Supplementary Information for

Palladium-Catalyzed Double C-H Activation: One-Pot Synthesis of Benzo[c]pyrazolo[1,2-a]cinnolin-1-ones from 5-Pyrazolones and Aryl Iodides

Zhoulong Fan,[a] *Kui Wu,*[b] *Li Xing,*[c] *Qizheng Yao*[b] *and Ao Zhang**[a]

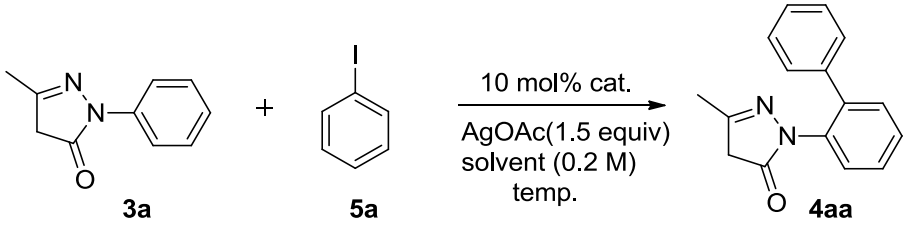
[a] CAS Key Laboratory of Receptor Research, and Synthetic Organic & Medicinal Chemistry Laboratory (SOMCL), Shanghai Institute of Materia Medica (SIMM), Chinese Academy of Sciences, Shanghai 201203, China. E-mail: **aozhang@simm.ac.cn**
[b] Department of Medicinal Chemistry, China Pharmaceutical University, Nanjing 210009, China
[c] Nano Science and Technology Institute, University of Science and Technology of China, Suzhou 215123, China

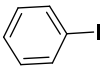
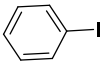
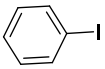
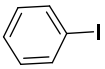
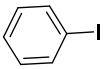
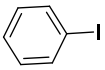
Table of Contents

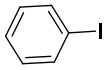
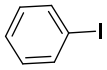
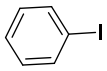
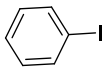
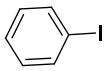
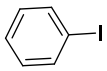
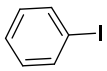
1. General Experimental Information: All reactions were performed in glassware containing a Tefloncoated stir bar. All solvents and chemical reagents were obtained from commercial sources and used without further purifications. ^{1}H and ^{13}C NMR spectra were recorded with tetramethylsilane as an internal reference. Low and high-resolution mass spectra were obtained in the EI mode. Flash column chromatography on silica gel (200-300 mesh) was used for the routine purification of reaction products. The column output was monitored by TLC on silica gel (100-200 mesh) precoated on glass plates (15 x 50 mm), and spots were visualized by UV light at 254 or 365 nM.

2. Optimization Results of the Reaction Conditions:

Table 1 Arylation of edaravone (**3a**) under different conditions.[a]

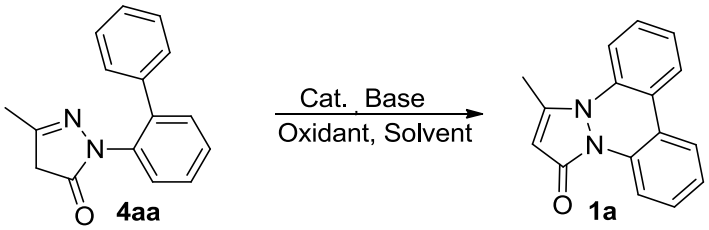


Entry	Substrate	Cat.	Solvent	Temp.	Time	Yield, %[b]
1	 (1.5eq)	$Pd(OAc)_2$**(0.1eq)**	CF_3COOH**(0.2M)**	100°C	23h	72%
2	 (2eq)	$Pd(OAc)_2$**(0.1eq)**	CF_3COOH**(0.2M)**	100°C	17h	75%
3	 (3eq)	$Pd(OAc)_2$**(0.1eq)**	CF_3COOH**(0.2M)**	100°C	8h	74%
4	 (4eq)	$Pd(OAc)_2$**(0.1eq)**	CF_3COOH**(0.2M)**	100°C	4h	75%
5	 (5eq)	$Pd(OAc)_2$**(0.1eq)**	CF_3COOH**(0.2M)**	100°C	2.5h	75%
6	 (5eq)	$PdCl_2$**(0.1eq)**	CF_3COOH**(0.2M)**	100°C	3h	52%

7	 (5eq)	$Pd(TFA)_2$**(0.1eq)**	CF_3COOH**(0.2M)**	100°C	3h	49%
8	 (5eq)	$Pd_2(dba)_3$**(0.1eq)**	CF_3COOH**(0.2M)**	100°C	4h	11%
9	 (5eq)	$Cu(OAc)_2$**(0.1eq)**	CF_3COOH**(0.2M)**	100°C	-	0
10	 (5eq)	$Pd(OAc)_2$**(0.1eq)**	CH_3COOH**(0.2M)**	100°C	3h	0
11	 (5eq)	$Pd(OAc)_2$**(0.1eq)**	CF_3COOH/ CH_3COOH**(1/1,0.2M)**	100°C	4h	24%
12	 (5eq)	$Pd(OAc)_2$**(0.1eq)**	CF_3COOH**(0.2M)**	80°C	3h	<5%
13	 (5eq)	**$Pd(OAc)_2$(0.1eq)**	**CF_3COOH(0.2M)**	**120°C**	**1.5h**	**82%**

[a] Unless stated otherwise, all reactions were carried out using edaravone **3a** (50 mg, 0.287 mmol), aryl iodide **5a** (1.5-5 equiv), Cat. (10 mol %), AgOAc (1.5 equiv), and Solvent (0.2 M) at 80-120 °C for 1.5-23 h. [b] Isolated yields.

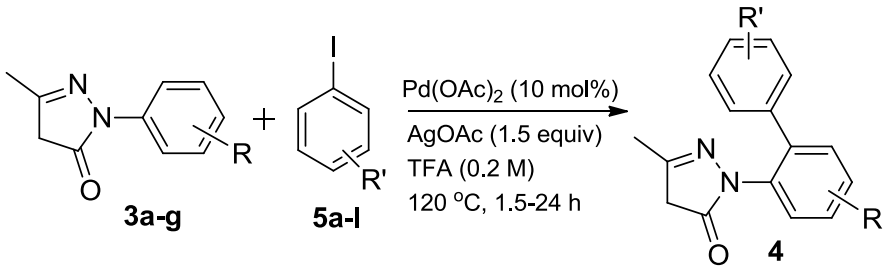
Table 3 Cyclization of **4aa** under different conditions.[a]



Entry	Cat.	Base	Oxidant	Solvent	Time	Yield, %[b]
1	$Pd(OAc)_2$	-	AgOAc	TFA **(0.2 M)**	24h	5%
2	$Pd(OAc)_2$	-	-	TFA **(0.2 M)**	24h	9%
3	$Pd(OAc)_2$	-	-	TFA **(0.2 M)**	24h	0
4	-	-	AgOAc	TFA **(0.2 M)**	24h	0
5	-	-	-	TFA **(0.2 M)**	24h	0
6	$Pd(OAc)_2$	K_2CO_3		TFA **(0.2 M)**	12h	17%
7	$Pd(OAc)_2$	Cs_2CO_3		TFA **(0.2 M)**	12h	12%
8	$Pd(OAc)_2$	CsF		TFA **(0.2 M)**	12h	8%
9	$Pd(OAc)_2$	$NaH_2PO_4.2H_2O$		TFA **(0.2 M)**	12h	6%
10	$Pd(OAc)_2$	K_2CO_3	AgOAc	TFA **(0.2 M)**	12h	25%
11	$Pd(OAc)_2$	K_2CO_3	Ag_2O	TFA **(0.2 M)**	12h	20%
12	$Pd(OAc)_2$	K_2CO_3	$K_2S_2O_8$	TFA **(0.2 M)**	12h	54%
13	$Pd(OAc)_2$	K_2CO_3	$Cu(OAc)_2$	TFA **(0.2 M)**	12h	trace
14	$Pd(OAc)_2$	K_2CO_3	$(NH_4)_2S_2O_8$	TFA **(0.2 M)**	12h	40%
15	$Pd(OAc)_2$	-	$K_2S_2O_8$	TFA **(0.2 M)**	12h	47%
16	$Pd(OAc)_2$	K_2CO_3	$K_2S_2O_8$	TFA **(0.1M)**	24h	55%
17[c]	$Pd(OAc)_2$	K_2CO_3	$K_2S_2O_8$	TFA **(0.1 M)**	24h	74%
18	$Pd(OAc)_2$	K_2CO_3	$K_2S_2O_8$	TFA **(0.05 M)**	24h	60%
19	$Pd(OAc)_2$	K_2CO_3	$K_2S_2O_8$	TFA **(0.03 M)**	24h	70%
20	$Pd(OAc)_2$	K_2CO_3	$K_2S_2O_8$	TFA **(0.02 M)**	24h	78%
21[c,d]	One-pot from **3a** + **5a**			TFA **(0.1 M)**	15h	76%
22[c,d]	One-pot from **3a** + **5a** (no Base)			TFA **(0.1 M)**	15h	66%

[a] Unless stated otherwise, all reactions were carried out using 5-pyrazolone **4aa** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol) in reflux TFA at 120 °C, the reaction time (12 - 24 h) was determined by TLC analysis. [b] Isolated yields. [c] Reaction run in TFA (0.1 M) in a sealed tube.[d] Experiment procedure following the synthesis of **1**.

3. General Procedure for Synthesis of Mono-arylation Products 4: To a stirred solution of 5-pyrazolones



(**3**)[1,2] (0.5 mmol), AgOAc (125 mg, 0.75 mmol) and $Pd(OAc)_2$ (11 mg, 0.05 mmol) in TFA (2.5 mL) was added aryl iodides (**5**) (2.5 mmol), the mixture was heated to 120 °C and monitored by TLC. After the starting material completely disappeared, the reaction mixture was filtered and the filtrate was concentrated. The residue was purified on a silica gel column with petroleum ether/ethyl acetate (2/1) to give the corresponding products **4** (**Table 2**).

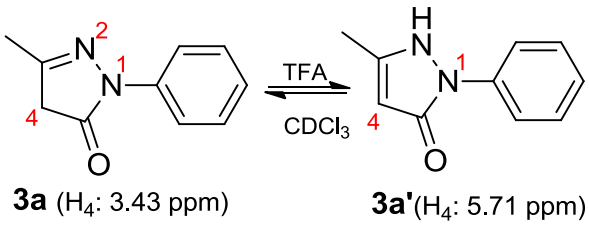
Table 2 Results of the reaction of 5-pyrazolones **3** with aryl iodides.[a]

Entry	**3a-g** (R=)	**5a-l** (R'=)	Time	Yield[b]
1	**3a** (H)	**5a** (H)	1.5 h	**4aa**, 82%
2[c]	**3a** (H)	**5b** (4'-Me)	2.5 h	**4ab**, 83%
3[c]	**3a** H)	**5c** (4'-F)	12 h	**4ac**, 87%
4[c]	**3a** (H)	**5d** (4'-Br)	13 h	**4ad**, 82%
5[c]	**3a** (H)	**5e** (4'-Bu^t)	4.5 h	**4ae**, 71%
6	**3a** (H)	**5f** (4'-CO_2Me)	14 h	**4af**, 85%
7	**3a** (H)	**5g** (3'-OMe)	4.5 h	**4ag**, 70%
8	**3a** (H)	**5h** (3'-CO_2Me)	12 h	**4ah**, 86%
9[c]	**3a** (H)	**5i** (3',5'-di-Me)	4 h	**4ai**, 68%
10	**3a** (H)	**5j** (3'-Cl)	10.5 h	**4aj**, 70%
11	**3a** (H)	**5k** (3'-F)	10 h	**4ak**, 90%
12	**3a** (H)	**5l** (3'-F-4'-Br)	24 h	**4al**, 76%
13	**3b** (4'-Me)	**5a** (H)	5 h	**4ba**, 91%
14	**3c** (4'-Cl)	**5a** (H)	5.5 h	**4ca**, 73%
15	**3d** (4'-NO_2)	**5a** (H)	22 h	**4da**, 49%
16	**3e** (3'-Me)	**5a** (H)	6 h	**4ea**, 64%
17	**3f** (3'-F)	**5a** (H)	5.5 h	**4fa**, 75%
18[d]	**3g** (3'-Cl-4'-Me)	**5a** (H)	20 h	**4ga**, 90%

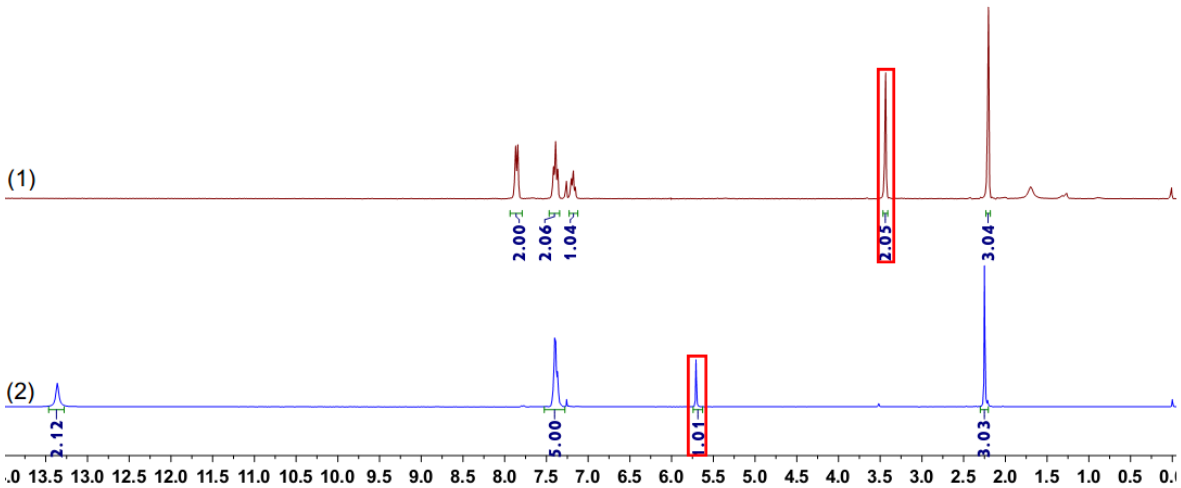
[a] Unless stated otherwise, all reactions were carried out using 5-pyrazolones **3** (0.5 mmol), aryl iodides **5** (2.5 mmol), $Pd(OAc)_2$ (0.05 mmol), AgOAc (0.75 mmol), and TFA (2.5 mL) at 120 °C for 1.5 - 24 h determined by TLC analysis. [b] Isolated yields. [c] Reaction run at 100 °C. [d] Sealed tube was employed.

4. General Procedure for One-pot Synthesis of Benzo[c]pyrazolo [1,2-a]cinnolines 1: To a stirred solution of 5-pyrazolones (**3**) (0.5 mmol) in TFA (2.5 mL), AgOAc (125 mg, 0.75 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and aryl iodides (**5**) (2.5 mmol) were added. The mixture was heated to 120 °C in a sealed tube till the starting material disappeared. After cooled to room temperature, $Pd(OAc)_2$ (11 mg, 0.05 mmol), $K_2S_2O_8$ (203 mg, 0.75 mmol), K_2CO_3 (138 mg, 1 mmol) and additional portion of TFA (2.5 mL) were added consecutively. The mixture was stirred at room temperature for 10 min under N_2 atmosphere, and then heated to 120 °C for 12-24 h in the sealed tube. The reaction mixture was filtered and the filtrate was concentrated. The residue was purified on a silica gel column with petroleum ether/ethyl acetate (1/3) as the eluent to afford the corresponding products **1**.

5. Determination of Tautomers 3a and 3a' in TFA by ^{1}H NMR:



3a (H_4: 3.43 ppm) **3a'**(H_4: 5.71 ppm)

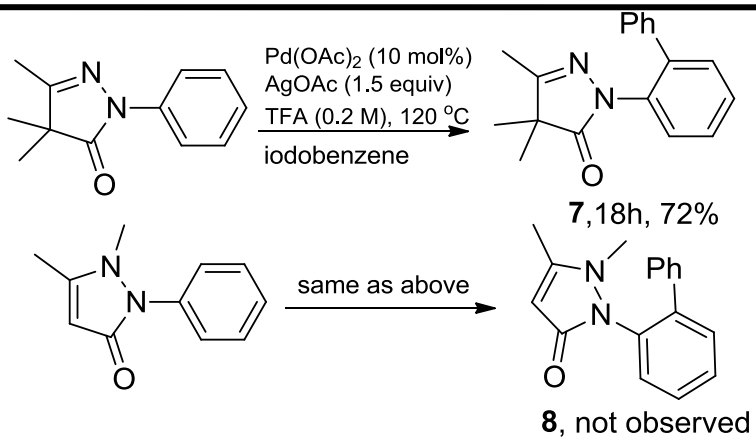


Compound 3a: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 3.43 (s, 2H), 2.20 (s, 3H).

Compound 3a': ^{1}H NMR (300 MHz, $CDCl_3$ + 2 drops TFA) δ 13.36 (s, 2H), 7.40 (m, 5H), 5.71 (s, 1H), 2.25 (s, 3H).

6. Additional Experiments for Mechanism Study:

(1) Two Additional Experiments: Two additional substrates (4,4-dimethyl or *N*-methyl) were employed for the same Pd-catalyzed C-H activation/arylation and compound **7** was obtained in 72% yield, whereas *N*-methyl product **8** was not observed(**Scheme 1**).



Scheme 1 Palladium-catalyzed C-H activation reaction of 1-phenyl 5-pyrazolones derivatives.

(2) Synthesis of 1-([1,1'-Biphenyl]-2-yl)-3,4,4-trimethyl-1H-pyrazol-5(4H)-one (7): To a stirred solution of 3,4,4-trimethyl-1-phenyl-1H-pyrazol-5(4H)-one[3] (20 mg, 0.1 mmol), AgOAc (25 mg, 0.15 mmol) and $Pd(OAc)_2$ (2 mg, 0.01 mmol) in TFA (1 mL), was added phenyl iodide (**5a**) (56 uL, 0.5 mmol). The mixture was heated to 120 °C and monitored by TLC. After completion, the mixture was filtered and the filtrate was evaporated to dryness in vacuo. The residue was separated on a silica gel column with petroleum ether/ethyl acetate (2/1) as the eluent to give product **7** (20 mg, 72% yield) as colorless oil.

7. Spectroscopic Data of All Products.

1-([1,1'-Biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (4aa):[4] White solid; mp = 101-103

^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 – 7.39 (m, 4H), 7.37 – 7.27 (m, 5H), 3.13 (s, 2H), 2.04 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.9, 155.4, 139.5, 138.9, 134.0, 130.4, 128.5, 128.0, 127.9, 127.8, 127.3, 126.8, 40.9, 16.5; **EI-MS** (m/z) 250 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{14}N_2O$, 250.1106; found, 250.1100.

3-Methyl-1-(4'-methyl-[1,1'-biphenyl]-2-yl)-1H-pyrazol-5(4H)-one (4ab): Colourless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 4H), 7.22 (d, J = 8.1 Hz, 2H), 7.15 (d, J = 8.5 Hz, 2H), 3.11 (s, 2H), 2.35 (s, 3H), 2.04 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.9, 155.5, 139.6, 136.4, 135.9, 133.9, 130.4, 128.5, 127.8, 127.7, 127.4, 40.9, 20.8, 16.5; **EI-MS** (m/z) 264 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{16}N_2O$, 264.1263; found, 264.1261.

1-(4'-Fluoro-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (4ac): White solid; mp = 163-165 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 (tt, J = 6.0, 3.3 Hz, 4H), 7.34 – 7.27 (m, 2H), 7.04 (t, J = 8.7 Hz, 2H), 3.16 (s, 2H), 2.07 (s,3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.9, 162.7, 160.7, 155.6, 138.6, 134.9, 134.8, 134.0, 130.3, 129.7, 129.6, 128.6, 128.0, 127.3, 114.8, 114.6, 40.9, 16.5; **EI-MS** (m/z) 268 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{13}FN_2O$, 268.1012; found, 268.1009.

1-(4'-Bromo-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (4ad): White solid; mp = 142-144 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.4 Hz, 2H), 7.46 – 7.36 (m, 4H), 7.21 (d, J = 8.4 Hz, 2H), 3.16 (s, 2H), 2.07 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.8, 155.7, 138.3, 137.9, 133.8, 130.9, 130.2, 129.6, 128.6, 128.3, 127.3, 121.1, 40.9, 16.6; **EI-MS** (m/z) 328 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{13}BrN_2O$, 328.0211; found, 328.0197.

1-(4'-(Tert-butyl)-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (4ae): Colourless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 – 7.42 (m, 4H), 7.39 (d, J = 8.3 Hz, 2H), 7.30 (s, 2H), 3.15 (s, 2H), 2.05 (s, 3H), 1.36 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.1, 155.4, 149.6, 139.5, 135.8, 134.0, 130.5, 128.5, 127.6(2), 127.4, 124.7, 40.9, 34.1, 30.9, 16.4; **EI-MS** (m/z) 306 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{20}H_{22}N_2O$, 306.1732; found, 306.1732.

Methyl 2'-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-[1,1'-biphenyl]-4-carboxylate (4af): Colourless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 – 8.00 (m, 2H), 7.48 – 7.39 (m, 6H), 3.92 (s, 3H), 3.15 (s, 2H), 2.05 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.8, 166.5, 155.9, 143.7, 138.1, 133.9, 130.2, 129.1, 128.9, 128.5, 128.4, 128.0, 127.2, 51.7, 40.9, 16.5; **EI-MS** (m/z) 308 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{18}H_{16}N_2O_3$, 308.1161; found, 308.1155.

1-(3'-Methoxy-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (4ag): Colourless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 – 7.42 (m, 4H), 7.28 (d, J = 3.0 Hz, 1H), 6.97 – 6.91 (m, 2H), 6.90 – 6.83 (m, 1H), 3.80 (s, 3H), 3.15 (s, 2H), 2.07 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.1, 158.9, 155.5, 140.2, 139.5, 133.9, 130.4, 128.8, 128.6, 128.0, 127.5, 120.4, 113.2, 112.8, 54.7, 40.9, 16.5; **EI-MS** (m/z) 280 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{16}N_2O_2$, 280.1212; found, 280.1209.

Methyl 2'-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-[1,1'-biphenyl]-3-carboxylate (4ah): Colourless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.97 (d, J = 7.9 Hz, 1H), 7.54 (d, J = 8.6 Hz, 1H), 7.44 (d, J = 10.0 Hz, 5H), 3.89 (s, 3H), 3.12 (s, 2H), 2.04 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.3, 166.9, 156.4, 139.5, 138.5, 134.4, 132.9, 130.7, 130.2, 129.5, 129.0, 128.8, 128.4, 127.8, 52.1, 41.4, 16.9; **EI-MS** (m/z) 308 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{18}H_{16}N_2O_3$, 308.1161; found, 308.1161.

1-(3',5'-Dimethyl-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (4ai): White solid; mp = 155-157 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.37 (m, 4H), 7.01 – 6.90 (m, 3H), 3.11 (s, 2H), 2.30 (s, 6H), 2.05 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.5, 155.6, 140.2, 139.1, 137.5, 134.3, 130.9, 129.0, 128.9, 128.1, 127.9, 126.2, 41.3, 21.3, 16.9; **EI-MS** (m/z) 278 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{18}H_{18}N_2O$, 278.1419; found, 278.1419.

1-(3'-Chloro-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (4aj): Colourless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 – 7.40 (m, 4H), 7.35 – 7.31 (m, 1H), 7.29 – 7.26 (m, 2H), 7.25 – 7.20 (m, 1H), 3.15 (s, 2H), 2.06 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 156.3, 141.0, 138.3, 134.3, 133.9, 130.6, 129.5, 129.0, 128.8, 128.5, 127.8, 127.3, 126.6, 41.4, 16.9; **EI-MS** (m/z) 284 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{13}ClN_2O$, 284.0716; found, 284.0718.

1-(3'-Fluoro-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (4ak): White solid; mp = 157-159 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 (s, 5H), 7.17 – 6.94 (m, 3H), 3.14 (s, 2H), 2.04 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 163.8, 161.3, 156.3, 141.5, 141.4, 138.5, 138.4, 134.3, 130.7, 129.8, 129.7, 129.0, 128.8, 127.7, 124.2(2), 115.4, 115.2, 114.2, 114.0, 41.4, 16.9; **EI-MS** (m/z) 268 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{13}FN_2O$, 268.1012; found, 268.1015.

1-(4'-Bromo-3'-fluoro-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (4al): Colourless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.48 – 7.37 (m, 4H), 7.12 (dd, *J* =

9.6, 2.0 Hz, 1H), 7.01 (dd, *J* = 8.2, 2.0 Hz, 1H), 3.19 (s, 2H), 2.09 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.8, 159.3, 157.3, 156.0, 140.4, 140.3, 137.0, 133.8, 132.8, 130.1, 128.7, 128.6, 127.3, 125.0, 124.9, 116.2, 116.0, 107.6, 107.4, 41.0, 16.5; **EI-MS** (m/z) 346 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{12}BrFN_2O$, 346.0117; found, 346.0124.

3-Methyl-1-(5-methyl-[1,1'-biphenyl]-2-yl)-1H-pyrazol-5(4H)-one (4ba): Colourless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.31 (m, 4H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.25 – 7.21 (m, 2H), 3.10 (s, 2H), 2.40 (s, 3H), 2.02 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.2, 155.3, 139.4, 138.9, 138.6, 131.4, 131.0, 128.5, 128.0, 127.7, 127.3, 126.7, 40.8, 20.8, 16.5; **EI-MS** (m/z) 264 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{16}N_2O$, 264.1263; found, 264.1255.

1-(5-Chloro-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (4ca): White solid; mp = 194-196 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 2.3 Hz, 1H), 7.40 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.37 – 7.29 (m, 6H), 3.11 (s, 2H), 2.03 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.9, 155.8, 141.0, 137.6, 134.0, 132.5, 130.4, 128.6, 127.9, 127.8(2), 127.3, 40.8, 16.5; **EI-MS** (m/z) 284 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{13}ClN_2O$, 284.0716; found, 284.0710.

3-Methyl-1-(5-nitro-[1,1'-biphenyl]-2-yl)-1H-pyrazol-5(4H)-one (4da): White solid; mp = 180-182 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 2.6 Hz, 1H), 8.26 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.65 (d, *J* = 8.7 Hz, 1H), 7.42 – 7.31 (m, 5H), 3.18 (s, 2H), 2.07 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.1, 156.6, 146.4, 139.4, 137.3, 128.2, 127.7, 127.5, 127.0, 125.8, 122.6, 40.9, 16.6; **EI-MS** (m/z) 295 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{13}N_3O_3$, 295.0957; found, 295.0955.

3-Methyl-1-(4-methyl-[1,1'-biphenyl]-2-yl)-1H-pyrazol-5(4H)-one (4ea): White solid; mp = 152-154 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 5H), 7.30 – 7.27 (m, 1H), 7.24 (d, *J* = 11.4 Hz, 2H), 3.12 (s, 2H), 2.40 (s, 3H), 2.04 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.5, 155.8, 139.3, 138.5, 137.2, 134.1, 130.7, 129.9, 128.5, 128.3, 128.2, 127.0, 41.4, 21.0, 17.0; **EI-MS** (m/z) 264 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{16}N_2O$, 264.1263; found, 264.1255.

1-(4-Fluoro-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (4fa): Off-white solid; mp = 167-169 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.27 (m, 6H), 7.20 – 7.11 (m, 2H), 3.12 (d, *J* = 0.9 Hz, 2H), 2.05 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.0, 163.2, 160.7, 156.3, 138.6, 135.9(2), 135.5, 135.4, 132.2, 132.1, 128.4, 128.3, 127.3, 116.0, 115.8, 114.8, 114.6, 41.3, 17.0; **EI-MS** (m/z) 268 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{13}FN_2O$, 268.1012; found, 268.1006.

1-(4-Chloro-5-methyl-[1,1'-biphenyl]-2-yl)-3-methyl-1H-pyrazol-5(4H)-one (4ga): White solid; mp = 162-164 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 7.36 – 7.28 (m, 6H), 3.10 (s, 2H), 2.42 (s, 3H), 2.04 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 156.2, 138.4, 137.0, 133.6, 132.9(2), 128.3, 128.2, 127.5, 41.3, 19.9, 17.0; **EI-MS** (m/z) 298 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{15}ClN_2O$, 298.0873; found, 298.0872.

3-Methyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1a):[5] White solid; mp= 118-120 ^{o}C; **IR** (υ_{max}): 2922, 2851, 1656, 1597, 1492, 1442, 1409, 1313, 993, 744 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.13 (dd, J = 8.4, 1.2 Hz, 1H), 7.85 (ddd, J = 13.8, 7.9, 1.5 Hz, 2H), 7.43 – 7.36 (m, 2H), 7.33 – 7.28 (m, 1H), 7.26 – 7.21 (m, 2H), 5.62 (s, 1H), 2.68 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.6, 143.7, 134.8, 133.3, 129.0, 128.2, 124.7, 124.4, 123.4, 121.7, 121.6, 118.5, 114.9, 99.3, 16.2; **EI-MS** (m/z) 248 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{12}N_2O$, 248.0950; found, 248.0949.

3,6-Dimethyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1b): White solid; mp = 160-162 ^{o}C; **IR** (υ_{max}): 2921, 2853, 1654, 1600, 1578, 1502, 1452, 1419, 1316, 989, 763 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.10 (d, *J* = 8.4 Hz, 1H), 7.72 (dd, *J* = 27.2, 8.0 Hz, 2H), 7.40 – 7.29 (m, 1H), 7.25 – 7.13 (m, 2H), 7.00 (d, *J* = 7.4 Hz, 1H), 5.58 (s, 1H), 2.65 (s, 3H), 2.35 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.0, 144.0, 139.0, 134.8, 133.6, 128.9, 126.0, 124.8, 123.7, 121.8, 119.2, 119.1, 115.8, 115.3, 99.6, 21.8, 16.7; **EI-MS** (m/z) 262 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{14}N_2O$, 262.1106; found, 262.1102.

6-(Tert-butyl)-3-methyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1c): Colourless oil; **IR** (υ_{max}): 2953, 2863, 1660, 1617, 1600, 1492, 1409, 1319, 998,769 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.15 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.84 – 7.79 (m, 2H), 7.45 (d, *J* = 1.8 Hz, 1H), 7.36 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H), 7.29 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.22 (ddd, *J* = 8.5, 7.4, 1.3 Hz, 1H), 5.63 (d, *J* = 1.0 Hz, 1H), 2.72 (s, 3H), 1.36 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.1, 152.4, 143.8, 135.1, 133.6, 129.1, 124.8, 123.6, 122.4, 121.9, 119.4, 119.1, 115.4, 112.6, 99.7, 35.1, 31.1, 16.7; **EI-MS** (m/z) 304 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{20}H_{20}N_2O$, 304.1576; found, 304.1570.

7-Methoxy-3-methyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1d): Colourless oil; **IR** (υ_{max}): 2920, 2850, 1639, 1599, 1579, 1504, 1412, 1298, 1225, 764 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.15 (d, *J* = 8.6 Hz, 1H), 7.77 (d, *J* = 7.4 Hz, 1H), 7.42 – 7.31 (m, 3H), 7.22 (t, *J* = 7.7 Hz, 1H), 6.87 – 6.79 (m, 1H), 5.56 (s, 1H), 3.87 (s, 3H), 2.63 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.7, 156.4,

143.4, 135.0, 129.2, 127.2, 124.2, 123.2, 121.7, 118.4, 116.3, 114.9, 113.6, 108.4, 98.1, 55.2, 15.8; **EI-MS** (m/z) 278 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{14}N_2O_2$, 278.1055; found, 278.1056.

Methyl 3-methyl-1-oxo-1H-benzo[c]pyrazolo[1,2-a]cinnoline-7-carboxylate (1e): Colourless oil; **IR** (υ_{max}): 2922, 2851, 1715, 1665, 1607, 1495, 1439, 1397, 1322, 1263, 986, 763 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.09 (d, *J* = 8.4 Hz, 1H), 8.51 (d, *J* = 1.9 Hz, 1H), 7.97 – 7.88 (m, 2H), 7.46 (d, *J* = 8.8 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.27 (d, *J* = 3.2 Hz, 1H), 5.69 (s, 1H), 3.97 (s, 3H), 2.71 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.9, 161.7, 144.4, 136.9, 135.0, 130.0(2), 126.3, 125.3, 125.2, 122.4, 121.8, 118.2, 115.5, 114.8, 101.4, 52.4, 16.9; **EI-MS** (m/z) 306 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{18}H_{14}N_2O_3$, 306.1004; found, 306.0999.

7-Chloro-3-methyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1f): White solid; mp = 197-199 ^oC; **IR** (υ_{max}): 2923, 2852, 1647, 1597, 1578, 1492, 1449, 1406, 1308, 989, 799, 763 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.09 (d, *J* = 8.3 Hz, 1H), 7.75 – 7.66 (m, 2H), 7.43 – 7.35 (m, 1H), 7.31 (d, *J* = 8.9 Hz, 1H), 7.25 – 7.18 (m, 2H), 5.62 (s, 1H), 2.64 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.9, 144.3, 135.3, 132.3, 130.7, 130.2, 128.4, 125.0, 123.8, 122.3, 117.9, 116.5, 115.4, 100.2, 16.6; **EI-MS** (m/z) 282 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{11}ClN_2O$, 282.0560; found, 282.0558.

7-Fluoro-3-methyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1g): Off-white solid; mp = 190-192 ^oC; **IR** (υ_{max}): 2923, 2853, 1659, 1599, 1581, 1507, 1436, 1403, 1319, 1212, 989, 796, 760 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.10 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.47 (dd, *J* = 9.4, 2.9 Hz, 1H), 7.42 – 7.30 (m, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.98 (ddd, *J* = 9.0, 7.5, 2.9 Hz, 1H), 5.60 (s, 1H), 2.63 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.6, 160.4, 158.4, 143.8, 134.9, 129.8, 129.7, 129.6, 124.4, 124.0(2), 121.9, 117.7(2), 116.6, 116.5, 115.0, 114.9, 114.8, 110.2, 110.0, 99.1, 15.9; **EI-MS** (m/z) 266 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{11}FN_2O$, 266.0855; found, 266.0857.

6-Chloro-3-methyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1h): Off-white solid; mp = 139-141 ^oC; **IR** (υ_{max}): 2923, 2851, 1658, 1633, 1599, 1487, 1417, 1296, 1103, 998, 758 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.07 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 13.1 Hz, 2H), 7.41 – 7.34 (m, 2H), 7.24 – 7.13 (m, 2H), 5.63 (s, 1H), 2.67 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.8, 144.3, 135.0, 134.5, 134.2, 129.8, 125.1, 125.0, 122.1, 120.6, 118.2, 115.4(2), 100.8, 16.6; **EI-MS** (m/z) 282 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{11}ClN_2O$, 282.0560; found, 282.0560.

3,7-Dimethyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1i): White solid; mp = 161-163 ^{o}C; **IR** (υ_{max}): 2919, 2855, 1645, 1598, 1581, 1507, 1449, 1409, 1311, 990, 767 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.12 (d, *J* = 7.3 Hz, 1H), 7.76 (d, *J* = 6.4 Hz, 1H), 7.57 (s, 1H), 7.38 – 7.30 (m, 1H), 7.24 – 7.15 (m, 2H), 7.03 (dd, *J* = 8.5, 1.2 Hz, 1H), 5.55 (s, 1H), 2.60 (s, 3H), 2.35 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.5, 143.4, 134.7, 134.3, 131.0, 128.8(2), 124.2, 123.7, 121.5, 121.2, 118.5, 114.9, 114.7, 98.6, 20.5, 16.0; **EI-MS** (m/z) 262 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{14}N_2O$, 262.1106; found, 262.1101.

3,10-Dimethyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1j): White solid; mp = 184-186 ^{o}C; **IR** (υ_{max}): 2923, 2857, 1684, 1601, 1495, 1421, 1318, 1213, 1140, 800 cm^{-1}; **^{1}H NMR** (400 MHz, MeOD) δ 8.71 (s, 1H), 7.77 (d, *J* = 6.4 Hz, 1H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.47 (d, *J* = 7.3 Hz, 1H), 7.27 (ddd, *J* = 8.5, 7.3, 1.5 Hz, 1H), 7.18 (td, *J* = 7.5, 1.1 Hz, 1H), 6.98 (d, *J* = 9.1 Hz, 1H), 5.59 (s, 1H), 2.63 (s, 3H), 2.31 (s, 3H); **^{13}C NMR** (126 MHz, MeOD) δ 161.5, 144.5, 138.9, 133.3, 132.1, 127.8, 125.5, 124.8, 122.7, 121.6, 120.6, 115.7, 115.0, 114.6, 97.8, 19.9, 14.9; **EI-MS** (m/z) 262 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{14}N_2O$, 262.1106; found, 262.1099.

10-Chloro-3-methyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1k): Off-white solid; mp = 195-197 ^{o}C; **IR** (υ_{max}): 2923, 2852, 1659, 1592, 1577, 1451, 1415, 1337, 987, 775 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.09 (d, *J* = 9.0 Hz, 1H), 7.80 – 7.73 (m, 2H), 7.42 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.25 (dd, *J* = 7.7, 1.2 Hz, 1H), 5.61 (s, 1H), 2.68 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.8, 144.4, 134.0, 133.6, 130.2, 129.5, 129.1, 125.2, 124.0, 122.0, 120.8(2), 116.8, 115.4, 99.8, 16.7; **EI-MS** (m/z) 282 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{11}ClN_2O$, 282.0560; found, 282.0558.

3,11-Dimethyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1l): Pale yellow solid; mp = 200-202 ^{o}C; **IR** (υ_{max}): 2923, 2853, 1645, 1602, 1578, 1501, 1451, 1419, 1337, 988, 762 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.02 (d, *J* = 8.6 Hz, 1H), 7.87 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.62 (s, 1H), 7.42 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.26 – 7.17 (m, 2H), 5.61 (s, 1H), 2.68 (s, 3H), 2.40 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.9, 143.8, 134.3, 133.9, 133.1, 130.2, 128.6, 125.0, 123.9, 122.5, 122.1, 118.8, 115.4, 115.3, 99.9, 21.2, 16.7; **EI-MS** (m/z) 262 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{14}N_2O$, 262.1106; found, 262.1098.

11-Fluoro-3-methyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1m): Pale yellow solid; mp =

178-180 ^{o}C; **IR** (υ_{max}): 2923, 2851, 1656, 1605, 1496, 1424, 1276, 1186, 917, 753 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.93 (d, *J* = 11.4 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.26 (d, *J* = 6.4 Hz, 1H), 7.21 (t, *J* = 8.1 Hz, 1H), 6.93 – 6.86 (m, 1H), 5.58 (s, 1H), 2.66 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.1, 161.9, 161.6, 144.7, 136.1, 136.0, 133.1, 128.6, 125.3, 123.8, 123.7, 123.6, 121.4, 115.6, 115.4, 115.2(2), 112.1, 111.8, 103.2, 102.9, 99.4, 16.6; **EI-MS** (m/z) 266 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{11}FN_2O$, 266.0855; found, 266.0848.

11-Chloro-3,10-dimethyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1r): White solid; mp = 182-184 ^{o}C; **IR** (υ_{max}): 2920, 2849, 1655, 1603, 1575, 1492, 1448, 1411, 1320, 994, 753 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 7.75 (d, *J* = 9.0 Hz, 1H), 7.58 (s, 1H), 7.37 (d, *J* = 8.3 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 5.57 (s, 1H), 2.66 (s, 3H), 2.38 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.6, 144.3, 135.3, 133.6, 133.5, 132.3, 128.8, 125.1, 123.9, 123.7, 121.2, 117.5, 115.7, 115.3, 99.5, 19.9, 16.6; **EI-MS** (m/z) 296 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{13}ClN_2O$, 296.0716; found, 296.0716.

10-Fluoro-3-methyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1o): Off-white solid; mp = 199-201 ^{o}C; **IR** (υ_{max}): 2923, 2851, 1642, 1603, 1500, 1453, 1433, 1273, 1191, 992, 892, 817, 777 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.13 (dd, *J* = 9.3, 5.3 Hz, 1H), 7.74 (d, *J* = 7.9 Hz, 1H), 7.48 – 7.38 (m, 2H), 7.36 – 7.29 (m, 1H), 7.26 – 7.19 (m, 1H), 7.05 (ddd, *J* = 9.3, 7.8, 2.8 Hz, 1H), 5.62 (d, *J* = 1.1 Hz, 1H), 2.67 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.3, 160.2, 158.3, 143.6, 133.6, 131.0, 129.0, 124.7, 123.6, 120.7, 120.6(2), 117.0, 116.9, 115.7, 115.5, 114.9, 108.3, 108.1, 99.5, 16.2; **EI-MS** (m/z) 266 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{11}FN_2O$, 266.0855; found, 266.0862.

10-Bromo-3-methyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1p): White solid; mp = 192-194 ^{o}C; **IR** (υ_{max}): 2924, 2852, 1644, 1588, 1485, 1418, 1312, 990, 817, 753 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.99 (d, *J* = 9.0 Hz, 1H), 7.83 (d, *J* = 2.2 Hz, 1H), 7.71 (d, *J* = 6.8 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.32 – 7.27 (m, 1H), 7.24 – 7.16 (m, 1H), 5.58 (s, 1H), 2.65 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.7, 144.4, 134.0, 133.9, 131.9, 129.4, 125.2, 124.9, 124.0, 121.0, 120.6, 117.8, 117.0, 115.3, 99.7, 16.7; **EI-MS** (m/z) 326 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{11}BrN_2O$, 326.0055; found, 326.0049.

11-Bromo-3-methyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1n): White solid; mp =

166-168 ^{o}C; **IR** (υ_{max}): 2923, 2851, 1664, 1604, 1588, 1485, 1416, 1313, 1258, 993, 751 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.31 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 7.36 – 7.28 (m, 2H), 7.22 (t, *J* = 7.4 Hz, 1H), 5.60 (s, 1H), 2.67 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.4, 144.3, 135.3, 133.2, 128.6, 127.5, 124.8, 123.3, 122.9, 122.8, 120.8, 117.7, 117.5, 115.0, 99.1, 16.2; **EI-MS** (m/z) 326 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{16}H_{11}BrN_2O$, 326.0055; found, 326.0059.

3,10,11-Trimethyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1q): Colourless oil; **IR** (υ_{max}): 2921, 2852, 1652, 1603, 1495, 1449, 1415, 1352, 1323, 895, 752 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.56 (s, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.27 (t, *J* = 3.4 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 5.60 (s, 1H), 2.66 (s, 3H), 2.31 (d, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.8, 143.6, 138.6, 133.5, 133.2, 128.0, 124.9, 123.5, 122.9, 122.2, 116.4, 116.1, 115.3, 99.7, 20.1, 19.6, 16.6; **EI-MS** (m/z) 276 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{18}H_{16}N_2O$, 276.1263; found, 276.1276.

1H-Benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1s): Pale yellow solid; mp = 126-128 ^{o}C; **IR** (υ_{max}): 2924, 2853, 1646, 1596, 1530, 1492, 1450, 1344, 1275, 744 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.16 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 3.8 Hz, 1H), 7.75 (dd, J = 7.8, 5.6 Hz, 2H), 7.39 – 7.31 (m, 1H), 7.29 – 7.24 (m, 1H), 7.22 – 7.16 (m, 1H), 7.12 (t, J = 7.7 Hz, 2H), 5.80 (d, J = 3.8 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.8, 133.8, 131.9, 129.6, 129.4, 126.6, 125.1, 124.8, 123.4, 121.9, 118.7, 118.0, 116.0, 111.8, 97.2; **EI-MS** (m/z) 234 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{15}H_{10}N_2O$, 234.0793; found, 234.0802.

3-Ethyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1t): White solid; mp = 104-106 ^{o}C; **IR** (υ_{max}): 2922, 2852, 1649, 1600, 1489, 1445, 1308, 747 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.11 (d, J = 8.4 Hz, 1H), 7.85 – 7.77 (m, 2H), 7.36 (dd, J = 14.8, 7.6 Hz, 2H), 7.31 – 7.26 (m, 1H), 7.22 (t, J = 7.5 Hz, 2H), 5.67 (s, 1H), 3.00 (q, J = 7.5 Hz, 2H), 1.39 – 1.34 (m, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.4, 151.0, 135.5, 134.0, 129.5, 128.6, 125.1, 124.8, 124.0, 122.4, 122.2, 119.2, 115.7, 115.3, 98.2, 23.2, 12.5.; **EI-MS** (m/z) 262 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{14}N_2O$, 276.1106; found, 262.1099.

3-Isopropyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1u): Colourless oil; **IR** (υ_{max}): 2974, 1658, 1599, 1554, 1502, 1487, 1442, 1300, 750 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.08 (d, J = 7.9

Hz, 1H), 7.84 (d, J = 7.8 Hz, 2H), 7.39 (dd, J = 17.1, 8.4 Hz, 2H), 7.33 (d, J = 7.1 Hz, 1H), 7.28 – 7.21 (m, 2H), 5.72 (s, 1H), 3.50 (p, J = 6.8 Hz, 1H), 1.40 (d, J = 6.7 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.8, 157.1, 135.8, 134.3, 129.5, 128.7, 125.4, 124.8, 124.3, 123.2, 122.3, 119.7, 116.0, 115.2, 97.7, 27.7, 22.5; **EI-MS** (m/z) 276 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{18}H_{16}N_2O$, 276.1263; found, 276.1268.

2,3-Dimethyl-1H-benzo[c]pyrazolo[1,2-a]cinnolin-1-one (1v): White solid; mp = 146-148 ^oC; **IR** (υ_{max}): 2921, 2852, 1645, 1610, 1491, 1442, 1384, 1320, 753 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.09 (d, J = 7.3 Hz, 1H), 7.87 – 7.78 (m, 2H), 7.37 (d, J = 8.8 Hz, 2H), 7.28 (d, J = 6.9 Hz, 1H), 7.25 – 7.18 (m, 2H), 2.62 (s, 3H), 2.00 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.0, 140.6, 135.3, 134.5, 129.4, 128.6, 124.7, 124.5, 124.0, 122.2(2), 119.6, 115.4, 115.1, 107.2, 14.46, 6.93; **EI-MS** (m/z) 262 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{17}H_{14}N_2O$, 262.1106; found, 262.1109.

Methyl 3-methyl-1-oxo-1H-benzo[c]pyrazolo[1,2-a]cinnoline-2-carboxylate (1w): White solid; mp = 165-167 ^oC; **IR** (υ_{max}): 2923, 2853, 1684, 1546, 1507, 1438, 1273, 1204, 751 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.15 (d, J = 8.4 Hz, 1H), 7.92 – 7.84 (m, 2H), 7.49 (dt, J = 7.8, 4.1 Hz, 1H), 7.45 – 7.36 (m, 3H), 7.27 (d, J = 2.4 Hz, 1H), 3.94 (s, 3H), 3.01 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 164.4, 159. 7, 150.0, 135.5, 131.8, 130.1, 128.5, 127.2, 125.2, 124.3(2), 122.4, 118.8, 118.1, 115.1, 100.7, 51.6, 15.7; **EI-MS** (m/z) 306 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{18}H_{14}N_2O_3$, 306.1004; found, 306.1011.

1-([1,1'-Biphenyl]-2-yl)-3,4,4-trimethyl-1H-pyrazol-5(4H)-one (7): Colourless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 (s, 4H), 7.36 – 7.25 (m, 5H), 1.95 (s, 3H), 1.07 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.9, 164.5, 140.2, 139.3, 134.5, 130.7, 128.8, 128.7, 128.3, 128.0, 127.8, 127.2, 48.5, 20.5, 13.2; **EI-MS** (m/z) 278 (M^+); **HRMS** (EI): m/z [M^+] calcd for $C_{18}H_{18}N_2O$, 278.1419; found, 278.1421.

Palladacycle (I): ^{1}H NMR (400 MHz, CD_3CN) δ 7.71 (d, *J* = 7.9 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 6.86 (t, *J* = 7.5 Hz, 1H), 5.52 (s, 1H), 2.08 (s, 3H).

8. References

1. K. J. Duffy, C. L. Erickson-Miller, D. F. Eppley, J. Jenkins, J. I. Luengo, N. Liu, A. T. Price, A. N. Shaw, S. Vison-Neau and K. Wiggall, *WO* 089457 A2, 2001.

2. D. Castagnolo, A. de Logu, M. Radi, B. Bechi, F. Manetti, M. Magnani, S. Supino, R. Meleddu, L. Chisu and M. Botta, *Bioorg. Med. Chem.* 2008, **16**, 8587.

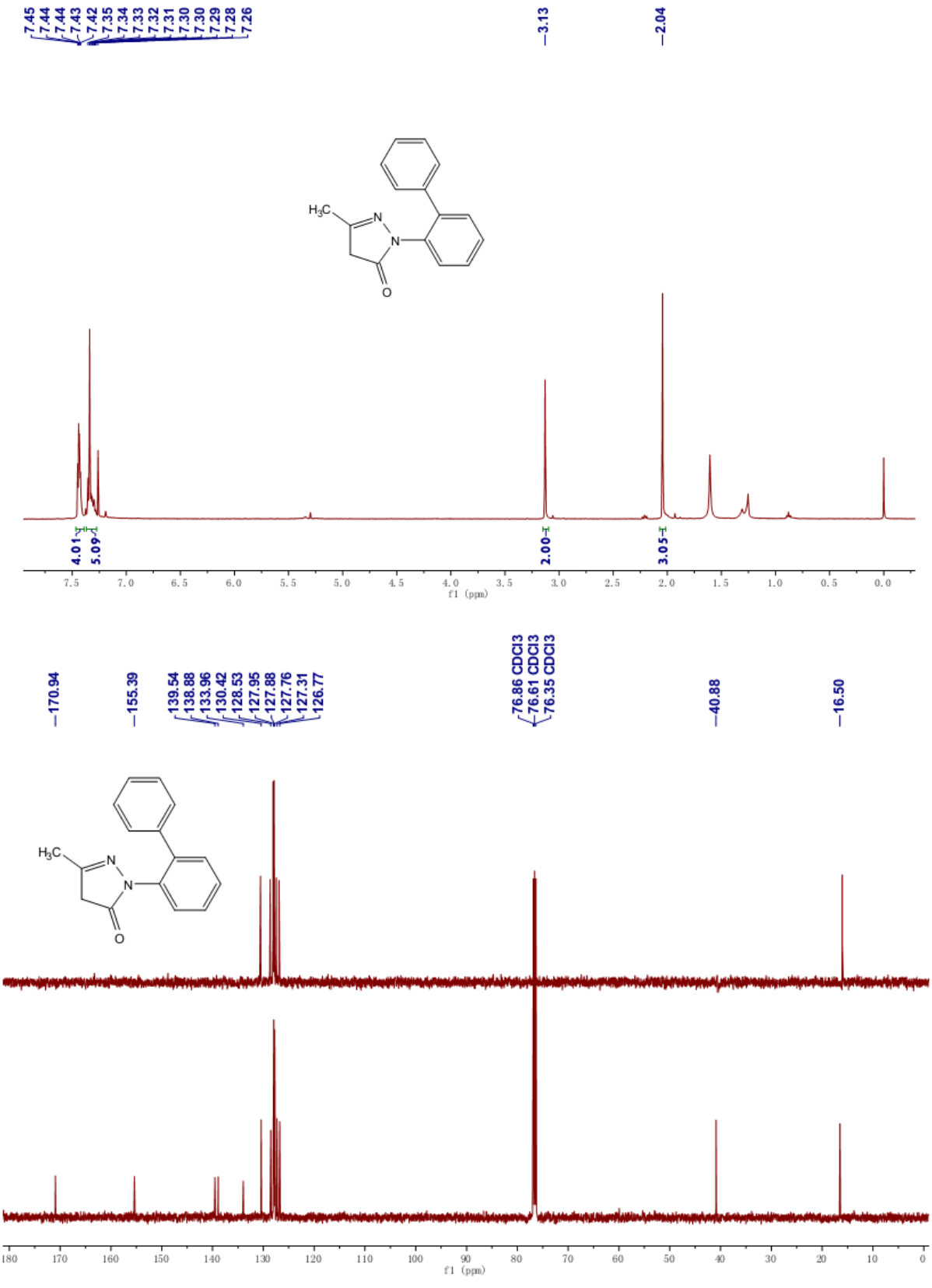
3. K. Watanabe, Y. Morinaka, K. Iseki, T. Watanabe, S. Yuki and H. Nishi, *Redox Rep.* 2003, **8**, 151.

4. W. F. Beech and M. Mendoza, *GB* 560892, 1944.

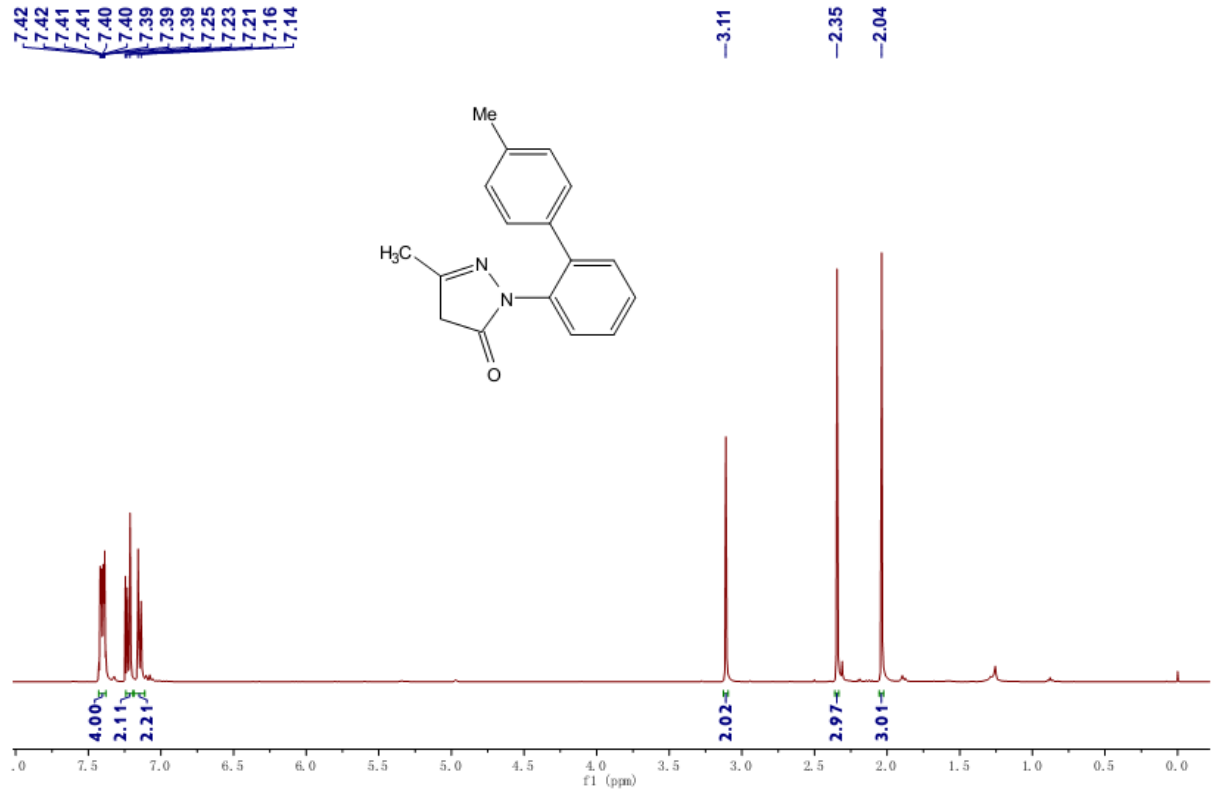
5. (a) E. Andre, A. Georges and A. Serge, *Comptes Rendus des Seances de l'Academie des Sciences, Serie C: Sciences Chimiques* 1967, **264**, 1855; (b) E. Andre and I. Georges, *Bulletin de la Societe Chimique de France* 1964, **11**, 2897; (c) E. Andre and P. Rene, *Bulletin de la Societe Chimique de France* 1962, 292.

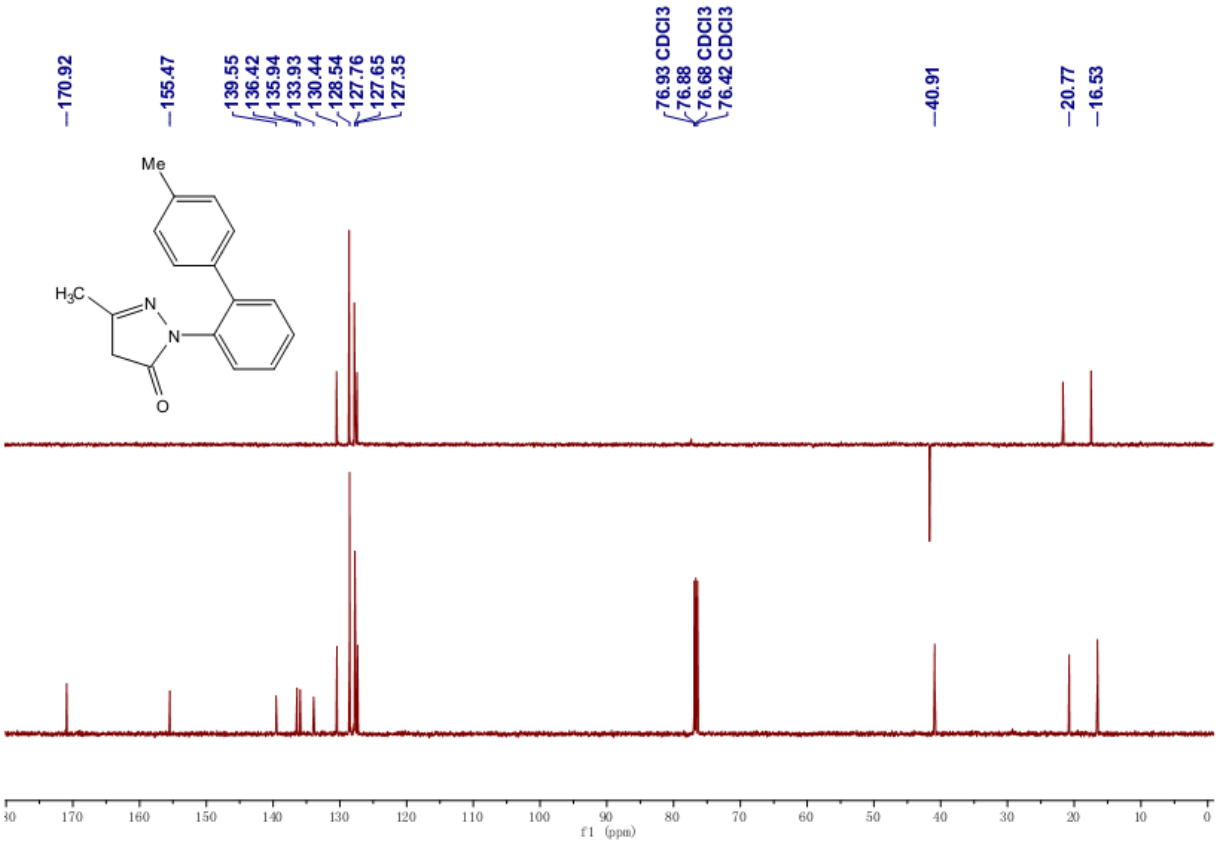
9. Copies of NMR Data for All New Compounds.

^{1}H and ^{13}C NMR spectra of compound **4aa.**

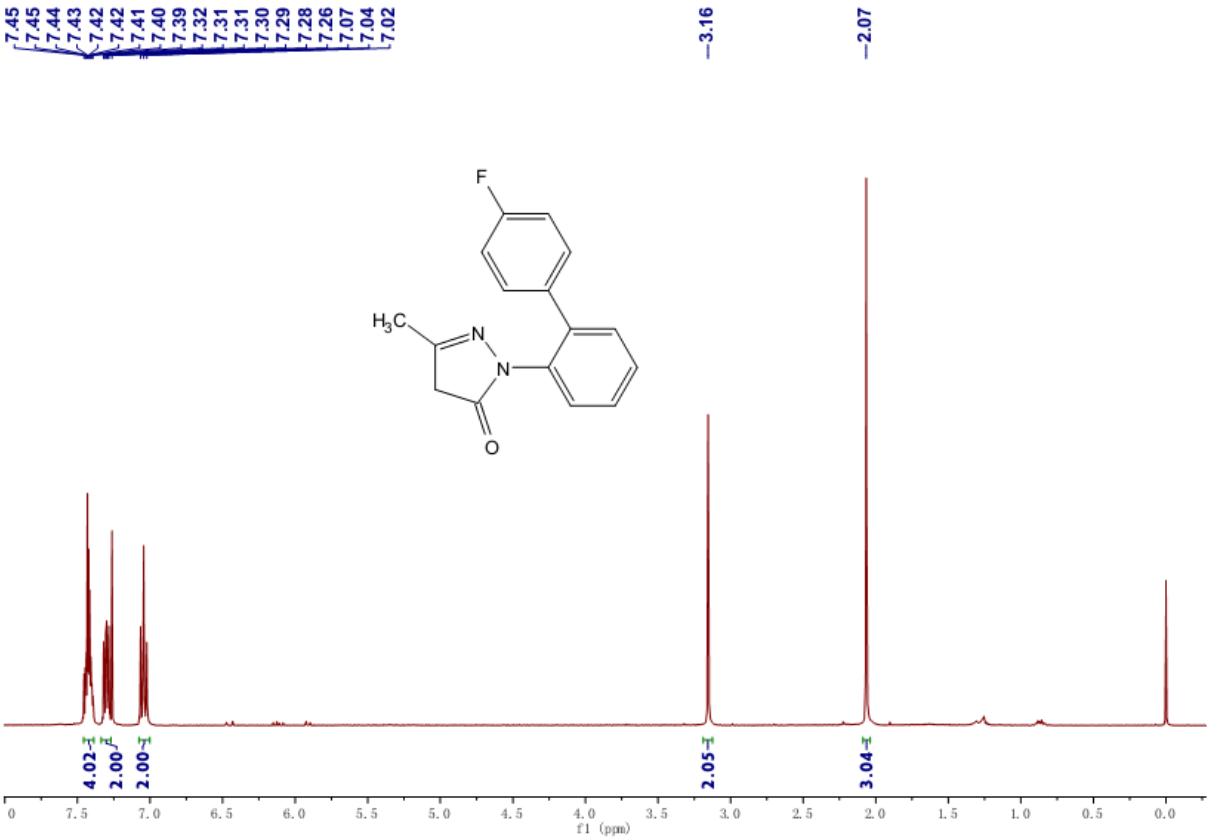


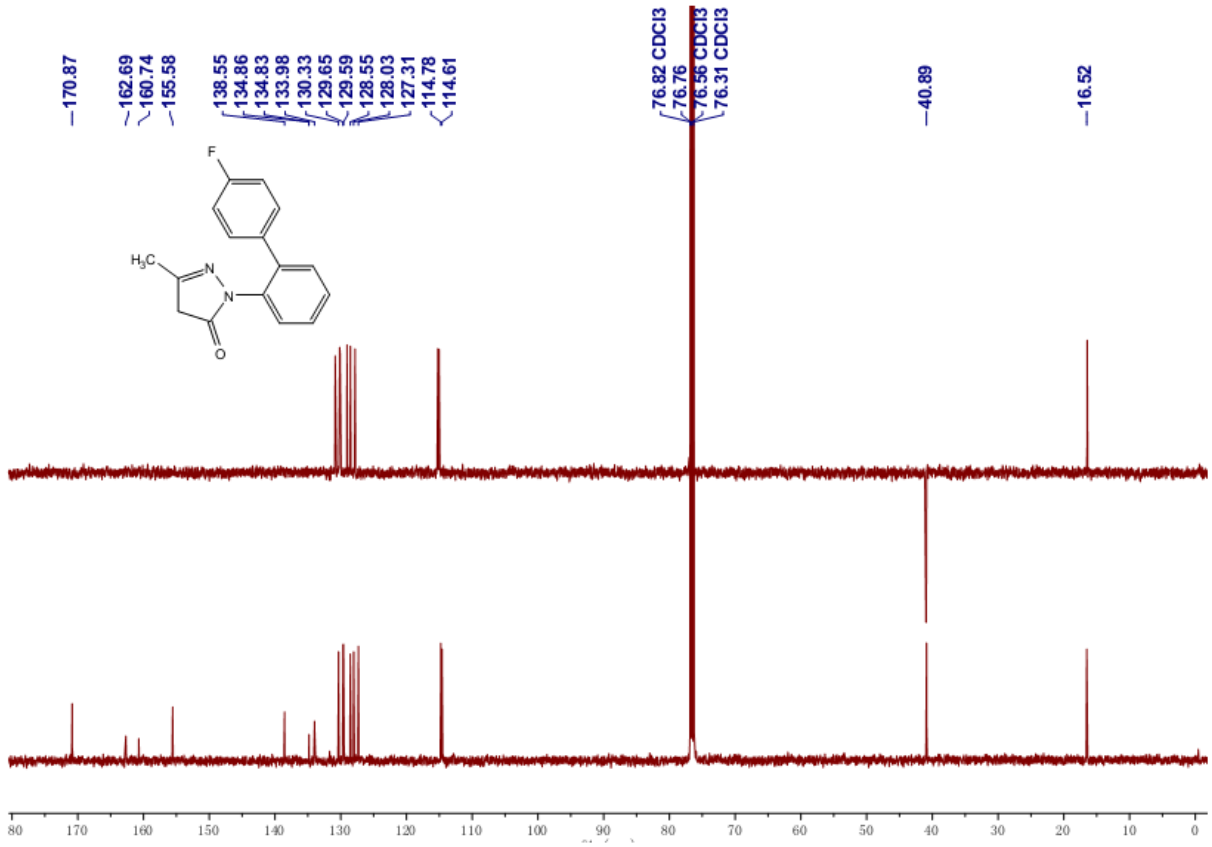
^{1}H and ^{13}C NMR spectra of compound **4ab**.



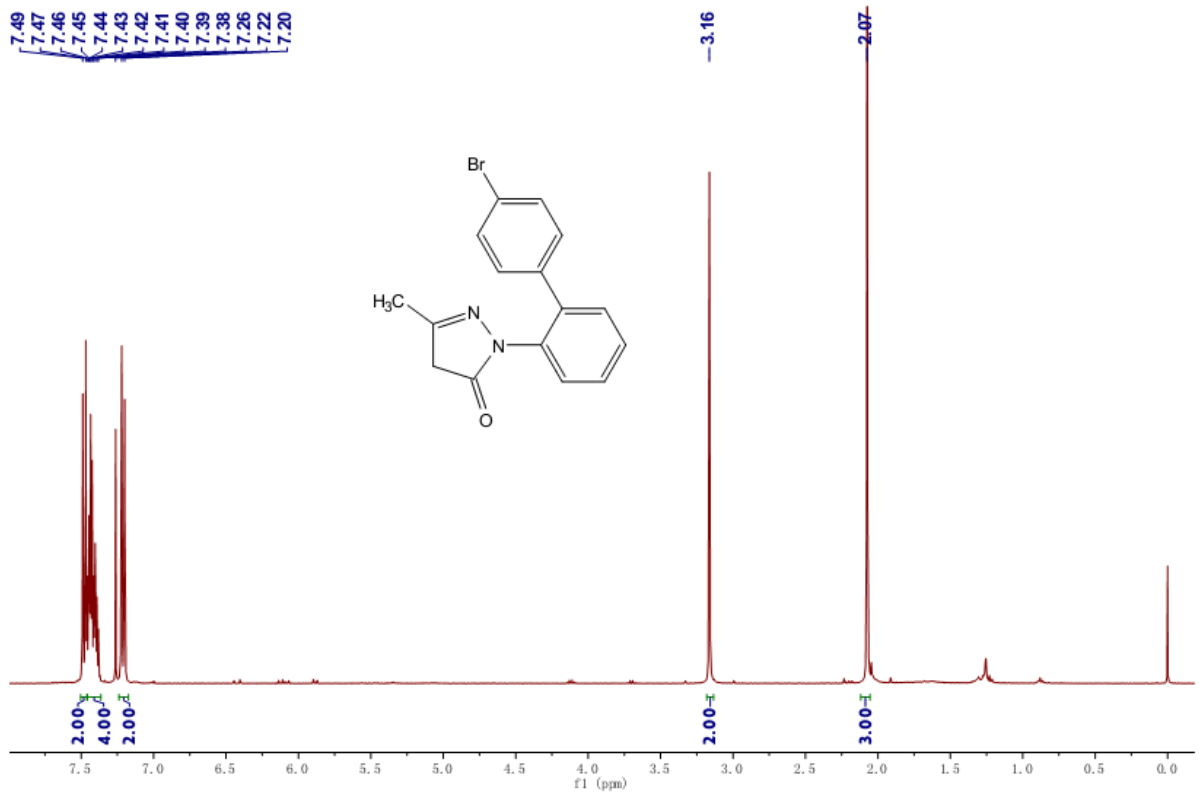


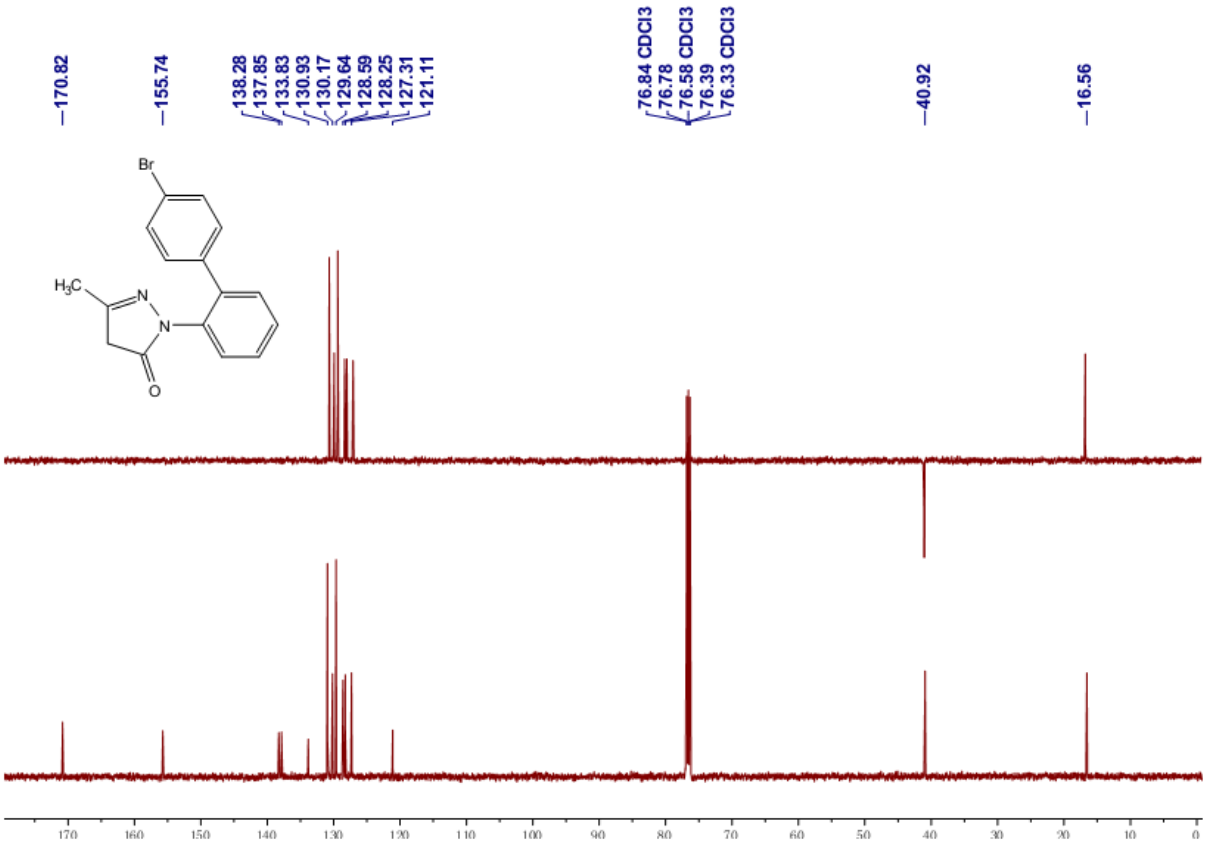
^{1}H and ^{13}C NMR spectra of compound **4ac.**



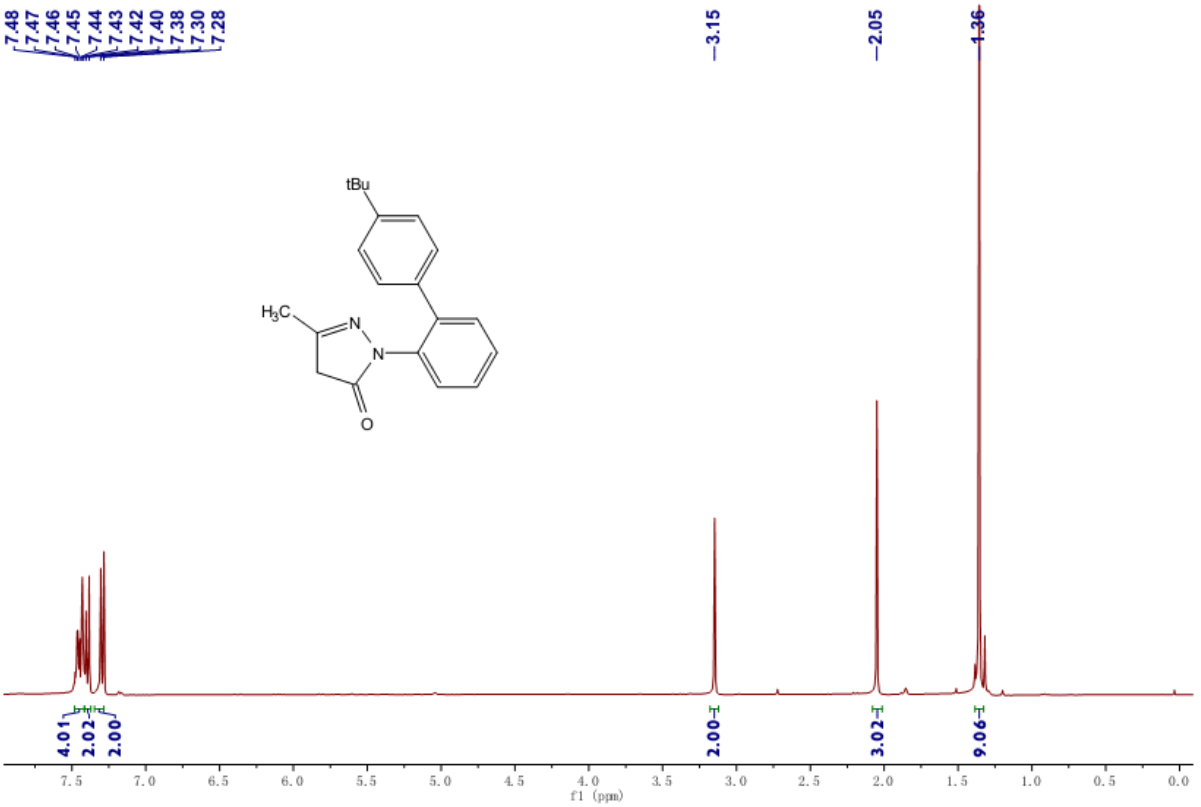


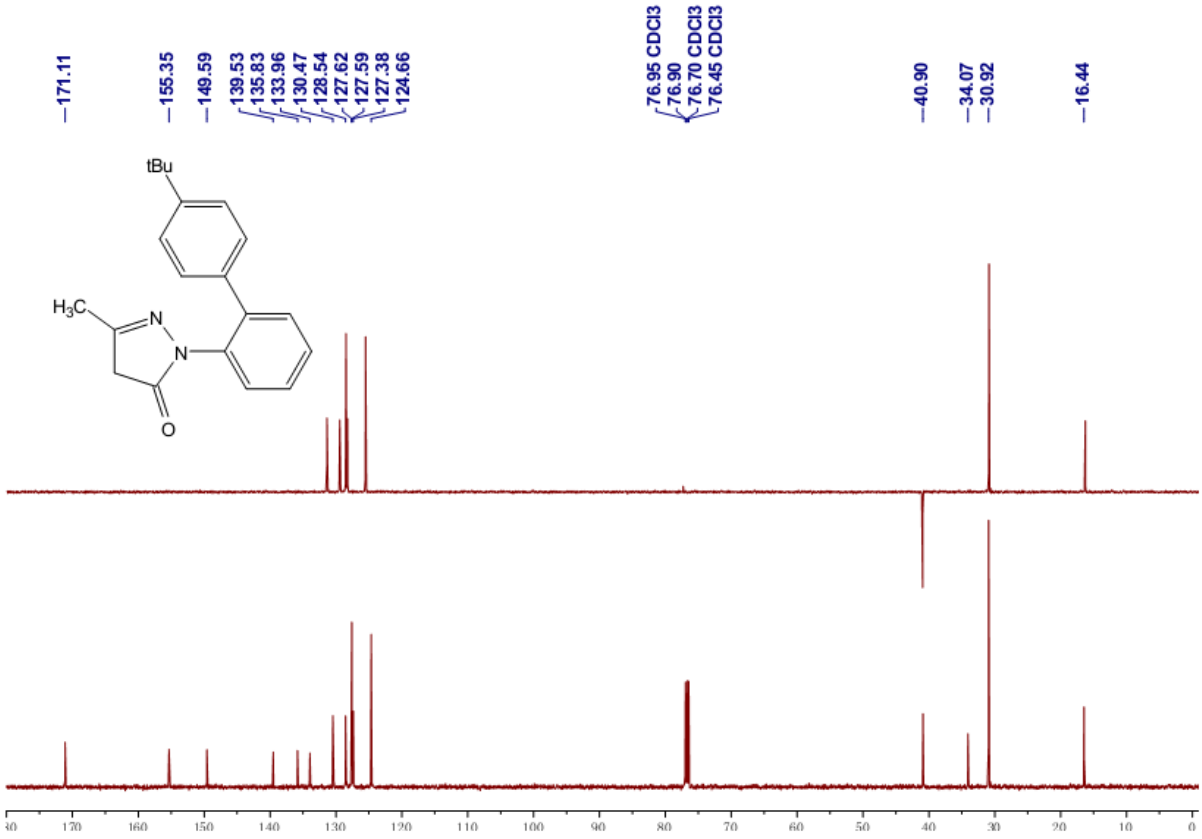
^{1}H and ^{13}C NMR spectra of compound **4ad.**



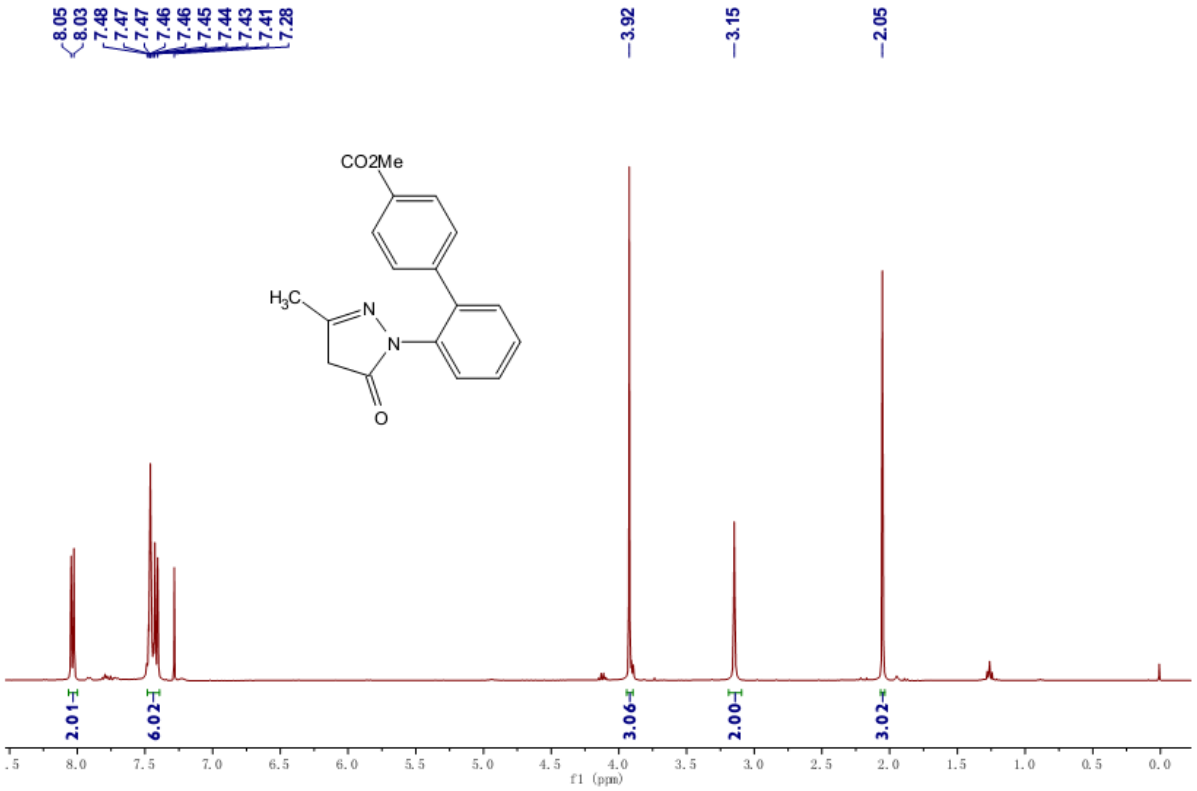


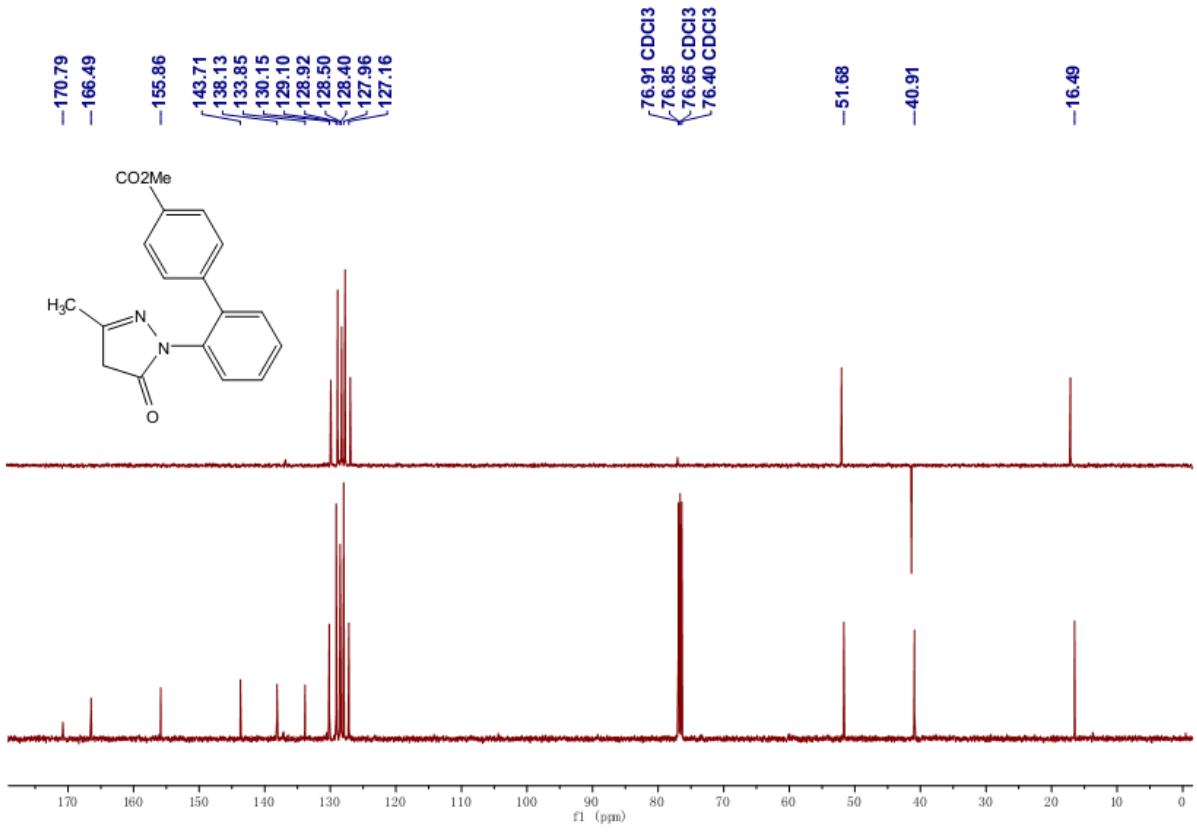
^{1}H and ^{13}C NMR spectra of compound **4ae.**



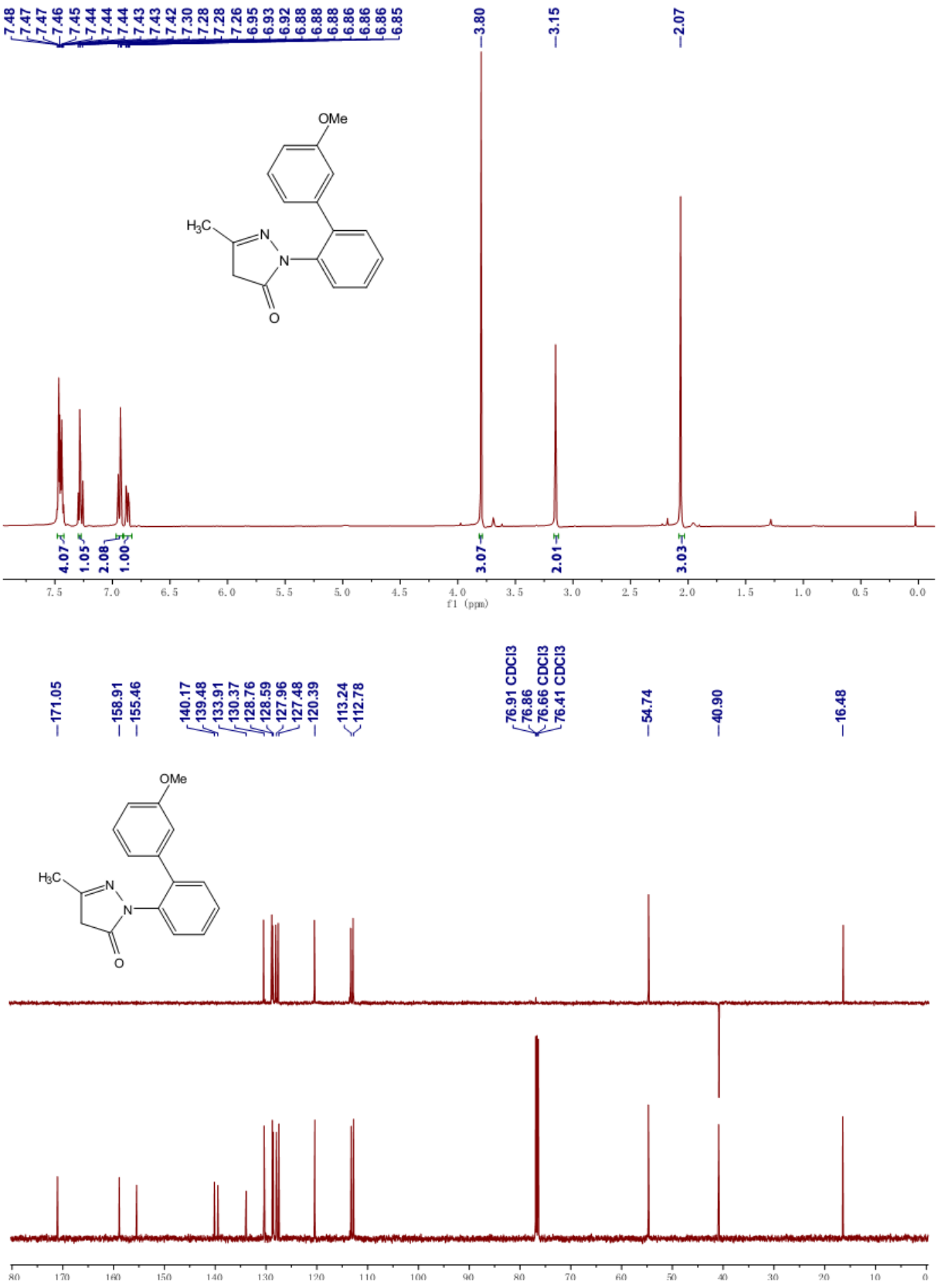


^{1}H and ^{13}C NMR spectra of compound **4af.**

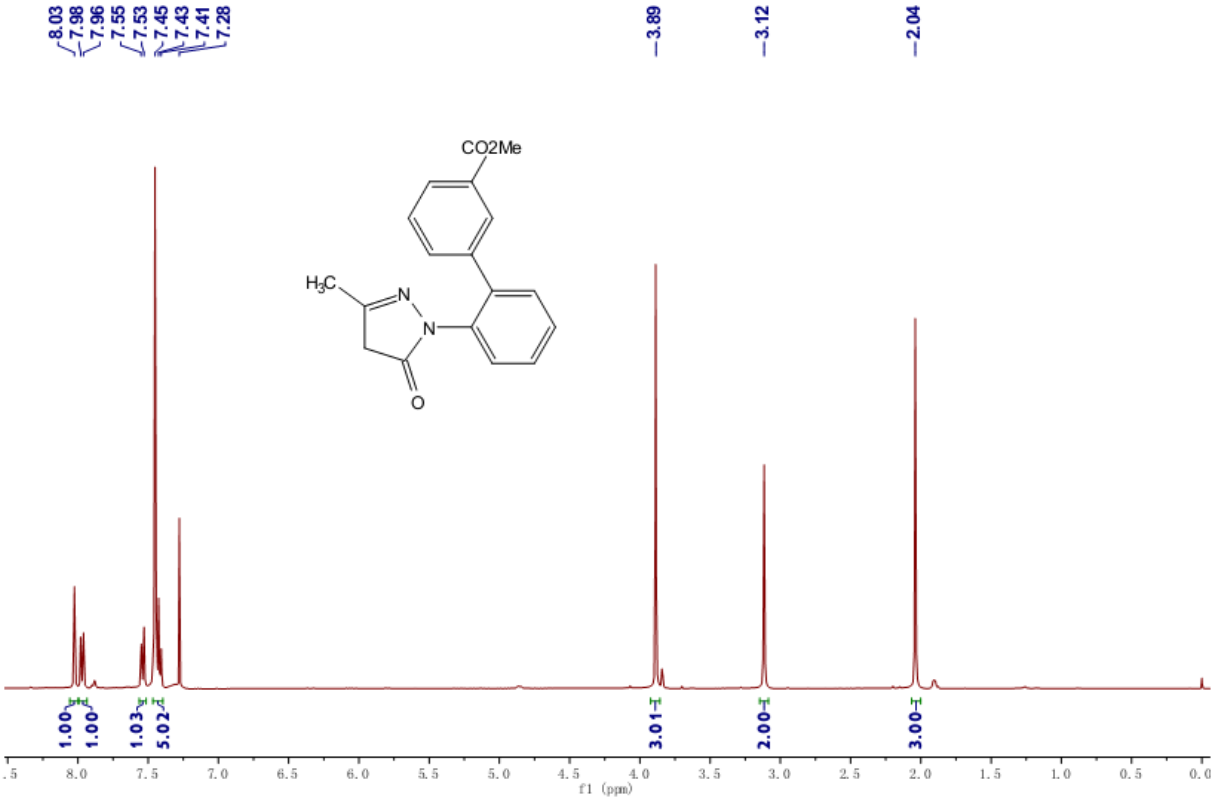


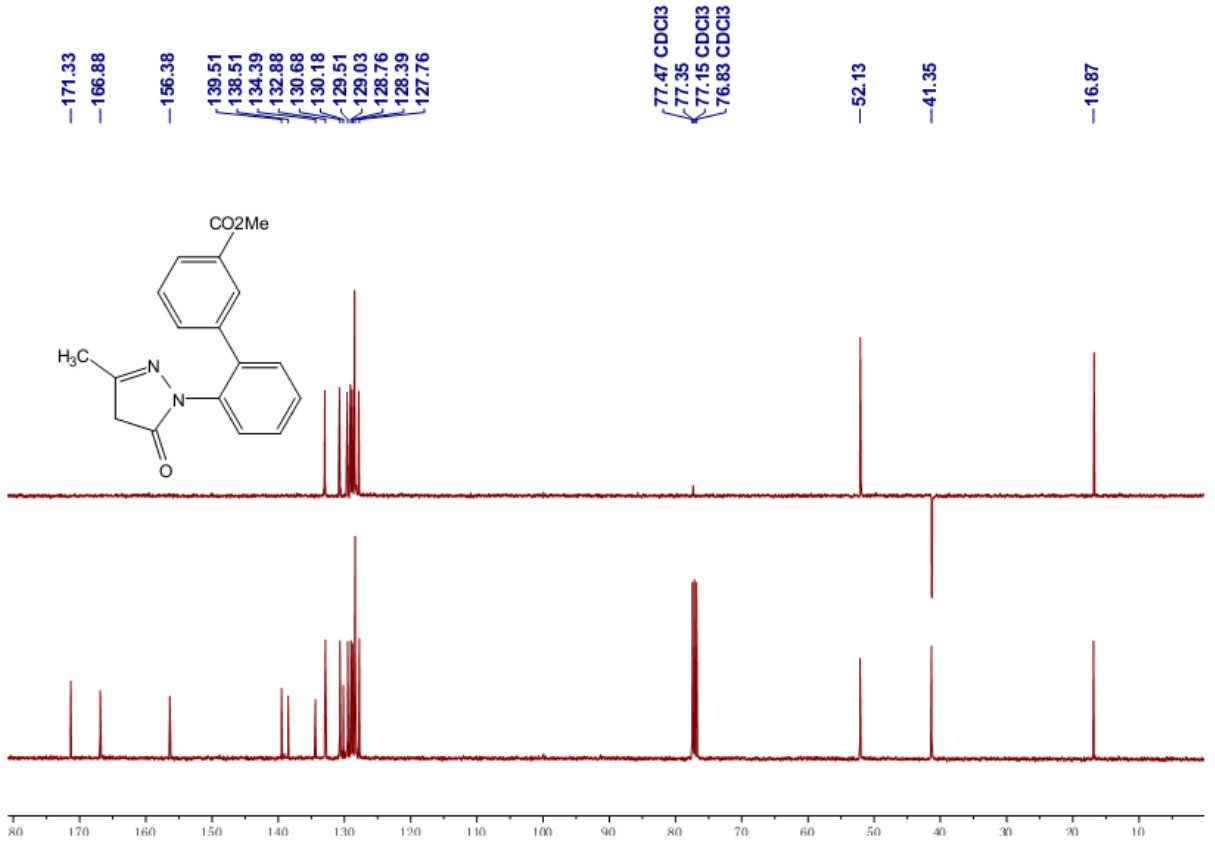


^{1}H and ^{13}C NMR spectra of compound **4ag.**

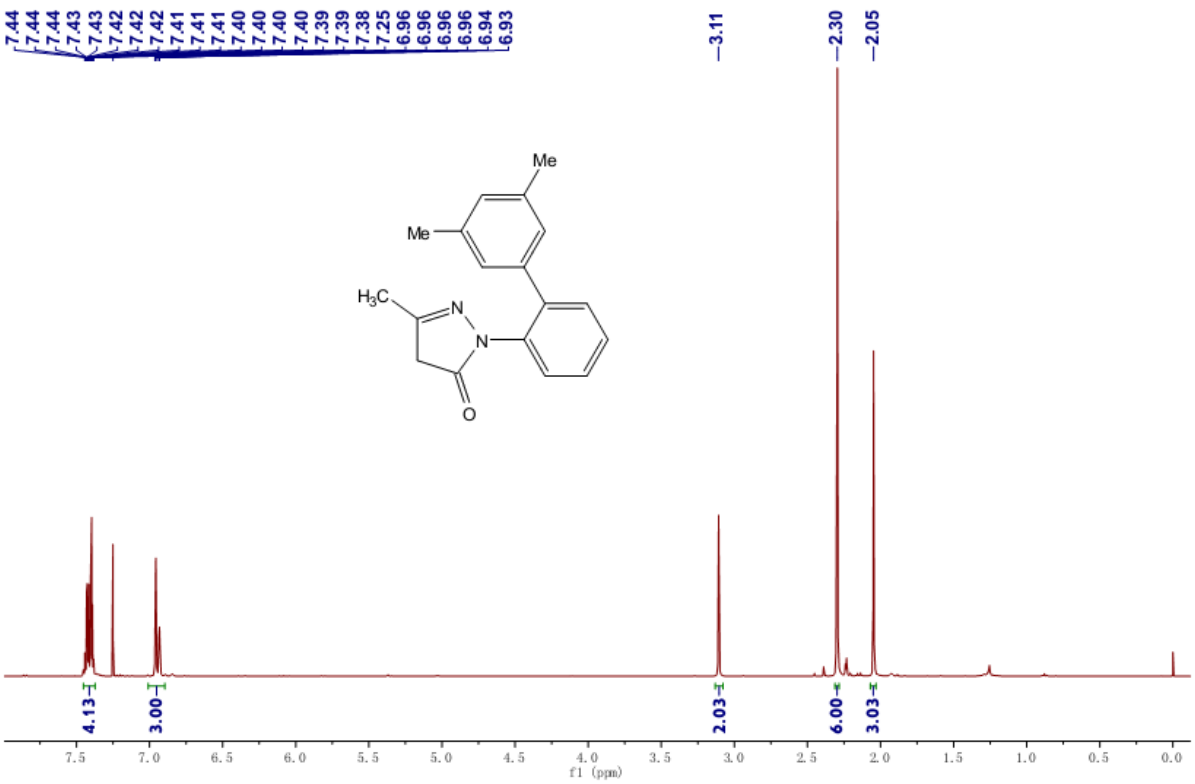


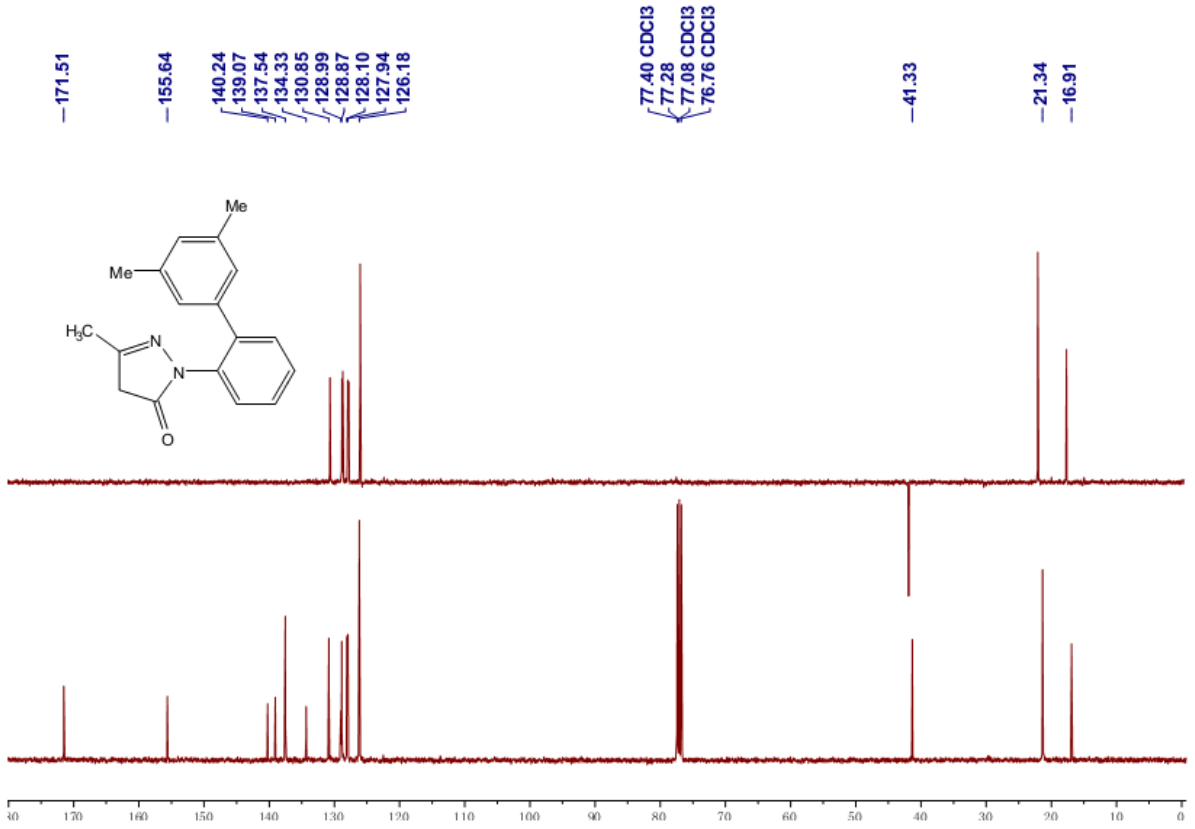
^{1}H and ^{13}C NMR spectra of compound **4ah.**



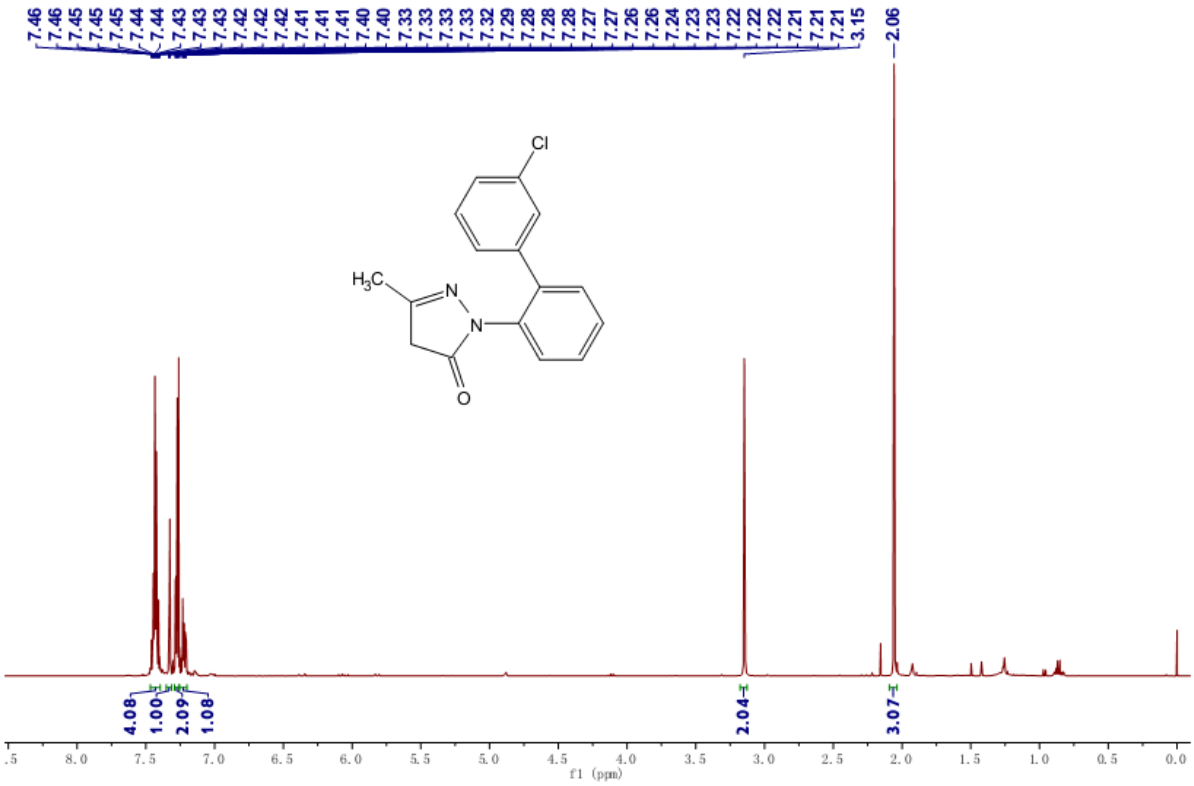


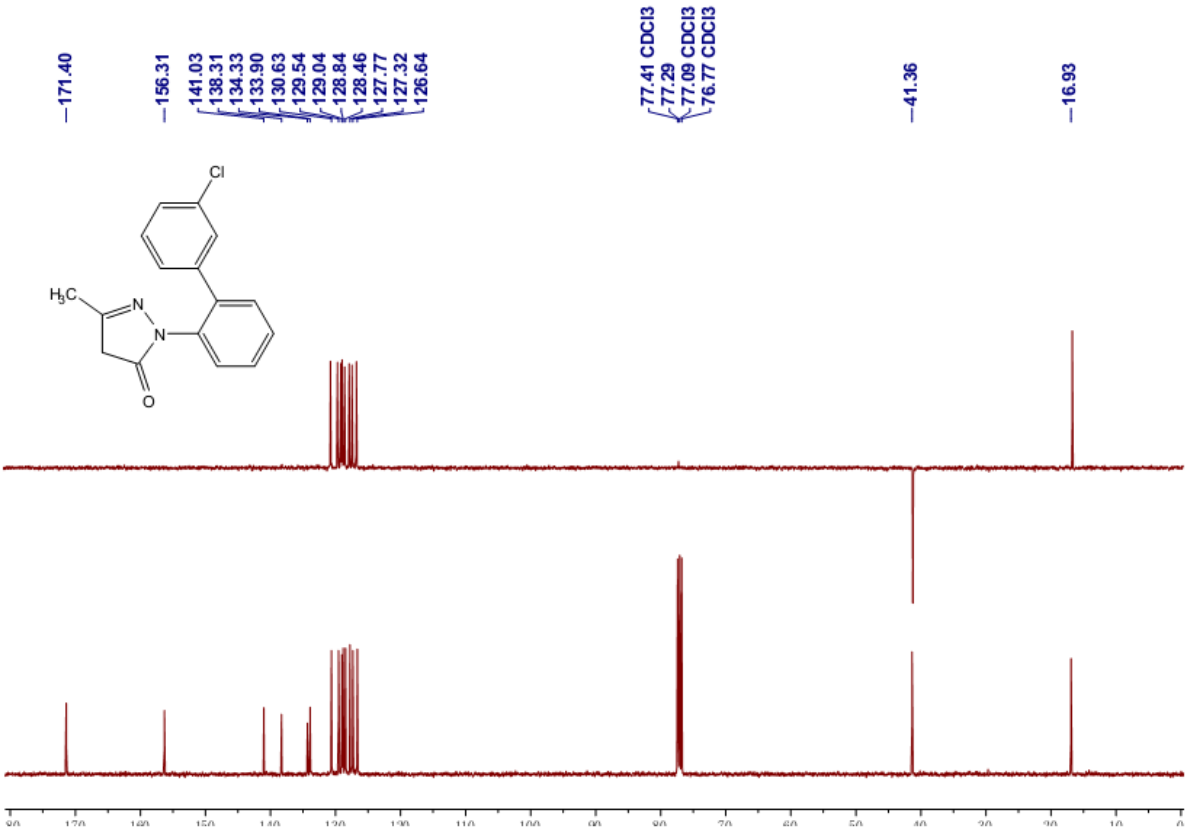
^{1}H and ^{13}C NMR spectra of compound **4ai.**



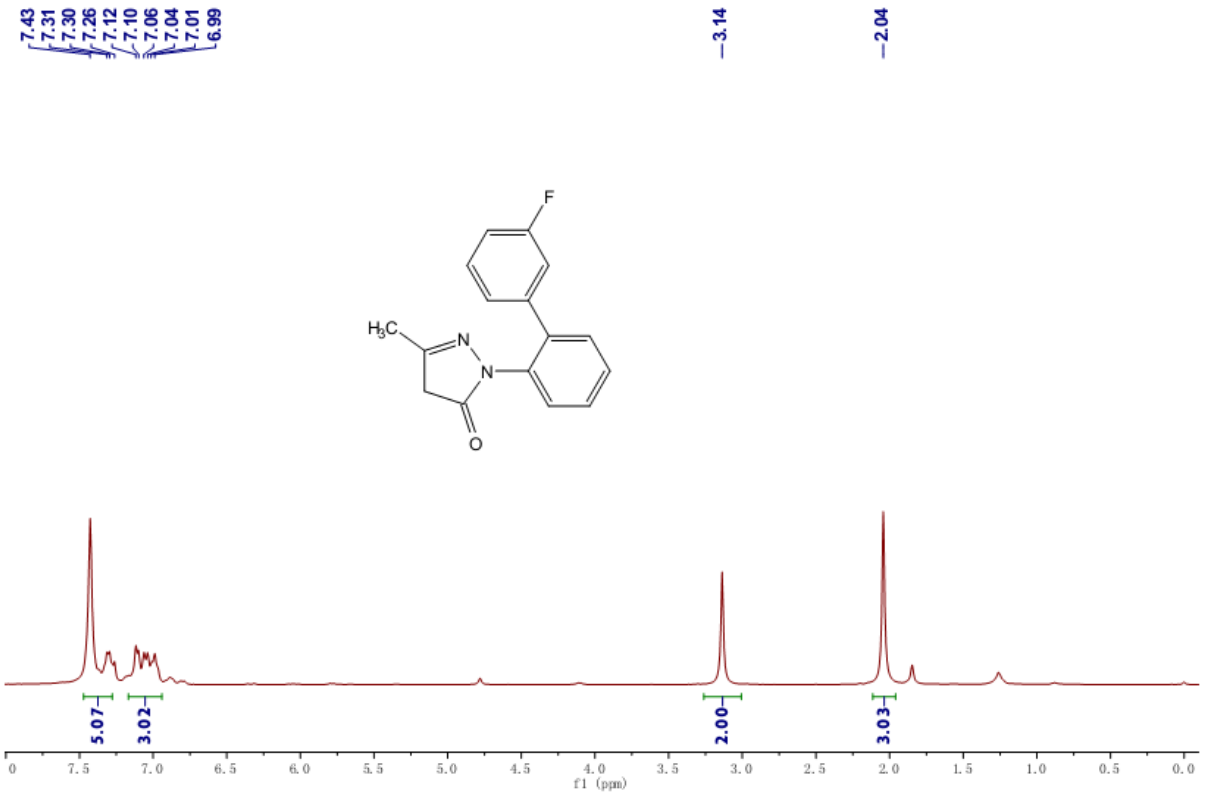


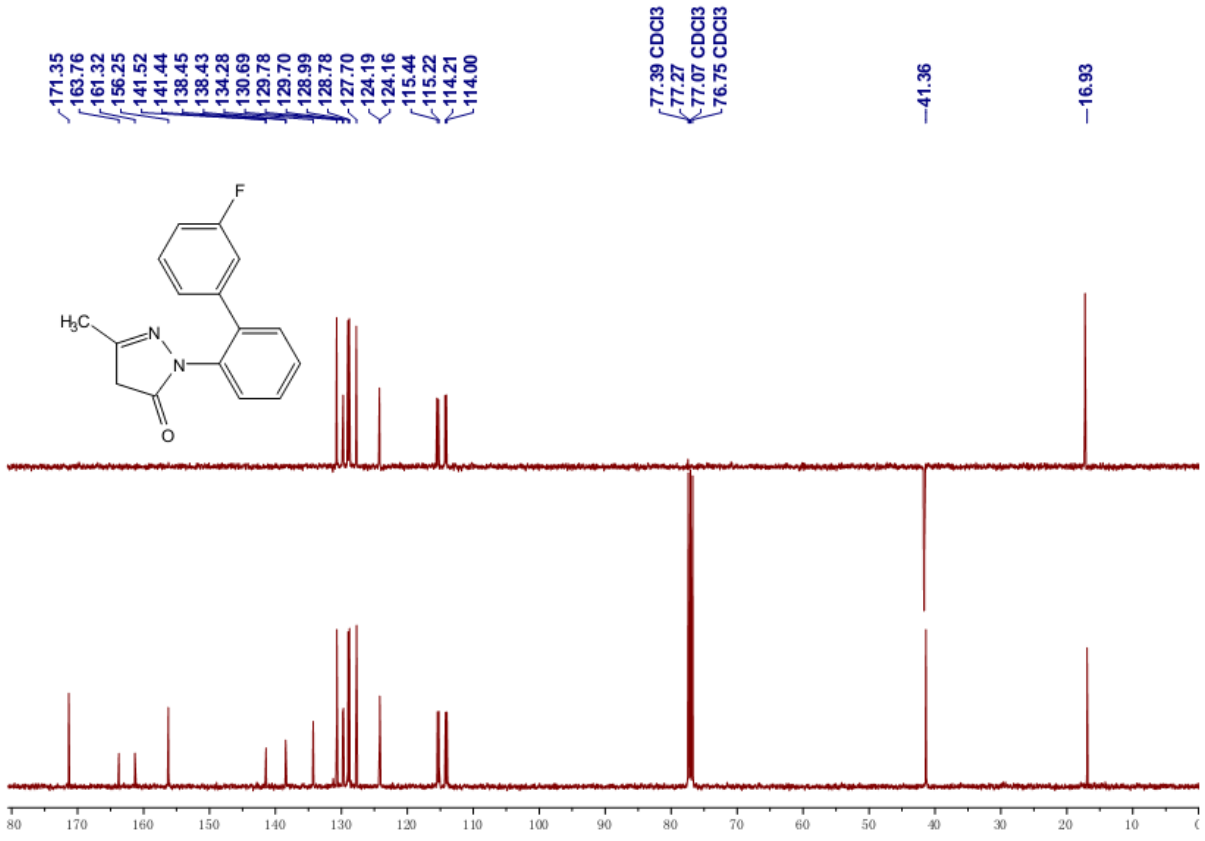
^{1}H and ^{13}C NMR spectra of compound **4aj.**



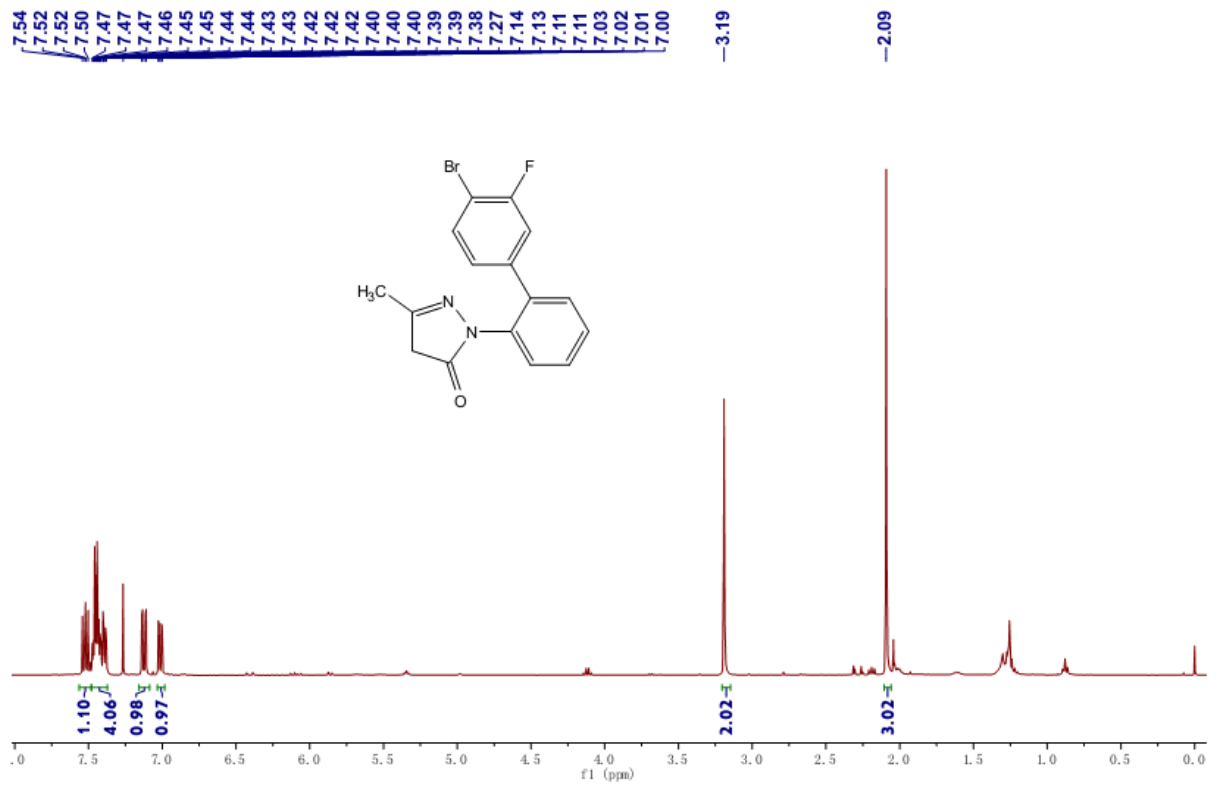


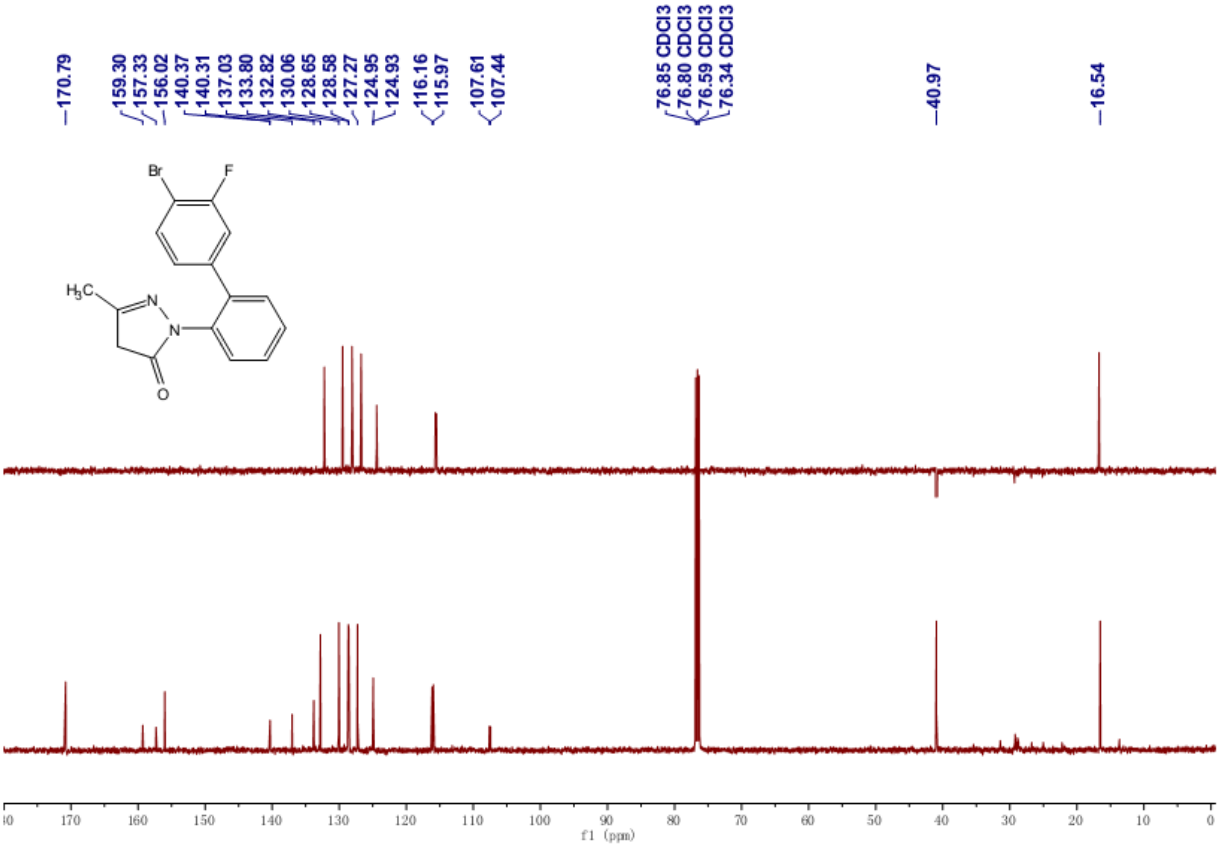
^{1}H and ^{13}C NMR spectra of compound **4ak.**



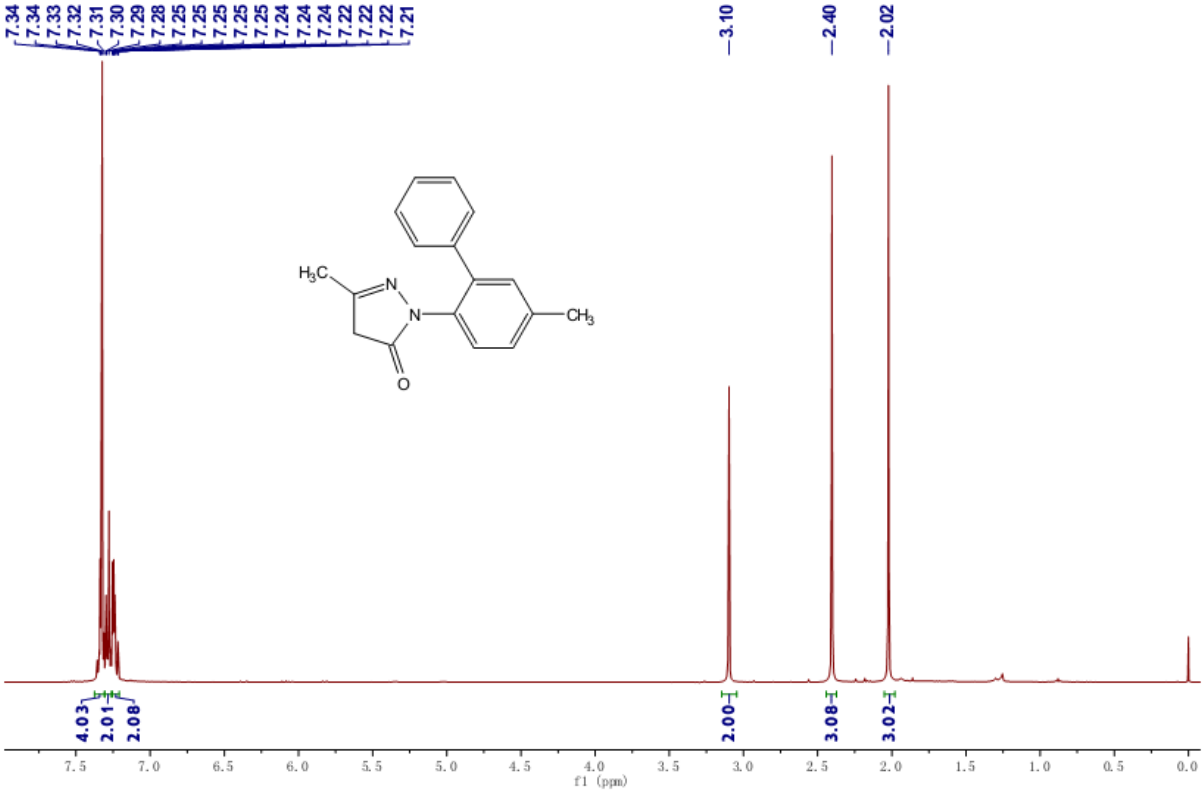


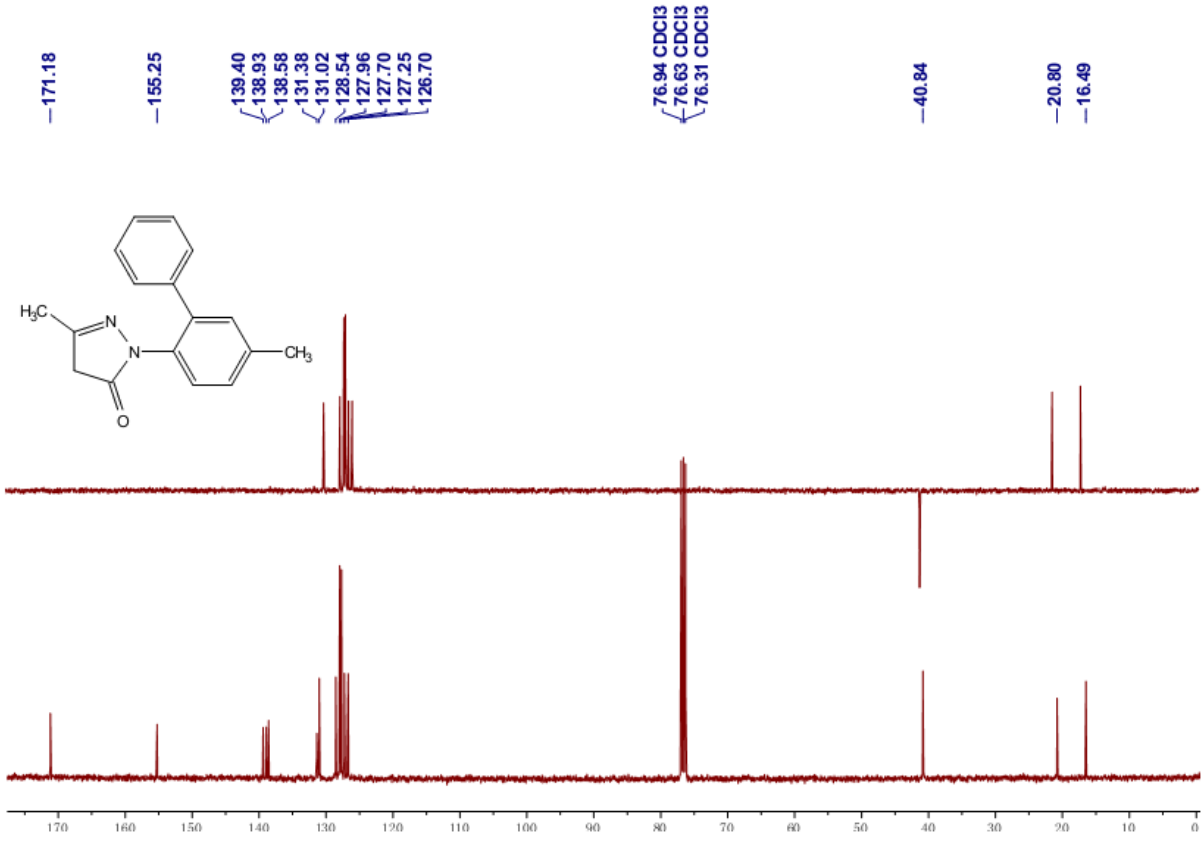
^{1}H and ^{13}C NMR spectra of compound **4al.**



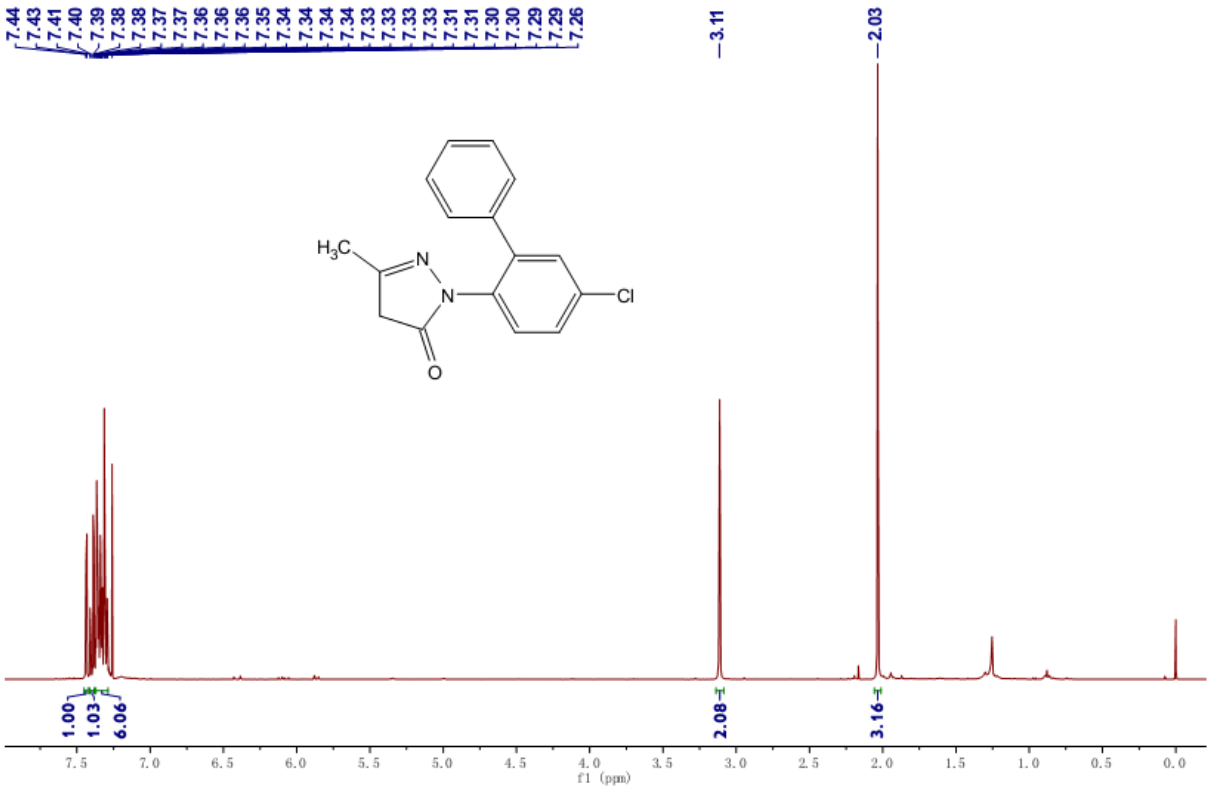


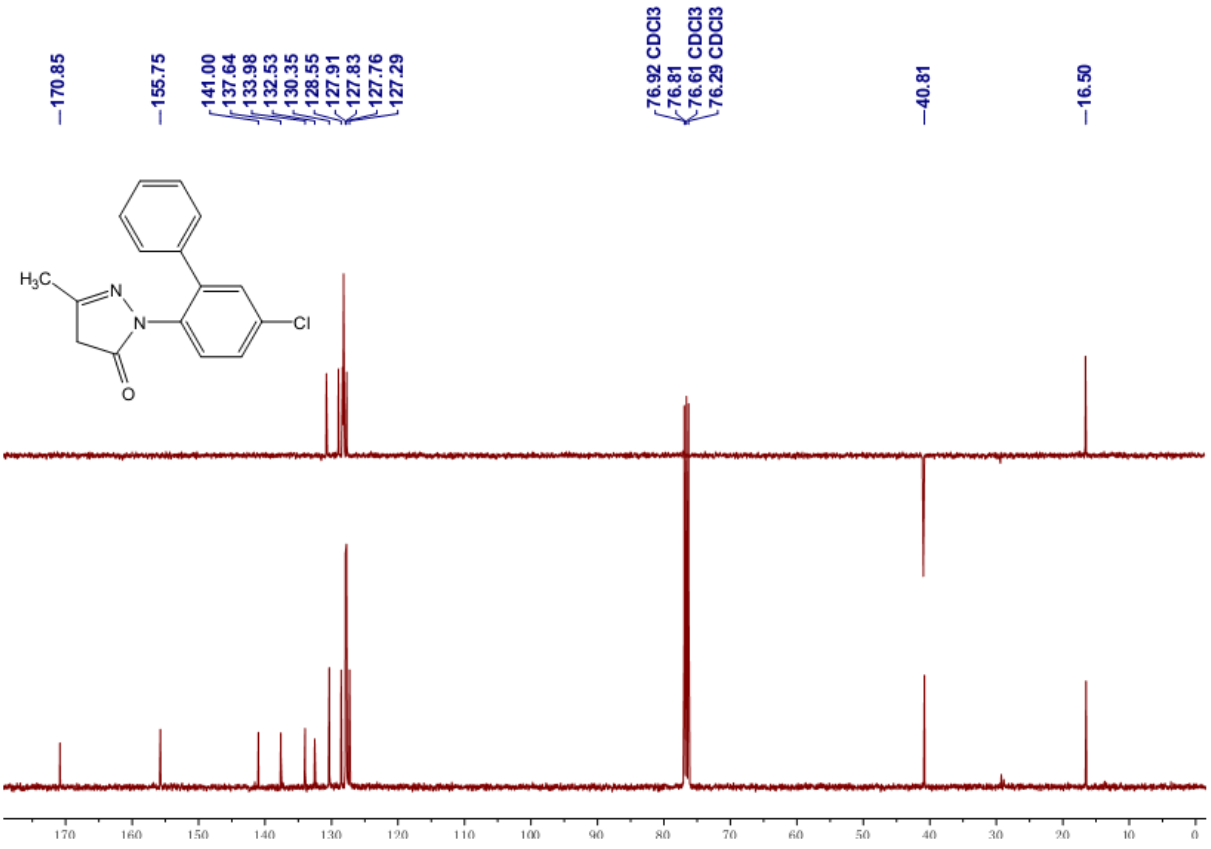
^{1}H and ^{13}C NMR spectra of compound **4ba.**



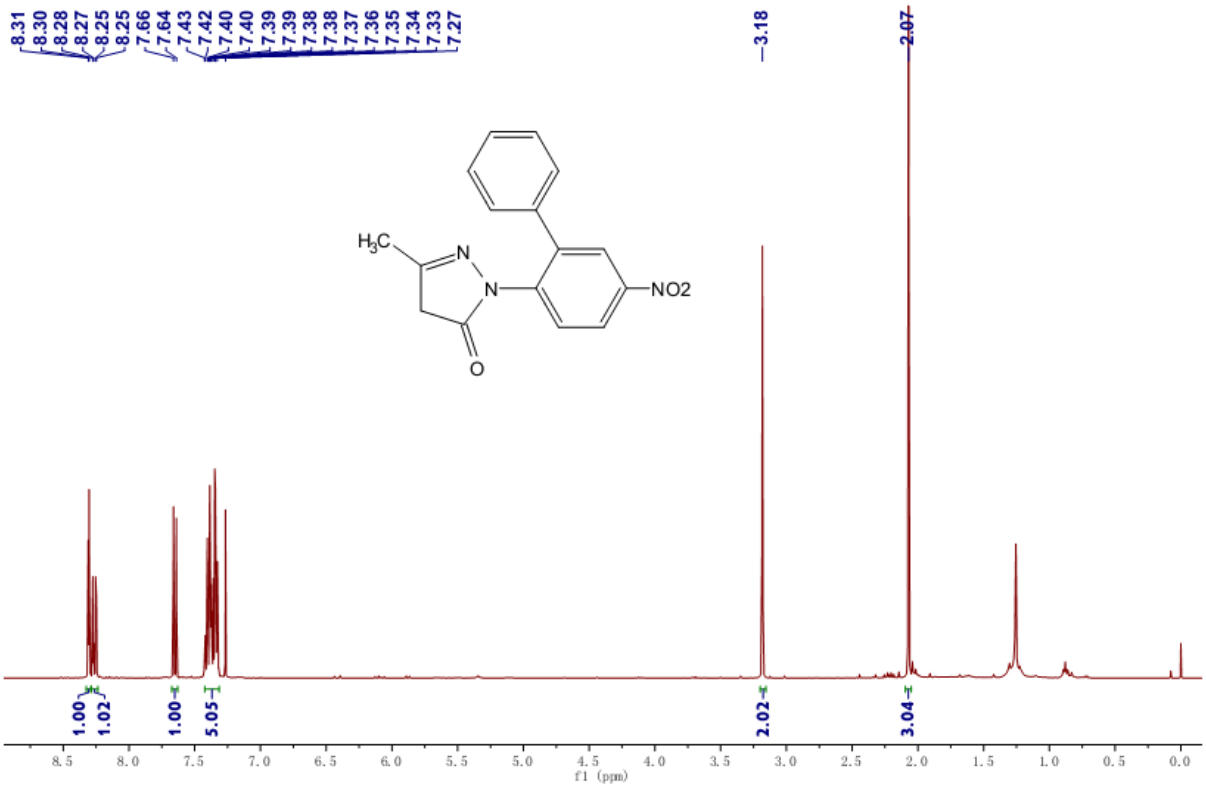


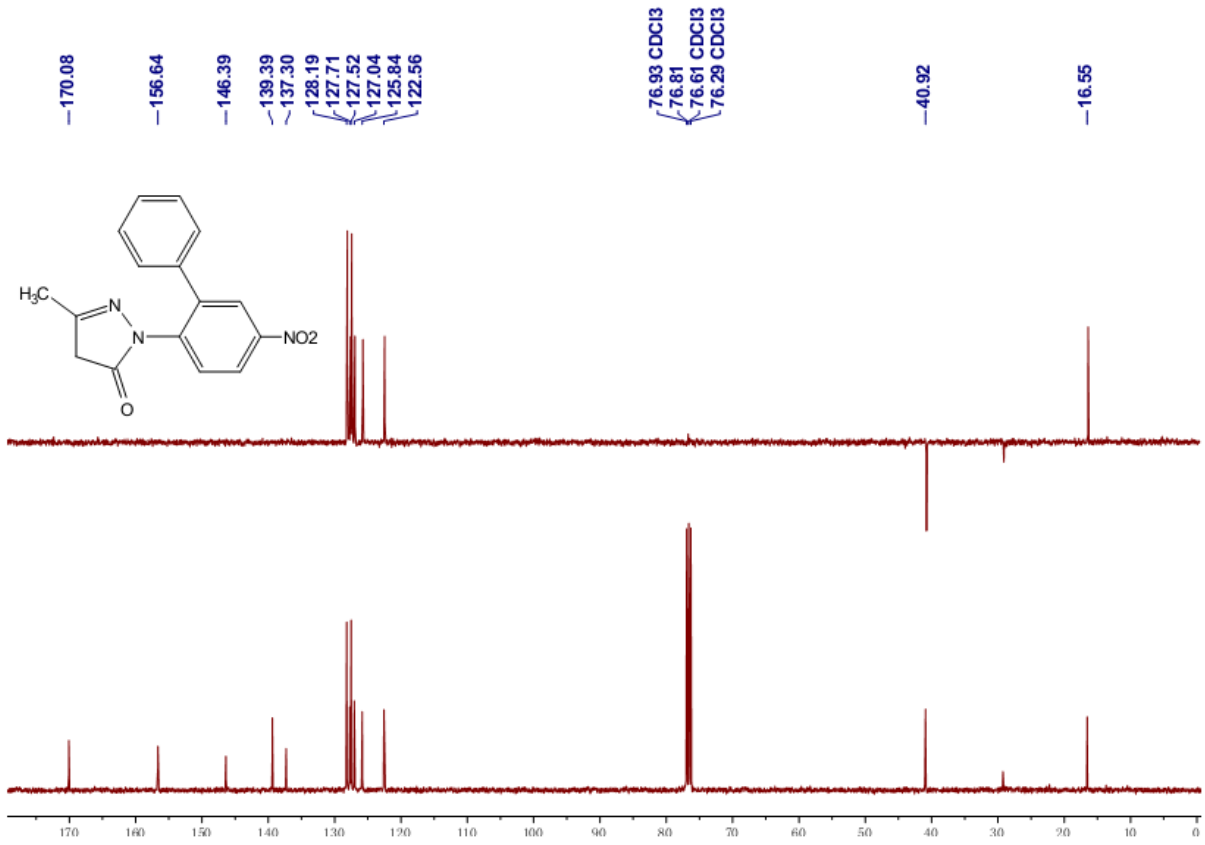
^{1}H and ^{13}C NMR spectra of compound **4ca.**



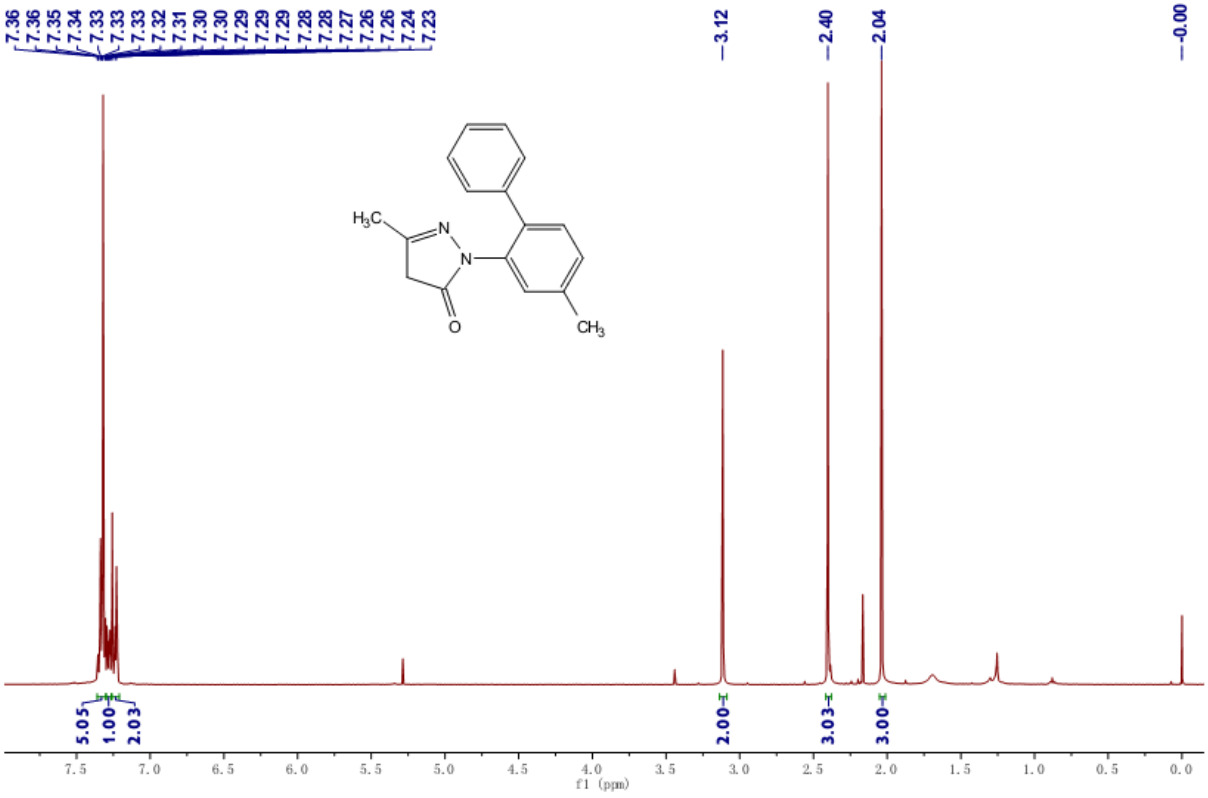


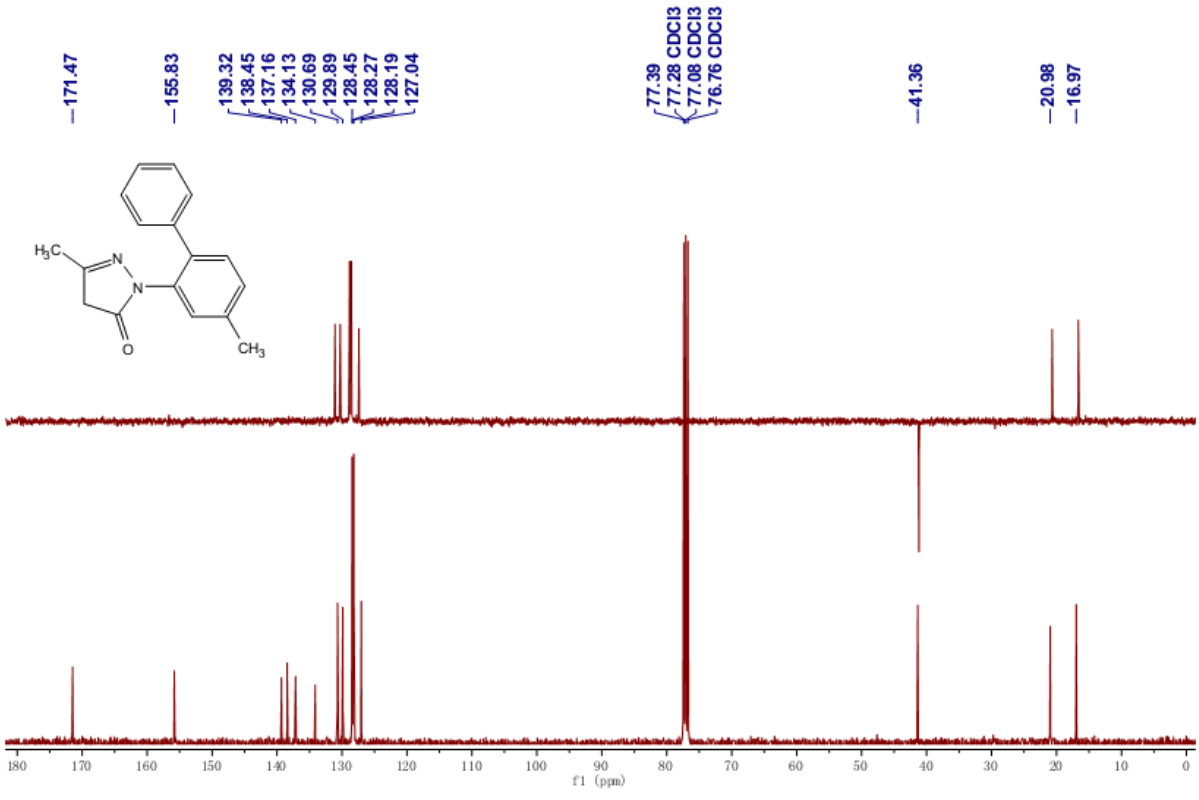
^{1}H and ^{13}C NMR spectra of compound **4da.**



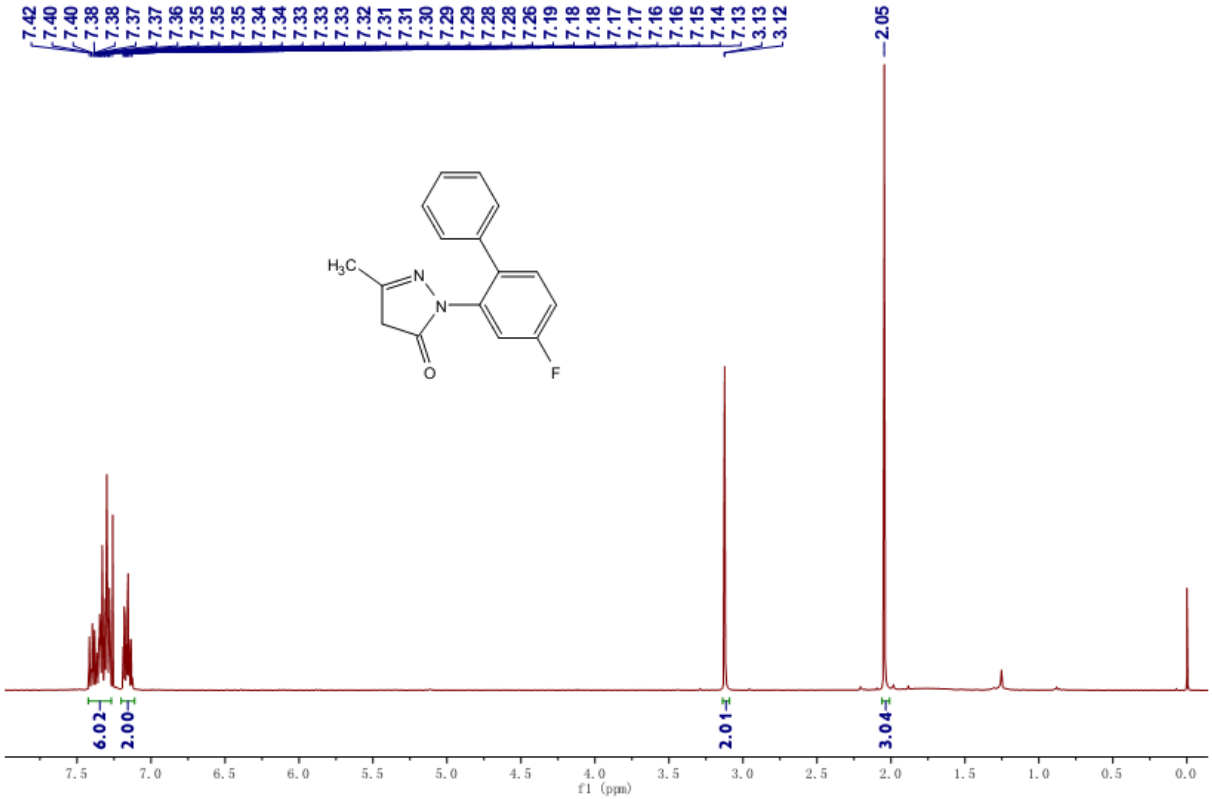


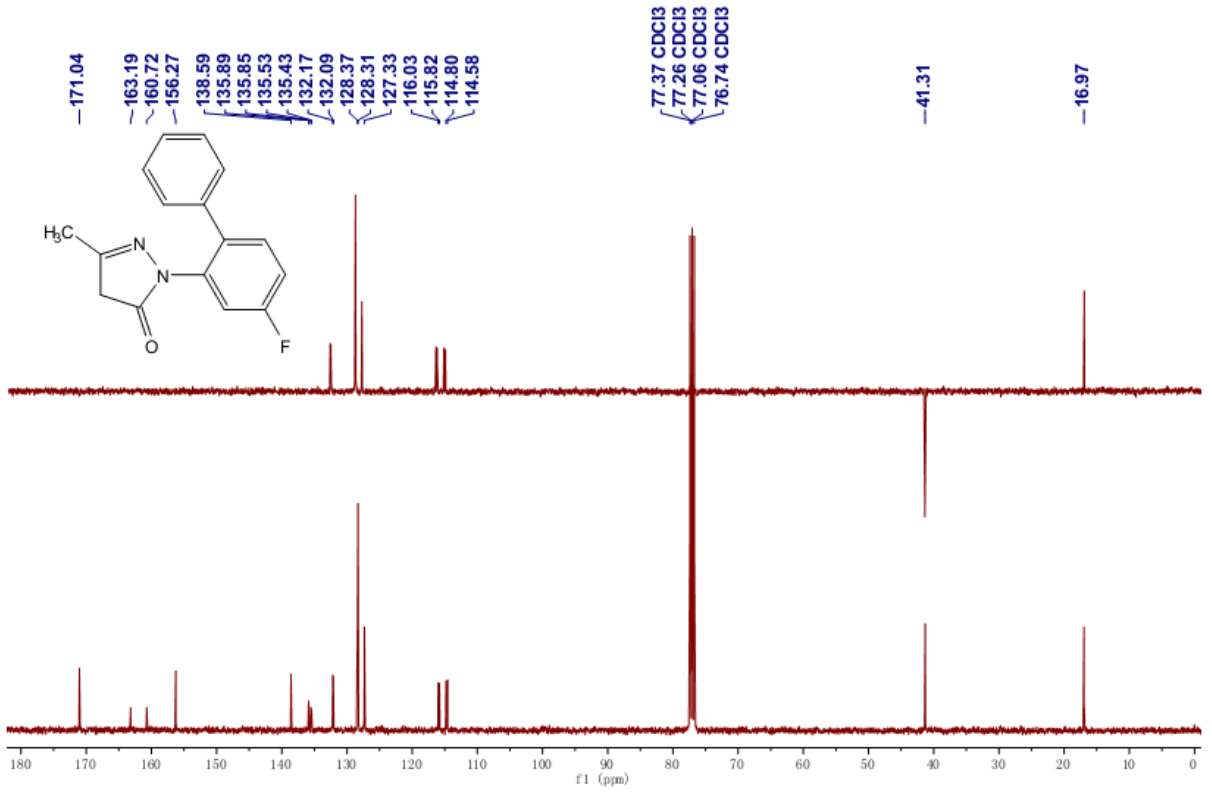
^{1}H and ^{13}C NMR spectra of compound **4ea.**



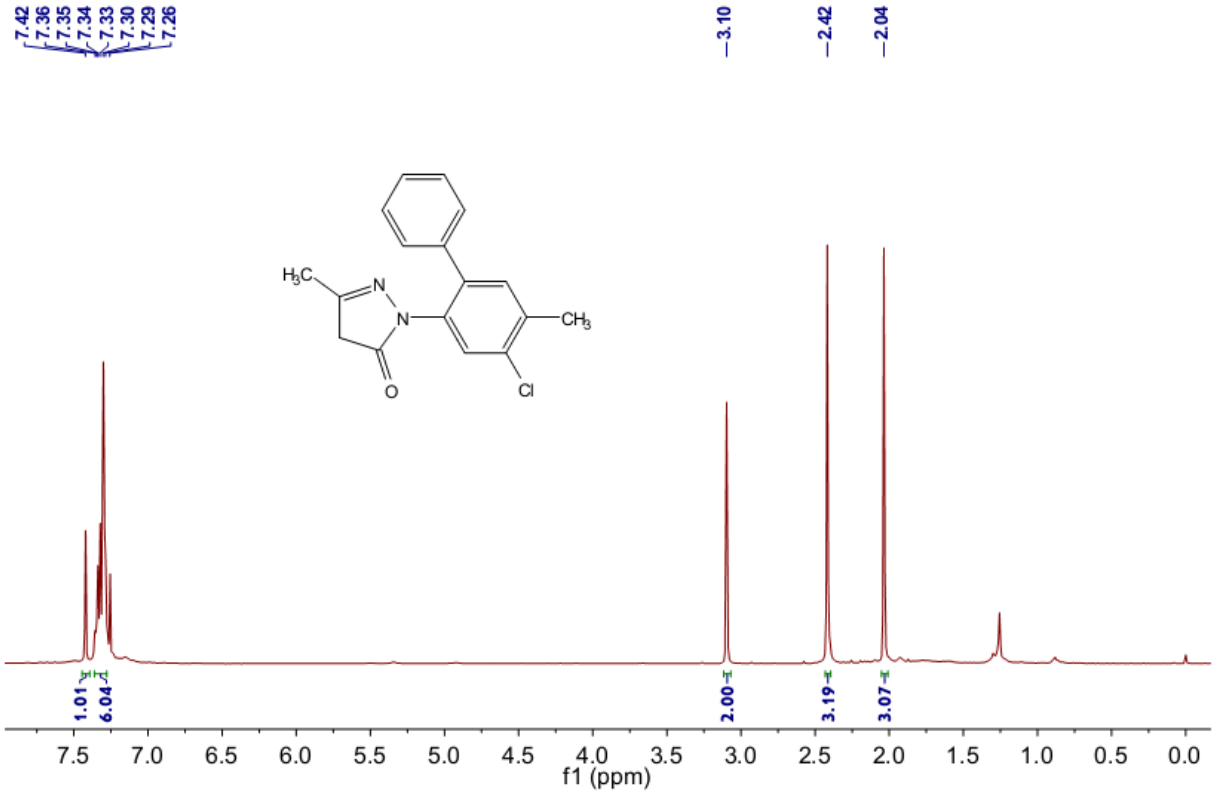


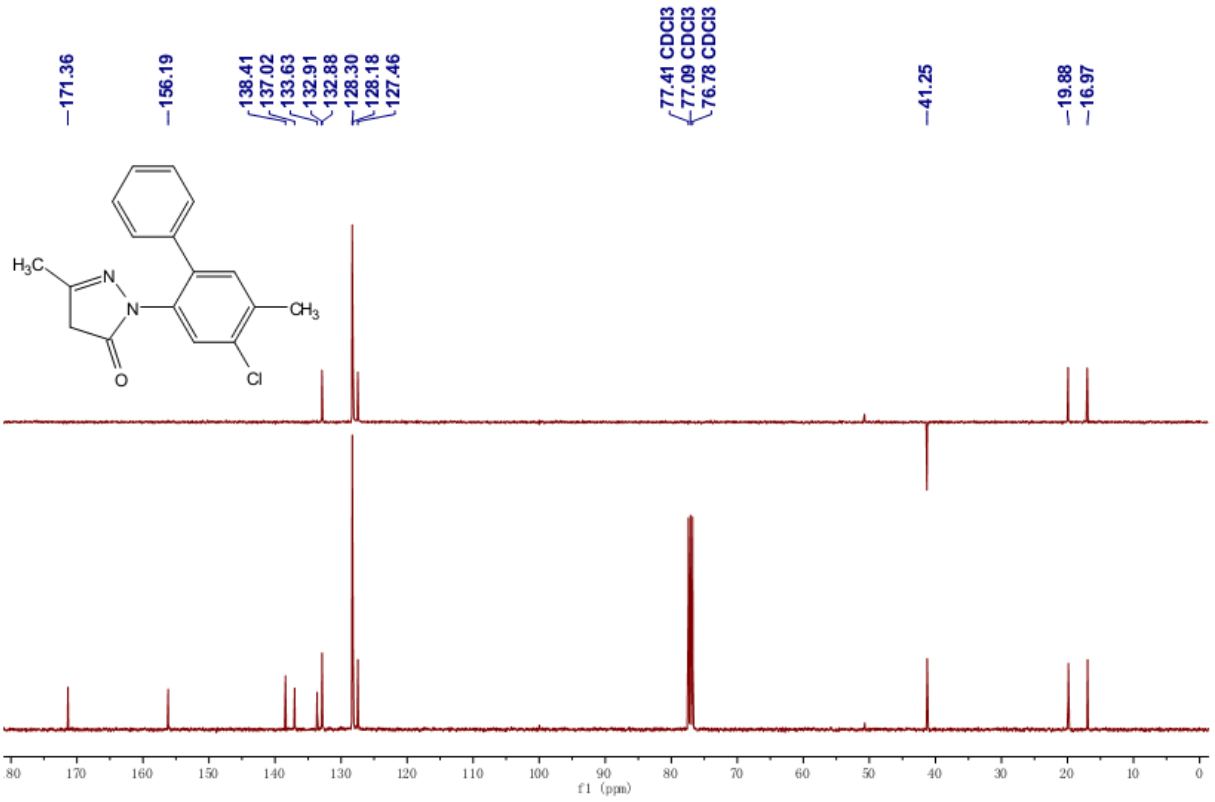
^{1}H and ^{13}C NMR spectra of compound **4fa.**



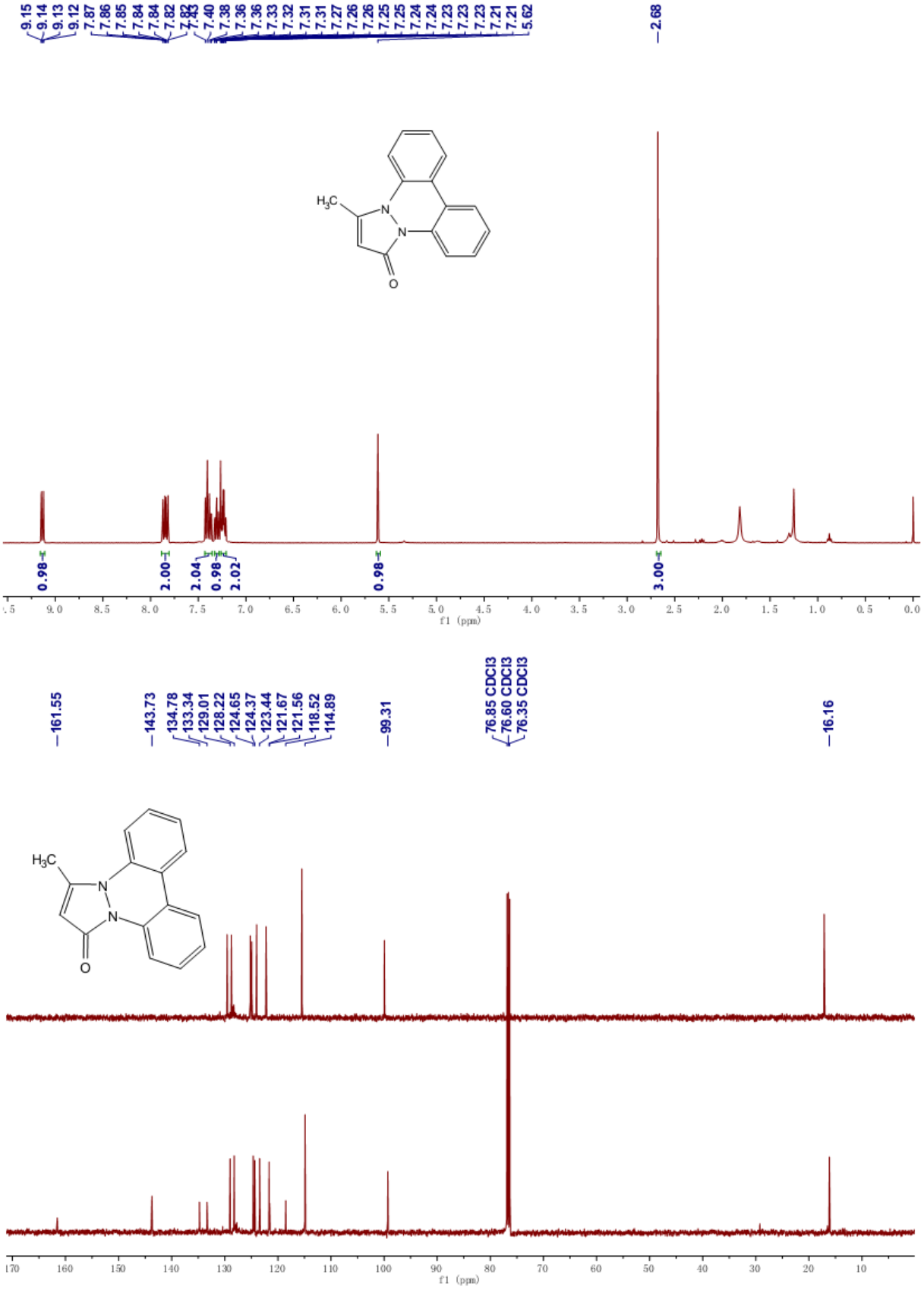


^{1}H and ^{13}C NMR spectra of compound **4ga.**

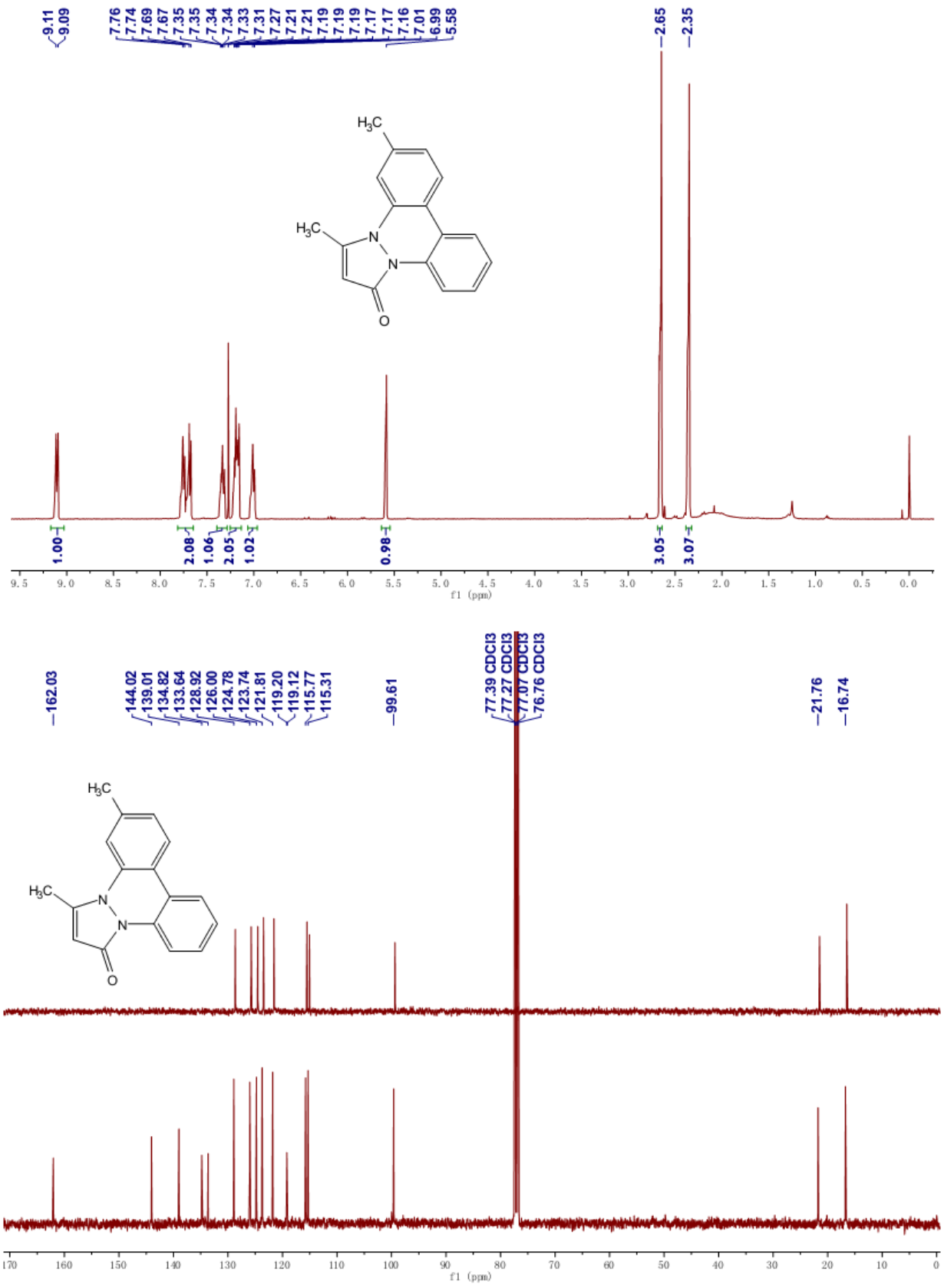




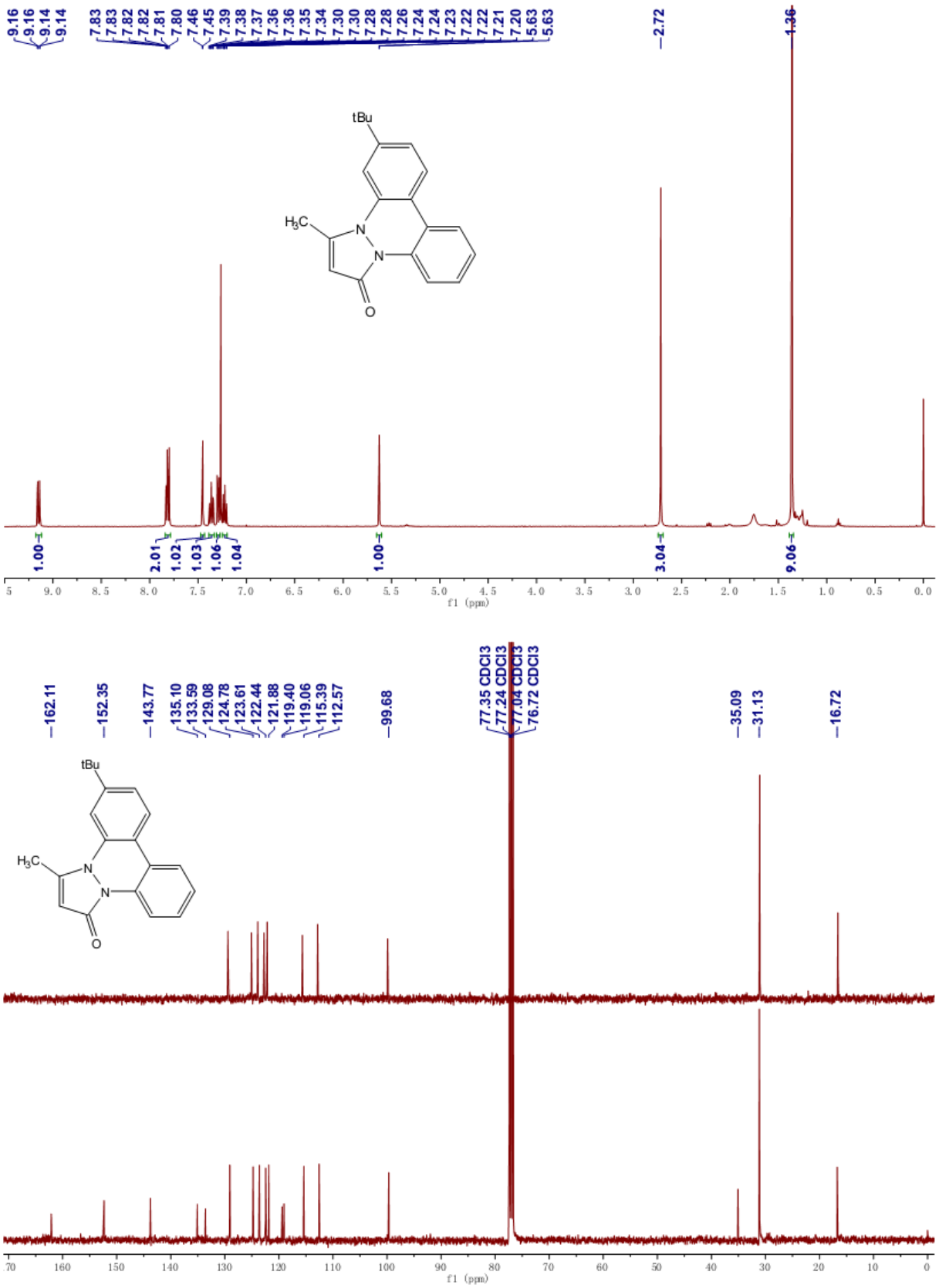
^{1}H and ^{13}C NMR spectra of compound **1a.**



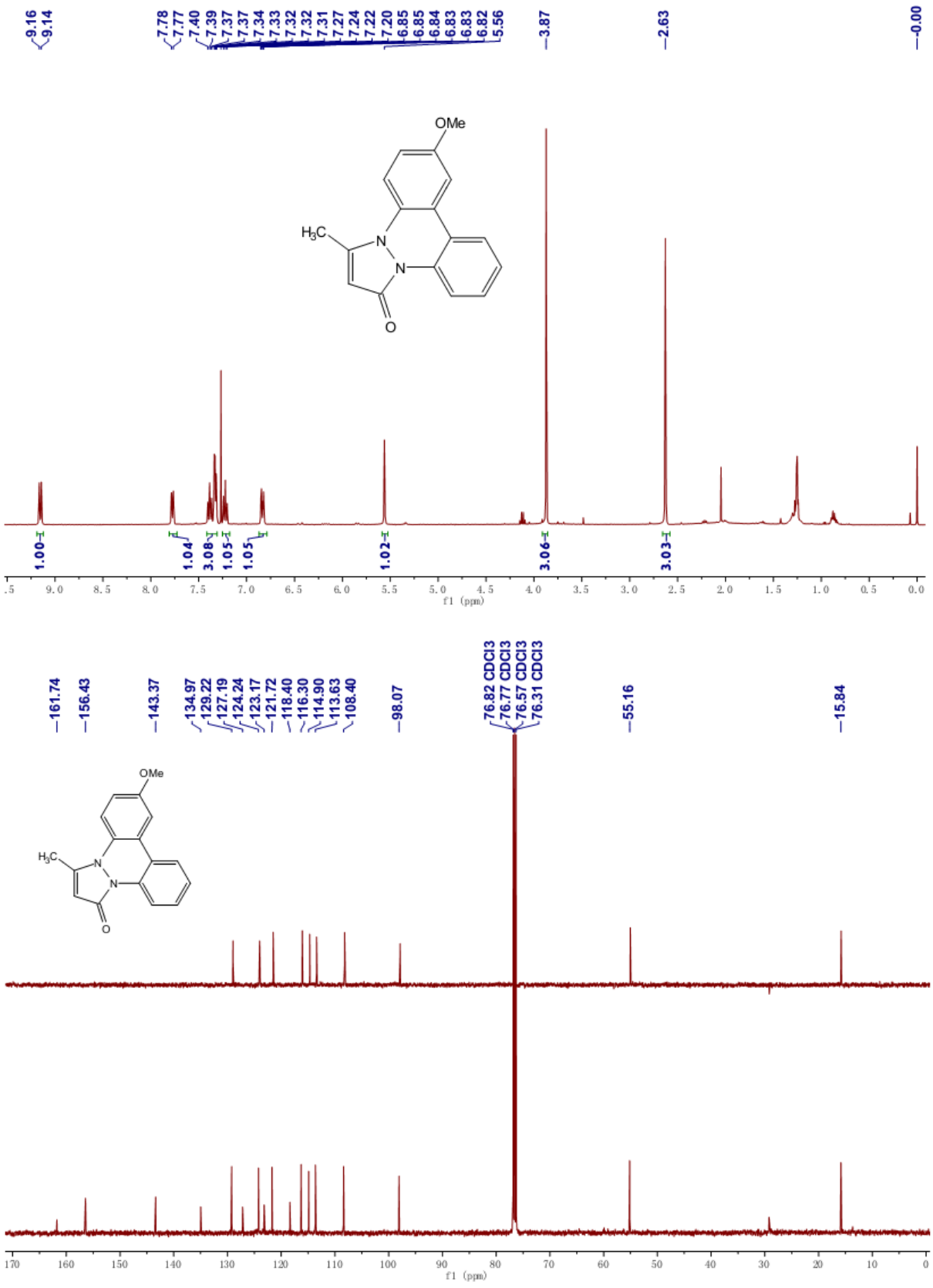
^{1}H and ^{13}C NMR spectra of compound **1b.**



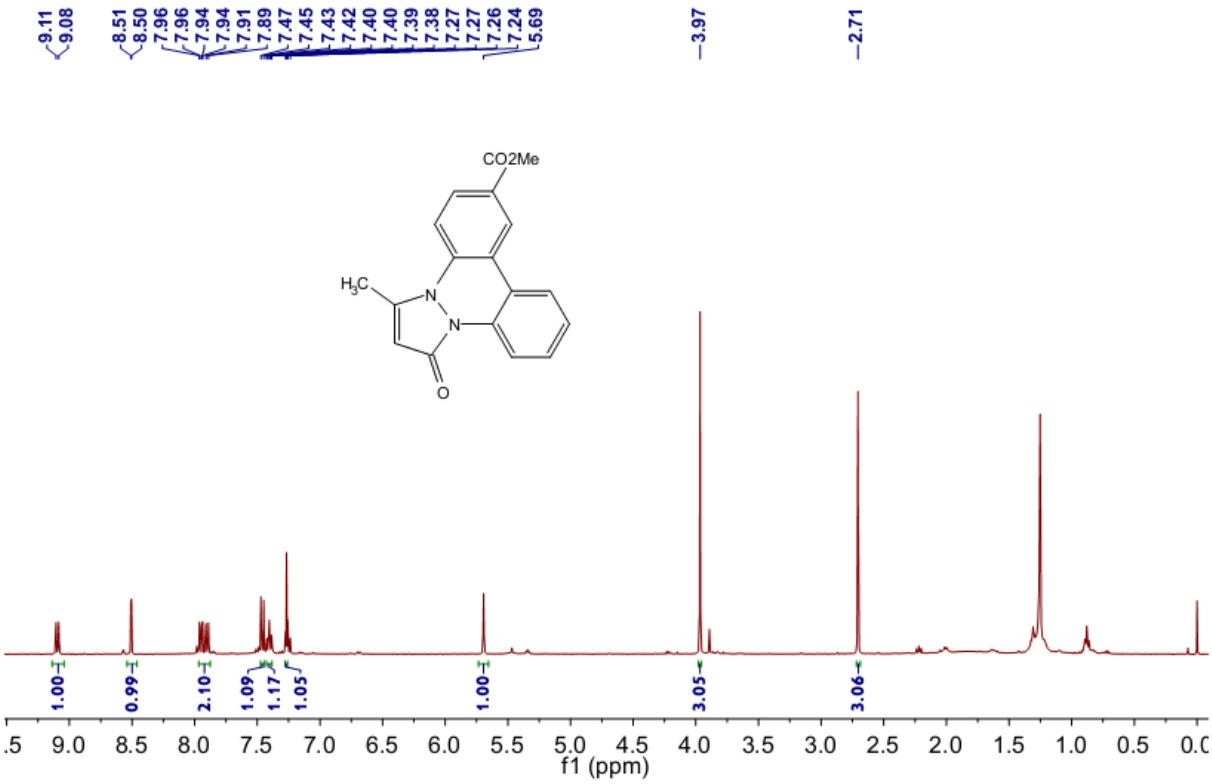
^{1}H and ^{13}C NMR spectra of compound **1c.**

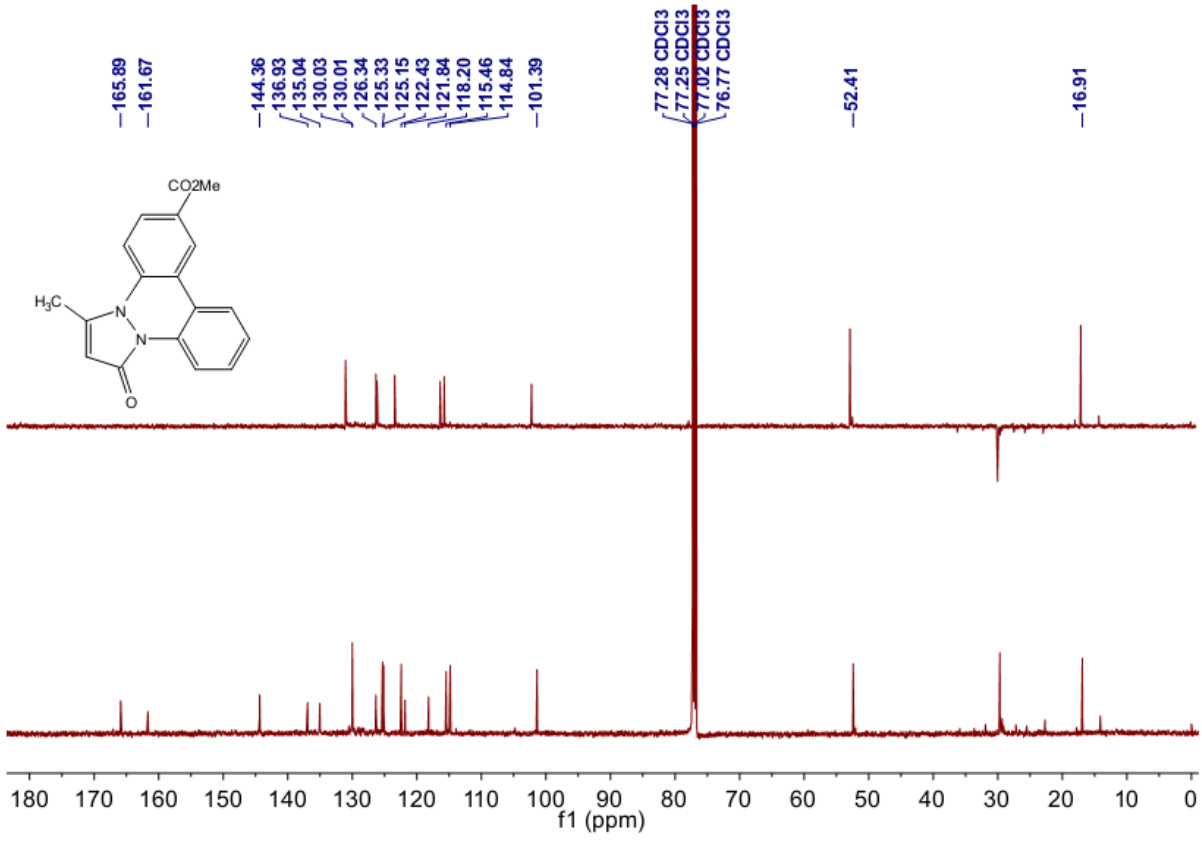


^{1}H and ^{13}C NMR spectra of compound **1d.**

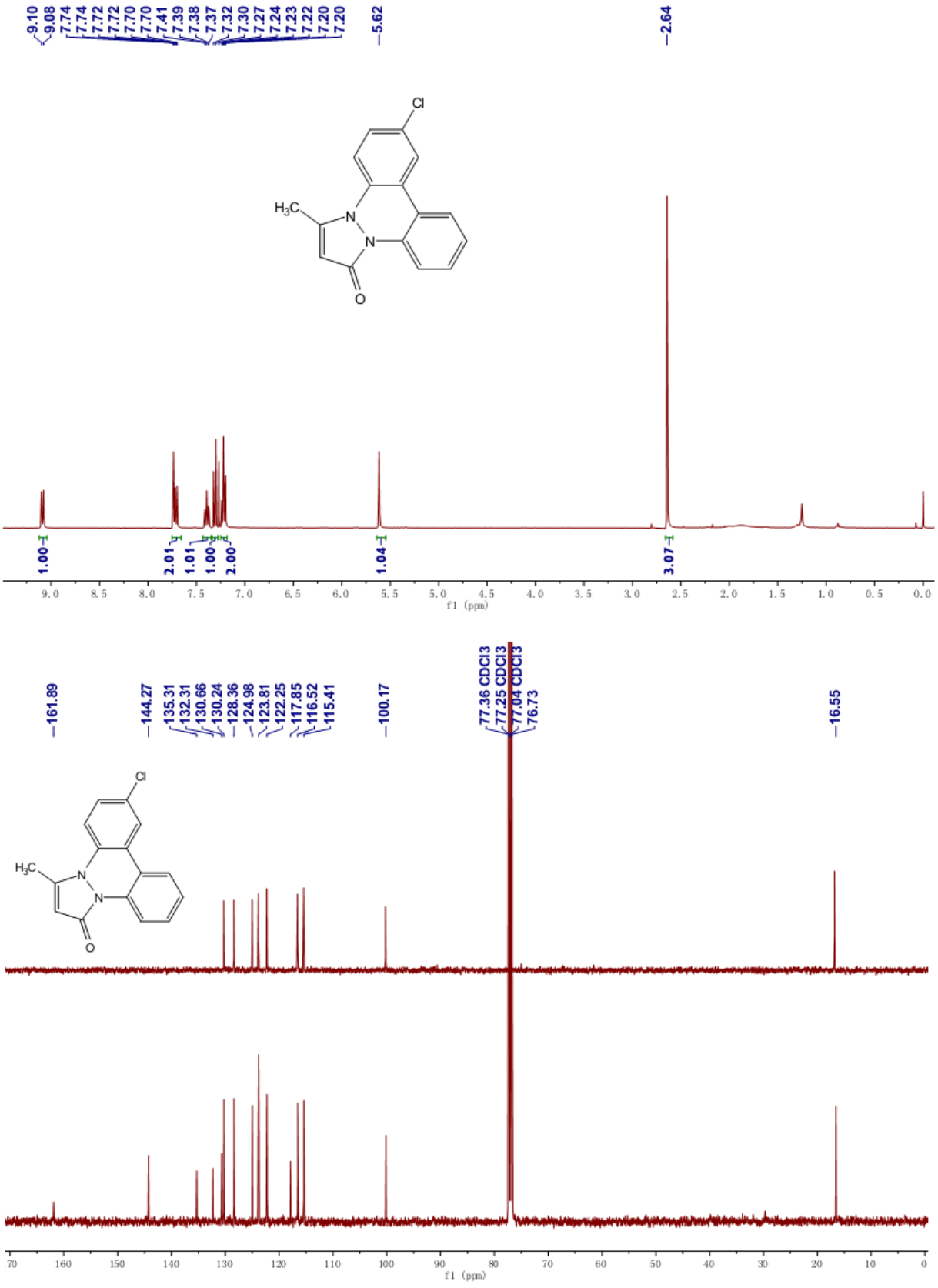


^{1}H and ^{13}C NMR spectra of compound **1e.**

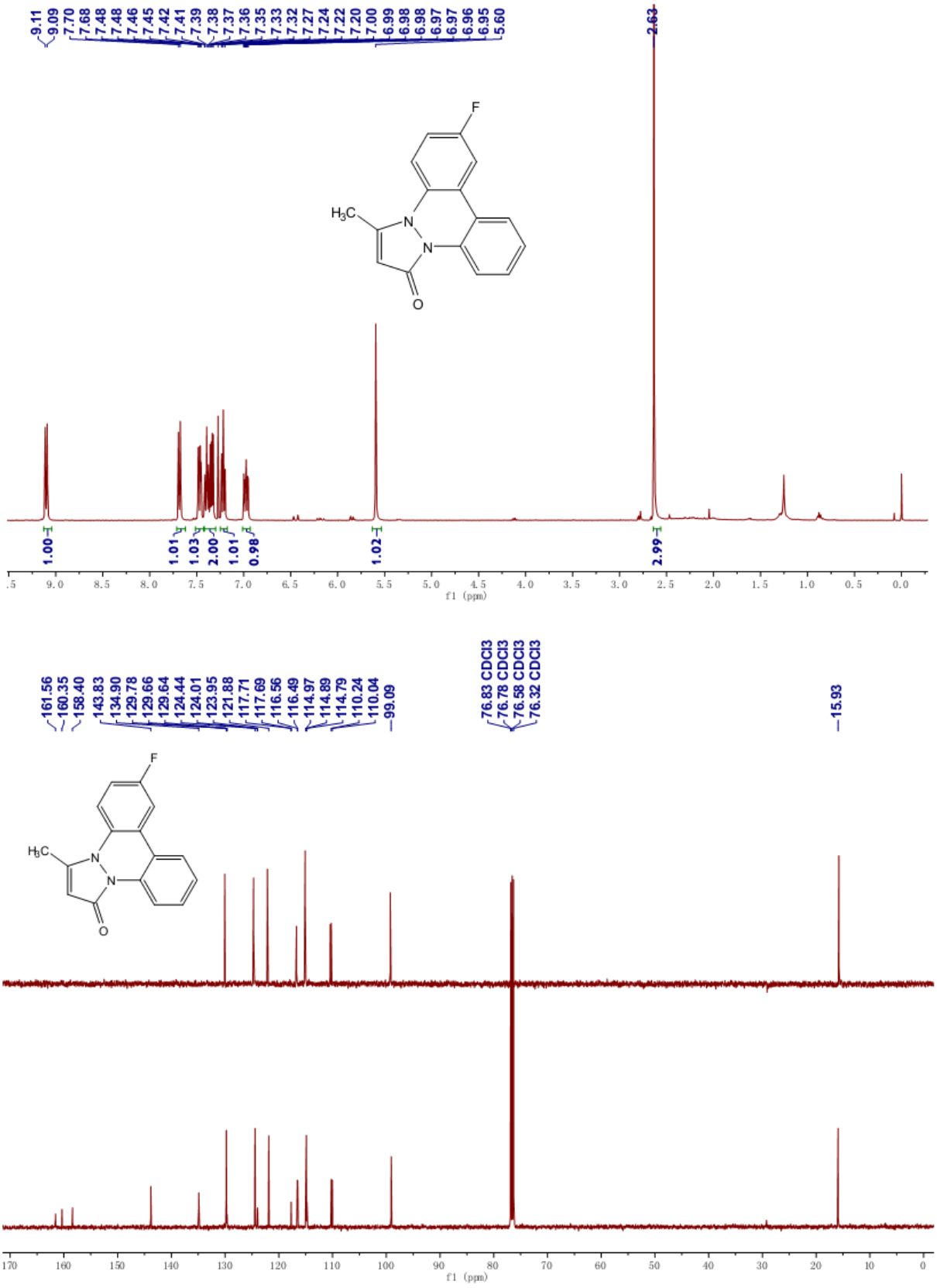




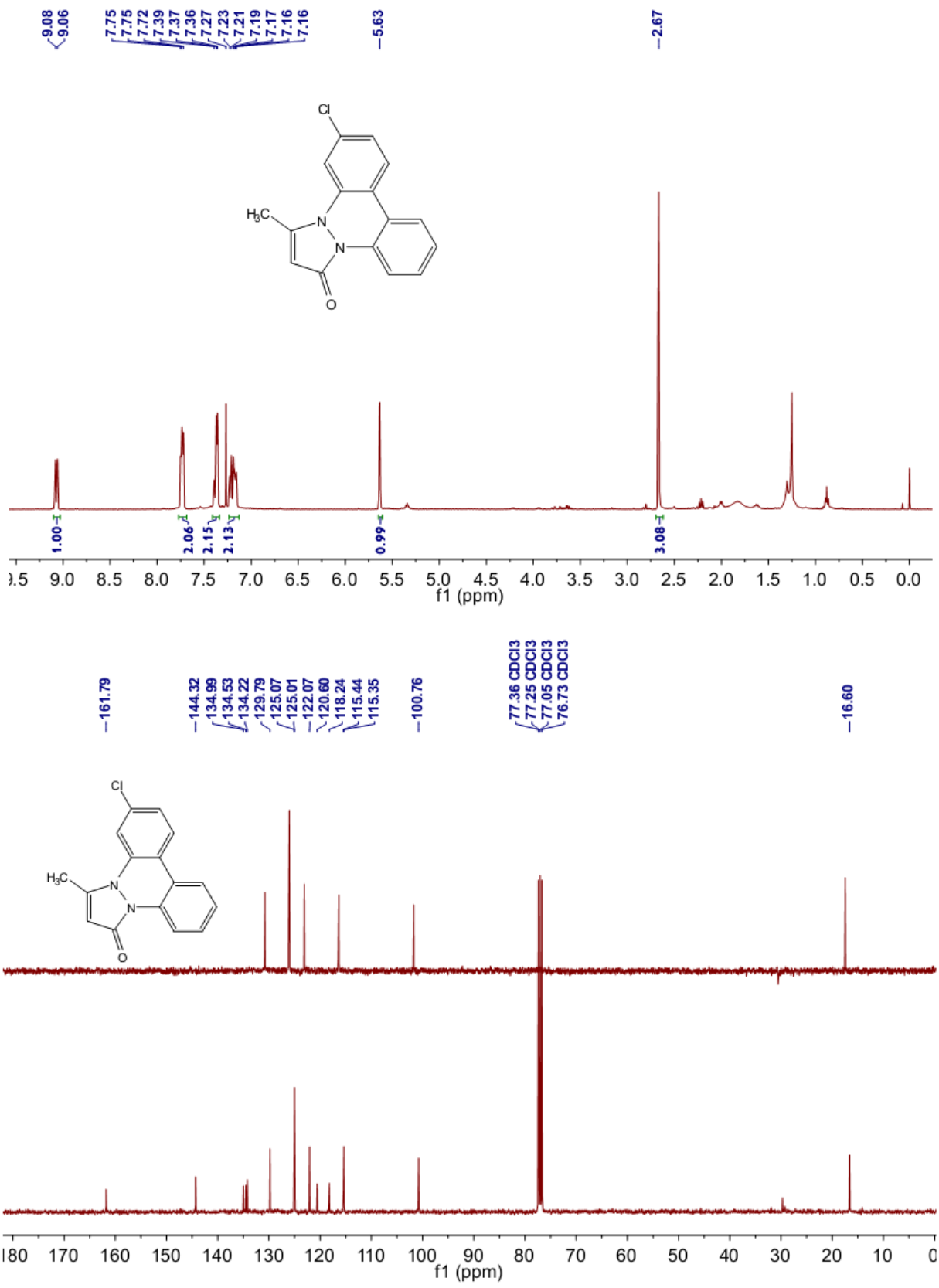
^{1}H and ^{13}C NMR spectra of compound **1f.**



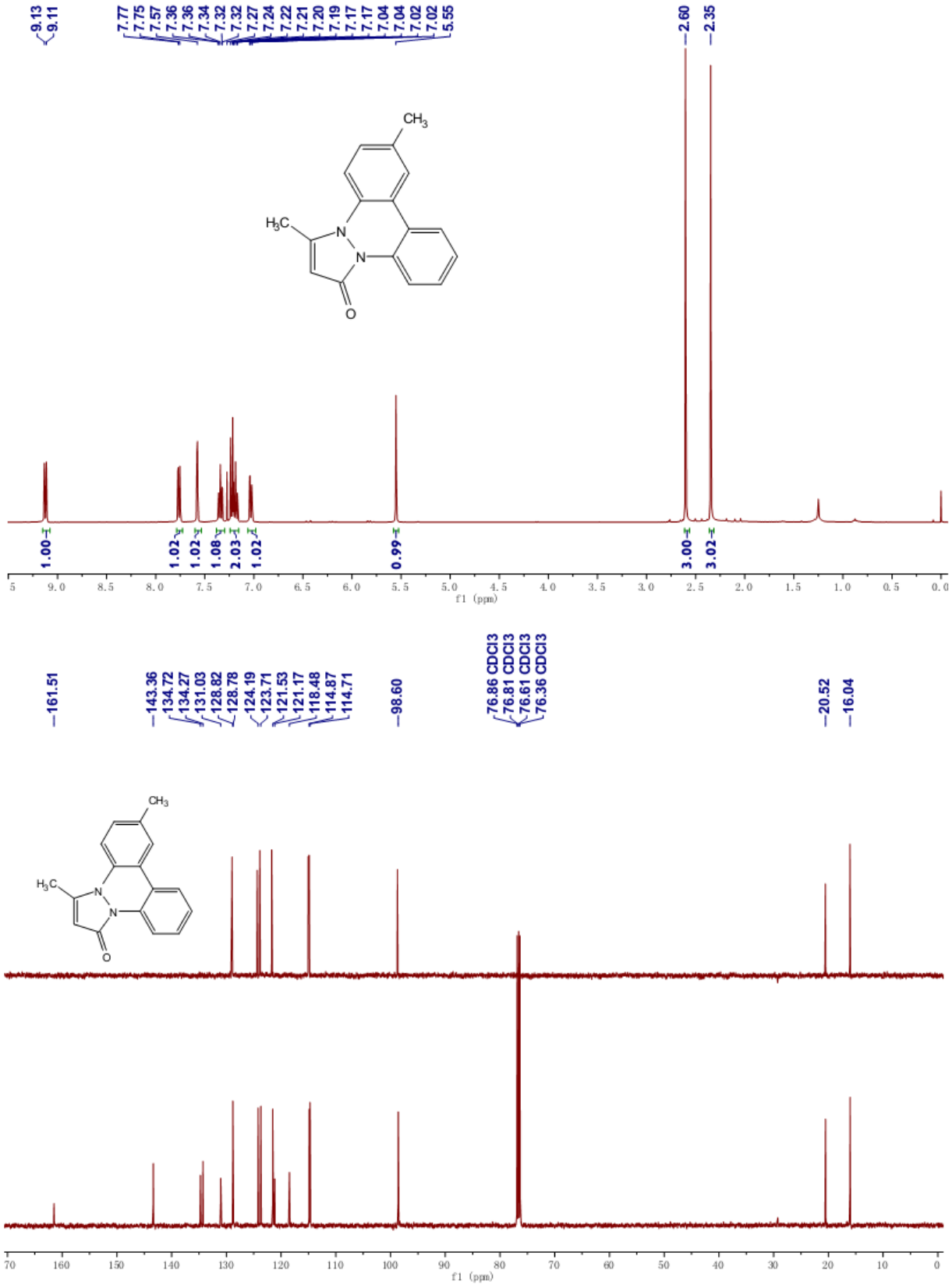
^{1}H and ^{13}C NMR spectra of compound **1g.**



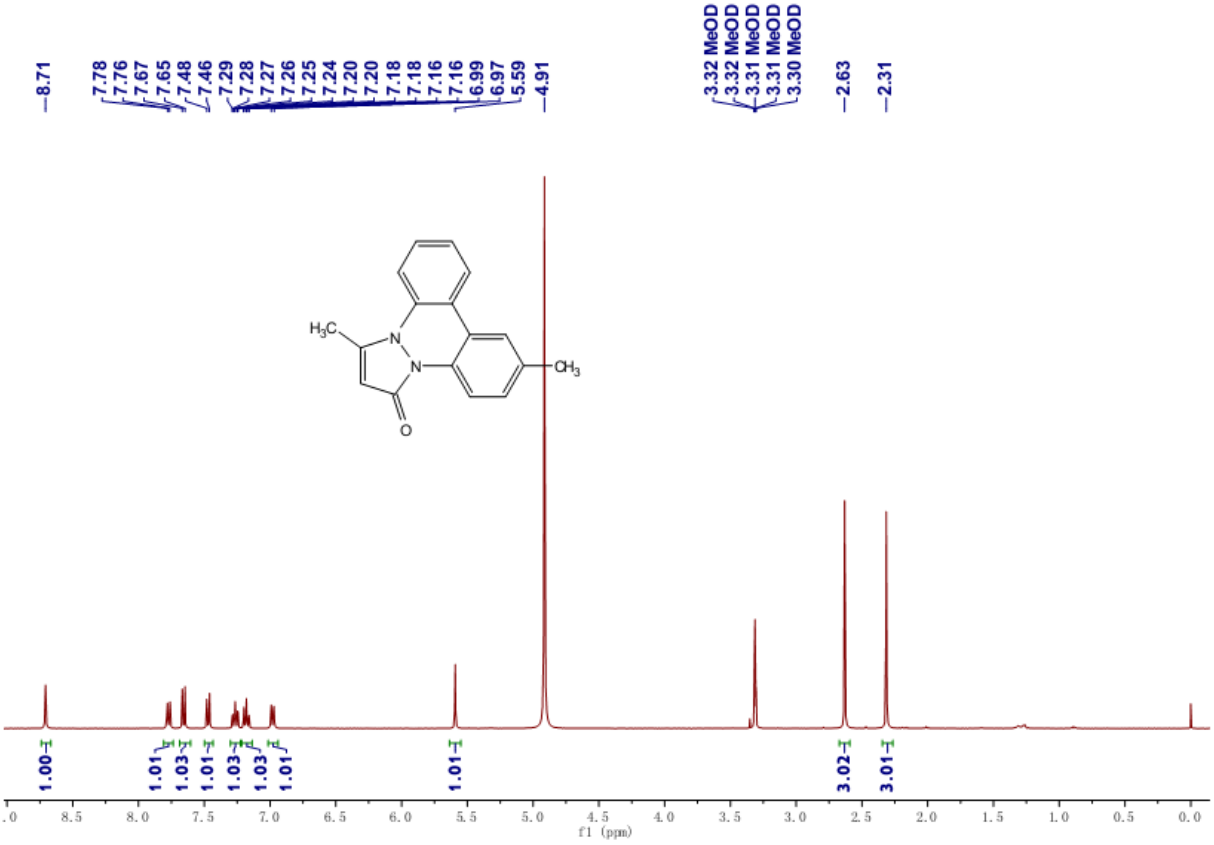
^{1}H and ^{13}C NMR spectra of compound **1h.**

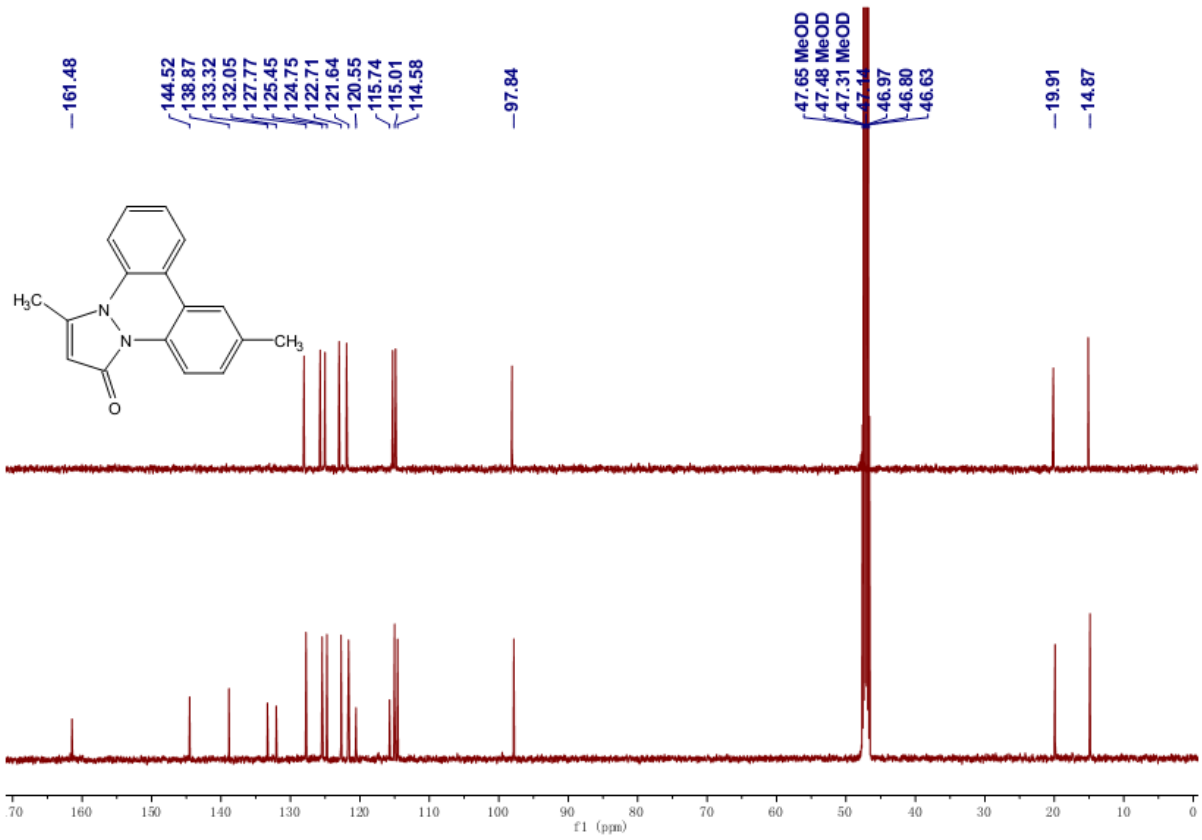


^{1}H and ^{13}C NMR spectra of compound **1i.**

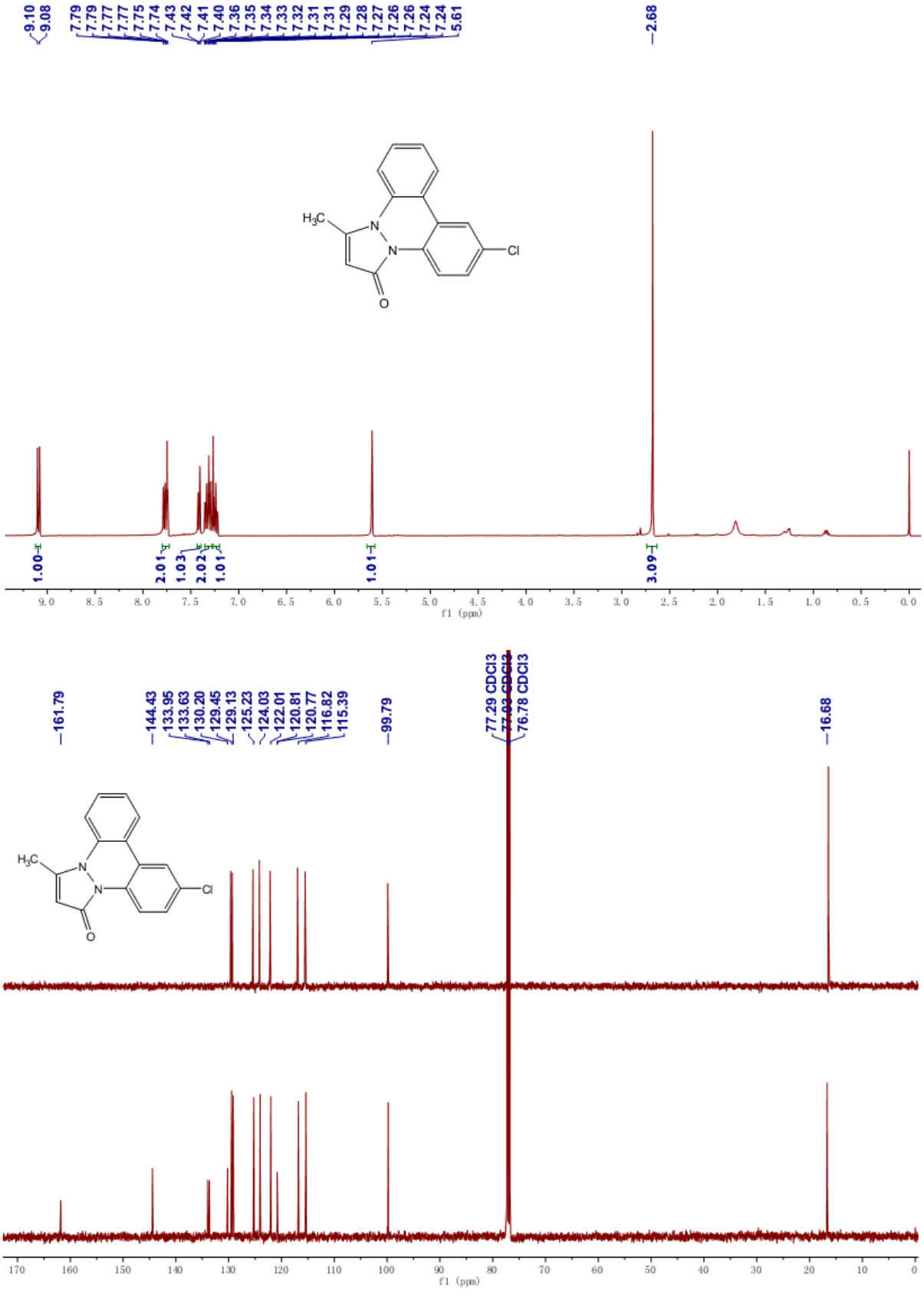


^{1}H and ^{13}C NMR spectra of compound **1j.**

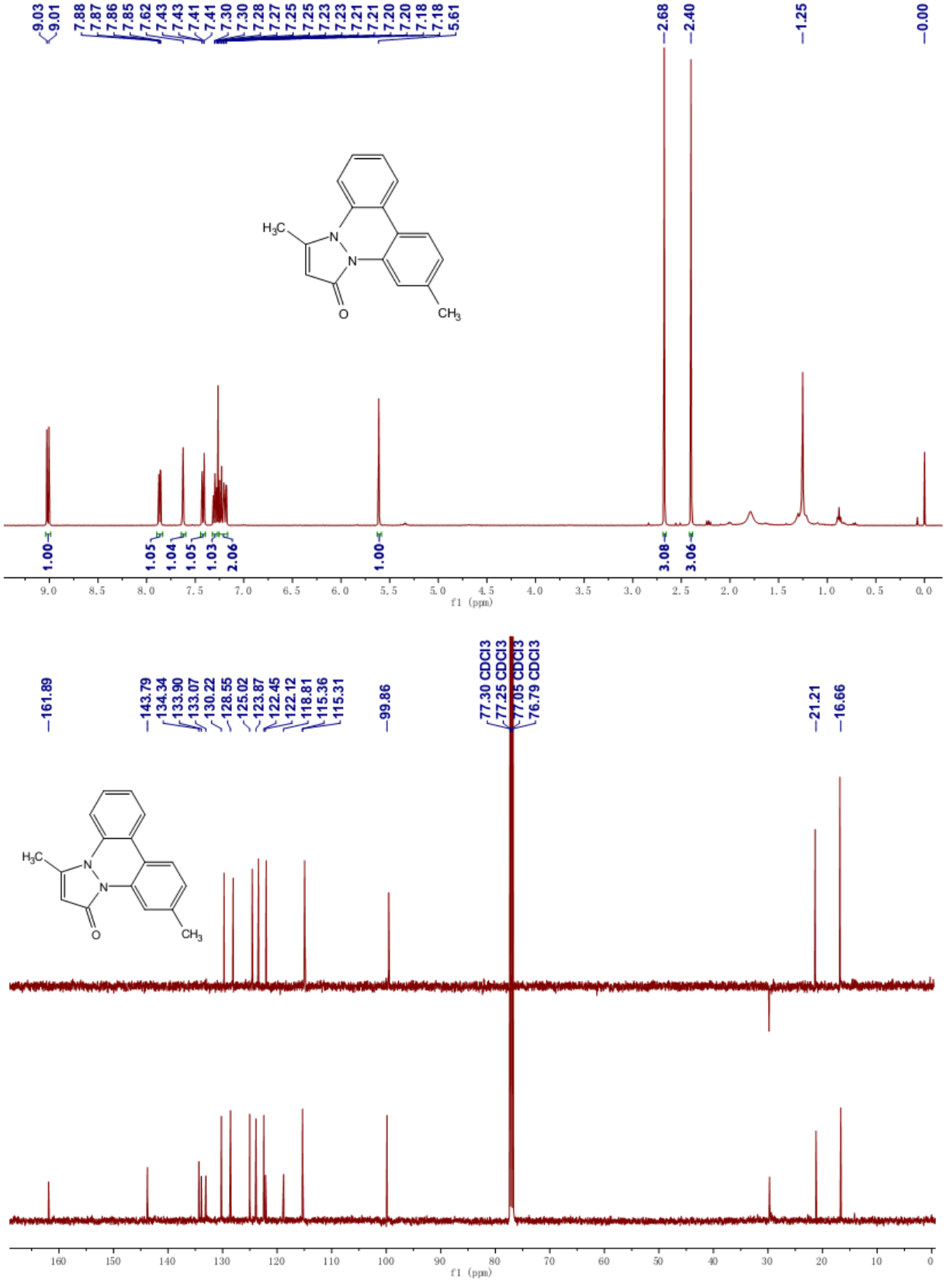




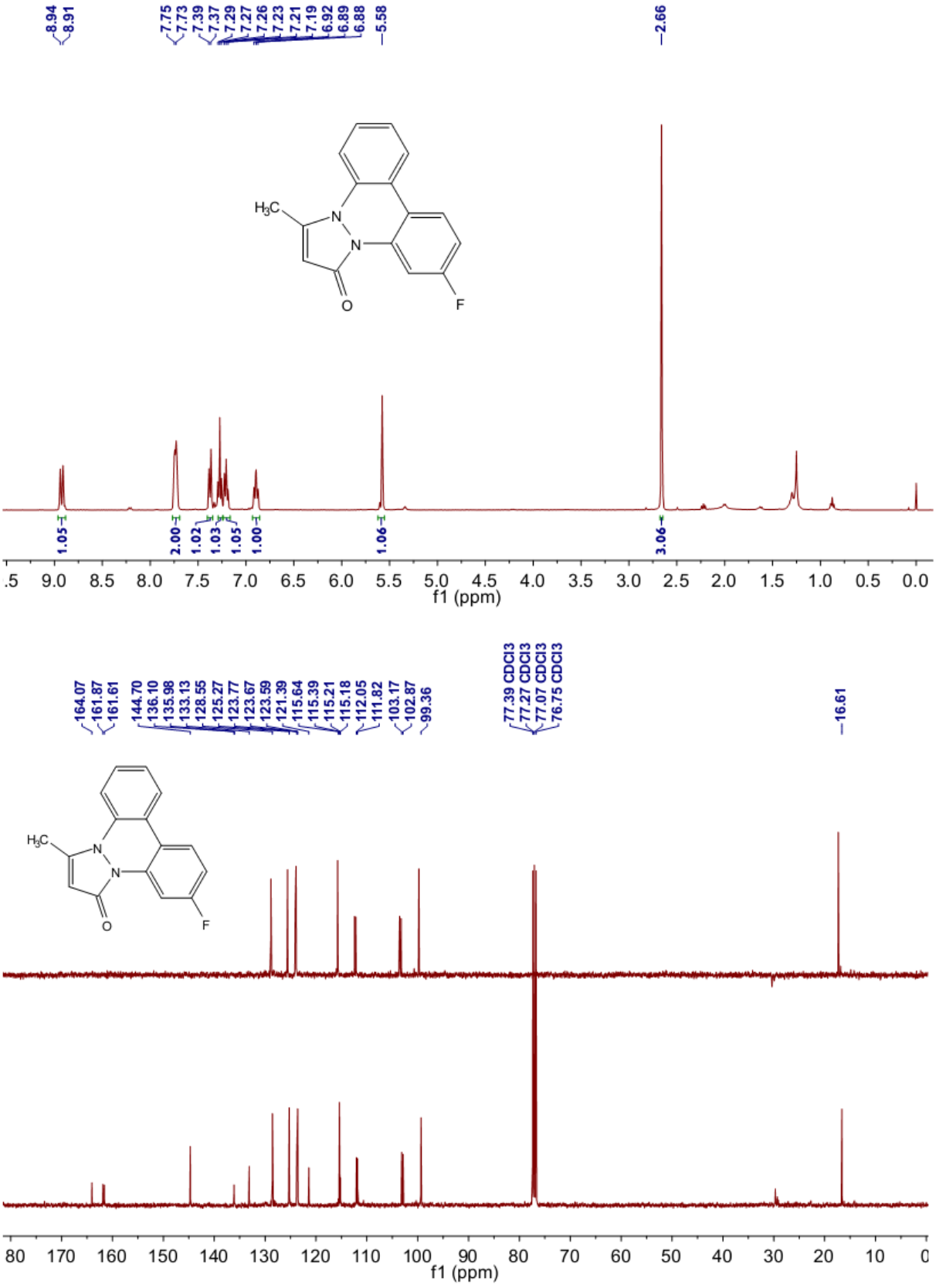
^{1}H and ^{13}C NMR spectra of compound **1k.**



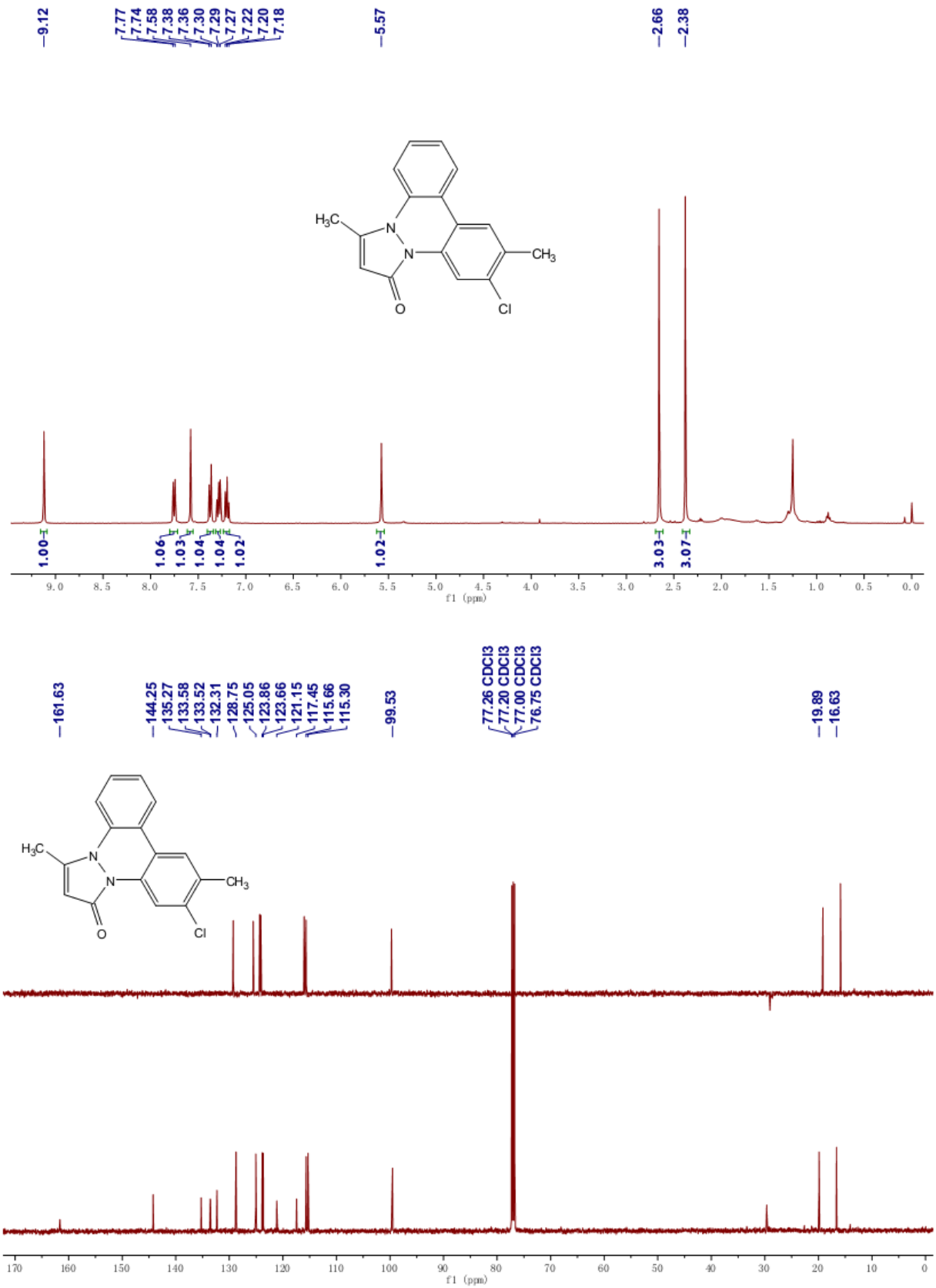
^{1}H and ^{13}C NMR spectra of compound **1l.**



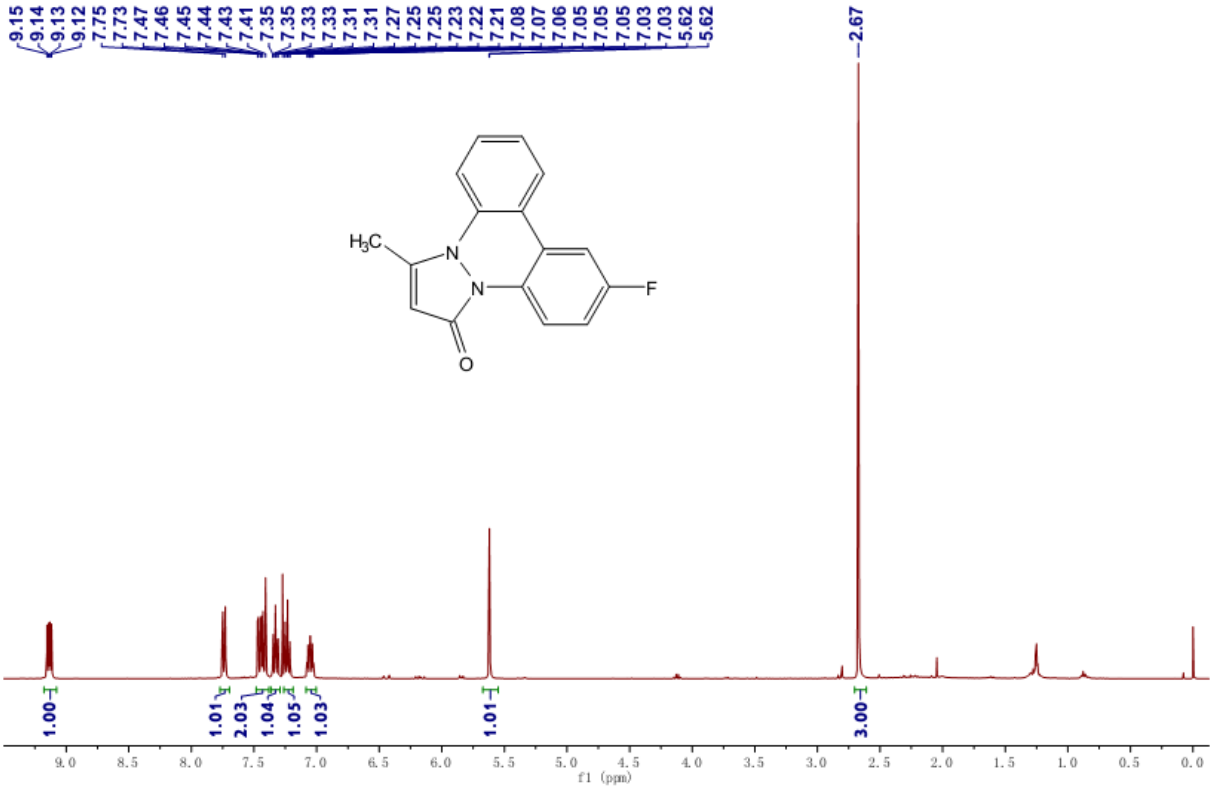
^{1}H and ^{13}C NMR spectra of compound **1m.**

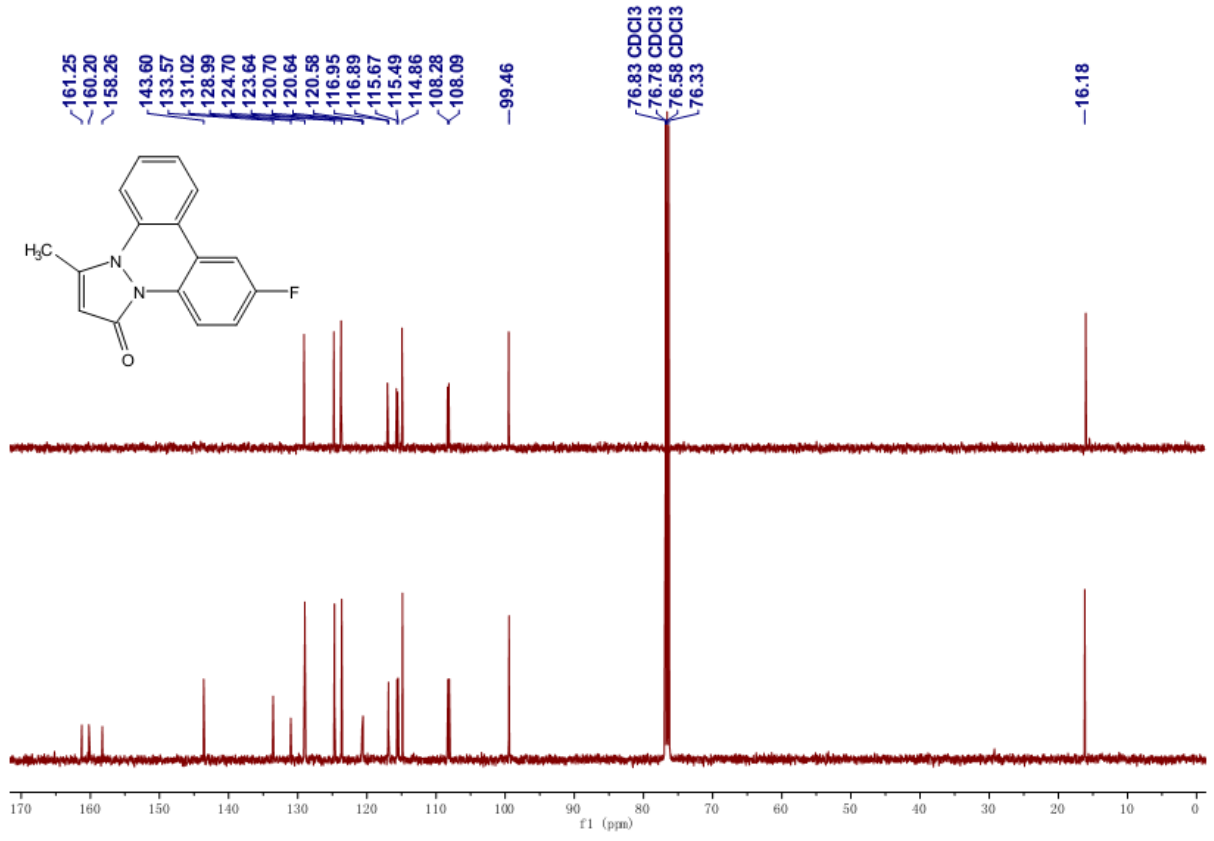


^{1}H and ^{13}C NMR spectra of compound **1r.**

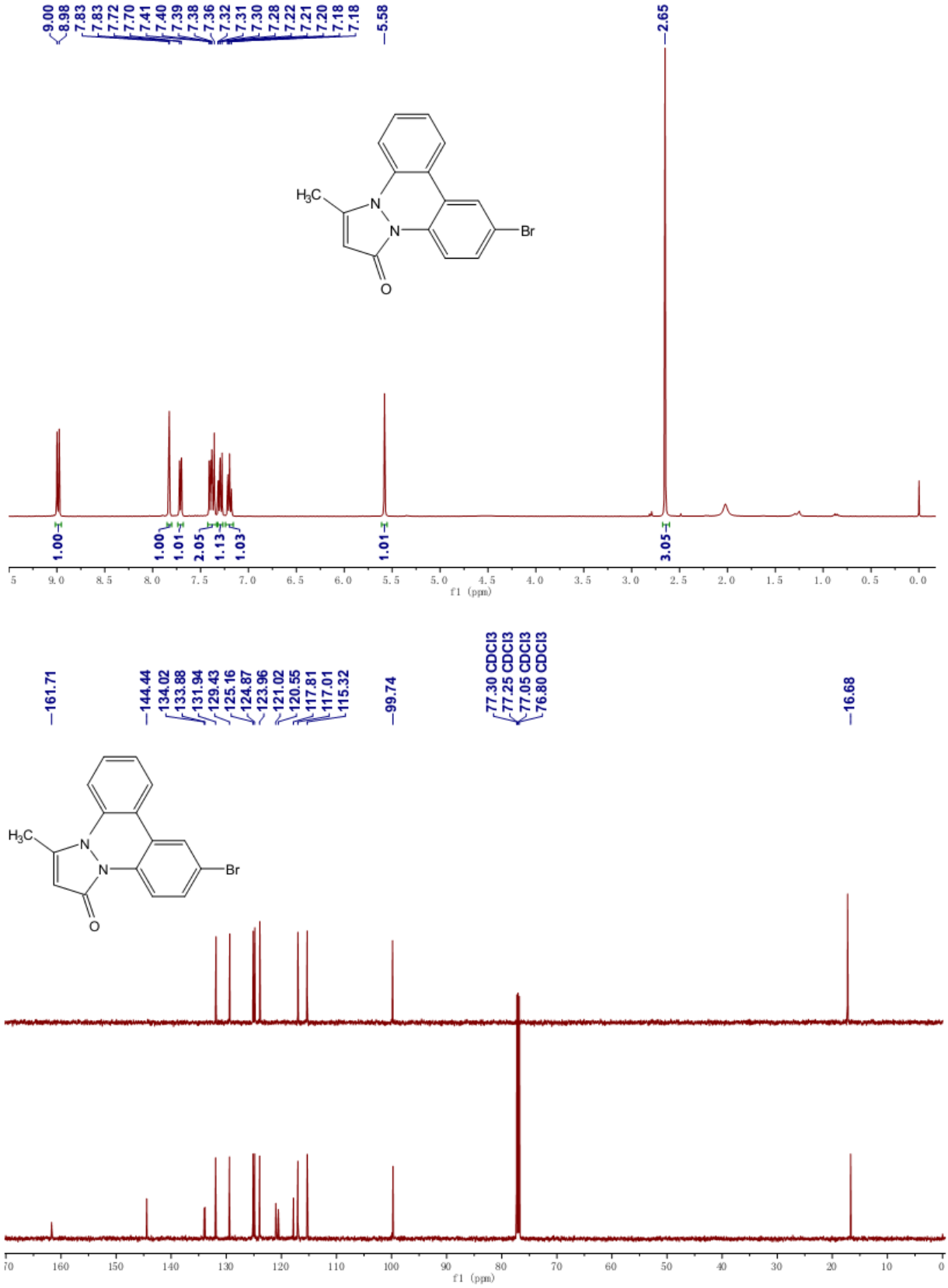


^{1}H and ^{13}C NMR spectra of compound **1o.**

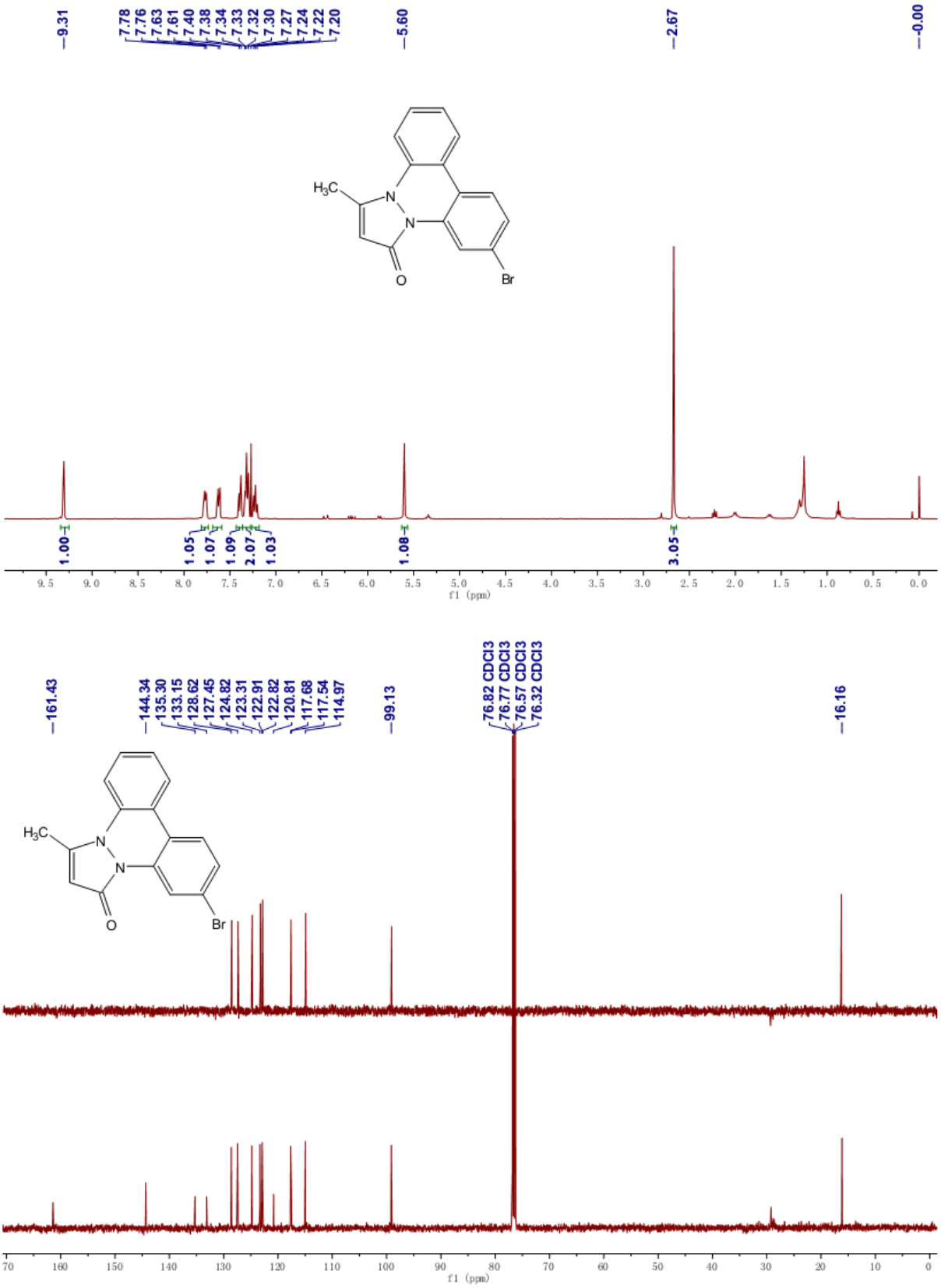




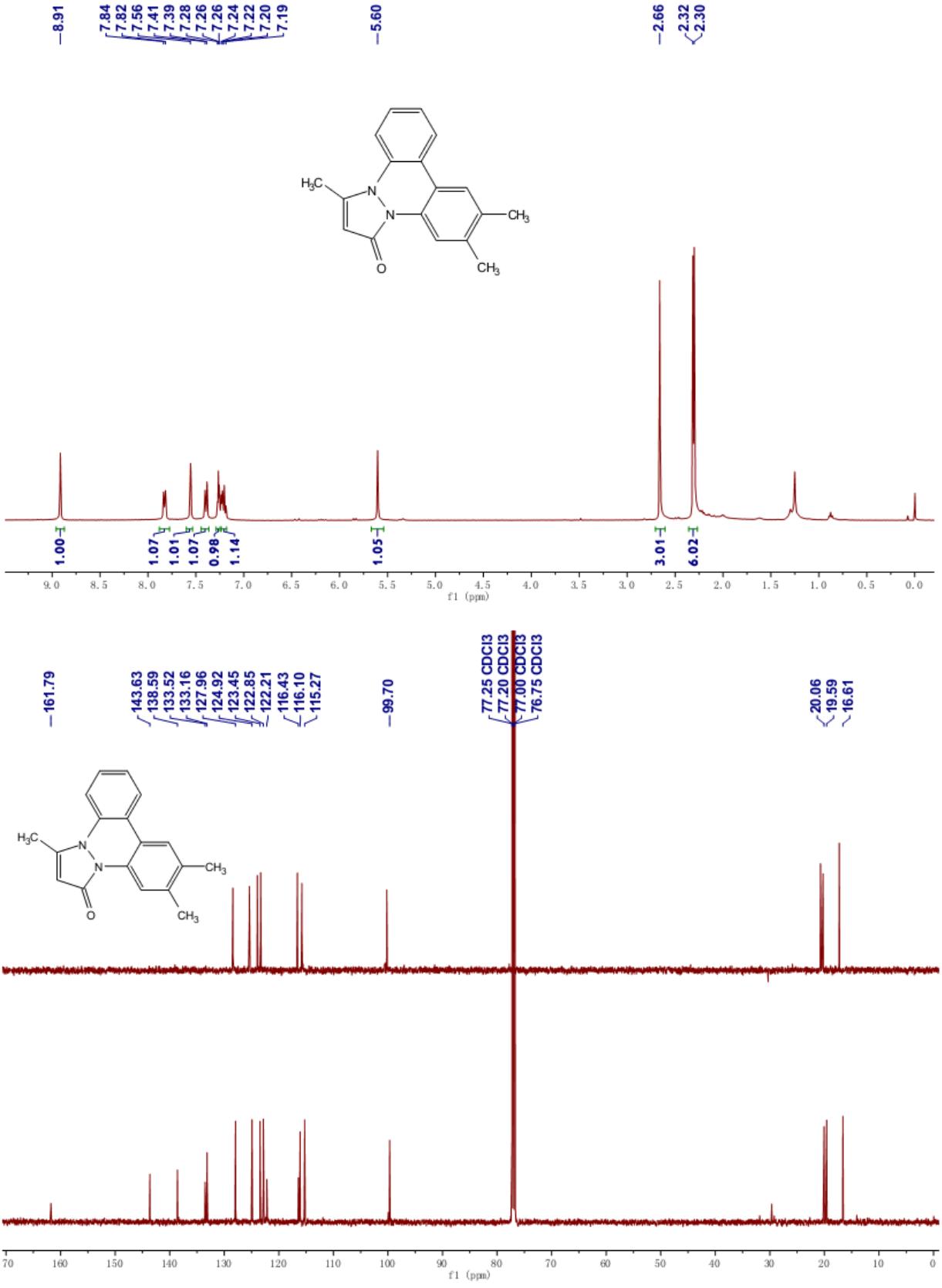
^{1}H and ^{13}C NMR spectra of compound **1p.**



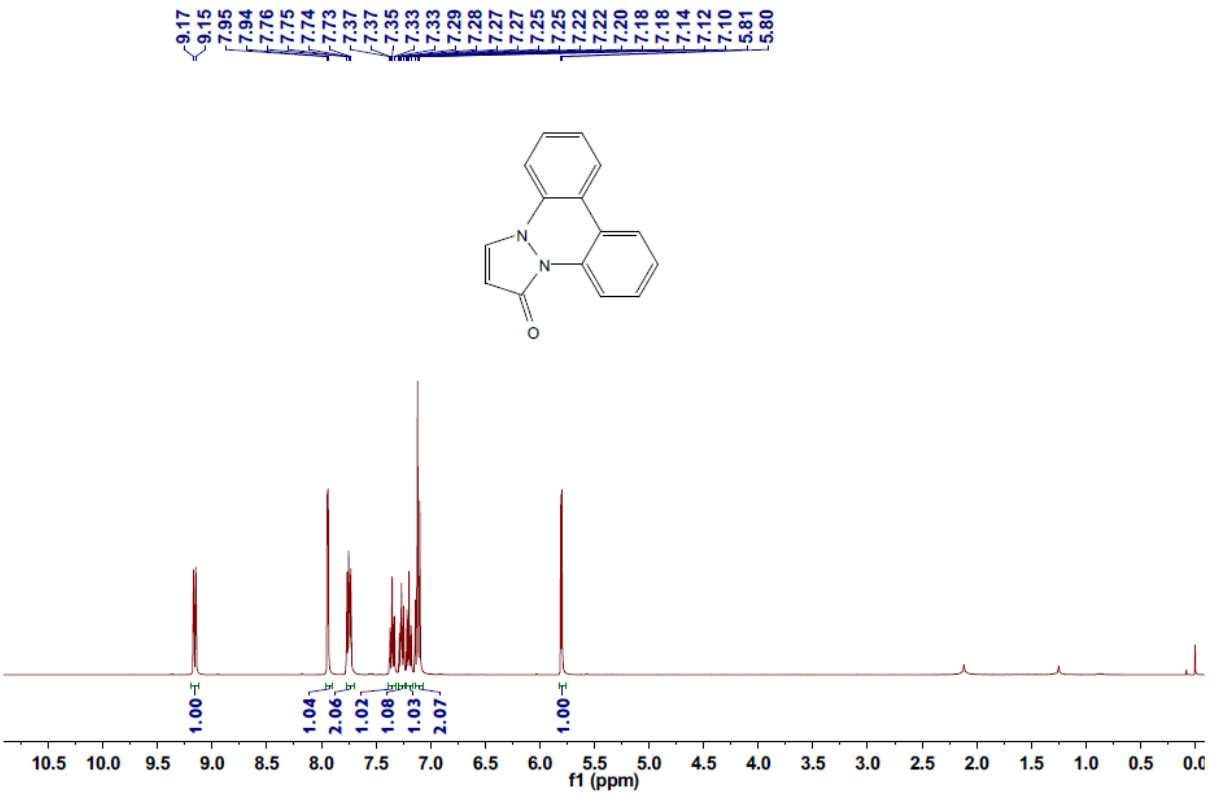
^{1}H and ^{13}C NMR spectra of compound **1n.**

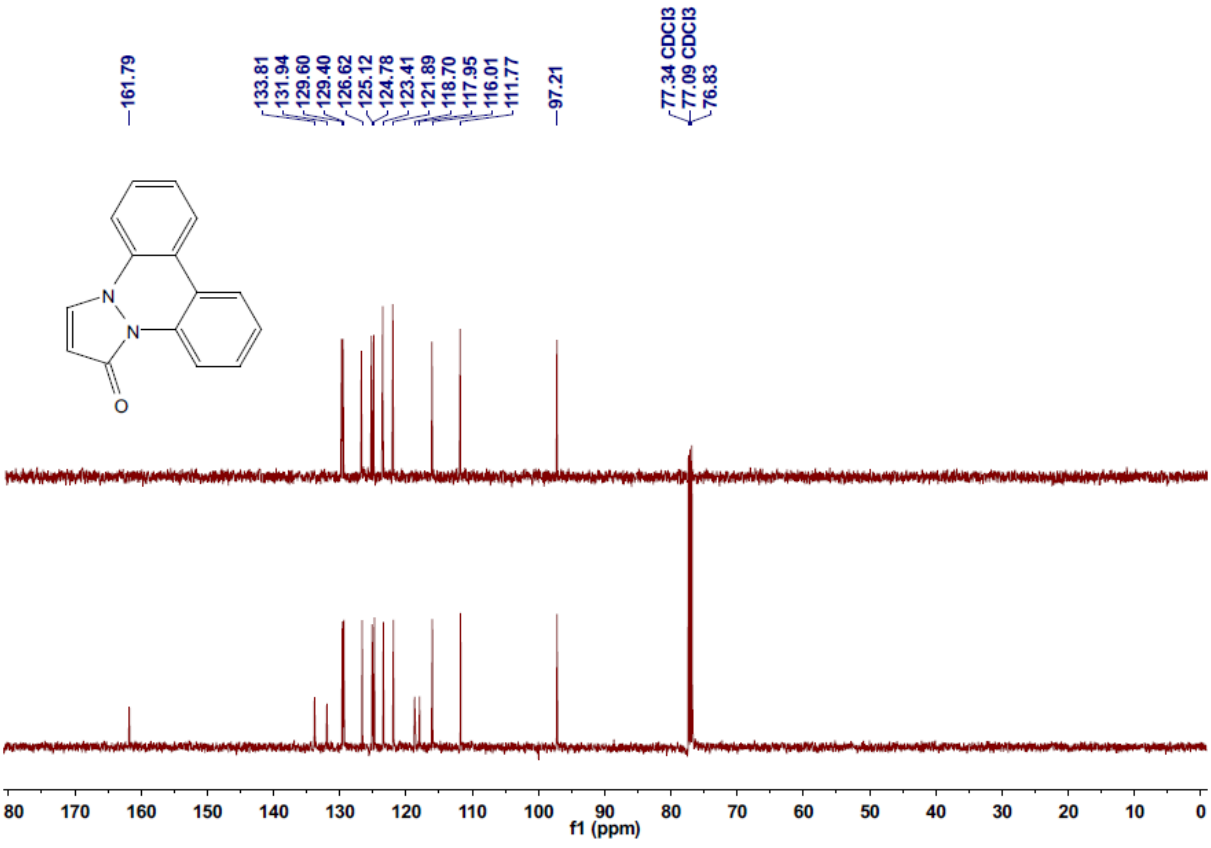


^{1}H and ^{13}C NMR spectra of compound **1q.**

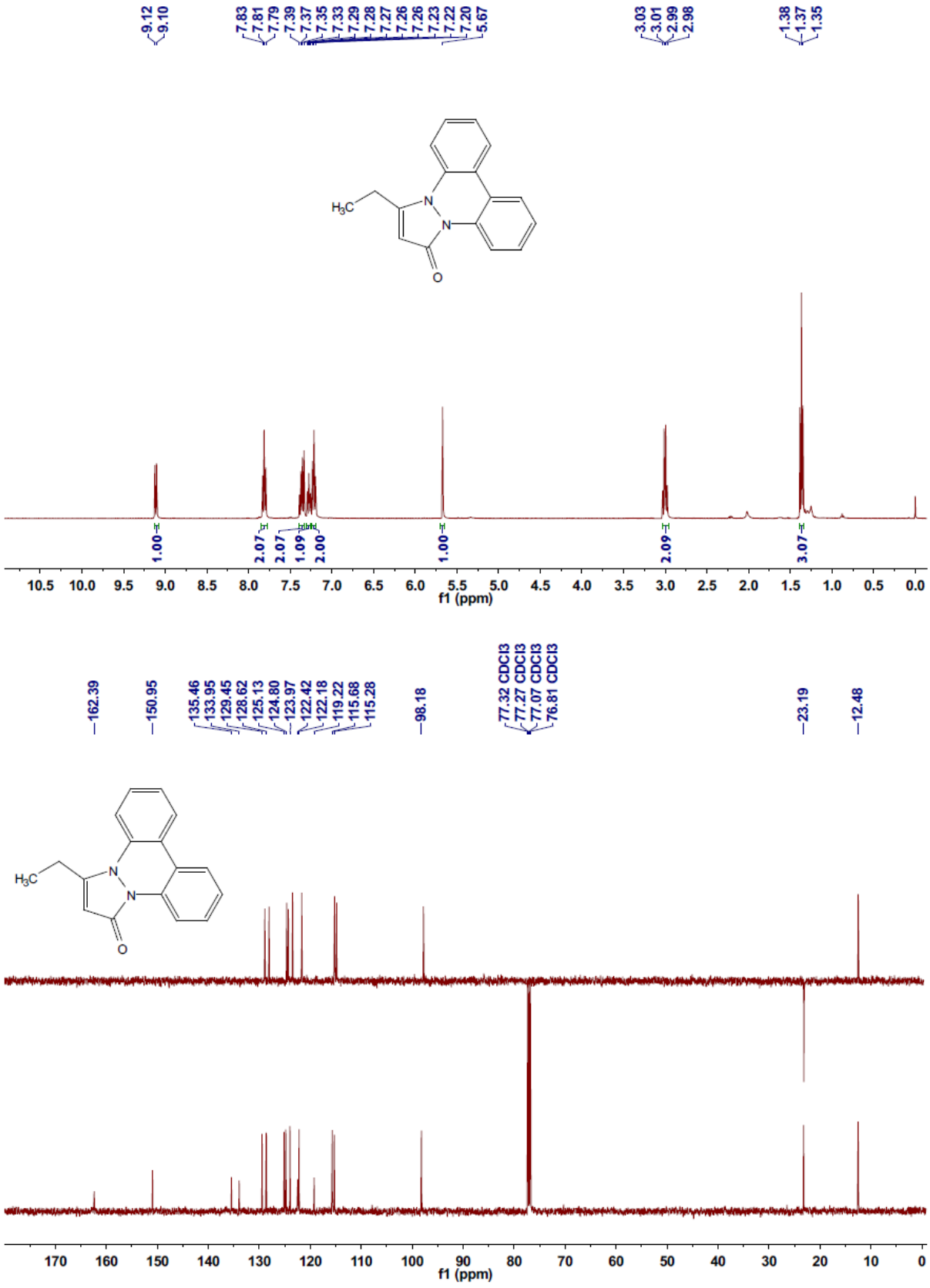


^{1}H and ^{13}C NMR spectra of compound **1s**.

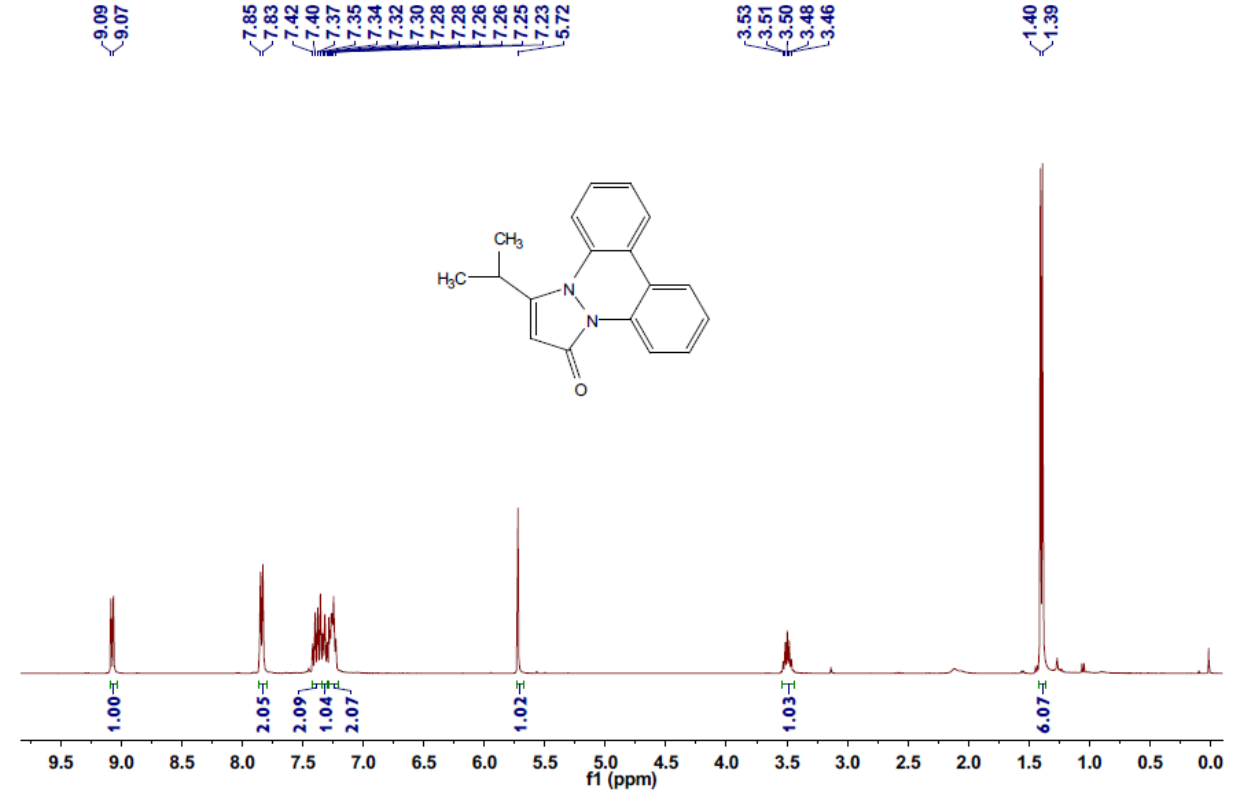


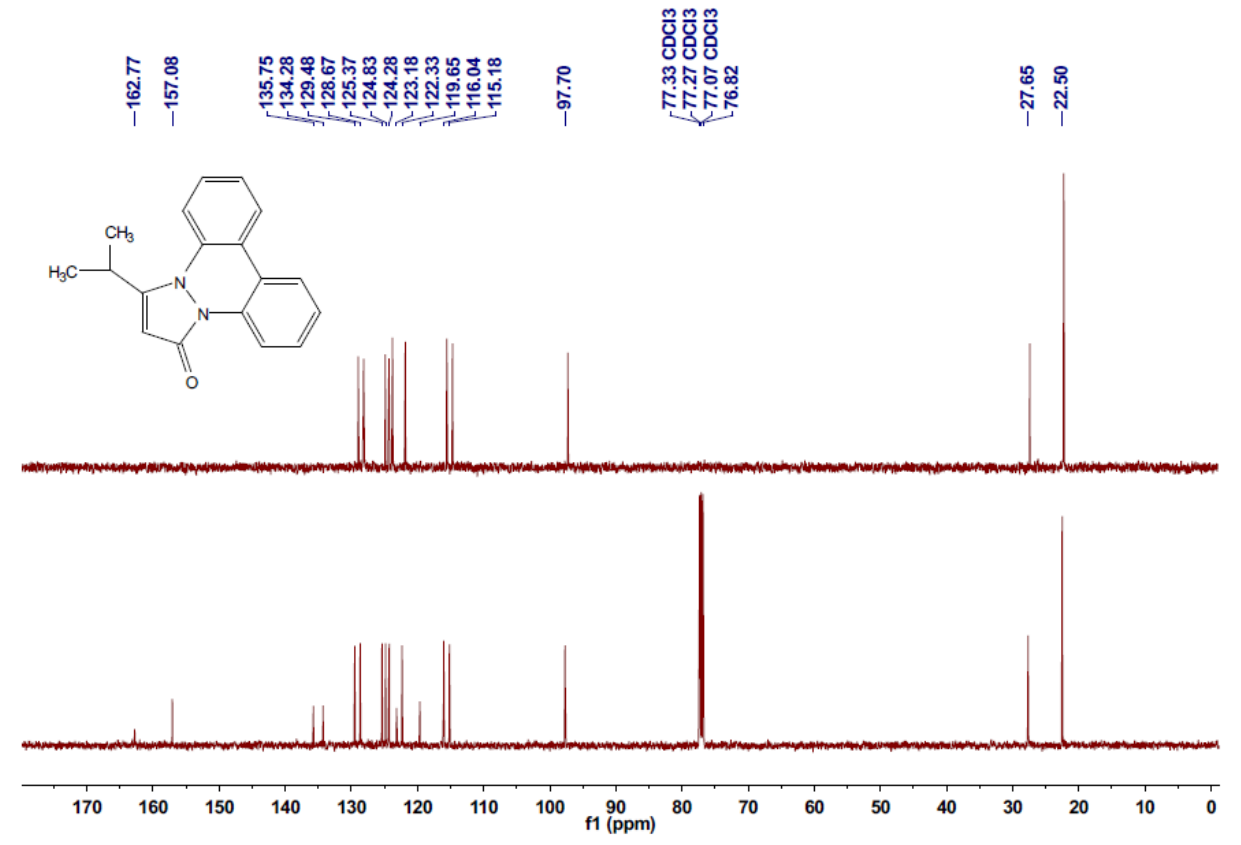


^{1}H and ^{13}C NMR spectra of compound **1t**.

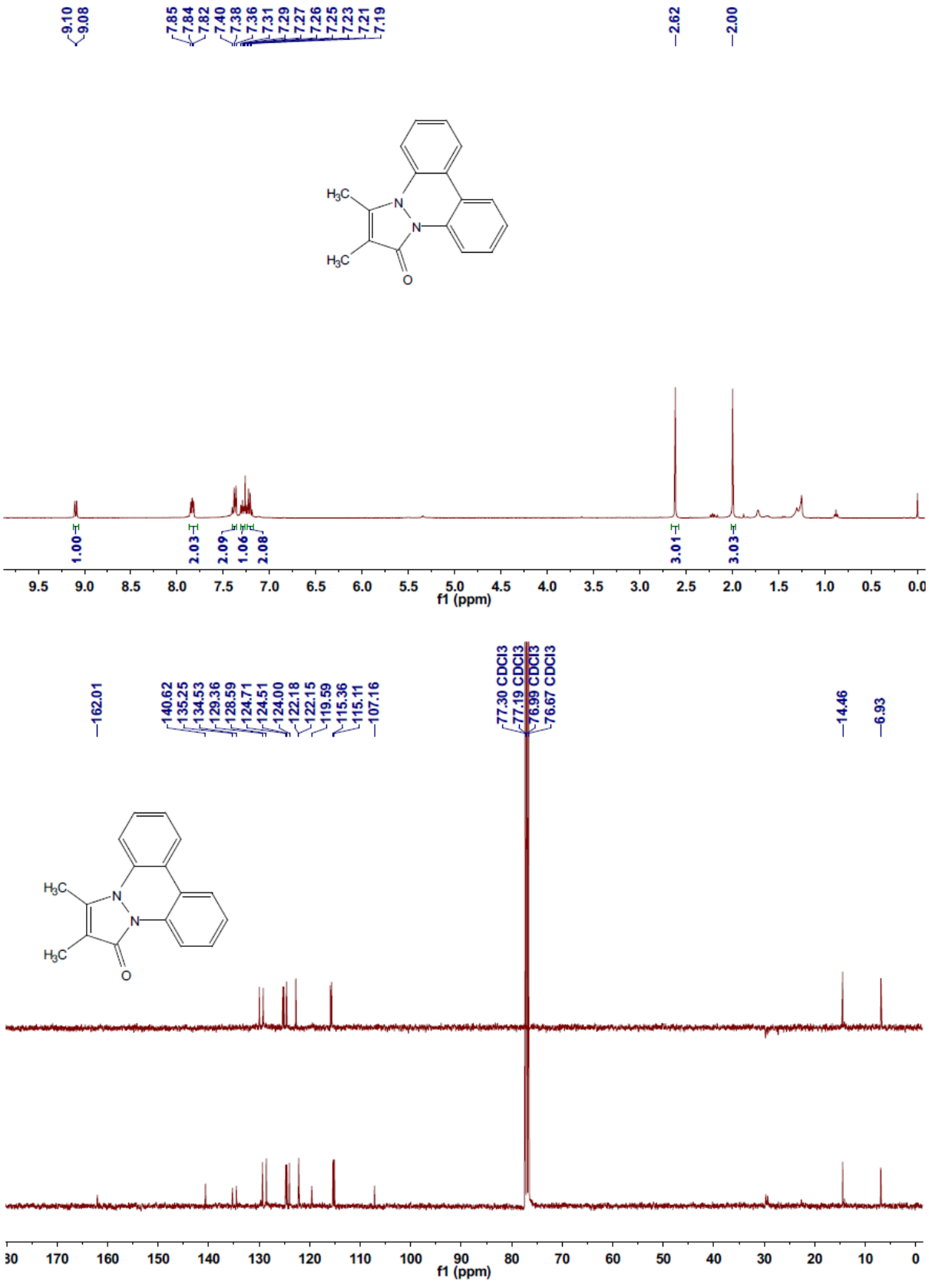


^{1}H and ^{13}C NMR spectra of compound **1u.**

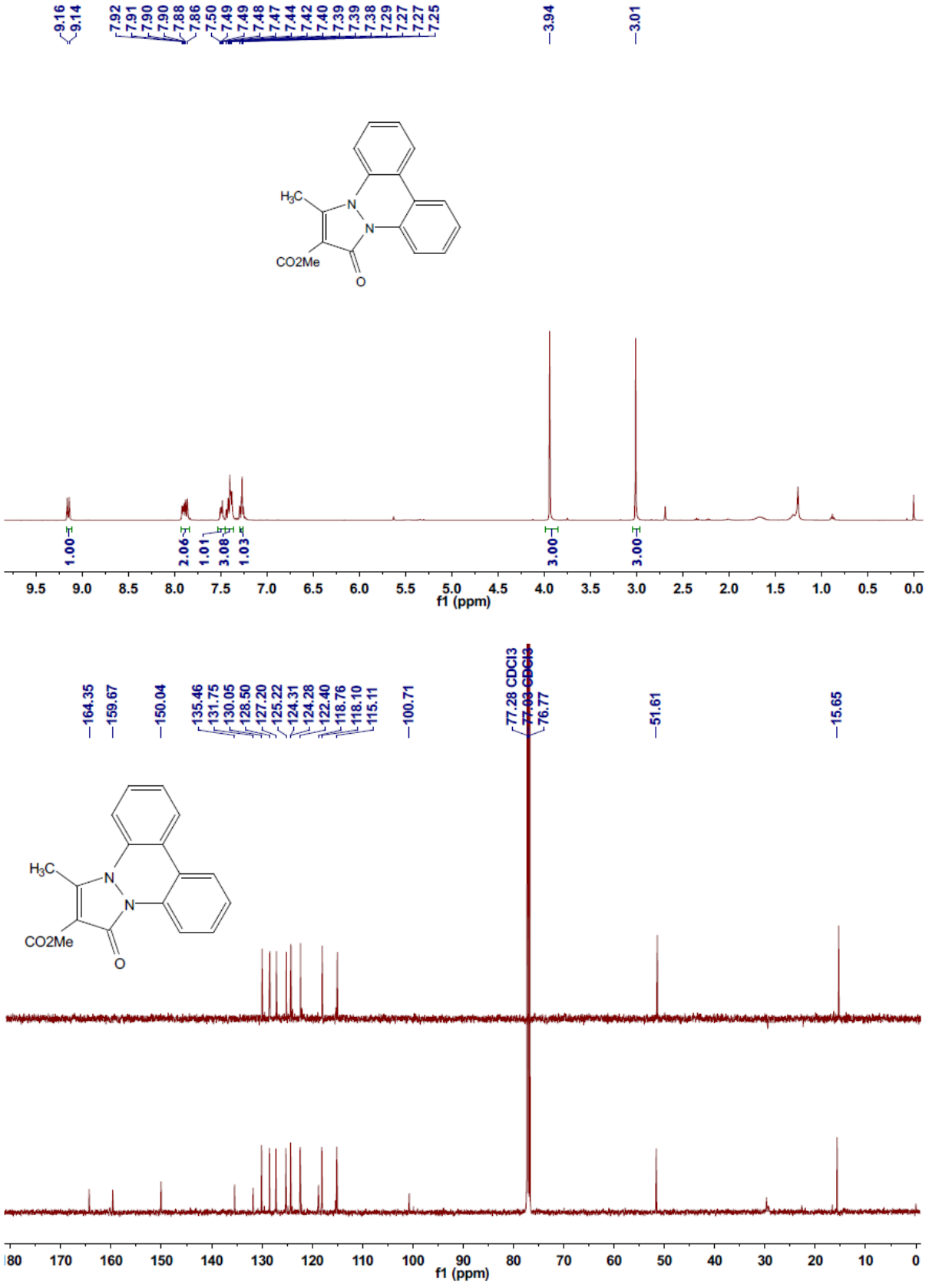




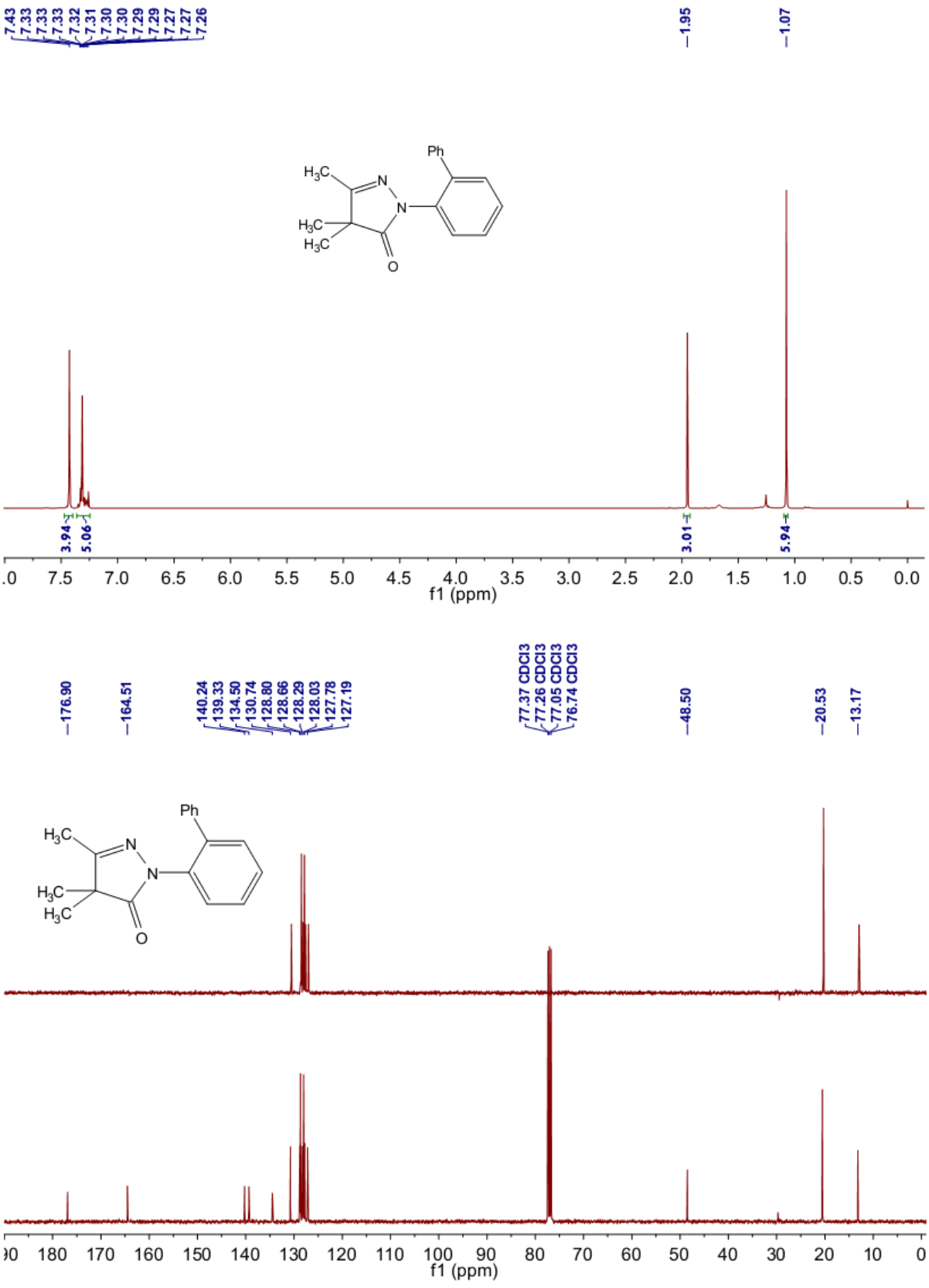
^{1}H and ^{13}C NMR spectra of compound **1y**



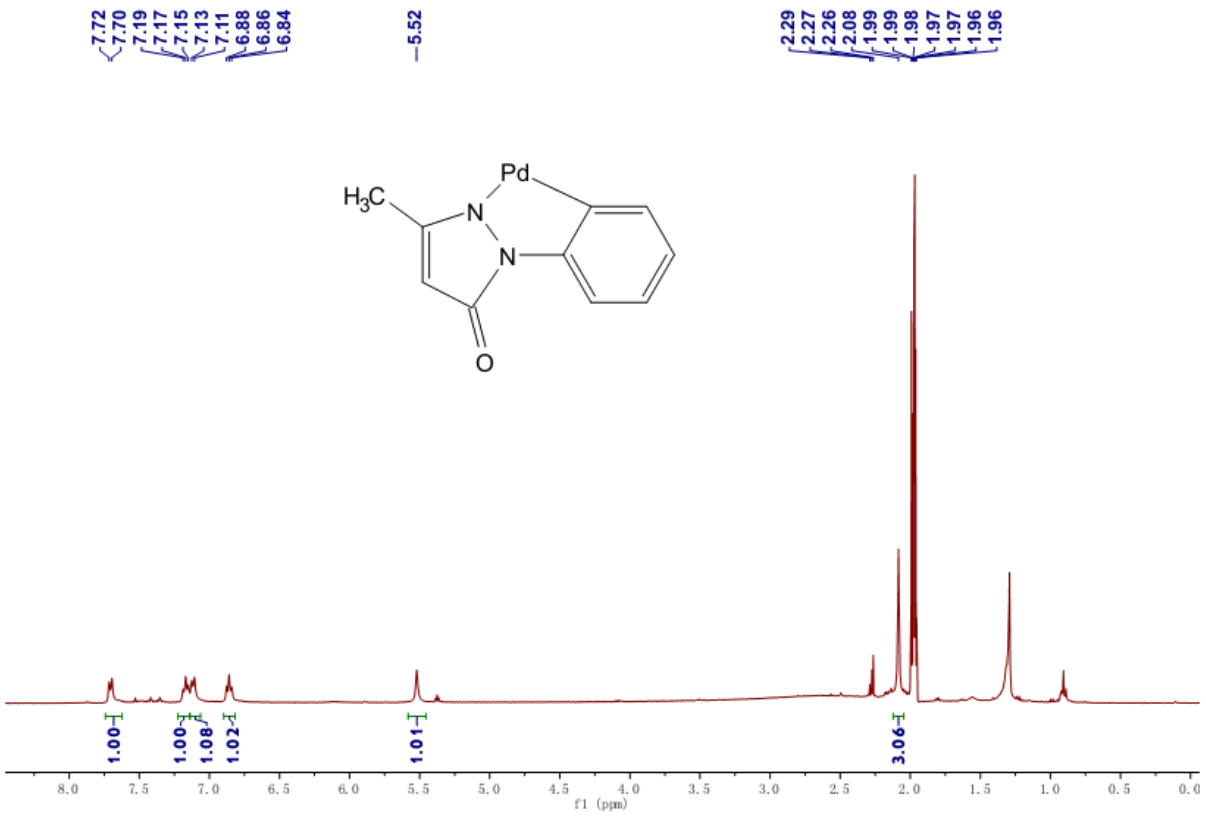
^{1}H and ^{13}C NMR spectra of compound **1w.**



^{1}H and ^{13}C NMR spectra of compound **7.**



^{1}H NMR spectra of compound **I.**



10. X-ray Data of Compound 1n.

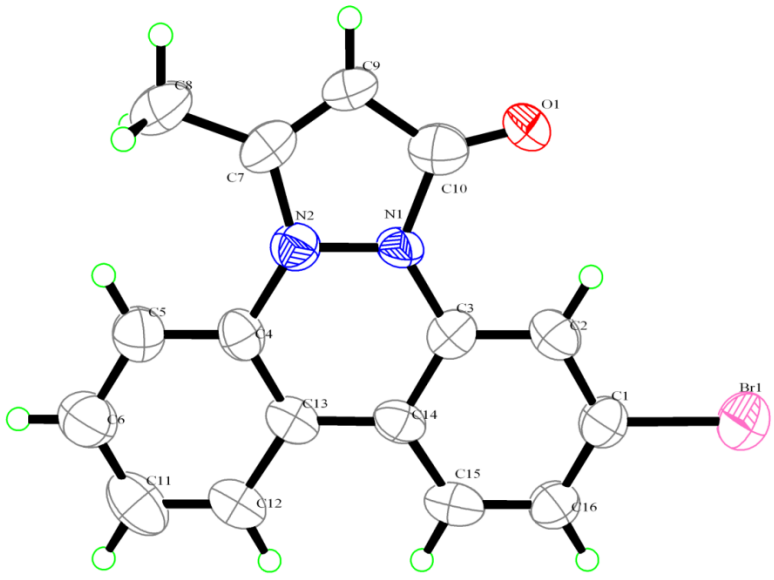


Table 4 Crystal data and structure refinement details for compound **1n**.

Identification code	2013251
Chemical formula	$C_{16}H_{11}BrN_2O$
Formula weight	326.01

Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal size	0.020 x 0.080 x 0.200 mm	
Crystal system	orthorhombic	
Space group	P c a 21	
Unit cell dimensions	a = 7.4355(4) Å	α = 90°
	b = 20.5015(12) Å	β = 90°
	c = 16.7167(9) Å	γ = 90°
Volume	2548.3(2) $Å^3$	
Z	4	
Density (calculated)	1.698 Mg/cm^3	
Absorption coefficient	3.222 mm^{-1}	
F(000)	1300	
Theta range for data collection	0.99 to 27.51°	
Index ranges	-9<=h<=9, -26<=k<=26, -21<=l<=21	
Reflections collected	39317	
Independent reflections	5862 [R(int) = 0.1042]	
Coverage of independent reflections	100.0%	
Absorption correction	multi-scan	
Structure solution technique	direct methods	
Structure solution program	SHELXS-97 (Sheldrick, 2008)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-97 (Sheldrick, 2008)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	5862 / 1 / 362	
Goodness-of-fit on F^2	0.907	
Δ/σ_{max}	0.863	
Final R indices	2893 data; I>2σ(I)	R1 = 0.0553, wR2 = 0.1352
	all data	R1 = 0.1439, wR2 = 0.1773
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.1000P)^2+0.0000P]$ where $P=(F_o^2+2F_c^2)/3$	
Absolute structure parameter	0.4(0)	
Largest diff. peak and hole	0.304 and -0.457 $eÅ^{-3}$	
R.M.S. deviation from mean	0.069 $eÅ^{-3}$	