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Ammonium Niobium Oxalate (ANO) as an efficient catalyst in the Paal-Knorr synthesis of *N*-substituted pyrroles

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1. General information

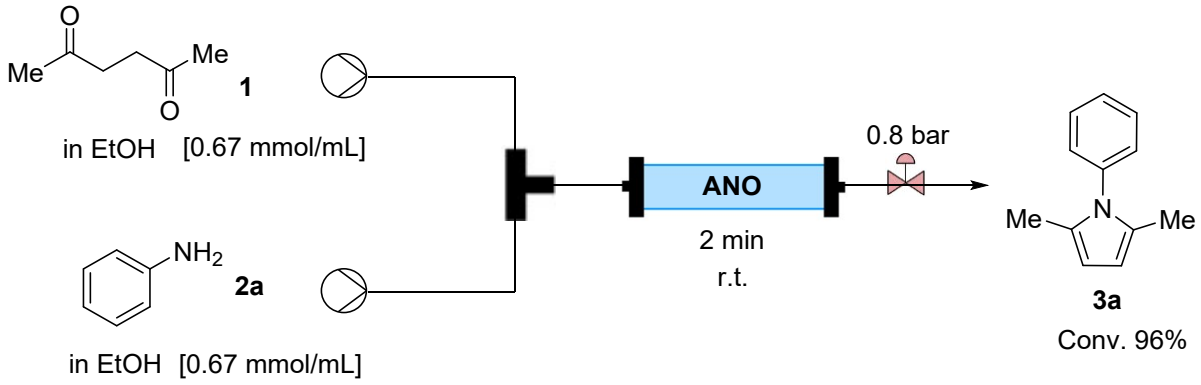
The reactions were monitored by TLC carried out on Merk silica gel (60 F_{254}) by using UV light as visualization agent, and the mixture between 5 % of vanillin in 10 % of H_2SO_4 under heating conditions as developing agent. Merck silica gel (particle size 0.040-0.063 mm) was used to flash chromatography. Hydrogen nuclear magnetic resonance spectra (^{1}H NMR) were obtained on Bruker Avance III HD 400 MHz employing a direct broadband probe at 400 MHz. The spectra were recorded in $CDCl_3$ solutions. The chemical shifts are reported in ppm, referenced to tetramethylsilane (TMS) as the internal reference. Coupling constants (*J*) are reported in Hertz. Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), td (triplet of doublet), and (multiplet). Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained on Bruker Avance III HD 400 MHz employing a direct broadband probe at 100 MHz. The chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$ (δ 77.16 ppm). High-resolution mass spectra (HRMS) were recorded in positive ion mode (APCI) using a Q-TOF spectrometer. Low-resolution mass spectra were obtained with a Shimadzu GC-MS-QP2010 mass spectrometer. Melting point (mp) values were measured in a Marte PFD III instrument. UV-Vis absorption spectroscopy was recorded using a Shimadzu UV-2600 spectrophotometer (data interval = 1.0 nm and slit = 1.0 mm) using three solvents: dichloromethane (DCM), dimethyl sulfoxide (DMSO), and ethanol (EtOH) at 250-500 nm range (concentration at 10 μM). For continuous flow experiments was used Asia Syrris Syringe Pump ASP-3.0, packed bed inox reactor (empty volume: 1.5 mL, length: 94 cm, internal diameter: 4.10 mm).

2. Experimental Section

2.1. General procedure for the synthesis of 2,5-dimethylpyrroles 3a-3d

In a round-bottomed flask were added equimolar amounts (0.5 mmol) of the aniline or amine derivative **2,** hexan-2,5-dione (**1**) and EtOH (1.5 mL) as solvent. In the sequence, ANO (0.023 g, 12 mol%) was added and the resulting mixture was vigorously stirred at room temperature for 30 min. After this time, the mixture was concentrated under vacuum, and the crude purified by column chromatography (silica gel) employing a mixture of hexane/ethyl acetate (99:1) as eluent.

2.2. Synthesis of 2,5-dimethyl-1-phenyl-1*H*-pyrrole 3a under flow conditions



In a flow line, a solution of hexan-2,5-dione **1** in EtOH (0.67 mmol/mL) was pumped through a T-mixer with a second stream containing aniline **2a** in EtOH (0.67 mmol/mL) using Syrris pumps in a flow rate of 0.375 mL/min for both pumps. The combined stream then flows through an inox packed bed reactor (empty volume: 1.5 mL, length: 9.4 cm, internal diameter: 4.10 mm) filled by ANO catalyst (1.136 g). The mentioned reactor was kept at the room temperature. All conversion values were calculated based on chromatographic profile (conversion of 96% to **3a**).

2.2.1 Recyclability test of the packed bed reactor under continuous flow conditions

In a flow line, a solution of hexan-2,5-dione **1** in EtOH (0.67 mmol/mL) was pumped through a T-mixer with a second stream containing aniline **2a** in EtOH (0.67 mmol/mL) using Syrris pumps in a flow rate of 0.375 mL/min for both pumps. The combined stream then flows through an inox packed bed reactor (empty volume: 1.5 mL, length: 9.4 cm, internal diameter: 4.10 mm) filled by ANO catalyst (1.136 g). The mentioned reactor was kept at the room temperature. After each reaction, EtOH was pumped through the packed bed reactor for 10 minutes. This procedure was repeated 6 times.

2.2.2 Image of the apparatus for the synthesis of 2,5-dimethyl-1-phenyl-1*H*-pyrrole 3a under flow conditions

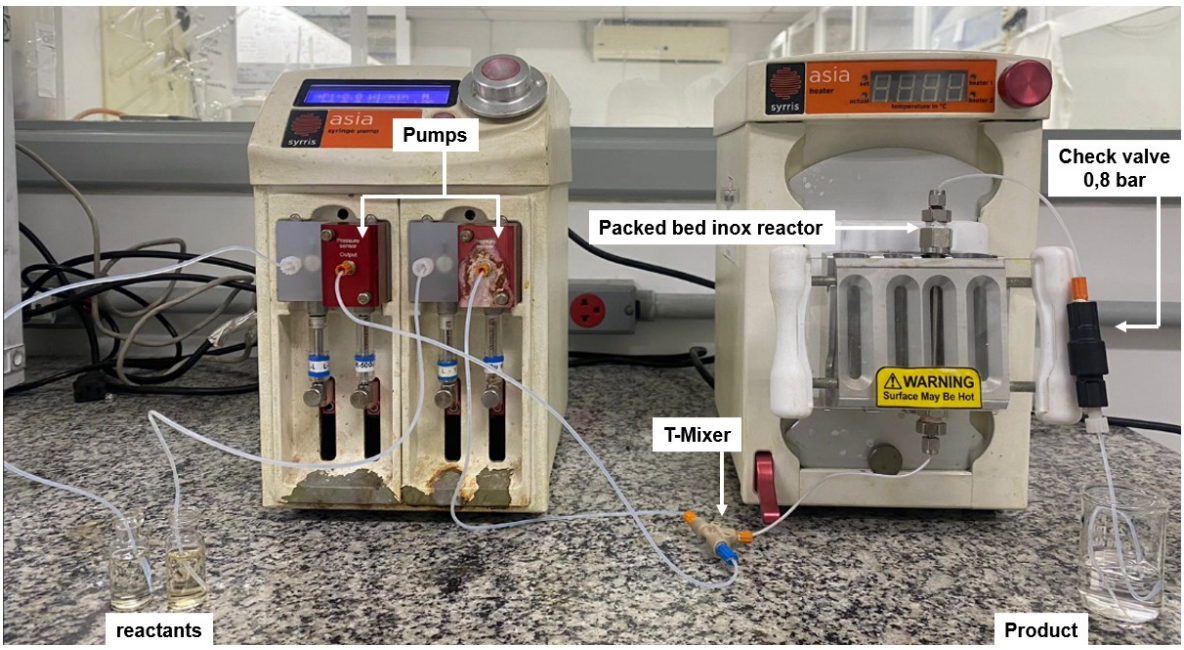


Figure S2. Image of Set up Continuous Flow for Synthesis of 2,5-dimethyl-1-phenyl-1*H*-pyrrole **3a** under flow conditions.

2.2.3 Chromatographic analysis of the synthesis of 2,5-dimethyl-1-phenyl-1*H*-pyrrole 3a under flow conditions

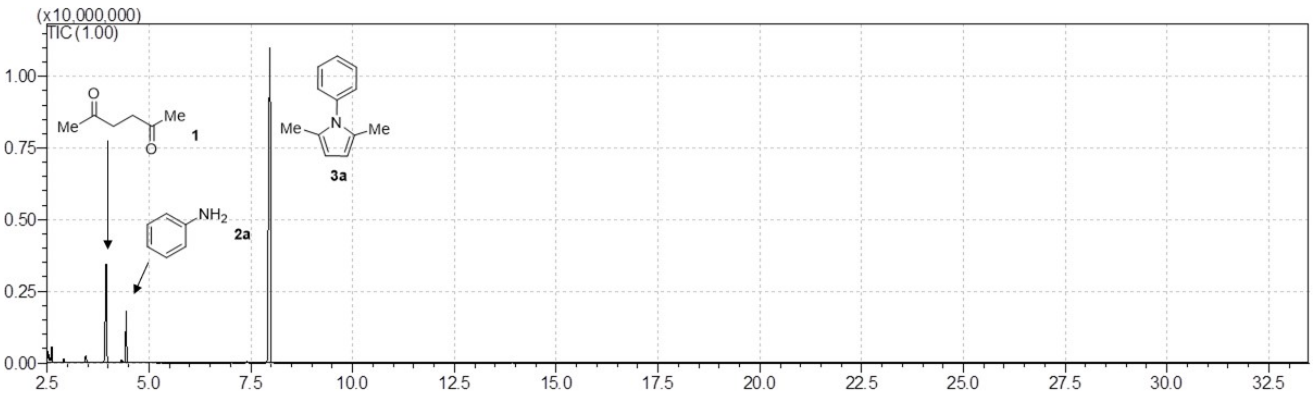


Figure S3. Chromatographic profile obtained by GC-MS after the optimized continuous flow conditions. Retention time: 3.92 min – hexan-2,5-dione, 4.43 min – aniline, 7.96 min - 2,5-dimethyl-1-phenyl-1*H*-pyrrole. *Experimental Conditions*: hexan-2,5-dione (0.5 mmol) in EtOH (0.75 mL), aniline (0.5 mmol) in EtOH (0.75 mL), packed bed inox filled with ANO catalyst (1.136 g) at room temperature and residence time of 5 min. Conversion of 92%. *Analyze Conditions*: oven programming, 50 °C for 2 min, heated for 20 °C/min until 280 °C and maintained 20 min.

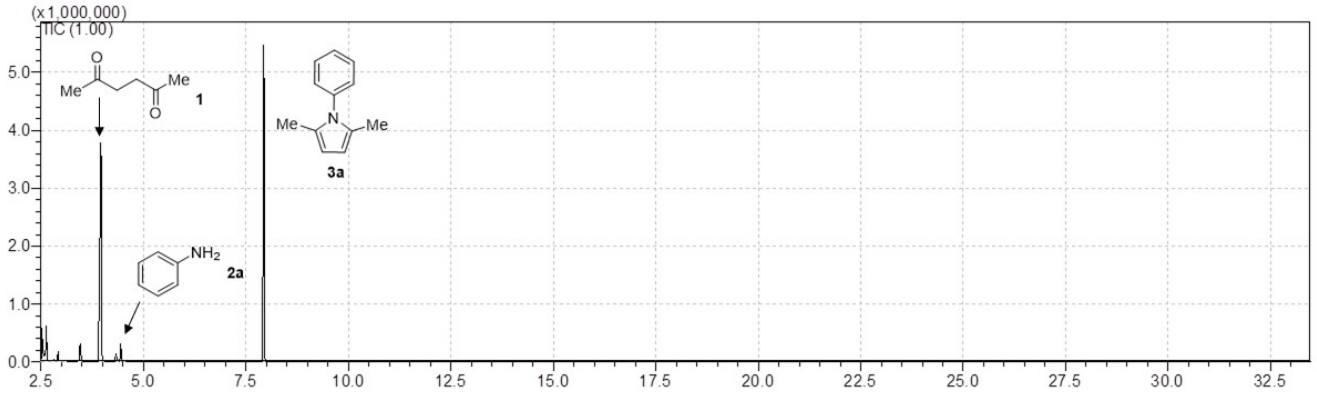


Figure S4. Chromatographic profile obtained by GC-MS after the optimized continuous flow conditions. Retention time: 3.92 min – hexan-2,5-dione, 4.43 min – aniline, 7.96 min - 2,5-dimethyl-1-phenyl-1*H*-pyrrole. *Experimental Conditions*: hexan-2,5-dione (0.5 mmol) in EtOH (0.75 mL), aniline (0.5 mmol) in EtOH (0.75 mL), packed bed inox filled with ANO catalyst (1.136 g) at room temperature and residence time of 3 min. Conversion of 96%. *Analyze Conditions*: oven programming, 50 °C for 2 min, heated for 20 °C/min until 280 °C and maintained 20 min.

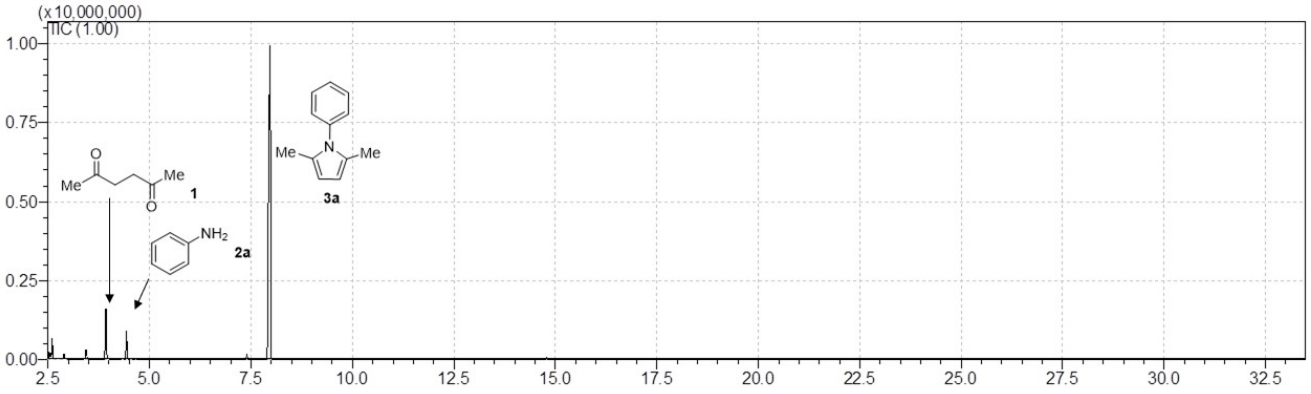
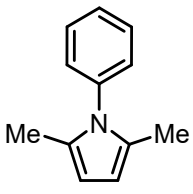


Figure S5. Chromatographic profile obtained by GC-MS after the optimized continuous flow conditions. Retention time: 3.92 min – hexan-2,5-dione, 4.43 min – aniline, 7.96 min - 2,5-dimethyl-1-phenyl-1*H*-pyrrole. *Experimental Conditions*: hexan-2,5-dione (0.5 mmol) in EtOH (0.75 mL), aniline (0.5 mmol) in EtOH (0.75 mL), packed bed inox filled with ANO catalyst (1.136 g) at room temperature and residence time of 2 min. Conversion of 96%. *Analyze Conditions*: oven programming, 50 °C for 2 min, heated for 20 °C/min until 280 °C and maintained 20 min.

2.1. Spectral data for the compounds 3a-3y

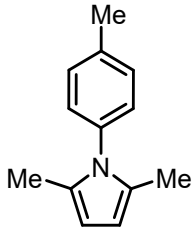
2,5-dimethyl-1-phenyl-1*H*-pyrrole (**3a**)[1]



Yield: 0.079 g (93%); yellow solid, mp: 50–52 °C; Lit.[1]: 49–50 °C. **^{1}H NMR** (400 MHz,

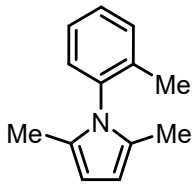
$CDCl_3$) δ (ppm) 7.45–7.35 (m, 3H), 7.21–7.18 (m, 2H), 5.90 (s, 2H), 2.02 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 139.1, 129.1, 128.8, 128.3, 127.7, 105.7, 13.1.

2,5-dimethyl-1-(*p*-tolyl)-1*H*-pyrrole (**3b**)[1]



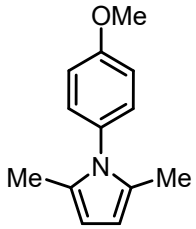
Yield: 0.074 g (80%); brown solid, mp: 44–46 °C; Lit.[1]: 43–44 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.25 (d, *J* = 7.9 Hz, 2H), 7.10–7.08 (m, 2H), 5.88 (s, 2H), 2.41 (s, 3H), 2.02 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 137.6, 136.5, 129.8, 128.9, 128.0, 105.5, 21.3, 13.1.

2,5-dimethyl-1-(o-tolyl)-1*H*-pyrrole (**3c**)[1]



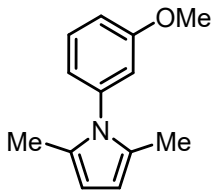
Yield: 0.090 g (97%); brown oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.40–7.36 (m, 1H), 7.15 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.04–7.00 (m, 2H); 5.91 (s, 2H), 3.77 (s, 3H), 1.96 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ (ppm) 156.0, 130.3, 129.5, 129.2, 127.7, 120.7, 112.1, 105.3, 55.8, 12.7.

1-(4-methoxyphenyl)-2,5-dimethyl-1*H*-pyrrole (**3d**)[1]



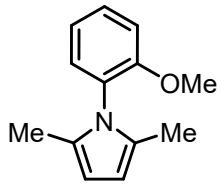
Yield: 0.091 g (90%); brown solid, mp: 58–59 °C; Lit.[1]: 55–57 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.14–7.10 (m, 2H), 6.98–6.94 (m, 2H), 5.88 (s, 2H), 3.85 (s, 3H), 2.01 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 159.9, 131.9, 129.3, 129.1, 114.3, 105.4, 55.6, 13.1.

1-(3-methoxyphenyl)-2,5-dimethyl-1*H*-pyrrole (**3e**)[1]



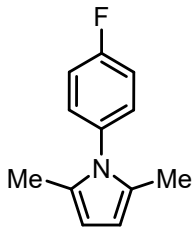
Yield: 0.097 g (96%); brown oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.37–7.33 (m, 1H), 6.95–6.92 (m, 1H), 6.82–6.79 (m, 1H), 6.76–6.75 (m, 1H), 5.89 (s, 2H), 3.82 (s, 3H), 2.05 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 160.2, 140.2, 129.8, 128.9, 120.7, 114.0, 113.6, 105.7, 55.5, 13.1.

1-(2-methoxyphenyl)-2,5-dimethyl-1*H*-pyrrole (**3f**)[1]



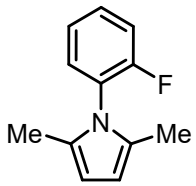
Yield: 0.100 g (99%); brown solid, mp: 63–64 °C; Lit.[1]: 62-63 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.40–7.36 (m, 1H), 7.16 (dd, J = 8.0, 1.8 Hz, 1H), 7.04–7.00 (m, 2H), 5.91 (s, 2H), 3.77 (s, 3H), 1.96 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 156.1, 130.3, 129.5, 129.2, 127.7, 120.7, 112.1, 105.3, 55.8, 12.7.

1-(4-fluorophenyl)-2,5-dimethyl-1*H*-pyrrole (**3g**)[1]



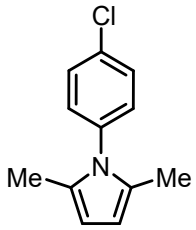
Yield: 0.090 g (95%); yellow solid, mp: 51–53 °C; Lit.[1]: 51–52 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.21–7.06 (m, 4H), 5.89 (s, 2H), 2.01 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 163.2, 160.7, 135.1 (d, *J* = 3.2 Hz), 129.9 (d, *J* = 8.5 Hz), 128.9, 116.1 (d, *J* = 22.6 Hz), 13.0.

1-(2-fluorophenyl)-2,5-dimethyl-1*H*-pyrrole (**3h**)[1]



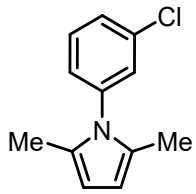
Yield: 0.092 g (97%); yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.42 – 7.32 (m, 1H), 7.29–7.15 (m, 3H), 5.93 (s, 2H), 2.01 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 158.5 (d, *J* = 250.6 Hz), 130.7, 129.8 (d, *J* = 7.7 Hz), 129.1, 126.7 (d, *J* = 13.1 Hz), 124.5 (d, *J* = 4.0 Hz), 116.7 (d, *J* = 20.3 Hz), 106.2, 12.5.

1-(4-chlorophenyl)-2,5-dimethyl-1*H*-pyrrole (**3i**)[1]



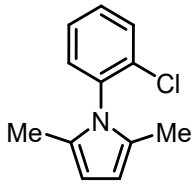
Yield: 0.101 g (98%); brown solid, mp: 56–57 °C; Lit.[1]: 56–57 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.44–7.41 (m, 2H), 7.16–7.13 (m, 2H), 5.90 (s, 2H), 2.02 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 137.6, 133.7, 129.6, 129.4, 128.8, 106.2, 13.1.

1-(3-chlorophenyl)-2,5-dimethyl-1*H*-pyrrole (**3j**)[2]



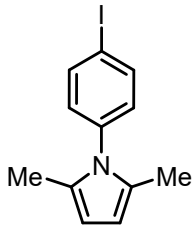
Yield: 0.098 g (95%); brown solid, mp: 45–47 °C; Lit.[2]: 39–40 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.39–7.37 (m, 2H), 7.24–7.22 (m, 1H), 7.13–7.10 (m, 1H), 5.90 (s, 2H), 2.03 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 140.4, 134.7, 130.1, 128.8, 128.7, 128.1, 126.7, 106.3, 13.1.

1-(2-chlorophenyl)-2,5-dimethyl-1*H*-pyrrole (**3k**)[2]



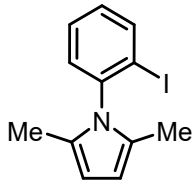
Yield: 0.101 g (98%); brown solid, mp: 43–45 °C; Lit.[2]: 45–47 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.55–7.52 (m, 1H), 7.39–7.35 (m, 2H), 7.30–7.27 (m, 1H), 5.93 (s, 2H), 1.96 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 136.9, 134.2, 130.7, 130.3, 129.7, 128.9, 127.7, 105.8, 12.6.

1-(4-iodophenyl)-2,5-dimethyl-1*H*-pyrrole (**3l**)[1]



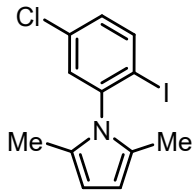
Yield: 0.121 g (81%); yellow solid, mp: 67–68 °C; Lit.[1]: 67–68 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.78 (d, J = 8.4 Hz, 2H), 6.96 (d, J = 8.4 Hz, 2H), 5.90 (s, 2H), 2.02 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 138.8, 138.4, 130.3, 128.8, 106.3, 93.0, 13.1.

1-(2-iodophenyl)-2,5-dimethyl-1*H*-pyrrole (**3m**)[3]



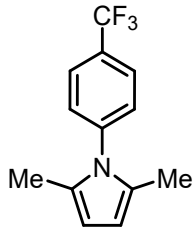
Yield: 0.129 g (87%); yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.95 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.47-7.43 (m, 1H), 7.27 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.15-7.11 (m, 1H), 5.93 (s, 2H), 1.95 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 142.2, 139.6, 129.9, 129.8, 129.2, 128.2, 105.8, 100.7, 12.9.

1-(5-chloro-2-iodophenyl)-2,5-dimethyl-1*H*-pyrrole (**3n**)[4]



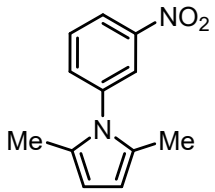
Yield: 0.159 g (96%); white solid, mp: 60–62 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.86 (d, *J* = 8.5 Hz, 1H), 7.29 (d, *J* = 2.4 Hz, 1H), 7.15 (dd, *J* = 8.5, 2.4 Hz, 1H), 5.92 (s, 2H), 1.96 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 143.6, 140.3, 135.1, 130.4, 130.1, 128.1, 106.3, 98.2, 12.9.

2,5-dimethyl-1-(4-(trifluoromethyl)phenyl)-1*H*-pyrrole (**3o**)[5]



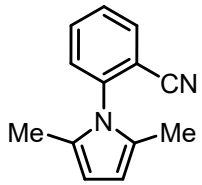
Yield: 0.114 g (95%); brown solid, mp: 56–58 °C; Lit.[5]: 55–57 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.74 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 5.93 (s, 2H), 2.05 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 142.4, 129.9 (q, *J* = 32.6 Hz), 128.8, 128.7, 126.4 (q, *J* = 3.7 Hz), 124.0 (q, *J*= 270 Hz), 106.7, 13.2.

2,5-dimethyl-1-(3-nitrophenyl)-1*H*-pyrrole (**3p**)[6]



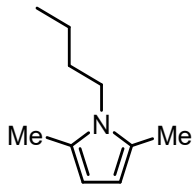
Yield: 0.103 g (95%); yellow solid, mp: 84–86 °C; Lit.[6]: 85–86 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 8.29–8.26 (m, 1H), 8.12–8.11 (m, 1H), 7.69–7.65 (m, 1H), 7.59–7.56 (m, 1H), 5.95 (s, 2H), 2.06 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 148.8, 140.3, 134.4, 130.1, 128.8, 123.4, 122.6, 107.1, 13.2.

2-(2,5-dimethyl-1*H*-pyrrol-1-yl)benzonitrile (**3q**)[6]



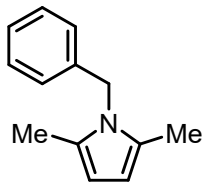
Yield: 0.056 g (57%); yellow solid, mp: 76–78 °C; Lit.[6]: 84–85 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.79 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.72 (td, *J* = 7.8, 1.6 Hz, 1H), 7.54 (td, *J* = 7.7, 1.2 Hz, 1H), 7.35 (dd, *J* = 8.0, 1.2 Hz, 1H), 5.96 (s, 2H), 2.02 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 142.1, 133.7, 133.6, 130.2, 128.9, 128.7, 116.0, 113.6, 107.1, 12.7.

1-butyl-2,5-dimethyl-1*H*-pyrrole (**3r**)[2]



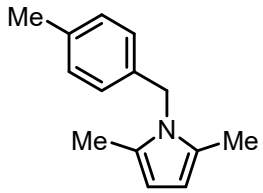
Yield: 0.047 g (62%); yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 5.75 (s, 1H), 3.76–3.68 (m, 1H), 2.21 (s, 3H), 1.68–1.48 (m, 2H), 1.45–1.30 (m, 1H), 0.95 (t, *J* = 7.4 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 127.4, 105.0, 43.5, 33.3, 20.3, 13.9, 12.6.

1-benzyl-2,5-dimethyl-1*H*-pyrrole (**3s**)[5]



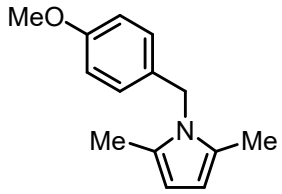
Yield: 0.077 g (83%); white solid, mp: 43–44 °C; Lit.[5]: 43–44 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.30–7.22 (m, 2H), 7.22–7.16 (m, 1H), 6.87 (d, *J* = 7.5 Hz, 2H), 5.85 (s, 2H), 4.98 (s, 2H), 2.12 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 138.6, 128.8, 128.0, 127.1, 125.7, 105.5, 46.8, 12.5.

2,5-dimethyl-1-(4-methylbenzyl)-1*H*-pyrrole (**3t**)[5]



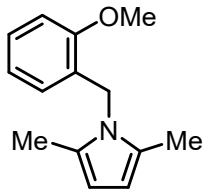
Yield: 0.080 g (80%); yellow solid, mp: 65–67 °C; Lit.[5]: 61–62 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.08 (d, *J* = 7.8 Hz, 2H), 6.77 (d, *J* = 7.8 Hz, 2H), 5.84 (s, 2H), 4.95 (s, 2H), 2.30 (s, 3H), 2.13 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 136.7, 135.6, 129.5, 128.1, 125.7, 105.4, 46.6, 21.1, 12.5.

1-(4-methoxybenzyl)-2,5-dimethyl-1*H*-pyrrole (**3u**)[5]



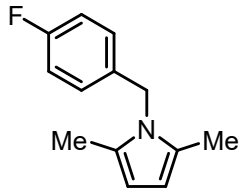
Yield: 0.083 g (77%); white solid, mp: 65–67 °C; Lit.[5]: 65–67 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 6.92–6.71 (m, 1H), 5.84 (d, *J* = 3.1 Hz, 1H), 4.93 (d, *J* = 2.5 Hz, 1H), 3.75 (s, 1H), 2.13 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 158.7, 130.6, 127.9, 126.9, 114.2, 105.4, 55.3, 46.2, 12.5.

1-(2-methoxybenzyl)-2,5-dimethyl-1*H*-pyrrole (**3v**)



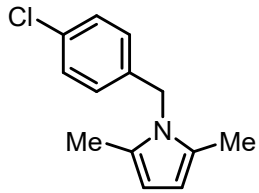
Yield: 0.089 g (83%); brown solid, mp: 73–75 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.19 (dd, *J* = 9.5, 4.8 Hz, 1H), 6.95–6.71 (m, 2H), 6.32–6.16 (m, 1H), 5.87 (dd, *J* = 6.3, 2.7 Hz, 2H), 5.06–4.86 (m, 2H), 3.88 (s, 3H), 2.12 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 156.1, 128.2, 127.9, 126.9, 126.1, 120.9, 109.6, 105.3, 55.3, 42.2, 12.3. HRMS calculated for $C_{14}H_{17}NNaO$ $[M+Na]^+$: 238.1202. Found: 238.1197.

1-(4-fluorobenzyl)-2,5-dimethyl-1*H*-pyrrole (**3w**)[7]



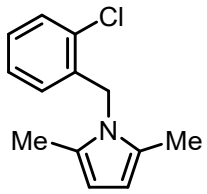
Yield: 0.083 g (82%); white solid, mp: 54–56 °C; Lit.[7]: 54–55 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 6.96 (m, 2H), 6.82 (dd, *J* = 8.4, 5.3 Hz, 2H), 5.85 (s, 2H), 4.95 (s, 2H), 2.12 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 161.9 (d, *J* = 245.0 Hz), 134.3 (d, *J* = 3.1 Hz), 127.9, 127.3 (d, *J* = 8.0 Hz), 115.6 (d, *J* = 21.5 Hz), 105.7, 46.1, 12.5.

1-(4-chlorobenzyl)-2,5-dimethyl-1*H*-pyrrole (**3x**)[5]



Yield: 0.040 g (36%); white solid, mp: 95-97 °C; Lit.[5]: 90–92 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.25 (d, *J* = 8.1 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 5.85 (s, 1H), 4.96 (s, 1H), 2.12 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 137.2, 132.9, 128.9, 127.9, 127.1, 105.8, 46.2, 12.5.

1-(2-chlorobenzyl)-2,5-dimethyl-1*H*-pyrrole (**3y**)[8]



Yield: 0.090 g (82%); yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.35 (d, J = 9.2 Hz, 1H), 7.24–7.04 (m, 2H), 6.24 (d, J = 7.5 Hz, 1H), 5.88 (s, 2H), 5.02 (s, 2H), 2.10 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 136.2, 131.7, 129.2, 128.3, 128.0, 127.5, 126.9, 105.8, 44.7, 12.3.

References

1. H. Lee, B and H. Kim, *Tetrahedron*, 2013, **69**, 6698-9708.
2. H. Zheng, Q. Shi, K. Du, Y. Mei and P. Zhang, *Mol. Divers.*, 2013, **17**, 245–250.
3. R. N. Patil and A. V. Kumar, *ChemistrySelect*, 2018, **3**, 9812–9818.
4. L. Zhang, S-H. Xiang, J. (J). Wang, J. Xiao, J-Q. Wang and B. Tan, *Nat. Commun.*, 2019, **10**, 566.
5. Y. Liu and Y. L. Hu, *J. Iran. Chem. Soc.*, 2018, **15**, 1033–1040.
6. K. Aghapoor, F. Mohsenzadeh, H. R. Darabi and S. Rastgar, *Res. Chem. Interm.*, 2018, **44**, 4063–4072.
7. H. Mahmoudi and A. A. Jafari, *ChemCatChem*, 2013, **5**, 3743–3749.
8. S. Cheraghi, D. Saberi and A. Heydari, *Catal Lett.*, 2014, **144**, 1339–1343.

Selected Spectra

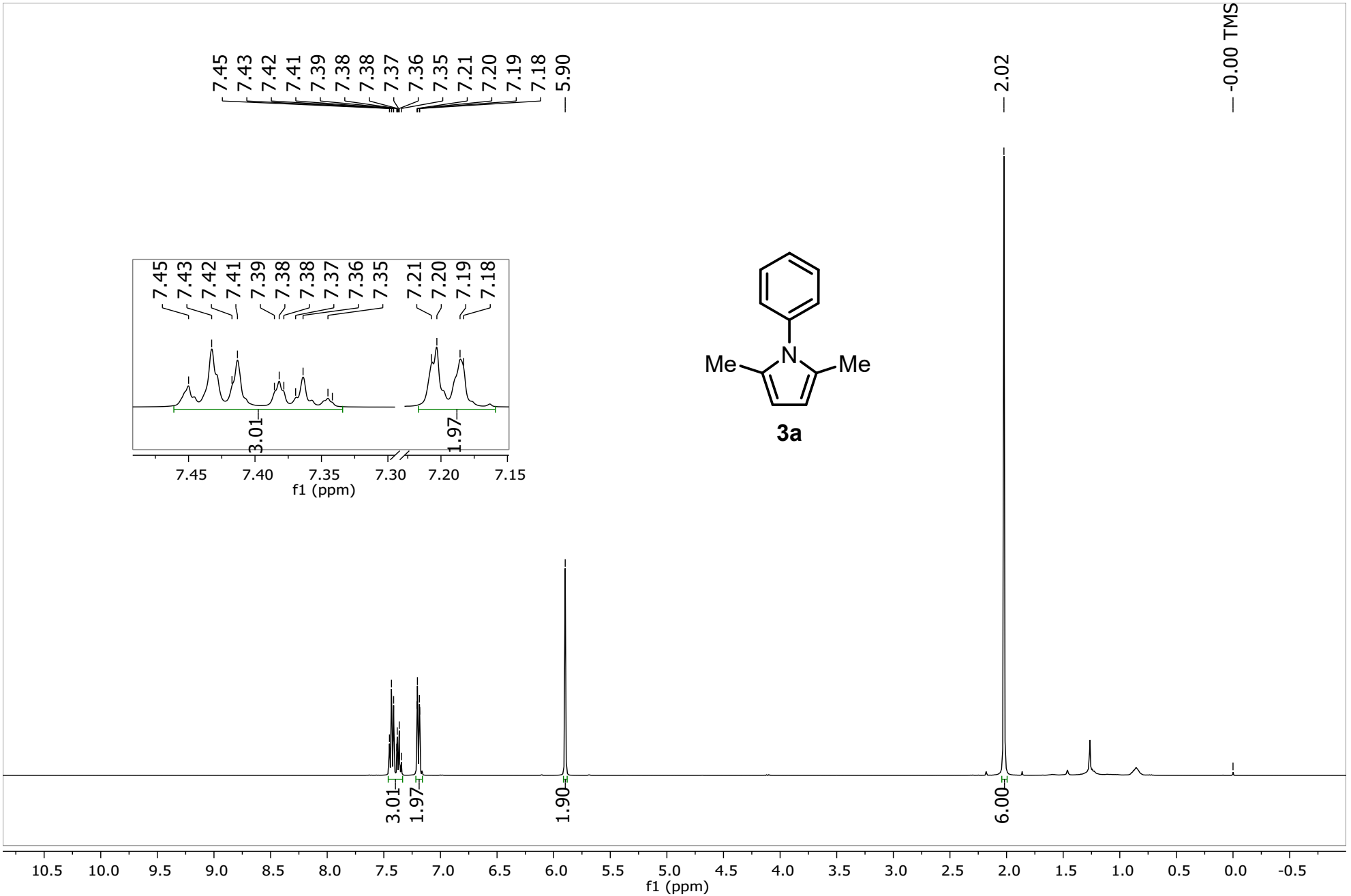


Figure 1. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3a**.

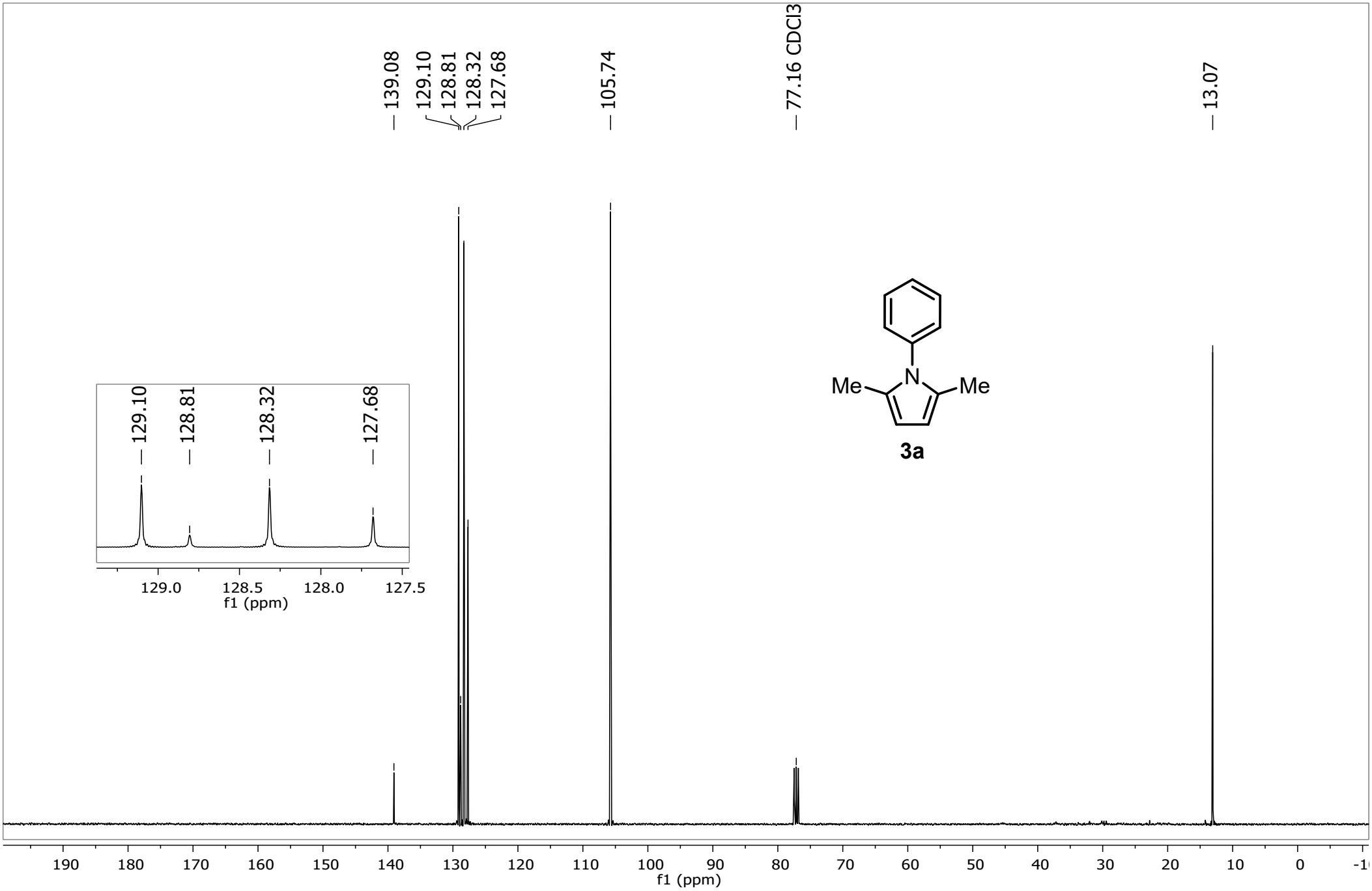


Figure 2. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3a**.

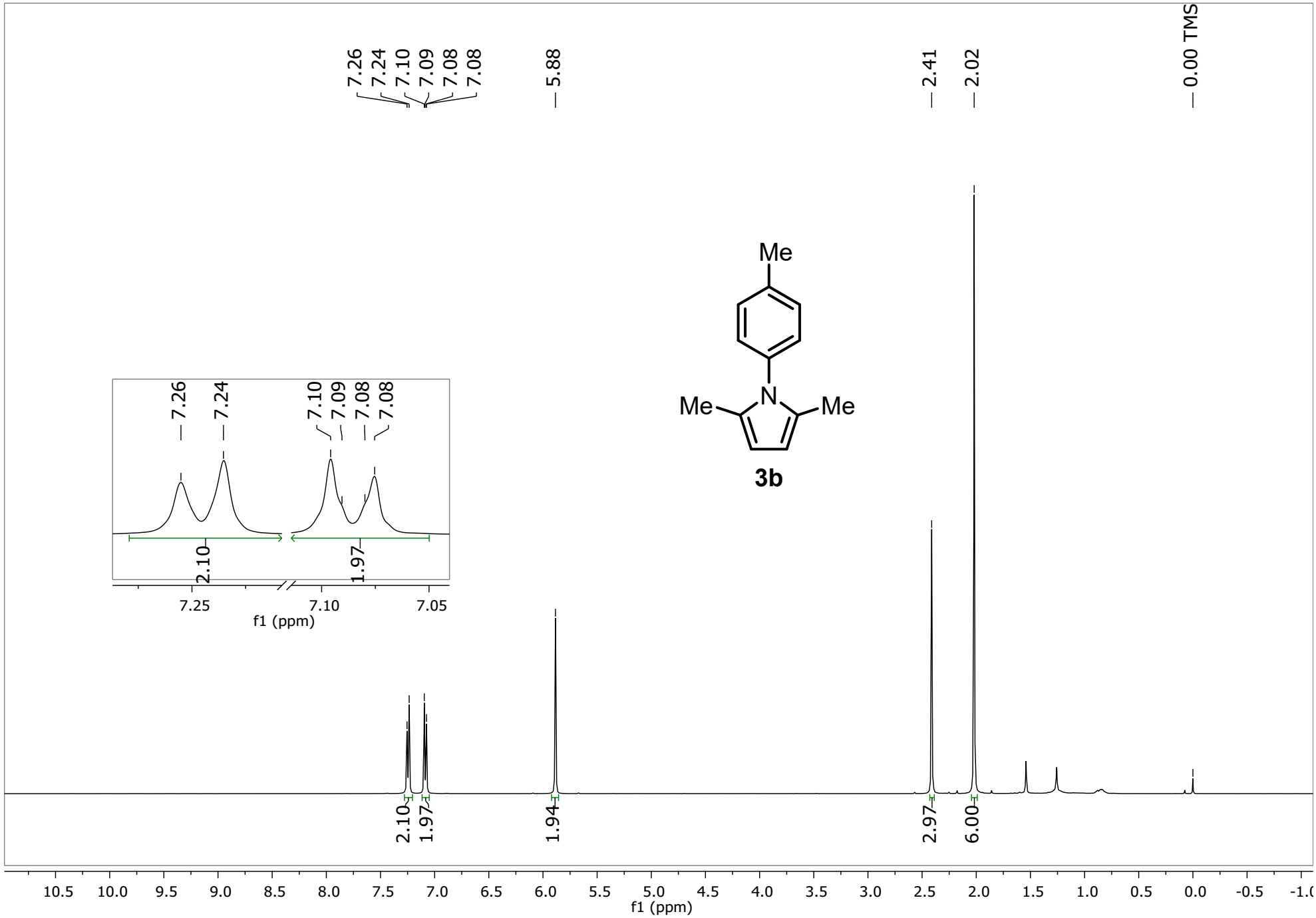


Figure 3. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3b**.

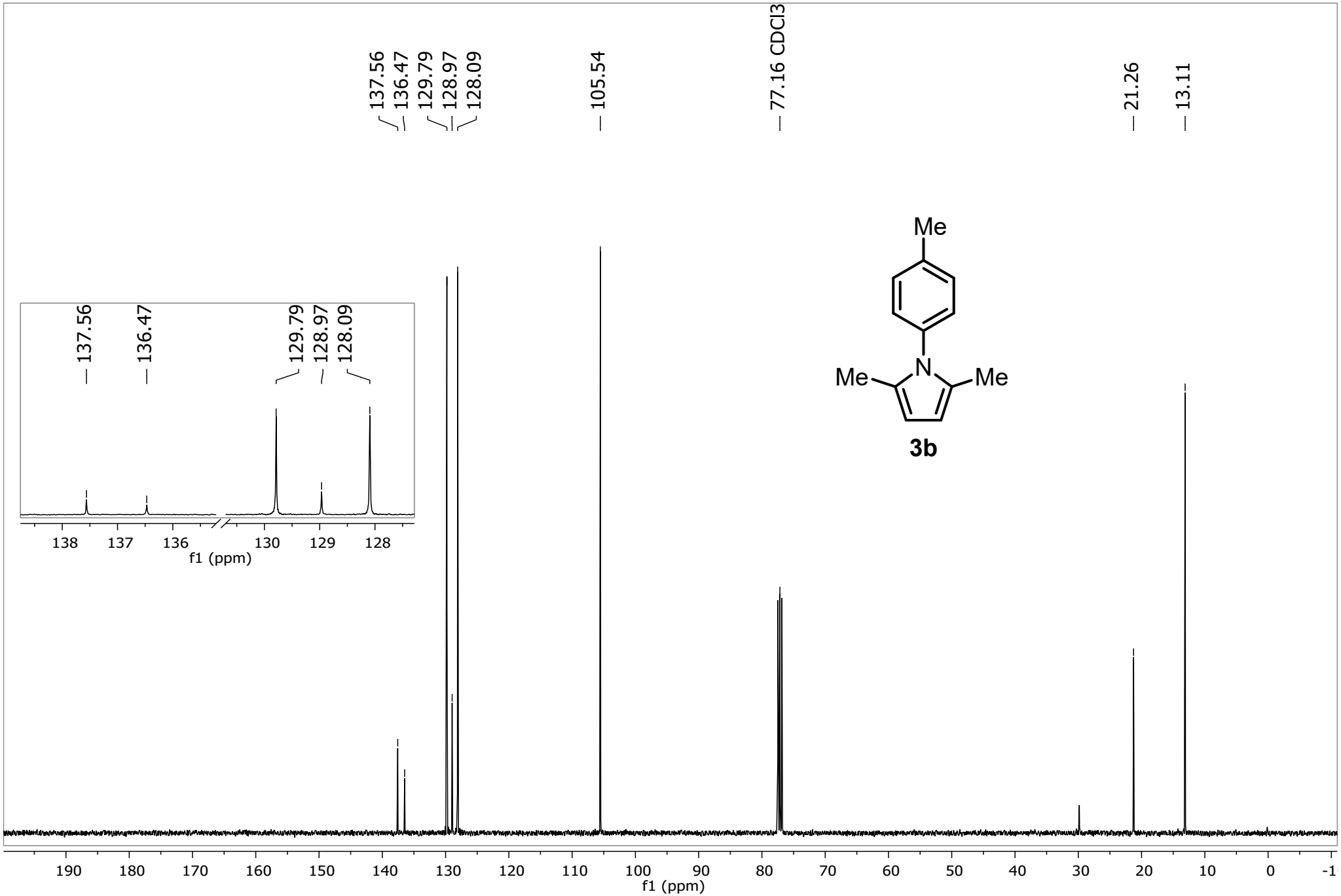


Figure 4. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3b**.

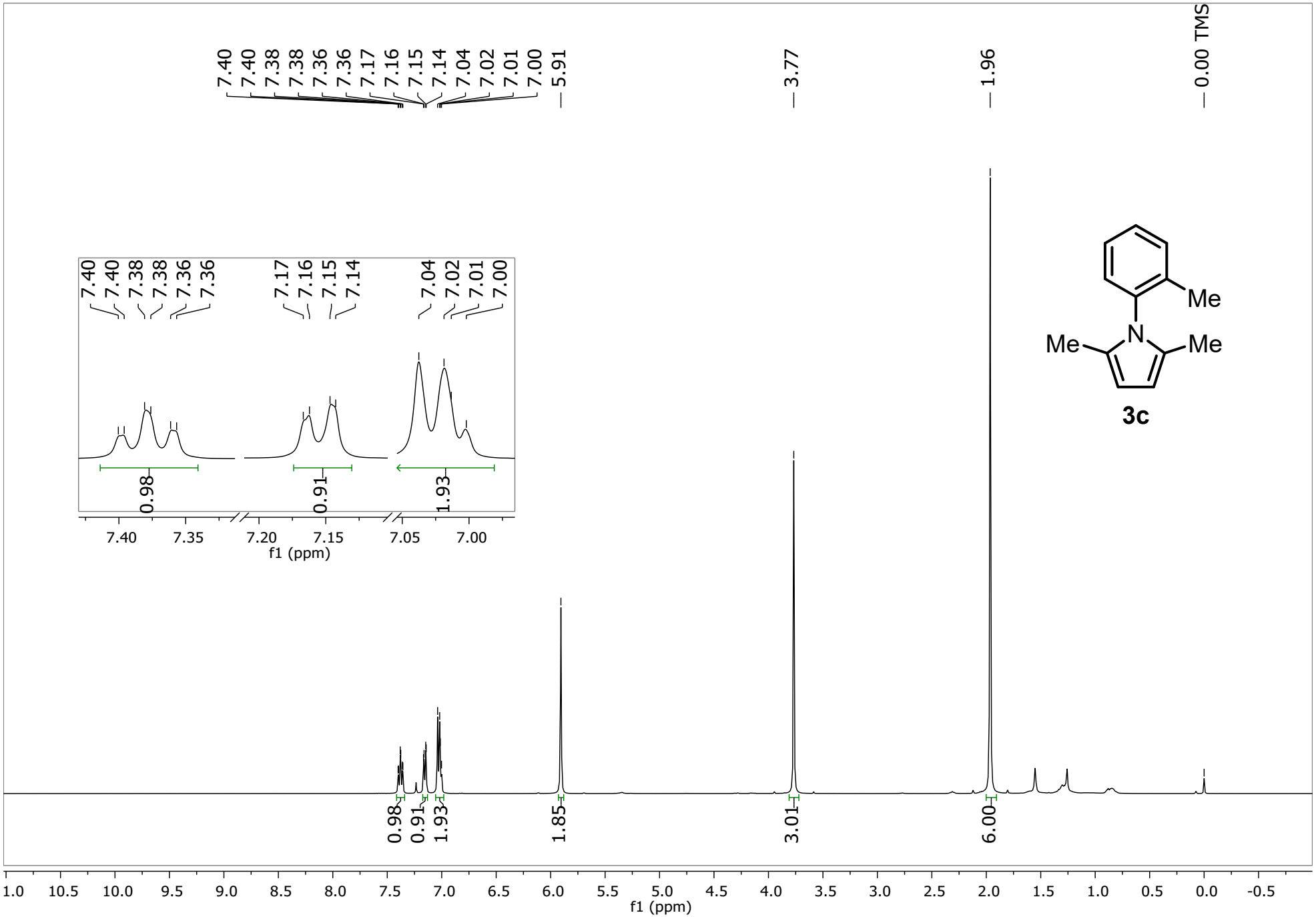


Figure 5. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3c**.

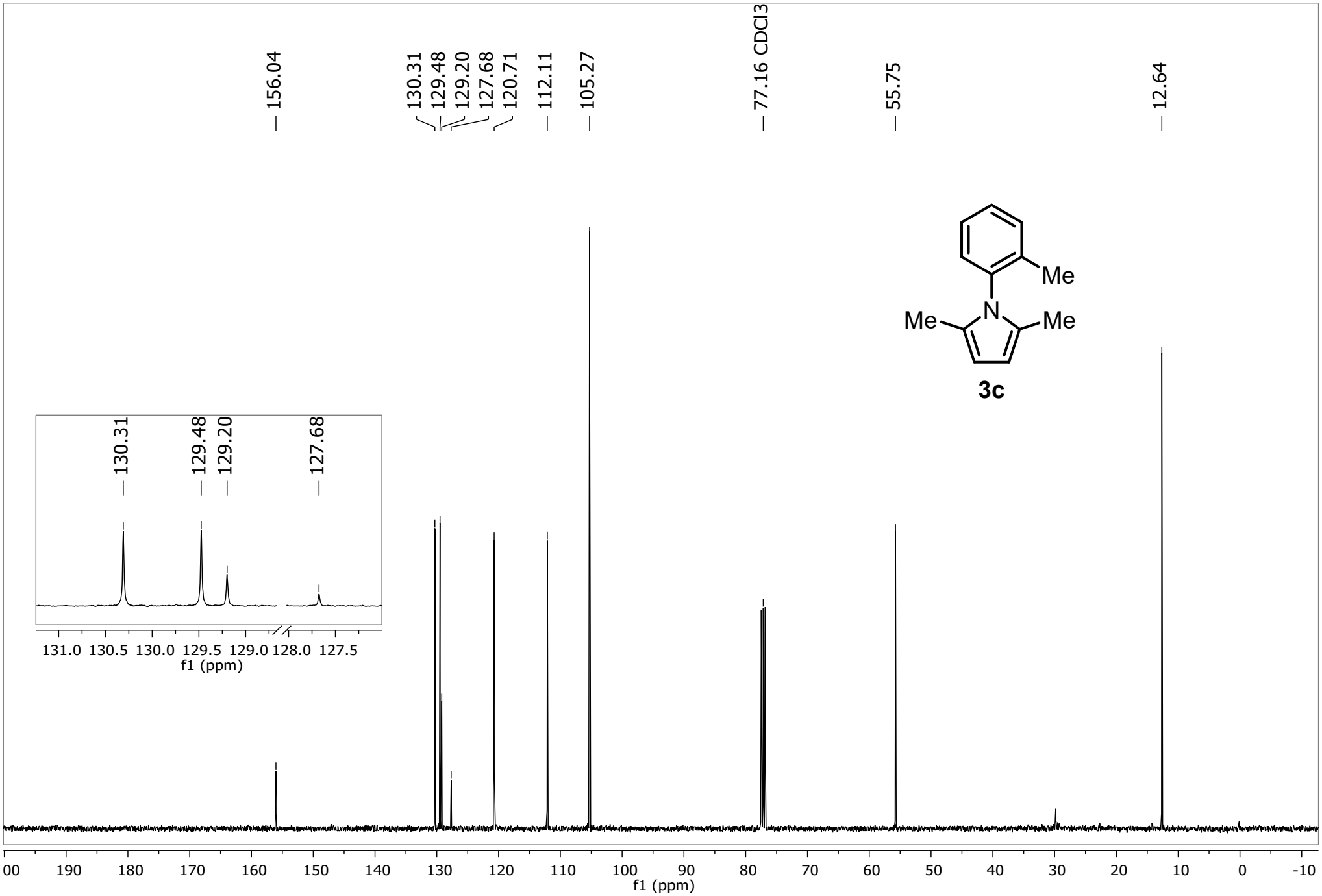


Figure 6. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3c**.

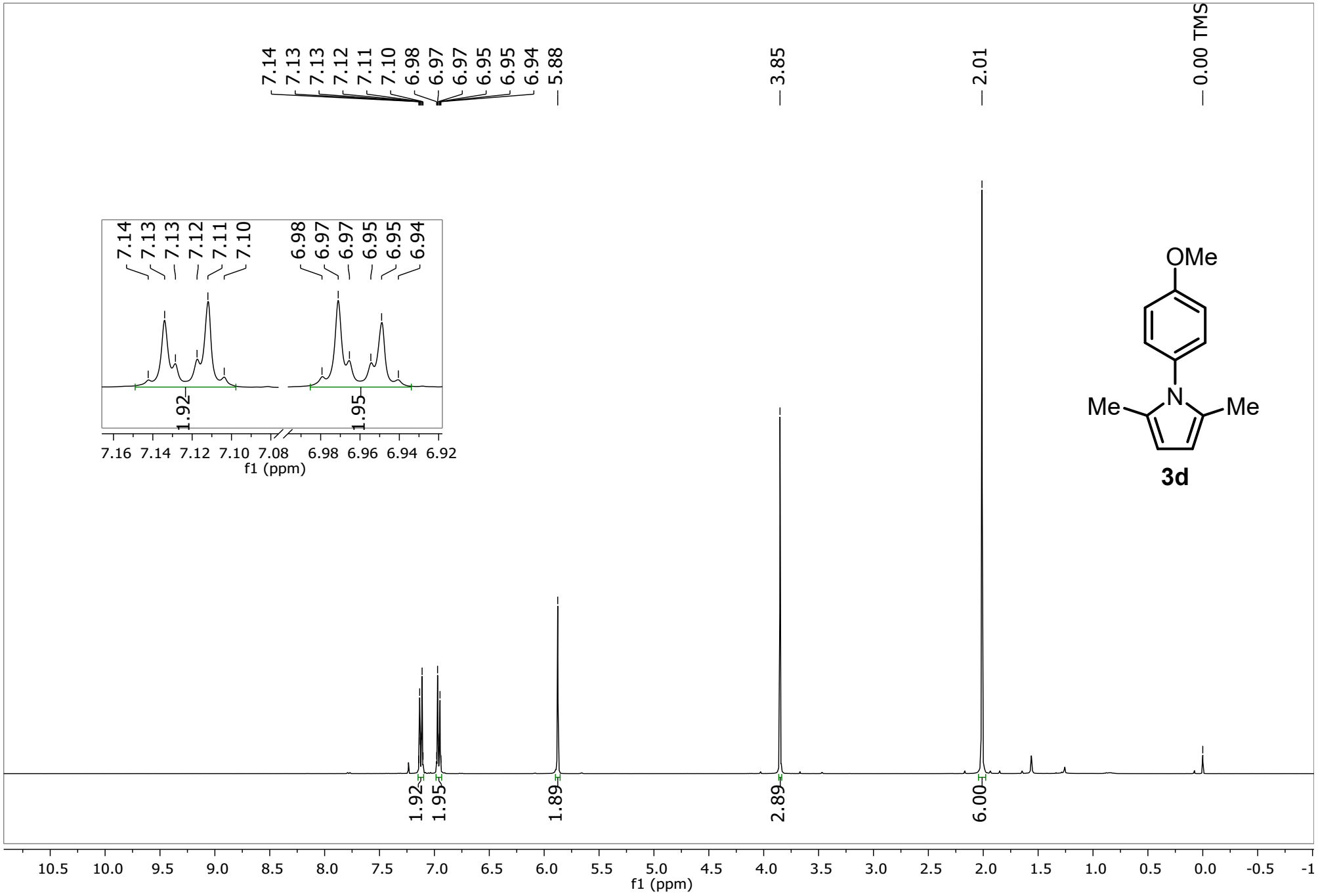


Figure 7. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3d**.

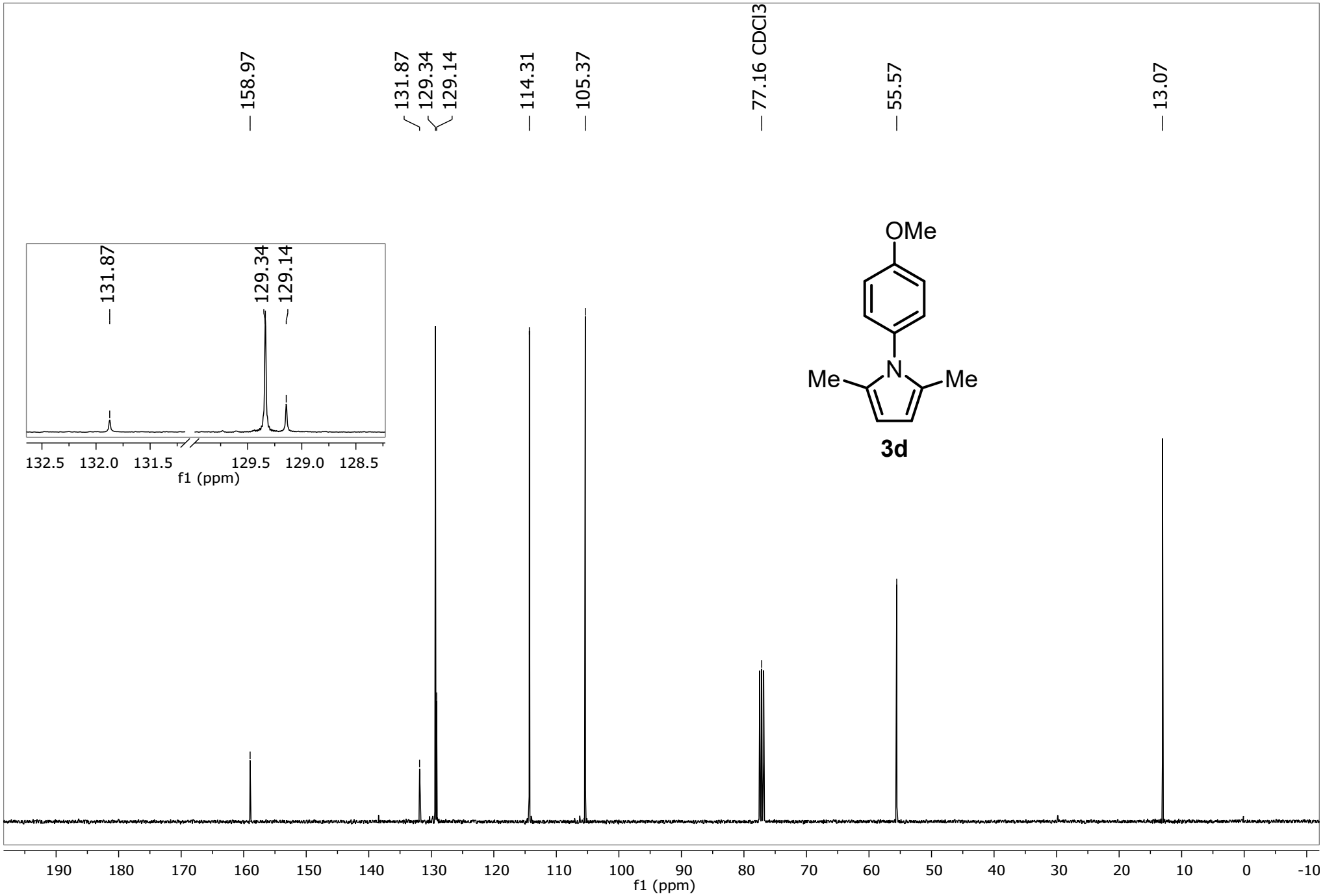


Figure 8. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3d**.

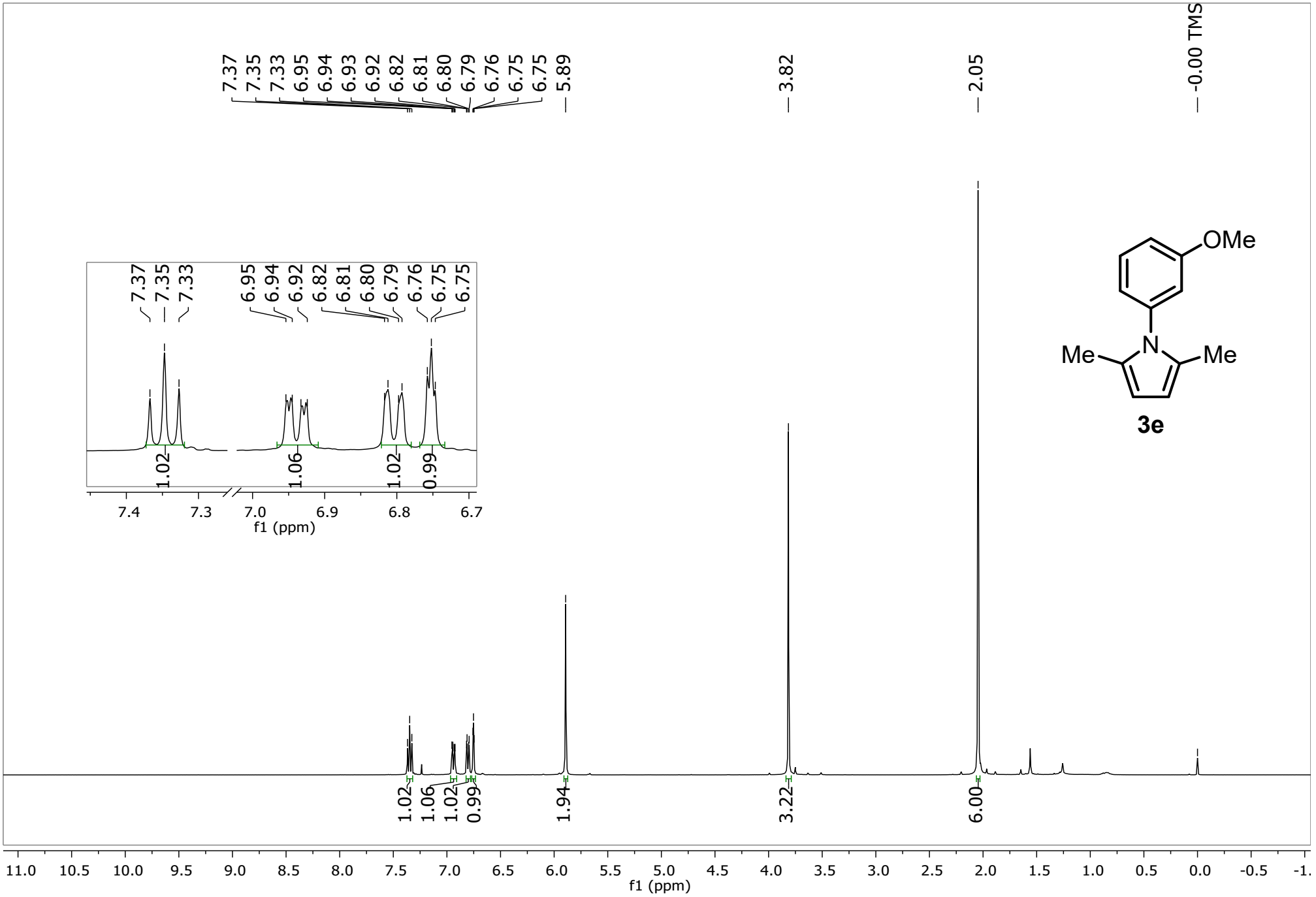


Figure 9. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3e**.

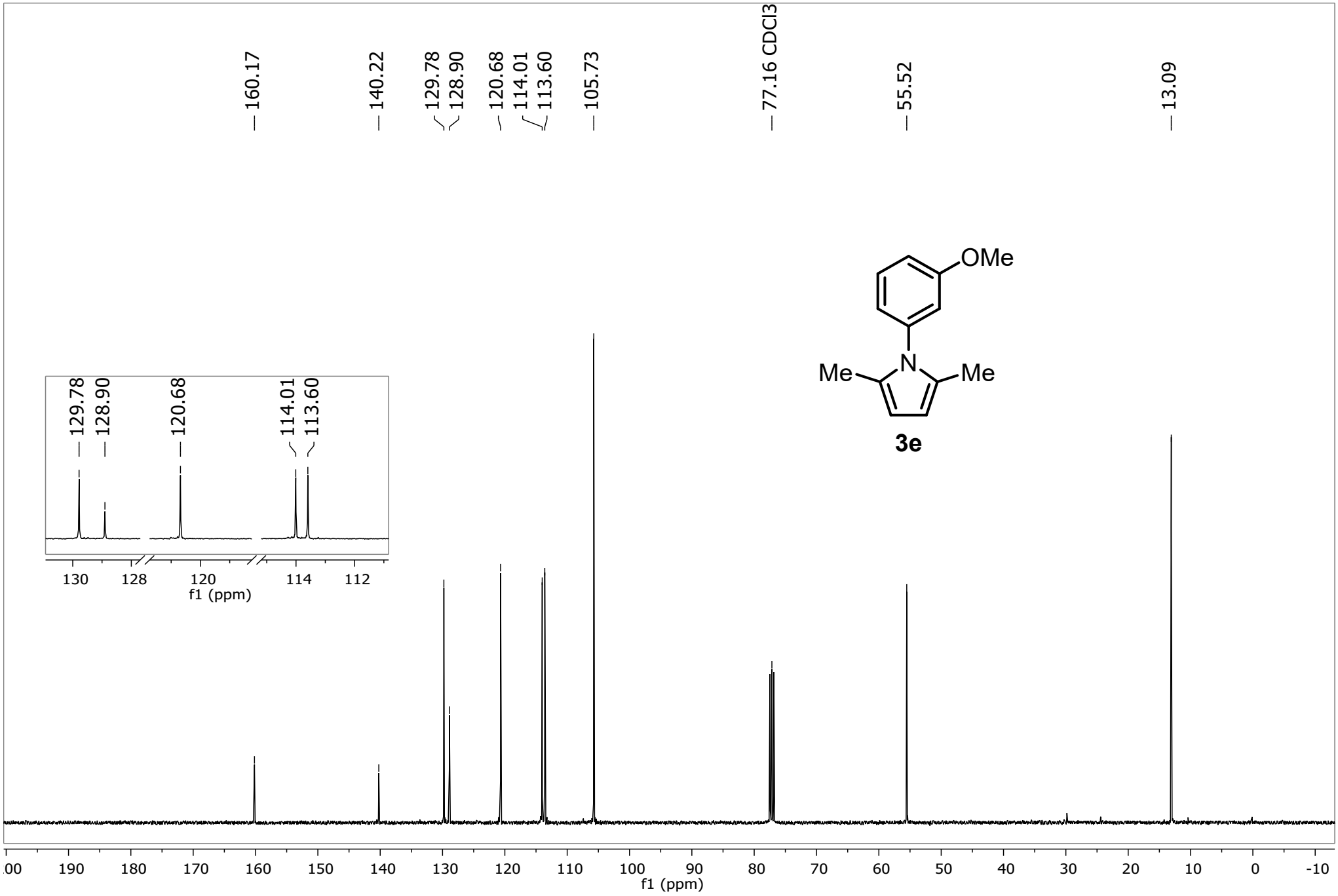


Figure 10. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3e**.

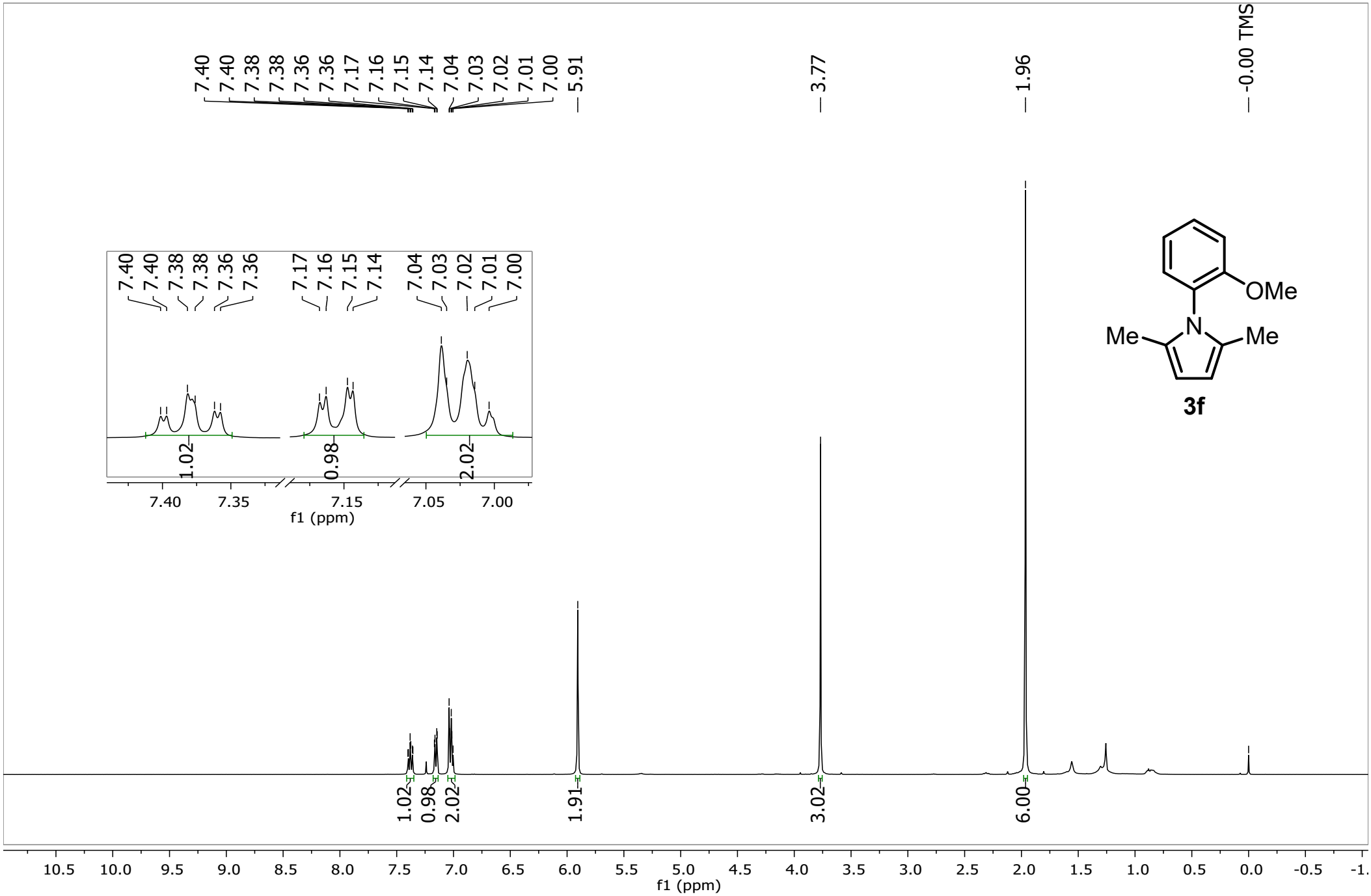


Figure 11. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3f**.

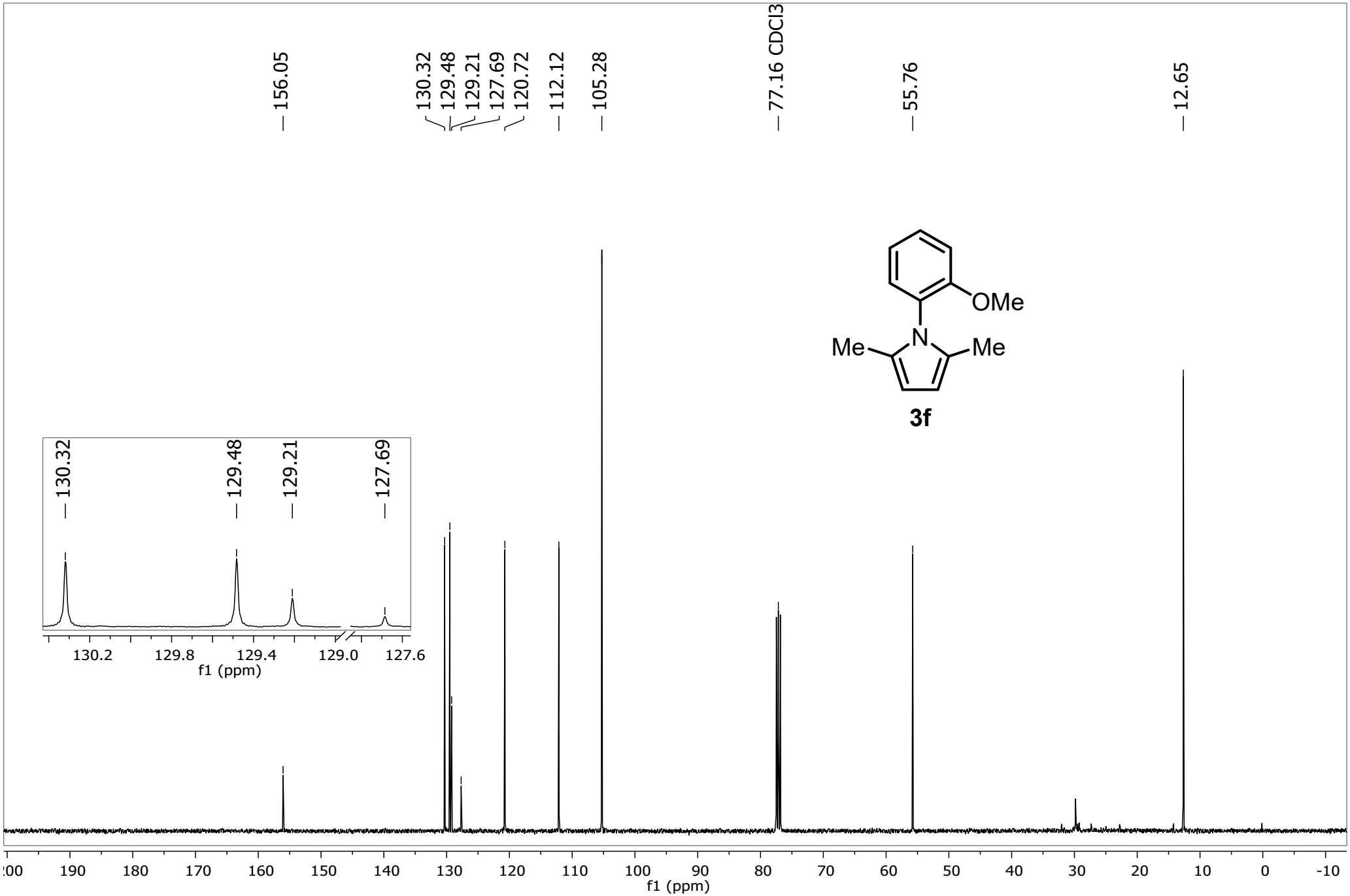


Figure 12. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3f**.

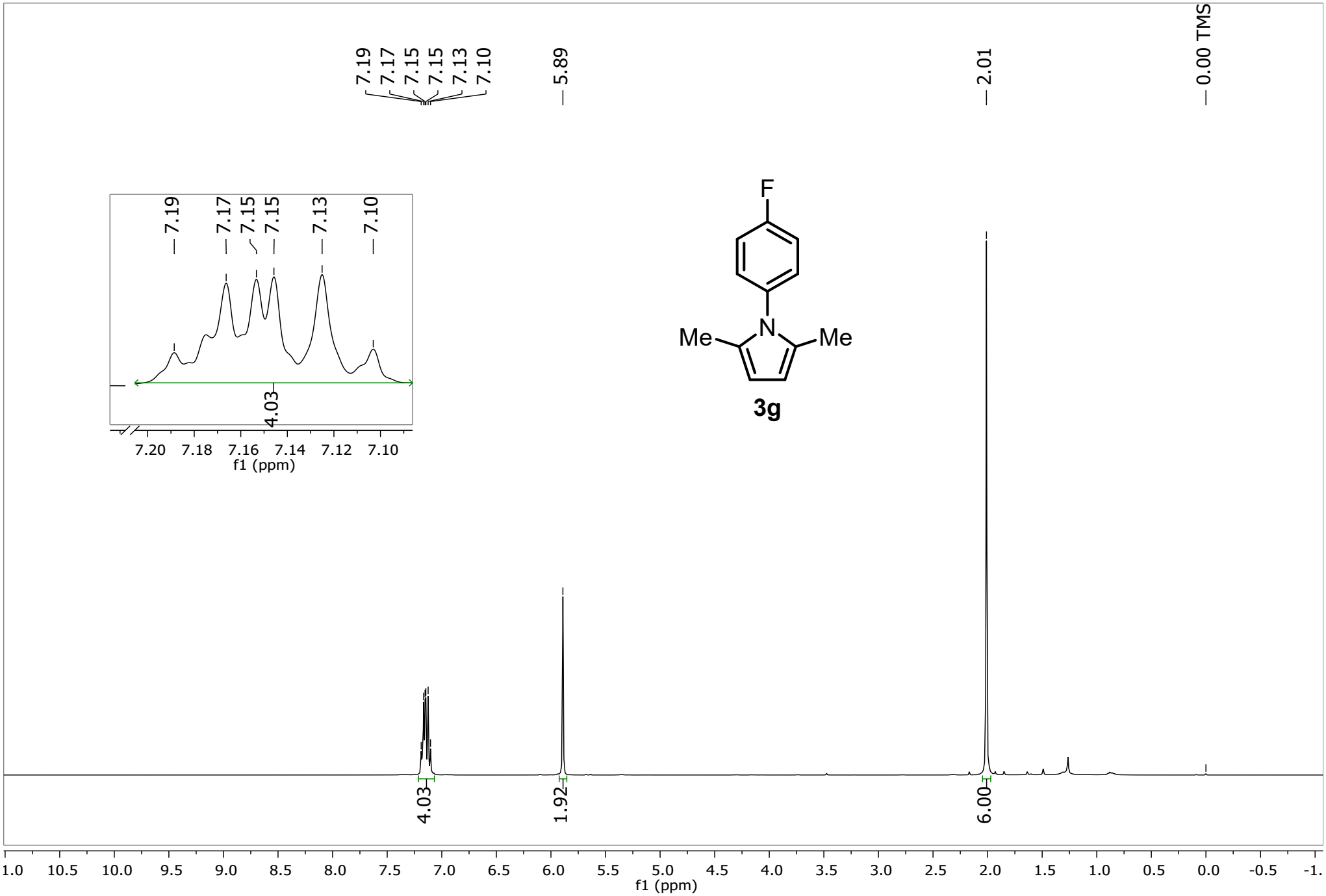


Figure 13 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3g**.

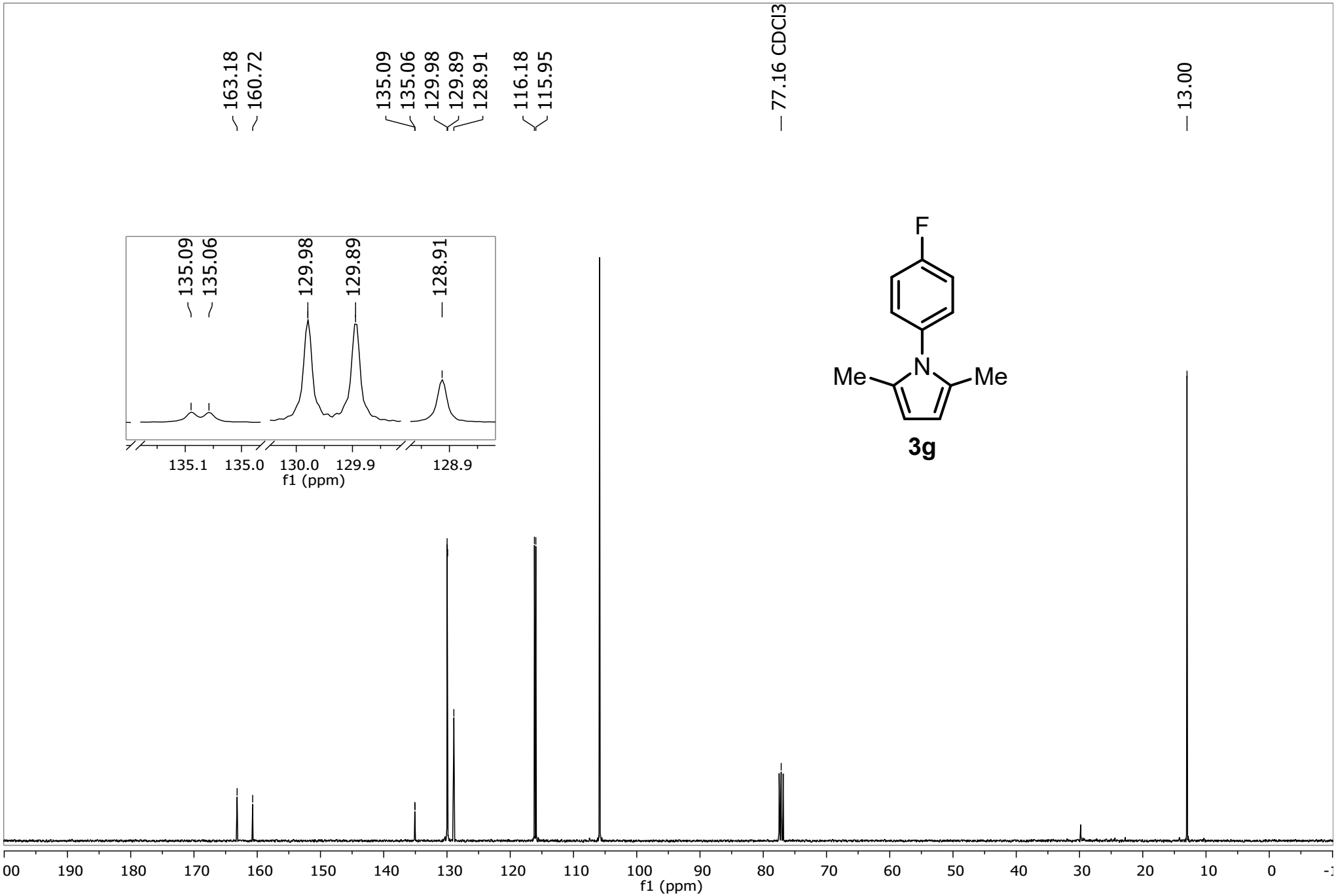


Figure 14. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3g**.

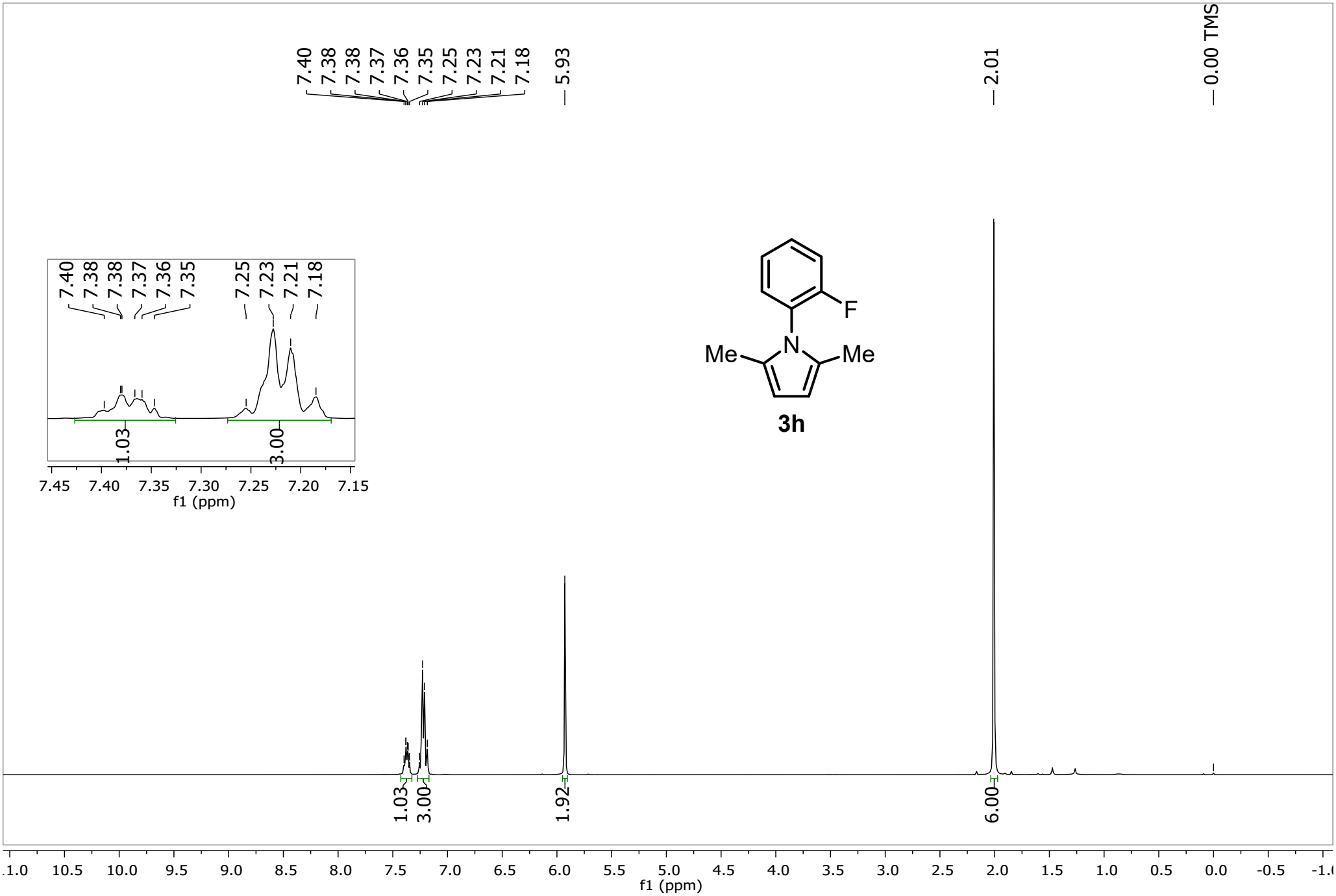


Figure 15. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3h**.

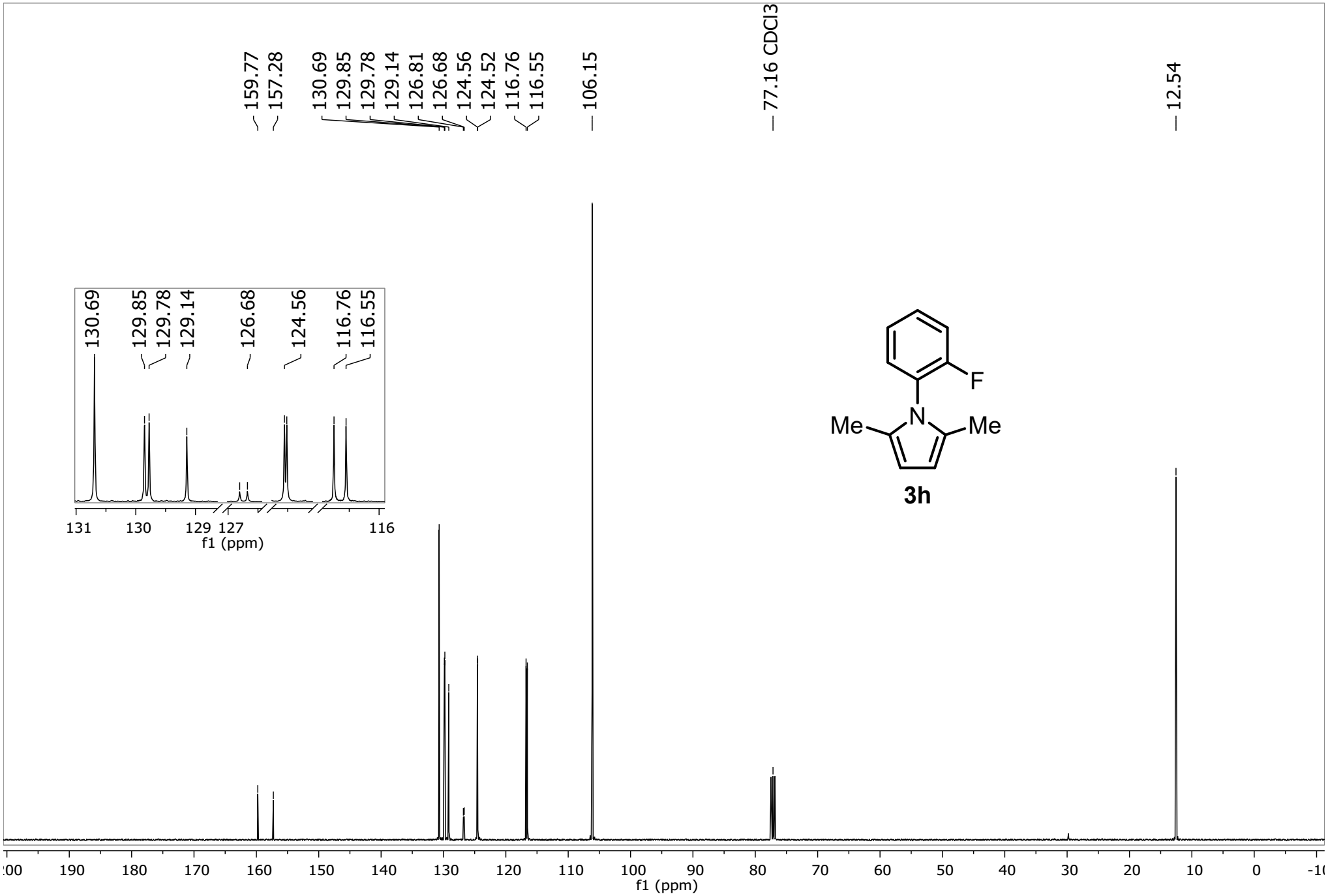


Figure 16. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3h**.

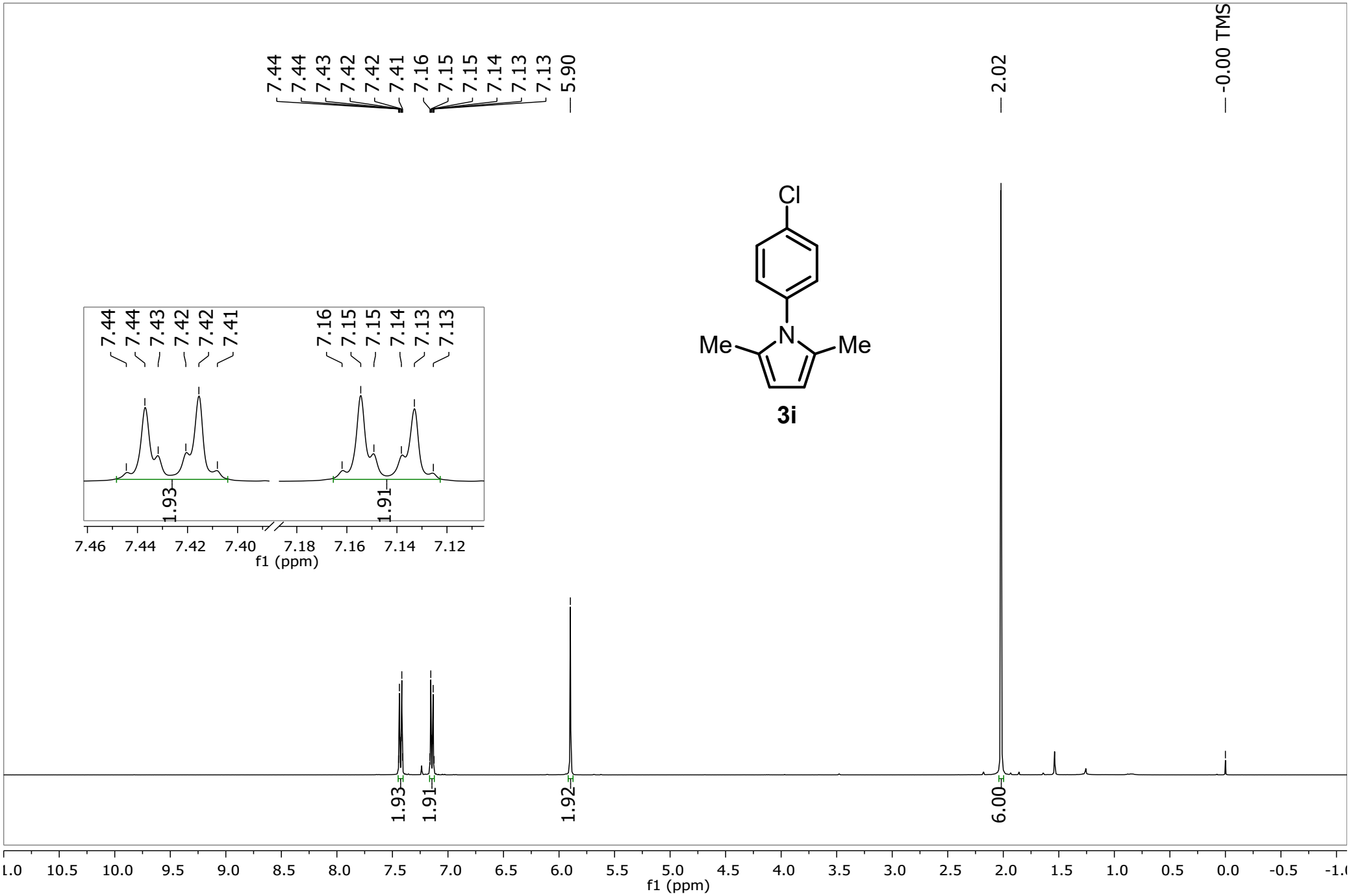


Figure 17. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3i**.

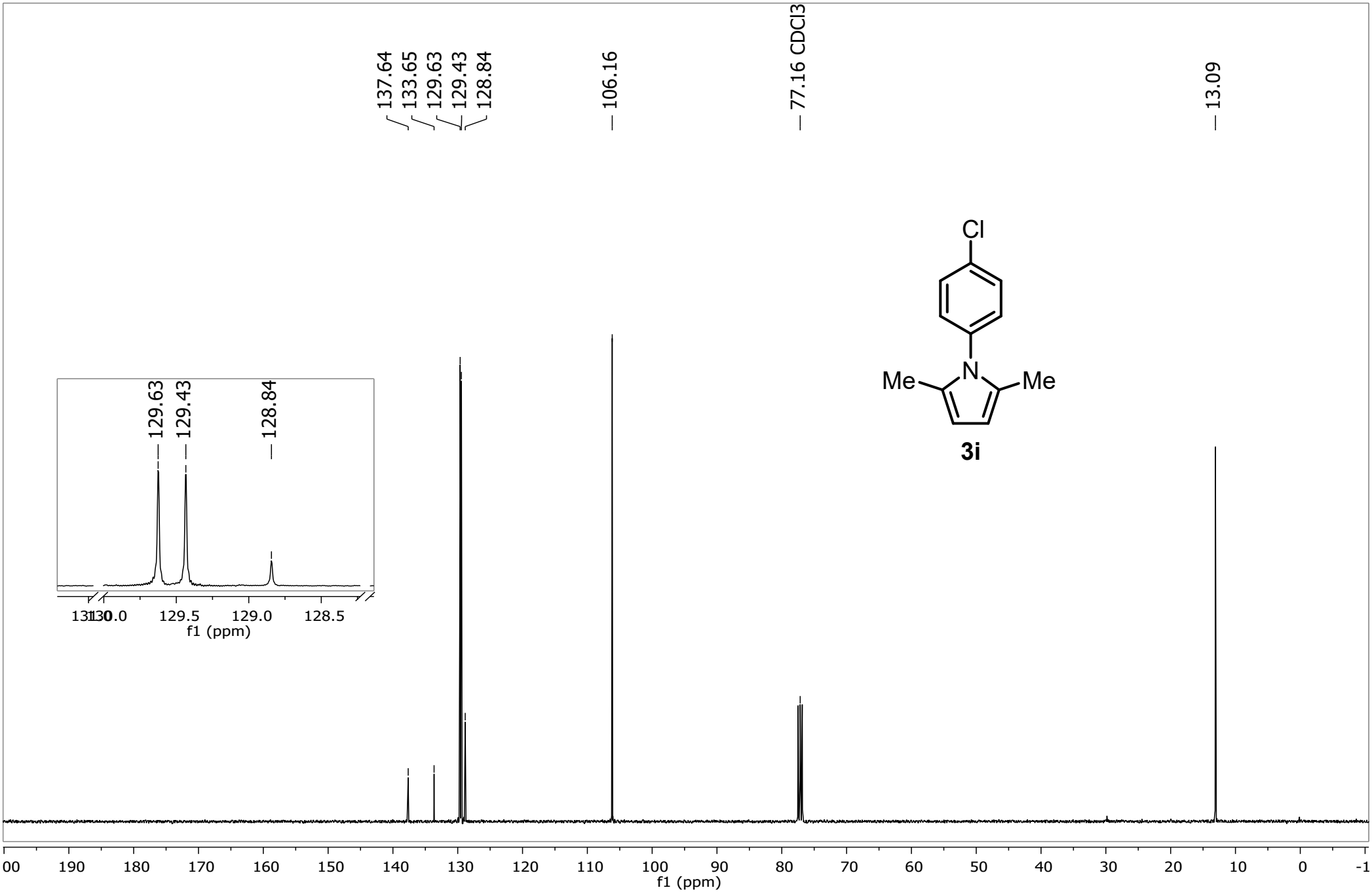


Figure 18. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3i**.

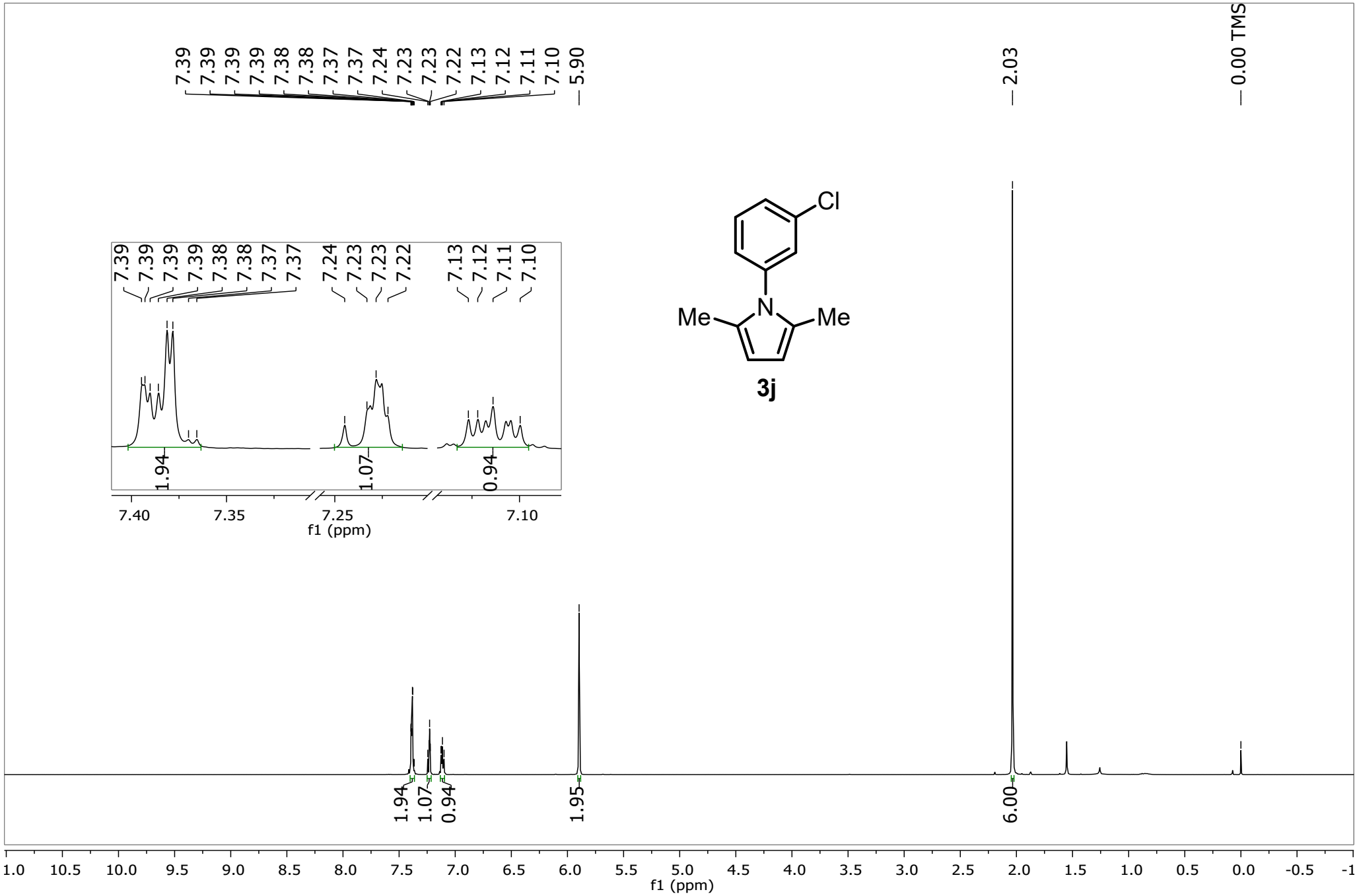


Figure 19. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3j**.

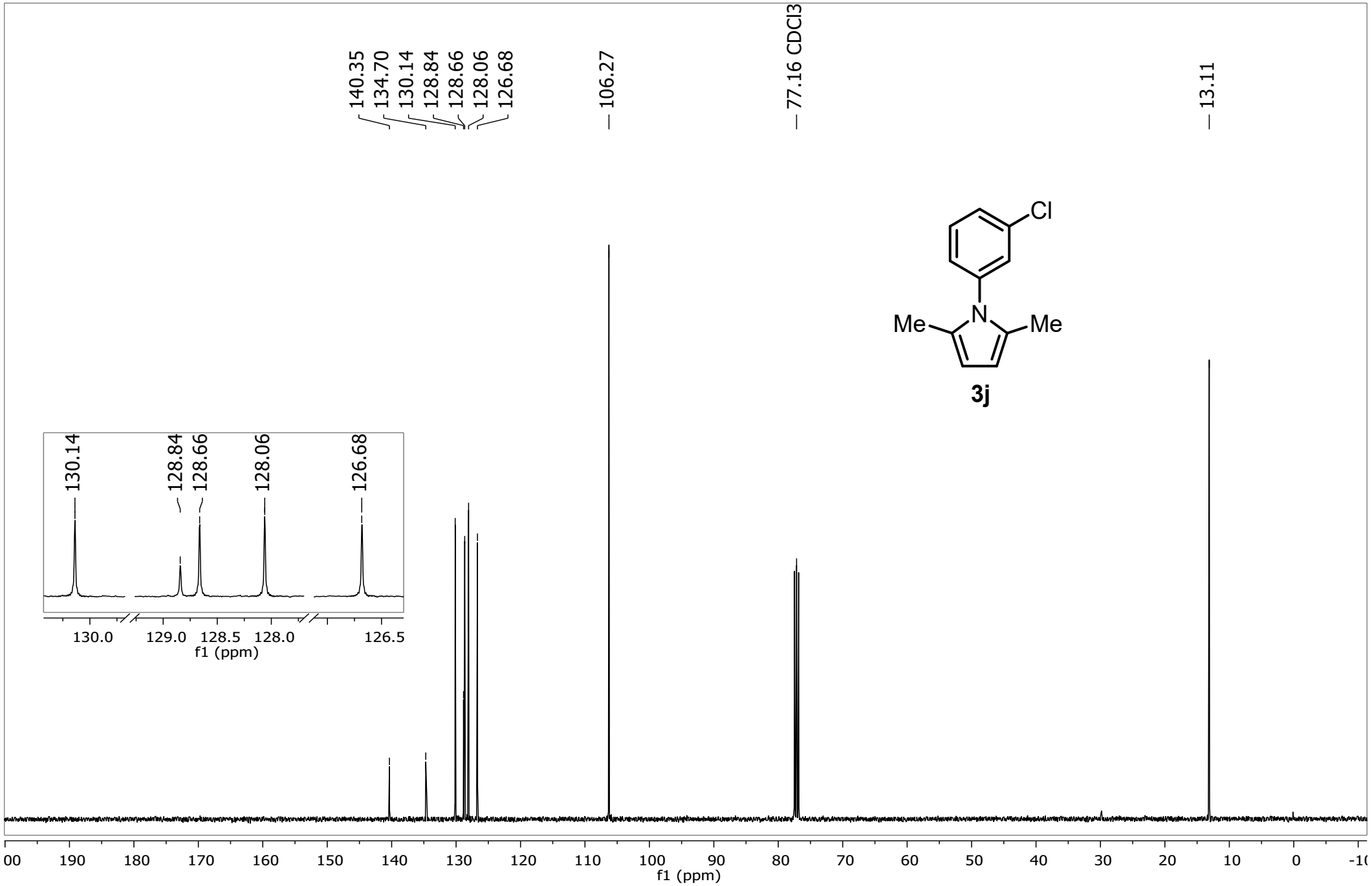


Figure 20. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3j**.

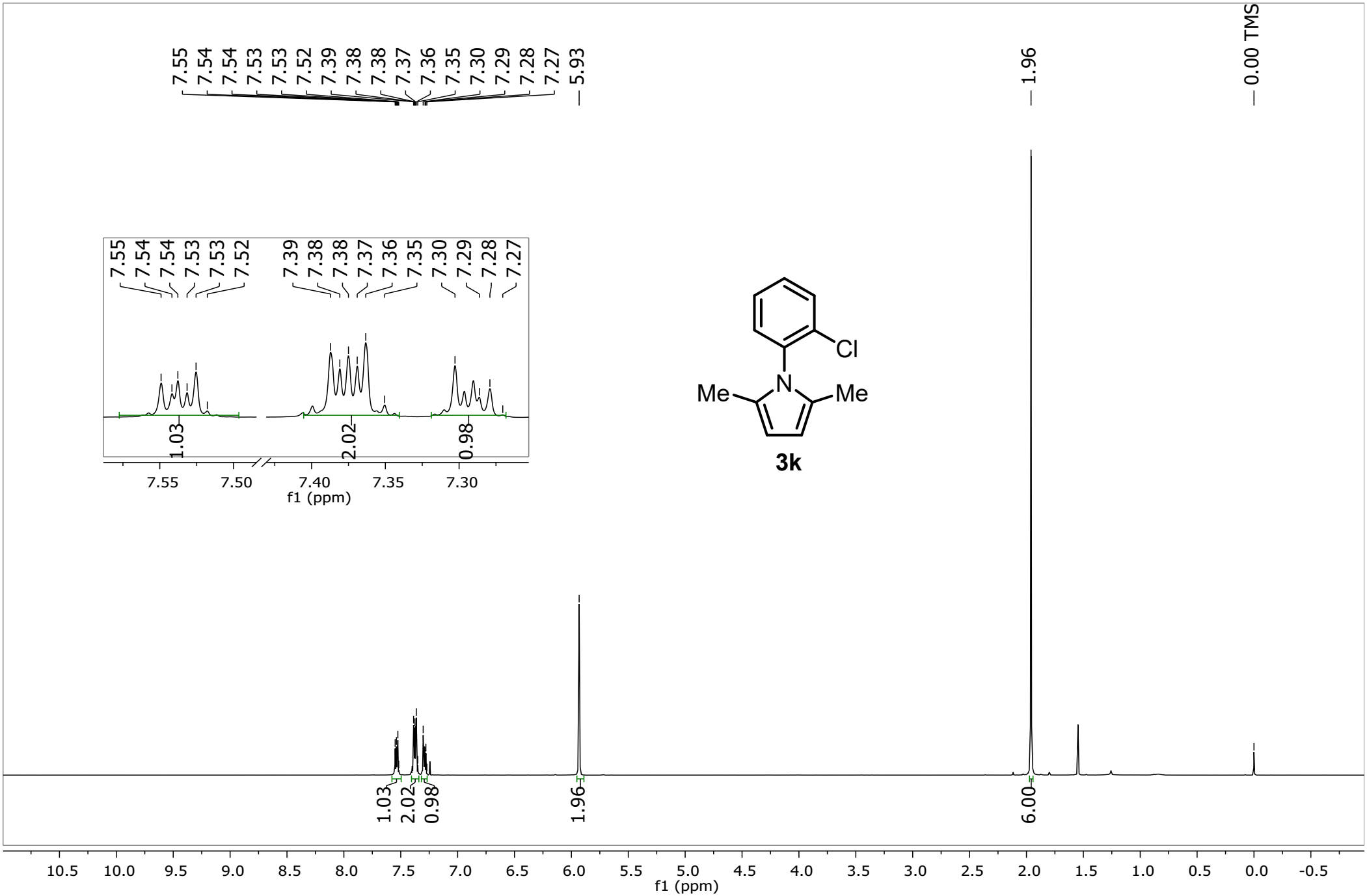


Figure 21. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3k**.

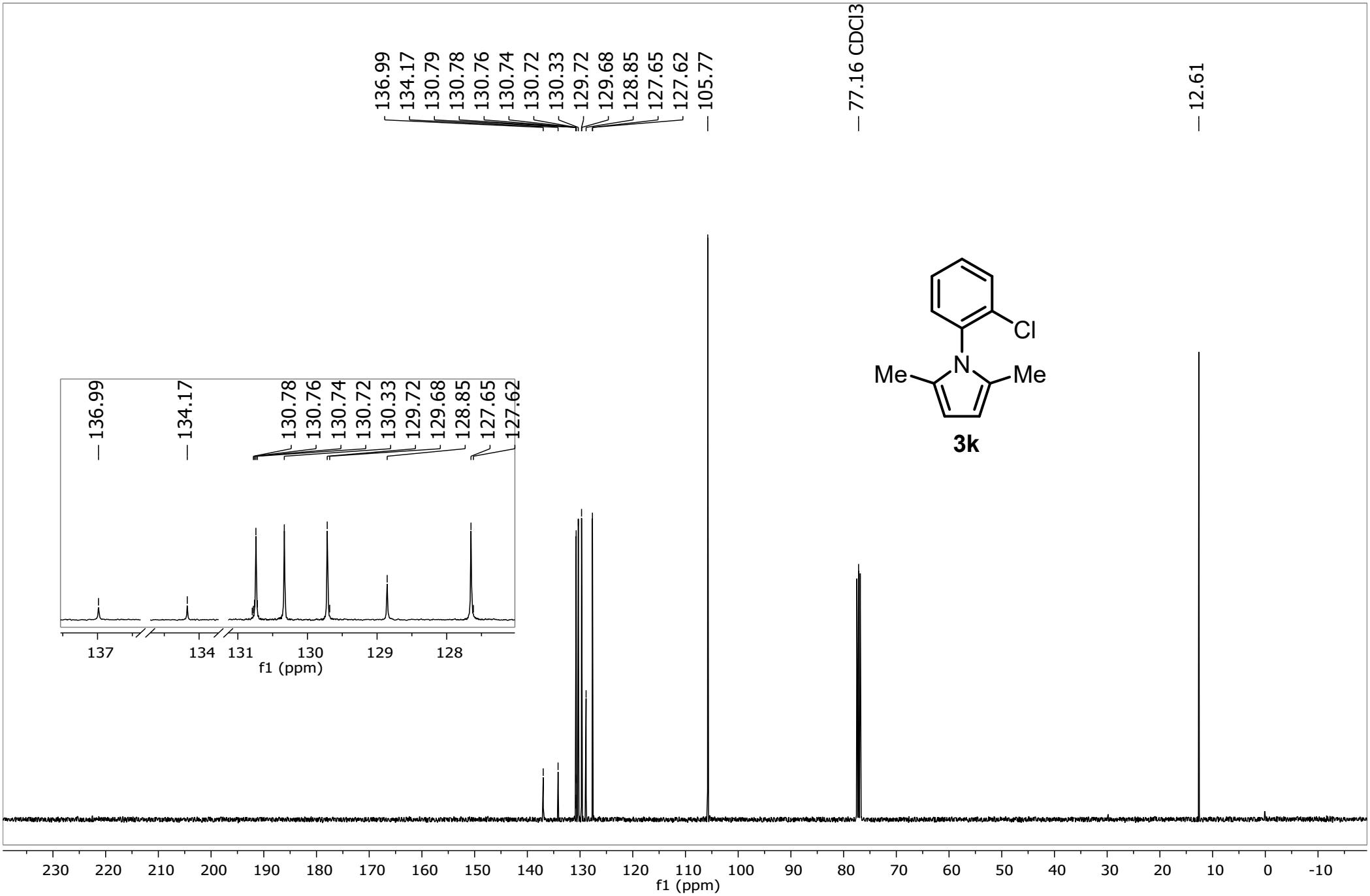


Figure 22. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3k**.

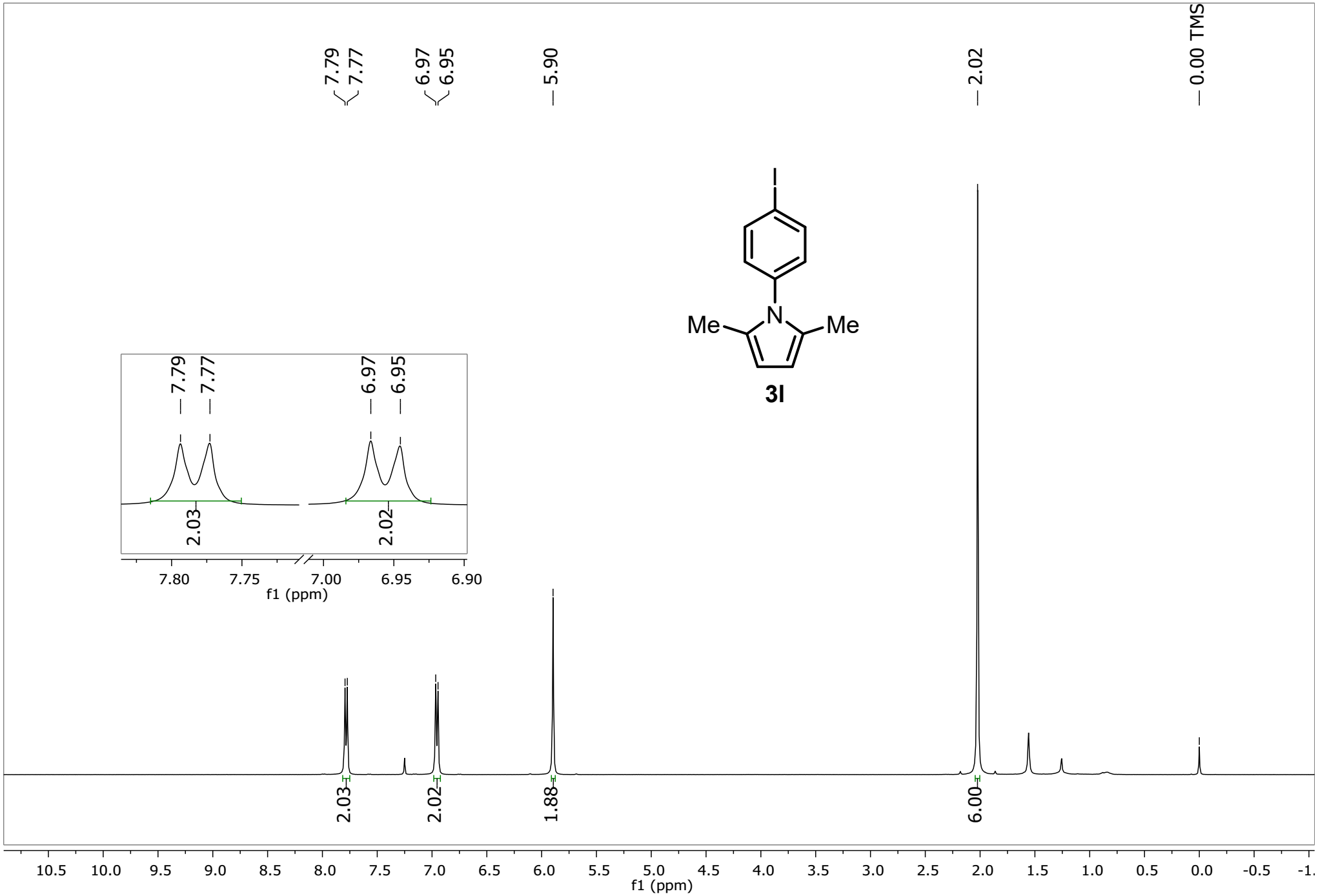


Figure 23. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3l**.

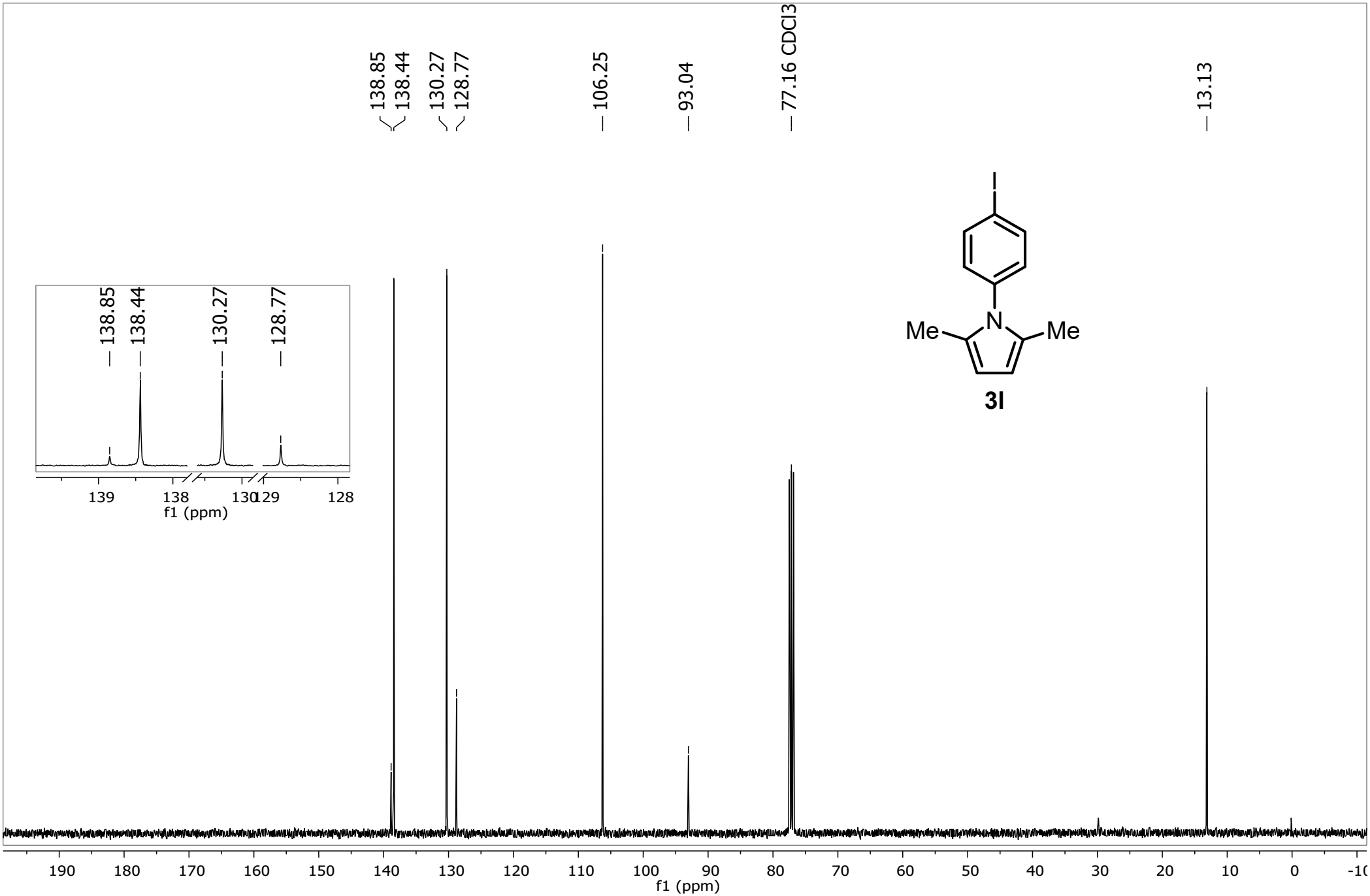


Figure 24. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3l**.

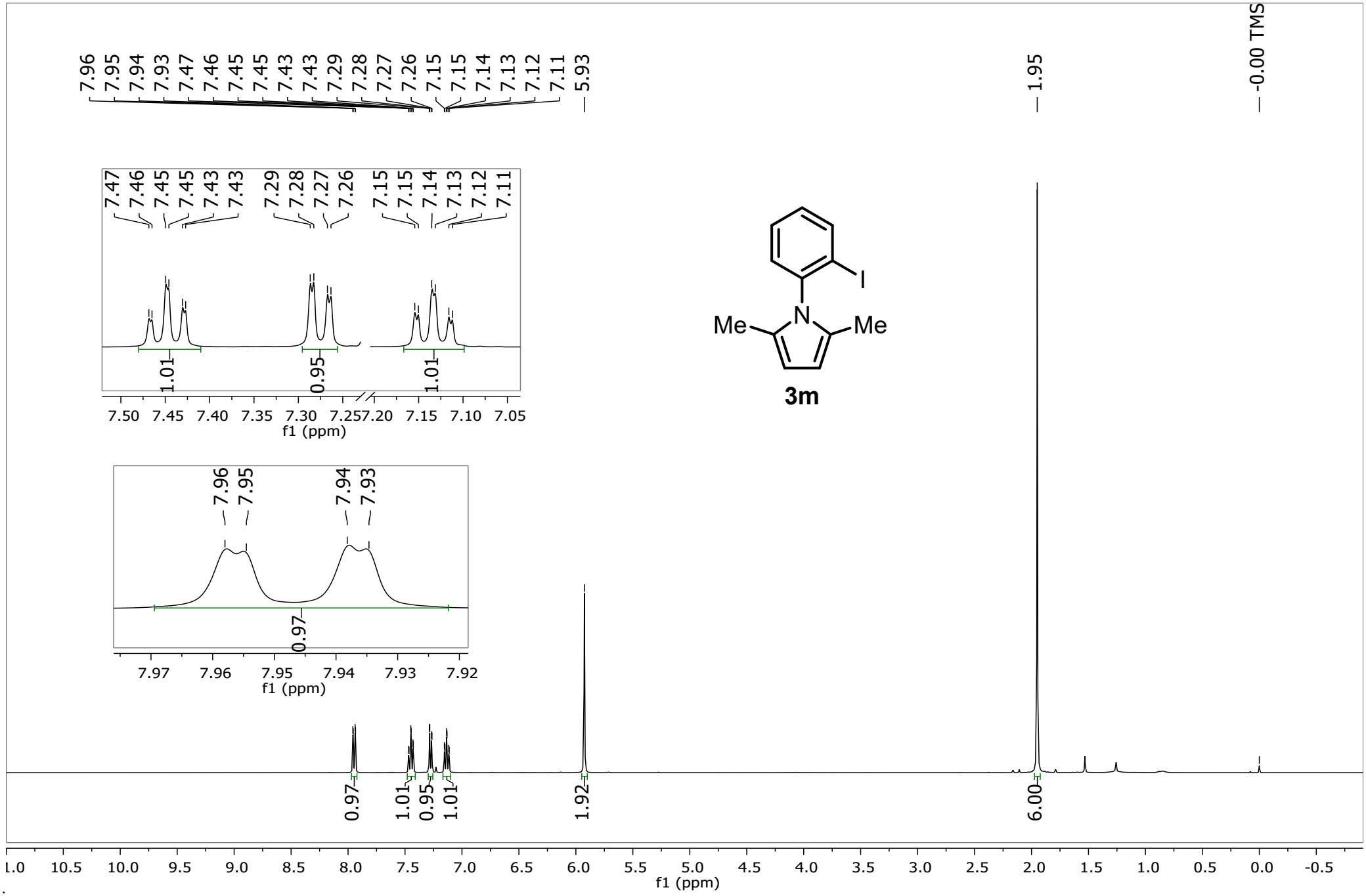


Figure 25. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3m**.

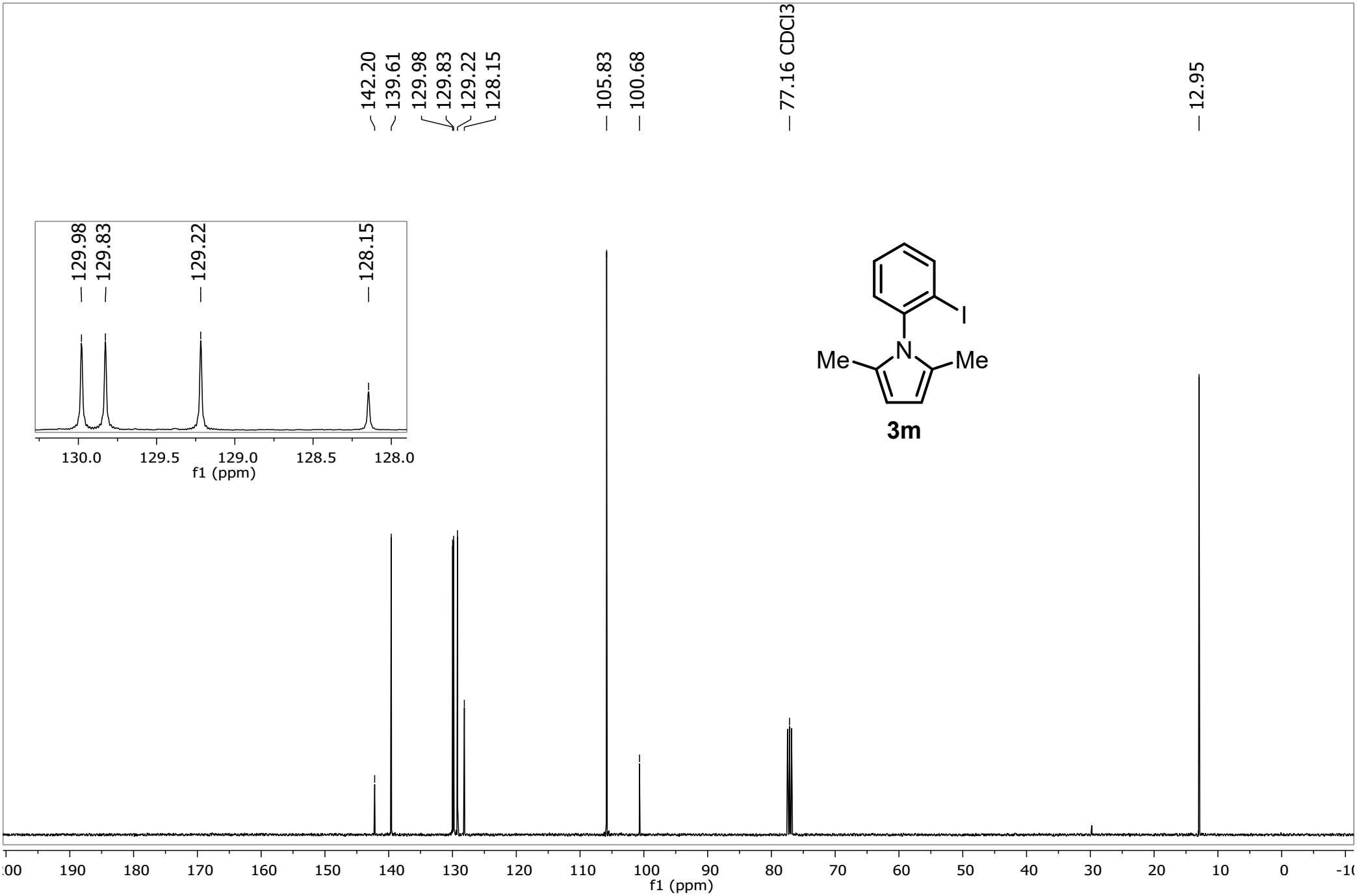


Figure 26. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3m**.

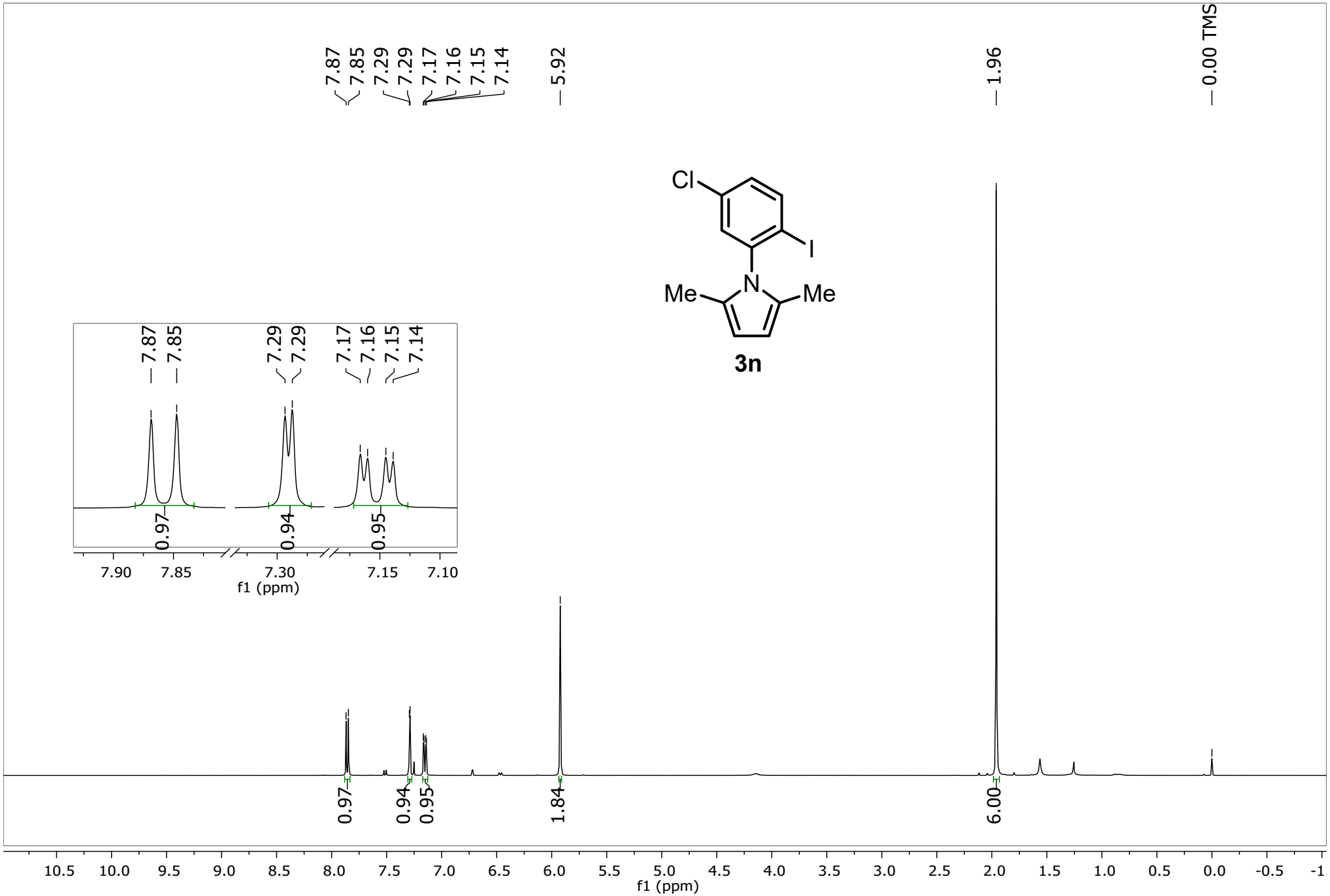


Figure 27. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3n**.

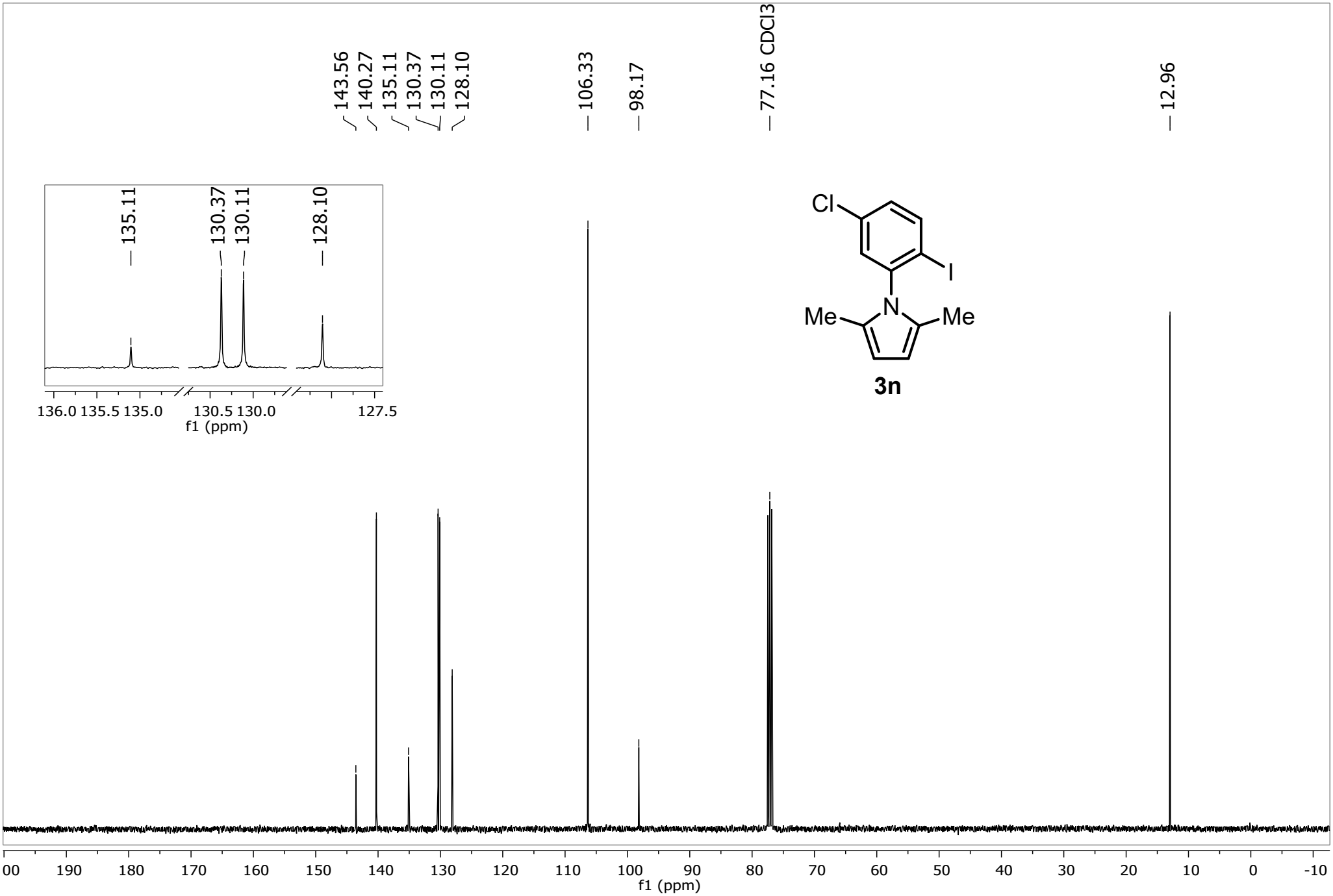


Figure 28. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3n**.

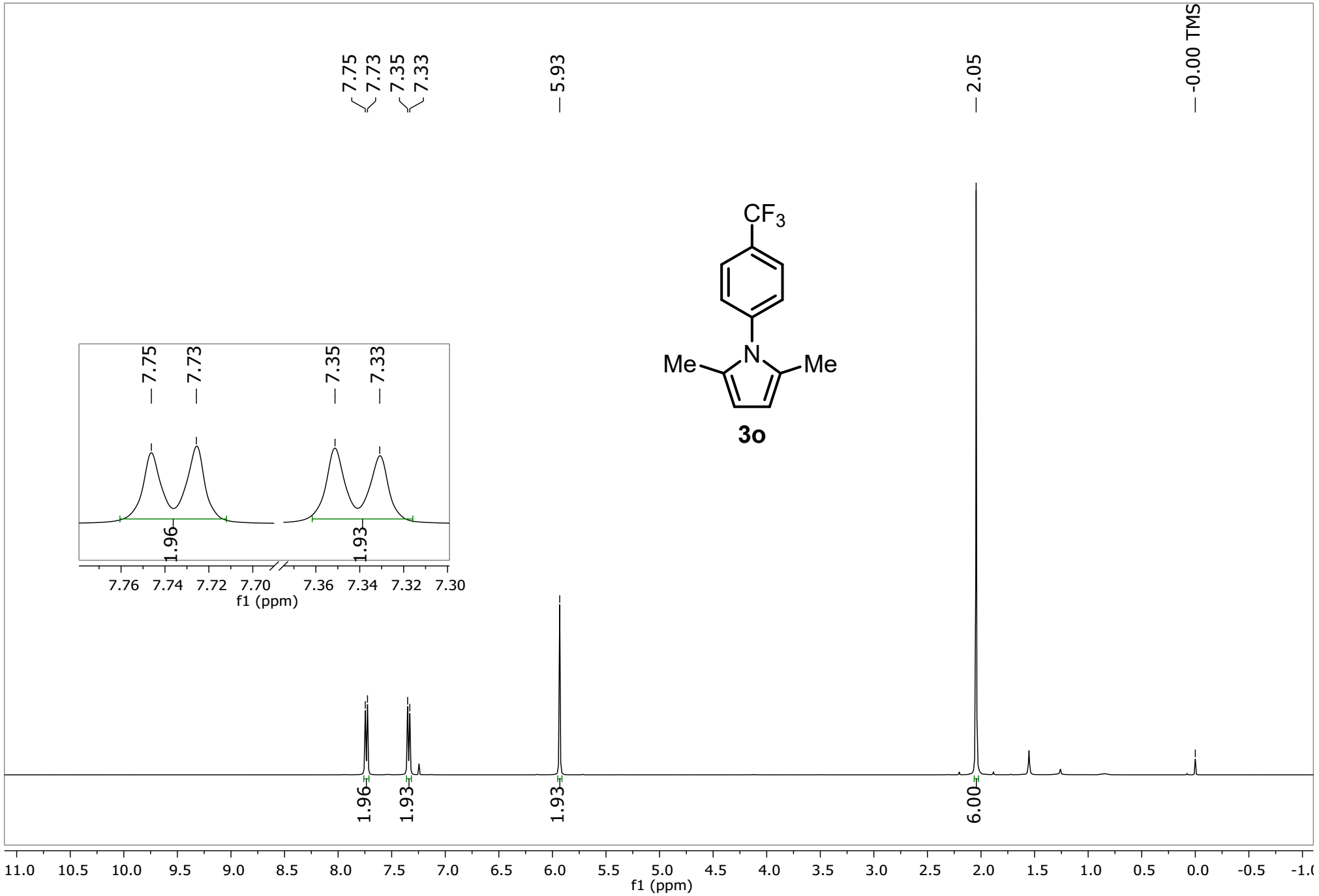


Figure 29. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3o**.

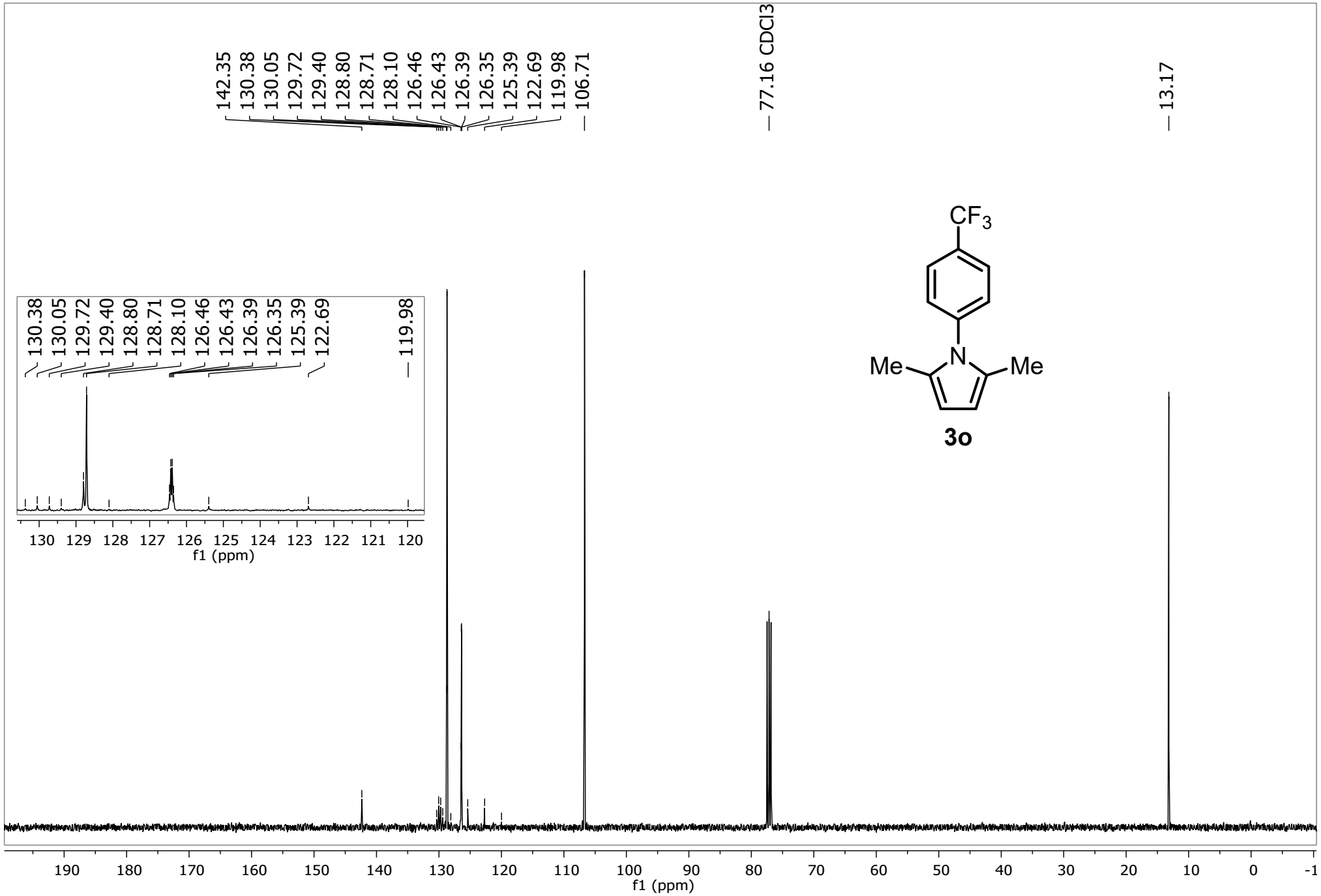


Figure 30. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound 3**o**.

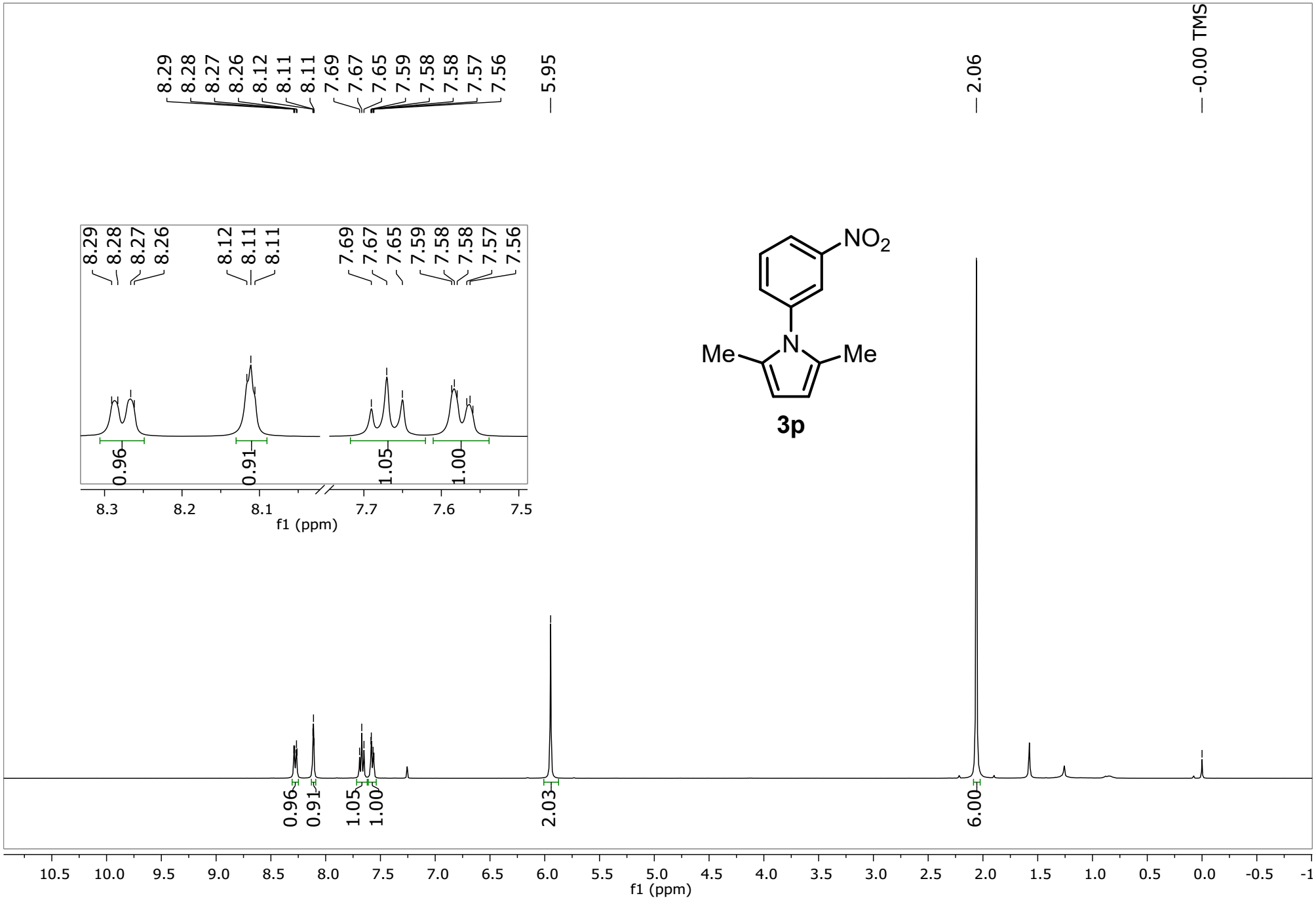


Figure 31. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3p**.

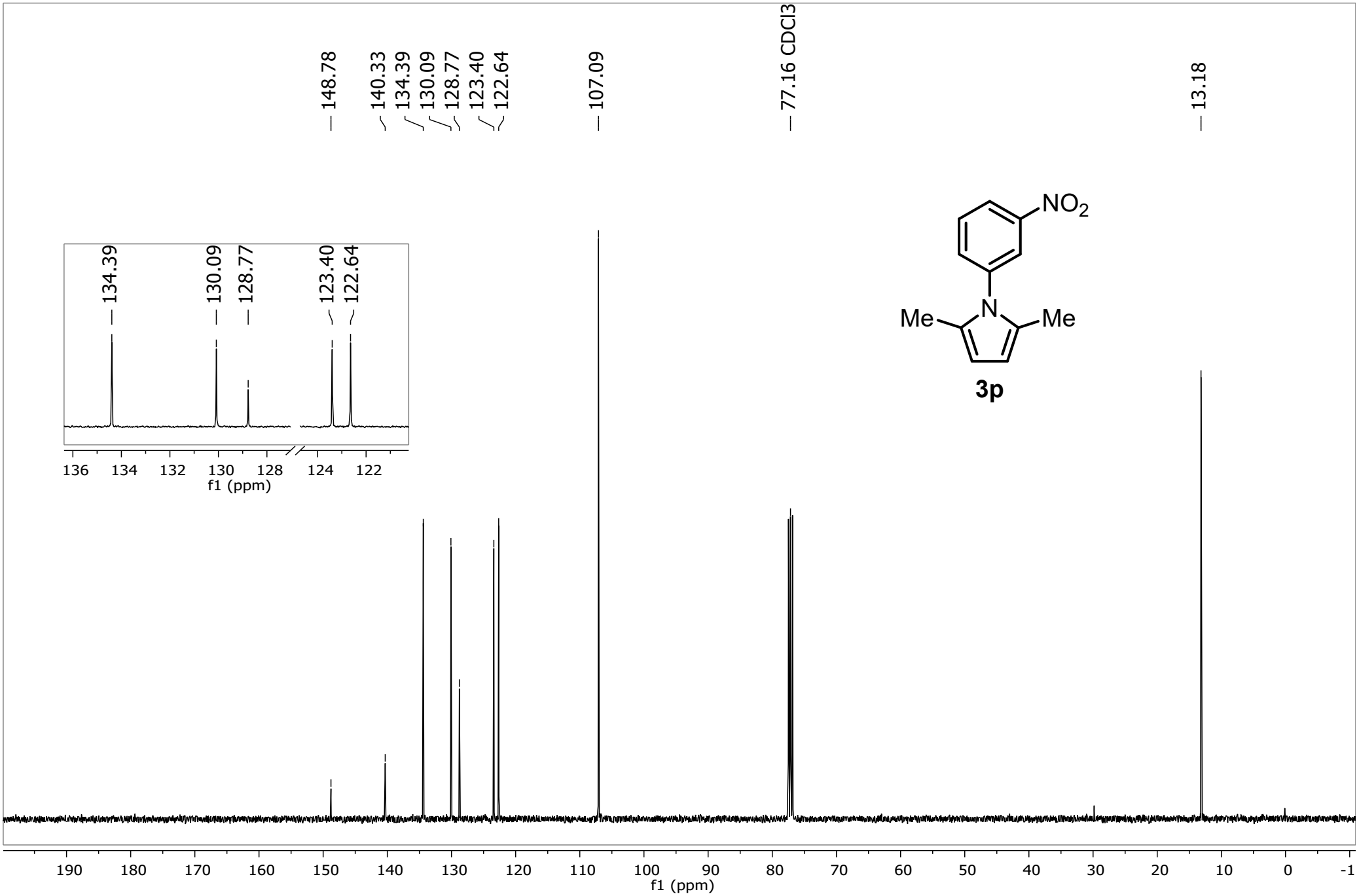


Figure 32. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3p**.

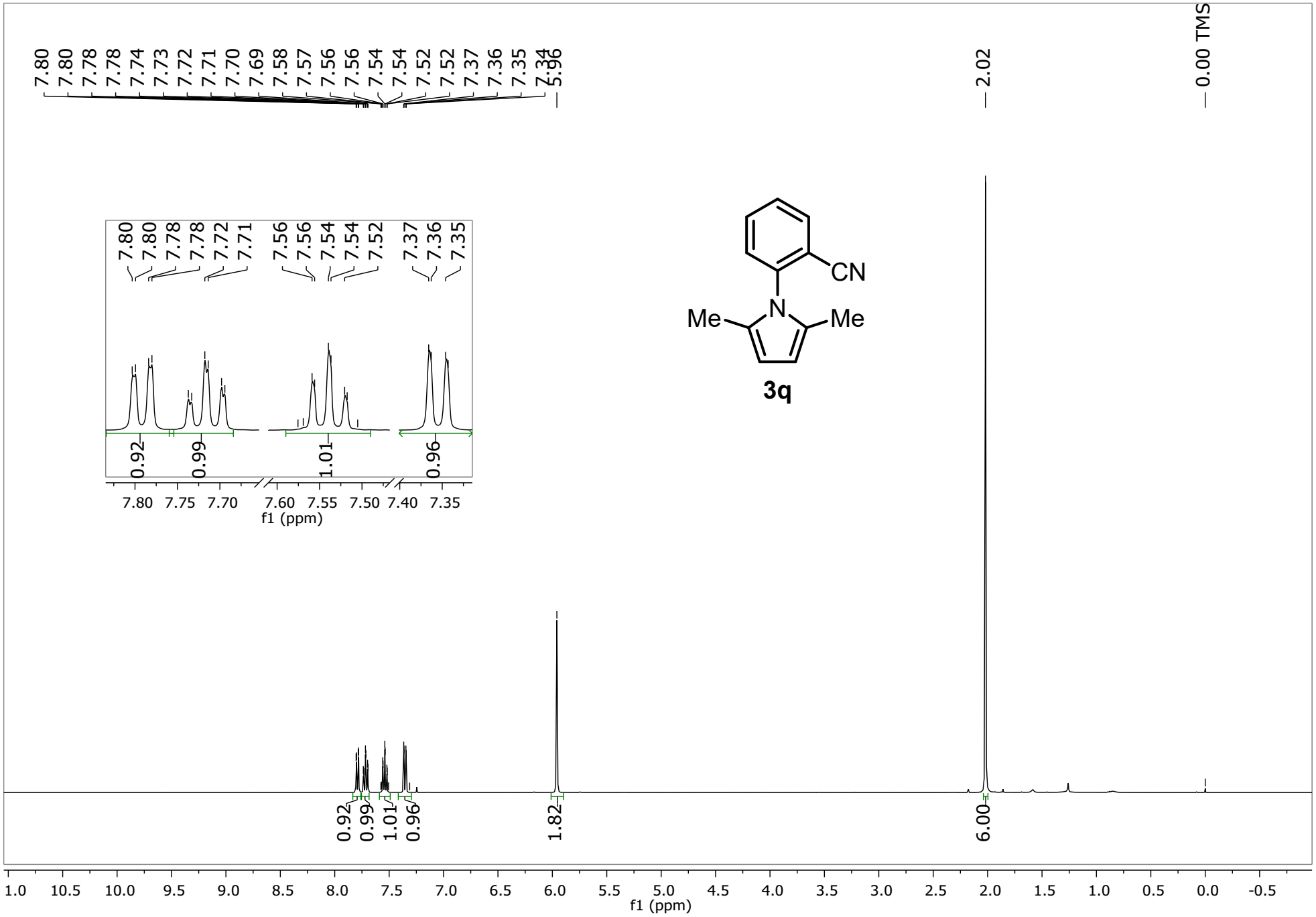


Figure 33. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3q**.

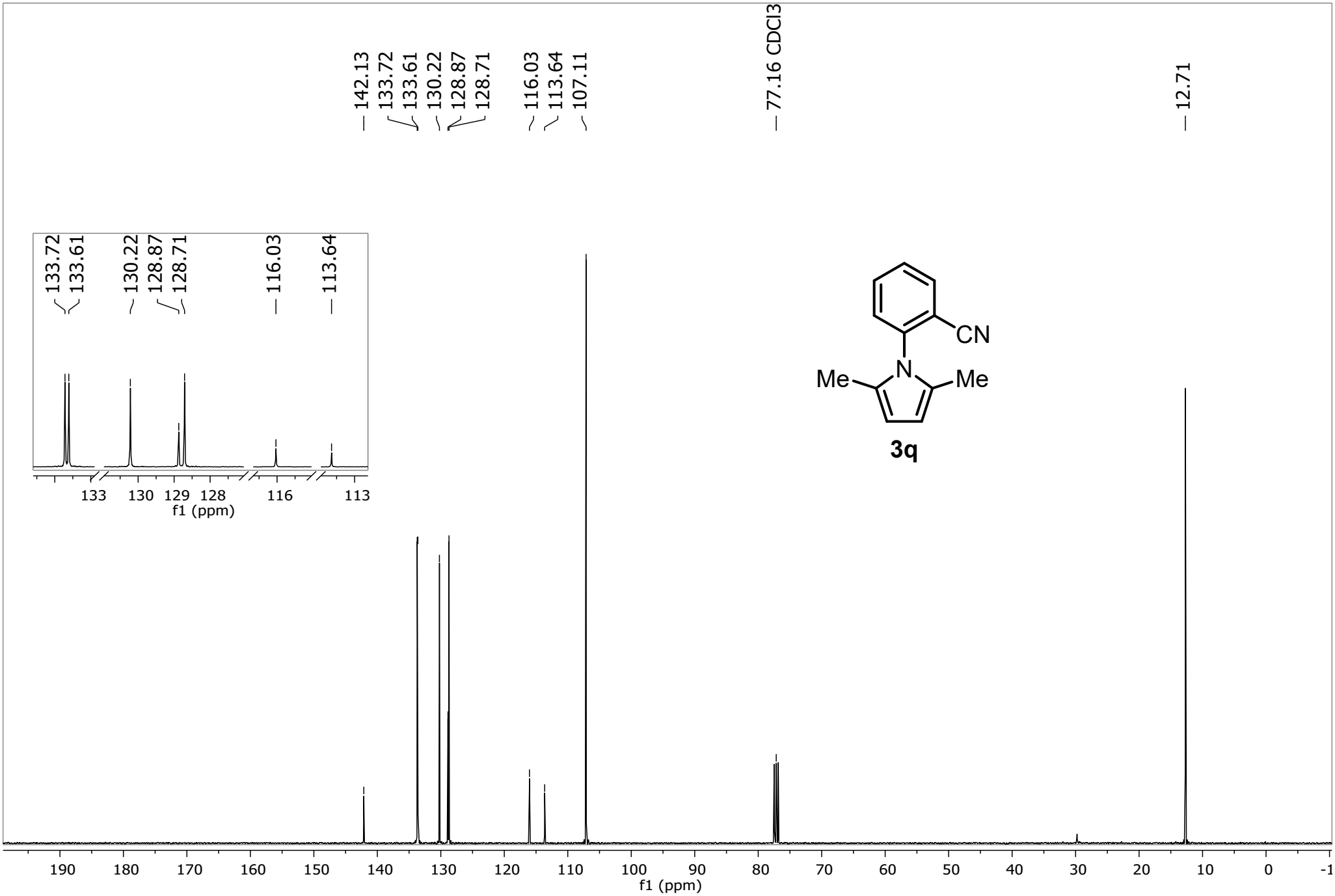


Figure 34. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3q**.

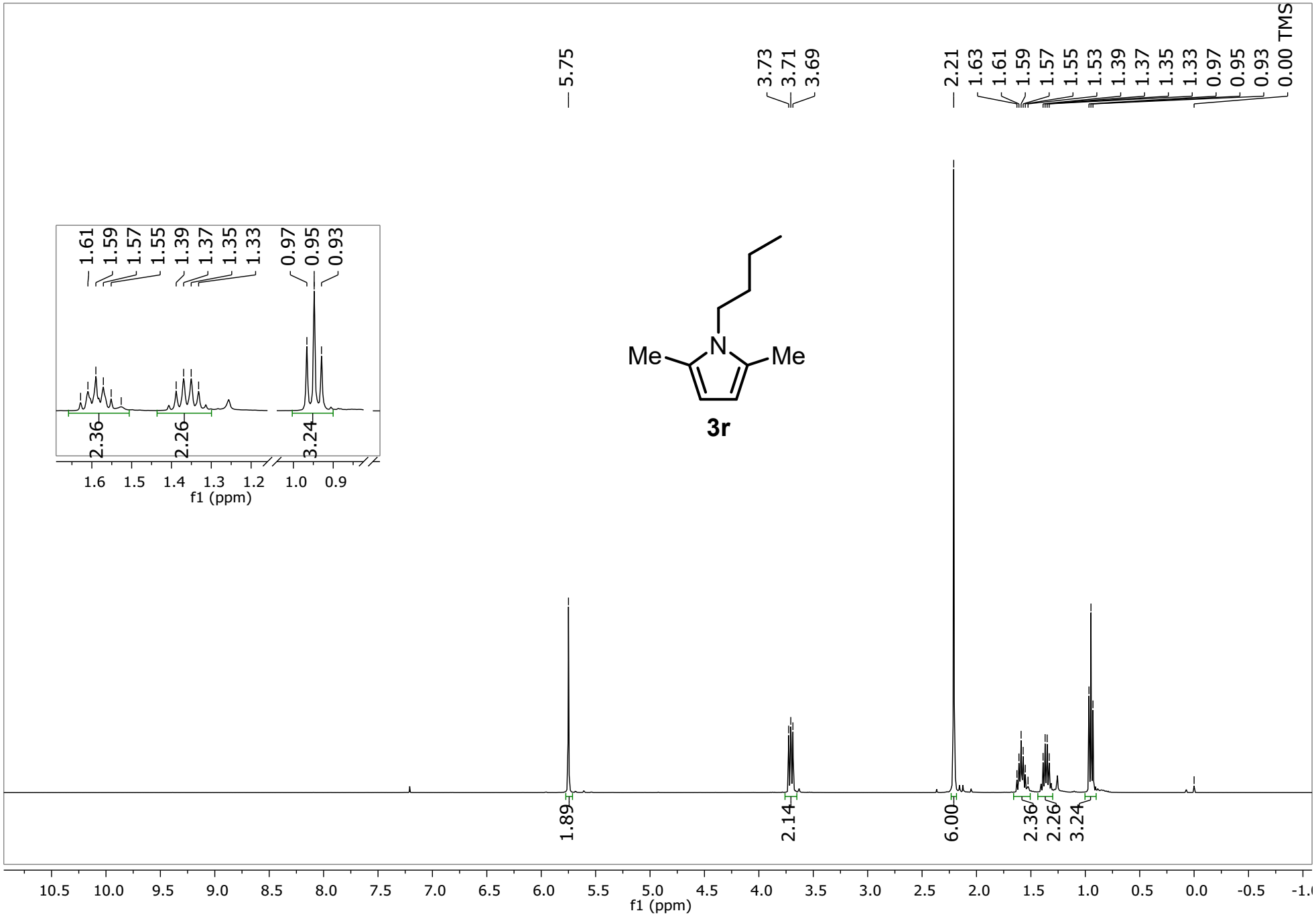


Figure 35. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3r**.

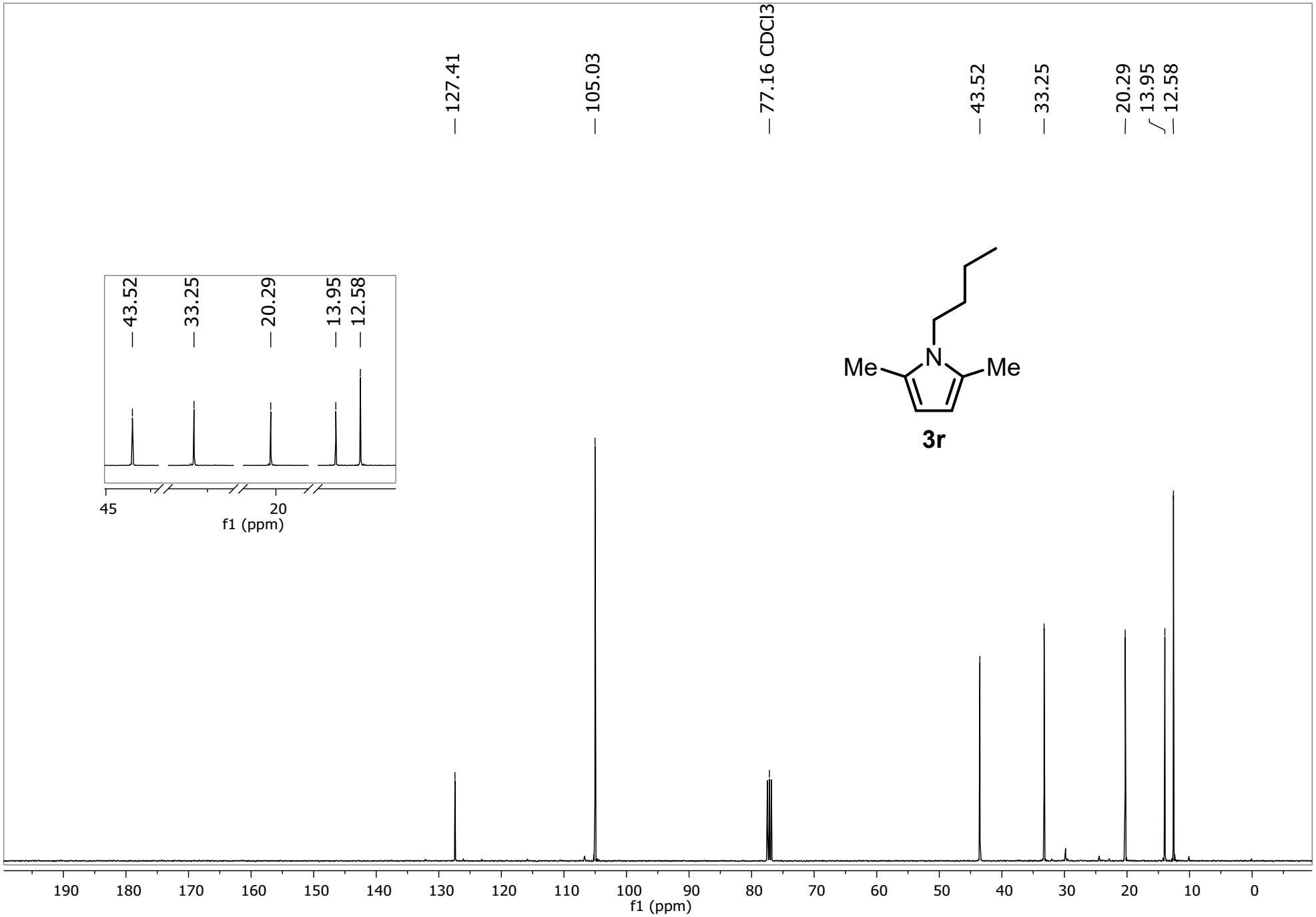


Figure 36. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3r**.

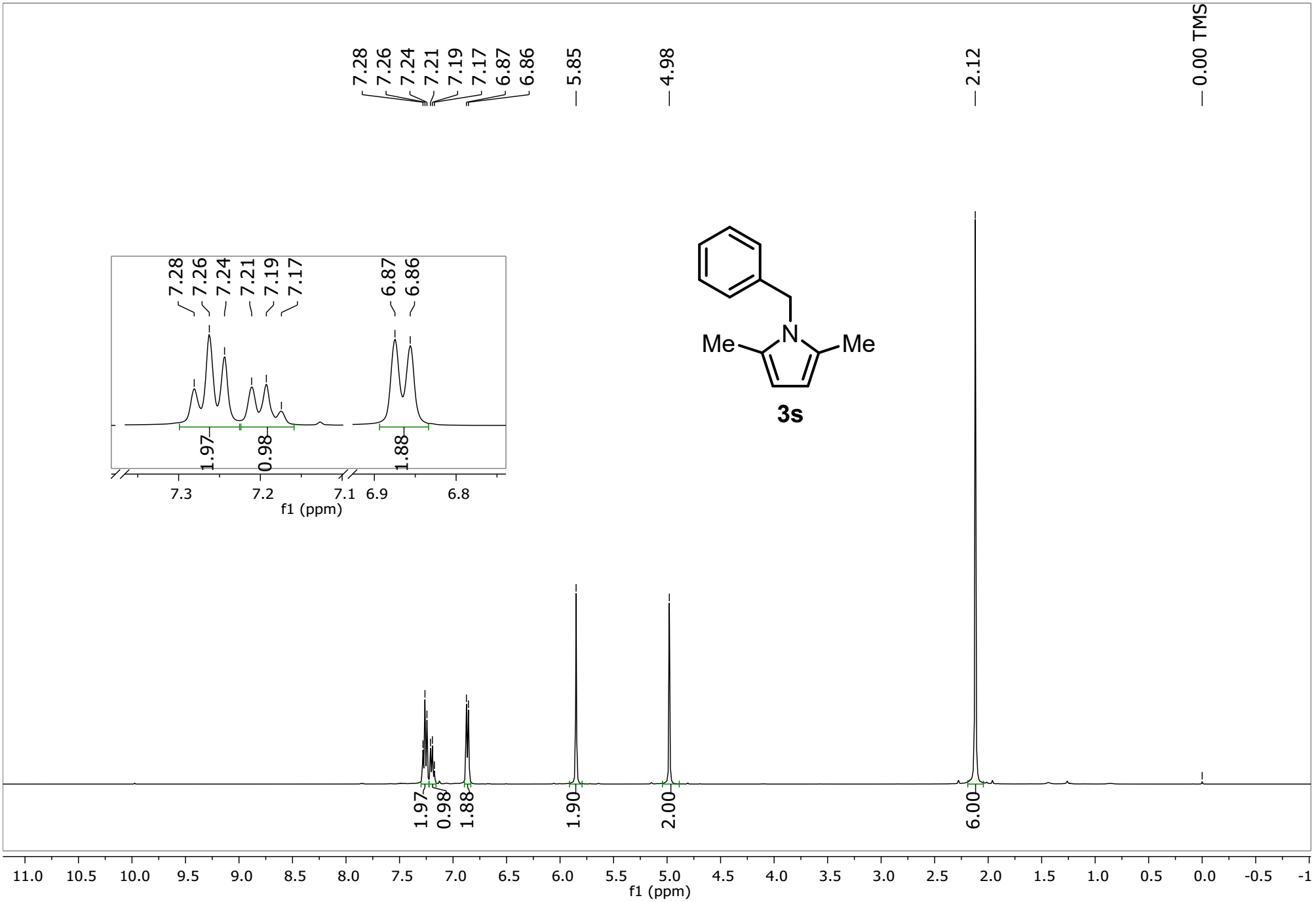


Figure 37. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3s**.

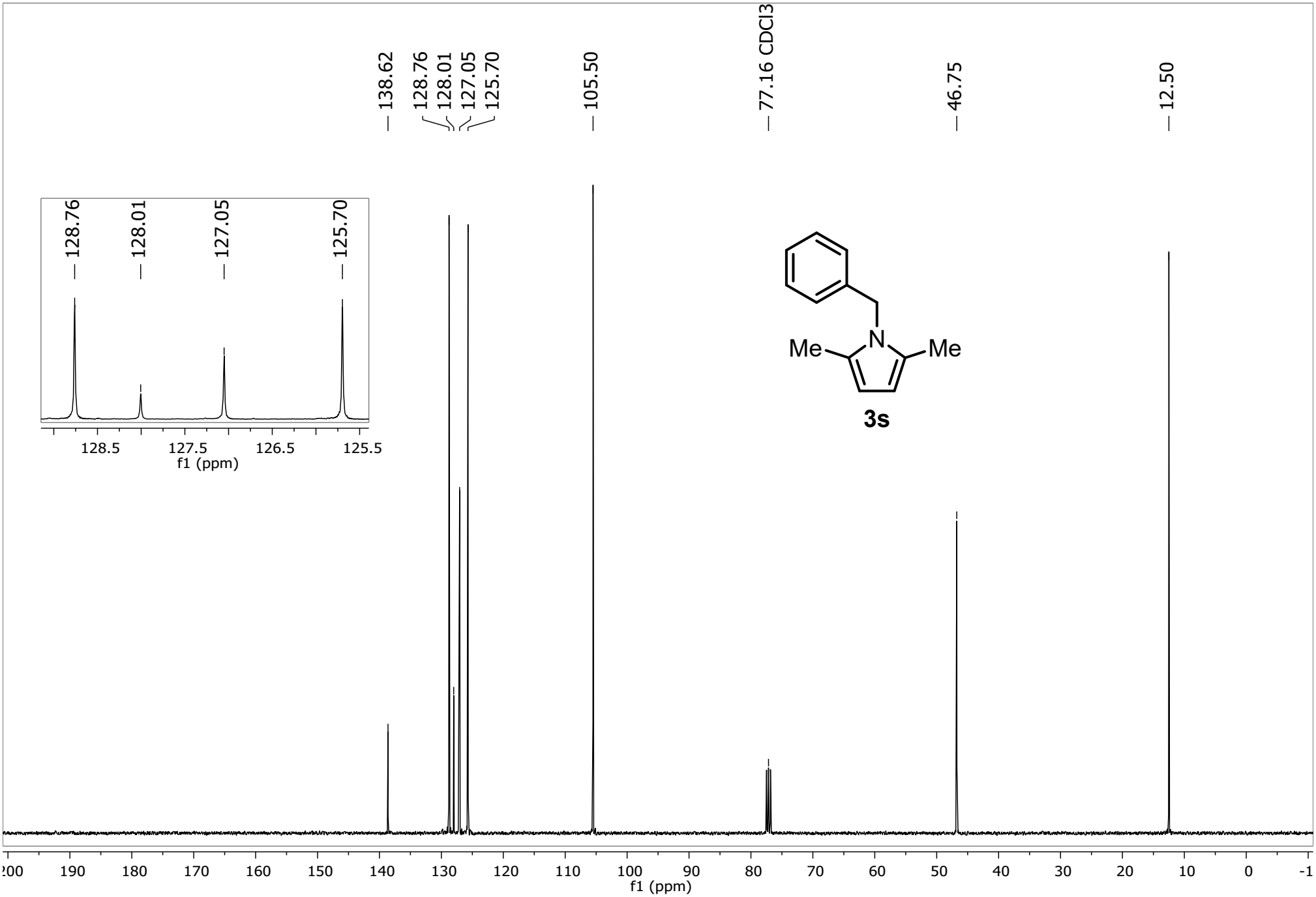


Figure 38. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3s**.

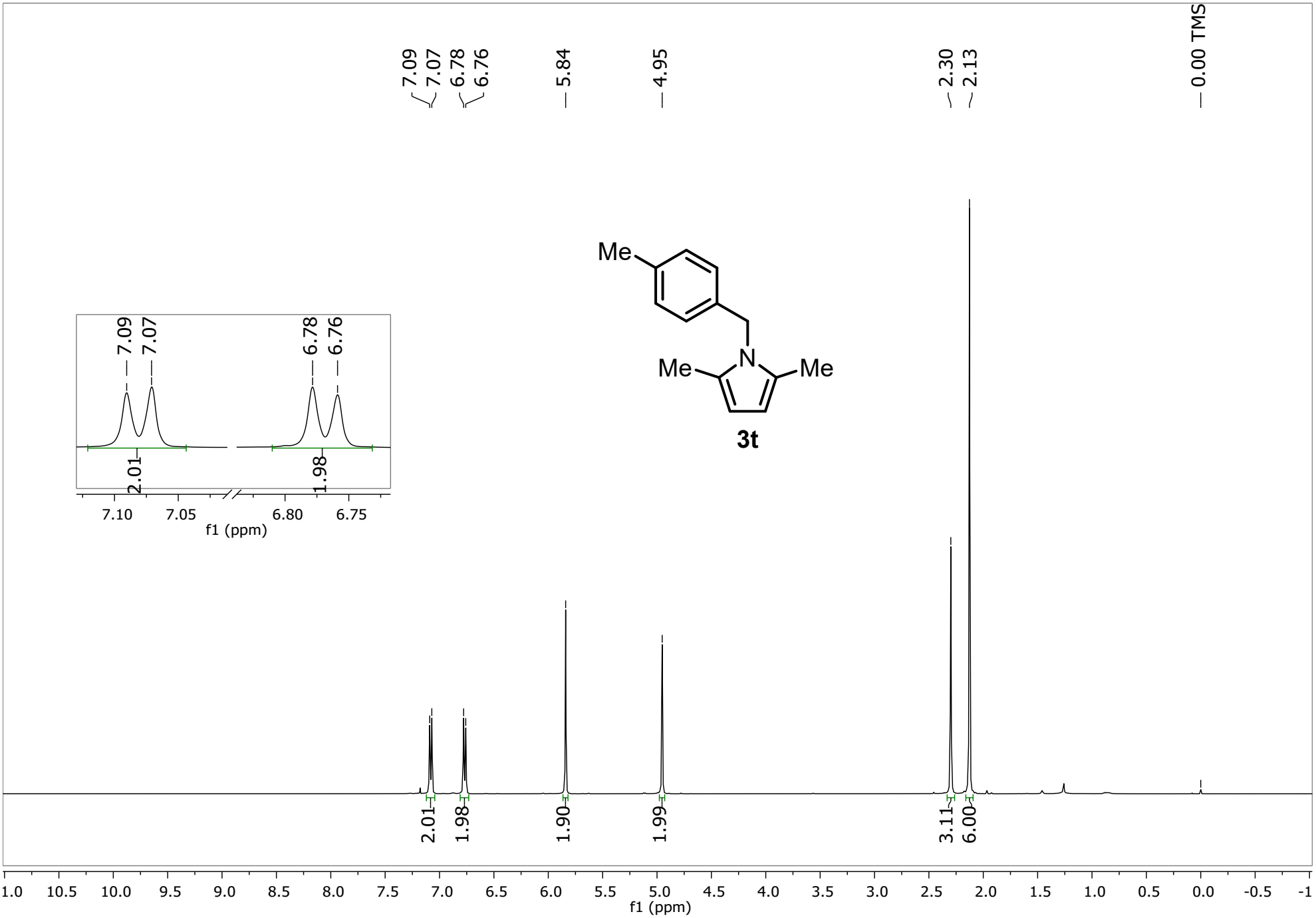


Figure 39. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3t**.

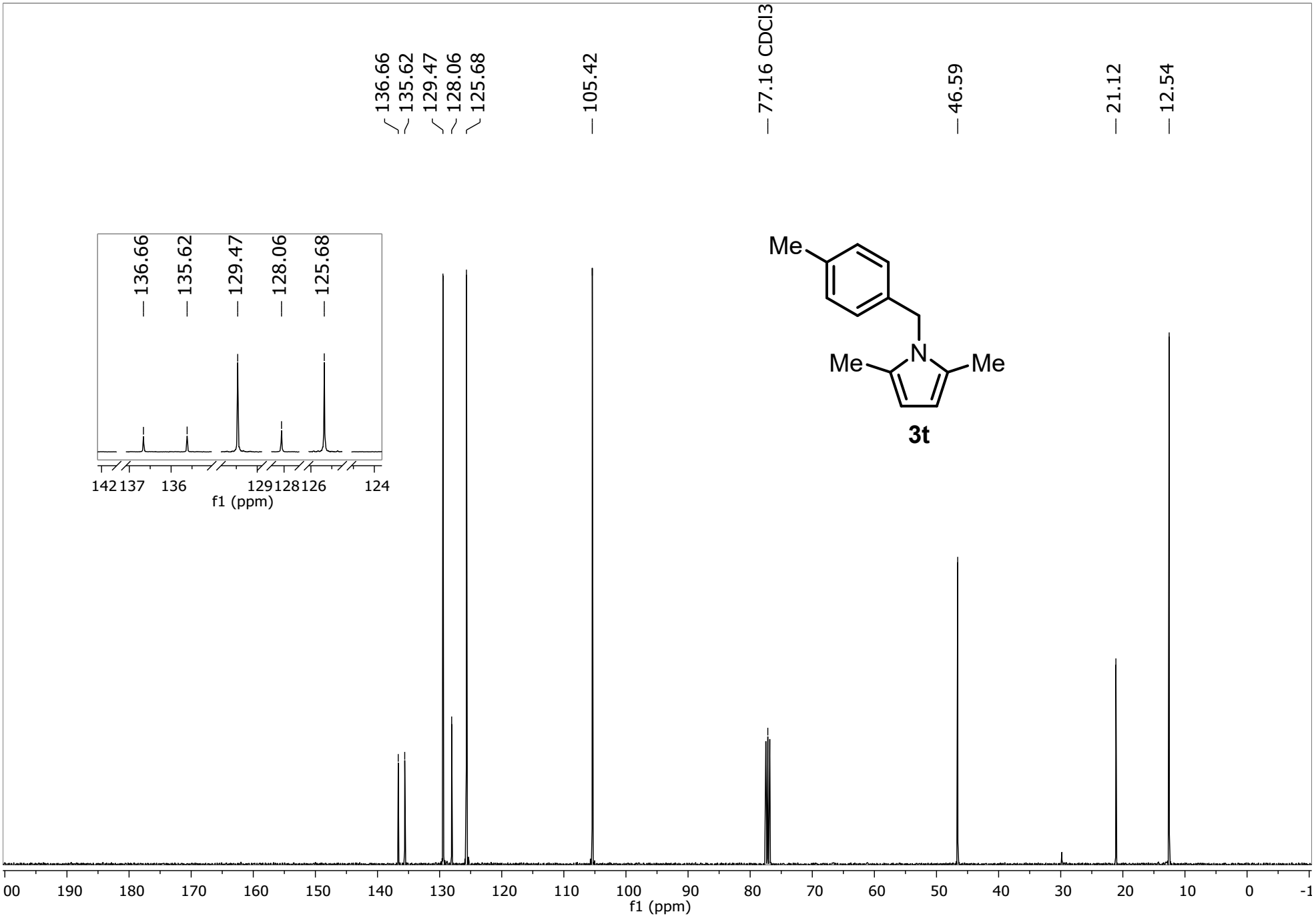


Figure 40. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3t**.

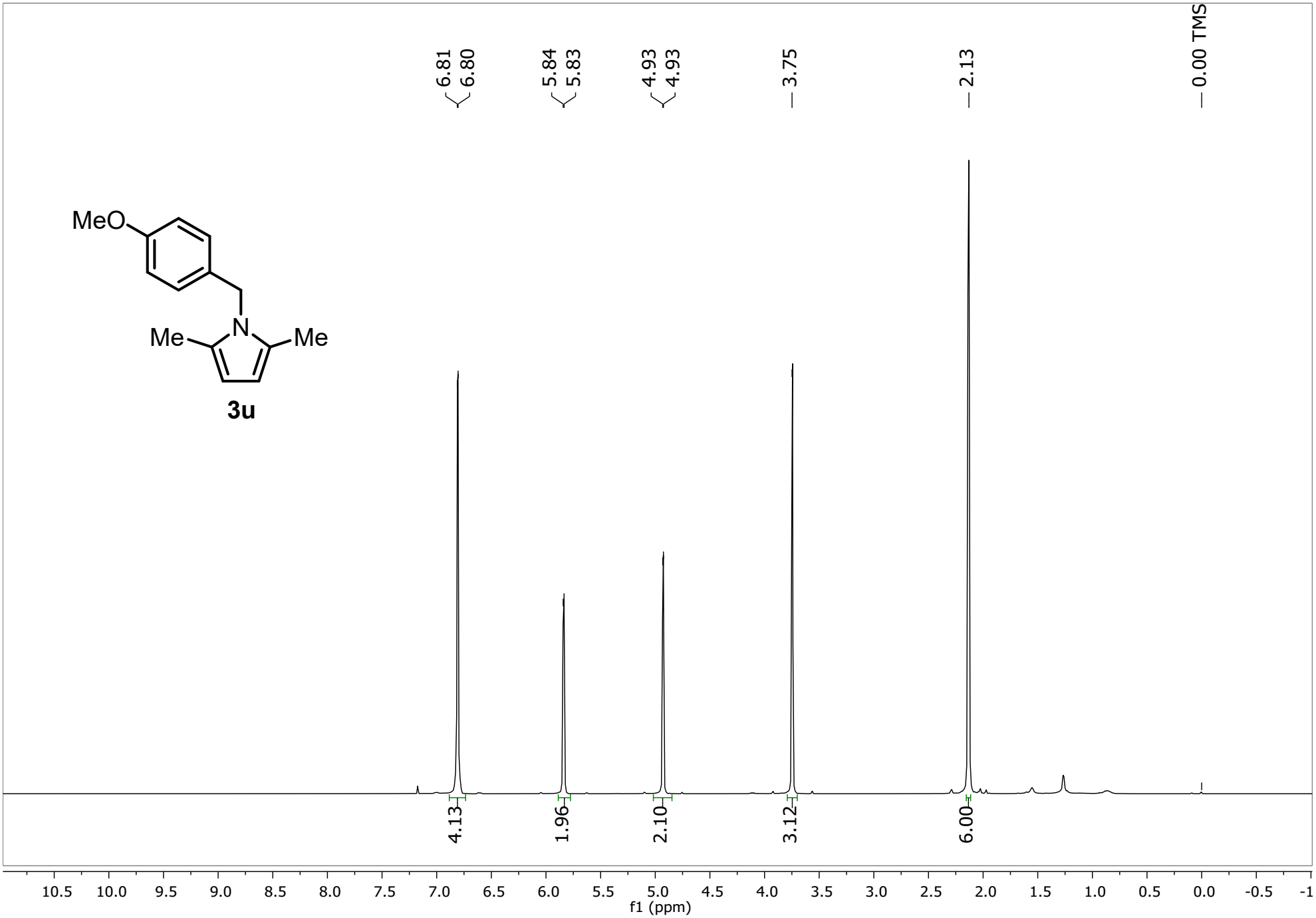


Figure 41. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3u**.

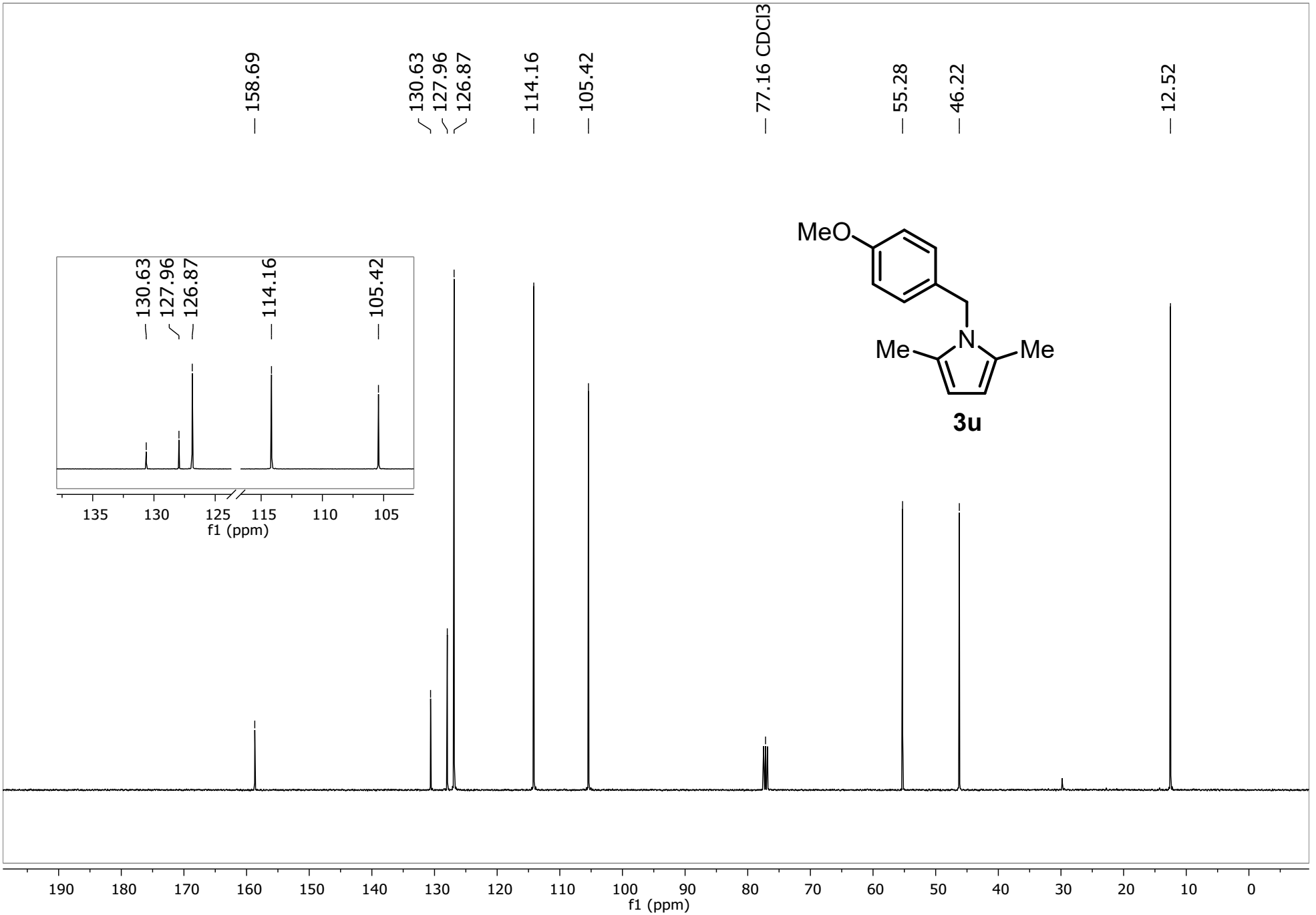


Figure 42. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3u**.

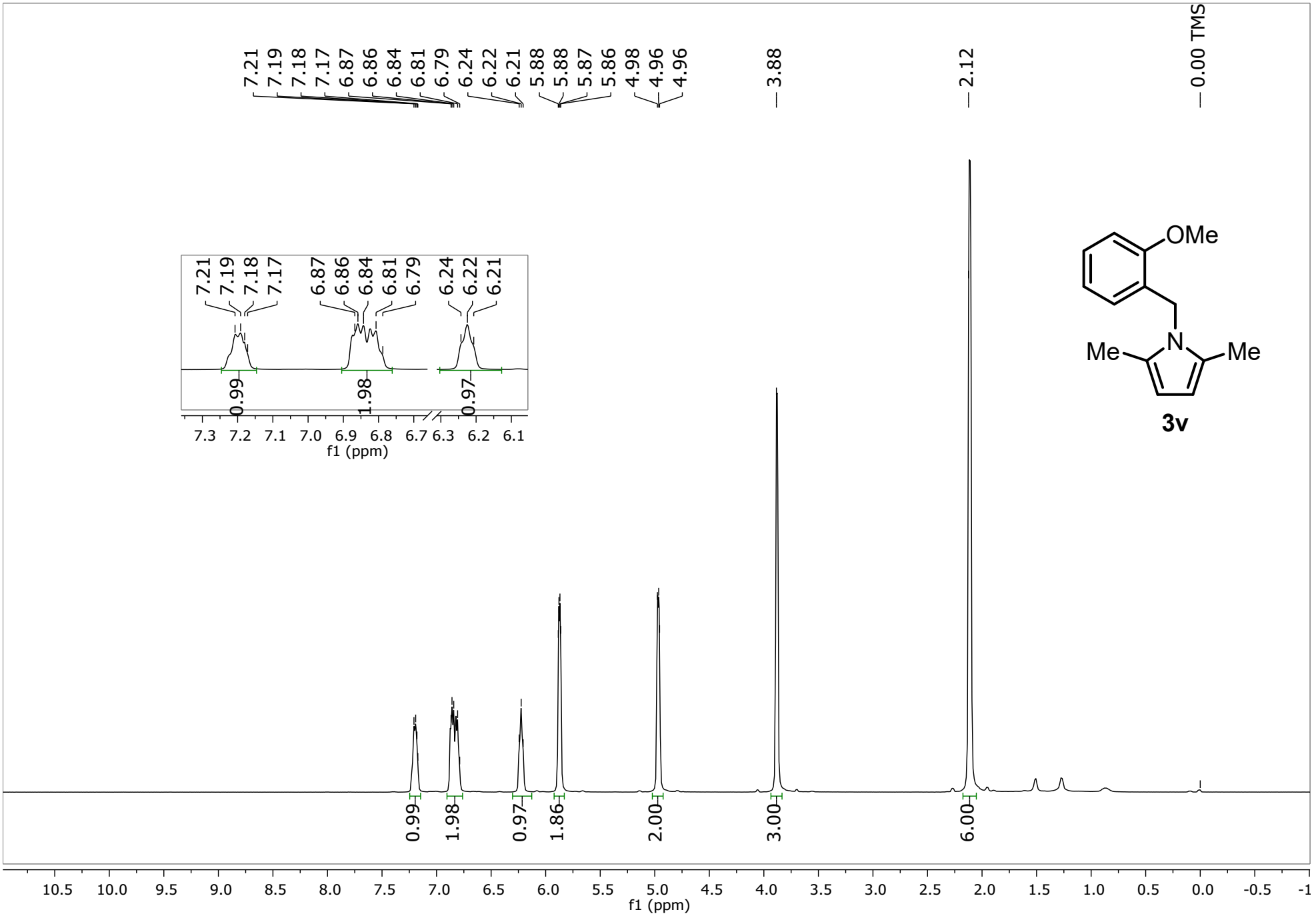


Figure 43. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3v**.

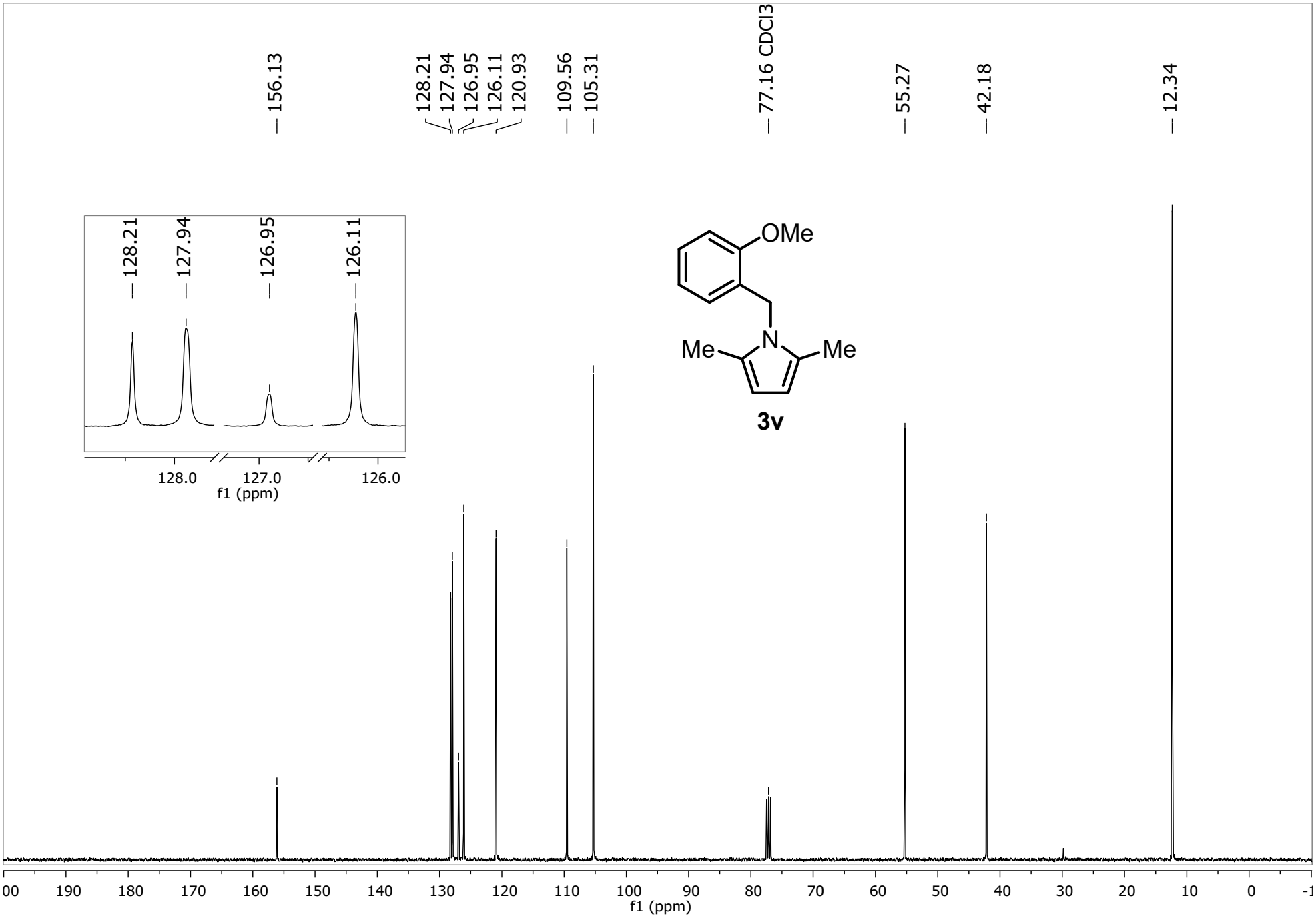


Figure 44. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3v**.

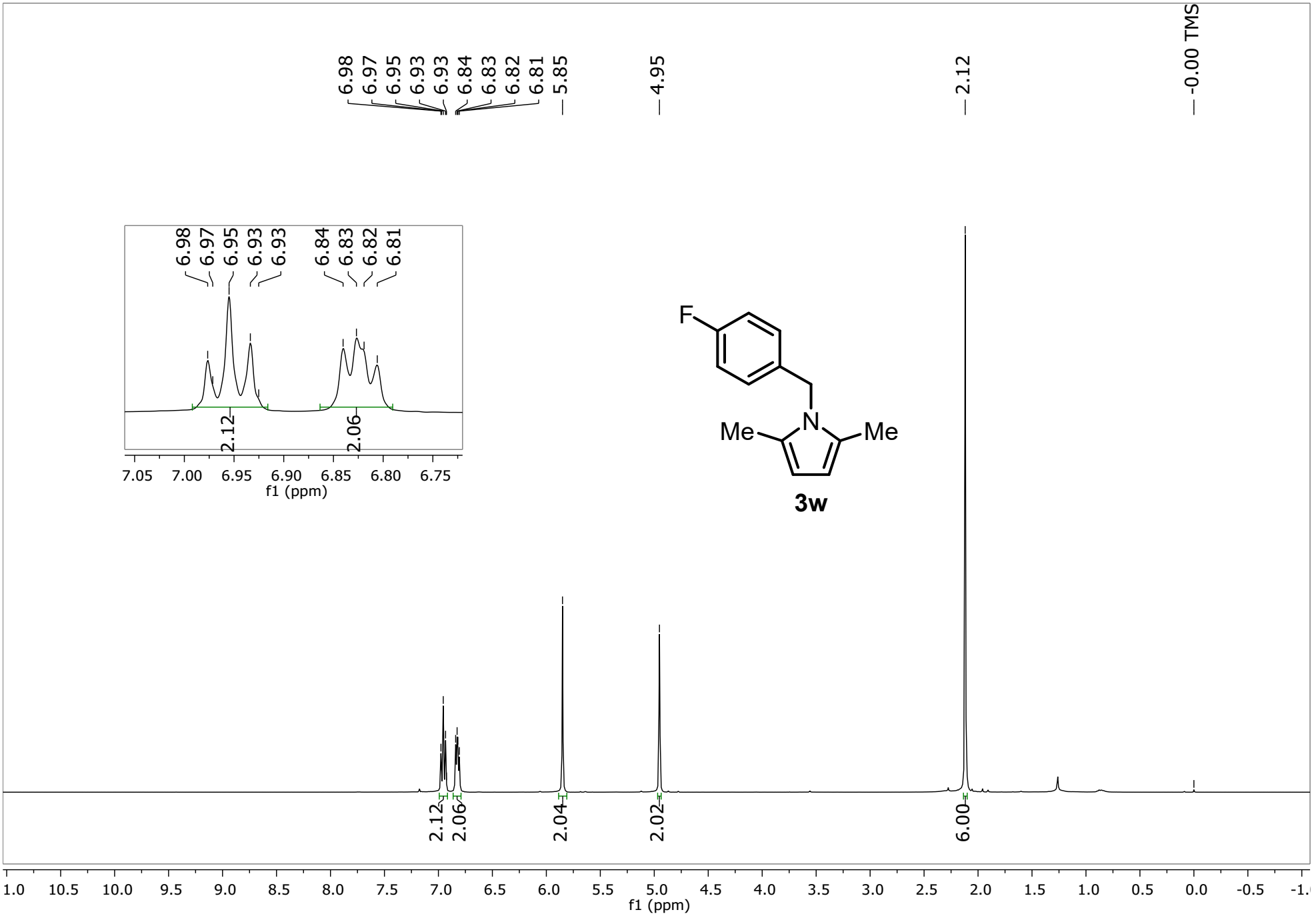


Figure 45. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3w**.

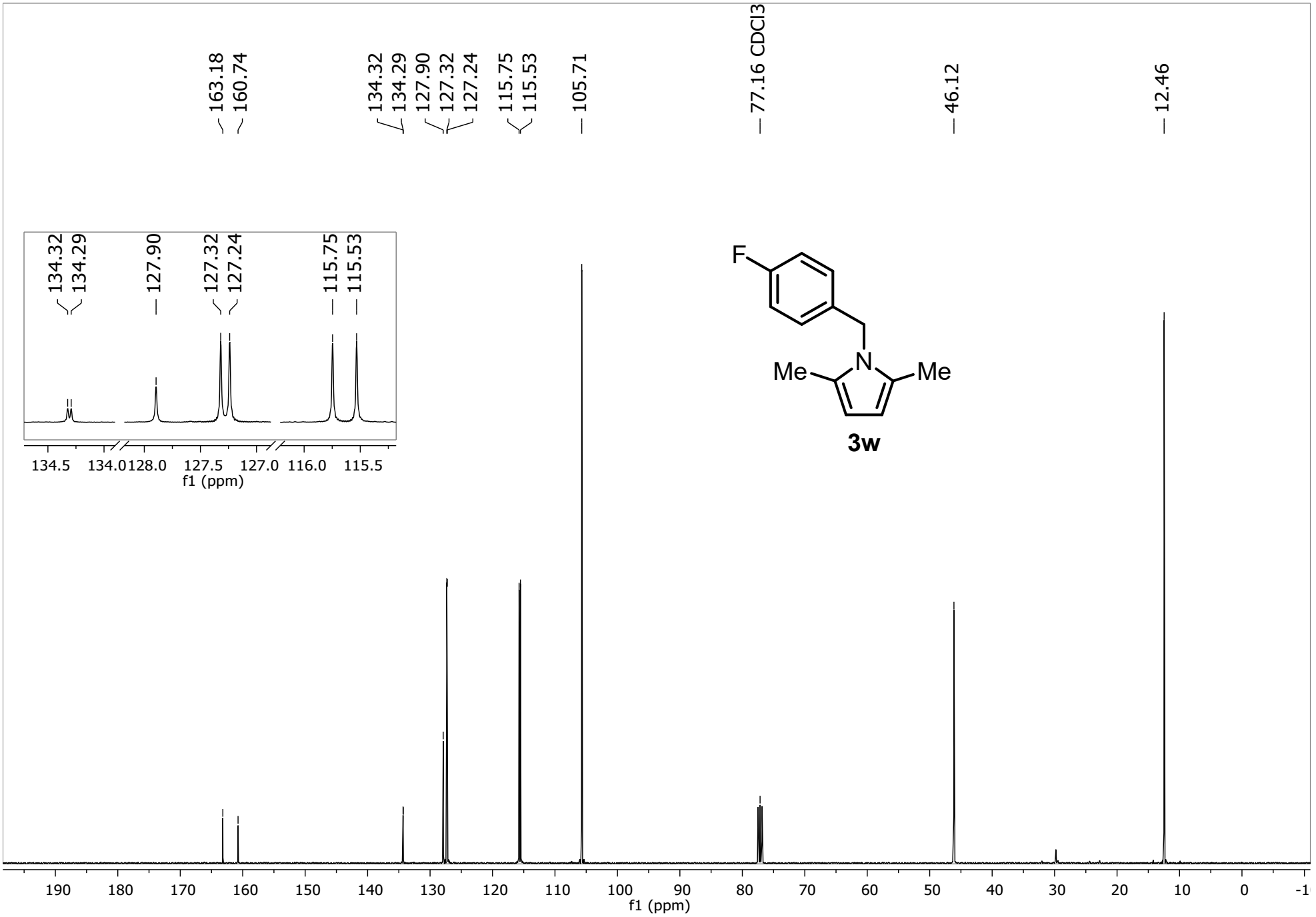


Figure 46. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3w**.

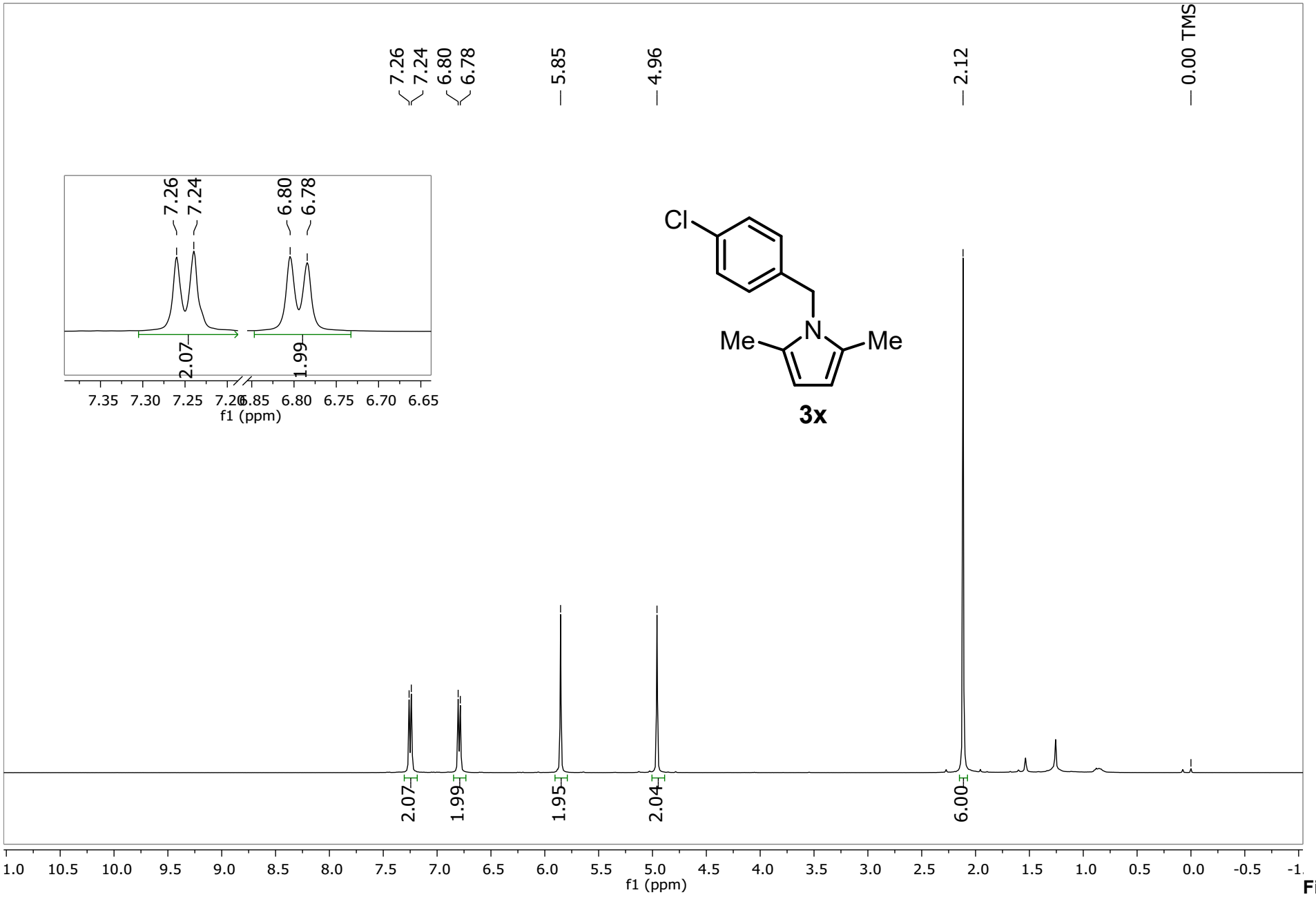


Figure 47. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3x**.

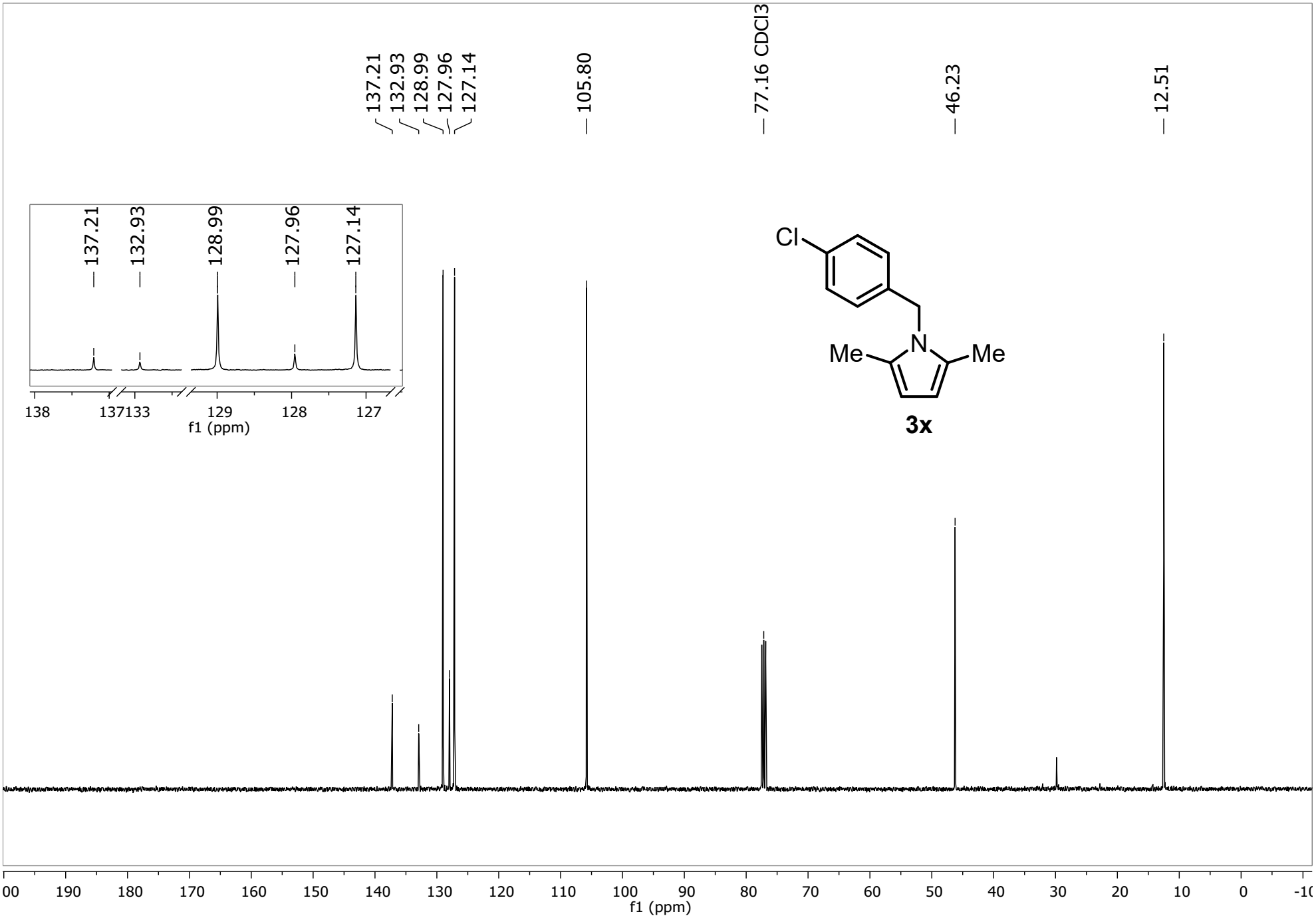


Figure 48. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3x**.

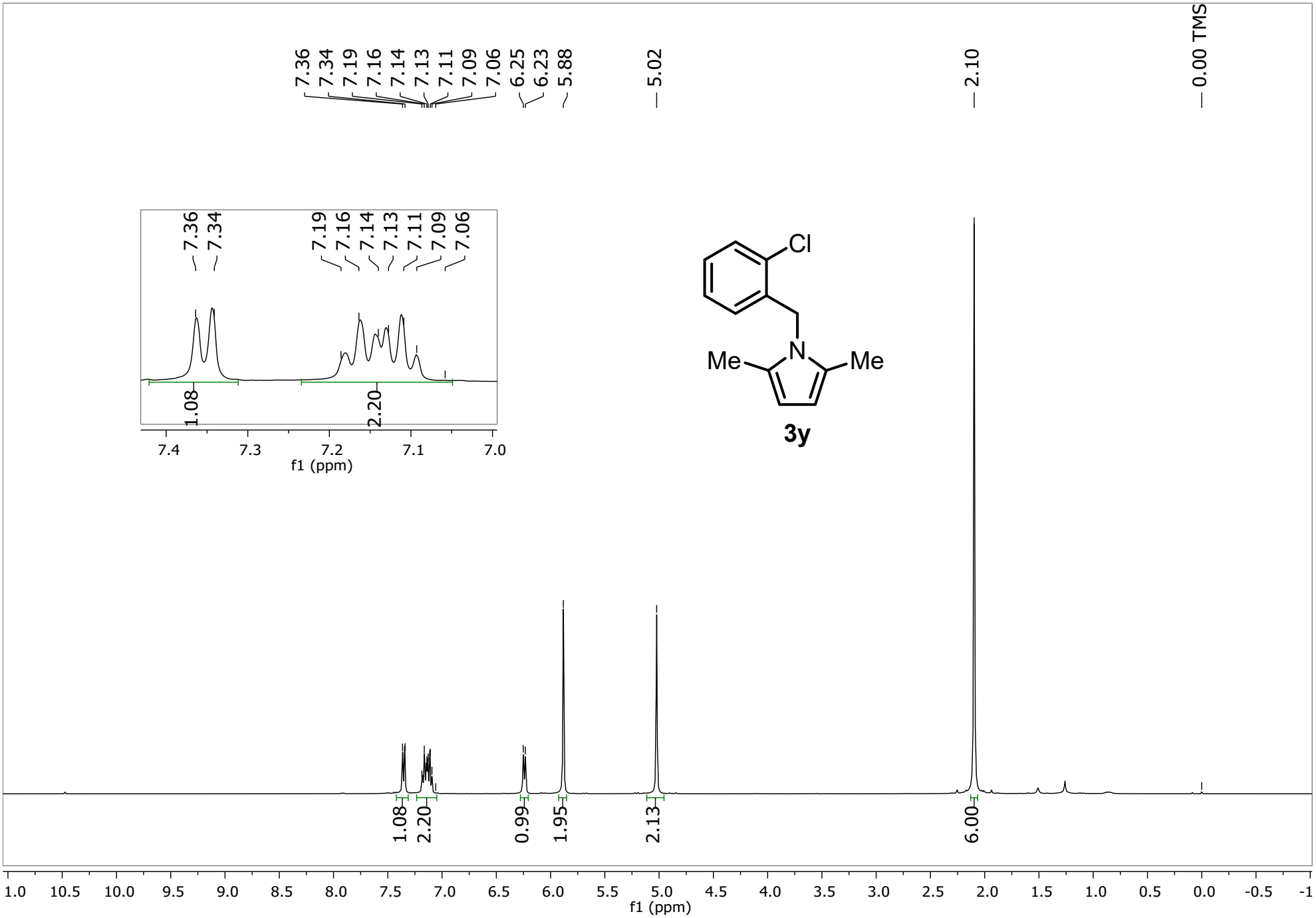


Figure 49. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the compound **3y**.

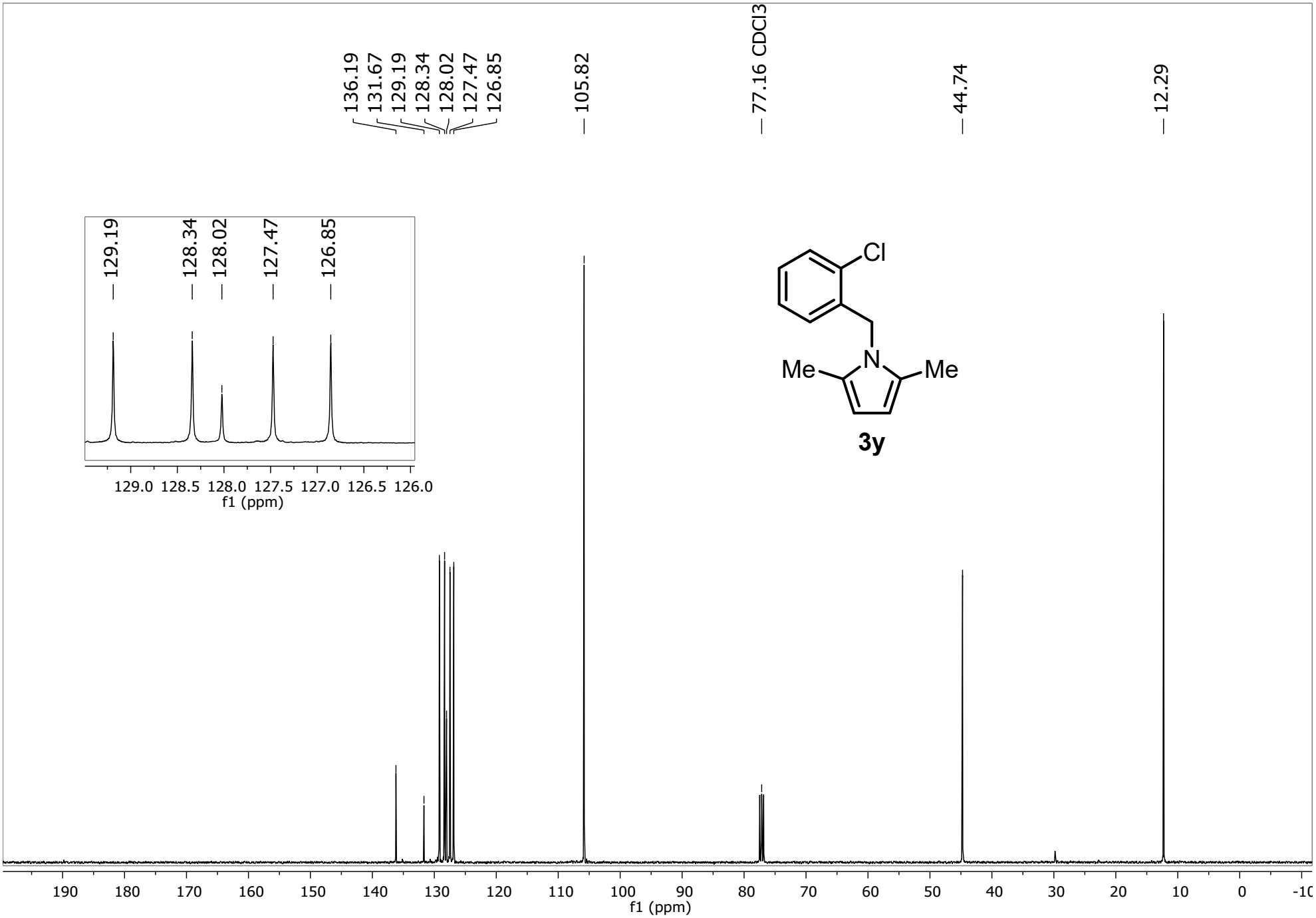


Figure 50. ^{13}C NMR (100 MHz, CDC_{l3}) spectrum of the compound **3y**.