Fischer Indole Synthesis in Low Melting Mixtures

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Supporting Information

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General Information

^{1}H NMR spectra were recorded on Bruker ADVANCE 400 MHz and 500 MHz spectrometers. ^{13}C NMR spectra were recorded on 100 MHz and 125 MHz spectrometers. Chemical shifts are expressed in δ units relative to tetramethylsilane (TMS) signal as internal reference in $CDCl_3$. FTIR spectra were recorded in $CHCl_3$ or neat. Column chromatography was performed on silica gel (60-120 mesh) using ethyl acetate and hexane as eluent.

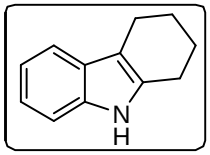
General Procedure for the preparation of indole derivatives:

In a typical experiment, 1.5 g of L-(+)-tartaric acid-DMU (30:70) mixture was heated to 70 ^{o}C to obtain a clear melt. To this melt, 1 mmol of aryl hydrazine.HCl and 1 mmol of aldehyde/ketone were added at 70 ^{o}C. The reaction was monitored by thin layer chromatography. After completion, the reaction mixture was quenched by adding water while still hot. The reaction mixture was cooled to room temperature and the solid that separated was filtered and washed with water (2 x 5 mL). The crude compound was dried under vacuum and recrystallized from ethanol to afford pure product. In case of liquid products, the reaction mixture was quenched with water and the aqueous layer was extracted with DCM (3 x 5 mL). The organic layer was washed with water (2 x 5 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude compound was purified by column chromatography over silica gel.

Experimental Section

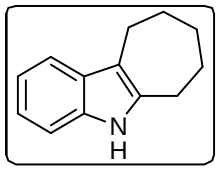
Spectral data for the indole derivatives obtained by the Fischer indole reaction between aldehyde/ketone and aryl hydrazine in tartaric acid-DMU melt:

3a. 2,3,4,9-Tetrahydro-1H-carbazole:



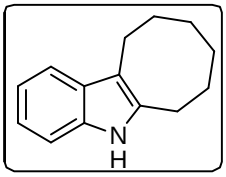
Colorless solid; Yield 97%; M.p. 118–120 ^{o}C; IR (neat): 3396, 1455, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.75–1.90 (m, 4H), 2.60–2.71 (m, 4H), 6.96–7.07 (m, 2H), 7.18 (dd, 1H, *J* = 7.6, 1.6 Hz) 7.38 (d, 1H, *J* = 7.6 Hz), 7.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 23.3, 23.4, 110.3, 110.5, 117.8, 119.2, 121.1, 128.0, 134.2, 135.8.

3b. 5,6,7,8,9,10-Hexahydrocyclohepta[b]indole:



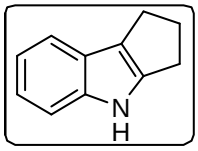
Colorless solid; Yield 98%; M.p. 145–147 ^{o}C; IR (neat): 3388, 1456, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.72–1.81 (m, 4H), 1.85–1.93 (m, 2H), 2.80 (t, 4H, *J* = 5.6 Hz), 7.05–7.12 (m, 2H), 7.20–7.25 (m, 1H), 7.44–7.50 (m, 1H), 7.62 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.8, 27.6, 28.8, 29.7, 31.9, 110.3, 113.8, 117.7, 119.1, 120.7, 129.3, 134.3, 137.5; HRMS calcd. for $C_{13}H_{16}N_1$ (M^{+}+1) 186.1283, found 186.1292.

3c. 6,7,8,9,10,11-Hexahydro-5H-cycloocta[b]indole:



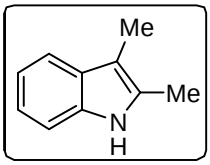
Colorless solid; Yield 96%; M.p. 73–74 ^{o}C; IR (neat): 3329, 1623, 1453, 1334, 742 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38–1.51 (m, 4H), 1.68–1.79 (m, 4H), 2.80–2.90 (m, 4H), 7.05–7.13 (m, 2H), 7.24–7.30 (m, 1H), 7.46–7.52 (m, 1H), 7.63 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.3, 26.0, 26.1, 29.6, 29.7, 110.4, 111.8, 117.8, 119.0, 120.7, 128.7, 135.1, 135.7; HRMS calcd. for $C_{14}H_{18}N_1$ (M^++1) 200.1439, found 200.1432.

3d. 1,2,3,4-Tetrahydrocyclopenta[b]indole:



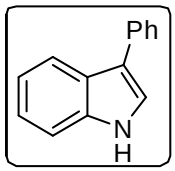
Colorless solid; Yield 97%; M.p. 101–103 ^{o}C; IR (neat): 3399, 1654, 1609, 1405, 1233, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.51–2.61 (m, 2H), 2.81–2.96 (m, 4H), 7.07–7.14 (m, 2H), 7.28–7.33 (m, 1H), 7.43–7.48 (m, 1H), 7.82 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.6, 26.0, 28.8, 111.4, 118.6, 119.6, 119.9, 120.6, 124.9, 141.1, 143.8; HRMS calcd. for $C_{11}H_{12}N_1$ (M^++1) 158.0970, found 158.0974.

3e. 2,3-Dimethyl-1H-indole:



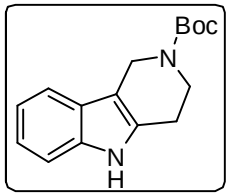
Colorless solid; Yield 88%; M.p. 104–106 ^{o}C; IR (neat): 3396, 1467, 740 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (s, 3H), 2.20 (s, 3H), 6.95–7.05 (m, 2H), 7.06–7.12 (m, 1H), 7.33–7.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 8.5, 11.6, 107.1, 110.2, 118.0, 119.1, 121.0, 129.5, 130.8, 135.3; HRMS calcd. for $C_{10}H_{12}N_1$ (M^++1) 146.0970, found 146.0970.

3f. 3-Phenyl-1H-indole:



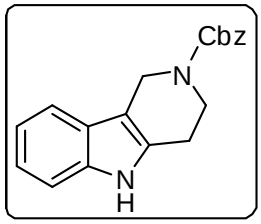
Colorless solid; Yield 87%; M.p. 85–86 ^{o}C; IR (neat): 3405, 3048, 1597, 1451, 1111, 741, 694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17–7.32 (m, 3H), 7.33 (d, 1H, J = 2.8 Hz), 7.39–7.51 (m, 3H), 7.65–7.75 (m, 2H), 7.95 (d, 1H, *J* = 7.6 Hz), 8.19 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 111.5, 118.5, 119.9, 120.4, 121.9, 122.5, 125.9, 126.1, 127.6, 128.9, 135.7, 136.8; HRMS calcd. for $C_{14}H_{12}N$ (M^++1) 194.0970, found 194.0966.

3g. Tert-butyl 3,4-dihydro-1H-pyrido[4,3-b]indole-2(5H)-carboxylate:



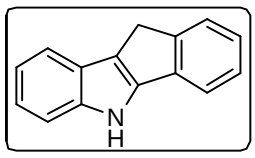
Pale yellow oil; Yield 85%; IR (neat): 3317, 1686, 1405, 1152, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.53 (s, 9H), 2.81 (t, 2H, *J* = 5.6 Hz), 3.83 (s, 2H), 4.67 (s, 2H), 6.96–7.21 (m, 2H), 7.31 (d, 1H, *J* = 7.6 Hz), 7.46 (br s, 1H), 8.15 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.6, 28.5, 28.6, 40.8, 41.6, 80.1, 107.5, 110.9, 117.6, 119.6, 121.6, 125.7, 128.4, 131.8, 132.3, 136.0, 155.4; HRMS calcd. for $C_{16}H_{21}N_2O_2$ (M^++1) 273.1603, found 273.1611.

3h. Benzyl 3,4-dihydro-1H-pyrido[4,3-b]indole-2(5H)-carboxylate:



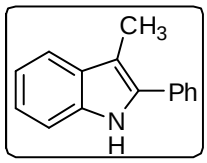
Colorless oil; Yield 94%; IR (neat): 3315, 1684, 1615, 1425, 1219, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.85 (s, 2H), 3.90 (d, 2H, *J* = 5.2 Hz), 4.75 (s, 2H), 5.22 (s, 2H), 7.09–7.20 (m, 2H), 7.29–7.48 (m, 7H), 8.0 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.5, 23.8, 41.5, 67.4, 107.1, 110.9, 117.7, 119.7, 121.8, 128.1, 128.2, 128.5, 128.6, 132.0, 136.0, 136.8, 156.1; HRMS calcd. for $C_{19}H_{19}N_2O_2$ (M^++H) 307.1447, found 307.1448.

3i. 5,10-Dihydroindeno[1,2-b]indole:



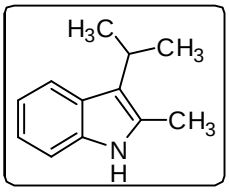
Colorless solid; Yield 97%; M.p. 232–234 ^oC; IR (neat): 3404, 1446, 737 cm^{-1}; ^1H NMR (400 MHz, MeOD): δ 2.92–2.98 (m, 2H), 6.66–6.67 (m, 2H) 6.79–6.86 (m, 1H), 6.95 (dd, 1H, *J* = 12.8, 5.6 Hz), 7.06 (d, 1H, *J* = 8.0 Hz), 7.13–7.23 (m, 3H); ^{13}C NMR (100 MHz, MeOD): δ 30.8, 113.1, 118.5, 119.4, 120.5, 121.5, 122.1, 125.6, 125.9, 126.3, 127.5, 136.8, 149.1, 145.0, 142.5; HRMS calcd. for $C_{15}H_{12}N_1$ (M^++1) 206.0970, found 206.0967.

3j. 3-Methyl-2-phenyl-1H-indole:



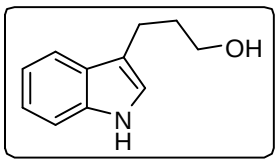
Colorless solid; Yield 97%; M.p. 93–94 ^{o}C; IR (neat): 3337, 3054, 1607, 1583, 1536, 1449, 1265 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3H), 7.03–7.13 (m, 2H), 7.20–7.26 (m, 2H), 7.33–7.39 (m, 2H), 7.42–7.47 (m, 2H), 7.50 (d, 1H, *J* = 7.6 Hz), 7.83 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.8, 108.8, 110.8, 119.1, 119.6, 122.4, 127.4, 127.8, 128.9, 130.2, 133.5, 134.1, 136.0; HRMS calcd. for $C_{15}H_{14}N$ (M^++H) 208.1126, found 208.1126.

3k. 3-Isopropyl-2-methyl-1H-indole:



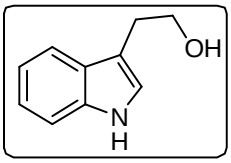
Yellow oil; Yield 95%; IR (neat): 3392, 2963, 1608, 1462, 1022 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.40 (d, 6H, *J* = 7.2 Hz), 2.35 (s, 3H), 3.17 (sep, 1H, *J* = 7.2 Hz), 7.01–7.11(m, 2H), 7.22 (d, 1H, *J* = 7.2 Hz), 7.58 (s, 1H), 7.65 (d, 1H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.2, 23.1, 26.0, 110.4, 117.9, 118.8, 119.5, 120.6, 127.5, 129.3, 135.5; HRMS calcd. for $C_{12}H_{16}N$ (M^++1) 174.1283, found 174.1289.

3l. 3-(1H-Indol-3-yl)propan-1-ol:



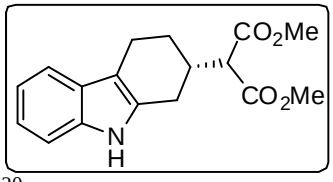
Yellow oil; Yield 80%; IR (neat): 3200–3500, 1457, 1024, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.96–2.03 (quin, 2H, J = 6.4 Hz), 2.86 (t, 2H, *J* = 7.6 Hz), 3.73 (t, 2H, *J* = 6.4 Hz), 6.99 (s, 1H), 7.10–7.16 (m, 1H), 7.17–7.23 (m, 1H), 7.35 (d, 1H, *J* = 8.0 Hz), 7.62 (d, 1H, *J* = 8.0 Hz), 8.0 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 33.0, 62.8, 111.2, 116.0, 119.0, 119.3, 121.4, 122.1, 127.6, 136.5; HRMS calcd. for $C_{11}H_{14}NO$ (M^++1) 176.1075, found 176.1078.

3m. 2-(1H-Indol-3-yl)ethanol:



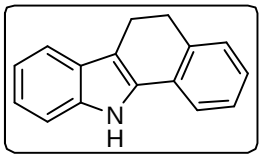
Colorless oil; Yield 90%; IR (neat): 3400–3100, 1660, 1493, 1282, 1034 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.05 (t, 2H, *J* = 6.0 Hz), 3.92 (t, 2H, *J* = 6.4 Hz), 7.09–7.18 (m, 2H), 7.19–7.25 (m, 1H), 7.38 (d, 1H, *J* = 8.4 Hz), 7.63 (d, 1H, *J* = 7.6 Hz), 8.10 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 28.8, 62.6, 111.2, 112.3, 118.9, 119.5, 122.2, 122.5, 127.4, 136.5; HRMS calcd. for $C_{10}H_{12}NO$ (M^++H) 162.0919, found 162.0924.

3n. (S)-Dimethyl 2-(2,3,4,9-tetrahydro-1H-carbazol-2-yl)malonate:



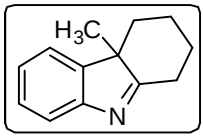
Colorless solid; Yield 97%; $[\alpha]^{20}_{D}$ = –28.20 (*c* 1.0, $CHCl_3$); M.p. 117–119 ^{o}C; IR (neat): 3200–3400, 2932, 1564, 1039 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.50–1.65 (m, 1H), 1.89–2.0 (m, 1H), 2.50–2.83 (m, 5H), 3.41 (d, 1H, *J* = 8.8 Hz, C**H**$(COOCH_3)_2$), 3.68 (s, 3H, COOC**H$_3$**), 3.70 (s, 3H, COOC**H$_3$**), 6.94–7.07 (m, 2H), 7.17 (d, 1H, *J* = 8.0 z), 7.37 (d, 1H, *J* = 7.6 Hz), 7.65 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.1, 27.1, 27.6, 34.8, 52.6 (COO**C**H_3), 52.7 (COO**C**H_3), 56.5 (**C**H$(COOCH_3)_2$), 109.5, 110.6, 117.9, 119.3, 121.3, 127.4, 132.4, 136.0, 169.1 (C=O), 169.2 (C=O); HRMS calcd. for $C_{17}H_{23}N_2O_3$ (M^++Na): 324.1212, found 324.1214.

3o. 6,7,8,9,10,11-Hexahydro-5H-cycloocta[b]indole:



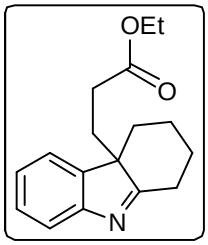
Colorless solid; Yield 96%; M.p. 162–163 ^{o}C; IR (neat): 3410, 3048, 1451, 1319, 743 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.95–3.01 (m, 2H), 3.03–3.10 (m, 2H), 7.09–7.20 (m, 3H), 7.22–7.29 (m, 2H), 7.32 (d, 1H, *J* = 6.8 Hz), 7.38 (d, 1H, *J* = 8.0 Hz), 7.55 (d, 1H, *J* = 7.8 Hz) 8.19 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.8, 29.7, 111.2, 112.8, 118.9, 119.9, 120.0, 122.5, 126.8, 126.9, 127.6, 128.6, 129.0, 133.2, 136.7, 137.1; HRMS calcd. for $C_{16}H_{14}N_1$ (M^++1) 220.1126, found 220.1125.

5a. 4a-Methyl-2,3,4,4a-tetrahydro-1H-carbazole:



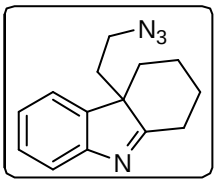
Pale yellow oil; Yield 99%; IR (neat): 1582, 1444, 1190 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16 (td, 1H, J = 13.2, 4.0 Hz), 1.30 (s, 3H), 1.33–1.48 (m, 1H), 1.64–1.86 (m, 2H), 2.12–2.32 (m, 2H), 2.58 (td, 1H, *J* = 13.2, 5.6 Hz), 2.86 (d, 1H, *J* = 13.2 Hz), 7.19 (t, 1H, *J* = 7.2 Hz), 7.25–7.38 (m, 2H), 7.59 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.9, 21.5, 29.1, 29.8, 38.7, 53.9, 120.3, 121.4, 124.9, 127.6, 146.9, 154.3, 190.3; HRMS calcd. for $C_{13}H_{16}N_1$ (M^++1) 186.1283, found 186.1276.

5b. Ethyl 3-(2,3,4,4a-tetrahydro-1H-carbazol-4a-yl)propanoate:



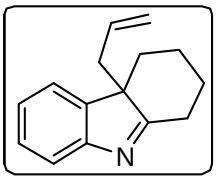
Colorless oil; Yield 94%; IR (neat): 2930, 1725, 1583, 1451, 1377, 1174, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.15 (t, 3H, J = 7.2 Hz, $COOCH_2C\mathbf{H_3}$), 1.18–1.27 (m, 1H), 1.35–1.49 (m, 1H), 1.52–1.66 (m, 2H), 1.66–1.74 (m, 1H), 1.79–1.93 (m, 1H), 2.11–2.25 (m, 2H), 2.31–2.47 (m, 2H), 2.55 (dt, 1H, *J* = 13.2, 5.6 Hz), 2.85–2.92 (m, 1H), 3.95–4.04 (m, 2H, $COOC\mathbf{H_2}CH_3$), 7.17–7.22 (m, 1H), 7.25–7.29 (m, 1H), 7.30–7.35 (m, 1H), 7.59 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (CH_3), 21.2, 28.6, 28.7, 29.1, 30.1, 38.3, 57.5, 60.5 (OCH_2), 120.4, 121.7, 125.1, 127.9, 143.9, 155.1, 173.1 (C=O), 188.6 (C=N); HRMS calcd. for $C_{17}H_{22}NO_2$ (M^++1): 272.1651, found 272.1651.

5c. 4a-(2-Azidoethyl)-2,3,4,4a-tetrahydro-1H-carbazole:



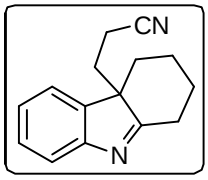
Colorless liquid; Yield 92%; IR (neat): 2920, 2857, 2157, 2091, 1584, 1446, 1258, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.18 (td, 1H, J = 13.6, 4.0 Hz), 1.40–1.51 (m, 1H), 1.66–1.75 (m, 1H), 1.76–1.86 (m, 1H), 2.07–2.15 (m, 1H), 2.18–2.26 (m, 1H), 2.32–2.44 (m, 2H), 2.55–2.65 (m, 2H, $C\mathbf{H_2}N_3$), 2.67–2.76 (m, 1H, $N{=}CC\mathbf{H}_2$), 2.89–2.97 (m, 1H, $N{=}CC\mathbf{H}_2$), 7.22 (d, 1H, *J* = 7.2 Hz), 7.27 (d, 1H, *J* = 7.6 Hz), 7.35 (t, 1H, *J* = 7.2 Hz), 7.61 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.3, 29.2, 30.3, 33.2, 39.0, 47.1 (CH_2N_3), 56.7, 120.6, 121.5, 125.2, 128.2, 143.5, 155.0, 188.4 (C=N); HRMS calcd. for $C_{14}H_{17}N_4$ (M^++H) 241.1453, found 241.1453.

5d. 4a-Allyl-2,3,4,4a-tetrahydro-1H-carbazole:



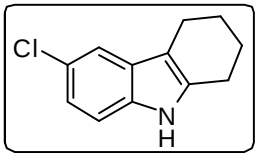
Pale yellow oil; Yield 90%; IR (neat): 2935, 1584, 1448, 920, 762 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.15 (td, 1H, *J* = 13.6, 4.0 Hz), 1.36–1.51 (m, 1H), 1.64–1.74 (m, 1H), 1.80–1.90 (m, 1H), 2.15–2.25 (m, 1H), 2.32–2.41 (m, 1H) 2.51–2.67 (m, 3H), 2.84–2.93 (m, 1H), 4.85 (d, 1H, *J* = 10.0 Hz), 4.94 (d, 1H, *J* = 16.8 Hz), 5.10–5.23 (m, 1H), 7.15–7.23 (m, 1H), 7.28–7.38 (m, 2H), 7.58 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2, 29.0, 30.3,. 37.0, 37.8, 57.8, 118.1, 120.2, 122.0, 124.8, 127.7, 132.3, 144.7, 155.0, 189.0; HRMS calcd. for $C_{15}H_{18}N_1$ (M^++1) 212.1439, found 212.1443.

5e. 3-(2,3,4,4a-Tetrahydro-1H-carbazol-4a-yl)propanenitrile:



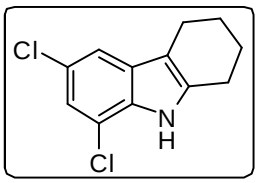
Pale yellow oil; Yield 90%; IR (neat): 1582, 1444, 1190 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.25 (td, 1H, *J* = 13.6, 4.8 Hz), 1.39–1.52 (m, 1H), 1.59 (t, 2H, *J* = 8.4 Hz), 1.74–1.86 (m, 2H), 2.15–2.30 (m, 2H), 2.32–2.41 (m, 1H), 2.47–2.58 (m, 2H), 2.91–3.0 (m, 1H), 7.23–7.30 (m, 2H), 7.35–7.41 (m, 1H), 7.62 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.1, 21.3, 29.1, 29.9, 30.3, 38.2, 57.4, 119.1, 120.9, 121.6, 125.7, 128.7, 142.4, 155.1, 187.3; HRMS calcd. for $C_{15}H_{17}N_2$ (M^++1) 225.1392, found 225.1393.

10. 6-Chloro-2,3,4,9-tetrahydro-1H-carbazole:



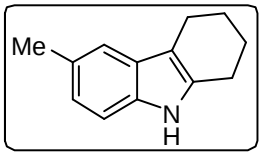
Colorless solid; Yield 97%; M.p. 162–163 ^oC; IR (neat): 3404, 2356, 1686, 1440, 799 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.80–1.96 (m, 4H), 2.66 (t, 2H, *J* = 6.0 Hz), 2.72 (t, 2H, *J* = 5.6 Hz), 7.05 (dd, 1H, *J* = 8.4, 1.6 Hz), 7.17 (d, 1H, *J* = 8.4 Hz), 7.41 (s, 1H), 7.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9, 23.1, 23.2, 23.4, 110.2, 111.3, 117.5, 121.2, 124.9, 129.1, 134.1, 135.9; HRMS calcd. for $C_{12}H_{13}NCl$ (M^++1) 206.0737, found 206.0736.

11. 6,8-Dichloro-2,3,4,9-tetrahydro-1H-carbazole:



Pale yellow solid; Yield 90%; M.p. 64–65 ^oC; IR (neat): 3437, 2928, 1571, 1465, 858 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.79–1.93 (m, 4H), 2.57–2.63 (m, 2H), 2.70 (t, 2H, *J* = 5.6 Hz), 7.07 (s, 1H), 7.28 (s, 1H), 7.86 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9, 23.0, 23.1, 23.3, 111.3, 116.1, 116.3, 120.3, 124.7, 129.8, 131.4, 136.6; HRMS calcd. for $C_{12}H_{11}Cl_2N$ (M^+) 240.0347, found 240.0340.

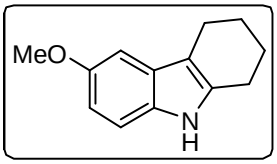
12. 6-Methyl-2,3,4,9-tetrahydro-1H-carbazole:



Colorless solid; Yield 96%; M.p. 142–144 ^oC; IR (neat): 3391, 2922, 1457, 795 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.81–1.94 (m, 4H), 2.43 (s, 3H), 2.64–2.73 (m, 4H), 6.92 (dd, 1H, *J* = 8.4, 1.2 Hz), 7.15 (d, 1H, *J* = 8.0 Hz), 7.24 (s, 1H), 7.54 (br s, 1H); ^{13}C NMR

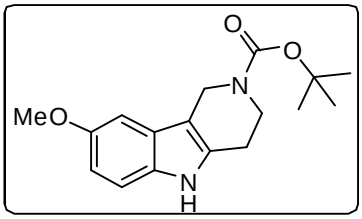
(100 MHz, $CDCl_3$): δ 21.1, 21.6, 23.3, 23.4, 23.5, 109.8, 110.1, 117.7, 122.5, 128.2, 128.4, 134.0, 134.4; HRMS calcd. for $C_{13}H_{16}N$ (M^++1) 186.1283, found 186.1289.

13. 6-Methoxy-2,3,4,9-tetrahydro-1H-carbazole:



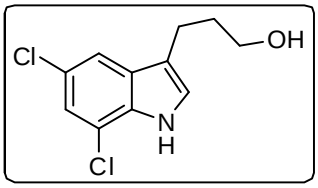
Colorless solid; Yield 95%; M.p. 106–108 ^oC; IR (neat): 3390, 2916, 1590, 1484, 1219, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.84–1.97 (m, 4H), 2.67–2.75 (m, 4H), 3.88 (s, 3H), 6.79 (dd, 1H, *J* = 8.8, 2.0 Hz), 6.92 (d, 1H, *J* = 2.4 Hz), 7.16 (d, 1H, *J* = 8.4 Hz), 7.59 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 23.3, 23.4, 23.5, 56.1, 100.4, 110.1, 110.6, 111.1, 128.3, 130.8, 135.2, 154.0; HRMS calcd. for $C_{13}H_{16}NO$ (M^++H) 202.1232, found 202.1228.

14. Tert-butyl 8-methoxy-3,4-dihydro-1H-pyrido[4,3-b]indole-2(5H)-carboxylate:



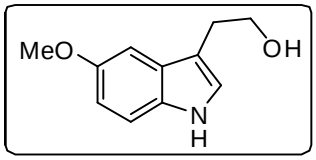
Colorless solid; Yield 88%; M.p. 174–176 ^oC (dec); IR (neat): 3304, 1674, 1426, 735 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.53 (s, 9H), 2.79 (s, 2H), 3.81 (s, 2H), 3.86 (s, 3H), 4.62 (s, 2H), 6.81 (d, 1H, *J* = 8.0 Hz), 6.91 (s, 1H), 7.19 (d, 1H, *J* = 7.0 Hz), 8.09 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 23.7, 28.6, 40.8, 41.6, 56.0, 80.0, 100.1, 107.3, 111.3, 111.5, 126.1, 131.1, 132.7, 133.3, 154.2, 155.4; HRMS calcd. for $C_{17}H_{23}N_2O_3$ (M^++1) 303.1709, found 303.1724.

15. 3-(5,7-Dichloro-1H-indol-3-yl)propan-1-ol:



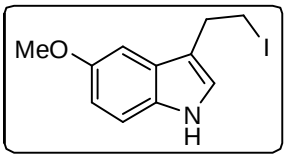
Pale yellow oil; Yield 90%; IR (neat): 3200–3400, 2932, 1564, 1039 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.95 (quin, 2H, *J* = 6.4 Hz, CH_2-C**H**$_2$-CH_2), 2.80 (t, 2H, *J* = 7.6 Hz), 3.71 (t, 2H, *J* = 6.4 Hz, C**H**$_2$-OH), 7.07 (d, 1H, *J* = 2.0 Hz), 7.18 (d, 1H, *J* = 1.6 Hz), 7.48 (d, 1H, *J* = 1.6 Hz), 8.27 (br s, 1H, N**H**); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.4, 32.9, 62.4 (CH_2-OH), 117.1, 117.2, 117.4, 121.6, 123.4, 125.0, 129.5, 132.3; HRMS calcd. for $C_{11}H_{12}NOCl_2$ (M^++1) 244.0296, found 244.0304.

16. 2-(5-Methoxy-1H-indol-3-yl)ethanol:



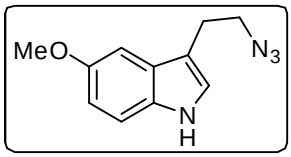
Colorless oil; Yield 92%; IR (neat): 3100–3400, 1493, 1282, 1034, 826 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.0 (t, 2H, *J* = 6.4 Hz), 3.87 (s, 3H), 3.90 (t, 2H, *J* = 6.4 Hz), 6.87 (dd, 1H, *J* = 8.8, 2.4 Hz), 7.05 (d, 2H, *J* = 2.2 Hz), 7.25 (d, 1H, *J* = 8.8 Hz), 8.04 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.8, 56.1, 62.7, 100.7, 112.0, 112.1, 112.5, 123.4, 127.9, 131.7, 154.1; HRMS calcd. for $C_{11}H_{14}NO_2$ (M^++H) 192.1025, found 192.1021.

16A. 3-(2-Iodoethyl)-5-methoxy-1H-indole:



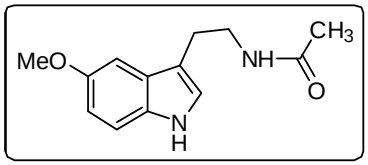
Colorless solid; Yield 97%; ^1H NMR (400 MHz, $CDCl_3$): δ 3.28–3.35 (m, 2H), 3.38–3.45 (m, 2H), 3.86 (s, 3H), 6.85 (dd, 1H, *J* = 8.8, 2.4 Hz), 6.98 (d, 1H, *J* = 2.4 Hz), 7.04 (d, 1H, *J* = 2.0 Hz), 7.24 (d, 1H, *J* = 2.4 Hz), 7.99 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 6.3, 30.5, 56.1, 100.4, 112.2, 112.5, 115.4, 122.8, 127.3, 131.4, 154.2.

16B. 3-(2-Azidoethyl)-5-methoxy-1H-indole:



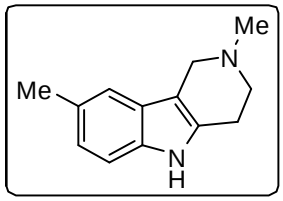
Colorless oil; Yield 96%; ^1H NMR (400 MHz, $CDCl_3$): δ 3.02 (t, 2H, *J* = 7.2 Hz), 3.55 (t, 2H, *J* = 7.2 Hz), 3.87 (s, 3H), 6.87 (dd, 1H, *J* = 8.8, 2.4 Hz), 7.01–7.04 (m, 2H), 7.23 (d, 1H, *J* = 8.8 Hz), 7.96 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.2, 51.7, 56.1, 100.5, 112.1, 112.5, 123.2, 127.6, 131.5, 154.2.

IV. N-(2-(5-Methoxy-1H-indol-3-yl)ethyl)acetamide:

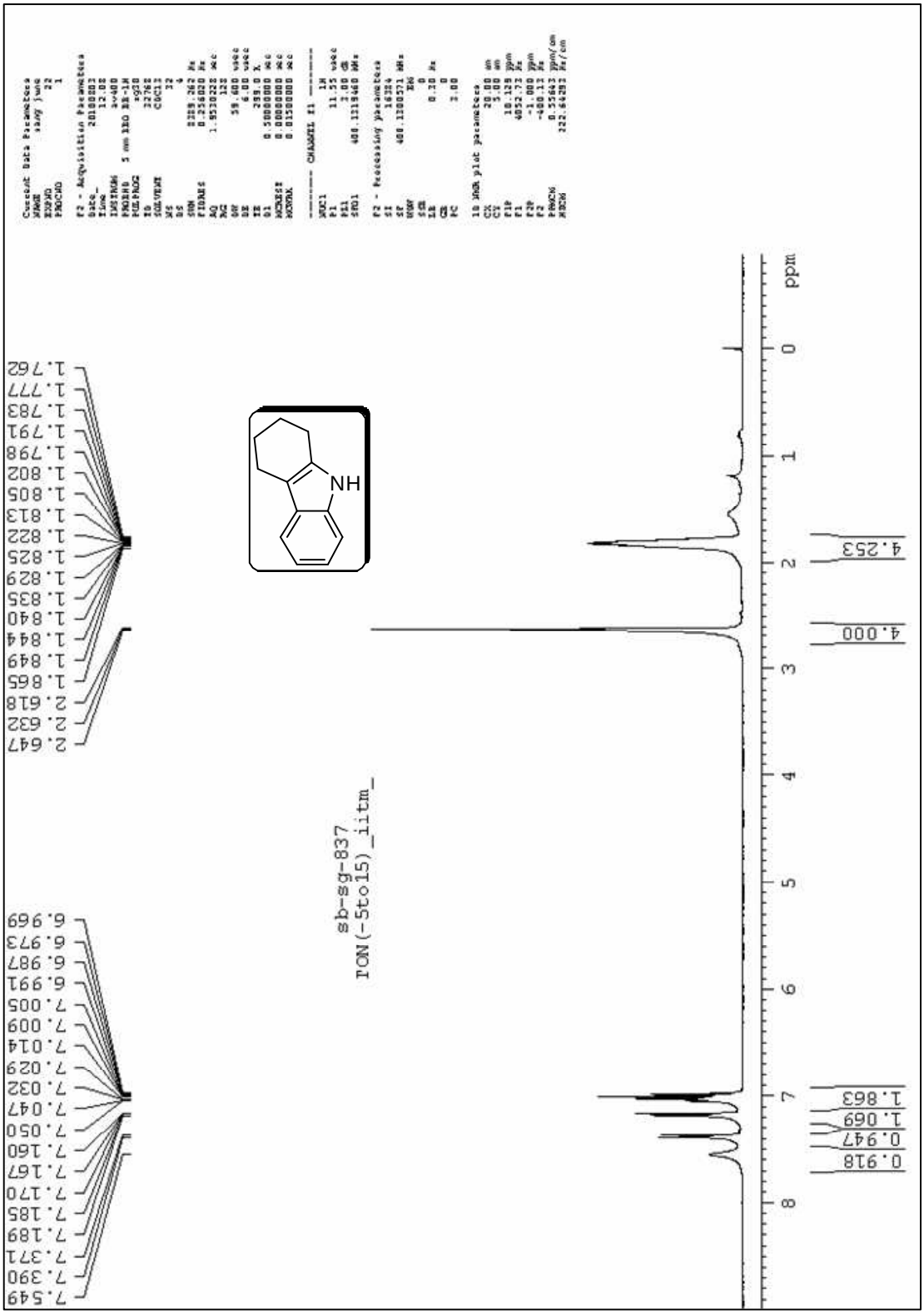


Colorless solid; Yield 95%; M.p. 118–120 ^oC; IR (neat): 3402, 1650, 1627, 1397, 1038 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.81 (s, 3H), 2.83 (t, 2H, *J* = 6.8 Hz), 3.47 (q, 2H, *J* = 6.4 Hz), 3.75 (s, 3H), 5.62 (br s, 1H), 6.76 (dd, 2H, *J* = 8.8, 2.4 Hz), 6.88 (d, 1H, *J* = 2.0 Hz), 6.93 (d, 1H, *J* = 2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.4, 25.4, 39.9, 56.1, 100.6, 112.2, 112.4, 112.6, 123.0, 127.8, 131.7, 154.1, 170.4; HRMS calcd. for $C_{13}H_{17}N_2O_2$ (M^++H) 233.1290, found 233.1289.

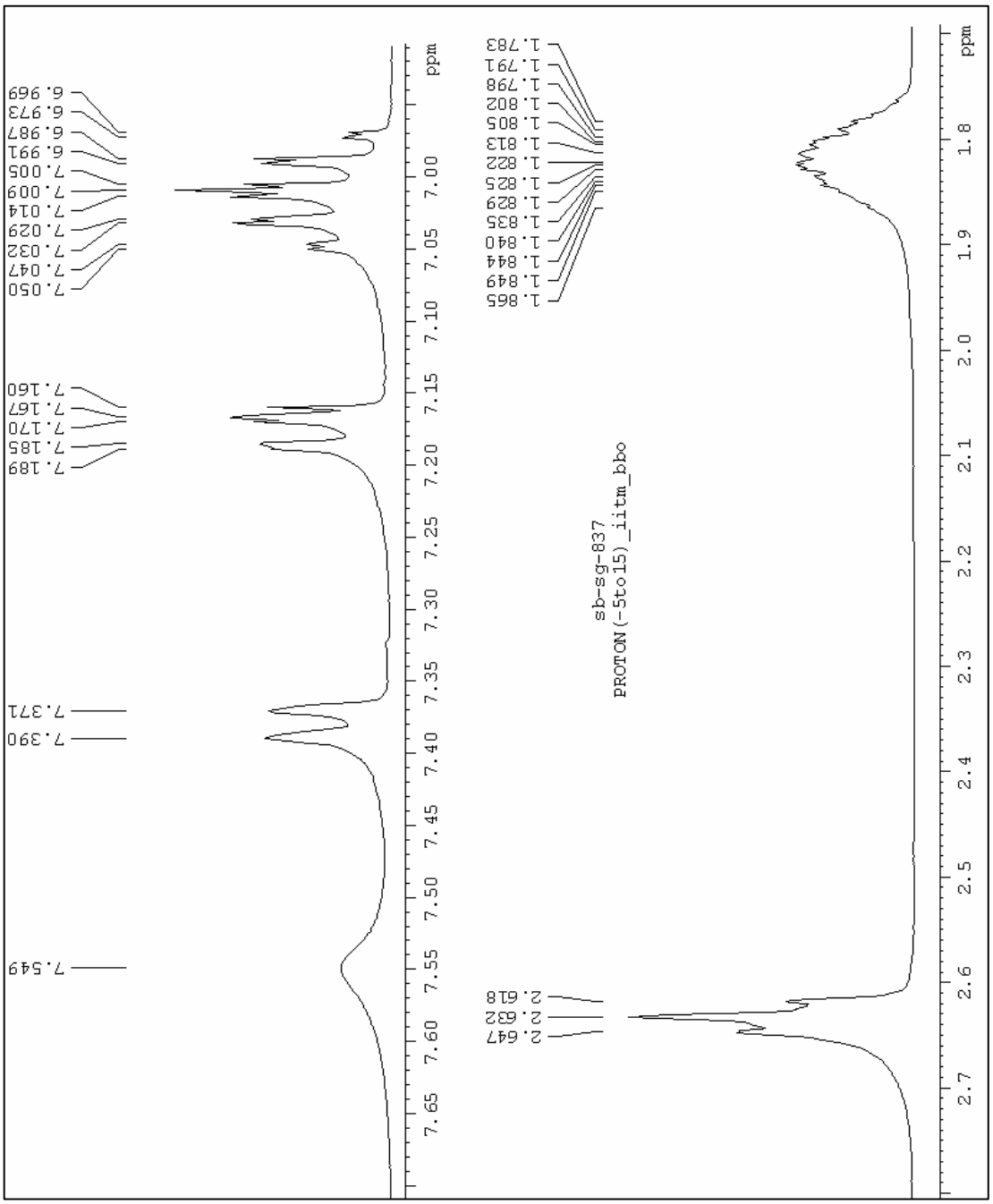
17. 2-Methyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole:



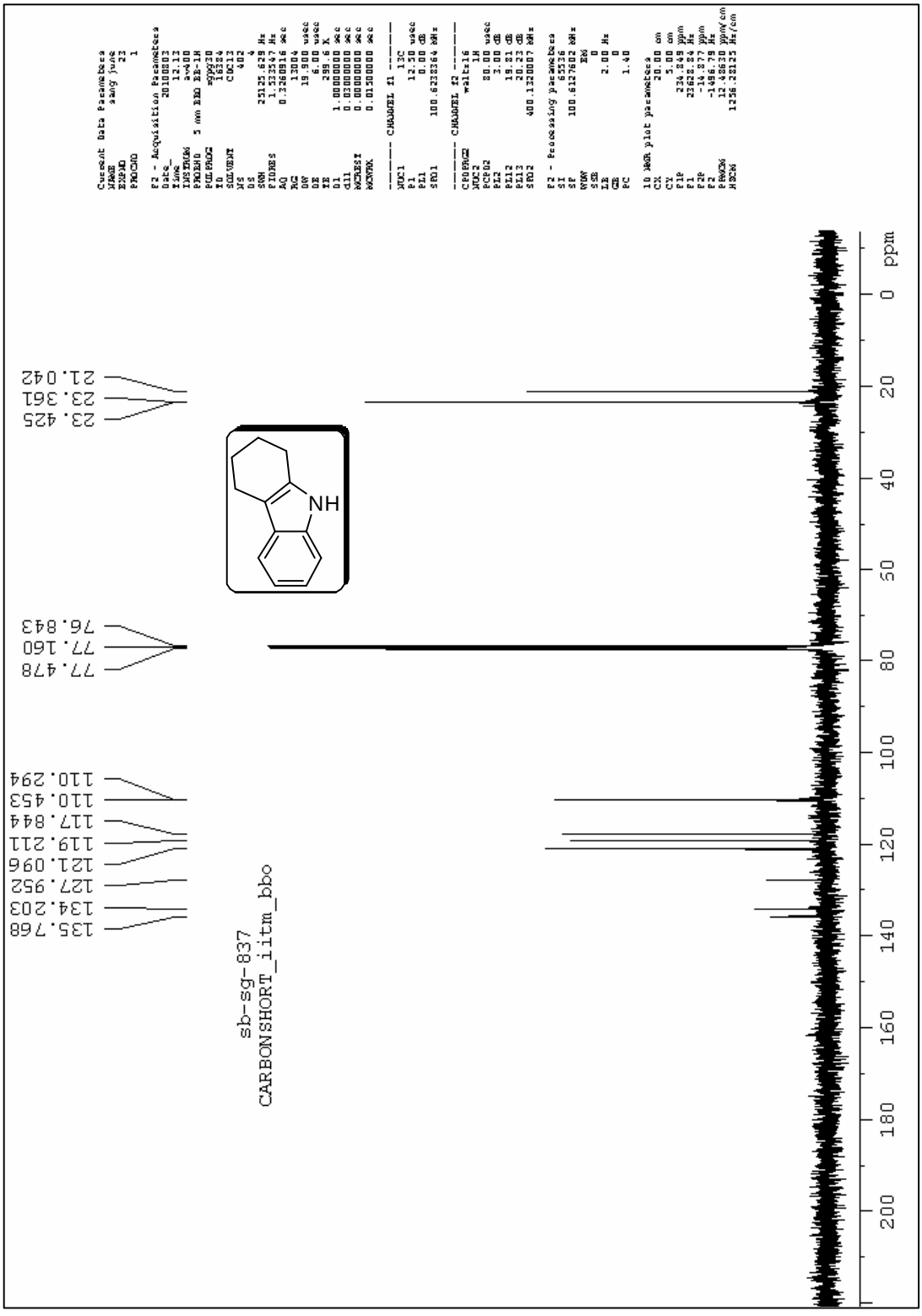
Colorless solid; Yield 91%; M.p. 97–99 ^{o}C; IR (neat): 3334, 2923, 1634, 1463, 795 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.43 (s, 3H), 2.58 (s, 3H), 2.85 (s, 4H), 3.69 (s, 2H), 6.94 (d, 1H, *J* = 8.4 Hz), 7.15 (s, 1H), 7.17 (d, 2H, *J* = 3.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 23.7, 45.7, 51.8, 52.5, 107.9, 110.4, 117.5, 122.8, 126.4, 128.6, 131.8, 134.5; HRMS calcd. for $C_{13}H_{17}N_2$ (M^++1) 201.1392, found 201.1384.



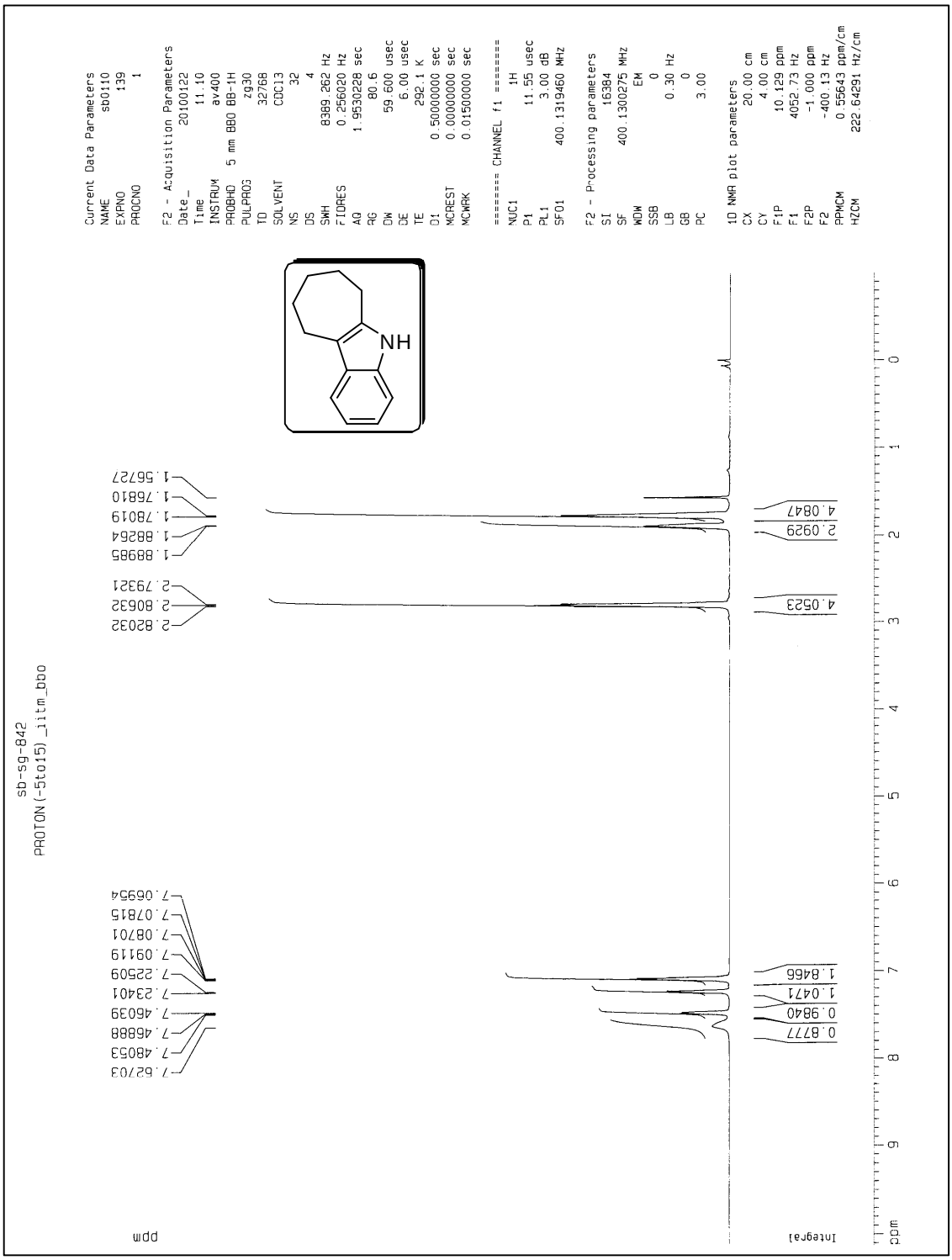
Expanded ^{1}H NMR spectra of compound **3a**



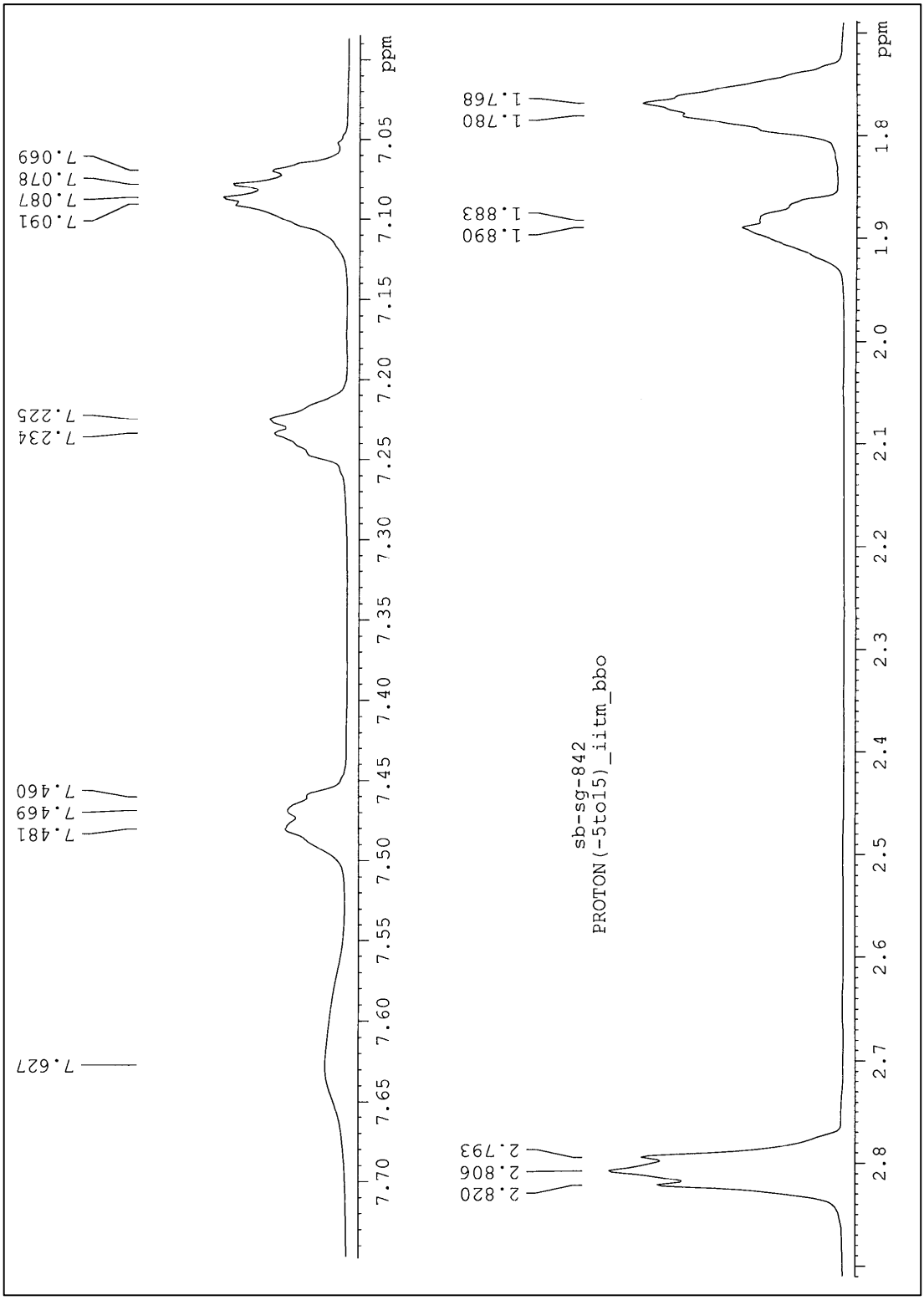
Expanded ^{1}H NMR spectrum of indole derivative **3a**



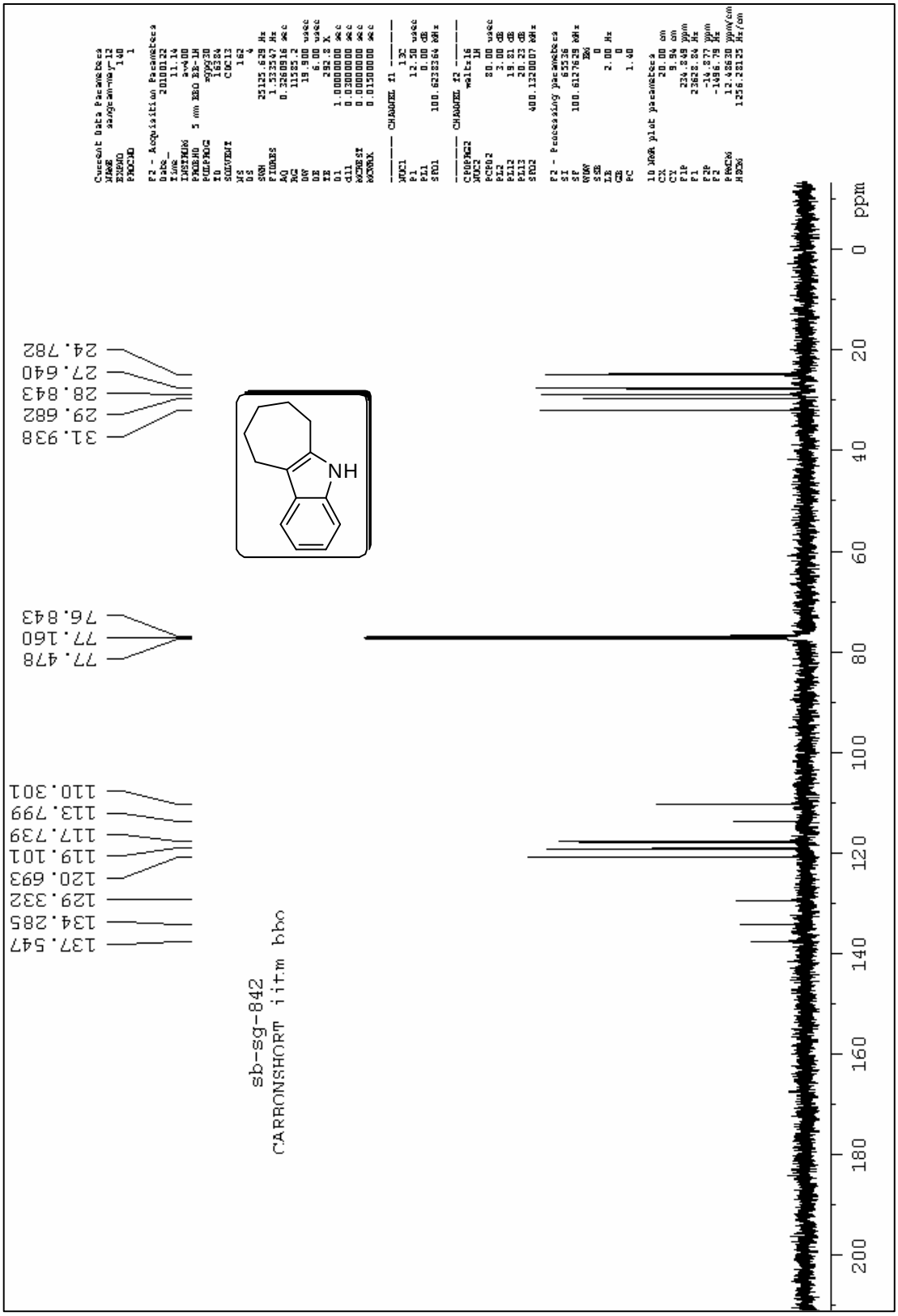
^{13}C NMR spectrum of indole derivative **3a**



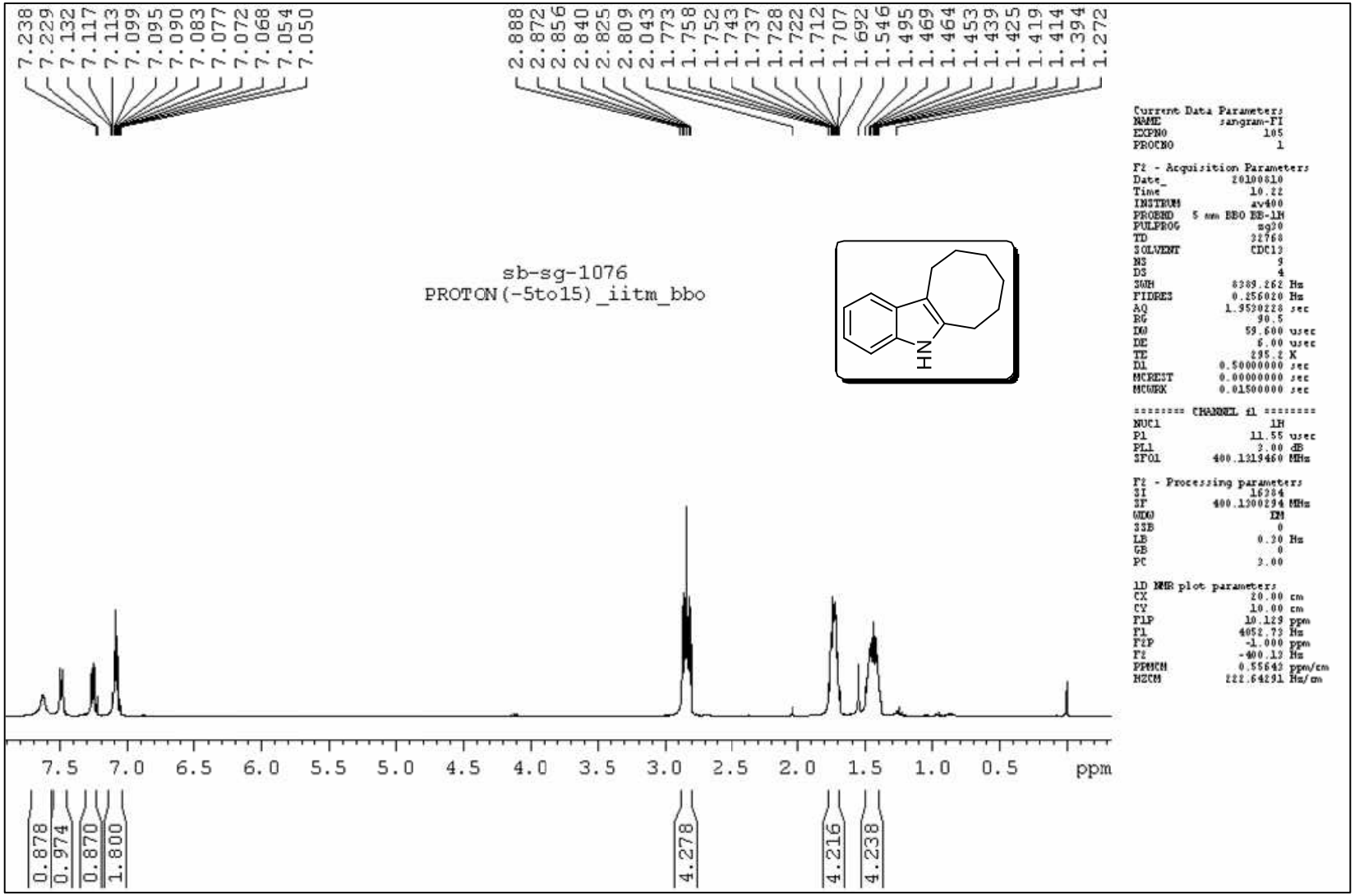
^{1}H NMR spectrum of indole derivative **3b**



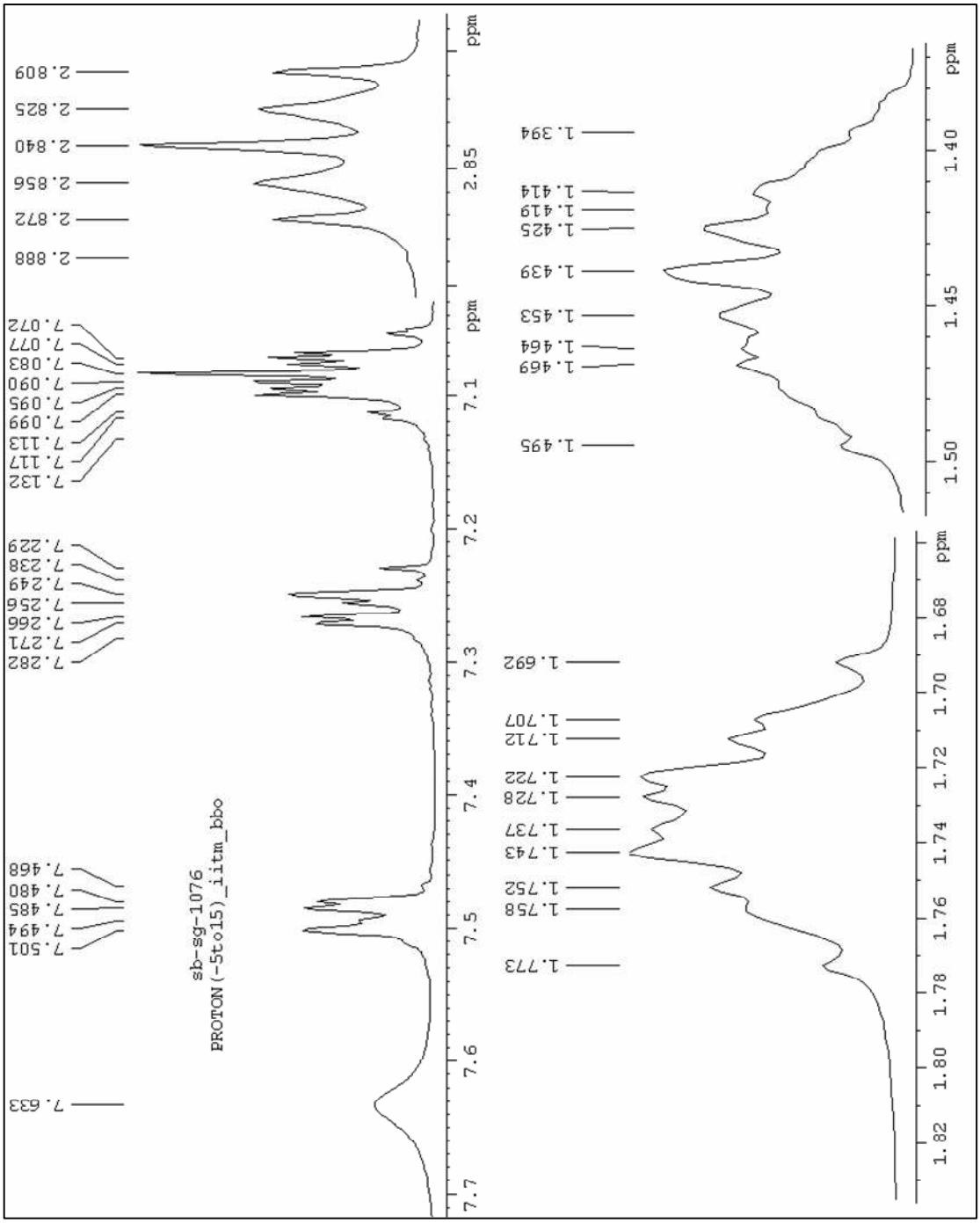
Expanded ^{1}H NMR spectrum of indole derivative **3b**



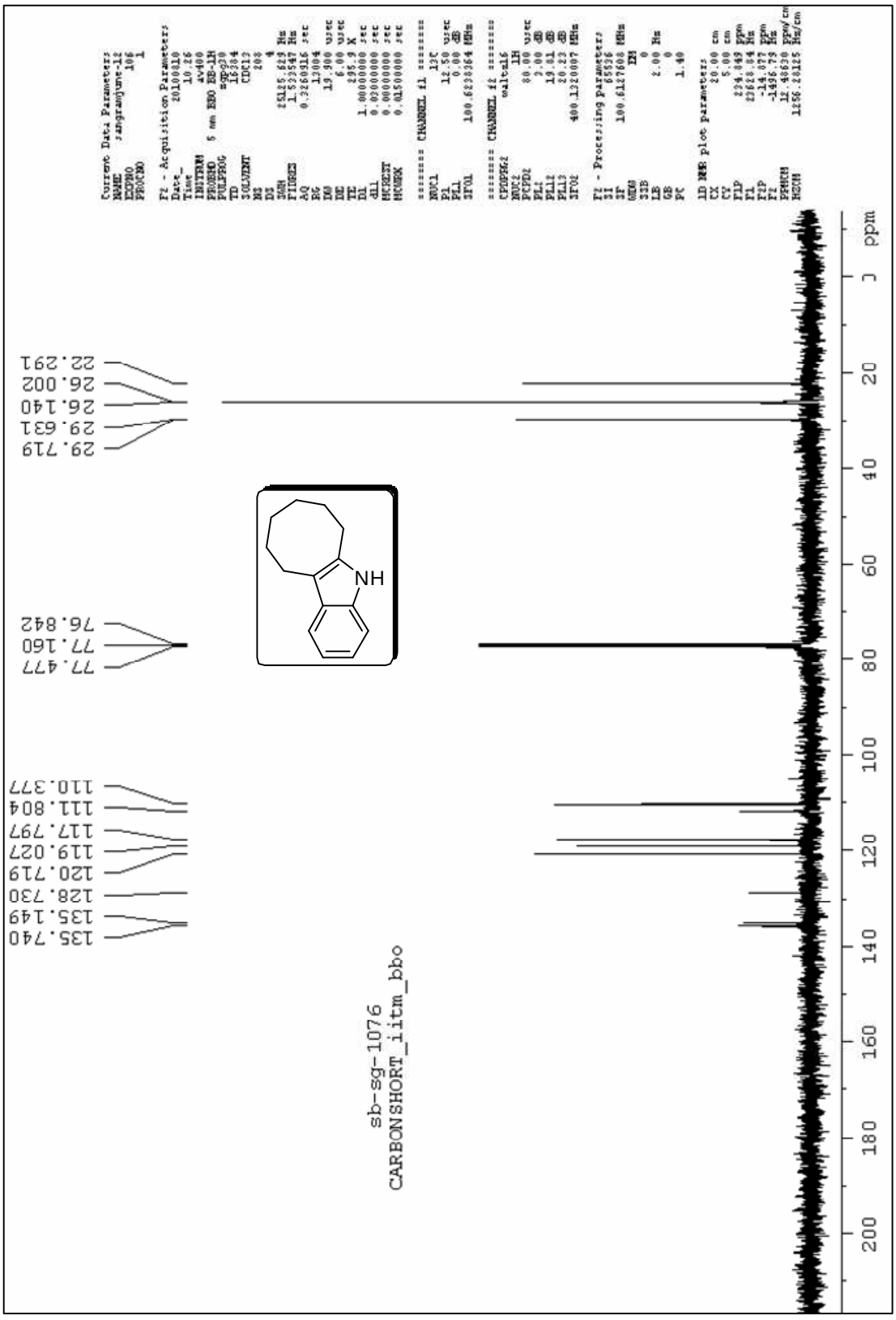
^{13}C NMR spectrum of indole derivative **3b**



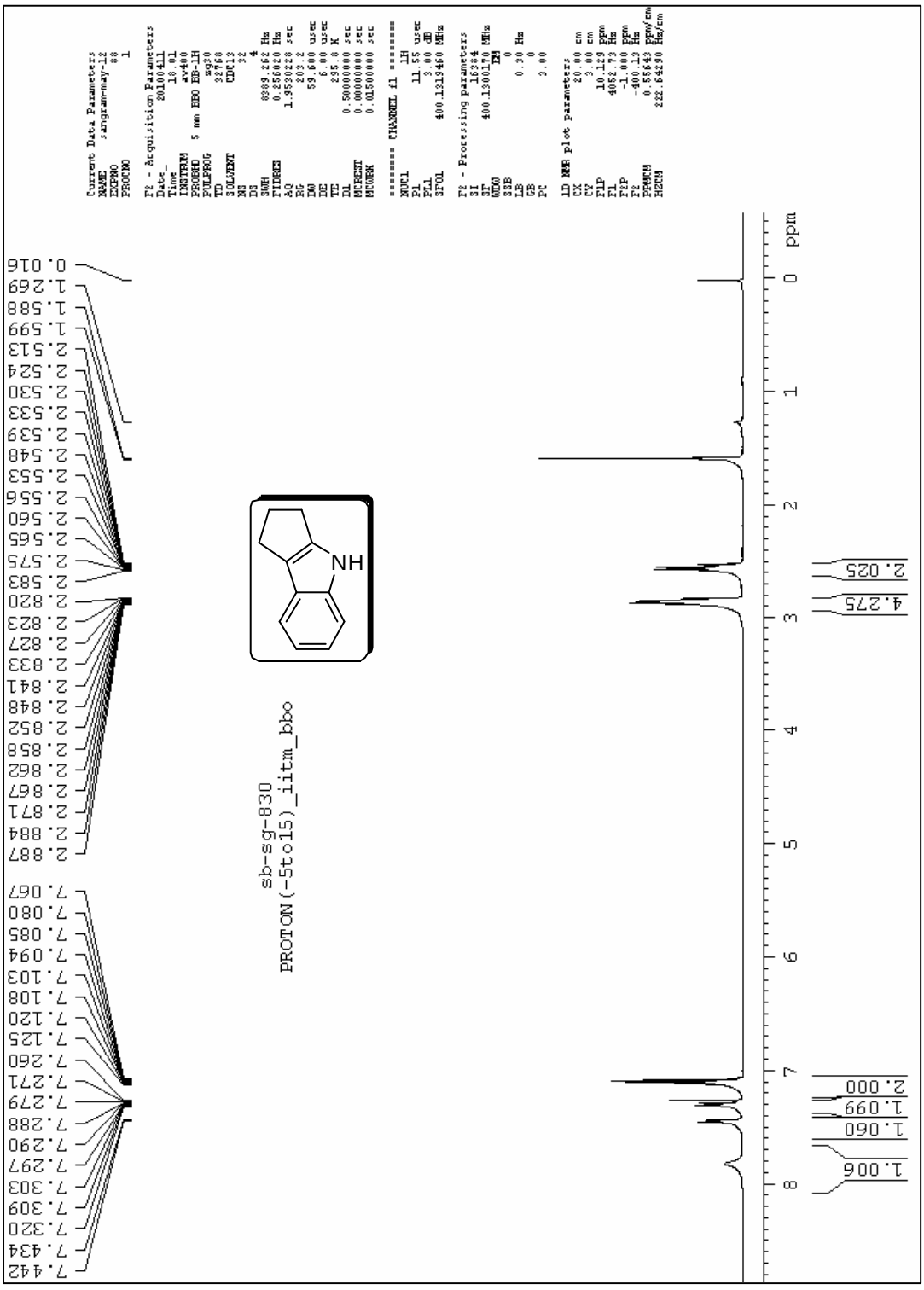
^{1}H NMR spectrum of indole derivative **3c**



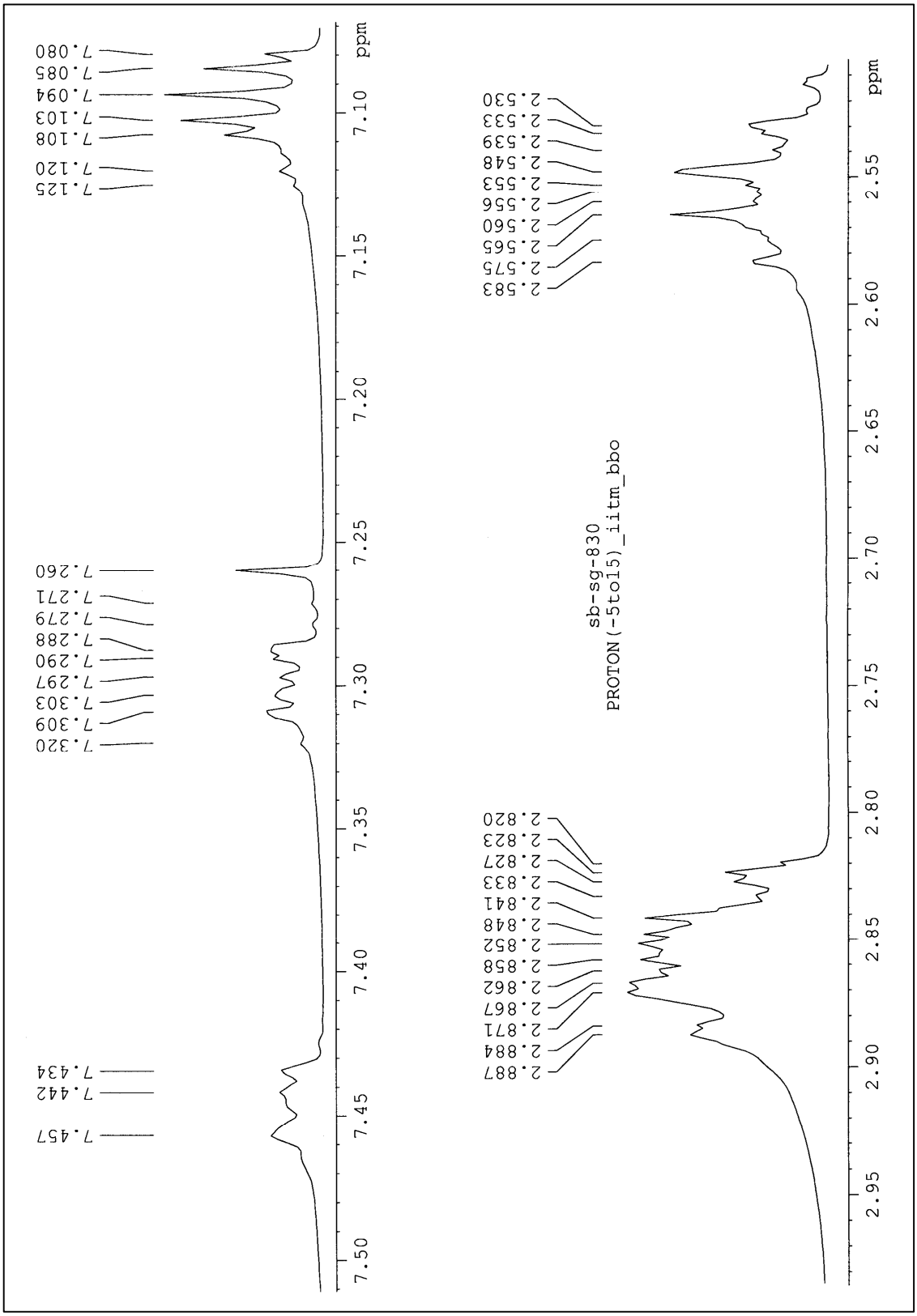
Expanded ^{1}H NMR spectrum of indole derivative **3c**



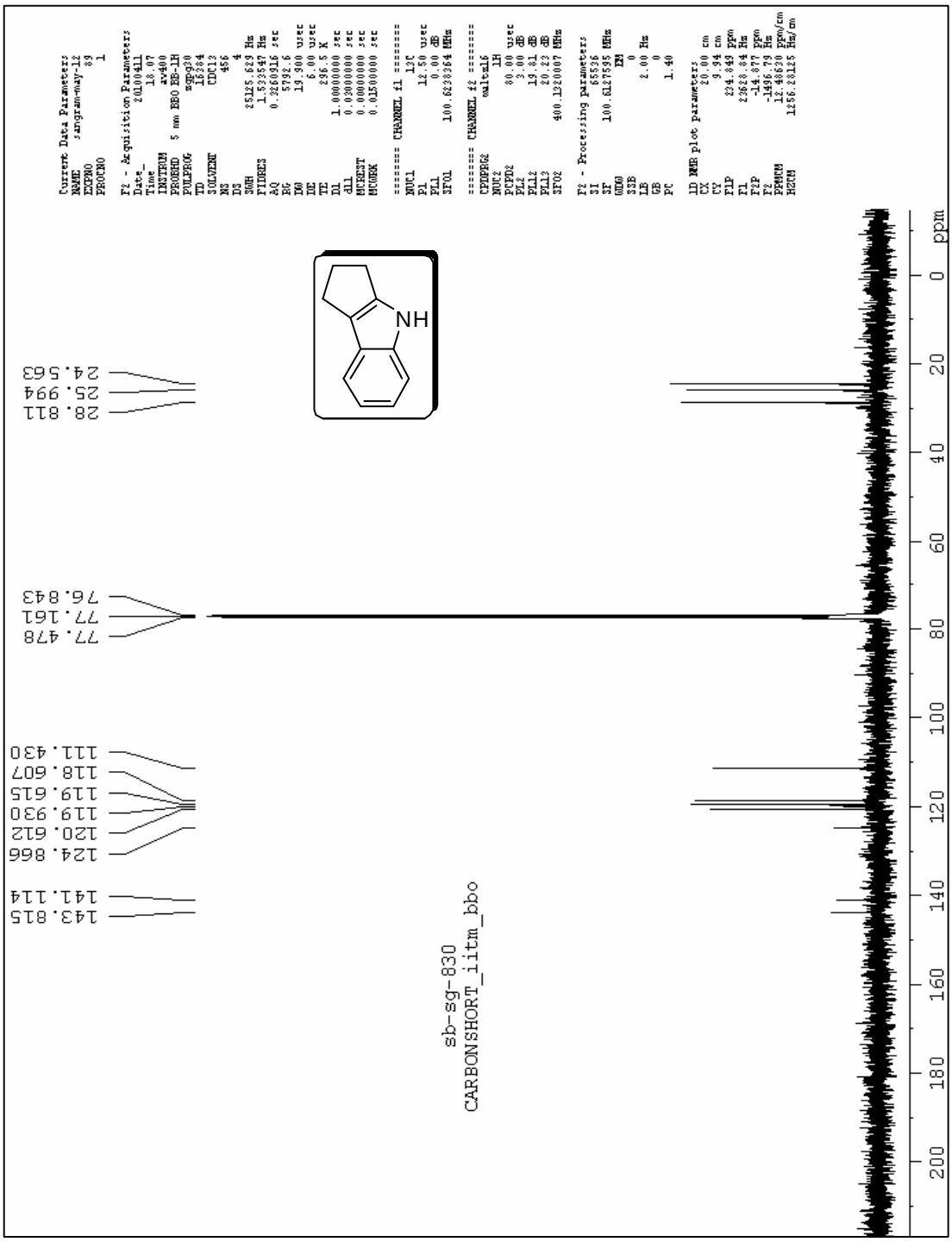
^{13}C NMR spectrum of indole derivative **3c**



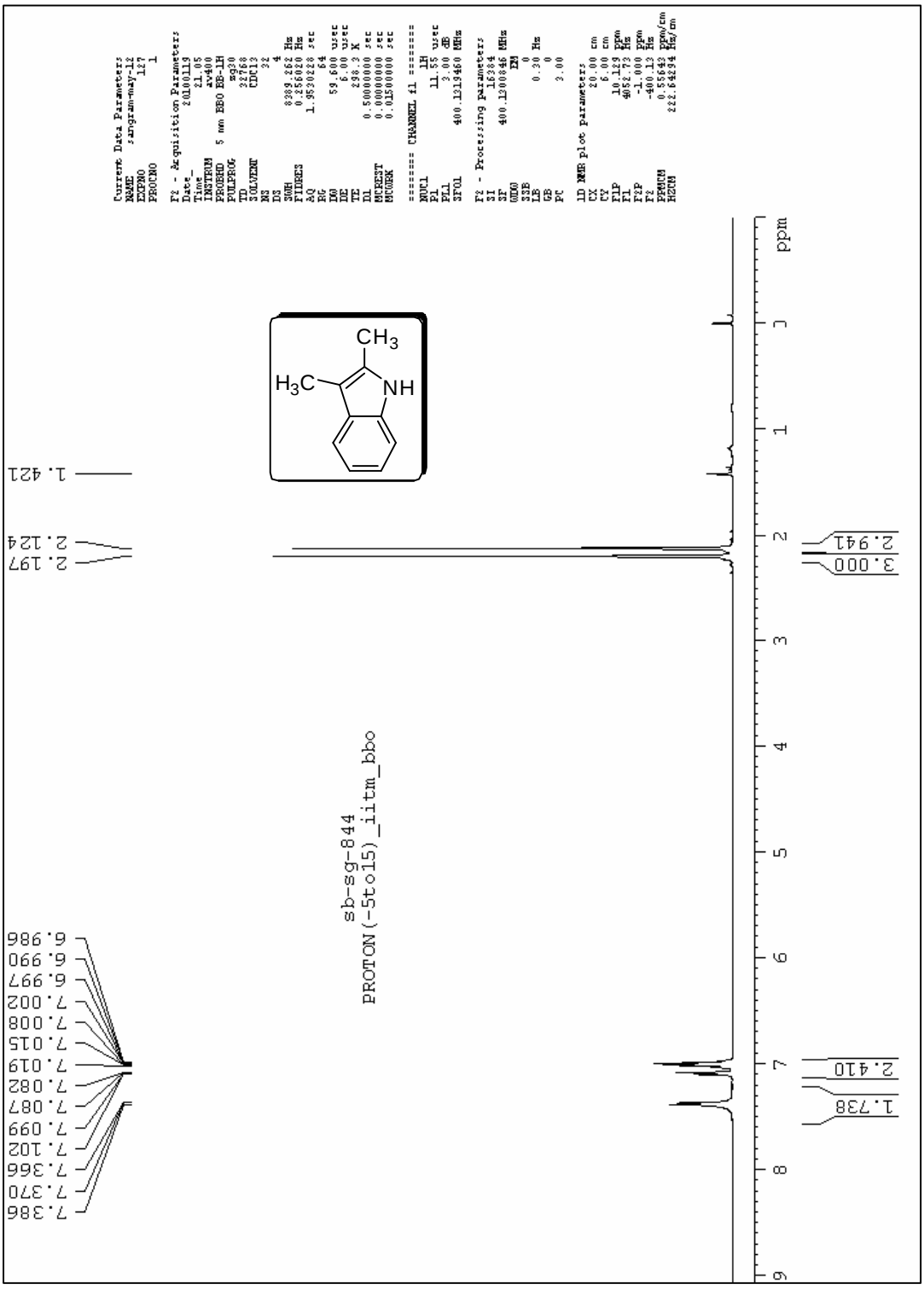
^{1}H NMR spectrum of indole derivative **3d**



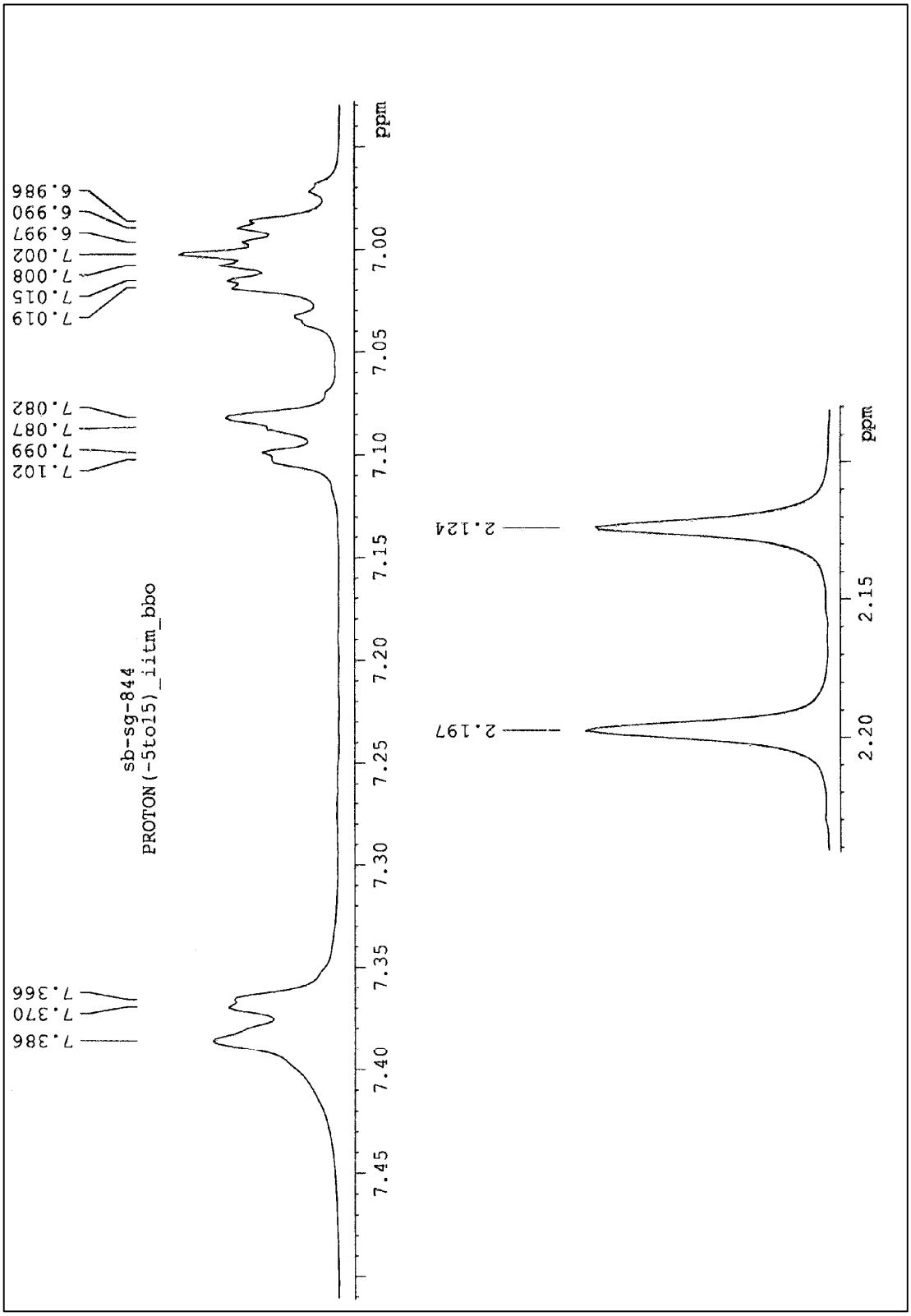
Expanded ^{1}H NMR spectrum of indole derivative **3d**



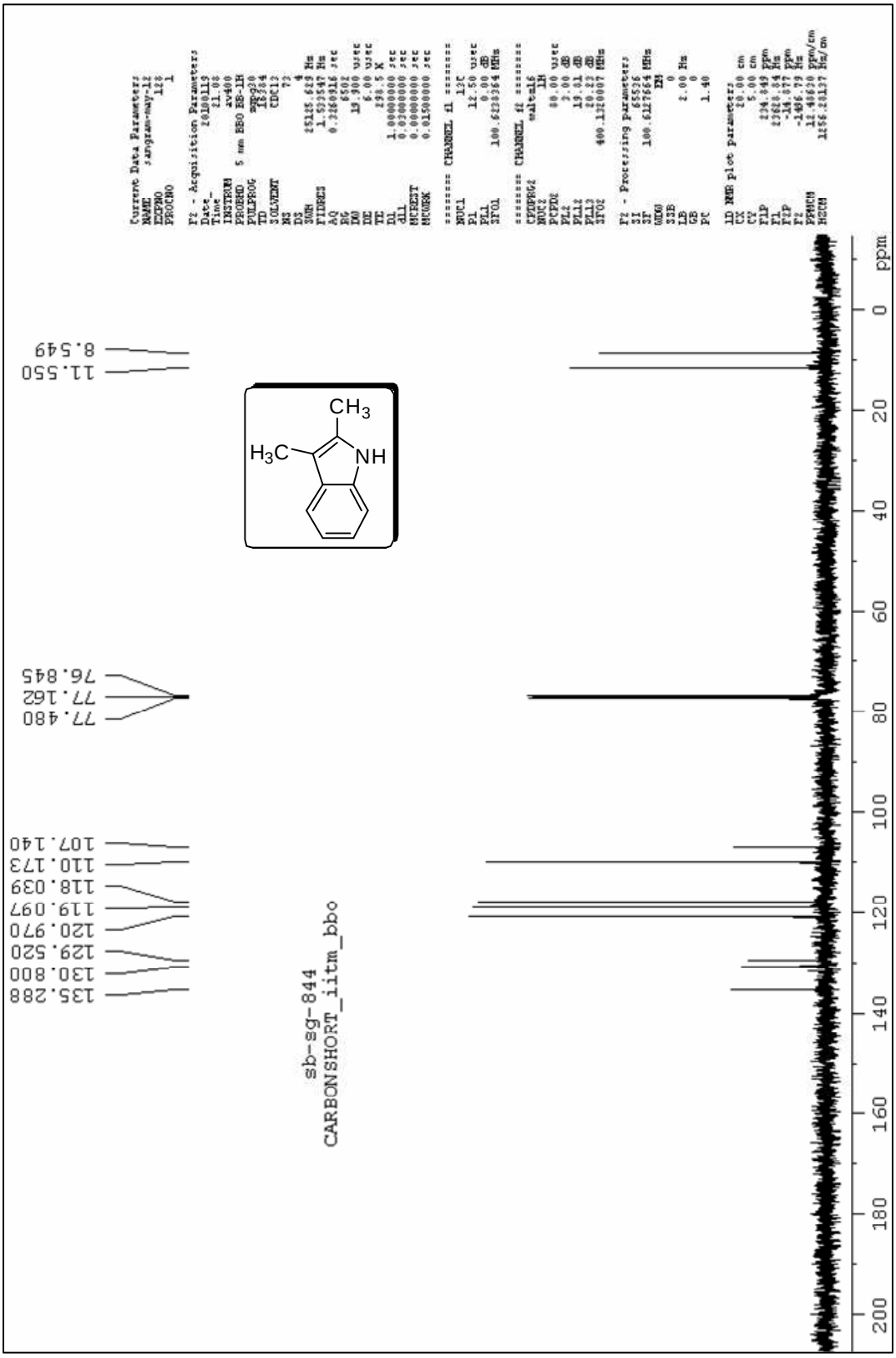
^{13}C NMR spectrum of indole derivative **3d**



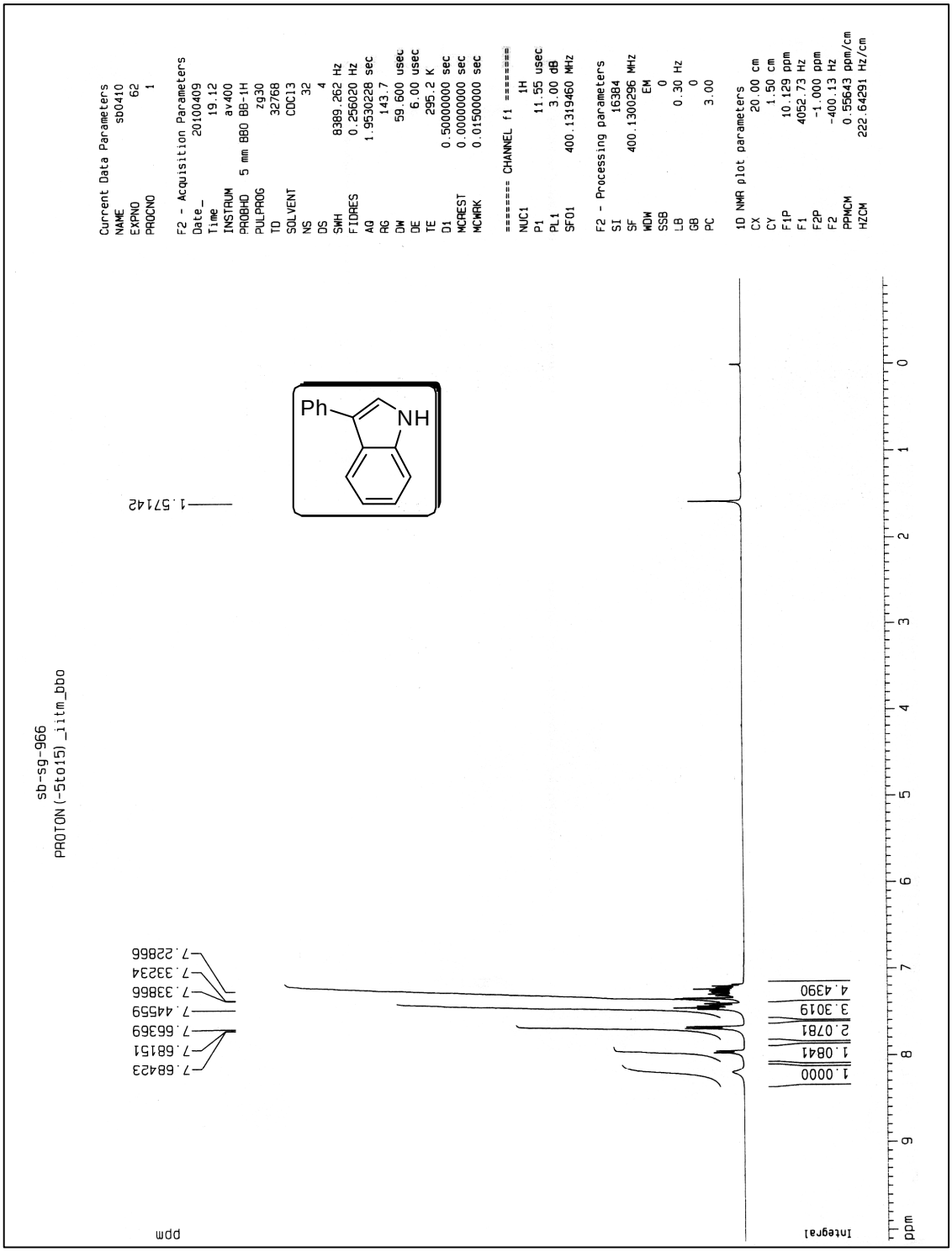
^{1}H NMR spectrum of indole derivative **3e**



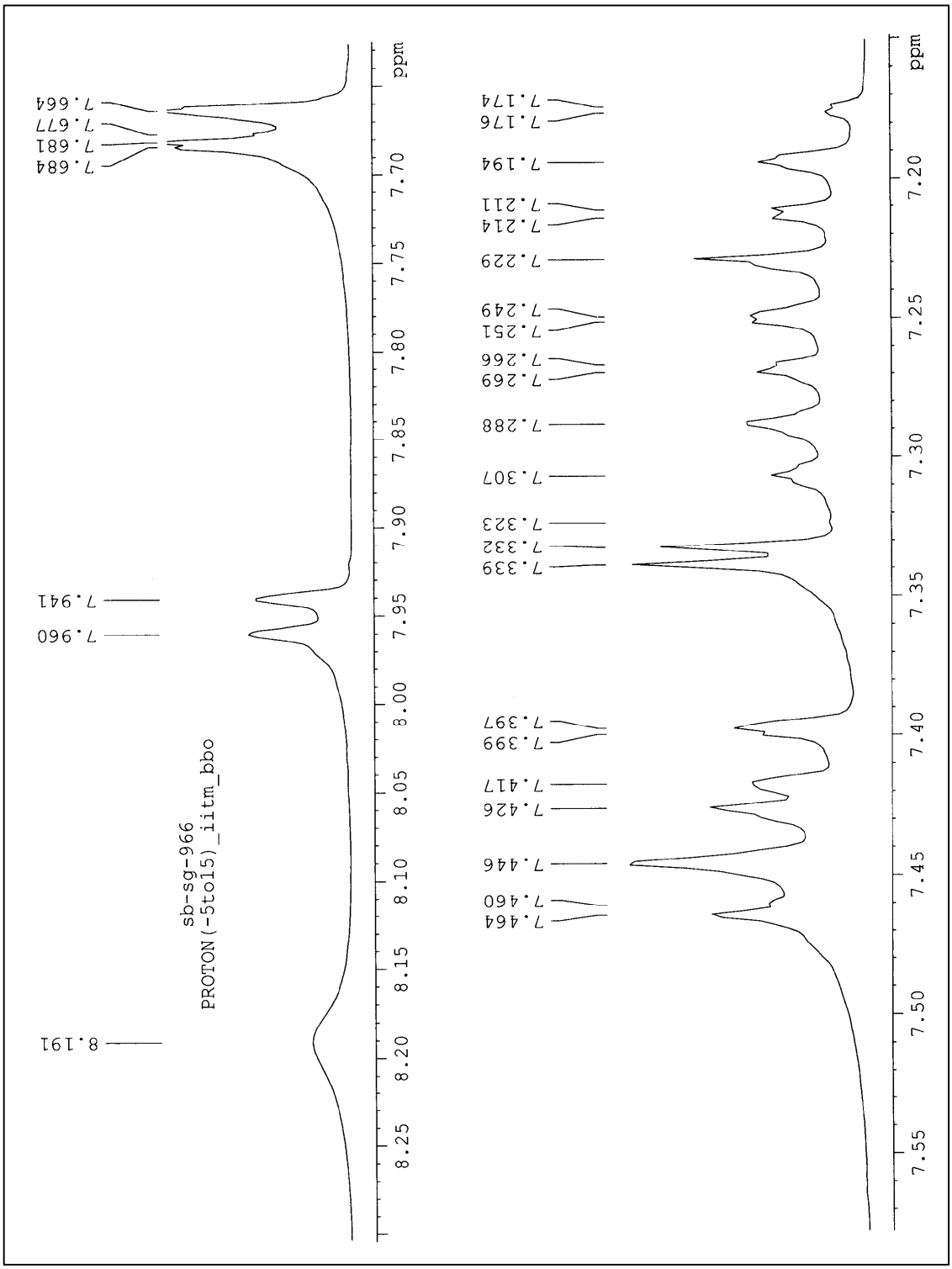
Expanded ^{1}H NMR spectrum of indole derivative **3e**



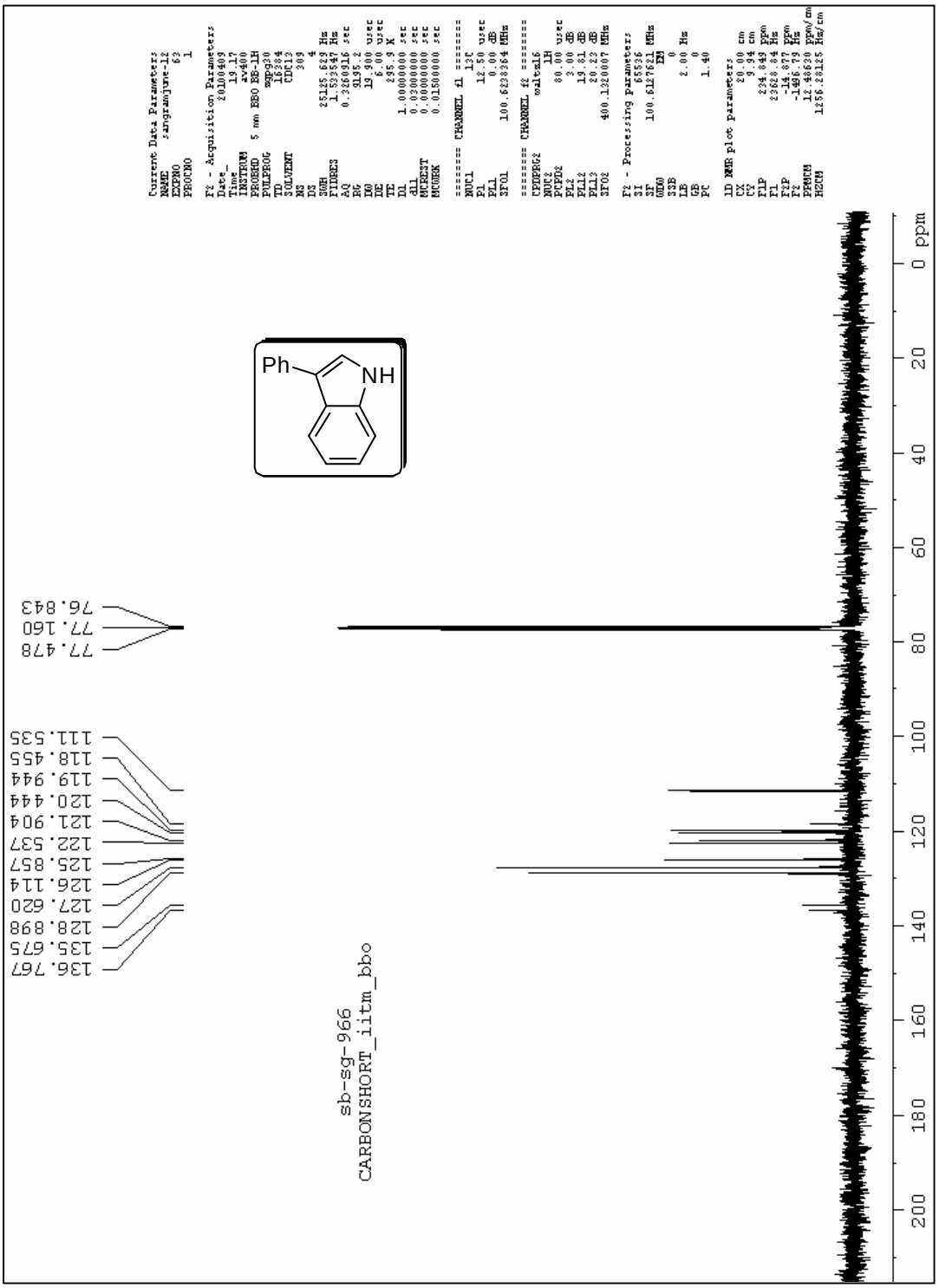
^{13}C NMR spectrum of indole derivative **3e**



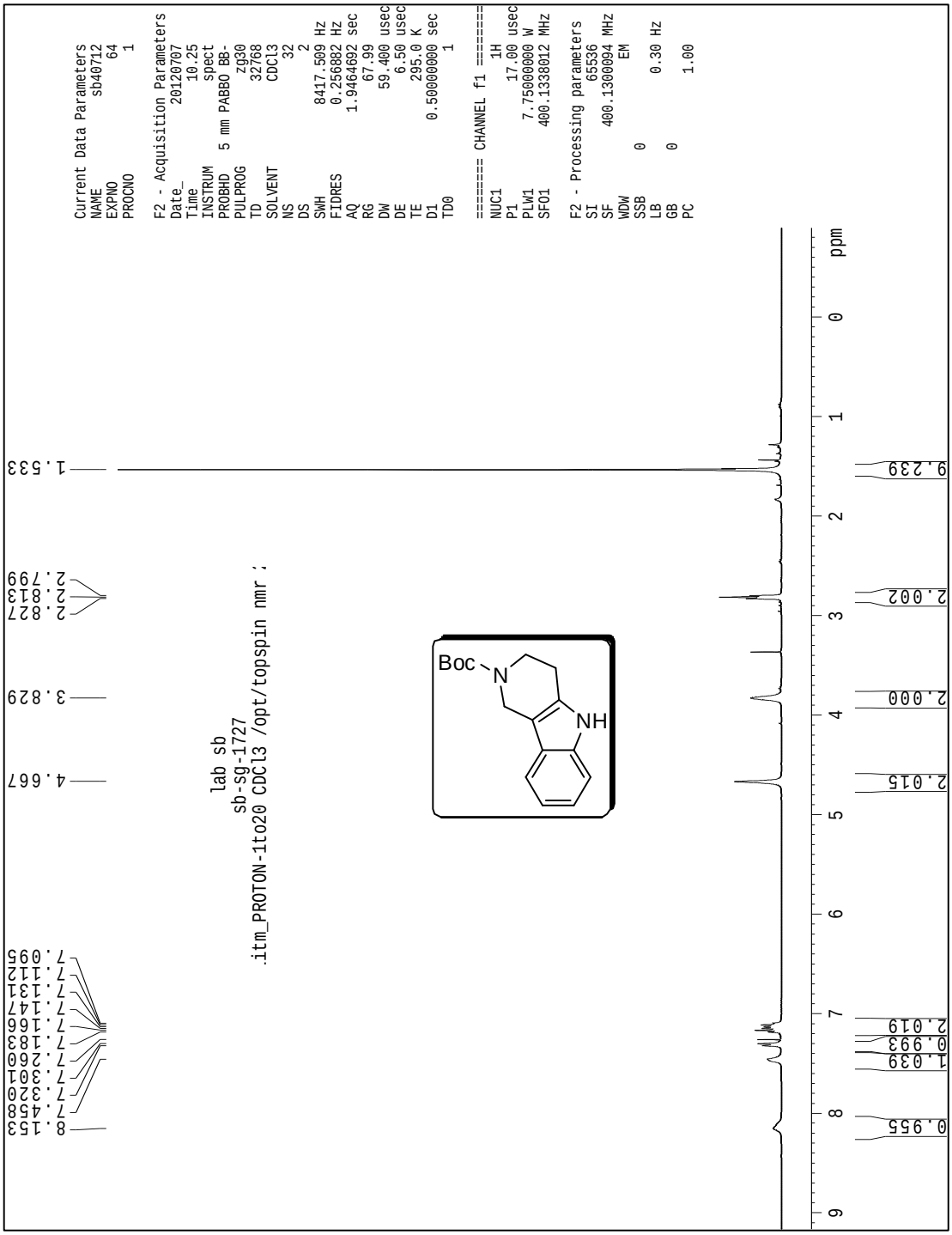
^{1}H NMR spectrum of indole derivative **3f**



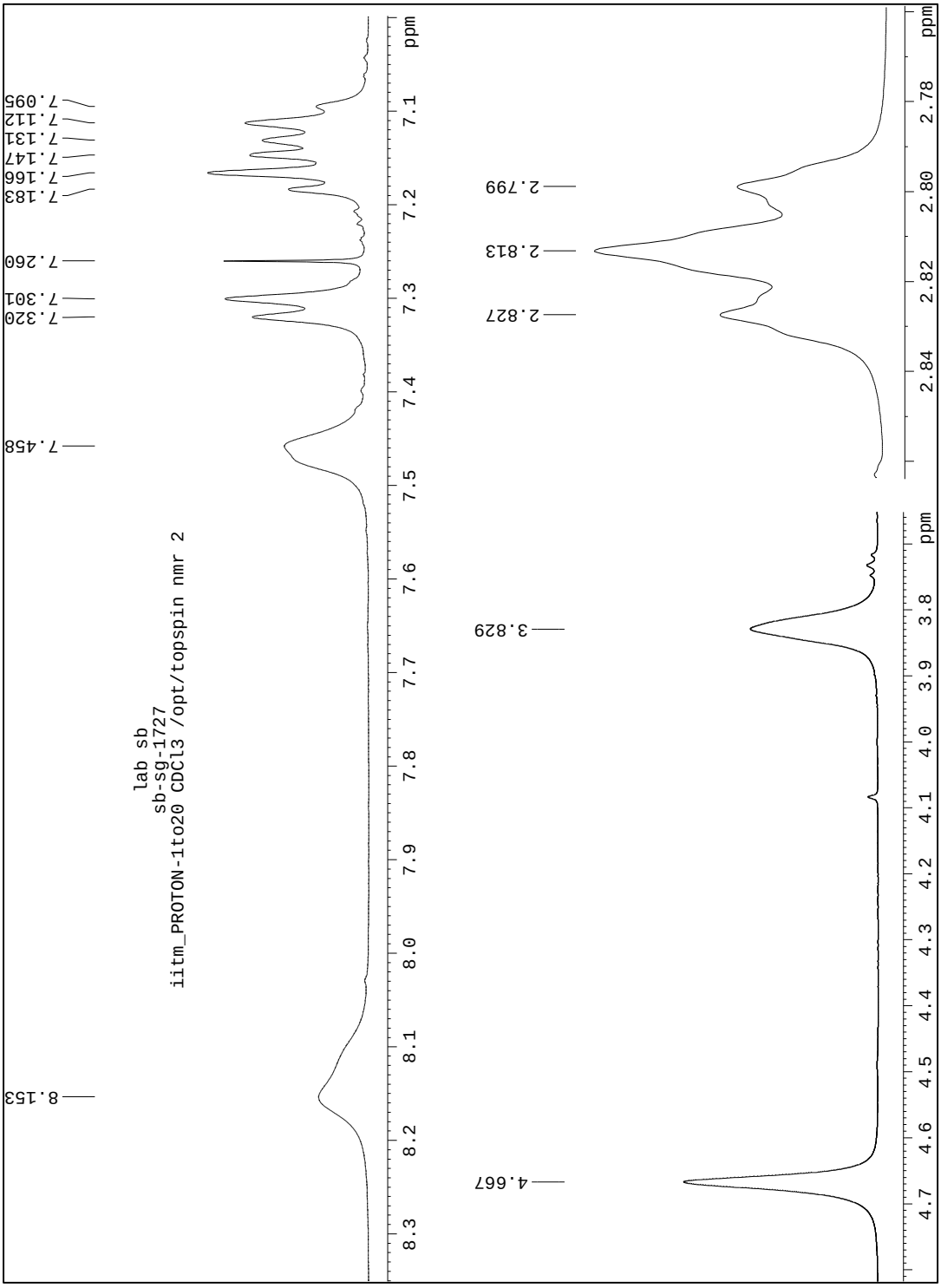
Expanded ^{1}H NMR spectrum of indole derivative **3f**



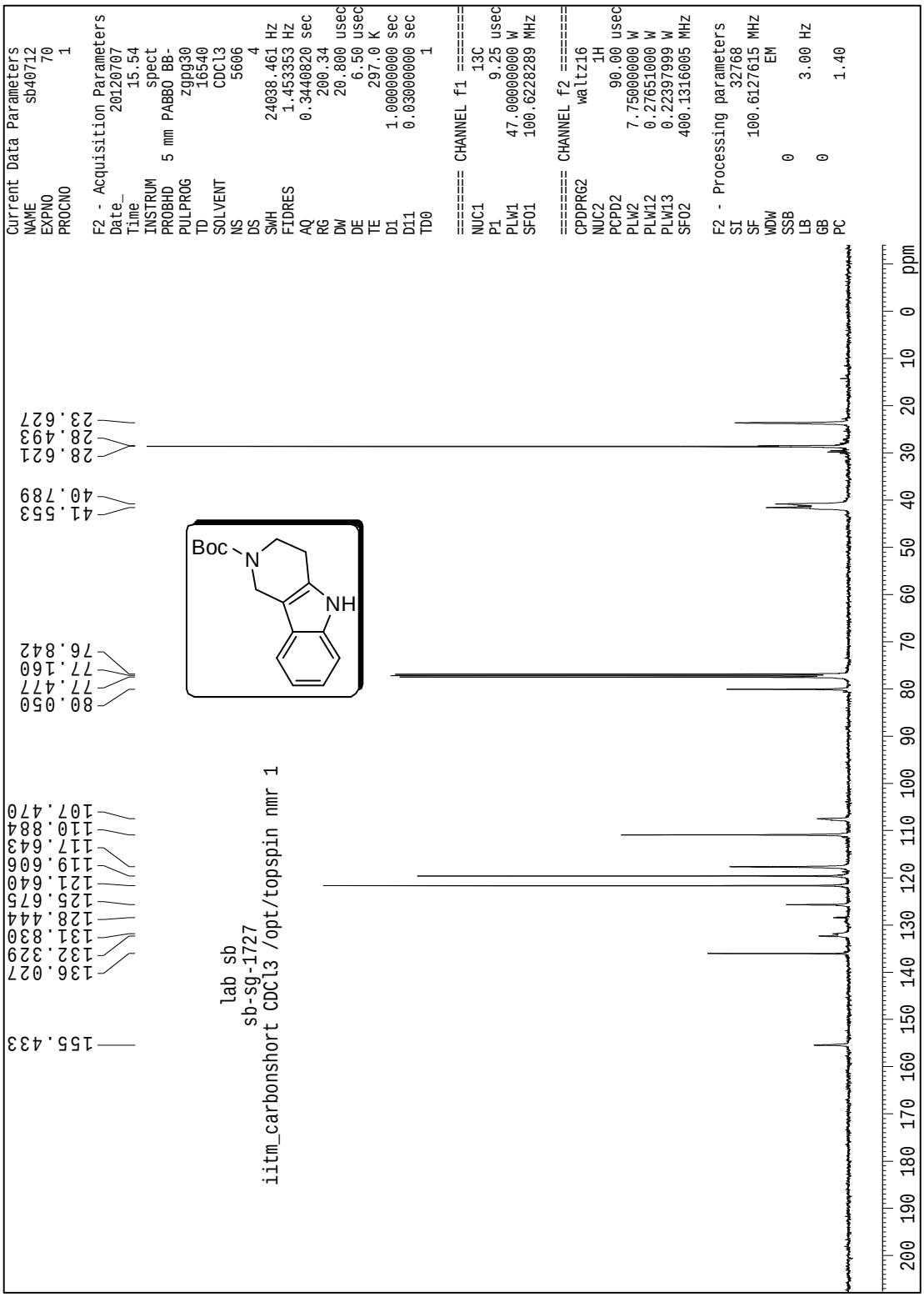
^{13}C NMR spectrum of indole derivative **3f**



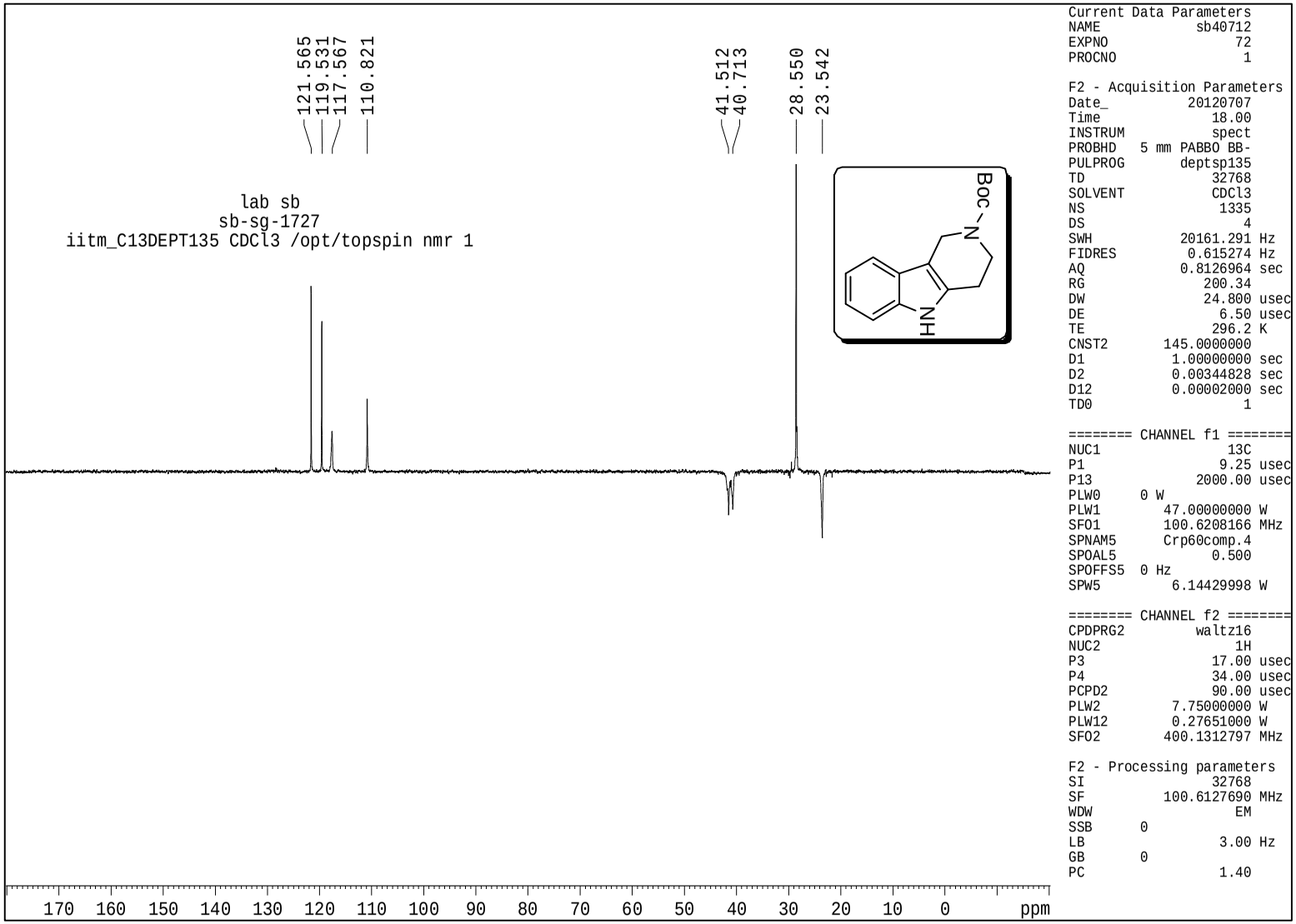
^{1}H NMR spectrum of indole derivative **3g**



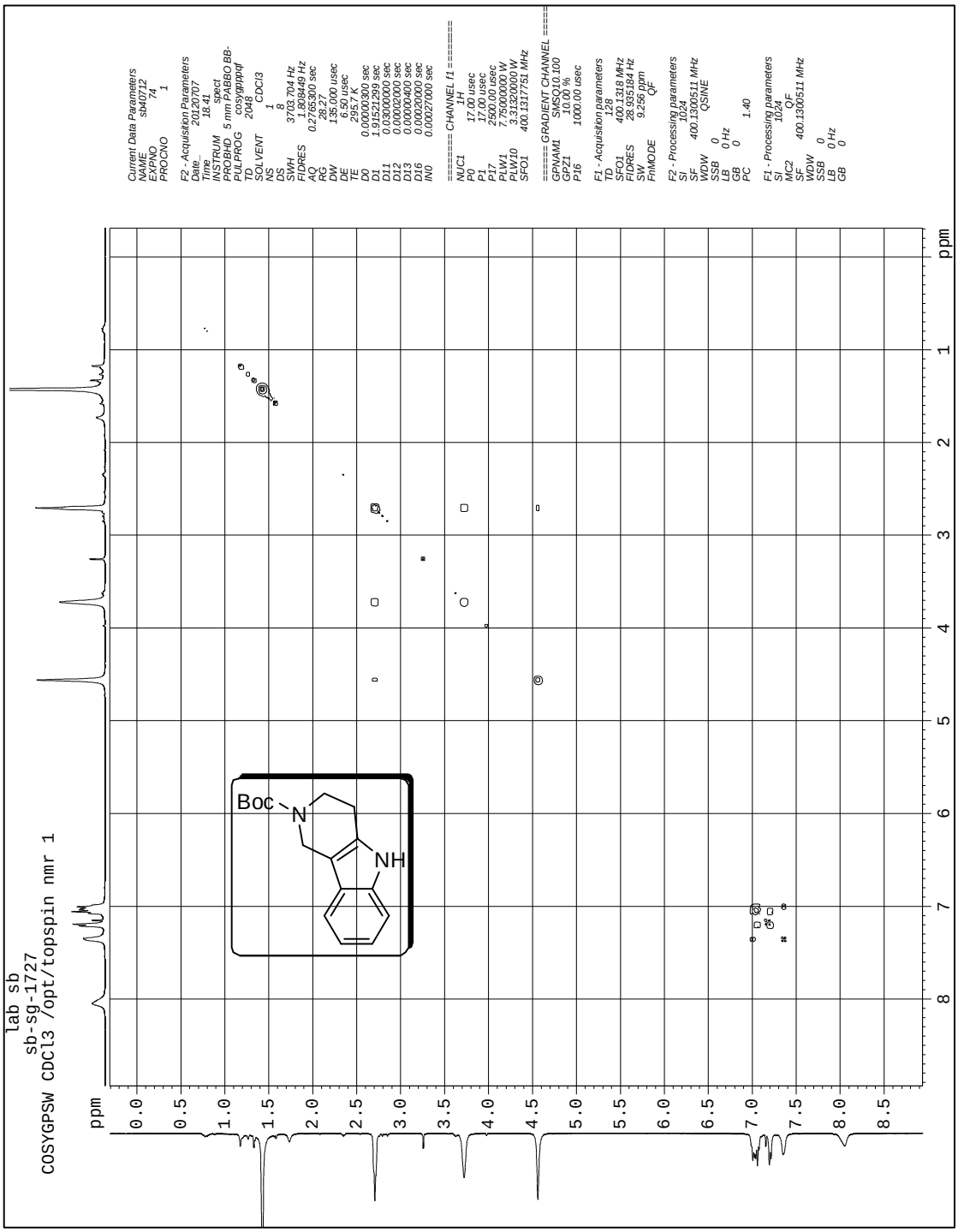
Expanded ^{1}H NMR spectrum of indole derivative **3g**



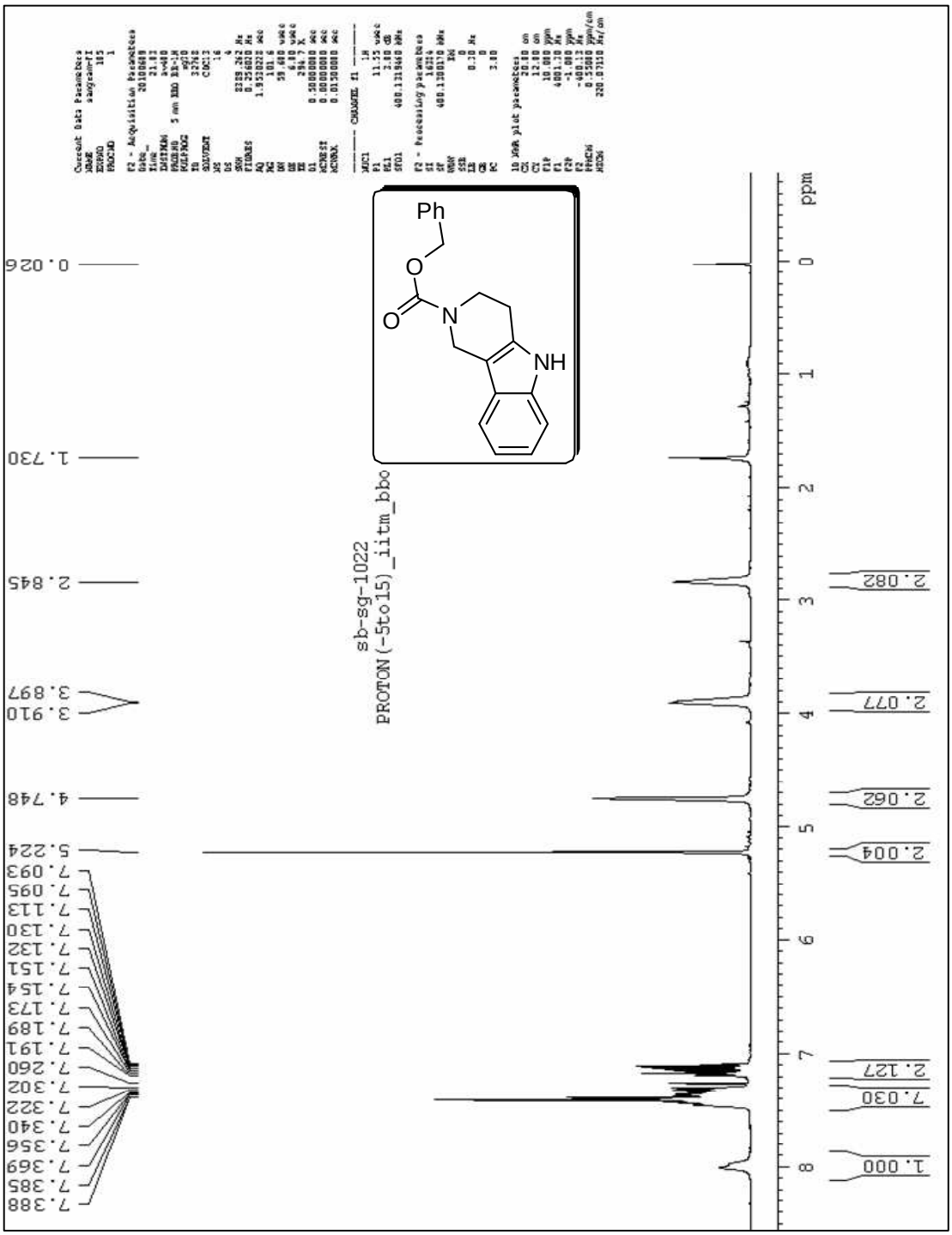
^{13}C NMR spectrum of indole derivative **3g**



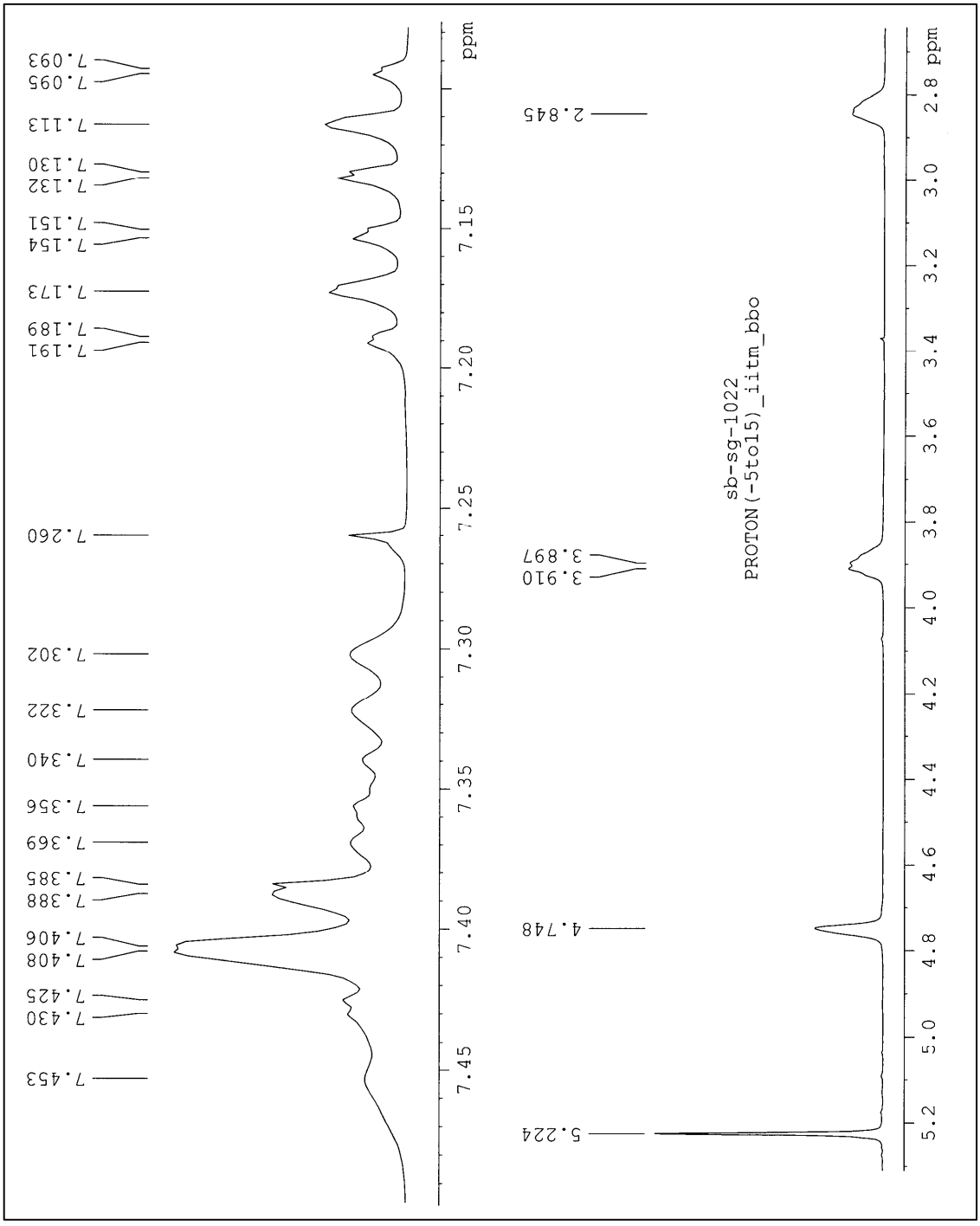
^{13}C DEPT NMR spectrum of indole derivative **3g**



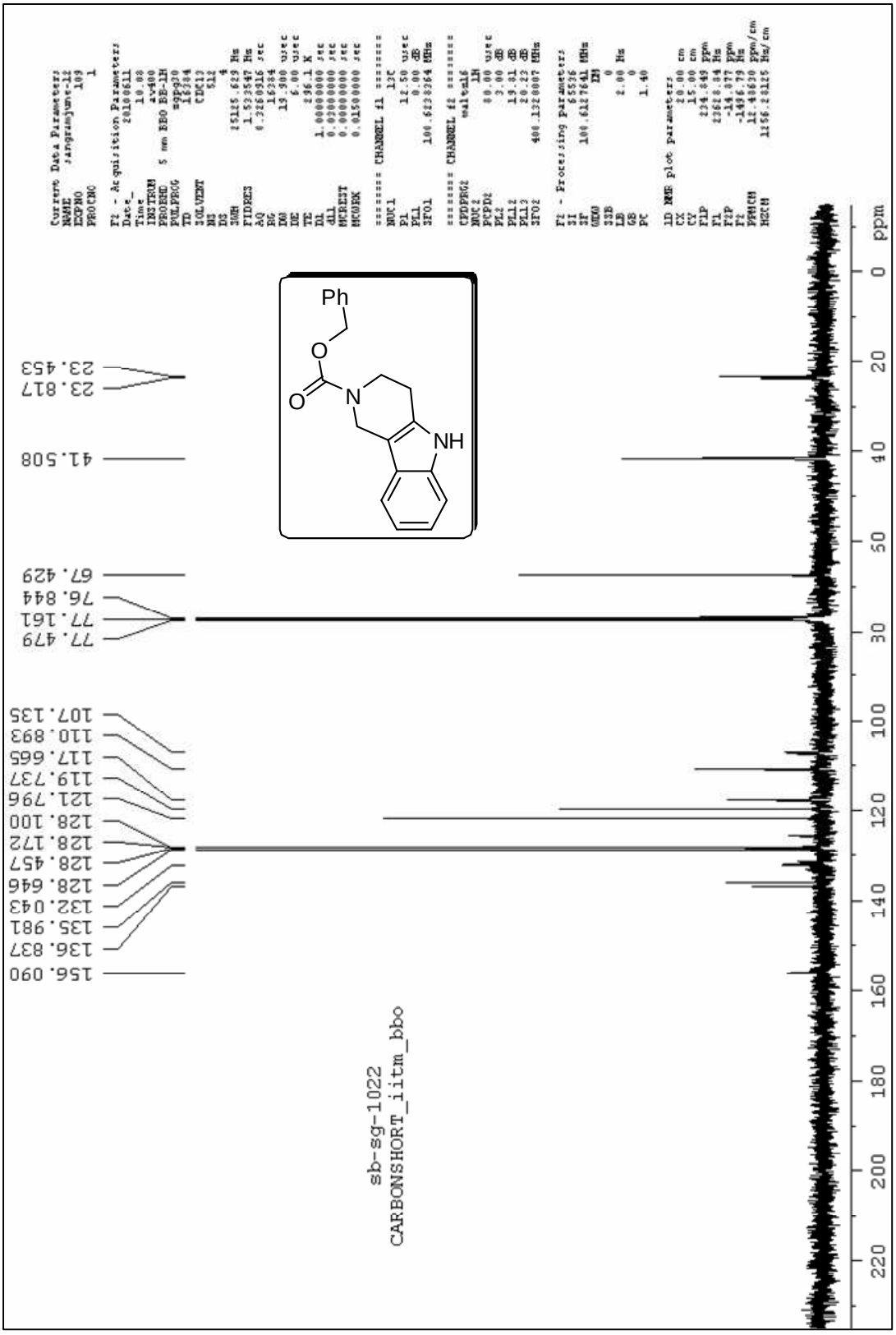
$^{11}H^{1}H$ COSY NMR spectrum of indole derivative **3g**



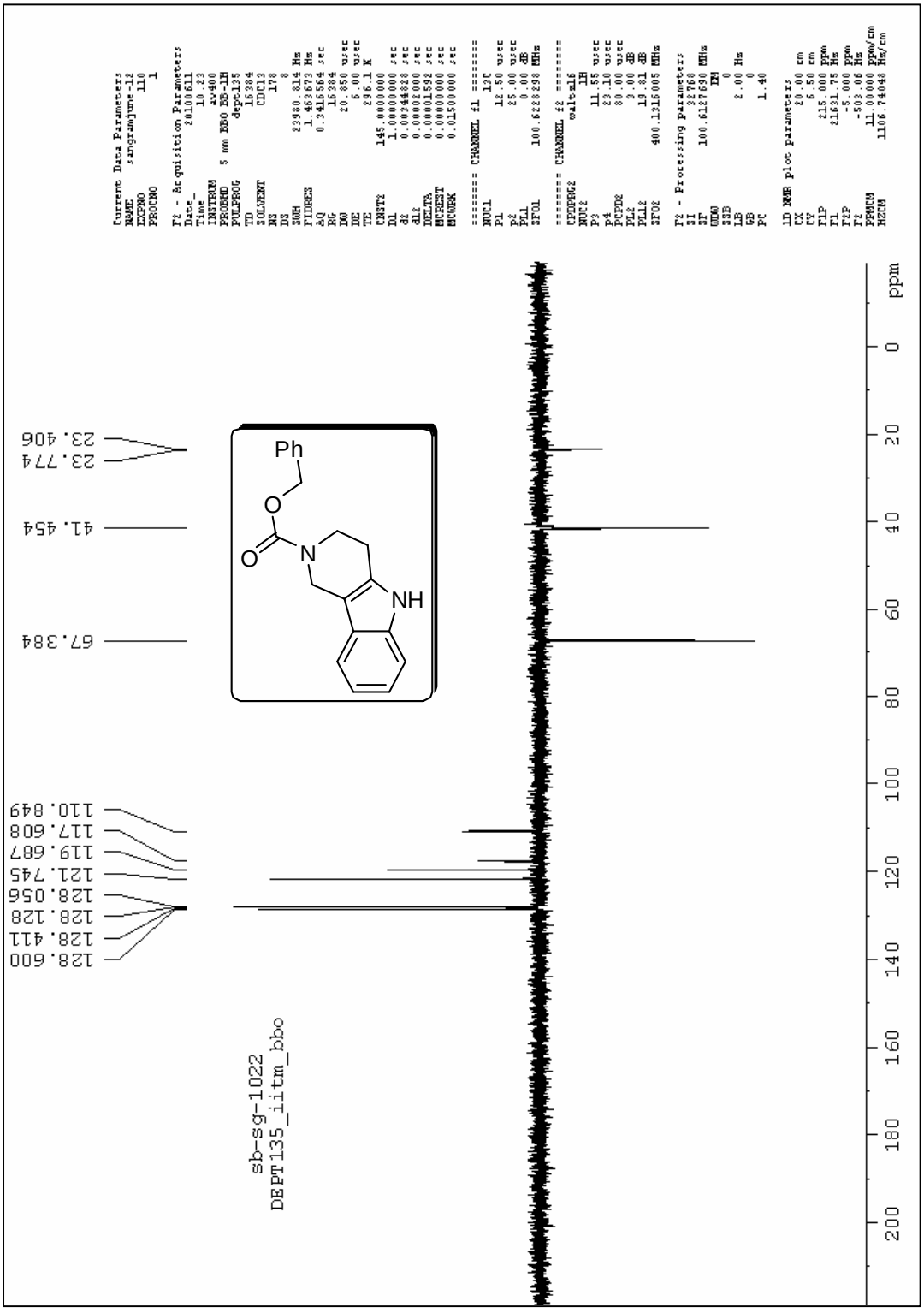
^{1}H NMR spectrum of indole derivative **3h**



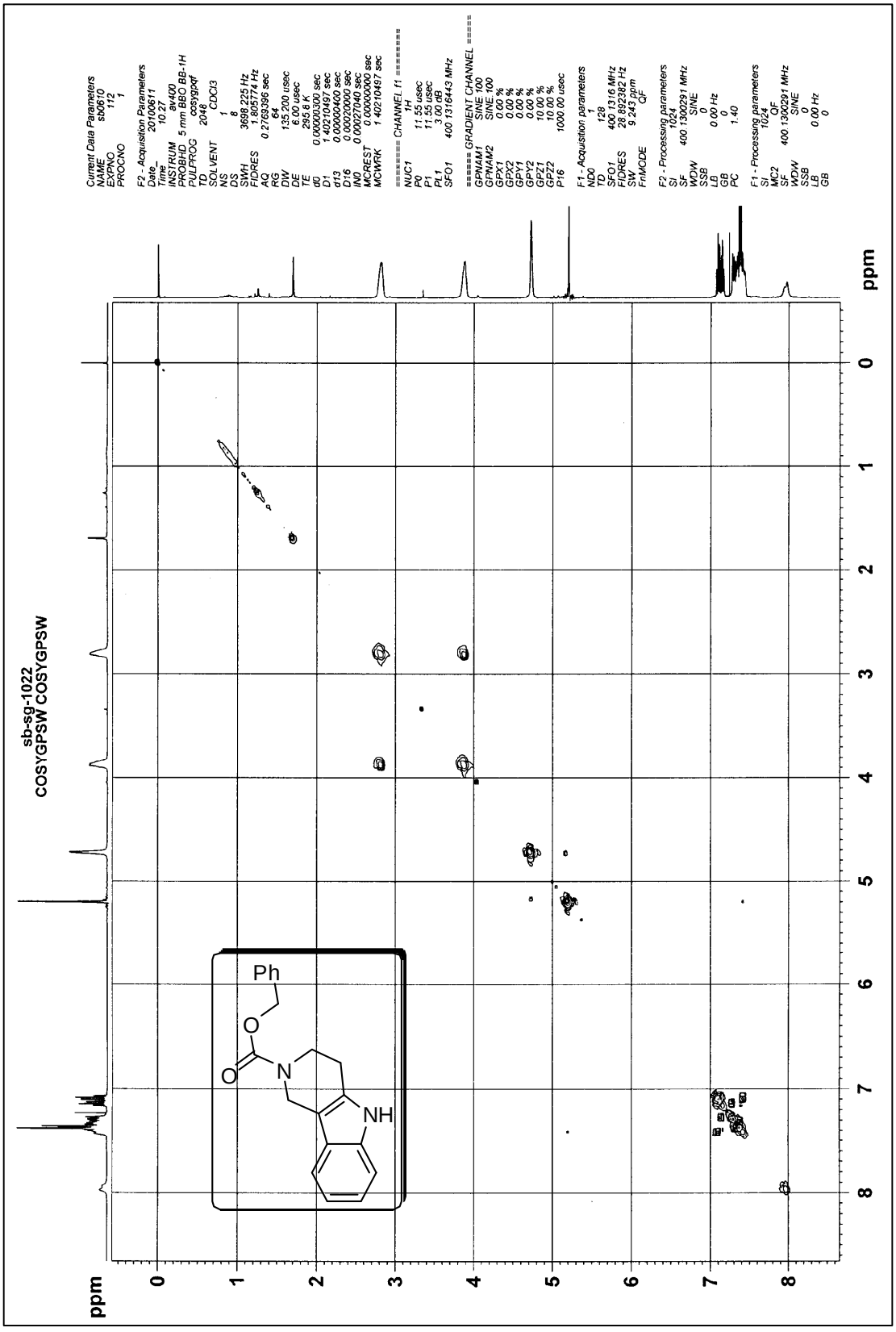
Expanded ^{1}H NMR spectrum of indole derivative **3h**



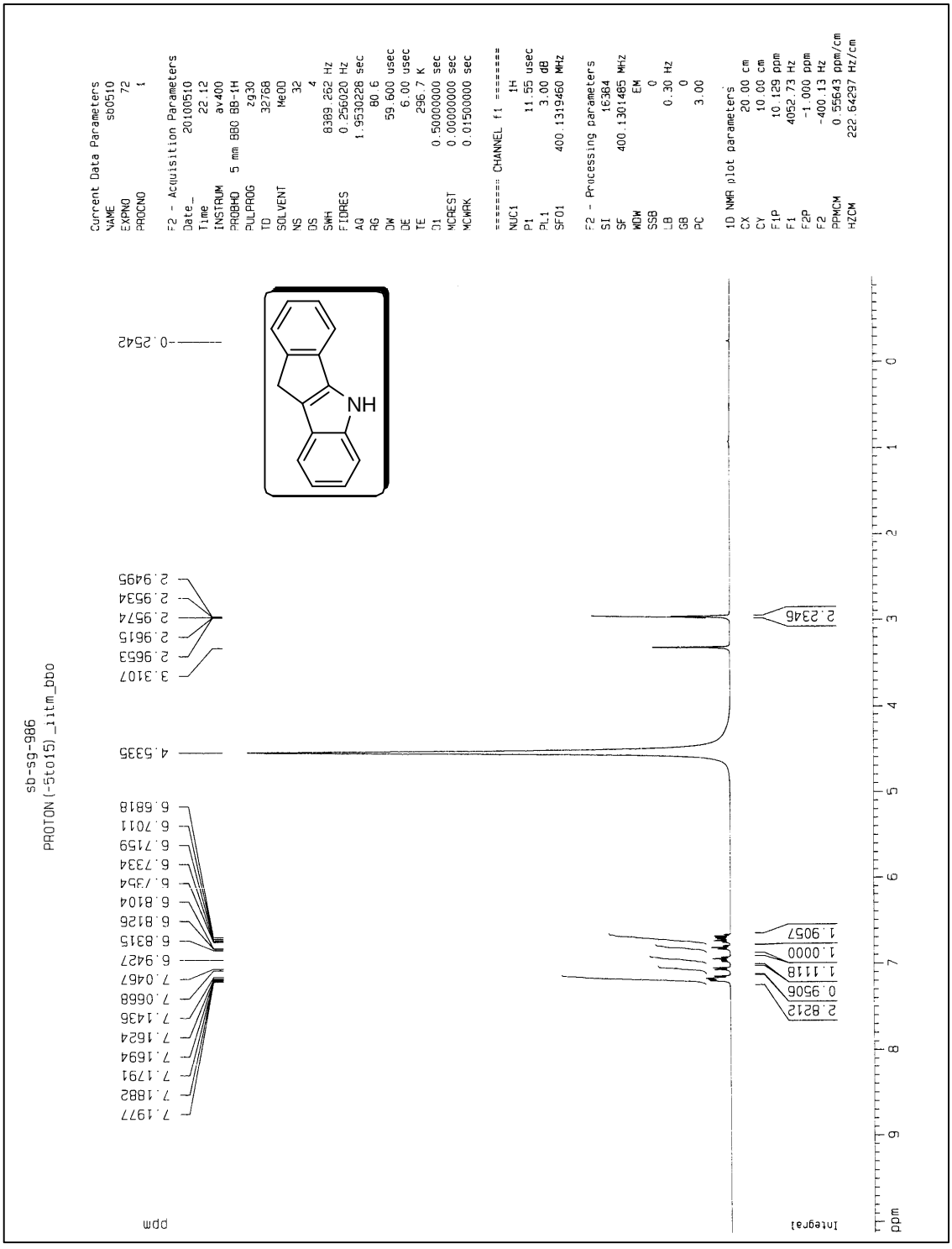
^{13}C NMR spectrum of indole derivative **3h**



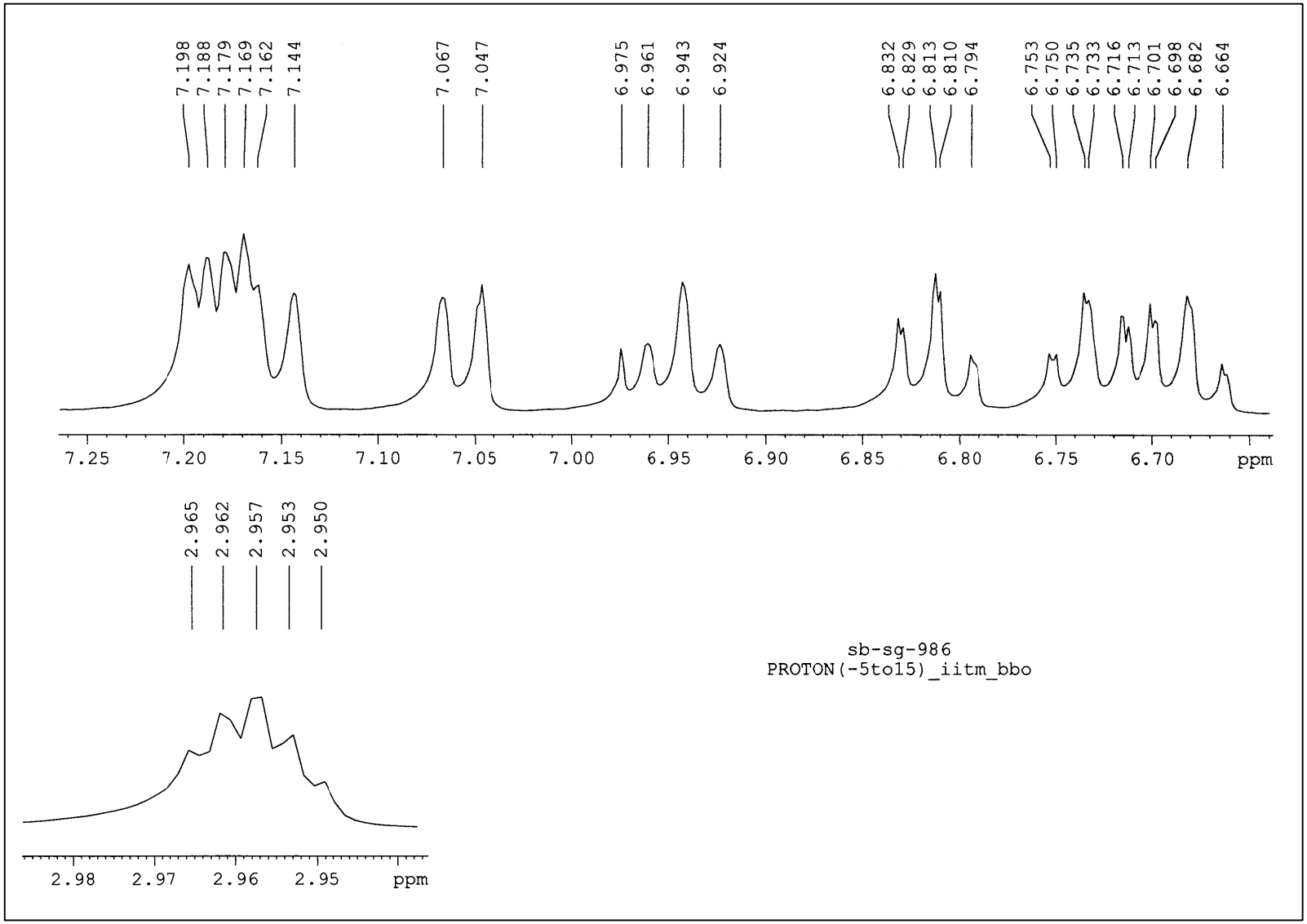
^{13}C DEPT NMR spectrum of indole derivative **3h**



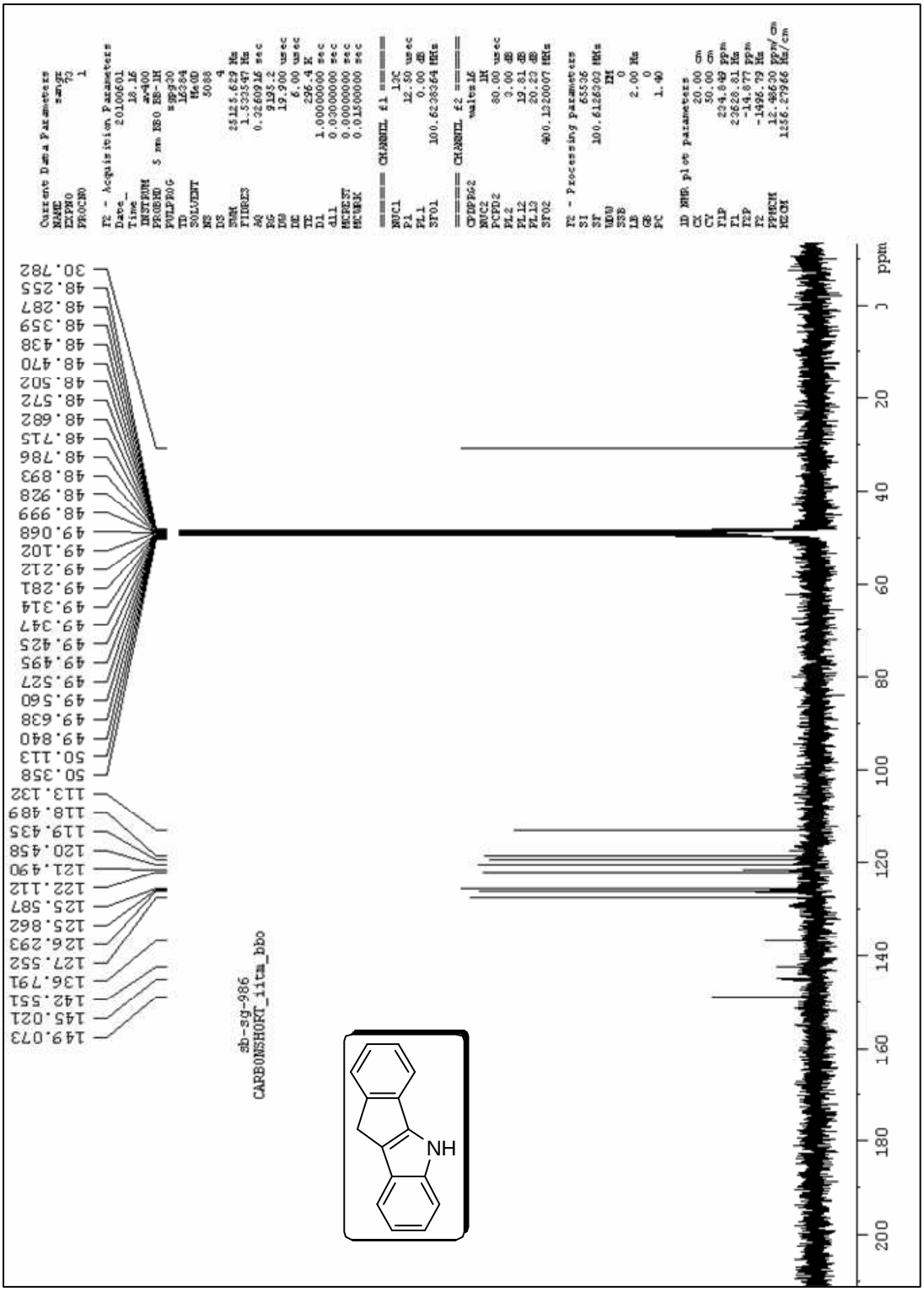
$^{1}H^{1}H$ COSY NMR spectrum of indole derivative **3h**



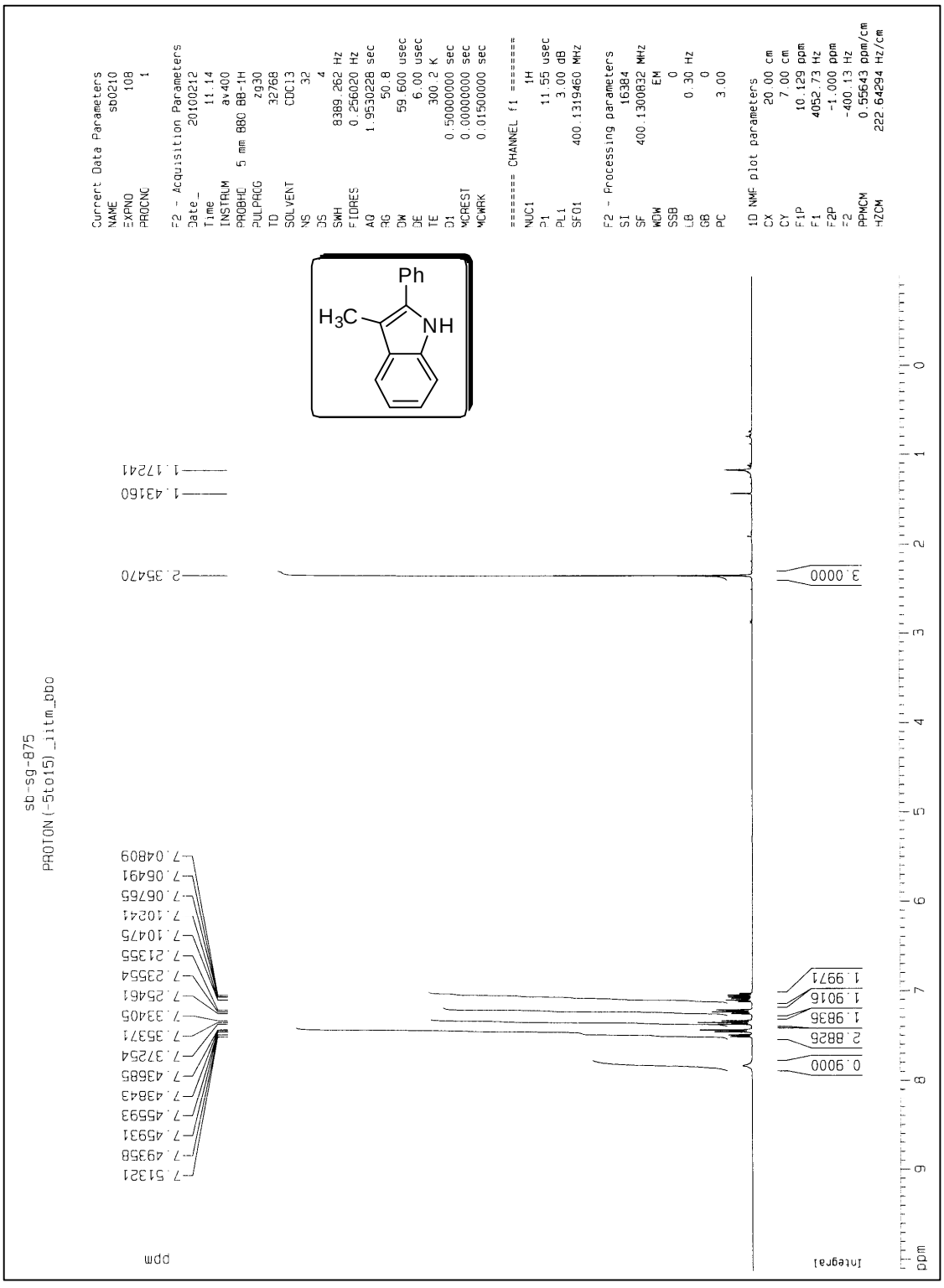
^{1}H NMR spectrum of indole derivative **3i**



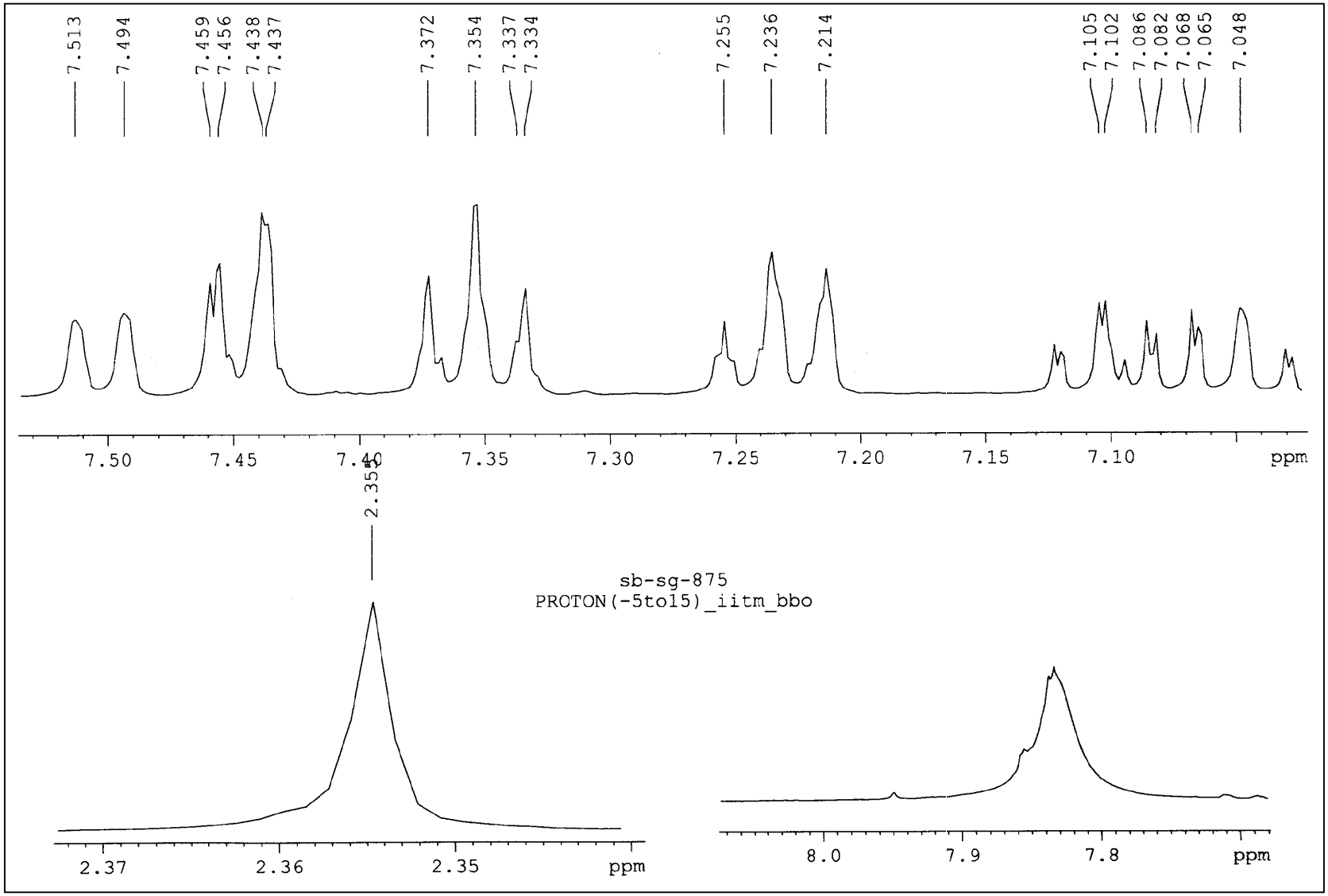
Expanded ^{1}H NMR spectrum of indole derivative **3i**



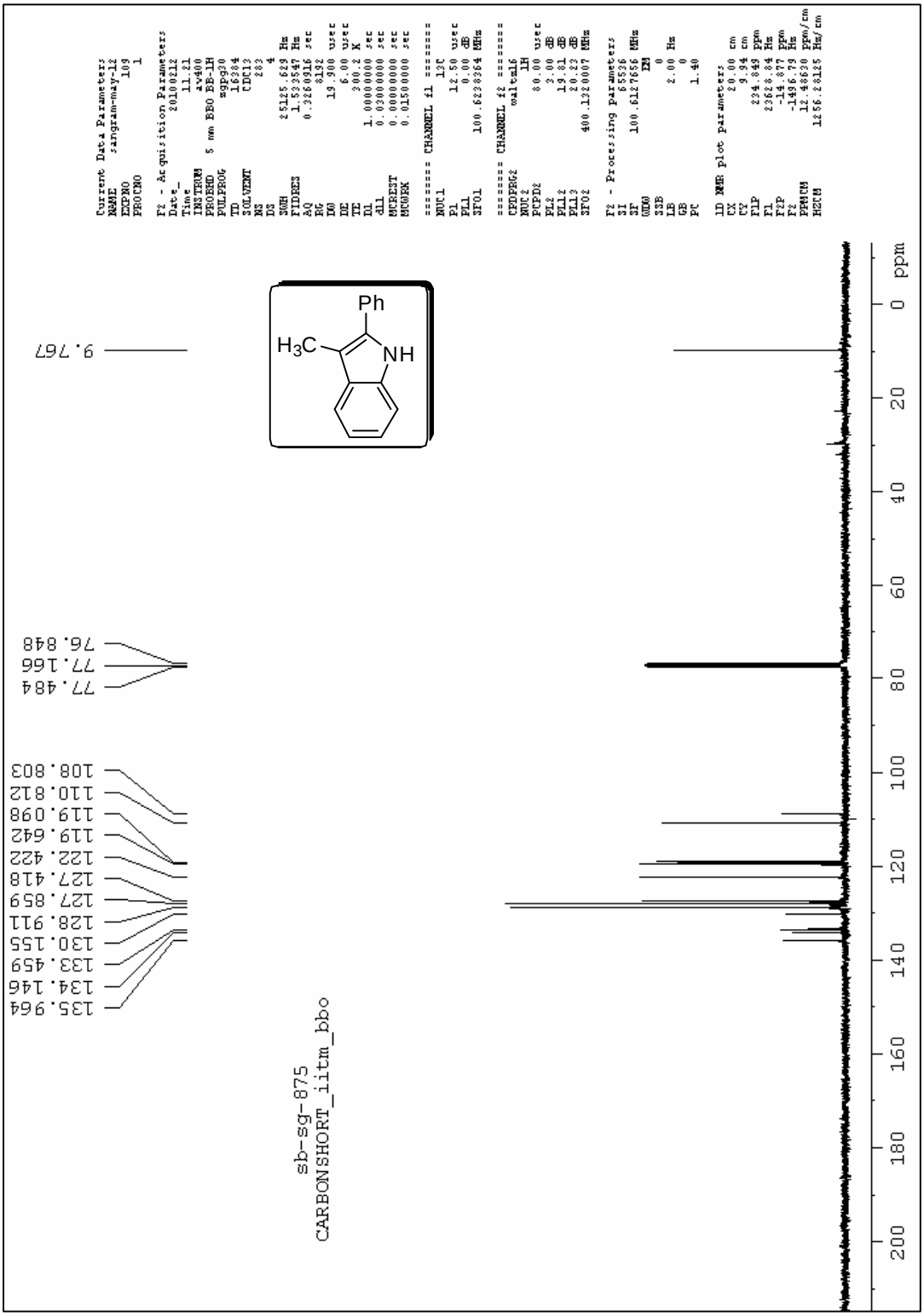
^{13}C NMR spectrum of indole derivative **3i**



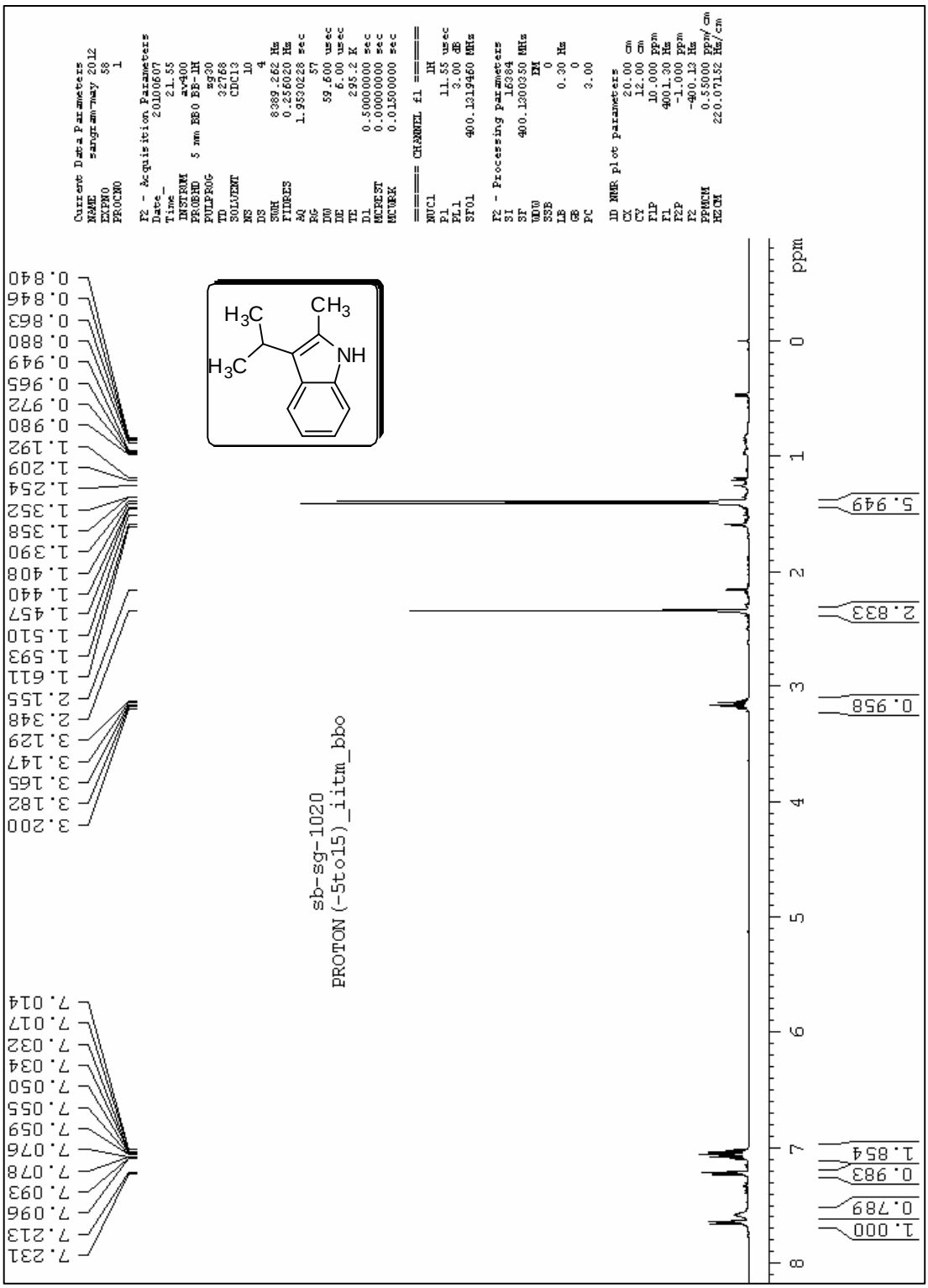
^{1}H NMR spectrum of indole derivative **3j**



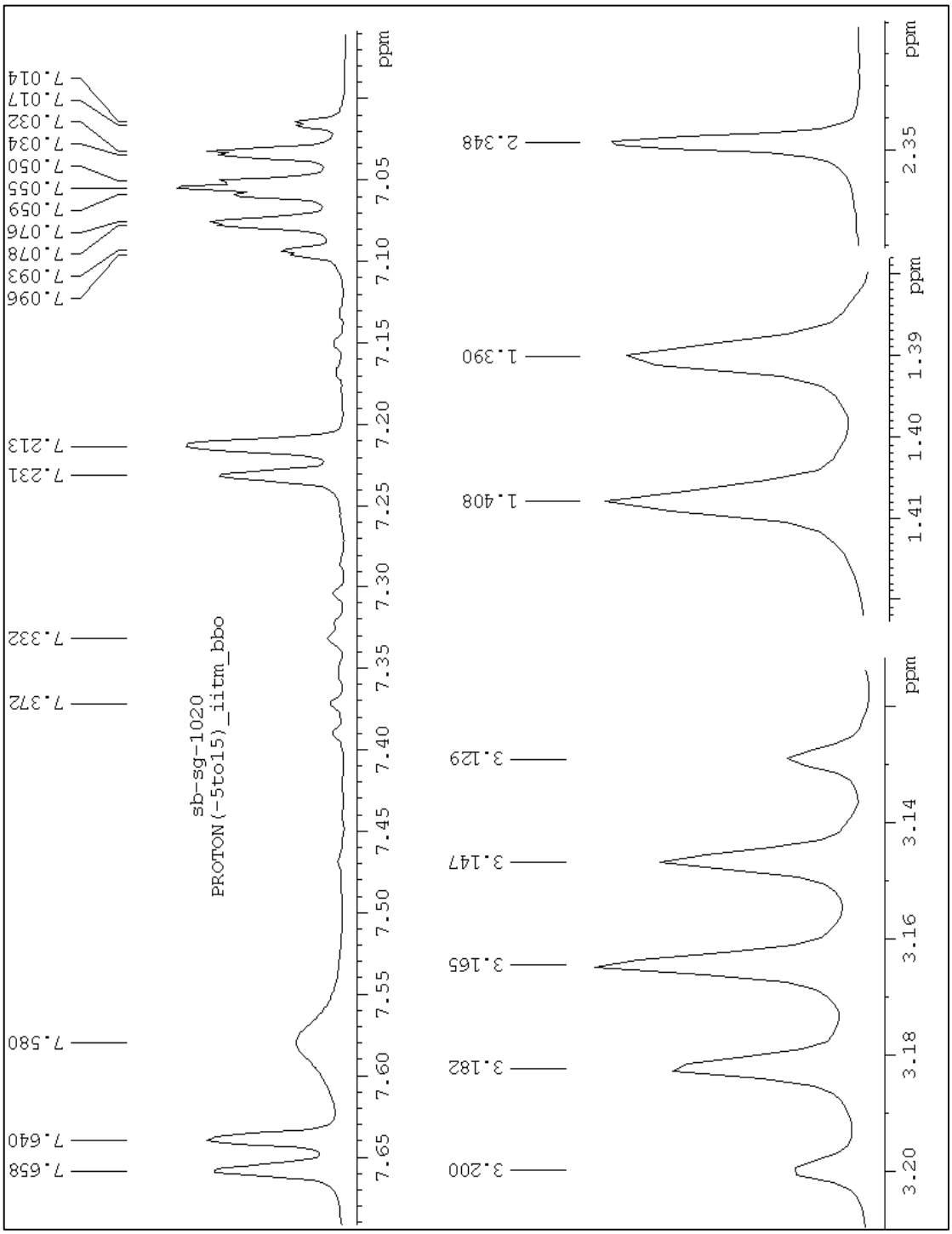
Expanded ^{1}H NMR spectrum of indole derivative **3j**



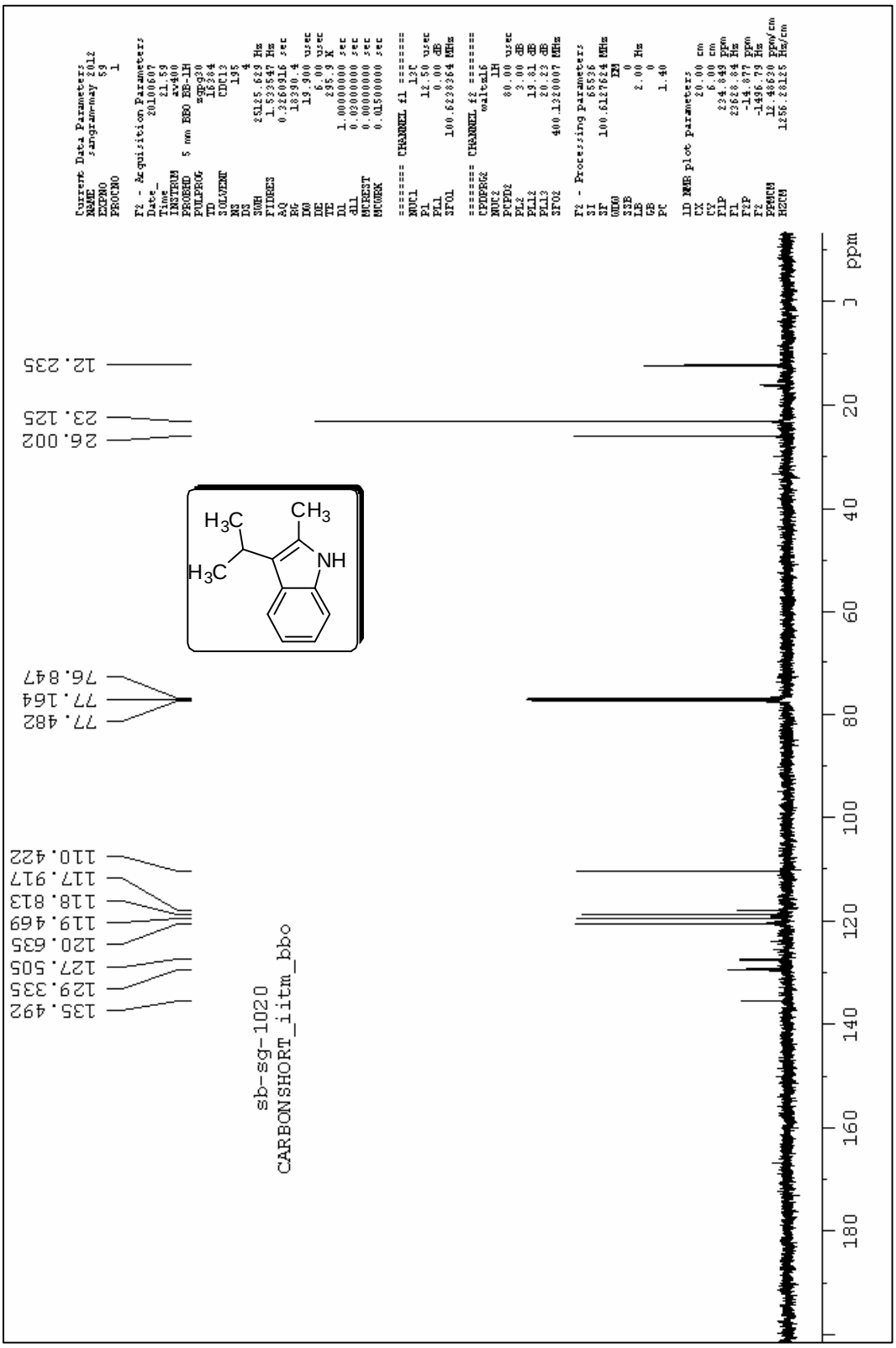
^{13}C NMR spectrum of indole derivative **3j**



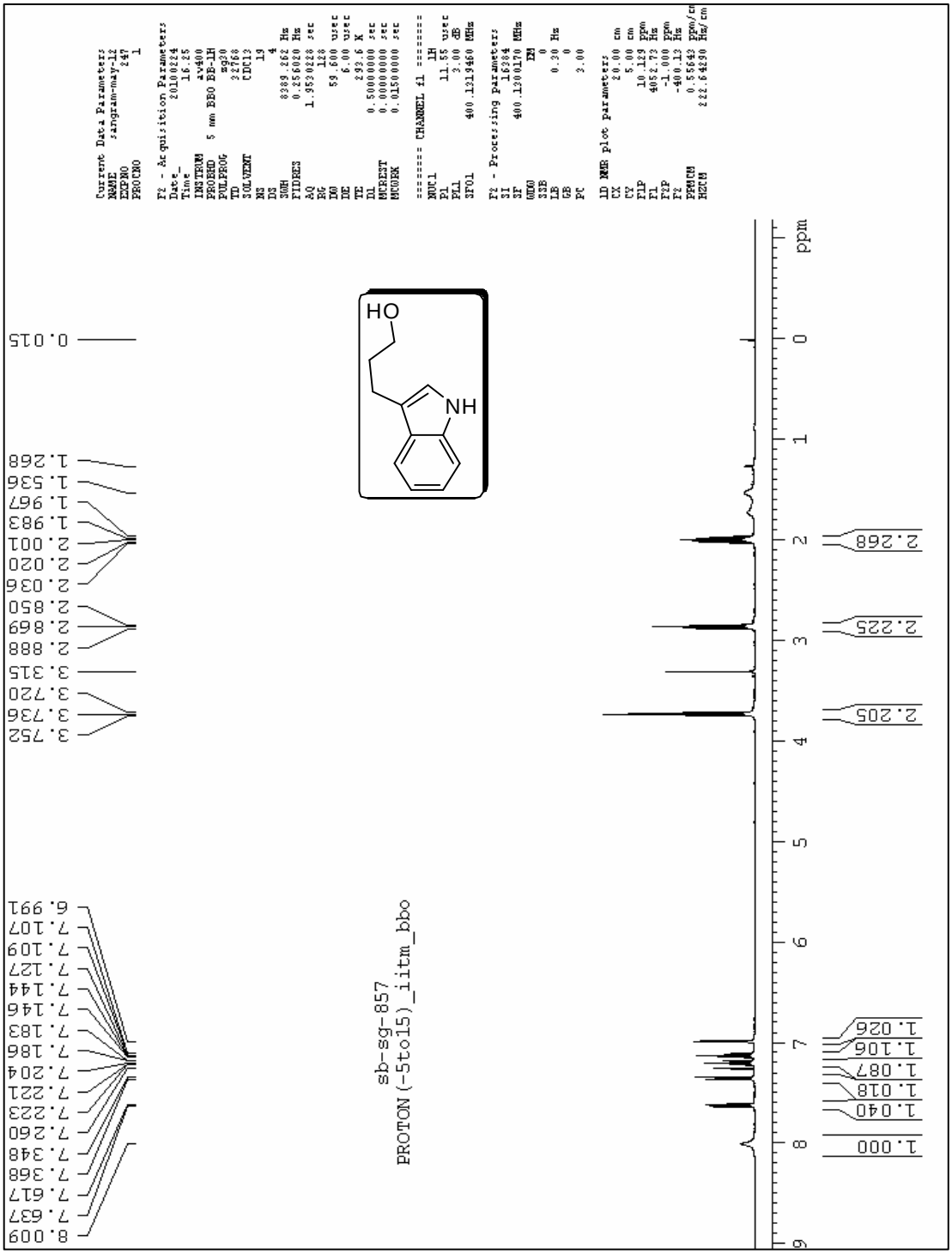
^{1}H NMR spectrum of indole derivative **3k**



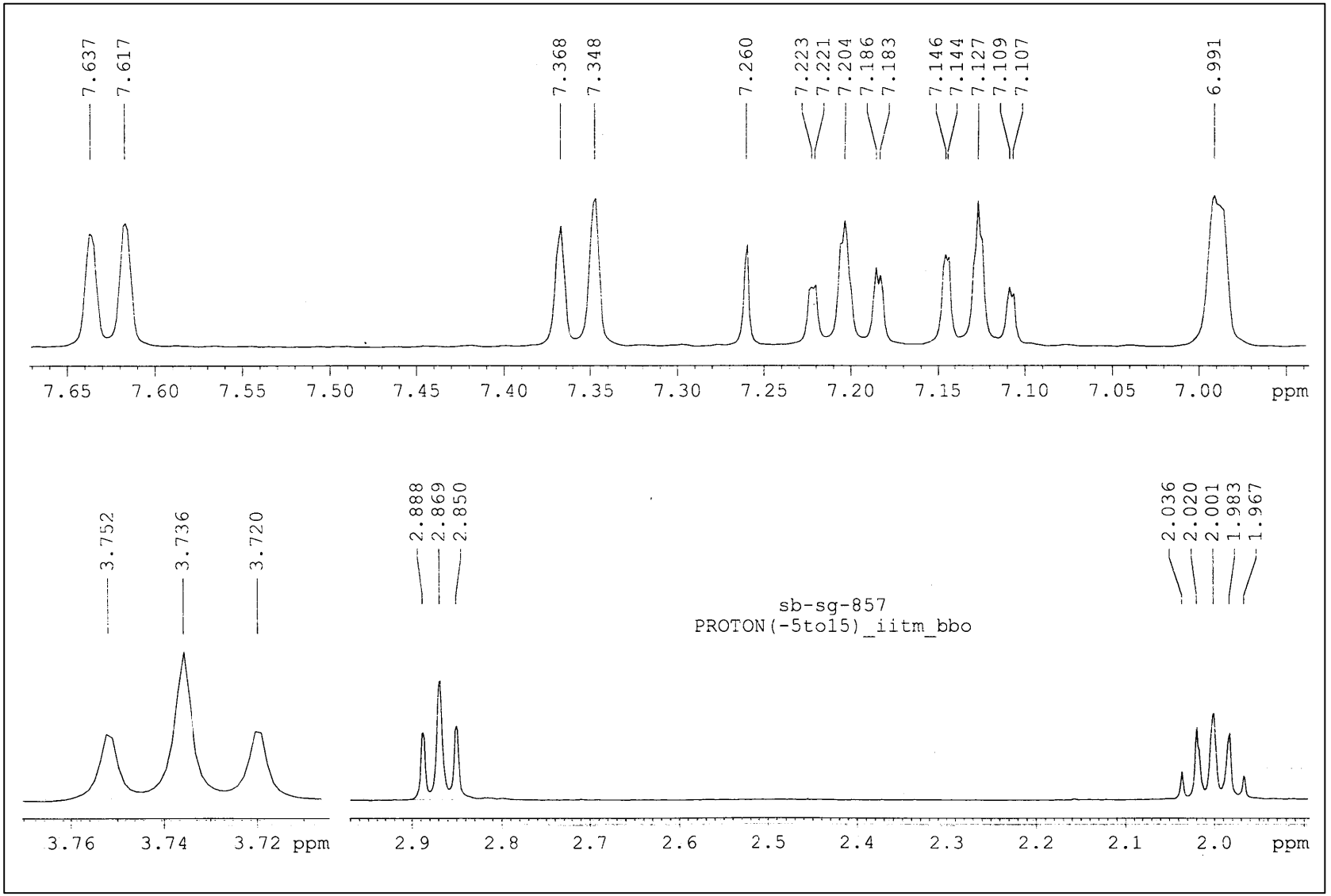
Expanded ^{1}H NMR spectrum of indole derivative **3k**



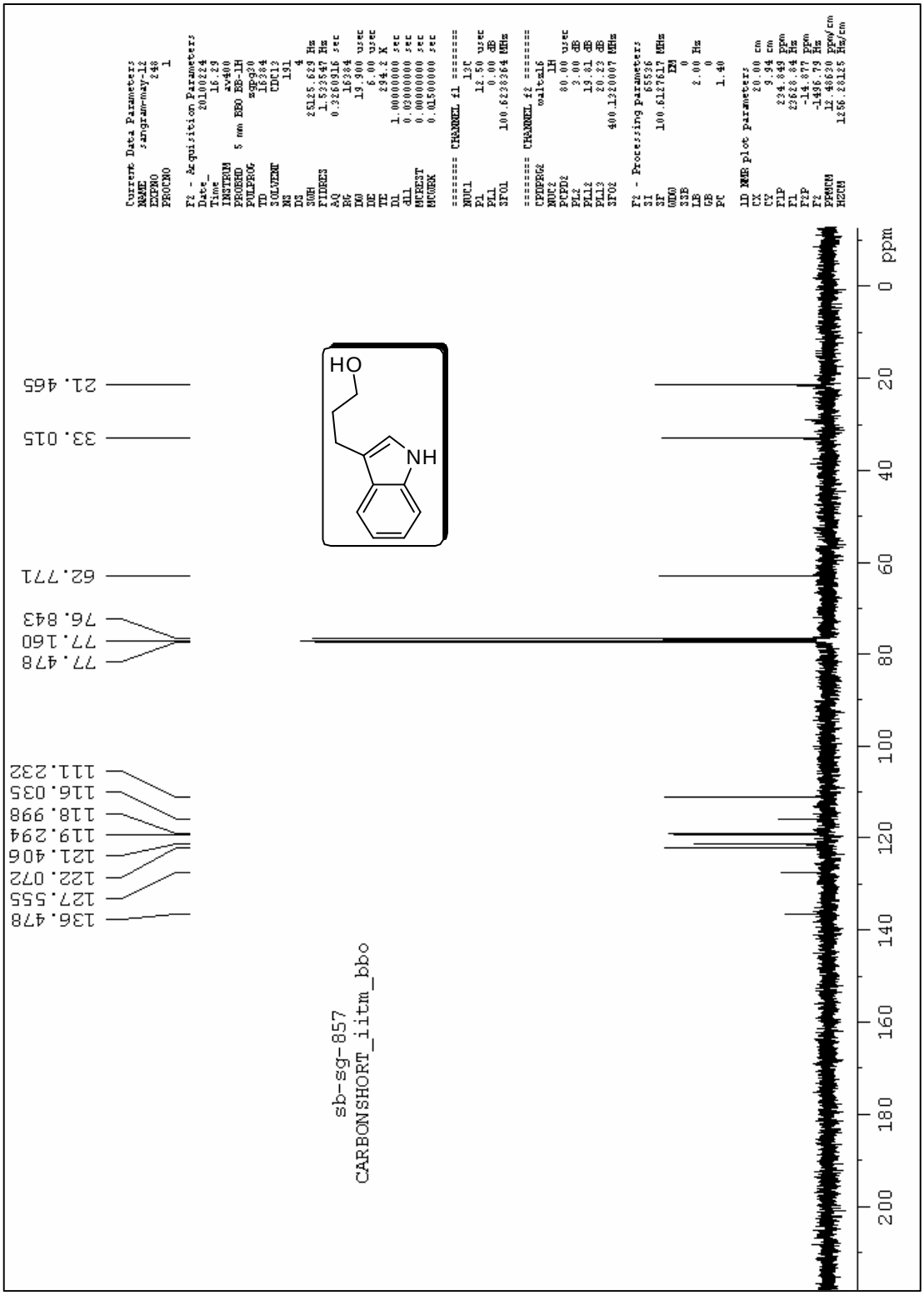
^{13}C NMR spectrum of indole derivative **3k**



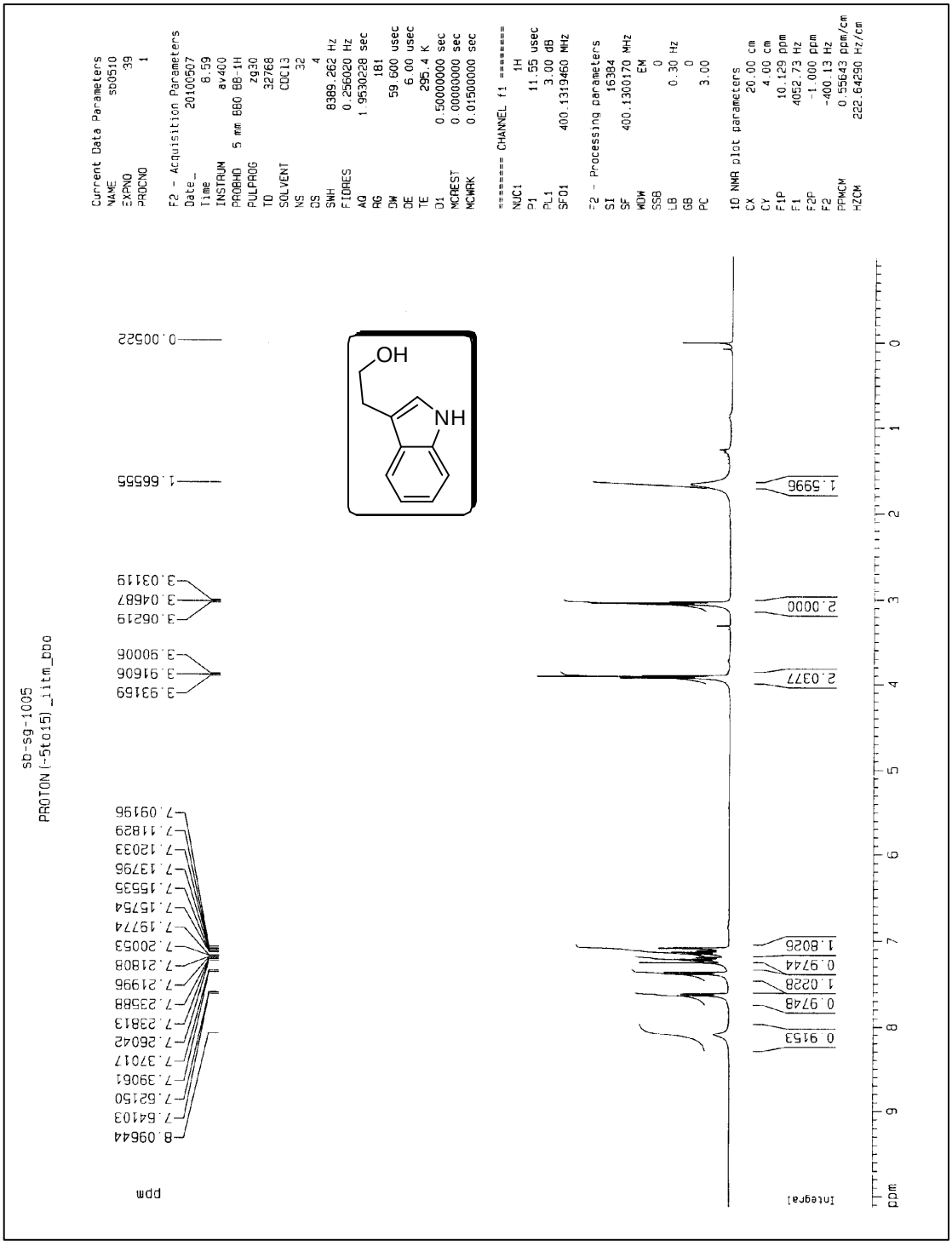
^{1}H NMR spectrum of indole derivative **3l**



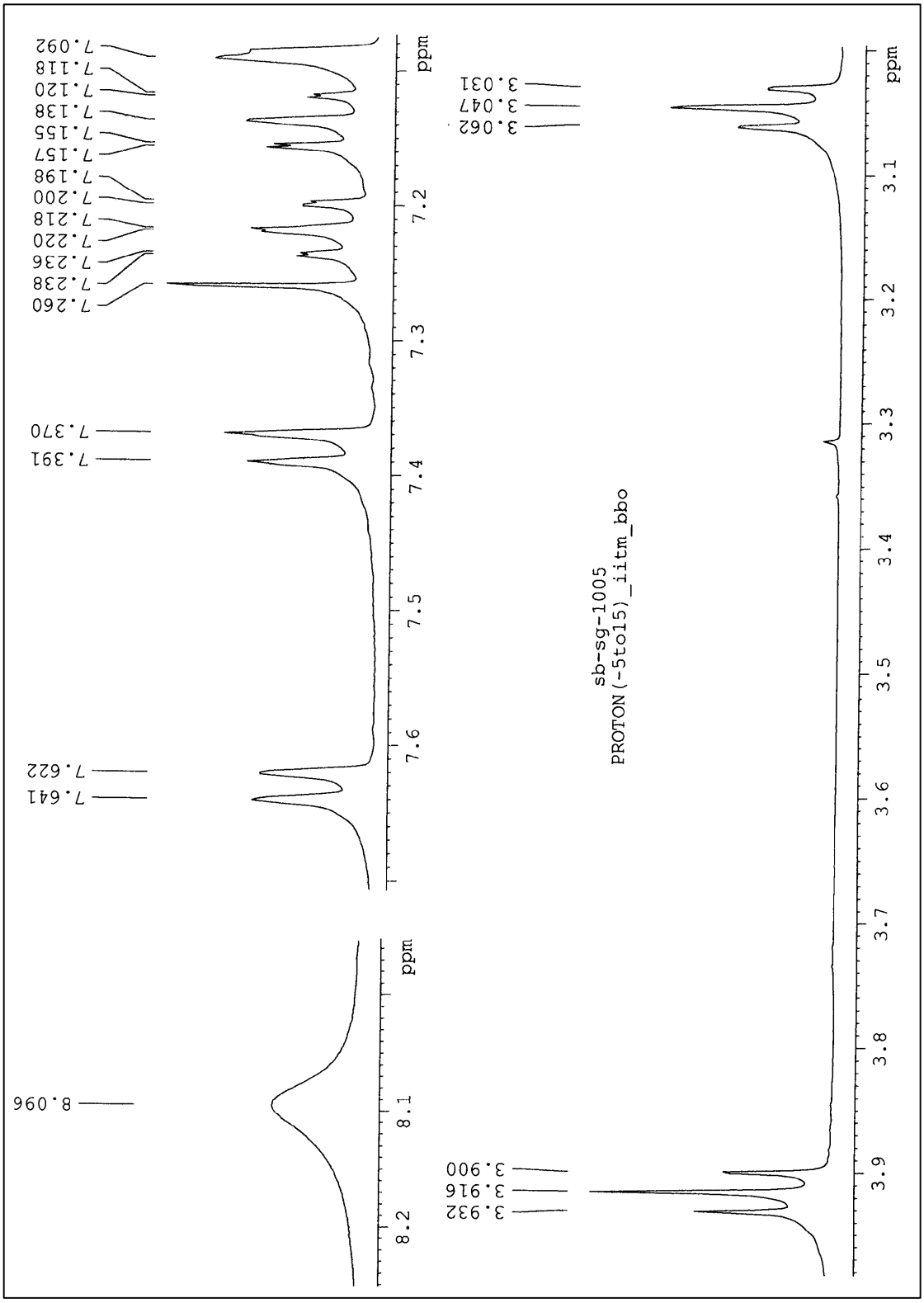
Expanded ^{1}H NMR spectrum of indole derivative **3l**



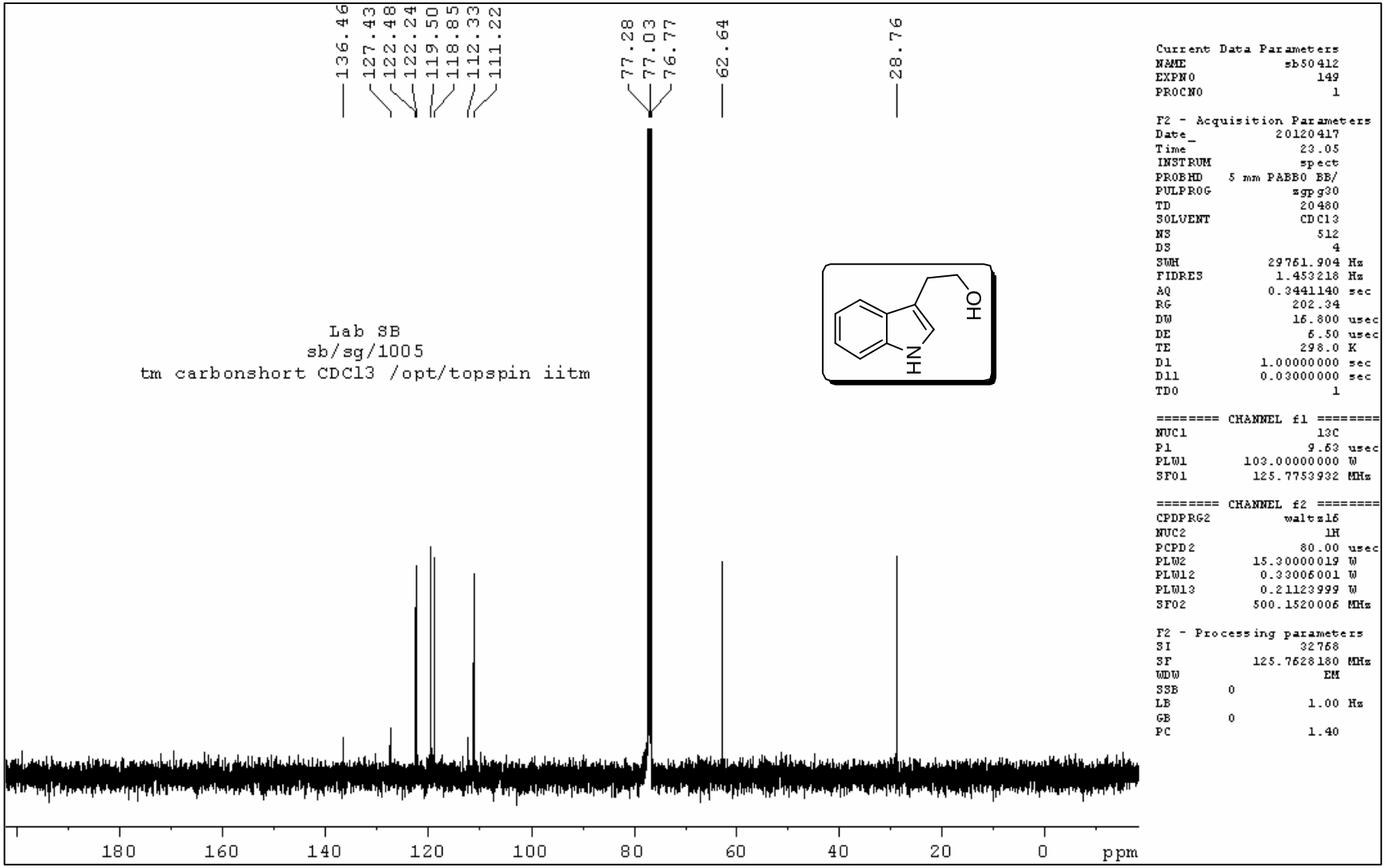
^{13}C NMR spectrum of indole derivative **3l**



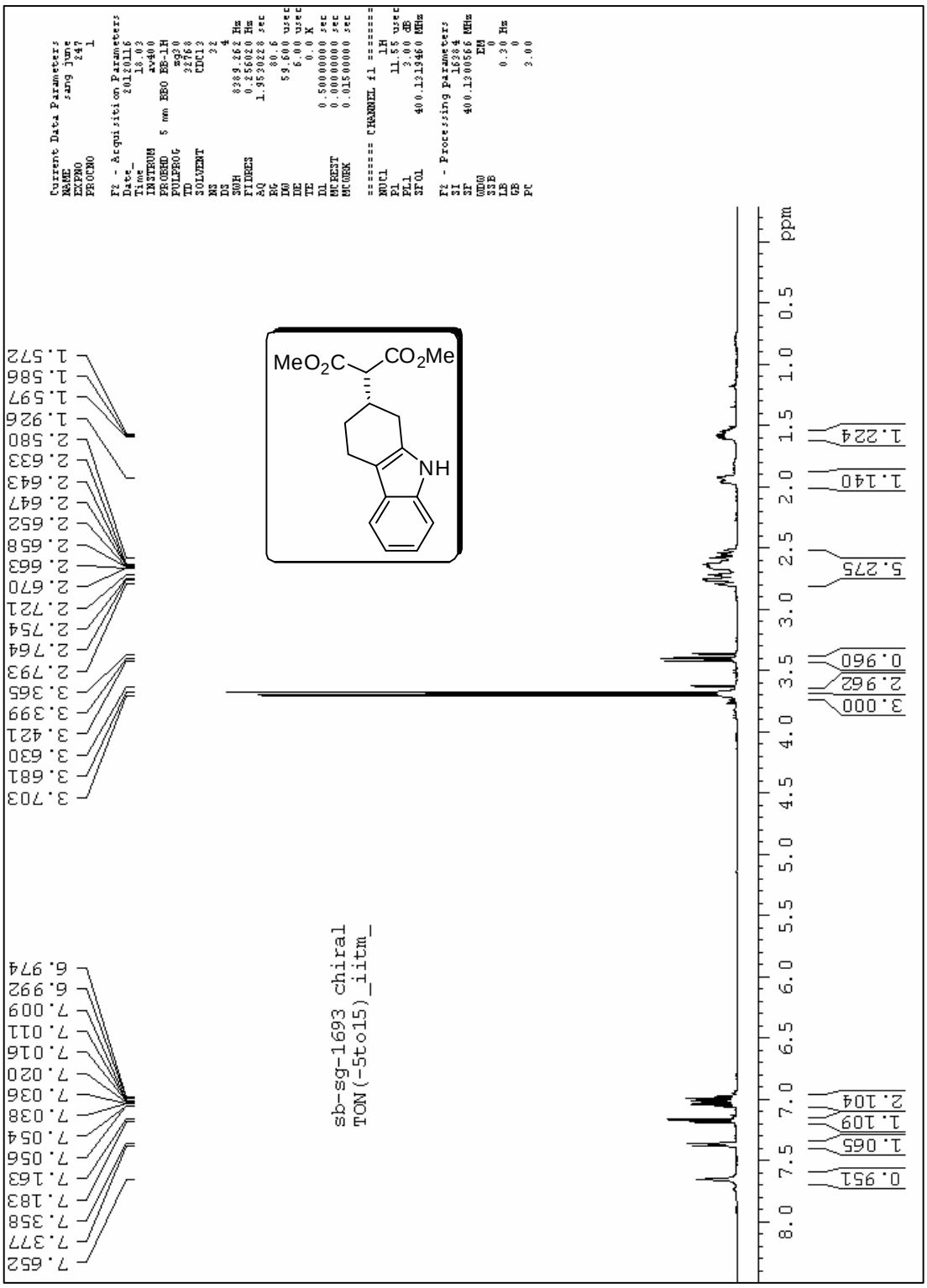
^{1}H NMR spectrum of indole derivative **3m**



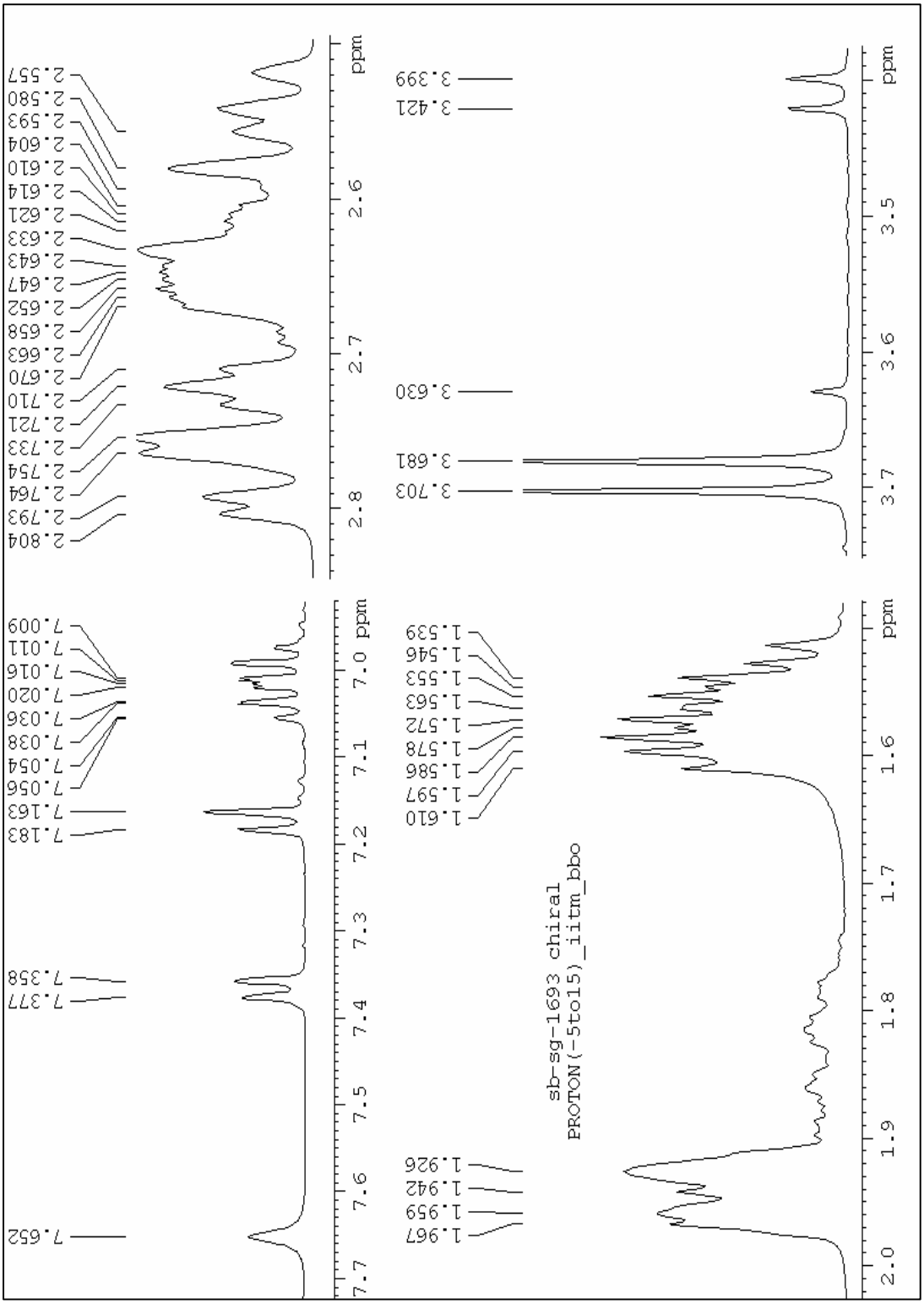
^{1}H NMR expansion spectrum of indole derivative **3m**



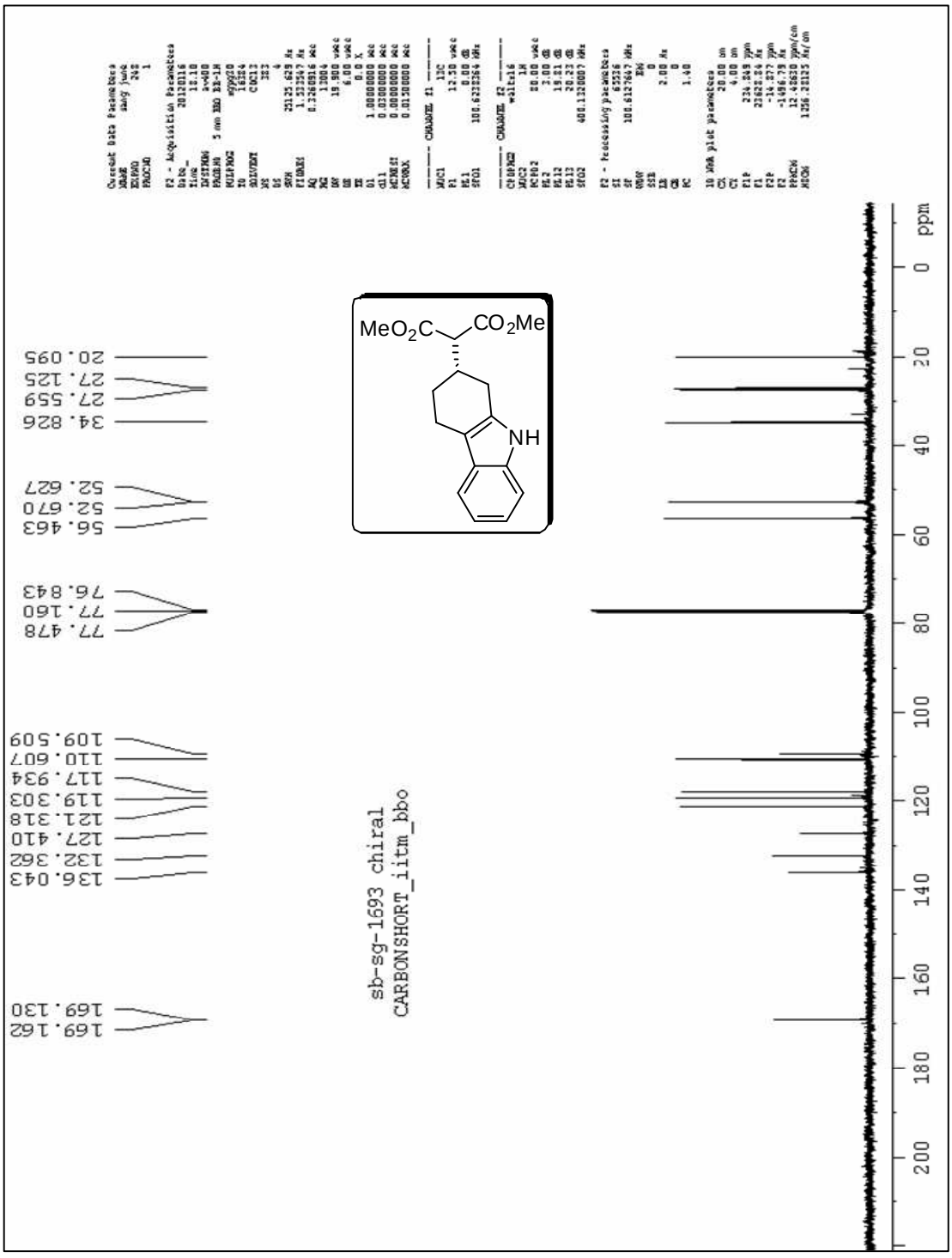
^{13}C NMR spectrum of indole derivative **3m**



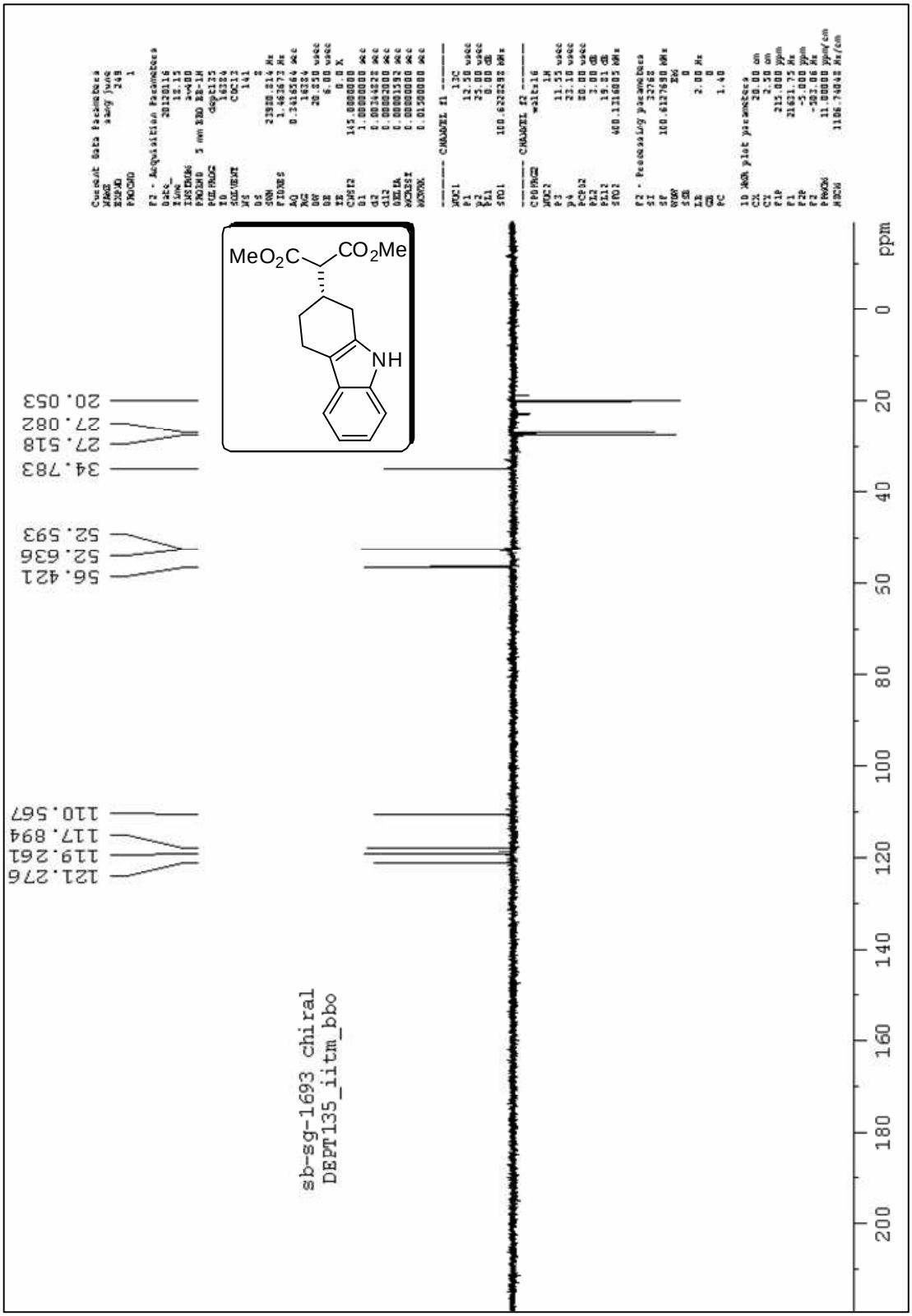
^{1}H NMR spectrum of indole derivative **3n**



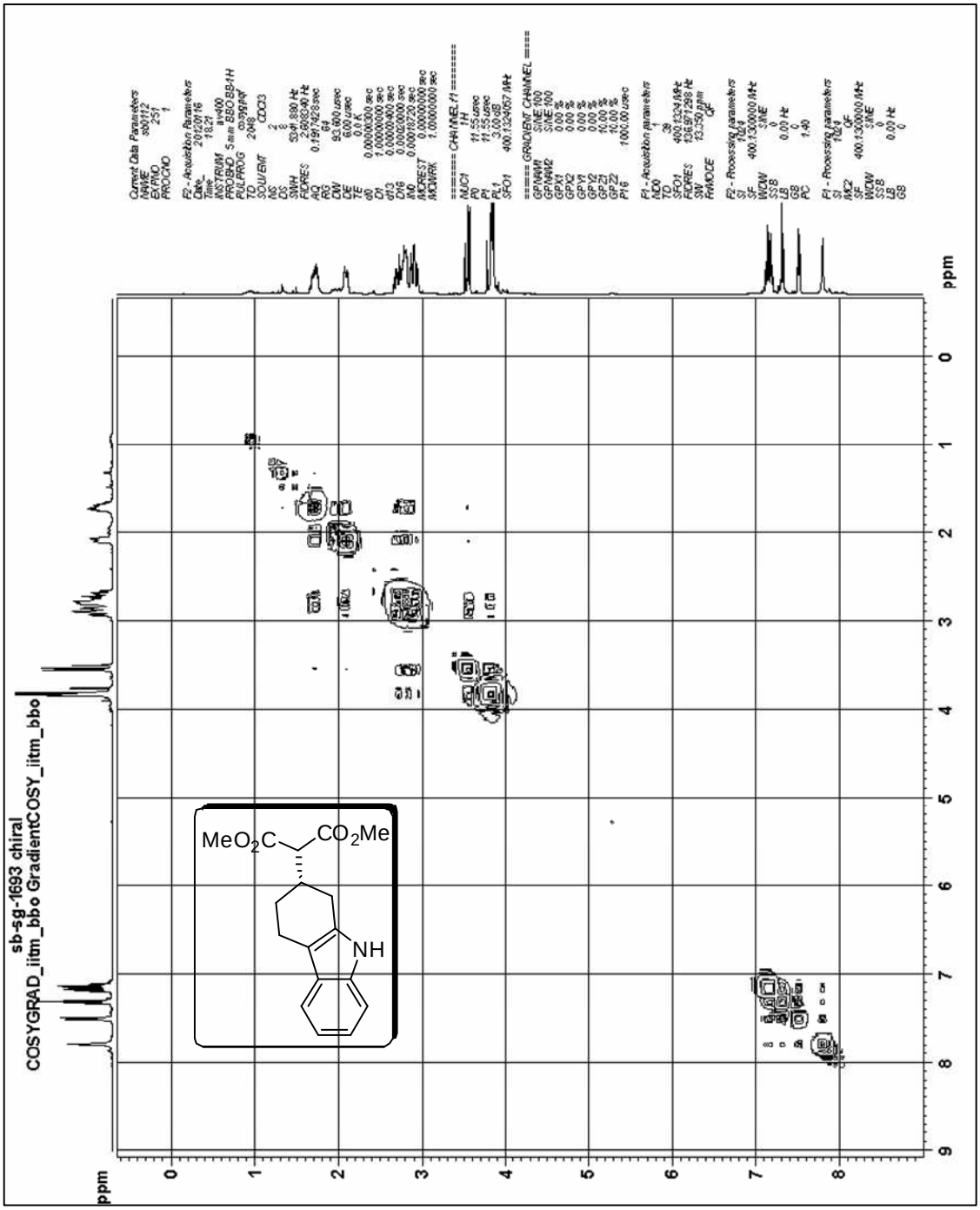
Expanded ^{1}H NMR spectrum of indole derivative **3n**



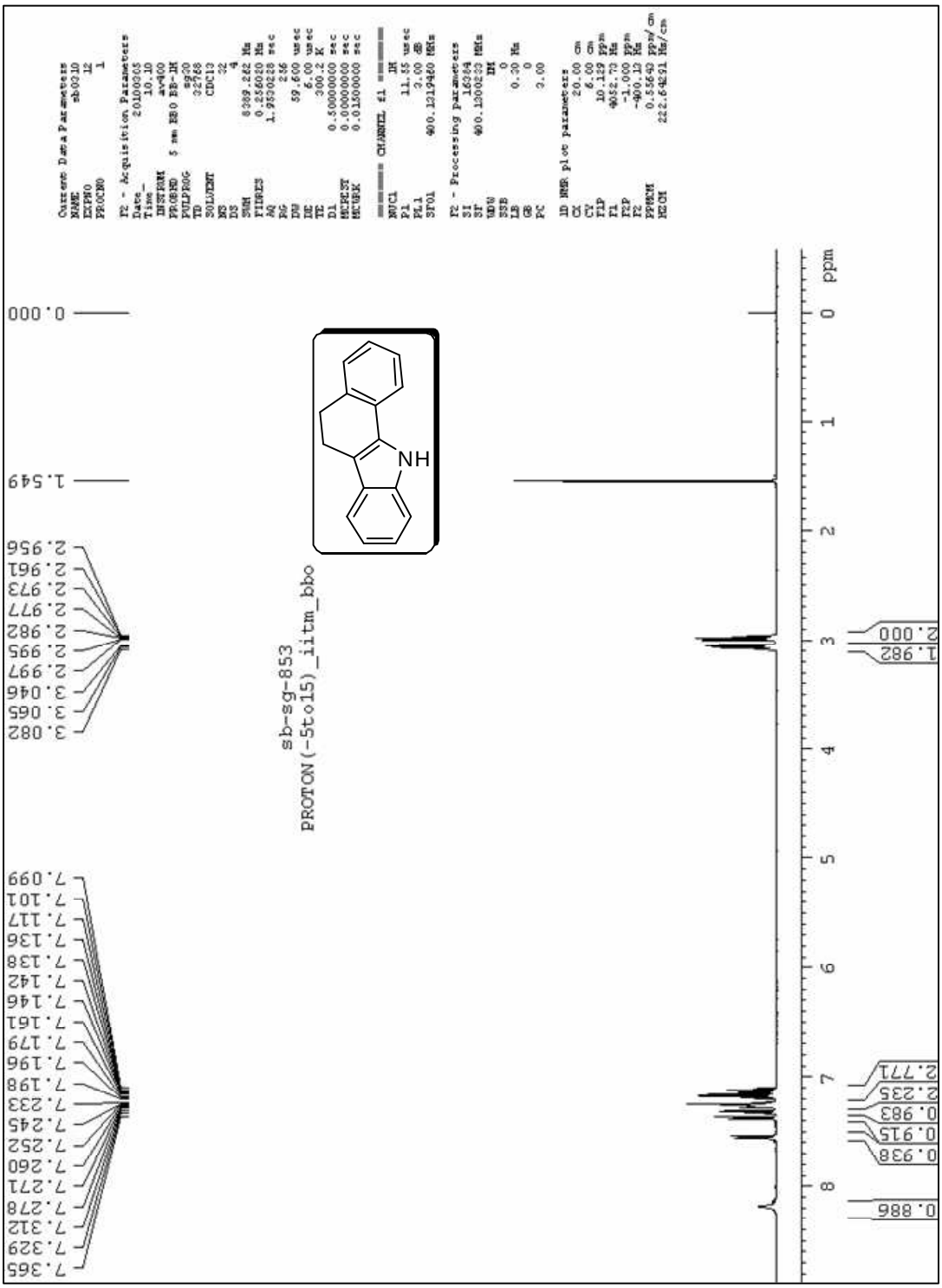
^{13}C NMR spectrum of indole derivative **3n**



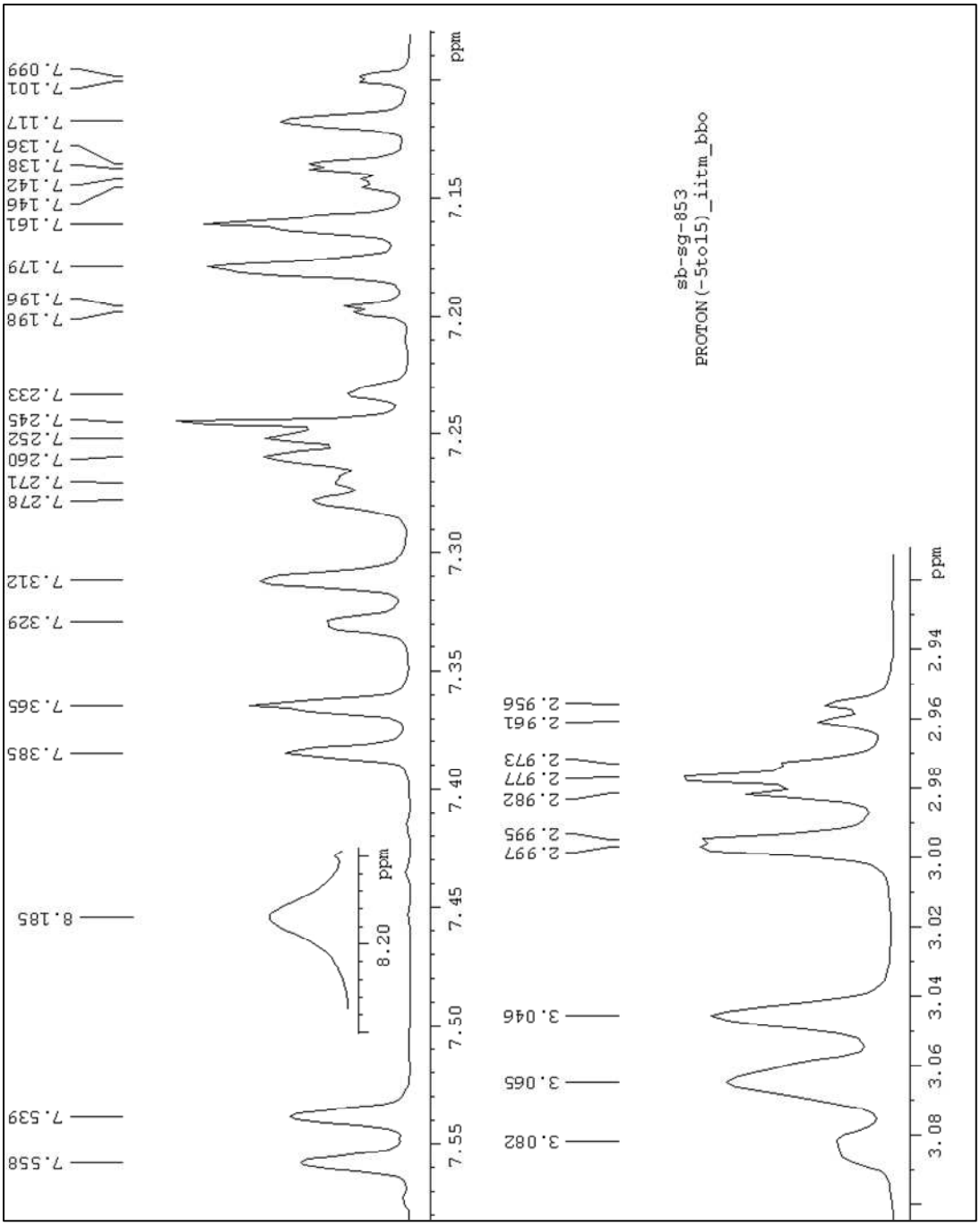
^{13}C DEPT NMR spectrum of indole derivative **3n**



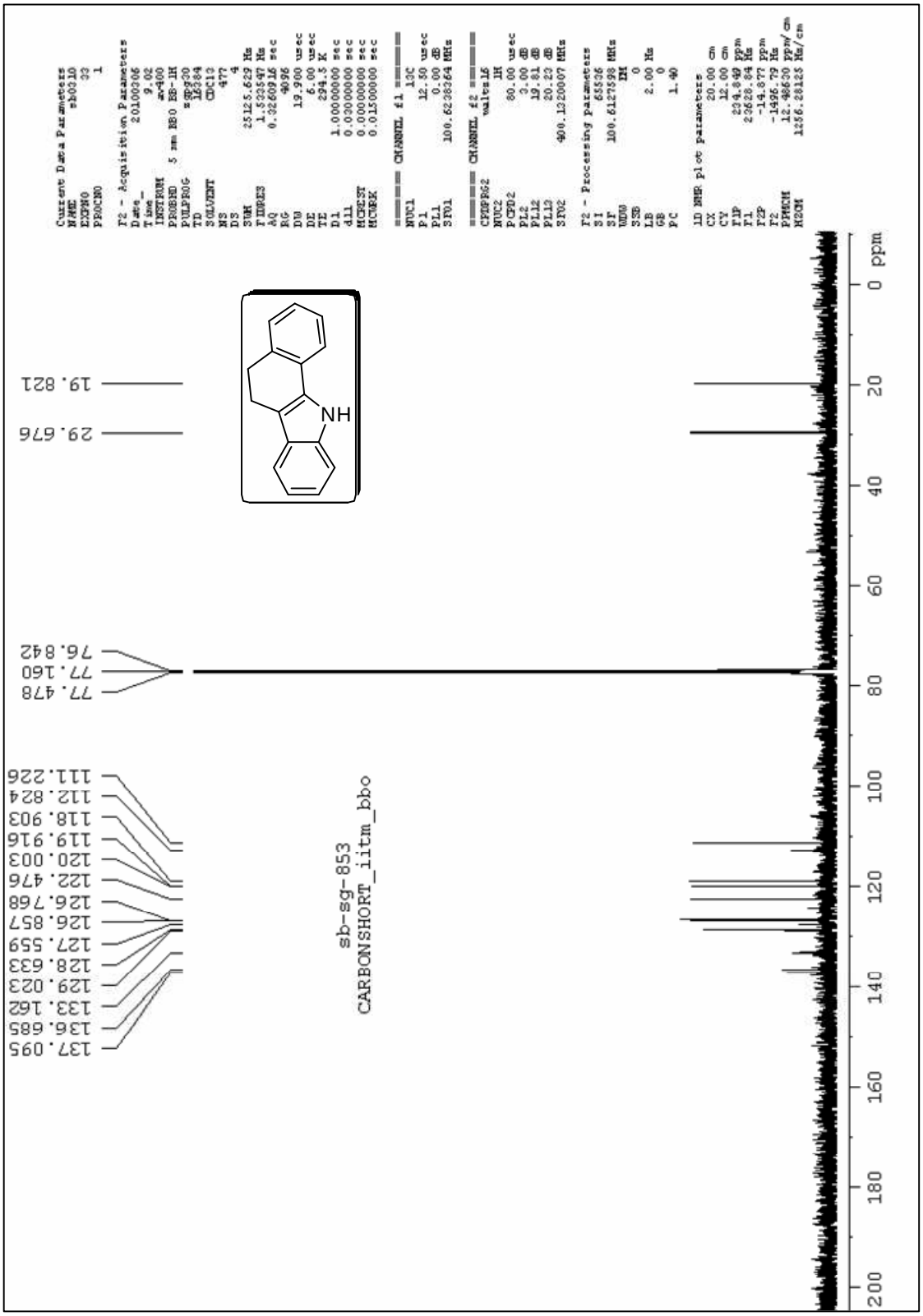
^{1}H ^{1}H COSY NMR spectrum of indole derivative **3n**



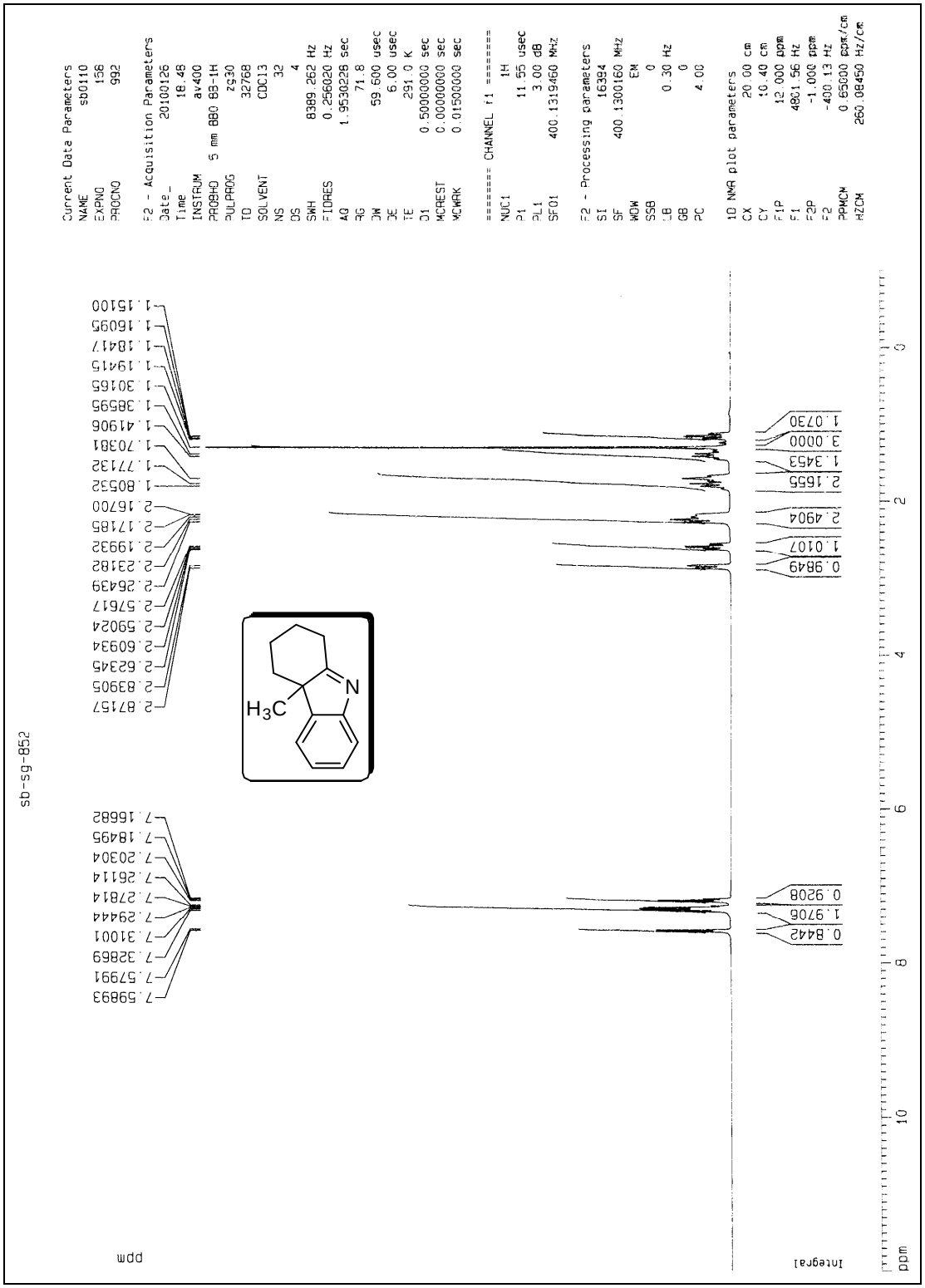
^{1}H NMR spectrum of indole derivative **3o**



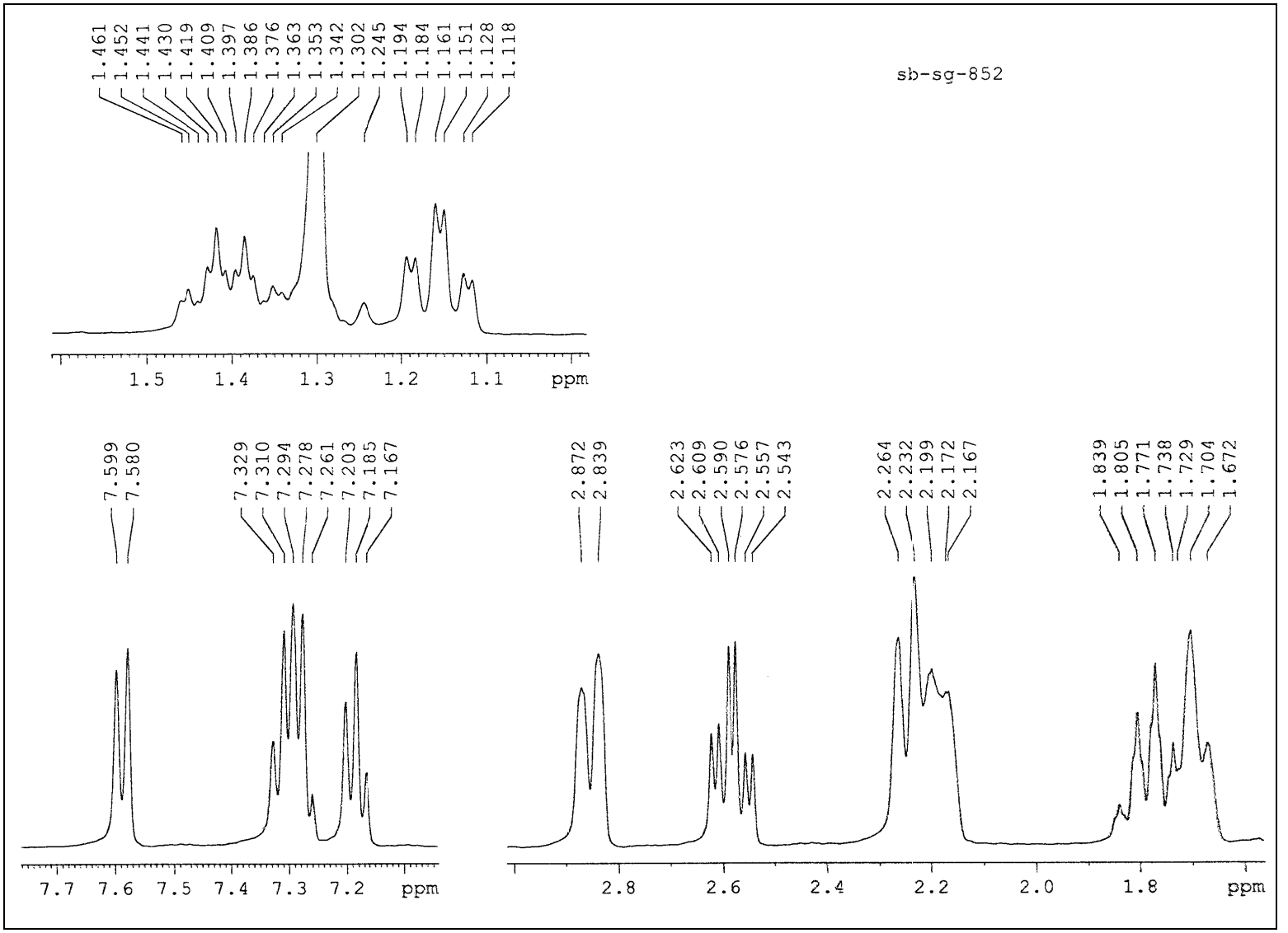
Expanded ^{1}H NMR spectrum of indole derivative **3o**



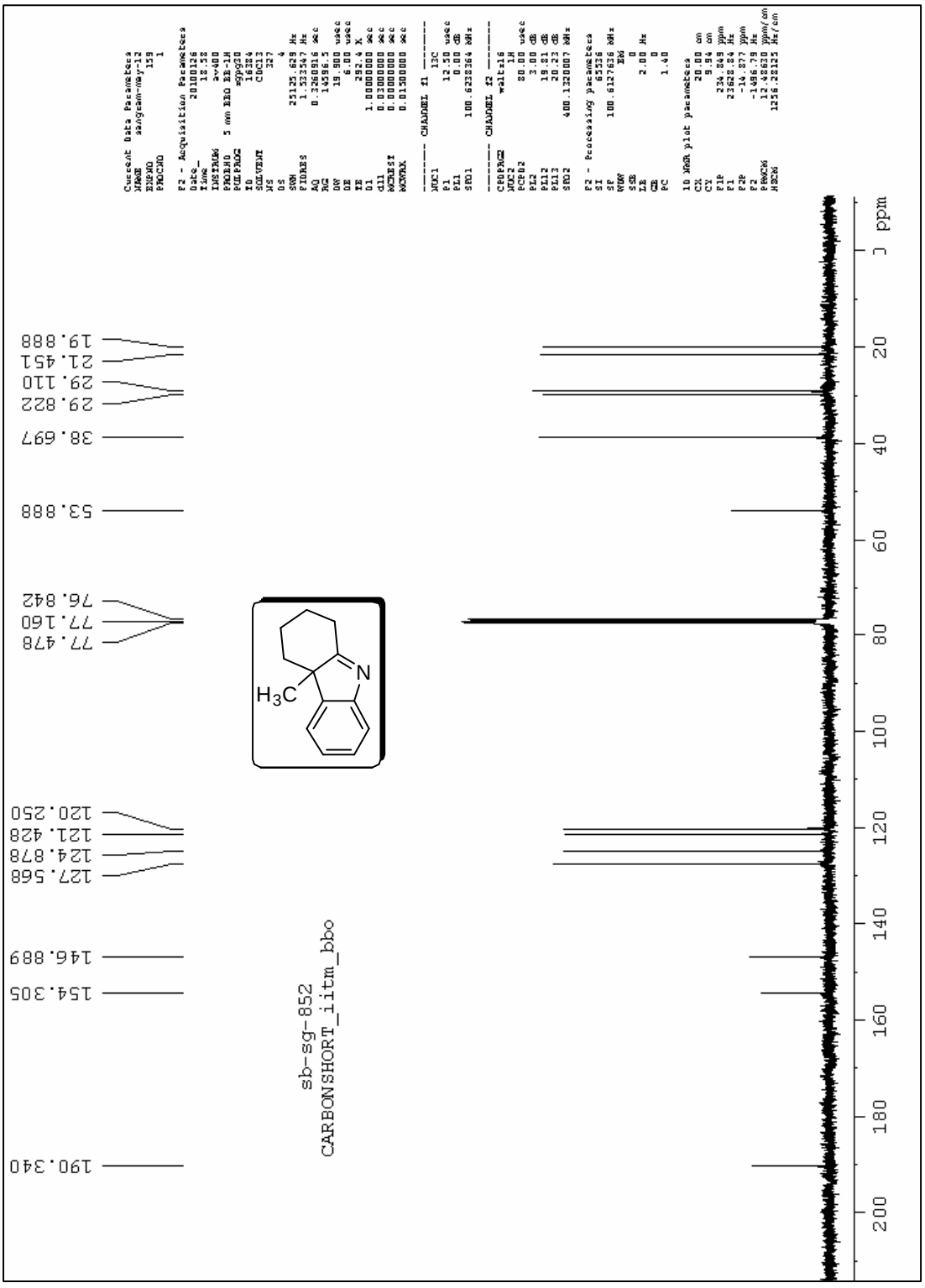
^{13}C NMR spectrum of indole derivative **3o**



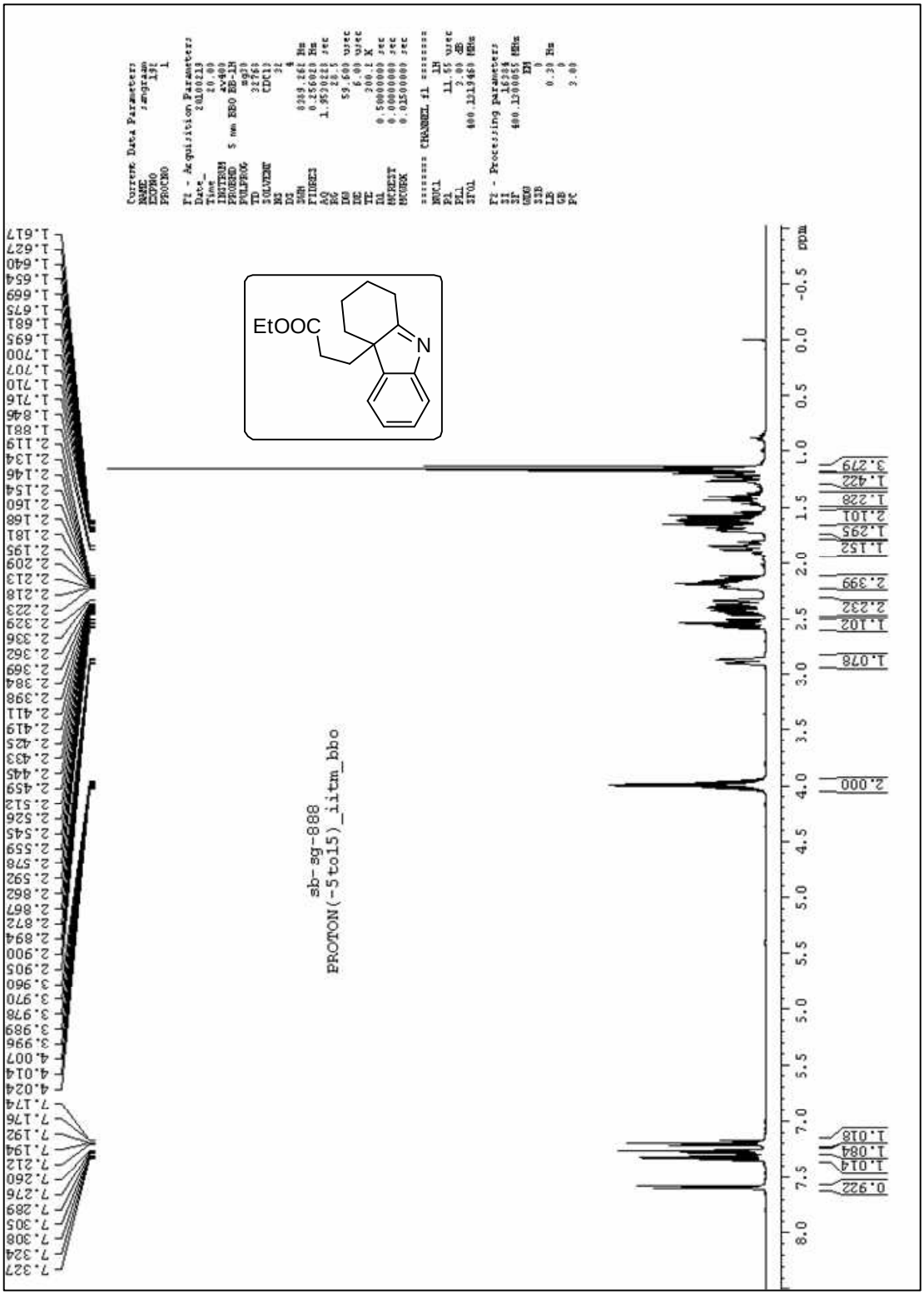
^{1}H NMR spectrum of indolenine derivative **5a**



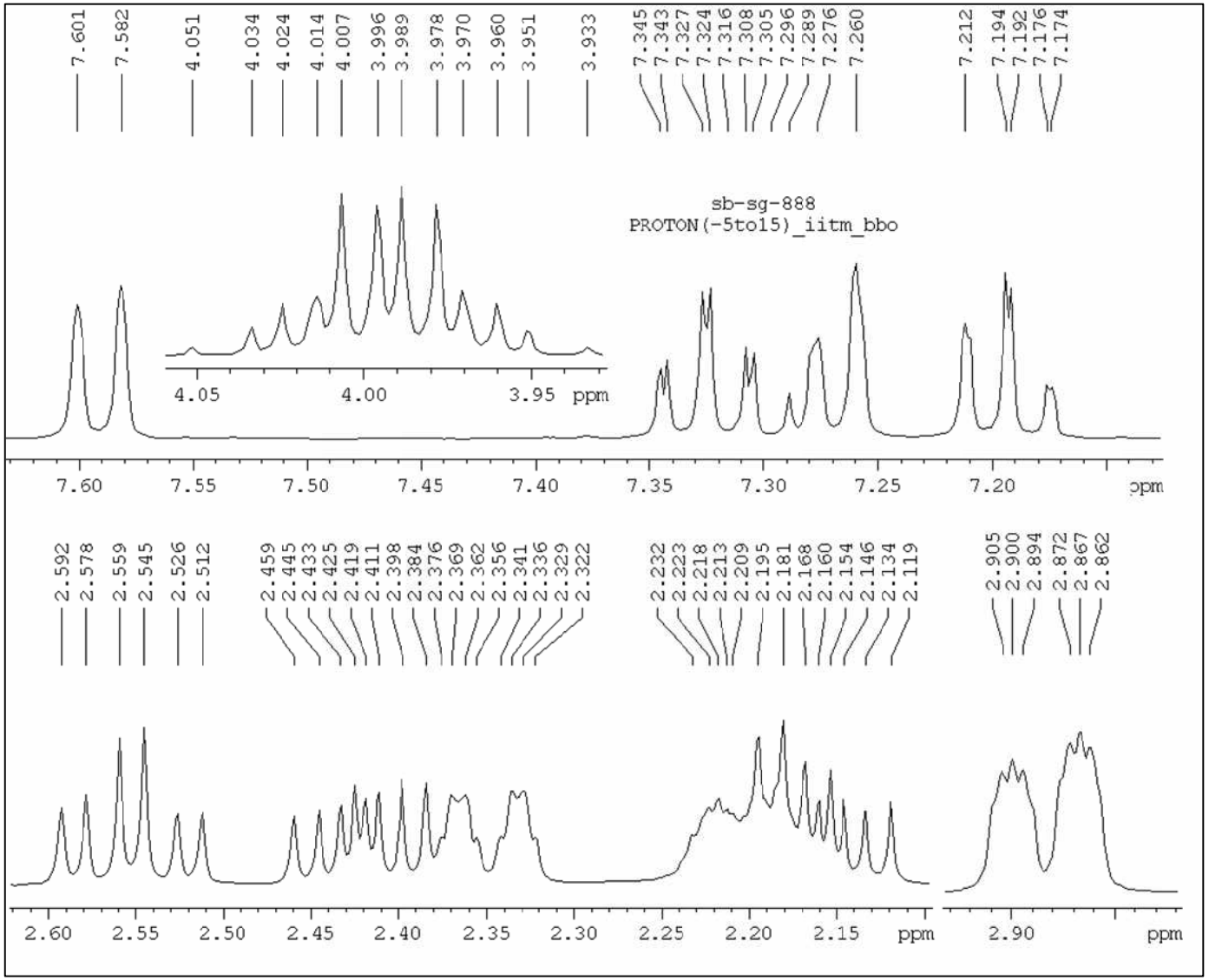
Expanded ^{1}H NMR spectrum of indolenine derivative **5a**



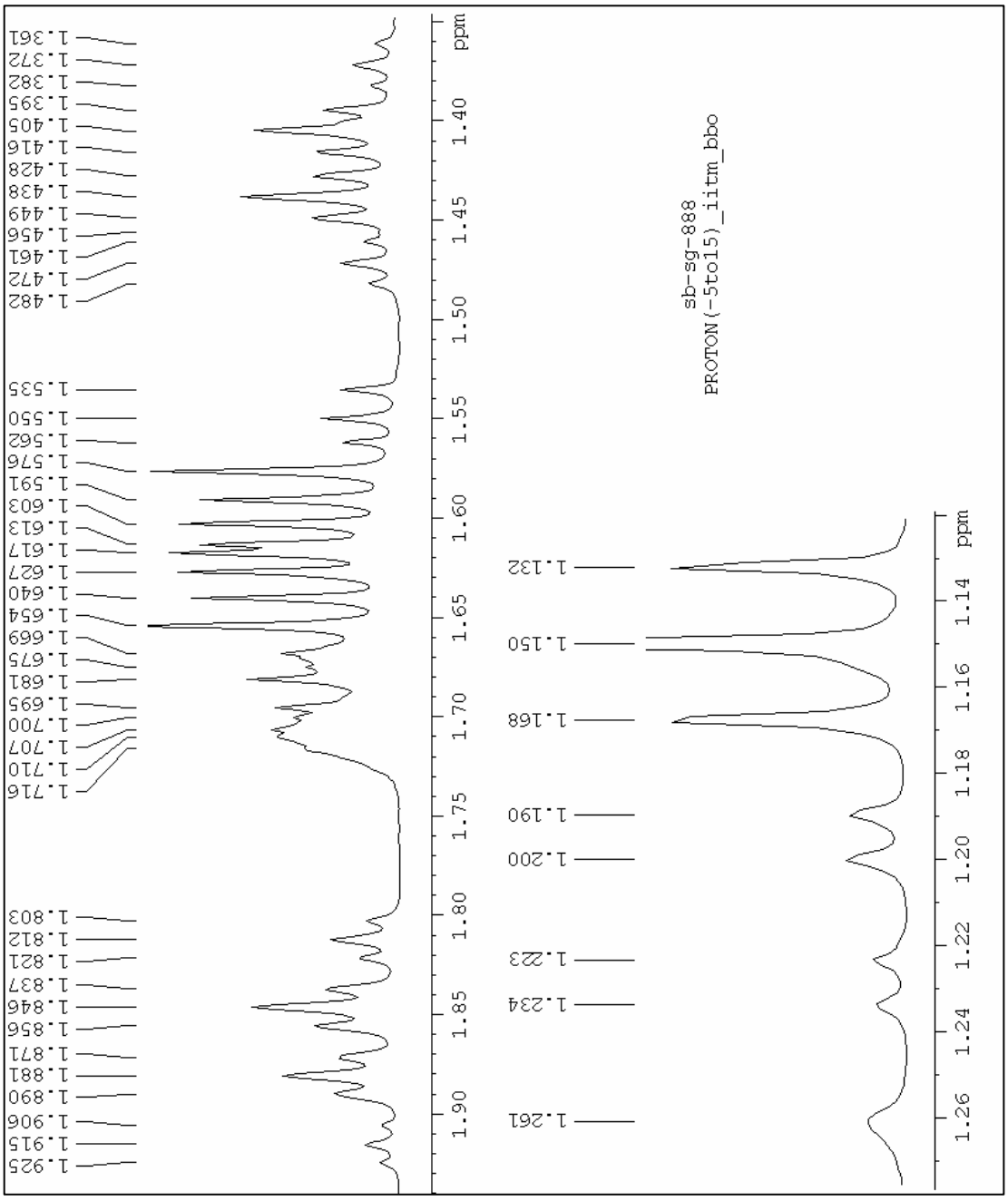
^{13}C NMR spectrum of indolenine derivative **5a**



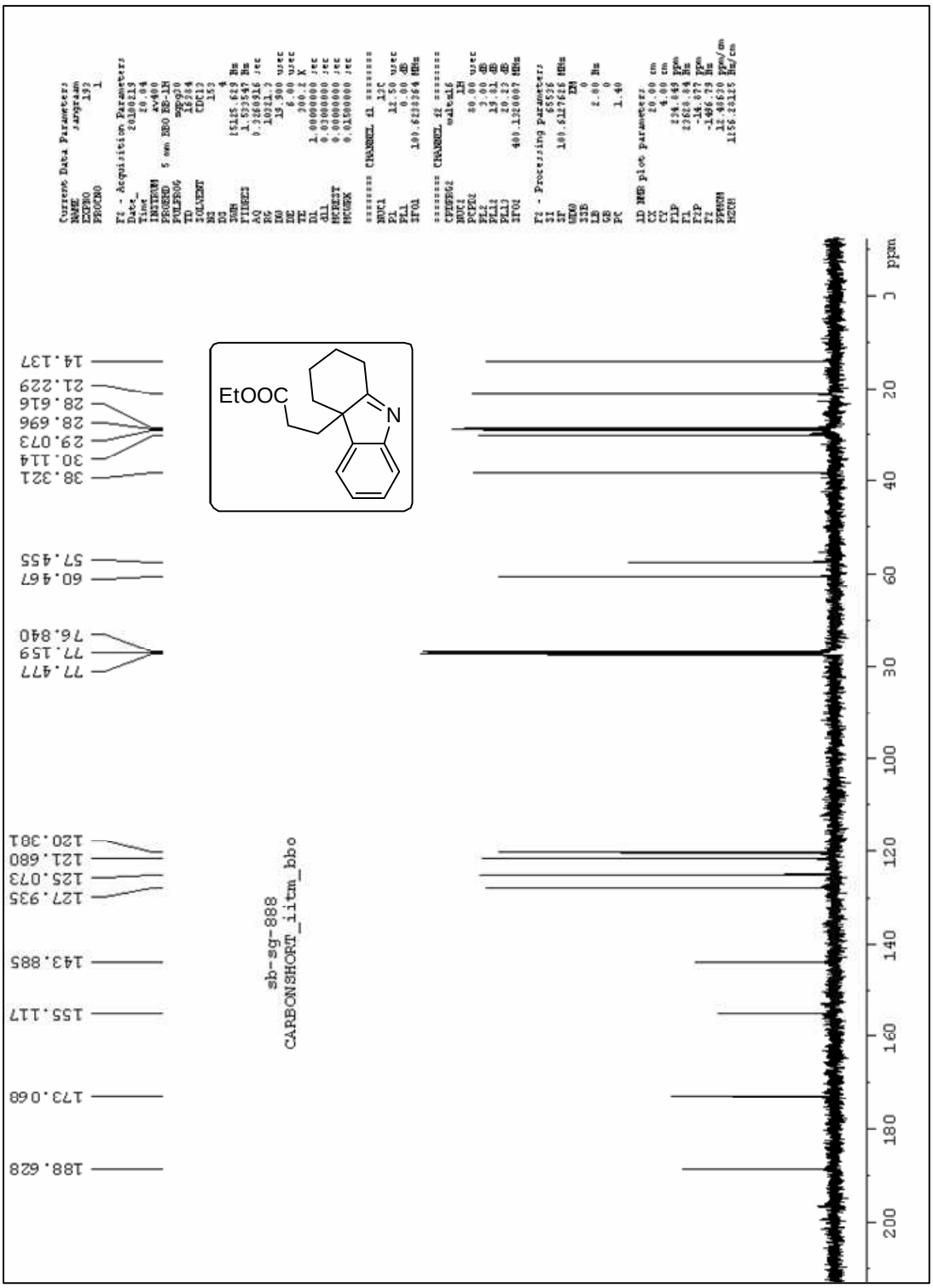
^{1}H NMR spectrum of indolenine derivative **5b**



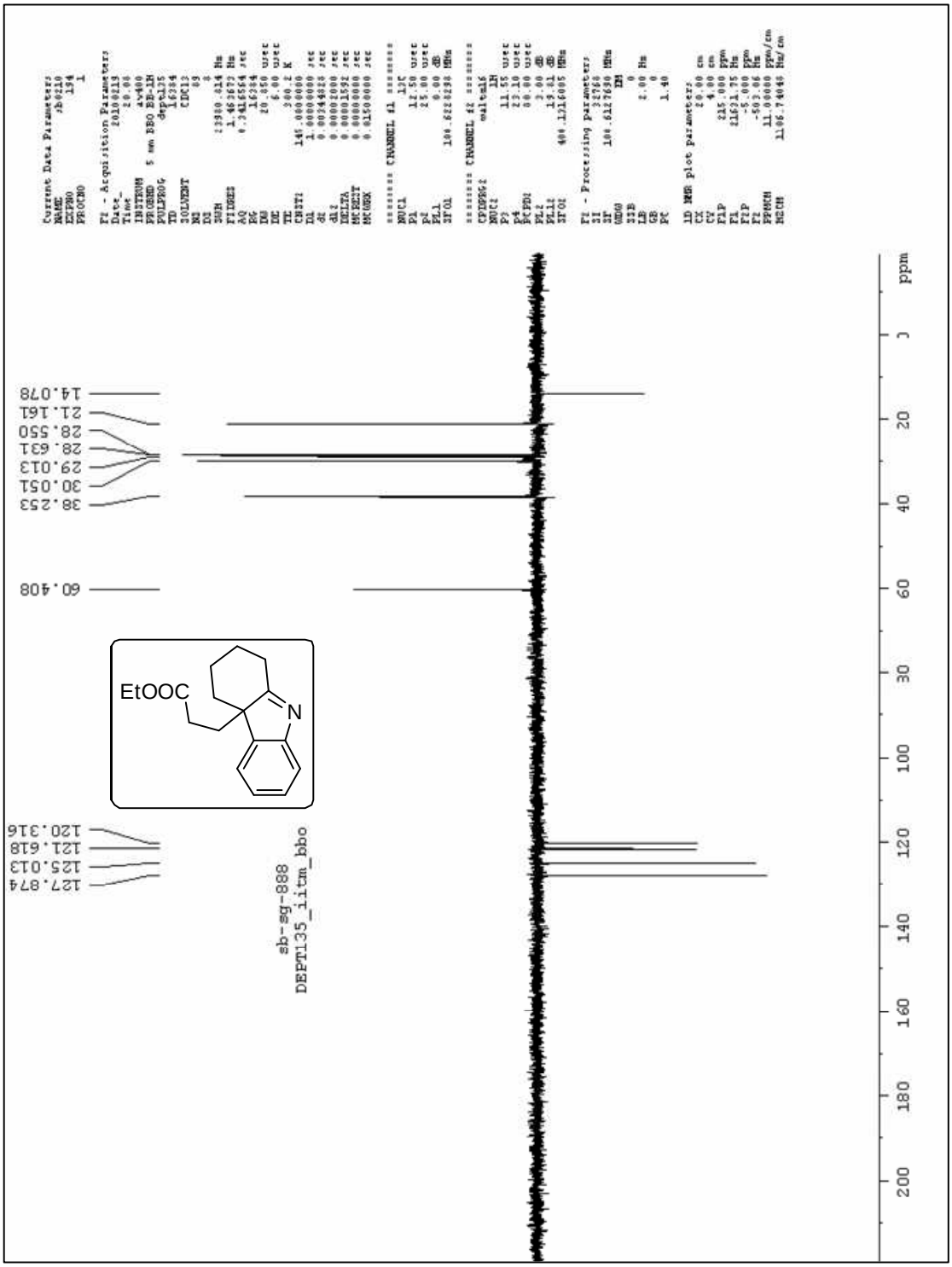
Expanded ^{1}H NMR spectrum of indolenine derivative **5b**



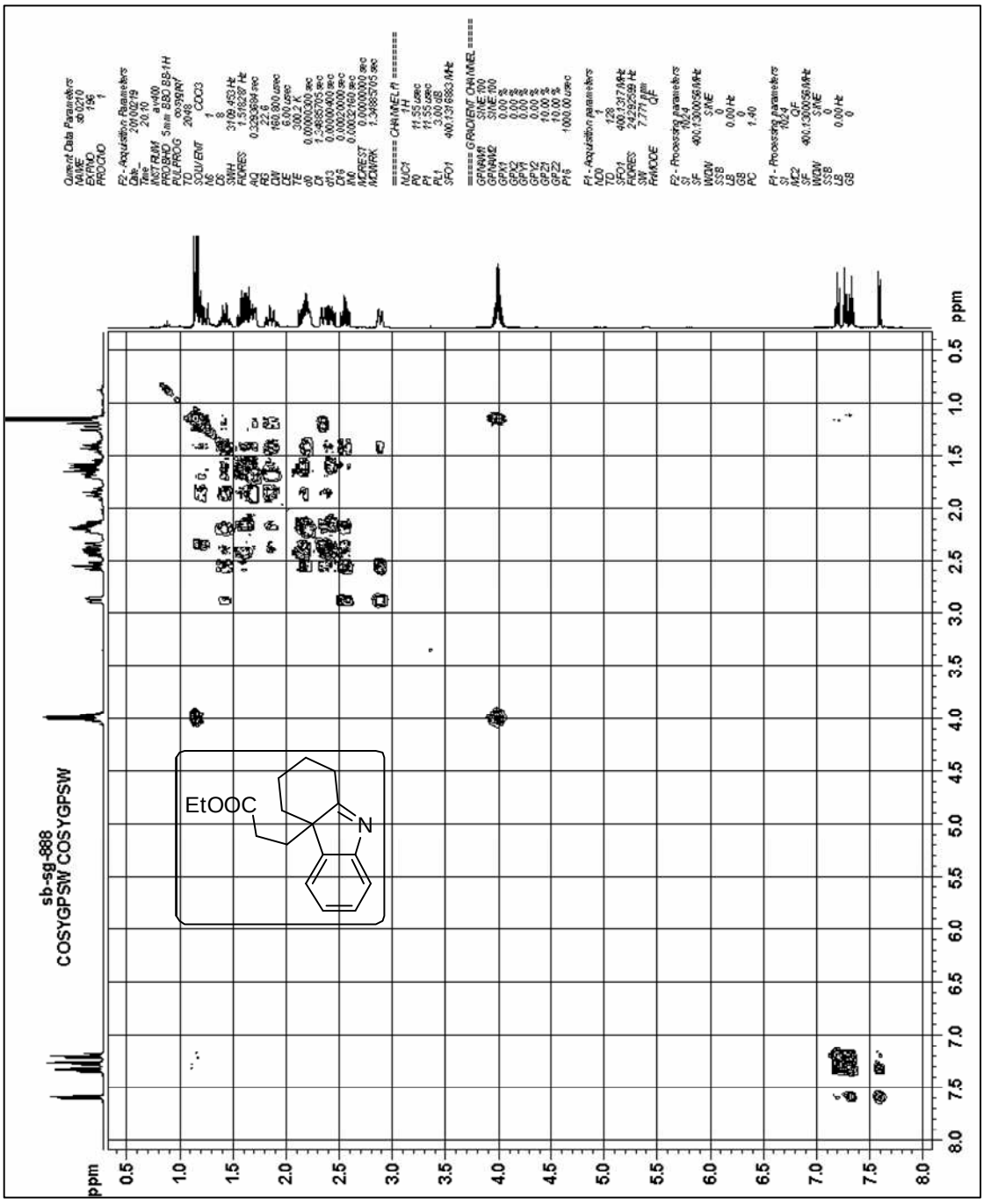
Expanded ^{1}H NMR spectrum of indolenine derivative **5b**



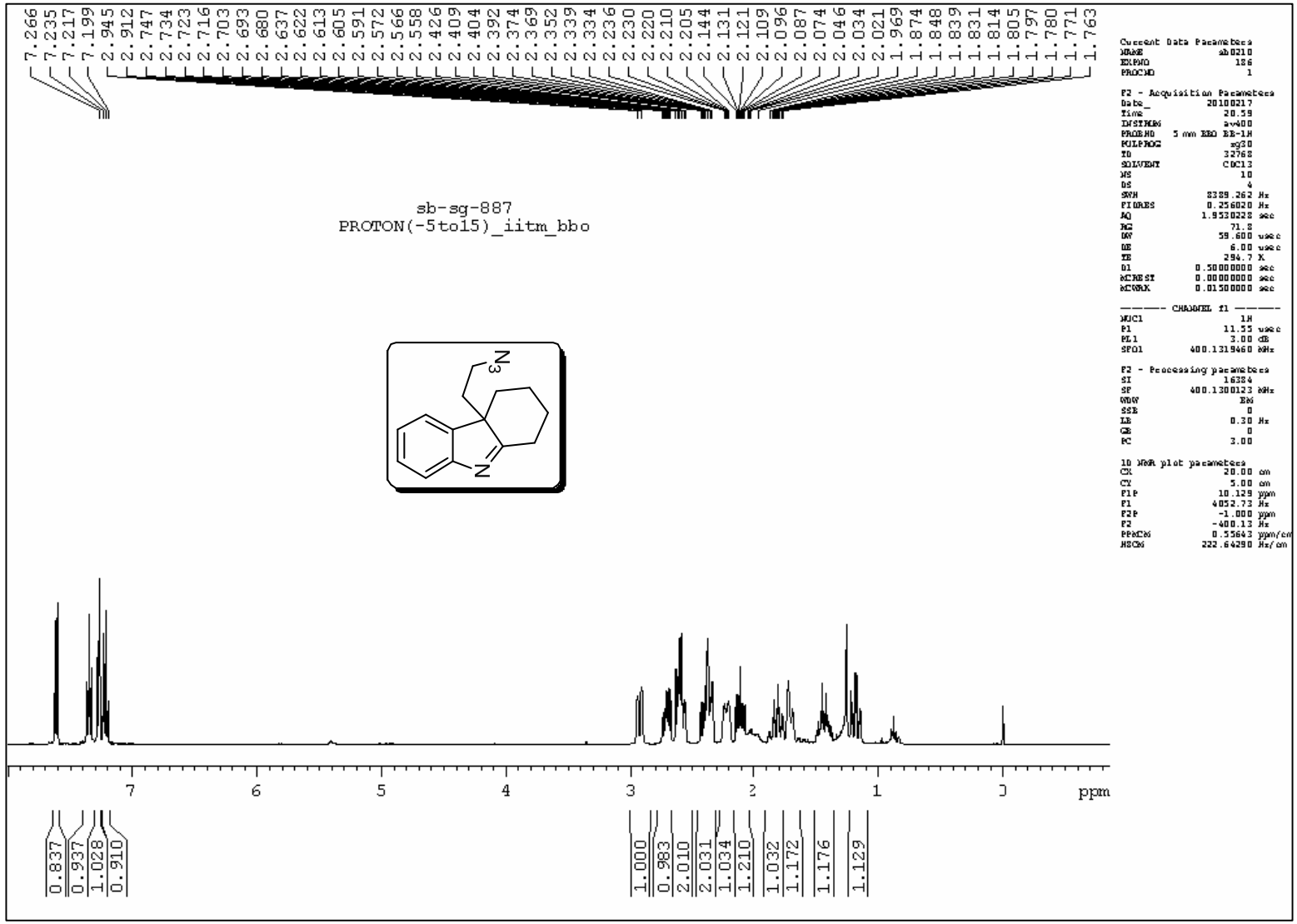
^{13}C NMR spectrum of indolenine derivative **5b**



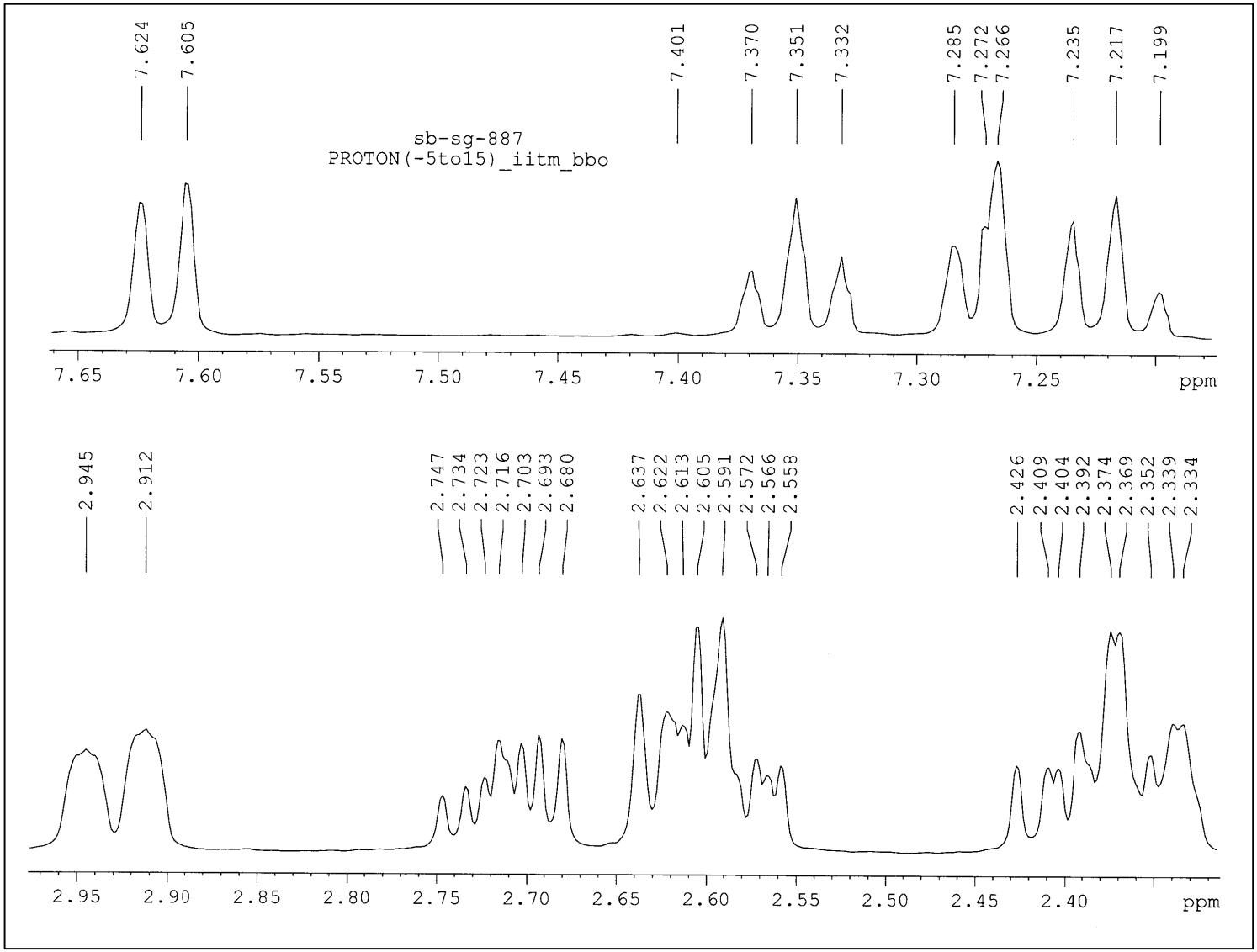
^{13}C DEPT NMR spectrum of indolenine derivative **5b**



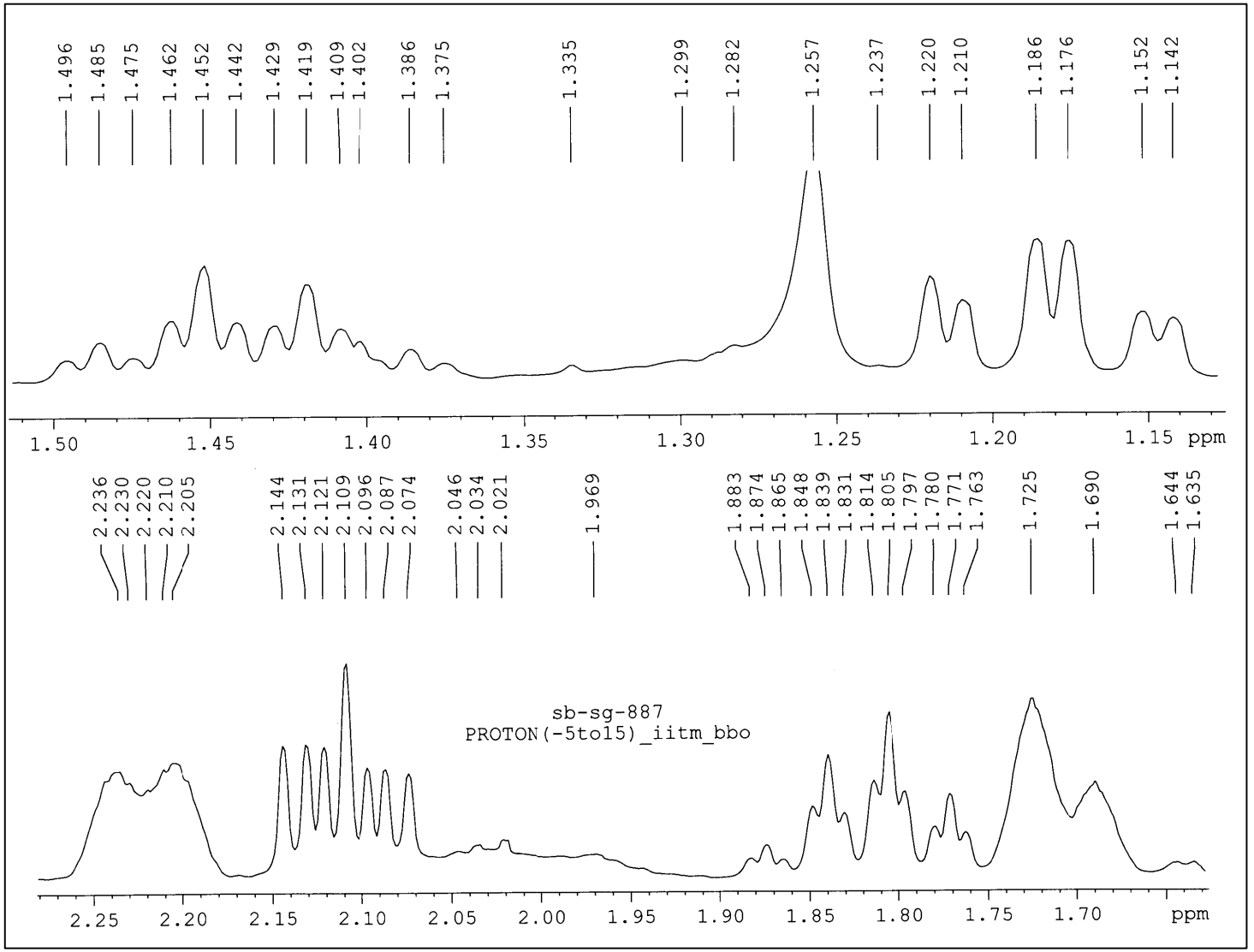
^{1}H-^{1}H COSY NMR spectrum of indolenine derivative **5b**



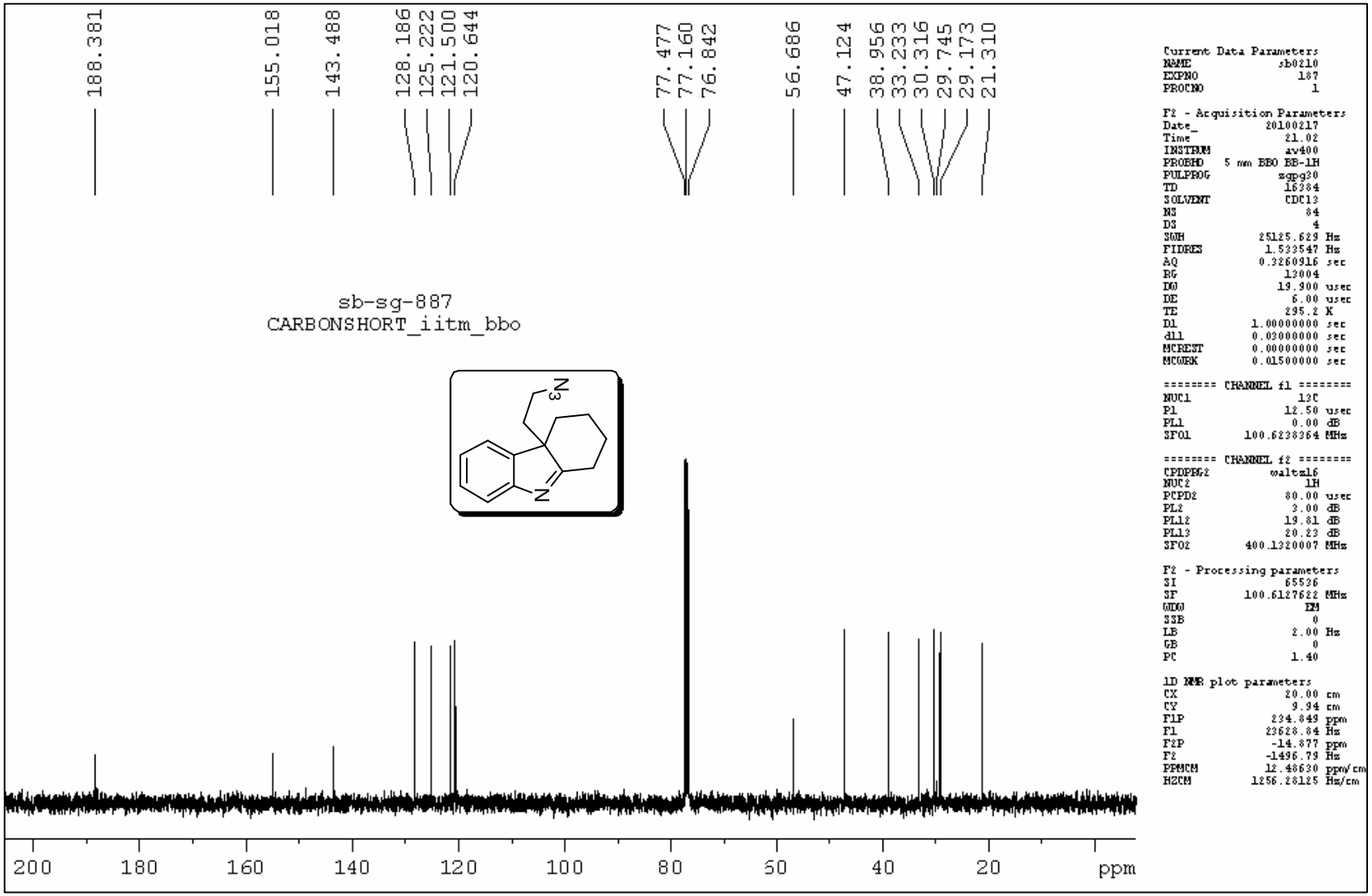
^{1}H NMR spectrum of indolenine derivative **5c**



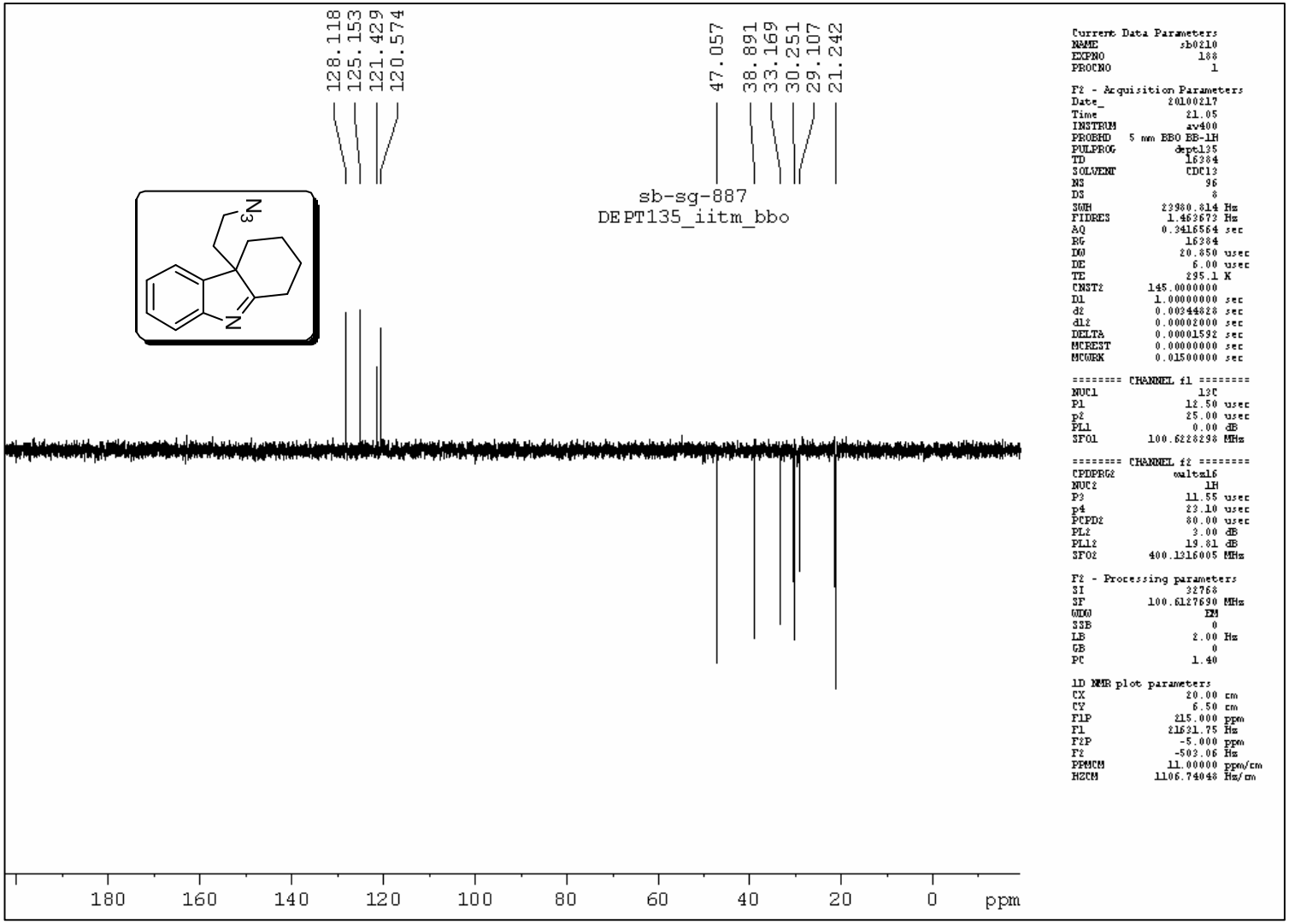
Expanded ^{1}H NMR spectrum of indolenine derivative **5c**



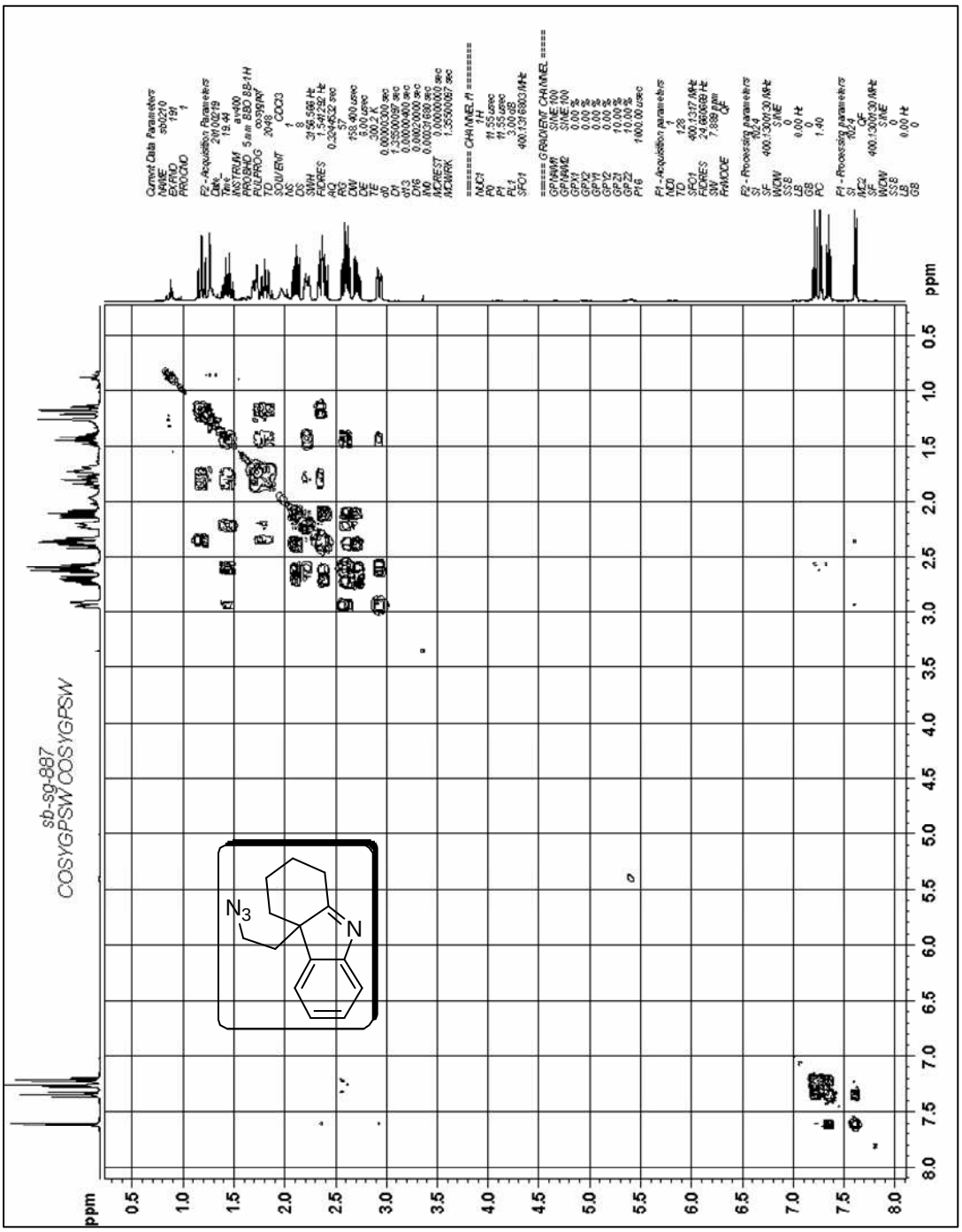
Expanded ^{1}H NMR spectrum of indolenine derivative **5c**



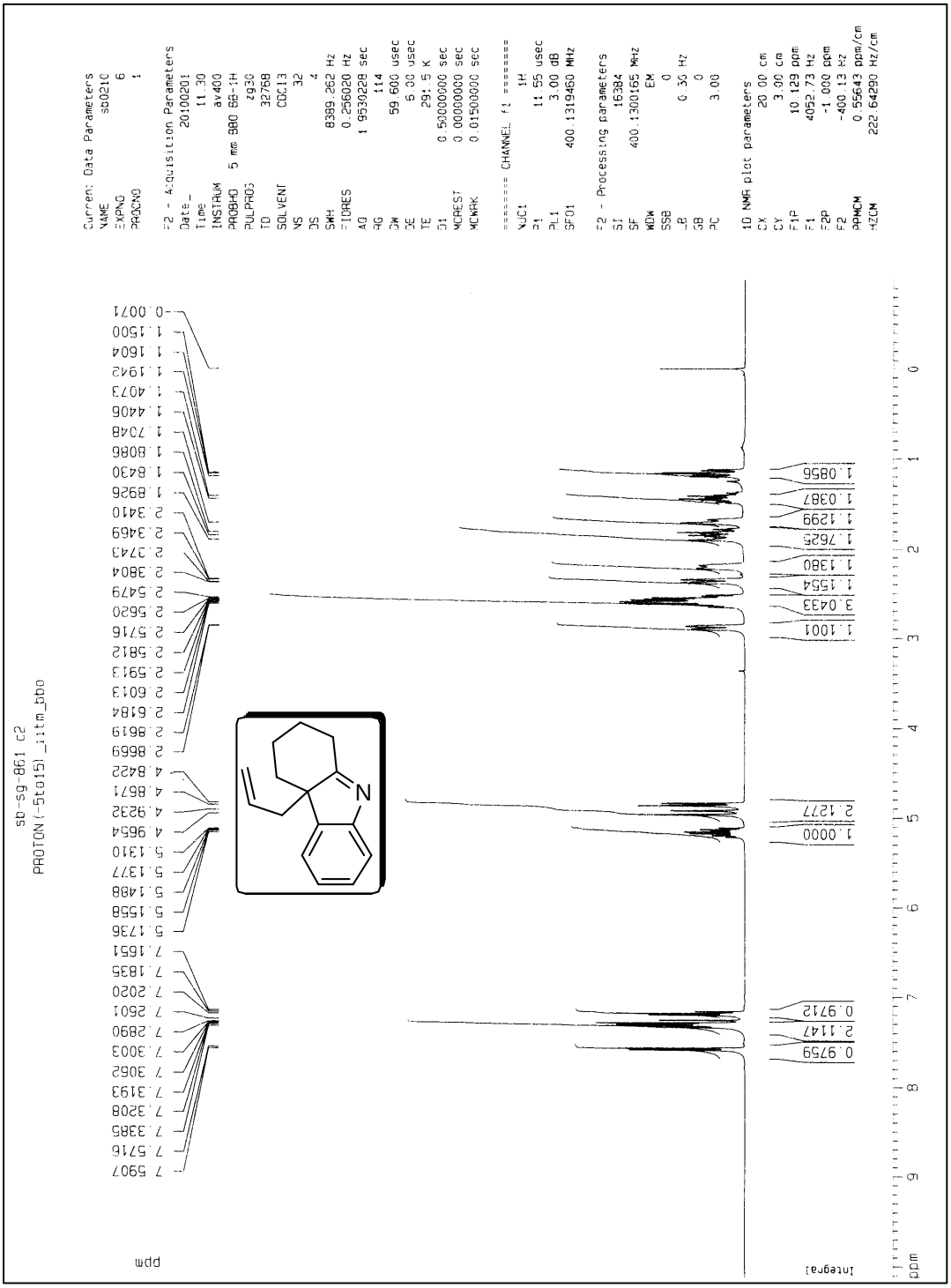
^{13}C NMR spectrum of indolenine derivative **5c**



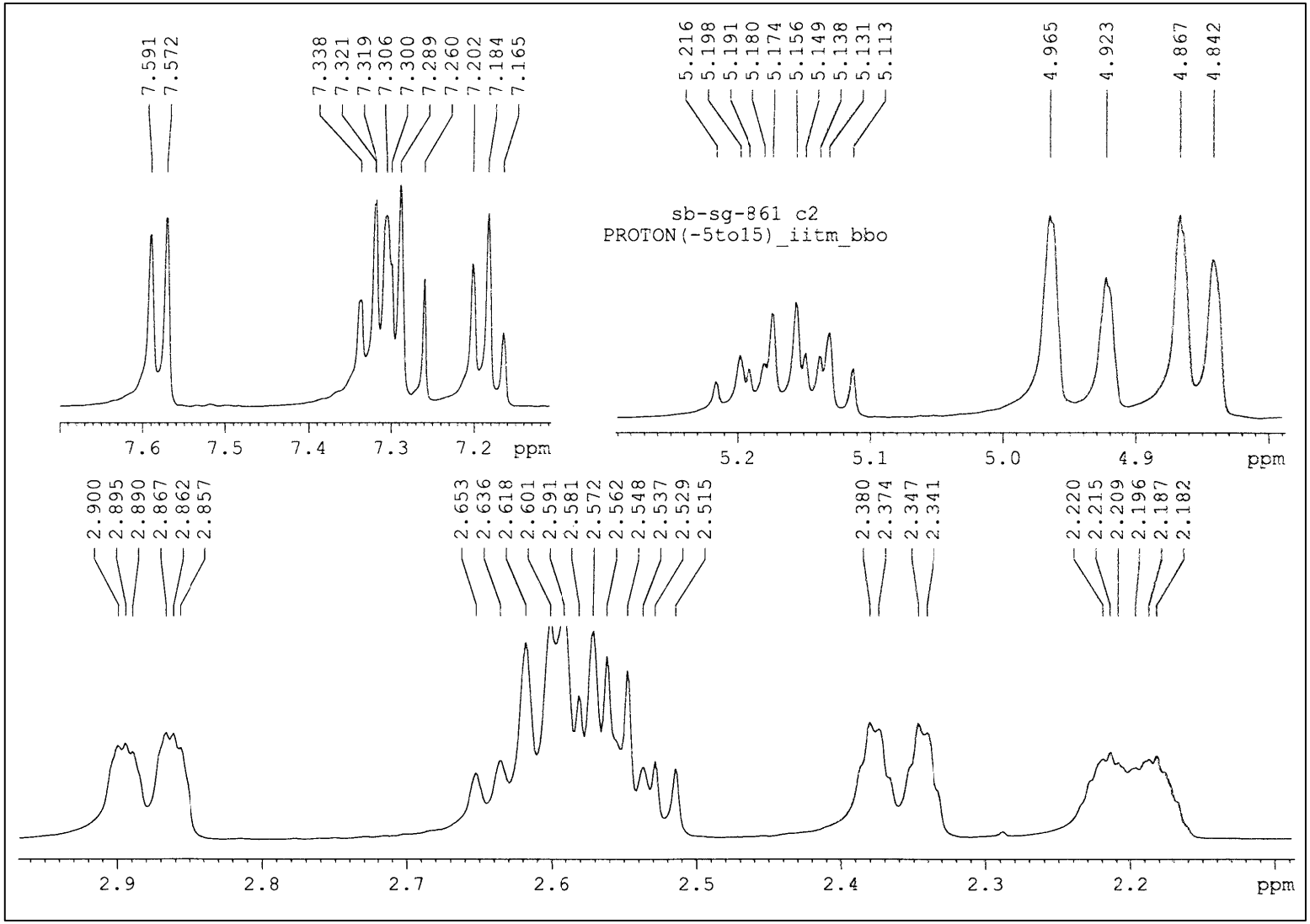
^{13}C DEPT NMR spectrum of indolenine derivative **5c**



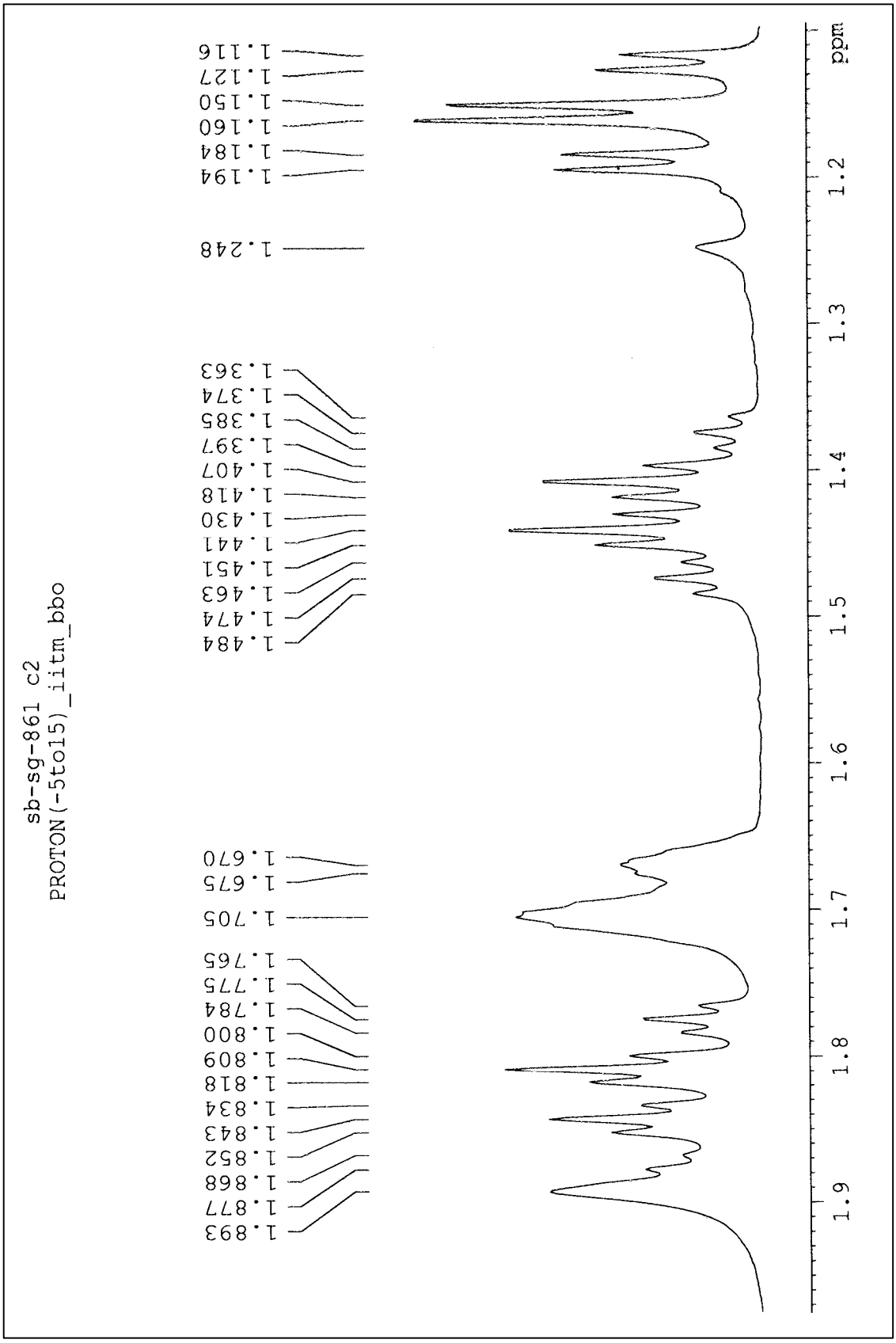
$^{1}H^{1}H$ COSY NMR spectrum of indolenine derivative **5c**



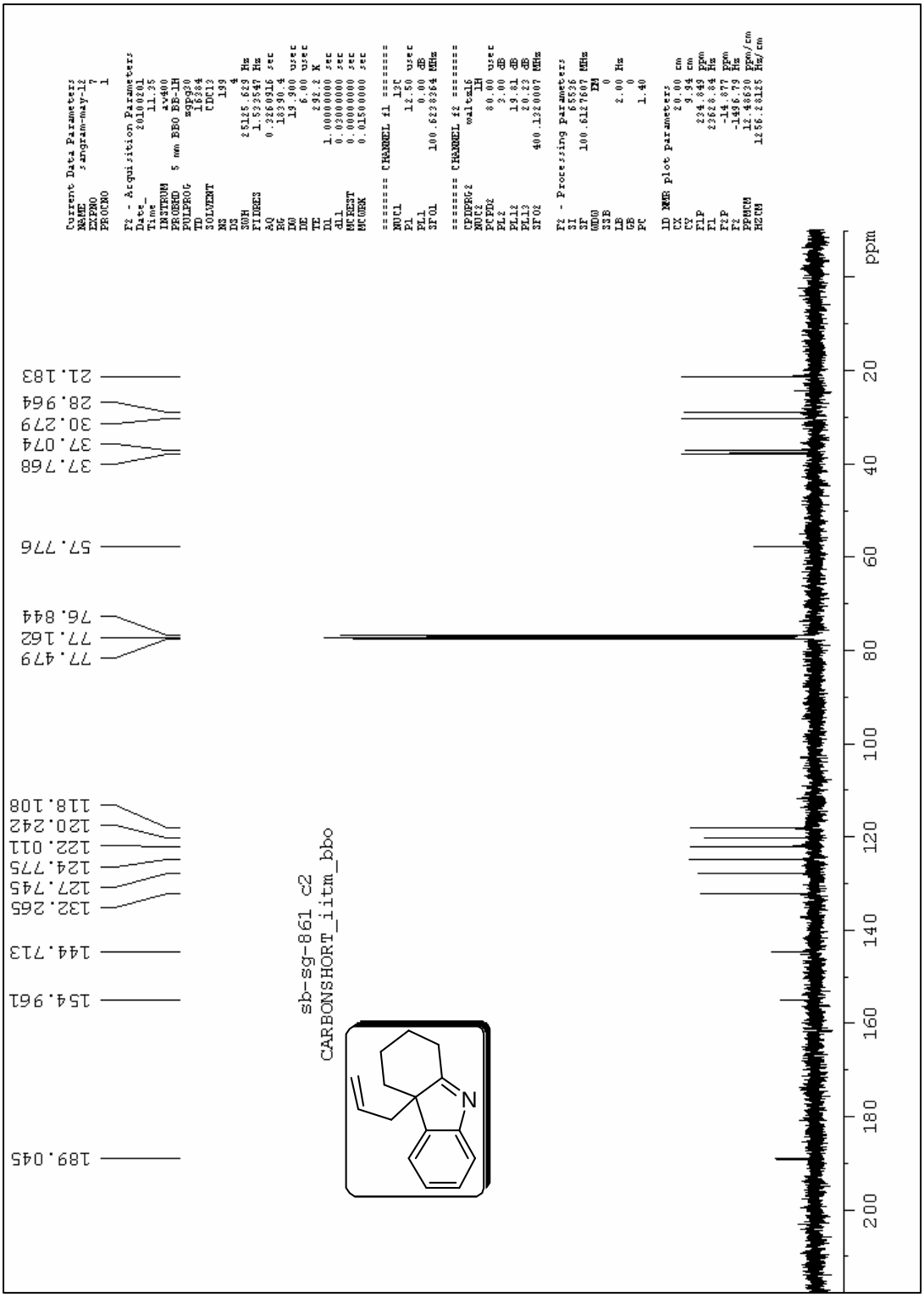
^{1}H NMR spectrum of indolenine derivative **5d**



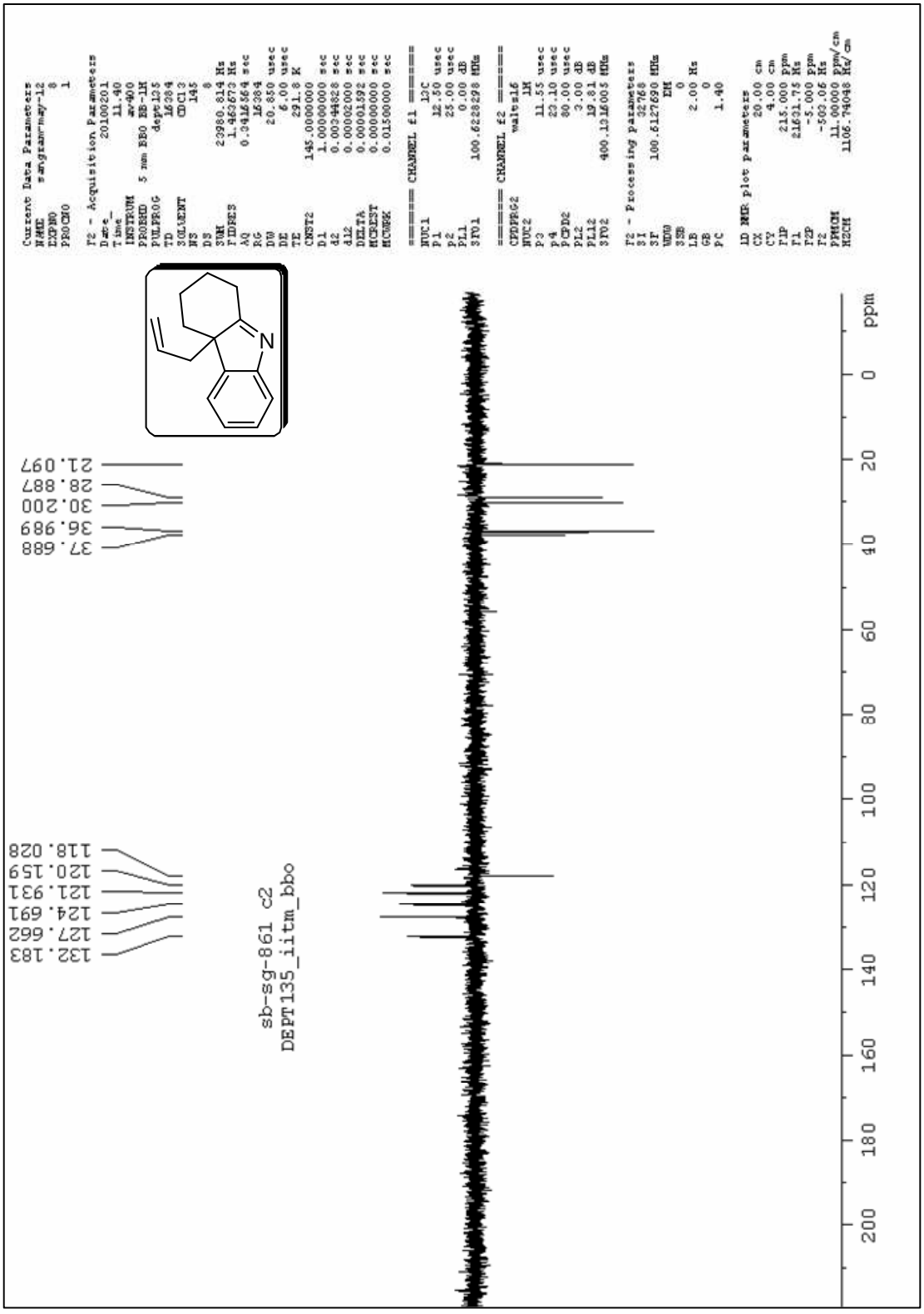
Expanded ^{1}H NMR spectrum of indolenine derivative **5d**



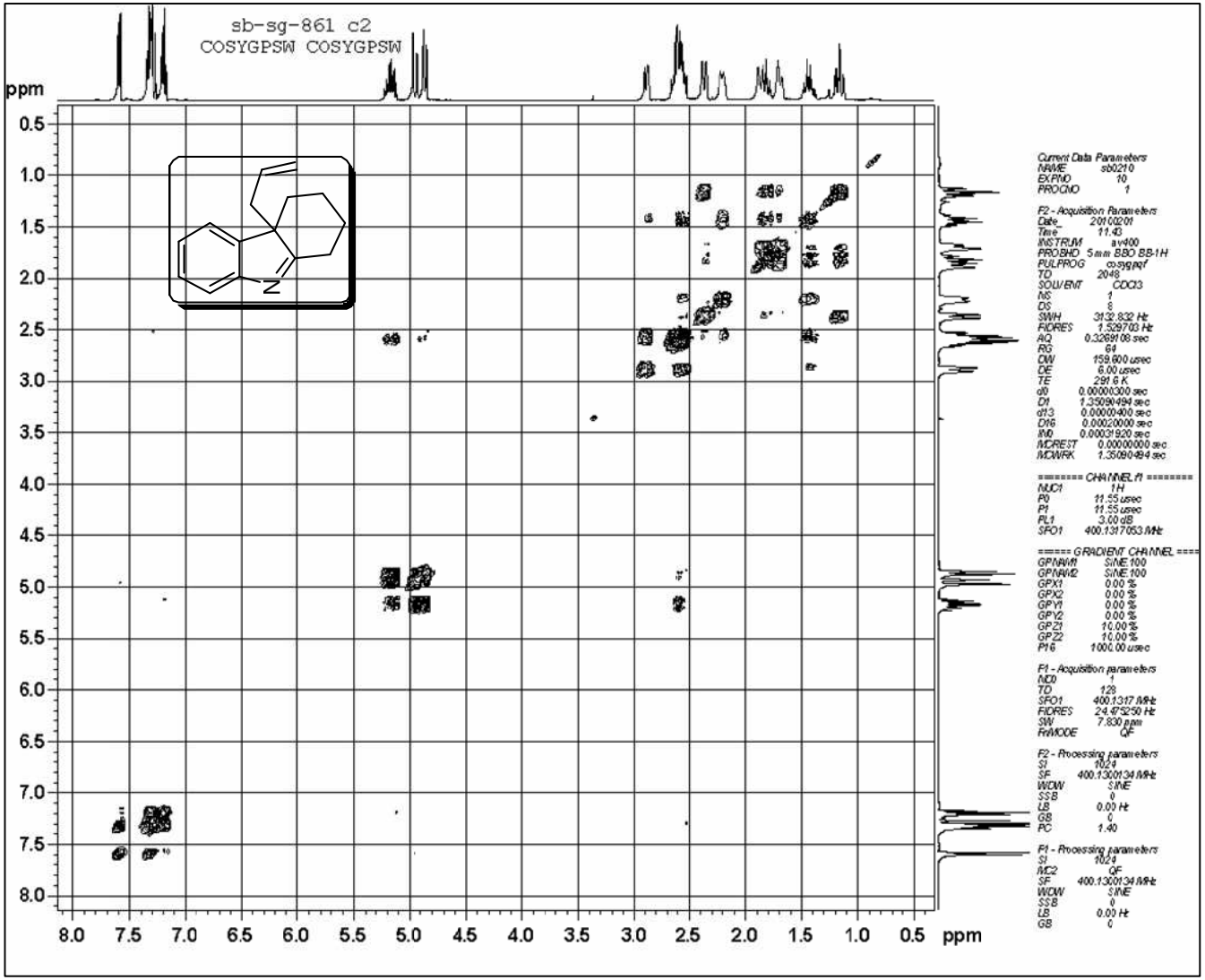
Expanded ^{1}H NMR spectrum of indolenine derivative **5d**



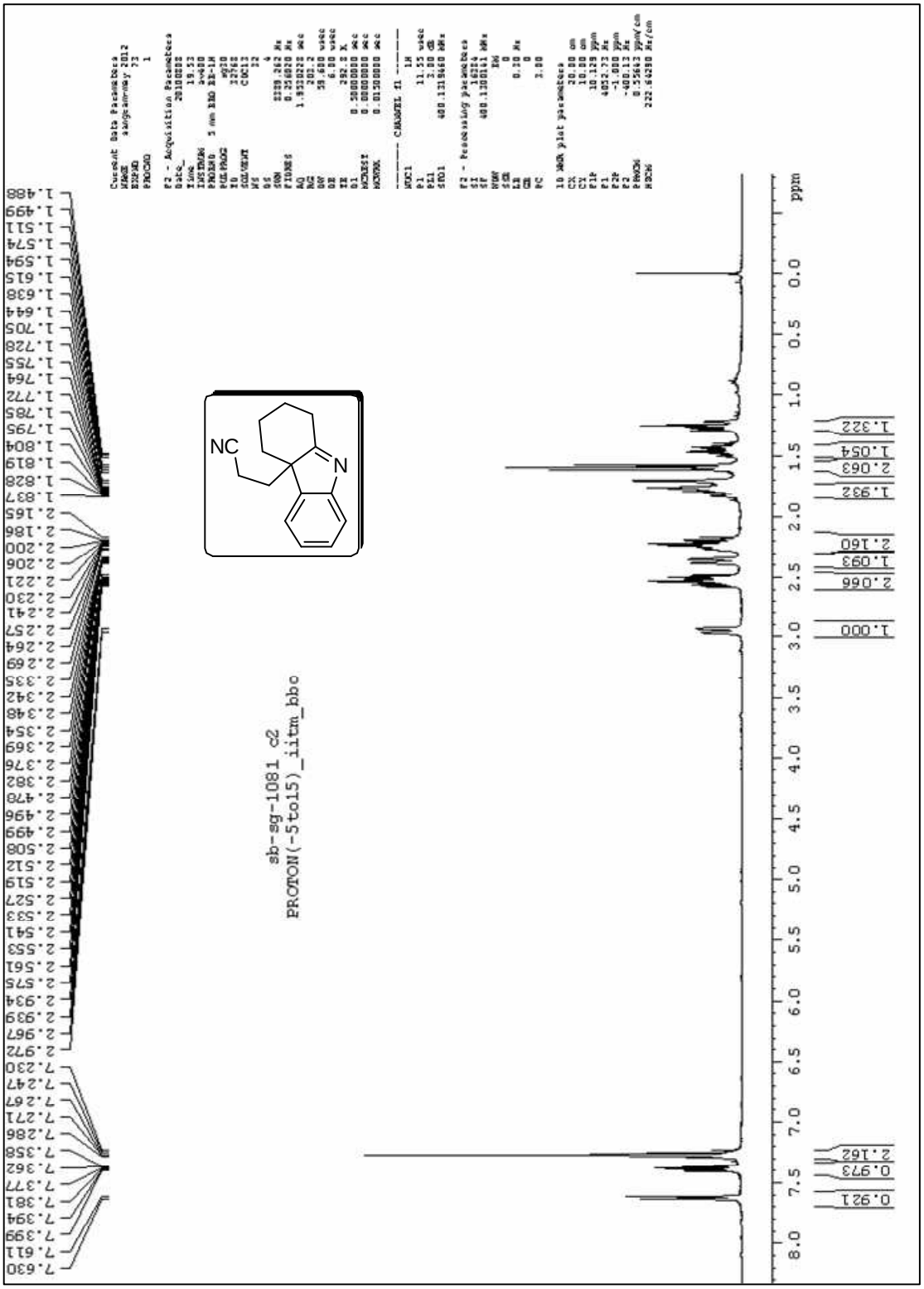
^{13}C NMR spectrum of indolenine derivative **5d**



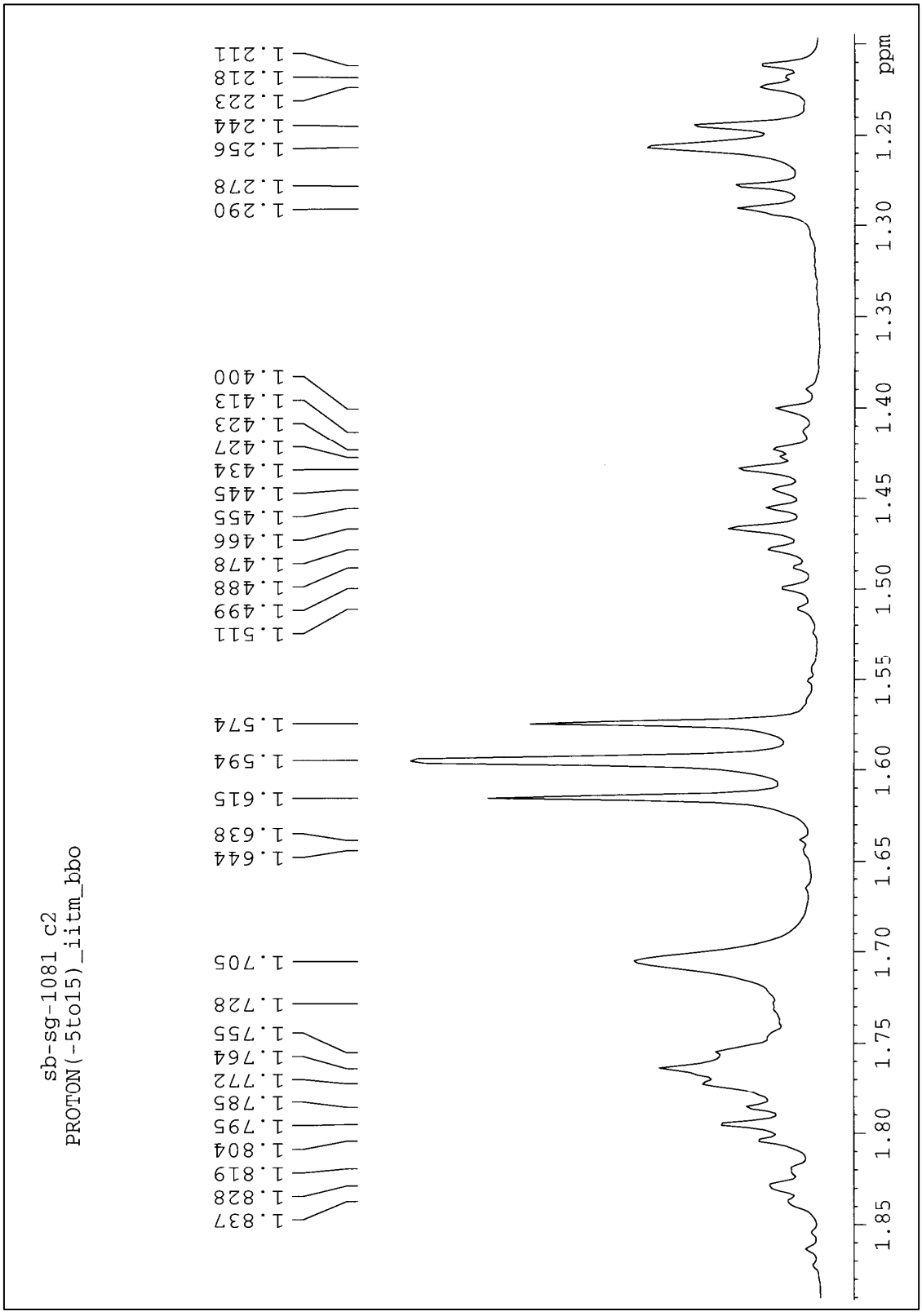
^{13}C DEPT NMR spectrum of indolenine derivative **5d**



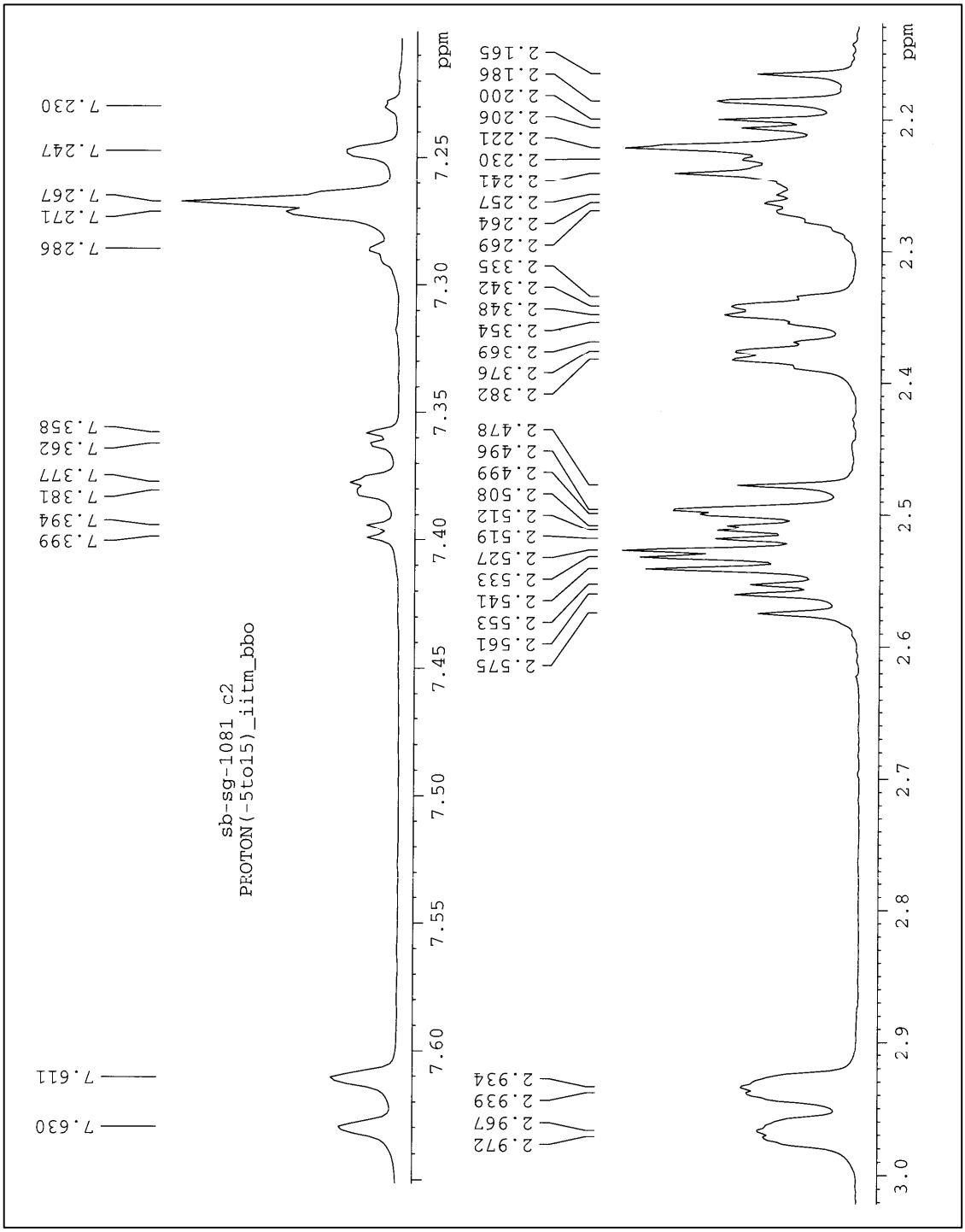
$^{1}H^{1}H$ COSY NMR spectrum of indolenine derivative **5d**



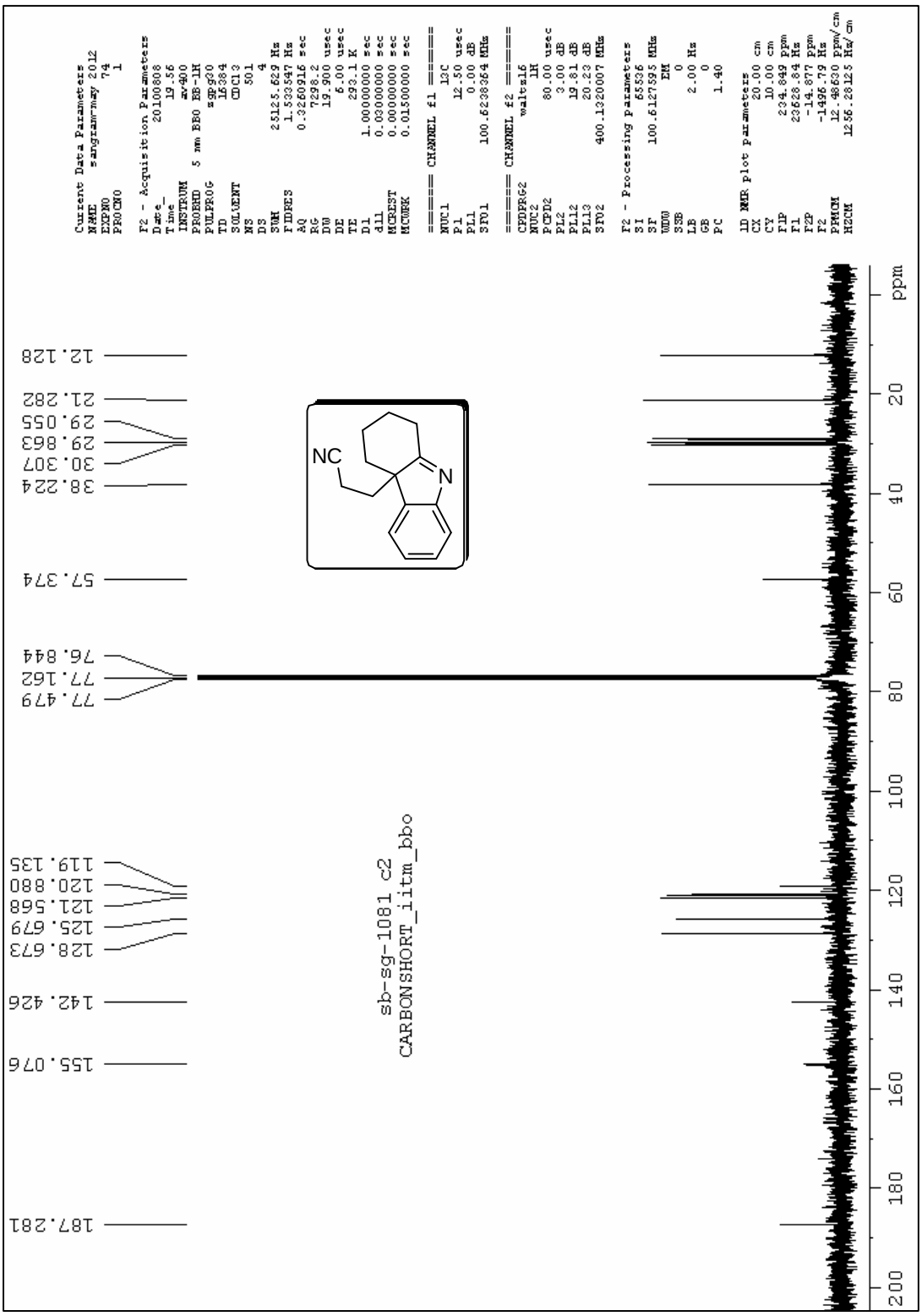
^{1}H NMR spectrum of indolenine derivative **5e**



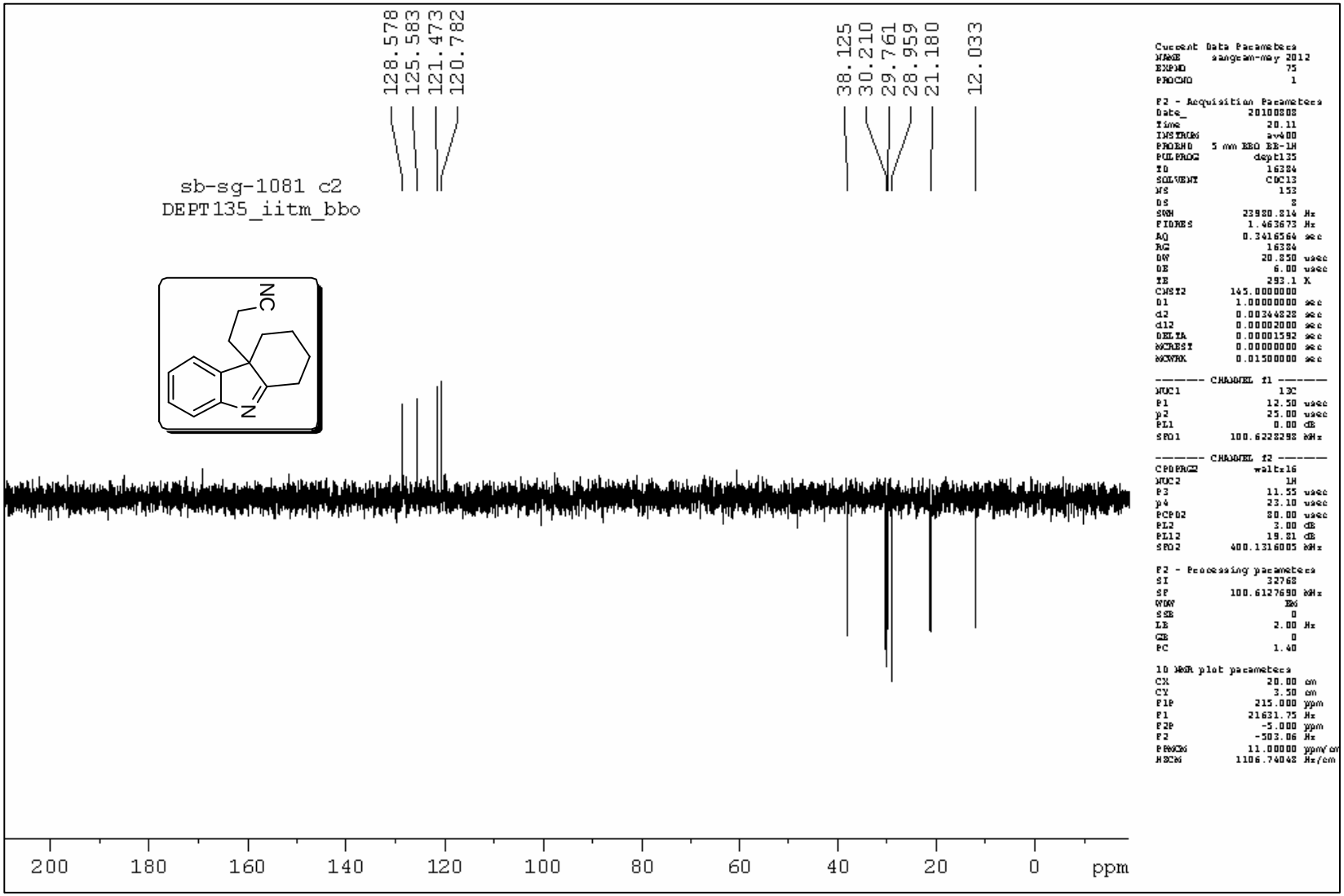
Expanded ^{1}H NMR spectrum of indolenine derivative **5e**



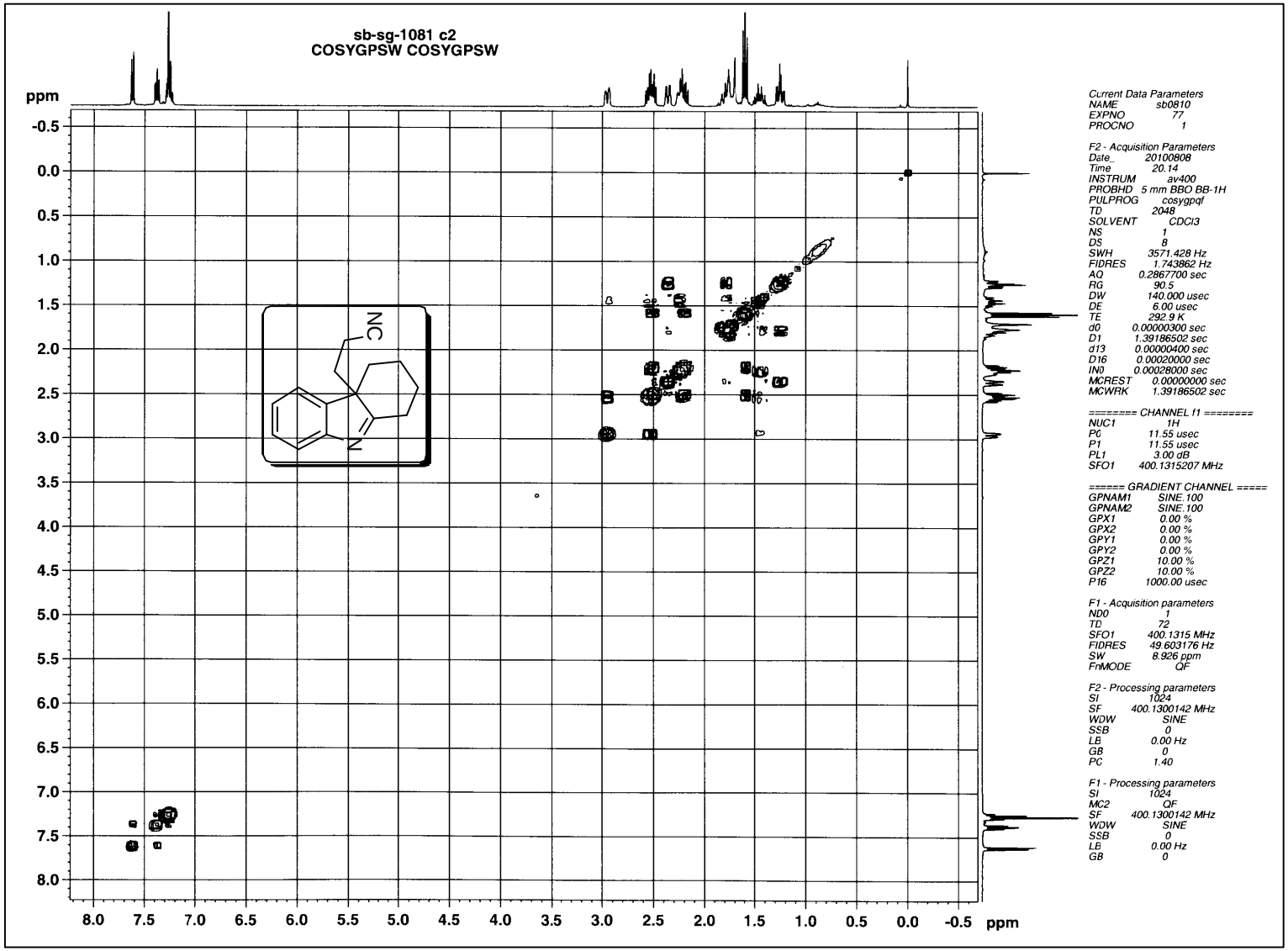
Expanded ^{1}H NMR spectrum of indolenine derivative **5e**



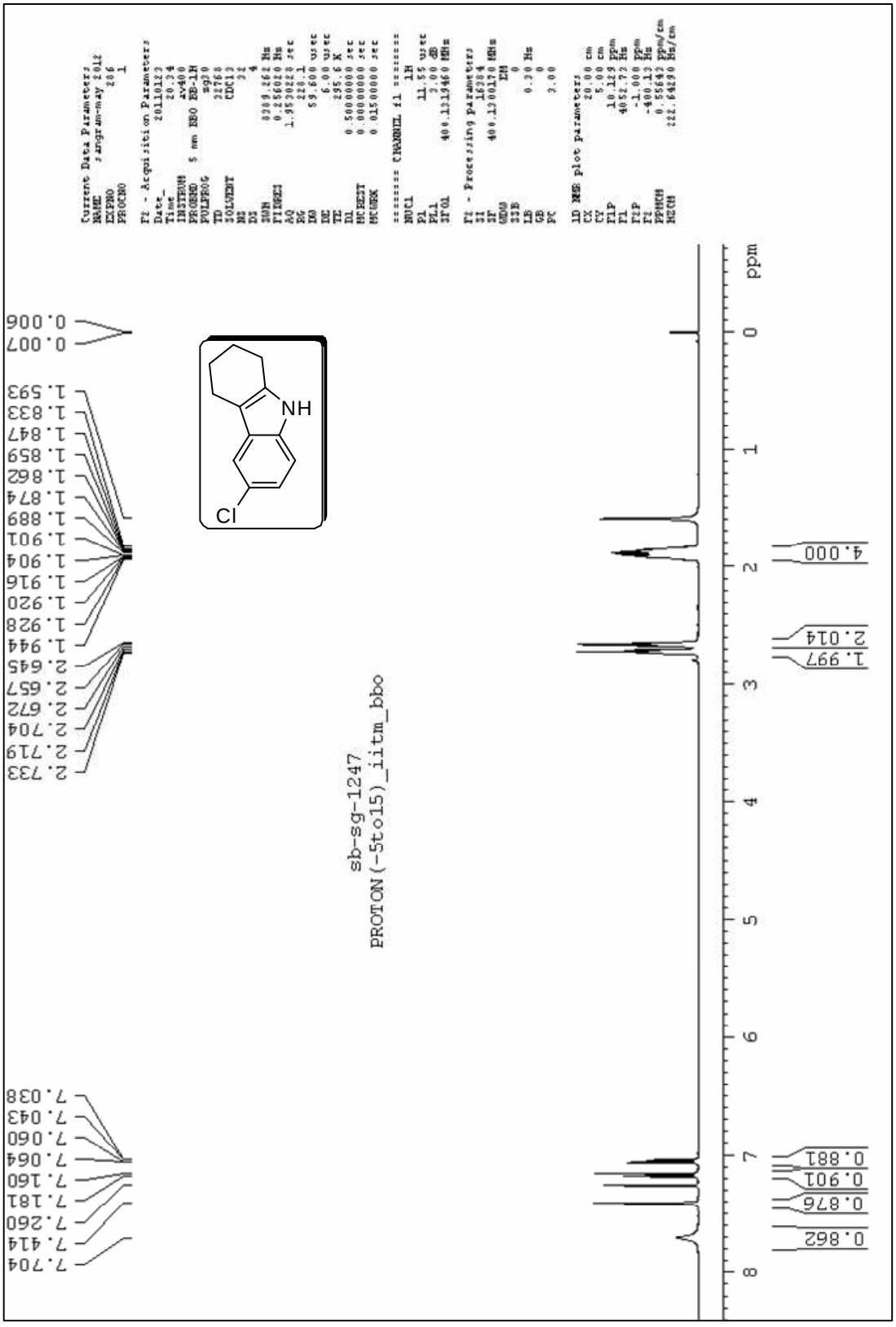
^{13}C NMR spectrum of indolenine derivative **5e**



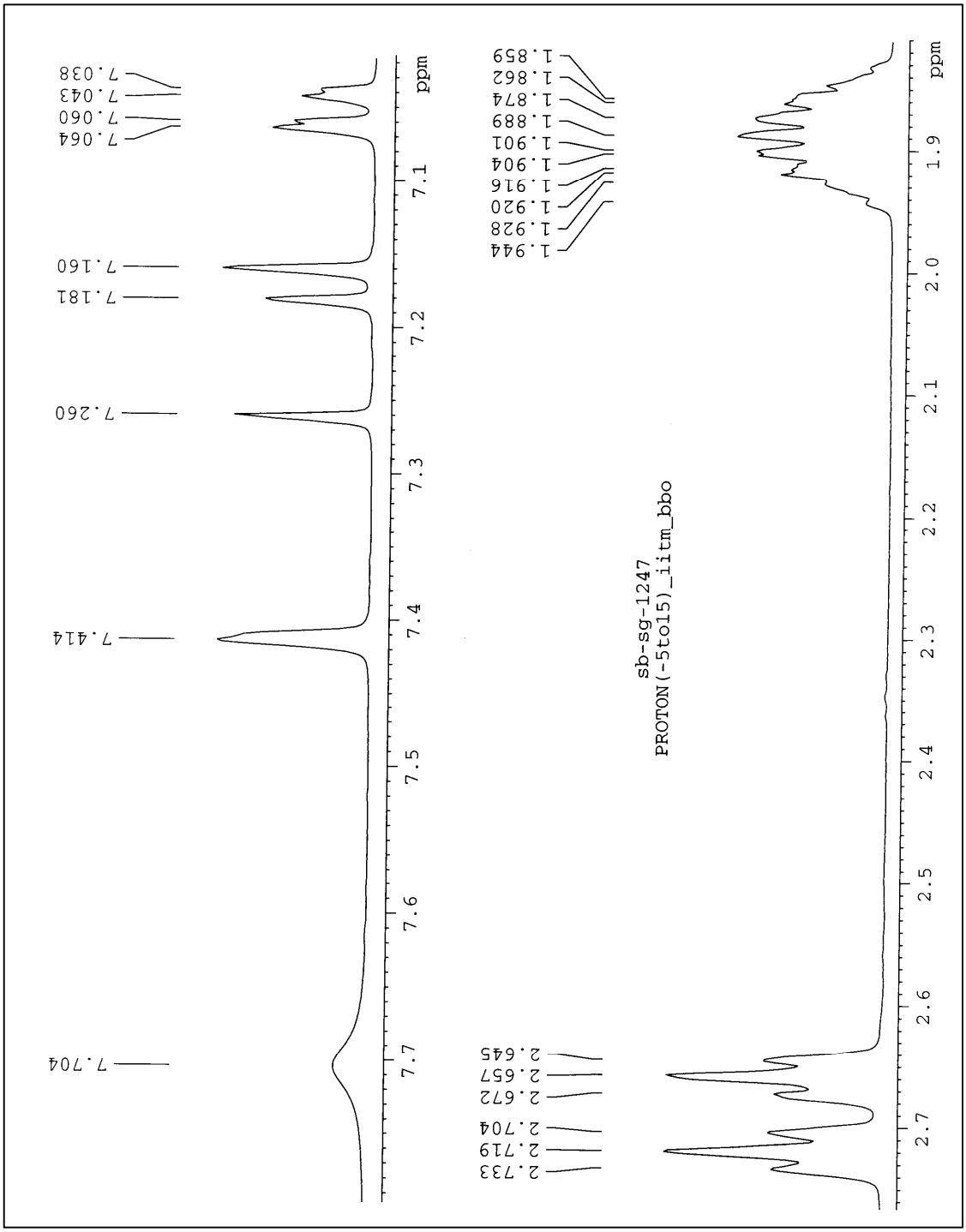
^{13}C DEPT NMR spectrum of indolenine derivative **5e**



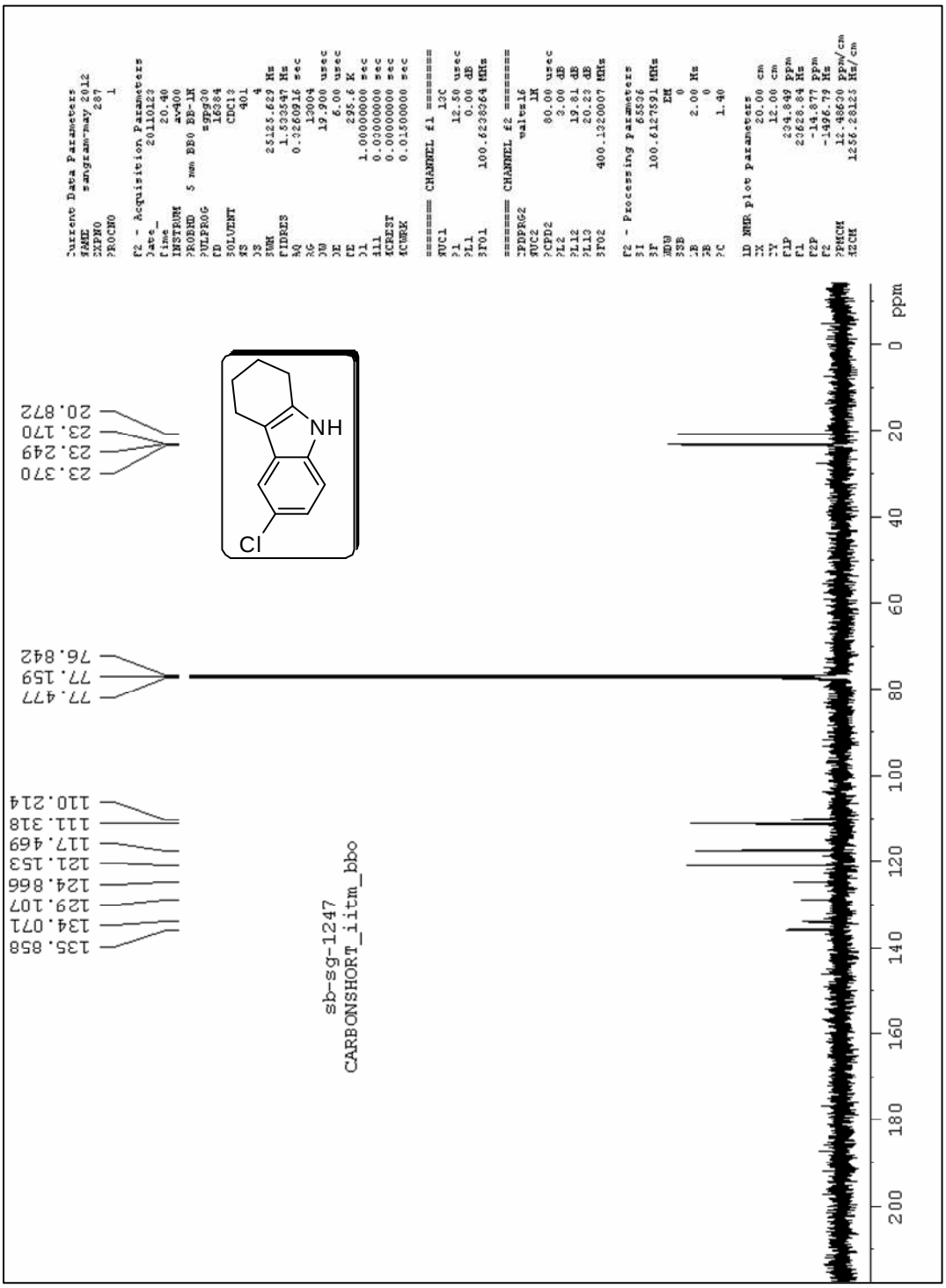
$^{1}H^{1}H$ COSY NMR spectrum of indolenine derivative **5e**



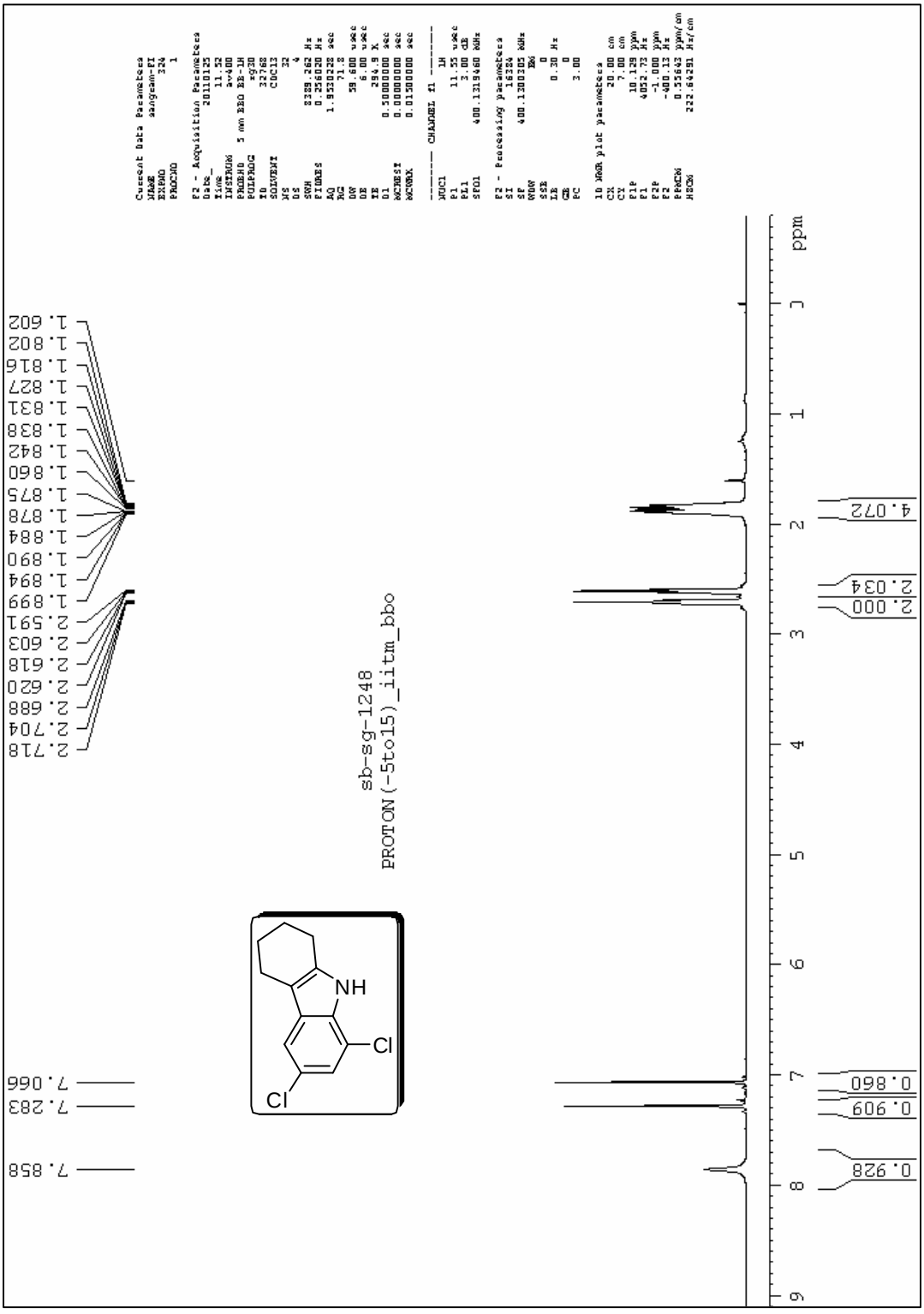
^{1}H NMR spectrum of indole derivative **10**



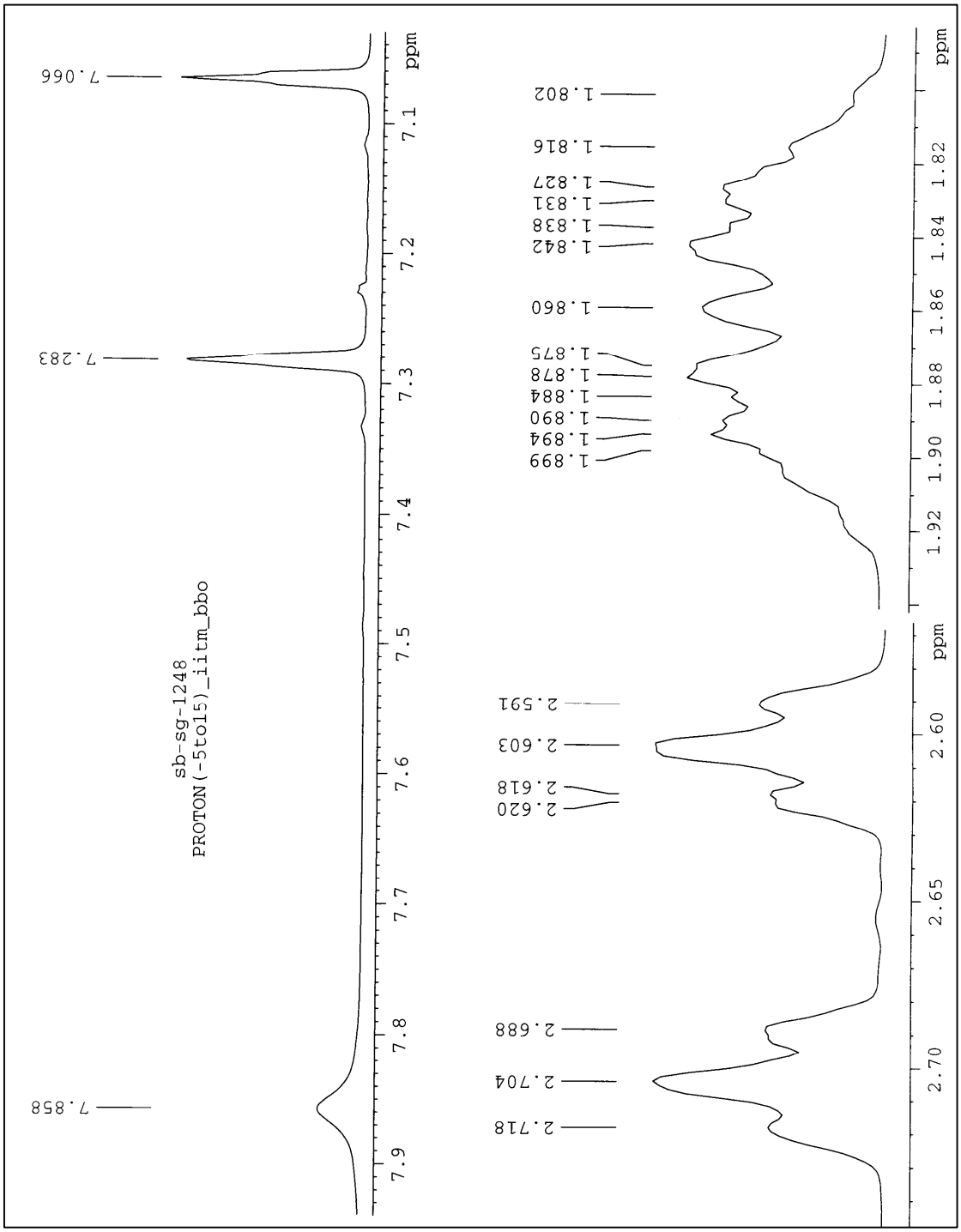
Expanded ^{1}H NMR spectrum of indole derivative **10**



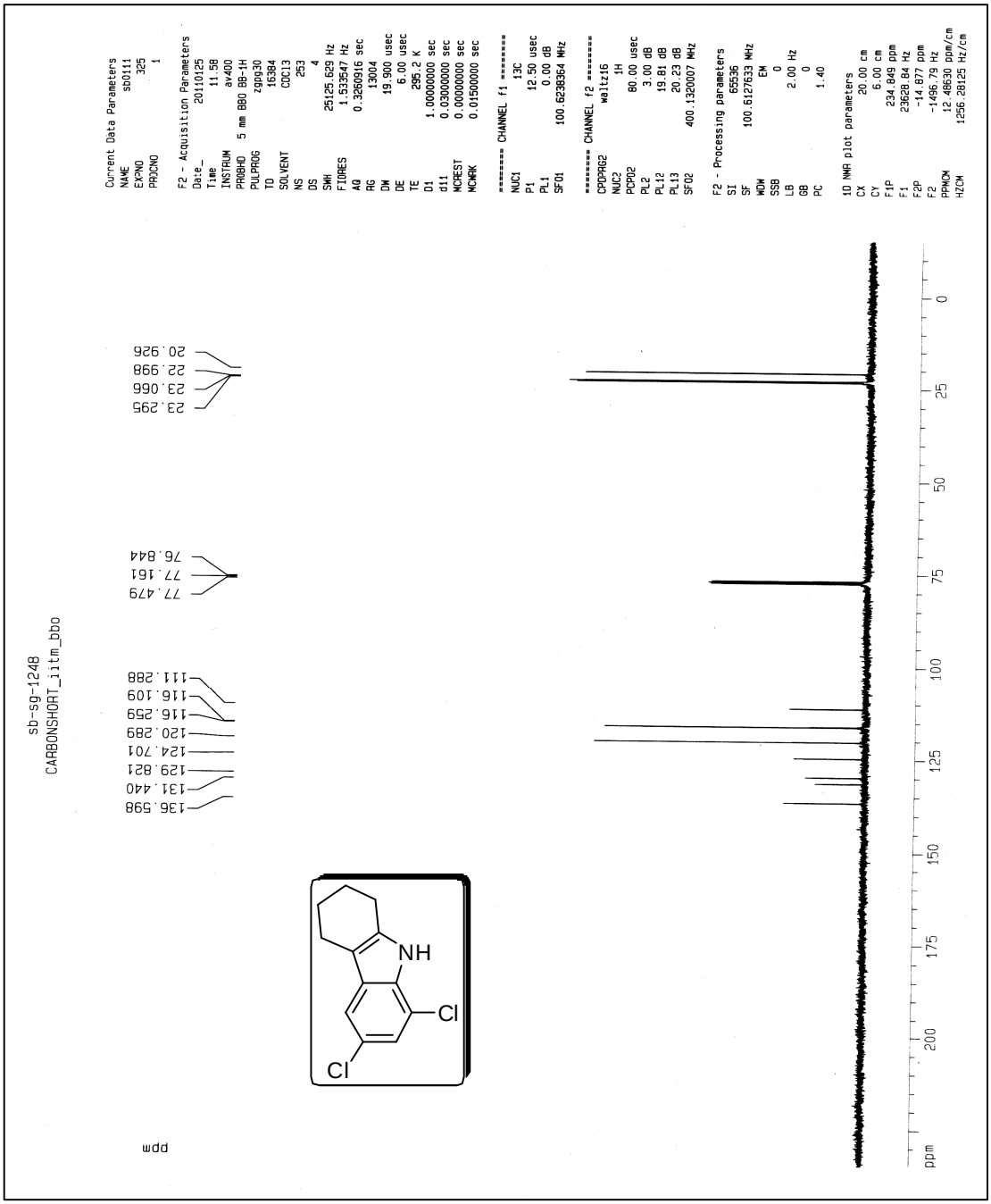
^{13}C NMR spectrum of indole derivative **10**



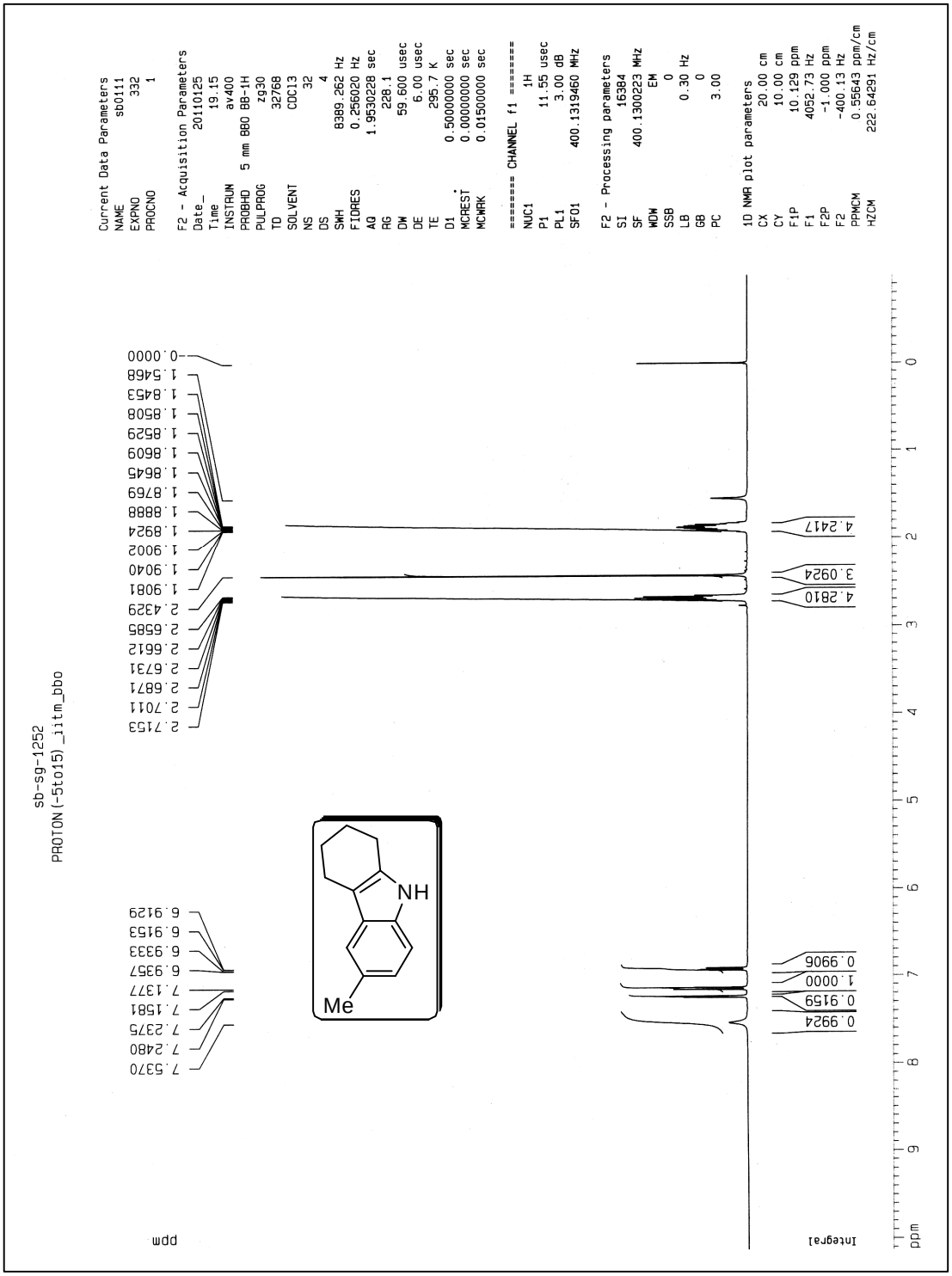
^{1}H NMR spectrum of indole derivative **11**



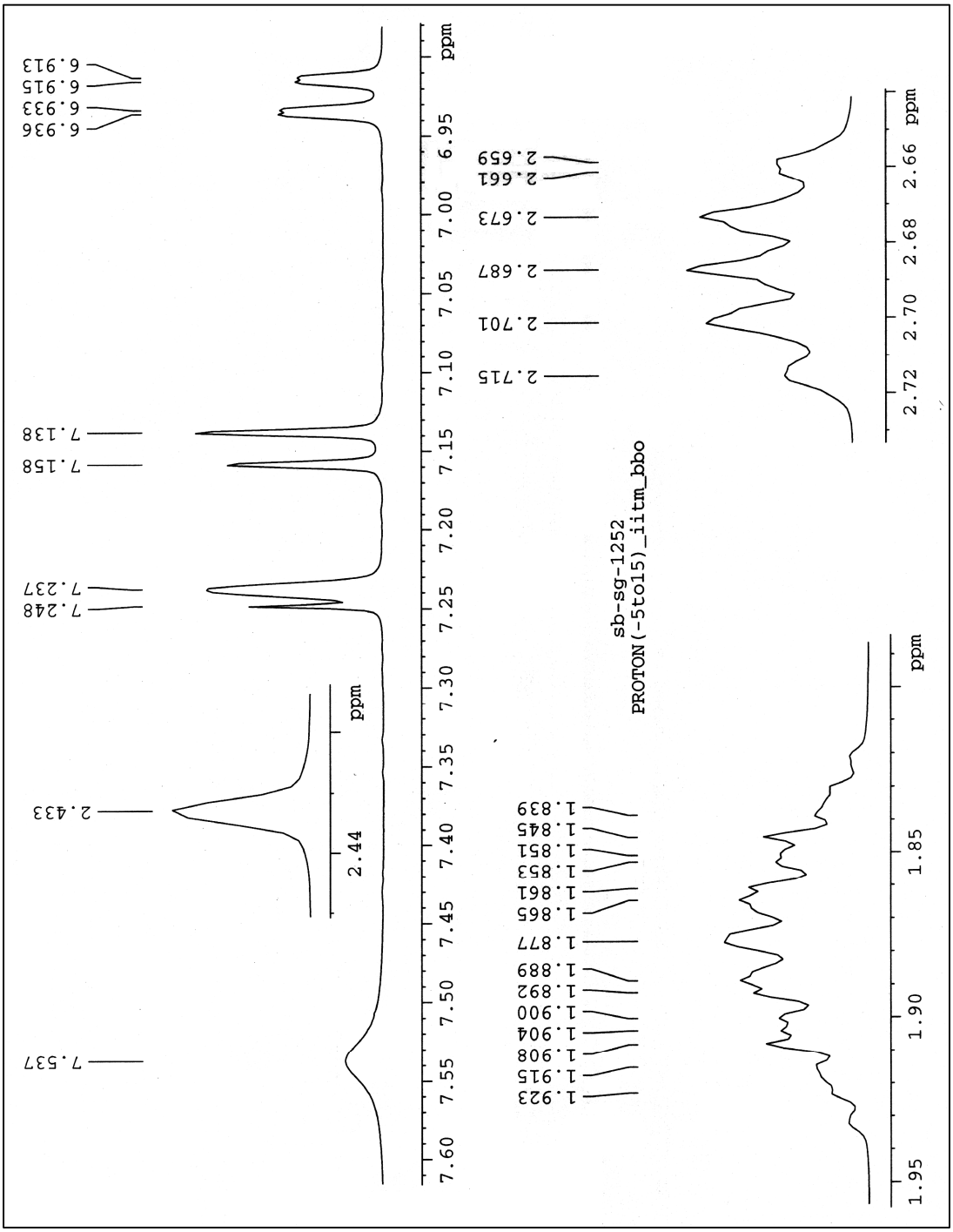
Expanded ^{1}H NMR spectrum of indole derivative **11**



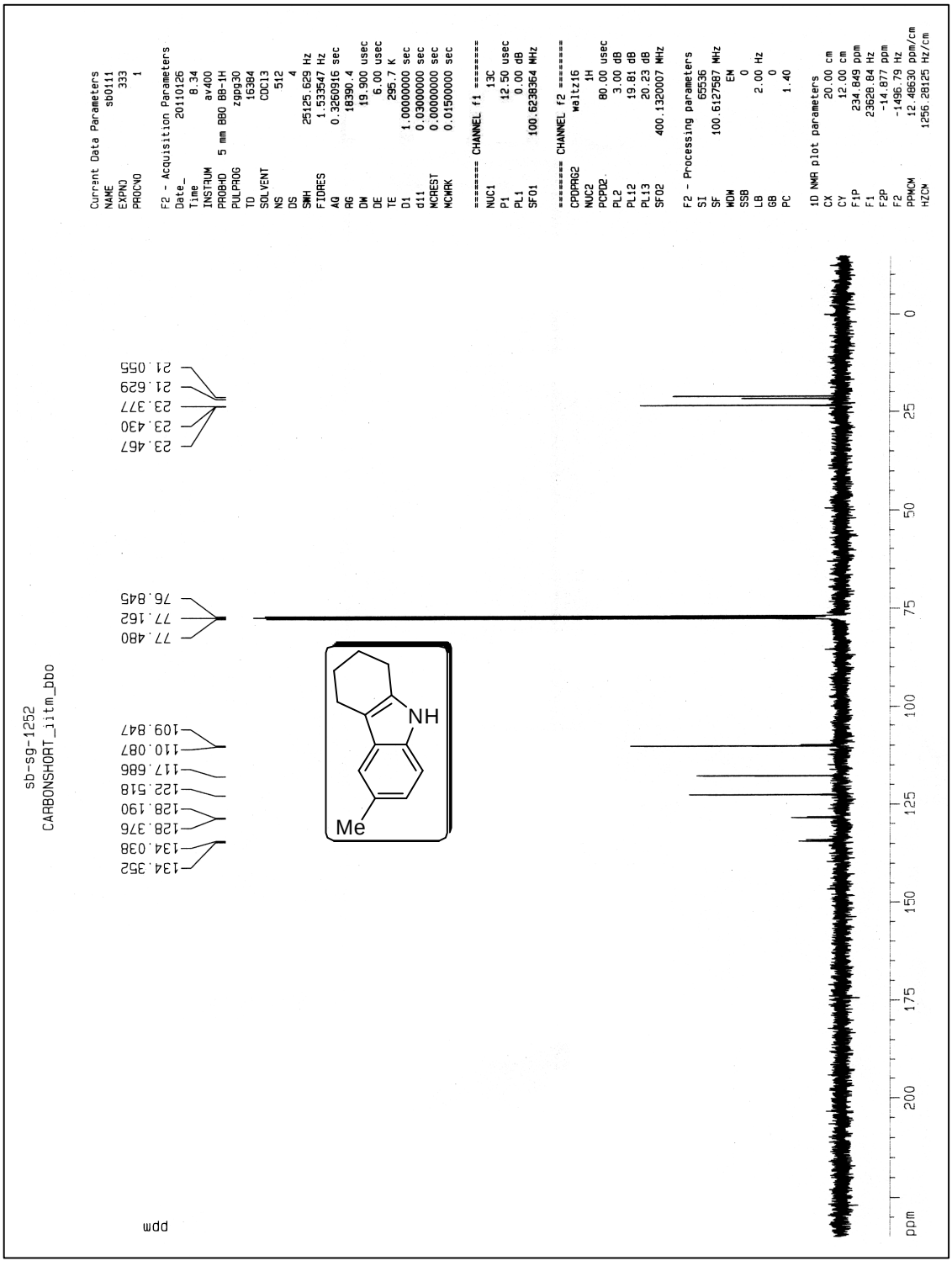
^{13}C NMR spectrum of indole derivative **11**



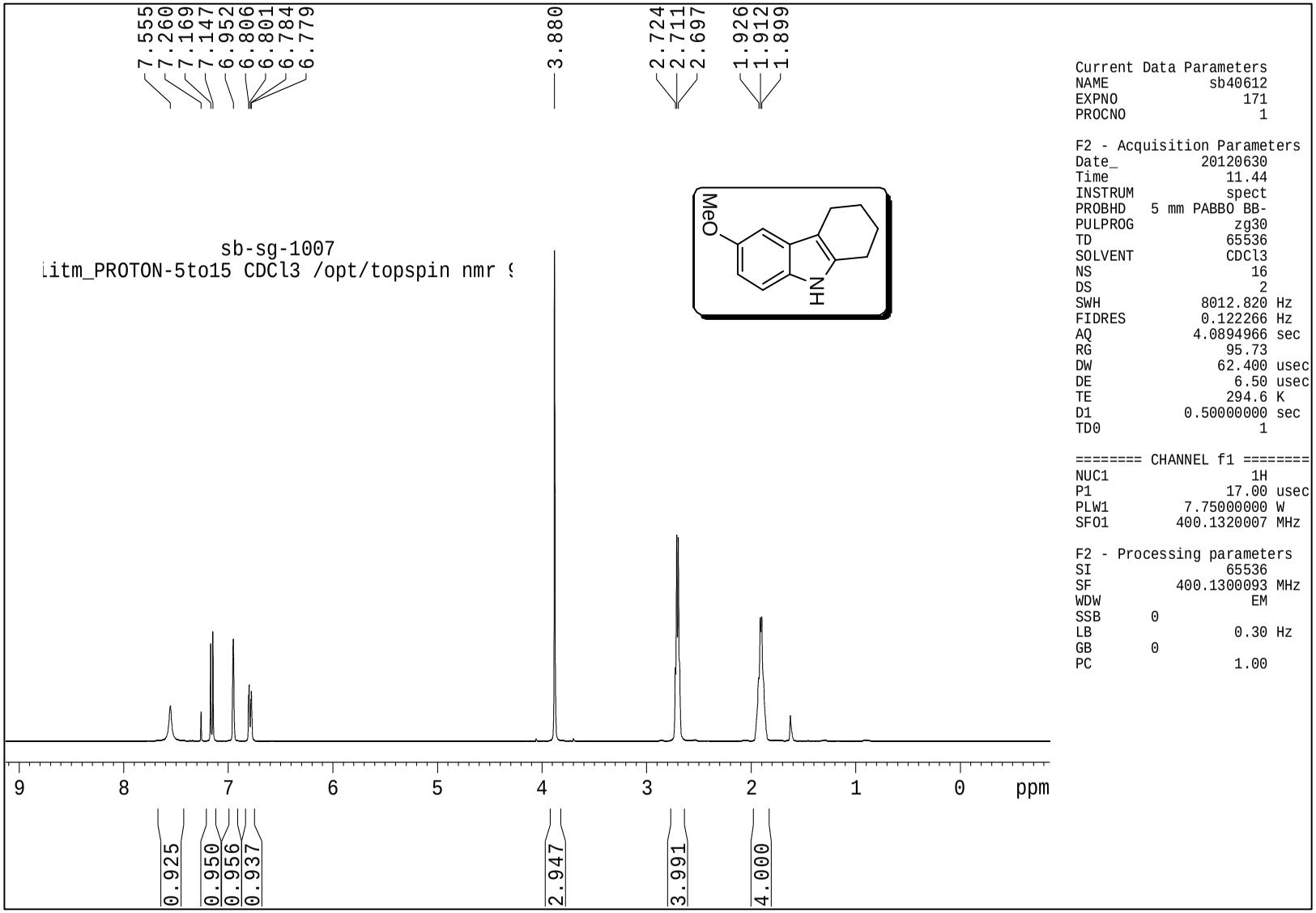
^{1}H NMR spectrum of indole derivative **12**



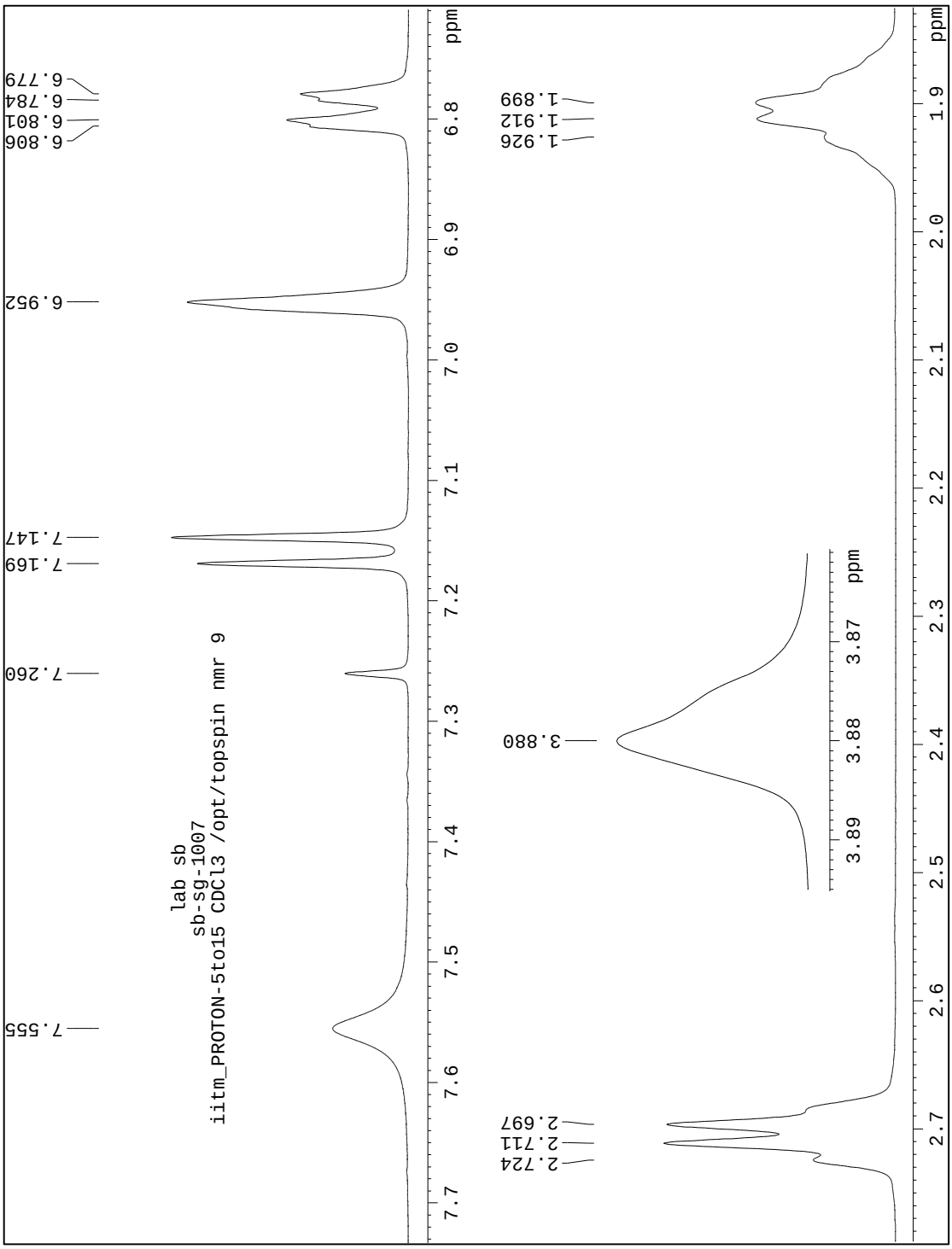
Expanded ^{1}H NMR spectrum of indole derivative **12**



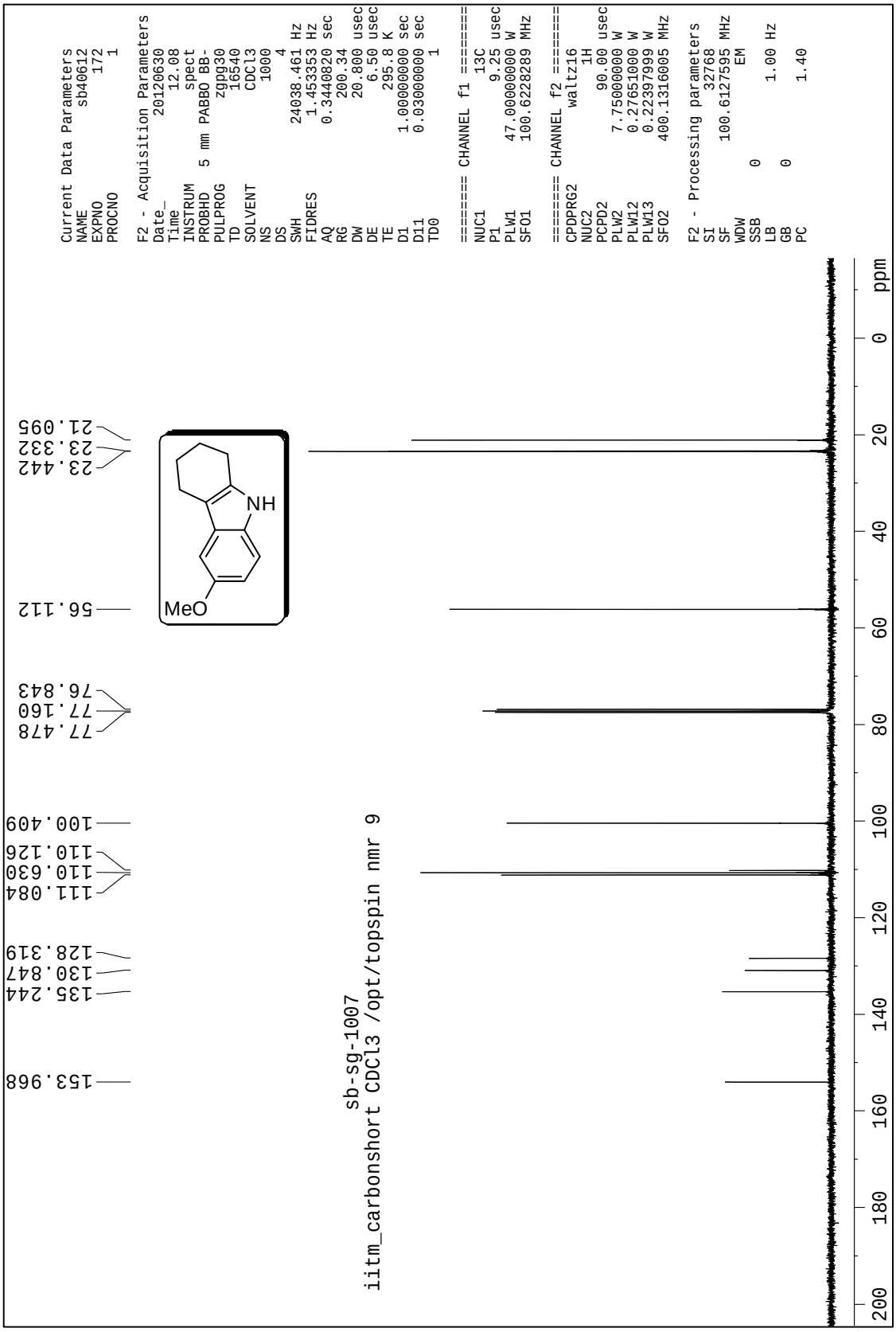
^{13}C NMR spectrum of indole derivative **12**



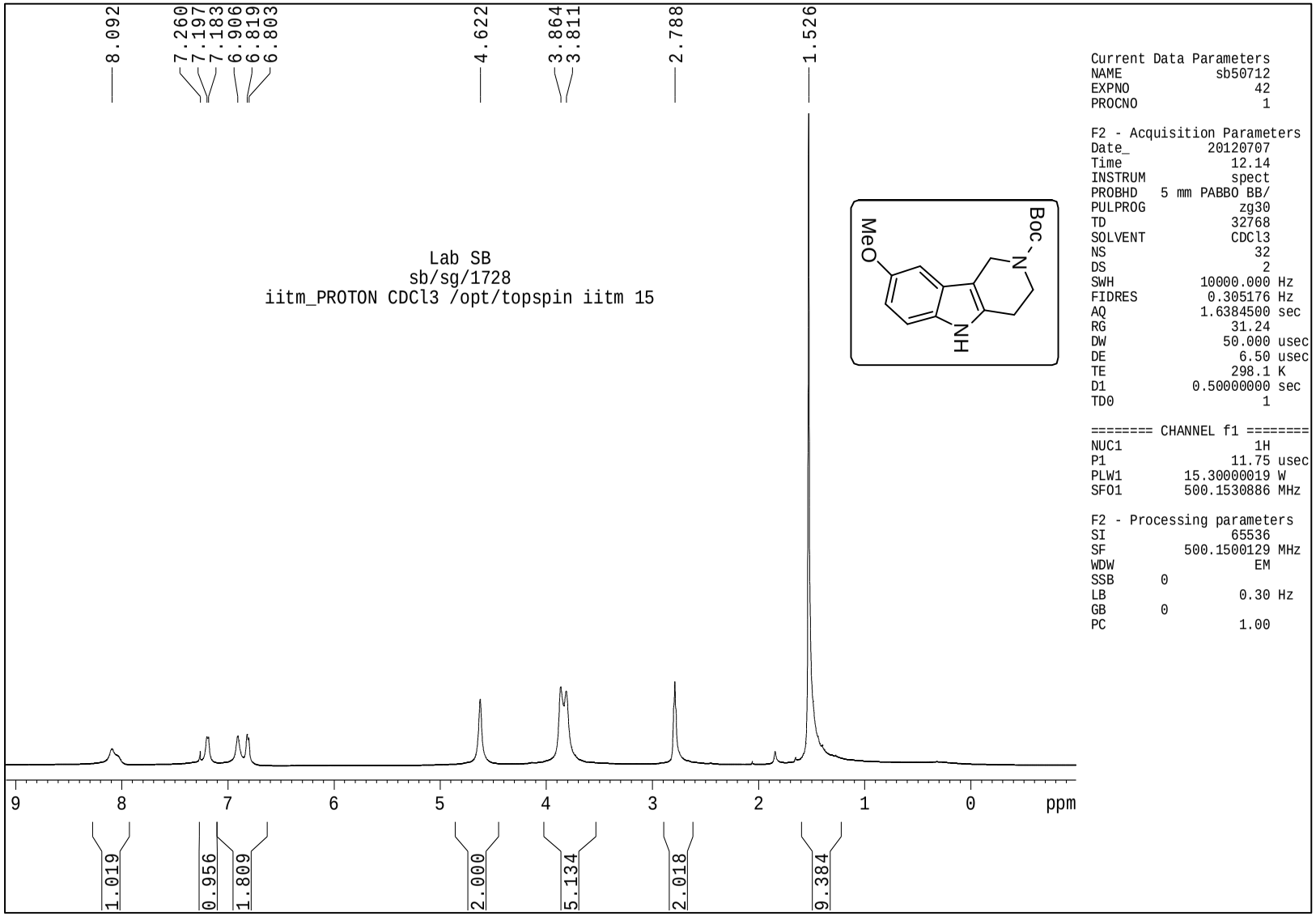
^{1}H NMR spectrum of indole derivative **13**



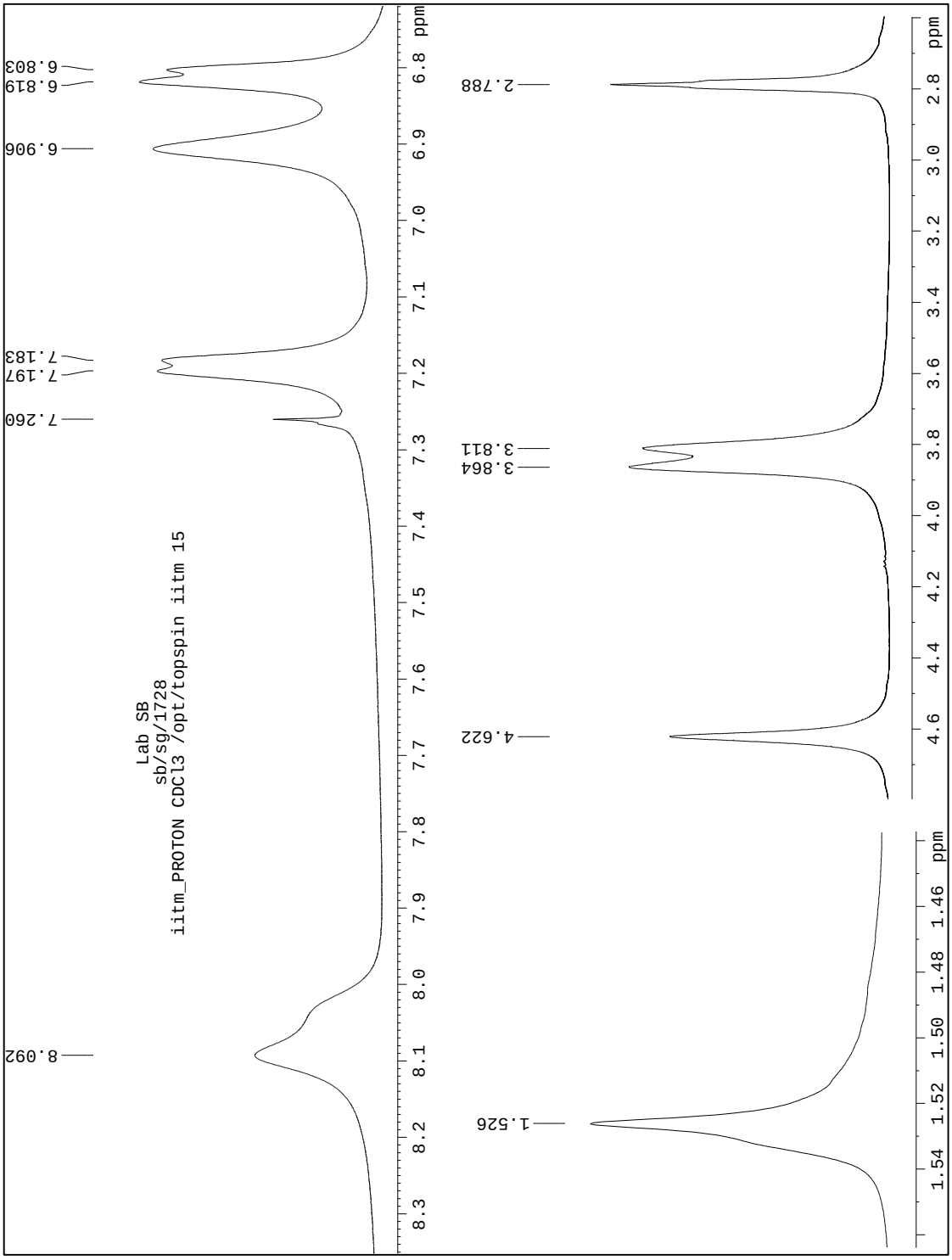
Expanded ^{1}H NMR spectrum of indole derivative **13**



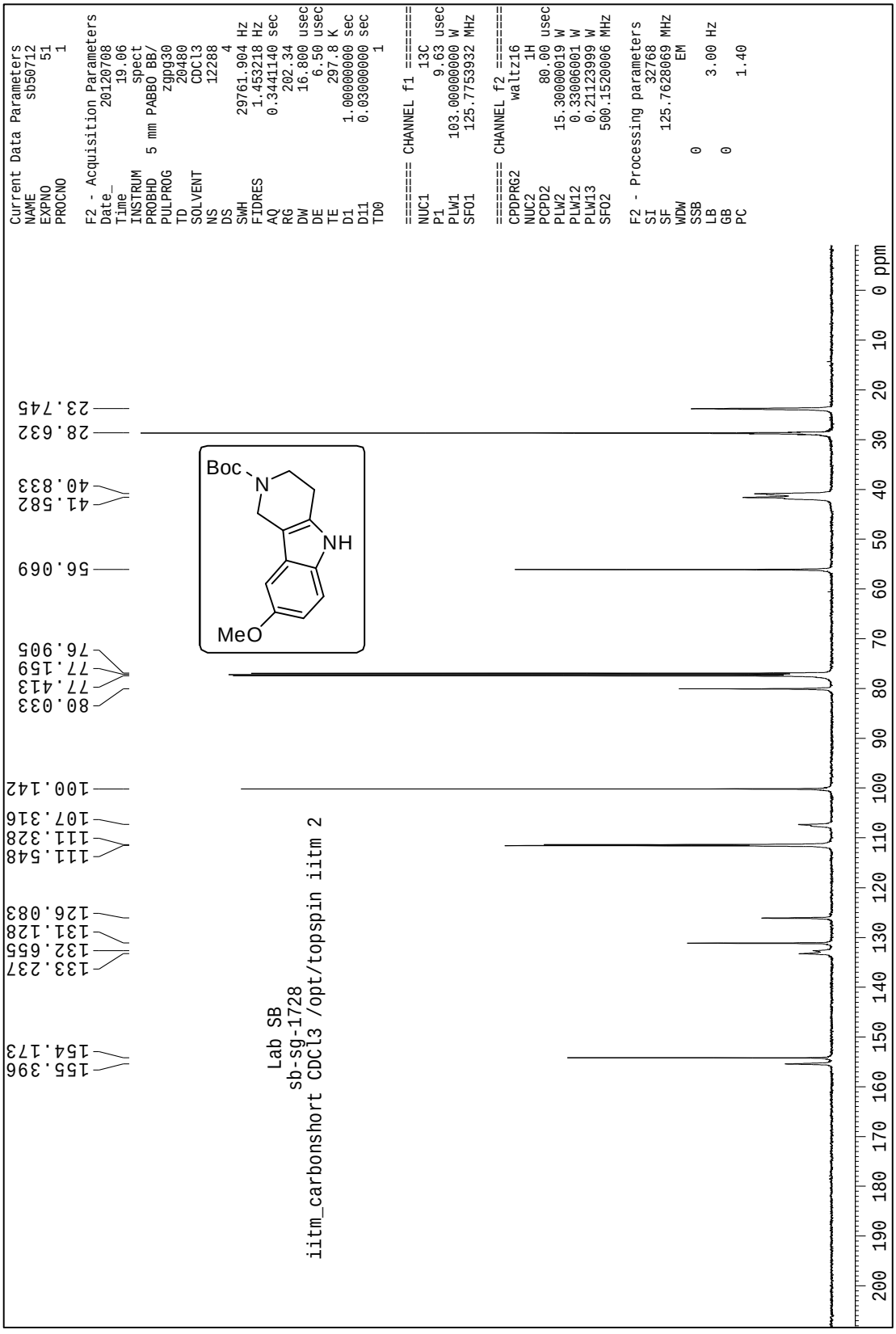
^{13}C NMR spectrum of indole derivative **13**



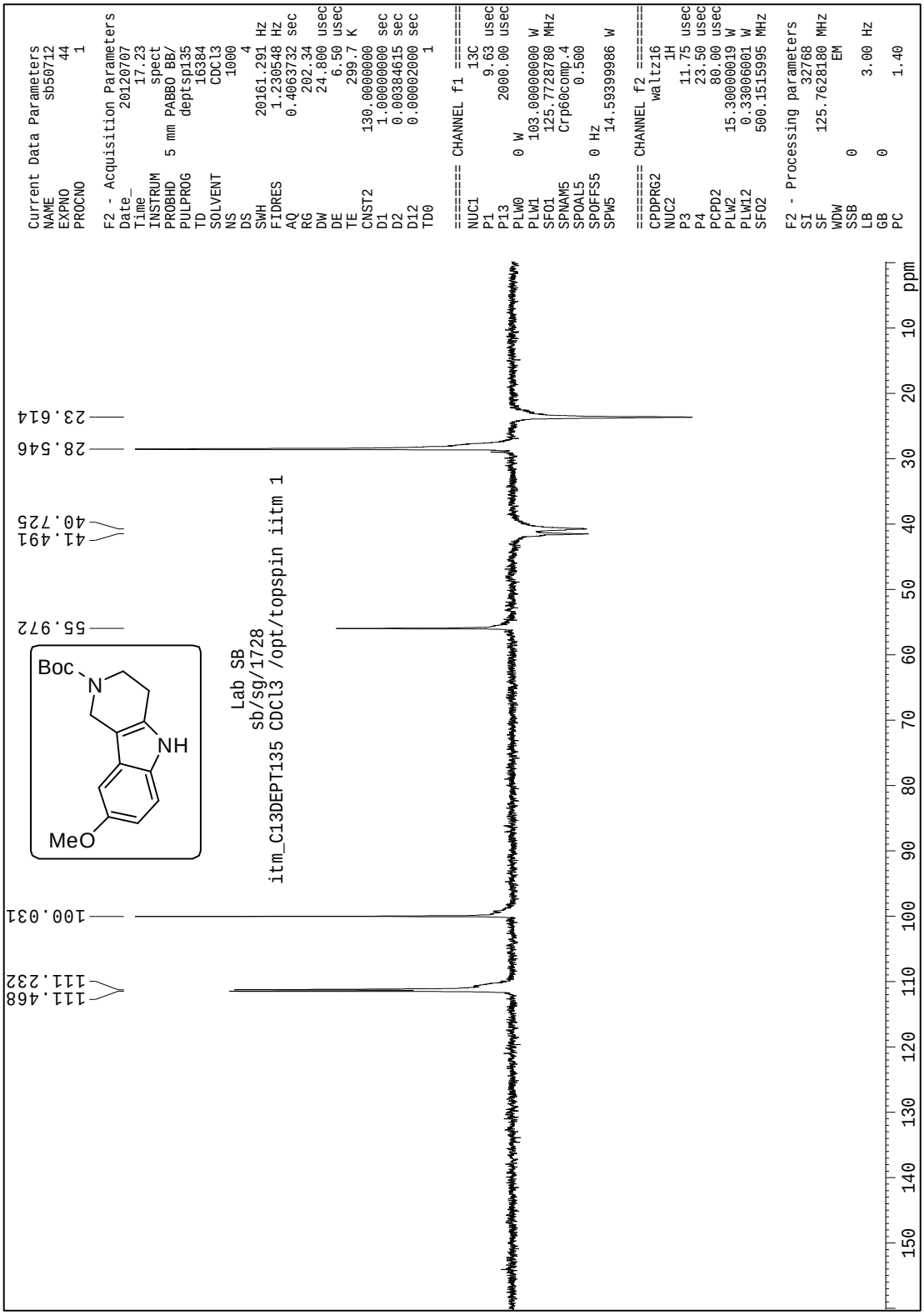
^{1}H NMR spectrum of indole derivative **14**



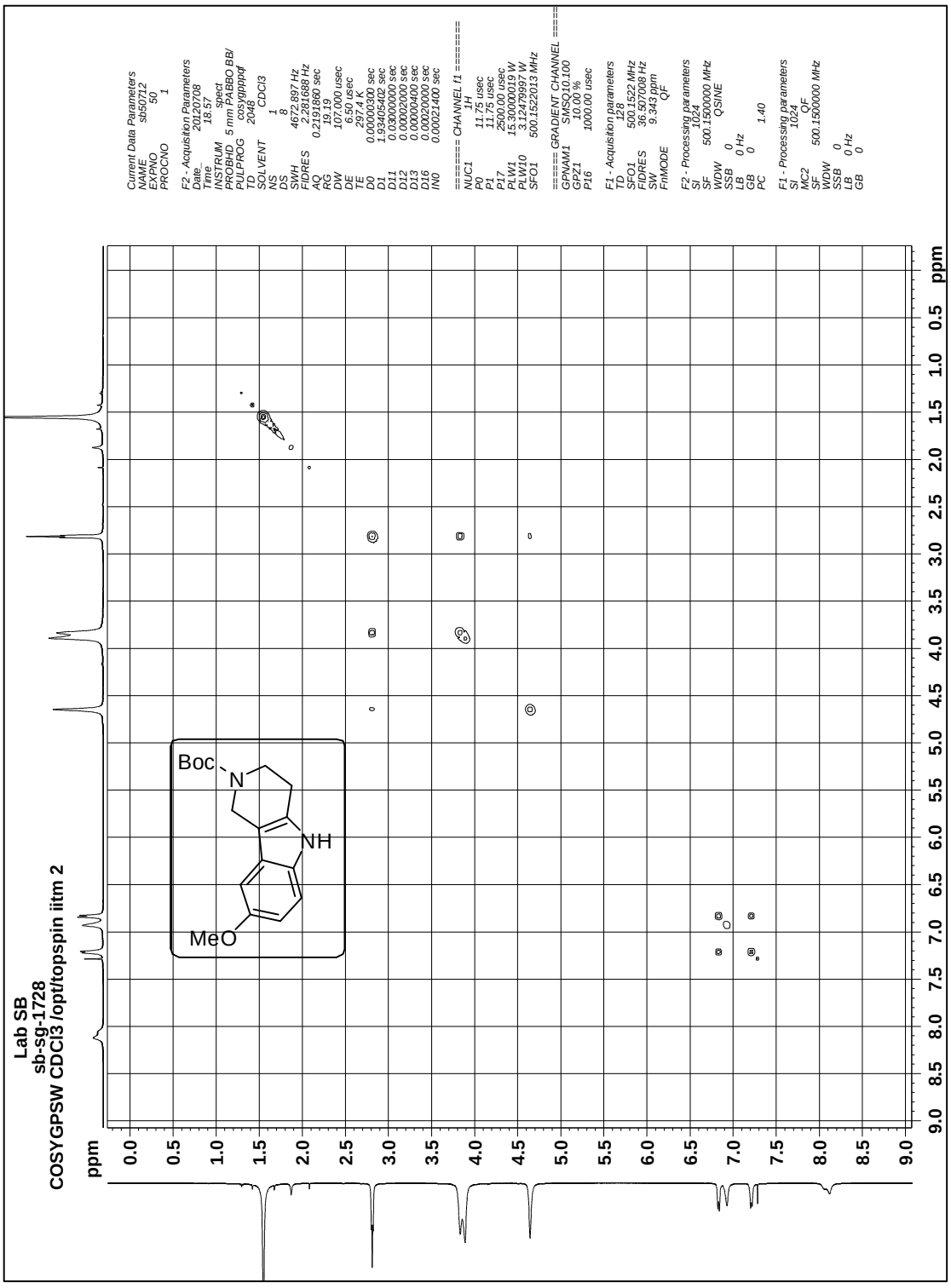
Expanded ^{1}H NMR spectrum of indole derivative **14**



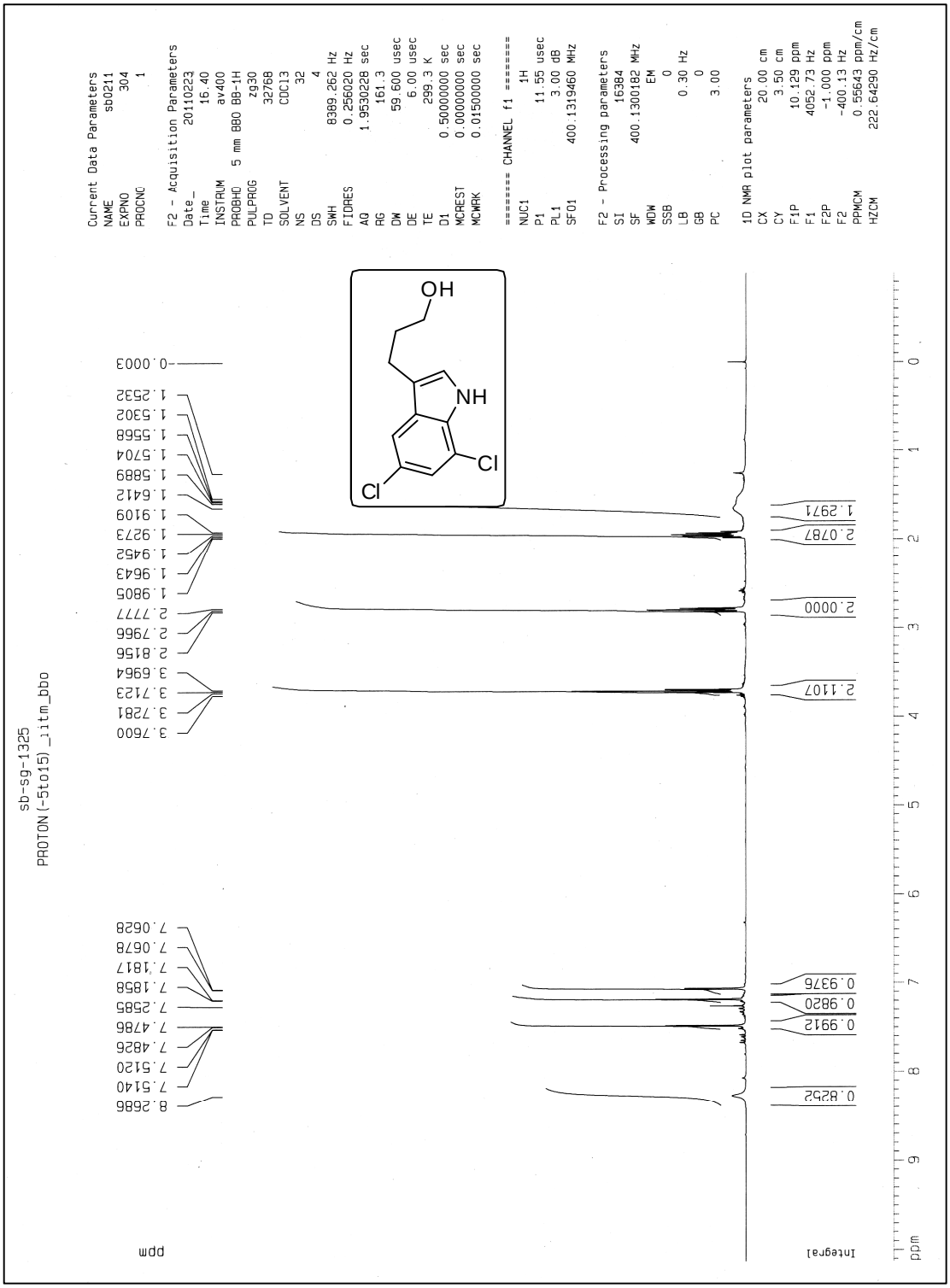
^{13}C NMR spectra of compound **14**



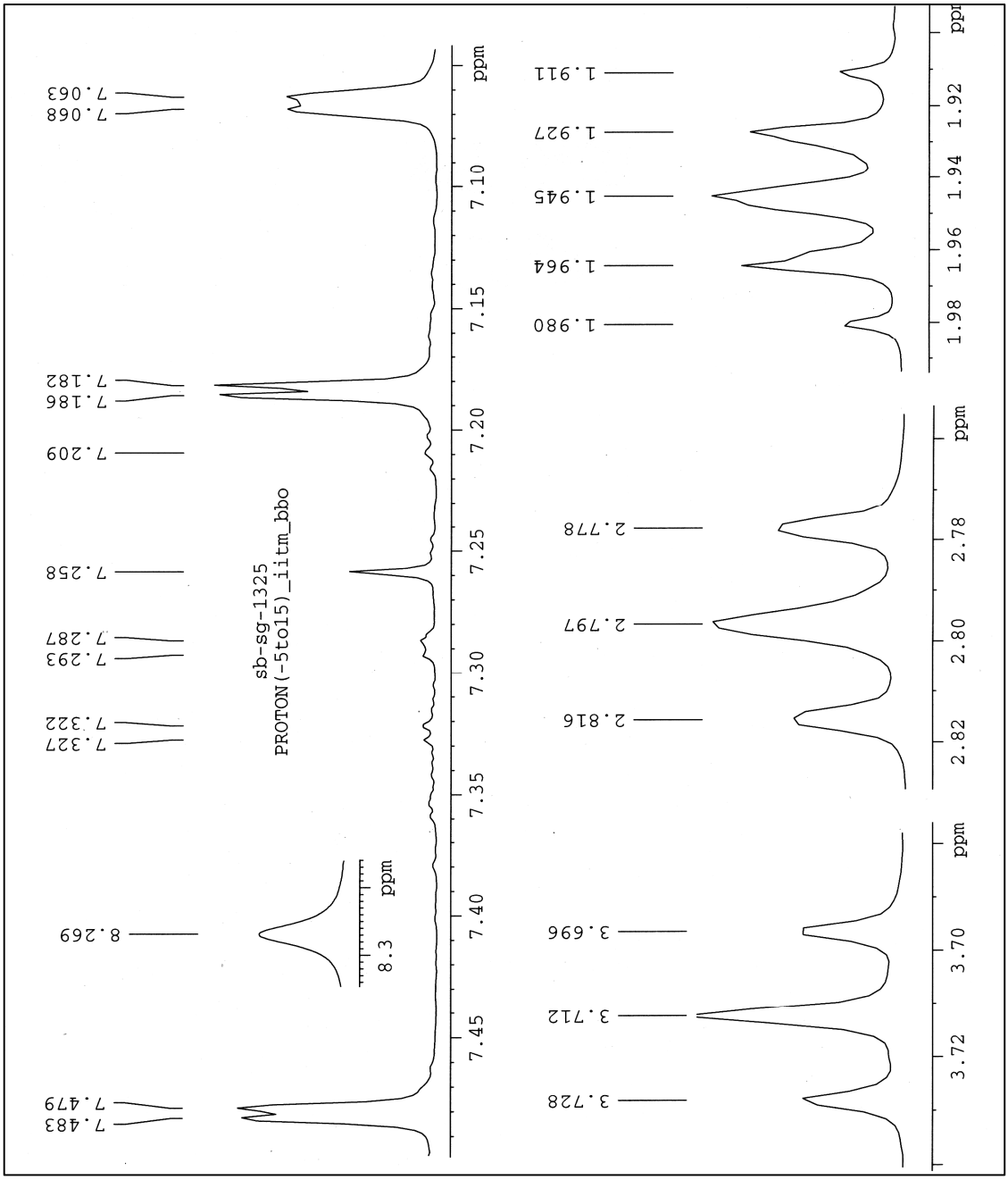
^{13}C DEPT NMR spectrum of indole derivative **14**



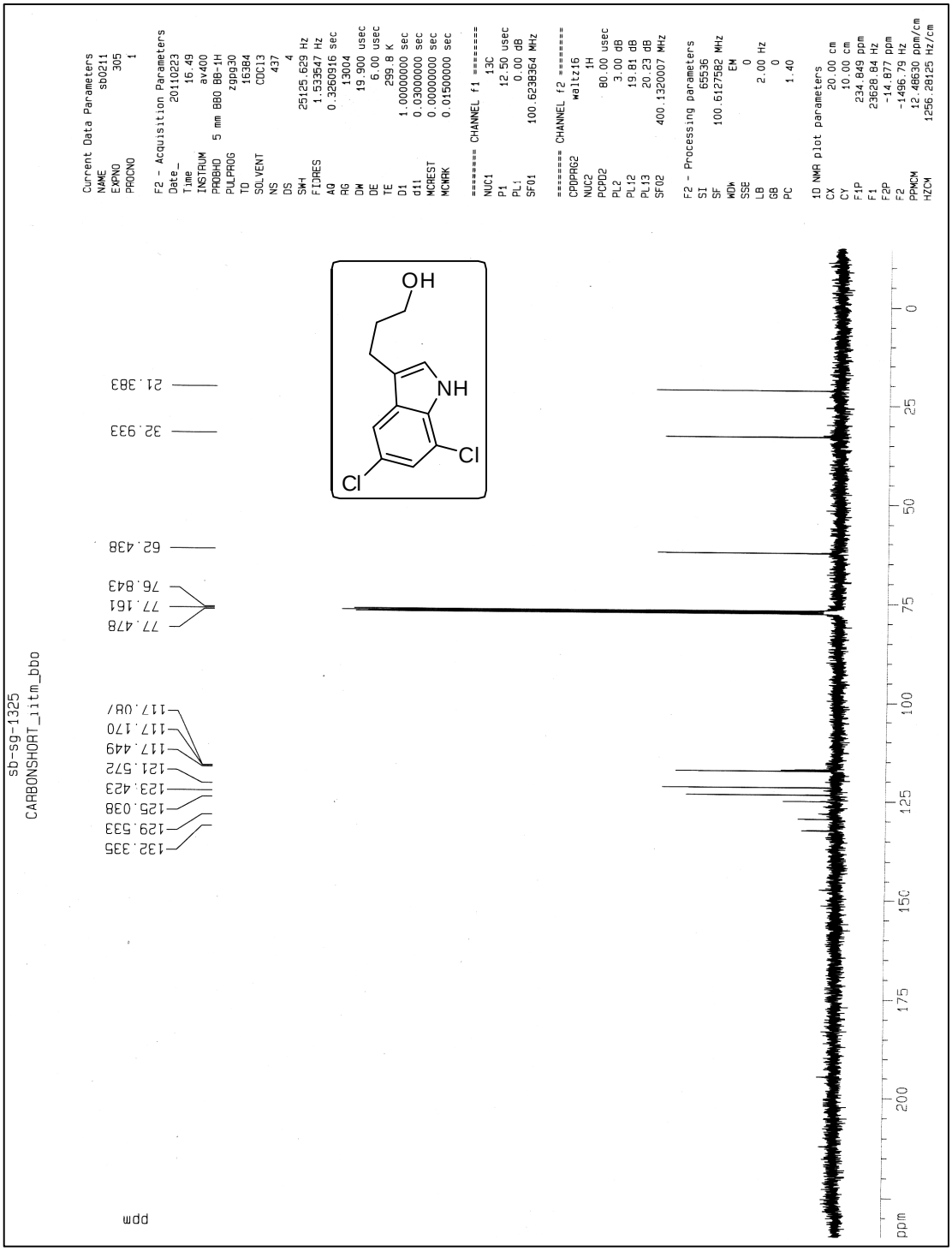
$^{1}H^{1}H$ COSY NMR spectrum of indole derivative **14**



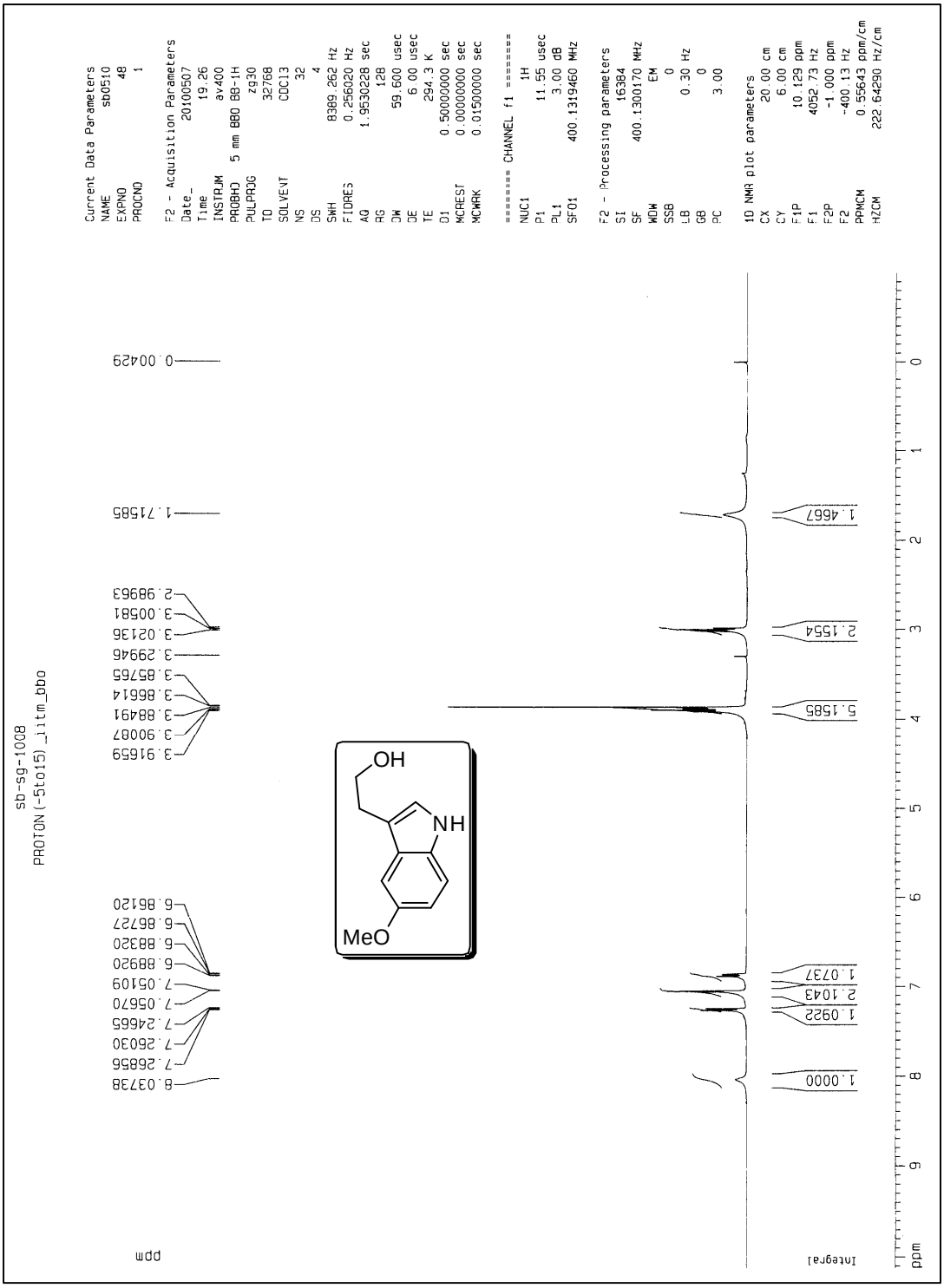
^{1}H NMR spectrum of indole derivative **15**



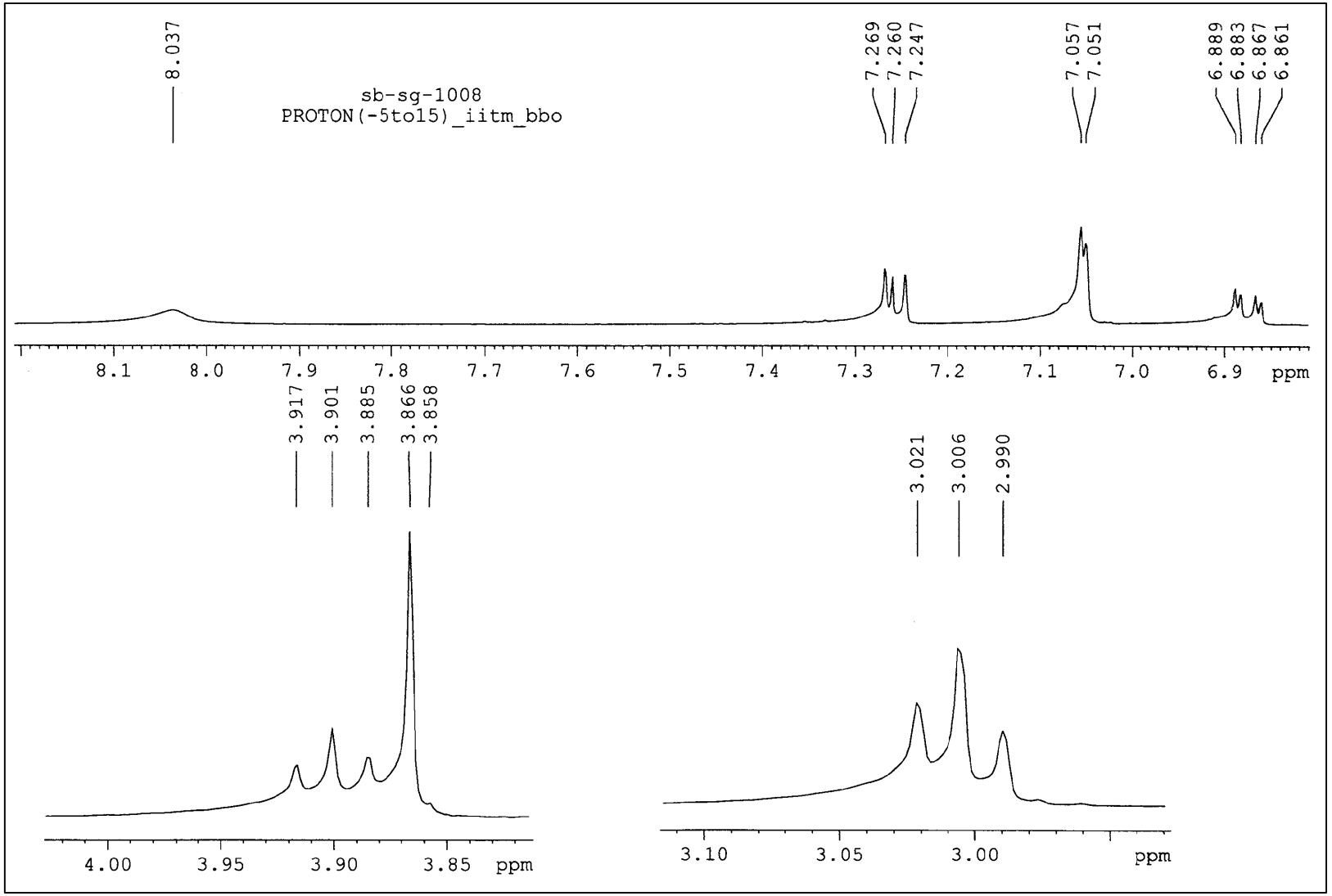
Expanded ^{1}H NMR spectrum of indole derivative **15**



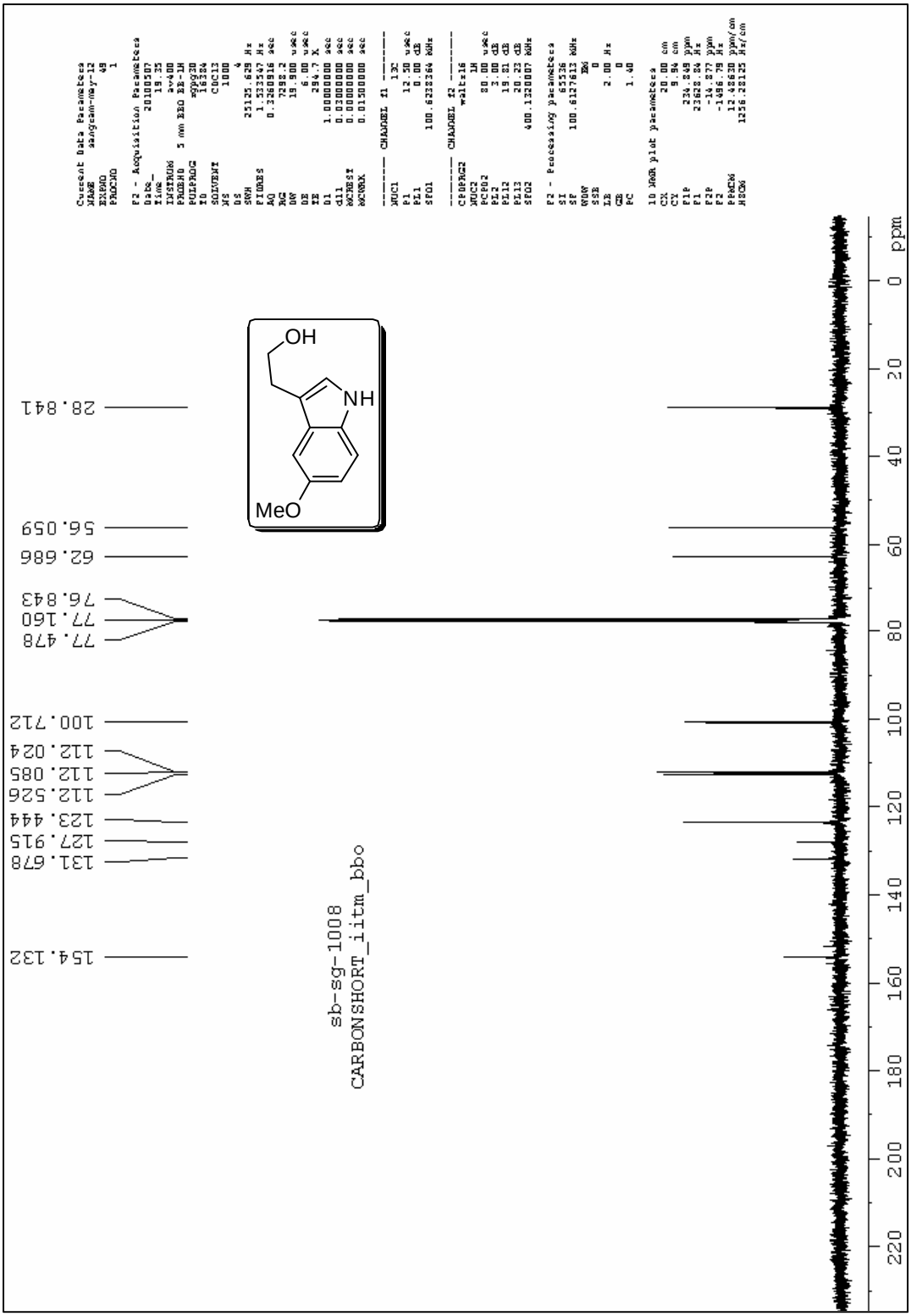
^{13}C NMR spectrum of indole derivative **15**



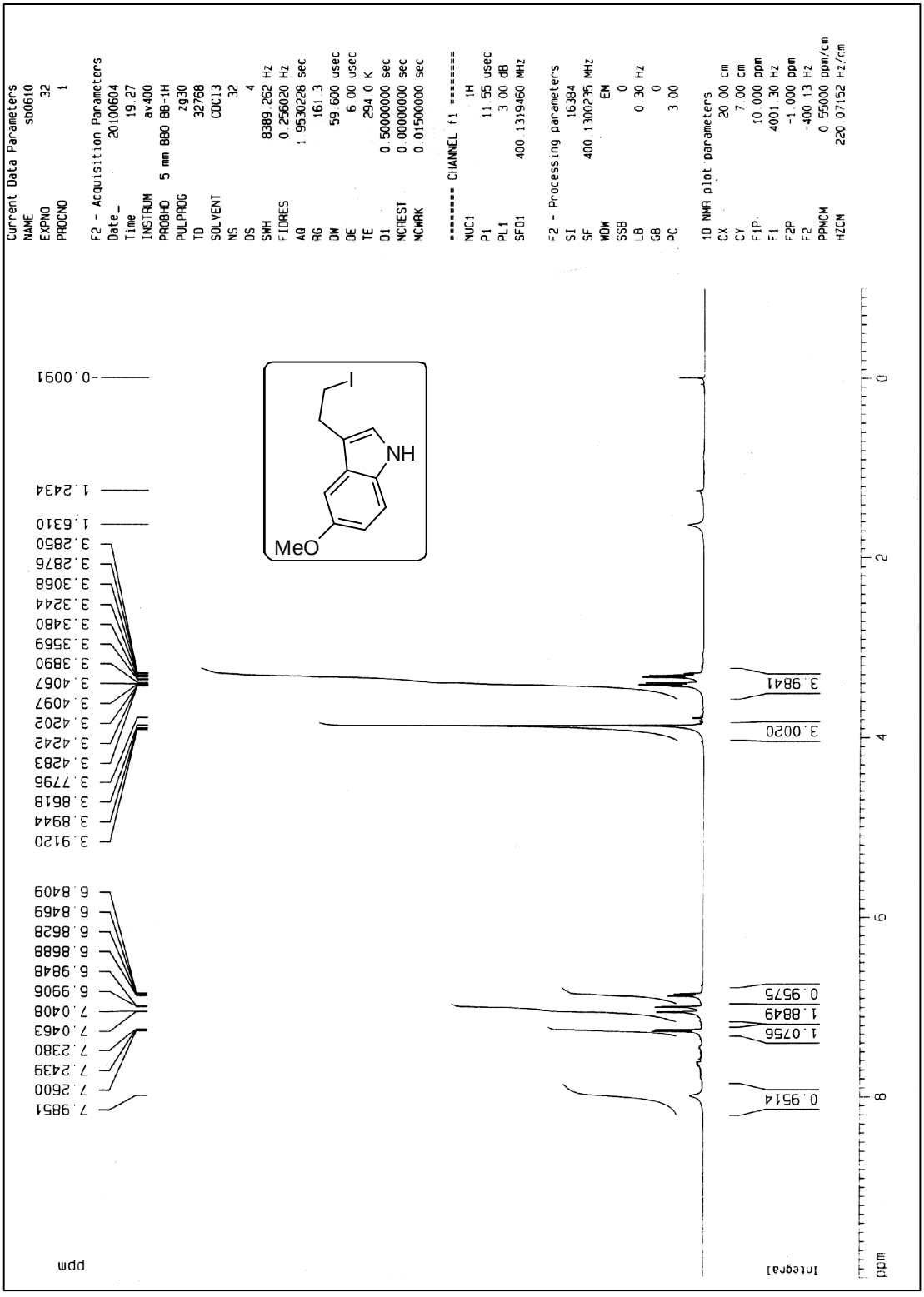
^{1}H NMR spectrum of indole derivative **16**



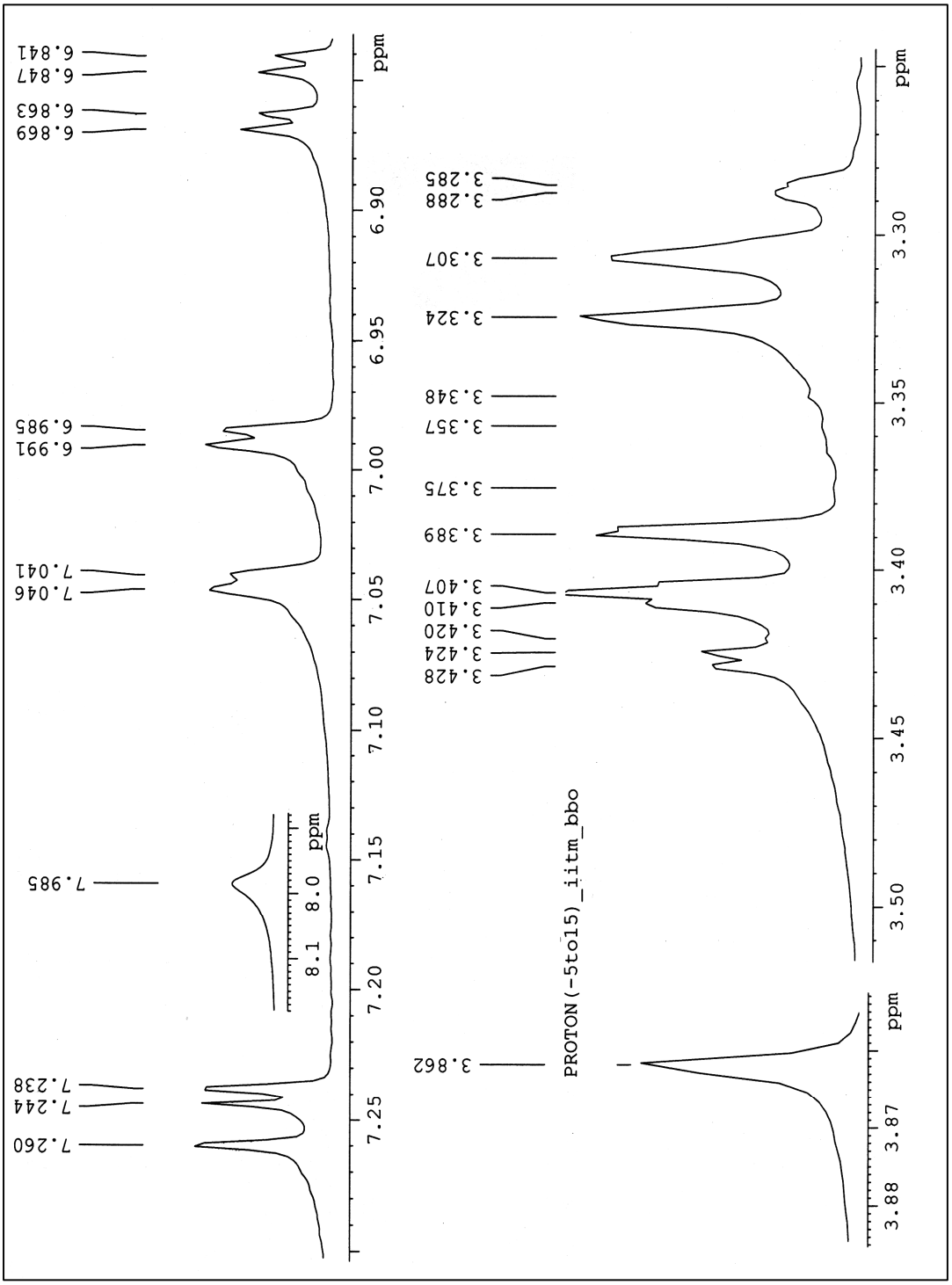
Expanded ^{1}H NMR spectrum of indole derivative **16**



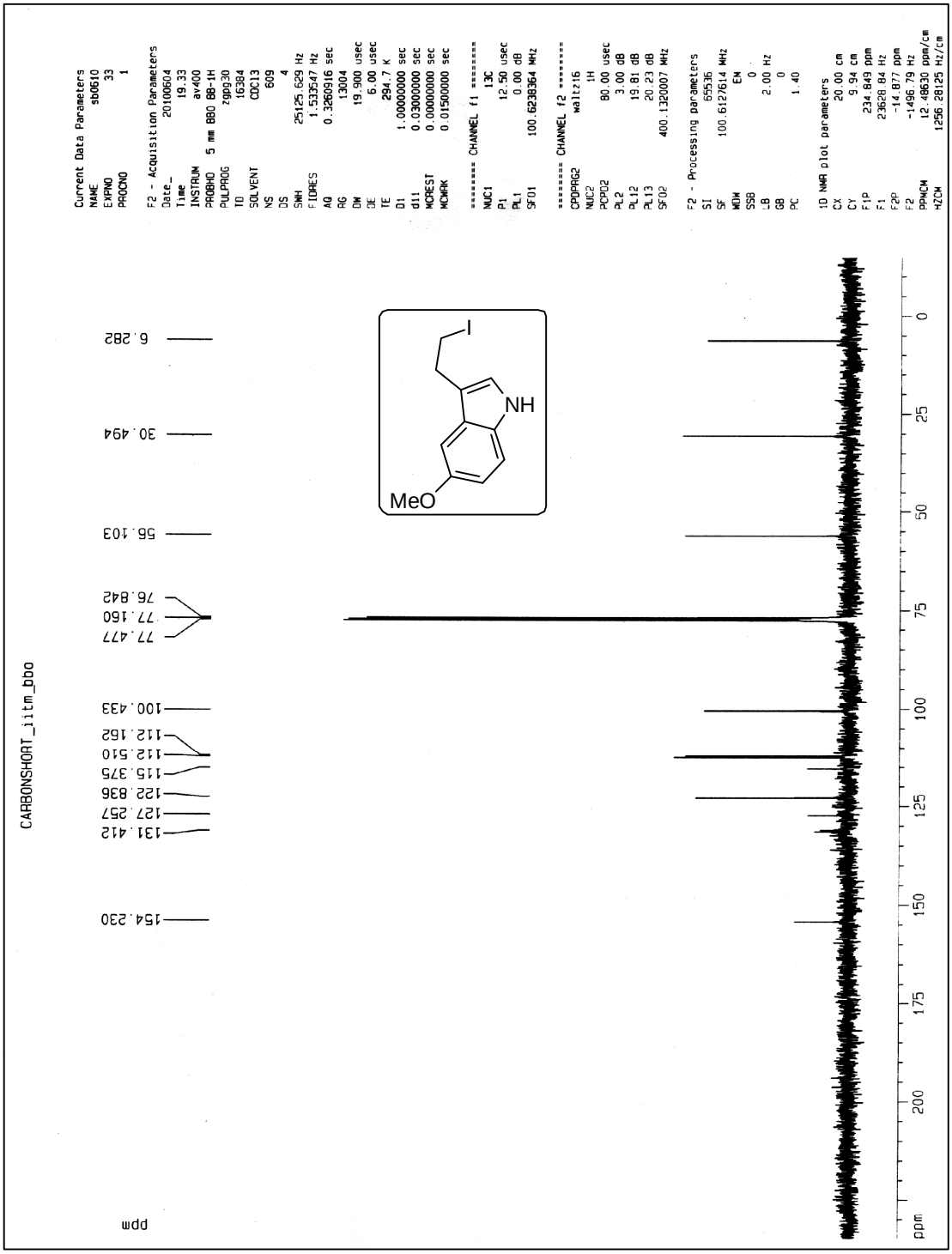
^{13}C NMR spectrum of indole derivative **16**



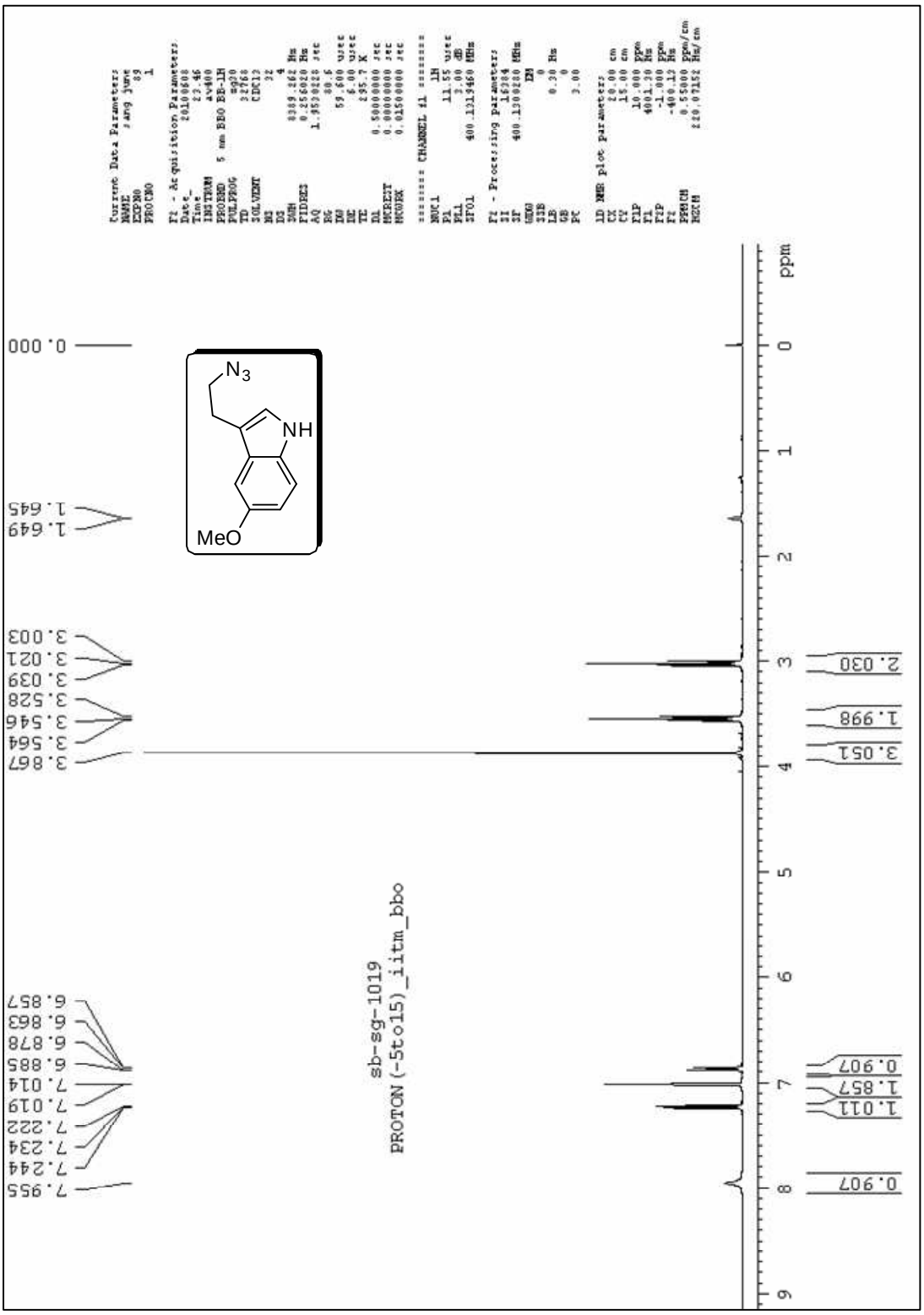
^{1}H NMR spectrum of indole derivative **16A**



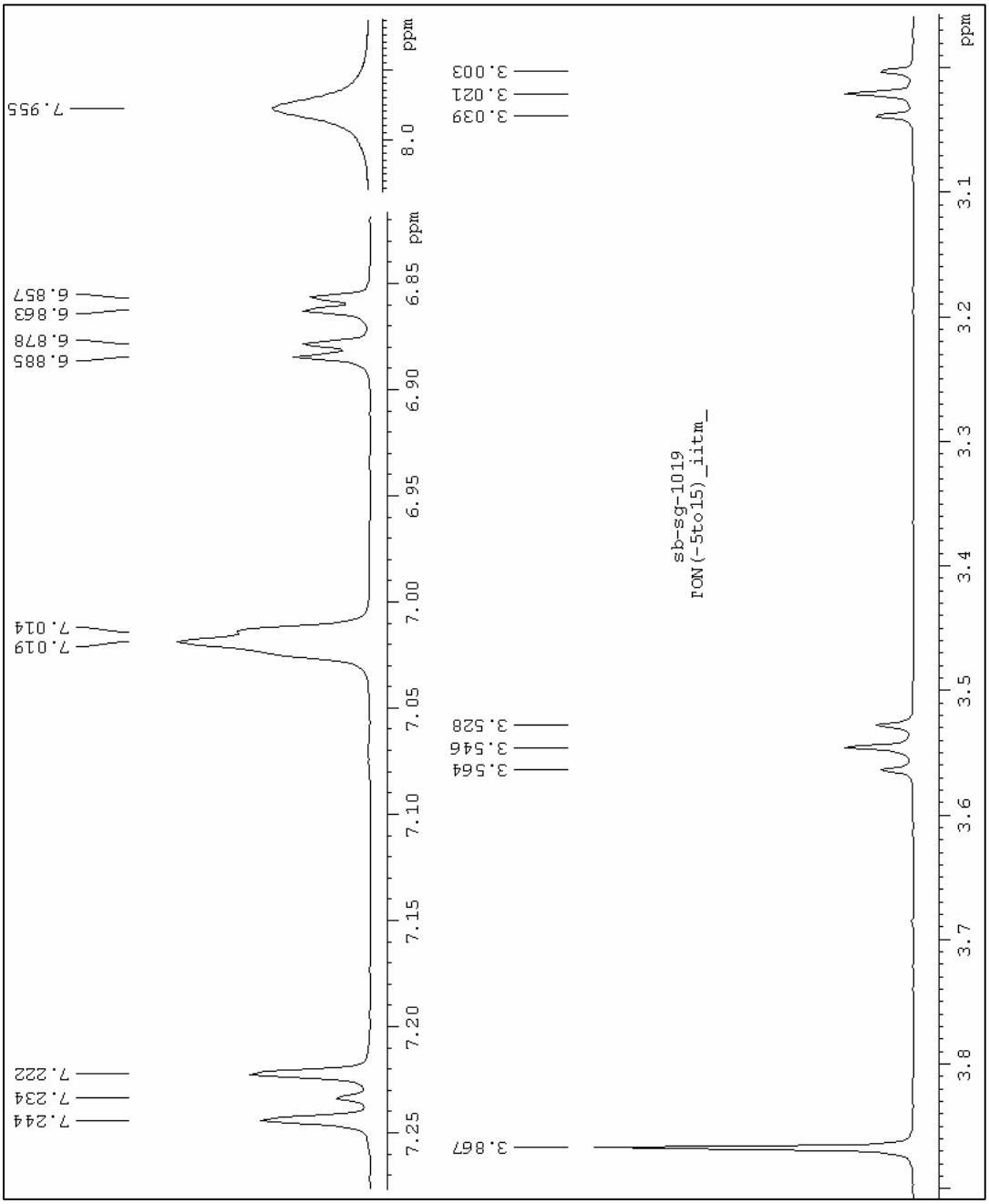
Expanded ^{1}H NMR spectrum of indole derivative **16A**



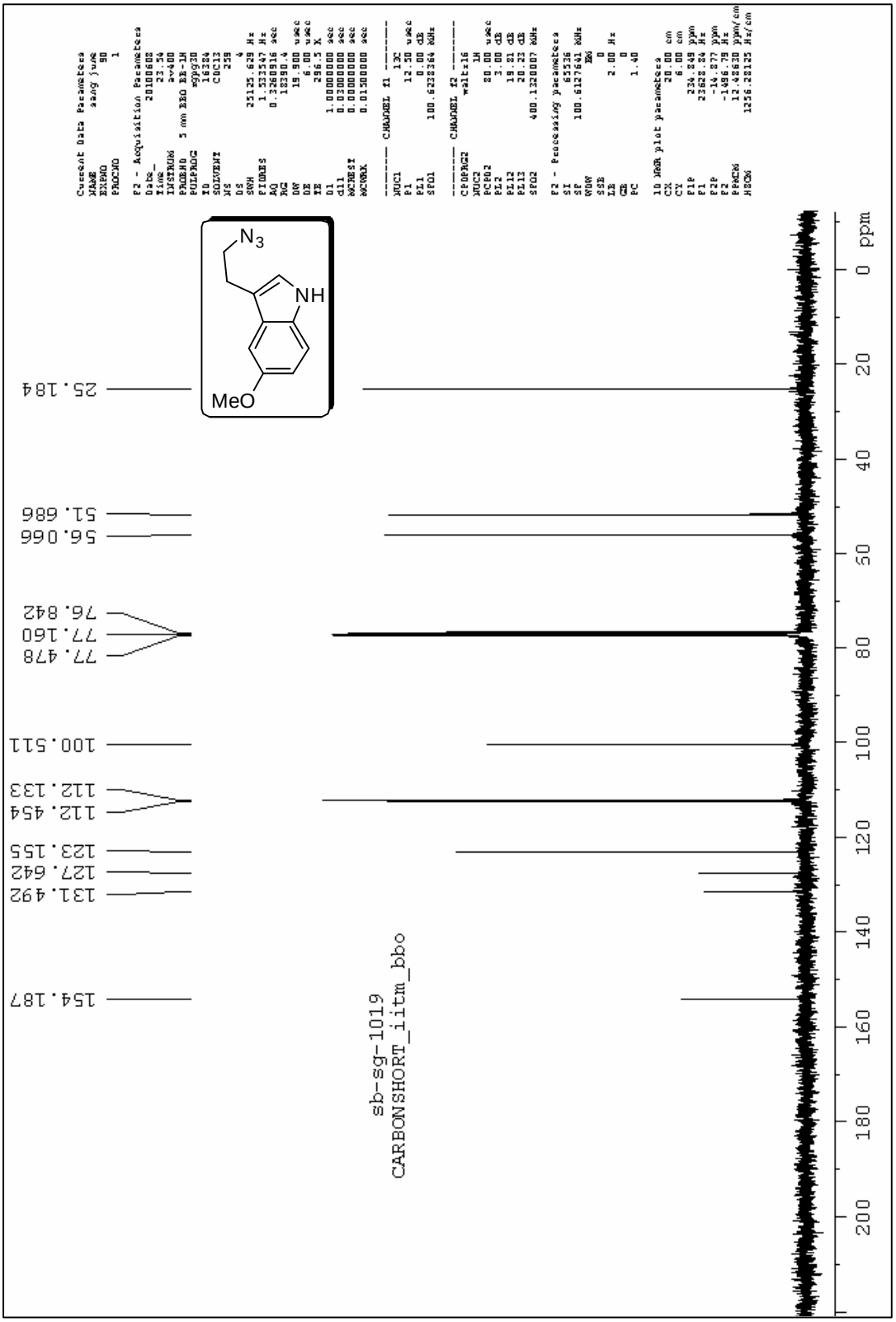
^{13}C NMR spectrum of indole derivative **16A**



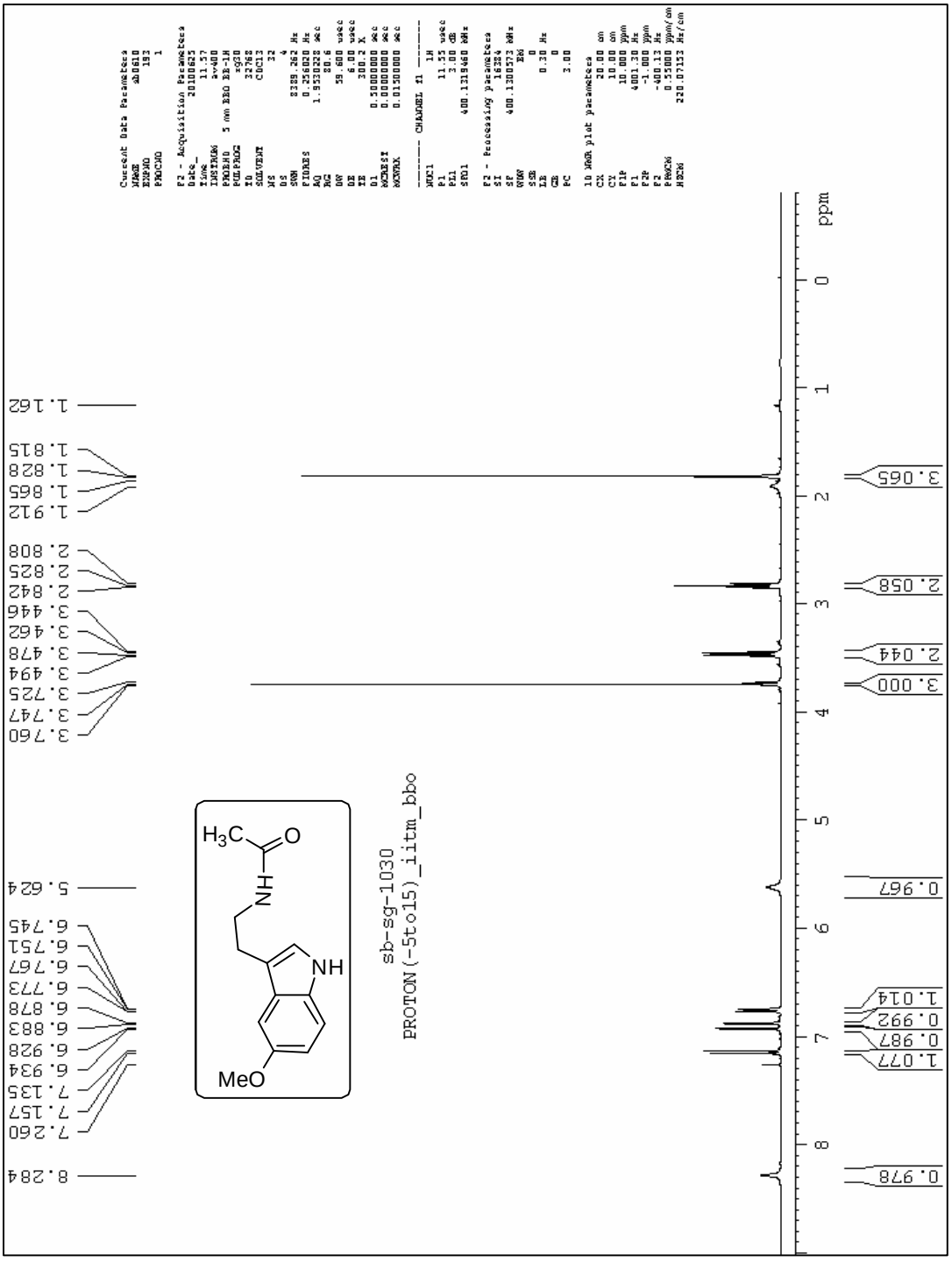
^{1}H NMR spectrum of indole derivative **16B**



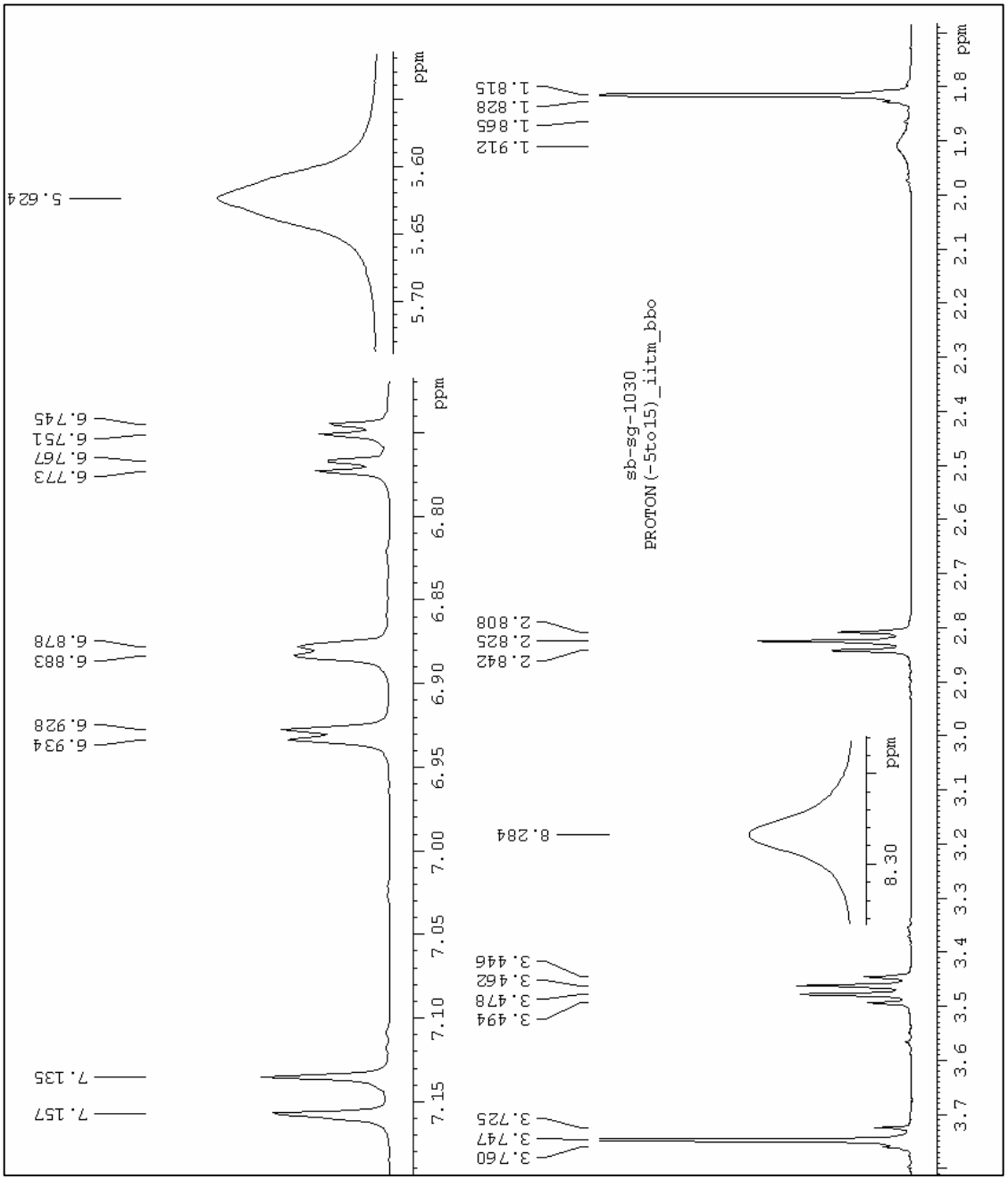
Expanded ^{1}H NMR spectrum of indole derivative **16B**



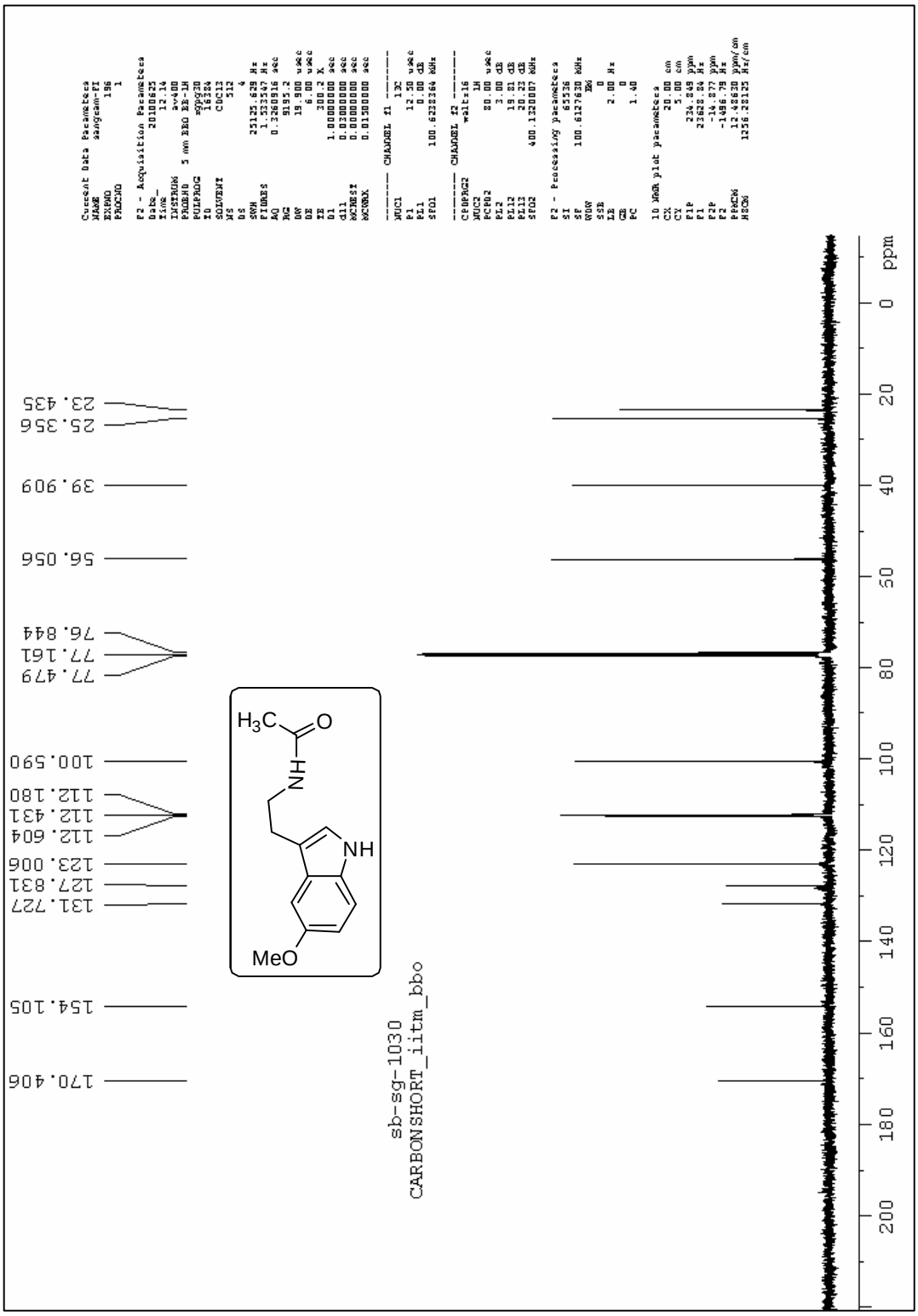
^{13}C NMR spectrum of indole derivative **16B**



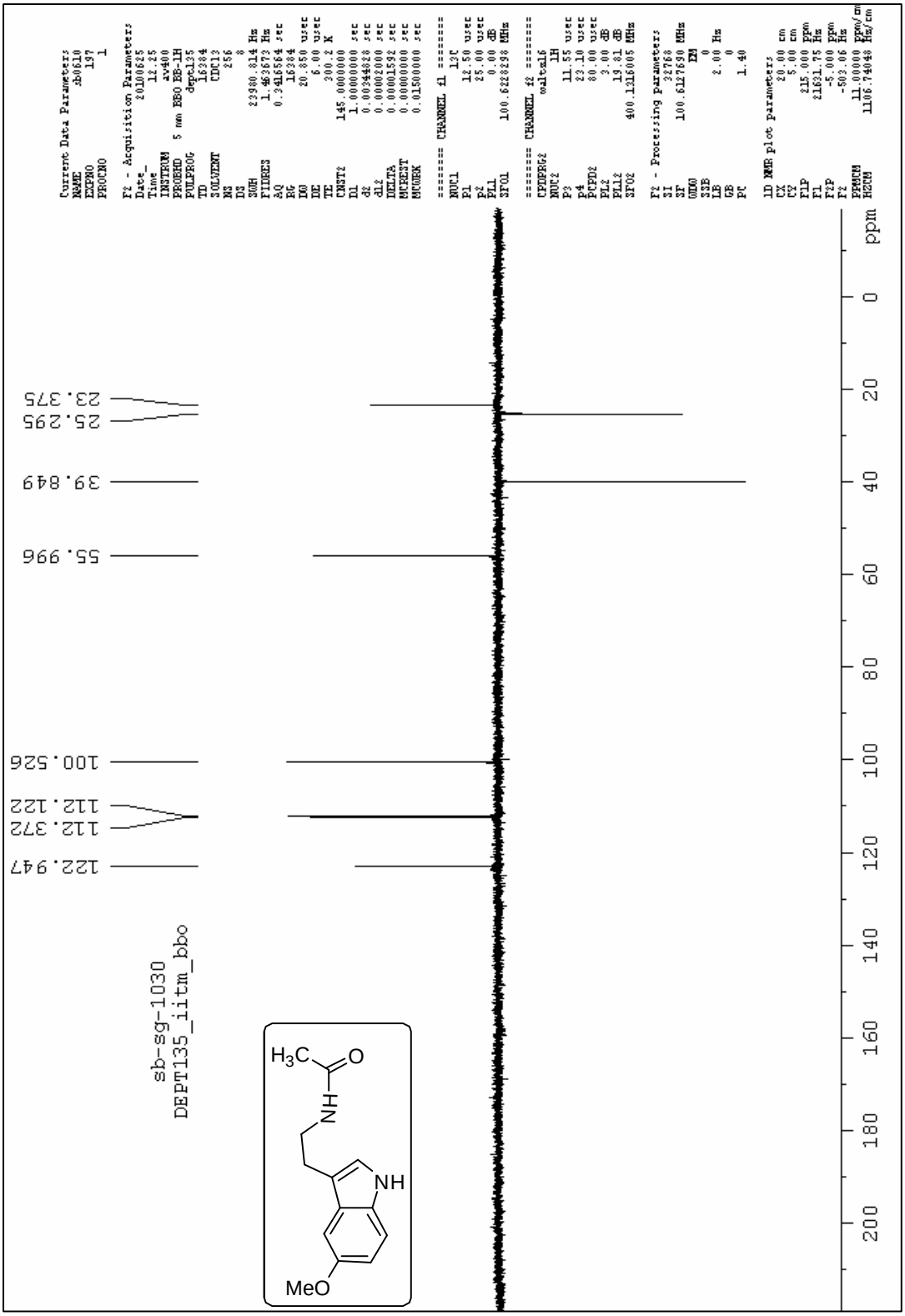
^{1}H NMR spectrum of indole derivative **IV**



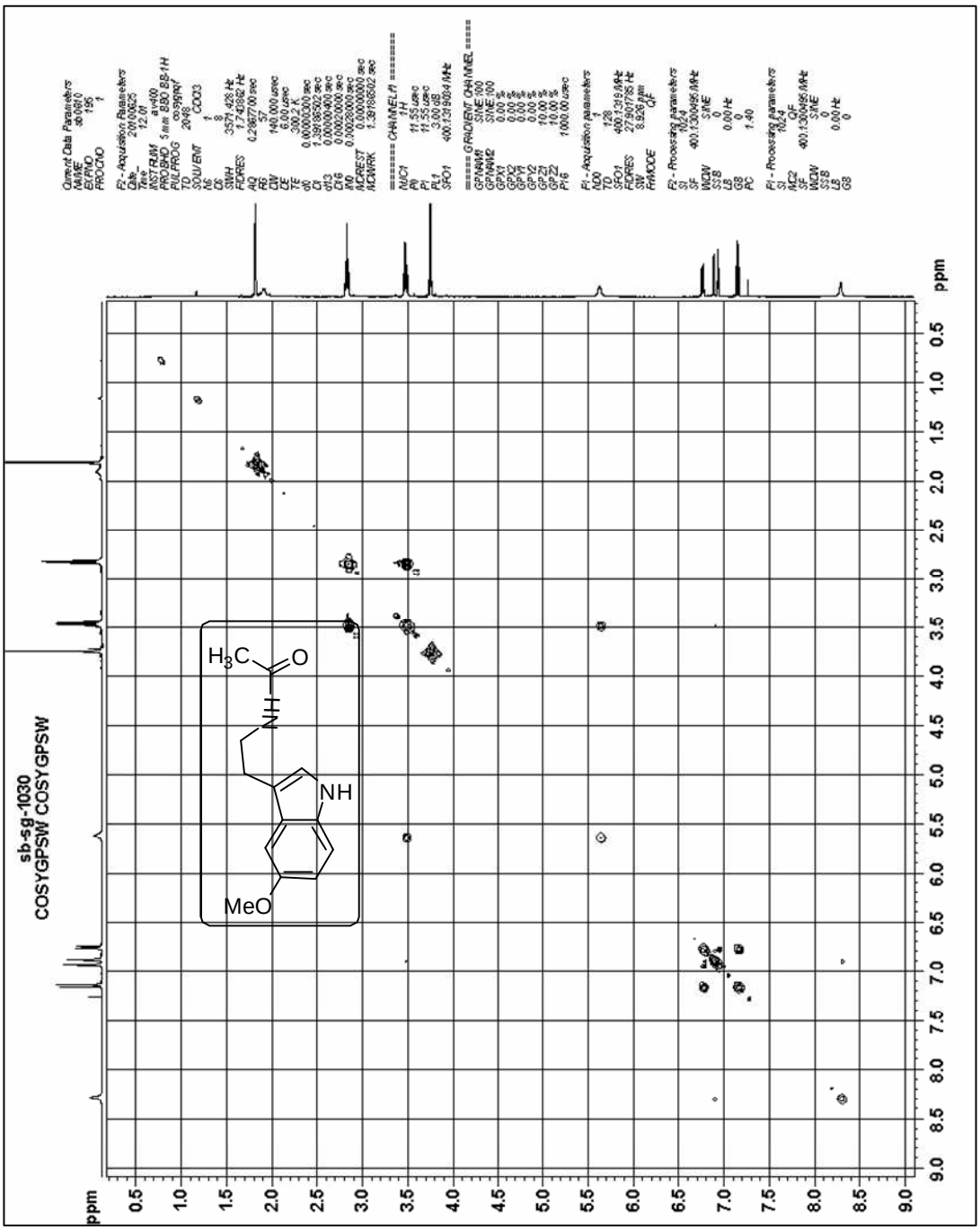
Expanded ^{1}H NMR spectrum of indole derivative **IV**



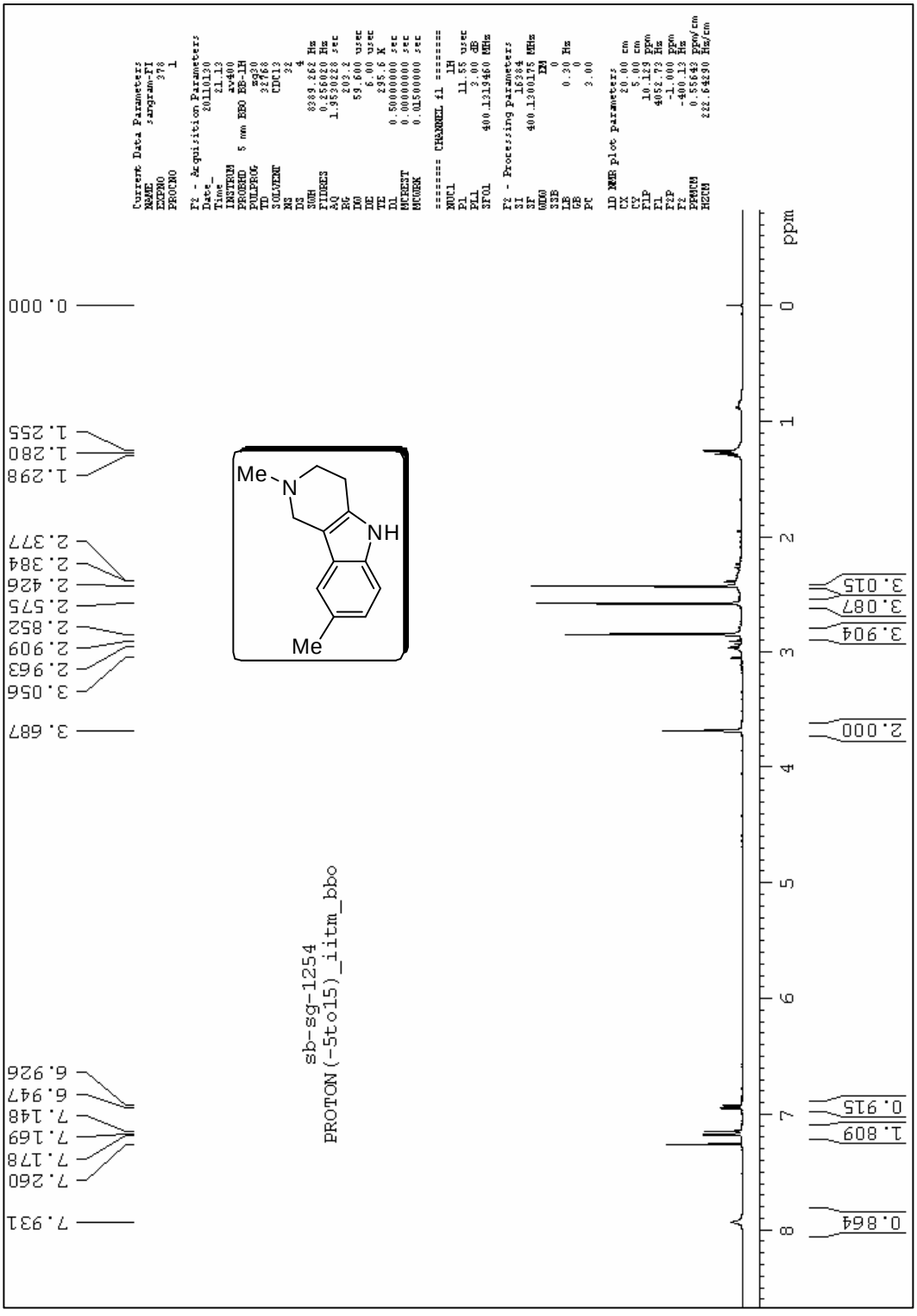
^{13}C NMR spectrum of indole derivative **IV**



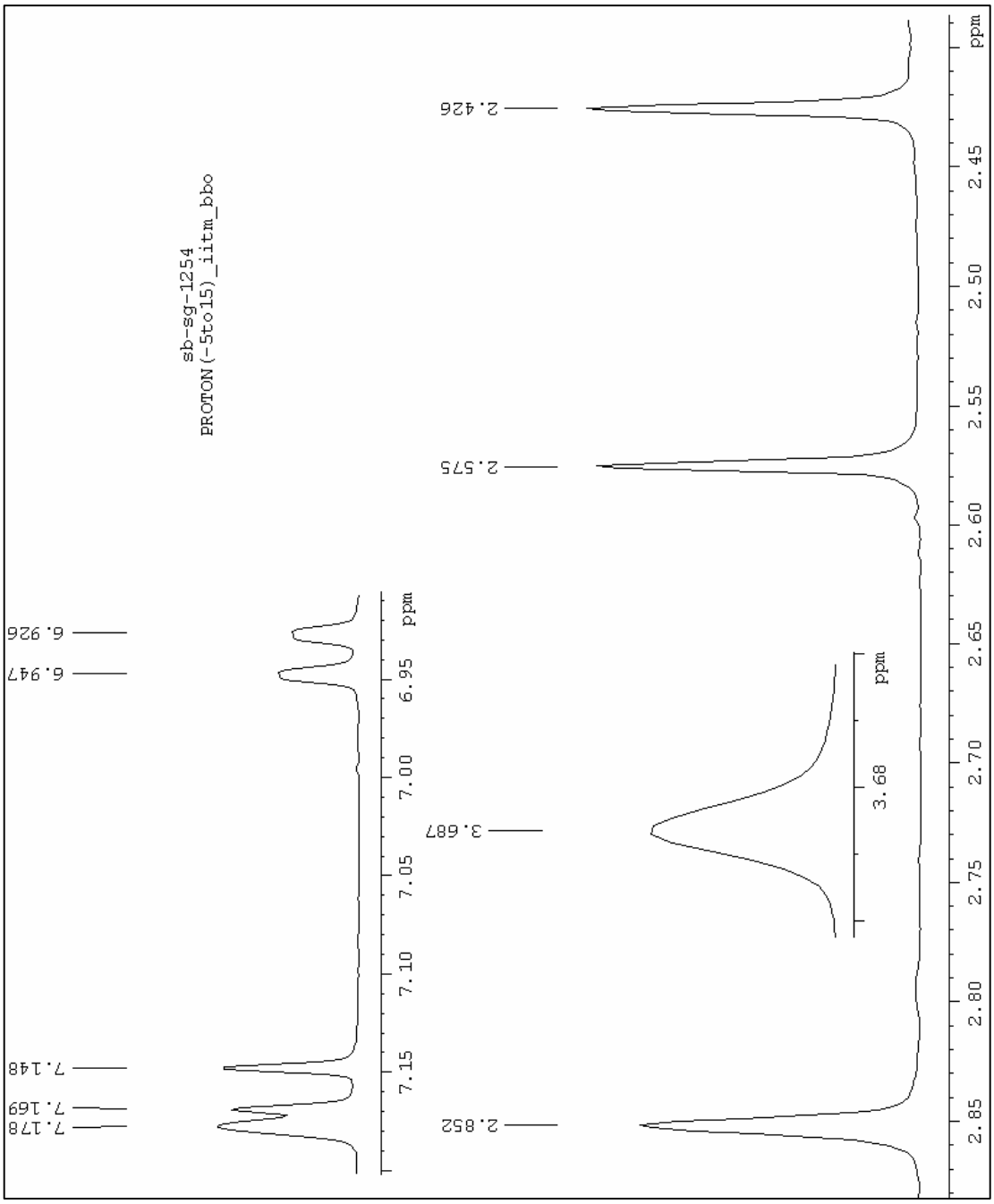
^{13}C DEPT NMR spectrum of indole derivative **IV**



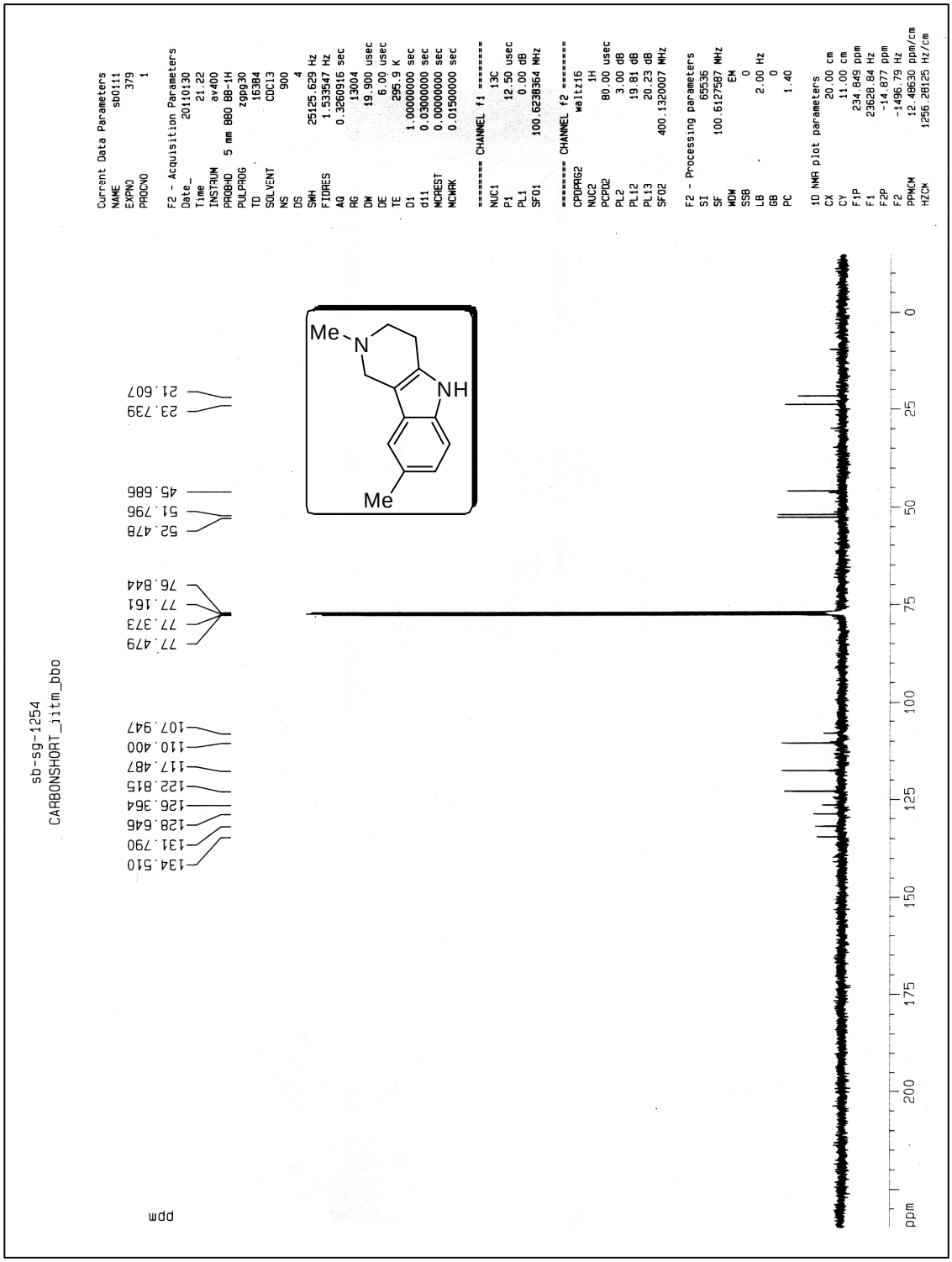
$^{1}H^{1}H$ COSY NMR spectrum of indole derivative **IV**



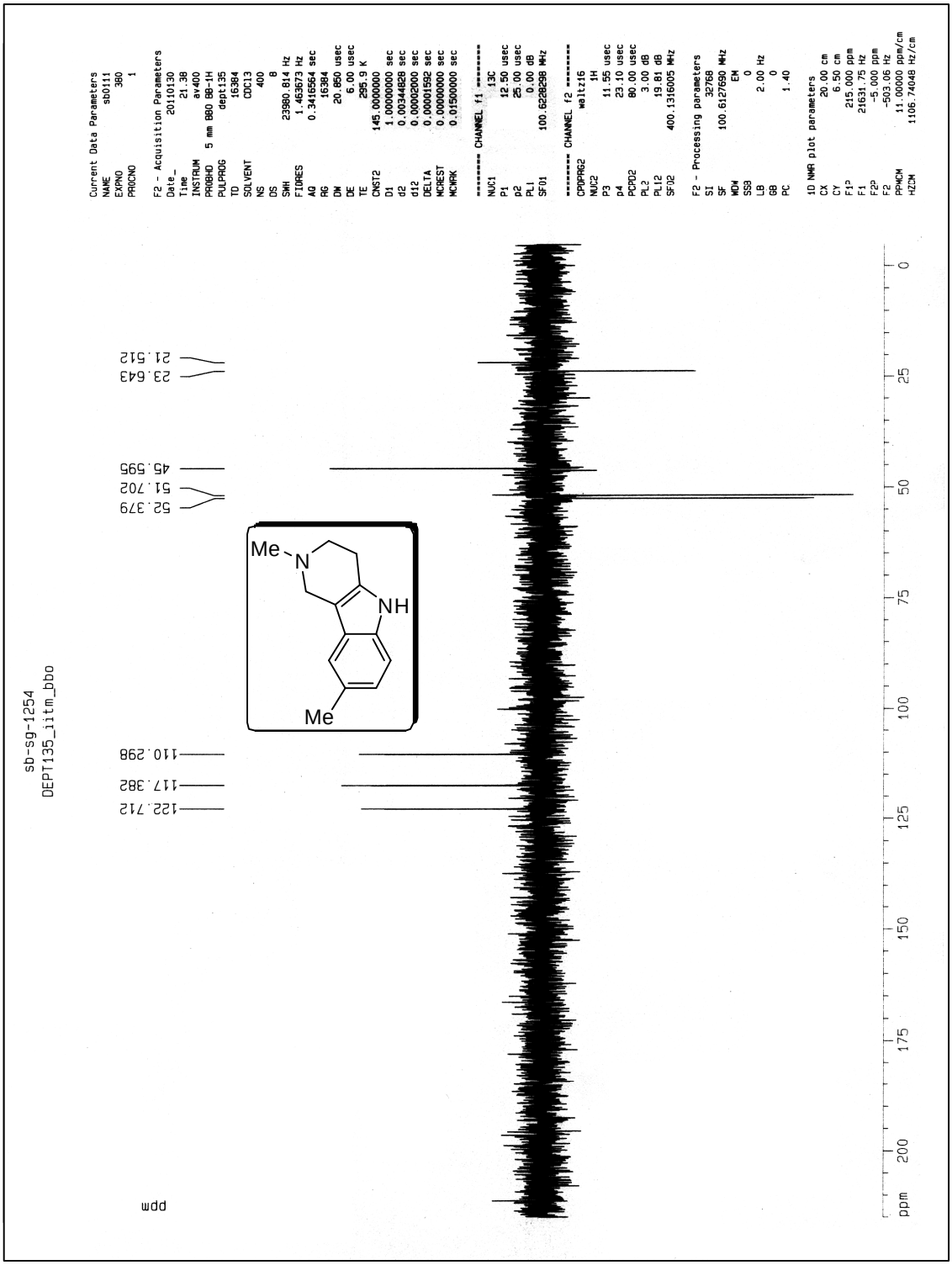
^{1}H NMR spectrum of indole derivative **17**



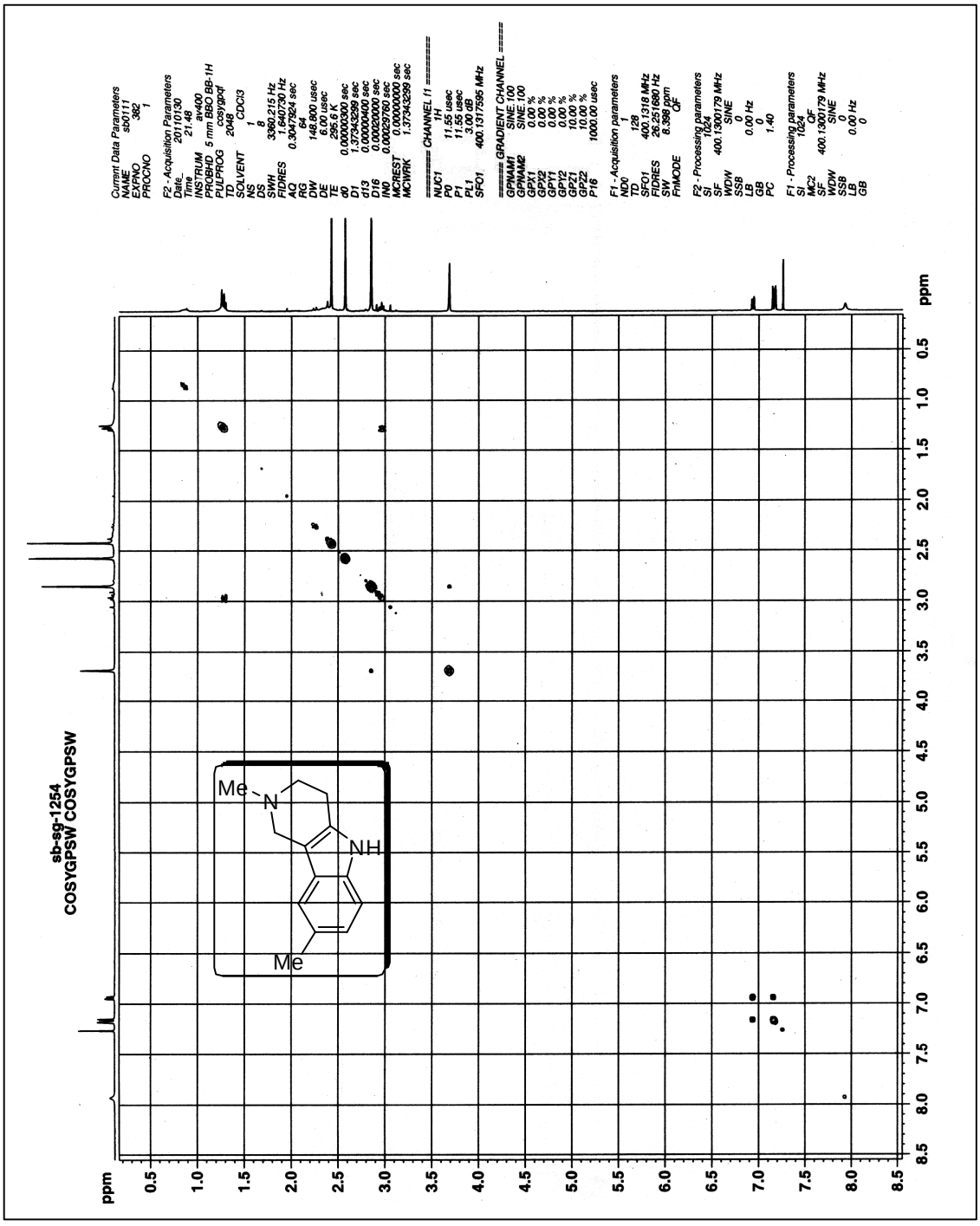
Expanded ^{1}H NMR spectrum of indole derivative **17**



^{13}C NMR spectrum of indole derivative **17**



^{13}C DEPT NMR spectrum of indole derivative **17**



^{1}H ^{1}H COSY NMR spectrum of indole derivative **17**