Supplementary Information (SI) for RSC Advances.

Design, synthesis and anticancer evaluation of novel hydrazide-2-oxindole analogues as GSK-3β kinase inhibitors

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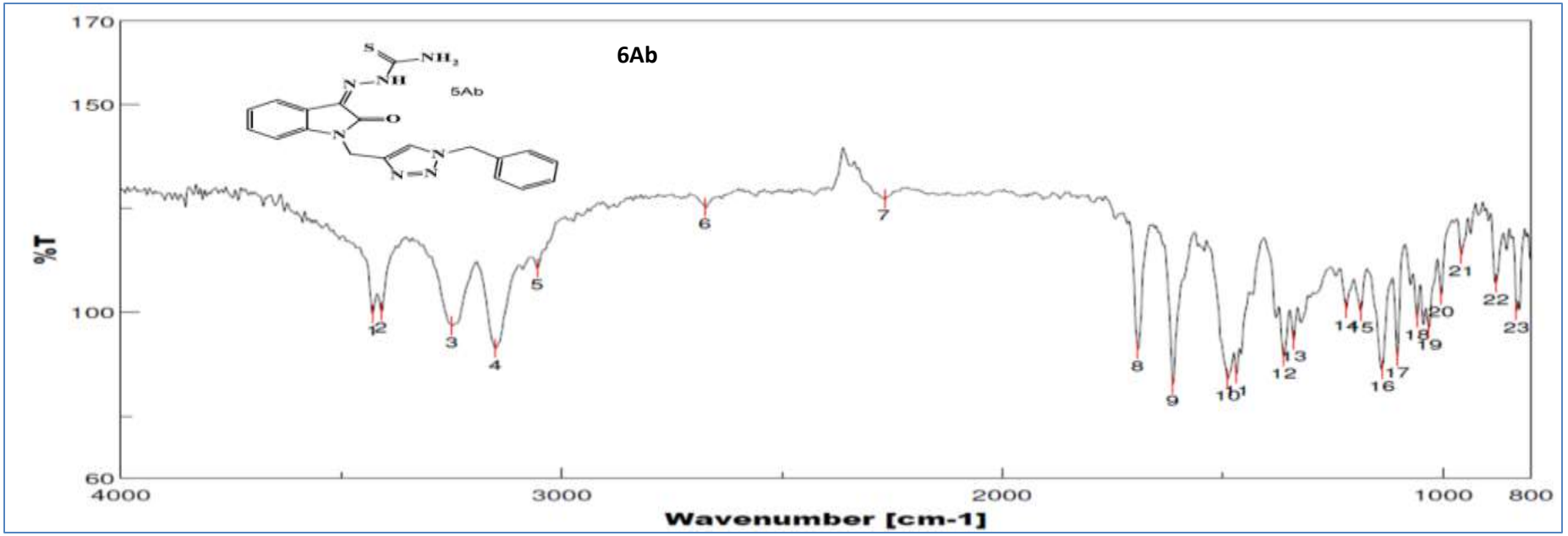
SUPPLEMENTARY FIGURES

Contents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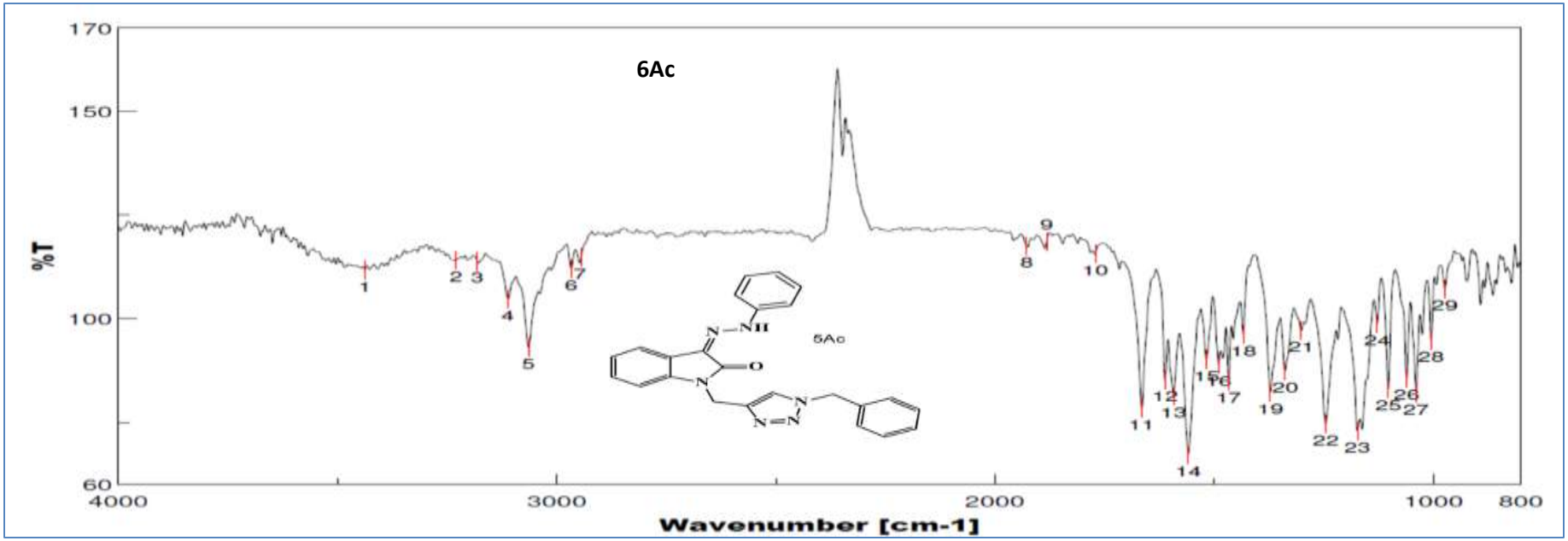
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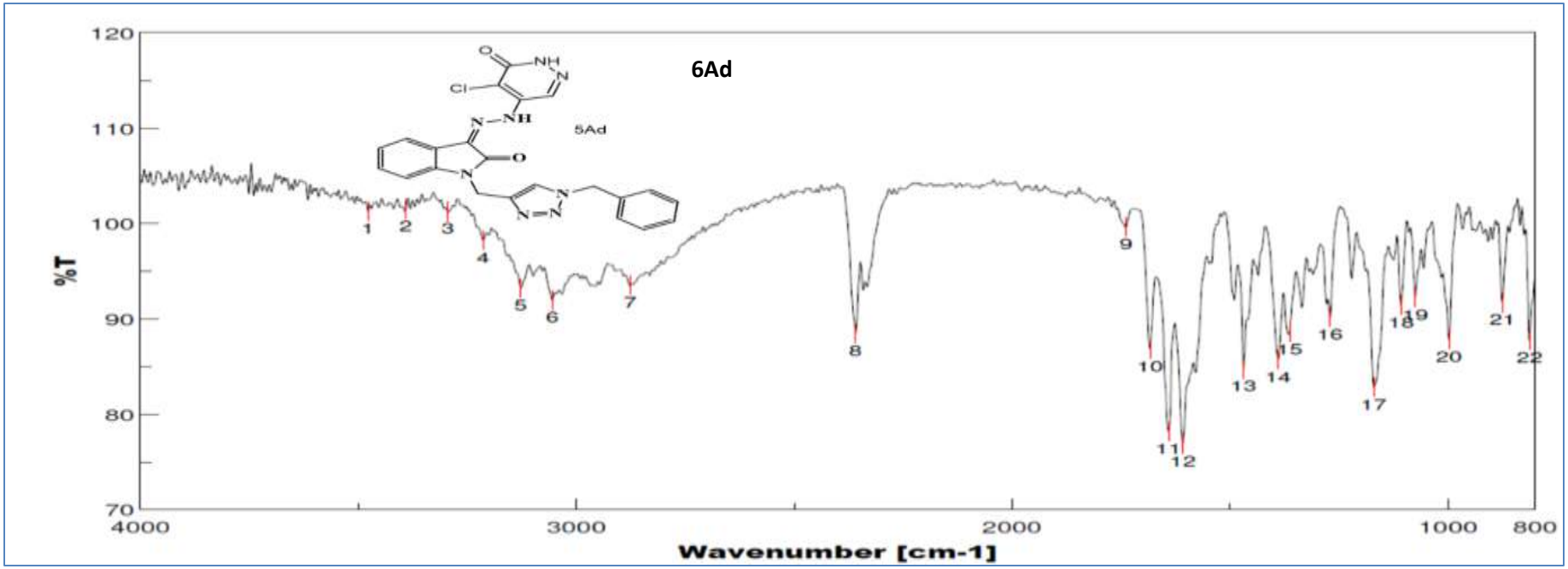
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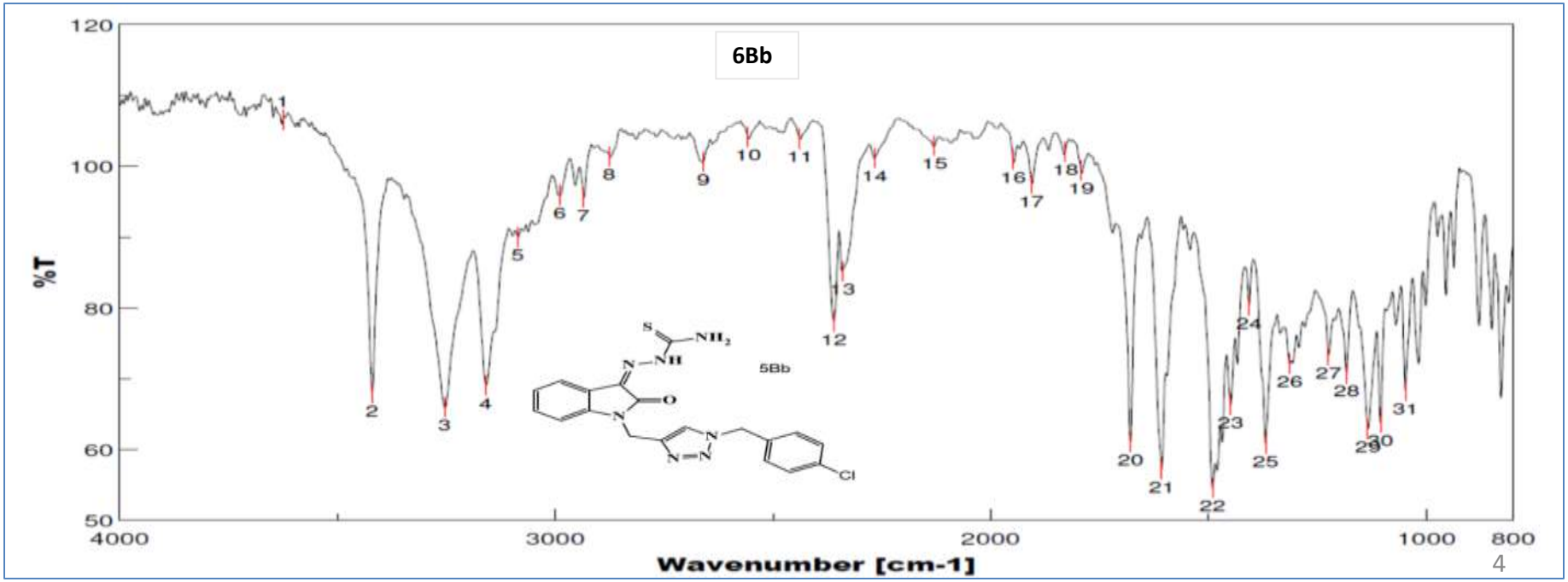
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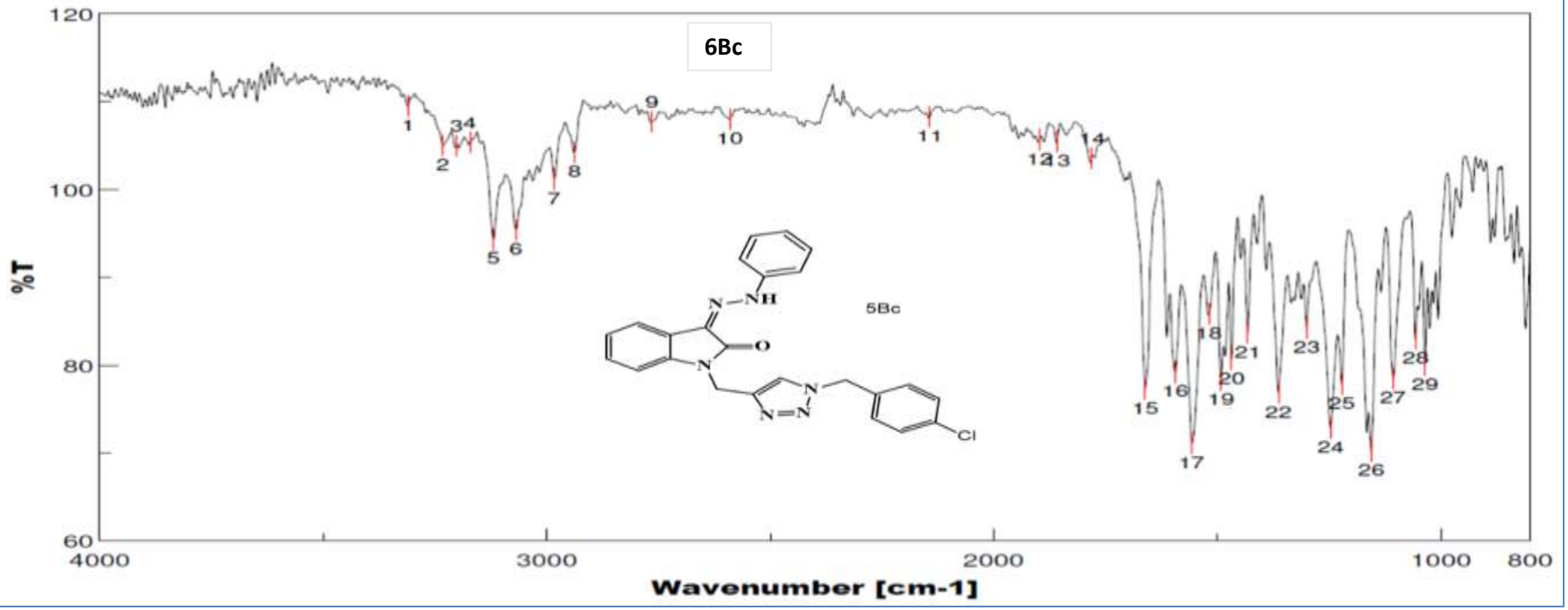
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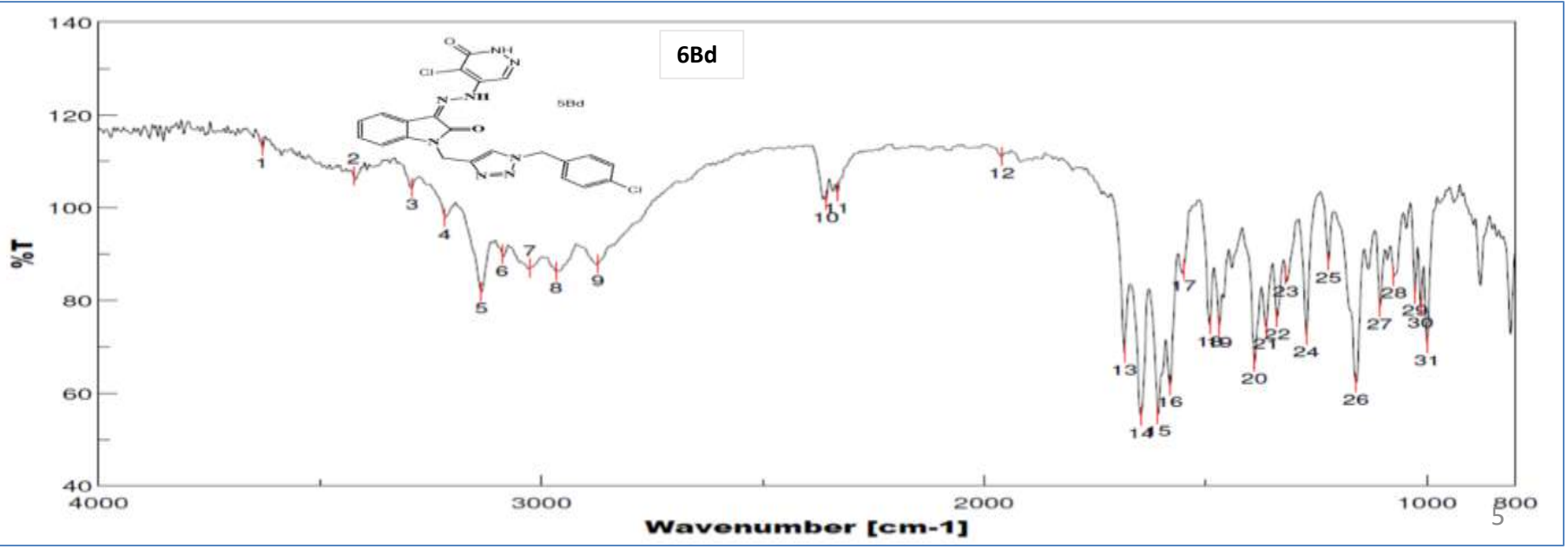
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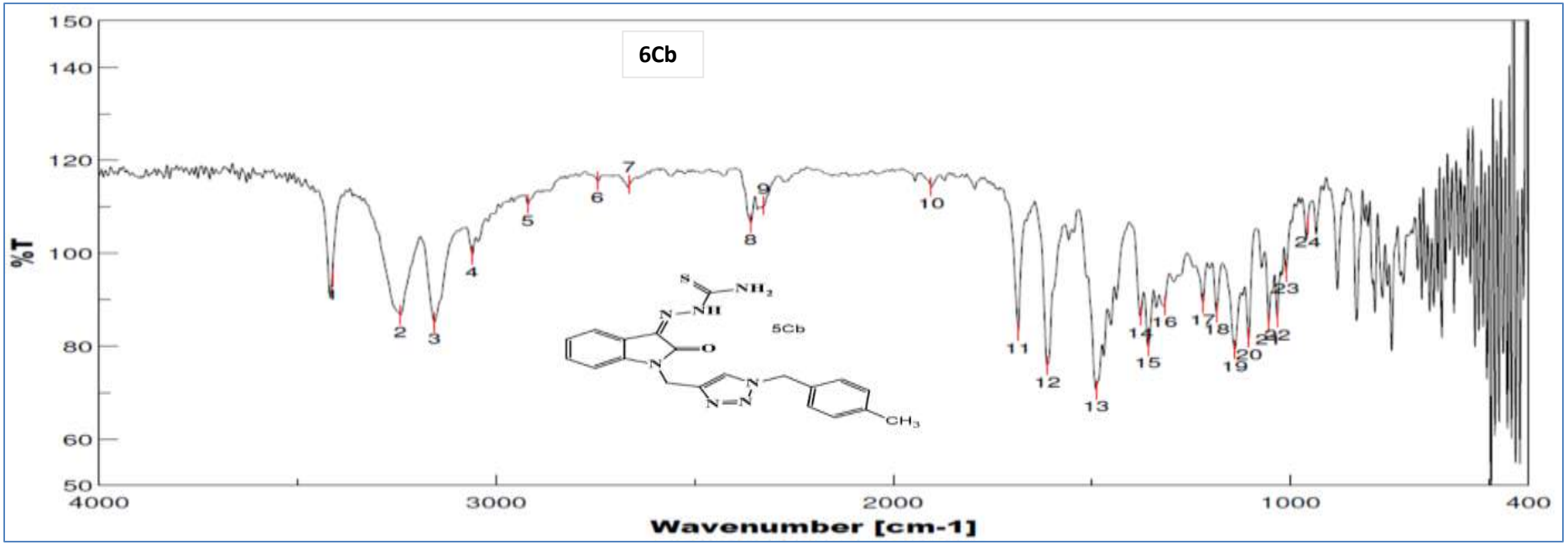
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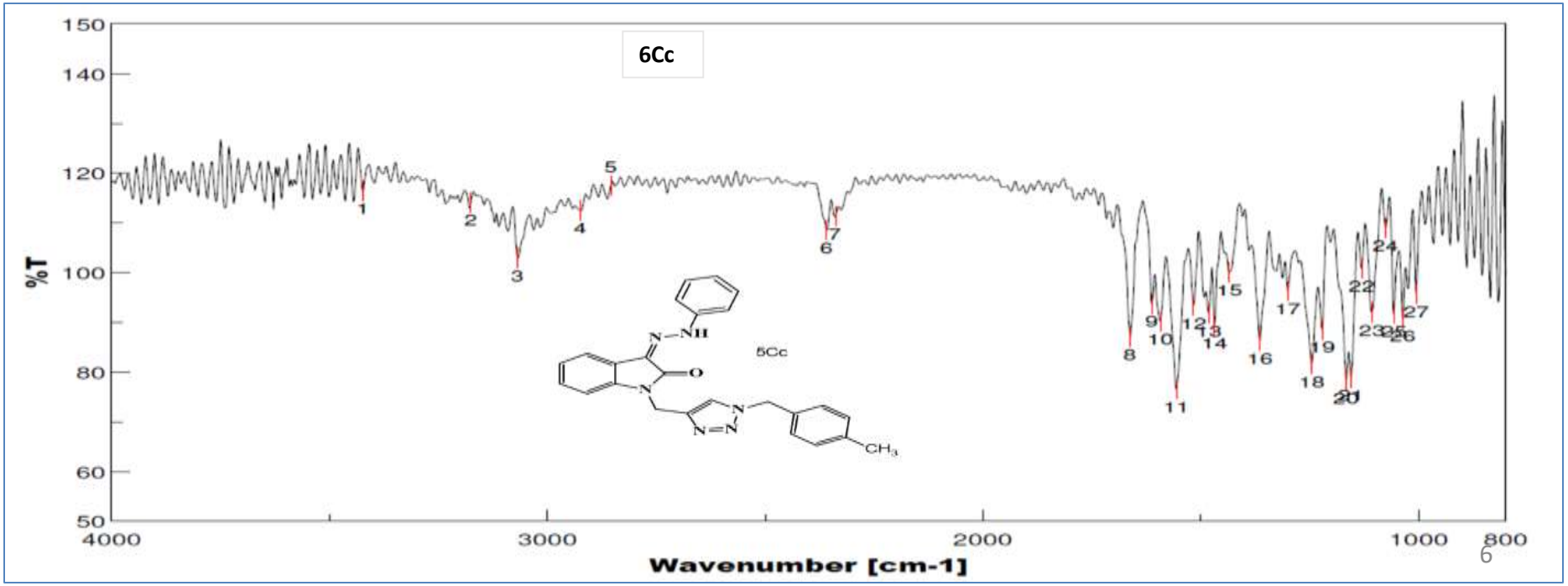
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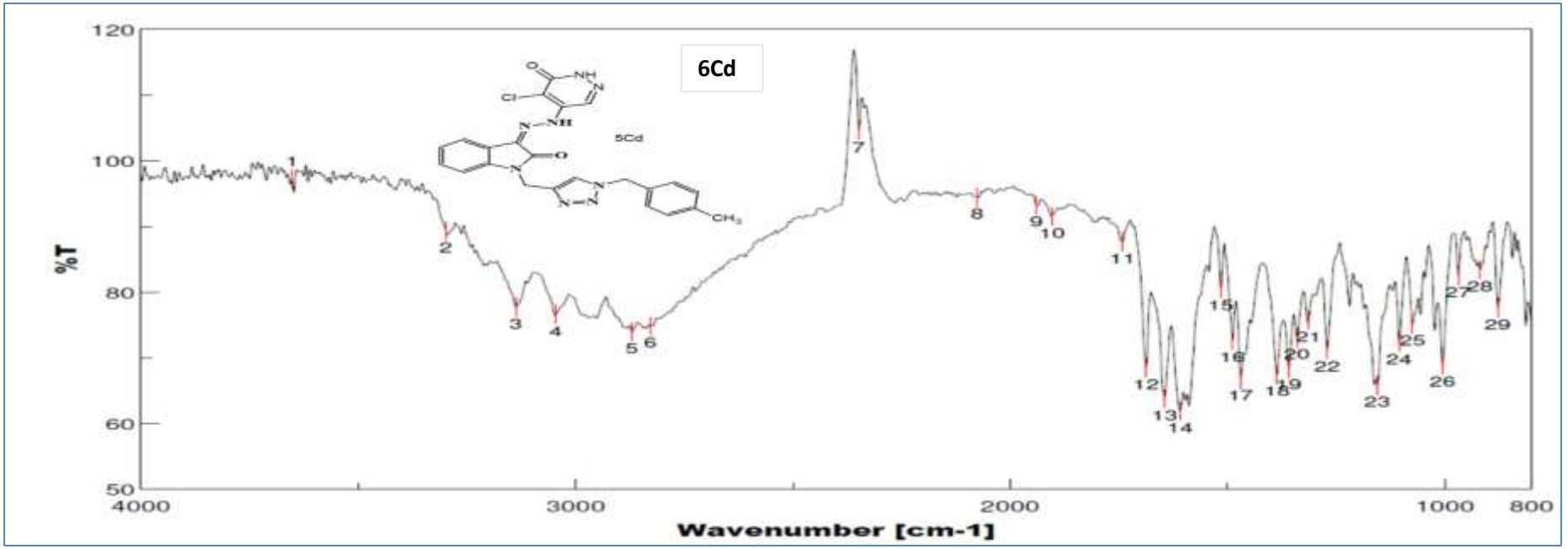
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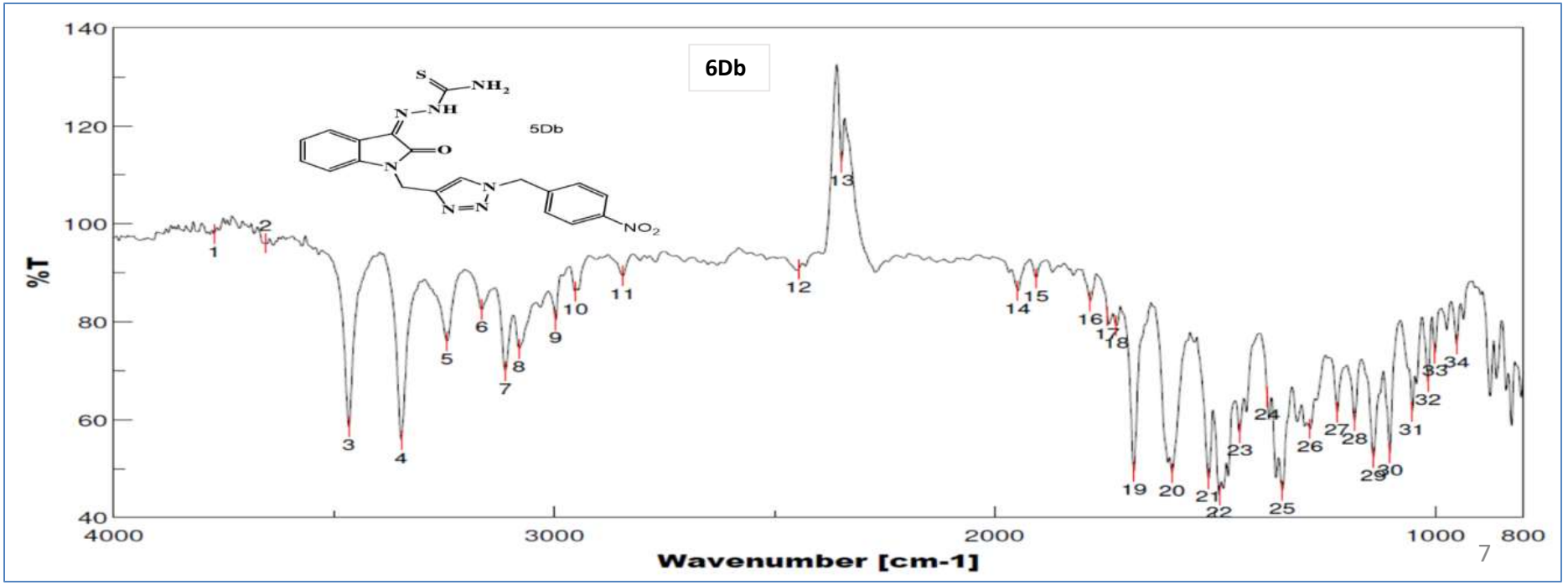
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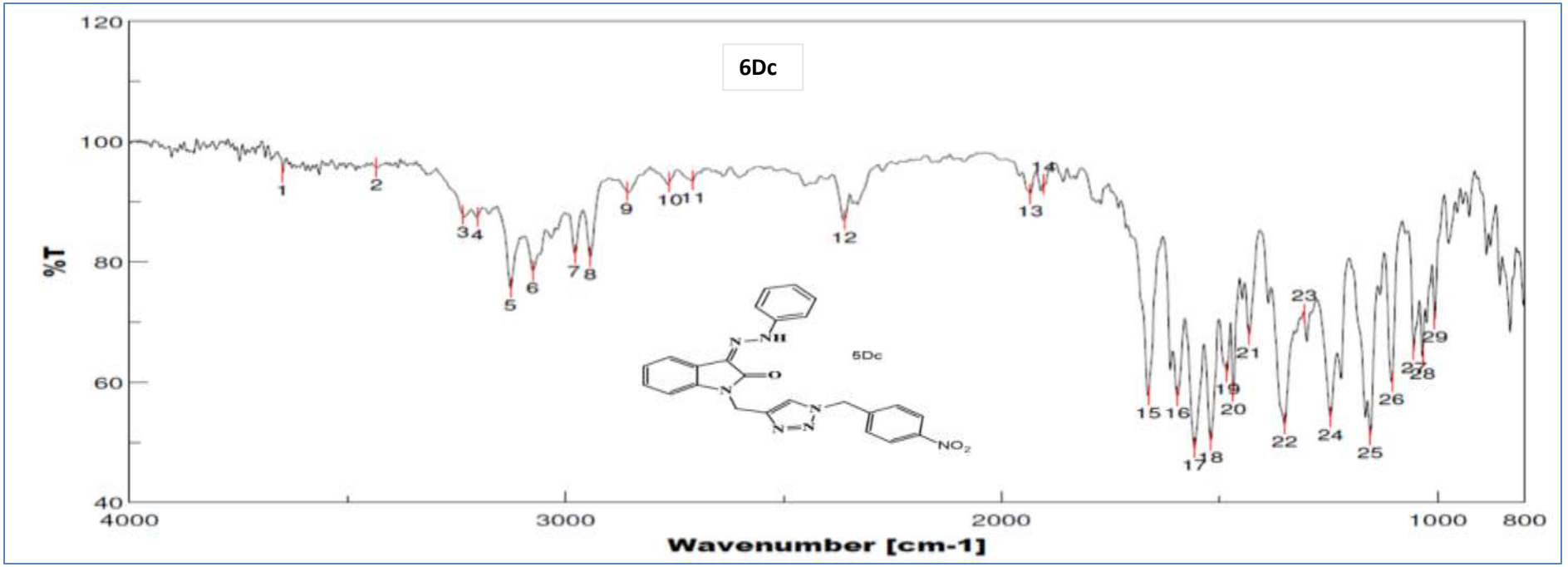
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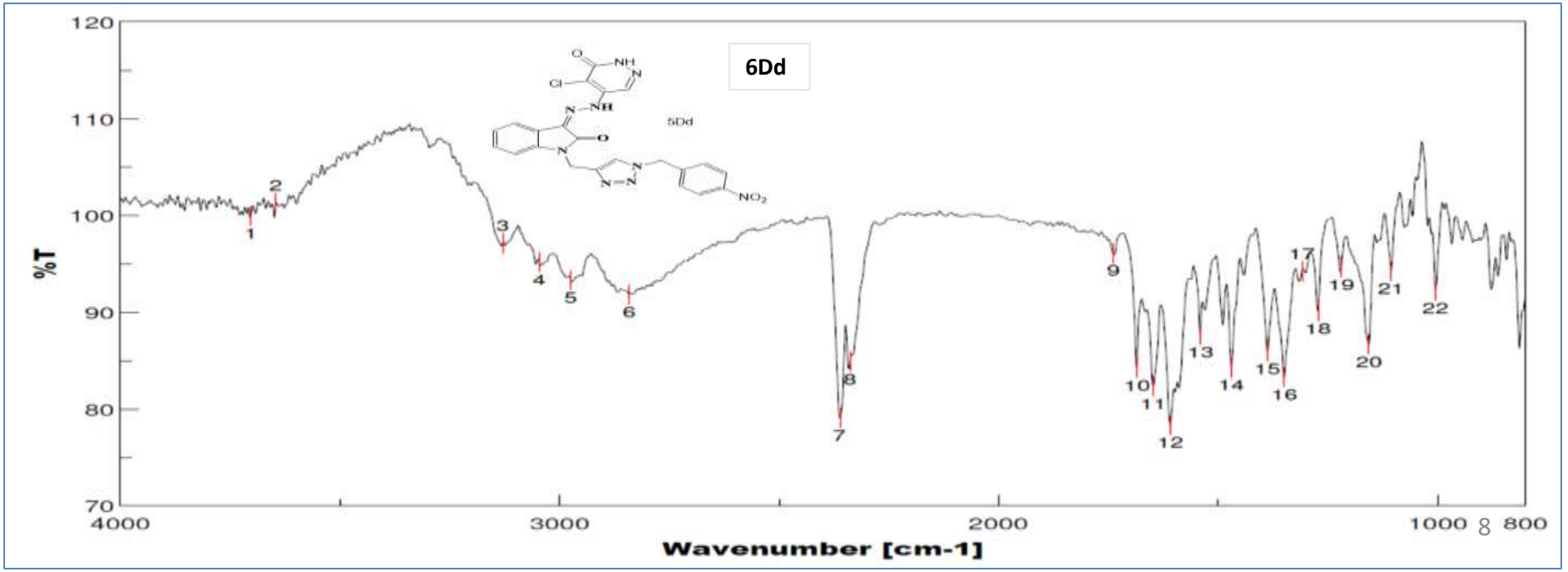
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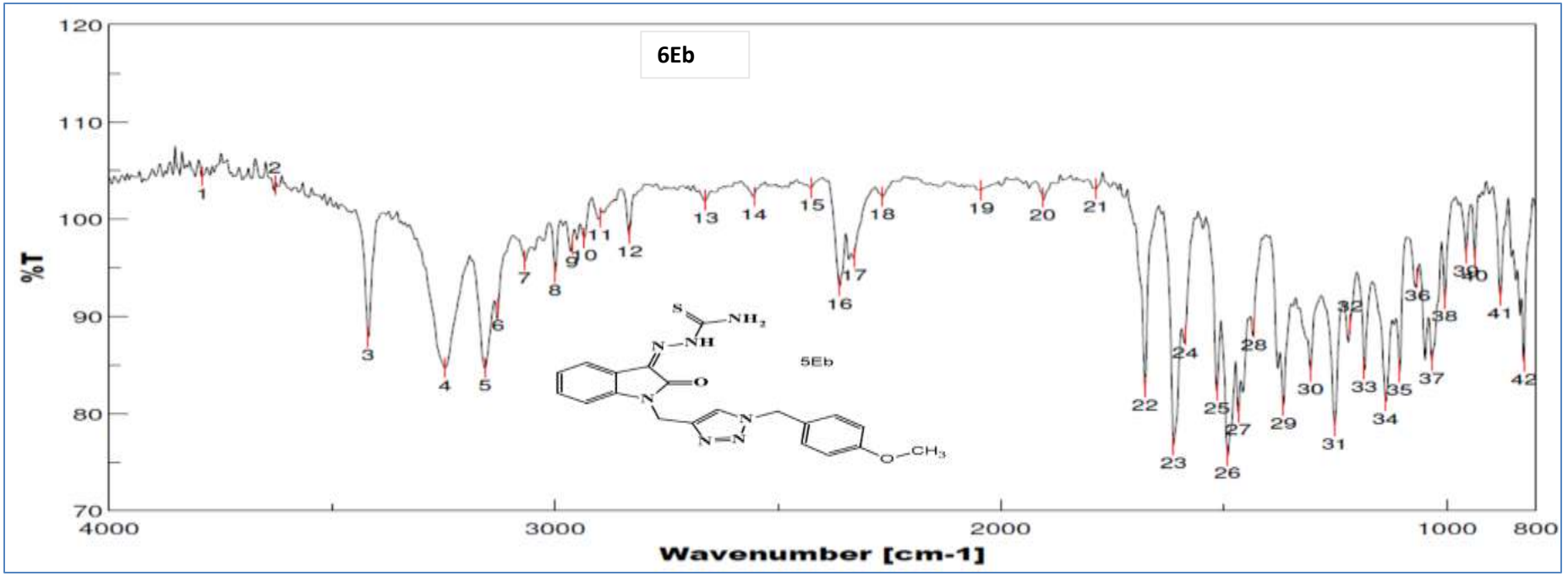
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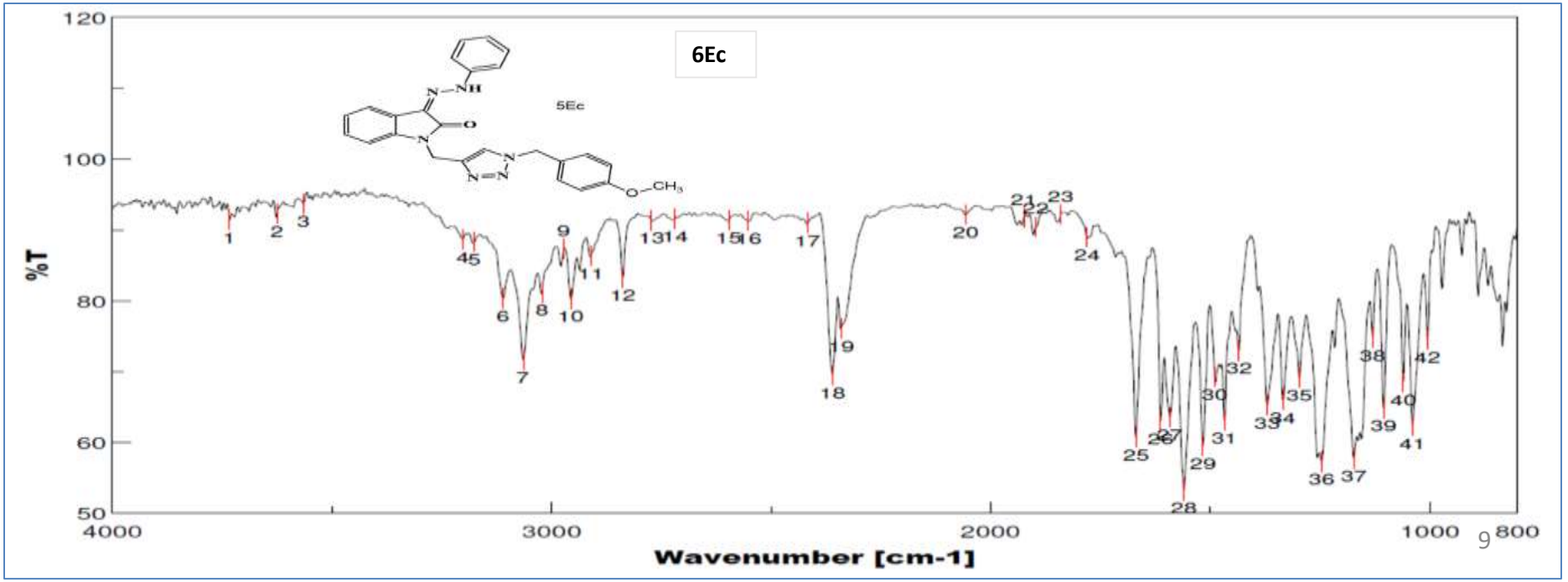
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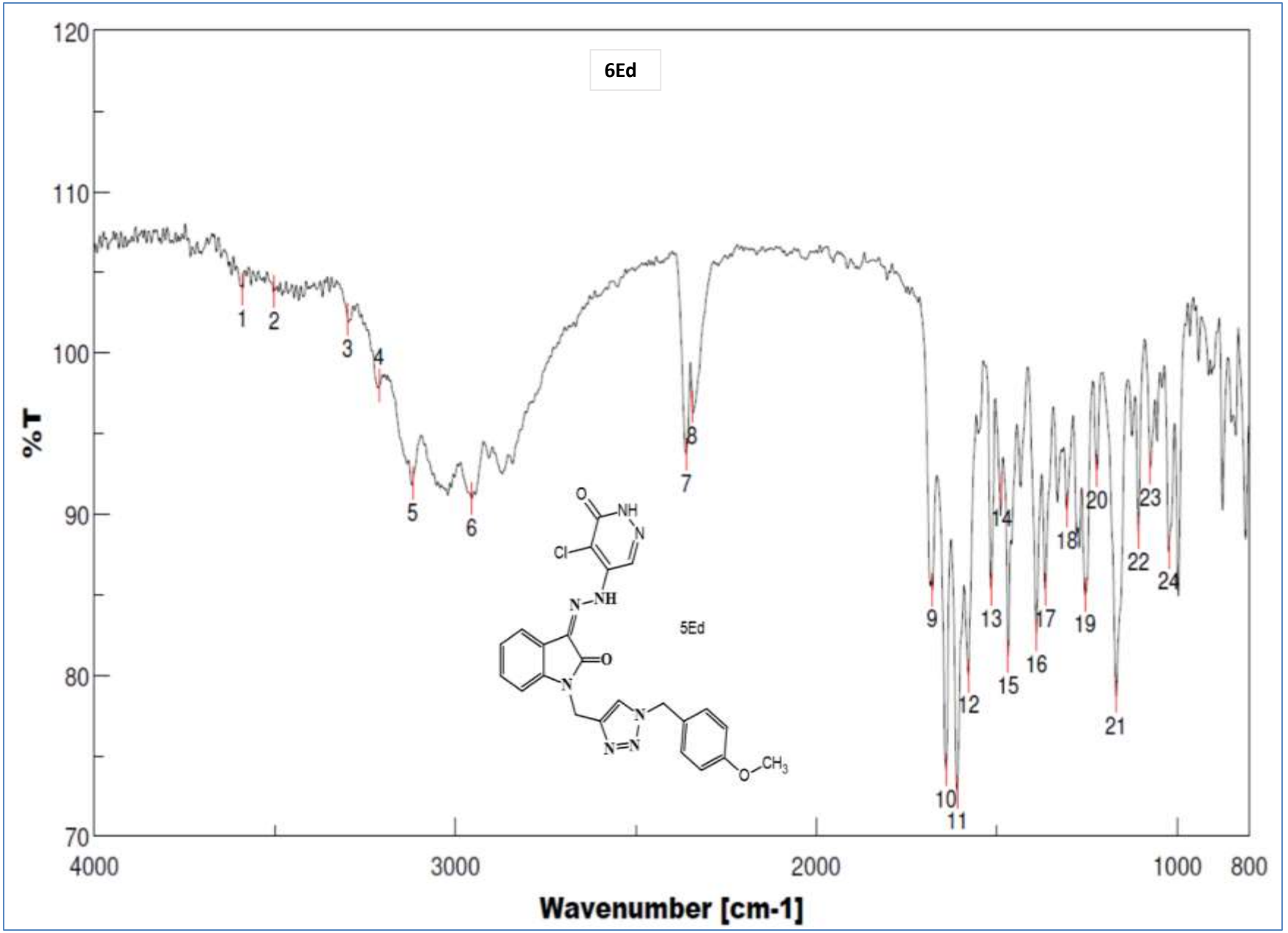
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110
100
90
80
70
%T
4000
3000
2000
1000
800
Wavenumber [cm-1]
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2
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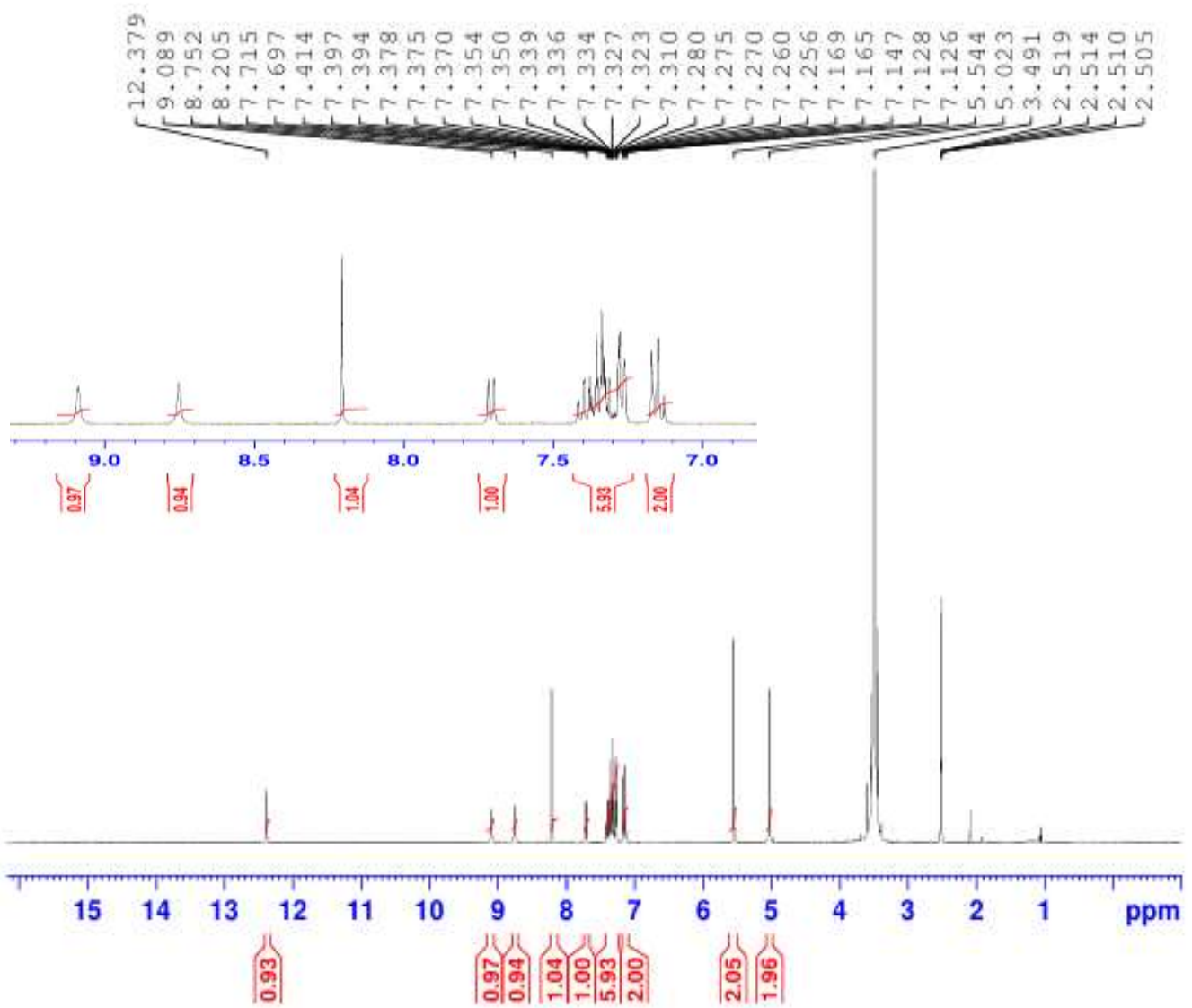
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
5Ed
O
NH
N
Cl
N–NH
O
N
N
N=N
O
CH3

6Ab
1H-NMR in DMSO



Chromatogen Analytical Solutions

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SOLVENT	DMSO	
NS	16	
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FIDRES	0.244532	Hz
AQ	4.0894465	sec
RG	73.11	
DW	62.400	usec
DE	17.09	usec
TE	295.9	K
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TD0	1	
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NUC1	1H	
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F2 - Processing parameters

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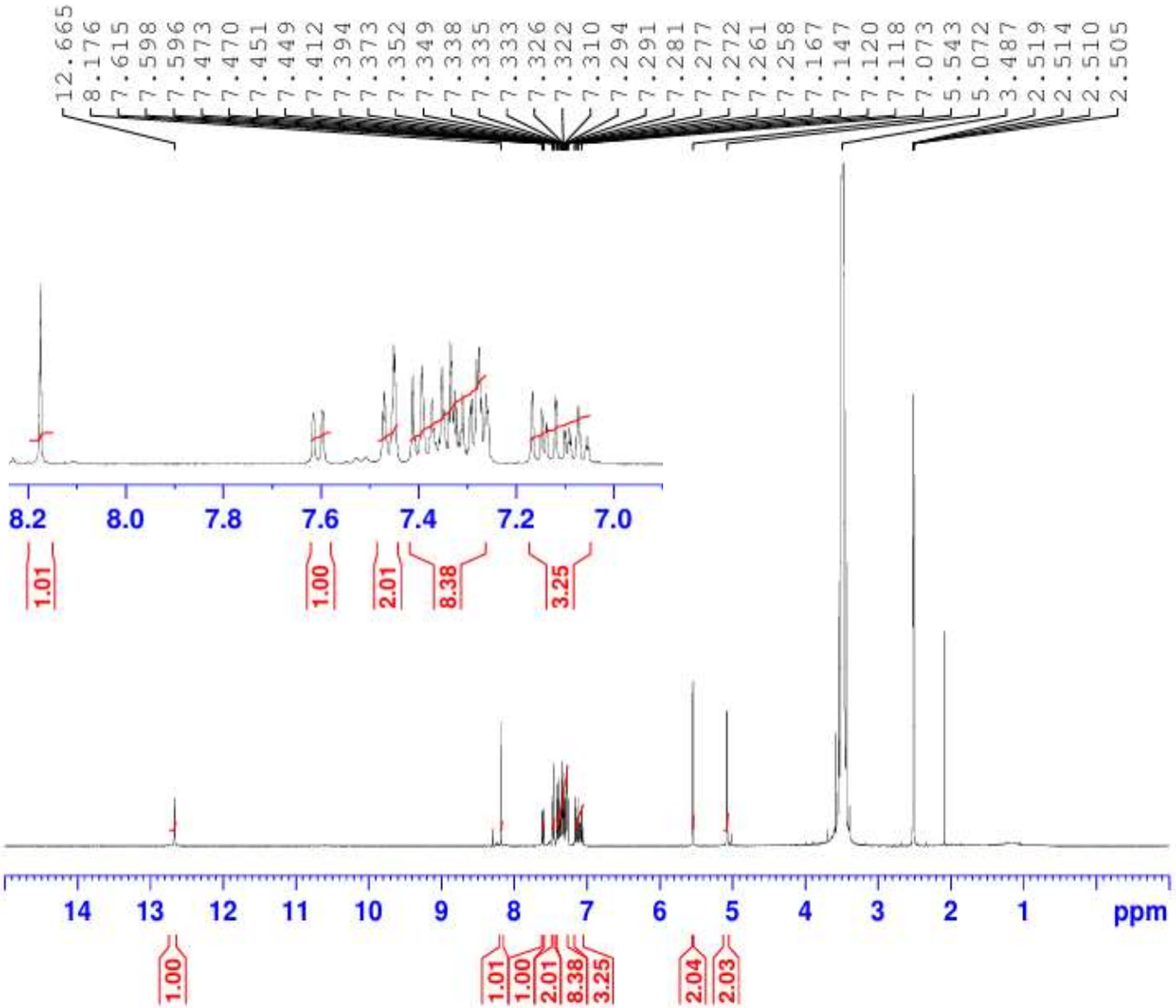
6Ac
1H-NMR in DMSO



Chromatogen Analytical Solutions

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PULPROG	zg30
TD	65536
SOLVENT	DMSO
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F2 - Processing parameters	
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WDW	EM
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GB	0
PC	1.00

INTPCL **6Ad**

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12.915

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8.238
7.756
7.730
7.447
7.428
7.411
7.379
7.357
7.345
7.319
7.287
7.273
7.245
7.224
7.197
7.182
7.161
5.560
5.085

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EXPNO 3
PROCNO 1

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PULPROG zg
TD 12818
SOLVENT DMSO
NS 258
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FIDRES 1.250245 Hz
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NUC1 1H
P1 13.50 usec
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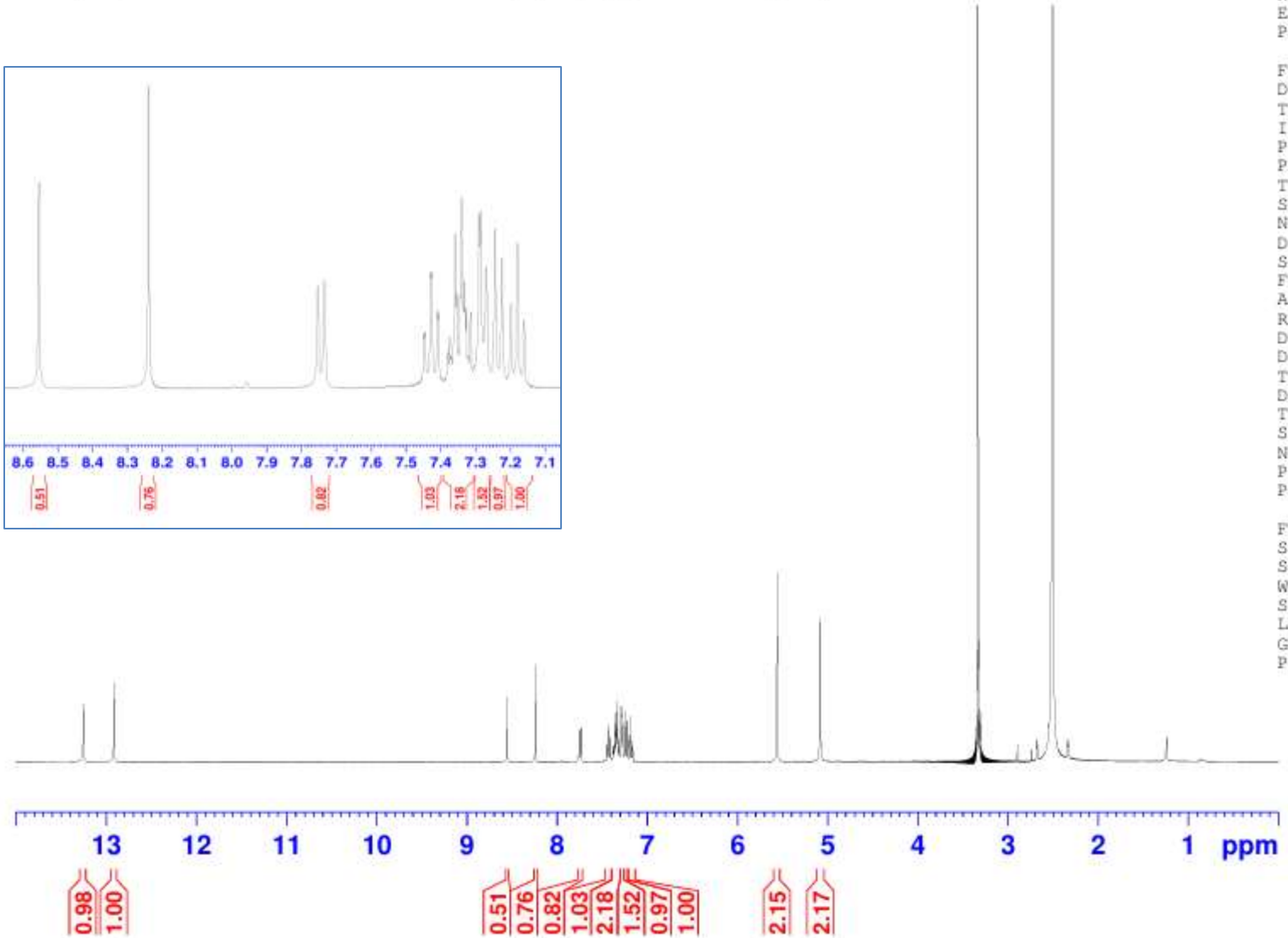

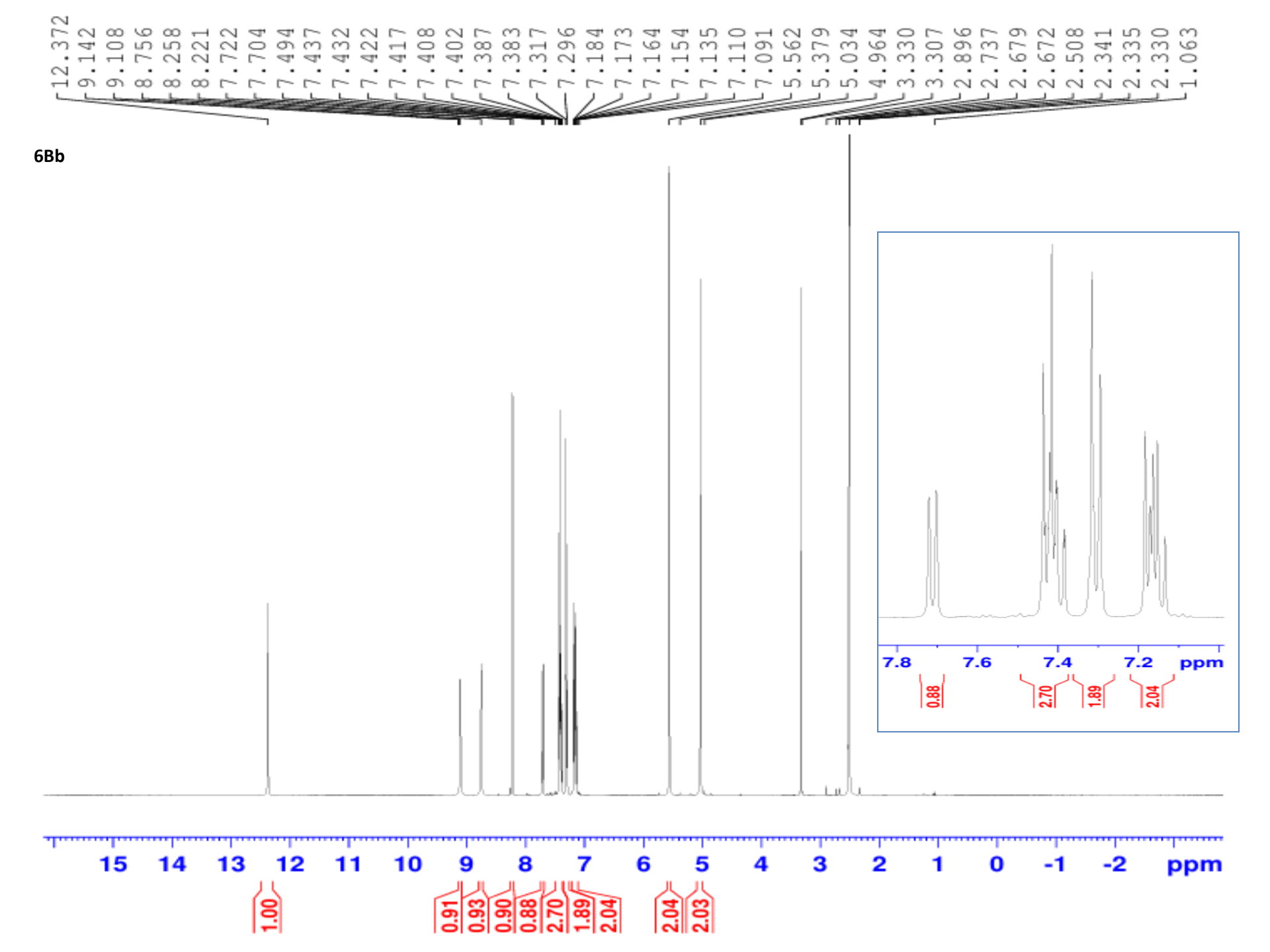
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7.173
7.164
7.154
7.135
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7.091
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4.964
3.330
3.307
2.896
2.737
2.679
2.672
2.508
2.341
2.335
2.330
1.063
6Bb
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 ppm
1.00
0.91
0.93
0.90
0.88
2.70
1.89
2.04
2.04
2.03
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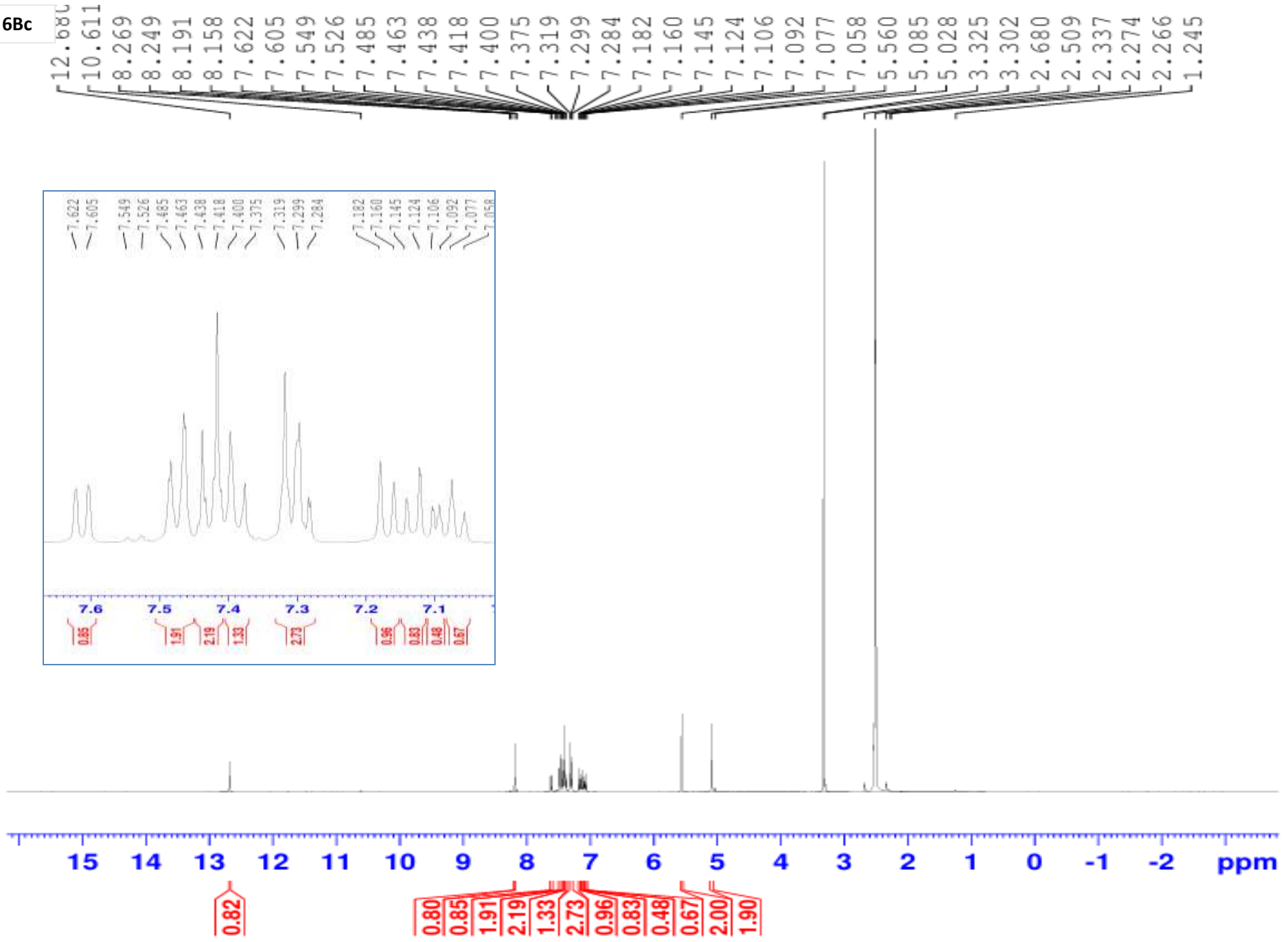
0.88
2.70
1.89
2.04

6Bc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7.418
7.400
7.375
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7.299
7.284
7.182
7.160
7.145
7.124
7.106
7.092
7.077
7.058
5.560
5.085
5.028
3.325
3.302
2.680
2.509
2.337
2.274
2.266
1.245
7.6
7.5
7.4
7.3
7.2
7.1
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1.91
2.19
1.33
2.73
0.96
0.83
0.48
0.67
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
ppm
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0.67
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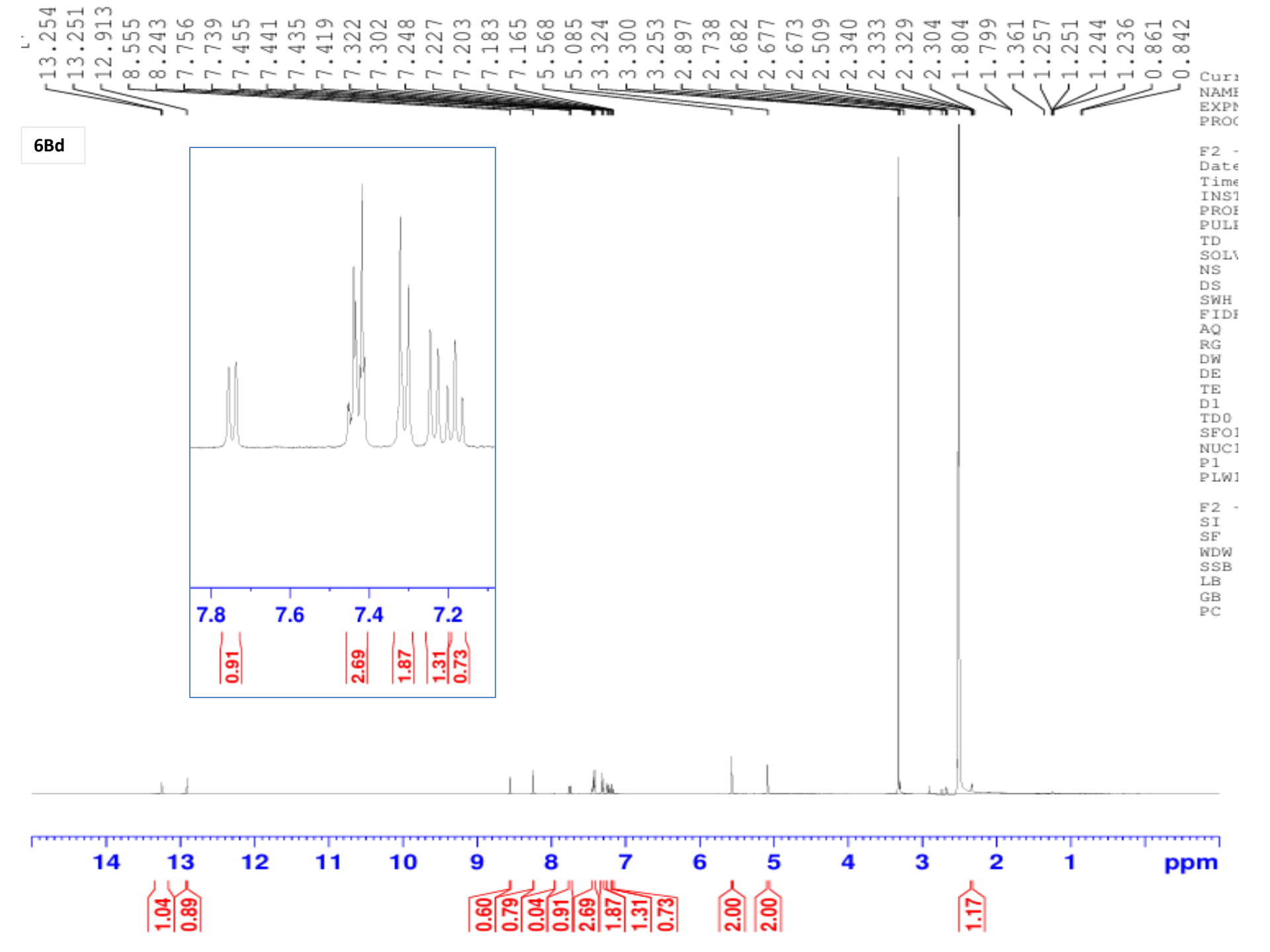
1.90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7.6
7.4
7.2
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1.87
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14
13
12
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10
9
8
7
6
5
4
3
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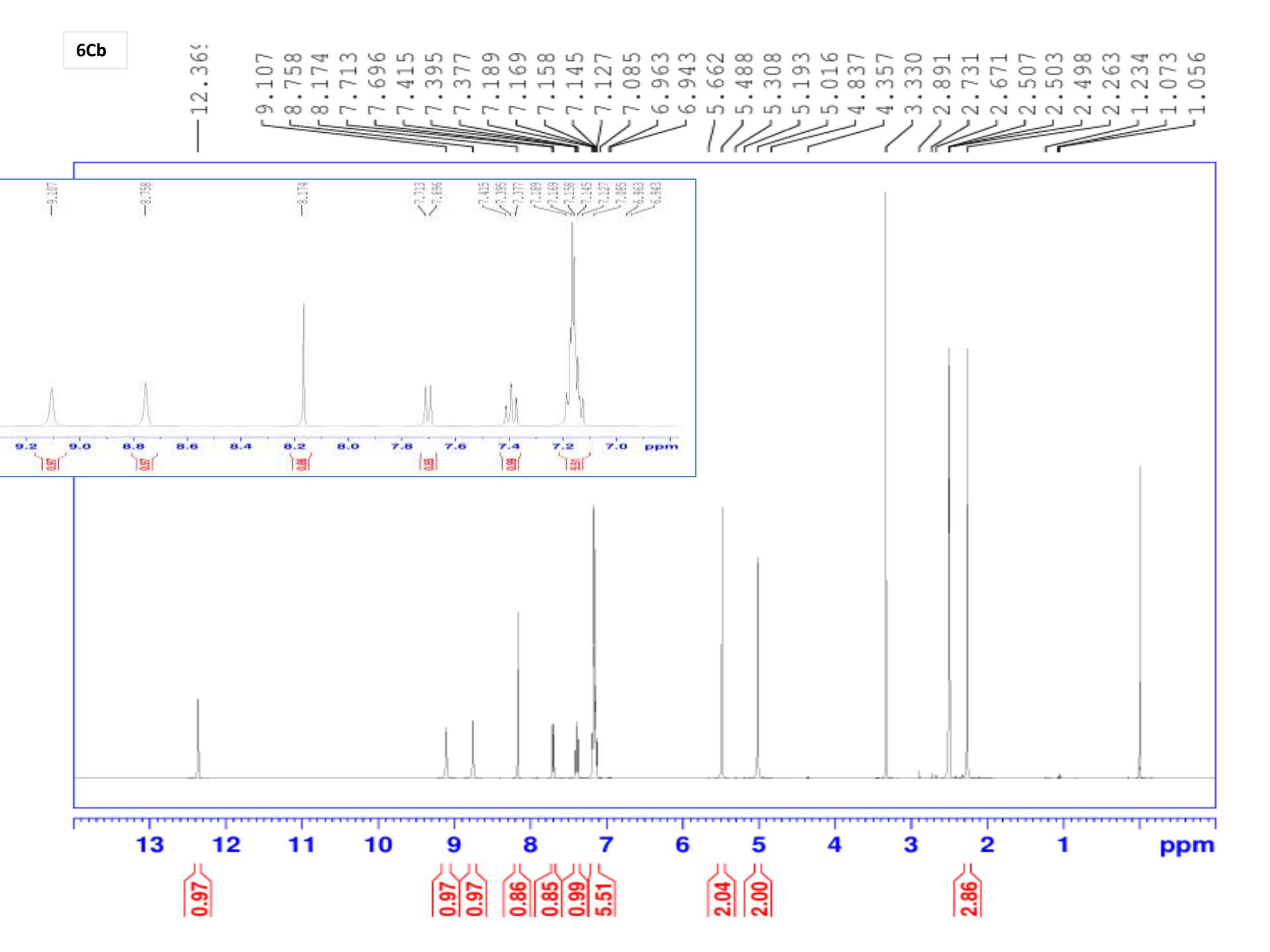
6Cb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6.963
6.943
5.662
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5.193
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4.837
4.357
3.330
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2.503
2.498
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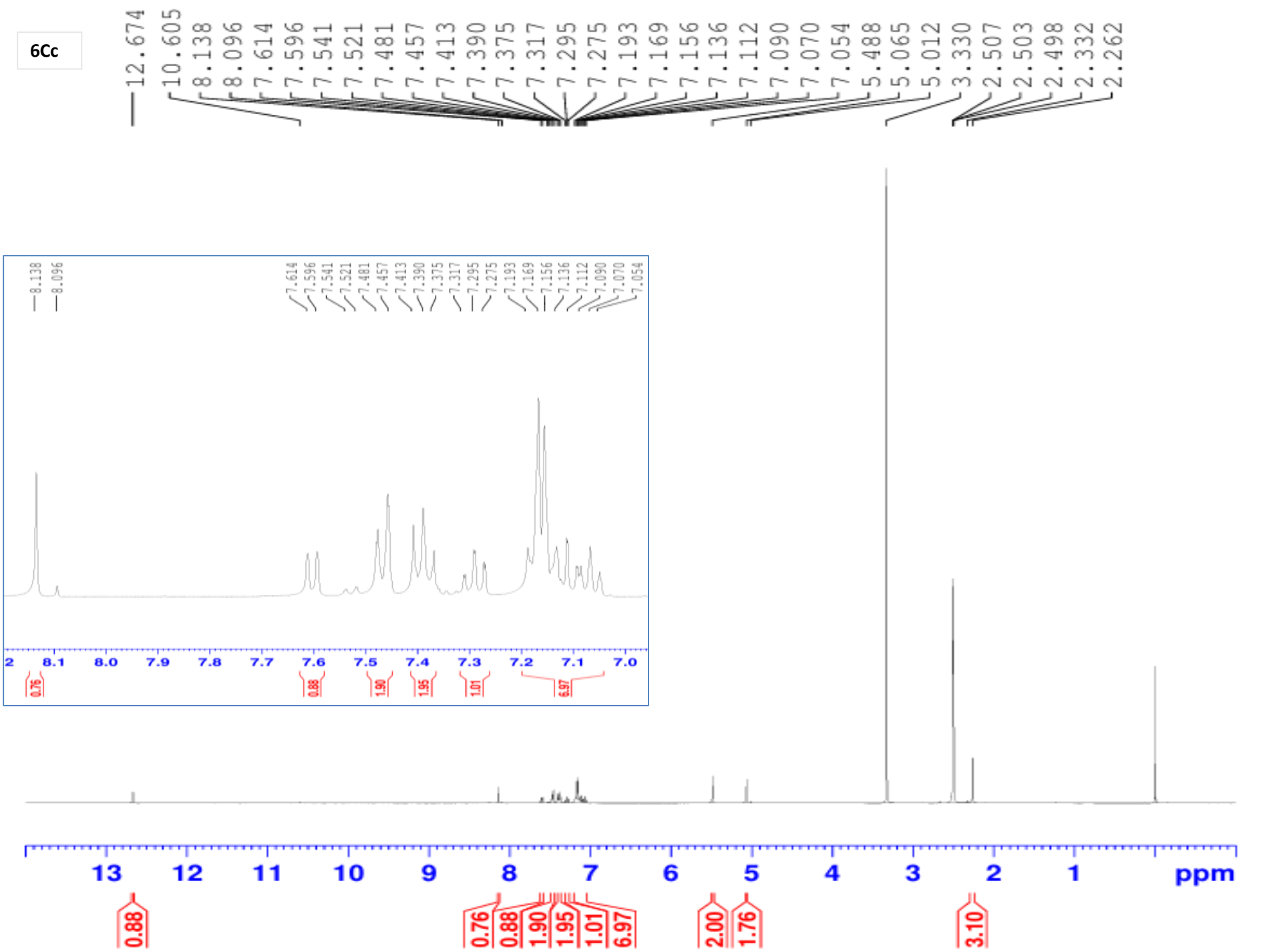
2.86

6Cc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7.295
7.275
7.193
7.169
7.156
7.136
7.112
7.090
7.070
7.054
5.488
5.065
5.012
3.330
2.507
2.503
2.498
2.332
2.262
13
12
11
10
9
8
7
6
5
4
3
2
1
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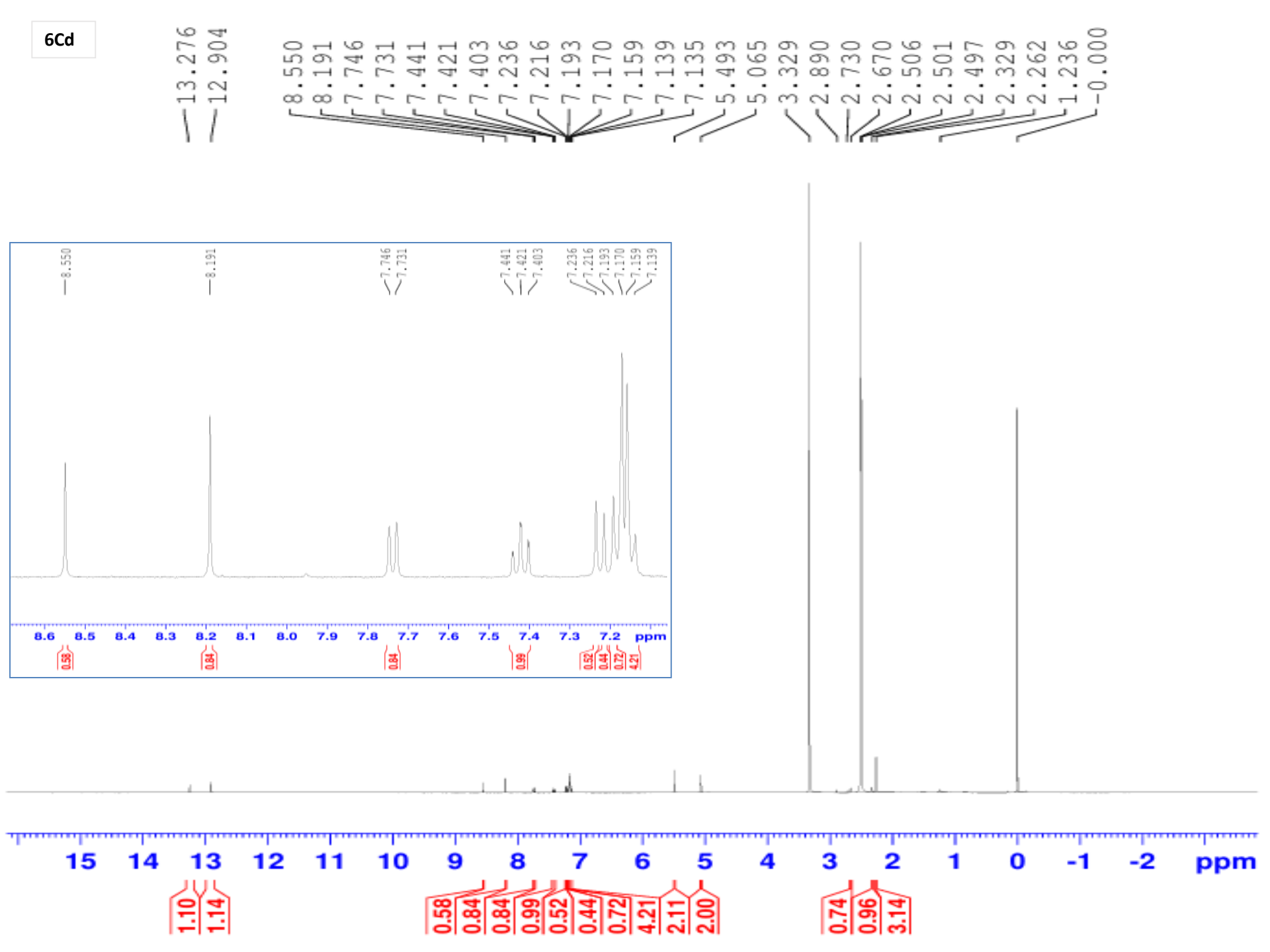
3.10

6Cd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7.170
7.159
7.139
7.135
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2.670
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2.501
2.497
2.329
2.262
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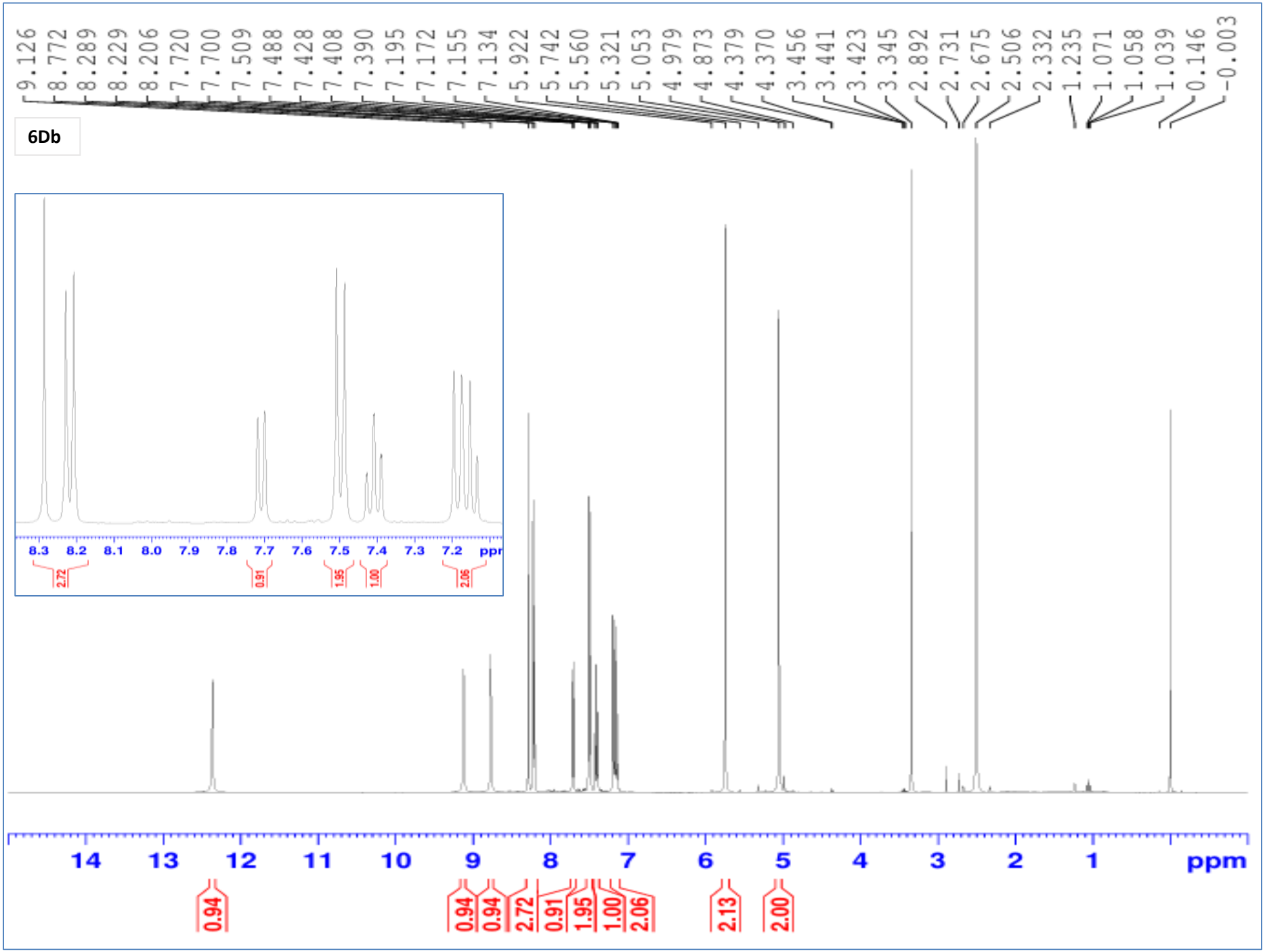
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7.172
7.155
7.134
5.922
5.742
5.560
5.321
5.053
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4.873
4.379
4.370
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3.441
3.423
3.345
2.892
2.731
2.675
2.506
2.332
1.235
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1.039
0.146
-0.003
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8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
ppm
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1.95
1.00
2.06
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
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0.94
0.94
2.72
0.91
1.95
1.00
2.06
2.13
2.00

12.703
12.675
10.619
8.259
8.229
8.208
7.619
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7.537
7.509
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7.480
7.461
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7.306
7.286
7.188
7.170
7.139
7.119
7.102
7.087
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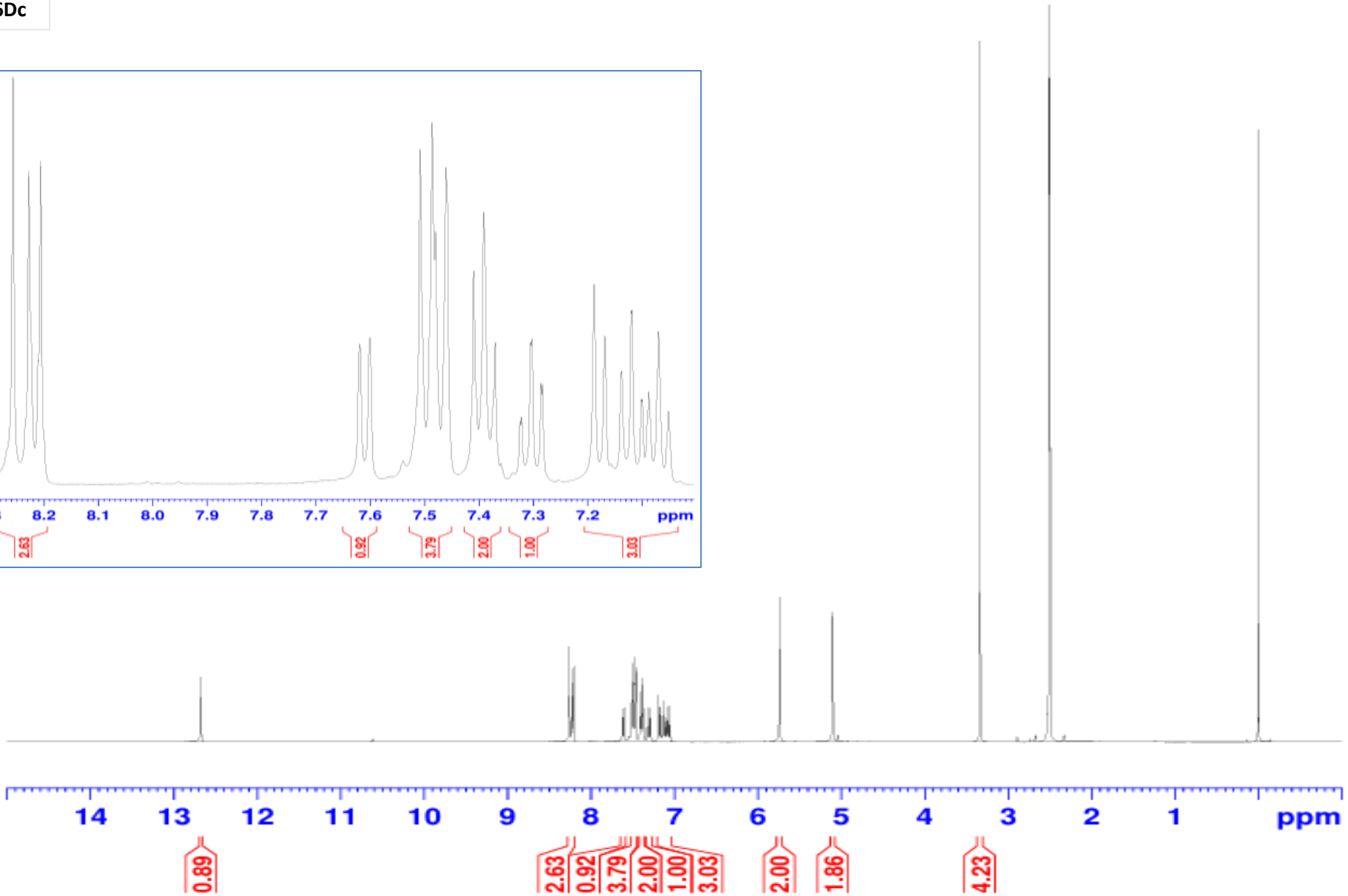
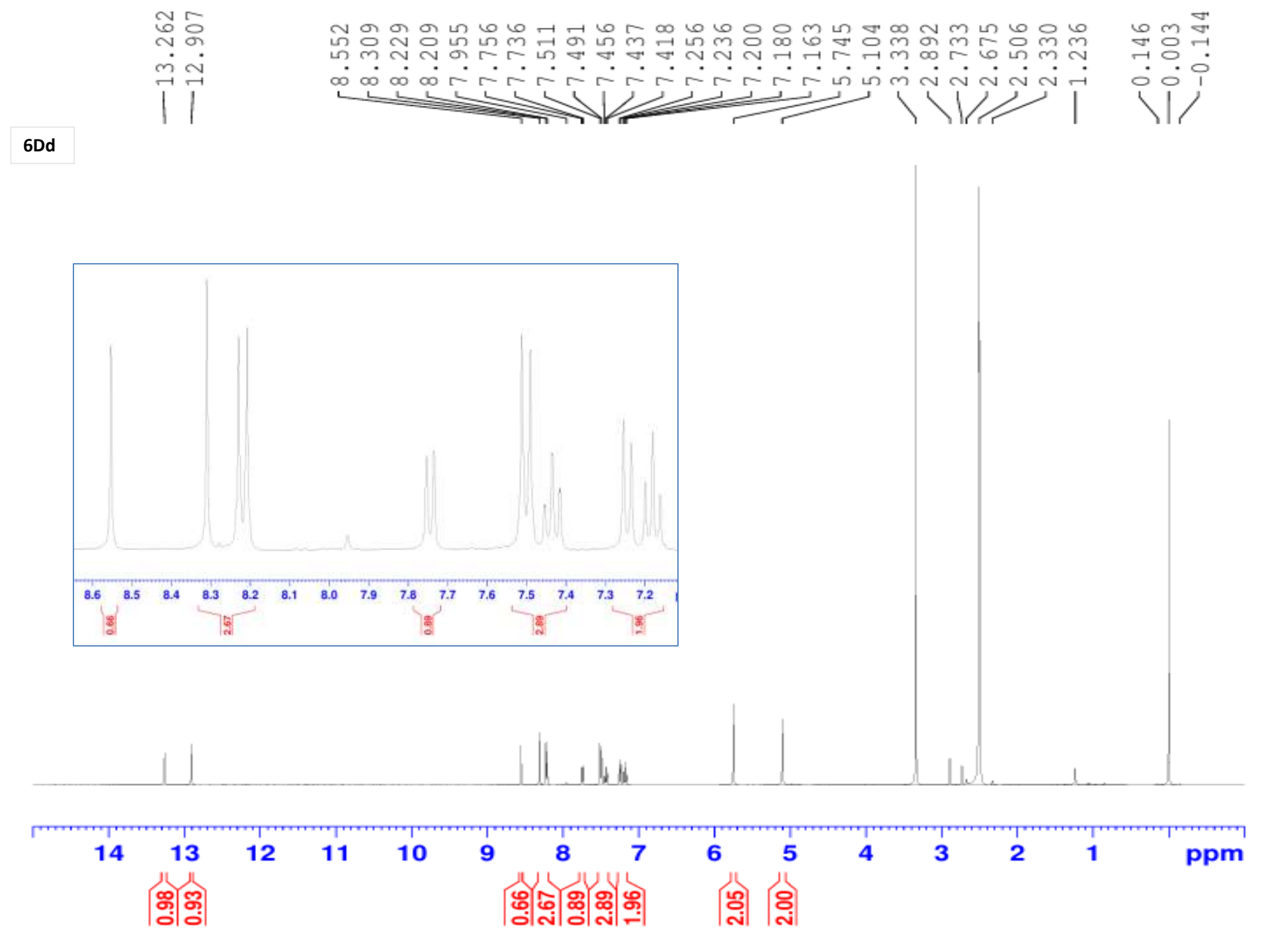
6Dc

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2.506
2.330
1.236
0.146
0.003
-0.144
6Dd
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2.89
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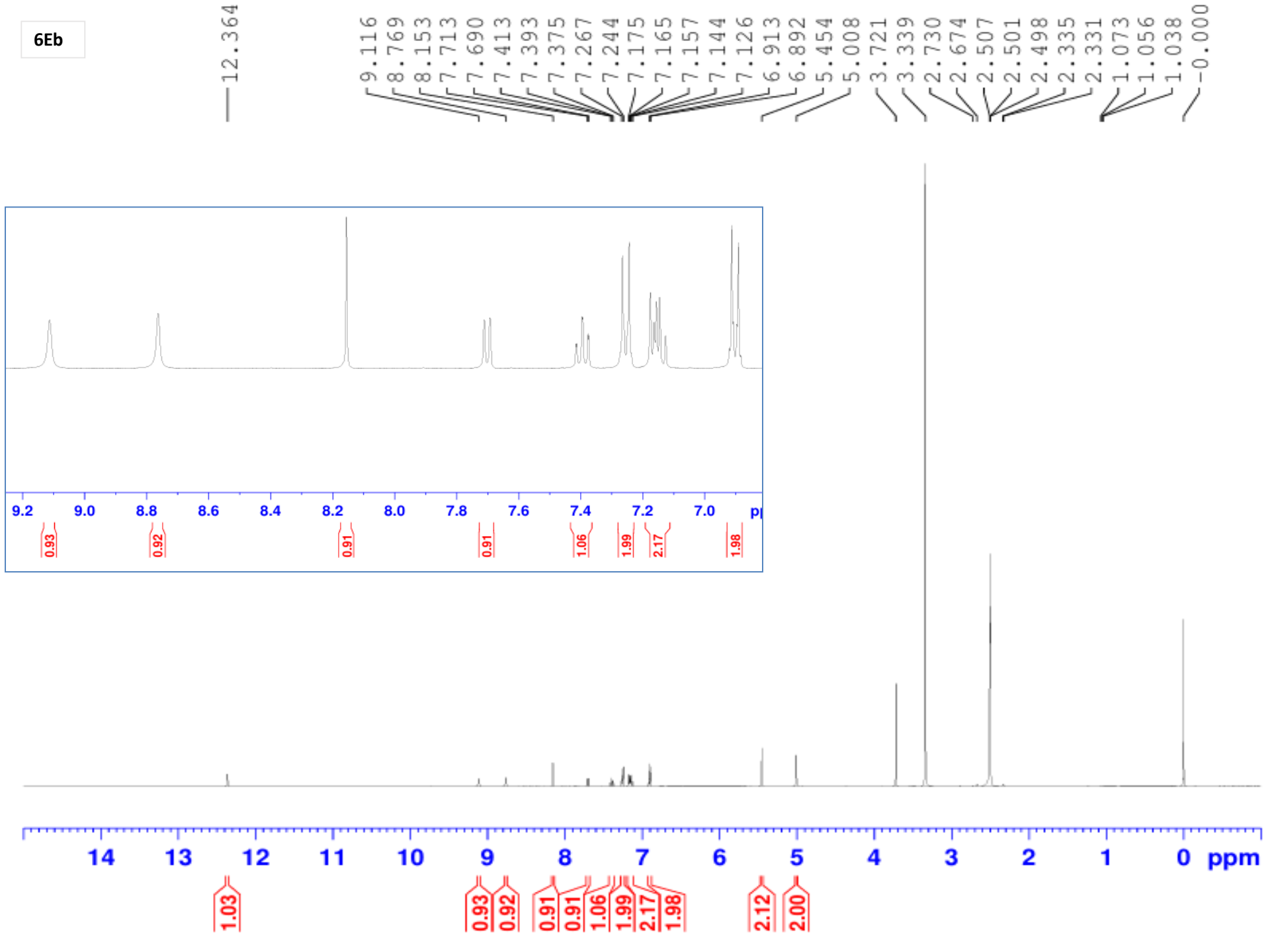
6Eb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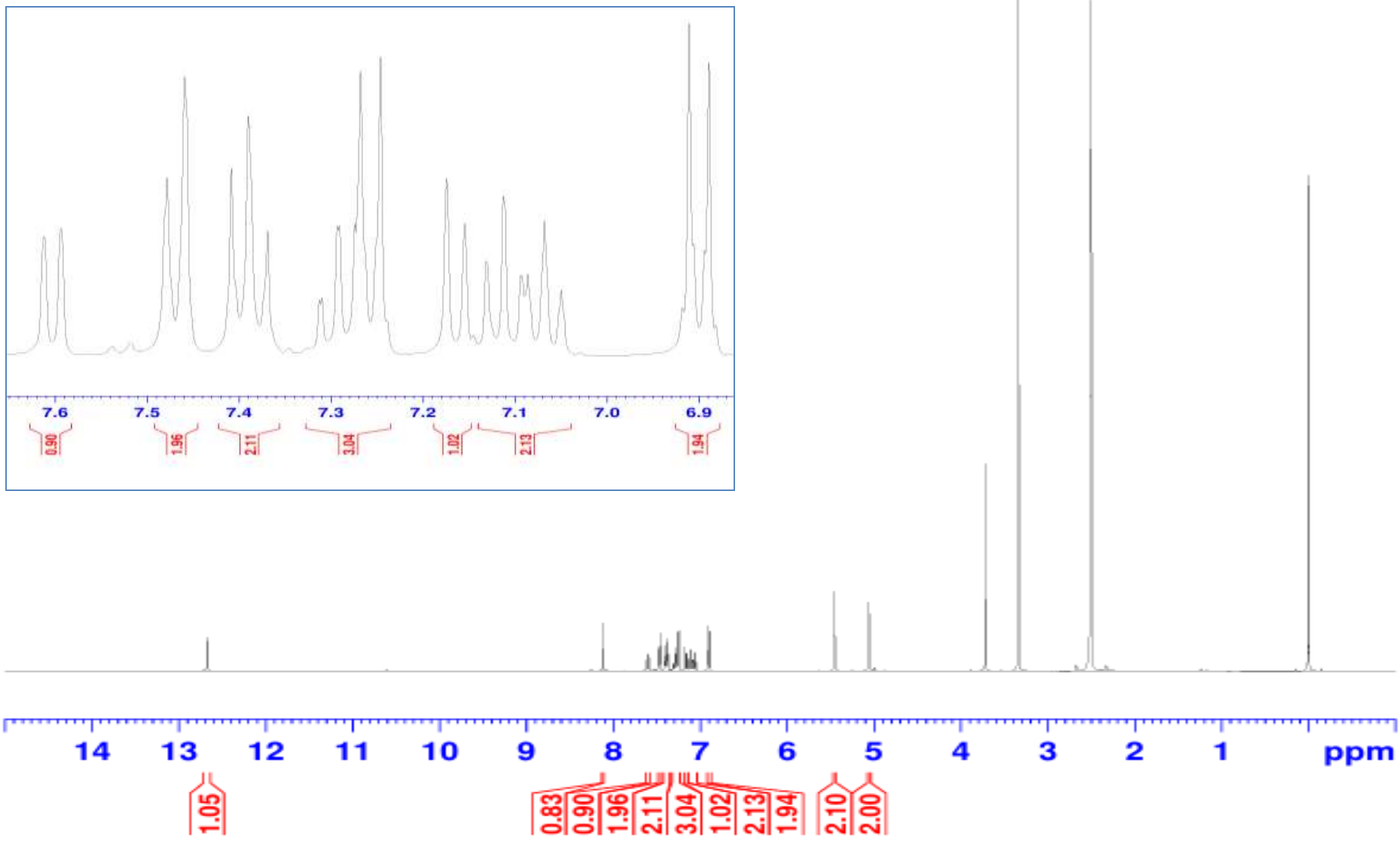
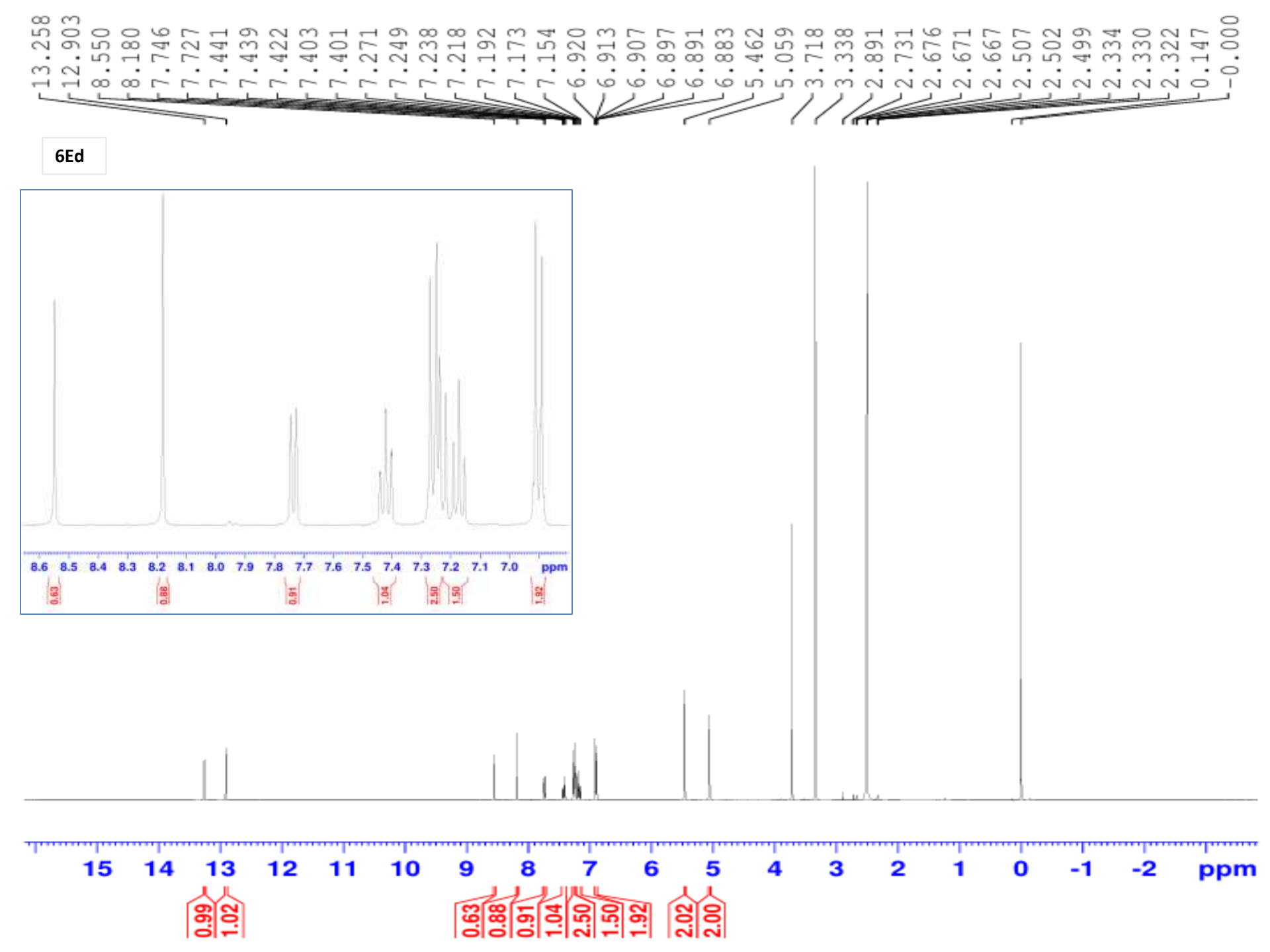
7.375
7.267
7.244
7.175
7.165
7.157
7.144
7.126
6.913
6.892
5.454
5.008
3.721
3.339
2.730
2.674
2.507
2.501
2.498
2.335
2.331
1.073
1.056
1.038
-0.000
9.2
9.0
8.8
8.6
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
0.93
0.92
0.91
0.91
1.06
1.99
2.17
1.98
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.03
0.93
0.92
0.91
0.91
1.06
1.99
2.17
1.98
2.12
2.00

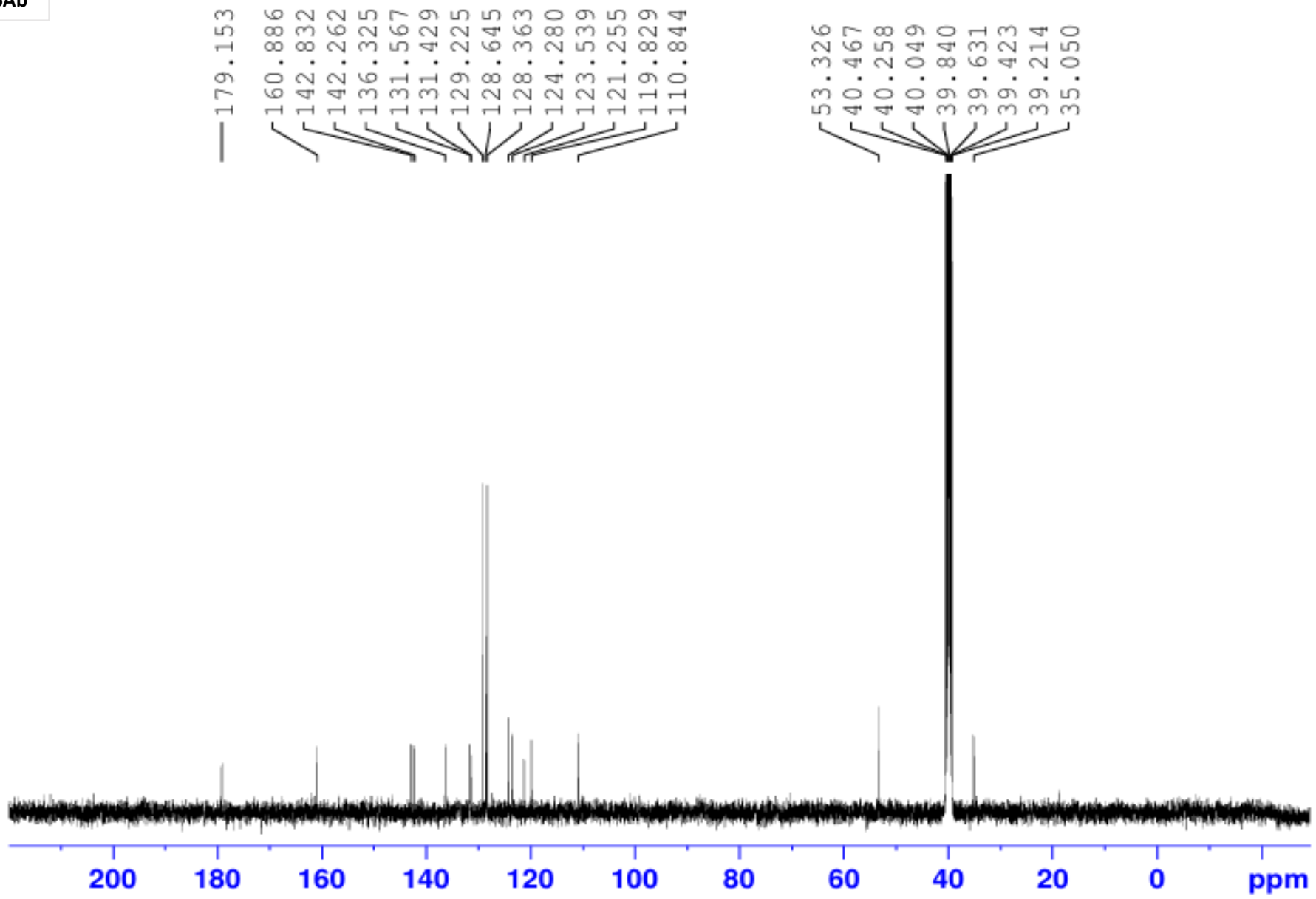
12.672 8.123 7.613 7.594 7.518 7.478 7.460 7.409 7.390 7.371 7.311 7.291 7.275 7.269 7.247 7.175 7.154 7.131 7.111 7.095 7.086 7.067 7.051 6.910 6.890 5.454 5.059 5.003 3.717 3.336 2.676 2.671 2.503 2.335 2.330 1.236 0.146 0.001

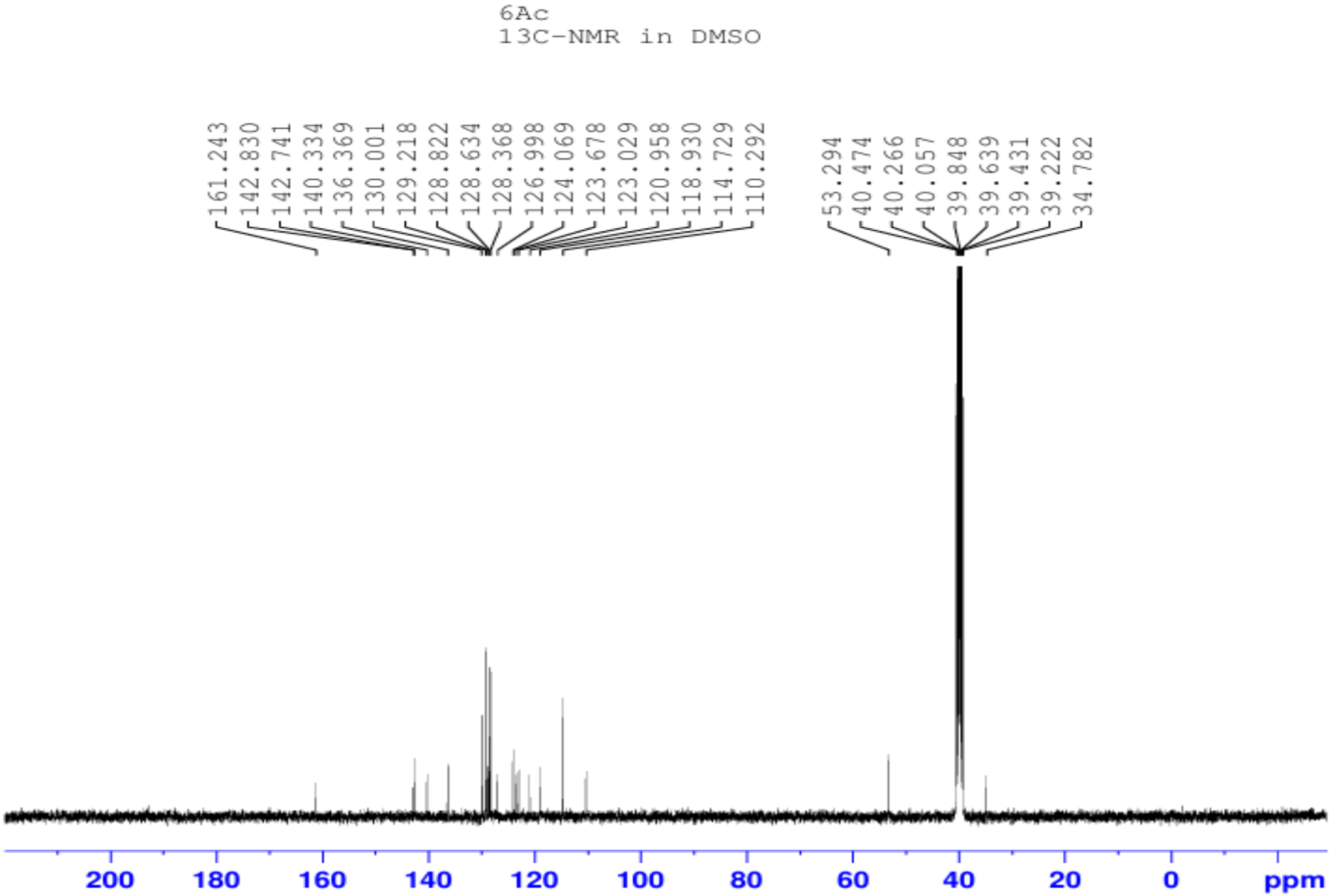
6Ec

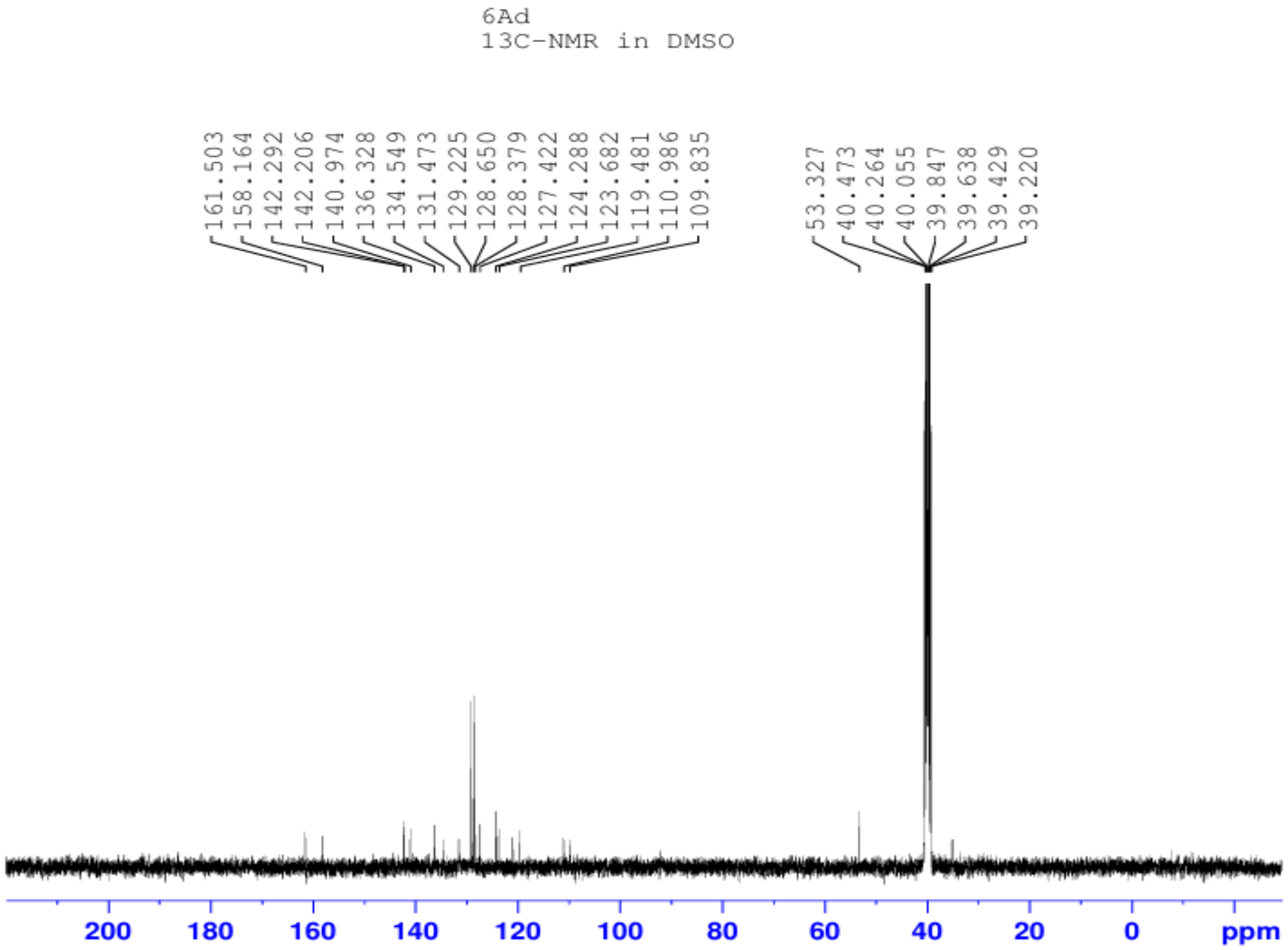


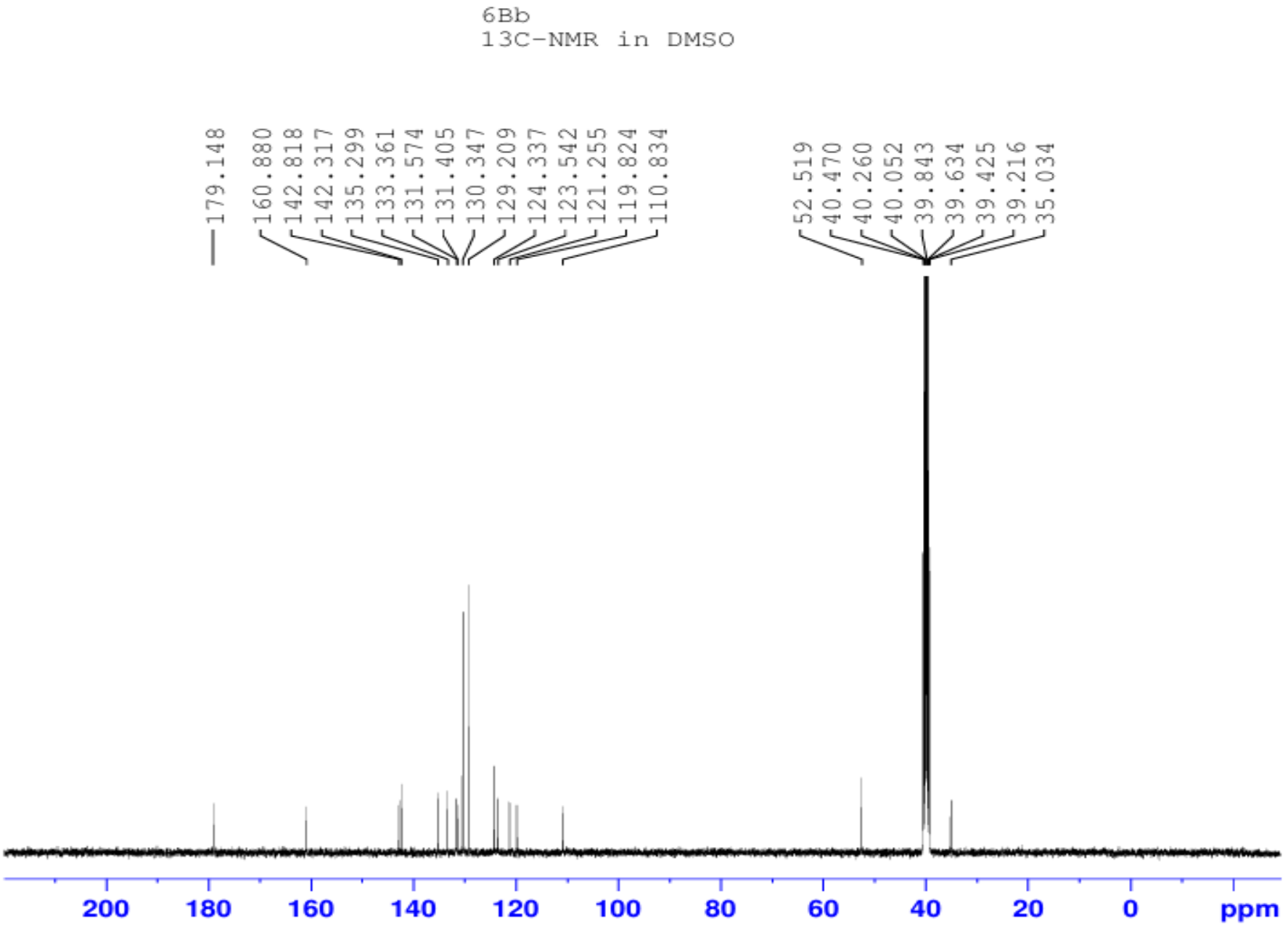

13.258
12.903
8.550
8.180
7.746
7.727
7.441
7.439
7.422
7.403
7.401
7.271
7.249
7.238
7.218
7.192
7.173
7.154
6.920
6.913
6.907
6.897
6.891
6.883
5.462
5.059
3.718
3.338
2.891
2.731
2.676
2.671
2.667
2.507
2.502
2.499
2.334
2.330
2.322
0.147
-0.000
6Ed
8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 ppm
0.63
0.88
0.91
1.04
2.50
1.50
1.92
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 ppm
0.99
1.02
0.63
0.88
0.91
1.04
2.50
1.50
1.92
2.02
2.00

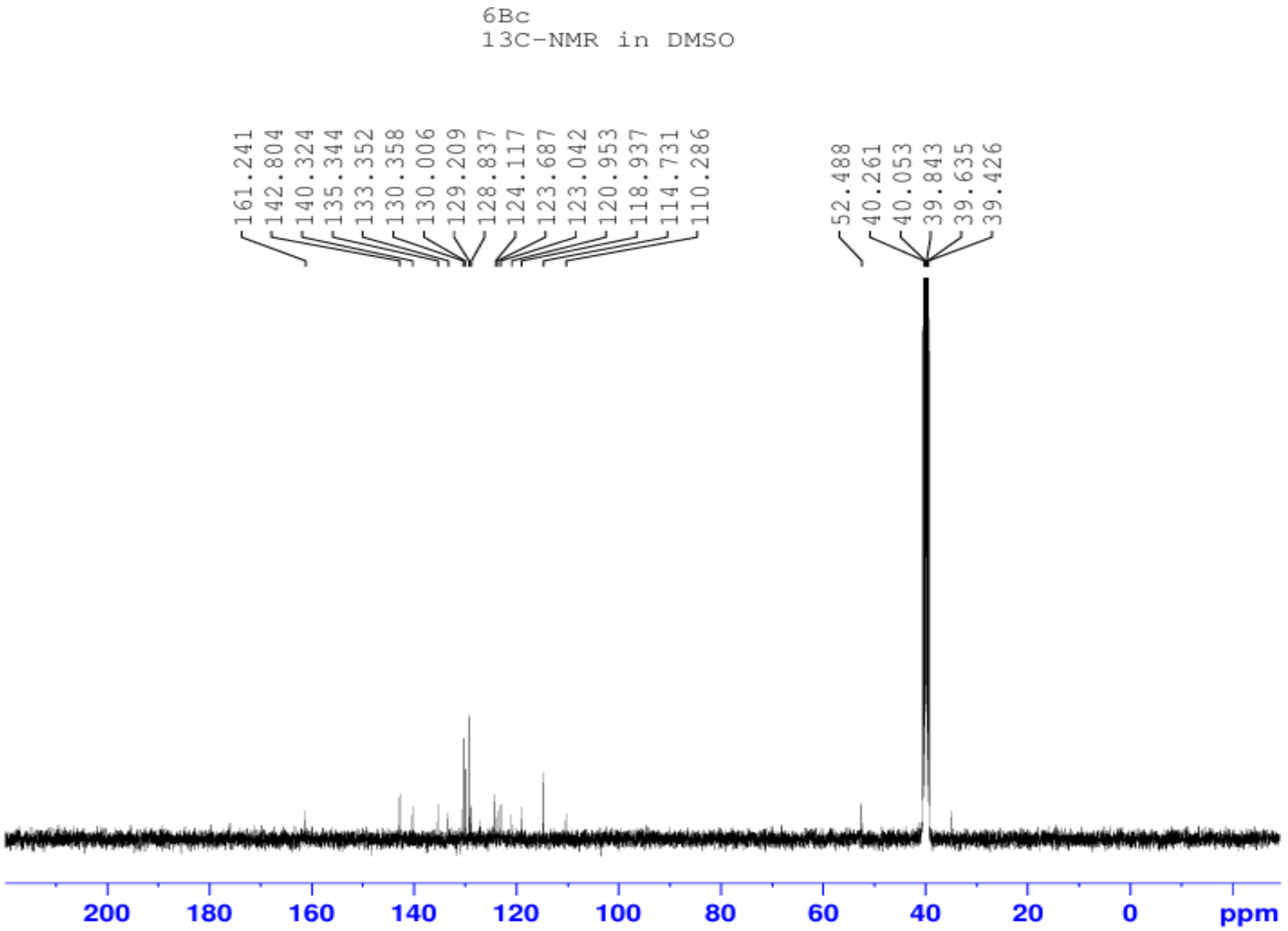
6Ab

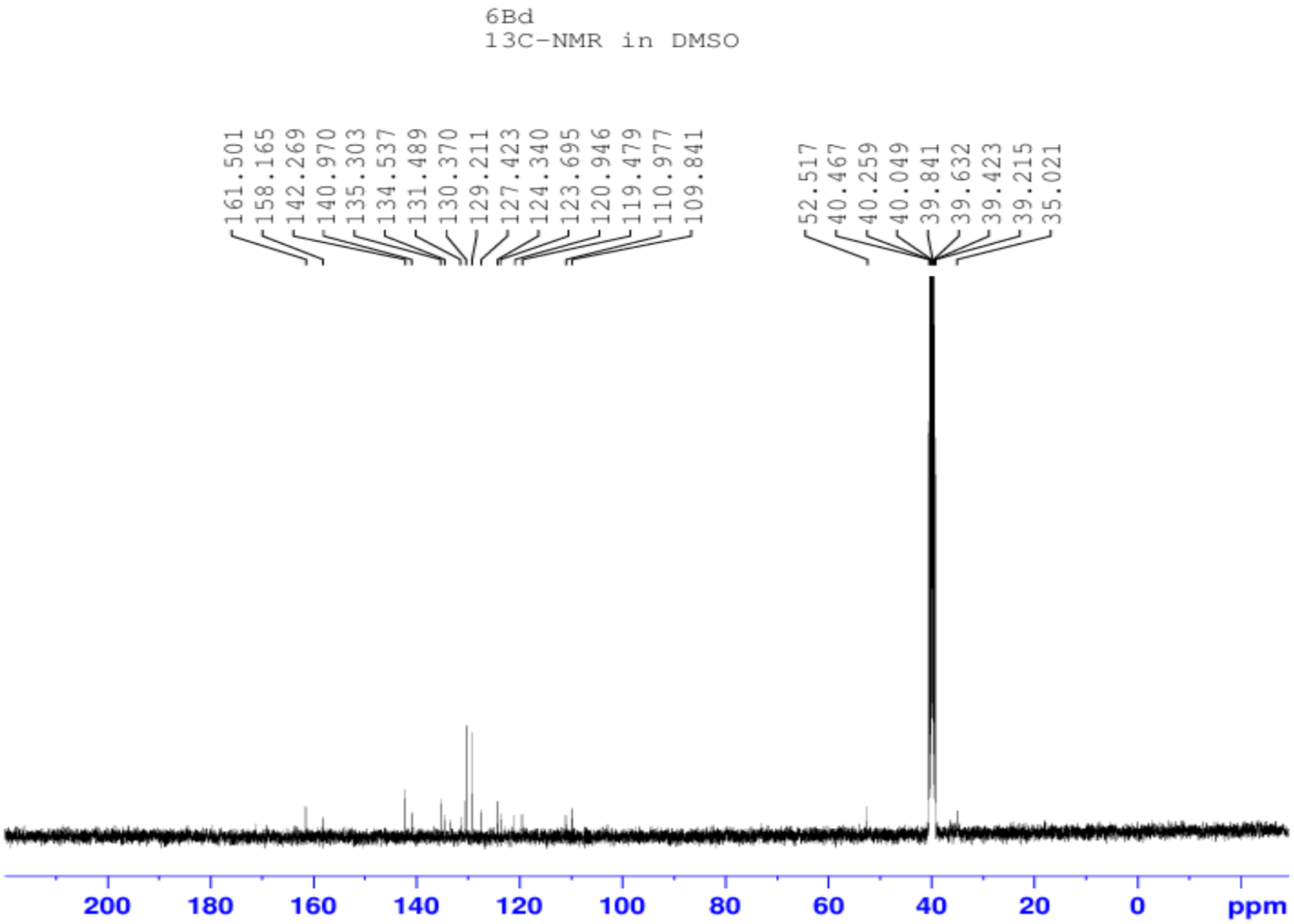

179.153
160.886
142.832
142.262
136.325
131.567
131.429
129.225
128.645
128.363
124.280
123.539
121.255
119.829
110.844
53.326
40.467
40.258
40.049
39.840
39.631
39.423
39.214
35.050
200
180
160
140
120
100
80
60
40
20
0
ppm

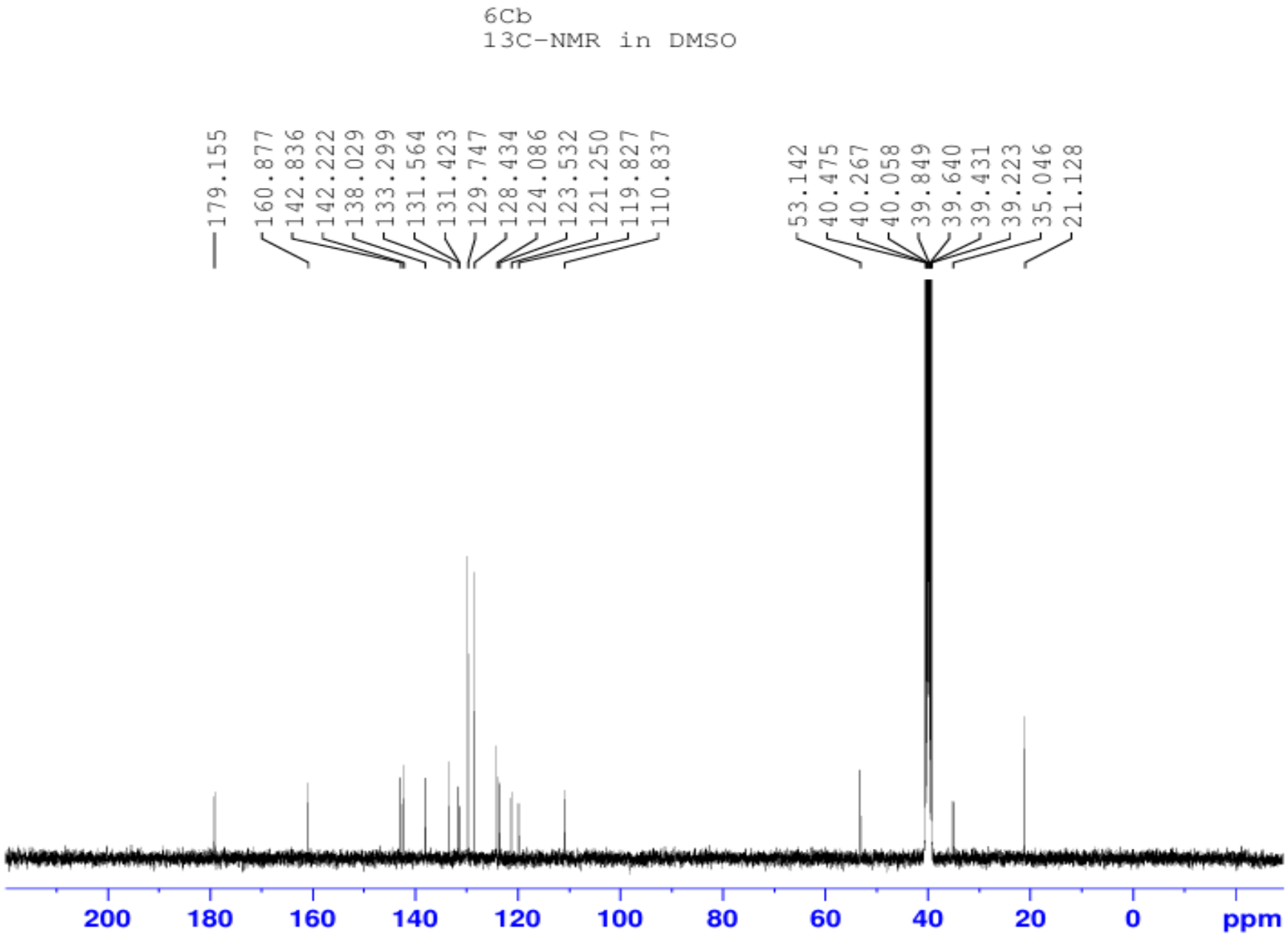

6Ac
13C-NMR in DMSO
161.243
142.830
142.741
140.334
136.369
130.001
129.218
128.822
128.634
128.368
126.998
124.069
123.678
123.029
120.958
118.930
114.729
110.292
53.294
40.474
40.266
40.057
39.848
39.639
39.431
39.222
34.782
200
180
160
140
120
100
80
60
40
20
0
ppm

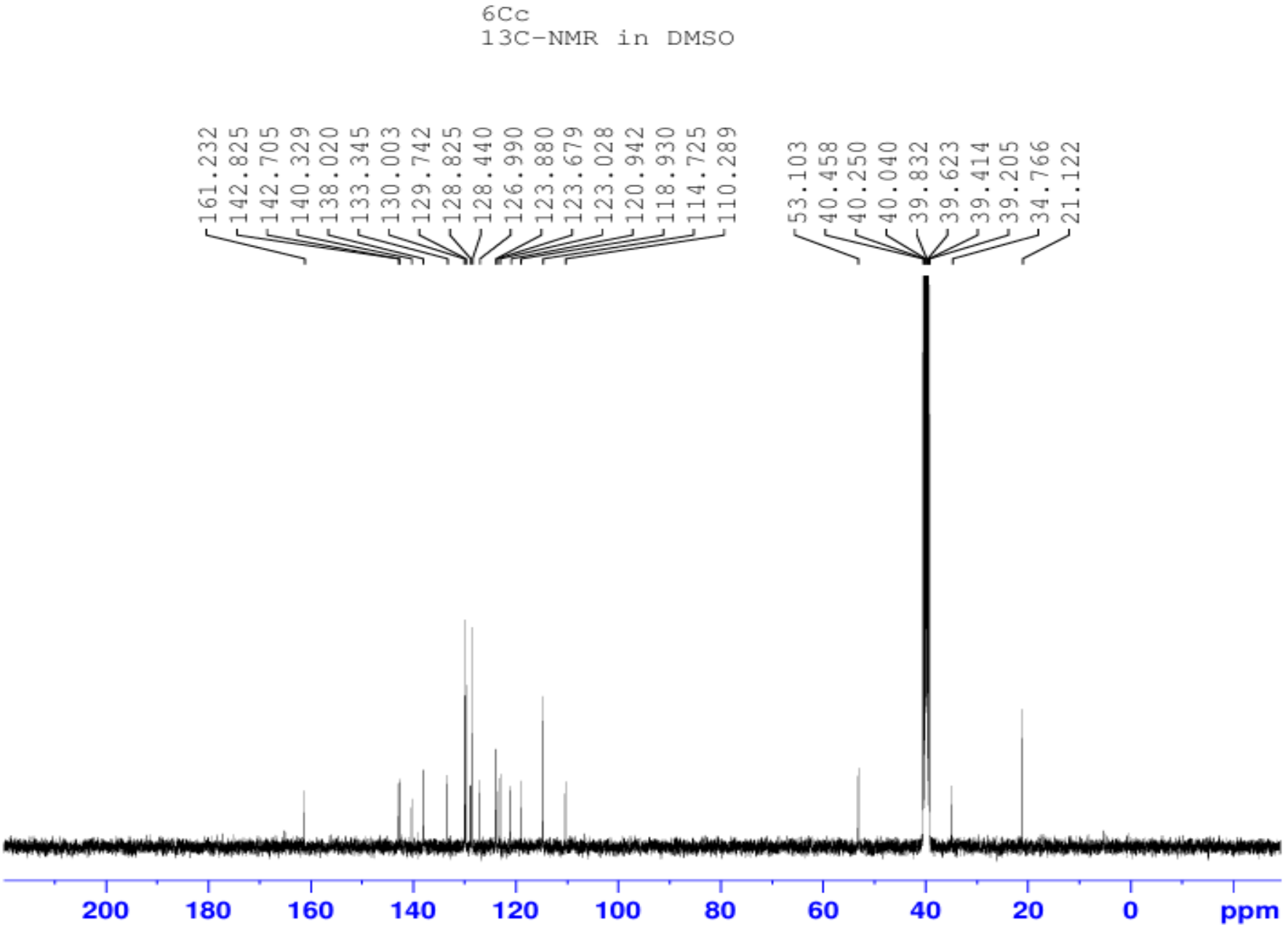

6Ad
13C-NMR in DMSO
161.503
158.164
142.292
142.206
140.974
136.328
134.549
131.473
129.225
128.650
128.379
127.422
124.288
123.682
119.481
110.986
109.835
53.327
40.473
40.264
40.055
39.847
39.638
39.429
39.220
200
180
160
140
120
100
80
60
40
20
0
ppm

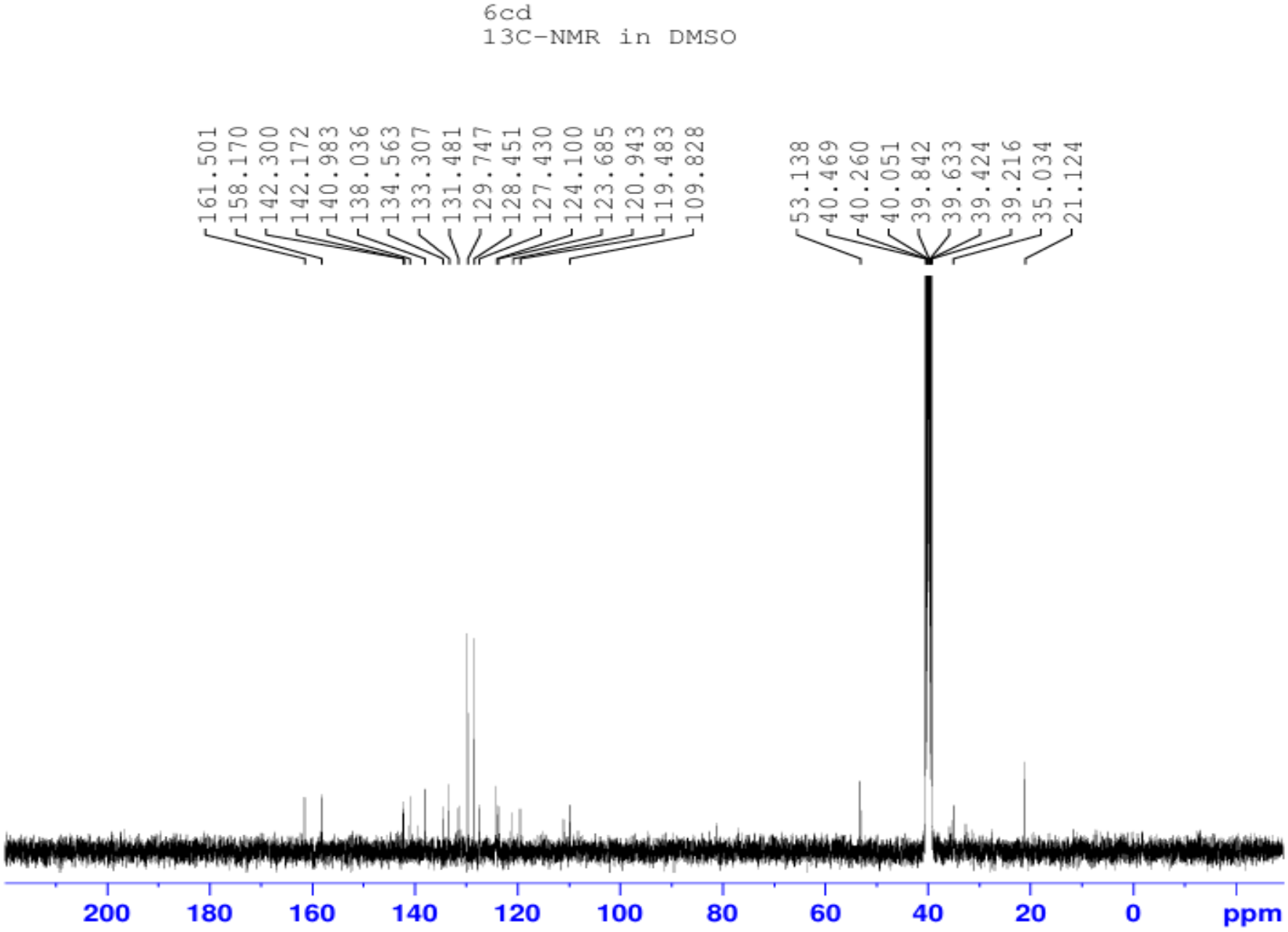

6Bb
13C-NMR in DMSO
179.148
160.880
142.818
142.317
135.299
133.361
131.574
131.405
130.347
129.209
124.337
123.542
121.255
119.824
110.834
52.519
40.470
40.260
40.052
39.843
39.634
39.425
39.216
35.034
200
180
160
140
120
100
80
60
40
20
0
ppm

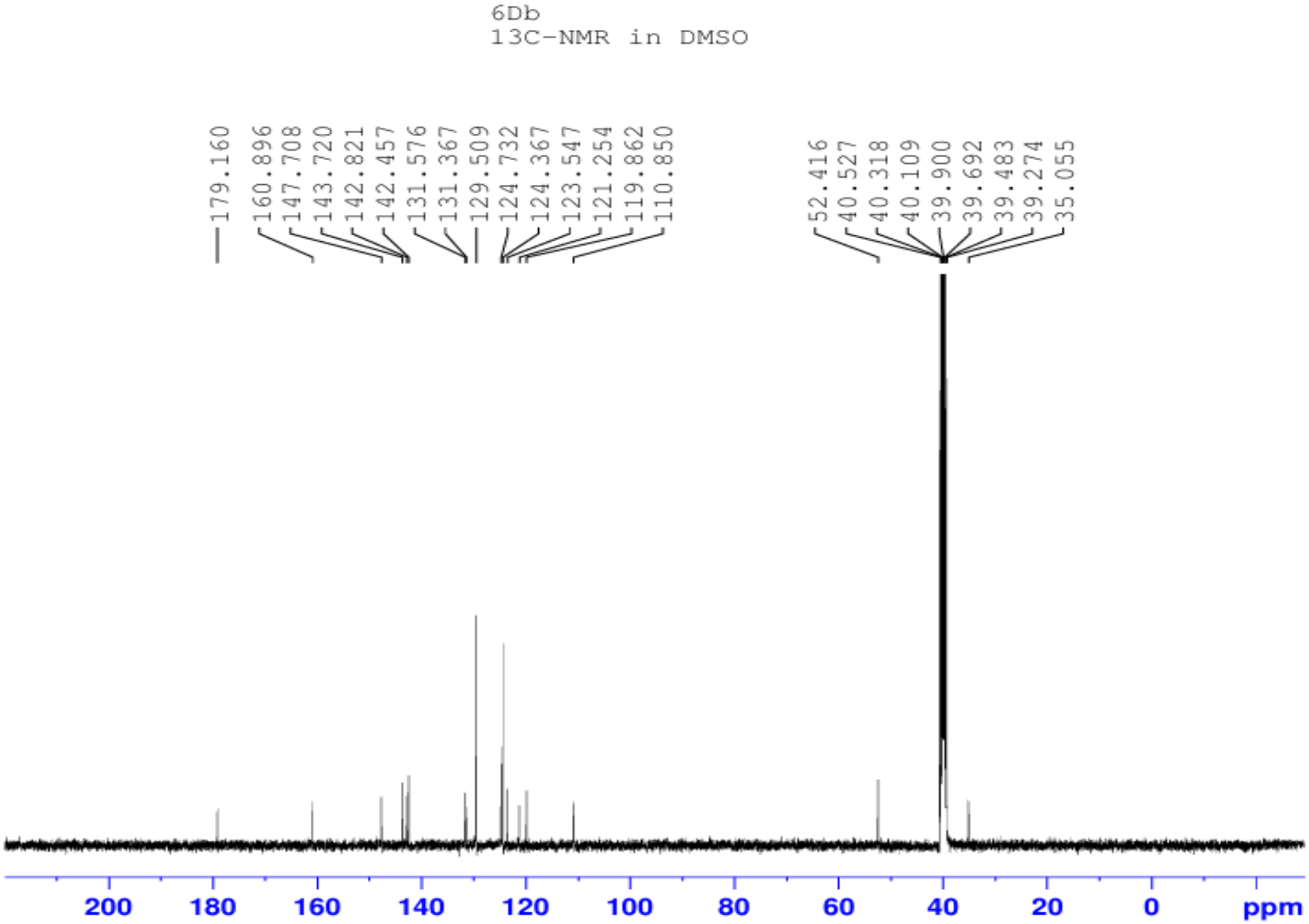

6Bc
13C-NMR in DMSO
161.241
142.804
140.324
135.344
133.352
130.358
130.006
129.209
128.837
124.117
123.687
123.042
120.953
118.937
114.731
110.286
52.488
40.261
40.053
39.843
39.635
39.426
200
180
160
140
120
100
80
60
40
20
0
ppm

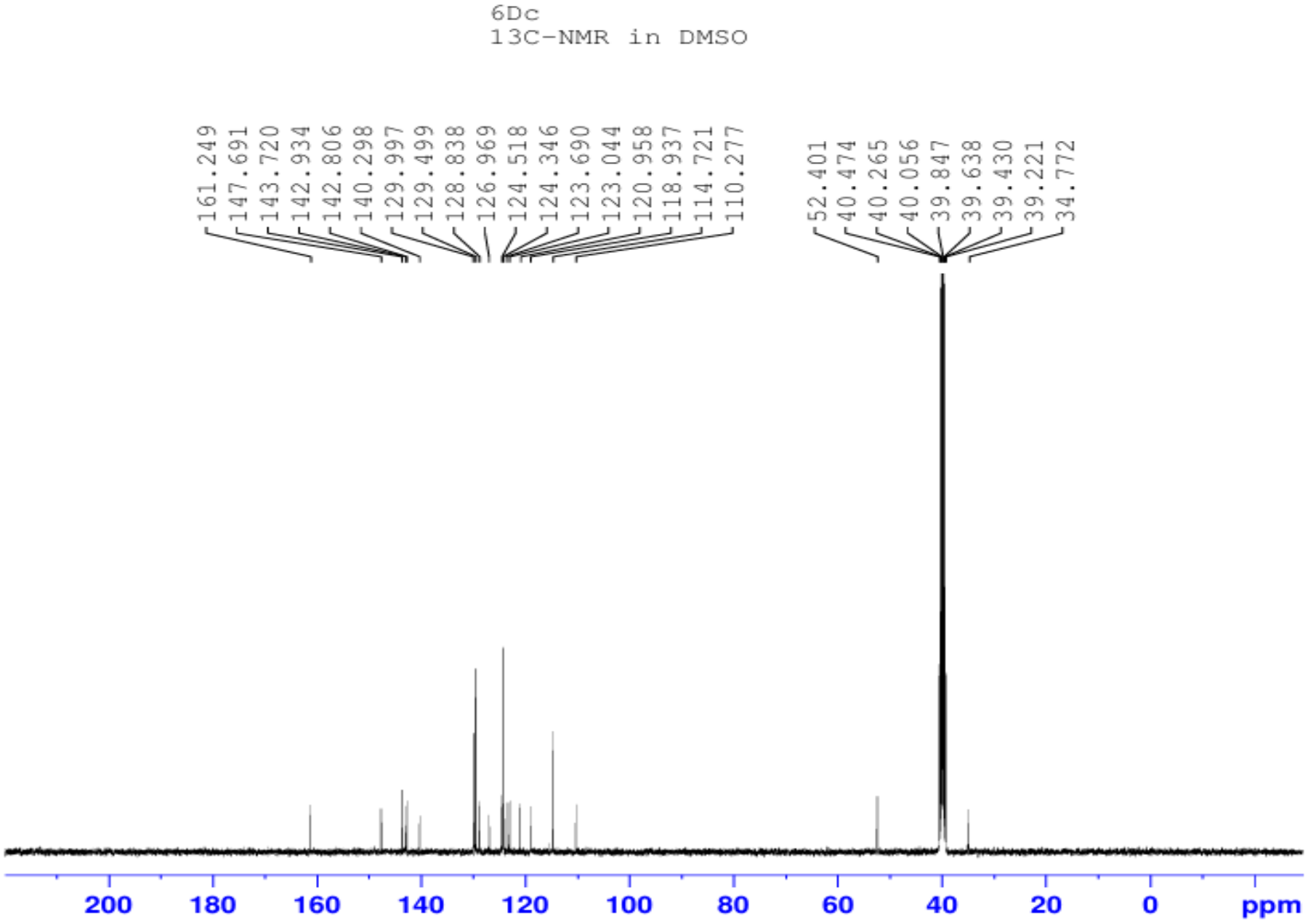

6Bd
13C-NMR in DMSO
161.501
158.165
142.269
140.970
135.303
134.537
131.489
130.370
129.211
127.423
124.340
123.695
120.946
119.479
110.977
109.841
52.517
40.467
40.259
40.049
39.841
39.632
39.423
39.215
35.021
200
180
160
140
120
100
80
60
40
20
0
ppm

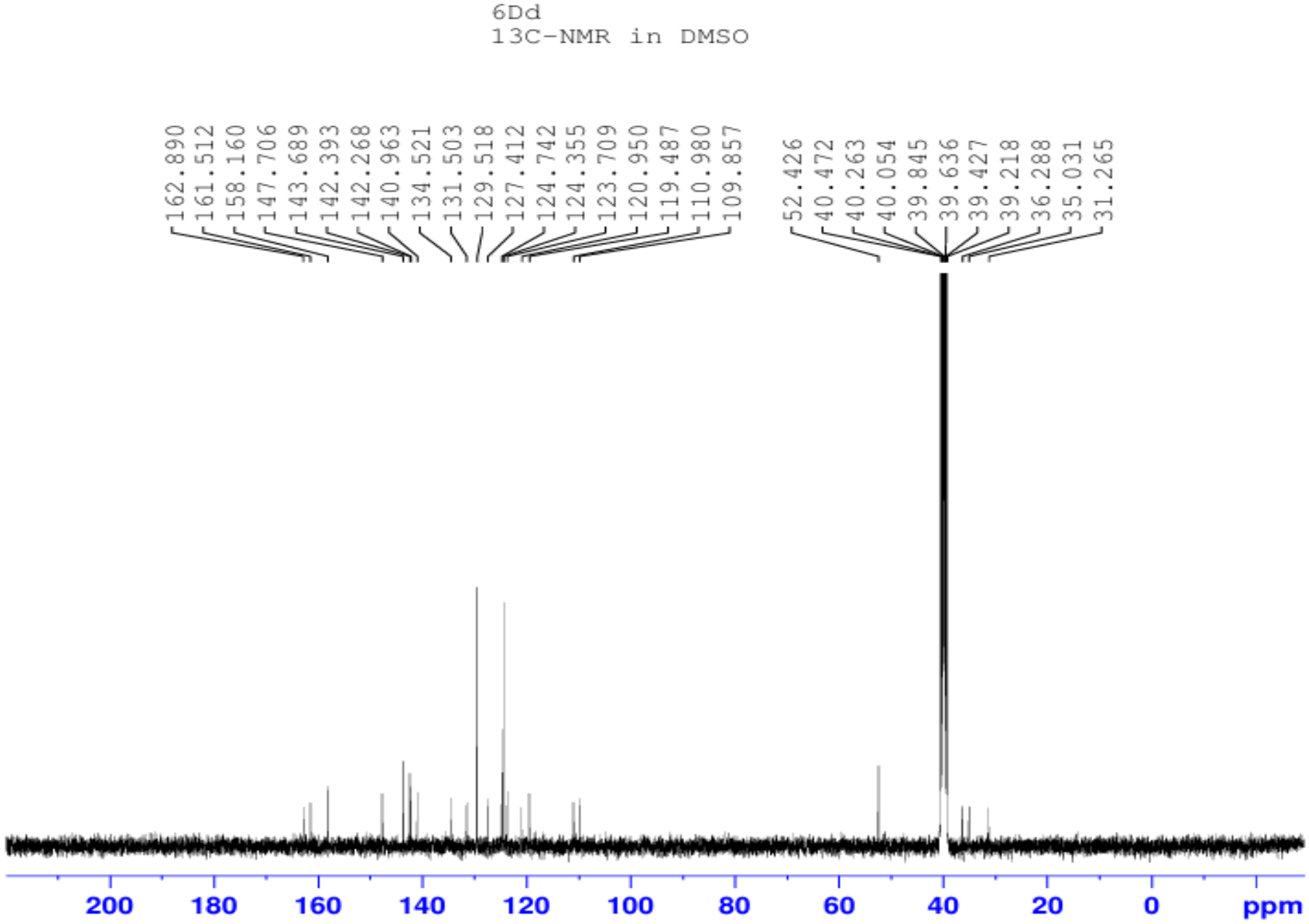

6Cb
13C-NMR in DMSO
179.155
160.877
142.836
142.222
138.029
133.299
131.564
131.423
129.747
128.434
124.086
123.532
121.250
119.827
110.837
53.142
40.475
40.267
40.058
39.849
39.640
39.431
39.223
35.046
21.128
200
180
160
140
120
100
80
60
40
20
0
ppm

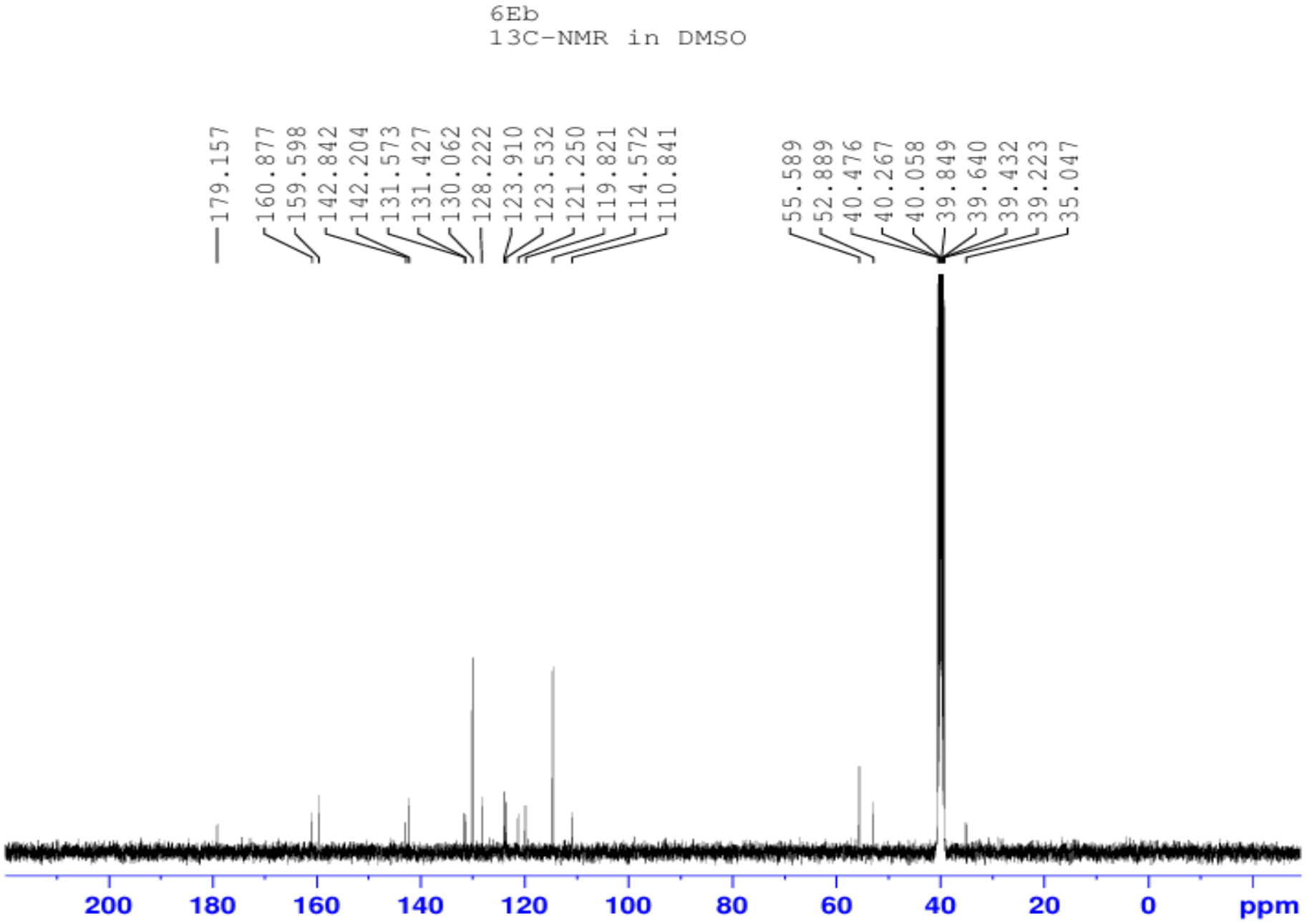

6Cc
13C-NMR in DMSO
161.232
142.825
142.705
140.329
138.020
133.345
130.003
129.742
128.825
128.440
126.990
123.880
123.679
123.028
120.942
118.930
114.725
110.289
53.103
40.458
40.250
40.040
39.832
39.623
39.414
39.205
34.766
21.122
200
180
160
140
120
100
80
60
40
20
0
ppm


6cd
13C-NMR in DMSO
161.501
158.170
142.300
142.172
140.983
138.036
134.563
133.307
131.481
129.747
128.451
127.430
124.100
123.685
120.943
119.483
109.828
53.138
40.469
40.260
40.051
39.842
39.633
39.424
39.216
35.034
21.124
200
180
160
140
120
100
80
60
40
20
0
ppm

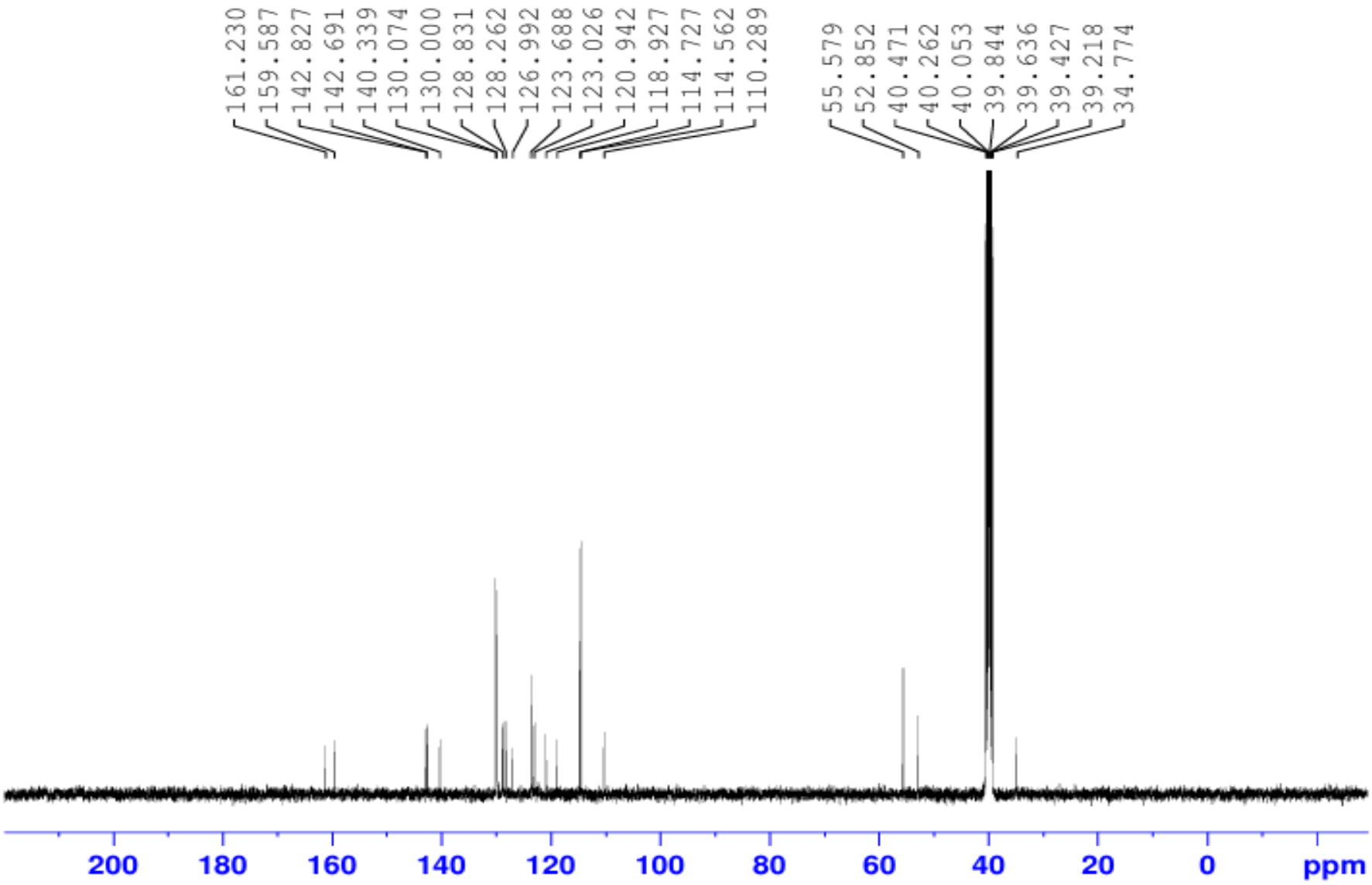

6Db
13C-NMR in DMSO
179.160
160.896
147.708
143.720
142.821
142.457
131.576
131.367
129.509
124.732
124.367
123.547
121.254
119.862
110.850
52.416
40.527
40.318
40.109
39.900
39.692
39.483
39.274
35.055
200
180
160
140
120
100
80
60
40
20
0
ppm

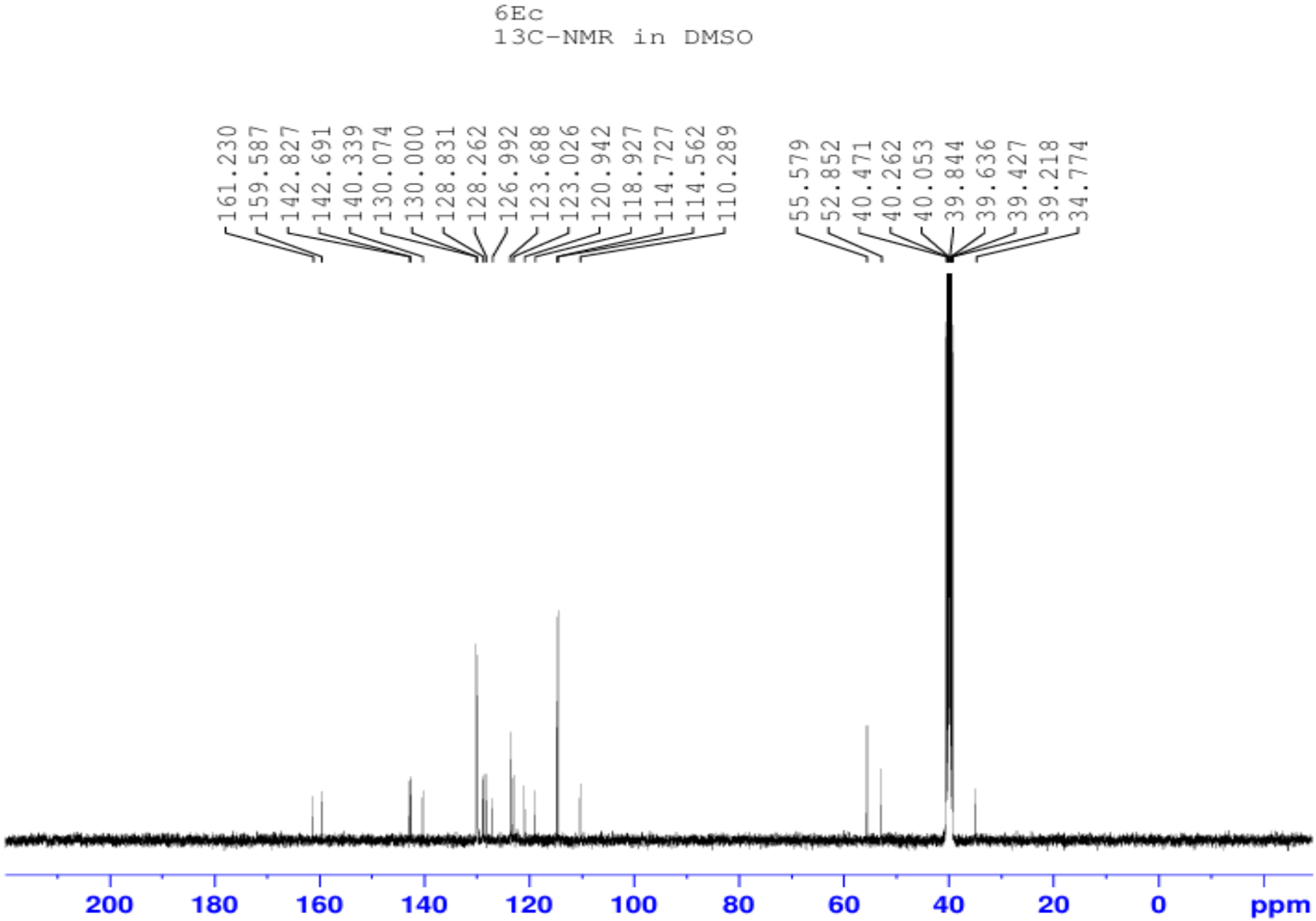

6Dc
13C-NMR in DMSO
161.249
147.691
143.720
142.934
142.806
140.298
129.997
129.499
128.838
126.969
124.518
124.346
123.690
123.044
120.958
118.937
114.721
110.277
52.401
40.474
40.265
40.056
39.847
39.638
39.430
39.221
34.772
200
180
160
140
120
100
80
60
40
20
0
ppm

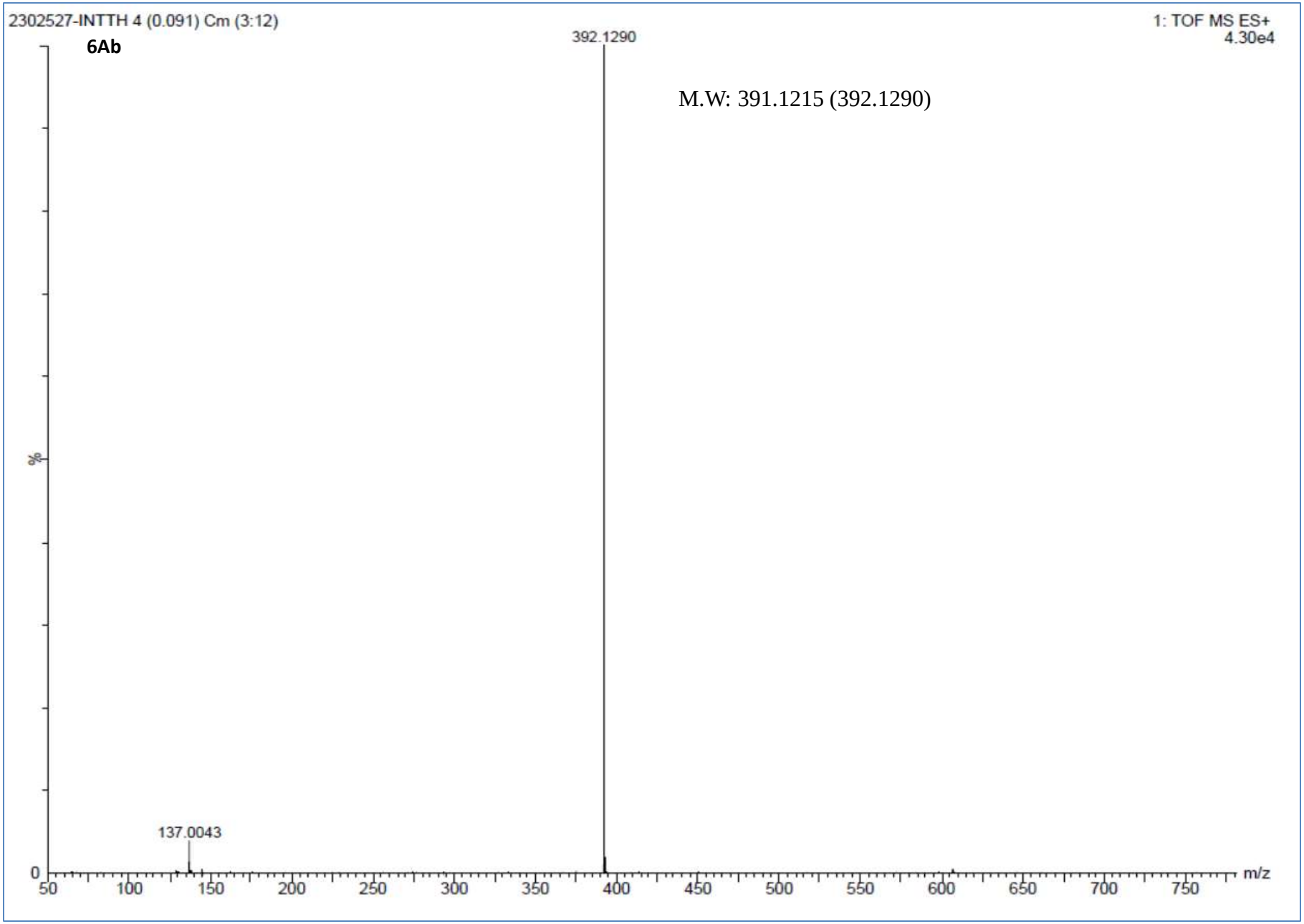

6Dd
13C-NMR in DMSO
162.890
161.512
158.160
147.706
143.689
142.393
142.268
140.963
134.521
131.503
129.518
127.412
124.742
124.355
123.709
120.950
119.487
110.980
109.857
52.426
40.472
40.263
40.054
39.845
39.636
39.427
39.218
36.288
35.031
31.265
200
180
160
140
120
100
80
60
40
20
0
ppm

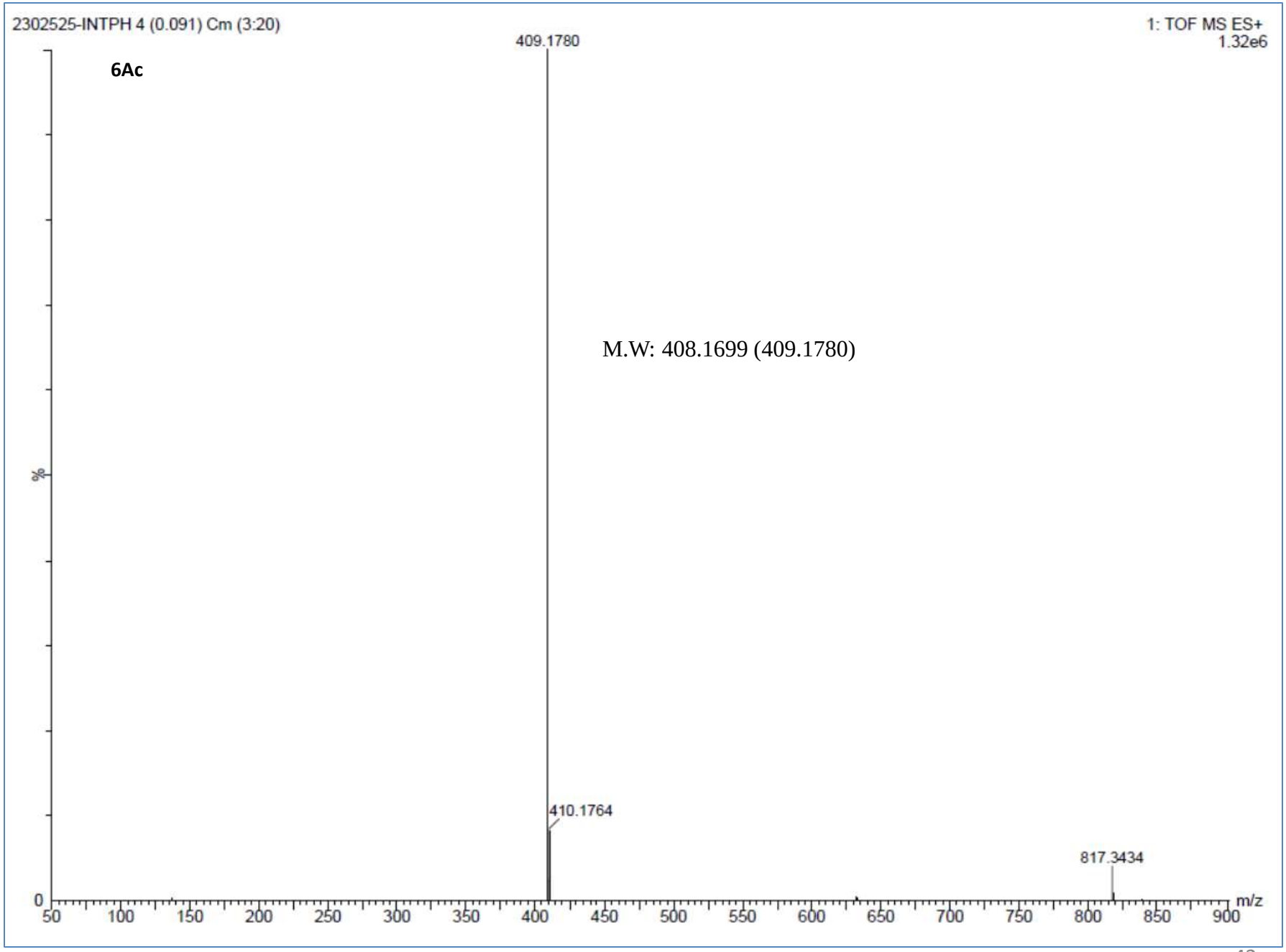

6Eb
13C-NMR in DMSO
179.157
160.877
159.598
142.842
142.204
131.573
131.427
130.062
128.222
123.910
123.532
121.250
119.821
114.572
110.841
55.589
52.889
40.476
40.267
40.058
39.849
39.640
39.432
39.223
35.047
200
180
160
140
120
100
80
60
40
20
0
ppm

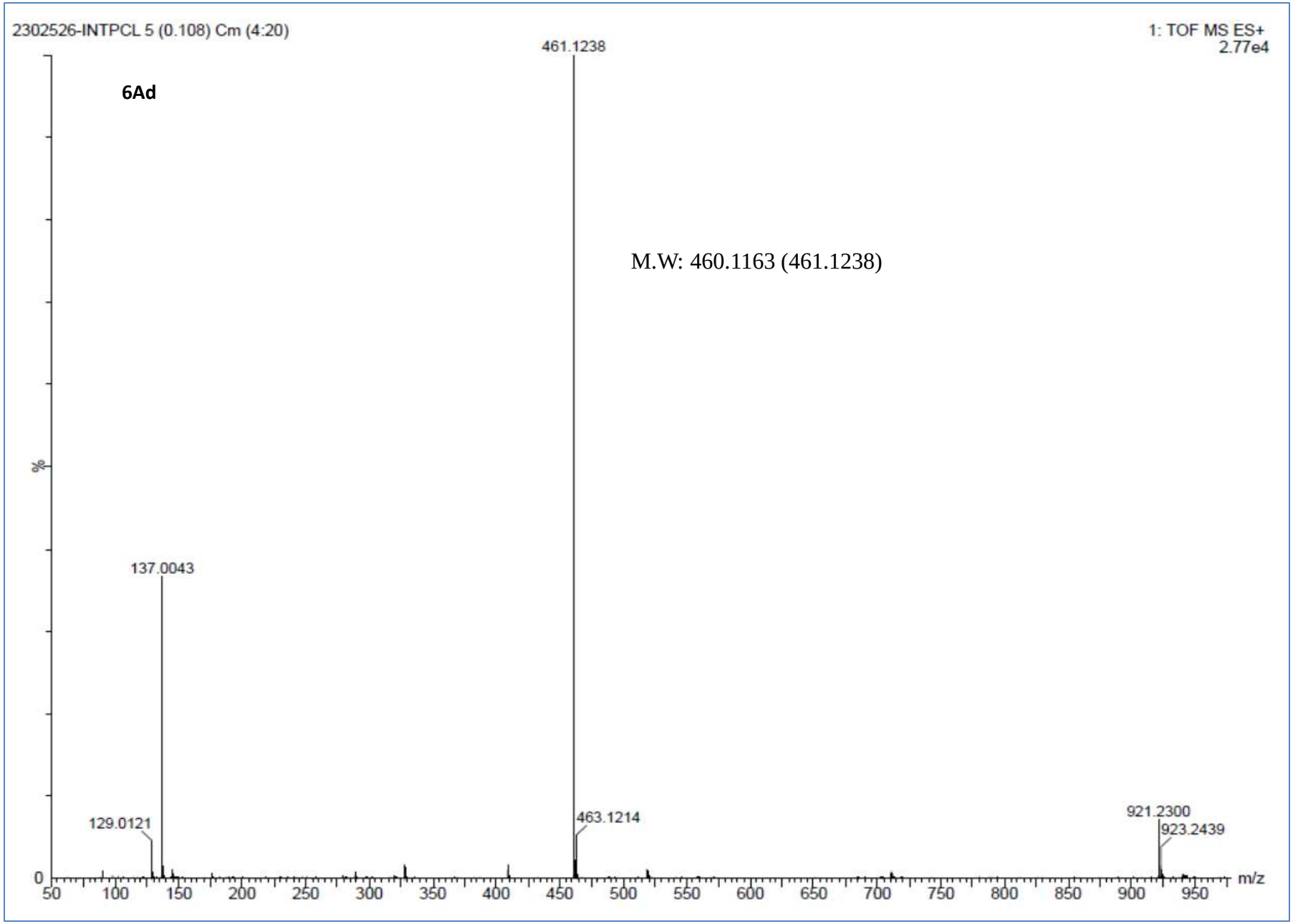
6Ec
13C-NMR in DMSO

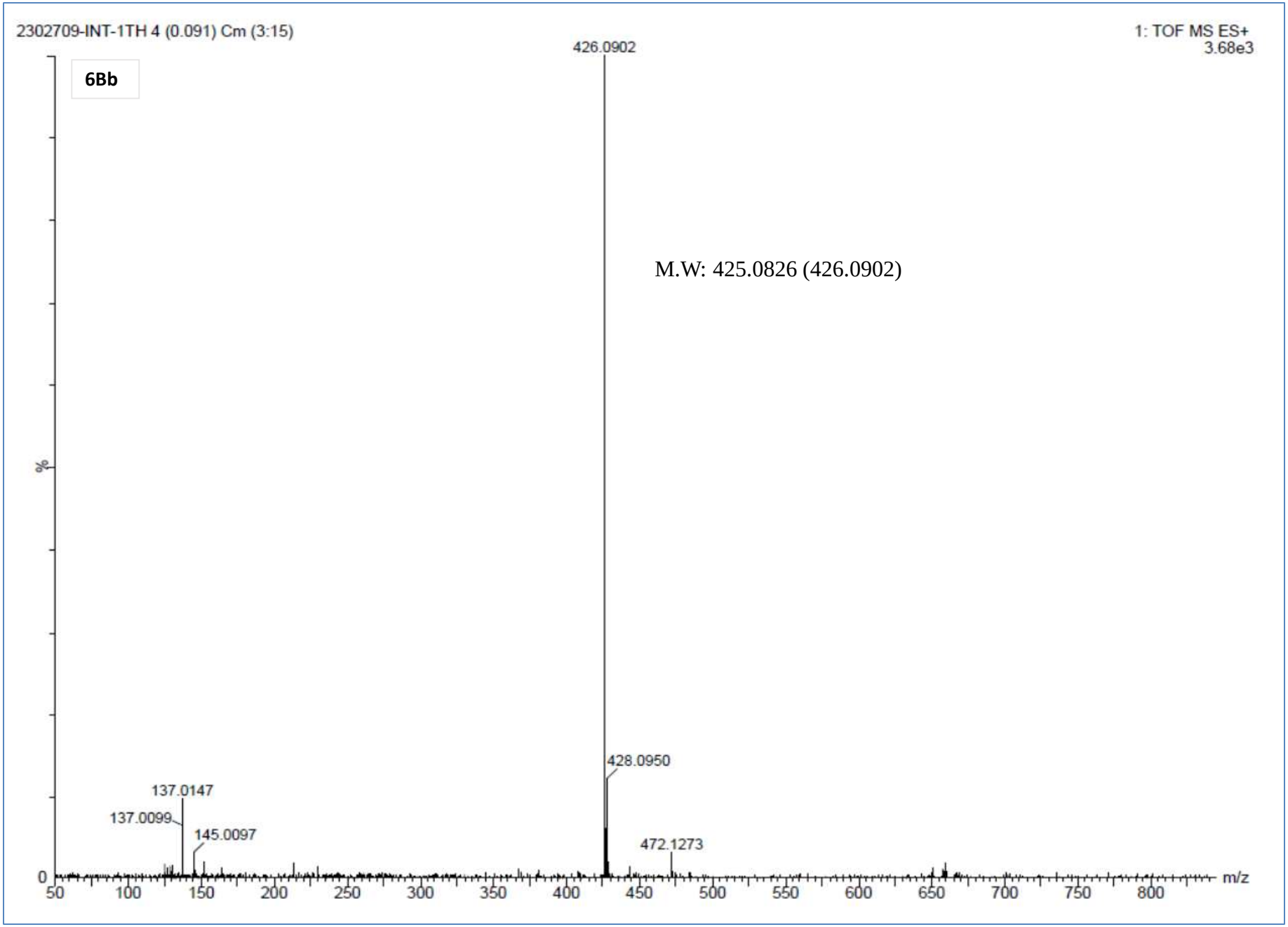


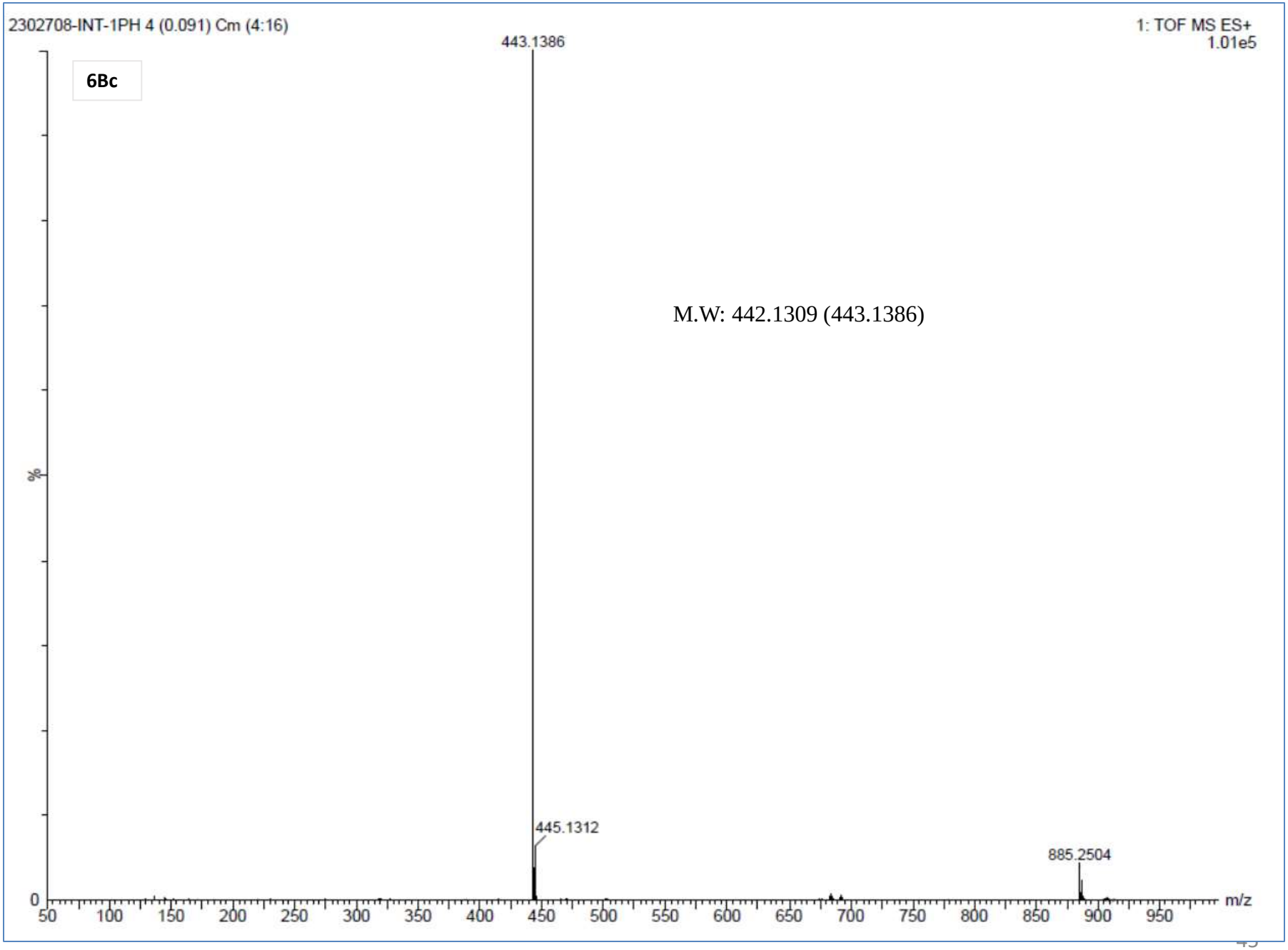

6Ec
13C-NMR in DMSO
161.230
159.587
142.827
142.691
140.339
130.074
130.000
128.831
128.262
126.992
123.688
123.026
120.942
118.927
114.727
114.562
110.289
55.579
52.852
40.471
40.262
40.053
39.844
39.636
39.427
39.218
34.774
200
180
160
140
120
100
80
60
40
20
0
ppm


2302527-INTTH 4 (0.091) Cm (3:12)
6Ab
1: TOF MS ES+
4.30e4
392.1290
M.W: 391.1215 (392.1290)
137.0043
%
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
m/z

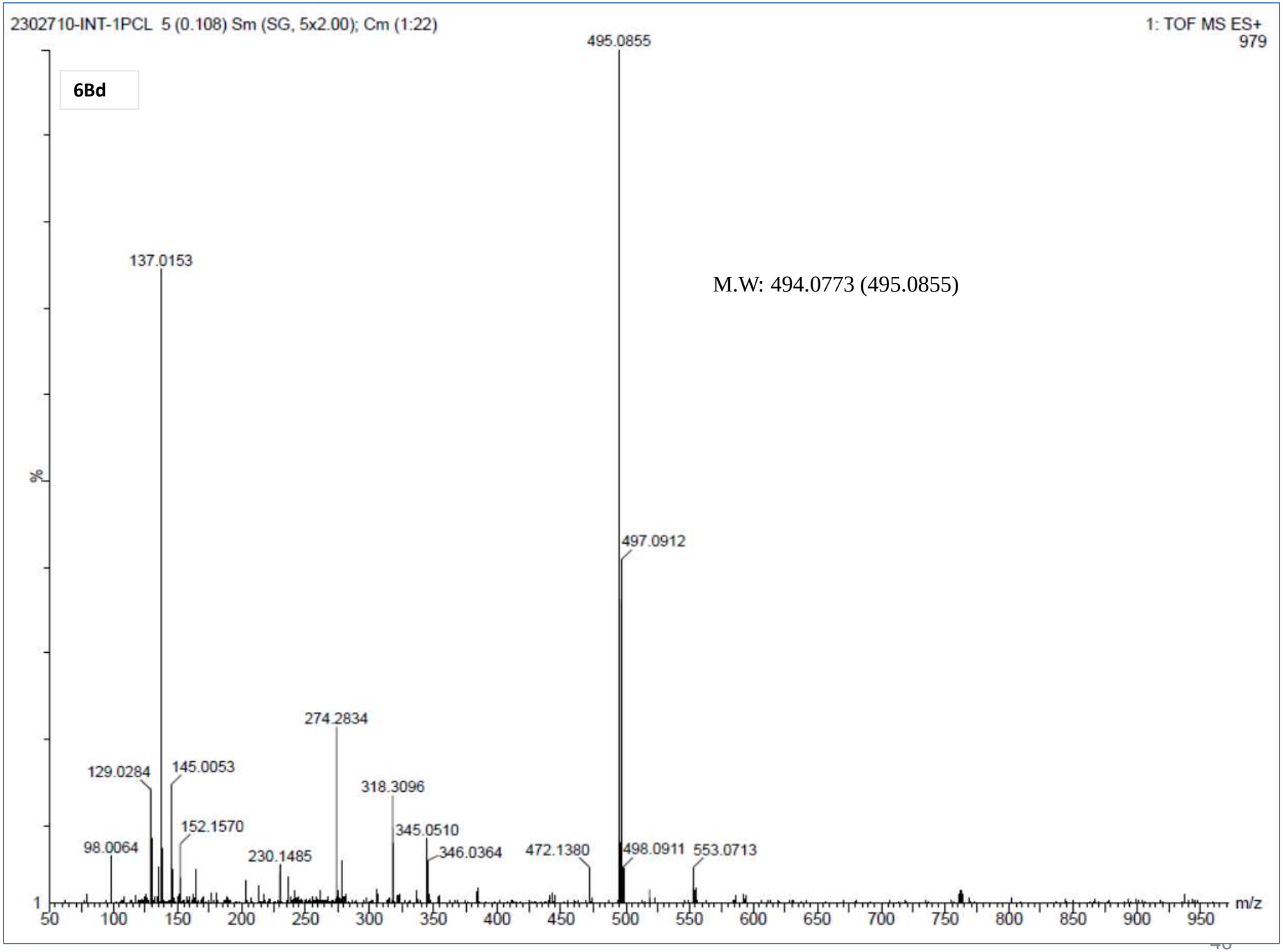

2302525-INTPH 4 (0.091) Cm (3:20)
1: TOF MS ES+
1.32e6
6Ac
409.1780
M.W: 408.1699 (409.1780)
%
410.1764
817.3434
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900
m/z

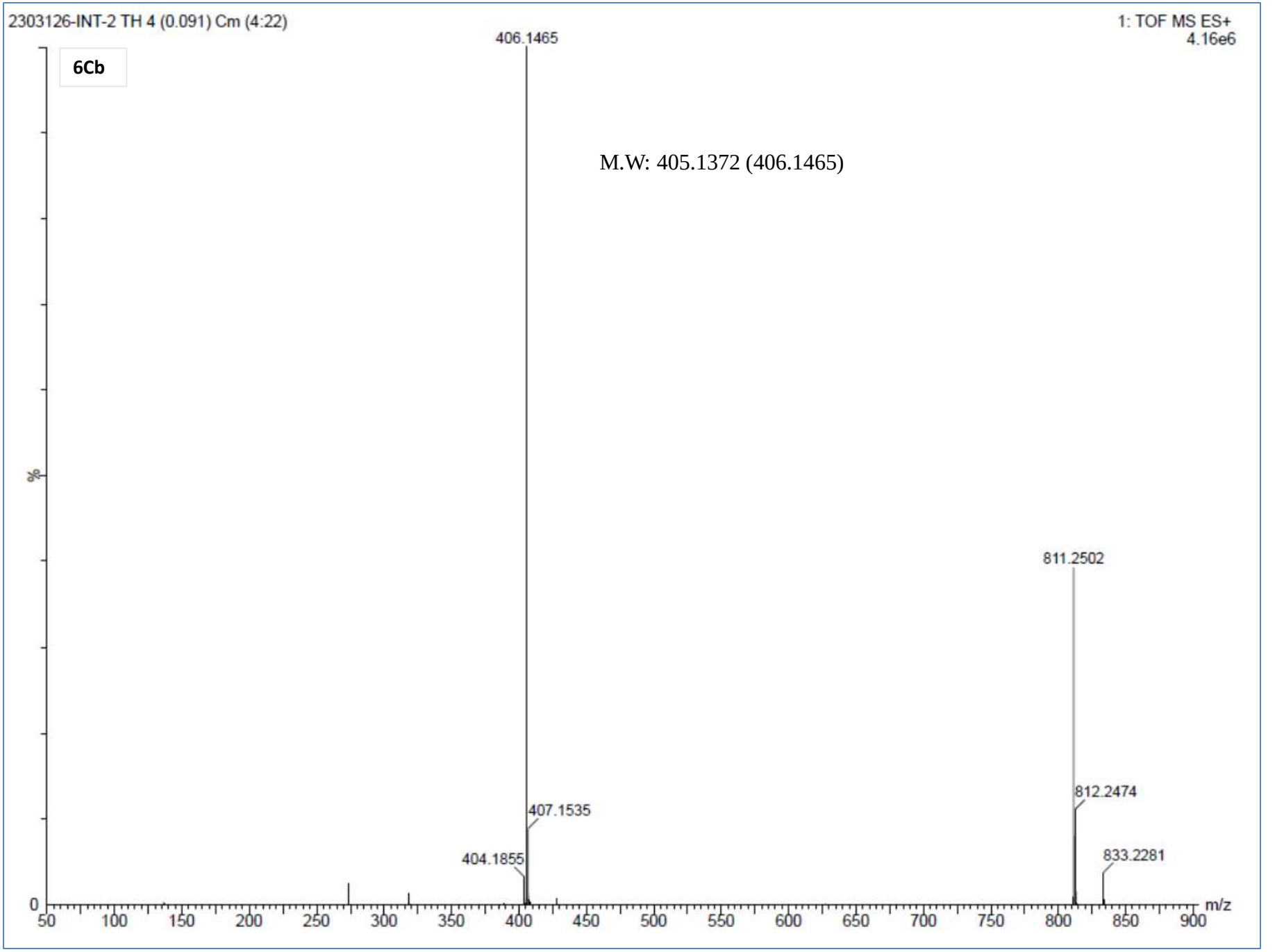

2302526-INTPCL 5 (0.108) Cm (4:20)
1: TOF MS ES+
2.77e4
6Ad
461.1238
M.W: 460.1163 (461.1238)
%
137.0043
129.0121
463.1214
921.2300
923.2439
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900
950
m/z

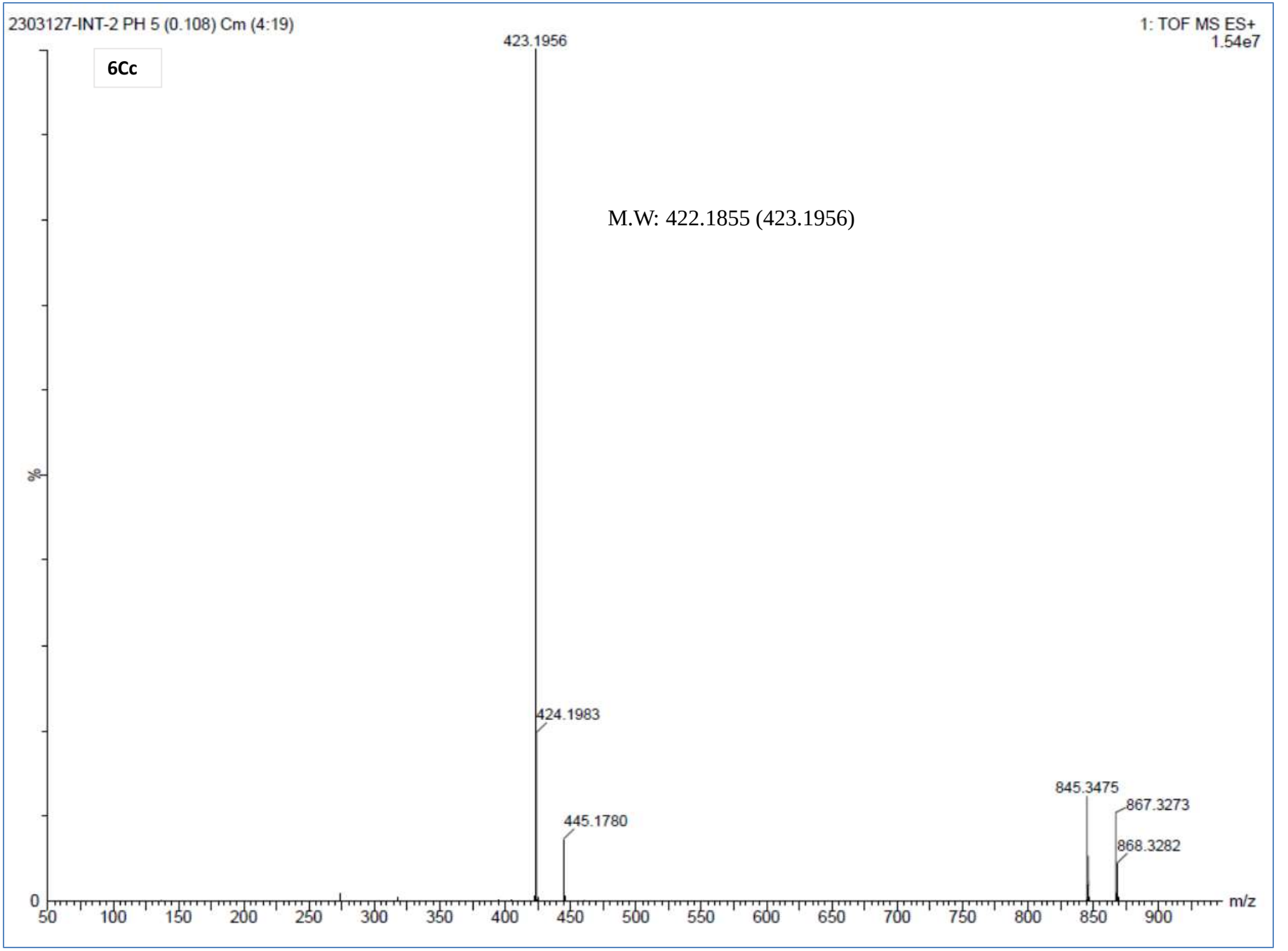

2302709-INT-1TH 4 (0.091) Cm (3:15)
1: TOF MS ES+
3.68e3
6Bb
426.0902
M.W: 425.0826 (426.0902)
%
428.0950
137.0147
137.0099
145.0097
472.1273
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
m/z

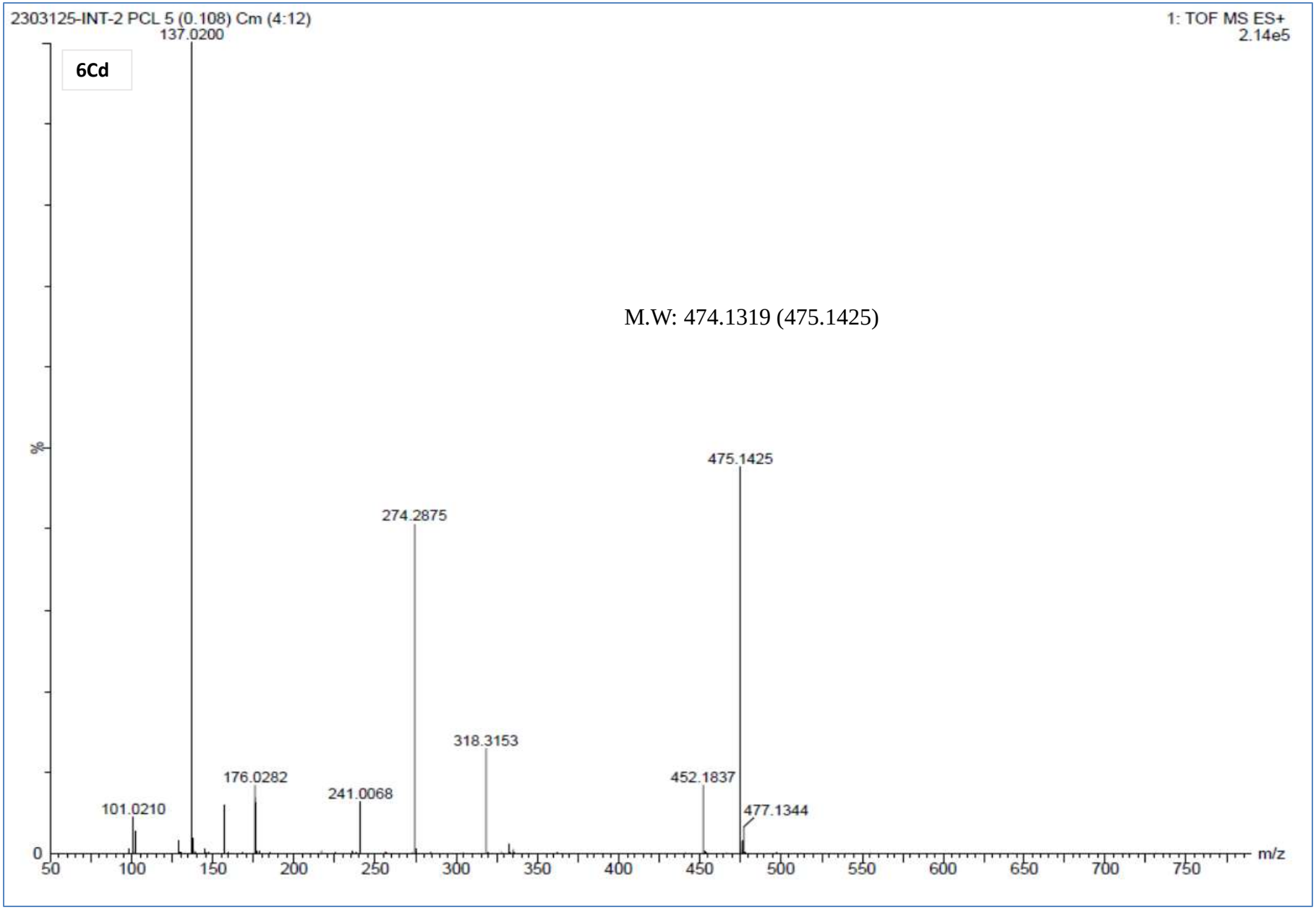


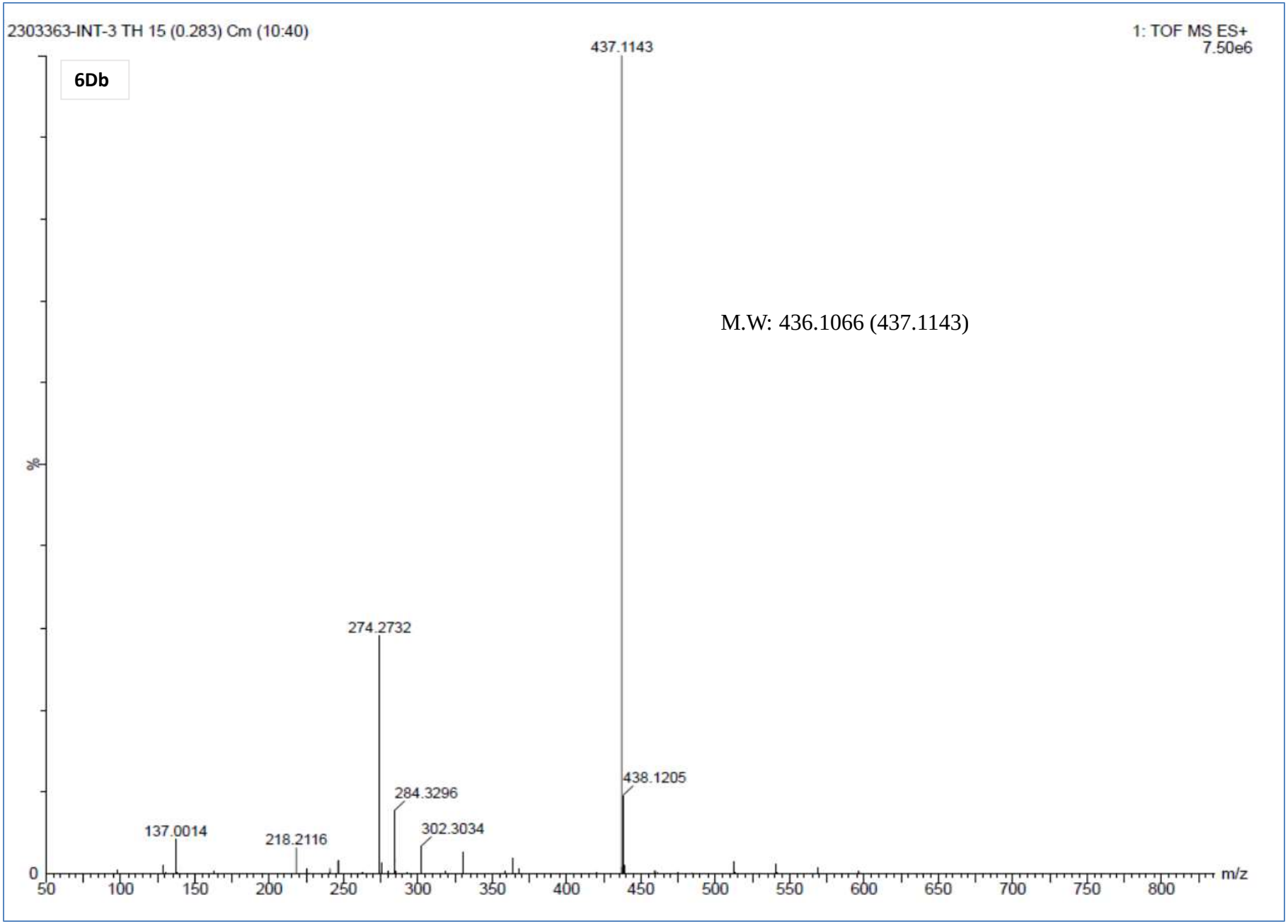
M.W: 442.1309 (443.1386)

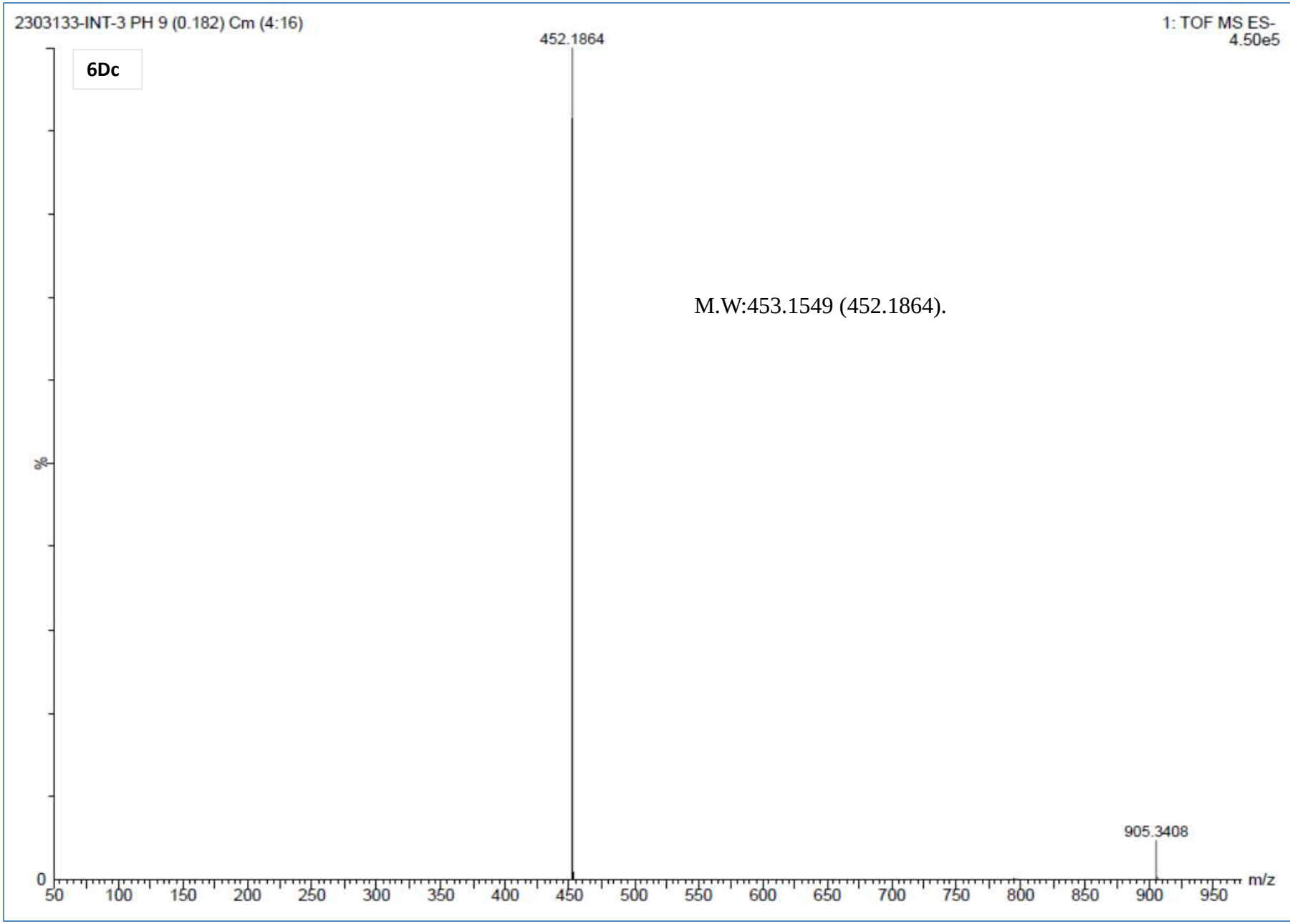

2302710-INT-1PCL 5 (0.108) Sm (SG, 5x2.00); Cm (1:22)
1: TOF MS ES+
979
6Bd
M.W: 494.0773 (495.0855)
%
m/z
495.0855
497.0912
137.0153
274.2834
129.0284
145.0053
318.3096
152.1570
345.0510
98.0064
230.1485
346.0364
472.1380
498.0911
553.0713
1
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900
950

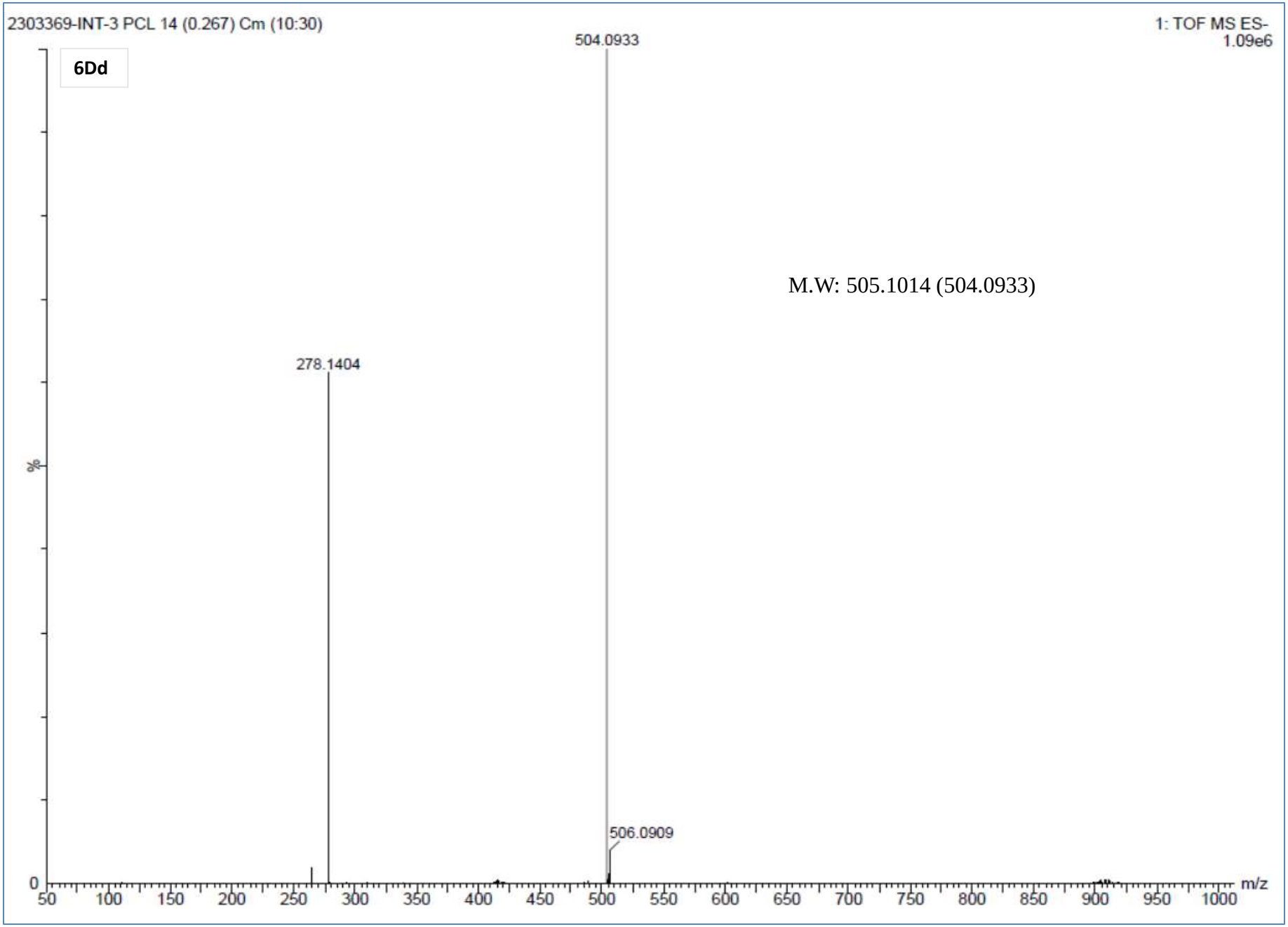

2303126-INT-2 TH 4 (0.091) Cm (4:22)
1: TOF MS ES+
4.16e6
6Cb
406.1465
M.W: 405.1372 (406.1465)
811.2502
812.2474
407.1535
404.1855
833.2281
%
0
m/z
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900


2303127-INT-2 PH 5 (0.108) Cm (4:19)
1: TOF MS ES+
1.54e7
6Cc
423.1956
M.W: 422.1855 (423.1956)
424.1983
445.1780
845.3475
867.3273
868.3282
%
0
m/z
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900

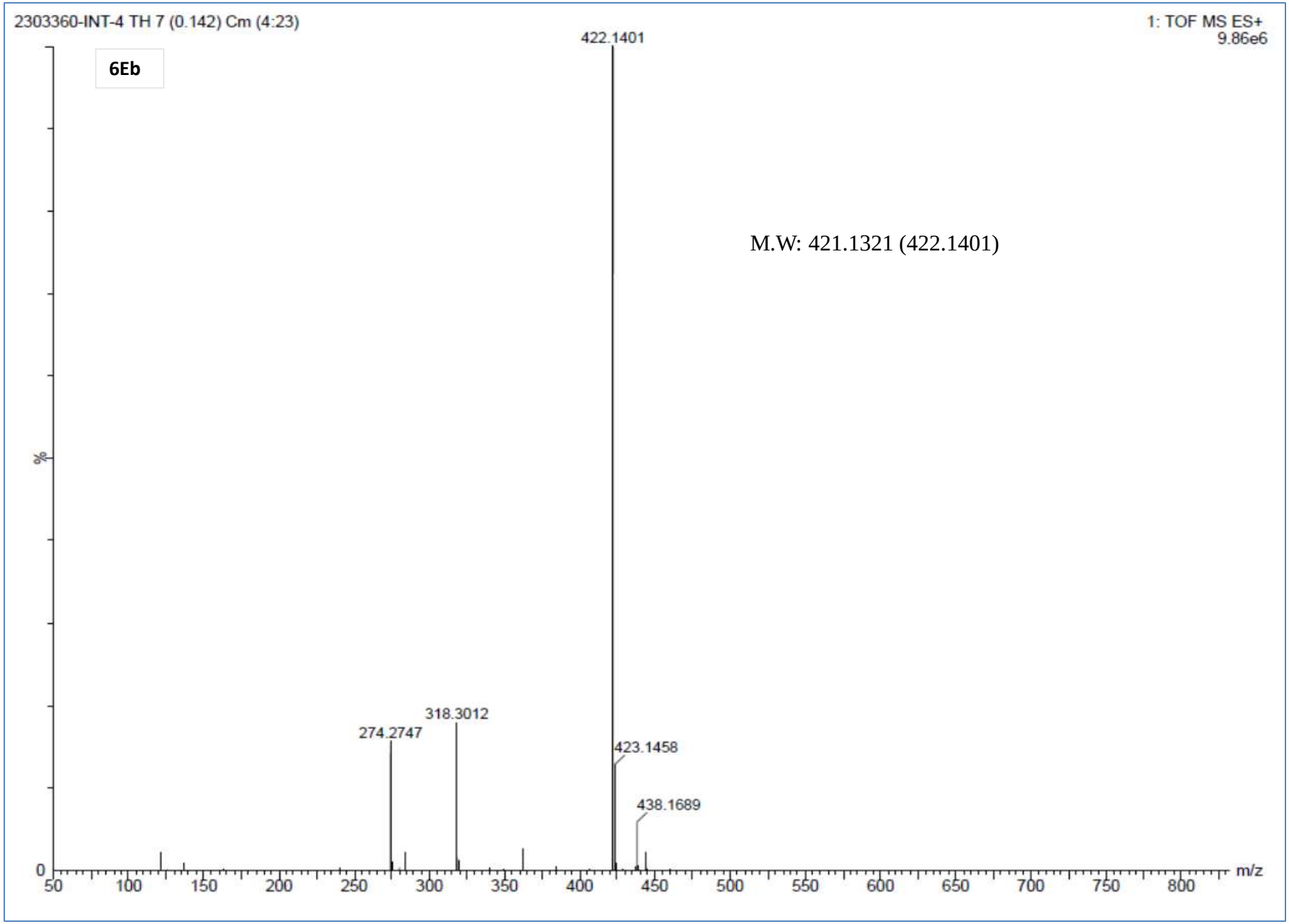

2303125-INT-2 PCL 5 (0.108) Cm (4:12)
1: TOF MS ES+
2.14e5
6Cd
137.0200
M.W: 474.1319 (475.1425)
%
475.1425
274.2875
318.3153
176.0282
452.1837
241.0068
101.0210
477.1344
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
m/z

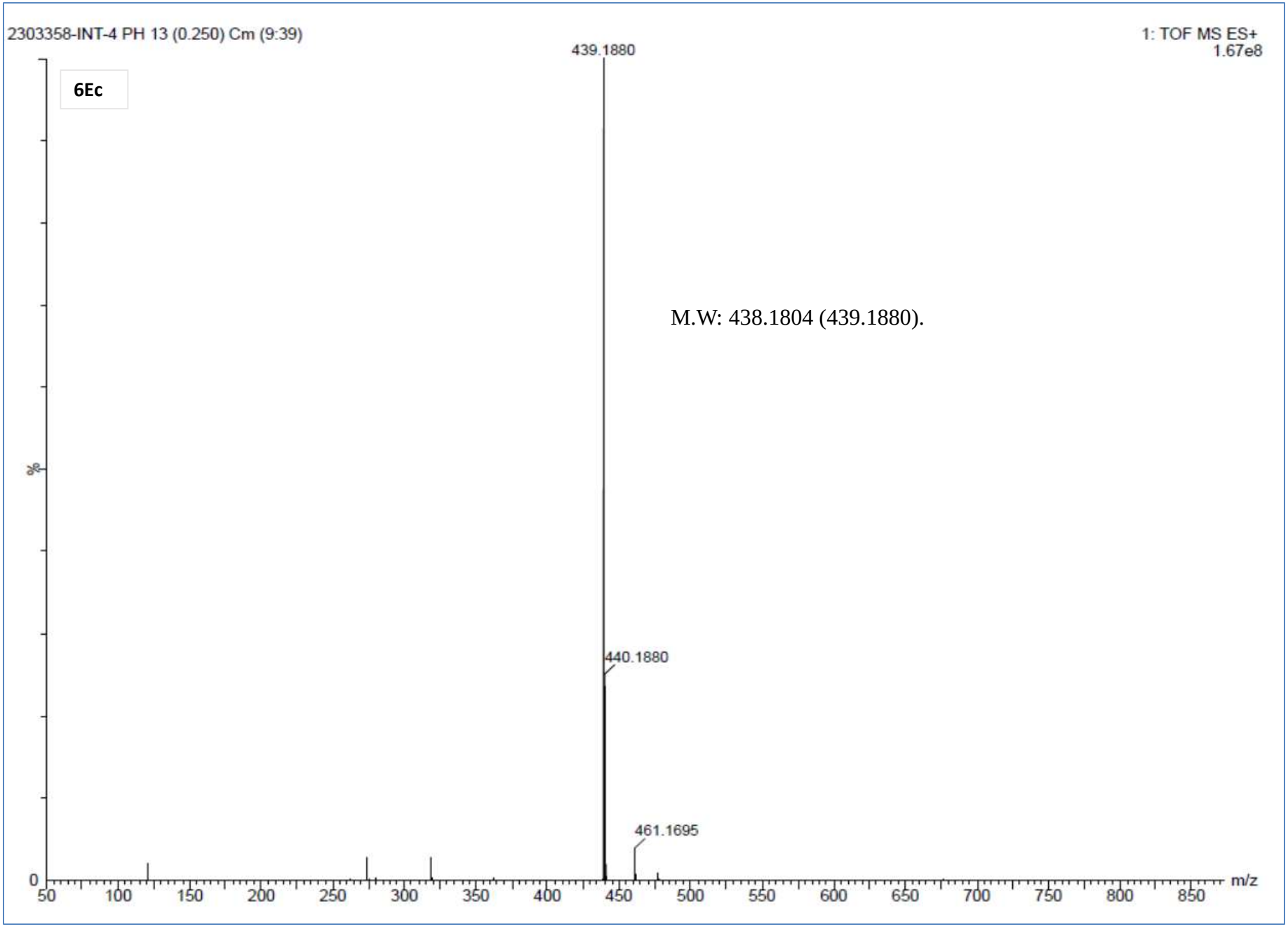

2303363-INT-3 TH 15 (0.283) Cm (10:40)
1: TOF MS ES+
7.50e6
6Db
437.1143
M.W: 436.1066 (437.1143)
%
274.2732
438.1205
284.3296
302.3034
137.0014
218.2116
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
m/z


2303133-INT-3 PH 9 (0.182) Cm (4:16)
1: TOF MS ES-
4.50e5
6Dc
452.1864
M.W:453.1549 (452.1864).
905.3408
%
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900
950
m/z

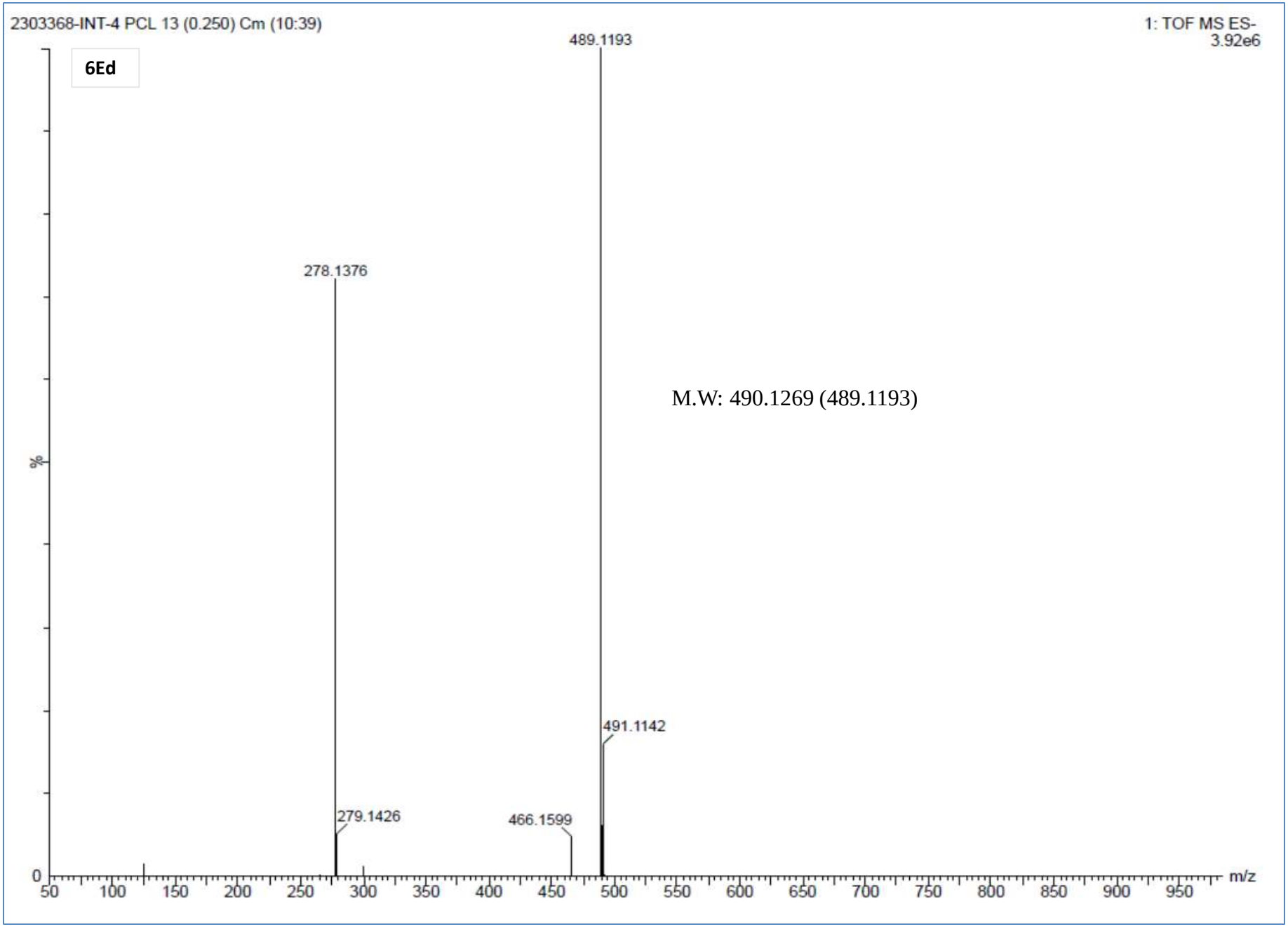


M.W: 505.1014 (504.0933)


2303360-INT-4 TH 7 (0.142) Cm (4:23)
1: TOF MS ES+
9.86e6
6Eb
422.1401
M.W: 421.1321 (422.1401)
318.3012
274.2747
423.1458
438.1689
%
0
m/z
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800

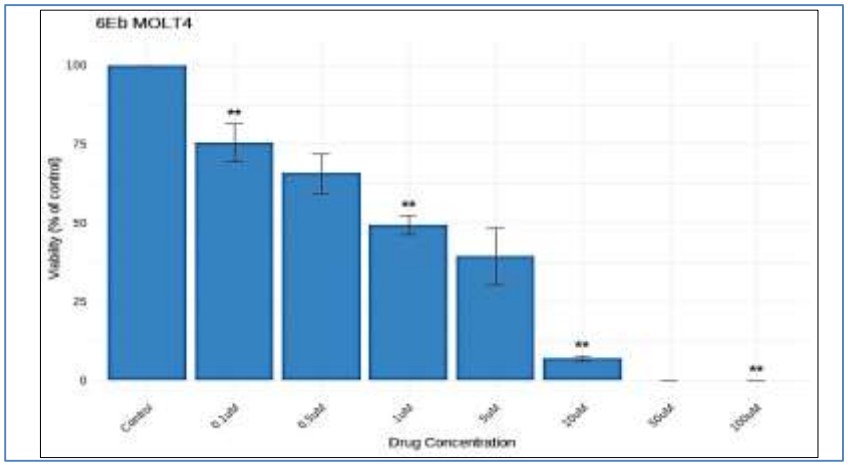


M.W: 438.1804 (439.1880).



M.W: 490.1269 (489.1193)

Supplementary Fig 1a and 1b: MTT assay using **6Eb** and **6Ec** in MOLT Cells



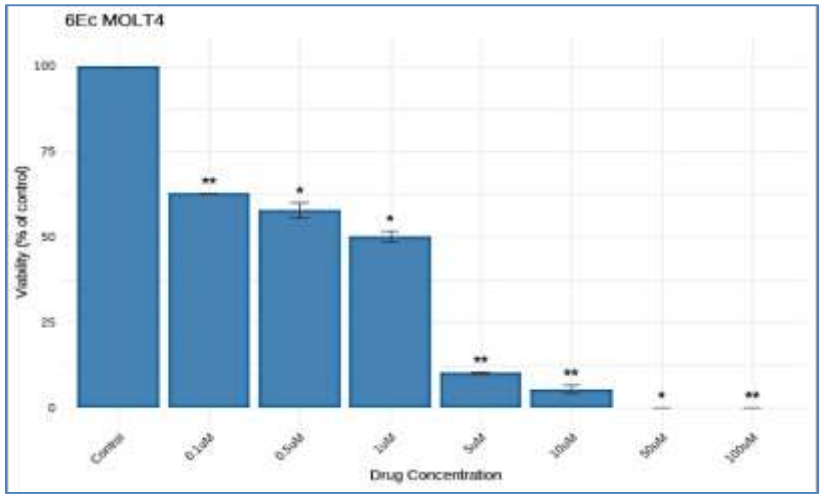


Fig 2: Western blot and quantitation of STAT3 in A) 6Eb and B) 6Ec