Divergent Reactions of Indoles with Aminobenzaldehydes: Indole Ring-Opening vs. Annulation and Facile Synthesis of Neocryptolepine

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Supporting Information

General Information: All solvents were purchased from commercial sources. Commercially available indoles were purchased and used as received. 2-amino-3,5-dibromobenzaldehyde was purchased and used as received. Toluene was distilled prior to use. *N*-methylindole was purified by distillation prior to use. Purification of reaction products was carried out by flash chromatography using Sorbent Technologies Standard Grade silica gel (60 Å, 230–400 mesh) or EMD Chromatographic Grade alumina (80–200 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60 F254 plates. Visualization was accomplished with UV light. Melting points were recorded on a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on an ATI Mattson Genesis Series FT-Infrared spectrophotometer. Proton nuclear magnetic resonance spectra (1H-NMR) were recorded on a Varian VNMRS-500 MHz and a Varian VNMRS-400 MHZ and were reported in ppm using the solvent as an internal standard (CDCl3 at 7.26 ppm, DMSO at 2.54 ppm). Data are reported as app = apparent, s = singlet, d = doublet, t = triplet, q = quartet, sex = sextet, m = multiplet, comp = complex, br = broad; coupling constant(s) in Hz. Proton-decoupled carbon nuclear magnetic resonance (13CNMR) spectra were recorded on a Varian VNMRS-500 MHz and a Varian VNMRS-400 MHz and are reported in ppm using the solvent as an internal standard (CDCl3 at 77.0 ppm, DMSO at 40.45 ppm). Mass spectra were recorded on a Finnigan LCQ-DUO mass spectrometer.

Starting materials 2-aminobenzaldehyde (**9a**) and 2-amino-3-formyl-4,6-dimethylbenzonitrile were prepared according to a literature procedure.[1] Starting materials 2-amino-4-chlorobenzaldehyde, 2-amino-4-(trifluoromethyl)benzaldehyde, 2-amino-4,5-dimethoxy-benzaldehyde were prepared in two steps from the corresponding anthranilic acid derivatives according to literature procedures.[2,3] 2-amino-3-methoxybenzaldehyde was prepared by reduction of the corresponding 2-nitrobenzaldehyde according to a literature procedure.[4] 2-amino-3, 5-dichlorobenzaldehyde was prepared by reduction of the corresponding 2-aminobenzonitrile according to a literature procedure.[4] Starting materials 2-(methylamino)benzaldehyde (**5a**) and 5-methoxy-2-(methylamino)benzaldehyde were prepared by methylation of the corresponding quinoline, followed by oxidative ring opening of the quinolinium iodide salt according to literature procedures.[5,6] The starting material N-benzylindole was prepared according to a literature procedure.[7]

The respective characterization data of starting materials 2-aminobenzaldehyde (**9a**),[1] 2-amino-3-formyl-4,6-dimethylbenzonitrile,[8] 2-amino-4-chlorobenzaldehyde,[8] 2-amino-4-(trifluoromethyl)-benzaldehyde,[8] 2-amino-3,5-dichlorobenzaldehyde,[8] 2-amino-4,5-dimethoxybenzaldehyde,[9] 2-

amino-3-methoxybenzaldehyde,[10] 2-(methylamino)benzaldehyde (**5a**),[6] 5-methoxy-2-(methylamino)benzaldehyde,[11] and N-benzylindole,[7] match what is reported in literature.

General Procedure A for the Synthesis of Quinoline Derivatives:

A mixture of the appropriate 2-aminobenzaldehyde (1.1 mmol, 1.1 equiv.), indole (1 mmol, 1 equiv.) and either *p*-TsOH (190 mg, 1 mmol, 1 equiv.) or TFA (114 mg, 76.6 μL, 1 mmol, 1 equiv.) in toluene (10 mL, 0.1 M) was stirred under nitrogen in a 25 mL round bottom flask at reflux for the indicated amount of time. After cooling to room temperature, the reaction mixture was washed with 1 M NaOH (30 mL) and the aqueous layer extracted with CH_2Cl_2 (3 x 40 mL). The combined organic layers were then dried with anhydrous sodium sulfate. The organic layer was concentrated under reduced pressure and the crude product was purified by flash chromatography on silica gel.

General Procedure B for the Synthesis of Neocryptolepine Derivatives 6a-6e:

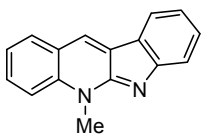
A mixture of the appropriate 2-(methylamino)benzaldehyde (0.5 mmol, 1 equiv.), indole (0.5 mmol, 1 equiv.) and *p*-TsOH (95 mg, 0.5 mmol, 1 equiv.) in absolute ethanol (5 mL, 0.1 M) was stirred open to air in a 25 mL round bottom flask at reflux for the indicated amount of time. After cooling to room temperature, the reaction mixture was washed with 1 M NaOH (30 mL) and the aqueous layer extracted with CH_2Cl_2 (3 x 40 mL). The combined organic layers were then dried with anhydrous sodium sulfate. The organic layer was concentrated under reduced pressure and the crude product was left in a capped 250 mL round bottom flask for 2.5 h. The crude product was subsequently purified by flash chromatography on alumina.

General Procedure C for the Synthesis of Neocryptolepine Derivatives 6a, 16, 17:

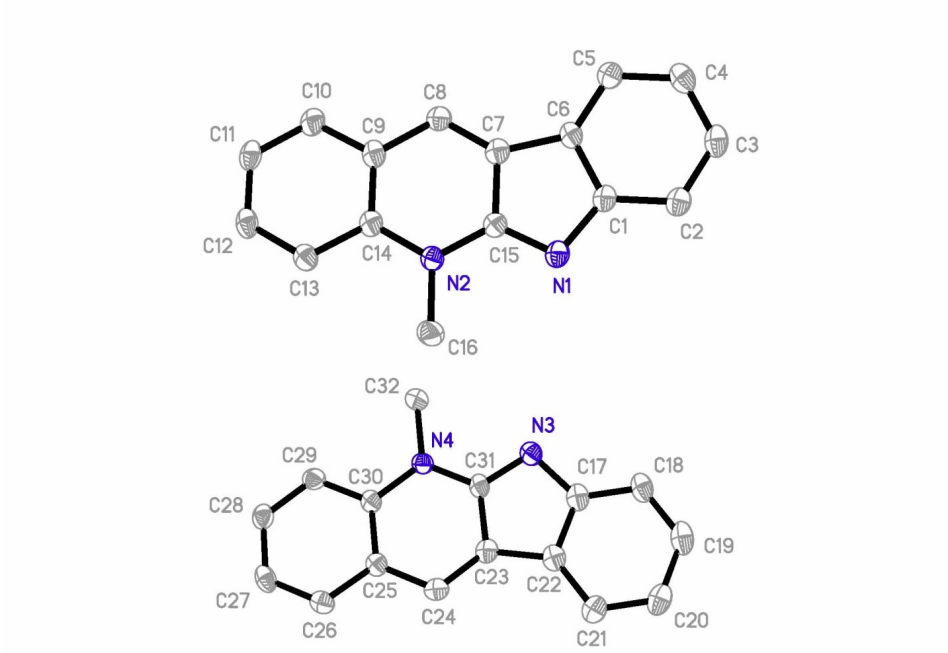
A mixture of compound **11a** (110 mg, 0.5 mmol, 1 equiv.) and the indicated amount of alkyl halide in acetonitrile (5 mL, 0.1 M) was stirred open to air in a 10 mL round bottom flask at reflux for 12 hours. After cooling to room temperature, the reaction mixture was washed with 1 M NaOH (30 mL) and the aqueous layer extracted with CH_2Cl_2 (3 x 40 mL). The combined organic layers were then dried with anhydrous sodium sulfate. The organic layer was concentrated under reduced pressure and the crude product was purified by flash chromatography on silica gel.

Characterization Data of Products

5-methyl-5H-indolo[2,3-b]quinoline (6a): Following general procedure B, compound **6a** was obtained as a red solid in 77% yield (89 mg). Alternatively, following general procedure C, compound **6a** was obtained as a red solid in 64% yield (74 mg). mp 105–108°C (CH_2Cl_2); Rf = 0.20 (MeOH/EtOAc 5/95 v/v); IR (KBr) cm^{-1}; 3294, 2857, 1689, 1450, 1341, 1145, 986, 782, 651. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.61, (app t, *J* = 7.9 Hz, 1H), 7.53–7.50 (comp, 2H), 7.31 (app t, *J* = 7.5 Hz, 1H), 7.17 (app t, *J* = 7.3 Hz, 1H), 4.13 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.6, 154.9, 136.4, 130.1, 129.6, 129.0, 127.7, 127.5, 123.6, 121.6, 120.8, 120.4, 119.6, 117.3, 113.8, 32.7; *m/z* (ESI-MS) 233.4 $[M]^+$.

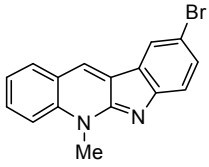


The structure was further elucidated by X-ray crystallography:



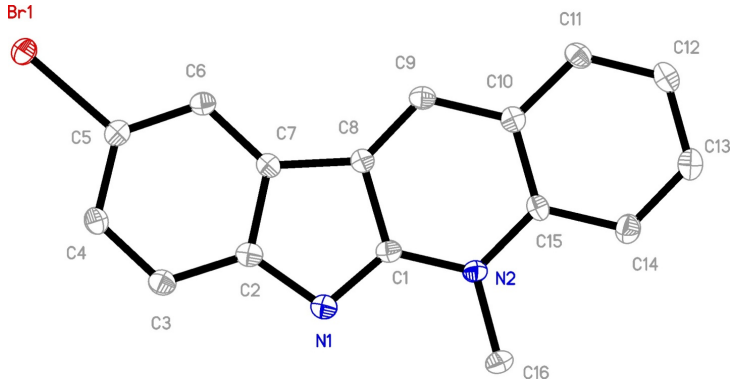
Suitable crystals were grown by slow evaporation of an EtOAc solution at room temperature over one day. The requisite CIF has been deposited with the CCDC (deposition # 828268).

9-bromo-5-methyl-5H-indolo[2,3-b]quinoline (6b): Following general procedure B, compound



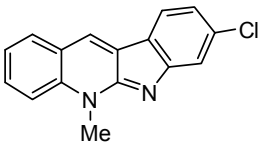
6b was obtained as a orange-red solid in 62% yield (96 mg). mp 215–217 °C (CH_2Cl_2); Rf = 0.20 (MeOH/EtOAc 2/98 v/v); IR (KBr) cm^{-1}; 3398, 2927, 1719, 1491, 1439, 1287, 1191, 1051, 757, 697. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.03 (s, 1H), 7.94 (d, *J* = 7.9 Hz, 1H), 7.78 (app t, 7.8 Hz, 1H), 7.70 (d, 8.6 Hz, 1H), 7.52 (s, 2H), 7.46 (app t, *J* = 7.4 Hz, 1H), 4.31 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.9, 153.6, 137.2, 132.0, 131.3, 130.4, 129.6, 126.8, 125.6, 123.9, 122.6, 120.9, 119.0, 114.5, 112.6, 33.5; *m/z* (ESI-MS) 311.4 $[M+H]^+$.

The structure was further elucidated by X-ray crystallography:



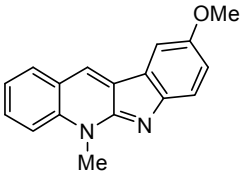
Suitable crystals were grown by slow evaporation of a CH_2Cl_2 solution at room temperature over one day. The requisite CIF has been deposited with the CCDC (deposition # 828272).

8-chloro-5-methyl-5H-indolo[2,3-b]quinoline (6c): Following general procedure B, compound



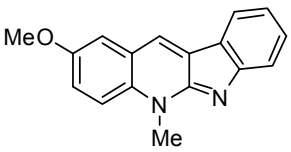
6c was obtained as a yellow-orange solid in 56% yield (75 mg). mp 162–165 °C (EtOAc); Rf = 0.55 (MeOH/EtOAc 2/98 v/v); IR (KBr) cm^{-1}; 2923, 1606, 1566, 1489, 1454, 1416, 1311, 1194, 1051, 866, 797, 752. ^1H NMR (500 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.96 (d, *J* =8.3 Hz, 1H), 7.89 (d, *J* =8.2 Hz, 1H), 7.79–7.73 (comp, 2H), 7.68 (s, 1H), 7.46 (app t, *J* = 7.7Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 4.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 156.6, 137.0, 135.0, 130.9, 130.2, 128.6, 127.4, 122.6, 122.4, 121.1, 120.2, 118.1, 114.5, 33.3; *m/z* (ESI-MS) 267.2 $[M+H]^+$.

9-methoxy-5-methyl-5H-indolo[2,3-b]quinoline (6d): Following general procedure C,



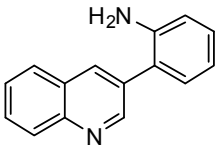
compound **6d** was obtained as a red-orange solid in 76% yield (100 mg). mp 146–148 °C (EtOAc); Rf = 0.27 (MeOH/EtOAc 2/98 v/v); IR (KBr) cm^{-1}; 3030, 2982, 2941, 2821, 1610, 1565, 1488, 1424, 1314, 1270, 1149, 1093, 1060, 973, 884, 834, 754. ^1H NMR (500 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.84–7.81 (comp, 2H), 7.67–7.61 (comp, 2H), 7.36 (app t, *J* = 7.6 Hz, 1H), 7.25 (d, *J* =2.3 Hz, 1H), 6.78 (dd, *J* =8.5, 2.3, 1H), 4.24 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 157.6, 157.2, 136.2, 129.8, 129.7, 128.0, 126.0, 122.0, 121.9, 121.3, 117.3, 114.2, 108.4, 101.8, 55.7, 33.1; *m/z* (ESI-MS) 263.3 $[M+H]^+$.

2-methoxy-5-methyl-5H-indolo[2,3-b]quinoline (6e): Following general procedure B,

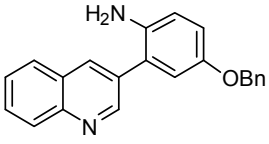


compound **6e** was obtained as a red solid in 59% yield (77 mg). mp 129–132°C (EtOAc); Rf = 0.23 (MeOH/EtOAc 5/95 v/v); IR (KBr) cm^{-1}; 2045, 3000, 2934, 2832, 1570, 1491, 1452, 1432, 1234, 1187, 1137, 1028, 807, 731. ^1H NMR (500 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.99 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* =8.0 Hz, 1H), 7.60 (d, *J* = 9.2 Hz, 1H), 7.54 (app t, *J* =7.5 Hz, 1H), 7.35 (dd, *J* = 9.3 Hz, 2.7 Hz, 1H), 7.29 (d, *J* =2.7 Hz, 1H), 7.20 (app t, *J* =7.4 Hz, 1H), 4.28 (s, 3H), 3.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.1, 156.0, 154.7, 132.0, 129.5, 128.7, 127.5, 123.9, 121.7, 121.2, 120.3, 119.6, 117.7, 115.6, 110.5, 55.0, 33.3; *m/z* (ESI-MS) 263.2 $[M+H]^+$.

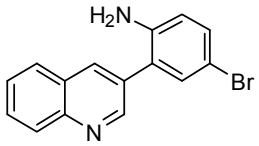
2-(quinolin-3-yl) aniline (11a): Following general procedure A, compound **11a** was obtained as



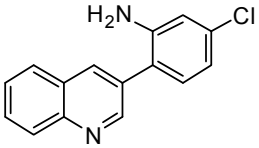
an off-white solid in 86% yield (189 mg). mp 119–120 °C (CH_2Cl_2); Rf = 0.2 (EtOAc/Hex 20/80 v/v); IR (KBr) cm^{-1}; 3416, 3319, 3218, 3024, 1635, 1566, 1499, 1490, 1465, 1446, 1307, 916, 784, 751, 740. ^1H NMR (500 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.22 (s, 1H), 8.14 (d, *J* = 8.3 Hz, 1H), 7.78 (d, *J* = 7.2 Hz, 1H), 7.71, (app t, *J* = 13.4 Hz, 1H), 7.55 (app t, *J* = 13.1 Hz, 1H), 7.19–7.23, (comp, 2H), 6.89 (t, *J* = 14.3 Hz, 1H), 6.81 (d, *J* = 7.9 Hz, 1H), 3.79 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.4, 146.7, 144.0, 135.3, 132.3, 130.7, 129.4, 129.3, 129.1, 127.8, 127.7, 126.8, 123.6, 118.9, 115.8; *m/z* (ESI-MS) 221.3 $[M+H]^+$.

4-(benzyloxy)-2-(quinolin-3-yl)aniline (11b): Following general procedure A, compound **11b** 

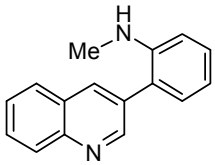
was obtained as a tan solid in 82% yield (267 mg). mp 115–116 °C (CH_2Cl_2); Rf = 0.15 (EtOAc/Hex 20/80 v/v); IR (KBr) cm^{-1}; 3405, 3216, 3029, 2922, 2871, 1644, 1498, 1465, 1452, 1410, 1360, 1282, 1256, 1170, 992, 787, 747, 696. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (d, *J* = 1.9 Hz, 1H), 8.25 (d, *J* = 1.7 Hz, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8.1Hz, 1H), 7.74 (app t, *J* = 7.6 Hz, 1H), 7.58 (app t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 7.4 Hz, 2H), 7.38 (app t, *J* = 7.4 Hz, 2H), 7.32 (d, *J* = 7.3 Hz, 1H), 6.91–6.93 (comp, 2H), 6.77 (d, *J* = 8.1 Hz, 1H), 5.04 (s, 2H), 3.55 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.0, 151.2, 147.0, 137.9, 137.2, 135.3, 132.3, 129.5, 129.1, 128.4, 127.8, 127.7, 127.4, 126.9, 124.7, 117.2, 116.3, 70.7; *m/z* (ESI-MS) 327.2 $[M+H]^+$.

4-bromo-2-(quinolin-3-yl)aniline (11c): Following general procedure A, compound **11c** was 

obtained as an off-white solid in 75% yield (224 mg). mp 157–159 °C (CH_2Cl_2); Rf = 0.15 (EtOAc/Hex 20/80 v/v); IR (KBr) cm^{-1}; 3421, 3205, 2924, 1635, 1570, 1488, 1463, 1403, 1356, 1337, 1298, 1282, 1256, 1160, 1128, 1087, 960, 915, 889, 858, 828, 808, 783, 769, 753, 705, 657, 617. ^{1}H NMR (500 MHz, DMSO) δ 8.98 (d, *J* = 1.7 Hz, 1H), 8.42 (s, 1H), 8.08 (s, 1H), 8.05 (d, *J* = 8.6 Hz, 1H), 7.13 (app t, *J* = 8.1 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.71 (app t, *J* = 7.3 Hz, 1H), 5.09 (br s, 2H); ^{13}C NMR (125 MHz, DMSO) δ 152.5, 146.6, 145.9, 134.8, 133.5, 133.3, 130.6, 130.2, 129.1, 127.2, 127.2, 126.4, 121.8, 116.9, 115.6; *m/z* (ESI-MS) 299.2 $[M+H]^+$.

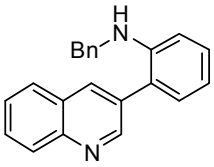
5-chloro-2-(quinolin-3-yl)aniline (11d): Following general procedure A, compound **11d** was 

obtained as an off-white solid in 81% yield (206 mg). mp 167–171 °C (CH_2CL_2); Rf = 0.25 (EtOAc/Hex 20/80 v/v); IR (KBr) cm^{-1}; 3443, 3290, 3173, 1634, 1606, 1589, 1565, 1493, 1422, 1407, 1259, 955, 904, 849, 796, 785, 748, 640, 410. ^{1}H NMR (500 MHz, DMSO) δ 8.90 (d, *J* = 2.1 Hz, 1H), 8.36 (d, *J* = 1.8 Hz, 1H), 8.00–8.05 (comp, 2H), 7.77 (app t, *J* = 7.7 Hz, 1H), 7.63 (app t, *J* = 7.4 Hz, 1H), 7.13 (d, *J* = 8.1 Hz, 1H), 6.87 (d, *J* = 2.0 Hz, 1H), 6.70, (dd, *J* = 2.1, 2.0 Hz, 1H), 5.37 (s, 2H); ^{13}C NMR (125 MHz, DMSO) δ 151.0, 147.6, 146.5, 135.0, 133.4, 132.1, 131.7, 129.3, 128.6, 128.2, 127.7, 126.7, 121.0, 116.2, 114.4: *m/z* (ESI-MS) 255.2 $[M+H]^+$.

N-methyl-2-(quinolin-3-yl)aniline (11e): Following general procedure A, compound **11e** was 

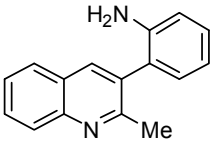
obtained as a pale yellow solid in 93% yield (218 mg). mp 100–101 °C (CH_2Cl_2); Rf = 0.25 (EtOAc/Hex 20/80 v/v); IR (KBr) cm^{-1}; 1606, 1578, 1567, 1510, 1492, 1466, 1423, 1407, 1361, 1337, 1313, 1289, 1170, 1127, 912, 787, 747. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 (d, *J* = 2.1 Hz, 1H), 8.19 (d, *J* = 1.9 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.80, (d, *J* = 8.1 Hz), 7.72 (app t, *J* = 7.5 Hz, 1H), 7.55 (app t, *J* = 7.5 Hz, 1H), 7.37 (app t, *J* = 7.7 Hz, 1H), 7.18 (dd, *J* = 1.4 and 1.4 Hz, 1H), 6.86 (app t, *J* = 7.4 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 1H), 4.01 (br s, 1H), 2.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.7, 147.0, 146.5, 135.6, 132.4, 130.4, 129.6, 129.3, 129.1, 127.9, 127.6, 126.8, 123.6, 117.1, 110.6, 30.6; *m/z* (ESI-MS) 235.3 $[M+H]^+$.

N-benzyl-2-(quinolin-3-yl)aniline (11f): Following general procedure A, compound **11f** was



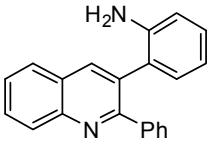
obtained as a off-white solid in 79% yield (245 mg). 80–82 °C (CH_2Cl_2); Rf = 0.30 (EtOAc/Hex 20/80 v/v); IR (KBr) cm^{-1}; 3436, 3055, 2985, 2305, 1595, 1504, 1426, 1158, 899, 752. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.08 (br s, 1H), 8.25 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.84, (d, *J* = 8.2 Hz, 1H), 7.75 (app t, *J* = 7.0 Hz, 1H), 7.58 (app t, *J* = 7.6 Hz, 1H), 7.20–7.34 (comp, 7H), 6.88 (app t, *J* = 7.2 Hz, 1 H), 6.77 (d, *J* = 8.2 Hz, 1H), 4.37 (br s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.6, 146.0, 145.2, 138.9, 135.7, 132.4, 130.7, 129.5, 129.4, 129.1, 128.5, 127.9, 127.7, 127.1, 127.0, 126.8, 123.8, 117.6, 111.2, 48.0; *m/z* (ESI-MS) 311.4 $[M+H]^+$.

2-(2-methylquinolin-3-yl)aniline (11g): Following general procedure A, compound **11g** was



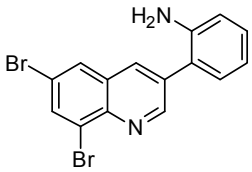
obtained as an off-white solid in 79% yield (185 mg). mp 114–115 °C (CH_2Cl_2); Rf = 0.2 (EtOAc/Hex 20/80 v/v); IR (KBr) cm^{-1}; 3456, 3315, 3197, 3053, 3019, 1619, 1492, 1447, 1416, 1372, 1301, 1195, 1146, 971, 664, 620, 579, 517, 472. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 1H), 7.95, (s, 1H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.68 (app t, *J* = 7.4 Hz, 1H), 7.47 (app t, *J* = 7.4 Hz, 1H), 7.22 (app t, *J* = 7.4 Hz, 1H), 7.05 (d, *J* = 7.1 Hz, 1H), 6.85 (app t, *J* = 7.4 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 3.57 (s, 2H), 2.60 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 147.2, 143.8, 136.9, 132.3, 130.1, 129.3, 129.0, 128.3, 127.3, 126.8, 125.8, 124.8, 118.2, 115.2, 23.6; *m/z* (ESI-MS) 235.3 $[M+H]^+$.

2-(2-phenylquinolin-3-yl)aniline (11h): Following general procedure A, compound **11h** was



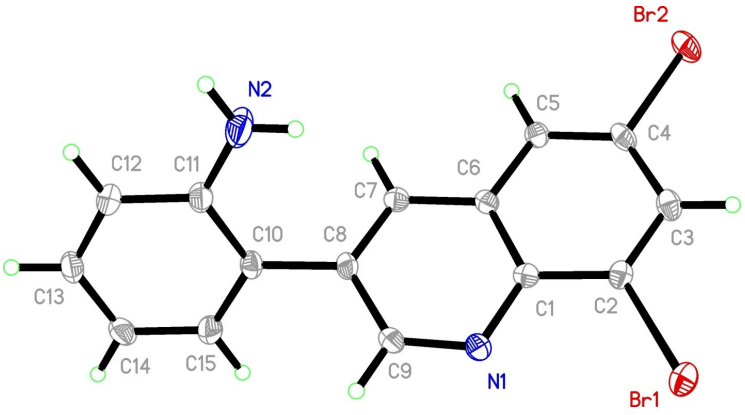
obtained as an off-white solid in 64% yield (189 mg). mp 150–152 °C (CH_2Cl_2); Rf = 0.2 (EtOAc/Hex 20/80 v/v); IR (KBr) cm^{-1}; 3465, 3312, 3200, 3050, 1628, 1498, 1485, 1455, 1439, 1404, 1307, 1265, 1157, 1024, 909, 767, 755, 744, 724, 694, 533. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.4 Hz, 1H), 8.20 (s, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.77 (app t, *J* = 7.4 Hz, 1H), 7.56–7.60 (comp, 3H), 7.26–7.30 (comp, 3H), 7.15 (app t, *J* =7.7 Hz, 1H), 7.05 (d, *J* = 7.4 Hz, 1H), 6.77 (app t, *J* = 7.4 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 3.49 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 147.6, 143.6, 140.0, 138.6, 131.5, 131.1, 129.7, 129.4, 129.2, 128.8, 128.2, 127.8, 127.3, 127.1, 126.7, 125.4, 118.5, 115.5; *m/z* (ESI-MS) 297.3 $[M+H]^+$.

2-(6,8-dibromoquinolin-3-yl)aniline (11i): Following general procedure A, compound **11i** was



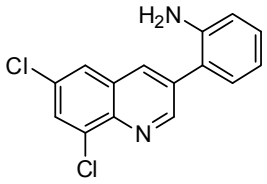
obtained as an off-white solid in 95% yield (359 mg). mp 195–198 °C (CH_2Cl_2); Rf = 0.20 (EtOAc/Hex 10/90 v/v); IR (KBr) cm^{-1}; 3467, 3352, 3064, 1619, 1581, 1495, 1455, 1311, 968, 918, 856, 750, 687, 504. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.15 (d, *J* = 15.4 Hz, 2H), 7.96 (s, 1H), 7.25 (app t, *J* = 7.7 Hz, 1H), 7.18 (d, *J* = 7.3 Hz, 1H), 6.91 (app t, *J* = 7.3 Hz, 1H), 6.84 (d, *J* = 7.9 Hz, 1H), 3.82 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8, 146.6, 142.4, 135.3, 135.3, 134.5, 130.4, 130.1, 129.7, 129.5, 125.3, 122.3, 120.1, 117.1, 110.3, 30.6; *m/z* (ESI-MS) 377.6 $[M+H]^+$.

The structure was further elucidated by X-ray crystallography:



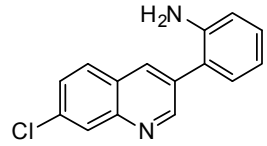
Suitable crystals were grown by slow evaporation of a CH_2Cl_2 solution at room temperature over one day. The requisite CIF has been deposited with the CCDC (deposition # 828270).

2-(6,8-dichloroquinolin-3-yl)aniline (11j): Following the general procedure A, compound **11j**



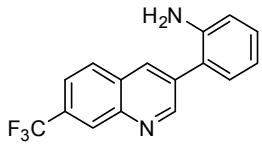
was obtained as an off-white solid in 86% yield (249 mg). mp 170–173 °C (CH_2Cl_2); Rf = 0.25 (EtOAc/Hex 20/80 v/v); IR (KBr) cm^{-1}; 3732, 3473, 3353, 3218, 3068, 1623, 1461, 1313, 1093, 1038, 986, 923, 853, 791, 752. ^1H NMR (500 MHz, $CDCl_3$) δ 9.13 (d, J = 2.1 Hz, 1H), 8.19, (d, J = 2.1 Hz, 1H), 7.81 (d, J = 2.1 Hz, 1H), 7.75, (d, J = 2.2 Hz, 1H), 7.24–7.27 (m, 1H), 7.19 (dd, J = 1.4 and 1.4 Hz, 1H), 6.91 (app t, J = 7.5 Hz, 1H), 6.84 (d, J = 8.1 Hz, 1H), 3.80 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.3, 143.9, 141.8, 134.8, 134.6, 134.5, 132.2, 130.7, 130.1, 129.9, 129.5, 125.6, 122.6, 119.3, 116.2; *m/z* (ESI-MS) 289.3 $[M+H]^+$.

2-(7-chloroquinolin-3-yl)aniline (11k): Following general procedure A, compound **11k** was



obtained as a white solid in 92% yield (234 mg). mp 170–173 °C (CH_2Cl_2): Rf = 0.25 (EtOAc/Hex 20/80 v/v); IR (KBr) cm^{-1}; 3417, 3297, 3193, 1631, 1487, 1404, 1347, 1289, 814, 751, 696, 615. ^1H NMR (500 MHz, $CDCl_3$) δ 8.98 (d, J = 1.7 Hz, 1H), 8.21 (s, 1H), 8.14 (d, J = 8.4 Hz), 7.75 (app t, J = 7.4 Hz, 1H), 7.59 (app t, J = 7.5 Hz, 1H), 7.30–7.32 (comp, 2H), 6.70 (d, J = 8.2 Hz, 1H), 3.80 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 147.3, 143.1, 135.6, 133.1, 132.0, 131.1, 129.8, 129.3, 127.8, 127.8, 127.2, 125.5, 117.4, 110.5; *m/z* (ESI-MS) 255.2 $[M+H]^+$.

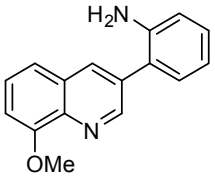
2-(7-(trifluoromethyl)quinolin-3-yl)aniline (11l): Following general procedure A, compound



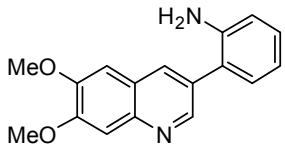
11l was obtained as an off-white solid in 86% yield (248 mg). mp 118–121 °C (CH_2Cl_2); Rf = 0.25 (EtOAc/Hex 20/80 v/v); IR (KBr) cm^{-1}; 3402, 3296, 3015, 1620, 1497, 1457, 1405, 1321, 1178, 1128, 1058, 965, 909, 826, 754, 692, 482. ^1H NMR (500 MHz, $CDCl_3$) δ 9.11 (d, J = 1.8 Hz, 1H), 8.39 (s, 1H), 8.29 (s, 1H), 7.91 (d, J = 8.4 Hz, 1H), 7.71 (d, J = 8.5 Hz, 1H), 7.25 (app t, J = 7.3 Hz, 1H), 7.20 (d, J = 7.4 Hz, 1H), 6.91 (t, J = 7.3 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 3.88 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.2, 146.1, 144.2, 135.4, 134.8, 131.3 (q, J_{C-F} =

32.2 Hz), 131.0, 130.1, 129.6, 129.2, 127.3 (q, $J_{C\text{-}F}$ = 4.5 Hz) , 124.1 (q, $J_{C\text{-}F}$ = 272.8 Hz), 123.3, 122.8 (q, $J_{C\text{-}F}$ = 3.1 Hz), 119.5, 116.5; *m/z* (ESI-MS) 289.3 $[M+H]^+$.

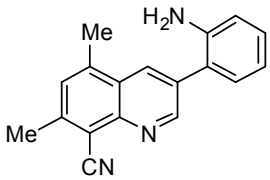
2-(8-methoxyquinolin-3-yl)aniline (11m): Following general procedure A, compound **11m** was obtained as a tan solid in 82% yield (205 mg). mp 195–198 °C (CH_2Cl_2); Rf = 0.20 (EtOAc/Hex 10/90 v/v); IR (KBr) cm^{-1}; 3330, 3209, 3012, 2944, 2840, 1618, 1572, 1490, 1453, 1373, 1267, 1166, 1113, 913, 558, 500. ^1H NMR (500 MHz, $CDCl_3$) δ 8.99 (d, *J* = 1.9 Hz, 1H), 8.13 (d, *J* = 1.9 Hz, 1H), 7.41 (app t, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.13–7.17 (comp, 2H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.82 (app t, *J* = 7.3 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 4.4 (s, 3H), 3.67 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.1, 149.9, 143.8, 138.7, 135.0, 132.8, 130.5, 129.2, 128.8, 127.0, 123.3, 119.3, 118.7, 115.7, 107.3, 55.7; *m/z* (ESI-MS) 251.2 $[M+H]^+$.



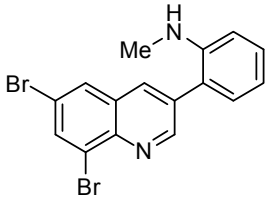
2-(6,7-dimethoxyquinolin-3-yl)aniline (11n): Following general procedure A, compound **11n** was obtained as a light purple solid in 44% yield (123 mg). mp 68–70 °C (CH_2Cl_2); Rf = 0.20 (EtOAc/Hex 50/50 v/v); IR (KBr) cm^{-1}; 3359, 3206, 3009, 2943, 1621, 1499, 1344, 1240, 1142, 1007, 852, 752, 489. ^1H NMR (500 MHz, $CDCl_3$) δ 8.81 (d, *J* = 1.5 Hz, 1H), 8.09 (d, *J* = 1.9 Hz, 1H), 7.45 (s, 1H), 7.18–7.23 (comp, 2H), 7.06 (s, 1H), 6.88 (app t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 4.05 (s, 3H), 4.02 (s, 3H), 3.78 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.6, 150.2, 148.8, 144.1, 144.0, 133.9, 130.8, 130.7, 129.1, 124. 2, 123.6, 119.0, 115.9, 107.7, 105.1, 56.2, 56.1; *m/z* (ESI-MS) 377.6 $[M+H]^+$.



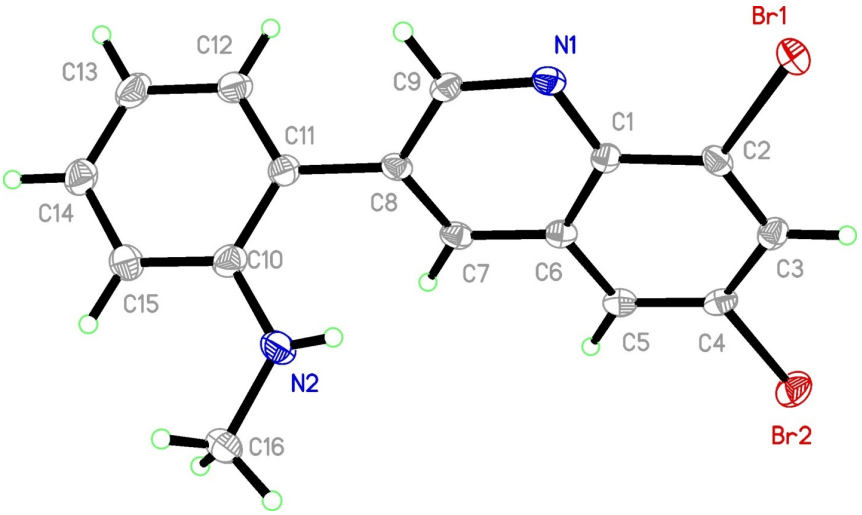
3-(2-aminophenyl)-5,7-dimethylquinoline-8-carbonitrile (11o): Following general procedure A, compound **11o** was obtained as an off-white solid in 85% yield (232 mg). mp 118–120 °C (CH_2Cl_2); Rf = 0.20 (EtOAc/Hex 20/80 v/v); IR (KBr) cm^{-1}; 3437, 3351, 3225, 3017, 2921, 2221, 1613, 1569, 1492, 1450, 1371, 1303, 1210, 913, 679, 486. ^1H NMR (500 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.34 (s, 1H), 7.23 (s, 1H), 7.16 (app t, *J* = 7.4 Hz, 1H), 7.09, (d, *J* = 7.3 Hz, 1H), 6.75–6.83 (comp, 2H), 3.55 (s, 2H), 2.63 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.6, 146.6, 145.9, 144.0, 139.9, 133.0, 132.3, 130.6, 129.5, 129.1, 125.2, 123.0, 118.8, 116.6, 116.1, 109.6, 21.0, 18.9; (ESI-MS) 273.1 $[M+H]^+$.



2-(6,8-dibromoquinolin-3-yl)-N-methylaniline(11p): Following general procedure A, compound **11p** was obtained as a pale yellow solid in 88% yield (344 mg). mp 195–198 °C (CH_2Cl_2); Rf = 0.20 (EtOAc/Hex 10/90 v/v); IR (KBr) cm^{-1}; 3301, 1591, 1515, 1460, 1317, 1165, 1077, 1033, 969, 747. ^1H NMR (500 MHz, $CDCl_3$) δ 9.00 (d, *J* = 2.1 Hz, 1H), 8.19 (d, *J* = 1.9 Hz, 1H), 8.14 (d, 8.4 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.72 (app t, *J* = 7.7 Hz, 1H), 7.55 (app t, *J* = 7.4 Hz, 1H), 7.37 (app t, *J* = 7.8 Hz, 1H), 6.86 (app t, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 4.01 (br s, 1H), 2.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8, 146.6, 142.4, 135.3, 135.3, 134.5, 130.4, 130.1, 129.7, 129.5, 125.3, 122.3, 120.1, 117.1, 110.3, 30.6: *m/z* (ESI-MS) 377.6 $[M+H]^+$.

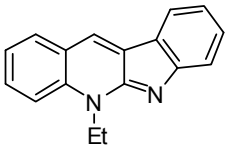


The structure was further elucidated by X-ray crystallography:



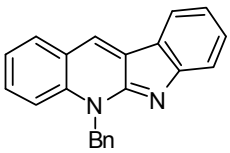
Suitable crystals were grown by slow evaporation from a CH_3OH solution at room temperature over one day. The requisite CIF has been deposited with the CCDC (deposition # 828271).

5-ethyl-5H-indolo[2,3-b]quinoline (16): Following general procedure C, compound **16** was



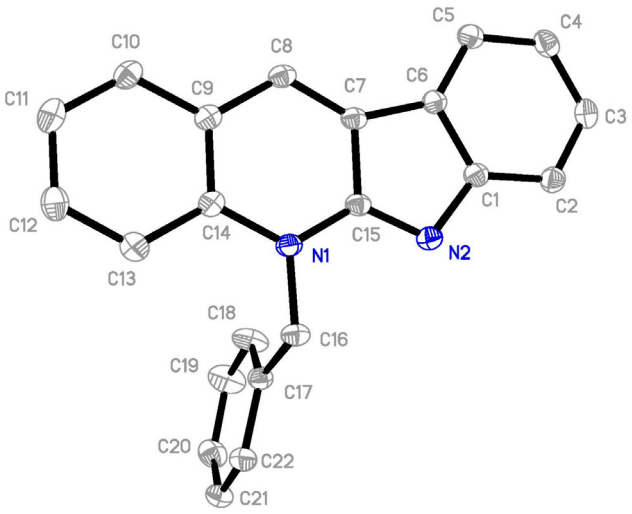
obtained as a red solid in 25% yield (31 mg). mp 131–134 °C (EtOAc); Rf = 0.38 (MeOH/EtOAc 2/98 v/v); IR (KBr) cm^{-1}; 3047, 2974, 2930, 1644, 1610, 1566, 1503, 1443, 1325, 1199, 1092, 747. ^1H NMR (500 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.05 (d, J = 7.1 Hz, 1H), 7.99 (d, J = 7.6 Hz, 1H), 7.78–7.76 (comp, 3H), 7.55 (app t, J = 7.2 Hz, 1H), 7.43 (app t, J = 7.1 Hz, 1H), 7.23 (app t, J = 7.0 Hz, 1H), 5.01 (q, J = 7.3 Hz, 2H), 1.61 (t, J = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.6, 155.5, 136.0, 130.6, 130.5, 129.5, 128.3, 124.1, 121.9, 121.3, 121.2, 120.0, 117.9, 114.3, 41.1, 13.2; *m/z* (ESI-MS) 247.2 $[M+H]^+$.

5-benzyl-5H-indolo[2,3-b]Quinoline (17): Following general procedure C, compound **17** was



obtained as a red solid in 39% yield (60 mg). mp 184–187 °C (EtOAc); Rf = 0.22 (EtOAc/Hexanes 25/75 v/v); IR (KBr) cm^{-1}; 3055, 3026, 2926, 2858, 1644, 1605, 1566, 1505, 1445, 1326, 1298, 1197, 1138, 1057, 857, 743. ^1H NMR (500 MHz, $CDCl_3$) δ 8.57 (app t, J =3.4 Hz, 1H), 8.10–8.08 (m, 1H), 7.98–7.96 (m, 1H), 7.78–7.75 (m, 1H), 7.64–7.56 (comp, 3H), 7.40–7.36 (m, 1H), 7.29–7.23 (comp, 7H), 6.19 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.8, 155.8, 136.5, 136.0, 136.0, 130.5, 130.2, 129.6, 129.1, 128.7, 128.6, 127.7, 126.9, 124.5, 122.1, 121.3, 120.2, 118.2, 115.3, 49.7; *m/z* (ESI-MS) 309.3 $[M+H]^+$.

The structure was further elucidated by X-ray crystallography:



Suitable crystals were grown by slow evaporation of an EtOAc solution at room temperature over one day. The requisite CIF has been deposited with the CCDC (deposition # 828269).

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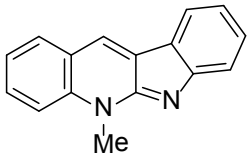
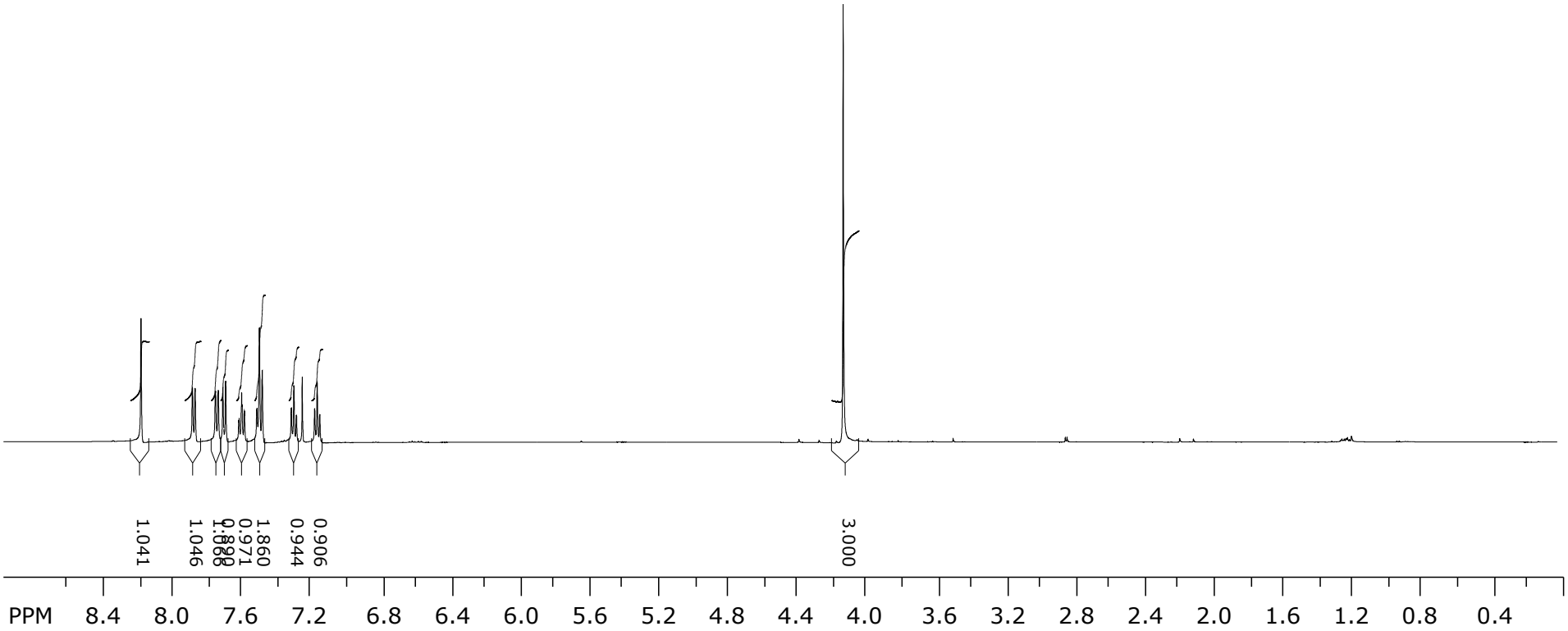
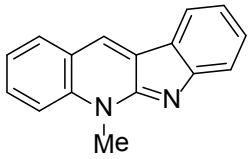
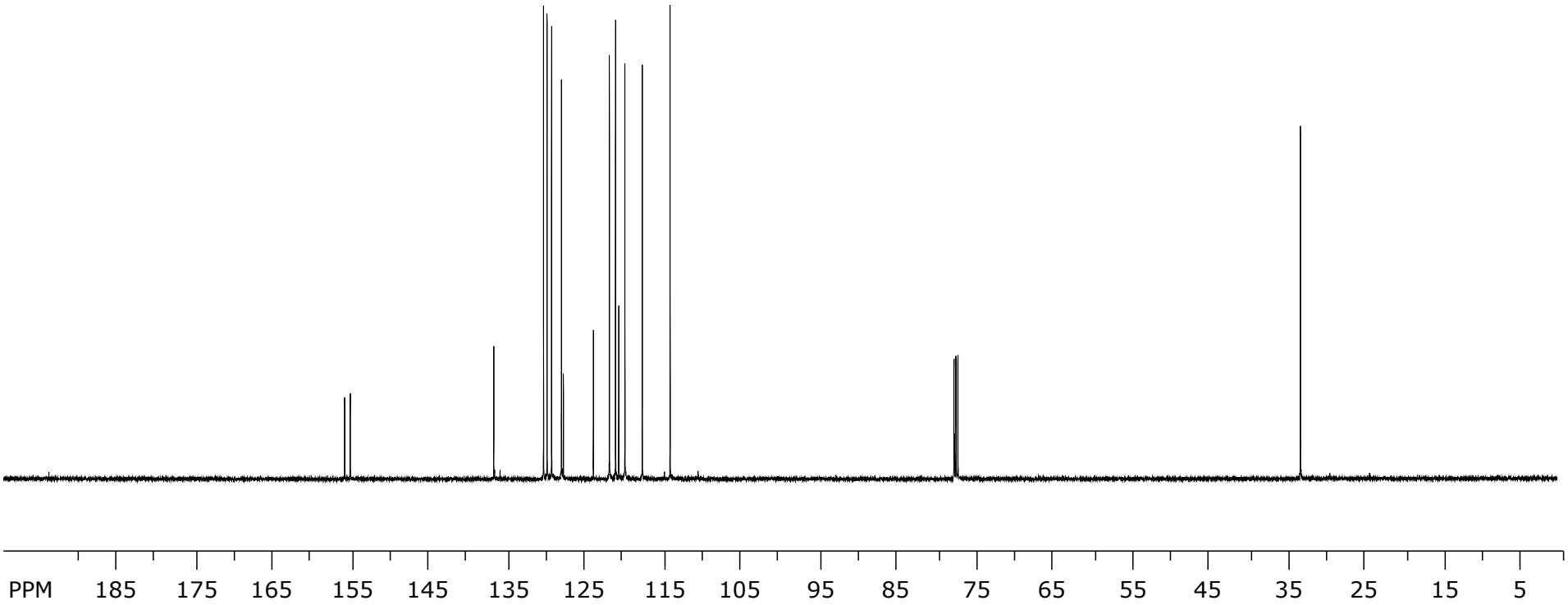
^{1}H NMR of **6a** in $CDCl_3$



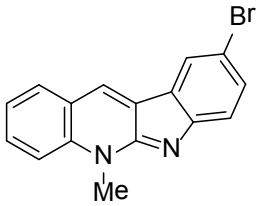


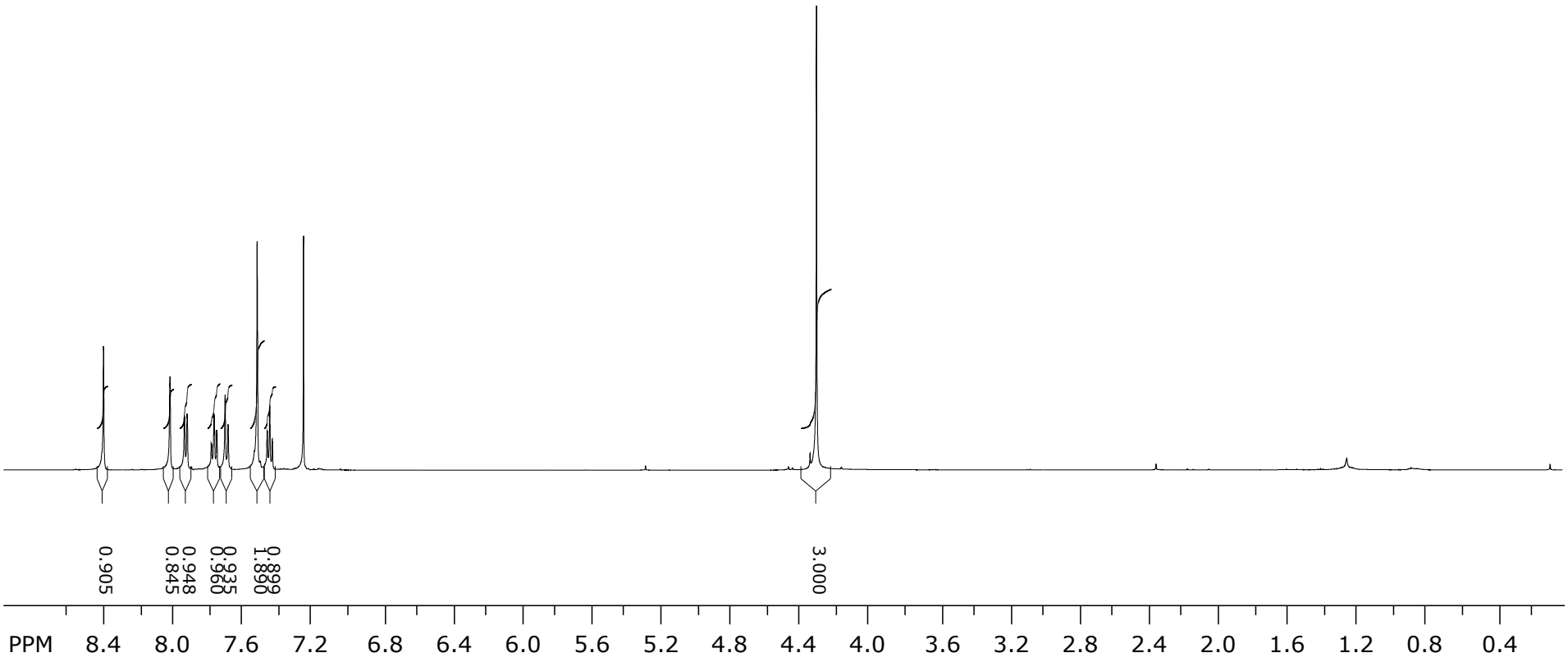
^{13}C NMR of **6a** in $CDCl_3$



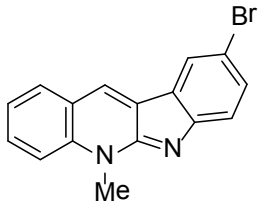


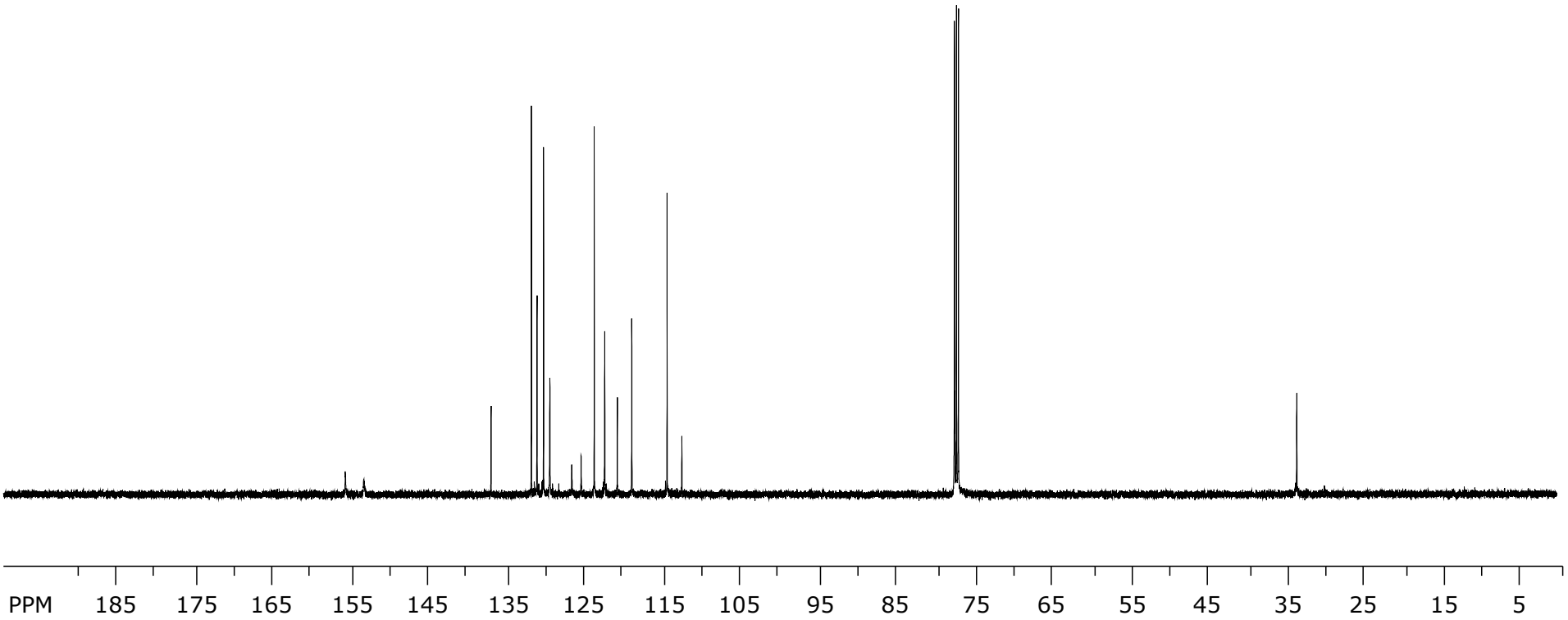
^{1}H NMR of **6b** in $CDCl_3$



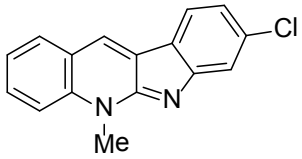


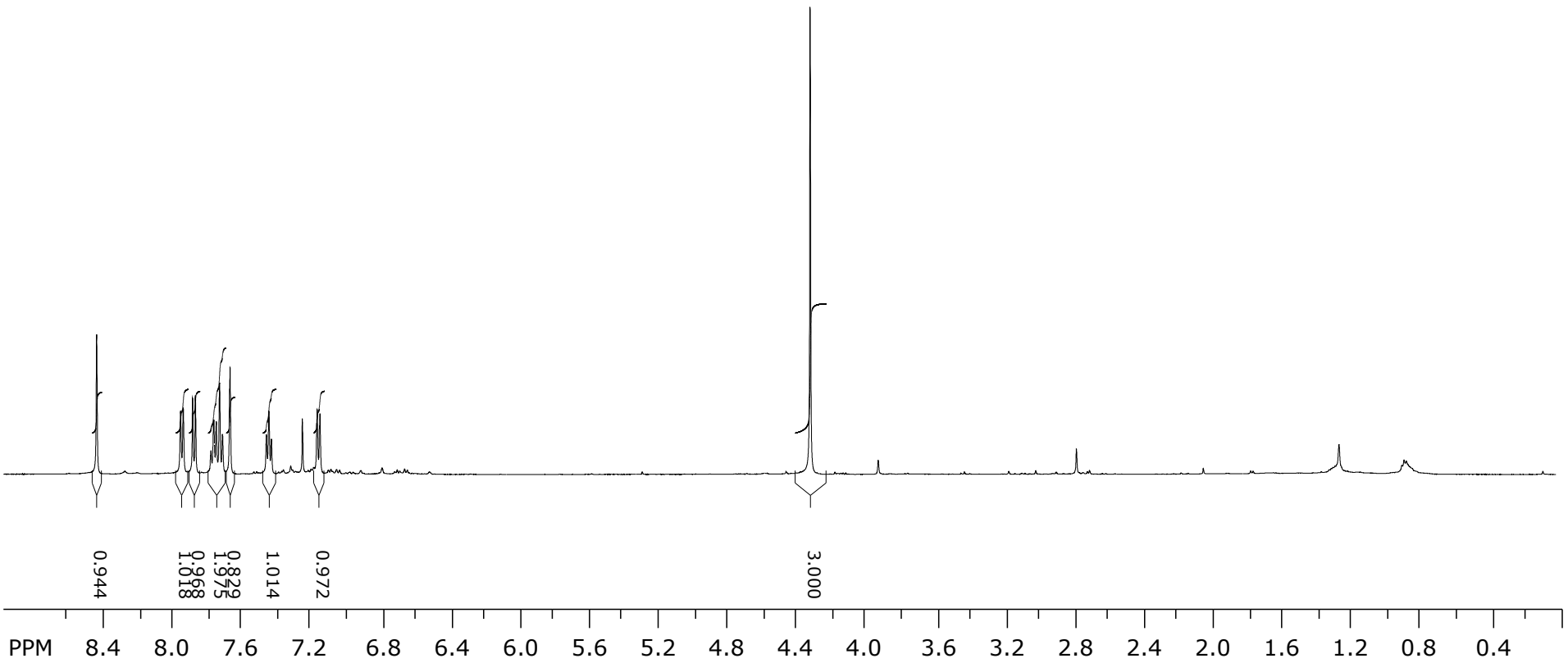
^{13}C NMR of **6b** in $CDCl_3$



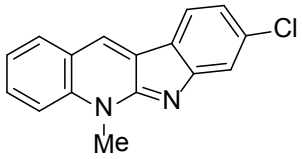


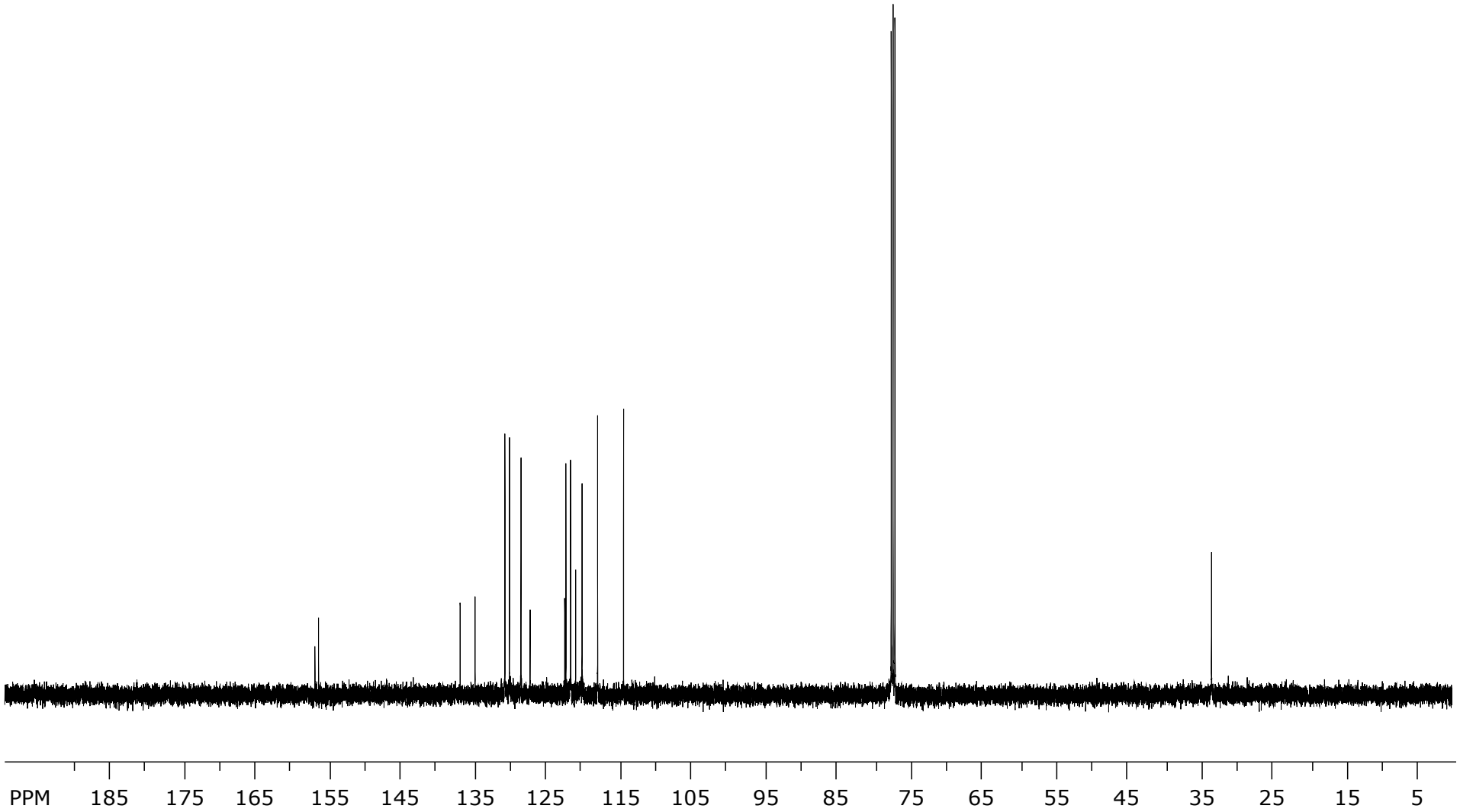
^{1}H NMR of **6c** in $CDCl_3$



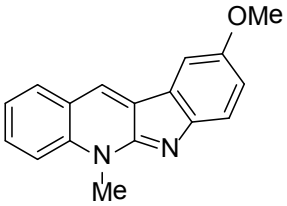


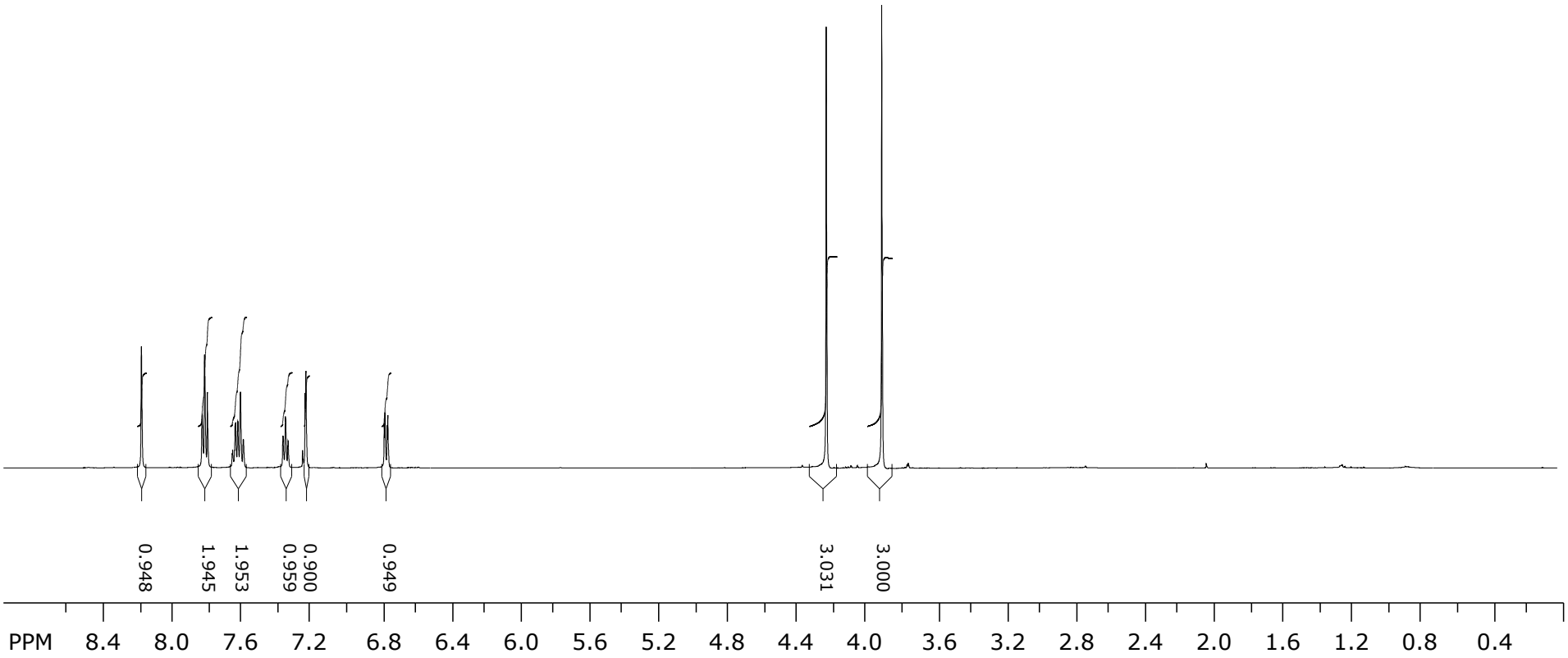
^{13}C NMR of **6c** in $CDCl_3$



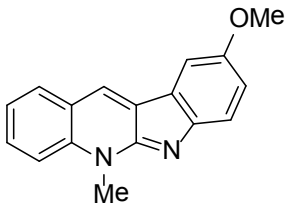


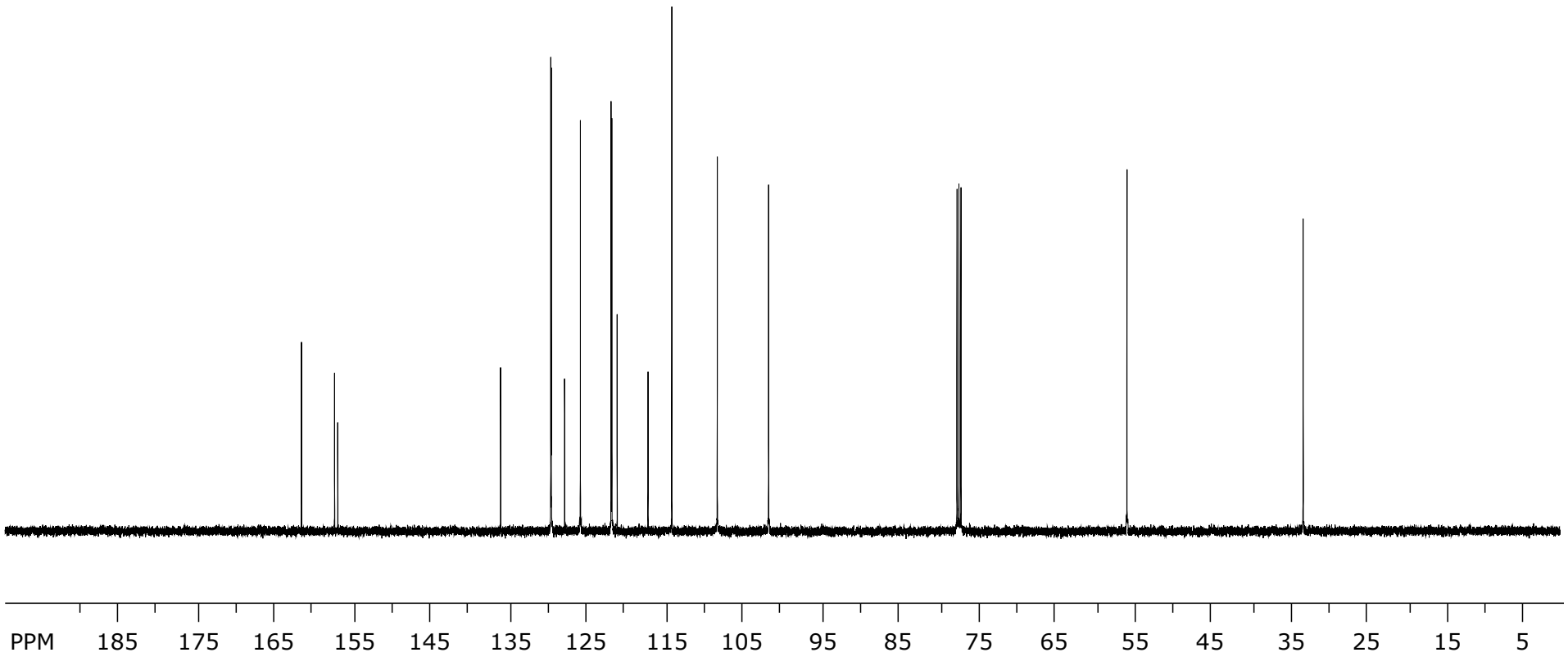
^{1}H NMR of **6d** in $CDCl_3$



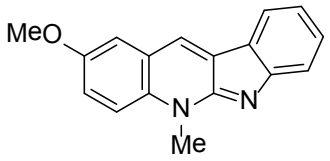


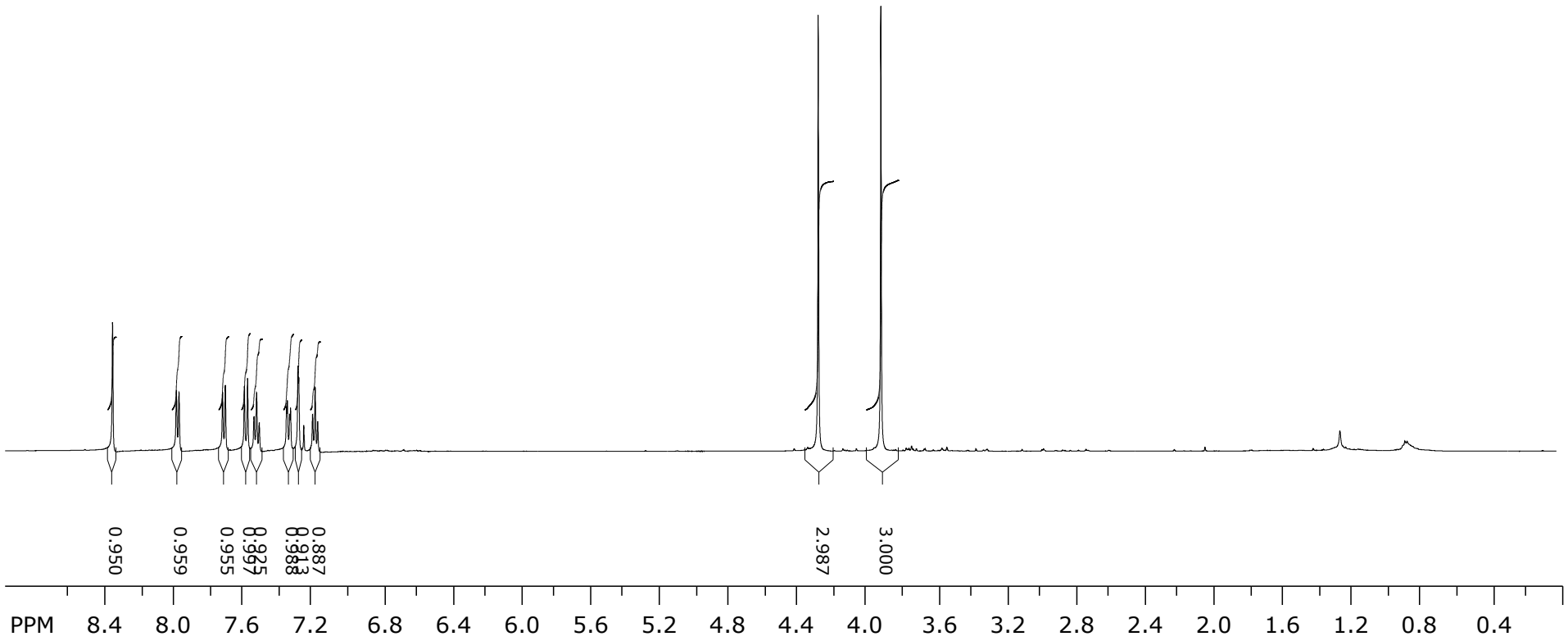
^{13}C NMR of **6d** in $CDCl_3$



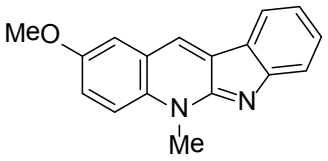


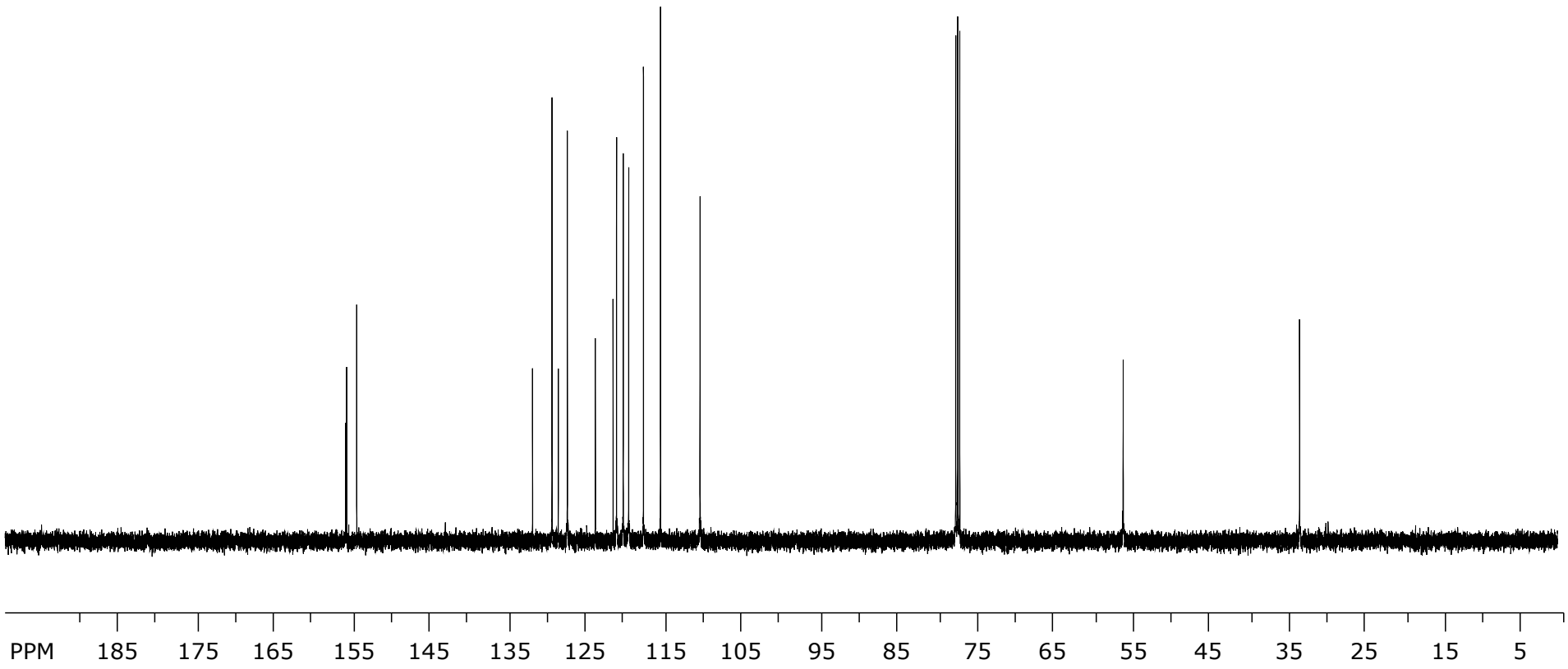
^{1}H NMR of **6e** in $CDCl_3$



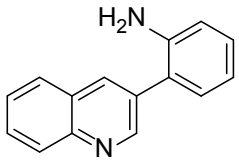


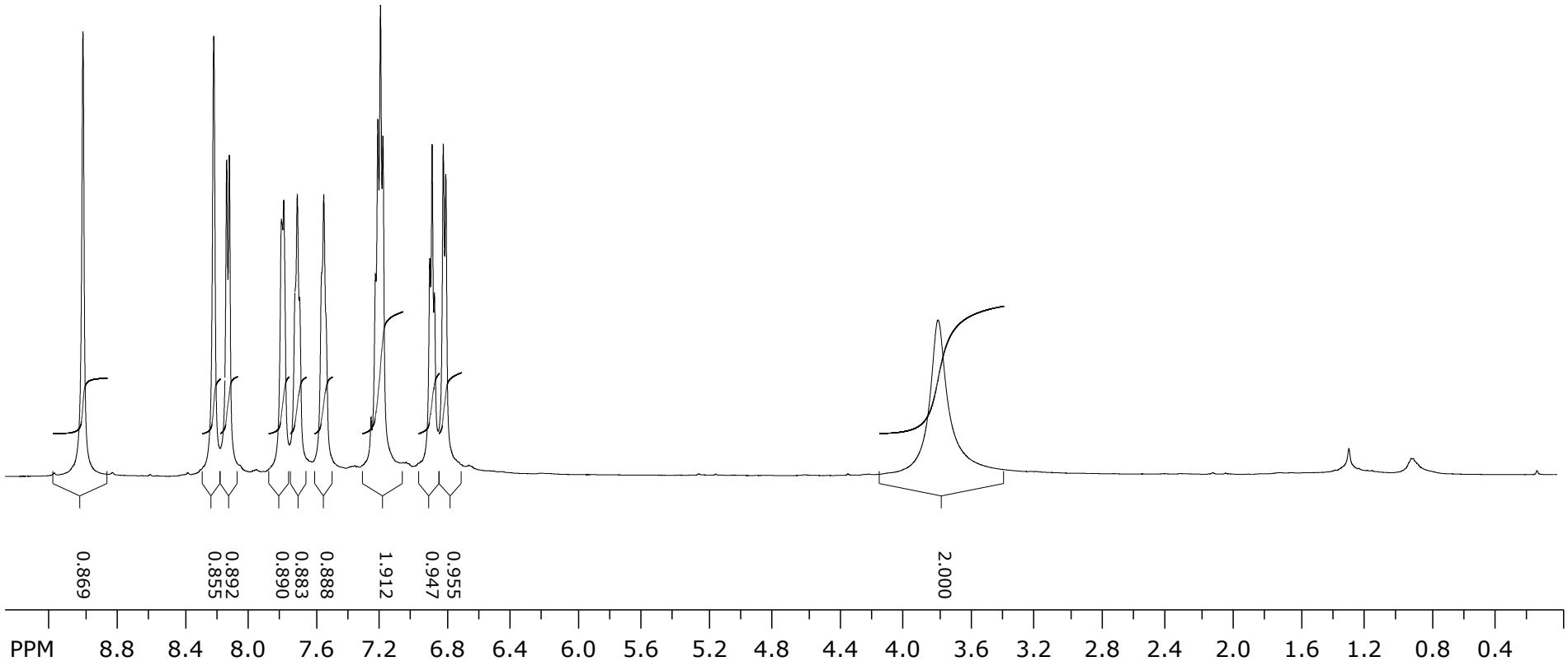
^{13}C NMR of **6e** in $CDCl_3$



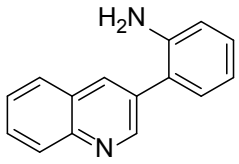


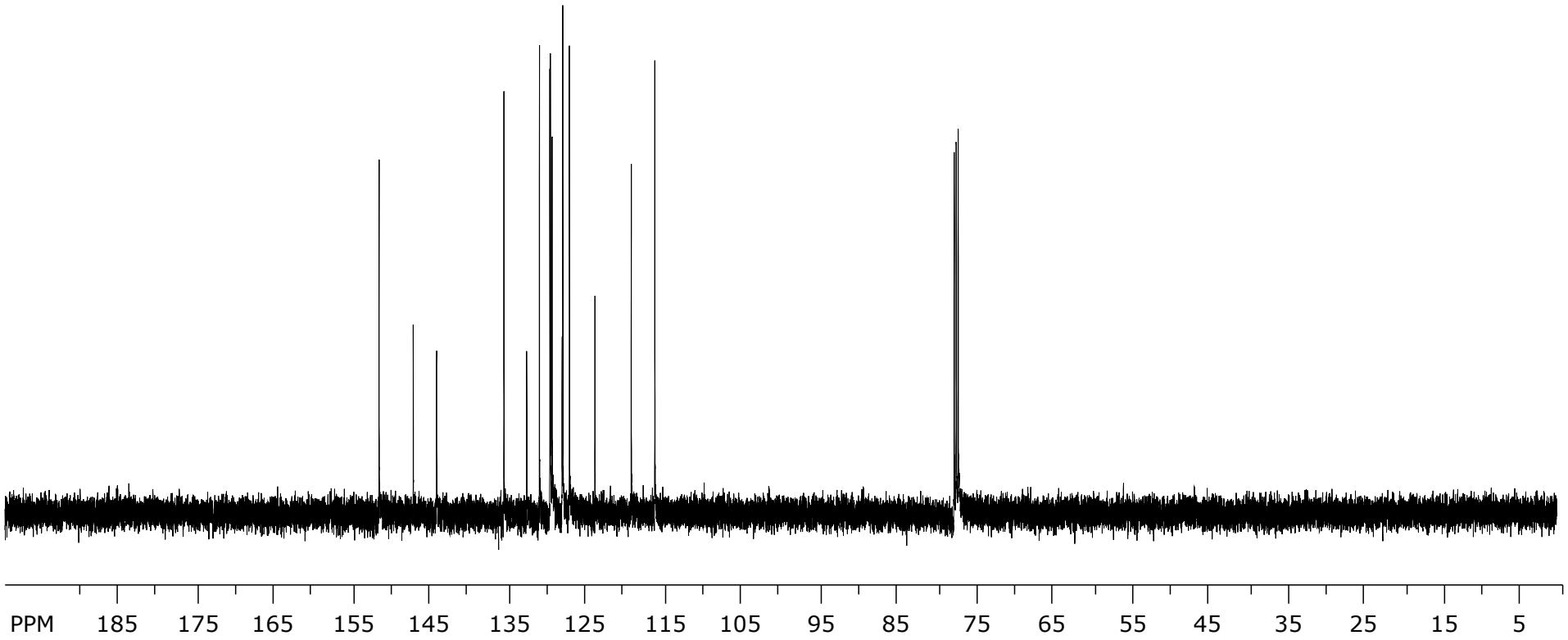
^{1}H NMR of **11a** in $CDCl_3$



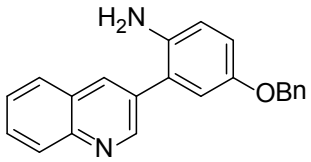


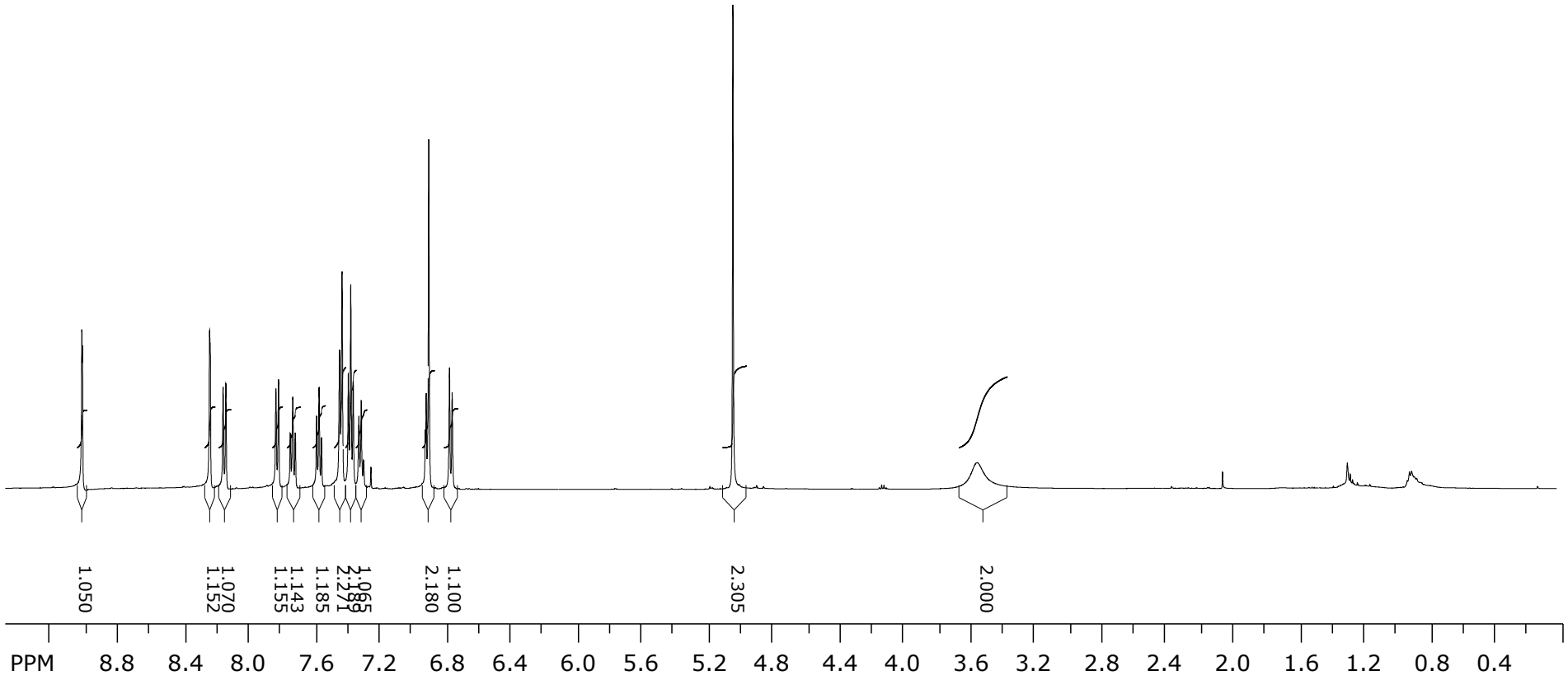
^{13}C NMR of **11a** in $CDCl_3$



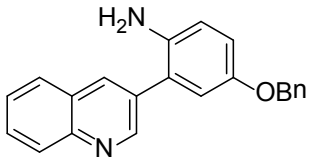


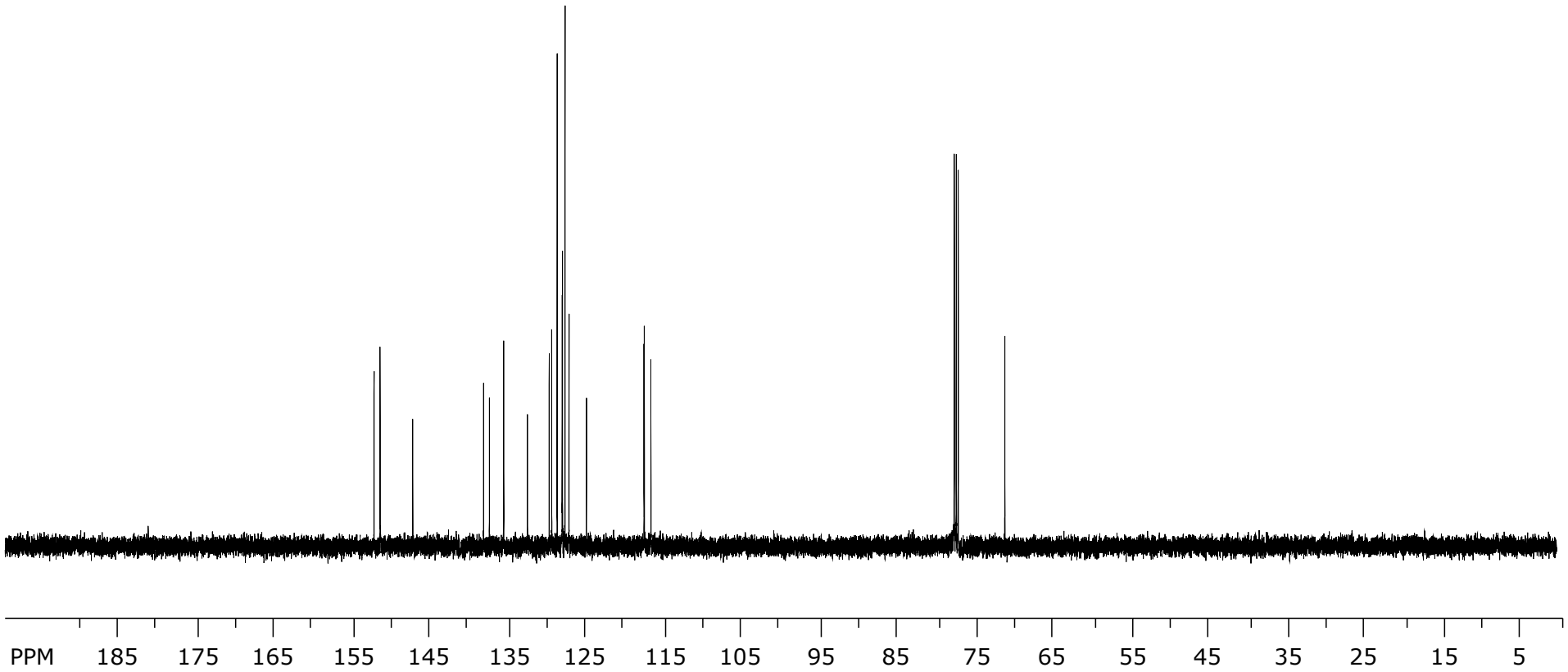
^{1}H NMR of **11b** in $CDCl_3$



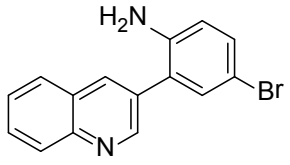


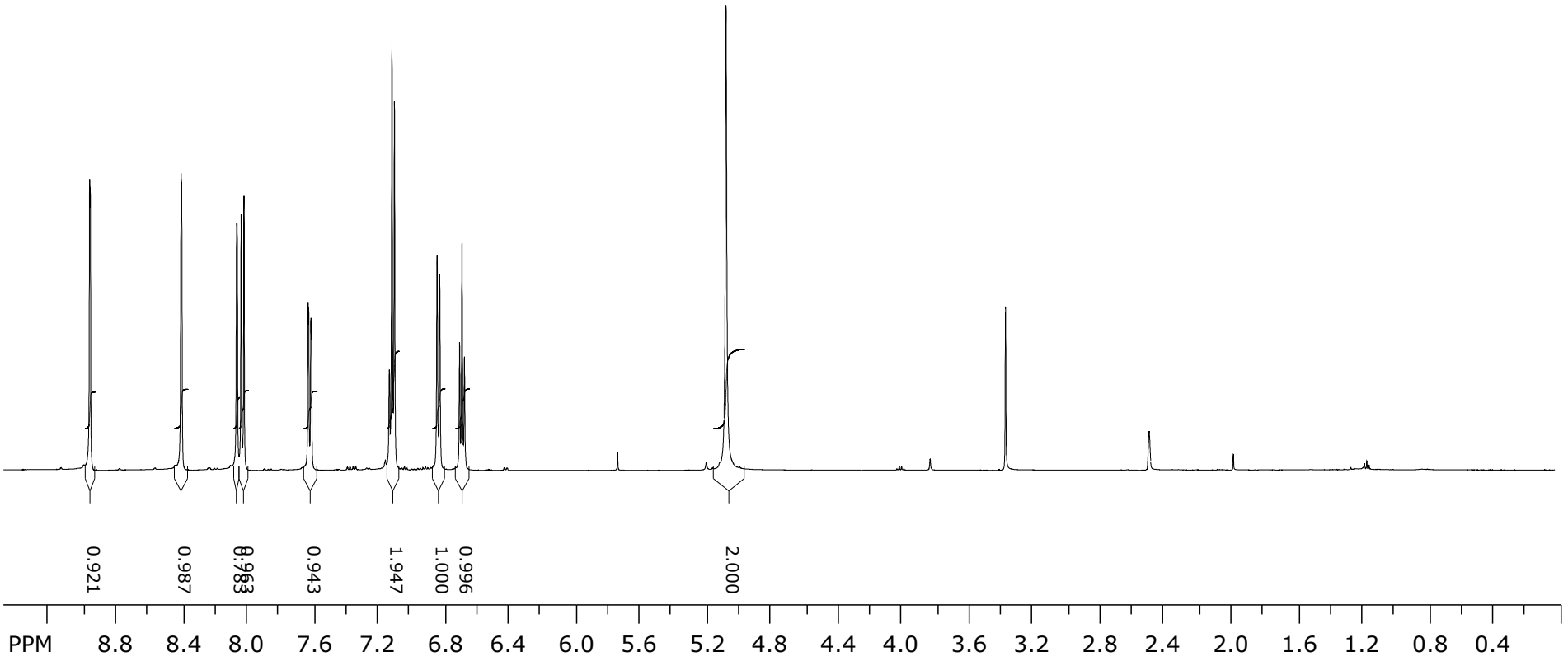
^{13}C NMR of **11b** in $CDCl_3$



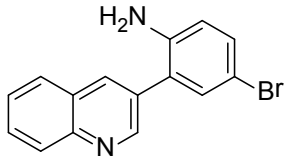


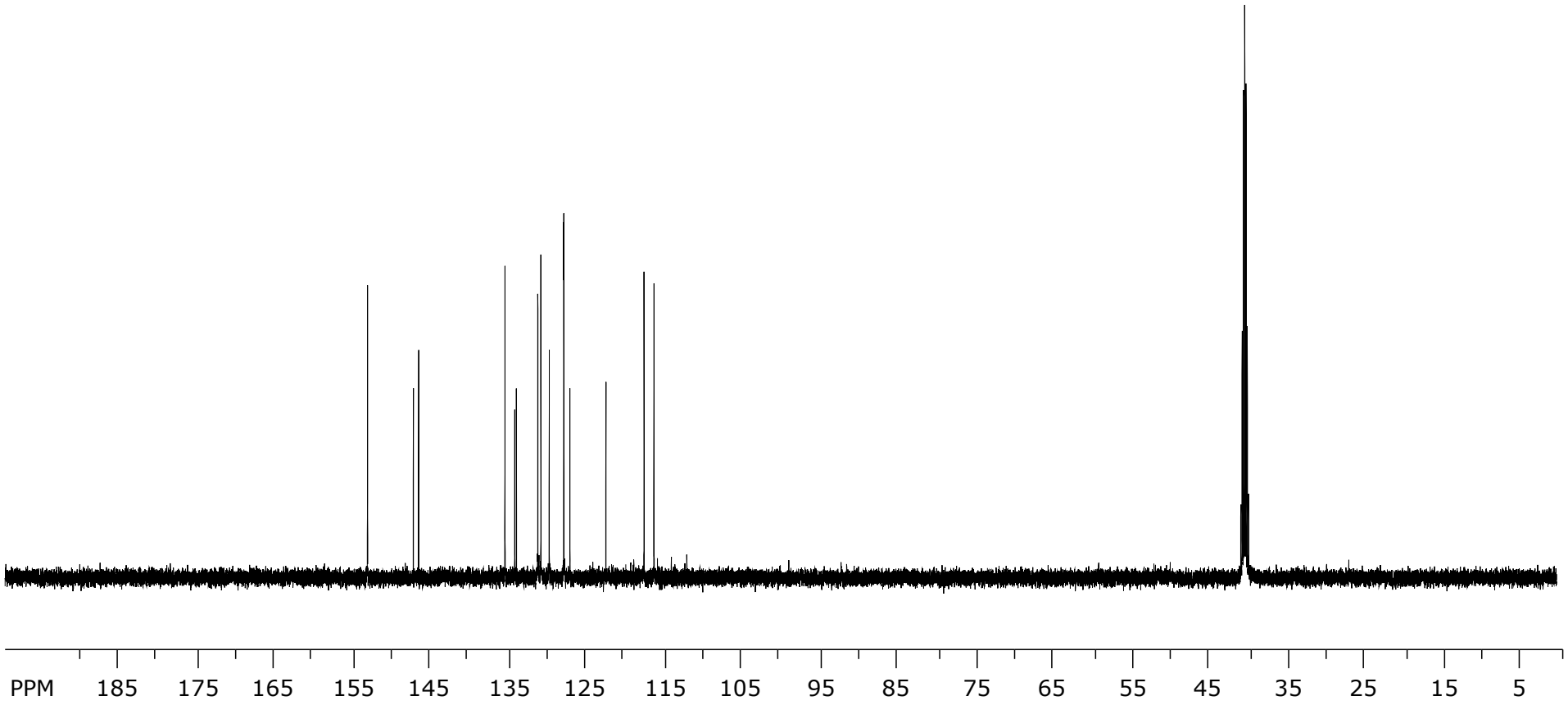
^{1}H NMR of **11c** in DMSO



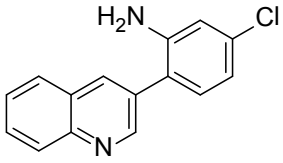


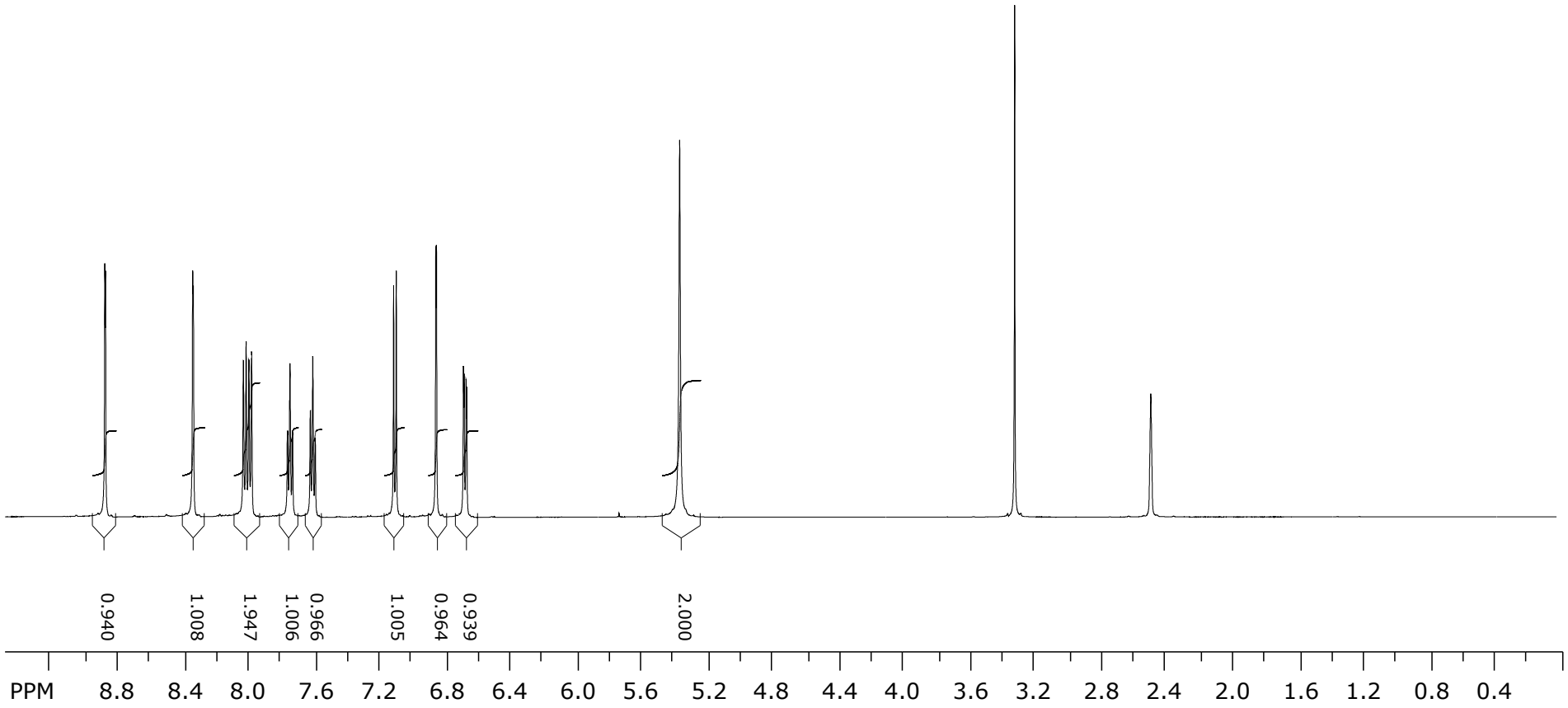
^{13}C NMR of **11c** in DMSO



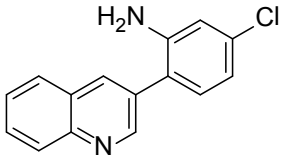


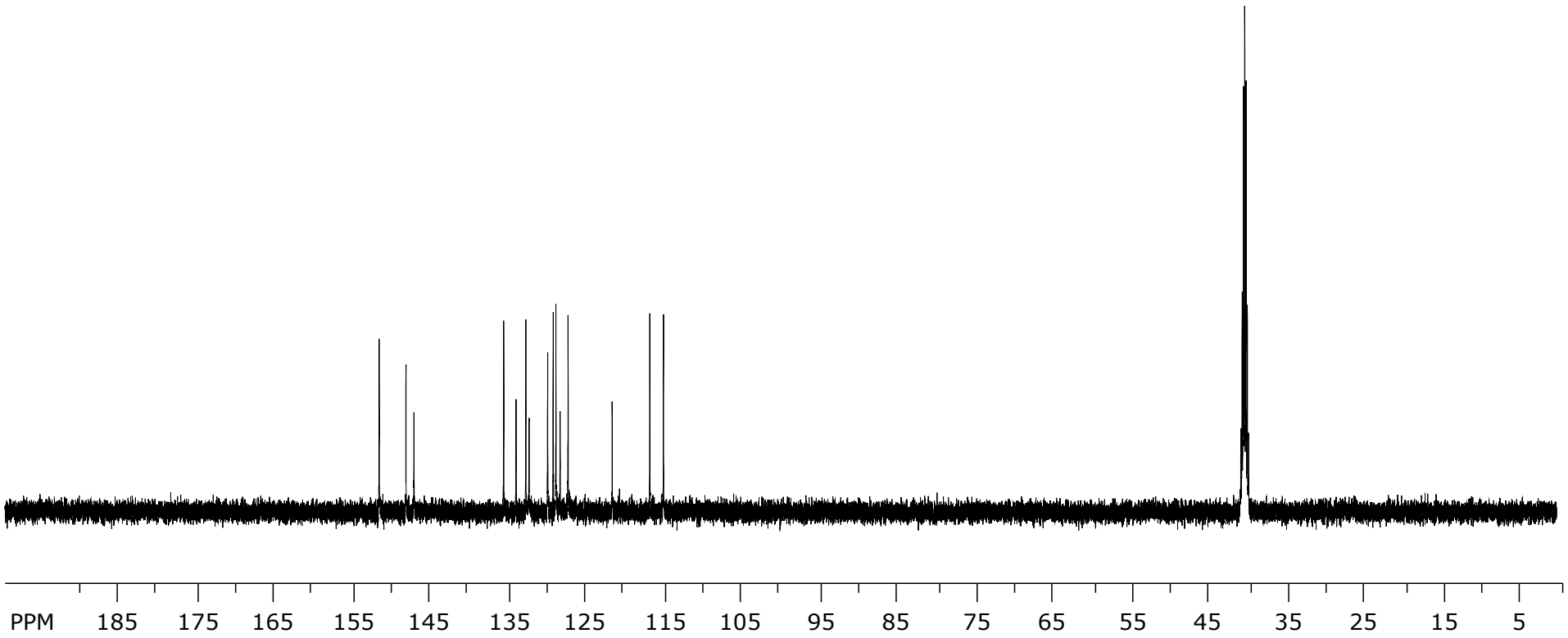
^{1}H NMR of **11d** in DMSO



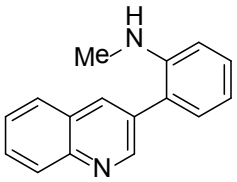


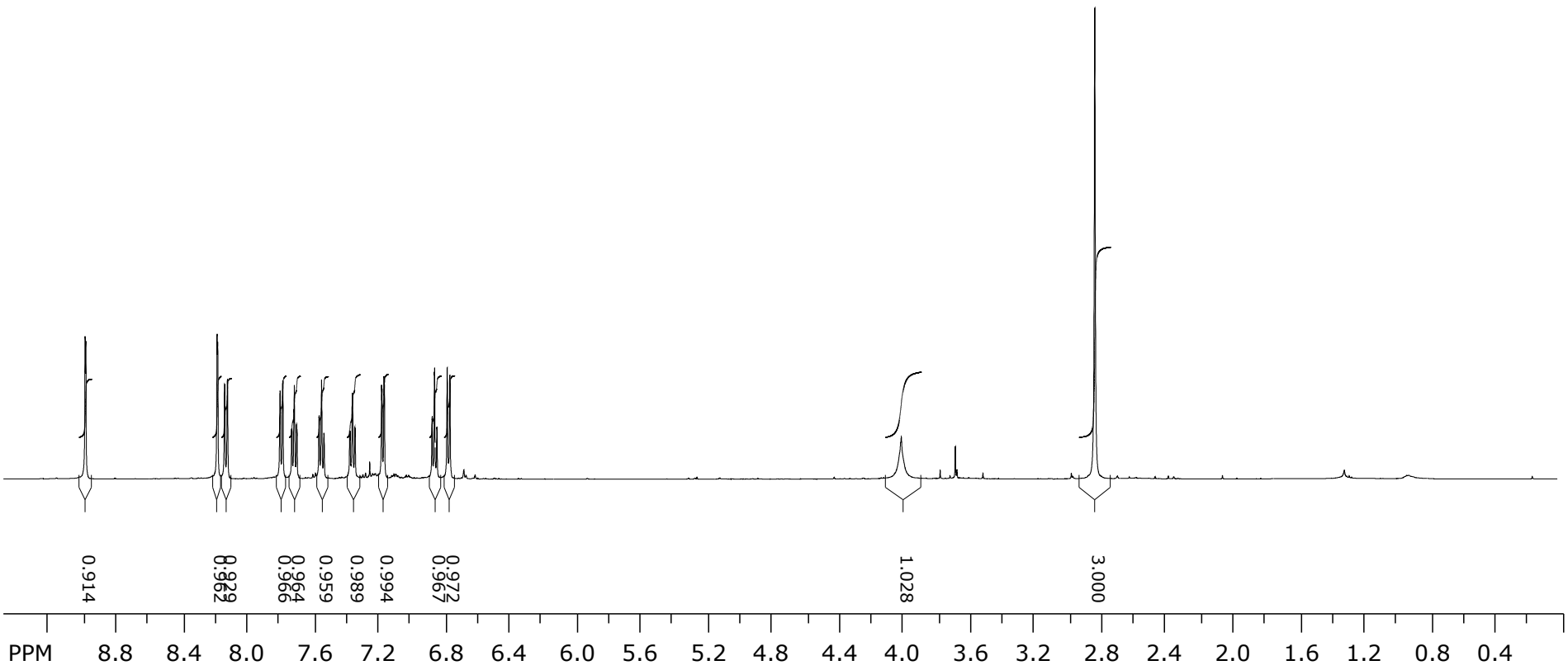
^{13}C NMR of **11d** in DMSO



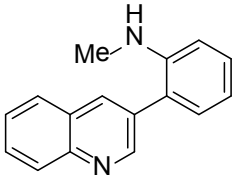


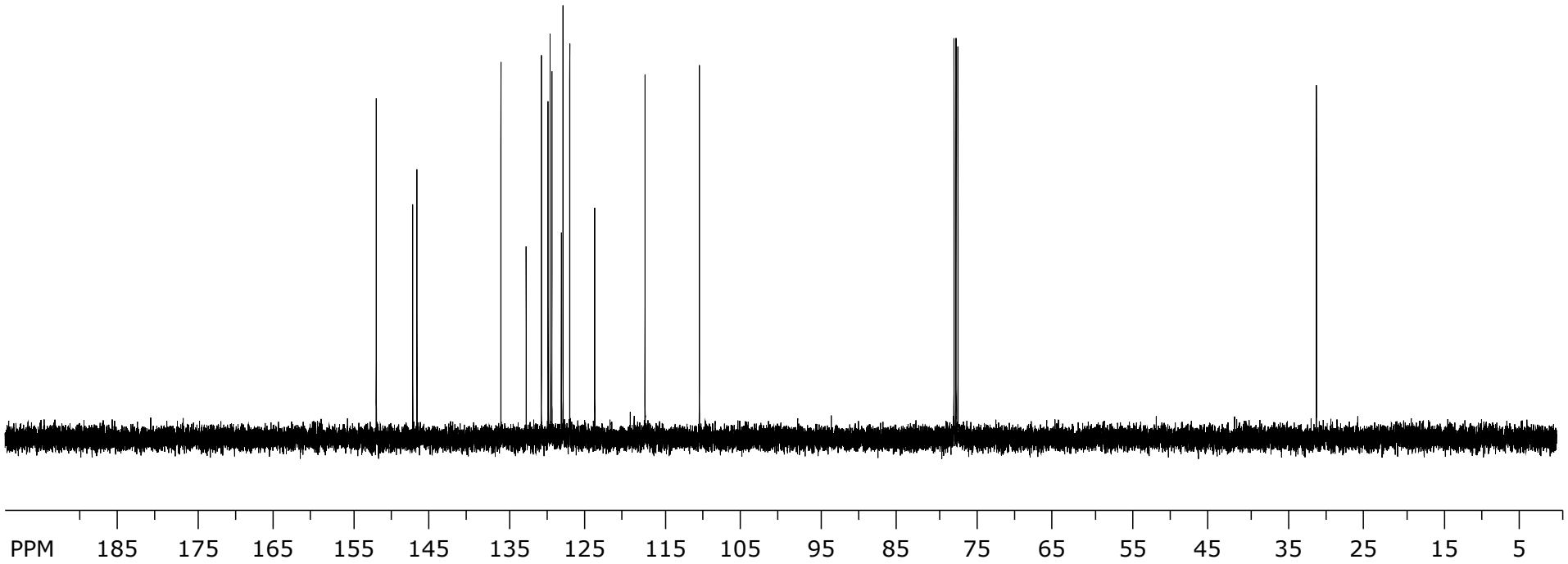
^{1}H NMR of **11e** in $CDCl_3$



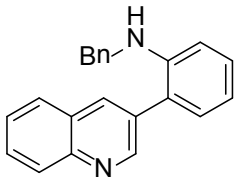


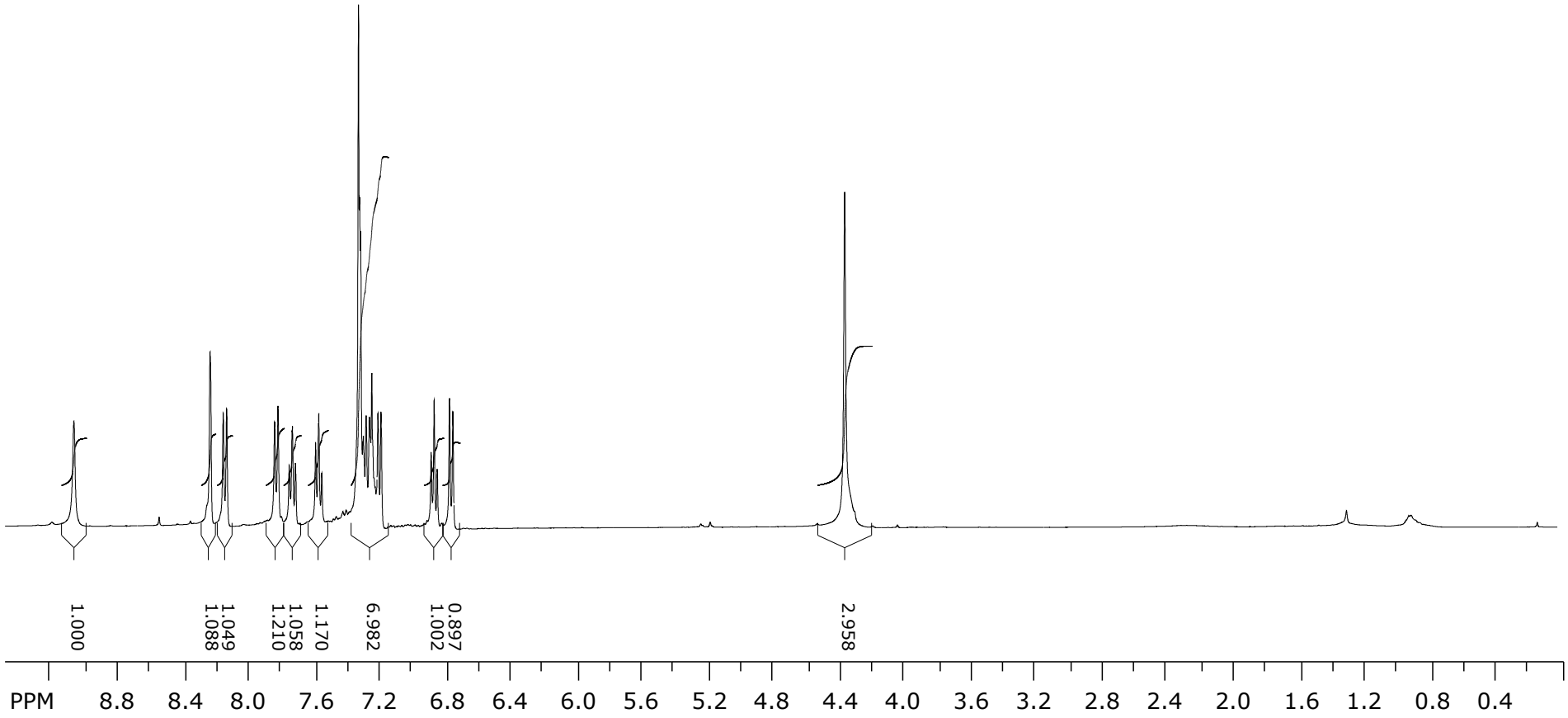
^{13}C NMR of **11e** in $CDCl_3$



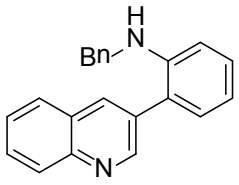


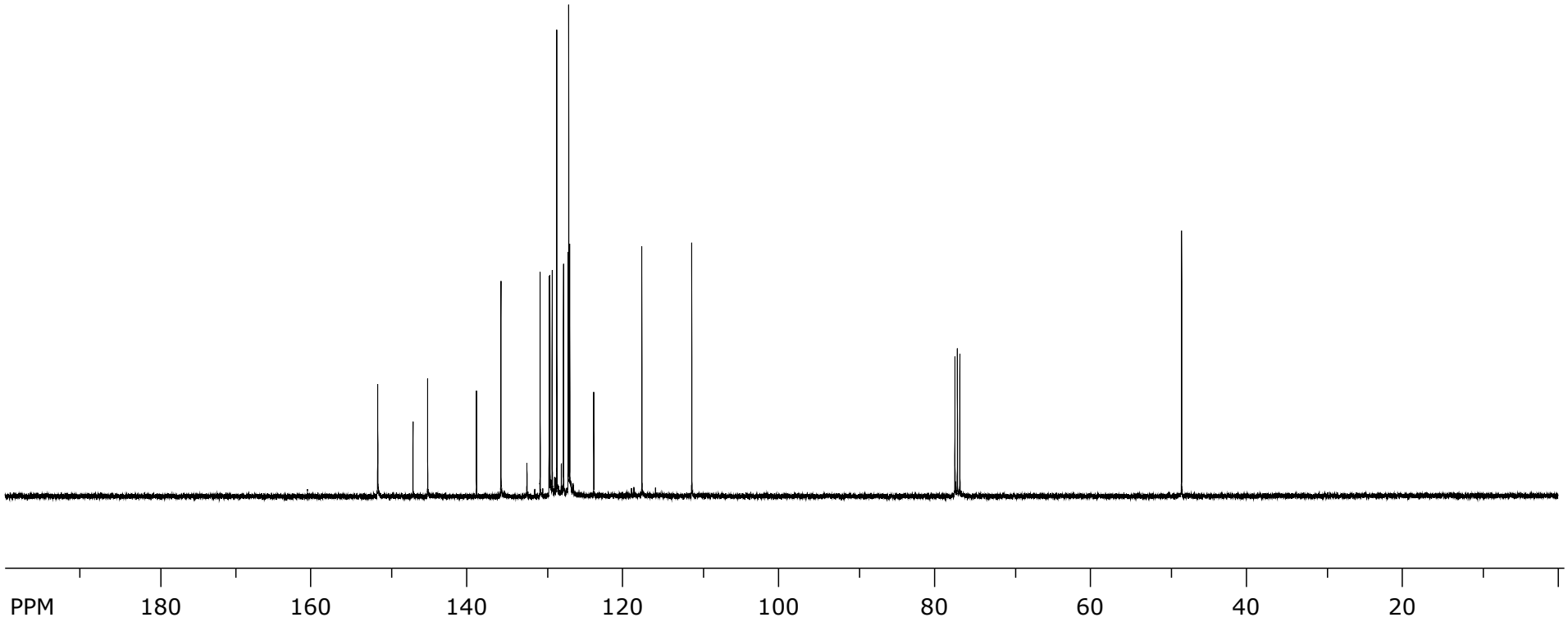
^{1}H NMR of **11f** in $CDCl_3$



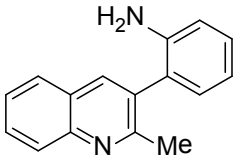


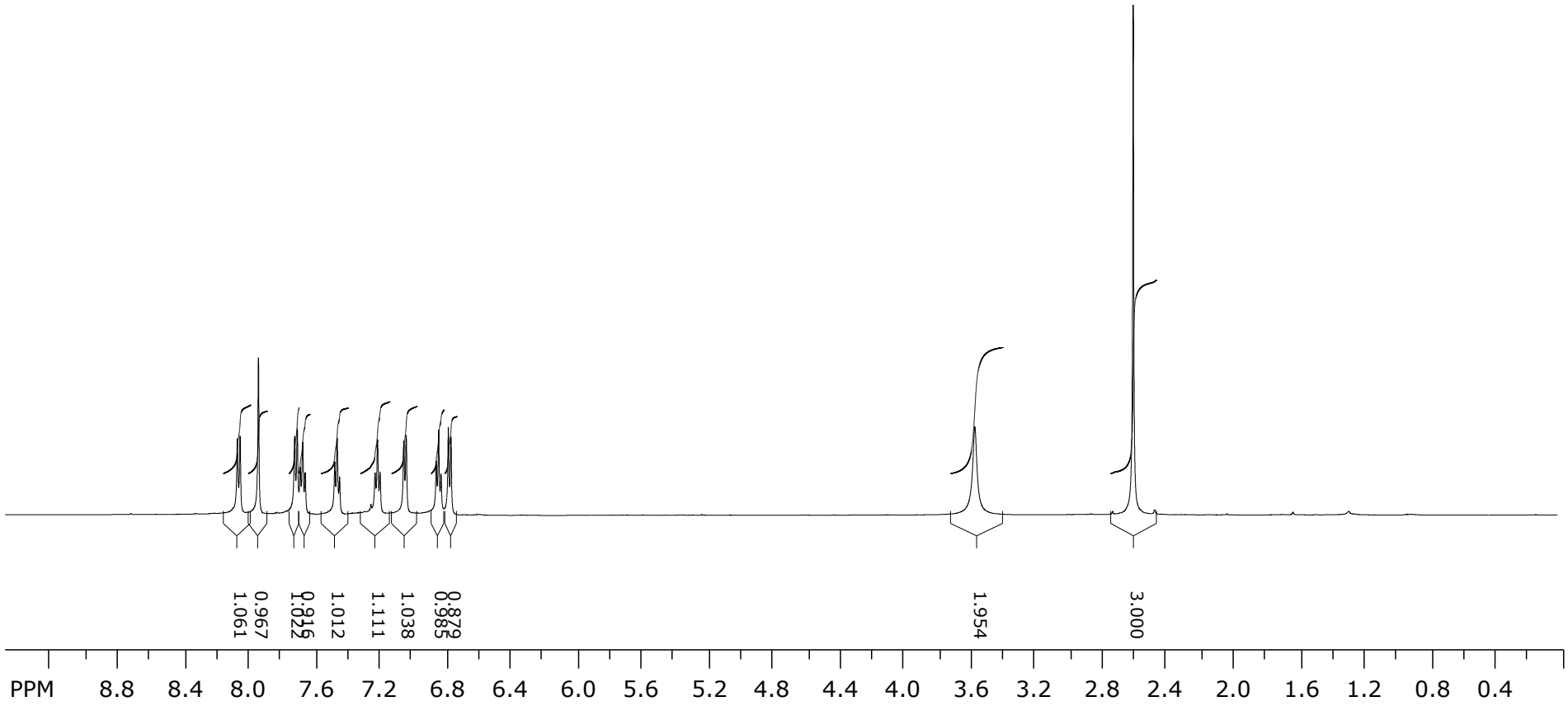
^{13}C NMR of **11f** in $CDCl_3$



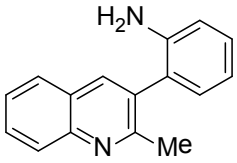


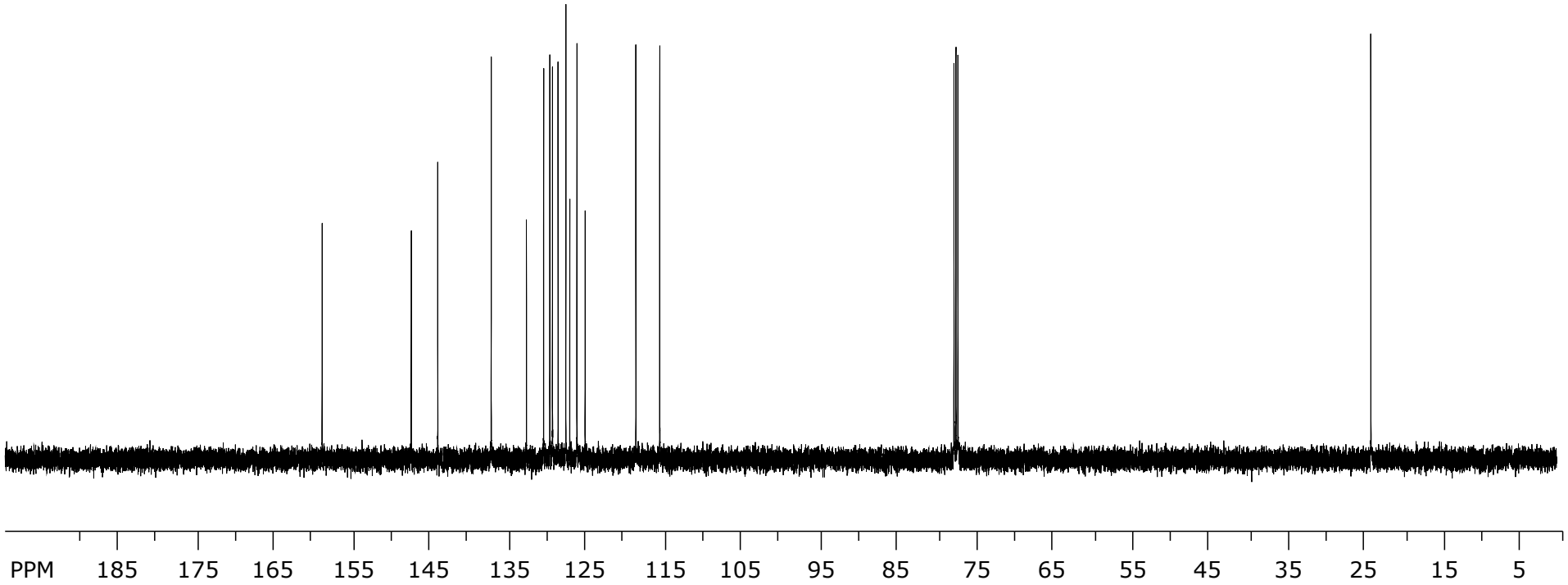
^{1}H NMR of **11g** in $CDCl_3$



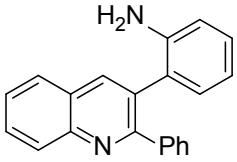


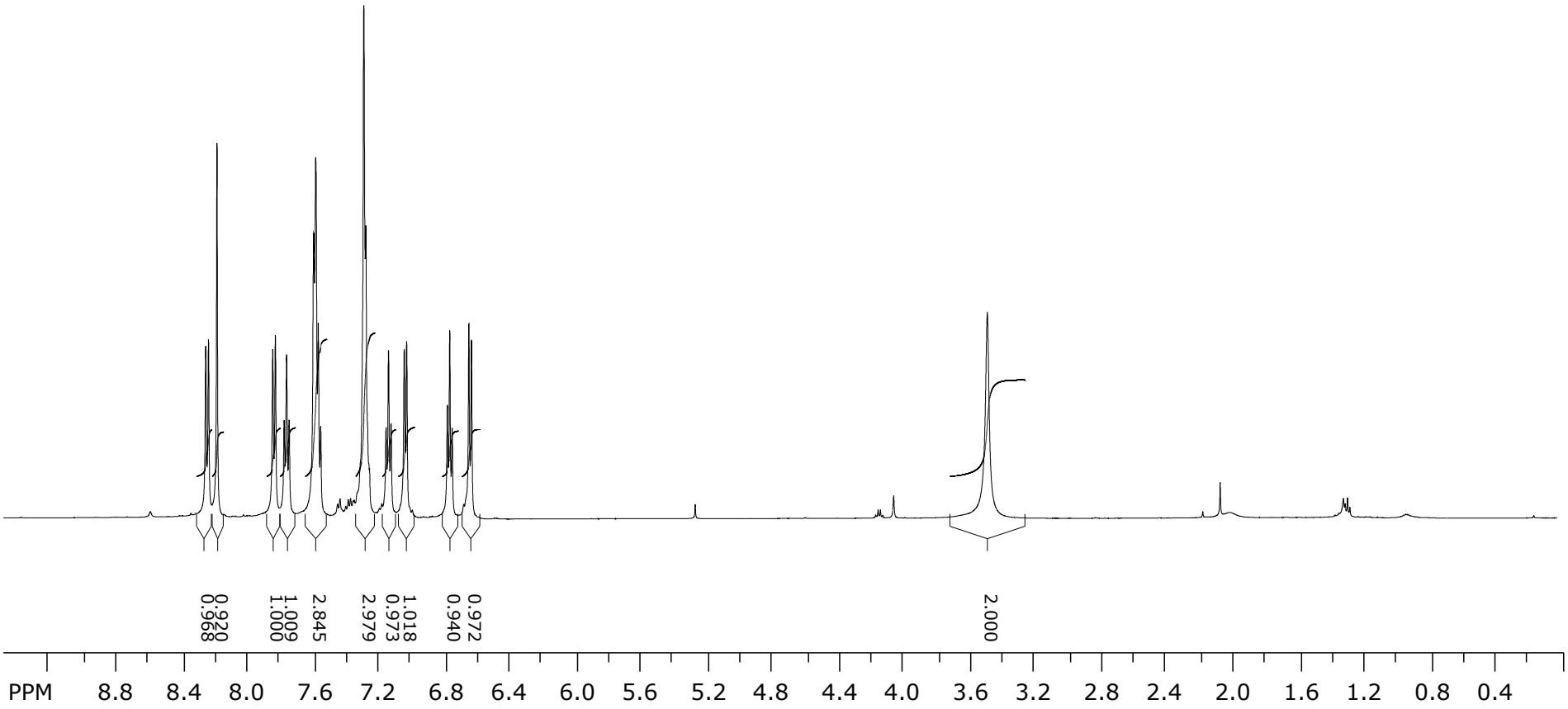
^{13}C NMR of **11g** in $CDCl_3$



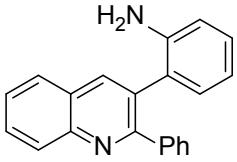


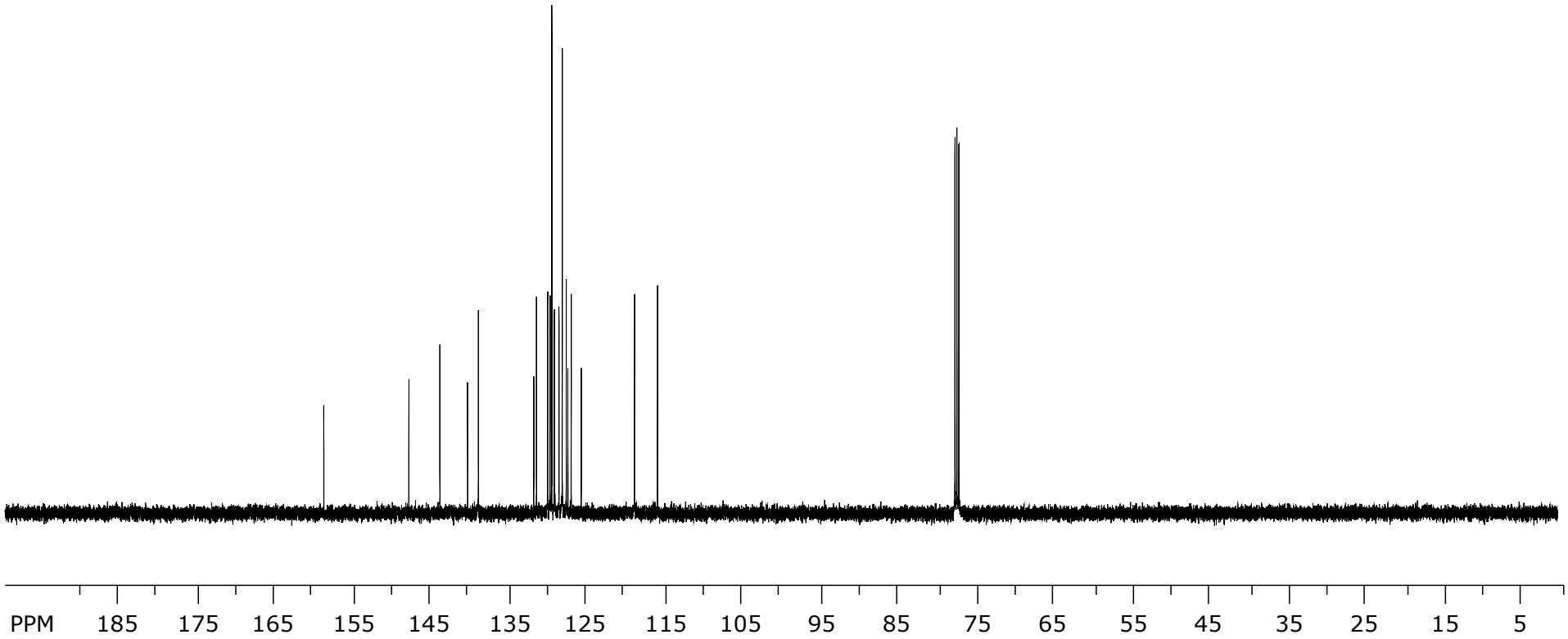
^{1}H NMR of **11h** in $CDCl_3$



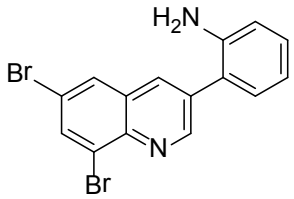


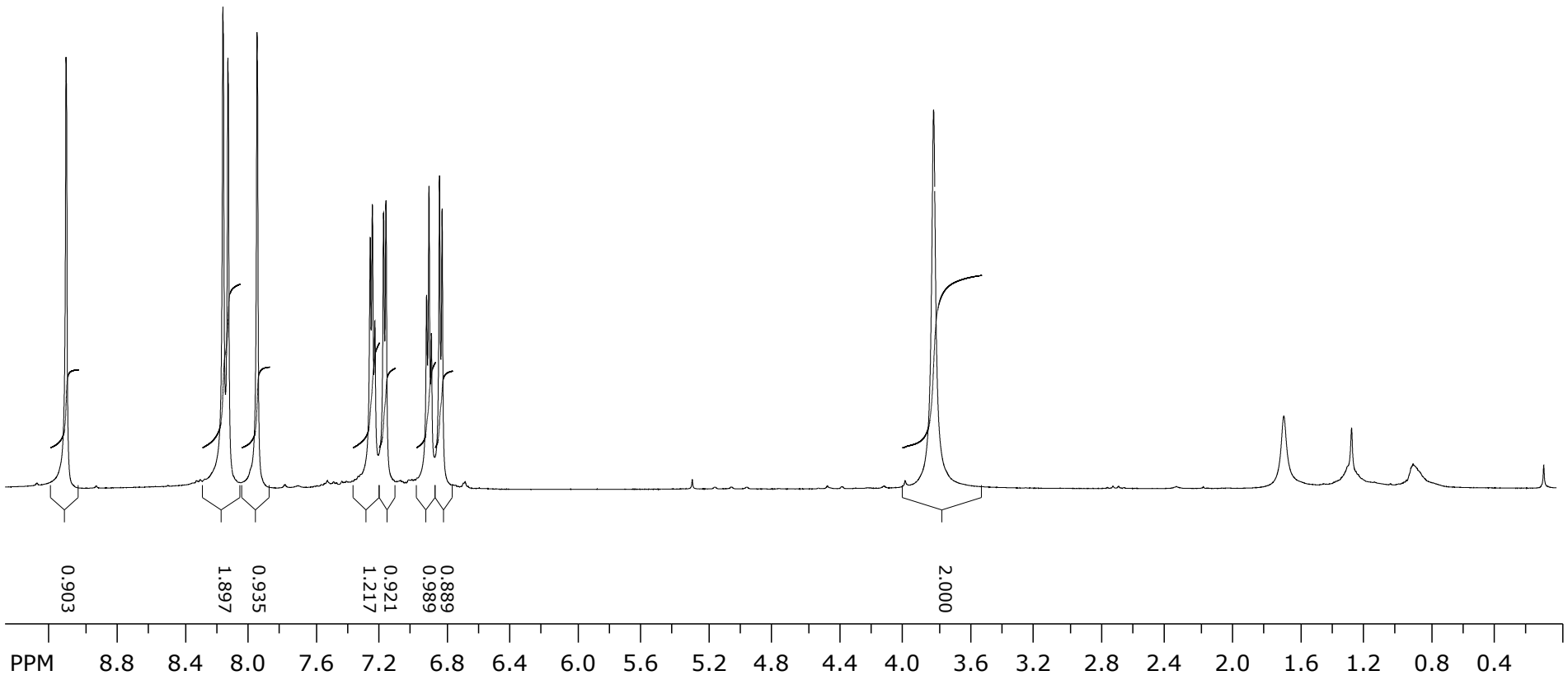
^{13}C NMR of **11h** in $CDCl_3$



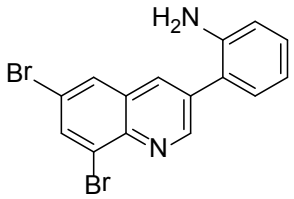


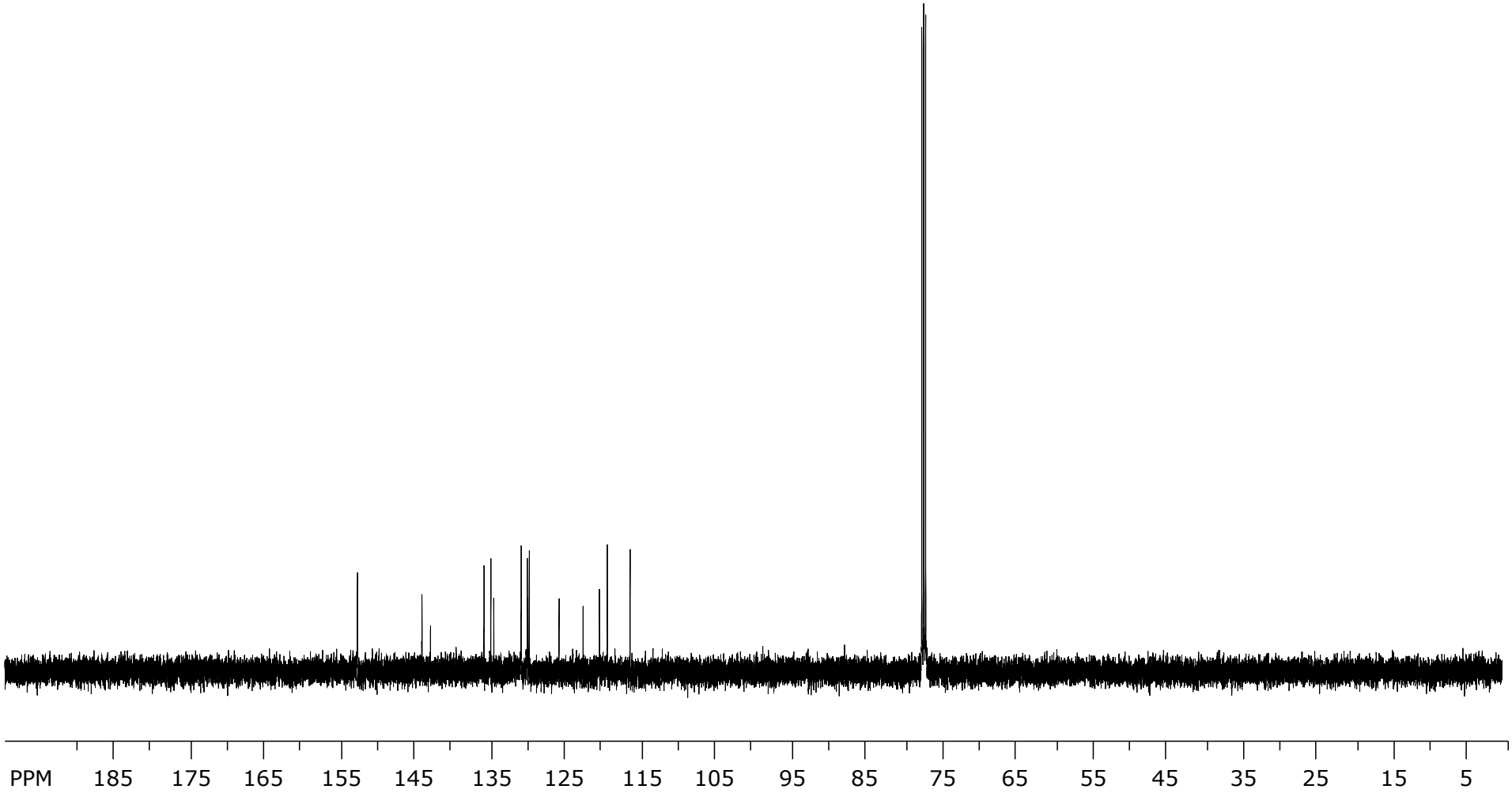
^{1}H NMR of **11i** in $CDCl_3$



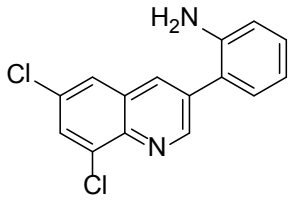


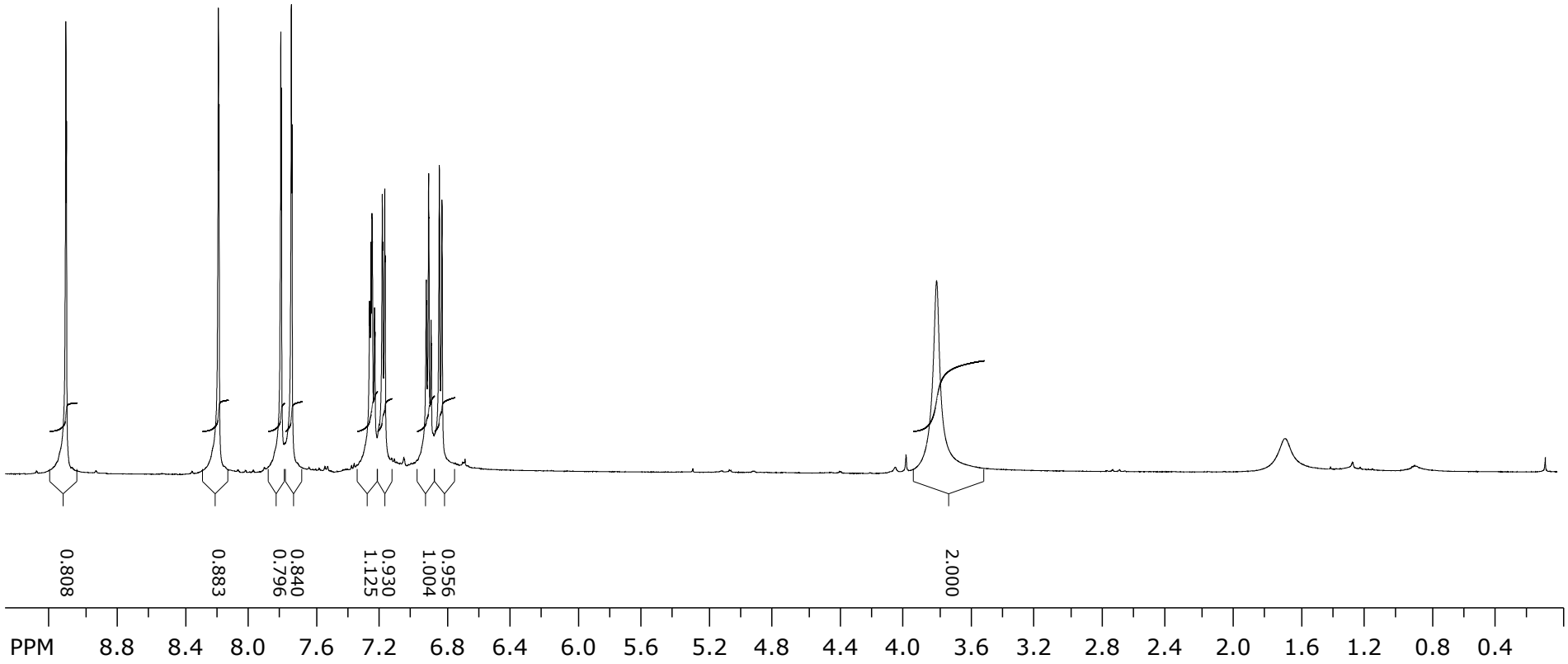
^{13}C NMR of **11i** in $CDCl_3$





^{1}H NMR of **11j** in $CDCl_3$





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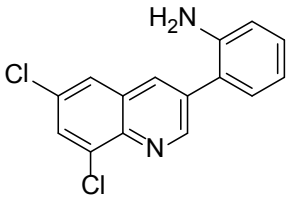
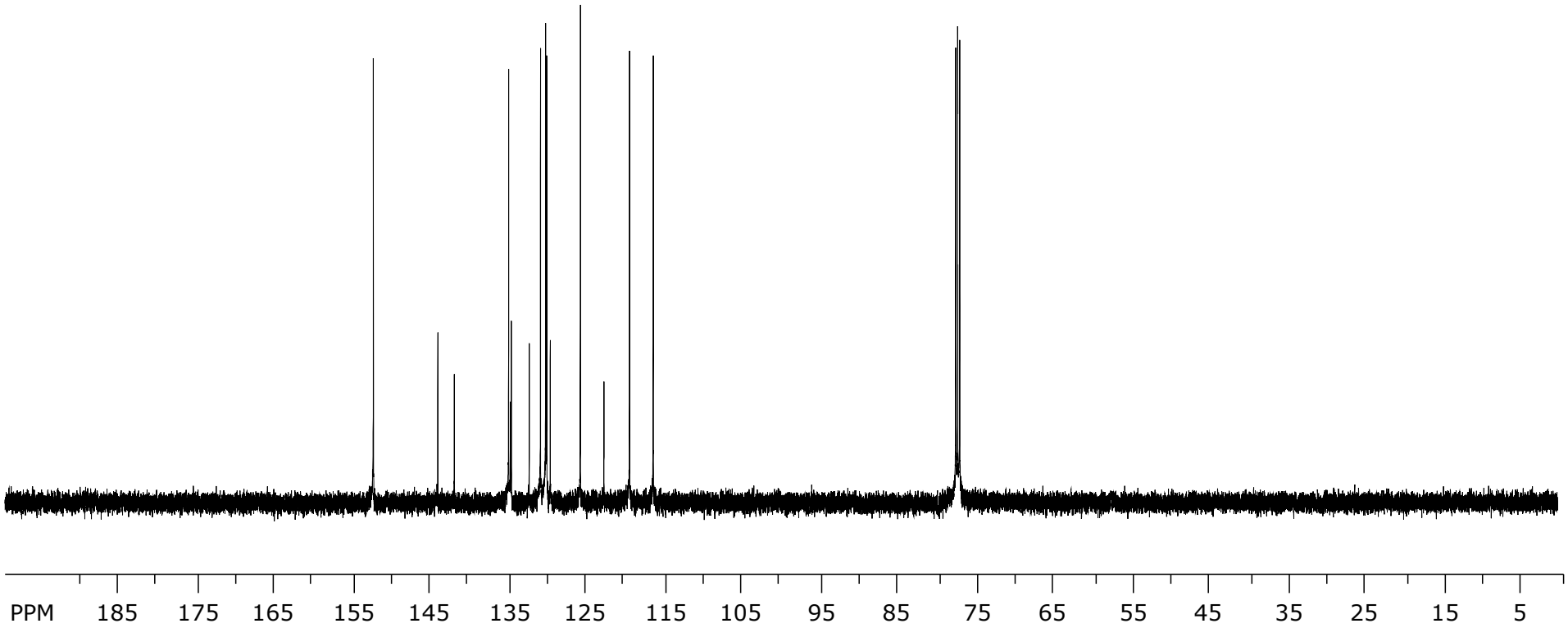
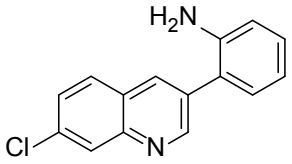
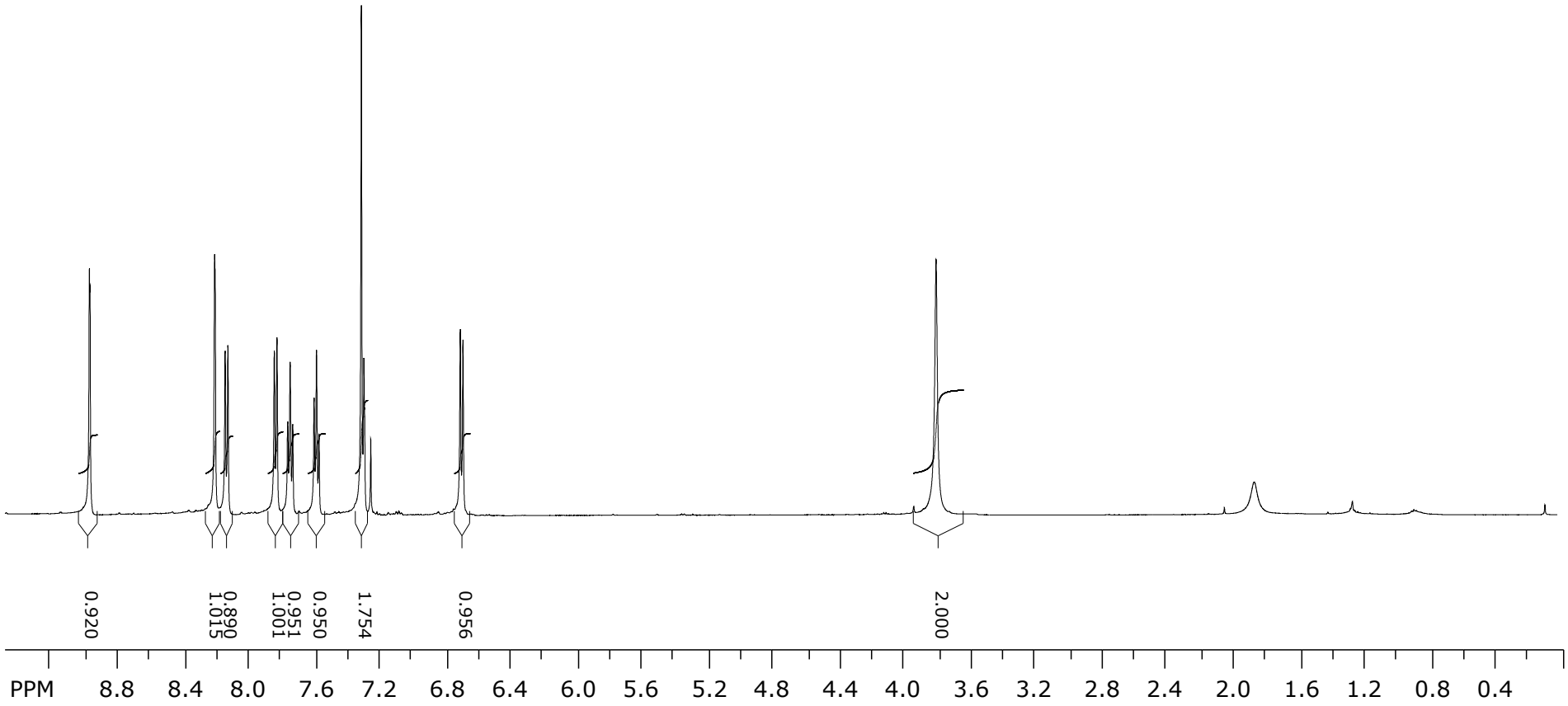


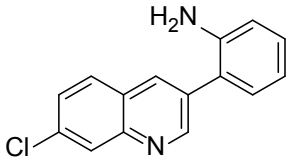


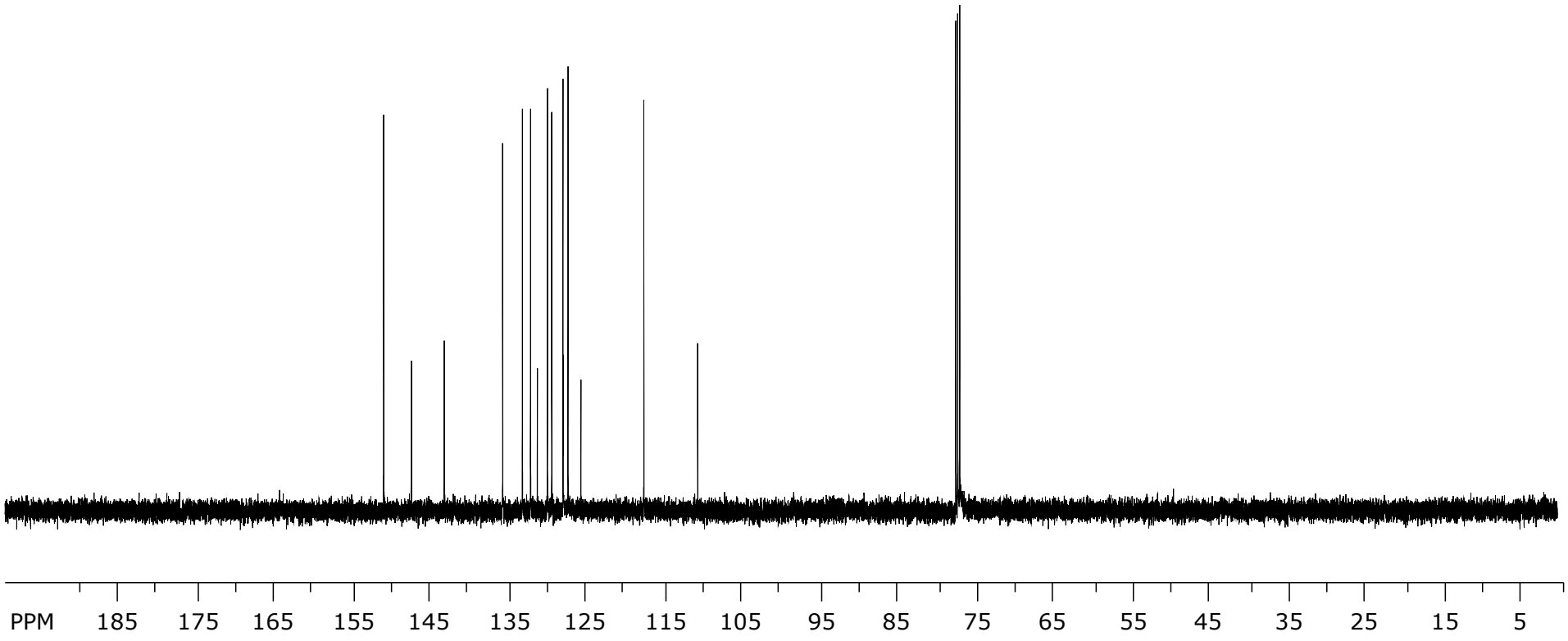
^{1}H NMR of **11k** in $CDCl_3$



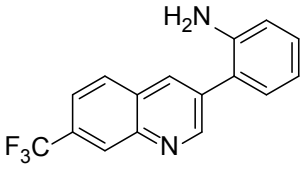


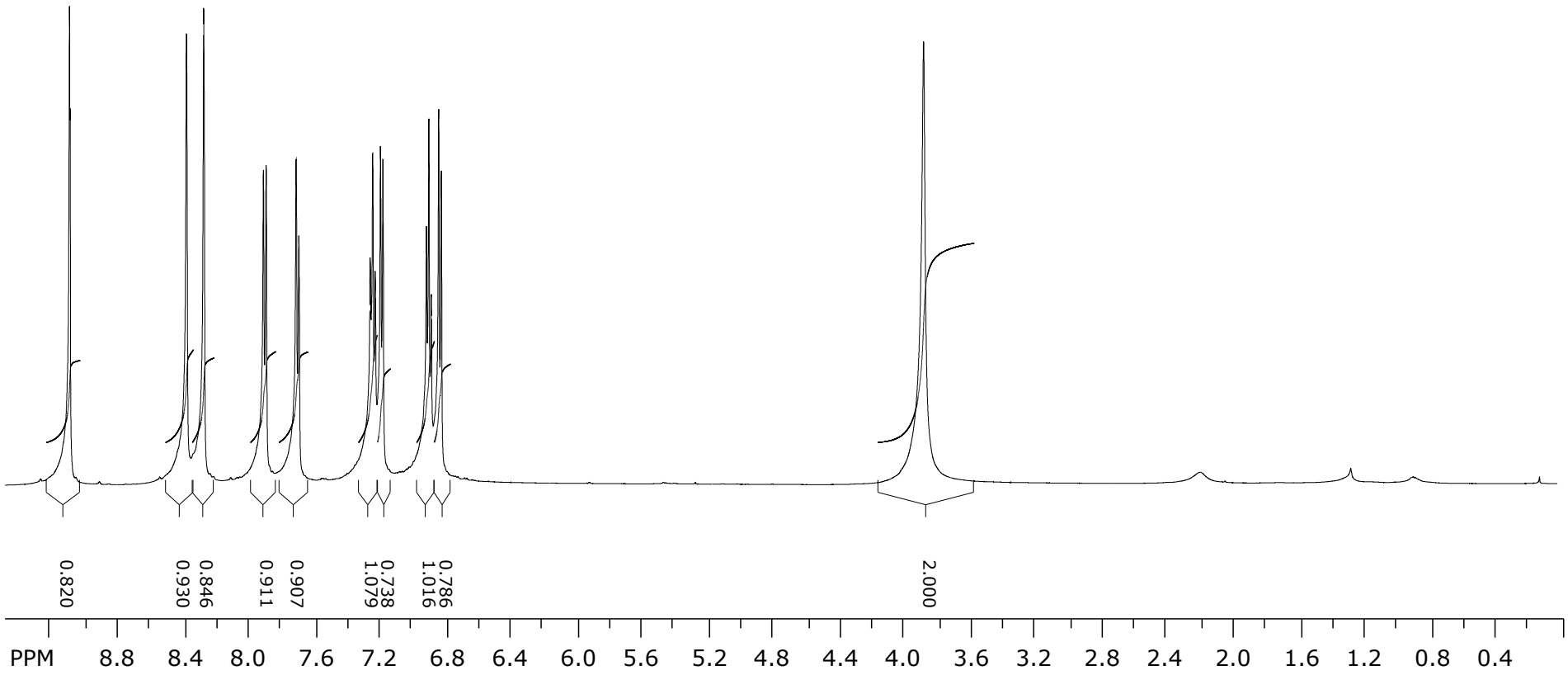
^{13}C NMR of **11k** in $CDCl_3$



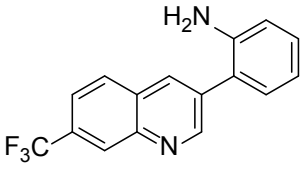


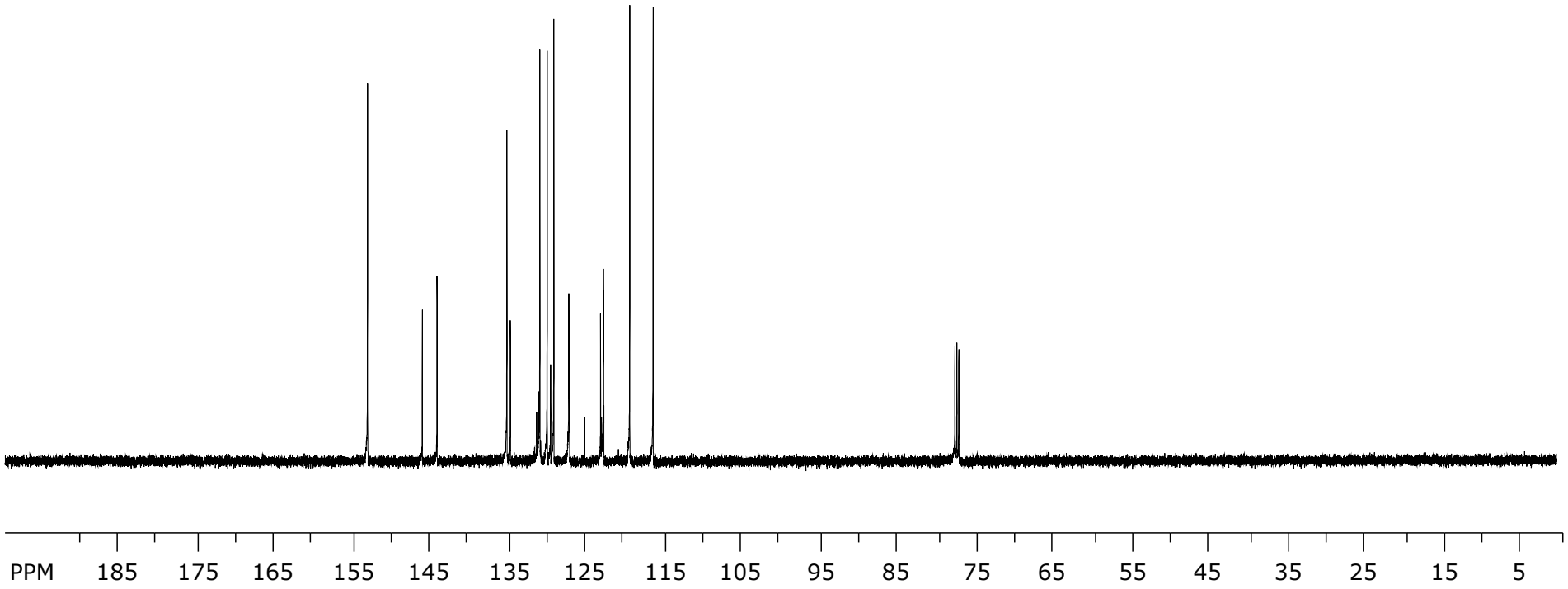
^{1}H NMR of **11l** in $CDCl_3$



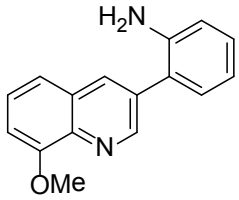


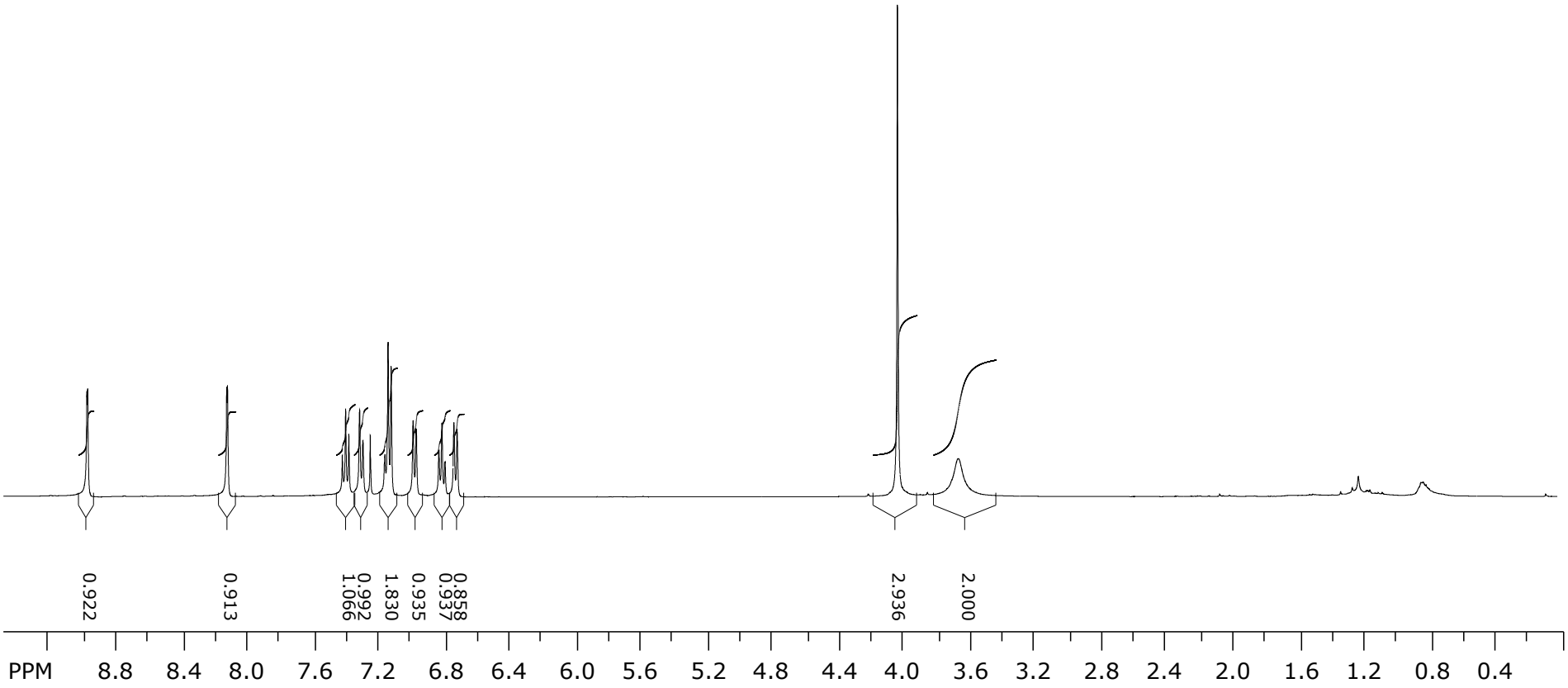
^{13}C NMR of **11l** in $CDCl_3$



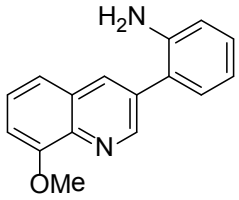


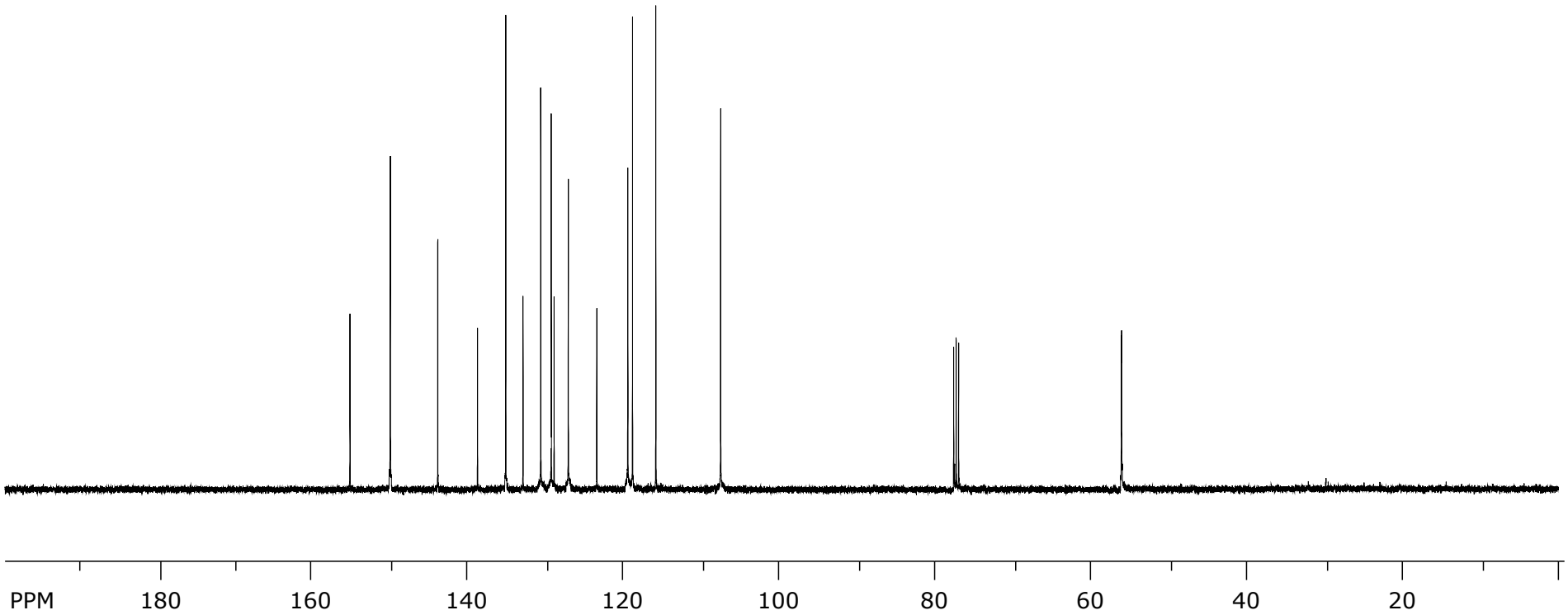
^{1}H NMR of **11m** in $CDCl_3$



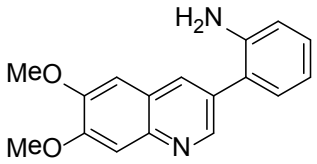


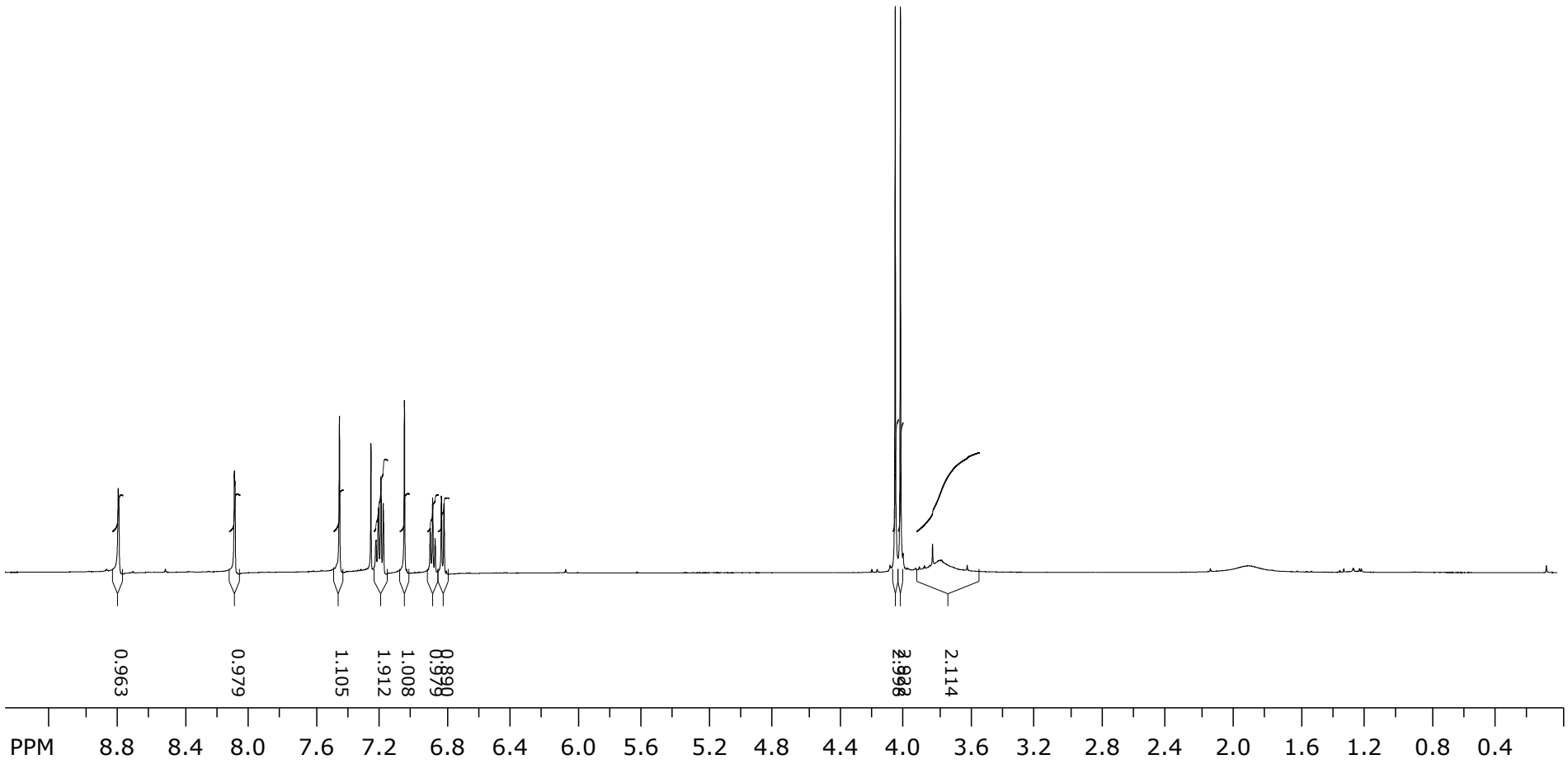
^{13}C NMR of **11m** in $CDCl_3$



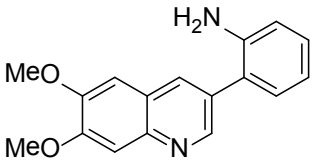


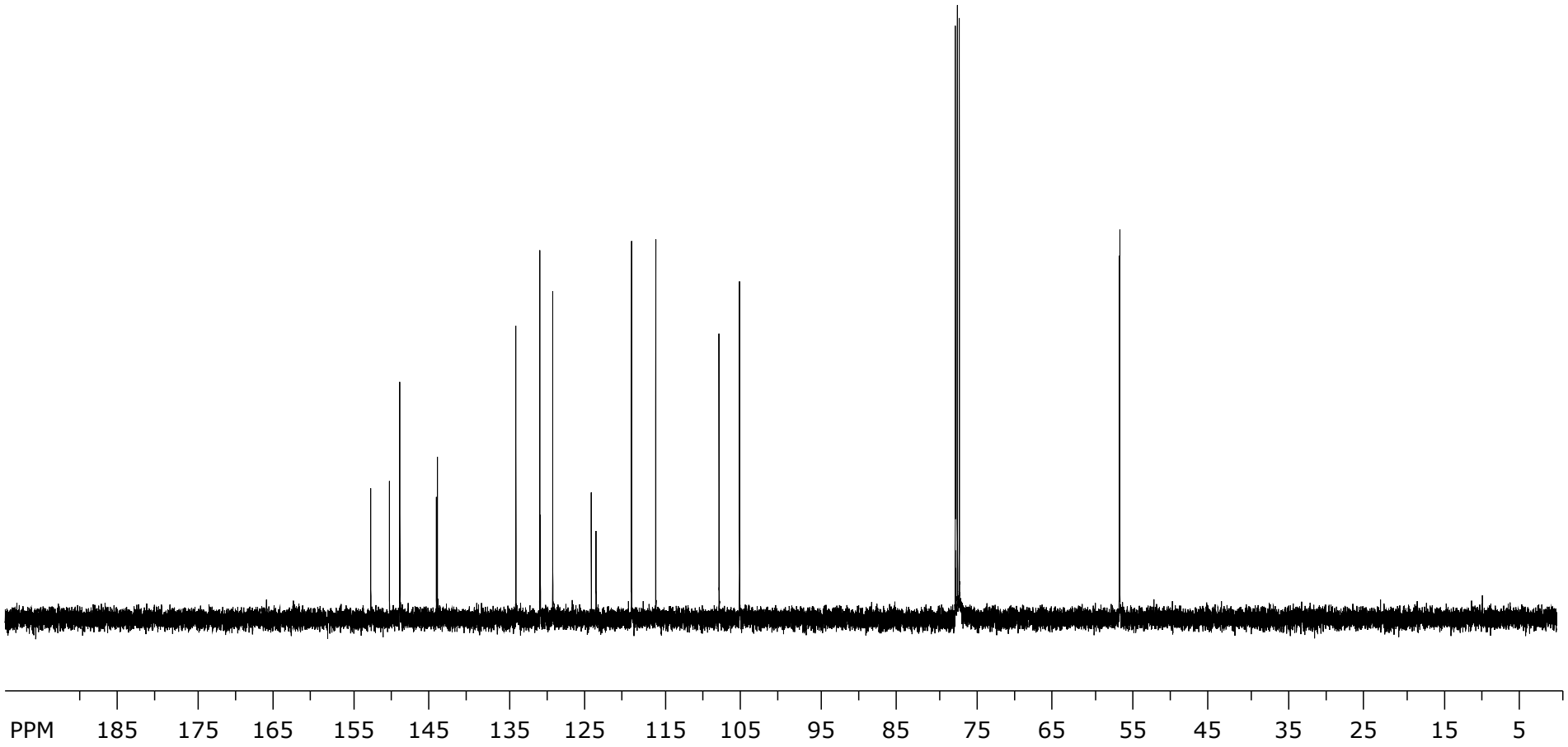
^{1}H NMR of **11n** in $CDCl_3$



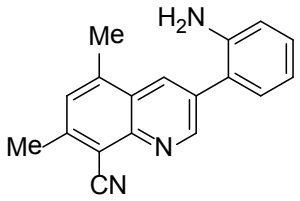


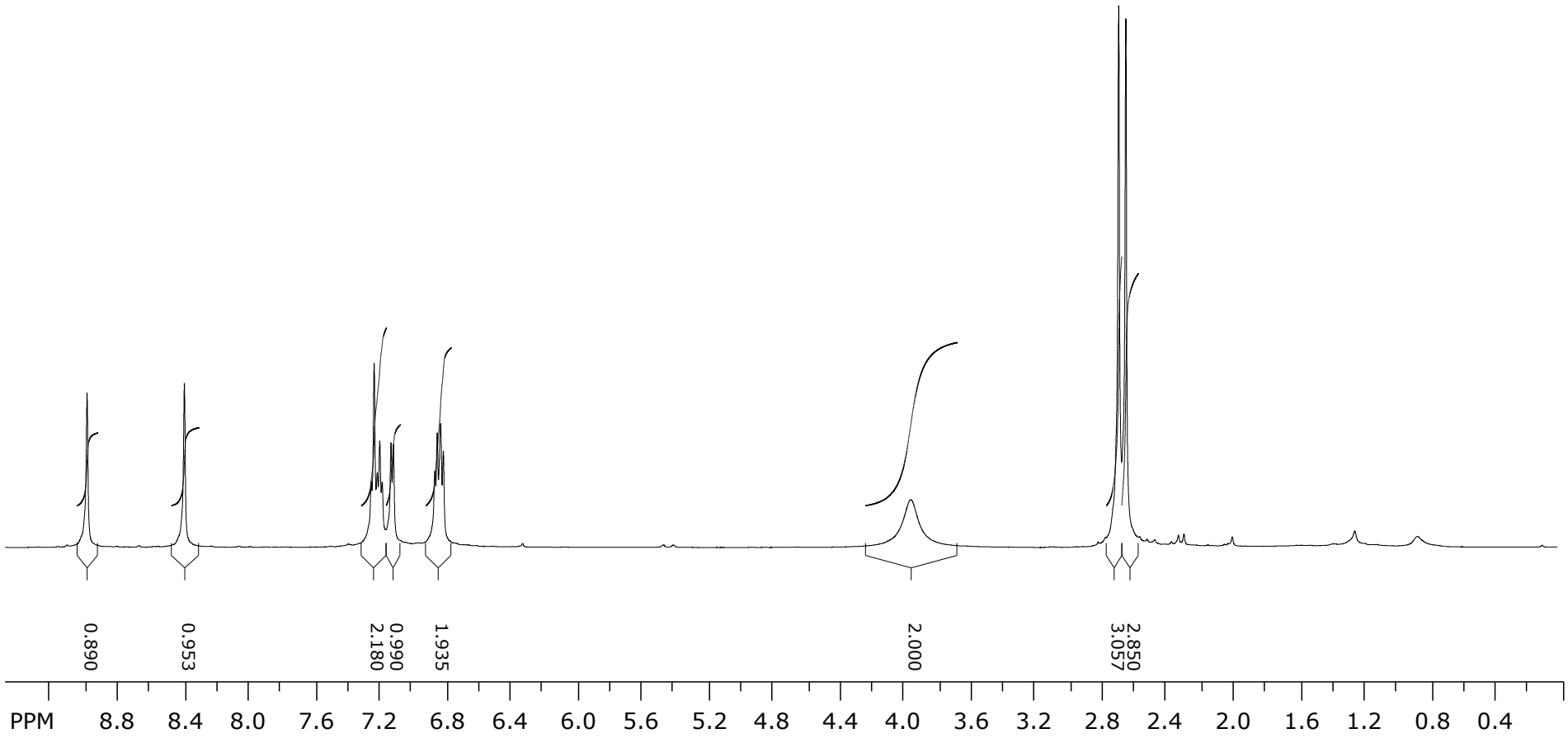
^{13}C NMR of **11n** in $CDCl_3$



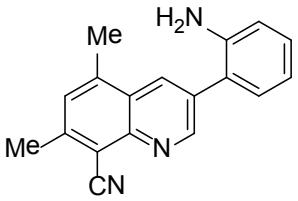


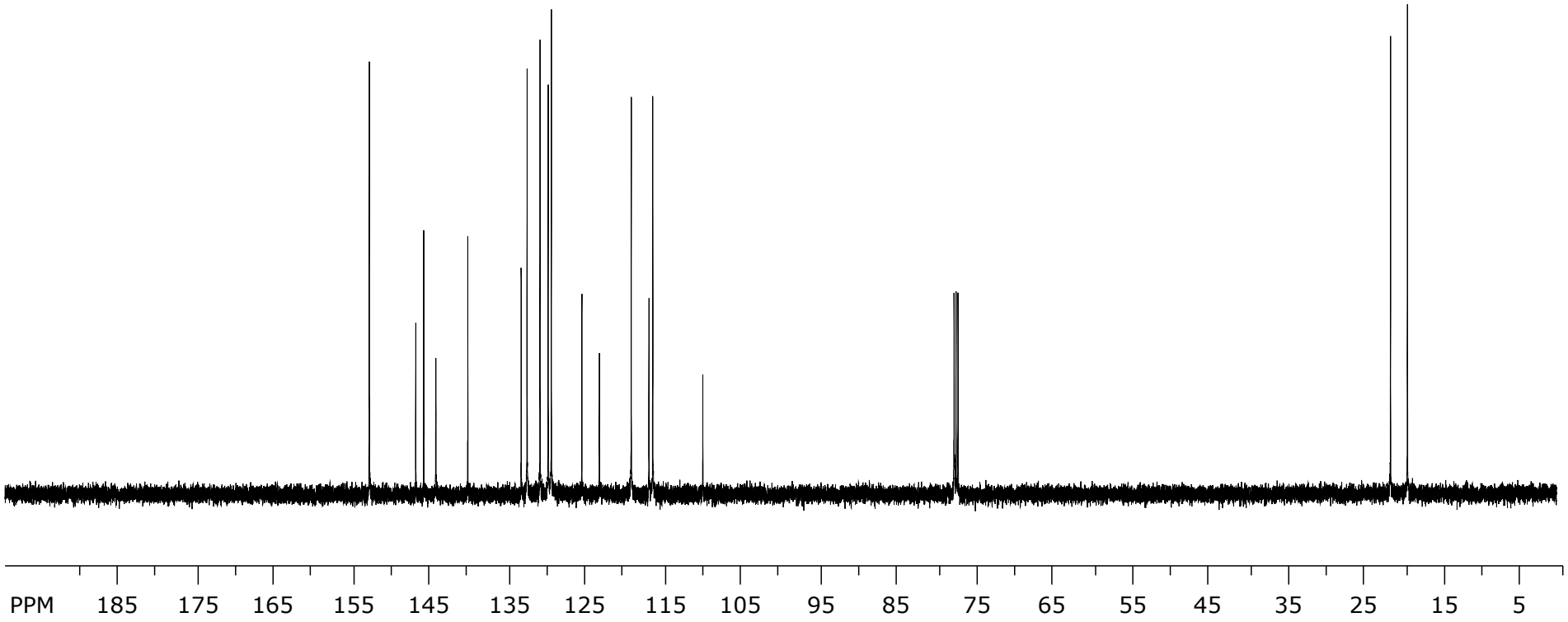
^{1}H NMR of **11o** in $CDCl_3$



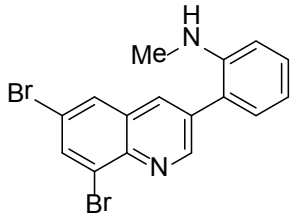


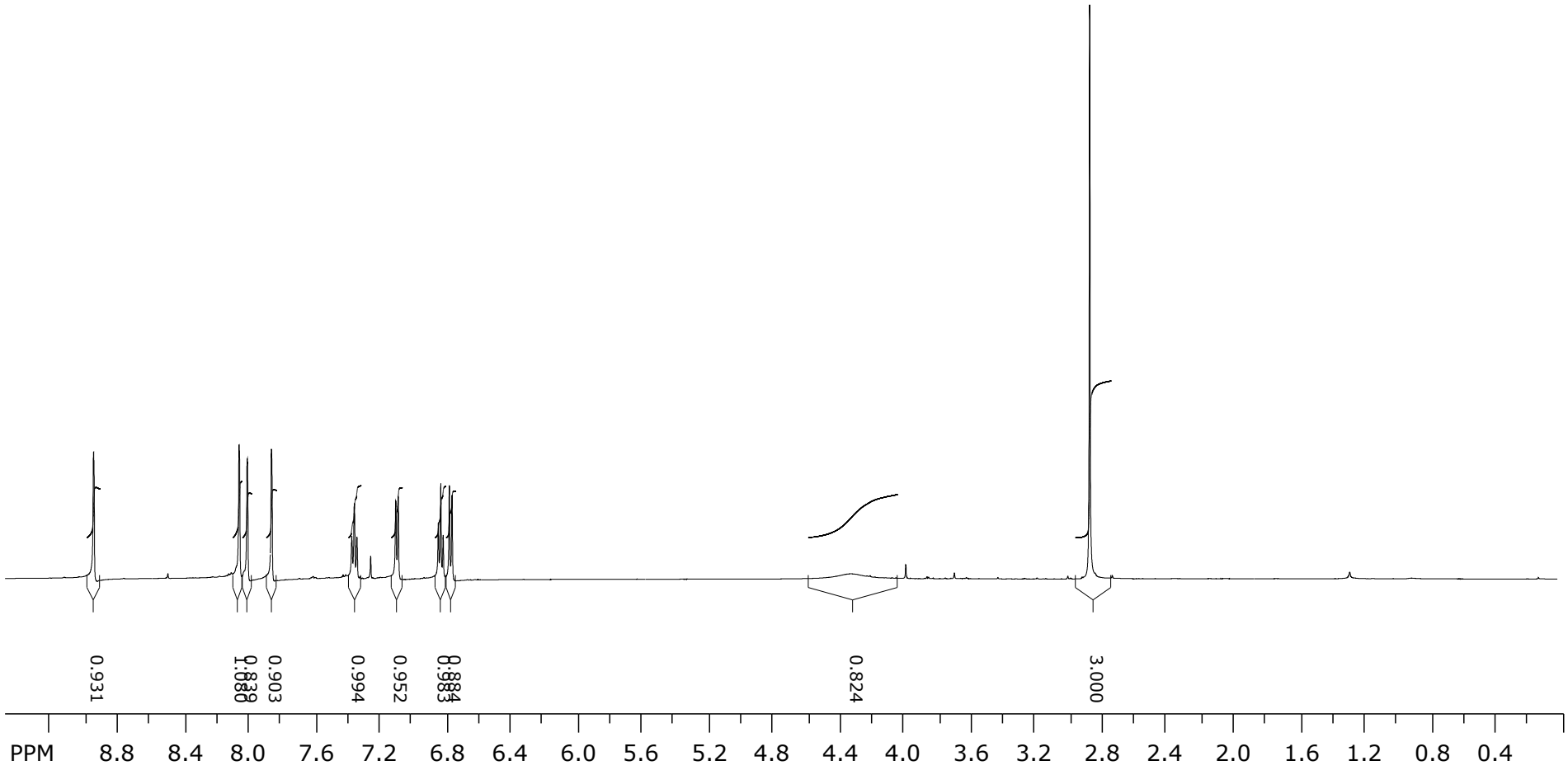
^{13}C NMR of **11o** in $CDCl_3$



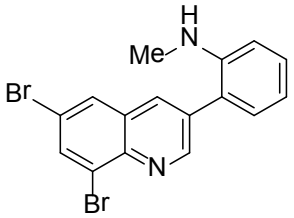


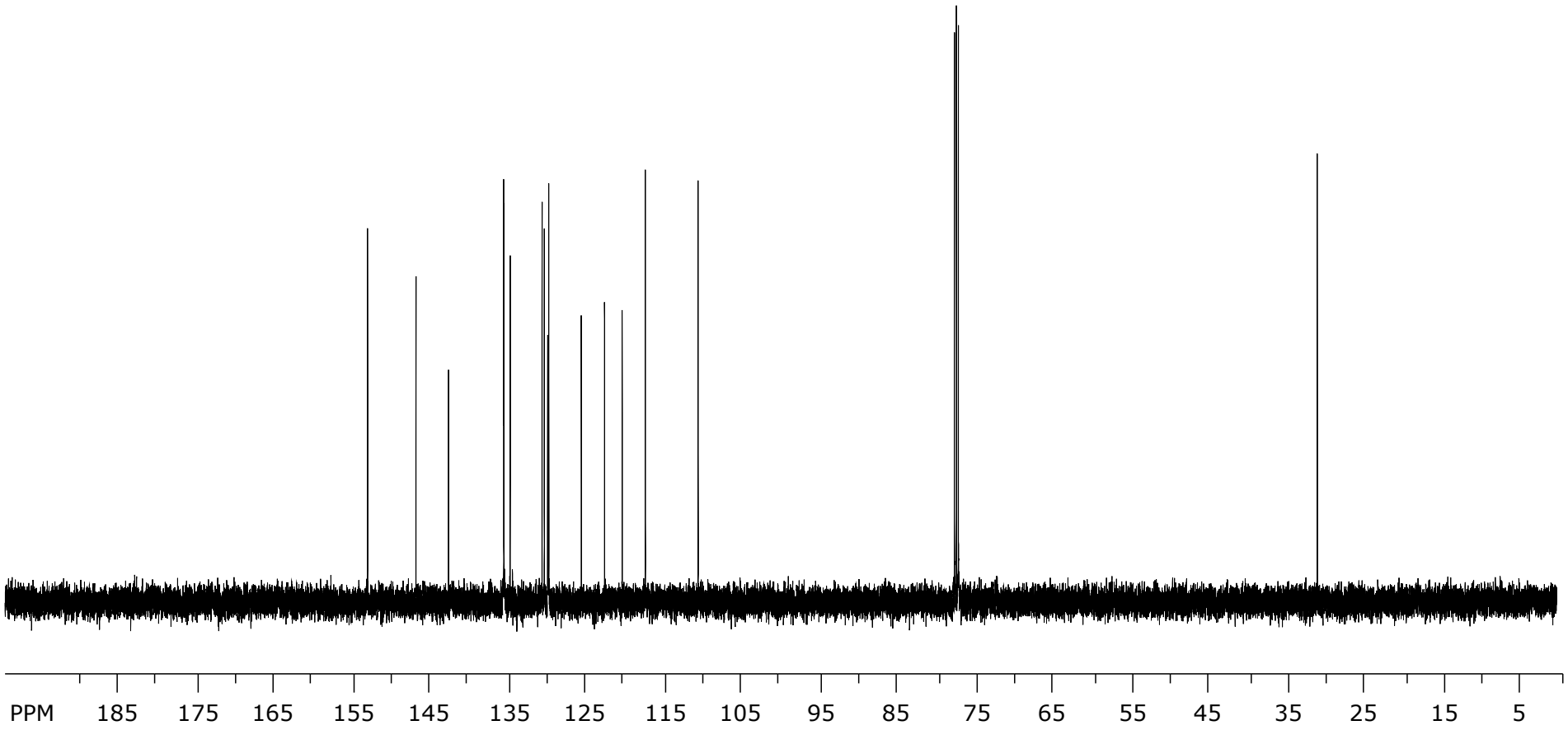
^{1}H NMR of **11p** in $CDCl_3$



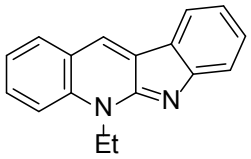


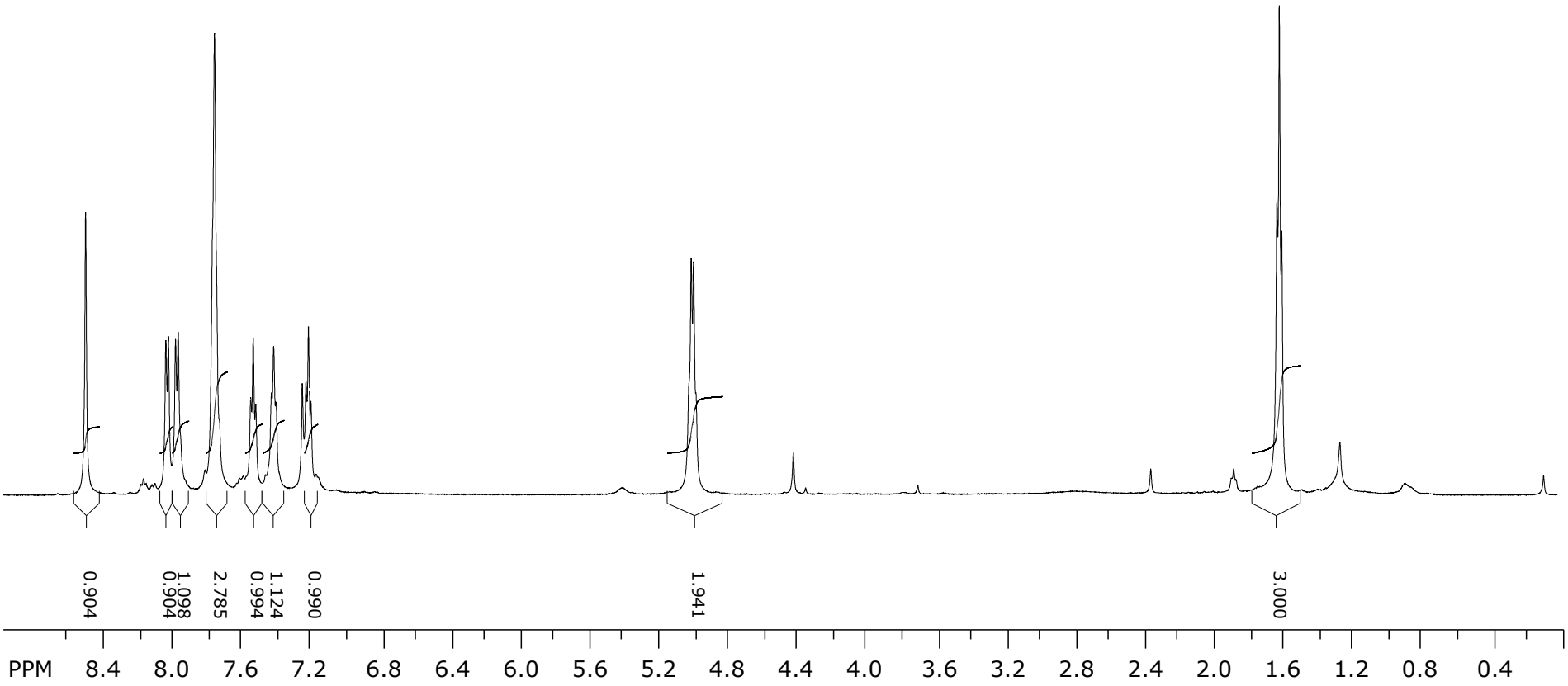
^{13}C NMR of **11p** in $CDCl_3$



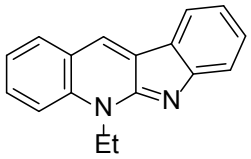


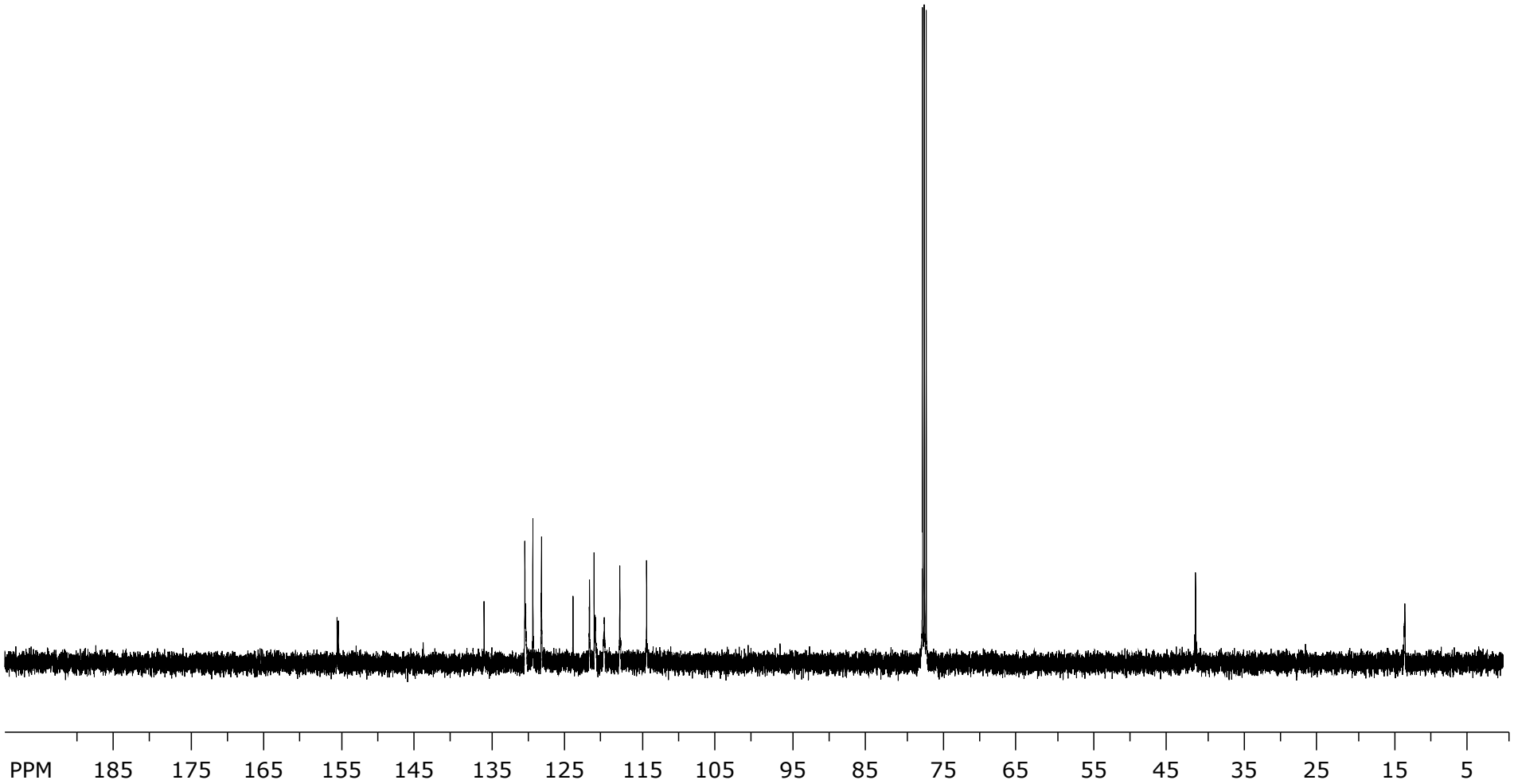
^{1}H NMR of **16** in $CDCl_3$



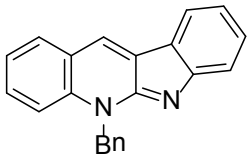


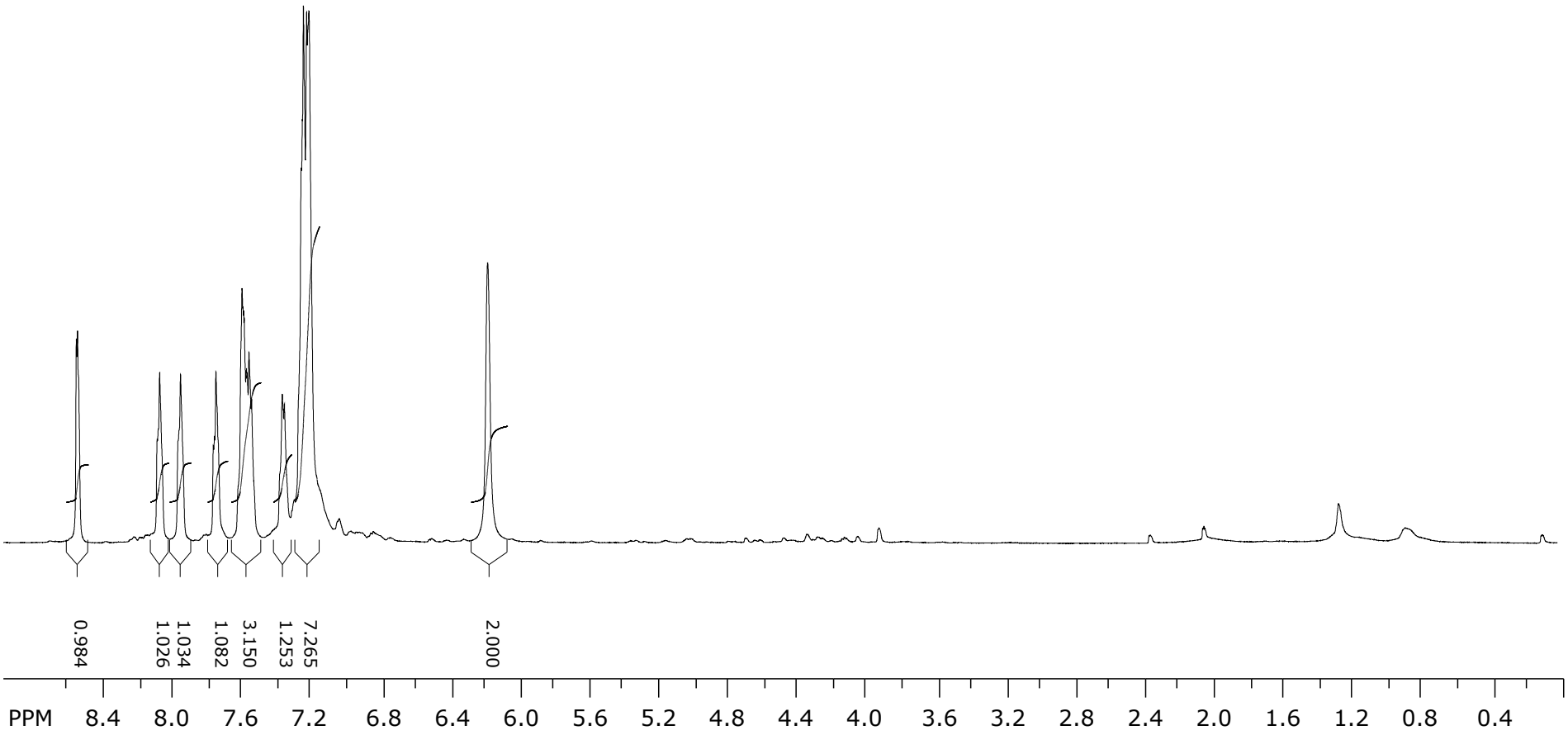
^{13}C NMR of **16** in $CDCl_3$





^{1}H NMR of **17** in $CDCl_3$





^{13}C NMR of **17** in $CDCl_3$