Total Synthesis of the Cytotoxic Anhydrophytosphingosine Pachastrissamine (Jaspine B)

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General Considerations

All reactions described were performed under an atmosphere of dry nitrogen using oven dried glassware unless otherwise specified. Flash chromatography was carried out with 230-400 mesh silica gel following the technique described by Still.[1] Concentration and removal of trace solvents was done via a rotary evaporator using dry ice/acetone condenser and vacuum from water or air aspirator.

All solvents, reagents, and starting materials were purchased from commercially available sources and were used without further purification unless otherwise specified. Diisopropylamine and dichloromethane was freshly distilled over calcium hydride. Tetrahydrofuran was freshly distilled over Na metal.

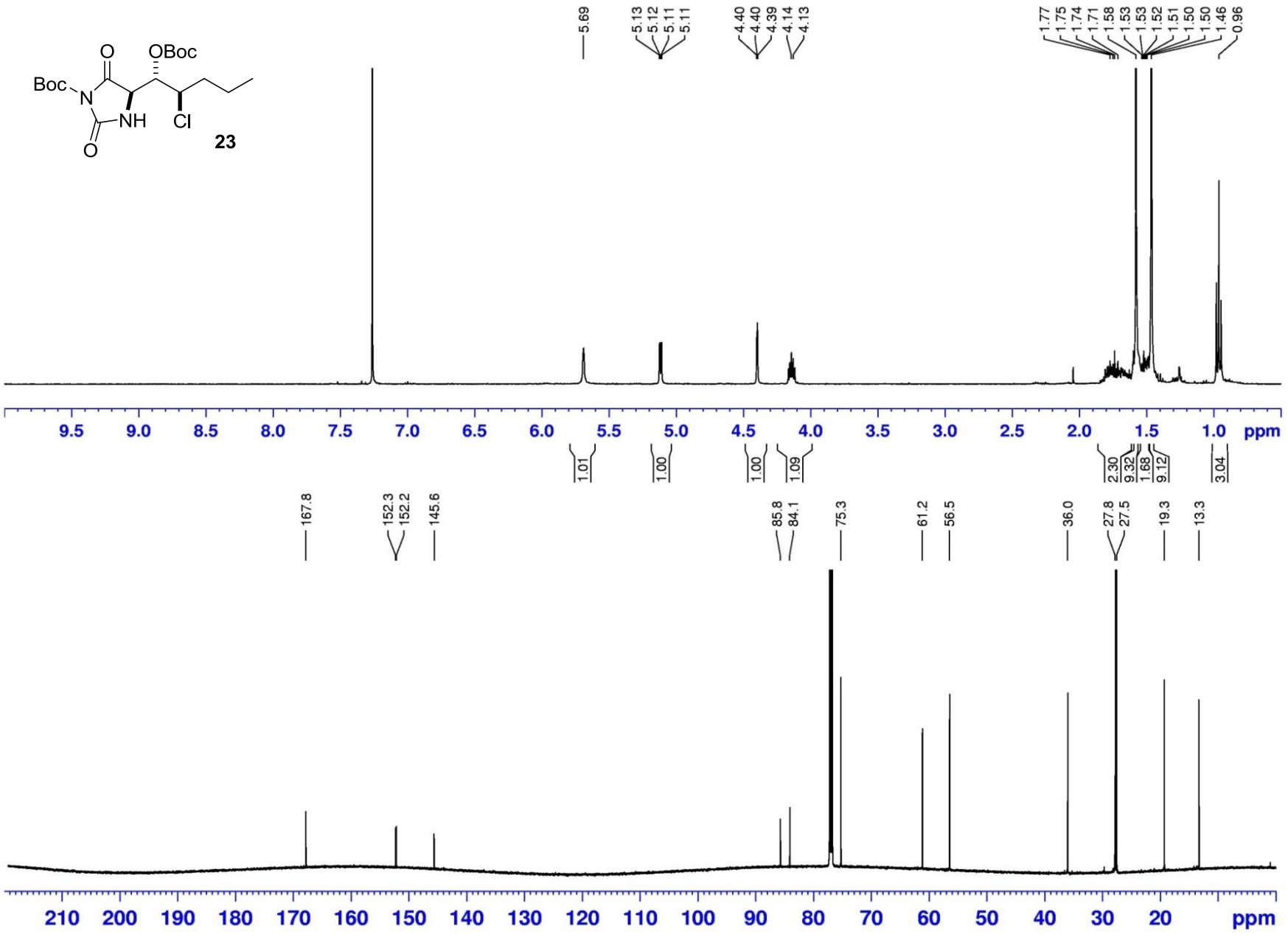
Nuclear magnetic resonance (NMR) spectra were recorded using deuterochloroform ($CDCl_3$). Signal positions (δ) are given in parts per million from tetramethylsilane (δ 0) and were measured relative to the signal of the solvent ($CDCl_3$: δ 7.26, ^{1}H NMR; δ 77.0, ^{13}C NMR). Coupling constants (*J* values) are given in Hertz (Hz) and are reported to the nearest 0.1 Hz. ^{1}H NMR spectral data are tabulated in the order: multiplicity (s, singlet; d, doublet; t, triplet; m, multiplet), number of protons, coupling constants. NMR spectra were recorded on a 400 MHz, 500 MHz, or 600 MHz (equipped with a QNP or TCI cryoprobe) spectrometer. Assignments of ^{1}H and ^{13}C NMR spectra are based on analysis of ^{1}H-^{1}H COSY, HSQC, HMBC, TOCSY and 1D NOESY spectra.

Infrared (IR) spectra were recorded on Fourier transform spectrophotometer. Only selected, characteristic absorption data are provided for each compound.

High resolution mass spectra were performed on a TOF LC/MS mass spectrometer (Ionization method: ESI).

Optical rotation was measured at 589 nm.

[1] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.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O
OBoc
NH
Cl
O
O
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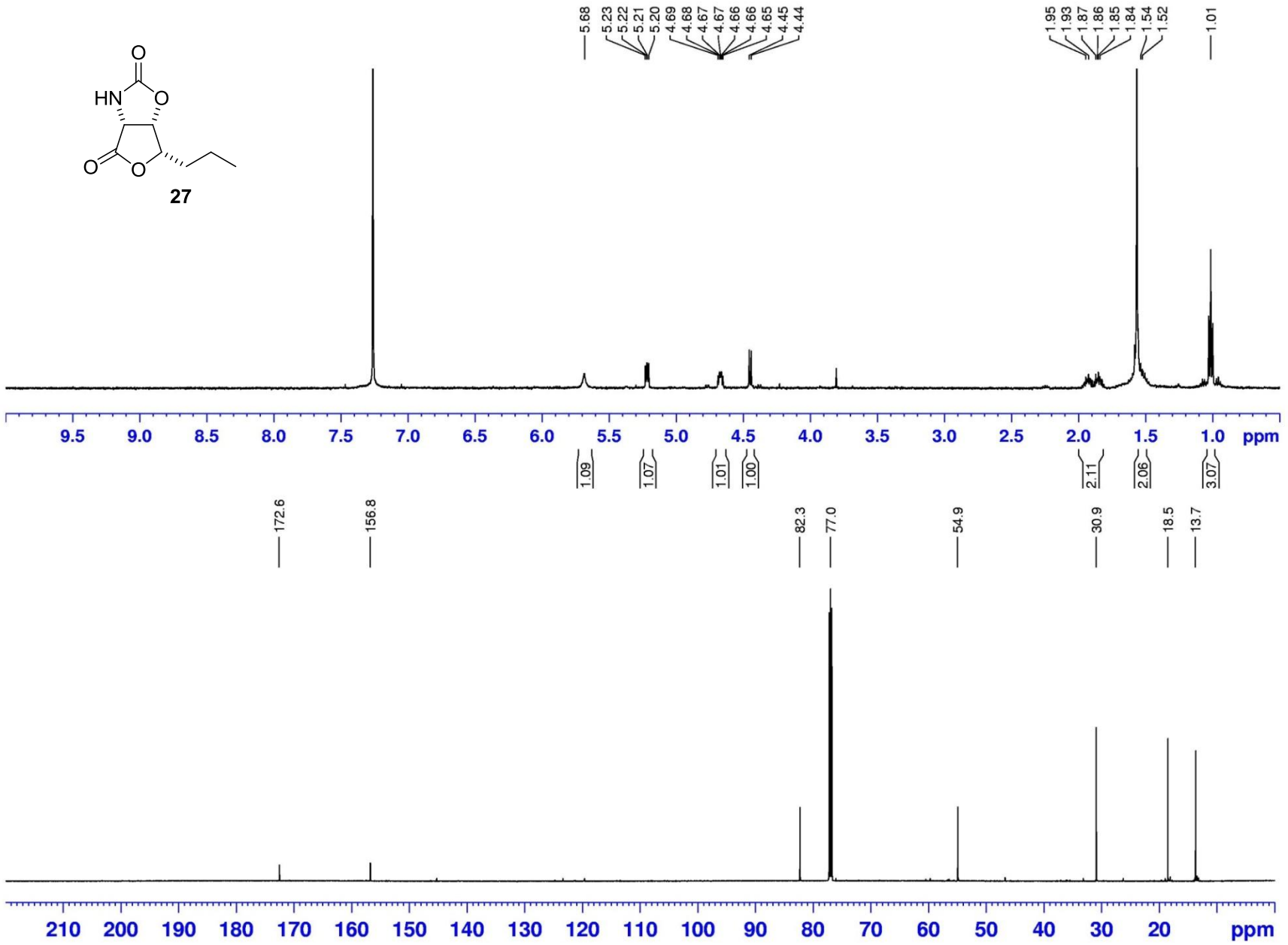
5.69
5.13
5.12
5.11
5.11
4.40
4.40
4.39
4.14
4.13
1.77
1.75
1.74
1.71
1.58
1.53
1.53
1.52
1.51
1.50
1.50
1.46
0.96
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.01
1.00
1.00
1.09
2.30
9.32
1.68
9.12
3.04
167.8
152.3
152.2
145.6
85.8
84.1
75.3
61.2
56.5
36.0
27.8
27.5
19.3
13.3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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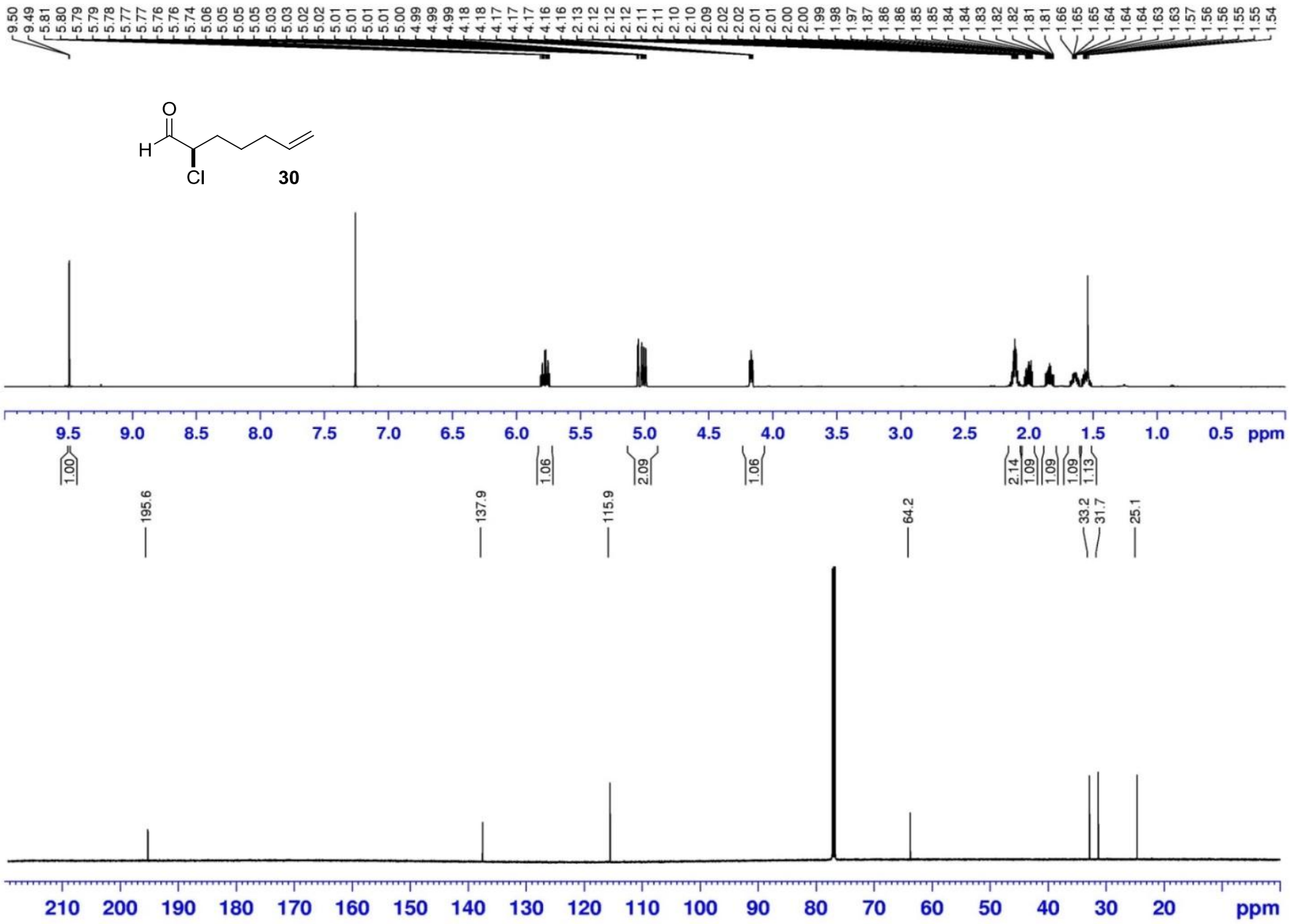
O
O
O
27
5.68
5.23
5.22
5.21
5.20
4.69
4.68
4.67
4.67
4.66
4.66
4.65
4.45
4.44
1.95
1.93
1.87
1.86
1.85
1.84
1.54
1.52
1.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.09
1.07
1.01
1.00
2.11
2.06
3.07
172.6
156.8
82.3
77.0
54.9
30.9
18.5
13.7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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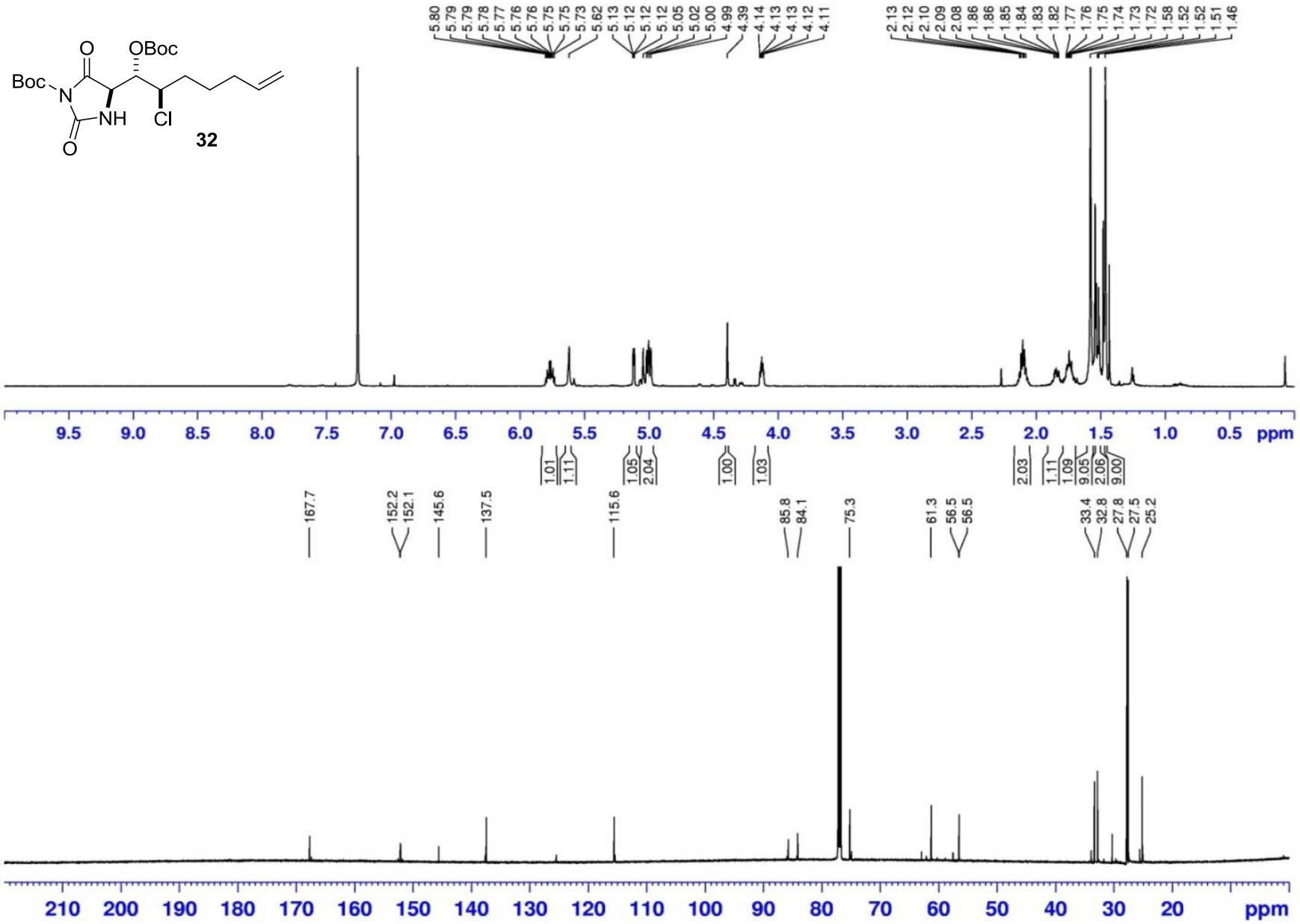
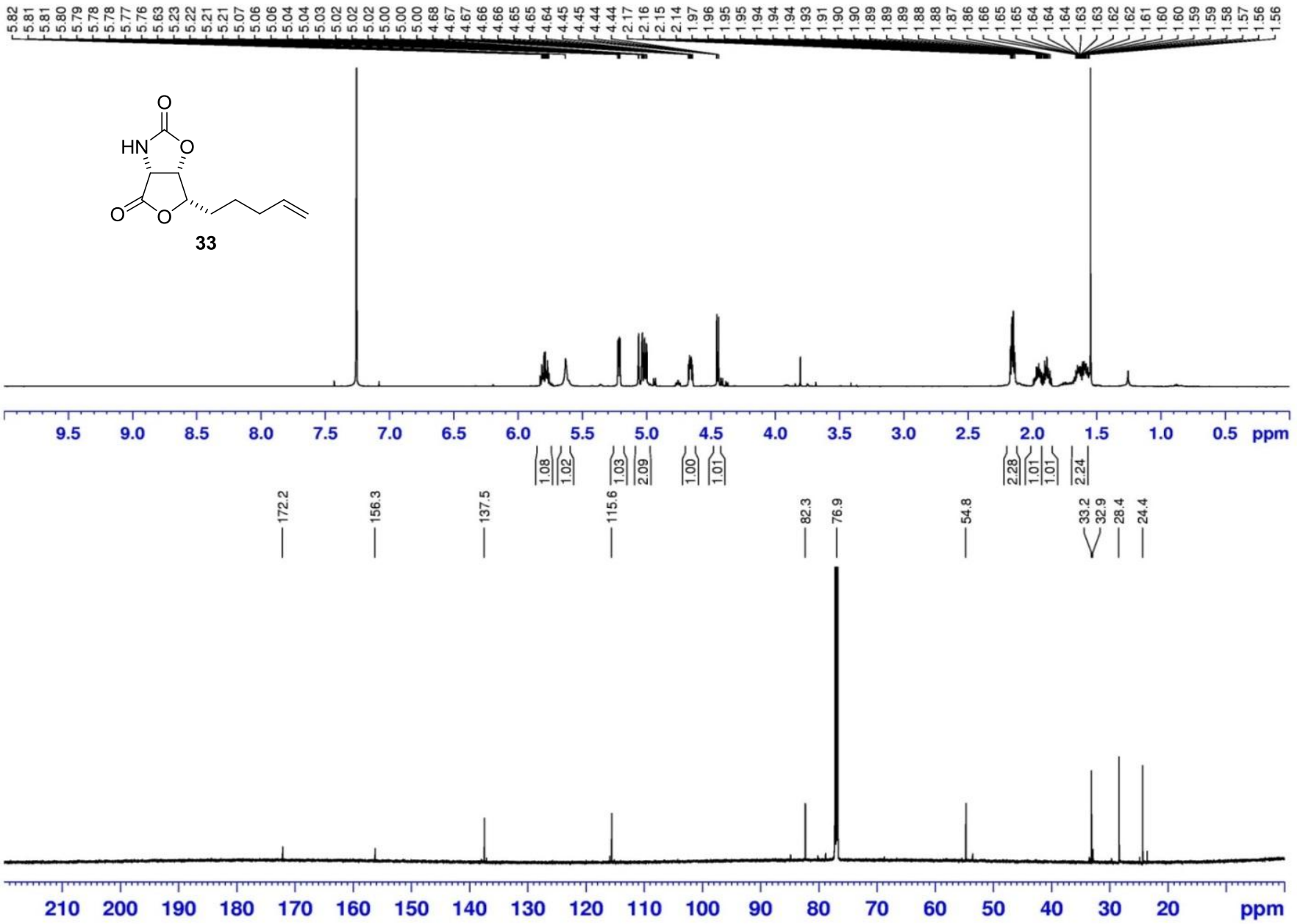
O
H
Cl
30
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00 1.06 2.09 1.06 2.14 1.09 1.09 1.09 1.13
195.6 137.9 115.9 64.2 33.2 31.7 25.1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


Boc
N
O
OBoc
NH
Cl
O
O
32
5.80 5.79 5.79 5.78 5.77 5.76 5.76 5.75 5.75 5.73 5.62 5.13 5.12 5.12 5.12 5.05 5.02 5.00 4.99 4.39 4.14 4.13 4.13 4.12 4.11
2.13 2.12 2.10 2.09 2.08 1.86 1.86 1.85 1.84 1.83 1.82 1.77 1.76 1.75 1.74 1.73 1.72 1.58 1.52 1.52 1.51 1.46
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 ppm
1.01 1.11 1.05 2.04 1.00 1.03 2.03 1.11 1.09 9.05 2.06 9.00
167.7 152.2 152.1 145.6 137.5 115.6 85.8 84.1 75.3 61.3 56.5 56.5 33.4 32.8 27.8 27.5 25.2
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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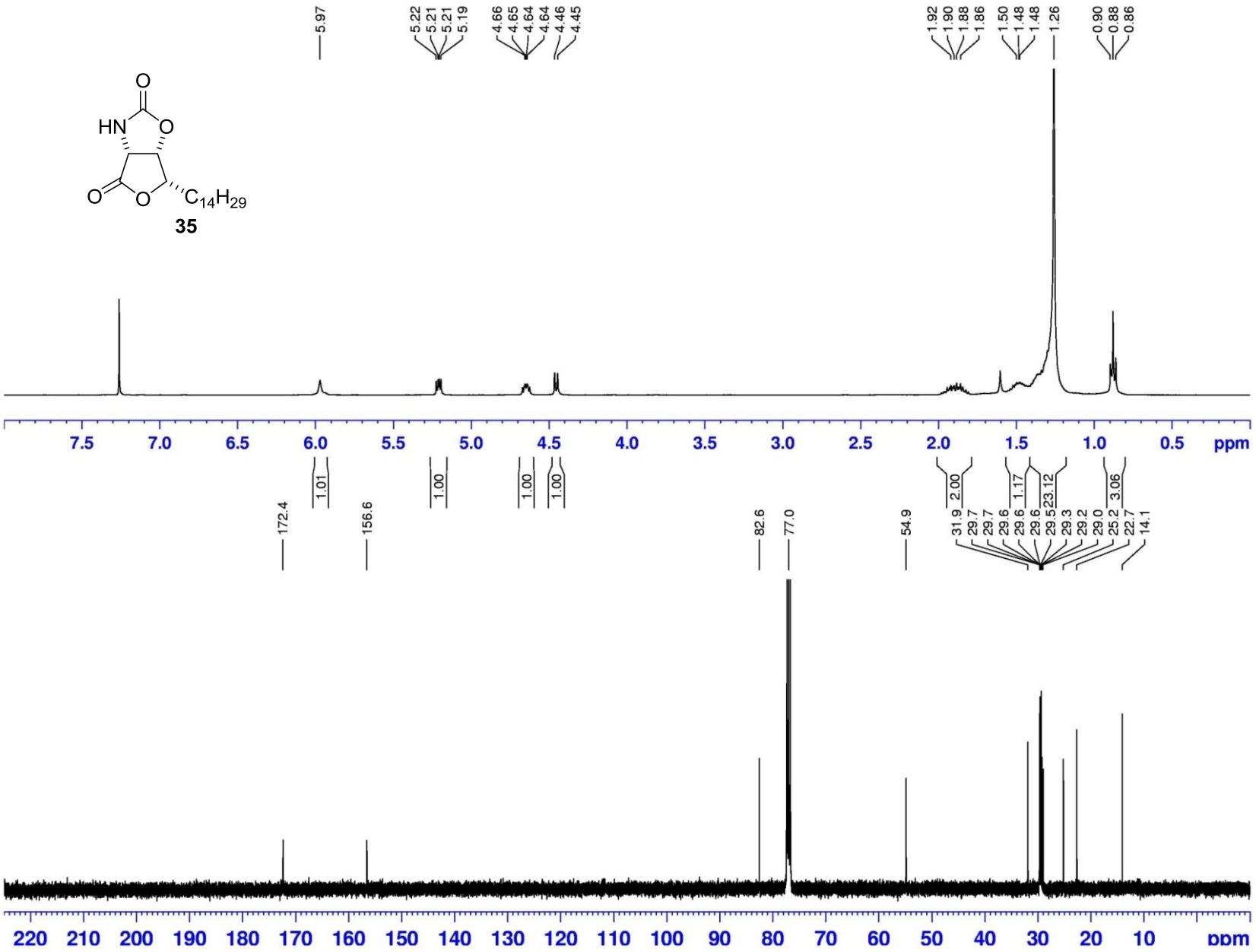
O
O
O
33
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.08 1.02 1.03 2.09 1.00 1.01 2.28 1.01 1.01 2.24
172.2 156.3 137.5 115.6 82.3 76.9 54.8 33.2 32.9 28.4 24.4
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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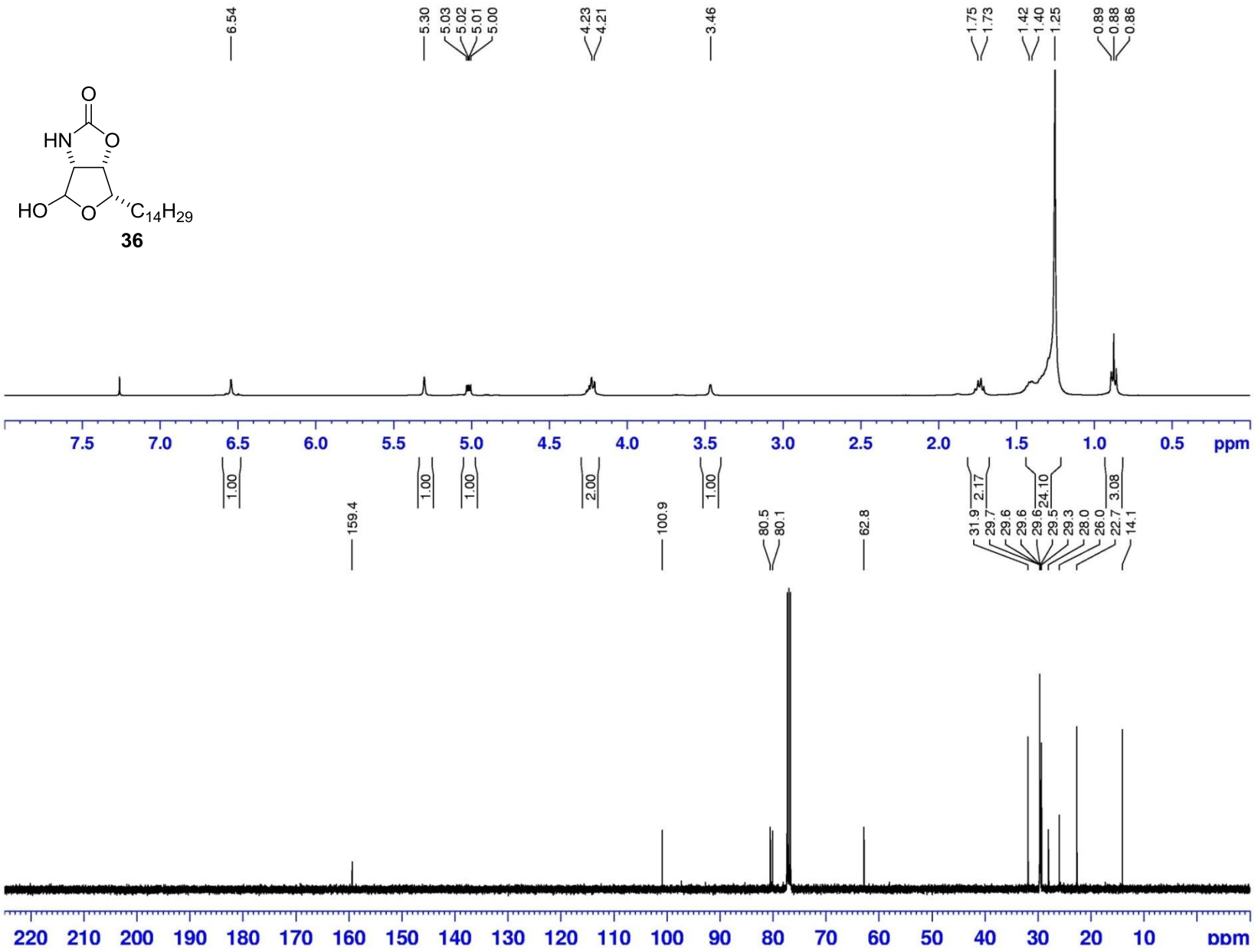
5.22
5.21
5.21
5.19
4.66
4.65
4.64
4.64
4.46
4.45
1.92
1.90
1.88
1.86
1.50
1.48
1.48
1.26
0.90
0.88
0.86
HN
O
O
O
O
C14H29
35
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.01
1.00
1.00
1.00
2.00
1.17
23.12
3.06
172.4
156.6
82.6
77.0
54.9
31.9
29.7
29.7
29.6
29.6
29.5
29.3
29.2
29.0
25.2
22.7
14.1
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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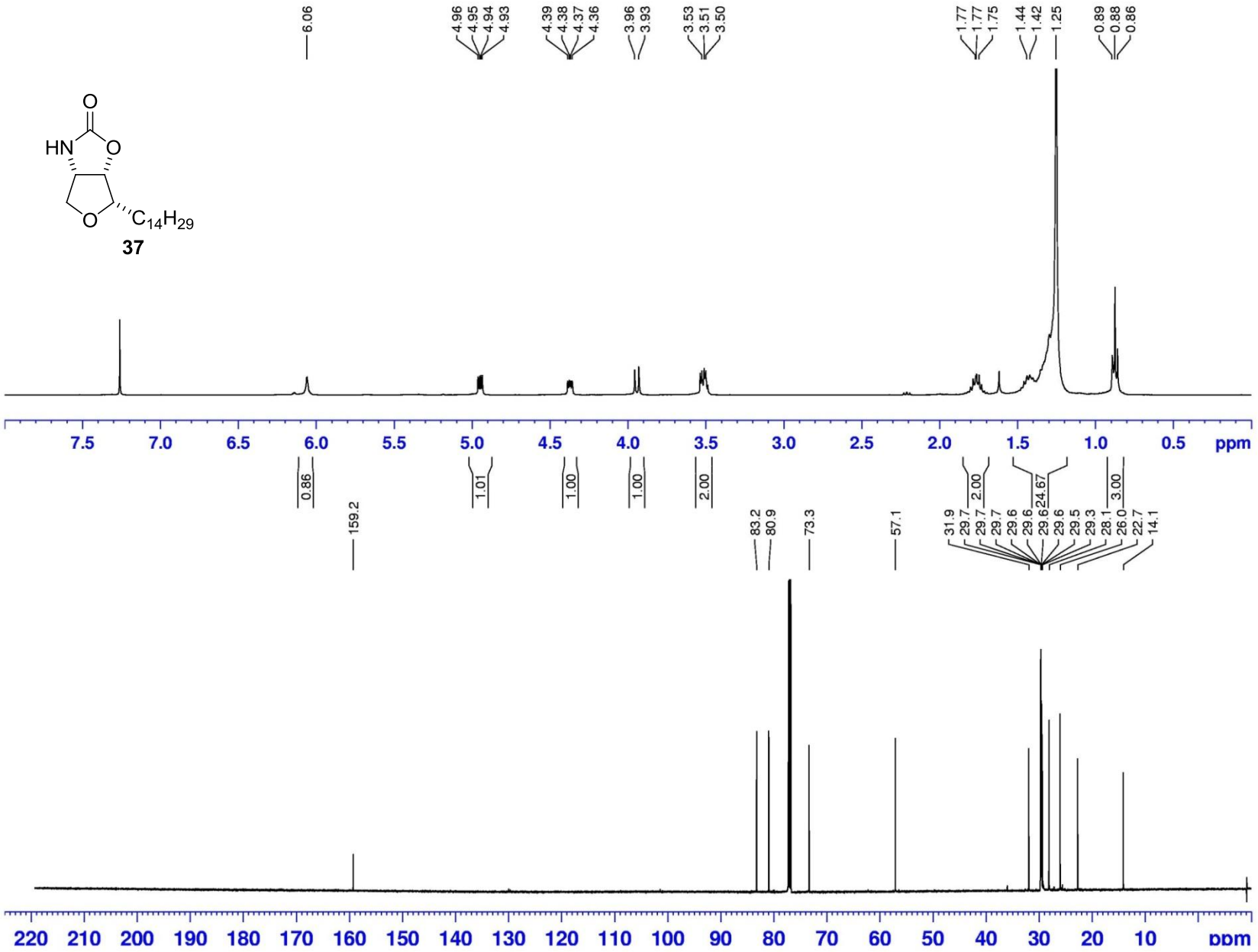
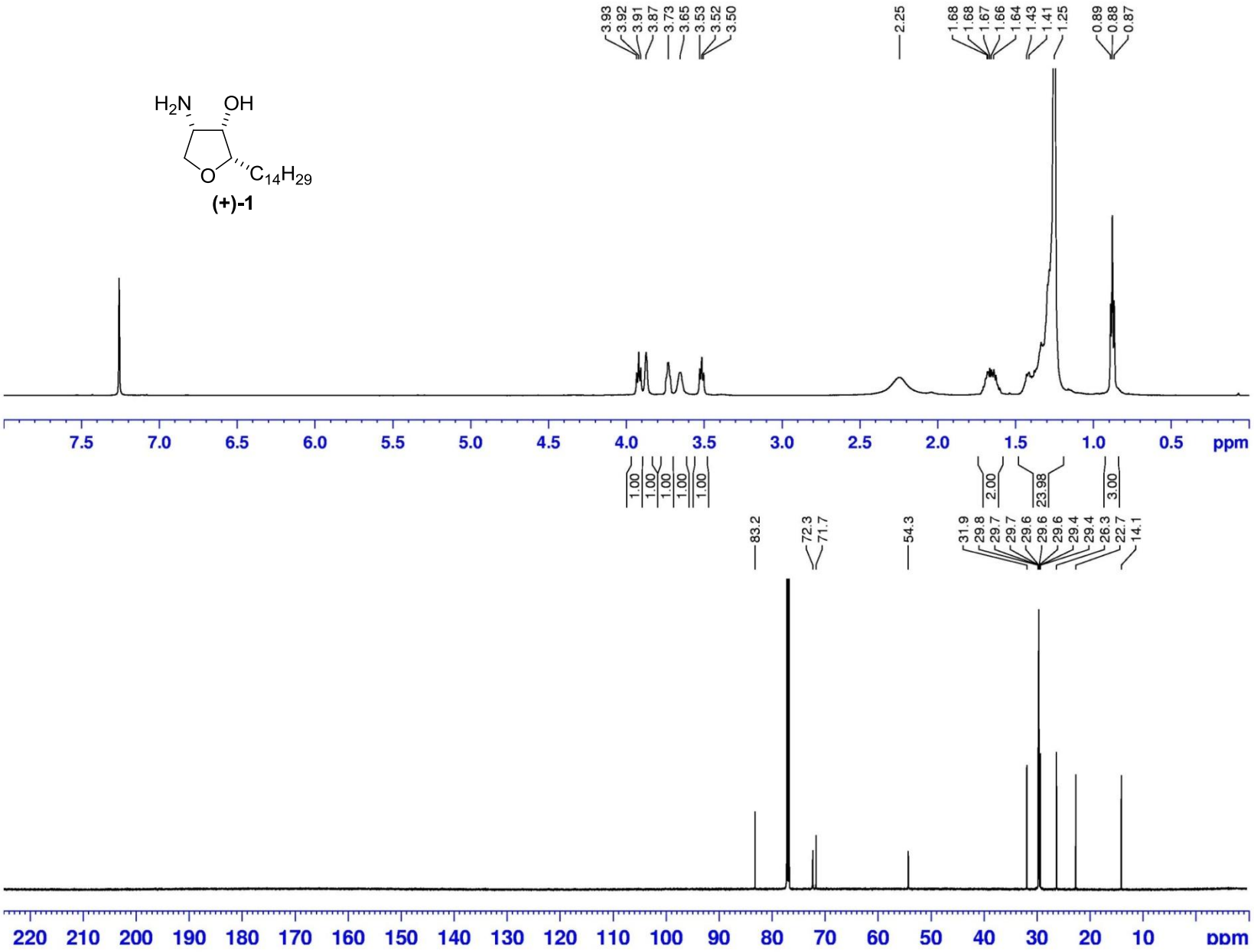
5.03
5.02
5.01
5.00
4.23
4.21
3.46
1.75
1.73
1.42
1.40
1.25
0.89
0.88
0.86
HN
O
O
HO
O
$C_{14}H_{29}$
36
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.00
1.00
2.00
1.00
2.17
24.10
3.08
159.4
100.9
80.5
80.1
62.8
31.9
29.7
29.6
29.6
29.6
29.5
29.3
28.0
26.0
22.7
14.1
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


6.06
4.96
4.95
4.94
4.93
4.39
4.38
4.37
4.36
3.96
3.93
3.53
3.51
3.50
1.77
1.77
1.75
1.44
1.42
1.25
0.89
0.88
0.86
HN
O
O
O
$C_{14}H_{29}$
37
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 ppm
0.86
1.01
1.00
1.00
2.00
2.00
24.67
3.00
159.2
83.2
80.9
73.3
57.1
31.9
29.7
29.7
29.7
29.6
29.6
29.6
29.6
29.5
29.3
28.1
26.0
22.7
14.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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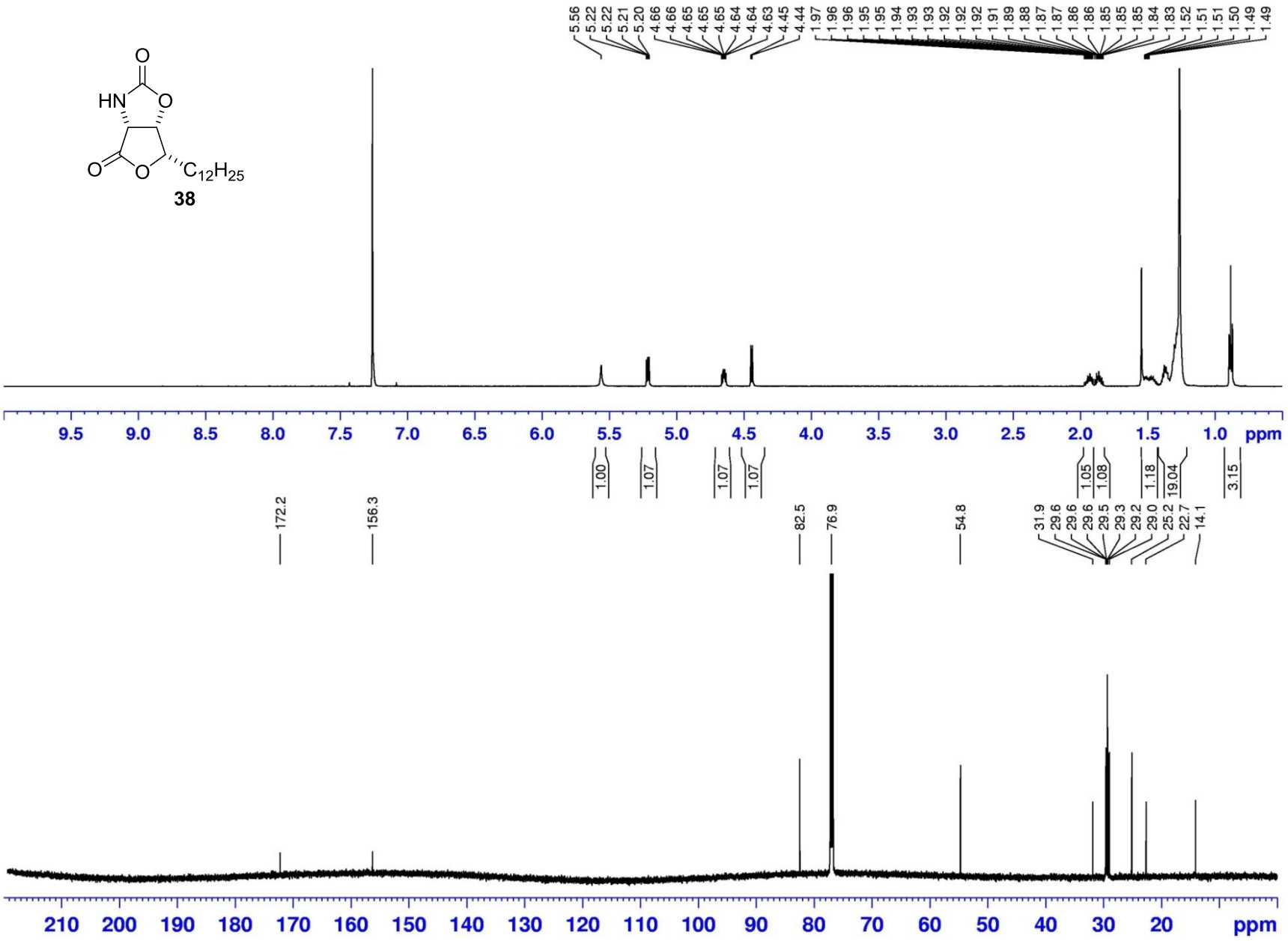
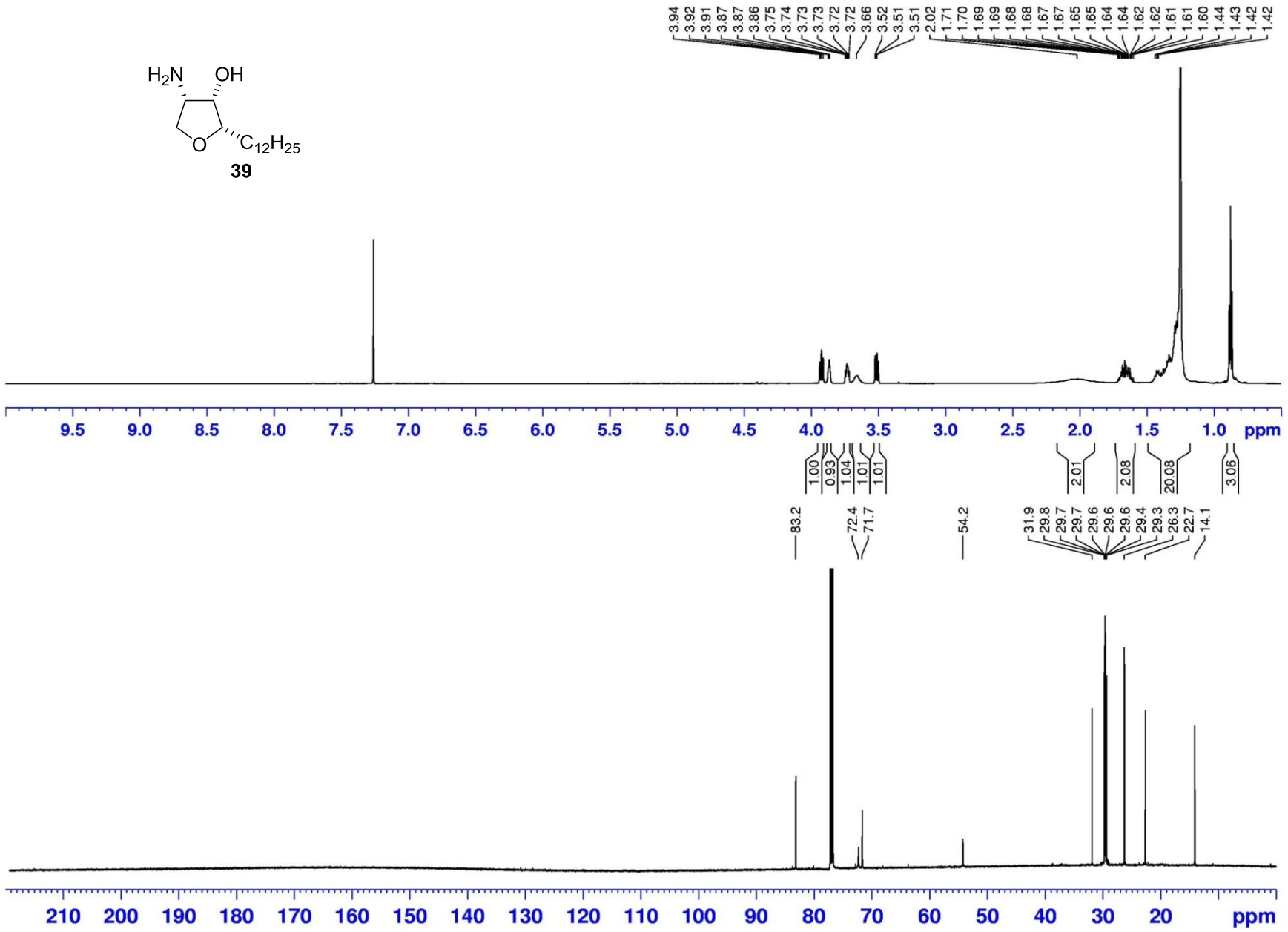
3.92
3.91
3.87
3.73
3.65
3.53
3.52
3.50
2.25
1.68
1.68
1.67
1.66
1.64
1.43
1.41
1.25
0.89
0.88
0.87
H2N
OH
O
C14H29
(+)-1
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.00
1.00
1.00
1.00
2.00
23.98
3.00
83.2
72.3
71.7
54.3
31.9
29.8
29.7
29.7
29.6
29.6
29.6
29.4
29.4
26.3
22.7
14.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


HN
O
O
O
O
$C_{12}H_{25}$
38
5.56 5.22 5.22 5.21 5.20 4.66 4.66 4.65 4.65 4.65 4.64 4.64 4.63 4.45 4.44 1.97 1.96 1.96 1.95 1.95 1.94 1.93 1.93 1.92 1.92 1.92 1.91 1.89 1.88 1.87 1.87 1.86 1.86 1.85 1.85 1.85 1.84 1.83 1.52 1.51 1.51 1.50 1.49 1.49
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 ppm
1.00 1.07 1.07 1.07 1.05 1.08 1.18 19.04 3.15
172.2 156.3 82.5 76.9 54.8 31.9 29.6 29.6 29.6 29.5 29.3 29.2 29.0 25.2 22.7 14.1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


H2N
OH
O
C12H25
39
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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 ppm
1.00 0.93 1.04 1.01 1.01 2.01 2.08 20.08 3.06
83.2 72.4 71.7 54.2 31.9 29.8 29.7 29.7 29.6 29.6 29.6 29.4 29.3 26.3 22.7 14.1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm