# Transition-metal catalyst free oxidative radical arylation of *N*-methyl pyrrole

Esma Kocaoğlu,[†] Muhammed A. Karaman,[†] Hatun Tokgöz[†] and Oktay TALAZ*[†]

†Karamanoğlu Mehmetbey University, Kamil Özdağ Science Faculty, Department of Chemistry, 70100, Karaman, Turkey

*Corresponding Author Email: otalaz@kmu.edu.tr

ORCID : 0000-0003-2209-5402

## 1. General Information

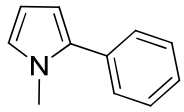
All reactions were carried out in air. All commercial reagents and chromatography solvents were used as obtained unless otherwise stated. Anhydrous solvents were distilled over appropriate drying agents prior to use. Analytical thin layer chromatography (TLC) was performed on Merck silica gel 60 $F_{254}$. Fluka Silica gel 60 (0.063-0.2 mm) was used for column chromatography.

TLC visualization was accomplished with UV light (254 nm) and by staining with ethanolic PMA (phosphomolybdic acid) solution. Elemental analyses were performed on a Leco CHNS-932. IR spectra were recorded on a Perkin Elmer Spectrum One FT-IR Spectrometer. High resolution mass spectra were measured on a Bruker Daltonics micrOTOF-Q. NMR spectra were recorded using a Varian 200 MHz NMR instrument ($^1$H NMR at 200 MHz, $^{13}$C NMR at 50 MHz) or a Varian 400 MHz instrument ($^1$H NMR at 400 MHz, $^{13}$C NMR at 100 MHz). $^1$H NMR data are reported as follows: chemical shift (δ ppm), multiplicity (s=singlet, d=dublet, dd=doublet of doublets, ddd=doublet of doublets of doublets, brs=broad singlet, t=triplet, q=quartet, quint=quintet, m=multiplet or otherwise stated), integration, coupling constant (*J*, Hz). $^{13}$C NMR data are given in terms of chemical shift (δ ppm).

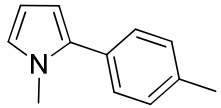
## 2. Experimental Procedures

### 2a. General Procedure for C-2 Arylation of Pyrrole with Phenylhydrazine Hydrochloride Salts

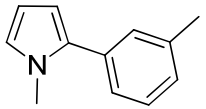
A two necked 10 mL flask equipped with magnetic stir bar (2x7 mm) was charged with pyrrole ( 10 mmol, 670 mg) and phenylhydrazine hydrochloride salt (0,5 mmol, 72 mg). Aqueous sodium hydroxide (0.5 M, 0.5 mL) was then added dropwise over a period of 0.5 hour. The resulting mixture was stirred in a two necked flask at room temperature 50-60 hour without closing the necks. Excess of pyrrole and water was evaporated with at room temperature, and the remaining solid was purified by flash columun chromatography (EtOAc/hexane %25).

**1-Methyl-2-phenyl-1*H*-pyrrole (8a)** 

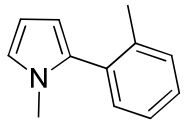
**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.41-7.29 (m, =CH, 5H), 6.73 (d, *J*= 1.8 Hz, CH, 1H), 6.23-6.21 (m, =CH, 2H), 3.67 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 134.83, 133.54, 128.87, 128.57, 126.96, 123.87, 108.84, 107.97, 35.32.

**1-Methyl-2-(*p*-tolyl)-1*H*-pyrrole (8b)** 

**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.33 (d, *J*= 8.0 Hz, =CH, 2H), 7.24 (dd, *J*= 8.8, 0.9 Hz, =CH, 2H), 6.73 (t, *J*= 2.2 Hz, =CH, 1H), 6.24 (m, =CH, 2H), 3.67 (s, $CH_3$, 3H), 2.41 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 136.74, 134.87, 13.71, 129,31, 128.86, 123.57, 35.25, 21.44.

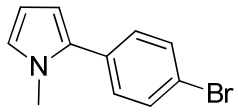
**1-Methyl-2-(*m*-tolyl)-1*H*-pyrrole (8c)** 

**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.37-7.16 (m, =CH, 4H), 6.76 (d, *J*= 1.91 Hz, =CH, 1H), 6.29-6.26 (m, =CH, 2H), 3.71 (s, $CH_3$, 3H), 2.45 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 138.21, 134.99, 133.57, 129.73, 128.49, 127.80, 125.99, 123.78, 108.81, 107.99, 35.31, 21.79.

**1-Methyl-2-(*o*-tolyl)-1*H*-pyrrole (8d)** 

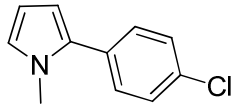
**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.20-7.14 (m, =CH, 4H), 6.64-6.63 (m, =CH, 4H), 6.13 (dd, *J*= 3.4, 2.8 Hz, =CH, 2H), 5.99 (dd, *J*= 3.5, 1. 8 Hz, =CH, 1H), 3.32 (s, $CH_3$, 3H), 2.11 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 138.23, 133.15, 131.21, 129.94, 127.91, 125.37, 121.64, 108.42, 107.23, 34.06, 20.06.

**2-(4-Bromophenyl)-1-methyl-1*H*-pyrrole (8e),**



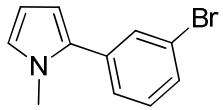

**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.52-7.49 (m, =CH, 2H), 7.27-7.24 (m, =CH, 2H), 6.73-6.71 (m, =CH, 1H), 6.23-6.18 (m, =CH, 2H), 3.64 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 133.54, 132.41, 132.22, 131.73, 130.27, 127.97, 124.38, 120.98, 109.22, 108.20, 35.34.

**2-(4-Chlorophenyl)-1-methyl-1*H*-pyrrole (8f),**




**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.41-7.33 (m, =CH, 4H), 6.74 (t, *J*= 2.2 Hz, =CH, 1H), 6.26-6.21 (m, =CH, 2H), 3.67 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 150.34, 134.81, 131.44, 129.02, 128.79, 128.24, 127.38, 125.76, 23.60.

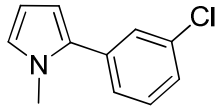
**2-(3-Bromophenyl)-1-methyl-1*H*-pyrrole (8g),**




**$^1$H NMR (400 MHz, CDCl3) δ** 7.54-7.27 (m, =CH, 4H), 6.72 (s, =CH, 1H), 6.23-6.19 (m, =CH, 2H), 3.66 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 135.57, 133.16, 131.55, 130.06, 129.81, 127.23, 124.55, 122.62, 109.61, 108.22, 35.35.

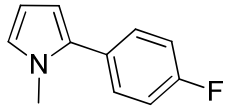
2-(3-chlorophenyl)-1-methyl-1*H*-pyrrole

**2-(3-Chlorophenyl)-1-methyl-1*H*-pyrrole (8h),**



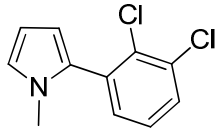
**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.29 (t, *J*= 1.74 Hz, =CH, 1H), 7.22-7.16 (m, =CH, 3H), 6.63-6.62 (m, =CH, 1H), 6.15-6.14 (m, =CH, 1H), 6.11-6.09 (m, =CH, 1H), 3.57 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 135.01, 134.16, 129.58, 128.39, 126.67, 126.55, 124.31, 109.31, 107.96, 29.71.

**2-(3-Florophenyl)-1-methyl-1*H*-pyrrole (8i),**



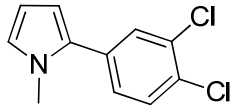

**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.35-7.32 (m, =CH, 2H), 7.09-7.04 (m, =CH, 2H), 6.69 (t, *J*= 2.3 Hz, =CH, 1H), 6.18-6.17 (m, =CH, 2H), 3.60 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 162.03 (d, *J*= 246.2 Hz, 1C), 133.66, 130.46 (d, *J*= 7.9 Hz, 2C), 129.56, 123.70, 115.44 (d, *J*= 21.4 Hz), 108.75, 107.88.

**2-(2,3-Dichlorophenyl)-1-methyl-1*H*-pyrrole (8j),**



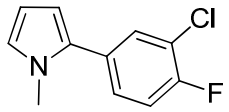

**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.48 (dd, *J*= 7.3, 2.4 Hz, =CH, 1H), 7.27-7.20 (m, =CH, 2H), 6.75-6.74 (m, =CH, 1H), 6.22 (dd, *J*= 3.5, 2.8 Hz, =CH, 1H), 6.15 (dd, *J*= 3.5, 2.8 Hz, =CH, 1H), 3.47 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 135.03, 133.73, 133.53, 131.23, 131.08, 130.31, 127.19, 123.00, 109.78, 107.78, 34.66.

**2-(3,4-dichlorophenyl)-1-methyl-1*H*-pyrrole (8k),**



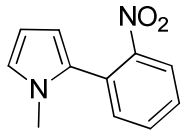

**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.48-7.44 (m, =CH, 2H), 7.24-7.21 (m, =CH, 1H), 6.73 (dd, *J*= 2.6, 1.9 Hz, =CH, 1H), 6.25 (dd, *J*= 3.6, 1.8 Hz, =CH, 1H), 6.20 (dd, *J*= 3.6, 2.7, =CH, 1H), 3.66 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 133.31, 132.42, 132.02, 130.66, 130.27, 130.01, 127.57, 124.61, 109.64, 108.14, 35.09.

**2-(3-Chloro-4-fluorophenyl)-1-methyl-1*H*-pyrrole (8l),**



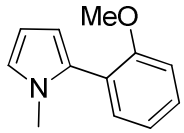

**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.44-7.41 (m, =CH, 1H), 7.27-7.22 (m, =CH, 1H), 7.19-7.13 (m, =CH, 1H), 6.73-6.71 (m, =CH, 1H), 6.22-6.18 (m, =CH, 2H), 3.64 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 158.99, 155.69, 132.42, 130.78, 128.50 (d, *J*= 69 Hz), 124.37, 121.07 (d, *J*= 17.8 Hz), 116.72 (d, *J*= 21.2 Hz, 109.49, 108.19, 35.29.

**1-Methyl-2-(2-nitrophenyl)-1*H*-pyrrole (8m),**



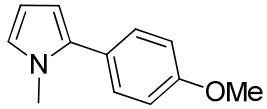

**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.94 (dd, *J*=8.1, 1.3, =CH, 1H), 7.61 (dd, *J*= 7.5, 1.4 Hz, =CH,1H), 7.53-7.45 (m, =CH, 2H), 6.76 (dd, *J*= 2.7, 1.8 Hz, =CH, 1H), 6.21 (dd, *J*= 3.6, 2.7 Hz, =CH, 1H), 6.14 (dd, *J*= 3.6, 1.8 Hz, 3.44 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 149.88, 133.40, 132.23, 128.67, 128.27, 127.93, 124.06, 123.62, 109.60, 108.06, 34.28.

**2-(2-Metoxyphenyl)-1-methyl-1*H*-pyrrole (8n),**



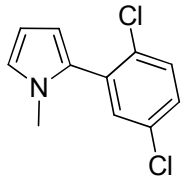

**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.38-7.31 (m, =CH, 2H), 7.06-6.98 (m, =CH,2H), 6.77 (d, *J*= 1.3 Hz, =CH, 1H), 6.27-6.25 (m, =CH, 2H), 6.19-6.18 (m, =CH, 2H), 3.84 (s, $CH_3$, 3H), 3.52 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 157.39, 132.36, 131.15, 129.14, 122.58, 122.41, 120.50, 110.70, 108.91, 107.49, 55.36, 34.52.

**2-(4-Metoxyphenyl)-1-methyl-1*H*-pyrrole (8o),**



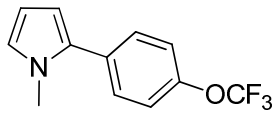
**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.23-7.21 (m, =CH, 2H), 6.85-6.83 (m, =CH, 2H), 6.59 (t, *J*= 2.2, =CH, 1H), 6.10-6.06 (m, =CH, 2H).3.73 (s, $CH_3$, 3H), 3.52 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 158.61, 134.36, 130.03, 125.93, 123.00, 113.78, 107.98, 107.56, 55.31, 34.92.

**2-(2,5-dichlorophenyl)-1-methyl-1*H*-pyrrole (8p),**



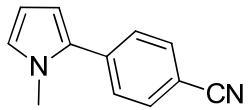

**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.40-7.35 (m, =CH, 2H), 7.29-7.26 (m, =CH, 1H), 7.75 (m, =CH, 1H), 6.22 (t, *J*= 3.10 Hz, =CH, 1H), 6.17 (dd, *J*= 3.5, 1.7 Hz, =CH, 1H), 3.49 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 134.14, 133.30, 132.52, 132.25, 130.56, 129.90, 129.09, 123.06, 109.96, 107.71, 34.41.

**1-Methyl-2-(4-(trifluoromethoxy)phenyl)-1*H*-pyrrole (8q),**



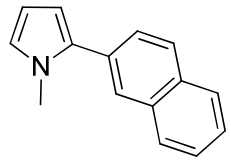

**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.42-7.40 (m, =CH, 2H), 7.25-7.23 (m, =CH, 2H), 6.74-6.73 (m, =CH, 1H), 6.24-6.20 (m, =CH, 2H), 3.66 (s, $CH_3$, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 150.10, 129.81, 127.61, 127.06, 127.04, 121.14, 120.85, 109.13, 107.91, 34.99.

**4-(1-Methyl-1*H*-pyrrole-2-yl)benzonitrile (8r),**




**$^1$H NMR (400 MHz, $CDCl_3$) δ** 7.67 (dd, *J*= 8.7, 0.7 Hz, =CH, 2H), 7.50 (dd, *J*= 8.7, 0.6 Hz, =CH, 2H), 6.78 (d, *J*= 2.0 Hz, =CH, 1H, 6.36-6.34 (m, =CH, 2H), 6.24-6.22 (m, =CH, 1H) ; **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 137.71, 132.60, 132.24, 128.26, 125.87, 119.02, 110.77, 109.66, 108.59, 35.45.

**1-Methyl-2-(naphthalene-2-yl)-1*H*-pyrrole (8s),**



**$^{1}$H NMR (400 MHz, $CDCl_3$) δ** 7.88 (t, *J*= 7.3 Hz, =CH, 2H), 7.71 (d, *J*= 8.8, =CH, 2H), 7.53-7.44 (m, =CH, 4H), 6.82 (m, =CH, 1H), 6.31-6.30 (m, =CH, 1H), 6.26-6.25 (m, =CH, 1H); **$^{13}$C NMR (100 MHz, $CDCl_3$) δ** 133.62, 133.32, 132.17, 131.23, 130.84, 128.78, 128.71, 128.18, 128.14, 126.26, 126.24, 125.82, 125.17, 122.38, 109.98, 107.52, 34.47.

**NMR Spectra of Compounds:**

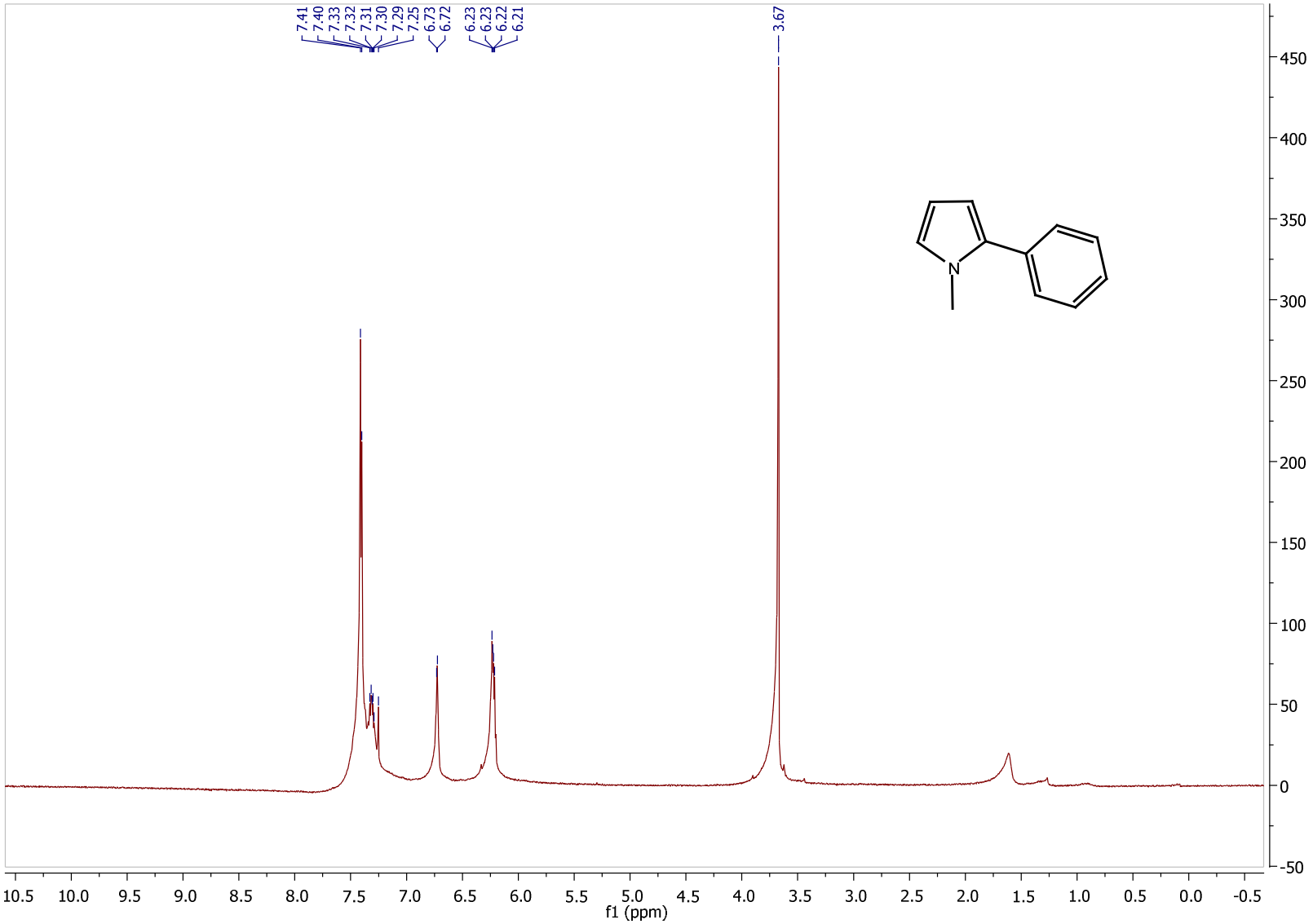



**Figure S1.** $^{1}$H-NMR spectra of compound **8a**.

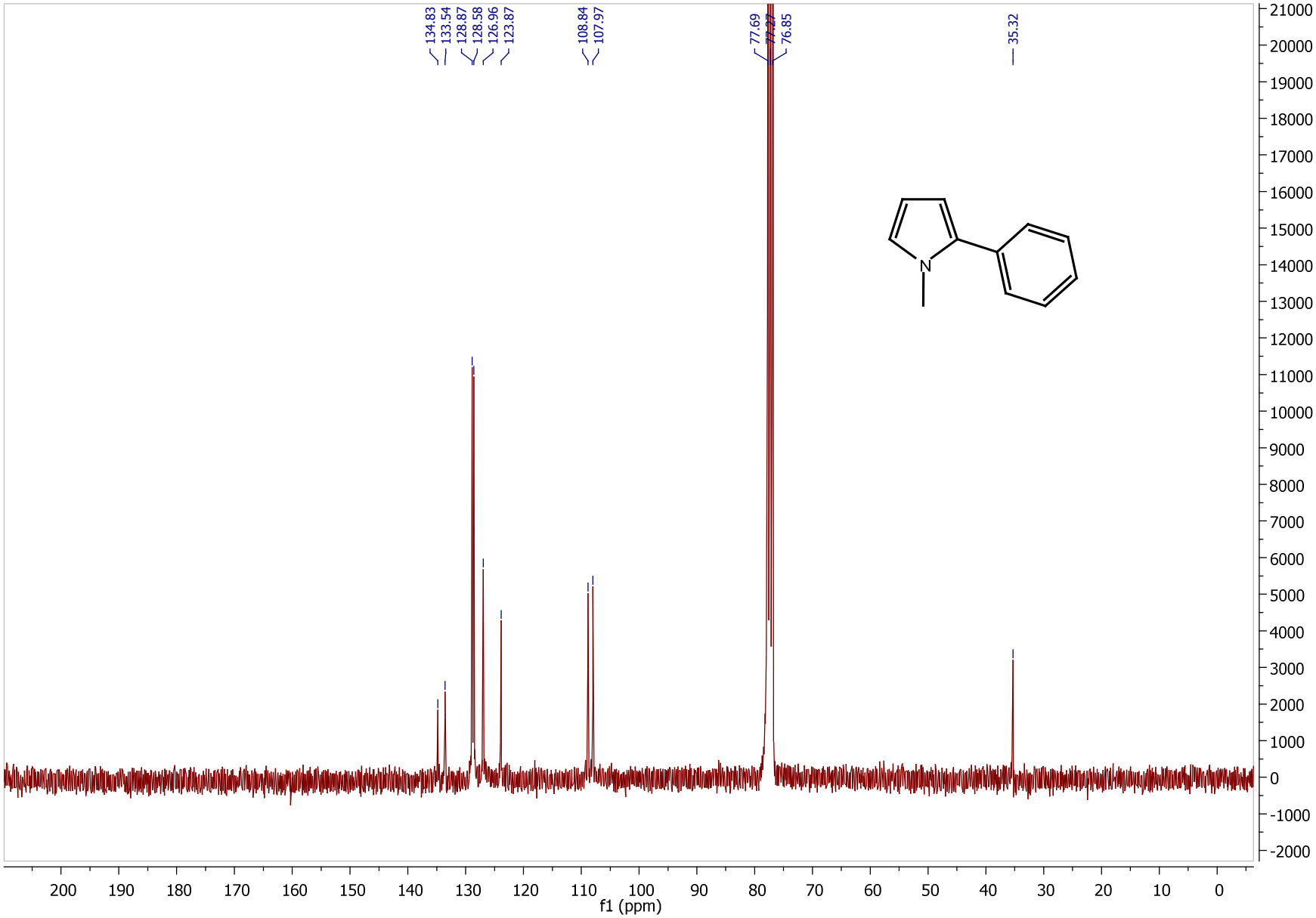



**Figure S2.** $^{13}$C-NMR spectra of compound **8a**.

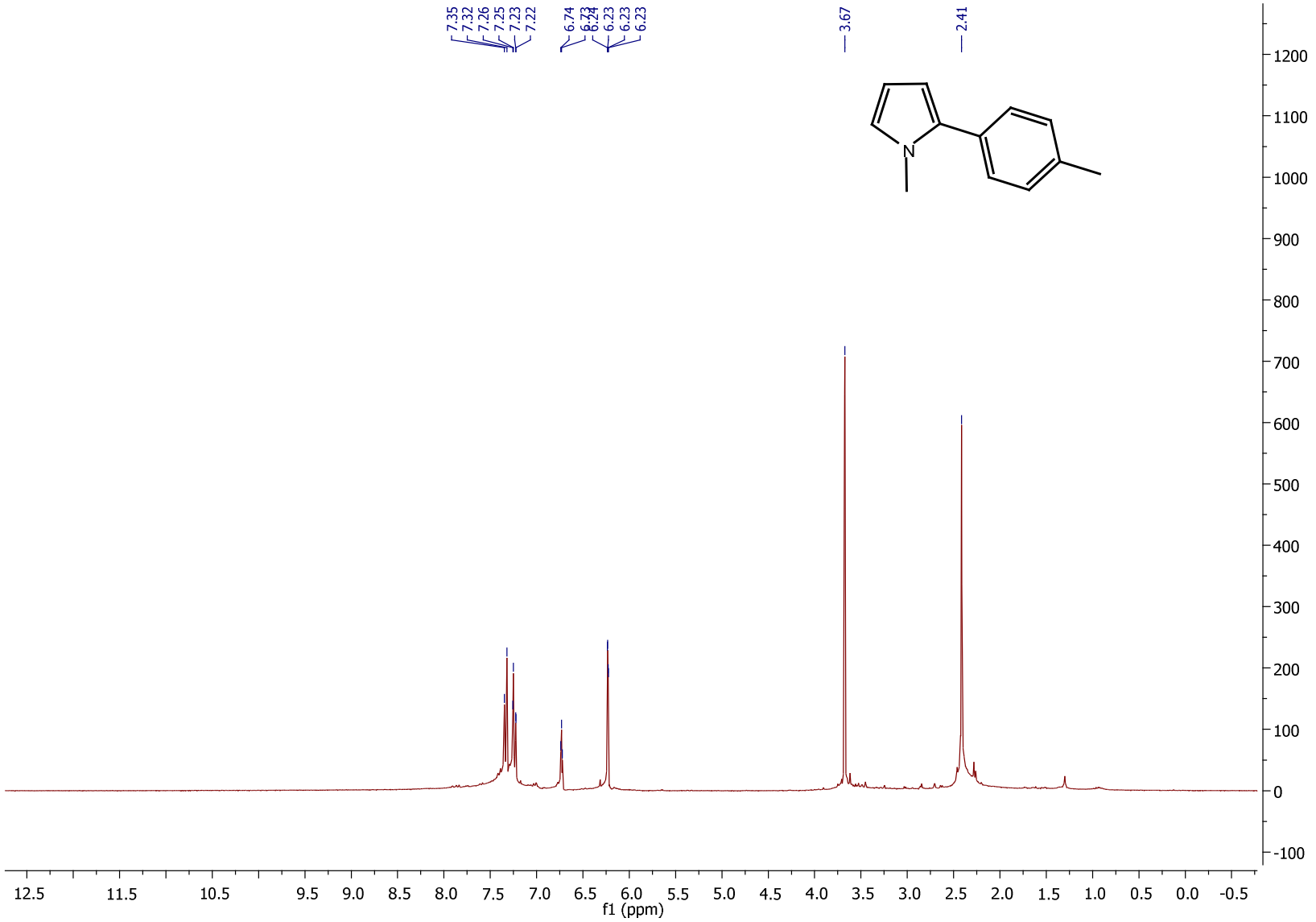



**Figure S3.** $^{1}$H-NMR spectra of compound **8b**.

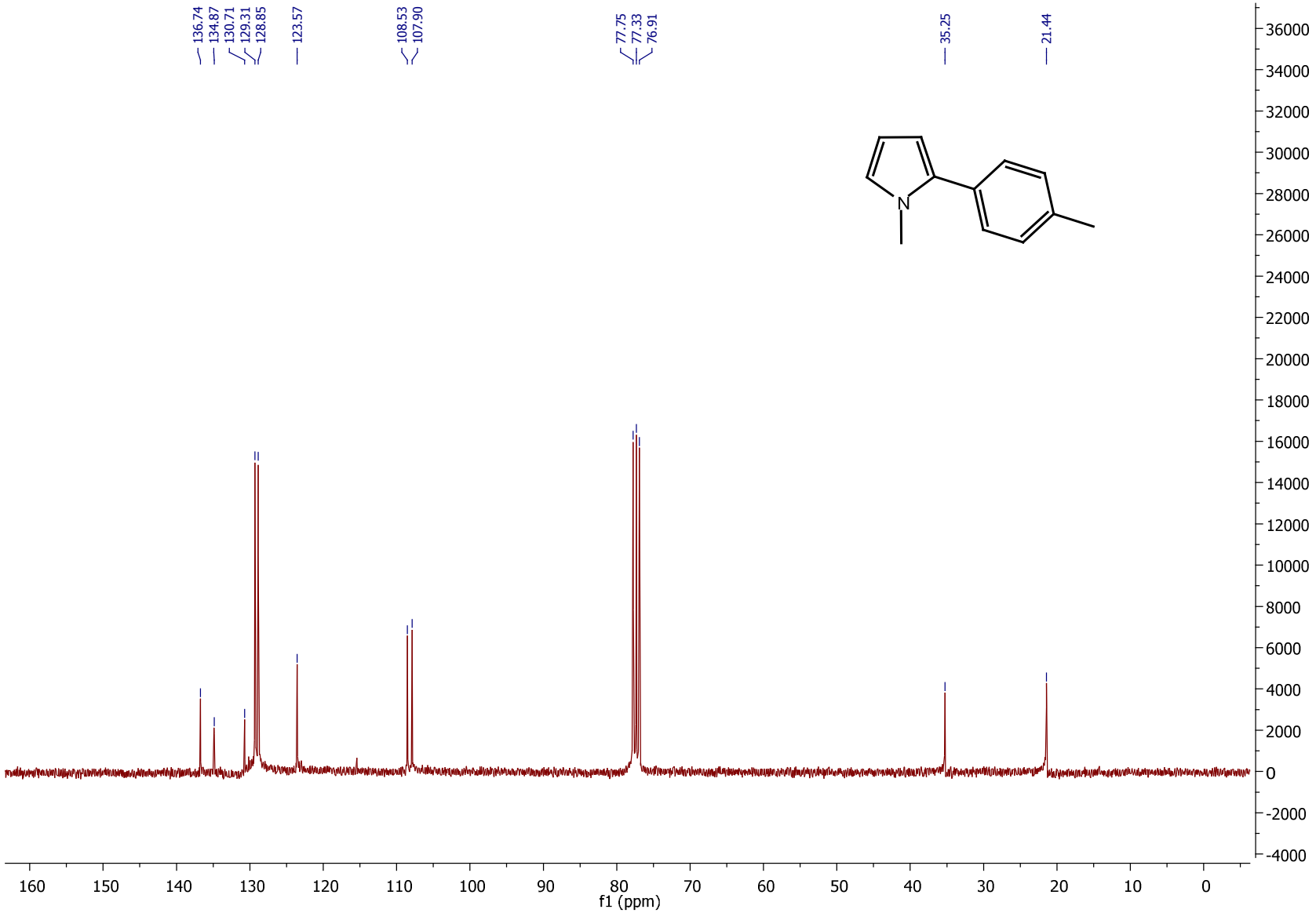



**Figure S4.** $^{13}$C-NMR spectra of compound **8b**.

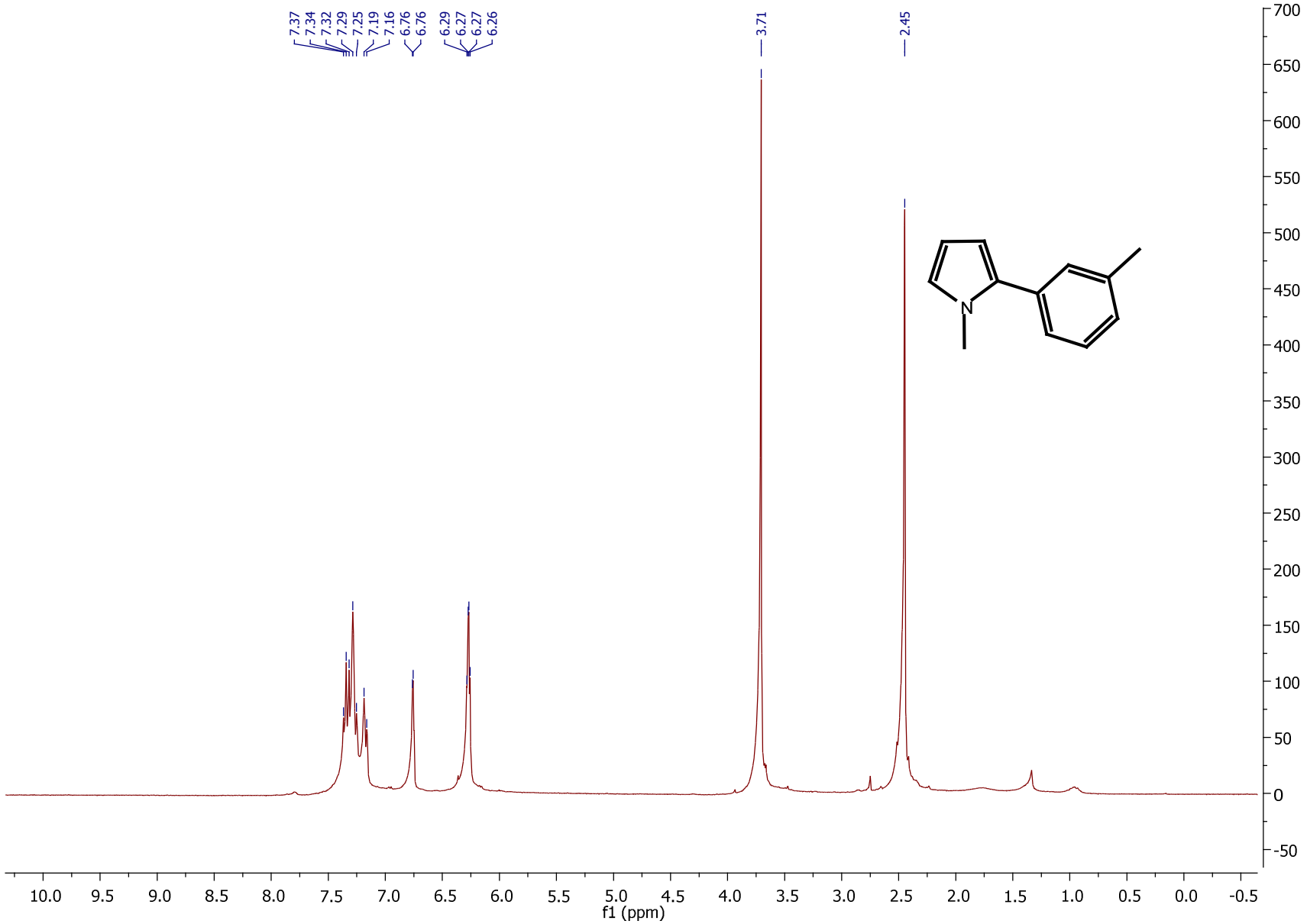



**Figure S5.** $^{1}$H-NMR spectra of compound **8c**.

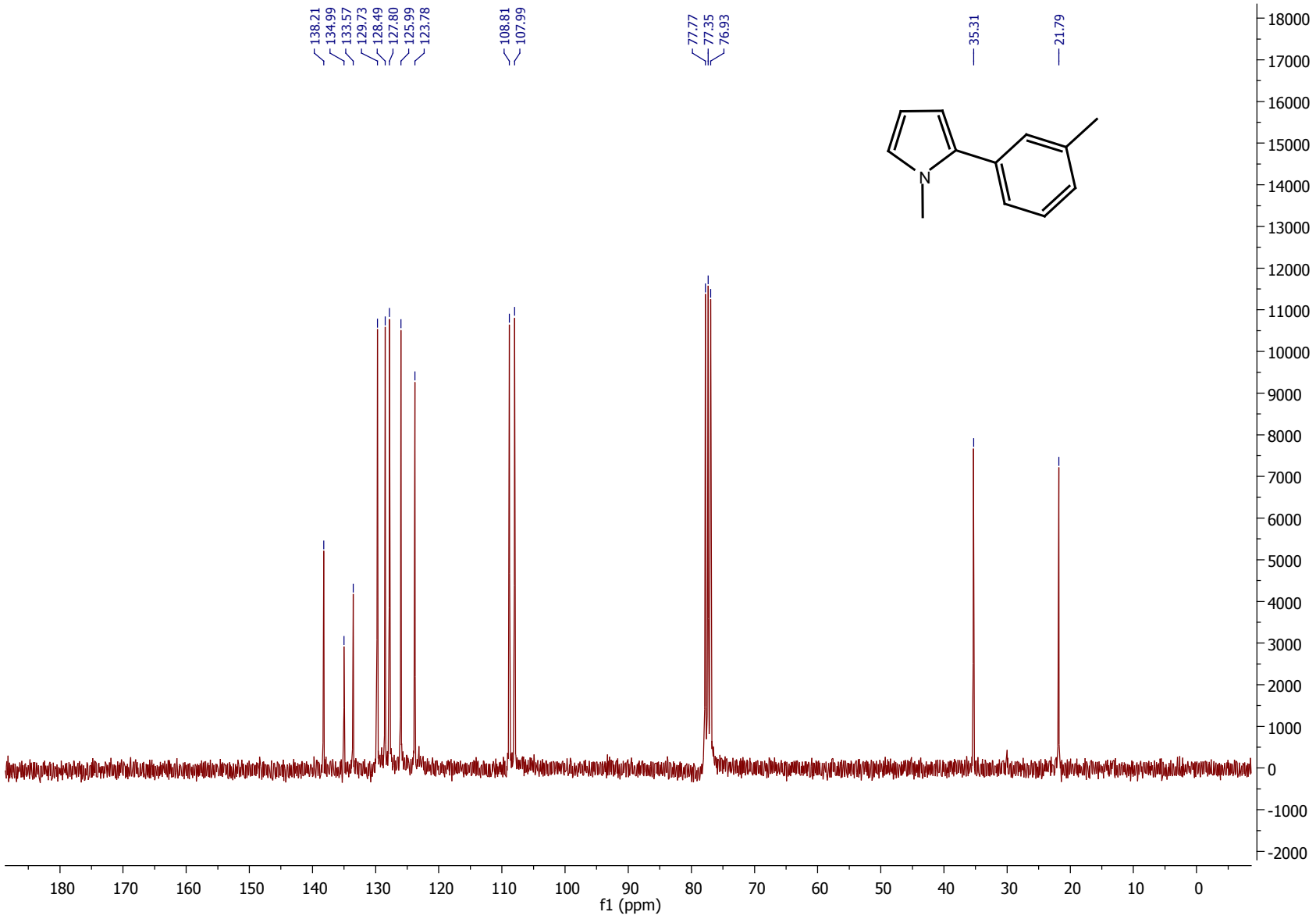



**Figure S6.** $^{13}$C-NMR spectra of compound **8c**.

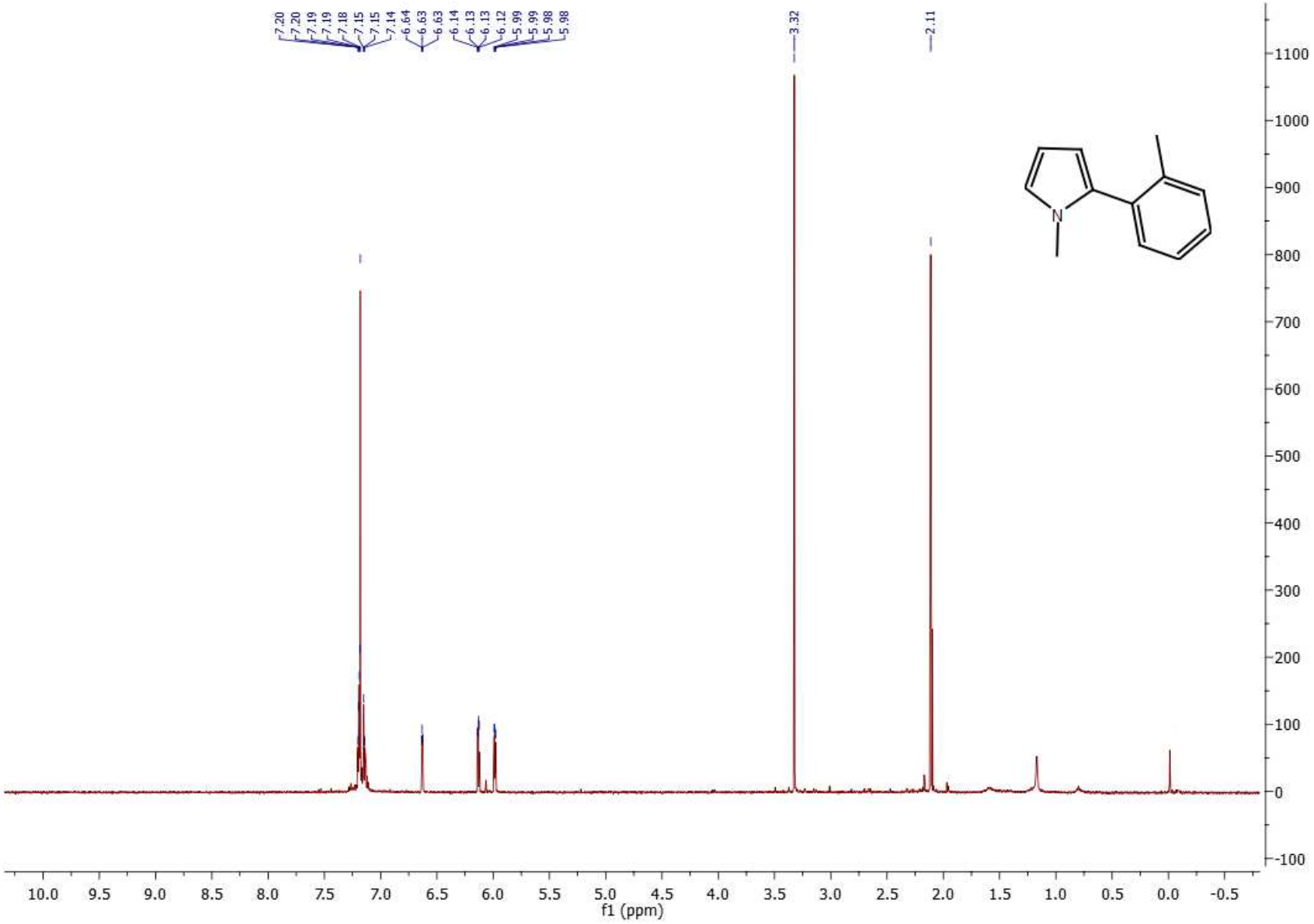



**Figure S7.** $^{1}$H-NMR spectra of compound **8d**.

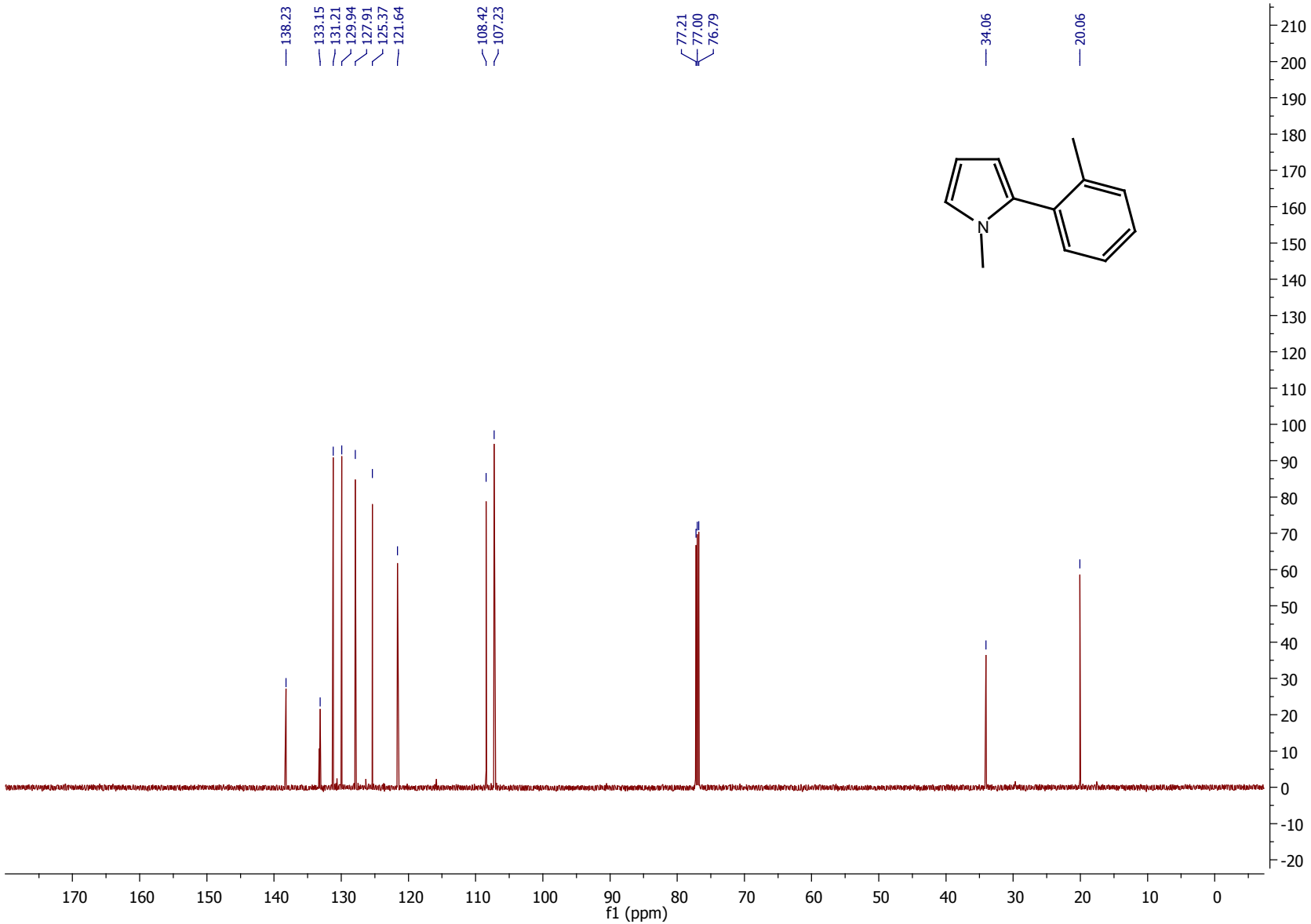



**Figure S8.** $^{13}$C-NMR spectra of compound **8d**.

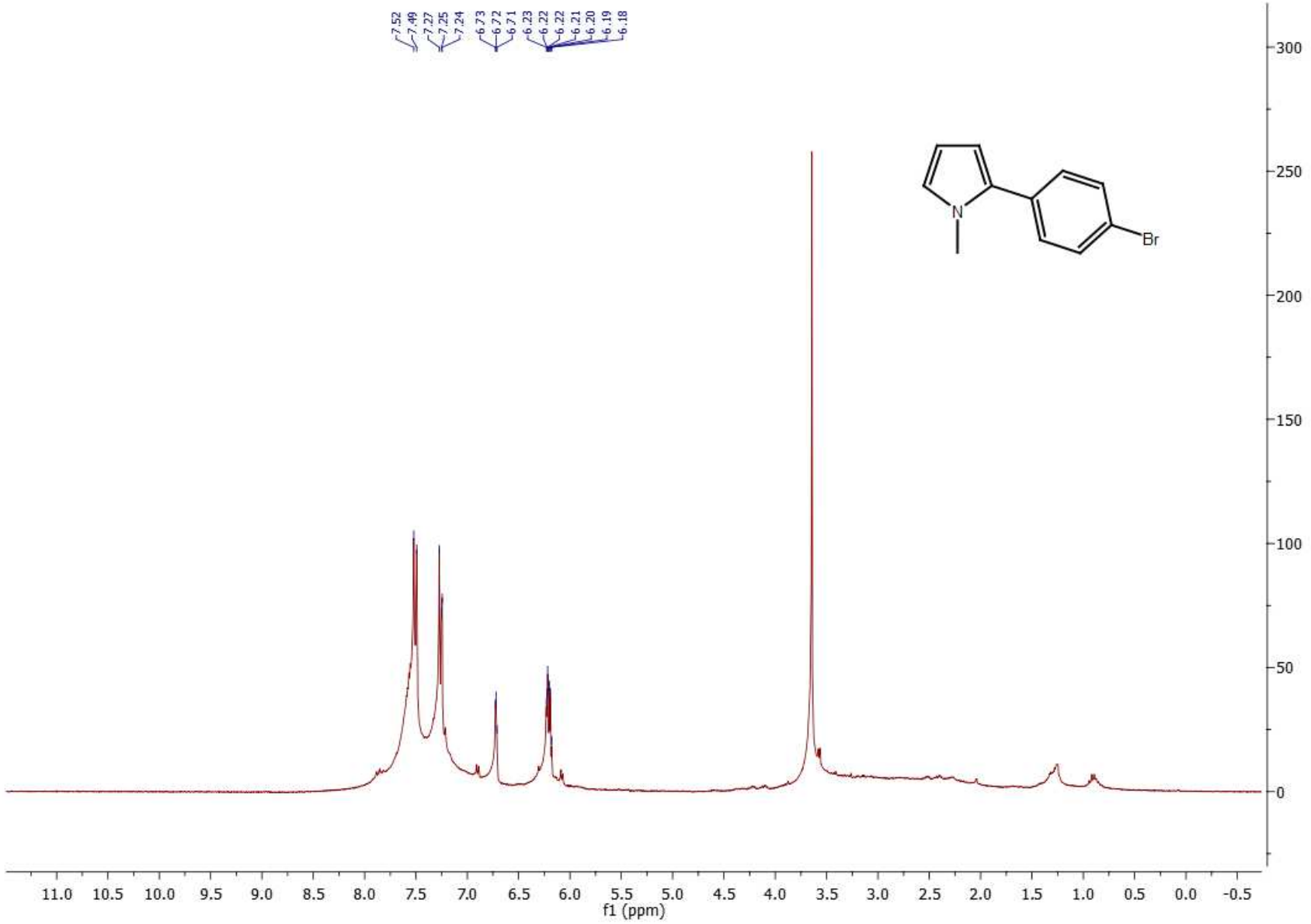



**Figure S9.** $^{1}$H-NMR spectra of compound **8e**.

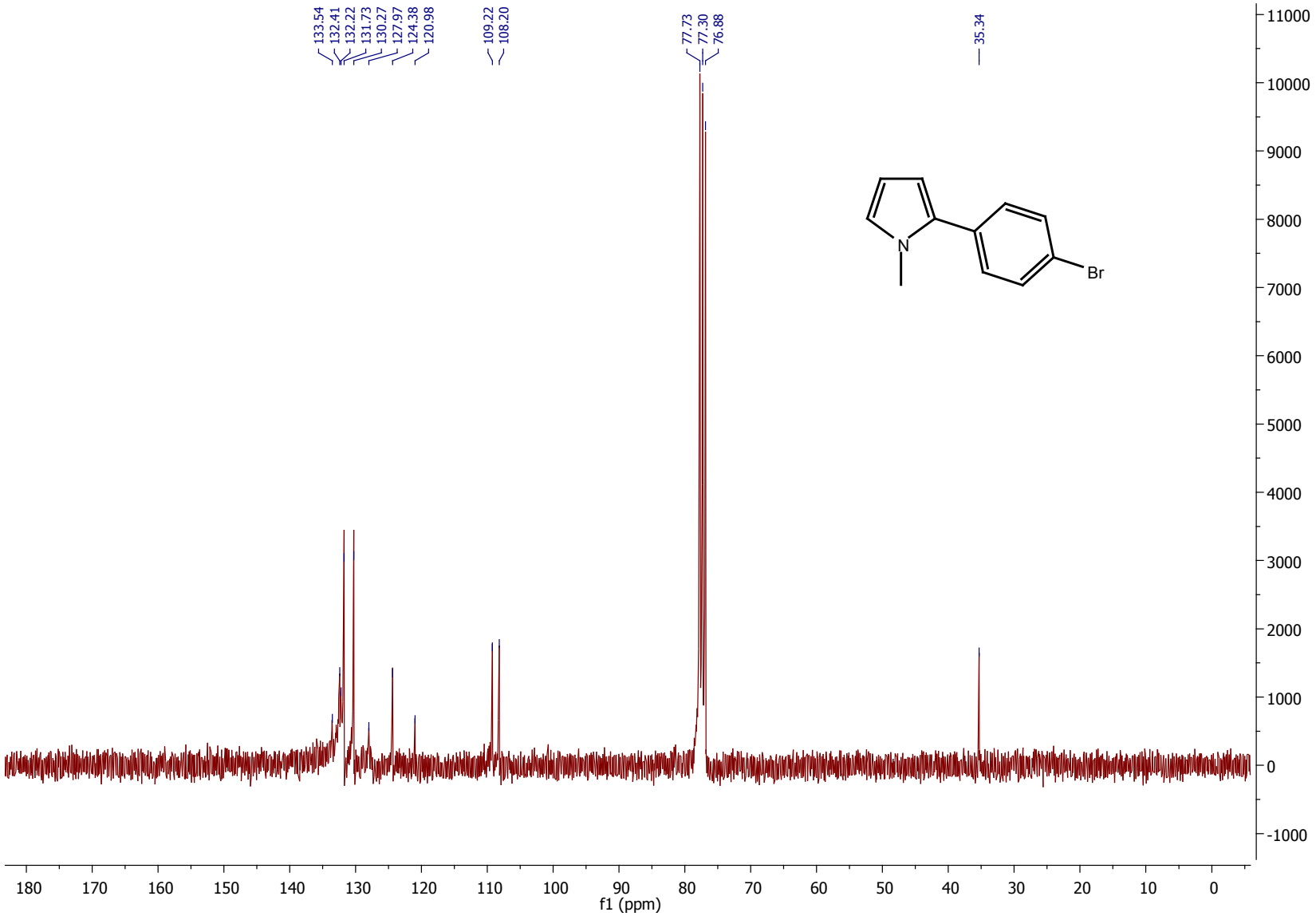



**Figure S10.** $^{13}$C-NMR spectra of compound **8e**.

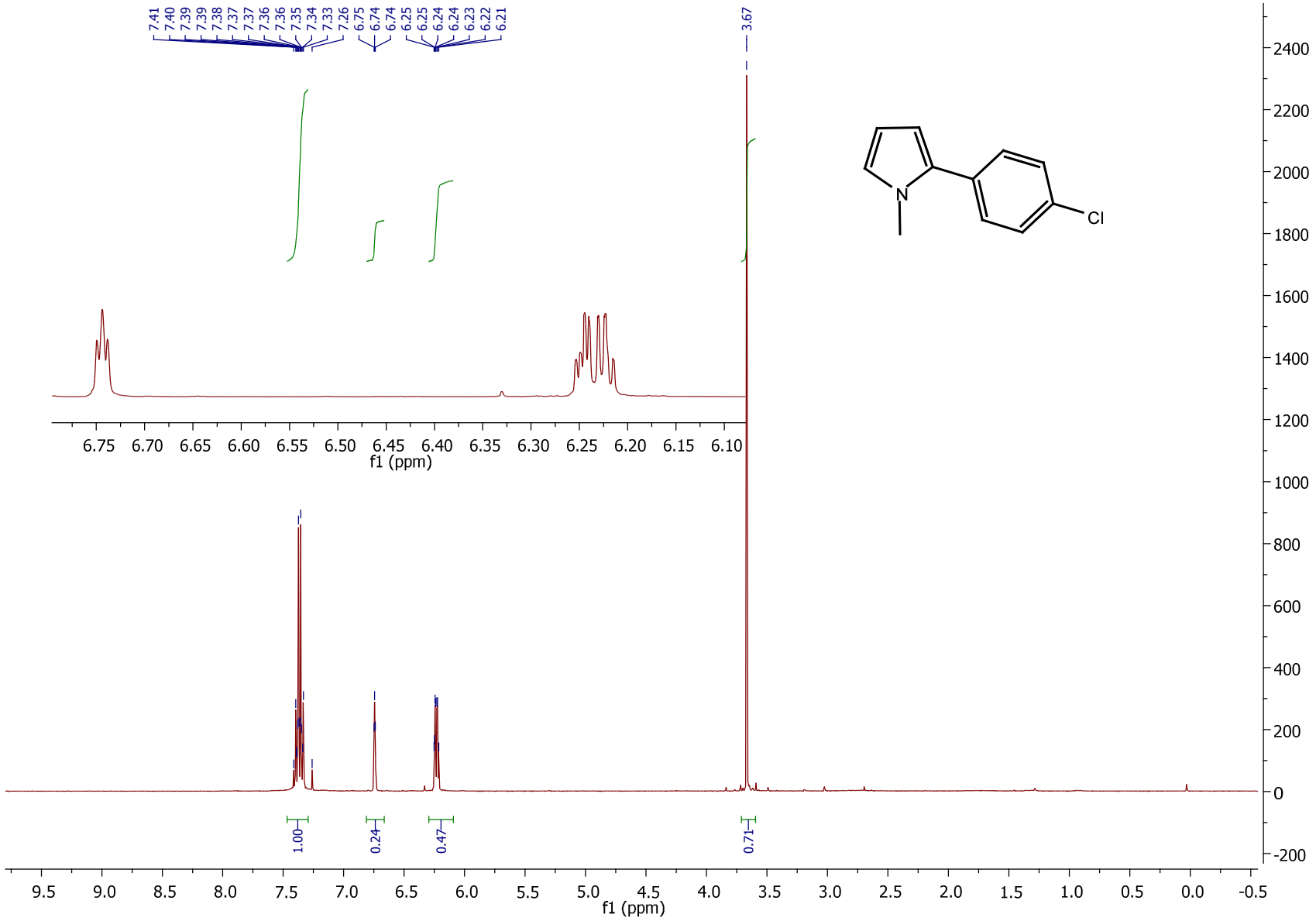



**Figure S11.** $^{1}$H-NMR spectra of compound **8f**.

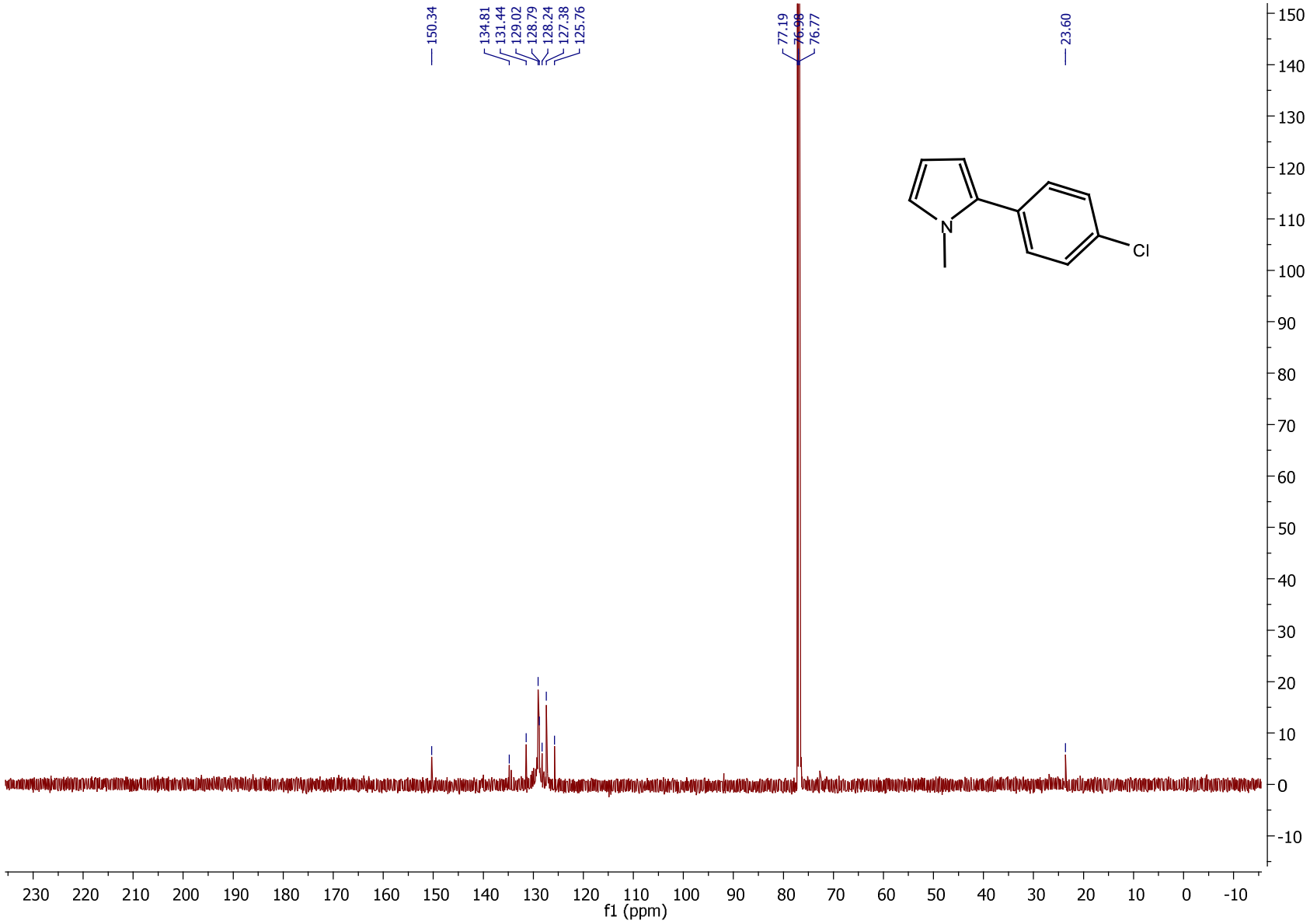



**Figure S12.** $^{13}$C-NMR spectra of compound **8f**.

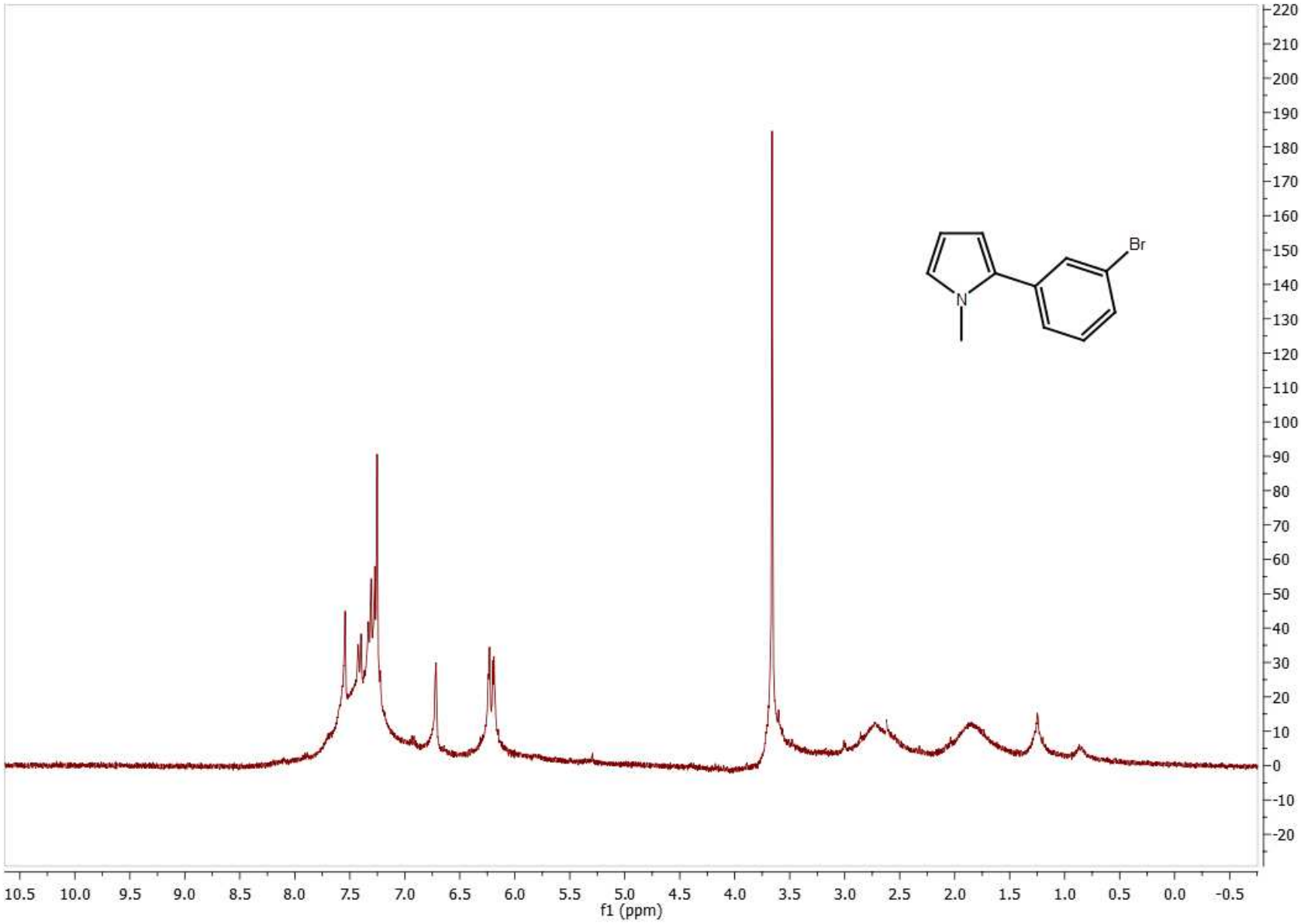



**Figure S13.** $^{1}$H-NMR spectra of compound **8g**.

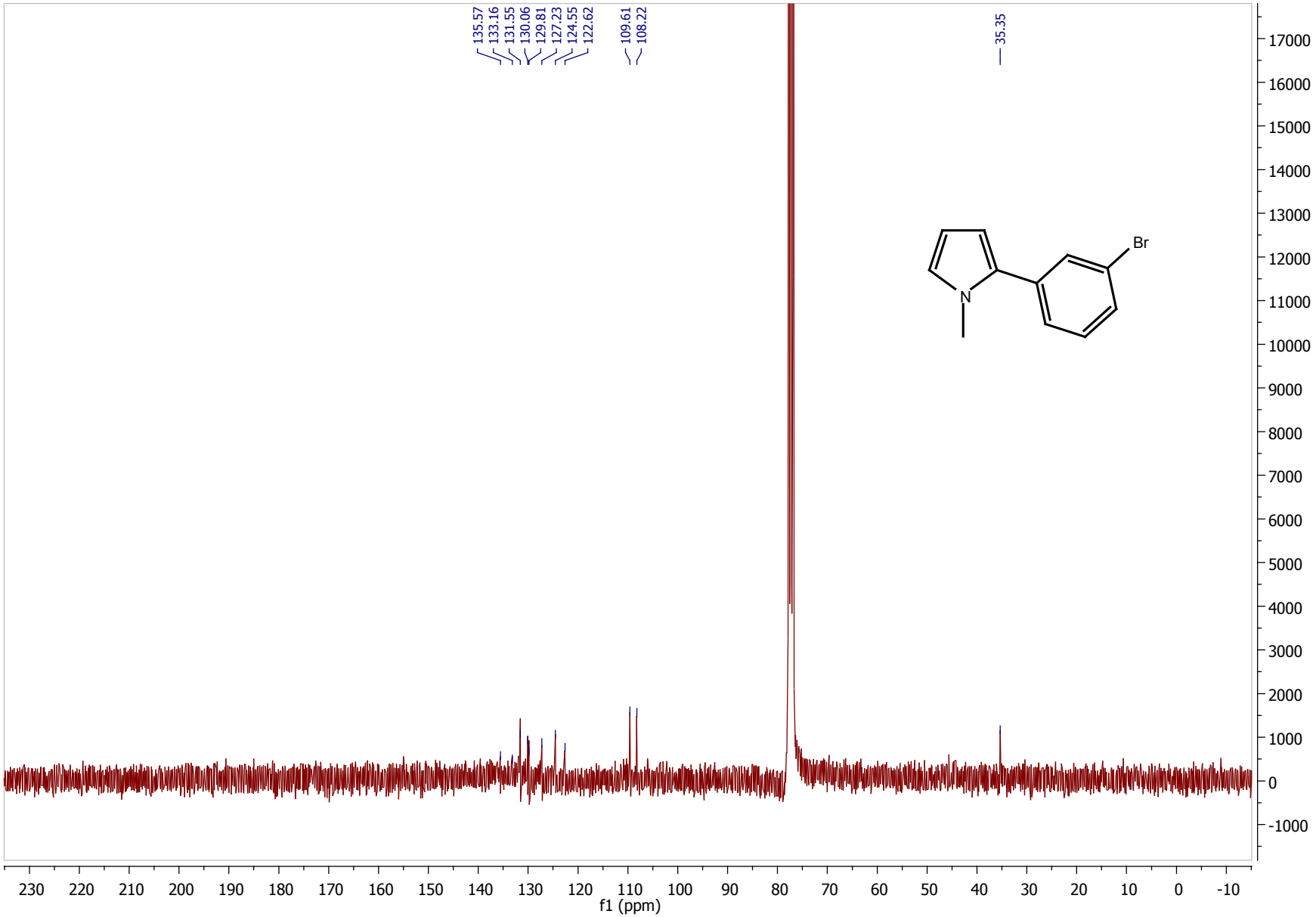



**Figure S14.** $^{13}$C-NMR spectra of compound **8g**.

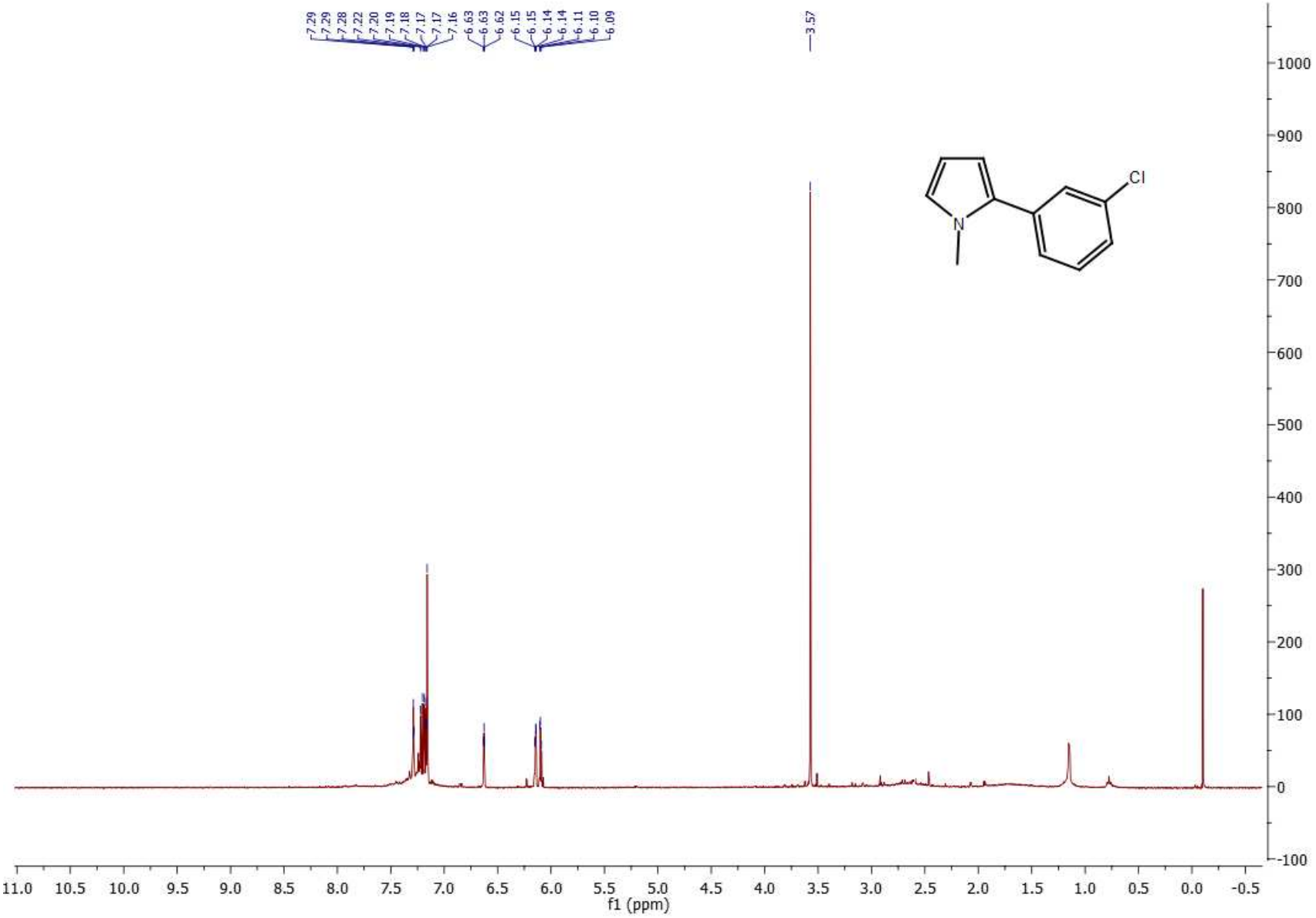



**Figure S15.** $^{1}$H-NMR spectra of compound **8h**.

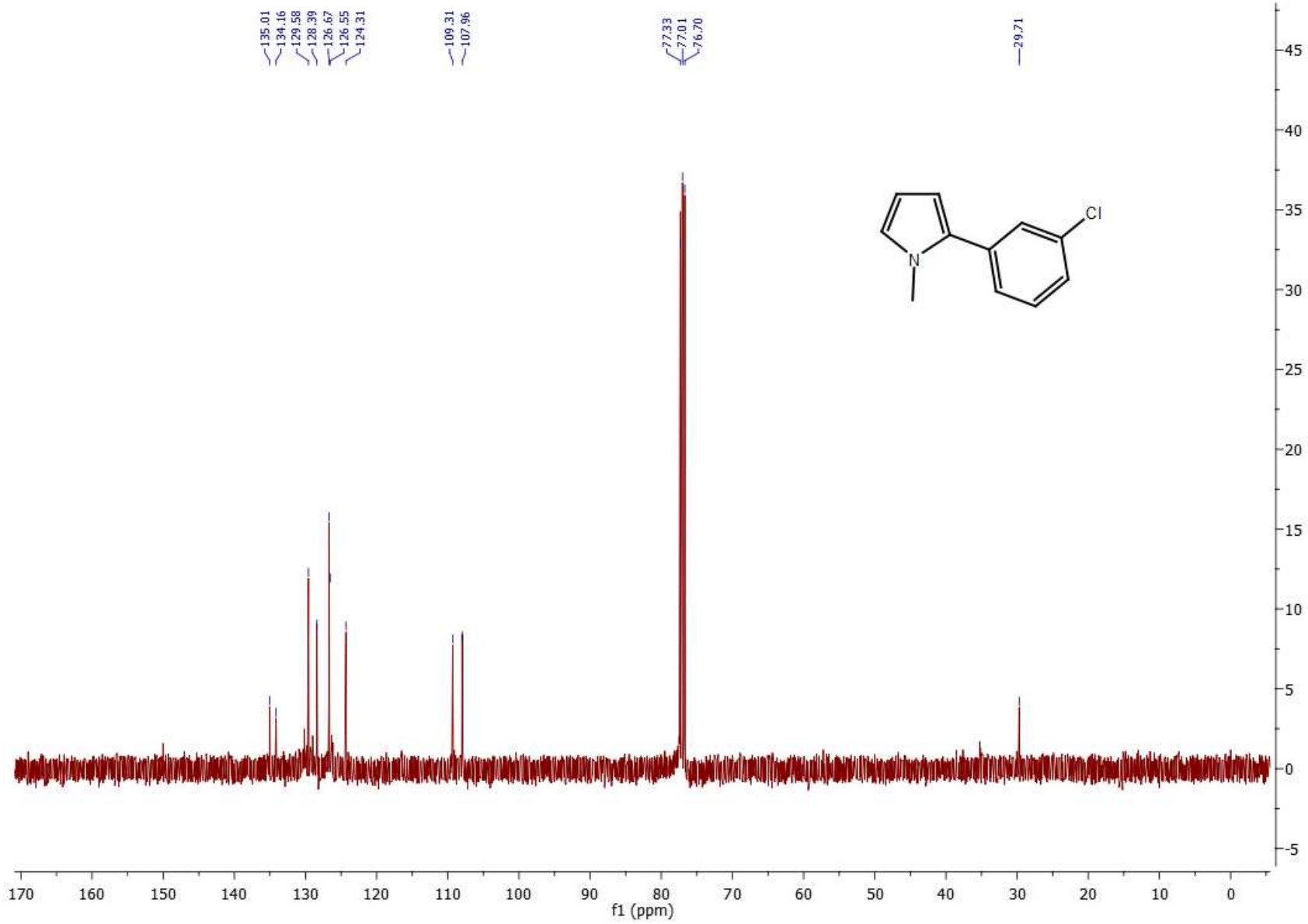



**Figure S16.** $^{13}$C-NMR spectra of compound **8h**.

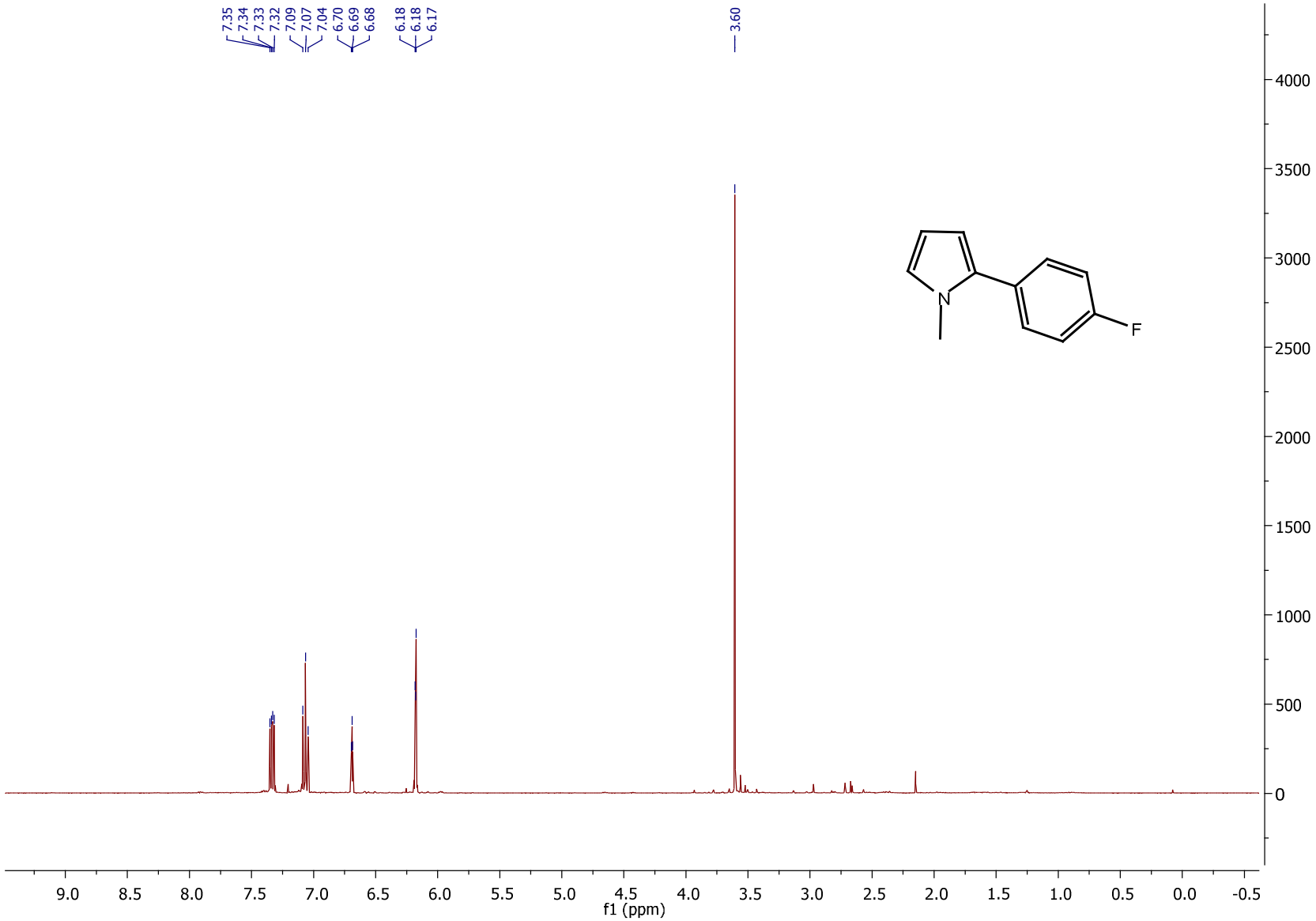



**Figure S17.** $^{1}$H-NMR spectra of compound **8i**.

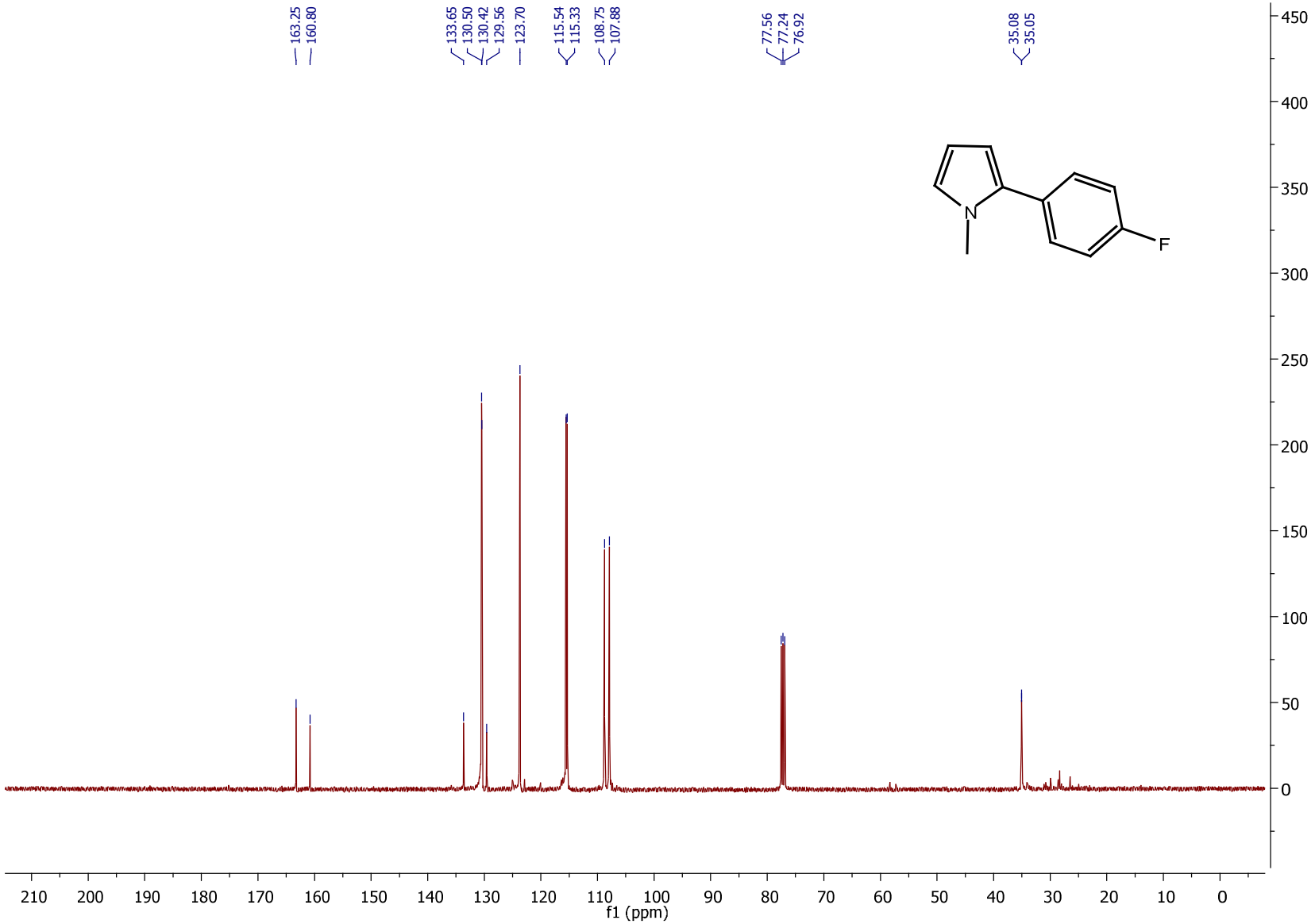



**Figure S18.** $^{13}$C-NMR spectra of compound **8i**.

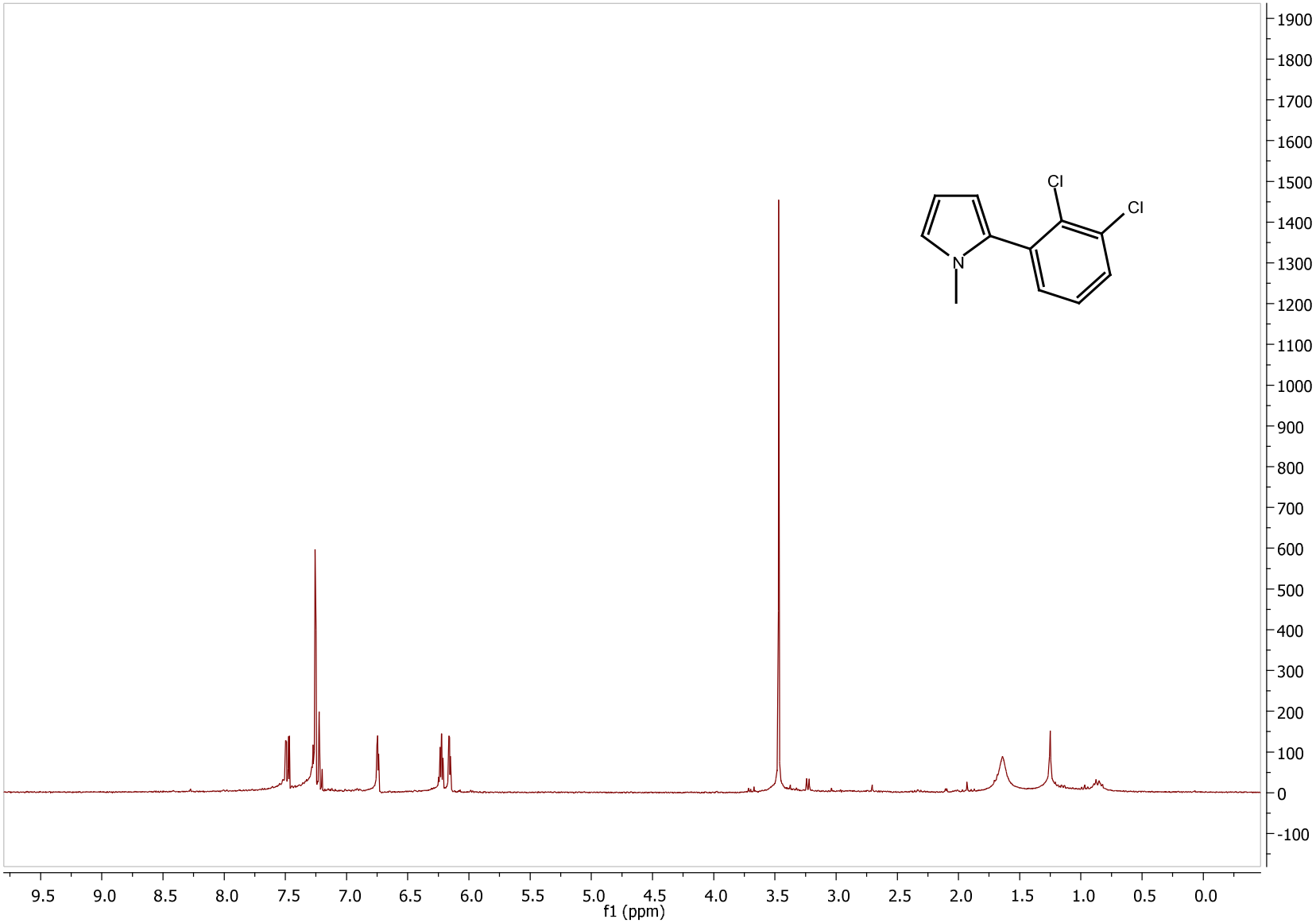



**Figure S19.** $^{1}$H-NMR spectra of compound **8j**.

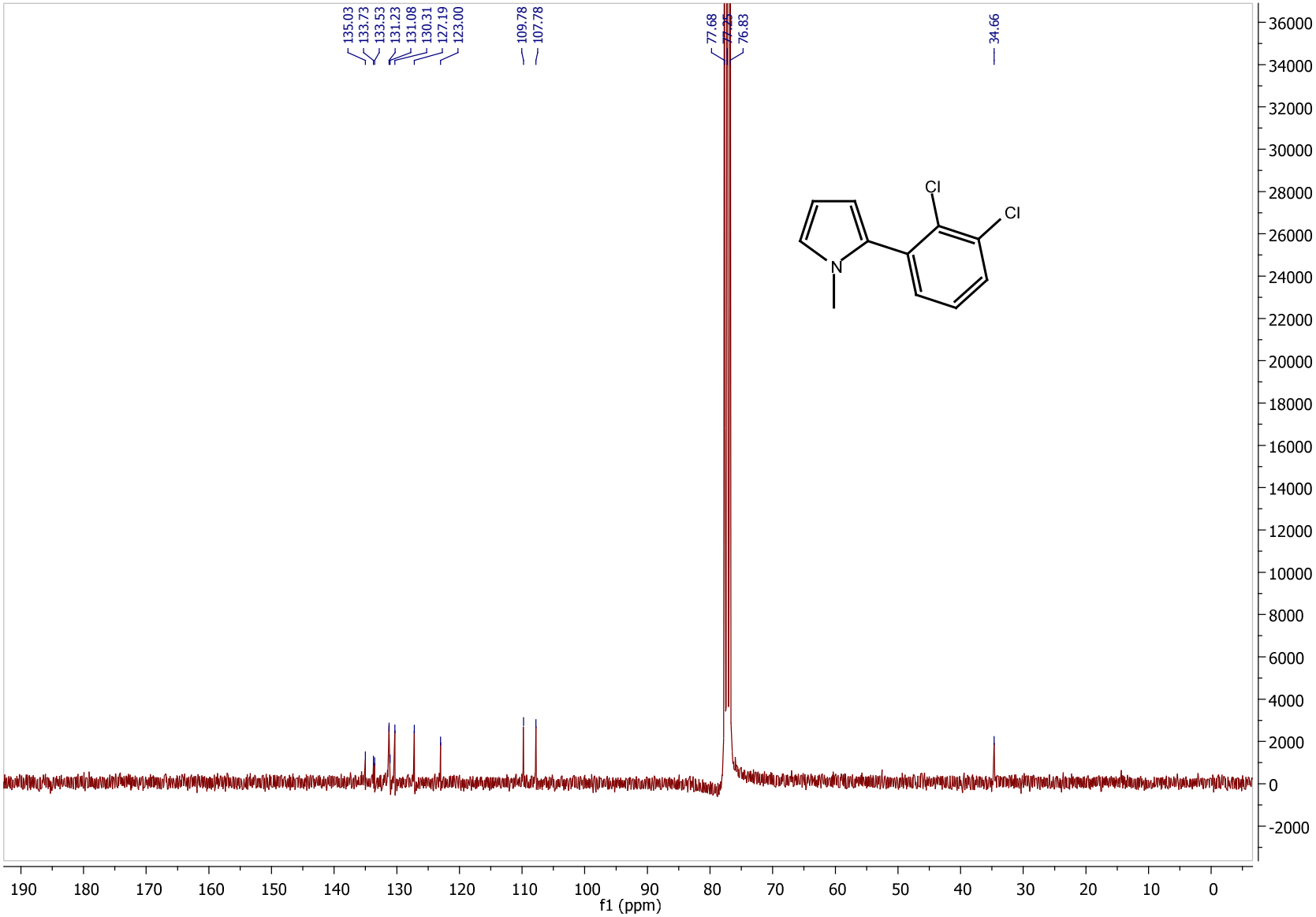



**Figure S20.** $^{13}$C-NMR spectra of compound **8j**.

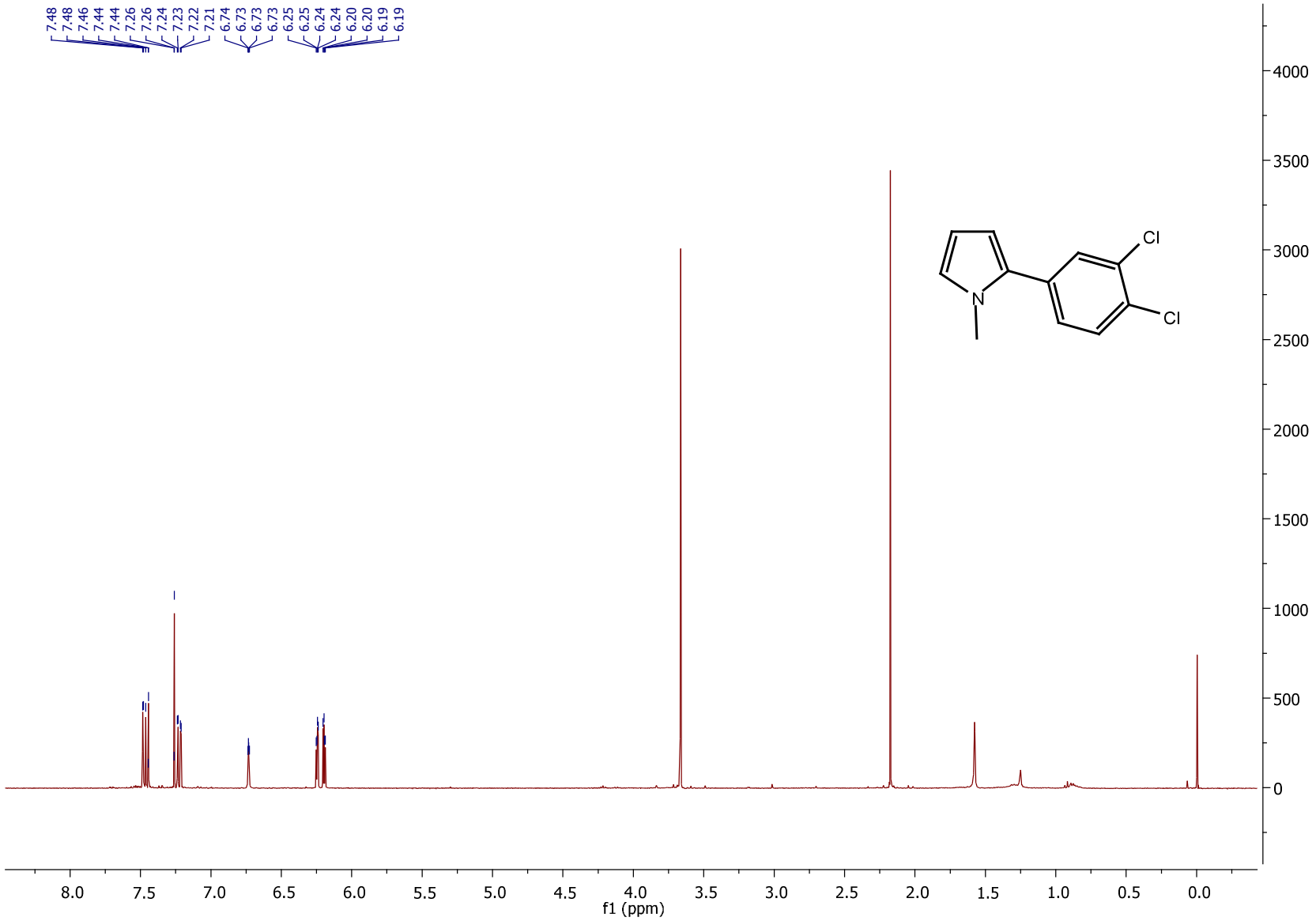



**Figure S21.** $^{1}$H-NMR spectra of compound **8k**.

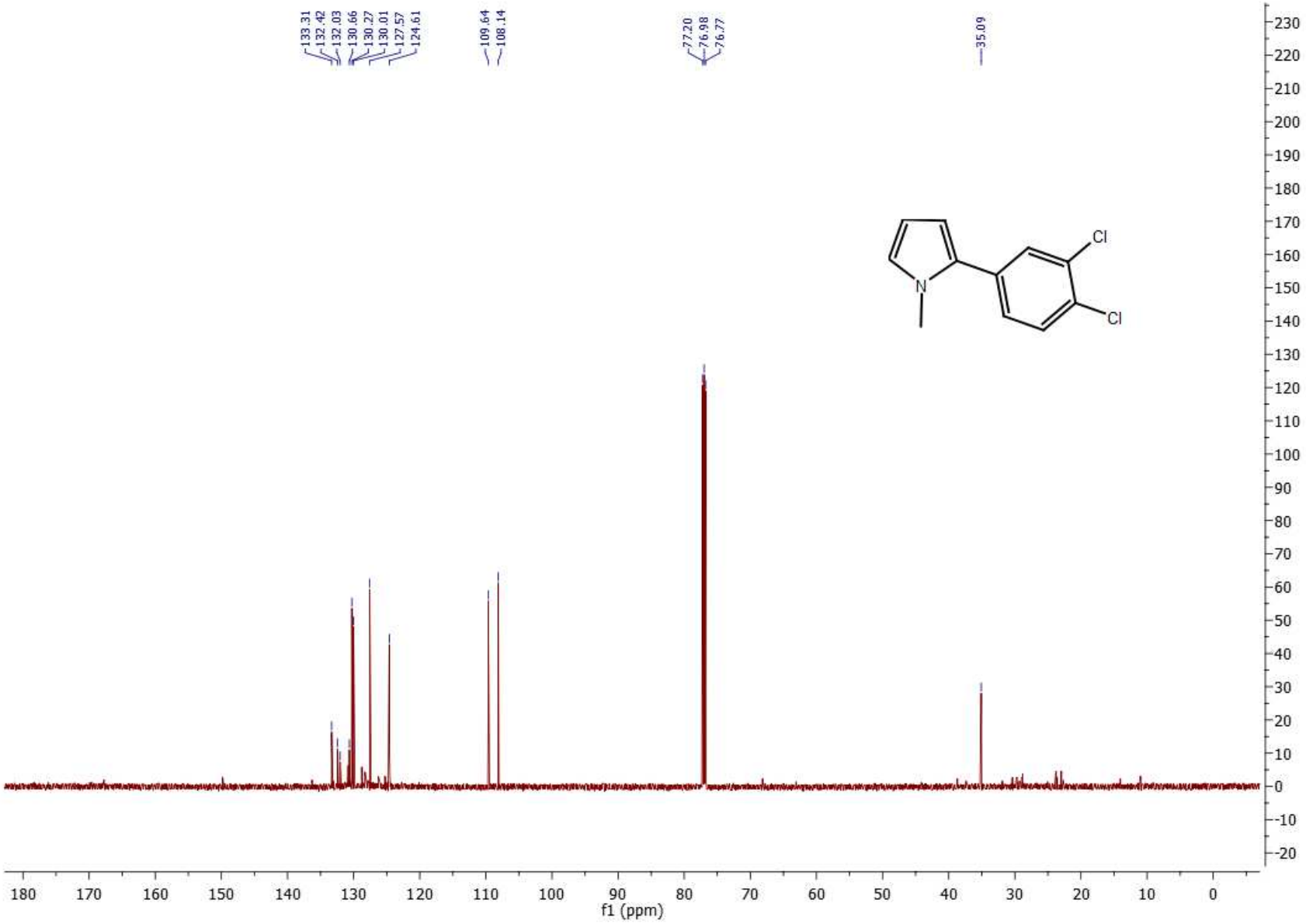



**Figure S22.** $^{13}$C-NMR spectra of compound **8k**.

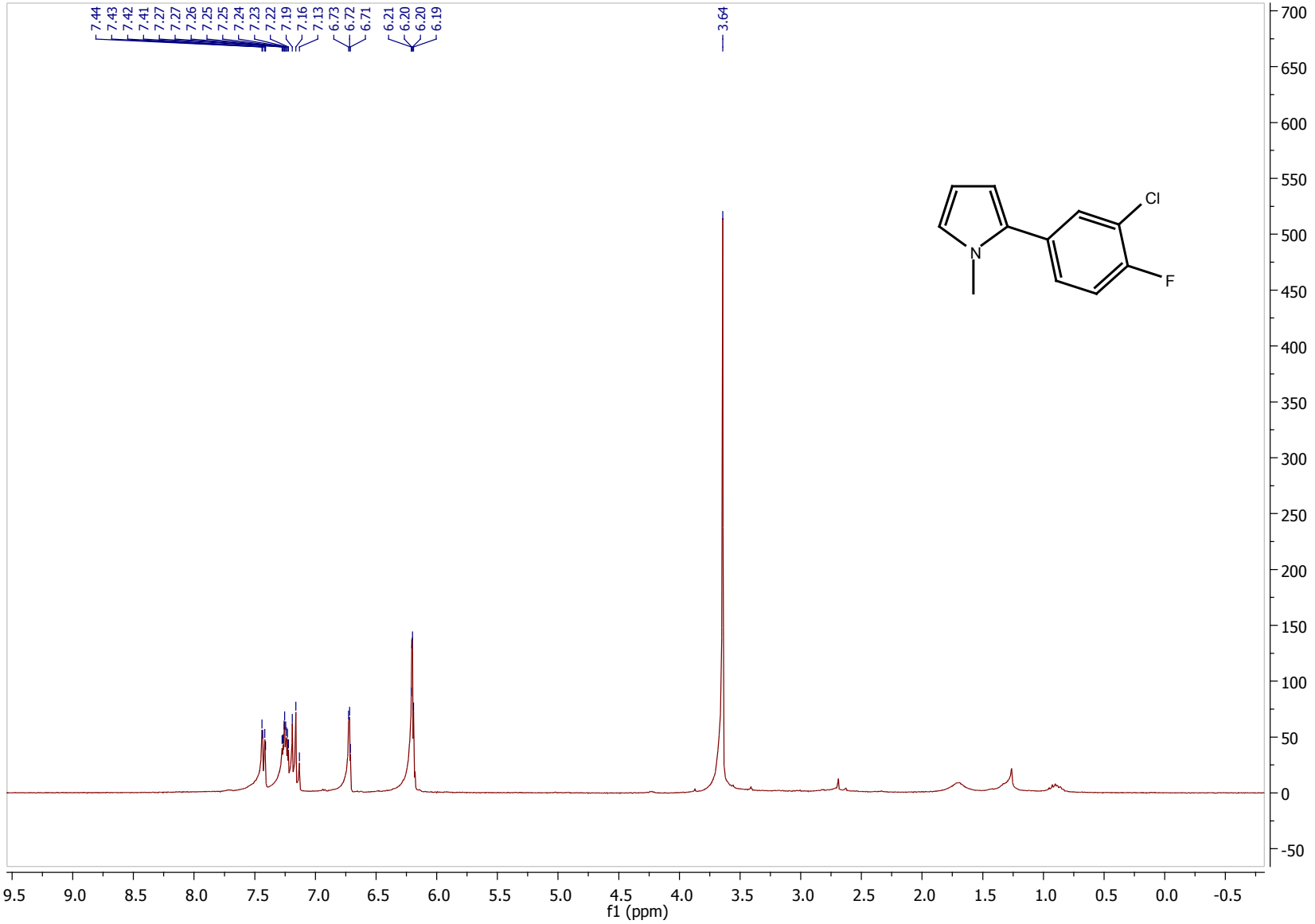



**Figure S23.** $^{1}$H-NMR spectra of compound **8l**.

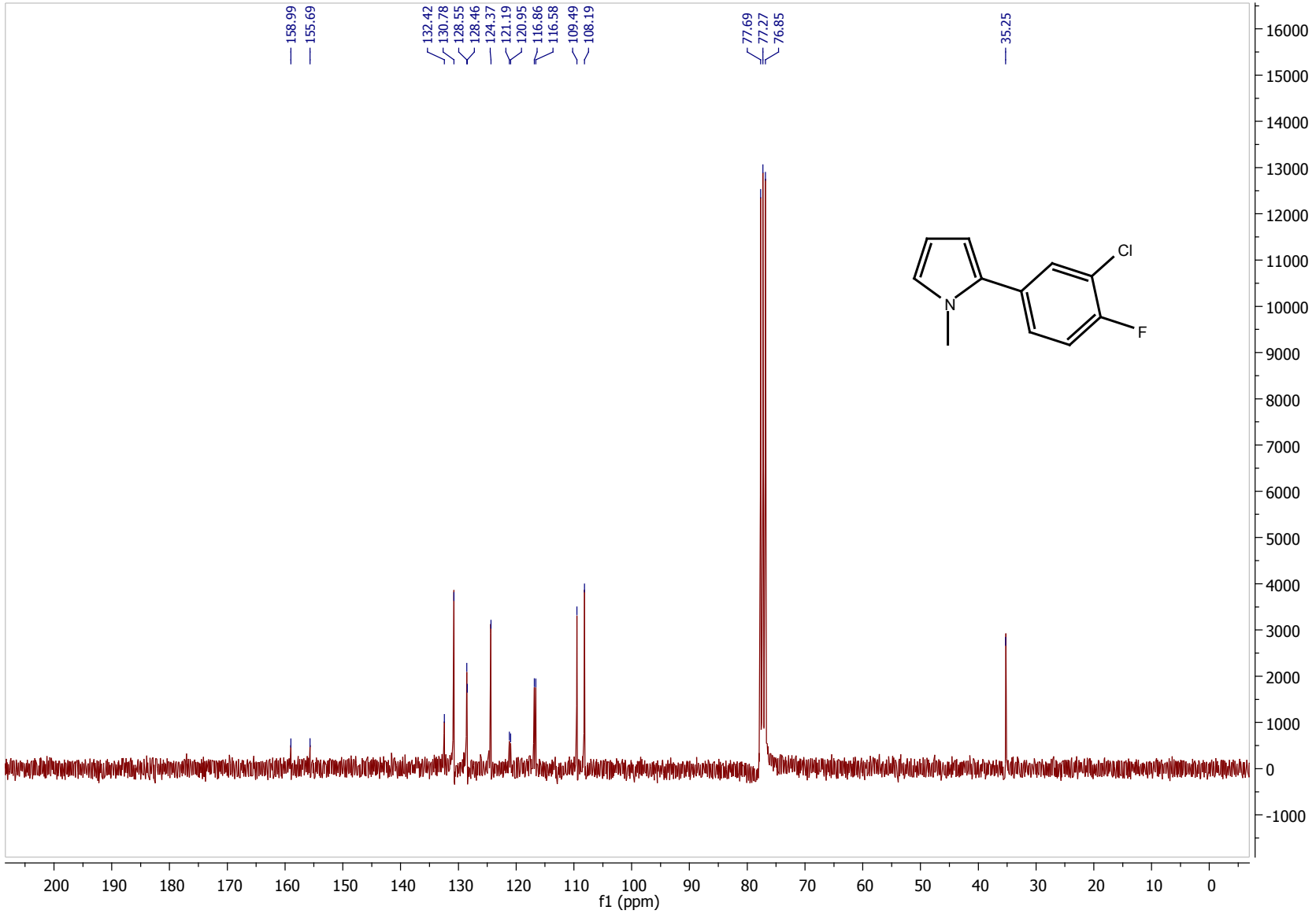



**Figure S24.** $^{13}$C-NMR spectra of compound **8l**.

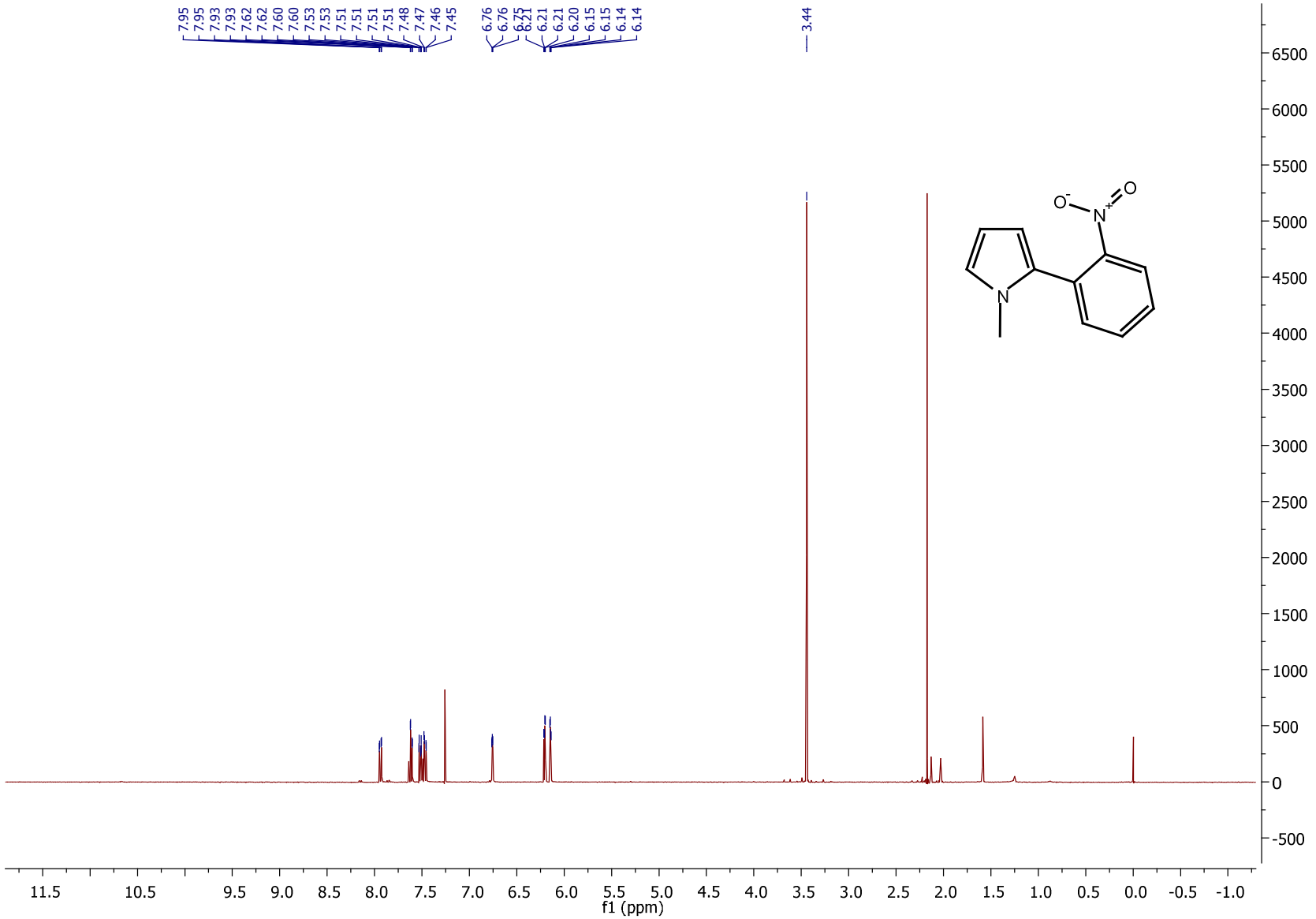



**Figure S25.** $^{1}$H-NMR spectra of compound **8m**.

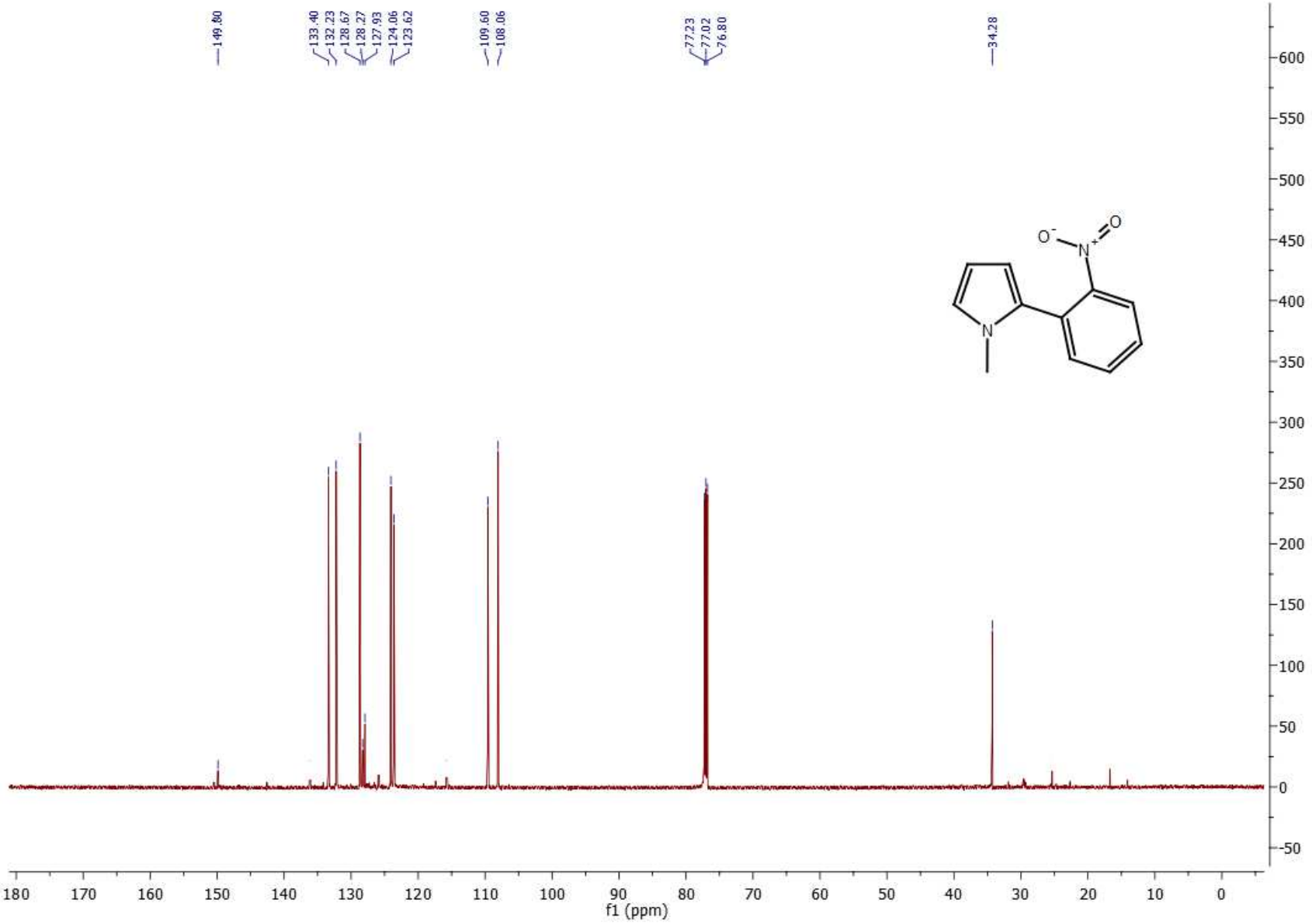



**Figure S26.** $^{13}$C-NMR spectra of compound **8m**.

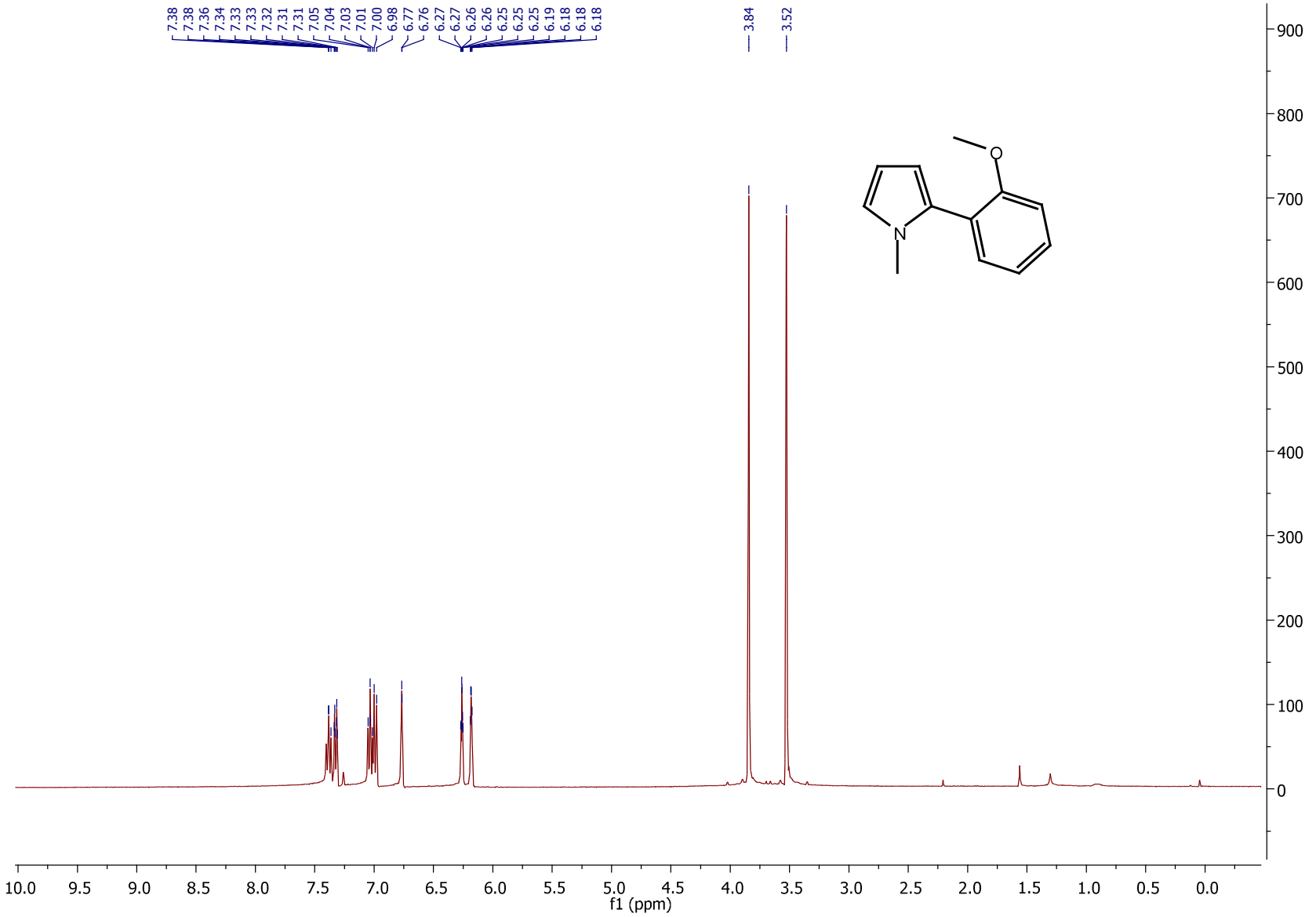



**Figure S27.** $^{1}$H-NMR spectra of compound **8n**.

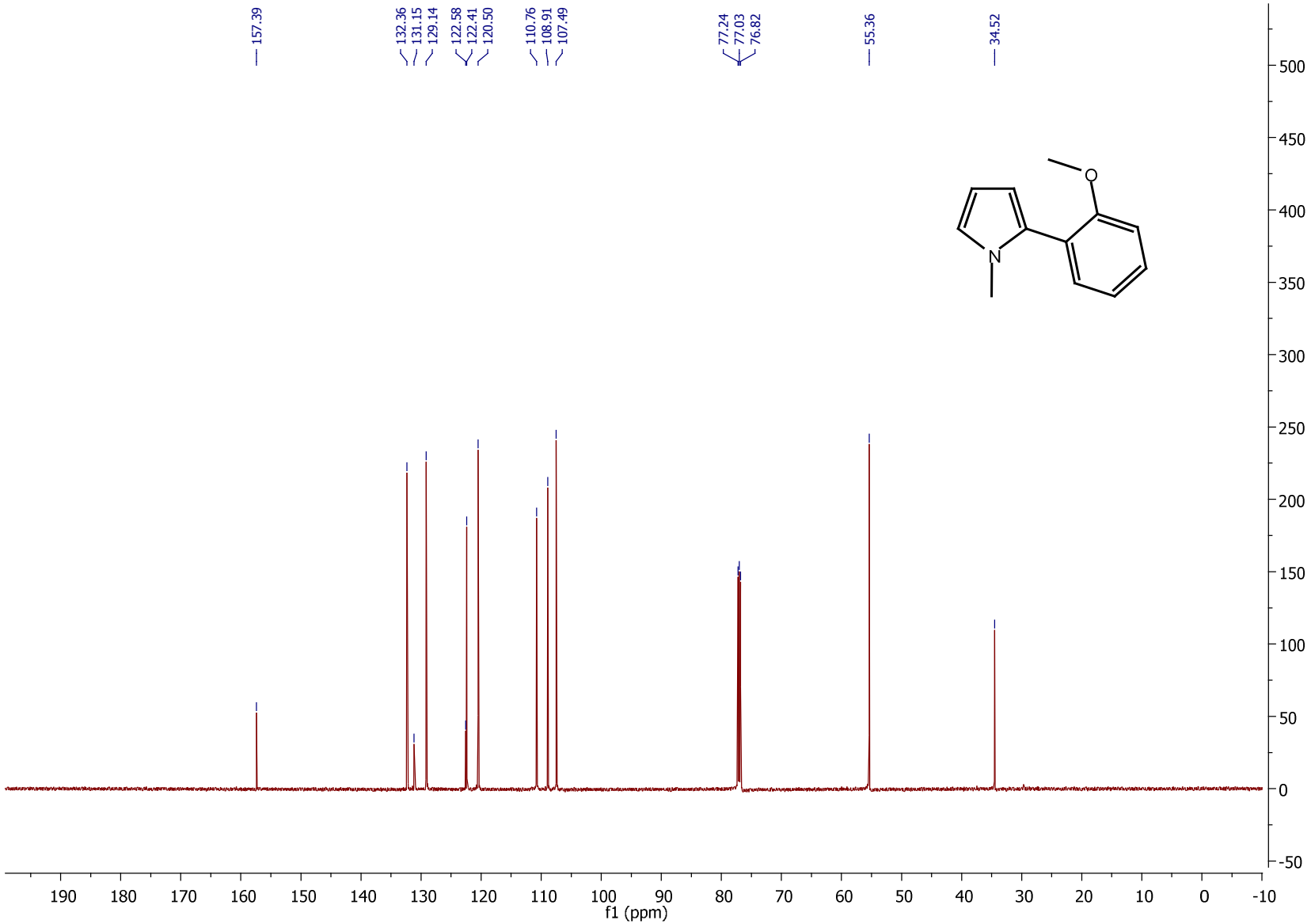



**Figure S28.** $^{13}$C-NMR spectra of compound **8n**.

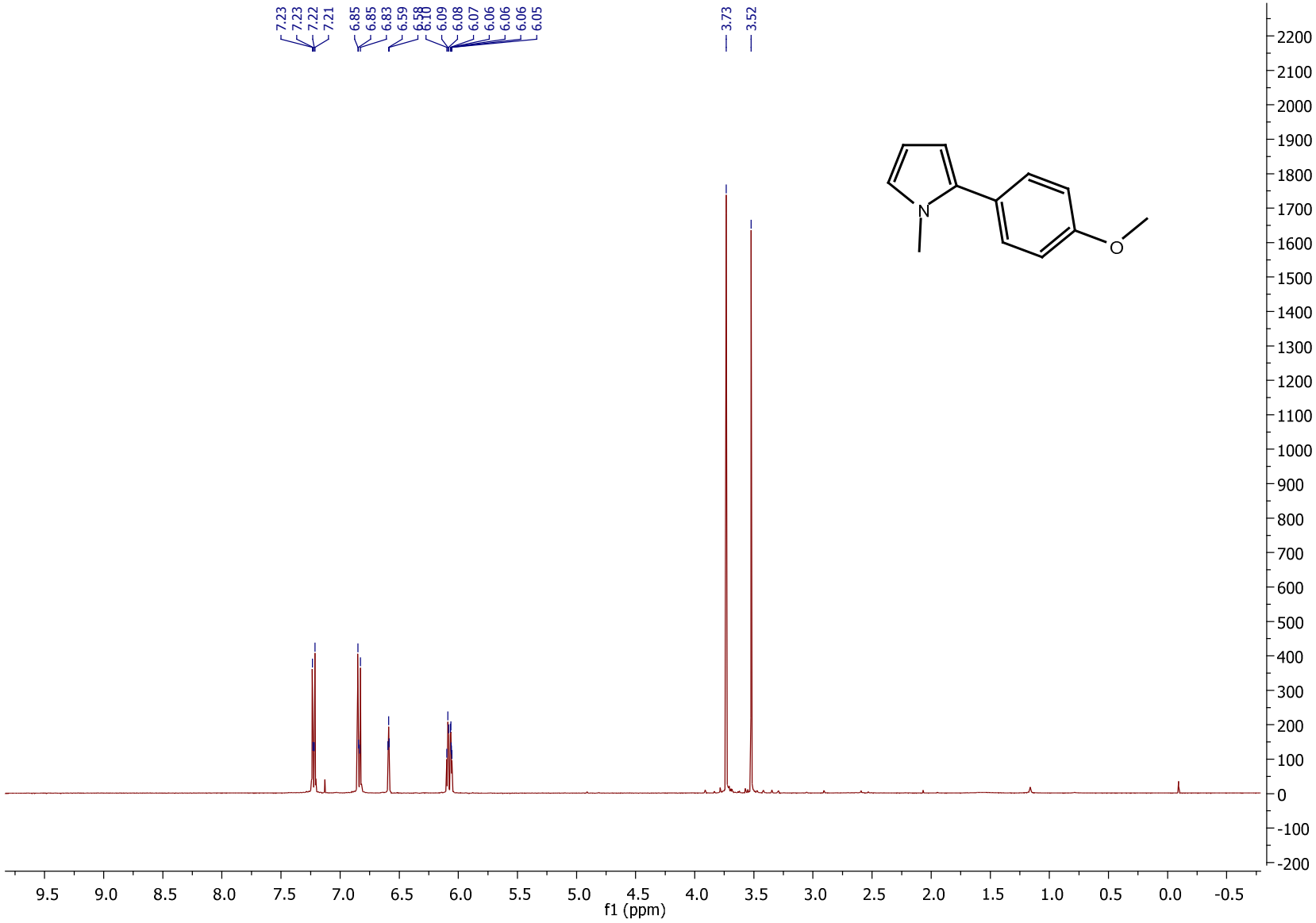



**Figure S29.** $^{1}$H-NMR spectra of compound **8o**.

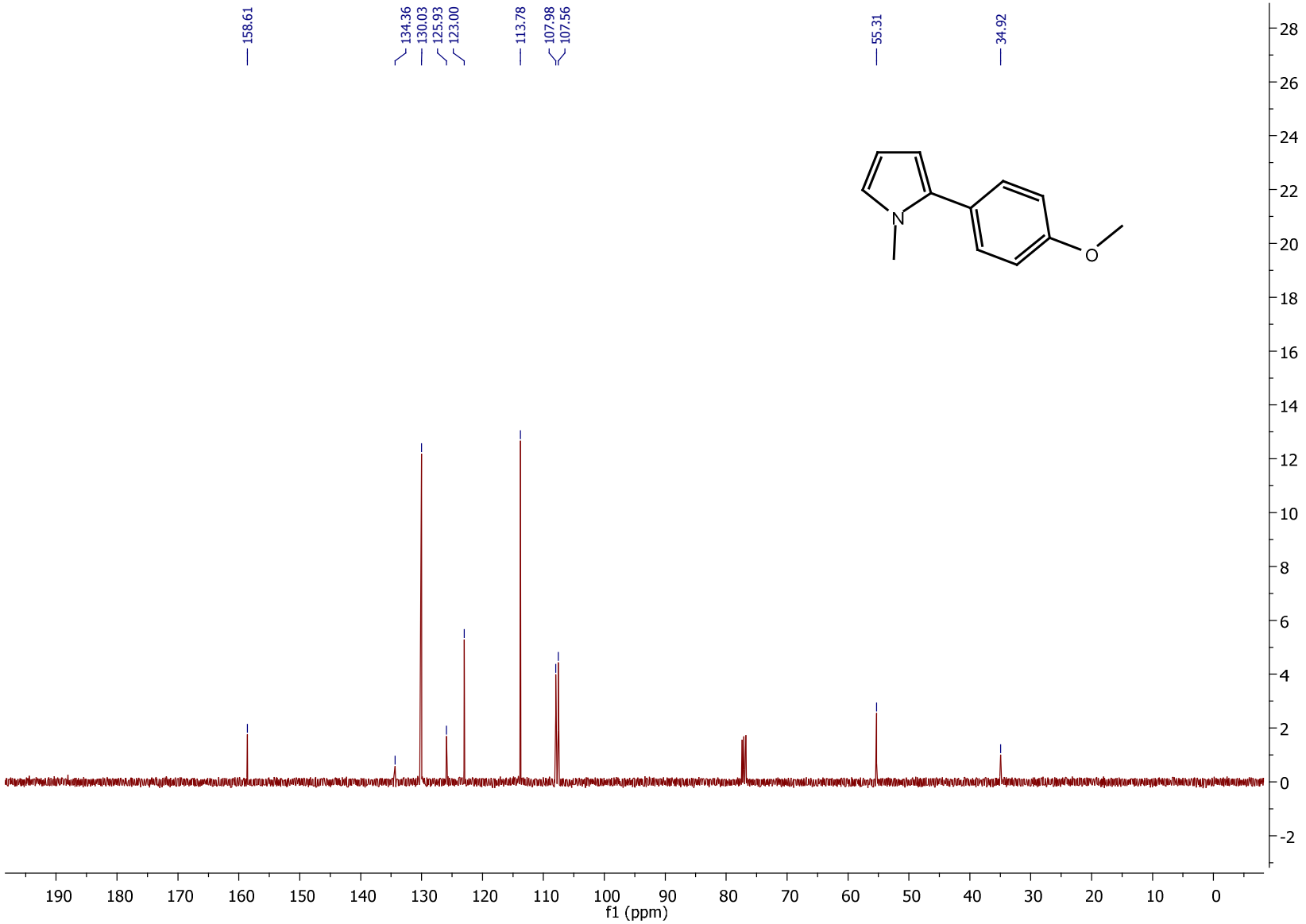



**Figure S30.** $^{13}$C-NMR spectra of compound **8o**.

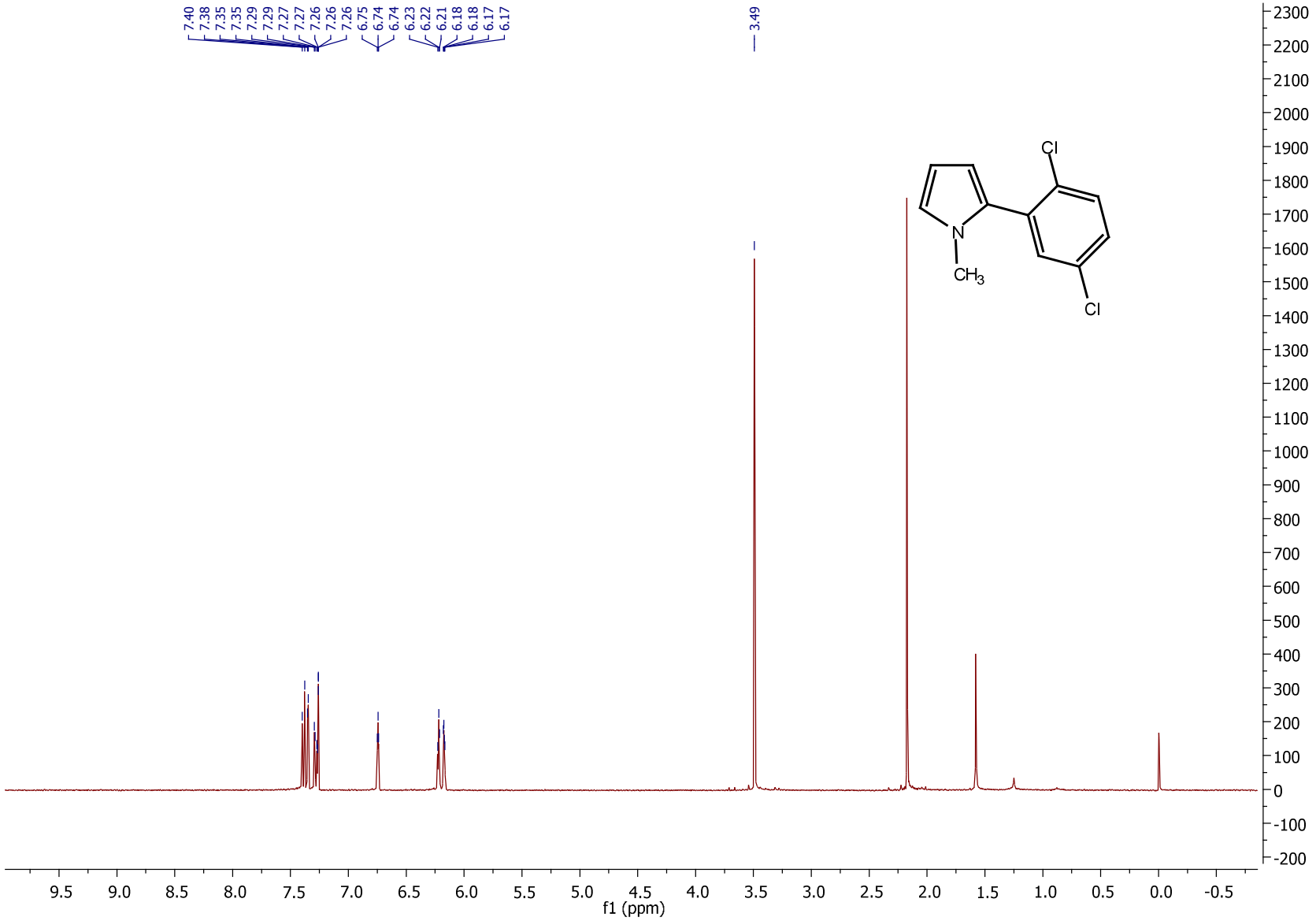



**Figure S31.** [1]H-NMR spectra of compound **8p**.

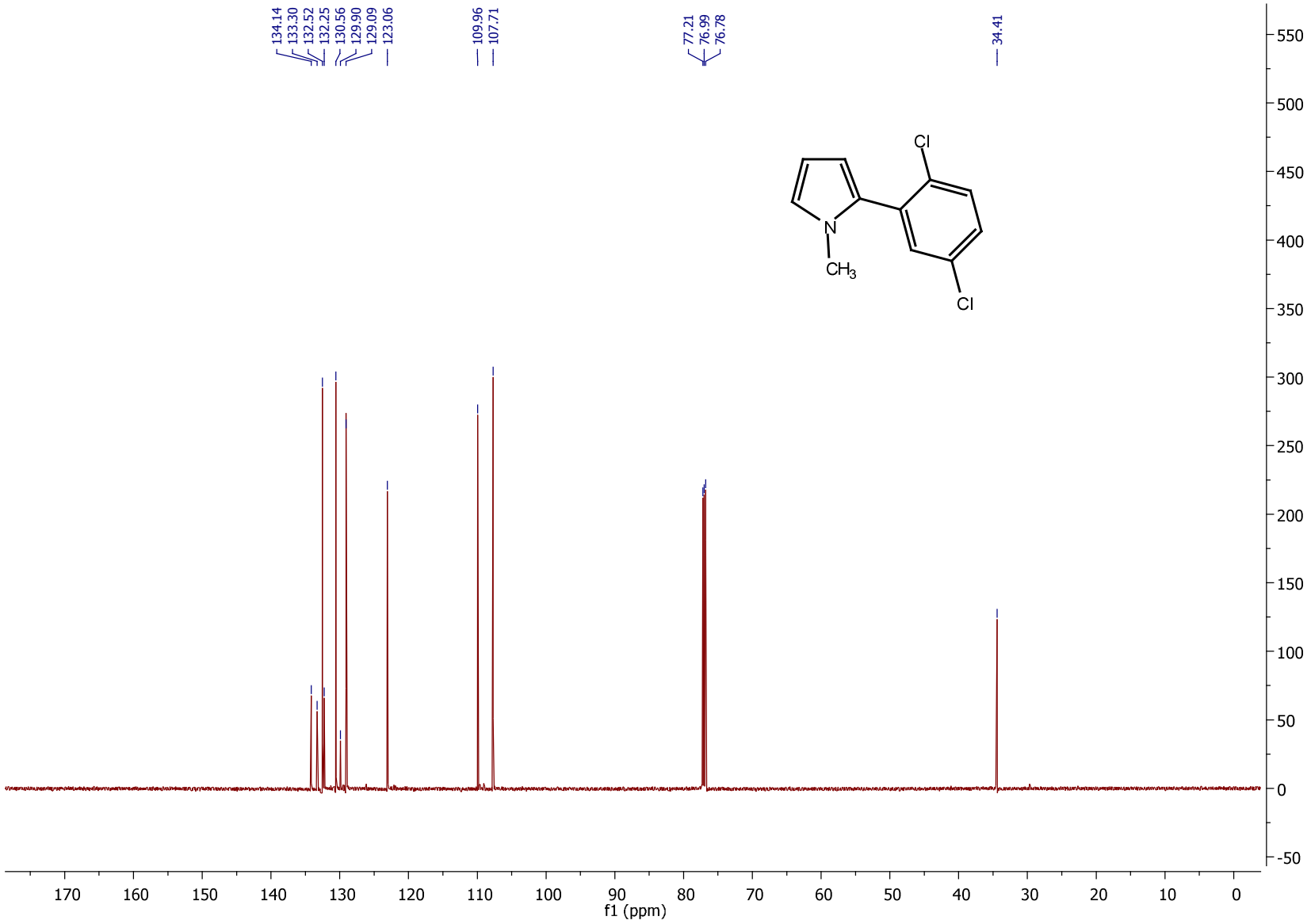



**Figure S32.** $^{13}$C-NMR spectra of compound **8p**.

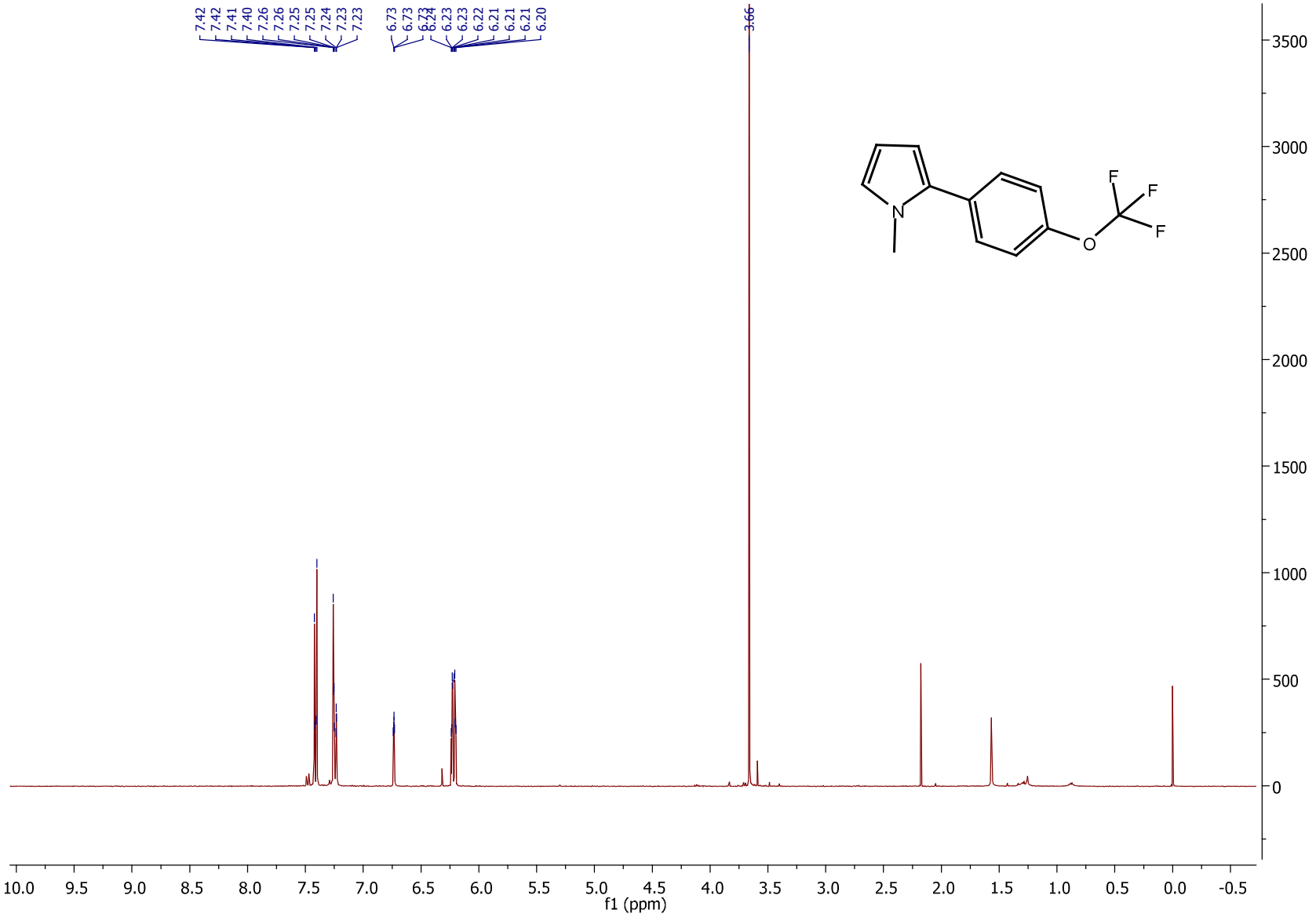



**Figure S33.** $^{1}$H-NMR spectra of compound **8q**.

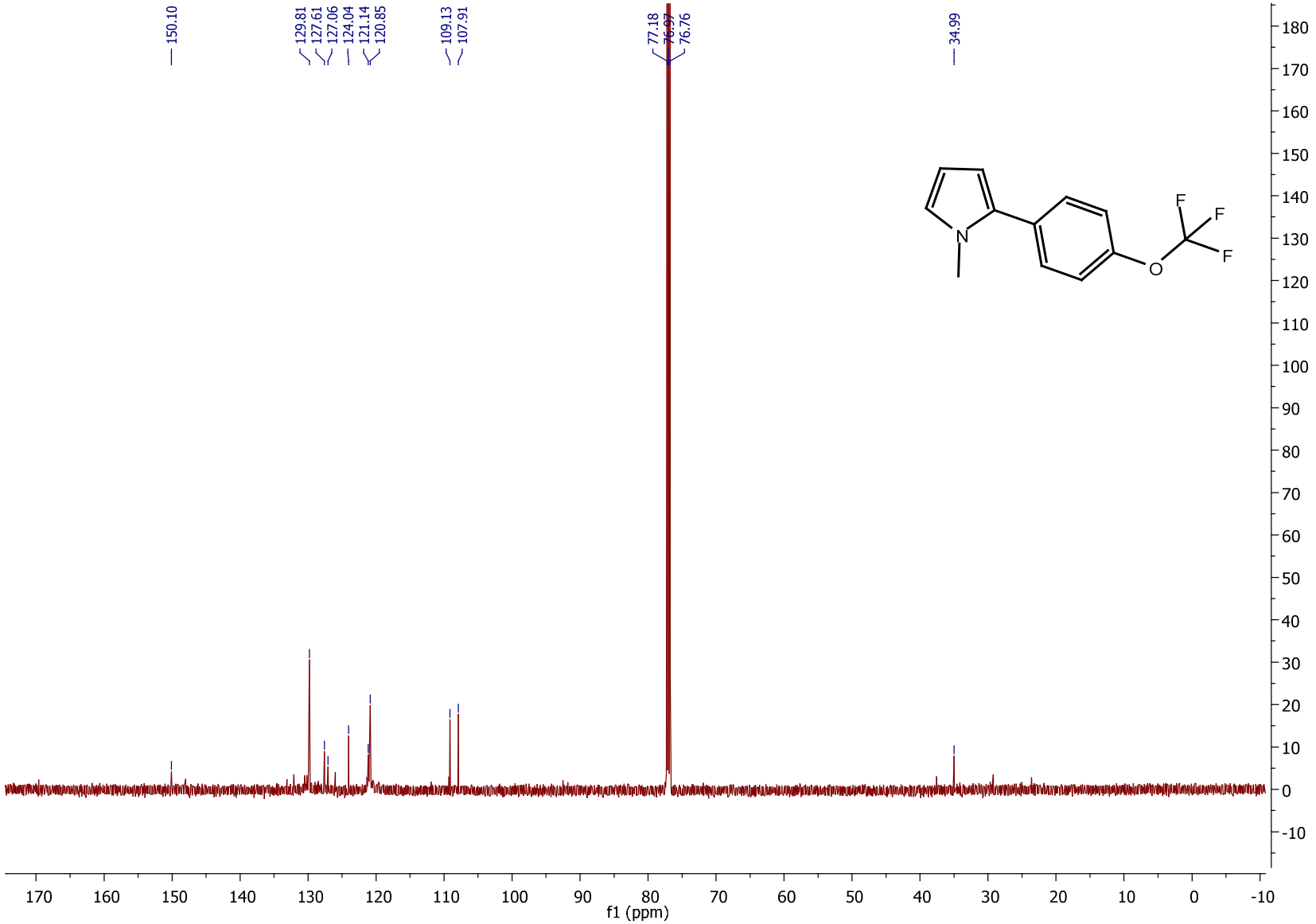



**Figure S34.** $^{13}$C-NMR spectra of compound **8q**.

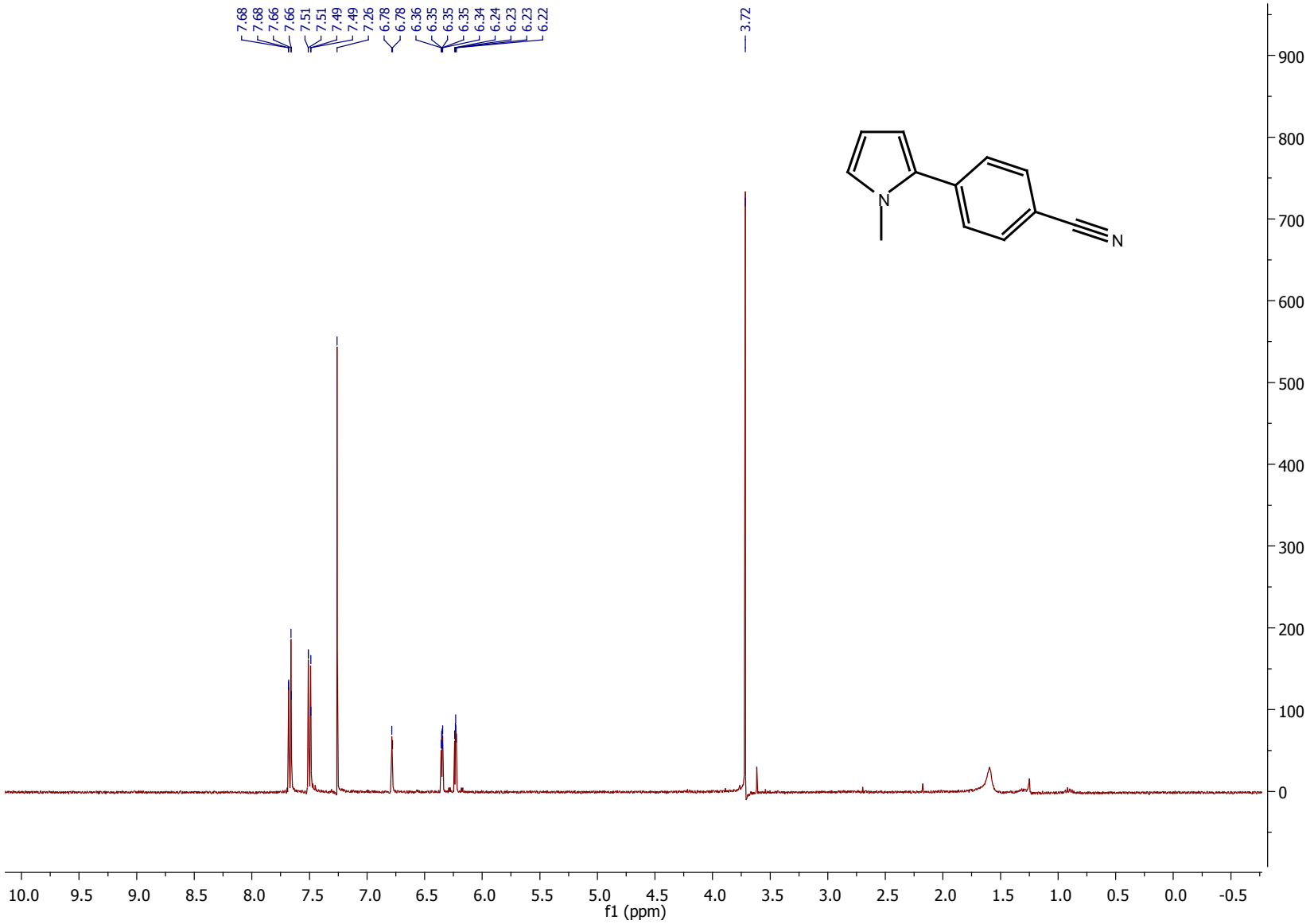



**Figure S35.** $^{1}$H-NMR spectra of compound **8r**.

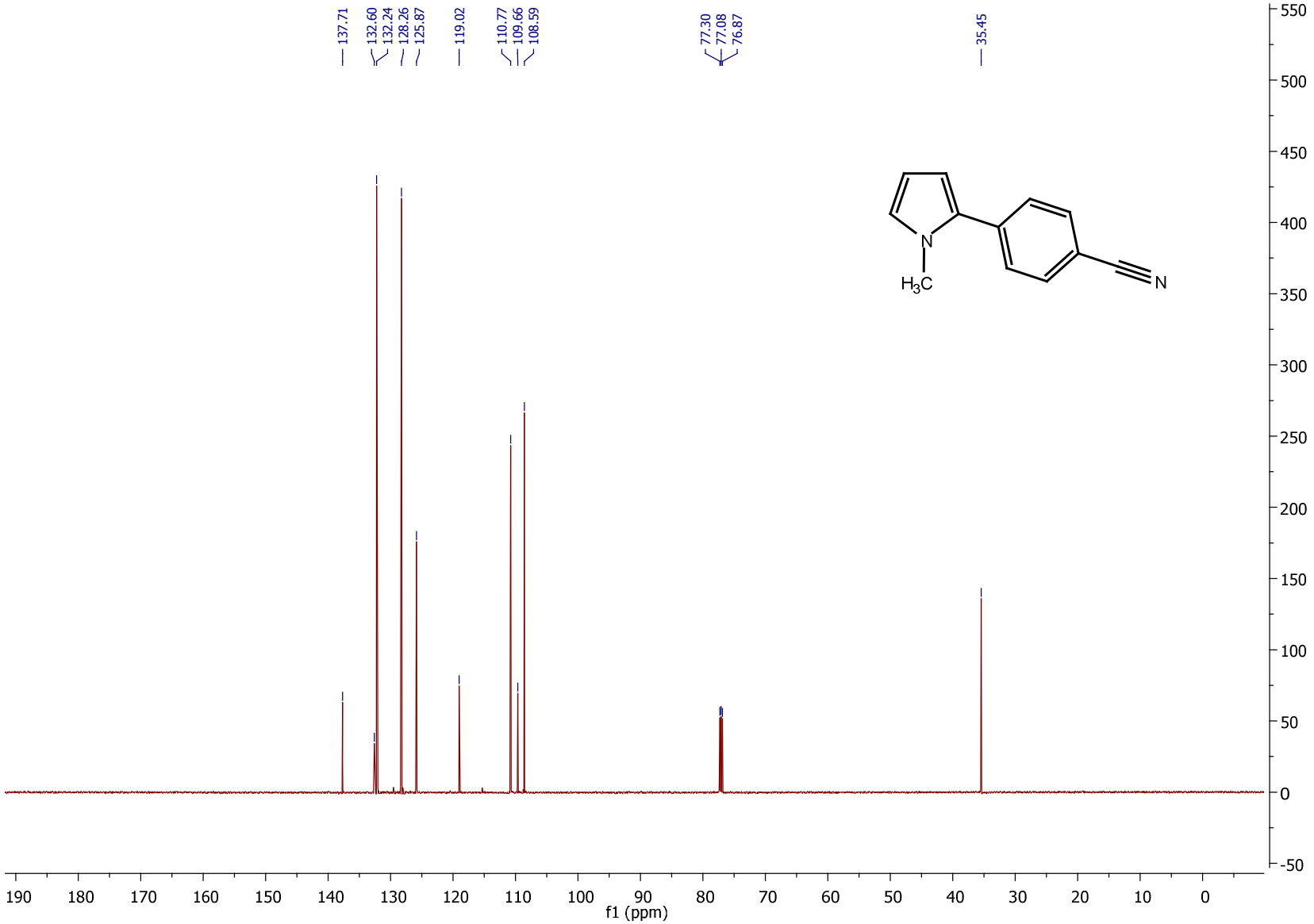



**Figure S36.** $^{13}$C-NMR spectra of compound **8r**.

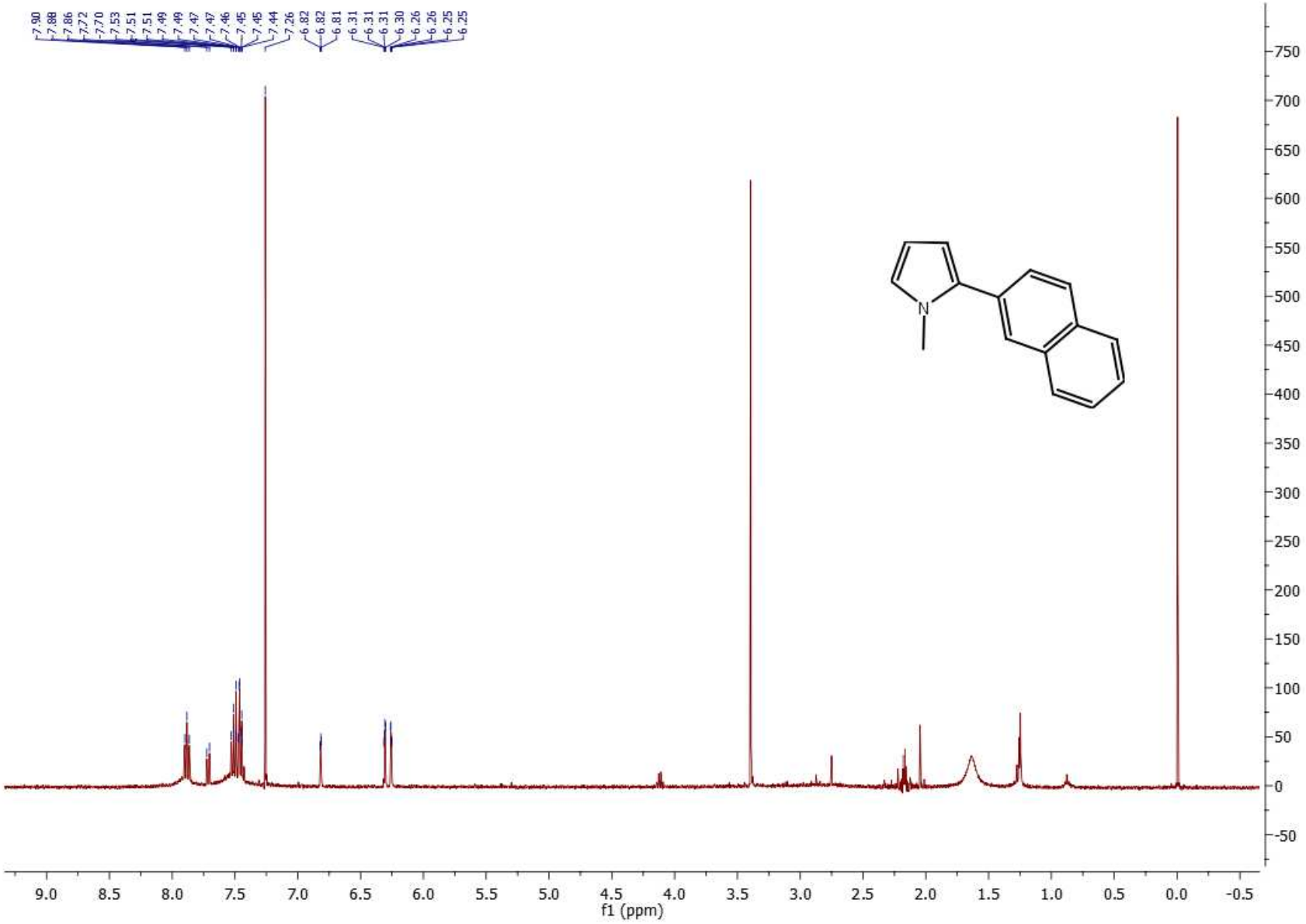



**Figure S37.** $^{1}$H-NMR spectra of compound **8s**.

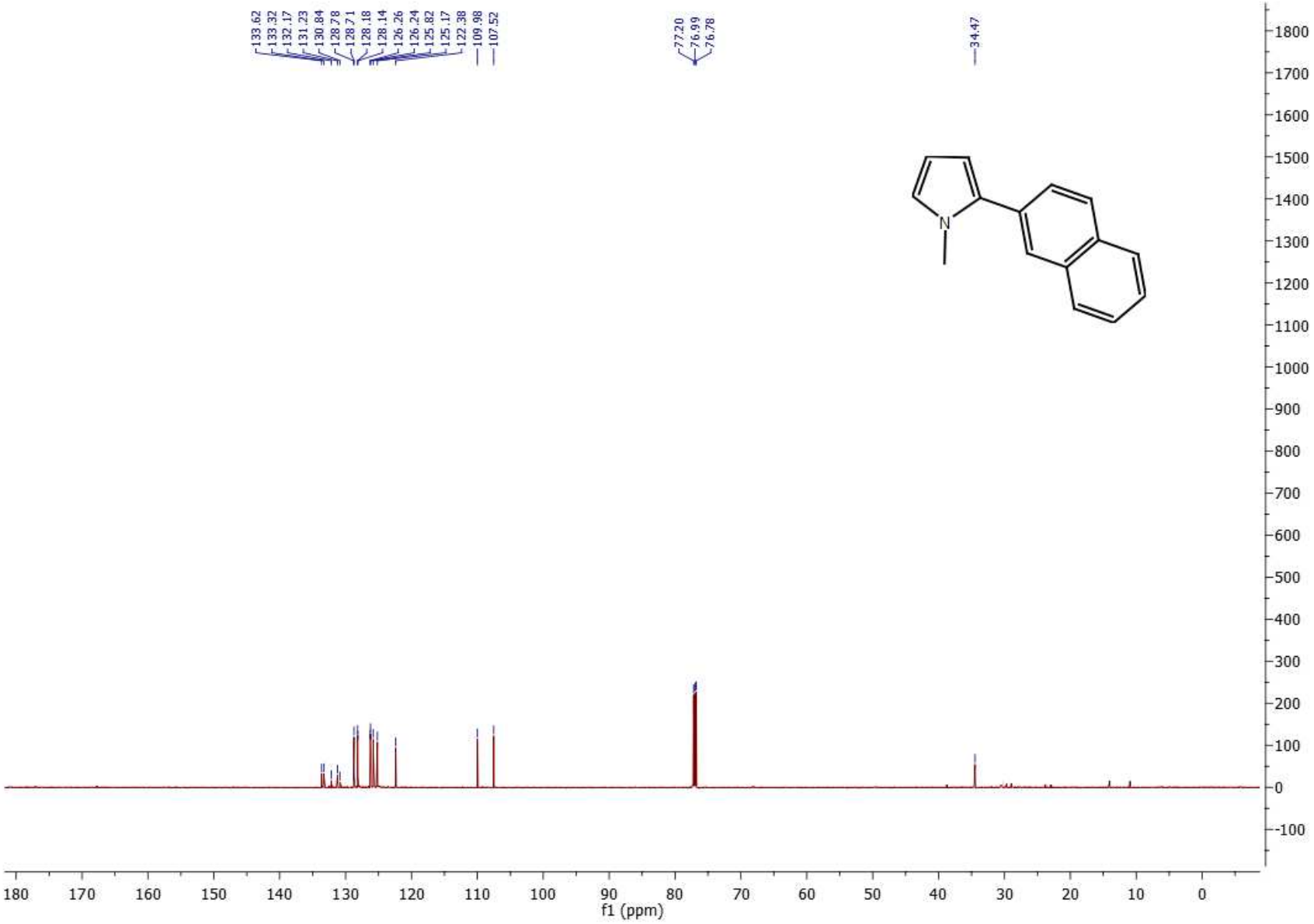



**Figure S38.** $^{13}$C-NMR spectra of compound **8s**.