Supplemental Data File

Synthesis of dihydronaphthalene analogues inspired by combretastatin A-4 and their biological evaluation as anticancer agents.

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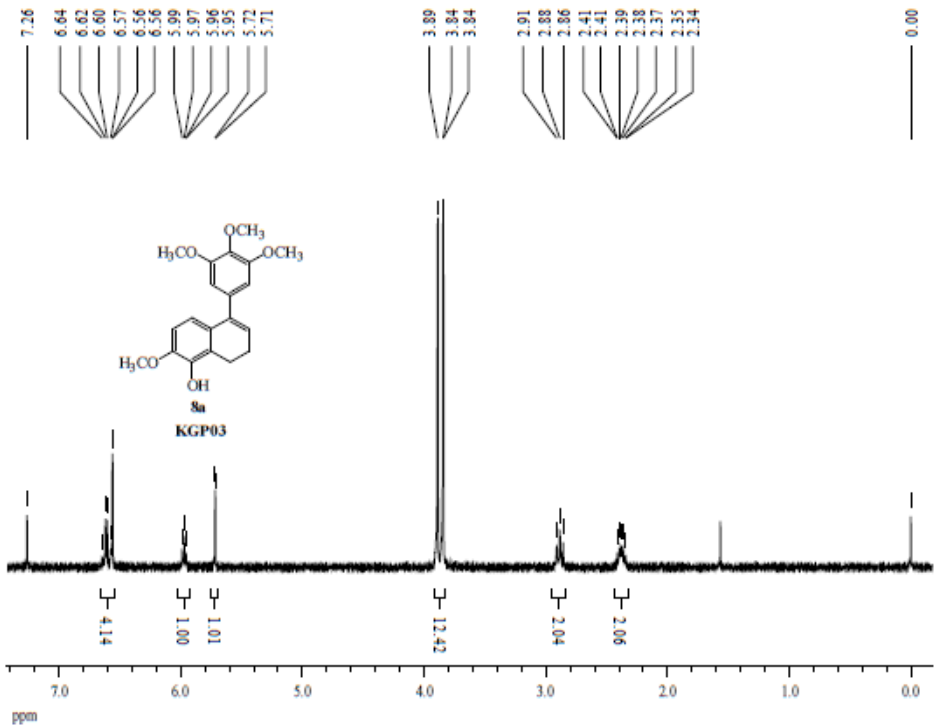
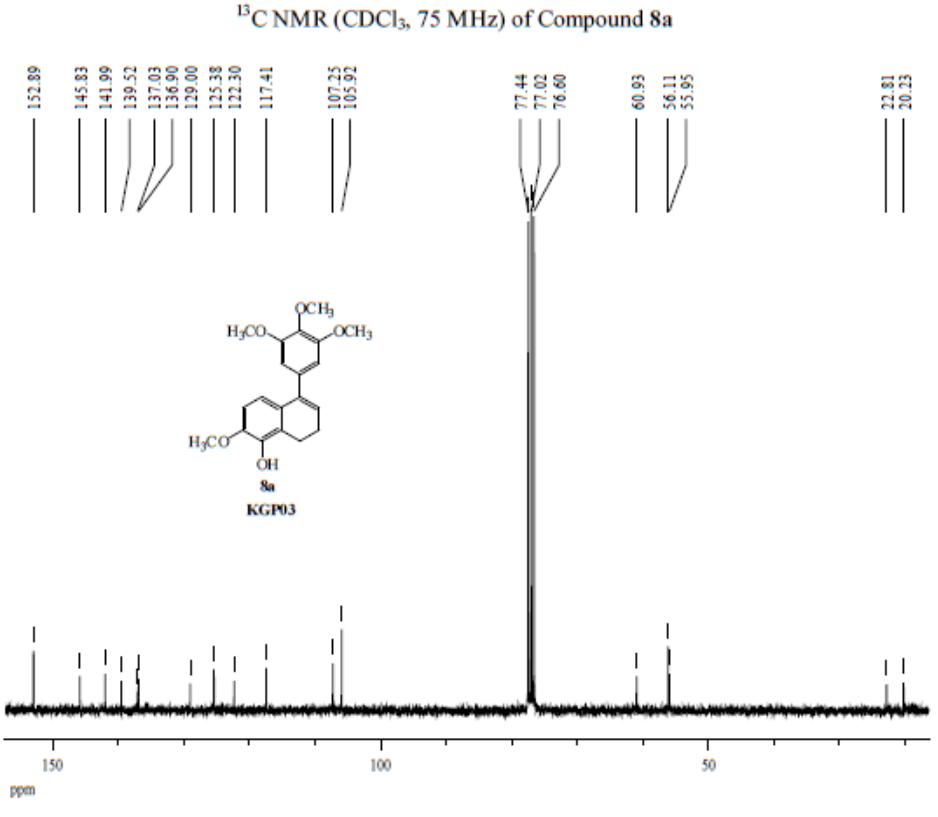
NOTE: Compound numbers containing the letter "a" are from Schemes 1 and 3, and those containing the letter "b" are from Schemes 2 and 4.

^{1}H NMR ($CDCl_3$, 300 MHz) of Compound **8a**

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137.03
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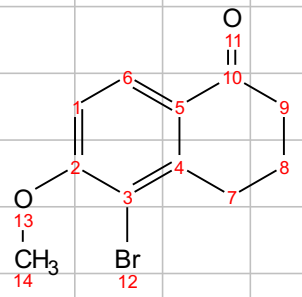
122.30
117.41
107.25
105.92
77.44
77.02
76.60
60.93
56.11
55.95
22.81
20.23
OCH3
H3CO
OCH3
H3CO
OH
8a
KGP03
150
100
50
ppm

CJM-II-86.10.fid

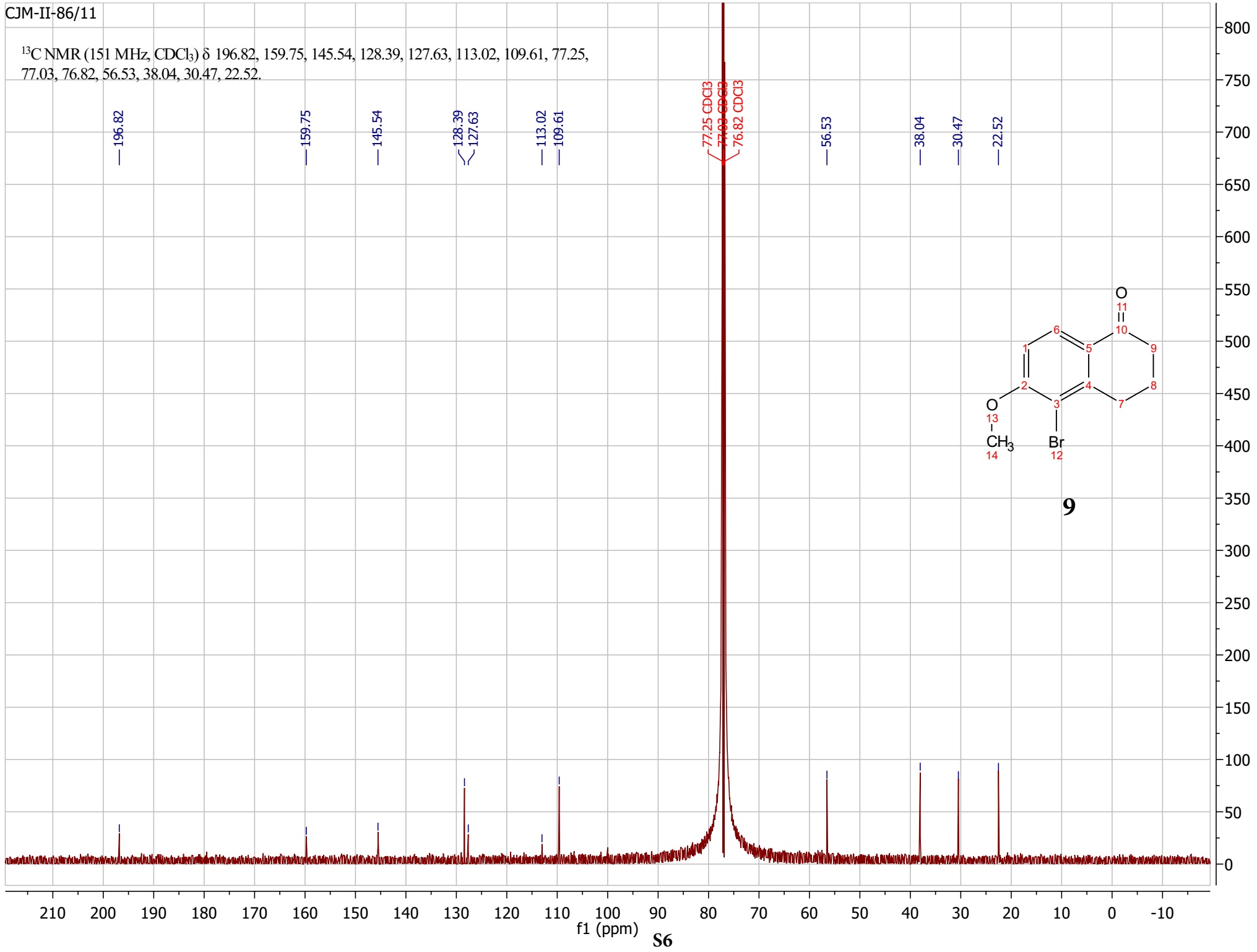
^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.7 Hz, 1H), 6.91 (d, *J* = 8.7 Hz, 1H), 4.00 (s, 3H), 3.06 (t, *J* = 6.2 Hz, 2H), 2.67 – 2.59 (m, 2H), 2.17 (p, *J* = 6.3 Hz, 2H).



9

CJM-II-86/11

^{13}C NMR (151 MHz, $CDCl_3$) δ 196.82, 159.75, 145.54, 128.39, 127.63, 113.02, 109.61, 77.25, 77.03, 76.82, 56.53, 38.04, 30.47, 22.52.



9

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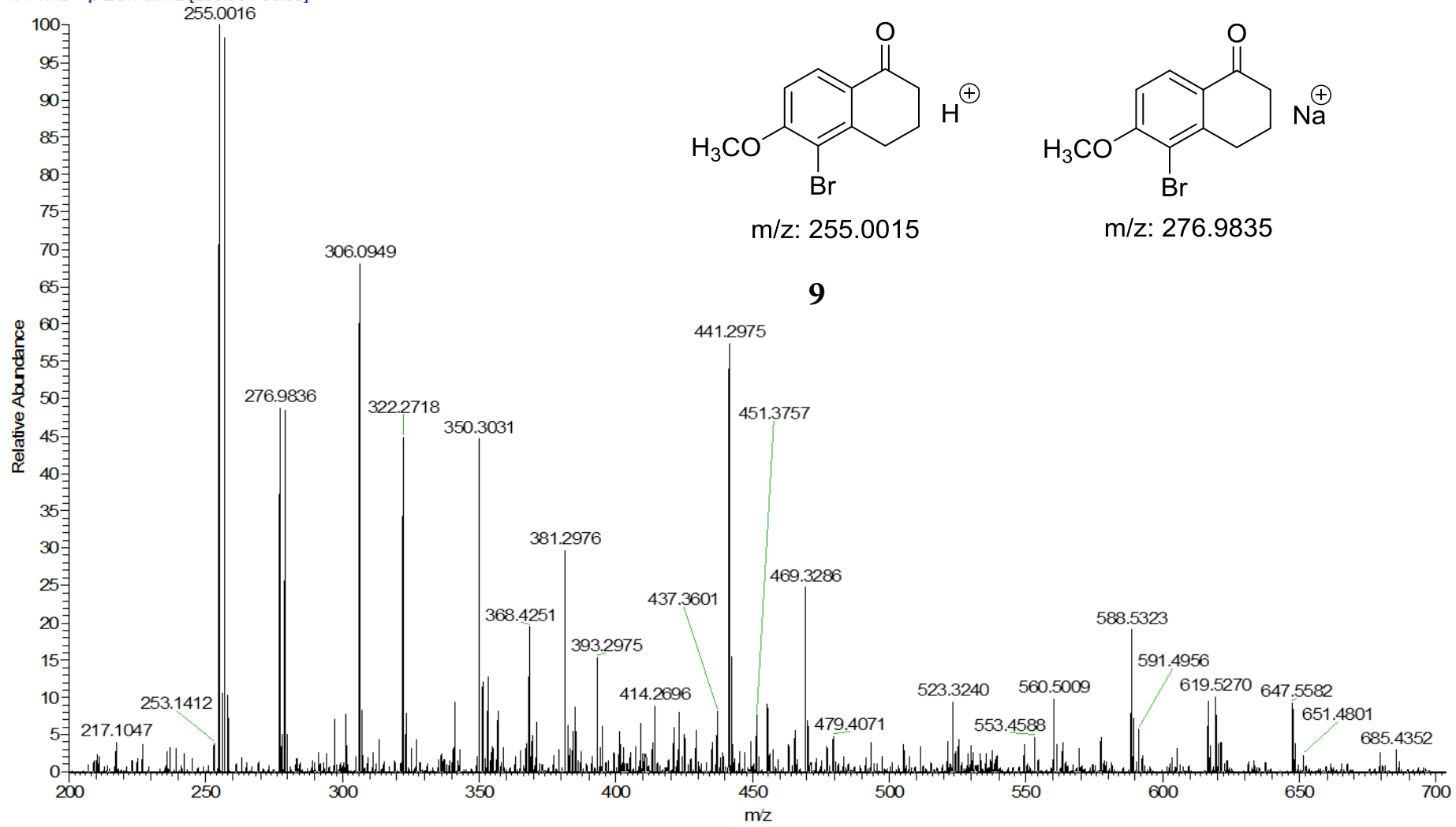


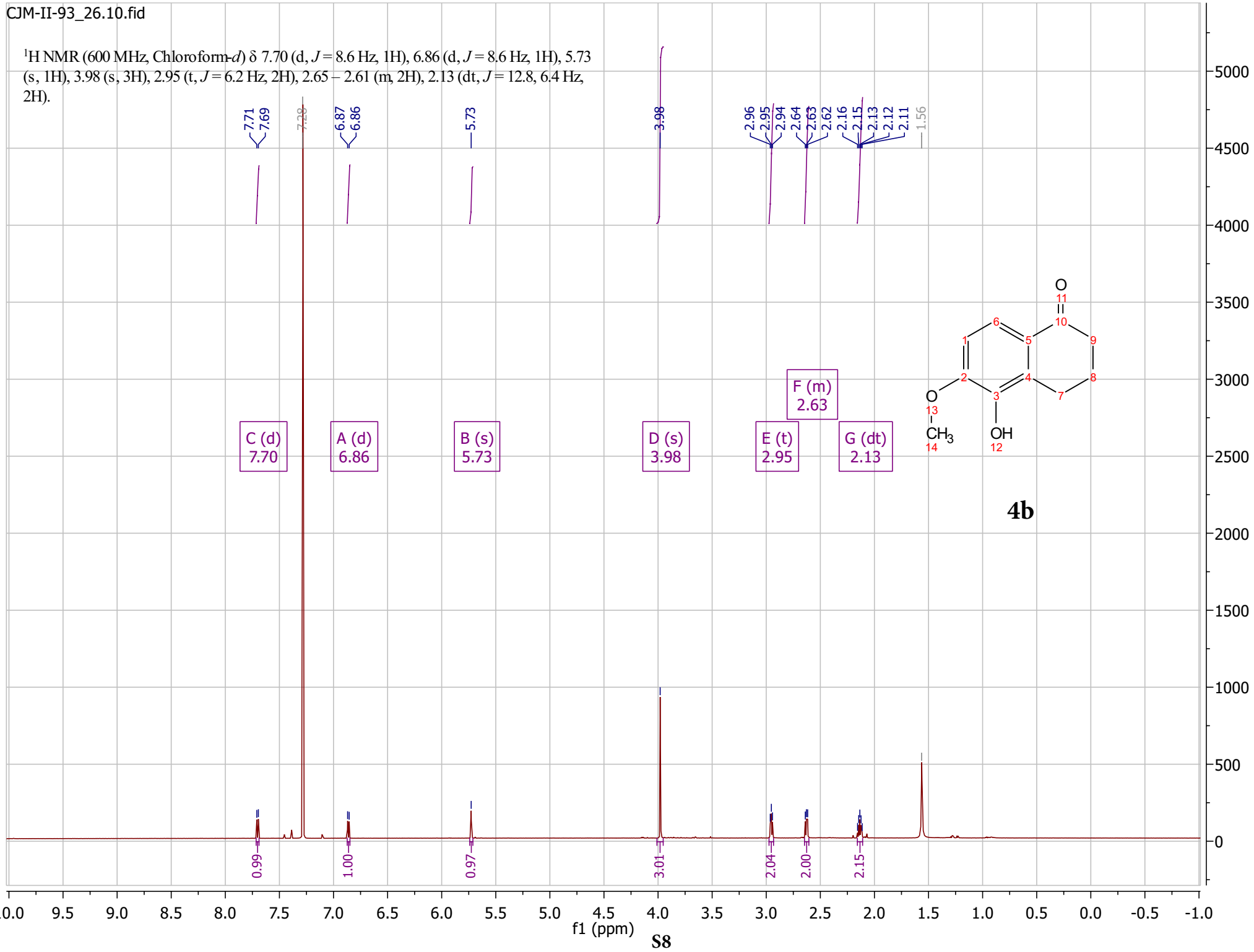
m/z: 255.0015

m/z: 276.9835

9

CJM-II-93_26.10.fid

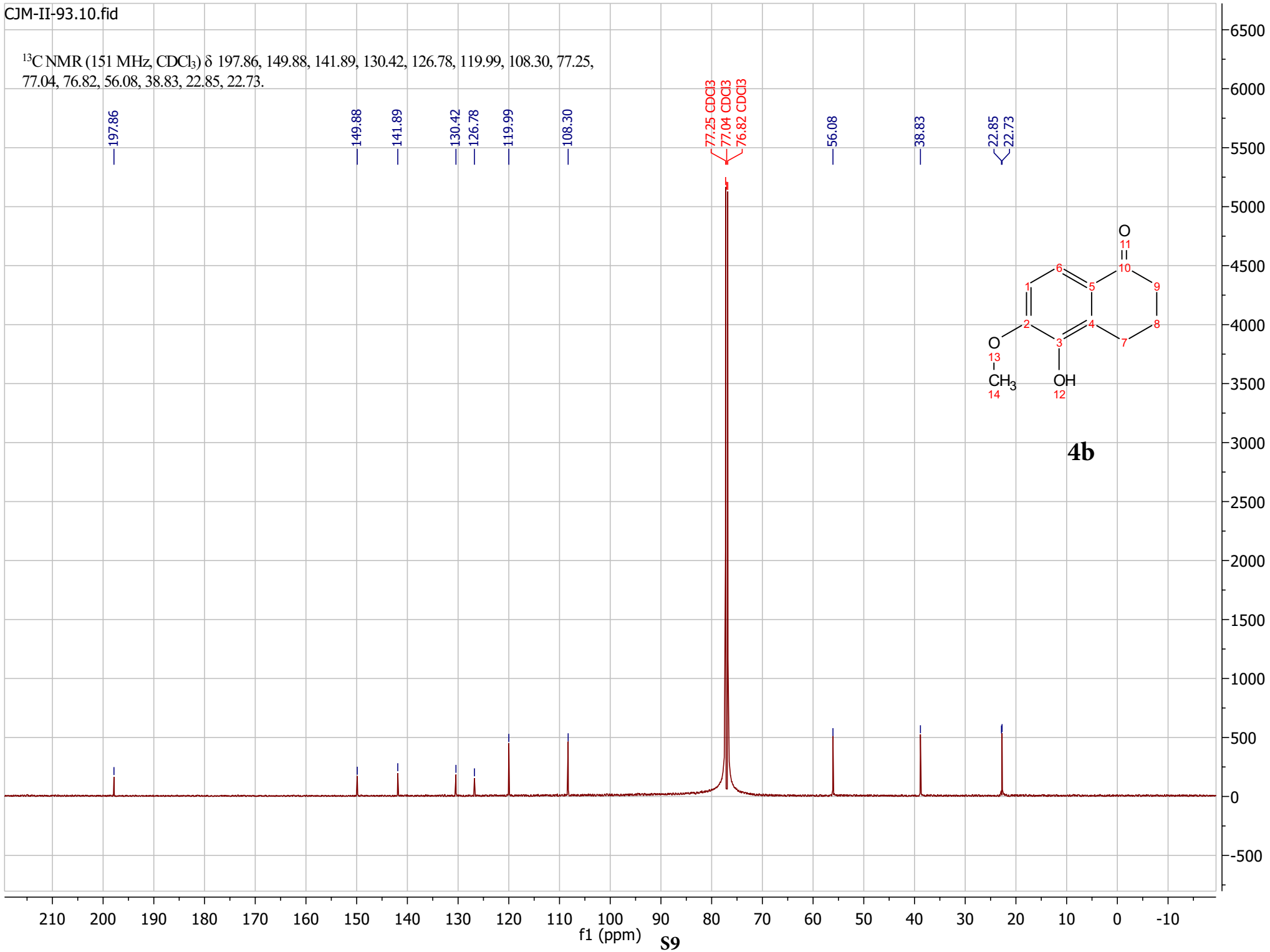
^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 8.6 Hz, 1H), 6.86 (d, *J* = 8.6 Hz, 1H), 5.73 (s, 1H), 3.98 (s, 3H), 2.95 (t, *J* = 6.2 Hz, 2H), 2.65 – 2.61 (m, 2H), 2.13 (dt, *J* = 12.8, 6.4 Hz, 2H).



4b

CJM-II-93.10.fid

^{13}C NMR (151 MHz, $CDCl_3$) δ 197.86, 149.88, 141.89, 130.42, 126.78, 119.99, 108.30, 77.25, 77.04, 76.82, 56.08, 38.83, 22.85, 22.73.



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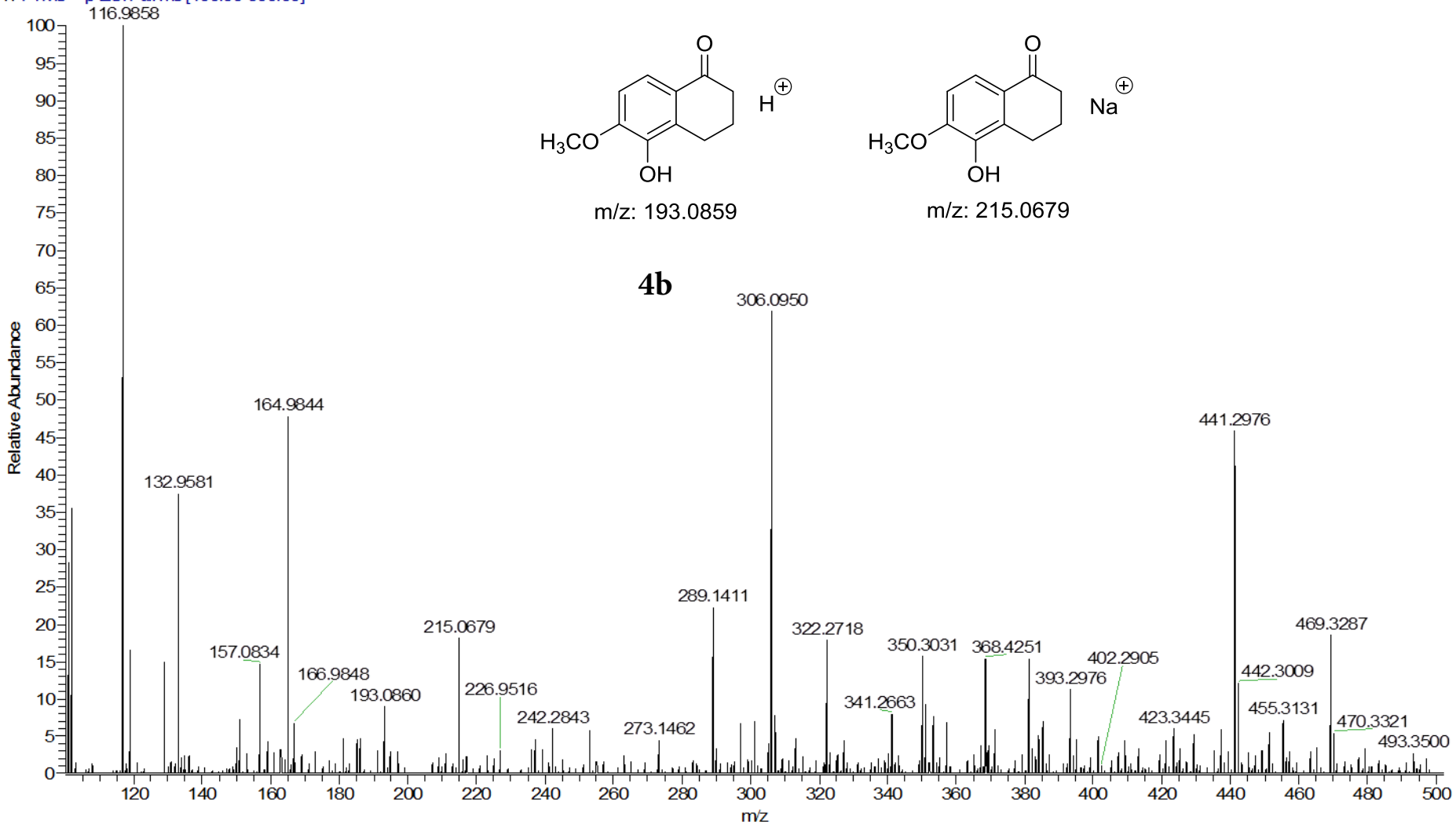

m/z: 193.0859

m/z: 215.0679

4b

CJM-II-95_4.10.fid

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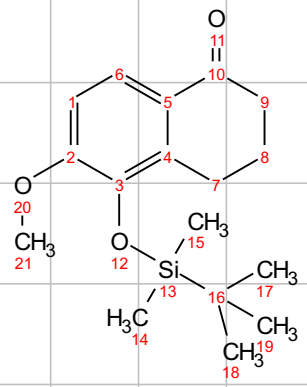
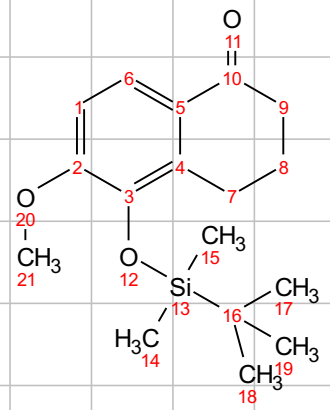


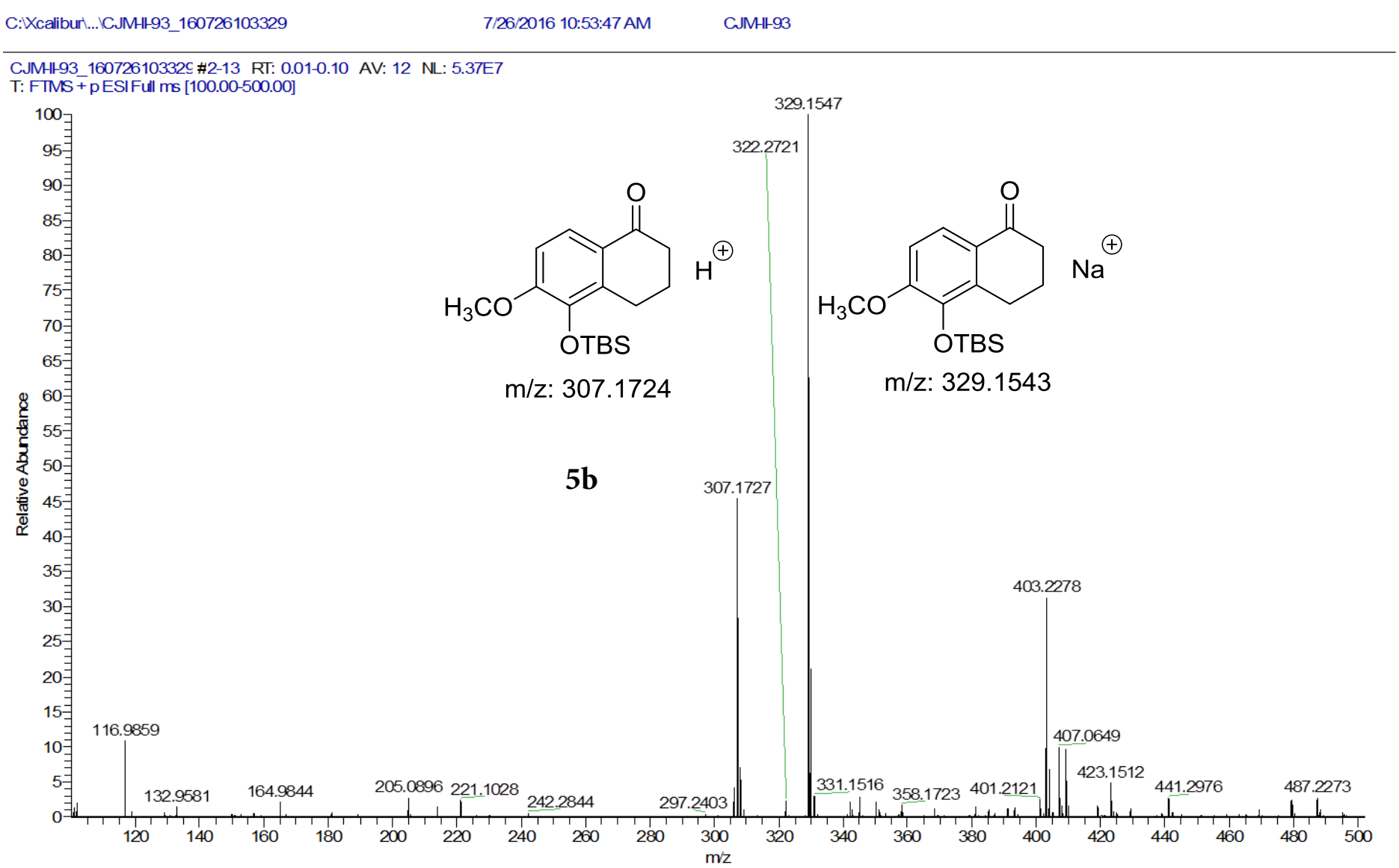
5b

CJM-II-95.10.fid

^{13}C NMR (151 MHz, $CDCl_3$) δ 197.96, 153.95, 141.28, 136.11, 126.75, 121.47, 109.19, 77.26, 77.04, 76.83, 54.94, 38.69, 26.05, 24.35, 22.85, 18.88, -3.84.



5b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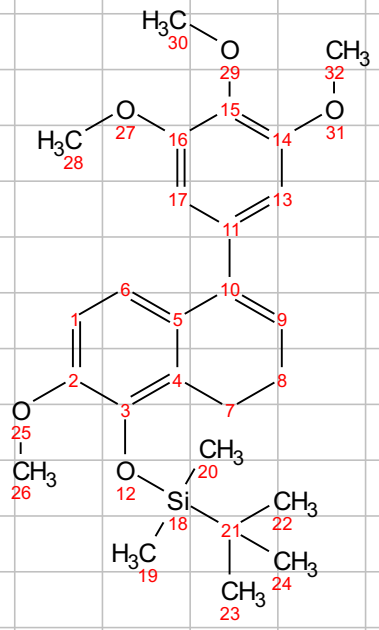
401.2121
358.1723
331.1516
297.2403
242.2844
221.1028
205.0896
164.9844
132.9581
116.9859
H3CO
OTBS
H
m/z: 307.1724
5b
Na
m/z: 329.1543
Relative Abundance
m/z

CJM-III-213_25.10.fid

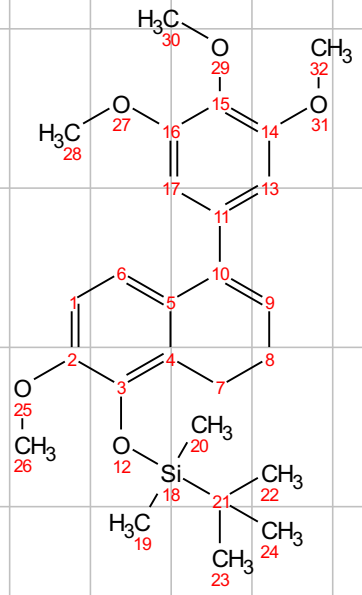
^{1}H NMR (600 MHz, Chloroform-*d*) δ 6.44 (d, *J* = 8.4 Hz, 1H), 6.40 (d, *J* = 8.5 Hz, 1H), 6.37 (s, 2H), 5.75 (t, *J* = 4.6 Hz, 1H), 3.69 (s, 3H), 3.65 (s, 6H), 3.58 (s, 3H), 2.69 – 2.64 (m, 2H), 2.13 (td, *J* = 7.9, 4.7 Hz, 2H), 0.83 (s, 9H), 0.00 (s, 6H).



7b

CJM-III-213_25.11.fid

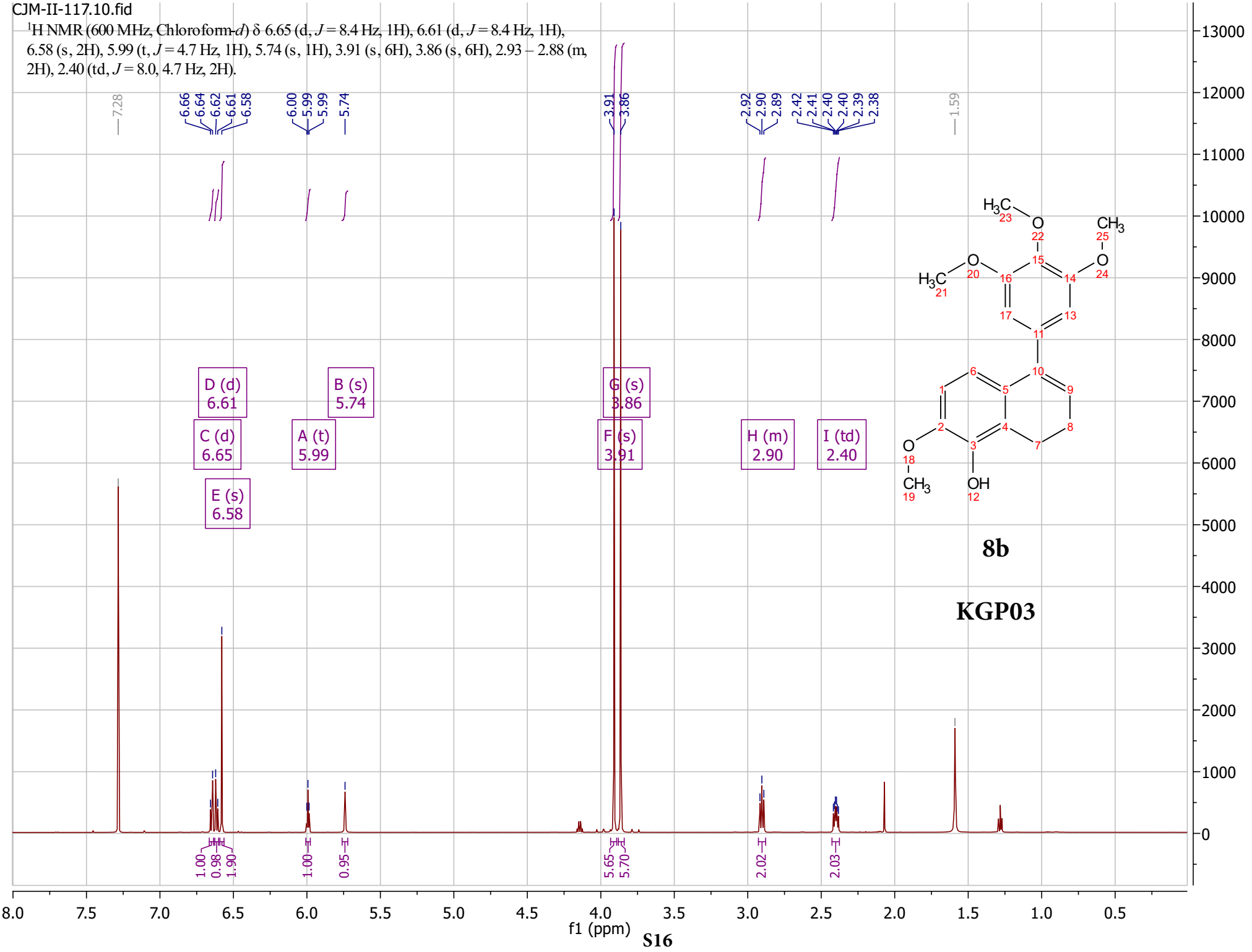
^{13}C NMR (151 MHz, $CDCl_3$) δ 152.86, 149.65, 141.40, 139.77, 137.03, 137.00, 128.70, 128.10, 124.94, 118.92, 108.09, 105.96, 77.24, 77.03, 76.82, 60.94, 56.13, 54.83, 26.08, 23.05, 21.73, 18.88, -3.91.



7b

CJM-II-117.10.fid

^{1}H NMR (600 MHz, Chloroform-*d*) δ 6.65 (d, *J* = 8.4 Hz, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 6.58 (s, 2H), 5.99 (t, *J* = 4.7 Hz, 1H), 5.74 (s, 1H), 3.91 (s, 6H), 3.86 (s, 6H), 2.93 – 2.88 (m, 2H), 2.40 (td, *J* = 8.0, 4.7 Hz, 2H).

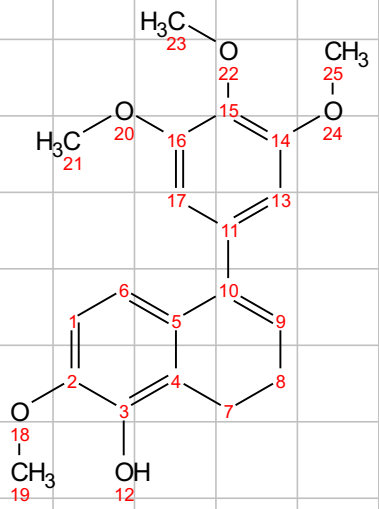


8b

KGP03

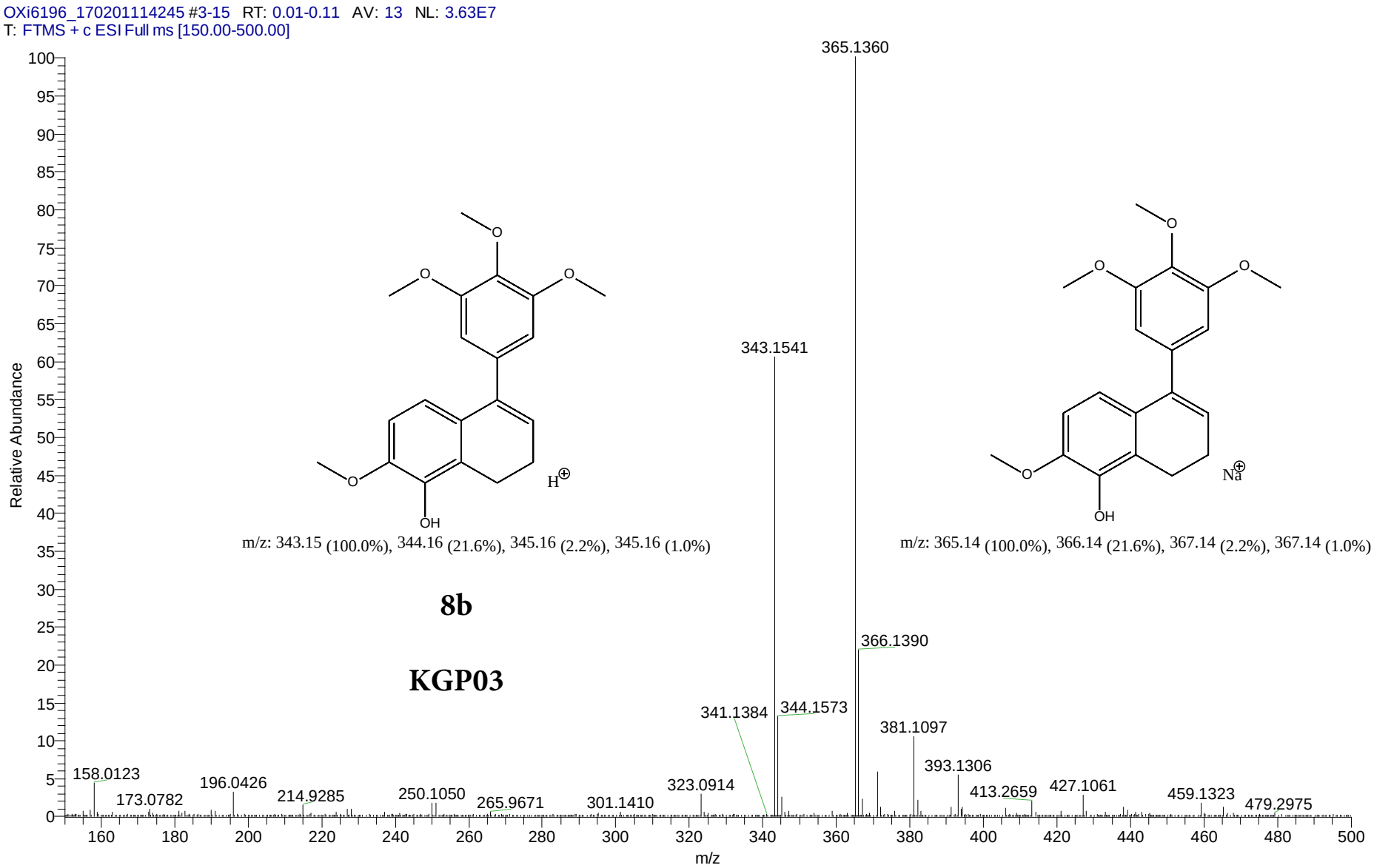
CJM-II-117_19.11.fid

^{13}C NMR (151 MHz, $CDCl_3$) δ 152.87, 145.82, 141.97, 139.51, 136.91, 132.80, 128.97, 125.41, 122.30, 117.42, 107.23, 105.84, 77.24, 77.03, 76.82, 60.96, 56.11, 55.96, 22.82, 20.23.



8b

KGP03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Relative Abundance
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366.1390
341.1384
344.1573
381.1097
393.1306
158.0123
173.0782
196.0426
214.9285
250.1050
265.9671
301.1410
323.0914
413.2659
427.1061
459.1323
479.2975
H
Na
OH
m/z: 343.15 (100.0%), 344.16 (21.6%), 345.16 (2.2%), 345.16 (1.0%)
m/z: 365.14 (100.0%), 366.14 (21.6%), 367.14 (2.2%), 367.14 (1.0%)

8b

KGP03

Data File C:\Chem32\1\Data\ZHE\20171002_OXi6196.D
Sample Name: OXi6196

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Sample Operator : SYSTEM
Acq. Instrument : 1200 HPLC Location : 1
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Inj Volume : No inj
Acq. Method : C:\CHEM32\1\METHODS\GRAD 2 50-90 ACN.M
Last changed : 4/30/2014 1:53:57 AM by ERICAP
Analysis Method : C:\CHEM32\1\METHODS\RT-ACNWASH 2.M
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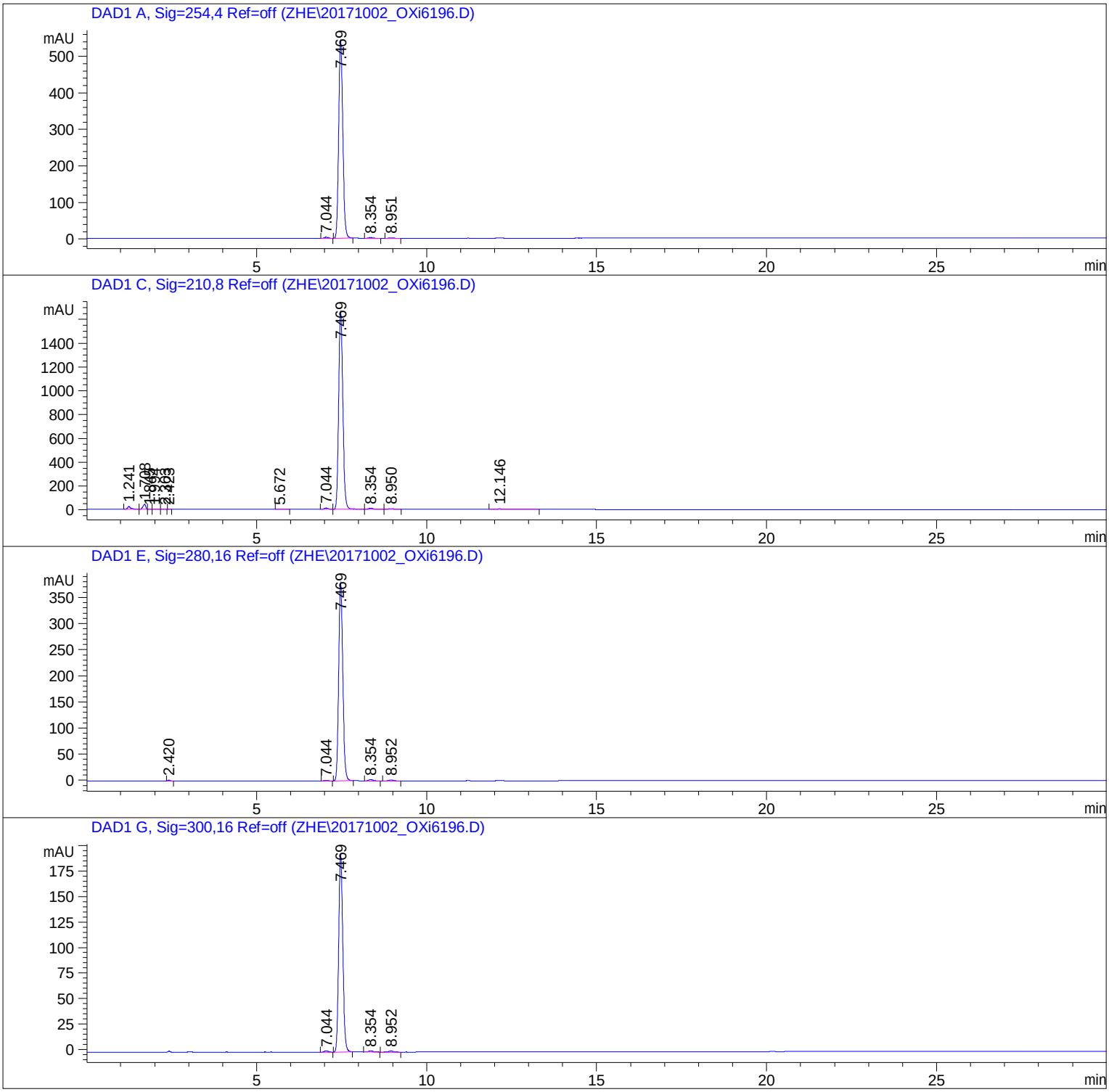
Method Info : General Column Wash Method

Sample Info : OXi6196
GRAD 2 50-90 ACN
20171002



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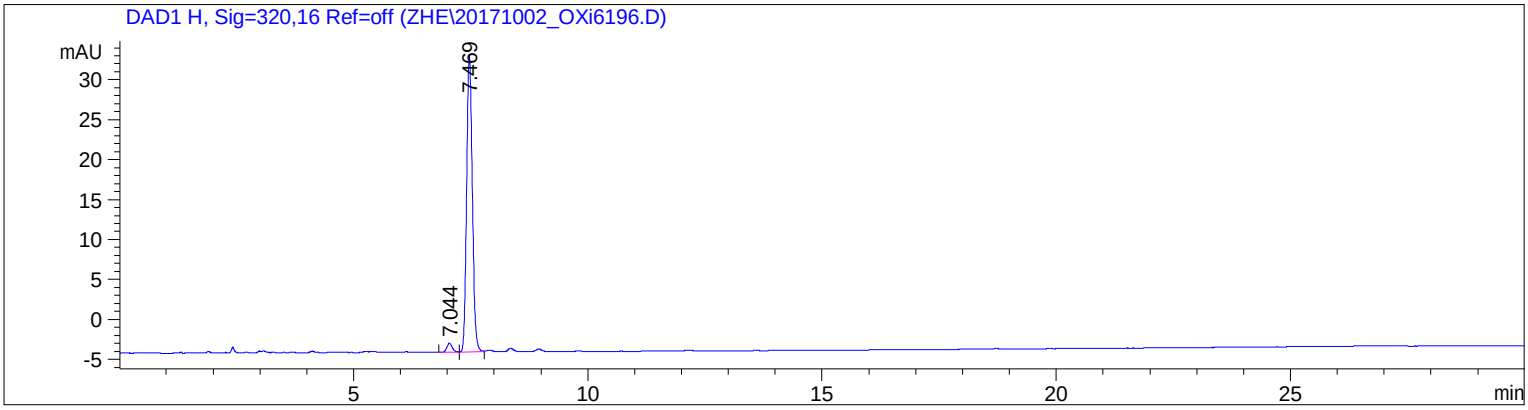

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Area Percent Report

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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	7.044	BB	0.1205	24.87840	3.20582	0.5455
2	7.469	BB	0.1289	4507.92627	542.74707	98.8435
3	8.354	BB	0.1312	16.42704	1.93128	0.3602
4	8.951	BB	0.1435	11.43703	1.21811	0.2508
Totals :				4560.66875	549.10229	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.241	BV	0.0892	152.59418	24.31470	1.0351
2	1.708	VB	0.0864	234.06787	42.40724	1.5877
3	1.845	BV	0.0791	6.16756	1.14120	0.0418
4	1.994	VB	0.0909	10.20336	1.58933	0.0692
5	2.303	BB	0.0755	12.08045	2.36802	0.0819
6	2.423	BB	0.0583	6.14344	1.69379	0.0417
7	5.672	VB	0.1305	10.41587	1.20932	0.0707
8	7.044	BV	0.1218	81.04125	10.29583	0.5497
9	7.469	VV	0.1304	1.40403e4	1664.50281	95.2370
10	8.354	VV	0.1397	86.48226	9.36422	0.5866
11	8.950	VB	0.1454	58.37324	6.11580	0.3960
12	12.146	BB	0.1712	44.60802	3.96630	0.3026
Totals :				1.47425e4	1768.96856	

Data File C:\Chem32\1\Data\ZHE\20171002_OXi6196.D
Sample Name: OXi6196

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.420	BB	0.0655	6.53248	1.53972	0.2039
2	7.044	BB	0.1188	8.33138	1.09431	0.2601
3	7.469	BB	0.1289	3152.02905	379.44495	98.4071
4	8.354	BB	0.1318	21.11969	2.46935	0.6594
5	8.952	BB	0.1395	15.03925	1.66302	0.4695
Totals :				3203.05186	386.21136	

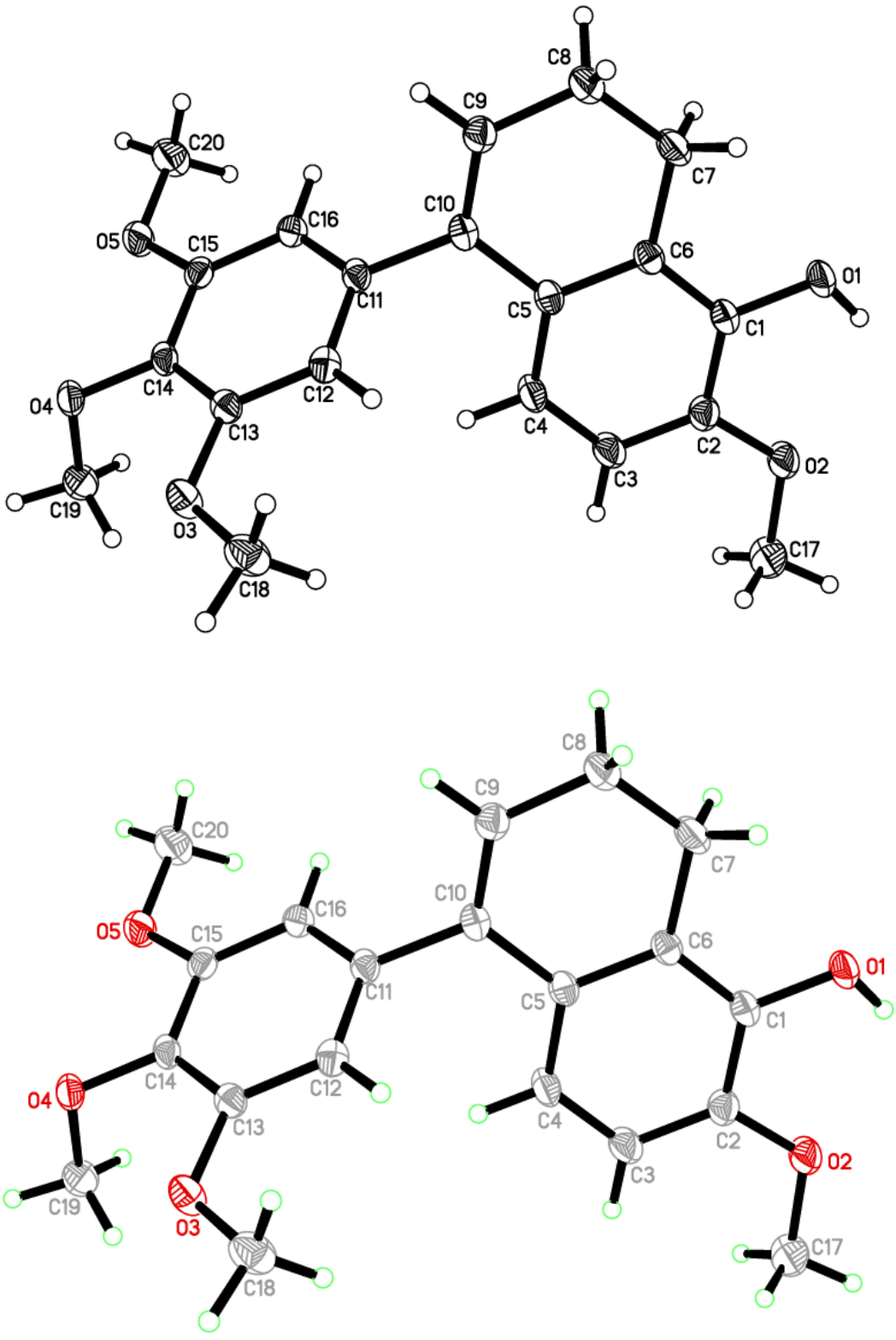
Signal 4: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.044	BB	0.1214	10.10590	1.29063	0.6137
2	7.469	BB	0.1289	1615.47058	194.48380	98.0960
3	8.354	BB	0.1324	11.78112	1.36897	0.7154
4	8.952	BB	0.1406	9.46903	1.03622	0.5750
Totals :				1646.82663	198.17962	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.044	BB	0.1224	8.92868	1.12732	2.8068
2	7.469	BB	0.1293	309.17801	37.06949	97.1932
Totals :				318.10669	38.19682	

*** End of Report ***



X-ray crystal structure of **KGP03**

X-ray Crystallographic Analysis:

X-ray crystallographic analysis of compound KGP03. Crystallographic data were collected on a crystal of KGP03 with dimensions 0.420 x 0.235 x 0.187 mm^3. Data were collected at 150(2) 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-S5). All data were processed using the Bruker AXS SHELXTL software, version 6.10.

Table 1. Crystal data and structure refinement for KGP03.

Identification code	KGP03	
Empirical formula	C20 H22 O5	
Formula weight	342.37	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 12.1996(5) Å	α= 90°.
	b = 6.7253(2) Å	β= 94.1342(15)°.
	c = 20.3499(9) Å	γ = 90°.
Volume	1665.28(11) $Å^3$	
Z	4	
Density (calculated)	1.366 Mg/m^3	
Absorption coefficient	0.098 mm^{-1}	
F(000)	728	
Crystal size	0.420 x 0.235 x 0.187 mm^3	
Theta range for data collection	3.191 to 28.360°.	
Index ranges	-15<=h<=16, -8<=k<=8, -27<=l<=24	
Reflections collected	29603	
Independent reflections	4152 [R(int) = 0.0358]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.944 and 0.923	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4152 / 0 / 234	
Goodness-of-fit on F^2	1.671	
Final R indices [I>2sigma(I)]	R1 = 0.0460, wR2 = 0.1310	

R indices (all data)	R1 = 0.0587, wR2 = 0.1366
Extinction coefficient	n/a
Largest diff. peak and hole	0.523 and -0.249 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for KGP03. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	339(1)	11402(1)	-1767(1)	26(1)
O(2)	1192(1)	8274(1)	-2345(1)	28(1)
O(3)	5613(1)	6023(1)	924(1)	23(1)
O(4)	4663(1)	3907(1)	1852(1)	21(1)
O(5)	2562(1)	4435(1)	2082(1)	26(1)
C(1)	1004(1)	10137(2)	-1391(1)	19(1)
C(2)	1464(1)	8465(2)	-1683(1)	22(1)
C(3)	2130(1)	7191(2)	-1305(1)	26(1)
C(4)	2344(1)	7582(2)	-638(1)	23(1)
C(5)	1911(1)	9243(2)	-342(1)	17(1)
C(6)	1225(1)	10545(2)	-728(1)	18(1)
C(7)	694(1)	12324(2)	-429(1)	28(1)
C(8)	1061(1)	12814(2)	279(1)	28(1)
C(9)	1733(1)	11274(2)	649(1)	22(1)
C(10)	2139(1)	9656(2)	370(1)	18(1)
C(11)	2818(1)	8175(2)	776(1)	18(1)
C(12)	3915(1)	7864(2)	651(1)	19(1)
C(13)	4532(1)	6447(2)	1012(1)	18(1)
C(14)	4056(1)	5321(2)	1492(1)	18(1)
C(15)	2960(1)	5636(2)	1614(1)	19(1)
C(16)	2347(1)	7089(2)	1261(1)	19(1)
C(17)	1737(1)	6739(2)	-2676(1)	34(1)
C(18)	6137(1)	7191(2)	454(1)	29(1)
C(19)	4798(1)	2111(2)	1490(1)	26(1)
C(20)	1438(1)	4734(2)	2219(1)	34(1)

Table 3. Bond lengths [Å] and angles [°] for KGP03.

O(1)-C(1)	1.3709(14)
O(2)-C(2)	1.3694(15)
O(2)-C(17)	1.4242(16)
O(3)-C(13)	1.3734(14)
O(3)-C(18)	1.4227(15)
O(4)-C(14)	1.3829(13)
O(4)-C(19)	1.4299(15)
O(5)-C(15)	1.3638(15)
O(5)-C(20)	1.4329(15)
C(1)-C(6)	1.3849(17)
C(1)-C(2)	1.4072(17)
C(2)-C(3)	1.3774(18)
C(3)-C(4)	1.3902(18)
C(4)-C(5)	1.3908(16)
C(5)-C(6)	1.4101(16)
C(5)-C(10)	1.4822(16)
C(6)-C(7)	1.5093(16)
C(7)-C(8)	1.5130(18)
C(8)-C(9)	1.4916(17)
C(9)-C(10)	1.3389(17)
C(10)-C(11)	1.5029(16)
C(11)-C(16)	1.3869(17)
C(11)-C(12)	1.3950(17)
C(12)-C(13)	1.3904(17)
C(13)-C(14)	1.3955(17)
C(14)-C(15)	1.3932(17)
C(15)-C(16)	1.3975(16)

C(2)-O(2)-C(17)	116.43(10)
C(13)-O(3)-C(18)	117.05(9)
C(14)-O(4)-C(19)	112.69(9)
C(15)-O(5)-C(20)	116.55(9)
O(1)-C(1)-C(6)	119.14(11)
O(1)-C(1)-C(2)	119.86(11)

C(6)-C(1)-C(2)	120.99(11)
O(2)-C(2)-C(3)	125.59(11)
O(2)-C(2)-C(1)	114.52(10)
C(3)-C(2)-C(1)	119.89(12)
C(2)-C(3)-C(4)	119.29(12)
C(3)-C(4)-C(5)	121.66(11)
C(4)-C(5)-C(6)	119.10(11)
C(4)-C(5)-C(10)	121.55(10)
C(6)-C(5)-C(10)	119.34(10)
C(1)-C(6)-C(5)	119.05(11)
C(1)-C(6)-C(7)	119.39(10)
C(5)-C(6)-C(7)	121.52(11)
C(6)-C(7)-C(8)	116.75(10)
C(9)-C(8)-C(7)	116.34(11)
C(10)-C(9)-C(8)	123.85(12)
C(9)-C(10)-C(5)	121.17(11)
C(9)-C(10)-C(11)	120.80(11)
C(5)-C(10)-C(11)	118.00(10)
C(16)-C(11)-C(12)	120.18(11)
C(16)-C(11)-C(10)	119.96(11)
C(12)-C(11)-C(10)	119.85(11)
C(13)-C(12)-C(11)	119.83(11)
O(3)-C(13)-C(12)	124.21(11)
O(3)-C(13)-C(14)	115.52(10)
C(12)-C(13)-C(14)	120.26(11)
O(4)-C(14)-C(15)	119.63(11)
O(4)-C(14)-C(13)	120.64(10)
C(15)-C(14)-C(13)	119.73(11)
O(5)-C(15)-C(14)	115.41(10)
O(5)-C(15)-C(16)	124.60(11)
C(14)-C(15)-C(16)	119.99(11)
C(11)-C(16)-C(15)	119.99(11)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for KGP03. 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)	30(1)	27(1)	20(1)	1(1)	-6(1)	11(1)
O(2)	36(1)	28(1)	19(1)	-3(1)	-6(1)	10(1)
O(3)	17(1)	22(1)	29(1)	6(1)	1(1)	2(1)
O(4)	25(1)	19(1)	18(1)	1(1)	-5(1)	5(1)
O(5)	26(1)	30(1)	23(1)	10(1)	6(1)	7(1)
C(1)	16(1)	18(1)	21(1)	3(1)	-2(1)	1(1)
C(2)	24(1)	22(1)	19(1)	0(1)	-2(1)	1(1)
C(3)	33(1)	20(1)	24(1)	-3(1)	-4(1)	9(1)
C(4)	28(1)	18(1)	22(1)	1(1)	-6(1)	6(1)
C(5)	17(1)	15(1)	19(1)	2(1)	-1(1)	-1(1)
C(6)	15(1)	16(1)	21(1)	2(1)	0(1)	0(1)
C(7)	29(1)	26(1)	27(1)	-2(1)	-6(1)	12(1)
C(8)	36(1)	22(1)	25(1)	-1(1)	-2(1)	10(1)
C(9)	23(1)	22(1)	20(1)	0(1)	-2(1)	1(1)
C(10)	17(1)	18(1)	20(1)	3(1)	-2(1)	-1(1)
C(11)	21(1)	16(1)	17(1)	-2(1)	-4(1)	2(1)
C(12)	22(1)	16(1)	18(1)	1(1)	-1(1)	-1(1)
C(13)	17(1)	18(1)	19(1)	-4(1)	-3(1)	0(1)
C(14)	21(1)	16(1)	16(1)	-2(1)	-5(1)	2(1)
C(15)	24(1)	18(1)	15(1)	-1(1)	-1(1)	1(1)
C(16)	19(1)	21(1)	18(1)	-2(1)	-1(1)	2(1)
C(17)	46(1)	32(1)	23(1)	-9(1)	-7(1)	9(1)
C(18)	22(1)	27(1)	39(1)	7(1)	8(1)	2(1)
C(19)	32(1)	20(1)	26(1)	1(1)	2(1)	6(1)
C(20)	28(1)	38(1)	35(1)	14(1)	12(1)	9(1)

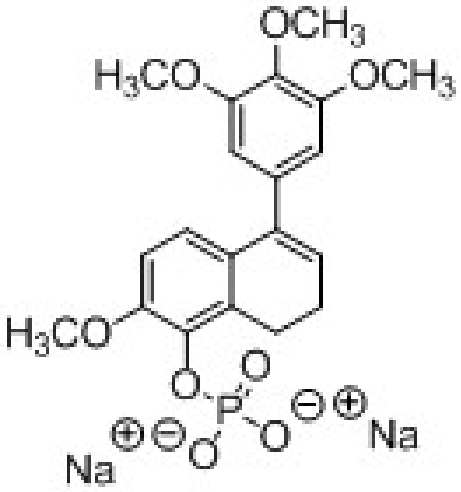
Table 5. Hydrogen bonds for KGP03 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(4)#1	0.90(2)	2.04(2)	2.8794(13)	155.2(15)
O(1)-H(1)...O(2)	0.90(2)	2.222(17)	2.6587(13)	109.5(13)

Symmetry transformations used to generate equivalent atoms:

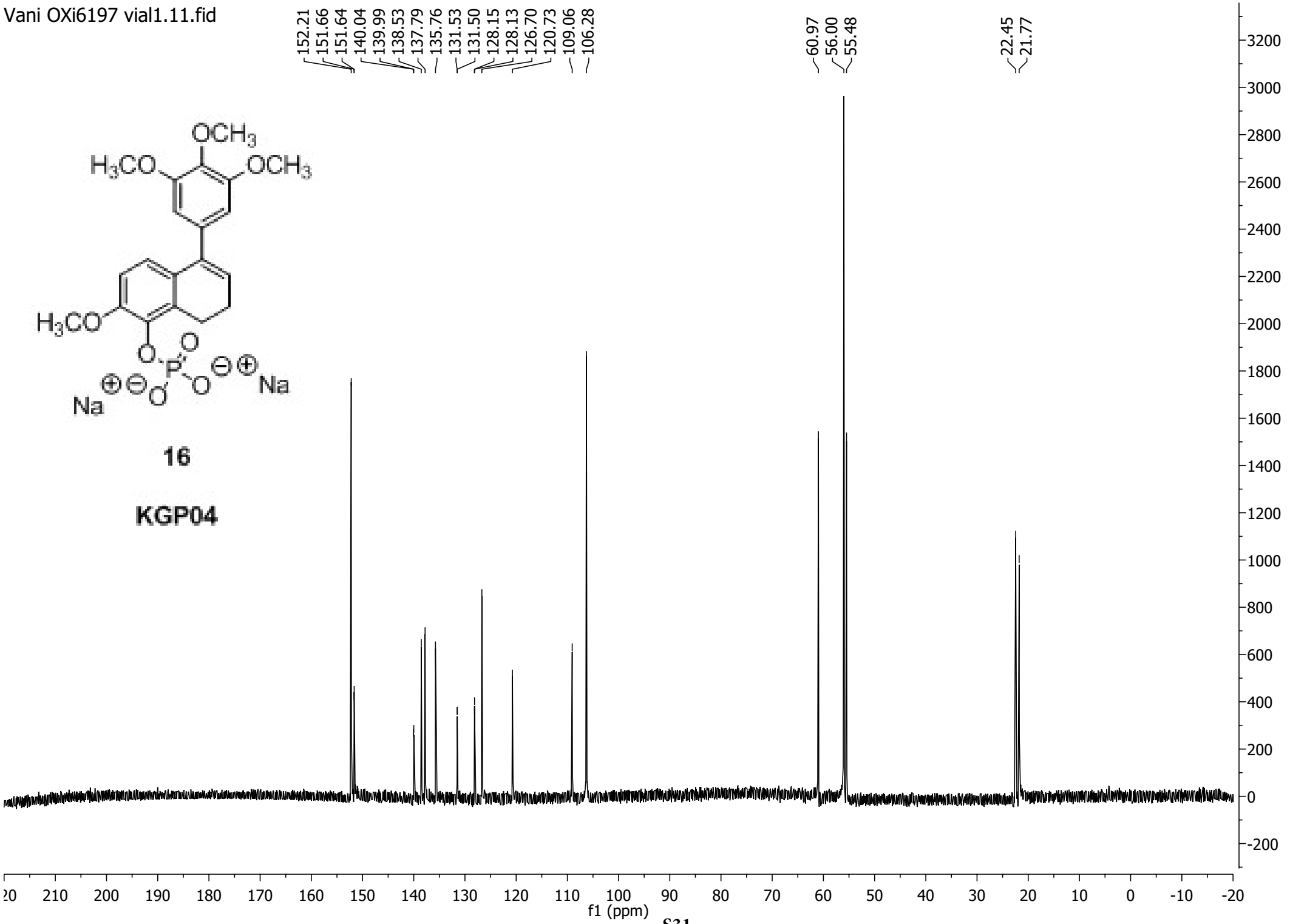
#1 x-1/2,-y+3/2,z-1/2

Vani OXi6197 vial1.10.fid



16

KGP04


Vani OXi6197 vial1.11.fid
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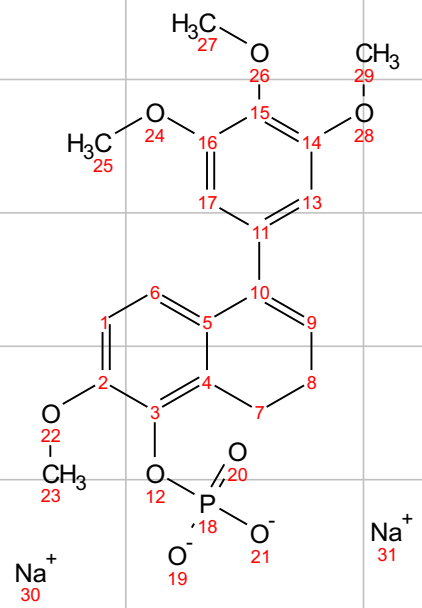
151.66
151.64
140.04
139.99
138.53
137.79
135.76
131.53
131.50
128.15
128.13
126.70
120.73
109.06
106.28
60.97
56.00
55.48
22.45
21.77
OCH3
H3CO
OCH3
H3CO
O
O
P
O
O
Na
Na
16
KGP04
f1 (ppm)

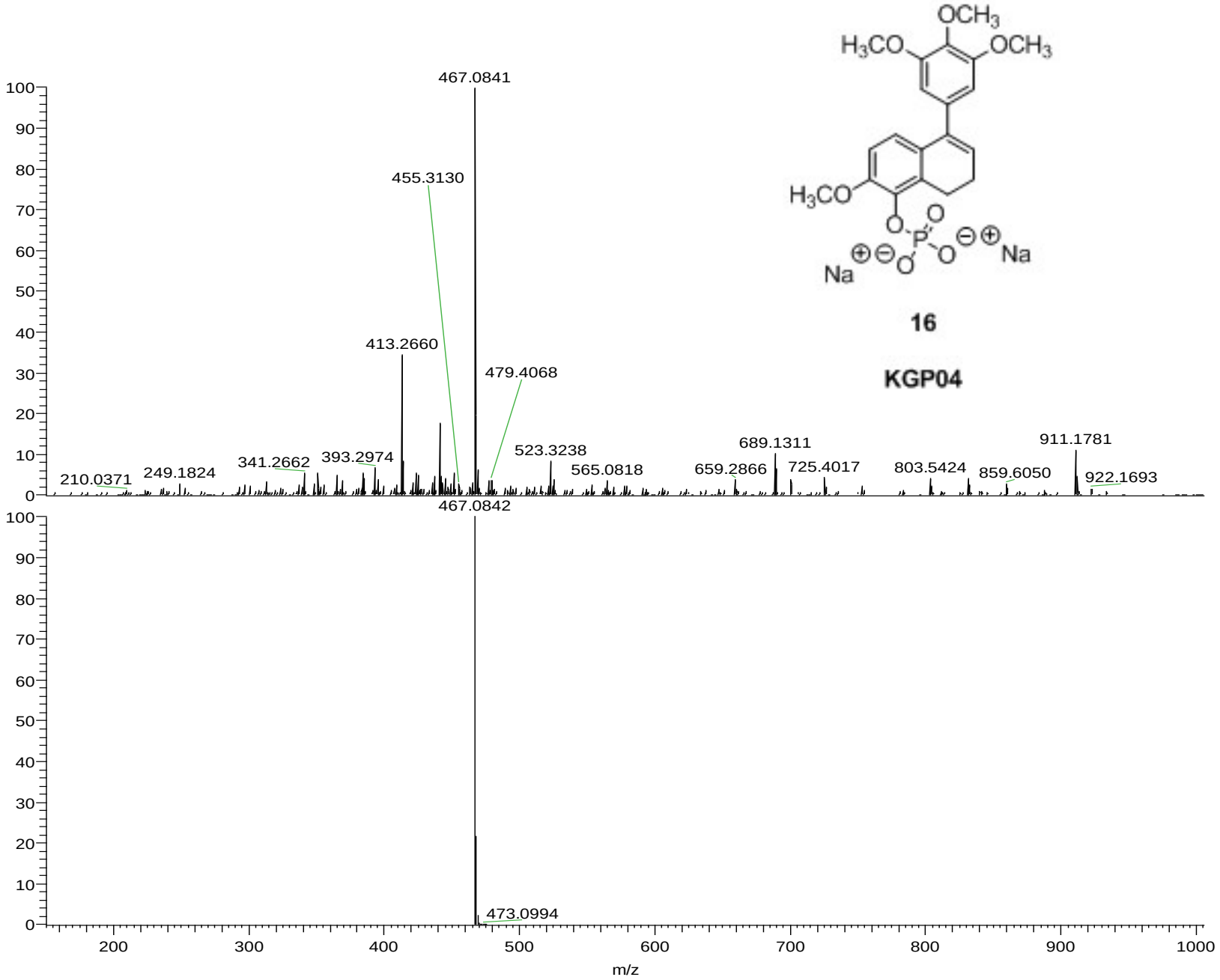
6197.10.fid

^{31}P NMR (243 MHz, D_2O) δ 0.54.



16

KGP04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413.2660
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523.3238
689.1311
911.1781
210.0371
249.1824
341.2662
393.2974
565.0818
659.2866
725.4017
803.5424
859.6050
922.1693
NL:
1.19E7
Madhavi's
OXi6197_+ESI#2-1
RT: 0.01-0.15 AV: 1
T: FTMS + p ESI Fu
ms [150.00-1000.00
16
KGP04
467.0842
473.0994
NL:
7.89E5
C 20 H 22 PO 8 Na 2:
C 20 H 22 P 1 O 8 Na 2
pa Chrg 1
m/z

Data File C:\Chem32\1\Data\ZHE\20170925 Vani OXi6197 Vial1.D
Sample Name: OXi6197

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Sample Operator : SYSTEM
Acq. Instrument : 1200 HPLC Location : 1
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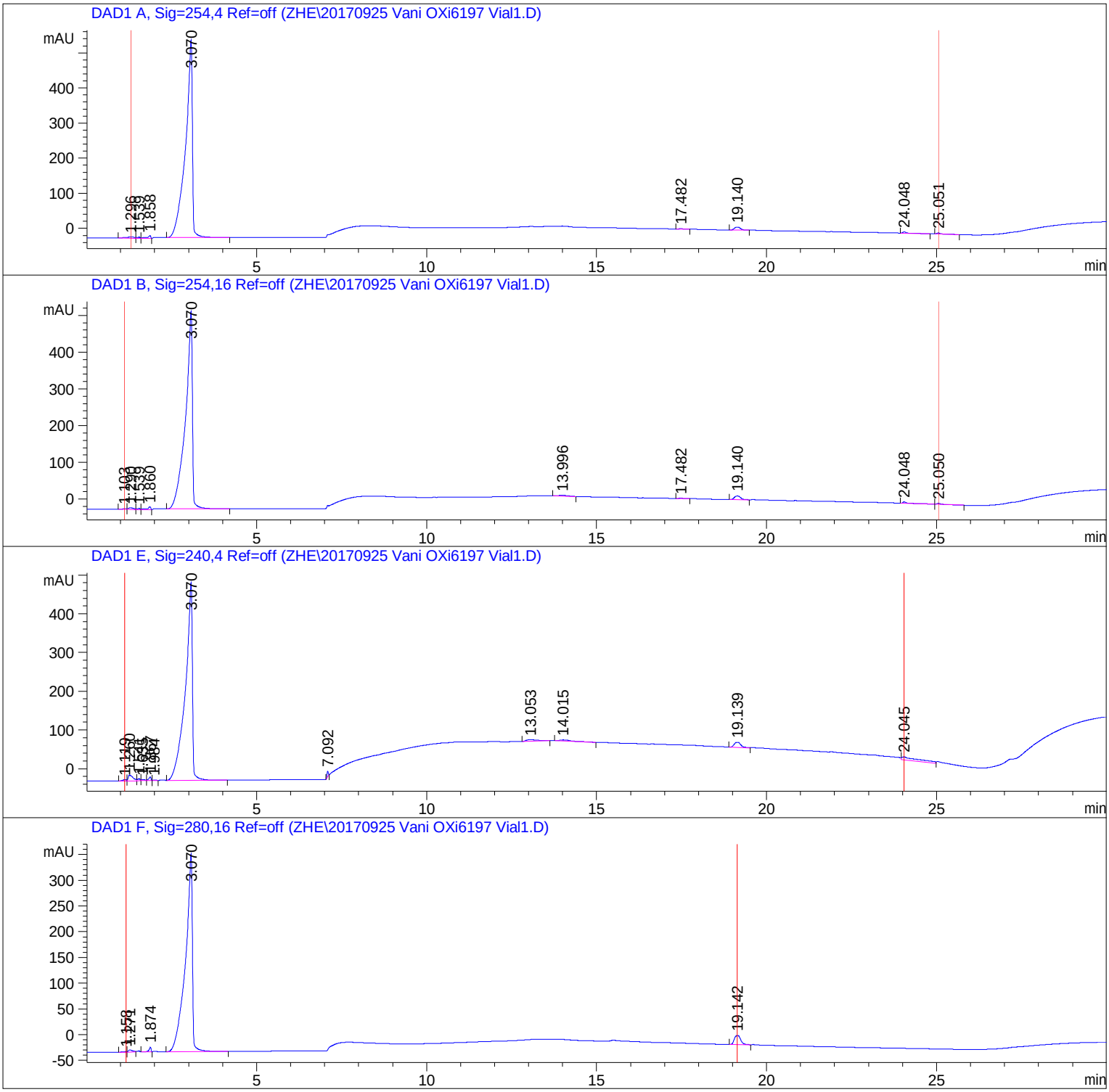
Inj Volume : No inj
Acq. Method : C:\Chem32\1\Methods\MASTERMETHOD2.M
Last changed : 12/2/2015 12:37:42 PM by Eric Lin
Analysis Method : C:\Chem32\1\Methods\KGP94_2.M
Last changed : 3/30/2015 10:52:31 AM by Graham
Sample Info : Master Method 2
OXi6197 (Vani Vial1)
with 0.1% TFA
20170925

Additional Info : Peak(s) manually integrated



Data File C:\Chem32\1\Data\ZHE\20170925 Vani OXi6197 Vial1.D
Sample Name: OXi6197

==========

Area Percent Report

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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	1.296	BV	0.2203	58.72168	3.75883	0.7077
2	1.539	VV	0.0836	19.94900	3.34274	0.2404
3	1.858	VB	0.1007	57.20063	8.07269	0.6893
4	3.070	BB	0.1875	7988.43213	563.10632	96.2718
5	17.482	BB	0.0960	11.76167	1.85554	0.1417
6	19.140	BB	0.2078	110.42595	8.59810	1.3308
7	24.048	BB	0.1124	30.82886	4.07009	0.3715
8	25.051	BB	0.1077	20.47215	2.78674	0.2467

Totals : 8297.79206 595.59105

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.103	BV	0.1210	14.26544	1.58503	0.1774
2	1.290	VV	0.1741	50.63790	4.33940	0.6296
3	1.539	VV	0.0823	19.82595	3.38714	0.2465
4	1.860	VB	0.1002	56.60329	8.03315	0.7038
5	3.070	BB	0.1879	7652.09180	538.05182	95.1425
6	13.996	BB	0.2857	37.01324	1.91302	0.4602
7	17.482	BB	0.0939	10.37951	1.68330	0.1291
8	19.140	BB	0.2078	128.46175	10.00571	1.5972
9	24.048	BV	0.1560	42.93175	3.79447	0.5338
10	25.050	VB	0.1426	30.56049	2.95647	0.3800

Totals : 8042.77112 575.74951

Signal 3: DAD1 E, Sig=240,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.119	BV	0.1003	22.11087	2.99043	0.2621
2	1.260	VV	0.1551	145.50647	14.75159	1.7250
3	1.541	VV	0.0754	27.96795	5.31454	0.3316
4	1.635	VV	0.1225	24.21500	2.70307	0.2871

Data File C:\Chem32\1\Data\ZHE\20170925 Vani OXi6197 Vial1.D
Sample Name: OXi6197

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
5	1.867	VB	0.0717	44.41597	9.65304	0.5265
6	1.984	BB	0.1087	6.57659	1.02770	0.0780
7	3.070	BB	0.1919	7438.32031	510.65103	88.1803
8	7.092	BB	0.0404	34.64425	14.25243	0.4107
9	13.053	BB	0.3346	95.22648	4.16650	1.1289
10	14.015	BB	0.3248	65.86151	2.90192	0.7808
11	19.139	BV	0.2182	183.04886	13.32661	2.1700
12	24.045	VV	0.4913	347.46405	8.67472	4.1191
Totals :				8435.35830	590.41356	

Signal 4: DAD1 F, Sig=280,16 Ref=off

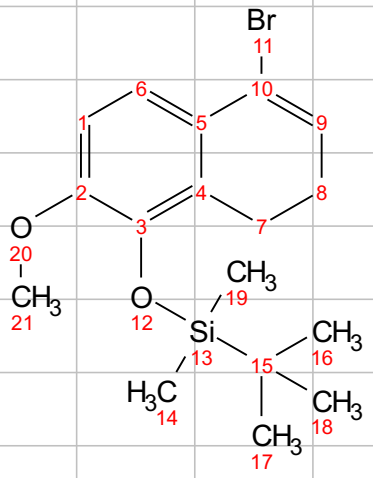
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.158	BV	0.1072	8.64392	1.03768	0.1495
2	1.271	VV	0.1391	37.98717	3.99077	0.6568
3	1.874	BB	0.0693	41.83498	8.82020	0.7233
4	3.070	BB	0.1880	5465.47412	384.15509	94.4977
5	19.142	BB	0.2075	229.76923	17.92632	3.9727
Totals :				5783.70942	415.93006	

==========

*** End of Report ***

221_8_PROTON_001
221_8

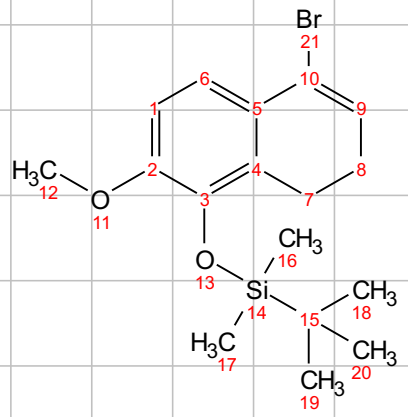
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.16 (d, *J* = 8.5 Hz, 1H), 6.69 (d, *J* = 8.5 Hz, 1H), 6.29 (t, *J* = 4.8 Hz, 1H), 3.80 (s, 3H), 2.86 – 2.82 (m, 2H), 2.29 (td, *J* = 8.0, 4.9 Hz, 2H), 1.00 (s, 9H), 0.16 (s, 6H).



14

CJM-IV-221_10.11.fid

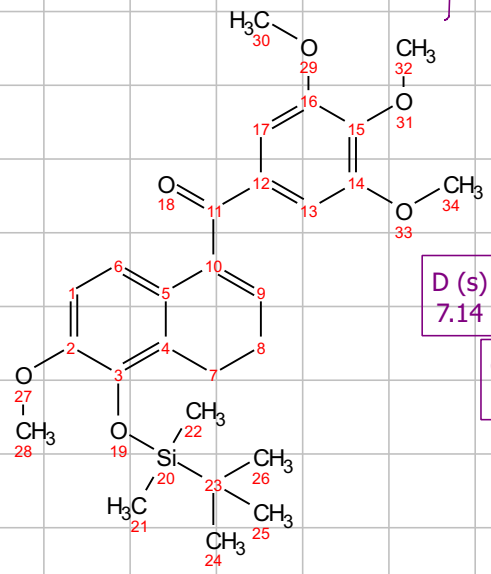
^{13}C NMR (151 MHz, $CDCl_3$) δ 150.59, 141.06, 128.16, 127.70, 126.69, 121.10, 120.06, 108.21, 54.85, 26.13, 26.04, 24.99, 21.47, -3.98.



14

222_55_PROTON_001
222_55

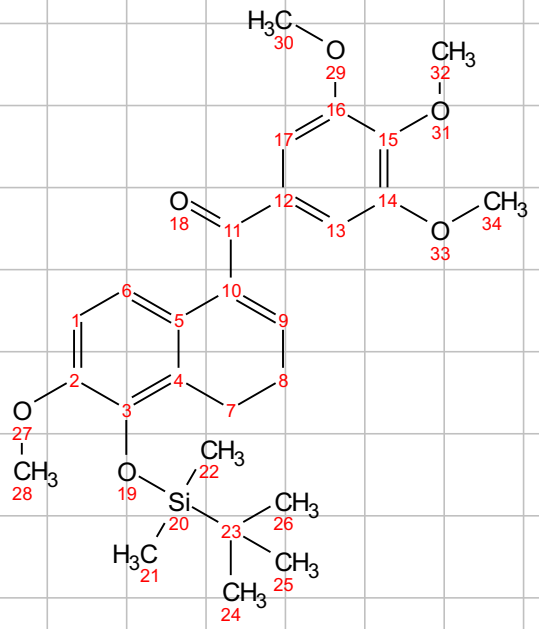
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.14 (s, 2H), 6.80 (d, *J* = 8.4 Hz, 1H), 6.63 (s, 1H), 6.32 (t, *J* = 4.7 Hz, 1H), 3.91 (s, 3H), 3.84 (s, 6H), 3.78 (s, 3H), 2.89 (t, *J* = 7.9 Hz, 2H), 2.43 (td, *J* = 7.9, 4.8 Hz, 2H), 1.01 (s, 9H), 0.17 (s, 6H).



12

222_55_CARBON_001
222_55

^{13}C NMR (126 MHz, cdcl$_3$) δ 196.38, 152.76, 150.19, 142.25, 141.54, 138.63, 133.05, 132.99, 127.25, 125.77, 119.18, 108.67, 107.40, 60.93, 56.20, 54.83, 26.03, 22.79, 21.34, 18.83, -4.01.



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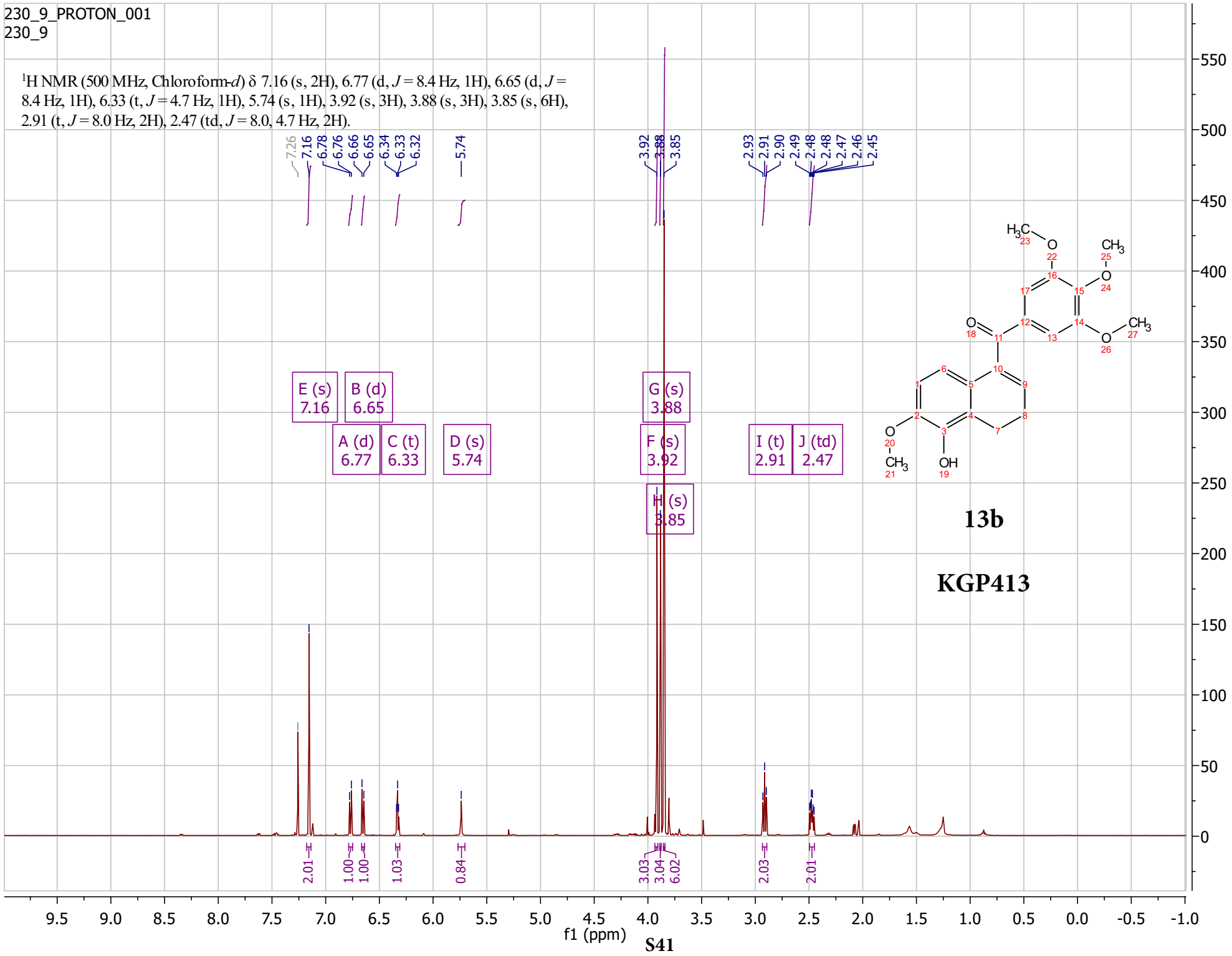
230_9_PROTON_001
230_9
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7.26
7.16
6.78
6.76
6.66
6.65
6.34
6.33
6.32
5.74
3.92
3.88
3.85
2.93
2.91
2.90
2.49
2.48
2.48
2.47
2.46
2.45
E (s) 7.16
B (d) 6.65
A (d) 6.77
C (t) 6.33
D (s) 5.74
G (s) 3.88
F (s) 3.92
H (s) 3.85
I (t) 2.91
J (td) 2.47
13b
KGP413
2.01
1.00
1.00
1.03
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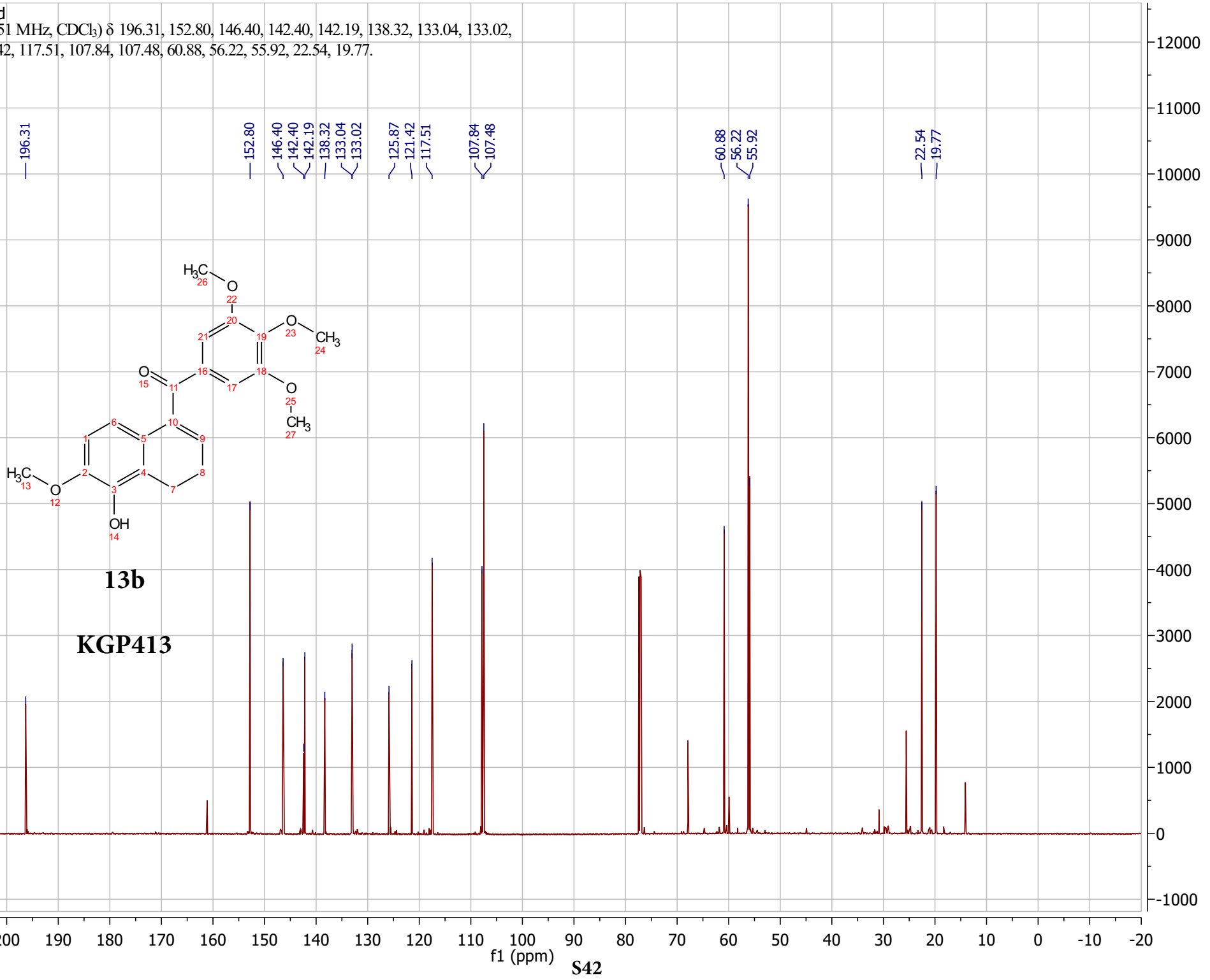
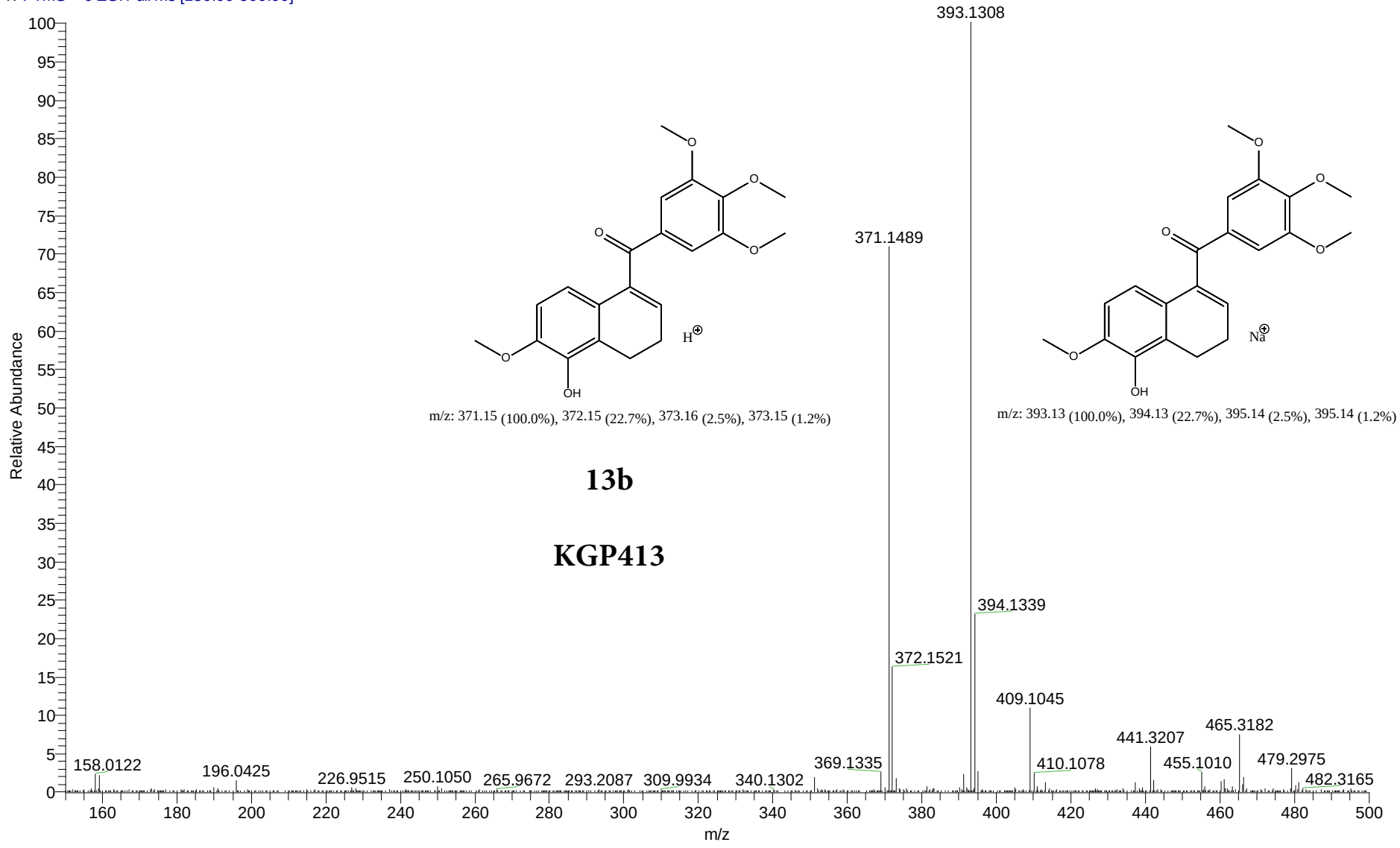
3.03
3.04
6.02
2.03
2.01
f1 (ppm)
S41

KGP413.10.fid

^{13}C NMR (151 MHz, $CDCl_3$) δ 196.31, 152.80, 146.40, 142.40, 142.19, 138.32, 133.04, 133.02, 125.87, 121.42, 117.51, 107.84, 107.48, 60.88, 56.22, 55.92, 22.54, 19.77.

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T: FTMS + c ESI Full ms [150.00-500.00]
Relative Abundance
m/z
393.1308
371.1489
394.1339
372.1521
409.1045
465.3182
441.3207
479.2975
455.1010
482.3165
410.1078
369.1335
158.0122
196.0425
226.9515
250.1050
265.9672
293.2087
309.9934
340.1302
m/z: 371.15 (100.0%), 372.15 (22.7%), 373.16 (2.5%), 373.15 (1.2%)
m/z: 393.13 (100.0%), 394.13 (22.7%), 395.14 (2.5%), 395.14 (1.2%)
13b
KGP413

Data File C:\Chem32\1\Data\Casey\CJM-V-223.D
Sample Name: CJM-V-223

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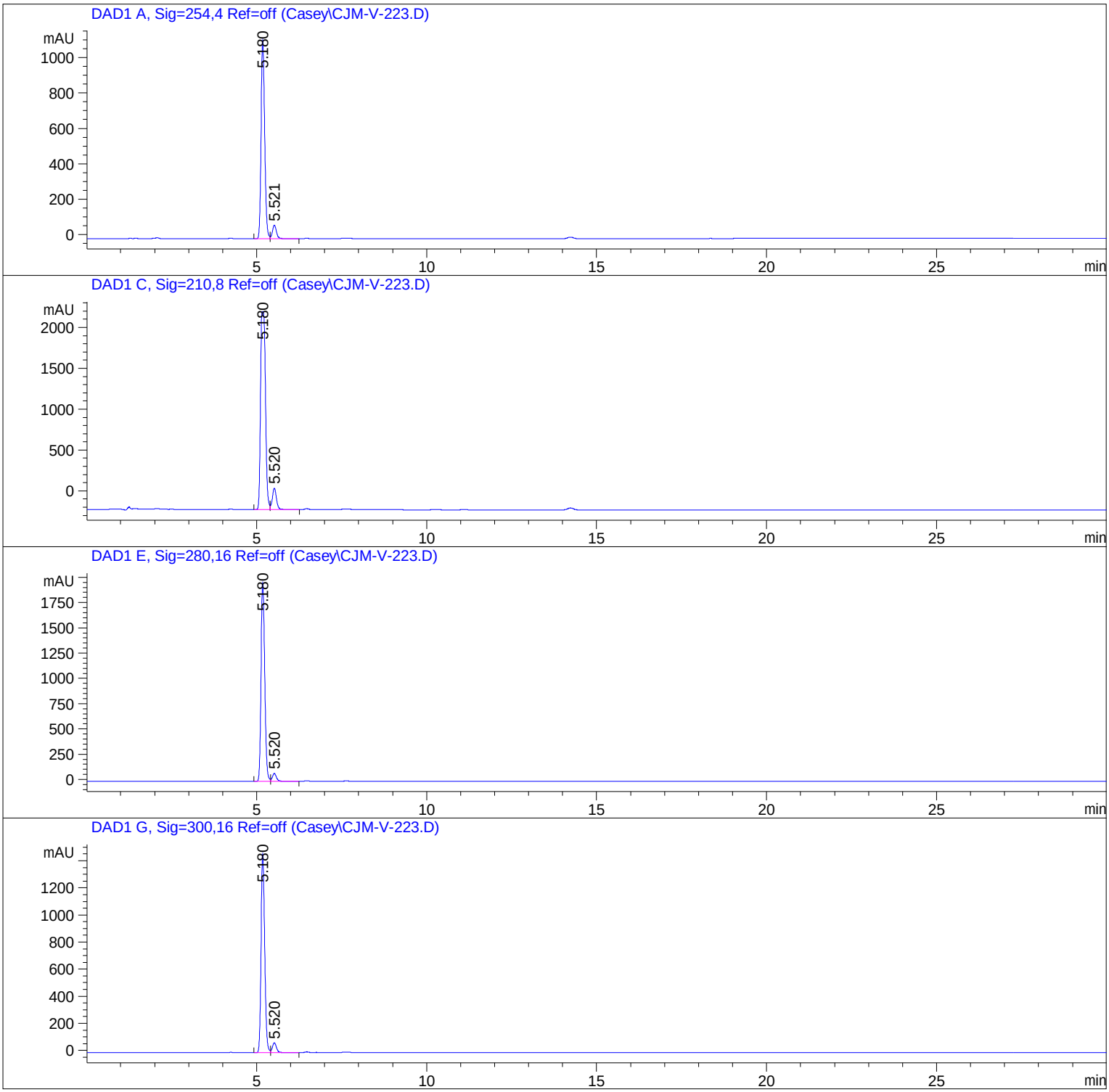
Analysis Method : C:\CHEM32\1\METHODS\RT-ACNWASH 2.M
Last changed : 7/9/2015 2:27:22 PM by Blake
Method Info : General Column Wash Method

Additional Info : Peak(s) manually integrated



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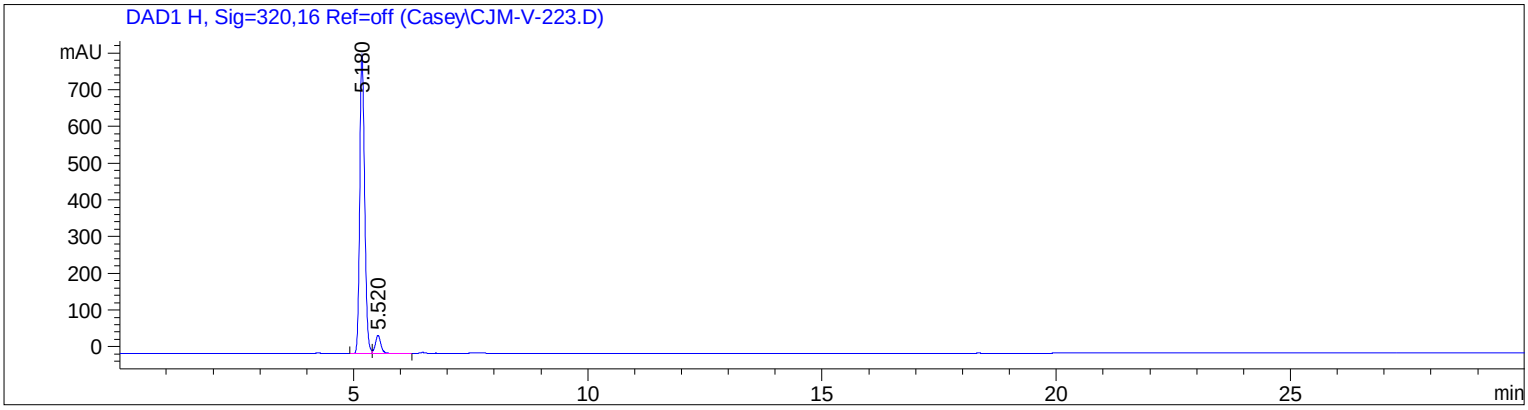
Sample Name: CJM-V-223



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Area Percent Report

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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	5.180	BV	0.1145	8328.20410	1123.58716	92.9875
2	5.521	VB	0.1234	628.06073	76.81297	7.0125
Totals :				8956.26483	1200.40012	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.180	BV	0.1638	2.44848e4	2424.16919	91.7750
2	5.520	VB	0.1247	2194.34351	264.87863	8.2250
Totals :				2.66791e4	2689.04782	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.180	BV	0.1210	1.50108e4	1966.61267	95.7647
2	5.520	VB	0.1268	663.86365	78.38828	4.2353
Totals :				1.56747e4	2045.00095	

Data File C:\Chem32\1\Data\Casey\CJM-V-223.D
Sample Name: CJM-V-223

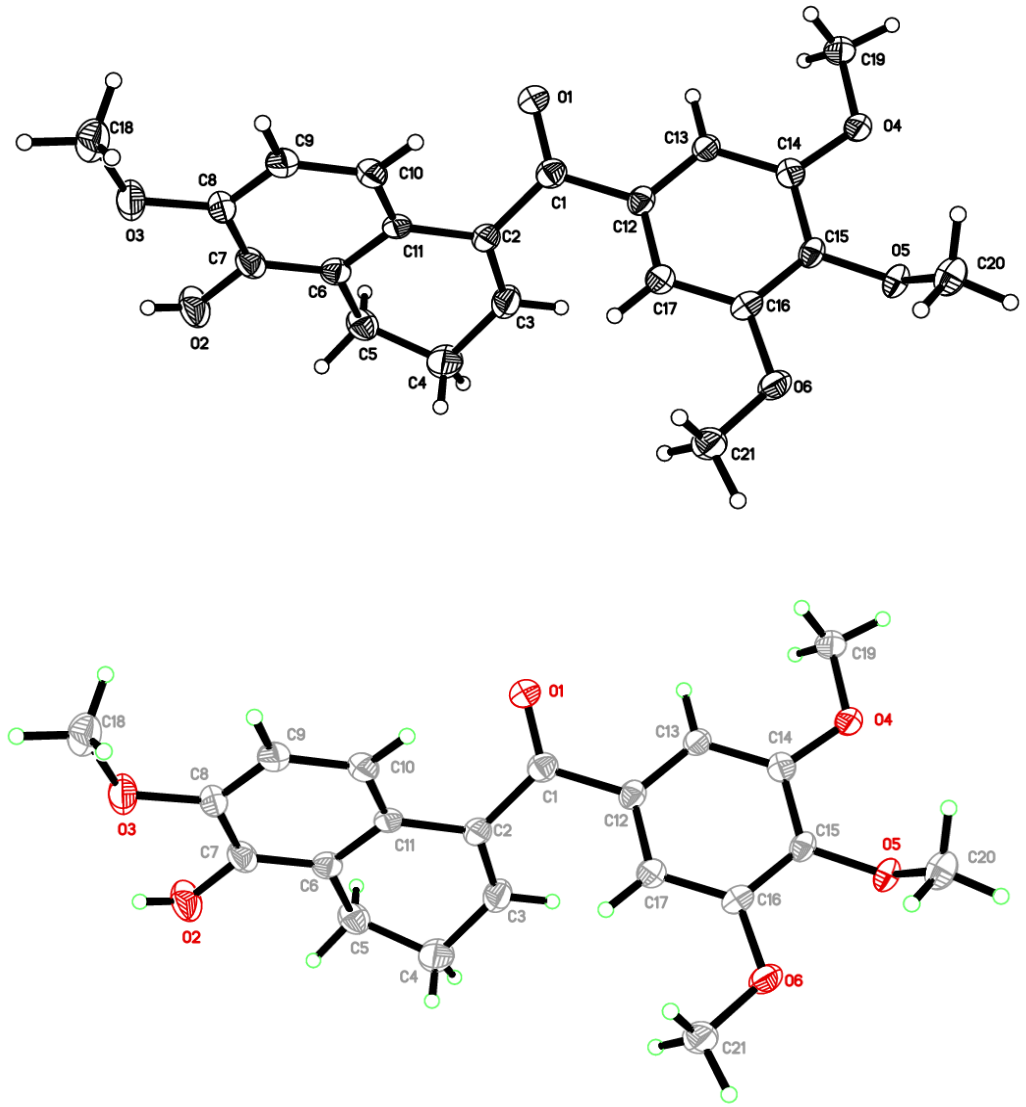
Signal 4: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.180	BV	0.1153	1.09799e4	1467.68677	94.6991
2	5.520	VB	0.1251	614.61560	73.83636	5.3009
Totals :				1.15945e4	1541.52312	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.180	BV	0.1144	6020.76904	813.01691	93.6785
2	5.520	VB	0.1240	406.28680	49.38525	6.3215
Totals :				6427.05585	862.40216	

*** End of Report ***



X-ray crystal structure of **KGP413**

X-ray Crystallographic Analysis:

X-ray crystallographic analysis of compound KGP413. Crystallographic data were collected on a crystal of KGP413 with dimensions 0.276 x 0.100 x 0.053 mm3. Data were collected at 150(2) 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-S5). All data were processed using the Bruker AXS SHELXTL software, version 6.10.

Table 1. Crystal data and structure refinement for KGP413.

Identification code	KGP413	
Empirical formula	C21 H22 O6	
Formula weight	370.38	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 2/c	
Unit cell dimensions	a = 56.225(4) Å	α= 90°.
	b = 4.6615(3) Å	β= 101.729(4)°.
	c = 14.0454(9) Å	γ = 90°.
Volume	3604.3(4) $Å^3$	
Z	8	
Density (calculated)	1.365 Mg/m^3	
Absorption coefficient	0.100 mm^{-1}	
F(000)	1568	
Crystal size	0.276 x 0.100 x 0.053 mm^3	
Theta range for data collection	2.220 to 26.376°.	
Index ranges	-69<=h<=70, -5<=k<=4, -17<=l<=17	
Reflections collected	16772	
Independent reflections	3661 [R(int) = 0.0589]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.995 and 0.972	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3661 / 0 / 252	
Goodness-of-fit on F^2	1.015	
Final R indices [I>2sigma(I)]	R1 = 0.0468, wR2 = 0.0937	
R indices (all data)	R1 = 0.0924, wR2 = 0.1113	

Extinction coefficient	n/a
Largest diff. peak and hole	0.224 and -0.226 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for KGP413. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	1314(1)	5006(3)	2944(1)	31(1)
O(2)	218(1)	6619(4)	3562(1)	39(1)
O(3)	218(1)	10104(3)	2050(1)	35(1)
O(4)	2198(1)	3468(3)	4800(1)	24(1)
O(5)	2218(1)	6154(3)	6480(1)	23(1)
O(6)	1840(1)	9126(3)	6846(1)	29(1)
C(1)	1322(1)	5492(4)	3807(1)	24(1)
C(2)	1095(1)	5639(4)	4200(1)	22(1)
C(3)	1090(1)	4425(5)	5060(1)	31(1)
C(4)	864(1)	4297(5)	5459(1)	40(1)
C(5)	640(1)	4043(4)	4656(1)	29(1)
C(6)	647(1)	6155(4)	3850(1)	22(1)
C(7)	436(1)	7337(4)	3321(1)	26(1)
C(8)	443(1)	9214(4)	2549(1)	26(1)
C(9)	662(1)	10026(4)	2350(1)	26(1)
C(10)	875(1)	8882(4)	2883(1)	25(1)
C(11)	871(1)	6903(4)	3617(1)	20(1)
C(12)	1561(1)	5814(4)	4499(1)	21(1)
C(13)	1765(1)	4456(4)	4284(1)	21(1)
C(14)	1986(1)	4664(4)	4933(1)	21(1)
C(15)	2004(1)	6199(4)	5801(1)	20(1)
C(16)	1802(1)	7647(4)	5988(1)	22(1)
C(17)	1580(1)	7467(4)	5340(1)	23(1)
C(18)	215(1)	12066(5)	1260(2)	39(1)
C(19)	2191(1)	1785(4)	3945(1)	28(1)
C(20)	2364(1)	8680(4)	6473(1)	29(1)
C(21)	1643(1)	10788(4)	7049(1)	30(1)

Table 3. Bond lengths [Å] and angles [°] for KGP413.

O(1)-C(1)	1.224(2)
O(2)-C(7)	1.374(2)
O(3)-C(8)	1.376(2)
O(3)-C(18)	1.435(2)
O(4)-C(14)	1.363(2)
O(4)-C(19)	1.428(2)
O(5)-C(15)	1.373(2)
O(5)-C(20)	1.438(2)
O(6)-C(16)	1.367(2)
O(6)-C(21)	1.428(2)
C(1)-C(2)	1.495(3)
C(1)-C(12)	1.496(3)
C(2)-C(3)	1.340(3)
C(2)-C(11)	1.477(3)
C(3)-C(4)	1.490(3)
C(4)-C(5)	1.513(3)
C(5)-C(6)	1.507(3)
C(6)-C(7)	1.381(3)
C(6)-C(11)	1.409(3)
C(7)-C(8)	1.399(3)
C(8)-C(9)	1.372(3)
C(9)-C(10)	1.386(3)
C(10)-C(11)	1.388(3)
C(12)-C(13)	1.395(3)
C(12)-C(17)	1.396(2)
C(13)-C(14)	1.389(3)
C(14)-C(15)	1.399(3)
C(15)-C(16)	1.391(3)
C(16)-C(17)	1.388(3)

C(8)-O(3)-C(18)	116.88(15)
C(14)-O(4)-C(19)	117.53(14)
C(15)-O(5)-C(20)	113.81(14)
C(16)-O(6)-C(21)	117.56(14)

O(1)-C(1)-C(2)	120.74(17)
O(1)-C(1)-C(12)	120.71(17)
C(2)-C(1)-C(12)	118.48(15)
C(3)-C(2)-C(11)	119.78(17)
C(3)-C(2)-C(1)	119.37(18)
C(11)-C(2)-C(1)	120.68(16)
C(2)-C(3)-C(4)	122.13(19)
C(3)-C(4)-C(5)	111.46(16)
C(6)-C(5)-C(4)	111.45(16)
C(7)-C(6)-C(11)	119.25(17)
C(7)-C(6)-C(5)	121.06(17)
C(11)-C(6)-C(5)	119.68(17)
O(2)-C(7)-C(6)	118.73(18)
O(2)-C(7)-C(8)	120.61(18)
C(6)-C(7)-C(8)	120.66(17)
C(9)-C(8)-O(3)	125.48(18)
C(9)-C(8)-C(7)	119.90(18)
O(3)-C(8)-C(7)	114.62(17)
C(8)-C(9)-C(10)	119.92(18)
C(9)-C(10)-C(11)	120.89(18)
C(10)-C(11)-C(6)	119.24(17)
C(10)-C(11)-C(2)	122.37(17)
C(6)-C(11)-C(2)	118.33(16)
C(13)-C(12)-C(17)	120.51(17)
C(13)-C(12)-C(1)	118.77(16)
C(17)-C(12)-C(1)	120.72(17)
C(14)-C(13)-C(12)	119.51(17)
O(4)-C(14)-C(13)	125.05(16)
O(4)-C(14)-C(15)	114.76(16)
C(13)-C(14)-C(15)	120.19(17)
O(5)-C(15)-C(16)	120.55(16)
O(5)-C(15)-C(14)	119.64(16)
C(16)-C(15)-C(14)	119.75(17)
O(6)-C(16)-C(17)	124.43(17)
O(6)-C(16)-C(15)	115.17(16)
C(17)-C(16)-C(15)	120.37(17)

C(16)-C(17)-C(12) 119.53(17)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for KGP413. 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)	25(1)	45(1)	21(1)	-6(1)	3(1)	1(1)
O(2)	21(1)	50(1)	48(1)	12(1)	11(1)	0(1)
O(3)	22(1)	45(1)	37(1)	10(1)	3(1)	6(1)
O(4)	21(1)	31(1)	20(1)	-3(1)	2(1)	4(1)
O(5)	21(1)	23(1)	21(1)	2(1)	-4(1)	-1(1)
O(6)	30(1)	34(1)	20(1)	-8(1)	-2(1)	8(1)
C(1)	25(1)	22(1)	22(1)	1(1)	4(1)	1(1)
C(2)	21(1)	25(1)	21(1)	-4(1)	3(1)	-3(1)
C(3)	25(1)	40(1)	25(1)	6(1)	0(1)	1(1)
C(4)	34(1)	60(2)	27(1)	11(1)	10(1)	-3(1)
C(5)	26(1)	31(1)	33(1)	3(1)	11(1)	-2(1)
C(6)	24(1)	21(1)	22(1)	-2(1)	6(1)	-1(1)
C(7)	19(1)	29(1)	31(1)	-3(1)	8(1)	-3(1)
C(8)	20(1)	30(1)	27(1)	-2(1)	3(1)	4(1)
C(9)	27(1)	31(1)	22(1)	2(1)	7(1)	3(1)
C(10)	21(1)	31(1)	24(1)	-1(1)	7(1)	-1(1)
C(11)	22(1)	22(1)	17(1)	-5(1)	4(1)	0(1)
C(12)	20(1)	22(1)	19(1)	3(1)	1(1)	-2(1)
C(13)	21(1)	23(1)	18(1)	0(1)	2(1)	-2(1)
C(14)	21(1)	19(1)	22(1)	5(1)	4(1)	1(1)
C(15)	19(1)	20(1)	18(1)	4(1)	-1(1)	-1(1)
C(16)	27(1)	20(1)	18(1)	-1(1)	1(1)	-1(1)
C(17)	22(1)	24(1)	21(1)	1(1)	4(1)	1(1)
C(18)	34(1)	43(1)	38(1)	10(1)	2(1)	10(1)
C(19)	27(1)	32(1)	24(1)	-7(1)	5(1)	2(1)
C(20)	29(1)	26(1)	29(1)	0(1)	-2(1)	-5(1)
C(21)	32(1)	29(1)	26(1)	-4(1)	3(1)	9(1)

Table 5. Hydrogen bonds for KGP413 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(19)-H(19C)...O(6)#1	0.98	2.61	3.226(2)	121.0
C(20)-H(20B)...O(5)#2	0.98	2.66	3.519(2)	147.0
C(20)-H(20C)...O(6)	0.98	2.59	3.104(2)	112.8
C(18)-H(18B)...O(2)#3	0.98	2.56	3.281(3)	130.2
O(2)-H(1)...O(3)	0.81(3)	2.26(3)	2.674(2)	112(3)
O(2)-H(1)...O(3)#4	0.81(3)	2.14(3)	2.924(2)	162(3)
C(19)-H(19C)...O(6)#1	0.98	2.61	3.226(2)	121.0
C(20)-H(20B)...O(5)#2	0.98	2.66	3.519(2)	147.0
C(20)-H(20C)...O(6)	0.98	2.59	3.104(2)	112.8
C(18)-H(18B)...O(2)#3	0.98	2.56	3.281(3)	130.2
O(2)-H(1)...O(3)	0.81(3)	2.26(3)	2.674(2)	112(3)
O(2)-H(1)...O(3)#4	0.81(3)	2.14(3)	2.924(2)	162(3)

Symmetry transformations used to generate equivalent atoms:

#1 x,-y+1,z-1/2 #2 -x+1/2,y+1/2,-z+3/2 #3 -x,y+1,-z+1/2

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

Table 5. Hydrogen bonds for kp72 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(19)-H(19C)...O(6)#1	0.98	2.61	3.226(2)	121.0
C(20)-H(20B)...O(5)#2	0.98	2.66	3.519(2)	147.0
C(20)-H(20C)...O(6)	0.98	2.59	3.104(2)	112.8
C(18)-H(18B)...O(2)#3	0.98	2.56	3.281(3)	130.2
O(2)-H(1)...O(3)	0.81(3)	2.26(3)	2.674(2)	112(3)
O(2)-H(1)...O(3)#4	0.81(3)	2.14(3)	2.924(2)	162(3)
C(19)-H(19C)...O(6)#1	0.98	2.61	3.226(2)	121.0
C(20)-H(20B)...O(5)#2	0.98	2.66	3.519(2)	147.0
C(20)-H(20C)...O(6)	0.98	2.59	3.104(2)	112.8
C(18)-H(18B)...O(2)#3	0.98	2.56	3.281(3)	130.2
O(2)-H(1)...O(3)	0.81(3)	2.26(3)	2.674(2)	112(3)
O(2)-H(1)...O(3)#4	0.81(3)	2.14(3)	2.924(2)	162(3)

Symmetry transformations used to generate equivalent atoms:

#1 x,-y+1,z-1/2 #2 -x+1/2,y+1/2,-z+3/2 #3 -x,y+1,-z+1/2

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

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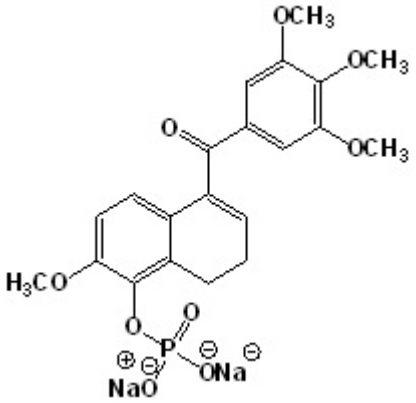
Vani_Oxi6197



18

KGP152

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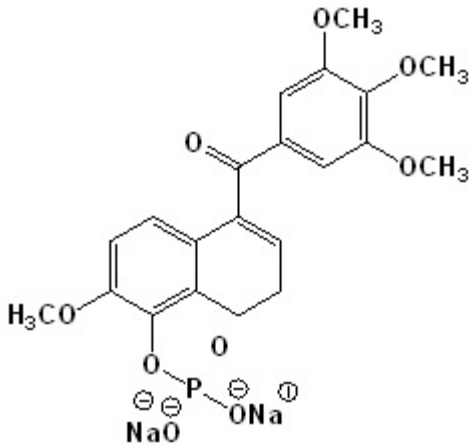

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KGP152

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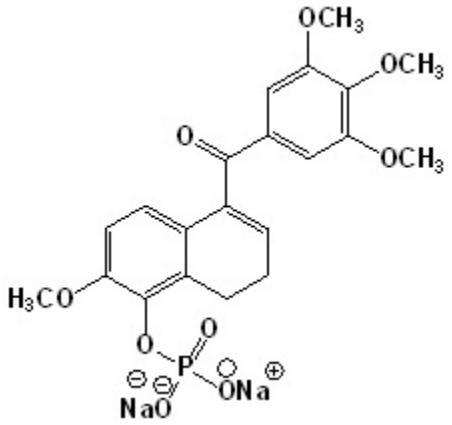

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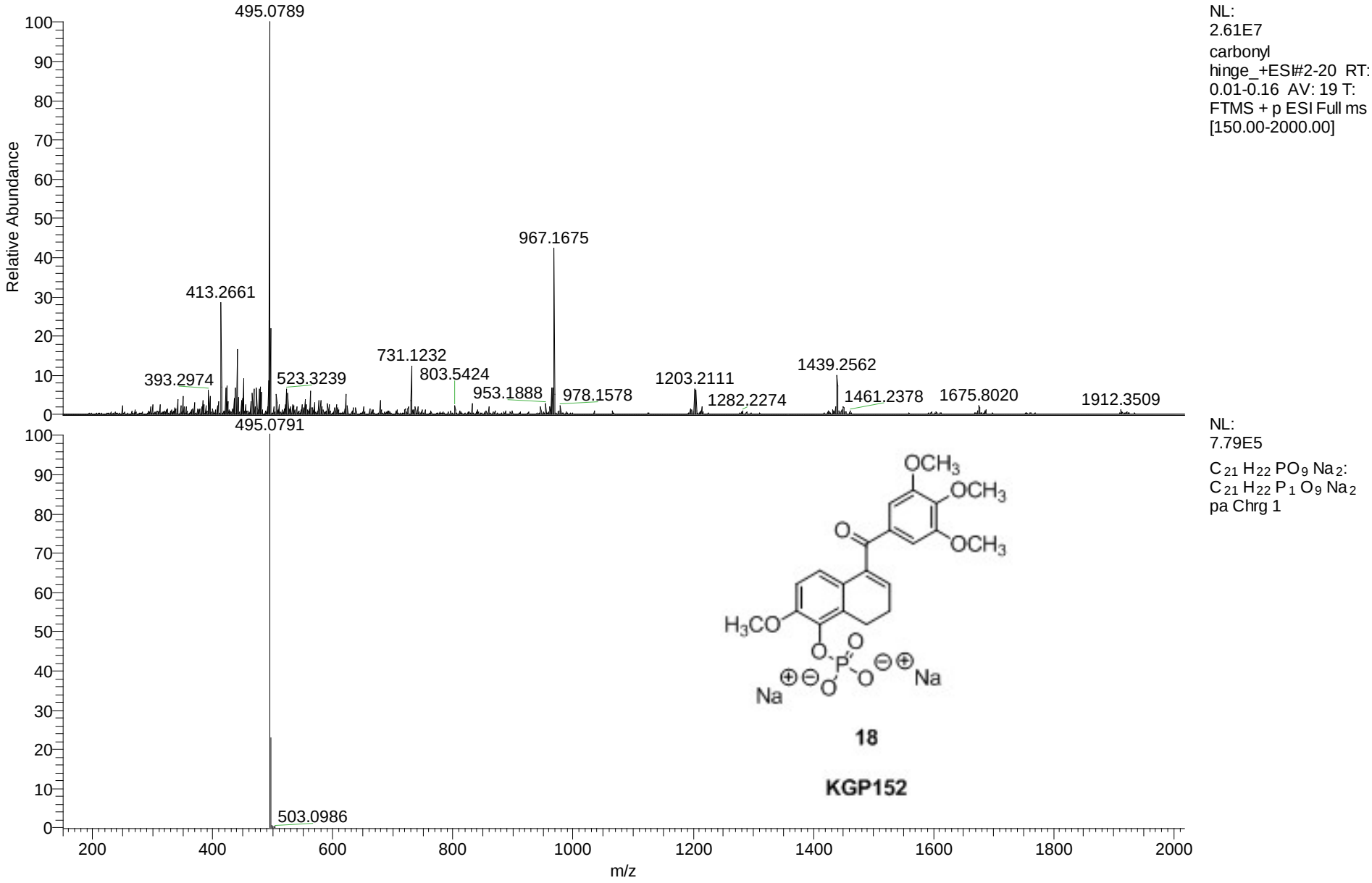
KGP152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carbonyl
hinge_+ESI#2-20 RT:
0.01-0.16 AV: 19 T:
FTMS + p ESI Full ms
[150.00-2000.00]
495.0791
503.0986
NL:
7.79E5
C21 H22 PO9 Na2:
C21 H22 P1 O9 Na2
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Na
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KGP152
m/z

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Sample Name: Benzoyl DHN salt

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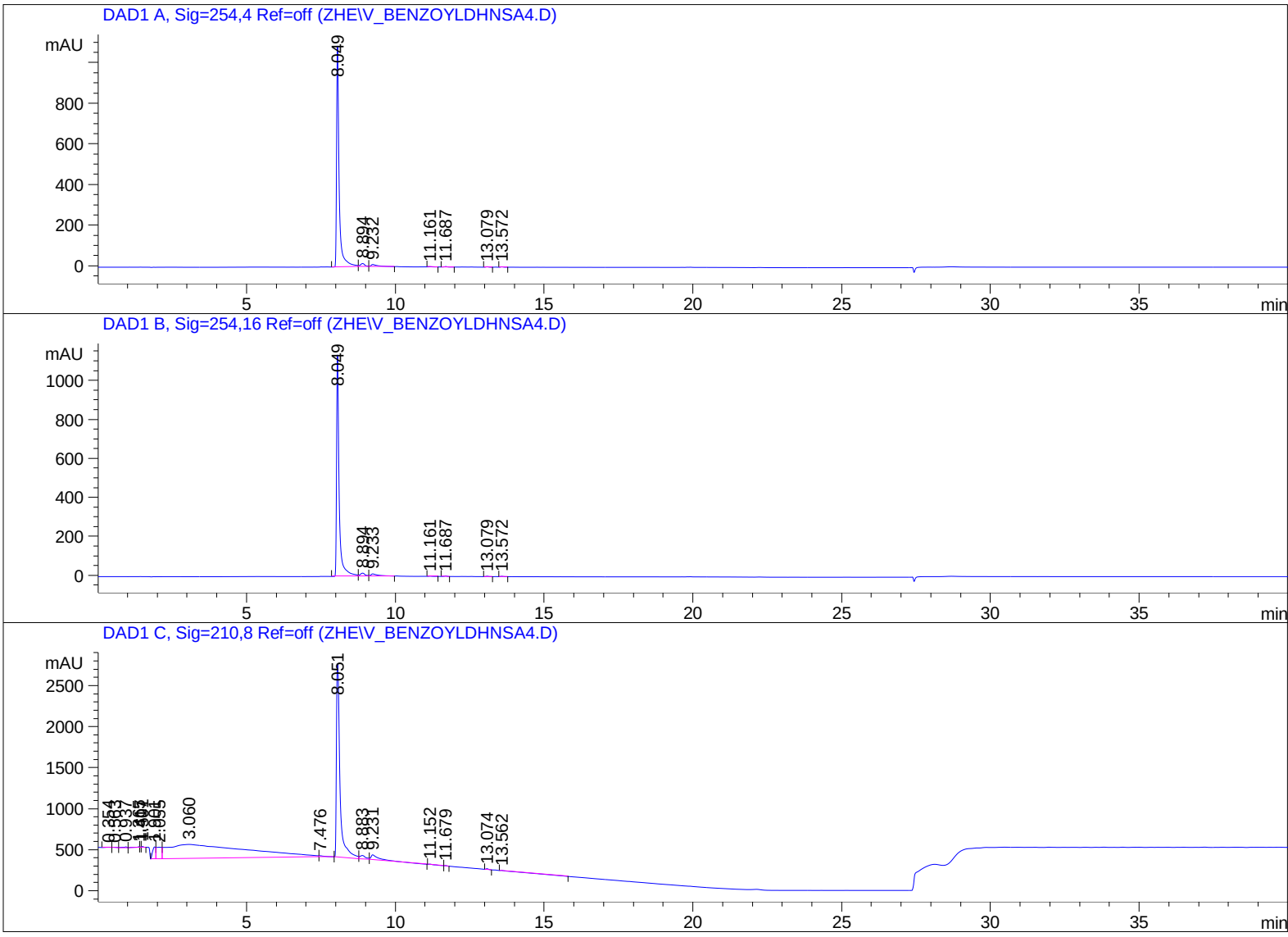

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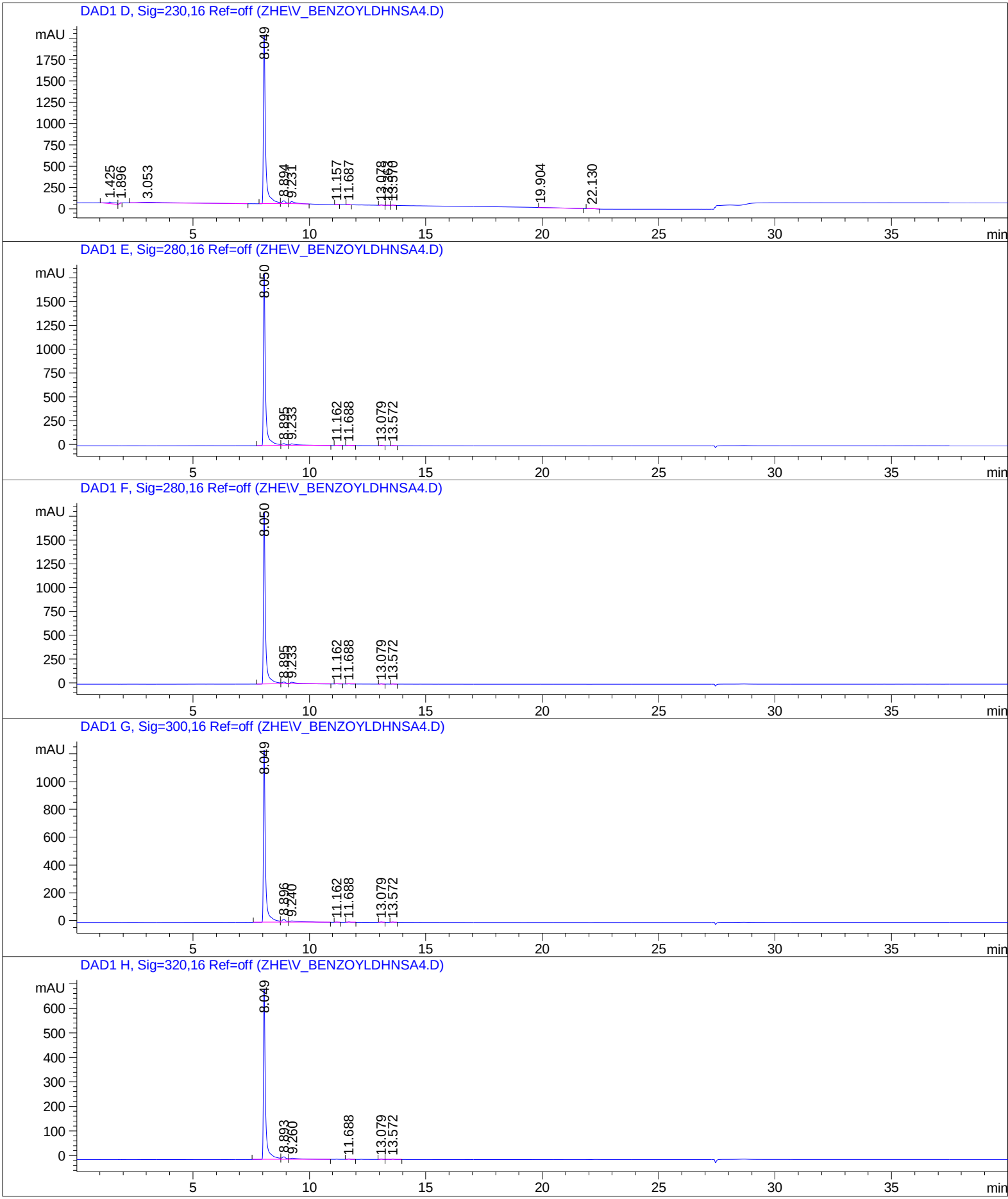

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Sample Name: Benzoyl DHN salt

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Area Percent Report

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Sorted By : Signal
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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	8.049	BV	0.0882	6579.05225	1093.93298	93.9567
2	8.894	VV	0.1712	185.73442	16.02457	2.6525
3	9.232	VB	0.2324	194.25351	11.08575	2.7742
4	11.161	BB	0.1017	6.67877	1.00323	0.0954
5	11.687	BB	0.0907	13.10749	2.16276	0.1872
6	13.079	BB	0.0854	11.79085	2.10245	0.1684
7	13.572	VB	0.0882	11.60197	1.98491	0.1657

Totals : 7002.21926 1128.29665

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.049	BV	0.0883	6884.68311	1142.31543	93.9984
2	8.894	VV	0.1733	188.51476	16.01816	2.5738
3	9.233	VB	0.2330	207.89497	11.83297	2.8384
4	11.161	BB	0.0998	6.75659	1.04007	0.0922
5	11.687	BB	0.0881	12.19330	2.08762	0.1665
6	13.079	BB	0.0852	12.60163	2.25334	0.1721
7	13.572	VB	0.0880	11.60913	1.99188	0.1585

Totals : 7324.25349 1177.53945

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.354	BV	0.2152	57.73859	4.17873	0.1005
2	0.563	VV	0.1775	58.07726	4.72132	0.1011
3	0.937	VB	0.1327	124.15131	12.20671	0.2161
4	1.365	BV	0.1588	116.42259	9.25145	0.2027

Data File C:\CHEM32\1\DATA\ZHE\V_BENZOYLDHNSA4.D
Sample Name: Benzoyl DHN salt

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
5	1.417	VV	0.0406	19.04517	6.81636	0.0332
6	1.501	VB	0.0586	43.99688	11.51662	0.0766
7	1.901	BV	0.1222	1106.77612	146.33044	1.9265
8	2.055	VV	0.1885	1854.98706	141.87375	3.2289
9	3.060	VV	2.2388	3.19199e4	172.18117	55.5617
10	7.476	VB	0.1705	189.76753	14.52080	0.3303
11	8.051	BV	0.1257	1.97345e4	2356.63037	34.3510
12	8.883	VV	0.1979	602.05365	43.38718	1.0480
13	9.231	VB	0.2937	1401.10352	61.99776	2.4388
14	11.152	BV	0.1226	38.26657	4.52592	0.0666
15	11.679	VB	0.0826	22.82174	4.25474	0.0397
16	13.074	BB	0.0822	48.23302	9.04336	0.0840
17	13.562	BB	0.3887	111.68531	3.53404	0.1944
Totals :				5.74495e4	3006.97072	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.425	BB	0.2899	496.31921	20.83771	3.1874
2	1.896	BB	0.1095	46.98227	6.89096	0.3017
3	3.053	BB	1.6689	903.74396	6.57787	5.8040
4	8.049	BV	0.0935	1.28374e4	1983.86572	82.4436
5	8.894	VV	0.1772	436.27634	36.05105	2.8018
6	9.231	VB	0.2336	473.19550	27.10887	3.0389
7	11.157	BB	0.0879	9.80778	1.73667	0.0630
8	11.687	VB	0.0848	24.09332	4.33475	0.1547
9	13.078	BB	0.0848	29.39844	5.29278	0.1888
10	13.363	BV	0.0854	7.89377	1.45315	0.0507
11	13.570	VB	0.0861	25.35130	4.47141	0.1628
12	19.904	VB	0.6470	212.59346	3.96855	1.3653
13	22.130	BB	0.2380	68.08338	4.22467	0.4372
Totals :				1.55711e4	2106.81415	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.050	BV	0.0890	1.10782e4	1819.90381	92.3952
2	8.895	VV	0.1950	288.56982	21.18053	2.4067
3	9.233	VB	0.3771	567.85303	19.08673	4.7360
4	11.162	BB	0.0996	11.89308	1.83455	0.0992

Data File C:\CHEM32\1\DATA\ZHE\V_BENZOYLDHNSA4.D
Sample Name: Benzoyl DHN salt

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
5	11.688	BB	0.0905	11.53965	1.90931	0.0962
6	13.079	BB	0.0839	20.55817	3.75307	0.1715
7	13.572	VB	0.0881	11.40272	1.95224	0.0951
Totals :				1.19901e4	1869.62023	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.050	BV	0.0890	1.10782e4	1819.90381	92.3952
2	8.895	VV	0.1950	288.56982	21.18053	2.4067
3	9.233	VB	0.3771	567.85303	19.08673	4.7360
4	11.162	BB	0.0996	11.89308	1.83455	0.0992
5	11.688	BB	0.0905	11.53965	1.90931	0.0962
6	13.079	BB	0.0839	20.55817	3.75307	0.1715
7	13.572	VB	0.0881	11.40272	1.95224	0.0951
Totals :				1.19901e4	1869.62023	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.049	BV	0.0891	7585.50195	1245.38721	91.7471
2	8.896	VV	0.1812	265.00891	21.29376	3.2053
3	9.240	VB	0.4501	364.04428	10.20599	4.4031
4	11.162	BB	0.0960	7.06348	1.14495	0.0854
5	11.688	BB	0.0885	16.16879	2.75573	0.1956
6	13.079	BB	0.0839	15.28931	2.79065	0.1849
7	13.572	VB	0.0883	14.76009	2.52256	0.1785
Totals :				8267.83681	1286.10085	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.049	BV	0.0892	4260.37939	698.56989	92.9384
2	8.893	VV	0.1840	130.38942	10.28179	2.8444
3	9.260	VB	0.4268	163.41396	4.90330	3.5648

Data File C:\CHEM32\1\DATA\ZHE\V_BENZOYLDHNSA4.D
Sample Name: Benzoyl DHN salt

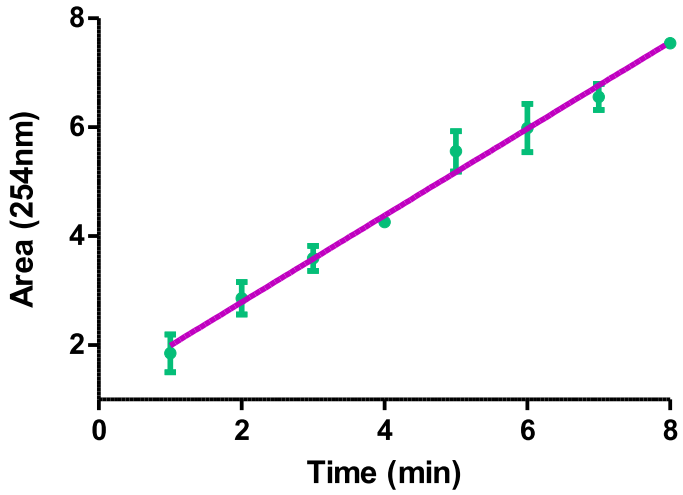
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
4	11.688	BB	0.0902	10.76002	1.78789	0.2347
5	13.079	BB	0.0847	9.05666	1.63390	0.1976
6	13.572	BB	0.1064	10.08892	1.36293	0.2201
Totals :				4584.08838	718.53970	

*** End of Report ***

Alkaline Phosphatase (ALP) Cleavage Assay (KGP04 converted to KGP03)

The enzymatic activity of alkaline phosphatase (from human placenta) was determined by using 4-nitrophenyl phosphate as substrate (Sigma-Aldrich). The cleavage of 40 μM phosphate prodrug KGP04 (**16**) with ALP was carried out by incubation at 37 °C in 10 mM glycine buffer solution (pH 8.6, with 2 mM $MgCl_2$) initially for 24 h, by which time all of KGP04 was converted to KGP03 (**8**) plus minor by-products. The rate release of the parent phenolic agent [KGP03] was monitored by HPLC (Agilent Technologies 1200 series, with a ZORBAX Eclipse XDB-18 column) isocratically in 60% acetonitrile and 40% water (containing 0.05% TFA) at 1 mL/min. The activity of ALP towards KGP04 was found to be 4.0 μM/min/enzyme unit.

Rate Study [Area at 254 nm Versus Time (min)]



Slope (rate curve) is 0.7962 (area/min).
Calibration curve KGP03 is y = 10.02x - 4.093.
The initial rate is 0.07946 uM/min.
200 uM [KGP04] & approx. 0.02 units ALP.
At different times, 5 ul (*3) of each resulting reaction mixture was diluted to 180 uL for HPLC analysis; KGP04 1.6 min and KGP03 5.3 min.

HPLC (left) for KGP04 (referred to as OXi6197) incubated (glycine-NaOH buffer) for 24 h without ALP (control).
HPLC (right) indicates KGP03 (referred to as OXi6196) that formed upon incubation (glycine-NaOH buffer) of KGP04 for 24 h with ALP (approximately 1U).