Pd-catalyzed assembly of spirooxindole natural products: a short synthesis of horsfiline

Nina Deppermann,[†] Heike Thomanek,[‡] Alexander H. G. P. Prenzel[§] and Wolfgang Maison[‡,*]

[†]*Dr. Knoell Consult GmbH, Dynamostrasse 19, 68165 Mannheim, Germany;* [‡]*Institute of Organic Chemistry, Justus-Liebig-University Giessen, Heinrich-Buff-Ring 58, 35392 Giessen, Germany;* [§] *tesa SE, Research & Development, Quickbornstrasse 24, 20253 Hamburg, Germany*

wolfgang.maison@org.chemie.uni-giessen.de

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1. Materials and Methods

TLC was performed on silica gel aluminum sheets. Reagents used for developing plates include cer-reagent (5 g molybdatophosphoric acid, 2.5 g cerium sulfate tetrahydrate, 25 ml sulfuric acid and 225 ml water), potassium permanganate (0.5% in 1N NaOH w/v) and detection by UV light was used when applicable. Flash column chromatography was performed on silica gel (60 – 200 µm). ^{1}H chemical shifts are referenced to residual non-deuterated solvent ($CDCl_3$, δ_H = 7.26 ppm; DMSO-d_6, δ_H = 2.50 ppm). ^{13}C chemical shifts are referenced to the solvent signal ($CDCl_3$, δ_C = 77.16 ppm; DMSO-d_6, δ_C = 128.06 ppm). NMR spectra were recorded on 400 (100), or 600 (150) MHz instruments. ESI mass spectra were recorded on a TOF instrument operated in positive or negative mode. Samples were dissolved in MeCN/MeOH-mixtures and directly injected *via* syringe.

Solvents were dried by distillation from sodium under nitrogen atmosphere prior to application. NaO*t*-Bu was prepared freshly by solution of sodium in dried *t*-BuOH and stored in an argon-glovebox.

The following compounds were prepared according to literature procedures: 2-bromo-5-methoxyaniline **7a**,[1] benzyl-(2-bromo-5-methoxyphenyl)-amine **7b**,[2] benzyl-(2-bromo-4-methoxyphenyl)-amine **7c**,[3] *N*-Boc-nipecotic acid[4].

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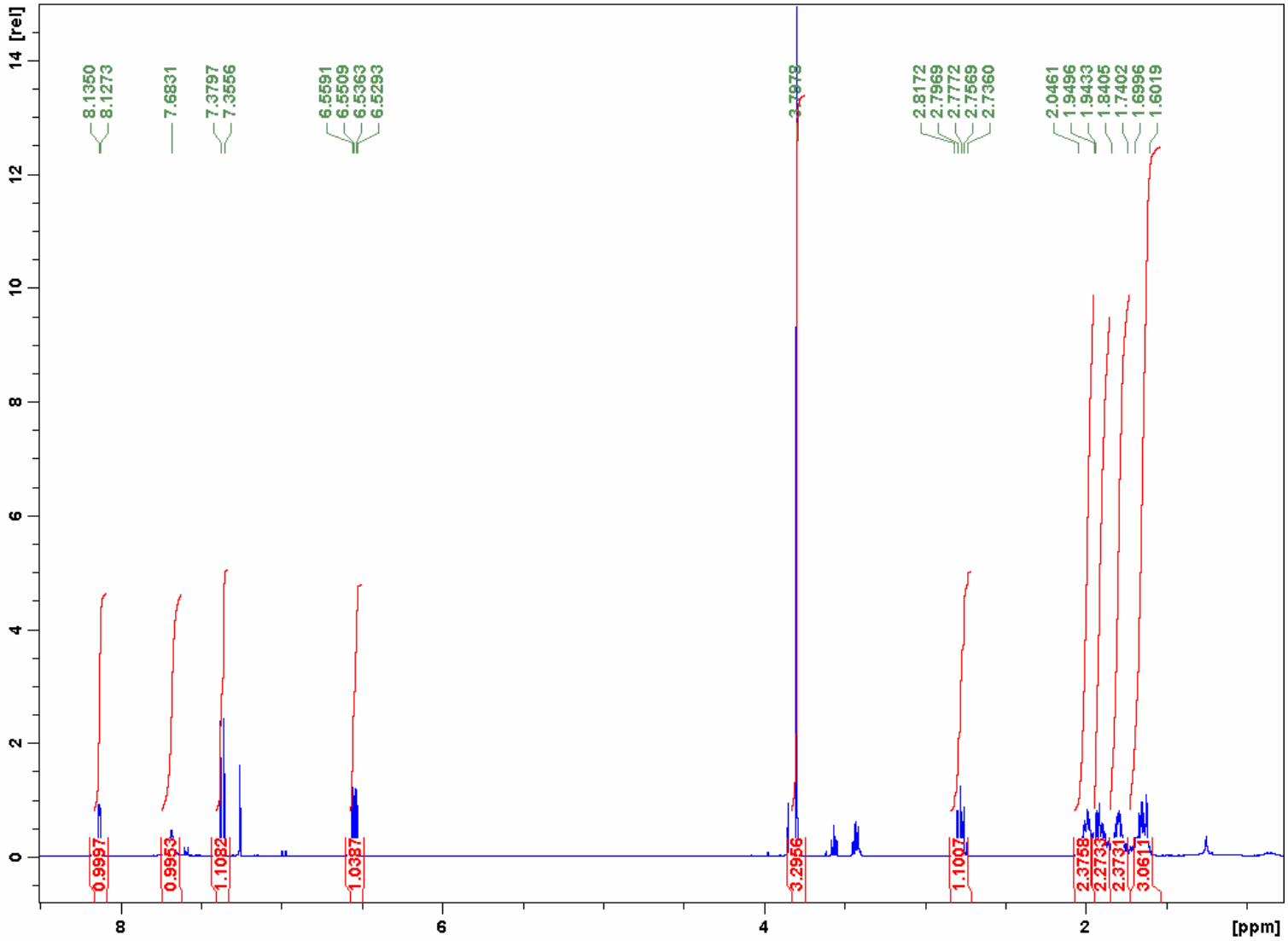
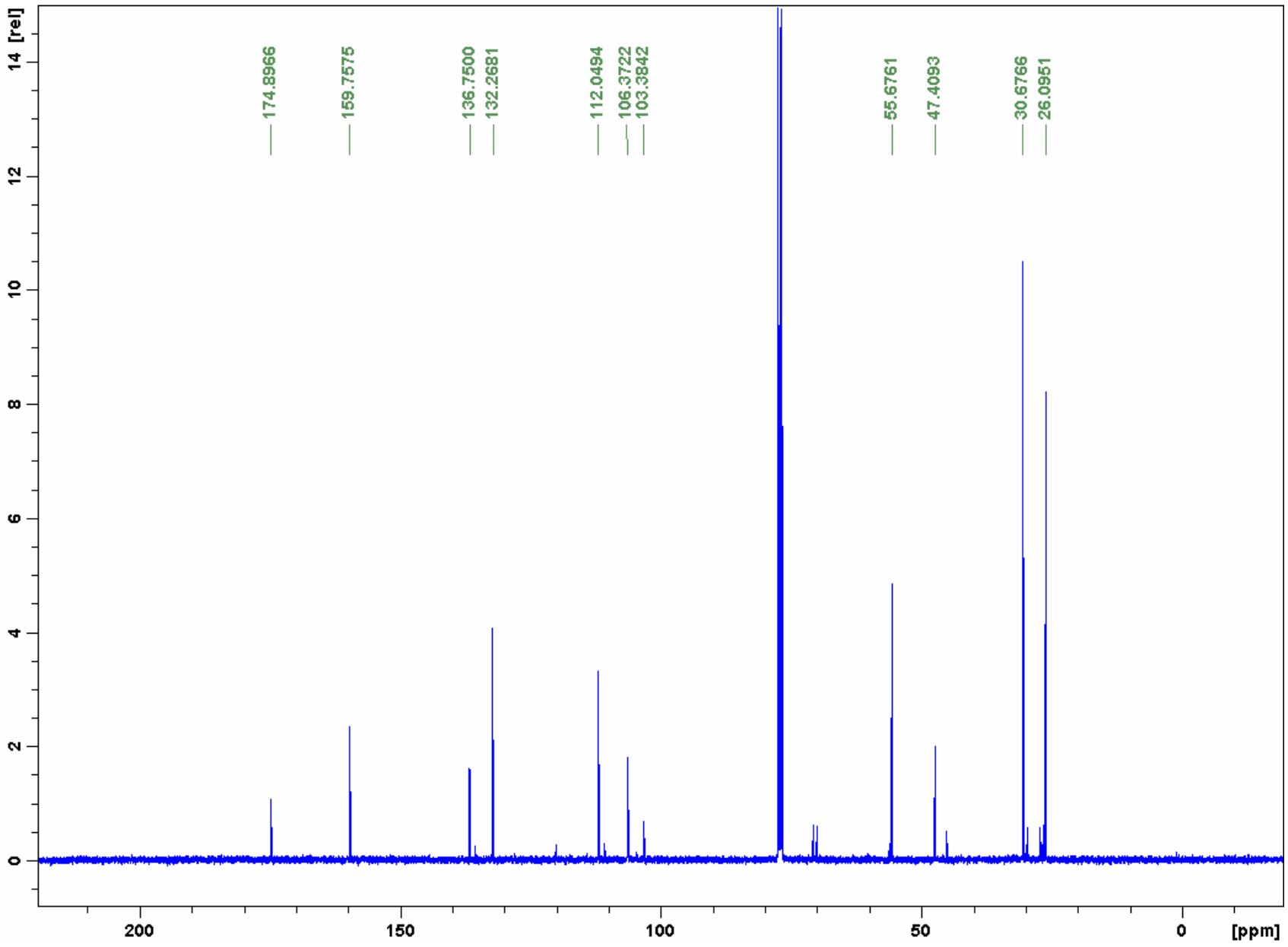
2. NMR-spectra for new compounds:

o-Bromoanilide 8a

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26.0951
14 [rel]
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10
8
6
4
2
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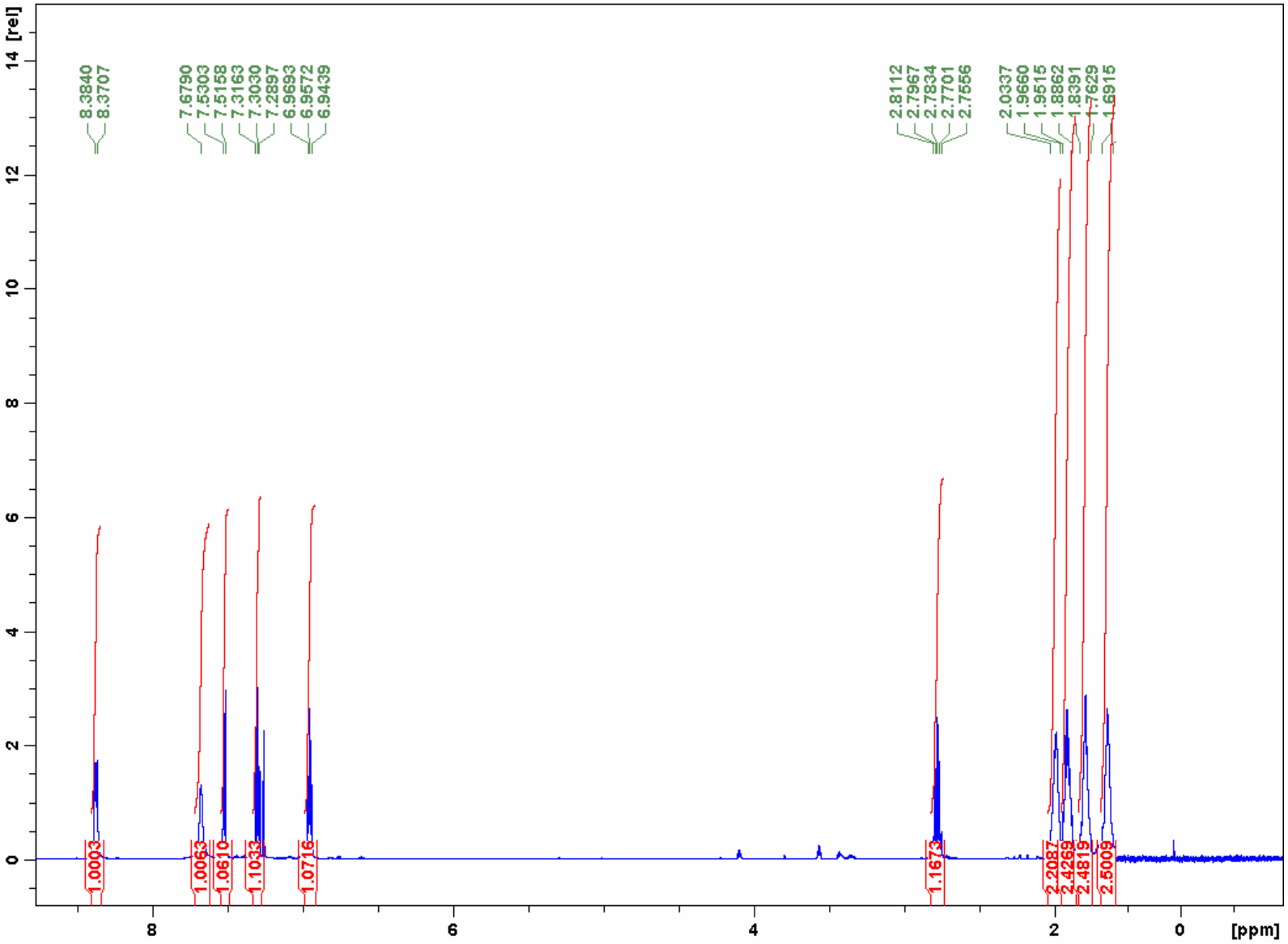
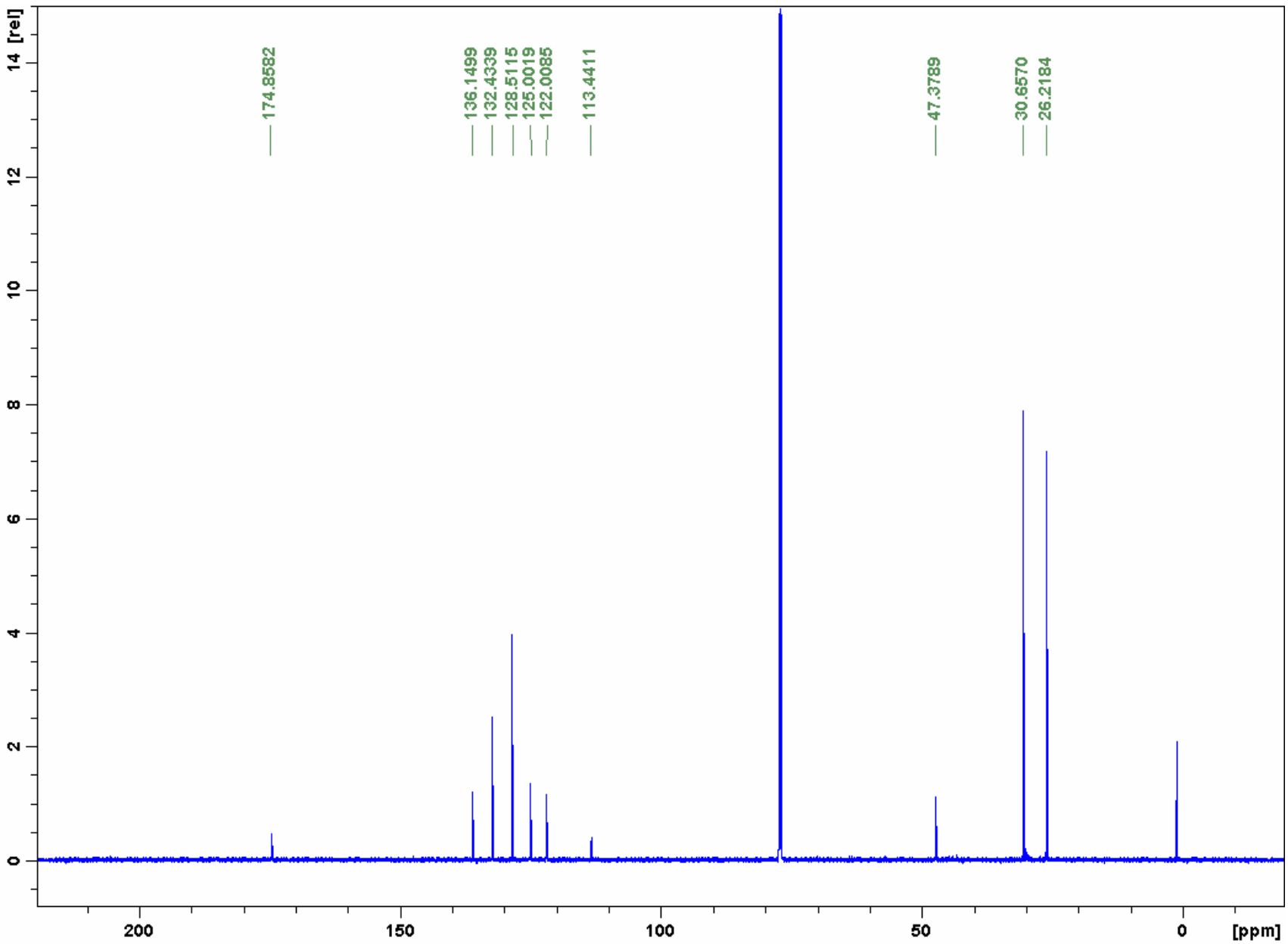
150
100
50
0
[ppm]

***o*-Bromoanilide Br-8c**

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[ppm]

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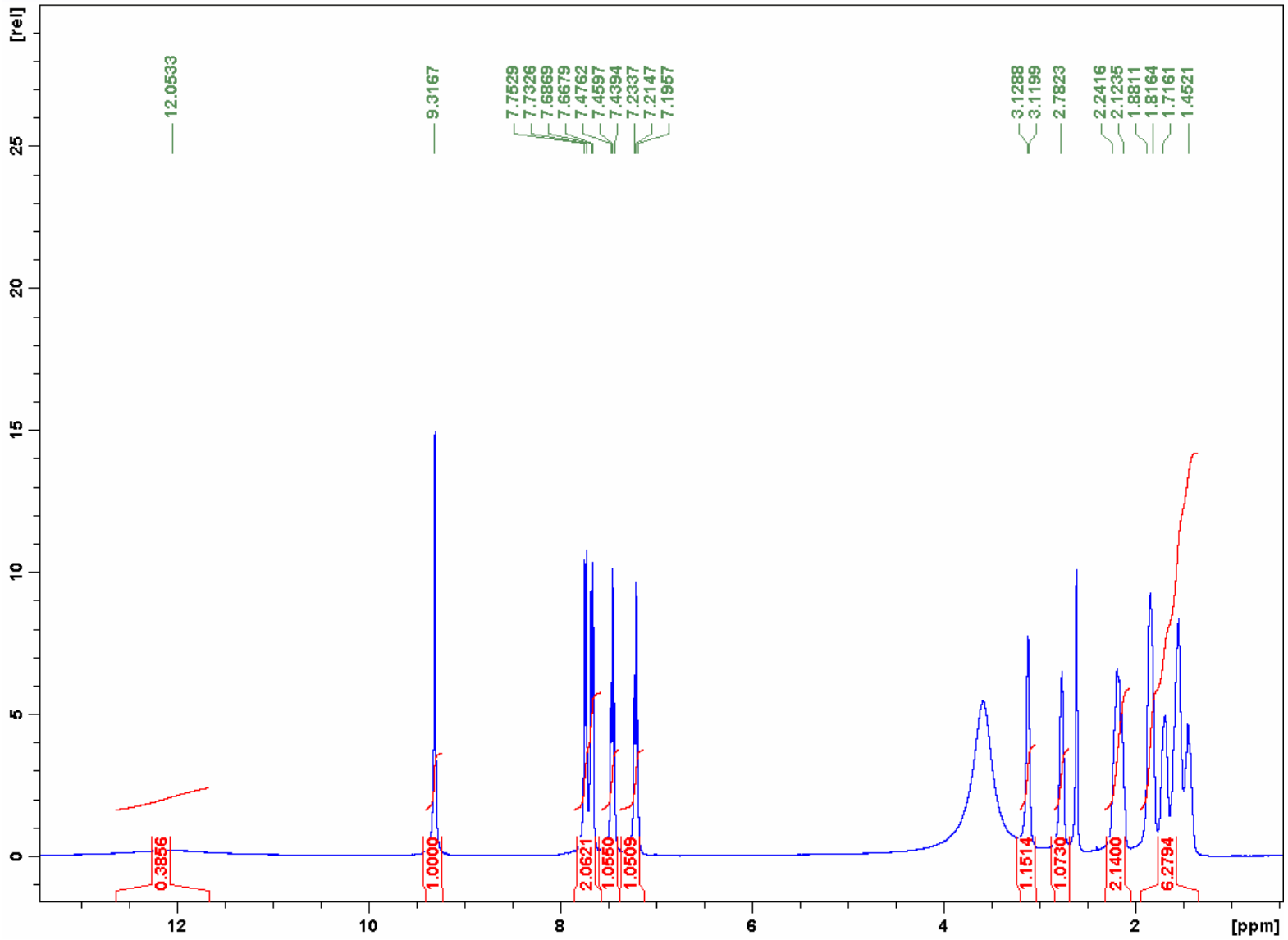

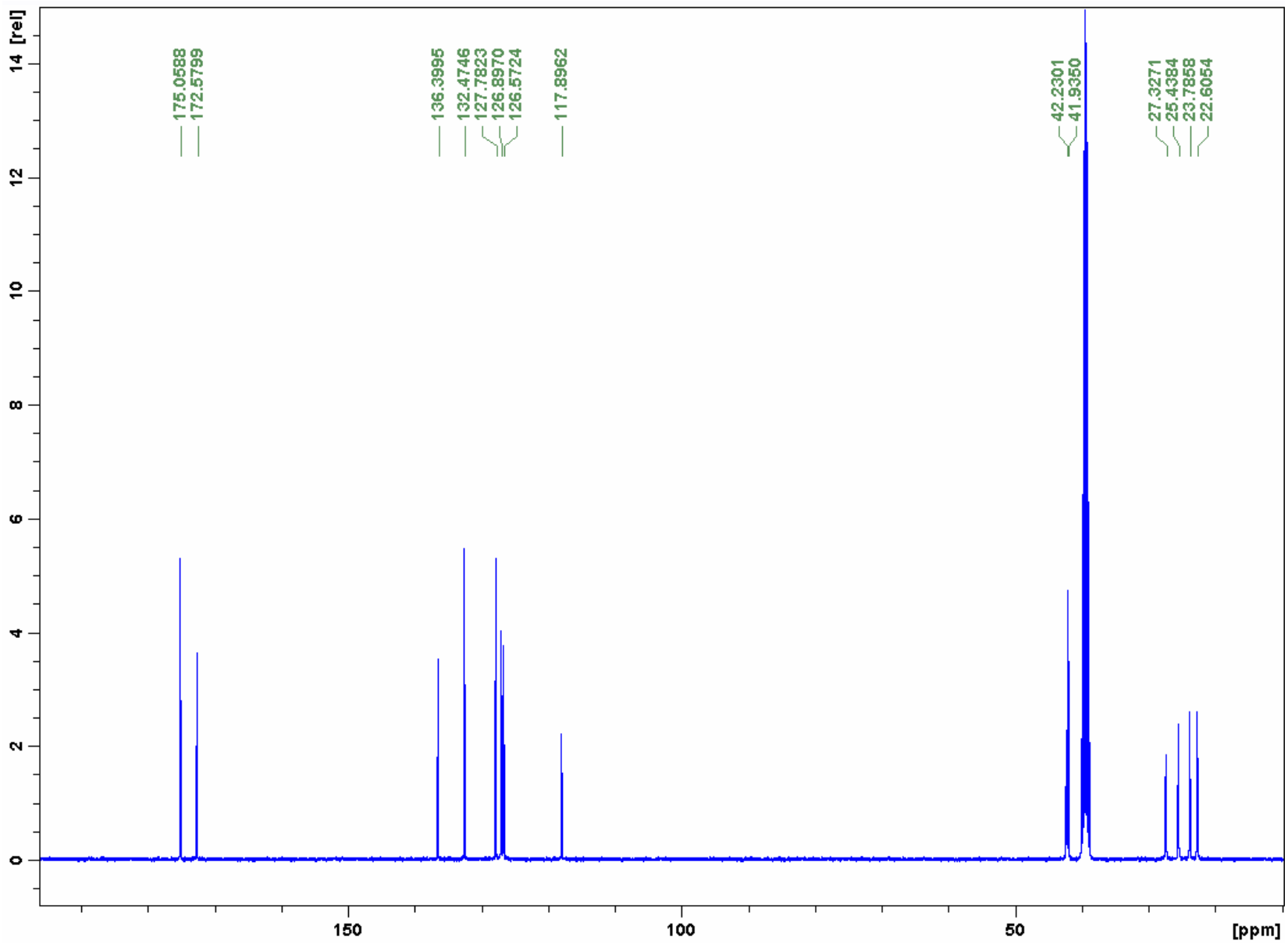
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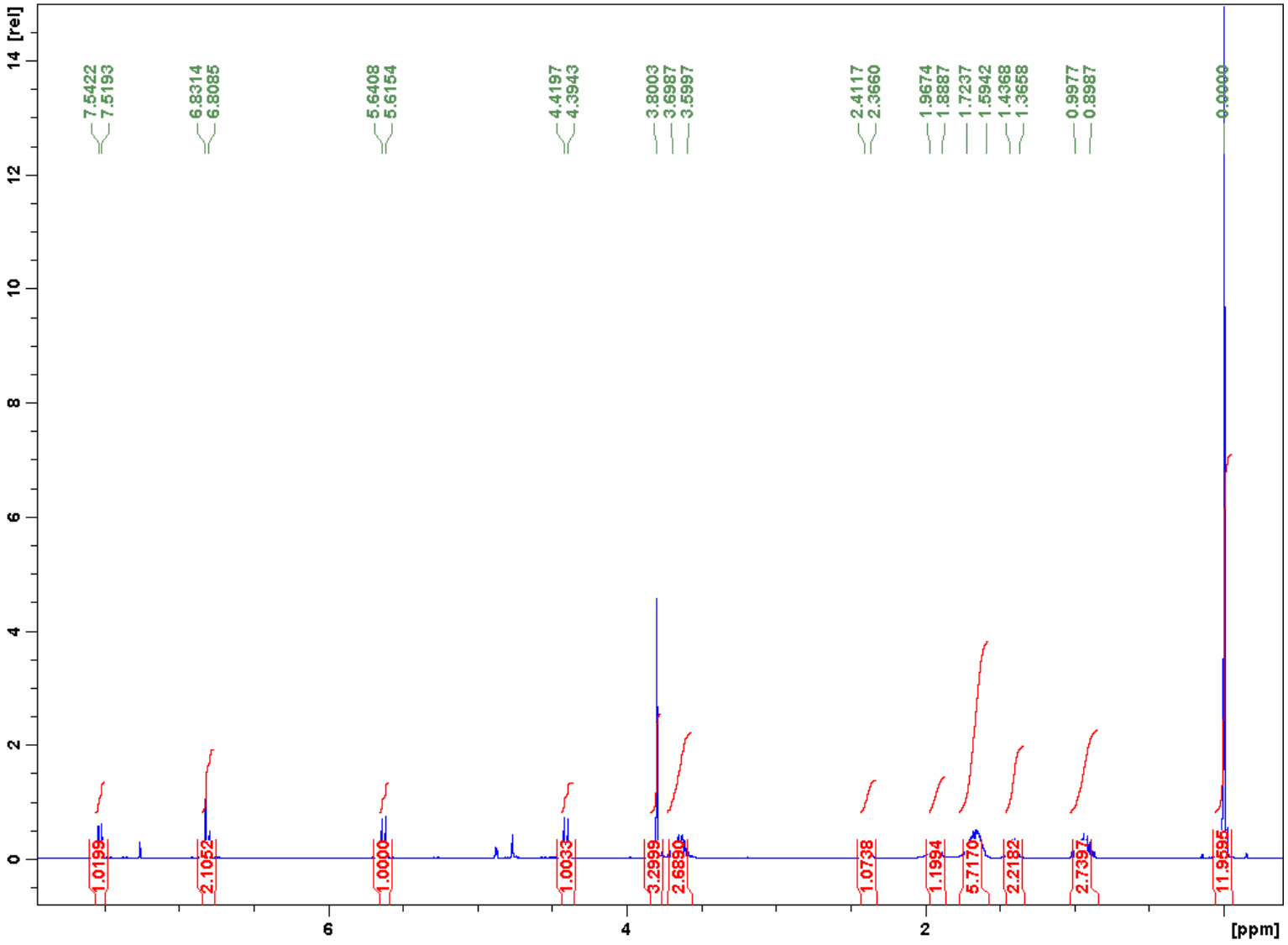

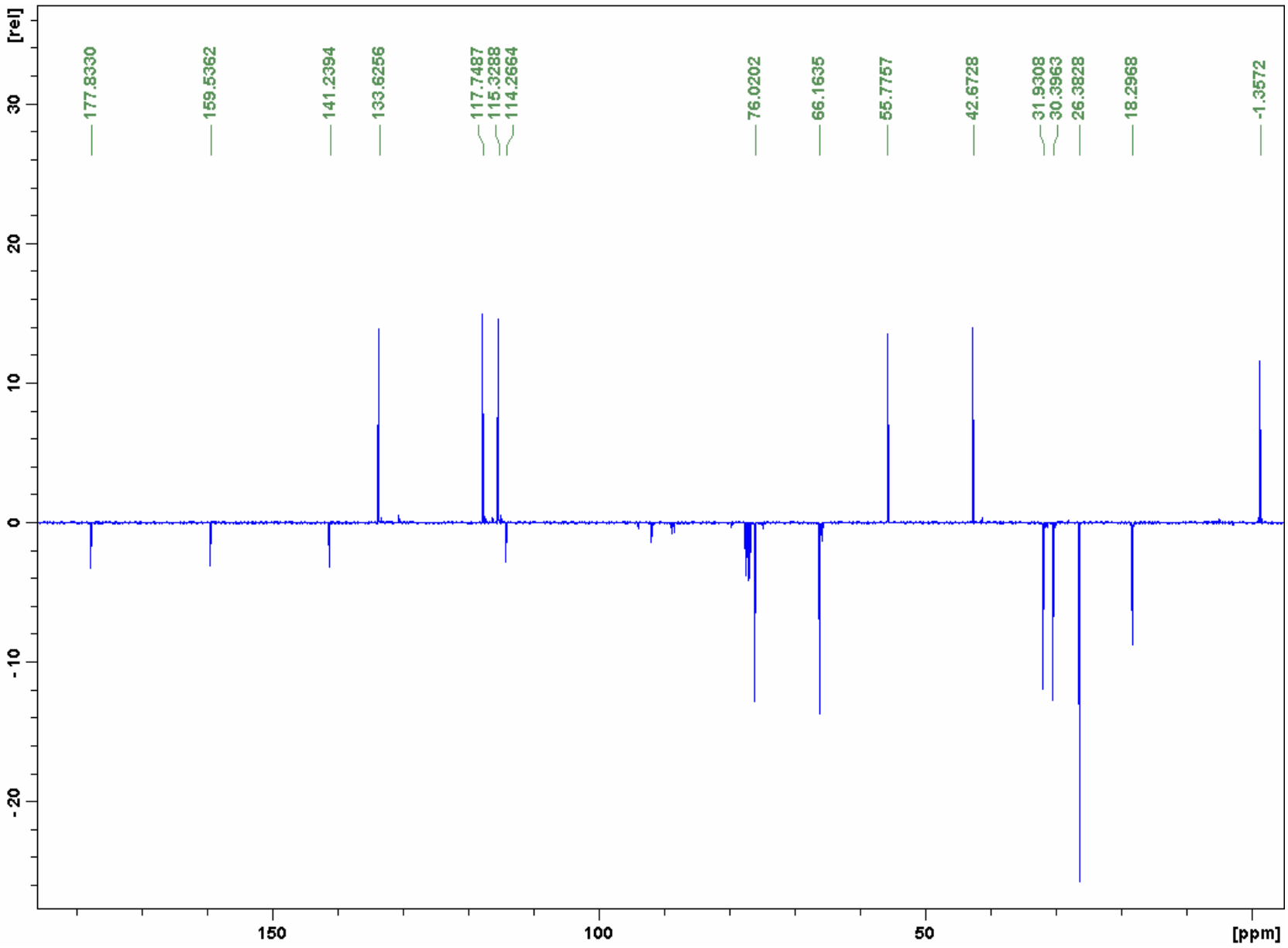
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- 10
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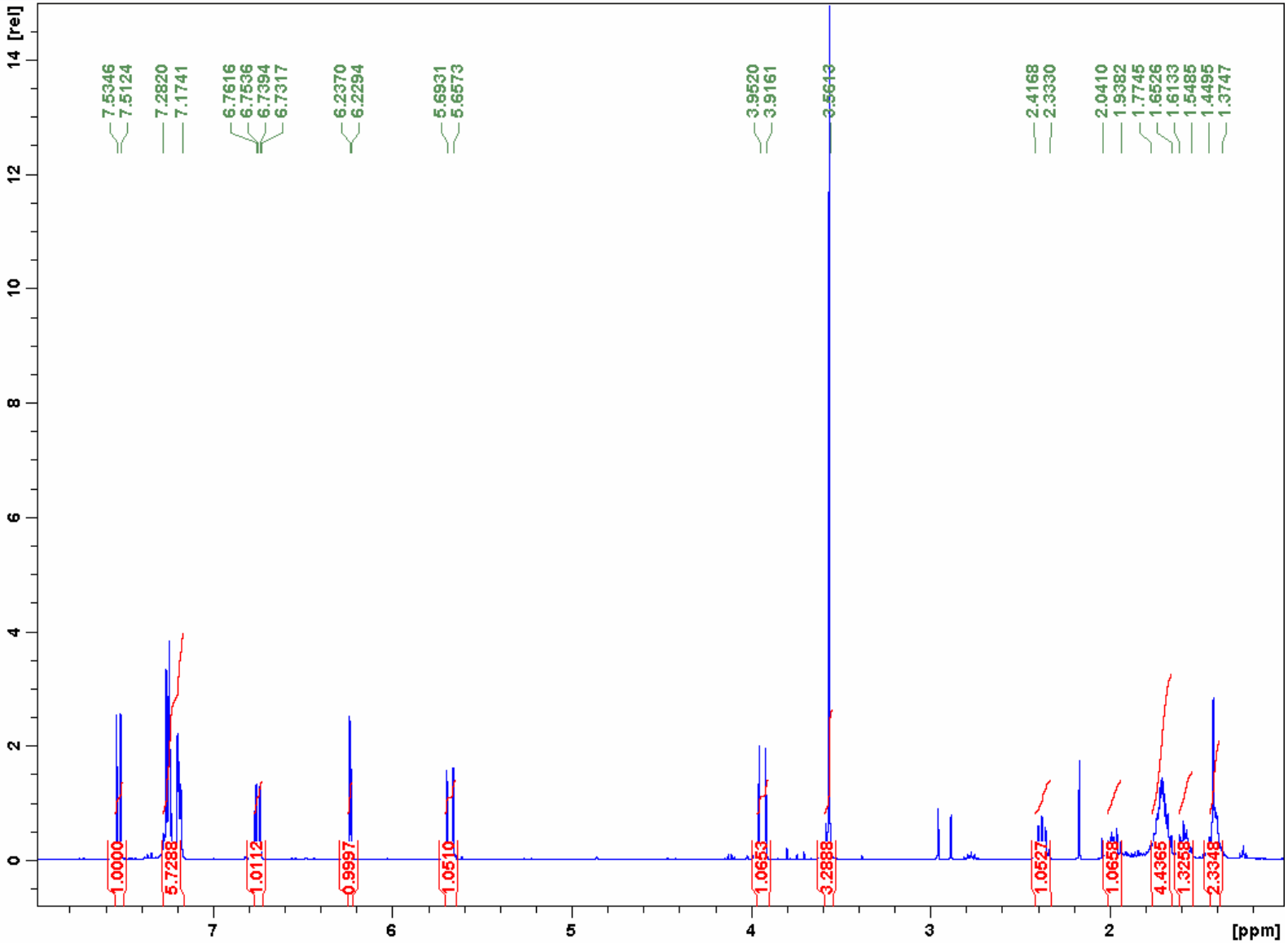

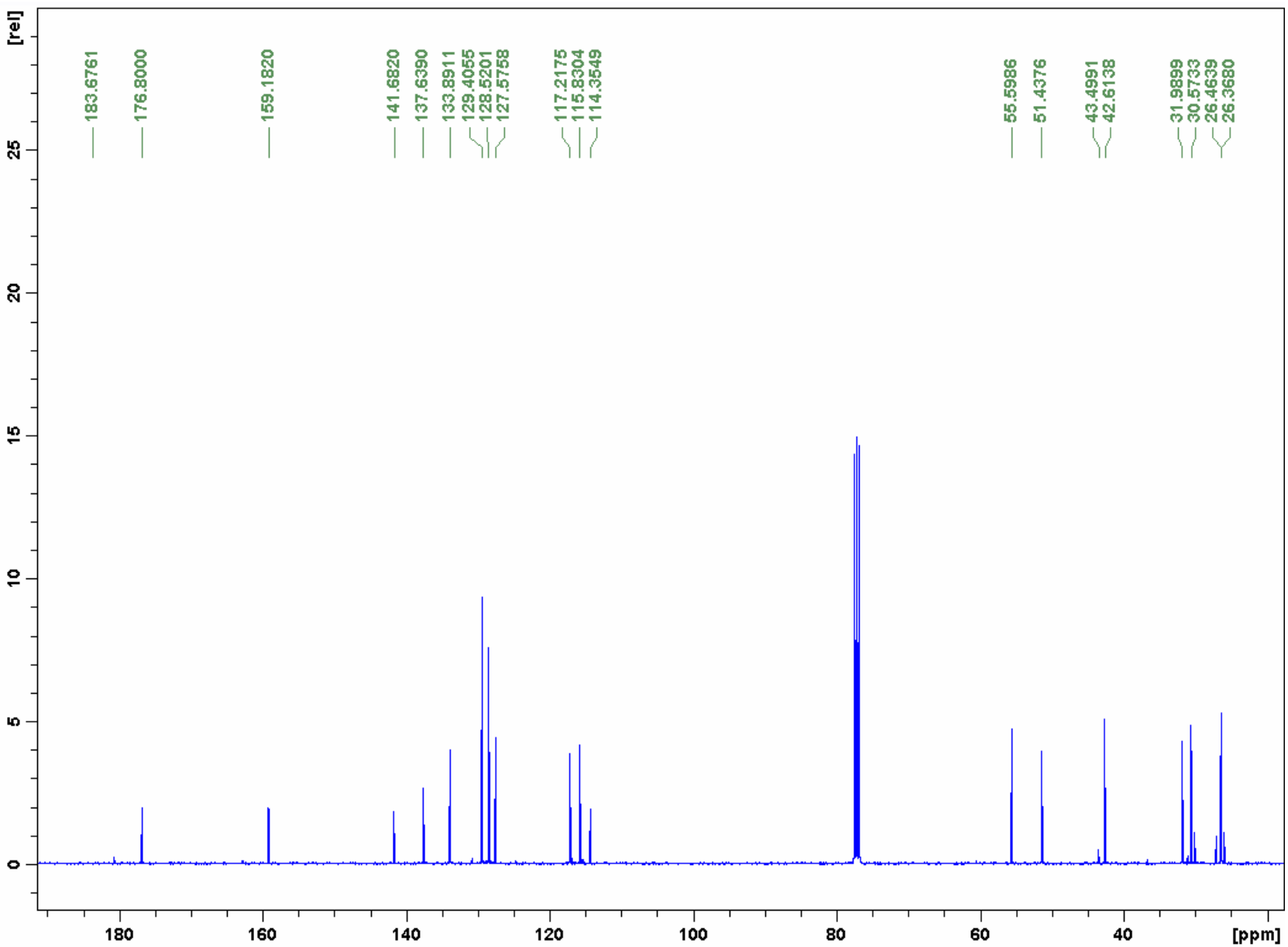
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30.5733
26.4639
26.3680
25
20
15
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5
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140
120
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80
60
40
[ppm]

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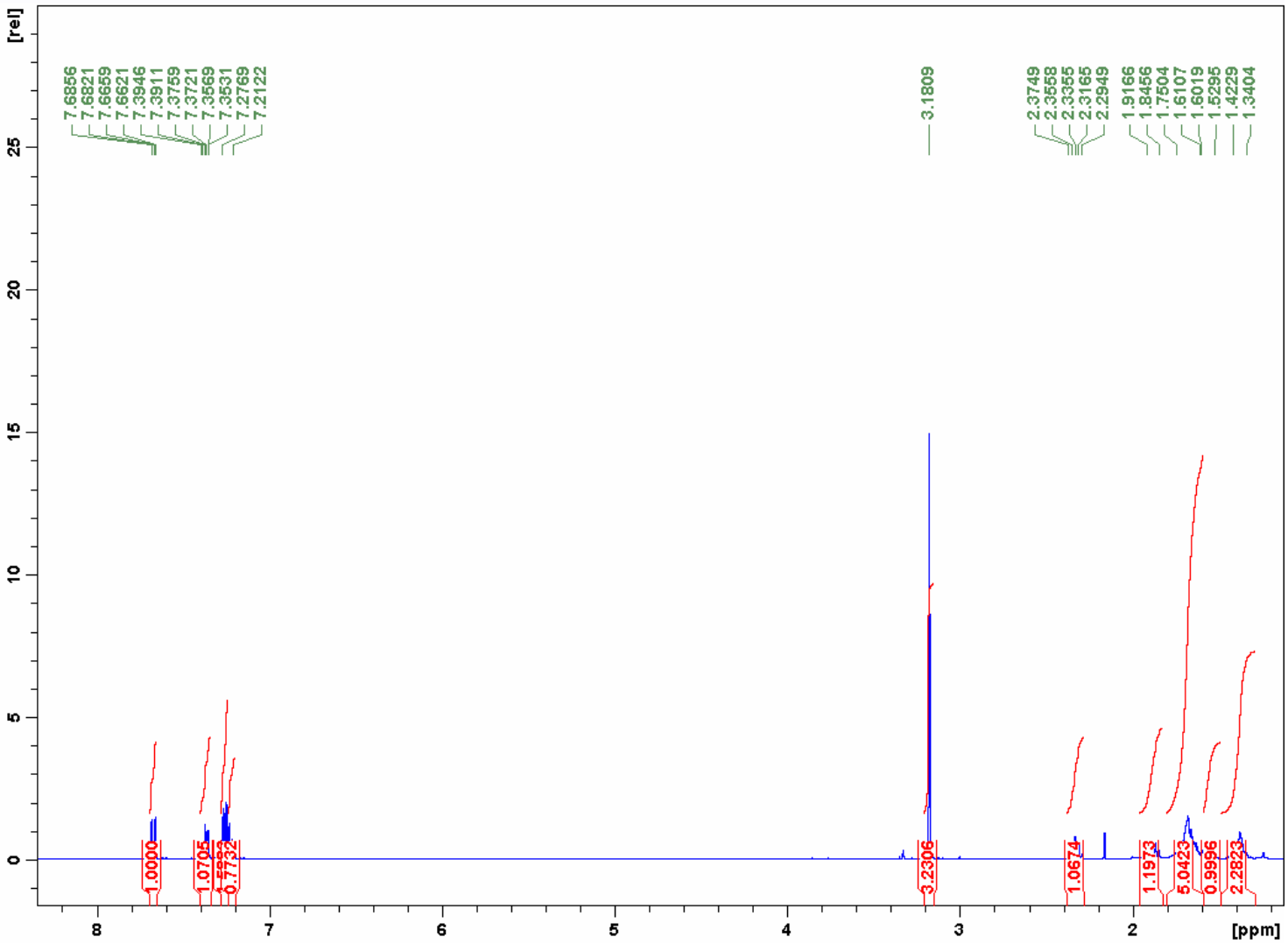

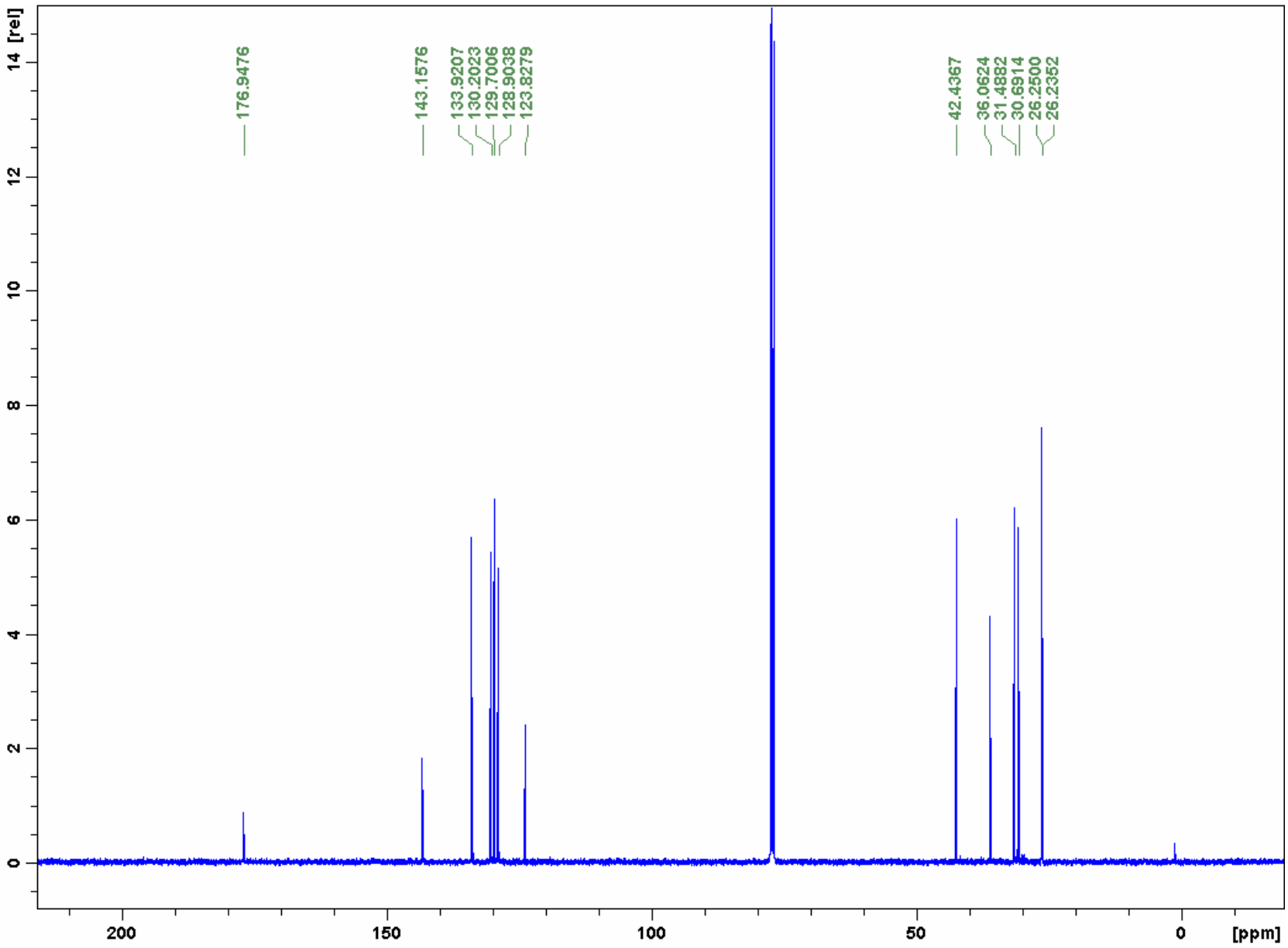
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26.2500
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6
4
2
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[ppm]

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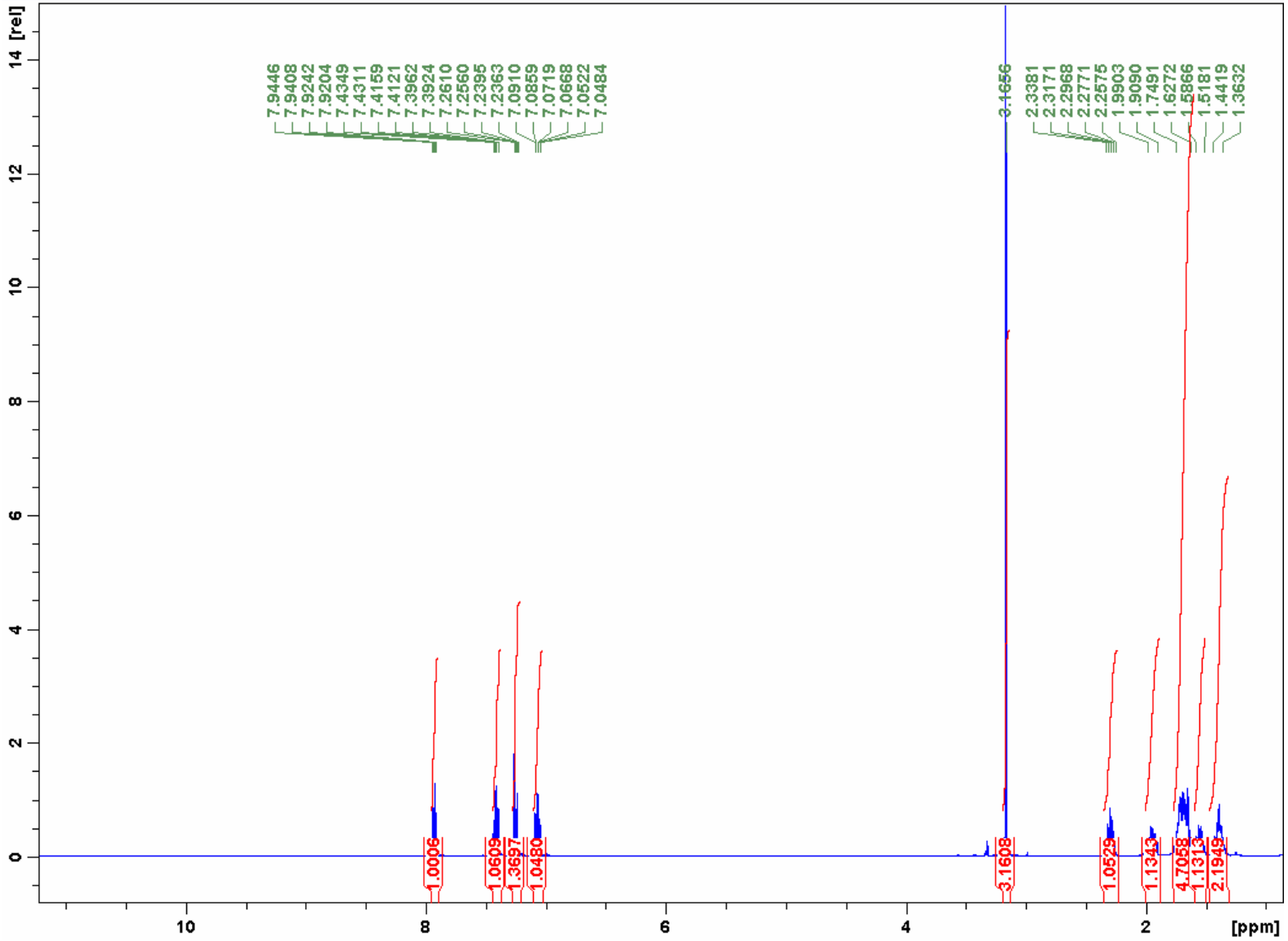

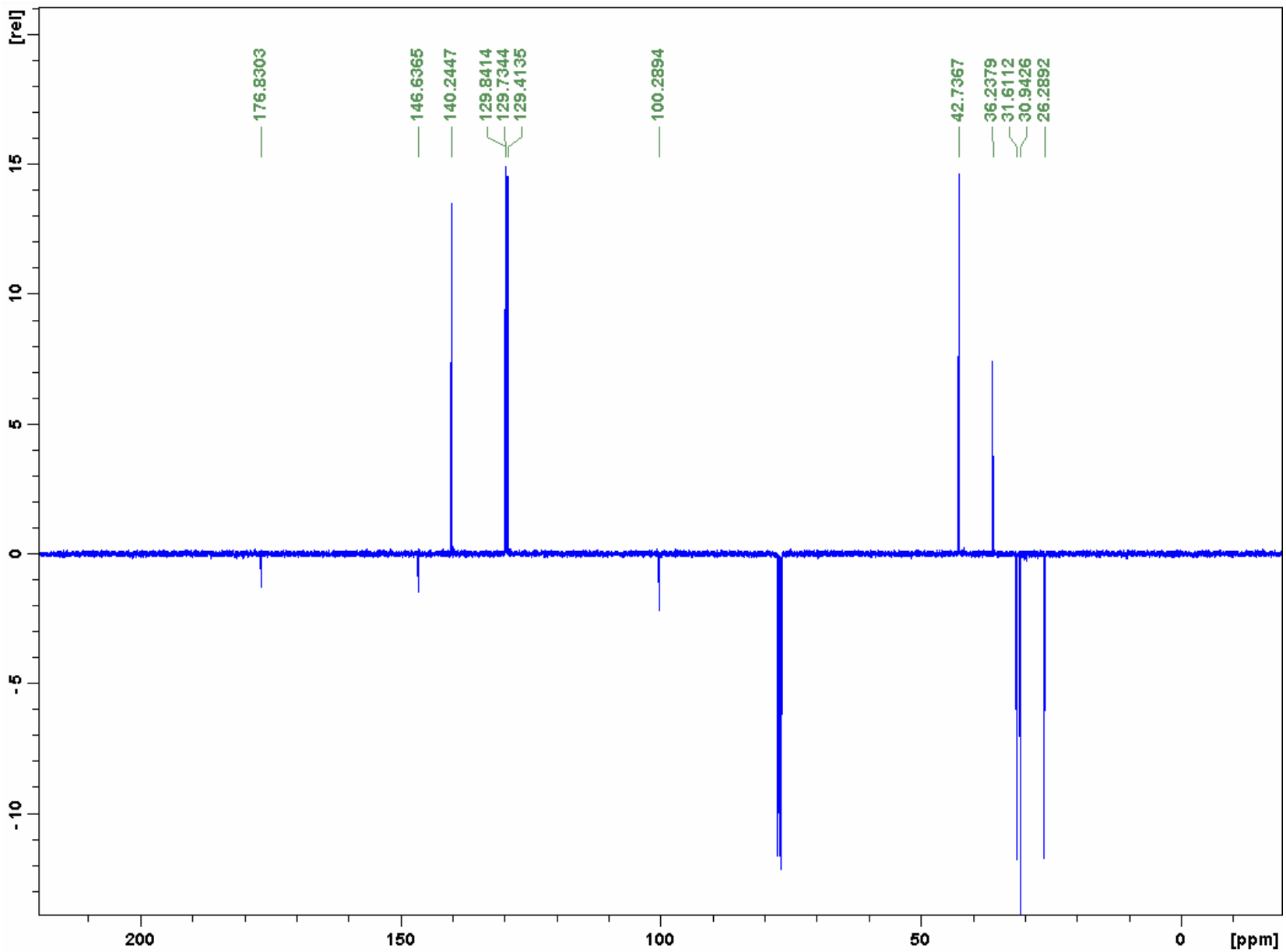
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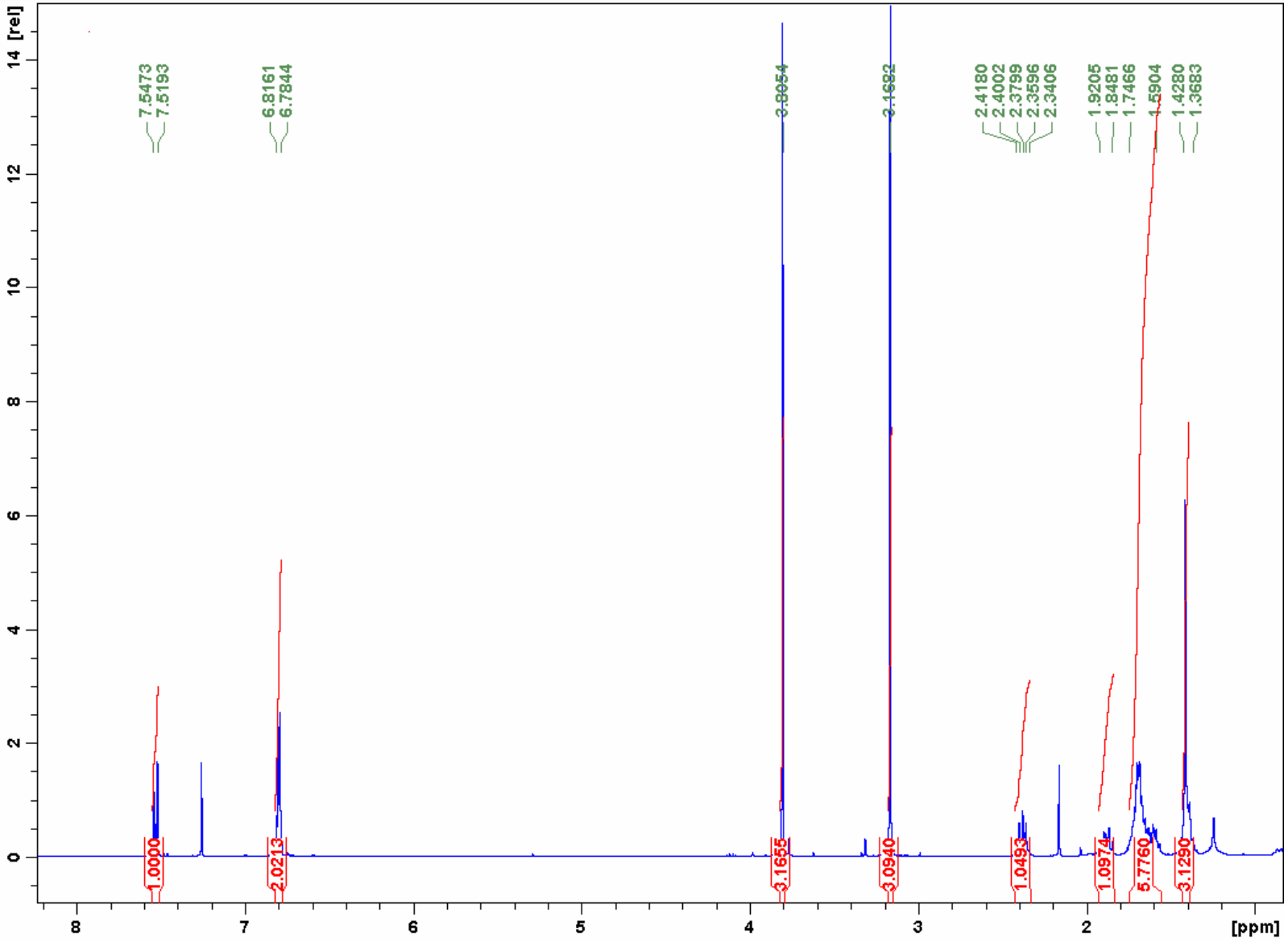

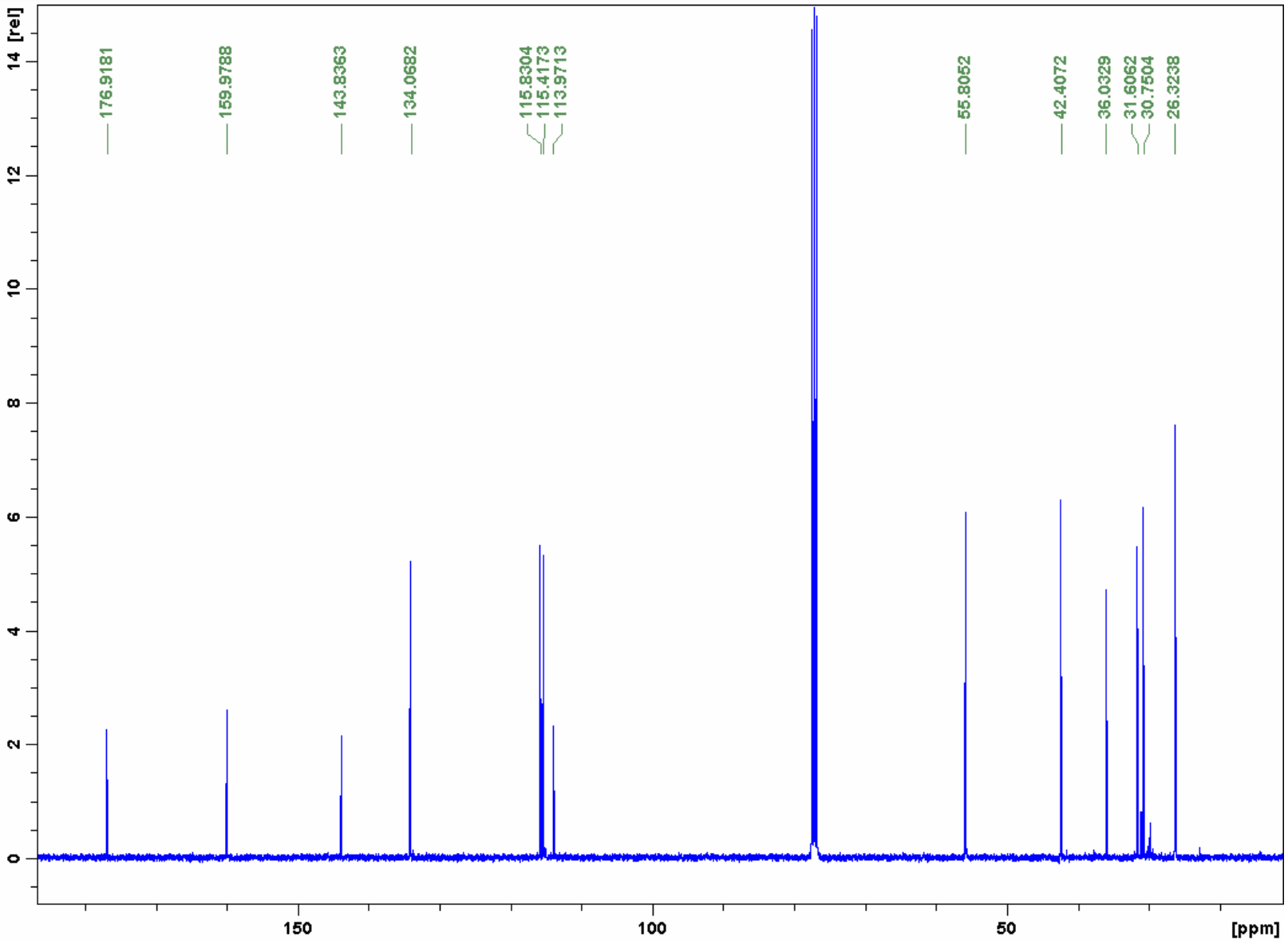
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2
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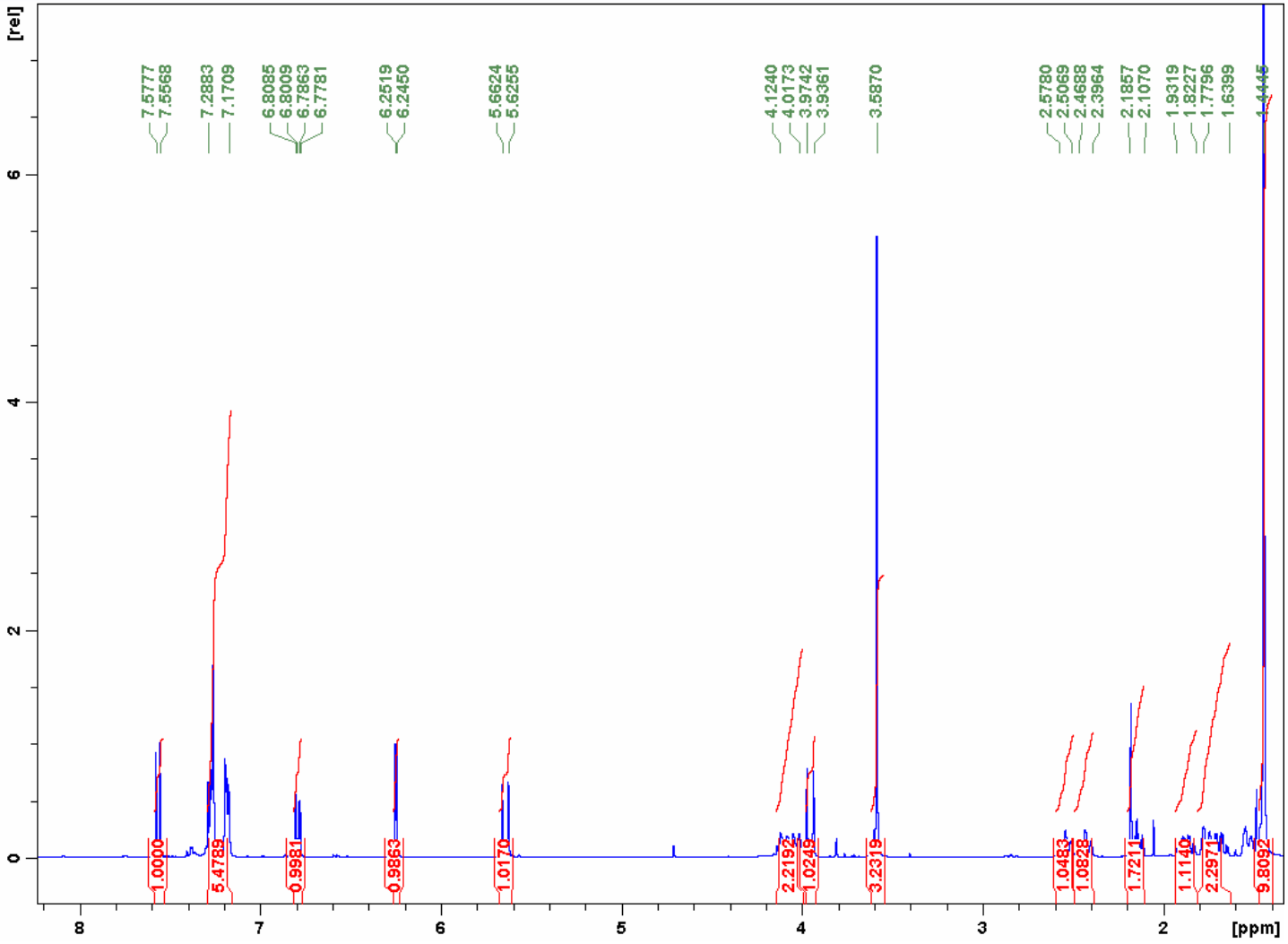
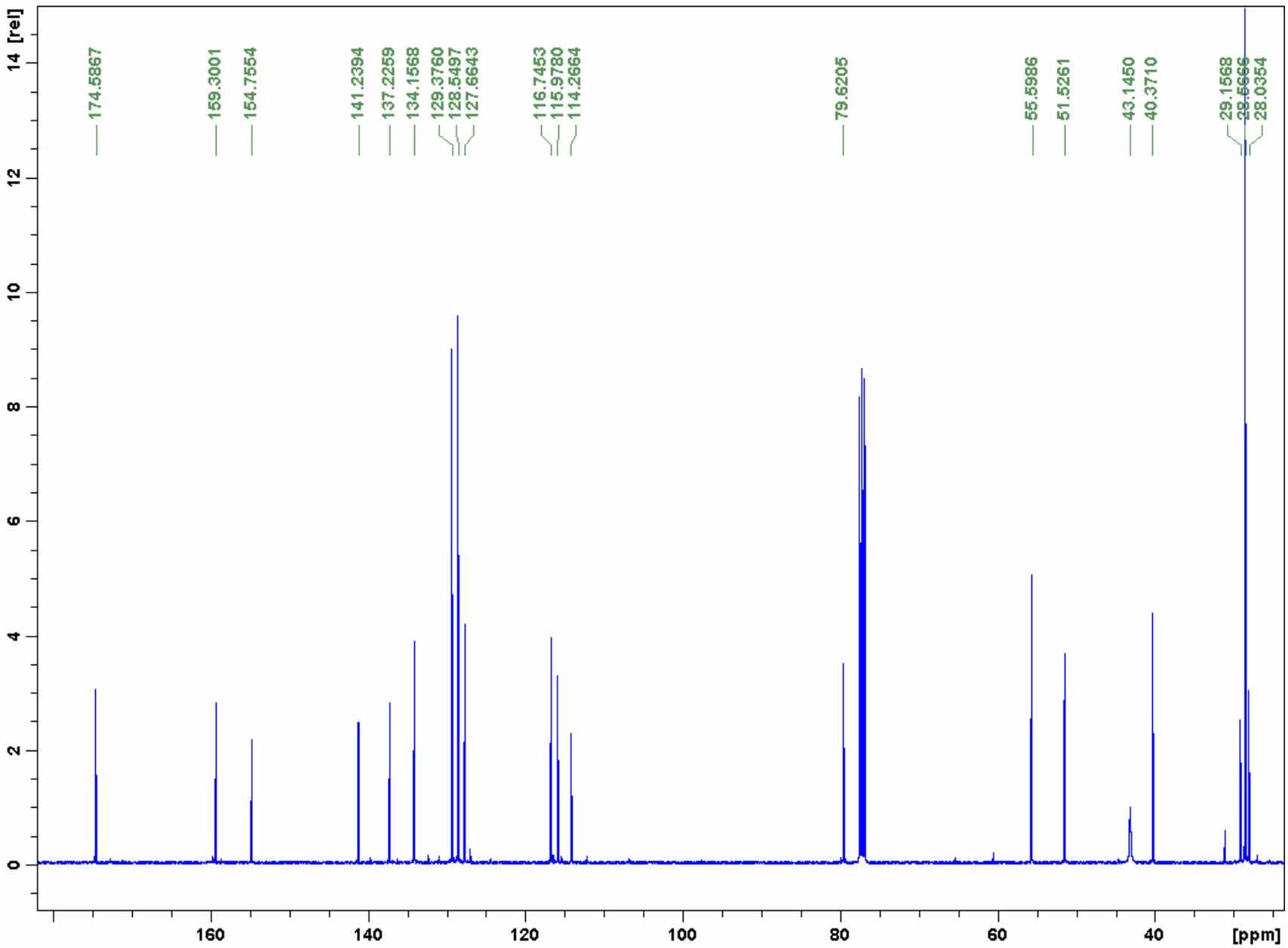
[ppm]

***N*-benzyl-*o*-bromoanilide 9e**

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14 [rel]
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0
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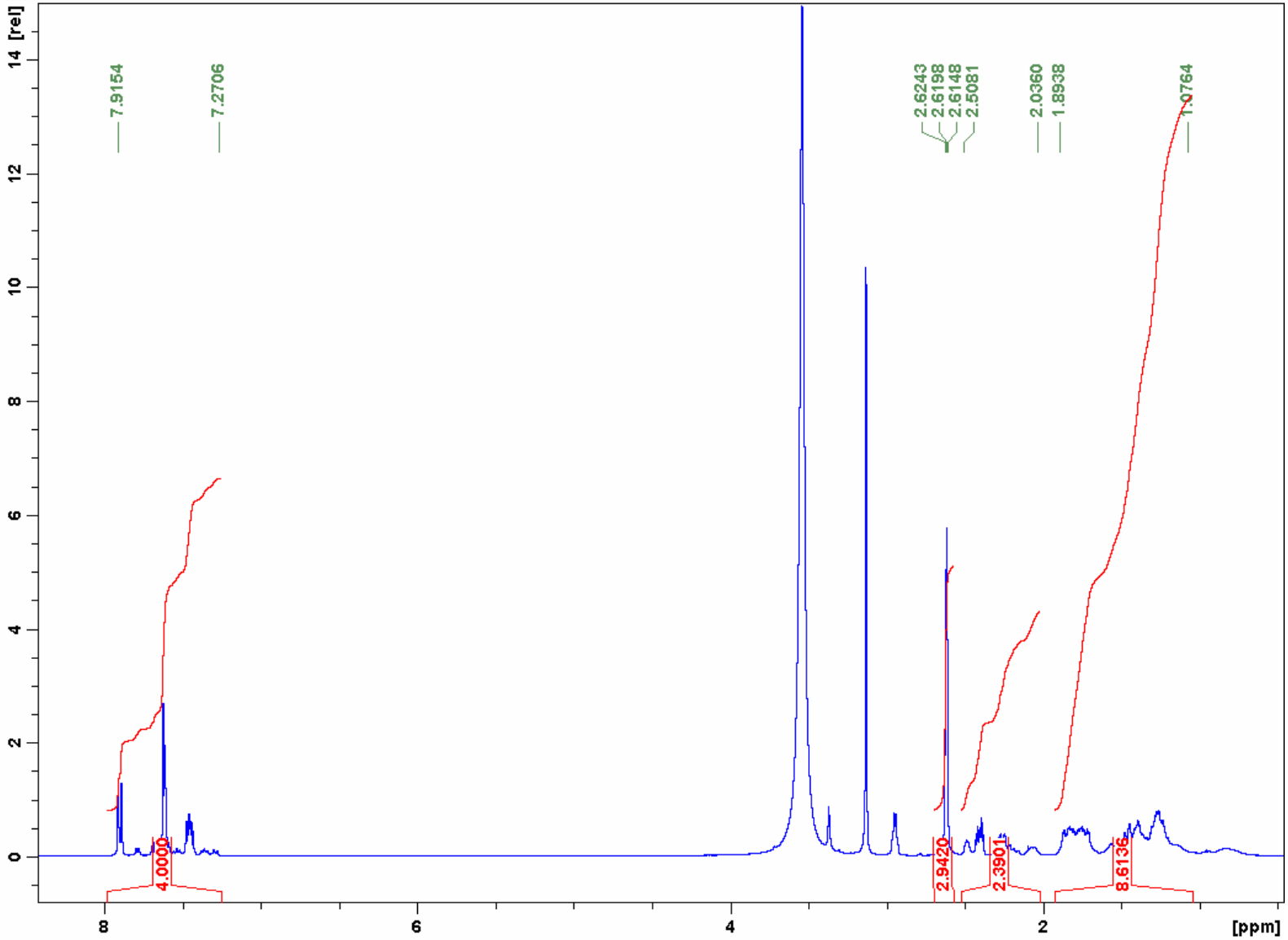
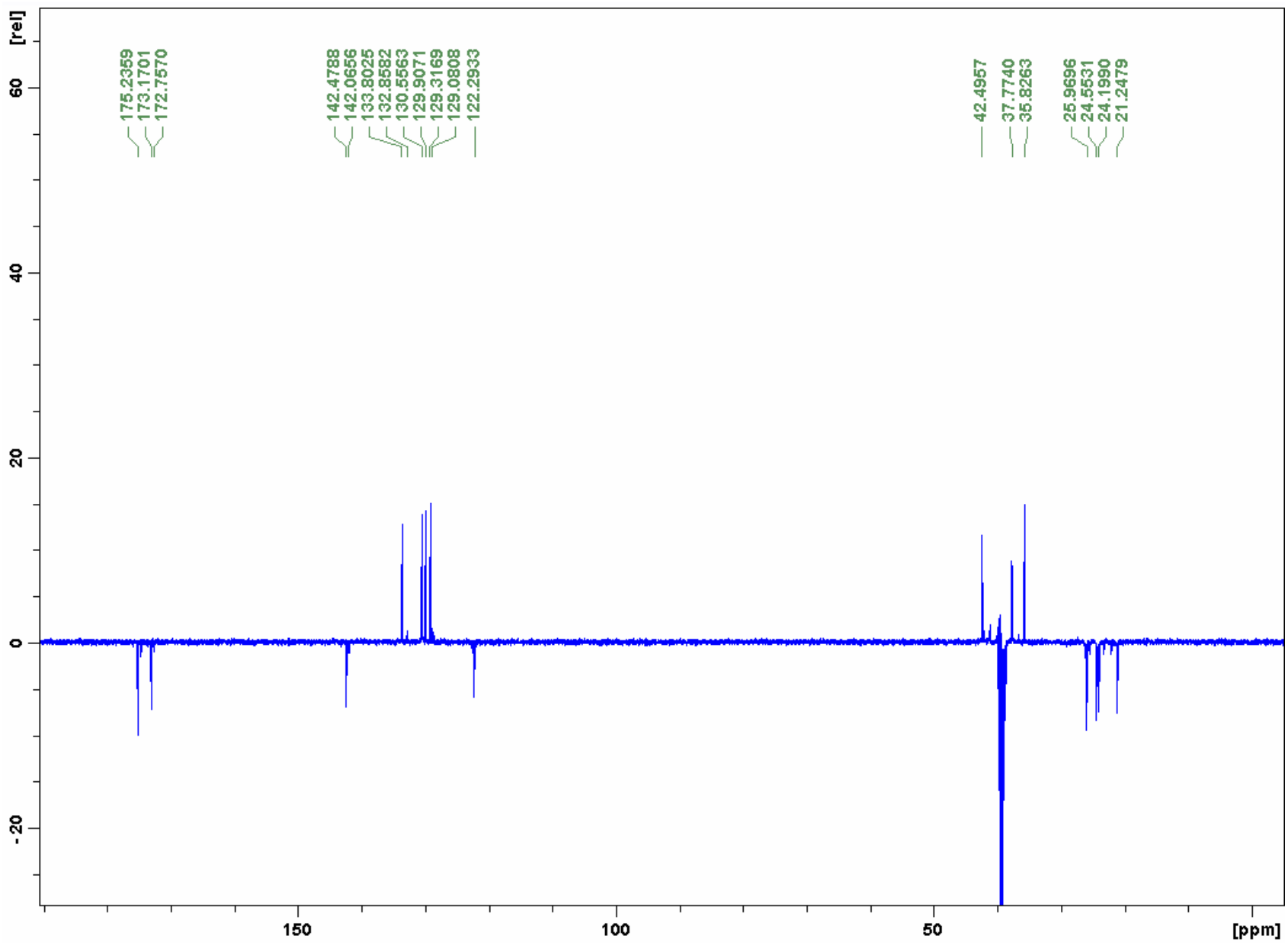
[ppm]

***N*-benzyl-*o*-bromoanilide 9f**

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24.5531
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20
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-20
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100
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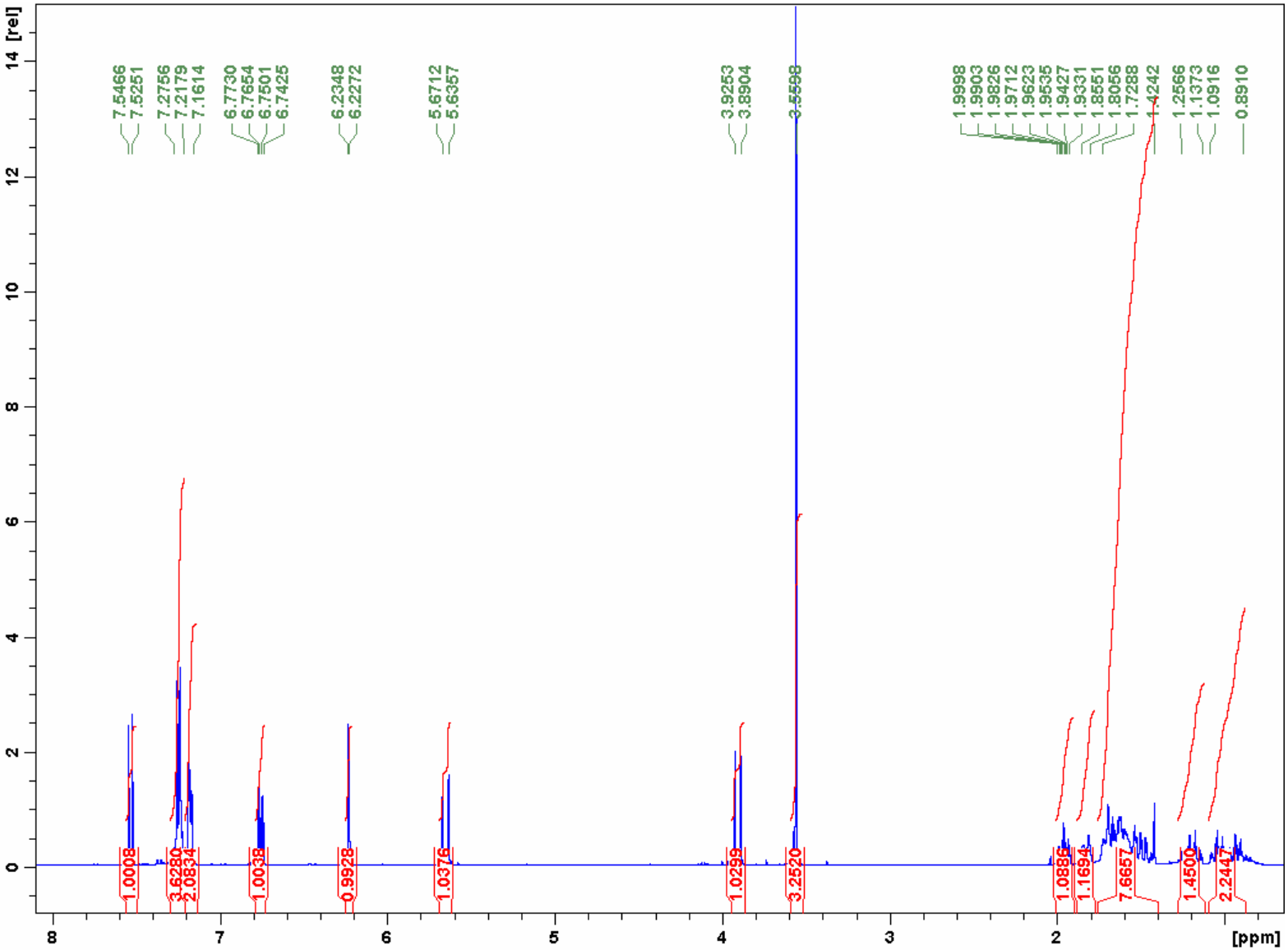
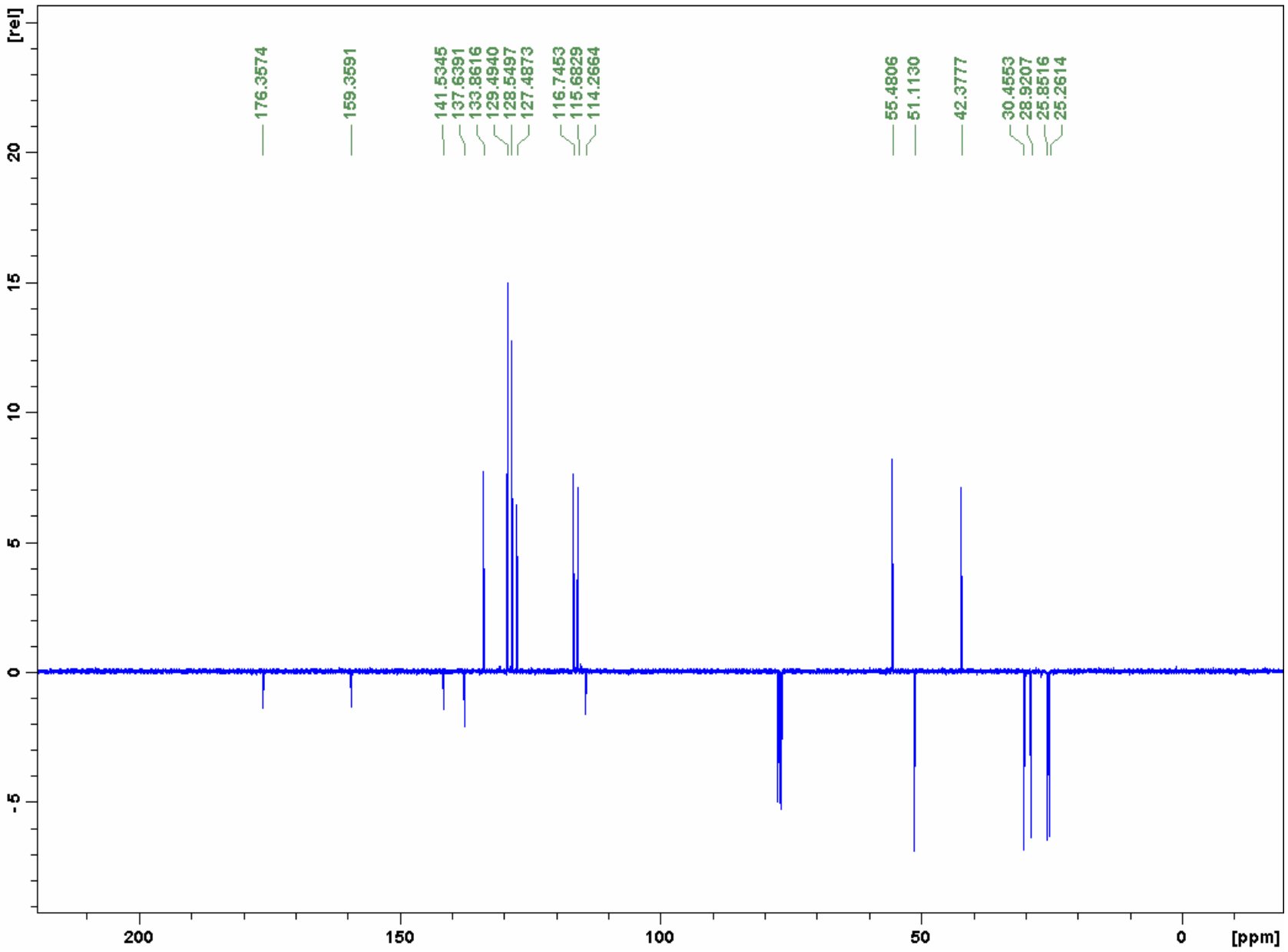
[ppm]

***N*-benzyl-*o*-bromoanilide 9g**

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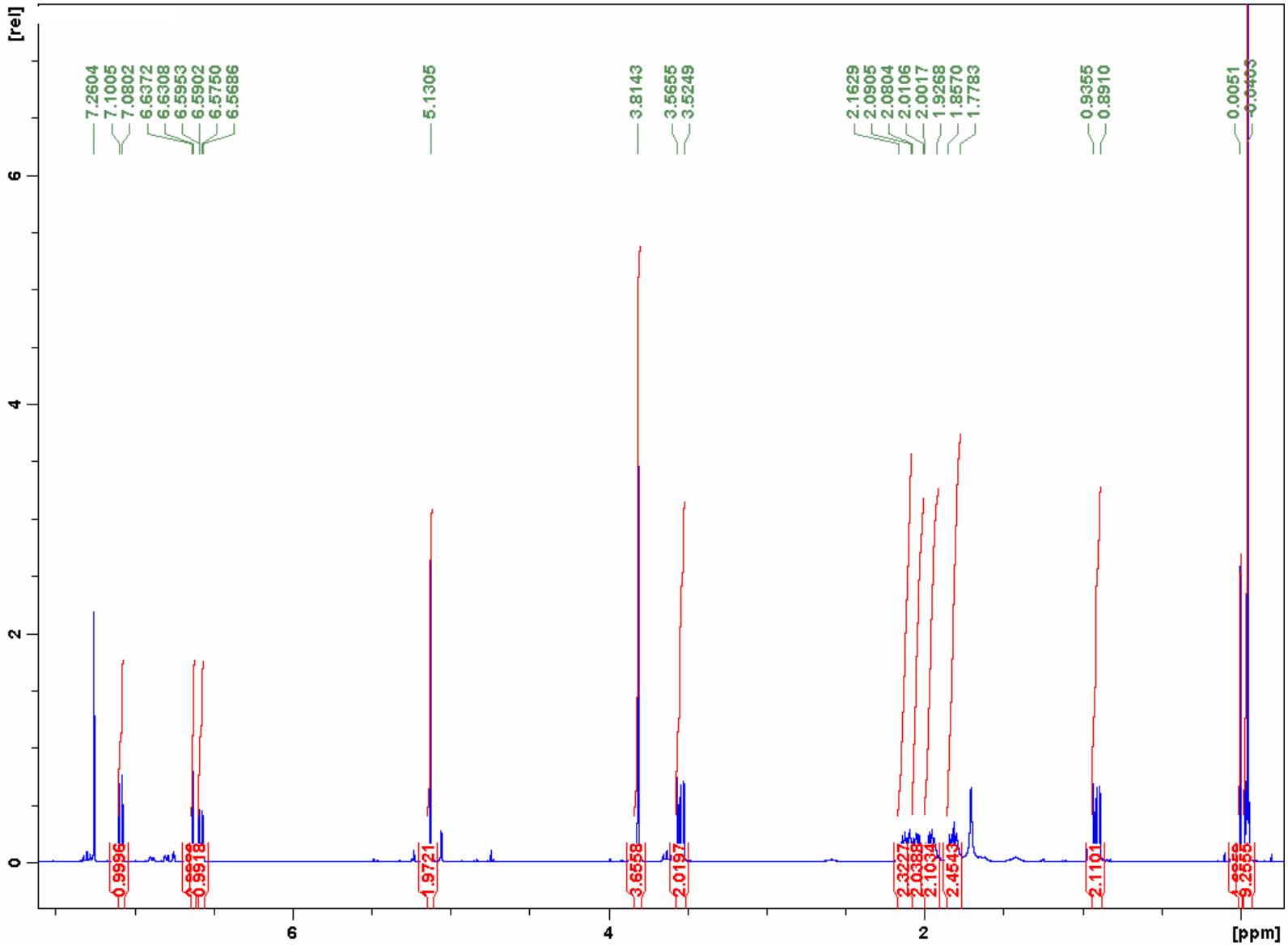
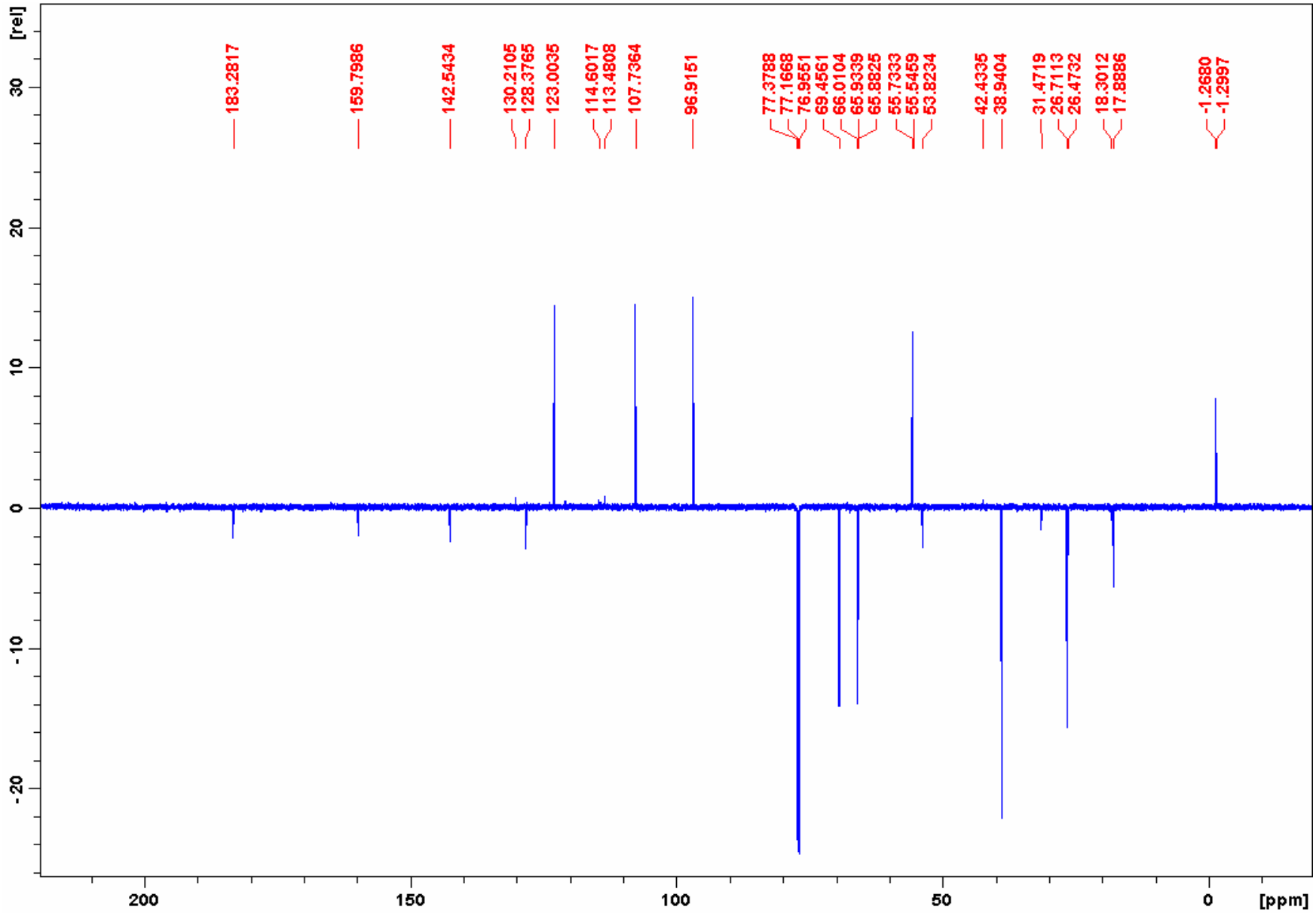
[ppm]

Spirooxindole 10a

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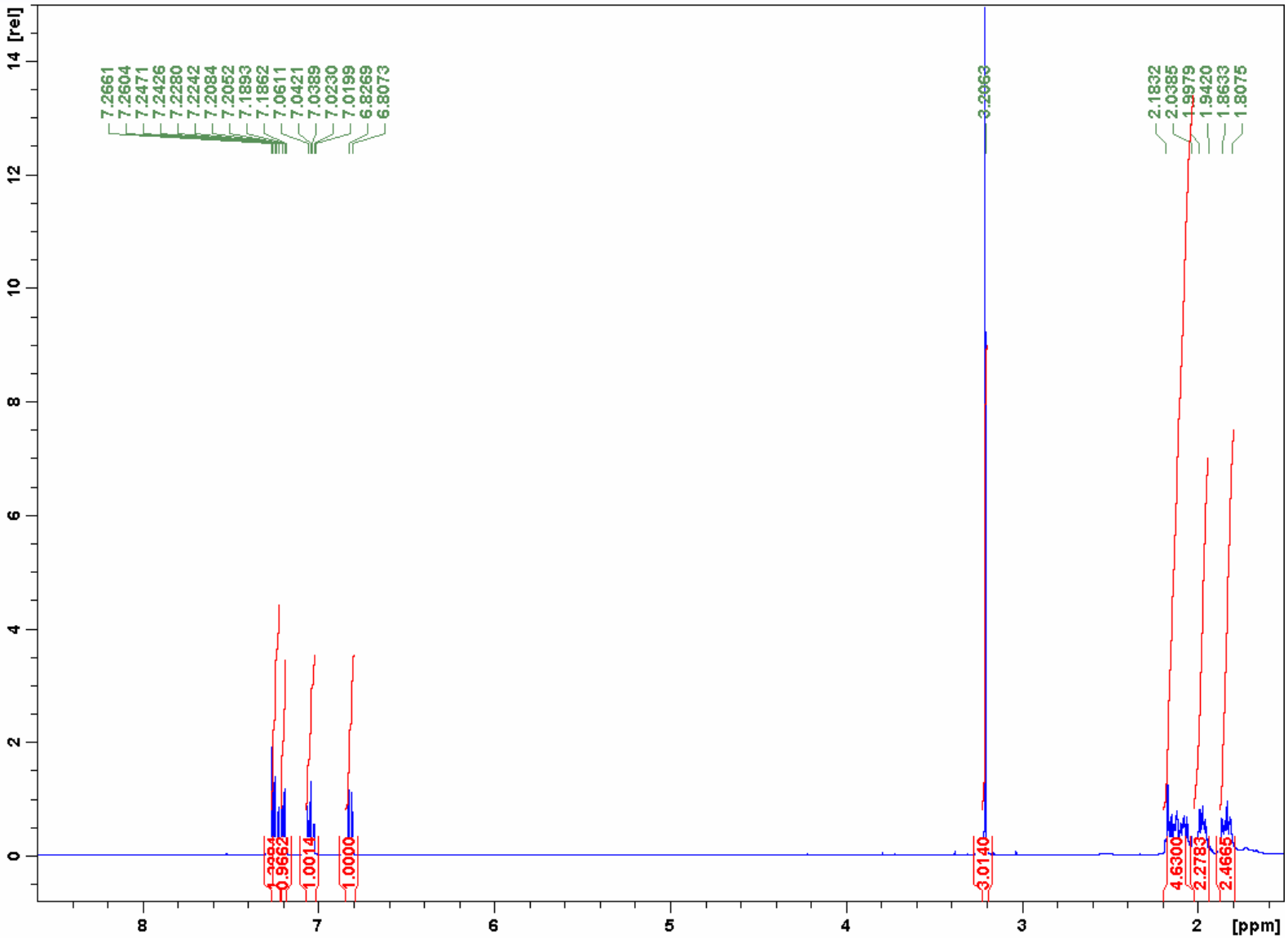

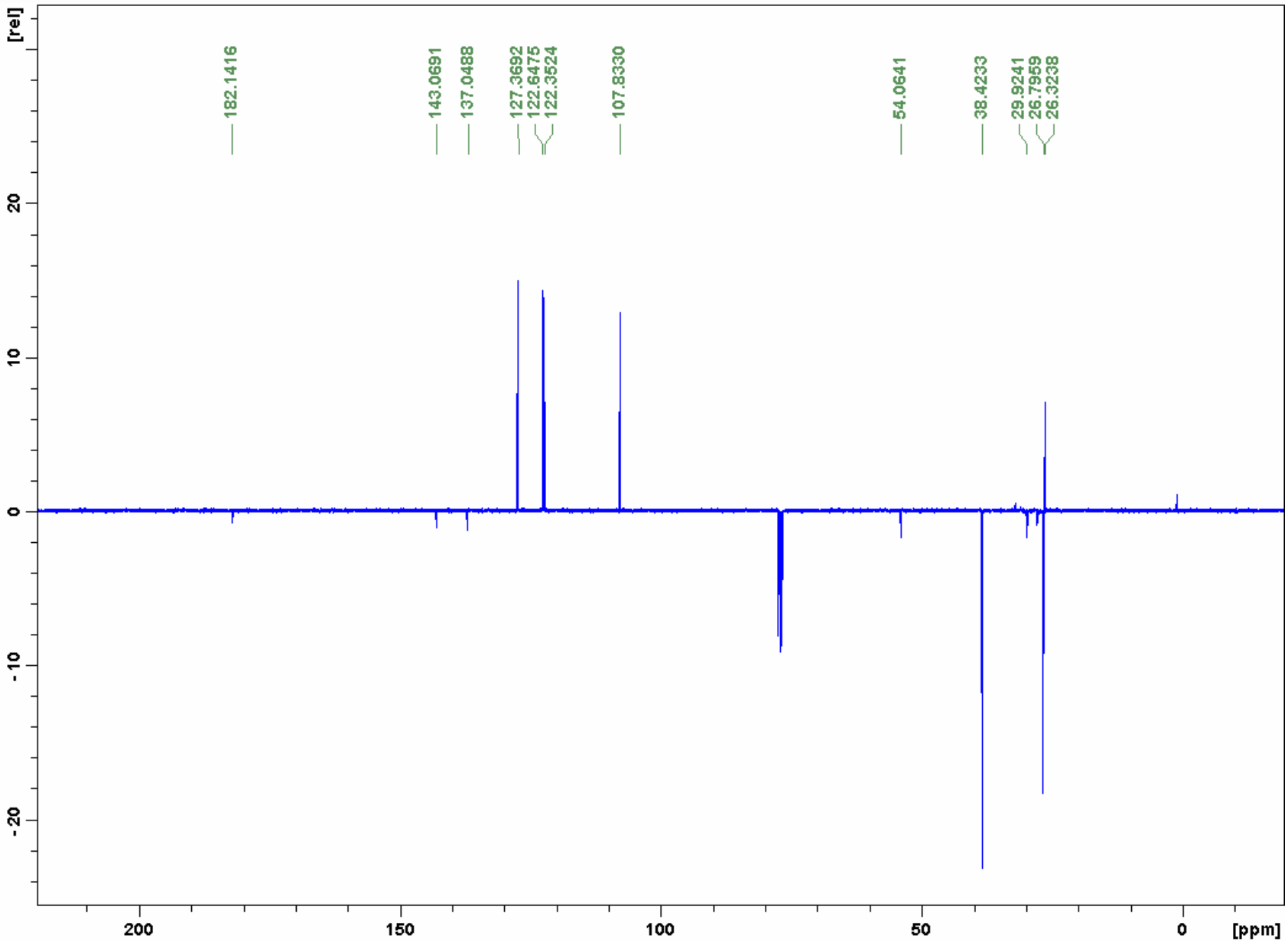
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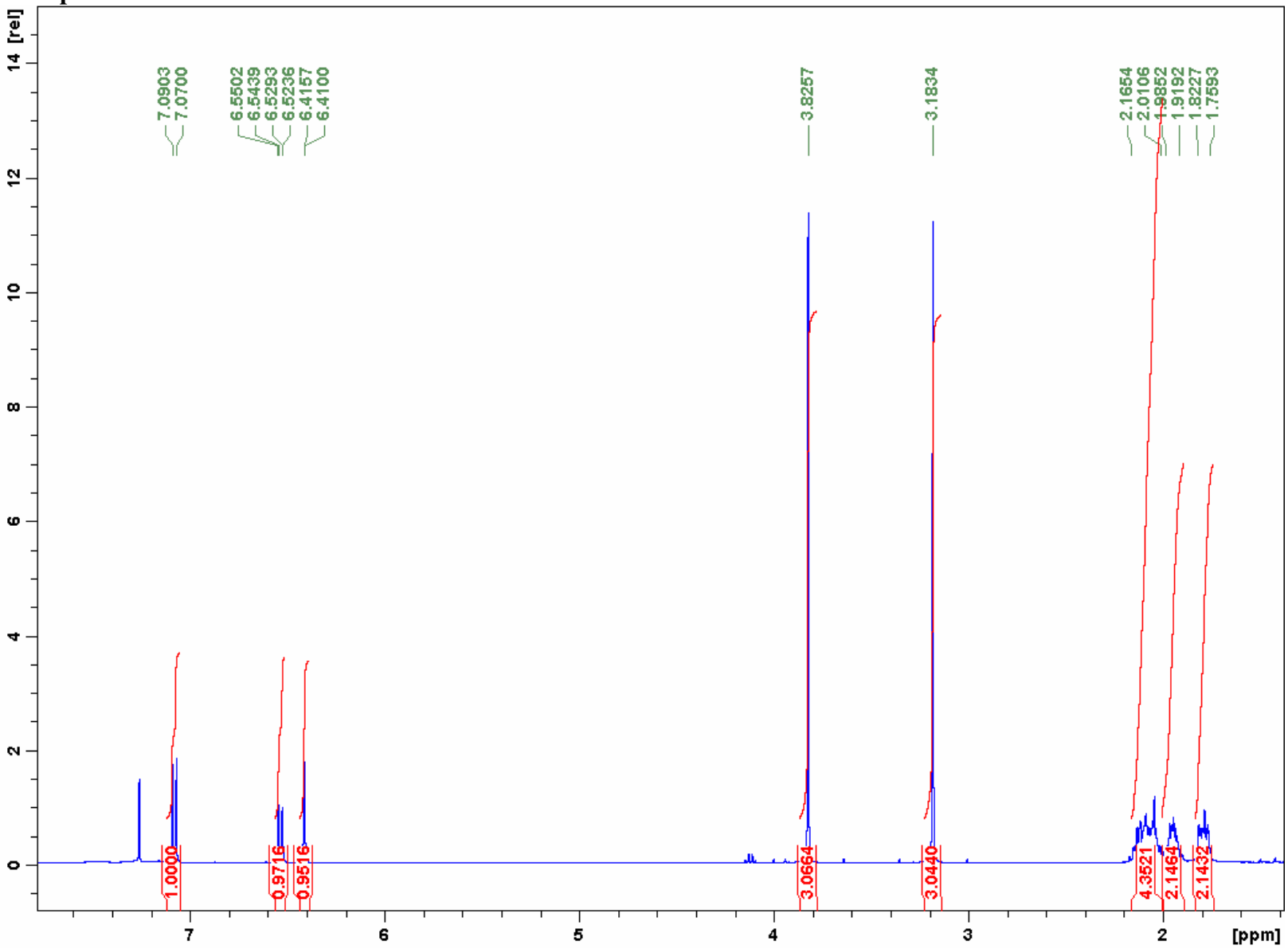
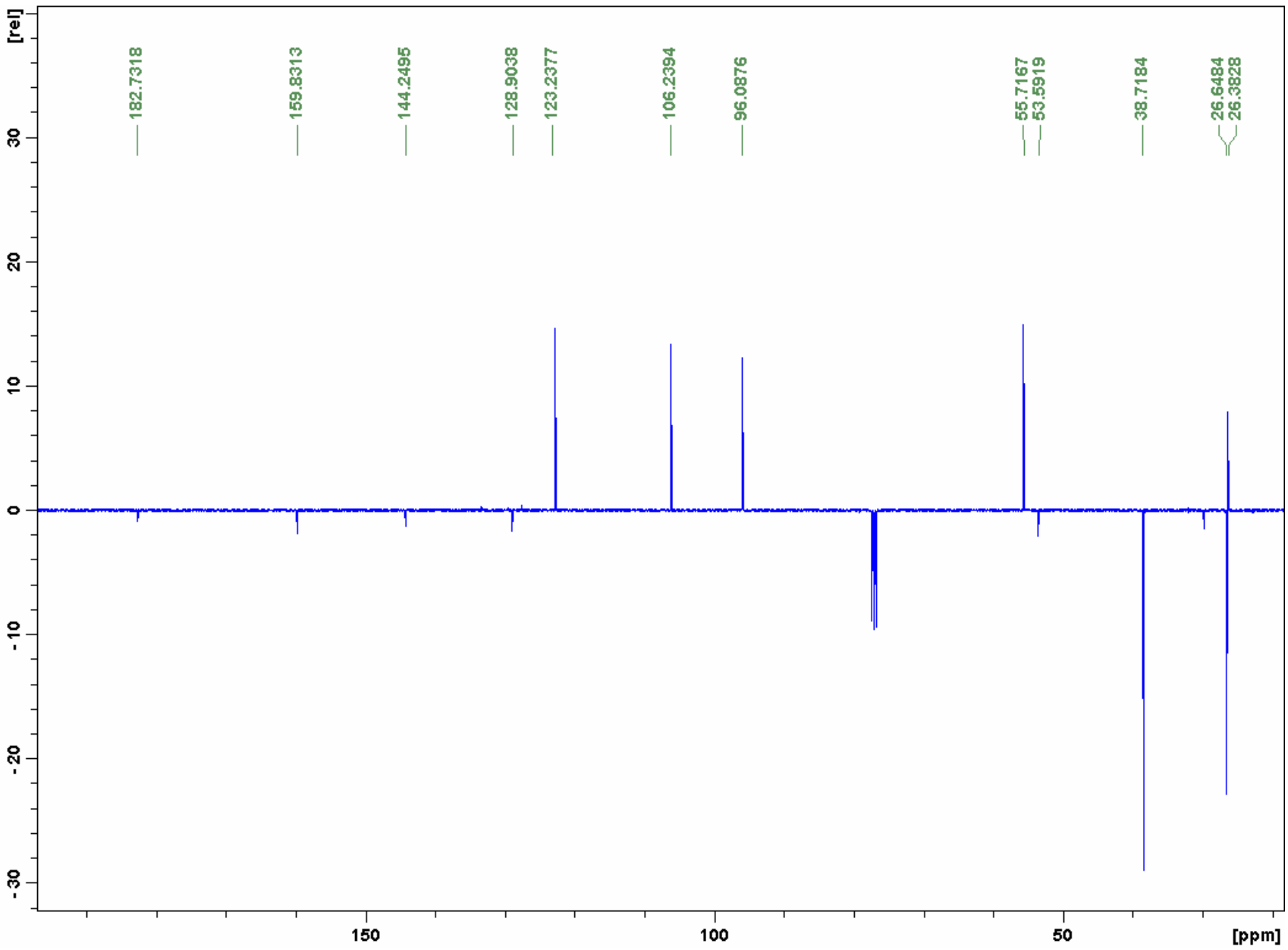
Spirooxindole 10d

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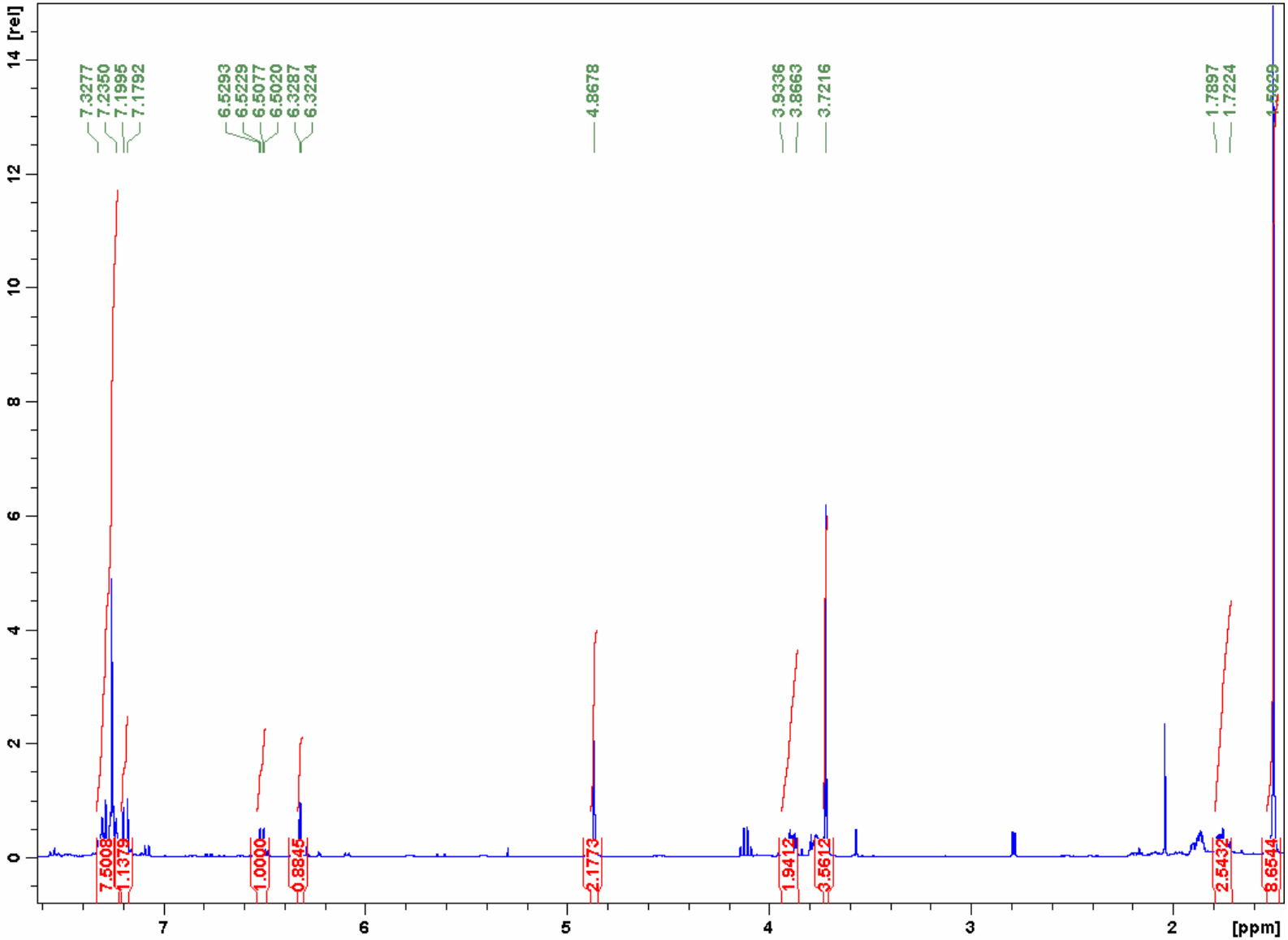
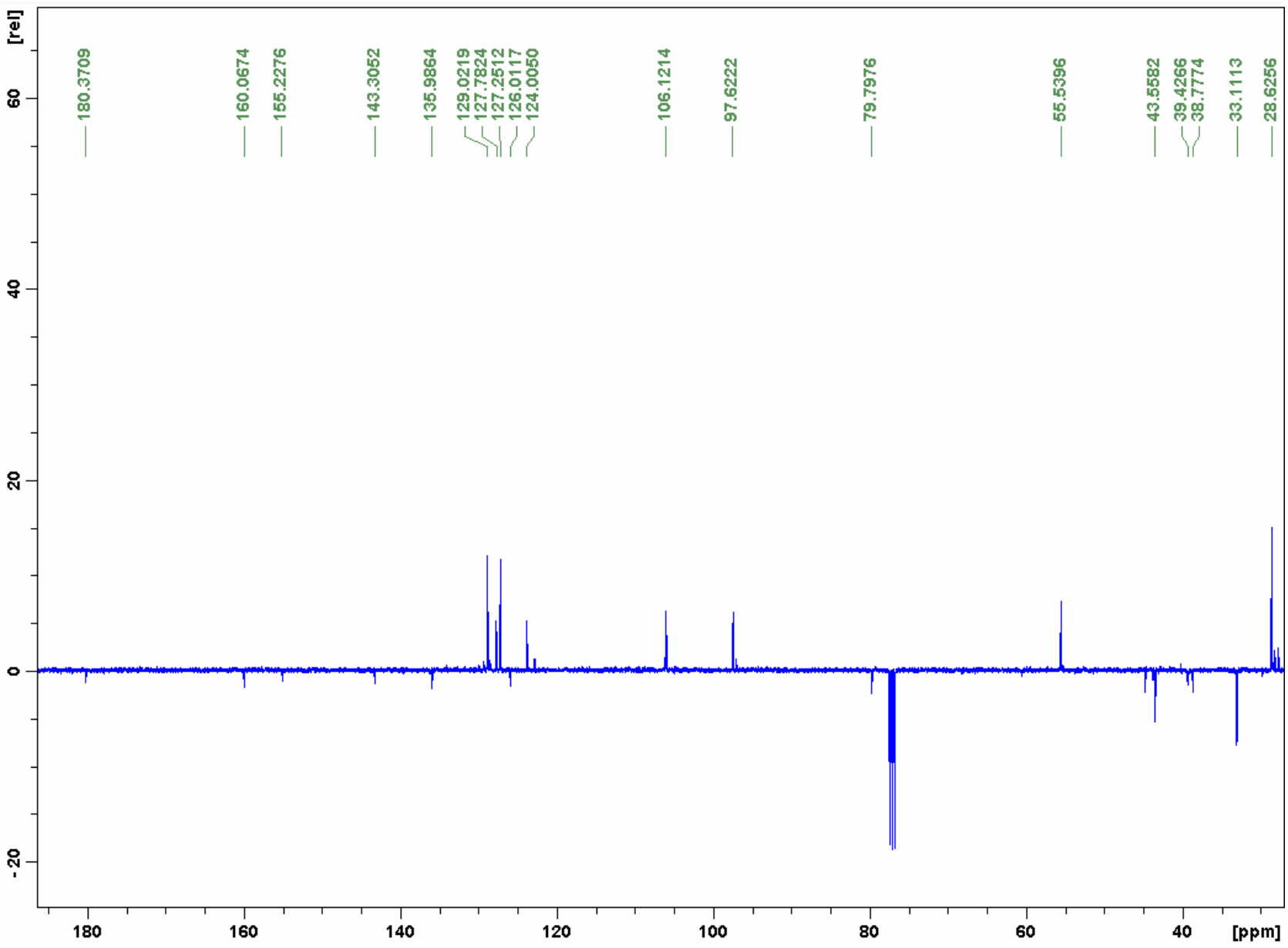
Spirooxindole 10e

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106.1214
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79.7976
55.5396
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140
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100
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60
40
[ppm]

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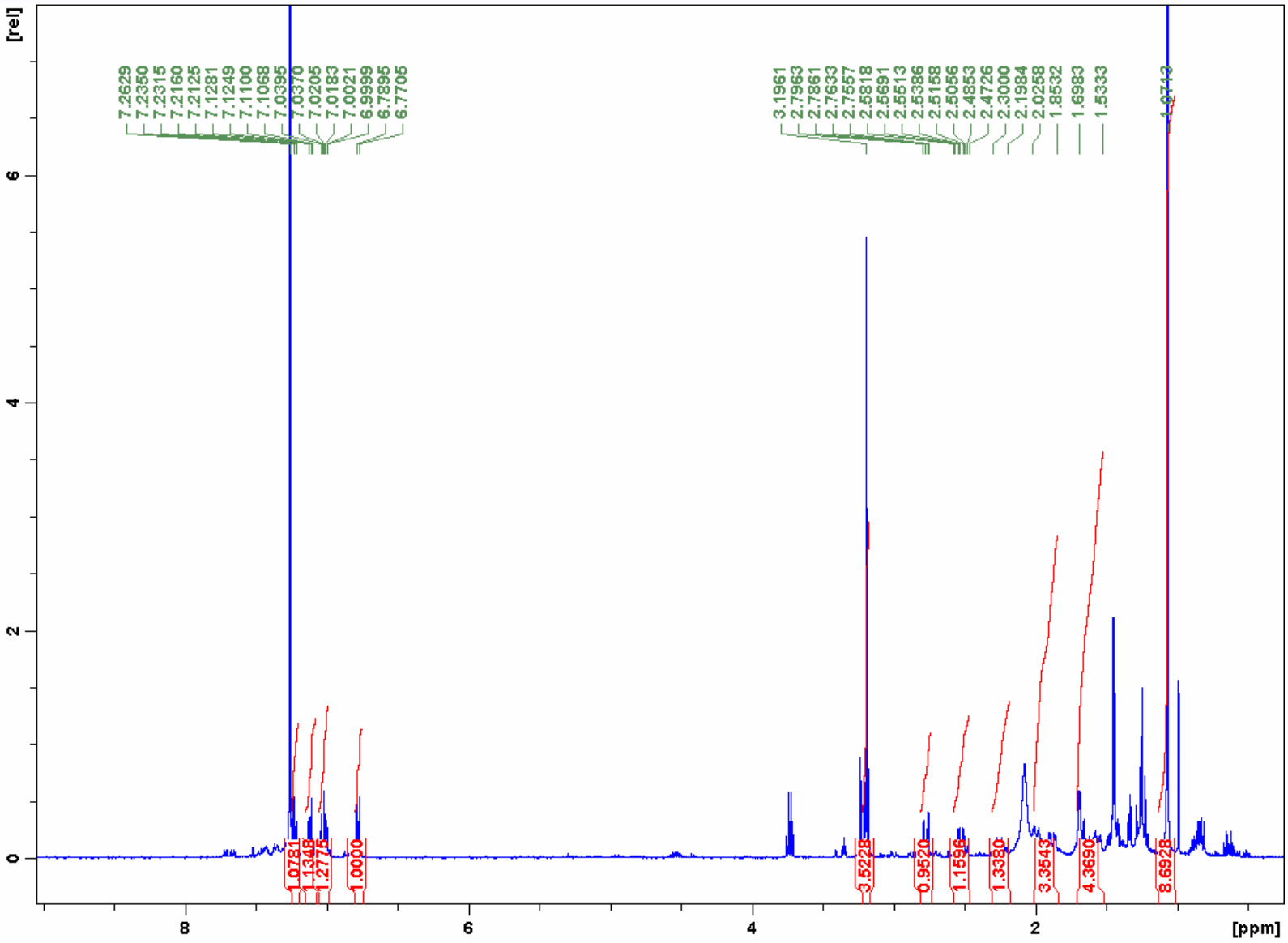
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7.0183
7.0021
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6.7895
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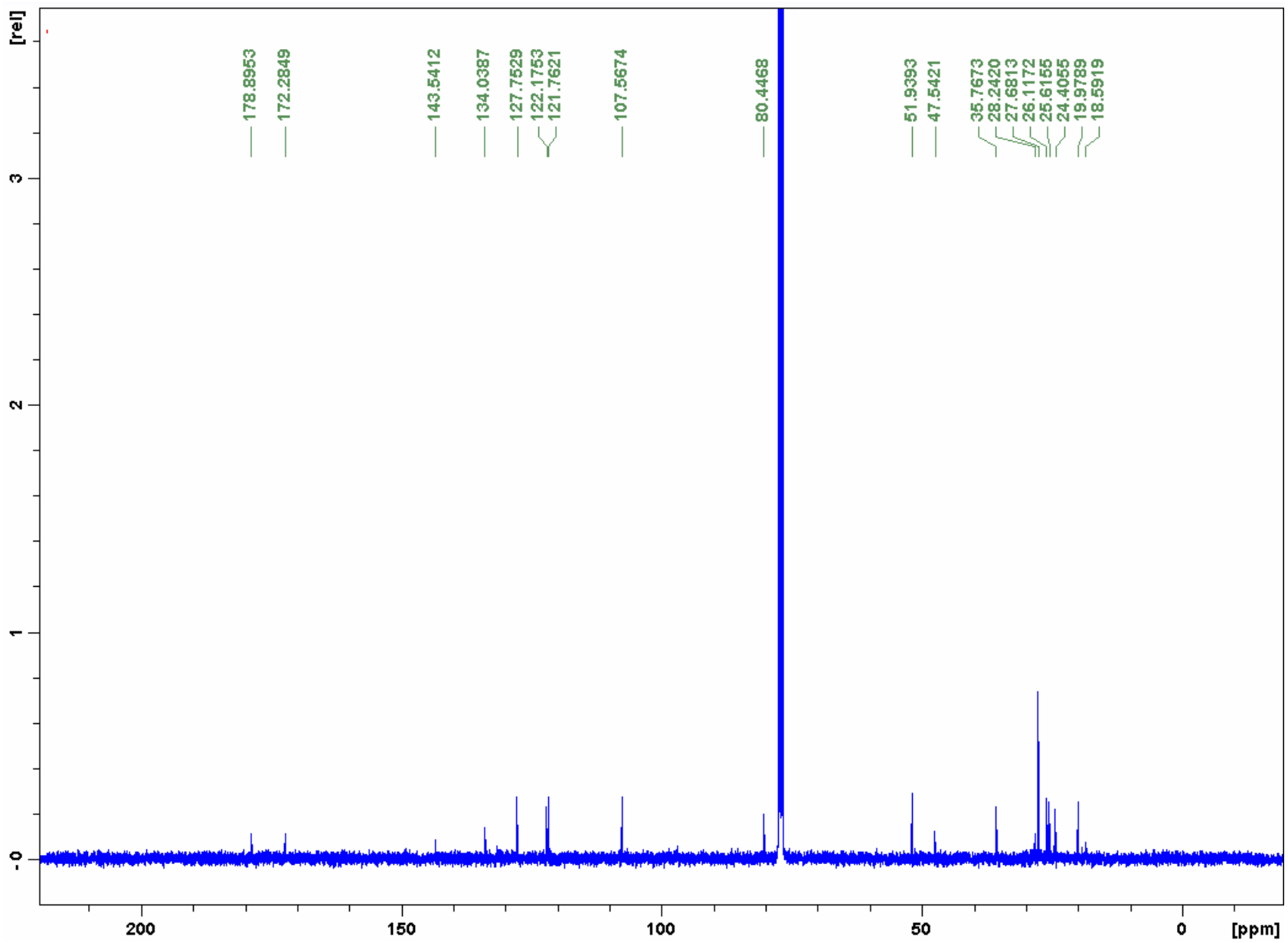
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2
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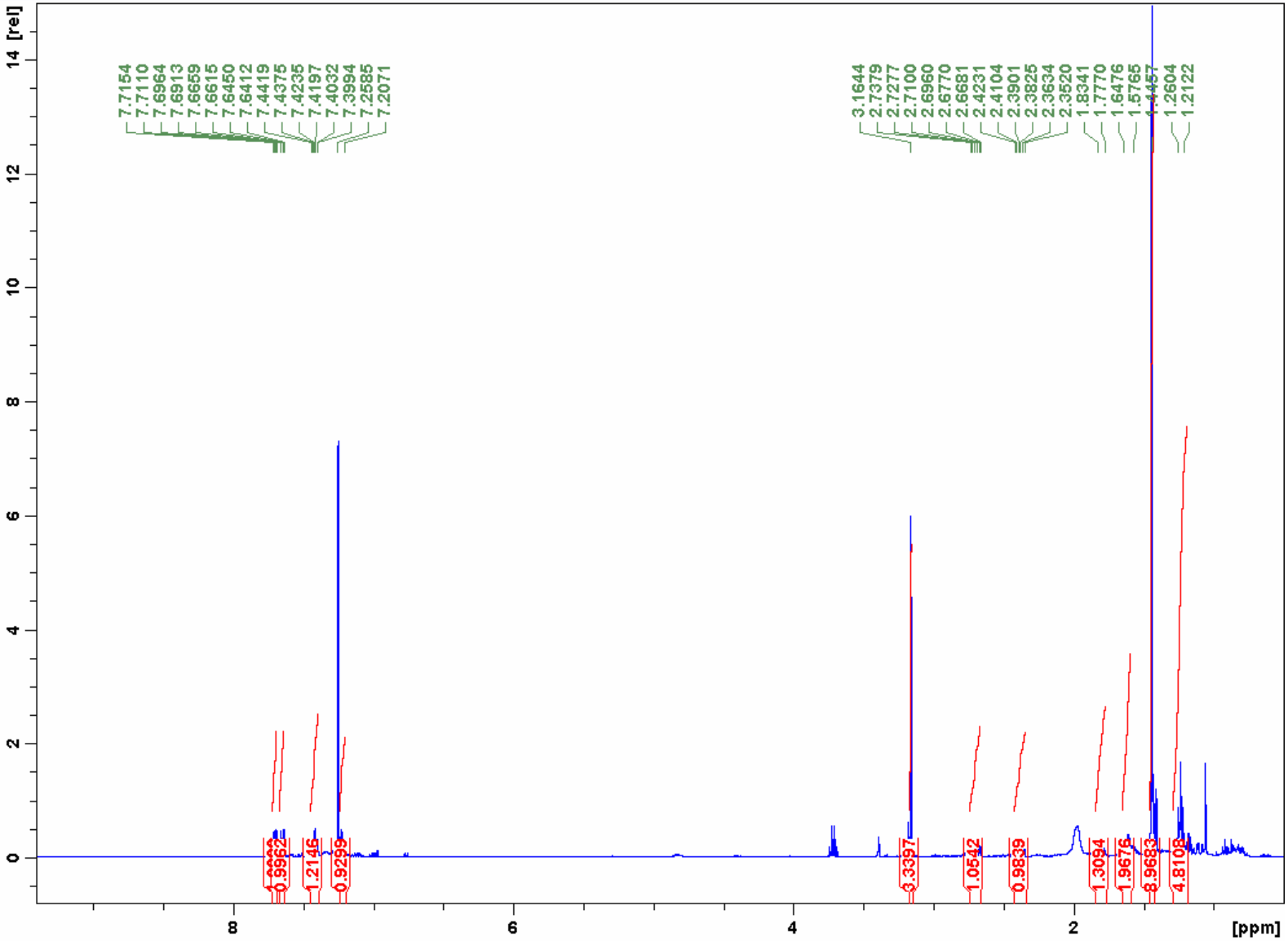
Slow 10f: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10
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6
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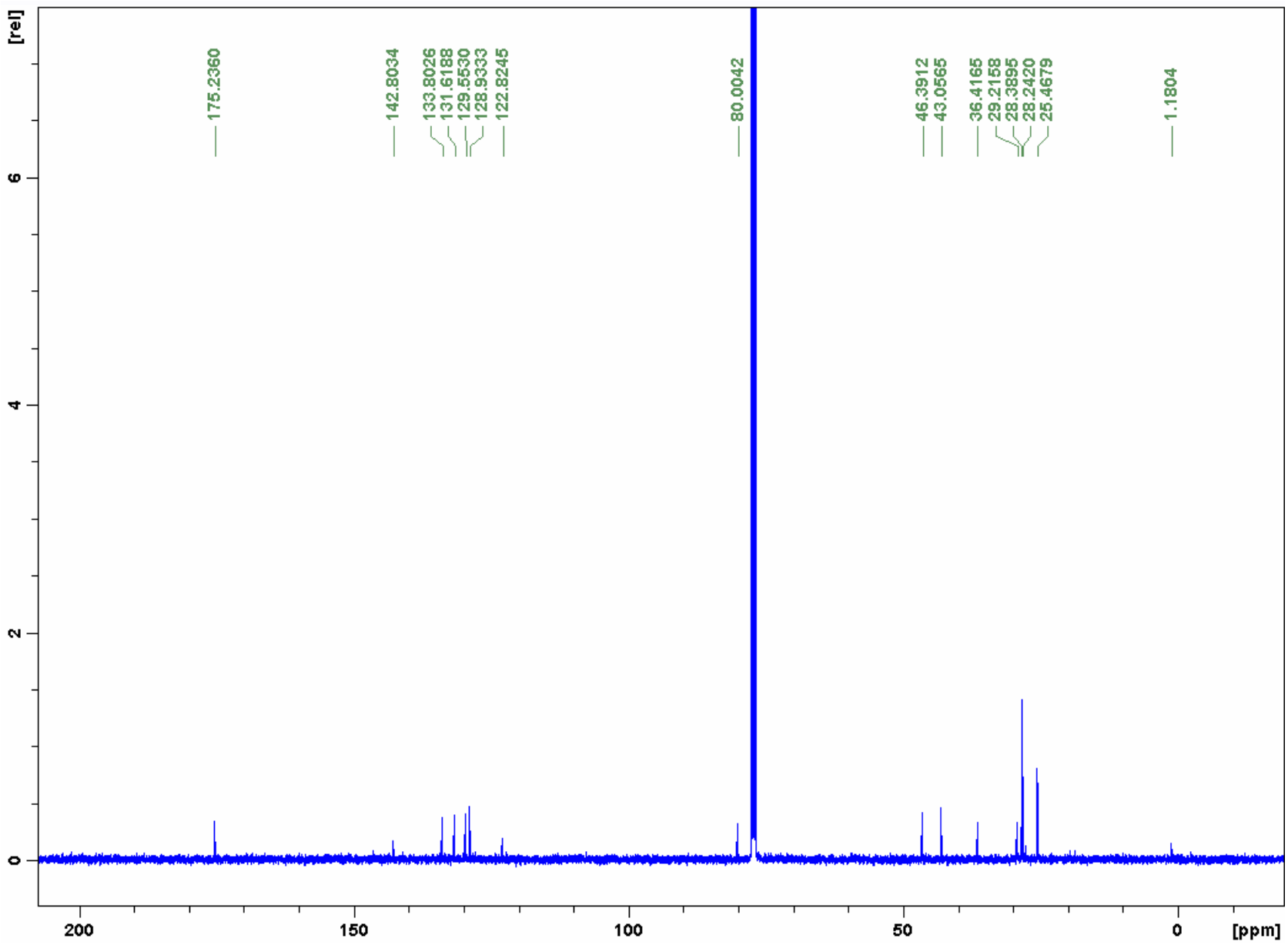
7.6913
7.6659
7.6615
7.6450
7.6412
7.4419
7.4375
7.4235
7.4197
7.4032
7.3994
7.2585
7.2071
3.1644
2.7379
2.7277
2.7100
2.6960
2.6770
2.6681
2.4231
2.4104
2.3901
2.3825
2.3634
2.3520
1.8341
1.7770
1.6476
1.5765
1.2604
1.2122
0.9962
1.2146
0.9299
3.3397
1.0542
0.9839
1.3094
1.9676
8.9683
4.8108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6
4
2
0
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142.8034
133.8026
131.6188
129.5530
128.9333
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46.3912
43.0565
36.4165
29.2158
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28.2420
25.4679
1.1804
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150
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50
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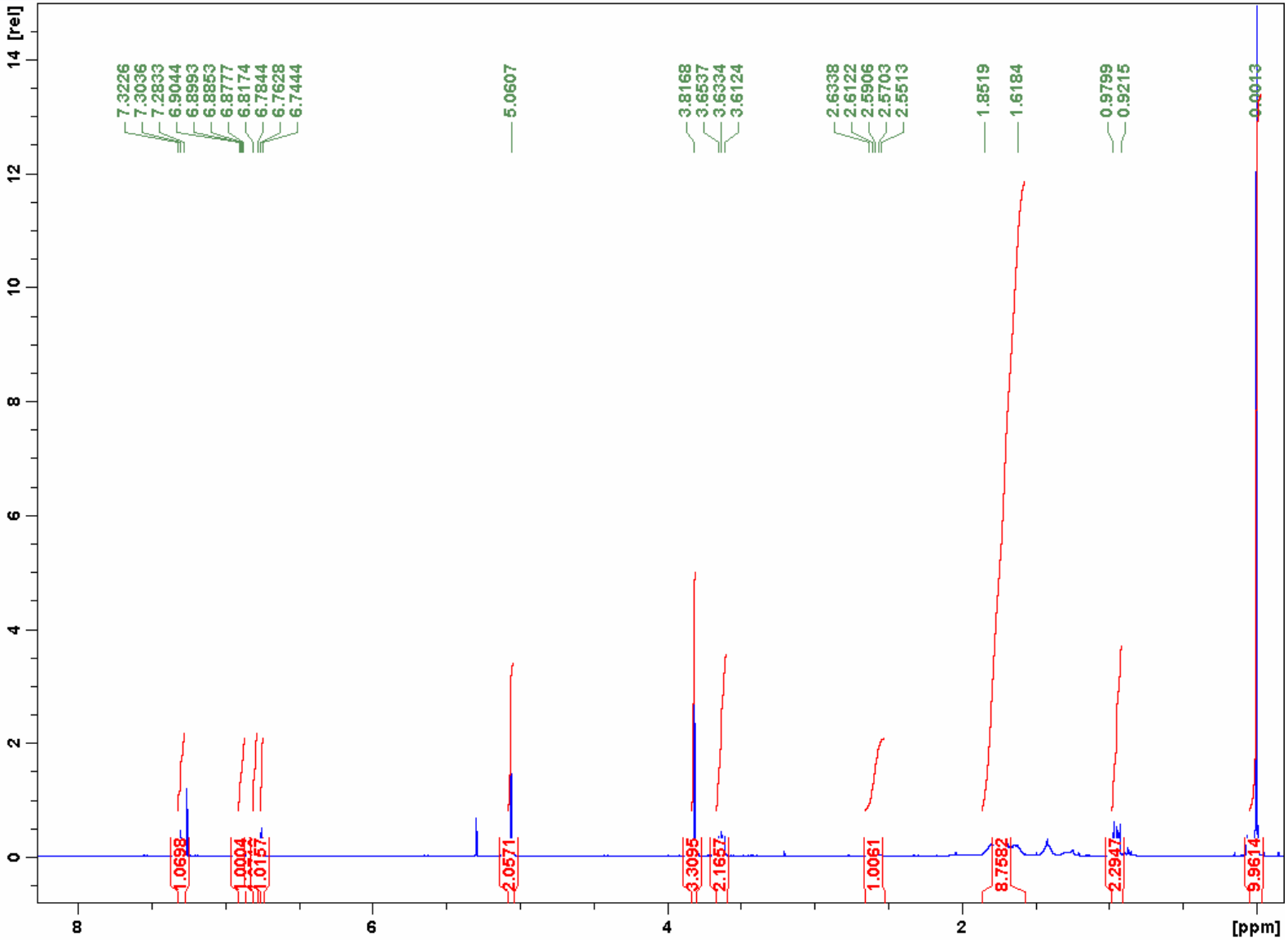
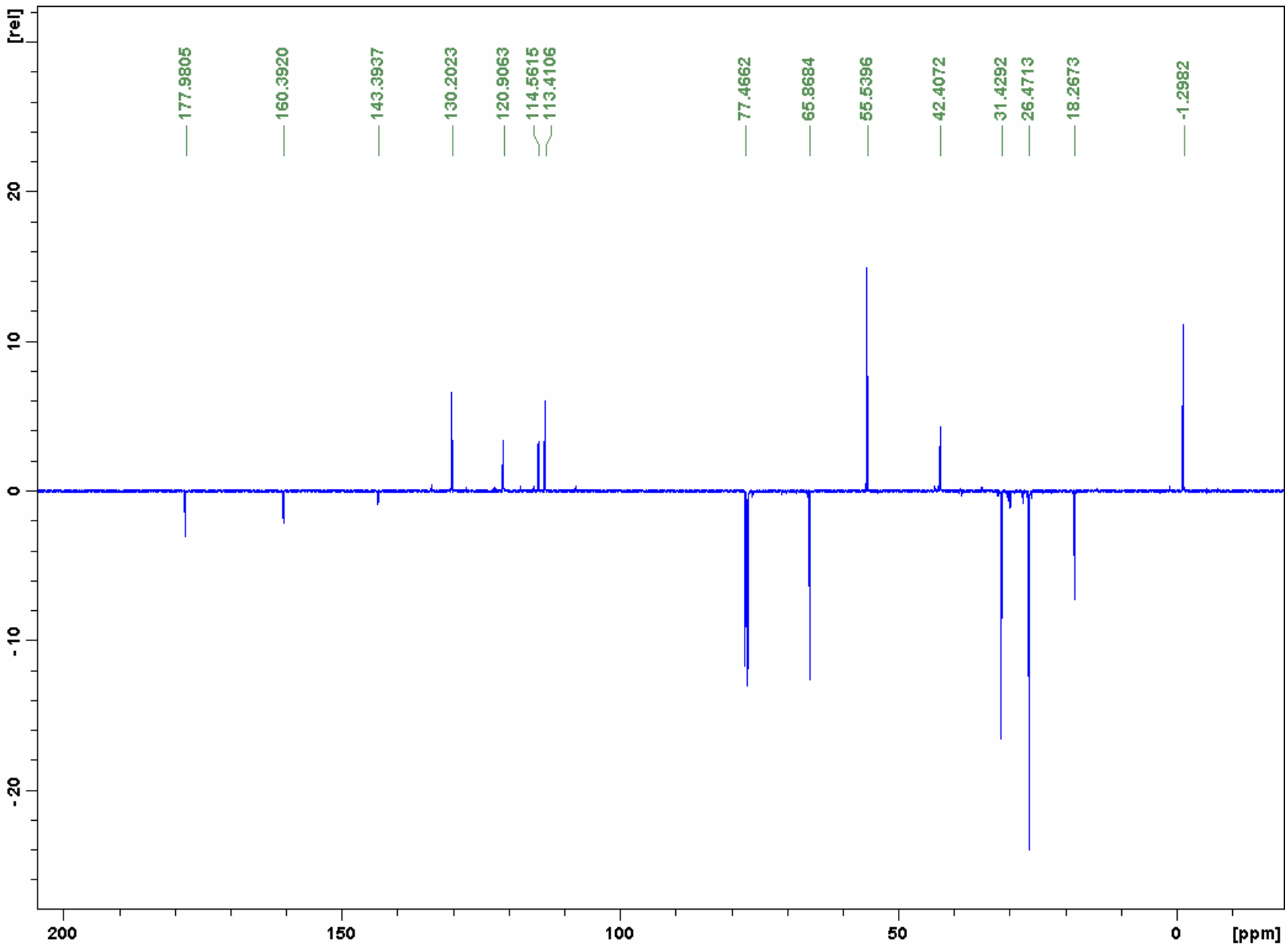
[ppm]

Dehalogenated side product 11a

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20
10
0
- 10
- 20
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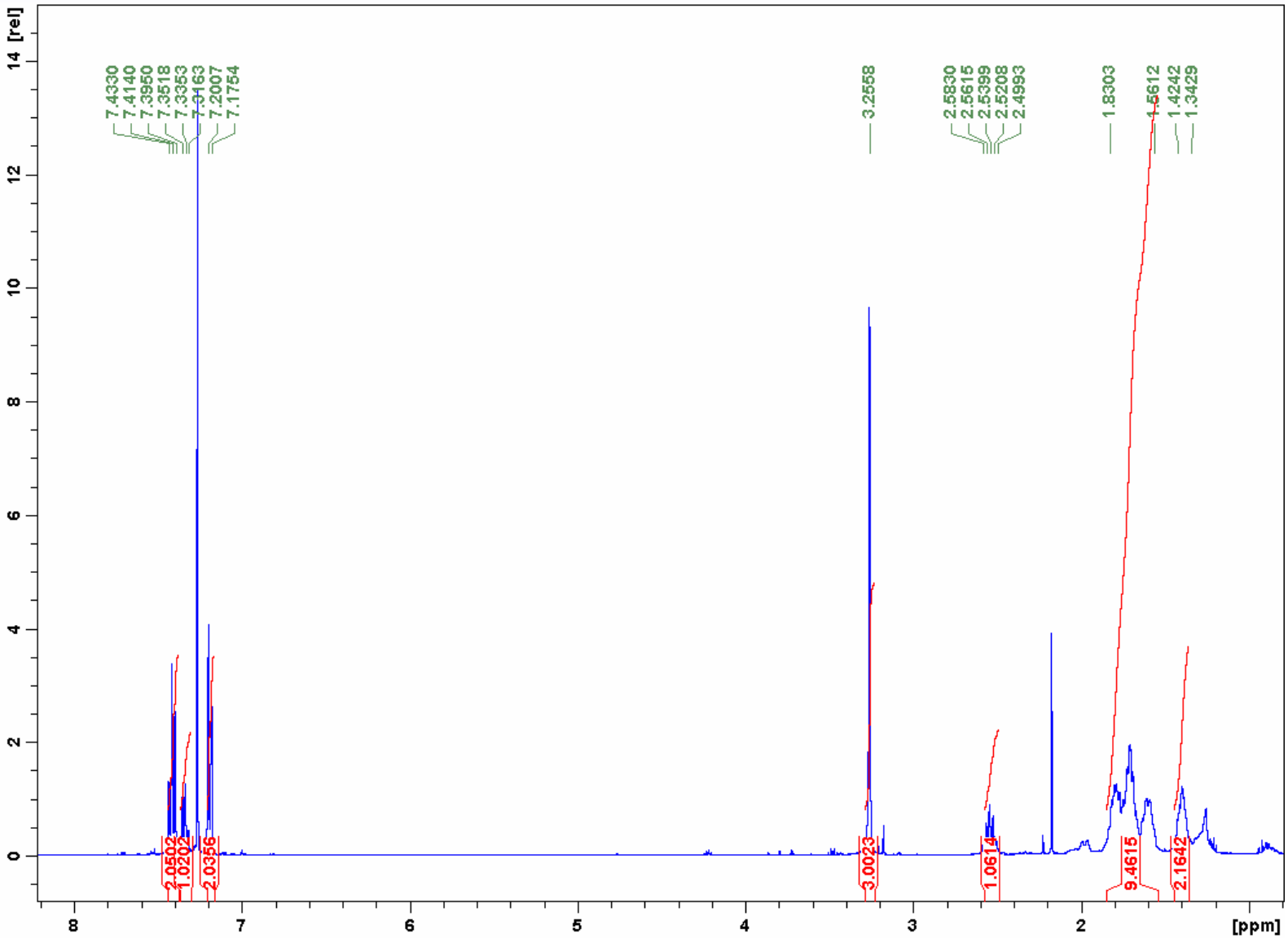
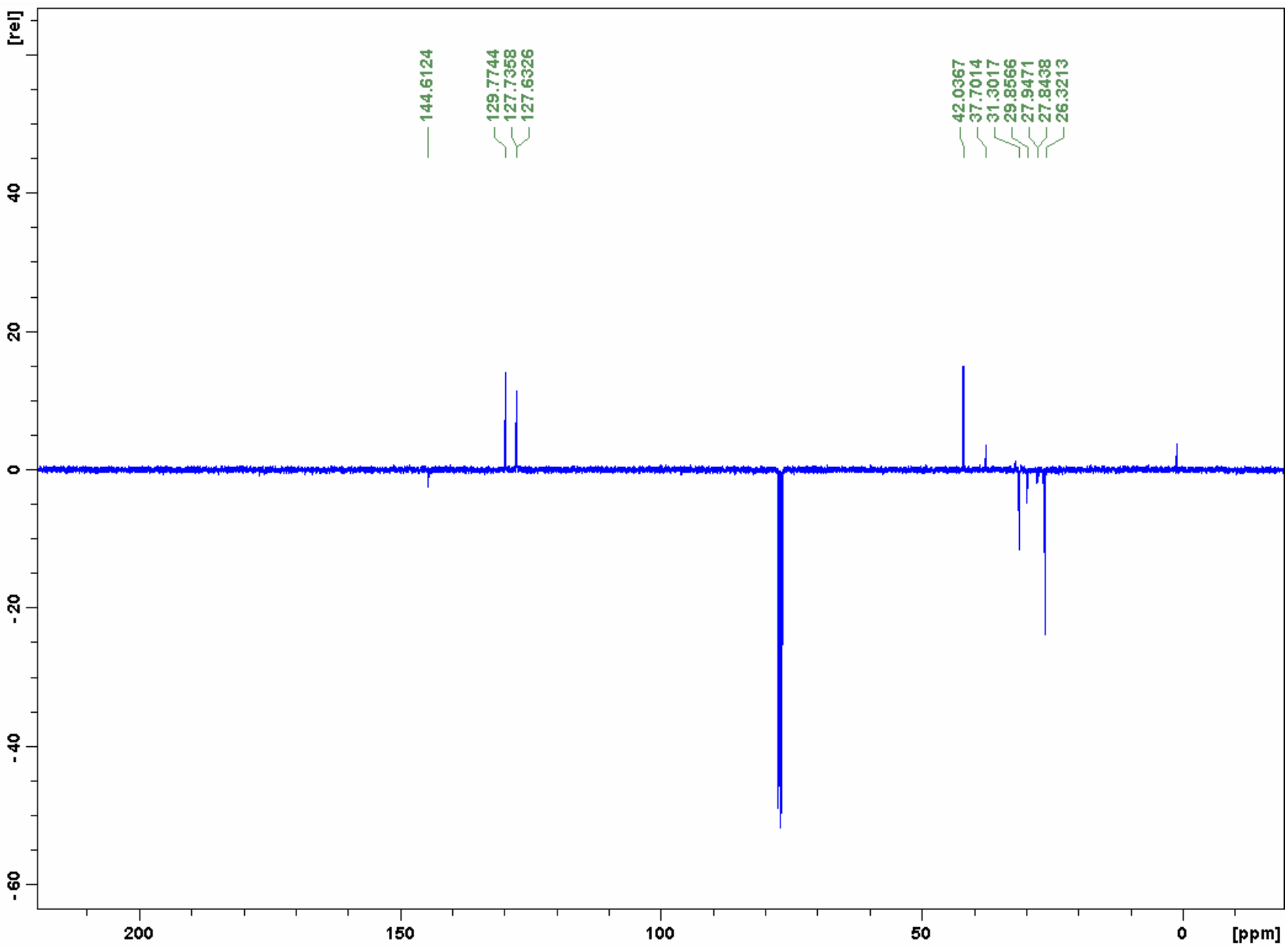
160.3920
143.3937
130.2023
120.9063
114.5615
113.4106
77.4662
65.8684
55.5396
42.4072
31.4292
26.4713
18.2673
-1.2982
200
150
100
50
0
[ppm]

Dehalogenated side product 11c

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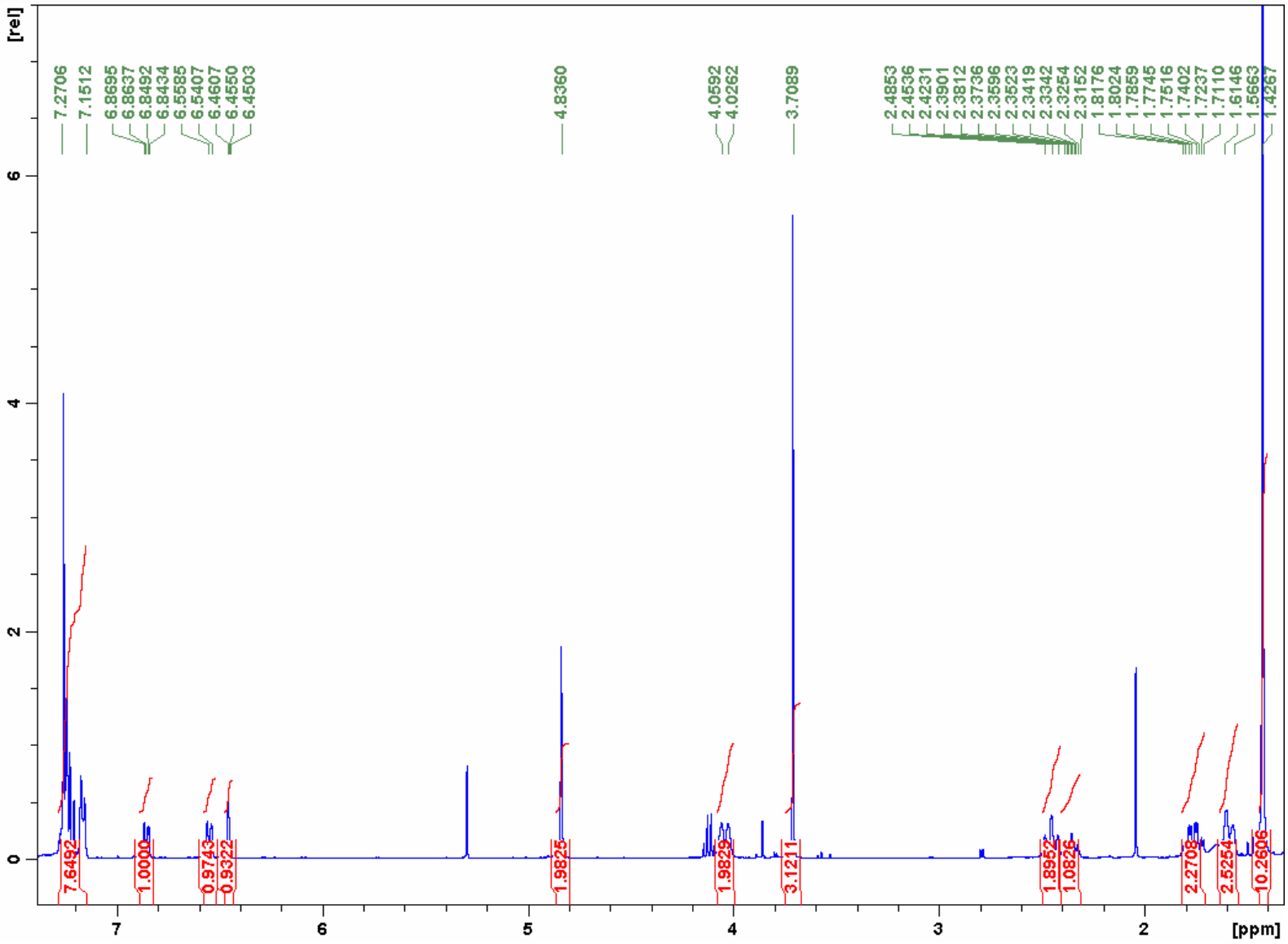
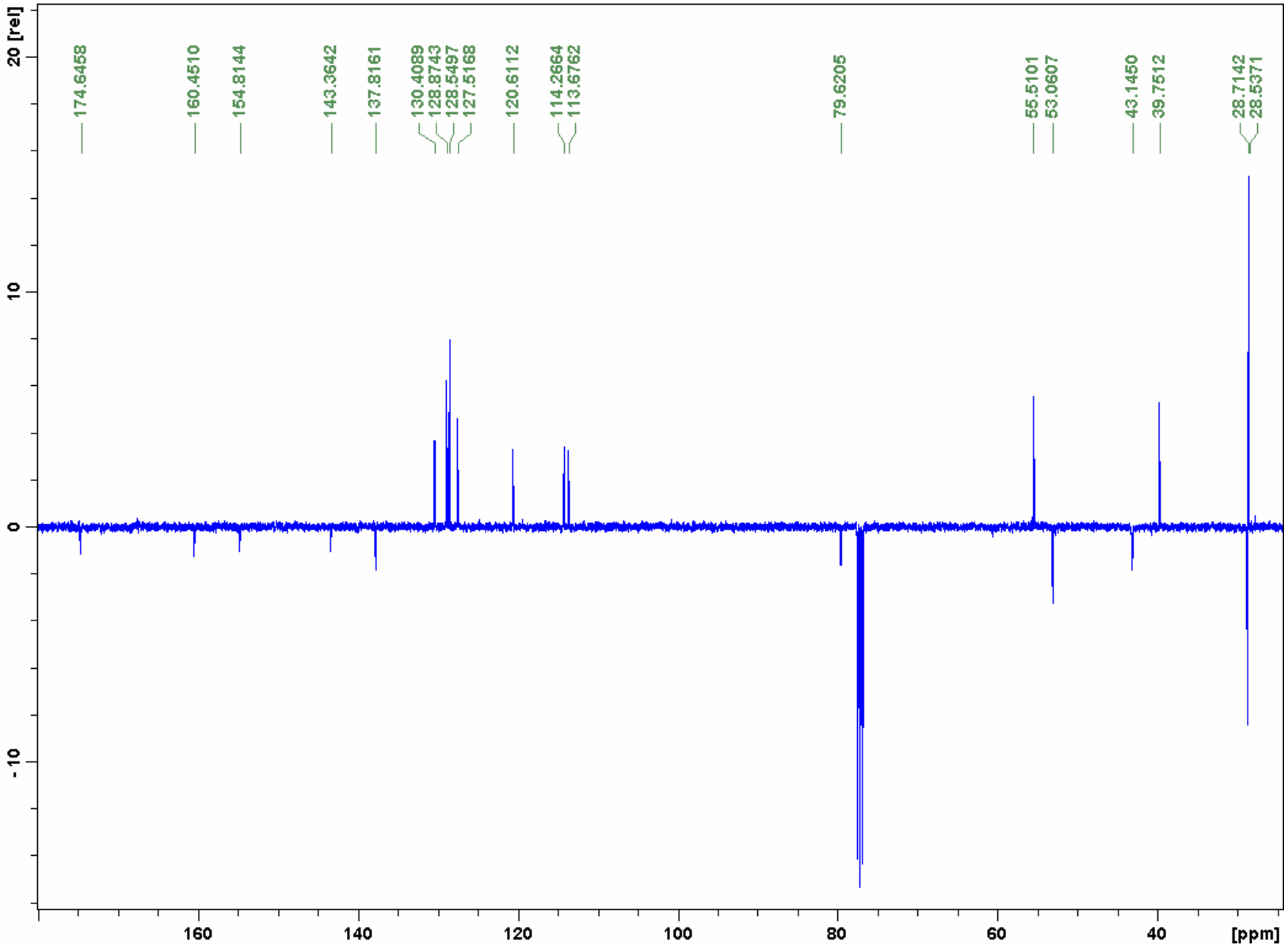
40
20
0
-20
-40
-60
144.6124
129.7744
127.7358
127.6326
42.0367
37.7014
31.3017
29.8566
27.9471
27.8438
26.3213
200
150
100
50
0
[ppm]

Dehalogenated side product 11e

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160.4510
154.8144
143.3642
137.8161
130.4089
128.8743
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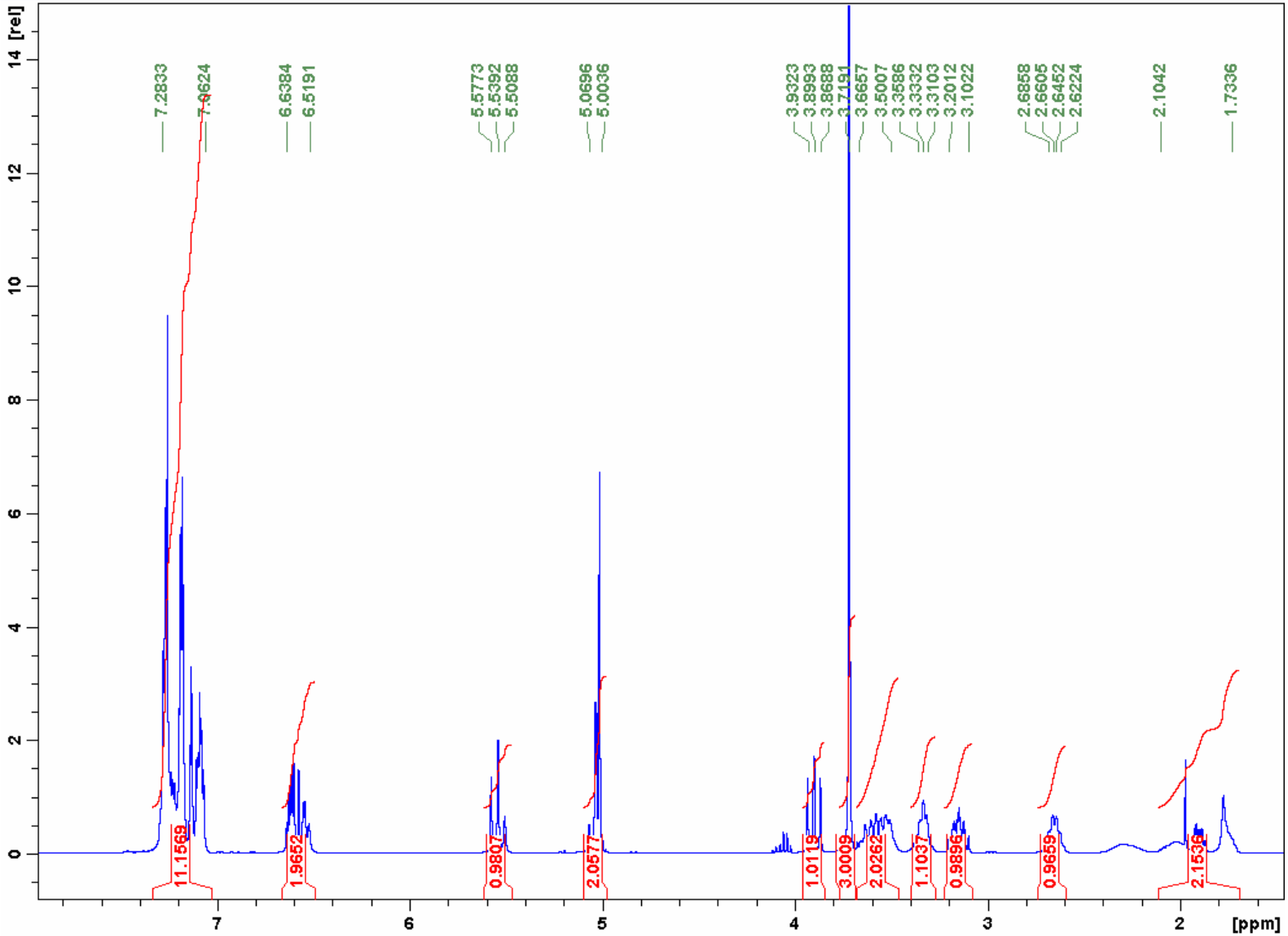
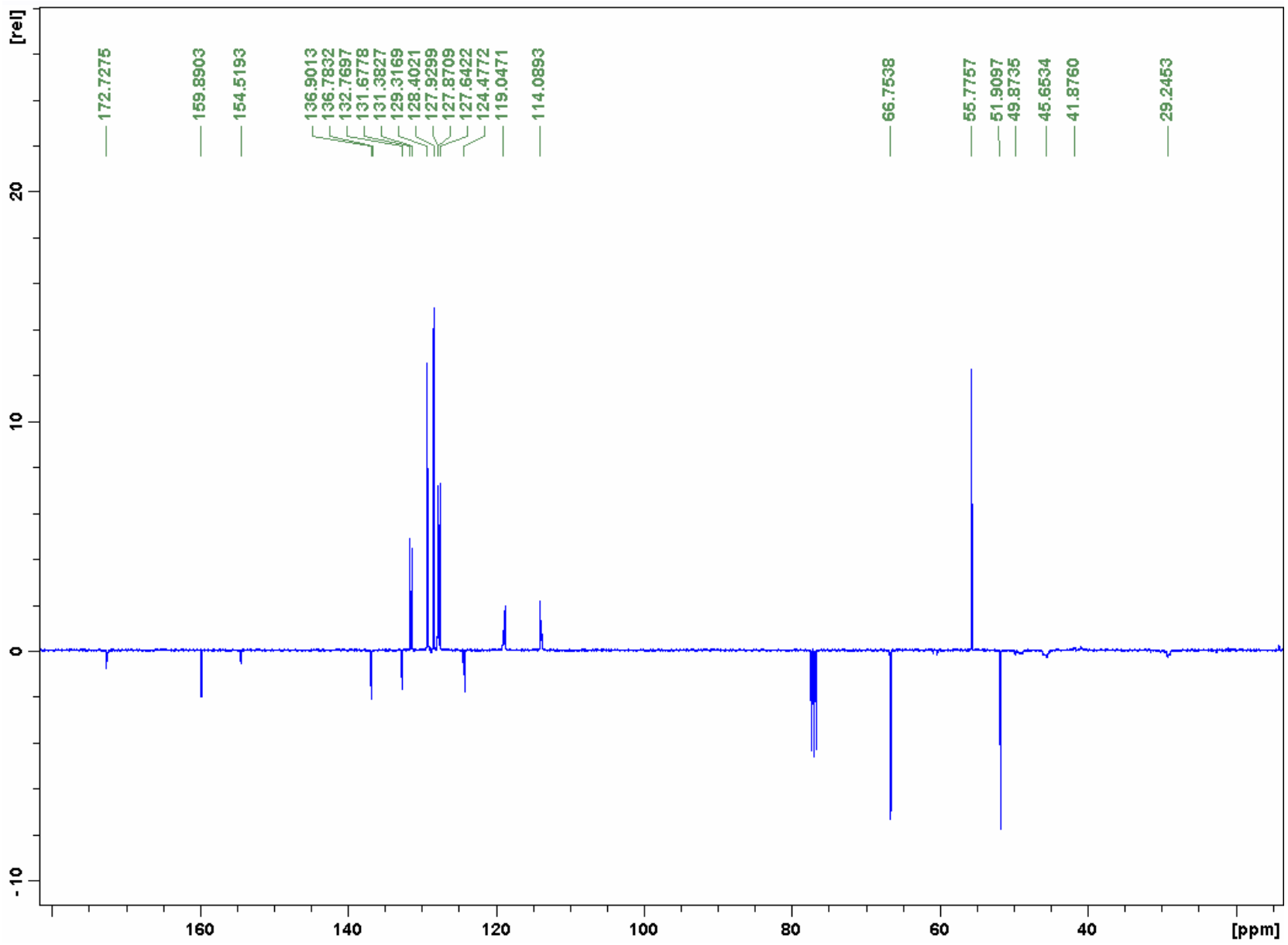
127.5168
120.6112
114.2664
113.6762
79.6205
55.5101
53.0607
43.1450
39.7512
28.7142
28.5371
20 [rel]
10
0
-10
160
140
120
100
80
60
40
[ppm]

***N*-Benzyl-*o*-bromoanilide 13 (mixture of diastereomers, rotamers, line broadening)**

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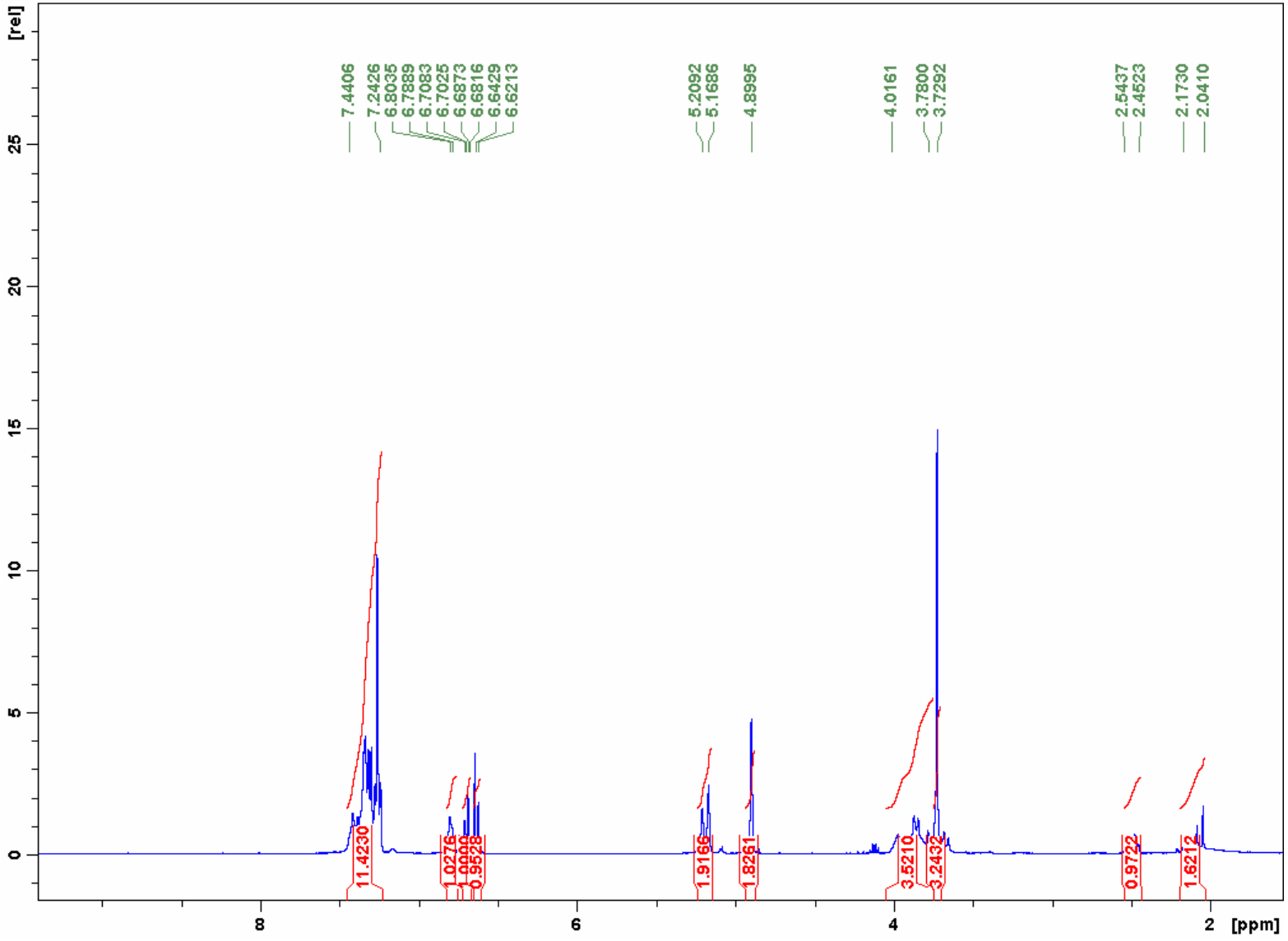
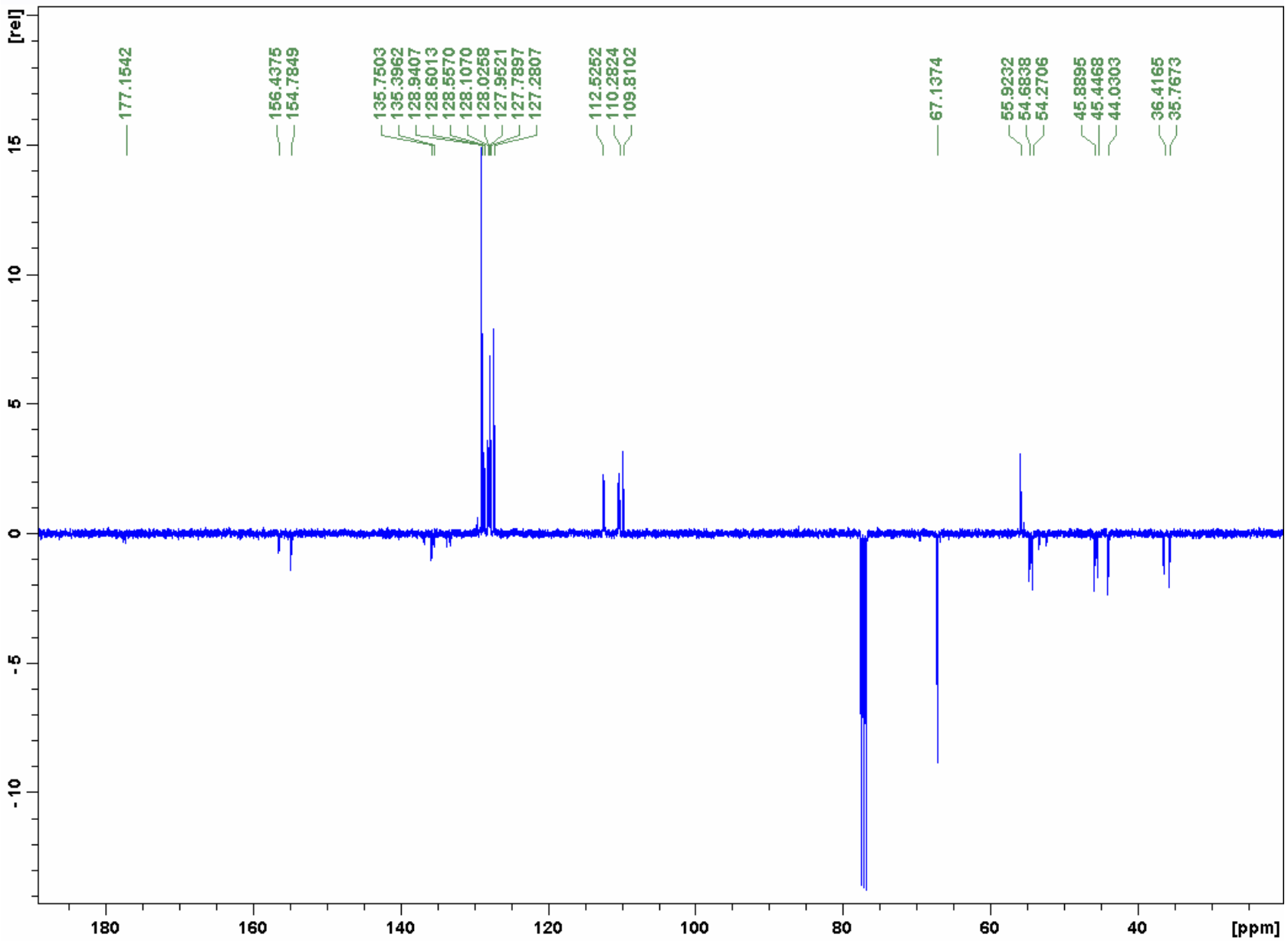
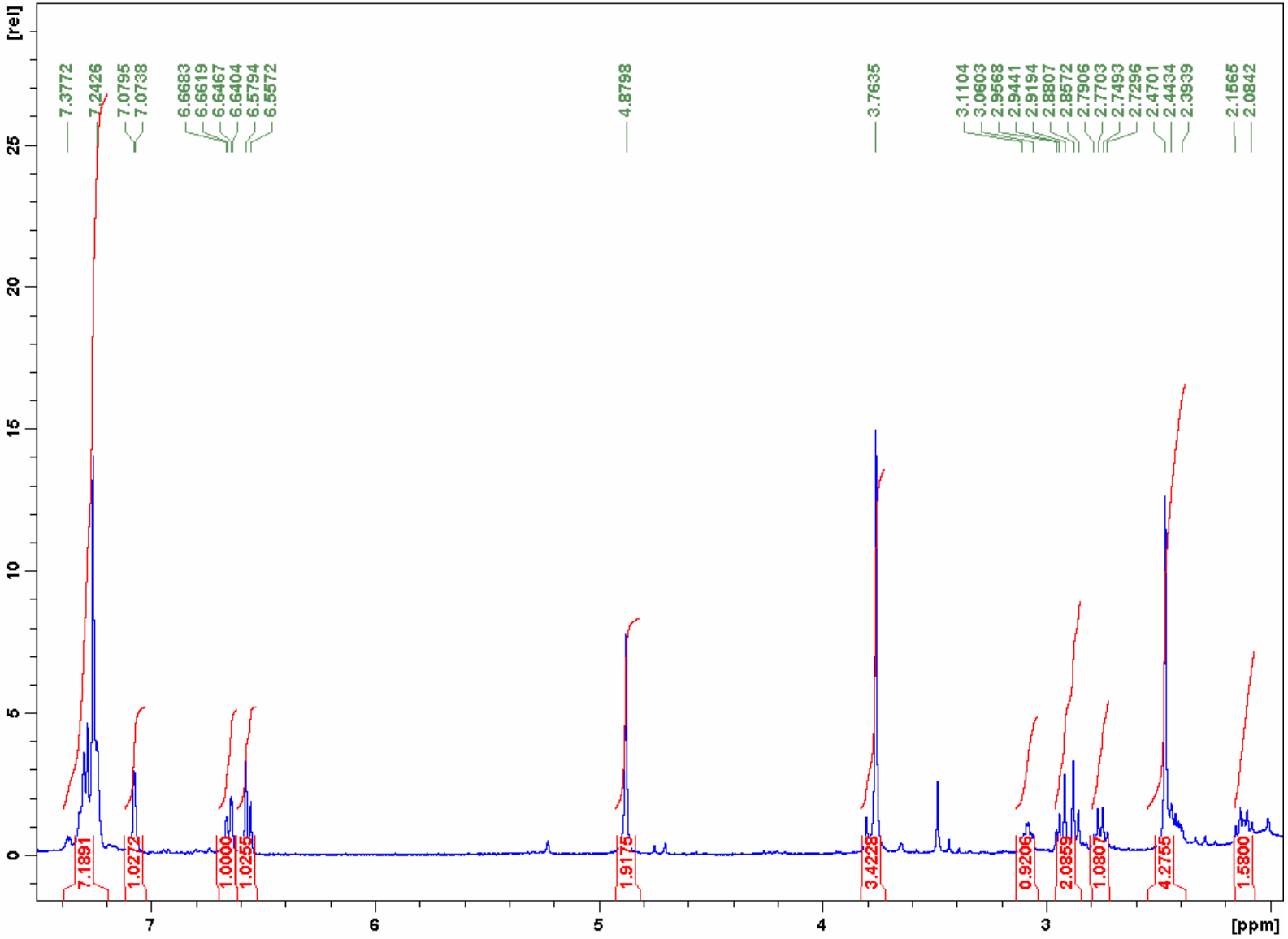
136.7832
132.7697
131.6778
131.3827
129.3169
128.4021
127.9299
127.8709
127.6422
124.4772
119.0471
114.0893
66.7538
55.7757
51.9097
49.8735
45.6534
41.8760
29.2453
160
140
120
100
80
60
40
[ppm]

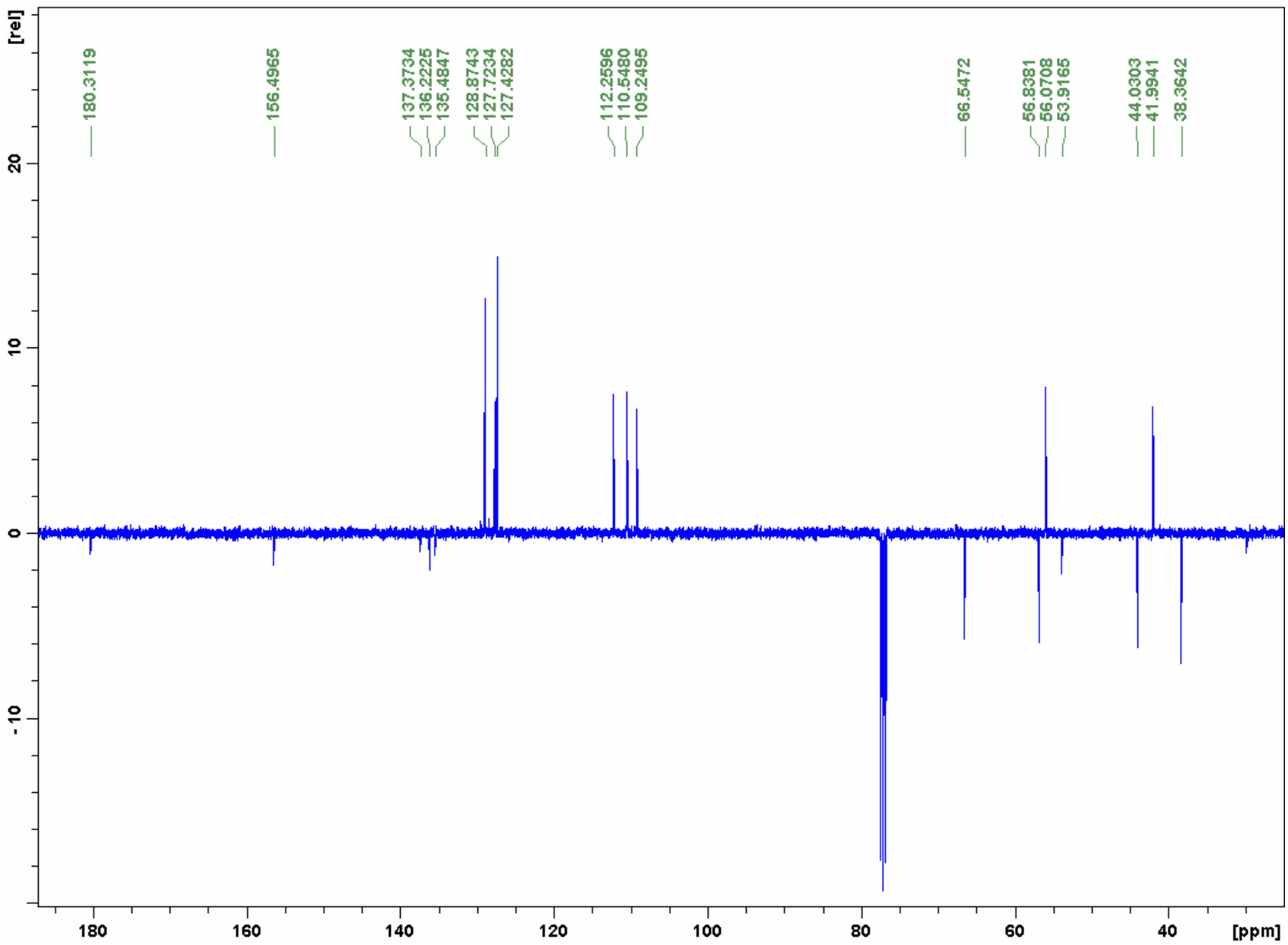
Spirooxindole 14 (mixture of rotamers)




[rel]
15
10
5
0
-5
-10
177.1542
156.4375
154.7849
135.7503
135.3962
128.9407
128.6013
128.5570
128.1070
128.0258
127.9521
127.7897
127.2807
112.5252
110.2824
109.8102
67.1374
55.9232
54.6838
54.2706
45.8895
45.4468
44.0303
36.4165
35.7673
180
160
140
120
100
80
60
40
[ppm]

***N*-Bn-Horsfiline 15**




[rel]
20
10
0
- 10
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135.4847
128.8743
127.7234
127.4282
112.2596
110.5480
109.2495
66.5472
56.8381
56.0708
53.9165
44.0303
41.9941
38.3642
180
160
140
120
100
80
60
40
[ppm]

1. References

(1) Uchiyama, M.; Kobayashi, F.; Nakamura, S.; Kajihara, Y.; Miyoshi, T.; Sakamoto, T.; Kondo, Y.; Morokuma, K. *J. Am. Chem. Soc.* **2007,** *130*, 472.
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