Electronic Supplementary Material (ESI) for RSC Advances.

α-Chymotrypsin and L-acylase aided synthesis of 5-hydroxy pipecolic acid via Jacobsen's hydrolytic kinetic resolution of epoxy amino acids.

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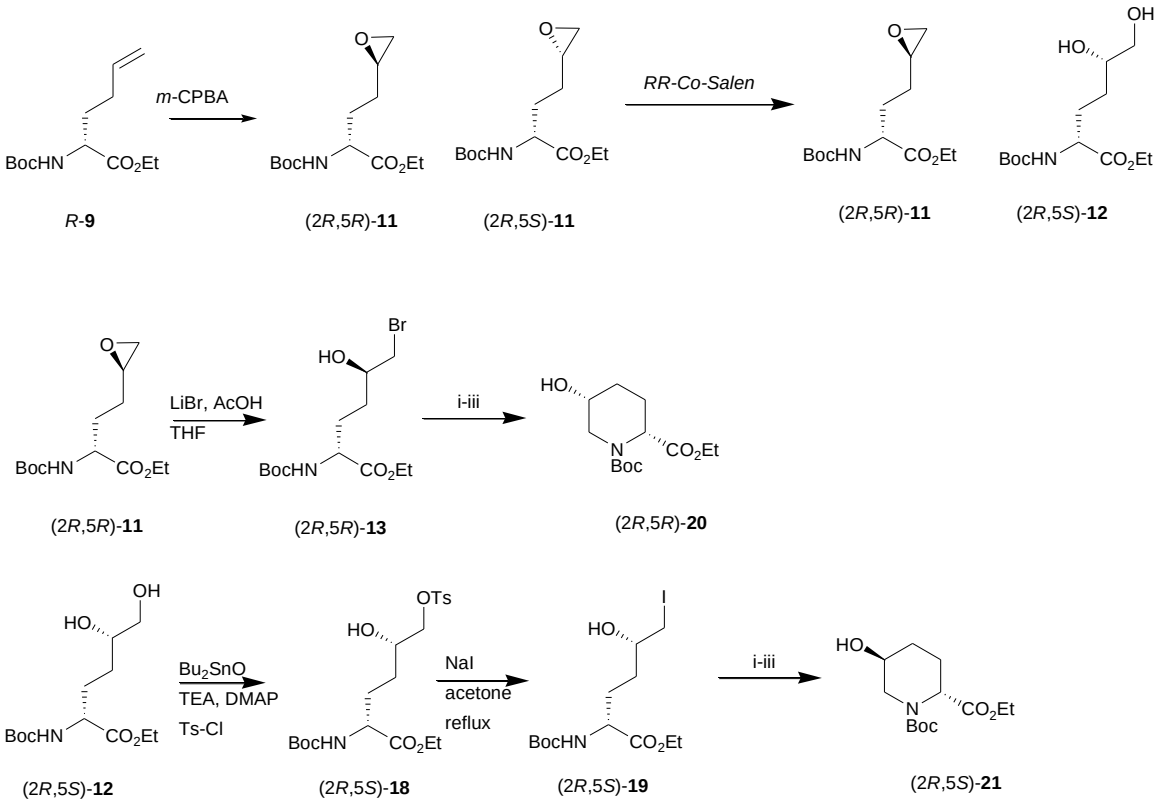


Scheme-7. Synthesis of (2*R*,5*R*) and (2*R*,5*S*)-5-hydroxypipecolic acid. i)TFA, ii) DIEA, THF, iii)Boc_2O

***m*-CPBA oxidation of (*R*)-9.**[1]

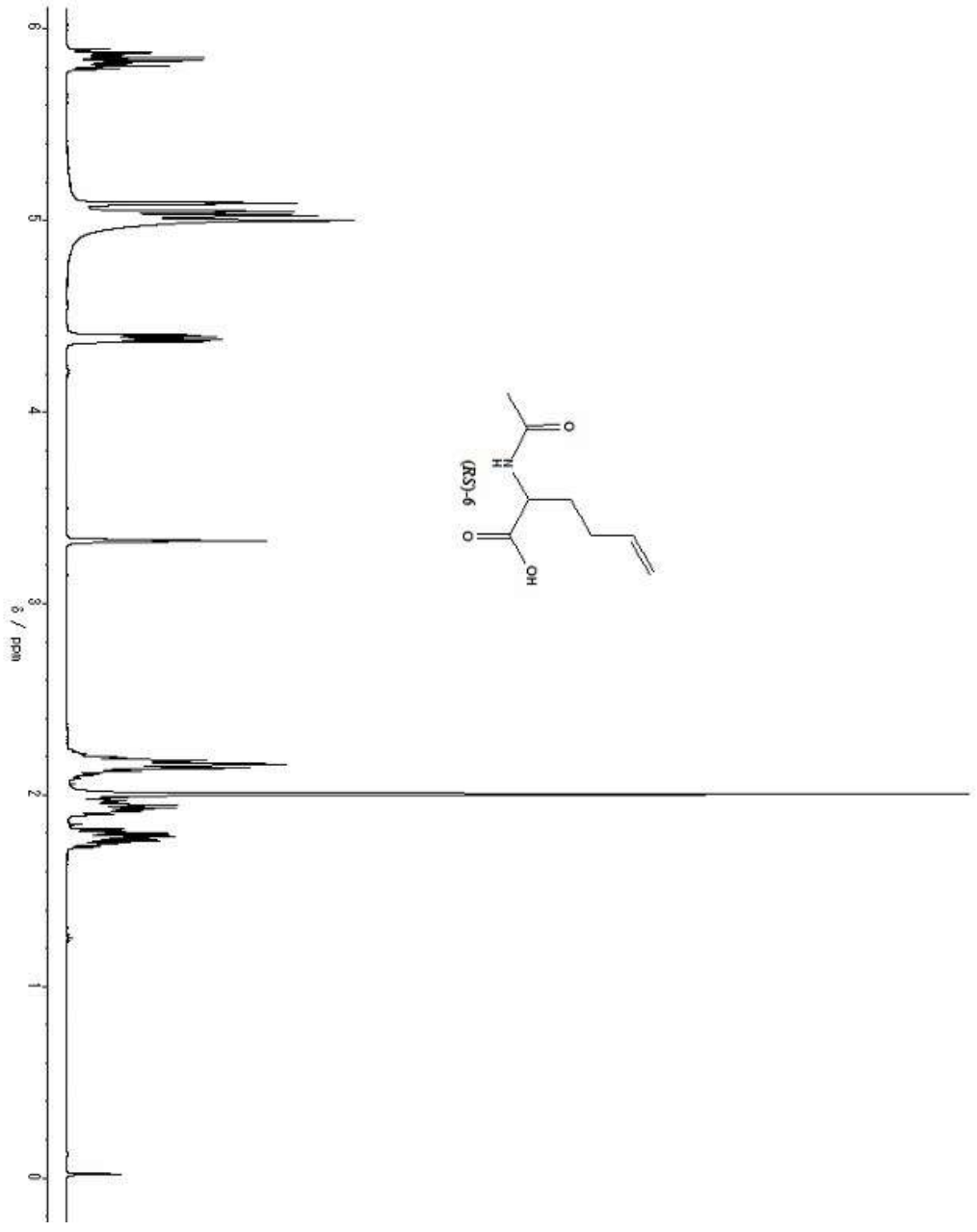
(*R*)-**9** (1.50 g, 5.84 mmol) was dissolved in DCM 30.0 mL and cooled to 0 °C. To this solution *m*-CPBA (2.00 g, 8.75 mmol) was added in one portion, and stirred, the ice-water bath was removed once the *m*-CPBA completely dissolved and allowed to stir at room temperature. After 24 h work up and purification similar to [(2*S*)-**12**], gave diastereomers of (2*R*)-**12** (1.45 g, 91 %) as an oil. (spectral data similar to (2*S*)-isomer).

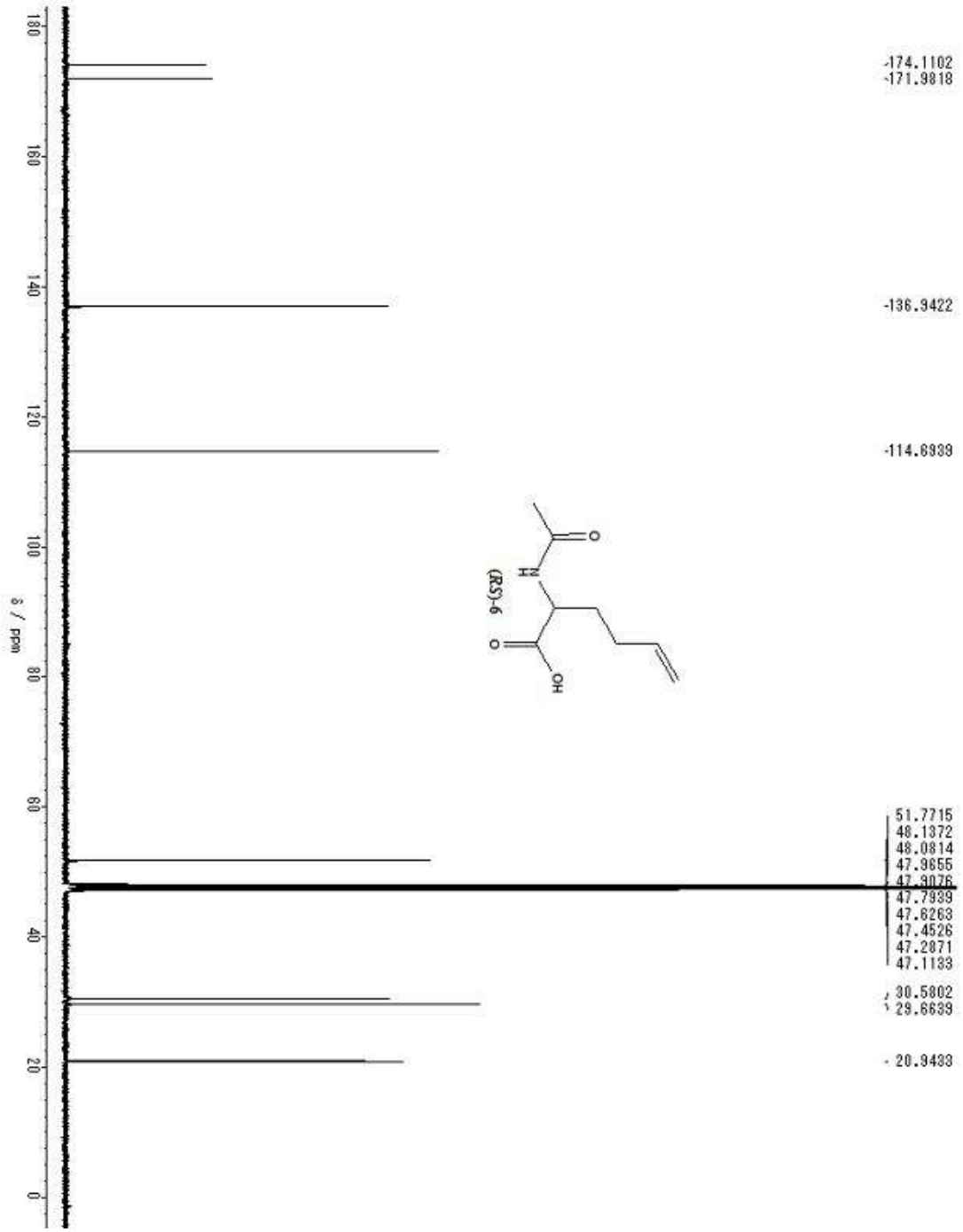
Jacobsen's Hydrolytic Kinetic Resolution (HKR).

(2*R*)-**12** (0.41 g, 1.50 mmol) was taken in a vial equipped with a stir bar, to this was added (*RR*)-Co-Salen (0.5 mol %, 5 mg), followed by acetic acid (12 µL) and THF (0.10 mL). Finally H_2O (0.83 mmol, 15 µL) was added in one portion at room temperature and stirred. After 48 h, work up and purification similar to [(2*S*) isomer] gave (2*R*,5*R*)-**12** (0.190 g, 46 %) and (2*R*,5*S*)-**13** (0.194 g, 44 %). (spectral data of both the compounds were similar to their (2*S*)-isomers).

Synthesis of (2*R*,5*R*)-20 and (2*R*,5*S*) 21. All the reaction were carried out in a exact manner similar to (2S)-isomers to get **(2*R*,5*R*)-20** and **(2*R*,5*S*)-21**, both as oil. (spectral data similar to their enatiomers)

[1] To improve the ee, (*R*)-**9** (2.42 g, 9.41 mmol) was again suspended in phosphate buffer (50 mL 0.1 M, pH 8.0) and treated with α-chymotrypsin (2 mg), after 24 h, usual work up gave (*R*)-9 in 95 % yield.


δ / ppm
(RS)-6


δ / ppm
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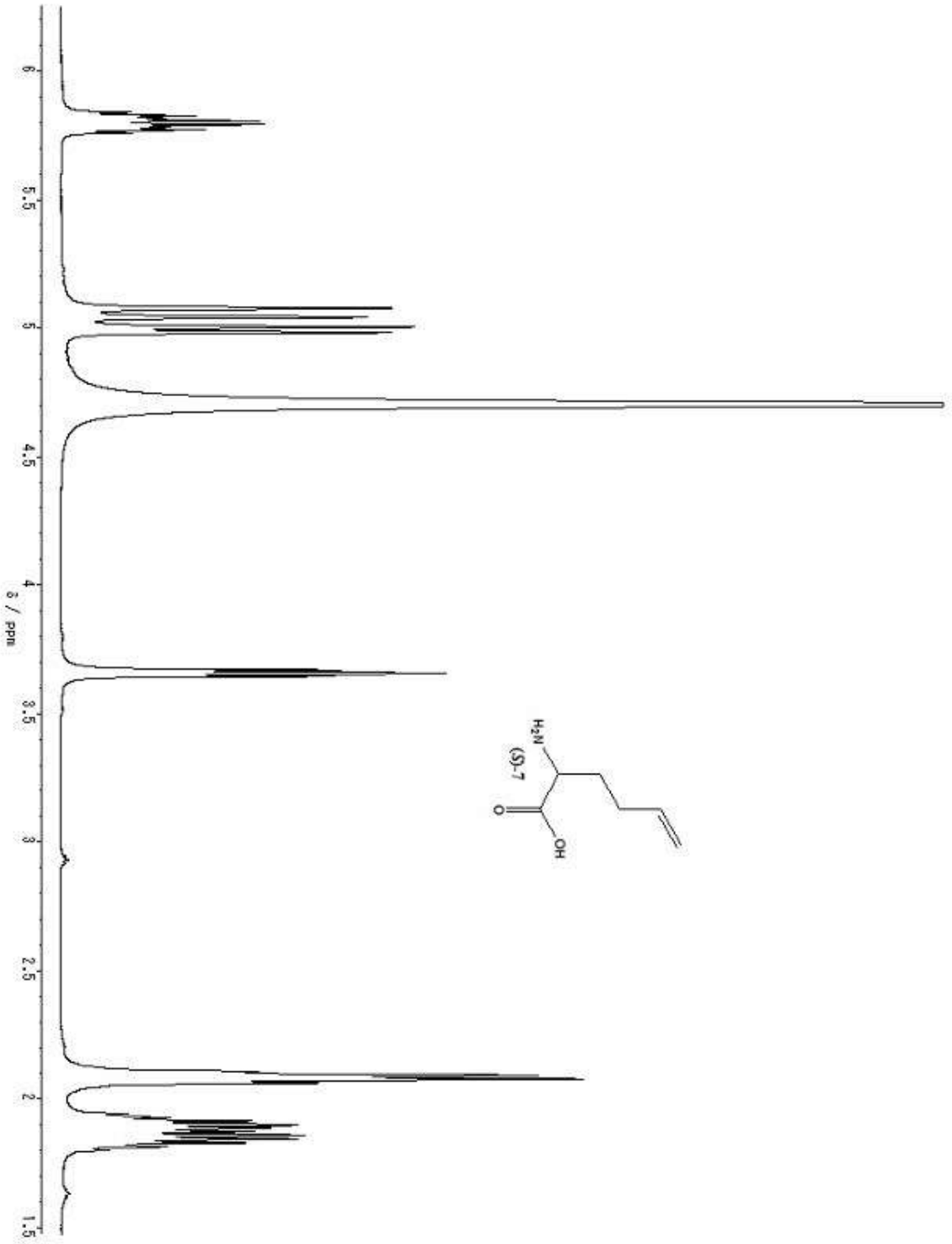
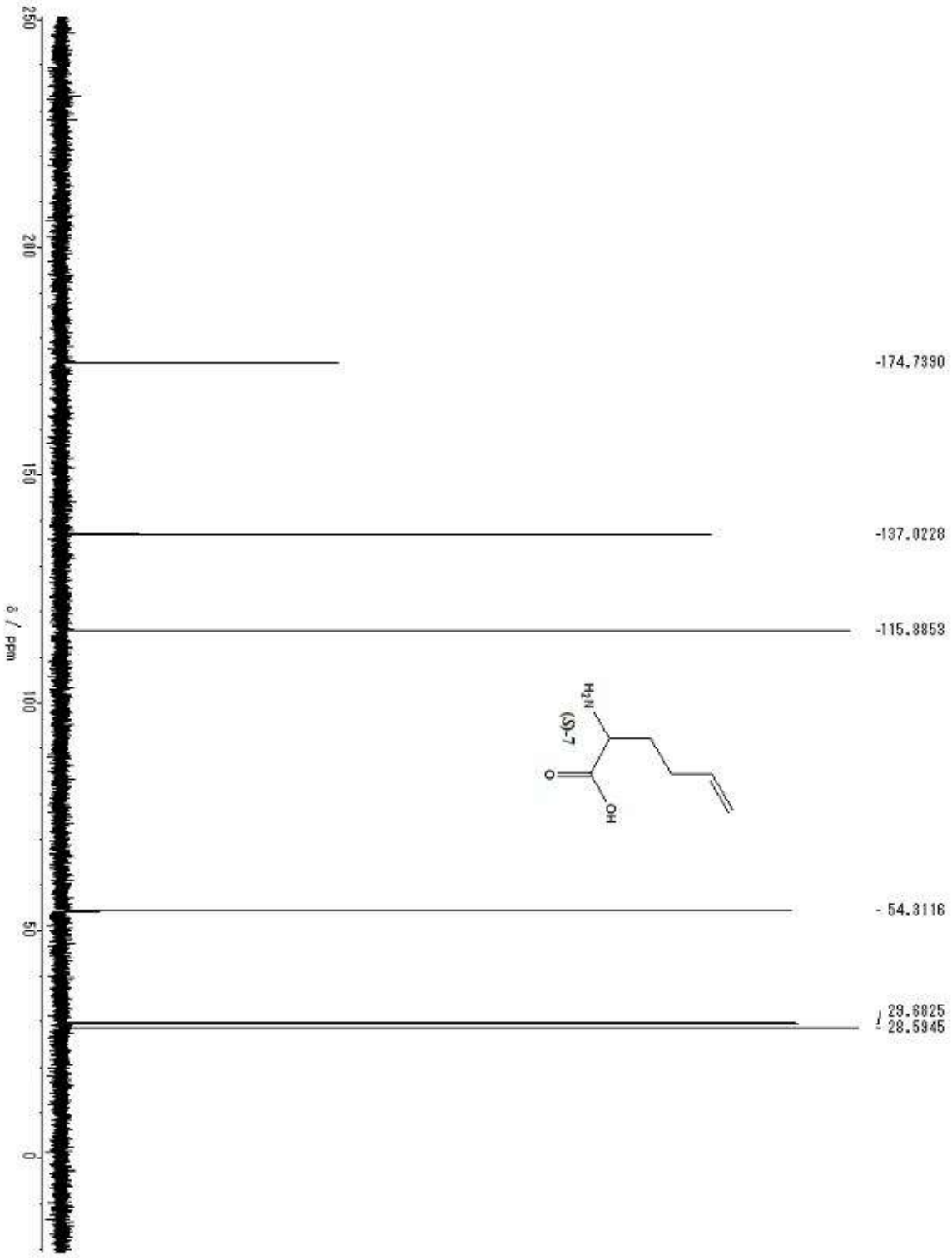
160
140
120
100
80
60
40
20
0
174.1102
171.9818
136.9422
114.6939
51.7715
48.1372
48.0814
47.9655
47.8076
47.7939
47.6263
47.4526
47.2871
47.1133
30.5802
29.6639
20.9433
(RS)-6
H
N
O
O
OH


6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
δ / ppm
H2N
(S)-7
O
OH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200
150
100
50
0
δ / ppm
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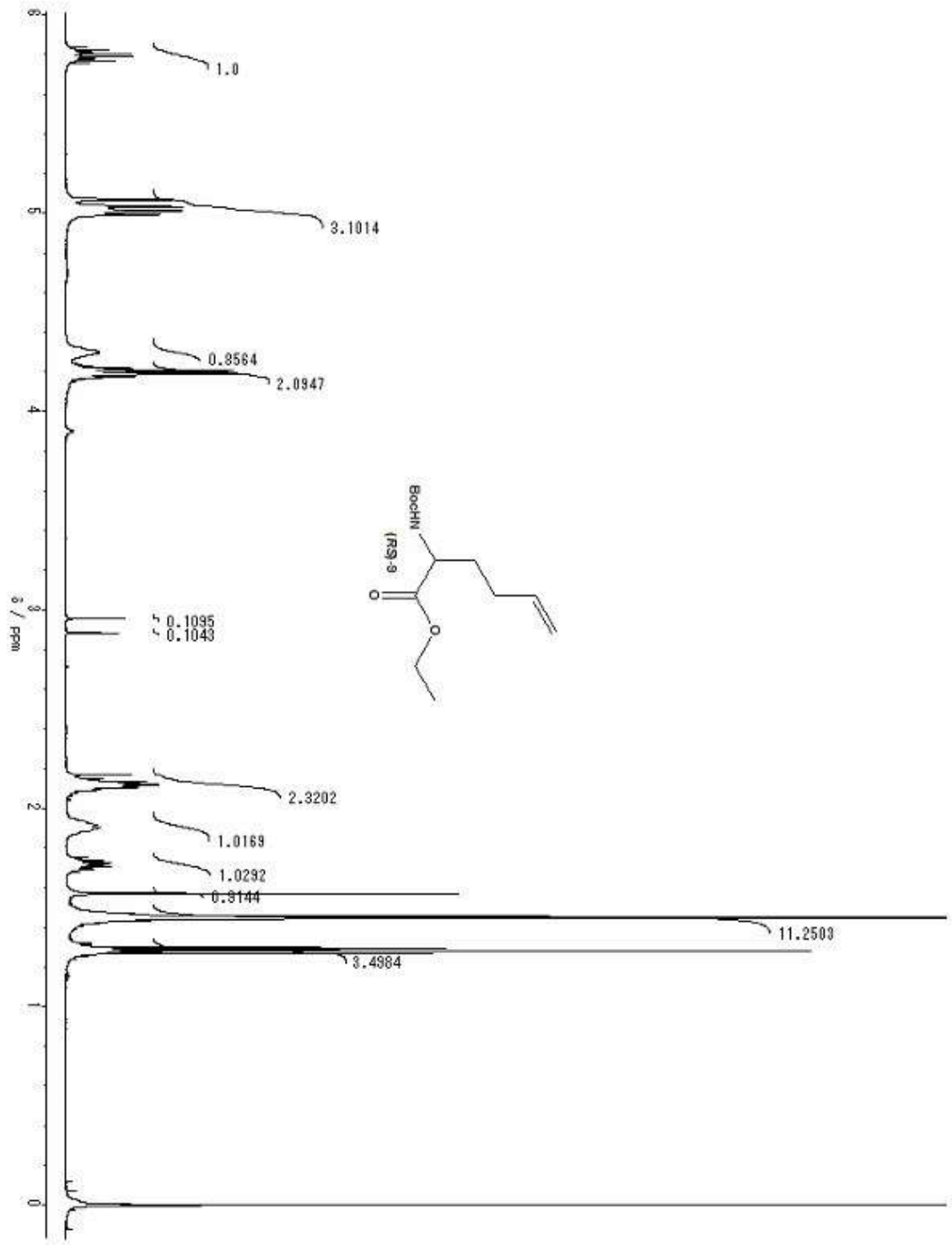
-115.8853
- 54.3116
29.6825
28.5945
(S)-7
H2N
O
OH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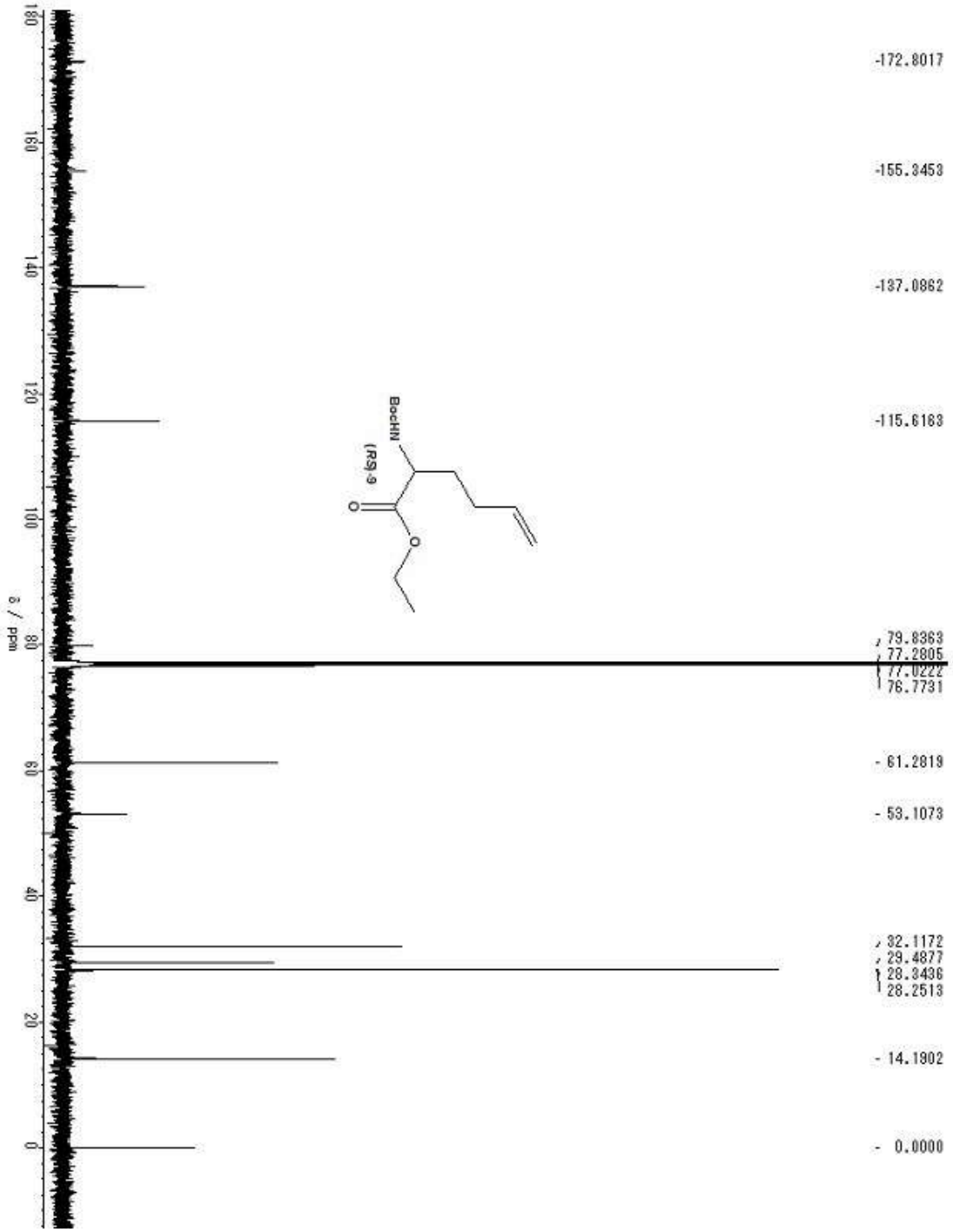
0.8564
2.0947
0.1095
0.1043
2.3202
1.0169
1.0292
0.8144
11.2503
3.4984
BocHN
(RS)-9
O
O
f1 / ppm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-115.6163
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76.7731
- 61.2819
- 53.1073
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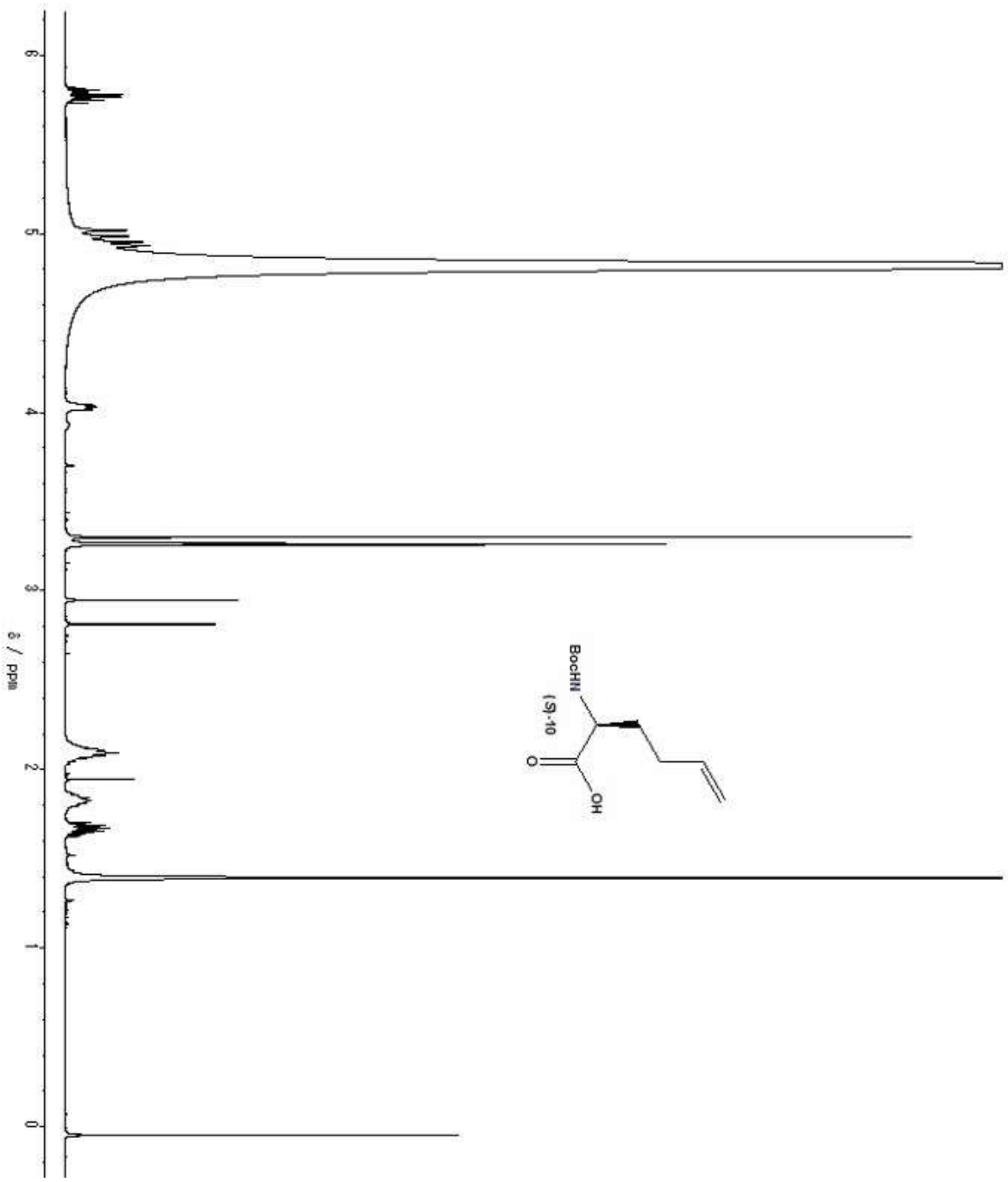
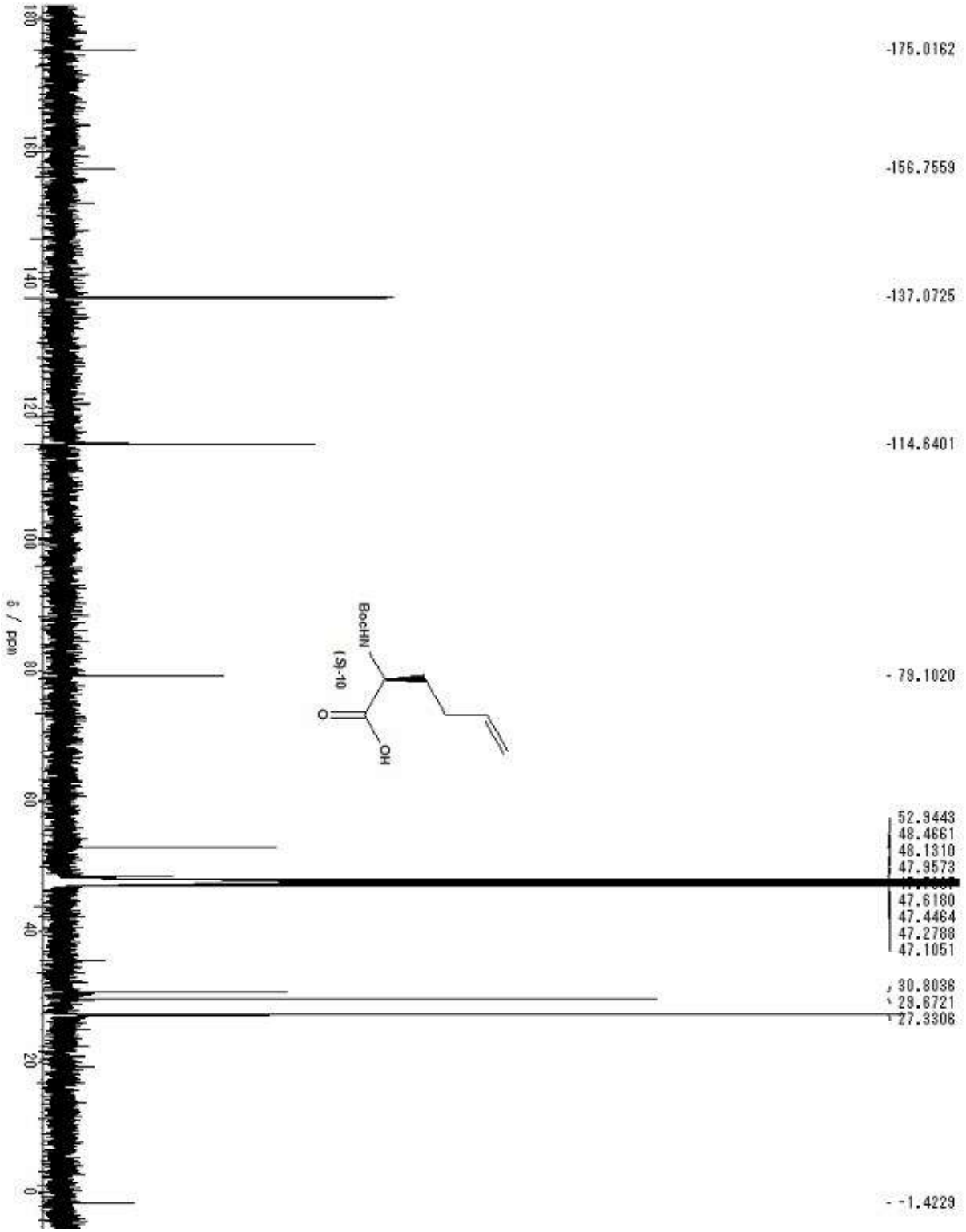
29.4877
28.3436
28.2513
- 14.1902
- 0.0000
δ / ppm
BocHN
(RS)-9


δ / ppm
BocHN
(S)-10
O
OH


δ / ppm
BocHN
(S)-10
O
OH
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156.7559
137.0725
114.6401
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52.9443
48.4661
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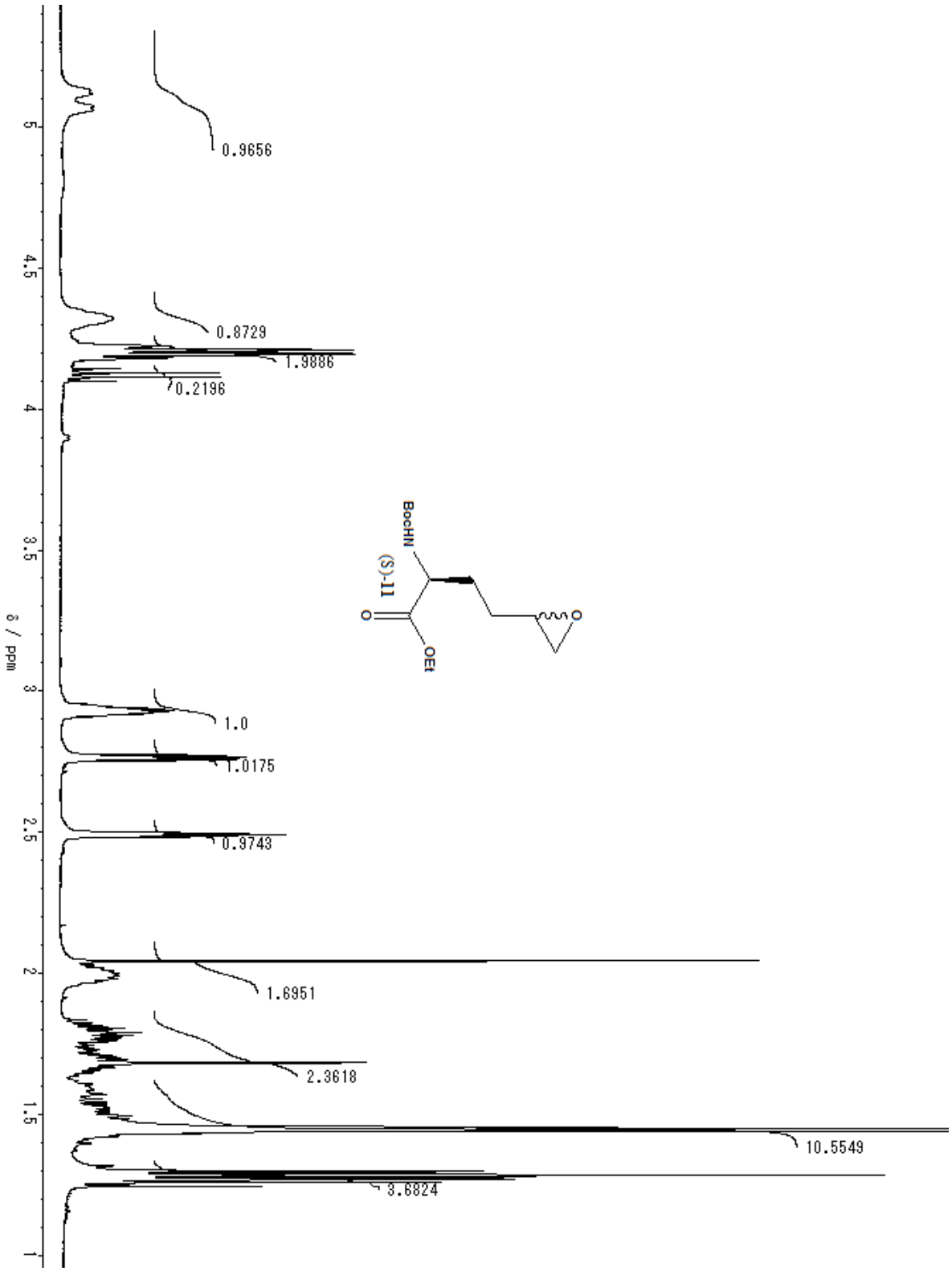
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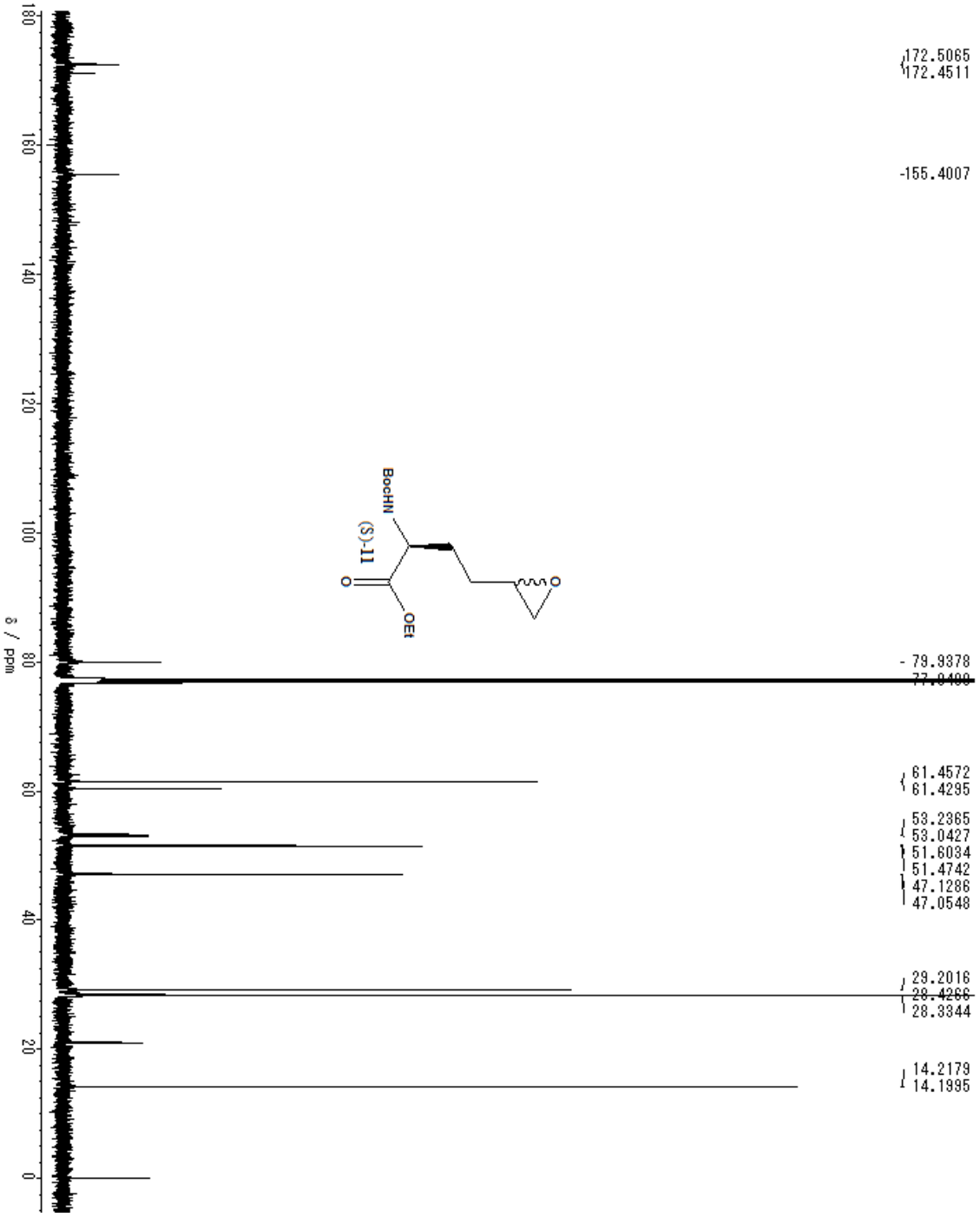
BocHN
(S)-11
O
OEt
O
δ / ppm


BocHN
(S)-11
O
OEt
O
δ / PPm
180
160
140
120
100
80
60
40
20
0
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172.4511
155.4007
79.9378
77.0488
61.4572
61.4295
53.2365
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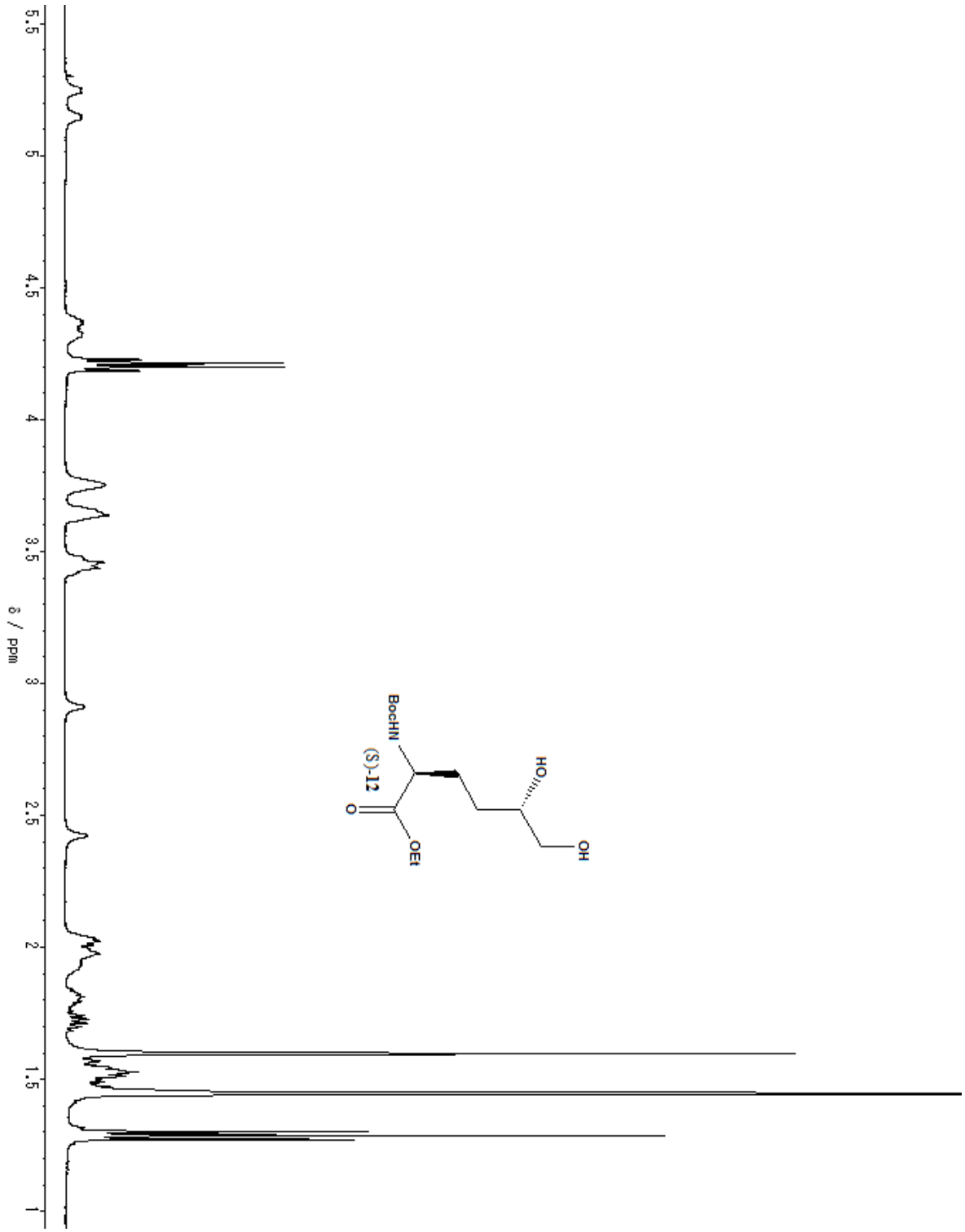
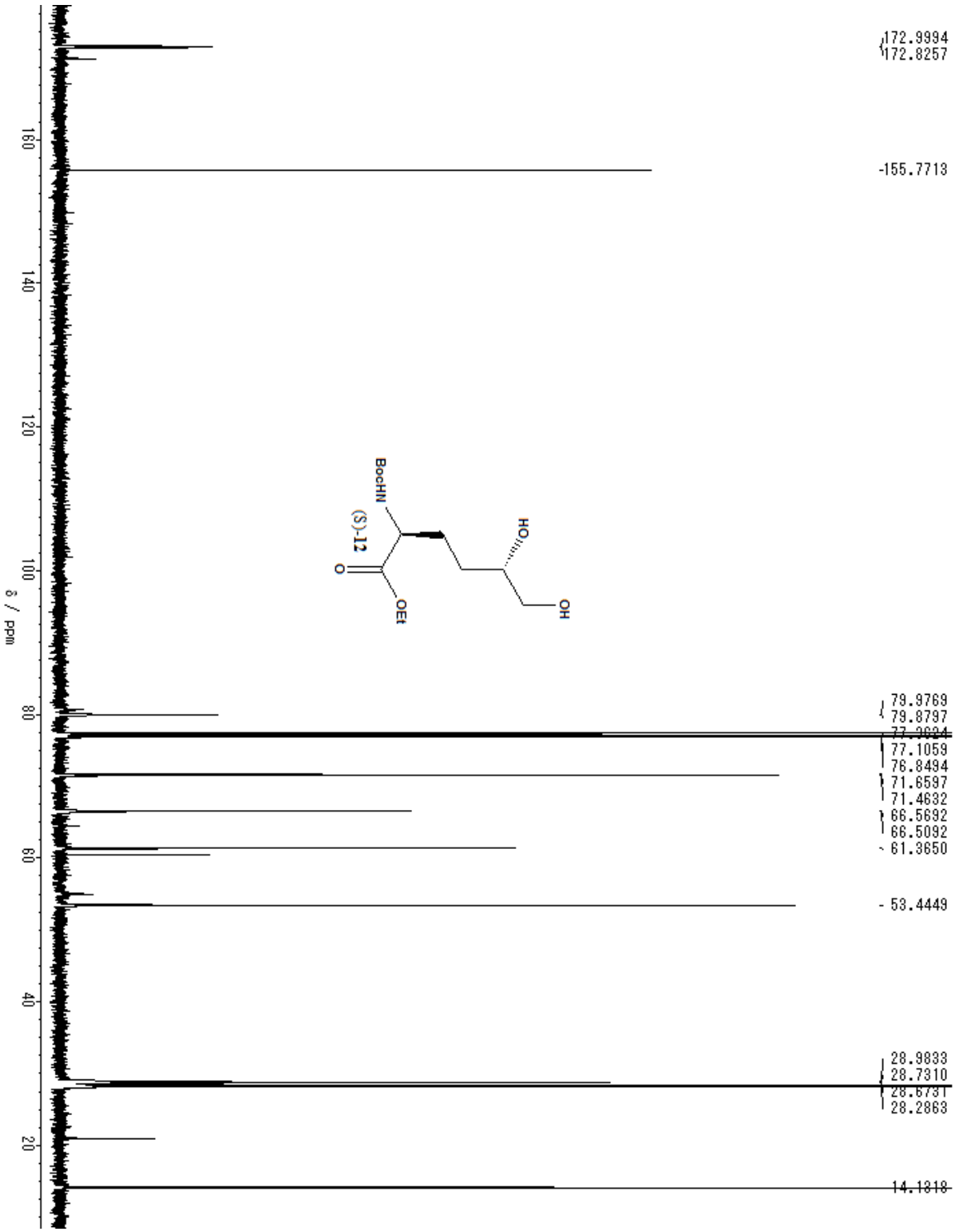
14.2179
14.1995


5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
δ / ppm
BocHN
(S)-12
O
OEt
HO
OH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71.4632
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61.3650
53.4449
28.9833
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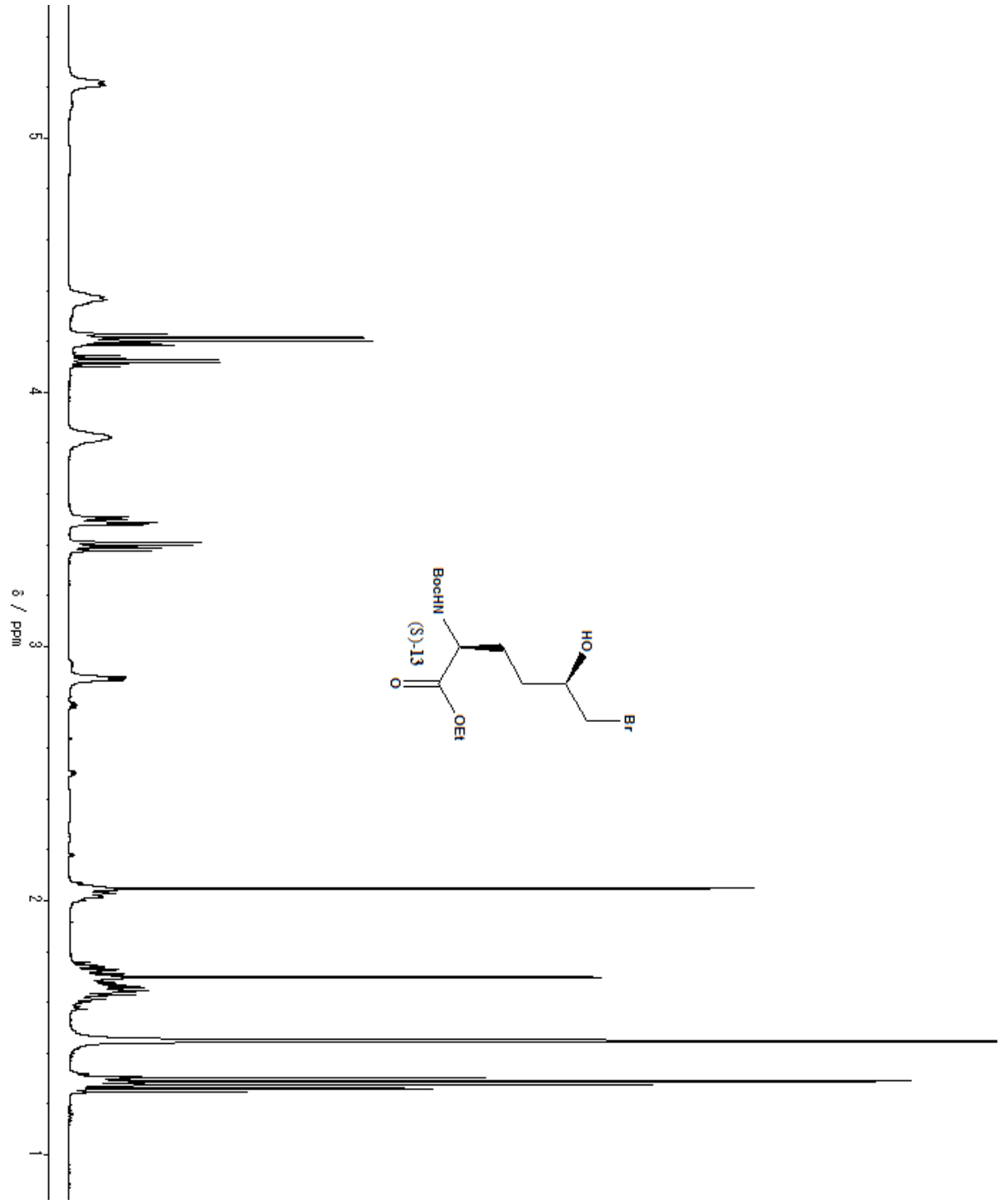
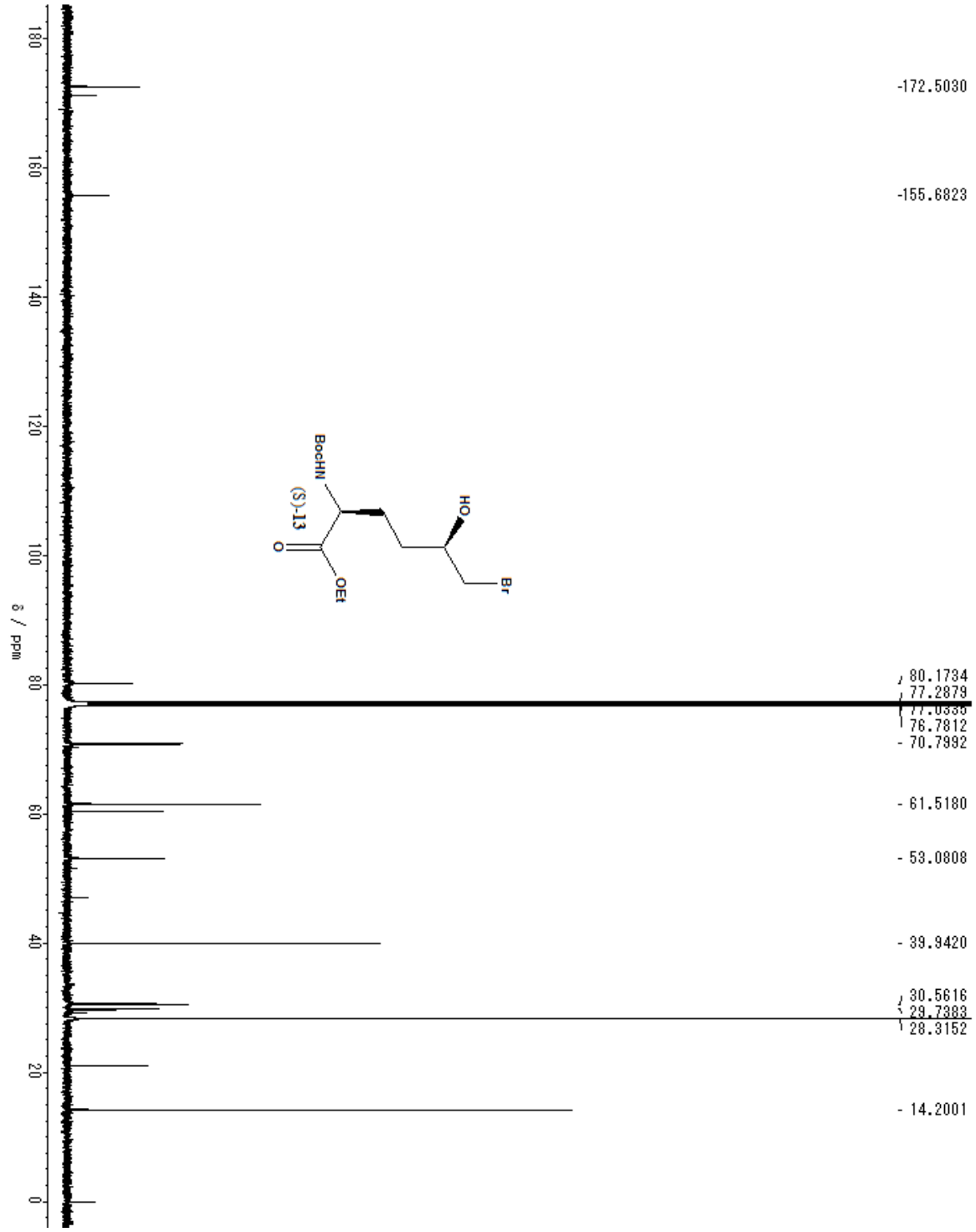
28.6731
28.2863
14.1318
δ / ppm
(S)-12
BocHN
HO
OEt
OH
O


BocHN
(S)-13
O
OEt
HO
Br
δ / ppm
1
2
3
4
5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(S)-13
O
OEt
HO
Br
δ / ppm
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160
140
120
100
80
60
40
20
0
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155.6823
80.1734
77.2879
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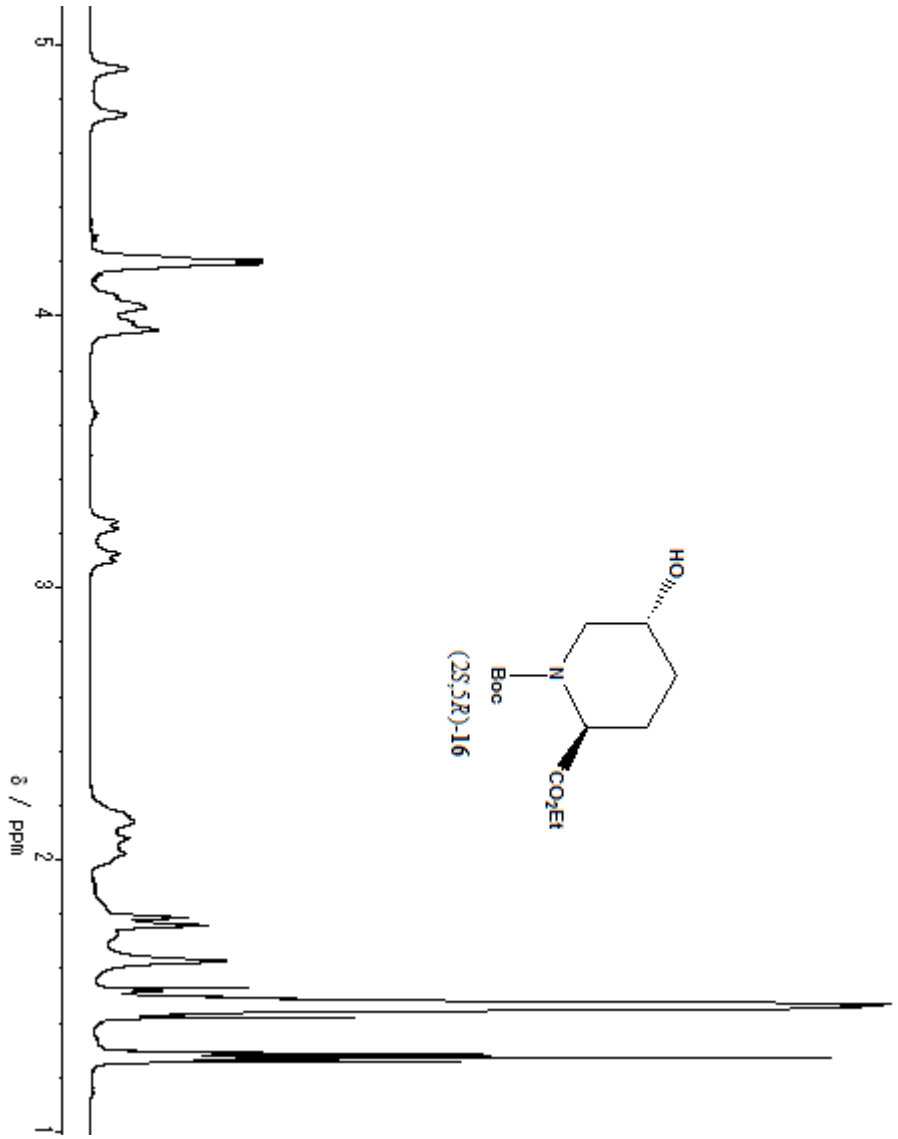
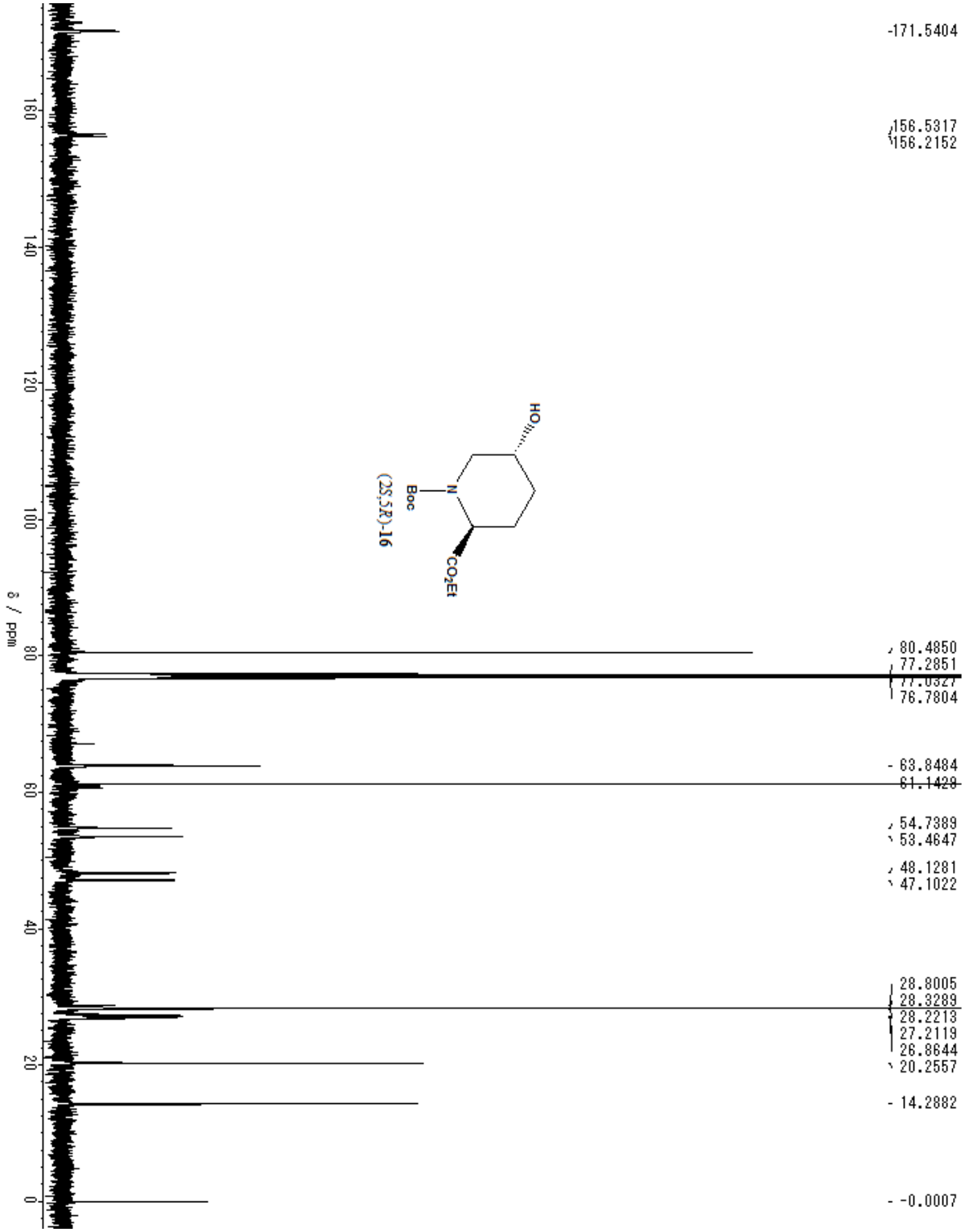
28.3152
14.2001



(2*S*,5*R*)-**16**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76.7804
63.8484
61.1428
54.7389
53.4647
48.1281
47.1022
28.8005
28.3289
28.2213
27.2119
26.8644
20.2557
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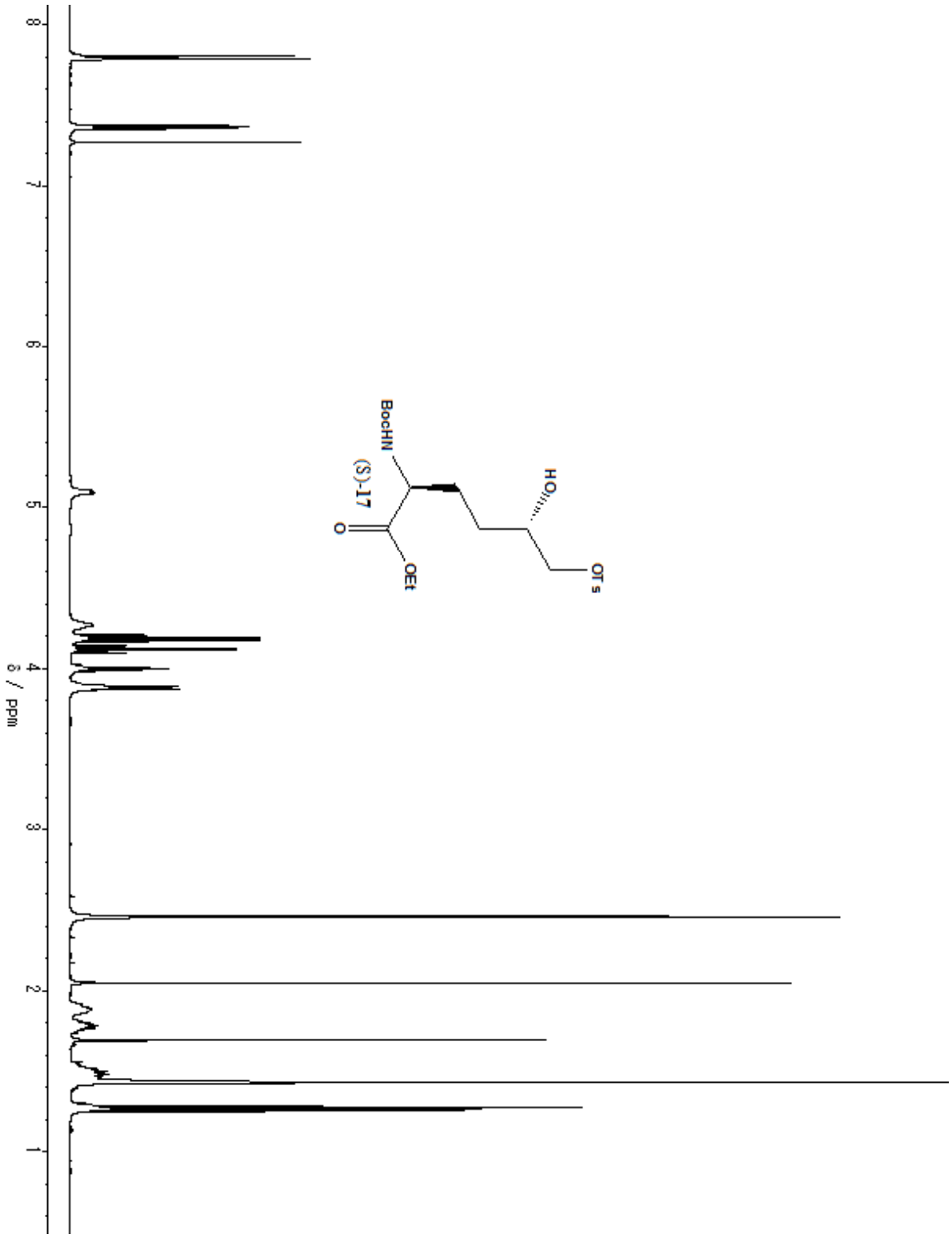
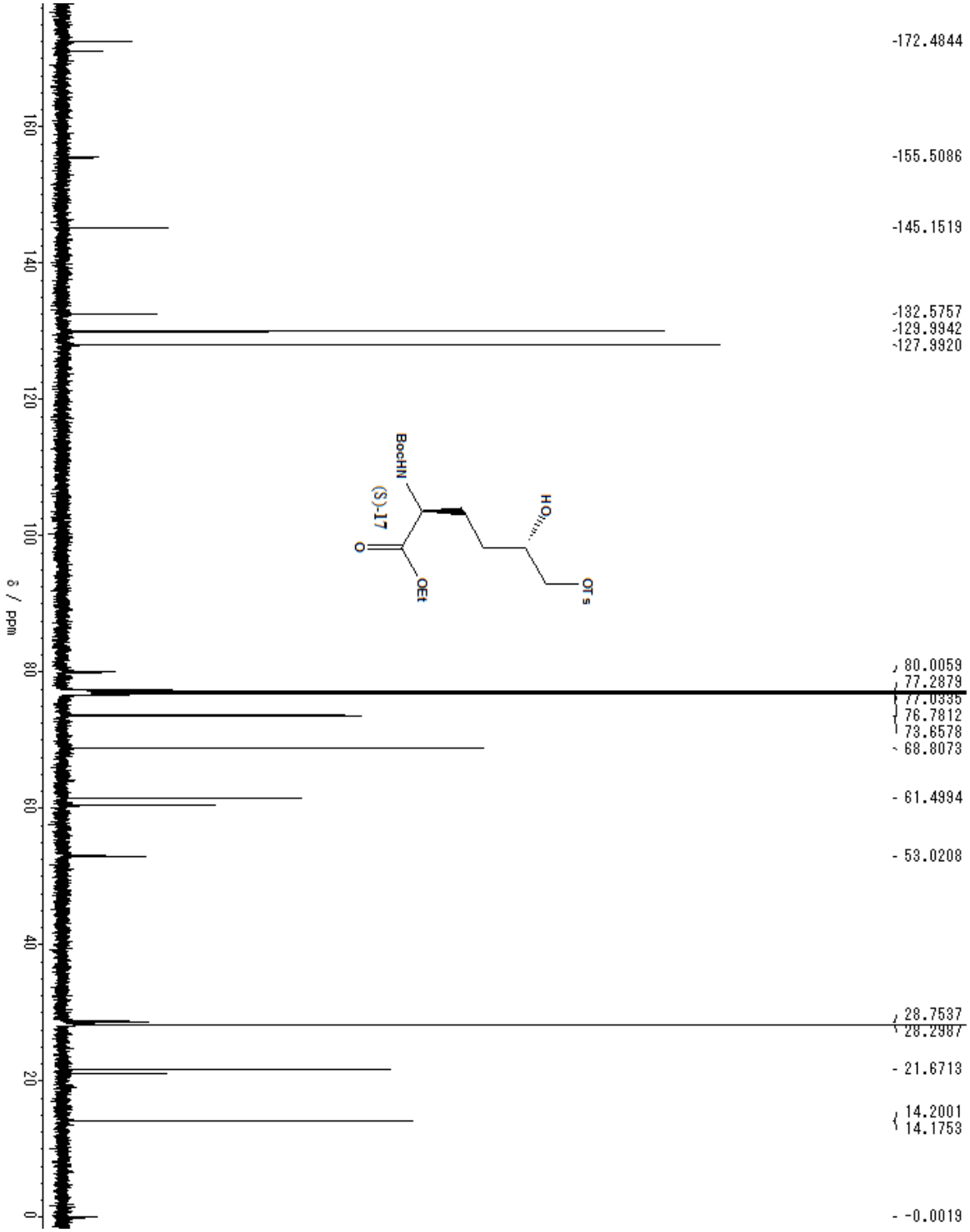
-0.0007
δ / ppm
HO
N
Boc
CO2Et
(2S,5R)-16


BocHN
(S)-17
O
OEt
HO
OTs
8
7
6
5
4
3
2
1
δ / ppm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-145.1519
-132.5757
-129.9942
-127.9920
BocHN
(S)-17
O
OEt
HO
OTs
80.0059
77.2879
77.0335
76.7812
73.6578
68.8073
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53.0208
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14.2001
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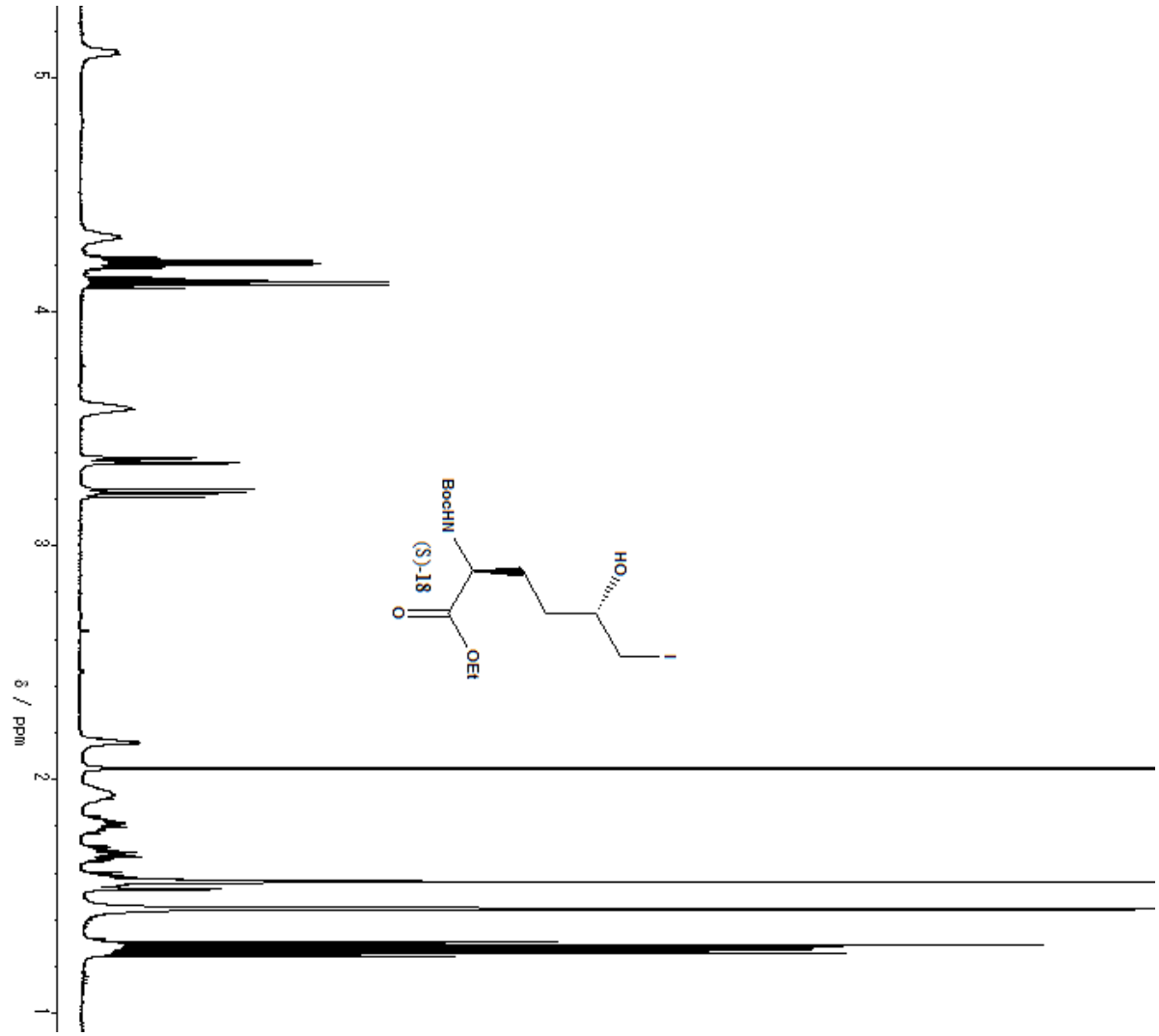
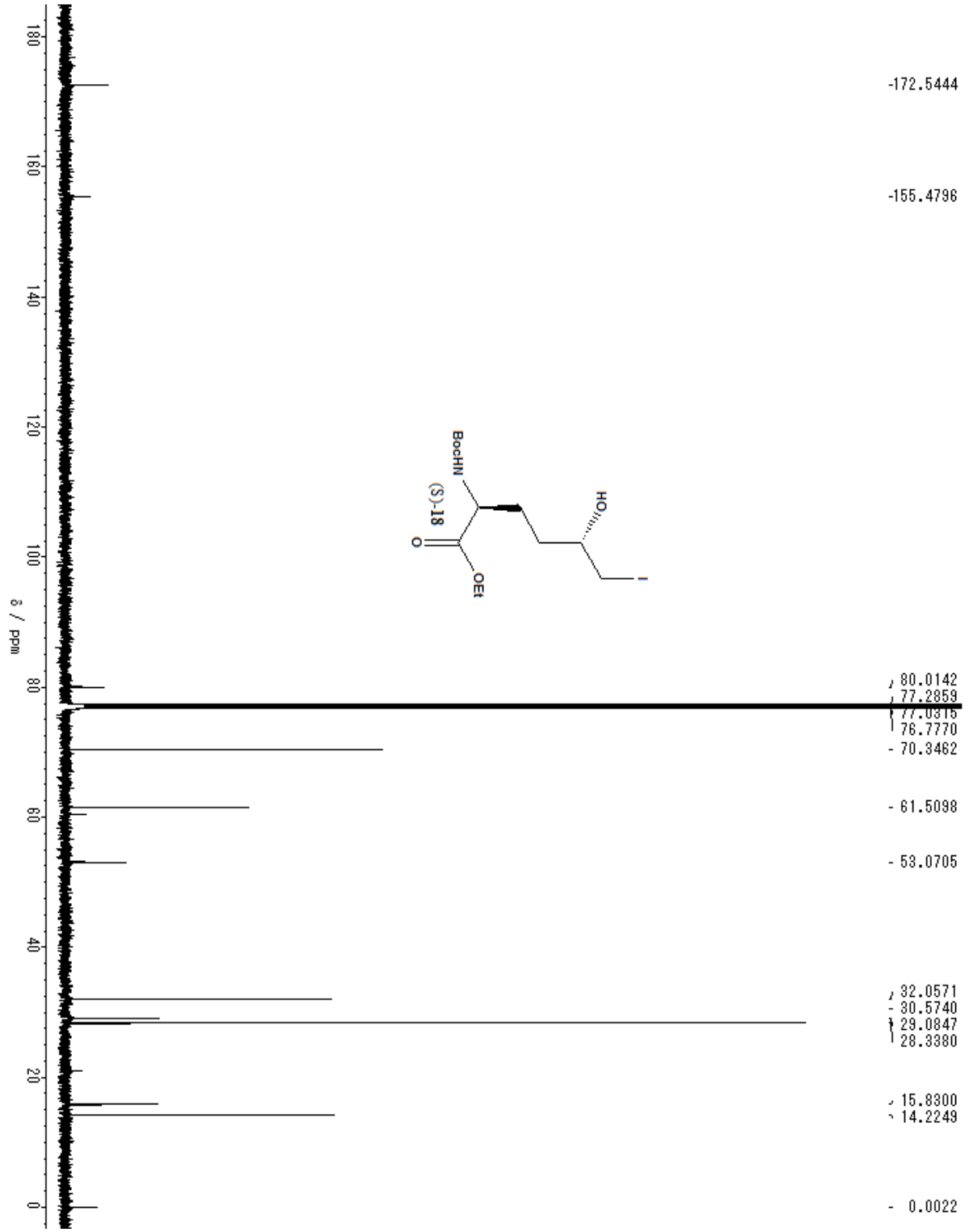
δ / ppm


BocHN
(S)-18
O
OEt
HO
I
δ / ppm
1
2
3
4
5


δ / ppm
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160
140
120
100
80
60
40
20
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77.2859
77.0315
76.7770
70.3462
61.5098
53.0705
32.0571
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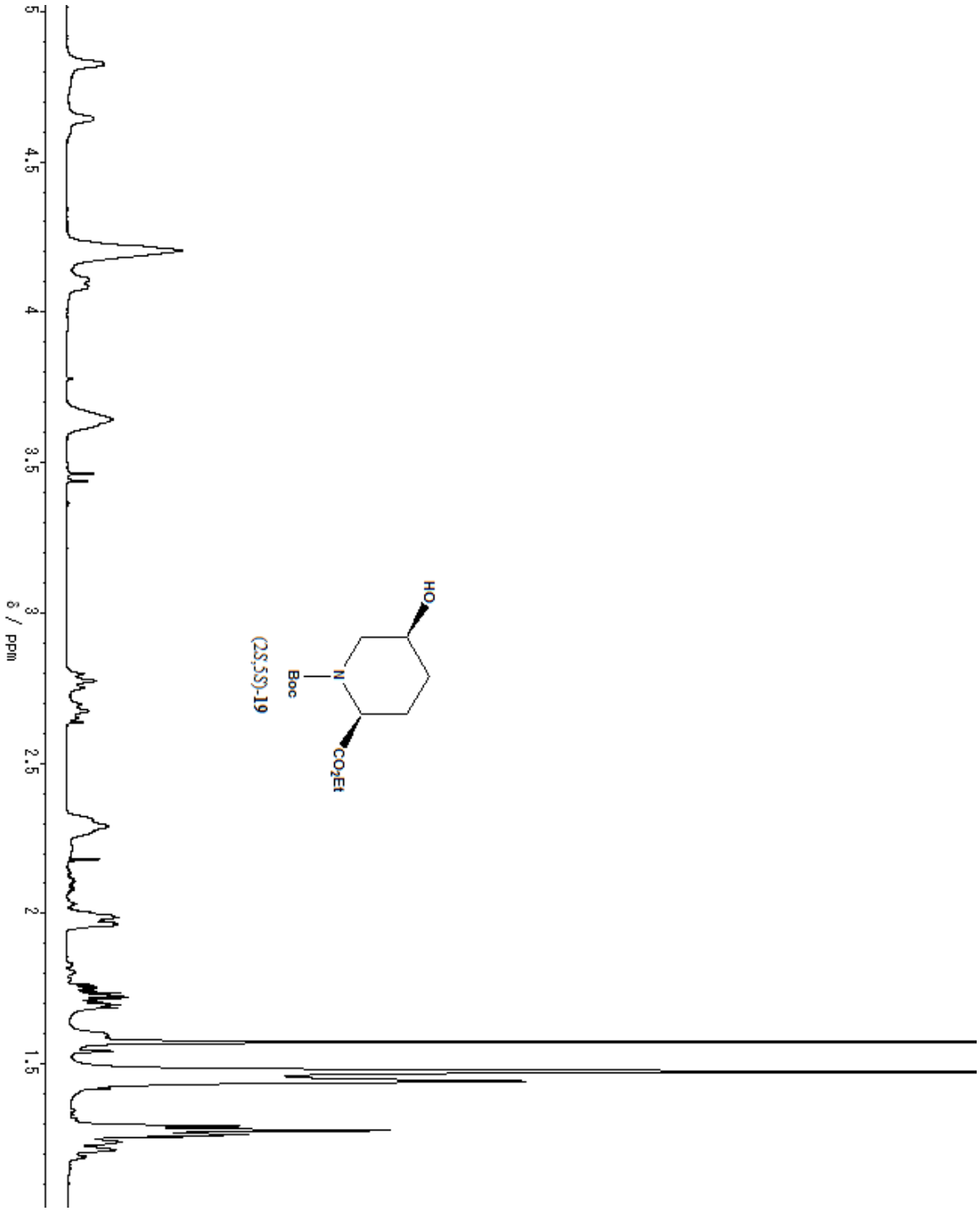
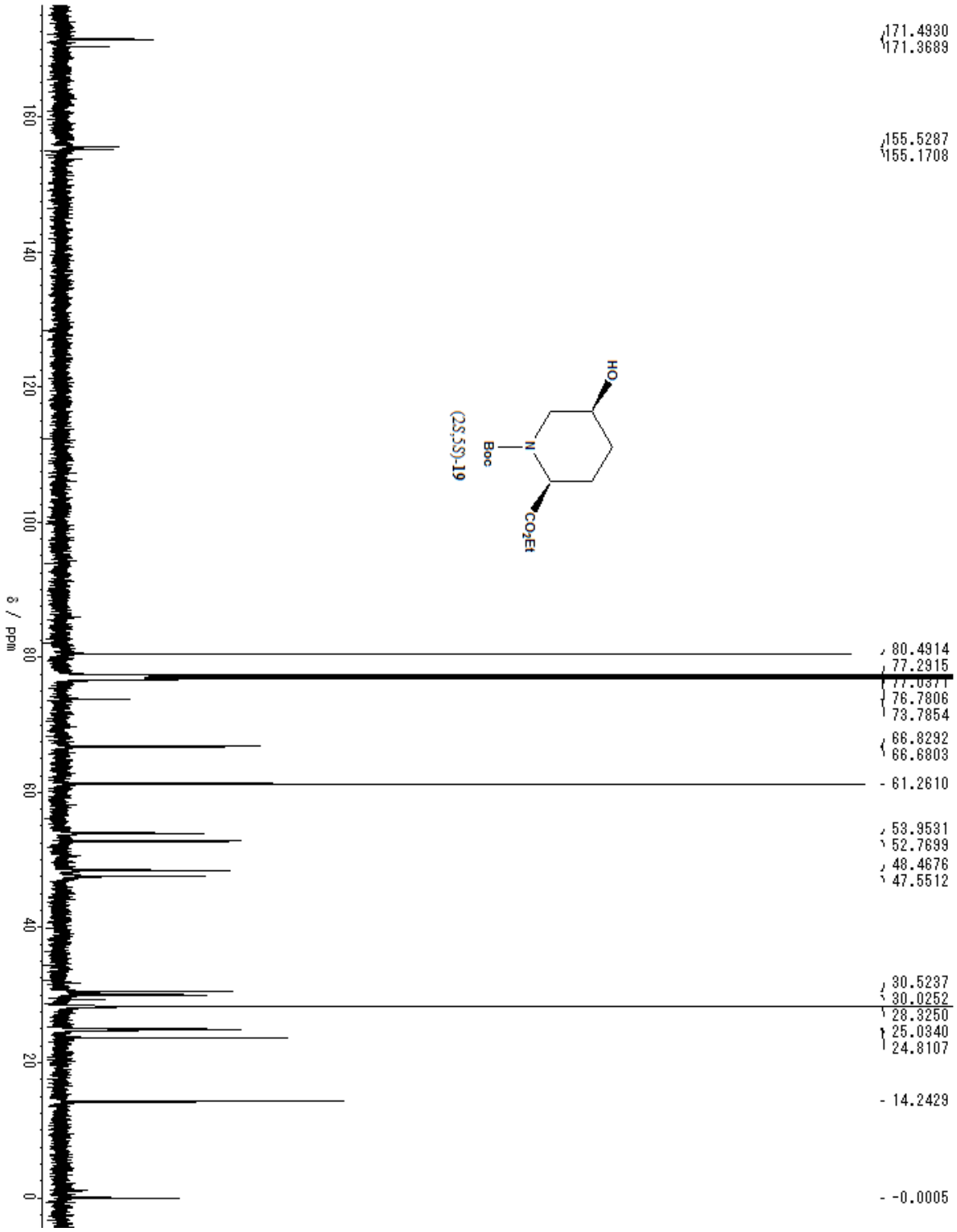
BocHN
(S)-18
O
OEt
HO
I


5
4.5
4
3.5
3
2.5
2
1.5
δ / ppm
HO
N
Boc
CO2Et
(2S,5S)-19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80.4914
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66.8292
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53.9531
52.7699
48.4676
47.5512
30.5237
30.0252
28.3250
25.0340
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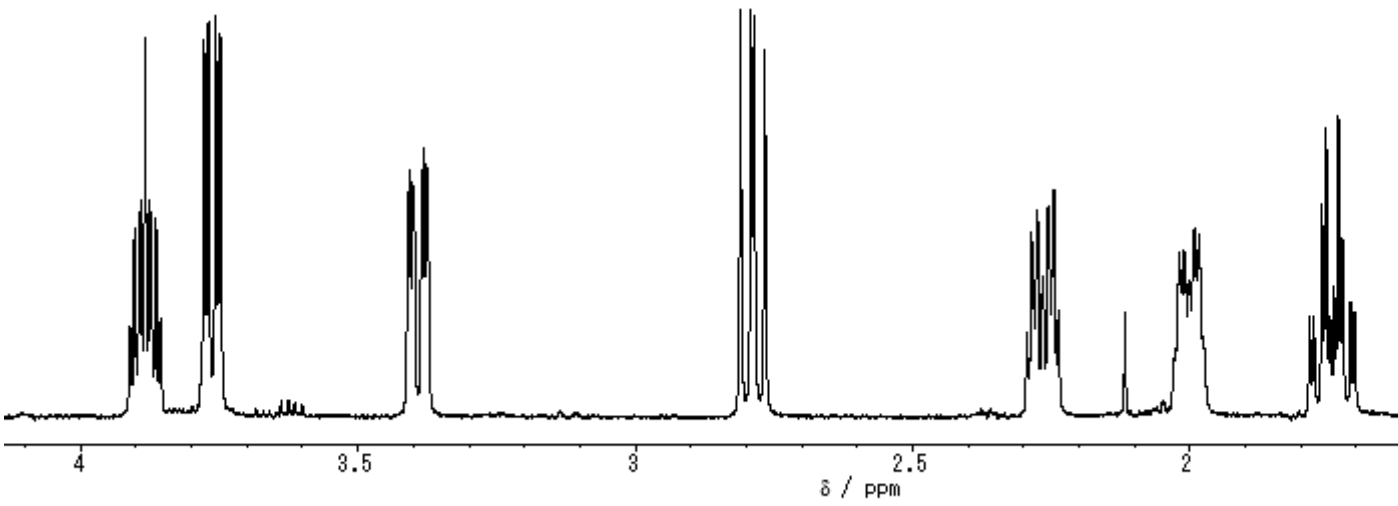
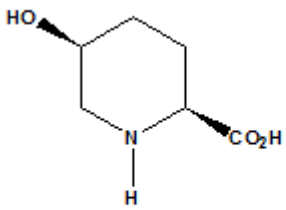
14.2429
-0.0005
δ / ppm
(2S,5S)-19
Boc
N
HO
CO2Et

1.HCl





2.HCl