Electronic Supplementary Information (ESI)

One-pot Synthesis of Substituted Isoindolin-1-ones *via* Lithiation and Substitution of *N'*-benzyl-*N,N*-dimethylureas

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Instrumentation and Chemicals

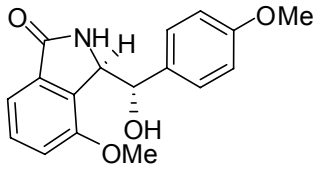
General. Melting point determinations were performed by the open capillary method using a Gallenkamp melting point apparatus and are reported uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV400 or AV500 spectrometer operating at 400 or 500 MHz for ^{1}H or 100 and 125 MHz for ^{13}C measurements. Chemical shifts δ are reported in parts per million (ppm) relative to TMS and coupling constants J are in Hz and have been rounded to the nearest whole number. The proton multiplicities are recorded as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Low-resolution mass spectra (see supplementary information) were recorded on a Quattro II spectrometer, electron impact (EI) at 70 eV and chemical ionization (CI) at 50 eV by the use of NH_3 as ionization gas. Atmospheric pressure chemical ionization mass spectra (APCI) were performed on a Waters LCT Premier XE instrument. Electrospray (ES) analyses were performed on a ZQ4000 spectrometer in positive and negative ionisation modes. Accurate mass data were obtained on a MAT900 instrument. IR spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrometer or a Perkin Elmer 1600 series FT-IR Spectrometer. Microanalyses were performed by Warwick analytical service at the University of Warwick. The X-ray single-crystal diffraction data were collected on a Nonius Kappa CCD diffractometer using graphite-monochromated Mo-K_α, (λ = 0.710 73 Å) radiation. Crystal and structure refinement data are shown in the supplementary information. The structures were solved by direct methods using SHELXS-96[1] and refined with all data on F^2 full-matrix least squares using SHELXL-97.[2] Non-hydrogen atoms were generally refined anisotropically. Hydrogen atom positions were located from difference Fourier maps and a riding model with atomic displacement parameters 1.2 times (1.5 times for methyl groups) those of the atom to which they are bonded was used for subsequent refinements. Full crystallographic data have been deposited with the CCDC, reference numbers 737411, 737415, 762623, and 762624 and can be obtained free of charge *via* http://www.ccdc.ac.uk/data_request/cif. Column chromatography was carried out using Fischer Scientific silica 60A (35-70 micron). Alkyllithiums were obtained from Aldrich Chemical Company and were estimated prior to use by the method of Watson and Eastham.[3] Other chemicals were obtained from Aldrich Chemical Company and used without further purification. THF was distilled from sodium benzophenone ketyl. Other solvents were purified by standard procedures.[4]

Experimental Procedures for the Synthesis of 3-Substituted Isoindolin-1-ones 4, 9-16 and 18-23 and their Characterization Data

A solution of *t*-BuLi in heptane (3.9 mL, 1.7 M, 6.6 mmol) was added to a cold (0 °C), stirred solution of *N*′-(substituted benzyl)-*N,N*-dimethylurea (2.0 mmol) in anhydrous THF (20 mL)

under N_2. Formation of the monolithium reagent was observed as a yellow solution and the dilithium reagent was observed as a reddish orange solution, after which the colour changed to deep red. The mixture was stirred at 0 °C for 6 h after which an electrophile (2.2 mmol), in anhydrous THF (8 mL) if solid, otherwise neat, was added. The mixture was stirred for 2 h at 0 °C then the cooling bath was removed and the mixture allowed to warm to room temperature. It was then diluted with Et_2O (10 mL) and quenched with aq. sat. NH_4Cl (10 mL). The organic layer was separated, washed with H_2O (2 x 10 mL), dried ($MgSO_4$), and evaporated under reduced pressure. The residue obtained was triturated with diethyl ether (20 ml) to give a white solid which was filtered and then washed with diethyl ether to give the pure product.

(*R)-3-((*S**)-Hydroxy(4-methoxyphenyl)methyl)-4-methoxyisoindolin-1-one (4)**



Yield: (0.49 g, 1.63 mmol, 81%); mp: 199–201 °C.

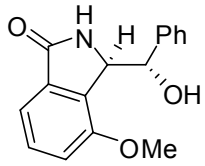
^{1}H NMR (400 MHz, DMSO-d_6): δ 8.77 (s, exch., 1H), 7.31 (app. t, J = 8 Hz, 1H), 7.16 (d, J = 8 Hz, 1H), 6.93 (d, J = 8 Hz, 1H), 6.89 (d, J = 9 Hz, 2H), 6.58 (d, J = 9 Hz, 2H), 5.73 (d, J = 3 Hz, exch., 1H), 5.39 (app. t, J = 3 Hz, 1H), 4.89 (d, J = 3 Hz, 1H), 3.97 (s, 3H), 3.60 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 169.7, 158.4, 155.0, 134.9, 131.6, 131.5, 130.1, 128.3, 114.9, 113.6, 112.5, 71.6, 61.5, 56.0, 55.1.

HRMS (CI): calcd for $C_{17}H_{18}NO_4$ [MH^+] 300.1230; found 300.1231.

FT (FT): ν_{max} 3304, 2872, 1677, 1604, 1512, 1273, 1048 cm^{-1}.

(*R)-3-((*S**)-(Hydroxy(phenyl)methyl)-4-methoxyisoindolin-1-one (9)**



Yield: 0.43 g (1.60 mmol, 80%); mp: 213–214 °C.

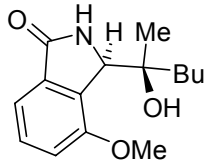
^{1}H NMR (500 MHz, DMSO-d_6): δ 8.79 (s, exch., 1H), 7.31 (app. t, J = 8 Hz, 1H), 7.16 (d, J = 8 Hz, 1H), 7.03–6.97 (m, 5H), 6.91 (d, J = 8 Hz, 1H), 5.82 (d, J = 4 Hz, exch., 1H), 5.43 (app. t, J = 4 Hz, 1H), 4.92 (d, J = 3 Hz, 1H), 3.98 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 175.0, 160.3, 144.8, 140.1, 136.8, 135.4, 132.6, 132.5, 132.4, 120.1, 118.8, 77.2, 66.6, 61.2.

HRMS (CI): calcd for $C_{16}H_{16}NO_3$ [MH^+] 270.1125; found 270.1125.

IR (FT): ν_{max} 3201, 3070, 1672, 1603, 1492, 1269, 1053 cm^{-1}.

(*R)-3-((*S**)-(2-Hydroxyhexyl)-4-methoxyisoindolin-1-one (10)**



Yield: 0.41 g (1.56 mmol, 78%); mp: 186–187 °C.

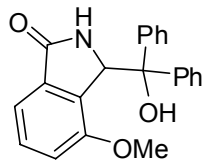
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (s, exch., 1H), 7.54 (dd, *J* = 1, 8 Hz, 1H), 7.49 (app. t, *J* = 8 Hz, 1H), 7.12 (dd, *J* = 1, 8 Hz, 1H), 4.72 (s, exch., 1H), 4.08 (s, 1H), 3.99 (s, 3H), 1.34 (s, 3H), 1.39–1.33 (m, 2H), 1.29–0.94 (m, 4H), 0.79 (t, *J* = 7 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.1, 154.3, 135.5, 132.5, 130.6, 117.5, 114.2, 74.7, 66.9, 56.5, 36.8, 25.6, 24.8, 23.6, 14.4.

HRMS (CI): calcd for $C_{15}H_{22}NO_3$ [MH^+] 264.1600; found 264.1596.

IR (FT): ν_{max} 3490, 3073, 1682, 1593, 1263, 1046 cm^{-1}.

3-(Hydroxydiphenylmethyl)-4-methoxyisoindolin-1-one (11)



Yield: 0.56 g (1.62 mmol, 81%); mp: 206–208 °C.

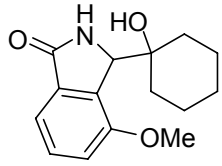
^{1}H NMR (500 MHz, DMSO-d_6): δ 7.89 (s, exch., 1H), 7.52–7.18 (m, 11H), 7.10 (d, *J* = 8 Hz, 1H), 6.94 (d, *J* = 8 Hz, 1H), 5.84 (s, exch., 1H), 5.76 (s, 1H), 3.19 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 169.7, 155.0, 145.8, 144.4, 136.2, 131.9, 130.2, 128.0, 127.4, 127.1, 126.9, 127.0, 126.8, 115.0, 113.9, 79.7, 64.3, 55.5. The two diastereoisomeric phenyl groups appeared as separated signals.

HRMS (ES^+): calcd for $C_{22}H_{20}NO_3$ [MH^+] 346.1438; found 346.1440.

IR (FT): ν_{max} 3301, 2981, 1690, 1599, 1491, 1267, 1038 cm^{-1}.

3-(1-Hydroxycyclohexyl)-4-methoxyisoindolin-1-one (12)



Yield: 0.41 g (1.57 mmol, 78%); mp: 206–207 °C.

^{1}H NMR (500 MHz, DMSO-d_6): δ 8.45 (s, exch., 1H), 7.43 (app. t, J = 8 Hz, 1H), 7.25 (d, J = 8 Hz, 1H), 7.22 (d, J = 8 Hz, 1H), 4.46 (s, 1H), 4.32 (s, exch., 1H), 3.88 (s, 3H), 1.54–0.96 (m, 10H).

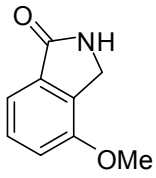
^{13}C NMR (125 MHz, DMSO-d_6): δ 169.8, 155.0, 135.9, 132.0, 130.2, 115.5, 114.6, 73.5, 65.5, 56.1, 38.8, 33.7, 25.8, 21.5, 21.4. The two diastereoisomeric sides of the cyclohexane ring appeared as separated signals.

HRMS (CI): calcd for $C_{15}H_{20}NO_3$ [MH^+] 262.1438; found 262.1435.

IR (FT): ν_{max} 3301, 2952, 1690, 1590, 1470, 1240, 1047 cm^{-1}.

Anal calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 69.13; H, 7.34; N, 5.48%.

4-methoxyisoindolin-1-one (13)



Yield: 0.27 g (1.65 mmol, 82%); mp: 190–192 °C.

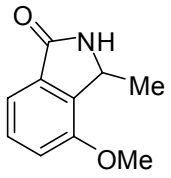
^{1}H NMR (500 MHz, DMSO-d_6): δ 8.60 (s, exch., 1H), 7.46 (app. t, J = 8 Hz, 1H), 7.26 (d, J = 8 Hz, 1H), 7.19 (d, J = 8 Hz, 1H), 4.29 (s, 2H), 3.88 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 170.3, 154.9, 134.6, 131.8, 129.9, 115.2, 113.5, 55.8, 43.0.

HRMS (CI): calcd for $C_9H_{10}NO_2$ [MH^+] 164.0706; found 164.0707.

IR (FT): ν_{max} 3286, 2870, 1682, 1585, 1440, 1266, 1052 cm^{-1}.

4-Methoxy-3-methylisoindolin-1-one (14)



Yield: 0.28 g (1.58 mmol, 79%); mp: 153–154 °C.

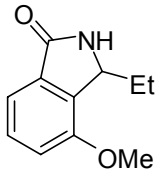
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (br s, exch., 1H), 7.47 (t, J = 8 Hz, 1H), 7.24 (d, J = 8 Hz, 1H), 7.15 (d, J = 8 Hz, 1H), 4.73 (q, J = 7 Hz, 1H), 3.92 (s, 3H), 1.55 (d, J = 7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 155.3, 136.8, 133.9, 130.1, 116.0, 113.6, 55.8, 52.0, 19.3.

HRMS CI): calcd for $C_{10}H_{12}NO_2$ [MH^+] 178.0863; found 178.0864.

IR (FT): ν_{max} 3071, 2971, 1680, 1602, 1493, 1267, 1057 cm^{-1}.

3-Ethyl-4-methoxyisoindolin-1-one (15)



Yield: 0.32 g (1.68 mmol, 84%); mp: 150–152 °C.

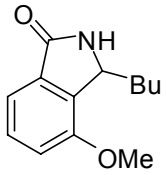
^{1}H NMR (500 MHz, DMSO-d_6): δ 7.72 (s, exch., 1 H, NH), 7.44 (app. t, J = 8 Hz, 1H), 7.23 (d, J = 8 Hz, 1H), 7.18 (d, J = 8 Hz, 1H), 4.57 (dd, J = 3, 7 Hz, 1H), 3.87 (s, 3H), 2.08 (ddq, J = 3, 14, 7 Hz, 1H), 1.59 (app. d quintet, J = 14, 7 Hz, 1H), 0.73 (app. t, J = 7 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 169.7, 155.1, 134.8, 134.4, 130.1, 115.0, 113.8, 56.1, 55.9, 25.0, 9.2.

HRMS (CI): calcd for $C_{11}H_{14}NO_2$ [MH^+] 192.1019; found 192.1018.

IR (FT): ν_{max} 3303, 2922, 1679, 1602, 1493, 1271, 1049 cm^{-1}.

3-Butyl-4-methoxyisoindolin-1-one (16)



Yield: 0.32 g (1.45 mmol, 72%); mp: 130–131 °C.

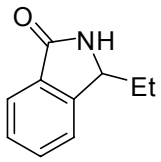
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57 (s, exch., 1H), 7.47–7.41 (m, 2H), 7.22 (dd, J = 2, 8 Hz, 1H), 4.69 (dd, J = 3, 7 Hz, 1H), 3.91 (s, 3H), 2.20 (m, 1H), 1.65 (m, 1H), 1.39–1.22 (m, 4H), 0.88 (t, J = 7 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.5, 155.3, 135.6, 134.2, 130.0, 116.1, 113.5, 56.4, 55.8, 32.4, 27.9, 23.0, 14.3.

HRMS (CI): calcd for $C_{13}H_{18}NO_2$ [MH^+] 220.1332; found 220.1332.

IR (FT): ν_{max} 3314, 2955, 1678, 1600, 1490, 1276, 1053 cm^{-1}.

3-Ethylisoindolin-1-one (18)



Yield: 0.25 g (1.55 mmol, 77%); mp: 103–105 °C (lit.[5] 104–105 °C).

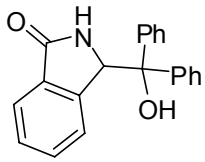
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46 (br, exch., 1H), 7.76 (d, *J* = 8 Hz, 1H), 7.46 (app. dt, *J* = 2, 8 Hz, 1H), 7.35 (app. t, *J* = 8 Hz, 1H), 7.21 (d, *J* = 8 Hz, 1H), 4.52 (dd, *J* = 5, 7 Hz, 1H), 1.94 (ddq, *J* = 5, 14, 7 Hz, 1H), 1.62 (app. d quintet, *J* = 14, 7 Hz, 1H), 0.87 (app. t, *J* = 7 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.6, 147.6, 132.3, 131.7, 128.5, 123.6, 122.4, 58.2, 27.3, 9.5.

HRMS (ACPI): calcd for $C_{10}H_{12}NO$ [MH^+] 162.0913; found 162.0919.

IR (FT): ν_{max} 3312, 2945, 1677, 1589, 1472, 1267, 1043 cm^{-1}.

3-(Hydroxydiphenylmethyl)isoindolin-1-one (19)



Yield: 0.47 g (1.49 mmol, 74%); mp: 189–191 °C.

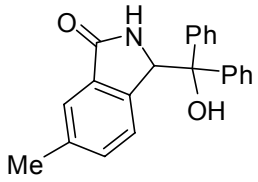
^{1}H NMR (500 MHz, DMSO-d_6): δ 8.20 (br, exch., 1H), 7.60 (d, *J* = 8 Hz, 1H), 7.52 (app. t, *J* = 8 Hz, 1H), 7.35 (d, *J* = 8 Hz, 1H), 7.30–7.00 (m, 11H), 6.44 (d, *J* = 6 Hz, 1H), 6.19 (s, exch., 1H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 170.3, 145.2, 145.1, 141.2, 134.2, 130.9, 129.6, 128.3, 128.2, 127.4, 127.3, 126.4, 126.3, 124.6, 122.8, 79.1, 67.5. The two diastereoisomeric phenyl groups appeared as separated signals.

HRMS (ES^+): calcd for $C_{21}H_{18}NO_2$ [MH^+] 316.1338; found 316.1338.

IR (FT): ν_{max} 3202, 2990, 1678, 1590, 1491, 1252, 1025 cm^{-1}.

3-(Hydroxydiphenylmethyl)-6-methylisoindolin-1-one (20)



Yield: 0.56 g (1.70 mmol, 85%); mp: 236–264 °C.

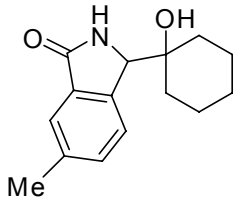
^{1}H NMR (500 MHz, DMSO-d_6): δ 8.12 (br, exch., 1H), 7.61–7.19 (m, 11H), 7.11 (d, *J* = 8 Hz, 1H), 6.26 (d, *J* = 8 Hz, 1H), 5.81 (s, exch., 1H), 5.72 (s, 1H), 2.33 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 172.40, 145.5, 145.2, 142.4, 137.6, 134.4, 131.8, 128.3, 128.2, 127.3, 127.2, 127.1, 127.0, 124.3, 123.0, 79.0, 63.4, 21.2. The two diastereoisomeric phenyl groups appeared as separated signals.

HRMS (ES^+): calcd for $C_{22}H_{20}NO_2$ [MH^+] 330.1494; found 330.1487.

IR (FT): ν_{max} 3278, 3000, 1678, 1591, 1493, 1251, 1040 cm^{-1}.

3-(1-Hydroxycyclohexyl)-6-methylisoindolin-1-one (21)



Yield: 0.35 g (1.43 mmol, 72%); mp: 235–237 °C.

^{1}H NMR (500 MHz, DMSO-d_6): δ 7.72 (br, exch., 1H), 6.56 (d, J = 8 Hz, 1H), 6.53 (s, 1H), 6.42 (d, J = 8 Hz, 1H), 4.00 (s, exch., 1H), 3.42 (s, 1H), 2.27 (s, 3H), 0.65–0.33 (m, 10H).

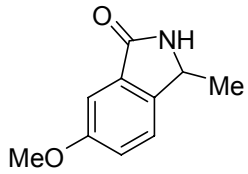
Compound **21** was only very slightly soluble in DMSO so that its ^{13}C NMR spectrum was not recorded.

HRMS (ES$^+$): calcd for $C_{15}H_{20}NO_2$ [MH$^+$] 264.1494; found 246.1498.

IR (FT): ν_{max} 3307, 2943, 1681, 1596, 1472, 1246, 1043 cm^{-1}.

Anal calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.81; H, 7.85; N, 5.80%.

6-Methoxy-3-methylisoindolin-1-one (22)



Yield: 0.27 g (1.52 mmol, 76%); mp: 160–161 °C.

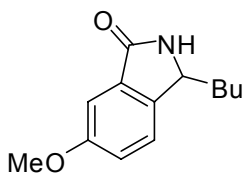
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (br, exch., 1H), 7.33 (d, J = 2 Hz, 1H), 7.31 (d, J = 8 Hz, 1H), 7.13 (dd, J = 2, 8 Hz, 1H), 4.66 (q, J = 7 Hz, 1H), 3.86 (s, 3H), 1.48 (d, J = 7 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.2, 160.0, 141.3, 133.0, 123.1, 120.2, 106.3, 55.7, 52.4, 20.4.

HRMS (ES$^+$): calcd for $C_{10}H_{12}NO_2$ [MH$^+$] 178.0863; found 178.0862.

IR (FT): ν_{max} 3165, 2979, 1679, 1600, 1487, 1261, 1046 cm^{-1}.

3-Butyl-6-methoxyisoindolin-1-one (23)



Yield: 0.34 g (1.55 mmol, 77%); mp: 145–147 °C.

^{1}H NMR (500 MHz, DMSO-d_6): δ 8.71 (br, exch., 1H), 7.44 (d, J = 8 Hz, 1H), 7.15–7.03 (m, 2H), 4.48 (dd, J = 3, 7 Hz, 1H), 3.81 (s, 3H), 1.84 (m, 1H), 1.48 (m, 1 H, 1H), 1.31–1.21 (m, 4H), 0.84 (t, J = 7 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 169.6, 159.5, 140.4, 134.3, 124.3, 119.4, 106.5, 56.0, 55.9, 34.4, 27.3, 22.6, 14.3.

HRMS (ES^+): calcd for $C_{13}H_{18}NO_2$ [MH^+] 220.1338; found 220.1347.

IR (FT): ν_{max} 3305, 2967, 1680, 1597, 1477, 1277, 1051 cm^{-1}.

References

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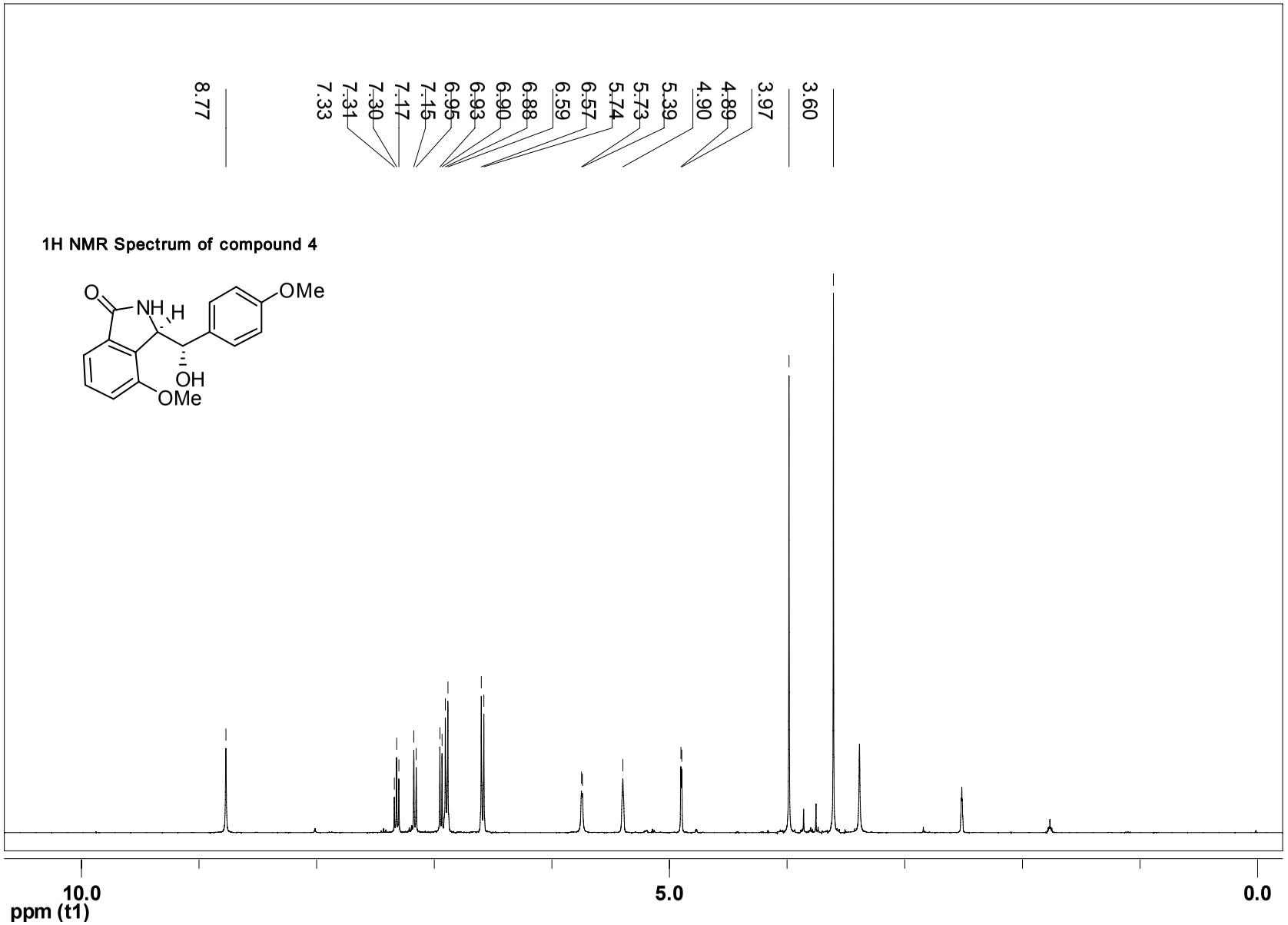
3 S. C. Watson and J. F. Eastham, *J. Organomet. Chem.*, 1967, **9**, 165.

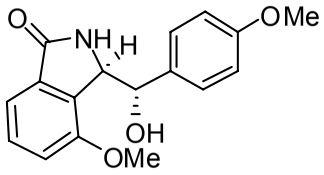
4 (*a*) *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; Longman: Harlow, 1989; (*b*) D. D. Perrin and W. L. F. Armarego, *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon: Oxford, 1988.

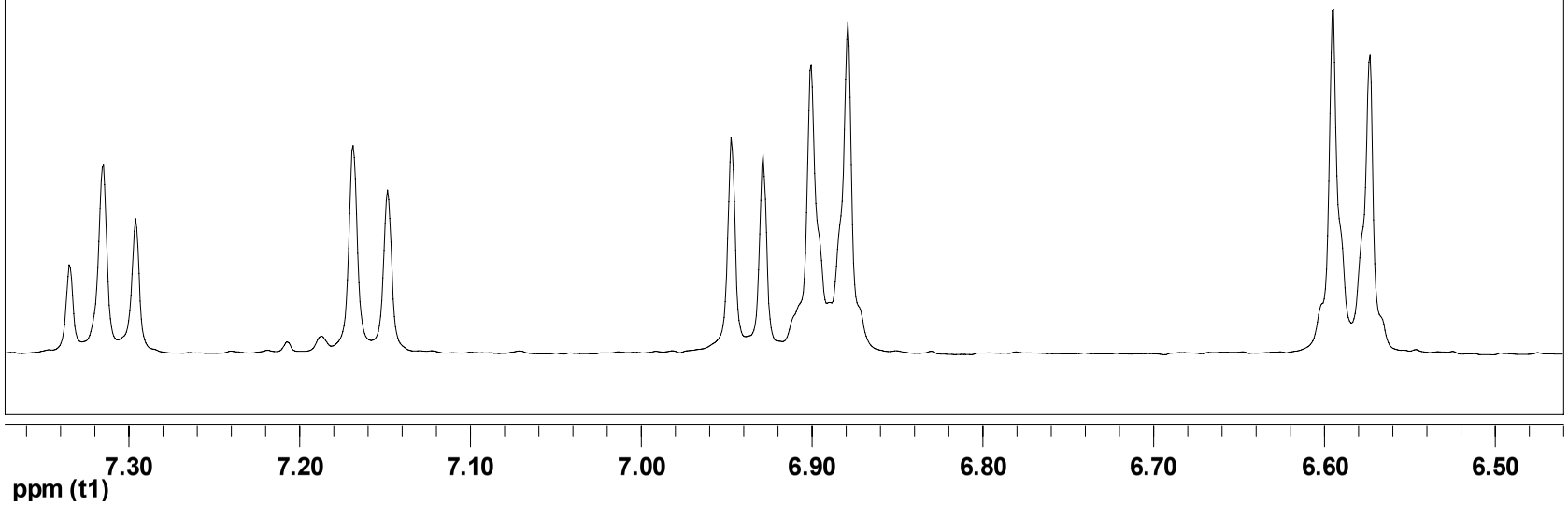
5 E. Deniau and D. Enders, *Tetrahedron*, 2001, **57**, 2581.

NMR Spectra for Some of the Synthesised Compounds

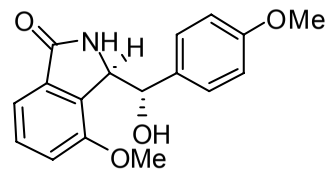

8.77
7.33
7.31
7.30
7.17
7.15
6.95
6.93
6.90
6.88
6.59
6.57
5.74
5.73
5.39
4.90
4.89
3.97
3.60
1H NMR Spectrum of compound 4
O
NH
H
OMe
OH
OMe
10.0
ppm (t1)
5.0
0.0

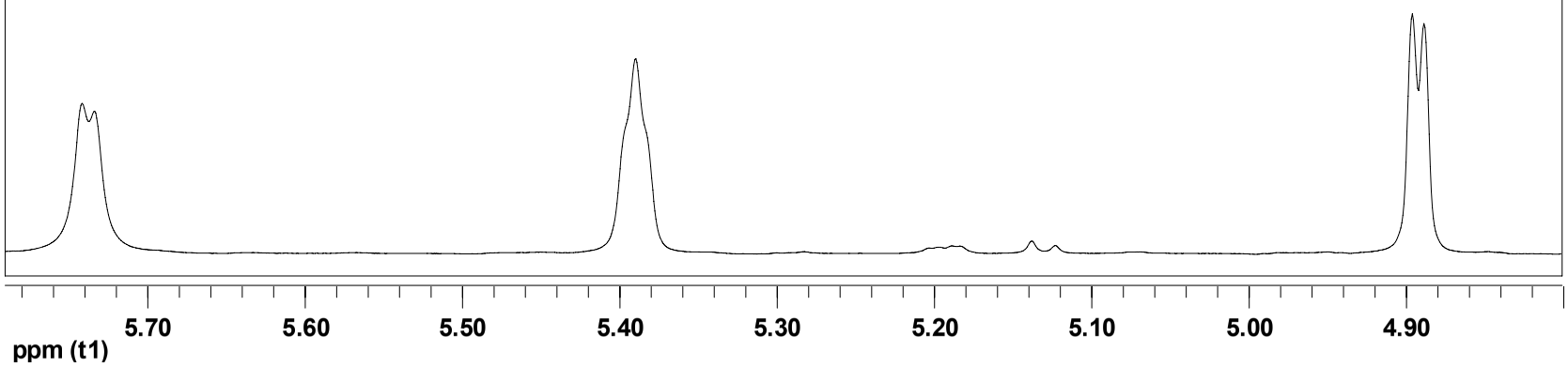
Expansion - 1H NMR Spectrum of compound 4

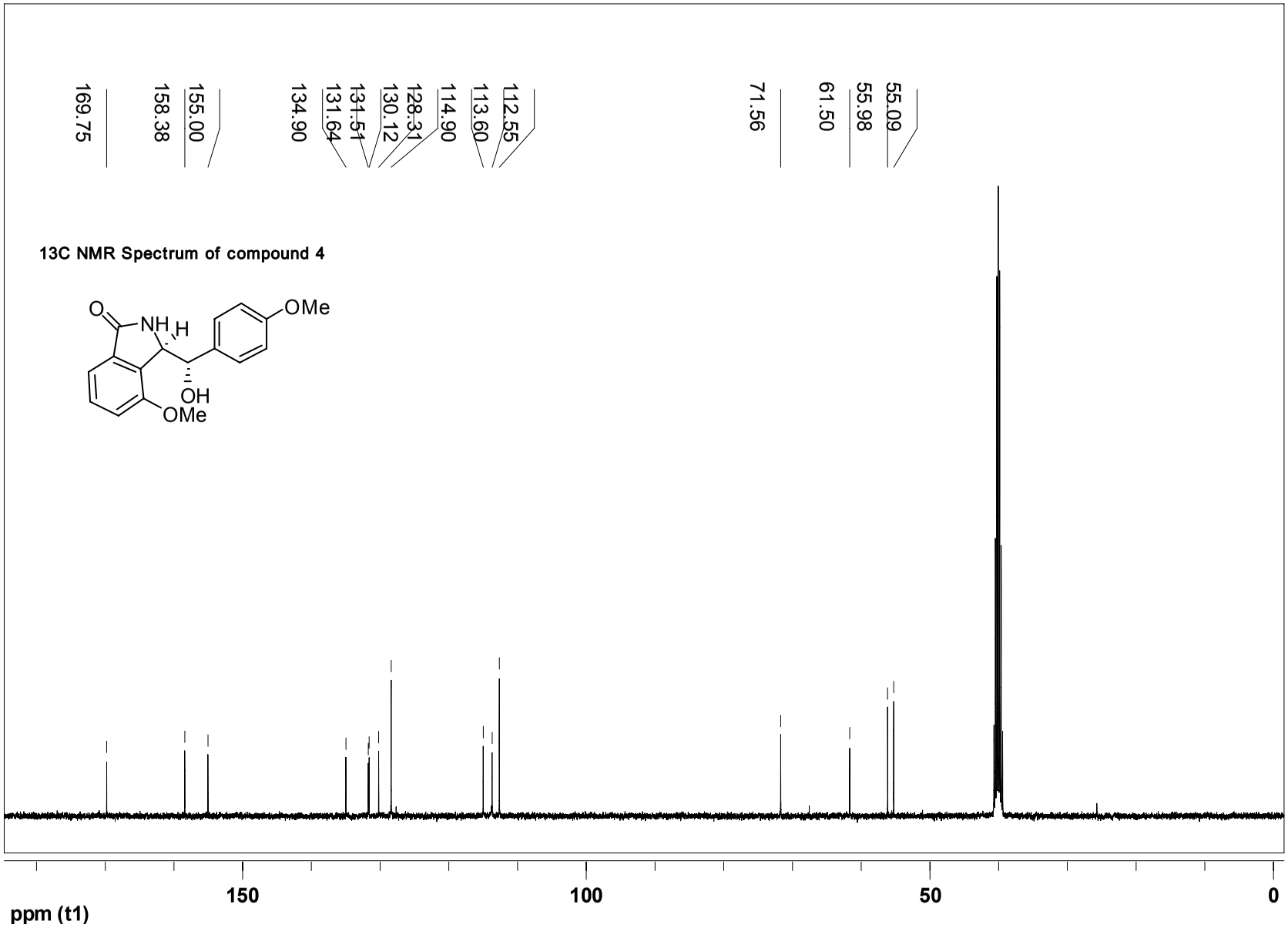


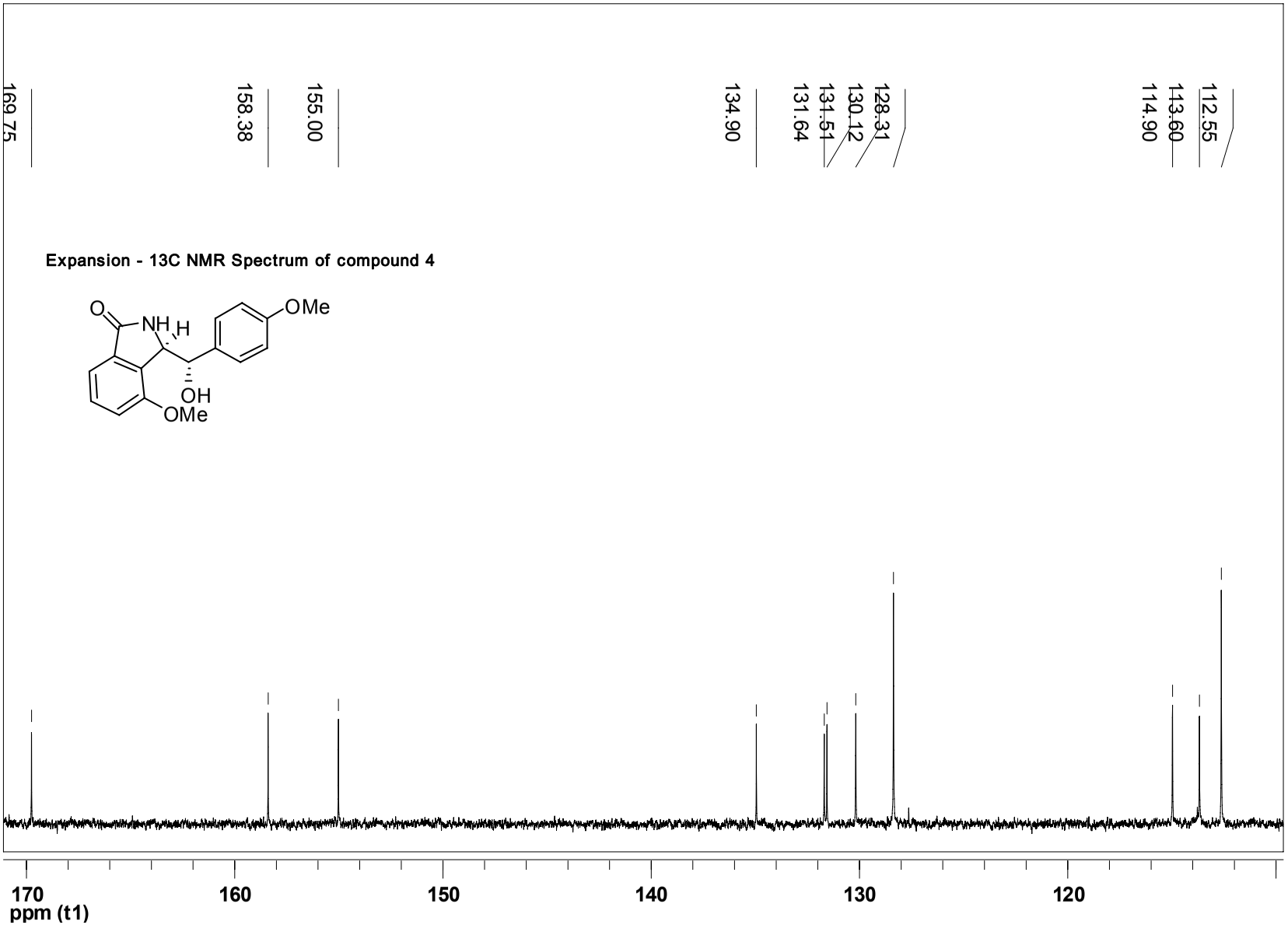


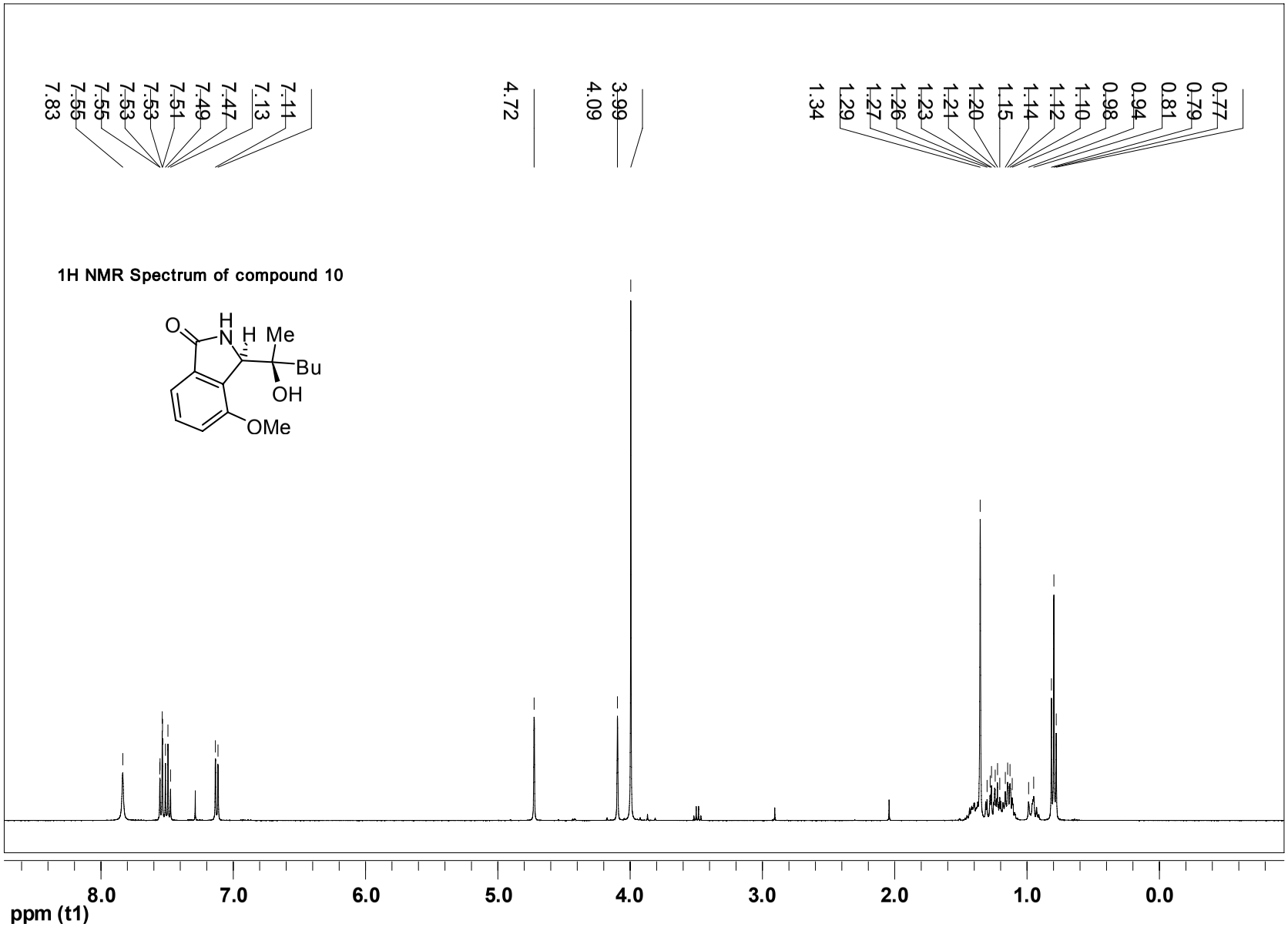
Expansion - 1H NMR Spectrum of compound 4



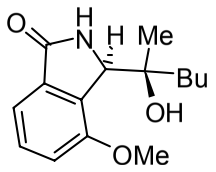


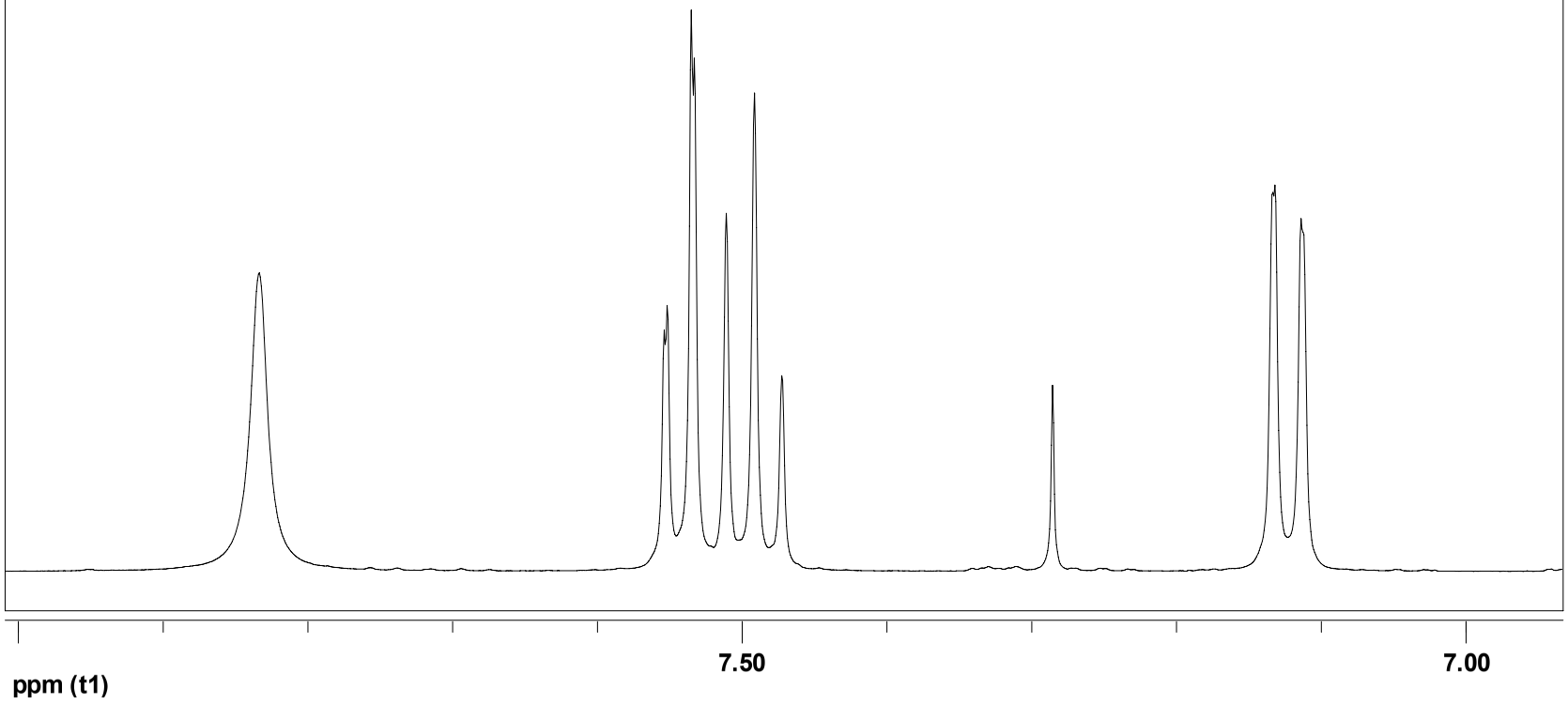

169.75
158.38
155.00
134.90
131.64
131.51
130.12
128.31
114.90
113.60
112.55
71.56
61.50
55.98
55.09
13C NMR Spectrum of compound 4
O
NH
H
OMe
OH
OMe
150
100
50
0
ppm (t1)

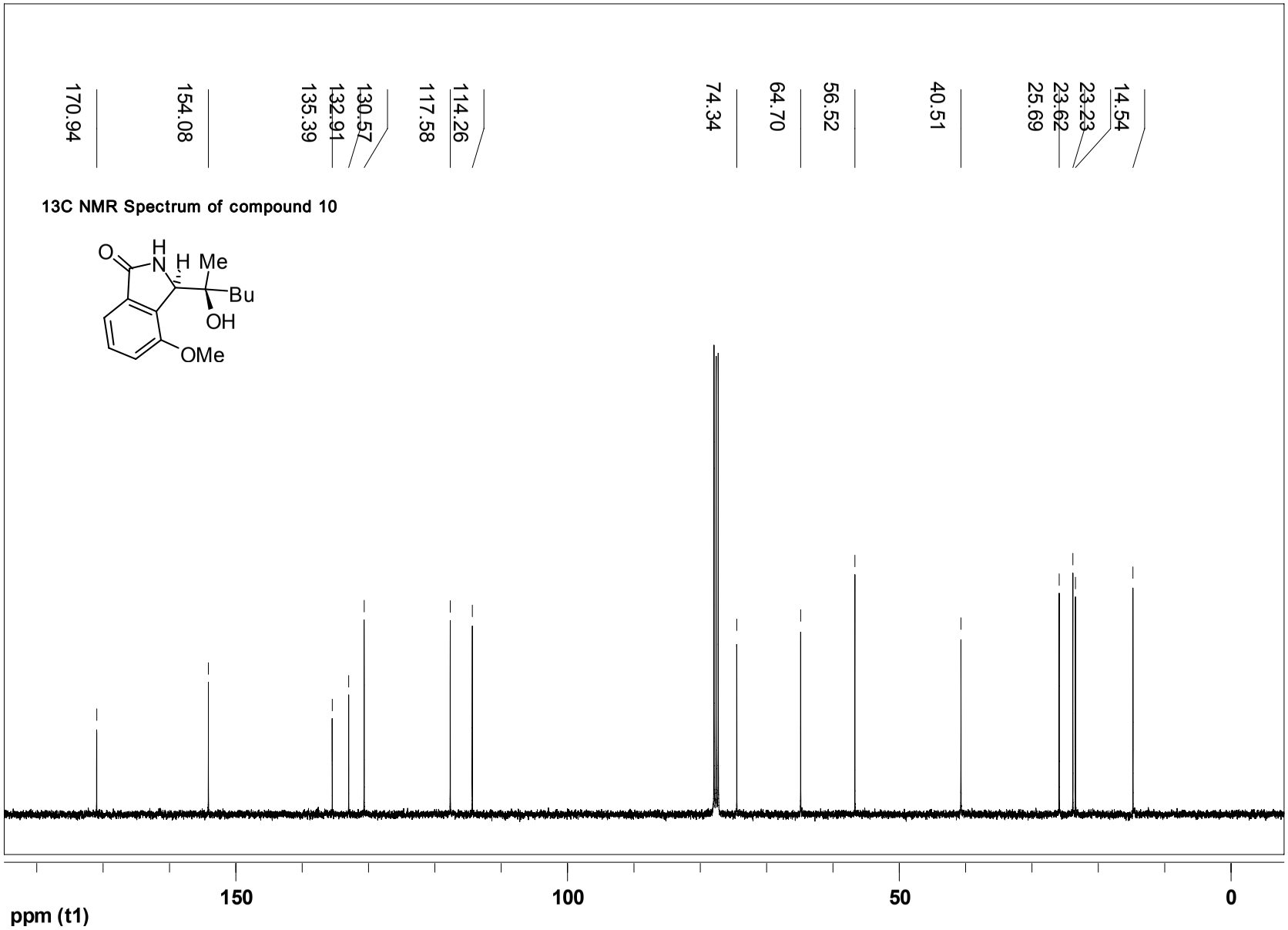

169.75
158.38
155.00
134.90
131.64
131.51
130.12
128.31
114.90
113.60
112.55
Expansion - 13C NMR Spectrum of compound 4
O
NH
H
OMe
OH
OMe
170
160
150
140
130
120
ppm (t1)

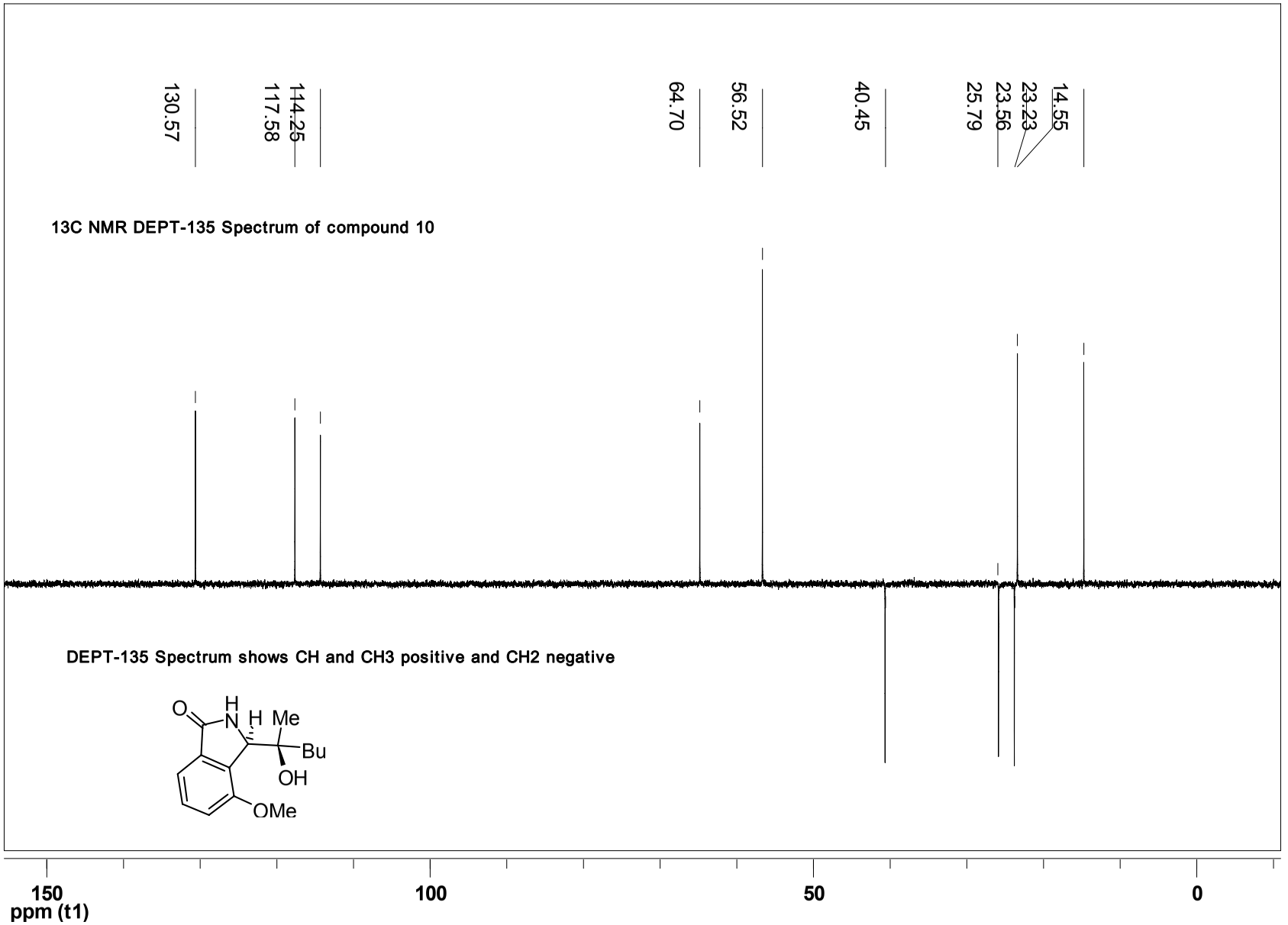

7.83
7.55
7.55
7.53
7.53
7.51
7.49
7.47
7.13
7.11
4.72
4.09
3.99
1.34
1.29
1.27
1.26
1.23
1.21
1.20
1.15
1.14
1.12
1.10
0.98
0.94
0.81
0.79
0.77
1H NMR Spectrum of compound 10
O
H
N
H
Me
Bu
OH
OMe
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

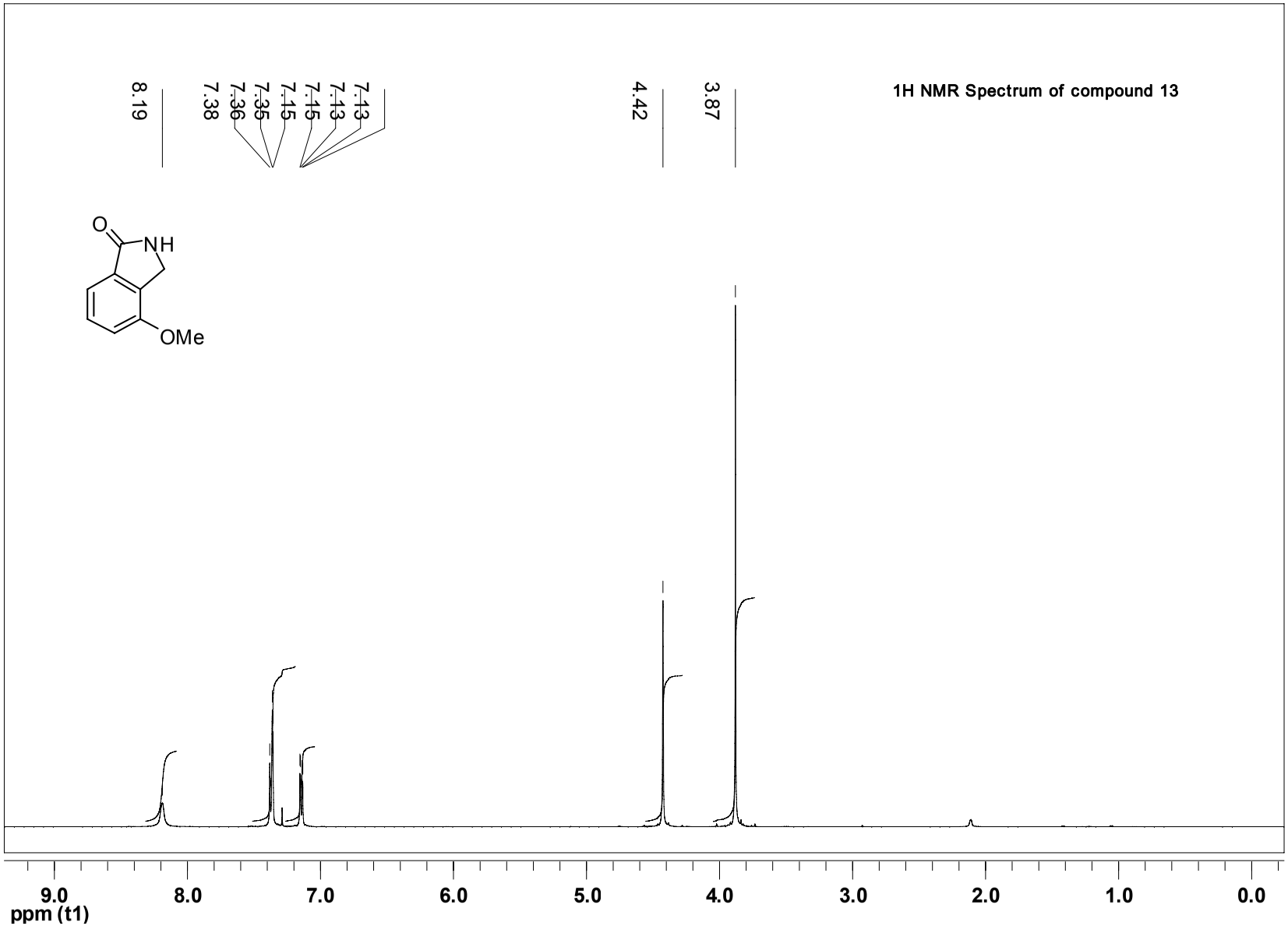
Expansion - 1H NMR Spectrum of compound 10

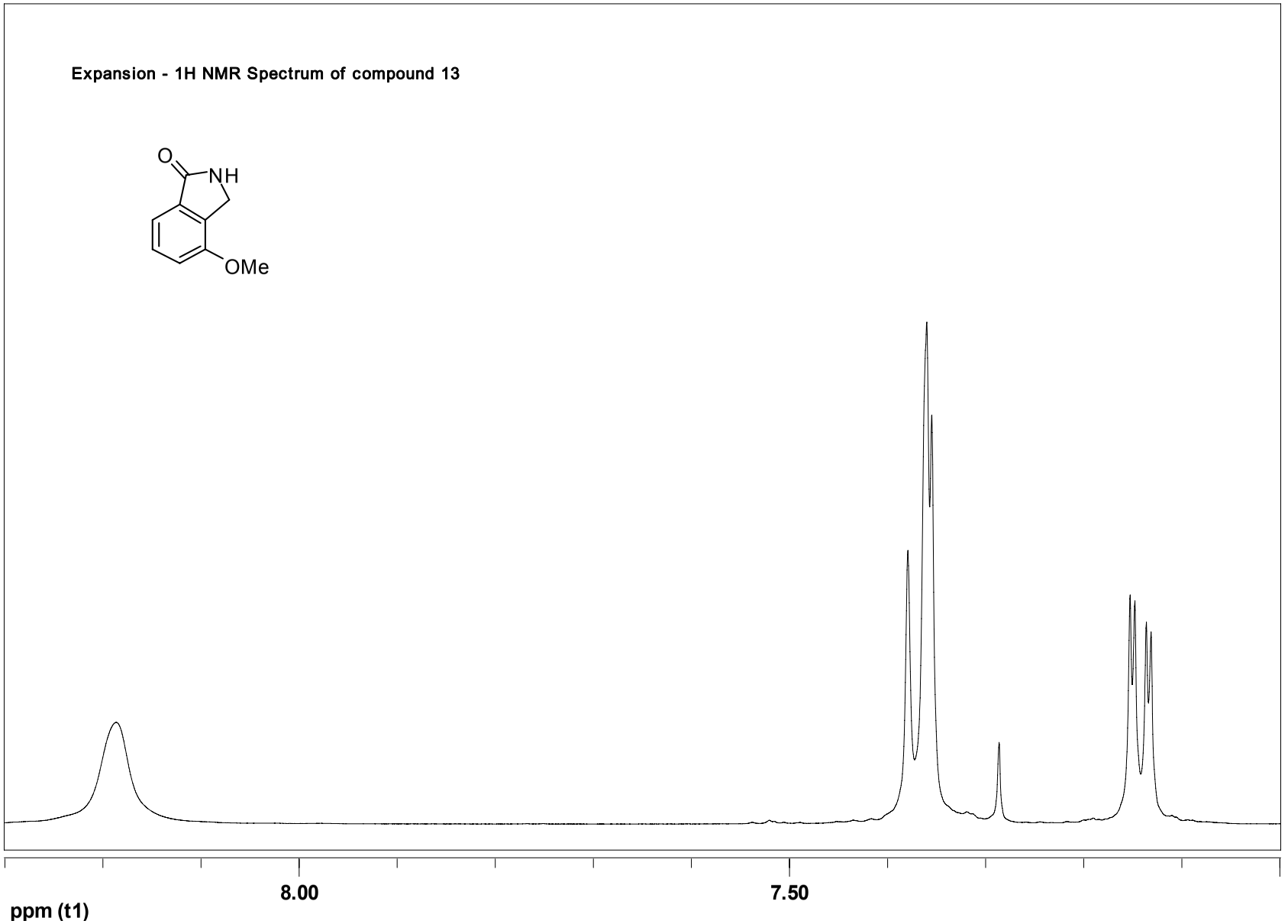


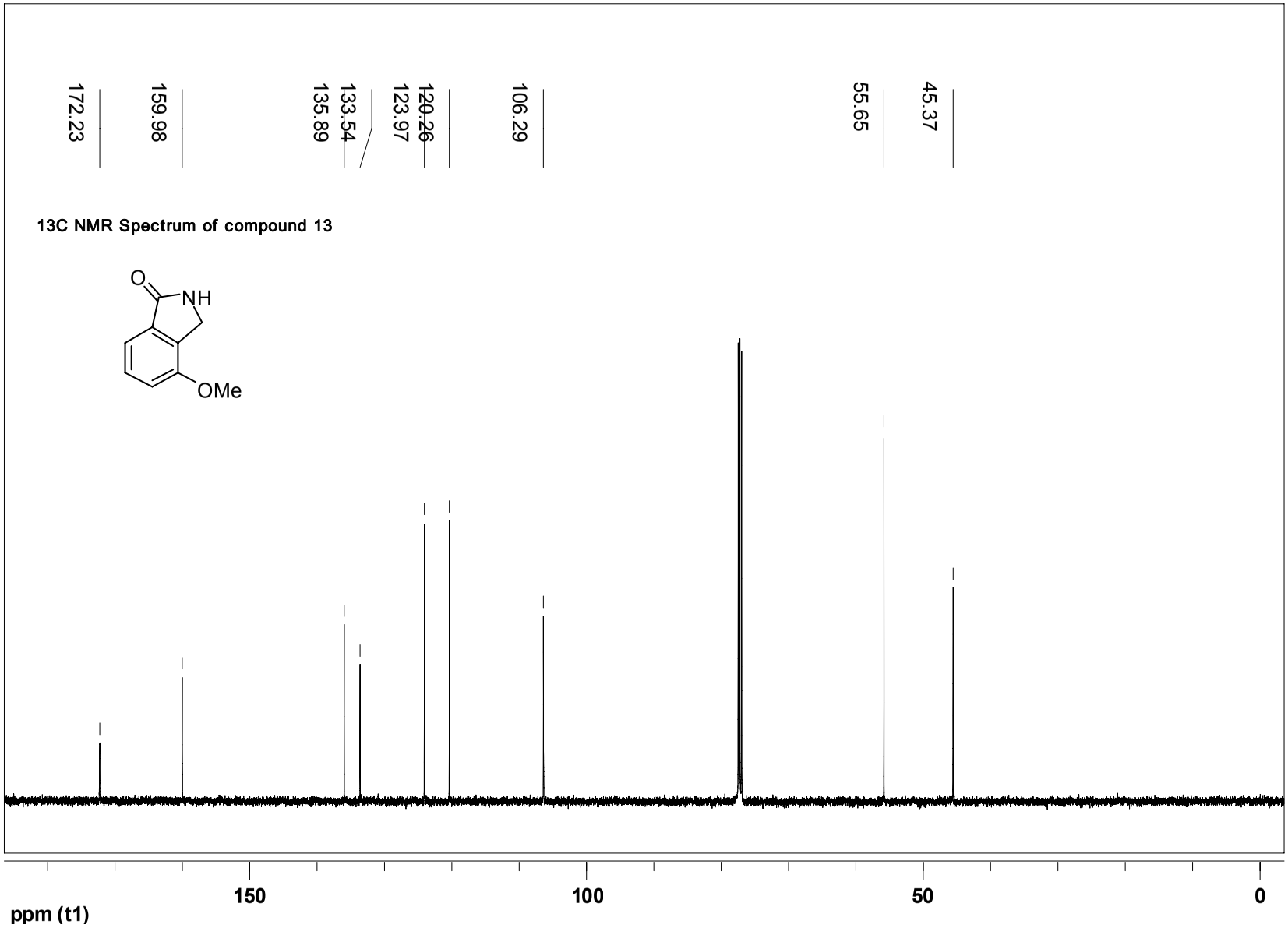


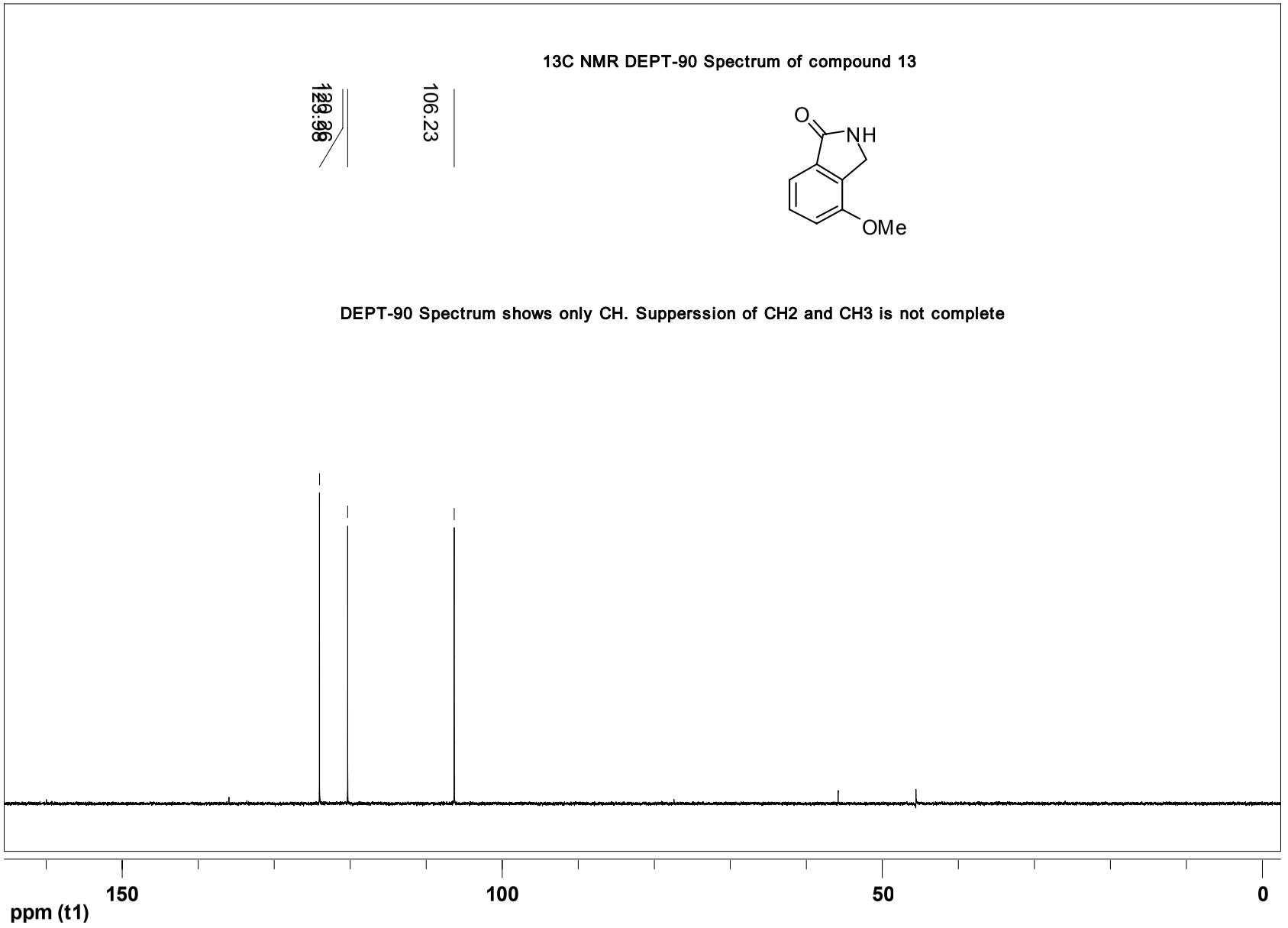

170.94
154.08
135.39
132.91
130.57
117.58
114.26
74.34
64.70
56.52
40.51
25.69
23.62
23.23
14.54
13C NMR Spectrum of compound 10
O
H
N
H
Me
Bu
OH
OMe
150
100
50
0
ppm (t1)

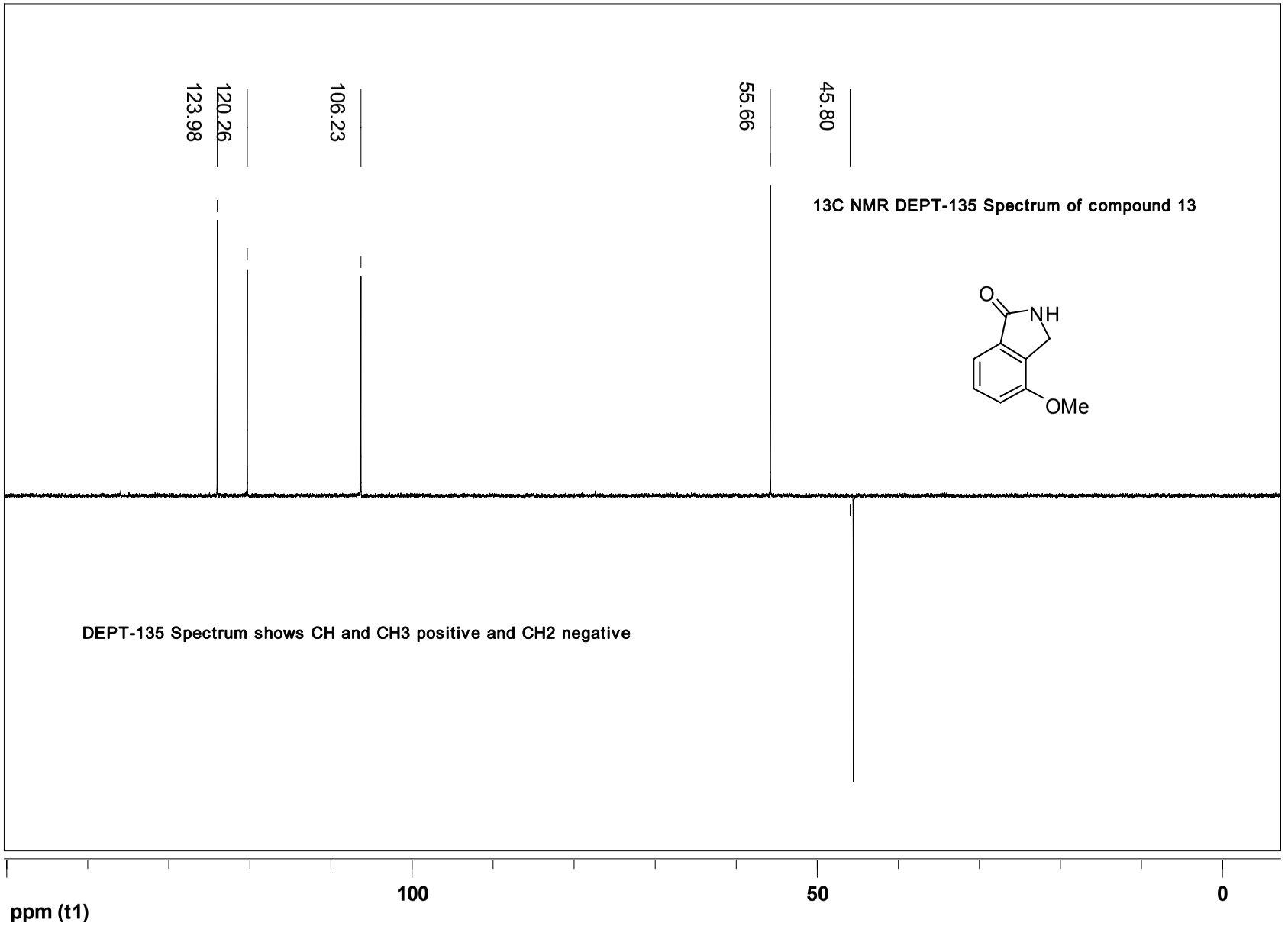

130.57
117.58
114.25
64.70
56.52
40.45
25.79
23.56
23.23
14.55
13C NMR DEPT-135 Spectrum of compound 10
DEPT-135 Spectrum shows CH and CH3 positive and CH2 negative
O
H
N
H
Me
Bu
OH
OMe
150
ppm (t1)
100
50
0

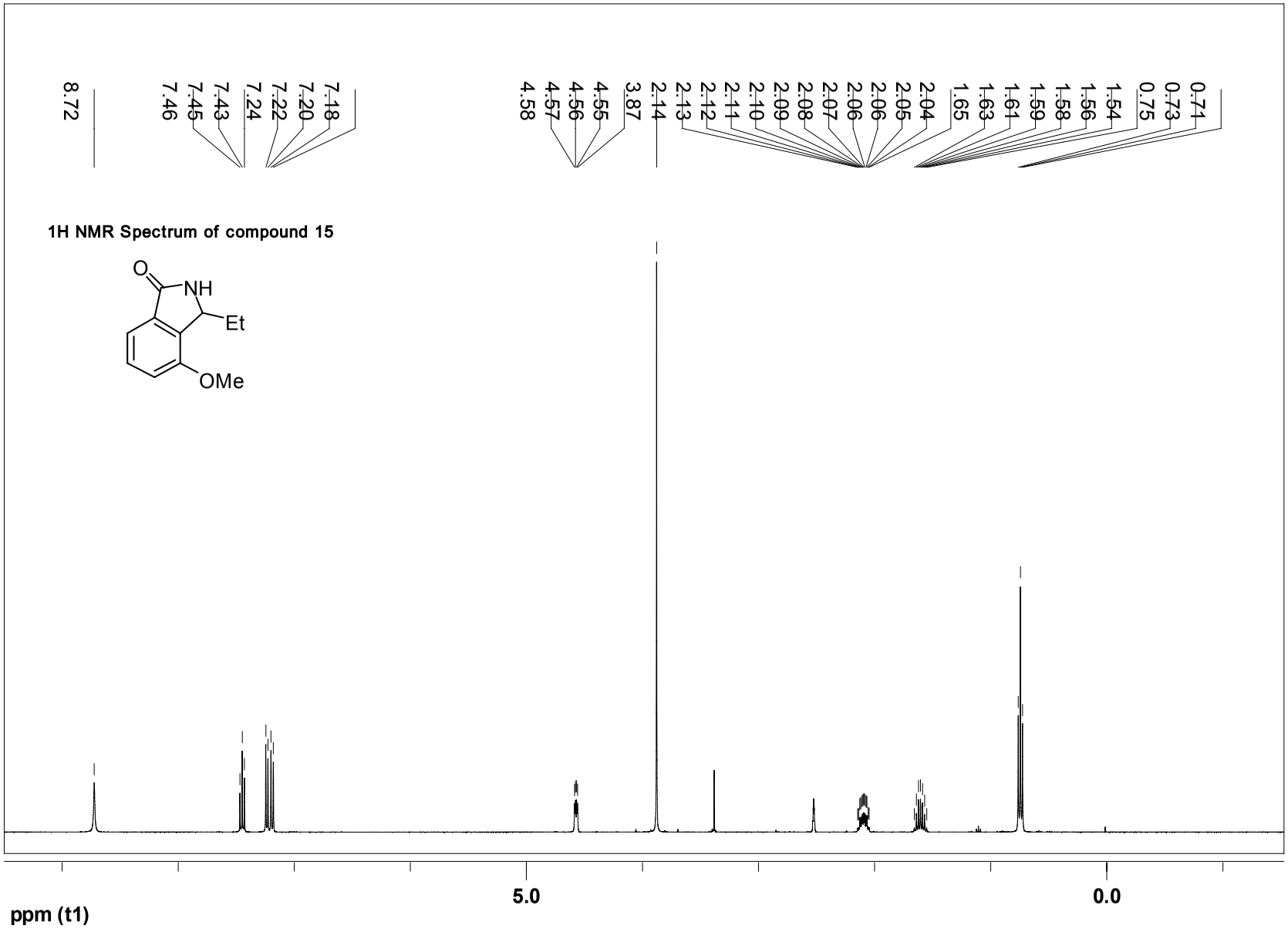

1H NMR Spectrum of compound 13
8.19
7.38
7.36
7.35
7.15
7.15
7.13
7.13
7.13
4.42
3.87
O
NH
OMe
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

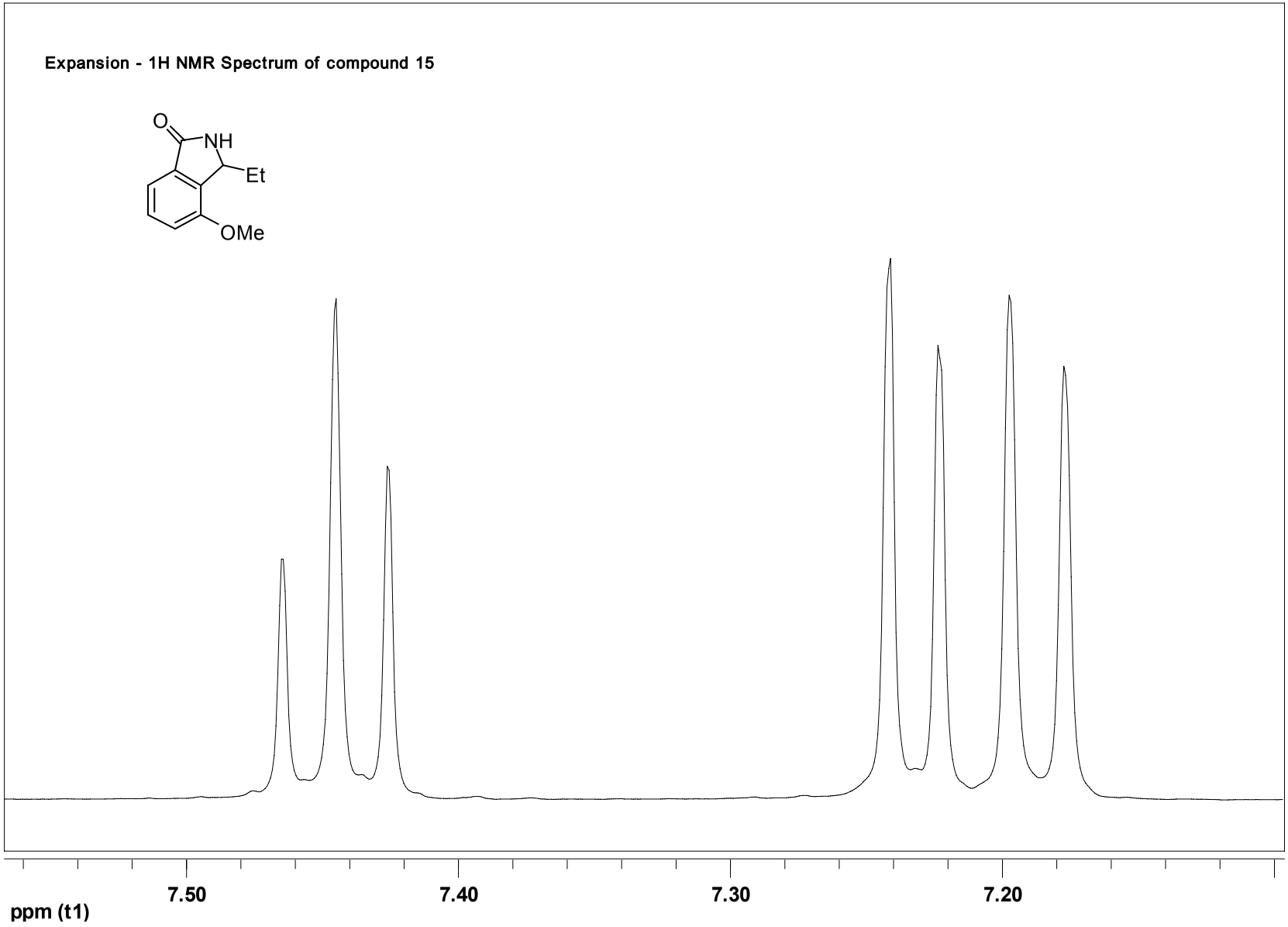

Expansion - 1H NMR Spectrum of compound 13
O
NH
OMe
8.00
7.50
ppm (t1)

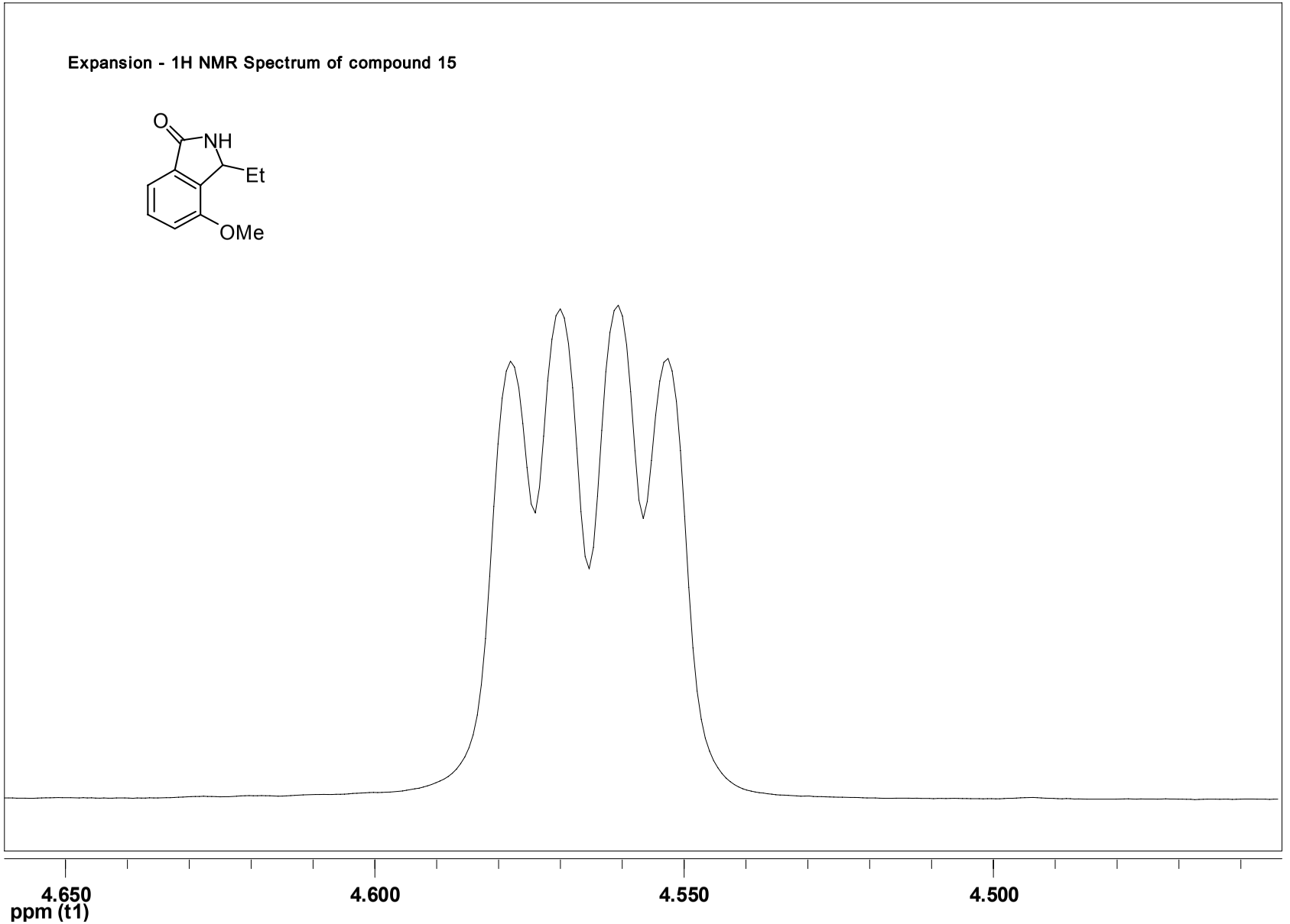

172.23
159.98
135.89
133.54
123.97
120.26
106.29
55.65
45.37
13C NMR Spectrum of compound 13
O
NH
OMe
150
100
50
0
ppm (t1)

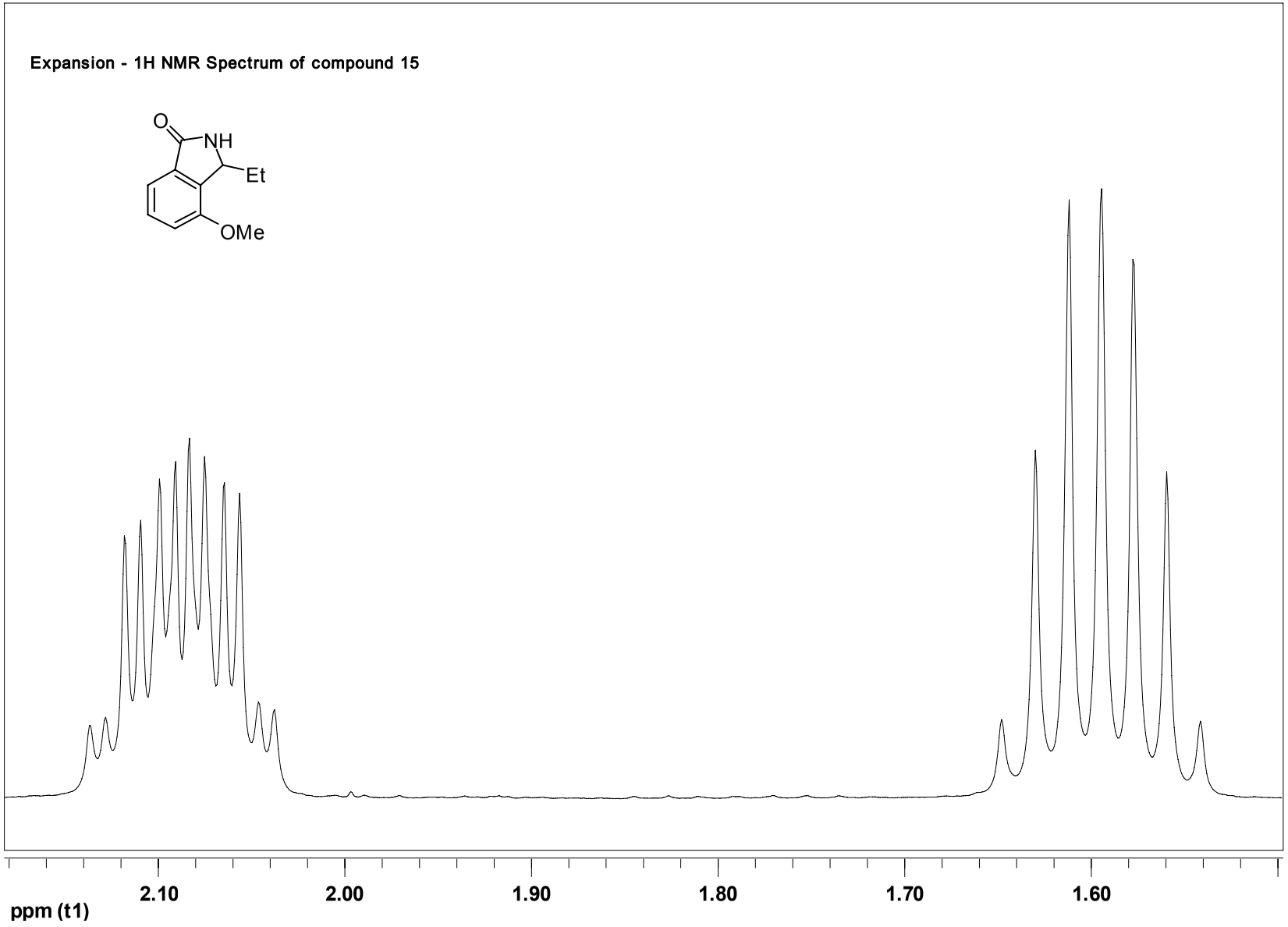

13C NMR DEPT-90 Spectrum of compound 13
129.96
129.86
106.23
O
NH
OMe
DEPT-90 Spectrum shows only CH. Supperssion of CH2 and CH3 is not complete
150
100
50
0
ppm (t1)

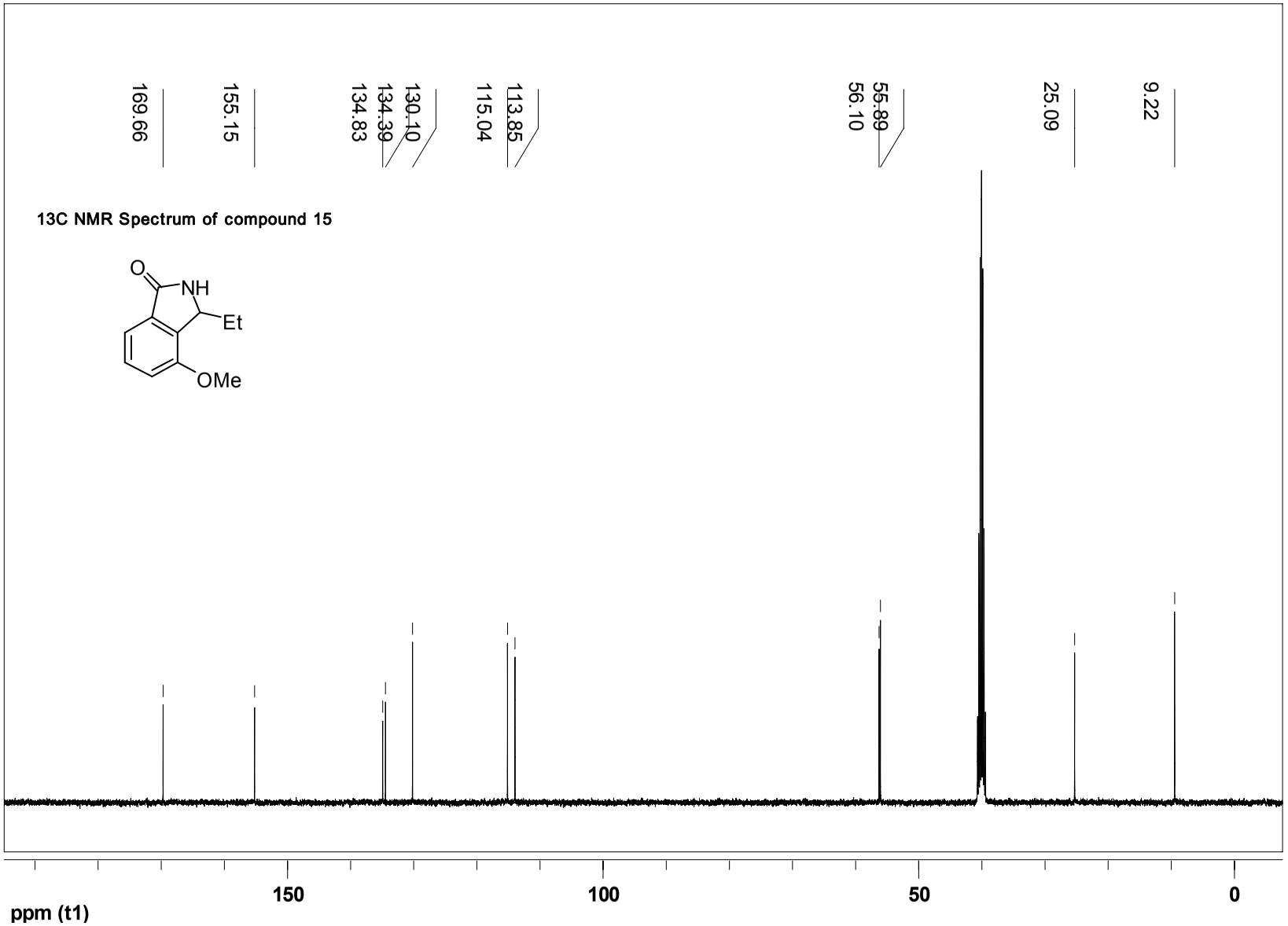

123.98
120.26
106.23
55.66
45.80
13C NMR DEPT-135 Spectrum of compound 13
O
NH
OMe
DEPT-135 Spectrum shows CH and CH3 positive and CH2 negative
100
50
0
ppm (t1)

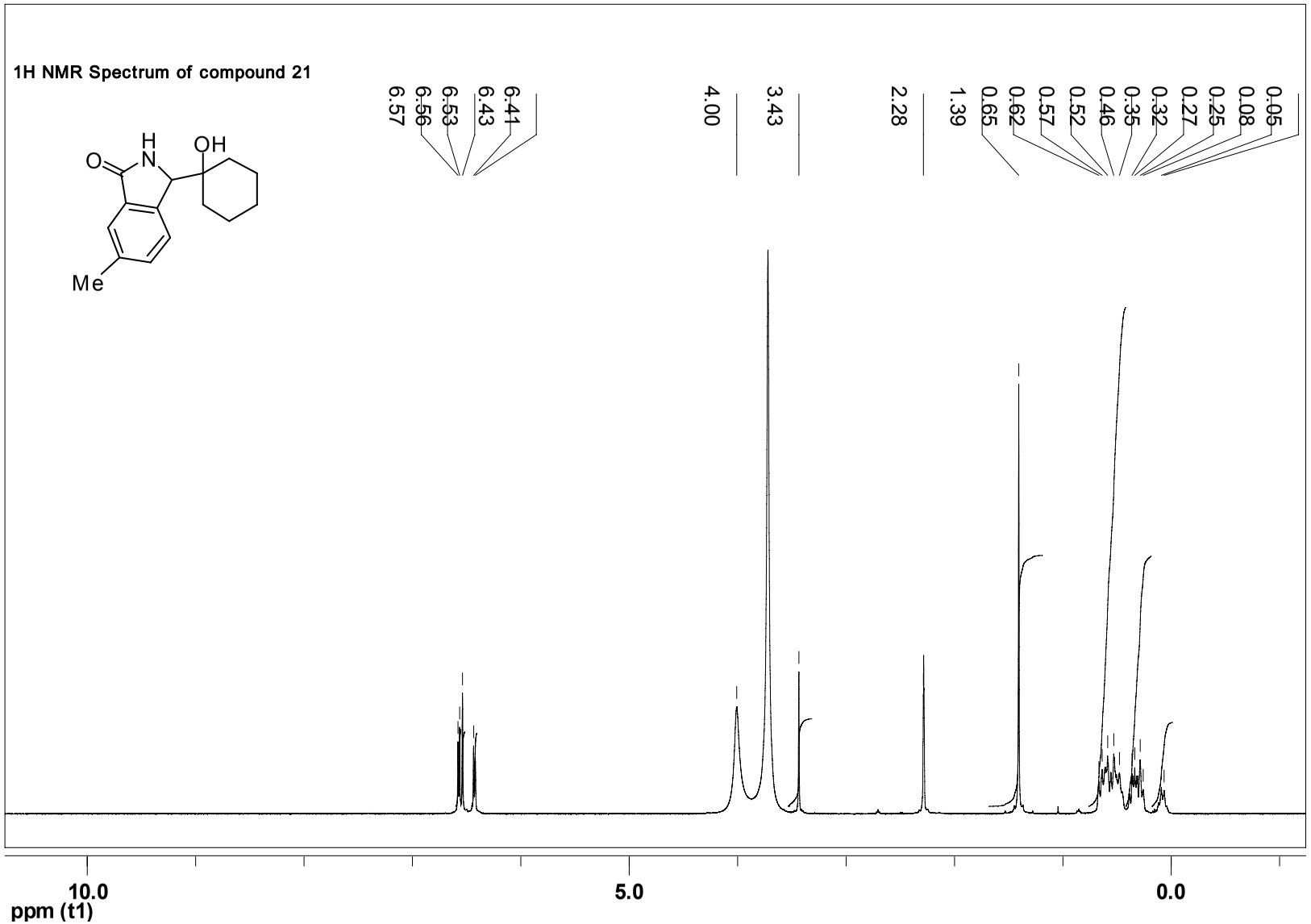

8.72
7.46
7.45
7.43
7.24
7.22
7.20
7.18
4.58
4.57
4.56
4.55
3.87
2.14
2.13
2.12
2.11
2.10
2.09
2.08
2.07
2.06
2.06
2.05
2.04
1.65
1.63
1.61
1.59
1.58
1.56
1.54
0.75
0.73
0.71
1H NMR Spectrum of compound 15
O
NH
Et
OMe
5.0
0.0
ppm (t1)

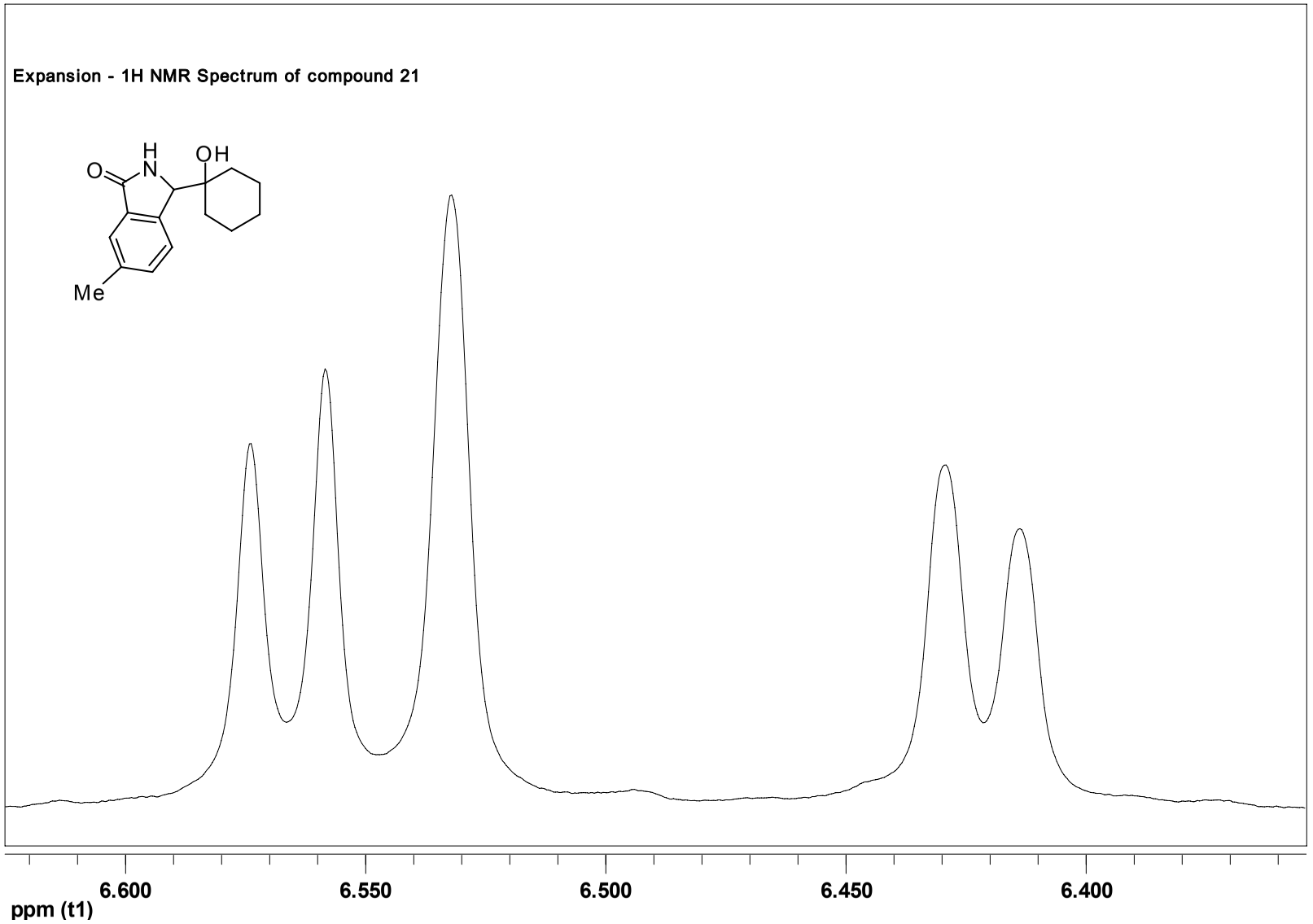

Expansion - 1H NMR Spectrum of compound 15
O
NH
Et
OMe
7.50
7.40
7.30
7.20
ppm (t1)

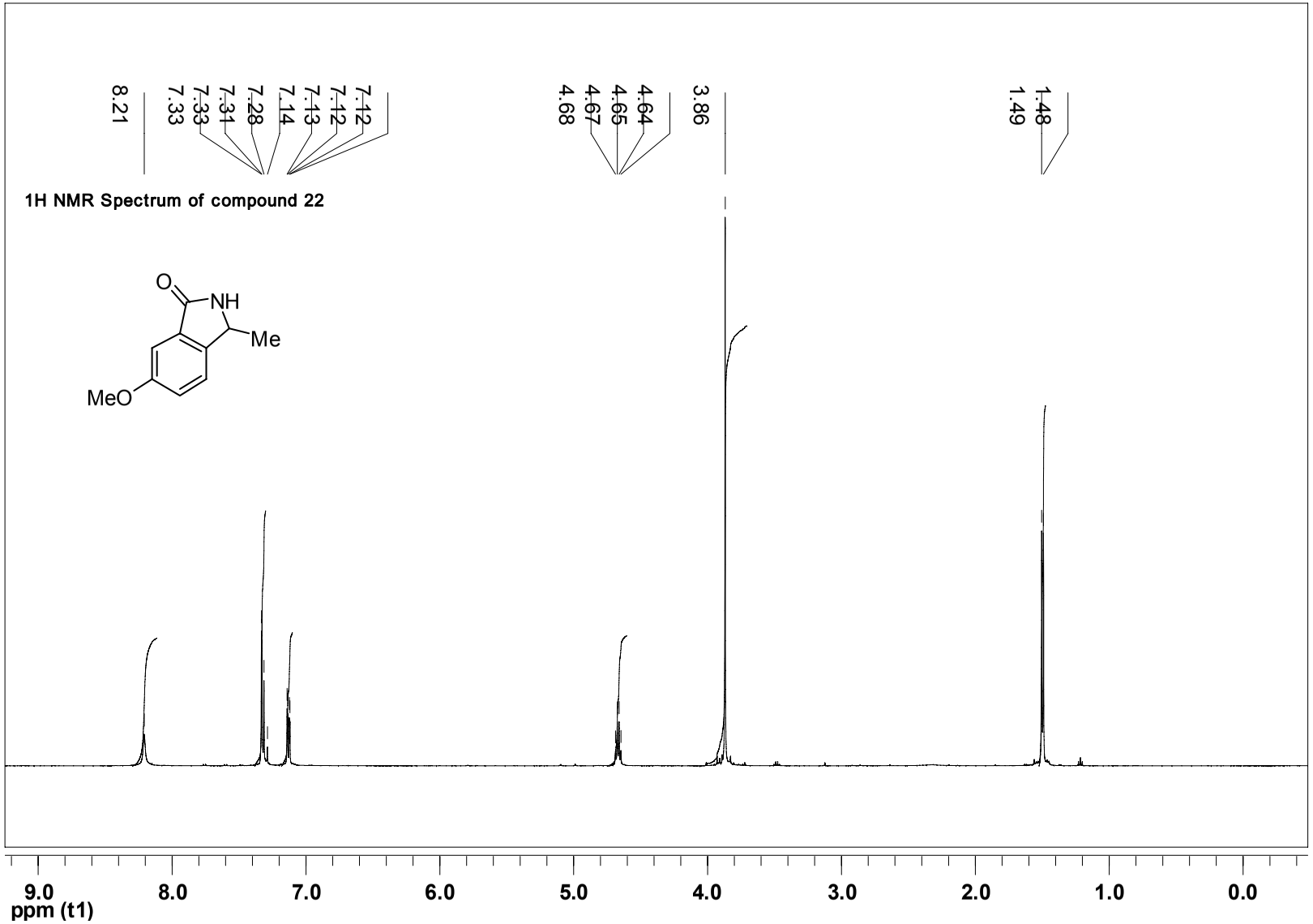

Expansion - 1H NMR Spectrum of compound 15
O
NH
Et
OMe
4.650
ppm (t1)
4.600
4.550
4.500


Expansion - 1H NMR Spectrum of compound 15
O
NH
Et
OMe
2.10
2.00
1.90
1.80
1.70
1.60
ppm (t1)

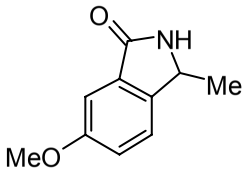

169.66
155.15
134.83
134.39
130.10
115.04
113.85
56.10
55.89
25.09
9.22
13C NMR Spectrum of compound 15
O
NH
Et
OMe
150
100
50
0
ppm (t1)


1H NMR Spectrum of compound 21
6.57
6.56
6.53
6.43
6.41
4.00
3.43
2.28
1.39
0.65
0.62
0.57
0.52
0.46
0.35
0.32
0.27
0.25
0.08
0.05
O
H
N
OH
Me
10.0
5.0
0.0
ppm (t1)

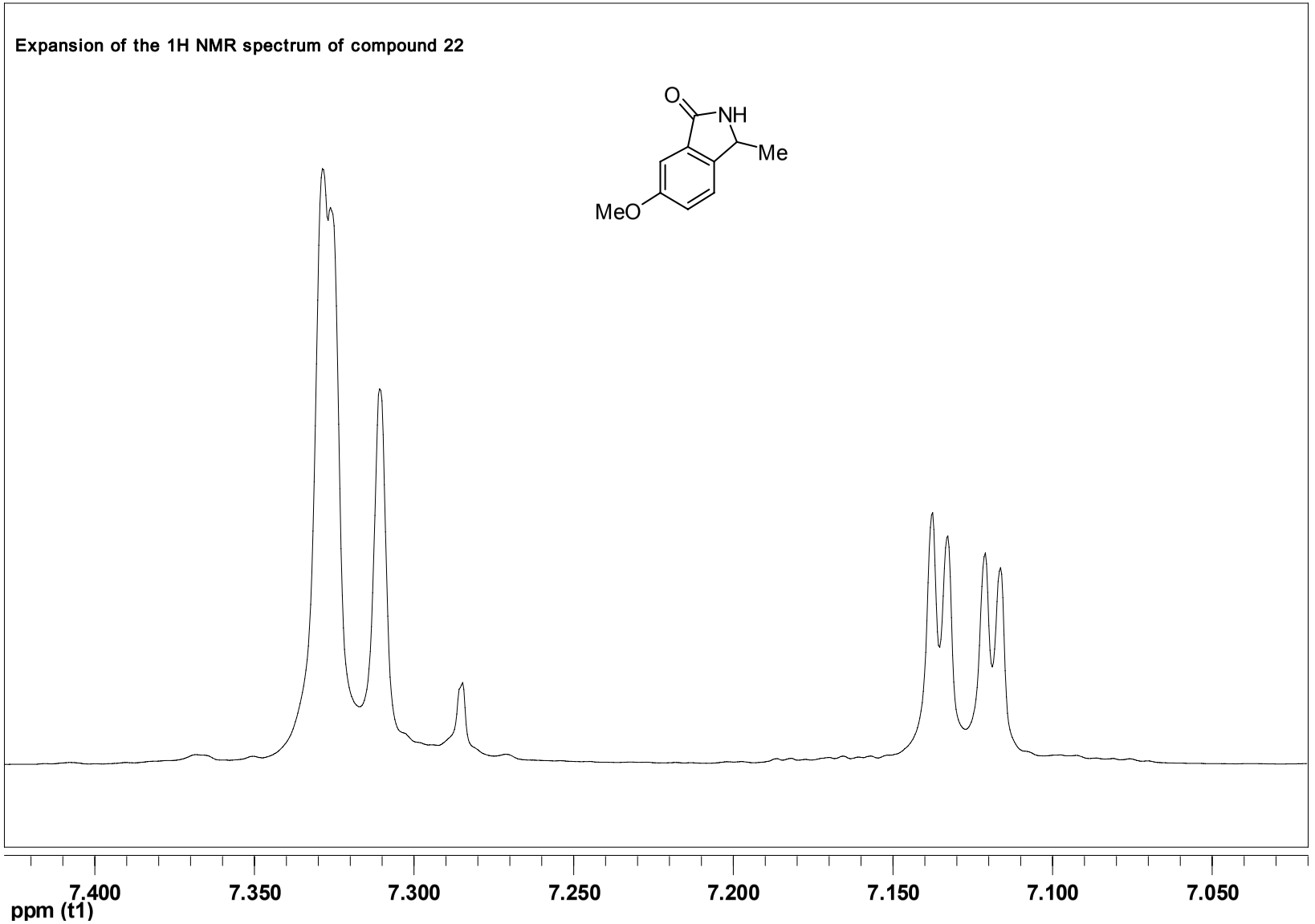

Expansion - 1H NMR Spectrum of compound 21
H
N
O
OH
Me
6.600
6.550
6.500
6.450
6.400
ppm (t1)

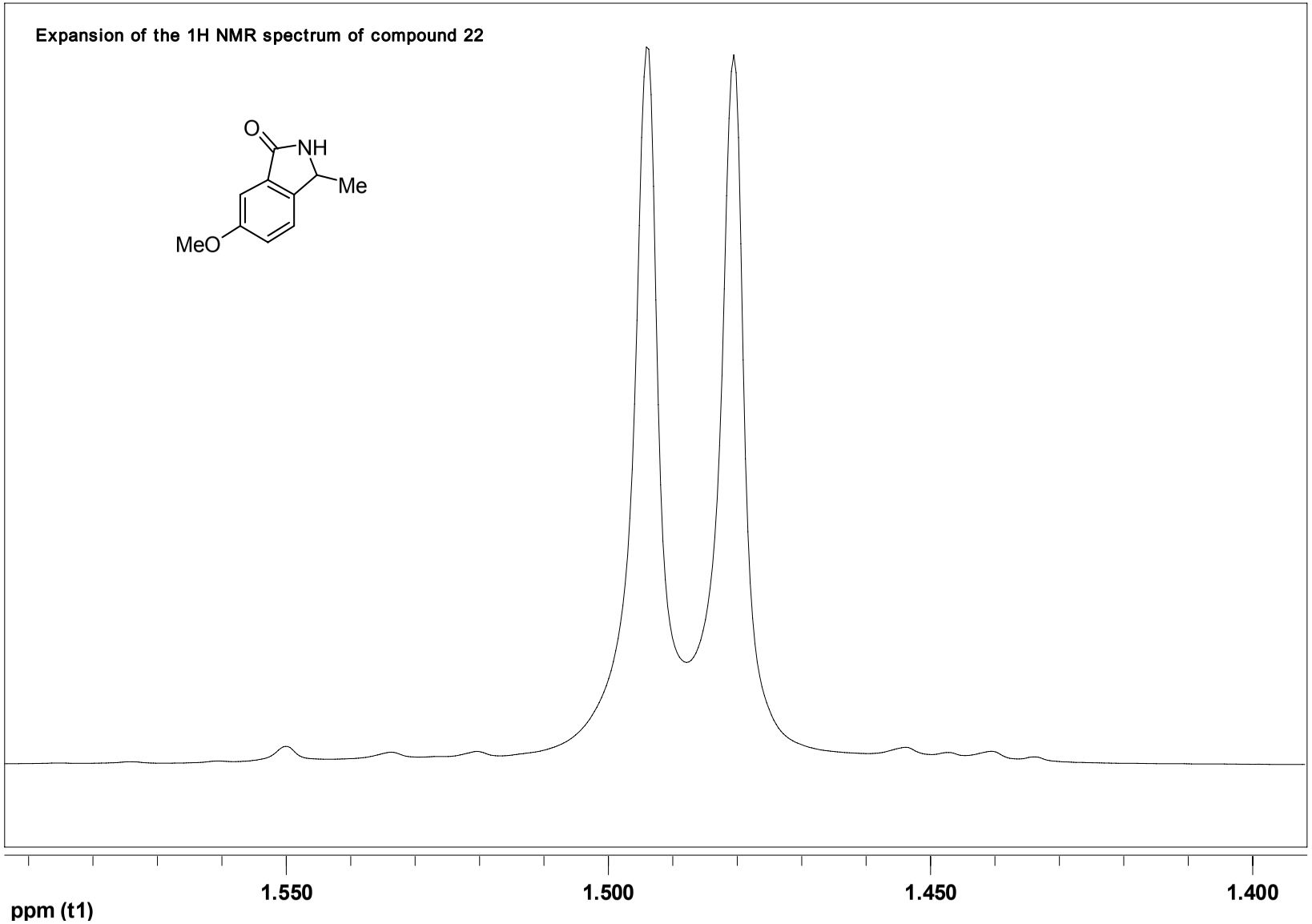

8.21
7.33
7.33
7.31
7.28
7.14
7.13
7.12
7.12
4.68
4.67
4.65
4.64
3.86
1.49
1.48
1H NMR Spectrum of compound 22
O
NH
Me
MeO
9.0
ppm (t1)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

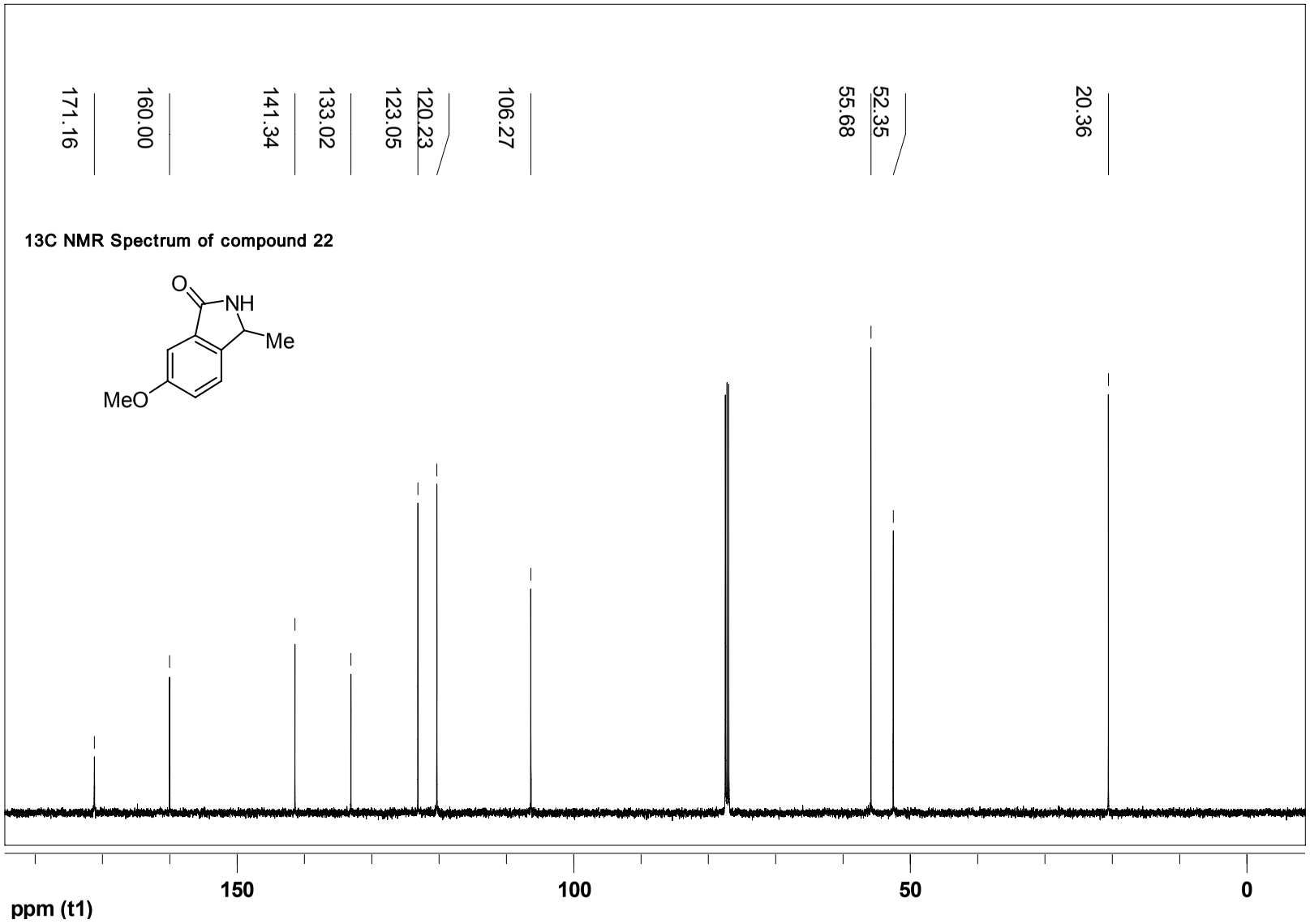
Expansion of the 1H NMR spectrum of compound 22

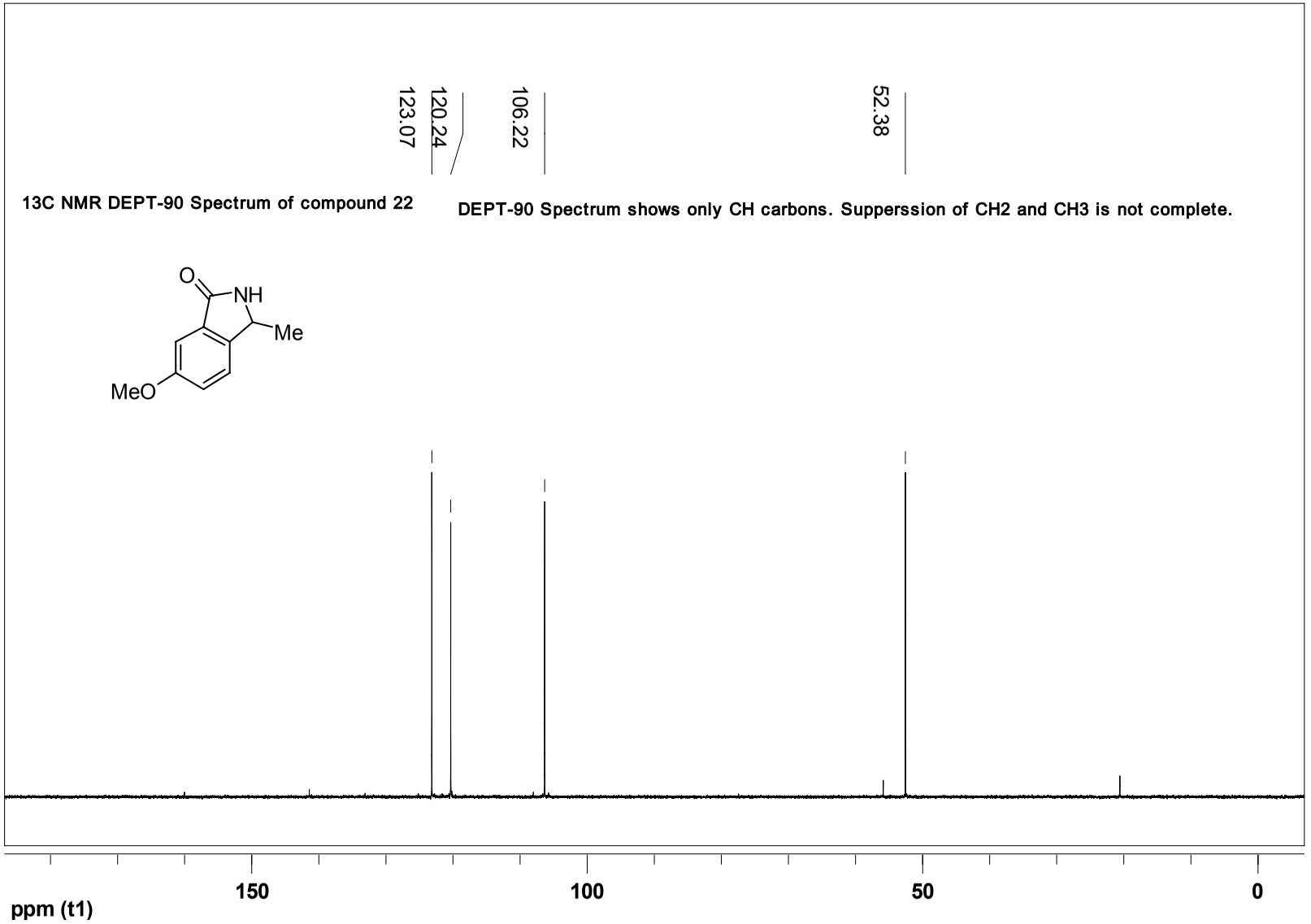


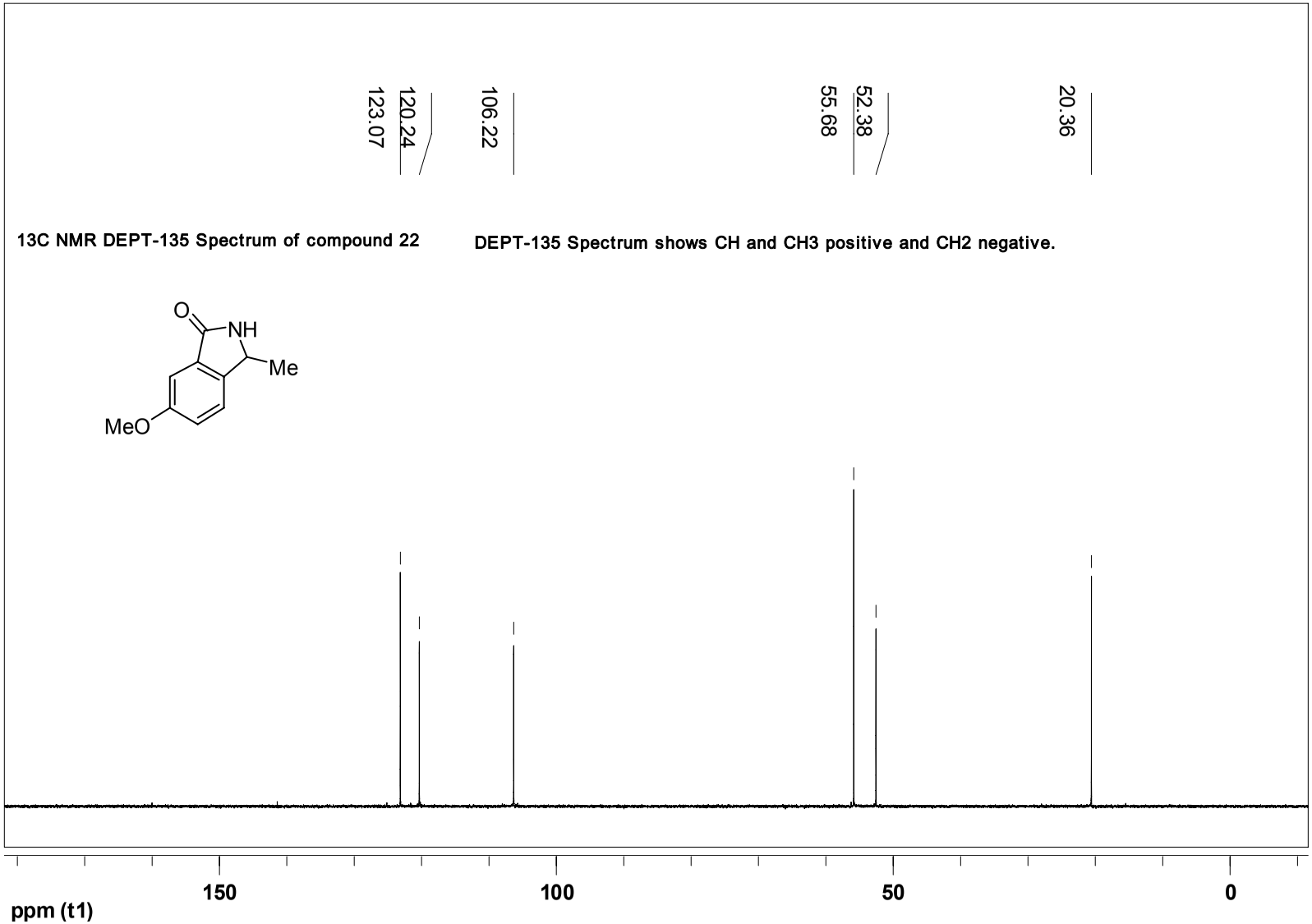
Expansion of the 1H NMR spectrum of compound 22

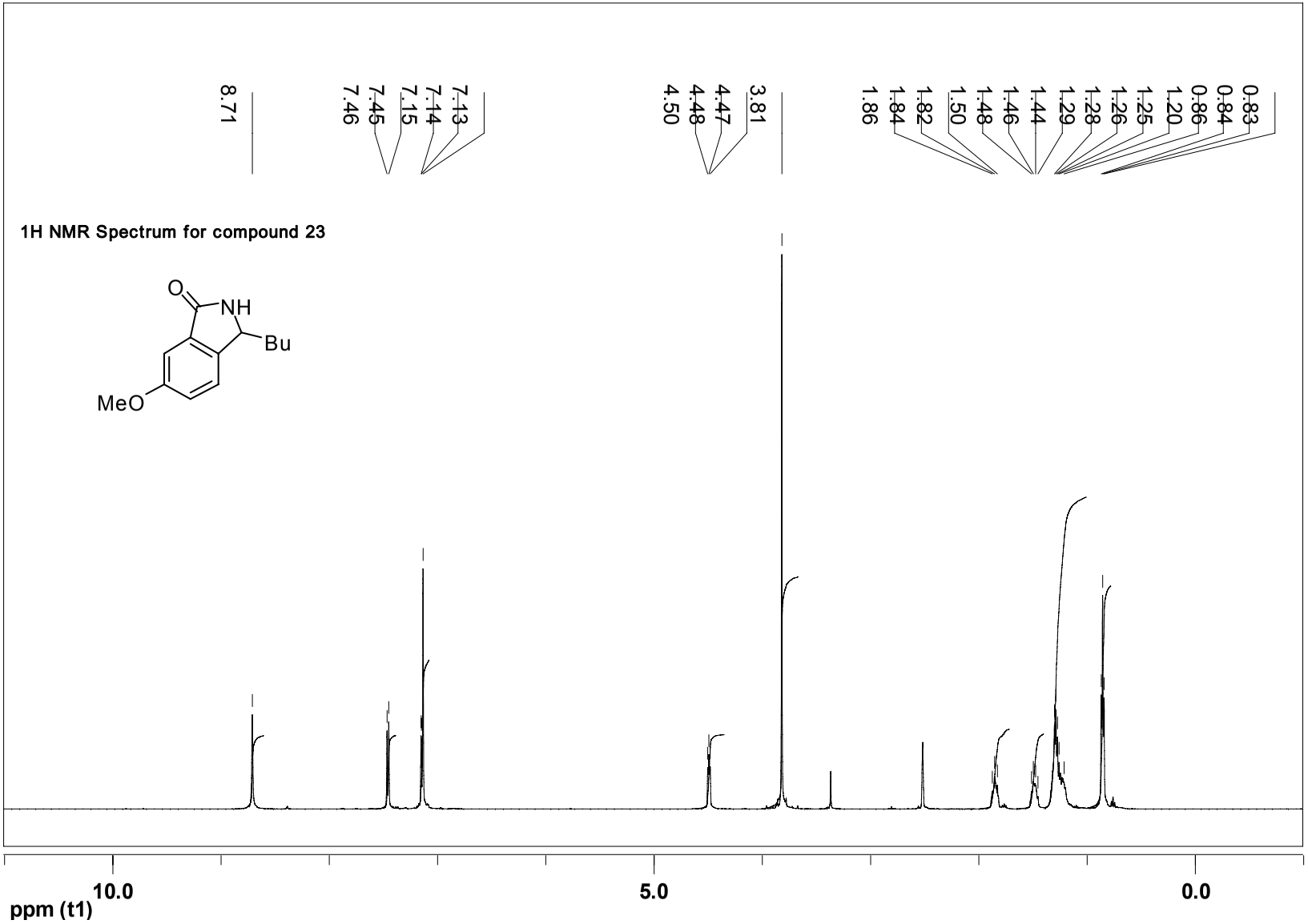


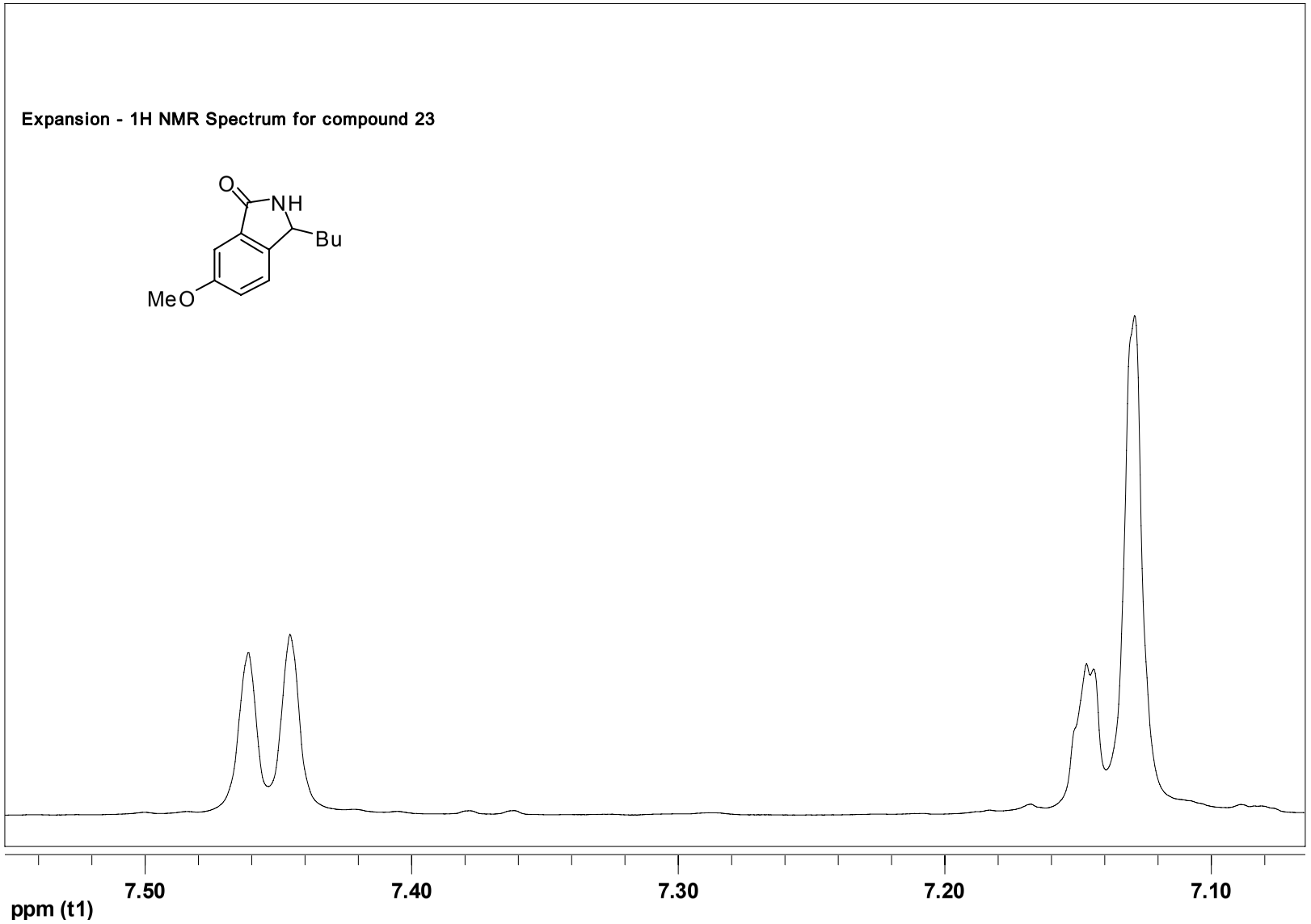

Expansion of the 1H NMR spectrum of compound 22
O
NH
Me
MeO
1.550
1.500
1.450
1.400
ppm (t1)

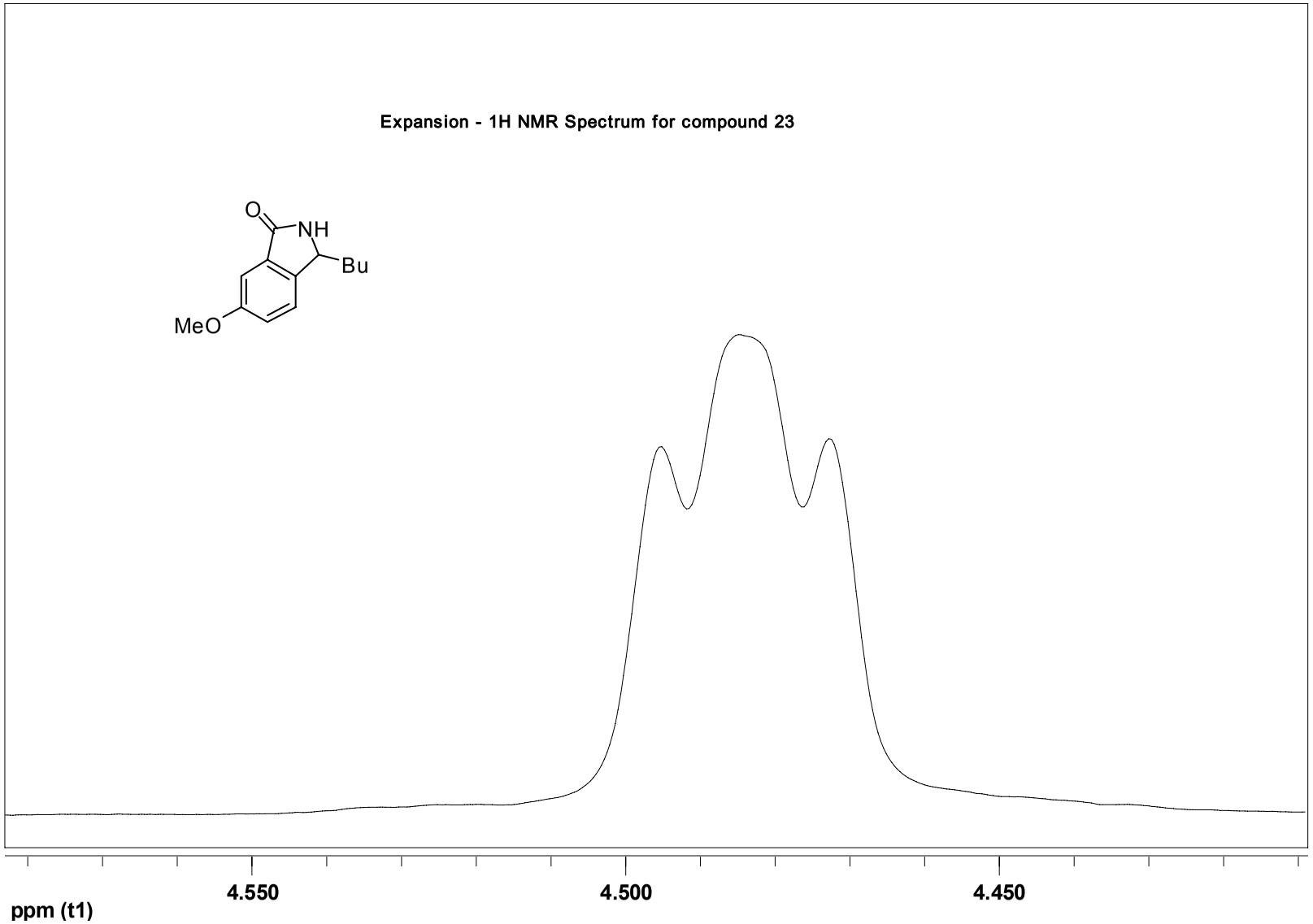

171.16
160.00
141.34
133.02
123.05
120.23
106.27
55.68
52.35
20.36
13C NMR Spectrum of compound 22
O
NH
Me
MeO
150
100
50
0
ppm (t1)

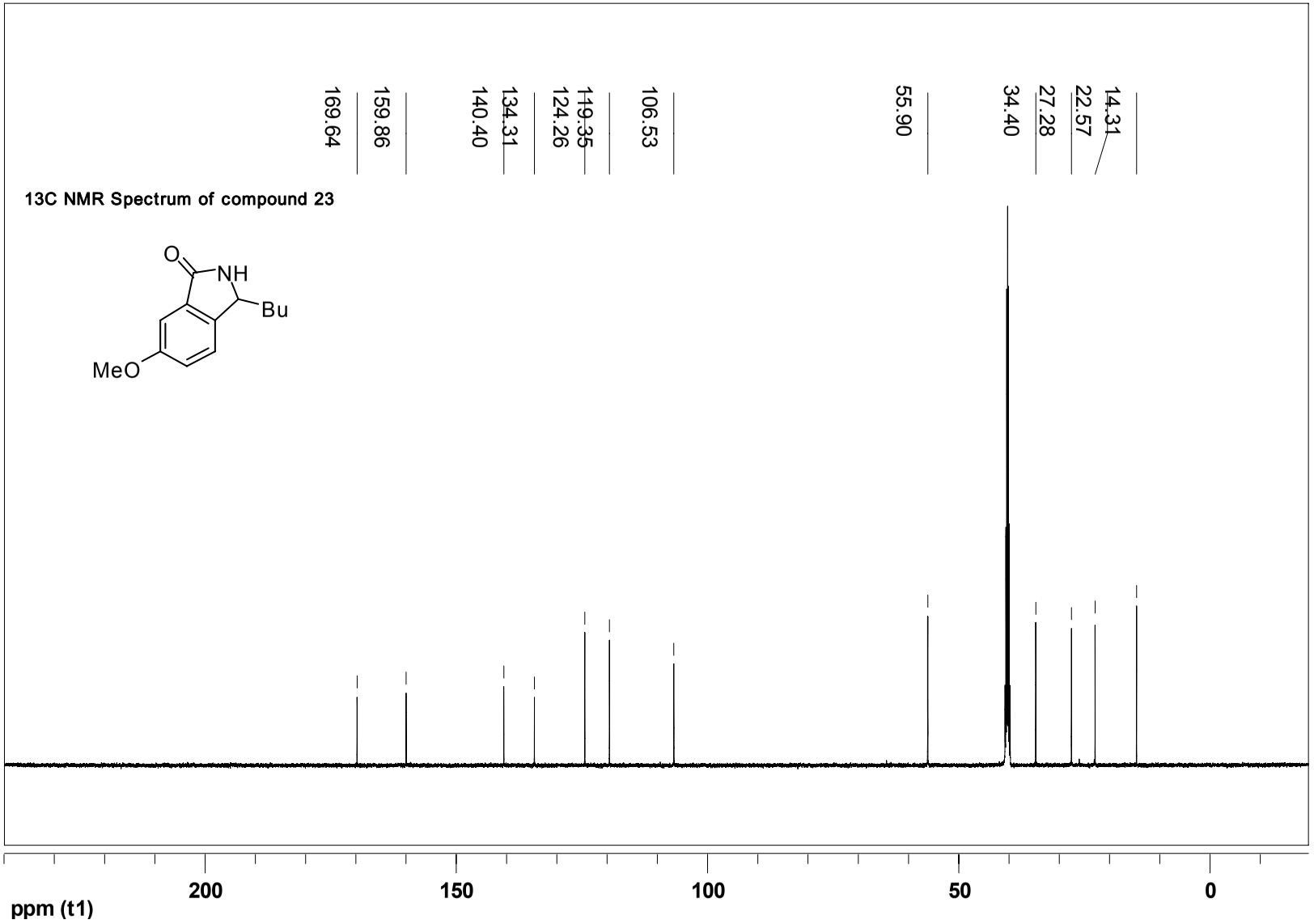

123.07
120.24
106.22
52.38
13C NMR DEPT-90 Spectrum of compound 22
DEPT-90 Spectrum shows only CH carbons. Supperssion of CH2 and CH3 is not complete.
O
NH
Me
MeO
150
100
50
0
ppm (t1)

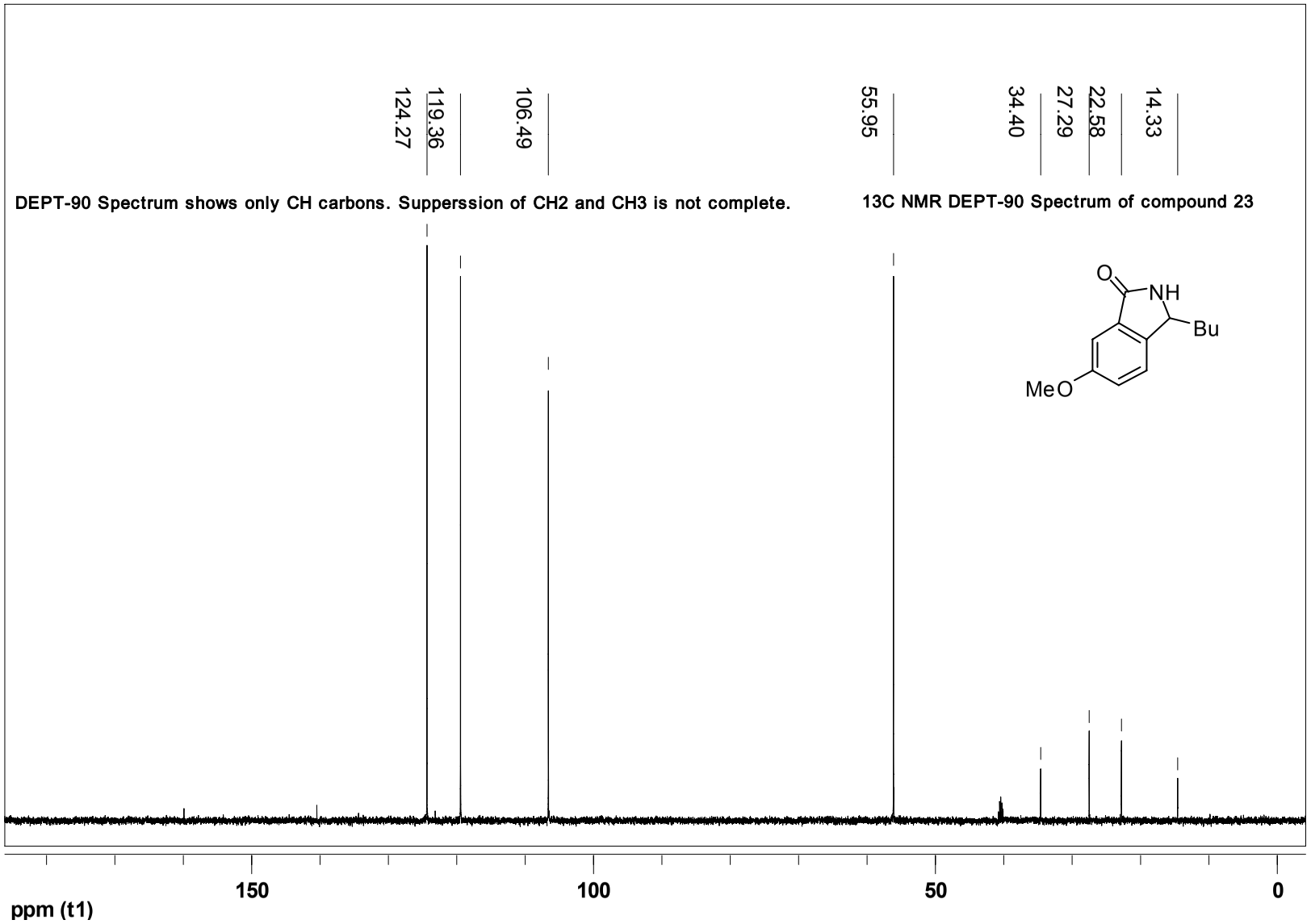

123.07
120.24
106.22
55.68
52.38
20.36
13C NMR DEPT-135 Spectrum of compound 22
DEPT-135 Spectrum shows CH and CH3 positive and CH2 negative.
O
NH
Me
MeO
150
100
50
0
ppm (t1)

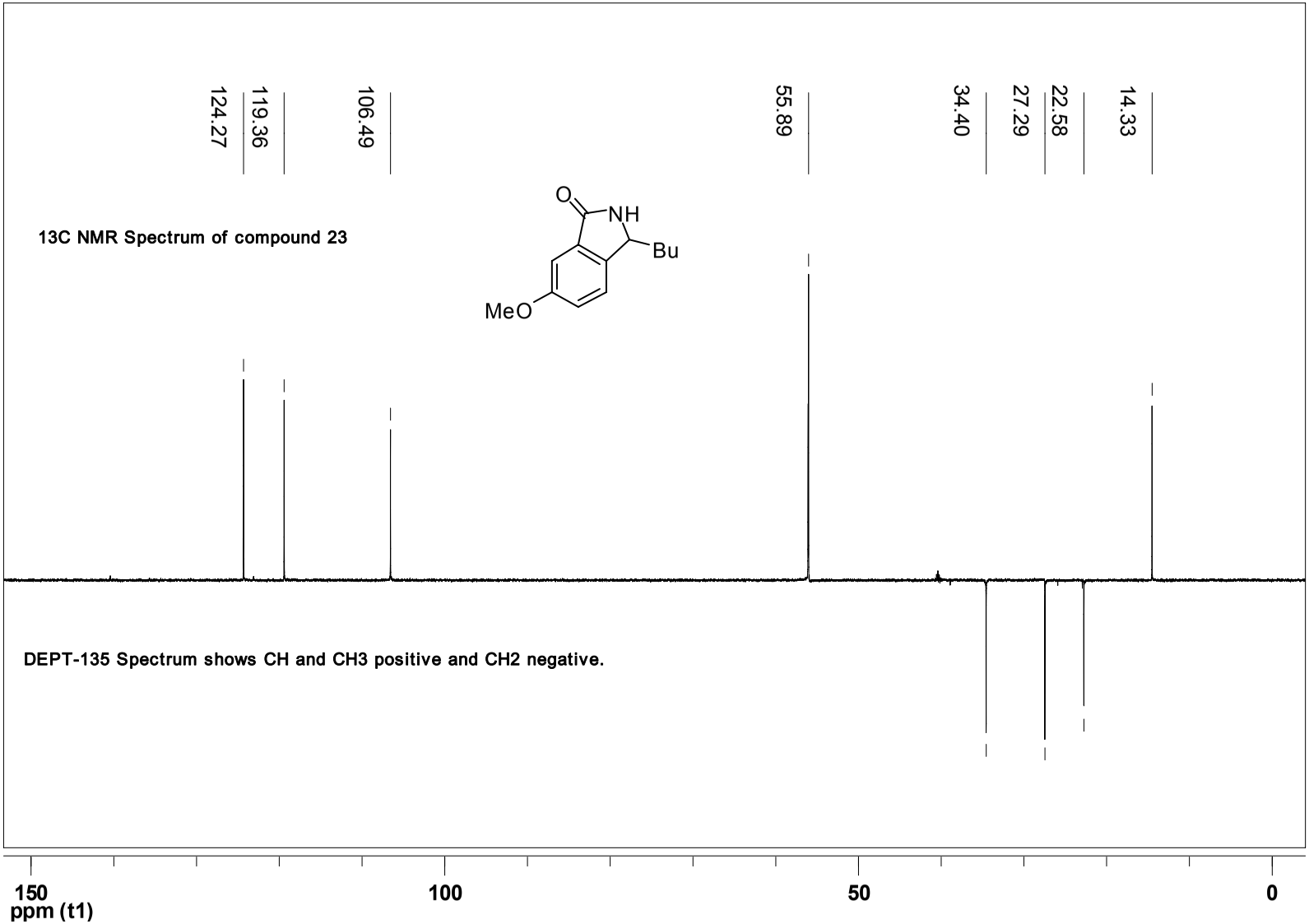

8.71
7.46
7.45
7.15
7.14
7.13
4.50
4.48
4.47
3.81
1.86
1.84
1.82
1.50
1.48
1.46
1.44
1.29
1.28
1.26
1.25
1.20
0.86
0.84
0.83
1H NMR Spectrum for compound 23
O
NH
Bu
MeO
10.0
5.0
0.0
ppm (t1)


Expansion - 1H NMR Spectrum for compound 23
O
NH
Bu
MeO
7.50
7.40
7.30
7.20
7.10
ppm (t1)

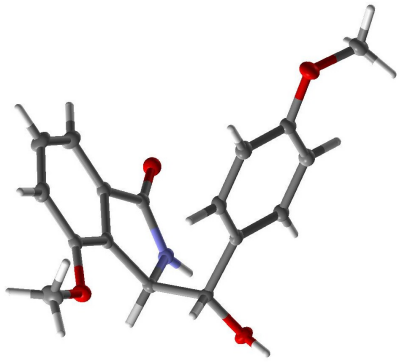
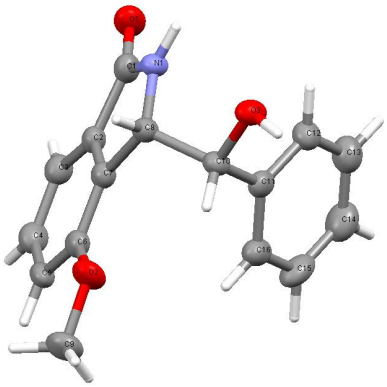

Expansion - 1H NMR Spectrum for compound 23
O
NH
Bu
MeO
4.550
4.500
4.450
ppm (t1)


169.64
159.86
140.40
134.31
124.26
119.35
106.53
55.90
34.40
27.28
22.57
14.31
13C NMR Spectrum of compound 23
O
NH
Bu
MeO
200
150
100
50
0
ppm (t1)

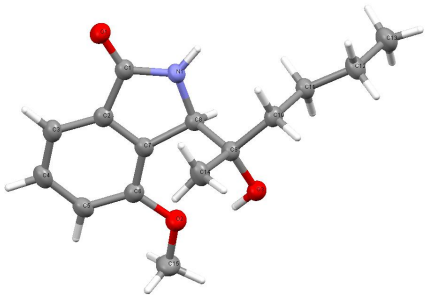
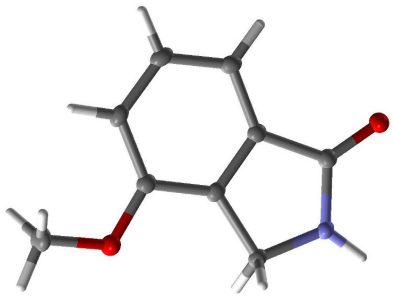

124.27
119.36
106.49
55.95
34.40
27.29
22.58
14.33
DEPT-90 Spectrum shows only CH carbons. Supperssion of CH2 and CH3 is not complete.
13C NMR DEPT-90 Spectrum of compound 23
O
NH
Bu
MeO
150
100
50
0
ppm (t1)


124.27
119.36
106.49
55.89
34.40
27.29
22.58
14.33
13C NMR Spectrum of compound 23
O
NH
Bu
MeO
DEPT-135 Spectrum shows CH and CH3 positive and CH2 negative.
150
ppm (t1)
100
50
0

Crystal and Structure Refinement Data of Compounds 4 and 9

Structure		
	4	**9**
CCDC reference	737415	762623
Empirical formula of crystal unit	$C_{17}H_{17}NO_4$	$C_{18}H_{19}NO_4$
Formula weight of crystal unit	299.32	313.34
Temperature/K	293(2)	150(2)
Crystal system	Centrosymmetric	Triclinic
Space group	P-1	P-1
a/Å	7.5240(3)	7.5698(6)
b/Å	9.4100(3)	9.2785(8)
c/Å	11.9960(5)	12.2934(10)
α/°	83.877(2)	78.473(4)
β/°	77.311(2)	82.365(4)
γ/°	68.559(2)	70.596(3)
V/Å^3	770.92(5)	795.91(11)
Z	2	2
ρ_{cal}/Mgm^{-3}	1.289	1.307
μ/mm^{-1}	0.092	0.093
Crystal size/mm^3	0.20 x 0.15 x 0.15	0.30 x 0.30 x 0.10
Reflections collected	5071	4991
Independent	3513	3467
R(int)	0.0334	0.0536
Parameters	202	238
R1	0.0570	0.0774
wR2	0.1277	0.1657

Crystal and Structure Refinement Data of Compounds 10 and 13

Structure		
	10	**13**
CCDC reference	762624	737411
Empirical formula of crystal unit	$C_{15}H_{21}NO_3$	$C_9H_9NO_2$
Formula weight of crystal unit	263.33	163.17
Temperature/K	150(2)	150(2)
Crystal system	Monoclinic	Triclinic
Space group	P21/a	P-1
a/Å	9.7517(5)	7.2640(5)
b/Å	13.5852(7)	7.8940(6)
c/Å	11.0154(4)	8.3280(8)
α/°	90	104.845(3)
β/°	95.266(3)	114.462(4)
γ/°	90	103.622(5)
V/Å^3	1453.15(12)	387.21(5)
Z	4	2
ρ_{cal}/Mgm^{-3}	1.204	1.400
μ/mm^{-1}	0.083	0.100
Crystal size/mm^3	0.30 x 0.06 x 0.06	0.25 x 0.24 x 0.18
Reflections collected	5380	2379
Independent	3240	1714
R(int)	0.0661	0.0301
Parameters	176	110
R1	0.0725	0.0512
wR2	0.1445	0.1220