# An Unusual Ambiphilic Carbenoid Equivalent in Amide-Cyclopropanation

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**General Information.** Dichloromethane was distilled from $P_2O_5$ prior to use. Commerically available ketones, and aldehydes were used as received (Lancaster, Acros, Aldrich, Tedia, RDH). Titanium tetrachloride was purchased from Fluka Chemie AG. Magnesium powder (ca 50 mesh) was purchased from Lancaster Synthesis Ltd. Flash chromatography was performed on silica gel 60 (230-400 mesh). All reactions were carried out under an atmosphere of $N_2$. $^1$H and $^{13}$C NMR spectra were recorded on a Varian VXR-400 MHz spectrometer at ambient temperature. High-resolution mass spectra were determined on a Jeol JMS-HX 110 spectrometer.

**General procedure for amide-cyclopropanation**:

To a 0 $^o$C suspension consisting of Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) was added over a 2-min period a solution of amide **4a** (219 mg, 1 mmol) in $CH_2Cl_2$ (1 mL) and THF (1 mL). After being stirred for 20 min at 0 $^o$C, the resulting green-black mixture was stirred for an additional 4 h at room temperature. The reaction mixture was recooled to 0 $^o$C. Saturated potassium carbonate solution (10 mL) was added and the mixture was diluted with ether (20 mL). The organic layer was separated, dried, evaporadted, and purified by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give ***N*-[1-(2-phenylethyl)cyclopropyl]morpholine 6a** (187 mg, 81% yield) as a colorless oil: IR (neat) 3083, 3062, 2952, 2933, 2890, 1673, 1602, 1584, 1495 cm$^{-1}$; $^1$H NMR (400 MHz, $C_6D_6$) δ 7.21-7.03 (m, 5 H), 3,53 (t, *J* = 4.4 Hz, 4 H), 2.46-2.42 (m, 6 H), 1.69-1.65 (m, 2 H), 0.53 (dd, *J* = 6.0, 4.4 Hz, 2 H), 0.31 (dd, *J* = 6.0, 4.4 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 142.50, 128.34, 128.13, 125.73, 67.63, 49.75, 44.23, 33.63, 32.43, 12.69; high-resolution MS m/e Calcd for $C_{15}H_{21}NO$: 231.1623. Found: 231.1616. Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 78.09; H, 9.10; N, 6.02.

***N*-[1-(2-phenylethyl)cyclopropyl]pyrrolidine 6b**: Following the general procedure, 203 mg of **4b** (1 mmol) and Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 153 mg (71%) of **6b** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ 7.20-7.07 (m, 5 H), 2.70-2.66 (m, 2 H), 2.51 (t, *J* = 5.6 Hz, 4 H), 1.74-1.70 (m, 2 H), 1.58-1.55 (m, 2 H), 0.67 (dd, *J* = 6.4, 4.8 Hz, 2 H), 0.29 (dd, *J*

= 6.4, 4.8 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 142.66, 128.27, 128.21, 125.64, 48.41, 40.01, 34.10, 33.14, 23.70, 10.91; high-resolution MS m/e Calcd for $C_{16}H_{23}N$: 229.1830. Found: 229.1823. Anal. Calcd for $C_{16}H_{23}N$: C, 83.79; H, 10.11; N, 6.11. Found: C, 83.67; H, 10.03; N, 6.07.

***N*-[1-(2-phenylethyl)cyclopropyl]pyrrolidine 6c**: Following the general procedure, 217 mg (1 mmol) of **4c** and Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 174 mg (76%) of **6c** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ 7.20-7.06 (m, 5 H), 2.57 (t, *J* = 5.6 Hz, 4 H), 2.49-2.45 (m, 2 H), 1.78-1.74 (m, 2 H), 1.48-1.43 (m, 4 H), 1.35-1.32 (m, 2 H), 0.63 (dd, *J* = 6.0, 4.0 Hz, 2 H), 0.39 (dd, *J* = 6.0, 4.0 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 142.75, 128.26, 128.10, 125.60, 50.70, 44.56, 33.73, 31.63, 26.65, 24.86, 13.30; high-resolution MS m/e Calcd for $C_{15}H_{21}N$: 215.1674. Found: 215.1665. Anal. Calcd for $C_{15}H_{21}N$: C, 83.67; H, 9.83; N, 6.50. Found: C, 83.43; H, 9.77; N, 6.60.

***N*-(1-phenylcyclopropyl]morpholine 6d**: Following the general procedure, 191 mg (1 mmol) of **4d** and Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 130 mg (64%) of **6d** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ 7.19-7.06 (m, 5 H), 3.52 (t, *J* = 4.8 Hz, 4 H), 2.32 (t, *J* = 4.8 Hz, 4 H), 0.84 (dd, *J* = 6.4, 4.0 Hz, 2 H), 0.66 (dd, *J* = 6.4, 4.0 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 136.92, 131.12, 127.67, 127.31, 67.27, 50.11, 49.35, 14.18; high-resolution MS m/e Calcd for $C_{13}H_{17}NO$: 203.1311. Found: 203.1308.

***N*-[1-(cyclohexyl)cyclopropyl]morpholine 6e**: Following the general procedure, 197 mg (1 mmol) of **4e** and Mg (288 mg, 12 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 153 mg (73%) of **6e** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ 3.53 (t, *J* = 4.8, 4 H), 2.32 (t, *J* = 4.8, 4 H), 1.72-1.55 (m, 6 H), 1.20-0.98 (m, 5 H), 0.54 (dd, *J* = 6.0, 4.4 Hz, 2 H), 0.26 (dd, *J* = 6.0, 4.4 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 67.77, 50.85, 48.97, 42.09, 31.24, 26.79, 26.49, 10.42; high-resolution MS m/e Calcd for $C_{13}H_{23}NO$: 209.1780. Found: 209.1771.

***N*,*N*-Dimethyl[1-(2-phenylethyl)cyclopropyl]amine 6f**: Following the general procedure, 177 mg (1 mmol) of **4f** and Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 142 mg (75%) of **6f** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ 7.19-7.04 (m, 5 H), 2.46-2.42 (m, 2 H), 2.26 (s,

6 H), 1.74-1.70 (m, 2 H), 0.63 (dd, *J* = 6.0, 4.0 Hz, 2 H), 0.36 (dd, *J* = 6.0, 4.0 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 142.53, 128.30, 128.08, 125.68, 44.07, 41.20, 33.51, 30.36, 13.57; high-resolution MS m/e Calcd for $C_{13}H_{19}N$: 189.1517. Found: 189.1516.

***N*,*N*-Diethyl[1-(2-phenylethyl)cyclopropyl]amine 6g**: Following the general procedure, 205 mg (1 mmol) of **4g** and Mg (288 mg, 12 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 145 mg (67%) of **6g** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ 7.20-7.06 (m, 5 H), 2.58 (q, *J* = 7.2, 4 H), 2.50-2.46 (m, 2 H), 1.72-1.68 (m, 2 H), 1.03 (t, *J* = 7.2, 6 H), 0.66 (dd, *J* = 6.0, 4.4 Hz, 2 H), 0.39 (dd, *J* = 6.0, 4.4 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 142.75, 128.30, 128.12, 125.64, 46.94, 42.30, 33.56, 33.09, 14.97, 13.54; high-resolution MS m/e Calcd for $C_{15}H_{23}N$: 217.1831. Found: 217.1828.

***N*-Benzyl-*N*-ethyl[1-(2-phenylethyl)cyclopropyl]amine 6h**: Following the general procedure, 267 mg (1 mmol) of **4h** and Mg (288 mg, 12 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 173 mg (62%) of **6h** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ 7.32-7.08 (m, 5 H), 3.74 (s, 2 H), 2.57 (q, *J* = 7.2, 2 H), 2.53-2.49 (m, 2 H), 1.78-1.74 (m, 2 H), 0.93 (t, *J* = 7.2, 3 H), 0.69 (dd, *J* = 6.4, 4.4 Hz, 2 H), 0.40 (dd, *J* = 6.4, 4.4 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 142.68, 141.77, 128.32, 128.13, 127.96, 127.91, 126.38, 125.66, 58.50, 45.85, 42.94, 34.33, 33.70, 14.73, 14.09; high-resolution MS m/e Calcd for $C_{20}H_{25}N$: 279.1987. Found: 279.1980.

***N*-Benzyl-*N*-methylcyclopropylamine 6i**: Following the general procedure, 149 mg (1 mmol) of **4i** and Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 82 mg (51%) of **6i** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ $^1$H NMR (400 MHz, $C_6D_6$) δ 7.26-7.11 (m, 5 H), 3.55 (s, 2 H), 2.16 (s, 3 H), 1.55 (tt, *J* = 7.2, 3.6 Hz, 1 H), 0.46-0.43 (m, 2 H), 0.33-0.29 (m, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 138.34, 129.33, 128.01, 126.81, 62.18, 41.86, 38.42, 7.06; high-resolution MS m/e Calcd for $C_{11}H_{15}N$: 161.1204. Found: 161.1201.

***N*-Benzyl-*N*-ethylcyclopropylamine 6j**: Following the general procedure, 163 mg (1 mmol) of **4j** and Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 88 mg (50%) of **6j** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ $^1$H NMR (400 MHz, $C_6D_6$) δ 7.29-7.11 (m, 5 H), 3.64 (s, 2 H),

2.52 (q, *J* = 7.2 Hz, 2 H), 1.63-1.58 (m, 1 H), 0.98 (t, *J* = 7.2 Hz, 3 H), 0.45-0.41 (m, 2 H), 0.33-0.29 (m, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 138.95, 129.27, 127.93, 126.67, 58.95, 48.19, 35.81, 11.90, 7.15; high-resolution MS m/e Calcd for $C_{12}H_{17}N$: 175.1361. Found: 175.1364**.**

**4-Benzyl-4-azaspiro[2.6]nonane 6k**: Following the general procedure, 203 mg (1 mmol) of **4k** and Mg (288 mg, 12 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 155 mg (72%) of **6k** as a colorless oil: IR (neat) 3062, 3026, 2923, 2853, 1493, 1462 cm$^{-1}$; $^1$H NMR (400 MHz, $C_6D_6$) δ 7.29-7.11 (m, 5 H), 3.82 (s, 2 H), 2.68 (t, *J* = 6.4 Hz, 2 H), 1.59-1.46 (m, 8 H), 0.74 (dd, *J* = 6.0, 3.6 Hz, 2 H), 0.35 (dd, *J* = 6.0, 3.6 Hz, 2 H); $^{13}$C NMR (1005 MHz, $CDCl_3$) δ 140.47, 128.40, 128.02, 126.51, 55.26, 49.47, 44.43, 34.63, 27.35, 25.83, 25.60, 16.64; high-resolution MS m/e Calcd for $C_{15}H_{21}N$: 215.1674. Found: 215.1680.

**4-Benzyl-4-azaspiro[2.4]heptane 6l**: Following the general procedure, 175 mg (1 mmol) of **4l** and Mg (288 mg, 12 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 138 mg (74%) of **6l** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ 7.36-7.11 (m, 5 H), 3.26 (s, 2 H), 2.65-2.62 (m, 2 H), 1.68-1.64 (m, 4 H), 0.75 (dd, *J* = 6.0, 4.8 Hz, 2 H), 0.28 (dd, *J* = 6.0, 4.8 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 139.84, 128.75, 128.17, 126.73, 55.13, 52.71, 47.16, 32.69, 22.26, 8.61; high-resolution MS m/e Calcd for $C_{13}H_{17}N$: 187.1354. Found: 187.1347.

**4-Benzyl-4-azaspiro[2.5]octane 6m**: To a -10 $^o$C suspension consisting of Mg (288 mg, 12 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) was added over a 2-min period a solution of amide **4m** (189 mg, 1 mmol) in $CH_2Cl_2$ (3 mL) and THF (1 mL). After being stirred for 16 h at -10 $^o$C, the reaction mixture was warmed to 0 $^o$C. Saturated potassium carbonate solution (10 mL) was added and the mixture was diluted with ether (20 mL). The organic layer was separated, dried, evaporadted, and purified by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 129 mg (64%) of **6m** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ 7.31-7.11 (m, 5 H), 3.76 (s, 2 H), 2.68 (t, *J* = 5.6 Hz, 2 H), 1.57-1.52 (m, 2 H), 1.27-1.23 (m, 4 H), 0.68 (dd, *J* = 5.6, 4.0 Hz, 2 H), 0.27 (dd, *J* = 6.0, 4.0 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 140.44, 128.68, 128.08, 126.57, 54.01, 47.73, 42.80, 27.79, 24.48, 18.29, 14.62; high-resolution MS m/e Calcd for $C_{14}H_{19}N$: 201.1518. Found: 201.1513.

**4-Benzyl-4-azaspiro[2.3]hexane 6n**: To a -10 $^o$C suspension consisting of Mg (288 mg, 12 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) was added over a 2-

min period a solution of amide **4n** (161 mg, 1 mmol) in $CH_2Cl_2$ (3 mL) and THF (1 mL). After being stirred for 16 h at -10 °C, the reaction mixture was warmed to 0 °C. Saturated potassium carbonate solution (10 mL) was added and the mixture was diluted with ether (20 mL). The organic layer was separated, dried, evaporadted, and purified by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 116 mg (67%) of **6n** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ 7.36-7.07 (m, 5 H), 3.25 (s, 2 H), 3.10 (t, *J* = 7.2 Hz, 2 H), 2.04 (t, *J* = 7.2 Hz, 2 H), 0.61 (dd, *J* = 7.6, 4.4 Hz, 2 H), 0.16 (dd, *J* = 7.8, 4.4 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 137.92, 128.38, 128.11, 126.73, 58.02, 51.35, 50.77, 26.62, 6.29; high-resolution MS m/e Calcd for $C_{12}H_{15}N$: 172.1204. Found: 173.1212.

***N*-[1-(2,2-ethylenedioxypropyl)cyclopropyl]morpholine 6o**: Following the general procedure, 215 mg (1 mmol) of **4o** and Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 159 mg (70%) of **6g** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ 3.53 (t, *J* = 4.8, 4 H), 3.47-3.43 (m, 4 H), 2.45 (t, *J* = 4.8, 4 H), 1.85 (s, 2 H), 1.39 (s, 3 H), 0.65 (t, *J* = 2.4 Hz, 2 H), 0.63 (t, *J* = 2.4 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 109.96, 67.16, 64.13, 49.10, 41.45, 38.76, 24.41, 13.53; high-resolution MS m/e Calcd for $C_{12}H_{21}NO_3$: 227.1522. Found: 227.1513.

***N*-[1-(2-phenylthioethyl)cyclopropyl]morpholine 6p**: Following the general procedure, 251 mg (1 mmol) of **4p** and Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 189 mg (72%) of **6p** as a colorless oil: $^1$H NMR (400 MHz, $C_6D_6$) δ 7.33-6.91 (m, 5 H), 3.45 (t, *J* = 4.8, 4 H), 2.78-2.74 (m, 2 H), 2.25 (t, *J* = 4.8, 4 H), 1.69-1.65 (m, 2 H), 0.45 (dd, *J* = 6.0, 4.4 Hz, 2 H), 0.26 (dd, *J* = 6.0, 4.4 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 136.56, 129.17, 128.81, 125.76, 67.51, 49.75, 44.03, 31.60, 31.24, 12.48; high-resolution MS m/e Calcd for $C_{15}H_{21}NOS$: 263.1344. Found: 263.1346.

***N*-[1-(4-trimethylsilyl-3-butynyl)cyclopropyl]morpholine 6q**: Following the general procedure, 239 mg (1 mmol) of **4q** and Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 141 mg (56%) of **6q** as a colorless oil: IR (neat) 2957, 2899, 2853, 2174, 1117 cm$^{-1}$; $^1$H NMR (400 MHz, $C_6D_6$) δ 3.43 (t, *J* = 4.8, 4 H), 2.25 (t, *J* = 4.8, 4 H), 2.14-2.10 (m, 2 H), 1.60-1.57 (m, 2 H), 0.44 (dd, *J* = 6.0, 4.0 Hz, 2 H), 0.24 (s, 9 H), 0.20 (dd, *J* = 6.0, 4.0 Hz, 2 H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 107.42, 84.59, 67.58, 49.65, 43.86, 30.53, 17.91, 12.36, 0.07; high-resolution MS m/e Calcd for $C_{14}H_{25}NOSi$: 251.1705. Found: 251.1707.

***N*-[1-(4-methyl-3-pentenyl)cyclopropyl]morpholine 6r**: Following the general procedure, 197 mg (1 mmol) of **4r** and Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 155 mg (74%) of **6r** as a colorless oil: IR (neat) 3009, 2958, 2927, 2914, 1675, 1116 $cm^{-1}$; $^1H$ NMR (400 MHz, $C_6D_6$) δ 5.17-5.12 (m, 1 H), 352 (t, *J* = 4.8, 4 H), 2.47 (t, *J* = 4.8, 4 H), 1.97-1.91 (m, 2 H), 1.67 (s, 3 H), 1.54 (s, 3 H), 1.51-1.47 (m, 2 H), 0.54 (dd, *J* = 6.0, 4.0 Hz, 2 H), 0.35 (dd, *J* = 6.0, 4.0 Hz, 2 H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 131.30, 124.50, 67.67, 49.70, 44.05, 29.82, 25.76, 25.62, 17.63, 12.73; high-resolution MS m/e Calcd for $C_{13}H_{23}NO$: 209.1780. Found: 209.1774.

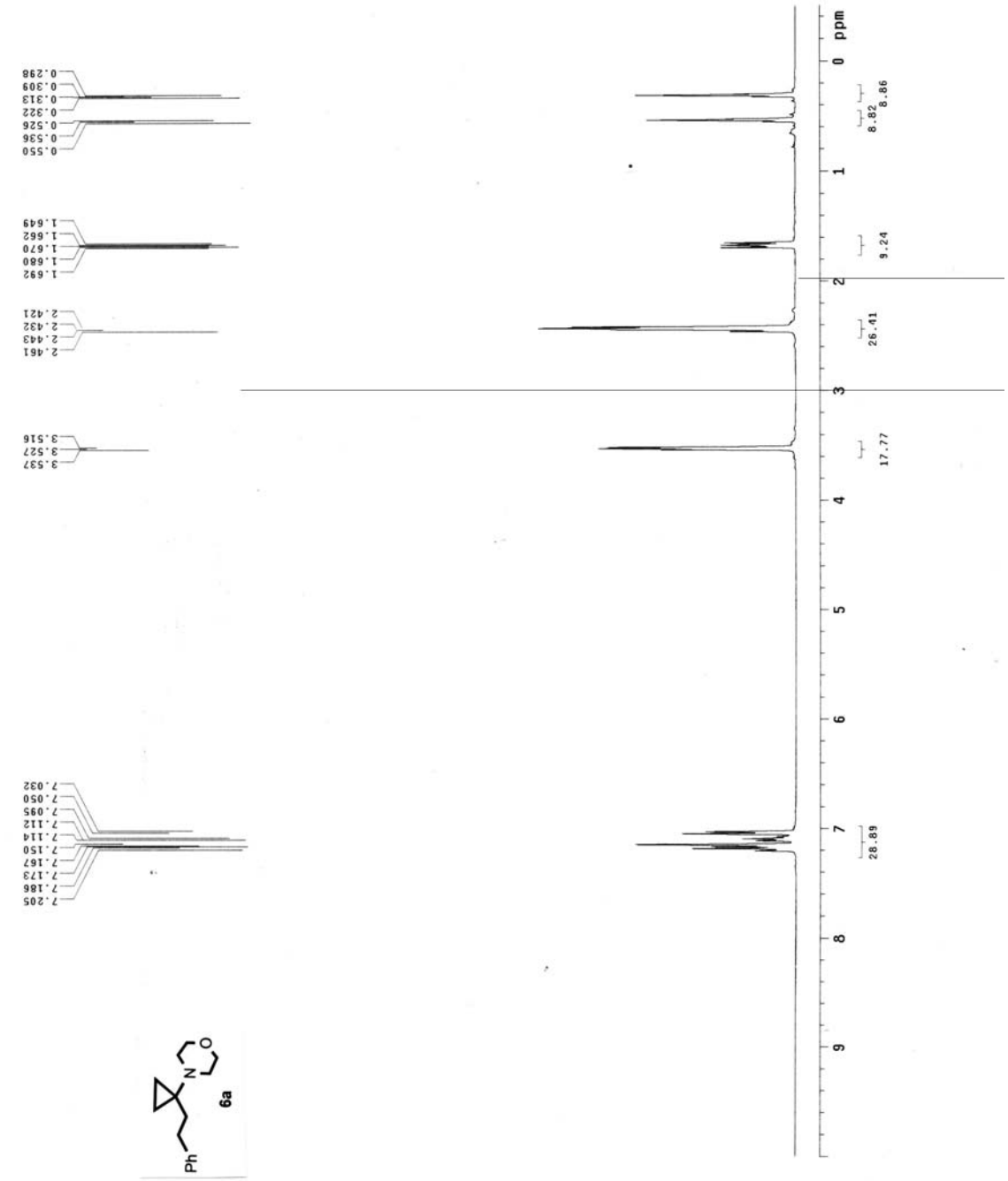
***N*-[1-(3-butenyl)cyclopropyl]morpholine 6s**: Following the general procedure, 169 mg (1 mmol) of **4s** and Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $CH_2Cl_2$, 0.8 mL) in $CH_2Cl_2$ (4 mL) gave a crude reaction mixture. Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 134 mg (74%) of **6s** as a colorless oil: IR (neat) 3077, 3002, 2954, 2929, 2852, 1678, 1452, 1117 $cm^{-1}$; $^1H$ NMR (400 MHz, $C_6D_6$) δ 5.77-5.67 (m, 1 H), 5.01 (dd, *J* = 16.8, 1.6 Hz, 1 H), 4.96 (dd, *J* = 8.8, 1.6 Hz, 1 H), 3.50 (t, *J* = 4.8, 4 H), 2.40 (t, *J* = 4.8, 4 H), 1.92-1.86 (m, 2 H), 1.48-1.44 (m, 2 H), 0.50 (dd, *J* = 6.0, 4.4 Hz, 2 H), 0.26 (dd, *J* = 6.0, 4.4 Hz, 2 H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 138.78, 114.15, 67.61, 49.64, 43.93, 31.40, 29.12, 12.66; high-resolution MS m/e Calcd for $C_{11}H_{19}NO$: 181.1467. Found: 181.1462.

***N*-[1-(2-phenylethyl)-2,2,3,3-tetradeuterocyclopropyl]morpholine 7a**: To a 0 °C suspension consisting of Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $ClCH_2CH_2Cl$, 0.8 mL) in $ClCH_2CH_2Cl$ (4 mL) was added over a 2-min period a solution of $CD_2Cl_2$ (0.3 mL, 4.5 mmol) and amide **4a** (219 mg, 1 mmol) in $ClCH_2CH_2C$ (1 mL) and THF (1 mL). After being stirred for 4 h at 0 °C, the resulting green-black mixture was stirred for an additional 6 h at room temperature. The reaction mixture was recooled to 0 °C. Saturated potassium carbonate solution (10 mL) was added and the mixture was diluted with ether (20 mL). The organic layer was separated, dried, evaporadted, and purified by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 185 mg (80%) of **7a** as a colorless oil: IR (neat) 3083, 3062, 2952, 2933, 2890, 2201, 1673, 1602, 1584, 1495 $cm^{-1}$; $^1H$ NMR (400 MHz, $C_6D_6$) δ 7.21-7.03 (m, 5 H), 3,53 (t, *J* = 4.4 Hz, 4 H), 2.45-2.42 (m, 6 H), 1.68-1.64 (m, 2 H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 142.46, 128.34, 128.13, 125.74, 67.58, 49.73, 43.95, 33.60, 32.20, 12.5-11.0 (multiplet) ; high-resolution MS m/e Calcd for $C_{15}H_{17}D_4NO$: 235.1874. Found: 235.1870.

**4-Benzyl-2,2,3,3-tetradeutero-4-azaspiro[2.6]nonane 7k**: To a 0 °C suspension consisting of Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $ClCH_2CH_2Cl$, 0.8 mL) in

$ClCH_2CH_2Cl$ (4 mL) was added over a 2-min period a solution of $CD_2Cl_2$ (0.3 mL, 4.5 mmol) and amide **4k** (203 mg, 1 mmol) in $ClCH_2CH_2C$ (1 mL) and THF (1 mL). After being stirred for 4 h at 0 °C, the resulting green-black mixture was stirred for an additional 6 h at room temperature. The reaction mixture was recooled to 0 °C. Saturated potassium carbonate solution (10 mL) was added and the mixture was diluted with ether (20 mL). Purification by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 150 mg (70%) of **7k** as a colorless oil: IR (neat) 3062, 3026, 2923, 2853, 2207, 1493, 1462 $cm^{-1}$; $^1H$ NMR (400 MHz, $C_6D_6$) δ 7.29-7.11 (m, 5 H), 3.82 (s, 2 H), 2.68 (t, *J* = 6.4 Hz, 2 H), 1.59-1.44 (m, 8 H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 140.72, 128.34, 128.01, 126.45, 55.28, 49.44, 44.10, 34.61, 27.37, 25.90, 25.70, 16.46-15.34 (multiplet); high-resolution MS m/e Calcd for $C_{13}H_{17}D_4N$: 187.1354. Found: 187.1347.

***N*-[1-(4-methyl-3-pentenyl)-2,2,3,3-tetradeuterocyclopropyl]morpholine 7r**: To a 0 °C suspension consisting of Mg (192 mg, 8 mmol) and $TiCl_4$ (0.8 mmol, 1 M in $ClCH_2CH_2Cl$, 0.8 mL) in $ClCH_2CH_2Cl$ (4 mL) was added over a 2-min period a solution of $CD_2Cl_2$ (0.3 mL, 4.5 mmol) and amide **4r** (197 mg, 1 mmol) in $ClCH_2CH_2C$ (1 mL) and THF (1 mL). After being stirred for 4 h at 0 °C, the resulting green-black mixture was stirred for an additional 6 h at room temperature. The reaction mixture was recooled to 0 °C. Saturated potassium carbonate solution (10 mL) was added and the mixture was diluted with ether (20 mL). The organic layer was separated, dried, evaporadted, and purified by flash chromatography on silica gel (elution with 1:6 ethyl acetate-hexane). to give 155 mg (74%) of **7r** as a colorless oil: IR (neat) 3009, 2958, 2927, 2914, 2204, 1675, 1116 $cm^{-1}$; $^1H$ NMR (400 MHz, $C_6D_6$) δ 5.17-5.12 (m, 1 H), 352 (t, *J* = 4.8, 4 H), 2.47 (t, *J* = 4.8, 4 H), 1.97-1.91 (m, 2 H), 1.67 (s, 3 H), 1.54 (s, 3 H), 1.50-1.46 (m, 2 H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 131.24, 124.48, 67.66, 49.67, 43.68, 29.62, 25.73, 25.61, 17.60, 12.5-11.3 (multiplet); high-resolution MS m/e Calcd for $C_{13}H_{19}D_4NO$: 213.2031. Found: 213.2029.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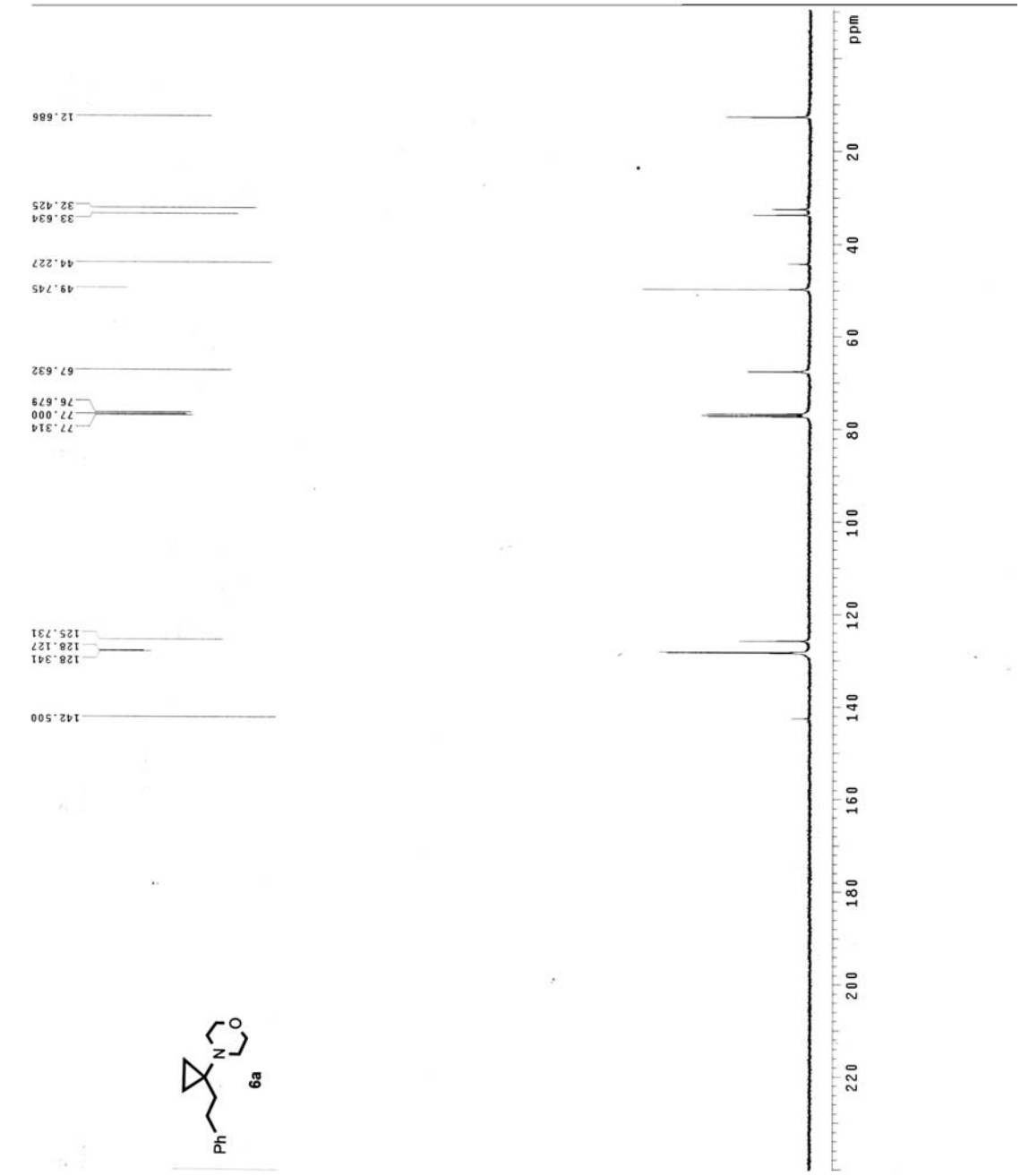
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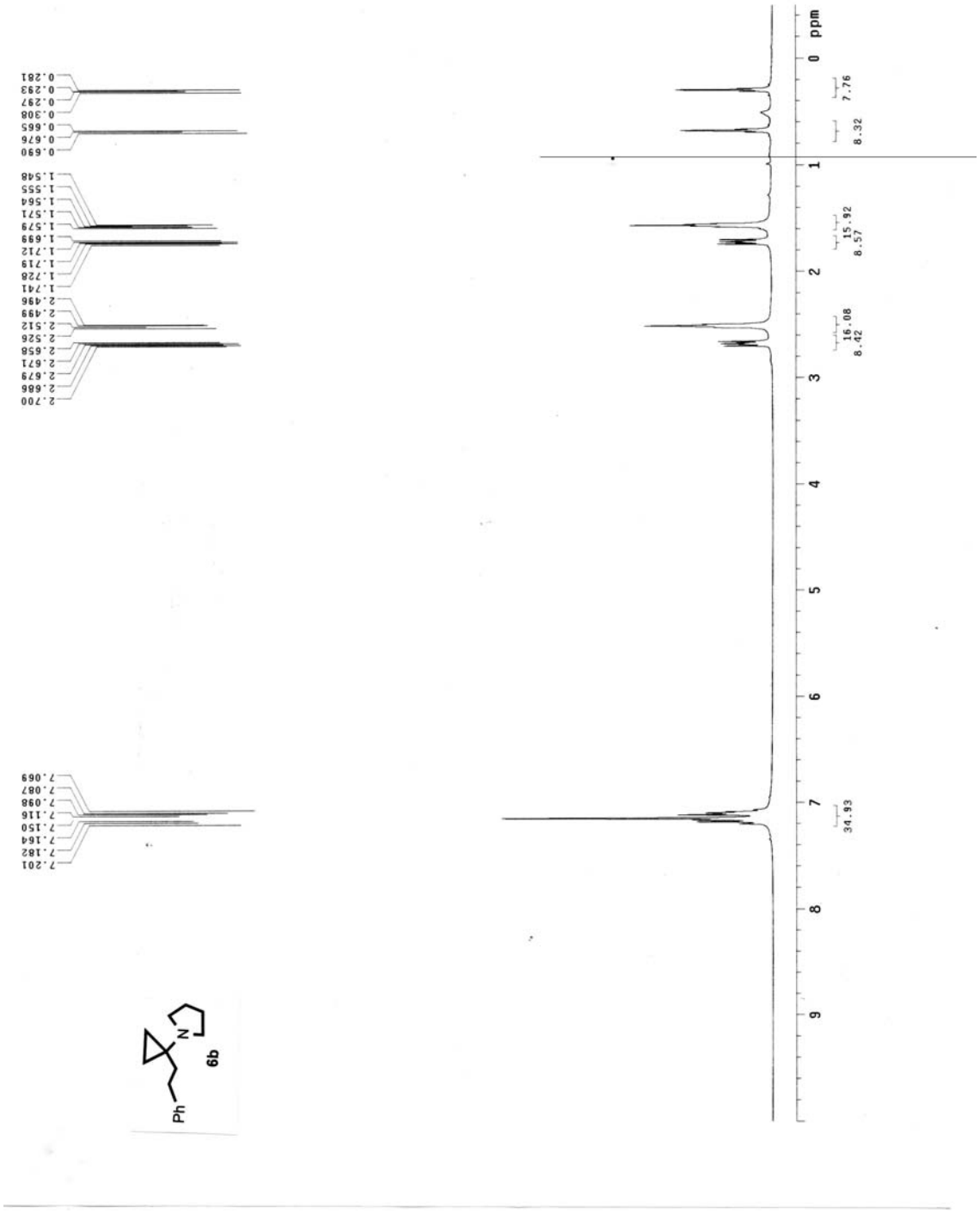
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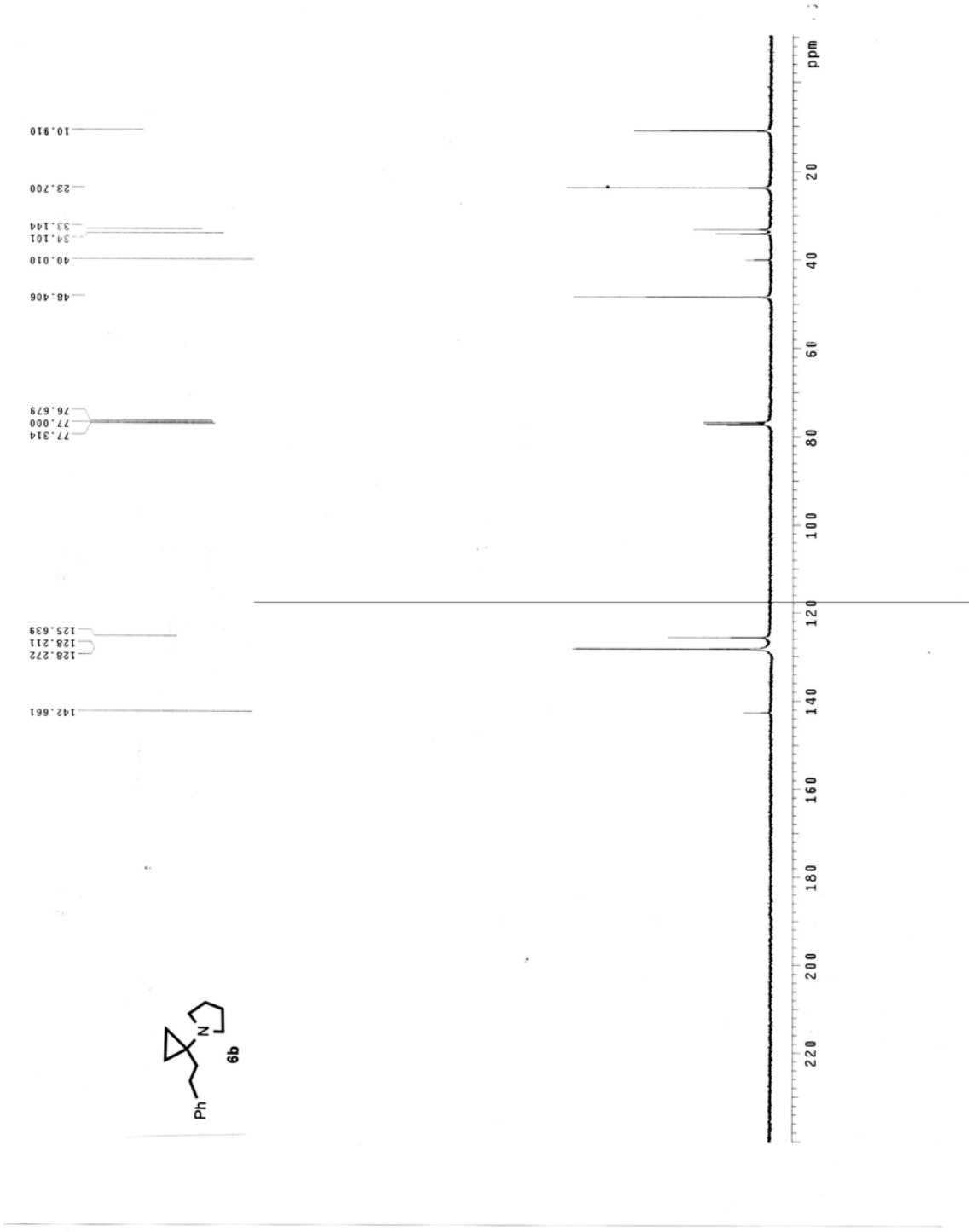
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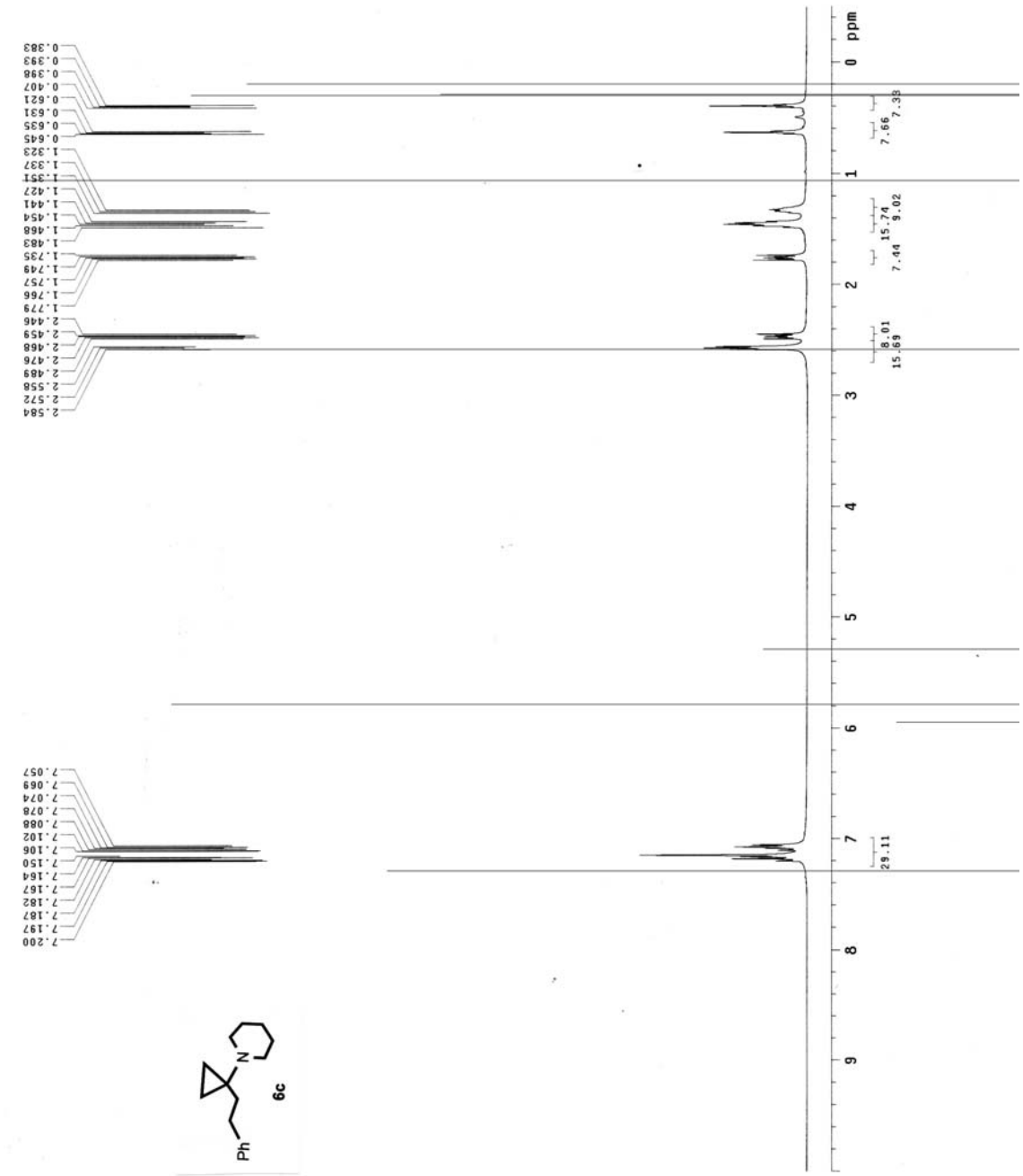
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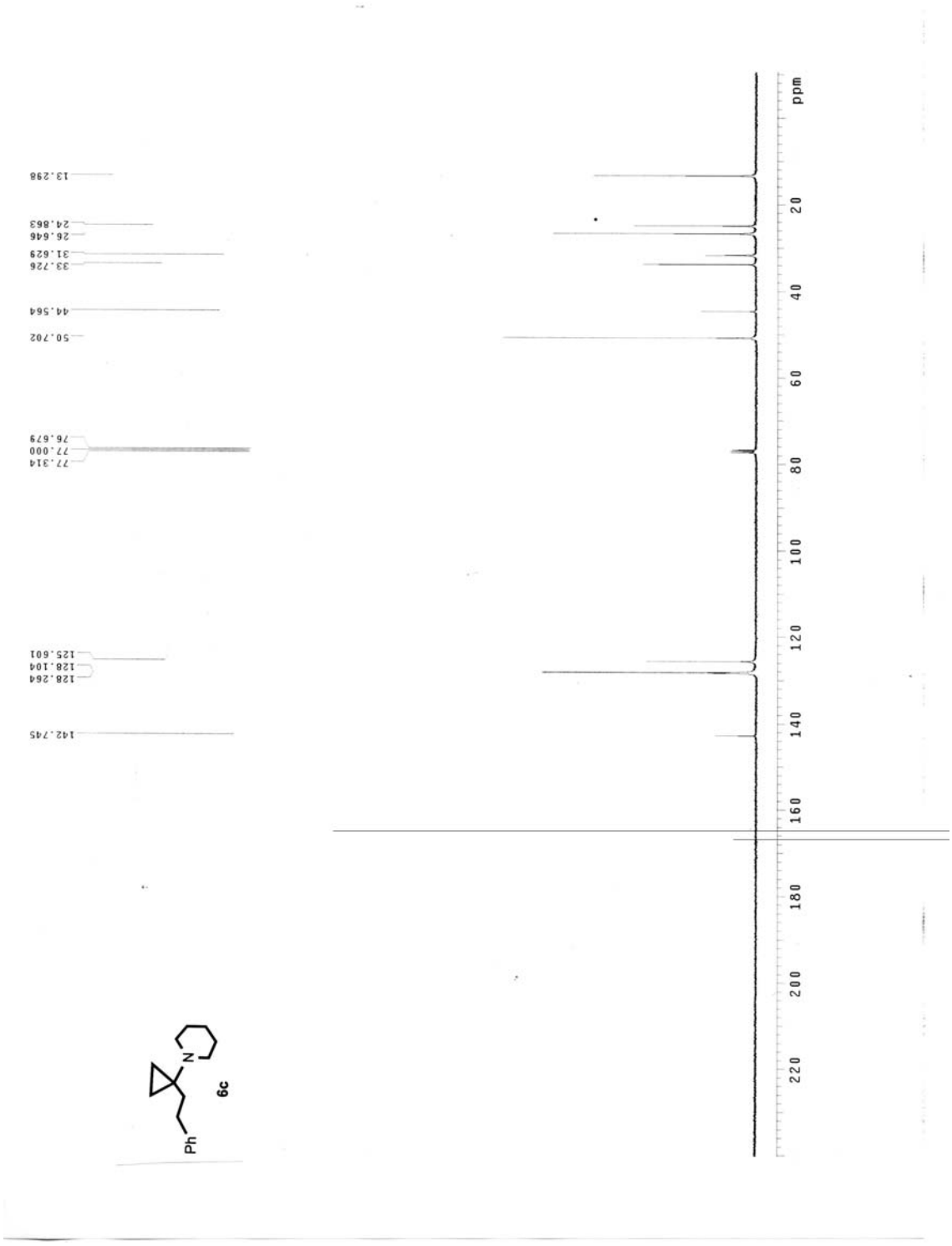
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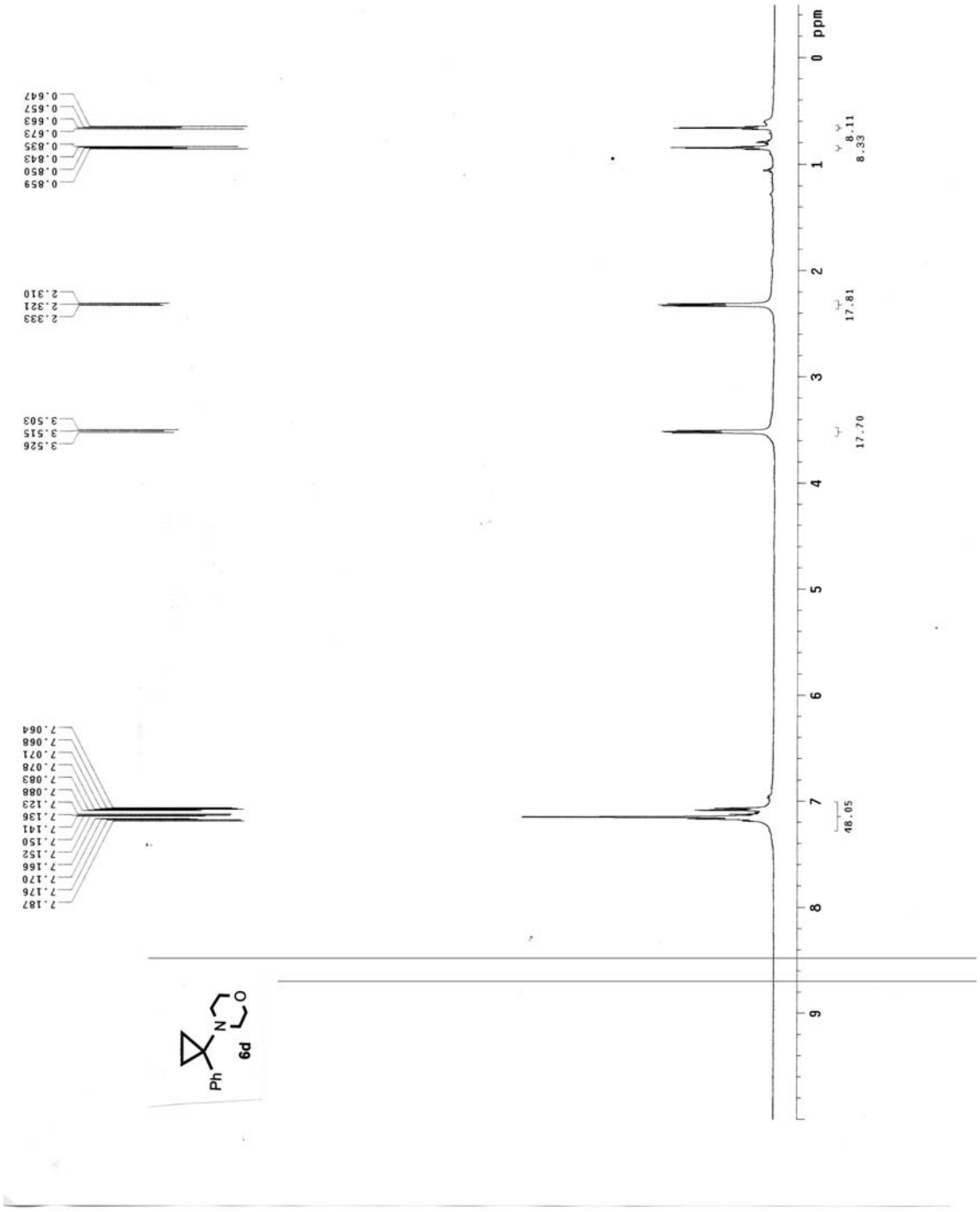
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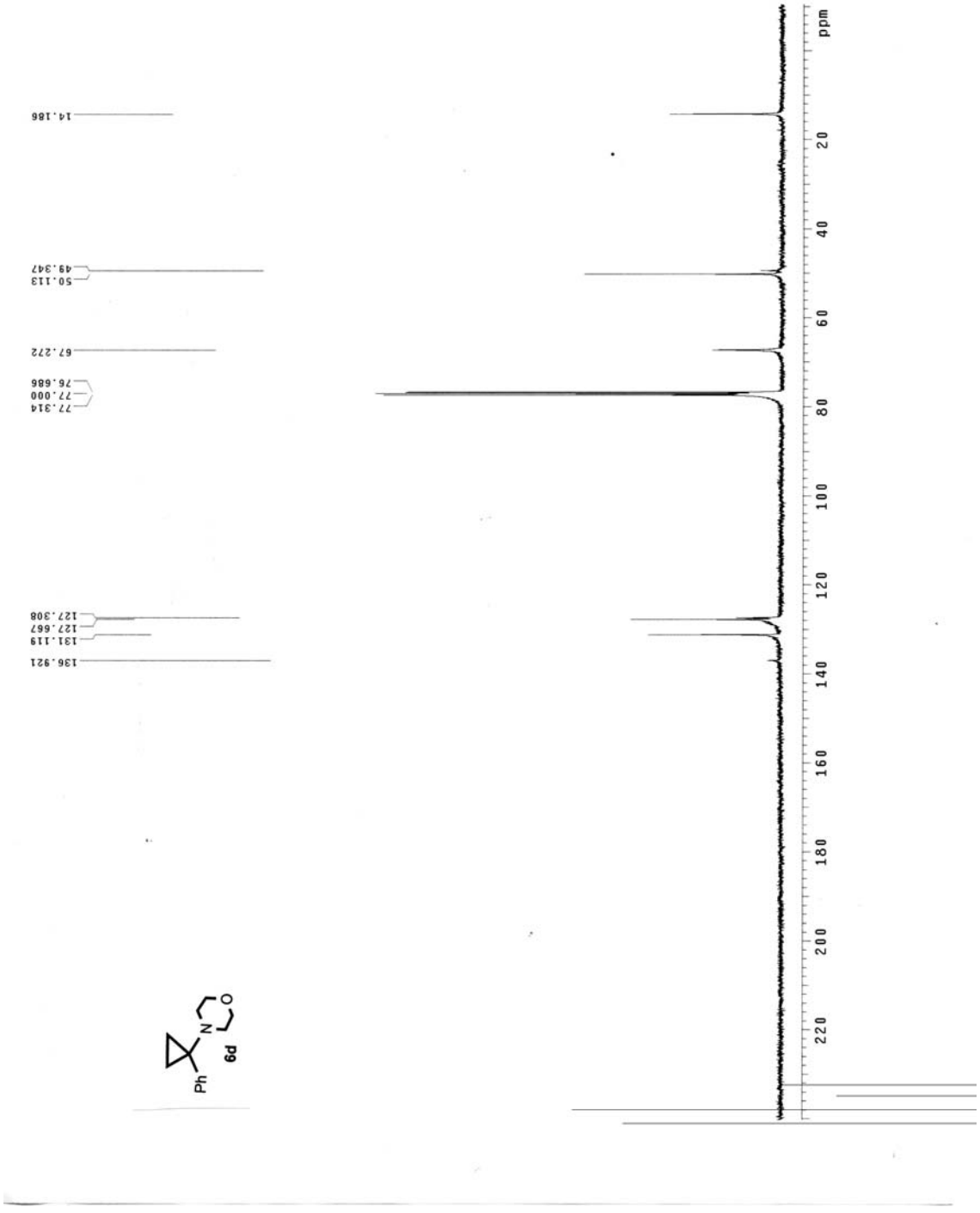
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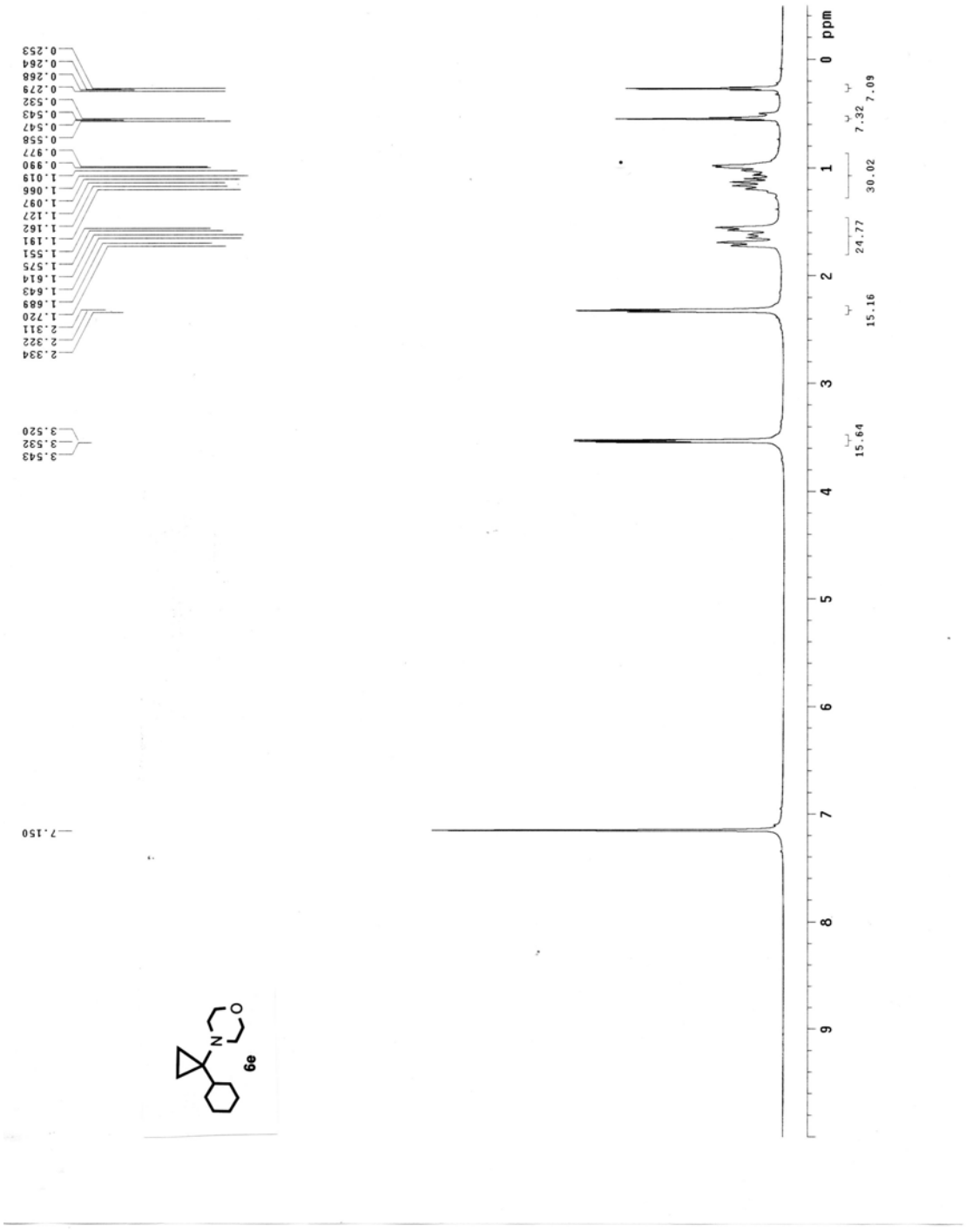
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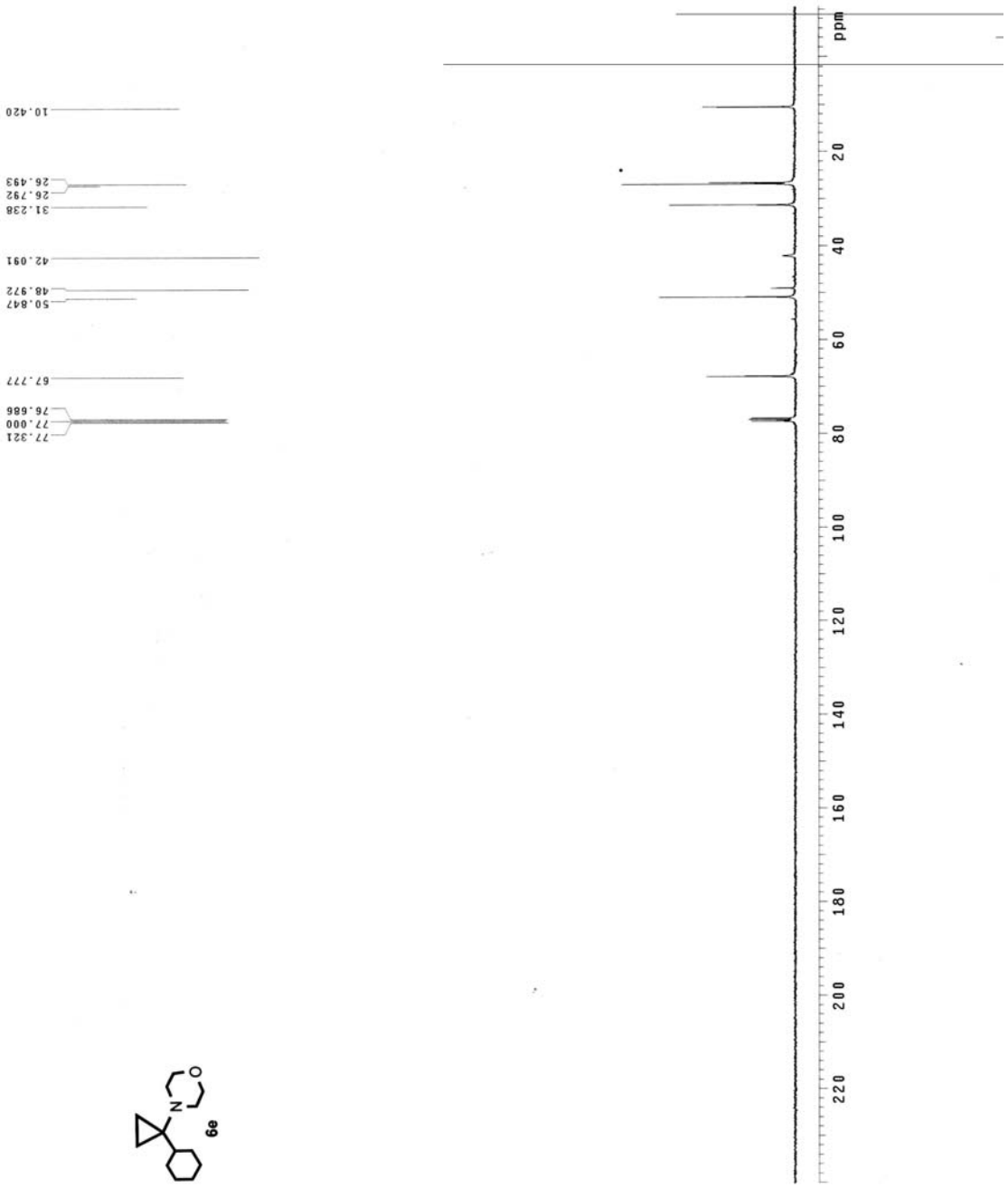
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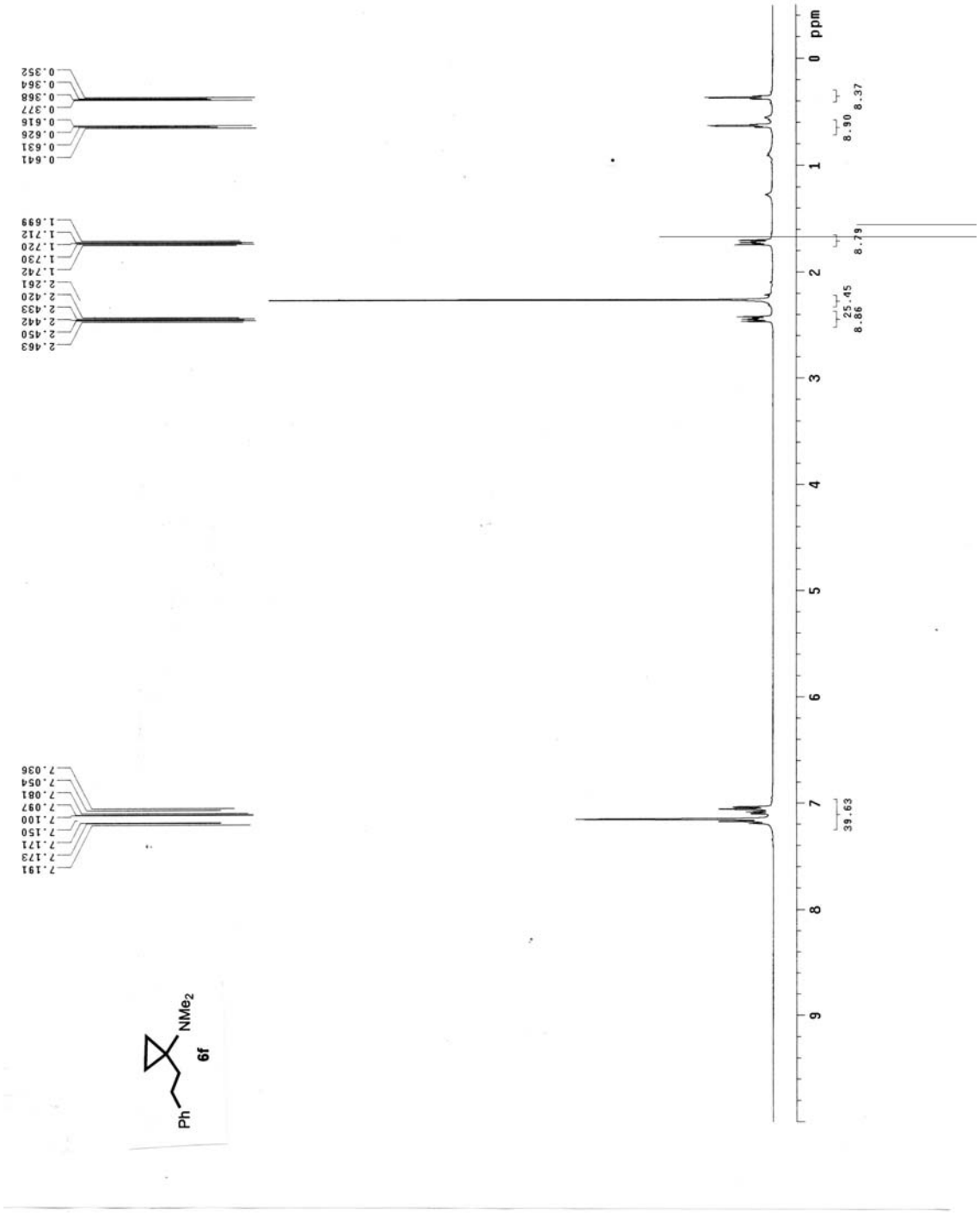
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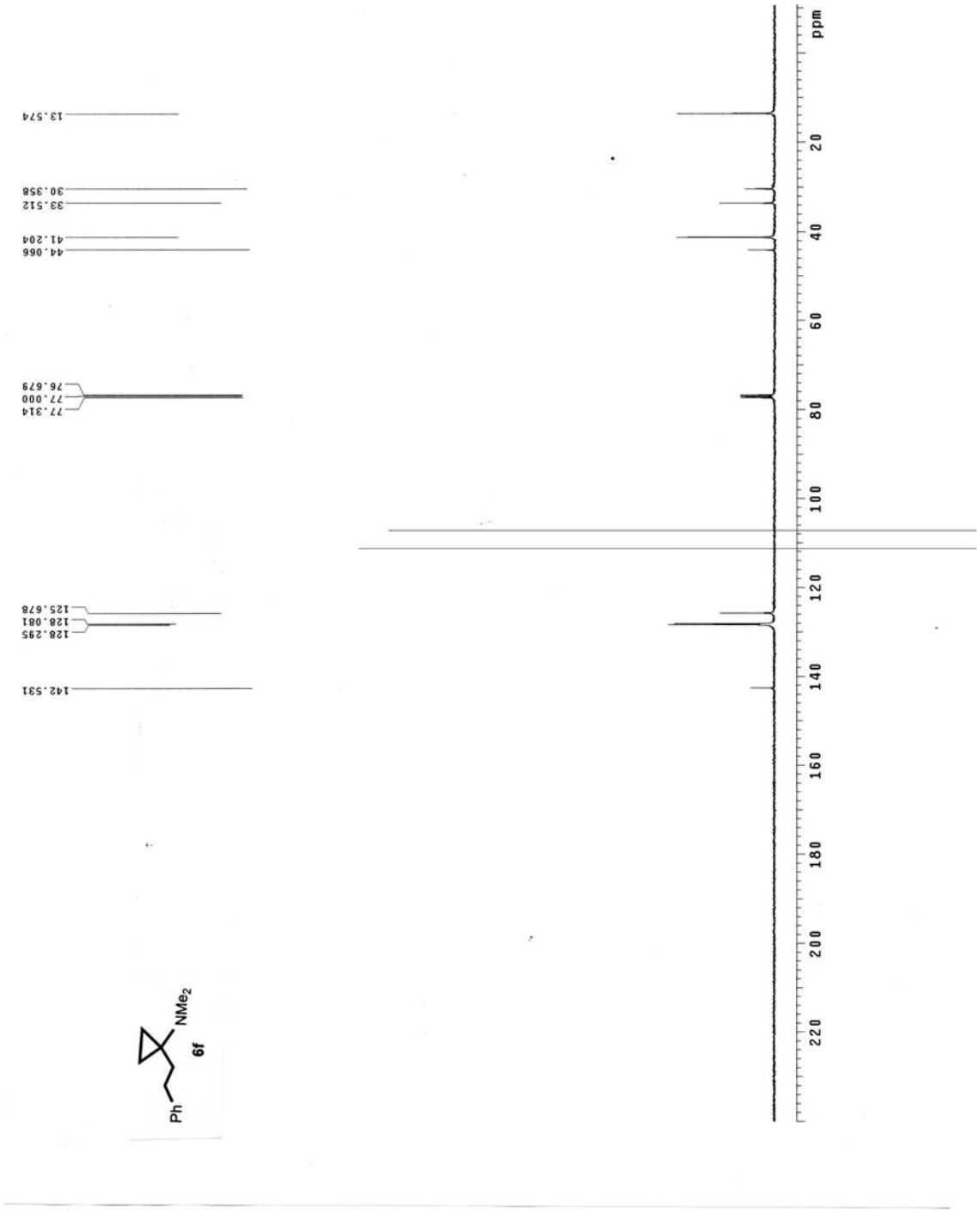
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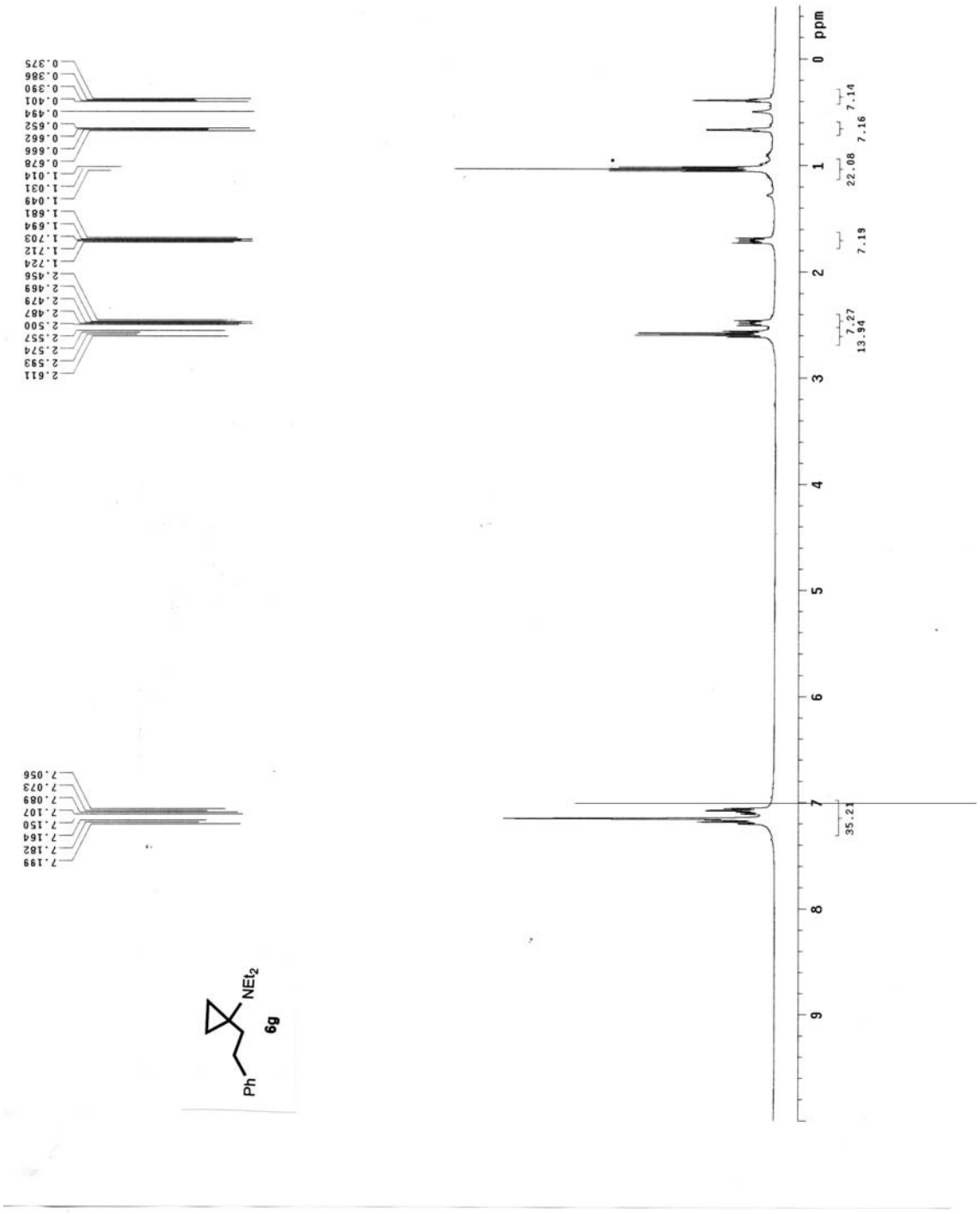
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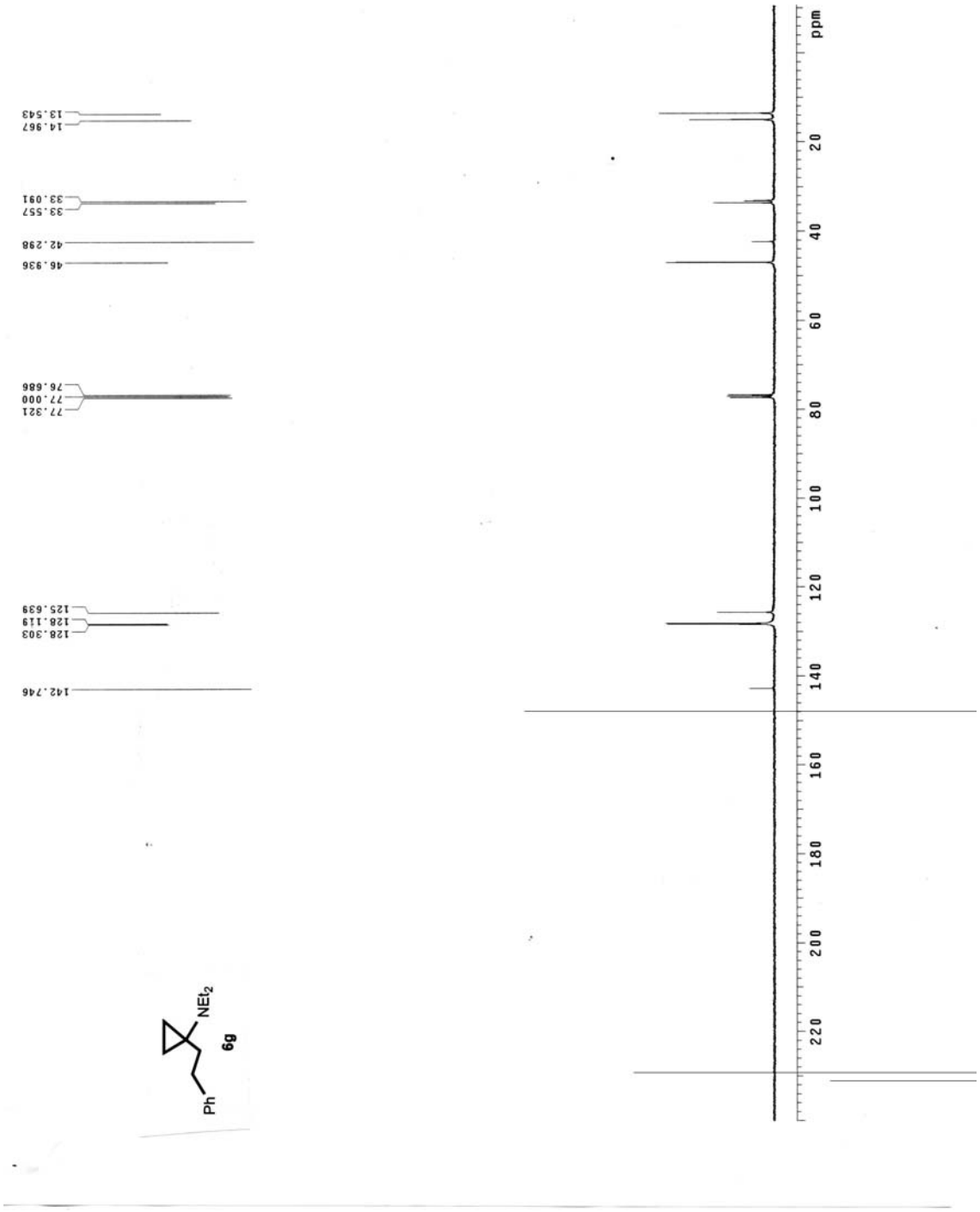
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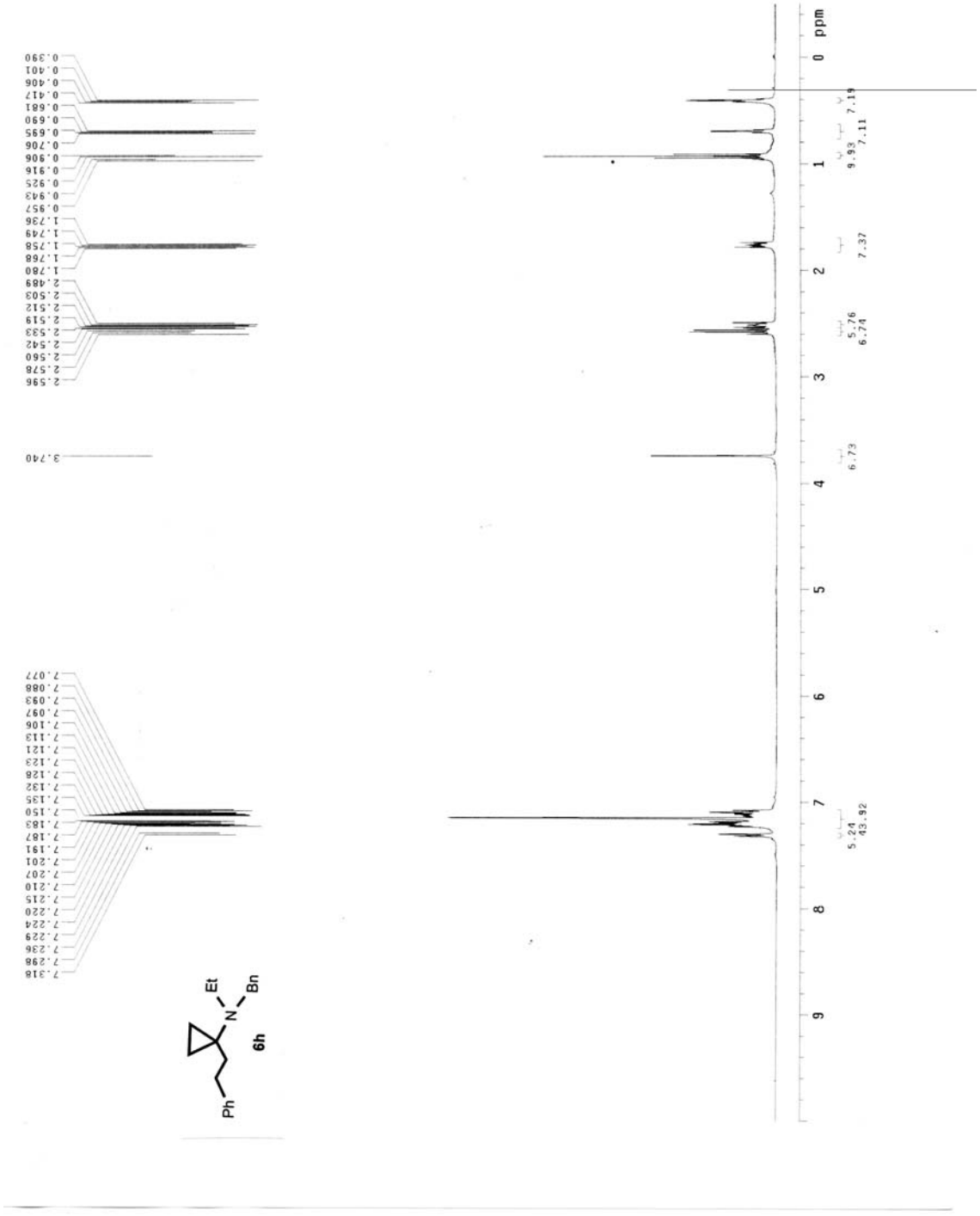
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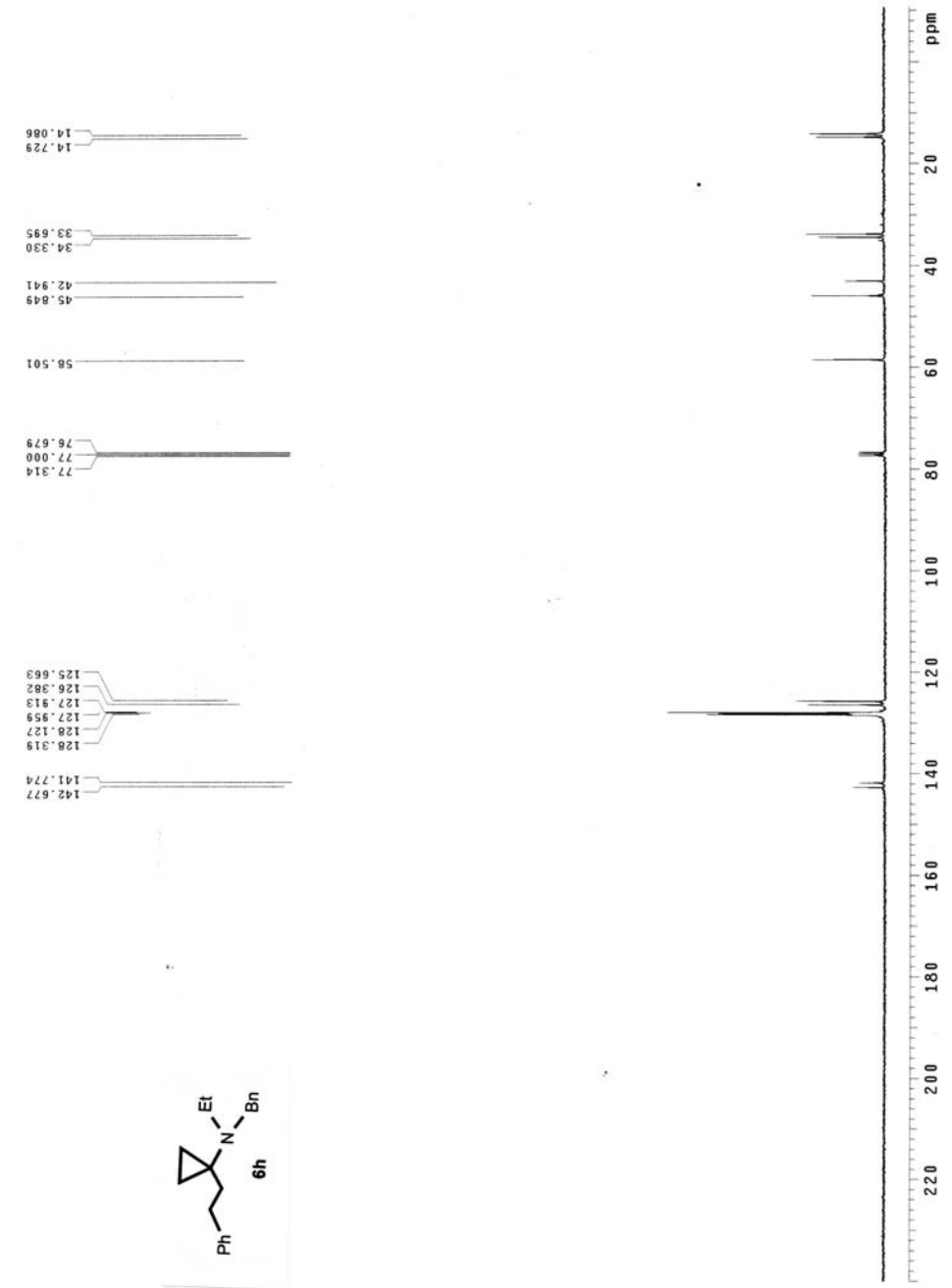
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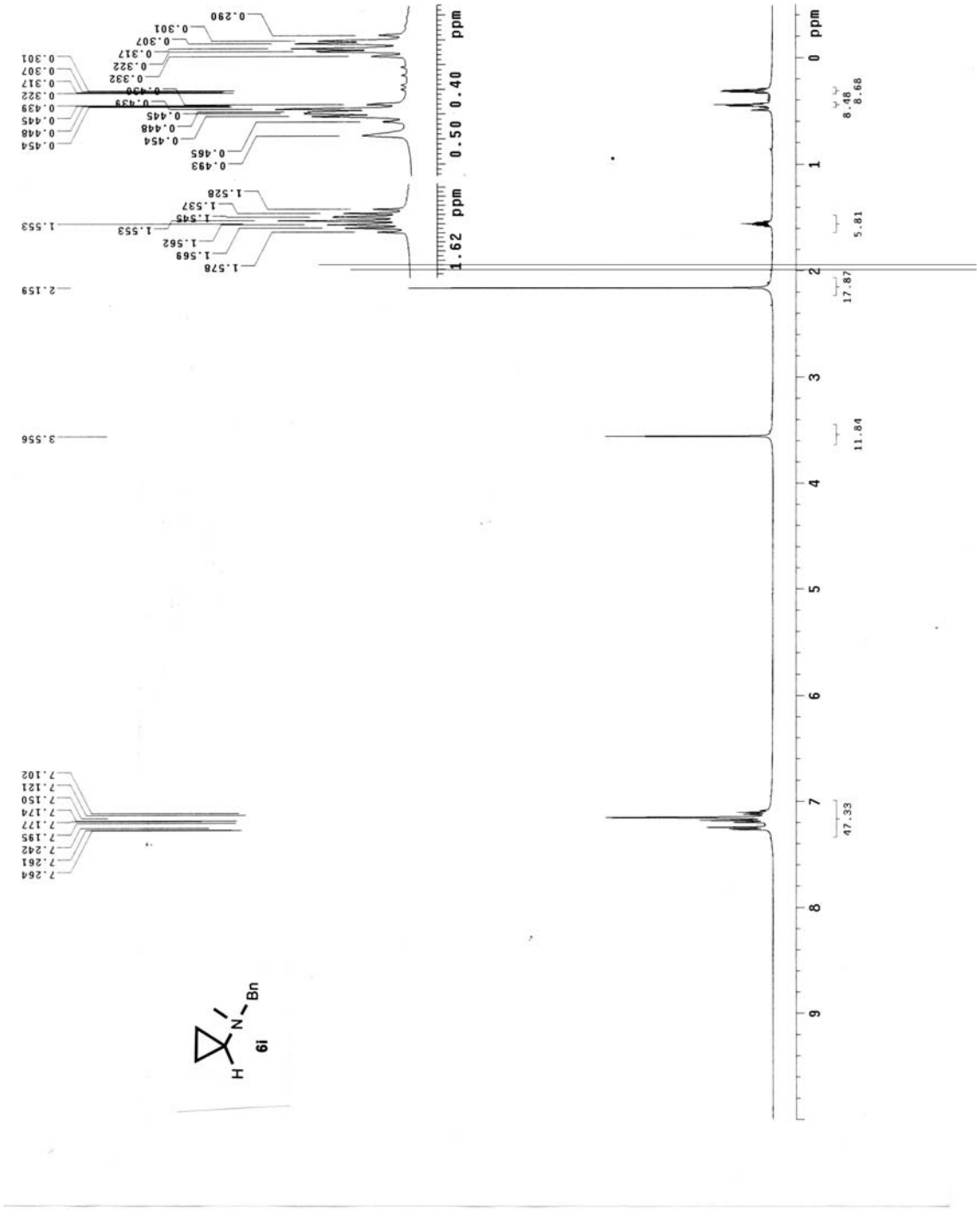
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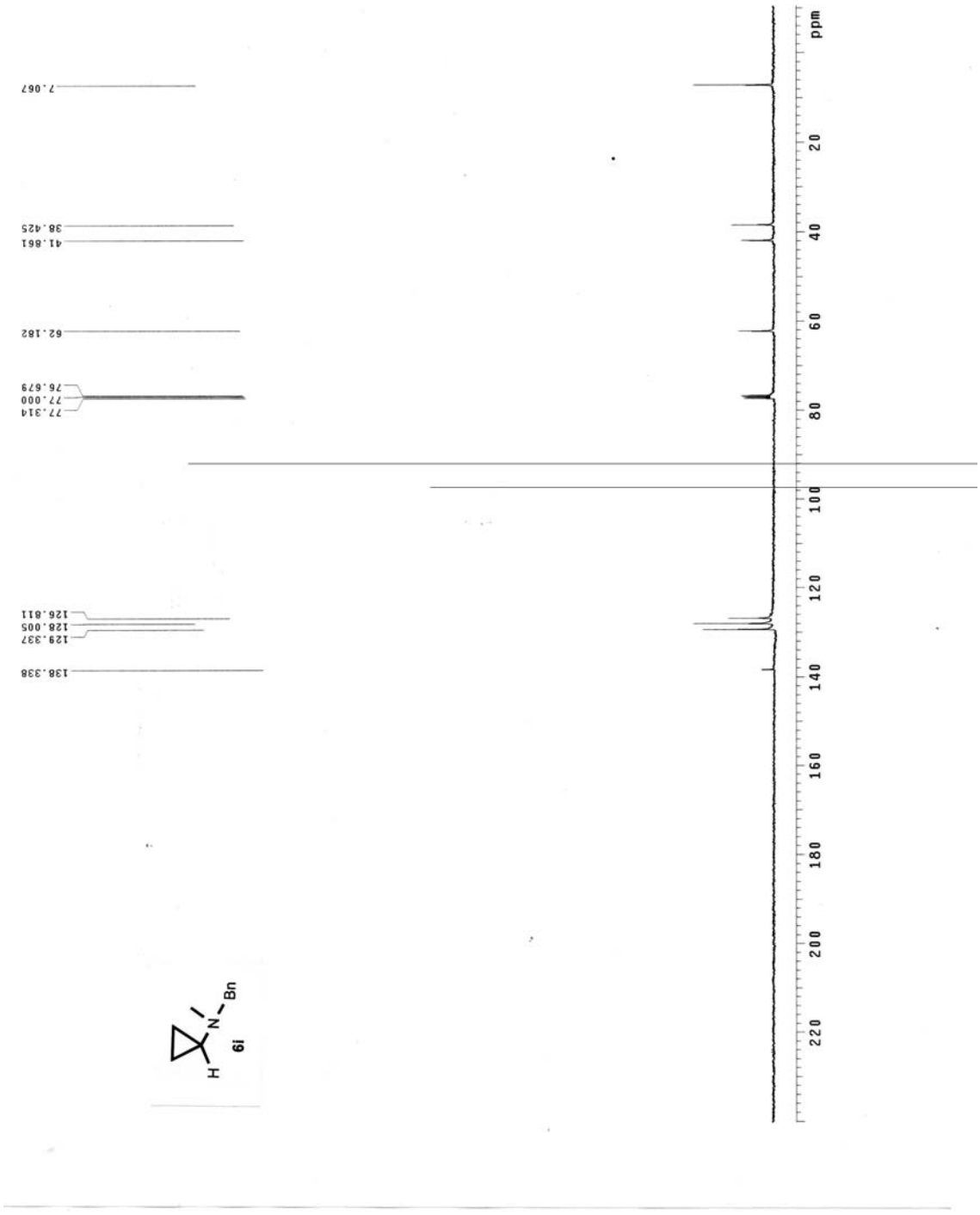
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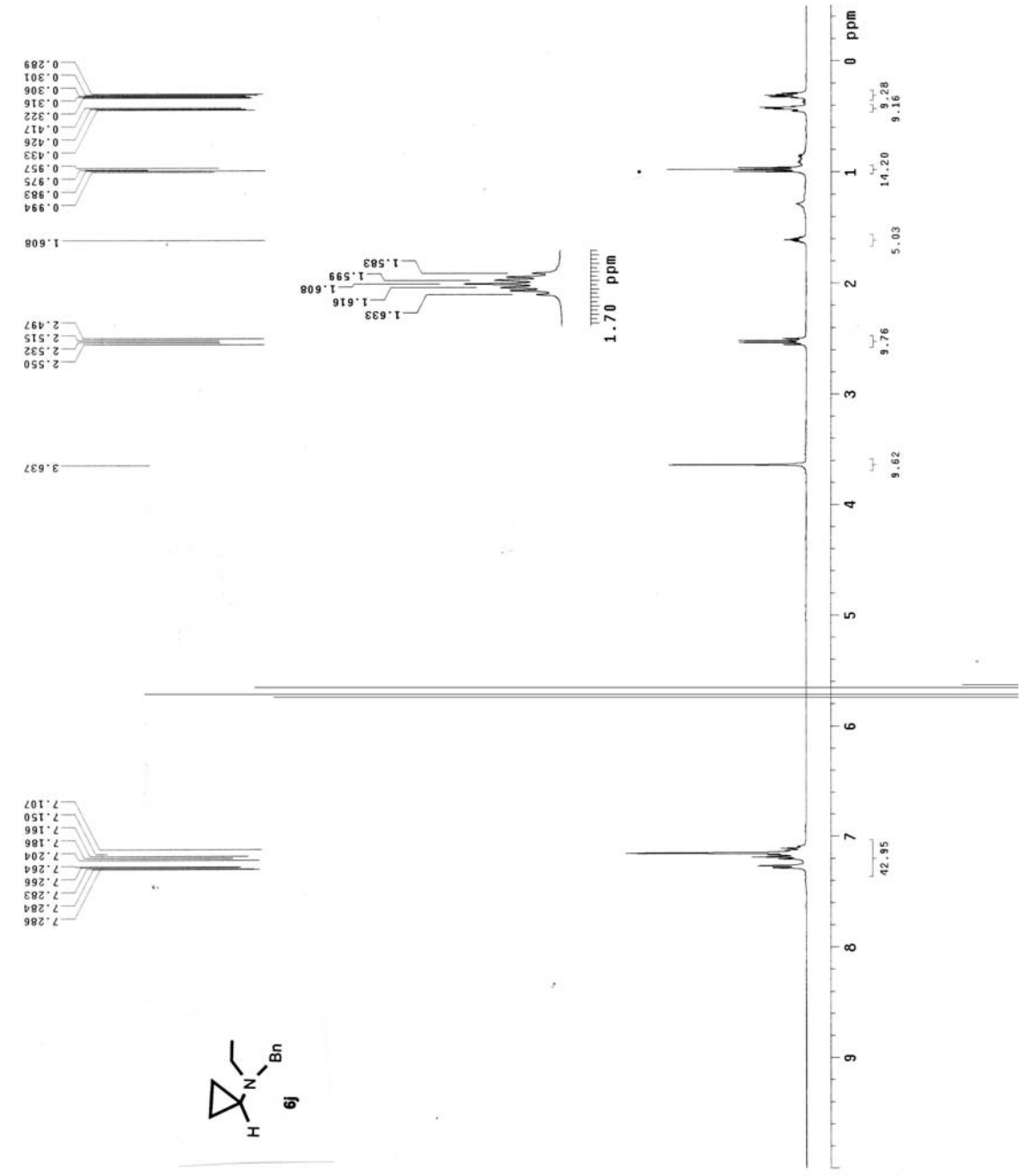
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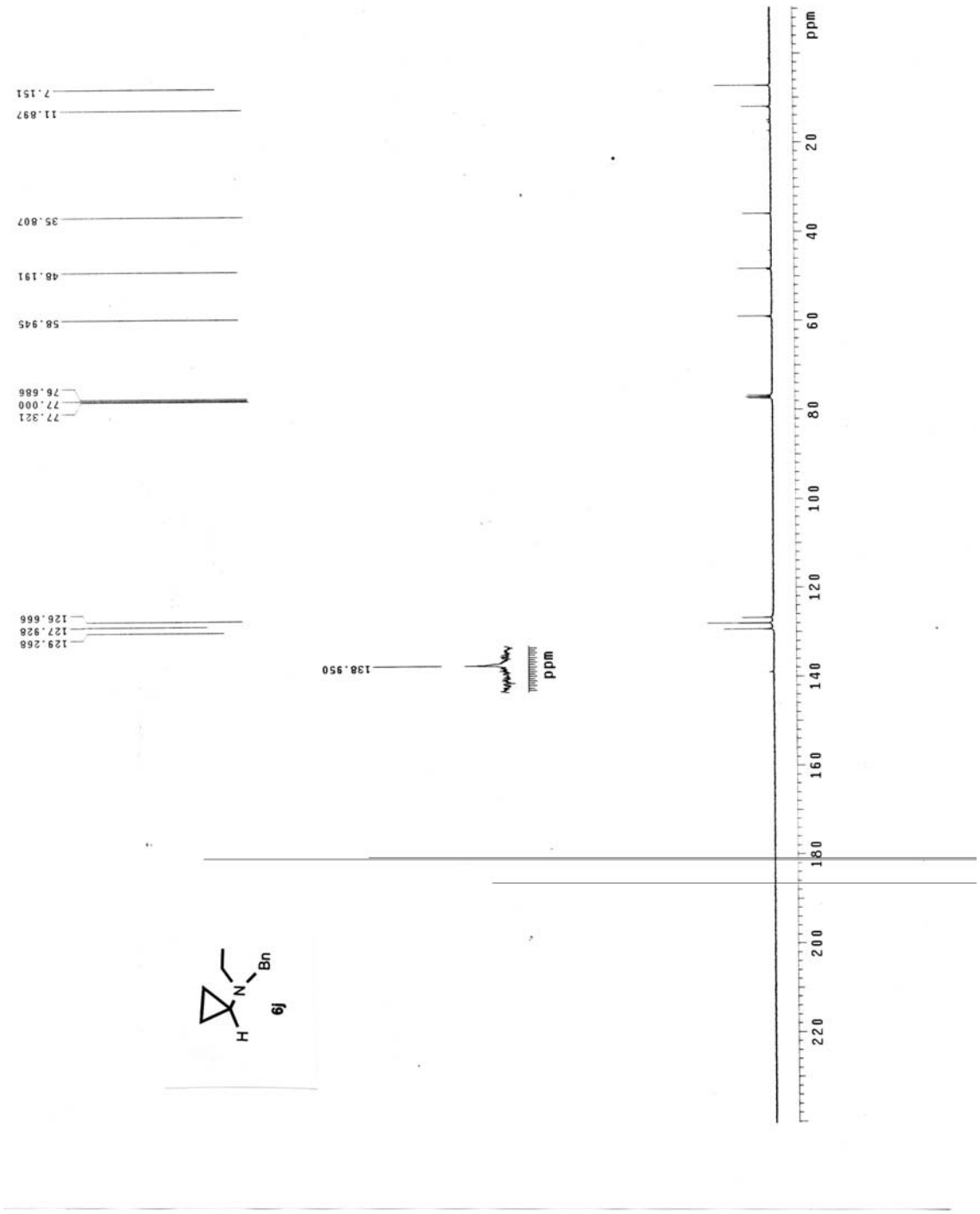
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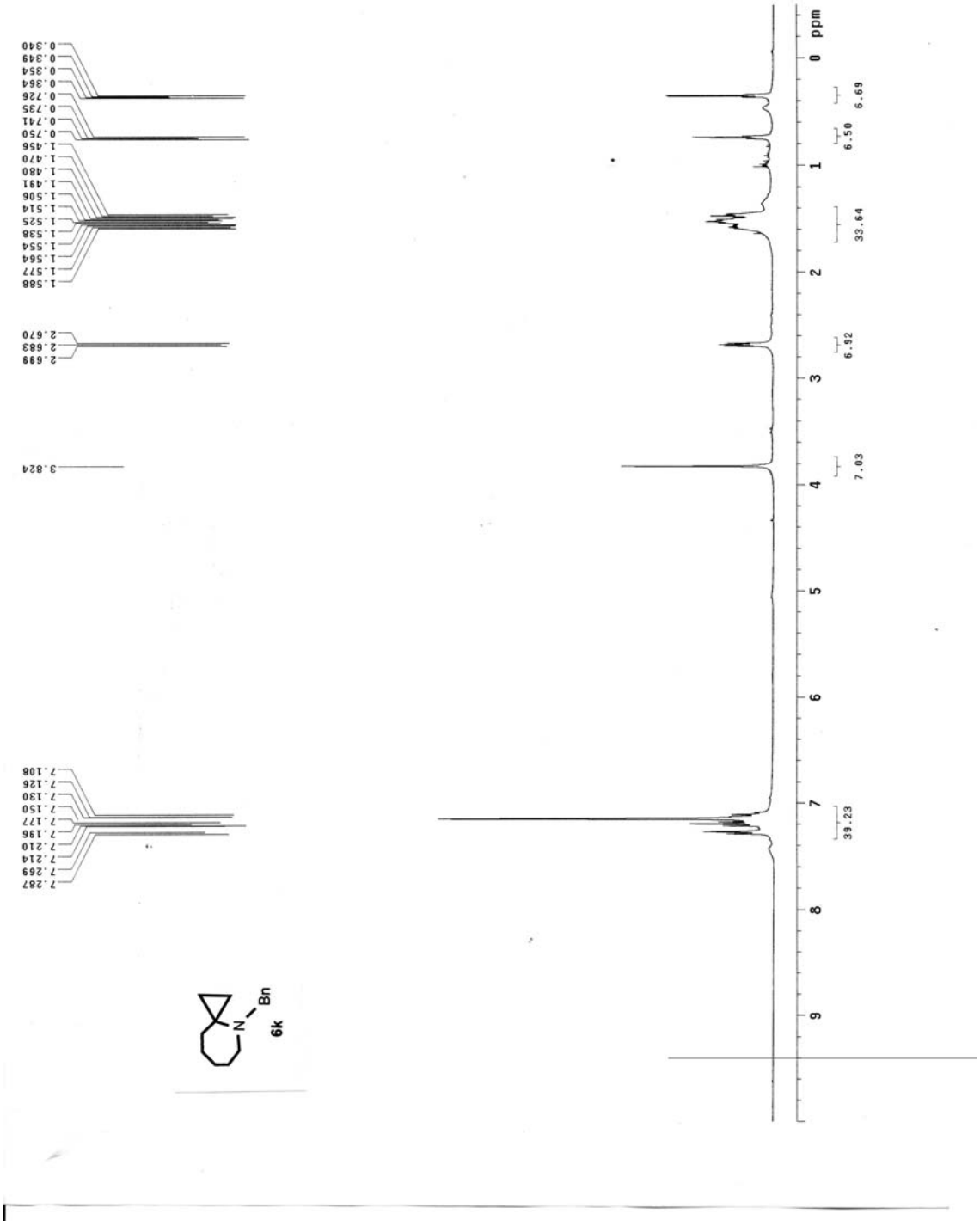
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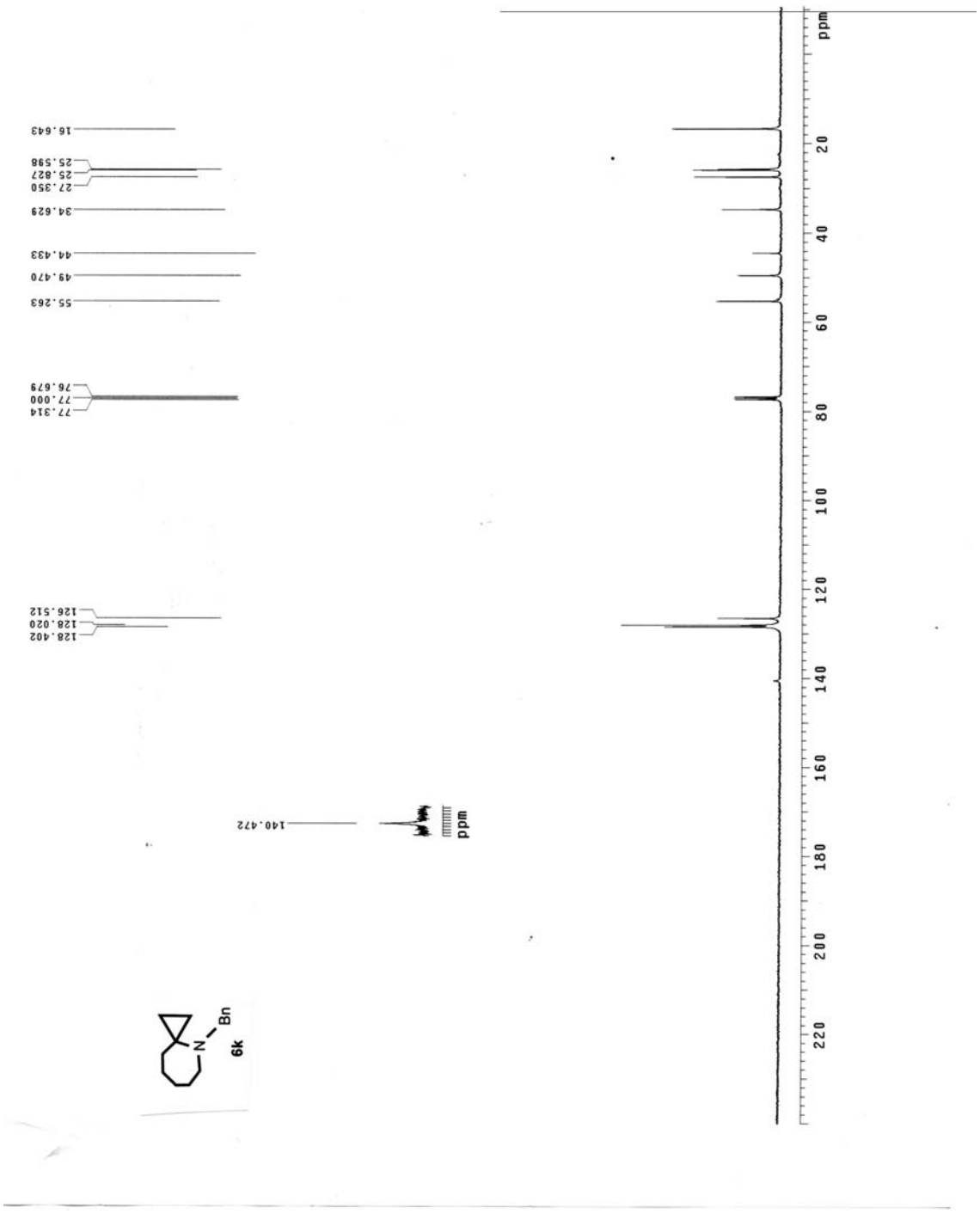
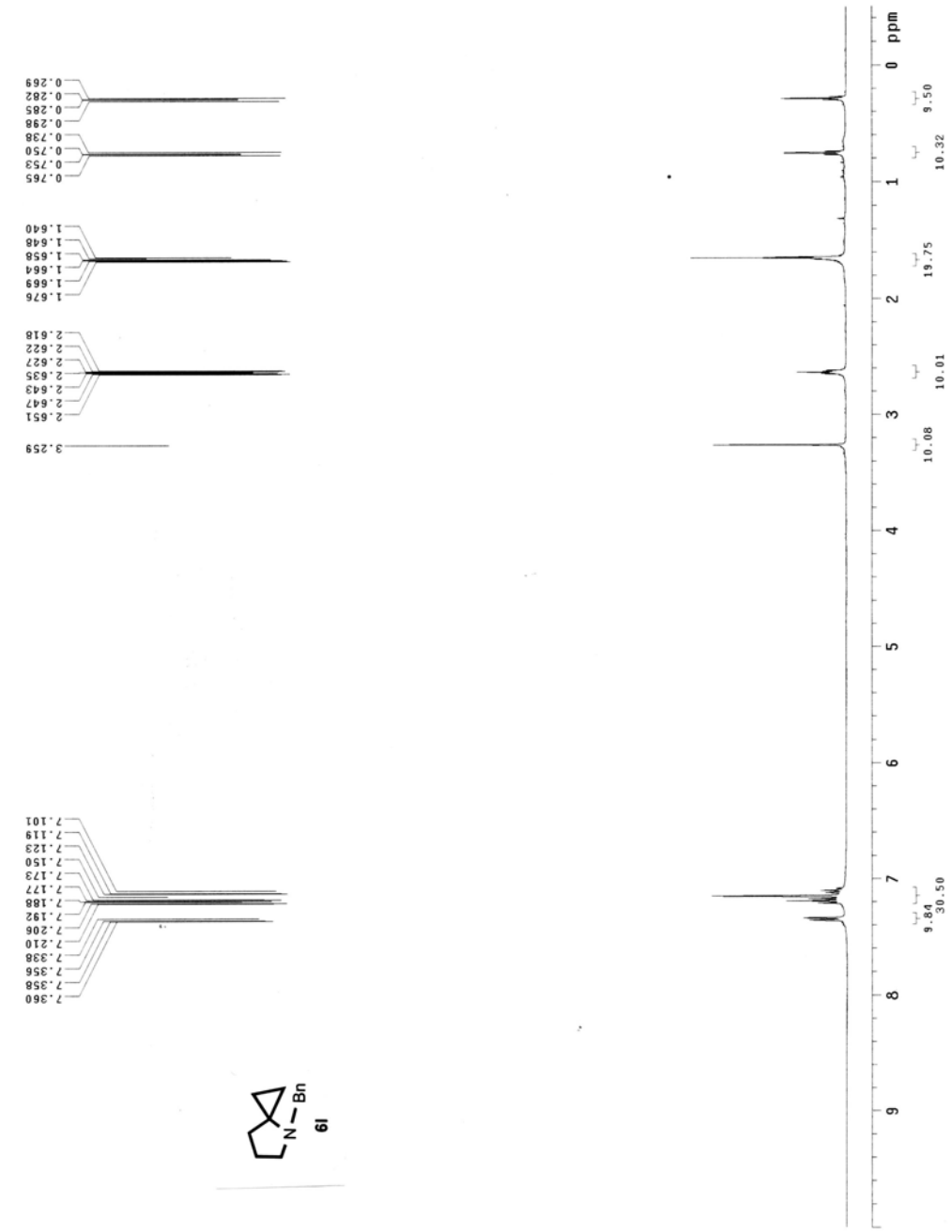
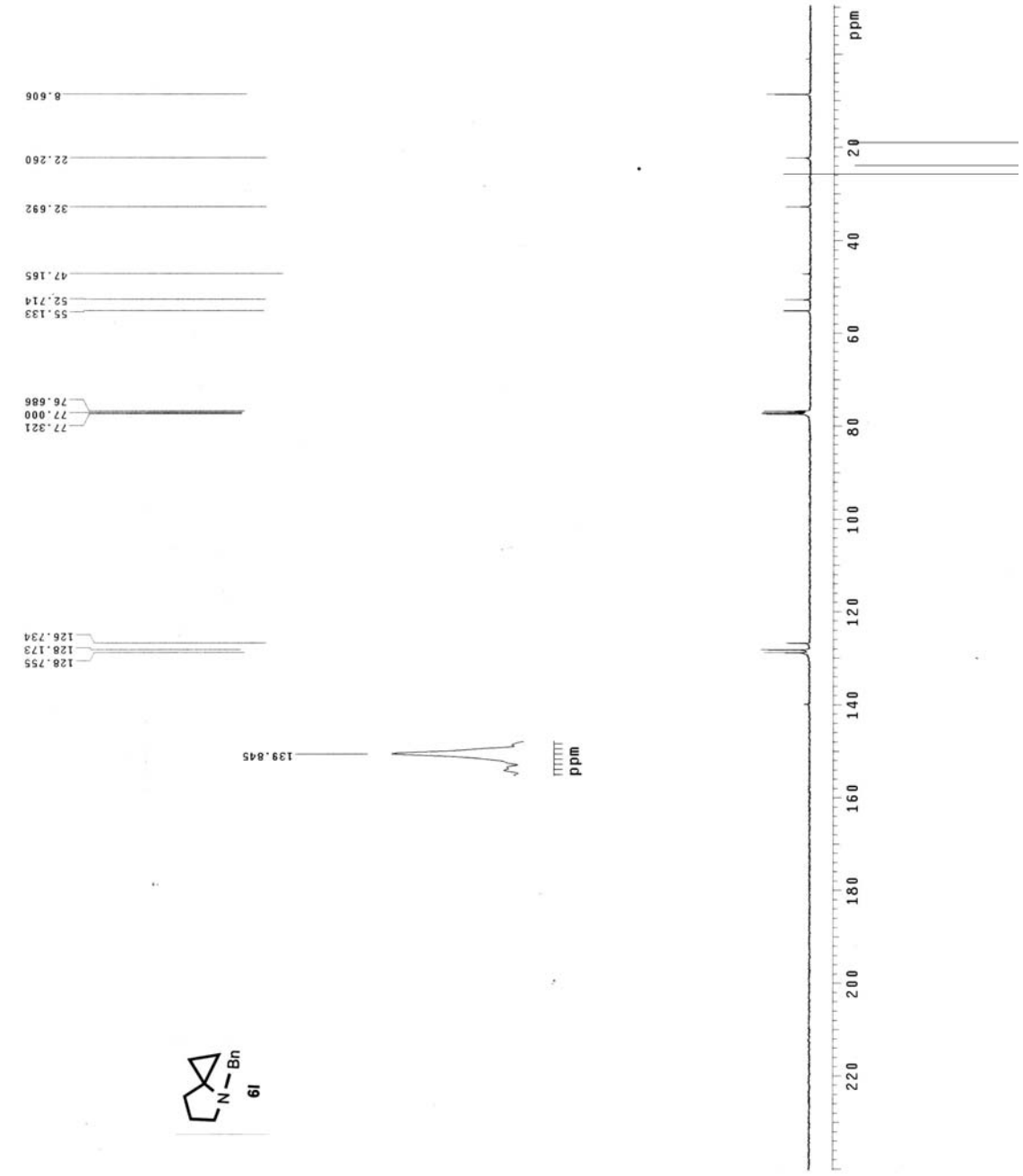
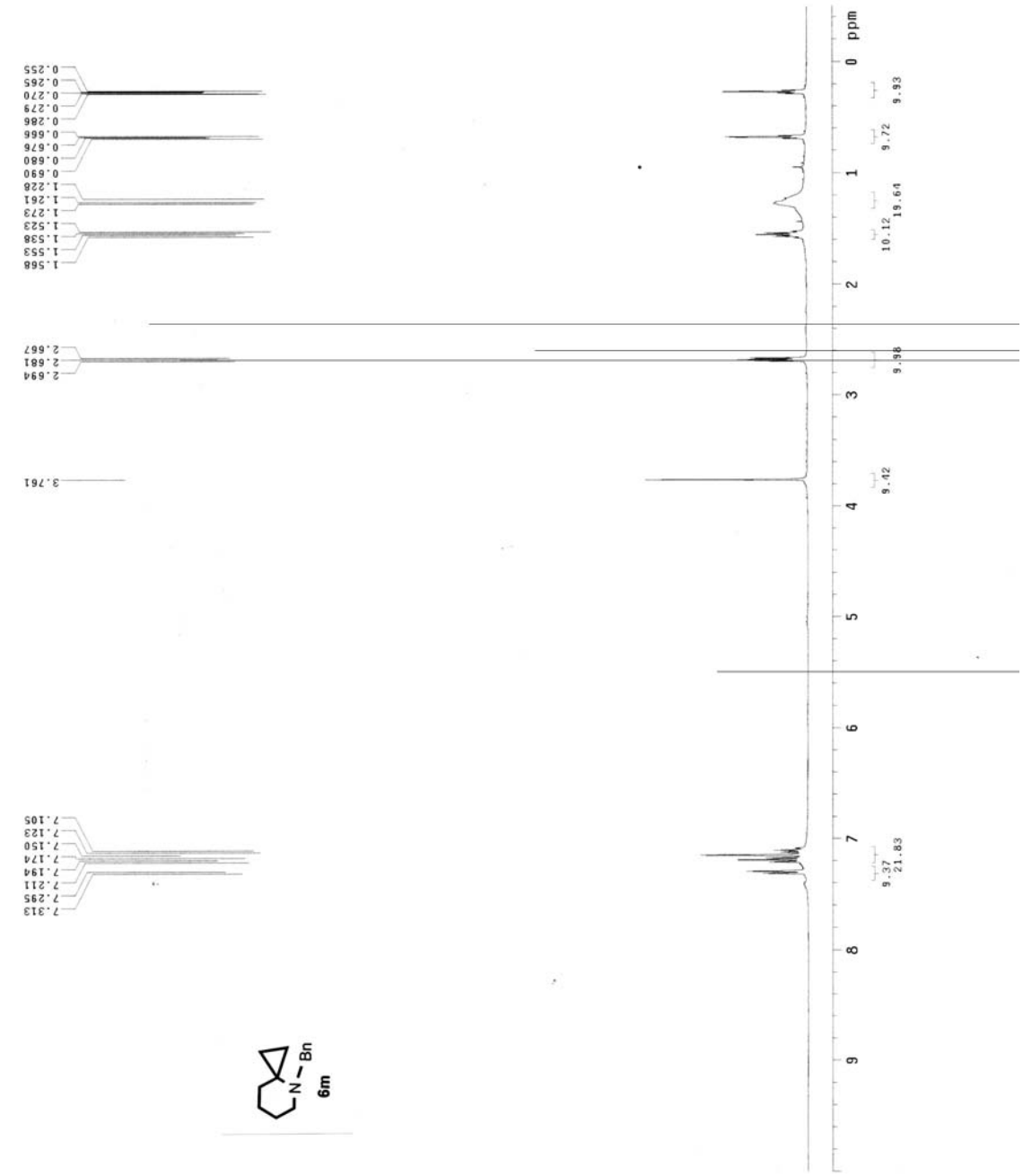
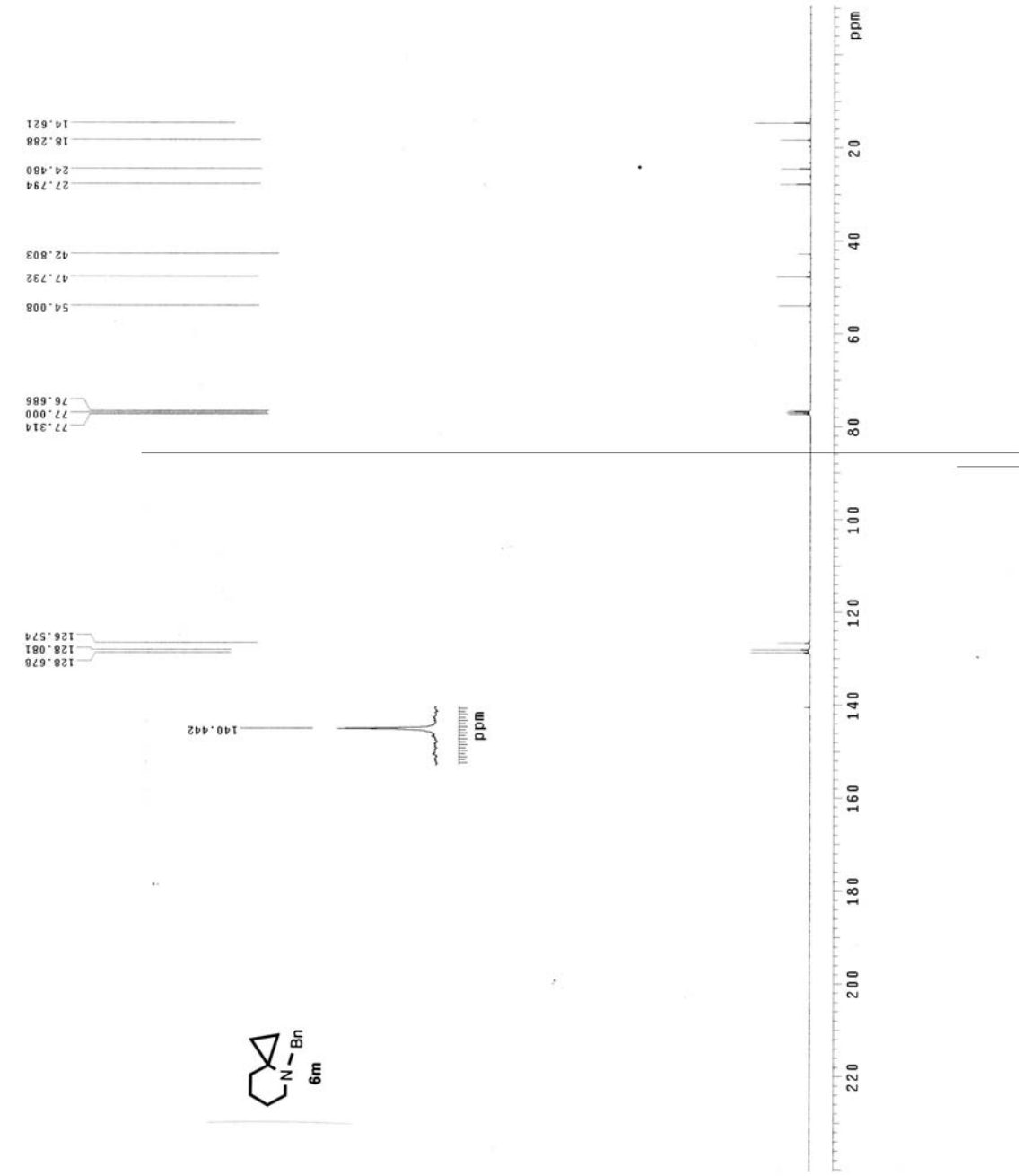
2.683
2.699
3.824
7.108
7.126
7.130
7.150
7.177
7.196
7.210
7.214
7.269
7.287
Bn
N
6k
ppm
0
1
2
3
4
5
6
7
8
9
6.69
6.50
33.64
6.92
7.03
39.23

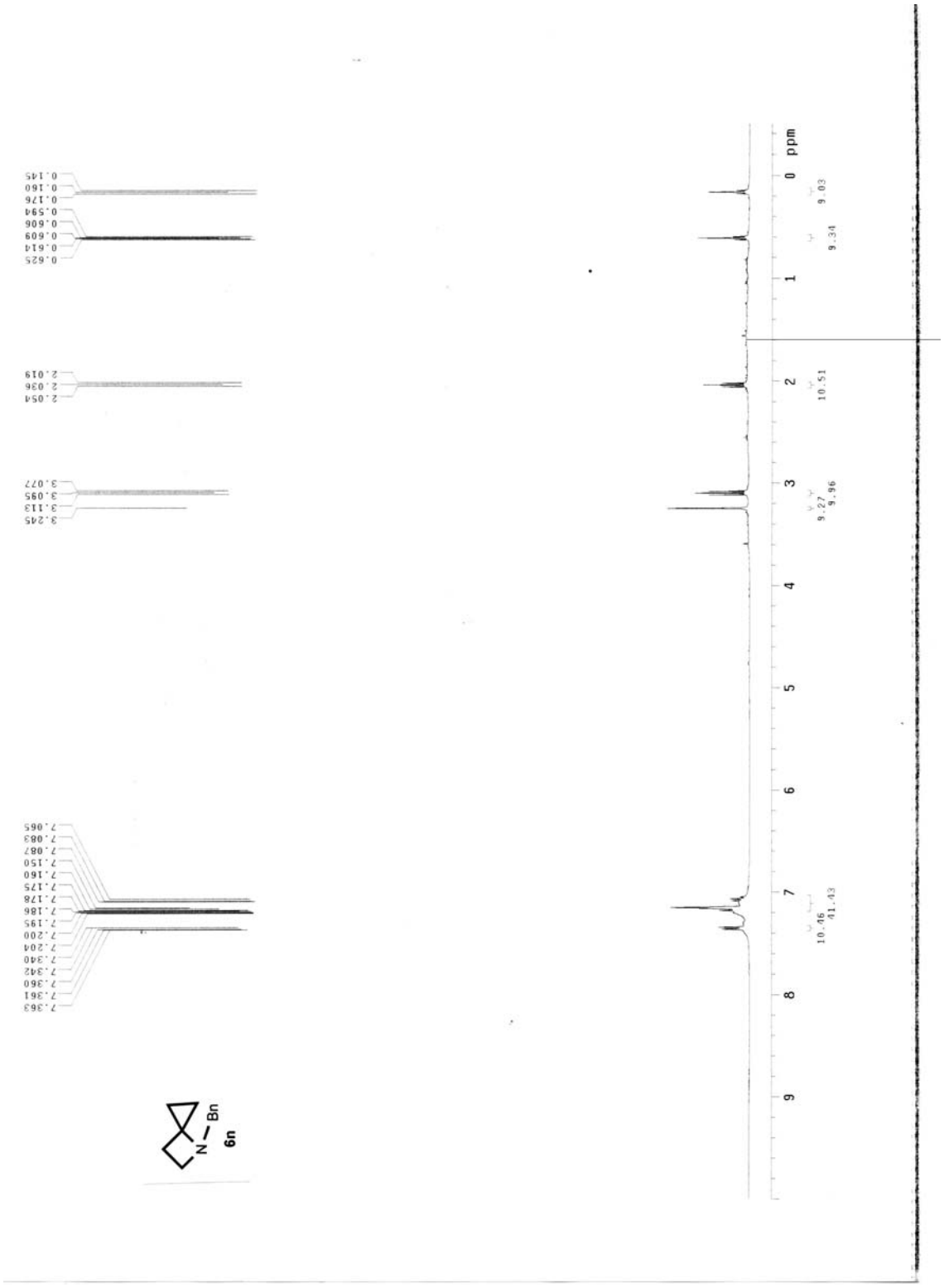

16.643
25.598
25.827
27.350
34.629
44.433
49.470
55.263
76.679
77.000
77.314
126.512
128.020
128.402
140.472
ppm
Bn
N
6k

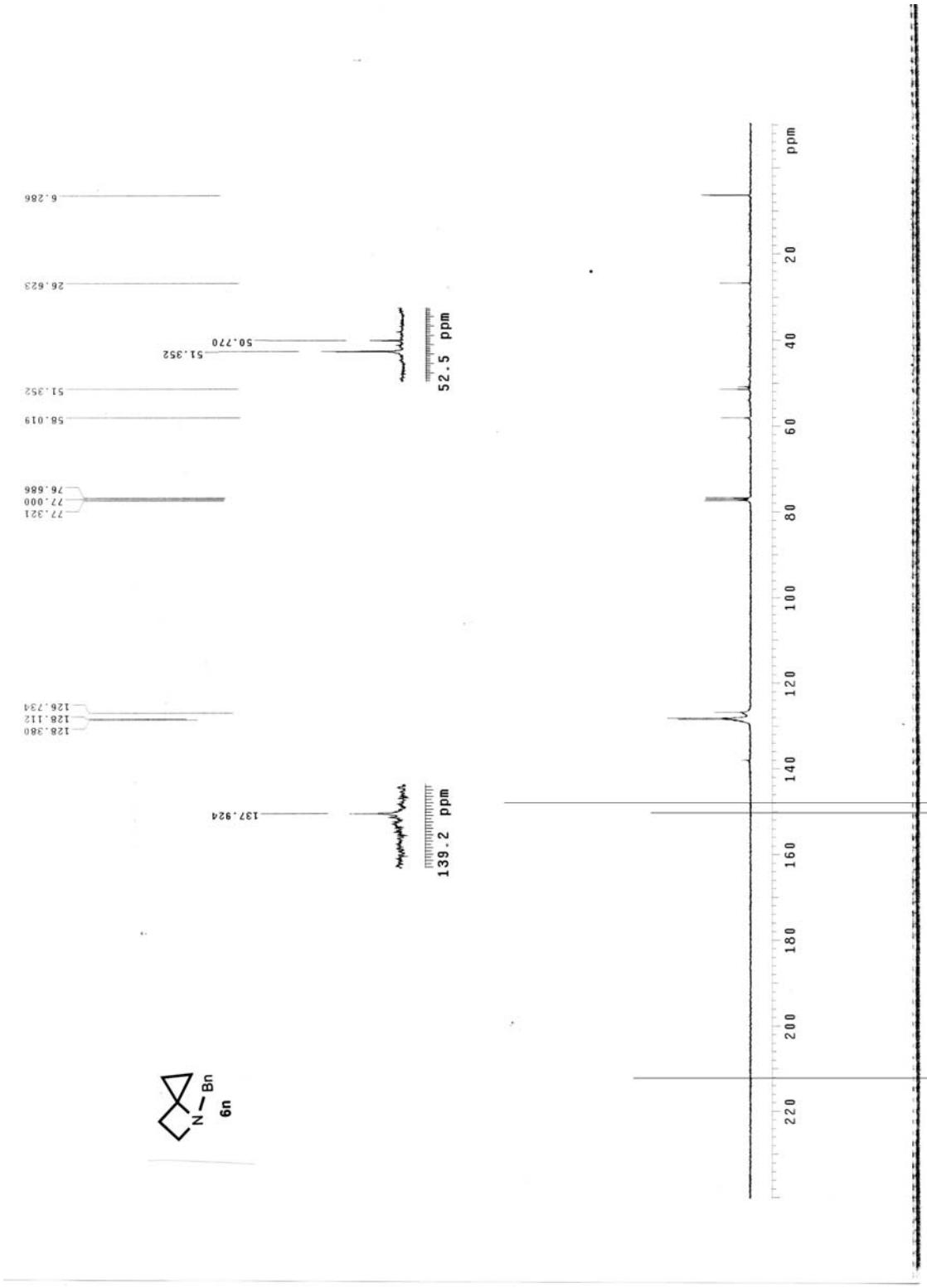

0.269
0.282
0.285
0.298
0.738
0.750
0.753
0.765
1.640
1.648
1.658
1.664
1.669
1.676
2.618
2.622
2.627
2.635
2.643
2.647
2.651
3.259
7.101
7.119
7.123
7.150
7.173
7.177
7.188
7.192
7.206
7.210
7.338
7.356
7.358
7.360
Bn
N
19
ppm
0
1
2
3
4
5
6
7
8
9
9.50
10.32
19.75
10.01
10.08
9.84
30.50

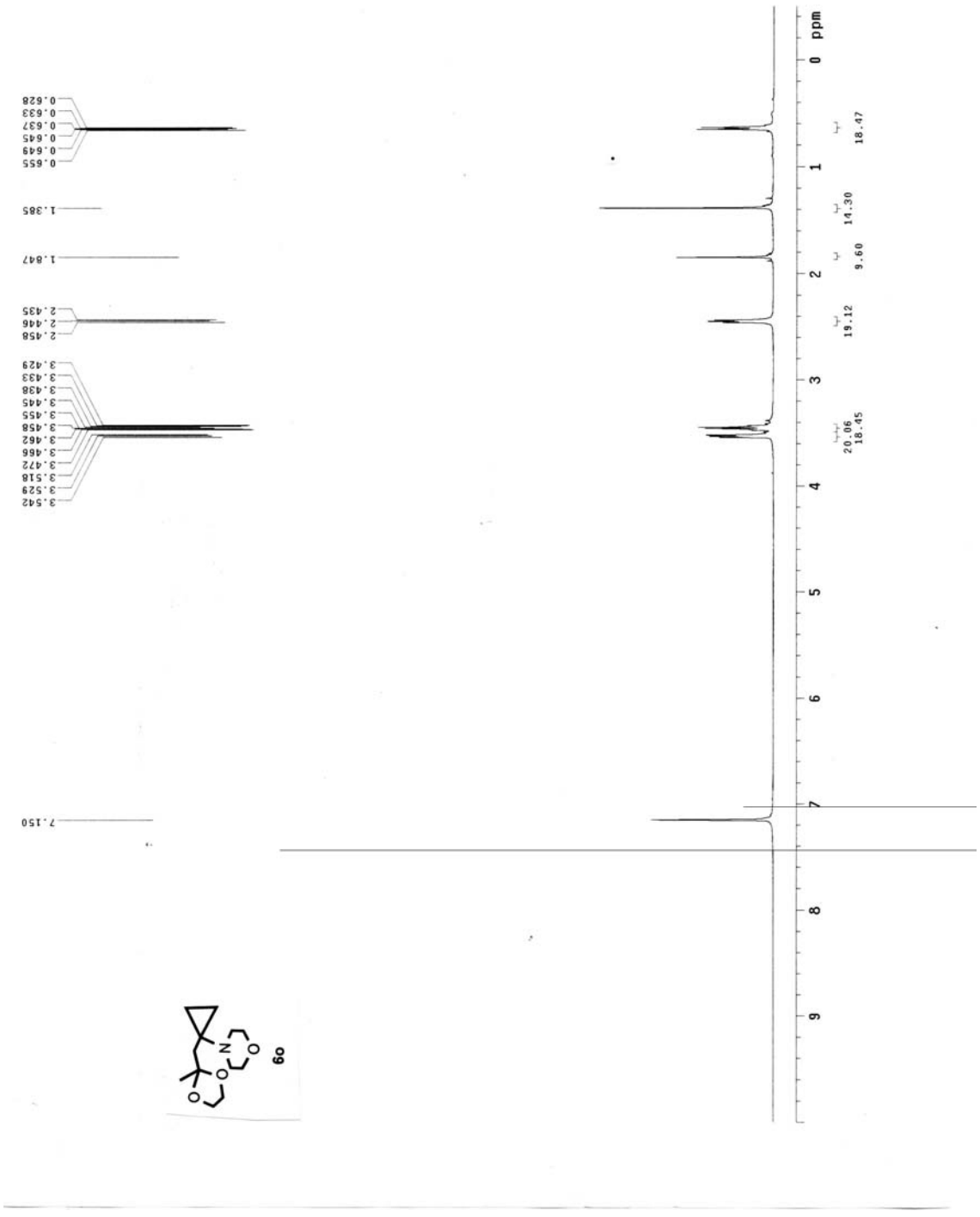

8.606
22.260
32.692
47.165
52.714
55.133
76.686
77.000
77.321
126.734
128.173
128.755
139.845
ppm
Bn
N
19
ppm
20
40
60
80
100
120
140
160
180
200
220

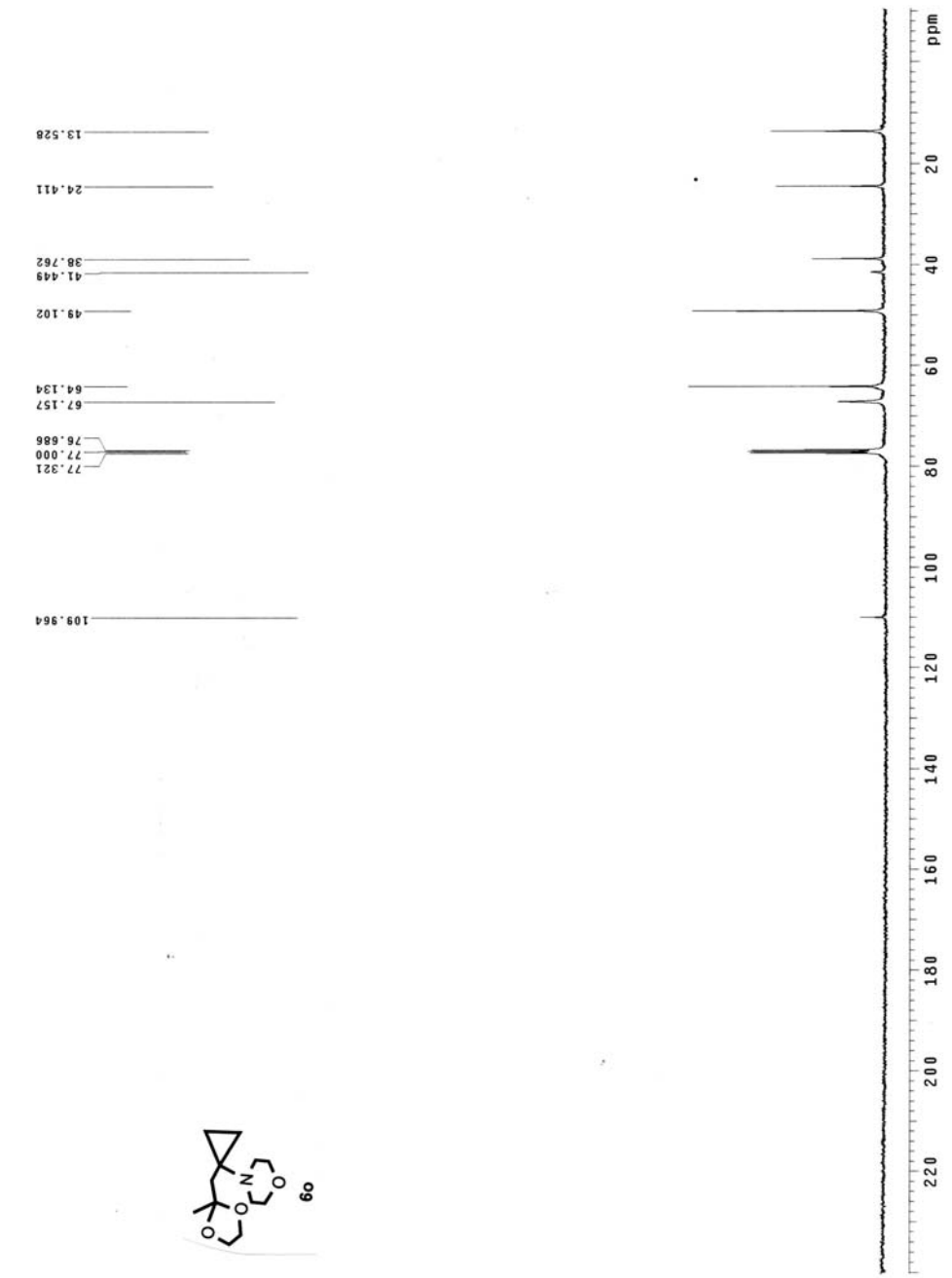

0.255
0.265
0.270
0.279
0.286
0.666
0.676
0.680
0.690
1.228
1.261
1.273
1.523
1.538
1.553
1.568
2.667
2.681
2.694
3.761
7.105
7.123
7.150
7.174
7.194
7.211
7.295
7.313
ppm
0
1
2
3
4
5
6
7
8
9
9.93
9.72
19.64
10.12
9.98
9.42
21.83
9.37
N
Bn
6m

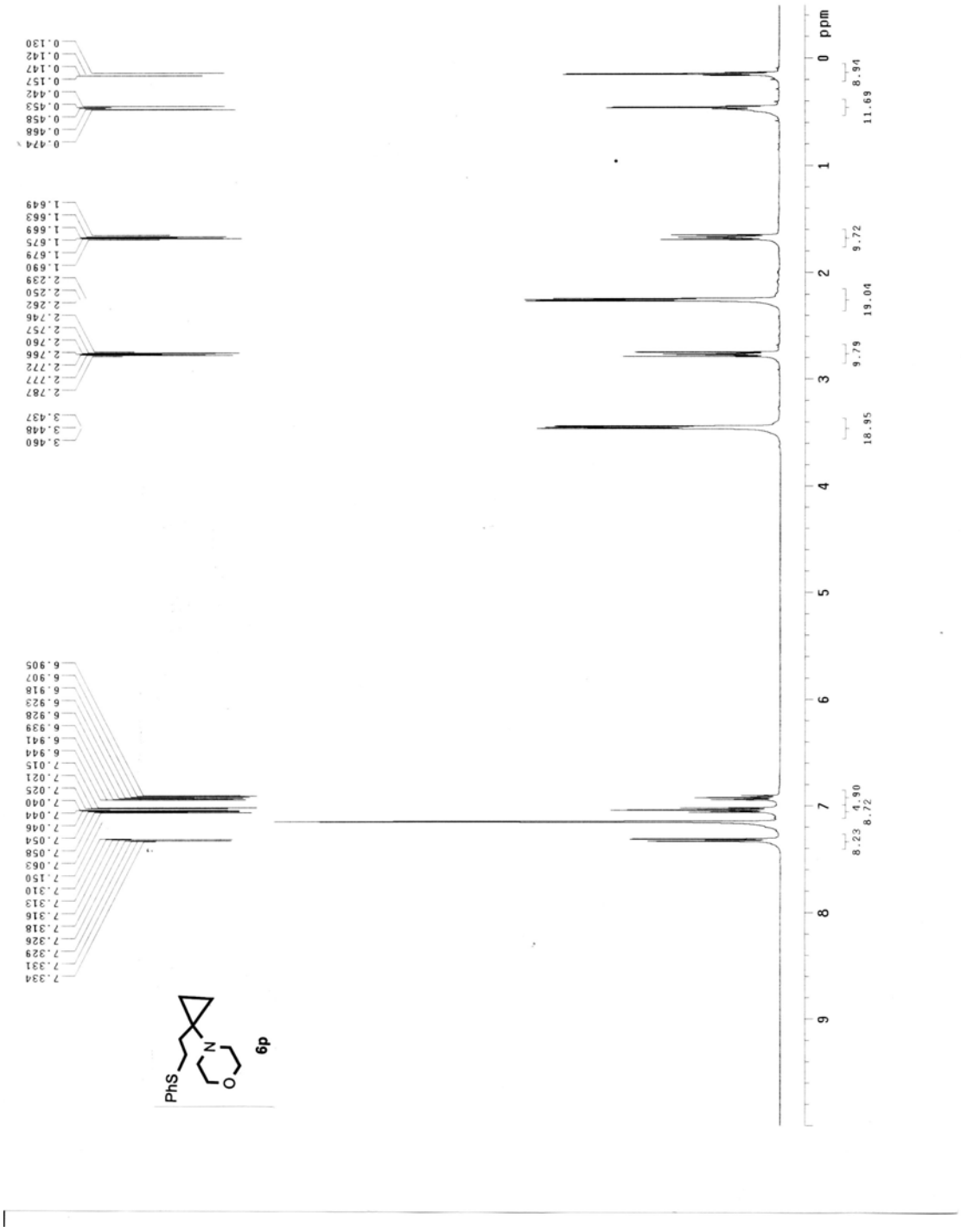

14.621
18.288
24.480
27.794
42.803
47.732
54.008
76.686
77.000
77.314
126.574
128.081
128.678
140.442
ppm
20
40
60
80
100
120
140
160
180
200
220
N
Bn
6m

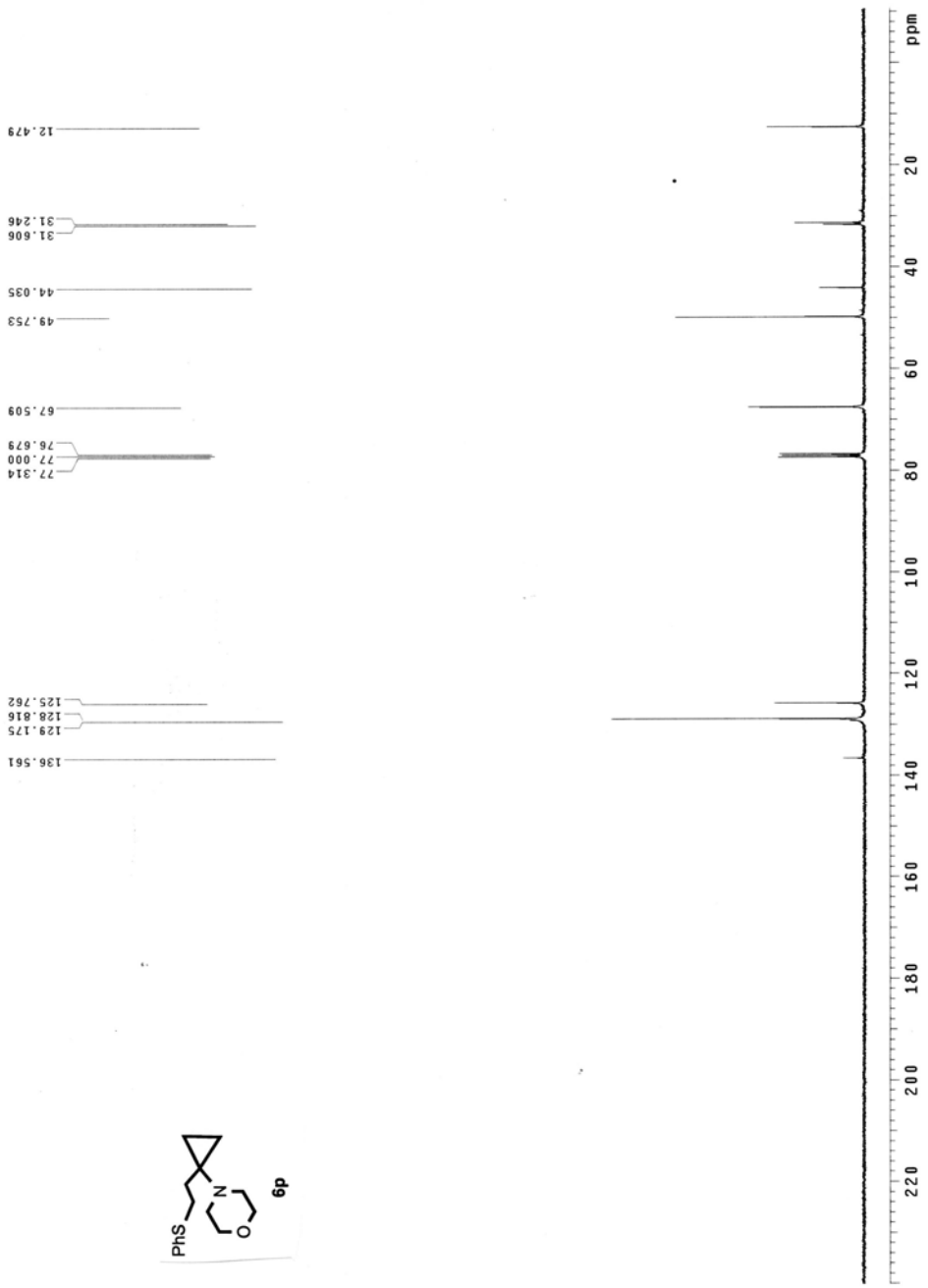

0.625
0.614
0.609
0.606
0.594
0.176
0.160
0.145
2.054
2.036
2.019
3.245
3.113
3.095
3.077
7.363
7.361
7.360
7.342
7.340
7.204
7.200
7.195
7.186
7.178
7.175
7.160
7.150
7.087
7.083
7.065
Bn
N
N
6n
ppm
0
1
2
3
4
5
6
7
8
9
9.03
9.34
10.51
9.27
9.96
10.46
41.43

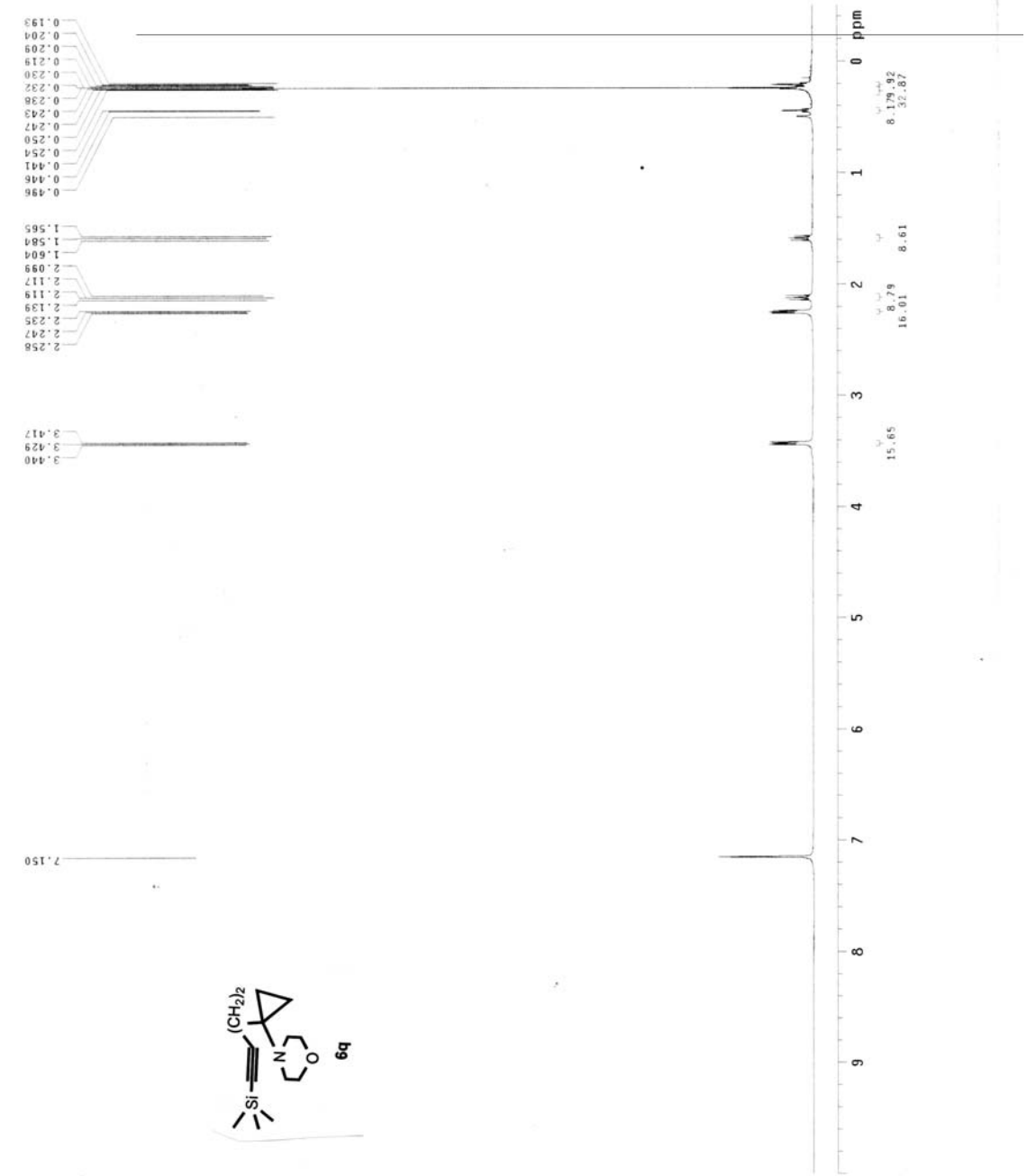

6.286
26.623
50.770
51.352
51.352
58.019
76.686
77.000
77.321
128.380
128.112
126.734
137.924
52.5 ppm
139.2 ppm
Bn
N
N
6n
ppm
20
40
60
80
100
120
140
160
180
200
220

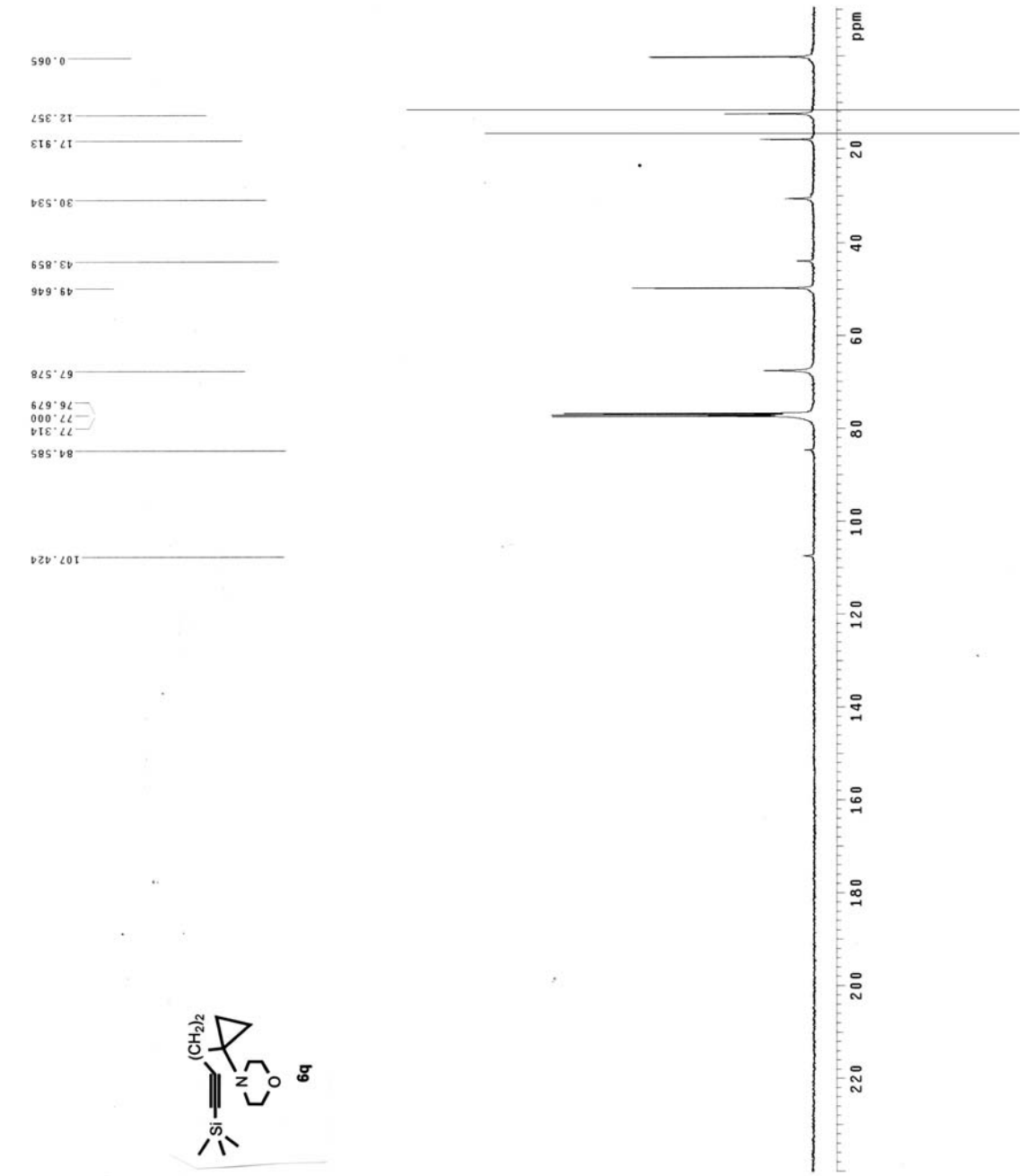

0.628
0.633
0.637
0.645
0.649
0.655
1.385
1.847
2.435
2.446
2.458
3.429
3.433
3.438
3.445
3.455
3.458
3.462
3.466
3.472
3.518
3.529
3.542
7.150
0 ppm
18.47
14.30
9.60
19.12
20.06
18.45
6o

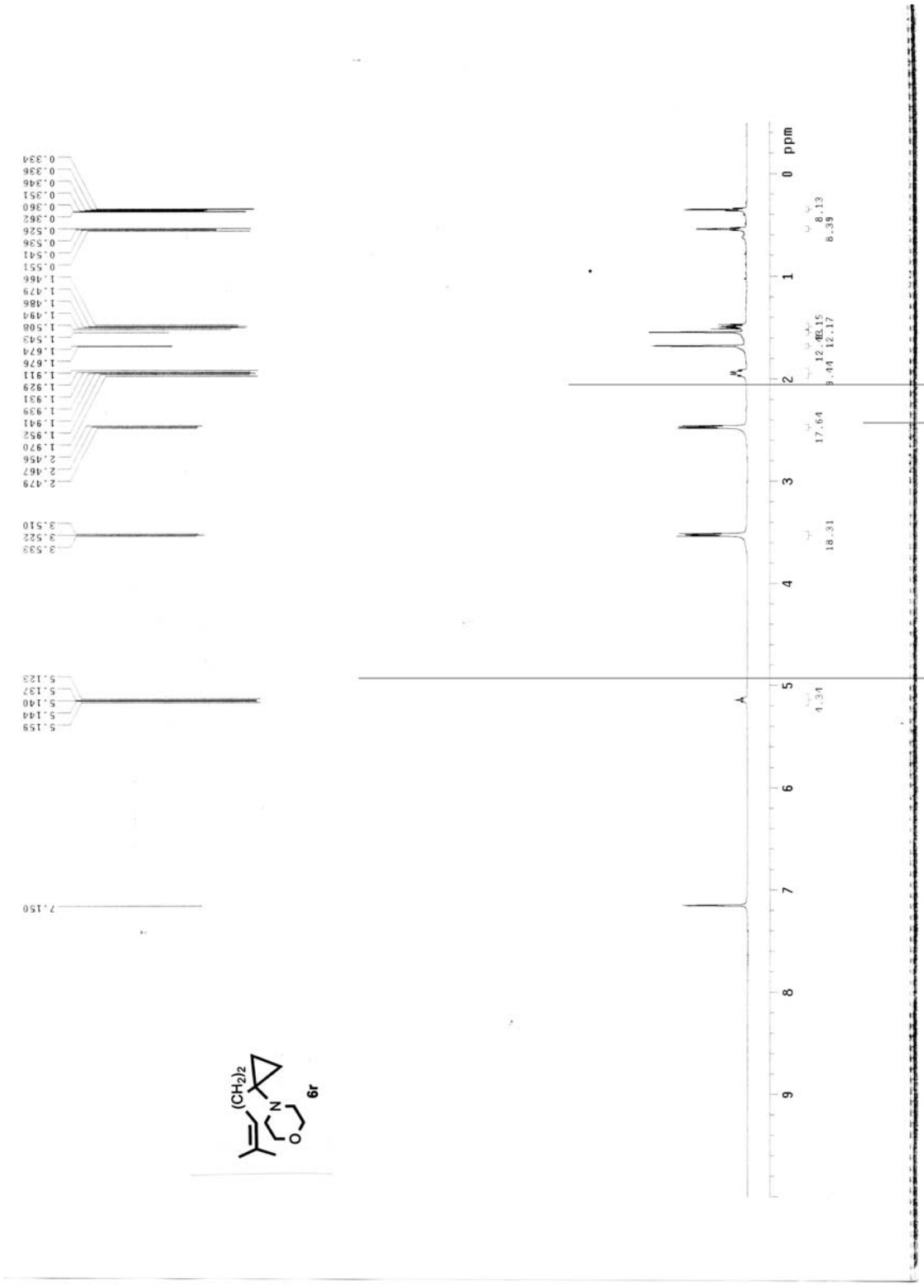

13.528
24.411
38.762
41.449
49.102
64.134
67.157
76.686
77.000
77.321
109.964
ppm
20
40
60
80
100
120
140
160
180
200
220
O
O
N
O
O
9o

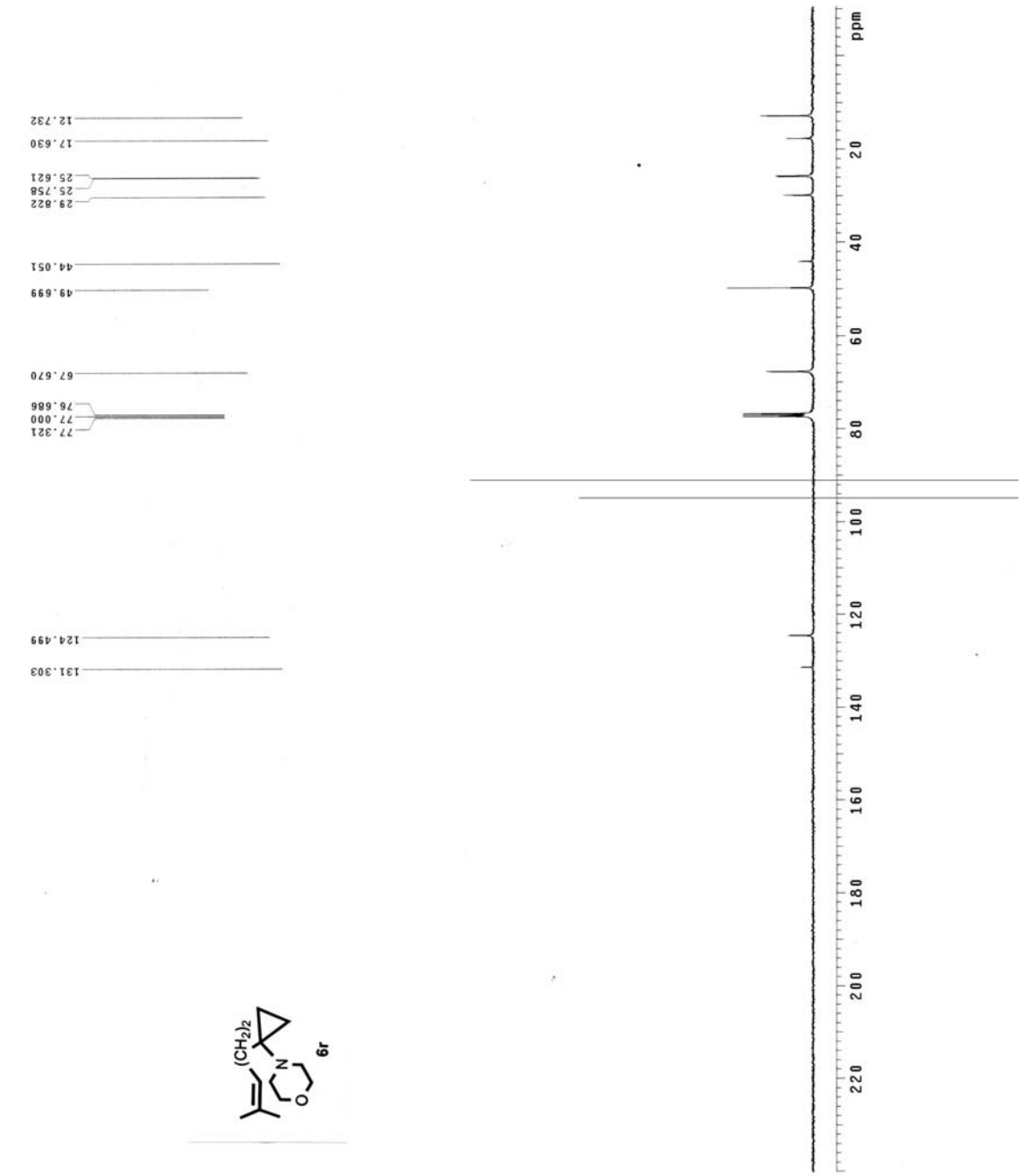

PhS
N
O
6p
ppm

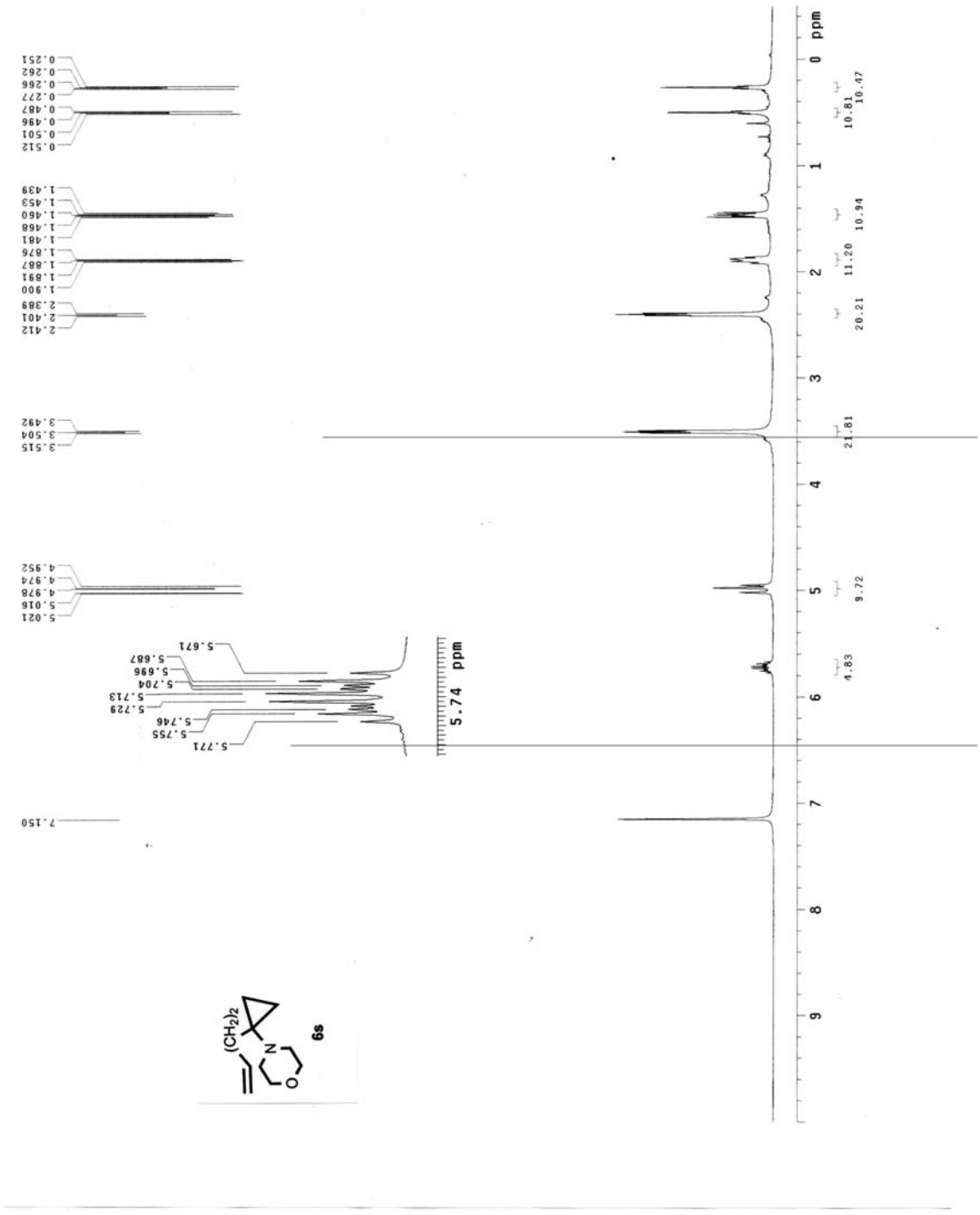

12.479
31.246
31.606
44.035
49.753
67.509
76.679
77.000
77.314
125.762
128.816
129.175
136.561
ppm
20
40
60
80
100
120
140
160
180
200
220
PhS
N
O
6p

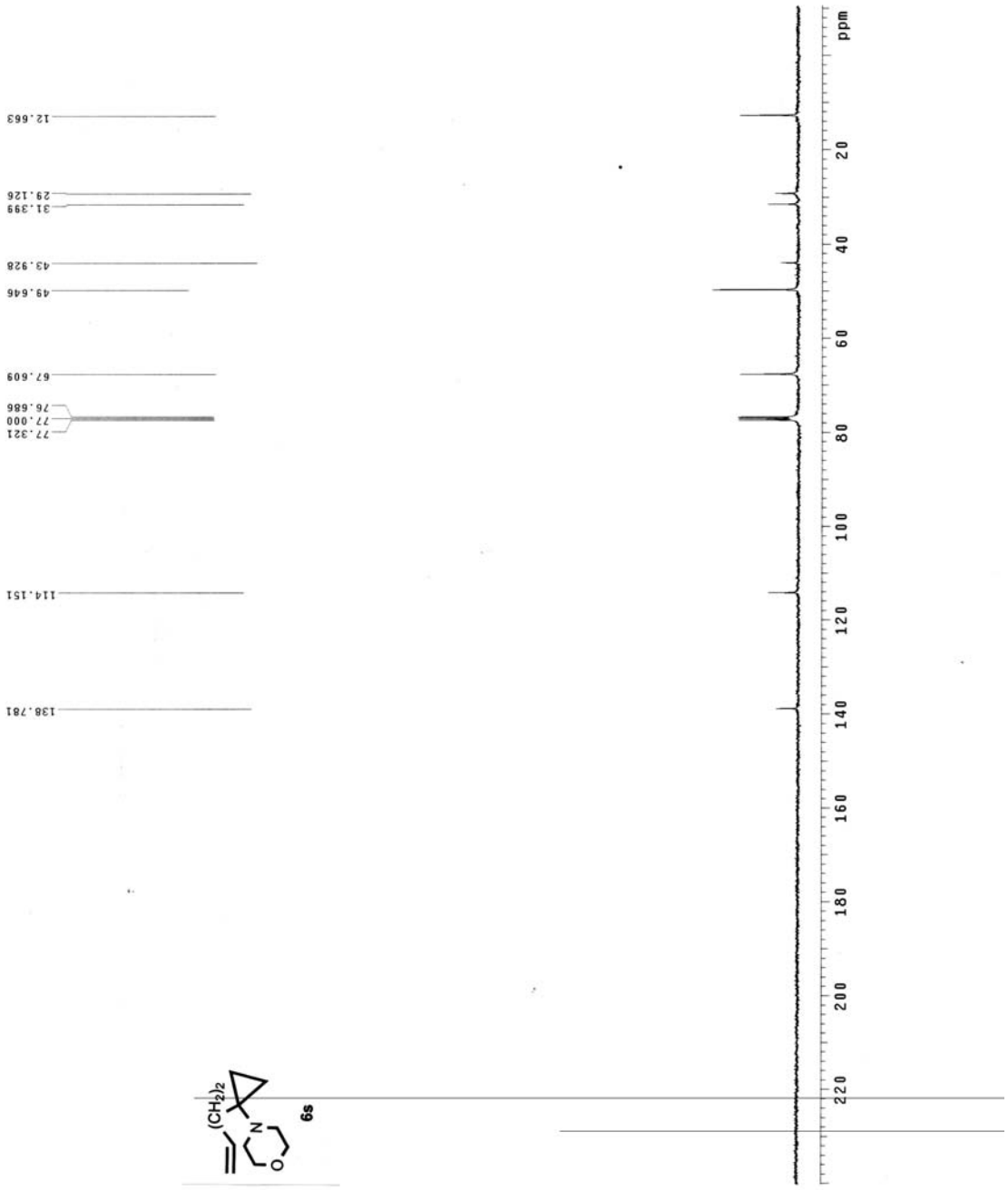

0.193
0.204
0.209
0.219
0.230
0.232
0.236
0.243
0.247
0.250
0.254
0.441
0.446
0.496
1.565
1.584
1.604
2.099
2.117
2.119
2.139
2.235
2.247
2.258
3.417
3.429
3.440
7.150
ppm
0
1
2
3
4
5
6
7
8
9
8.179.92
32.87
8.61
8.79
16.01
15.65
(CH2)2
Si
N
O
6q

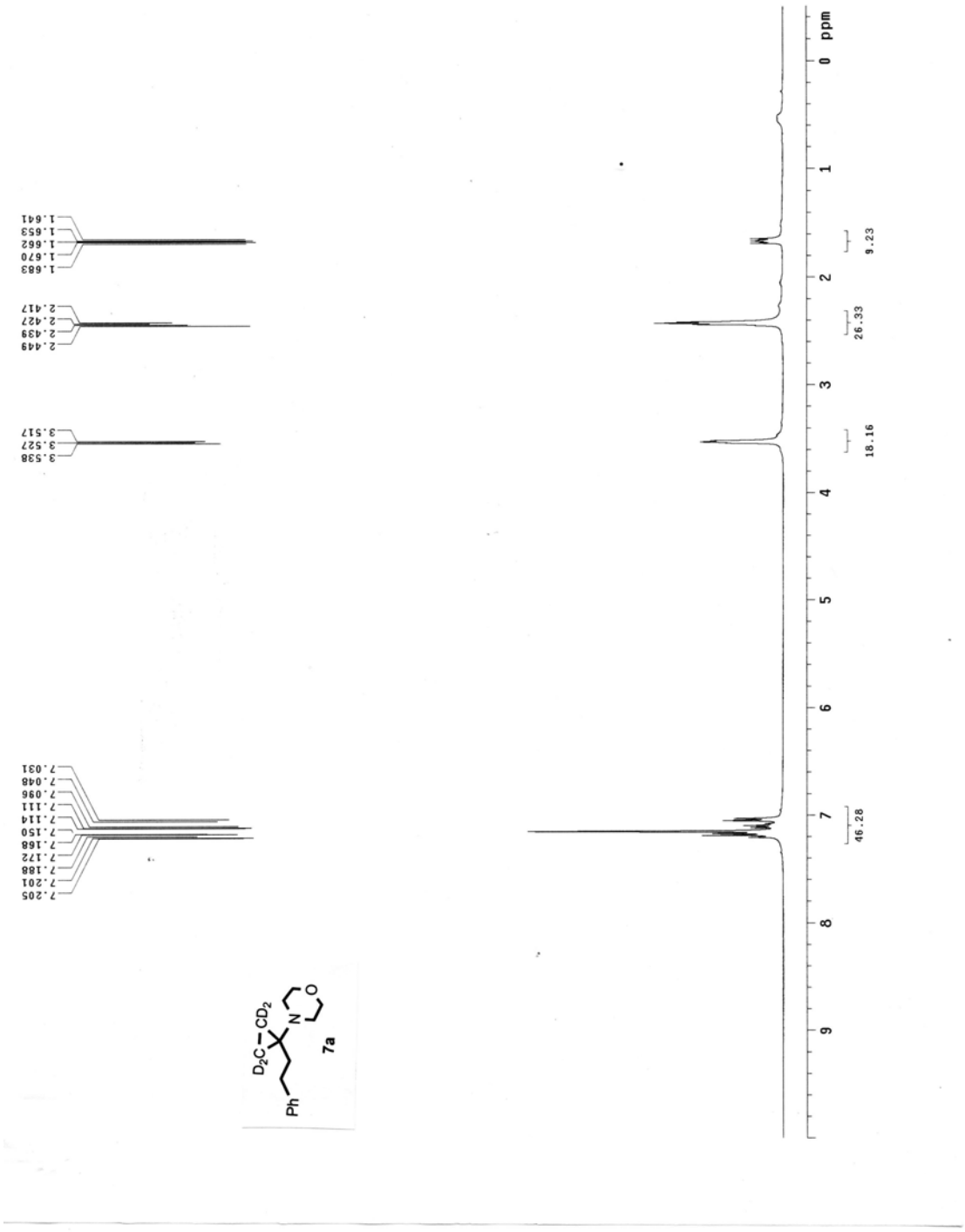

0.065
12.357
17.913
30.534
43.859
49.646
67.578
76.679
77.000
77.314
84.585
107.424
ppm
20
40
60
80
100
120
140
160
180
200
220
(CH2)2
Si
N
O
6q

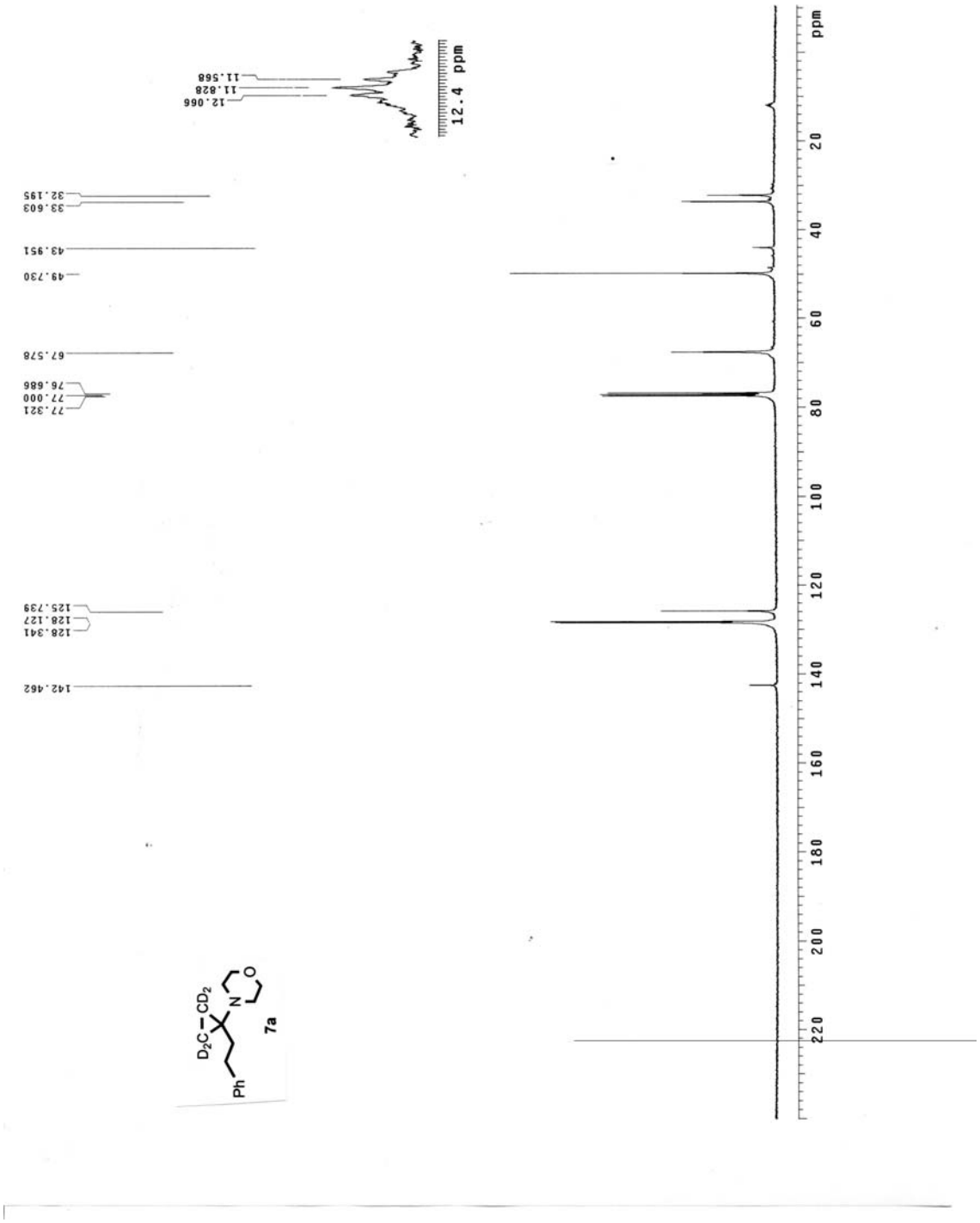

(CH2)2
N
O
6r

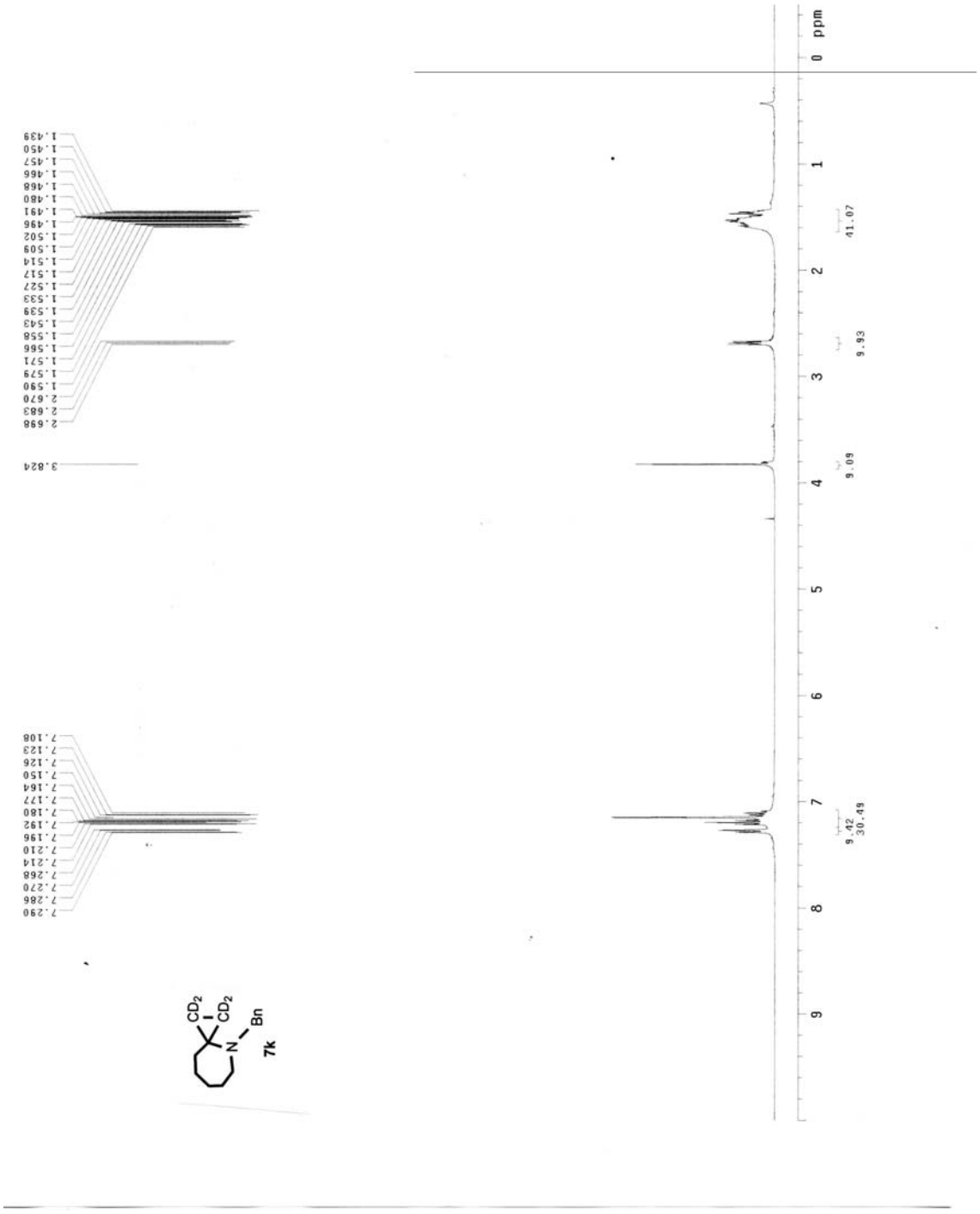

12.732
17.630
25.621
25.758
29.822
44.051
49.699
67.670
76.686
77.000
77.321
124.499
131.303
(CH2)2
N
O
6r
ppm
20
40
60
80
100
120
140
160
180
200
220

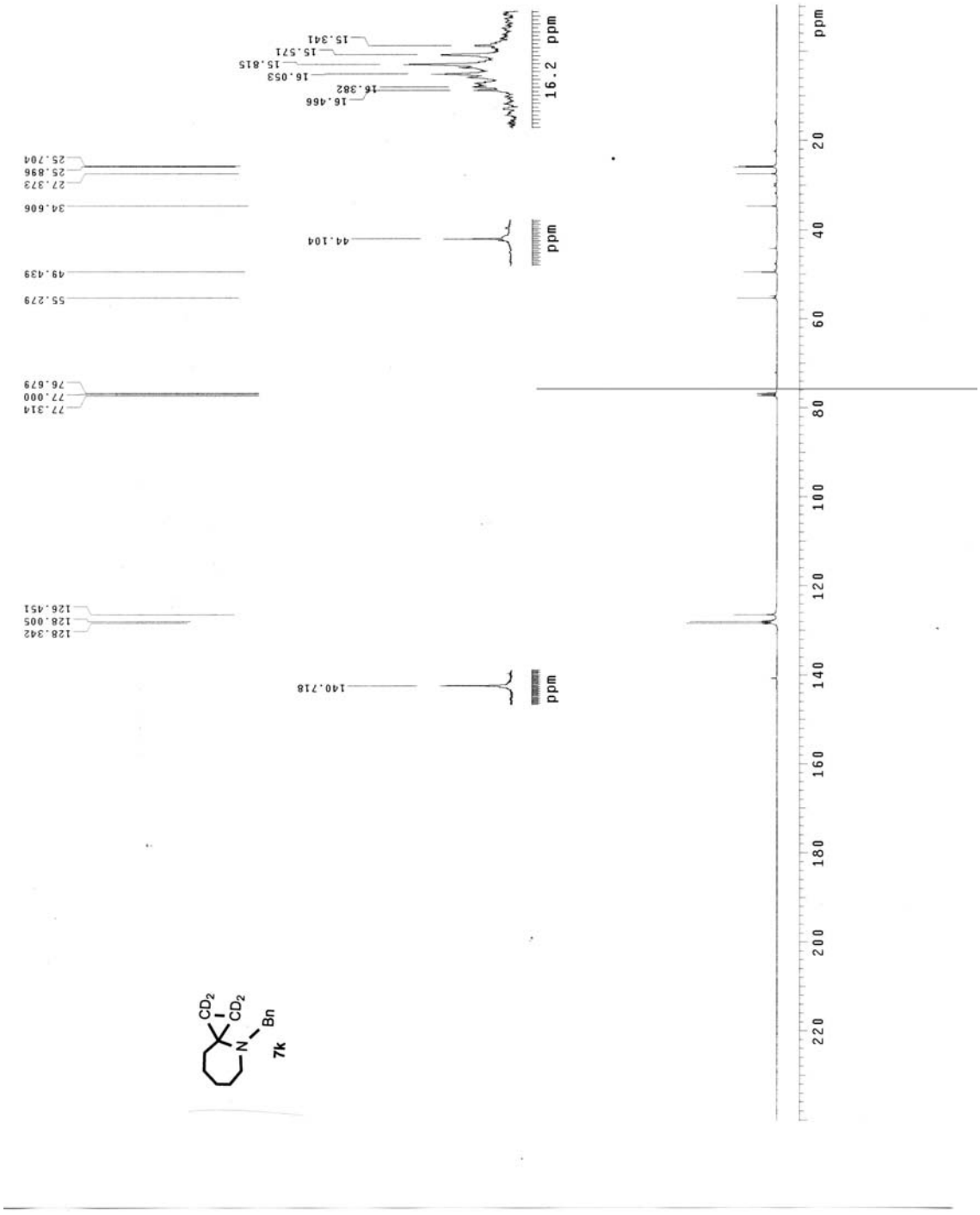

6s
5.74 ppm

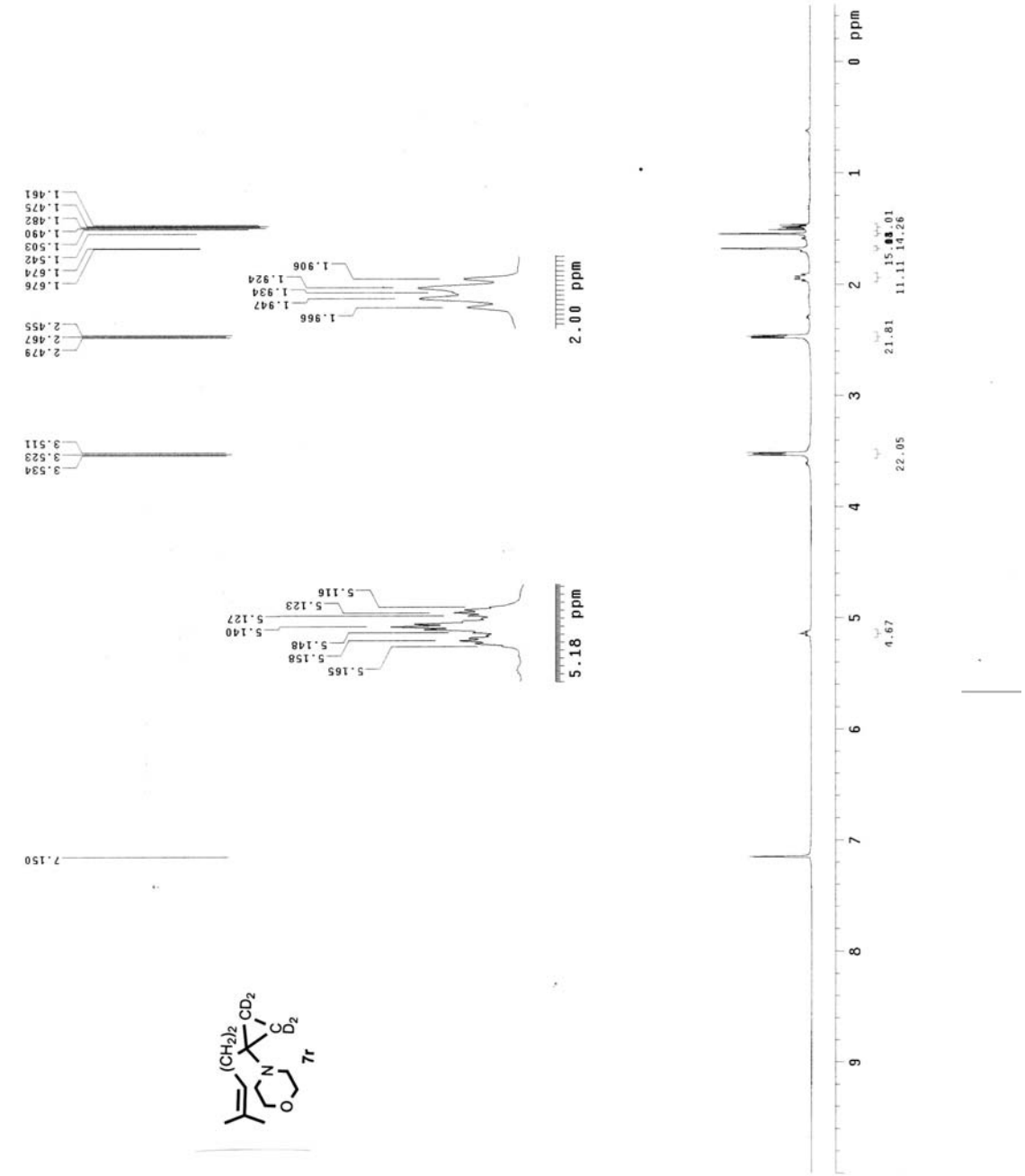

12.663
29.126
31.399
43.928
49.646
67.609
76.686
77.000
77.321
114.151
138.781
ppm
20
40
60
80
100
120
140
160
180
200
220
(CH2)2
N
O
6s

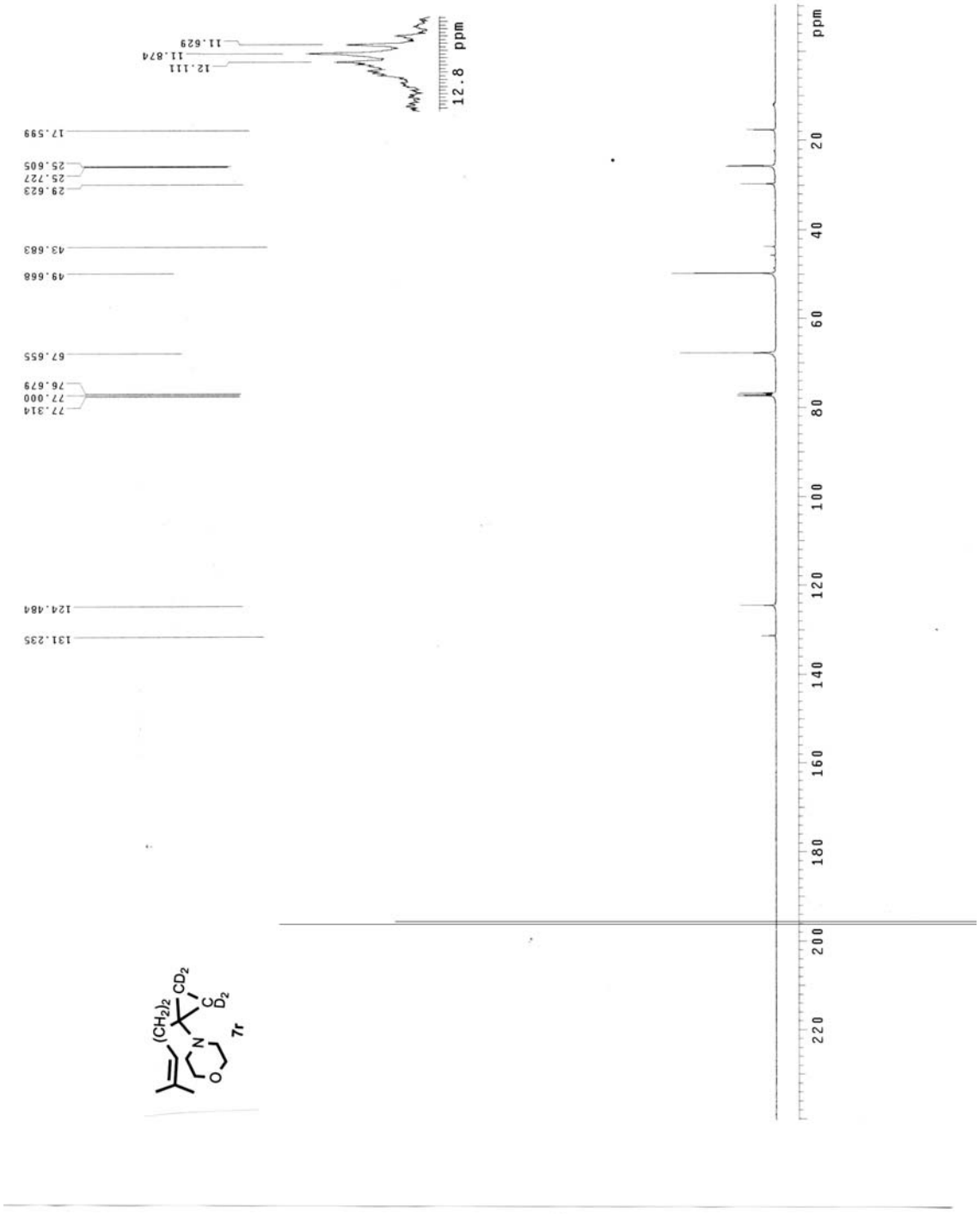

7.205
7.201
7.188
7.172
7.168
7.150
7.114
7.111
7.096
7.048
7.031
3.538
3.527
3.517
2.449
2.439
2.427
2.417
1.683
1.670
1.662
1.653
1.641
D2C
CD2
N
O
Ph
7a
46.28
18.16
26.33
9.23
ppm


12.066
11.828
11.568
12.4 ppm
32.195
33.603
43.951
49.730
67.578
76.686
77.000
77.321
125.739
128.127
128.341
142.462
ppm
20
40
60
80
100
120
140
160
180
200
220
D2C—CD2
N
O
Ph
7a


1.439
1.450
1.457
1.466
1.468
1.480
1.491
1.496
1.502
1.509
1.514
1.517
1.527
1.533
1.539
1.543
1.558
1.566
1.571
1.579
1.590
2.670
2.683
2.698
3.824
7.108
7.123
7.126
7.150
7.164
7.177
7.180
7.192
7.196
7.210
7.214
7.268
7.270
7.286
7.290
CD2
CD2
N
Bn
7k
0 ppm
1
2
3
4
5
6
7
8
9
41.07
9.93
9.09
9.42
30.49


15.341
15.571
15.815
16.053
16.382
16.466
16.2
ppm
25.704
25.896
27.373
34.606
44.104
49.439
55.279
76.679
77.000
77.314
128.342
128.005
126.451
140.718
ppm
ppm
20
40
60
80
100
120
140
160
180
200
220
ppm
CD2
CD2
N
Bn
7k


7.150
5.165
5.158
5.148
5.140
5.127
5.123
5.116
5.18 ppm
3.534
3.523
3.511
2.479
2.467
2.455
1.906
1.947
1.934
1.924
1.866
2.00 ppm
1.676
1.674
1.542
1.503
1.490
1.482
1.475
1.461
0 ppm
4.67
22.05
21.81
15.01
11.11 14.26


11.629
11.874
12.111
12.8 ppm
17.599
25.605
25.727
29.623
43.683
49.668
67.655
76.679
77.000
77.314
124.484
131.235
ppm
20
40
60
80
100
120
140
160
180
200
220
(CH3)2
CD2
D2
N
O
7r