Supplementary material

Stereoselective synthesis of carbohydrate fused pyrano[3,2-c]pyranones as anticancer agents

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General experimental procedures

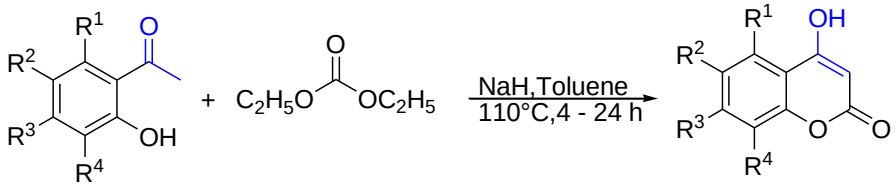
Synthesis of 2-C-formyl galactal 1a and 2-C-formyl glucal 1b: In a 100 mL round bottom flask 30 mL anhydrous DMF was added followed by dropwise addition of $POCl_3$ (0.6 mL, 21.6 mmol) at 0 °C and resulting mixture was stirred for 30 min under Argon atmosphere. A solution (dissolved in anhydrous DMF) of 3,4,6-tri-*O*-benzyl-D-galactal (2.99 g, 7.20 mmol) was added to this dropwise within 30 min. The resulting reaction mixture was stirred at 0 °C to room temperature for 5 h which shows disappearance of starting material (TLC). Reaction mixture was quenched by slow addition of (within 30 min) of chilled $NaHCO_3$ (30 mL) solution at 0 °C. Mixture was extracted with ethyl acetate (3 × 30 mL).and combined organic layer washed with brine solution (3 × 30 mL).then dried over anhydrous Na_2SO_4. The combined organic layer was evaporated under vaccume to get crude residue which was purified though flash column chromatography and pure 2-C-formyl galactal **1a** was isolated in 94% isolated yield (3.0 g). Similarly using 3,4,6-tri-*O*-benzyl-D-galucal and adopting above protocol 2-C-formyl glucal **1b** was obtained in 54% (1.7g) isolated yield [1].

Synthesis of 4-hydroxycoumarins 1-10: In an oven dried 100 mL round bottom flask 2-hydroxyacetophenone (0.4 mL, 3.67 mmol) was suspended in anhydrous toluene (20 mL) at room temperature. The mixture was placed to ice bath at 0 °C and sodium hydride (880 mg, 36.7 mmol) was added to this under Argon atmosphere. The reaction mixture was vigorously stirred for 20 min at same temperature then warm to room temperature. Diethylcarbonate (1.3 mL, 11.01mmol) was added to this and reaction mixture was refluxed (110 °C) for 4h. After completion of reaction (4 h) the reaction mixture was cooled to room temperature then filtered through Buchner funnel under vacuum. The solid residue thus obtained was suspended in ice cold water (50 mL) and acidified by adding 2 N HCl dropwise (pH 1-2). The solid precipitate obtained was filtered through Buchner funnel under vaccum till dryness to get almost pure 4-hydroxycoumarin **1** in 81% yield (482 mg) [2]. Similar reaction protocol was adopted for the synthesis of substituted 4-hydroxycoumarins **2-10** using respective substituted 2-hydroxyacetophenones and results are summarized in table S1

References

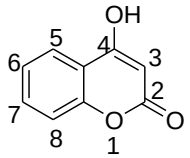
1. Ramesh N., Balasubramanian K.K, *Tetrahedron Lett.*1991, 32: 3875-3878.
2. Jian W, Haibing G, Saofa S, Jiayao H, Lei W, Shiyong P, *Adv.Synth.Catal*.2013, 355:2550-2557.

Table S1. Synthesis of 4-hydroxy coumarins **1-10**.



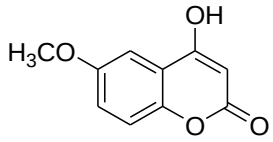
1-10

Entry	R^1	R^2	R^3	R^4	Product	Time (h)	Yield (%)
1	H	H	H	H	**1**	4	81
2	H	OCH_3	H	H	**2**	4	68
3	H	Cl	H	H	**3**	4	68
4	H	CH_3	H	H	**4**	4	92
5	H	Br	H	H	**5**	4	81
6	H	$-C_6H_4-$		H	**6**	4	55
7	H	H	F	H	**7**	5	85
8	H	Cl	H	Cl	**8**	24	50
9	H	H	OCH_3	OCH_3	**9**	5	56
10	OCH_3	H	OCH_3	H	**10**	5	94



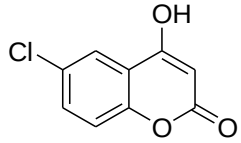
1

4-hydroxy-2H-benzopyran-2-one (1). ^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.53 (brs,1H,OH), 7.82 (dd, *J* = 1.6 Hz, 8Hz,1H, H-7), 7.66-7.62 (m, 1H, H-6), 7.36 (dd, *J* = 8.0 Hz,7.2 Hz, 1H, H-7), 5.60 (s, 1H, H-3), ^{13}C NMR (100 MHz, DMSO-*d6*): δ 166.0, 162.3, 153.9, 133.1, 124.3, 123.6, 116.8, 116.2, 91.4, HRMS(ESI), calcd, m/z $C_9H_6O_3$, $[M+H]^+$163.0389;Found: 163.0420.



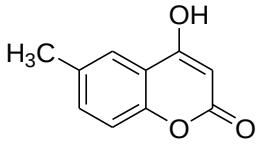
2

4-hydroxy-6-methoxy-2H-benzopyran-2-one (2). ^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.52 (brs, 1H, OH), 7.30 (dd, *J* = 4.0 Hz, *J* = 8.0 Hz, 1H, H-7), 7.22-7.19 (m, 2H, ArH), 5.59 (s, 1H, H-3), 3.80 (s, 1H, OCH_3), ^{13}C NMR (100 MHz, DMSO-*d6*): δ 165.8, 162.5, 155.7, 148.3, 120.7, 118.0, 116.6, 105.4, 91.6, 56.0 (OCH_3), HRMS(ESI), calcd, m/z $C_{10}H_8O_4$, $[M+H]^+$ 193.0495; Found: 193.0513.



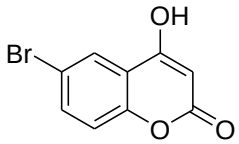
3

6-Chloro-4-hydroxy-2H-benzopyran-2-one (3) ^{1}H NMR (400 MHz, DMSO-*d6*): δ 7.89 (d, *J* = 2.4 Hz, 1H, H-5), 7.79 (dd, *J* = 2.4 Hz and *J* = 8.8 Hz, 1H, H-8),7.35 (d, *J* = 8.8 Hz, 1H, H-7), 5.62 (s, 1H, H-3), ^{13}C NMR (100 MHz, DMSO-*d6*): δ 164.8, 161.8, 152.9, 135.6, 125.7, 119.2, 118.2, 116.1, 92.1, HRMS(ESI), calcd, m/z $C_9H_5ClO_3$, $[M+H]^+$ 196.9999; Found: 197.0014.



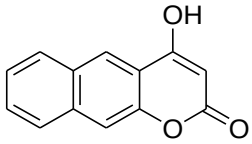
4

4-hydroxy-6 methyl-2H-benzopyran-2-one (4) (400 MHz, DMSO-*d6*): δ 7.59 (s, 1H, H-5), 7.43 (dd, *J* = 1.6 Hz and *J* = 8 Hz), 7.24 (d, *J* = 8.4 Hz, 1H, H-7), 5.56 (s, 1H), 2.35 (s, 3H, CH_3), ^{13}C NMR (100 MHz, DMSO-*d6*): δ 166.1, 162.5, 152.1, 133.9, 133.5, 123.2, 116.5, 115.9, 91.3, 20.7 (CH_3), HRMS(ESI), calcd, m/z $C_{10}H_8O_3$, $[M+H]^+$ 177.0546; Found: 177.0563.



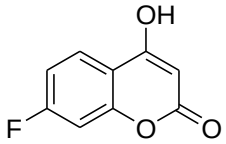
5

6-bromo-4-hydroxy-2H-benzopyran-2-one(5) ^{1}H NMR (400 MHz, DMSO-*d6*): δ 7.90.(d, *J* = 2 Hz, 1H, H-5), 7.79 (dd, *J* = 2.0 Hz and *J* = 7.2 Hz, 1H, H-7), 7.35 (d, *J* = 7.2 Hz, 1H, H-8), 5.58 (s, 1H, H-3), ^{13}C NMR (100 MHz, DMSO-*d6*): δ 164.9, 161.7, 152.6, 132.8, 128.4, 122.8, 118.9, 117.7, 92.1, HRMS(ESI), calcd, m/z $C_9H_5BrO_3$, $[M+H]^+$ 240.9495;Found: 240.9509.



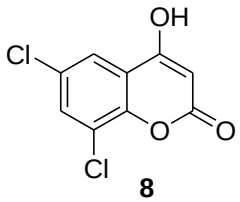
6

4-hydroxy-2H-benzo[g]benzopyran-2-one (6). ^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.68 (brs, 1H, OH), 8.36-8.33 (m, 1H), 8.05 - 8.02 (m, 1H), 7.82 (s, 2H), 7.73-7.70 (m, 2H), 5.71 (s, 1H, H-3), ^{13}C NMR (100 MHz, DMSO-*d6*): δ 167.0, 162.2, 151.1, 135.2, 129.2, 128.5, 127.7, 124.0, 122.6, 122.1, 119.4, 111.5, 91.1 HRMS(ESI), calcd, m/z $C_{13}H_8O_3$, $[M+H]^+$ 213.0546; Found: 213.0567.



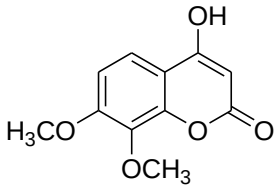
7

7-flouro-4-hydroxy-2H-benzopyran-2-one (7) ^{1}H NMR (400 MHz, DMSO-*d6*): δ 7.85 (dd, *J* = 6.4 Hz, *J* = 8.8 Hz, H-7), 7.33 (dd, *J* = 2.4 Hz and *J* = 10.0 Hz, H-5), 7.21 (td, *J* = 2.4 Hz and *J* = 11.2 Hz, H-6), 5.55 (s, 1H, H-3), ^{13}C NMR, (100 MHz, DMSO-*d6*): δ 165.8, 162.2, 155.3, 155.1, 125.9, 125.8, 113.2, 112.3, 112.1, 104.4, 104.1, 90.4, HRMS(ESI), calcd, m/z $C_9H_5FO_3$, $[M+H]^+$ 180.0223;Found: 181.0304.



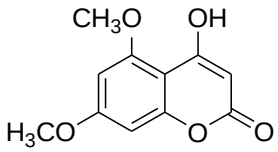
8

6, 8-dichloro-4-hydroxy-2H-benzopyran-2-one (8). ^{1}H NMR (400 MHz, DMSO-*d6*): δ 7.95 (d, *J* = 2.4 Hz, 1H, H-8), 7.73(d, *J* = 2.4 Hz, 1H, H-5), 5.58 (s, 1H, H-3), ^{13}C NMR (100 MHz, DMSO-*d6*): δ 165.4, 160.9, 148.6, 132.2, 128.2, 122.1, 121.7, 119.5, 91.9, HRMS(ESI), calcd, m/z $C_9H_4Cl_2O_3$, $[M+H]^+$ 230.9610; Found: 230.9625.



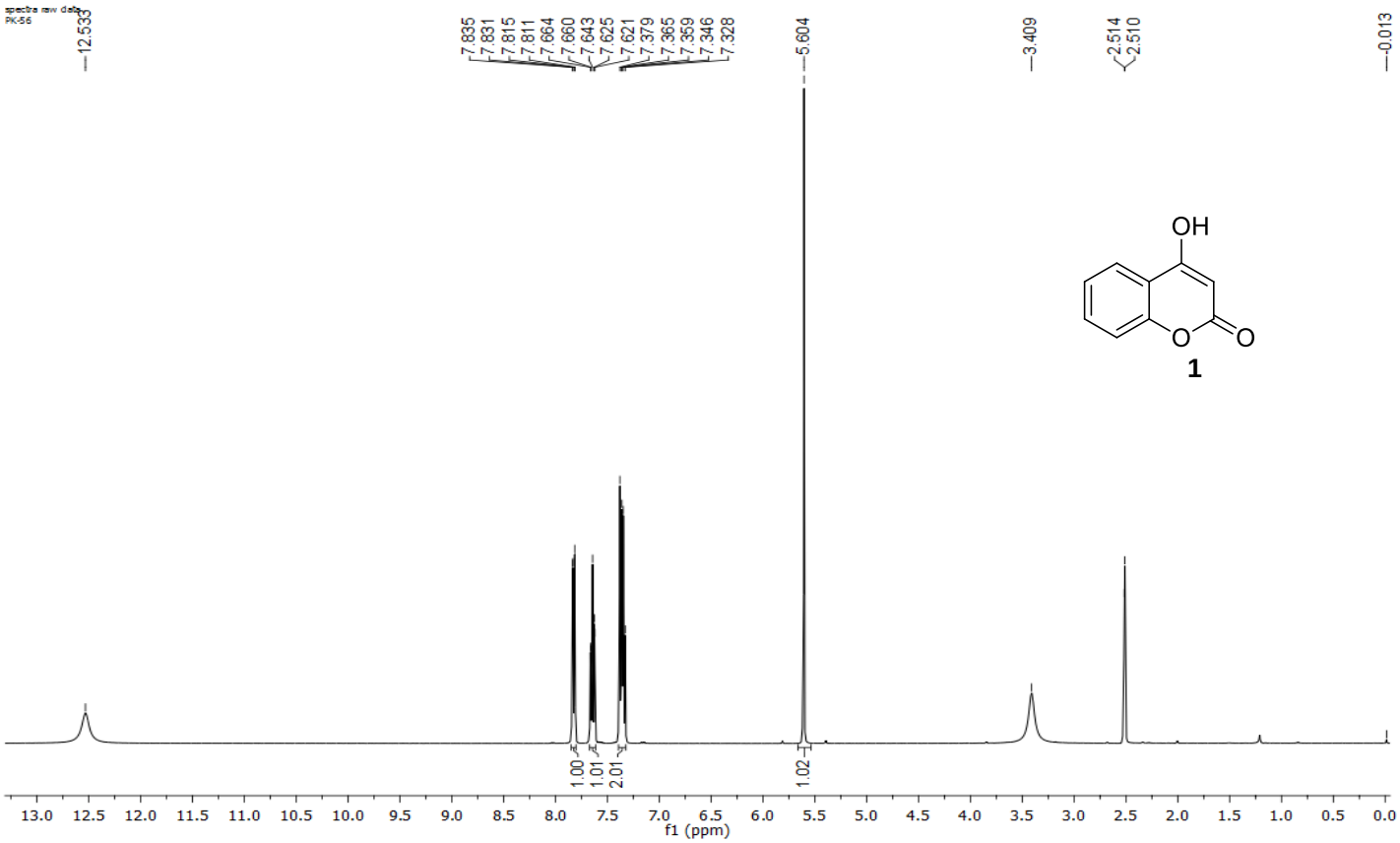
9

4-hydroxy-7,8-dimethoxy-2H-benzopyran-2-one (9). ^{1}H NMR (400 MHz, DMSO-*d6*): δ 7.53 (d, *J* = 8.8 Hz, 1H, H-5), 7.08 (d, *J* = 9.2 Hz, 1H, H-6), 5.45 (s, 1H, H-3), 3.89 (s, 1H, OCH_3), 3.79 (s, 1H, OCH_3), ^{13}C NMR (100 MHz, DMSO-*d6*): δ 166.4, 162.3, 156.0, 148.0, 135.7, 118.7, 110.5, 109.0, 89.1, 61.1 (OCH_3), 56.7 (OCH_3**),** HRMS(ESI), calcd, m/z $C_{11}H_{10}O_5$, $[M+H]^+$ 223.0601;Found: 223.0611.



10

4-hdroxy-5,7-dimethoxy-2H-benzopyran-2-one (10). ^{1}H NMR (400 MHz, DMSO-*d6*): δ 11.14 (s, 1H, OH), 6.56 (d, *J* = 2.4 Hz, 1H, H-6), 6.48 (d, *J* = 2 Hz, 1H, H-8), 5.33 (s, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), ^{13}C NMR (100 MHz, DMSO-*d6*): δ 168.0, 163.7, 162.1, 158.8, 157.4, 95.8, 94.0, 88.6, 56.9, 56.4 (OCH_3), HRMS(ESI), calcd, m/z $C_{11}H_{10}O_5$, $[M+H]^+$ 223.0601; Found: 223.0611.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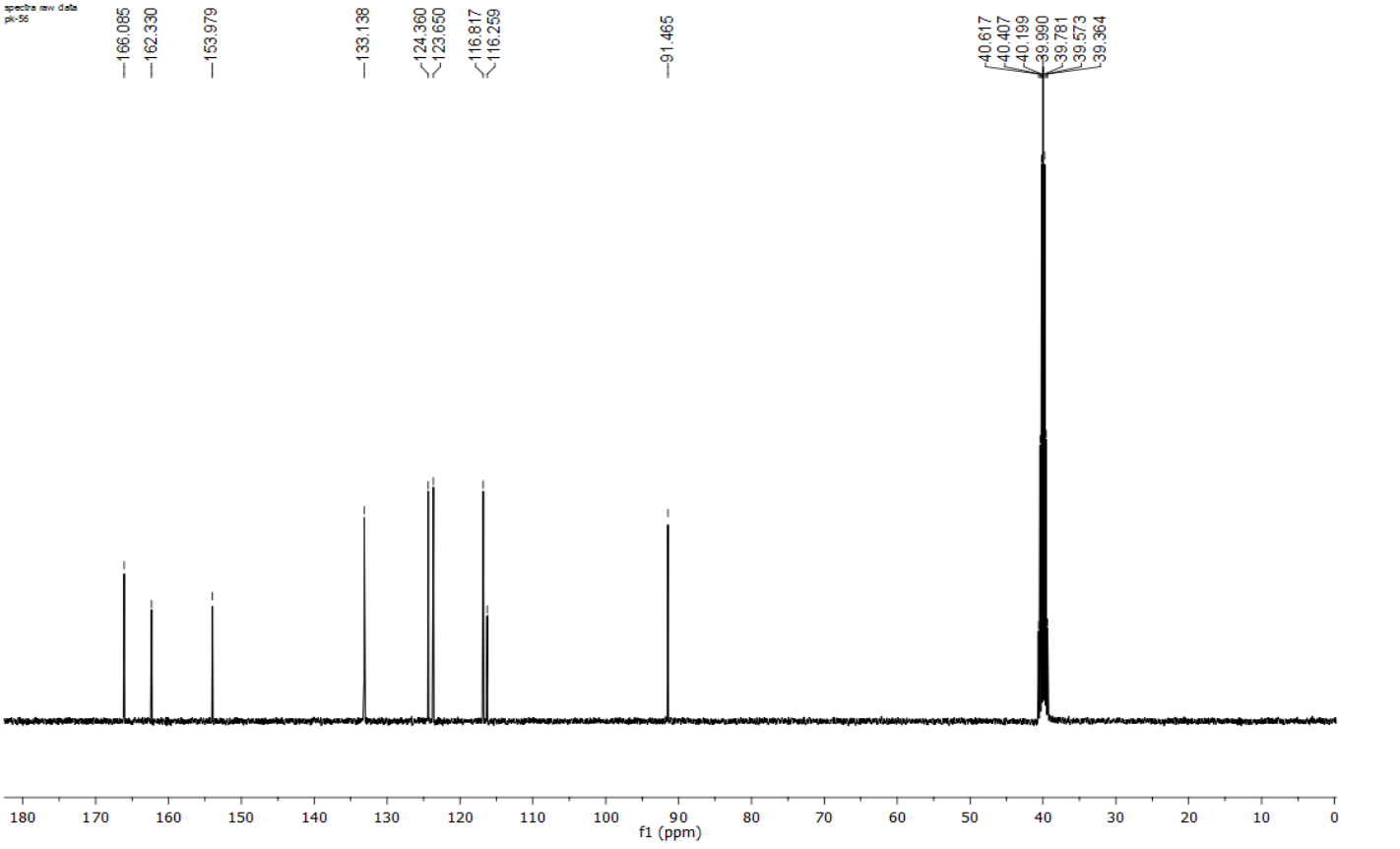
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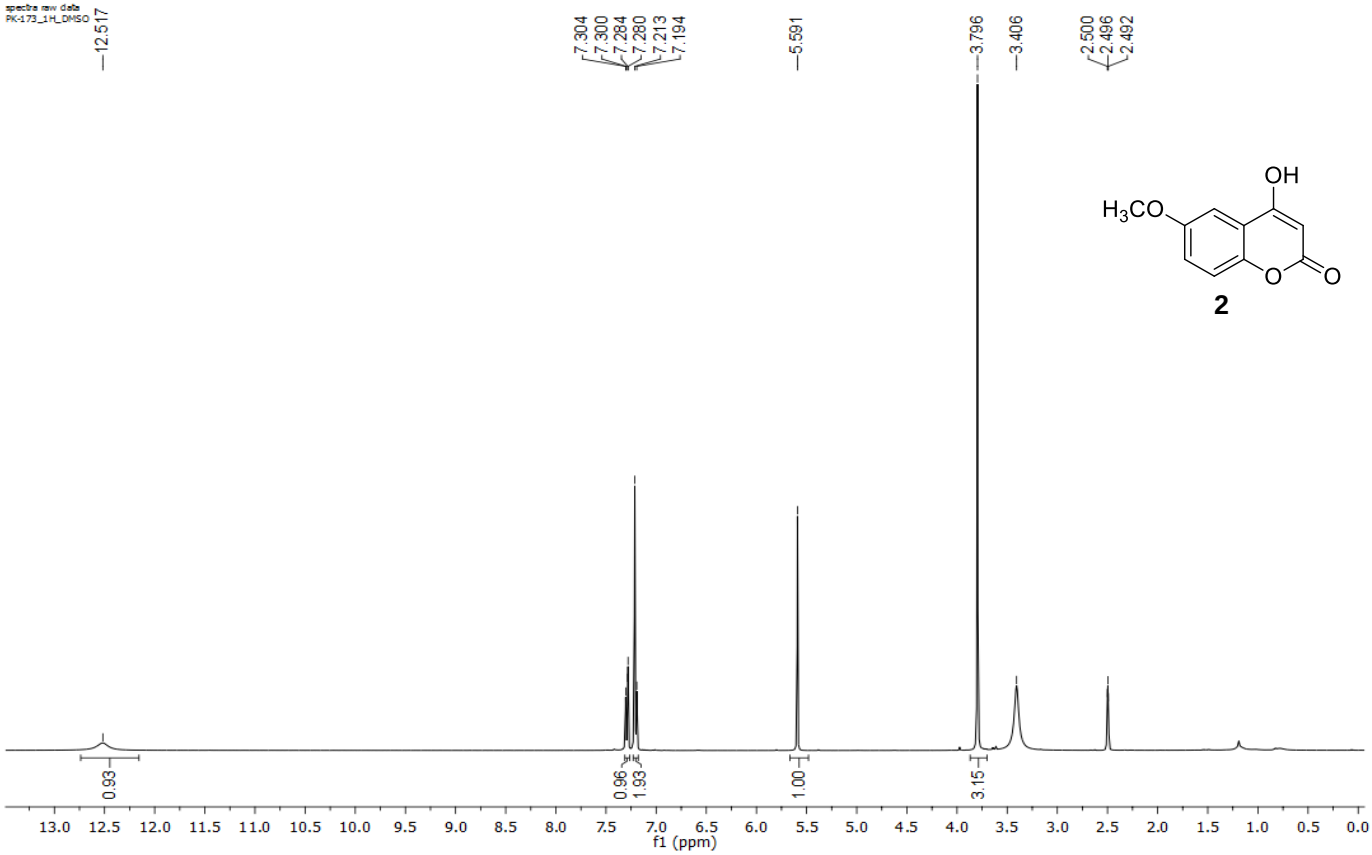
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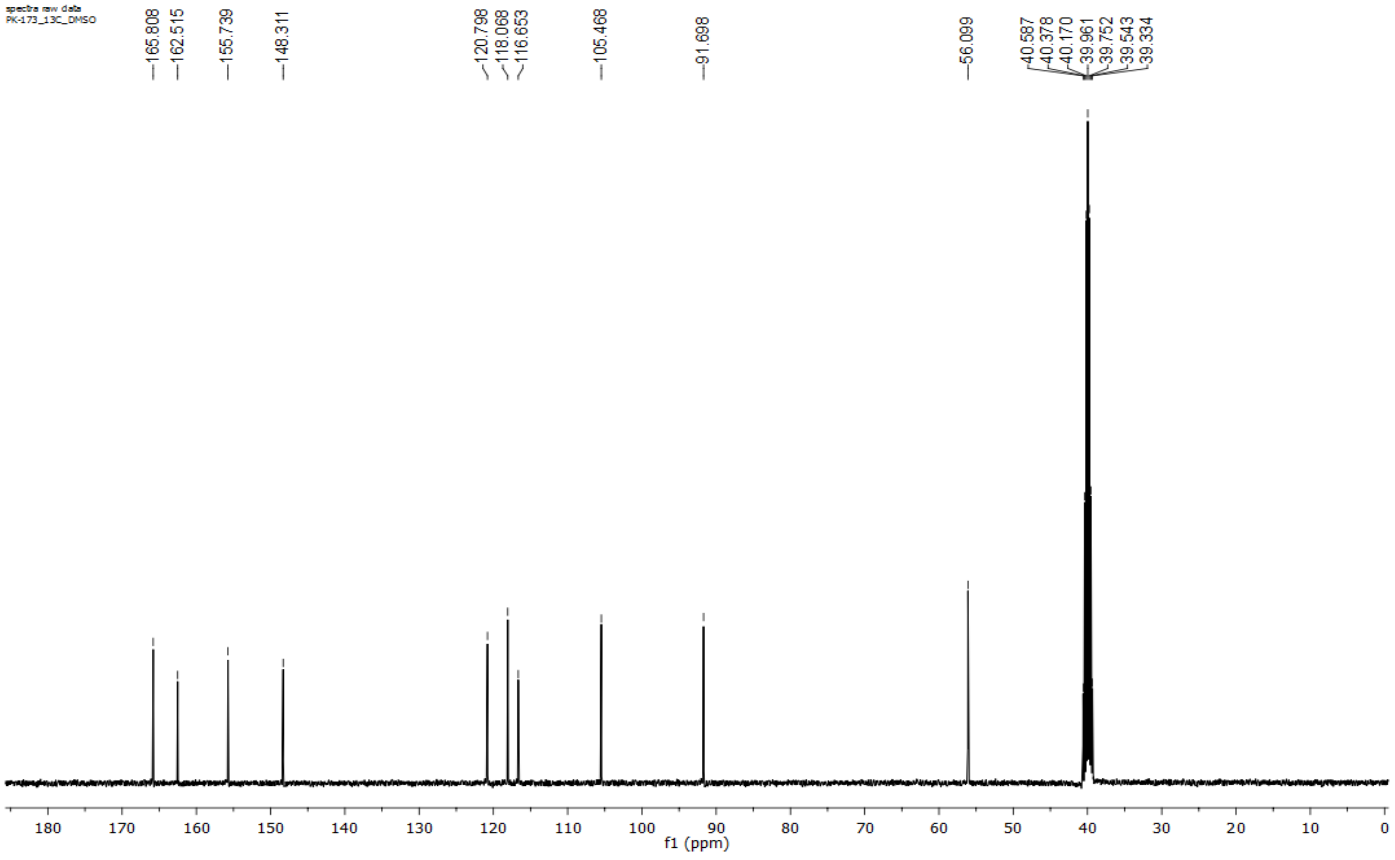
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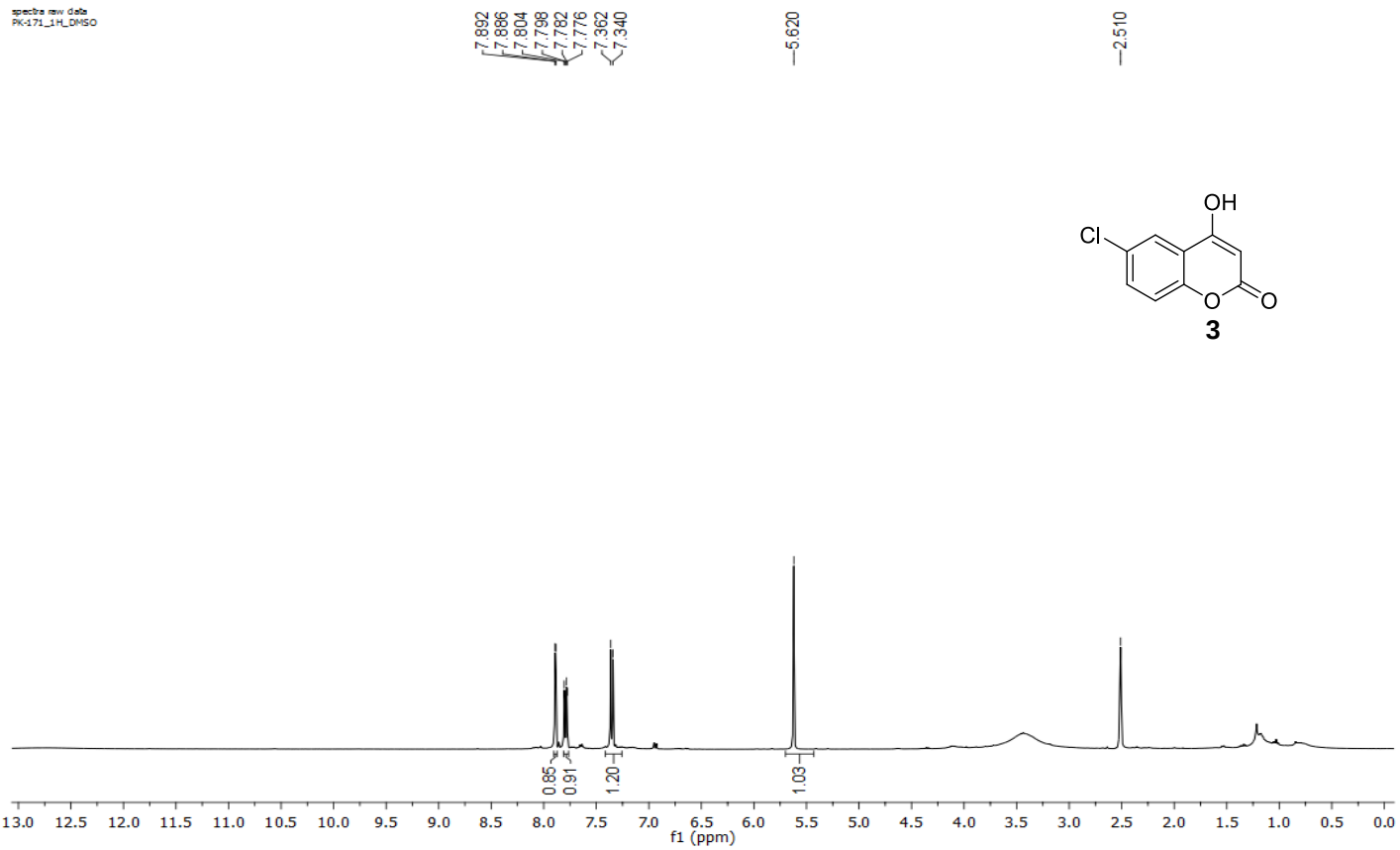
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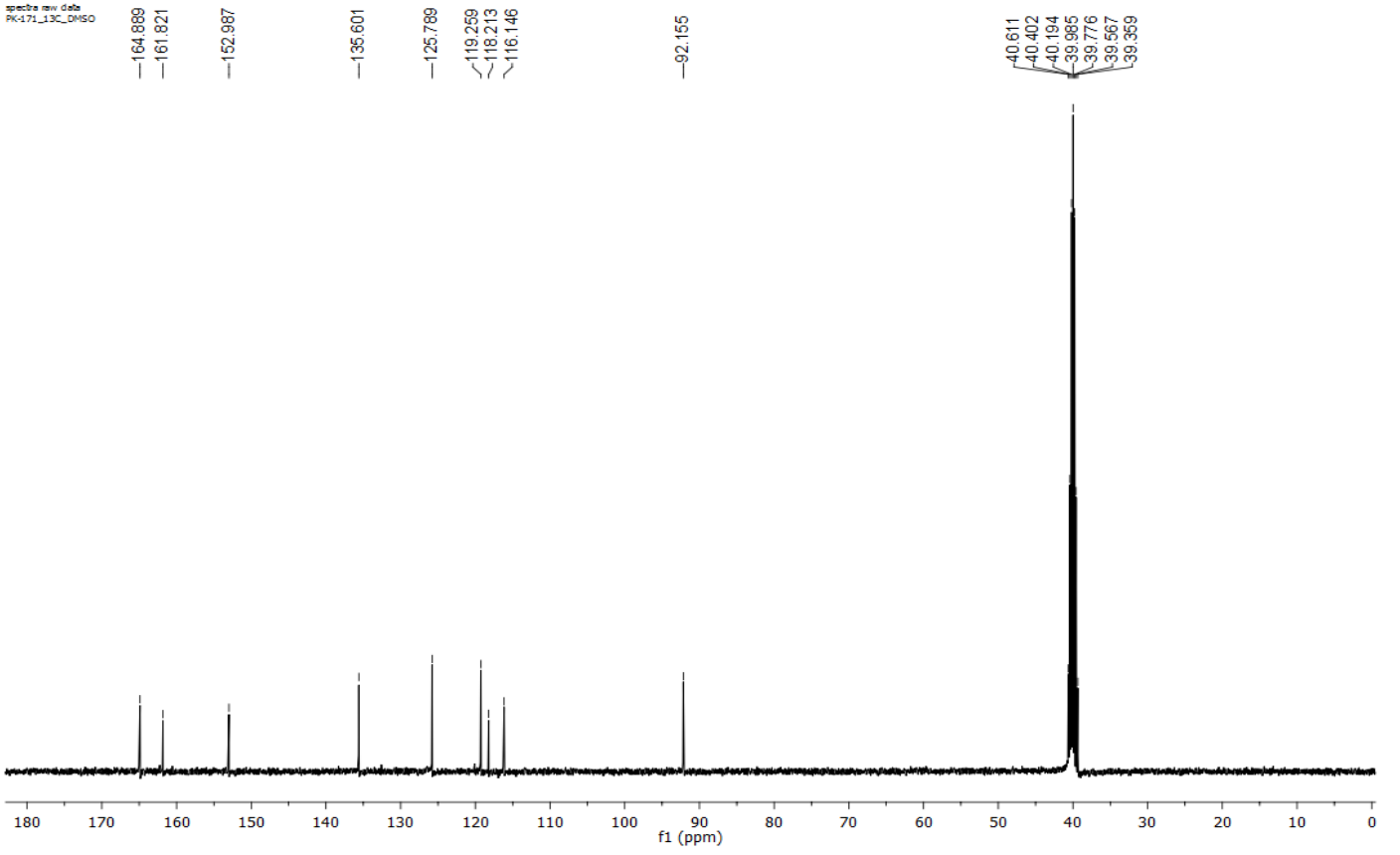
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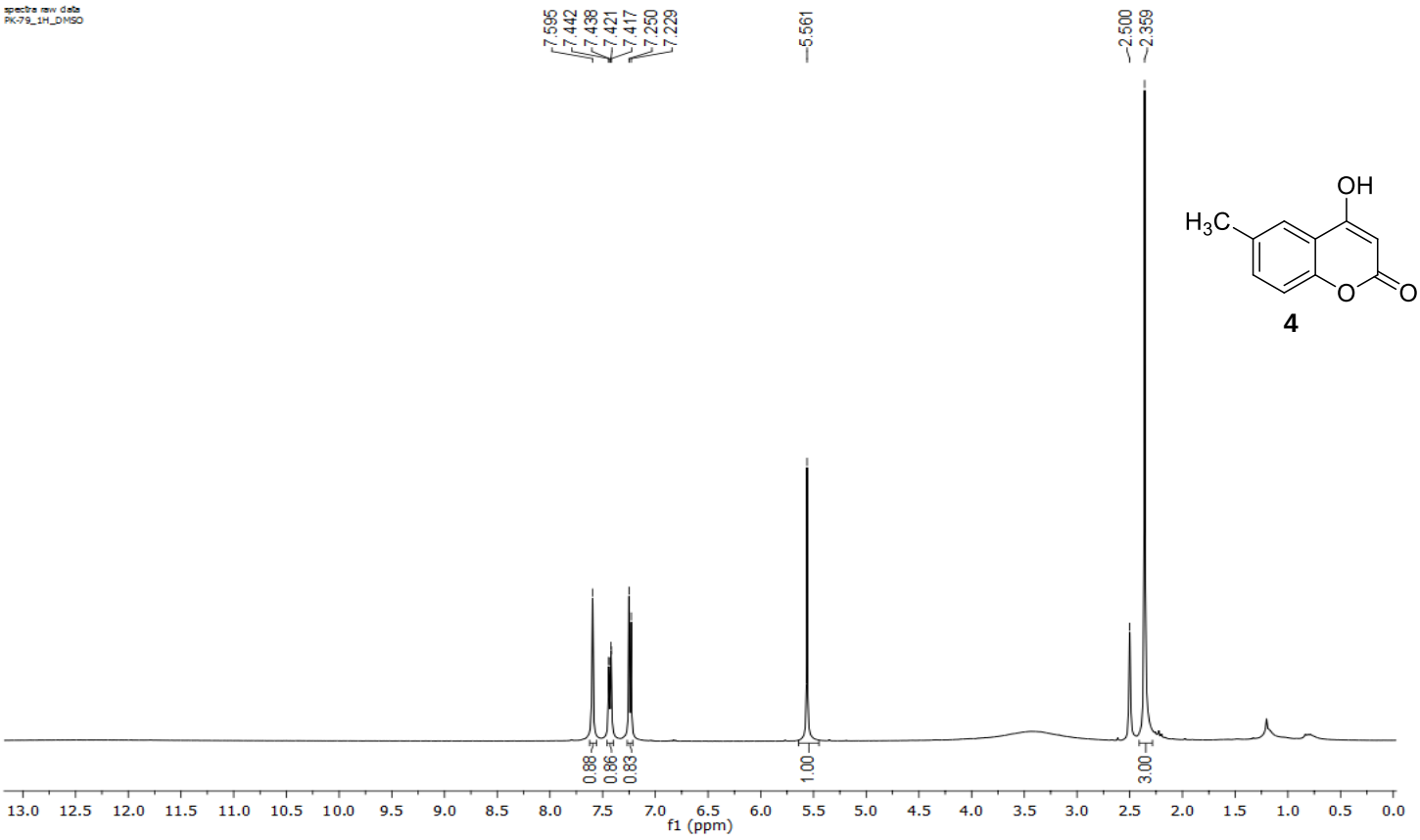
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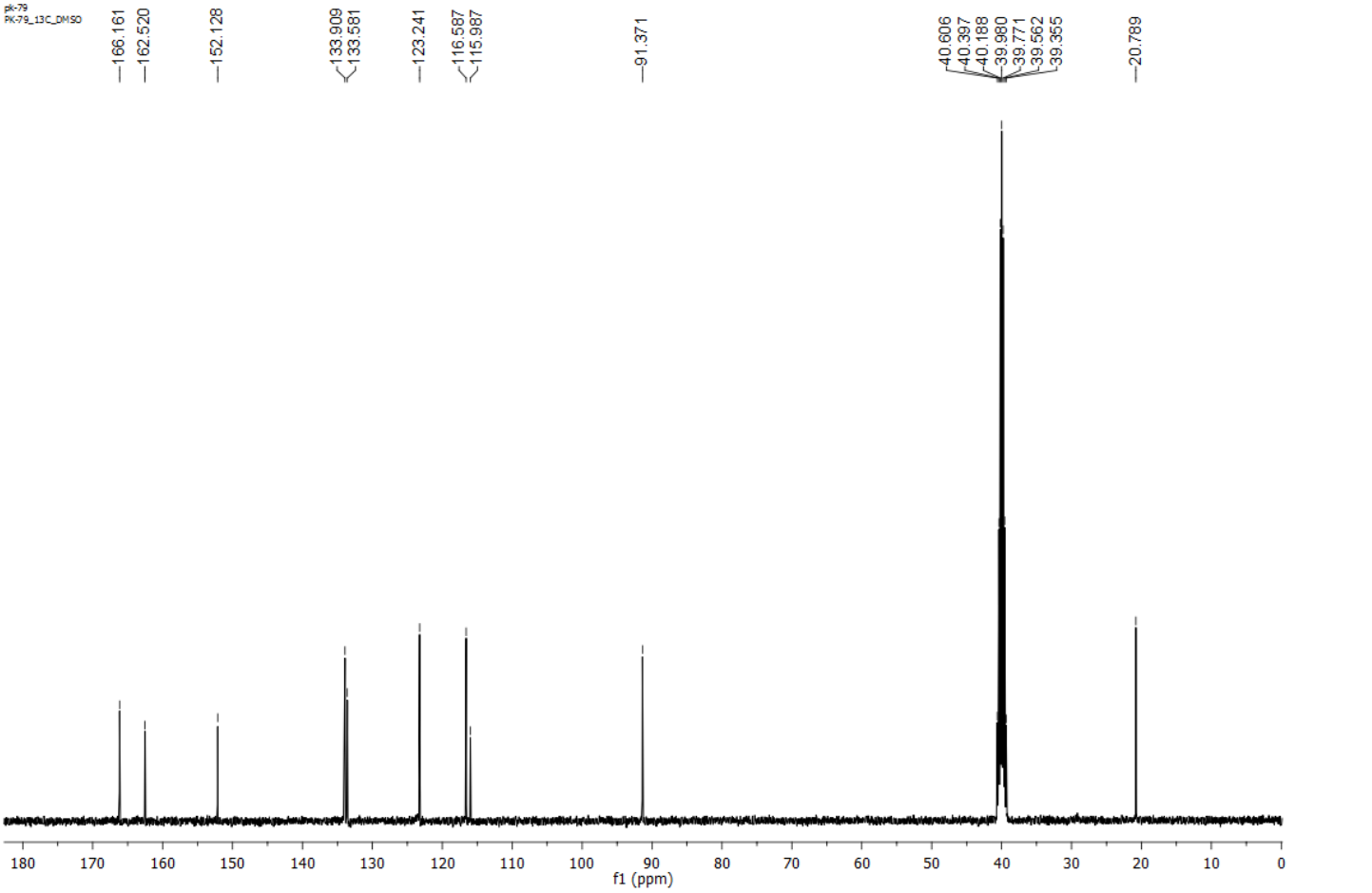
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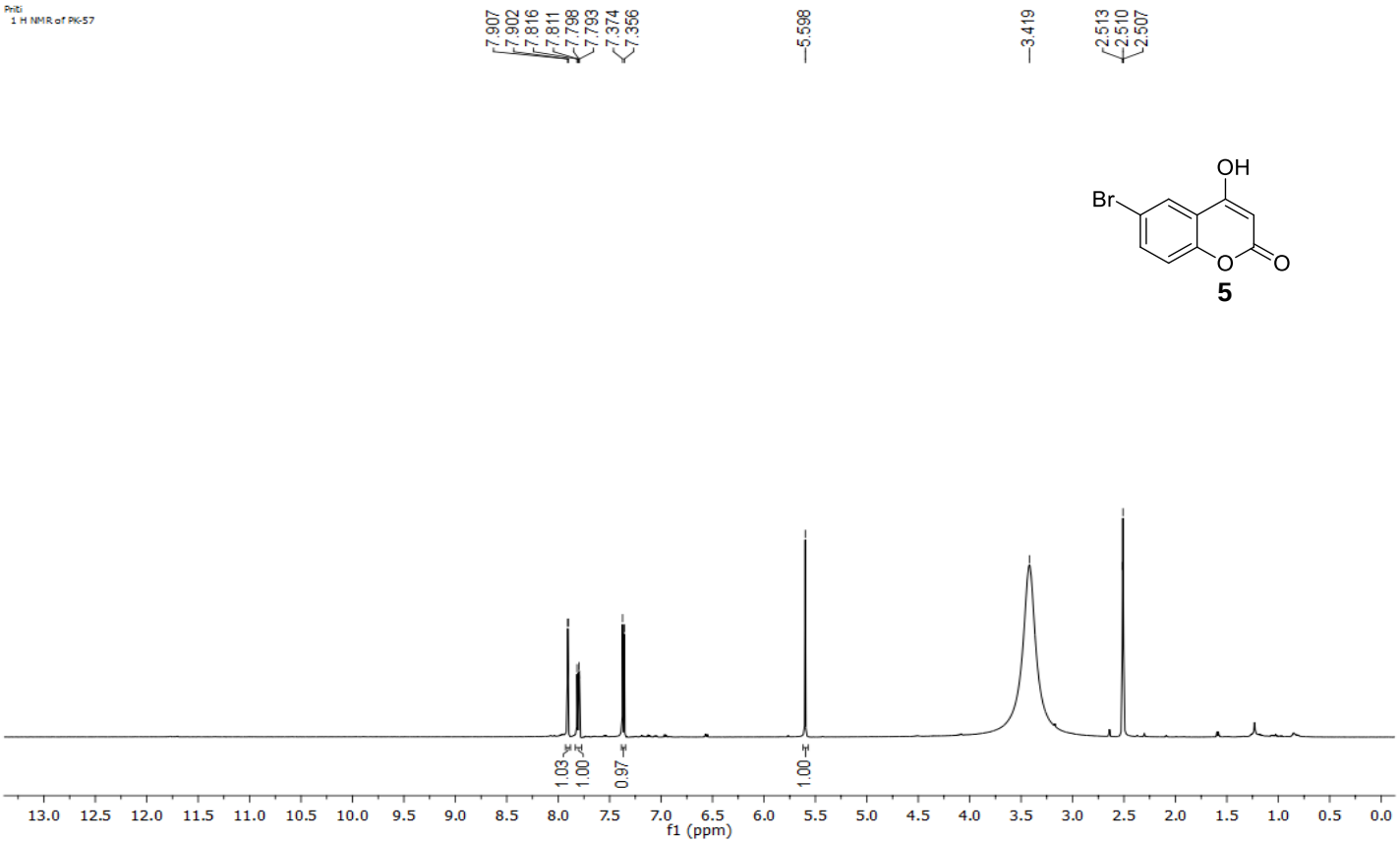
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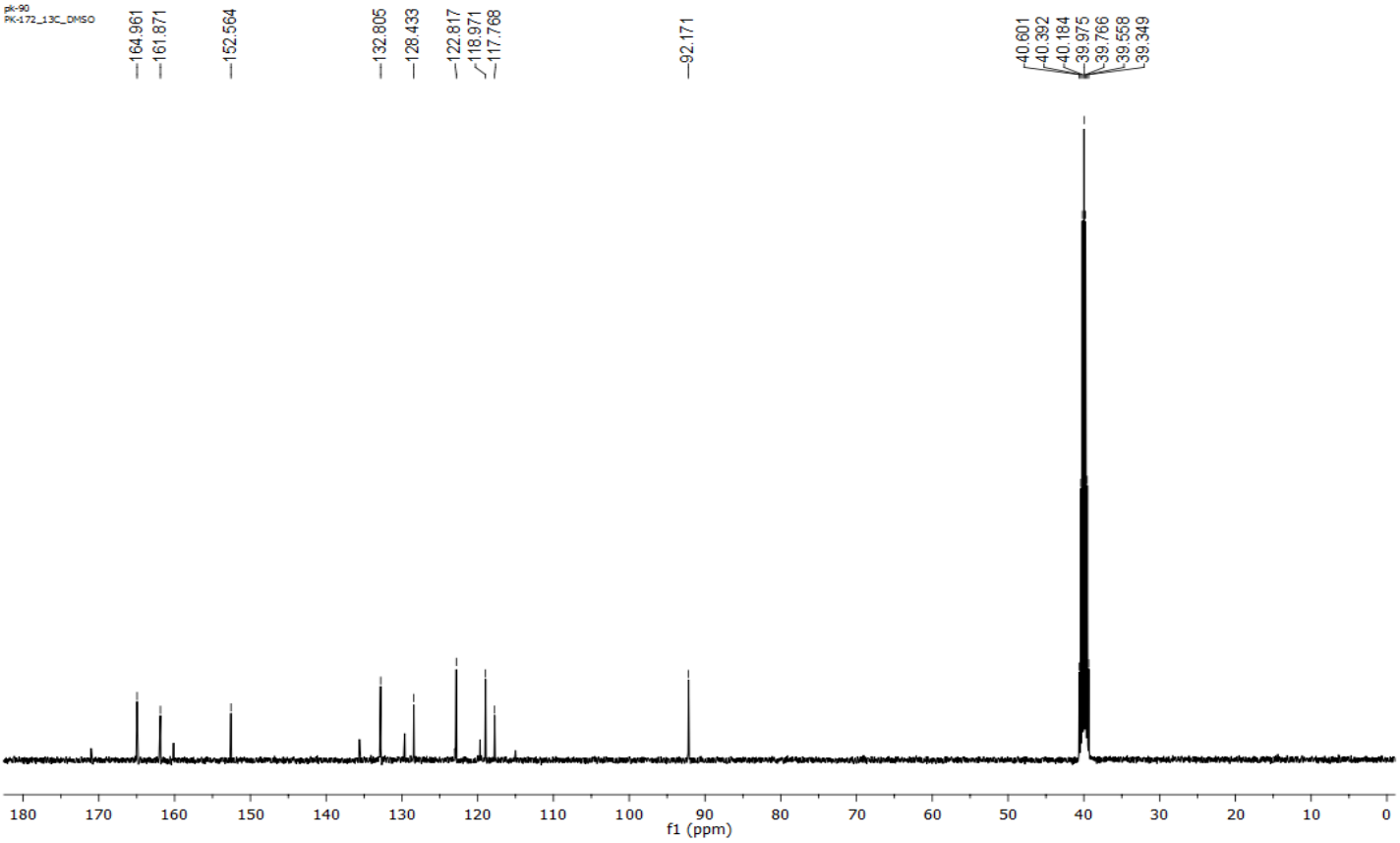
5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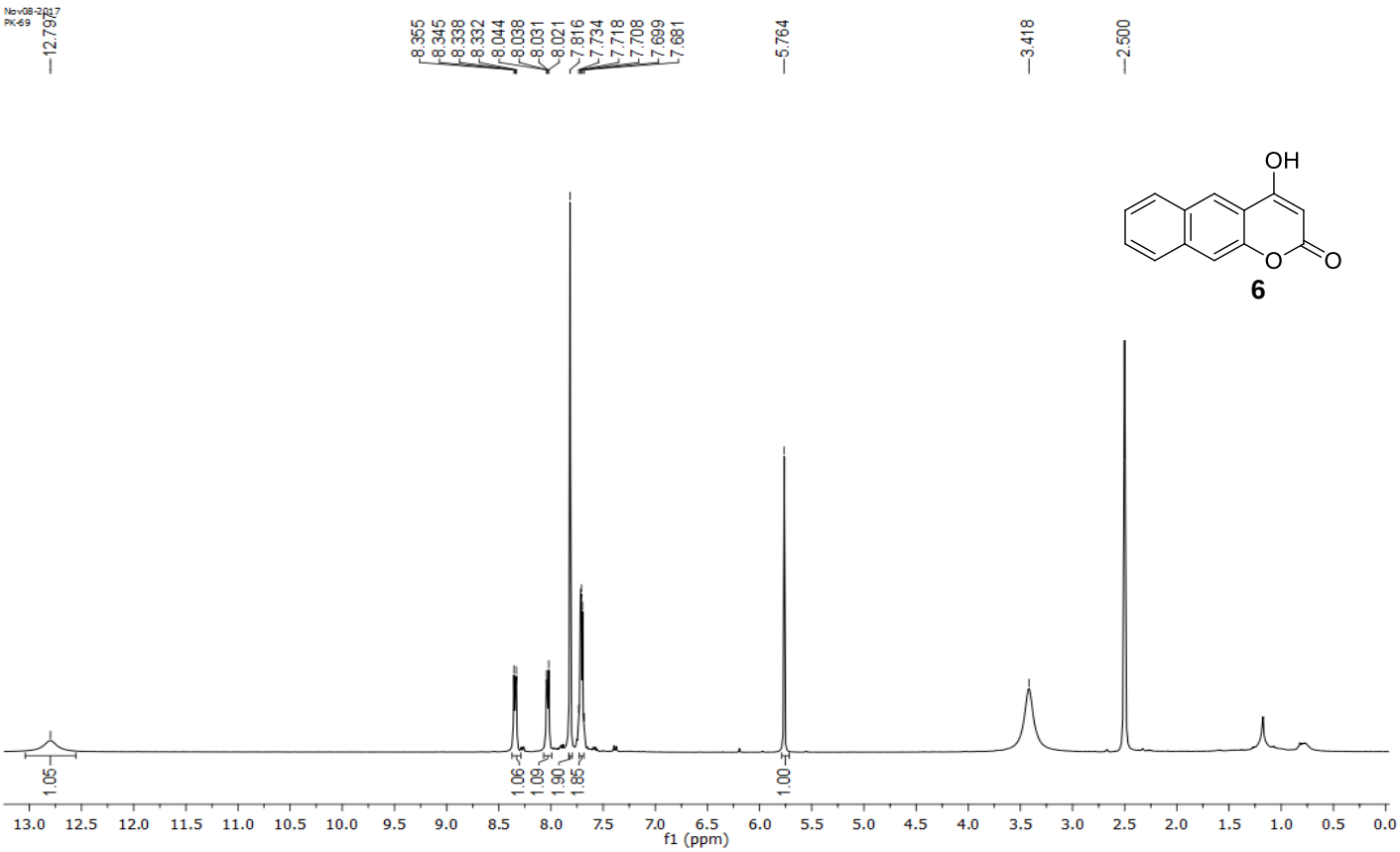
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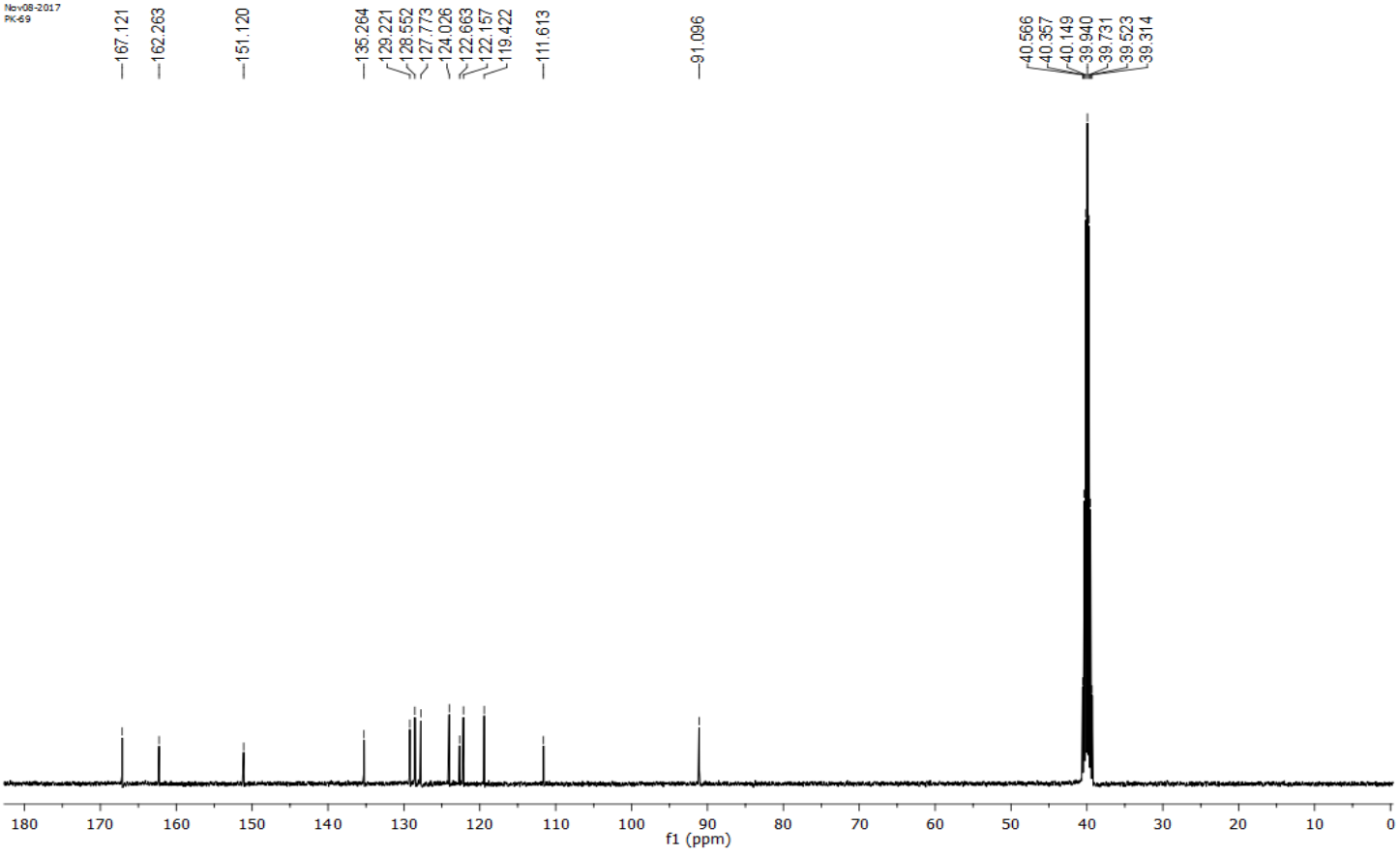
6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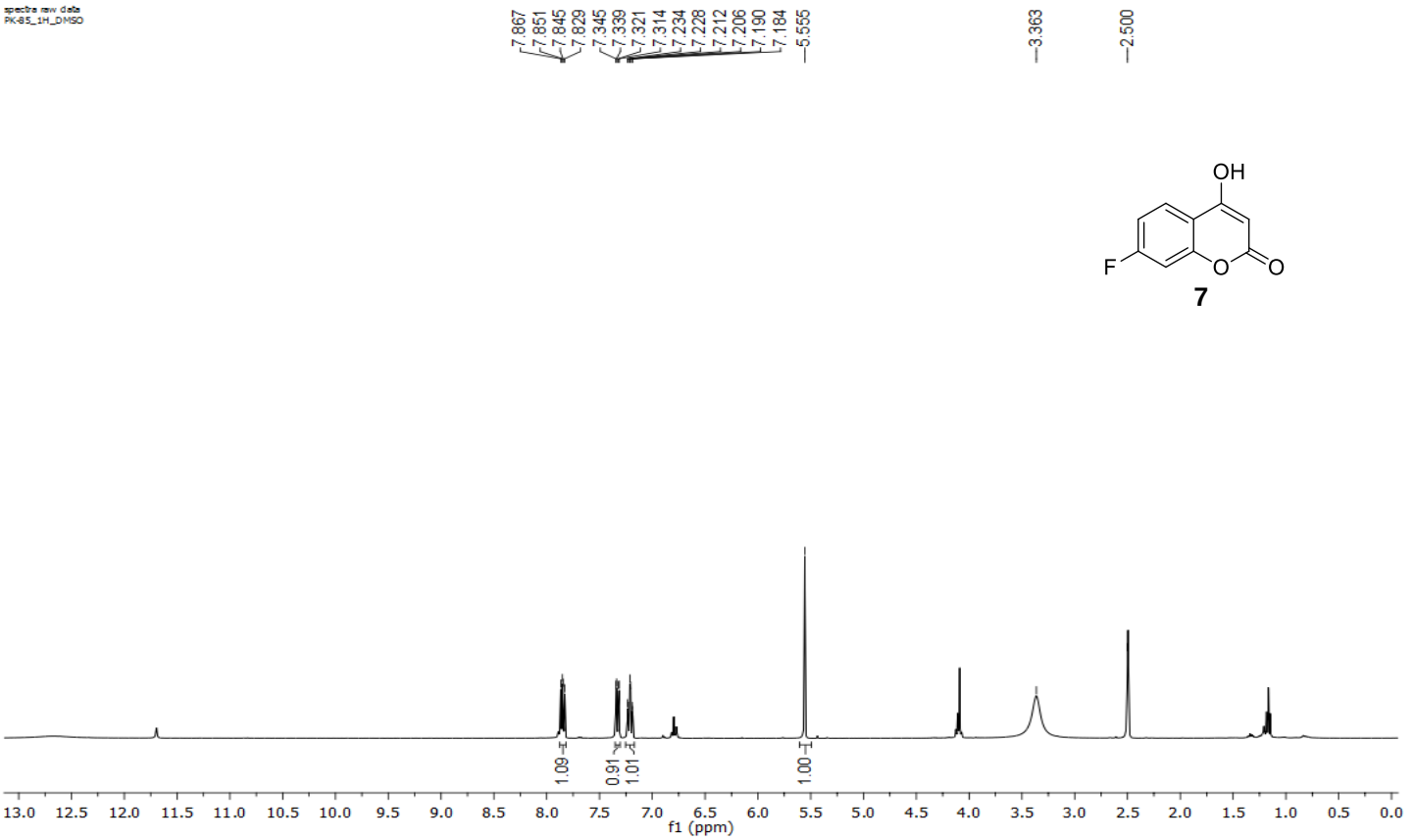
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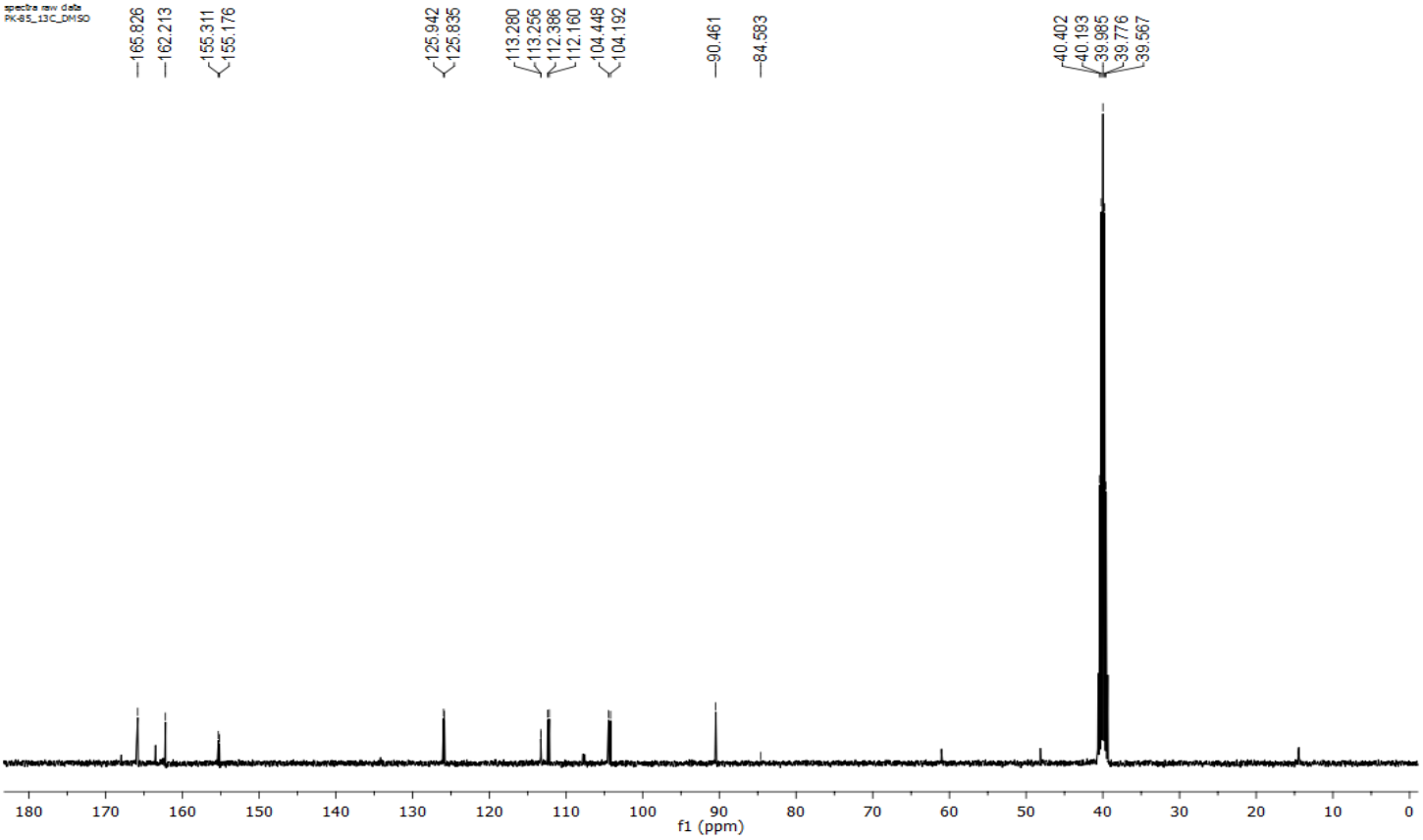
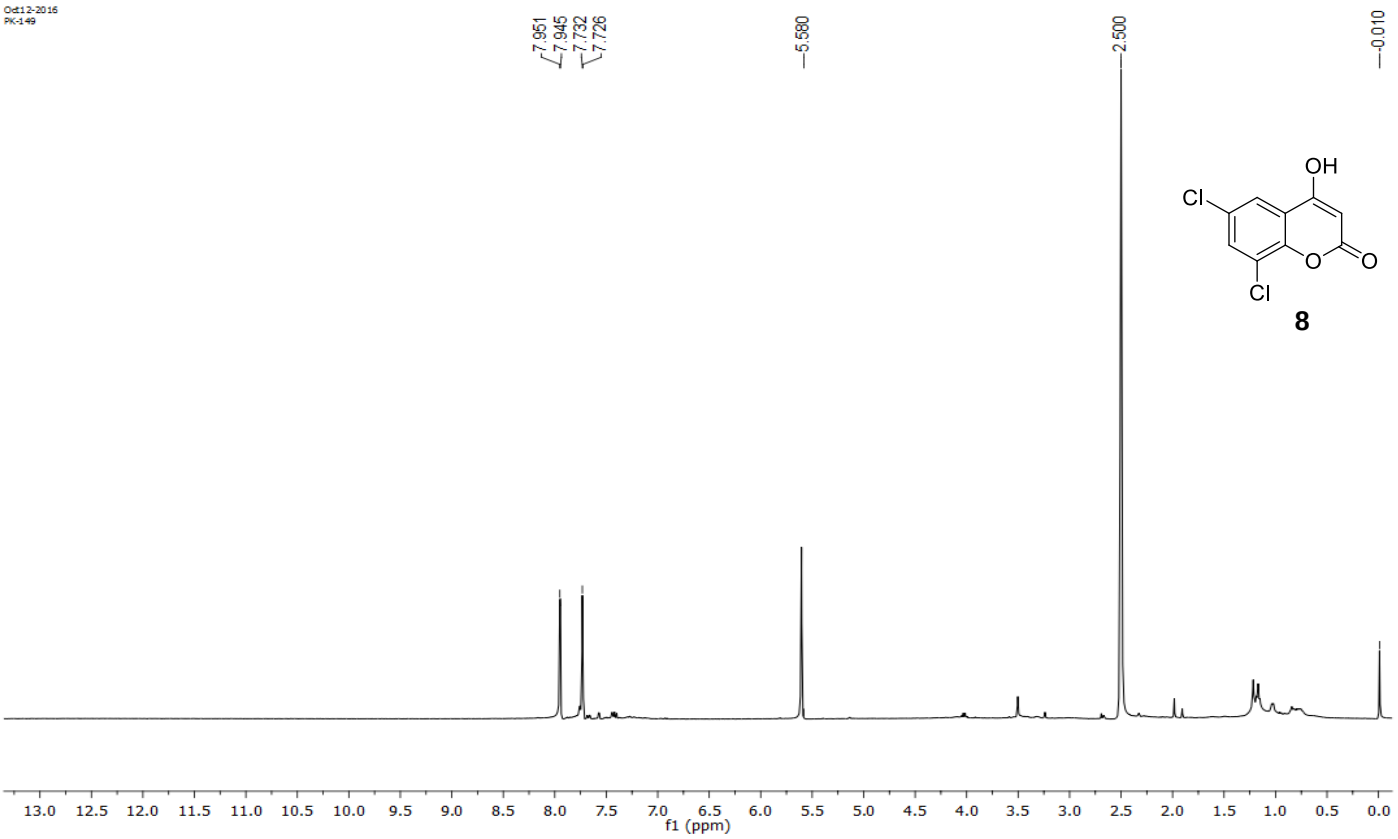
1.01
1.00
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

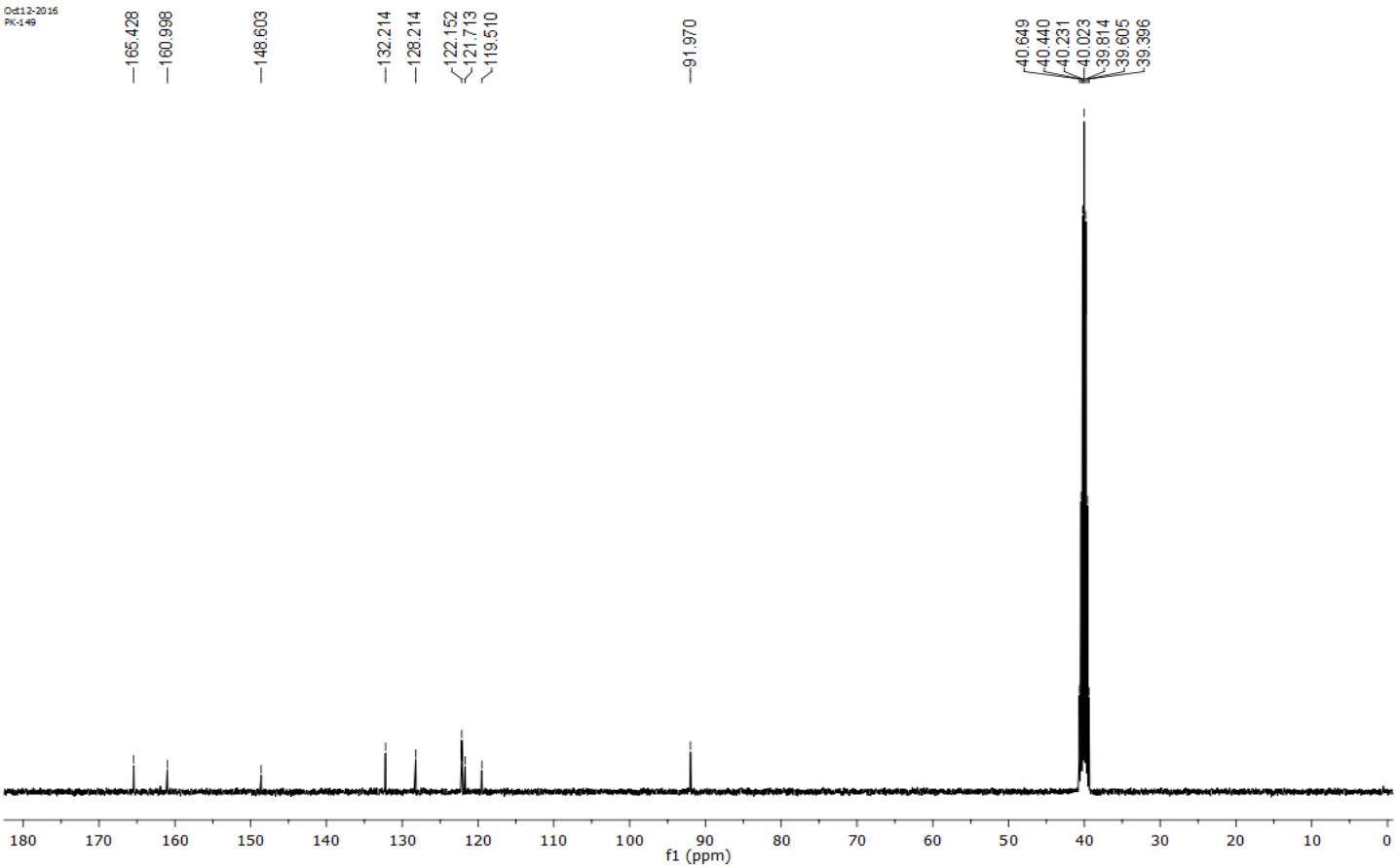
OH
F
O
O

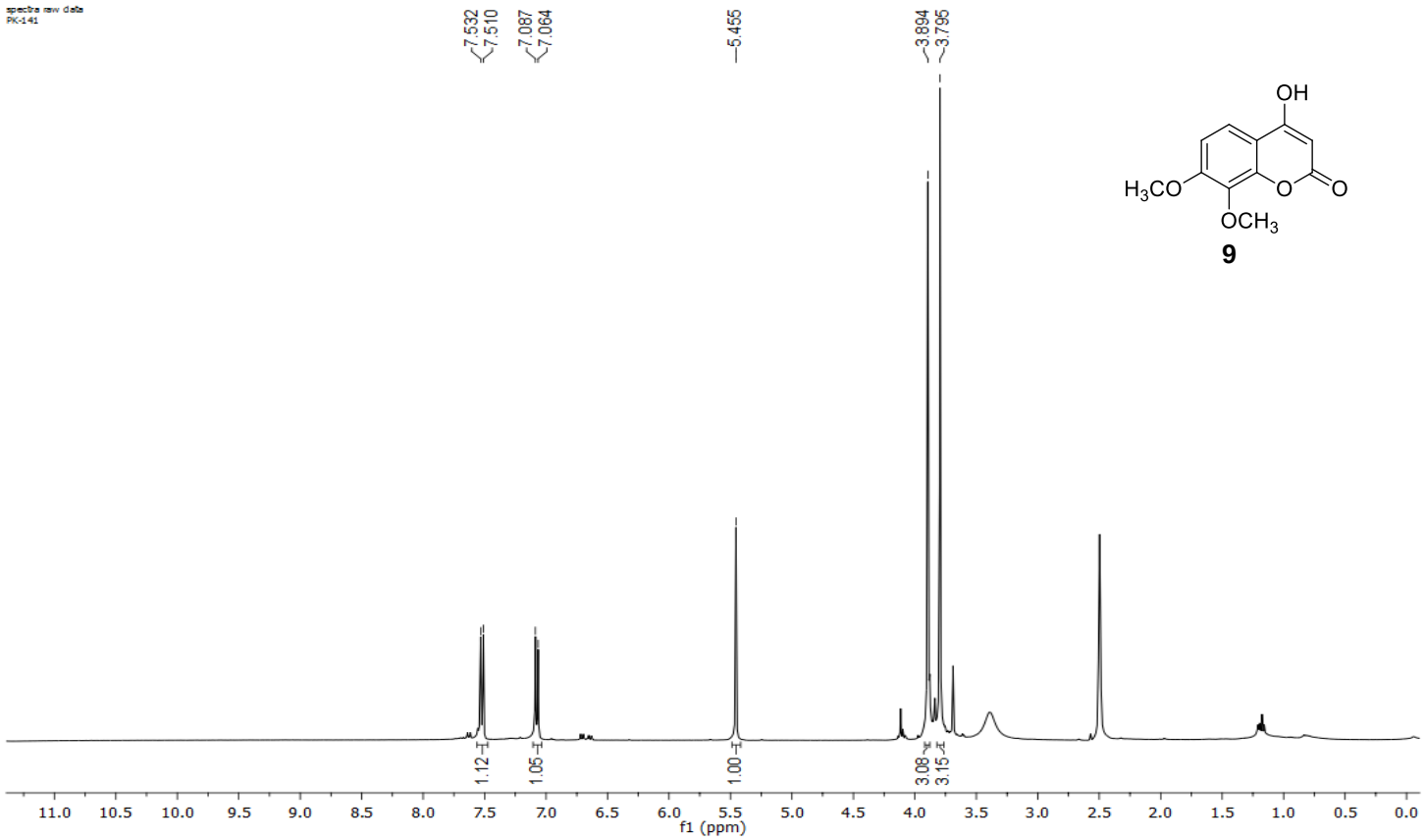
7

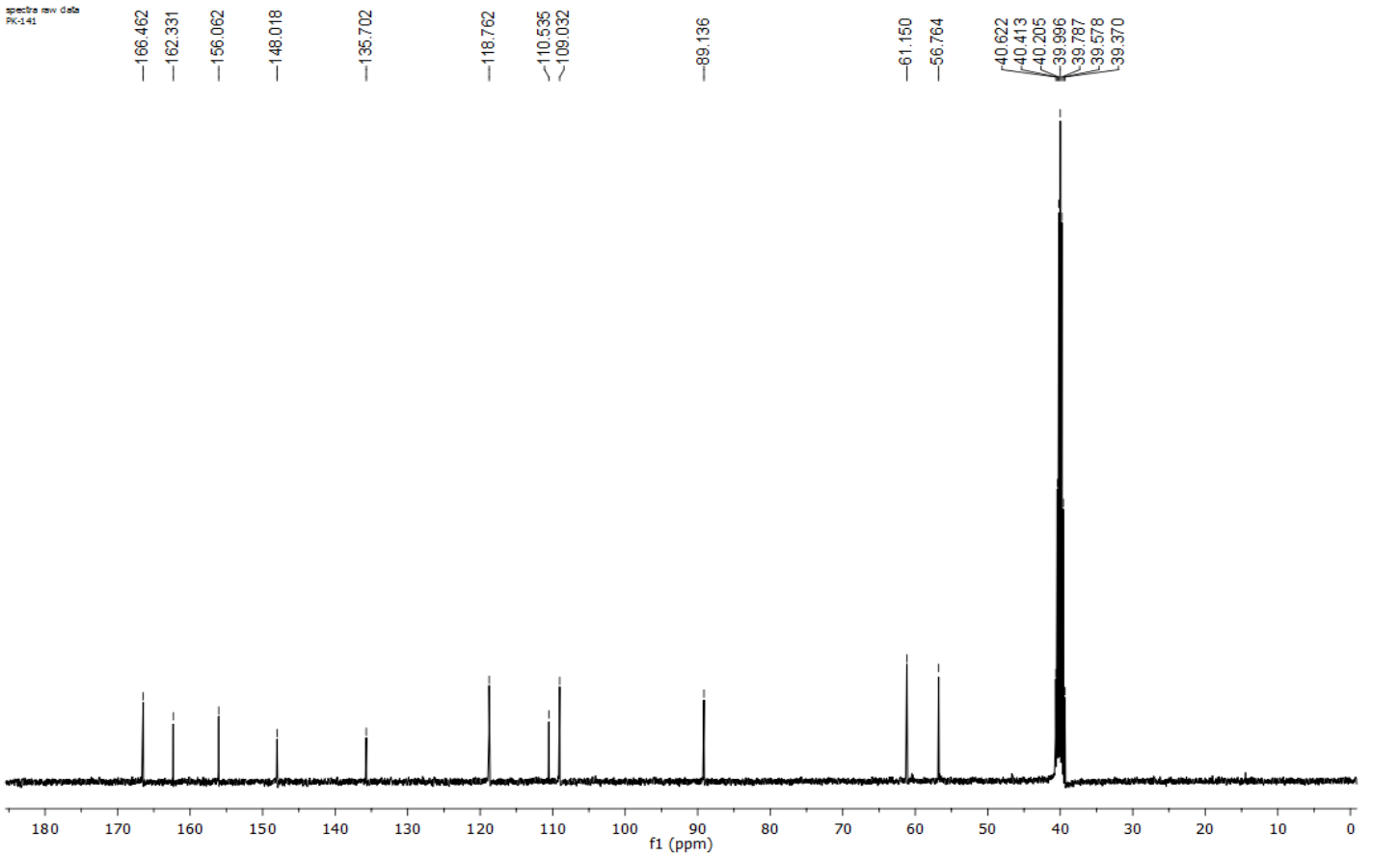

spectra raw data
PK-85_13C_DMSO
165.826
162.213
155.311
155.176
125.942
125.835
113.280
113.256
112.386
112.160
104.448
104.192
90.461
84.583
40.402
40.193
39.985
39.776
39.567
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

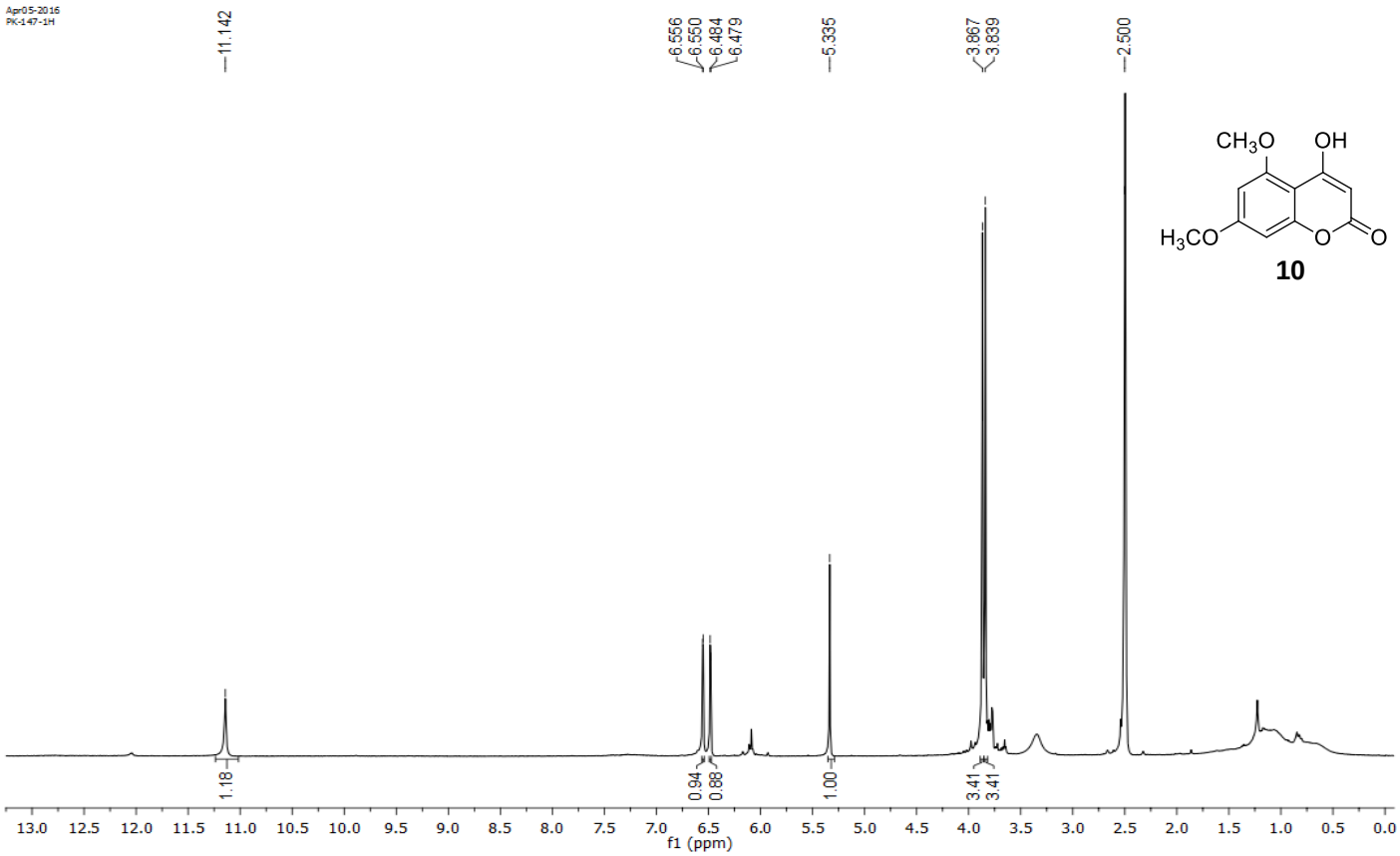

Oct12-2016
PK-149
7.951
7.945
7.732
7.726
5.580
2.500
0.010
OH
Cl
Cl
O
O
f1 (ppm)

8


Oct12-2016
PK-149
165.428
160.998
148.603
132.214
128.214
122.152
121.713
119.510
91.970
40.649
40.440
40.231
40.023
39.814
39.605
39.396
f1 (ppm)

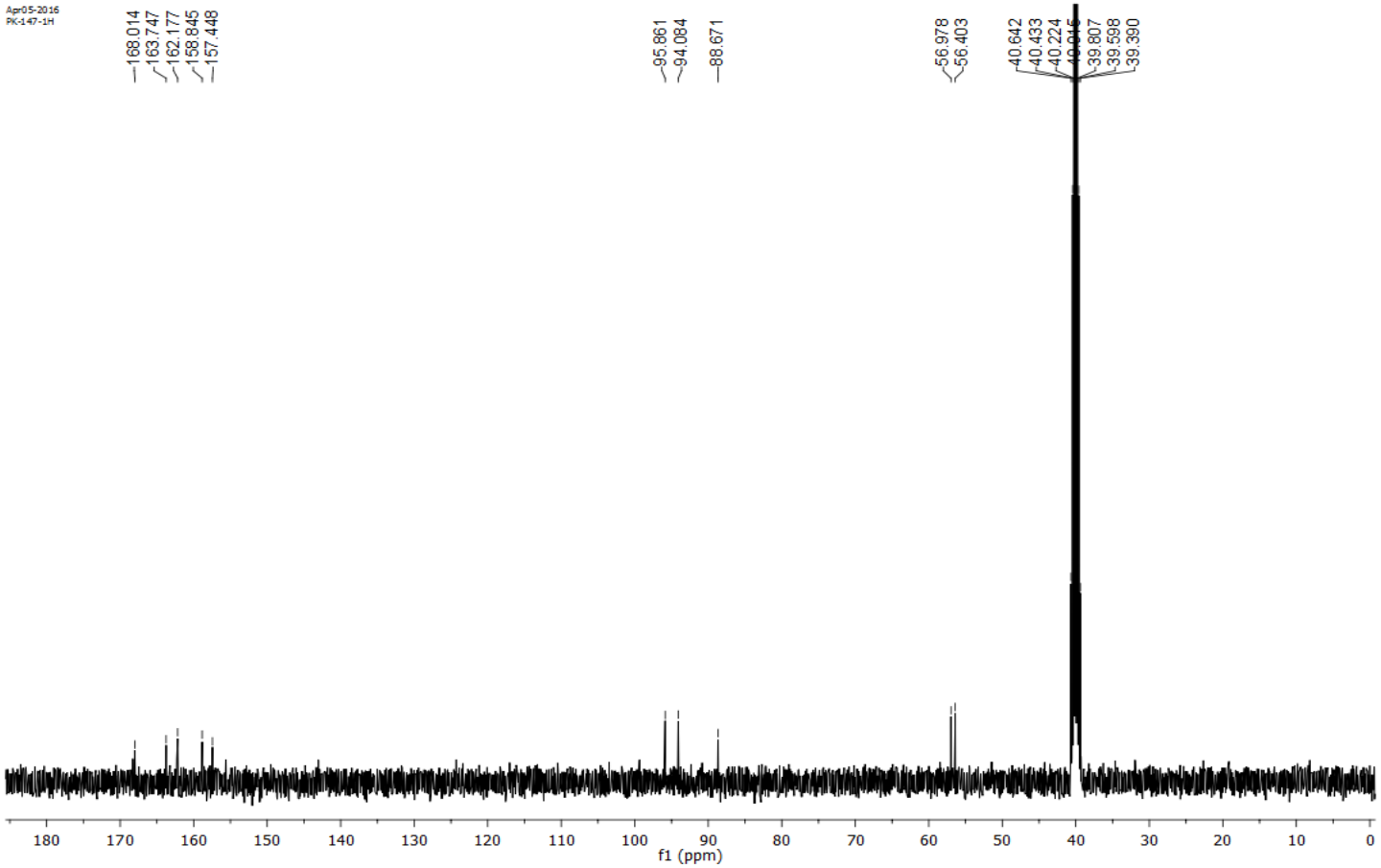

spectra raw data
PK-141
7.532
7.510
7.087
7.064
5.455
3.894
3.795
OH
H3CO
O
O
OCH3
9
1.12
1.05
1.00
3.08
3.15
f1 (ppm)

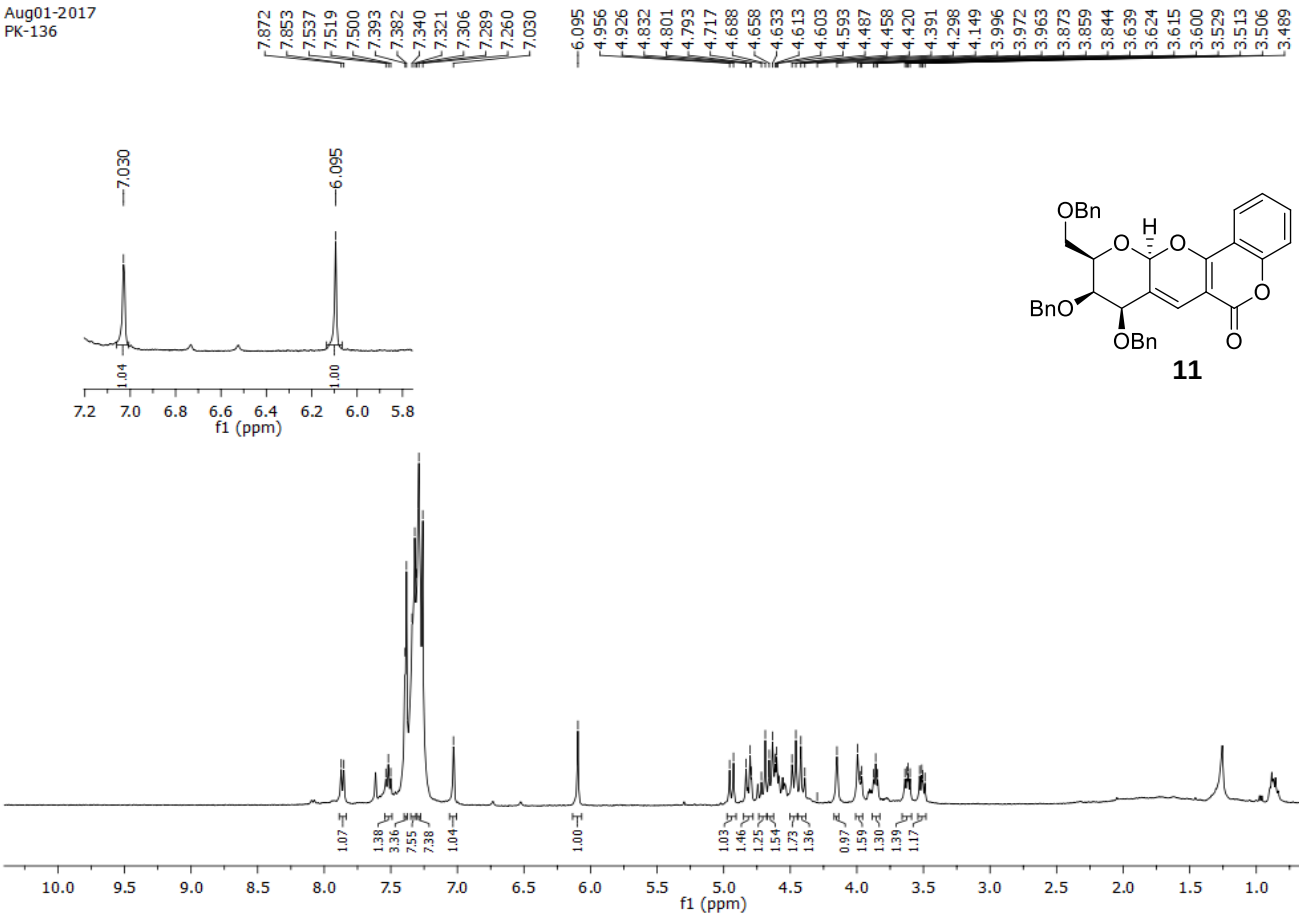

spectra raw data
PK-141
166.462
162.331
156.062
148.018
135.702
118.762
110.535
109.032
89.136
61.150
56.764
40.622
40.413
40.205
39.996
39.787
39.578
39.370
f1 (ppm)

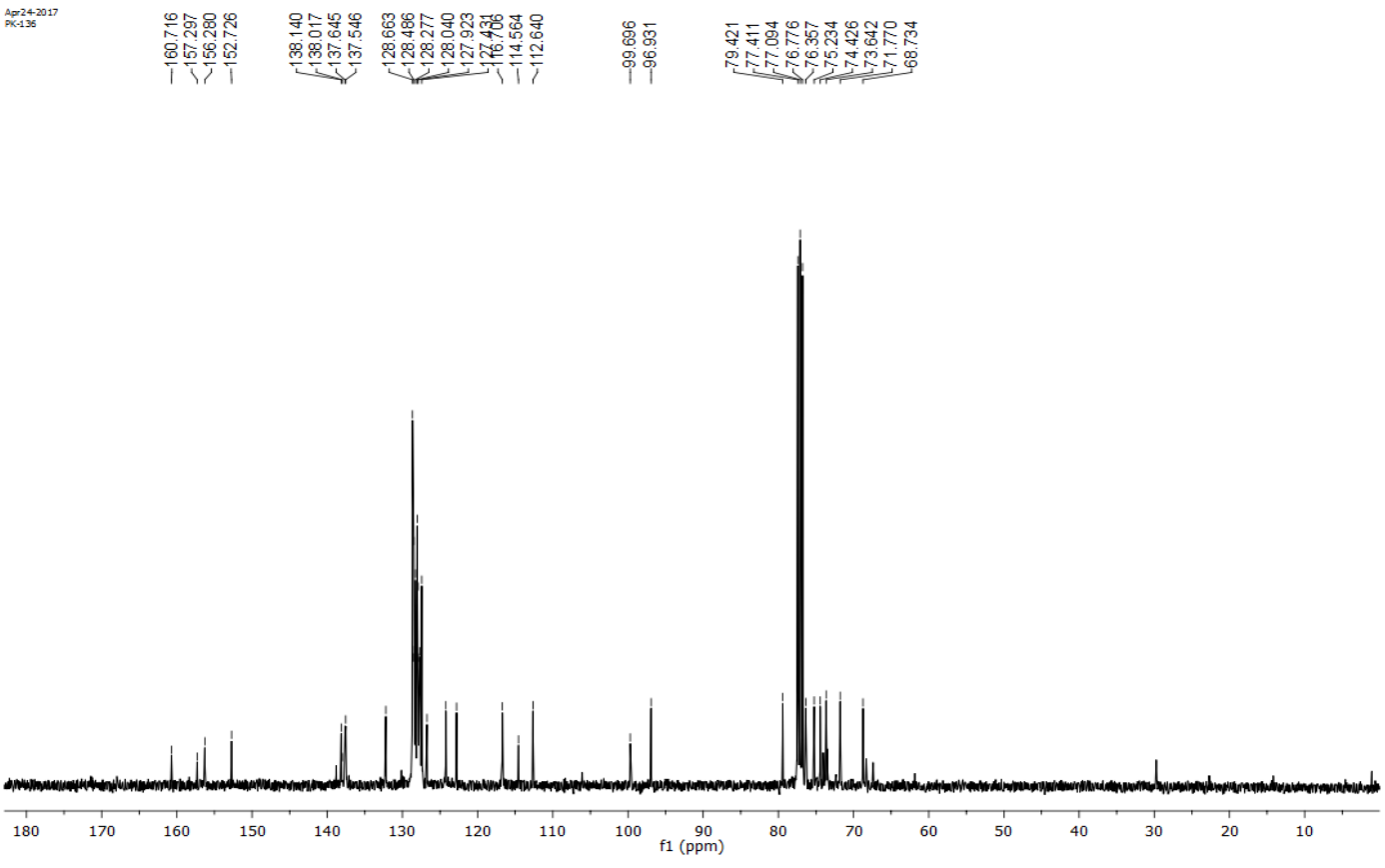

Apr05-2016
PK-147-1H
11.142
6.556
6.550
6.484
6.479
5.335
3.867
3.839
2.500
1.18
0.94
0.88
1.00
3.41
3.41
f1 (ppm)

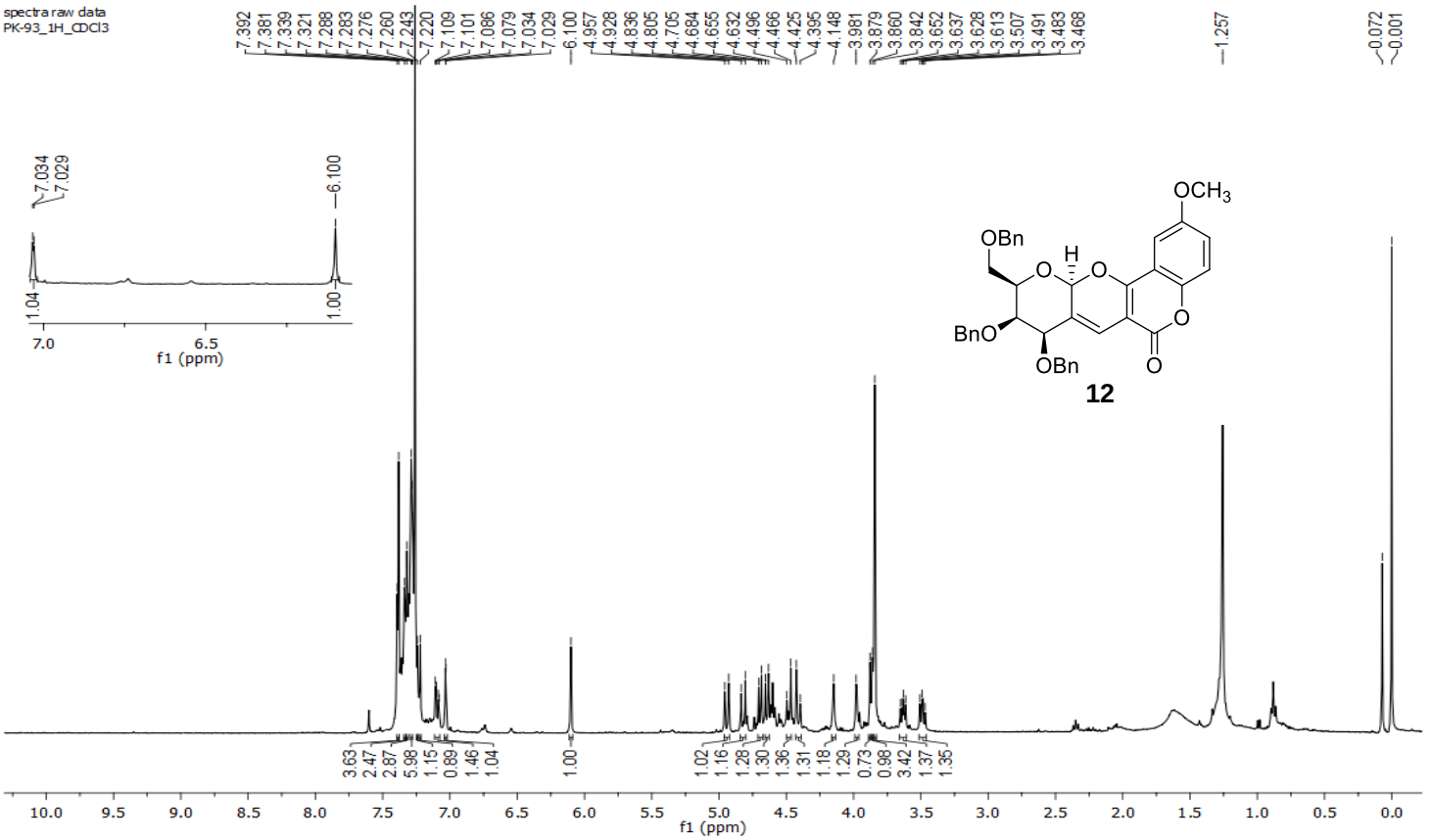
CH3O
OH
H3CO
O
O

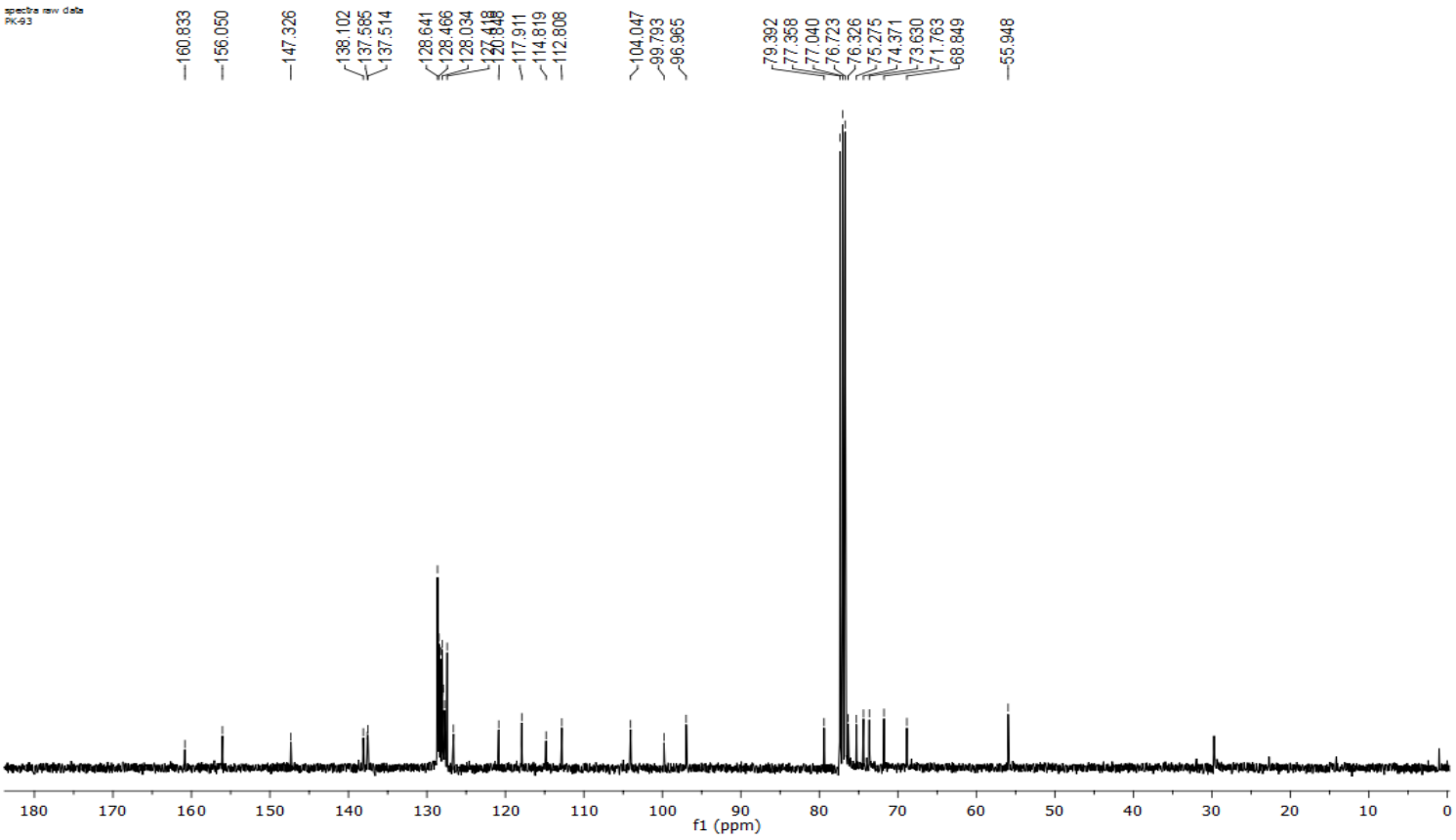
10

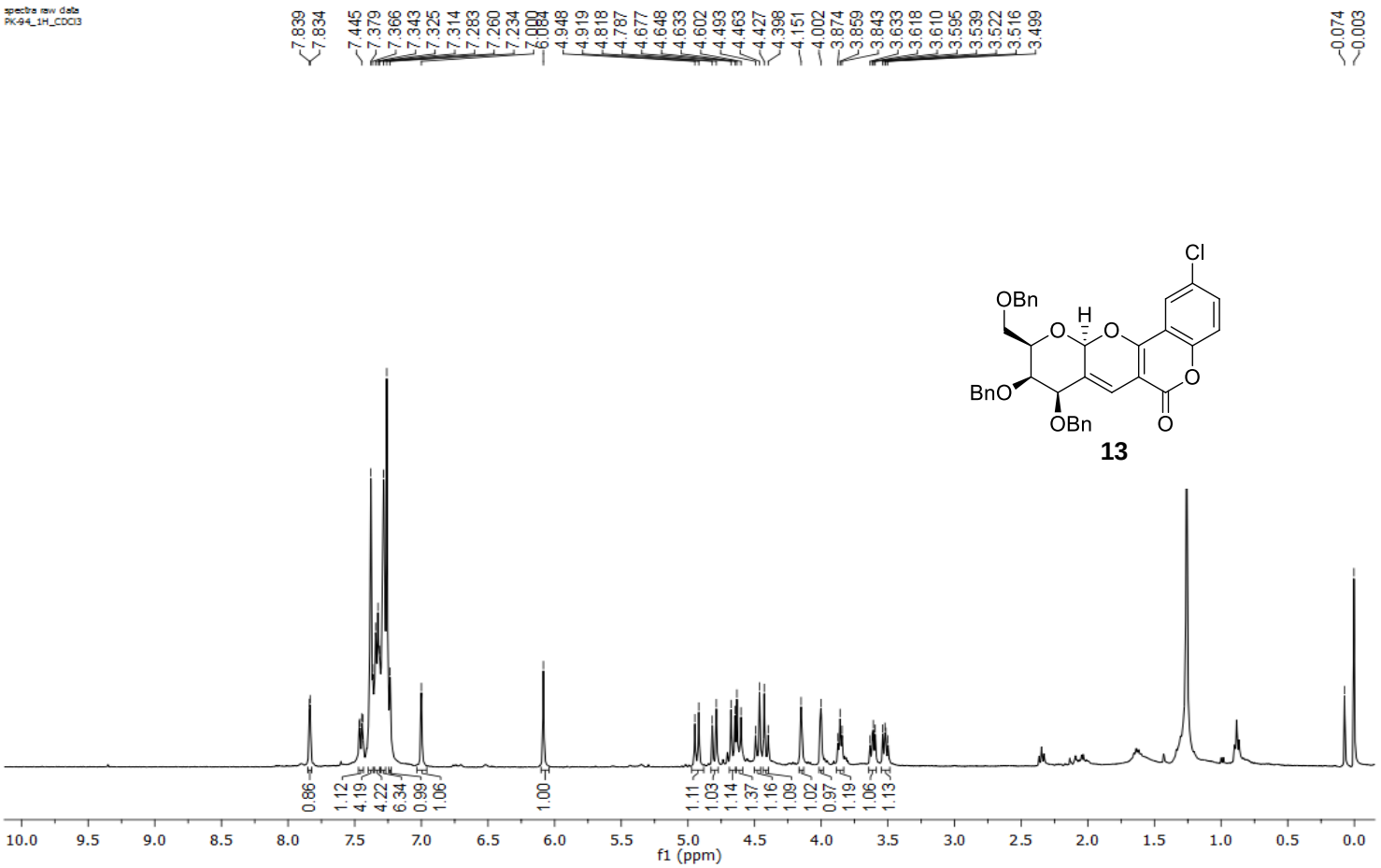

Apr05-2016
PK-147-1H
168.014
163.747
162.177
158.845
157.448
95.861
94.084
88.671
56.978
56.403
40.642
40.433
40.224
39.807
39.598
39.390
f1 (ppm)

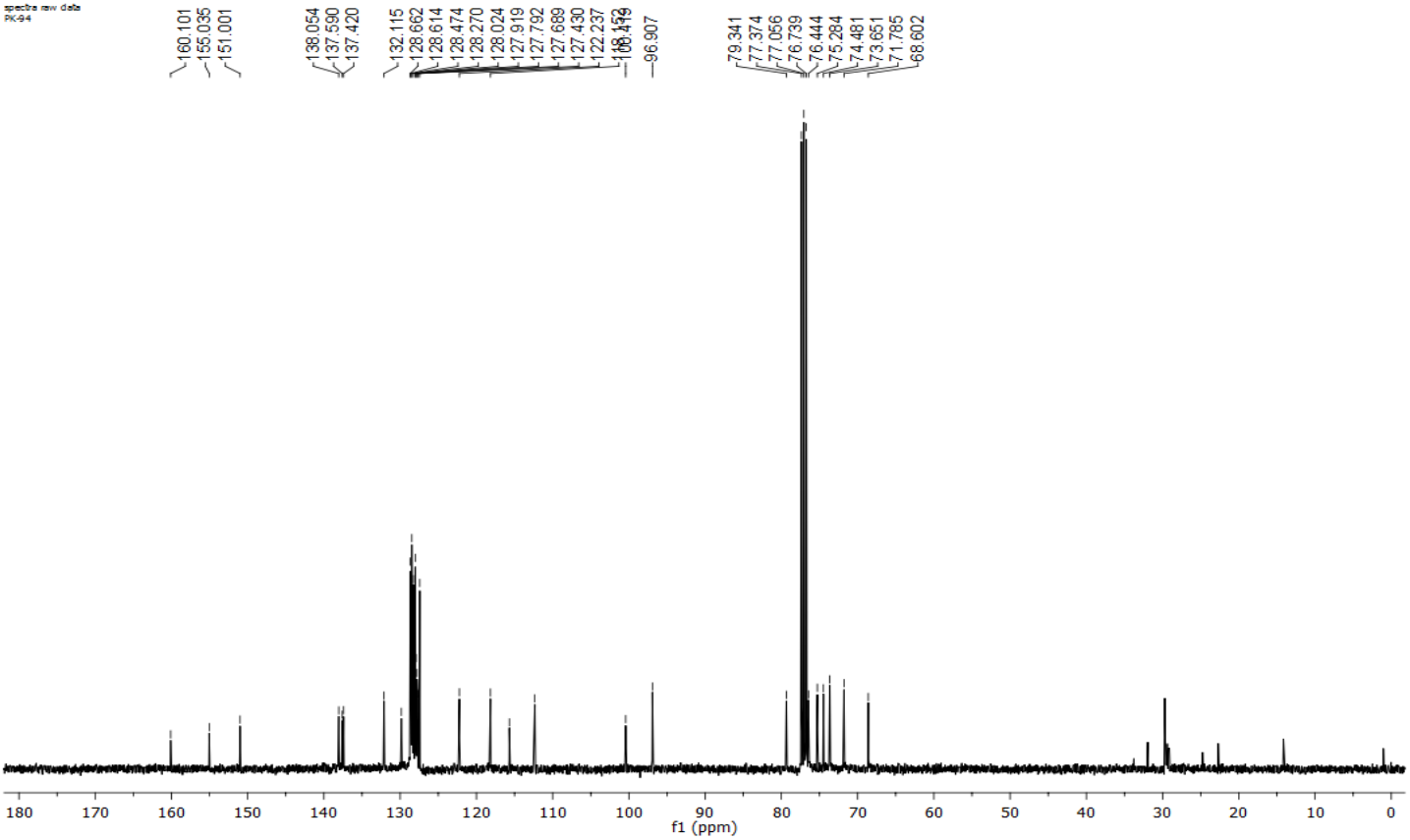

Aug01-2017
PK-136
7.872 7.853 7.537 7.519 7.500 7.393 7.382 7.340 7.321 7.306 7.289 7.260 7.030
6.095
4.956 4.926 4.832 4.801 4.793 4.717 4.688 4.658 4.633 4.613 4.603 4.593 4.487 4.458 4.420 4.391 4.298 4.149 3.996 3.972 3.963 3.873 3.859 3.844 3.639 3.624 3.615 3.600 3.529 3.513 3.506 3.489
7.030
6.095
1.04
1.00
7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8
f1 (ppm)
OBn
H
O
O
BnO
O
OBn
O
11
1.07 1.38 3.36 7.55 7.38 1.04 1.00 1.03 1.46 1.25 1.54 1.73 1.36 0.97 1.59 1.30 1.39 1.17
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
f1 (ppm)

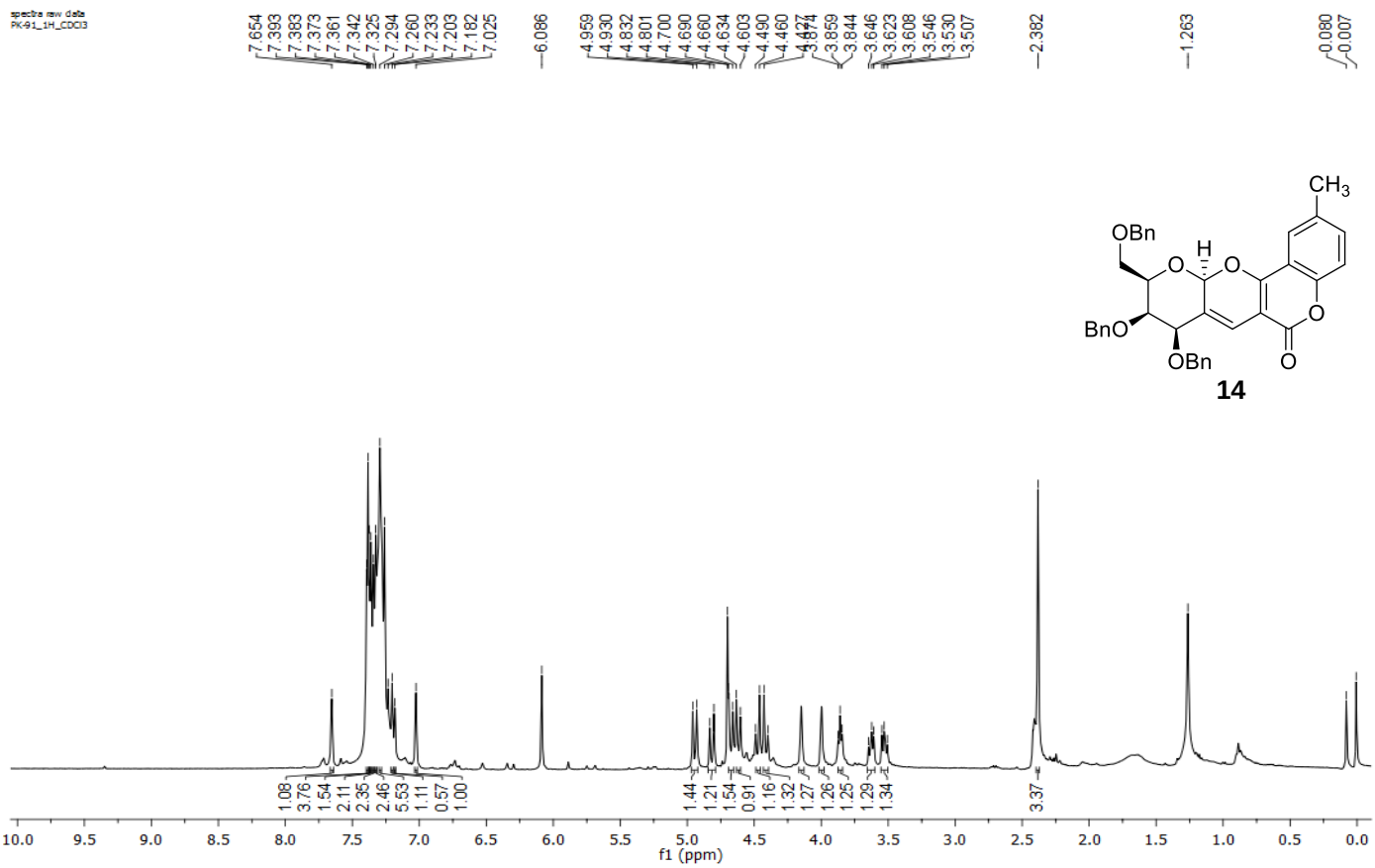

Apr24-2017
PK-136
160.716 157.297 156.280 152.726 138.140 138.017 137.645 137.546 128.663 128.486 128.277 128.040 127.923 127.431 116.706 114.564 112.640 99.696 96.931 79.421 77.411 77.094 76.776 76.357 75.234 74.426 73.642 71.770 68.734
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

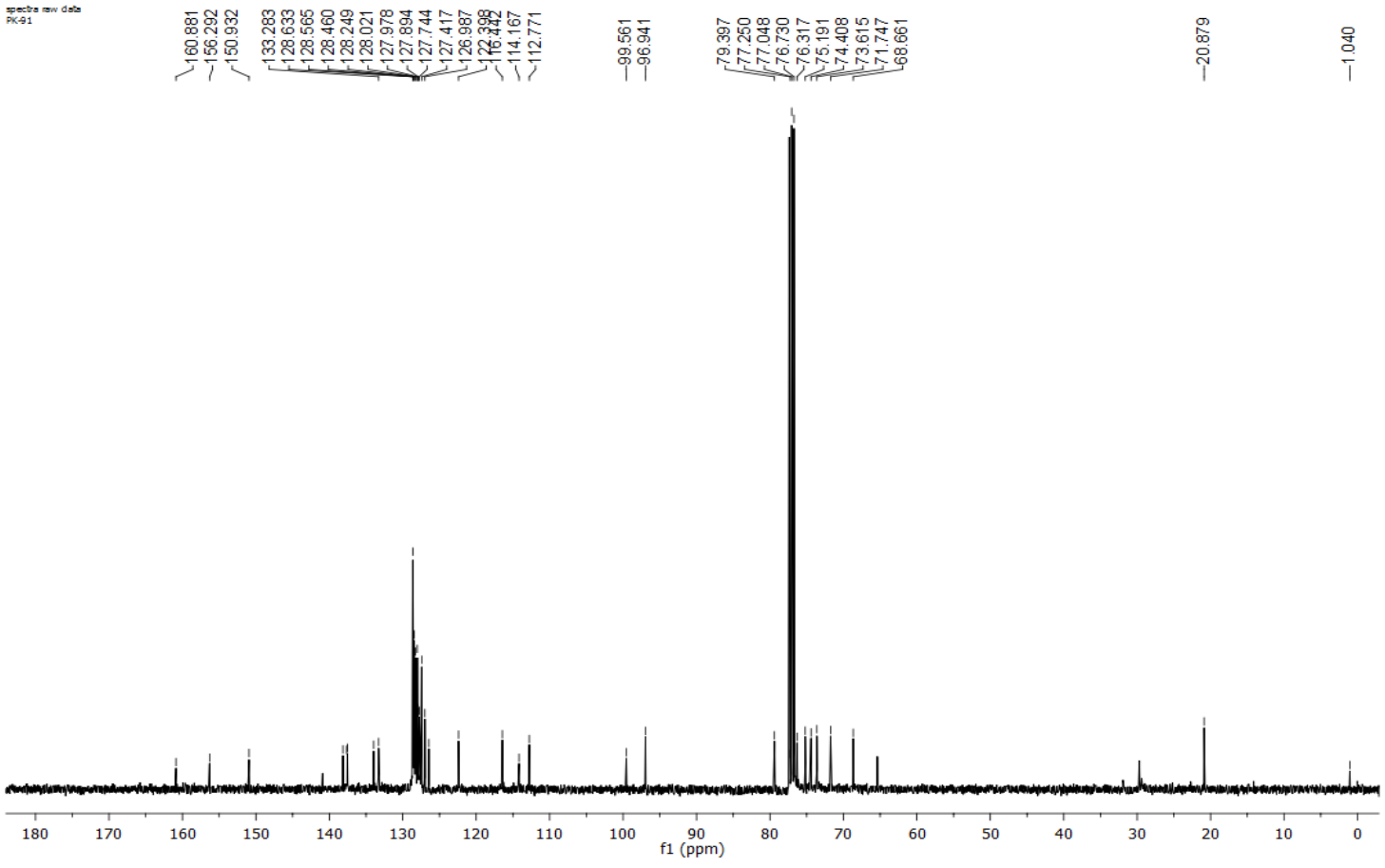

spectra raw data
PK-93_1H_CDCl3
OCH3
OBn
H
O
BnO
OBn
O
12
f1 (ppm)

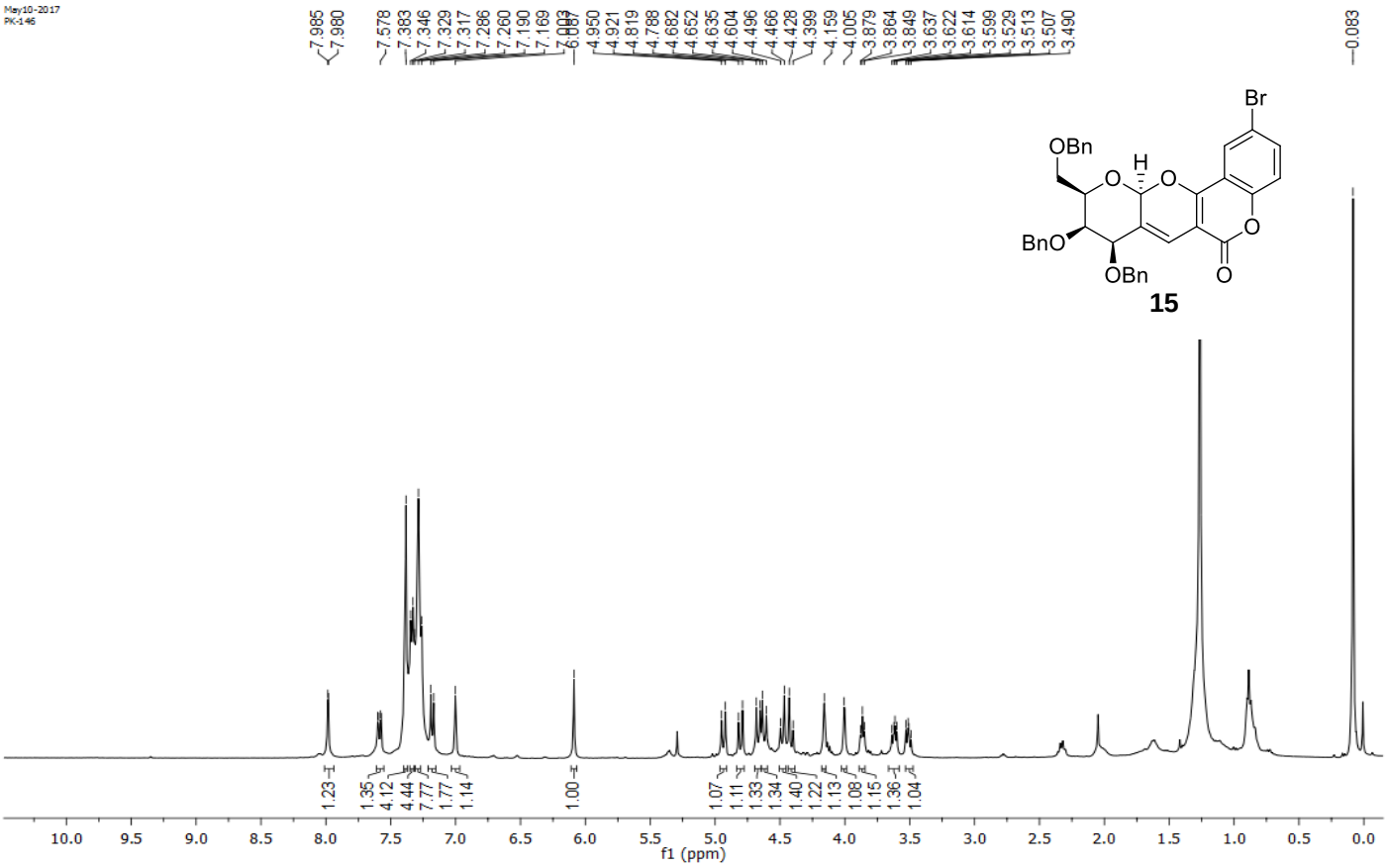

spectra raw data
PK-93
f1 (ppm)

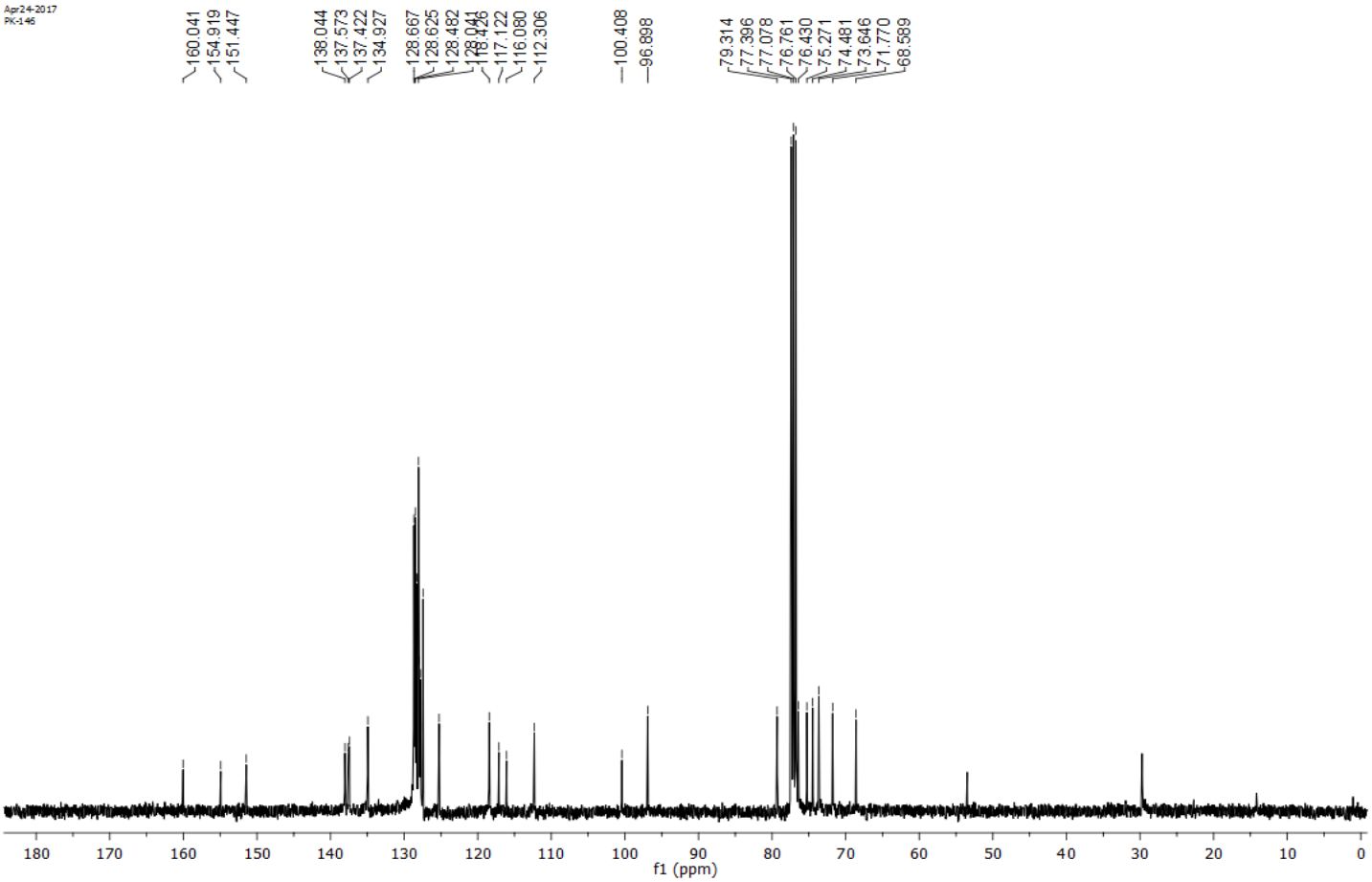

spectra raw data
PK-94_1H_CDCl3
7.839
7.834
7.445
7.379
7.366
7.343
7.325
7.314
7.283
7.260
7.234
6.084
4.948
4.919
4.818
4.787
4.677
4.648
4.633
4.602
4.493
4.463
4.427
4.398
4.151
4.002
3.874
3.859
3.843
3.633
3.618
3.610
3.595
3.539
3.522
3.516
3.499
0.074
0.003
Cl
OBn
H
O
O
O
BnO
OBn
O
13
0.86
1.12
4.19
4.22
6.34
0.99
1.06
1.00
1.11
1.03
1.14
1.37
1.16
1.09
1.02
0.97
1.19
1.06
1.13
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
f1 (ppm)

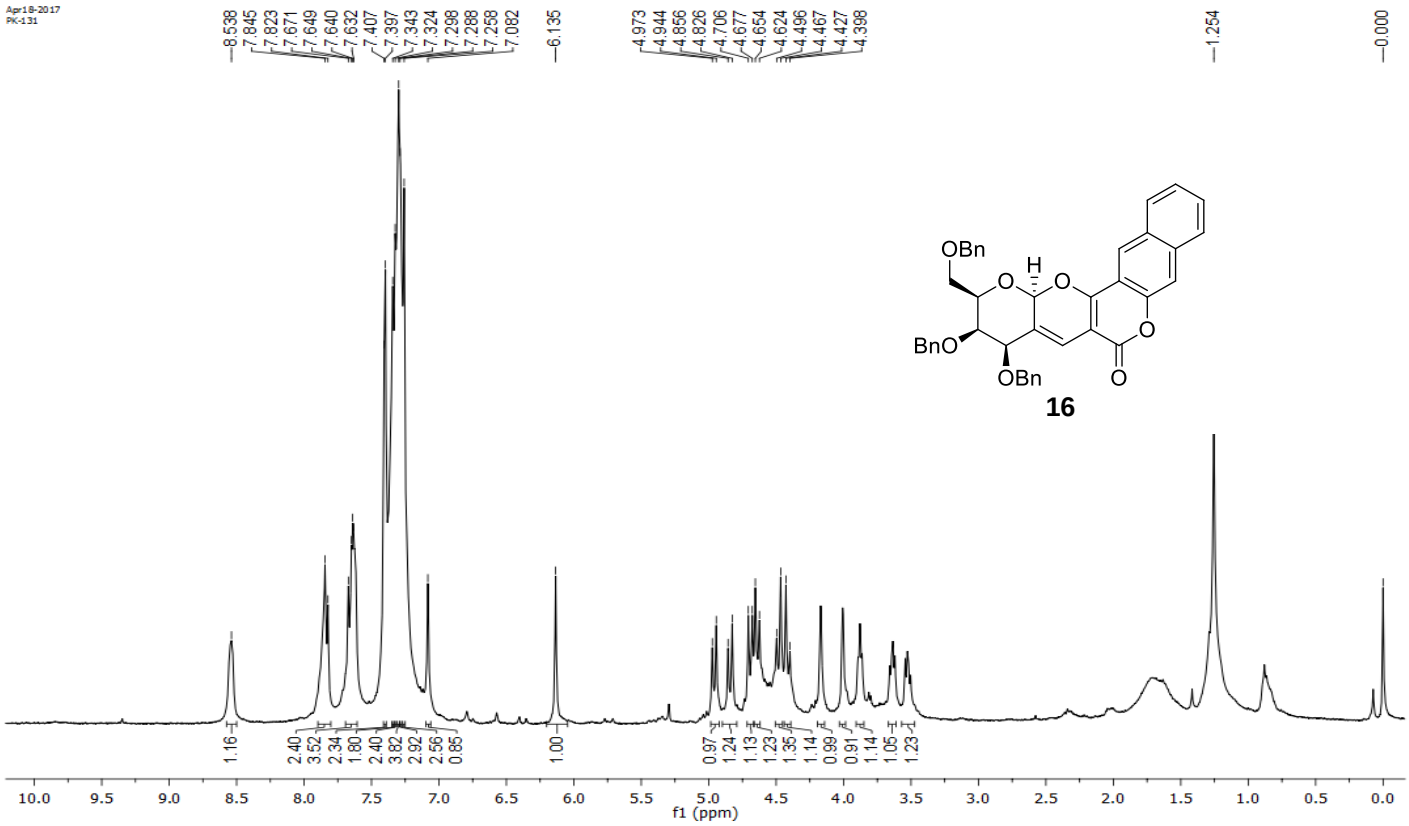

spectra raw data
PK-94
160.101
155.035
151.001
138.054
137.590
137.420
132.115
128.662
128.614
128.474
128.270
128.024
127.919
127.792
127.689
127.430
122.237
96.907
79.341
77.374
77.056
76.739
76.444
75.284
74.481
73.651
71.785
68.602
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


spectra raw data
PK-91_1H_CDCl3
7.654
7.393
7.383
7.373
7.361
7.342
7.325
7.294
7.260
7.233
7.203
7.182
7.025
6.086
4.959
4.930
4.832
4.801
4.700
4.690
4.660
4.634
4.603
4.490
4.460
3.859
3.844
3.646
3.623
3.608
3.546
3.530
3.507
2.382
1.263
0.080
0.007
CH3
OBn
H
O
O
O
BnO
OBn
O
14
1.08
3.76
1.54
2.11
2.35
2.46
5.53
1.11
0.57
1.00
1.44
1.21
1.54
0.91
1.16
1.32
1.27
1.26
1.25
1.29
1.34
3.37
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
f1 (ppm)


spectra raw data
PK-91
160.881
156.292
150.932
133.283
128.633
128.565
128.460
128.249
128.021
127.978
127.894
127.744
127.417
126.987
122.398
116.442
114.167
112.771
99.561
96.941
79.397
77.250
77.048
76.730
76.317
75.191
74.408
73.615
71.747
68.661
20.879
1.040
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

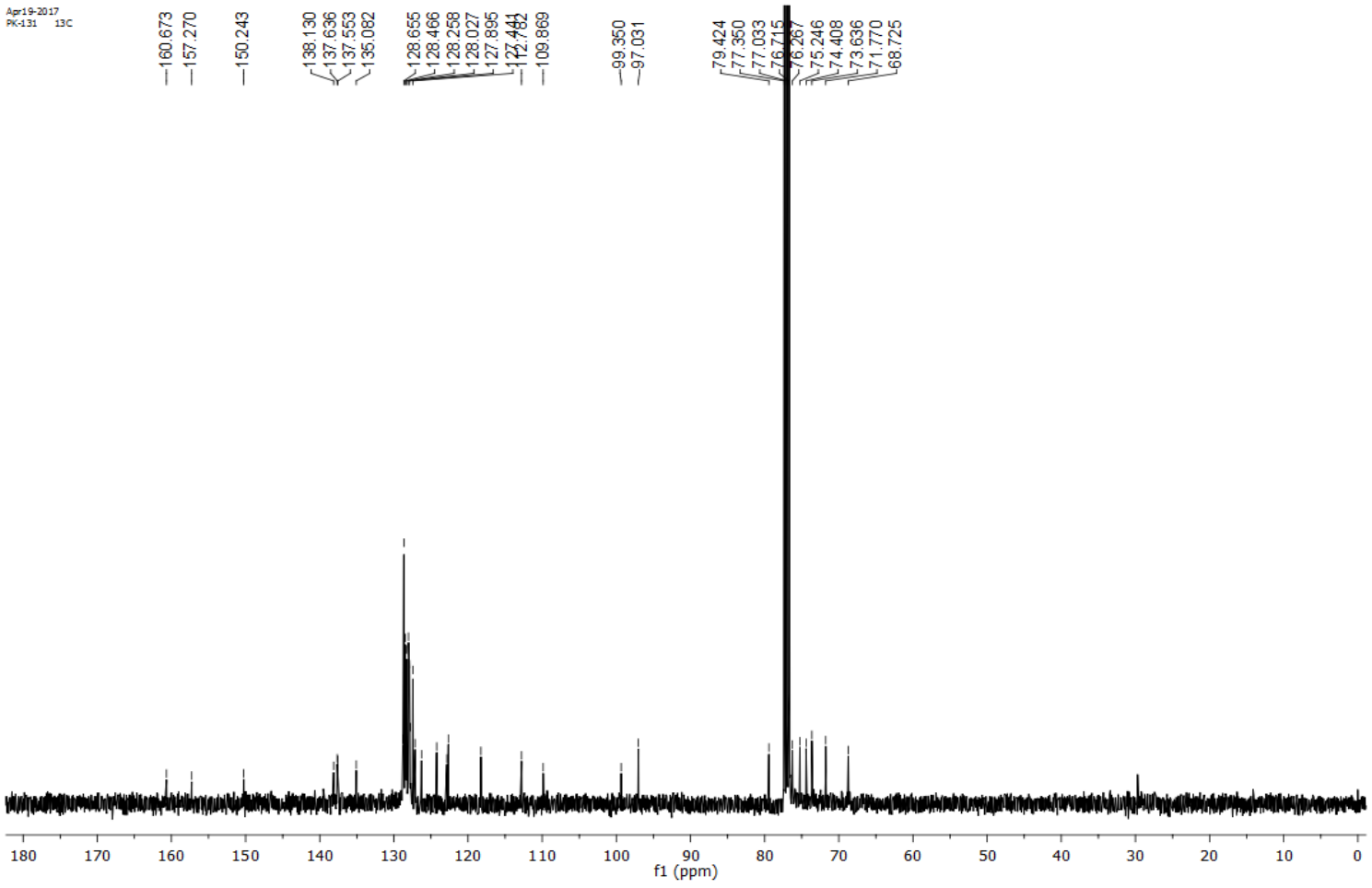

May10-2017
PK-146
7.985
7.980
7.578
7.383
7.346
7.329
7.317
7.286
7.260
7.190
7.169
6.087
4.950
4.921
4.819
4.788
4.682
4.652
4.635
4.604
4.496
4.466
4.428
4.399
4.159
4.005
3.879
3.864
3.849
3.637
3.622
3.614
3.599
3.529
3.513
3.507
3.490
0.083
Br
OBn
H
O
O
O
BnO
OBn
O
O
15
1.23
1.35
4.12
4.44
7.77
1.77
1.14
1.00
1.07
1.11
1.33
1.34
1.40
1.22
1.13
1.08
1.15
1.36
1.04
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
f1 (ppm)

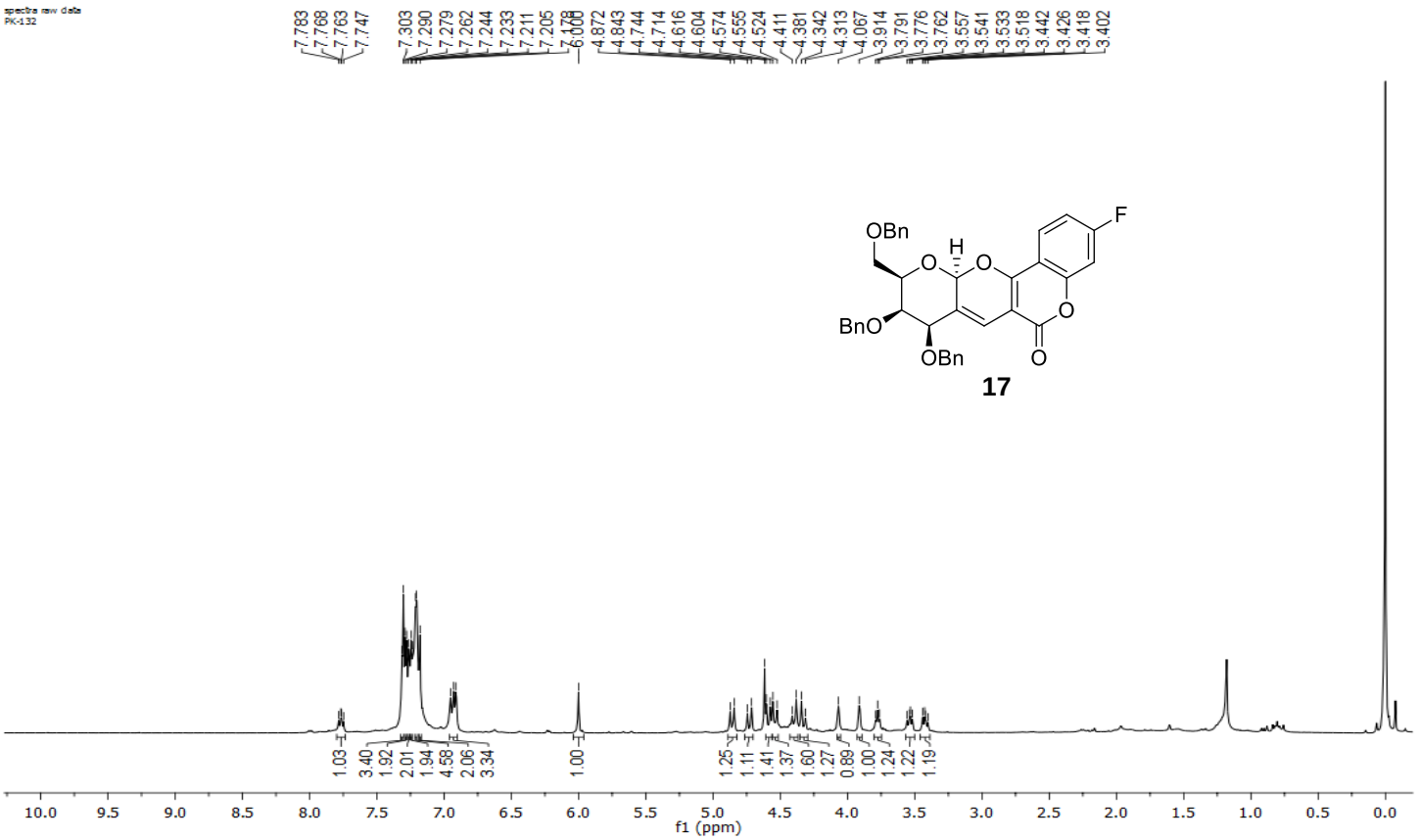

Apr24-2017
PK-146
160.041
154.919
151.447
138.044
137.573
137.422
134.927
128.667
128.625
128.482
128.041
117.122
116.080
112.306
100.408
96.898
79.314
77.396
77.078
76.761
76.430
75.271
74.481
73.646
71.770
68.589
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

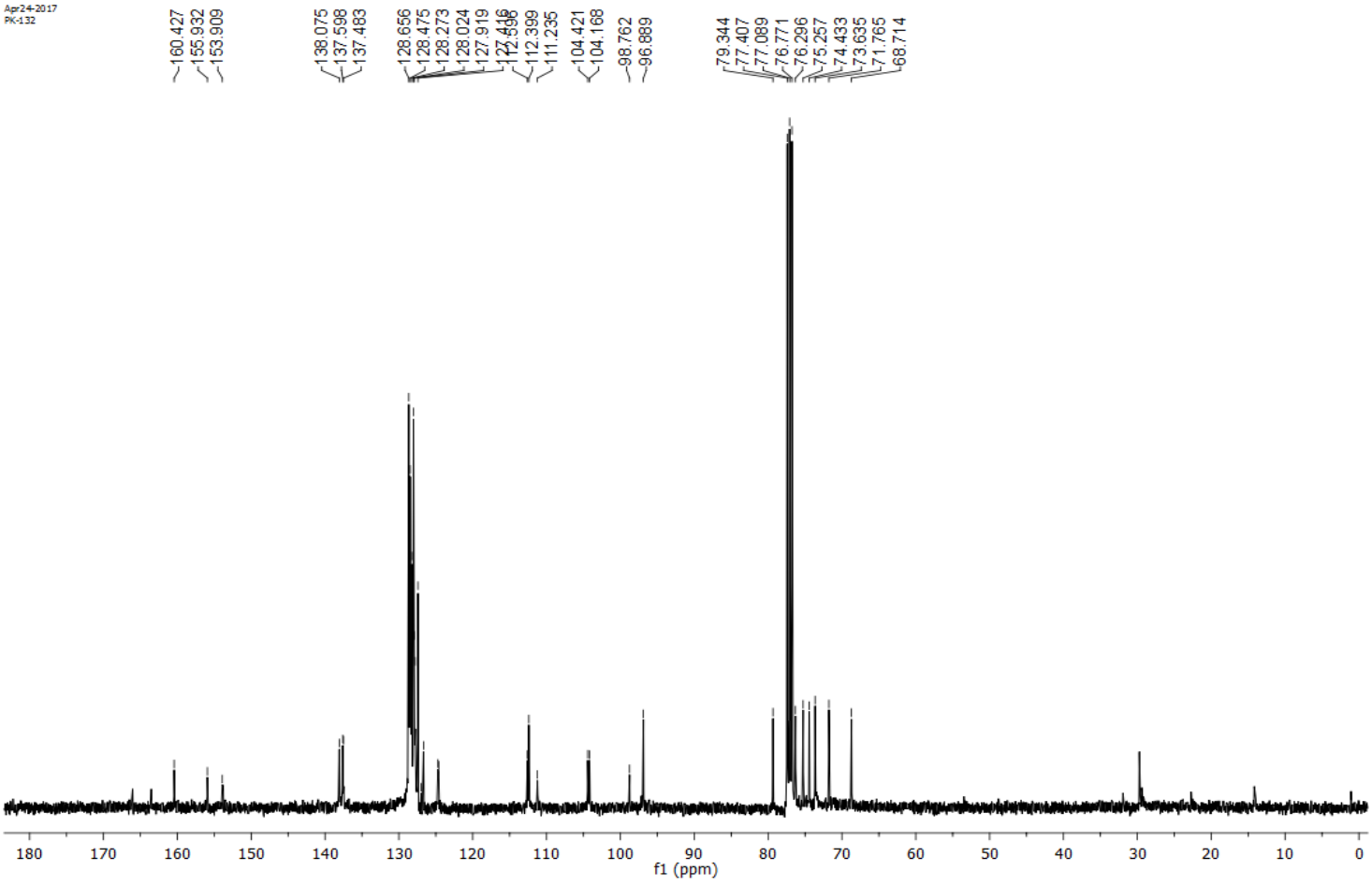

Apr18-2017
PK-131
8.538
7.845
7.823
7.671
7.649
7.640
7.632
7.407
7.397
7.343
7.324
7.298
7.288
7.268
7.082
6.135
4.973
4.944
4.856
4.826
4.706
4.677
4.654
4.624
4.496
4.467
4.427
4.398
1.254
0.000
1.16
2.40
3.52
2.34
1.80
2.40
3.82
2.92
2.56
0.85
1.00
0.97
1.24
1.13
1.23
1.35
1.14
0.99
0.91
1.14
1.05
1.23
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
f1 (ppm)

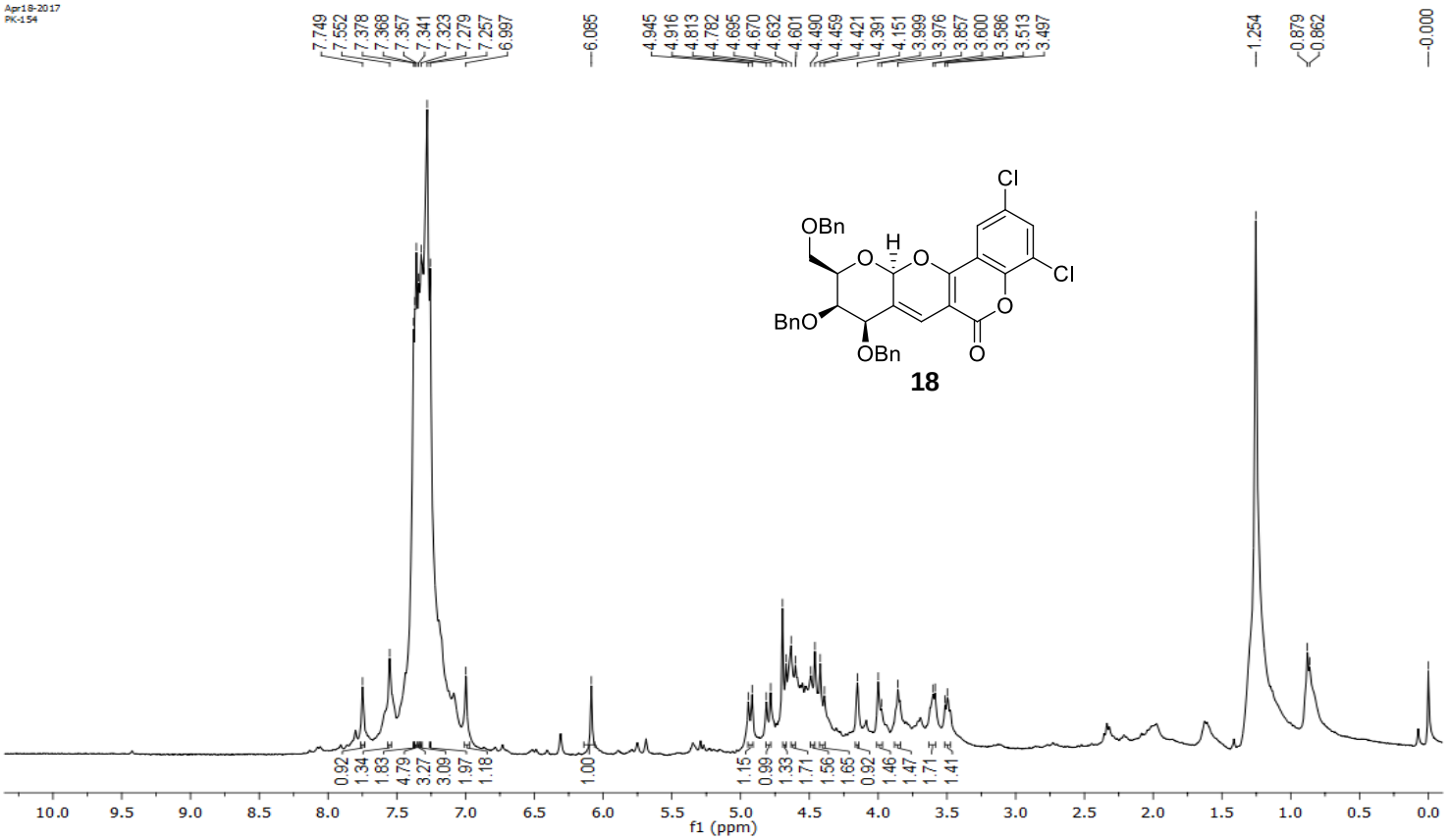
OBn
H
O
O
BnO
OBn
O
O

16


Apr19-2017
PK-131 13C
160.673
157.270
150.243
138.130
137.636
137.553
135.082
128.655
128.466
128.258
128.027
127.895
112.762
109.869
99.350
97.031
79.424
77.350
77.033
76.715
76.267
75.246
74.408
73.636
71.770
68.725
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

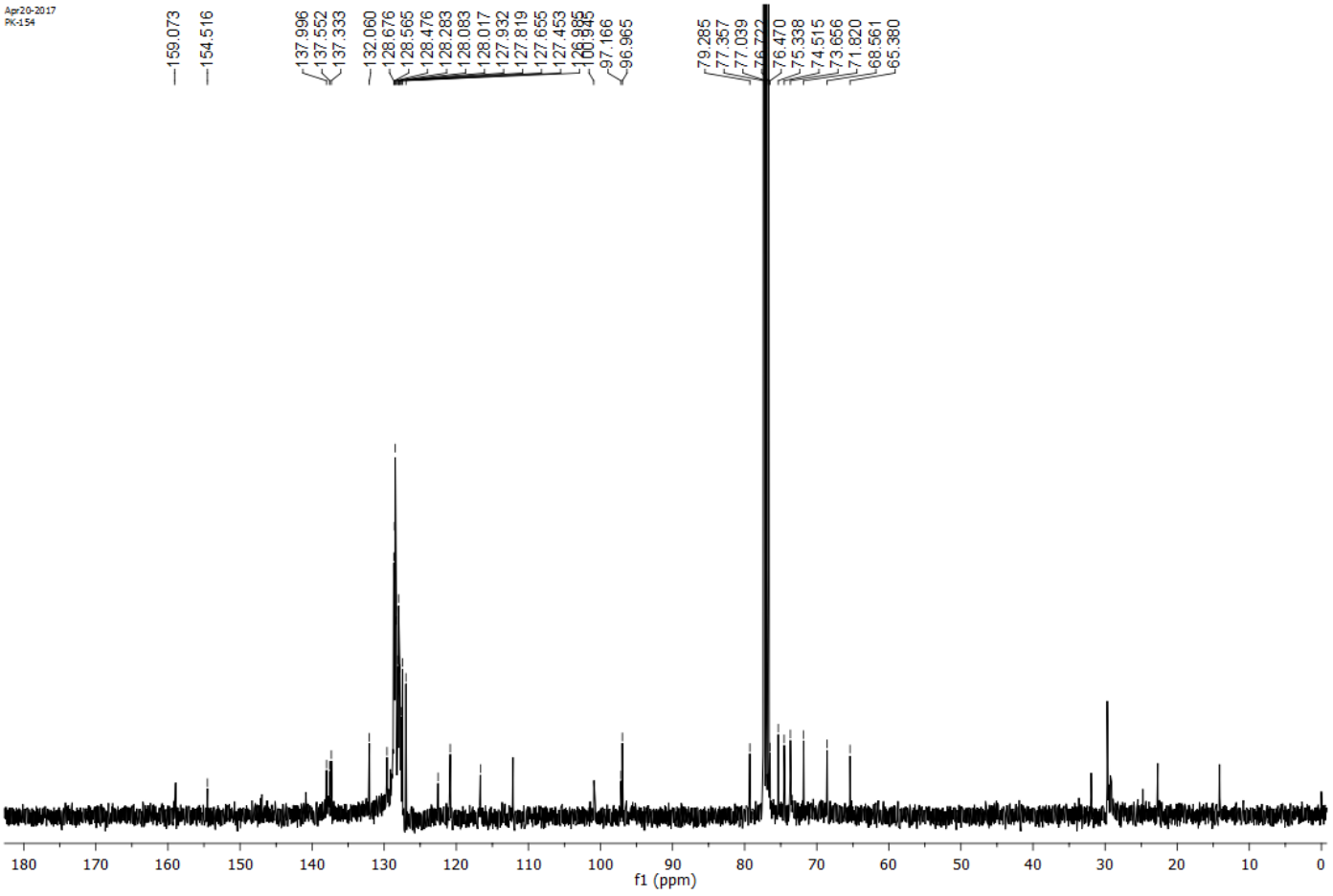

spectra raw data
PK-132
7.783
7.768
7.763
7.747
7.303
7.290
7.279
7.262
7.244
7.233
7.211
7.205
7.178
7.000
4.872
4.843
4.744
4.714
4.616
4.604
4.574
4.555
4.524
4.411
4.381
4.342
4.313
4.067
3.914
3.791
3.776
3.762
3.557
3.541
3.533
3.518
3.442
3.426
3.418
3.402
OBn
H
O
O
F
BnO
OBn
O
O
17
1.03
3.40
1.92
2.01
1.94
4.58
2.06
3.34
1.00
1.25
1.11
1.41
1.37
1.60
1.27
0.89
1.00
1.24
1.22
1.19
f1 (ppm)

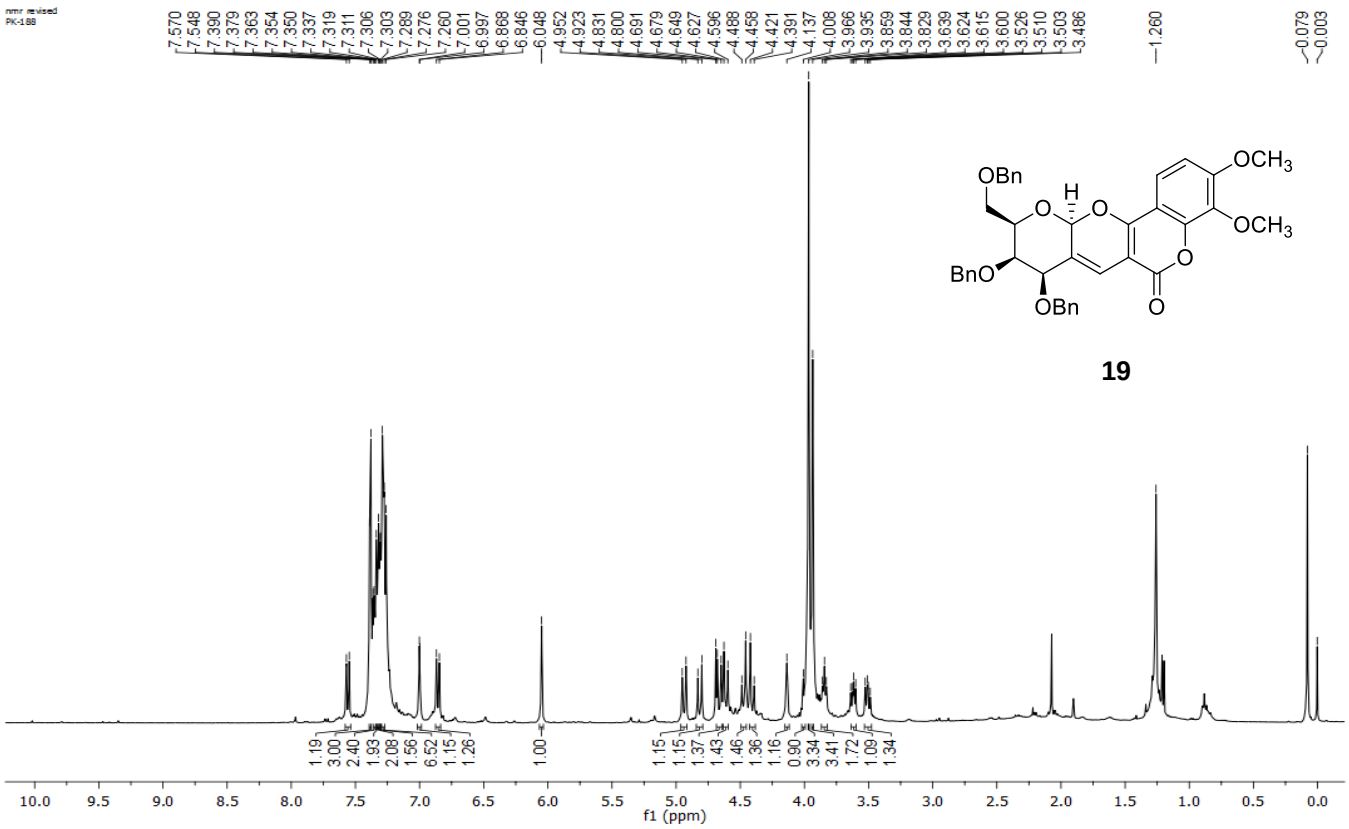

Apr24-2017
PK-132
160.427
155.932
153.909
138.075
137.598
137.483
128.656
128.475
128.273
128.024
127.919
112.399
111.235
104.421
104.168
98.762
96.889
79.344
77.407
77.089
76.771
76.296
75.257
74.433
73.635
71.765
68.714
f1 (ppm)


Apr18-2017
PK-154
7.749
7.552
7.378
7.368
7.357
7.341
7.323
7.279
7.257
6.997
6.085
4.945
4.916
4.813
4.782
4.695
4.670
4.632
4.601
4.490
4.459
4.421
4.391
4.151
3.999
3.976
3.857
3.600
3.586
3.513
3.497
1.254
0.879
0.862
0.000
0.92
1.34
1.83
4.79
3.27
3.09
1.97
1.18
1.00
1.15
0.99
1.33
1.71
1.56
1.65
0.92
1.46
1.47
1.71
1.41
f1 (ppm)

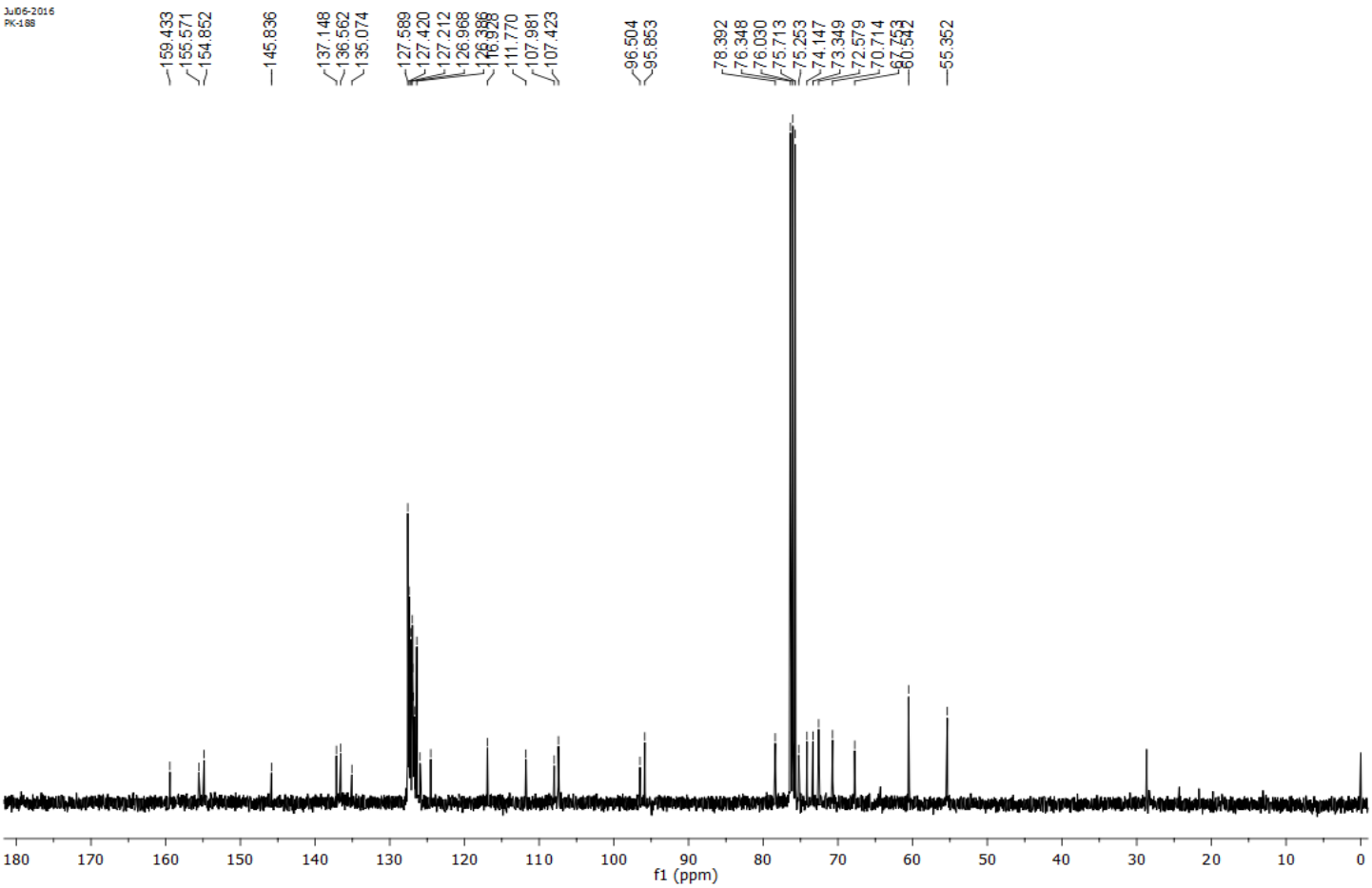
Cl
OBn
H
O
O
Cl
BnO
O
OBn
O

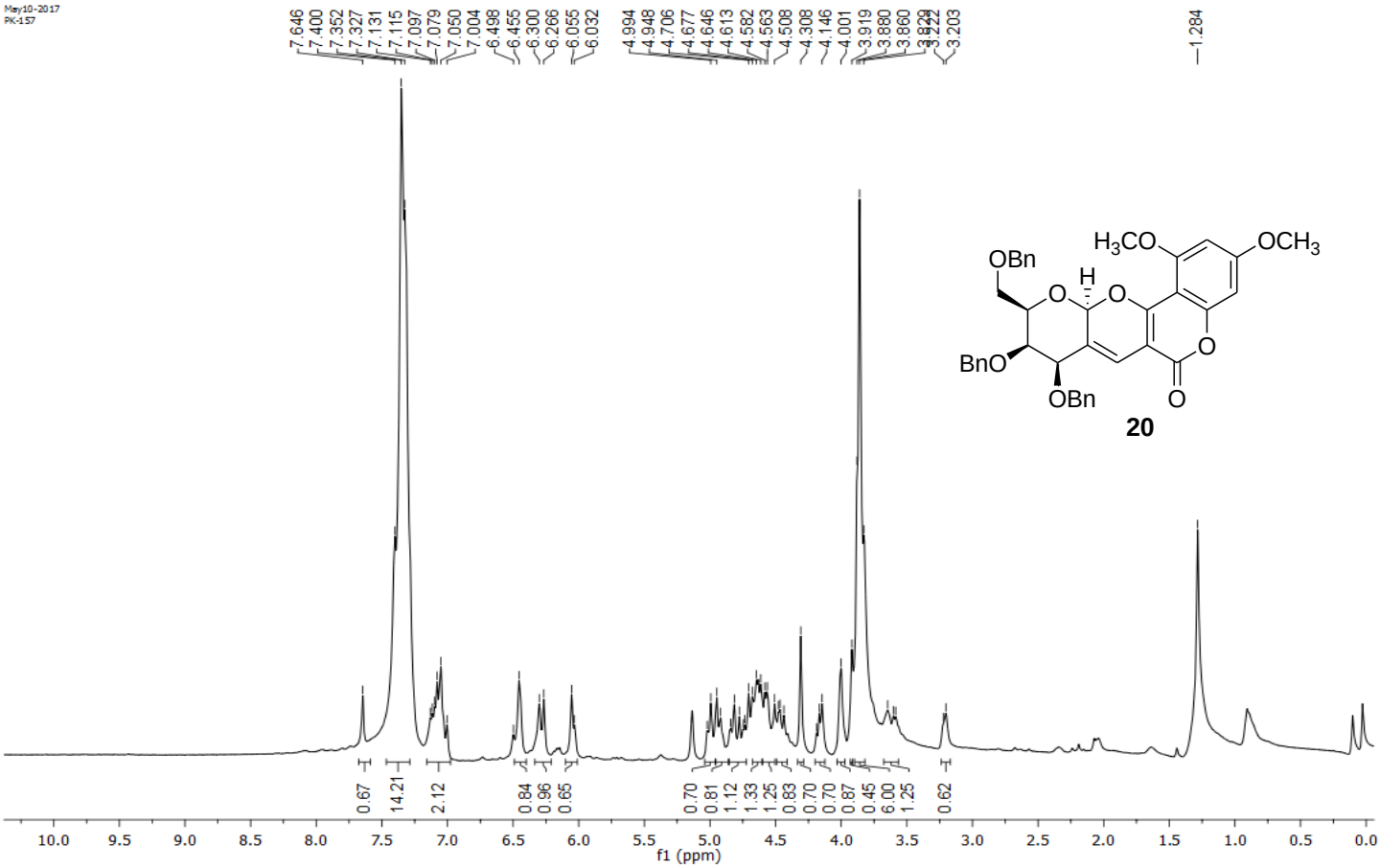
18


Apr20-2017
PK-154
159.073
154.516
137.996
137.552
137.333
132.060
128.676
128.565
128.476
128.283
128.083
128.017
127.932
127.819
127.655
127.453
126.985
126.945
97.166
96.965
79.285
77.357
77.039
76.722
76.470
75.338
74.515
73.656
71.820
68.561
65.380
f1 (ppm)



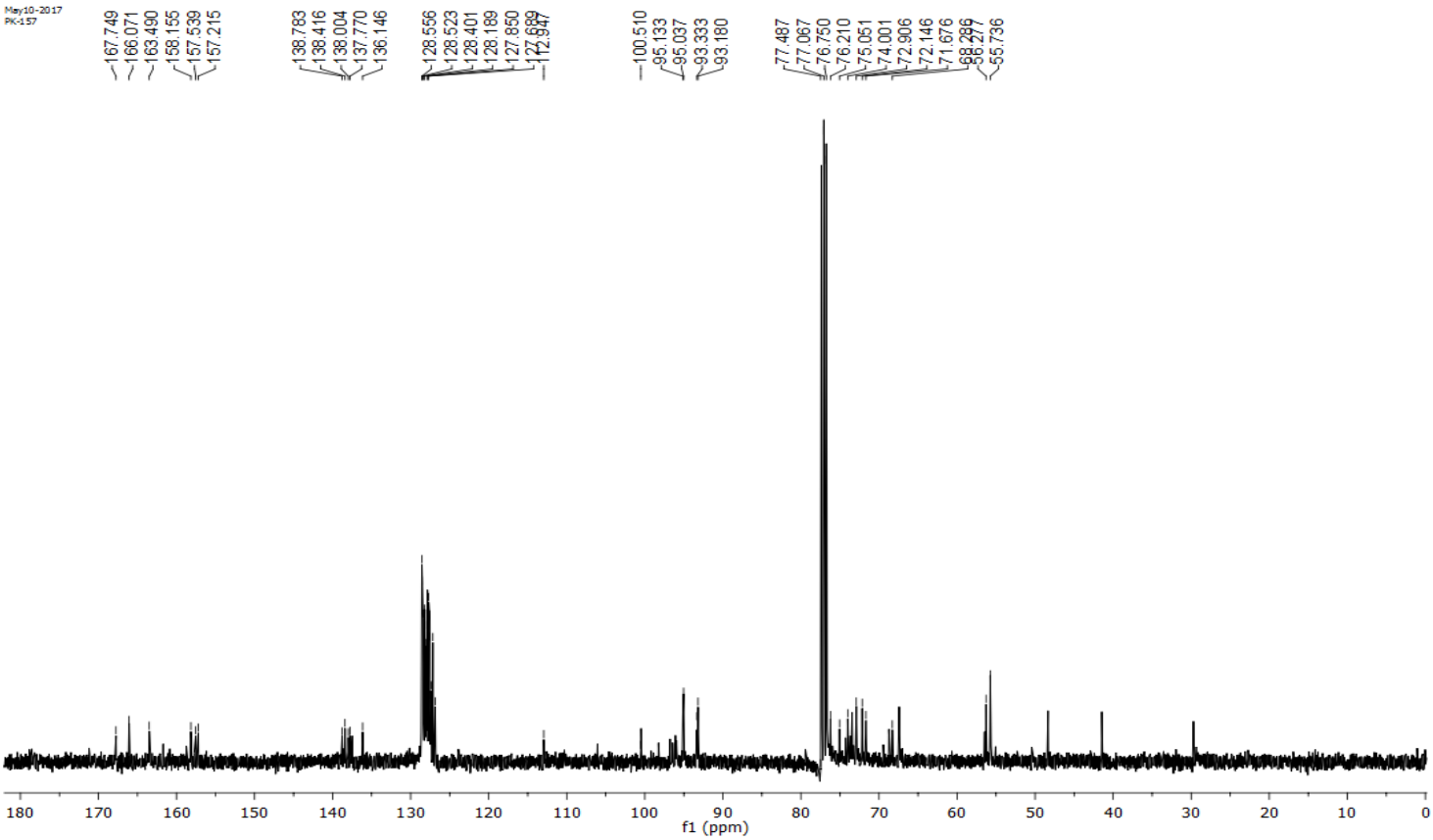
19

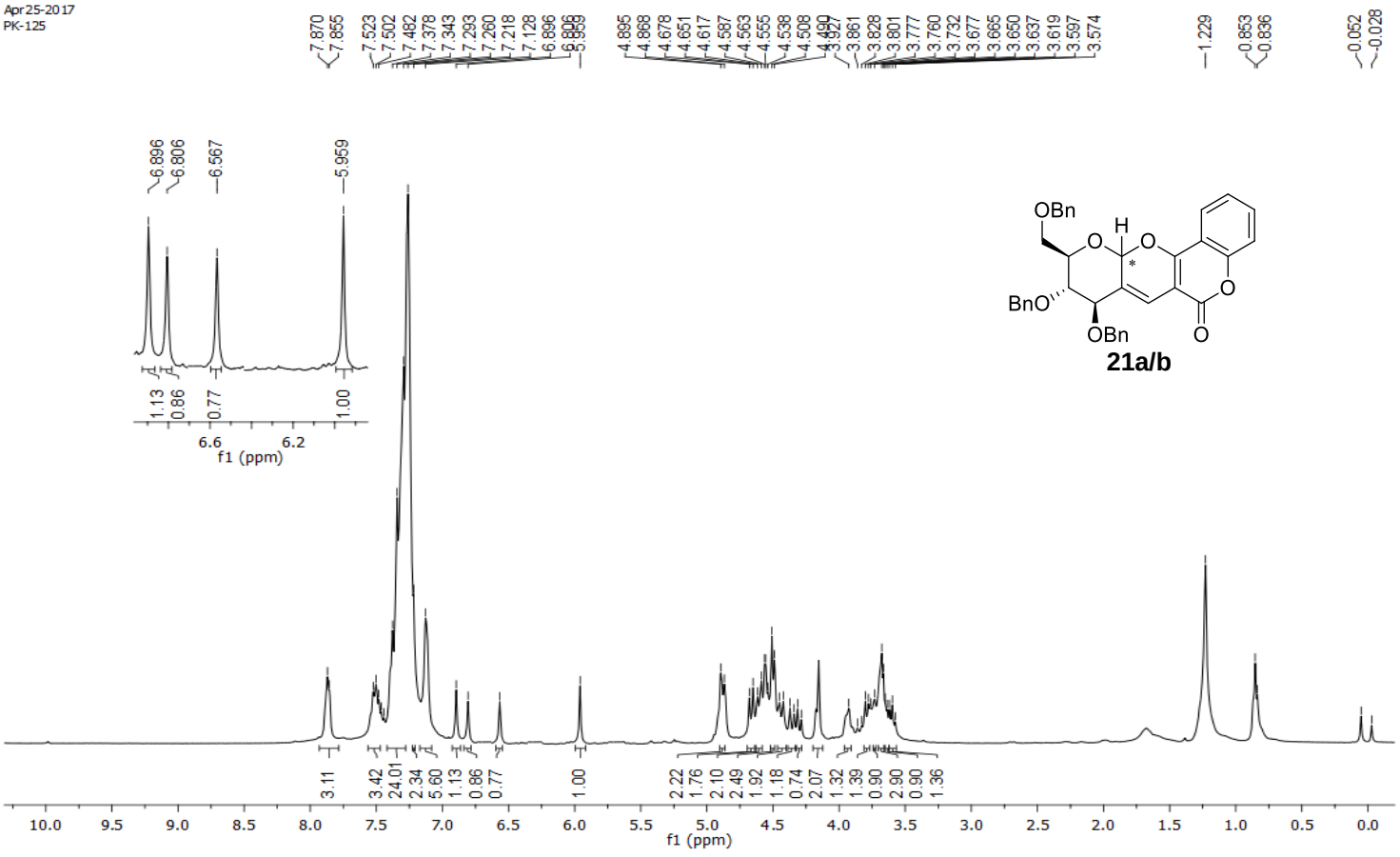


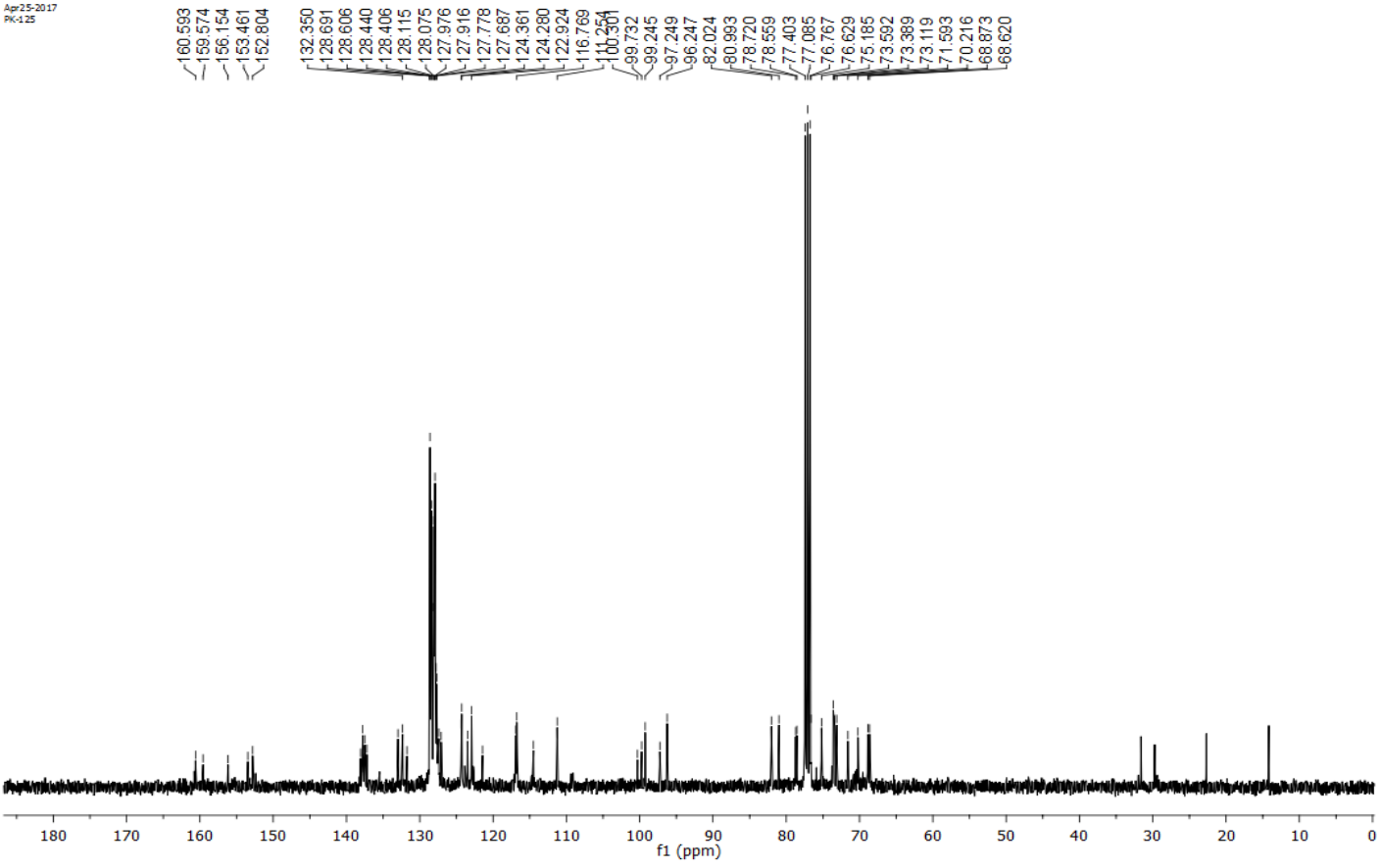

May10-2017
PK-157
7.646
7.400
7.352
7.327
7.131
7.115
7.097
7.079
7.050
7.004
6.498
6.455
6.300
6.266
6.055
6.032
4.994
4.948
4.706
4.677
4.646
4.613
4.582
4.563
4.508
4.308
4.146
4.001
3.919
3.880
3.860
3.829
3.822
3.203
1.284
0.67
14.21
2.12
0.84
0.96
0.65
0.70
0.81
1.12
1.33
1.25
0.83
0.70
0.70
0.87
0.45
6.00
1.25
0.62
f1 (ppm)

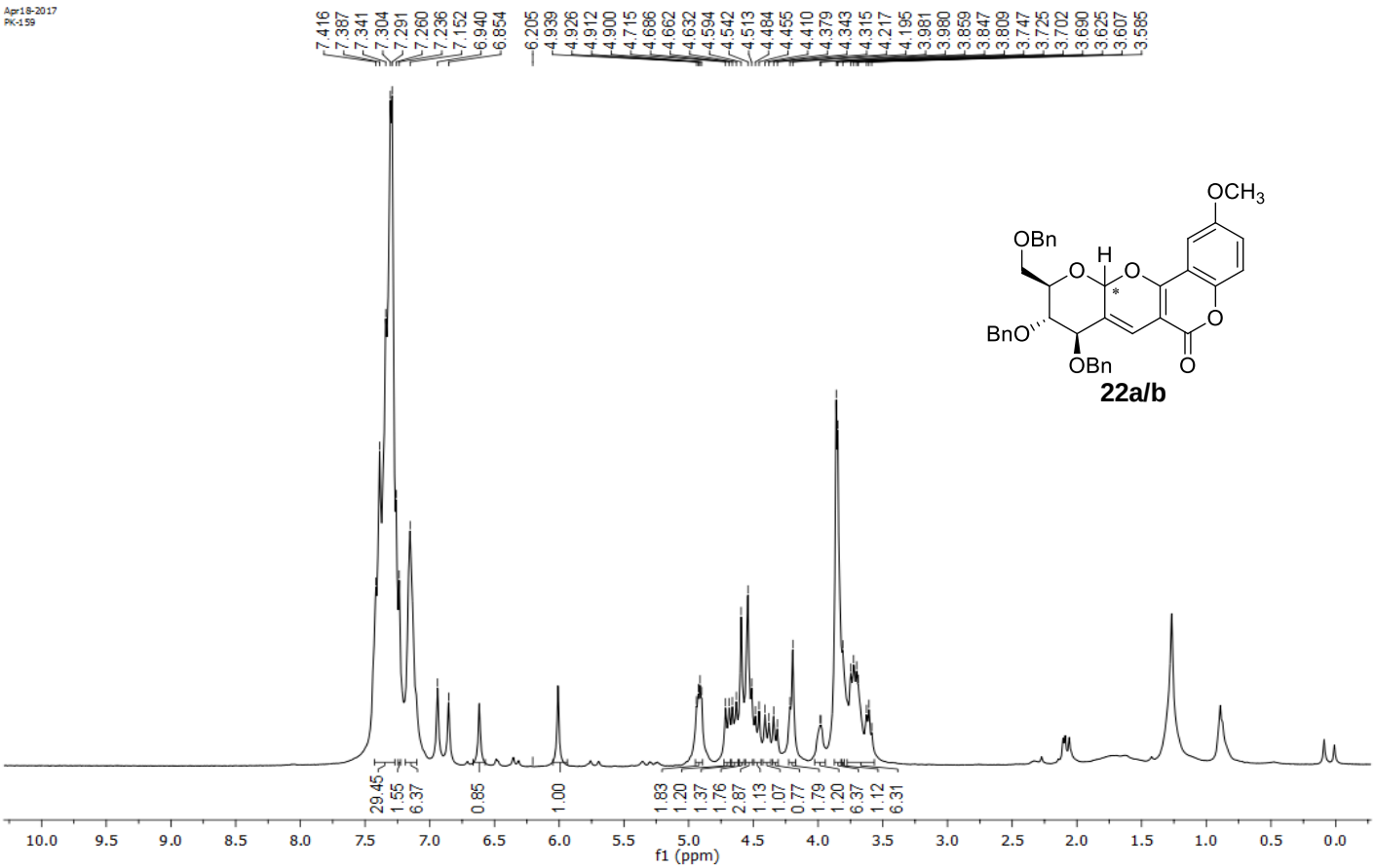
H3CO
OCH3
OBn
H
O
O
BnO
O
OBn
O

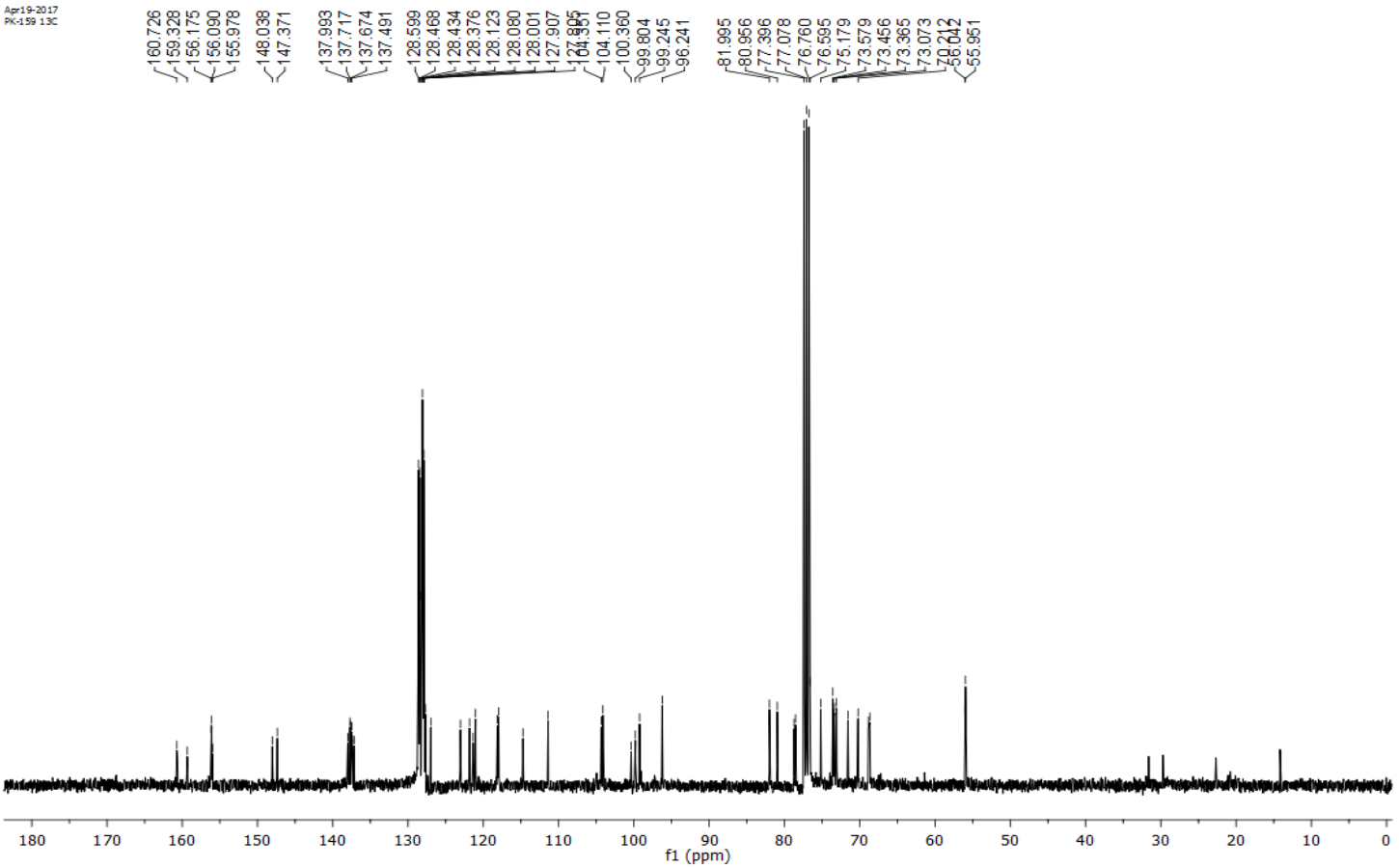
20

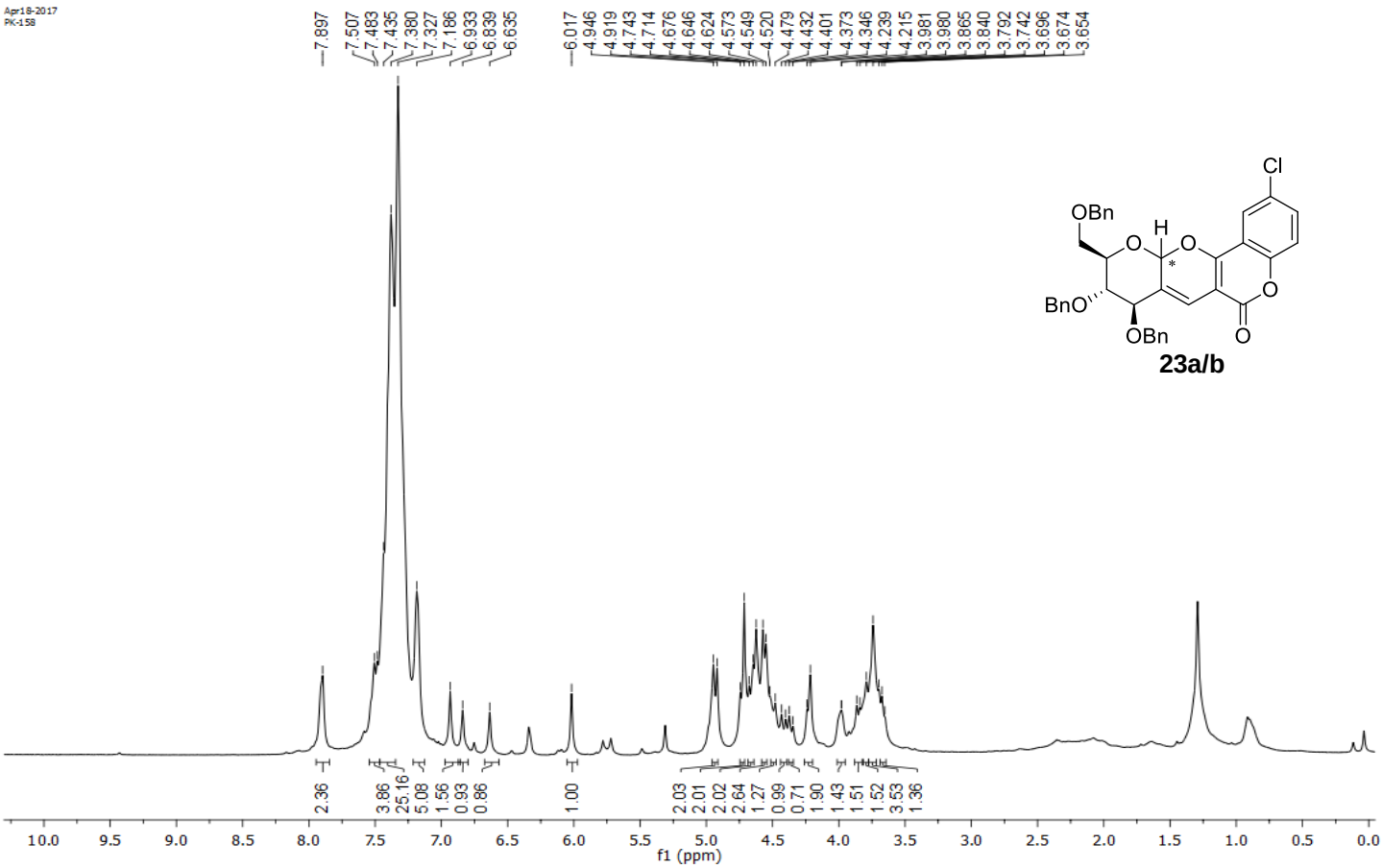

May10-2017
PK-157
167.749
166.071
163.490
158.155
157.539
157.215
138.783
138.416
138.004
137.770
136.146
128.556
128.523
128.401
128.189
127.850
100.510
95.133
95.037
93.333
93.180
77.487
77.067
76.750
76.210
75.051
74.001
72.906
72.146
71.676
68.277
55.736
f1 (ppm)


Apr 25-2017
PK-125
OBn
H
O
O
O
BnO
OBn
O
O
*
21a/b
f1 (ppm)


Apr 25-2017
PK-125
f1 (ppm)

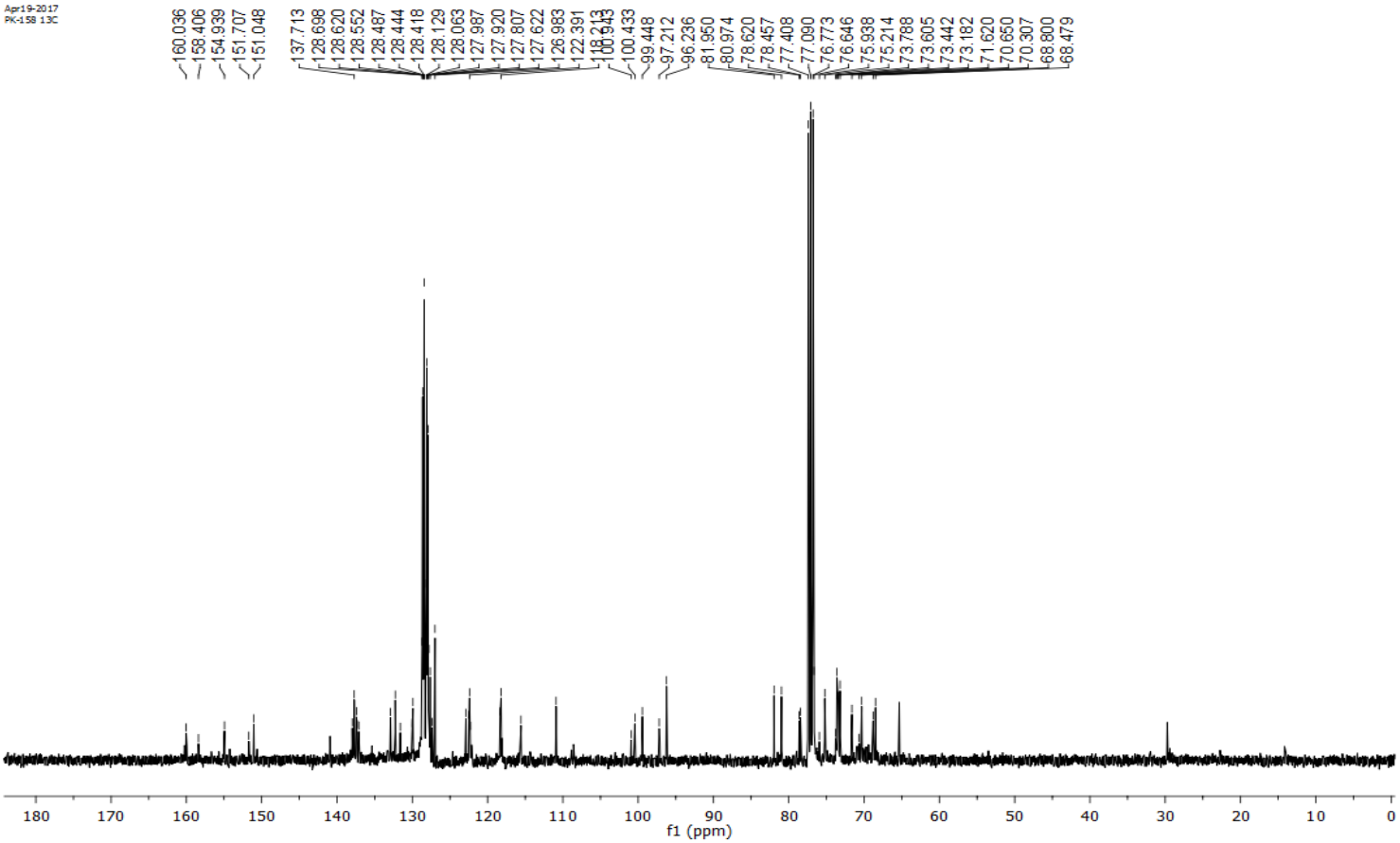

Apr18-2017
PK-159
7.416
7.387
7.341
7.304
7.291
7.260
7.236
7.152
6.940
6.854
6.205
4.939
4.926
4.912
4.900
4.715
4.686
4.662
4.632
4.594
4.542
4.513
4.484
4.455
4.410
4.379
4.343
4.315
4.217
4.195
3.981
3.980
3.859
3.847
3.809
3.747
3.725
3.702
3.690
3.625
3.607
3.585
OCH3
OBn
H
O
O
*
BnO
O
OBn
O
22a/b
29.45
1.55
6.37
0.85
1.00
1.83
1.20
1.37
1.76
2.87
1.13
1.07
0.77
1.79
1.20
6.37
1.12
6.31
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
f1 (ppm)

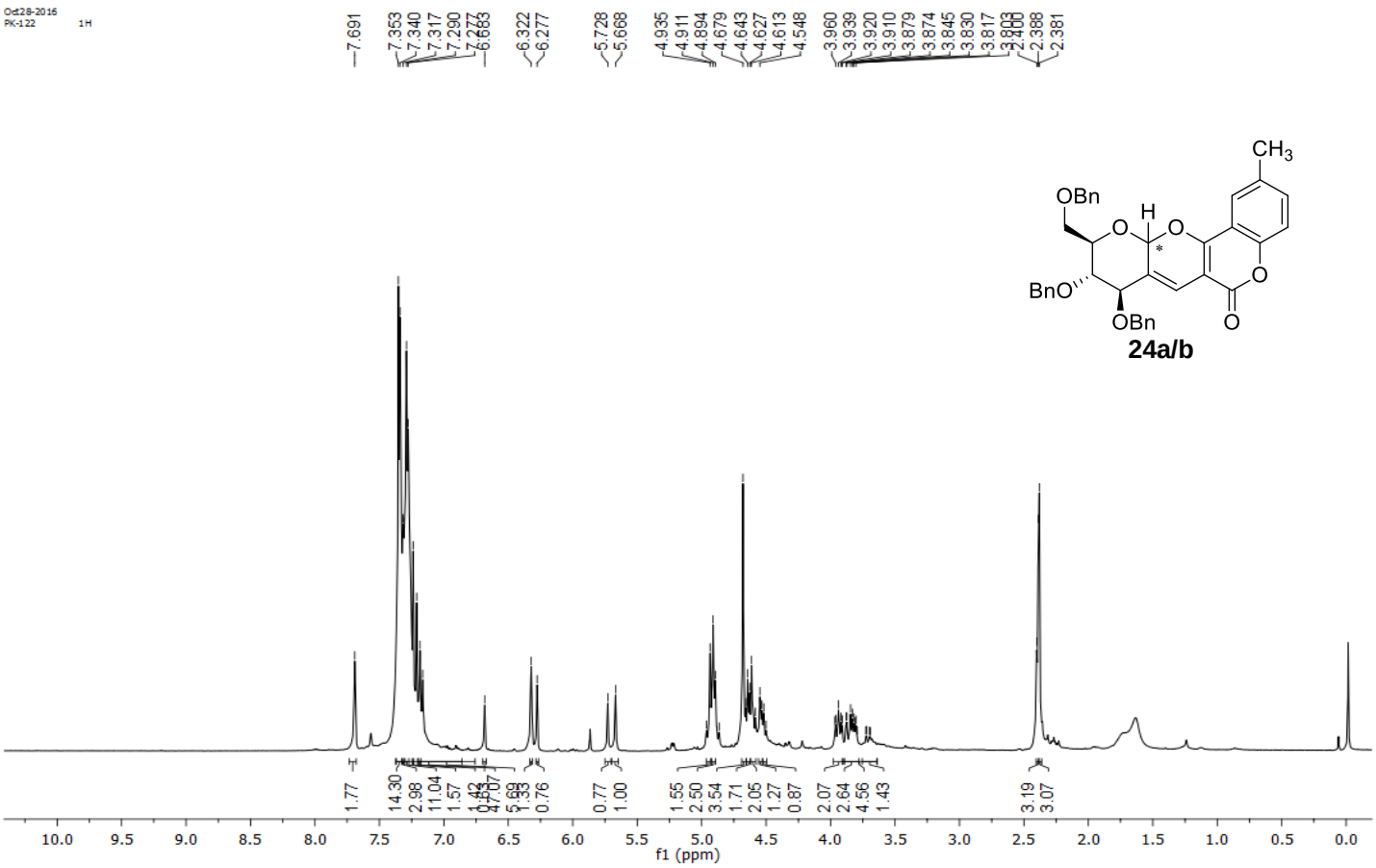

Apr19-2017
PK-159 13C
160.726
159.328
156.175
156.090
155.978
148.038
147.371
137.993
137.717
137.674
137.491
128.599
128.468
128.434
128.376
128.123
128.080
128.001
127.907
104.110
100.360
99.804
99.245
96.241
81.995
80.956
77.396
77.078
76.760
76.595
75.179
73.579
73.456
73.365
73.073
70.212
56.042
55.951
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Apr18-2017
PK-158
7.897
7.507
7.483
7.436
7.380
7.327
7.186
6.933
6.839
6.635
6.017
4.946
4.919
4.743
4.714
4.676
4.646
4.624
4.573
4.549
4.520
4.479
4.432
4.401
4.373
4.346
4.239
4.215
3.981
3.980
3.865
3.840
3.792
3.742
3.696
3.674
3.654
2.36
3.86
25.16
5.08
1.56
0.93
0.86
1.00
2.03
2.01
2.02
2.64
1.27
0.99
0.71
1.90
1.43
1.51
1.52
3.53
1.36
f1 (ppm)

Cl
OBn
H
O
O
*
O
BnO
OBn
O

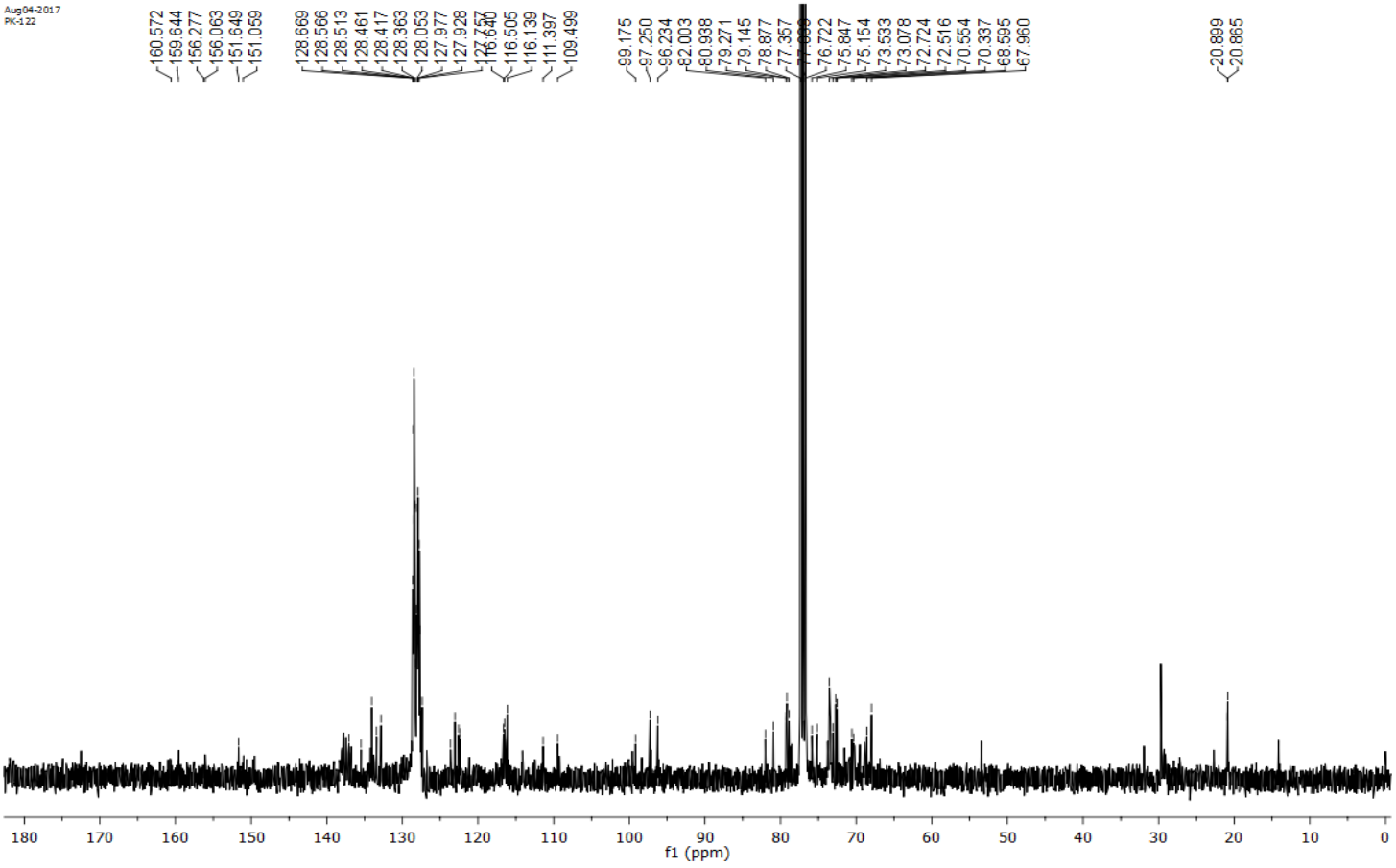
23a/b

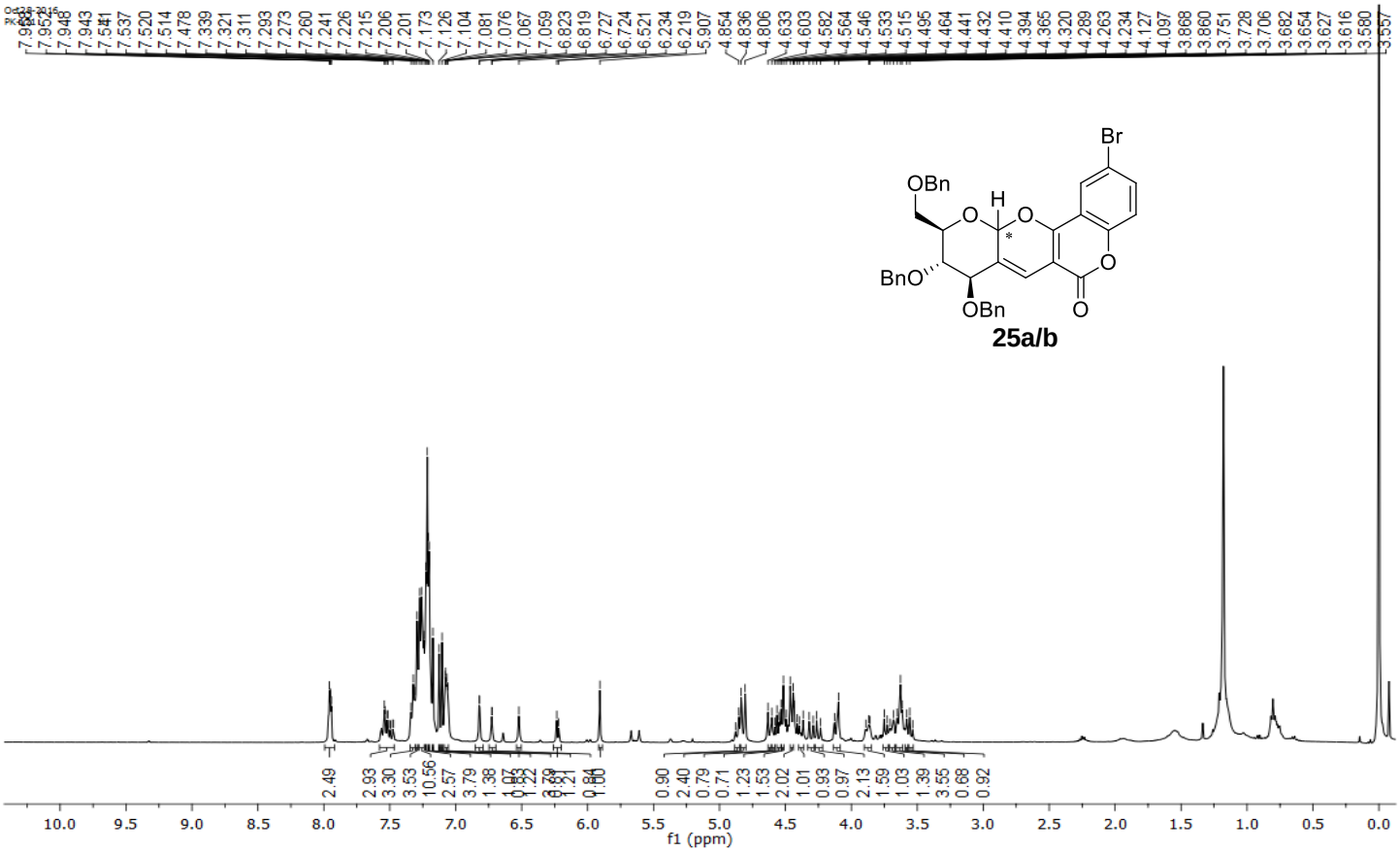

Apr19-2017
PK-158 13C
160.036
158.406
154.939
151.707
151.048
137.713
128.698
128.620
128.552
128.487
128.444
128.418
128.129
128.063
127.987
127.920
127.807
127.622
126.983
122.391
118.213
100.943
100.433
99.448
97.212
96.236
81.950
80.974
78.620
78.457
77.408
77.090
76.773
76.646
75.938
75.214
73.788
73.605
73.442
73.182
71.620
70.650
70.307
68.800
68.479
f1 (ppm)


Oct28-2016
PK-122 1H
7.691
7.353
7.340
7.317
7.290
7.277
6.683
6.322
6.277
5.728
5.668
4.935
4.911
4.894
4.679
4.643
4.627
4.613
4.548
3.960
3.939
3.920
3.910
3.879
3.874
3.845
3.830
3.817
3.803
2.400
2.388
2.381
1.77
14.30
2.98
11.04
1.57
1.43
0.83
4.07
5.69
1.33
0.76
0.77
1.00
1.55
2.50
3.54
1.71
2.05
1.27
0.87
2.07
2.64
4.56
1.43
3.19
3.07
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
f1 (ppm)

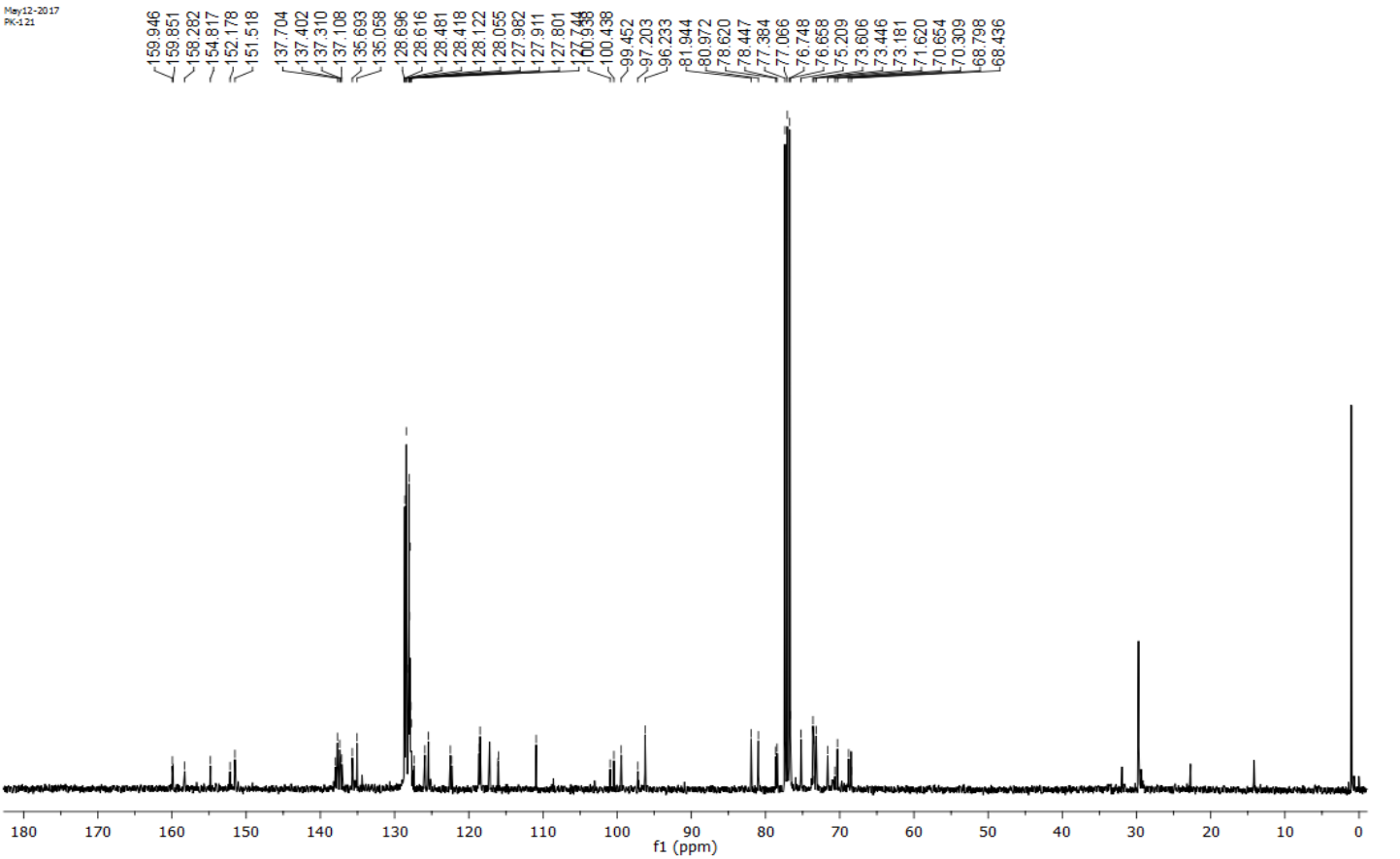
CH3
OBn
H
O
O
*
O
BnO
OBn
O

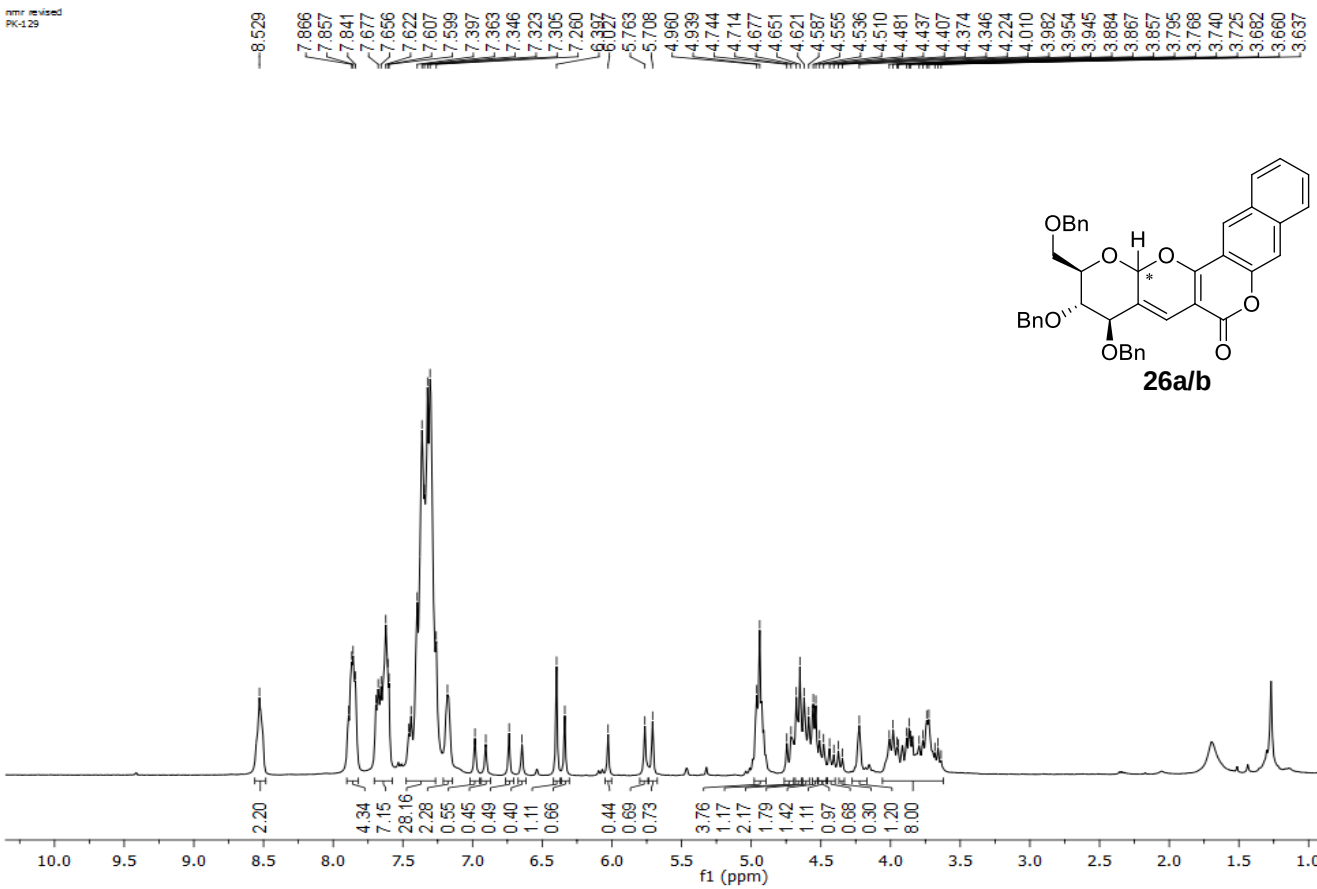
24a/b

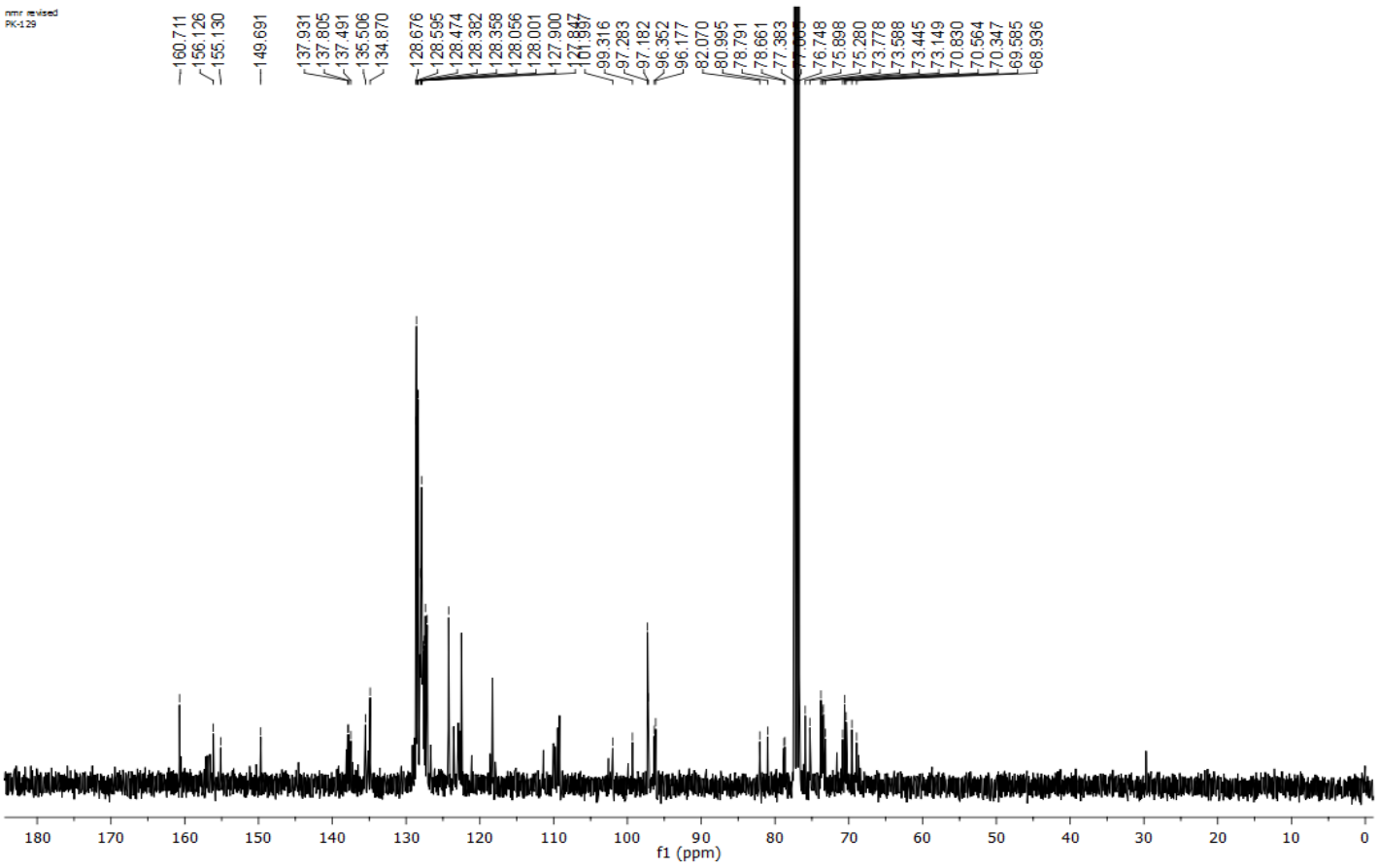

Aug04-2017
PK-122
160.572
159.644
156.277
156.063
151.649
151.059
128.669
128.566
128.513
128.461
128.417
128.363
128.053
127.977
127.928
127.757
116.640
116.505
116.139
111.397
109.499
99.175
97.250
96.234
82.003
80.938
79.271
79.145
78.877
77.357
76.722
75.847
75.154
73.533
73.078
72.724
72.516
70.554
70.337
68.595
67.960
20.899
20.865
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

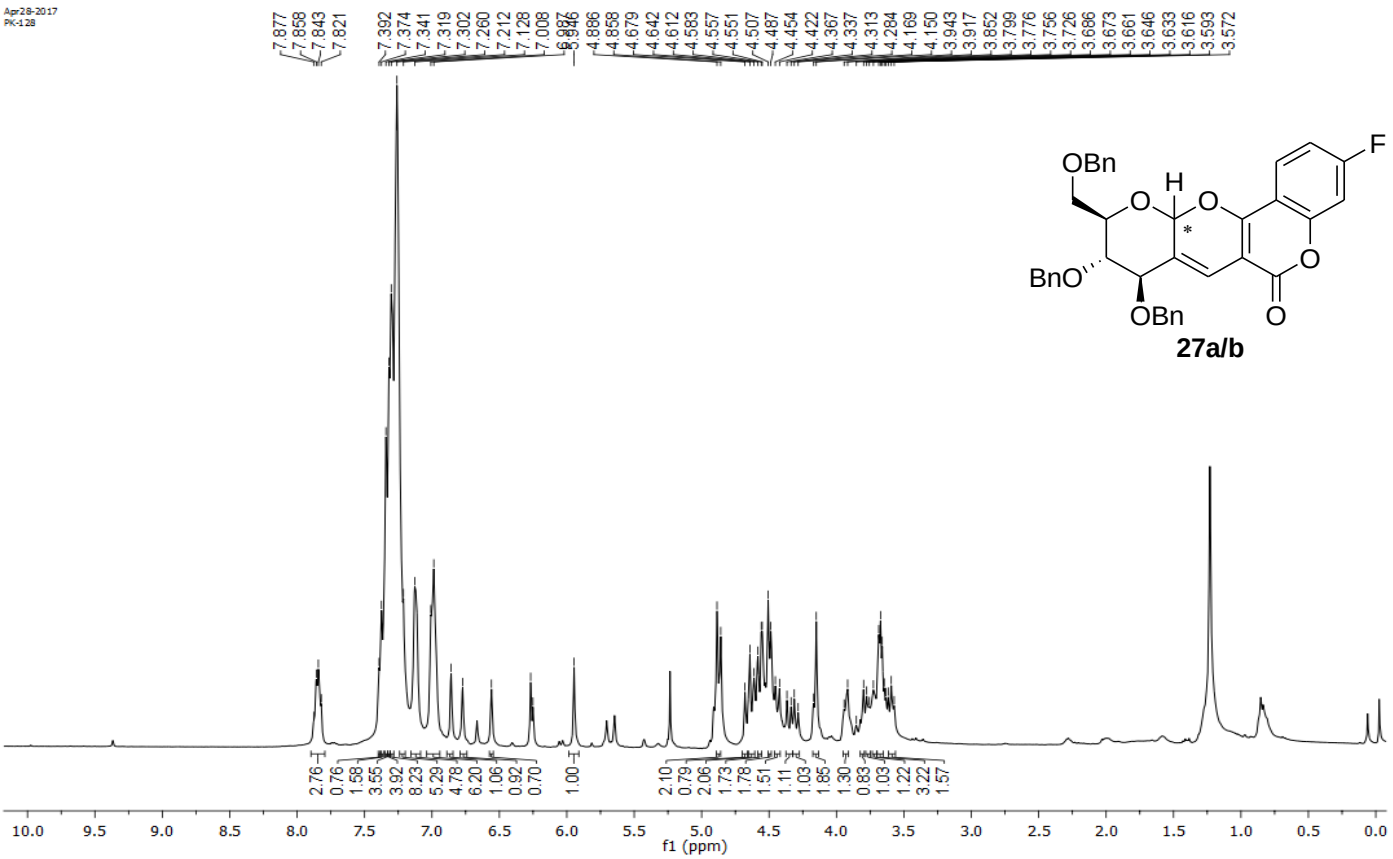


25a/b



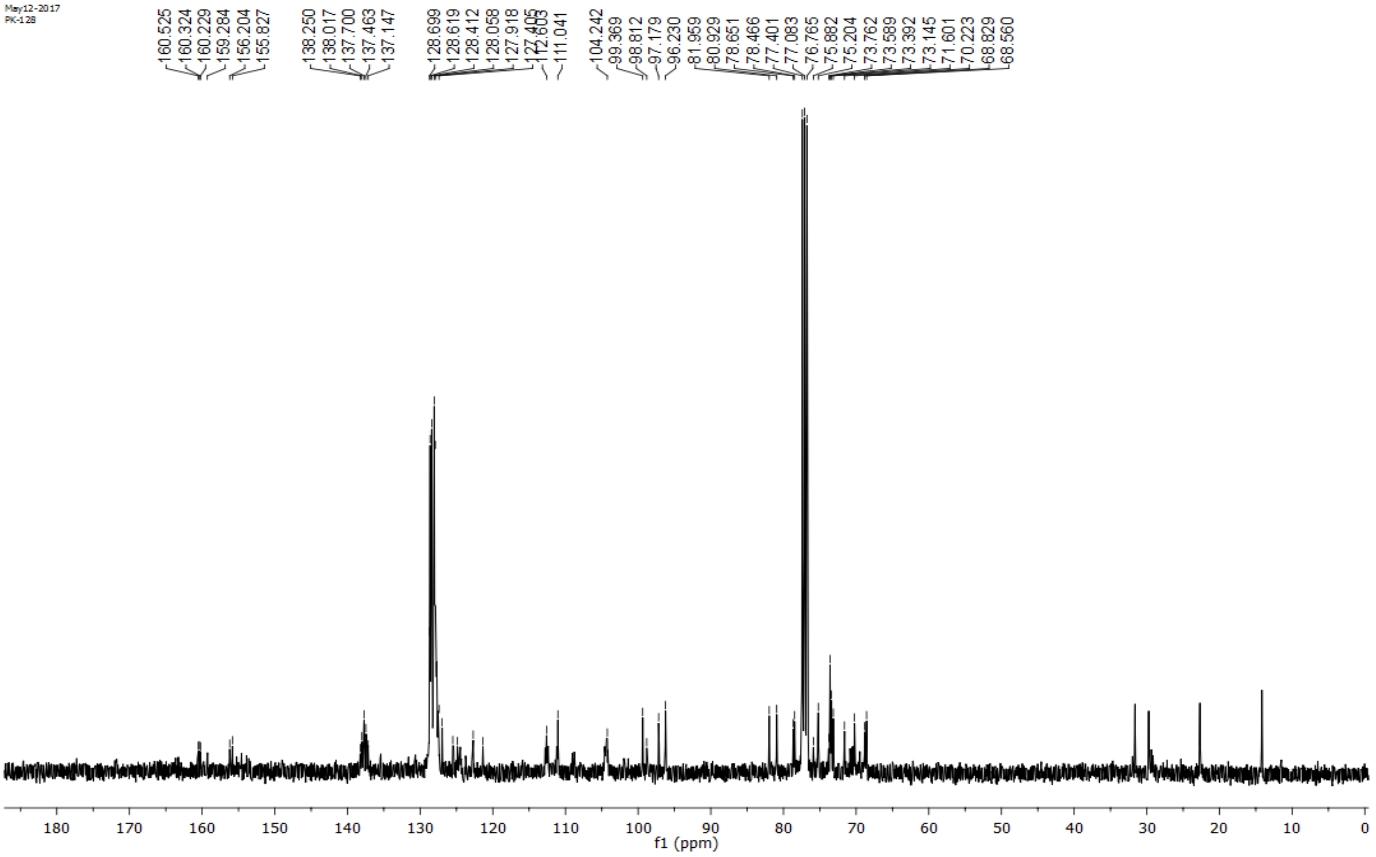

nmr revised
PK-129
OBn
H
O
O
*
O
BnO
OBn
O
26a/b
f1 (ppm)

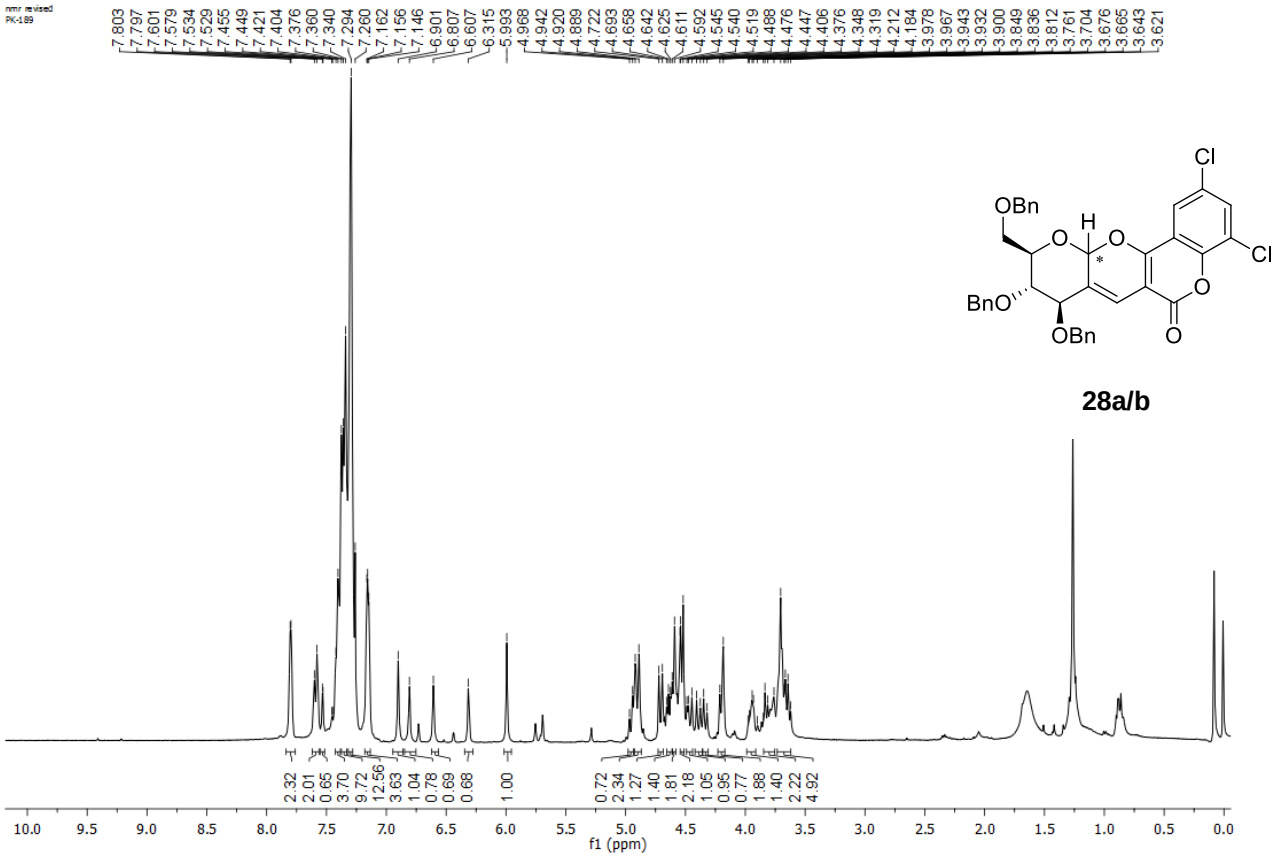

nmr revised
PK-129
f1 (ppm)


Apr28-2017
PK-128
7.877
7.858
7.843
7.821
7.392
7.374
7.341
7.319
7.302
7.260
7.212
7.128
7.008
6.887
4.886
4.858
4.679
4.642
4.612
4.583
4.557
4.551
4.507
4.487
4.454
4.422
4.367
4.337
4.313
4.284
4.169
4.150
3.943
3.917
3.852
3.799
3.776
3.756
3.726
3.686
3.673
3.661
3.646
3.633
3.616
3.593
3.572
2.76
0.76
1.58
3.55
3.92
8.23
5.29
4.78
6.20
1.06
0.92
0.70
1.00
2.10
0.79
2.06
1.73
1.78
1.51
1.11
1.03
1.85
1.30
0.83
1.03
1.22
3.22
1.57
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
f1 (ppm)

OBn
H
O
O
F
*
BnO
OBn
O
O

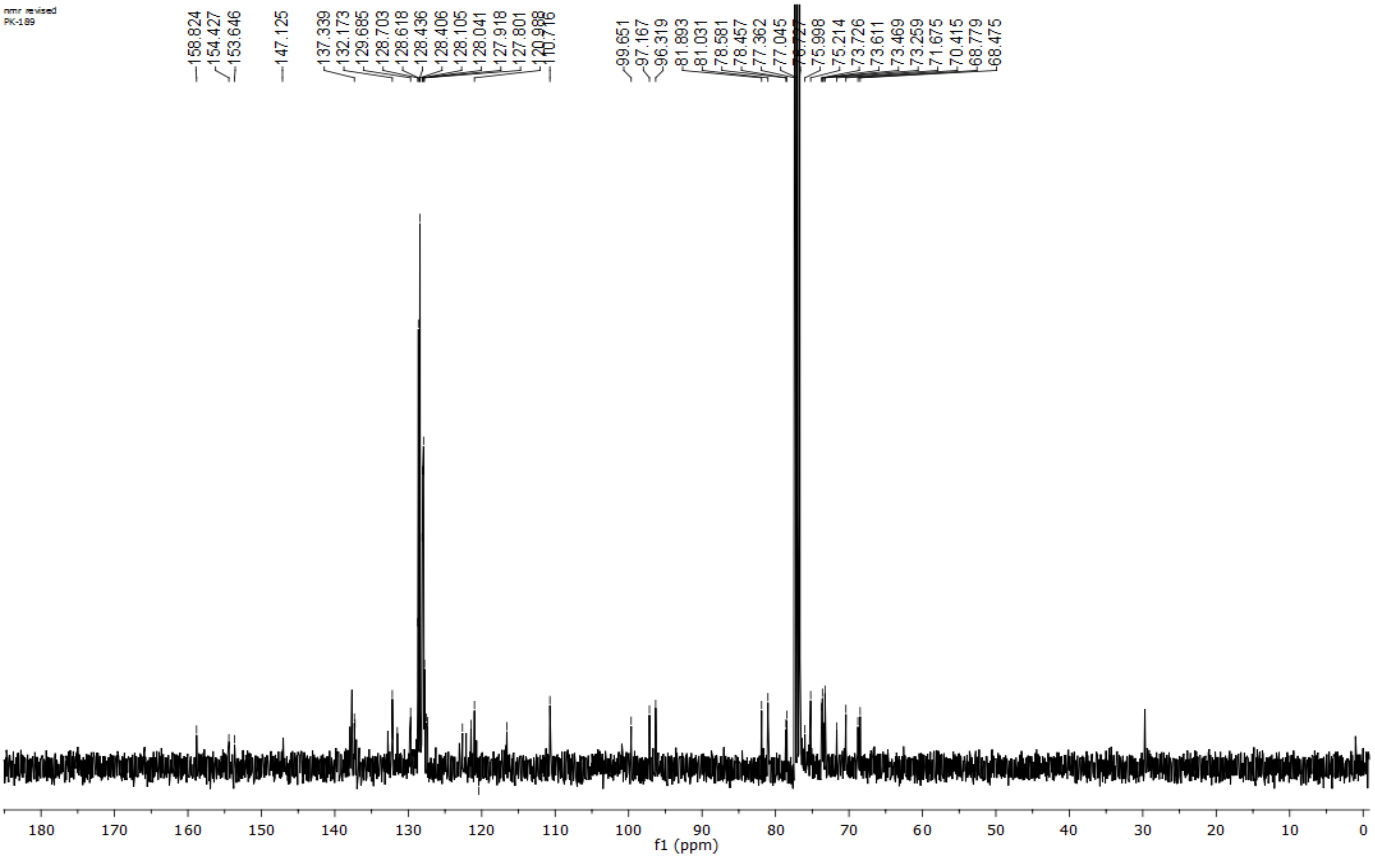
27a/b

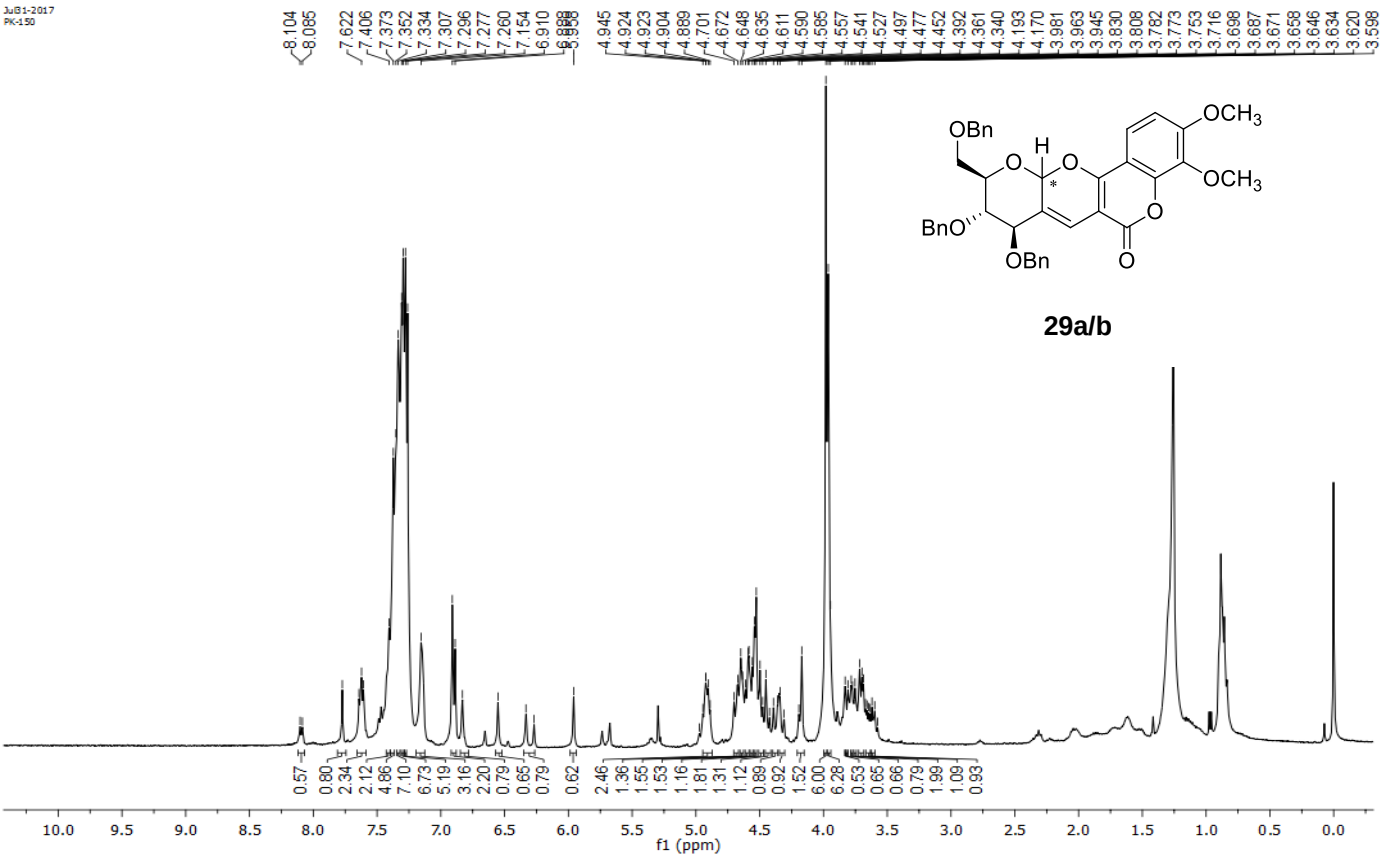

May12-2017
PK-128
160.525
160.324
160.229
159.284
156.204
155.827
138.250
138.017
137.700
137.463
137.147
128.699
128.619
128.412
128.058
127.918
127.405
127.083
112.603
111.041
104.242
99.369
98.812
97.179
96.230
81.959
80.929
78.651
78.466
77.401
77.083
76.765
75.882
75.204
73.762
73.589
73.392
73.145
71.601
70.223
68.829
68.560
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


nmr revised
PK-189
7.803
7.797
7.601
7.579
7.534
7.529
7.455
7.449
7.421
7.404
7.376
7.360
7.340
7.294
7.260
7.162
7.156
7.146
6.901
6.807
6.607
6.315
5.993
4.968
4.942
4.920
4.889
4.722
4.693
4.658
4.642
4.625
4.611
4.592
4.545
4.540
4.519
4.488
4.476
4.447
4.406
4.376
4.348
4.319
4.212
4.184
3.978
3.967
3.943
3.932
3.900
3.849
3.836
3.812
3.761
3.704
3.676
3.665
3.643
3.621
2.32
2.01
0.65
3.70
9.72
12.56
3.63
1.04
0.78
0.69
0.68
1.00
0.72
2.34
1.27
1.40
1.81
2.18
1.05
0.95
0.77
1.88
1.40
2.22
4.92
f1 (ppm)

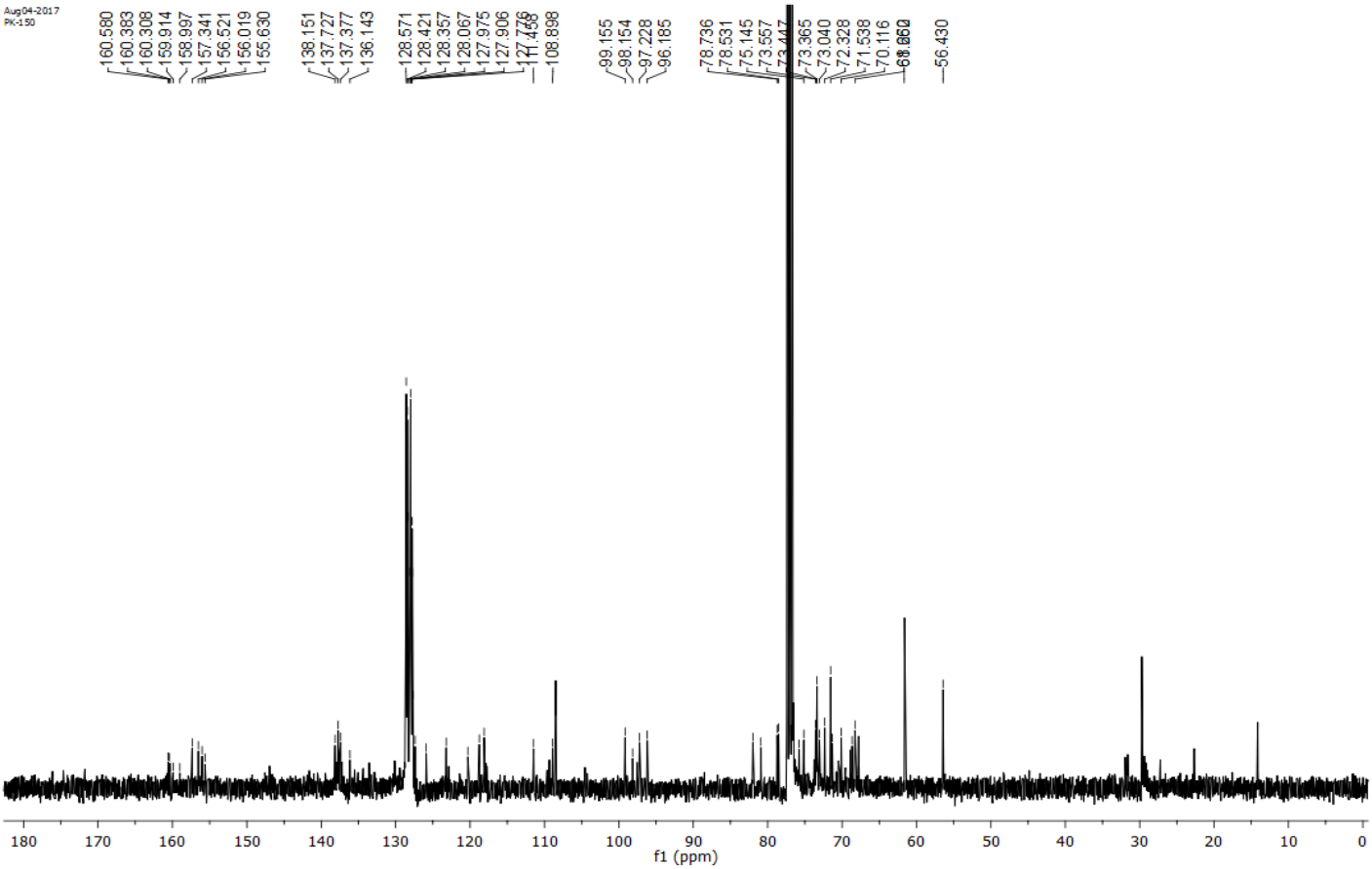
Cl
OBn
H
O
O
Cl
*
BnO
O
OBn
O

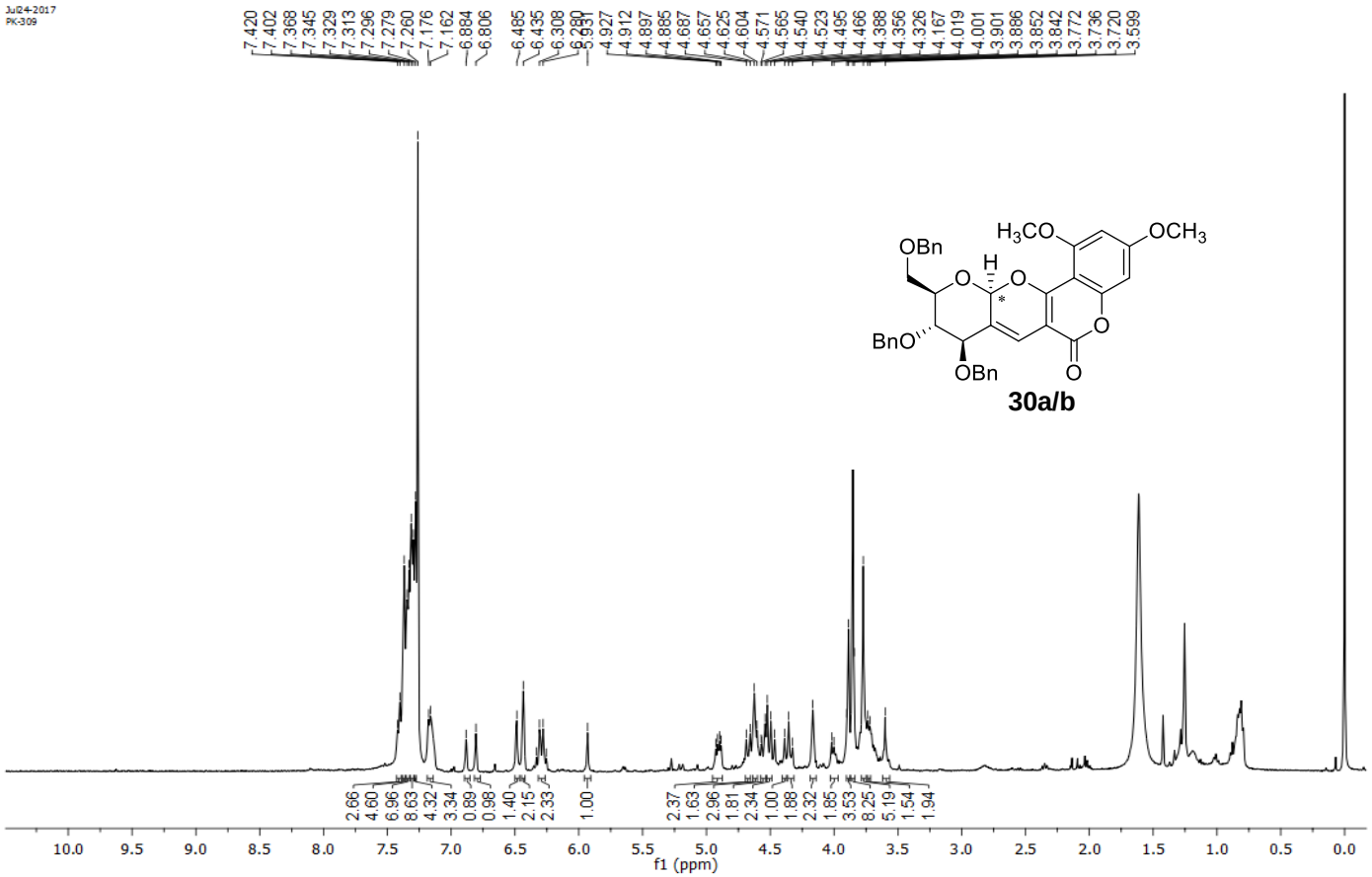
28a/b

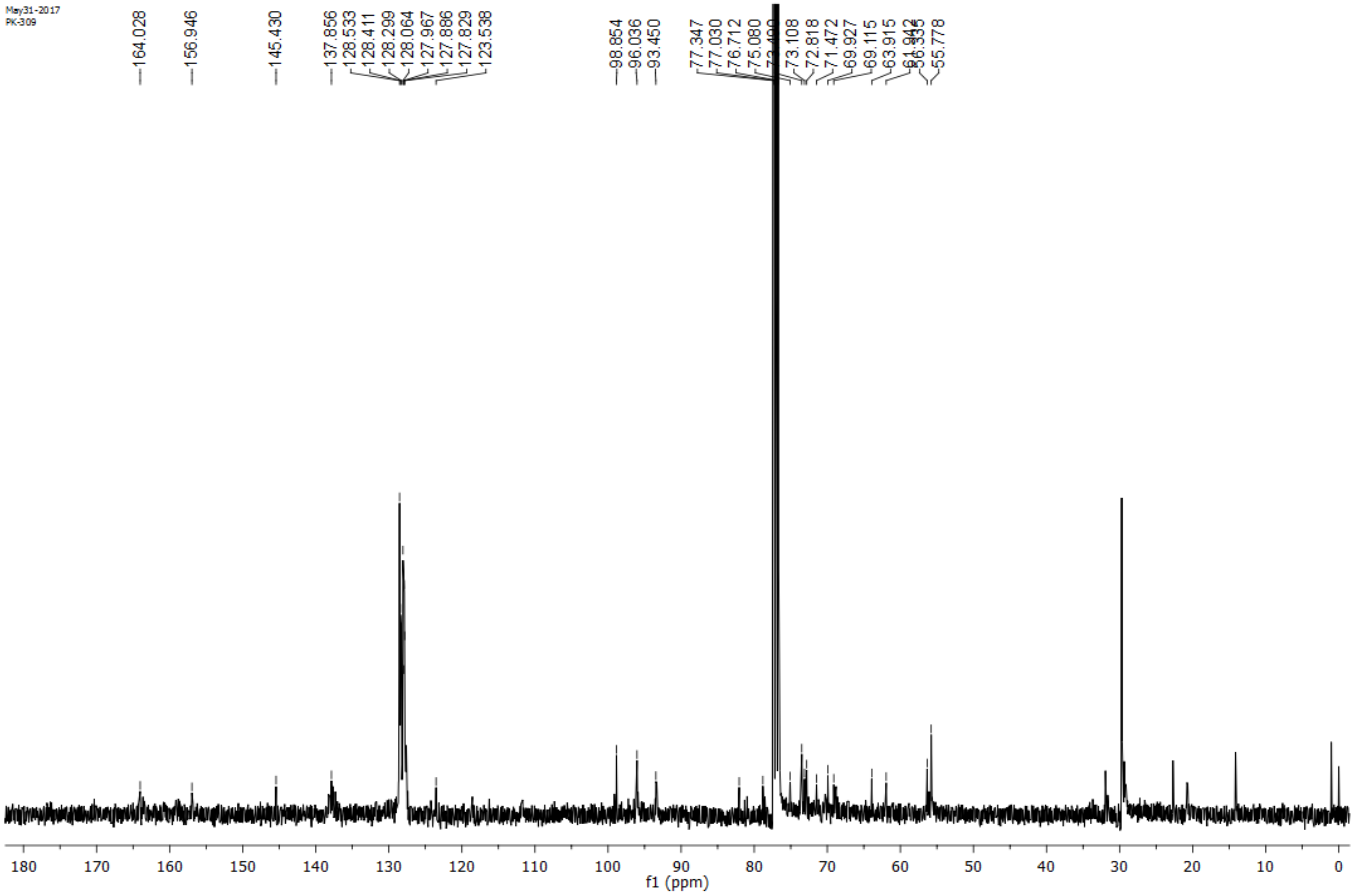

nmr revised
PK-189
158.824
154.427
153.646
147.125
137.339
132.173
129.685
128.703
128.618
128.436
128.406
128.105
128.041
127.918
127.801
110.776
99.651
97.167
96.319
81.893
81.031
78.581
78.457
77.362
77.045
75.998
75.214
73.726
73.611
73.469
73.259
71.675
70.415
68.779
68.475
f1 (ppm)


JuB1-2017
PK-150
OBn
H
O
O
OCH3
OCH3
BnO
O
OBn
O
*
f1 (ppm)

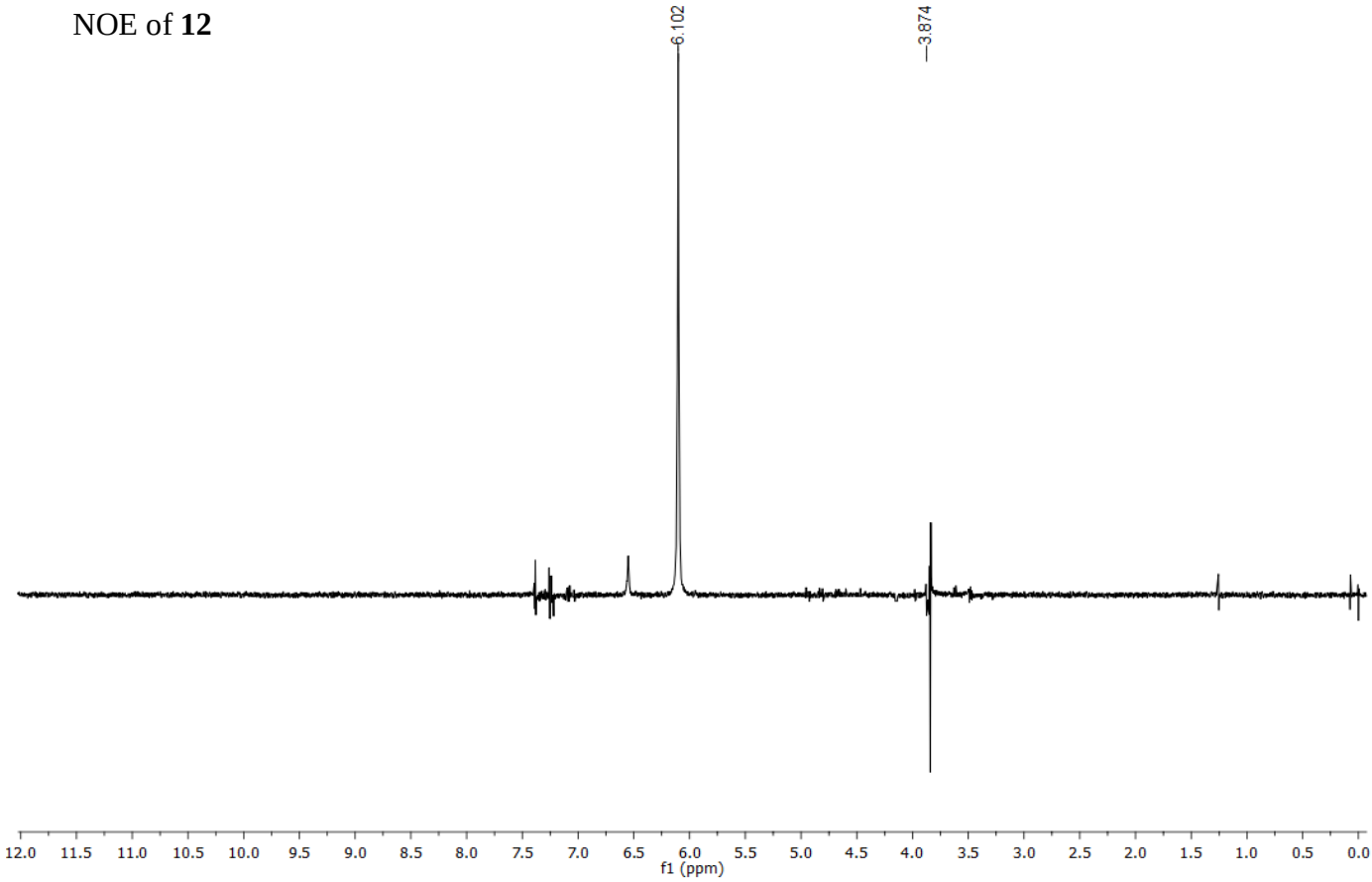
29a/b


Aug04-2017
PK-150
f1 (ppm)

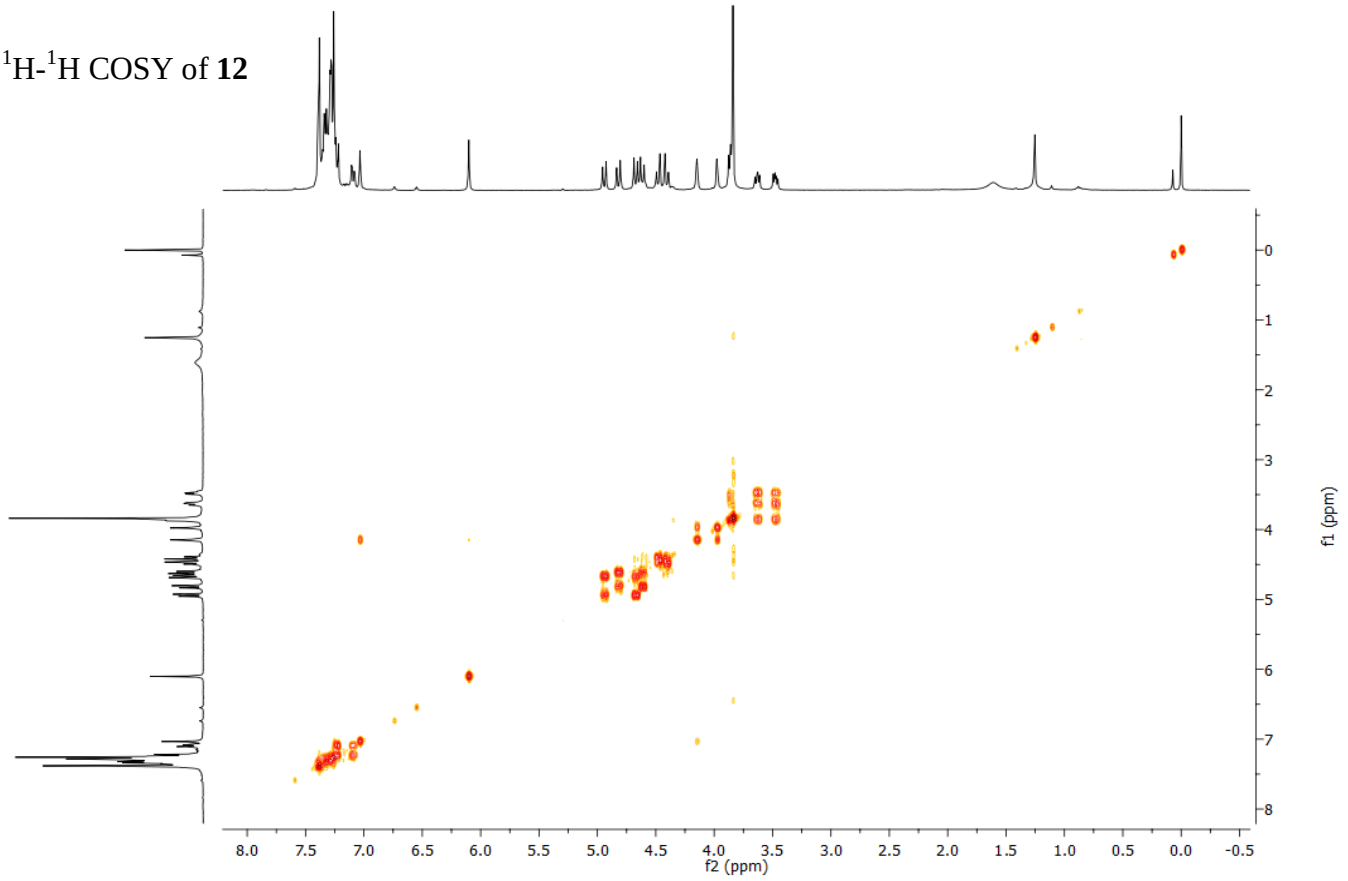

Jul24-2017
PK-309
7.420
7.402
7.368
7.345
7.329
7.313
7.296
7.279
7.260
7.176
7.162
6.884
6.806
6.485
6.435
6.308
6.280
5.931
4.927
4.912
4.897
4.885
4.687
4.657
4.625
4.604
4.571
4.565
4.540
4.523
4.495
4.466
4.388
4.356
4.326
4.167
4.019
4.001
3.901
3.886
3.852
3.842
3.772
3.736
3.720
3.599
OBn
H
O
O
H3CO
OCH3
BnO
OBn
O
O
*
30a/b
2.66
4.60
6.96
8.63
4.32
3.34
0.89
0.98
1.40
2.15
2.33
1.00
2.37
1.63
2.96
1.81
2.34
1.00
1.88
2.32
1.85
3.53
8.25
5.19
1.54
1.94
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
f1 (ppm)


May31-2017
PK-309
164.028
156.946
145.430
137.856
128.533
128.411
128.299
128.064
127.967
127.886
127.829
123.538
98.854
96.036
93.450
77.347
77.030
76.712
75.080
73.108
72.818
71.472
69.927
69.115
63.915
61.942
56.335
55.778
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

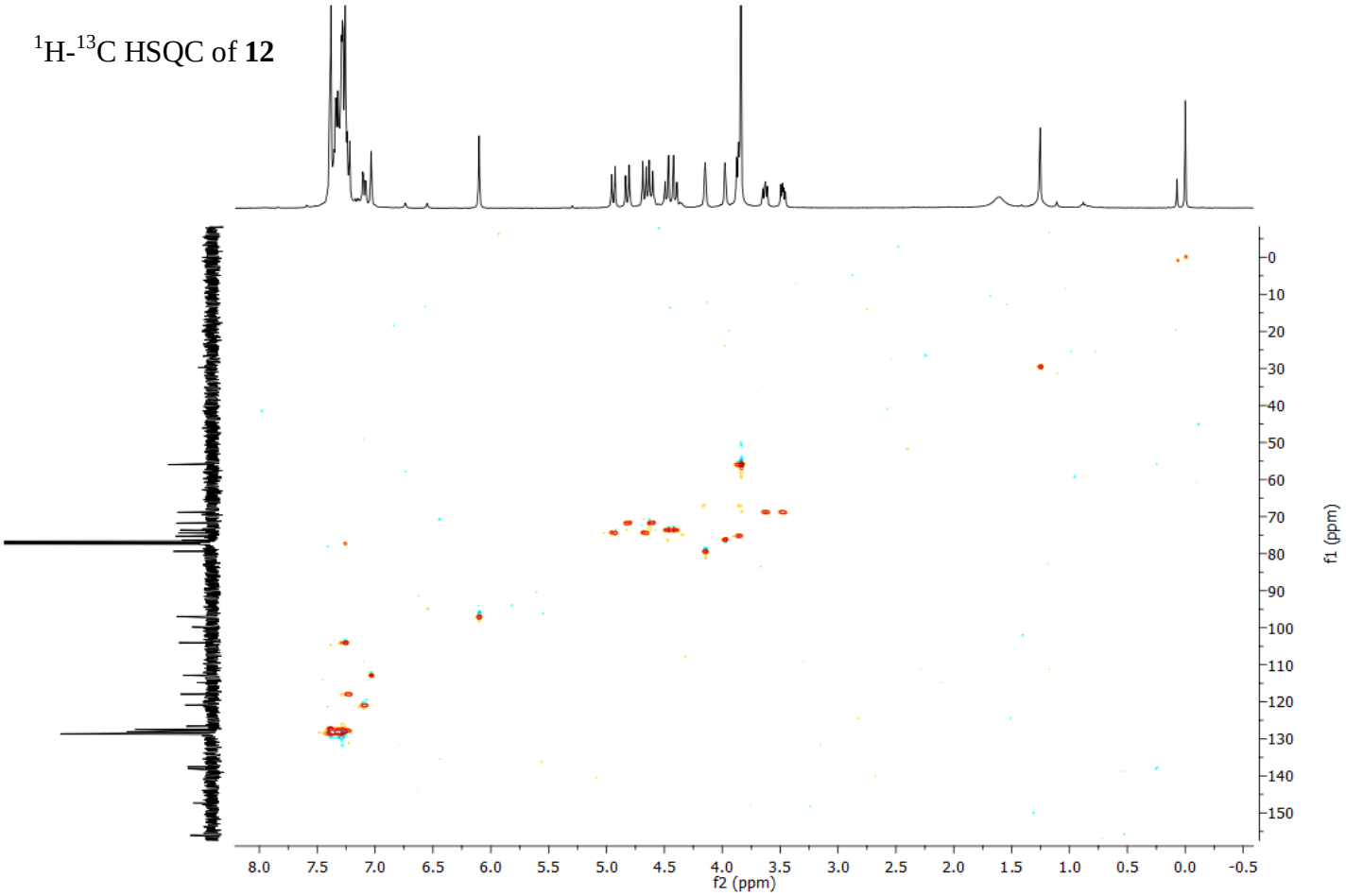
NOE of **12**

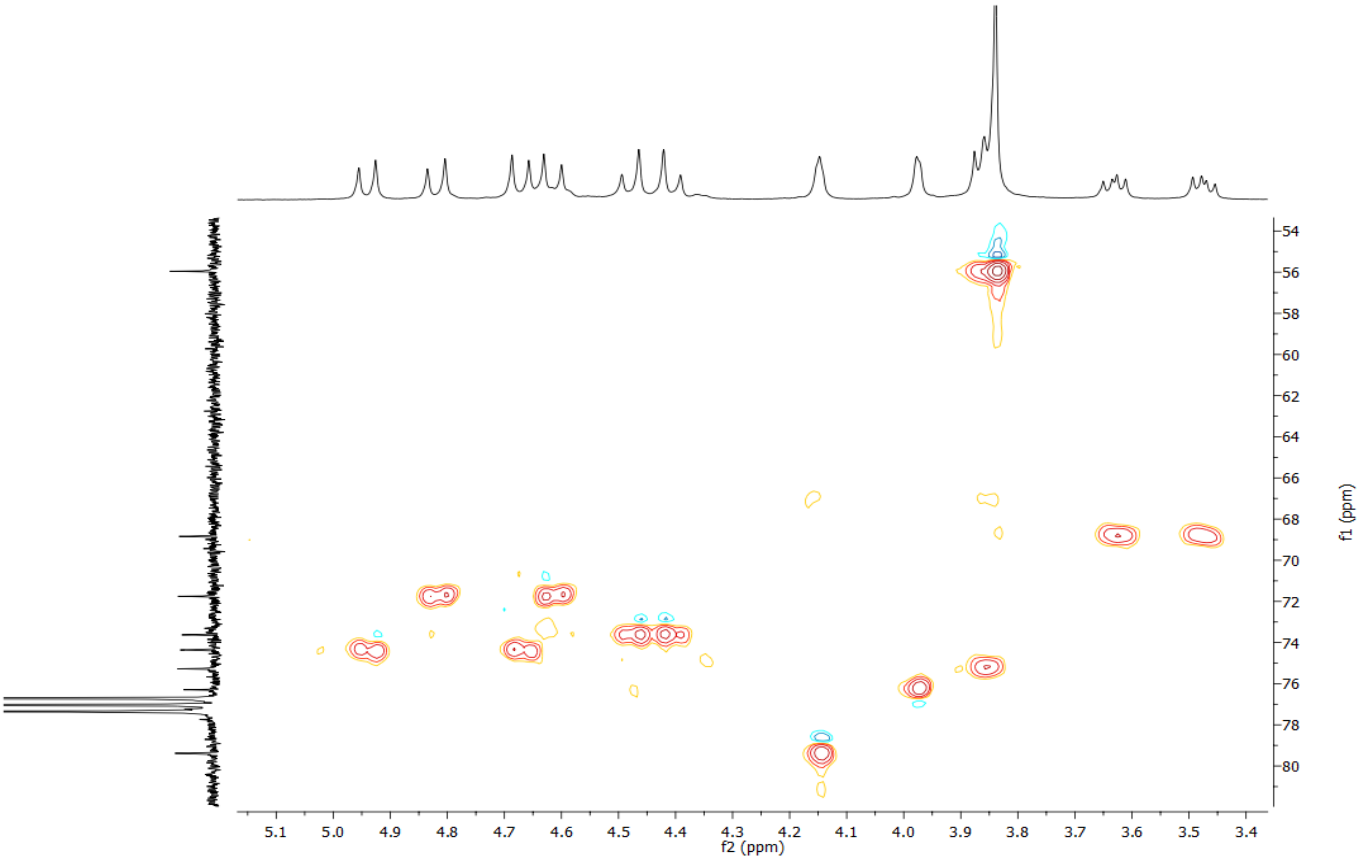


^{1}H-^{1}H COSY of **12**

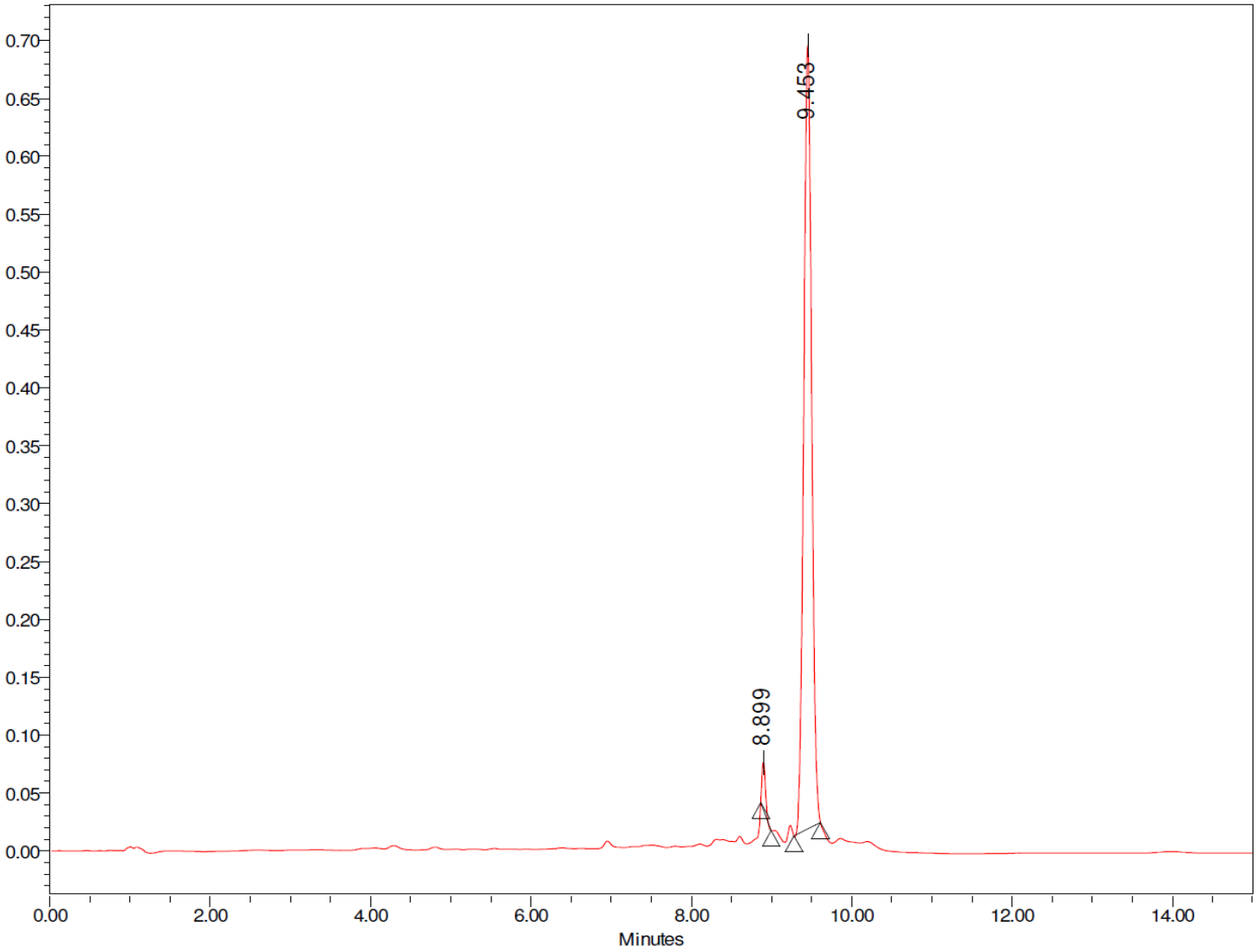


^{1}H-^{13}C HSQC of **12**





HPLC data of **12**

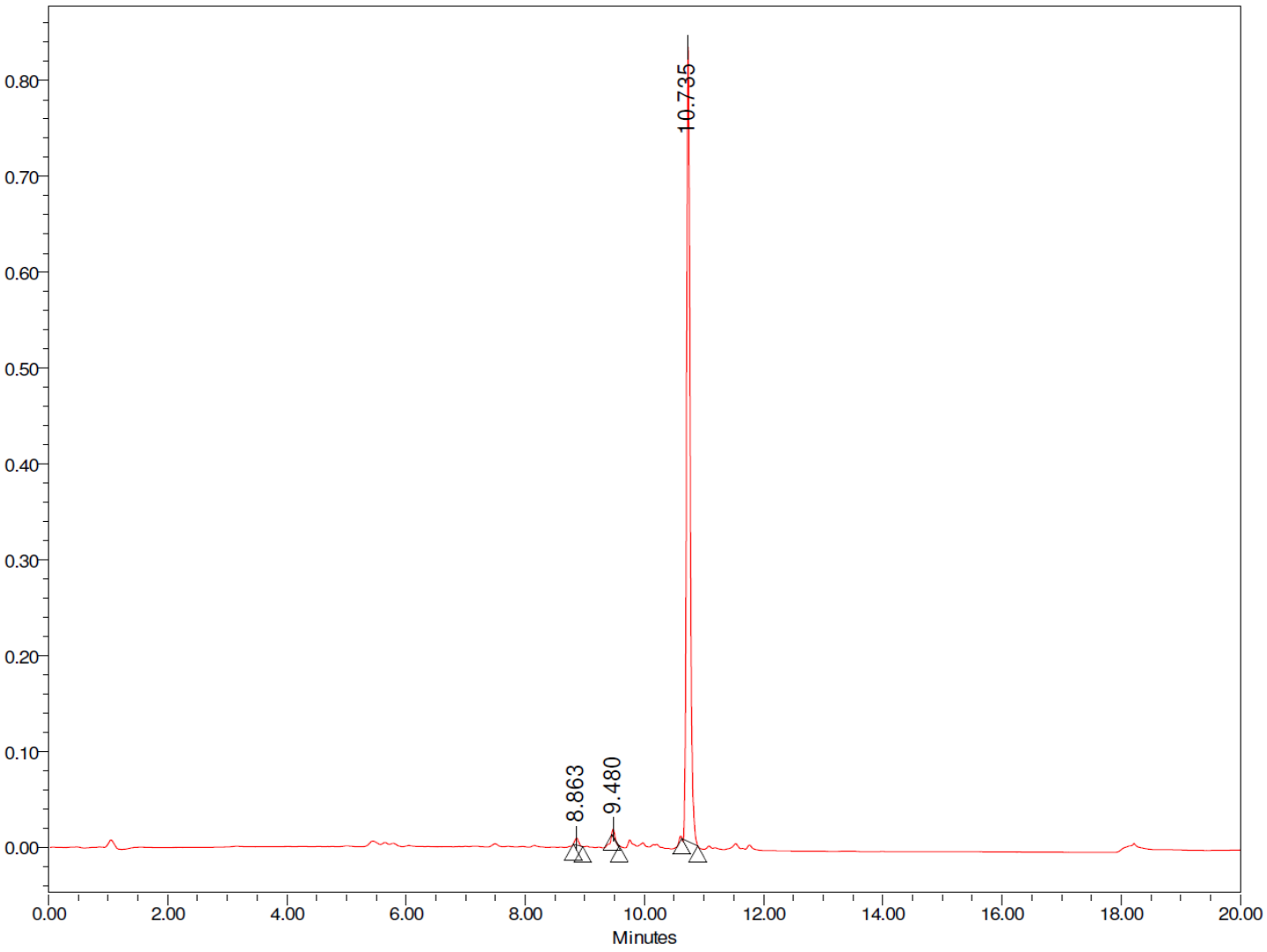


Peak Summary with Statistics

Name:

	Sample Name	Vial	Inj	Retention Time (min)	Area	% Area	Height
1	pk-12	28	1	9.453	4632759	97.35	676652
2	pk-12	28	1	8.899	125962	2.65	40885
Mean				9.176			
Std. Dev.				0.392			
% RSD				4.27			

HPLC data of **13**

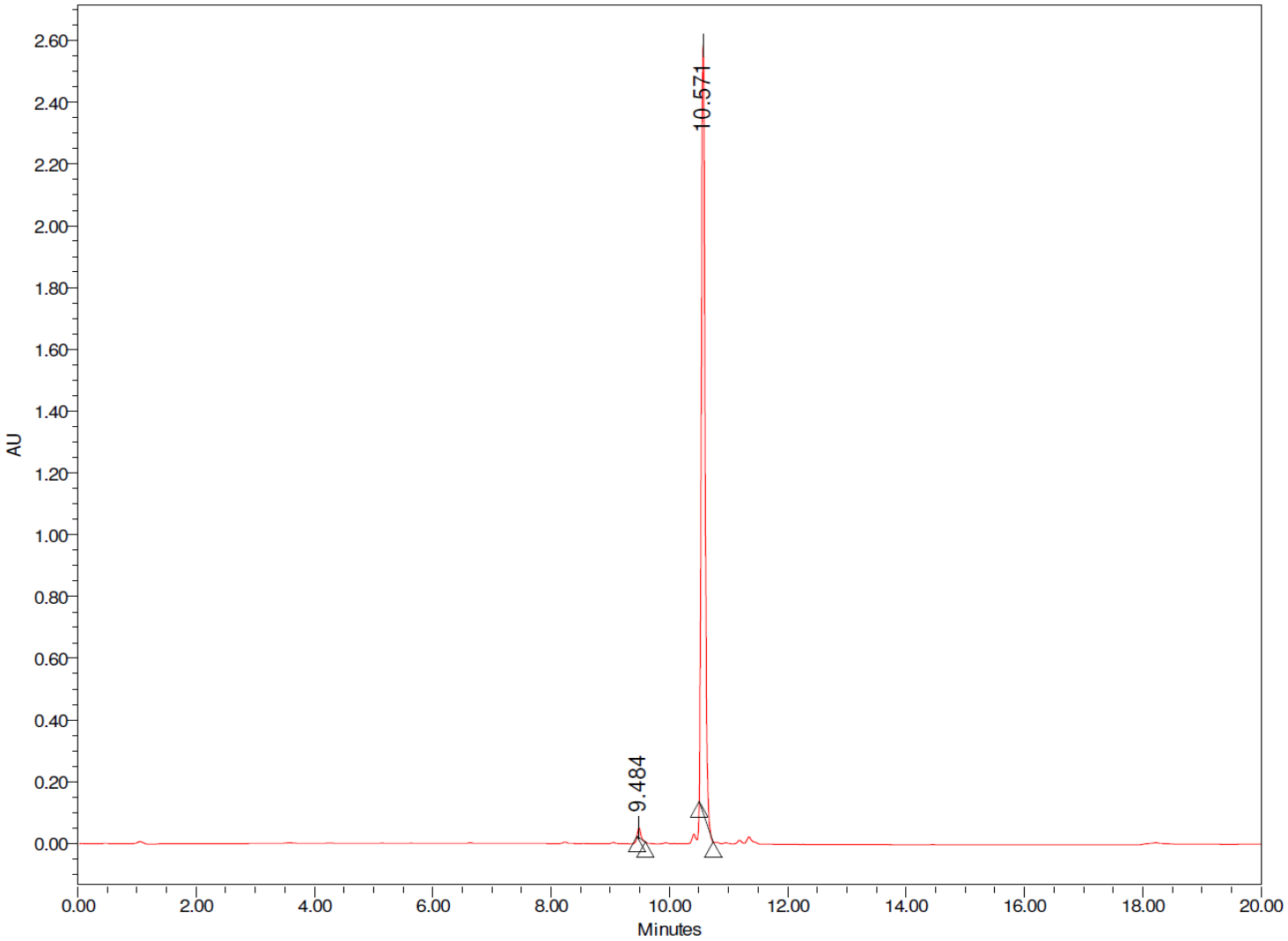


Peak Summary with Statistics

Name:

	Sample Name	Vial	Inj	Retention Time (min)	Area	% Area	Height
1	PK-13	29	1	8.863	30908	0.89	7275
2	PK-13	29	1	10.735	3422118	98.44	828679
3	PK-13	29	1	9.480	23164	0.67	8187
Mean				9.693			
Std. Dev.				0.954			
% RSD				9.84			

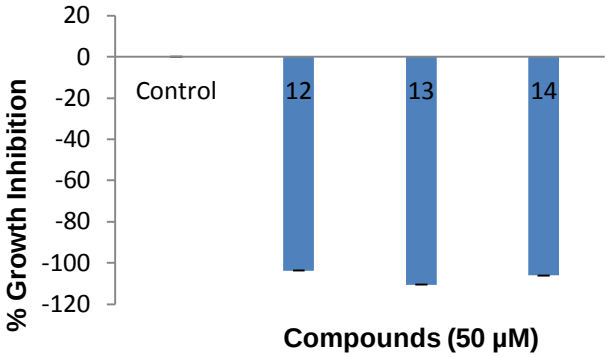
HPLC data of **14**



Peak Summary with Statistics

Name:

	Sample Name	Vial	Inj	Retention Time (min)	Area	% Area	Height
1	PK-14	30	1	10.571	10599283	99.02	2484772
2	PK-14	30	1	9.484	104385	0.98	32554
Mean				10.028			
Std. Dev.				0.768			
% RSD				7.66			



compounds	% Inhibition±SD
Control	0±0.022
12	-103.79±0.002
13	-110.62±0.025
14	-106.12±0.004

Fig S1. Growth inhibition assay for compound **12**, **13** and **14** against in HEK 293cells.

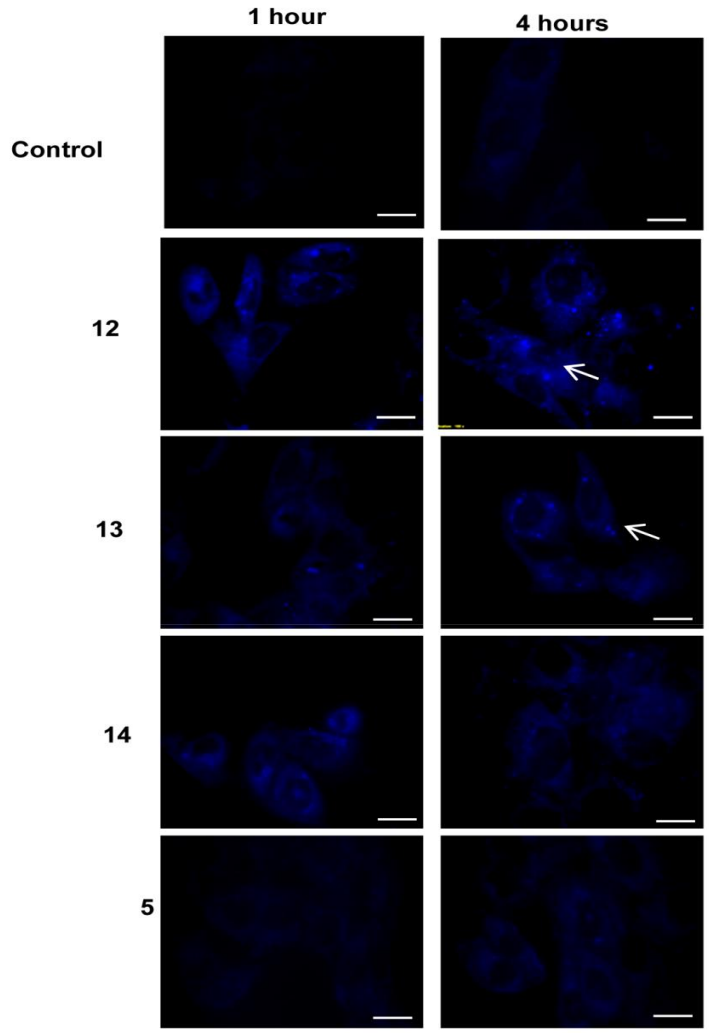


Fig. S2. Cellular uptake of Galactal fused pyrano-pyranones 12, 13 and 14. MCF 7 cells were grown on coverslips and treated with compounds for different time points as shown. Fluorescence microscopic images showed increase uptake and intracellular accumulation (arrows) of these compounds by cancer cells as compared to parent compound **5.** Scale bar = 10 µm.