

# **One-Step Synthesis of Diverse Pyridine-containing Heterocycles with 3-Ethoxycyclobutanones at Room Temperature**

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## I. Materials and Methods

All commercial materials (Alfa Aesar, Aladdin, J&K Chemical LTD., Beijing Ouhe Technology Co.Ltd.) were used without further purification. All solvents were analytical grade. Anhydrous dichloromethane, acetonitrile, 1, 2-dichloroethane were obtained through refluxing over CaH<sub>2</sub> and redistillation. The <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a 400 MHz spectrometer in CDCl<sub>3</sub> using TMS or solvent peak as a standard. All <sup>13</sup>C NMR spectra were recorded with complete proton decoupling. Mass spectra were recorded on a Thermo Fisher Orbitrap Fusion Mass Spectrometer (ESI). All IR spectra were recorded on a Bruker company equipment (ATR). All reactions were carried out in oven-dried glassware with a rubber seal. Analytical TLC was performed on Yantai Chemical Industry Research Institute silica gel 60 F254 plates and flash column chromatography was performed on Qingdao Haiyang Chemical Co. Ltd silica gel 60 (200-300mesh). The rotavapor was BUCHI's Rotavapor R-3. Substituted 3-ethoxycyclobutanones was prepared according to the literature reports.<sup>1,2</sup>

All the reactions were carried out under a nitrogen atmosphere except the optimization study involving oxygen. Silica gel plates (GF254) were used for TLC monitoring and silica gel (230-400 mesh) was used for flash column chromatography. All final compounds were characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR and Waters UPLC-mass spectroscopy. Copies of NMR spectra are included for all final compounds. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on Bruker models Avance DPX 400 (400 MHz) spectrometers. <sup>1</sup>H NMR spectra are reported in parts per million (ppm) downfield of TMS and were measured relative to the signals for CHCl<sub>3</sub> (7.26 ppm), Acetone-d6 (d 2.05) and DMSO-d6 (d 2.50). All <sup>13</sup>C NMR spectra were reported in ppm and were obtained with <sup>1</sup>H decoupling. In reporting spectral data, the format ( $\delta$ ) chemical shift (multiplicity, J values in Hz, integration) was used with the following abbreviations: s = singlet, brs = broad singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet, brm = broad multiplet. MS analyses were carried out on Waters UPLC-Mass instrument.

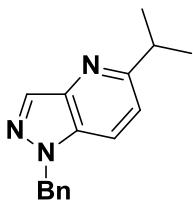
## II. General procedure for the synthesis of heterocyclics

Substituted heterocyclic amines (1.0 equiv, 0.30 mmol) and substituted 3-ethoxycyclobutanones (1.0 equiv) were dissolved in anhydrous dichloromethane (2 ml) in a round bottom flask. Following that, BF<sub>3</sub>•OEt<sub>2</sub> (1.0 equiv) was added slowly into the reaction solution. Then the reaction mixture was stirred at room temperature under atmosphere of Argon for 6-12 h. The reaction was monitored by TLC and LC-MS. After completion of the reaction, Et<sub>3</sub>N (1~2 drops) was added to quench the reaction. The reaction mixture was diluted with dichloromethane (15 ml) and washed once with saturated aqueous NaHCO<sub>3</sub> (10 ml) and once with water (10 ml). Then organic layer was dried over MgSO<sub>4</sub> and concentrated on rotavapor under reduced pressure. Finally the residue was purified by silical gel column chromatography to give corresponding heterocyclic products.

## III. References

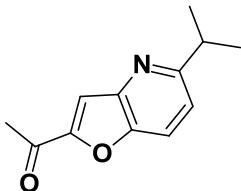
- [1] Matsuo , J.; Sasaki, S.; Hoshikawa, T.; Ishibashi, H. *Org.Lett.* **2009**. 11. 3822.
- [2] Matsuo J.;Okuno,R; Takeuchi, K.; Kawano,M; Ishibashi,H. *Tetrahedron Lett.* **2010**. 51. 3736

#### IV. Data of products



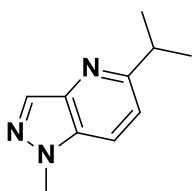
##### 3. 1-benzyl-5-isopropyl-1H-pyrazolo[4,3-b]pyridine

Following the general procedure **II**, amine (104 mg, 0.60 mmol),  $\text{BF}_3\text{-OEt}_2$  (73  $\mu\text{l}$ , 0.60 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 9h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **3** (126 mg, white solid) was isolated in 84% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.22 (s, 1H), 7.55 (d,  $J=8.8\text{Hz}$ , 1H), 7.28 (m, 3H), 7.19 (d, 2H), 7.14 (d,  $J=8.8\text{Hz}$ , 1H), 5.57 (s, 2H), 3.19 (m, 1H), 1.34 (d, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 163.4, 141.8, 136.5, 133.8, 131.6, 129.0, 128.1, 127.4, 119.2, 117.9, 53.9, 36.7, 23.0; HRMS (ESI) calcd for  $\text{C}_{16}\text{H}_{17}\text{N}_3$   $[\text{M}+\text{H}]^+$ : 252.1495, found 252.1502.



##### 4a. 1-(5-isopropylfuro[3,2-b]pyridin-2-yl)ethanone

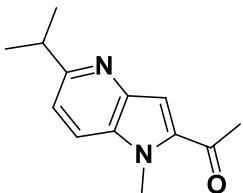
Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3\text{-OEt}_2$  (36  $\mu\text{l}$ , 0.30 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 10h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4a** (33 mg, colorless oil) was isolated in 55% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.98 (d,  $J=8.0\text{Hz}$ , 1H), 7.44 (d, 1H), 7.22 (d,  $J=8.0\text{Hz}$ , 1H), 3.19 (m, 1H), 2.65 (s, 3H), 1.37 (d, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 163.2, 141.3, 133.3, 131.9, 119.1, 117.5, 36.8, 36.0, 23.0; HRMS (ESI) calcd for  $\text{C}_{12}\text{H}_{13}\text{NO}_2$   $[\text{M}+\text{H}]^+$ : 204.1019, found 204.1024.



##### 4b. 5-isopropyl-1-methyl-1H-pyrazolo[4,3-b]pyridine

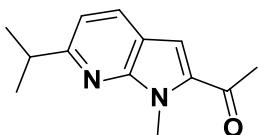
Following the general procedure **II**, amine (0.60 mmol),  $\text{BF}_3\text{-OEt}_2$  (73  $\mu\text{l}$ , 0.60 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 10h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4b** (87 mg, yellow solid) was isolated in 83% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.16 (s, 1H), 7.68 (d,  $J=8.8\text{Hz}$ , 1H), 7.23 (d,  $J=8.8\text{Hz}$ , 1H), 4.07 (s, 3H), 3.22 (m, 1H), 1.36 (d, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 163.2, 141.3, 133.3, 131.9, 119.1, 117.5, 36.8, 36.0, 23.0; HRMS (ESI) calcd

for C<sub>10</sub>H<sub>13</sub>N<sub>3</sub> [M+H]<sup>+</sup>: 176.1182, found 176.1188.



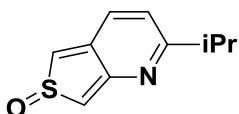
#### **4c. 1-(5-isopropyl-1-methyl-1H-pyrrolo[3,2-b]pyridin-2-yl)ethanone**

Following the general procedure **II**, amine (0.30 mmol), BF<sub>3</sub>•OEt<sub>2</sub> (36 ul, 0.60 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4c** (48 mg, yellow solid) was isolated in 74% yield. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 7.65 (d, J=8.7Hz, 1H), 7.41 (s, 1H), 7.21 (d, J=8.7Hz, 1H), 4.05 (s, 3H), 3.20 (m, 1H), 2.63 (s, 3H), 1.36 (d, 6H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 192.2, 163.3, 142.8, 136.5, 132.5, 118.9, 118.5, 111.6, 36.8, 32.4, 28.3, 23.1; HRMS (ESI) calcd for C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>O [M+H]<sup>+</sup>: 217.1335, found 217.1340.



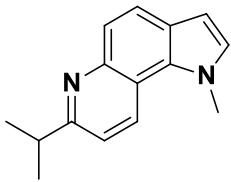
#### **4d. 1-(6-isopropyl-1-methyl-1H-pyrrolo[2,3-b]pyridin-2-yl)ethanone**

Following the general procedure **II**, amine (0.30 mmol), BF<sub>3</sub>•OEt<sub>2</sub> (36 ul, 0.60 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 11h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4d** (43 mg, primrose yellow oil) was isolated in 66% yield. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 7.90 (d, J=8.4Hz, 1H), 7.17 (s, 1H), 7.03 (d, J=8.4Hz, 1H), 4.15 (s, 3H), 3.16 (m, 1H), 2.60 (s, 3H), 1.36 (d, 6H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 191.6, 166.4, 149.5, 134.5, 131.3, 116.4, 115.2, 109.6, 37.1, 30.9, 27.7, 22.9; HRMS (ESI) calcd for C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>O [M+H]<sup>+</sup>: 217.1335, found 217.1343.



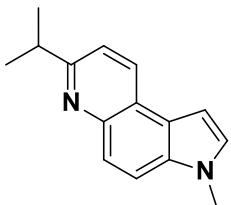
#### **4e. 2-isopropylthieno[3,4-b]pyridine**

Following the general procedure **II**, amine (0.20 mmol), BF<sub>3</sub>•OEt<sub>2</sub> (24 ul, 0.20 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 8h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4e** (34 mg, yellow oil) was isolated in 87% yield. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 9.26 (s, 1H), 8.78 (d, J=1.2Hz, 1H), 7.97 (d, J=1.5Hz, 1H), 7.63 (d, J=5.5Hz, 1H), 3.63 (m, 1H), 1.29 (d, 6H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 203.0, 158.7, 147.7, 135.2, 131.1, 125.3, 36.2, 19.2; HRMS (ESI) calcd for C<sub>10</sub>H<sub>11</sub>NSO [M+H]<sup>+</sup>: 194.0634, found 194.0637.



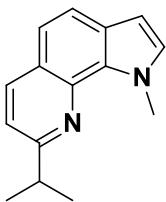
**4f. 7-isopropyl-1-methyl-1H-pyrrolo[2,3-f]quinolone**

Following the general procedure **II**, amine (0.60 mmol),  $\text{BF}_3\cdot\text{OEt}_2$  (72 ul, 0.60 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 10h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 20:1). Finally, compound **4f** (102 mg, white solid) was isolated in 76% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.69 (d,  $J=8.8\text{Hz}$ , 1H), 7.89 (d,  $J=8.8\text{Hz}$ , 1H), 7.75 (d,  $J=8.8\text{Hz}$ , 1H), 7.37 (d,  $J=8.8\text{Hz}$ , 1H), 7.07 (d,  $J=2.9\text{Hz}$ , 1H), 6.61 (d,  $J=2.9\text{Hz}$ , 1H), 4.23 (s, 3H), 3.29 (m, 1H), 1.42 (d, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 164.2, 146.7, 129.6, 129.3, 129.2, 125.4, 124.4, 122.1, 117.4, 116.9, 102.4, 38.3, 37.1, 22.9; HRMS (ESI) calcd for  $\text{C}_{15}\text{H}_{16}\text{N}_2$  [ $\text{M}+\text{H}]^+$ : 225.1386, found 225.1392



**4g. 7-isopropyl-3-methyl-3H-pyrrolo[3,2-f]quinolone**

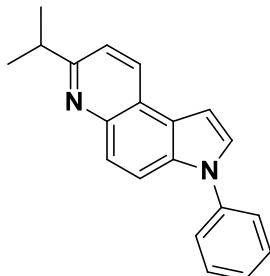
Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3\cdot\text{OEt}_2$  (36 ul, 0.30 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4g** (48 mg, white solid) was isolated in 71% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.46 (d,  $J=8.5\text{Hz}$ , 1H), 7.83 (d,  $J=9.0\text{Hz}$ , 1H), 7.69 (d,  $J=9.0\text{Hz}$ , 1H), 7.39 (d,  $J=8.5\text{Hz}$ , 1H), 7.16 (d,  $J=3.0\text{Hz}$ , 1H), 6.97 (d,  $J=3.0\text{Hz}$ , 1H), 3.92 (s, 3H), 3.28 (m, 1H), 1.41 (d, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 164.5, 144.6, 132.8, 131.7, 127.8, 123.5, 123.0, 121.7, 118.3, 114.1, 100.4, 37.3, 33.4, 23.0; HRMS (ESI) calcd for  $\text{C}_{15}\text{H}_{16}\text{N}_2$  [ $\text{M}+\text{H}]^+$ : 225.1386, found 225.1392.



**4h. 8-isopropyl-1-methyl-1H-pyrrolo[3,2-h]quinolone**

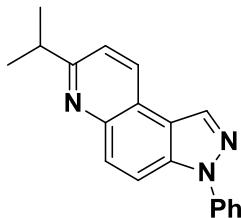
Following the general procedure **II**, amine (0.60 mmol),  $\text{BF}_3\cdot\text{OEt}_2$  (72 ul, 0.60 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 10h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4h** (110 mg, white solid) was isolated in 82% yield. Melting point: 57-58°C.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$

(ppm) 8.12 (d,  $J=8.3\text{Hz}$ , 1H), 7.71 (d,  $J=8.5\text{Hz}$ , 1H), 7.40 (d,  $J=8.5\text{Hz}$ , 1H), 7.26 (d,  $J=8.3\text{Hz}$ , 1H), 7.16 (d,  $J=2.8\text{Hz}$ , 1H), 6.65 (d,  $J=2.8\text{Hz}$ , 1H), 4.60 (s, 3H), 3.29 (m, 1H), 1.49 (d, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 164.5, 139.7, 136.2, 129.9, 129.5, 128.0, 123.7, 120.9, 119.3, 117.3, 102.1, 38.1, 36.9, 22.7; HRMS (ESI) calcd for  $\text{C}_{15}\text{H}_{16}\text{N}_2$  [ $\text{M}+\text{H}]^+$ : 225.1386, found 225.1393.



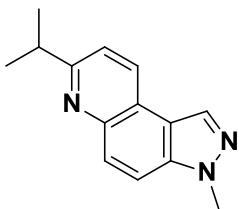
#### 4i. 7-isopropyl-3-phenyl-3H-pyrrolo[3,2-f]quinolone

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 9h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4i** (55 mg, yellow solid) was isolated in 64% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.51 (d, 1H), 7.84 (s, 1H), 7.56 (m, 4H), 7.43 (m, 3H), 7.16 (d, 1H), 3.30 (m, 1H), 1.43 (d, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 165.0, 145.0, 139.6, 132.1, 131.9, 129.9, 127.2, 127.2, 125.0, 124.2, 124.0, 121.7, 118.5, 115.2, 102.6, 37.3, 23.0; HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{18}\text{N}_2$  [ $\text{M}+\text{H}]^+$ : 287.1543, found 287.1550.



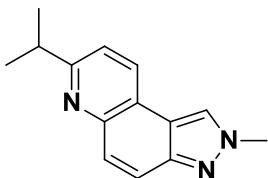
#### 4j. 7-isopropyl-3-phenyl-3H-pyrazolo[4,3-f]quinolone

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 9h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4j** (74 mg, brown solid) was isolated in 86% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.57 (s, 1H), 8.50 (d,  $J=8.4\text{Hz}$ , 1H), 8.00 (d,  $J=9.3\text{Hz}$ , 1H), 7.95 (d,  $J=9.3\text{Hz}$ , 1H), 7.76 (d, 2H), 7.58 (t, 2H), 7.49 (d,  $J=8.4\text{Hz}$ , 1H), 7.43 (t, 1H), 3.30 (m, 1H), 1.43 (d, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 166.1, 145.5, 139.9, 136.7, 134.1, 131.6, 129.8, 129.7, 127.5, 123.6, 120.8, 120.4, 120.0, 114.3, 37.3, 22.9; HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{17}\text{N}_3$  [ $\text{M}+\text{H}]^+$ : 288.1495, found 288.1502.



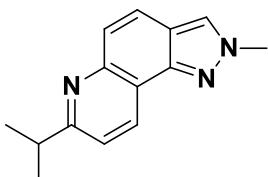
**4k. 7-isopropyl-3-methyl-3H-pyrazolo[4,3-f]quinolone**

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 9h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4k** (58 mg, white solid) was isolated in 52% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.44 (d,  $J=8.4\text{Hz}$ , 1H), 8.35 (s, 1H), 7.95 (d,  $J=9.2\text{Hz}$ , 1H), 7.67 (d,  $J=9.2\text{Hz}$ , 1H), 7.45 (d,  $J=8.4\text{Hz}$ , 1H), 4.17 (s, 3H), 3.27 (m, 1H), 1.41 (d, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 165.6, 145.2, 137.6, 131.8, 131.5, 129.2, 120.9, 119.8, 119.0, 113.1, 37.2, 36.1, 22.9; HRMS (ESI) calcd for  $\text{C}_{14}\text{H}_{15}\text{N}_3$   $[\text{M}+\text{H}]^+$ : 226.1339, found 226.1346.



**4l. 7-isopropyl-2-methyl-2H-pyrazolo[4,3-f]quinolone**

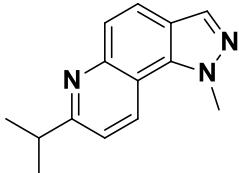
Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 10h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4l** (54 mg, yellow solid) was isolated in 79% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.23 (d,  $J=8.4\text{Hz}$ , 1H), 8.17 (s, 1H), 7.83 (d,  $J=9.2\text{Hz}$ , 1H), 7.78 (d,  $J=9.2\text{Hz}$ , 1H), 7.33 (d,  $J=8.4\text{Hz}$ , 1H), 4.20 (s, 3H), 3.24 (m, 1H), 1.39 (d, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 165.5, 147.2, 146.7, 131.6, 129.4, 123.7, 121.1, 120.8, 118.8, 118.0, 40.3, 37.0, 22.9; HRMS (ESI) calcd for  $\text{C}_{14}\text{H}_{15}\text{N}_3$   $[\text{M}+\text{H}]^+$ : 226.1339, found 226.1346.



**4m. 7-isopropyl-2-methyl-2H-pyrazolo[3,4-f]quinolone**

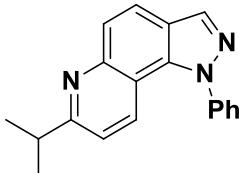
Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 10h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4m** (52 mg, yellow solid) was isolated in 77% yield. Melting point: 81-82°C.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$

(ppm) 8.75 (d,  $J=8.4$ Hz, 1H), 7.89 (s, 1H), 7.72 (d,  $J=9.2$ Hz, 1H), 7.69 (d,  $J=9.2$ Hz, 1H), 7.41 (d,  $J=8.4$ Hz, 1H), 4.25 (s, 3H), 3.26 (m, 1H), 1.41 (d, 6H);  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 167.0, 148.6, 145.8, 130.7, 125.0, 124.9, 121.7, 119.1, 118.7, 118.6, 40.2, 37.2, 22.9; IR (ATR) 2955, 2863, 1614, 1590, 1560, 1469, 1431, 1399, 1373, 1355, 1331, 1289, 1251, 1209, 1158, 1129, 1103, 1081, 1026, 995, 976, 926, 879, 848, 826, 779, 728, 681, 659  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{14}\text{H}_{15}\text{N}_3$  [ $\text{M}+\text{H}]^+$ : 226.1339, found 226.1346



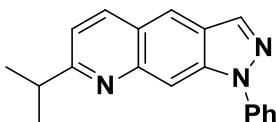
#### 4n. 7-isopropyl-1-methyl-1H-pyrazolo[3,4-f]quinolone

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3\cdot\text{OEt}_2$  (36 ul, 0.30 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4n** (34 mg, pale yellow oil) was isolated in 50% yield.  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.69 (d,  $J=8.6$ Hz, 1H), 8.02 (s, 1H), 7.88 (d,  $J=8.7$ Hz, 1H), 7.73 (d,  $J=8.7$ Hz, 1H), 7.47 (d,  $J=8.6$ Hz, 1H), 4.50 (s, 3H), 3.30 (m, 1H), 1.42 (d, 6H);  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 166.9, 148.8, 135.3, 133.3, 130.2, 124.0, 122.8, 121.2, 118.5, 115.0, 40.6, 37.2, 22.8; HRMS (ESI) calcd for  $\text{C}_{14}\text{H}_{15}\text{N}_3$  [ $\text{M}+\text{H}]^+$ : 226.1339, found 226.1344.



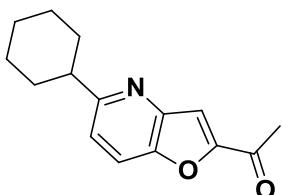
#### 4o-1. 7-isopropyl-1-phenyl-1H-pyrazolo[3,4-f]quinolone

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3\cdot\text{OEt}_2$  (36 ul, 0.30 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4o-1** (55 mg, pale yellow solid) was isolated in 64% yield. Melting point: 79-80°C.  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.23 (s, 1H), 7.94 (d,  $J=8.9$ Hz, 1H), 7.85 (d,  $J=8.9$ Hz, 1H), 7.79 (d,  $J=8.9$ Hz, 1H), 7.59 (m, 5H), 7.16 (d,  $J=8.9$ Hz, 1H), 3.23 (m, 1H), 1.36 (d, 6H);  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 167.2, 148.8, 141.6, 135.7, 135.6, 130.3, 129.8, 129.4, 127.1, 124.7, 122.4, 121.3, 118.1, 114.5, 37.2, 22.7; IR (ATR) 3065, 2966, 2923, 2867, 1612, 1596, 1580, 1500, 1453, 1403, 1361, 1314, 1297, 1206, 1183, 1145, 1087, 1071, 1018, 999, 960, 922, 879, 841, 831, 769, 720  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{17}\text{N}_3$  [ $\text{M}+\text{H}]^+$ : 288.1495, found 288.1503.



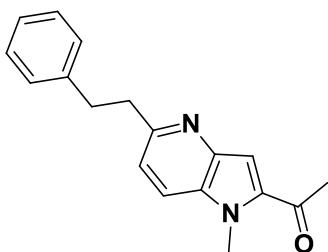
#### **4o-2. 7-isopropyl-1-phenyl-1H-pyrazolo[4,3-g]quinolone**

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and 2,2-dimethyl 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **4o-2** (14 mg, colorless oil) was isolated in 16% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.47 (s, 1H), 8.44 (s, 1H), 8.27 (s, 1H), 8.24 (d, 1H), 7.88 (d, 2H), 7.56 (t, 2H), 7.36 (t, 1H), 7.28 (d, 1H), 3.27 (m, 1H), 1.42 (d, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 169.2, 146.4, 140.5, 139.3, 137.7, 136.1, 129.6, 126.5, 125.9, 122.9, 122.5, 119.8, 117.9, 107.2, 37.8, 22.4; HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{17}\text{N}_3$   $[\text{M}+\text{H}]^+$ : 288.1495, found 288.1502.



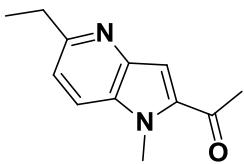
#### **5a. 1-(5-isopropylfuro[3,2-b]pyridin-2-yl)ethanone**

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 10h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5a** (50 mg, colorless oil) was isolated in 69% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.00 (d,  $J=8.8\text{Hz}$ , 1H), 7.46 (s, 1H), 7.23 (d,  $J=8.8\text{Hz}$ , 1H), 2.84 (t, 1H), 2.67 (s, 3H), 2.00 (d, 2H), 1.91 (d, 2H), 1.78 (m, 1H), 1.67 (q, 2H), 1.41 (q, 2H), 1.36 (m, 1H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 189.6, 167.1, 161.9, 151.7, 132.8, 118.8, 117.1, 110.3, 47.0, 33.2, 26.8, 26.5, 26.0; HRMS (ESI) calcd for  $\text{C}_{15}\text{H}_{17}\text{NO}_2$   $[\text{M}+\text{H}]^+$ : 244.1332, found 244.1336.



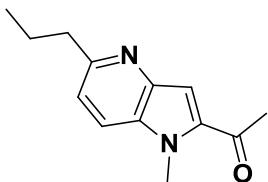
#### **5b. 1-(1-methyl-5-phenethyl-1H-pyrrolo[3,2-b]pyridin-2-yl)ethanone**

Following the general procedure **II**, amine (0.20 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (24 ul, 0.20 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5b** (45 mg, colorless oil) was isolated in 81% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.61 (d,  $J=8.4\text{Hz}$ , 1H), 7.41 (s, 1H), 7.26 (m, 5H), 7.09 (d,  $J=8.4\text{Hz}$ , 1H), 4.05 (s, 3H), 3.22 (m, 2H), 3.11 (m, 2H), 2.65 (s, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 192.2, 157.1, 143.1, 141.8, 136.6, 132.3, 128.7, 128.5, 126.1, 120.6, 118.7, 111.4, 40.6, 36.7, 32.5, 28.3; HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$ : 279.1492, found 279.1498.



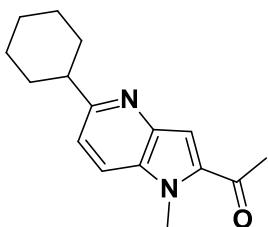
**5c. 1-(5-ethyl-1-methyl-1H-pyrrolo[3,2-b]pyridin-2-yl)ethanone**

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 20:1). Finally, compound **5c** (52mg, white solid) was isolated in 86% yield. Melting point: 95–96°C.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.63 (d,  $J=8.7\text{Hz}$ , 1H), 7.36 (s, 1H), 7.17 (d,  $J=8.7\text{Hz}$ , 1H), 4.04 (s, 3H), 2.93 (q, 2H), 2.62 (s, 3H), 1.35 (t, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 192.2, 159.4, 143.0, 136.5, 132.3, 119.8, 118.8, 111.4, 32.4, 31.8, 28.3, 14.6; IR (ATR) 3047, 2966, 2921, 2852, 1913, 1672, 1565, 1505, 1467, 1441, 1417, 1394, 1354, 1327, 1300, 1214, 1196, 1170, 1151, 1103, 1062, 1018, 981, 964, 932, 822, 801, 781, 752, 686  $\text{cm}^{-1}$ ; HRMS (ESI) calcd for  $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O} [\text{M}+\text{H}]^+$ : 203.1179, found 203.1186.



**5d. 1-(1-methyl-5-propyl-1H-pyrrolo[3,2-b]pyridin-2-yl)ethanone**

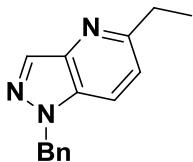
Following the general procedure **II**, amine (0.20 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (24 ul, 0.20 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 20:1). Finally, compound **5d** (29mg, yellow oil) was isolated in 67% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.62 (d,  $J=8.7\text{Hz}$ , 1H), 7.37 (s, 1H), 7.16 (d,  $J=8.7\text{Hz}$ , 1H), 4.04 (s, 3H), 2.87 (t, 2H), 2.63 (s, 3H), 1.80 (m, 2H), 1.35 (t, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 192.2, 158.2, 143.0, 136.5, 132.3, 120.4, 118.6, 111.4, 40.8, 32.4, 28.3, 23.8, 14.0; HRMS (ESI) calcd for  $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O} [\text{M}+\text{H}]^+$ : 217.1335, found 217.1342.



**5e. 1-(5-cyclohexyl-1-methyl-1H-pyrrolo[3,2-b]pyridin-2-yl)ethanone**

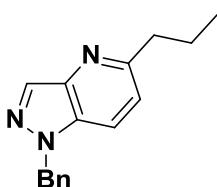
Following the general procedure **II**, amine (0.20 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (24 ul, 0.20 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 10h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 15:1). Finally, compound **5e** (40mg, white solid) was isolated in 78% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.64 (d,  $J=8.7\text{Hz}$ , 1H), 7.40

(s, 1H), 7.18 (d, J=8.7Hz, 1H), 4.04 (s, 3H), 2.84 (m, 1H), 2.63 (s, 3H), 1.98 (d, 2H), 1.87 (d, 2H), 1.77 (d, 1H), 1.58 (q, 2H), 1.44 (q, 2H), 1.30 (m, 1H);  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 192.2, 162.4, 142.8, 136.5, 132.5, 118.9, 118.8, 111.6, 47.1, 33.5, 32.4, 28.3, 26.8, 26.3; HRMS (ESI) calcd for  $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O} [\text{M}+\text{H}]^+$ : 257.1648, found 257.1656.



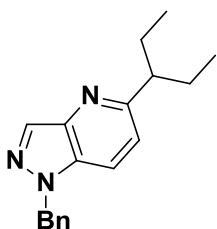
### 5f. 1-benzyl-5-ethyl-1H-pyrazolo[4,3-b]pyridine

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 10h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5f** (62mg, pale yellow oil) was isolated in 87% yield.  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.20 (s, 1H), 7.55 (d, J=8.8Hz, 1H), 7.28 (m, 3H), 7.19 (d, 2H), 7.12 (d, J=8.8Hz, 1H), 5.58 (s, 2H), 2.94 (q, 2H), 1.35 (t, 3H);  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 159.6, 142.0, 136.5, 133.8, 131.5, 129.0, 128.2, 127.4, 120.6, 117.9, 53.9, 31.7, 14.4; HRMS (ESI) calcd for  $\text{C}_{15}\text{H}_{15}\text{N}_3 [\text{M}+\text{H}]^+$ : 238.1339, found 238.1348.



### 5g. 1-benzyl-5-propyl-1H-pyrazolo[4,3-b]pyridine

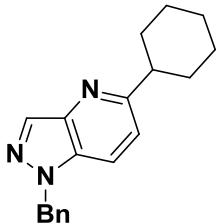
Following the general procedure **II**, amine (0.20 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.20 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 10h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5g** (29mg, brown solid) was isolated in 58% yield.  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.18 (s, 1H), 7.52 (d, J=8.8Hz, 1H), 7.28 (m, 3H), 7.16 (d, 2H), 7.08 (d, J=8.8Hz, 1H), 5.55 (s, 2H), 2.85 (t, 2H), 1.76 (m, 2H), 0.96 (t, 3H);  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 158.4, 142.0, 136.5, 133.7, 131.5, 129.0, 128.2, 127.4, 121.1, 117.7, 53.9, 40.6, 23.7, 14.1; HRMS (ESI) calcd for  $\text{C}_{16}\text{H}_{17}\text{N}_3 [\text{M}+\text{H}]^+$ : 252.1495, found 252.1501.



### 5h. 1-benzyl-5-(pentan-3-yl)-1H-pyrazolo[4,3-b]pyridine

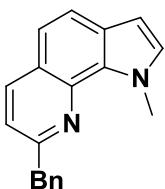
Following the general procedure **II**, amine (0.20 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.20 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room

temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 15:1). Finally, compound **5h** (43mg, pale yellow oil) was isolated in 77% yield. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.23 (s, 1H), 7.55 (d, J=8.8Hz, 1H), 7.28 (m, 3H), 7.22 (d, 2H), 7.07 (d, J=8.8Hz, 1H), 5.57 (s, 2H), 2.69 (m, 1H), 1.74 (m, 4H), 0.78 (t, 6H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 161.5, 141.9, 136.4, 133.8, 131.6, 129.0, 128.2, 127.5, 120.4, 117.6, 53.8, 51.8, 28.7, 12.3; HRMS (ESI) calcd for C<sub>18</sub>H<sub>21</sub>N<sub>3</sub> [M+H]<sup>+</sup>: 280.1808, found 280.1816.



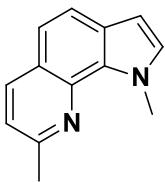
### **5i. 1-benzyl-5-cyclohexyl-1H-pyrazolo[4,3-b]pyridine**

Following the general procedure **II**, amine (0.20 mmol), BF<sub>3</sub>·OEt<sub>2</sub> (24 ul, 0.20 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 11h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 15:1). Finally, compound **5i** (47mg, white solid) was isolated in 80% yield. Melting point: 78-79°C. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.22 (s, 1H), 7.55 (d, J=8.8Hz, 1H), 7.28 (m, 3H), 7.19 (d, 2H), 7.12 (d, J=8.8Hz, 1H), 5.56 (s, 2H), 2.83 (m, 1H), 1.97 (d, 2H), 1.88 (d, 2H), 1.75 (m, 1H), 1.58 (q, 2H), 1.44 (q, 2H), 1.40 (m, 1H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 162.6, 141.7, 136.4, 133.8, 131.5, 129.0, 128.1, 127.4, 119.7, 117.8, 53.8, 47.0, 33.3, 26.7, 26.2; IR (ATR) 3061, 3028, 2926, 2856, 2114, 1774, 1604, 1568, 1493, 1452, 1428, 1409, 1377, 1328, 1301, 1261, 1176, 1157, 1133, 1103, 1076, 1049, 1028, 949, 892, 868, 847, 819, 798, 776, 744, 723, 694 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>19</sub>H<sub>21</sub>N<sub>3</sub> [M+H]<sup>+</sup>: 292.1808, found 292.1815.



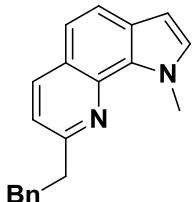
### **5j. 8-benzyl-1-methyl-1H-pyrrolo[3,2-h]quinoline**

Following the general procedure **II**, amine (0.30 mmol), BF<sub>3</sub>·OEt<sub>2</sub> (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 9h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5j** (73mg, yellow solid) was isolated in 90% yield. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.76 (d, 1H), 7.72 (d, J=8.8Hz, 1H), 7.33 (d, J=8.8Hz, 1H), 7.31 (m, 5H), 7.25 (m, 1H), 7.10 (d, J=2.8Hz, 1H), 6.61 (d, J=2.8Hz, 1H), 4.53 (s, 3H), 4.49 (s, 2H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 147.3, 146.1, 139.5, 130.1, 129.4, 129.0, 128.7, 128.5, 127.8, 126.5, 124.4, 121.8, 120.0, 119.2, 115.4, 102.0, 39.2, 38.2; HRMS (ESI) calcd for C<sub>19</sub>H<sub>16</sub>N<sub>2</sub> [M+H]<sup>+</sup>: 273.1386, found 273.1392.



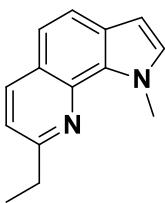
**5k. 1,8-dimethyl-1H-pyrrolo[3,2-h]quinoline**

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 8h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5k** (54mg, colorless oil) was isolated in 92% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.06 (d,  $J=8\text{Hz}$ , 1H), 7.66 (d,  $J=8.8\text{Hz}$ , 1H), 7.35 (d,  $J=8.8\text{Hz}$ , 1H), 7.20 (d,  $J=8\text{Hz}$ , 1H), 7.13 (d,  $J=2.8\text{Hz}$ , 1H), 6.61 (d,  $J=2.8\text{Hz}$ , 1H), 4.55 (s, 3H), 2.74 (s, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 156.0, 147.1, 139.9, 136.2, 129.6, 128.0, 123.4, 120.8, 119.3, 119.1, 102.1, 37.9, 25.5; HRMS (ESI) calcd for  $\text{C}_{13}\text{H}_{12}\text{N}_2$  [ $\text{M}+\text{H}]^+$ : 197.1073, found 197.1080.



**5l. 1-methyl-8-phenethyl-1H-pyrrolo[3,2-h]quinoline**

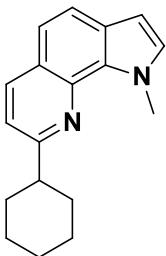
Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 8h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5l** (75mg, yellow solid) was isolated in 88% yield. Melting point: 80-81°C.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.09 (d,  $J=8\text{Hz}$ , 1H), 7.72 (d,  $J=8.5\text{Hz}$ , 1H), 7.40 (d,  $J=8.5\text{Hz}$ , 1H), 7.31 (m, 4H), 7.25 (m, 1H), 7.19 (d,  $J=8.5\text{Hz}$ , 1H), 7.18 (d,  $J=2.8\text{Hz}$ , 1H), 6.66 (d,  $J=2.8\text{Hz}$ , 1H), 4.56 (s, 3H), 3.35 (m, 4H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 158.6, 142.3, 139.9, 136.2, 129.7, 129.6, 128.6, 128.5, 128.0, 126.0, 123.7, 121.0, 119.3, 118.8, 102.2, 40.5, 38.0, 35.3; HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{18}\text{N}_2$  [ $\text{M}+\text{H}]^+$ : 287.1543, found 287.1549.



**5m. 8-ethyl-1-methyl-1H-pyrrolo[3,2-h]quinolone**

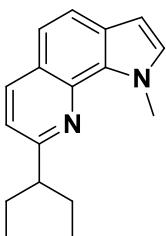
Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 11h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5m** (pale yellow

oil) was isolated in 95% yield. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.09 (d, J=8.3Hz, 1H), 7.69 (d, J=8.5Hz, 1H), 7.38 (d, J=8.5Hz, 1H), 7.22 (d, J=8.3Hz, 1H), 7.15 (d, J= 2.8Hz, 1H), 6.63 (d, J= 2.8Hz, 1H), 4.58 (s, 3H), 3.05 (q, 2H), 1.48 (t, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 160.7, 139.9, 136.1, 129.8, 129.5, 128.0, 123.6, 120.8, 119.3, 118.3, 102.1, 38.0, 32.0, 13.4; HRMS (ESI) calcd for C<sub>14</sub>H<sub>14</sub>N<sub>2</sub> [M+H]<sup>+</sup>: 211.1230, found 211.1237.



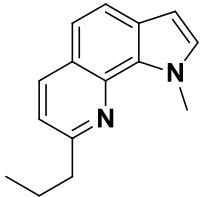
### **5n. 8-cyclohexyl-1-methyl-1H-pyrrolo[3,2-h]quinolone**

Following the general procedure **II**, amine (0.30 mmol), BF<sub>3</sub>·OEt<sub>2</sub> (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5n** (74mg, pale yellow solid) was isolated in 93% yield. Melting point: 126-127°C. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.09 (d, J=8.3Hz, 1H), 7.69 (d, J=8.5Hz, 1H), 7.37 (d, J=8.5Hz, 1H), 7.22 (d, J=8.3Hz, 1H), 7.15 (d, J= 2.8Hz, 1H), 6.62 (d, J= 2.8Hz, 1H), 4.58 (s, 3H), 2.91 (t, 1H), 2.11 (d, 2H), 1.95 (d, 2H), 1.84 (m, 1H), 1.70 (q, 2H), 1.50 (q, 2H), 1.38 (m, 1H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 163.8, 139.8, 136.1, 129.9, 129.4, 127.9, 123.7, 120.8, 119.3, 117.6, 102.1, 47.0, 38.1, 33.1, 26.9, 26.5; IR (ATR) 3102, 2918, 2872, 2848, 2106, 1707, 1931, 1607, 1595, 1541, 1524, 1501, 1461, 1447, 1416, 1400, 1364, 1348, 1327, 1291, 1261, 1238, 1208, 1184, 1146, 1129, 1071, 1056, 999, 959, 904, 890, 867, 853, 834, 801, 792, 756, 743, 714, 687 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>18</sub>H<sub>20</sub>N<sub>2</sub> [M+H]<sup>+</sup>: 265.1699, found 265.1705.



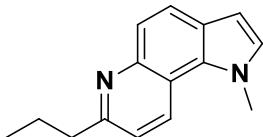
### **5o. 1-methyl-8-(pentan-3-yl)-1H-pyrrolo[3,2-h]quinolone**

Following the general procedure **II**, amine (0.30 mmol), BF<sub>3</sub>·OEt<sub>2</sub> (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5o** (71mg, brown solid) was isolated in 94% yield. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.09 (d, J=8.3Hz, 1H), 7.69 (d, J=8.5Hz, 1H), 7.39 (d, J=8.5Hz, 1H), 7.18 (d, J=8.3Hz, 1H), 7.15 (d, J= 2.8Hz, 1H), 6.63 (d, J= 2.8Hz, 1H), 4.56 (s, 3H), 2.76 (m, 1H), 1.94 (m, 2H), 1.82 (m, 2H), 0.86 (t, 6H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 162.6, 140.1, 135.8, 129.9, 129.4, 127.8, 123.8, 120.8, 119.3, 102.1, 51.9, 38.1, 28.5, 12.3; HRMS (ESI) calcd for C<sub>17</sub>H<sub>20</sub>N<sub>2</sub> [M+H]<sup>+</sup>: 253.1699, found 253.1707.



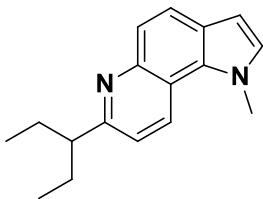
**5p. 1-methyl-8-(pentan-3-yl)-1H-pyrrolo[3,2-h]quinolone**

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 10h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5p** (62mg, pale yellow oil) was isolated in 92% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.08 (d,  $J=8.3\text{Hz}$ , 1H), 7.67 (d,  $J=8.5\text{Hz}$ , 1H), 7.37 (d,  $J=8.5\text{Hz}$ , 1H), 7.20 (d,  $J=8.3\text{Hz}$ , 1H), 7.14 (d,  $J=2.8\text{Hz}$ , 1H), 6.62 (d,  $J=2.8\text{Hz}$ , 1H), 4.56 (s, 3H), 2.99 (t, 2H), 1.95 (q, 2H), 1.05 (t, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 159.7, 139.9, 136.1, 129.9, 129.5, 128.0, 123.6, 120.8, 119.3, 118.8, 102.1, 41.0, 38.0, 22.5, 14.1; HRMS (ESI) calcd for  $\text{C}_{15}\text{H}_{16}\text{N}_2$  [ $\text{M}+\text{H}]^+$ : 225.1386, found 225.1394.



**5q. 1-methyl-7-propyl-1H-pyrrolo[2,3-f]quinoline**

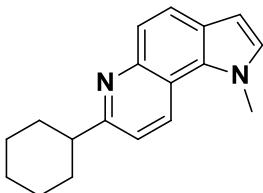
Following the general procedure **II**, amine (0.20 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (24 ul, 0.20 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 20:1). Finally, compound **5q** (38mg, white solid) was isolated in 84% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.68 (d,  $J=8.4\text{Hz}$ , 1H), 7.89 (d,  $J=8.8\text{Hz}$ , 1H), 7.74 (d,  $J=8.8\text{Hz}$ , 1H), 7.33 (d,  $J=8.4\text{Hz}$ , 1H), 7.09 (d,  $J=2.9\text{Hz}$ , 1H), 6.62 (d,  $J=2.9\text{Hz}$ , 1H), 4.25 (s, 3H), 2.97 (t, 2H), 1.87 (q, 2H), 1.03 (t, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 159.1, 146.6, 129.5, 128.8, 125.3, 124.4, 121.8, 119.7, 116.6, 102.3, 41.0, 38.2, 23.5, 14.1; HRMS (ESI) calcd for  $\text{C}_{15}\text{H}_{16}\text{N}_2$  [ $\text{M}+\text{H}]^+$ : 225.1386, found 225.1392.



**5r. 1-methyl-7-(pentan-3-yl)-1H-pyrrolo[2,3-f]quinoline**

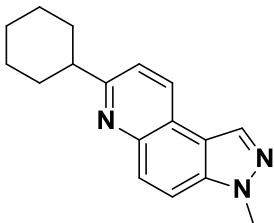
Following the general procedure **II**, amine (0.20 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (24 ul, 0.20 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 20:1). Finally, compound **5r** (37mg, colorless oil) was isolated in 73% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.68 (d,  $J=8.8\text{Hz}$ , 1H), 7.90 (d,  $J=8.4\text{Hz}$ , 1H), 7.77 (d,  $J=8.5\text{Hz}$ , 1H), 7.29 (d,  $J=8.8\text{Hz}$ , 1H), 7.07 (d,  $J=2.8\text{Hz}$ , 1H), 6.61 (d,

$J = 2.8\text{Hz}$ , 1H), 4.23 (s, 3H), 2.80 (m, 1H), 1.82 (m, 4H), 0.85 (t, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 162.6, 140.1, 135.8, 129.9, 129.4, 127.8, 123.8, 120.8, 119.3, 102.1, 51.9, 38.1, 28.5, 12.3; HRMS (ESI) calcd for  $\text{C}_{17}\text{H}_{20}\text{N}_2$  [ $\text{M}+\text{H}]^+$ : 253.1699, found 253.1703.



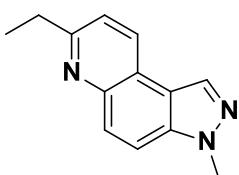
### 5s. 7-cyclohexyl-1-methyl-1H-pyrrolo[2,3-f]quinoline

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 20:1). Finally, compound **5s** (62mg, white solid) was isolated in 78% yield. Melting point: 113-114°C.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.67 (d,  $J=8.8\text{Hz}$ , 1H), 7.89 (d,  $J=9.2\text{Hz}$ , 1H), 7.75 (d,  $J=9.2\text{Hz}$ , 1H), 7.34 (d,  $J=8.8\text{Hz}$ , 1H), 7.07 (d,  $J=2.8\text{Hz}$ , 1H), 6.61 (d,  $J=2.8\text{Hz}$ , 1H), 4.22 (s, 3H), 2.94 (m, 1H), 2.08 (d, 2H), 1.92 (d, 2H), 1.85 (m, 1H), 1.67 (q, 2H), 1.54 (q, 2H), 1.38 (m, 1H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 163.3, 146.7, 129.6, 129.2, 129.1, 125.3, 124.4, 122.0, 117.9, 116.9, 102.4, 47.4, 38.3, 33.2, 26.8, 26.3; HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{20}\text{N}_2$  [ $\text{M}+\text{H}]^+$ : 265.1699, found 265.1705.



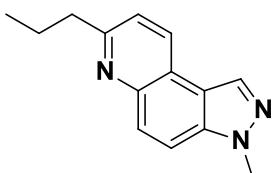
### 5t. 7-cyclohexyl-3-methyl-3H-pyrazolo[4,3-f]quinolone

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3 \cdot \text{OEt}_2$  (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5t** (59mg, yellow oil) was isolated in 74% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.44 (d,  $J=8.4\text{Hz}$ , 1H), 8.34 (s, 1H), 7.95 (d,  $J=9.2\text{Hz}$ , 1H), 7.67 (d,  $J=9.2\text{Hz}$ , 1H), 7.44 (d,  $J=8.4\text{Hz}$ , 1H), 4.17 (s, 3H), 2.93 (t, 1H), 2.04 (d, 2H), 1.95 (d, 2H), 1.84 (m, 1H), 1.70 (q, 2H), 1.50 (q, 2H), 1.35 (m, 1H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 164.8, 145.2, 137.5, 131.8, 131.5, 129.1, 120.9, 120.2, 119.0, 113.1, 47.5, 36.1, 33.3, 26.8, 26.3; HRMS (ESI) calcd for  $\text{C}_{17}\text{H}_{19}\text{N}_3$  [ $\text{M}+\text{H}]^+$ : 266.1652, found 266.1657.



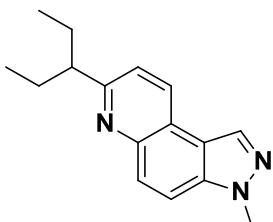
### **5u. 7-ethyl-3-methyl-3H-pyrazolo[4,3-f]quinolone**

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3\cdot\text{OEt}_2$  (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5u** (42mg, brown solid) was isolated in 66% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.42 (d, 1H), 8.34 (s, 1H), 7.94 (d, 1H), 7.67 (d, 1H), 7.42 (d, 1H), 4.17 (s, 3H), 3.02 (q, 2H), 1.41 (t, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 161.8, 145.4, 137.5, 131.8, 131.5, 129.0, 121.5, 120.7, 119.0, 113.2, 36.1, 32.2, 14.4; HRMS (ESI) calcd for  $\text{C}_{13}\text{H}_{13}\text{N}_3$  [ $\text{M}+\text{H}]^+$ : 212.1182, found 212.1188.



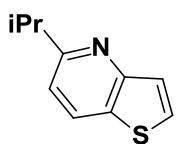
### **5v. 3-methyl-7-propyl-3H-pyrazolo[4,3-f]quinolone**

Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3\cdot\text{OEt}_2$  (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5v** (51mg, colorless oil) was isolated in 75% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.42 (d,  $J=8.4\text{Hz}$ , 1H), 8.34 (s, 1H), 7.96 (d,  $J=9.2\text{Hz}$ , 1H), 7.67 (d,  $J=9.2\text{Hz}$ , 1H), 7.41 (d,  $J=8.4\text{Hz}$ , 1H), 4.16 (s, 3H), 2.97 (t, 2H), 1.86 (m, 2H), 1.03 (t, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 160.6, 145.3, 137.5, 131.8, 131.4, 128.9, 122.1, 120.8, 119.0, 113.3, 41.1, 36.1, 23.6, 14.1; HRMS (ESI) calcd for  $\text{C}_{14}\text{H}_{15}\text{N}_3$  [ $\text{M}+\text{H}]^+$ : 226.1339, found 226.1345.



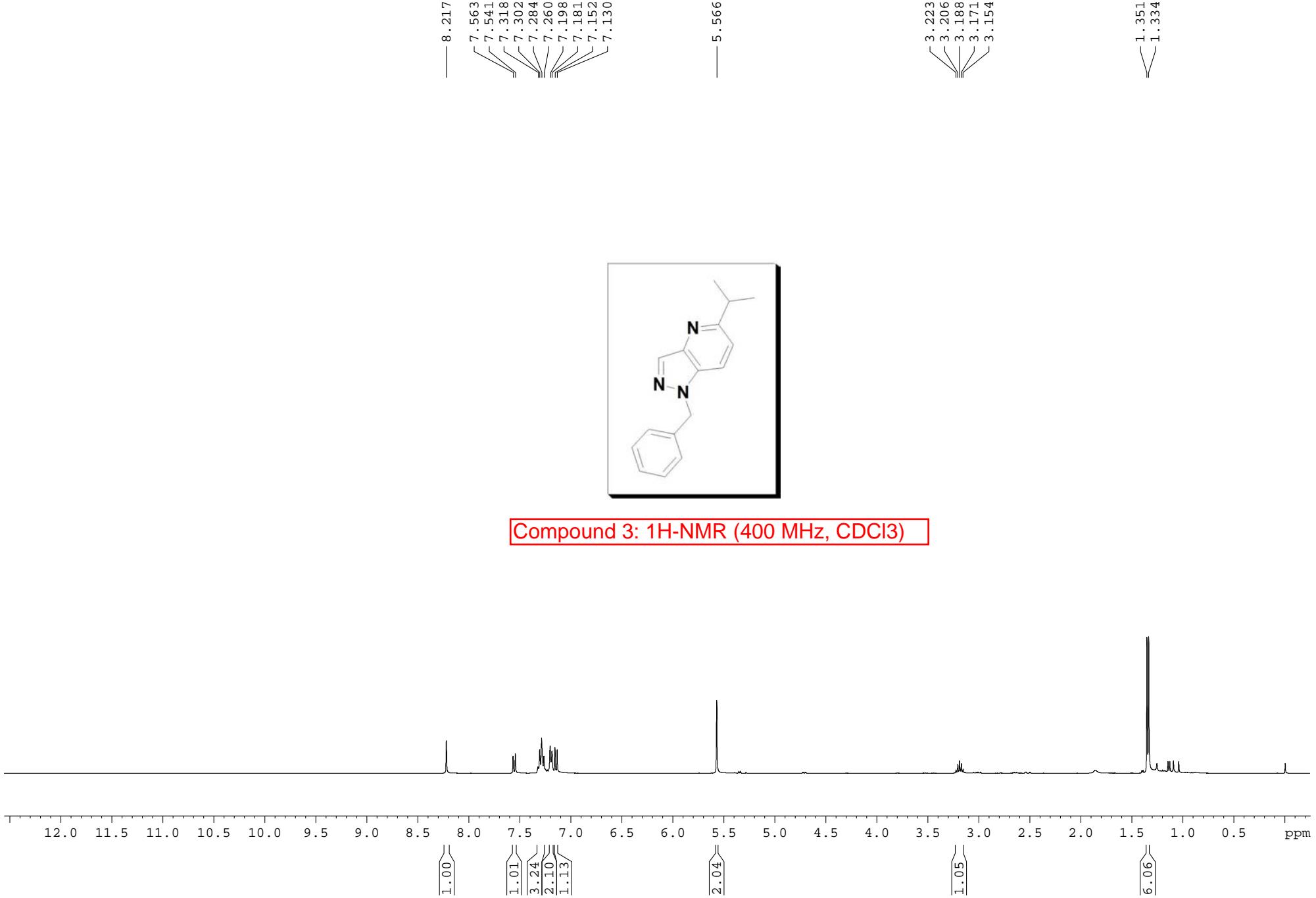
### **5w. 3-methyl-7-(pentan-3-yl)-3H-pyrazolo[4,3-f]quinolone**

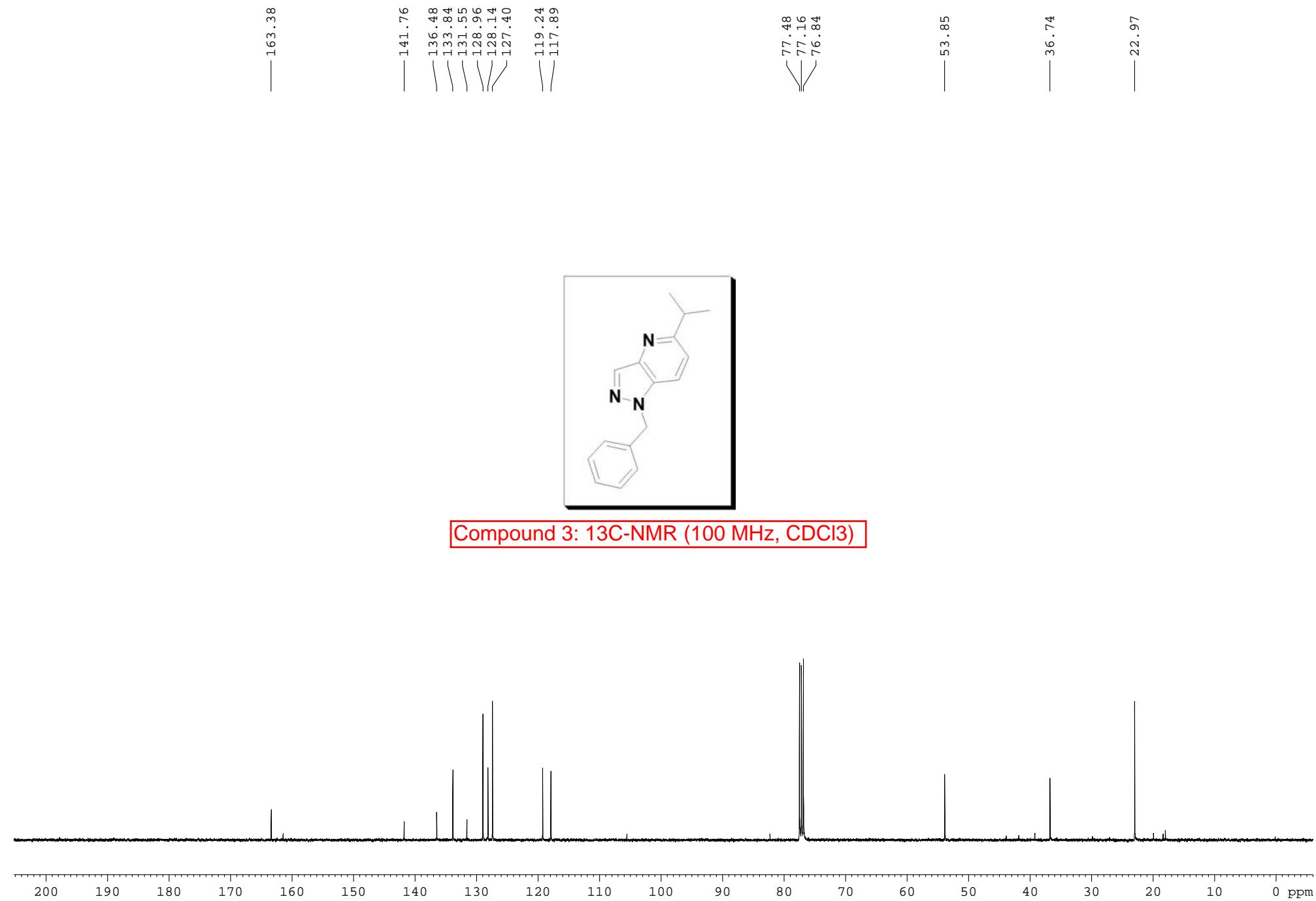
Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3\cdot\text{OEt}_2$  (36 ul, 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 10:1). Finally, compound **5w** (45mg, yellow oil) was isolated in 59% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.43 (d,  $J=8.4\text{Hz}$ , 1H), 8.36 (s, 1H), 7.98 (d,  $J=9.2\text{Hz}$ , 1H), 7.68 (d,  $J=9.2\text{Hz}$ , 1H), 7.38 (d,  $J=8.4\text{Hz}$ , 1H), 4.18 (s, 3H), 2.79 (m, 1H), 1.81 (m, 4H), 0.83 (t, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 163.8, 145.4, 144.3, 137.6, 131.8, 131.2, 129.3, 121.1, 119.0, 113.0, 52.2, 36.1, 28.5, 12.3; HRMS (ESI) calcd for  $\text{C}_{16}\text{H}_{19}\text{N}_3$  [ $\text{M}+\text{H}]^+$ : 254.1652, found 254.1659.

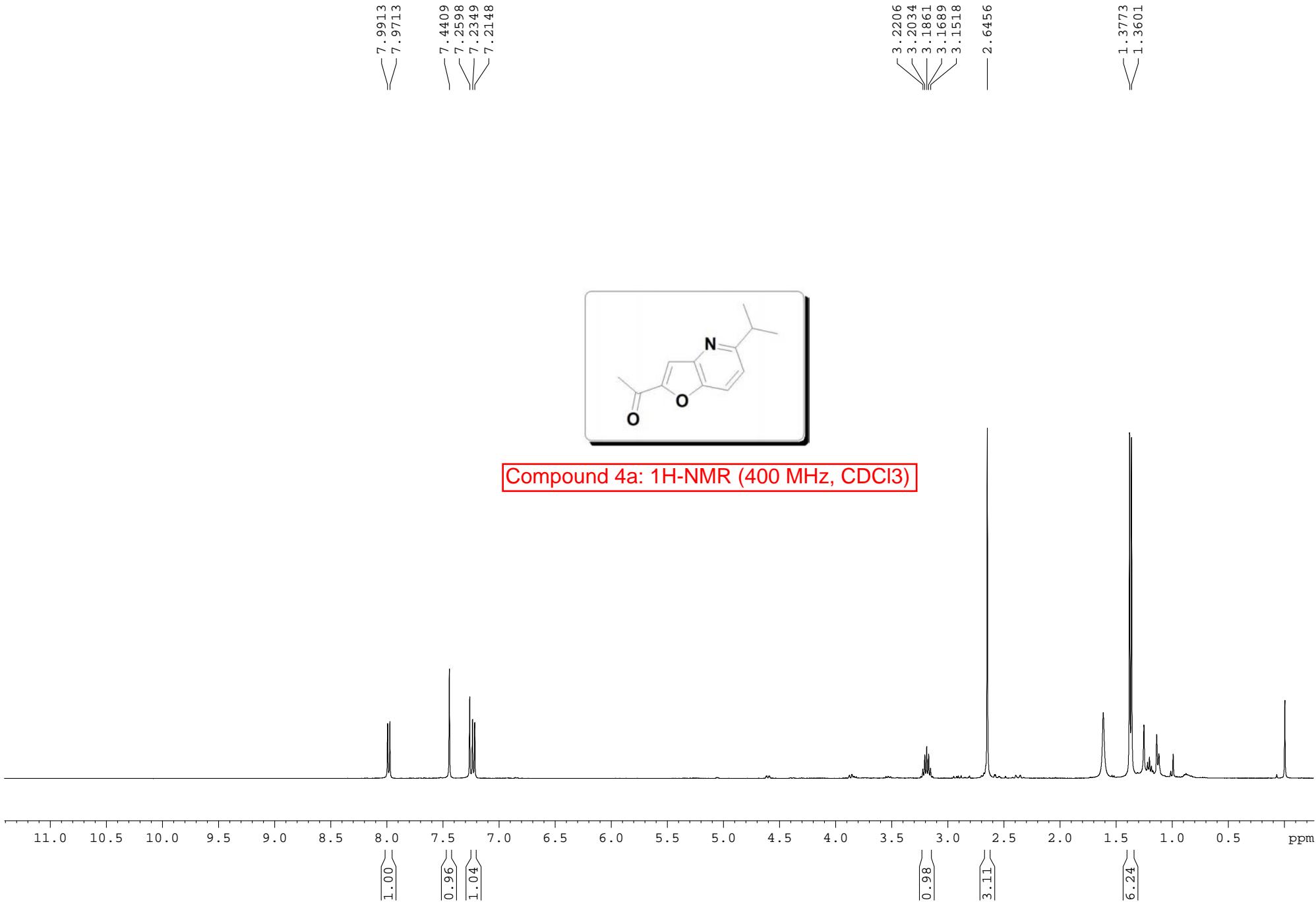


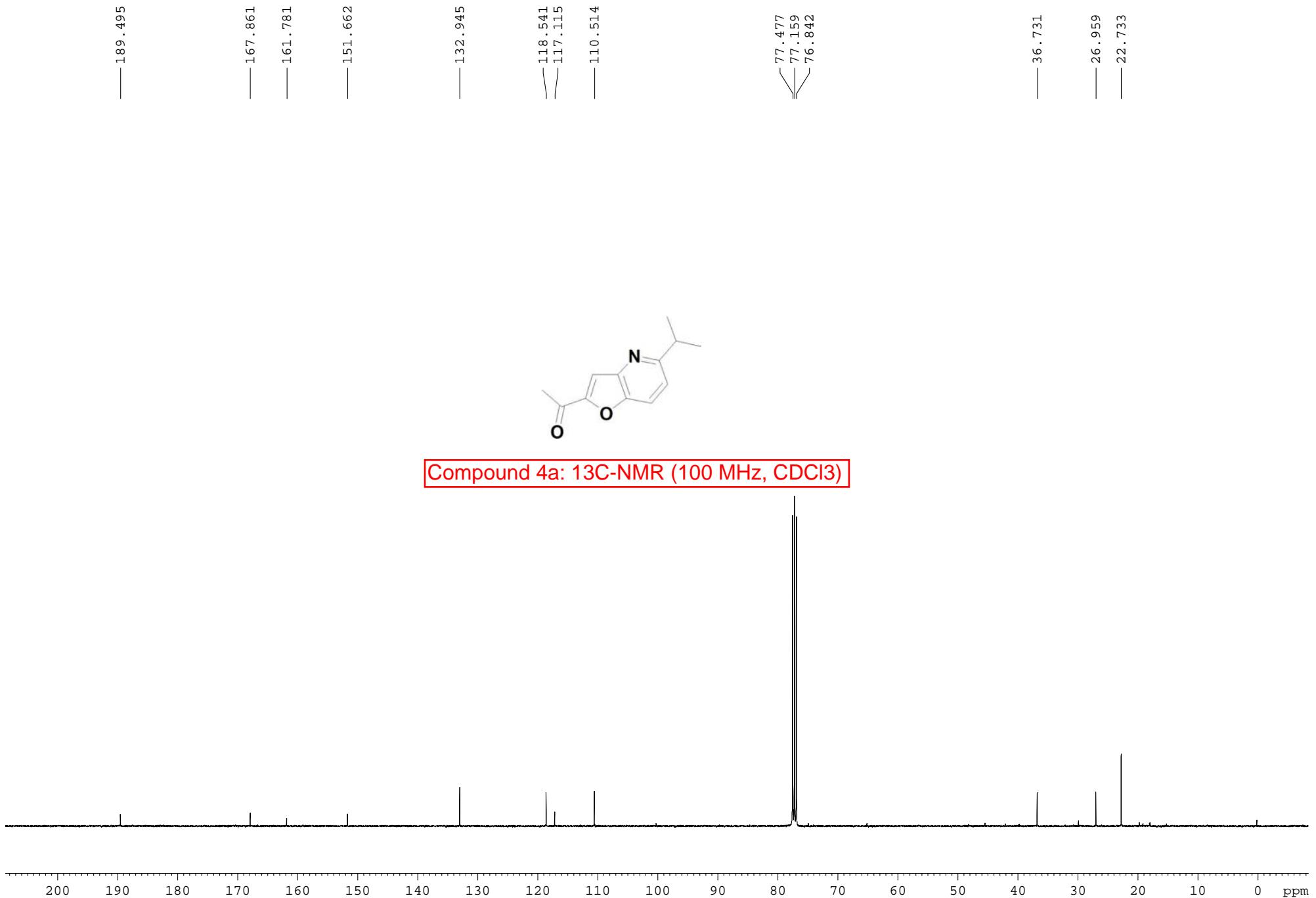
**5x. 5-isopropylthieno[3,2-b]pyridine**

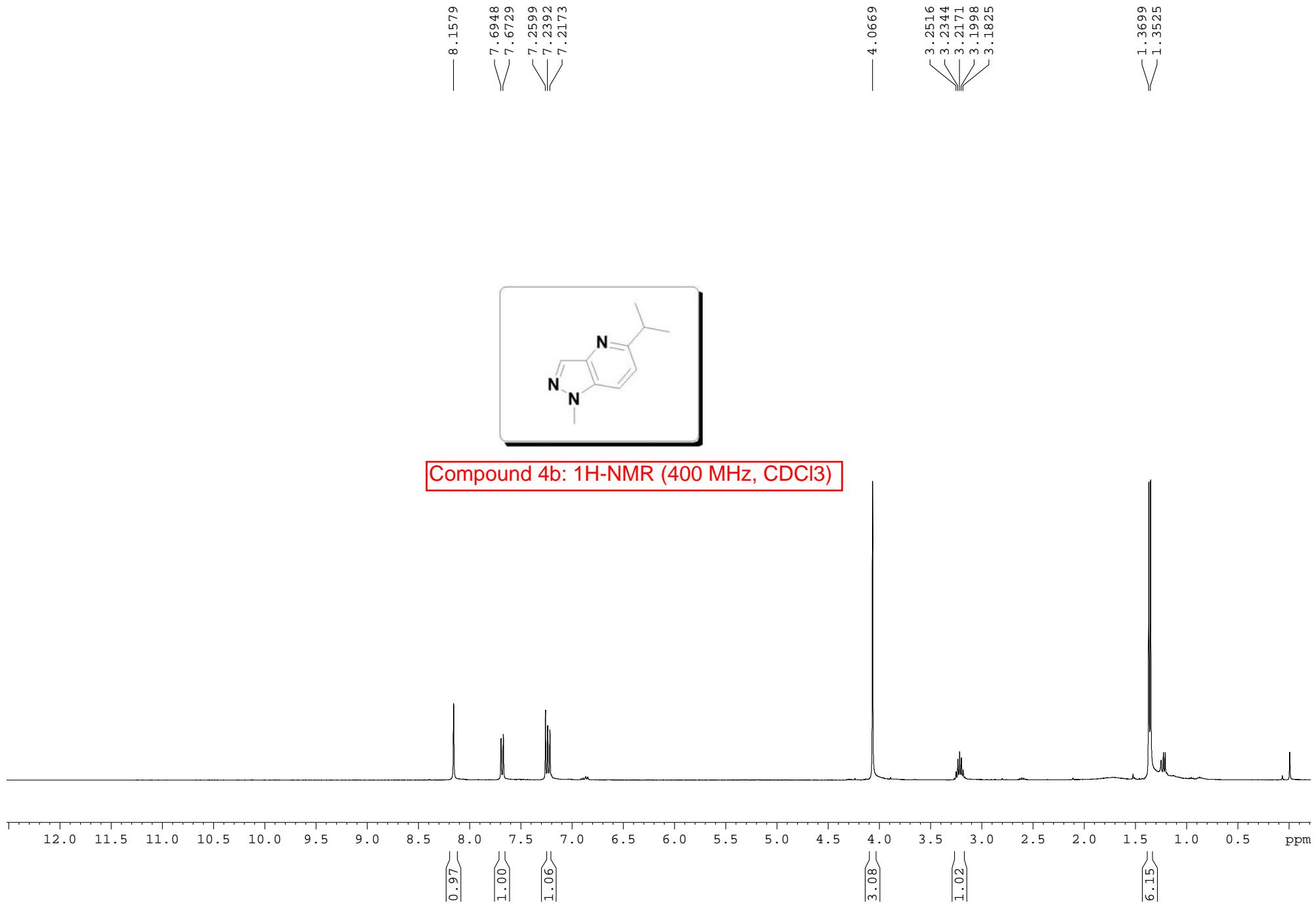
Following the general procedure **II**, amine (0.30 mmol),  $\text{BF}_3\cdot\text{OEt}_2$  (36  $\mu\text{l}$ , 0.30 mmol) and substituted 3-ethoxycyclobutanone (1.0 equiv) were used. The reaction mixture was stirred at room temperature for 12h under Ar protection. After completion of the reaction, the residue was purified by silical gel column chromatography (Hexane: Ether = 20:1). Finally, compound **5x** (47mg, pale yellow solid) was isolated in 89% yield.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.11 (d,  $J=8.4\text{Hz}$ , 1H), 7.70 (d,  $J=5.2\text{Hz}$ , 1H), 7.53 (d,  $J=5.2\text{Hz}$ , 1H), 7.18 (d,  $J=8.4\text{Hz}$ , 1H), 3.2 (m, 1H), 1.37 (d, 6H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 165.4, 155.7, 130.9, 130.8, 130.3, 125.2, 116.5, 36.8, 23.1; HRMS (ESI) calcd for  $\text{C}_{10}\text{H}_{11}\text{NS} [\text{M}+\text{H}]^+$ : 178.0685, found 178.0691.

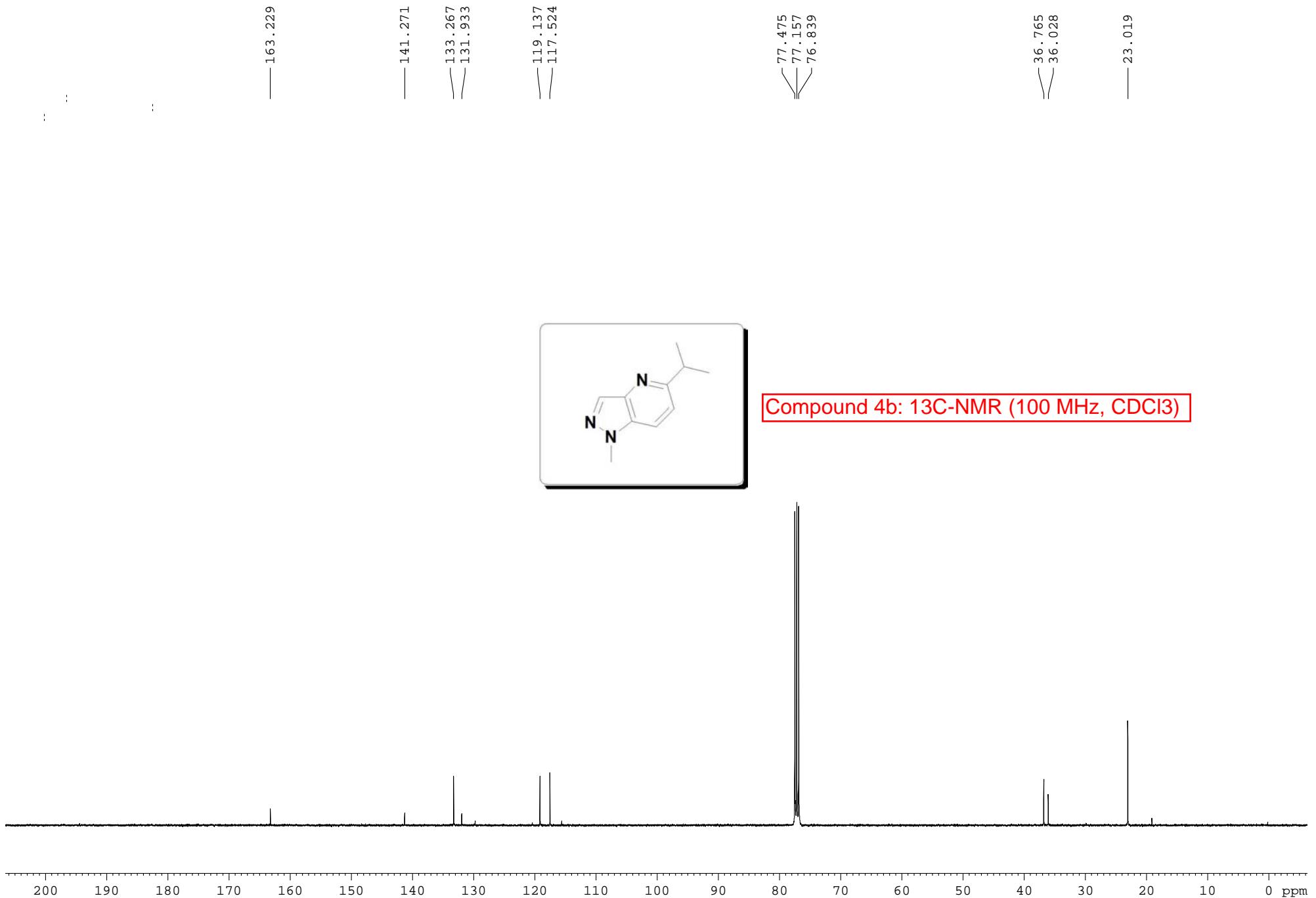


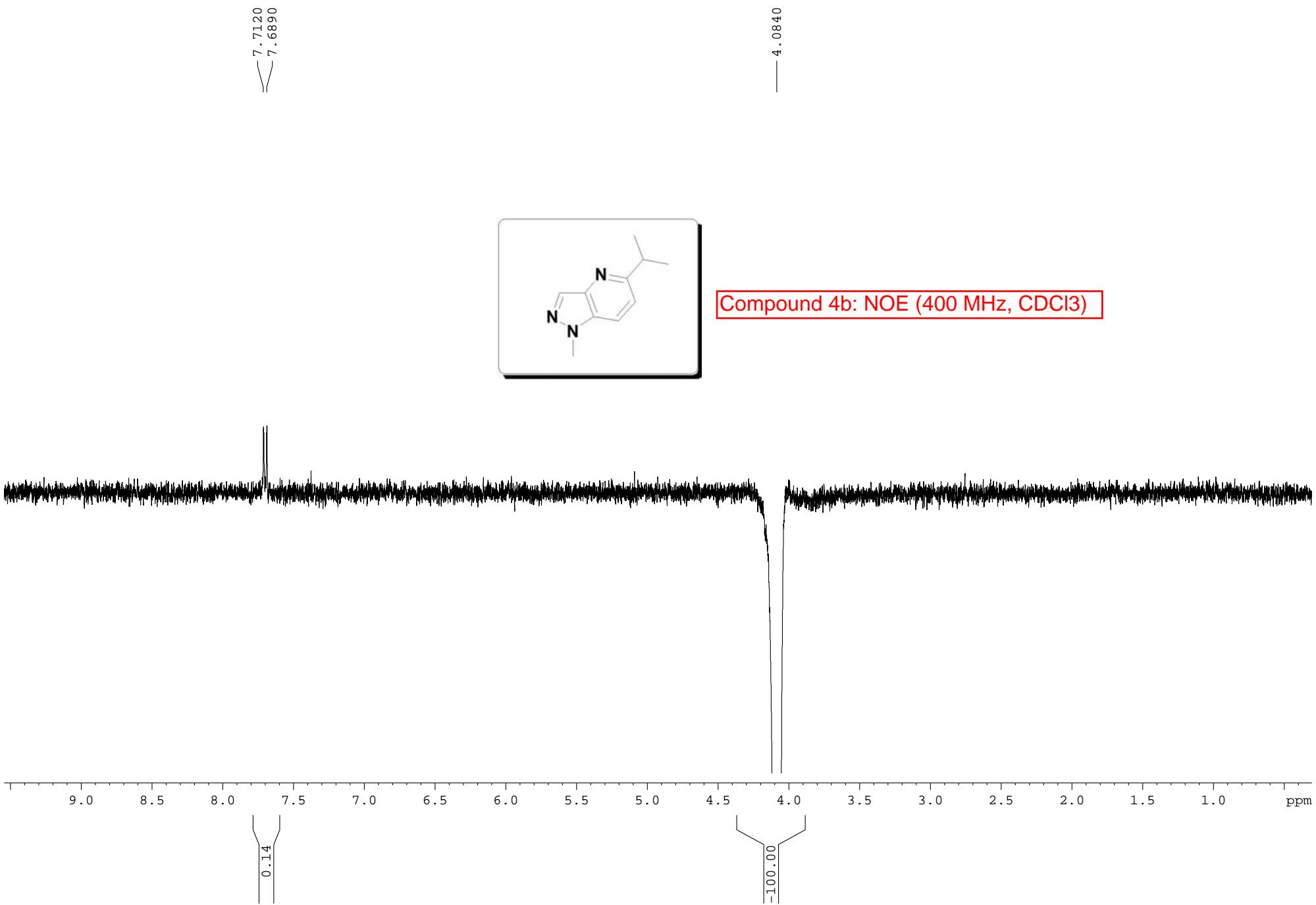




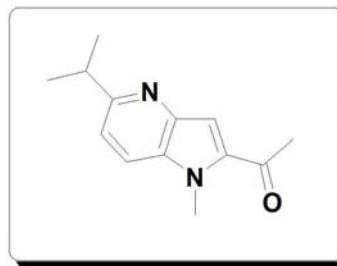




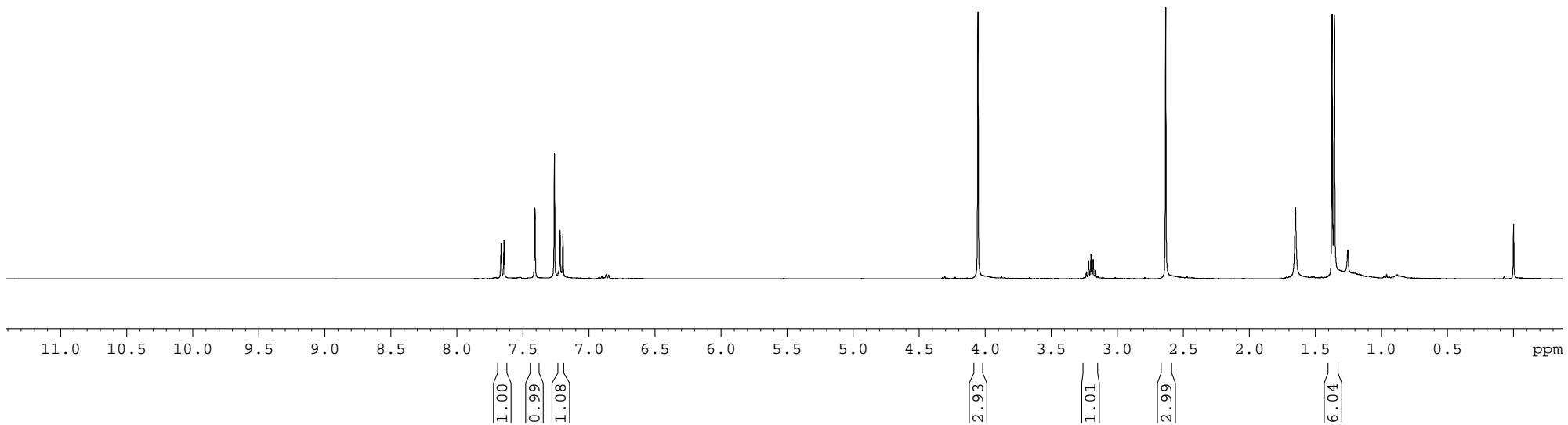


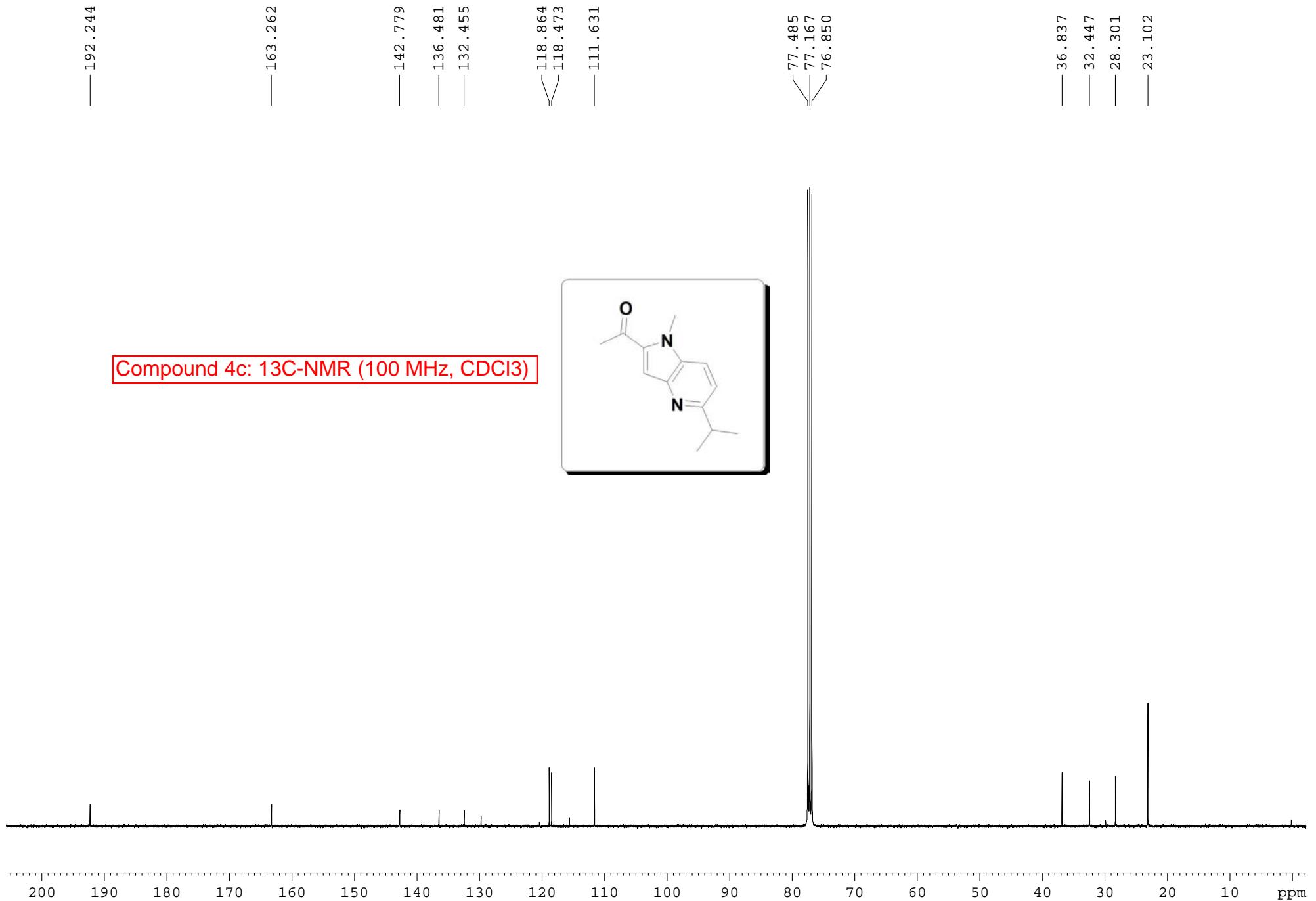


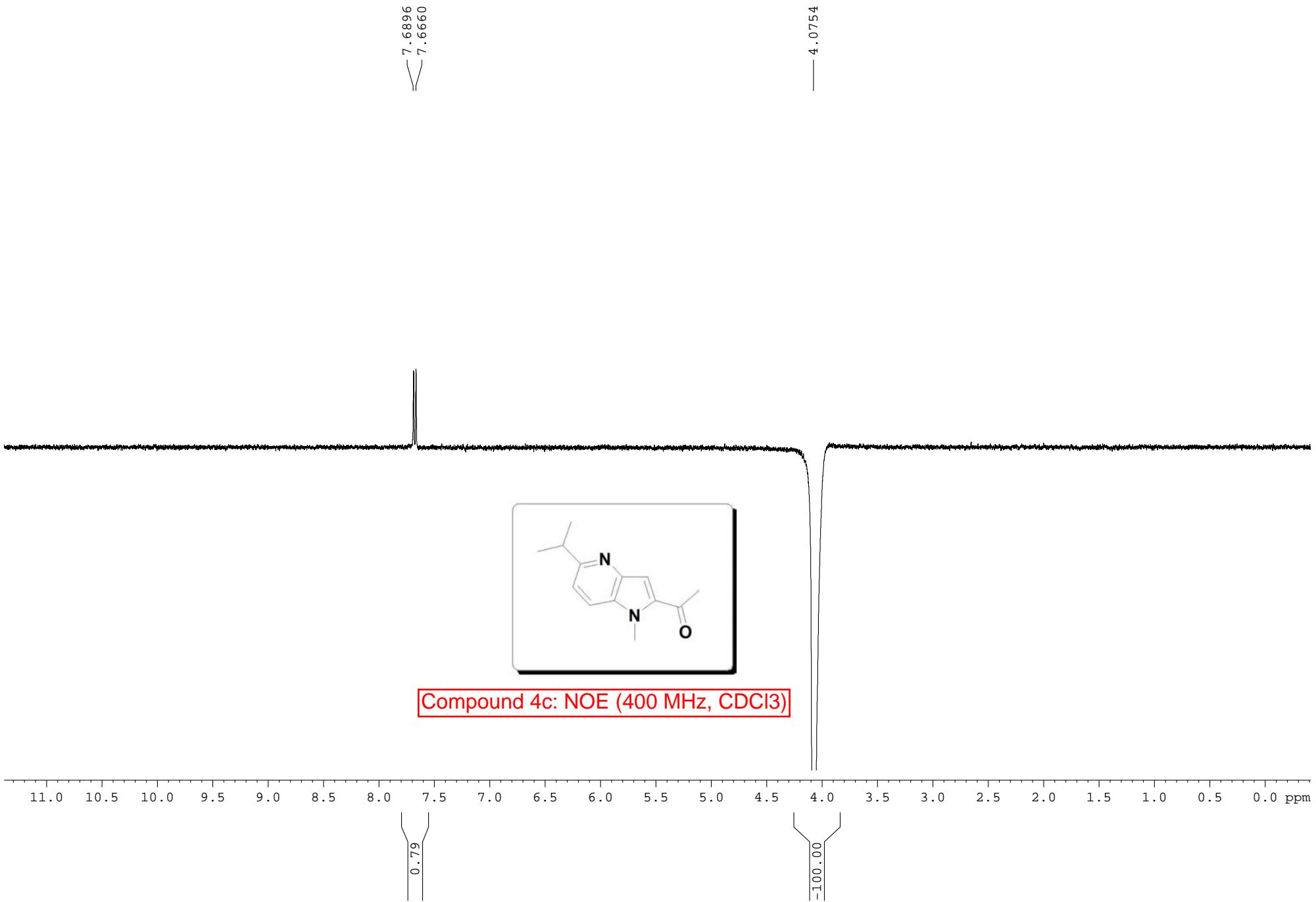
Compound 4b: NOE (400 MHz,  $\text{CDCl}_3$ )

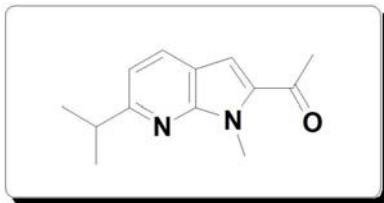


Compound 4c:  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )

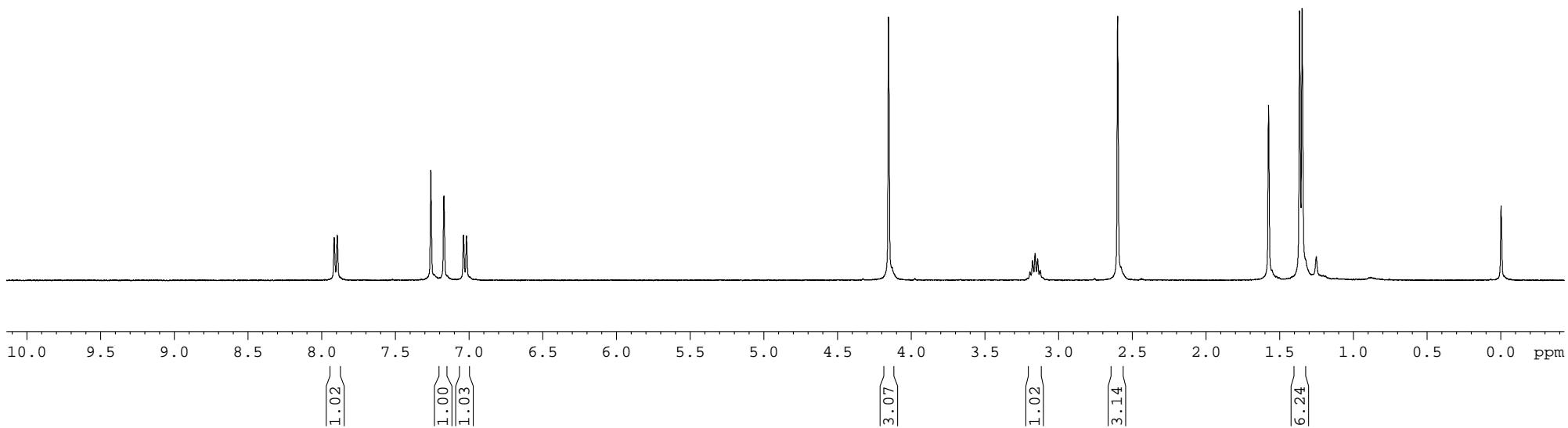








### Compound 4d: $^1\text{H}$ -NMR (400 MHz, CDCl<sub>3</sub>)



— 191.5872

— 166.4358

— 149.5349

— 134.5400

— 131.3359

— 116.4259

— 115.2412

— 109.5626

— 77.4804

— 77.1629

— 76.8455

— 37.0550

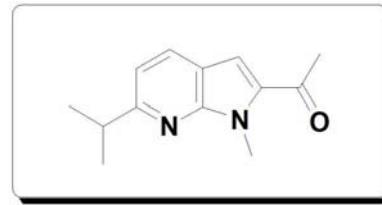
— 30.9345

— 27.6602

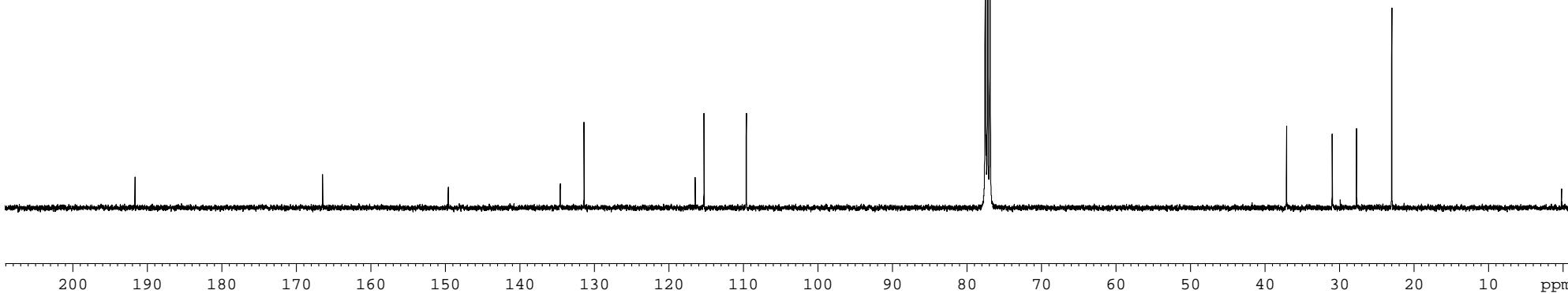
— 22.9419

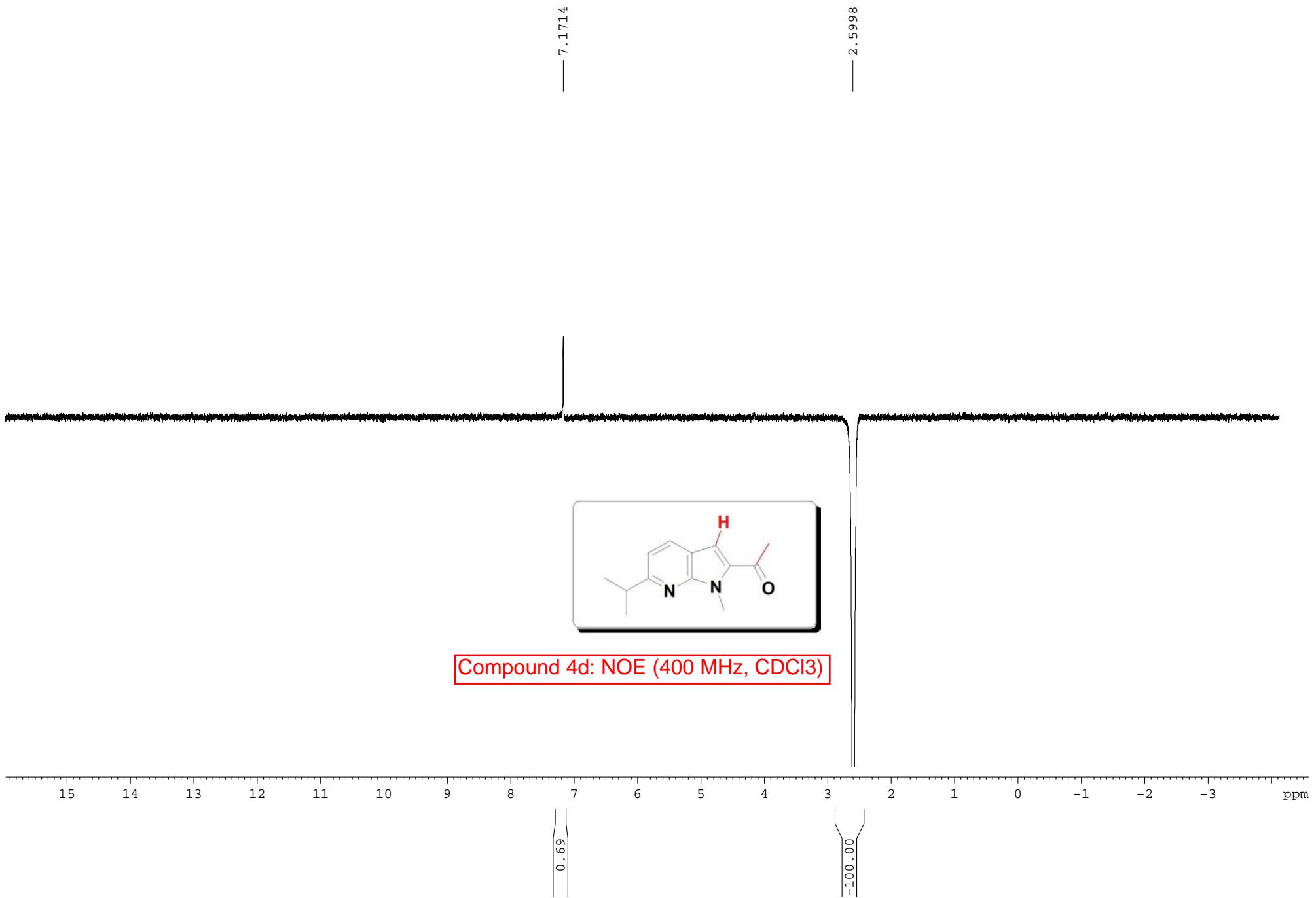
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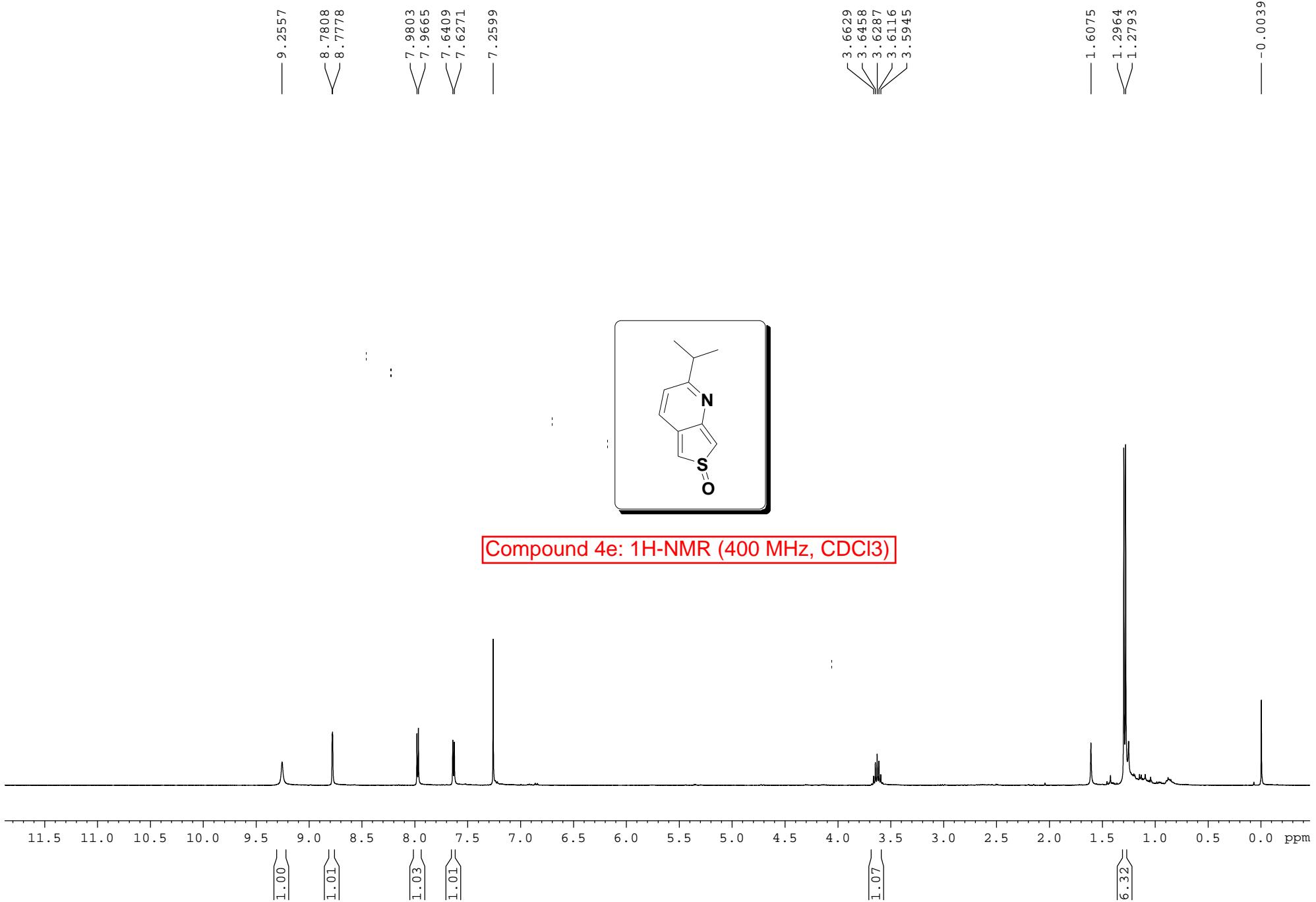
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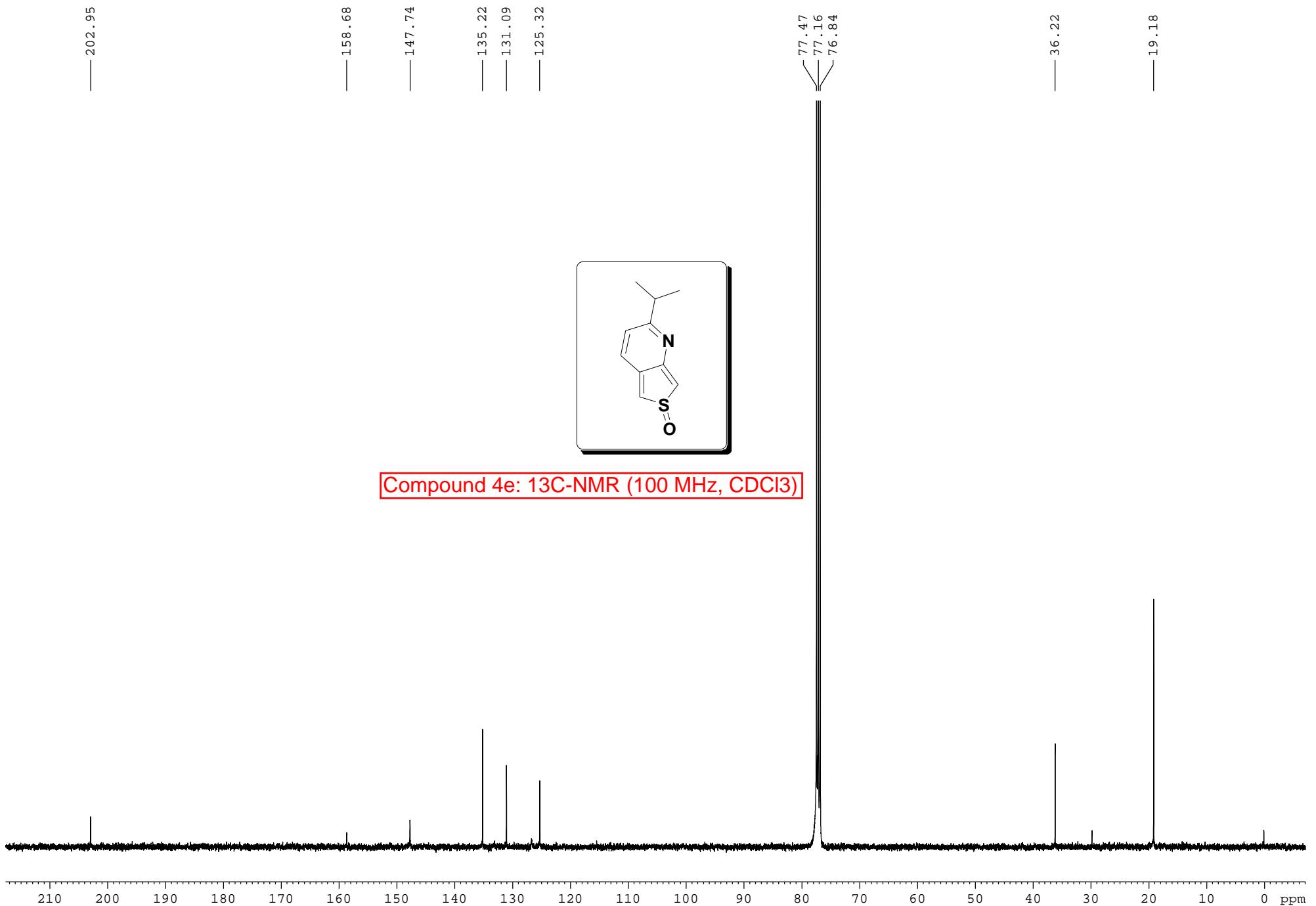


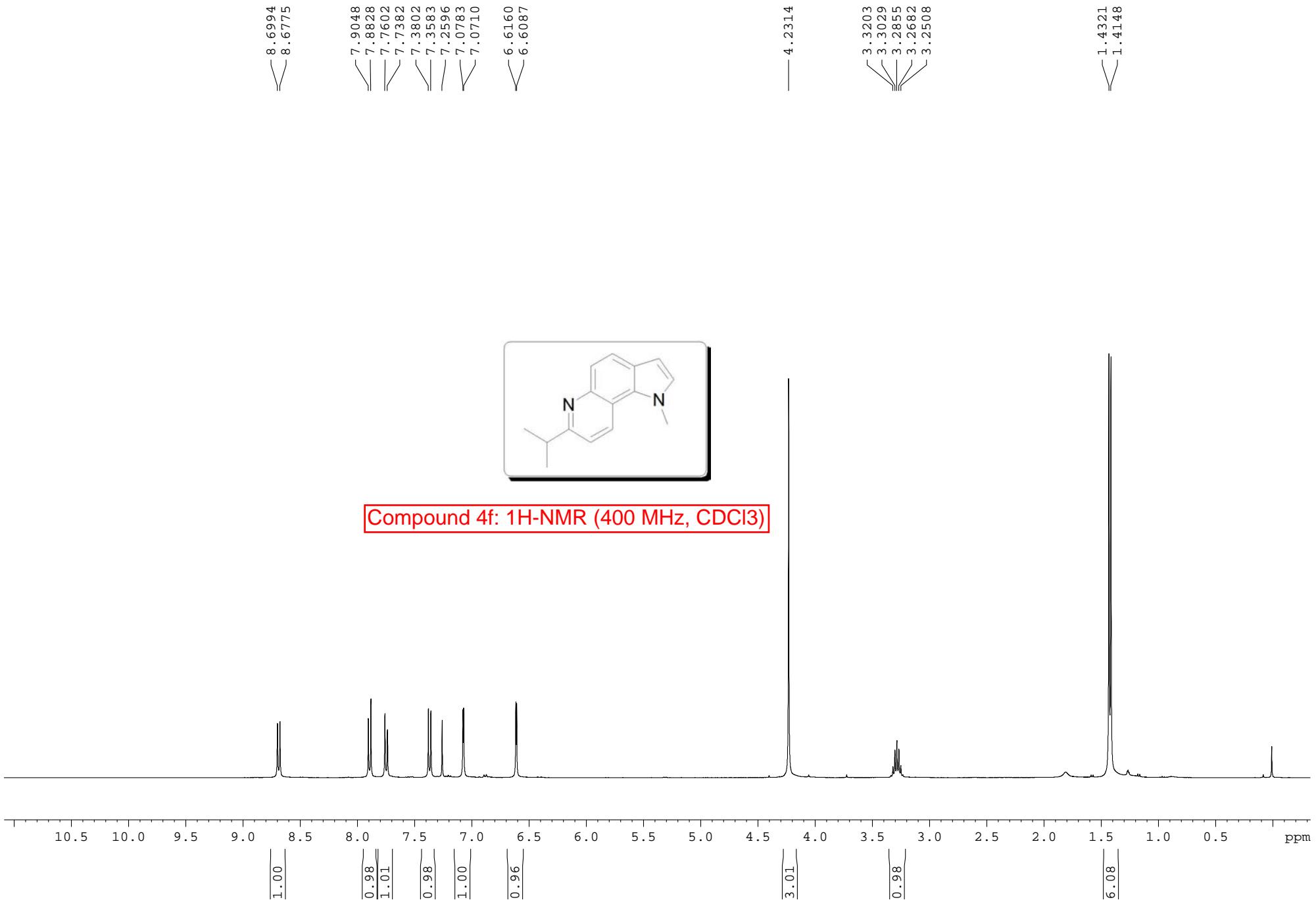
Compound 4d: 13C-NMR (100 MHz, CDCl3)

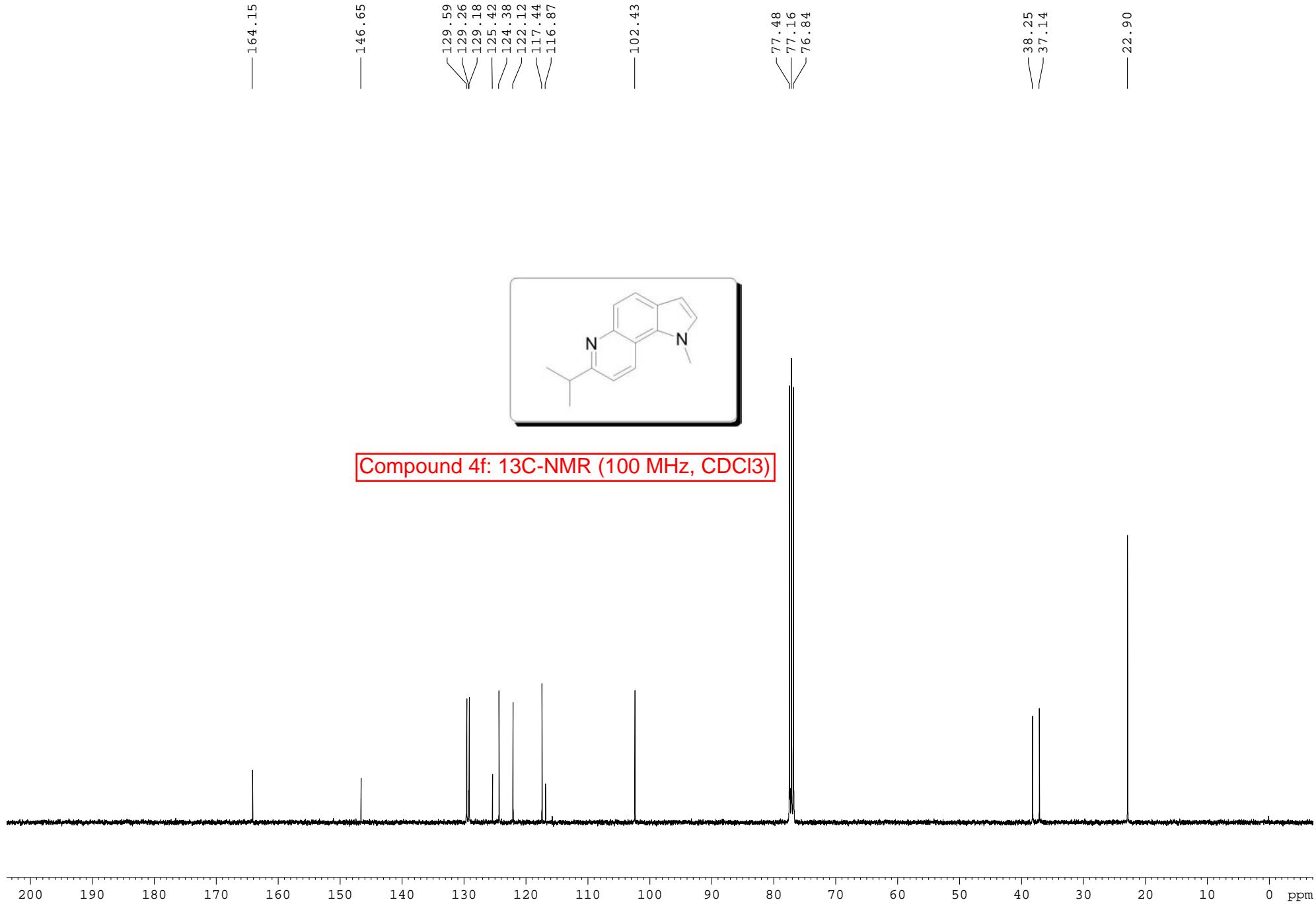


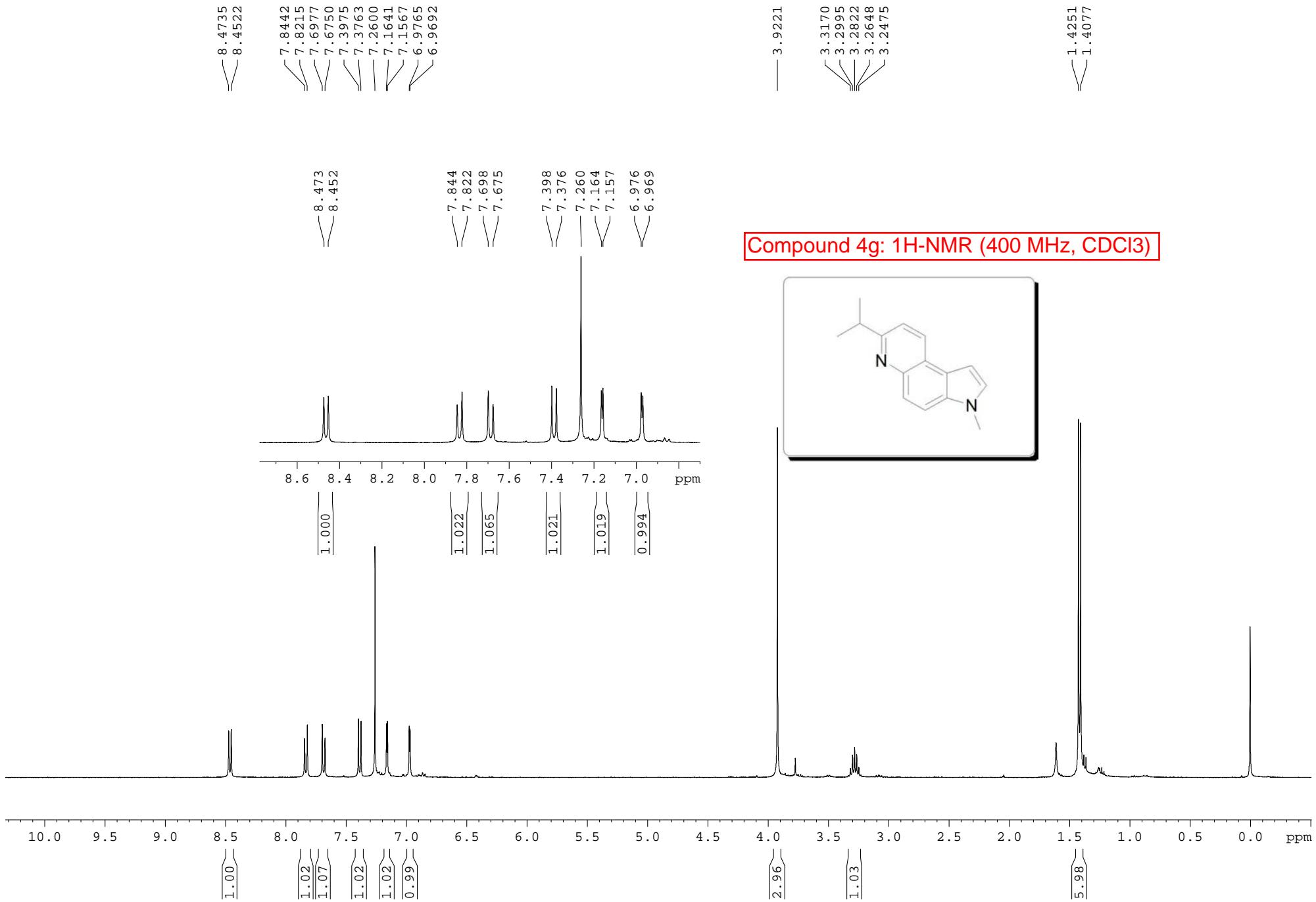


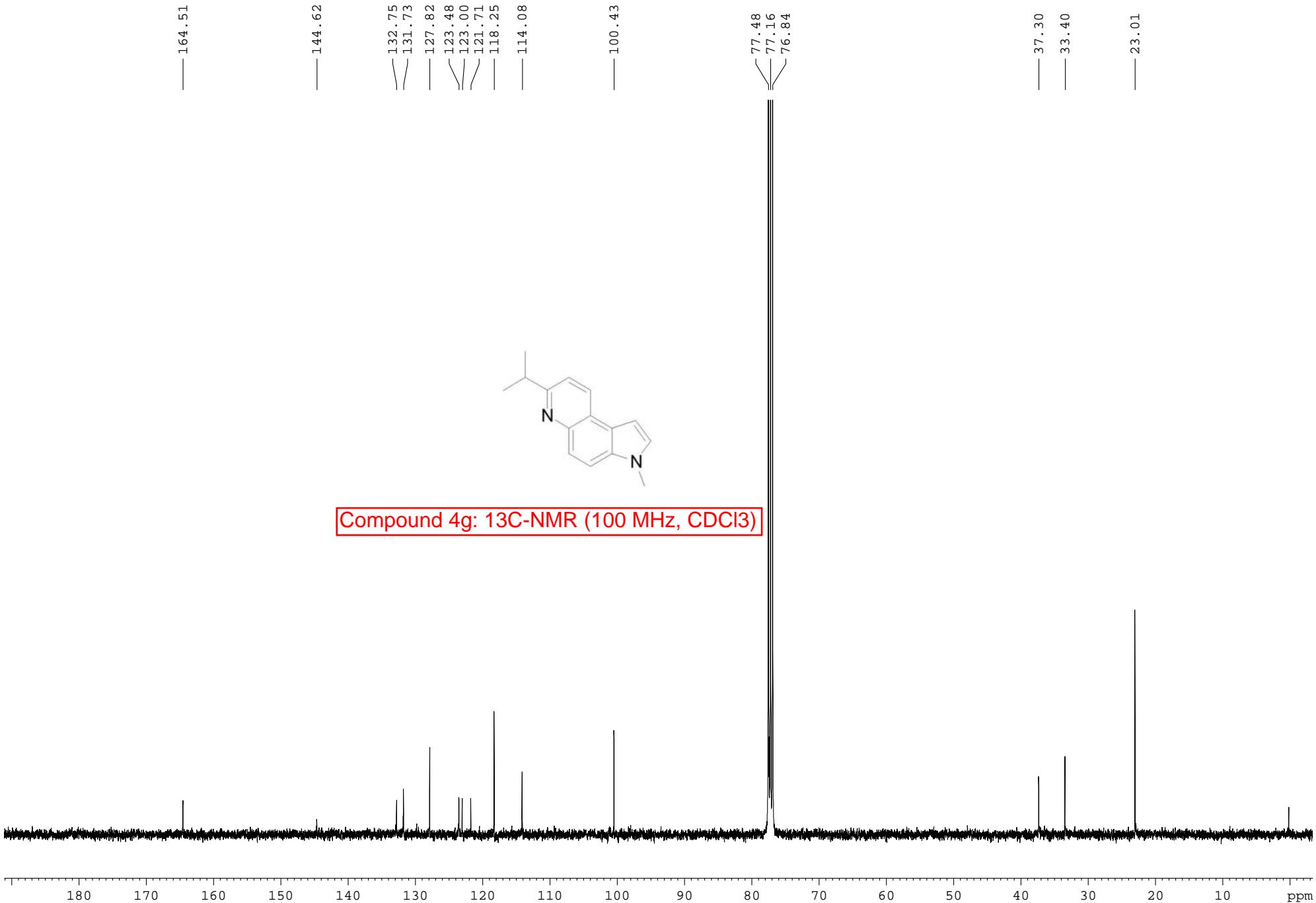




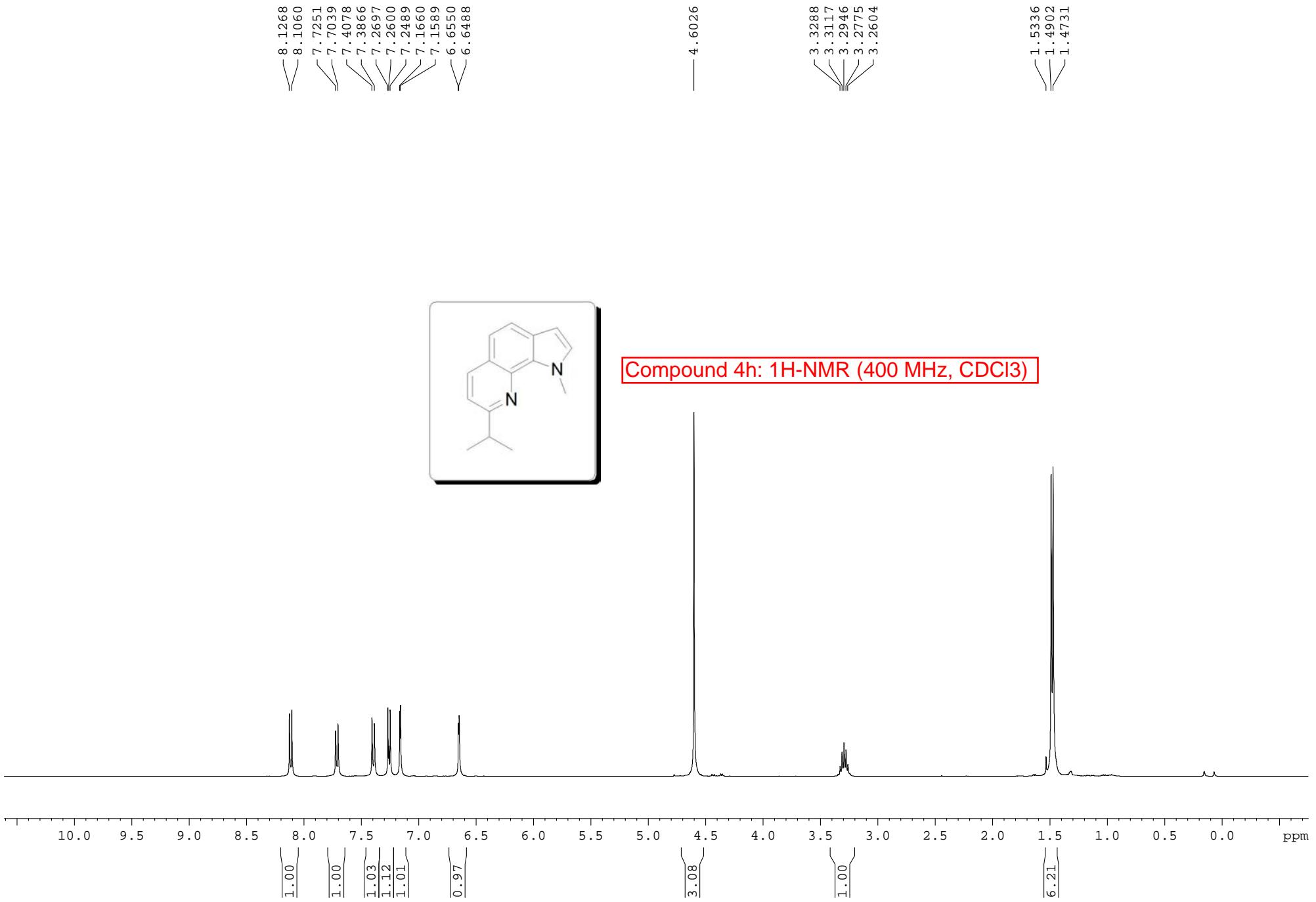


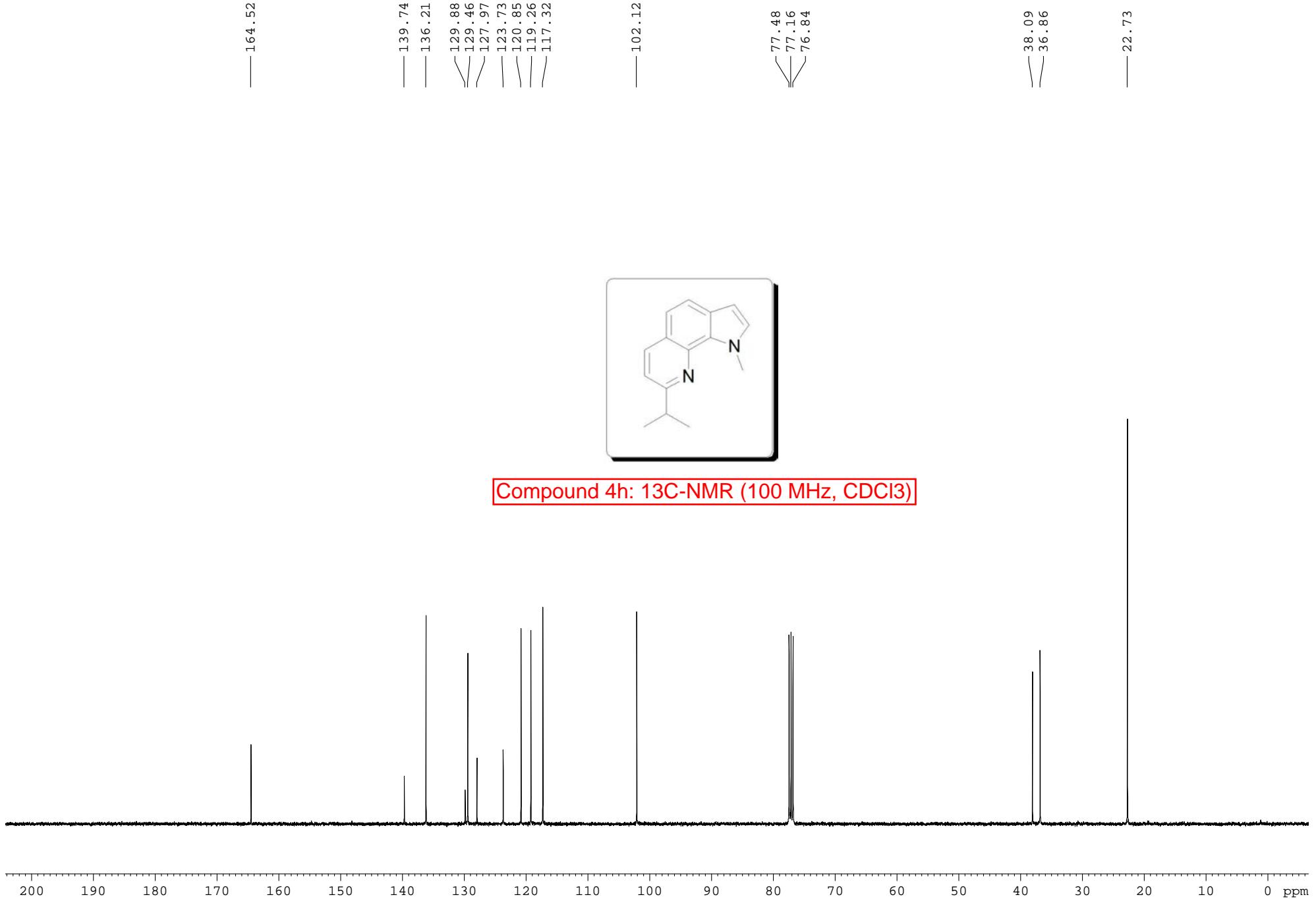


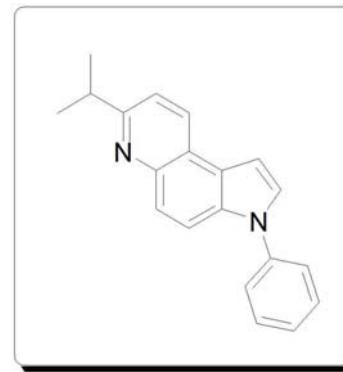




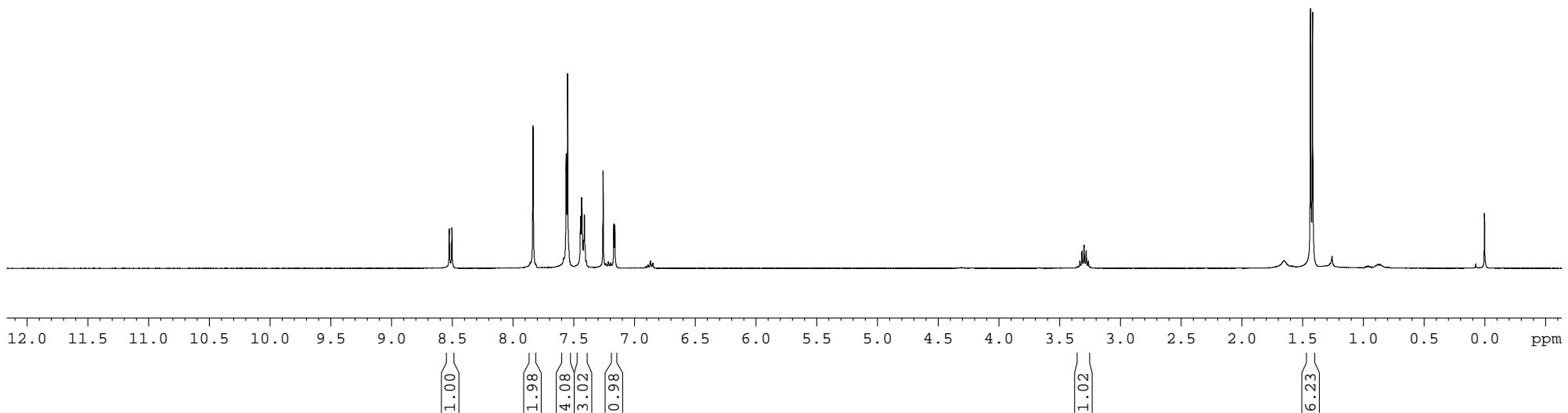
Compound 4g:  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ )

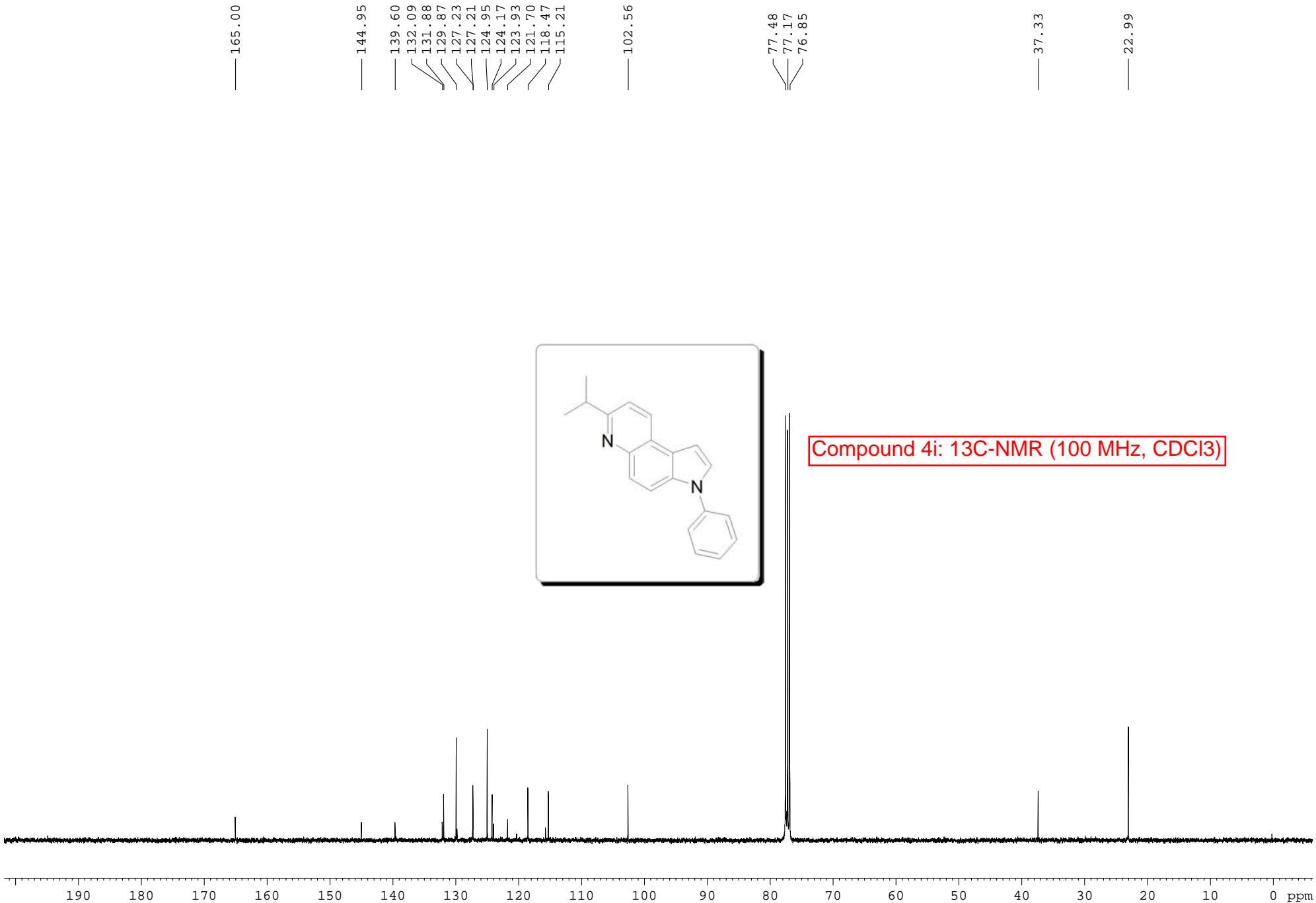


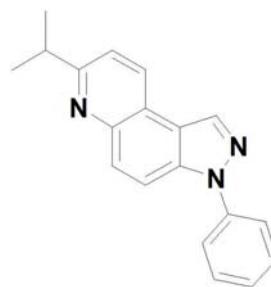




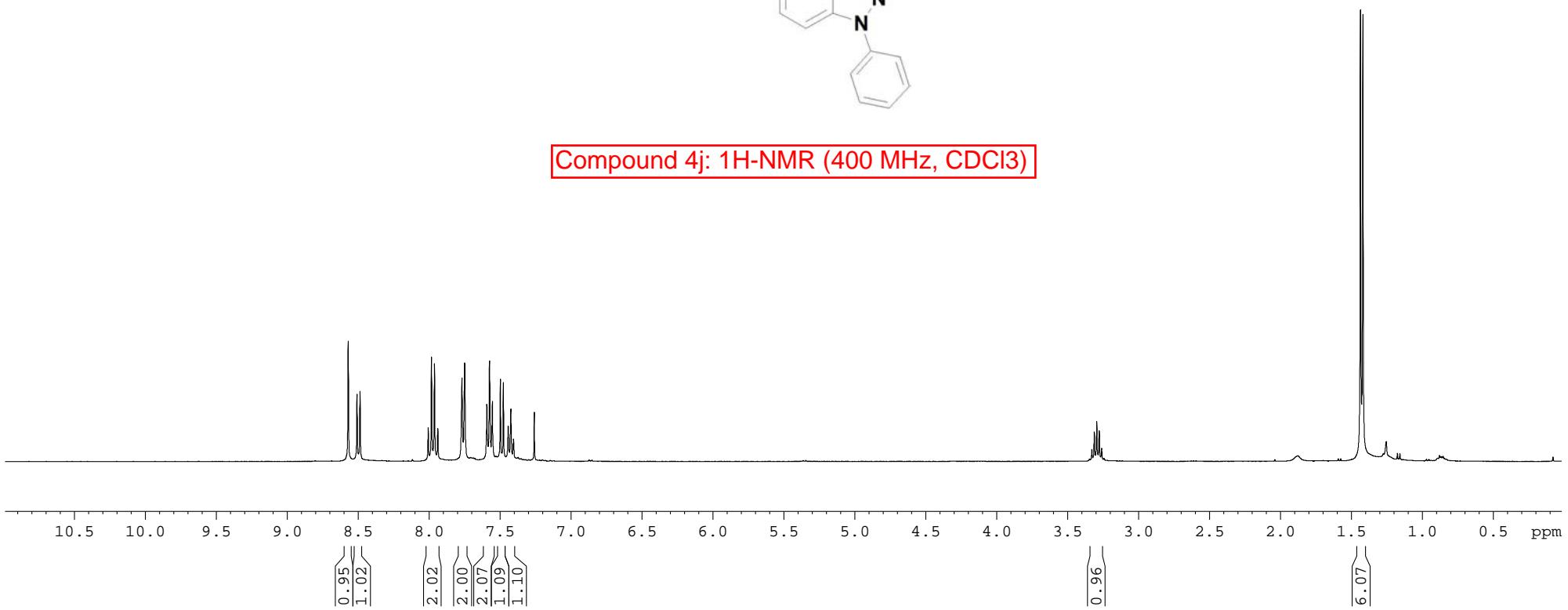
Compound 4i:  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )

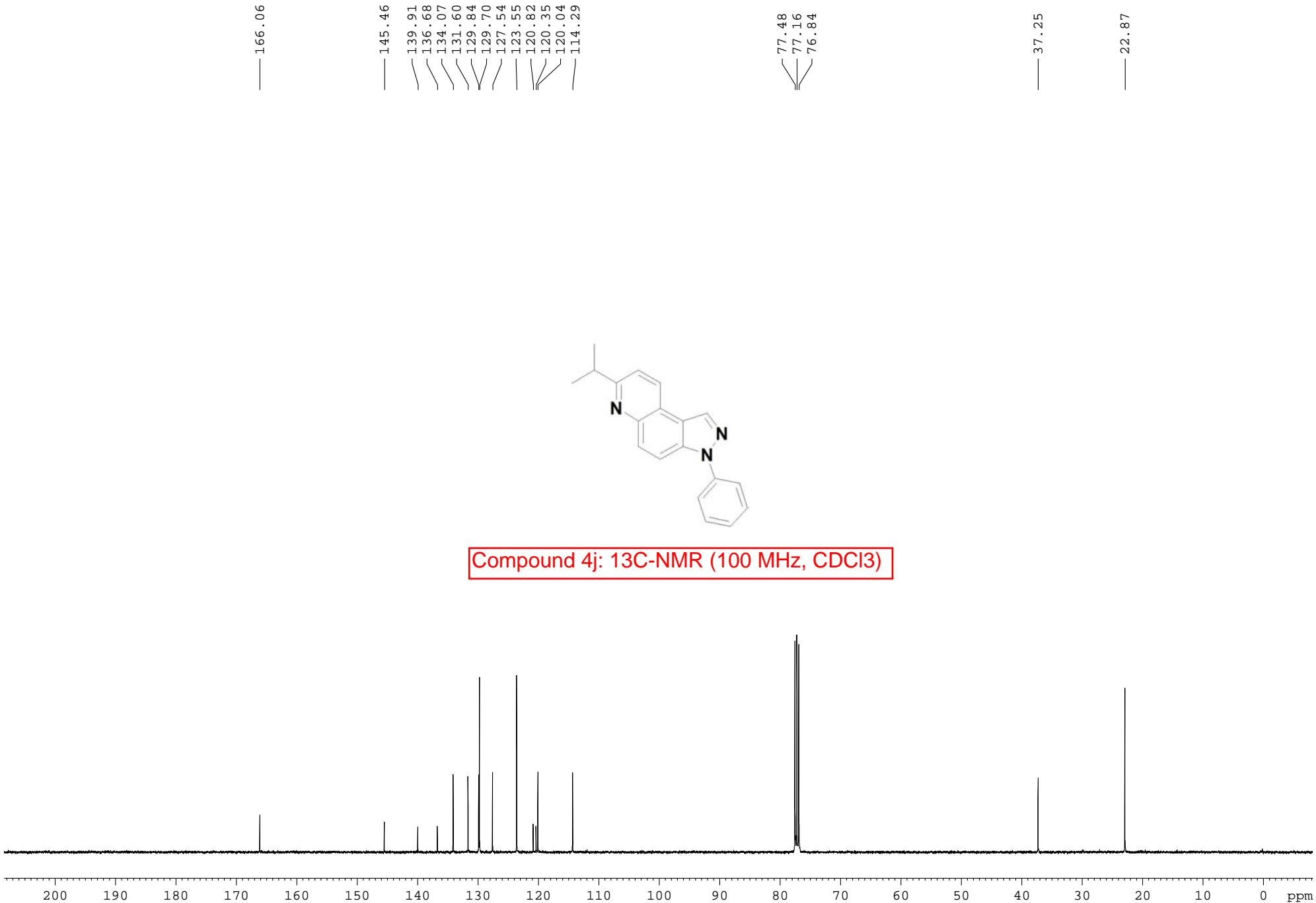






Compound 4j:  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )



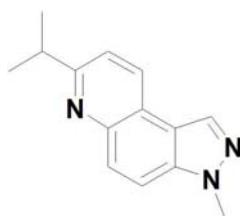


8.4509  
8.4299  
8.3461  
7.9657  
7.9426  
7.6810  
7.6580  
7.4622  
7.4411  
7.2599

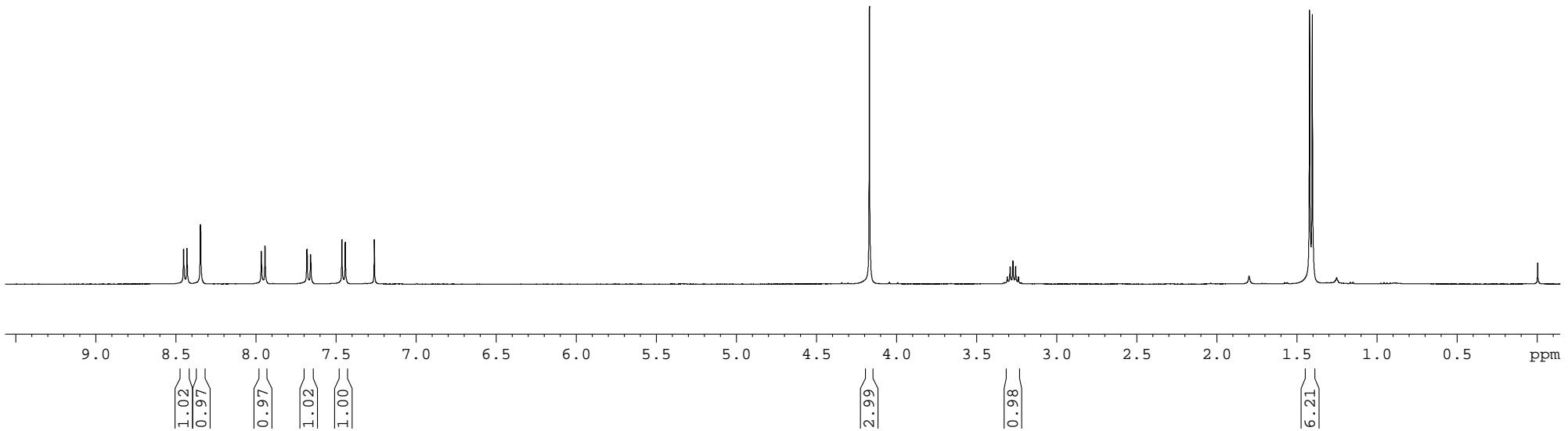
— 4.1707

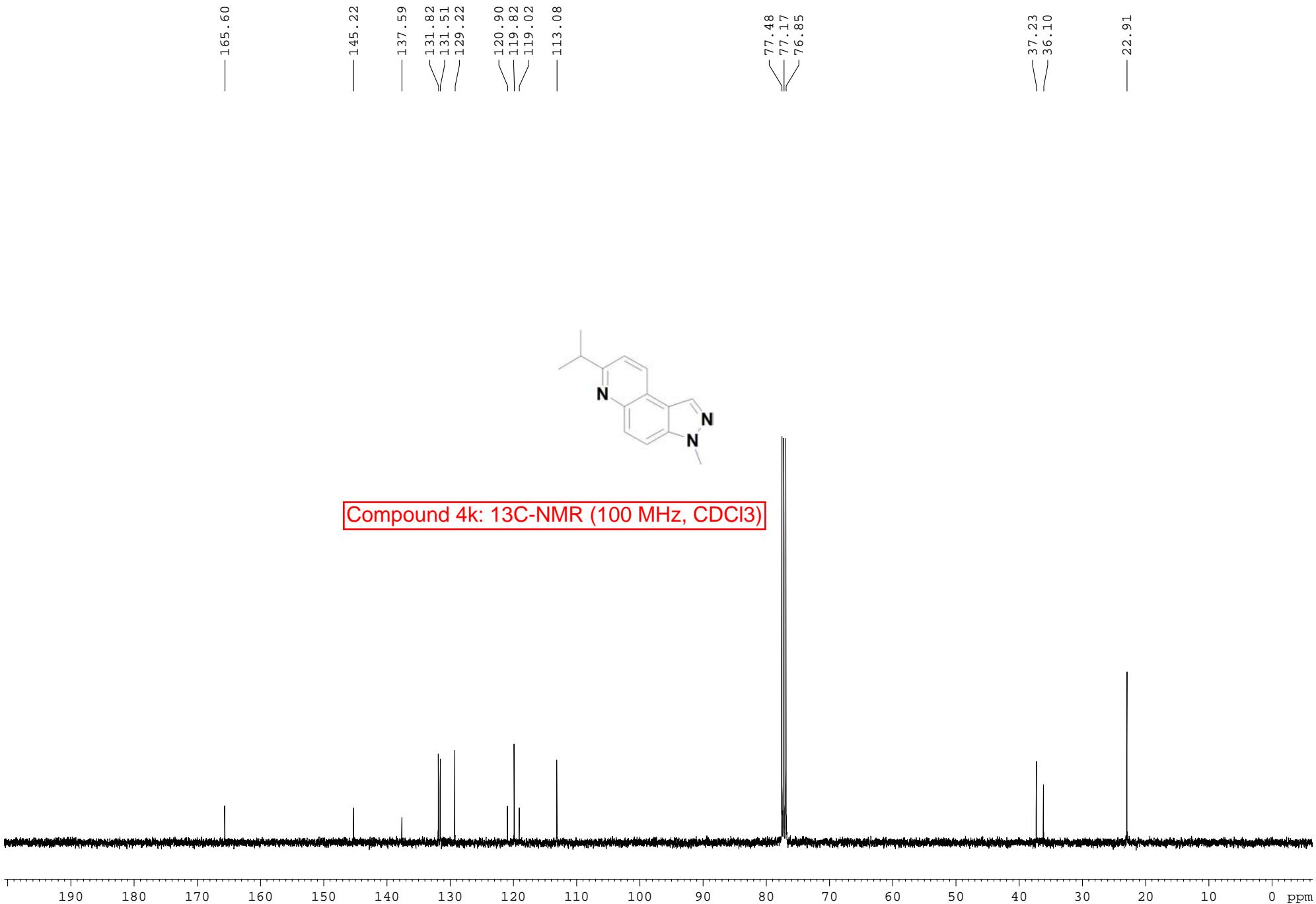
3.3095  
3.2921  
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3.2574  
3.2401

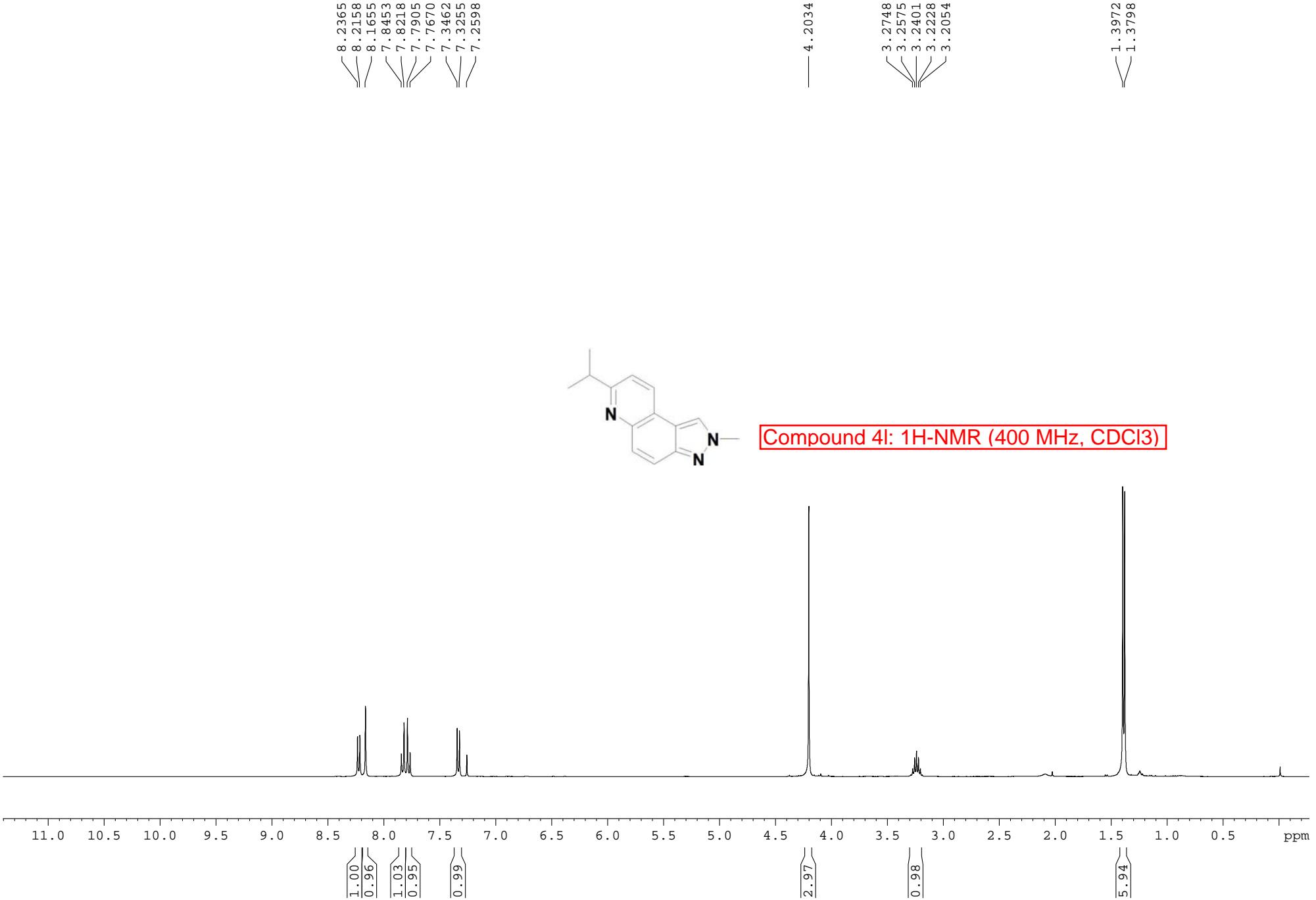
1.4219  
1.4045

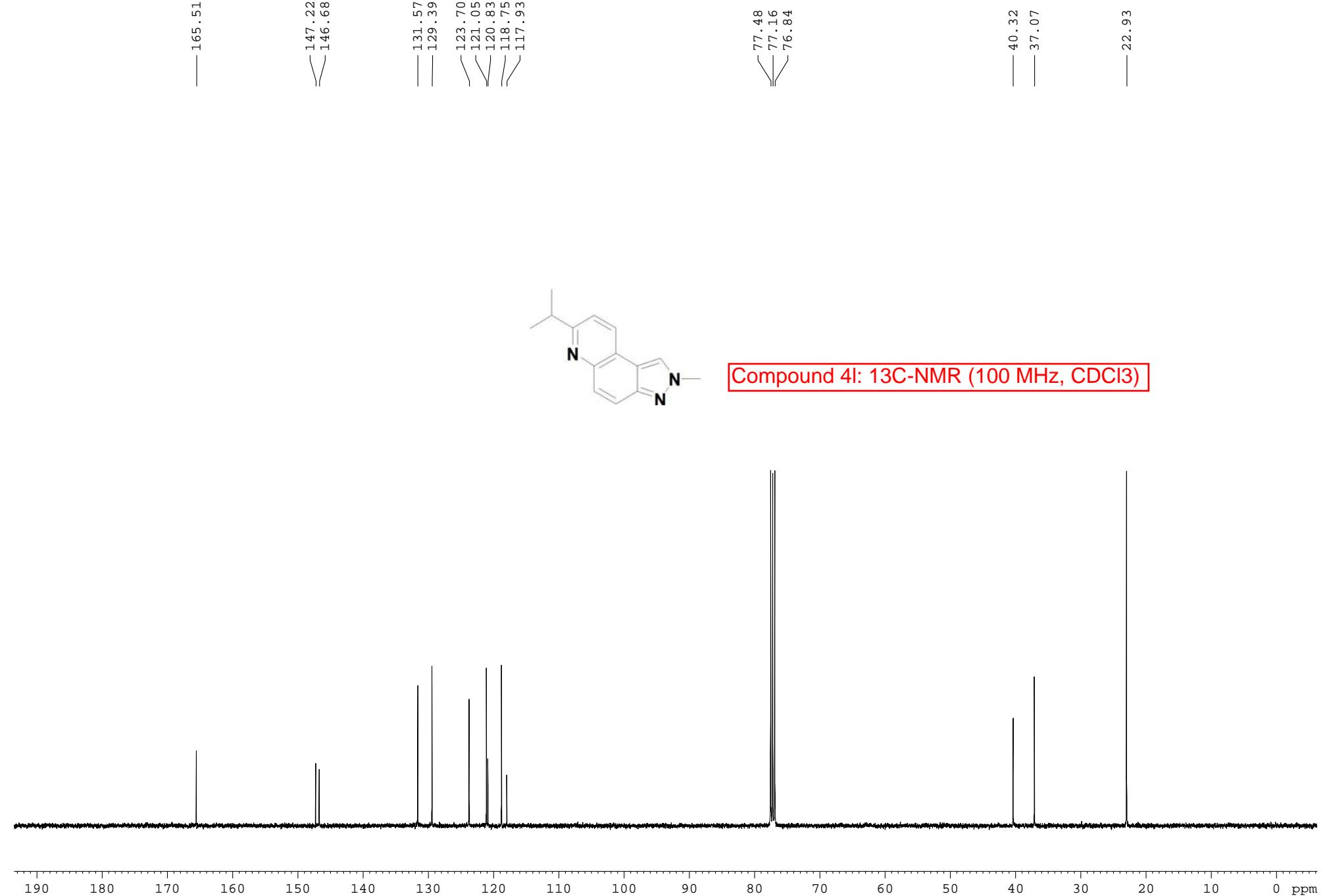


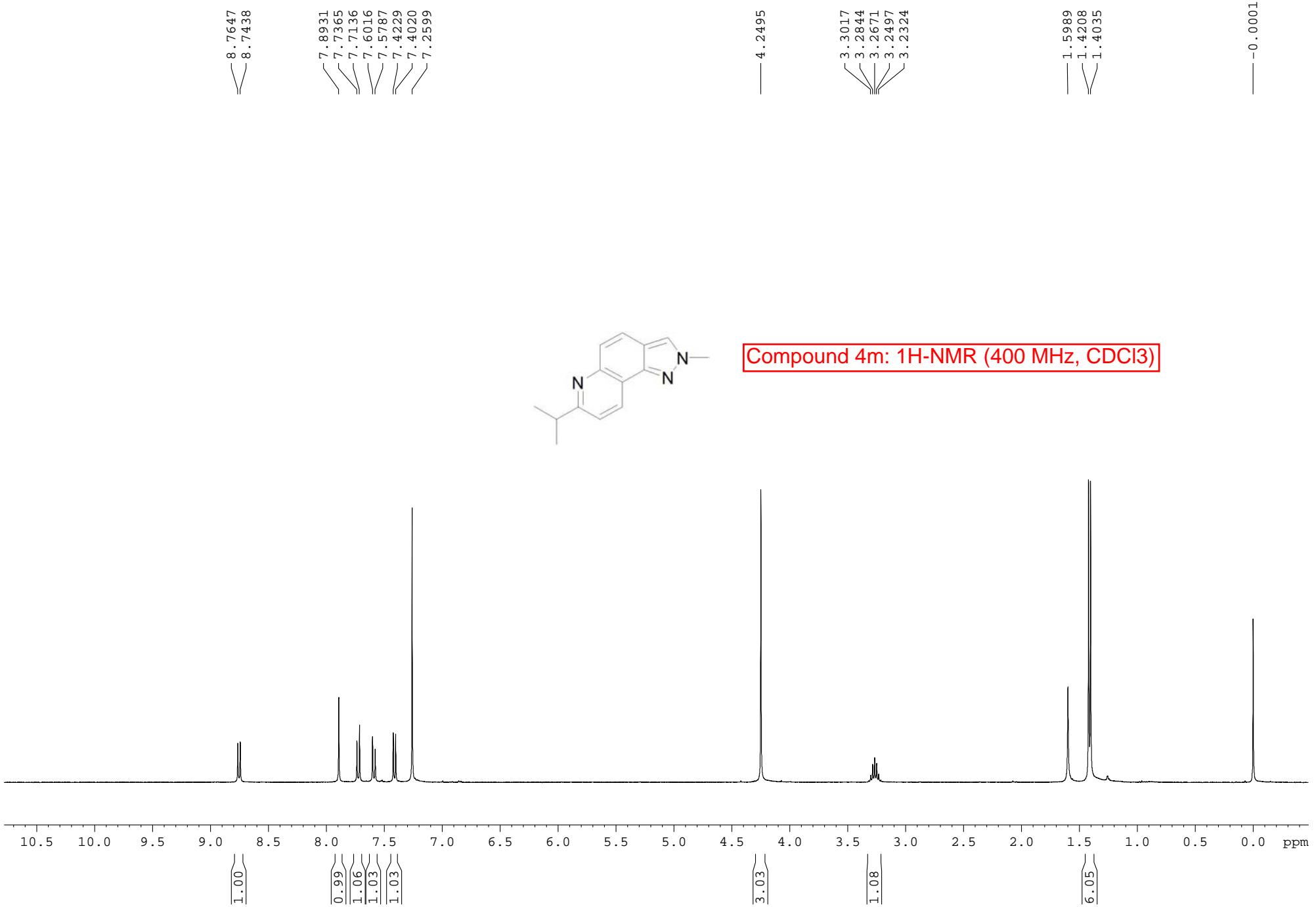
Compound 4k:  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )

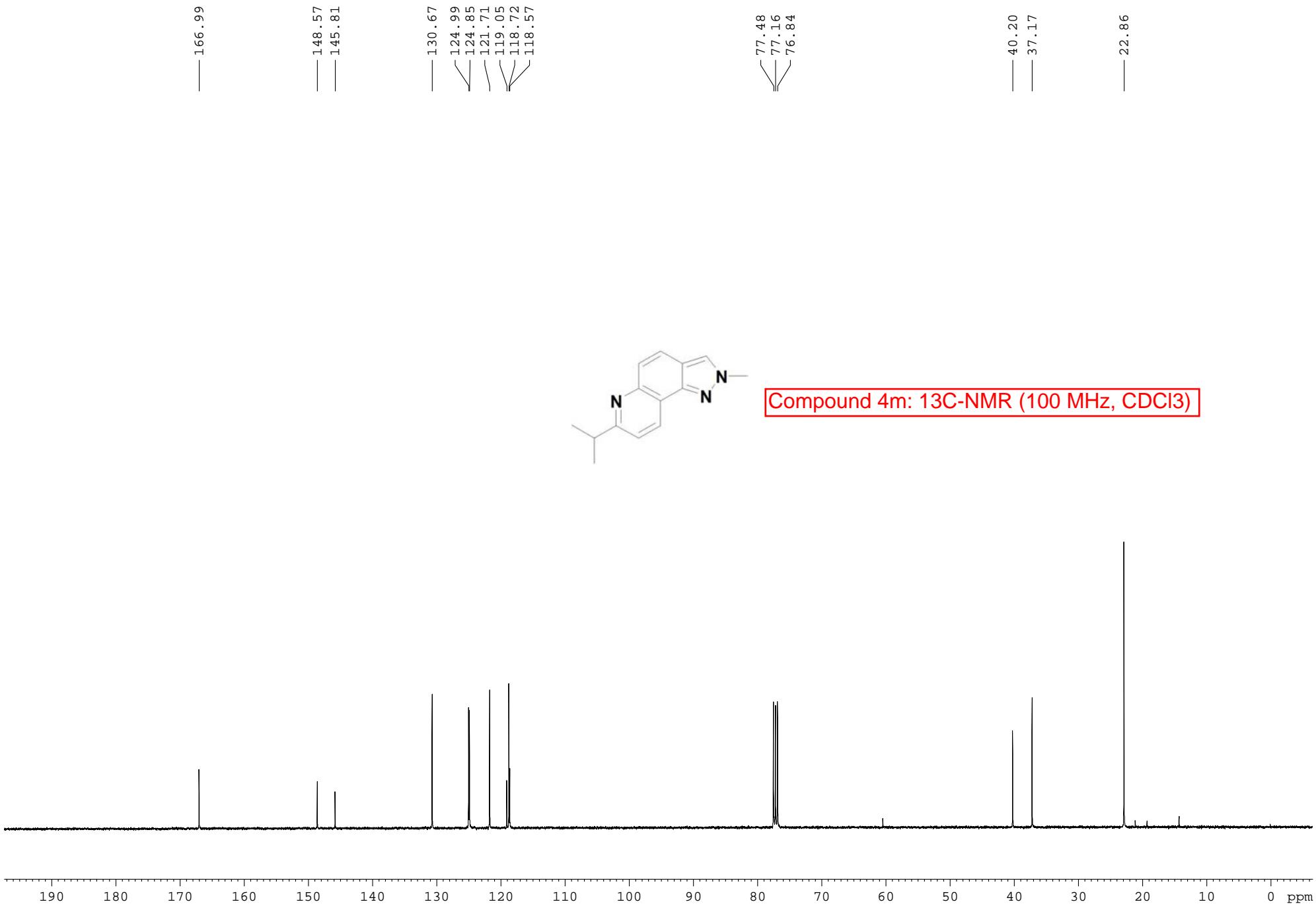


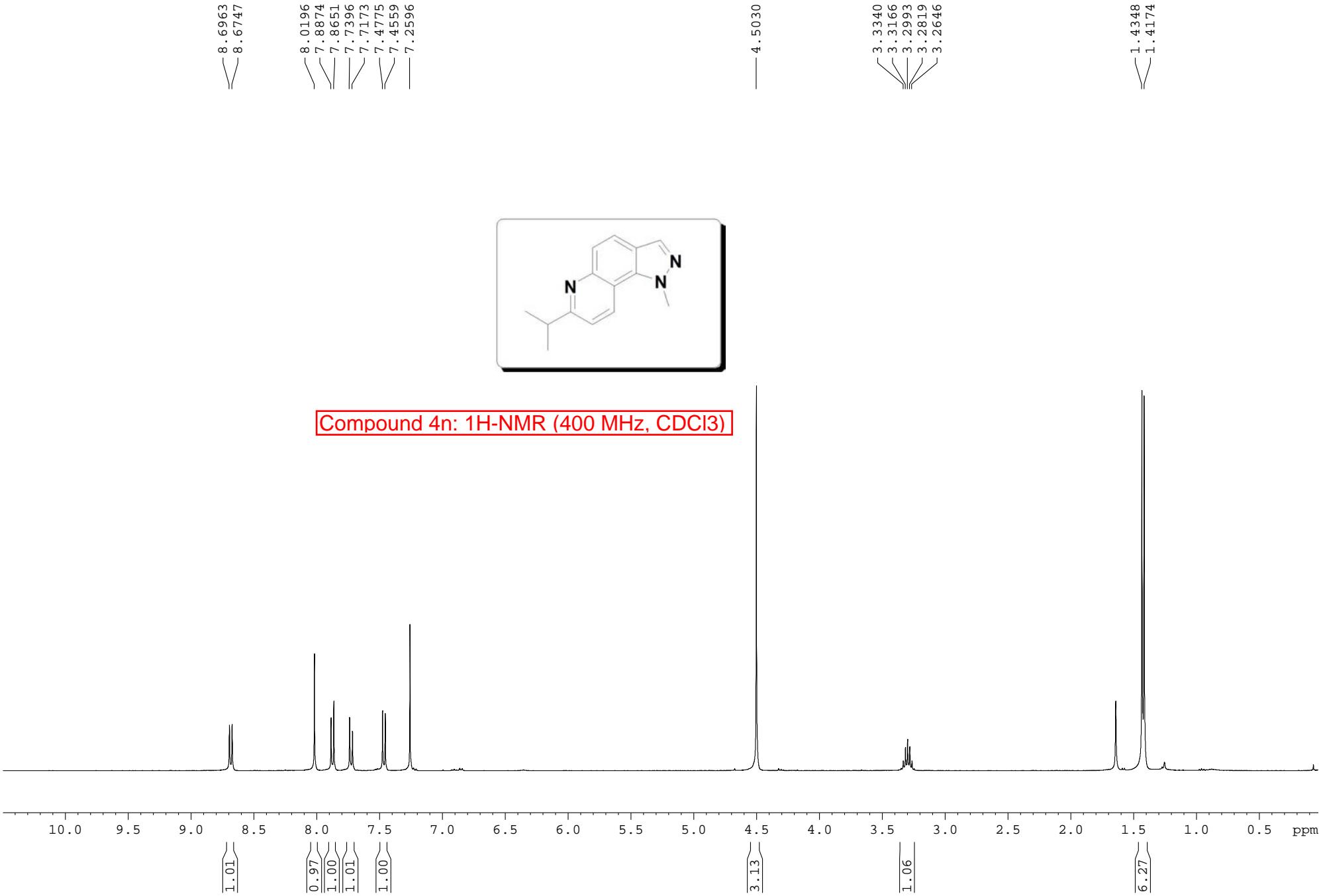


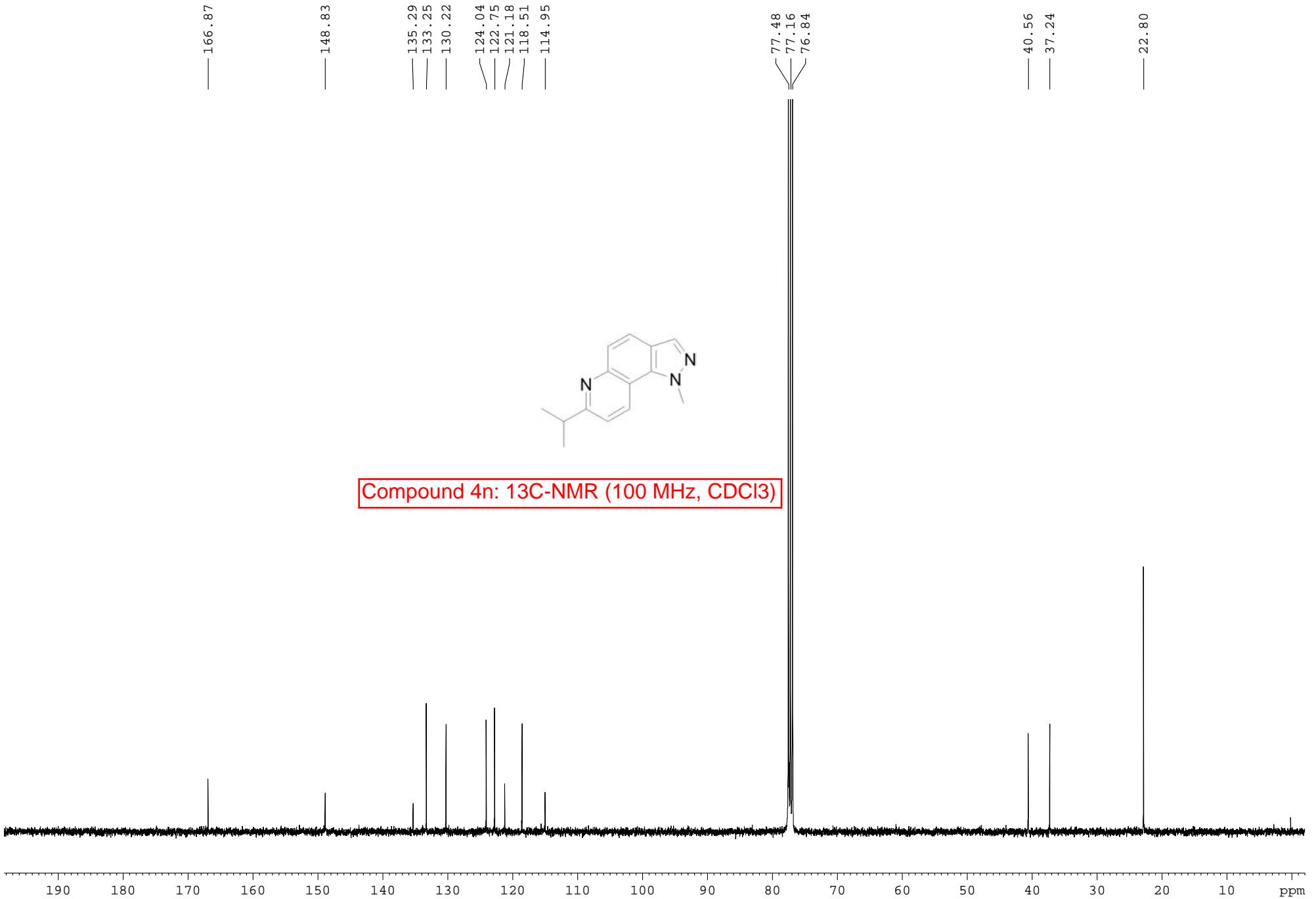


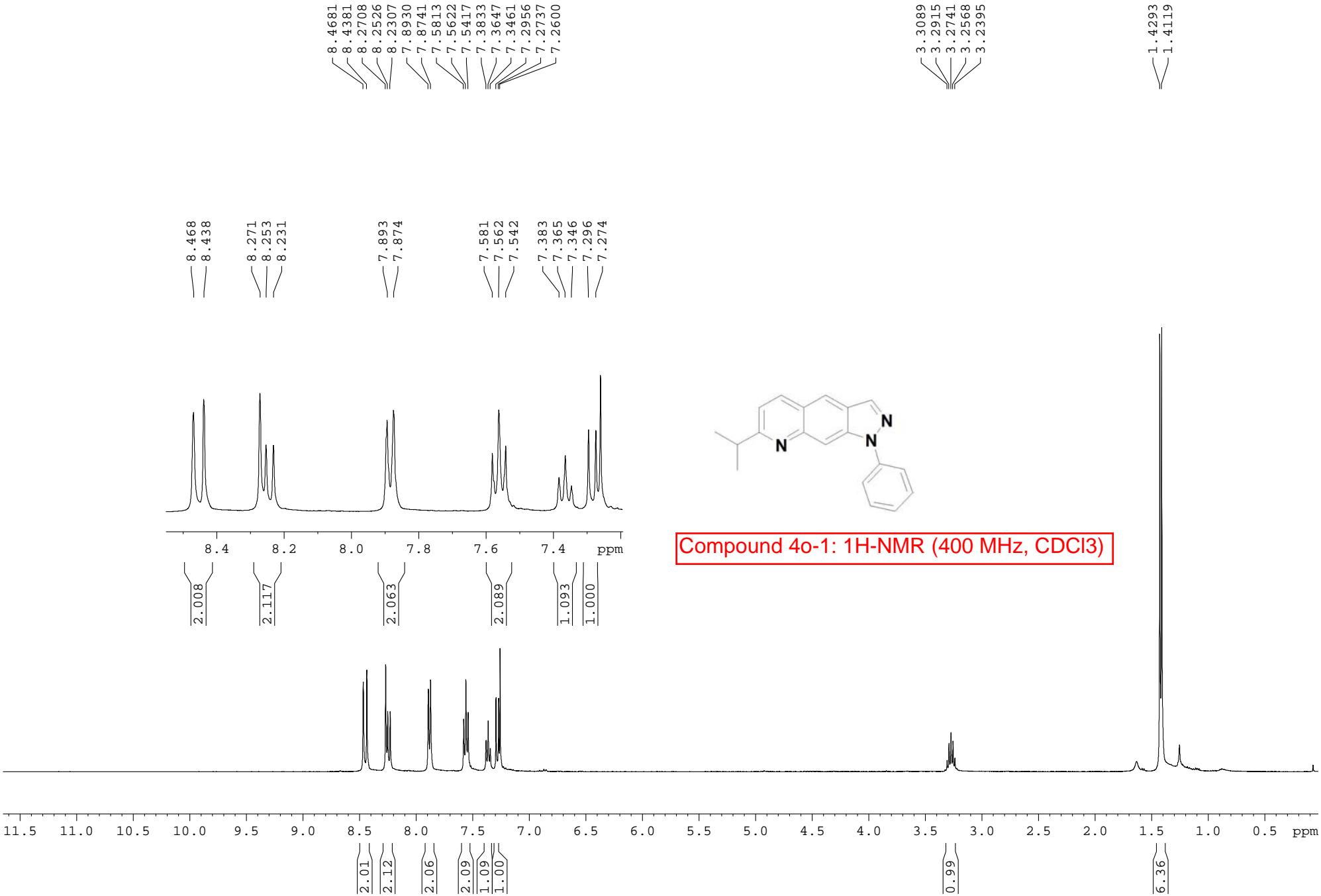


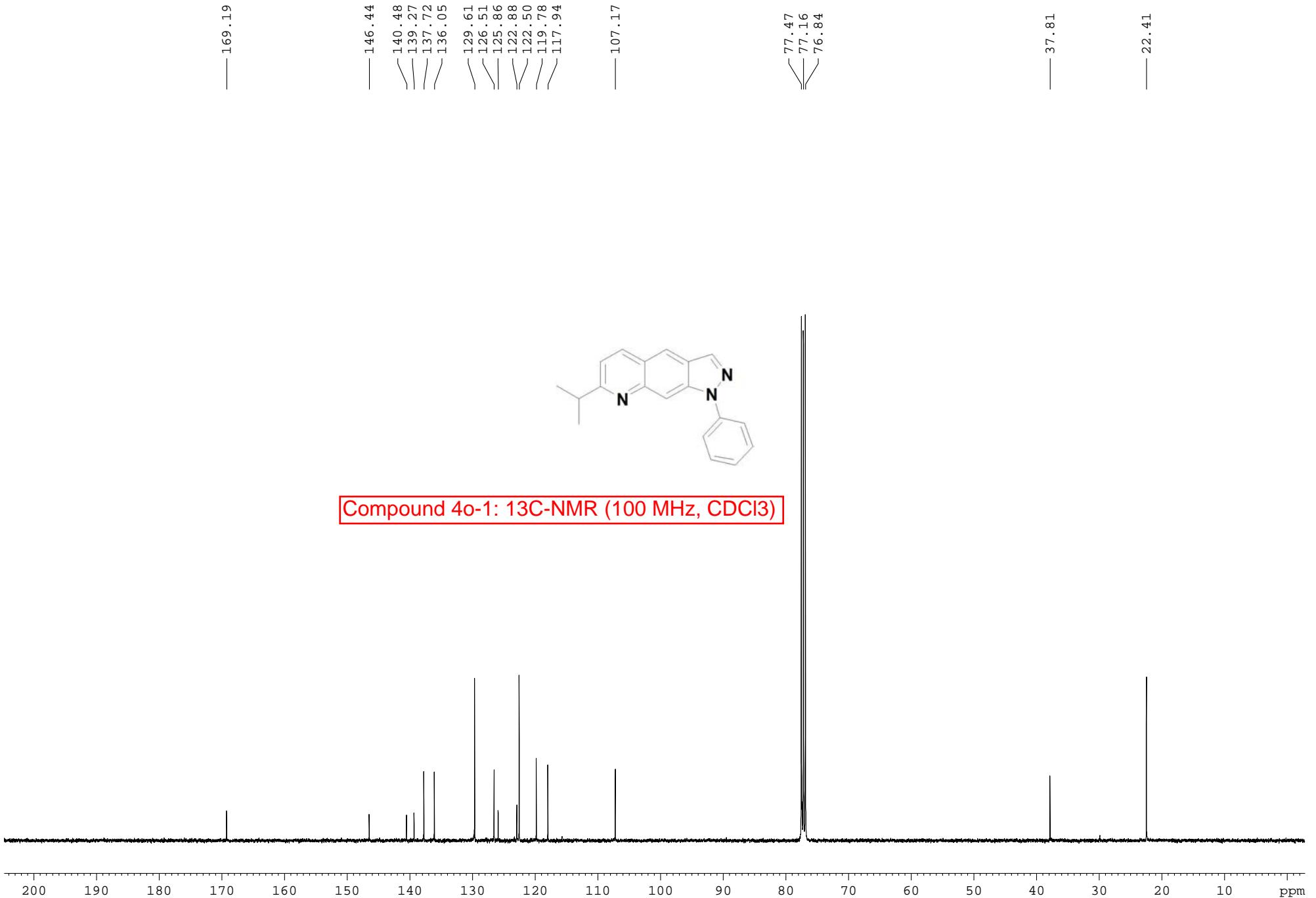


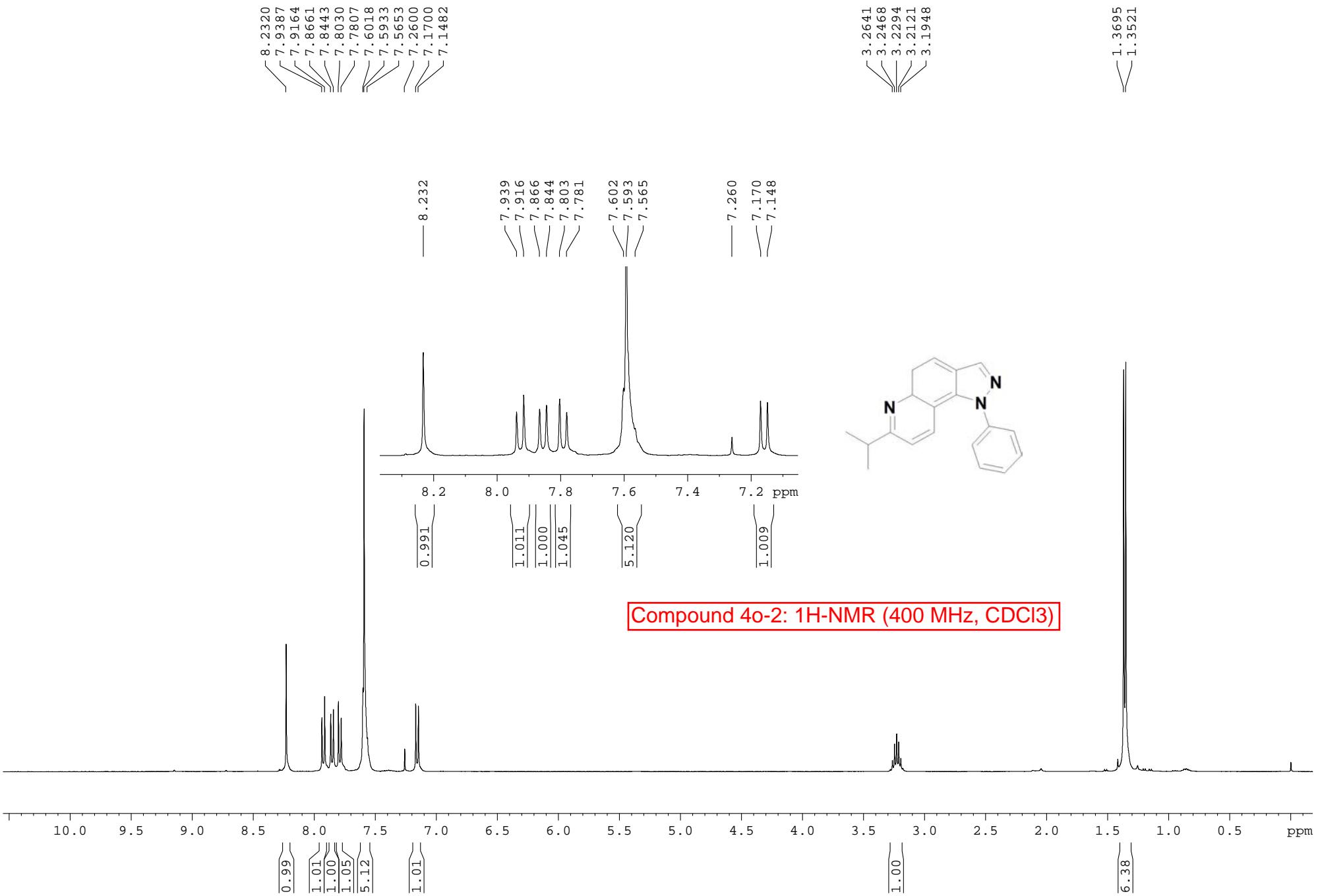


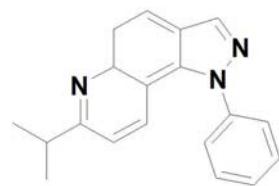




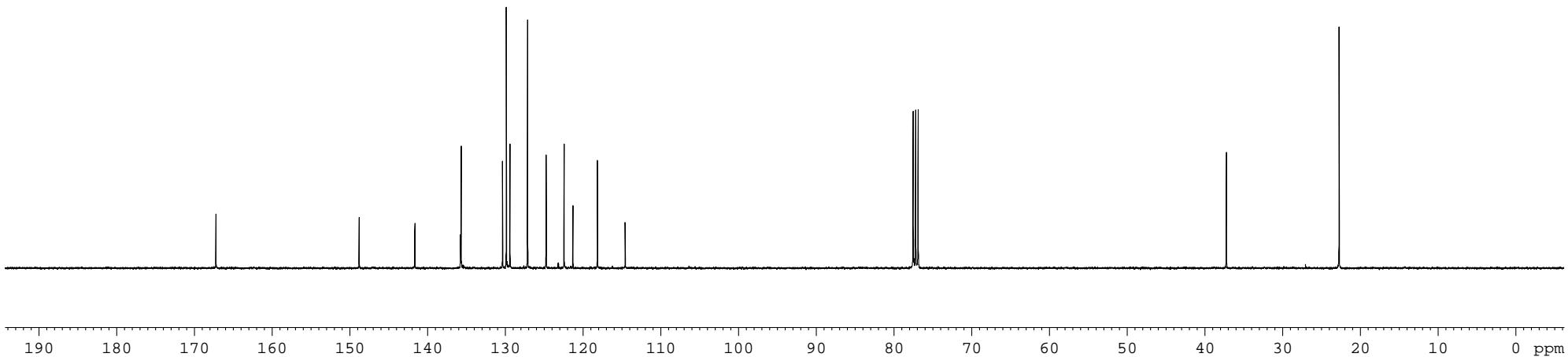






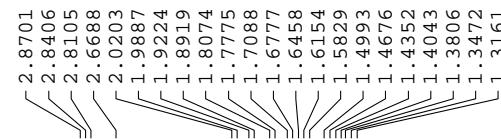
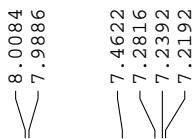


Compound 4o-2: <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)

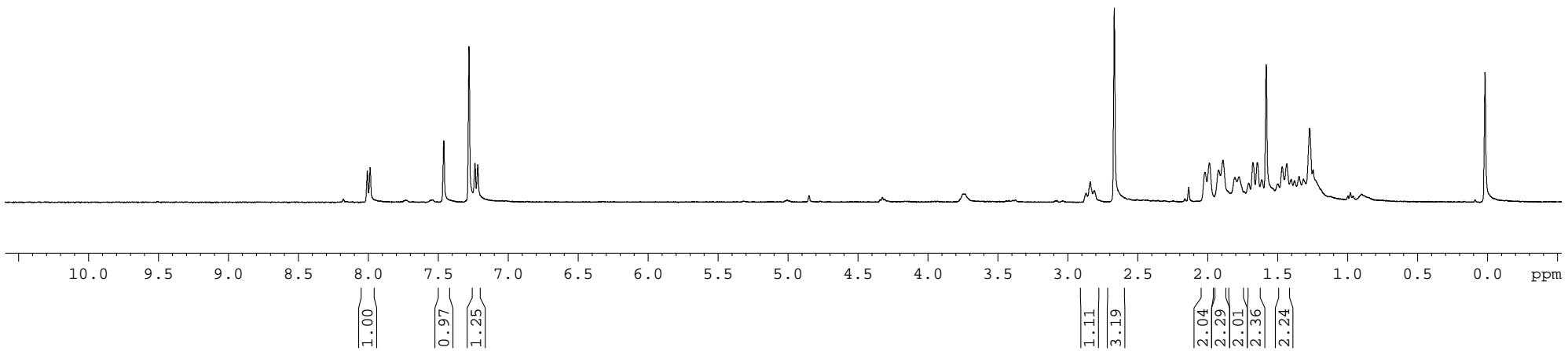
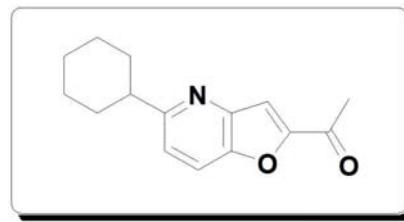


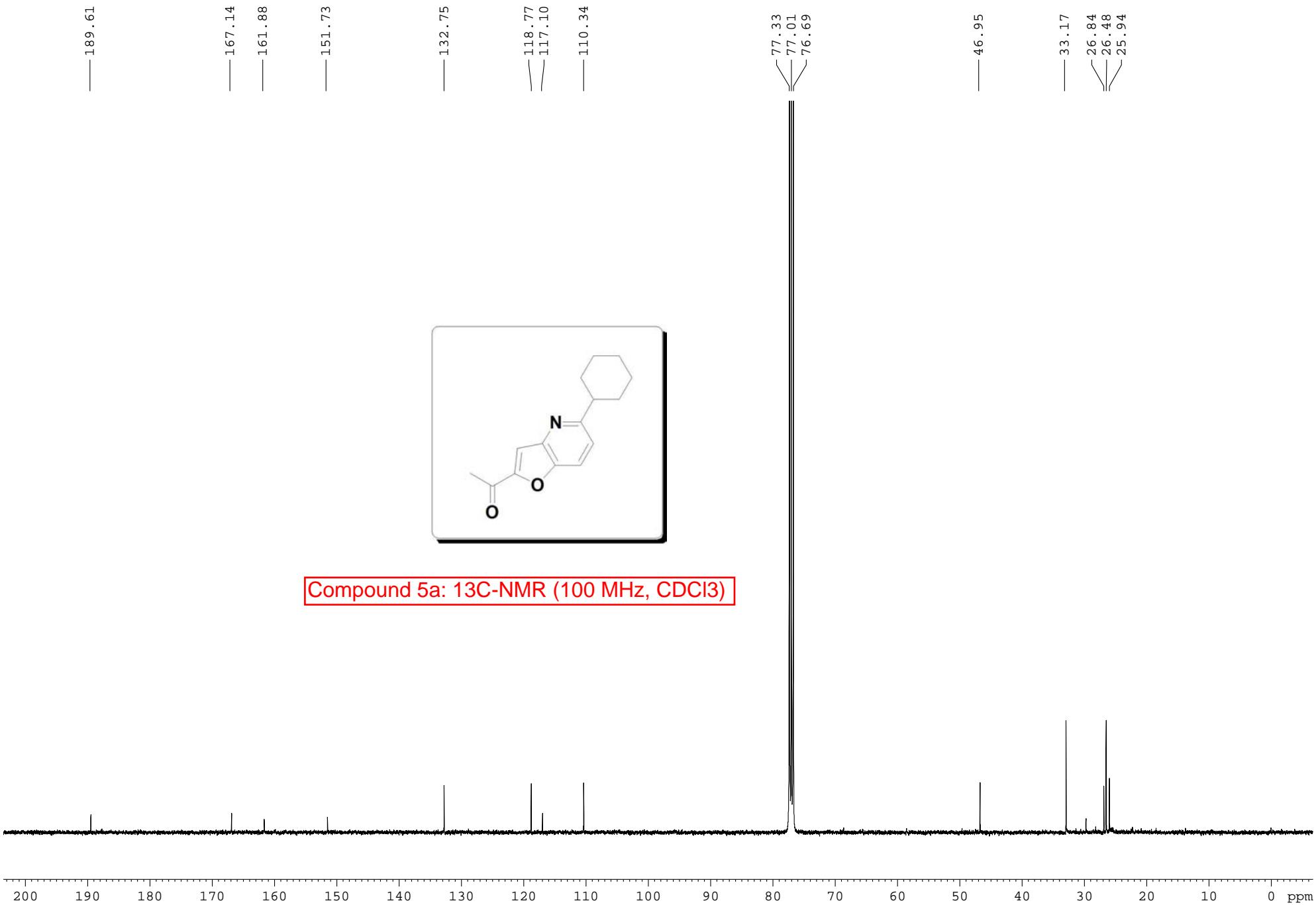
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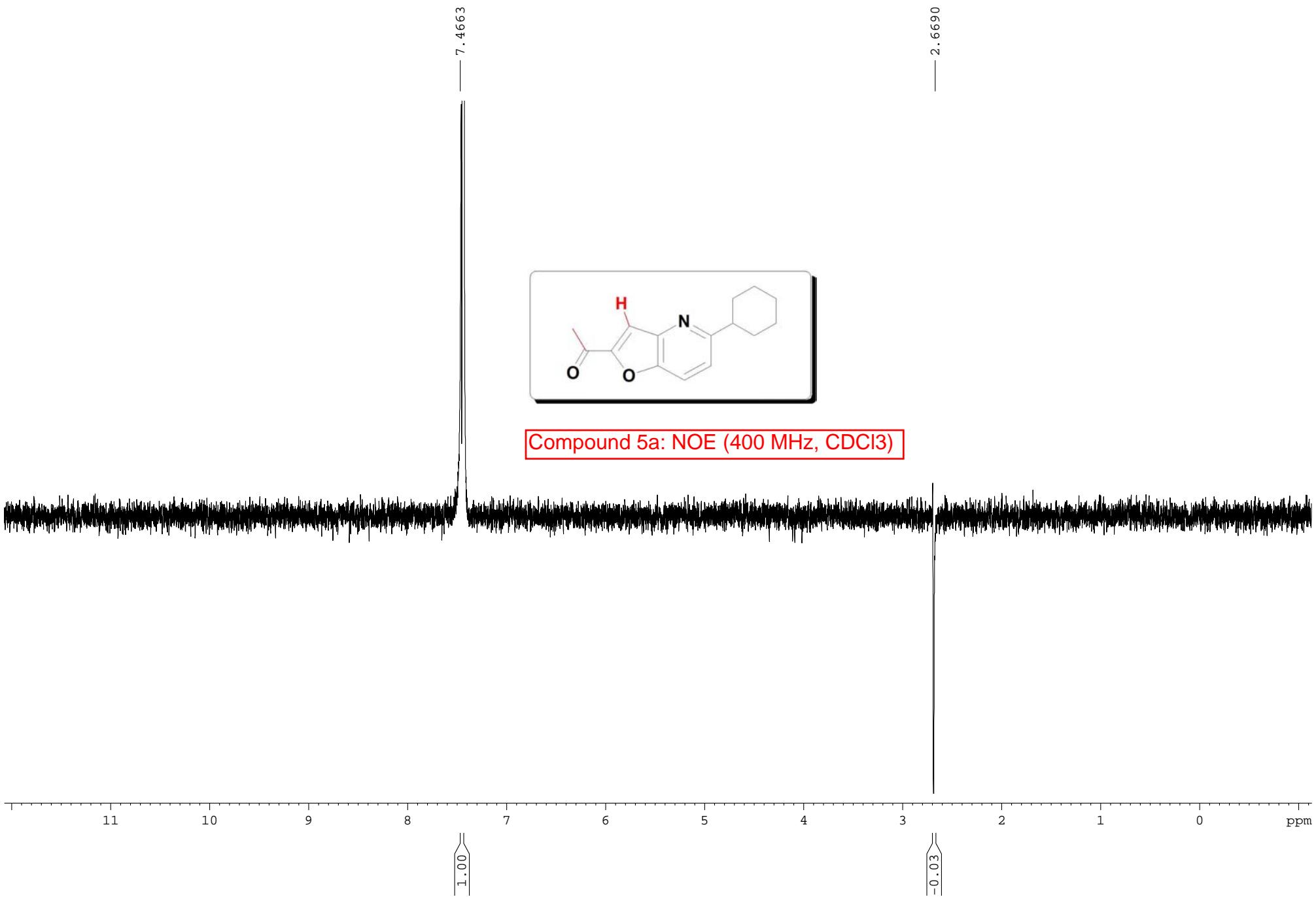
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SOLVENT CDCl3  
NS 16  
DS 2

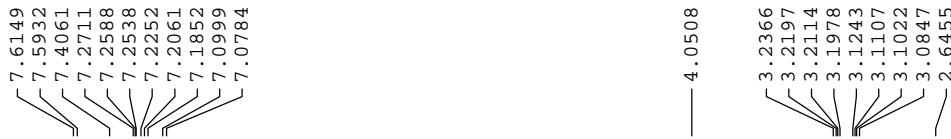


Compound 5a: 1H-NMR (400 MHz, CDCl3)

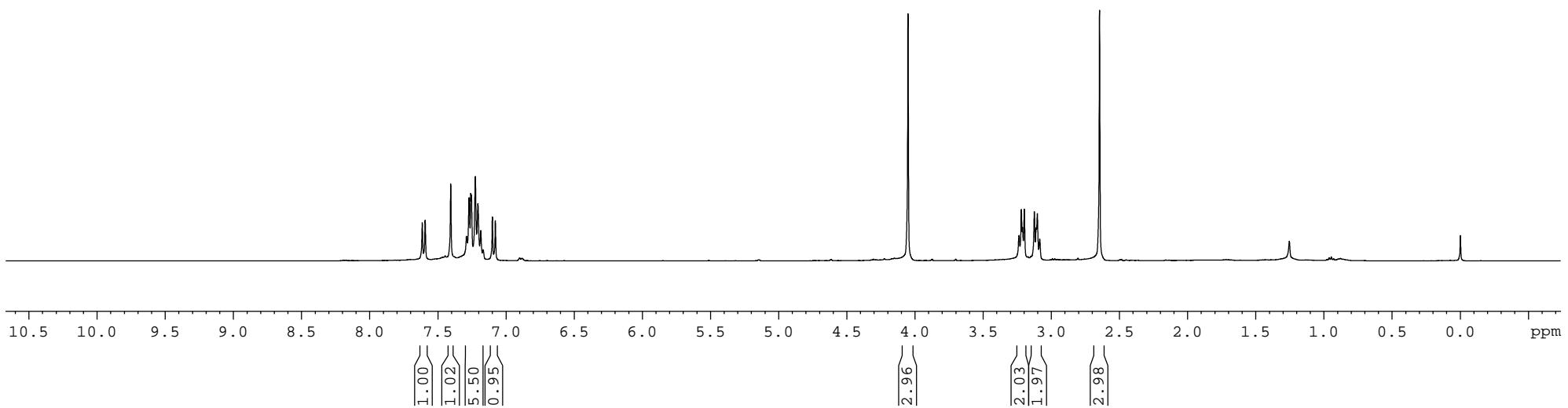


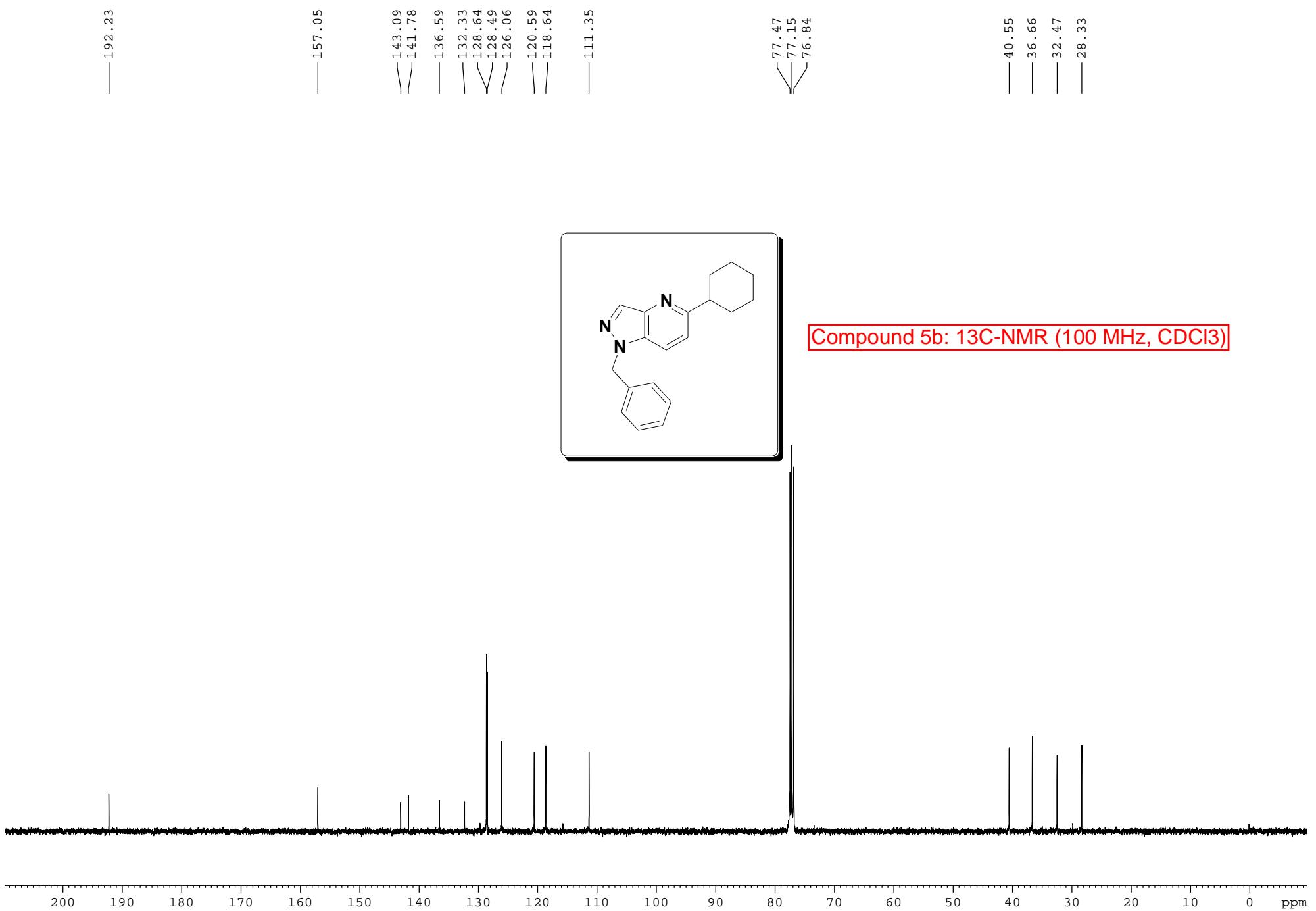


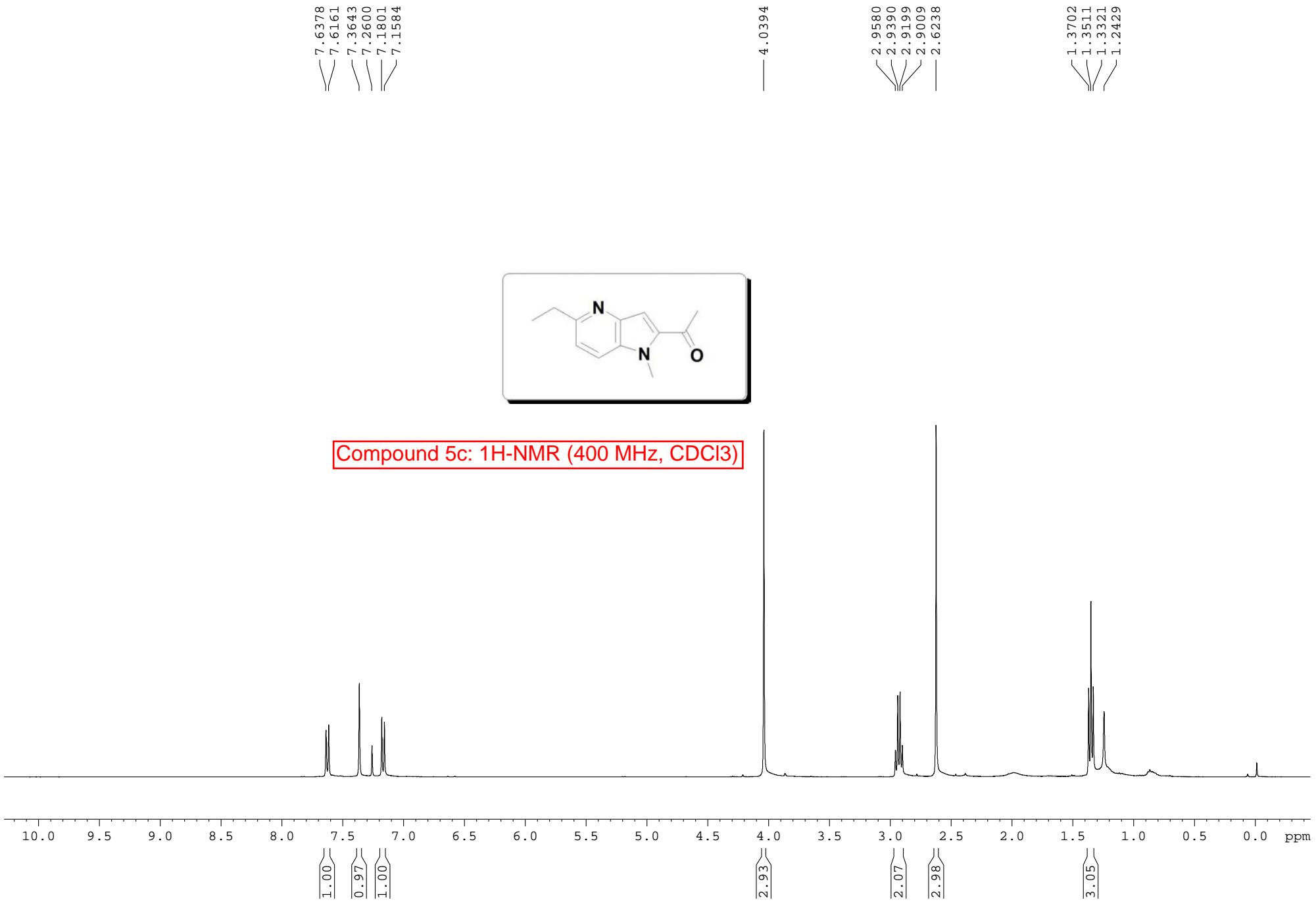


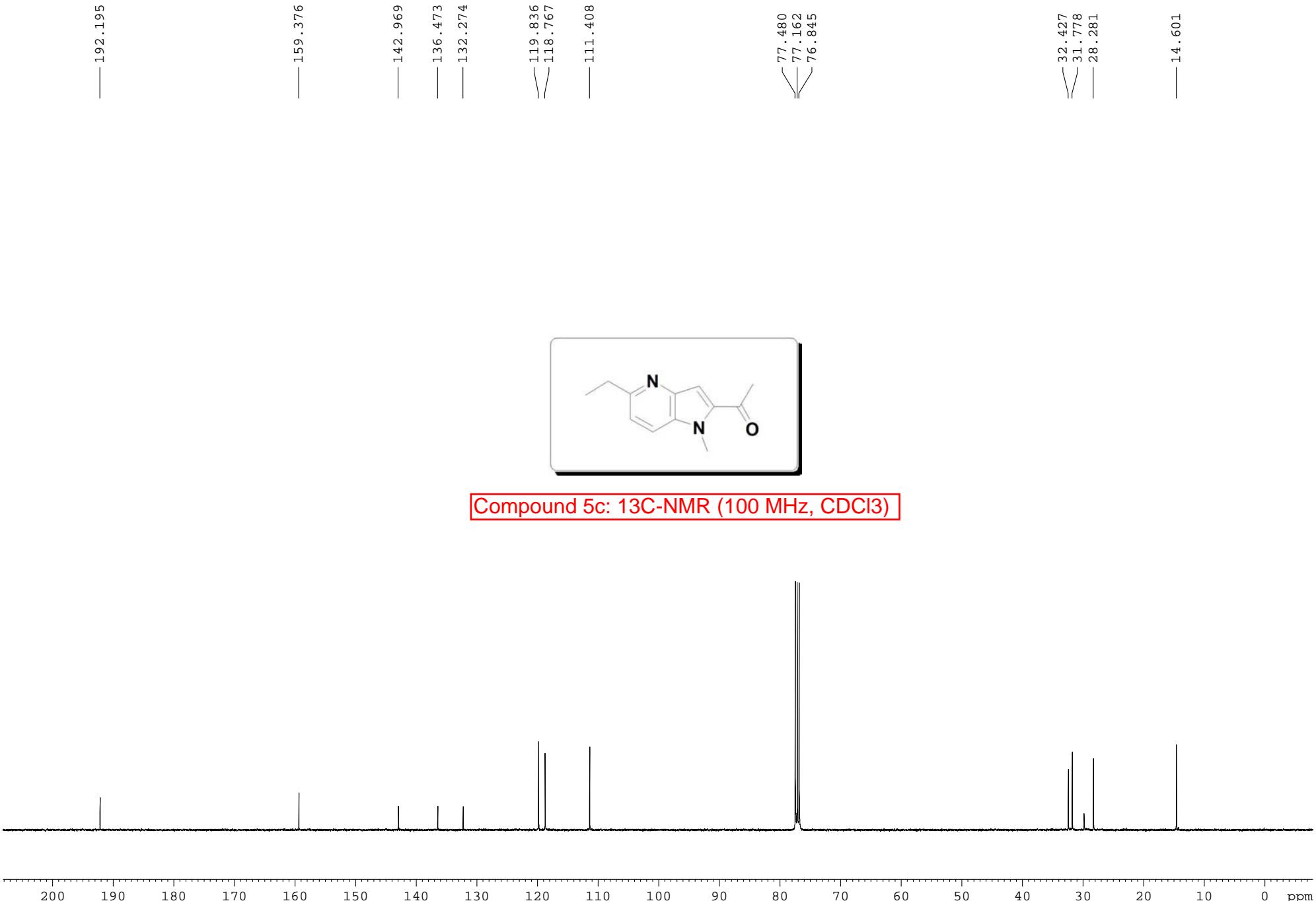


Compound 5b:  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )



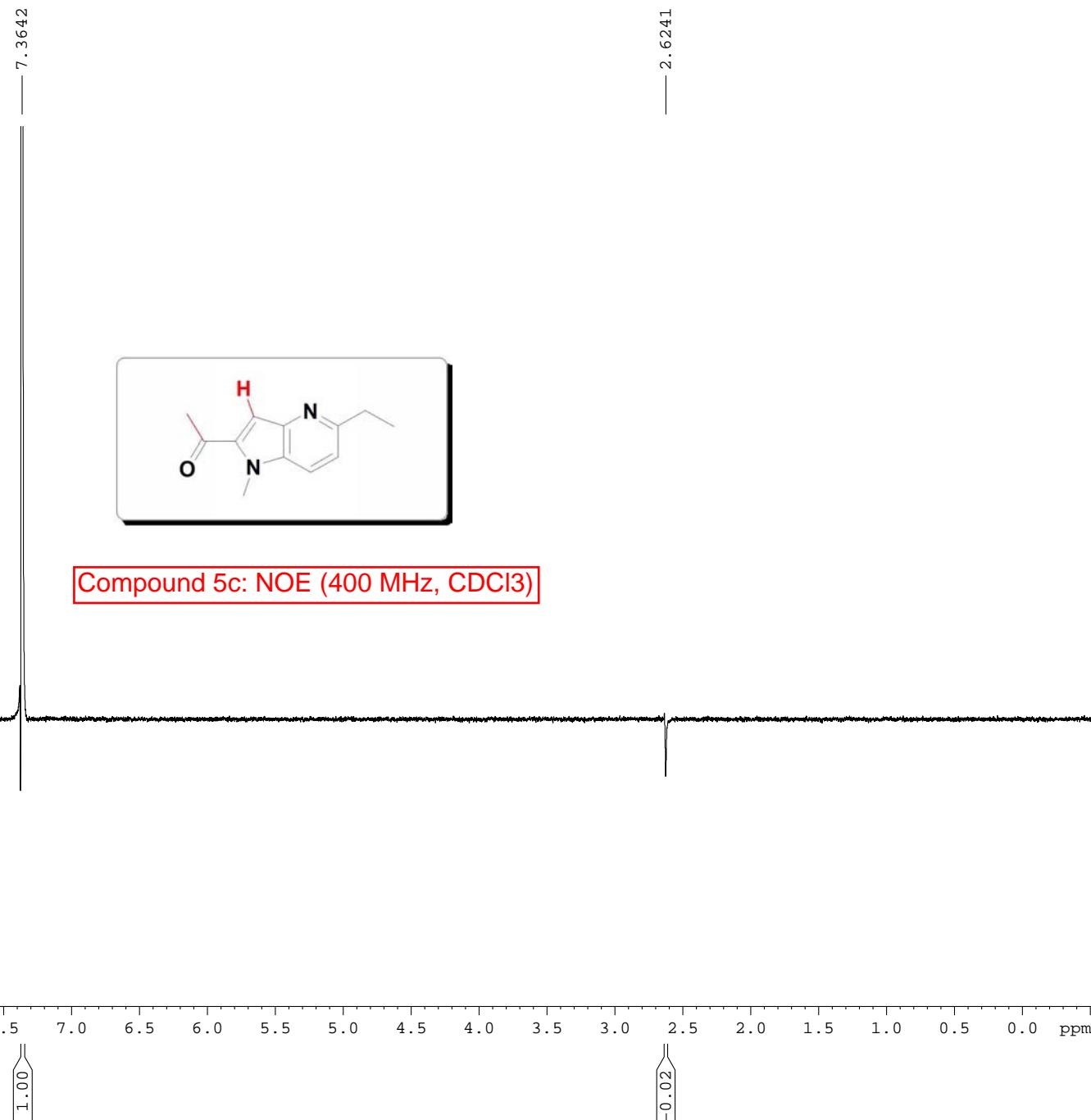






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PROCNO 1

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PULPROG selnogp  
TD 65536  
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DS 4  
SWH 8223.685 Hz  
FIDRES 0.125483 Hz  
AQ 3.9846387 sec  
RG 209.25  
DW 60.800 usec  
DE 6.50 usec  
TE 298.7 K  
D1 1.0000000 sec  
D8 0.5000000 sec  
D16 0.0002000 sec  
D20 0.24879999 sec  
TD0 1



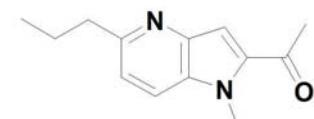
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7.1672  
7.1455

— 4.0438

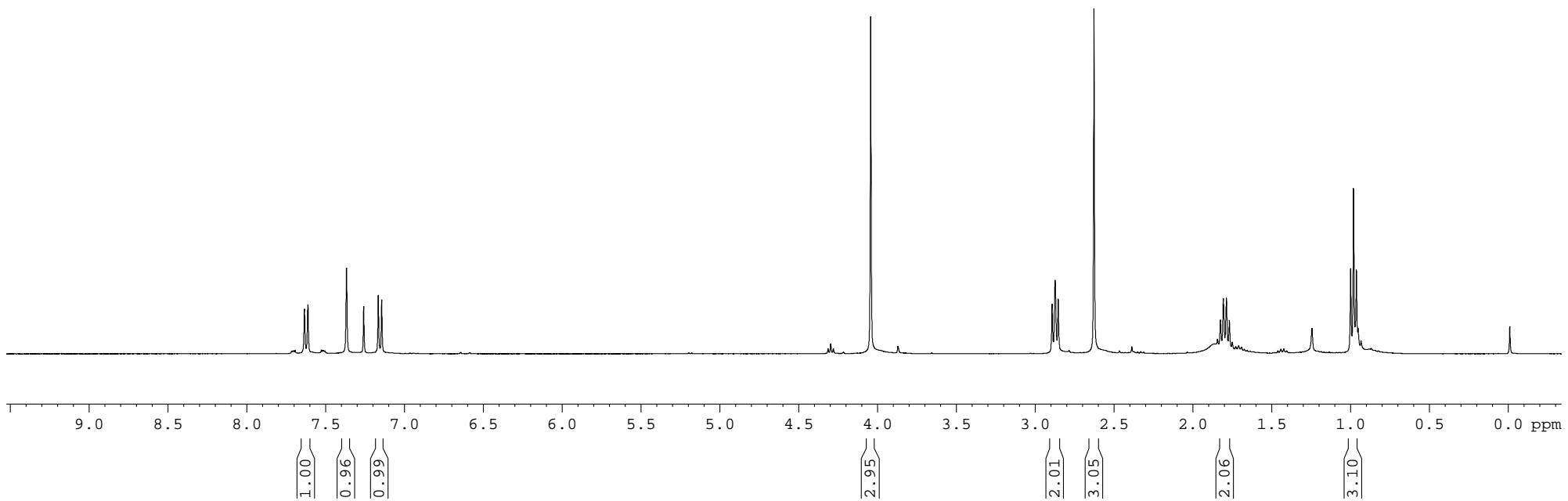
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2.8545  
2.6276

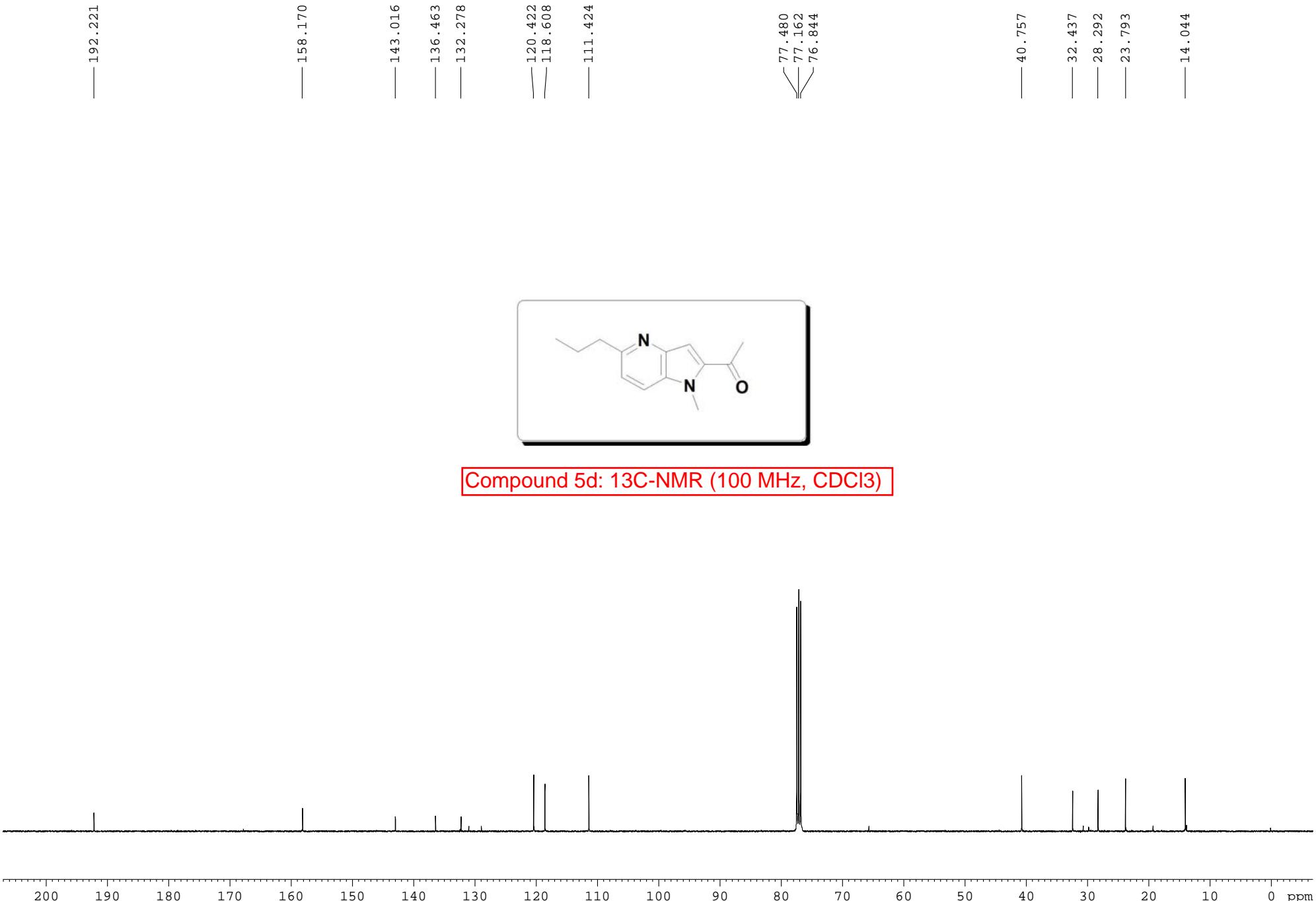
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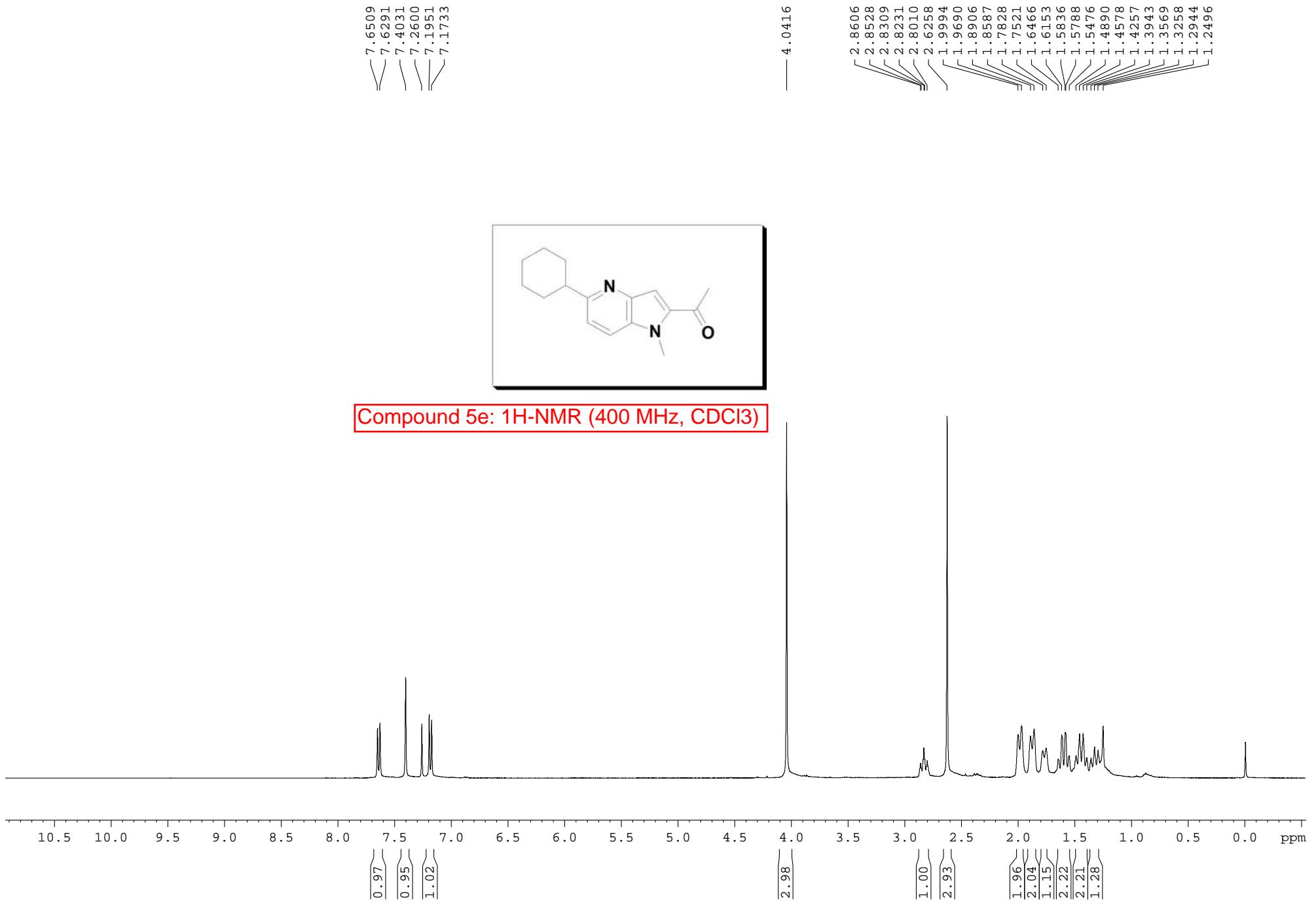
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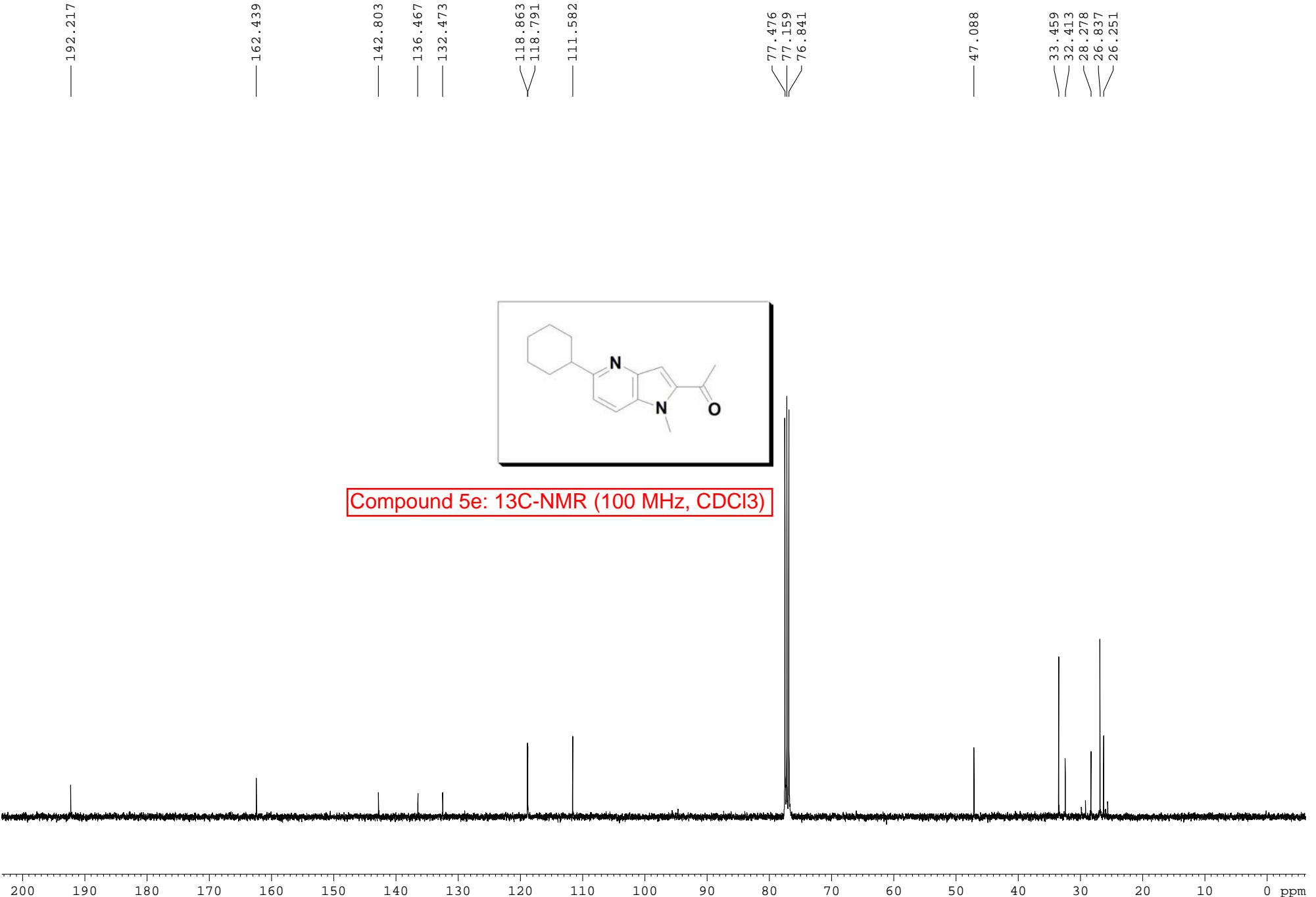


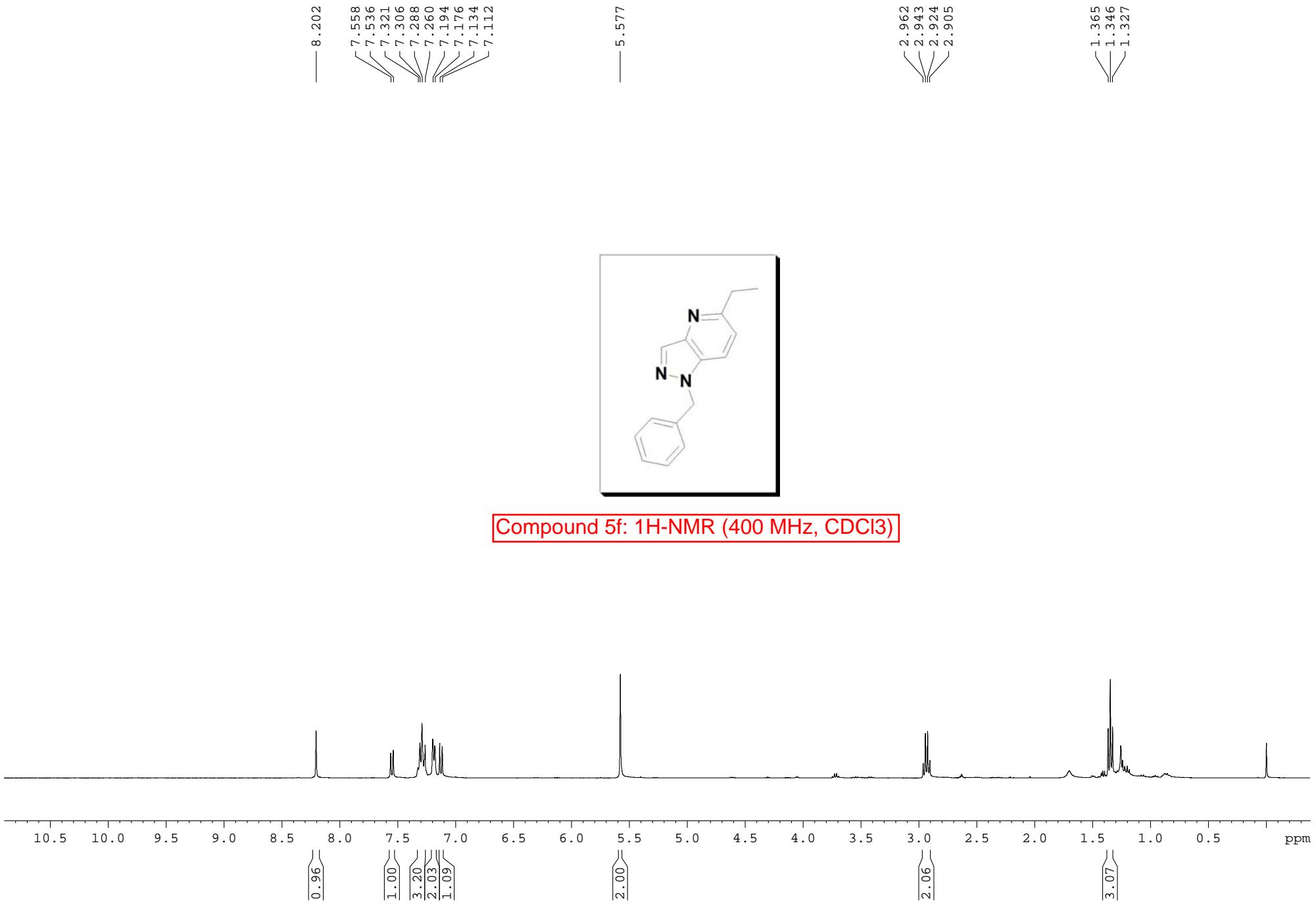
Compound 5d: <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)

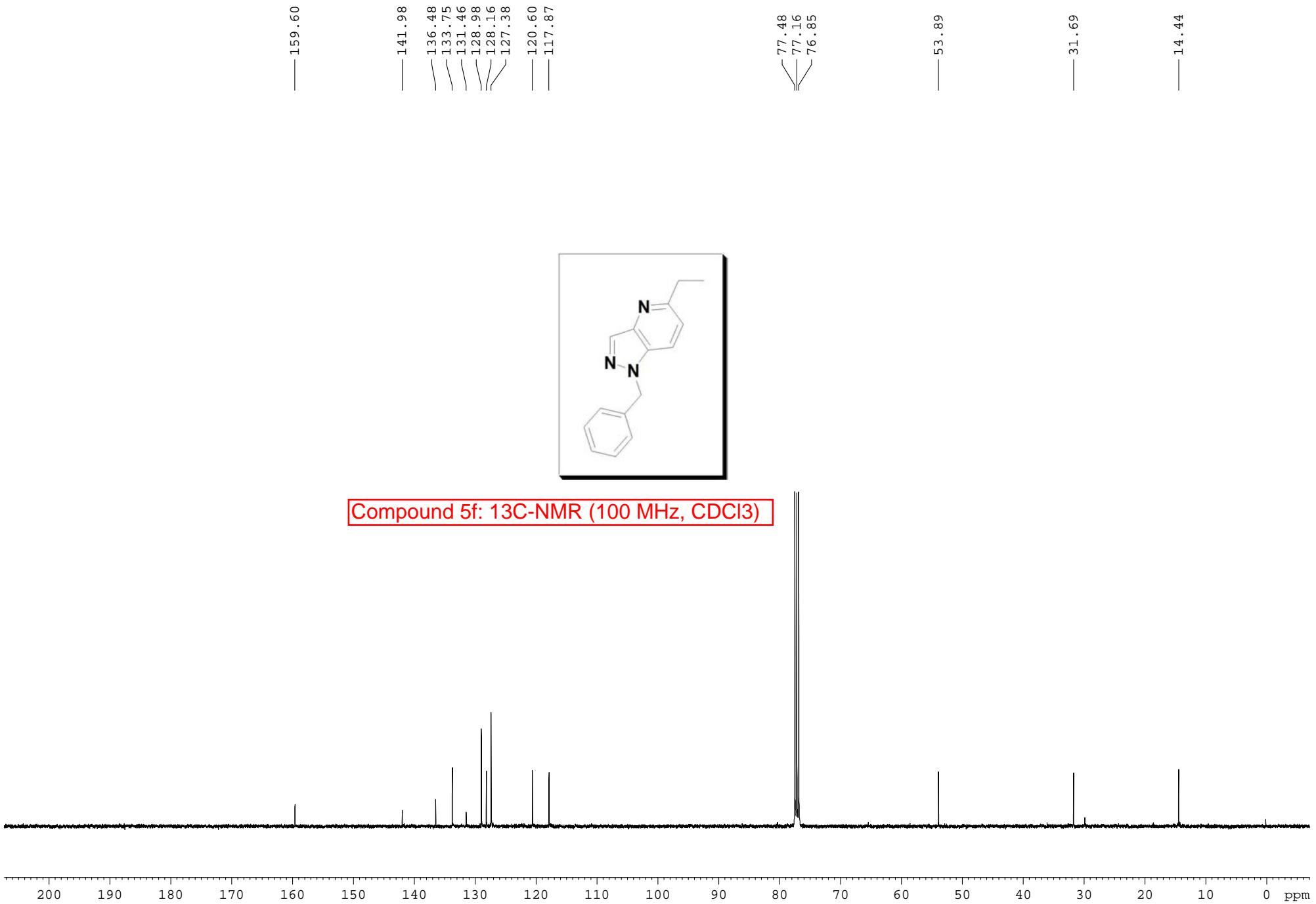






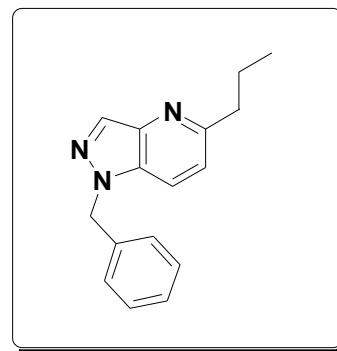




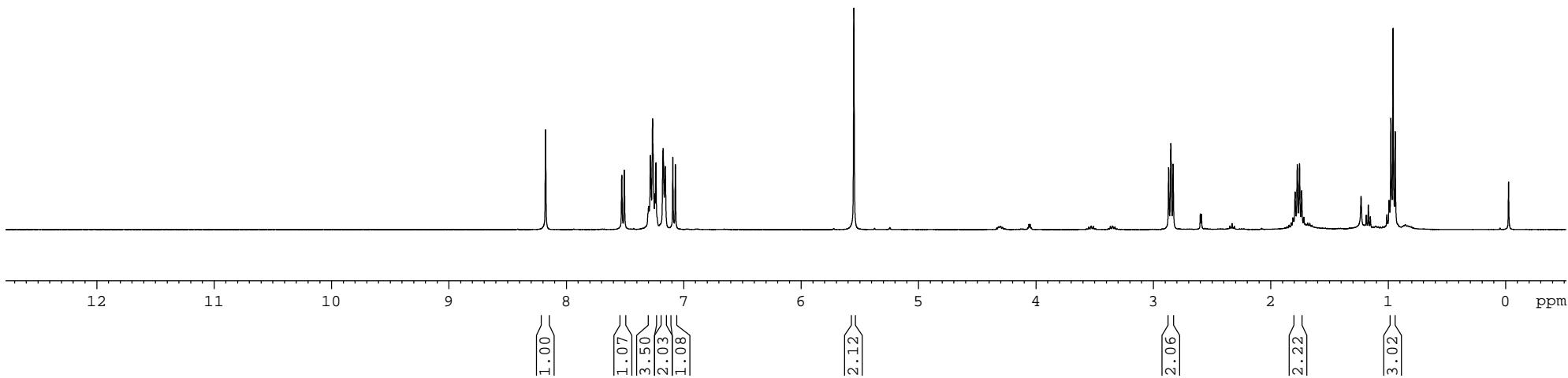


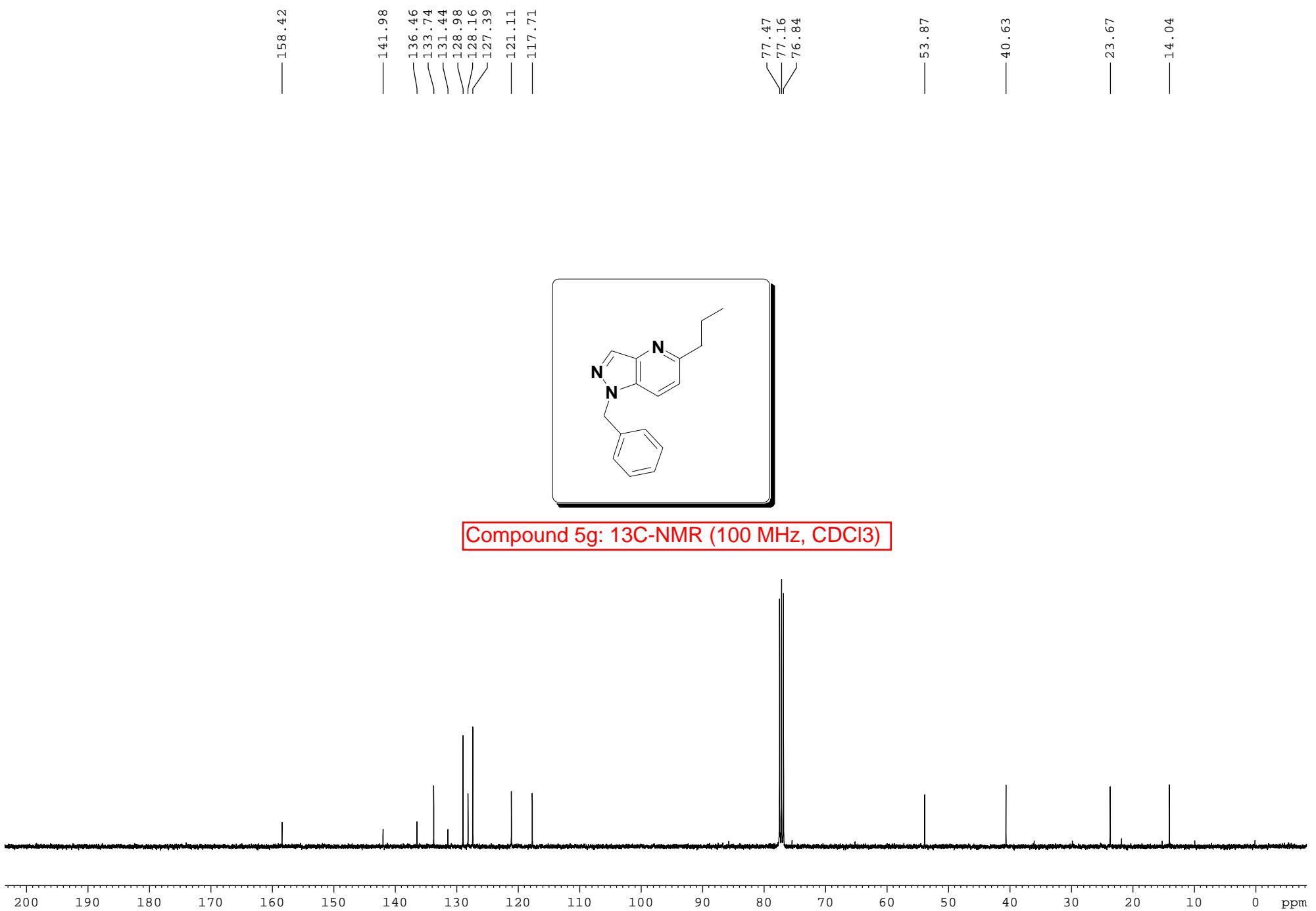
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FIDRES 0.125483 Hz  
AQ 3.9845889 sec  
RG 144.49  
DW 60.800 usec



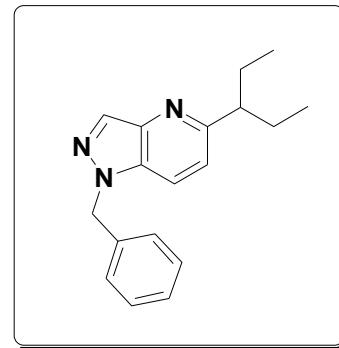
Compound 5g: 1H-NMR (400 MHz, CDCl3)



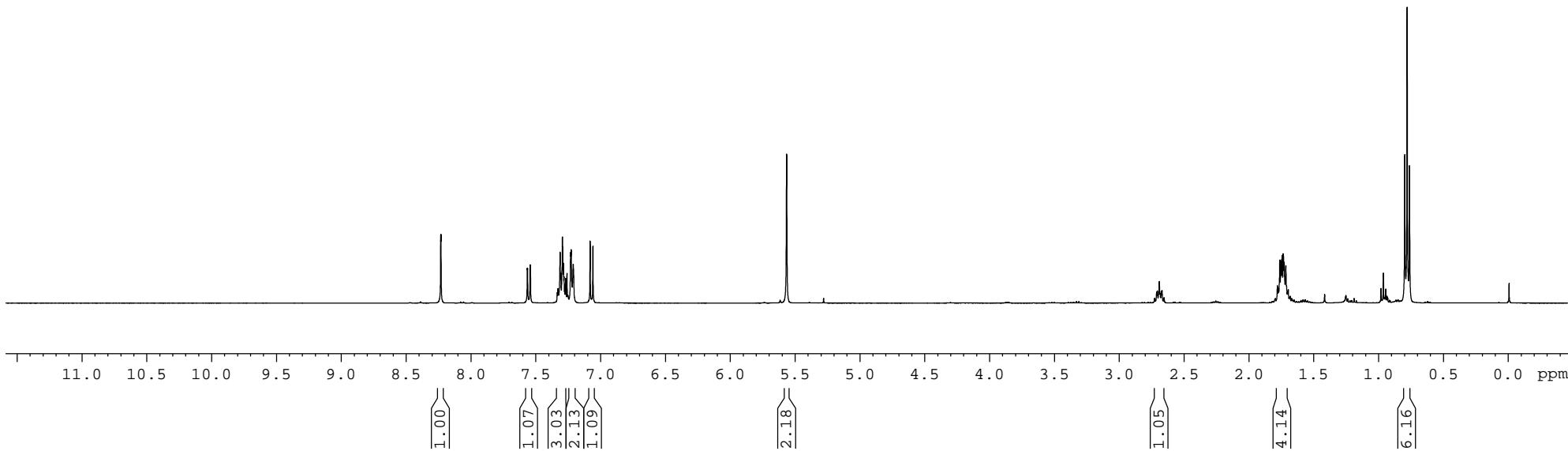


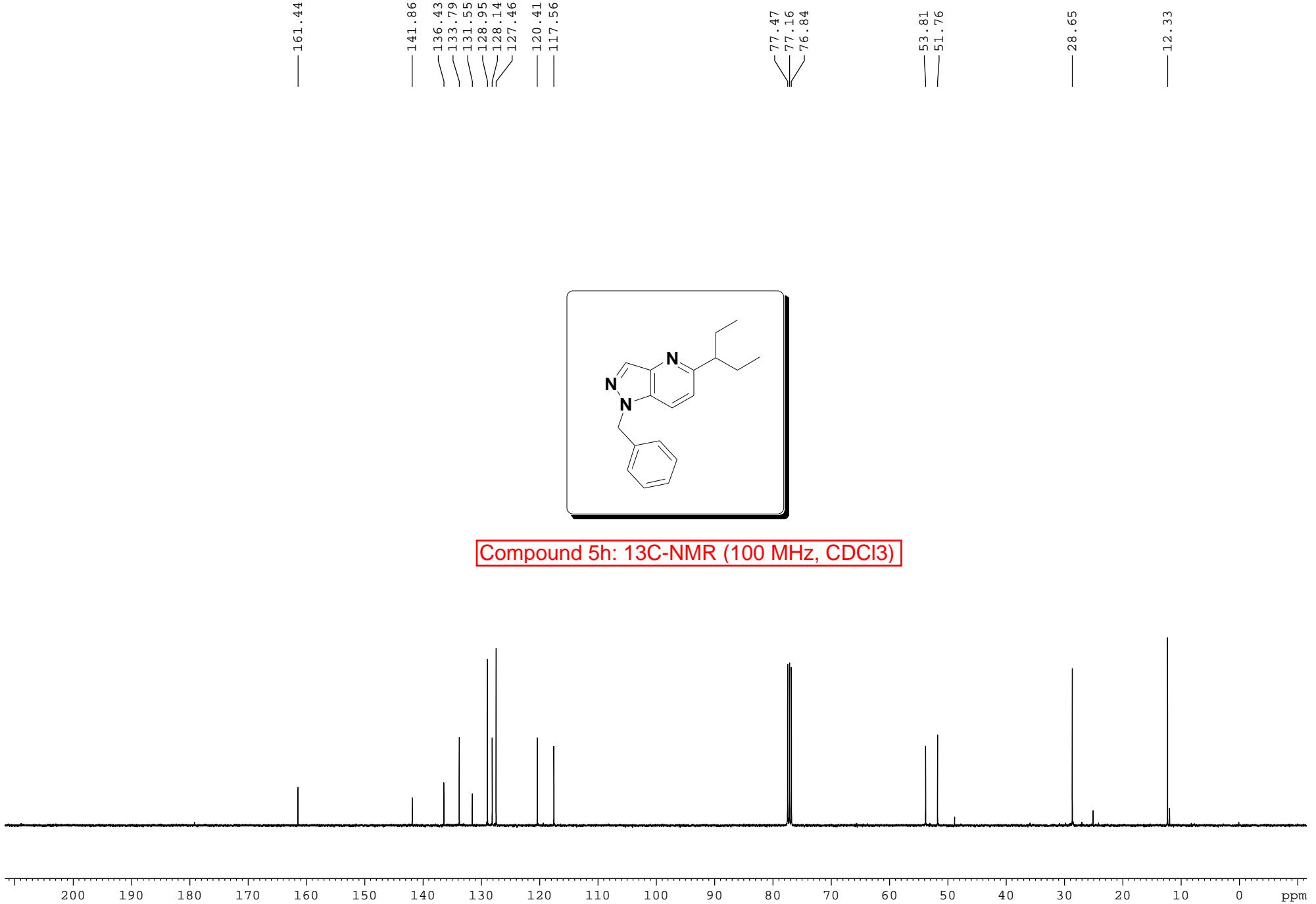
Current Data Parameters  
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EXPNO 10  
PROCNO 1

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PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2  
SWH 8012.820 Hz  
FIDRES 0.122266 Hz  
AQ 4.0894465 sec  
RG 32.58  
DW 62.400 usec  
\_1



Compound 5h: 1H-NMR (400 MHz, CDCl3)

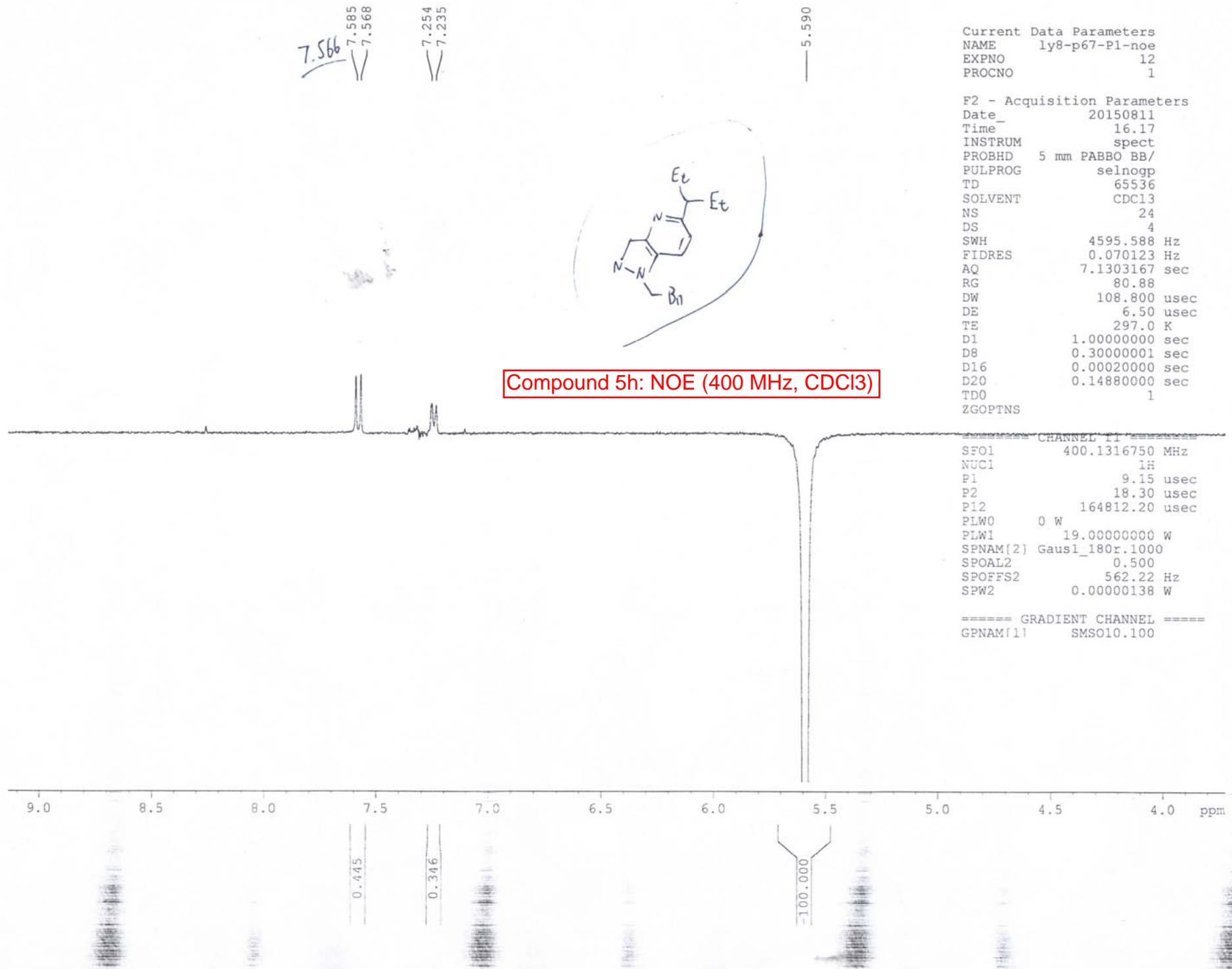




Current Data Parameters  
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EXPNO 12  
PROCNO 1

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Time 16.17  
INSTRUM spect  
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PULPROG selnogp  
TD 65536  
SOLVENT CDCl3  
NS 24  
DS 4  
SWH 4595.588 Hz  
FIDRES 0.070123 Hz  
AQ 7.1303167 sec  
RG 80.88  
DW 108.800 usec  
DE 6.50 usec  
TE 297.0 K  
D1 1.0000000 sec  
D8 0.3000001 sec  
D16 0.00020000 sec  
D20 0.14880000 sec  
TDO 1  
ZGOPTNS

Compound 5h: NOE (400 MHz, CDCl3)



Current Data Parameters  
NAME ly9-p11-twice-160415-  
EXPNO 10  
PROCNO 1

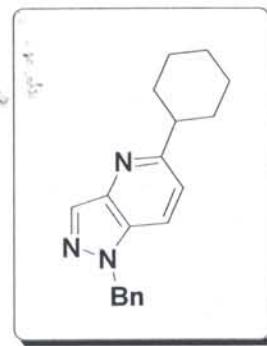
E2 - Acquisition Parameters  
Date\_ 20160415  
Time 15.42  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2

8.2141

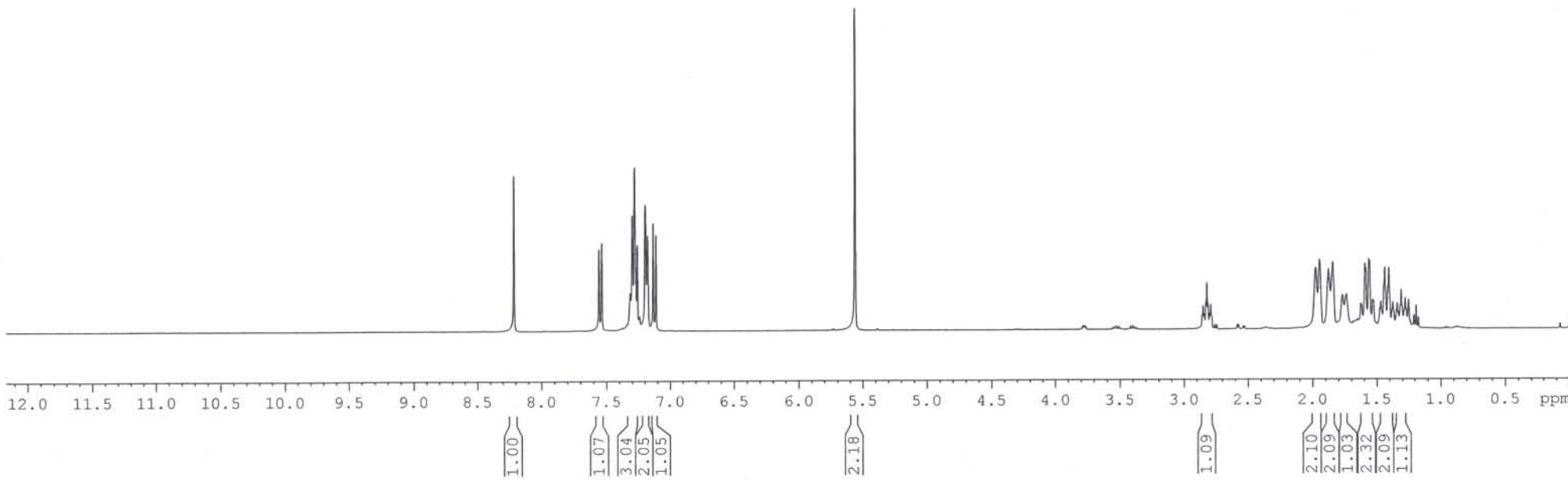
7.5579  
7.5360  
7.2996  
7.2812  
7.2590  
7.1975  
7.1791  
7.1346  
7.1127

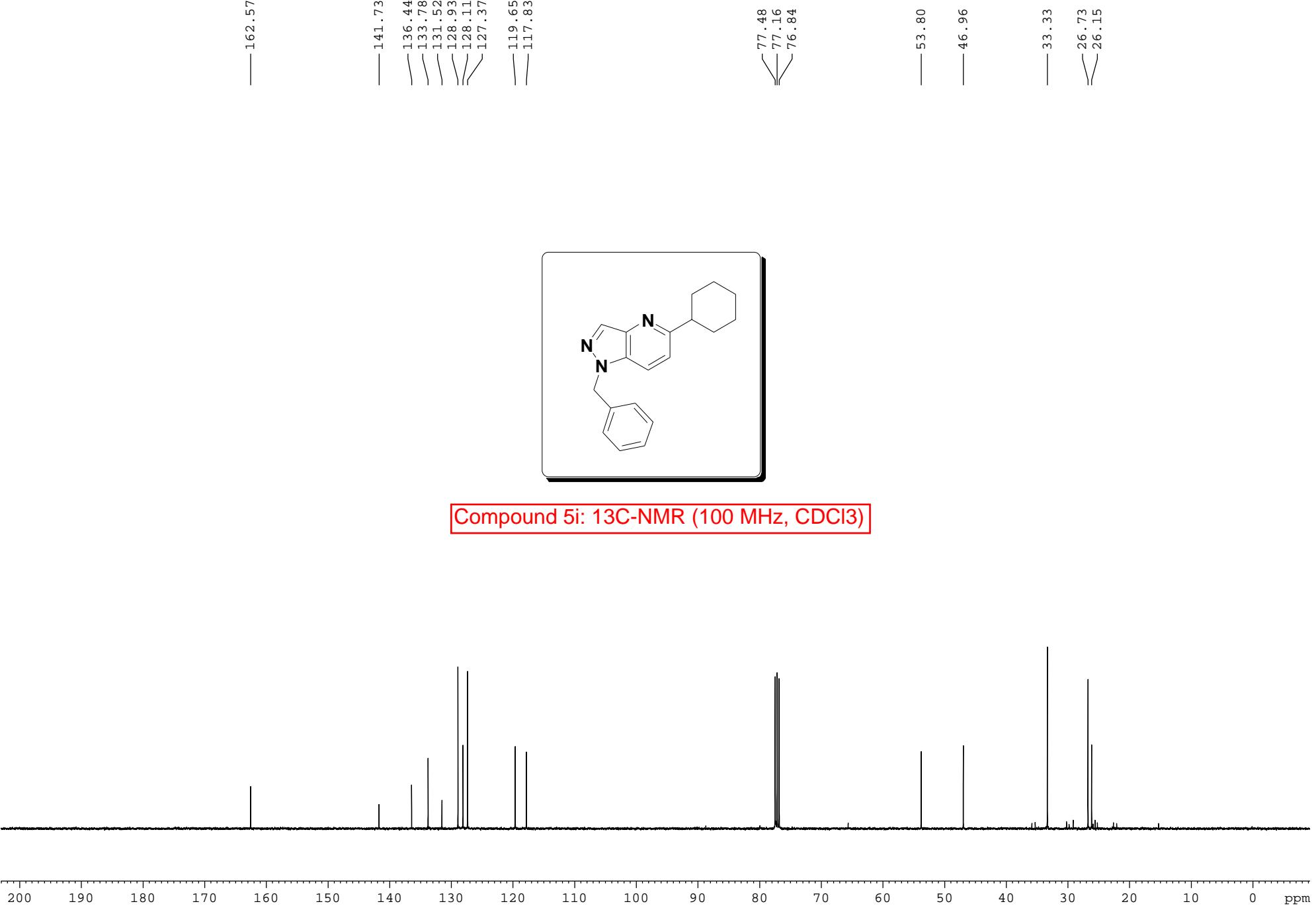
5.5611

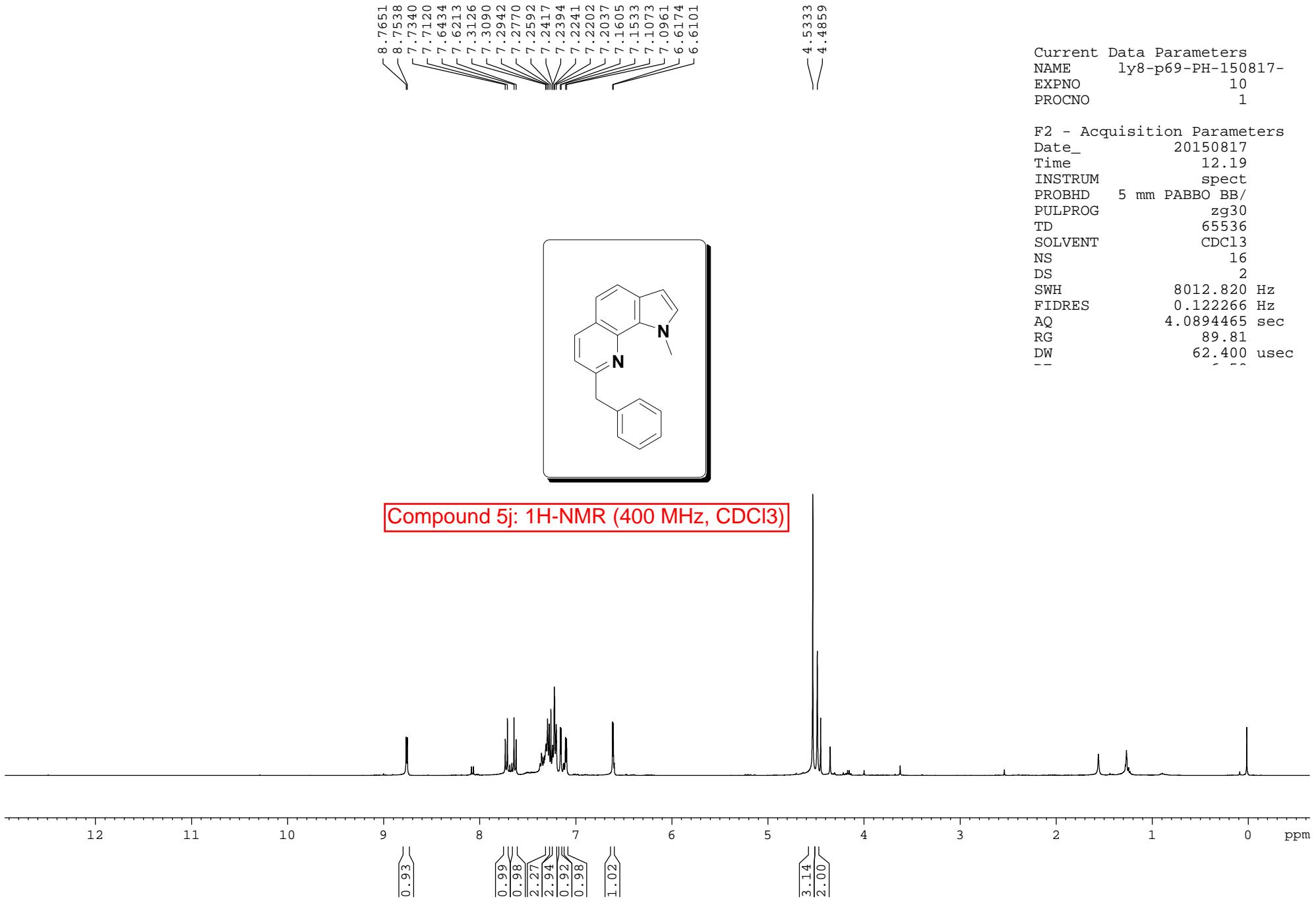
2.8590  
2.8510  
2.8427  
2.8294  
2.8212  
2.8129  
2.8002  
2.7912  
2.7833  
1.9765  
1.9469  
1.8775  
1.8456  
1.7693  
1.5951  
1.5879  
1.5637  
1.5574  
1.6193  
1.4124  
1.4052  
1.3736  
1.3459  
1.3393

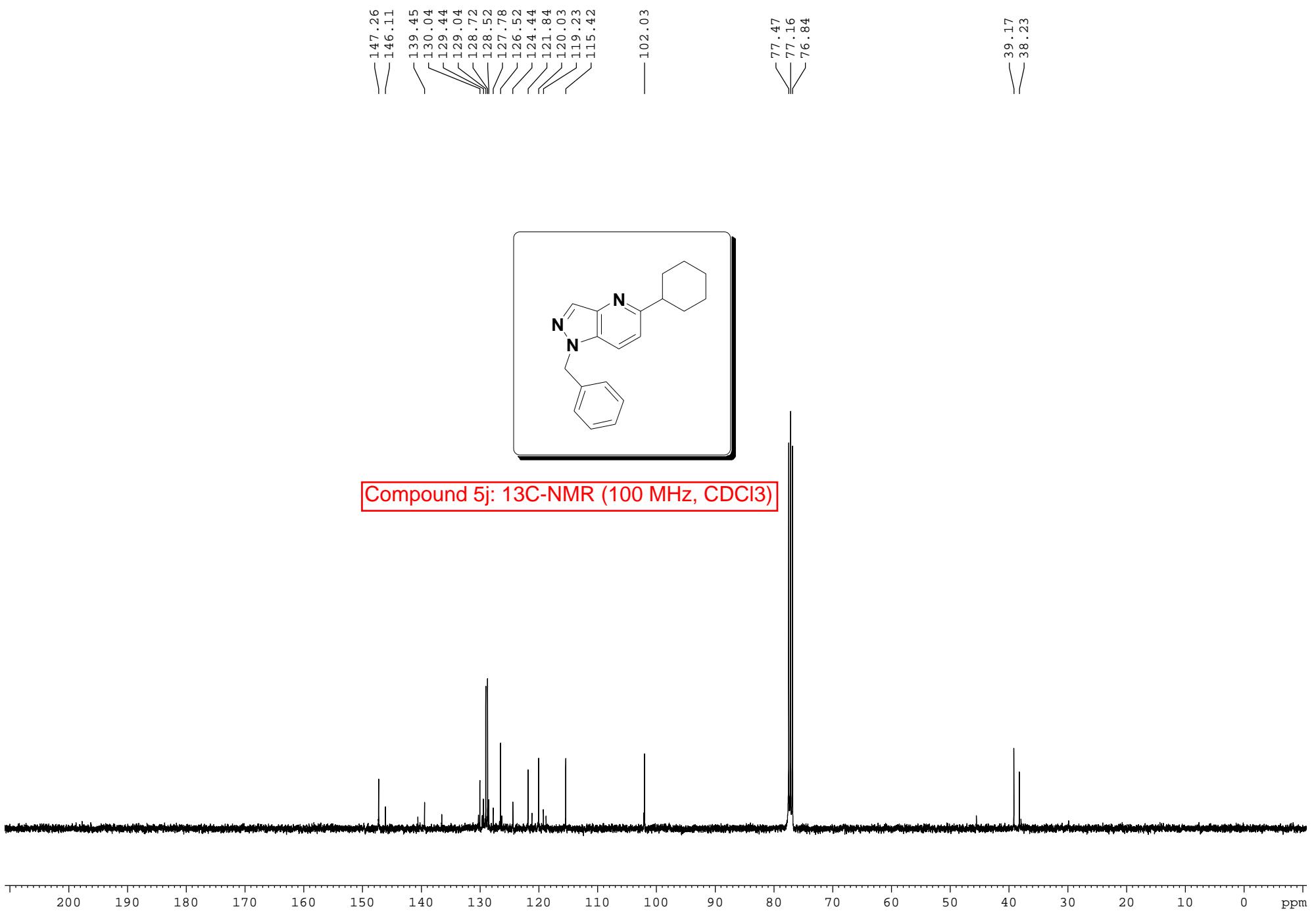


Compound 5i: 1H-NMR (400 MHz, CDCl3)



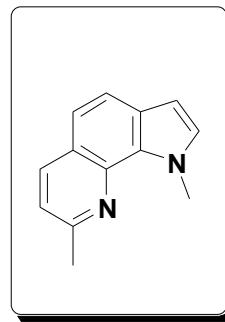




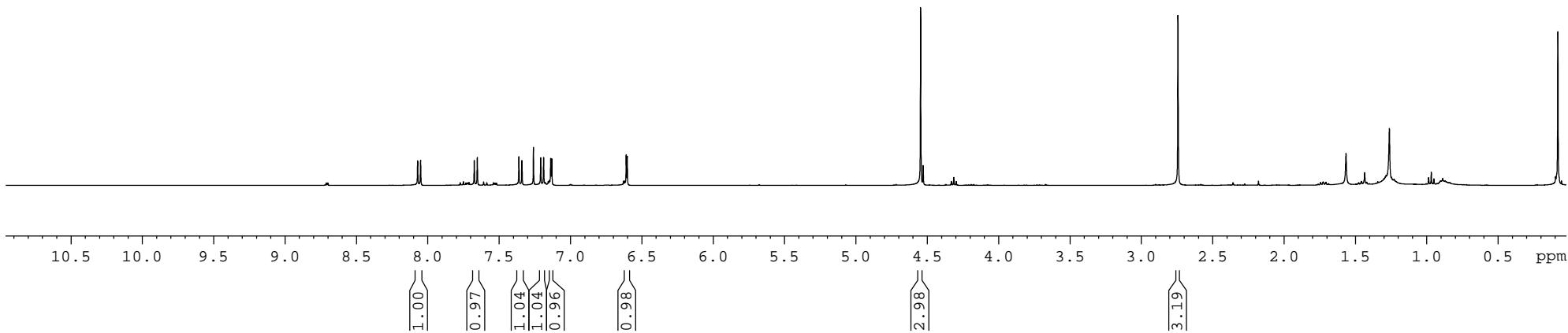


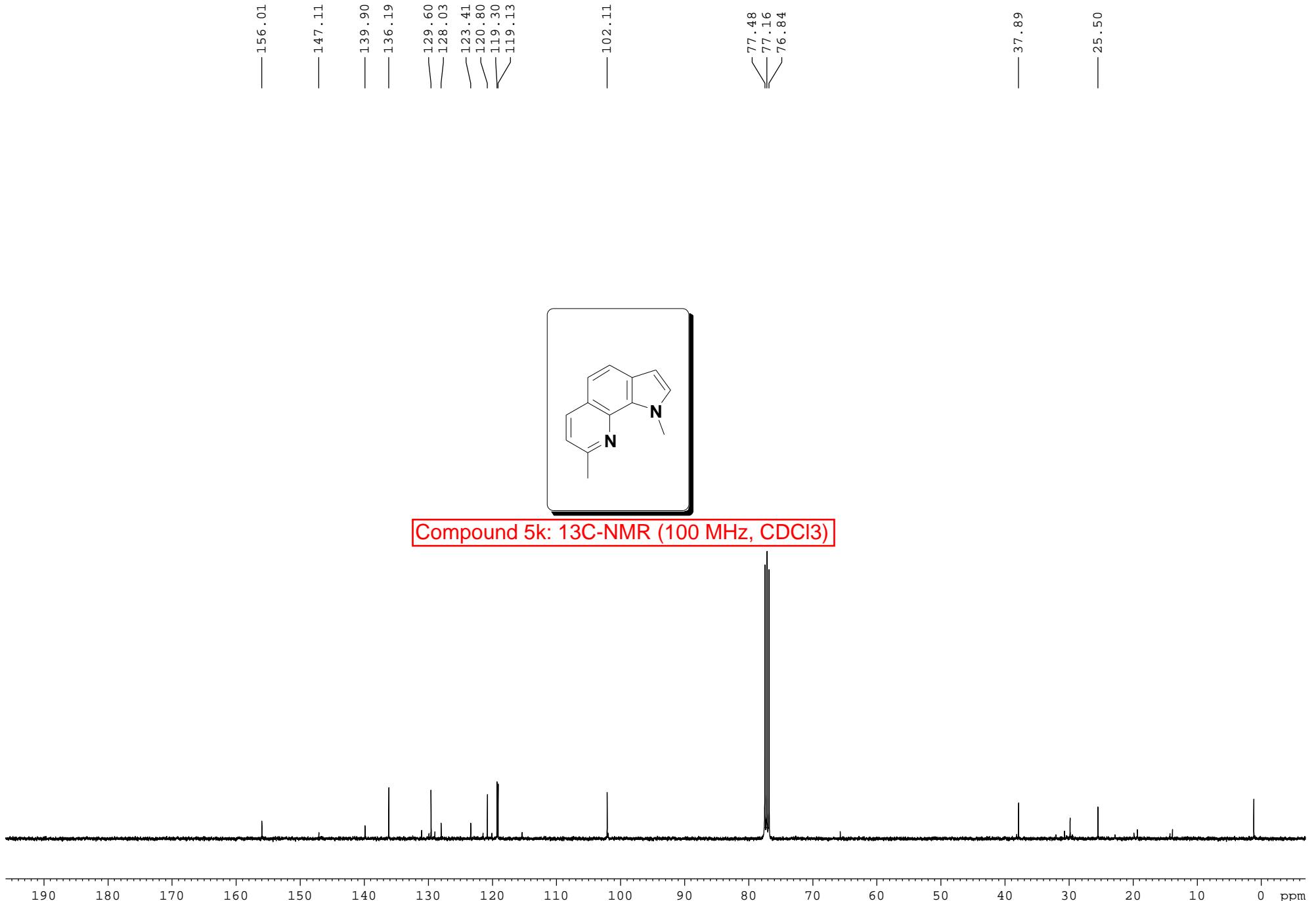
Current Data Parameters  
NAME ly8-p62-150804-  
EXPNO 10  
PROCNO 1

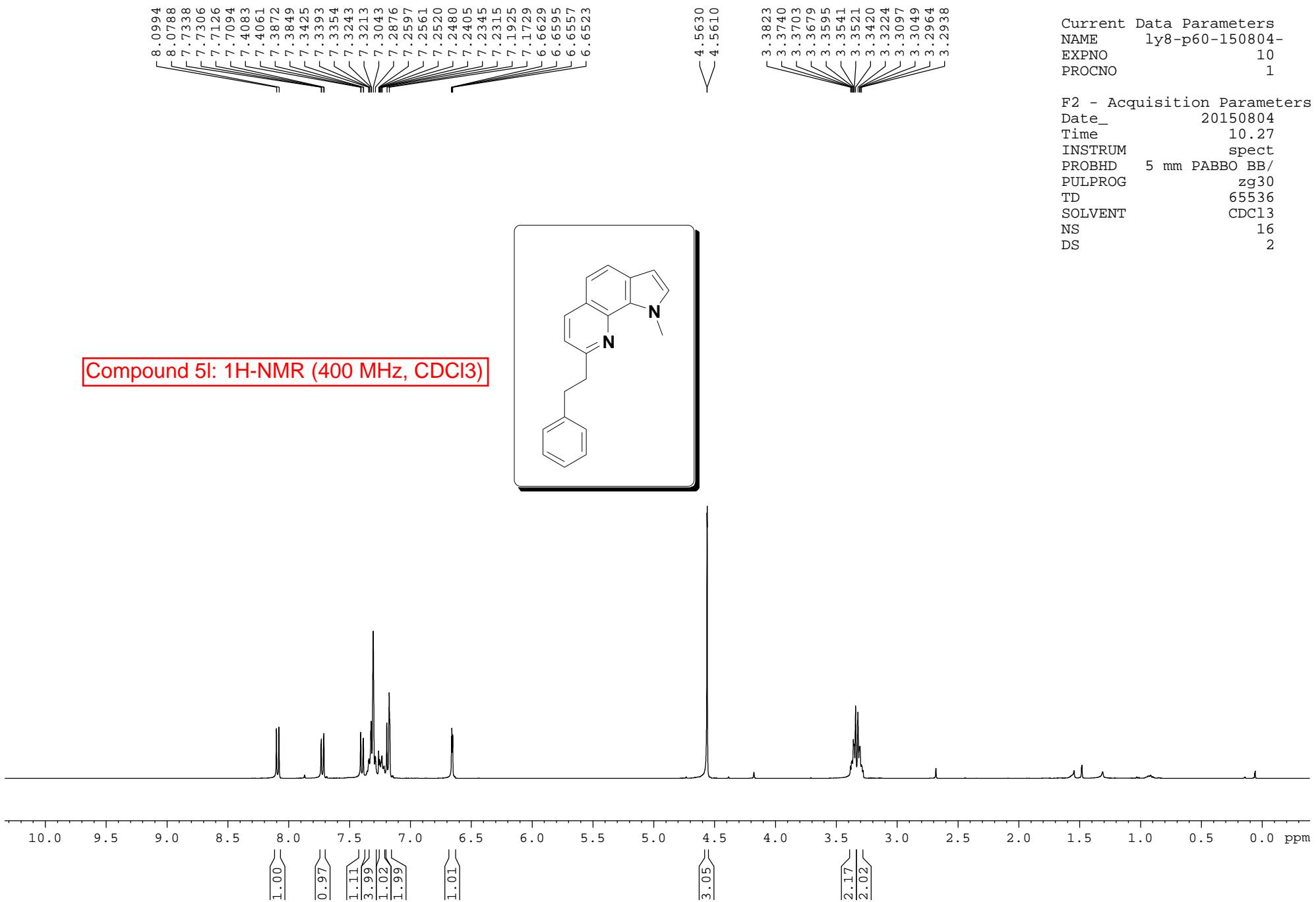
F2 - Acquisition Parameters  
Date\_ 20150804  
Time 22.24  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2

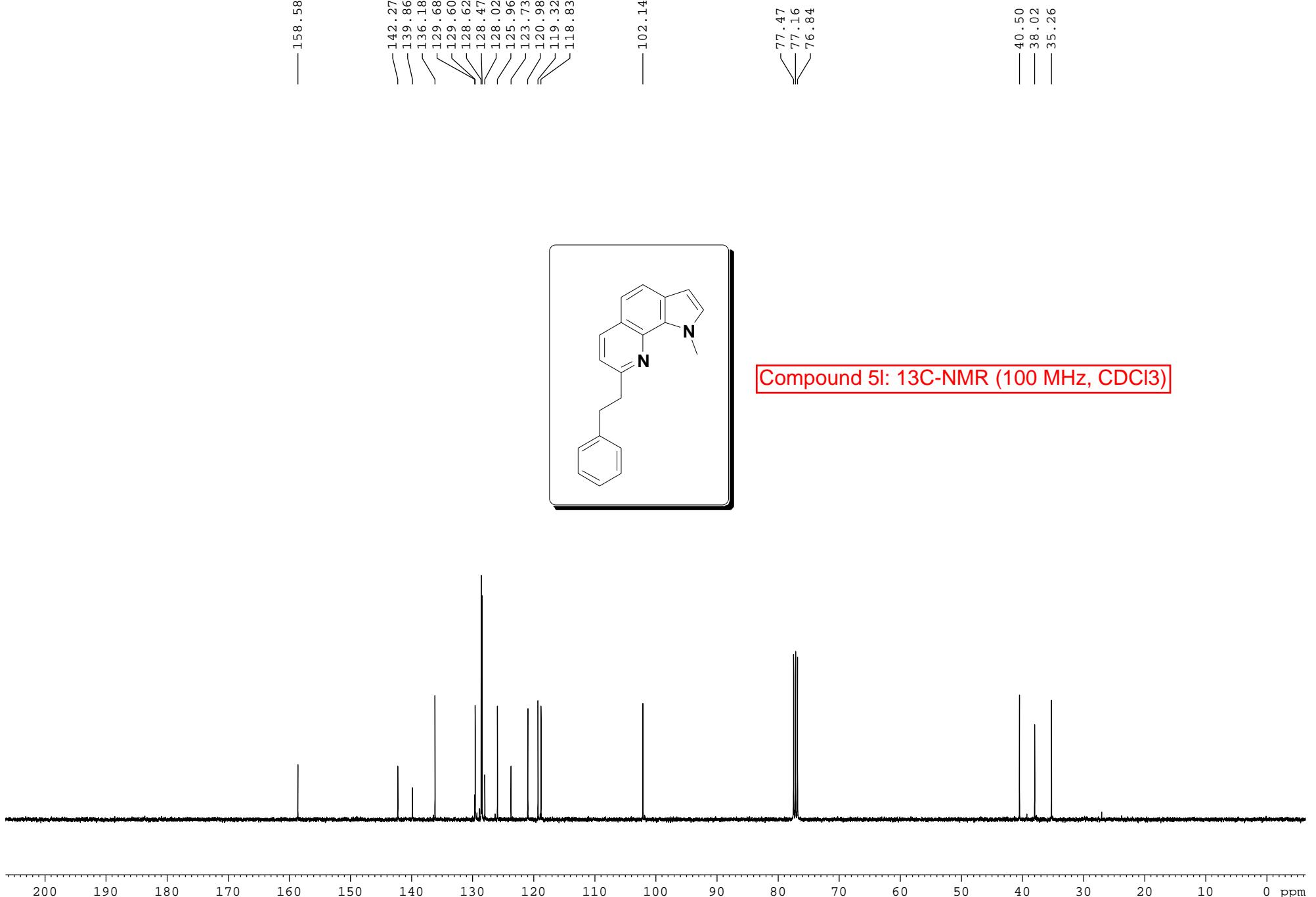


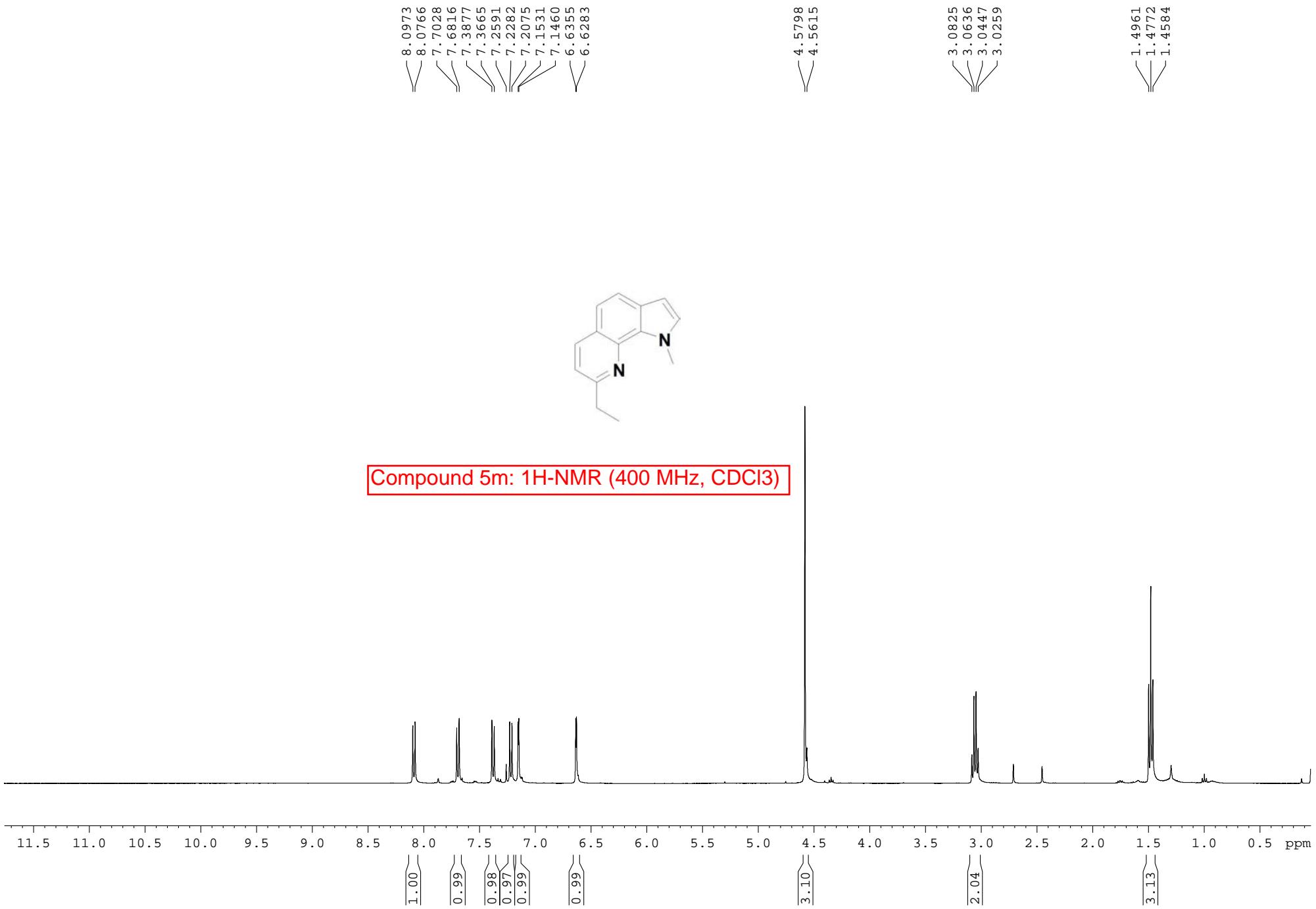
Compound 5k: 1H-NMR (400 MHz, CDCl3)





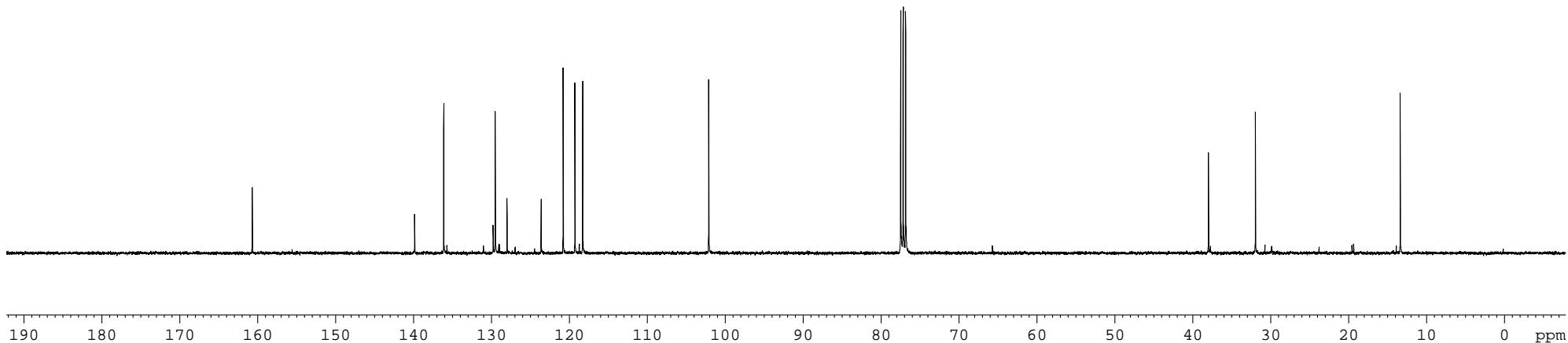


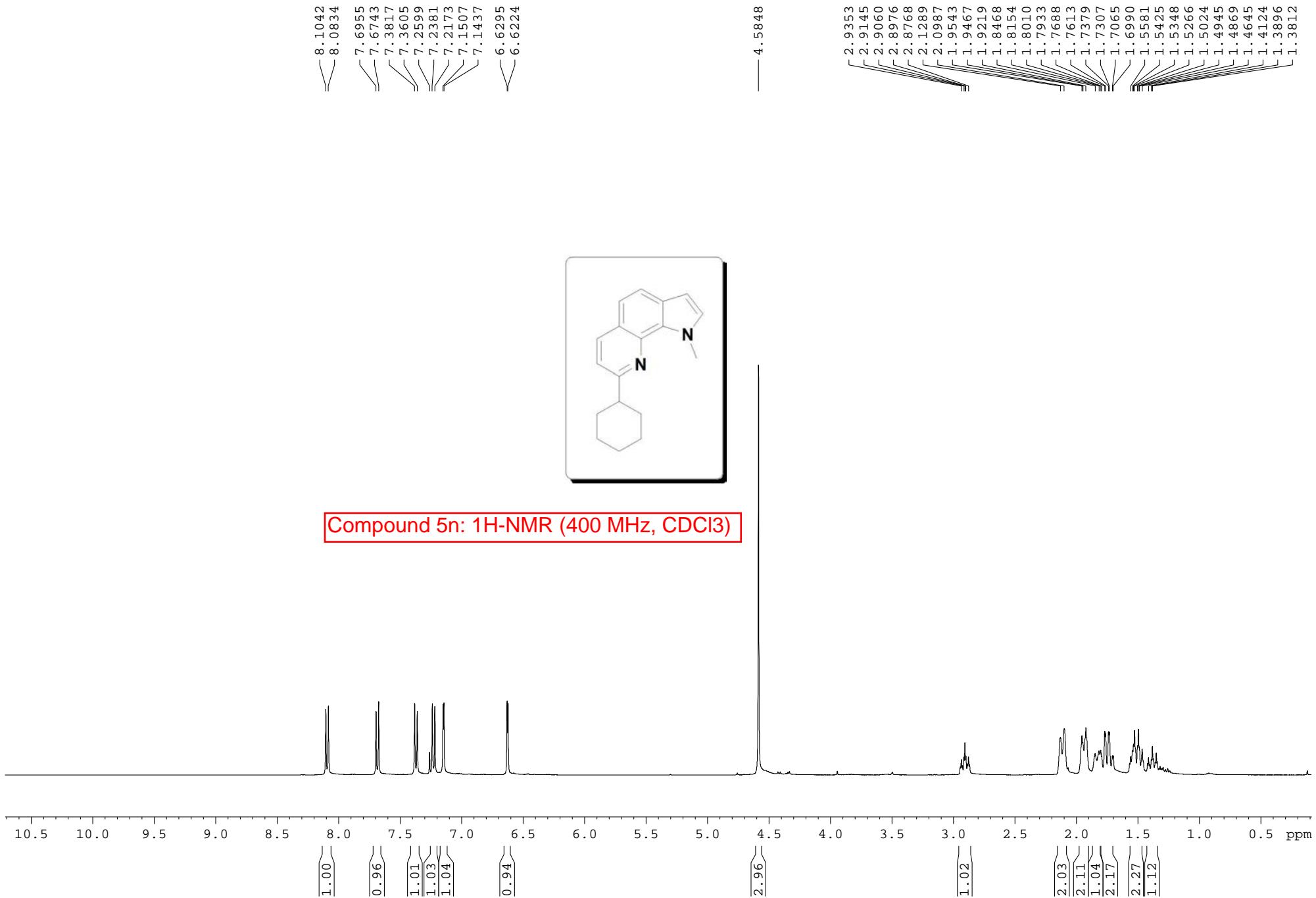


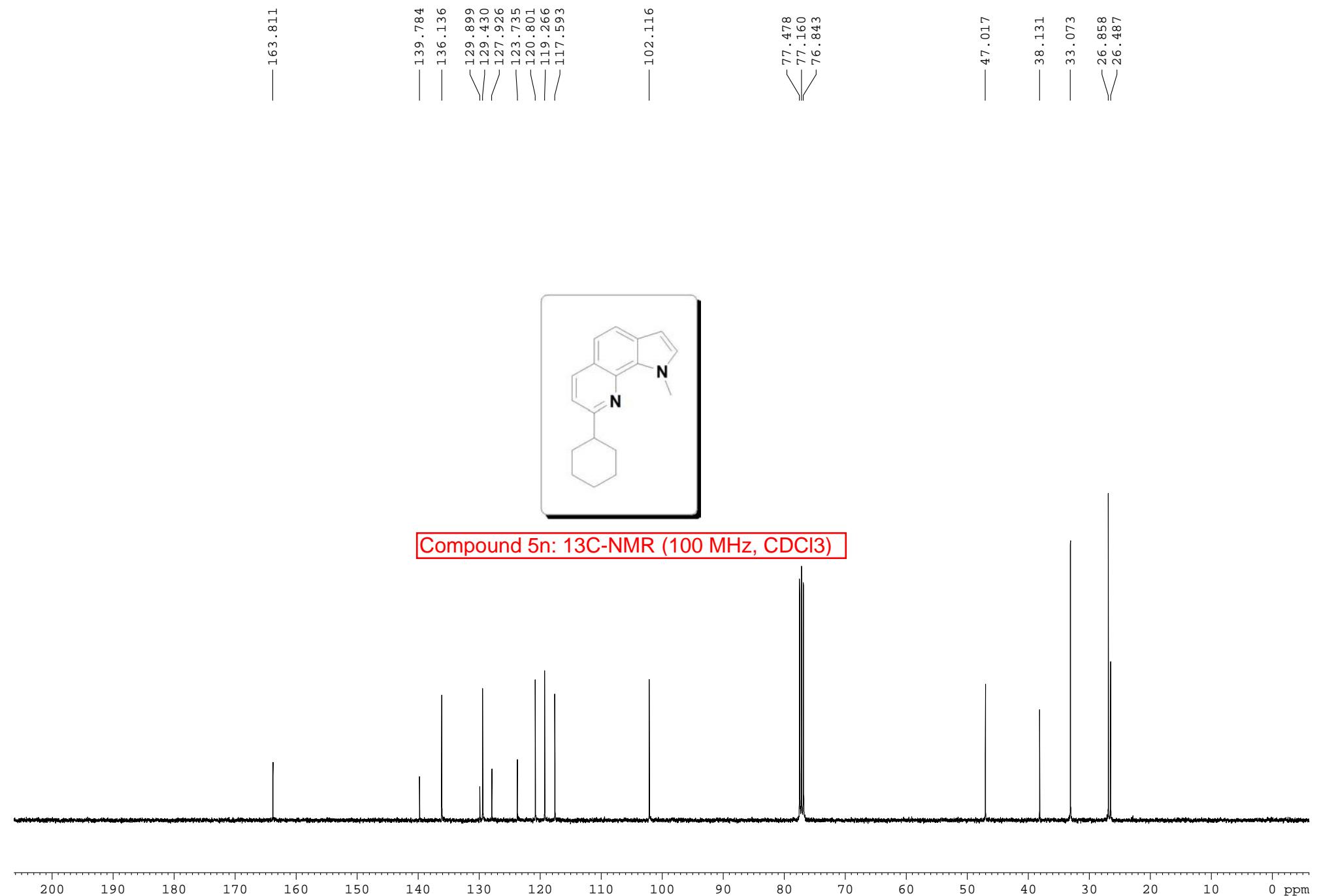


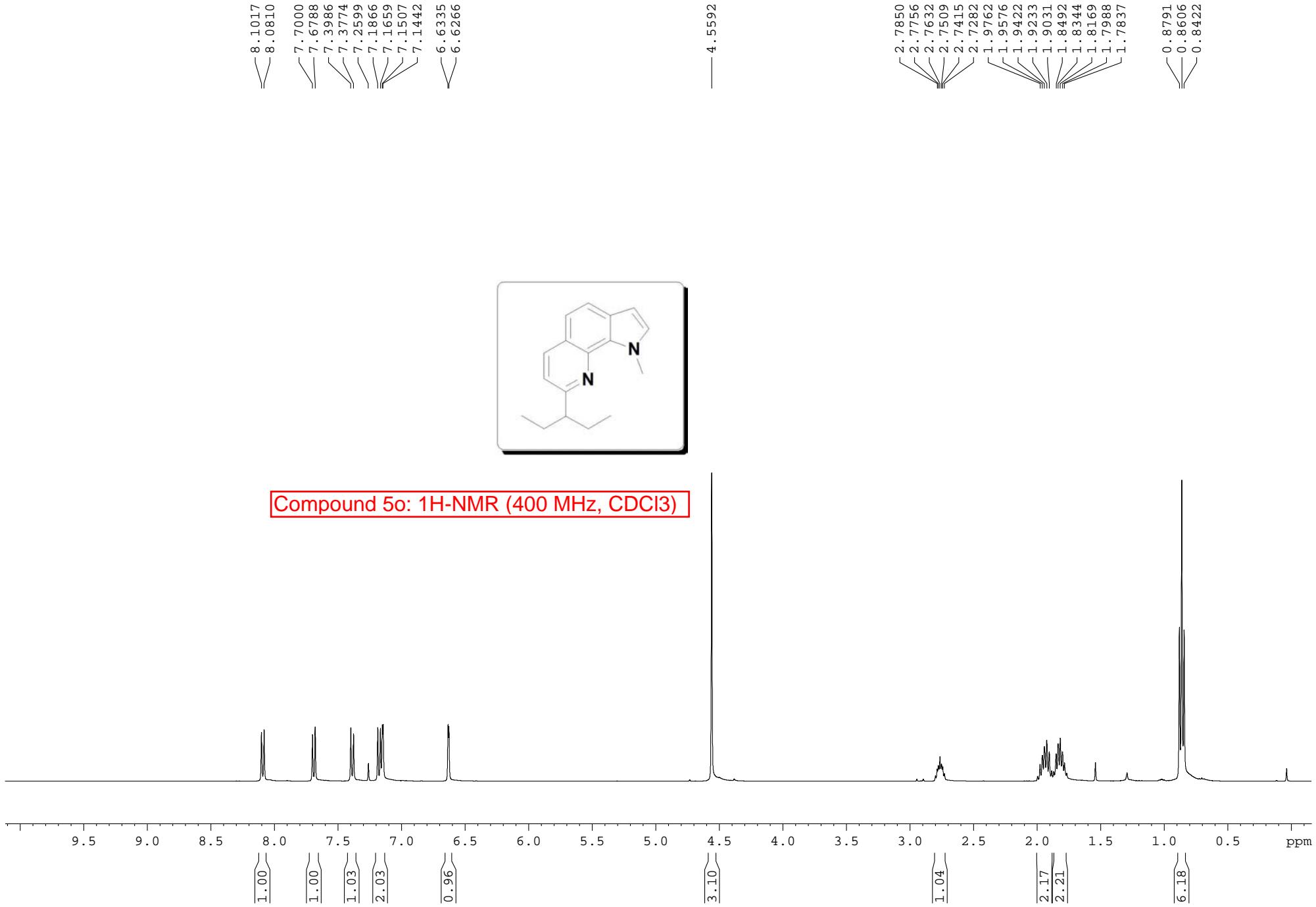


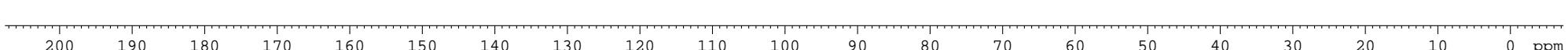
Compound 5m:  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ )



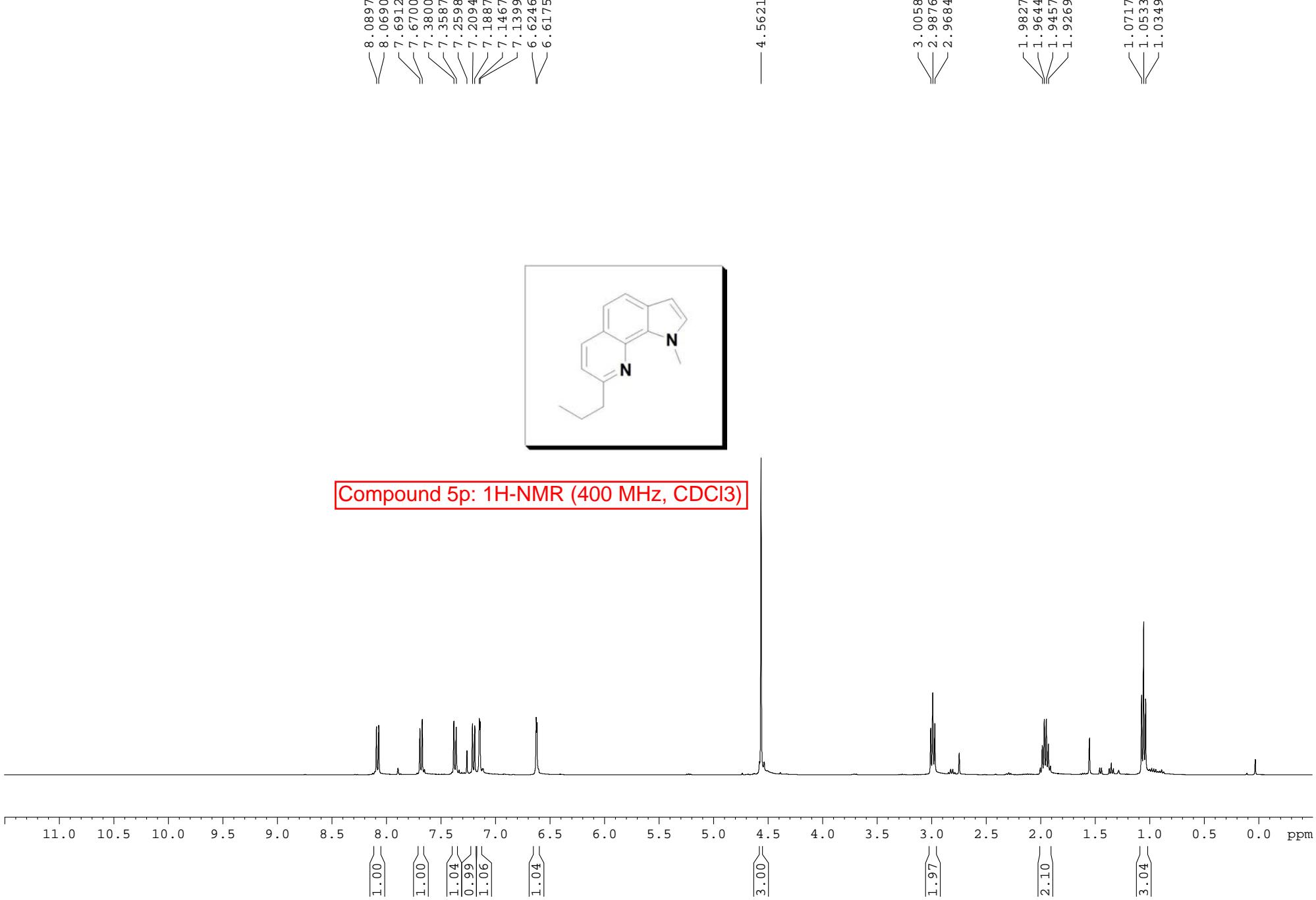


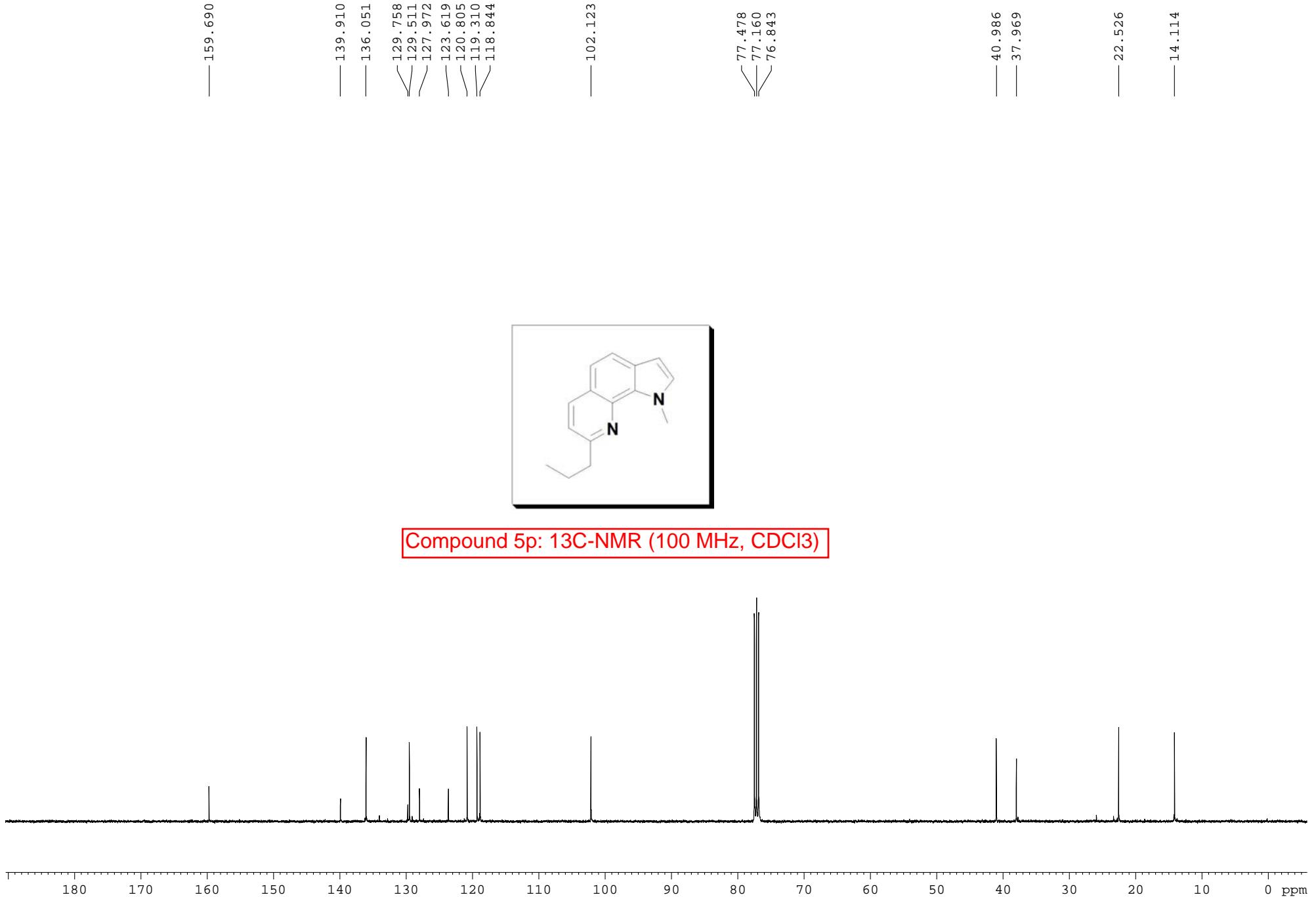






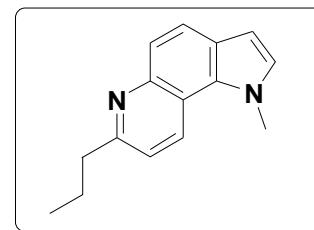
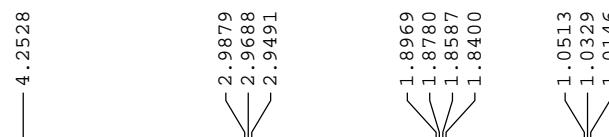
Compound 5o: <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)



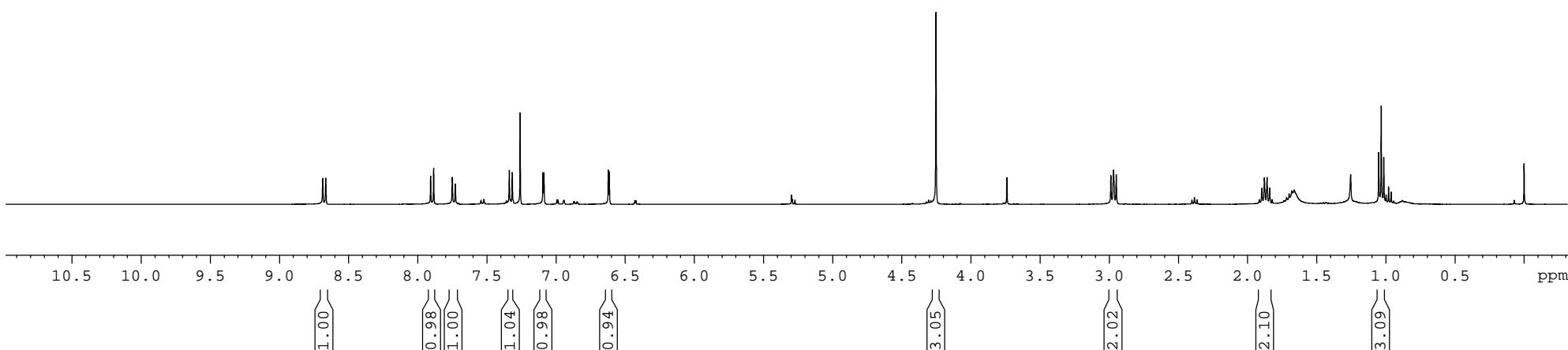


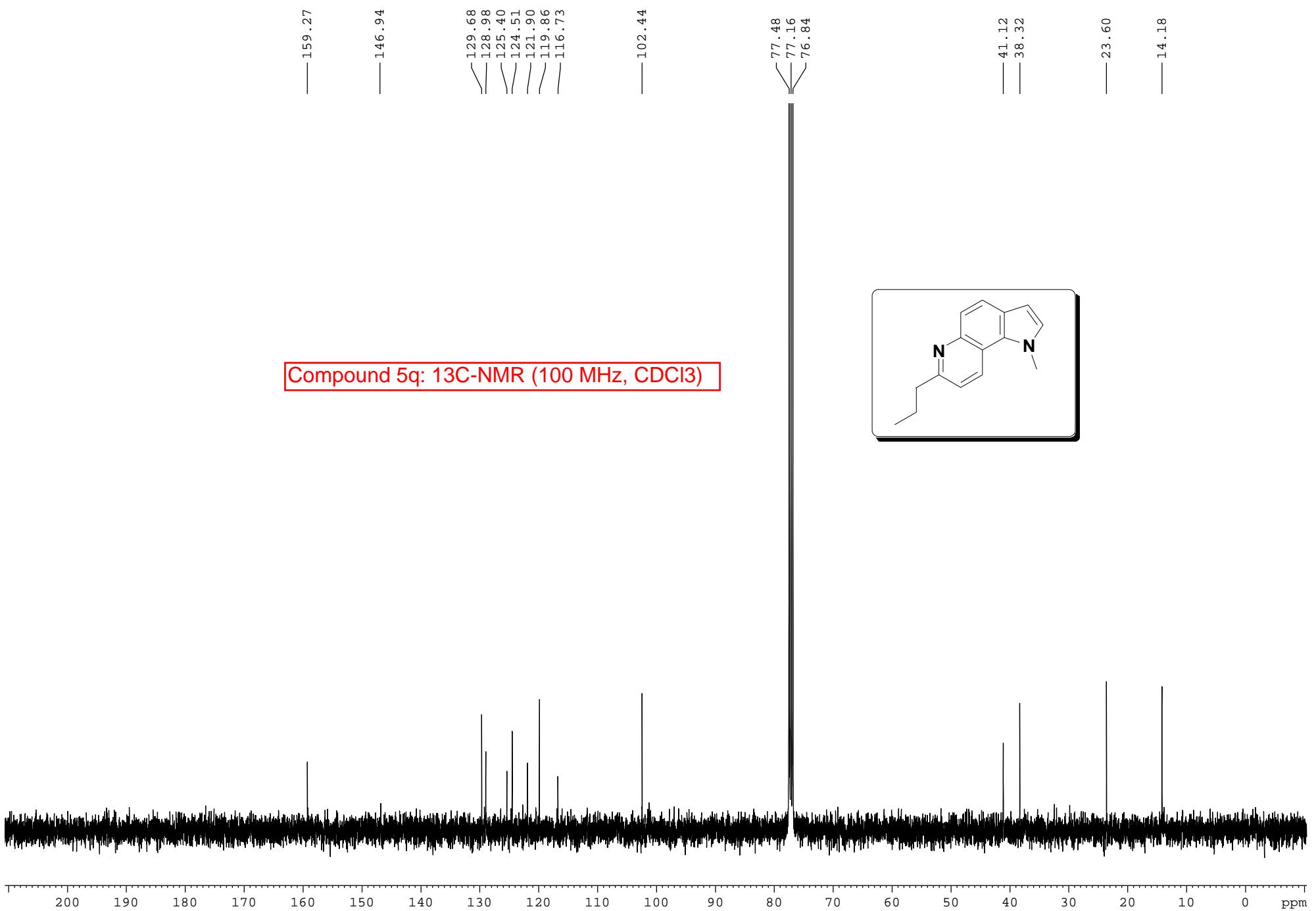
Current Data Parameters  
NAME ly8-p64-3P-150808-  
EXPNO 10  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20150808  
Time 17.34  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2  
SWH 8012.820 Hz  
FIDRES 0.122266 Hz  
AQ 4.0894465 sec  
RG 128.61  
DW 62.400 usec  
--



Compound 5q: 1H-NMR (400 MHz, CDCl3)

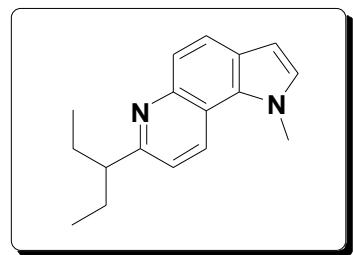




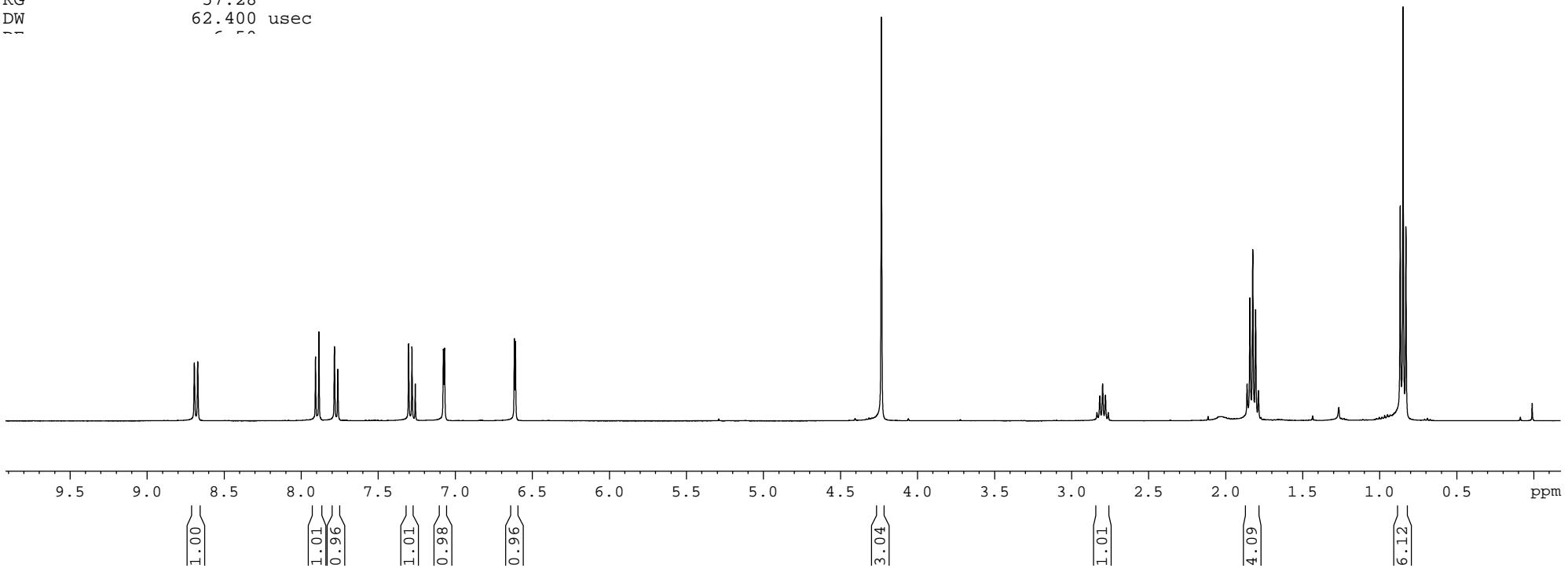


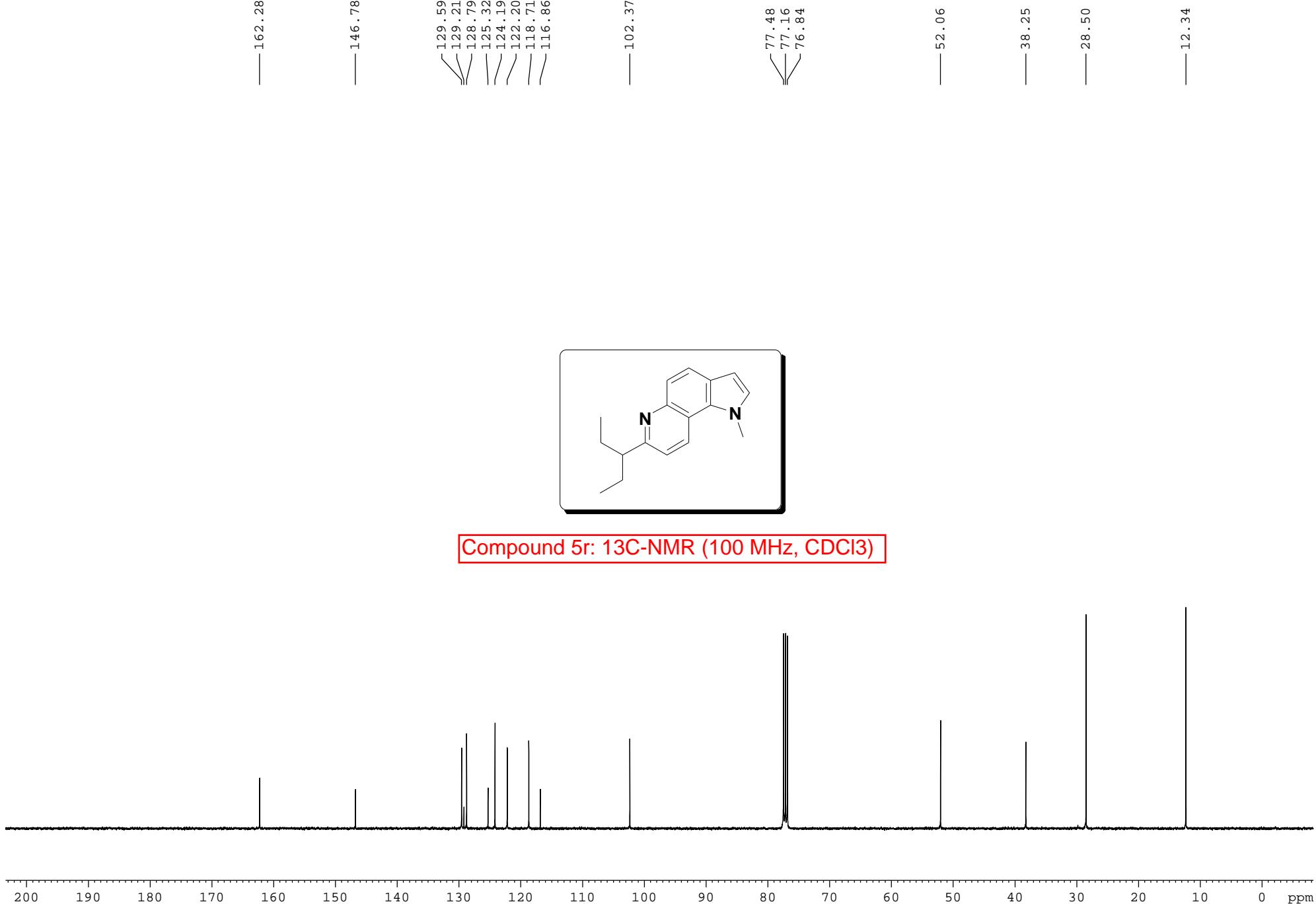
Current Data Parameters  
 NAME ly8-150805-  
 EXPNO 10  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20150805  
 Time 22.07  
 INSTRUM spect  
 PROBHD 5 mm PABBO BB/  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 8012.820 Hz  
 FIDRES 0.122266 Hz  
 AQ 4.0894465 sec  
 RG 57.28  
 DW 62.400 usec



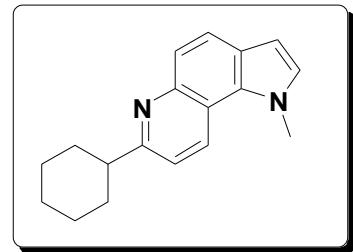
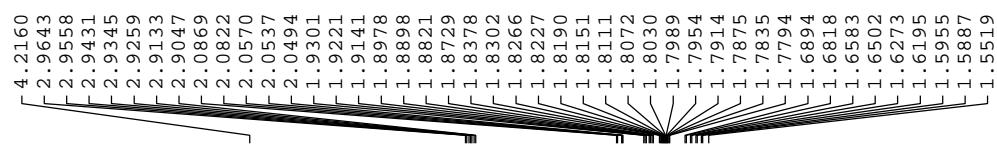
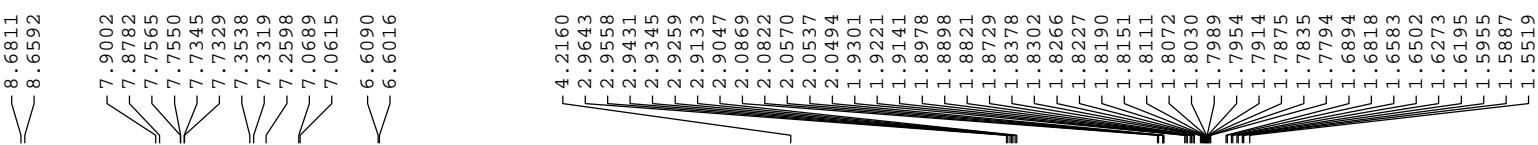
Compound 5r: 1H-NMR (400 MHz, CDCl3)



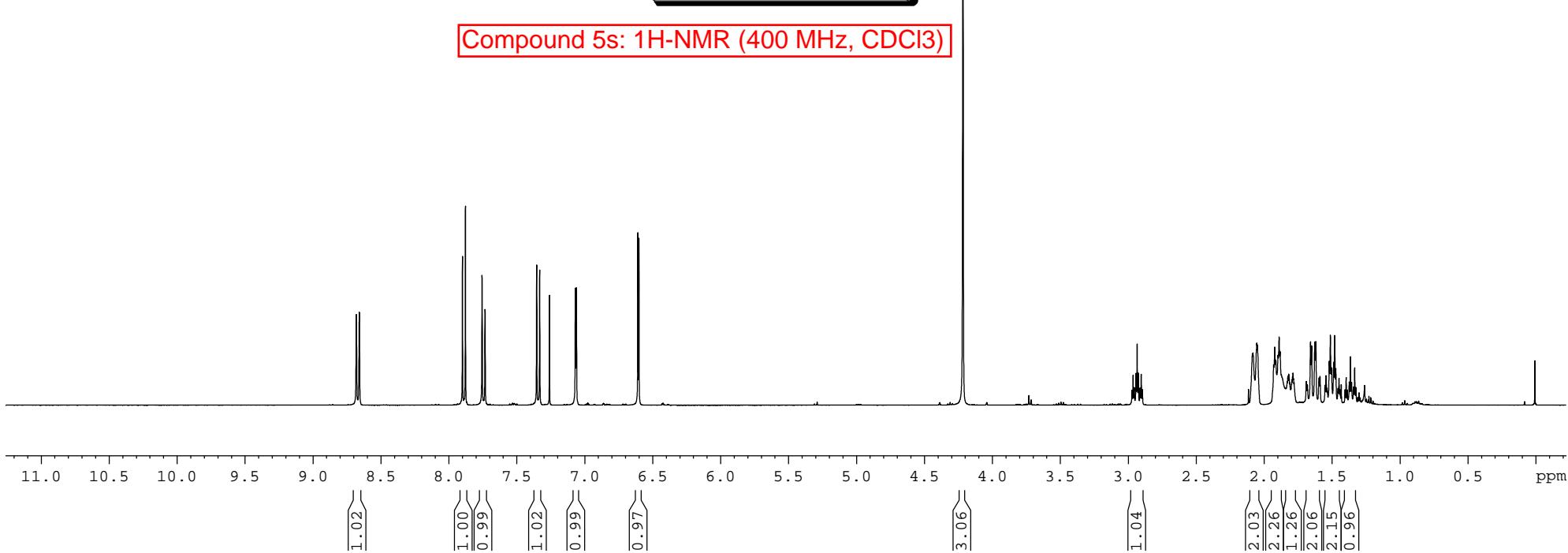


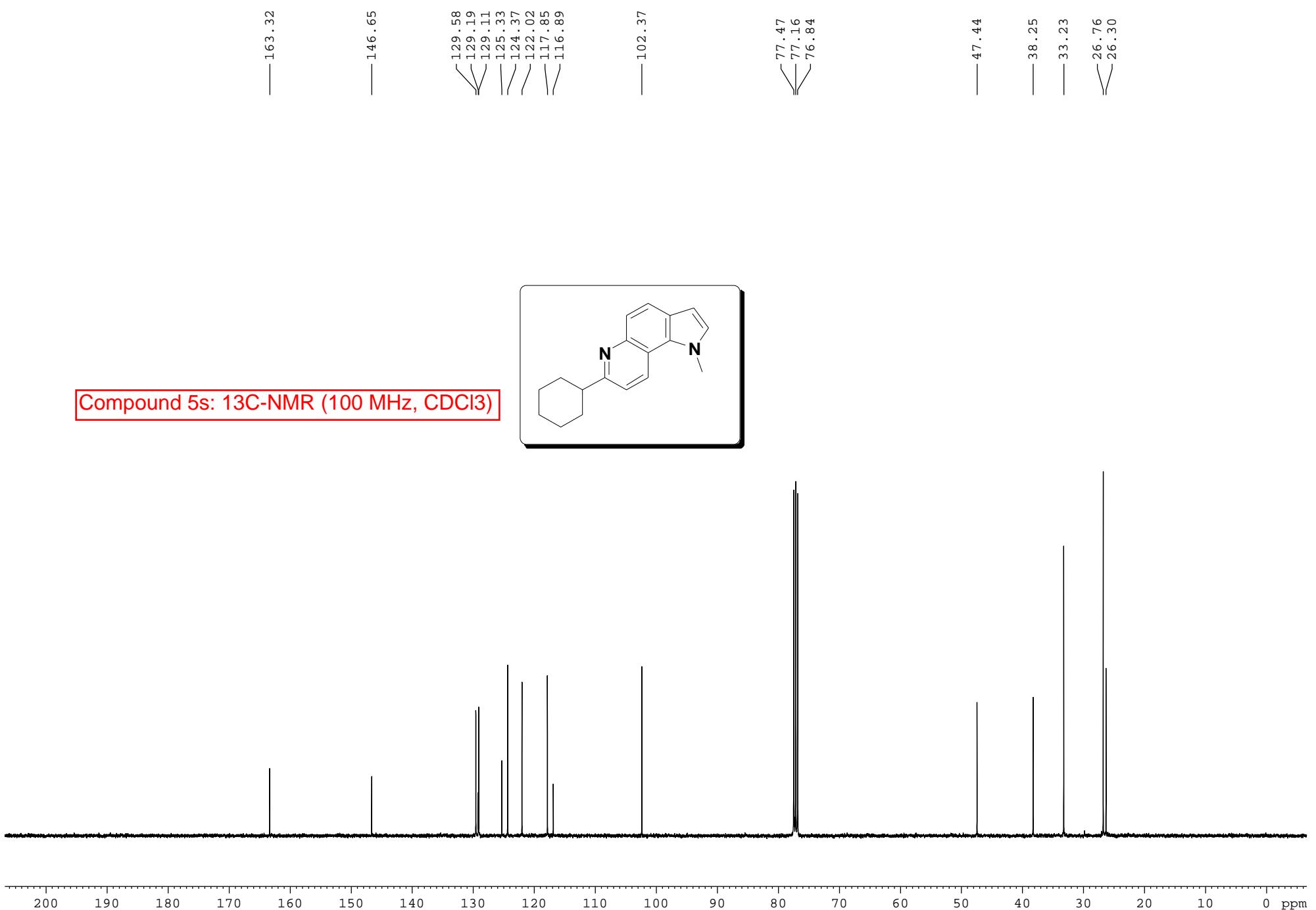
Current Data Parameters  
NAME 1y8-p64-hex-150805-  
EXPNO 10  
PROCNO 1

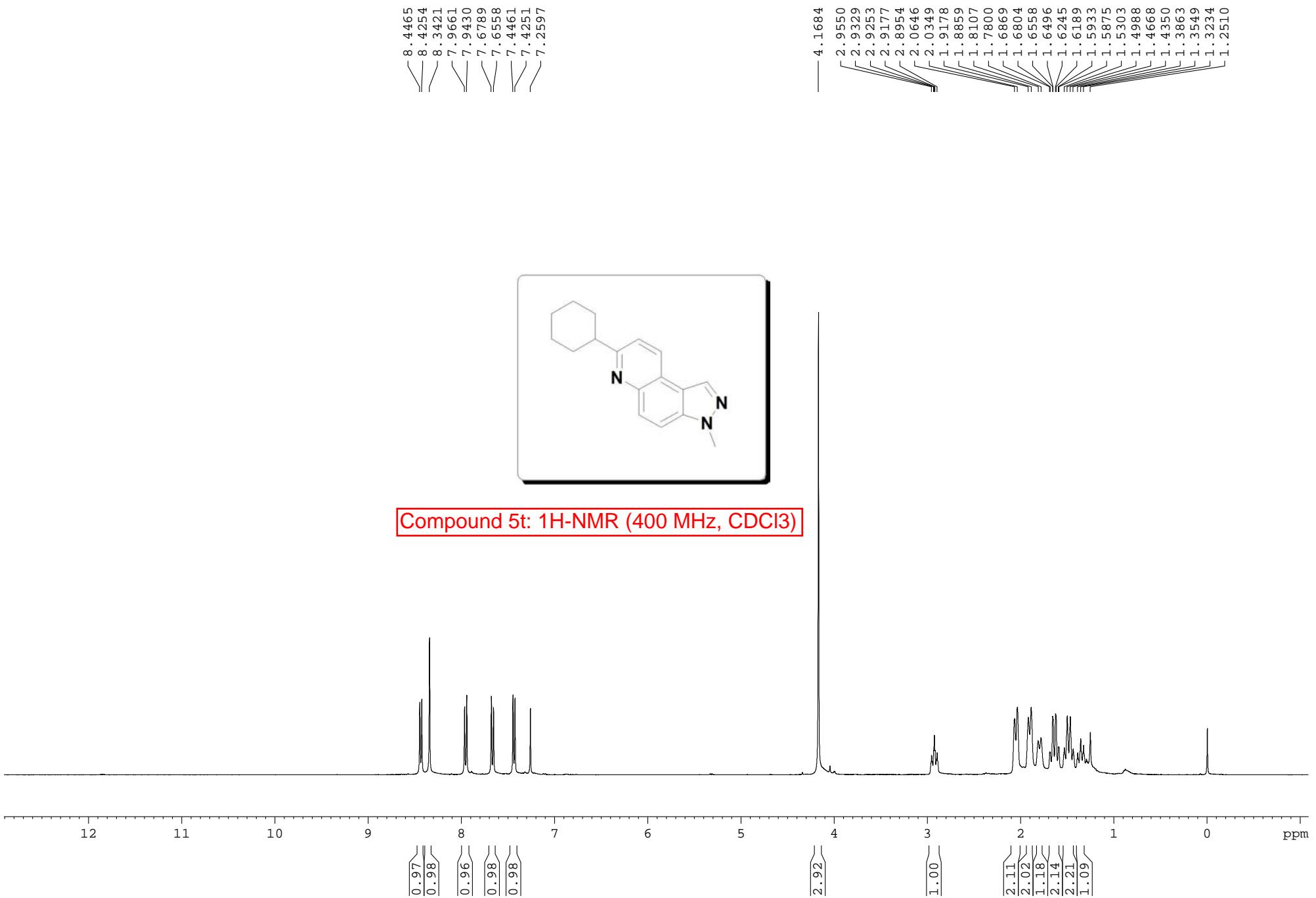
F2 - Acquisition Parameters  
Date\_ 20150806  
Time 0.06  
INSTRUM spect  
PROBHD 5 mm PABBO BB/  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2

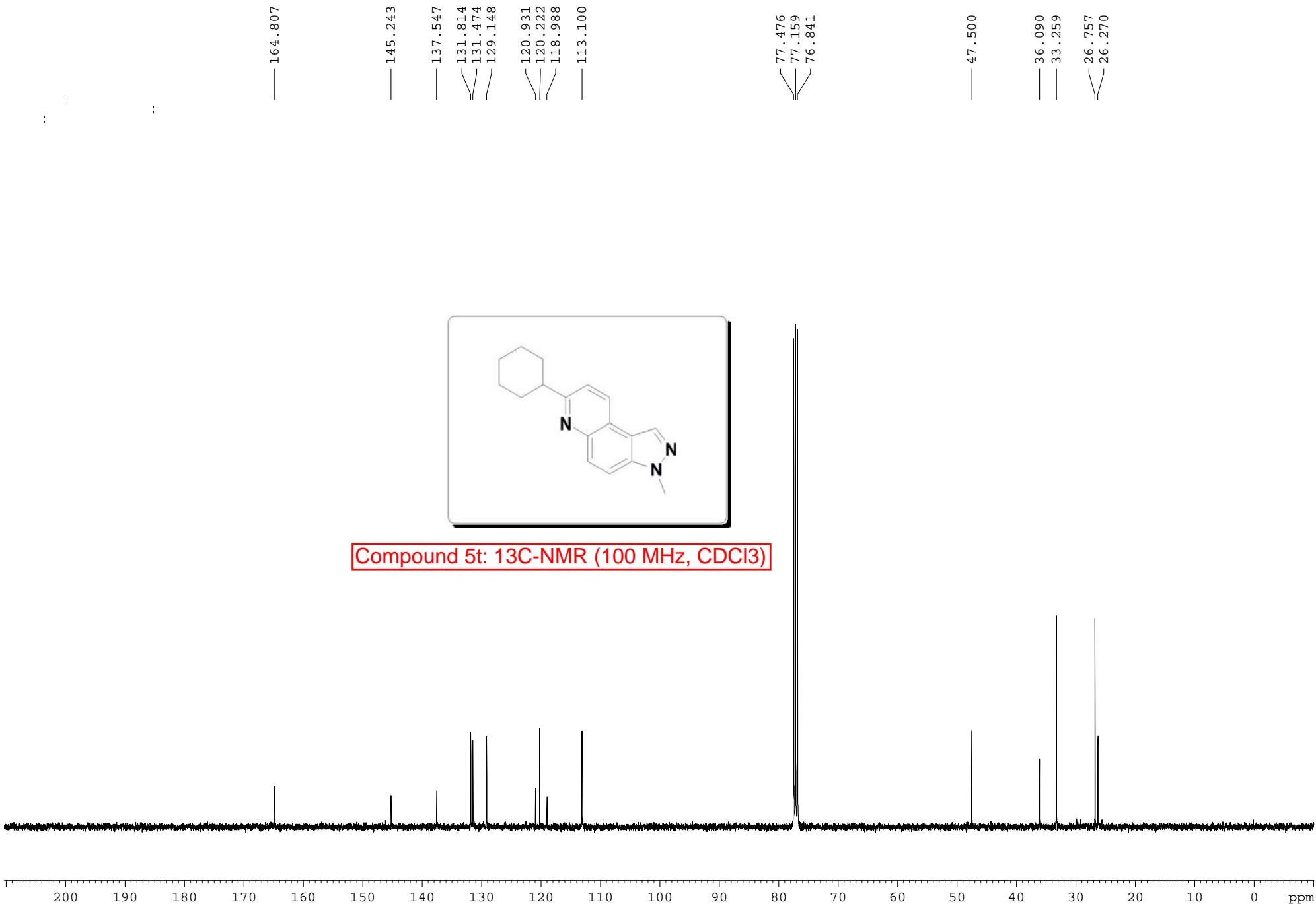


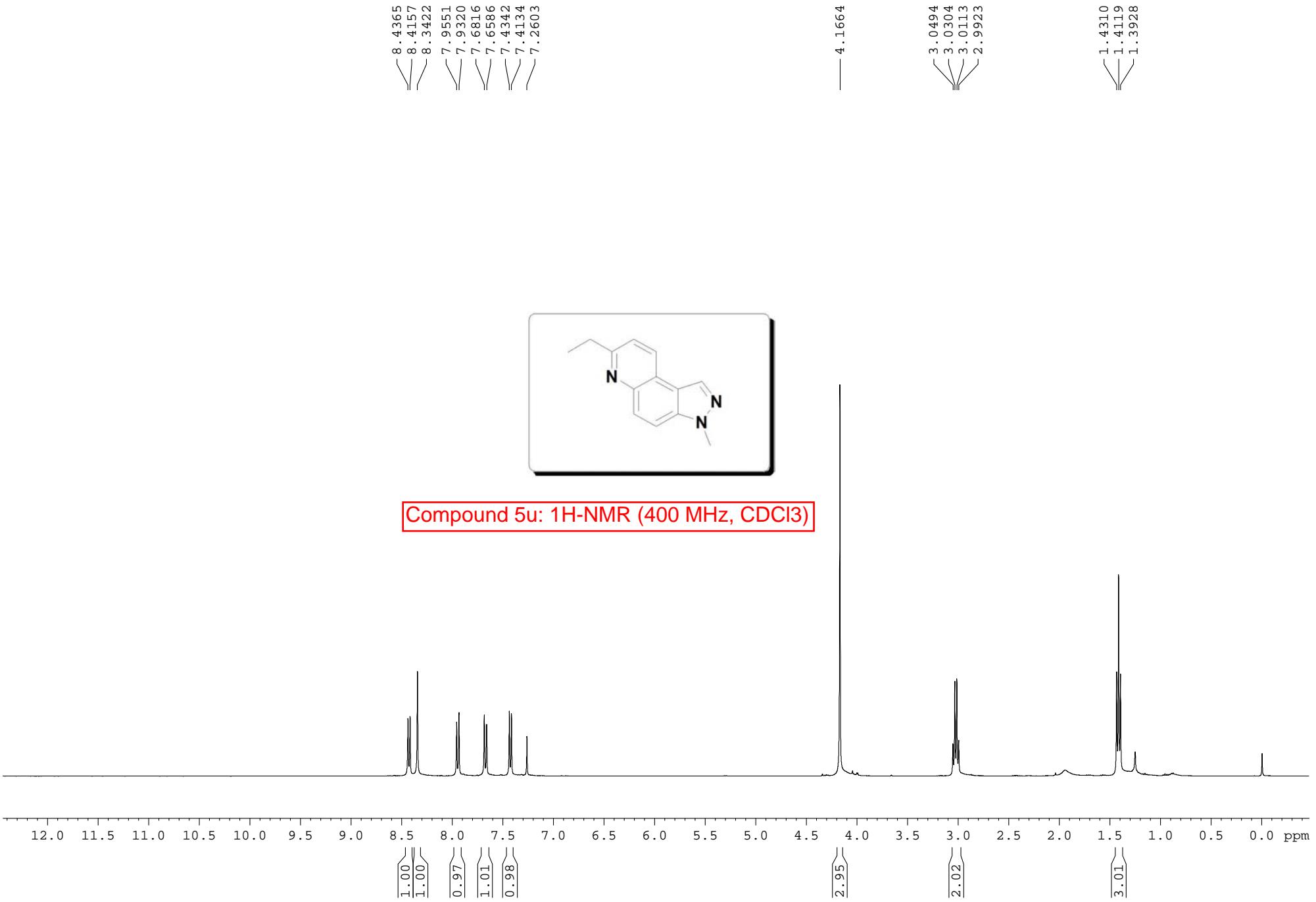
Compound 5s: 1H-NMR (400 MHz, CDCl3)

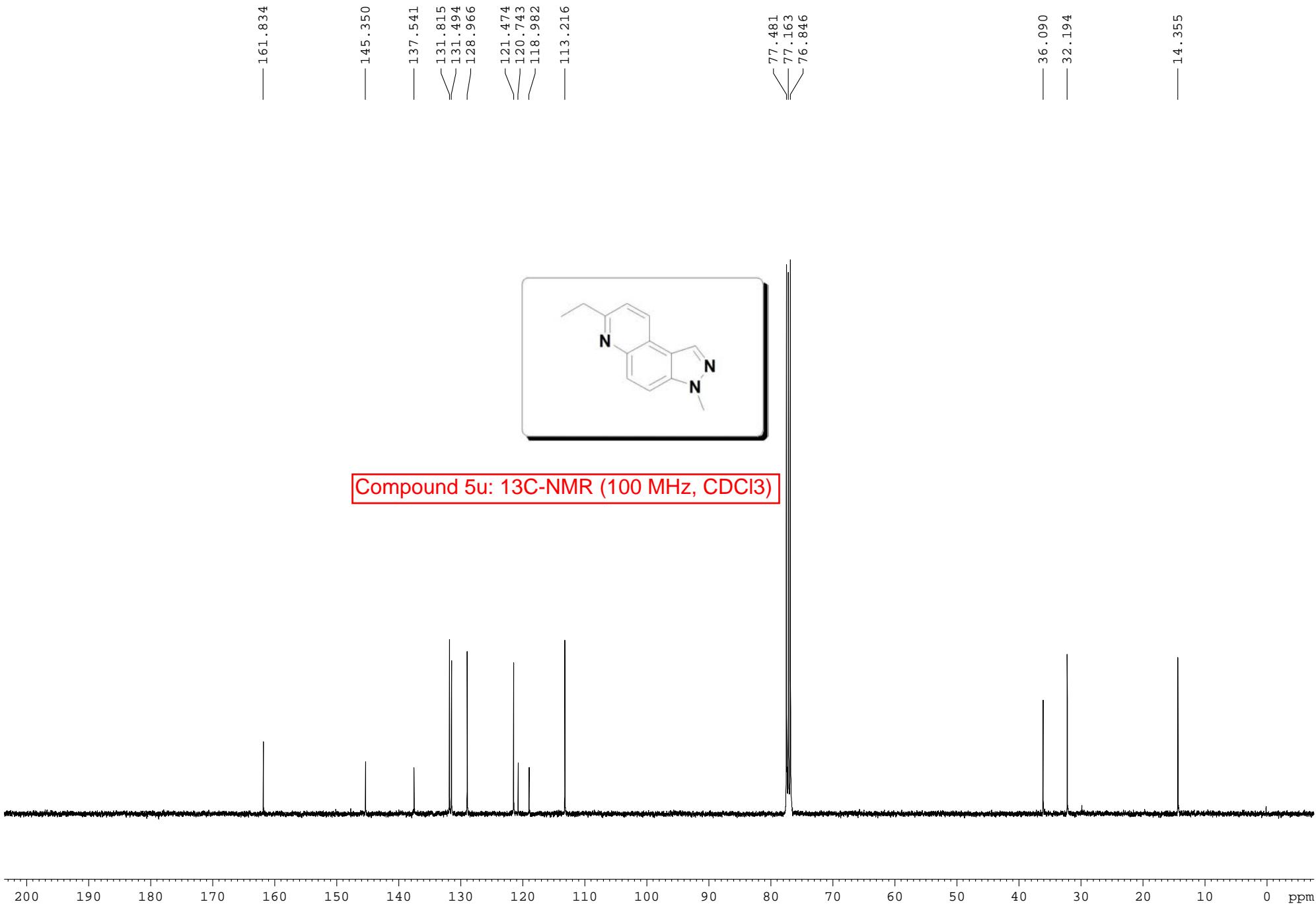


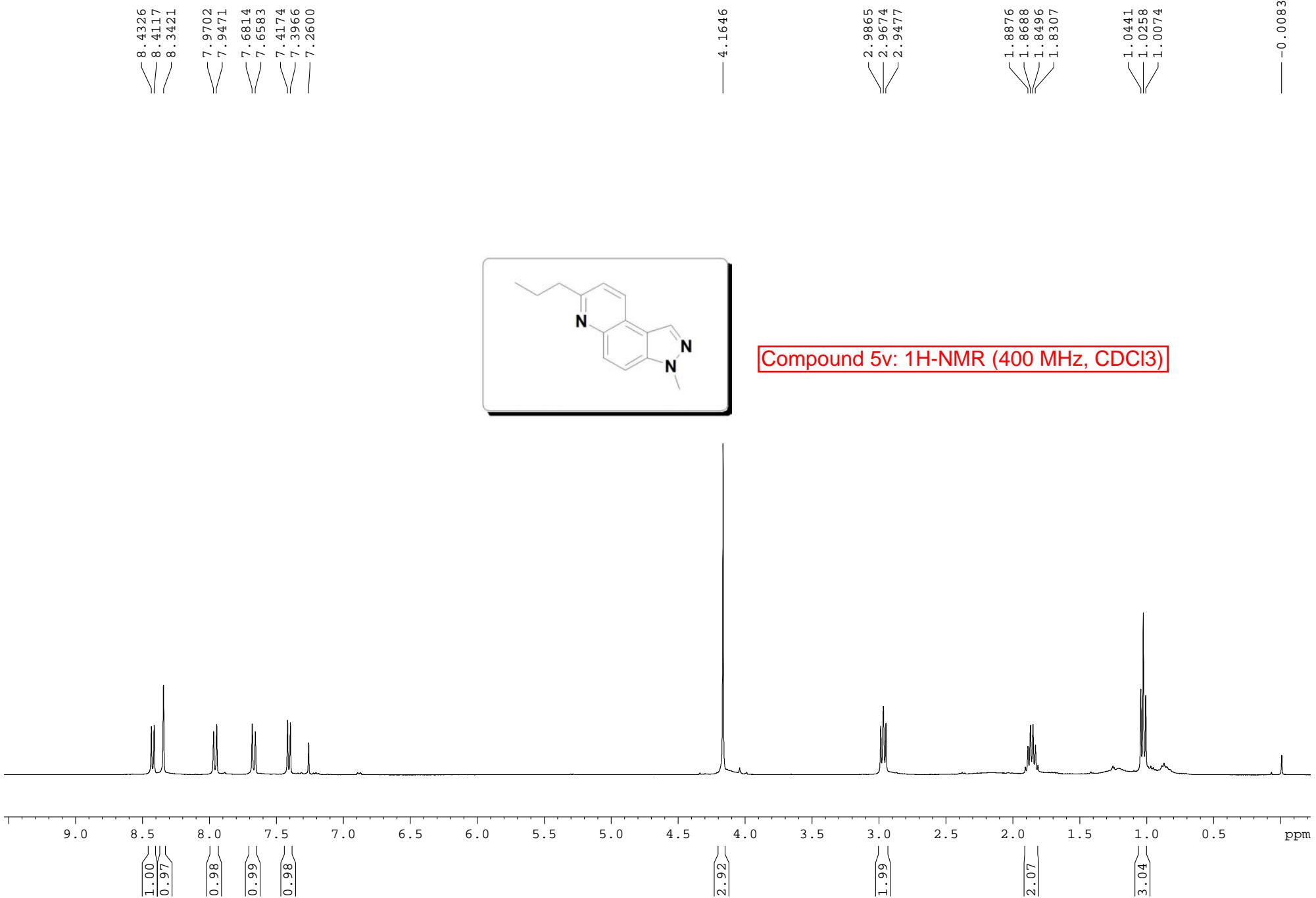


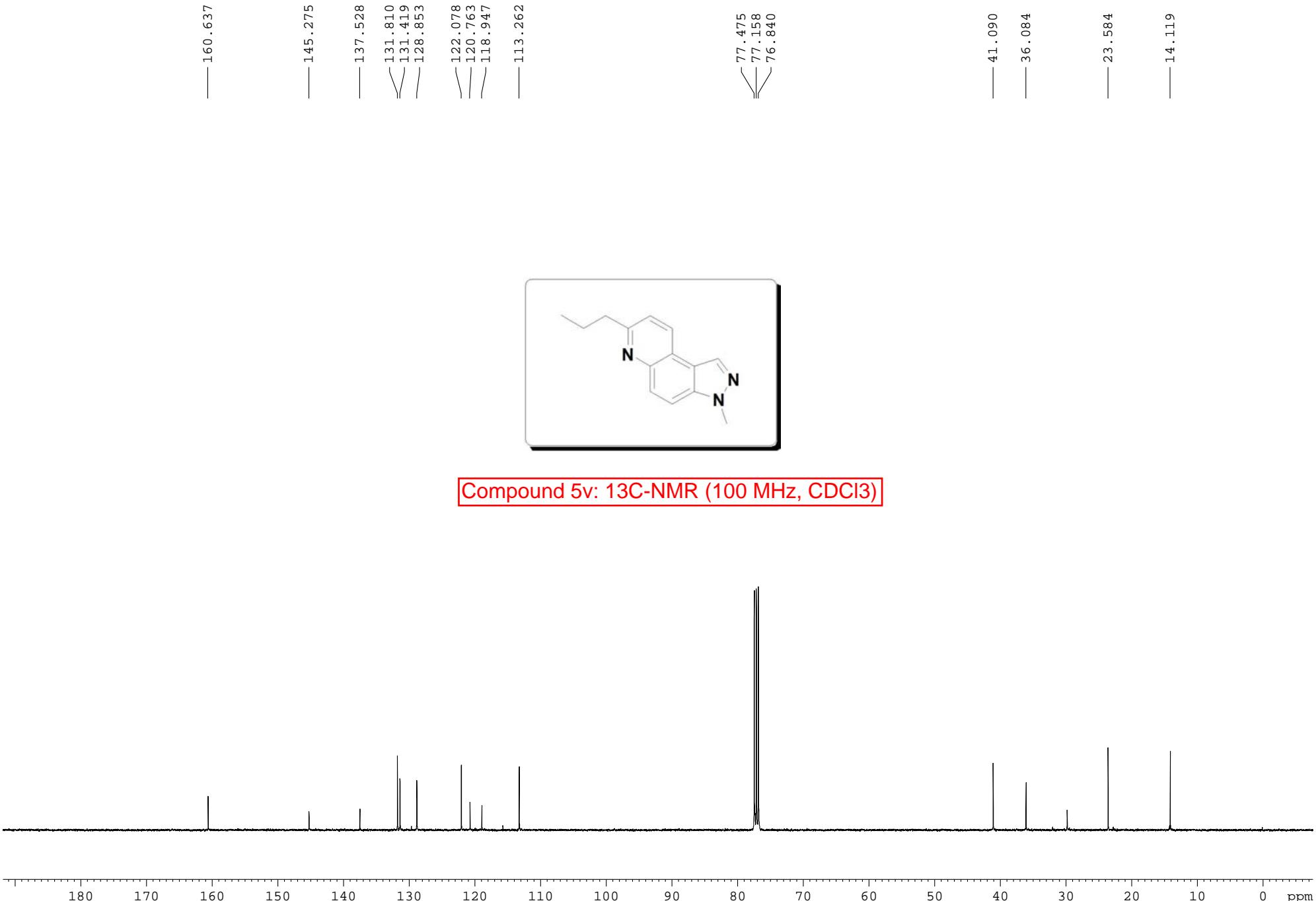












8.4514

8.4305  
8.3570

7.9932  
7.9702

7.6900  
7.6668

7.3904  
7.3694

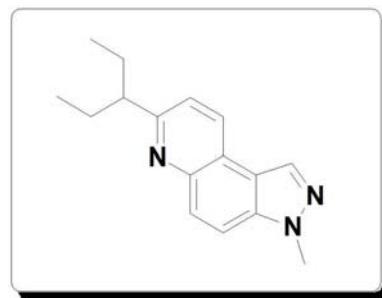
7.2602

4.1816

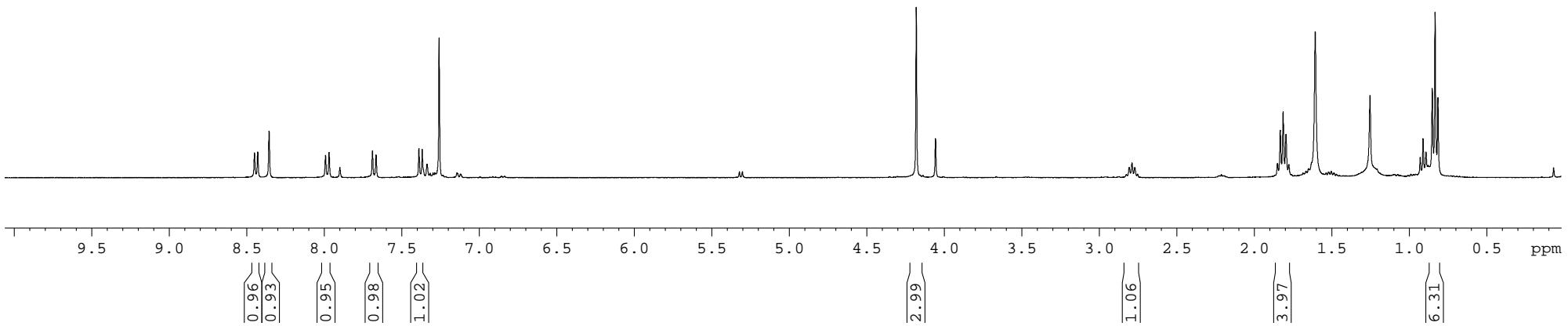
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2.8069  
2.7894  
2.7707  
2.7540

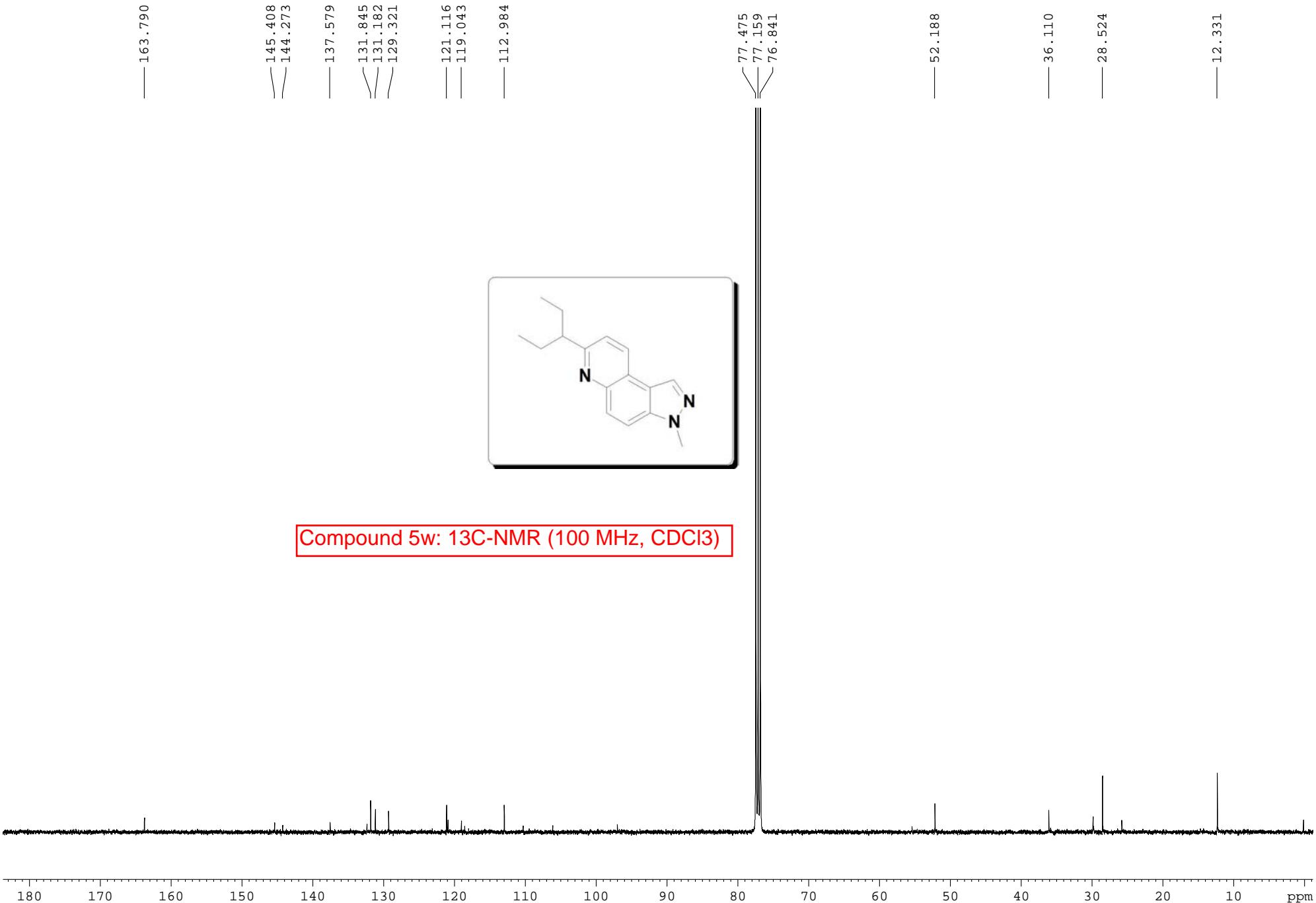
1.8511  
1.8327  
1.8141  
1.7957  
1.7779

0.8524  
0.8340  
0.8155



Compound 5w: 1H-NMR (400 MHz, CDCl<sub>3</sub>)





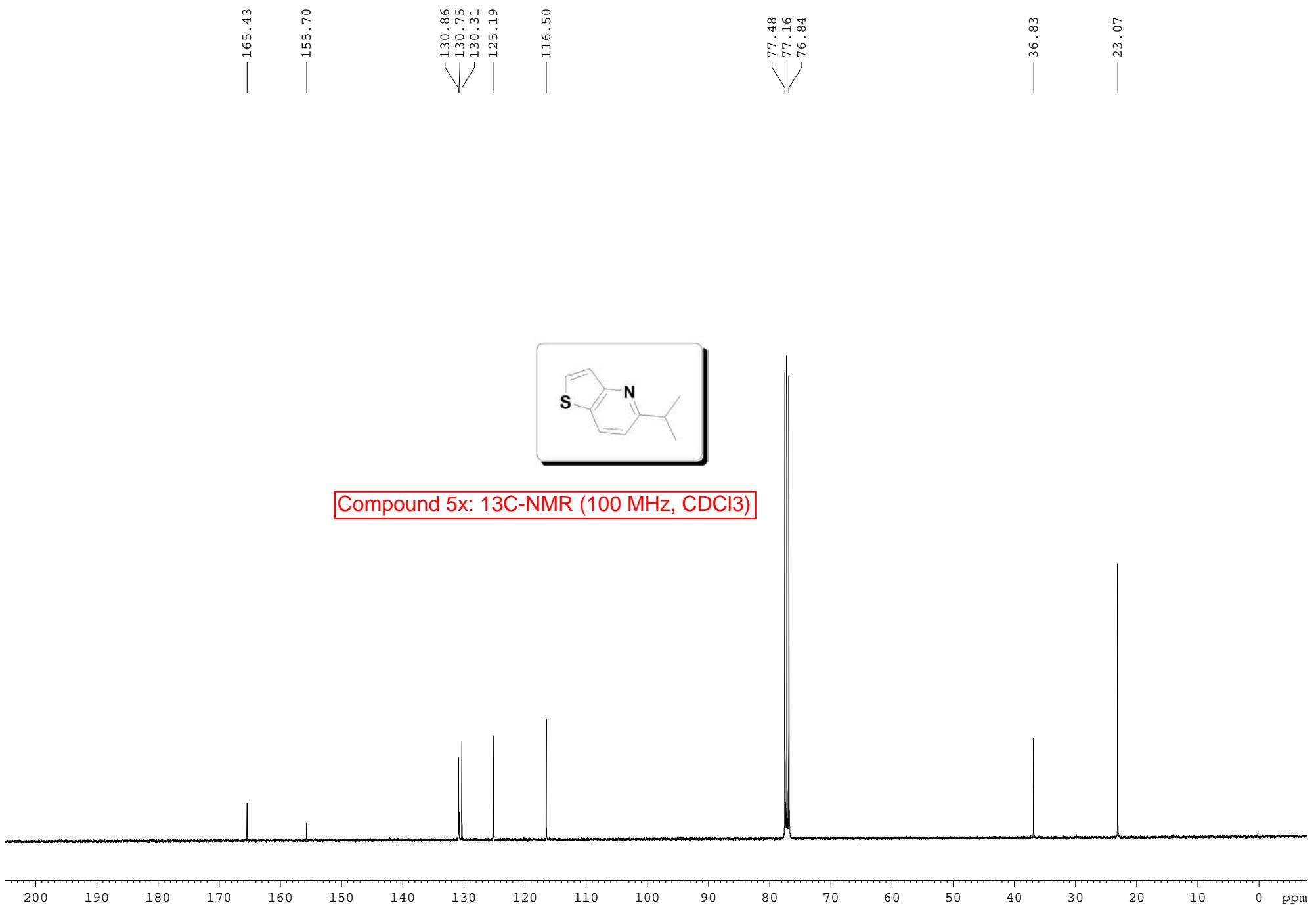
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Current Data Parameters
NAME      ly8-p137-P-20151208
EXPNO     10
PROCNO    1

F2 - Acquisition Parameters
Date_      20151208
Time       17.28
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zg30
TD        65536
SOLVENT    CDC13
NS         16
DS         2
SWH        8223.685 Hz
FIDRES   0.125483 Hz
AQ        3.9846387 sec
RG        144.49
DW        60.800 usec
DE        6.50  usec
TE        298.5 K
D1        1.0000000 sec
TD0           1

```

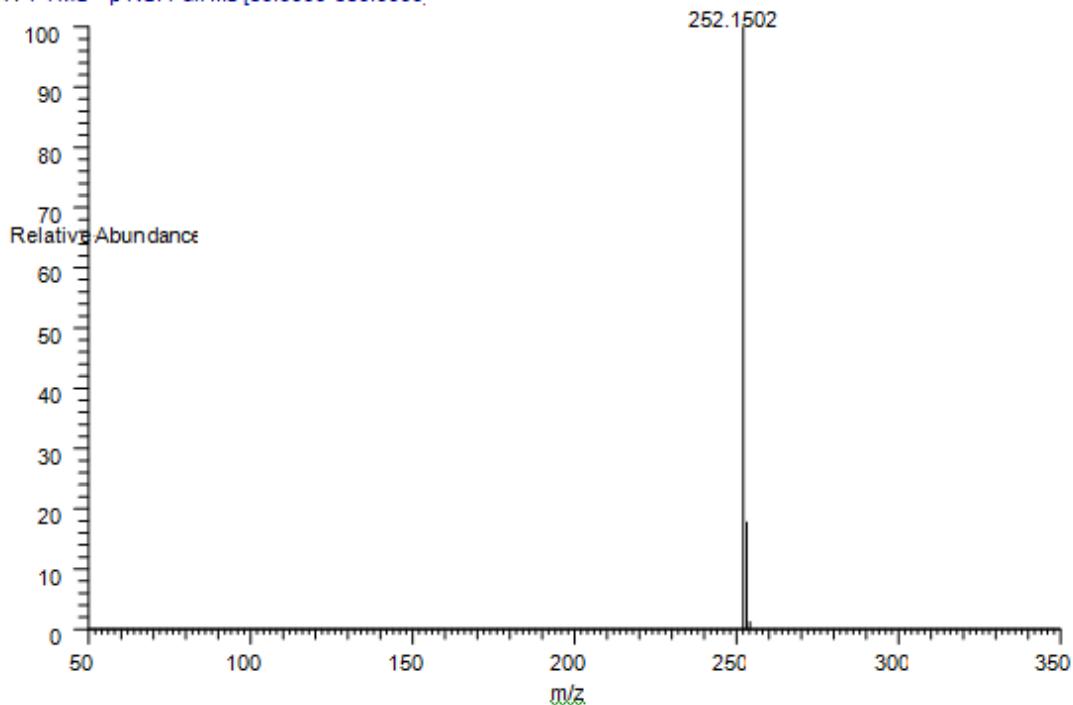




## HRMS (ESI)

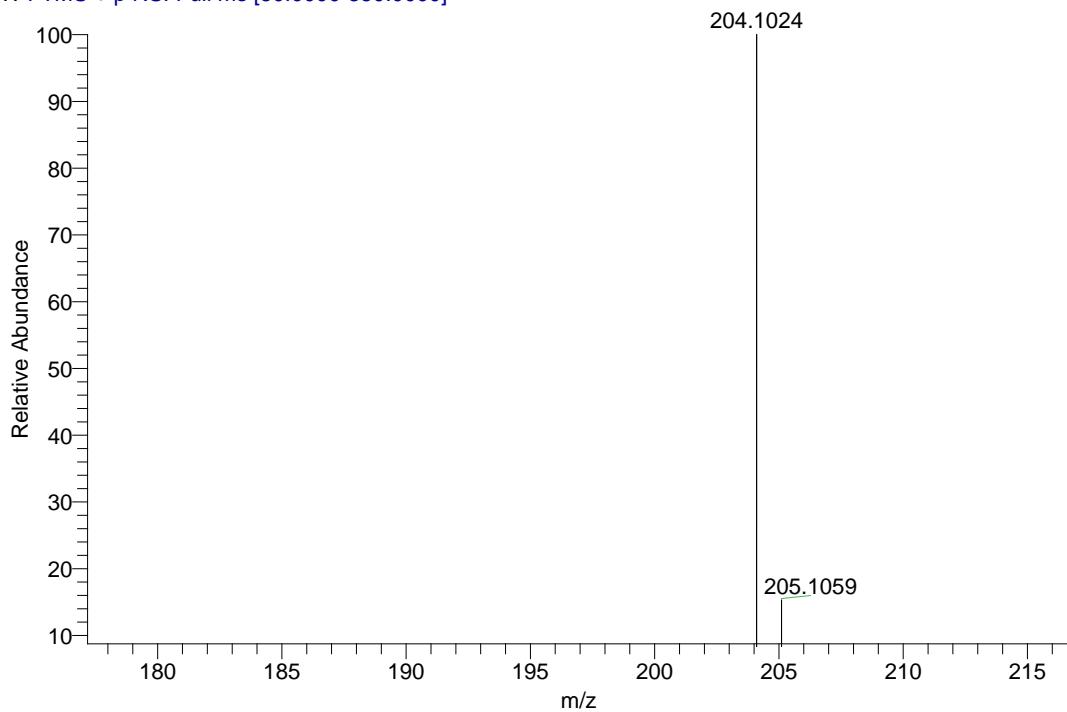
### 3 1-benzyl-5-isopropyl-1H-pyrazolo[4,3-b]pyridine

MS160221-2-E #956 RT: 8.53 AV: 1 NL: 7.92E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



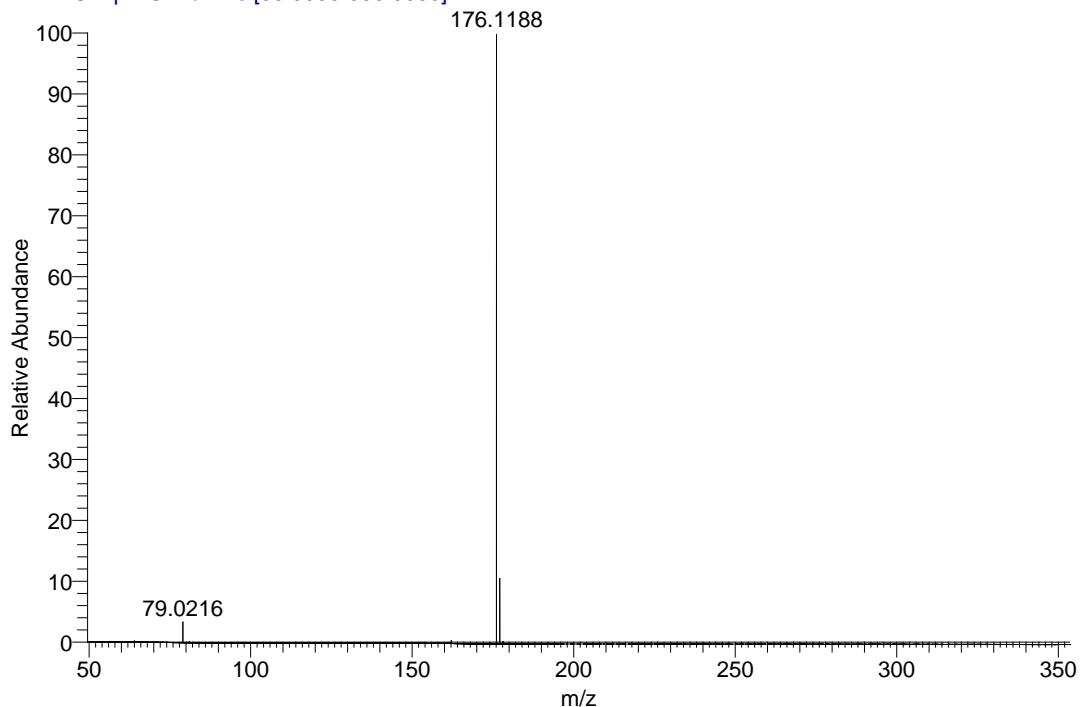
### 4a. 1-(5-isopropylfuro[3,2-b]pyridin-2-yl)ethanone

MS160221-2-E #633 RT: 6.07 AV: 1 NL: 9.12E3  
T: FTMS + p NSI Full ms [50.0000-350.0000]



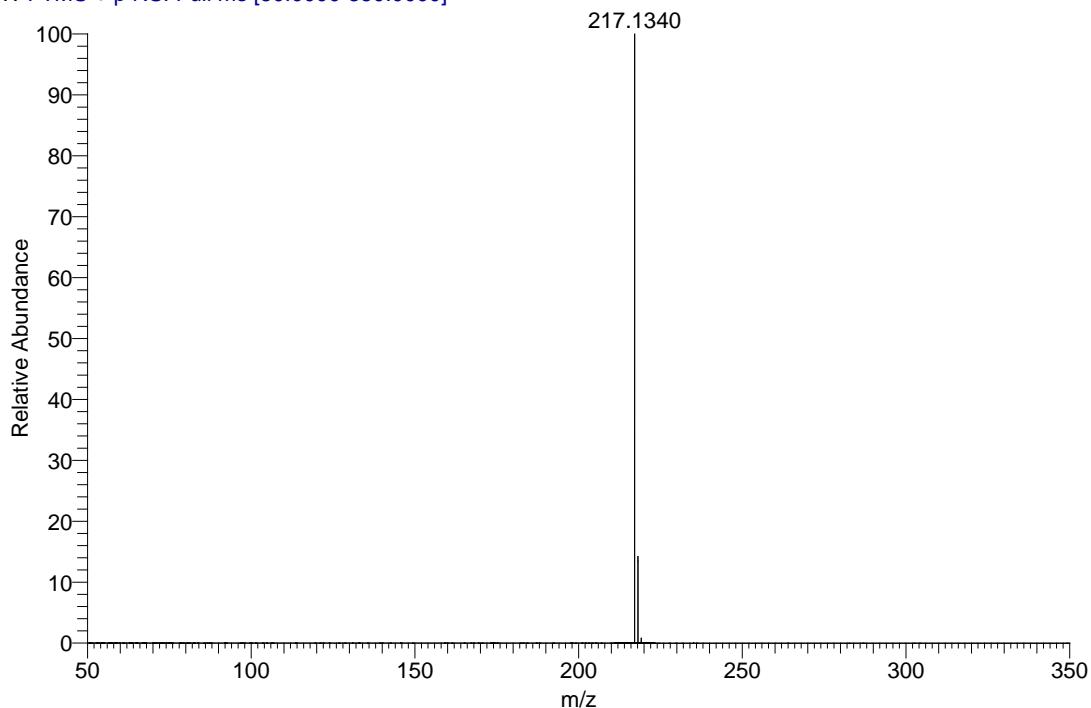
**4b. 5-isopropyl-1-methyl-1H-pyrazolo[4,3-b]pyridine**

MS160221-2-C #759-788 RT: 7.48-7.73 AV: 30 NL: 3.24E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



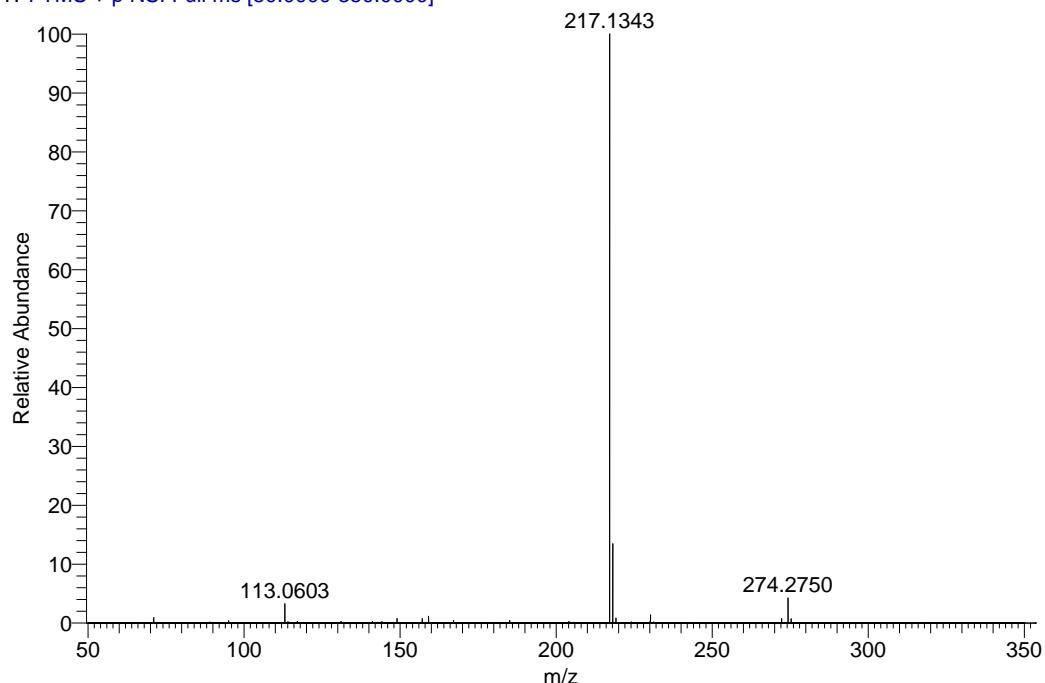
**4c. 1-(5-isopropyl-1-methyl-1H-pyrrolo[3,2-b]pyridin-2-yl)ethanone**

MS160221-12-H #970 RT: 8.71 AV: 1 NL: 8.11E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



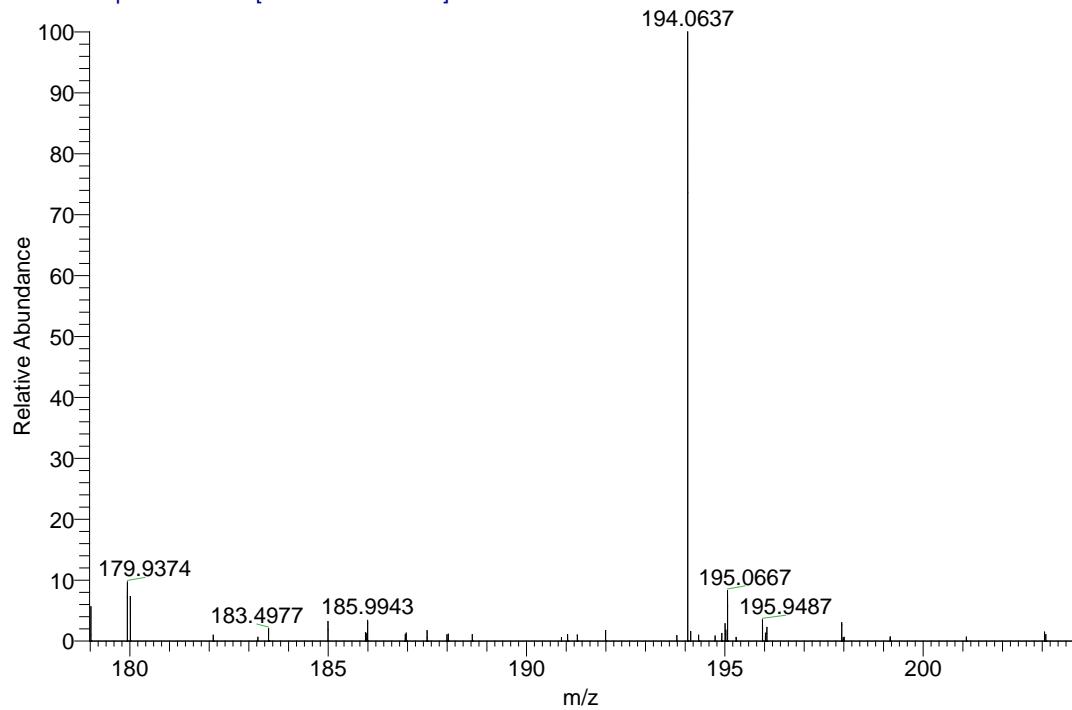
**4d. 1-(2-isopropyl-6-methyl-6H-pyrrolo[3,4-b]pyridin-7-yl)ethanone**

MS160221-2-D #1196-1288 RT: 11.17-12.00 AV: 93 NL: 4.95E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



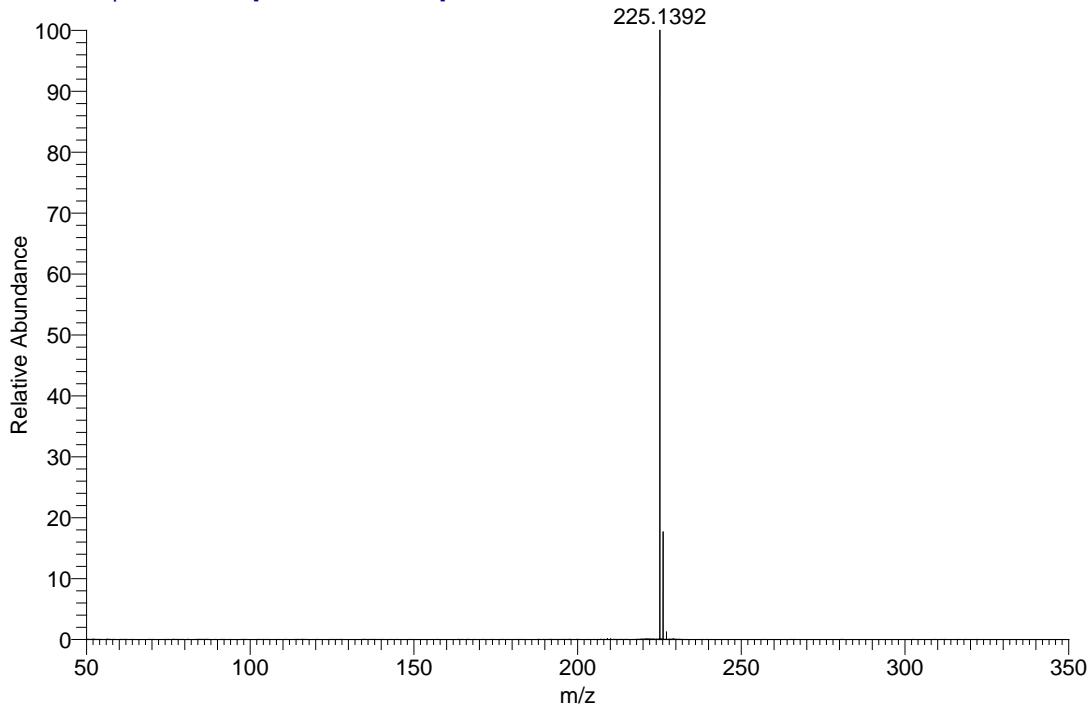
**4e. 2-isopropylthieno[3,4-b]pyridine**

MS160221-1-A #662 RT: 6.23 AV: 1 NL: 3.60E6  
T: FTMS + p NSI Full ms [50.0000-350.0000]



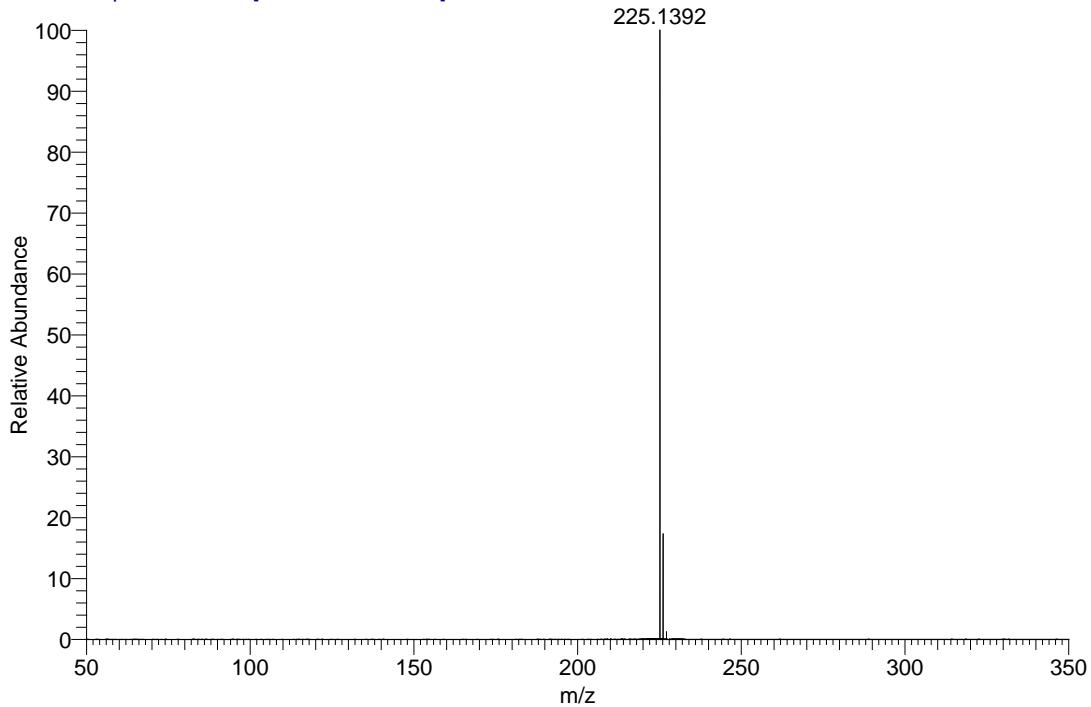
**4f. 7-isopropyl-1-methyl-1H-pyrrolo[2,3-f]quinolone**

MS160221-10-D #1013 RT: 9.07 AV: 1 NL: 7.41E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



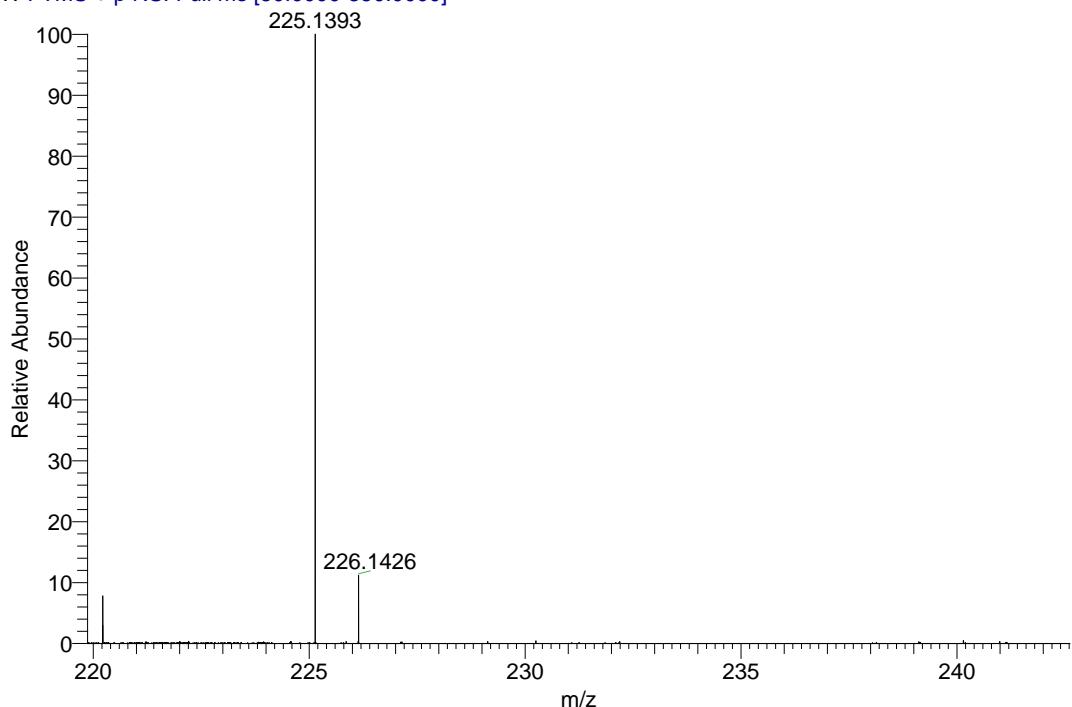
**4g. 7-isopropyl-3-methyl-3H-pyrrolo[3,2-f]quinolone**

MS160221-10-E #1007 RT: 9.02 AV: 1 NL: 7.02E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



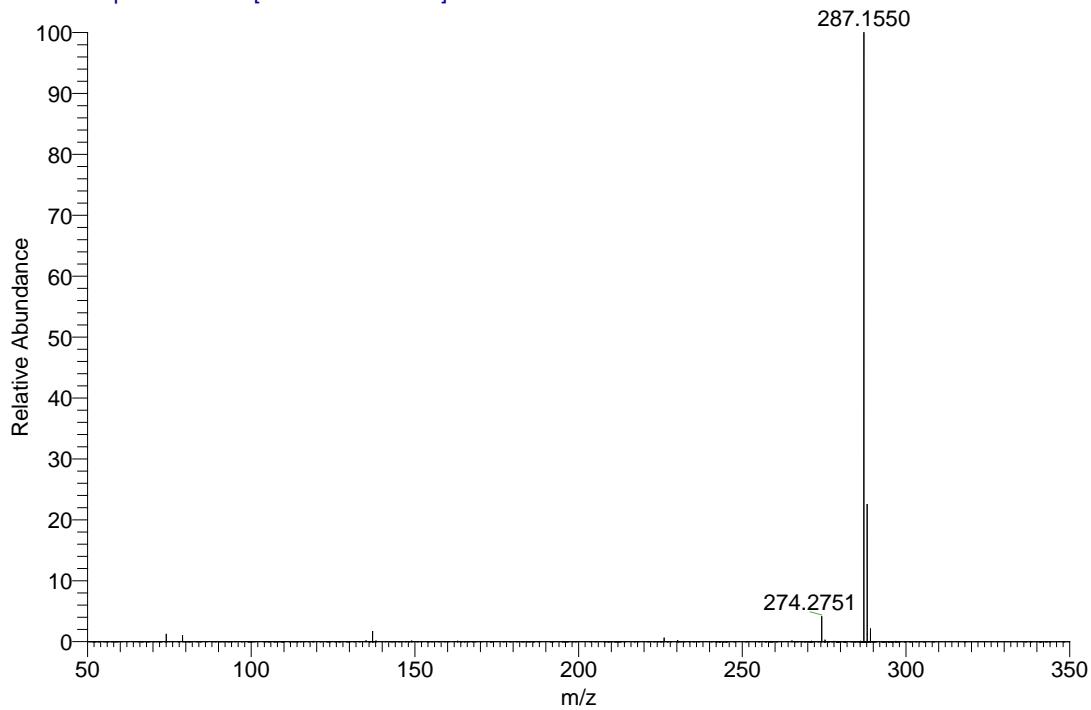
#### 4h. 8-isopropyl-1-methyl-1H-pyrrolo[3,2-h]quinolone

MS160221-10-H\_160226171838 #785 RT: 7.84 AV: 1 NL: 1.15E7  
T: FTMS + p NSI Full ms [50.0000-350.0000]



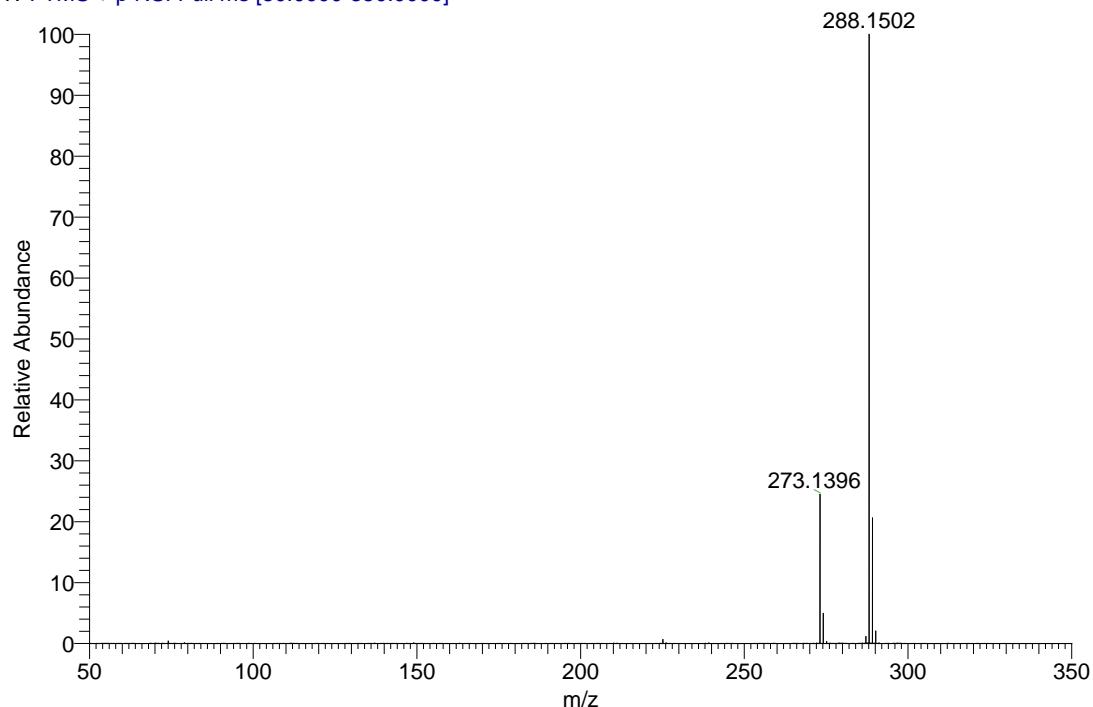
#### 4i. 7-isopropyl-3-phenyl-3H-pyrrolo[3,2-f]quinolone

MS160221-11-F #1220 RT: 10.93 AV: 1 NL: 2.50E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



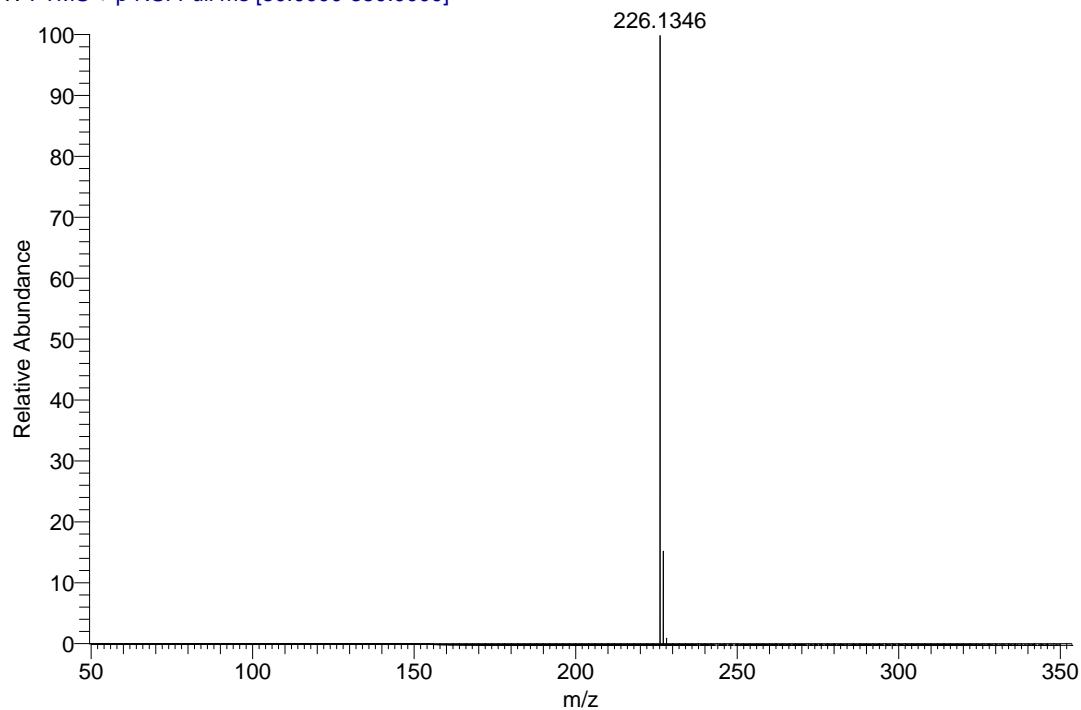
**4j. 7-isopropyl-3-phenyl-3H-pyrazolo[4,3-f]quinolone**

MS160221-12-D #1431 RT: 12.83 AV: 1 NL: 4.45E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



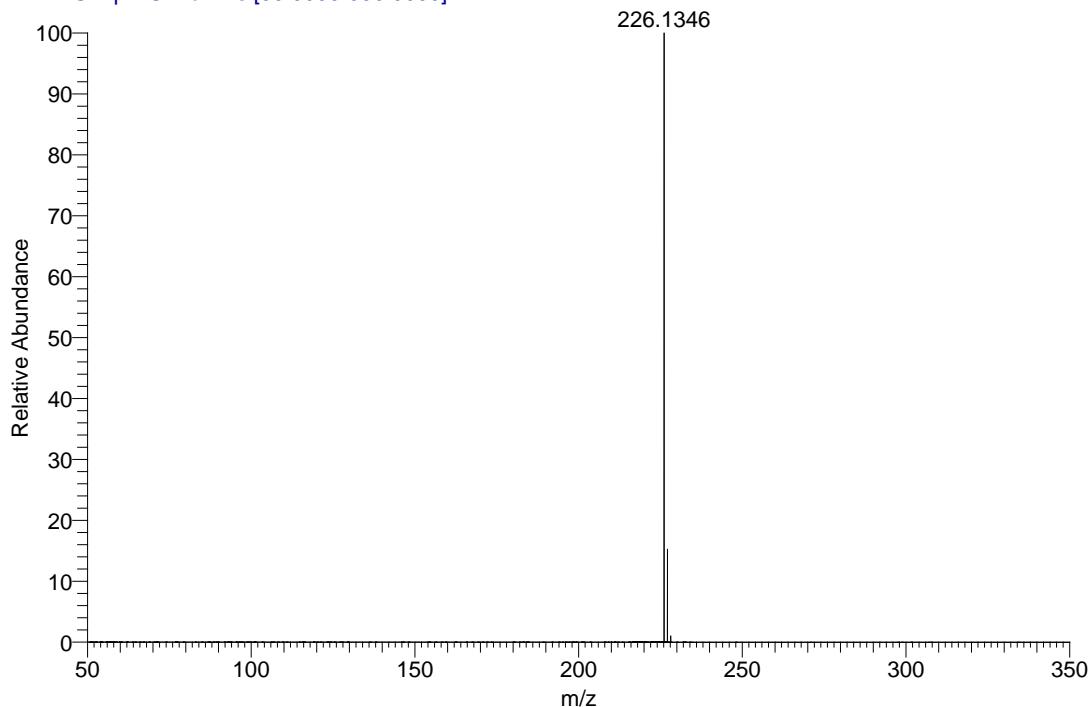
**4k. 7-isopropyl-3-methyl-3H-pyrazolo[4,3-f]quinolone**

MS160221-12-A #1050-1115 RT: 9.40-9.98 AV: 66 NL: 7.47E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



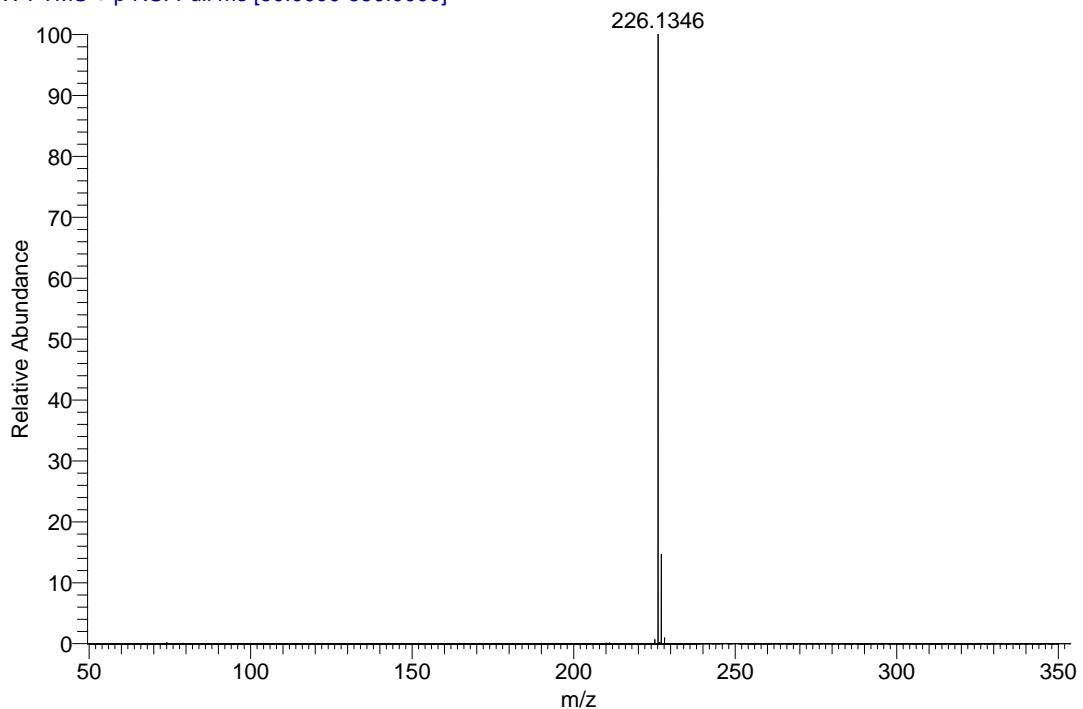
**4l. 7-isopropyl-2-methyl-2H-pyrazolo[4,3-f]quinolone**

MS160221-12-B #989 RT: 8.86 AV: 1 NL: 8.39E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



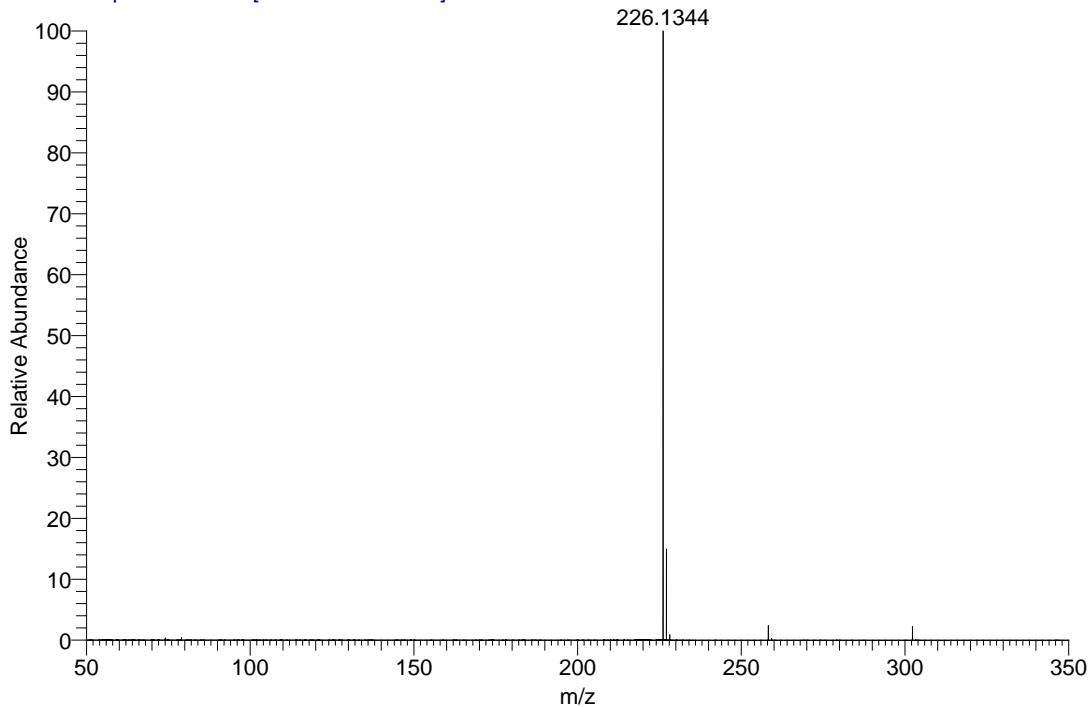
**4m. 7-isopropyl-2-methyl-2H-pyrazolo[3,4-f]quinolone**

MS160221-12-C #965-1055 RT: 8.66-9.46 AV: 91 NL: 7.39E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



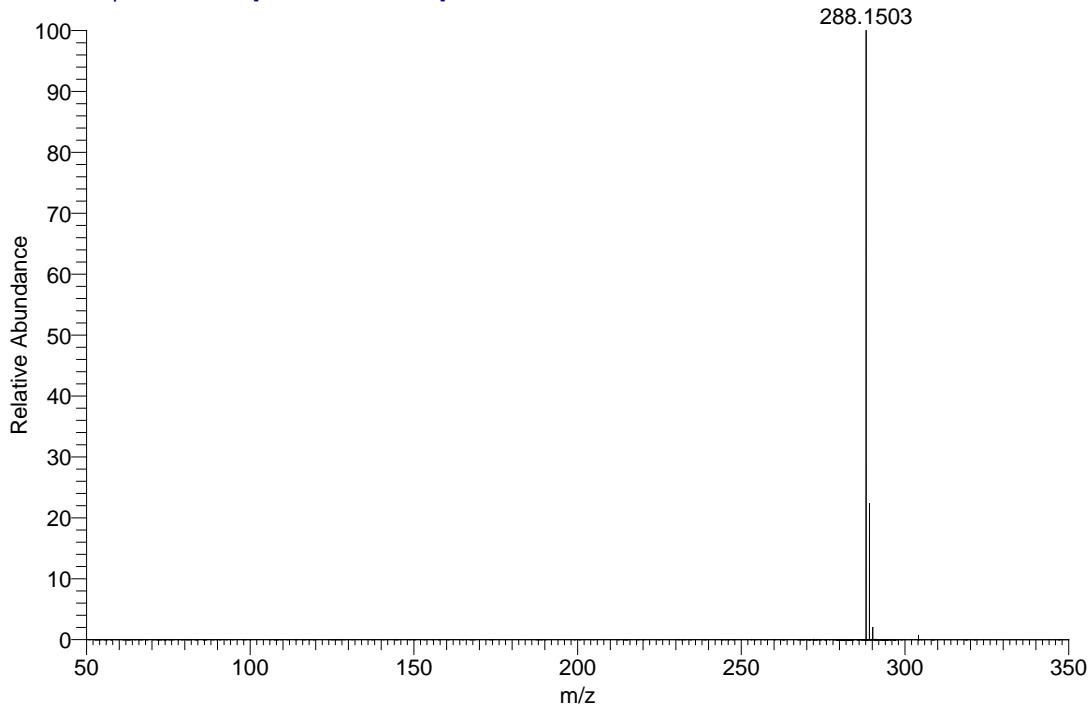
#### 4n. 7-isopropyl-1-methyl-1H-pyrazolo[3,4-f]quinolone

MS160221-11-E #1324 RT: 11.85 AV: 1 NL: 4.94E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



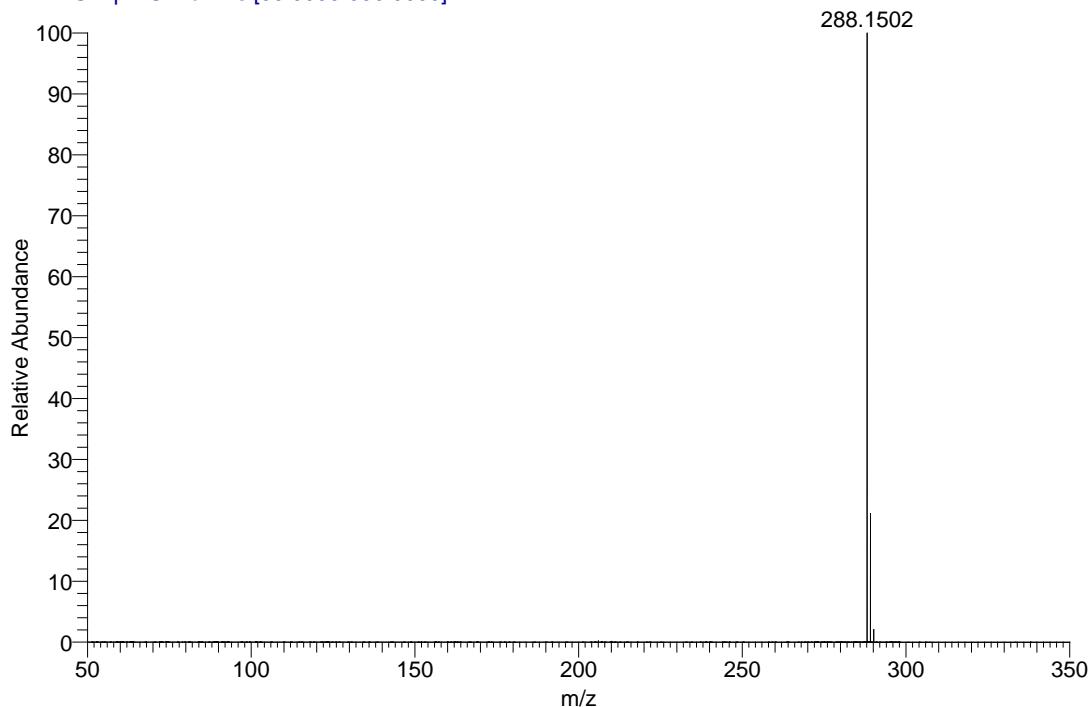
#### 4o-1. 7-isopropyl-1-phenyl-1H-pyrazolo[3,4-f]quinolone

MS160221-1-C #1116 RT: 10.01 AV: 1 NL: 6.31E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



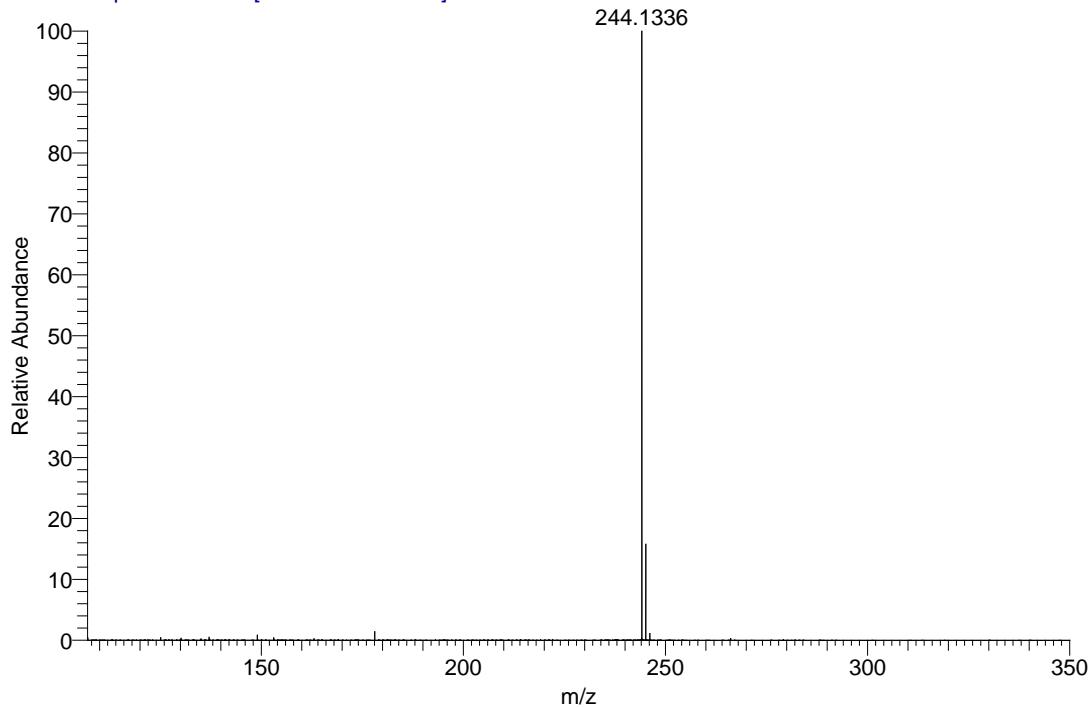
**4o-2. 7-isopropyl-1-phenyl-1H-pyrazolo[4,3-g]quinolone**

MS160221-1-B #1353 RT: 12.11 AV: 1 NL: 6.51E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



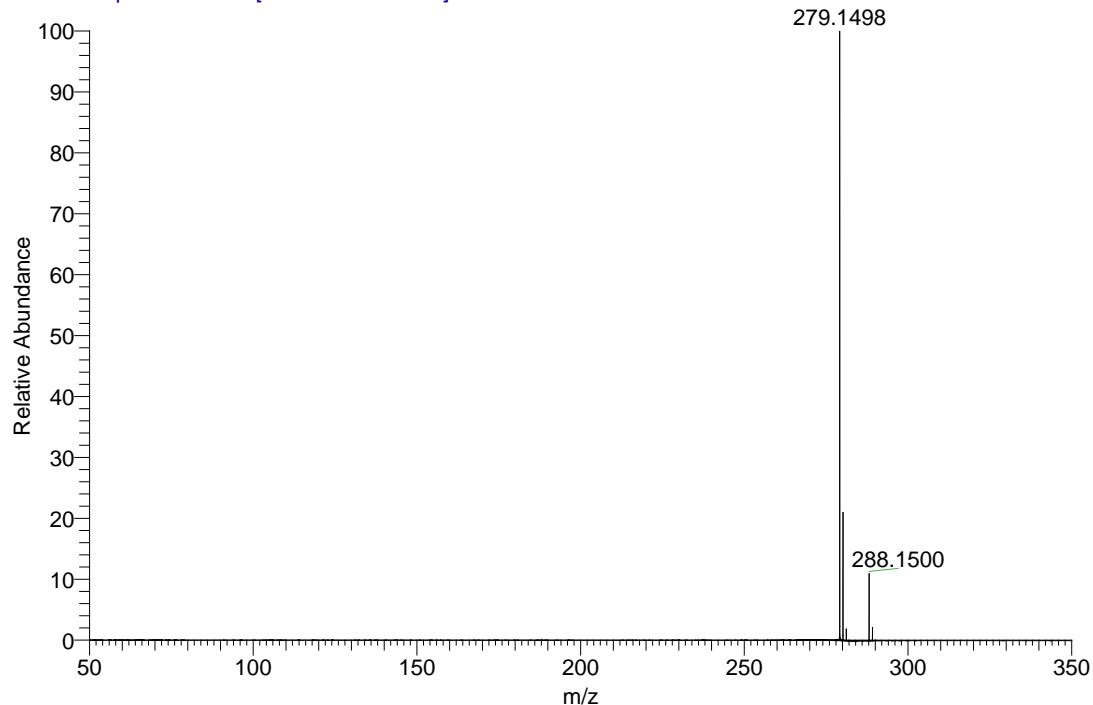
**5a. 1-(5-isopropylfuro[3,2-b]pyridin-2-yl)ethanone**

MS160221-3-A\_160226160031 #344 RT: 3.06 AV: 1 NL: 2.08E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



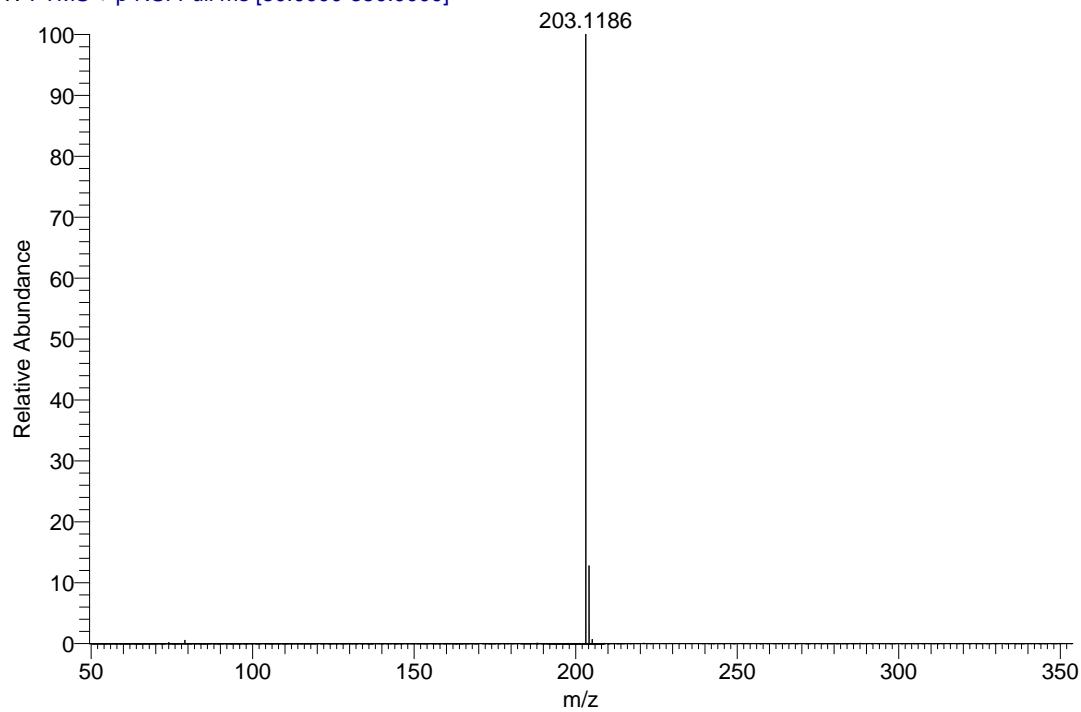
**5b.**

MS160221-1-D #1452 RT: 12.98 AV: 1 NL: 4.61E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



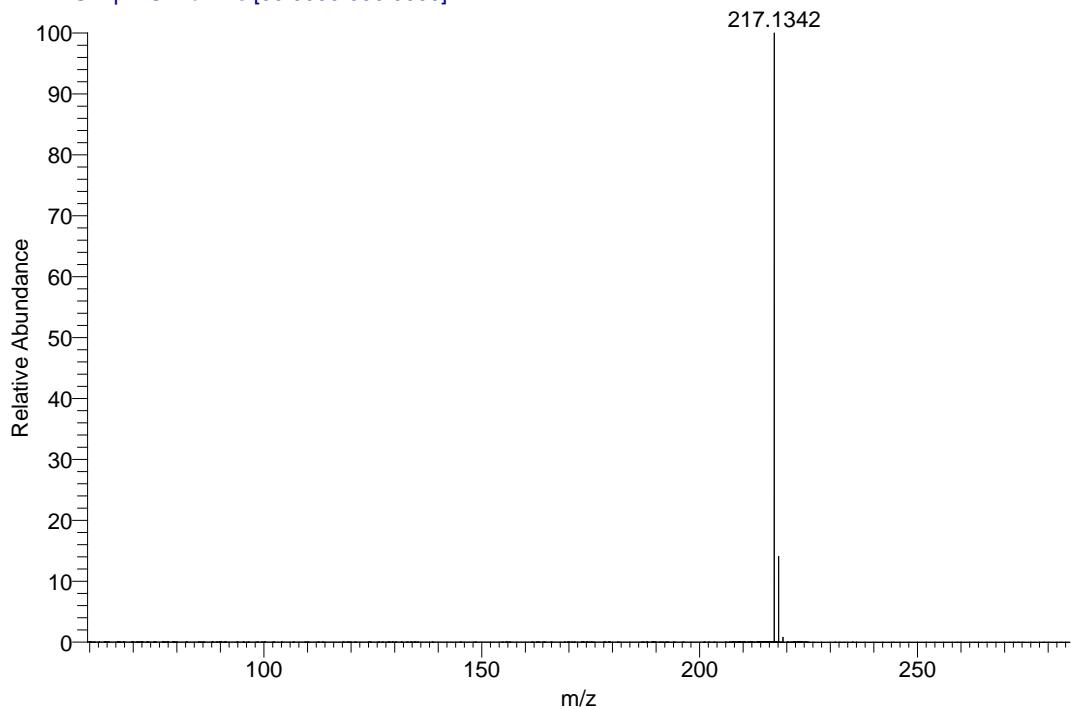
**5c. 1-(5-ethyl-1-methyl-1H-pyrrolo[3,2-b]pyridin-2-yl)ethanone**

MS160221-1-F #879-892 RT: 7.93-8.05 AV: 14 NL: 6.62E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



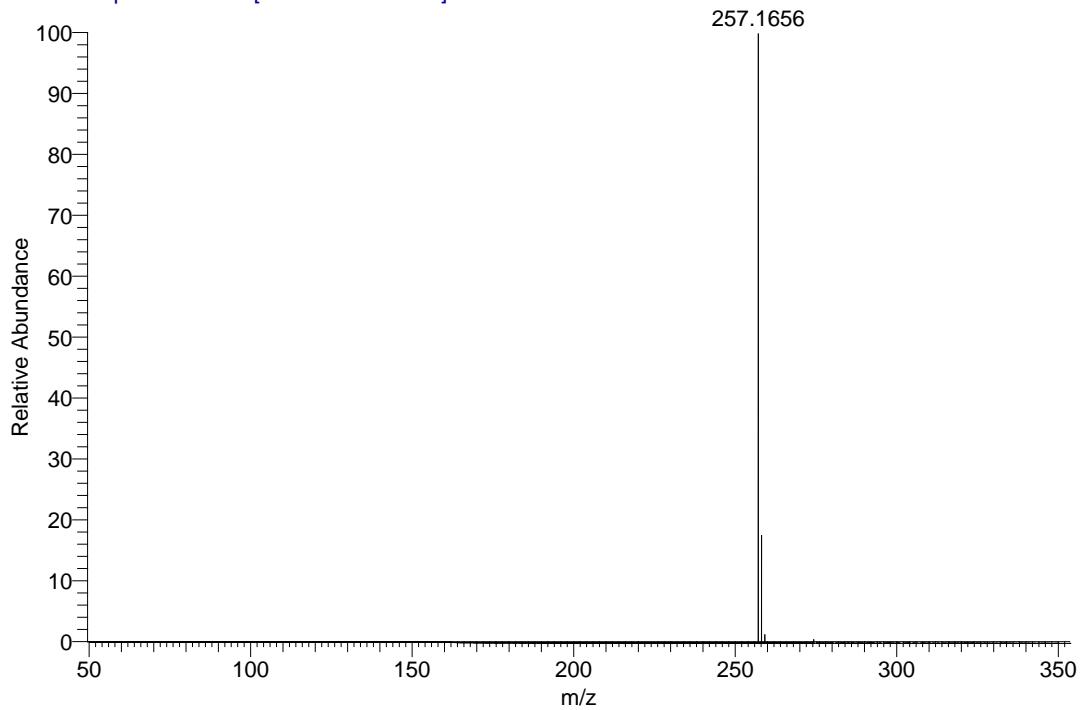
**5d. 1-(1-methyl-5-propyl-1H-pyrrolo[3,2-b]pyridin-2-yl)ethanone**

MS160221-1-E #1003 RT: 8.95 AV: 1 NL: 7.37E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



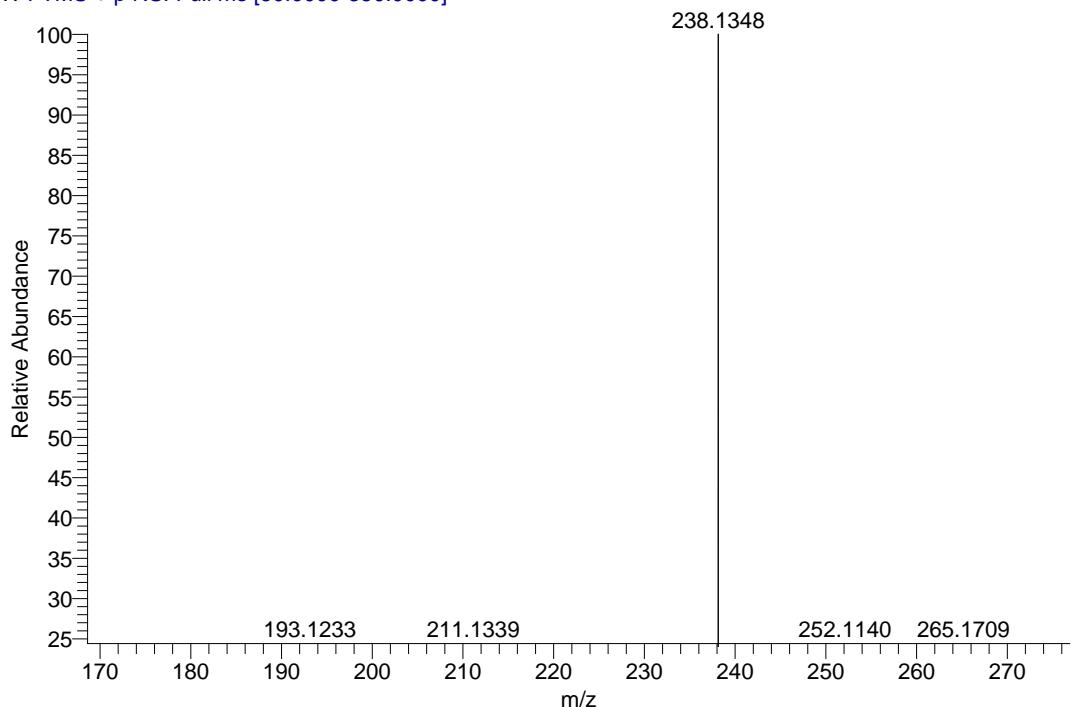
**5e.**

MS160221-1-G #1293-1348 RT: 11.66-12.16 AV: 56 NL: 6.97E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



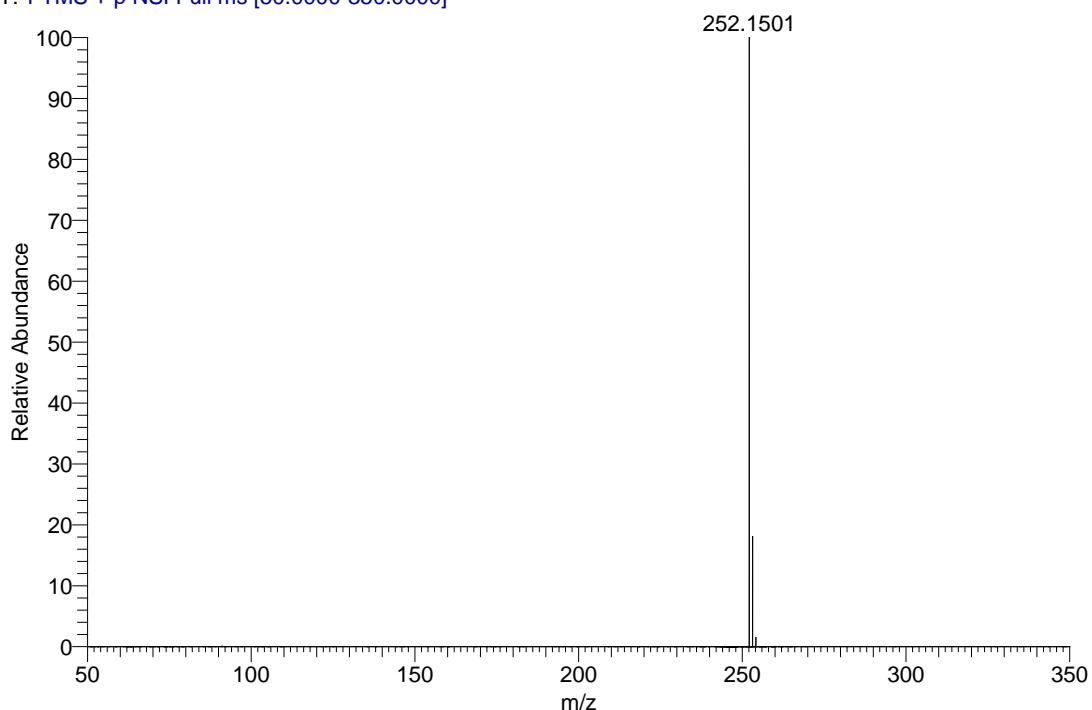
### 5f. 1-benzyl-5-ethyl-1H-pyrazolo[4,3-b]pyridine

MS160221-2-A #1439 RT: 12.87 AV: 1 NL: 3.30E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



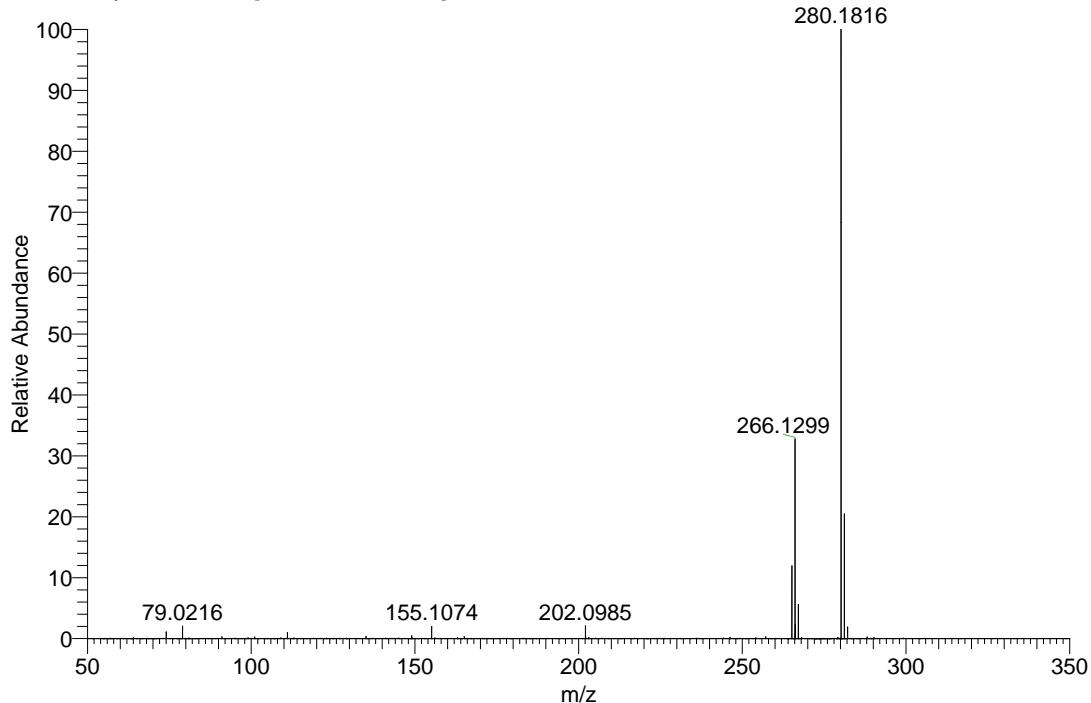
### 5g. 1-benzyl-5-propyl-1H-pyrazolo[4,3-b]pyridine

MS160221-2-F #1063 RT: 9.49 AV: 1 NL: 7.46E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



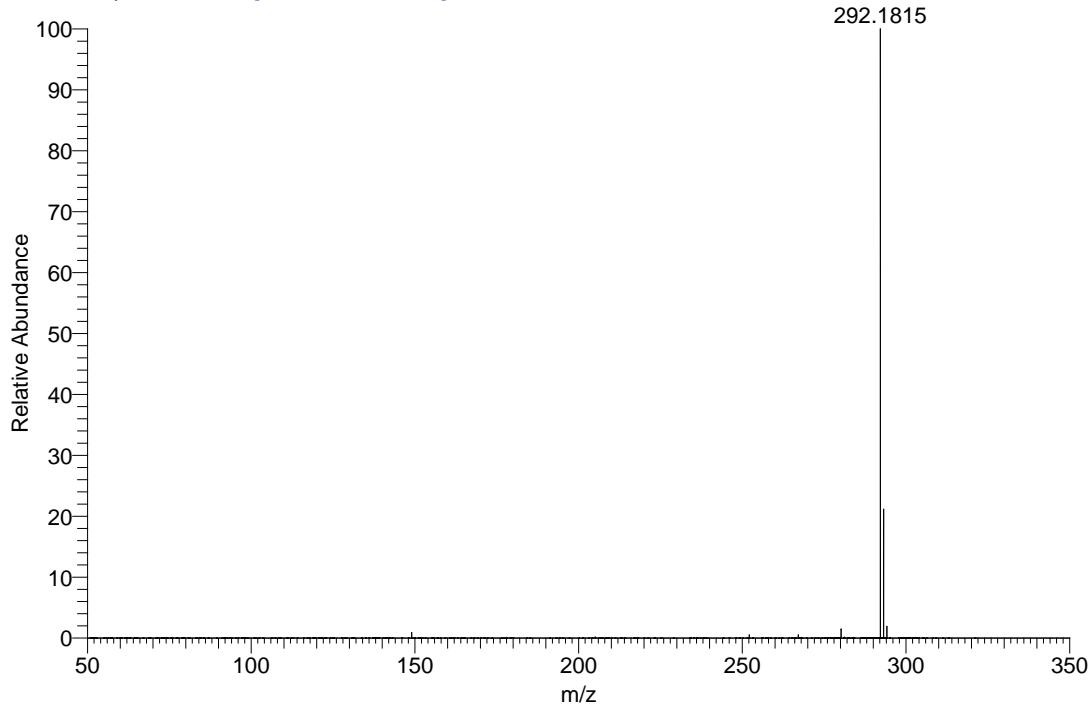
**5h. 1-benzyl-5-(pentan-3-yl)-1H-pyrazolo[4,3-b]pyridine**

MS160221-1-H #1164 RT: 10.46 AV: 1 NL: 1.92E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



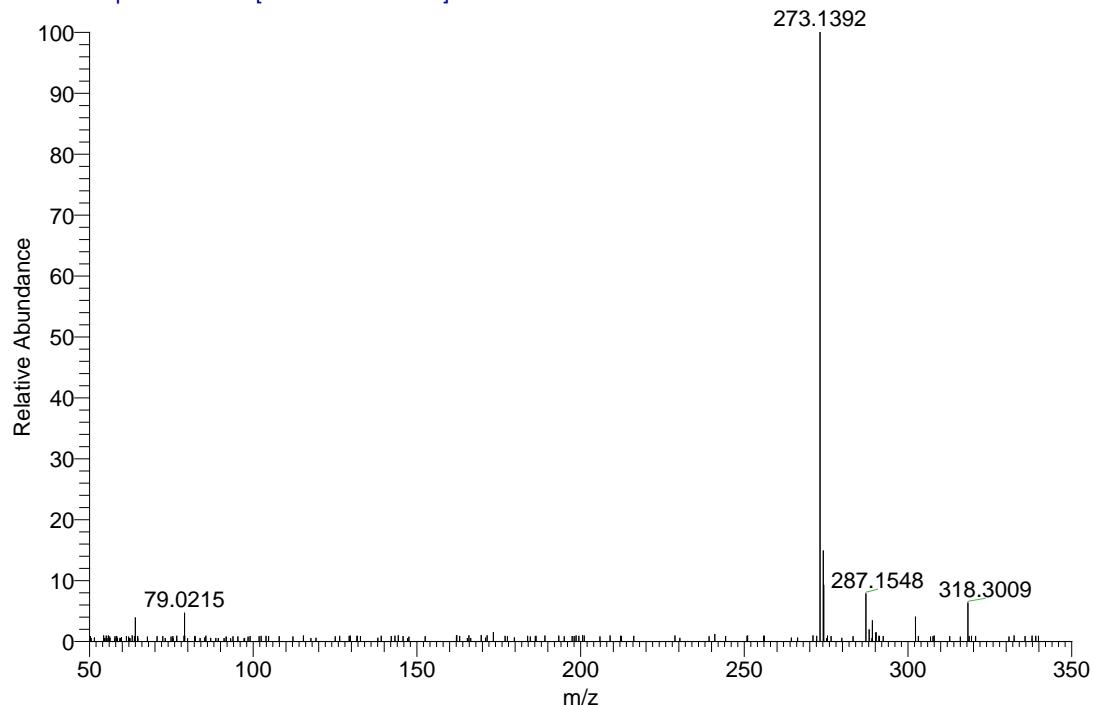
**5i. 1-benzyl-5-cyclohexyl-1H-pyrazolo[4,3-b]pyridine**

MS160221-2-G #1196 RT: 11.62 AV: 1 NL: 3.68E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



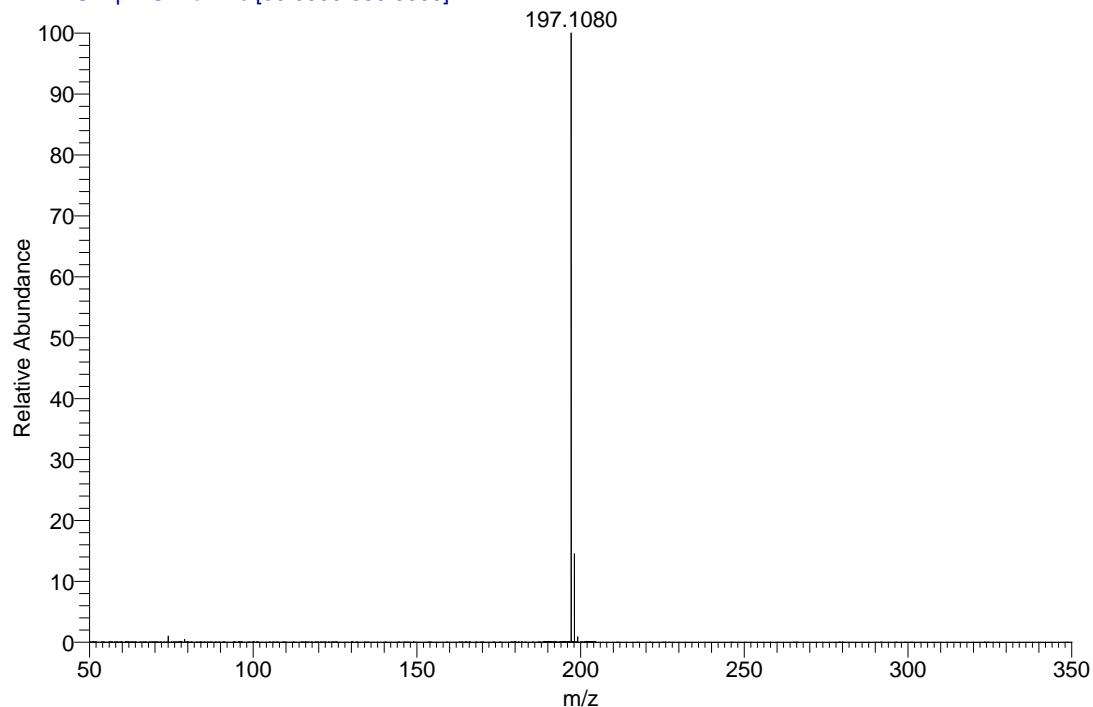
**5j. 8-benzyl-1-methyl-1H-pyrrolo[3,2-h]quinoline**

MS160221-11-C\_160226180817 #523 RT: 5.31 AV: 1 NL: 5.97E4  
T: FTMS + p NSI Full ms [50.0000-350.0000]



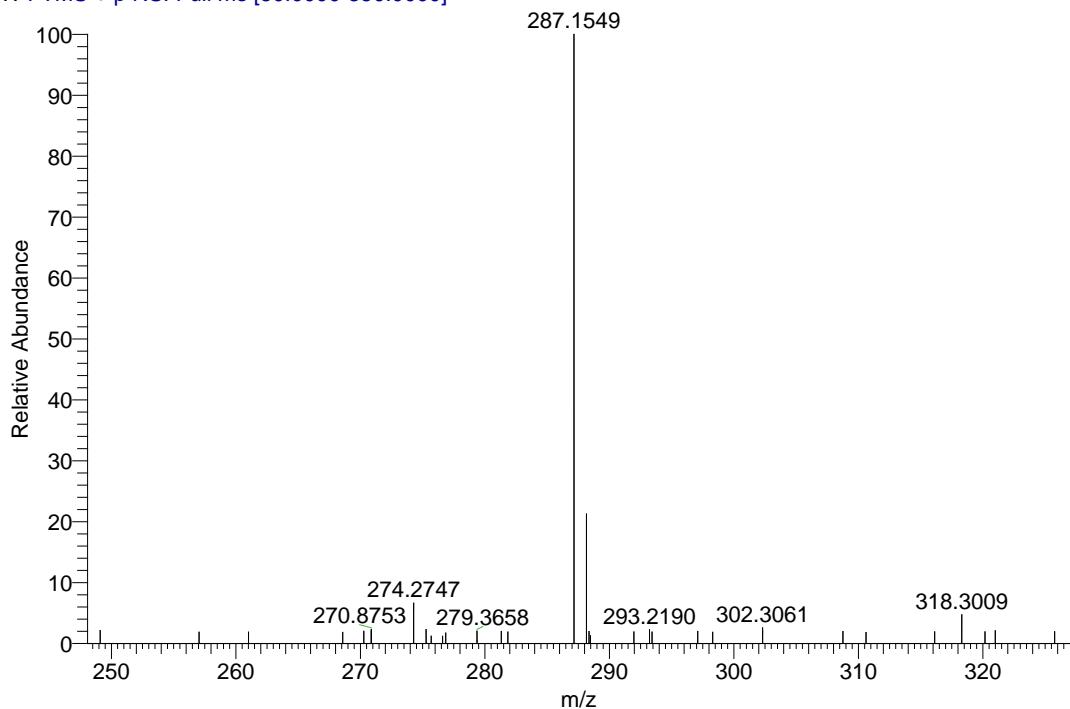
**5k. 1,8-dimethyl-1H-pyrrolo[3,2-h]quinoline**

MS160221-10-G #1185 RT: 10.60 AV: 1 NL: 4.83E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



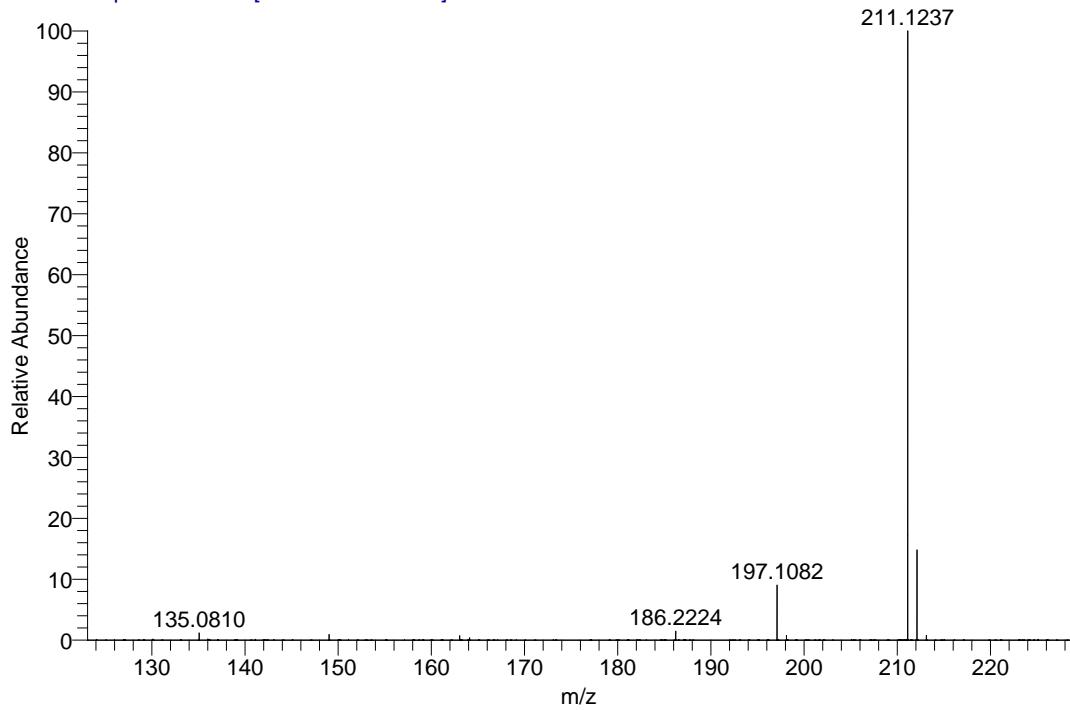
### 5l. 1-methyl-8-phenethyl-1H-pyrrolo[3,2-h]quinoline

MS160221-11-B\_160226175228 #531 RT: 5.28 AV: 1 NL: 2.55E4  
T: FTMS + p NSI Full ms [50.0000-350.0000]



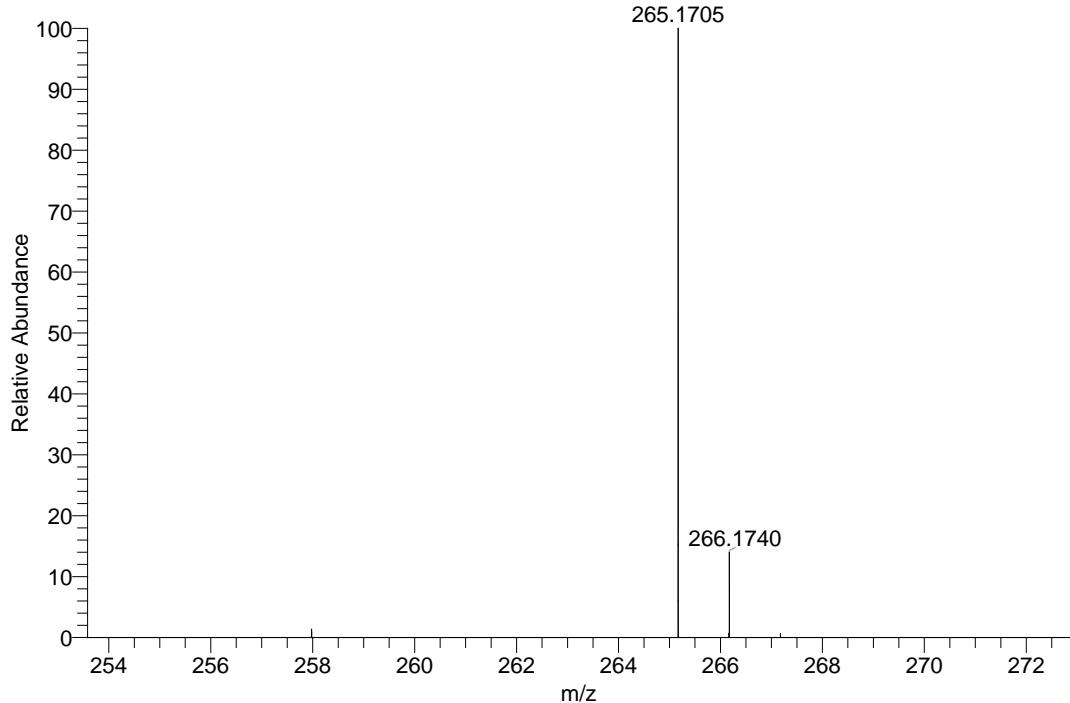
### 5m. 8-ethyl-1-methyl-1H-pyrrolo[3,2-h]quinolone

MS160221-10-F #1230 RT: 11.02 AV: 1 NL: 5.20E8  
T: FTMS + p NSI Full ms [50.0000-350.0000]



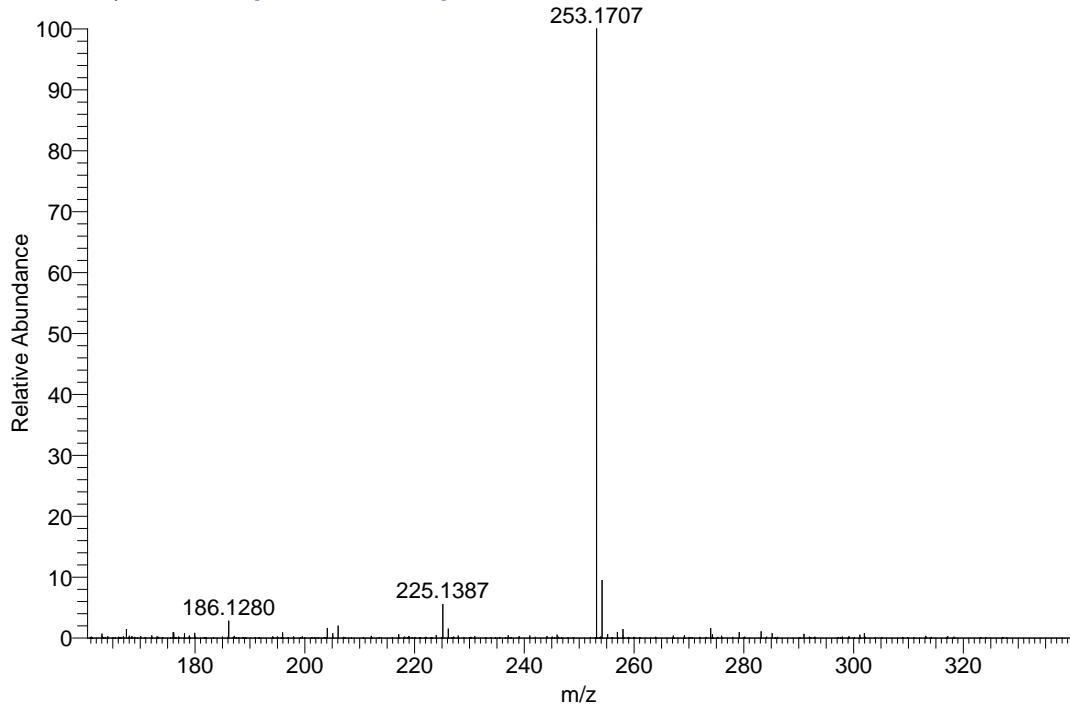
**5n. 8-cyclohexyl-1-methyl-1H-pyrrolo[3,2-h]quinolone**

MS160221-11-D\_160226182403 #618 RT: 6.50 AV: 1 NL: 8.39E4  
T: FTMS + p NSI Full ms [50.0000-350.0000]



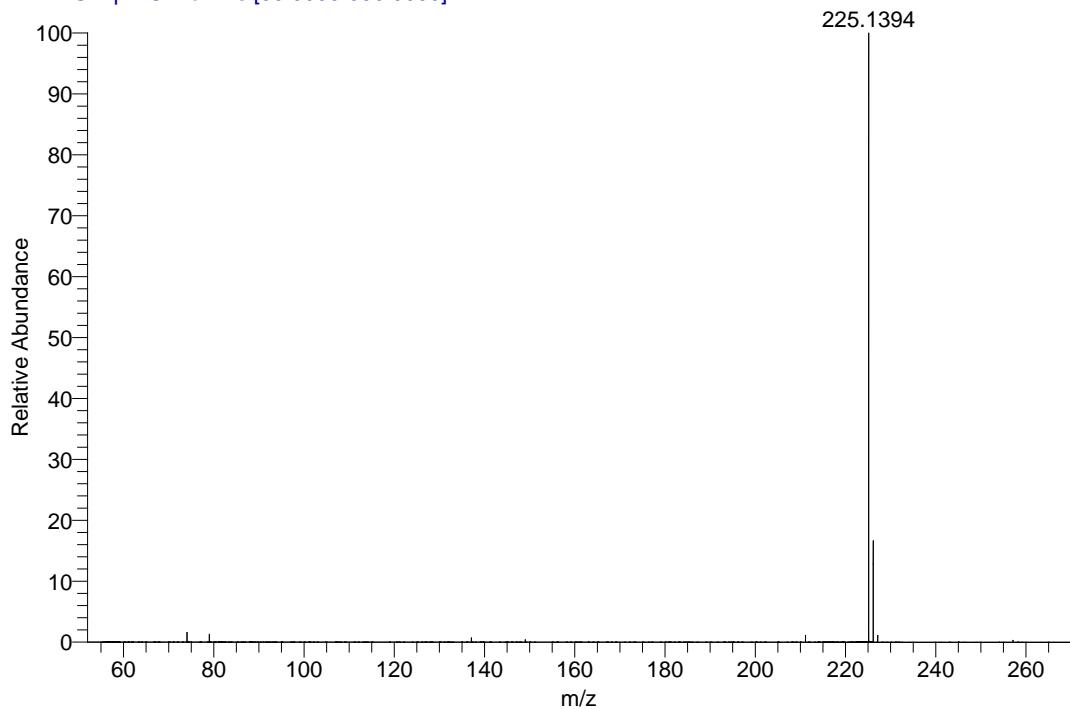
**5o. 1-methyl-8-(pentan-3-yl)-1H-pyrrolo[3,2-h]quinolone**

MS160221-11-A\_160226173644 #718 RT: 7.07 AV: 1 NL: 1.51E7  
T: FTMS + p NSI Full ms [50.0000-350.0000]



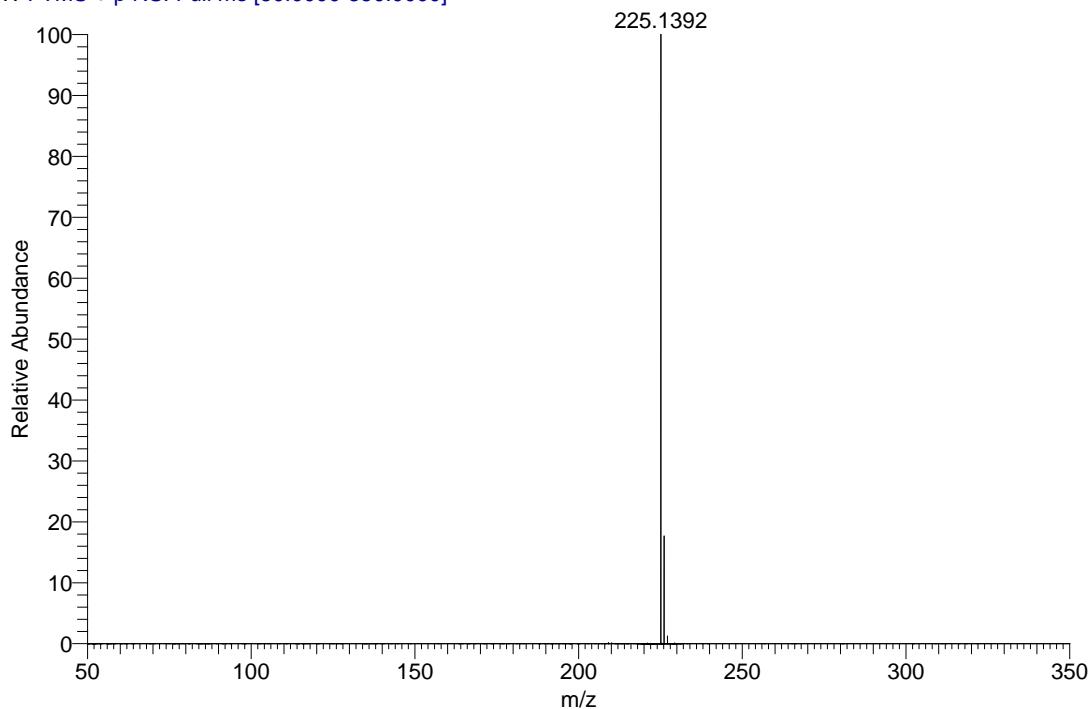
### 5p. 1-methyl-8-(pentan-3-yl)-1H-pyrrolo[3,2-h]quinolone

MS160221-11-G #1448 RT: 12.97 AV: 1 NL: 2.30E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



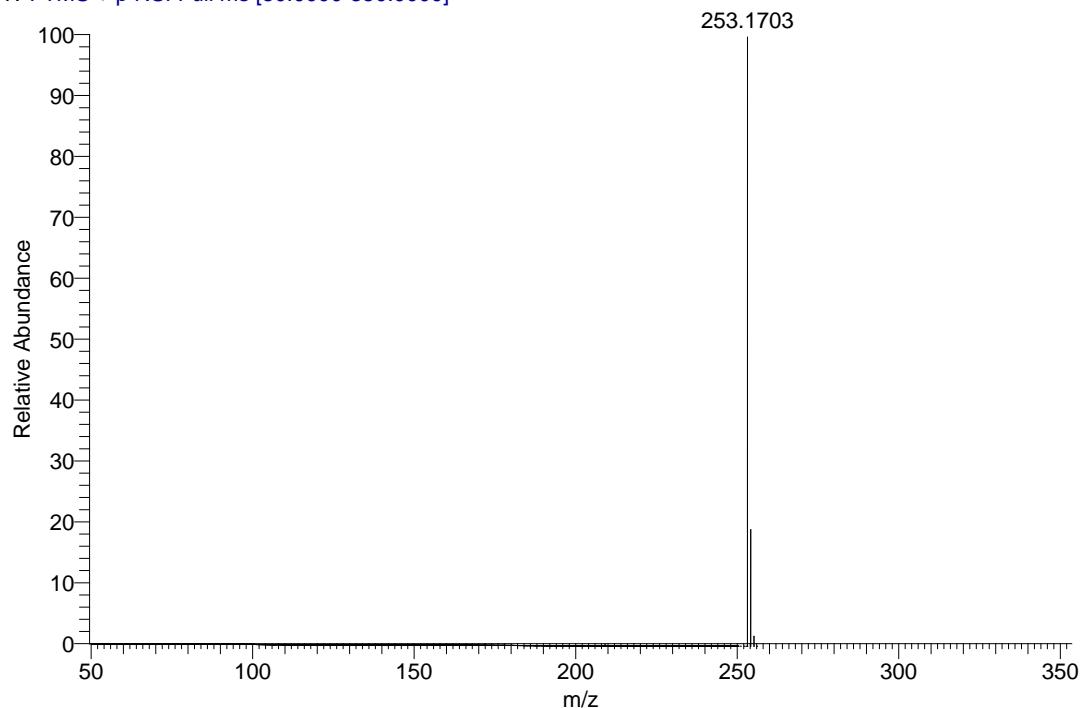
### 5q. 1-methyl-7-propyl-1H-pyrrolo[2,3-f]quinoline

MS160221-10-D #1013 RT: 9.07 AV: 1 NL: 7.41E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



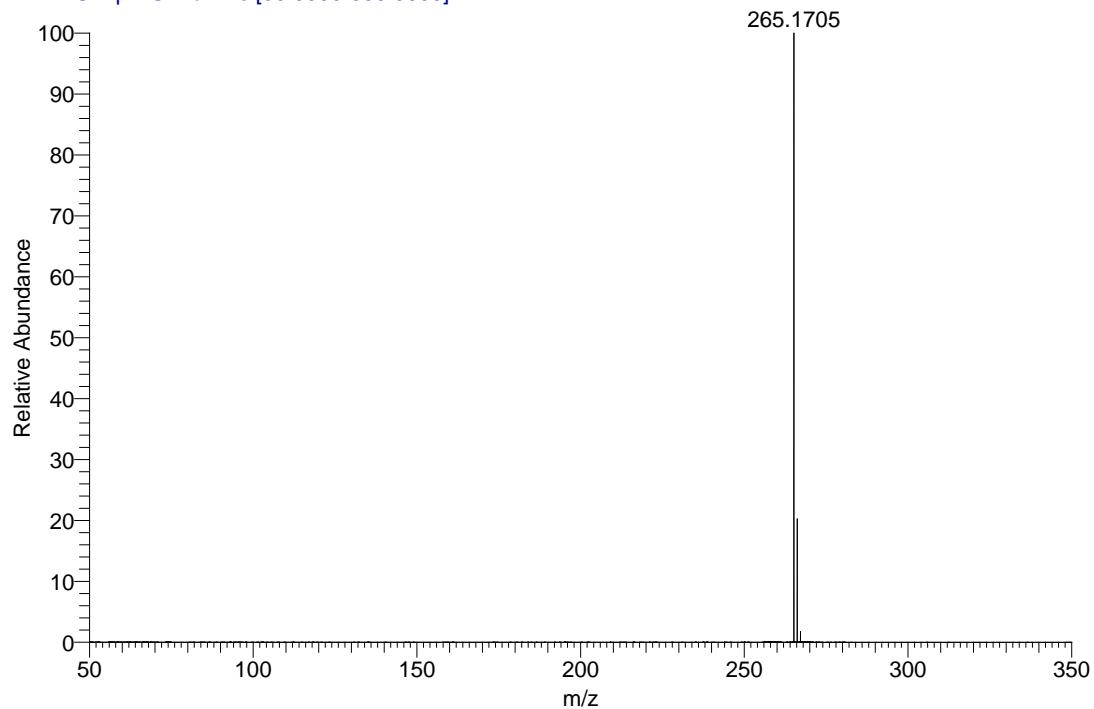
**5r. 1-methyl-7-(pentan-3-yl)-1H-pyrrolo[2,3-f]quinoline**

MS160221-10-B #1099-1142 RT: 9.91-10.30 AV: 44 NL: 5.60E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



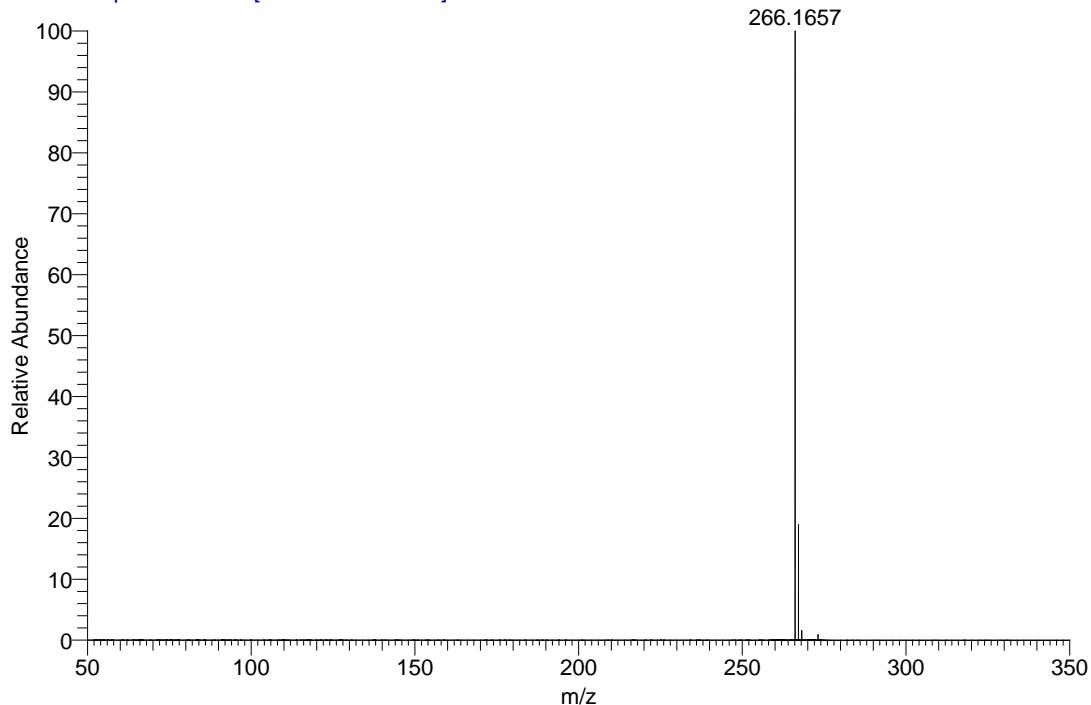
**5s. 7-cyclohexyl-1-methyl-1H-pyrrolo[2,3-f]quinoline**

MS160221-10-C #1254 RT: 11.23 AV: 1 NL: 6.36E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



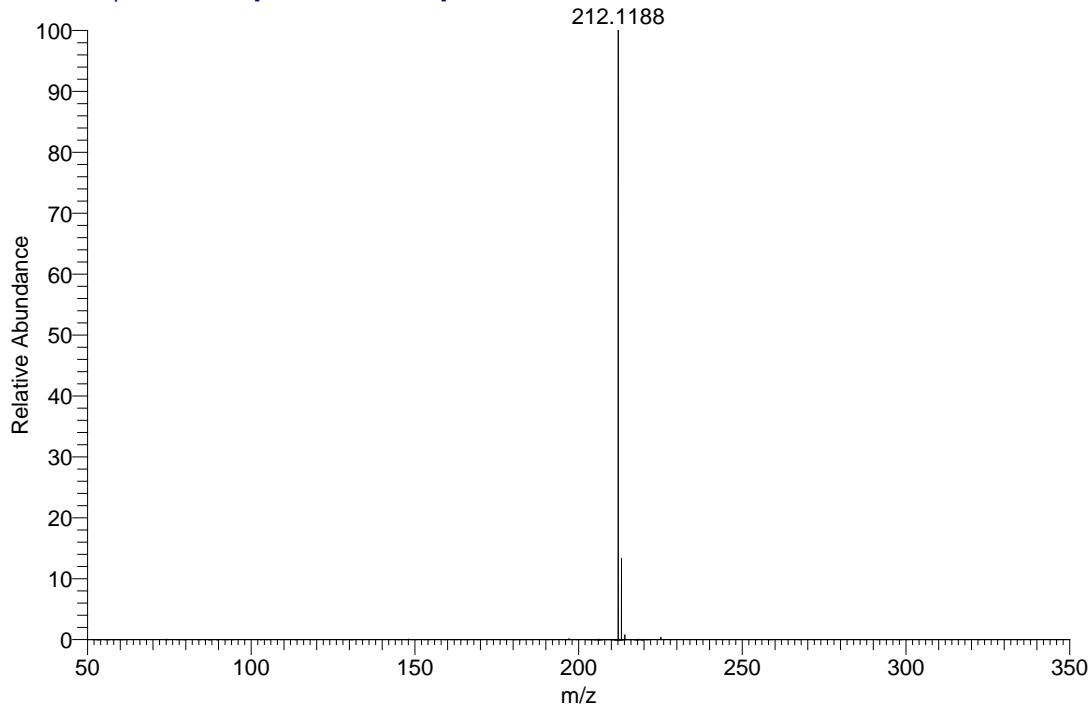
**5t. 7-cyclohexyl-3-methyl-3H-pyrazolo[4,3-f]quinolone**

MS160221-11-H #1410 RT: 12.62 AV: 1 NL: 5.93E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



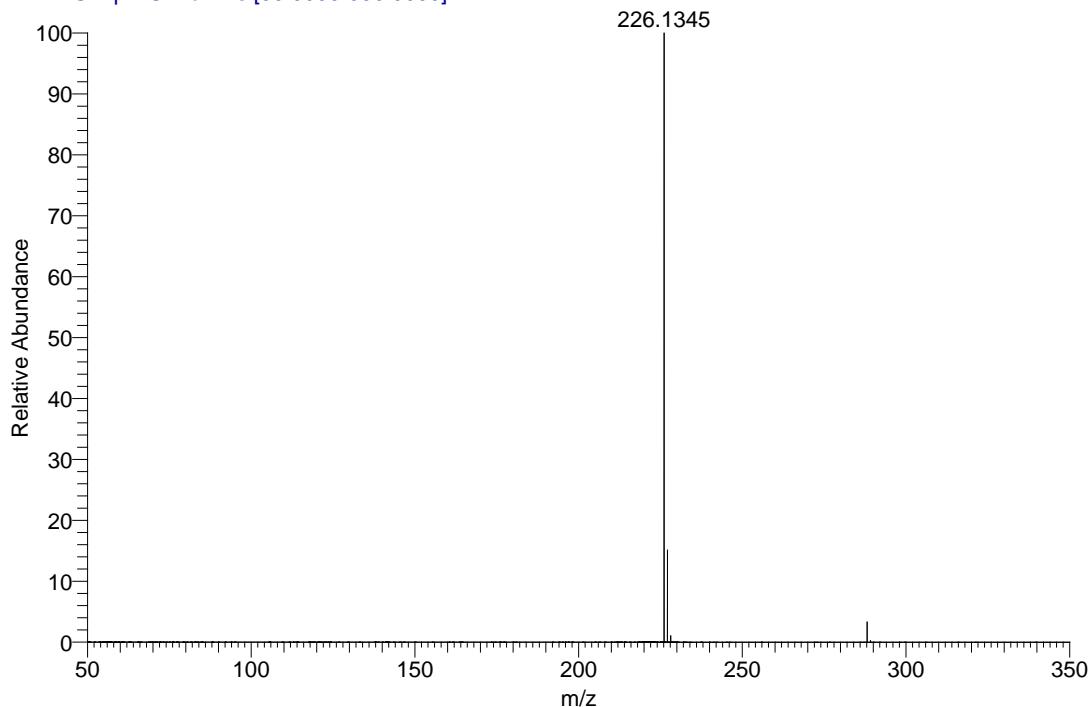
**5u. 7-ethyl-3-methyl-3H-pyrazolo[4,3-f]quinolone**

MS160221-12-G #949 RT: 8.49 AV: 1 NL: 7.35E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



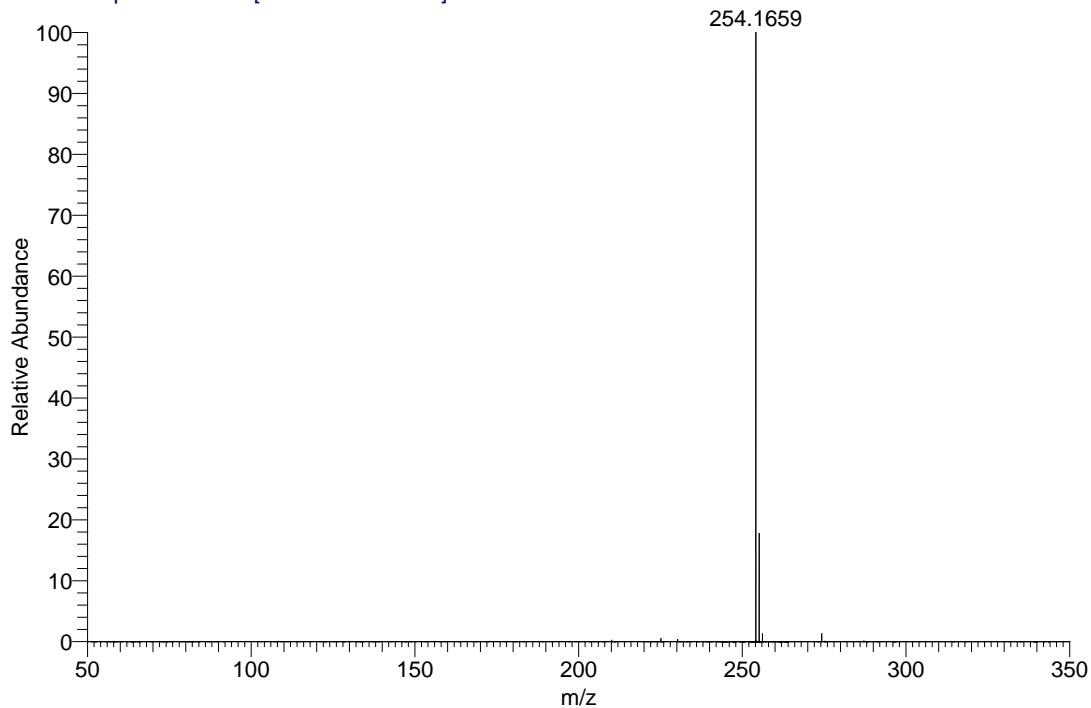
### 5v. 3-methyl-7-propyl-3H-pyrazolo[4,3-f]quinolone

MS160221-12-E #1159 RT: 10.39 AV: 1 NL: 7.16E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]



### 5w. 3-methyl-7-(pentan-3-yl)-3H-pyrazolo[4,3-f]quinolone

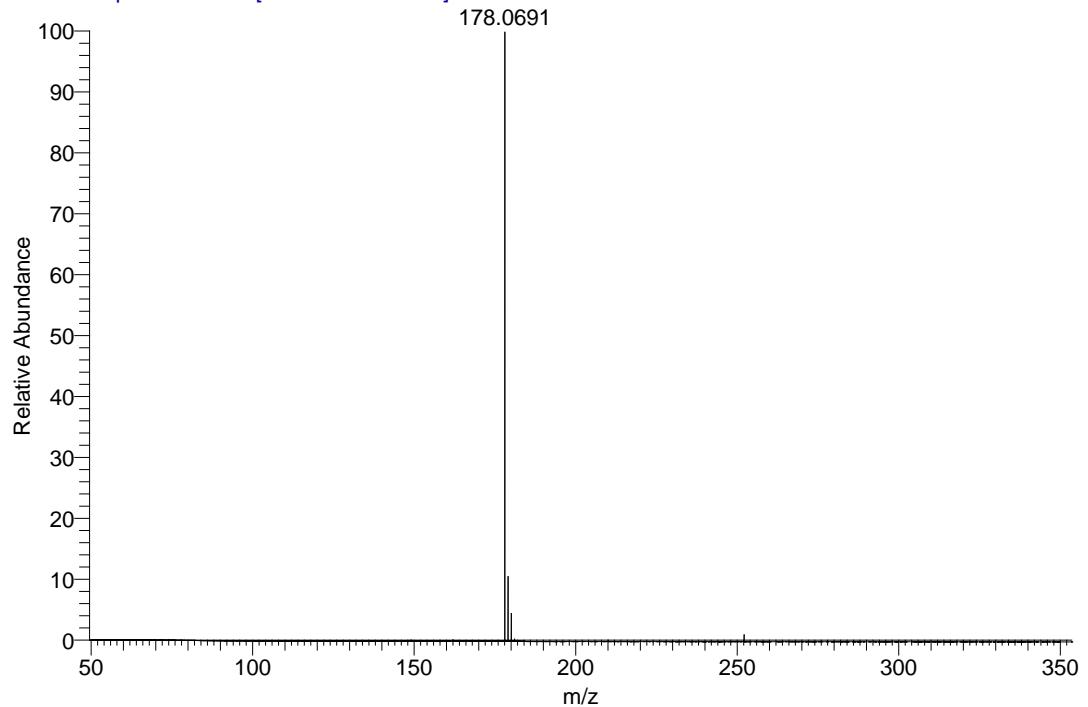
MS160221-12-F #1305 RT: 11.66 AV: 1 NL: 7.70E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]

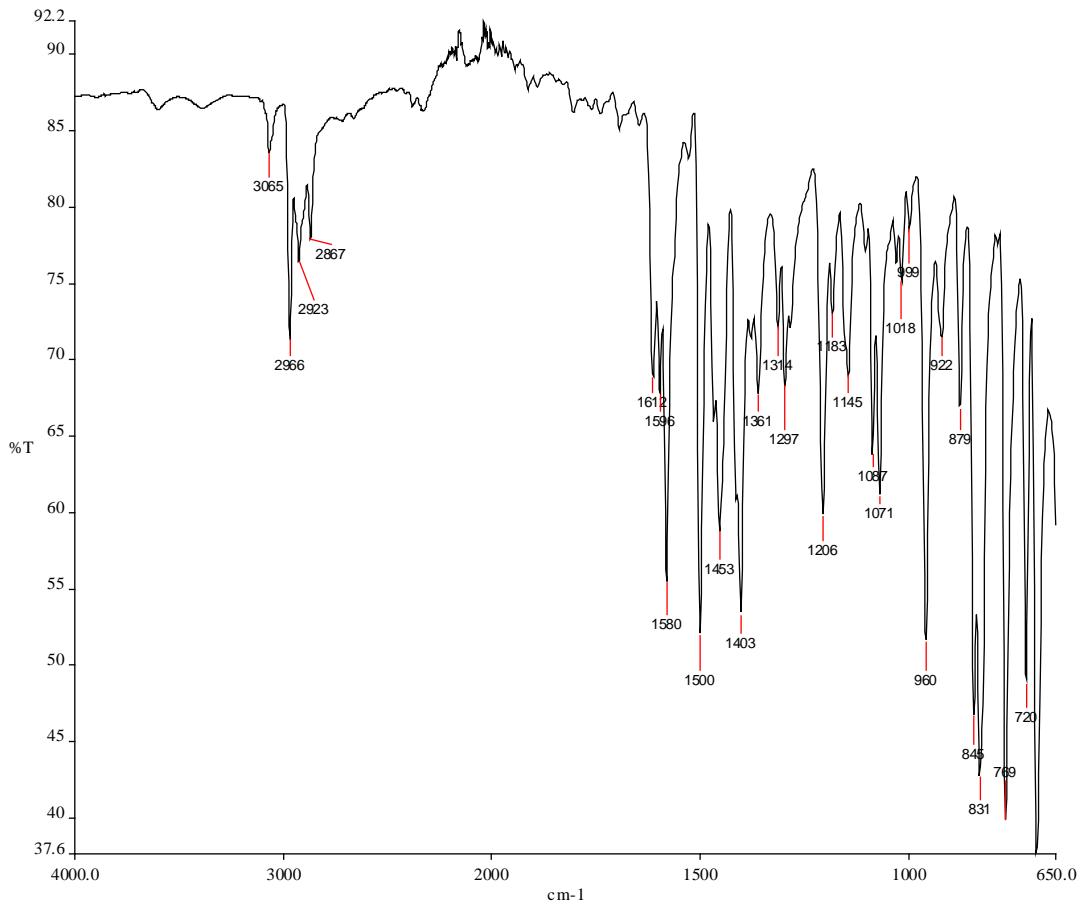


**5x.**

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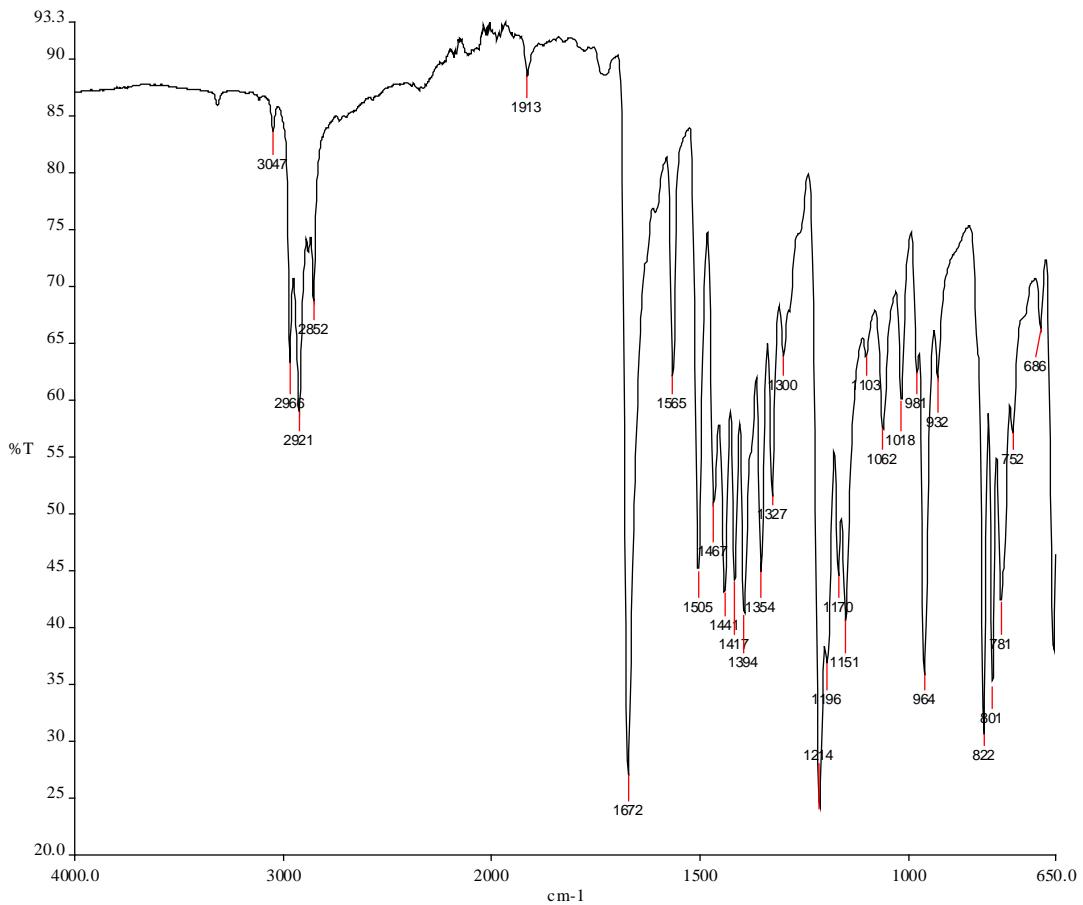
MS160221-2-H #1026-1042 RT: 9.26-9.41 AV: 17 NL: 4.98E9  
T: FTMS + p NSI Full ms [50.0000-350.0000]





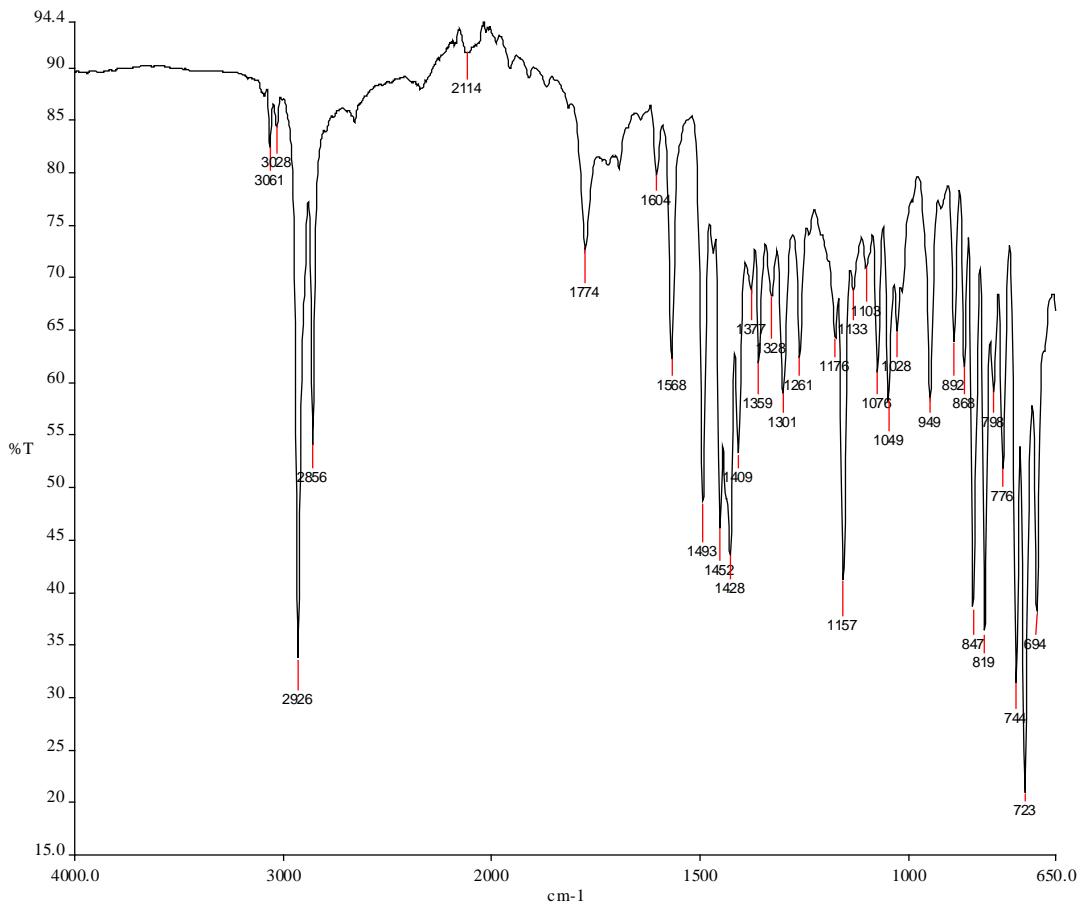
1

**Compound 4o-1. 7-isopropyl-1-phenyl-1H-pyrazolo[3,4-f]quinolone**



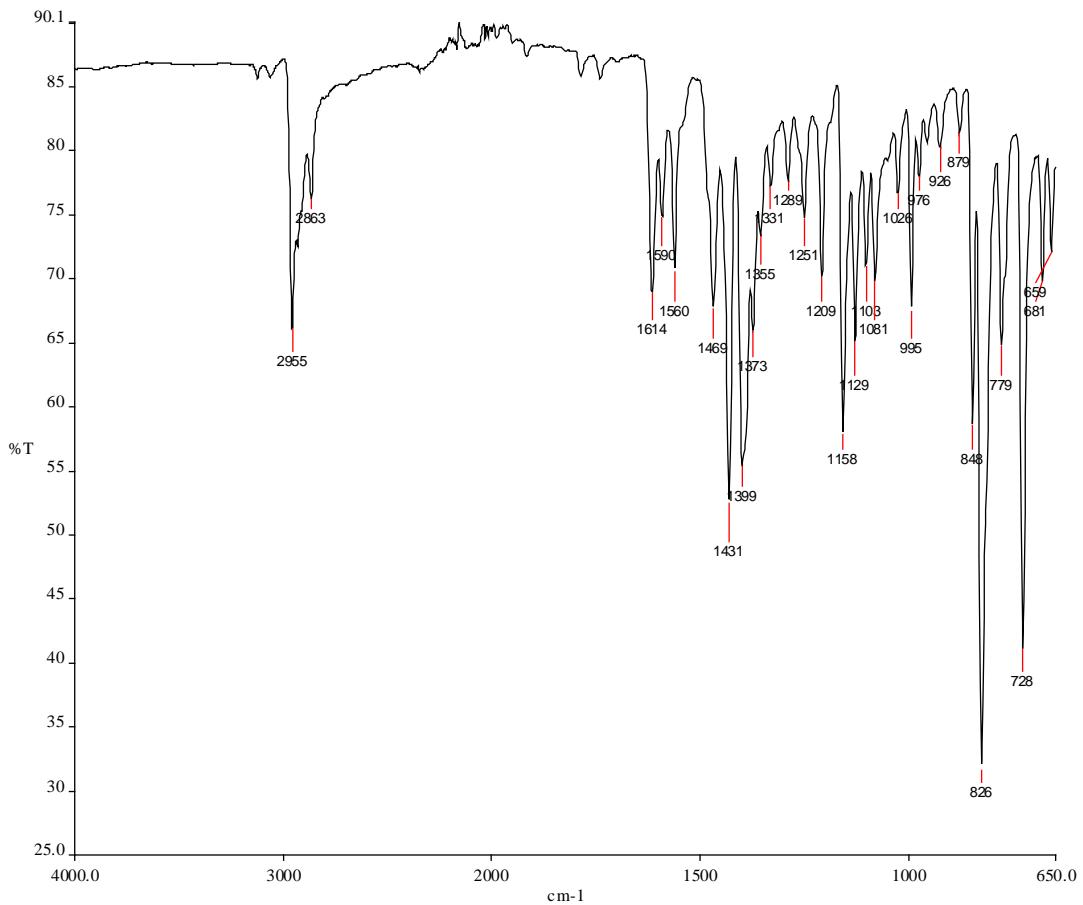
2

**Compound 5c. 1-(5-ethyl-1-methyl-1H-pyrrolo[3,2-*b*]pyridin-2-yl)ethanone**



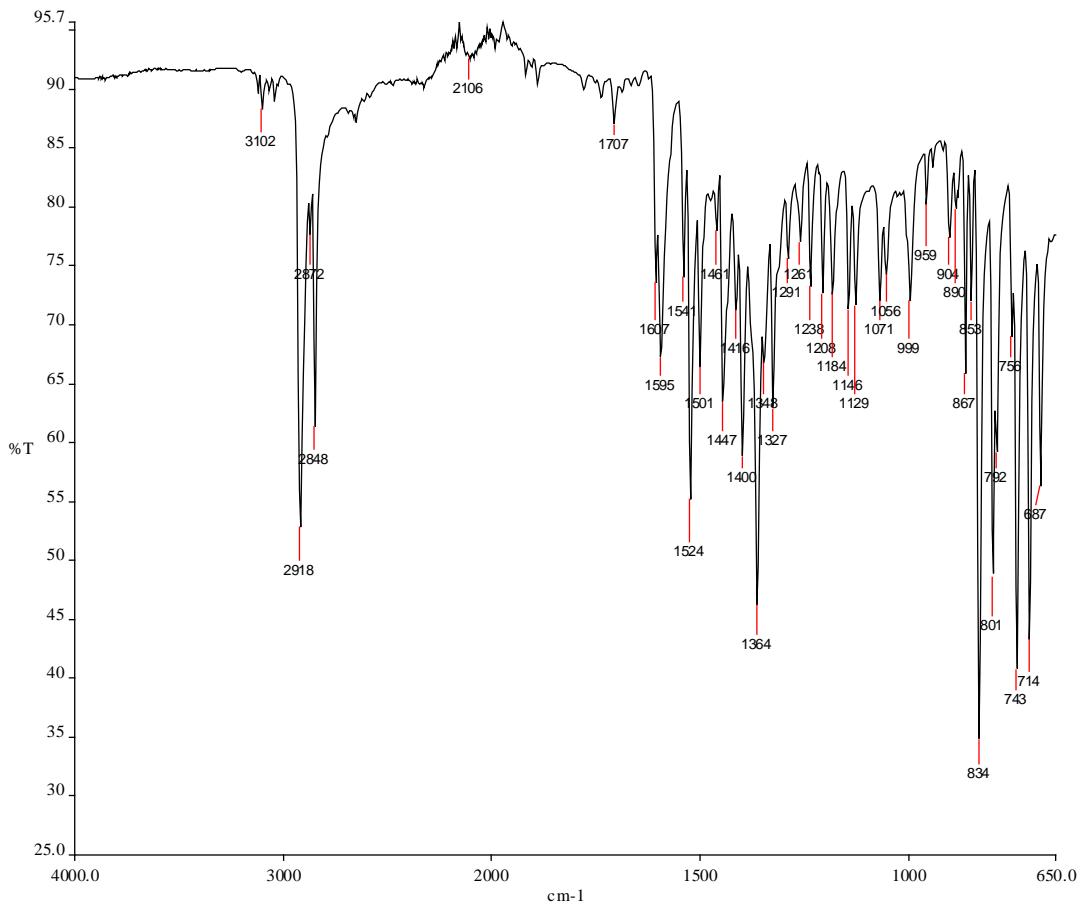
3

**Compound 5i. 1-benzyl-5-cyclohexyl-1H-pyrazolo[4,3-*b*]pyridine**



4

**Compound 4m. 7-isopropyl-2-methyl-2H-pyrazolo[3,4-f]quinolone**



5

**Compound 5n. 8-cyclohexyl-1-methyl-1H-pyrrolo[3,2-h]quinolone**