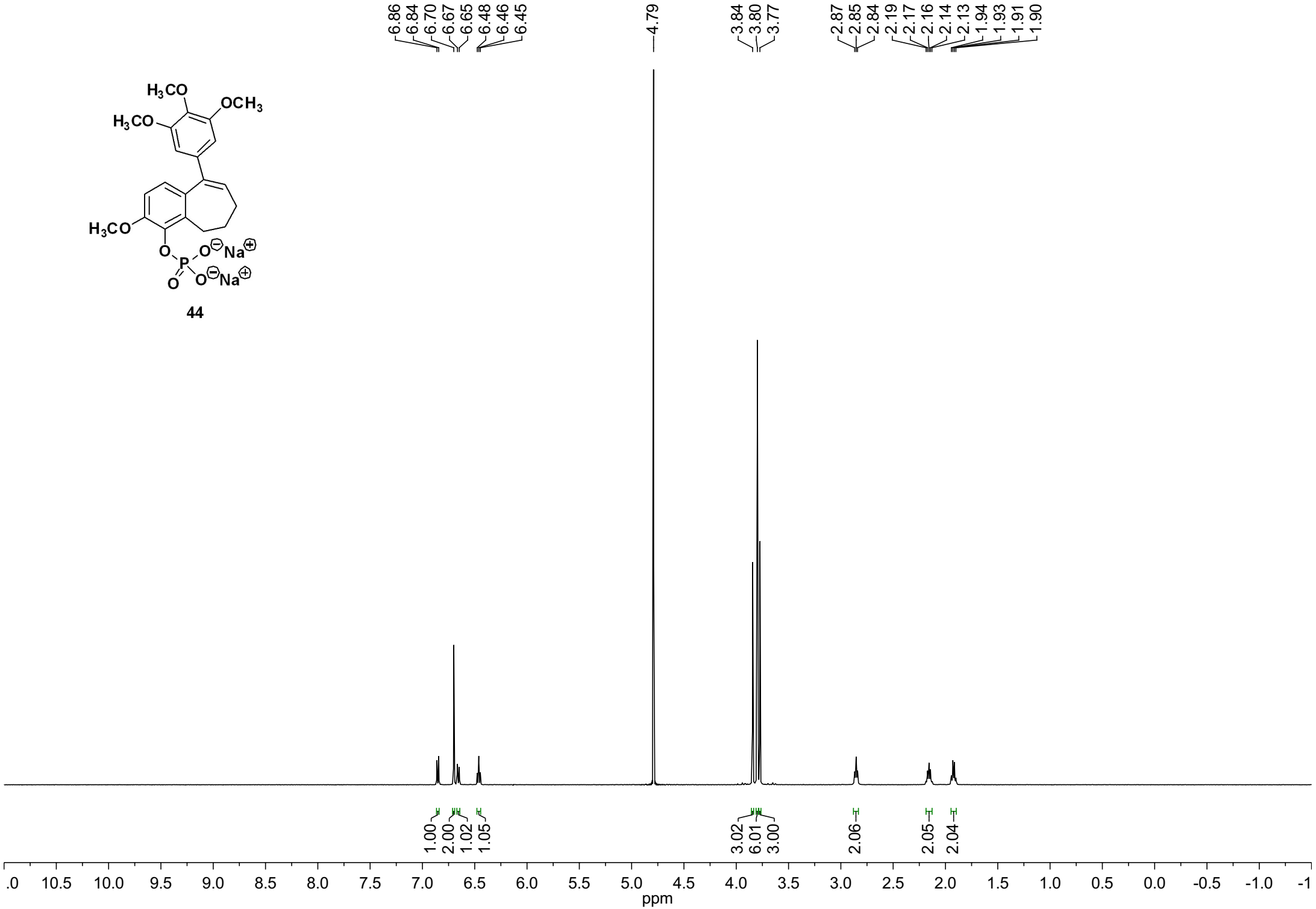
C:\Xcalibur\...\LD-I-65-1_130327121414 3/27/2013 4:53:38 PM LD-I-65-1

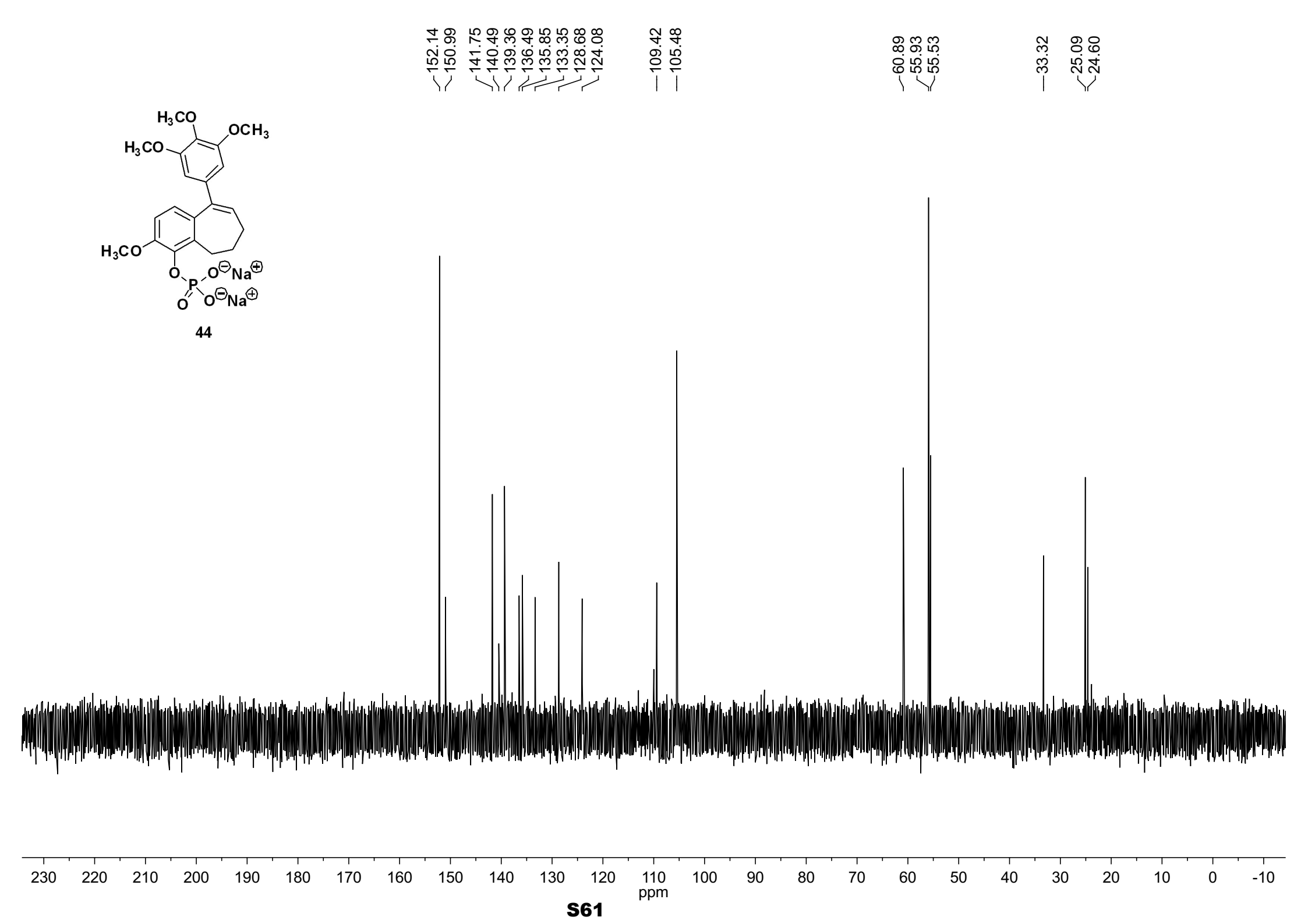




H3CO
OCH3
H3CO
H3CO
O
P
O
Na
O
Na
O

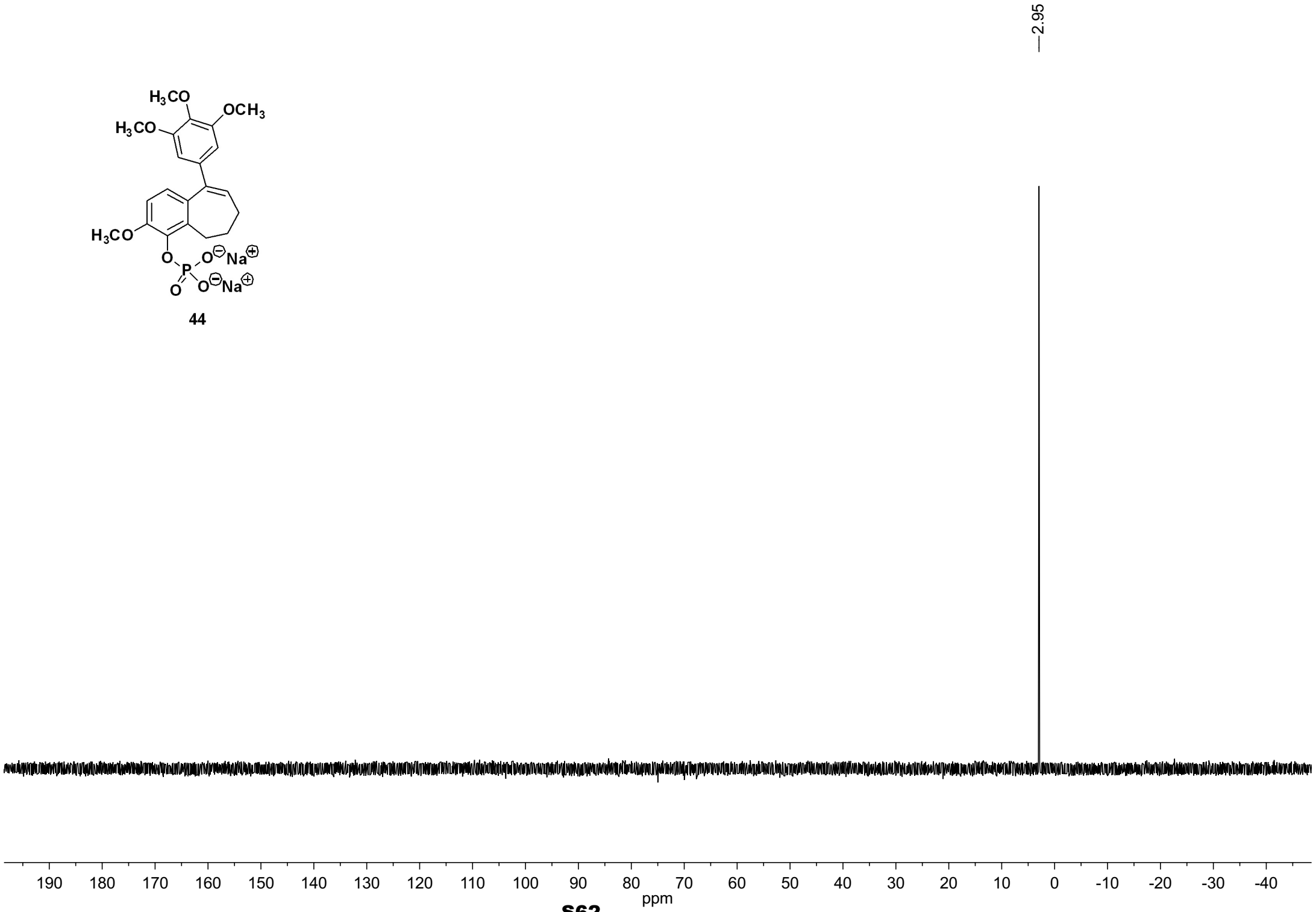
44


6.86
6.84
6.70
6.67
6.65
6.48
6.46
6.45
4.79
3.84
3.80
3.77
2.87
2.85
2.84
2.19
2.17
2.16
2.14
2.13
1.94
1.93
1.91
1.90
1.00
2.00
1.02
1.05
3.02
6.01
3.00
2.06
2.05
2.04
ppm


152.14
150.99
141.75
140.49
139.36
136.49
135.85
133.35
128.68
124.08
109.42
105.48
60.89
55.93
55.53
33.32
25.09
24.60
H3CO
OCH3
H3CO
H3CO
O
P
O
O
Na
O
Na
44
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

H3CO
OCH3
H3CO
H3CO
O
O
Na
P
O
O
Na

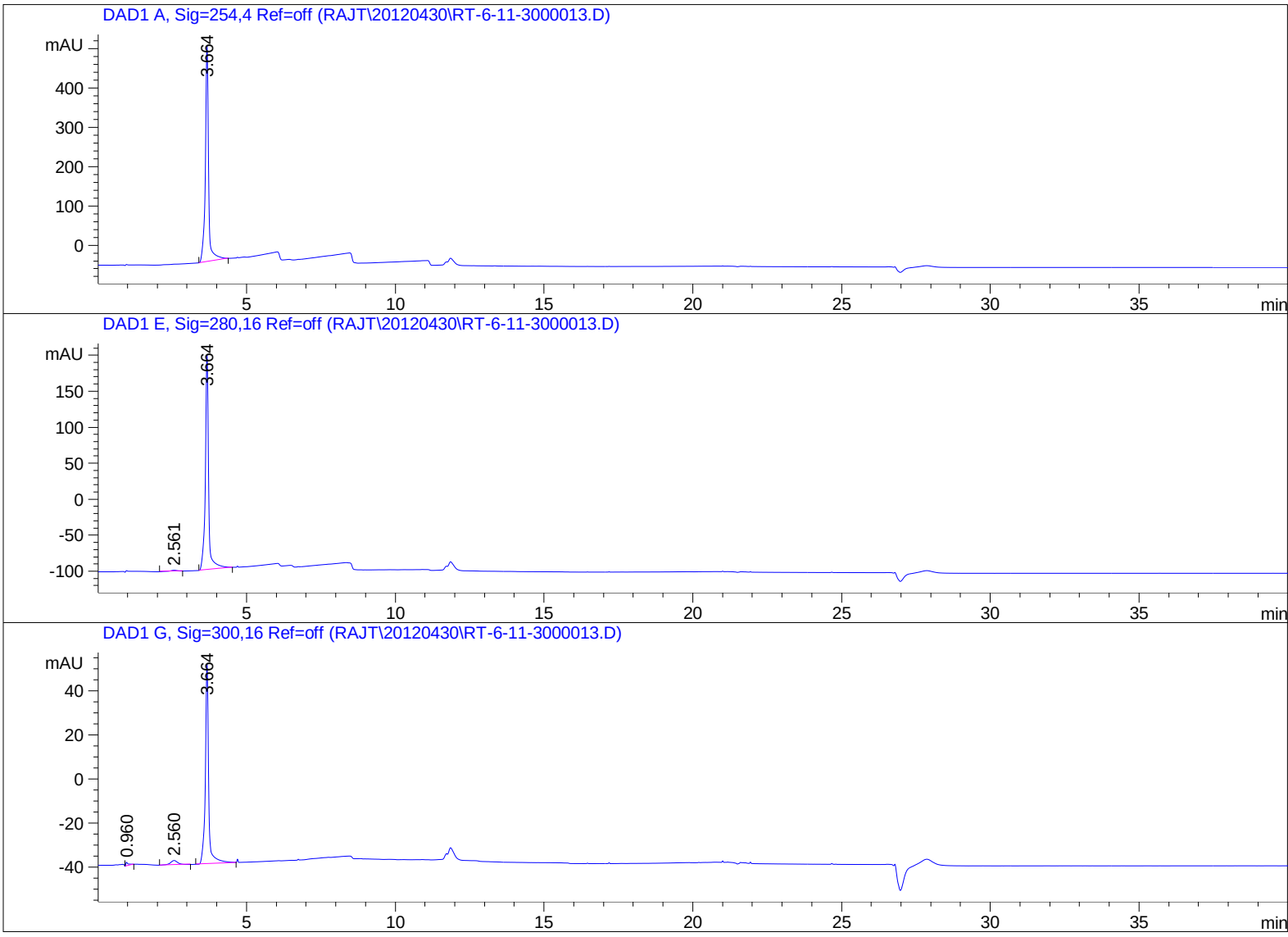
44


2.95
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
ppm

Data File C:\CHEM32\1\DATA\RAJT\20120430\RT-6-11-3000013.D
Sample Name: RT-6-11-3

HPLC Traces of Compound 44

```
==========================================================================
Acq. Operator   : RajT.
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 5/1/2012 4:39:02 AM
Acq. Method     : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed    : 5/1/2012 4:07:09 AM by RajT.
Analysis Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed    : 3/28/2012 11:50:33 AM by Erica P
Sample Info     : RT-6-11-3
                  10 uL
```



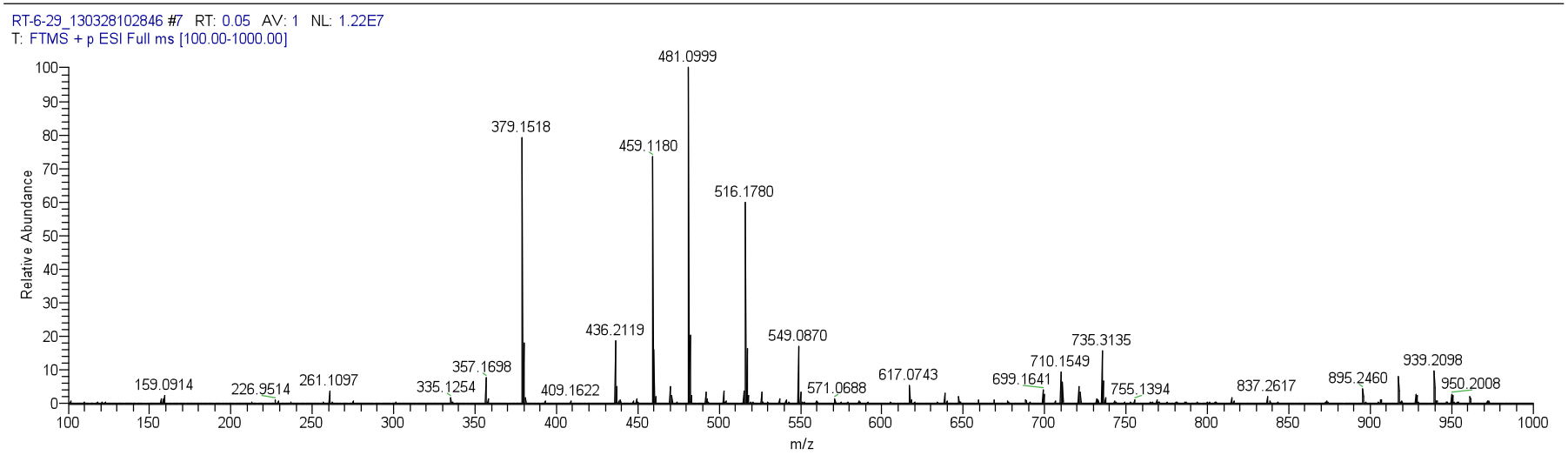
Data File C:\CHEM32\1\DATA\RAJT\20120430\RT-6-11-3000013.D
Sample Name: RT-6-11-3

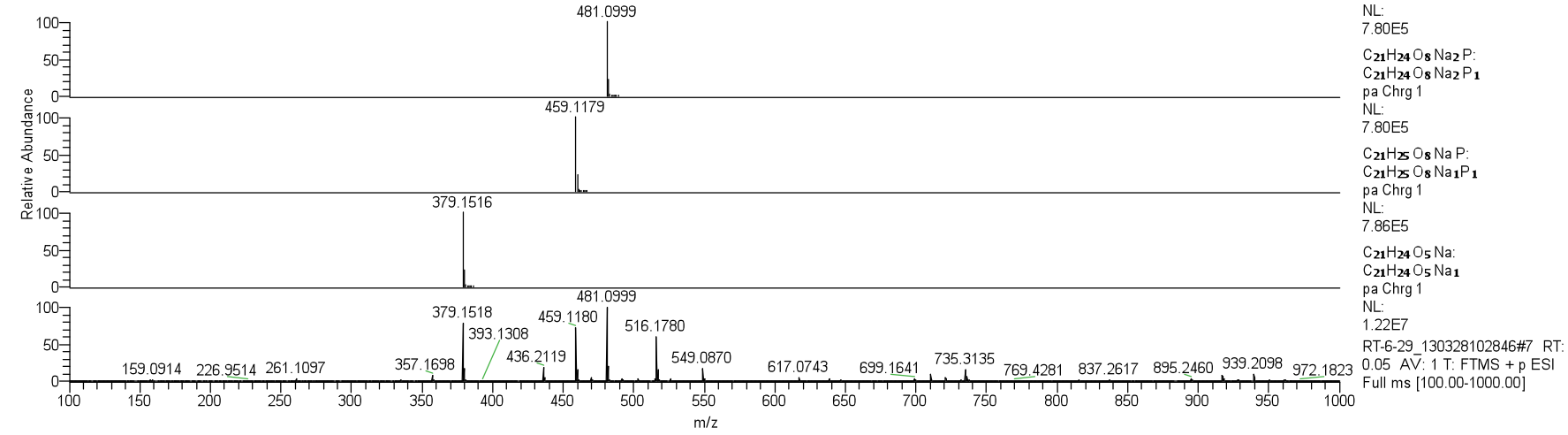
HPLC Traces of Compound 44

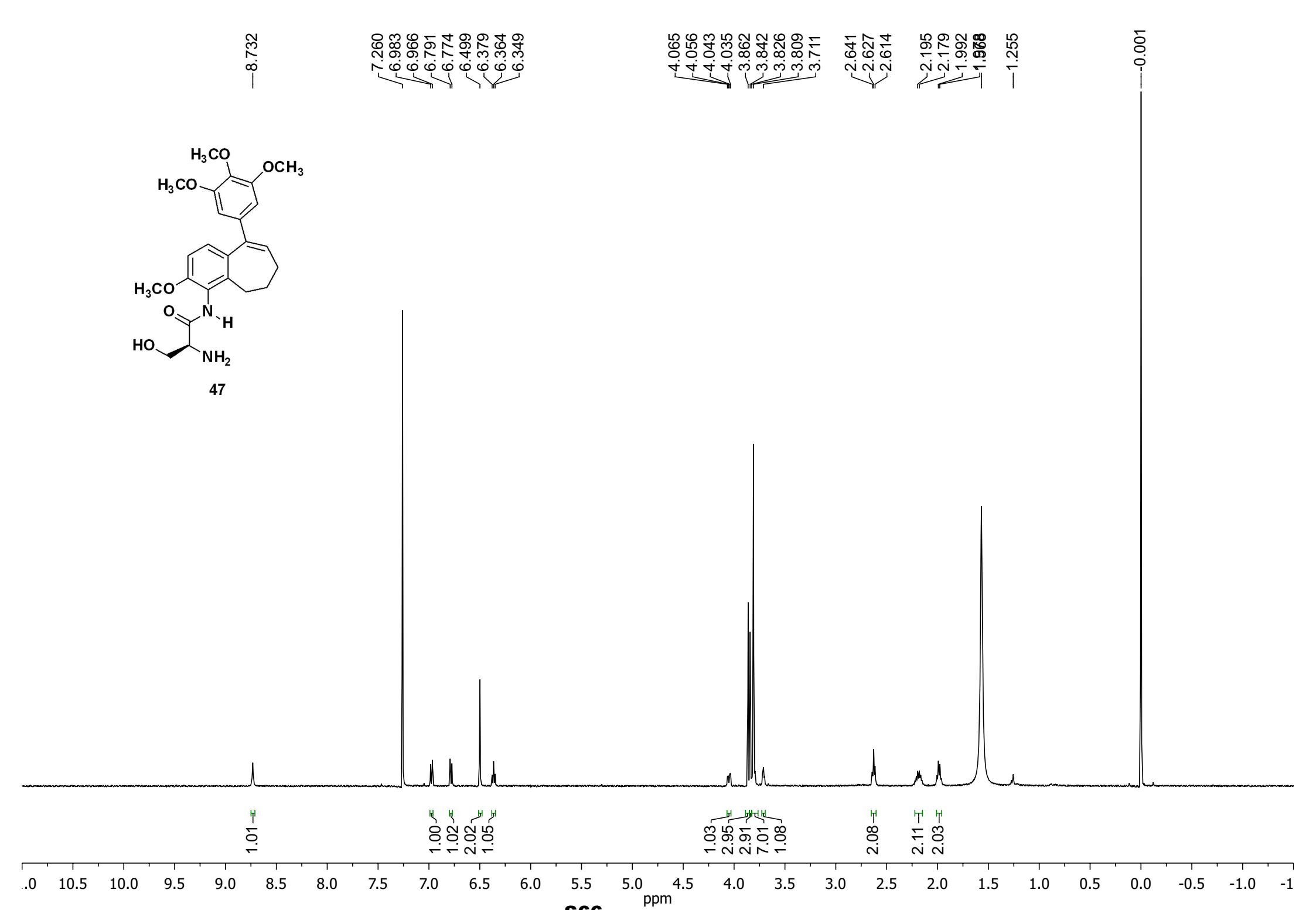
```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.664 BB    0.1124 4163.92969  549.24536 100.0000

Totals :                  4163.92969  549.24536



Signal 2: DAD1 E, Sig=280,16 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   2.561 BB    0.2526   25.22306    1.45211   1.0891
   2   3.664 BB    0.1134 2290.73706  298.77597  98.9109

Totals :                  2315.96012  300.22808



Signal 3: DAD1 G, Sig=300,16 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.960 BB    0.0865   10.72702    1.68029   1.4187
   2   2.560 BB    0.2635   34.55238    1.96197   4.5697
   3   3.664 BV    0.1152  710.83453   90.96315  94.0116

Totals :                   756.11394   94.60541


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

HRMS of Compound 44

C:\Xcalibur\...\RT-6-29_130328102846 3/28/2013 10:28:47 AM RT-6-29

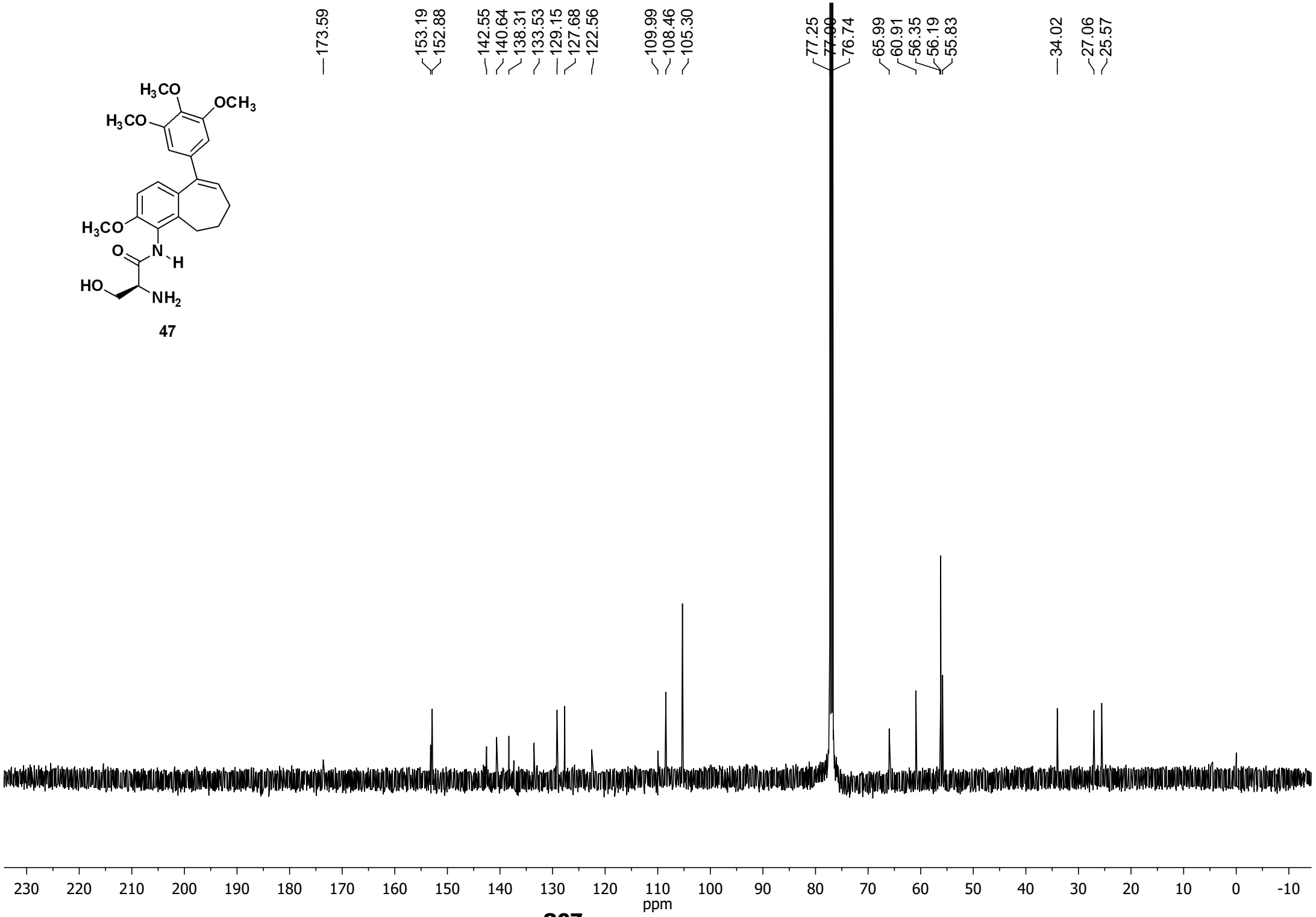





8.732
7.260
6.983
6.966
6.791
6.774
6.499
6.379
6.364
6.349
4.065
4.056
4.043
4.035
3.862
3.842
3.826
3.809
3.711
2.641
2.627
2.614
2.195
2.179
1.992
1.255
0.001
H3CO
OCH3
H3CO
H3CO
O
N
H
HO
NH2
47
1.01
1.00
1.02
2.02
1.05
1.03
2.95
2.91
7.01
1.08
2.08
2.11
2.03
ppm

H3CO
OCH3
H3CO
H3CO
O
N
H
HO
NH2

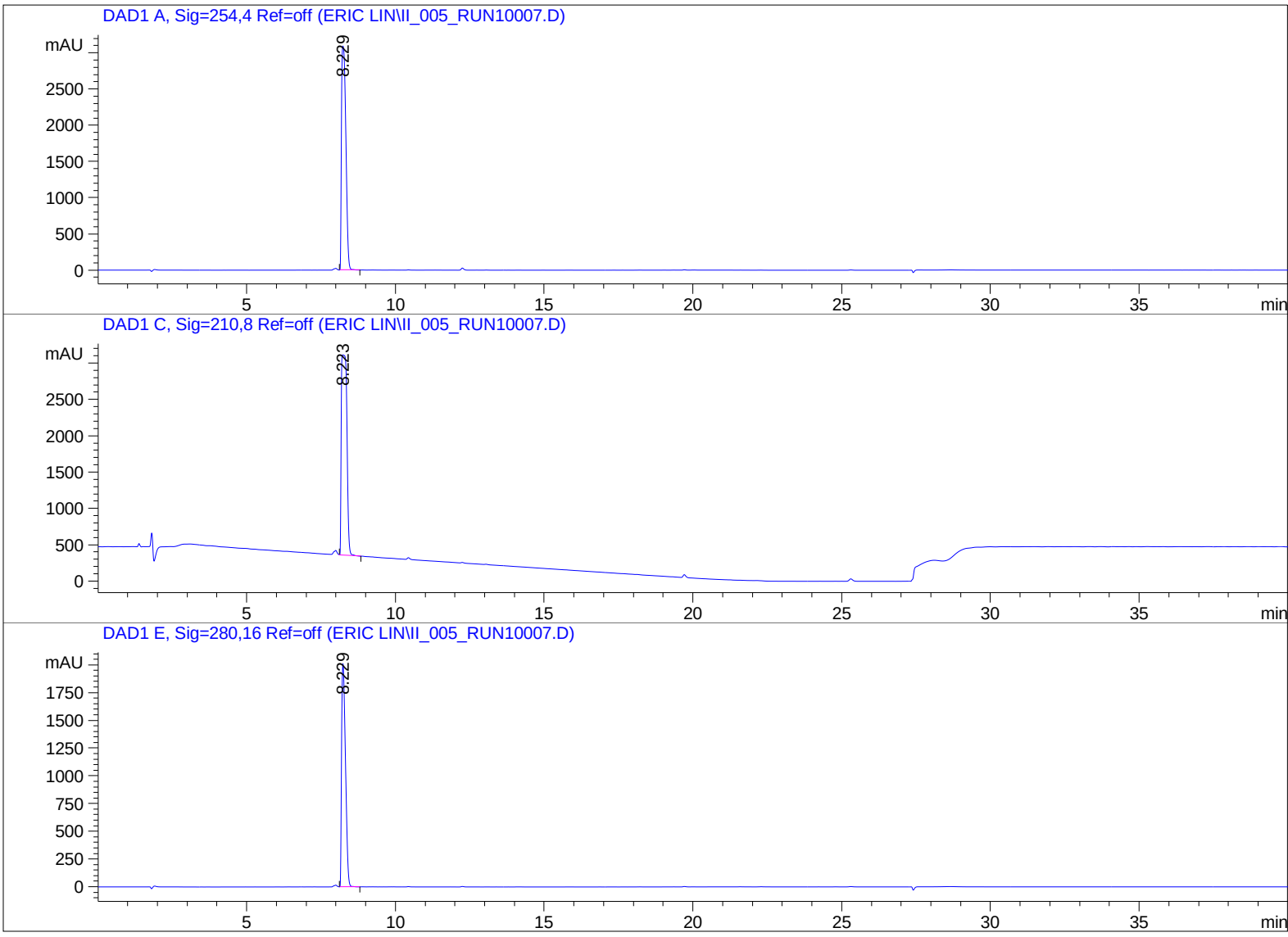
47


173.59
153.19
152.88
142.55
140.64
138.31
133.53
129.15
127.68
122.56
109.99
108.46
105.30
77.25
77.00
76.74
65.99
60.91
56.35
56.19
55.83
34.02
27.06
25.57
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

Data File C:\CHEM32\1\DATA\ERIC LIN\II_005_RUN10007.D
Sample Name: CML_II_005_run1

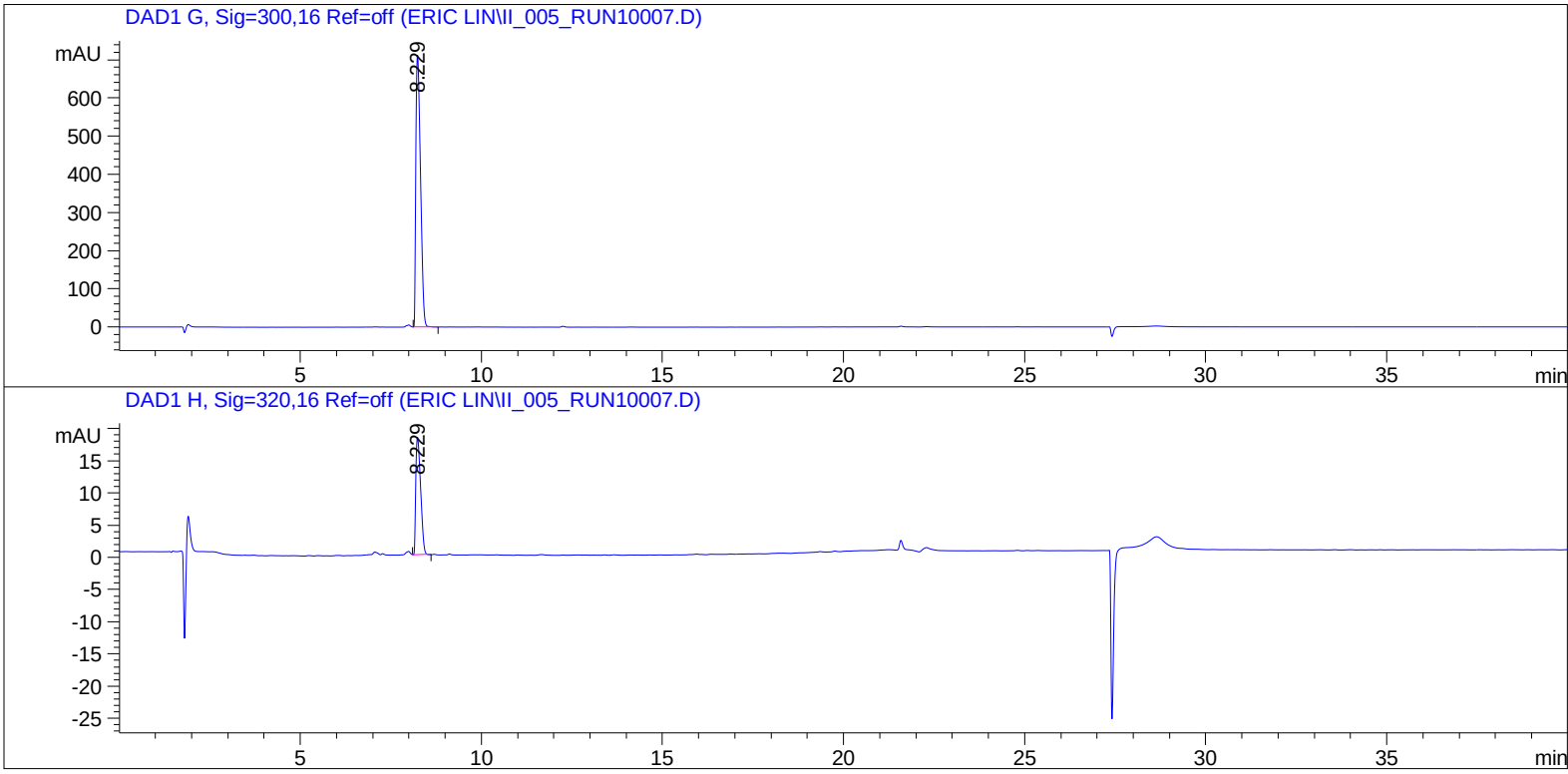
HPLC Traces of Compound 47

```
==========================================================================
Acq. Operator   : ERIC LIN
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 8/26/2012 6:28:39 PM
Acq. Method     : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed    : 8/26/2012 6:29:45 PM by ERIC LIN
                  (modified after loading)
Analysis Method : C:\CHEM32\1\DATA\ERIC LIN\II_005_RUN10007.D\DA.M (MASTERMETHOD.M)
Last changed    : 8/26/2012 8:08:08 PM by ERIC LIN
Sample Info     :
```



Data File C:\CHEM32\1\DATA\ERIC LIN\II_005_RUN10007.D
Sample Name: CML_II_005_run1

HPLC Traces of Compound 47



==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.229	VV	0.1674	3.16497e4	3092.45068	100.0000
Totals :				3.16497e4	3092.45068	

Signal 2: DAD1 C, Sig=210,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.223	VV	0.1718	3.58401e4	2754.71655	100.0000
Totals :				3.58401e4	2754.71655	

HPLC Traces of Compound 47

Signal 3: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.229	VV	0.1462	1.83095e4	2011.87817	100.0000
Totals :				1.83095e4	2011.87817	

Signal 4: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.229	VB	0.1406	6393.18701	712.86285	100.0000
Totals :				6393.18701	712.86285	

Signal 5: DAD1 H, Sig=320,16 Ref=off

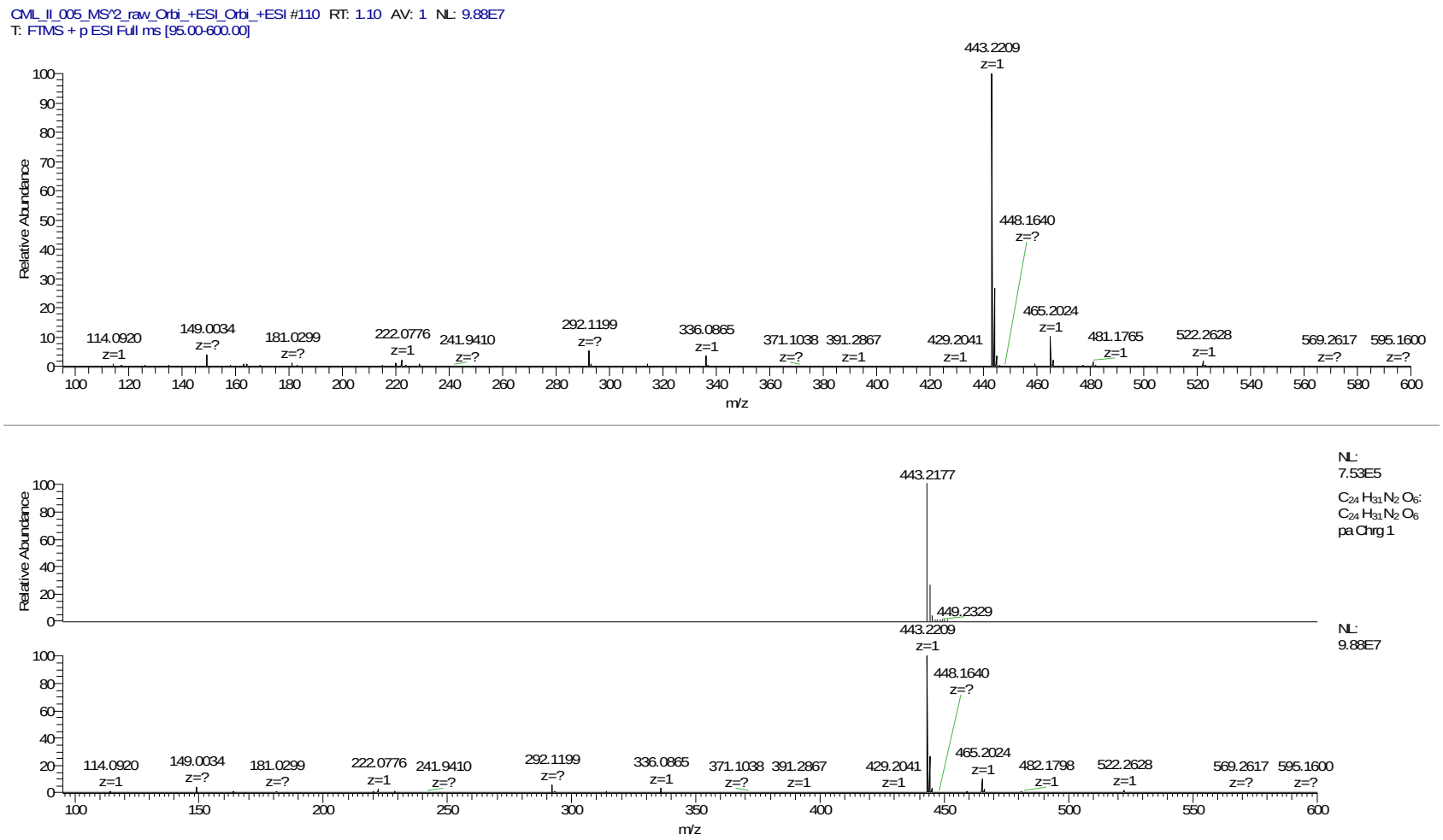
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.229	VB	0.1486	169.87639	18.24767	100.0000
Totals :				169.87639	18.24767	

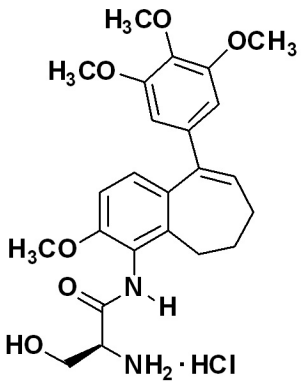
==========

*** End of Report ***

HRMS of Compound 47

CML_II_005_MS^2_raw_Orbi_+ESI_Orbi_+ESI 8/20/2012 12:52:35 PM

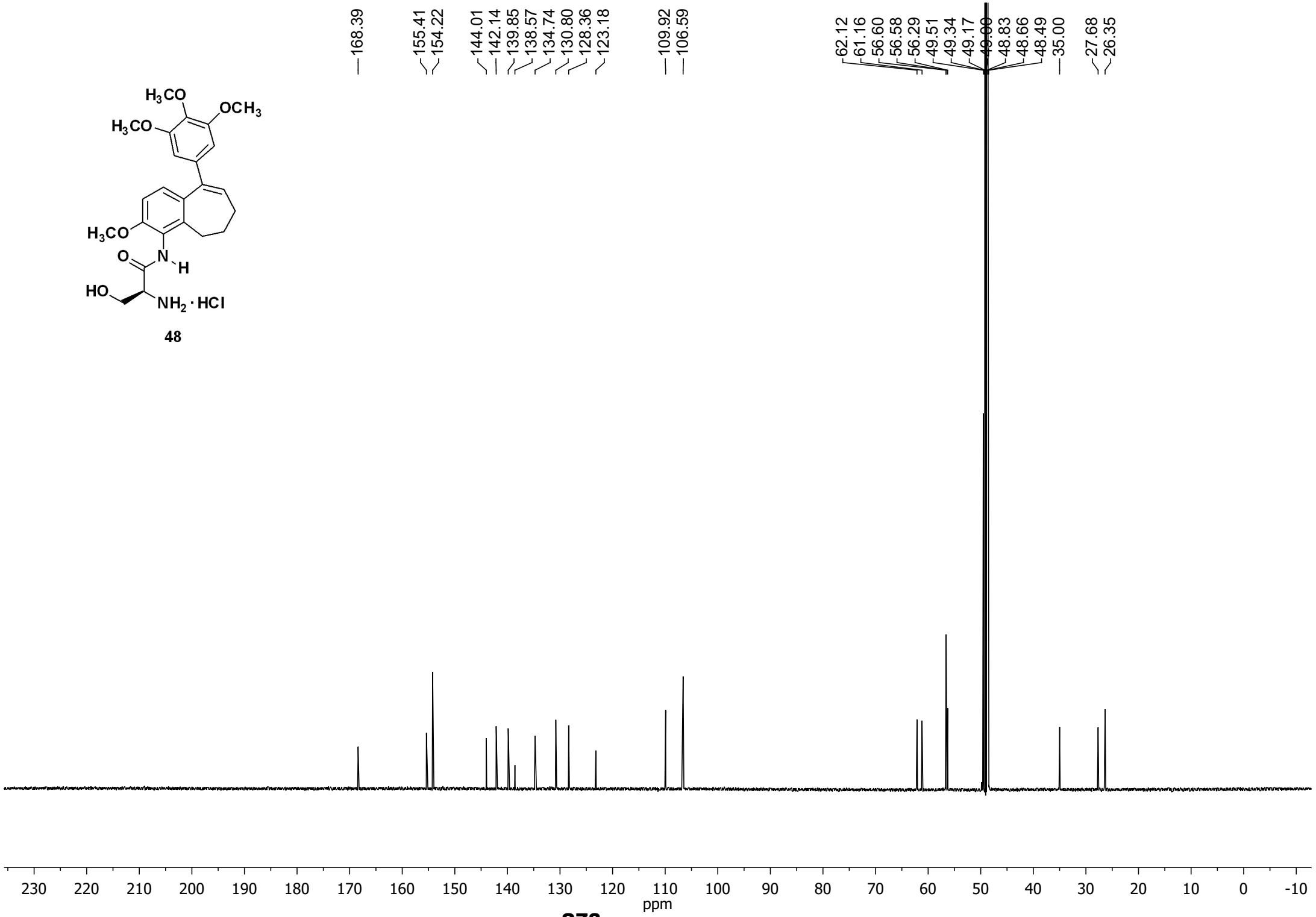




48

H3CO
OCH3
H3CO
H3CO
O
N
H
HO
NH2 · HCl

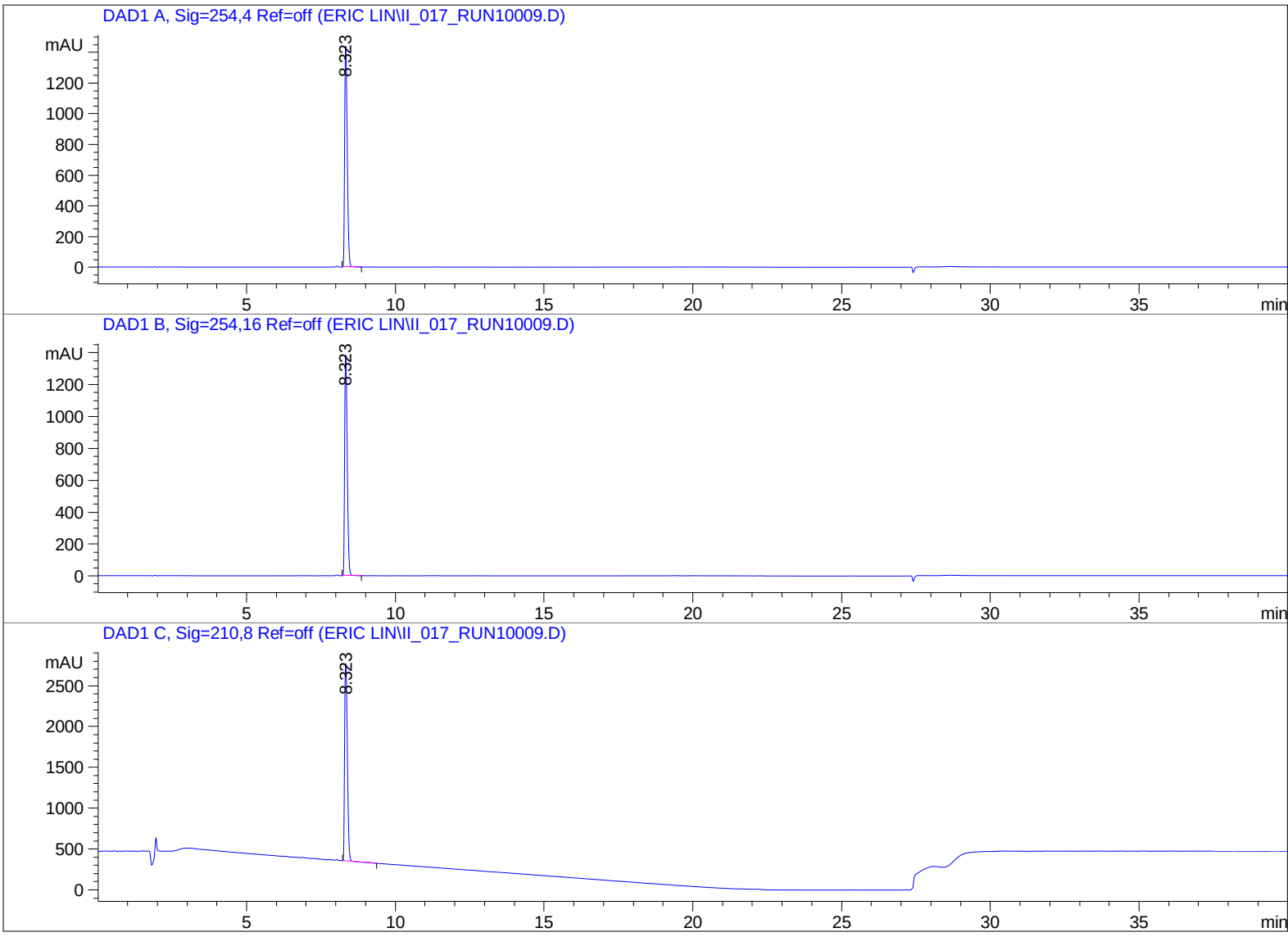
48


168.39
155.41
154.22
144.01
142.14
139.85
138.57
134.74
130.80
128.36
123.18
109.92
106.59
62.12
61.16
56.60
56.58
56.29
49.51
49.34
49.17
48.83
48.66
48.49
35.00
27.68
26.35
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

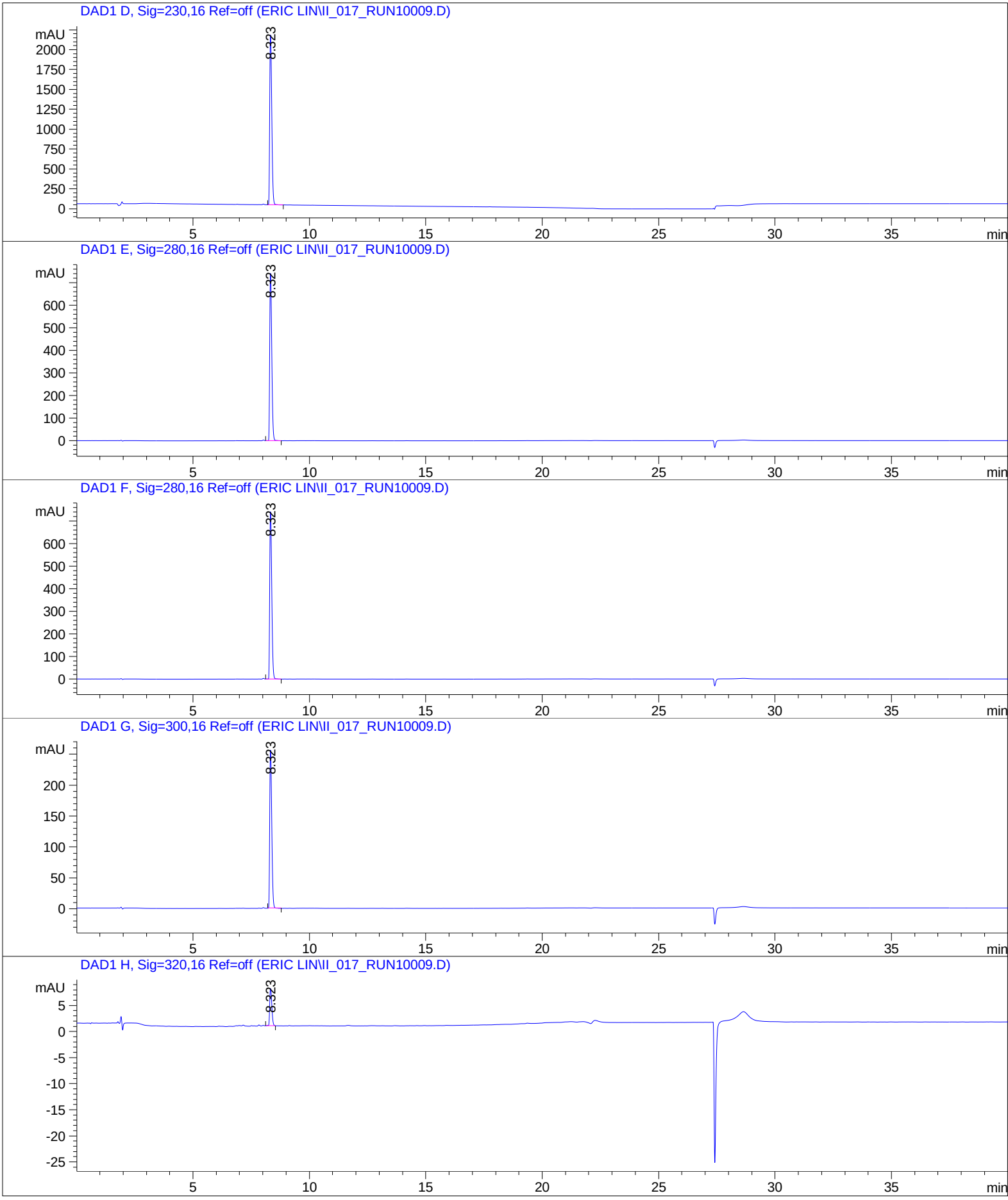
Data File C:\CHEM32\1\DATA\ERIC LIN\II_017_RUN10009.D
Sample Name: CML_II_017_run1

HPLC Traces of Compound 48

```
==========================================================================
Acq. Operator   : ERIC LIN
Acq. Instrument : Instrument 1                    Location :   -
Injection Date  : 8/26/2012 8:14:29 PM
Acq. Method     : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed    : 8/26/2012 8:11:49 PM by ERIC LIN
                  (modified after loading)
Analysis Method : C:\CHEM32\1\DATA\ERIC LIN\II_017_RUN10009.D\DA.M (MASTERMETHOD.M)
Last changed    : 8/26/2012 9:04:41 PM by ERIC LIN
Sample Info     :
```



HPLC Traces of Compound 48



HPLC Traces of Compound 48

```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.323 VV    0.0949 8745.86328 1439.63110 100.0000

Totals :                  8745.86328 1439.63110



Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.323 VB    0.0948 8403.83496 1384.48010 100.0000

Totals :                  8403.83496 1384.48010



Signal 3: DAD1 C, Sig=210,8 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.323 VB    0.1035 1.56445e4  2416.47046 100.0000

Totals :                  1.56445e4  2416.47046



Signal 4: DAD1 D, Sig=230,16 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.323 VV    0.0977 1.31259e4  2134.97778 100.0000

Totals :                  1.31259e4  2134.97778
```

HPLC Traces of Compound 48

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.323	VB	0.0948	4502.56006	741.66730	100.0000
Totals :				4502.56006	741.66730	

Signal 6: DAD1 F, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.323	VB	0.0948	4502.56006	741.66730	100.0000
Totals :				4502.56006	741.66730	

Signal 7: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.323	BB	0.0949	1553.26367	255.71465	100.0000
Totals :				1553.26367	255.71465	

Signal 8: DAD1 H, Sig=320,16 Ref=off

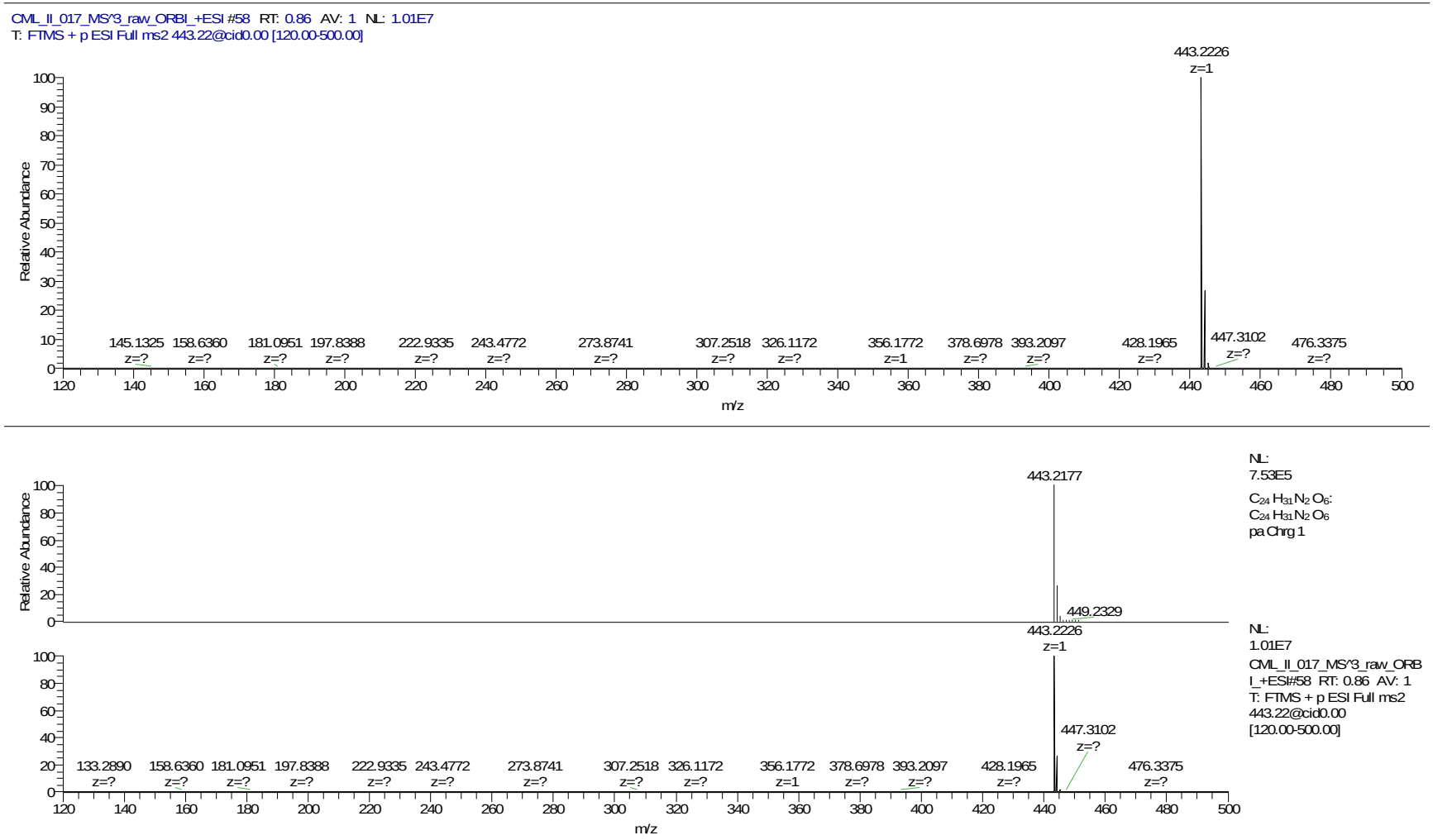
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.323	BB	0.0998	45.32738	7.16882	100.0000
Totals :				45.32738	7.16882	

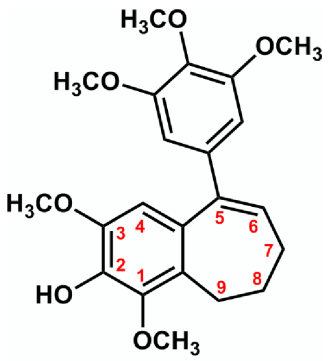
==========

*** End of Report ***

HRMS of Compound 48

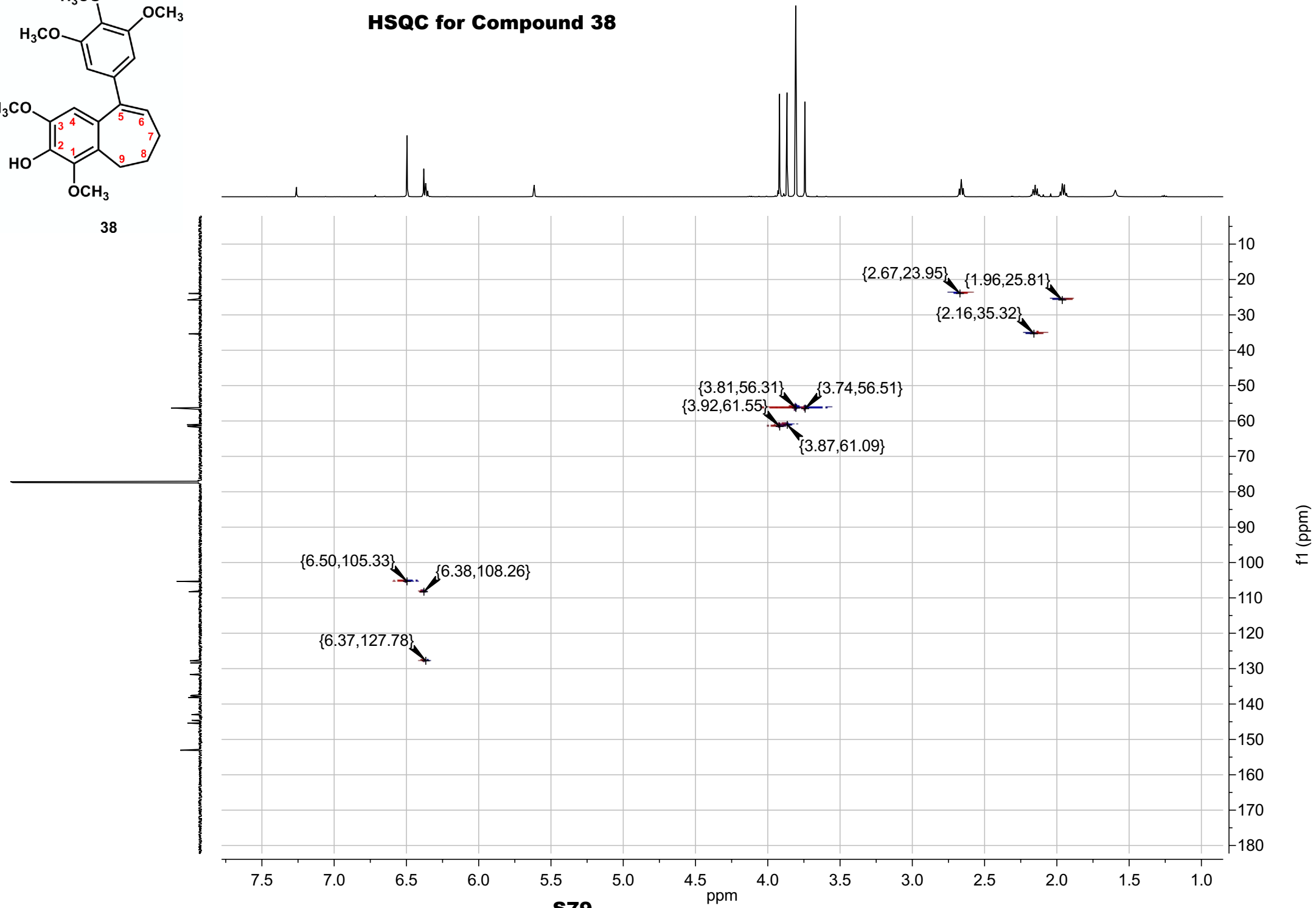
CML_II_017_MS^3_raw_ORBI_+ESI 8/26/2012 11:33:23 PM

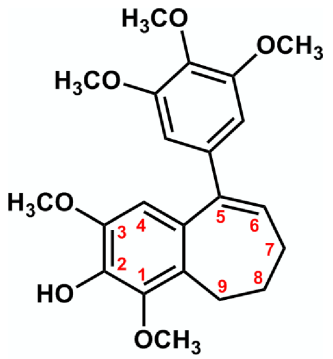




38

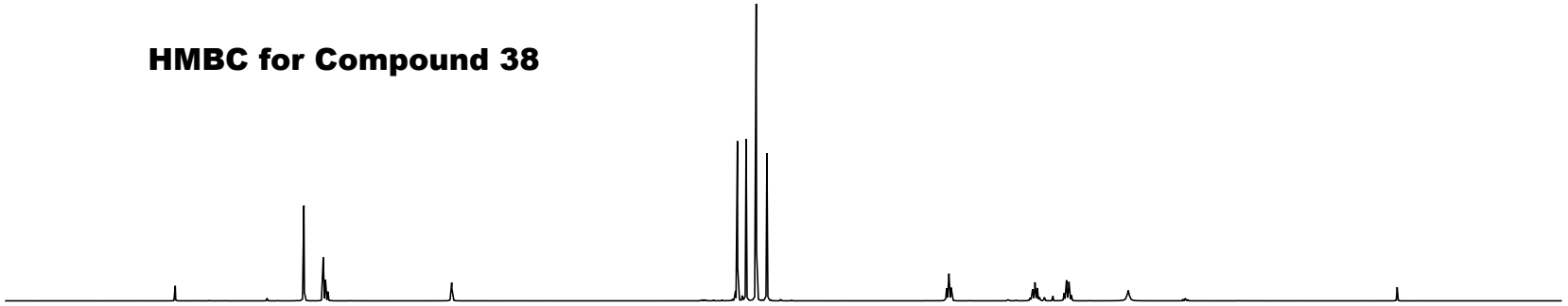
HSQC for Compound 38

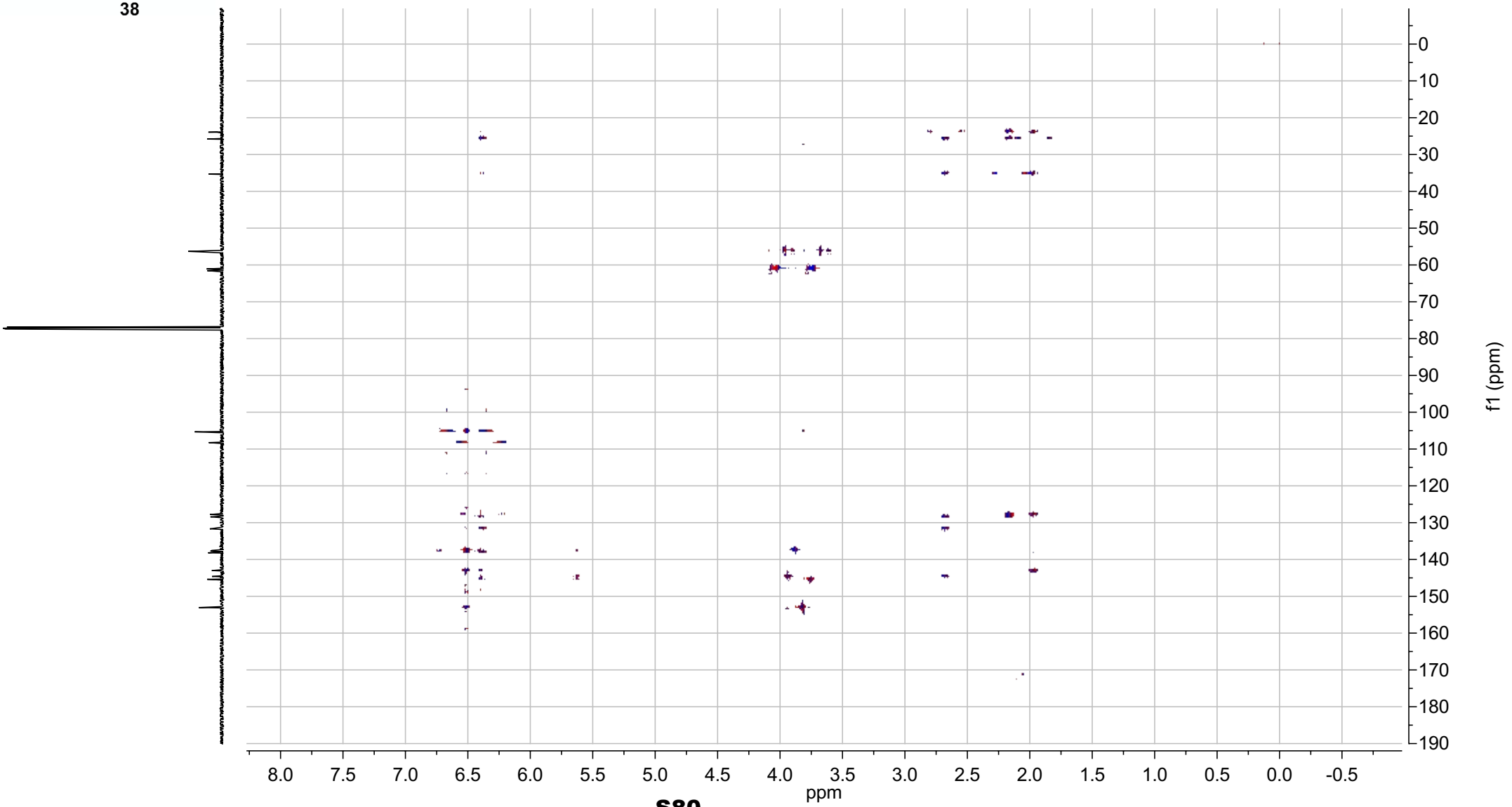


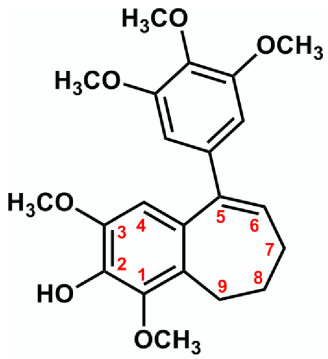


38

HMBC for Compound 38

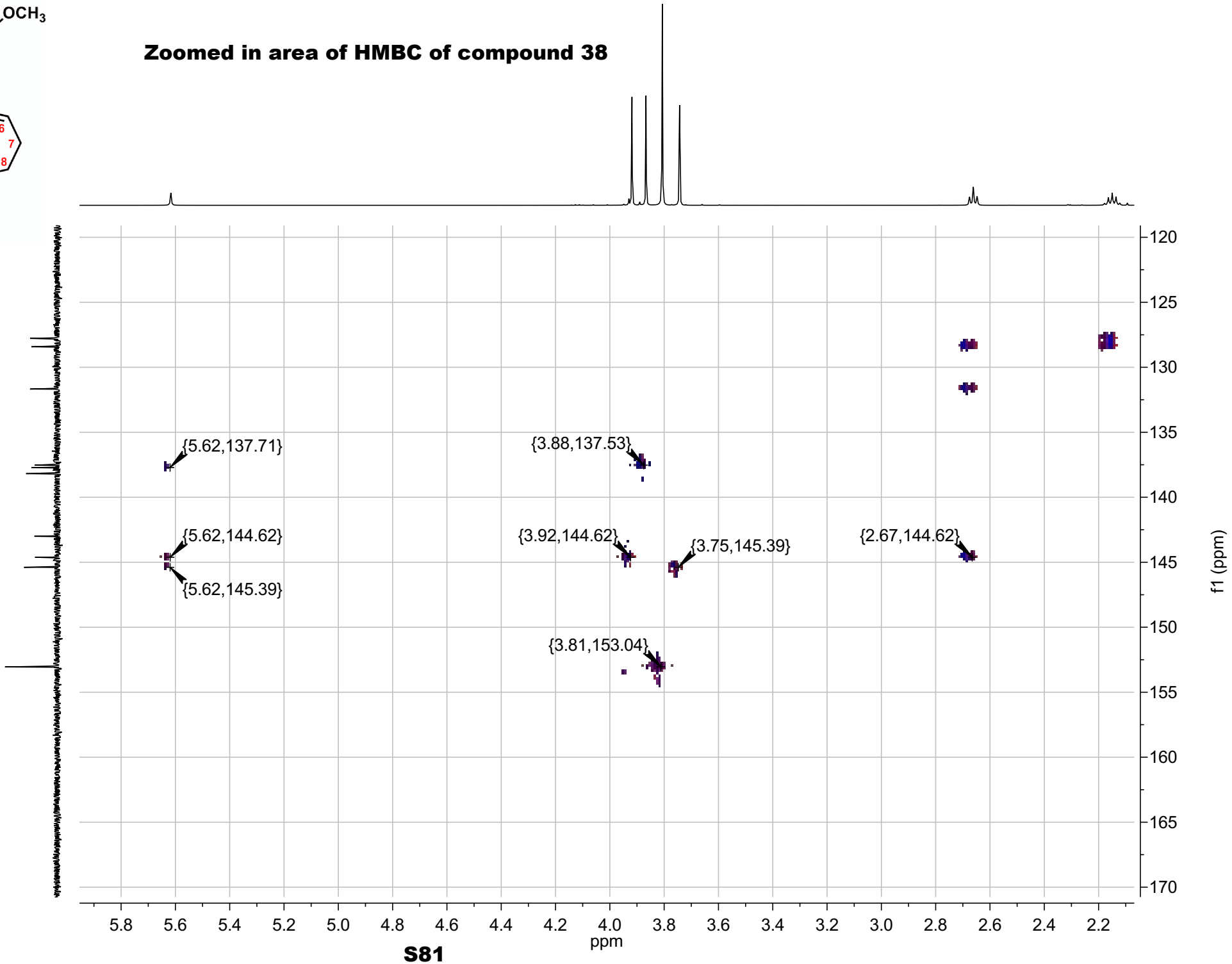






38

Zoomed in area of HMBC of compound 38



The regio demethylation en route to final compound 38 was determined by the HSQC and HMBC of compound 38. The HSQC revealed a total of ten C-H correlations as expected with the key coordination of the carbon at the 4 position (127.78 ppm) to the proton at 6.37 ppm. The HMBC revealed the coordination of the free phenol proton to a total of three carbons; the carbon at position 3 (145.39 ppm) which is also coordinated to the methoxy protons (3.75 ppm) at position 3, the carbon at position 1 (144.62 ppm) which is also coordinated to the methoxy protons (3.92 ppm) at position 1 and the aliphatic protons (2.67 ppm) at position 9, and the coordination to carbon at position 2 (137.71 ppm) for which the phenol substituent is attached. The assignment of 137.71 ppm to the carbon at position 2 was determined by the observed coupling to the phenolic proton in addition to the absence of coupling of the phenolic proton to the carbon at position 4 (127.78 ppm) which was established by the HSQC.

X-ray Crystallographic Analysis:

X-ray crystallographic analysis of compound **38**.[S1] Crystallographic data were collected on a crystal of **38** with dimensions 0.20 x 0.18 x 0.10 mm^3. Data were collected at 110 K on a Bruker X8 Apex using Mo KR radiation (λ = 0.71073 Å). The structure was solved by direct methods after correction of the data using SADABS. Crystallographic data and definement details for the complex mentioned herein is found in the Supporting Information (Table S1-S4). The thermal ellipsoid plots at 50% probability for compound **38** is displayed in Figure S1 and Figures S2. All data were processed using the Bruker AXS SHELXTL software, version 6.10.

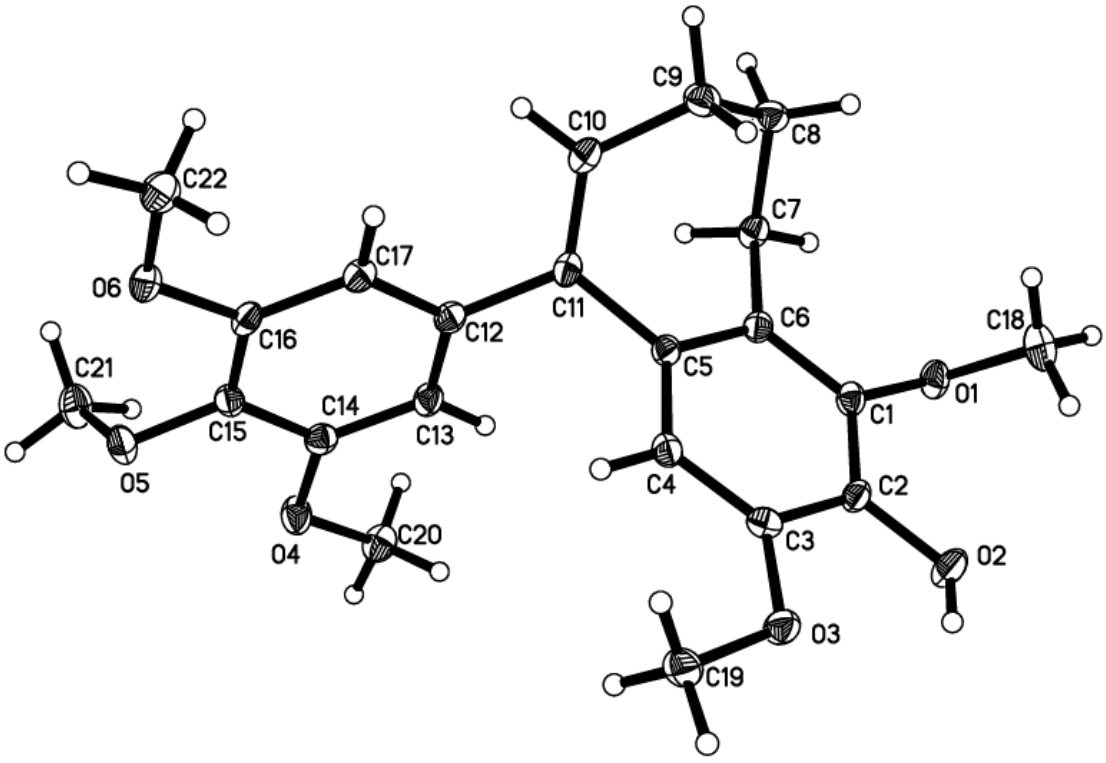


Figure S1. X-ray crystallogaphy of compound **38**

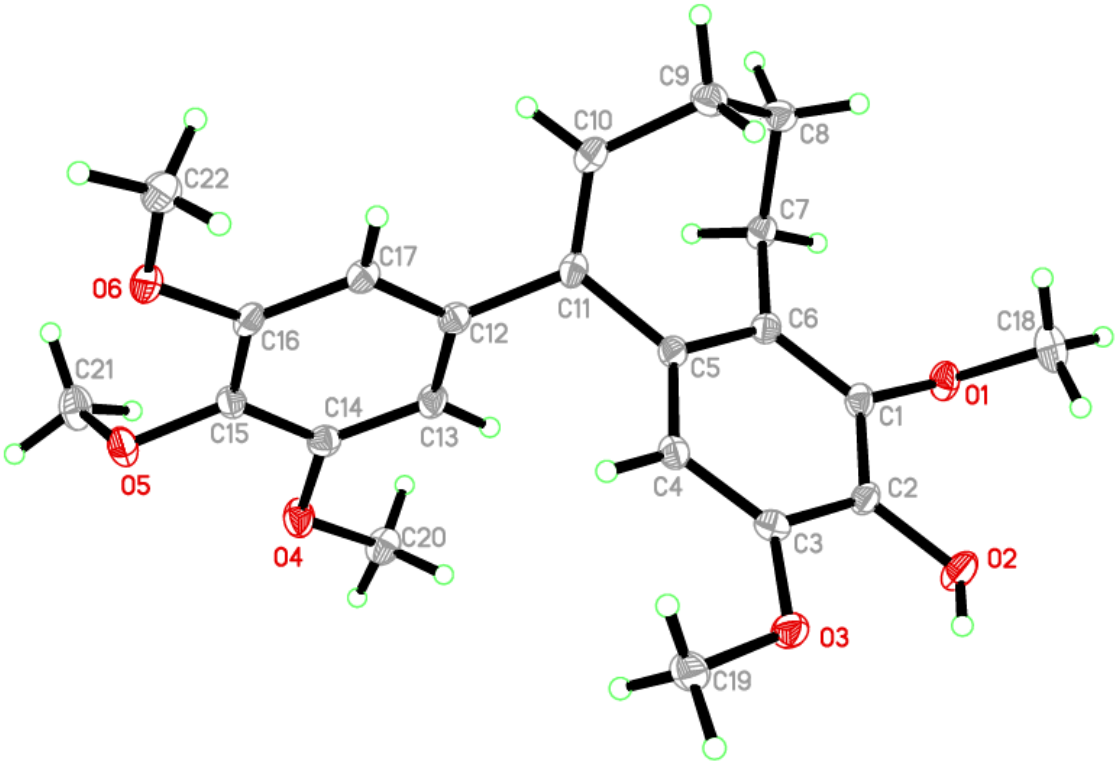


Figure S2. X-ray crystallography of compound **38**

Table S1. Crystal data and structure refinement for **38**

Identification code	kp63	
Empirical formula	C22 H26 O6	
Formula weight	386.43	
Temperature	110(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 5.1754(3) Å	α= 90°.
	b = 11.8147(7) Å	β= 90°.
	c = 30.8093(18) Å	γ = 90°.
Volume	1883.86(19) $Å^3$	
Z	4	
Density (calculated)	1.362 Mg/m^3	
Absorption coefficient	0.099 mm^{-1}	
F(000)	824	
Crystal size	0.20 x 0.18 x 0.10 mm^3	
Theta range for data collection	1.32 to 28.34°.	
Index ranges	-6<=h<=6, -15<=k<=15, -41<=l<=35	
Reflections collected	17128	
Independent reflections	4660 [R(int) = 0.0450]	
Completeness to theta = 28.34°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9907 and 0.9806	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4660 / 0 / 262	
Goodness-of-fit on F^2	1.231	
Final R indices [I>2sigma(I)]	R1 = 0.0393, wR2 = 0.0961	
R indices (all data)	R1 = 0.0468, wR2 = 0.1101	
Largest diff. peak and hole	0.241 and -0.267 $e.Å^{-3}$	

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **38**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(2)	6188(3)	1777(1)	1255(1)	21(1)
O(3)	9569(2)	3137(1)	1643(1)	18(1)
O(1)	2618(2)	2567(1)	683(1)	18(1)
O(6)	9213(2)	9929(1)	1555(1)	18(1)
O(5)	6103(2)	9665(1)	2243(1)	18(1)
O(4)	2878(2)	7889(1)	2305(1)	20(1)
C(5)	5822(3)	5215(1)	997(1)	13(1)
C(9)	5668(3)	5989(2)	91(1)	18(1)
C(2)	6132(3)	2910(1)	1168(1)	14(1)
C(7)	2100(3)	4910(1)	479(1)	16(1)
C(3)	7829(3)	3656(1)	1374(1)	15(1)
C(6)	4137(3)	4473(1)	785(1)	14(1)
C(10)	5642(3)	6782(1)	473(1)	18(1)
C(11)	5791(3)	6442(1)	887(1)	14(1)
C(4)	7635(3)	4802(1)	1296(1)	14(1)
C(1)	4326(3)	3315(1)	874(1)	14(1)
C(8)	3170(3)	5295(2)	40(1)	18(1)
C(17)	7590(3)	8200(1)	1221(1)	15(1)
C(13)	4324(3)	7147(1)	1608(1)	16(1)
C(16)	7617(3)	9001(1)	1552(1)	14(1)
C(15)	5982(3)	8892(1)	1908(1)	15(1)
C(12)	5924(3)	7276(1)	1247(1)	15(1)
C(14)	4351(3)	7953(1)	1936(1)	15(1)
C(20)	1001(3)	7006(1)	2323(1)	20(1)
C(19)	11307(3)	3853(2)	1877(1)	19(1)
C(18)	3801(4)	1828(2)	376(1)	26(1)
C(22)	10967(4)	10039(2)	1198(1)	21(1)
C(21)	3908(3)	10401(2)	2267(1)	22(1)

Table S3. Bond lengths [Å] and angles [°] for **38**.

O(2)-C(2)	1.3657(19)
O(3)-C(3)	1.3701(19)
O(3)-C(19)	1.429(2)
O(1)-C(1)	1.3814(19)
O(1)-C(18)	1.426(2)
O(6)-C(16)	1.3728(19)
O(6)-C(22)	1.432(2)
O(5)-C(15)	1.3797(19)
O(5)-C(21)	1.432(2)
O(4)-C(14)	1.370(2)
O(4)-C(20)	1.427(2)
C(5)-C(6)	1.398(2)
C(5)-C(4)	1.403(2)
C(5)-C(11)	1.489(2)
C(9)-C(10)	1.504(2)
C(9)-C(8)	1.539(2)
C(2)-C(1)	1.385(2)
C(2)-C(3)	1.398(2)
C(7)-C(6)	1.505(2)
C(7)-C(8)	1.531(2)
C(3)-C(4)	1.378(2)
C(6)-C(1)	1.399(2)
C(10)-C(11)	1.339(2)
C(11)-C(12)	1.485(2)
C(17)-C(16)	1.392(2)
C(17)-C(12)	1.394(2)
C(13)-C(14)	1.390(2)
C(13)-C(12)	1.394(2)
C(16)-C(15)	1.391(2)
C(15)-C(14)	1.396(2)
C(3)-O(3)-C(19)	116.97(12)
C(1)-O(1)-C(18)	113.57(13)
C(16)-O(6)-C(22)	116.69(13)

C(15)-O(5)-C(21)	113.84(13)
C(14)-O(4)-C(20)	116.92(13)
C(6)-C(5)-C(4)	120.35(14)
C(6)-C(5)-C(11)	119.88(14)
C(4)-C(5)-C(11)	119.69(15)
C(10)-C(9)-C(8)	113.87(14)
O(2)-C(2)-C(1)	118.81(14)
O(2)-C(2)-C(3)	121.03(15)
C(1)-C(2)-C(3)	120.16(14)
C(6)-C(7)-C(8)	113.65(13)
O(3)-C(3)-C(4)	126.44(15)
O(3)-C(3)-C(2)	113.92(14)
C(4)-C(3)-C(2)	119.64(15)
C(5)-C(6)-C(1)	118.54(15)
C(5)-C(6)-C(7)	120.91(14)
C(1)-C(6)-C(7)	120.52(14)
C(11)-C(10)-C(9)	123.94(15)
C(10)-C(11)-C(12)	121.01(14)
C(10)-C(11)-C(5)	120.55(15)
C(12)-C(11)-C(5)	118.44(14)
C(3)-C(4)-C(5)	120.37(15)
O(1)-C(1)-C(2)	119.29(14)
O(1)-C(1)-C(6)	119.76(14)
C(2)-C(1)-C(6)	120.89(14)
C(7)-C(8)-C(9)	111.80(14)
C(16)-C(17)-C(12)	119.73(15)
C(14)-C(13)-C(12)	119.97(15)
O(6)-C(16)-C(17)	123.60(15)
O(6)-C(16)-C(15)	115.79(14)
C(17)-C(16)-C(15)	120.61(15)
O(5)-C(15)-C(16)	120.04(15)
O(5)-C(15)-C(14)	120.47(15)
C(16)-C(15)-C(14)	119.34(15)
C(13)-C(12)-C(17)	119.96(15)
C(13)-C(12)-C(11)	119.69(14)
C(17)-C(12)-C(11)	120.32(15)

O(4)-C(14)-C(13)	124.06(15)
O(4)-C(14)-C(15)	115.57(14)
C(13)-C(14)-C(15)	120.36(15)

Symmetry transformations used to generate equivalent atoms:

Table S4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **38**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(2)	23(1)	12(1)	28(1)	3(1)	-6(1)	0(1)
O(3)	20(1)	15(1)	19(1)	2(1)	-6(1)	-1(1)
O(1)	18(1)	14(1)	23(1)	-3(1)	-3(1)	-2(1)
O(6)	20(1)	14(1)	20(1)	0(1)	-1(1)	-5(1)
O(5)	19(1)	17(1)	19(1)	-6(1)	-4(1)	1(1)
O(4)	25(1)	17(1)	19(1)	-4(1)	7(1)	-4(1)
C(5)	15(1)	12(1)	13(1)	-1(1)	3(1)	1(1)
C(9)	20(1)	20(1)	15(1)	0(1)	2(1)	-2(1)
C(2)	17(1)	10(1)	16(1)	1(1)	1(1)	0(1)
C(7)	14(1)	14(1)	19(1)	0(1)	-2(1)	0(1)
C(3)	15(1)	18(1)	12(1)	1(1)	0(1)	0(1)
C(6)	15(1)	13(1)	14(1)	0(1)	2(1)	-1(1)
C(10)	19(1)	13(1)	21(1)	2(1)	0(1)	-2(1)
C(11)	15(1)	11(1)	18(1)	-1(1)	2(1)	0(1)
C(4)	15(1)	14(1)	14(1)	-2(1)	0(1)	-1(1)
C(1)	15(1)	13(1)	16(1)	-2(1)	2(1)	-2(1)
C(8)	20(1)	20(1)	16(1)	2(1)	-3(1)	0(1)
C(17)	15(1)	13(1)	17(1)	1(1)	1(1)	1(1)
C(13)	16(1)	13(1)	18(1)	0(1)	0(1)	-4(1)
C(16)	13(1)	10(1)	20(1)	2(1)	-4(1)	0(1)
C(15)	17(1)	13(1)	15(1)	-2(1)	-4(1)	3(1)
C(12)	16(1)	12(1)	16(1)	1(1)	-2(1)	3(1)
C(14)	15(1)	15(1)	16(1)	1(1)	0(1)	2(1)
C(20)	19(1)	18(1)	24(1)	1(1)	5(1)	-1(1)
C(19)	18(1)	20(1)	19(1)	0(1)	-5(1)	-4(1)
C(18)	29(1)	22(1)	26(1)	-10(1)	0(1)	-2(1)
C(22)	21(1)	20(1)	22(1)	1(1)	1(1)	-5(1)
C(21)	20(1)	20(1)	27(1)	-7(1)	0(1)	3(1)

S1. Crystallographic data for structure **38** (deposition number CCDC 953837) reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

X-ray Crystallographic Analysis:

X-ray crystallographic analysis of compound **39**.[S2] Crystallographic data were collected on a crystal of **39** with dimensions 0.24 x 0.23 x 0.19 mm^3. Data were collected at 110 K on a Bruker X8 Apex using Mo KR radiation (λ = 0.71073 Å). The structure was solved by direct methods after correction of the data using SADABS. Crystallographic data and definement details for the complex mentioned herein is found in the Supporting Information (Table S5-S9). The thermal ellipsoid plots at 50% probability for compound **39** is displayed in Figure S3 and Figures S4. All data were processed using the Bruker AXS SHELXTL software, version 6.10.

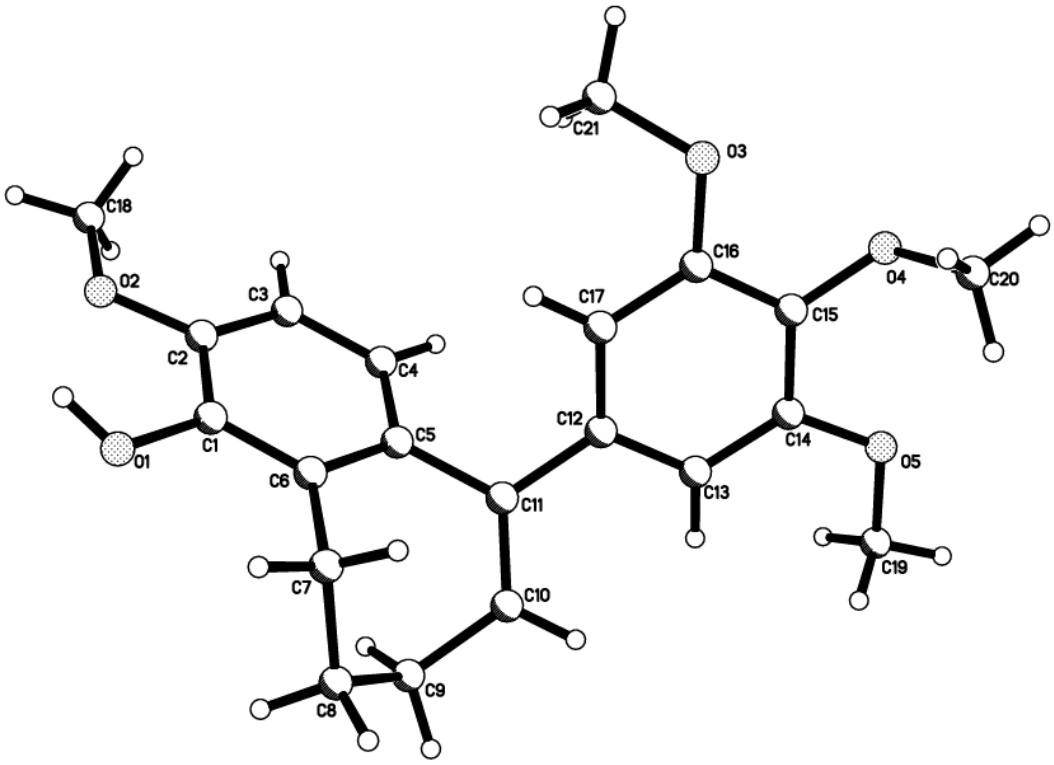


Figure S3. X-ray crystallography of compound **39**

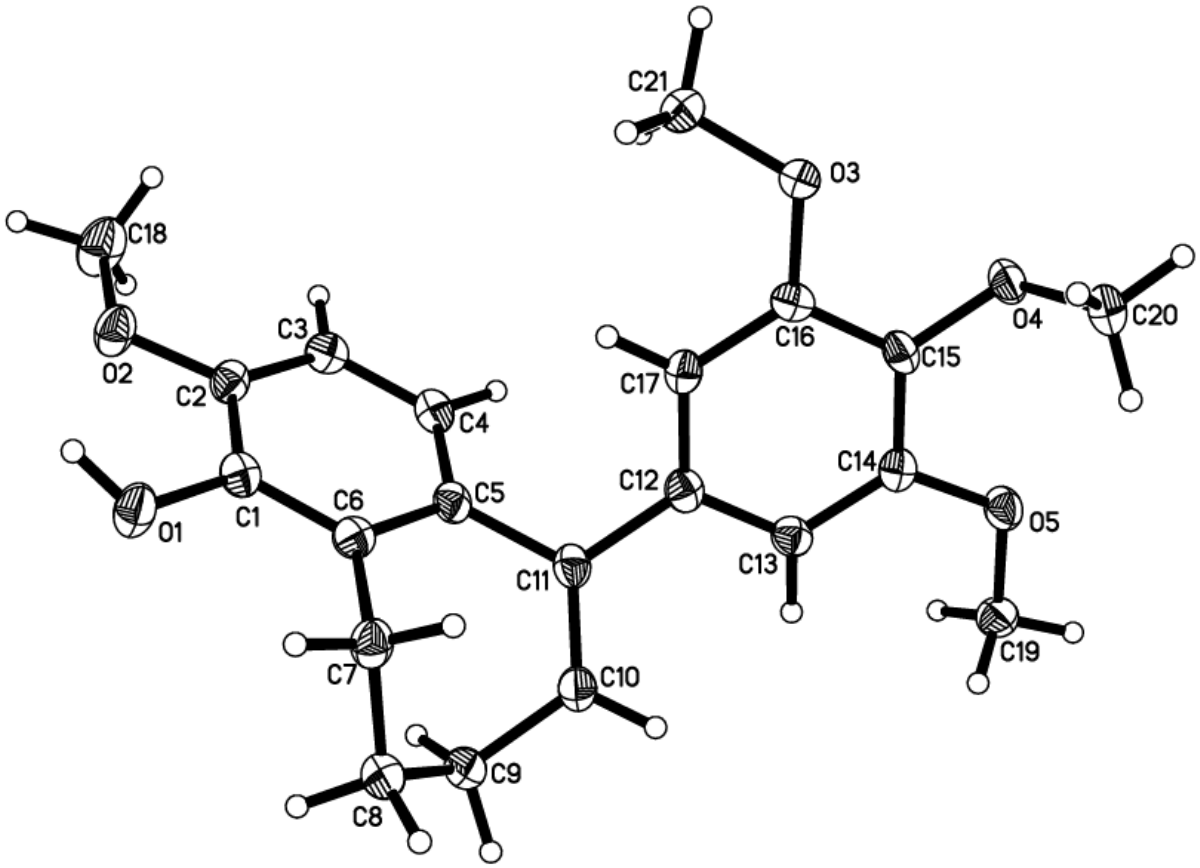


Figure S4. X-ray crystallography of compound **39**

Table S5. Crystal data and structure refinement for compound **39**.

Identification code	kp16	
Empirical formula	C21 H24 O5	
Formula weight	356.40	
Temperature	110(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 16.8122(12) Å	α= 90°.
	b = 10.9319(8) Å	β= 90°.
	c = 19.7517(14) Å	γ = 90°.
Volume	3630.2(5) $Å^3$	
Z	8	
Density (calculated)	1.304 Mg/m^3	
Absorption coefficient	0.092 mm^{-1}	
F(000)	1520	
Crystal size	0.24 x 0.23 x 0.19 mm^3	
Theta range for data collection	2.39 to 26.46°.	
Index ranges	-16<=h<=21, -13<=k<=12, -12<=l<=24	
Reflections collected	23164	
Independent reflections	3721 [R(int) = 0.0492]	
Completeness to theta = 26.46°	99.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9826 and 0.9782	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3721 / 0 / 243	
Goodness-of-fit on F^2	1.016	
Final R indices [I>2sigma(I)]	R1 = 0.0383, wR2 = 0.0834	
R indices (all data)	R1 = 0.0631, wR2 = 0.0945	
Largest diff. peak and hole	0.235 and -0.189 $e.Å^{-3}$	

Table S6. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **39**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	
O(1)	6395(1)	3926(1)	2768(1)	28(1)
O(2)	6631(1)	1736(1)	2218(1)	27(1)
O(3)	2227(1)	2486(1)	1280(1)	22(1)
O(4)	1432(1)	3679(1)	289(1)	24(1)
O(5)	2104(1)	5563(1)	-372(1)	24(1)
C(1)	6003(1)	3635(2)	2180(1)	21(1)
C(2)	6115(1)	2490(2)	1876(1)	21(1)
C(3)	5728(1)	2207(1)	1279(1)	22(1)
C(4)	5227(1)	3065(1)	987(1)	22(1)
C(5)	5111(1)	4209(1)	1279(1)	20(1)
C(6)	5506(1)	4501(1)	1888(1)	20(1)
C(7)	5361(1)	5719(1)	2230(1)	24(1)
C(8)	5734(1)	6812(2)	1863(1)	29(1)
C(9)	5610(1)	6737(2)	1093(1)	28(1)
C(10)	4792(1)	6295(2)	902(1)	24(1)
C(11)	4569(1)	5123(1)	965(1)	21(1)
C(12)	3761(1)	4712(1)	761(1)	20(1)
C(13)	3341(1)	5326(1)	254(1)	21(1)
C(14)	2562(1)	5001(1)	109(1)	20(1)
C(15)	2195(1)	4043(1)	458(1)	20(1)
C(16)	2619(1)	3416(1)	950(1)	19(1)
C(17)	3398(1)	3748(1)	1102(1)	20(1)
C(18)	6800(1)	578(2)	1913(1)	37(1)
C(19)	2490(1)	6476(2)	-773(1)	25(1)
C(20)	824(1)	4457(2)	555(1)	29(1)
C(21)	2724(1)	1556(1)	1572(1)	24(1)

Table S7. Bond lengths [Å] and angles [°] for **39**.

O(1)-C(1)	1.3717(18)
O(1)-H(1)	0.89(2)
O(2)-C(2)	1.3740(18)
O(2)-C(18)	1.4300(19)
O(3)-C(16)	1.3762(18)
O(3)-C(21)	1.4368(18)
O(4)-C(15)	1.3846(18)
O(4)-C(20)	1.4299(19)
O(5)-C(14)	1.3688(18)
O(5)-C(19)	1.4300(18)
C(1)-C(6)	1.387(2)
C(1)-C(2)	1.402(2)
C(2)-C(3)	1.380(2)
C(3)-C(4)	1.386(2)
C(3)-H(3)	0.9500
C(4)-C(5)	1.391(2)
C(4)-H(4)	0.9500
C(5)-C(6)	1.411(2)
C(5)-C(11)	1.488(2)
C(6)-C(7)	1.513(2)
C(7)-C(8)	1.533(2)
C(7)-H(7A)	0.9900
C(7)-H(7B)	0.9900
C(8)-C(9)	1.537(2)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(10)	1.505(2)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(10)-C(11)	1.340(2)
C(10)-H(10)	0.9500
C(11)-C(12)	1.486(2)
C(12)-C(17)	1.392(2)
C(12)-C(13)	1.397(2)

C(13)-C(14)	1.386(2)
C(13)-H(13)	0.9500
C(14)-C(15)	1.397(2)
C(15)-C(16)	1.387(2)
C(16)-C(17)	1.390(2)
C(17)-H(17)	0.9500
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800

C(1)-O(1)-H(1)	109.8(14)
C(2)-O(2)-C(18)	116.75(13)
C(16)-O(3)-C(21)	115.67(12)
C(15)-O(4)-C(20)	113.70(12)
C(14)-O(5)-C(19)	116.23(12)
O(1)-C(1)-C(6)	118.85(14)
O(1)-C(1)-C(2)	120.40(14)
C(6)-C(1)-C(2)	120.74(14)
O(2)-C(2)-C(3)	125.60(14)
O(2)-C(2)-C(1)	114.15(13)
C(3)-C(2)-C(1)	120.25(14)
C(2)-C(3)-C(4)	119.27(15)
C(2)-C(3)-H(3)	120.4
C(4)-C(3)-H(3)	120.4
C(3)-C(4)-C(5)	121.43(14)
C(3)-C(4)-H(4)	119.3
C(5)-C(4)-H(4)	119.3

C(4)-C(5)-C(6)	119.37(14)
C(4)-C(5)-C(11)	121.10(14)
C(6)-C(5)-C(11)	119.52(14)
C(1)-C(6)-C(5)	118.93(14)
C(1)-C(6)-C(7)	120.82(14)
C(5)-C(6)-C(7)	120.20(14)
C(6)-C(7)-C(8)	114.16(13)
C(6)-C(7)-H(7A)	108.7
C(8)-C(7)-H(7A)	108.7
C(6)-C(7)-H(7B)	108.7
C(8)-C(7)-H(7B)	108.7
H(7A)-C(7)-H(7B)	107.6
C(7)-C(8)-C(9)	111.76(13)
C(7)-C(8)-H(8A)	109.3
C(9)-C(8)-H(8A)	109.3
C(7)-C(8)-H(8B)	109.3
C(9)-C(8)-H(8B)	109.3
H(8A)-C(8)-H(8B)	107.9
C(10)-C(9)-C(8)	112.85(14)
C(10)-C(9)-H(9A)	109.0
C(8)-C(9)-H(9A)	109.0
C(10)-C(9)-H(9B)	109.0
C(8)-C(9)-H(9B)	109.0
H(9A)-C(9)-H(9B)	107.8
C(11)-C(10)-C(9)	122.58(15)
C(11)-C(10)-H(10)	118.7
C(9)-C(10)-H(10)	118.7
C(10)-C(11)-C(12)	121.24(14)
C(10)-C(11)-C(5)	120.60(14)
C(12)-C(11)-C(5)	118.06(13)
C(17)-C(12)-C(13)	119.24(14)
C(17)-C(12)-C(11)	119.96(14)
C(13)-C(12)-C(11)	120.72(14)
C(14)-C(13)-C(12)	120.16(14)
C(14)-C(13)-H(13)	119.9
C(12)-C(13)-H(13)	119.9

O(5)-C(14)-C(13)	124.07(14)
O(5)-C(14)-C(15)	115.44(13)
C(13)-C(14)-C(15)	120.49(14)
O(4)-C(15)-C(16)	120.20(14)
O(4)-C(15)-C(14)	120.45(13)
C(16)-C(15)-C(14)	119.25(14)
O(3)-C(16)-C(15)	116.76(14)
O(3)-C(16)-C(17)	122.83(13)
C(15)-C(16)-C(17)	120.40(14)
C(16)-C(17)-C(12)	120.43(14)
C(16)-C(17)-H(17)	119.8
C(12)-C(17)-H(17)	119.8
O(2)-C(18)-H(18A)	109.5
O(2)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
O(2)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
O(5)-C(19)-H(19A)	109.5
O(5)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
O(5)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
O(4)-C(20)-H(20A)	109.5
O(4)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
O(4)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
O(3)-C(21)-H(21A)	109.5
O(3)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
O(3)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table S8. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **39**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	33(1)	26(1)	24(1)	-3(1)	-8(1)	8(1)
O(2)	30(1)	24(1)	28(1)	-4(1)	-5(1)	10(1)
O(3)	19(1)	20(1)	27(1)	3(1)	-1(1)	-1(1)
O(4)	17(1)	26(1)	29(1)	-2(1)	-4(1)	-2(1)
O(5)	20(1)	29(1)	22(1)	6(1)	-3(1)	-2(1)
C(1)	18(1)	26(1)	19(1)	-1(1)	1(1)	0(1)
C(2)	17(1)	24(1)	22(1)	3(1)	3(1)	3(1)
C(3)	21(1)	21(1)	24(1)	-3(1)	4(1)	1(1)
C(4)	19(1)	28(1)	20(1)	-1(1)	0(1)	-2(1)
C(5)	14(1)	24(1)	21(1)	2(1)	3(1)	0(1)
C(6)	17(1)	22(1)	21(1)	1(1)	4(1)	0(1)
C(7)	22(1)	25(1)	25(1)	-3(1)	-2(1)	5(1)
C(8)	25(1)	25(1)	36(1)	-2(1)	-7(1)	0(1)
C(9)	23(1)	26(1)	35(1)	6(1)	-5(1)	-4(1)
C(10)	19(1)	26(1)	28(1)	4(1)	-3(1)	0(1)
C(11)	16(1)	25(1)	21(1)	1(1)	1(1)	1(1)
C(12)	18(1)	23(1)	21(1)	-3(1)	2(1)	2(1)
C(13)	19(1)	22(1)	21(1)	0(1)	3(1)	-1(1)
C(14)	20(1)	22(1)	17(1)	-2(1)	0(1)	3(1)
C(15)	15(1)	23(1)	22(1)	-5(1)	-2(1)	-1(1)
C(16)	21(1)	18(1)	19(1)	-3(1)	4(1)	-1(1)
C(17)	19(1)	21(1)	21(1)	-1(1)	-1(1)	4(1)
C(18)	46(1)	29(1)	37(1)	-8(1)	-6(1)	17(1)
C(19)	26(1)	25(1)	24(1)	5(1)	-3(1)	-3(1)
C(20)	17(1)	32(1)	37(1)	3(1)	-3(1)	1(1)
C(21)	25(1)	21(1)	27(1)	1(1)	-1(1)	2(1)

Table S9. Hydrogen bonds for **39** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(3)#1	0.89(2)	2.03(2)	2.8229(16)	148(2)
O(1)-H(1)...O(2)	0.89(2)	2.20(2)	2.6589(16)	111.5(17)

Symmetry transformations used to generate equivalent atoms:

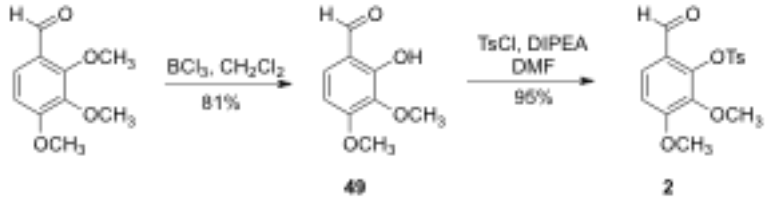
#1 x+1/2,y,-z+1/2

S2. Crystallographic data for structure **39** (deposition number CCDC 941978) reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

Mechanistic Speculation Regarding Selective Demethylation with Ionic Liquid

In the case of the selective demethylation of *ortho*-dimethoxybenzosuberone **18** resulting in the 1-hydroxy-2-methoxy derivative **21**, the argument can be advanced that the methoxy group located *para* to the carbonyl group is partially stabilized by a charge separated resonance contributor rendering the oxygen atom of that methoxy group somewhat less nucleophilic for coordination with the ionic liquid, which most likely precedes the chloride attack to liberate chloromethane. Related dimethoxytetralone and dimethyoxyindanone systems that undergo selective demethylation with this same ionic liquid are described by Kemperman and co-workers.[S3] Interestingly, with the trimethoxybenzosuberone analogue **16**, it is the methoxy group *para* to the fused-ring carbonyl moiety that is selectively cleaved, however in this case it is likely that the two *ortho*-flanking methoxy groups aid in the coordination of the chloroaluminate anion to the central methoxy group, facilitating selective demethylation at that position.

Scheme And Experimentals for Precursor Steps of Compound 2



Scheme S1. Precursor steps to compound **2**

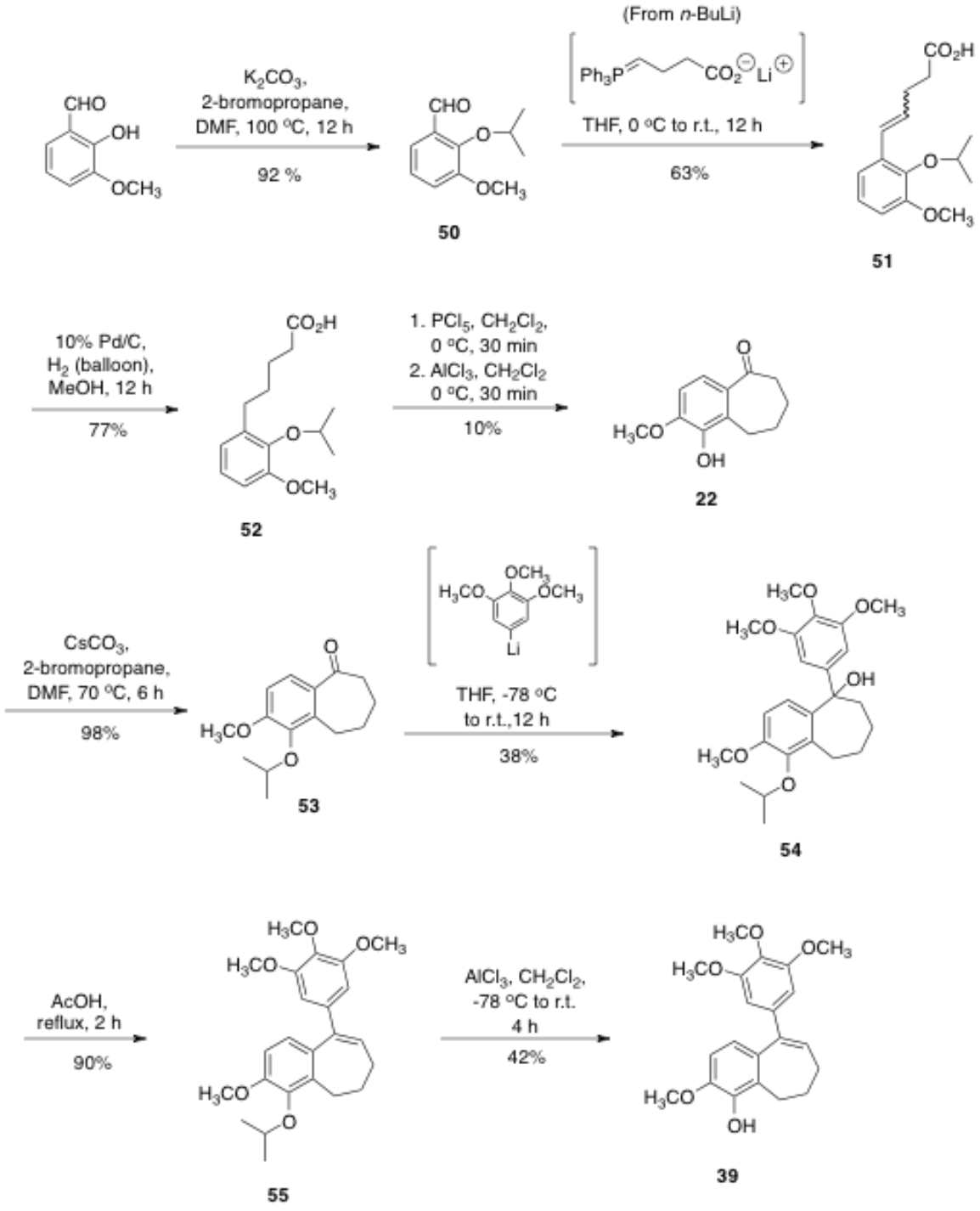
2-Hydroxy-3-4-dimethoxybenzaldehyde ***(49).***[S4,S5] 2,3,4-Trimethoxybenzaldehyde (5.00 g, 25.5 mmol) was dissolved in dry CH_2Cl_2 (15 mL) at 0 ºC under nitrogen. Anhydrous BCl_3 (28.0 mL, 1.0 M soln in CH_2Cl_2) was added dropwise, and the reaction mixture stirred for 5 h. The reaction was quenched with H_2O (10 mL), and the aqueous phase was extracted with CH_2Cl_2 (2 × 25 mL). The organic extract was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was subjected to flash column chromatography (silica gel, 30:70 EtOAc-hexanes) to yield aldehyde **49** (3.75 g, 20.6 mmol, 81% yield) as a white powder.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 11.2 (1H, s, O*H*-2), 9.75 (1H, s, C*H*O-1a), 7.29 (1H, d, *J* = 9.0 Hz, H-6), 6.61 (1H, d, *J* = 9.0 Hz, H-5), 3.95 (3H, s, OCH_3-4), 3.91 (3H, s, OCH_3-3). **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 194.9 (CH, C-1a), 159.4 (C, C-4), 155.7 (C, C-2), 136.2 (C, C-3), 130.2 (CH, C-6), 116.6 (C, C-1), 104.0 (CH, C-5), 60.8 (CH_3, O*C*H_3-3), 56.3 (CH_3, O*C*H_3-4).

2-Tosyloxy-3,4-dimethoxybenzyldehyde ***(2).***[S5] To a stirred solution of aldehyde **49** (2.0 g, 11.0 mmol), DIPEA (4.0 mL, 23.0 mmol) in anhydrous DMF (10 mL) at rt, *p*-TsCl (4.18 g, 22.0 mmol) was added in portions. The reaction mixture was stirred 12 h and quenched with H_2O (10 mL). The solution was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and evaporated

under reduced pressure. The crude product was subjected to flash column chromatography (silica gel, 10:90 EtOAc-hexanes) to afford aldehyde **2** (3.50 g, 10.4 mmol, 95% yield) as a white solid. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 9.86 (1H, s, C*H*O-1a), 7.86 (2H, d, *J* = 8.35 Hz, H-2′, -6′), 7.68 (1H, d, *J* = 8.8 Hz, H-6), 7.37 (2H, d, *J* = 8.35 Hz, H-3′, -5′), 6.94 (1H, d, *J* = 8.8 Hz, H-5), 3.94 (3H, s, OCH_3-4), 3.74 (3H, s, OCH_3-3), 2.48 (3H, s, CH_3-4′). **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 187.0 (CH, C-1a), 158.9 (C, C-4), 145.8 (C, C-2), 145.1 (C, C-3), 142.3 (C, C-3), 132.8 (C, C-1′), 129.9 (CH, C-3′,-5′), 128.4 (C, C-2′,-6′), 124.0 (C, C-1), 123.9 (CH, C-6), 110.6 (CH, C-5), 61.0 (CH_3, O*C*H_3-3), 56.4 (CH_3, O*C*H_3-4), 21.8 (CH_3, *C*H_3-4′).

Scheme and Experimentals for Alternative Route to Compound 39



Scheme S2. Alternative synthetic route to compound **39**

2-Isopropoxy-3-methoxybenzaldehyde ***(50).***[S6] Commercially available *o*-vanillin (10.2 g, 60.7 mmol) was dissolved in DMF (50 mL). To this solution was added 2-bromopropane (20.0 g, 162.4 mmol) and K_2CO_3 (28.0 g, 203.0 mmol). The reaction mixture was heated to 100 °C and stirred for 12 h. The reaction was quenched with H_2O (50 mL) and was then extracted with EtOAc (4 x 50 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, evaporated under reduced pressure, and purified using flash chromatography with a pre-packed 100 g silica column [solvent A: EtOAc, solvent B: hexanes; gradient, 5%A / 95%B (1 CV), 5%A / 95%B → 29%A / 71%B (7 CV); flow rate, 40 mL/min; monitored at 254 and 280 nm]. The isopropyl protected *o*-vanillin **50** (10.8 g, 55.8 mmol, 92% yield) was obtained as a yellow oil. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 10.44 (1 H, d, J = 0.7 Hz), 7.40 (1 H, dd, J = 7.5, 1.9 Hz), 7.11 (1 H, dd, J = 8.0, 1.8 Hz), 7.08 (1 H, td, J = 7.8, 0.8 Hz), 4.62 (1 H, p, J = 6.2 Hz), 3.86 (3 H, s), 1.30 (6 H, d, J = 6.2).

5-(2-Isopropoxy-3-methoxyphenyl)pent-4-enoic acid ***(51)***. (3-Carboxypropyl)triphenylphosponium bromide (9.10 g, 21.2 mmol) was dissolved in THF (50 mL) and cooled to 0 °C. *n*-BuLi (24.0 mL, 1.75 M in hexanes) was added to the solution and stirred for 1 h, warmed to ambient temperature and stirred for 15 min, then cooled to 0 °C. Isopropyl protected *o*-vanillin intermediate **50** (2.02 g, 10.4 mmol) was dissolved in THF (5 mL) and was then added to the phosphine ylide solution. The solution was allowed to warm to ambient temperature while stirring for 12 h. The reaction was quenched with aqueous 2M HCl (30 mL) and extracted with EtOAc (4 x 25 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, evaporated under reduced pressure, and purified using flash chromatography

with a pre-packed 100 g silica column [solvent A: EtOAc, solvent B: hexanes; gradient: 5%A / 95%B (1 CV), 5%A /95%B → 52% A / 48%B (7 CV); flow rate, 12 mL/min; monitored at 254 and 280 nm]. The combined *E* and *Z* isomers of alkene analogue **51** (1.72 g, 6.51 mmol, 63% yield) was obtained as a yellow oil.

5-(2-Isopropoxy-3-methoxyphenyl)pentanoic acid ***(52).*** (5-(2-isopropoxy-3-methoxyphenyl)pent-4-enoic acid intermediate **51** (7.49 g, 28.3 mmol) was dissolved in MeOH (100 mL). 10% Pd/C (1.3 g) was added to the solution and stirred for 10 min at ambient temperature. Hydrogen balloons were then added to the sealed system and allowed to stir for 12 h. The solution was filtered through CELITE and washed with EtOAc (4 x 25 mL). The combined organic extracts were evaporated under reduced pressure, and purified using flash chromatography with a pre-packed 100 g silica column [solvent A: EtOAc, solvent B: hexanes; gradient: 12%A / 88%B (1 CV), 12%A / 88%B → 100%A / 0%B (15 CV); flow rate, 40 mL/min; monitored at 254 and 280 nm]. The carboxylic acid analogue **52** (5.78 g, 21.7 mmol, 77% yield) was obtained as a clear oil. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 6.95 (1 H, t, J = 7.9 Hz), 6.75 (2 H, m), 4.46 (1 H, p, J = 6.2 Hz), 2.66 (2 H, t, J = 7.3 Hz), 2.38 (2 H, t, J = 7.2 Hz), 1.66 (4 H, m), 1.28 (d, J = 6.2 Hz).

1-Hydroxy-2-methoxybenzosuber-5-one ***(22).***[S5] 5-(2-isopropoxy-3-methoxyphenyl)pentanoic acid **52** (4.68 g, 17.6 mmol) was dissolved in CH_2Cl_2 (250 mL) and cooled to 0 °C. Phosphorous pentachloride (5.03 g, 24.1 mmol) was added to the solution and stirred for 30 min at 0 °C. The excess phosphorous pentachloride and CH_2Cl_2 was removed under reduced pressure. Aluminum chloride was diluted in CH_2Cl_2 (250 mL) and cooled to 0 °C added. The crude acyl chloride intermediate was then

dissolved in CH_2Cl_2 (10 mL), added to the aluminum chloride solution, and stirred for 30 min at 0 °C. The reaction was quenched with H_2O (30 mL) and extracted with CH_2Cl_2 (4 x 50 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, evaporated under reduced pressure, and purified by flash chromatography using 10% EtOAc/90% hexanes as eluent. The ketone analogue **22** (0.355 g, 1.72 mmol, 10% yield) was obtained as a white solid. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.34 (1 H, d, J = 8.5 Hz), 6.79 (1 H, d, J = 8.5 Hz), 5.79 (1 H, s), 3.94 (3 H, s), 3.02 (2 H, m), 2.71 (2 H, m), 1.82 (4 H, m). **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 205.2, 149.4, 142.6, 133.4, 127.8, 121.0, 108.0, 56.2, 40.9, 24.6, 23.2, 21.5.

1-Isopropoxy-2-methoxybenzosuber-5-one ***(53).***[S8] 1-Hydroxy-2-methoxybenzosuber-5-one analogue **22** (0.261 g, 1.27 mmol) was dissolved in DMF (10 mL). To this solution was added 2-bromopropane (0.196 g, 1.60 mmol) and Cs_2CO_3 (1.45 g, 4.44 mmol). The reaction mixture was heated to 100 °C and stirred for 6 h. The reaction was quenched with H_2O (20 mL) and extracted with EtOAc (4 x 25 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, evaporated under reduced pressure, and purified using flash chromatography with a pre-packed 25 g silica column [solvent A: EtOAc, solvent B: hexanes; gradient: 5%A / 95%B → 7%A / 93%B (1 CV), 7%A / 93%B → 60%A / 40%B (12 CV); flow rate, 25 mL/min; monitored at 254 and 280 nm]. The isopropyl protected benzosuberone analogue **53** (0.308 g, 1.24 mmol, 98% yield) was obtained as a yellow oil. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.51 (1 H, d, J = 8.6 Hz), 6.82 (1 H, d, J = 8.6 Hz), 4.41 (1 H, p, J = 6.1 Hz), 3.88 (3 H, s), 3.03 (2 H, m), 2.70 (2 H, m), 1.80 (4 H, m), 1.29 (6 H, d, J = 6.2 Hz).

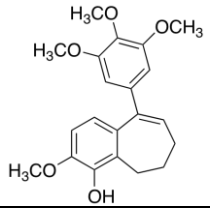
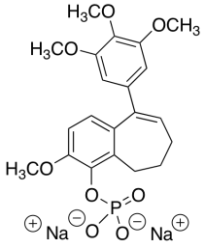
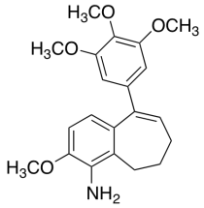
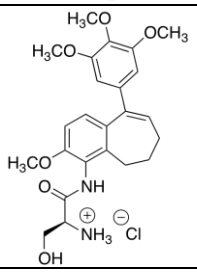
1-Isopropoxy-2-methoxy-5-(3′,4′,5′-trimethoxyphenyl)-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-ol ***(54).***[S8] 3,4,5-Trimethoxybromobenzene (0.113 g, 0.457 mmol) was dissolved in THF (5 mL) and cooled to -78 °C. To this solution was added *n*-BuLi (0.20 mL, 2.3 M in hexanes) and the solution was allowed to stir for 1 h. 1-Isopropoxy-2-methoxybenzosuber-5-one analogue **53** (0.079 g, 0.320 mmol) was dissolved in THF (2 mL) and was added to the aryl lithium solution. The reaction was allowed to warm to ambient temperature over 12 h and was quenched with H_2O (5 mL). The organic solvent was removed under reduced pressure. The aqueous mixture was extracted with EtOAc (4 x 10 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, evaporated under reduced pressure, and purified using flash chromatography with a pre-packed 25 g silica column [solvent A: EtOAc, solvent B: hexanes; gradient, 7%A / 93%B (1 CV), 7%A / 93%B → 60%A / 40%B (10 CV), 60%A / 40%B (2 CV); flow rate, 25 mL/min; monitored at 254 and 280 nm]. The tertiary alcohol analogue **54** (0.051g, 0.123 mmol, 38% yield) was obtained as a yellow oil.

4-Isopropoxy-3-methoxy-9-(3′,4′,5′-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulene ***(55).***[S8] Tertiary alcohol intermediate **54** (0.048 g, 0.115 mmol) was dissolved in AcOH (8 mL) and refluxed for 6 h. The reaction was quenched with H_2O and extracted with Et_2O (4 x 10 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, evaporated under reduced pressure, and purified using flash chromatography with a pre-packed 10 g silica column [solvent A: EtOAc, solvent B: hexanes; gradient: 7%A / 93%B (4 CV), 7%A / 93%B → 60%A / 40%B (19 CV); flow rate, 25 mL/min; monitored at 254 and 280 nm]. Alkene analogue **55** (0.041 g, 0.104 mmol, 90% yield) was obtained as a yellow oil. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 6.73 (2 H, s), 6.47 (2 H, s),

6.33 (1 H, t, J = 7.2 Hz), 4.51 (1 H, p, J = 6.1 Hz), 3.86 (3 H, s), 3.85 (3 H, s), 3.80 (6 H, s), 2.78 (2 H, t, J = 6.9 Hz), 2.14 (2 H, p, J = 6.9 Hz), 1.96 (2 H, q, J = 7.0 Hz), 1.34 (6 H, d, J = 6.1 Hz).

3-Methoxy-9-(3′,4′,5′-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulen-4-ol **)** ***(39).***[S5,S8,S9] Aluminum chloride (0.057 g, 0.427 mmol) was dissolved in CH_2Cl_2 (2 mL) and cooled to 0 °C. Alkene intermediate **55** (0.041 g, 0.099 mmol) was dissolved in CH_2Cl_2 (2 mL) and added to aluminum chloride solution. The solution was allowed to stir for 30 min at 0 °C. The reaction was quenched with H_2O and extracted with CH_2Cl_2 (4 x 10 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, evaporated under reduced pressure, and purified using flash chromatography with a pre-packed 10 g silica column [solvent A: EtOAc, solvent B: hexanes; gradient: 7%A / 93%B (1 CV), 7%A / 93%B → *60*%A / 40%B (13 CV), 60%A / 40%B (2 CV); flow rate, 40 mL/min; monitored at 254 and 280 nm]. Alkene analogue **39** (0.015 g, 0.042 mmol, 42% yield) was obtained as a white solid. **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 6.71 (1 H, d, J = 8.4 Hz), 6.57 (1 H, d, J = 8.4 Hz), 6.50 (2 H, s), 6.34 (1 H, t, J = 7.4 Hz), 5.73 (1 H, s), 3.91 (3 H, s), 3.86 (3 H, s), 3.80 (6 H, s), 2.76 (2 H, t, J = 6.9 Hz), 2.14 (2 H, p, J = 7.1 Hz), 1.96 (2 H, q, 7.1 Hz).**^{13}C NMR** ($CDCl_3$, 125 MHz): δ 153.0, 145.2, 142.9, 142.5, 138.6, 137.4, 134.4, 127.9, 127.4, 121.0, 107.8, 105.4, 61.1, 56.3, 56.1, 33.8, 25.9, 23.7.

HRMS, *m/z*: observed 357.1699 $[M + H]^+$, calcd for $C_{21}H_{25}O_5^+$, 357.1697.

Compound Number	Compound	cLogP
39		3.95 ± 0.55 (3.93)
44 – Calculated without Na+		2.42 ± 1.57* (2.28)
45		3.73 ± 0.47 (3.51)
48 – Calculated without Cl^-		0.88 ± 1.81 (1.98)

http://www.vcclab.org/lab/alogps/ is the online application used to calculate the first log P given. This number is an average of eight algorithms calculating log P. The number in parenthesis is the log P generated by chemdraw. Numbers with asterisks had one unreliable log P calculations. Citations for the online application:

1. Tetko, I. V.; Gasteiger, J.; Todeschini, R.; Mauri, A.; Livingstone, D.; Ertl, P.; Palyulin, V. A.; Radchenko, E. V.; Zefirov, N. S.; Makarenko, A. S.; Tanchuk, V. Y.; Prokopenko, V. V. Virtual computational chemistry laboratory - design and description, *J. Comput. Aid. Mol. Des.*, **2005**, 19, 453-63.
2. VCCLAB, Virtual Computational Chemistry Laboratory, http://www.vcclab.org, 2005.

cLog P: a distribution coefficient that describes how well a compound will partition itself between octanol and water (thus describing it's lipophilicity). This partition coefficient describes the "druglikeness," and is thought that if the cLogP is less than 5, the compound is a good candidate as a drug because hydrophobic compounds are more likely to distribute to lipid bilayers of cells.

Supplementary References and Notes

S1. Crystallographic data for structure **38** (deposition number CCDC 953837) reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

S2. Crystallographic data for structure **39** (deposition number CCDC 941978) reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

S3. Kemperman, G.; Roeters, T.; Hilberink, P. Eur. J. Org. Chem. 2003, 1681-1686.

S4. Baker, W.; Smith, H.A. *J. Chem. Soc.* **1931,** 2542-2549.

S5. Pinney, K.G.; Sriram, M.; George, C.; Tanpure, R.P. Efficient method for preparing functionalized benzosuberenes useful as cytotoxic agents. PCT Int. Appl. **2012,** WO 2012068284 A2 20120524.

S6. Delaby, R.; Tsatsa, G.; Jehdrot, M.C. *Bulleting de la Societe Chimique de France,* **1956**, 1830-1833.

S7. Horton, W.J.; Pitchforth, L.L. *J. Org. Chem.* **1960,** *25,* 131-132.

S8. Sriram, M.; Hall, J.J.; Grohman, N.C.; Strecker, T.E.; Wootton, T.; Franken, A.; Trawick, M.L.; Pinney, K.G. *Bioorg. Med. Chem.* **2008,** *16,* 8161-8171.

S9. Chen, Z.; O'Donnell, C.J.; Maderna, A. *Tetrahedron Letters*, **2012**, *53*, 64-66.