Design, synthesis, and biological evaluation of substrate competitive inhibitors of C-Terminal Binding Protein (CtBP)

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b. Division of Hematology, Oncology, & Palliative Care and Department of Human and Molecular Genetics, and Massey Cancer Center, Virginia Commonwealth University, Richmond, VA 23298, United States

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Supporting Information

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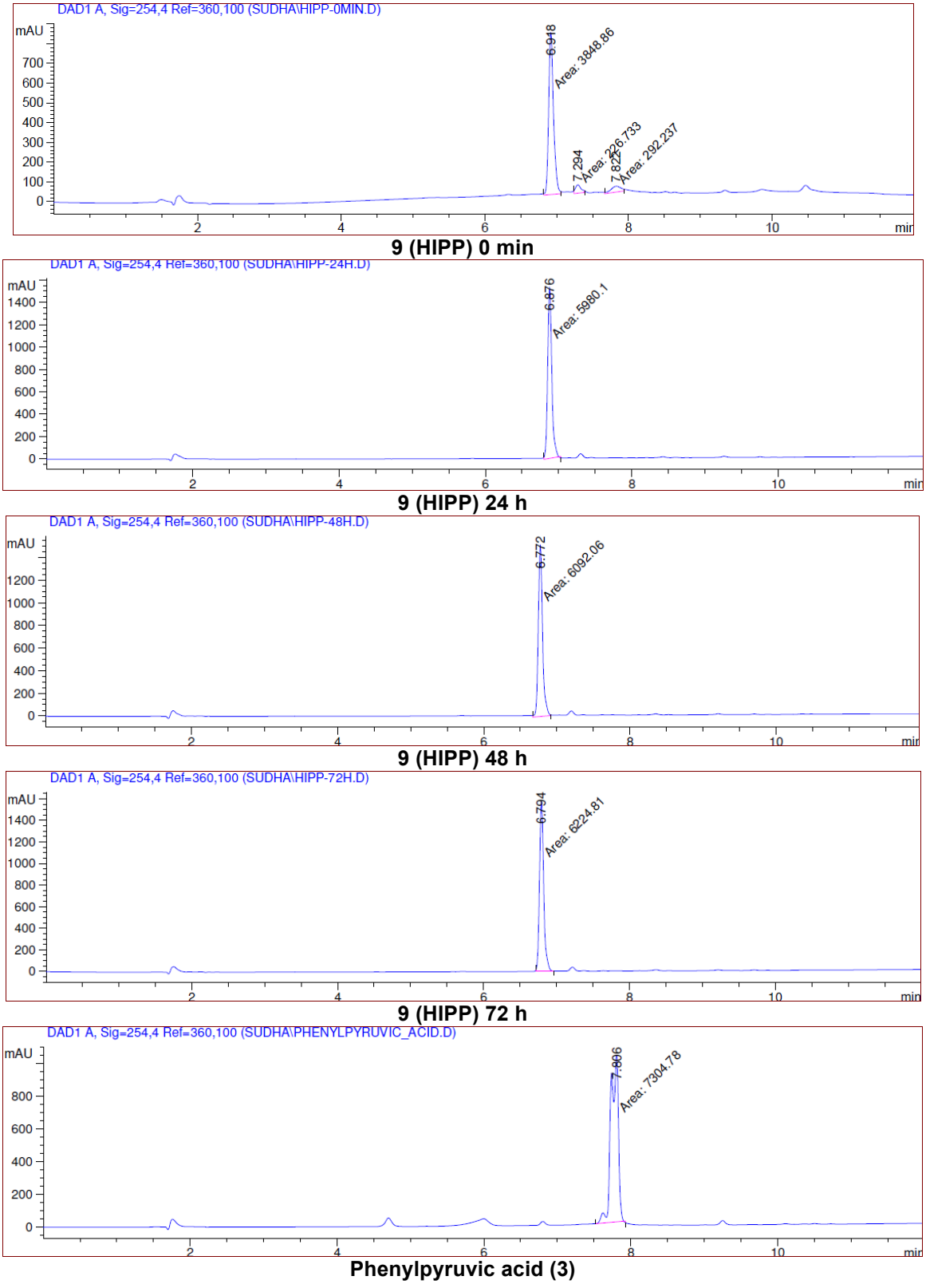
Table S1. Inhibition of recombinant CtBP by Initial Set of Designed Inhibitors from Schemes **1** and **2.**

Compound	IC_{50} (μM)[a]
MTOB (1)	300
3	116.3
4	>300
5	>300
6	>300
7	>300
8	>300
9	0.24
10	>300
11	>300
12	>300
13	>300

a. Data represents the average of two replicates.

Figure S2. Stability of 9 (A), 14g (B), and 14h (C) to hydrolysis under aqueous conditions.

A.



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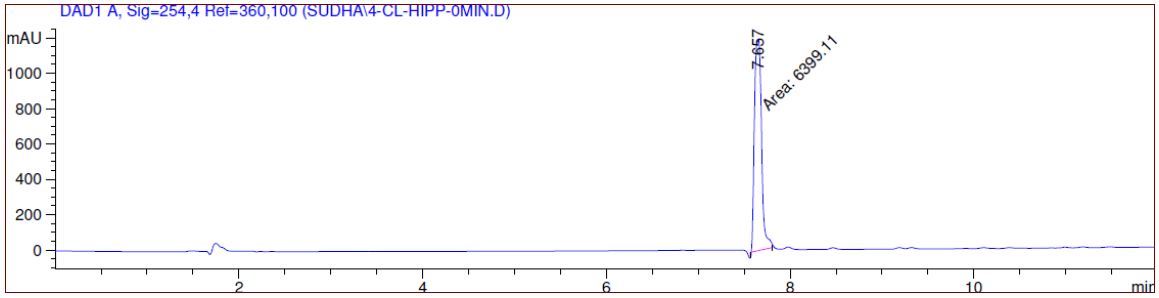
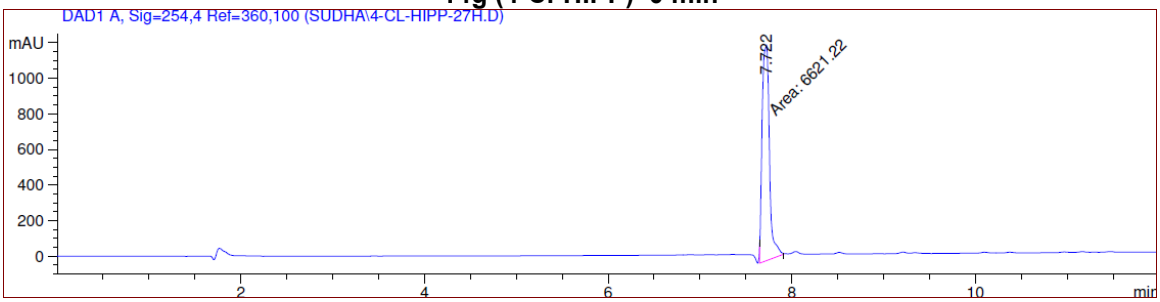


14g (4-Cl-HIPP) 0 min



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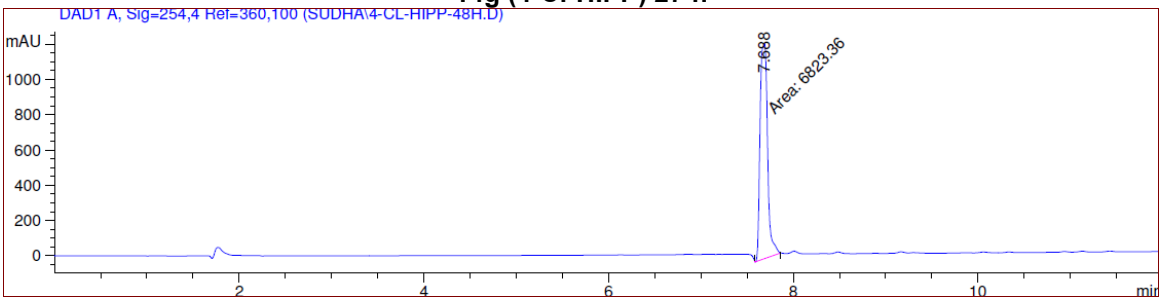
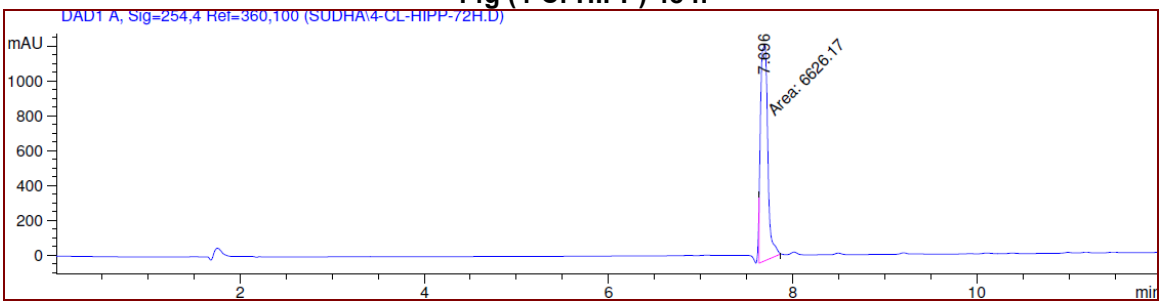
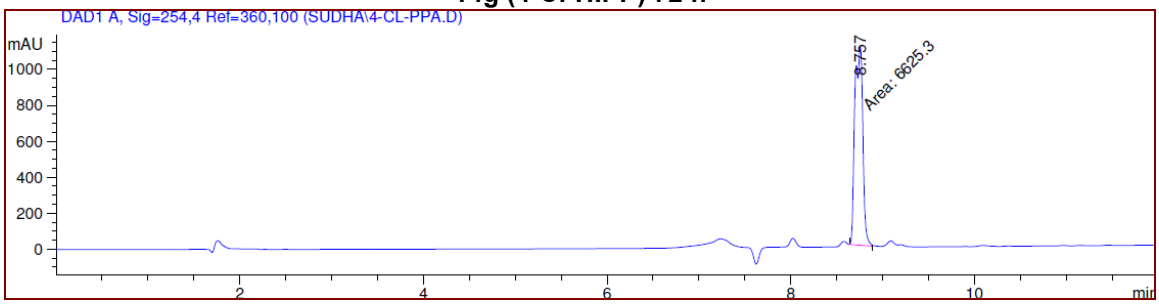


14g (4-Cl-HIPP) 48 h

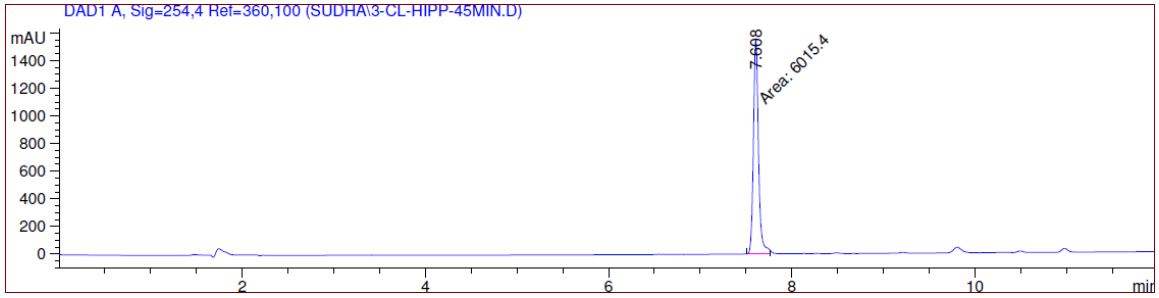


14g (4-Cl-HIPP) 72 h



4-Cl-phenylpyruvic acid (17g)

C.



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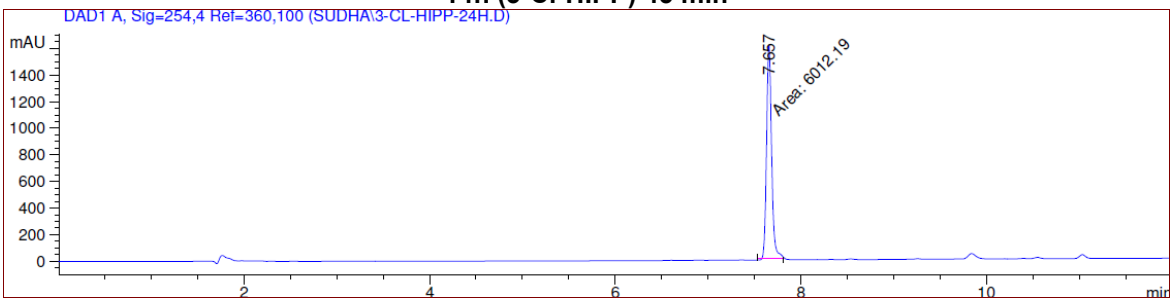
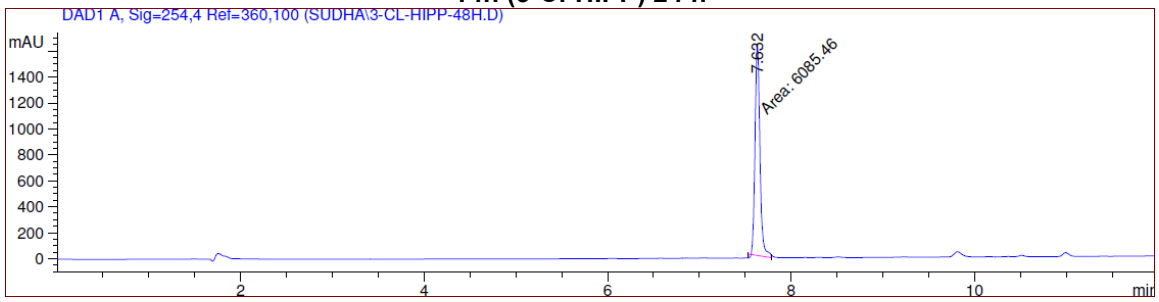
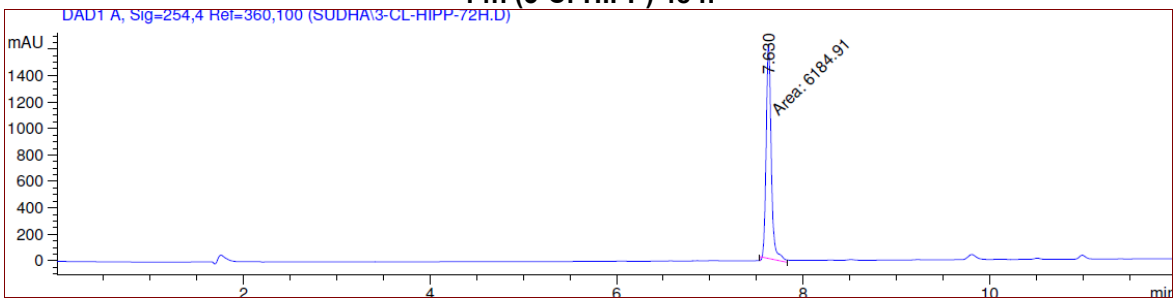


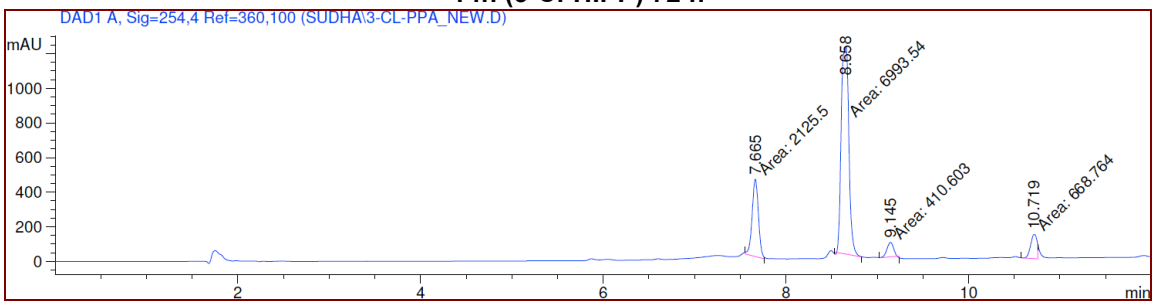
14h (3-Cl-HIPP) 24 h



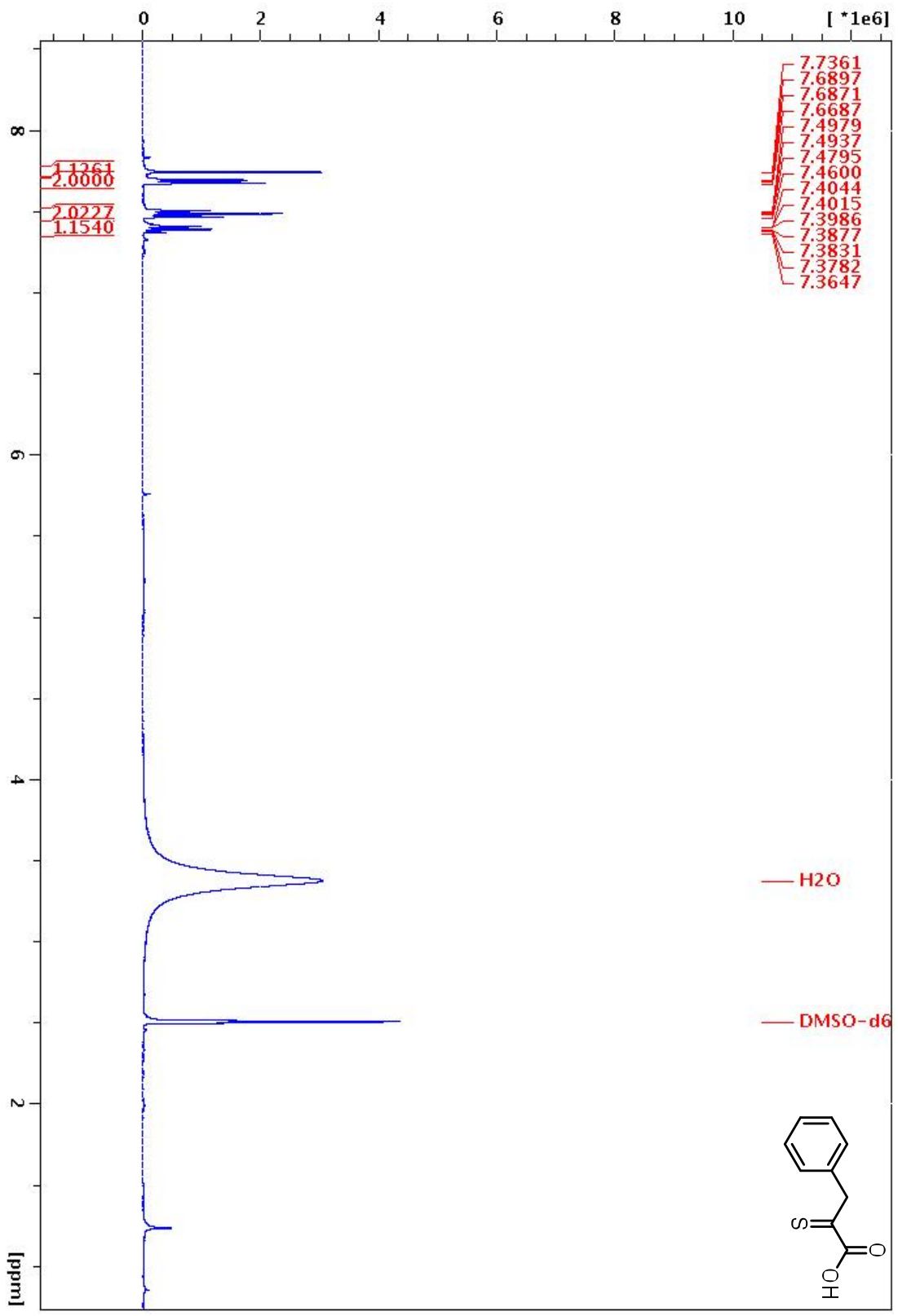
14h (3-Cl-HIPP) 48 h



14h (3-Cl-HIPP) 72 h



4-Cl-phenylpyruvic acid (17h)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6
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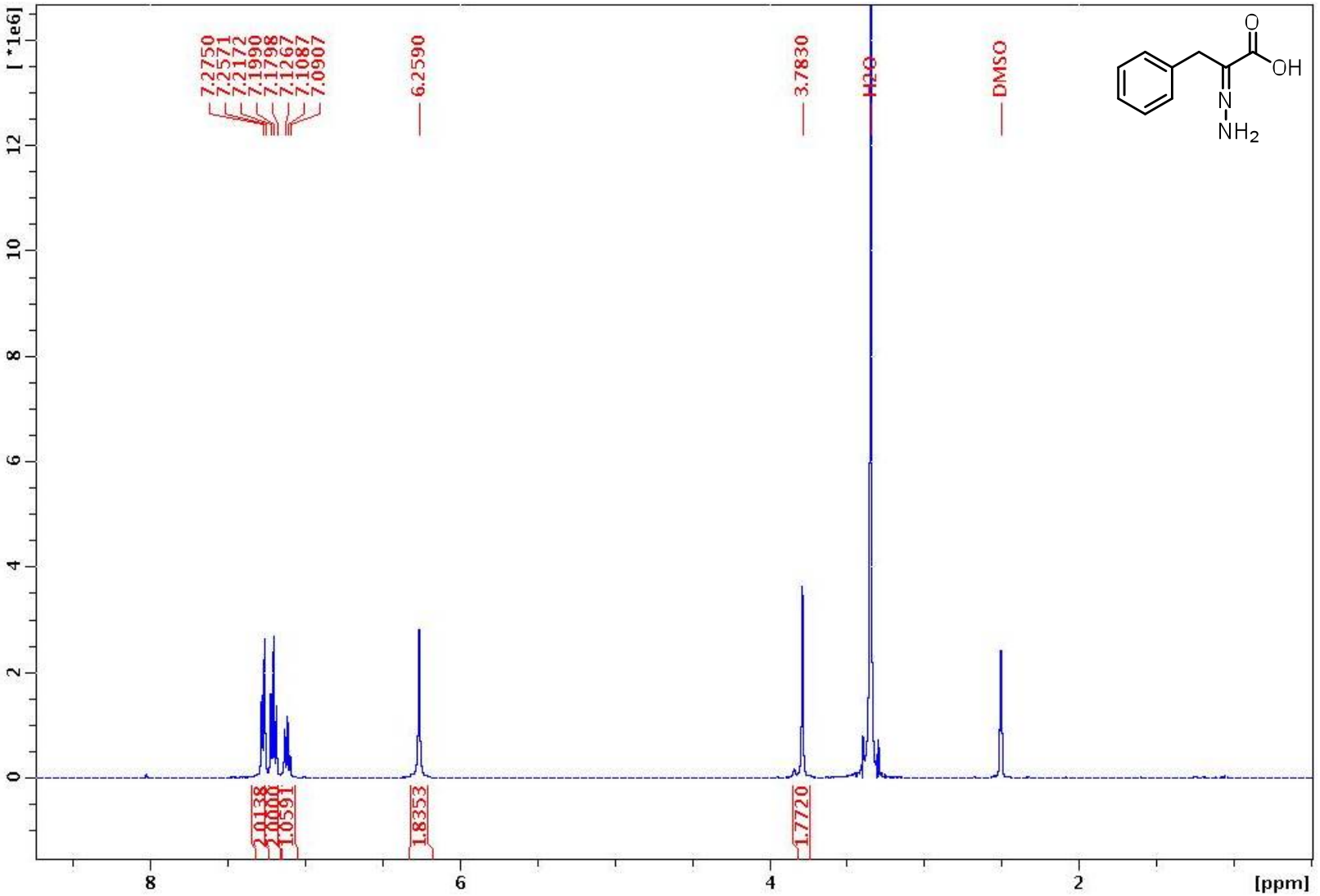
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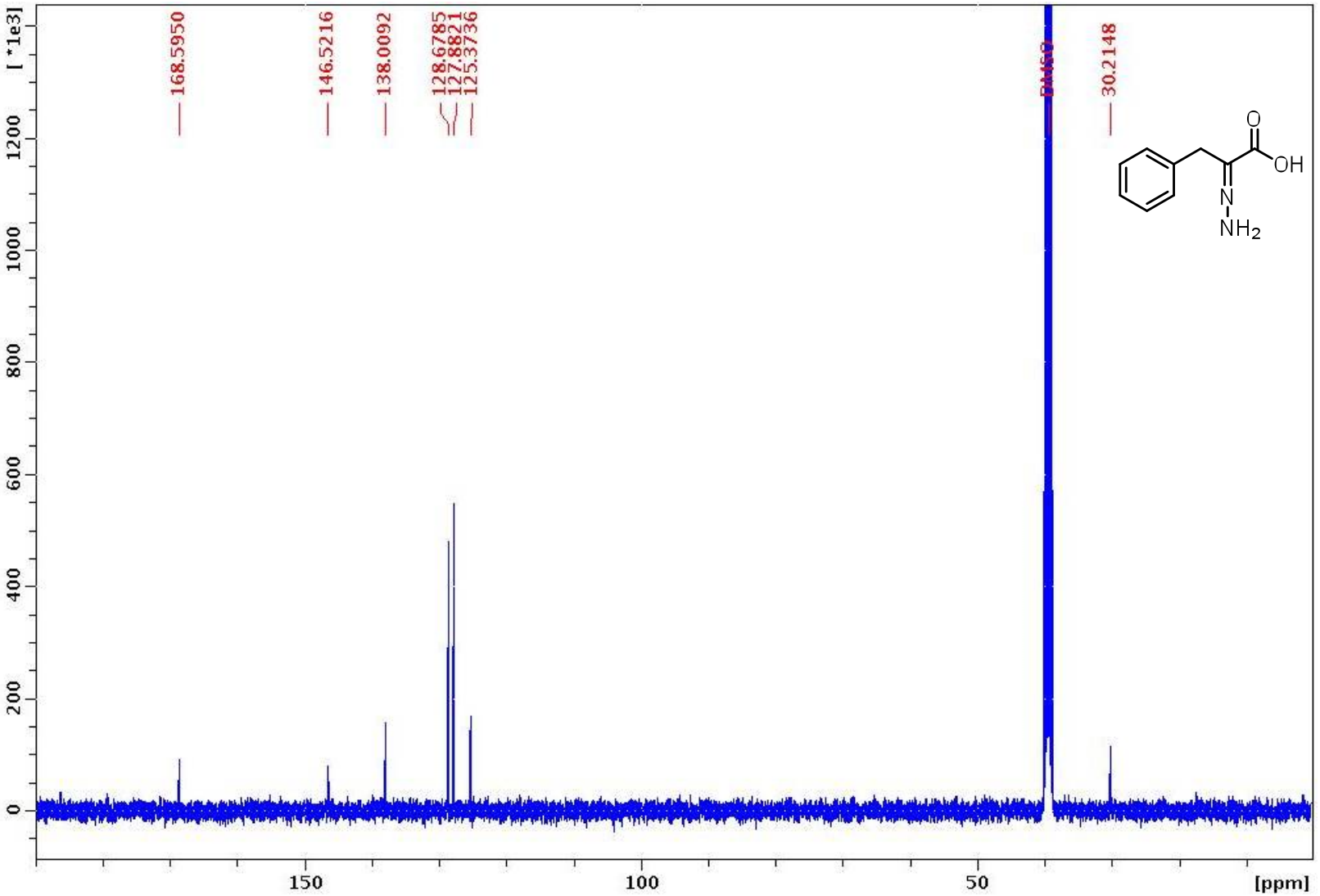
N
NH2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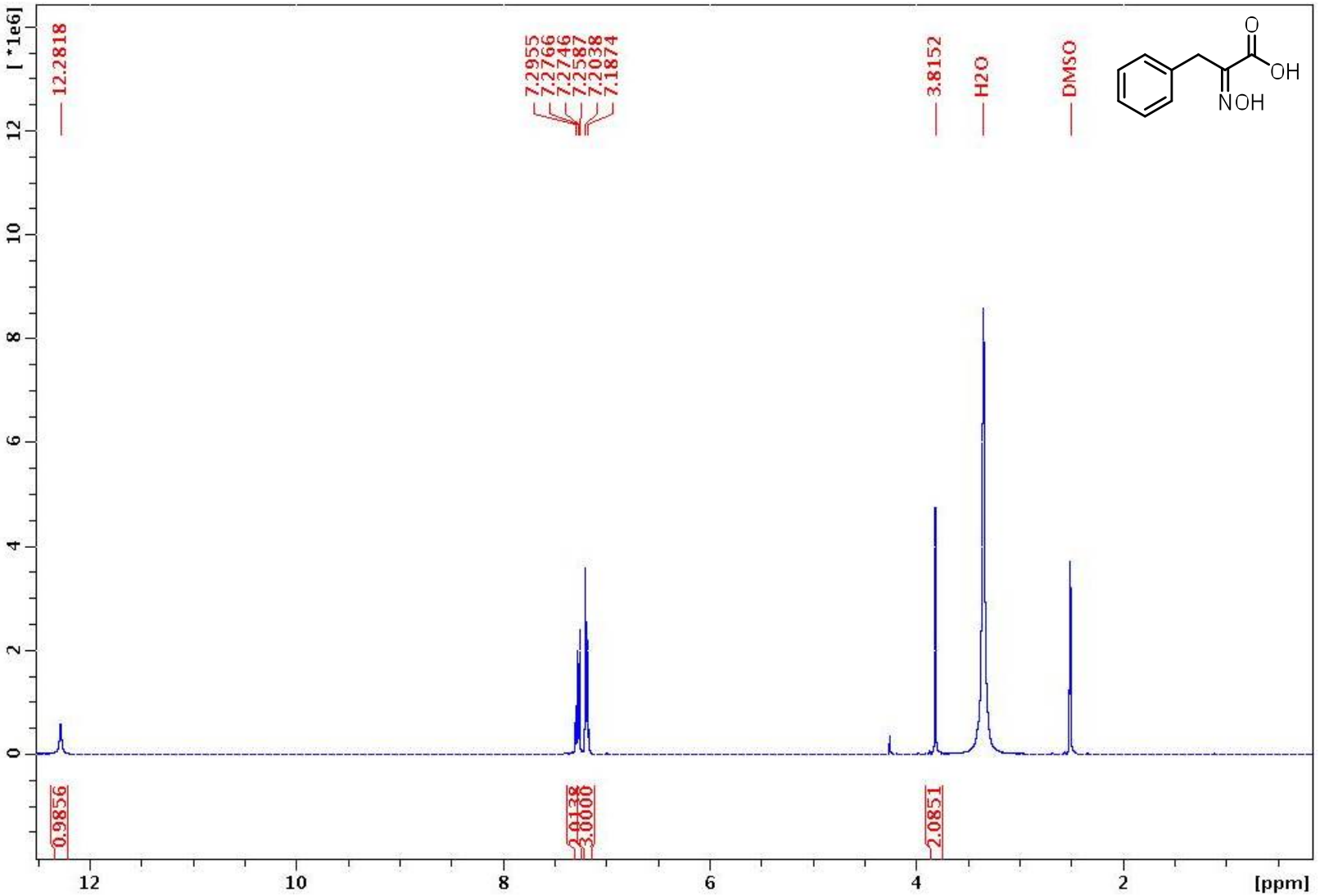
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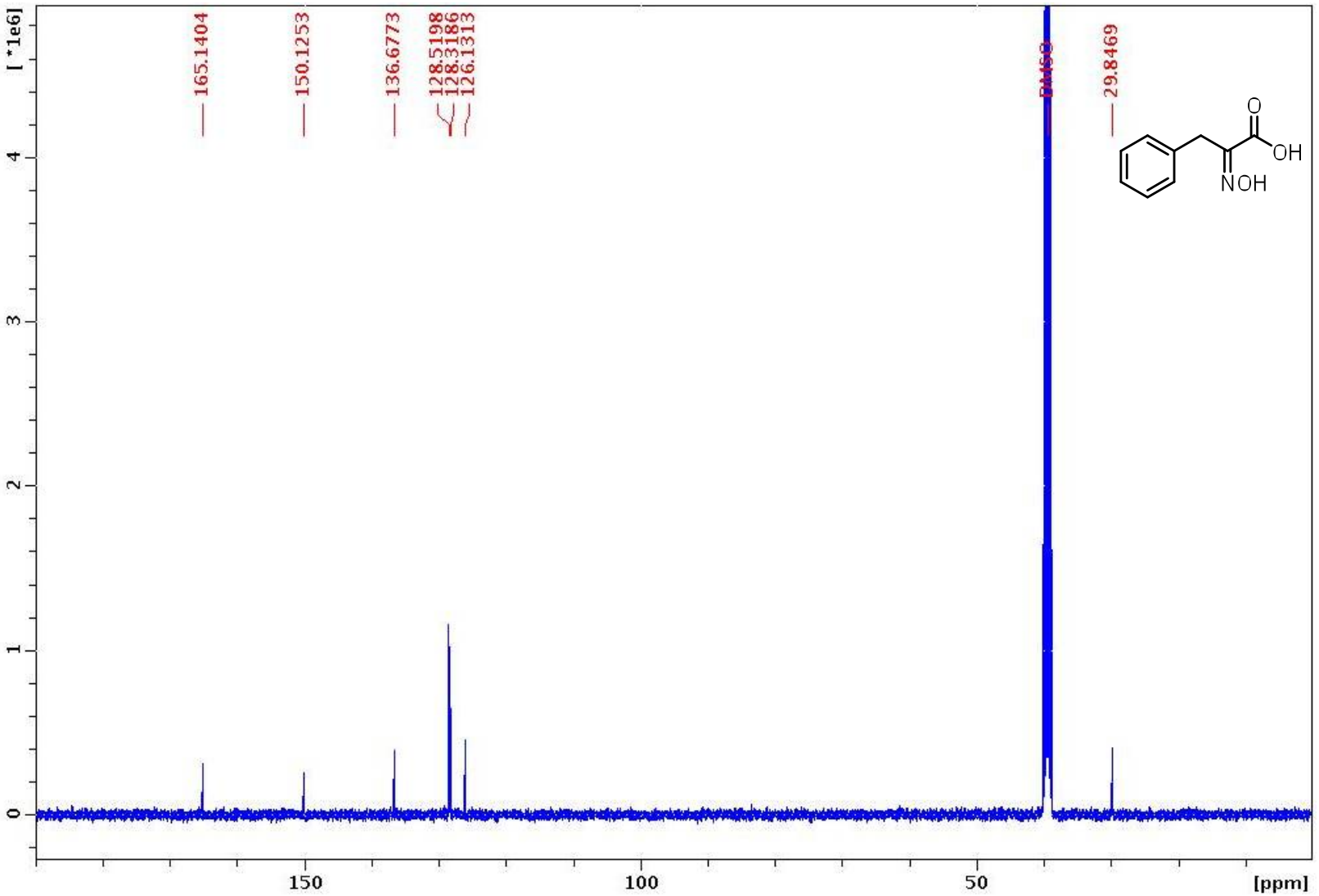
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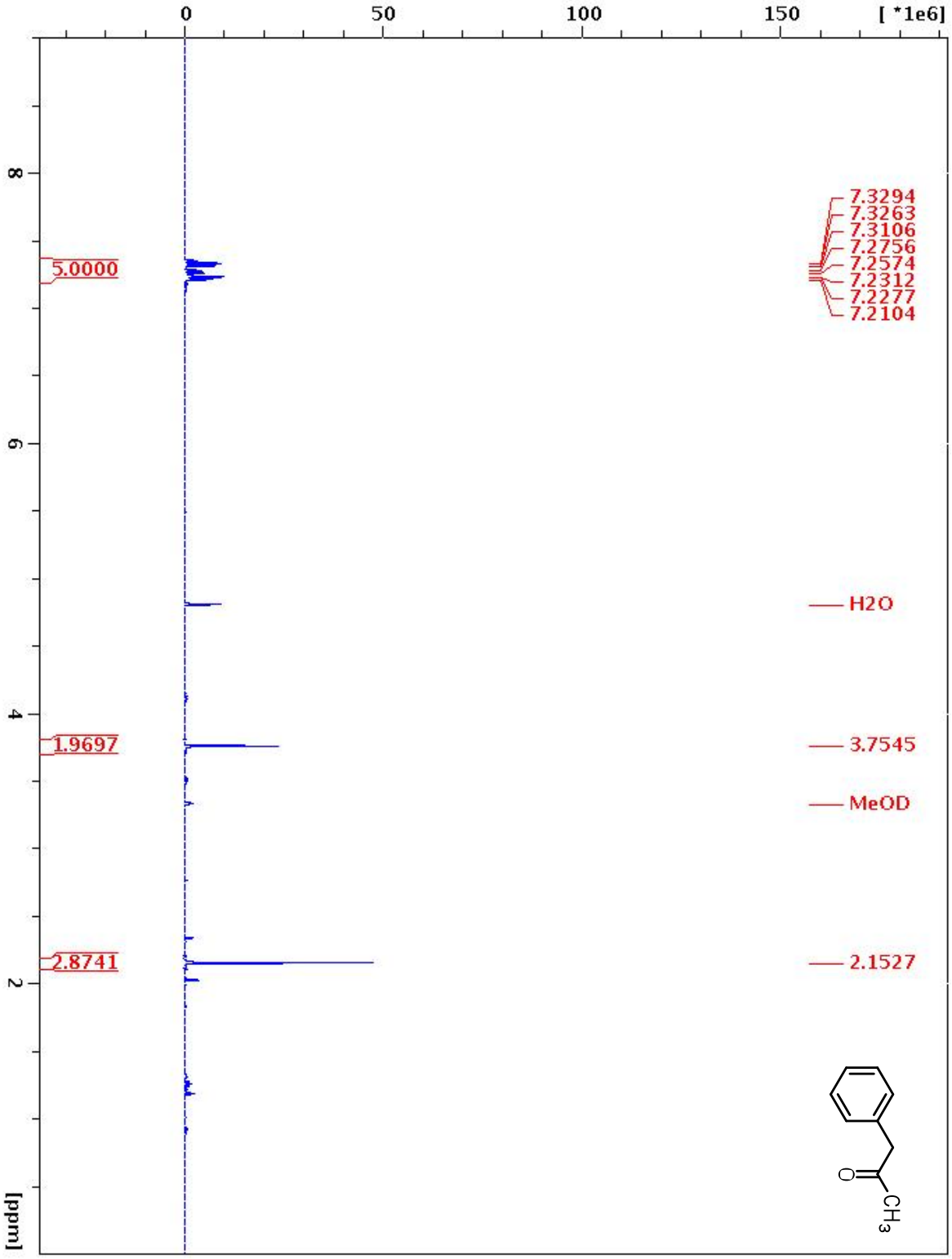
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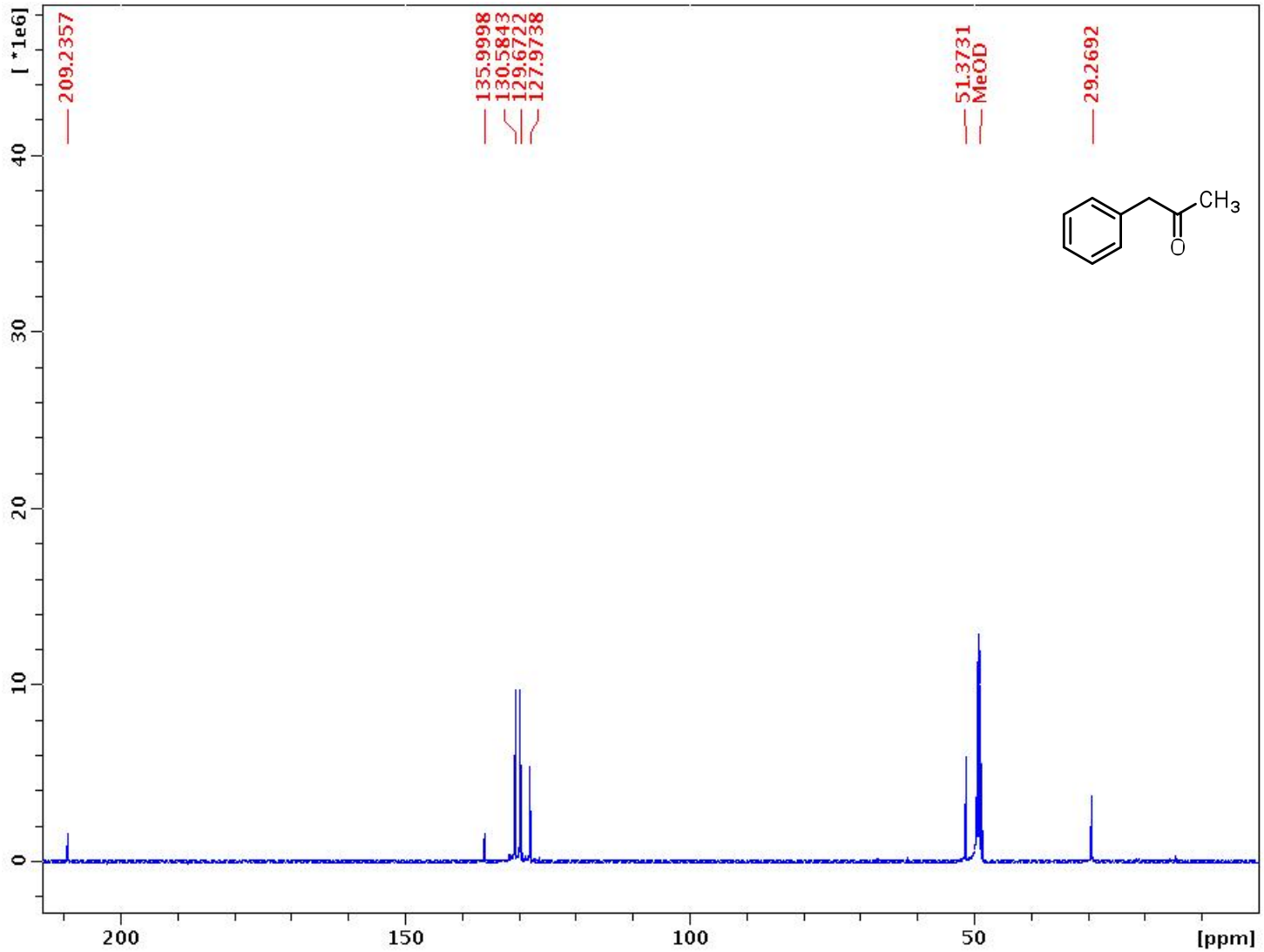
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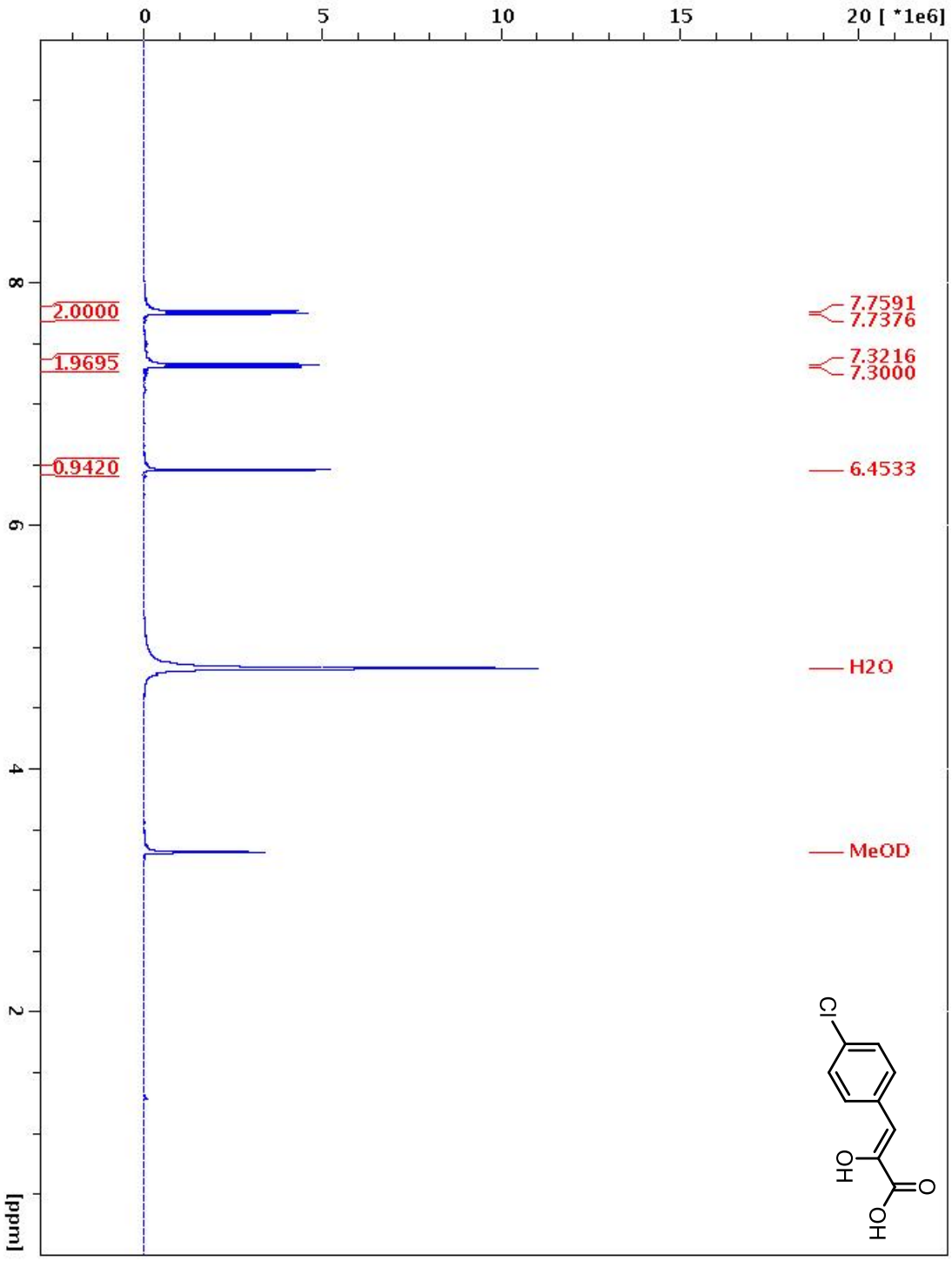
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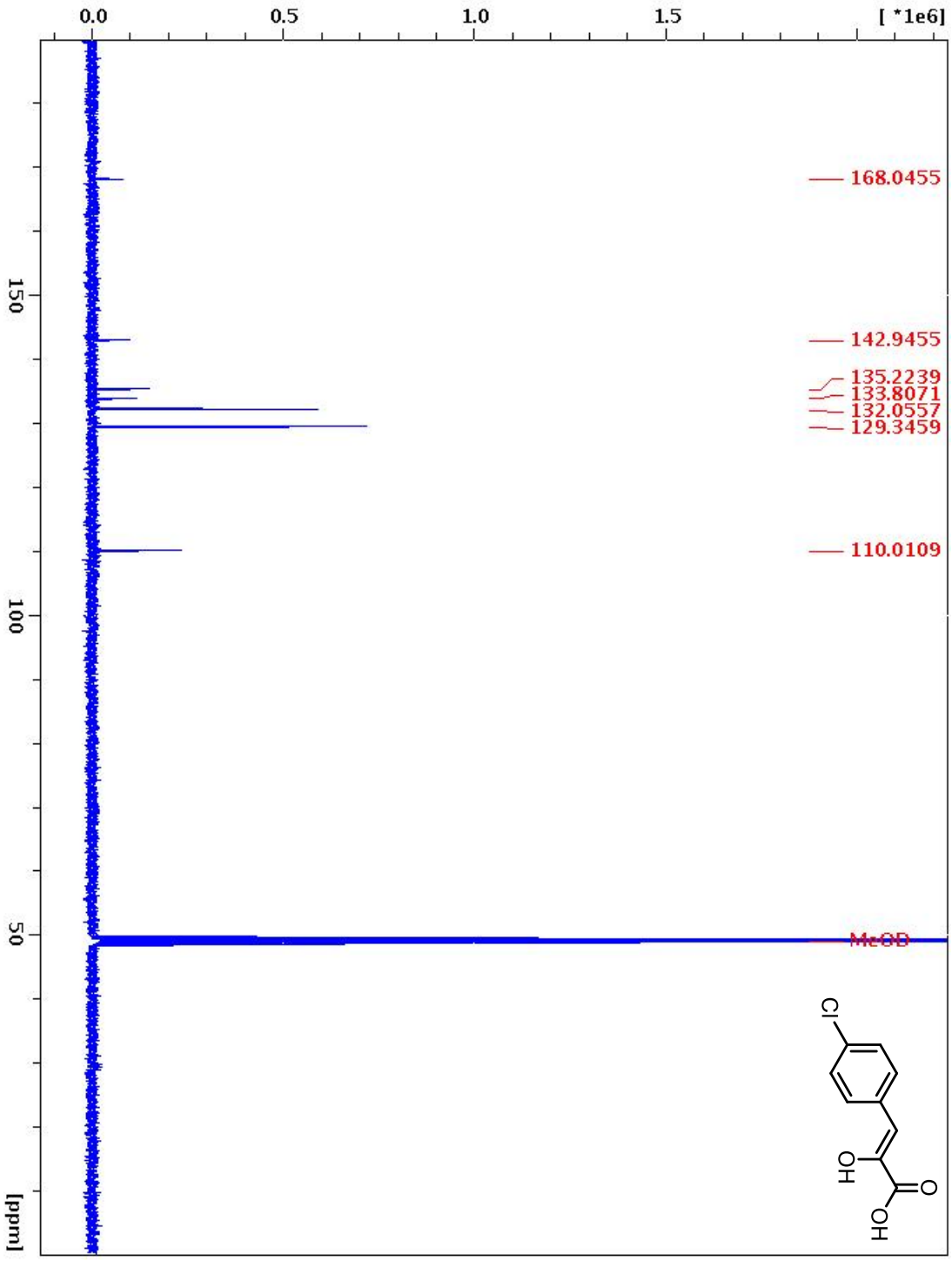
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O
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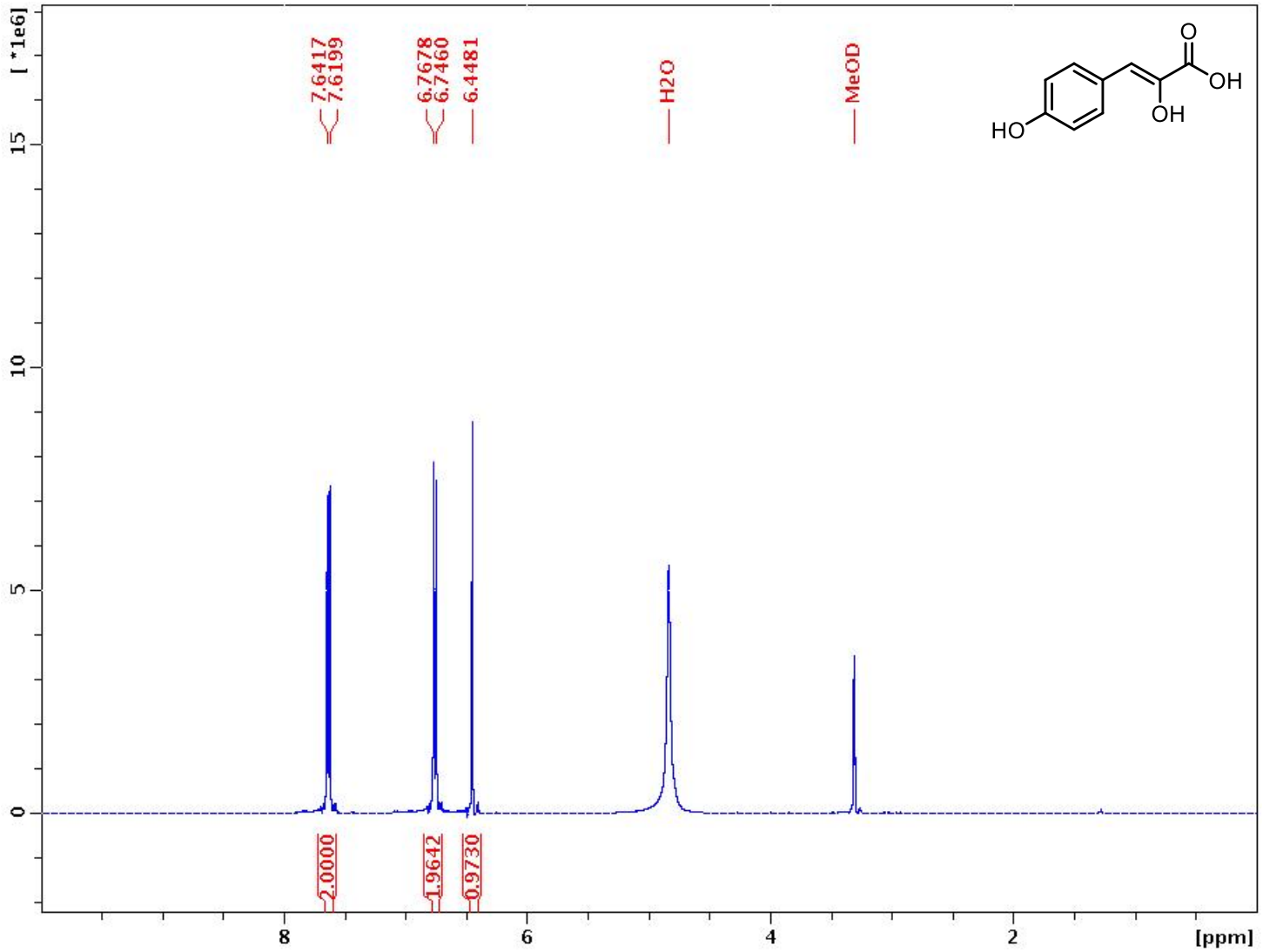
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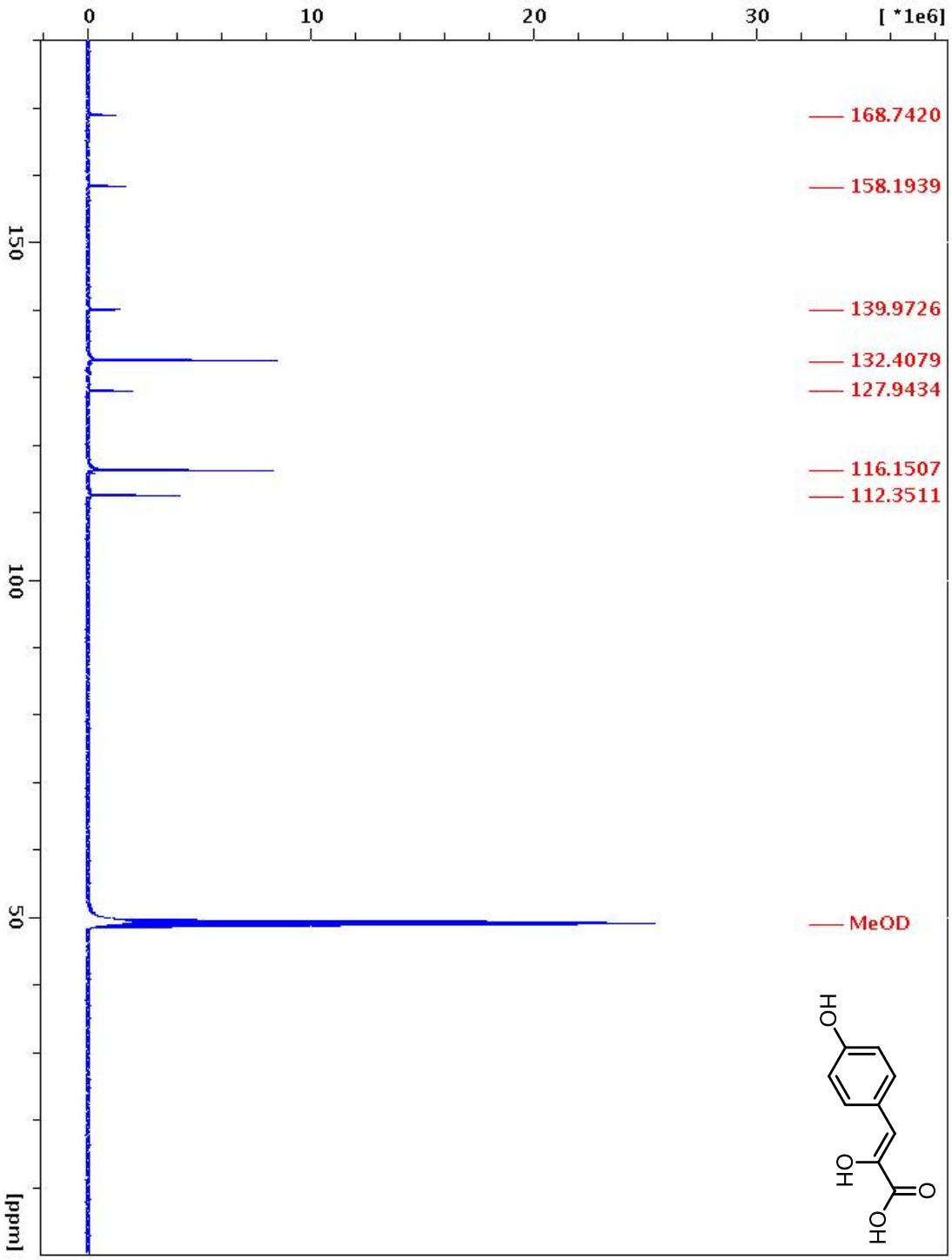
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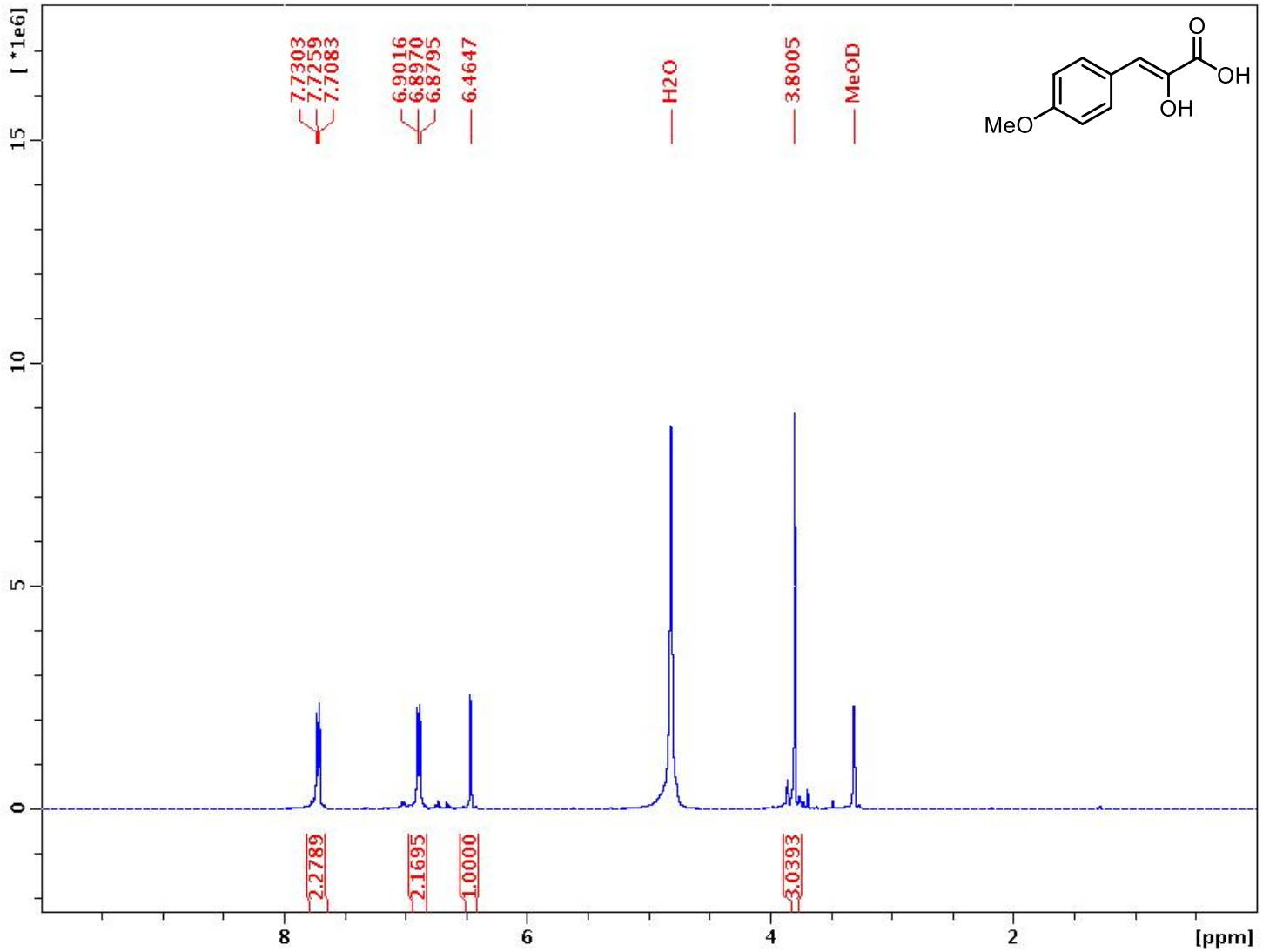
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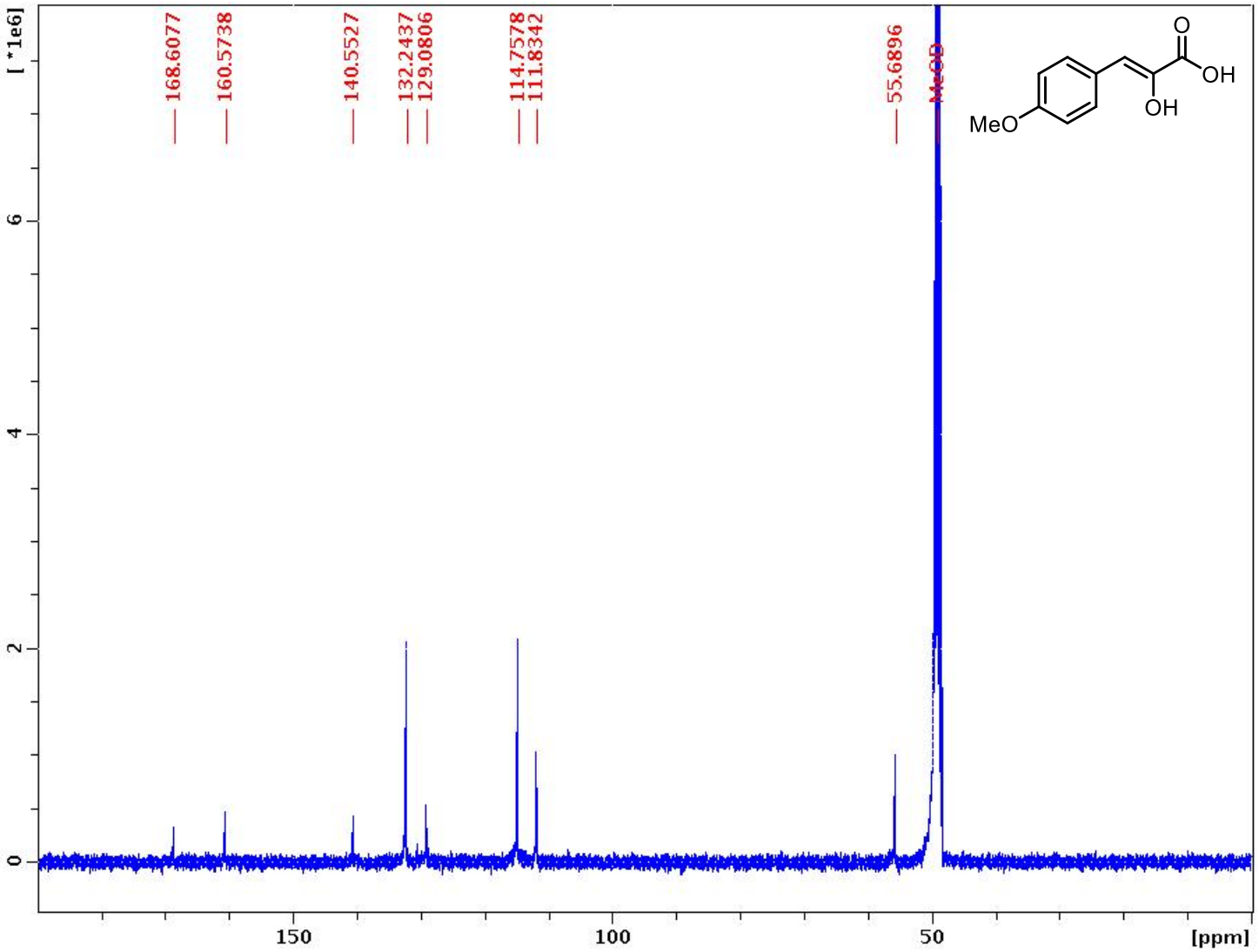
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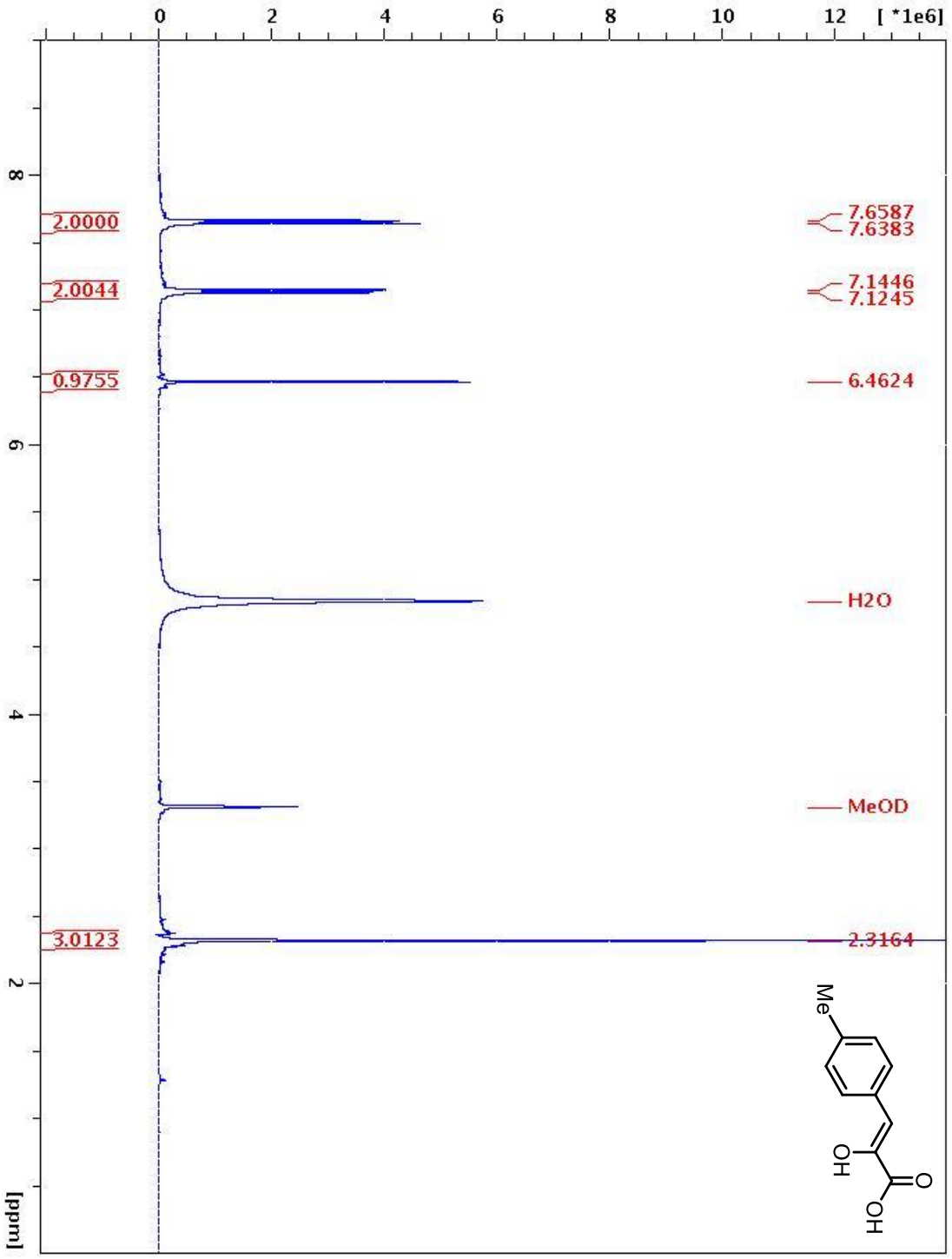
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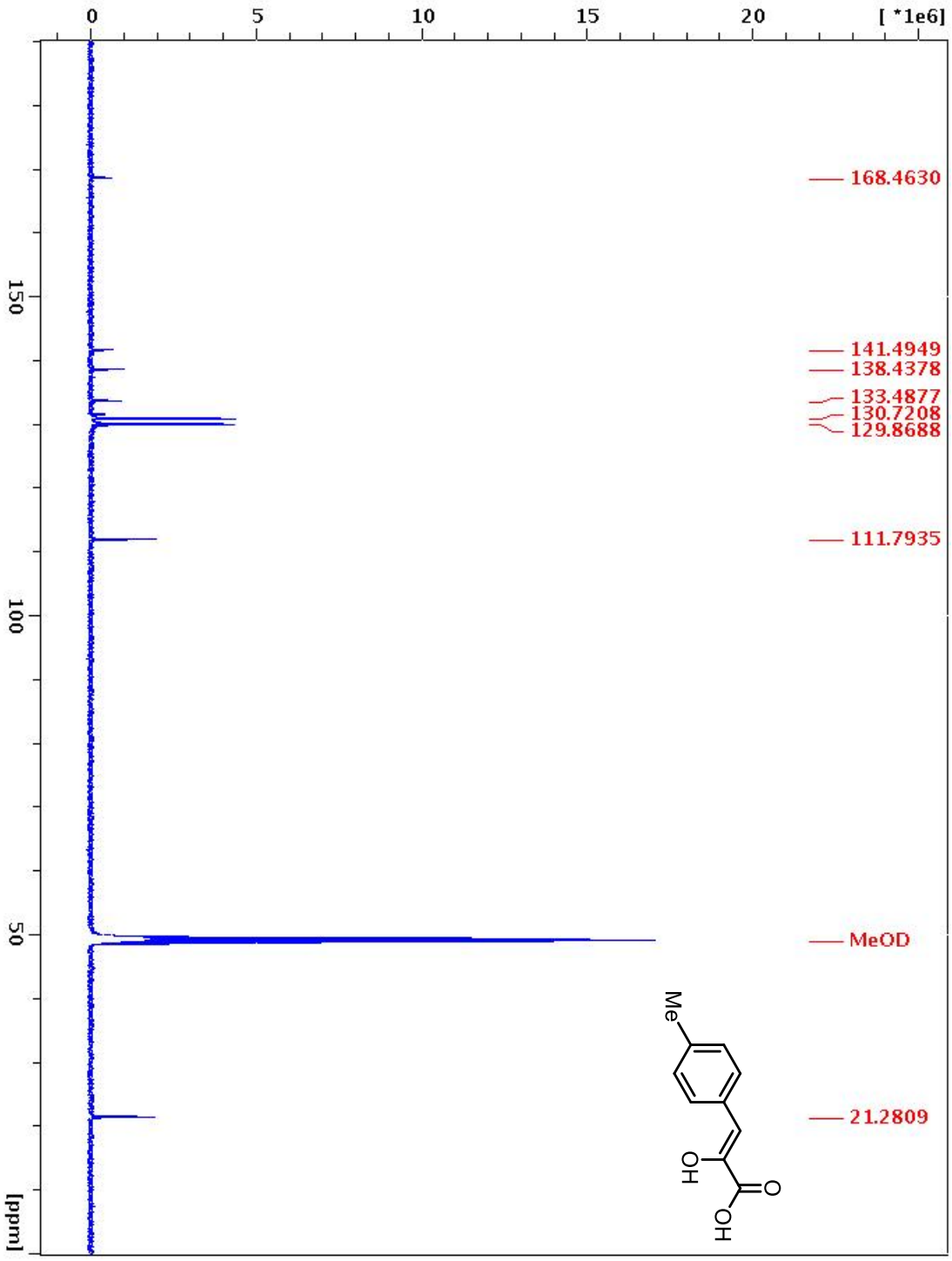
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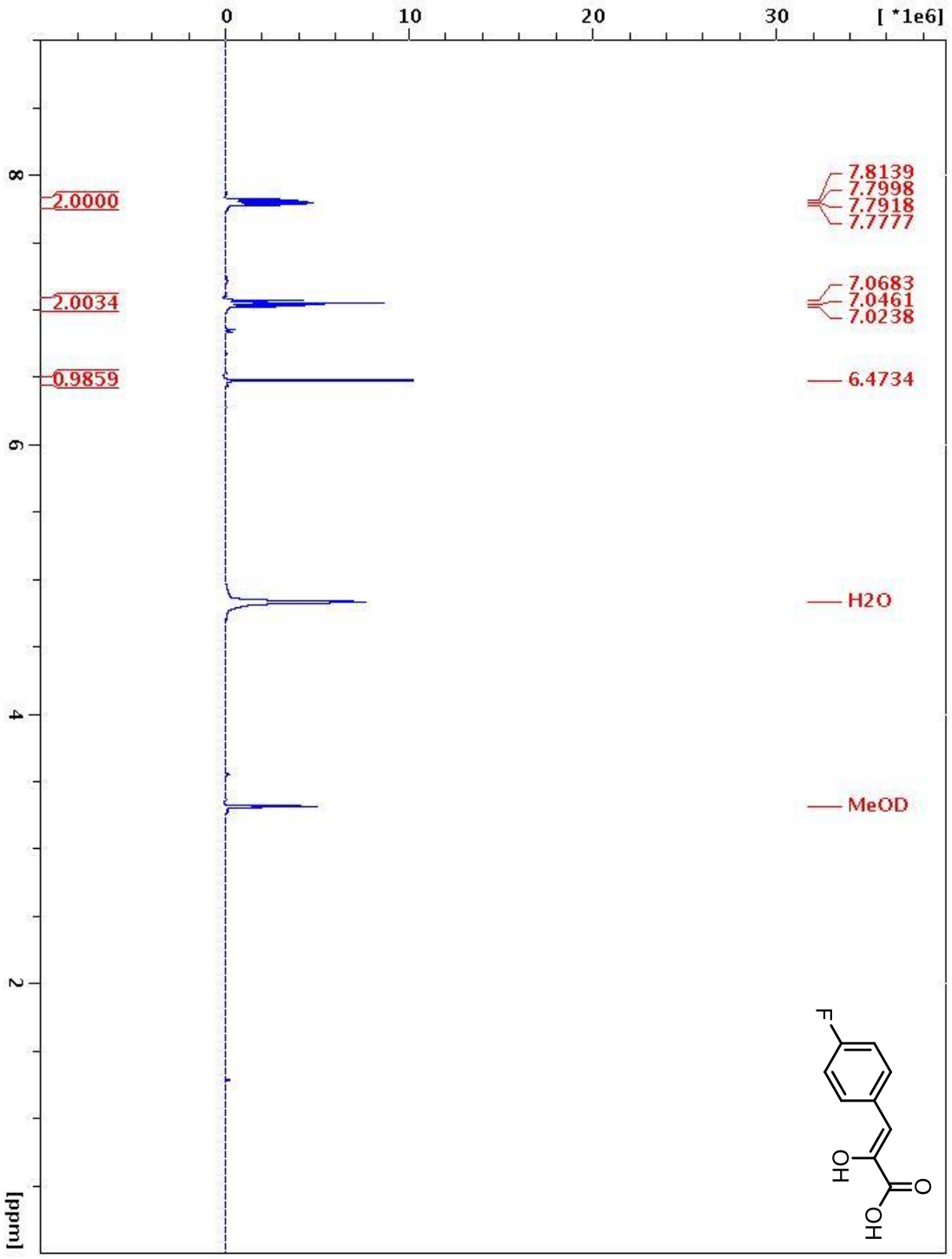
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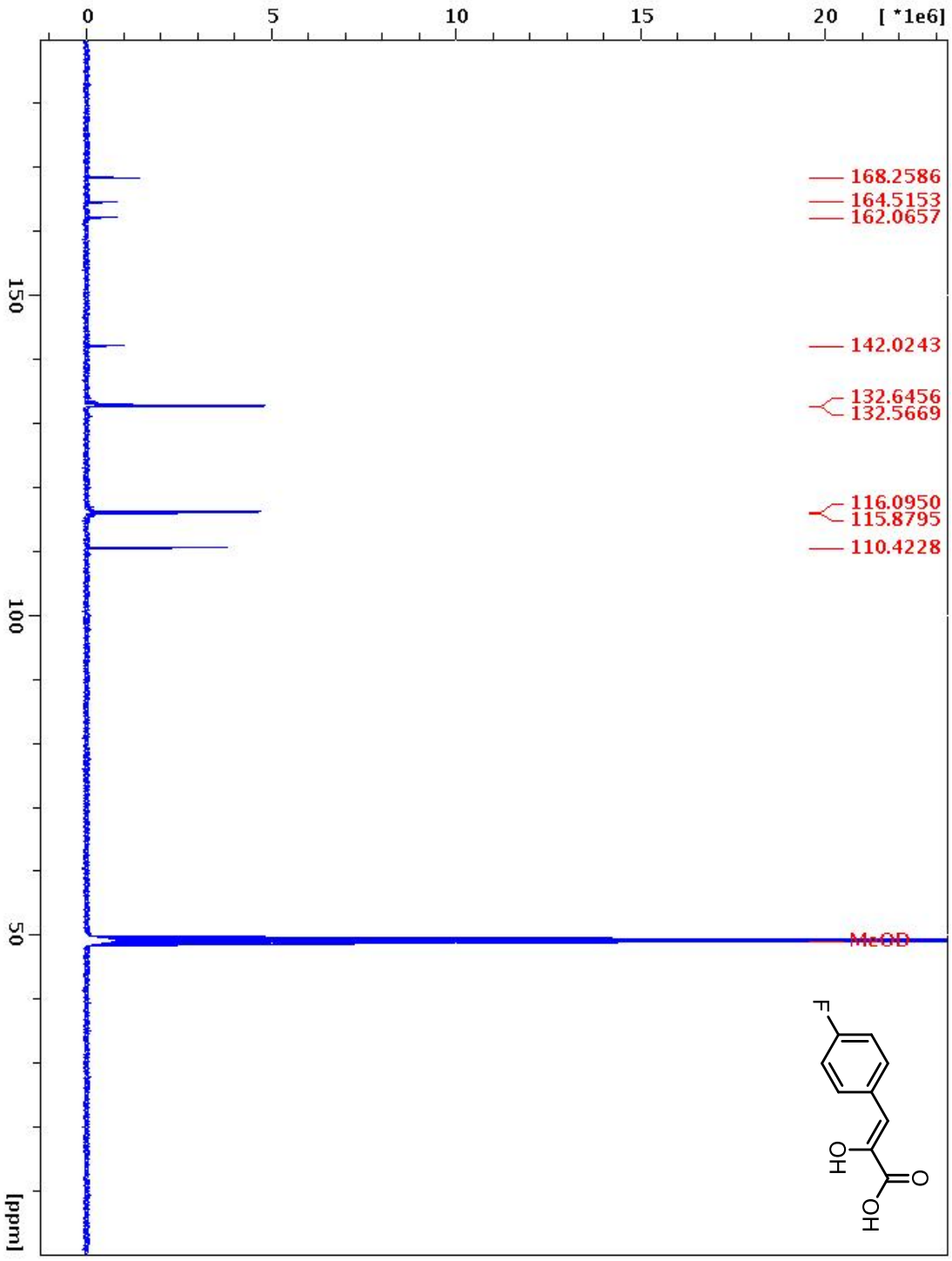
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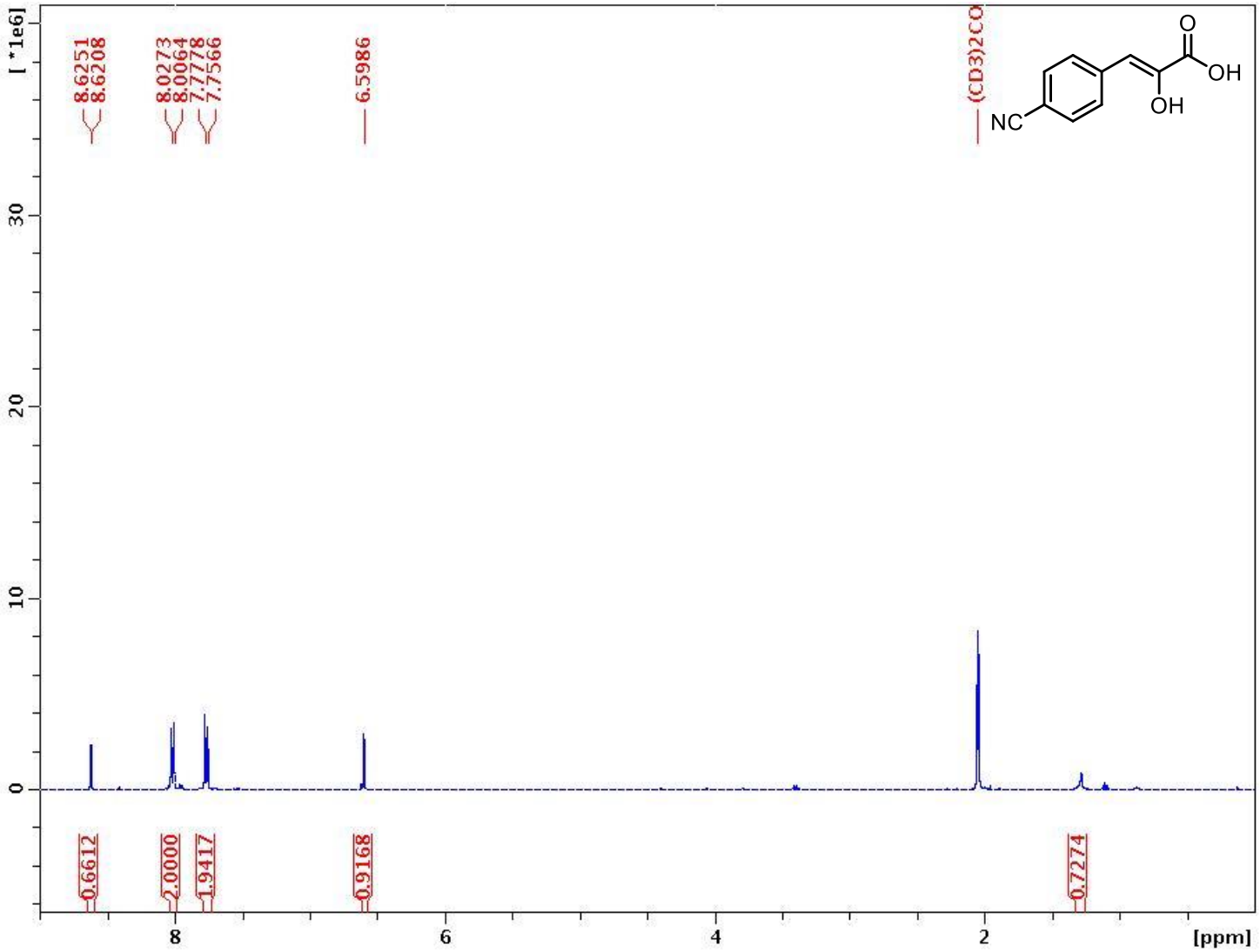
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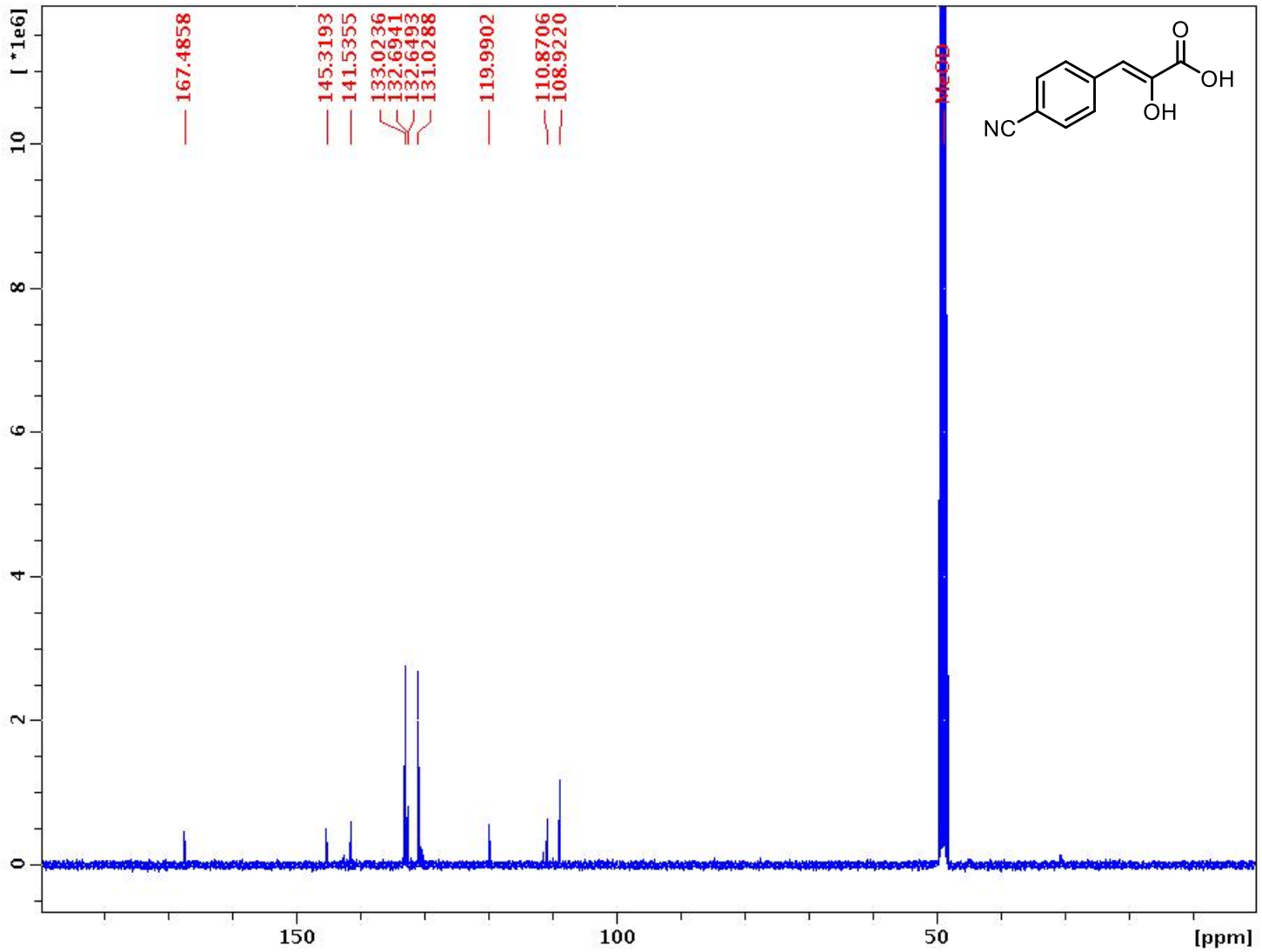
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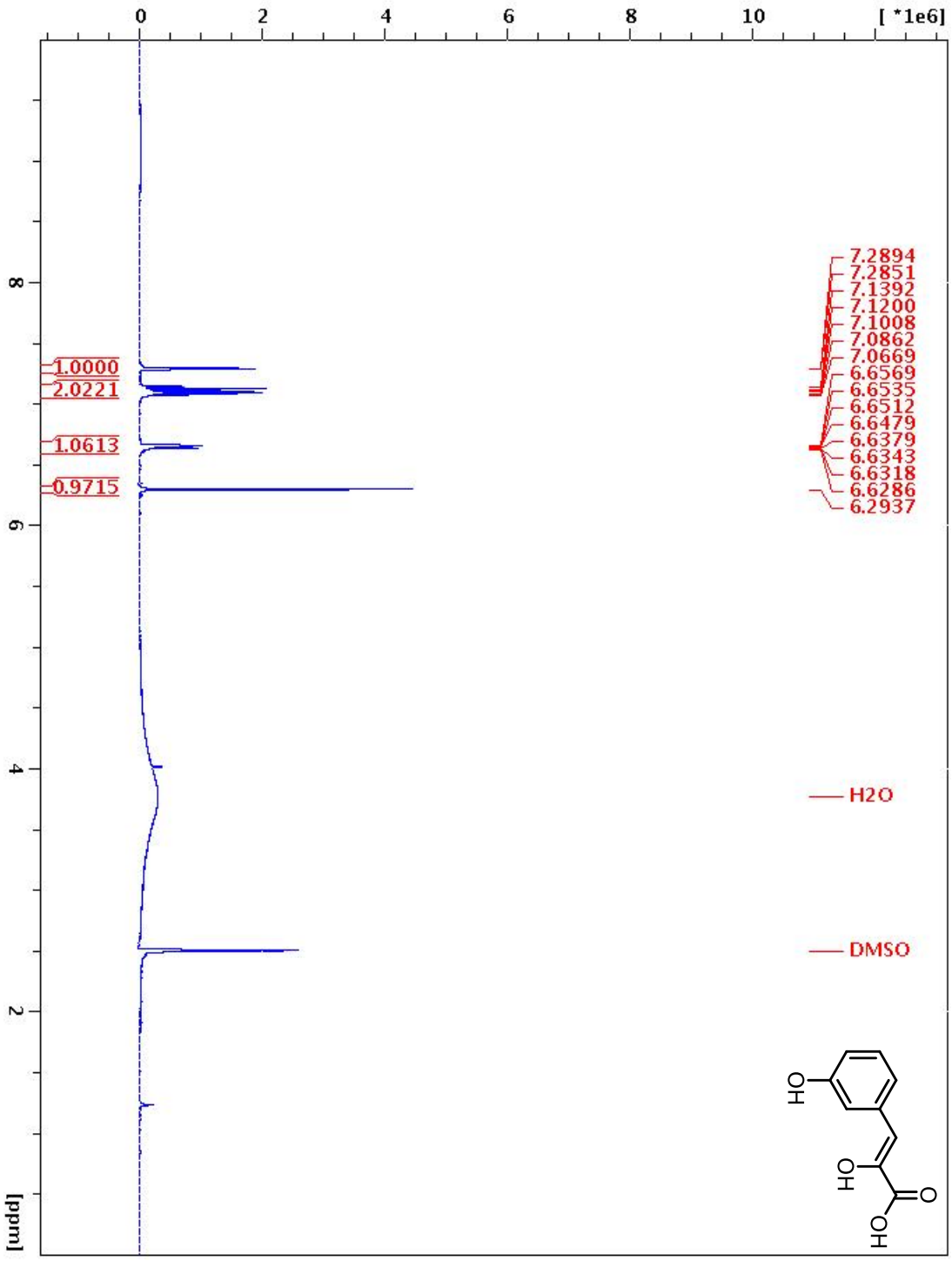
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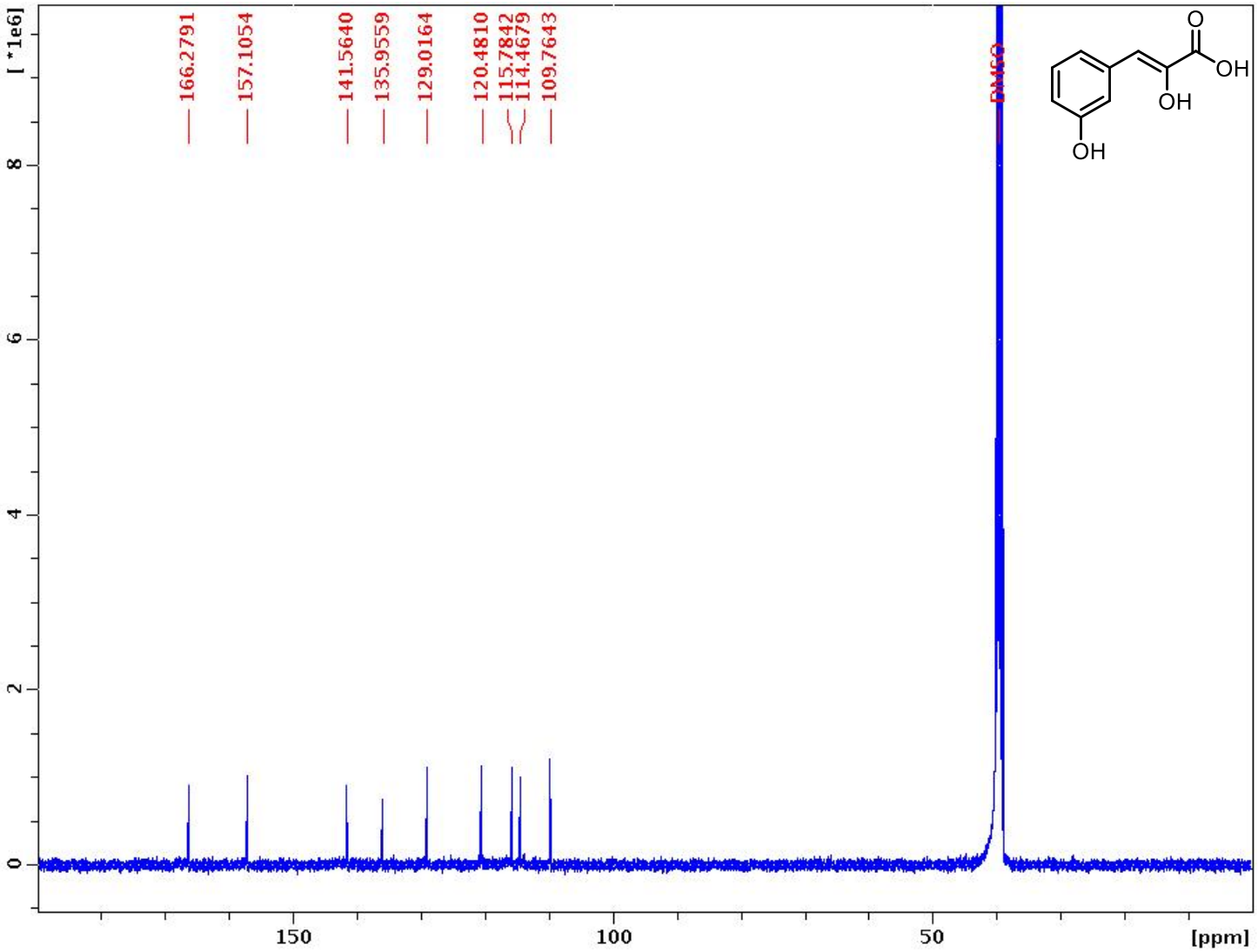
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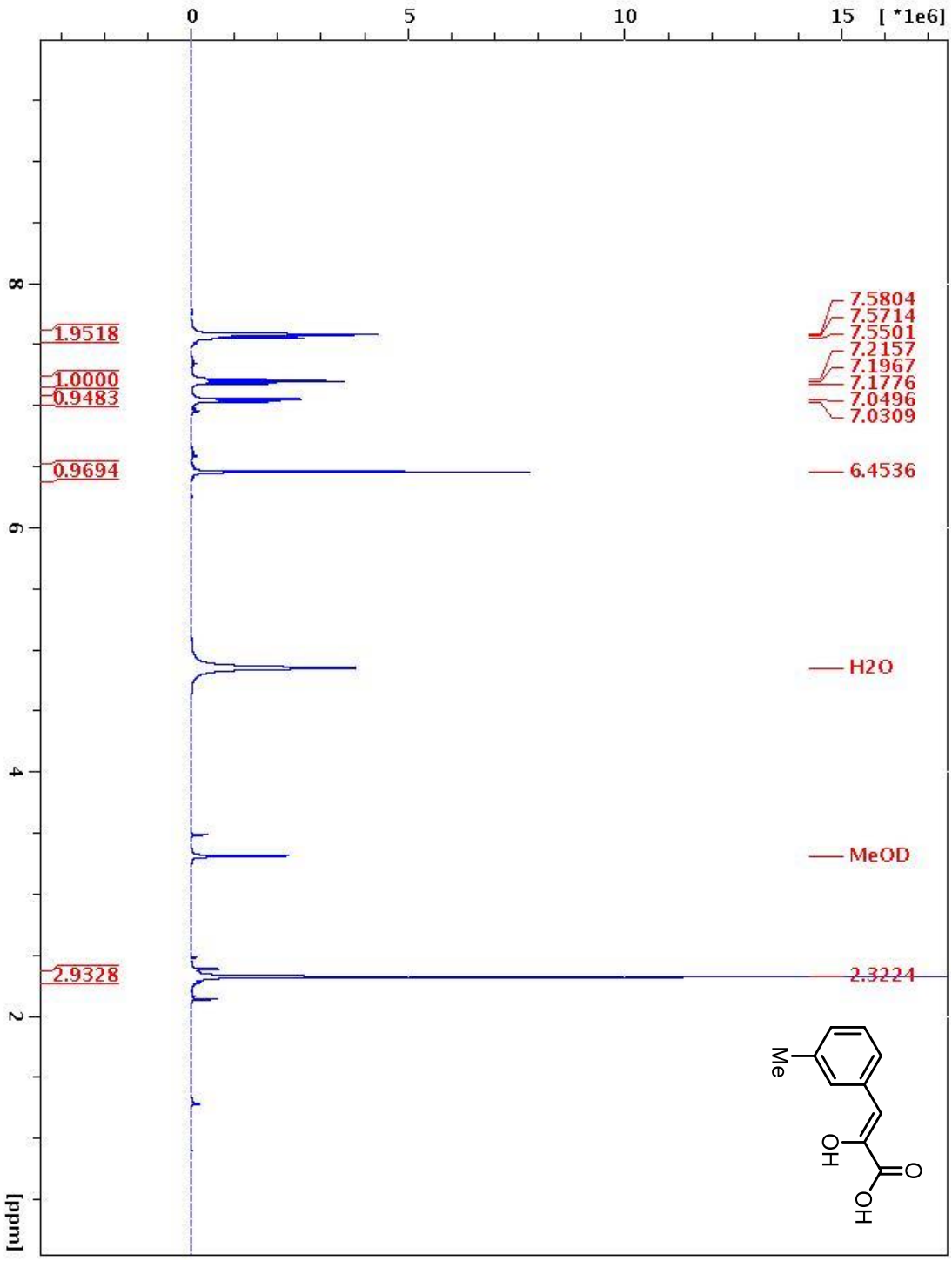
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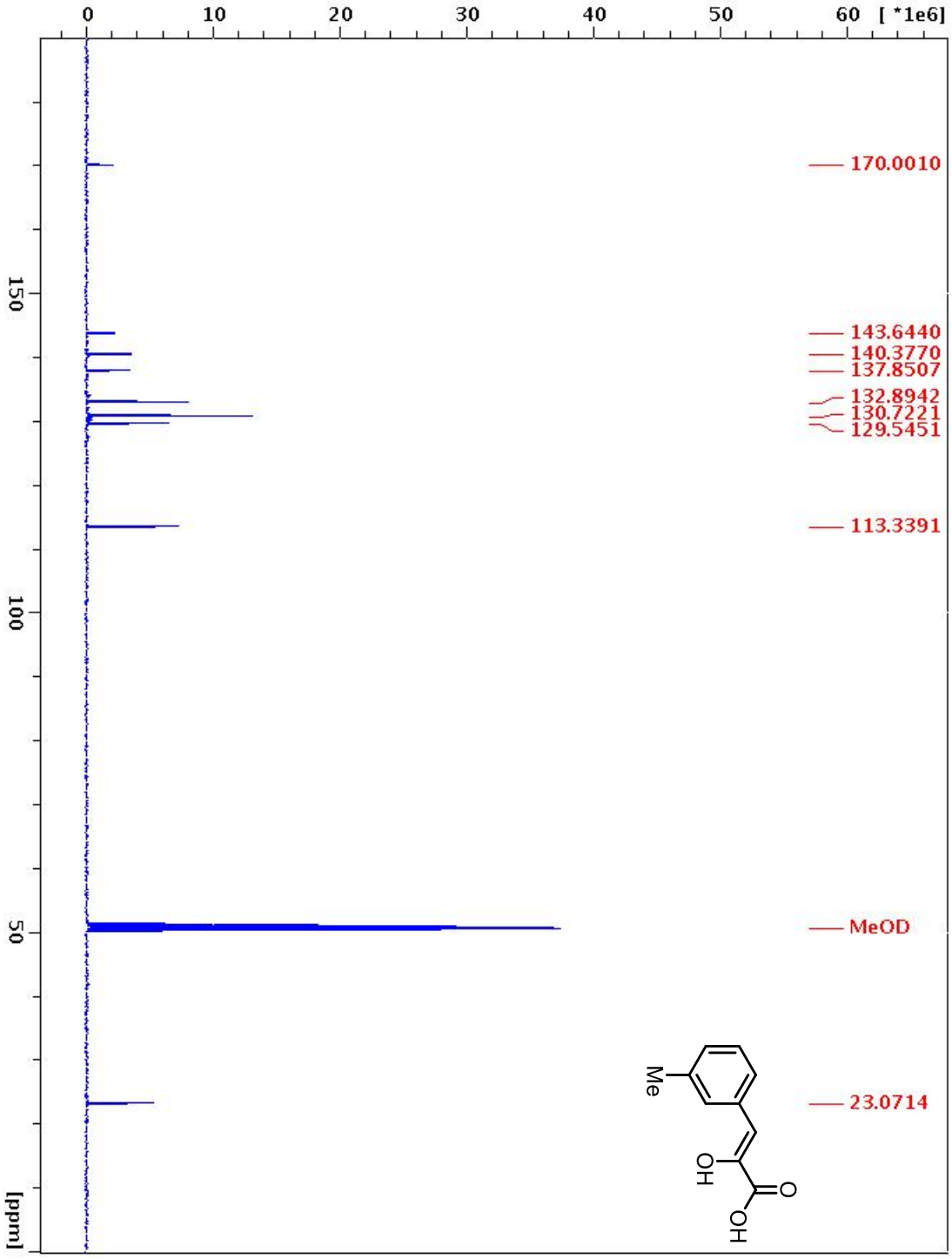
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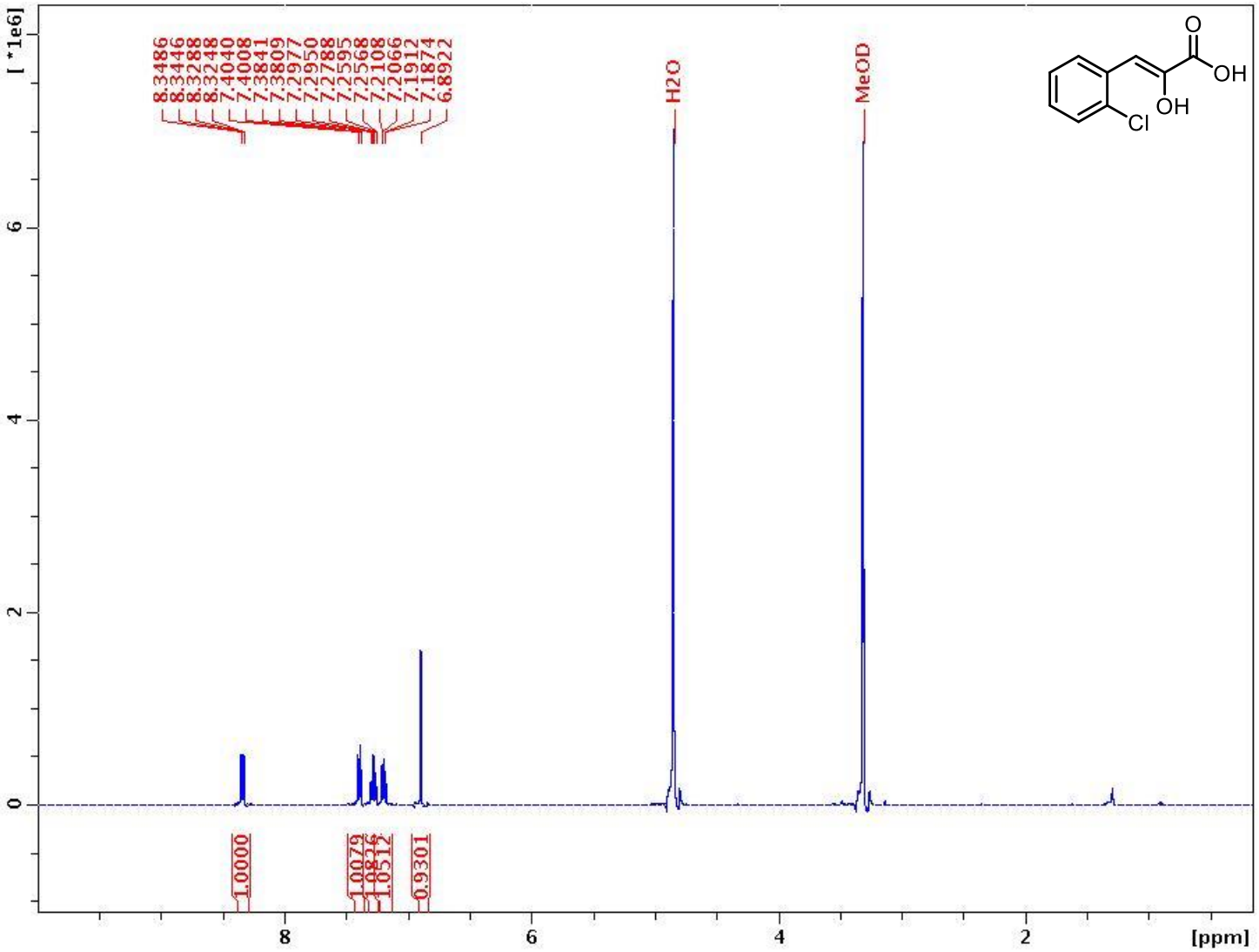
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7.2595
7.2568
7.2108
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7.1912
7.1874
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H2O
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O
OH
OH
Cl
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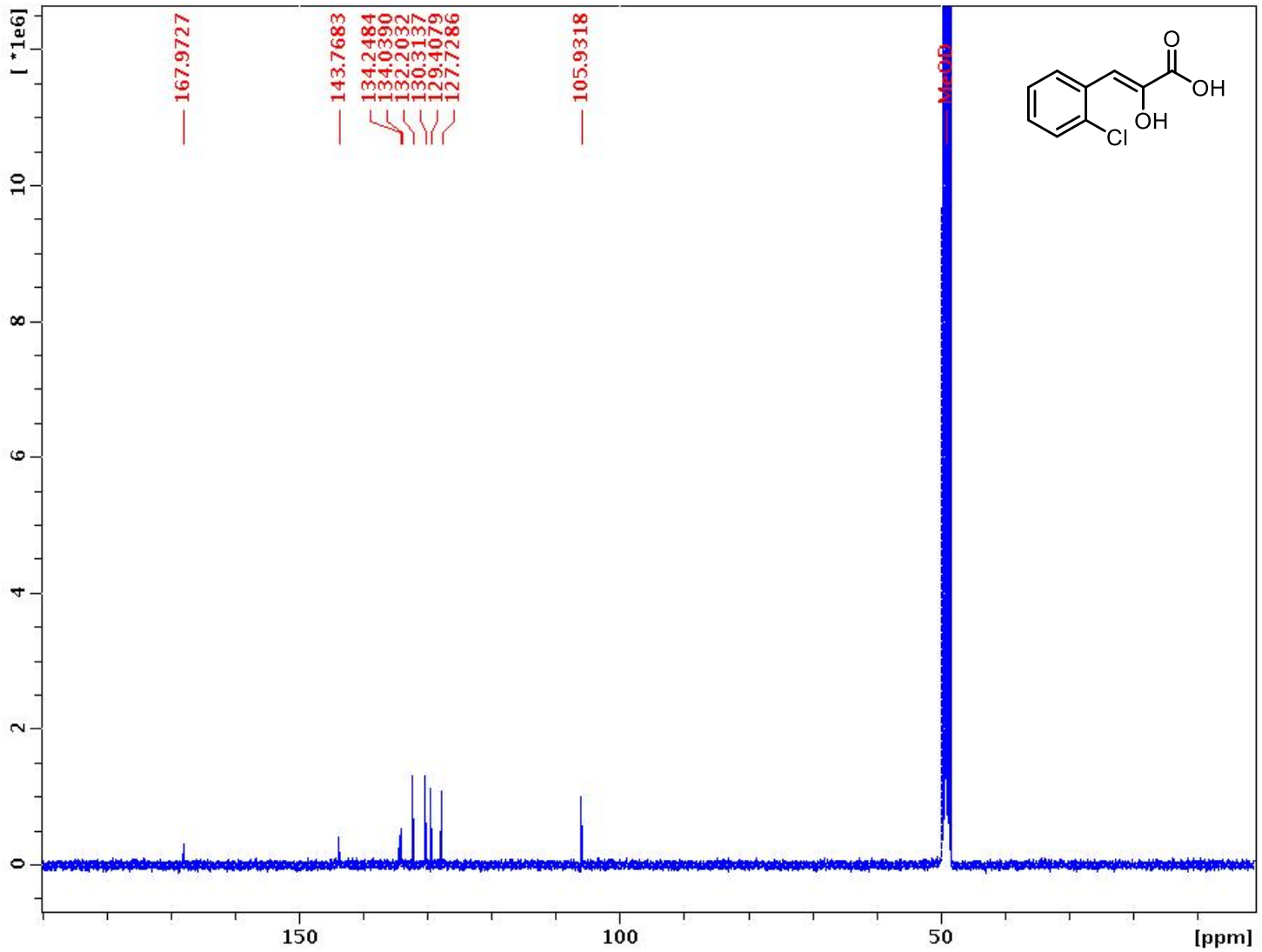
[ppm]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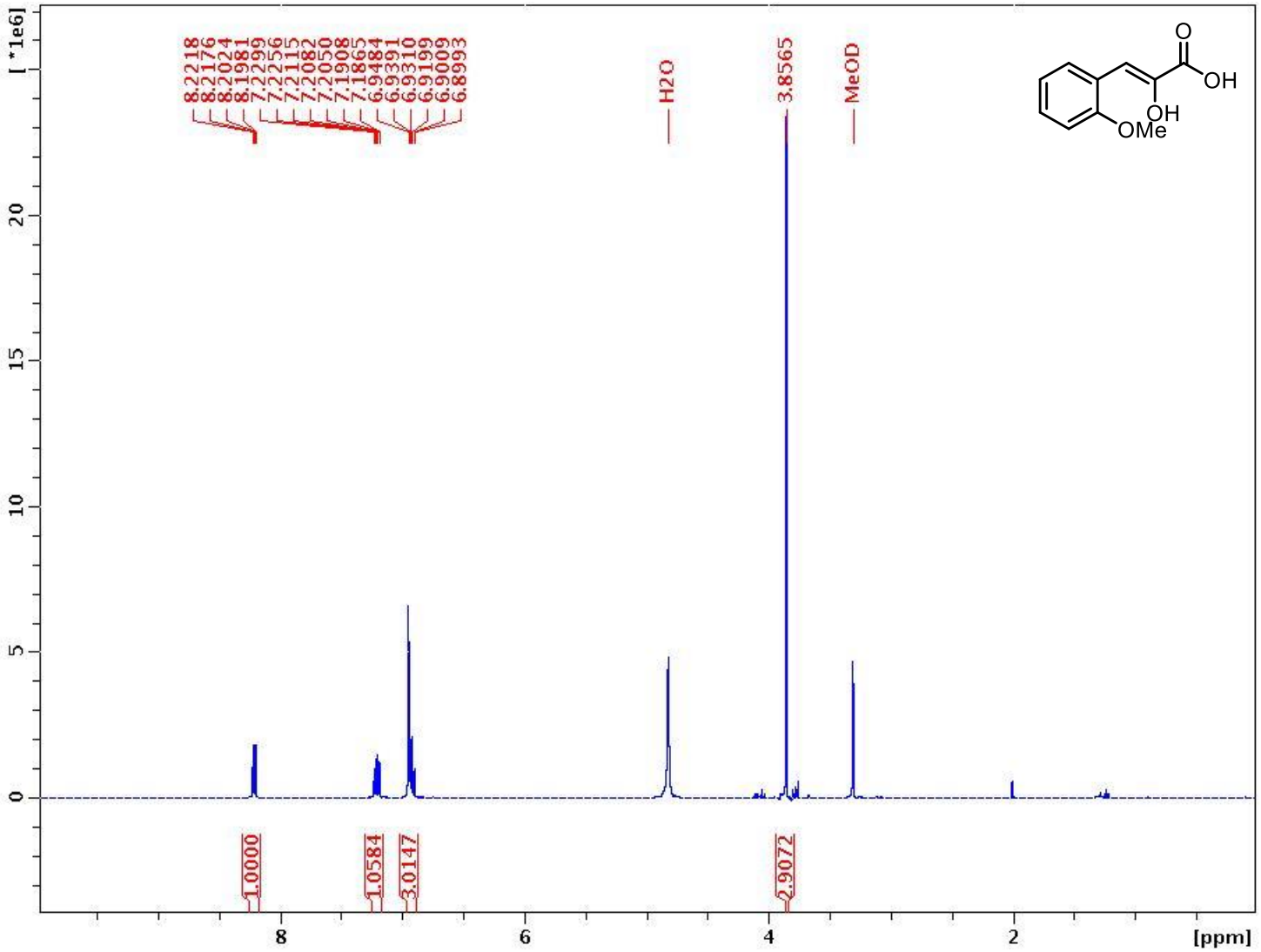
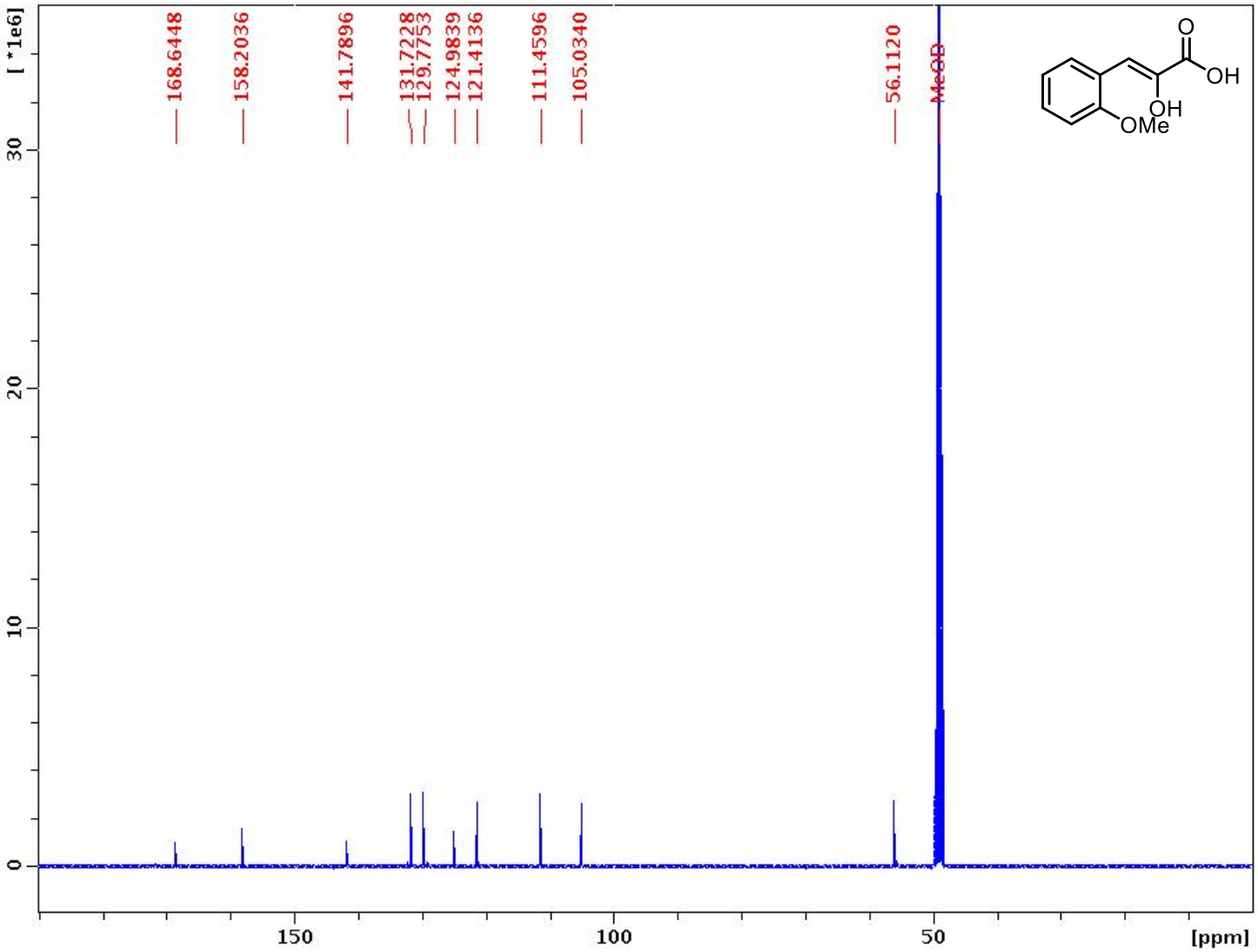
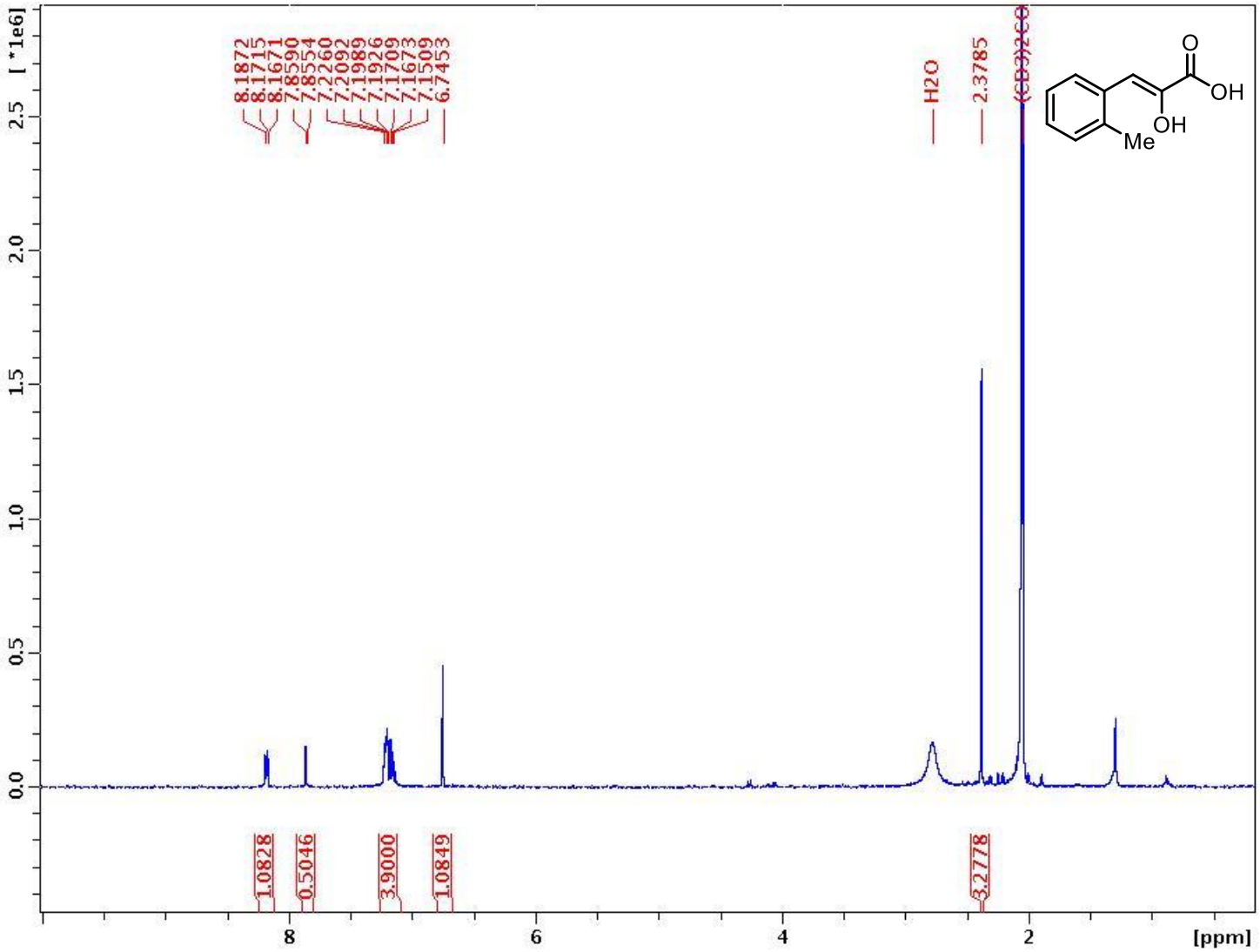
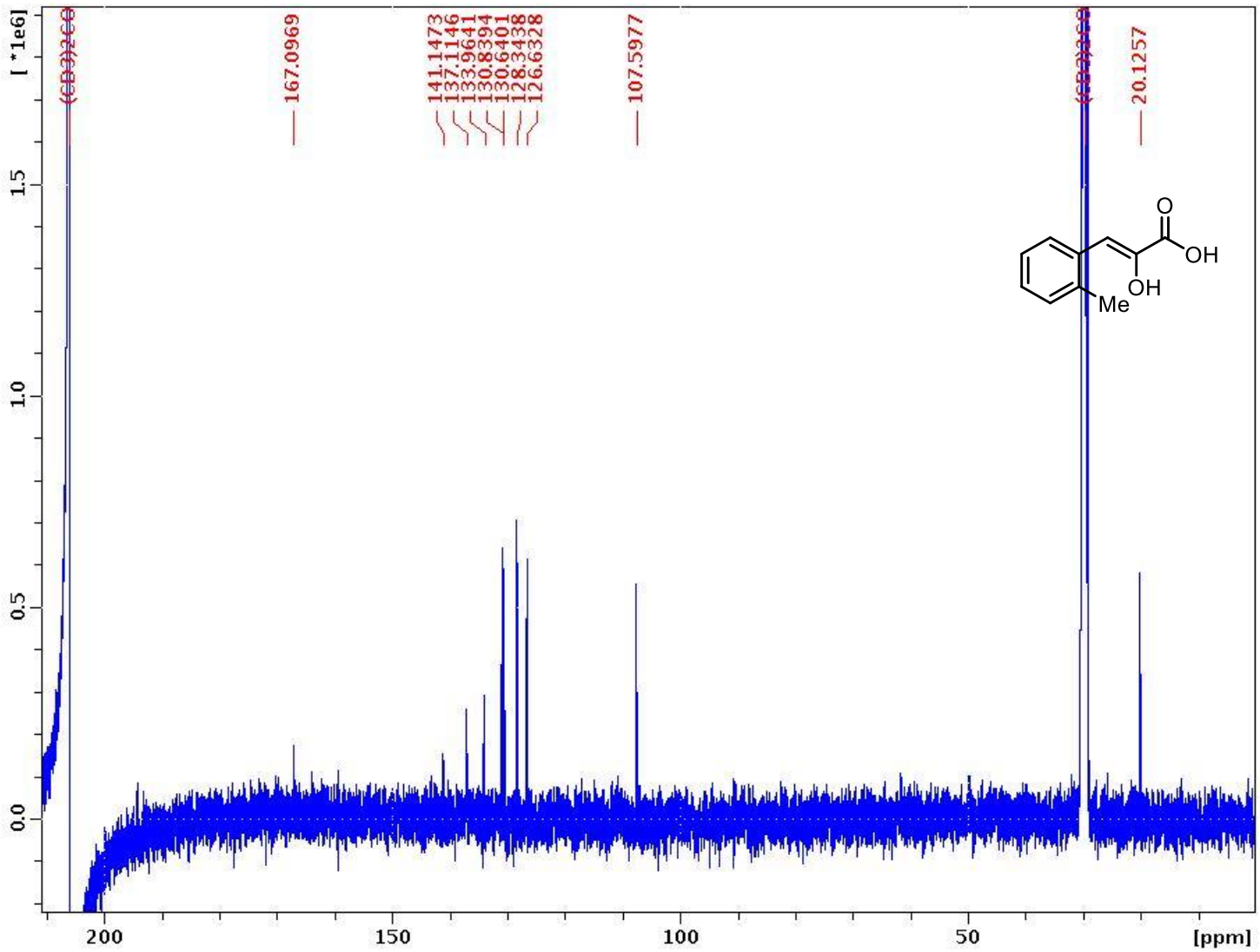
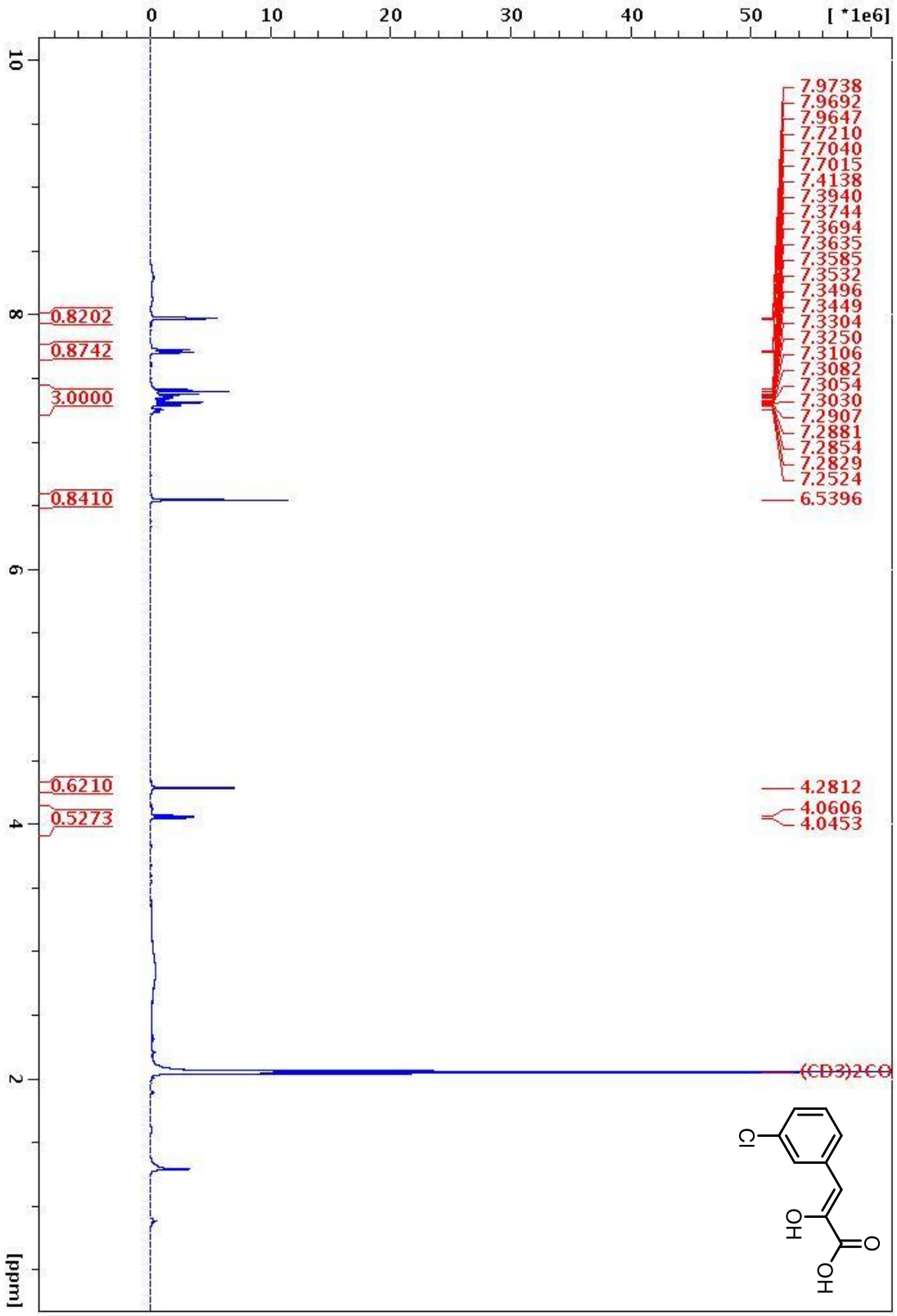
143.7683
134.2484
134.0390
132.2032
130.3137
129.4079
127.7286
105.9318
O
OH
OH
Cl
[*1e6]
10
8
6
4
2
0
150
100
50
[ppm]

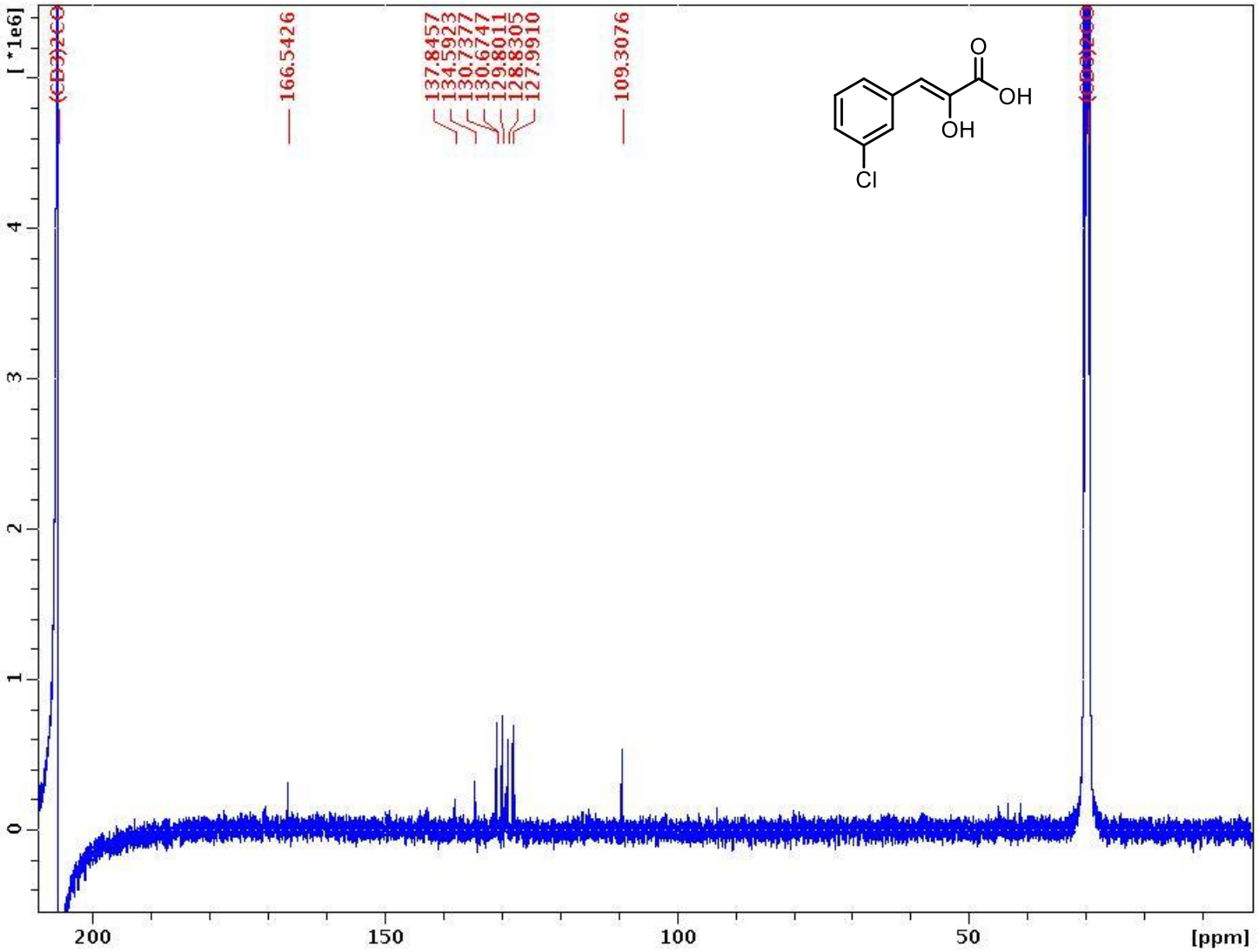

[*1e6]
0
5
10
15
20
8.2218
8.2176
8.2024
8.1981
7.2299
7.2256
7.2115
7.2082
7.2050
7.1908
7.1865
6.9484
6.9391
6.9310
6.9199
6.9009
6.8993
H2O
3.8565
MeOD
OH
OH
OMe
1.0000
1.0584
3.0147
2.9072
8
6
4
2
[ppm]

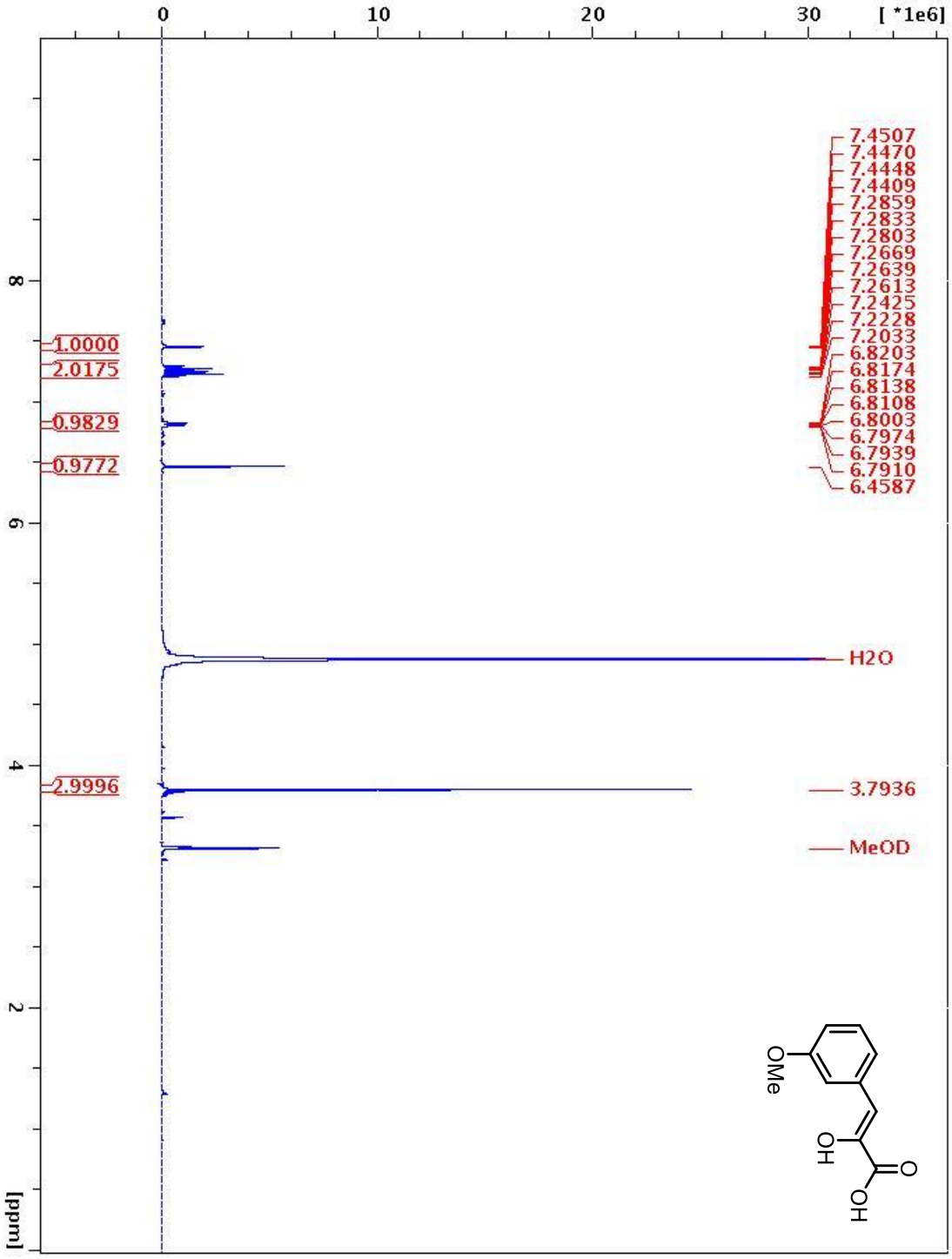

[*1e6]
30
20
10
0
168.6448
158.2036
141.7896
131.7228
129.7753
124.9839
121.4136
111.4596
105.0340
56.1120
MeOD
150
100
50
[ppm]
O
OH
OH
OMe

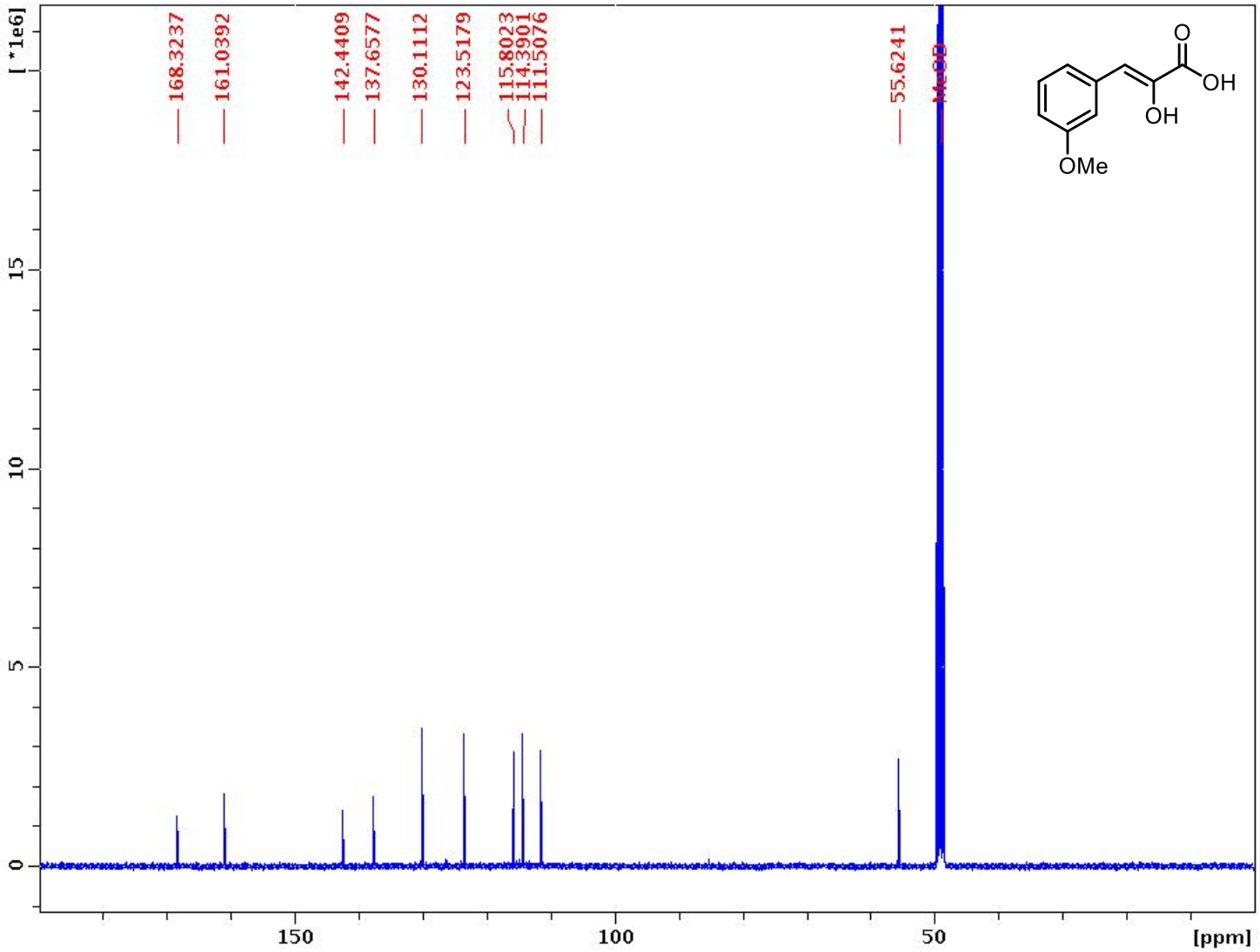

8.1872
8.1715
8.1671
7.8590
7.8554
7.2260
7.2092
7.1989
7.1926
7.1709
7.1673
7.1509
6.7453
H2O
2.3785
(CD3)2CO
O
OH
OH
Me
[*1e6]
2.5
2.0
1.5
1.0
0.5
0.0
1.0828
0.5046
3.9000
1.0849
3.2778
8
6
4
2
[ppm]

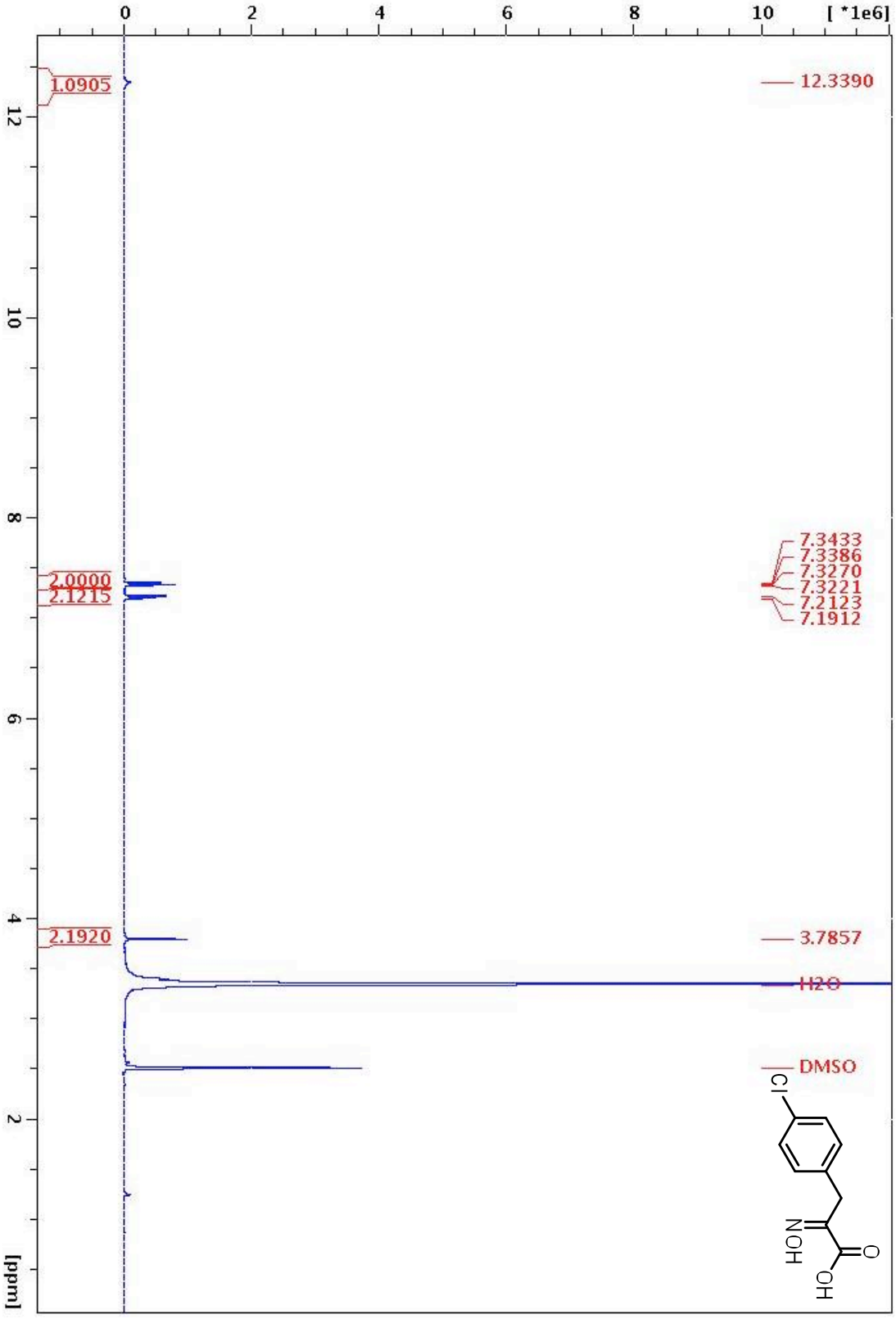

[*1e6]
1.5
1.0
0.5
0.0
167.0969
141.1473
137.1146
133.9641
130.8394
130.6401
128.3438
126.6328
107.5977
20.1257
O
OH
OH
Me
200
150
100
50
[ppm]

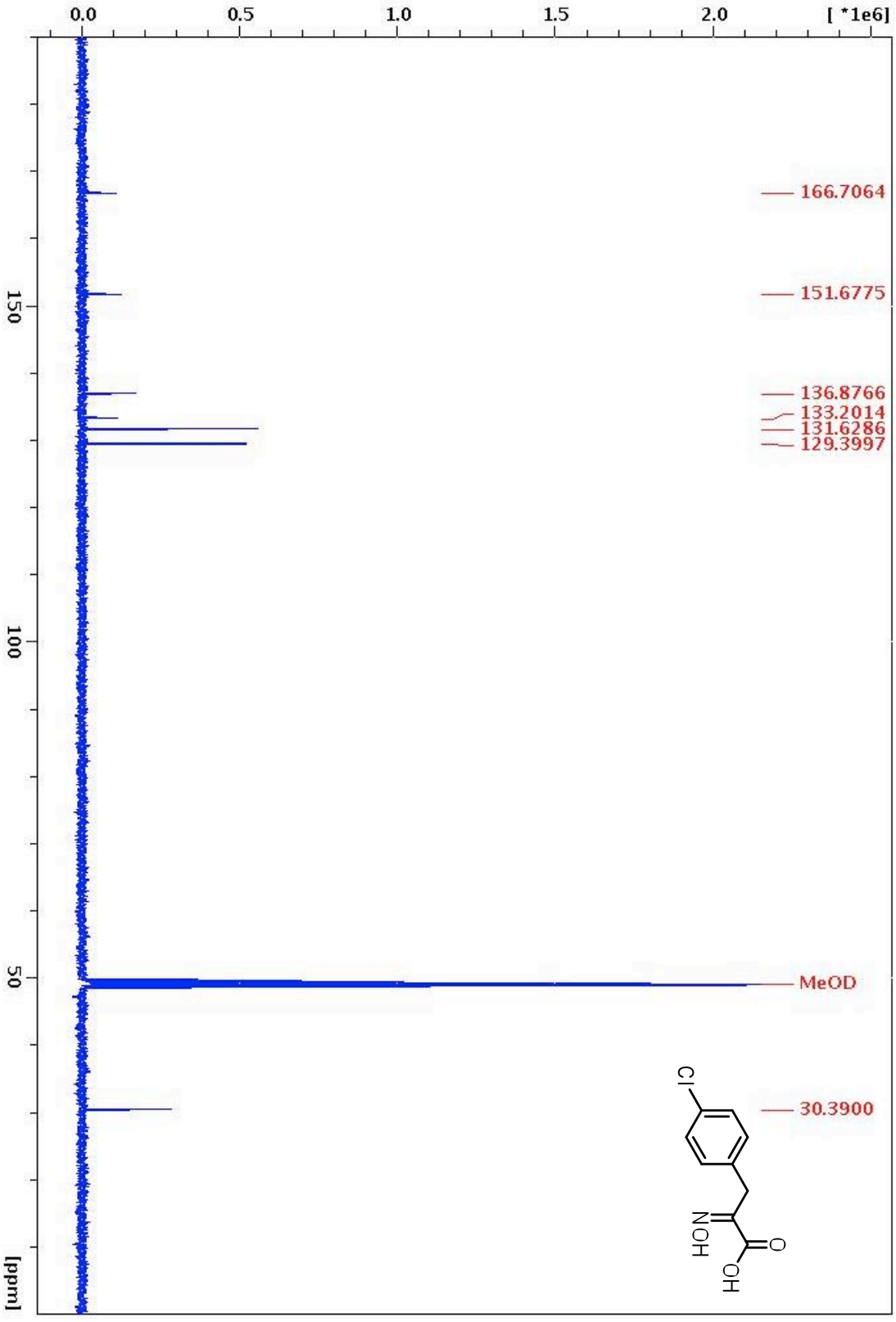

0
10
20
30
40
50
[*1e6]
10
8
6
4
2
[ppm]
0.8202
0.8742
3.0000
0.8410
0.6210
0.5273
7.9738
7.9692
7.9647
7.7210
7.7040
7.7015
7.4138
7.3940
7.3744
7.3694
7.3635
7.3585
7.3532
7.3496
7.3449
7.3304
7.3250
7.3106
7.3082
7.3054
7.3030
7.2907
7.2881
7.2854
7.2829
7.2524
6.5396
4.2812
4.0606
4.0453
(CD3)2CO
Cl
OH
O
OH

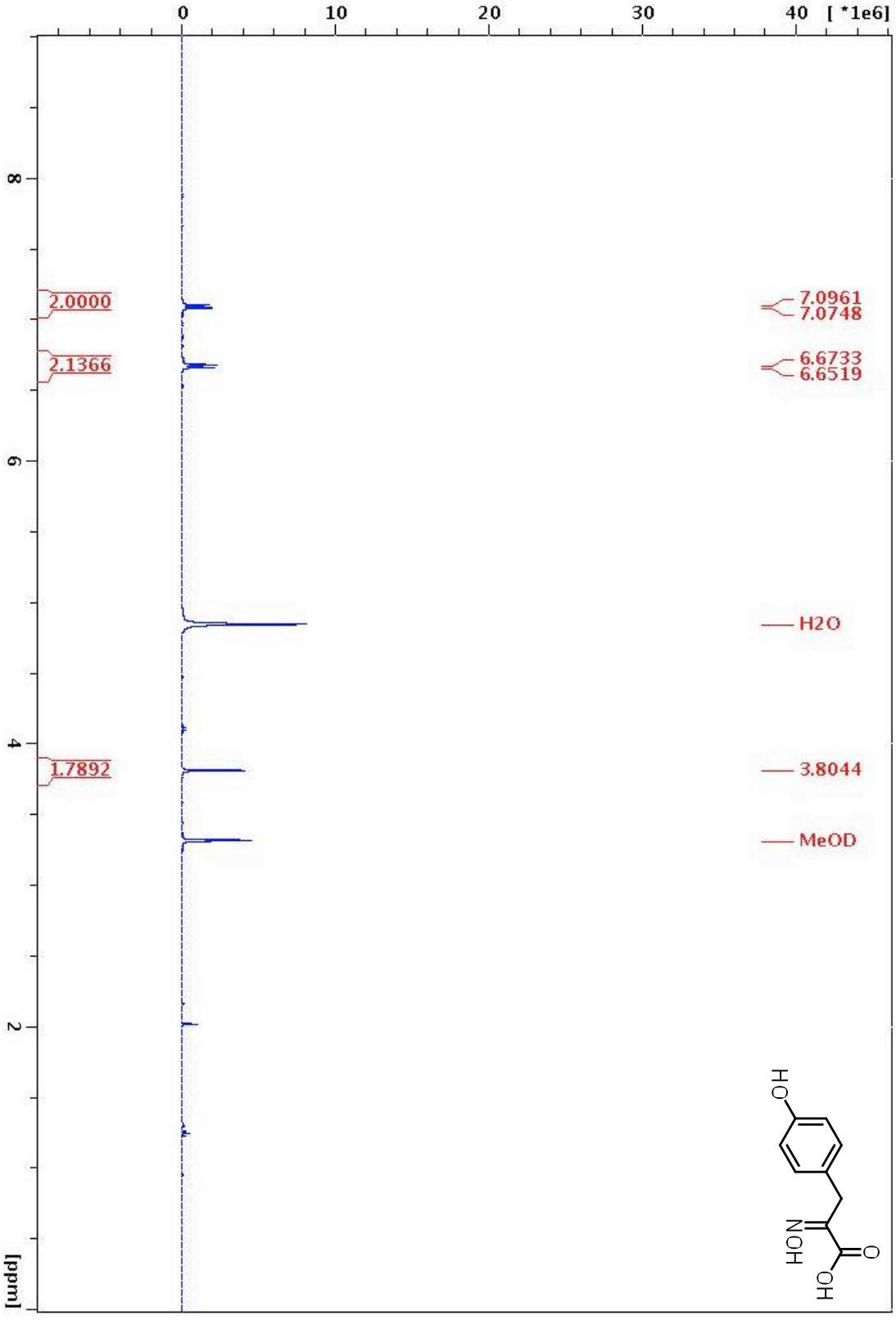

[*1e6]
0
1
2
3
4
166.5426
137.8457
134.5923
130.7377
130.6747
129.8011
128.8305
127.9910
109.3076
O
OH
OH
Cl
200
150
100
50
[ppm]

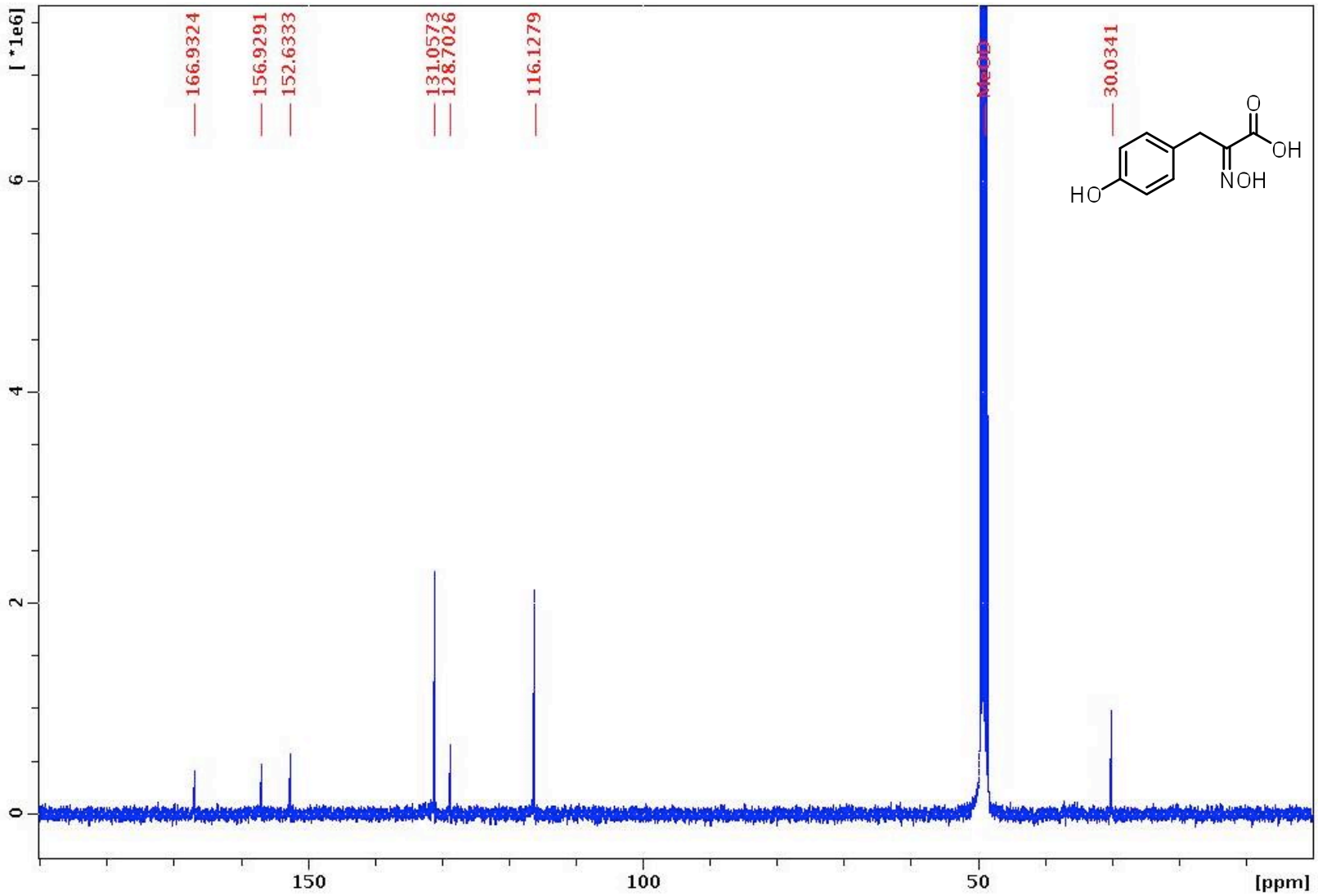

0
10
20
30
[*1e6]
8
6
4
2
[ppm]
1.0000
2.0175
0.9829
0.9772
2.9996
7.4507
7.4470
7.4448
7.4409
7.2859
7.2833
7.2803
7.2669
7.2639
7.2613
7.2425
7.2228
7.2033
6.8203
6.8174
6.8138
6.8108
6.8003
6.7974
6.7939
6.7910
6.4587
H2O
3.7936
MeOD
OMe
OH
O
OH

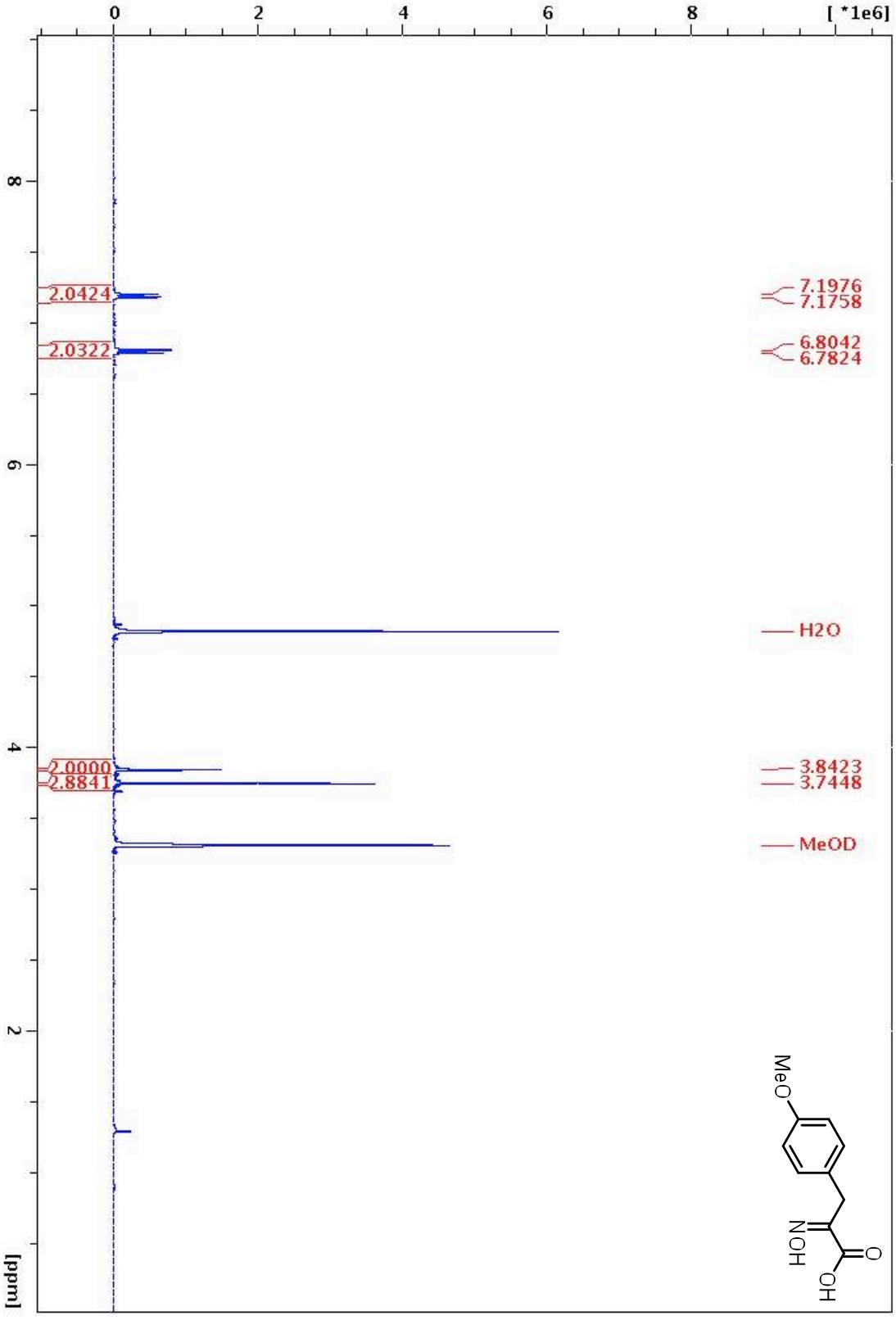

[*1e6]
15
10
5
0
168.3237
161.0392
142.4409
137.6577
130.1112
123.5179
115.8023
114.3901
111.5076
55.6241
O
OH
OH
OMe
150
100
50
[ppm]

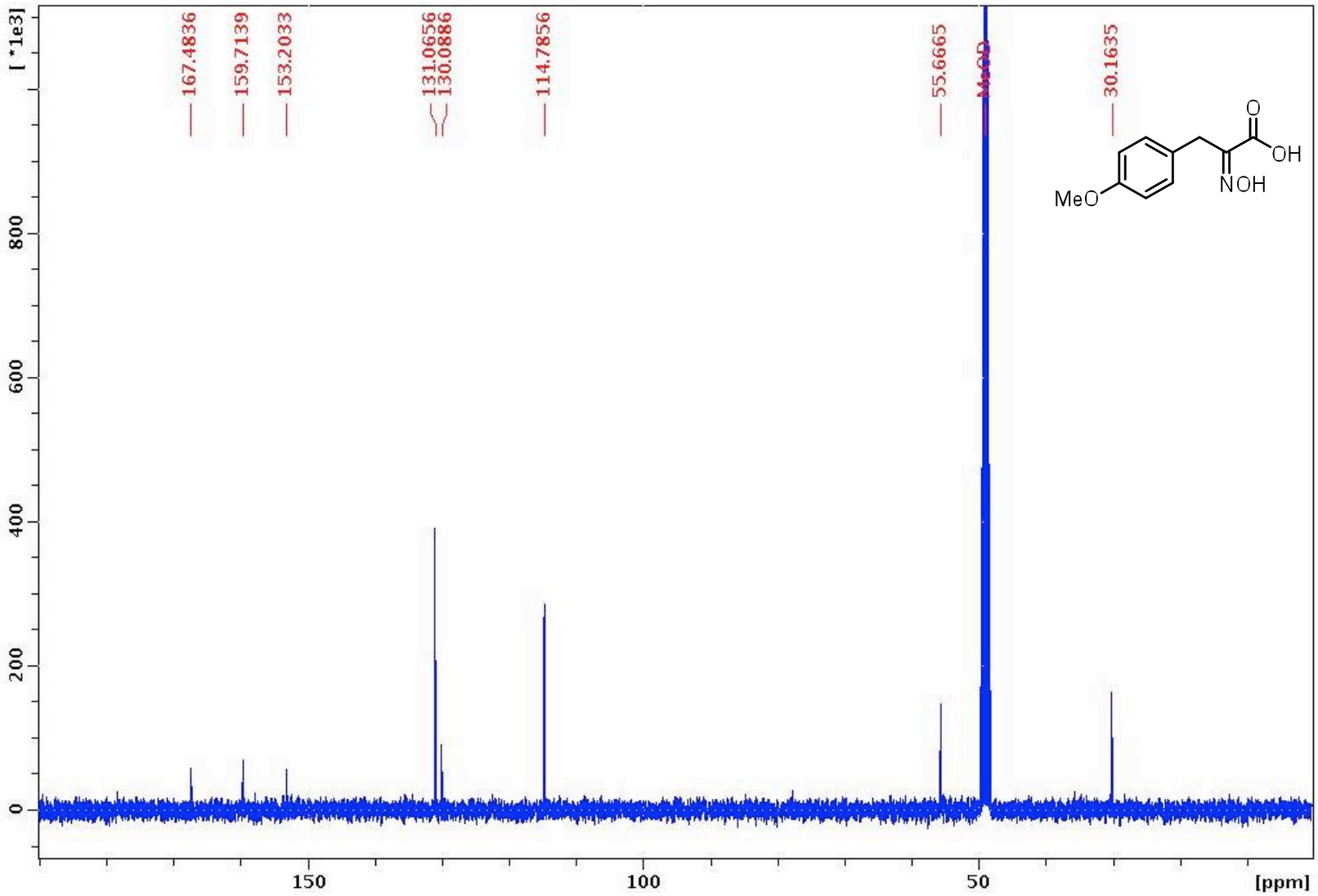

0
2
4
6
8
10
[*1e6]
12
10
8
6
4
2
[ppm]
1.0905
2.0000
2.1215
2.1920
12.3390
7.3433
7.3386
7.3270
7.3221
7.2123
7.1912
3.7857
H2O
DMSO
Cl
N
OH
O
OH

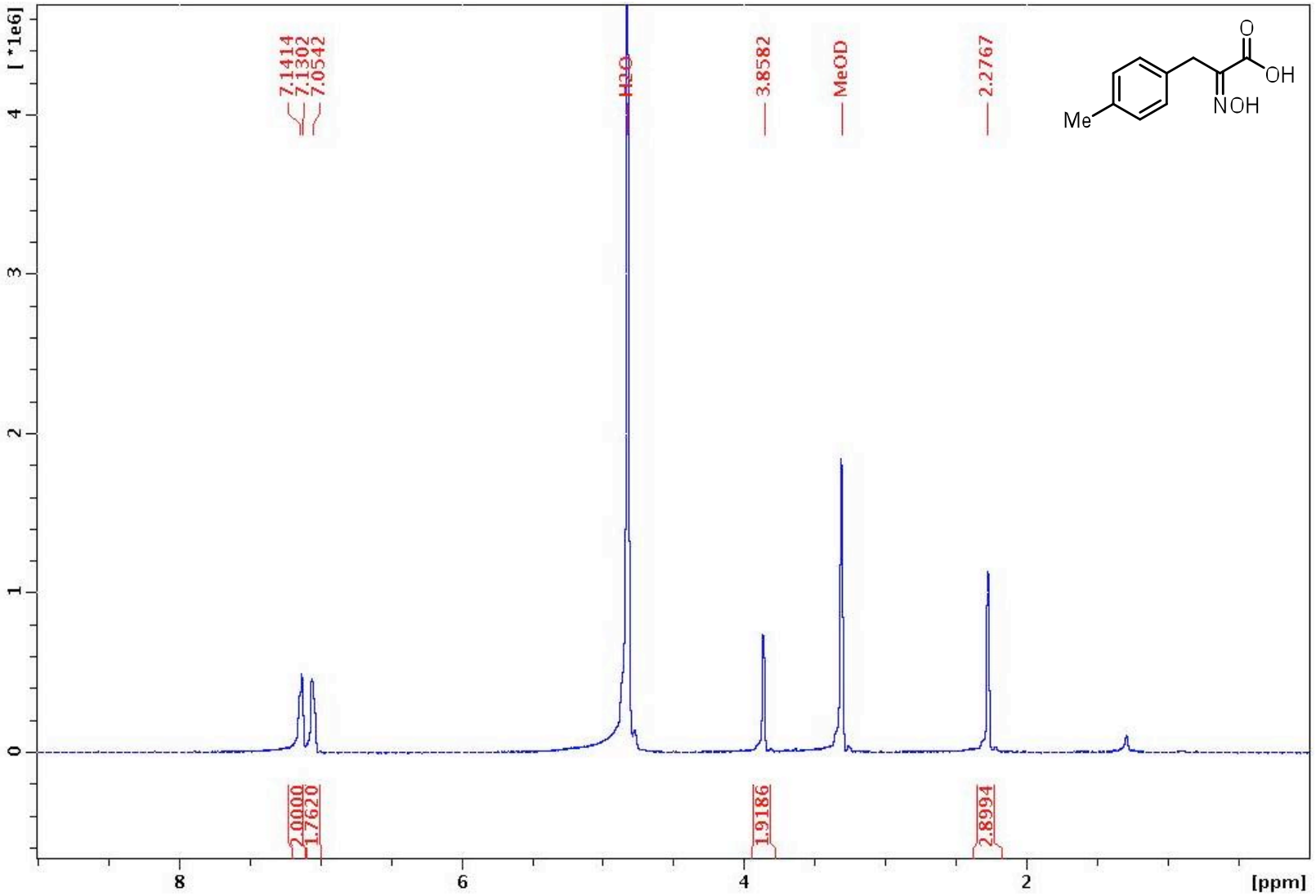

0.0
0.5
1.0
1.5
2.0
[*1e6]
150
100
50
[ppm]
166.7064
151.6775
136.8766
133.2014
131.6286
129.3997
MeOD
30.3900
Cl
HO
N
OH
O

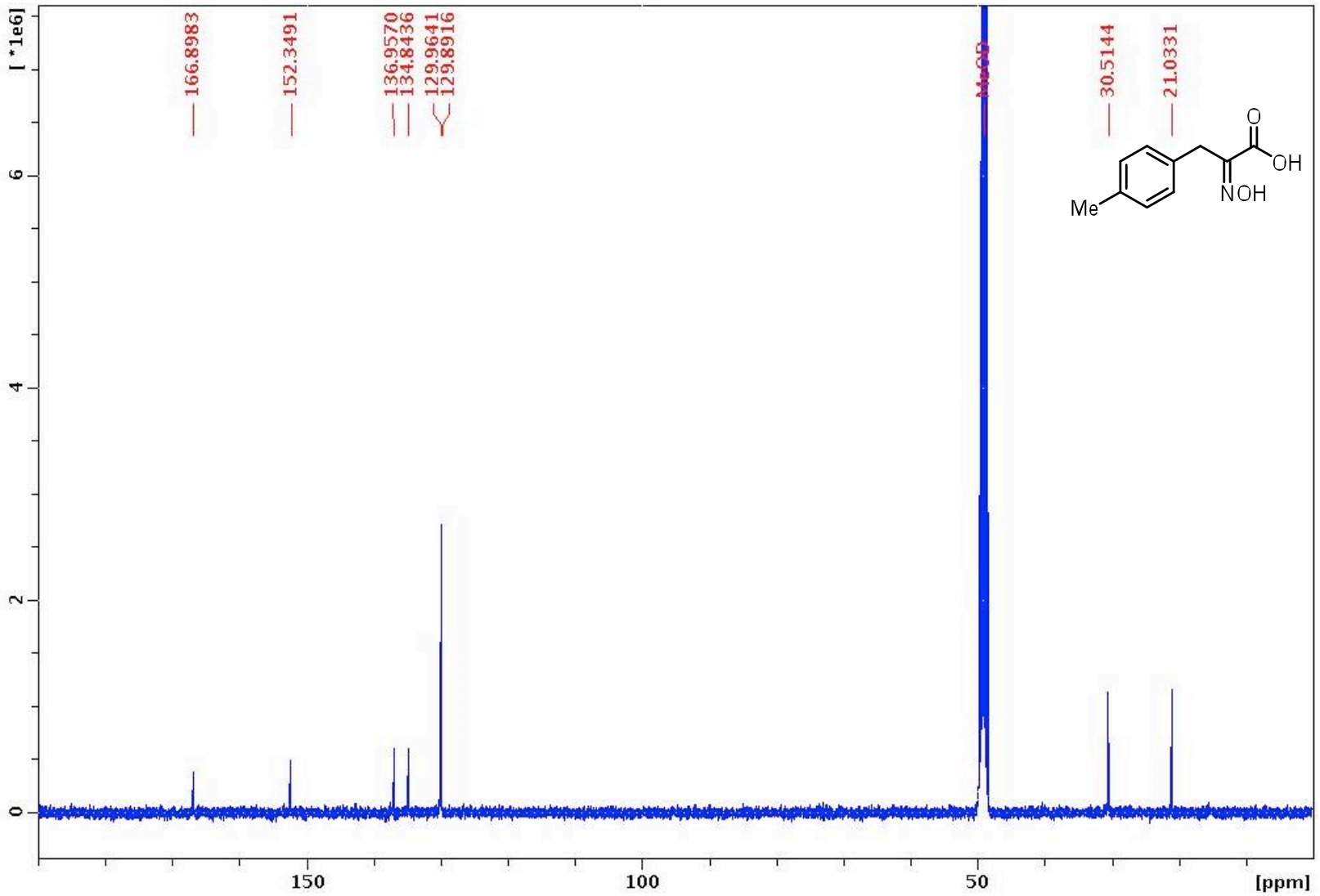

0
10
20
30
40
[*1e6]
8
6
4
2
[ppm]
2.0000
2.1366
1.7892
7.0961
7.0748
6.6733
6.6519
H2O
3.8044
MeOD
HO
N
OH
O
OH

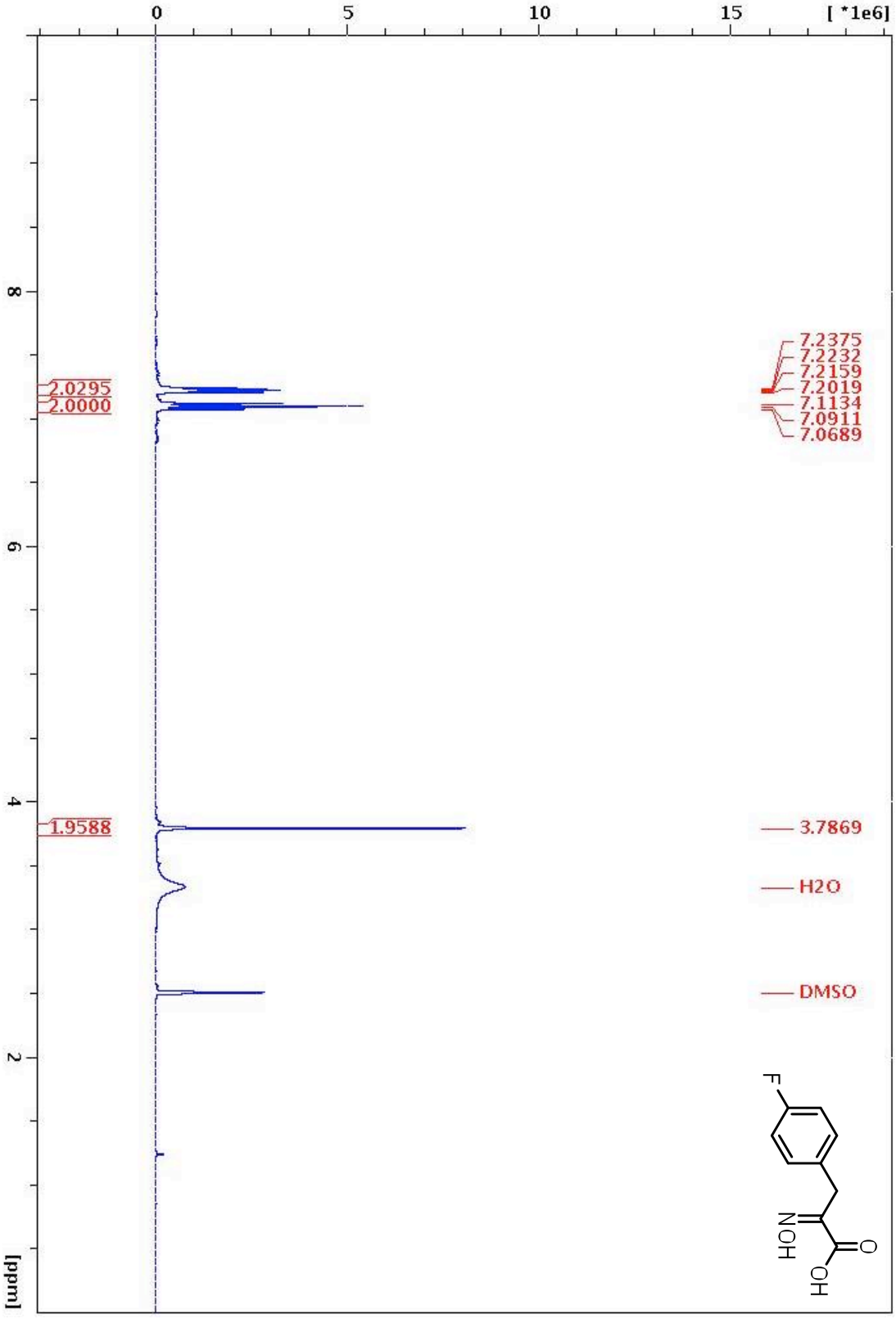

[*1e6]
166.9324
156.9291
152.6333
131.0573
128.7026
116.1279
30.0341
0
2
4
6
150
100
50
[ppm]
HO
NOH
OH
O

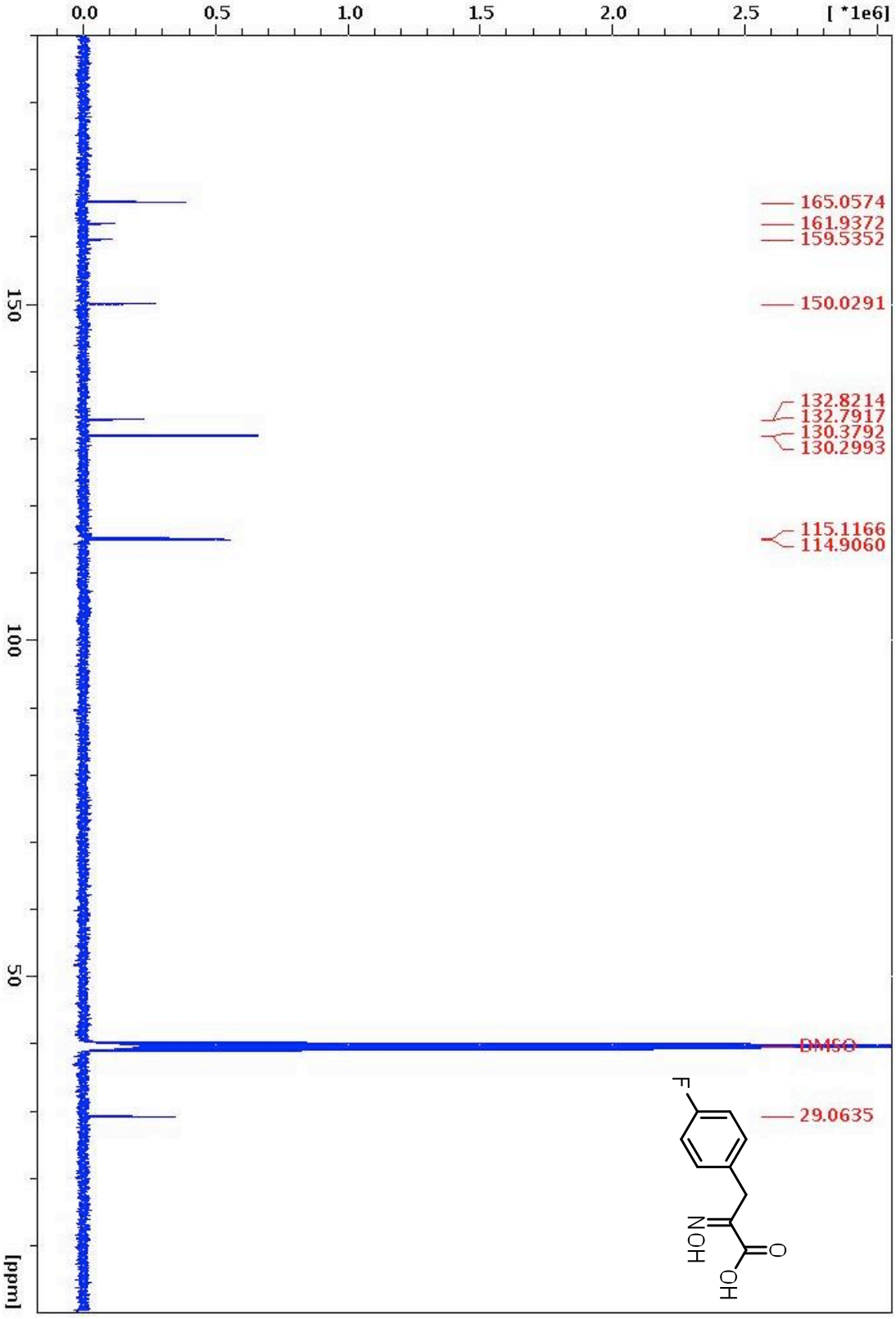

0
2
4
6
8
[*1e6]
8
6
4
2
[ppm]
2.0424
2.0322
2.0000
2.8841
7.1976
7.1758
6.8042
6.7824
H2O
3.8423
3.7448
MeOD
MeO
NOH
O
OH

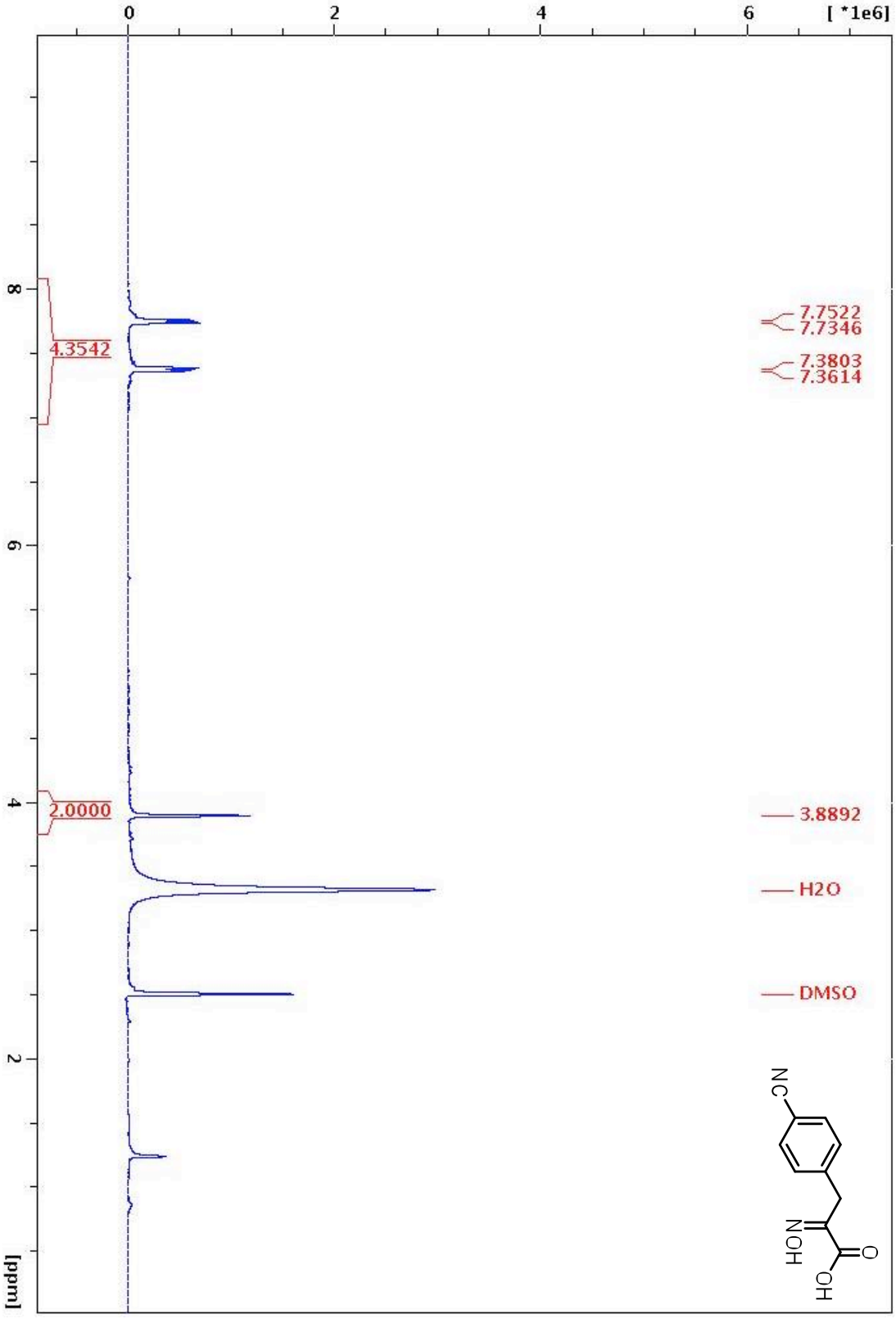

[*1e3]
800
600
400
200
0
167.4836
159.7139
153.2033
131.0656
130.0886
114.7856
55.6665
30.1635
150
100
50
[ppm]
O
OH
NOH
MeO

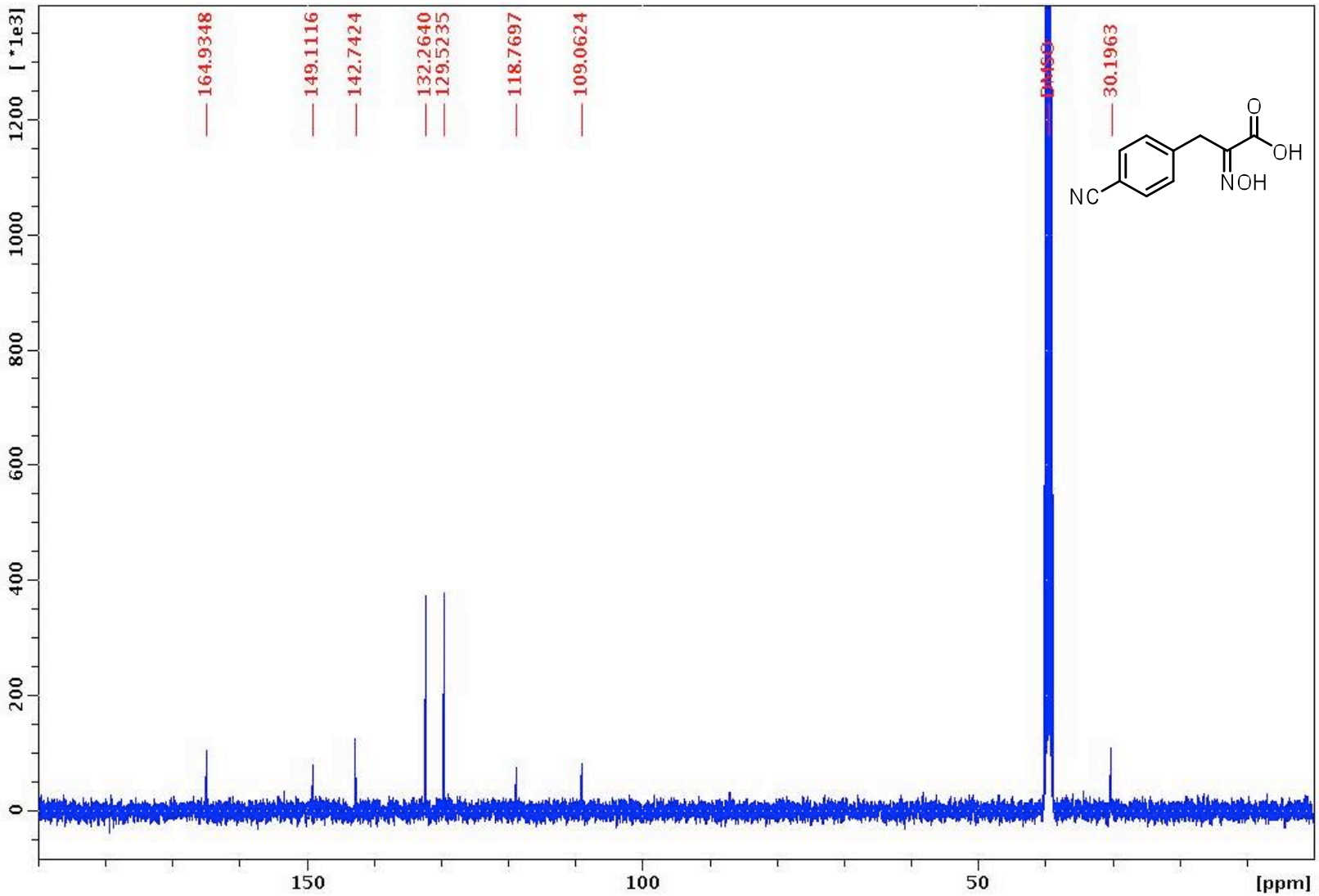

[*1e6]
4
3
2
1
0
7.1414
7.1302
7.0542
H2O
3.8582
MeOD
2.2767
2.0000
1.7620
1.9186
2.8994
8
6
4
2
[ppm]
O
OH
NOH
Me

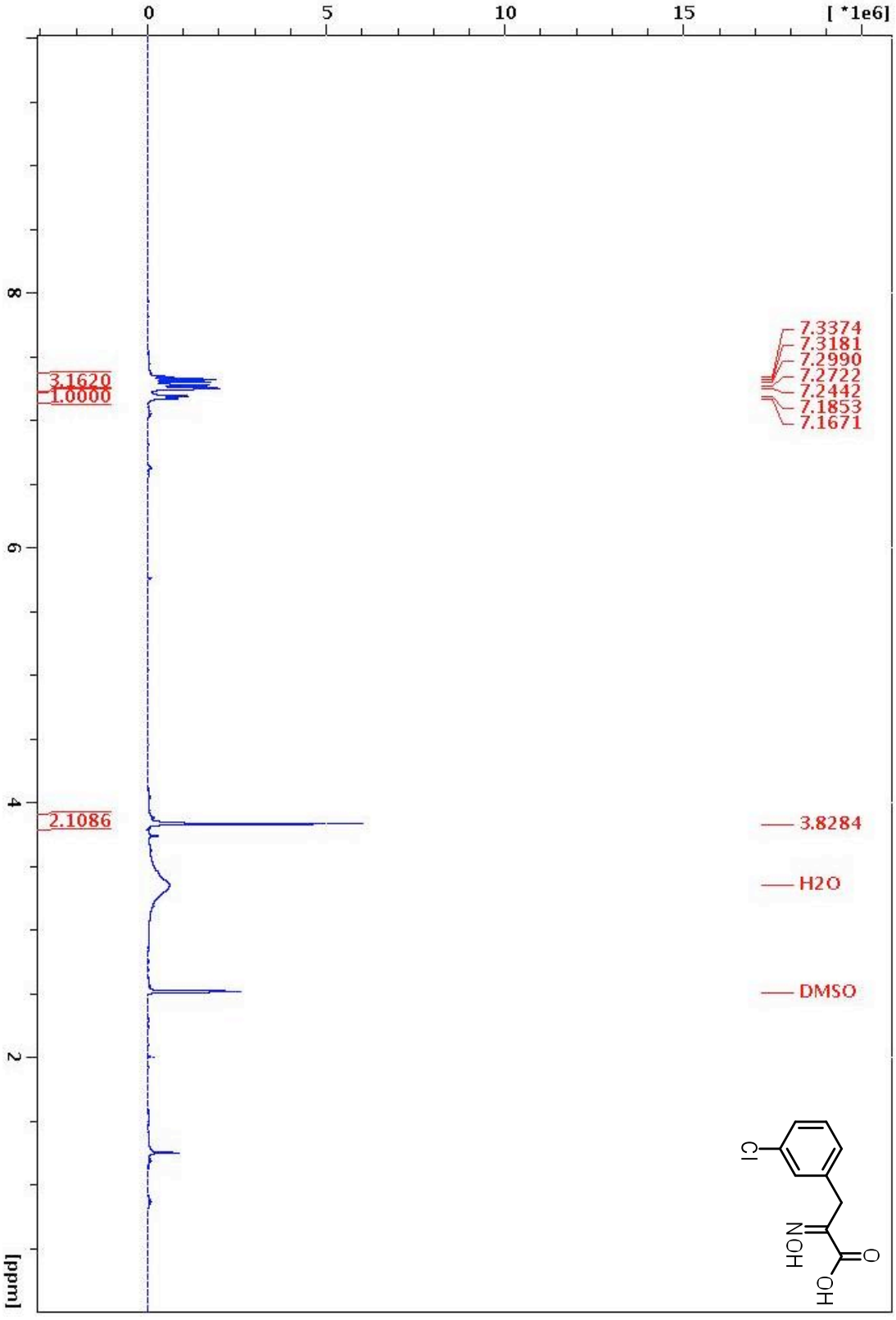

[*1e6]
166.8983
152.3491
136.9570
134.8436
129.9641
129.8916
30.5144
21.0331
0
2
4
6
150
100
50
[ppm]
O
OH
NOH
Me

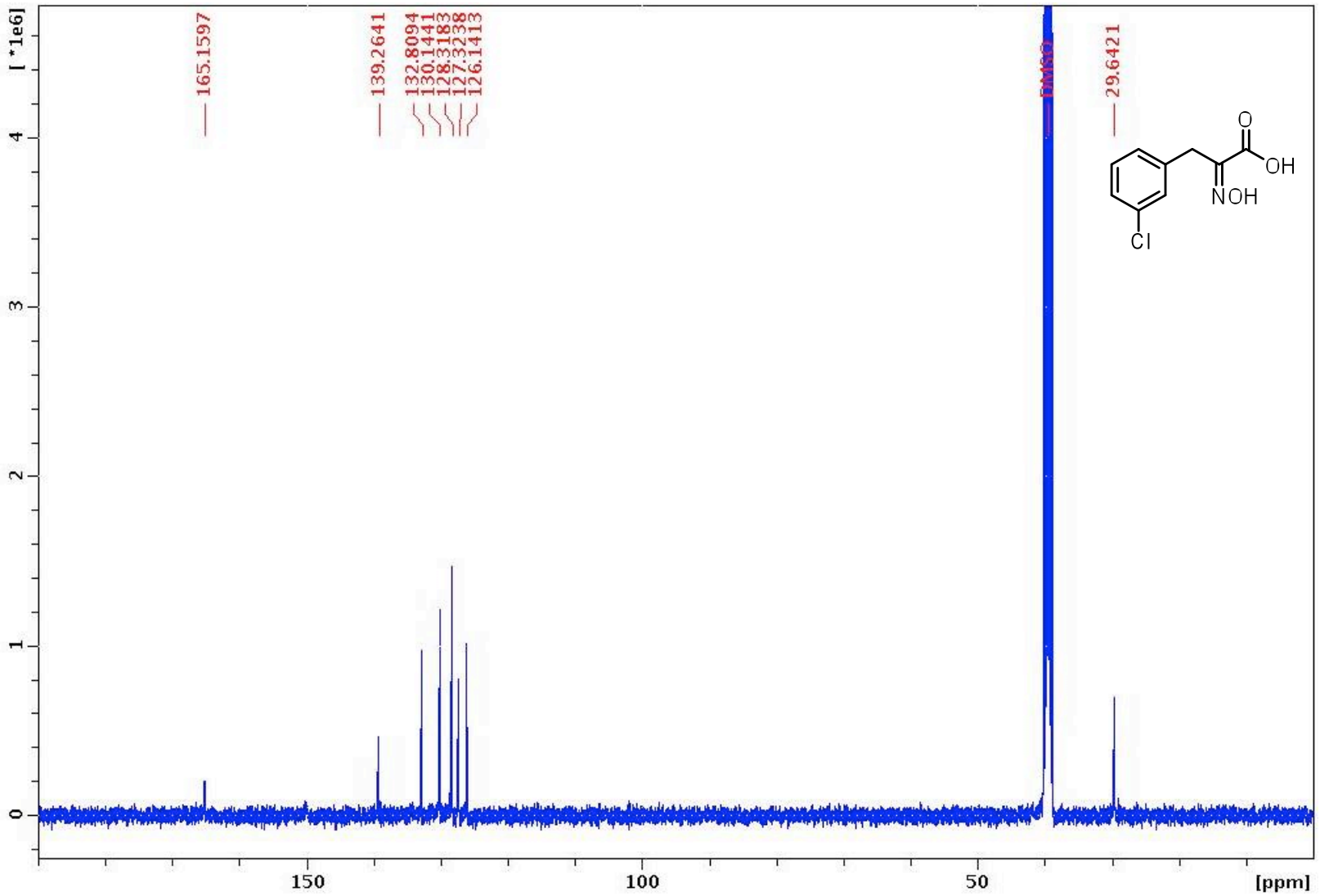

0
5
10
15
[*1e6]
8
6
4
2
[ppm]
2.0295
2.0000
1.9588
7.2375
7.2232
7.2159
7.2019
7.1134
7.0911
7.0689
3.7869
H2O
DMSO
F
NOH
O
OH

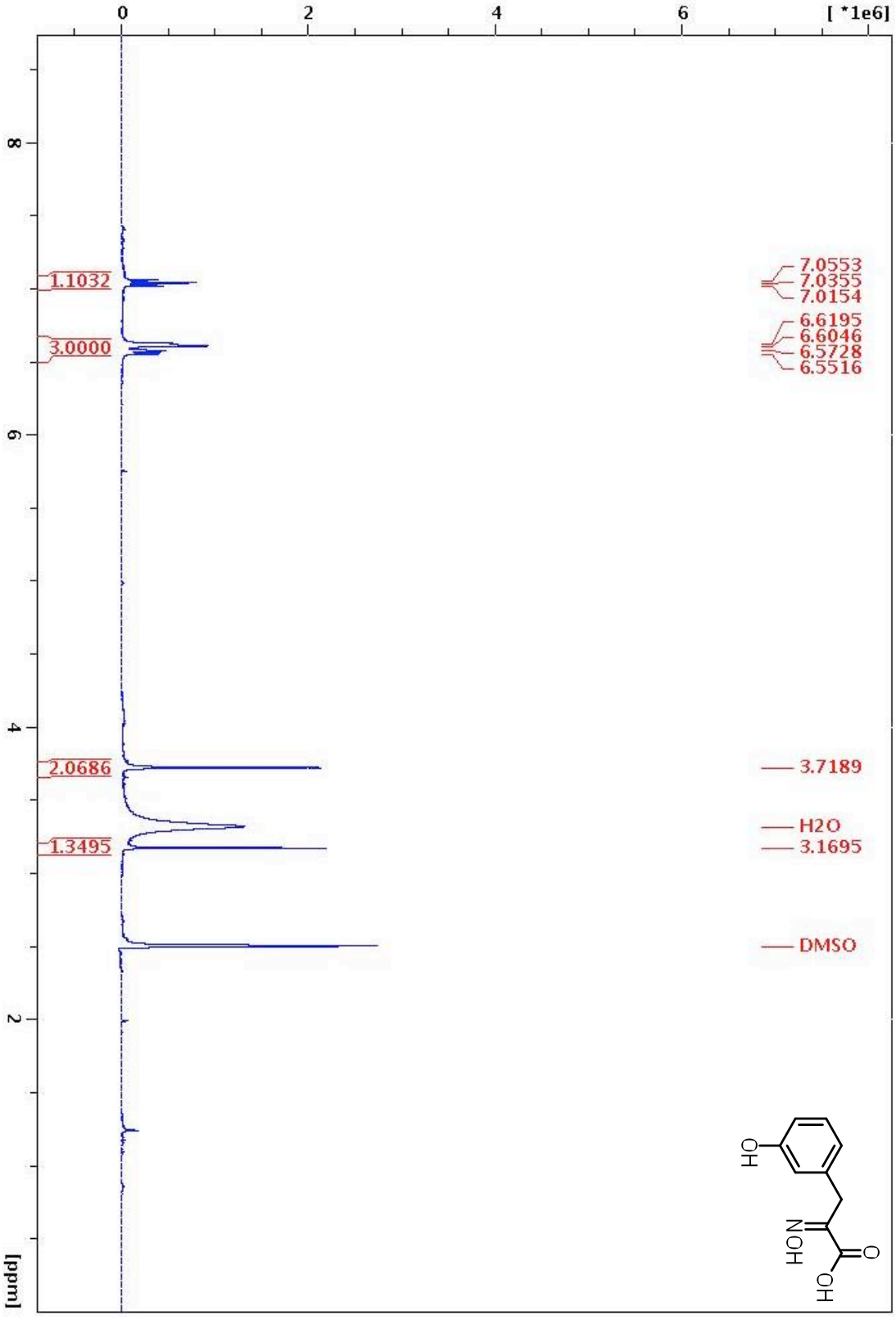

0.0
0.5
1.0
1.5
2.0
2.5
[*1e6]
150
100
50
[ppm]
165.0574
161.9372
159.5352
150.0291
132.8214
132.7917
130.3792
130.2993
115.1166
114.9060
DMSO
29.0635
F
NOH
O
OH

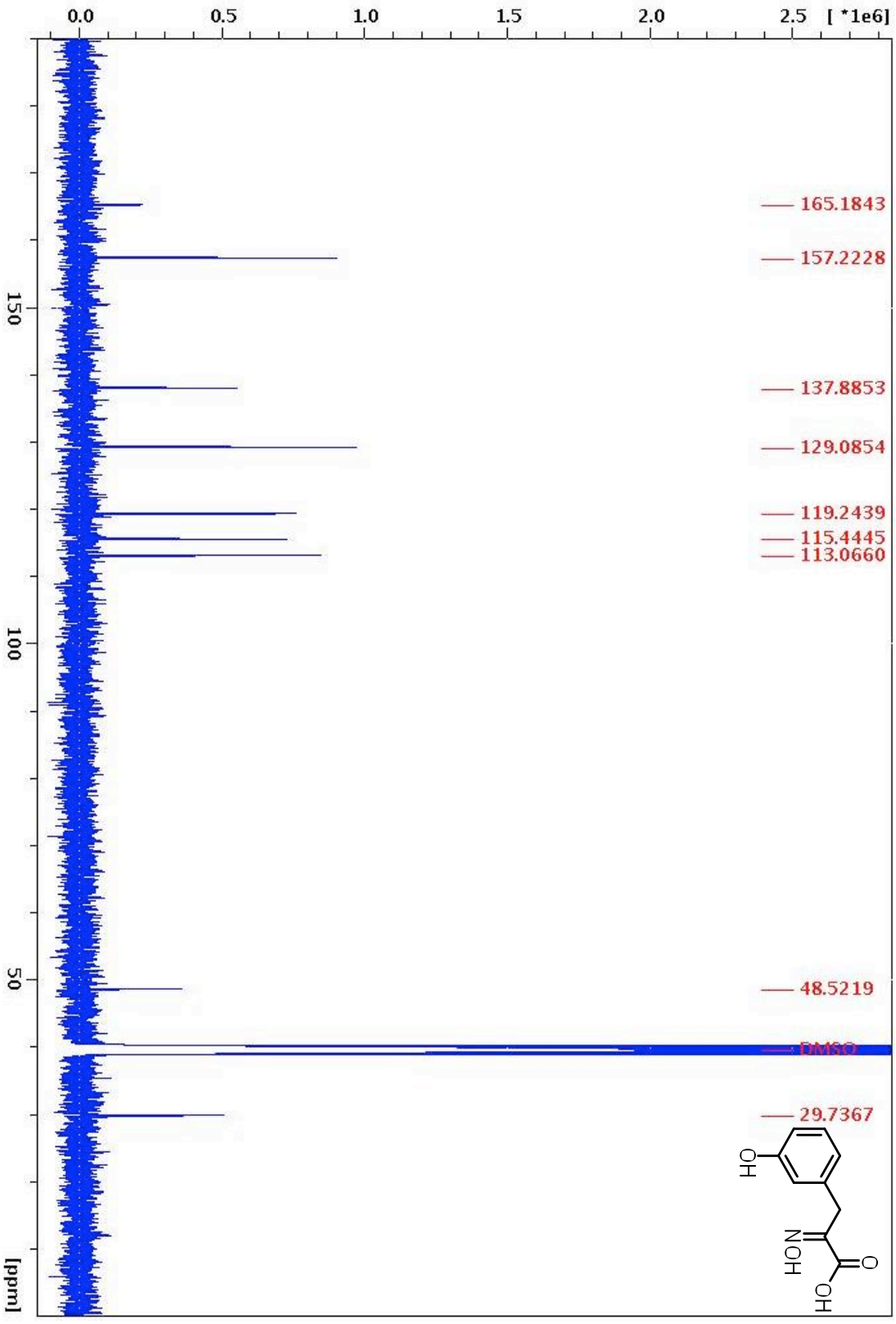

0
2
4
6
[*1e6]
8
6
4
2
[ppm]
4.3542
2.0000
7.7522
7.7346
7.3803
7.3614
3.8892
H2O
DMSO
N
OH
O
HO

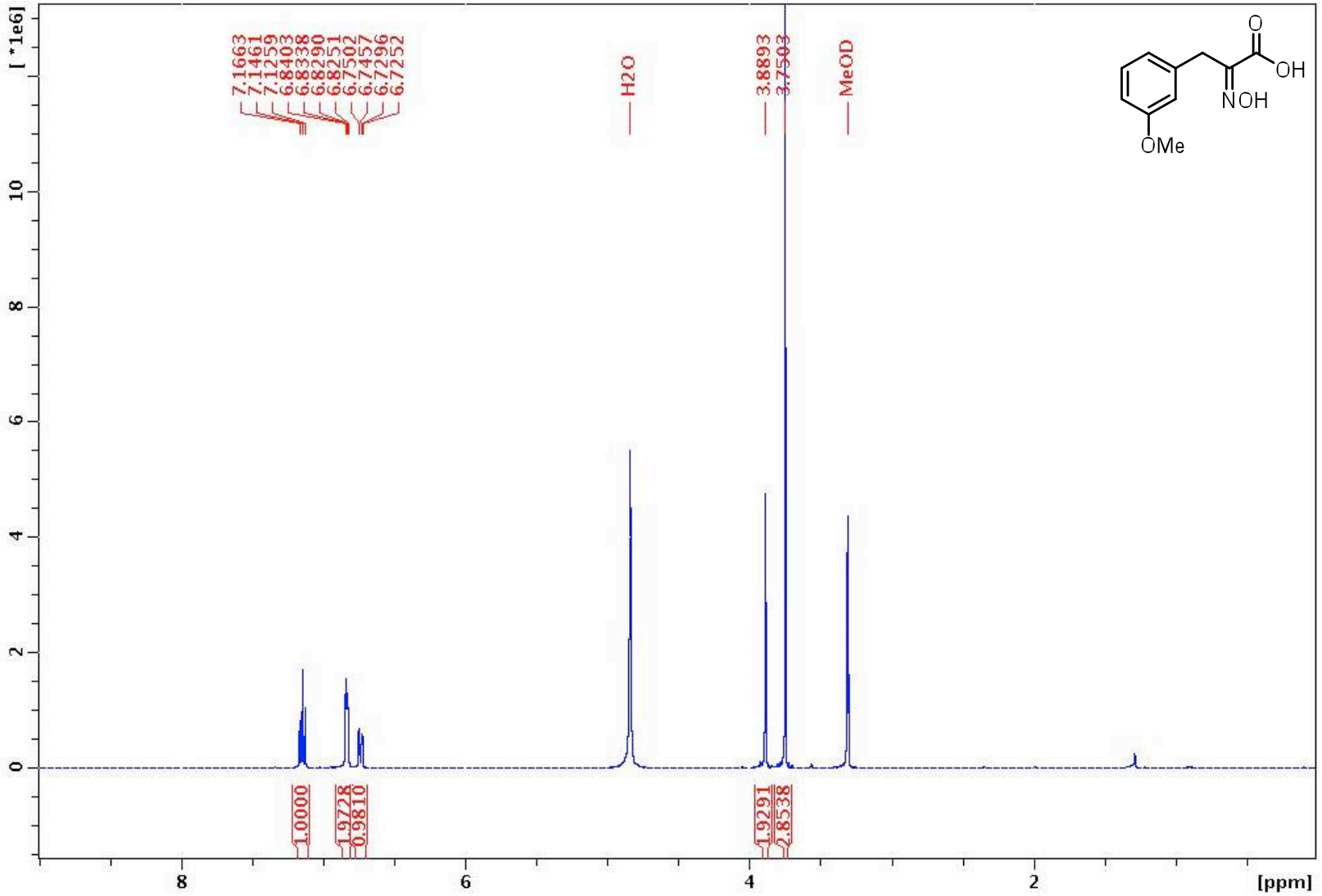

164.9348
149.1116
142.7424
132.2640
129.5235
118.7697
109.0624
30.1963
[*1e3]
1200
1000
800
600
400
200
0
150
100
50
[ppm]
O
OH
NOH
NC

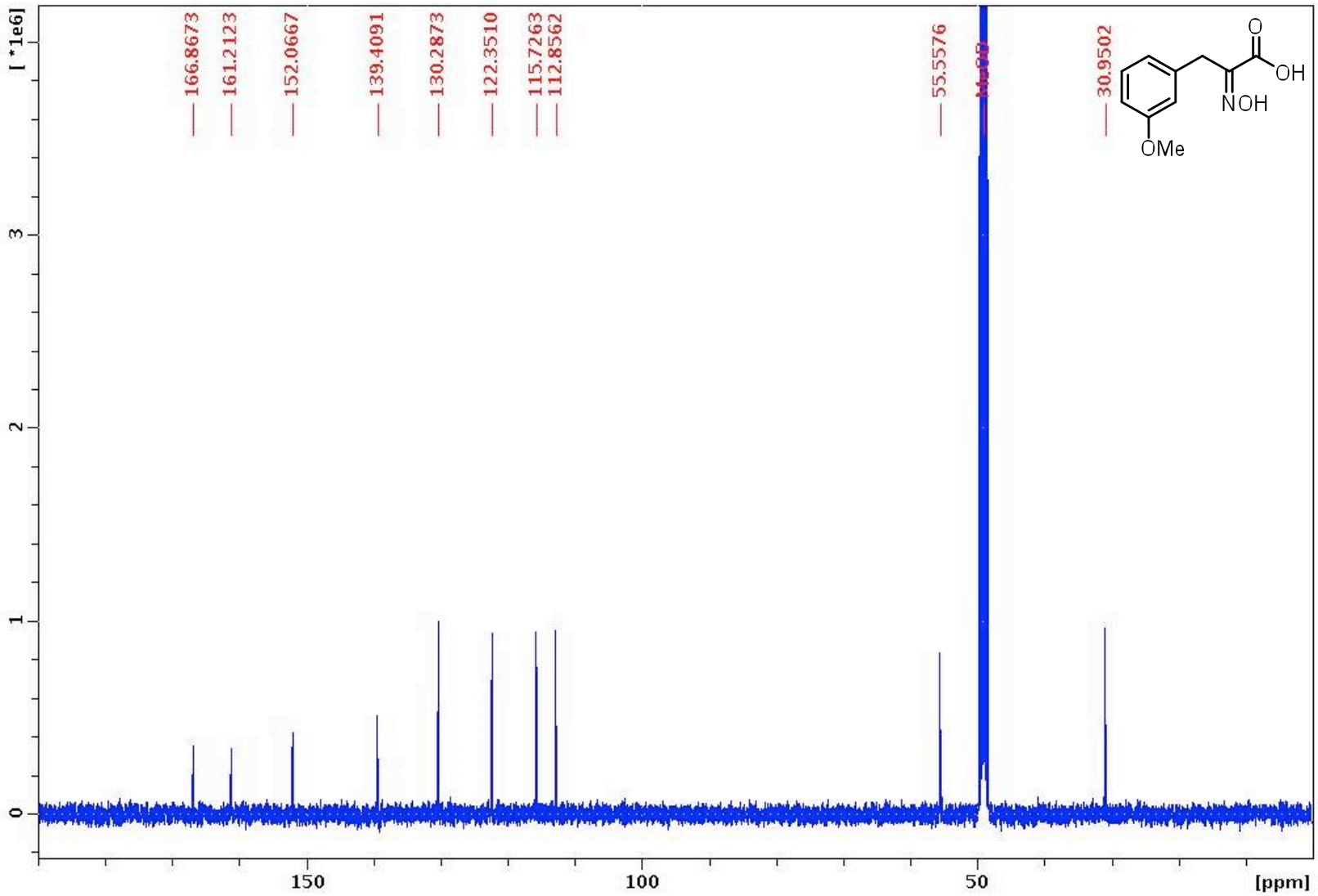

0
5
10
15
[*1e6]
8
6
4
2
[ppm]
3.1620
1.0000
2.1086
7.3374
7.3181
7.2990
7.2722
7.2442
7.1853
7.1671
3.8284
H2O
DMSO
Cl
N
OH
O
OH

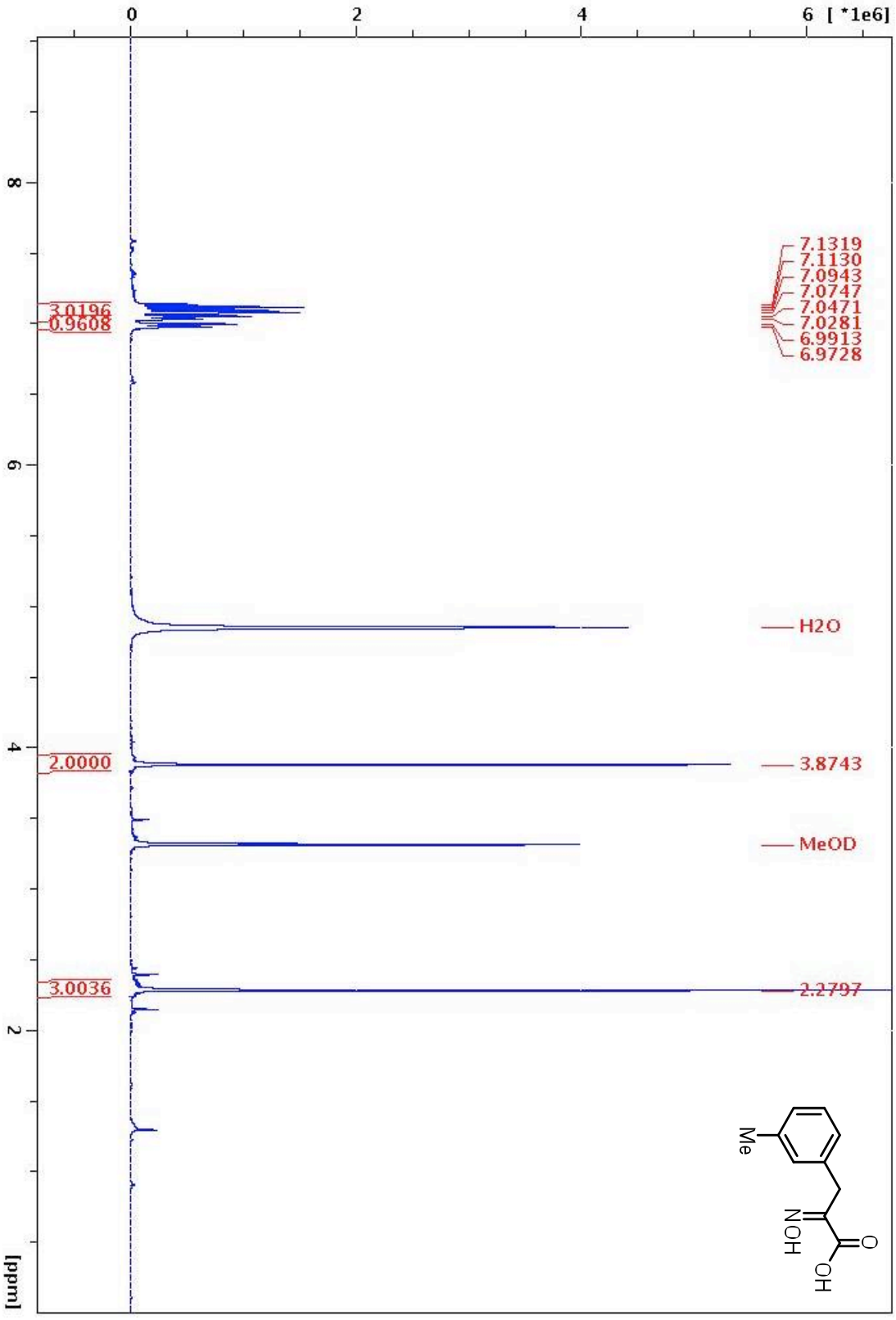

[*1e6]
4
3
2
1
0
165.1597
139.2641
132.8094
130.1441
128.3183
127.3238
126.1413
DMSO
29.6421
O
OH
NOH
Cl
150
100
50
[ppm]

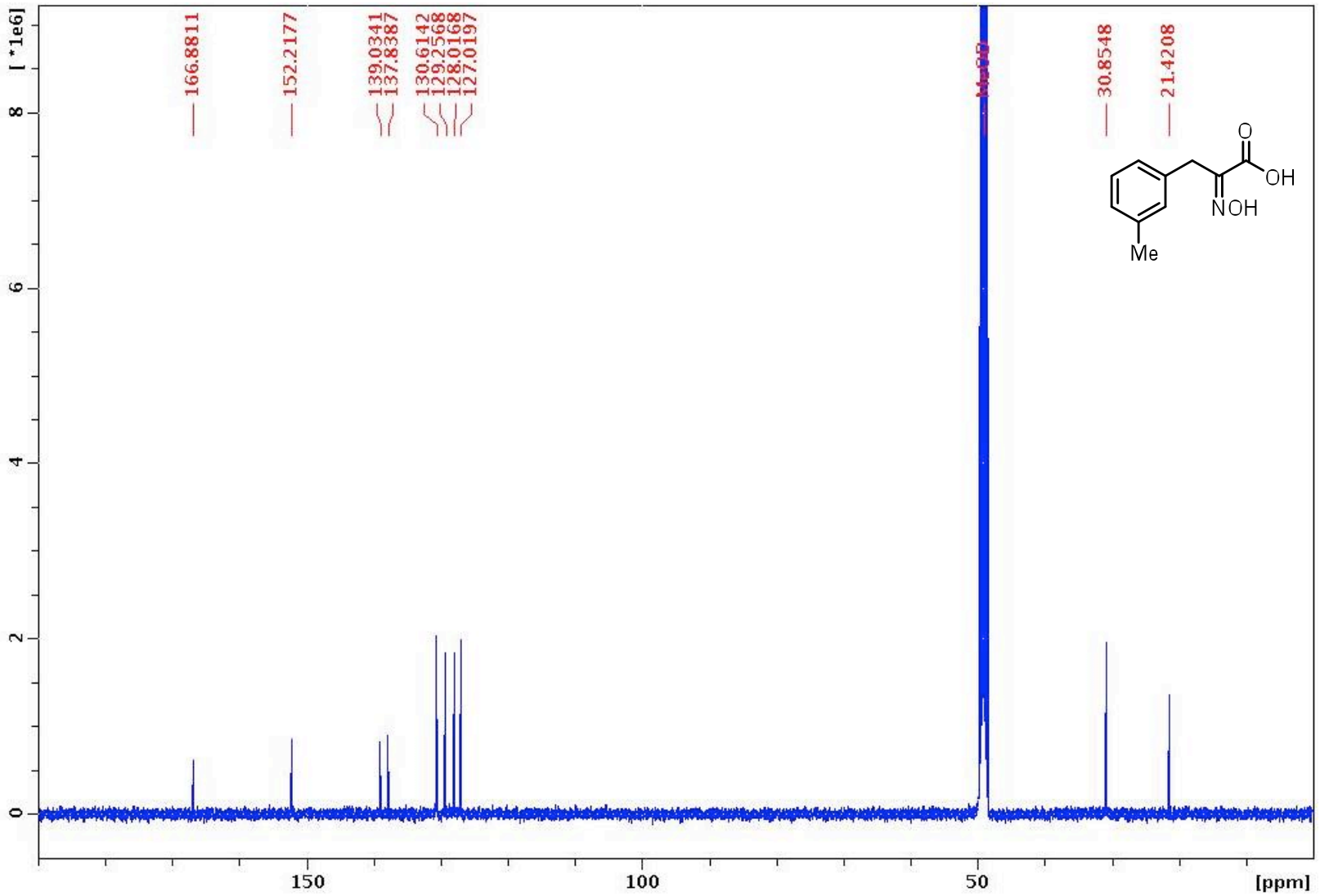

0
2
4
6
[*1e6]
8
6
4
2
[ppm]
1.1032
3.0000
2.0686
1.3495
7.0553
7.0355
7.0154
6.6195
6.6046
6.5728
6.5516
3.7189
H2O
3.1695
DMSO
HO
HO
N
OH
O

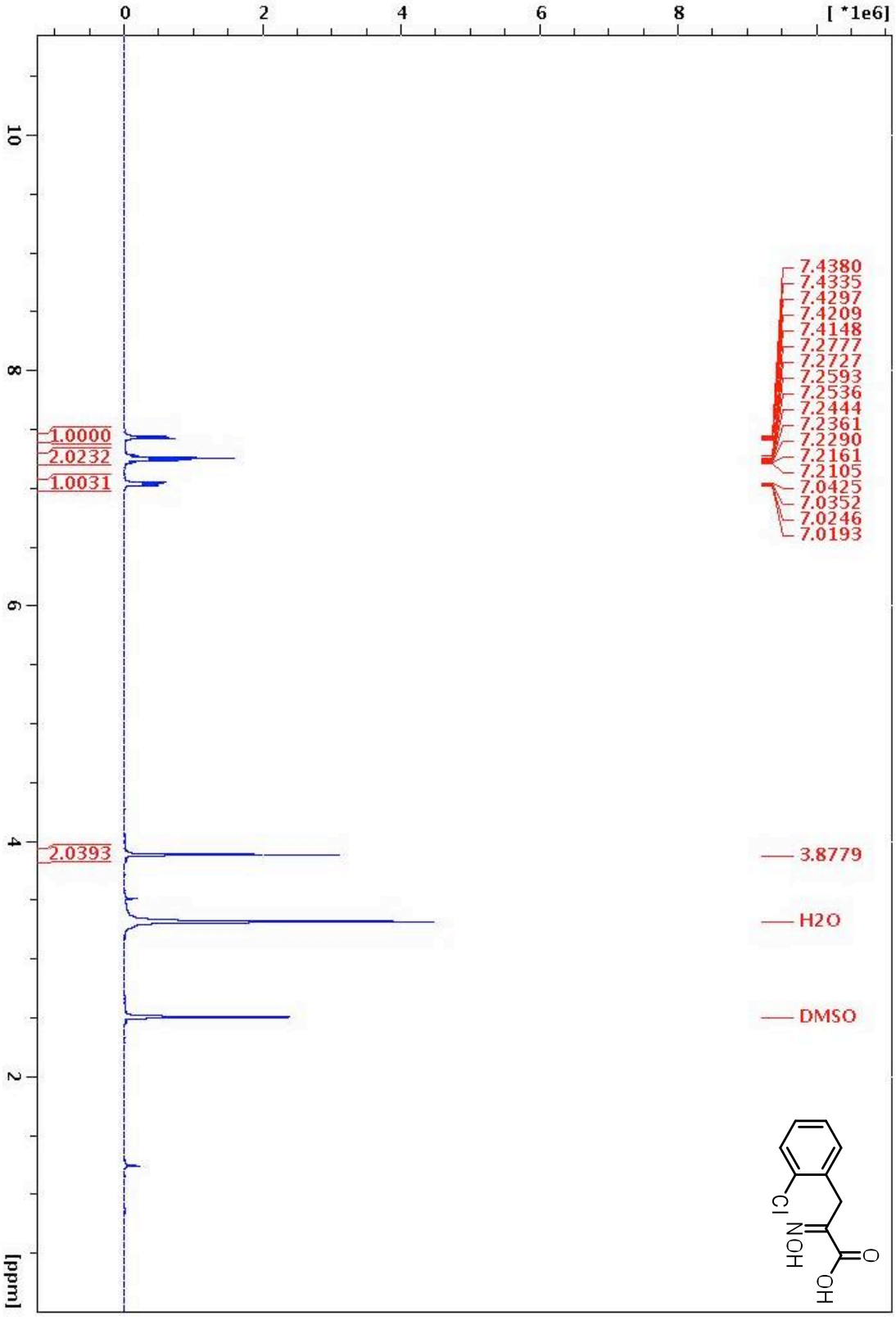

0.0
0.5
1.0
1.5
2.0
2.5
[*1e6]
150
100
50
[ppm]
165.1843
157.2228
137.8853
129.0854
119.2439
115.4445
113.0660
48.5219
DMSO
29.7367
OH
NOH
O
OH

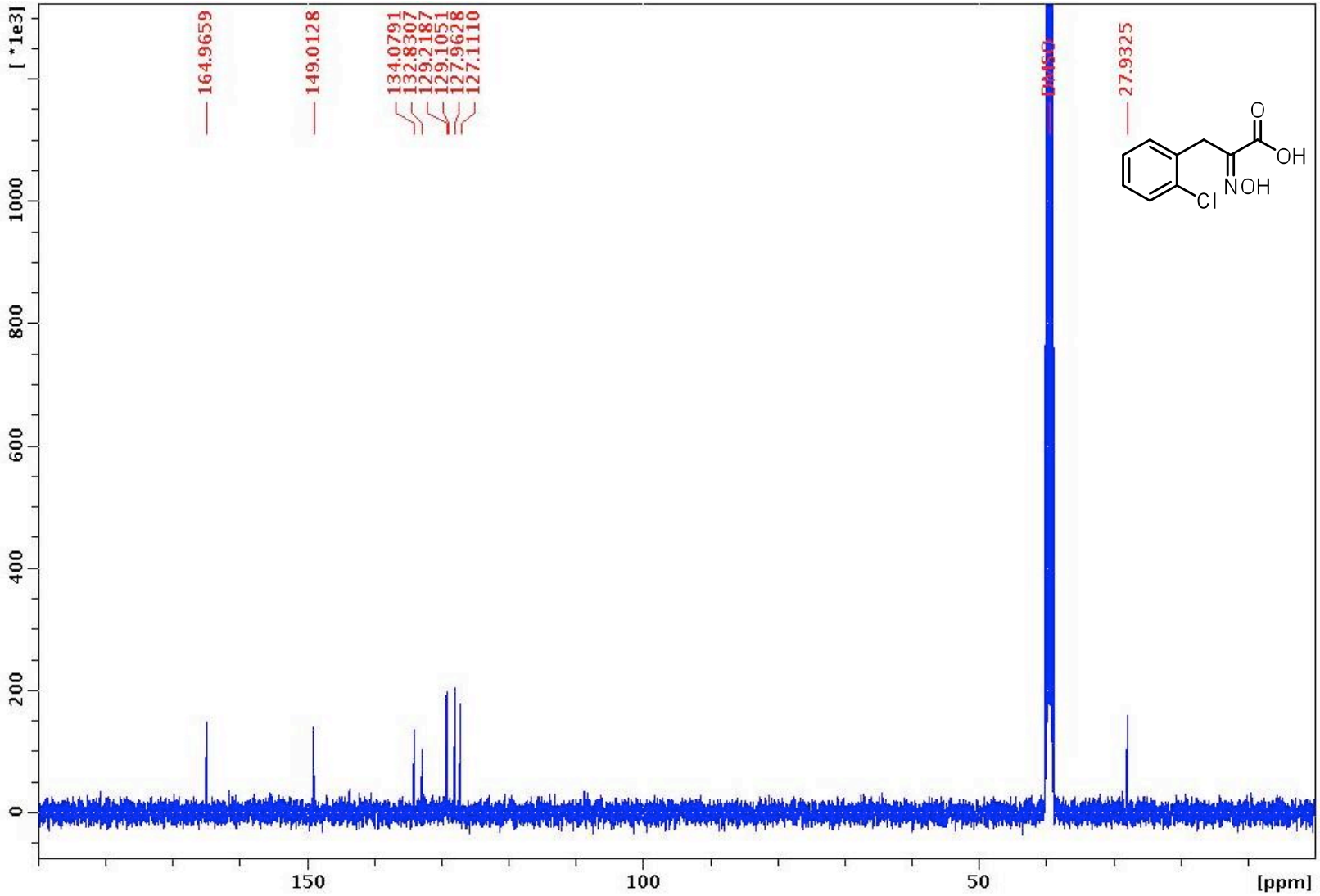

[*1e6]
10
8
6
4
2
0
7.1663
7.1461
7.1259
6.8403
6.8338
6.8290
6.8251
6.7502
6.7457
6.7296
6.7252
H2O
3.8893
3.7503
MeOD
1.0000
1.9728
0.9810
1.9291
2.8538
8
6
4
2
[ppm]
O
OH
NOH
OMe

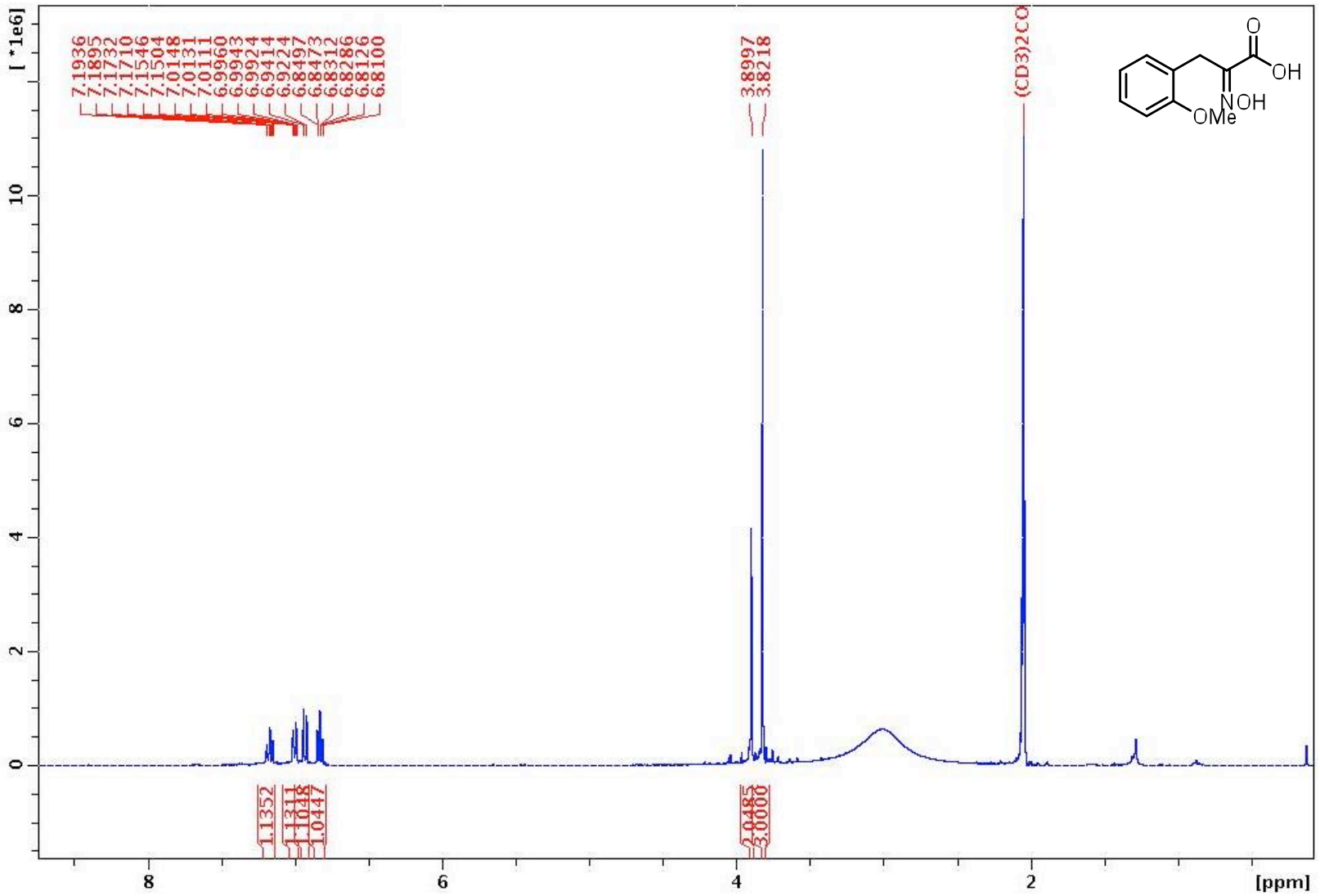

[*1e6]
166.8673
161.2123
152.0667
139.4091
130.2873
122.3510
115.7263
112.8562
55.5576
30.9502
O
OH
NOH
OMe
0
1
2
3
150
100
50
[ppm]


0
2
4
6 [*1e6]
8
6
4
2
[ppm]
7.1319
7.1130
7.0943
7.0747
7.0471
7.0281
6.9913
6.9728
3.0196
0.9608
H2O
2.0000
3.8743
MeOD
3.0036
2.2797
Me
NOH
O
OH


166.8811
152.2177
139.0341
137.8387
130.6142
129.2568
128.0168
127.0197
30.8548
21.4208
[*1e6]
8
6
4
2
0
150
100
50
[ppm]
O
OH
NOH
Me


0
2
4
6
8
[*1e6]
10
8
6
4
2
[ppm]
1.0000
2.0232
1.0031
2.0393
7.4380
7.4335
7.4297
7.4209
7.4148
7.2777
7.2727
7.2593
7.2536
7.2444
7.2361
7.2290
7.2161
7.2105
7.0425
7.0352
7.0246
7.0193
3.8779
H2O
DMSO
Cl
NOH
O
OH


[*1e3]
1000
800
600
400
200
0
164.9659
149.0128
134.0791
132.8307
129.2187
129.1051
127.9628
127.1110
27.9325
150
100
50
[ppm]
O
OH
NOH
Cl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7.0148
7.0131
7.0111
6.9960
6.9943
6.9924
6.9414
6.9224
6.8497
6.8473
6.8312
6.8286
6.8126
6.8100
3.8997
3.8218
(CD3)2CO
OH
N
OH
OMe
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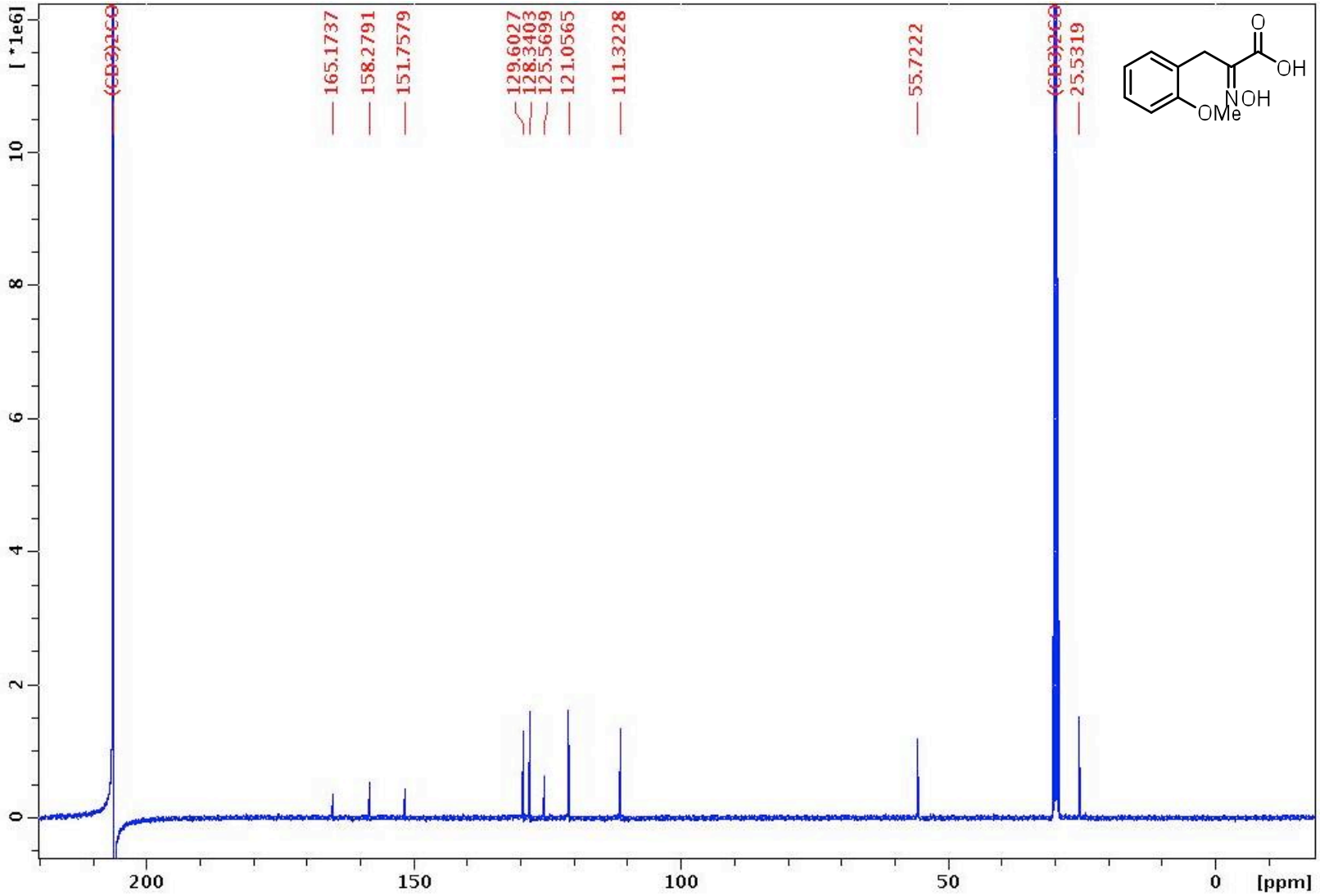
1.1311
1.1048
1.0447
2.0485
3.0000
8
6
4
2
[ppm]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150
100
50
0
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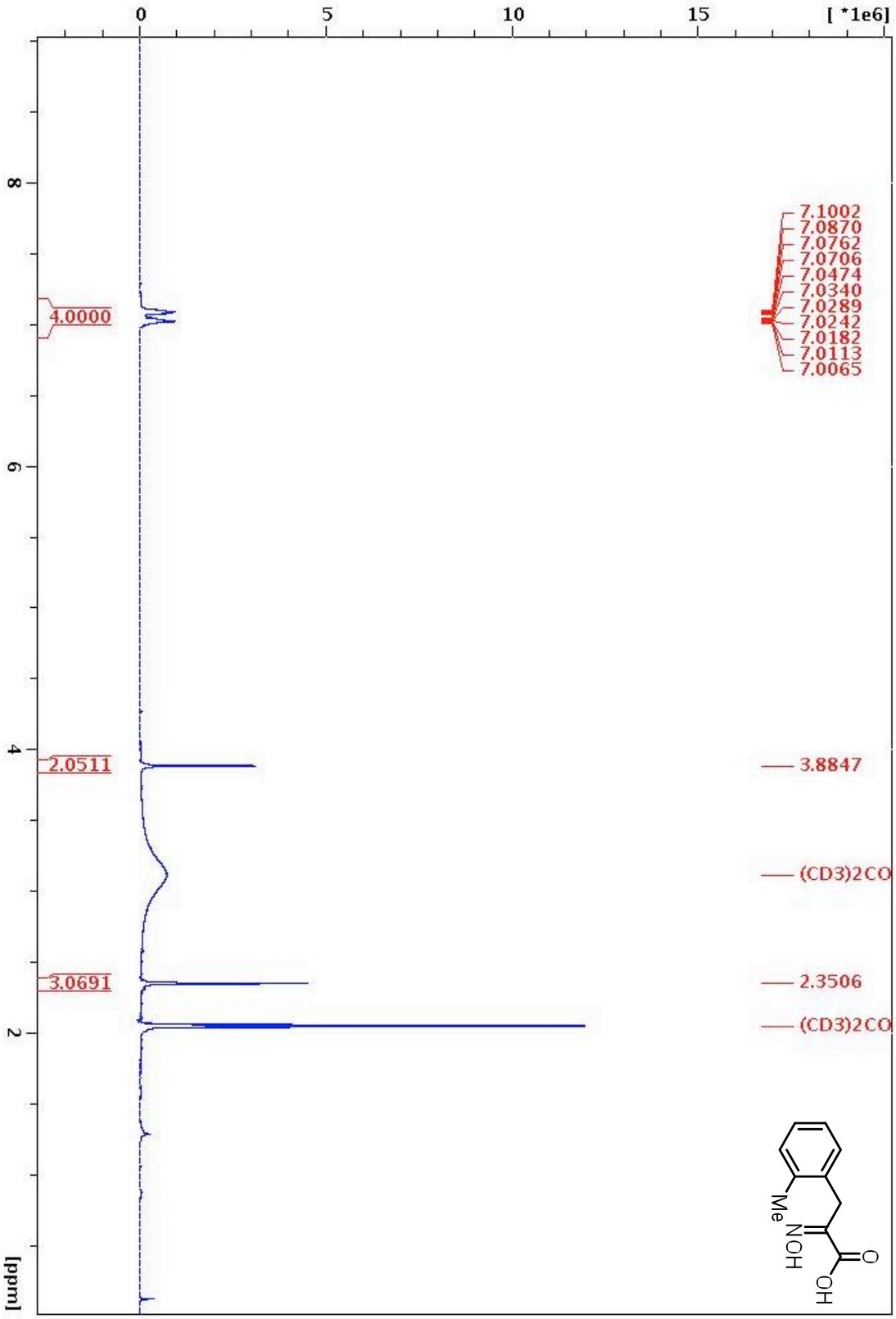
O
OH
NOH
OMe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6
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7.0340
7.0289
7.0242
7.0182
7.0113
7.0065
4.0000
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3.0691
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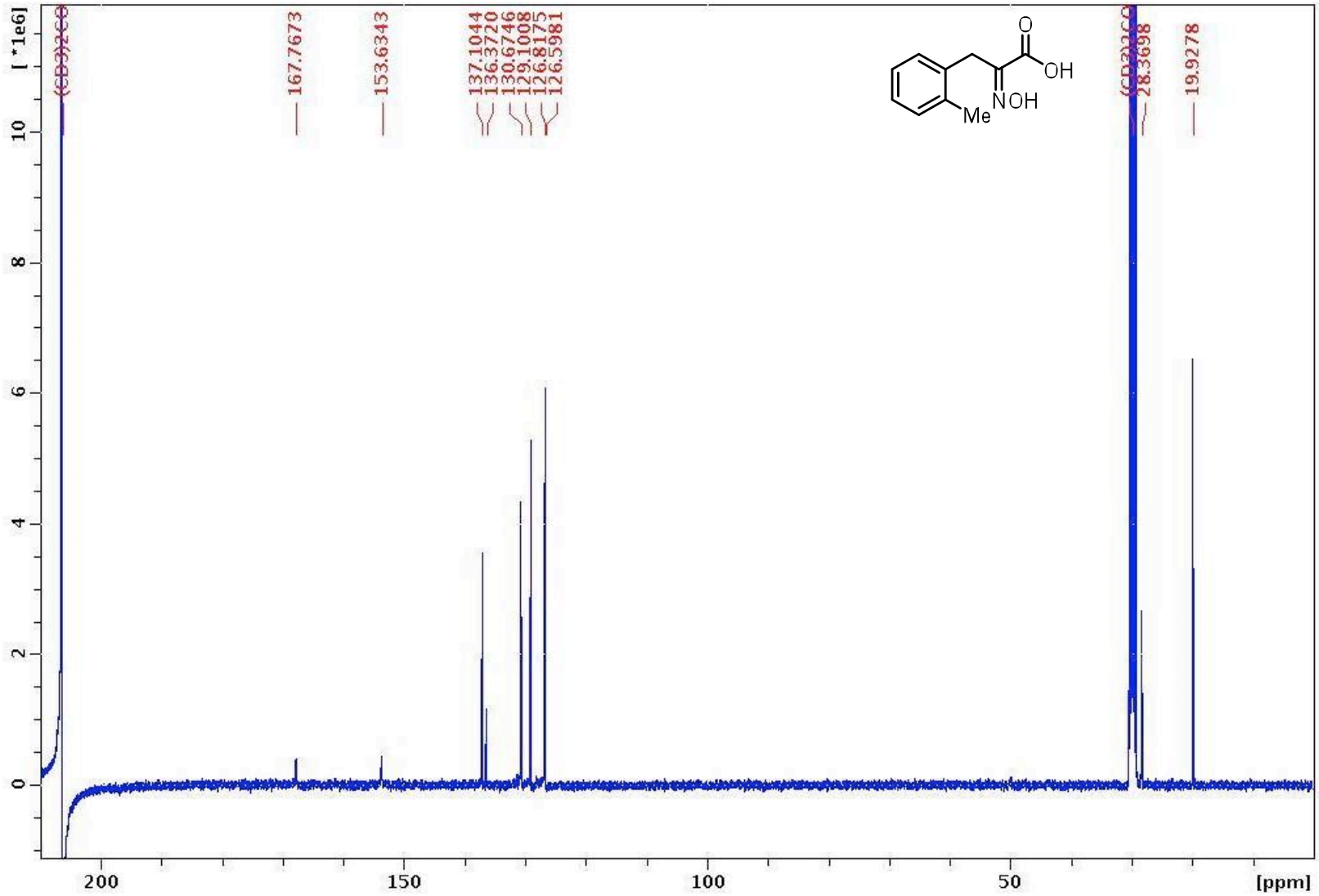
(CD3)2CO
2.3506
(CD3)2CO
Me
NOH
O
OH


[*1e6]
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8
6
4
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126.5981
28.3698
19.9278
O
OH
NOH
Me
200
150
100
50
[ppm]