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Supporting Information

Synthesis of New Tetracyclic Benzodiazepine-Fused Isoindolinones Using Recyclable Mesoporous Silica Nanoparticles

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1. General Information

All the commercially available chemicals and solvents were used without further purification. All reagents used to prepare the substrates were purchased from Sigma-Aldrich, Innochem, Aladdin. Morphology characterizations of MSNs were performed by TEM (Ht-7700, Japan) at an acceleration voltage of 120 kV and SEM (Hitachi S4800, Japan). The hydrodynamic diameter and zeta potential of MSNs were measured by Malvern Nano HT ZetaSizer (Malvern, UK). N_2 adsorption-desorption isotherm was conducted in a Micromeritics ASAP 2460 (Micromeritics, USA). TLC was performed using aluminum plates coated with SiO_2 (Merck 60, F-254) and visualized with UV light at 254 nm. Flash column chromatography was performed with silica gel (200-300 mesh). Melting points were determined on a Fargo MP-1D instrument. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker-DRX (400 or 600 MHz and 100 or 150 MHz, respectively) instruments in $CDCl_3$ and DMSO-*d6*. High-resolution mass spectra (HRMS) were recorded on a Thermo Scientific Q Exactive (ESI).

2. Preparation of mesoporous silica nanoparticles

MSNs with a particle size of 100 nm were synthesized by sol-gel method, with base as catalyst, hexadecyl trimethyl ammonium bromide (CTAB) as template, and tetraethyl orthosilicate (TEOS) as silica precursor. Specifically, 112 mL deionized water was added to a round bottom flask and 29-wt% NH_3 in water was used to adjust the pH of water to about 11. When the temperature of the solution rose to 50 ℃, 0.14 g of CTAB was added under stirring, and then 0.7 mL of TEOS was added dropwise to the solution. After stirring for 2 hours, the sample was centrifugated at 12000 r/min for 5 mins and then the precipitation was washed three times with ethanol and water respectively. The templates were removed by extraction. Simply, the sample was dispersed in acidic ethanol (ethanol: 37.2% HCl=100:1 v:v) stirring at 79 ℃ for 24 h and then the template-removed MSNs were washed thoroughly with ethanol and distilled water and dried for 12 h under vacuum at 50 ℃.

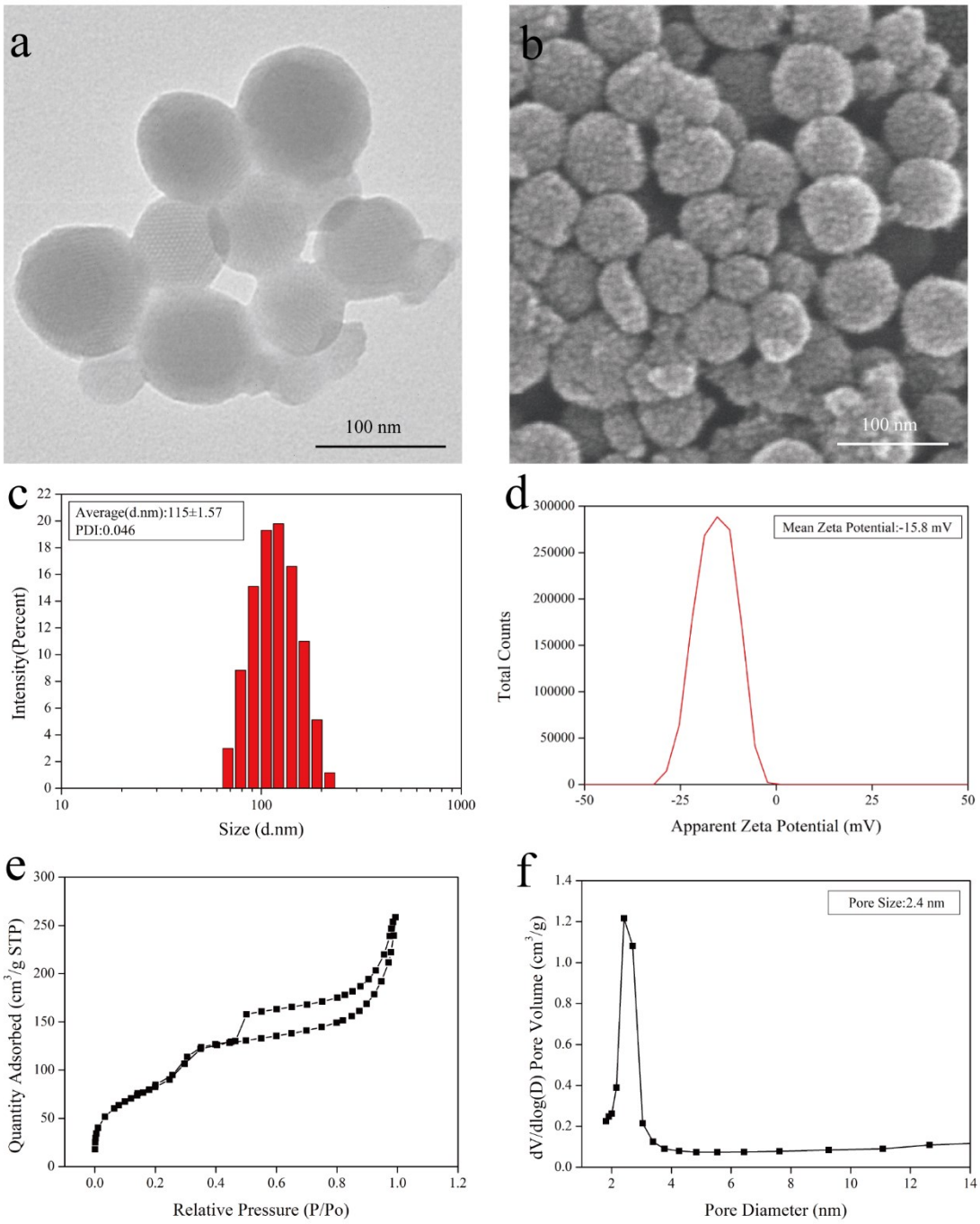


Figure S1. Characterization of the mesoporous silica nanoparticles (MSNs). TEM (a) and SEM (b) of MSNs; Hydrodynamic size distribution (c) and Zeta potential (d) of MSNs; Nitrogen adsorption-desorption isotherm of MSNs at 77 K (e) and the pore size distribution curves of MSNs (f).

Morphology characterizations of MSNs were performed by Transmission Electron Microscopy (TEM, Ht-7700, Japan) at an acceleration voltage of 120 kV and Scanning Electron Microscope (SEM, Hitachi S4800, Japan). As shown in Figure S1a and S1b, MSNs appeared regular spheres with obvious pore channels. The hydrodynamic diameter and zeta potential of MSNs were measured by Malvern Nano HT ZetaSizer

(Malvern, UK), the results showed that the average size of MSNs was about 115 nm and the potential was -15.8 mV (Figure S1c and S1d), each test was repeated three times.

Table S1. Nitrogen adsorption/ desorption isotherms measurement data and pore characteristic of MSNs.

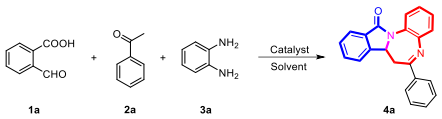
Sample	BET surface area (m^2/g)	Pore volume (cm^3/g)	Pore Size (nm)
MSNs	311.03	0.42	2.4

N_2 adsorption-desorption isotherm was conducted in a Micromeritics ASAP-2460 (Micromeritics, USA). The surface areas and pore size distribution of MSNs were obtained through Brunauer-Emmett-Teller (BET) and Barret-Joyner-Halenda (BJH) method, respectively. MSNs exhibited a typical IV mesoporous nitrogen adsorption-desorption isotherm with a pore diameter of 2.4 nm (Figure S1e and S1f). And the surface area of MSNs calculated by BET was 311.03 m^2/g (Table S1).

3. Optimization of reaction conditions

Initially, 2-formylbenzoic acid **1a** (0.5 mmol), acetophenone **2a** (0. 5 mmol) and 1,2-diaminobenzene **3a** (1.5 mmol) were used as model substrates to optimize the reaction conditions in the presence of 10-wt% MSNs (Table S2). Compound **4a** was obtained in 9% yield when the reaction was performed in DCE (Table S2, entry1). Encouraged by this result, we further examined the reactivity in other solvents (Table S2, entries 2-7). To our satisfaction, product **4a** was afforded in 88% yield when the reaction was carried out in acetic acid (Table S2, entry 7). Other solvents such as EtOH, DMSO, DMF, H_2O and toluene turned out to be less efficient, and failed to generate compound **4a** (Table S2, entries 2-6). Other solid catalysts, such as SiO_2, amberlyst-15 (A-15) and montmorillonite-K10 (Mont-K10) could also catalyze this transformation, giving compound **4a** in 35-59% yields (Table S2, entries 8-10). We also found that compound **4a** was afforded in 33% yield when the reaction was carried out in AcOH only (Table S2, entry 11), indicating the effectiveness of the MSNs catalysts. According to above optimizations, the optimal reaction conditions entailed 2-formylbenzoic acid **1a** (0.5 mmol), acetophenone **2a** (0.5 mmol), 1,2-diaminobenzene **3a** (1.5 mmol), MSNs (10-wt%), AcOH (2 mL), 100 ℃, 24 h (Table 1, entry 7).

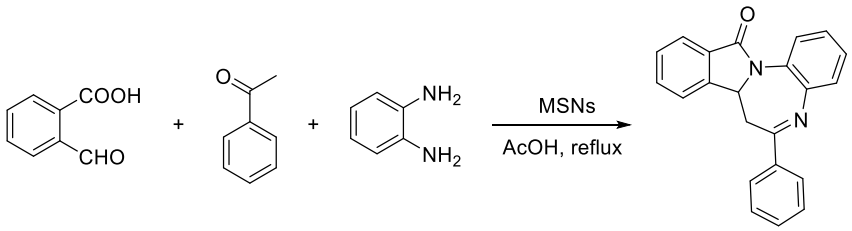
Table S2. Optimization of the reaction conditions [a]



Entry	Catalyst (wt%)	Solvent	T (℃)	**4a** (%)[b]
1	MSNs	DCE	80	9
2	MSNs	EtOH	80	0
3	MSNs	DMSO	80	0
4	MSNs	DMF	80	0
5	MSNs	H_2O	80	0
6	MSNs	Toluene	80	0
7	**MSNs**	**AcOH**	**100**	**88**
8	SiO_2	AcOH	100	59
9	A-15	AcOH	100	35
10	Mont-K10	AcOH	100	39
11	-	AcOH	100	33

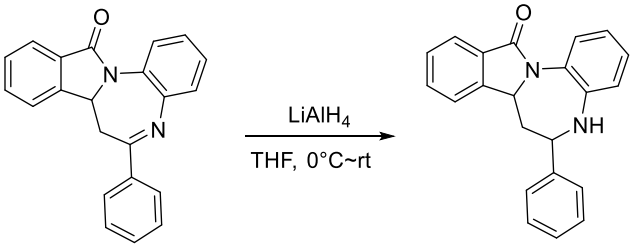
[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), **3a** (1.5 mmol), catalyst (10-wt%), solvent (2 mL), 24 h. [b] NMR yields determined by ^{1}H NMR using the triphenylmethane as an internal standard.

4. General Procedure for the Synthesis of Compounds 4a-4r



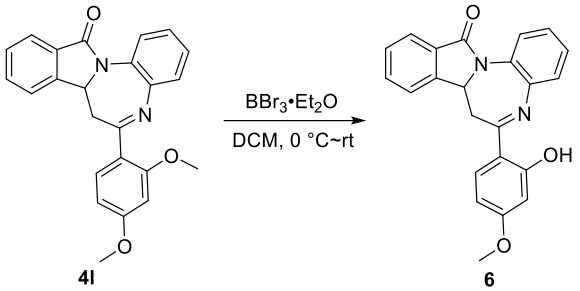
To a microwave reaction tube were added 2-formylbenzoic acid (75 mg, 0.5 mmol), acetophenone (59 μL, 0.5 mmol), *o*-phenylenediamine (162 mg, 1.5 mmol), MSNs (30 mg, 10-wt%) and AcOH (2 mL). The tube was then sealed, and the mixture was stirred at 120 ℃ for 24 h. Upon completion of the reaction (monitored by TLC), the solvent was evaporated, and the residue was purified by silica gel chromatography using petroleum ether/ethyl acetate to afford the product **4a** (136 mg, yield: 84%). Compound **4b**-**4r** were prepared following the same procedure.

5. Preparation of Compounds 5-7



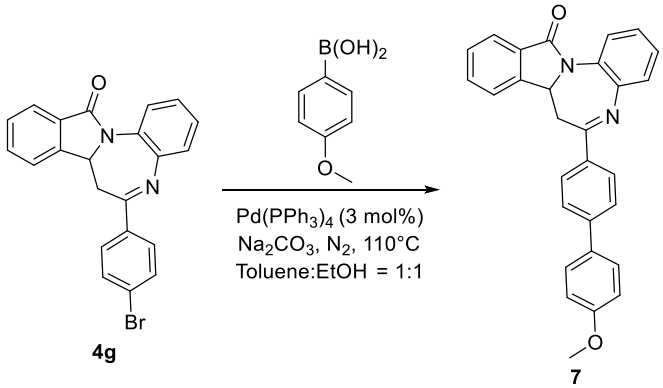
4a **5**

To a solution of **4a** (0.5 mmol) in dry THF (5 mL) was added dropwise a THF solution (3 mL) of $LiAlH_4$ (0.6 mmol) at 0 °C. The resulting solution was stirred at room temperature until completion of the reaction (monitored by TLC), after evaporation of the solvent, the residue was purified by silica gel chromatography using petroleum ether/ethyl acetate to afford the product **5** (146 mg, yield: 90%).



4l **6**

To a solution of **4l** (0.5 mmol) in DCM was added dropwise an Et_2O solution (0.75 mL) of BBr_3 (0.75 mmol) at 0 °C. The resulting mixture was stirred at room temperature until completion of the reaction (monitored by TLC), after evaporation of the solvent, the residue was purified by silica gel chromatography using petroleum ether/ethyl acetate to afford the product **6** (150 mg, yield: 81%).



4g **7**

To a round bottom flask were added **4g** (0.5 mmol), (4-methoxyphenyl)boric acid (0.6 mmol), $Pd(PPh_3)_4$ (3 mol%), solvent (5 mL, toluene: EtOH = 1:1) and Na_2CO_3 (1.25 mmol, dissolved in a small amount of water). The mixture was stirred at 110 °C for 24 h under nitrogen atmosphere. Upon completion of the reaction (monitored by TLC), the equivalent of water and EtOAc were added to the residue. The phases were separated and the aqueous phase was extracted with EtOAc (15 mL × 3). The organic

layer was washed with brine and dried over Na_2SO_4, then filtered, and concentrated to give the residue which was purified by silica gel chromatography using petroleum ether/ethyl acetate to afford the product **7** (156 mg, yield: 73%).

6. Reuse Experiment

To a microwave reaction tube were added 2-formylbenzoic acid (75 mg, 0.5 mmol), acetophenone (59 μL, 0.5 mmol), *o*-phenylenediamine (162 mg, 1.5 mmol), MSNs (30 mg, 10-wt%) and AcOH (2 mL). Then the tube was sealed, and the mixture was stirred at 120 ℃ for 24 h. After completion of the reaction, the NMR yields was determined by ^{1}H NMR using triphenylmethane (122 mg, 0.5 mmol) as an internal standard. Then the residue was filtered and washed thoroughly with EtOH: H_2O (1:1), followed by drying at 120 ℃ under vacuum for 24 h to give the recycled MSNs catalysts for the next cycle.

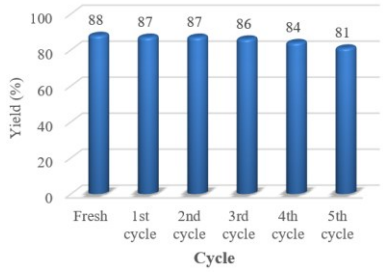
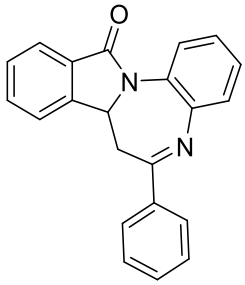


Figure S2. NMR yield obtained for each cycle.

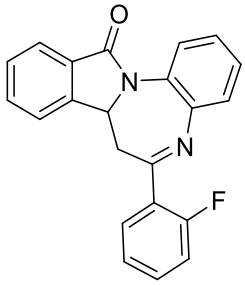
7. Characterization Data

6-phenyl-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4a)



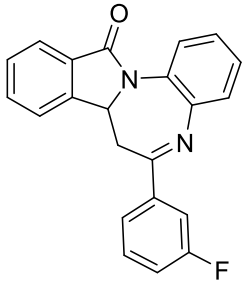
Yield 84% (136 mg); white solid; m.p. 160~161 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.09 - 8.02 (m, 2H), 8.00 - 7.95 (m, 1H), 7.77 (d, *J* = 7.1 Hz, 1H), 7.73 - 7.69 (m, 1H), 7.68 - 7.61 (m, 2H), 7.60 - 7.49 (m, 4H), 7.24 - 7.16 (m, 2H), 6.06 (t, *J* = 5.7 Hz, 1H), 4.12 (dd, *J* = 18.5, 5.7 Hz, 1H), 3.94 (dd, *J* = 18.5, 5.9 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 197.5, 157.2, 148.6, 148.1, 136.1, 133.7, 132.1, 129.9, 128.8, 128.7, 128.3, 128.2, 124.3, 122.3, 121.7, 121.2, 119.8, 110.9, 55.6, 42.0. **HRMS (ESI) m/z**: calculated for $C_{22}H_{16}N_2O$ $[M+H]^+$: 325.1341, found: 325.1342.

6-(2-fluorophenyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4b)



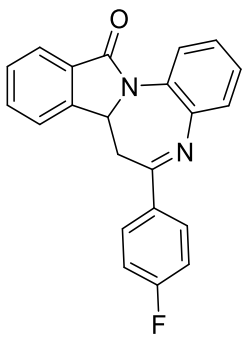
Yield 91% (156 mg); white solid; m.p. 128~129 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 7.98 - 7.89 (m, 2H), 7.81 - 7.77 (m, 1H), 7.73 - 7.64 (m, 3H), 7.61 - 7.52 (m, 2H), 7.39 - 7.30 (m, 2H), 7.26 - 7.16 (m, 2H), 6.04 (t, *J* = 5.7 Hz, 1H), 4.09 - 4.00 (m, 1H), 3.89 - 3.79 (m, 1H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 195.3, 161.1 (d, *J* = 254 Hz), 157.2, 148.4, 148.3, 135.6 (d, *J* = 9 Hz), 132.1, 130.3 (d, *J* = 2 Hz), 129.8, 128.8, 128.4, 124.9, 124.8 (d, *J* = 4 Hz), 124.8, 124.3, 122.2, 121.4 (d, *J* = 43 Hz), 119.8, 116.9 (d, *J* = 23 Hz), 110.8, 55.4, 46.0. **HRMS (ESI) m/z**: calculated for $C_{22}H_{15}FN_2O$ $[M+H]^+$: 343.1247, found: 343.1246.

6-(3-fluorophenyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4c)



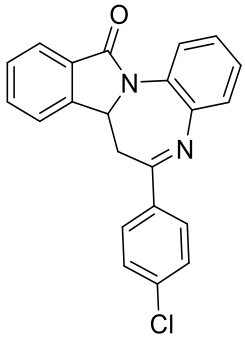
Yield 85% (145 mg); white solid; m.p. 157~158 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.07 - 7.94 (m, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.85 - 7.79 (m, 1H), 7.76 (d, *J* = 7.0 Hz, 1H), 7.73 - 7.68 (m, 1H), 7.68 - 7.62 (m, 1H), 7.62 - 7.48 (m, 4H), 7.26 - 7.14 (m, 2H), 6.05 (t, *J* = 5.7 Hz, 1H), 4.16 (dd, *J* = 18.7, 5.5 Hz, 1H), 3.97 (dd, *J* = 18.7, 6.0 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 196.6, 162.14 (d, *J* = 244 Hz), 157.2, 148.5, 148.3, 138.3 (d, *J* = 6 Hz), 132.1, 131.0, 130.9, 129.8, 128.8, 128.4, 124.4 (d, *J* = 2 Hz), 124.3, 121.9 (d, *J* = 61 Hz), 121.2, 120.6 (d, *J* = 22 Hz), 119.8, 114.7 (d, *J* = 23 Hz), 110.9, 55.4, 42.2. **HRMS (ESI) m/z**: calculated for $C_{22}H_{15}FN_2O$ $[M+H]^+$: 343.1247, found : 343.1246.

6-(4-fluorophenyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4d)



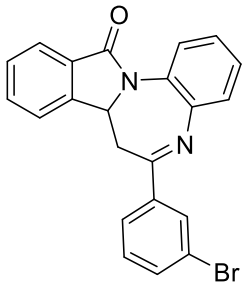
Yield 70% (120 mg); white solid; m.p. 151~152 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.20 - 8.08 (m, 2H), 8.01 - 7.90 (m, 1H), 7.76 (d, *J* = 7.0 Hz, 1H), 7.73 - 7.67 (m, 1H), 7.67 - 7.61 (m, 1H), 7.61 - 7.49 (m, 2H), 7.35 (t, *J* = 8.9 Hz, 2H), 7.26 - 7.15 (m, 2H), 6.04 (t, *J* = 5.7 Hz, 1H), 4.12 (dd, *J* = 18.5, 5.7 Hz, 1H), 3.93 (dd, *J* = 18.5, 6.0 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 196.1, 165.3 (d, *J* = 251 Hz), 157.2, 148.6, 148.3, 132.9 (d, *J* = 3 Hz), 132.1, 131.3 (d, *J* = 10 Hz), 129.8, 128.8, 128.4, 124.3, 122.2, 121.6, 121.2, 119.8, 115.8 (d, *J* = 21 Hz), 110.9, 55.5, 42.0. **HRMS (ESI) m/z**: calculated for $C_{22}H_{15}FN_2O$ $[M+H]^+$: 343.1247, found: 343.1246.

6-(4-chlorophenyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4e)



Yield 63% (113 mg); white solid; m.p. 191~192 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 7.98 (d, *J* = 8.6 Hz, 2H), 7.93 - 7.87 (m, 1H), 7.69 (d, *J* = 7.1 Hz, 1H), 7.66 - 7.61 (m, 1H), 7.59 - 7.55 (m, 1H), 7.55 - 7.45 (m, 4H), 7.17 - 7.08 (m, 2H), 5.98 (t, *J* = 5.7 Hz, 1H), 4.06 (dd, *J* = 18.6, 5.6 Hz, 1H), 3.87 (dd, *J* = 18.6, 6.0 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 196.6, 157.2, 148.5, 148.3, 138.6, 134.8, 132.1, 130.1, 129.8, 128.8, 128.8, 128.4, 124.3, 122.2, 121.6, 121.2, 119.8, 110.9, 55.4, 42.1. **HRMS (ESI) m/z**: calculated for $C_{22}H_{15}ClN_2O$ $[M+H]^+$: 359.0951, found: 359.0952.

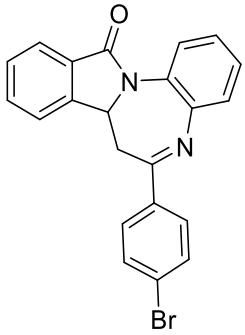
6-(3-bromophenyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4f)



Yield 75% (150 mg); white solid; m.p. 162~163 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.17 (s, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.98 - 7.92 (m, 1H), 7.89 - 7.82 (m, 1H), 7.75 (d, *J* = 7.0 Hz, 1H), 7.72 - 7.68 (m, 1H), 7.67 - 7.61 (m, 1H), 7.61 - 7.52 (m, 2H), 7.48 (t, *J* = 7.9 Hz, 1H), 7.24 - 7.17 (m, 2H), 6.03 (t, *J* = 5.7 Hz, 1H), 4.16 (dd, *J* = 18.8, 5.5 Hz, 1H), 3.98 (dd, *J* = 18.8, 6.0 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 196.6, 157.2, 148.5, 148.2, 138.1, 136.2, 132.1, 131.0, 130.8, 129.8, 128.8, 128.4, 127.1, 124.3, 122.2, 122.2, 121.6, 121.2, 119.8, 110.9, 55.4, 42.1. **HRMS (ESI) m/z**: calculated for $C_{22}H_{15}BrN_2O$ $[M+H]^+$: 403.0446, found: 403.0446.

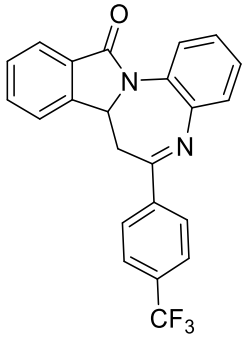
6-(4-bromophenyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-

one (4g)



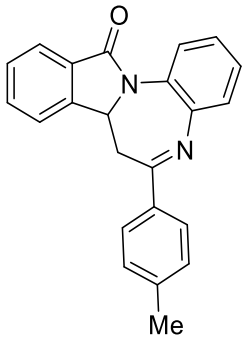
Yield 83% (166 mg); white solid; m.p. 194~195 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 7.97 - 7.86 (m, 3H), 7.74 - 7.61 (m, 4H), 7.59 - 7.54 (m, 1H), 7.54 - 7.44 (m, 2H), 7.17 - 7.10 (m, 2H), 5.97 (t, *J* = 5.7 Hz, 1H), 4.05 (dd, *J* = 18.6, 5.6 Hz, 1H), 3.86 (dd, *J* = 18.6, 6.0 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 196.8, 157.2, 148.5, 148.3, 135.2, 132.1, 131.8, 130.2, 129.8, 128.8, 128.4, 127.8, 124.3, 122.2, 121.6, 121.2, 119.8, 110.8, 55.4, 42.0. **HRMS (ESI) m/z**: calculated for $C_{22}H_{15}BrN_2O$ $[M+H]^+$: 403.0446, found: 403.0447.

6-(4-(trifluoromethyl)phenyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4h)



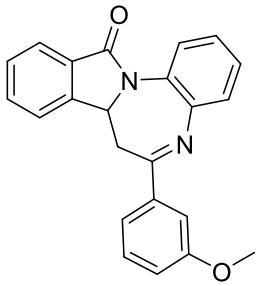
Yield 55% (107 mg); white solid; m.p. 183~184 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.21 (d, *J* = 8.2 Hz, 2H), 8.02 - 7.95 (m, 1H), 7.90 (d, *J* = 8.3 Hz, 2H), 7.77 (d, *J* = 7.0 Hz, 1H), 7.73 - 7.63 (m, 2H), 7.63 - 7.51 (m, 2H), 7.25 - 7.17 (m, 2H), 6.06 (t, *J* = 5.6 Hz, 1H), 4.22 (dd, *J* = 18.7, 5.4 Hz, 1H), 4.03 (dd, *J* = 18.8, 6.1 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 197.1, 157.2, 148.5, 148.1, 139.2, 132.9 (q, *J* = 32 Hz), 132.1, 129.9, 129.0, 128.8, 128.4, 125.7 (q, *J* = 4 Hz), 124.4, 123,7 (q, *J* = 270 Hz), 122.3, 121.7, 121.2, 119.8, 110.9, 55.4, 42.3. **HRMS (ESI) m/z**: calculated for $C_{23}H_{15}F_3N_2O$ $[M+H]^+$: 393.1215, found: 393.1215.

6-(*p*-tolyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4i)



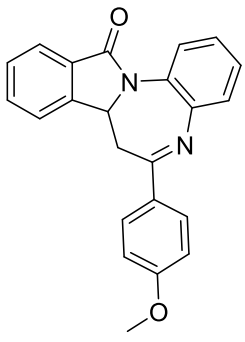
Yield 86% (145 mg); white solid; m.p. 158~159 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.02 - 7.89 (m, 3H), 7.76 (d, *J* = 7.2 Hz, 1H), 7.73 - 7.67 (m, 1H), 7.64 - 7.59 (m, 1H), 7.58 - 7.50 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.22 - 7.14 (m, 2H), 6.05 (t, *J* = 5.8 Hz, 1H), 4.05 (dd, *J* = 18.4, 5.9 Hz, 1H), 3.87 (dd, *J* = 18.4, 5.9 Hz, 1H), 2.36 (s, 3H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 197.0, 157.2, 148.7, 148.3, 144.2, 133.7, 132.1, 129.8, 129.3, 128.7, 128.4, 128.3, 124.3, 122.2, 121.6, 121.2, 119.8, 110.9, 55.6, 42.0, 21.1. **HRMS (ESI) m/z**: calculated for $C_{23}H_{18}N_2O$ $[M+H]^+$: 339.1497, found: 339.1498.

6-(3-methoxyphenyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4j)



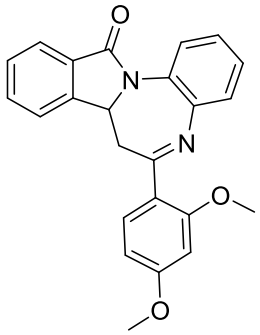
Yield 75% (132 mg); white solid; m.p. 129~130 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 7.96 (d, *J* = 6.5 Hz, 1H), 7.76 (d, *J* = 7.0 Hz, 1H), 7.73 - 7.67 (m, 1H), 7.67 - 7.59 (m, 2H), 7.60 - 7.53 (m, 2H), 7.53 - 7.49 (m, 1H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.26 - 7.15 (m, 3H), 6.04 (t, *J* = 5.7 Hz, 1H), 4.11 (dd, *J* = 18.6, 5.6 Hz, 1H), 3.95 (dd, *J* = 18.6, 5.9 Hz, 1H), 3.79 (s, 3H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 197.3, 159.4, 157.2, 148.6, 148.3, 137.5, 132.1, 129.9, 129.8, 128.7, 128.4, 124.3, 122.2, 121.6, 121.2, 120.7, 119.9, 119.8, 112.6, 110.9, 55.5, 55.4, 42.1. **HRMS (ESI) m/z**: calculated for $C_{23}H_{18}N_2O_2$ $[M+H]^+$: 355.1447, found: 355.1447.

6-(4-methoxyphenyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4k)



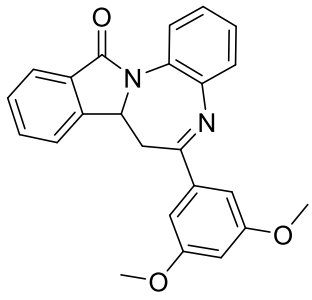
Yield 76% (134 mg); white solid; m.p. 152~153 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.02 (d, *J* = 8.9 Hz, 2H), 7.98 - 7.95 (m, 1H), 7.76 (d, *J* = 7.2 Hz, 1H), 7.73 - 7.68 (m, 1H), 7.64 - 7.58 (m, 1H), 7.58 - 7.49 (m, 2H), 7.27 - 7.11 (m, 2H), 7.02 (d, *J* = 8.9 Hz, 2H), 6.05 (t, *J* = 5.8 Hz, 1H), 4.02 (dd, *J* = 18.2, 6.0 Hz, 1H), 3.89 - 3.79 (m, 4H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 195.8, 163.5, 157.2, 148.7, 148.3, 132.1, 130.6, 129.8, 129.2, 128.7, 128.4, 124.3, 122.2, 121.6, 121.2, 119.8, 113.9, 110.9, 55.7, 55.6, 41.7. **HRMS (ESI) m/z**: calculated for $C_{23}H_{18}N_2O_2$ $[M+H]^+$: 355.1447, found: 355.1447.

6-(2,4-dimethoxyphenyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4l)



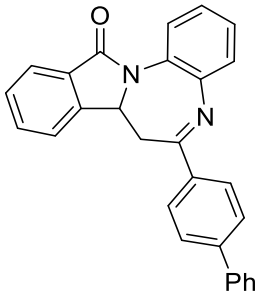
Yield 75% (144 mg); white solid; m.p. 117~118 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 7.97 - 7.92 (m, 1H), 7.83 (d, *J* = 8.7 Hz, 1H), 7.74 (d, *J* = 6.5 Hz, 1H), 7.72 - 7.66 (m, 1H), 7.60 - 7.53 (m, 3H), 7.23 - 7.17 (m, 2H), 6.65 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.61 (d, *J* = 2.2 Hz, 1H), 6.04 (t, *J* = 5.9 Hz, 1H), 3.89 - 3.79 (m, 4H), 3.76 (s, 3H), 3.66 (dd, *J* = 18.2, 5.9 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 195.8, 164.8, 161.1, 157.1, 148.8, 148.3, 132.2, 132.1, 129.8, 128.7, 128.3, 124.3, 122.2, 121.6, 121.2, 119.8, 119.5, 110.8, 106.3, 98.4, 55.9, 55.9, 55.7, 47.0. **HRMS (ESI) m/z**: calculated for $C_{24}H_{20}N_2O_3$ $[M+H]^+$: 385.1552, found: 385.1553.

6-(3,5-dimethoxyphenyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4m)



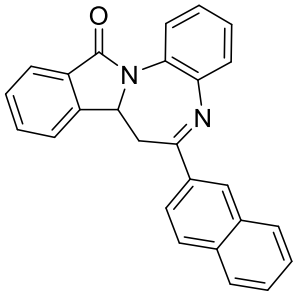
Yield 74% (143 mg); white solid; m.p. 150~151 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 7.99 - 7.94 (m, 1H), 7.75 (d, *J* = 6.9 Hz, 1H), 7.73 - 7.67 (m, 1H), 7.65 - 7.61 (m, 1H), 7.60 - 7.51 (m, 2H), 7.27 - 7.17 (m, 2H), 7.14 (d, *J* = 2.3 Hz, 2H), 6.77 (t, *J* = 2.2 Hz, 1H), 6.03 (t, *J* = 5.7 Hz, 1H), 4.10 (dd, *J* = 18.7, 5.6 Hz, 1H), 3.95 (dd, *J* = 18.7, 5.9 Hz, 1H), 3.77 (s, 6H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 197.2, 160.6, 157.3, 148.6, 148.3, 138.2, 132.1, 129.8, 128.7, 128.5, 124.3, 122.2, 121.6, 121.2, 119.8, 110.9, 105.8, 105.8, 55.5, 55.5, 42.0. **HRMS (ESI) m/z**: calculated for $C_{24}H_{20}N_2O_3$ $[M+H]^+$: 385.1552, found: 385.1552.

6-([1,1'-biphenyl]-4-*yl*)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4n)



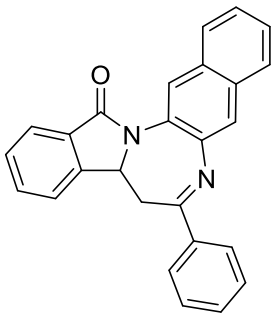
Yield 82% (164 mg); white solid; m.p. 213~214 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.12 (d, *J* = 8.5 Hz, 2H), 8.02 - 7.97 (m, 1H), 7.82 (d, *J* = 8.5 Hz, 2H), 7.79 (d, *J* = 7.0 Hz, 1H), 7.77 - 7.70 (m, 3H), 7.68 - 7.63 (m, 1H), 7.62 - 7.54 (m, 2H), 7.53 - 7.46 (m, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 7.27 - 7.14 (m, 2H), 6.08 (t, *J* = 5.7 Hz, 1H), 4.14 (dd, *J* = 18.5, 5.8 Hz, 1H), 3.96 (dd, *J* = 18.5, 5.9 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 197.1, 157.3, 148.7, 148.3, 145.0, 138.7, 135.0, 132.2, 129.8, 129.1, 128.9, 128.8, 128.5, 127.0, 126.9, 124.3, 122.2, 121.6, 121.2, 119.8, 110.9, 55.6, 42.1. **HRMS (ESI) m/z**: calculated for $C_{28}H_{20}N_2O$ $[M+H]^+$: 401.1654, found: 401.1655.

6-(naphthalen-2-*yl*)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4o)



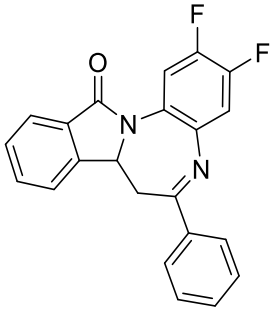
Yield 88% (164 mg); white solid; m.p. 185~186 ℃; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ 8.75 (s, 1H), 8.16 - 7.91 (m, 5H), 7.81 (d, *J* = 6.9 Hz, 1H), 7.73 - 7.64 (m, 3H), 7.63 - 7.51 (m, 3H), 7.27 - 7.13 (m, 2H), 6.13 (t, *J* = 5.8 Hz, 1H), 4.25 (dd, *J* = 18.4, 5.9 Hz, 1H), 4.05 (dd, *J* = 18.3, 6.0 Hz, 1H). **^{13}C NMR** (100 MHz, DMSO-*d6*) δ 197.5, 157.2, 148.7, 148.3, 135.2, 133.4, 132.2, 132.1, 130.7, 129.8, 129.6, 128.9, 128.8, 128.4, 128.4, 127.6, 127.0, 124.4, 123.4, 122.2, 121.6, 121.2, 119.8, 110.9, 55.6, 42.3. **HRMS (ESI) m/z**: calculated for $C_{26}H_{18}N_2O$ $[M+H]^+$: 375.1497, found: 375.1497.

7-phenyl-8,8*a*-dihydro-13*H*-naphtho[2',3':2,3][1,4]diazepino[7,1-*a*]isoindol-13-one (4p)



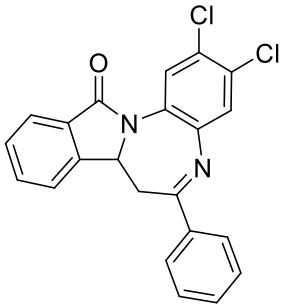
Yield 86% (160 mg); white solid; m.p. 185~186 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.15 (d, *J* = 7.4 Hz, 1H), 8.04 - 7.96 (m, 3H), 7.92 - 7.84 (m, 1H), 7.77 (s, 1H), 7.68 - 7.62 (m, 1H), 7.63 - 7.56 (m, 2H), 7.56 - 7.51 (m, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.44 - 7.37 (m, 2H), 6.20 (dd, *J* = 7.2, 5.3 Hz, 1H), 4.00 (dd, *J* = 18.1, 5.1 Hz, 1H), 3.51 (dd, *J* = 18.1, 7.4 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.0, 161.3, 149.2, 149.0, 136.2, 134.1, 132.4, 130.8, 130.5, 130.2, 129.2, 128.9, 128.4, 128.2, 127.4, 124.5, 124.3, 123.6, 122.8, 117.5, 105.7, 55.4, 43.0. **HRMS (ESI) m/z**: calculated for $C_{26}H_{18}N_2O$ $[M+H]^+$: 375.1497, found: 375.1496.

2,3-difluoro-6-phenyl-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4q)



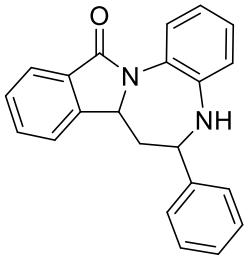
Yield 81% (145 mg); white solid; m.p. 218~219 ℃; **^{1}H NMR** (600 MHz, DMSO-*d6*) δ 8.02 (d, *J* = 7.6 Hz, 2H), 7.94 (d, *J* = 6.7 Hz, 1H), 7.84 (dd, *J* = 10.9, 7.5 Hz, 1H), 7.75 (t, *J* = 8.2 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.59 - 7.55 (m, 2H), 7.53 (t, *J* = 7.8 Hz, 2H), 6.01 (t, *J* = 5.8 Hz, 1H), 4.18 (dd, *J* = 18.6, 5.2 Hz, 1H), 3.96 (dd, *J* = 18.6, 6.5 Hz, 1H).**^{13}C NMR** (150 MHz, DMSO-*d6*) δ 198.1, 159.7, 149.1, 147.8 (t, *J* = 15 Hz), 146.2 (t, *J* = 15 Hz), 144.1 (d, *J* = 10.5 Hz), 136.6, 134.2, 130.6, 129.3, 129.2, 128.7, 128.5, 128.2 (d, *J* = 12 Hz), 124.9, 121.7, 107.6 (d, *J* = 19.5 Hz), 99.7 (d, *J* = 24 Hz), 56.5, 42.2. **HRMS (ESI) m/z**: calculated for $C_{22}H_{14}F_2N_2O$ $[M+H]^+$: 361.1152, found: 361.1150.

2,3-dichloro-6-phenyl-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (4r)



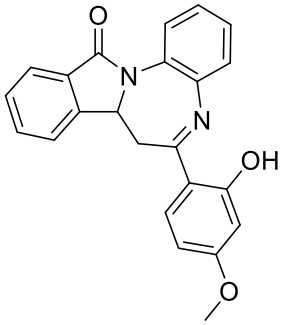
Yield 76% (149 mg); white solid; m.p. 226~227 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 6.9 Hz, 1H), 8.02 - 7.94 (m, 2H), 7.88 (s, 1H), 7.68 - 7.45 (m, 7H), 6.08 (t, *J* = 6.1 Hz, 1H), 3.75 (dd, *J* = 18.2, 6.1 Hz, 1H), 3.56 (dd, *J* = 18.2, 6.3 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.7, 159.6, 148.2, 135.9, 134.3, 131.3, 130.6, 129.4, 129.0, 128.2, 128.1, 126.7, 126.3, 124.0, 122.4, 121.6, 111.7, 55.7, 43.5. **HRMS (ESI) m/z**: calculated for $C_{22}H_{14}Cl_2N_2O$ $[M+H]^+$: 393.0561, found: 393.0561.

6-phenyl-7*a*,12-dihydro-7*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindole (5)



Yield 90% (146 mg); white solid; m.p. 168~169 ℃; H. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 - 7.93 (m, 1H), 7.81 - 7.68 (m, 2H), 7.55 - 7.47 (m, 1H), 7.46 - 7.34 (m, 2H), 7.33 - 7.28 (m, 2H), 7.27 - 7.25 (m, 1H), 7.24 - 7.15 (m, 4H), 5.64 - 5.58 (m, 1H), 5.15 - 4.88 (m, 1H), 3.16 - 2.65 (m, 1H), 2.95 - 2.85 (m, 1H), 2.33 - 2.16 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.0, 157.4, 148.6, 148.3, 148.0, 144.2, 143.9, 133.1, 131.9, 129.6, 129.5, 128.9, 128.7, 128.5, 127.9, 127.8, 125.7, 125.4, 124.2, 123.4, 122.8, 122.6, 122.2, 122.1, 122.0, 120.4, 110.5, 109.8, 70.6, 70.5, 57.7, 57.3, 44.6, 42.4. **HRMS (ESI) m/z**: calculated for $C_{22}H_{18}N_2$ $[M+H]^+$: 327.1497, found: 327.1498.

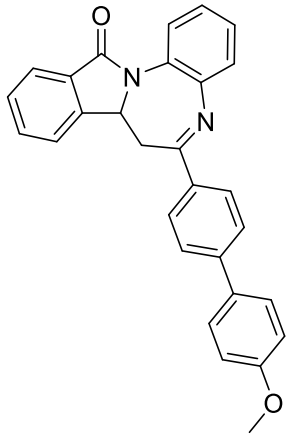
6-(2-hydroxy-4-methoxyphenyl)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (6)



Yield 81% (150 mg); white solid; m.p. 232~233 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 15.09 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.68 - 7.60 (m, 2H), 7.58 - 7.53 (m, 1H), 7.52 - 7.42 (m, 2H), 7.37 - 7.31 (m, 2H), 7.19 (d, *J* = 9.1 Hz, 1H), 6.34 (d, *J* = 2.6 Hz, 1H), 6.24 (dd, *J* = 9.0, 2.6 Hz, 1H), 5.56 (d, *J* = 5.8 Hz, 1H), 3.75 (s, 3H), 3.65 (dd, *J* = 14.4,

1.7 Hz, 1H), 3.37 (dd, *J* = 14.5, 7.3 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.8, 167.6, 165.3, 164.1, 143.3, 142.6, 132.3, 132.2, 130.0, 129.4, 129.3, 129.3, 129.2, 126.6, 126.4, 124.6, 121.9, 112.4, 106.7, 101.3, 69.1, 55.3, 32.1. **HRMS (ESI) m/z**: calculated for $C_{23}H_{18}N_2O_3$ $[M+H]^+$: 371.1396, found: 371.1396.

6-(4'-methoxy-[1,1'-biphenyl]-4-*yl*)-7,7*a*-dihydro-12*H*-benzo[2,3][1,4]diazepino[7,1-*a*]isoindol-12-one (7)

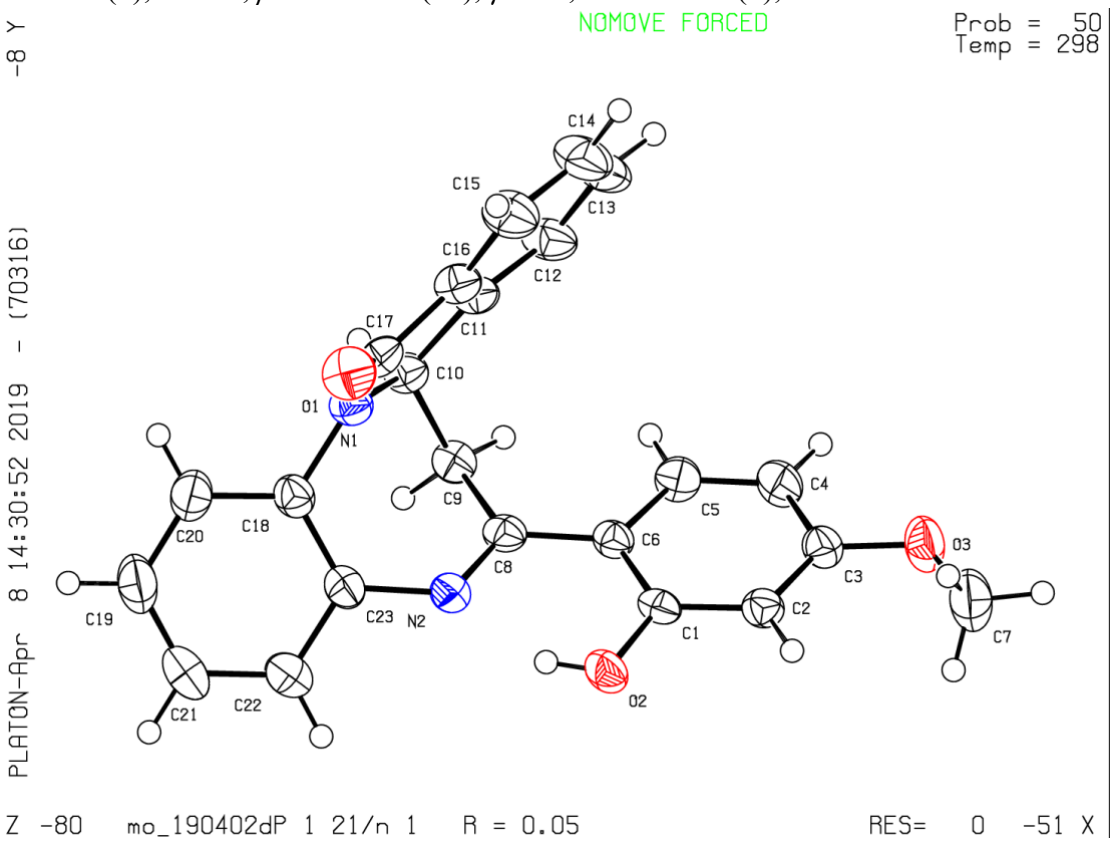


Yield 73% (156 mg); white solid; m.p. 166~167 ℃; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.5 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.85 (d, *J* = 7.3 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.62 - 7.51 (m, 4H), 7.50 - 7.40 (m, 2H), 7.31 - 7.20 (m, 2H), 6.99 (d, *J* = 8.8 Hz, 2H), 6.19 - 6.08 (m, 1H), 3.95 - 3.82 (m, 4H), 3.51 (dd, *J* = 18.0, 7.1 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.4, 160.1, 157.7, 148.8, 148.4, 146.3, 134.2, 132.0, 131.8, 129.9, 129.1, 128.9, 128.8, 128.4, 126.8, 124.1, 122.8, 122.3, 122.1, 120.7, 114.5, 110.1, 55.4, 55.4, 43.4. **HRMS (ESI) m/z**: calculated for $C_{29}H_{22}N_2O_2$ $[M+H]^+$: 431.1760, found: 431.1761.

8. X-ray Crystallographic Data

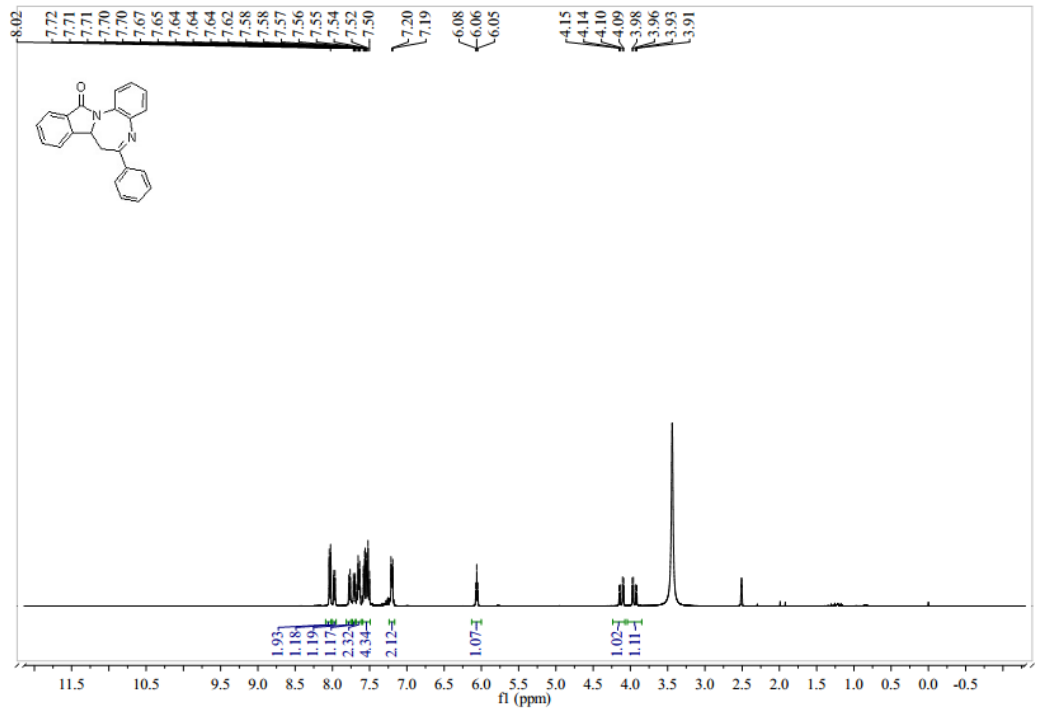
X-ray Single Crystal Structure Analysis of **6**

X-ray crystallographic data of **6**: CCDC (1908638), T = 298K, $C_{23}H_{18}N_2O_3$, Mr = 370.39, monoclinic, space group: P 21/n, a = 9.7282 (15), b = 14.5036 (12), c = 13.5002(9), $\alpha = 90$, $\beta = 108.564$ (12), $\gamma = 90$, V = 1805.7 (4), Z = 4.

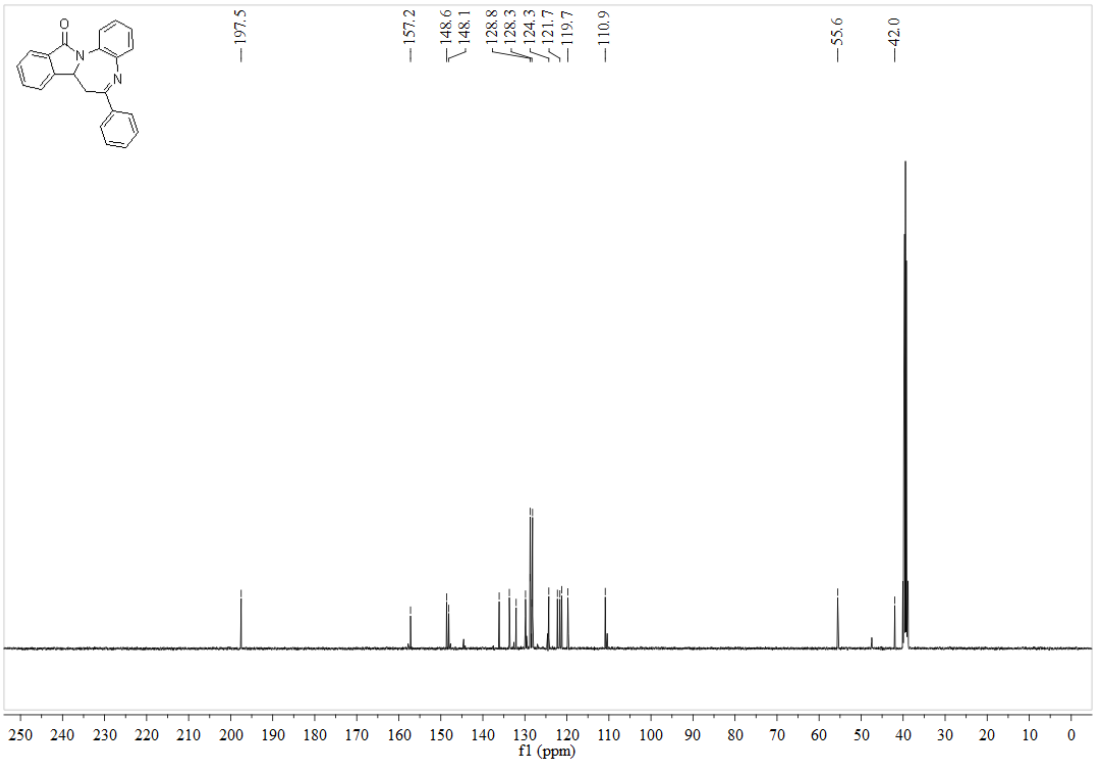


9. Representative NMR Spectra

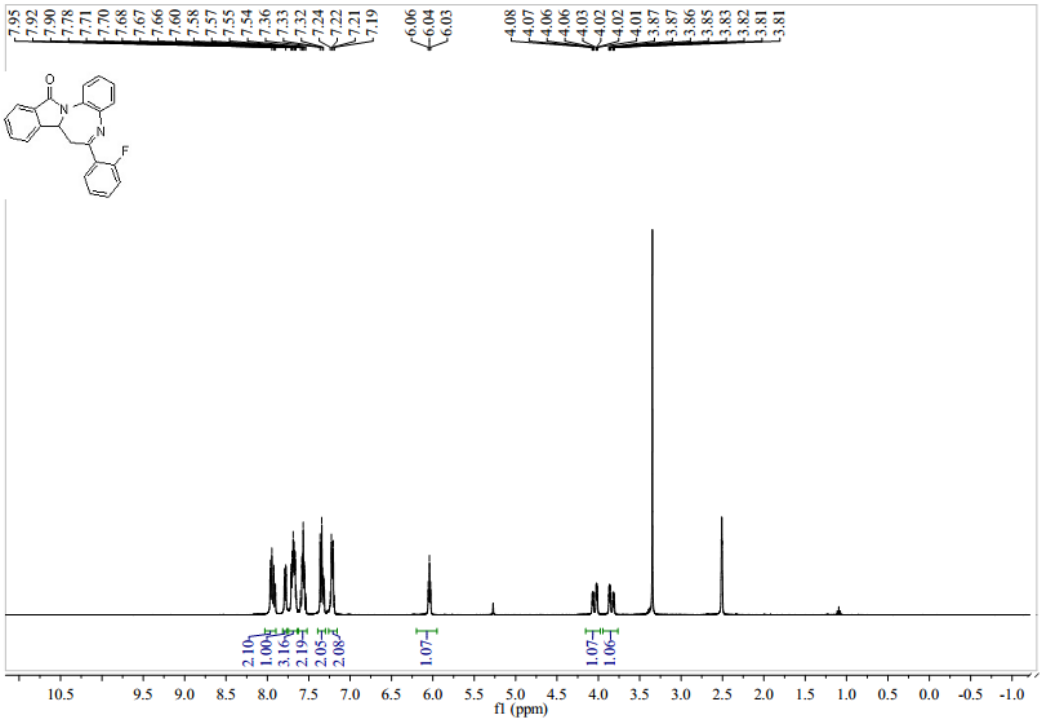
^{1}H NMR spectrum of compound 4a



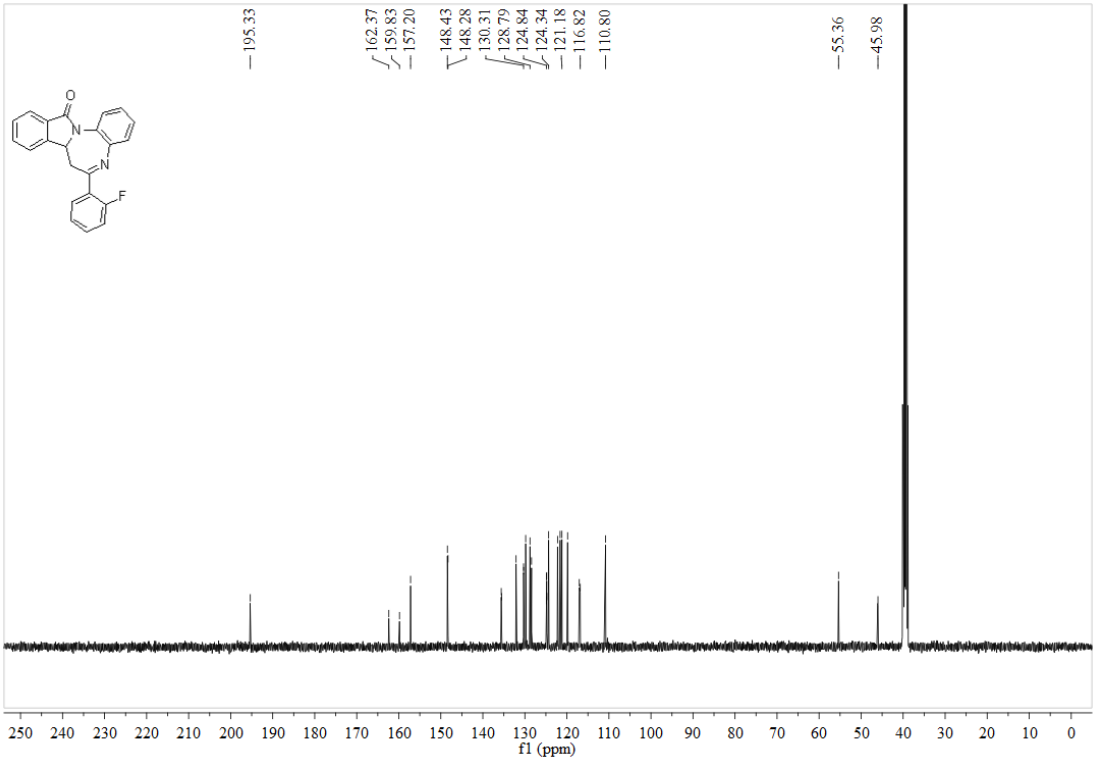
^{13}C NMR spectrum of compound 4a



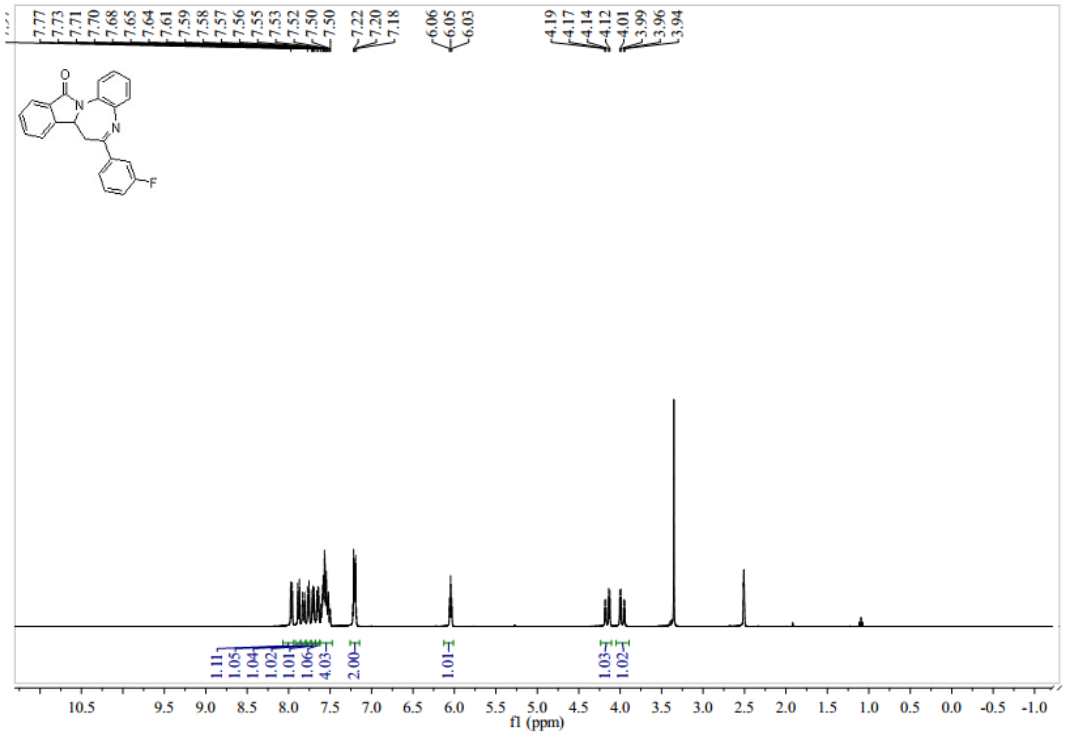
^{1}H NMR spectrum of compound 4b



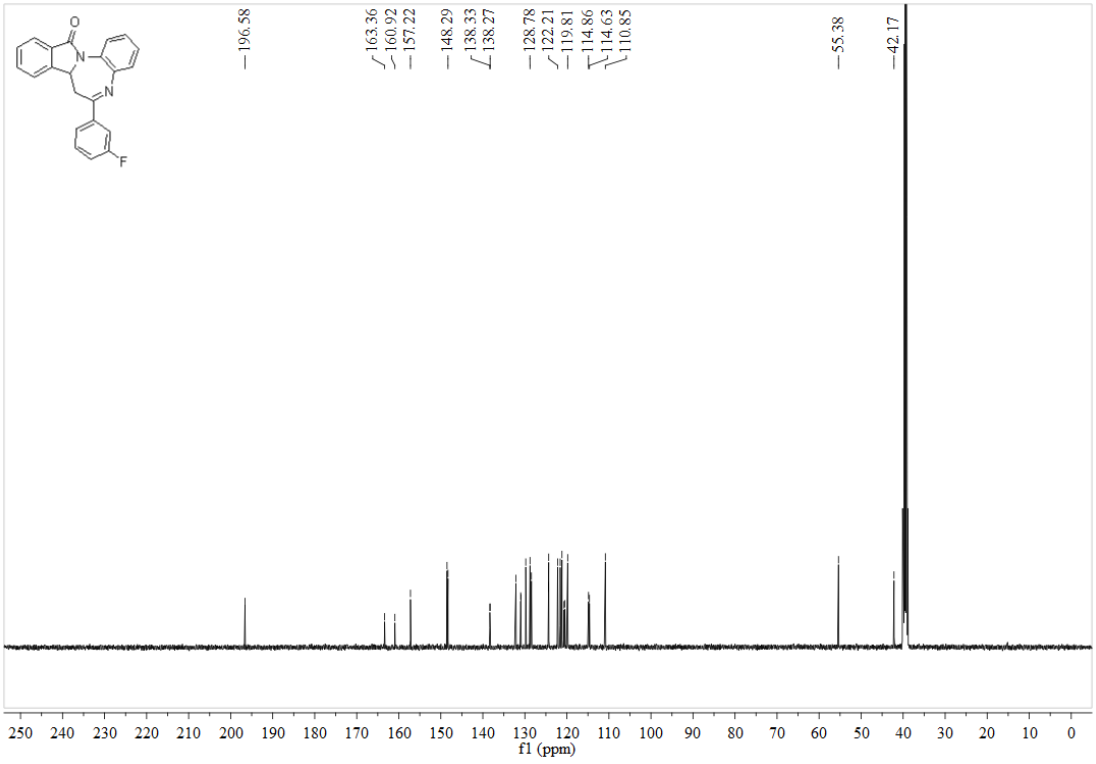
^{13}C NMR spectrum of compound 4b



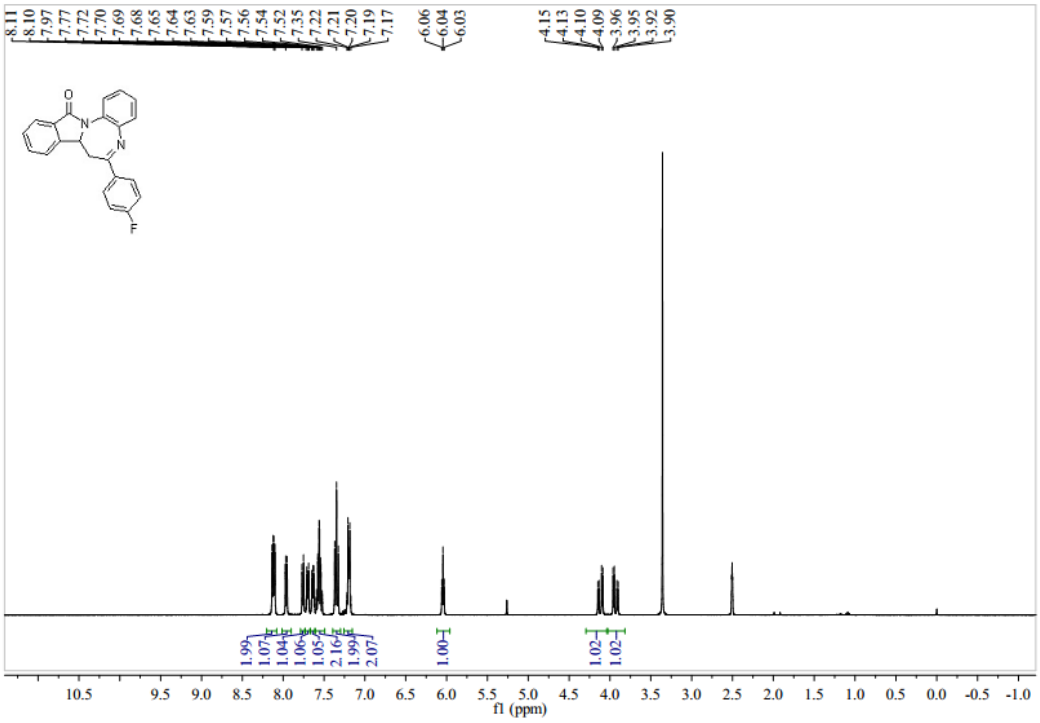
^{1}H NMR spectrum of compound 4c



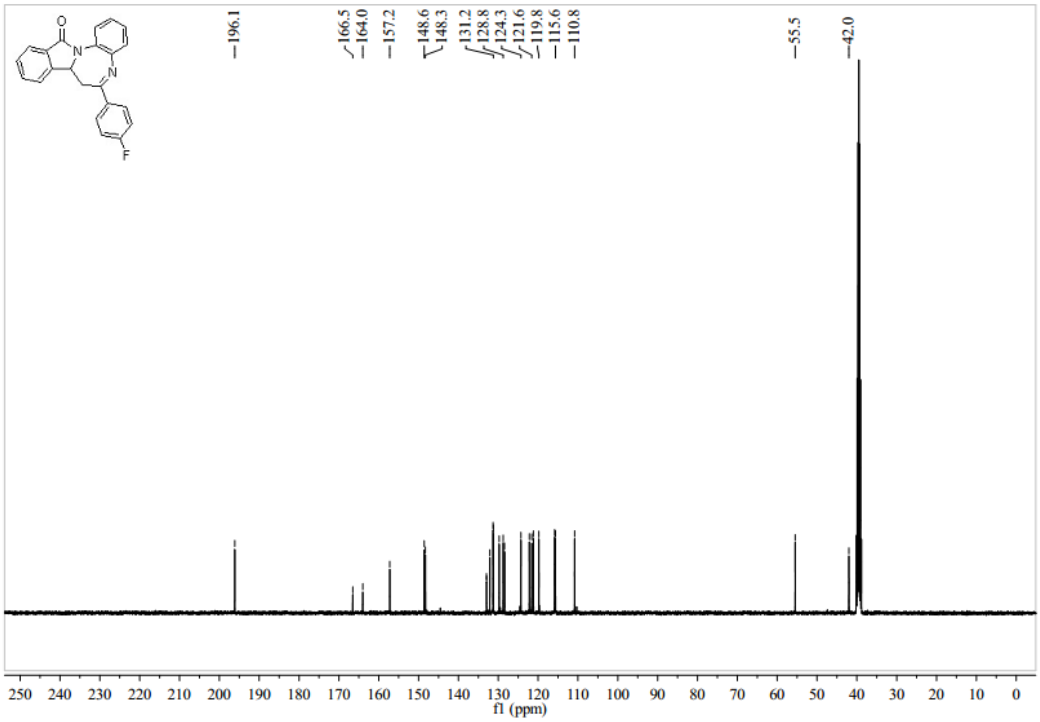
^{13}C NMR spectrum of compound 4c



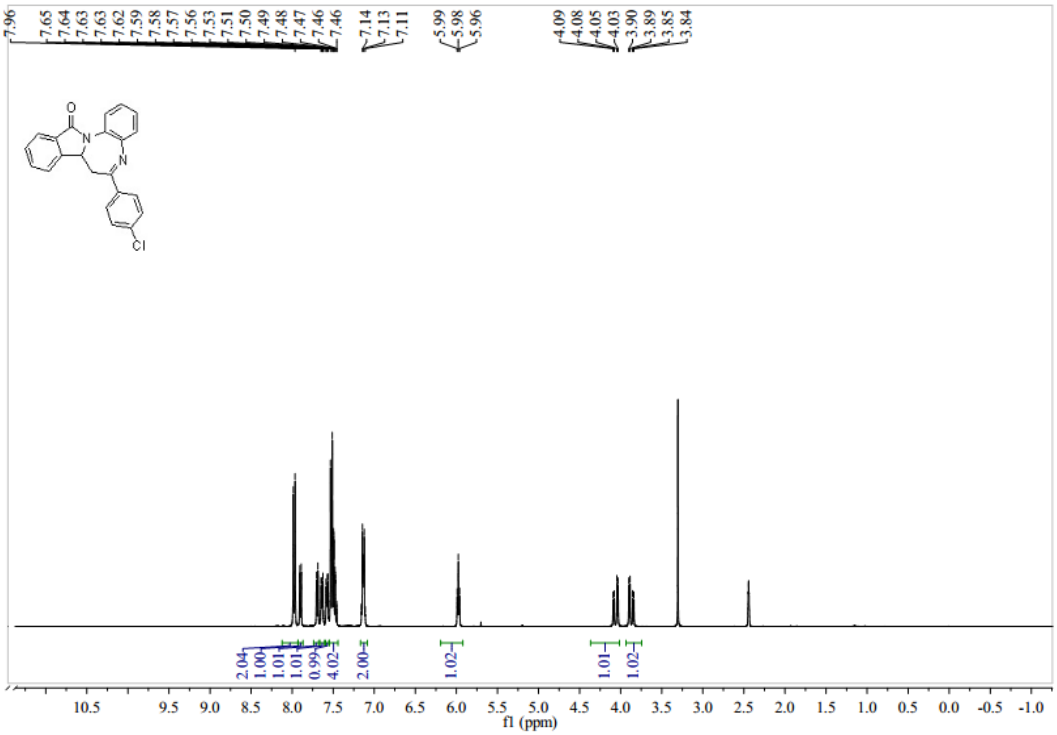
^{1}H NMR spectrum of compound 4d



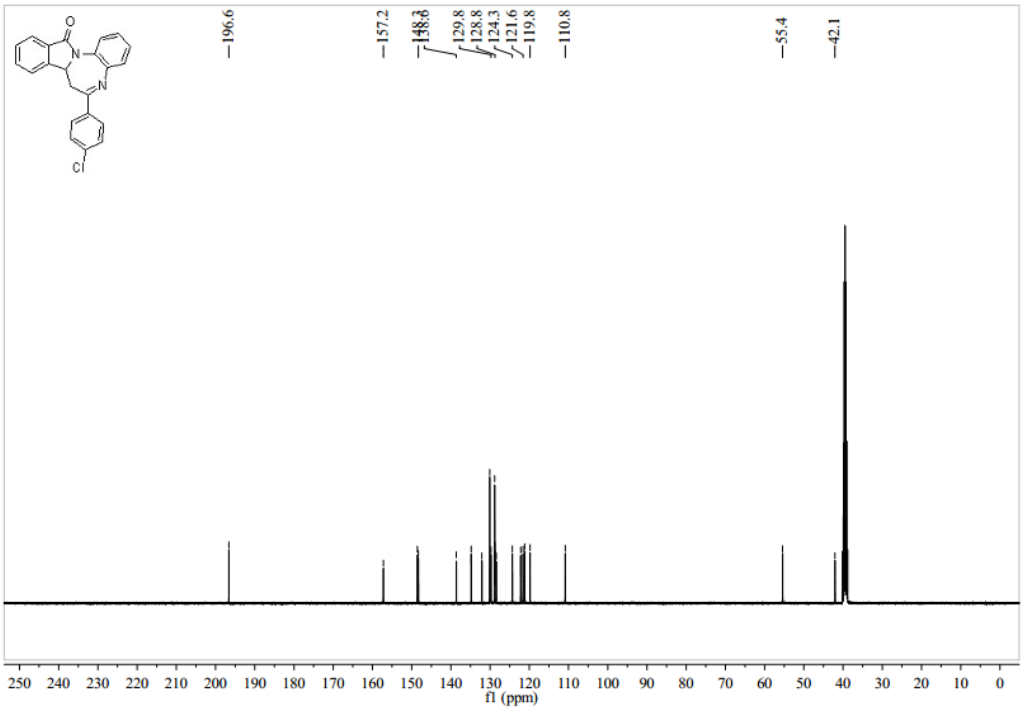
^{13}C NMR spectrum of compound 4d



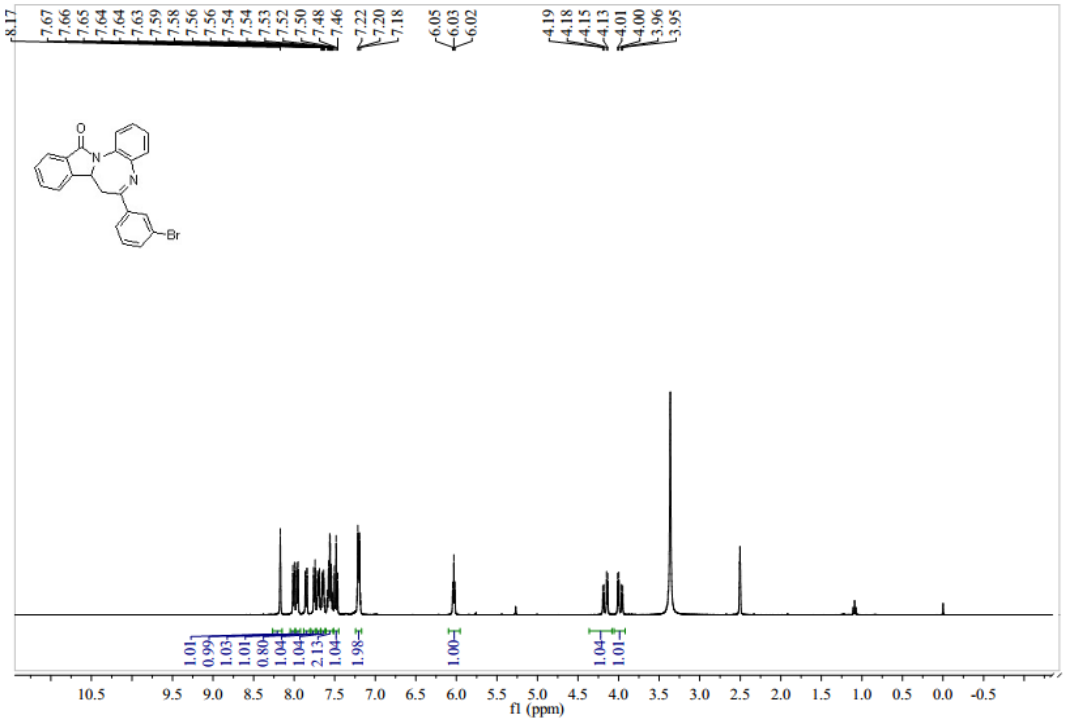
^{1}H NMR spectrum of compound 4e



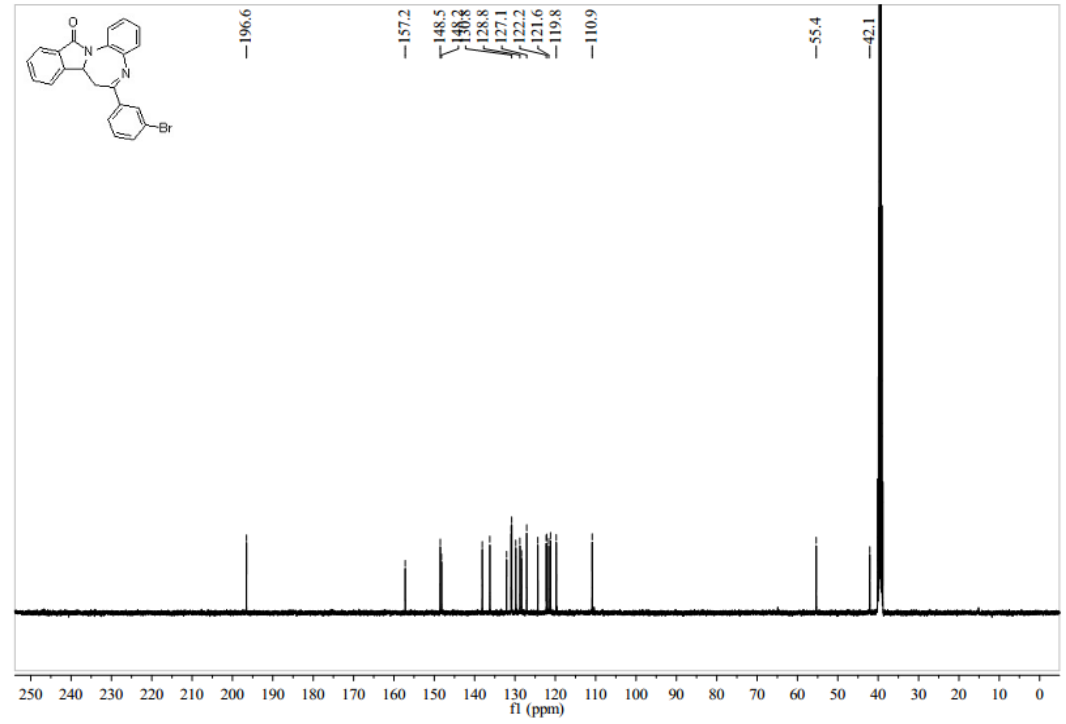
^{13}C NMR spectrum of compound 4e



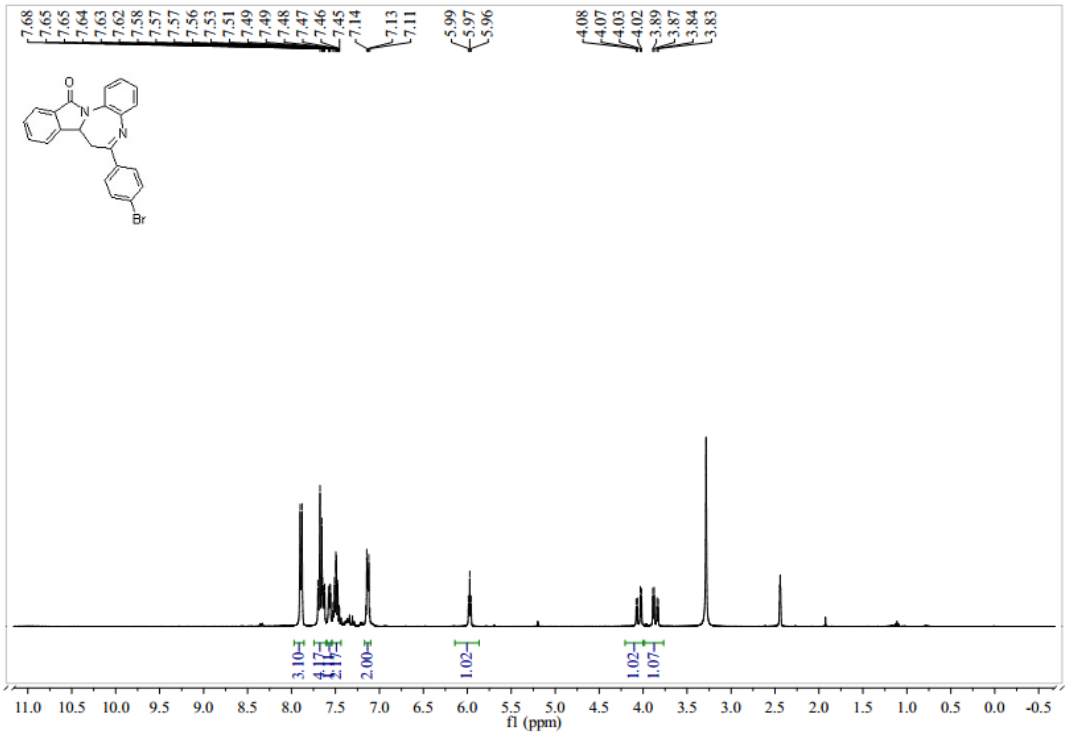
^{1}H NMR spectrum of compound 4f



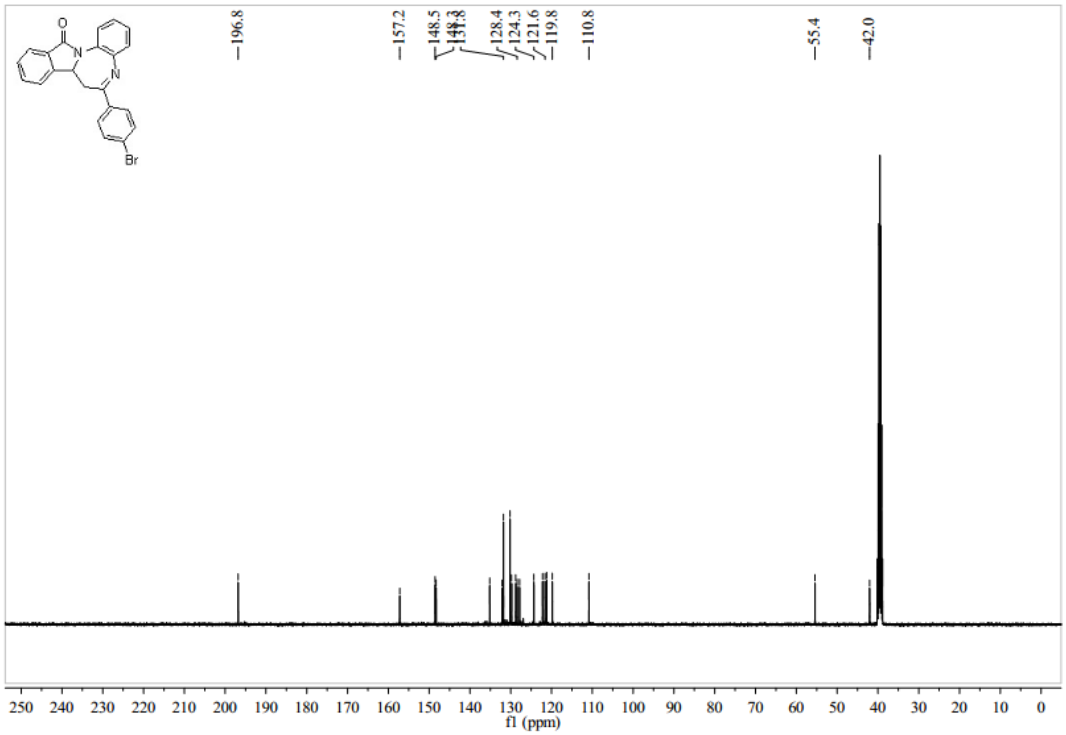
^{13}C NMR spectrum of compound 4f



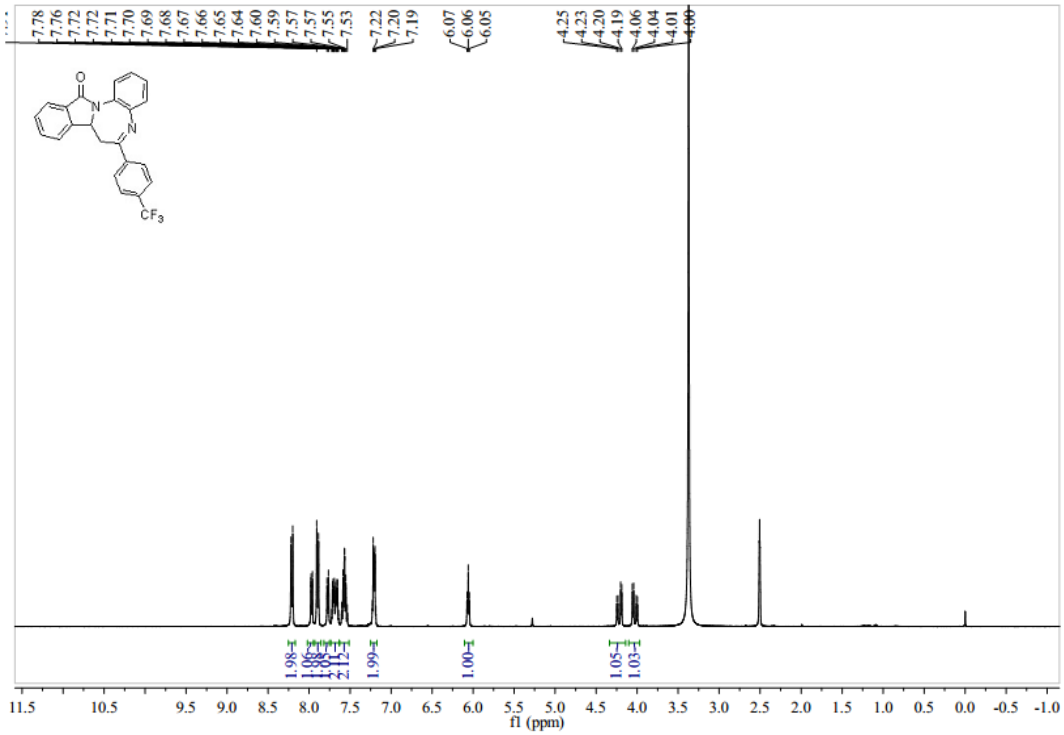
^{1}H NMR spectrum of compound 4g



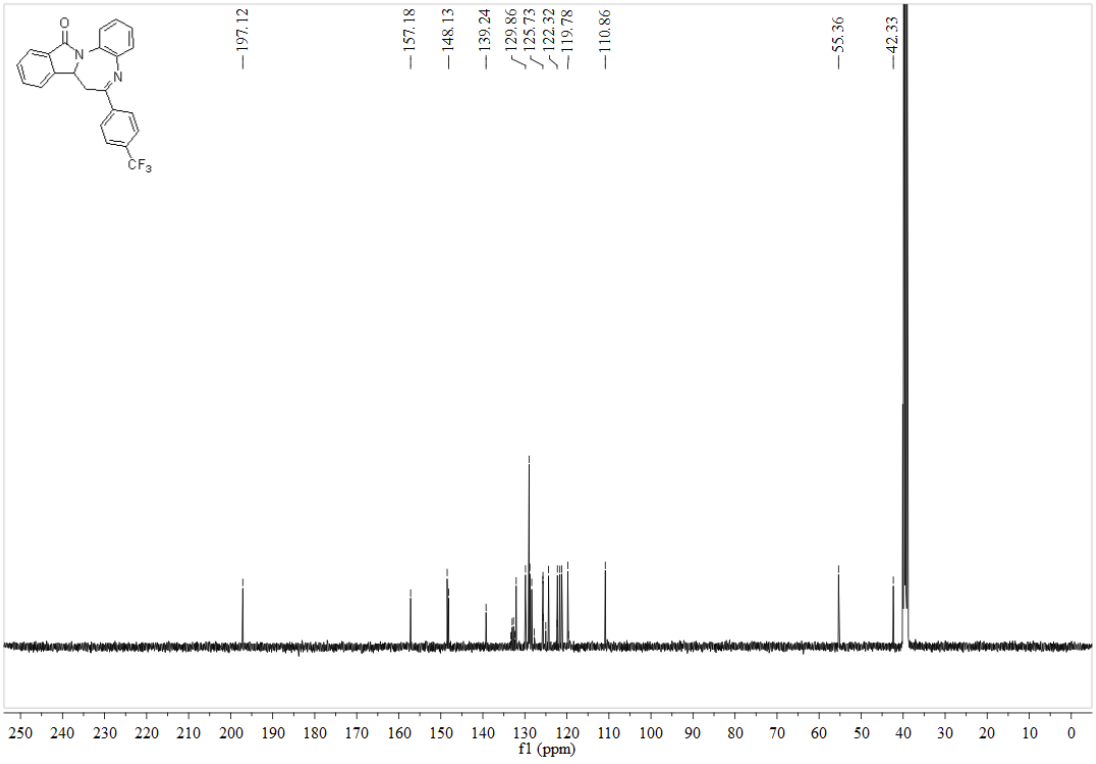
^{13}C NMR spectrum of compound 4g



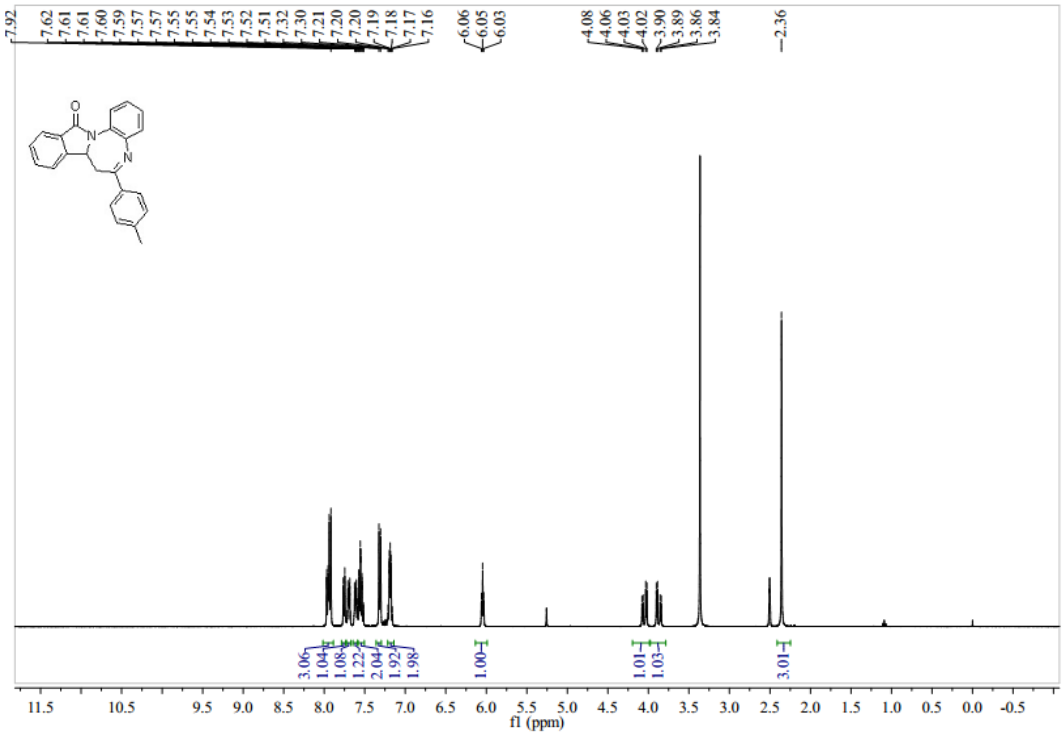
^{1}H NMR spectrum of compound 4h



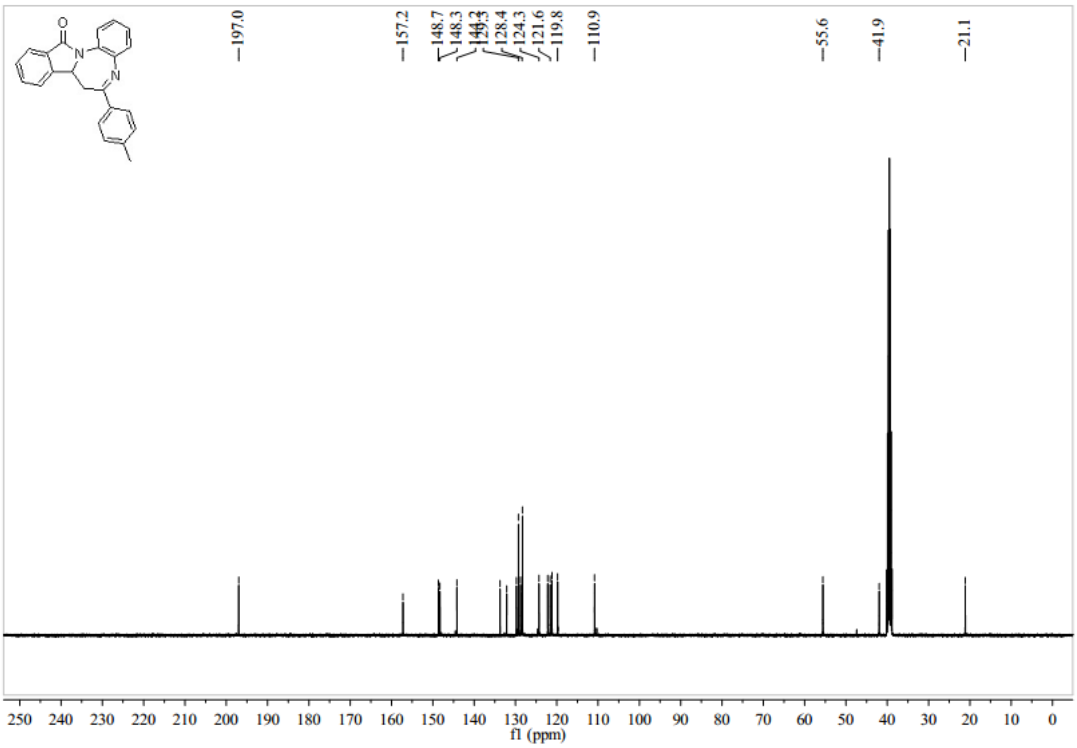
^{13}C NMR spectrum of compound 4h



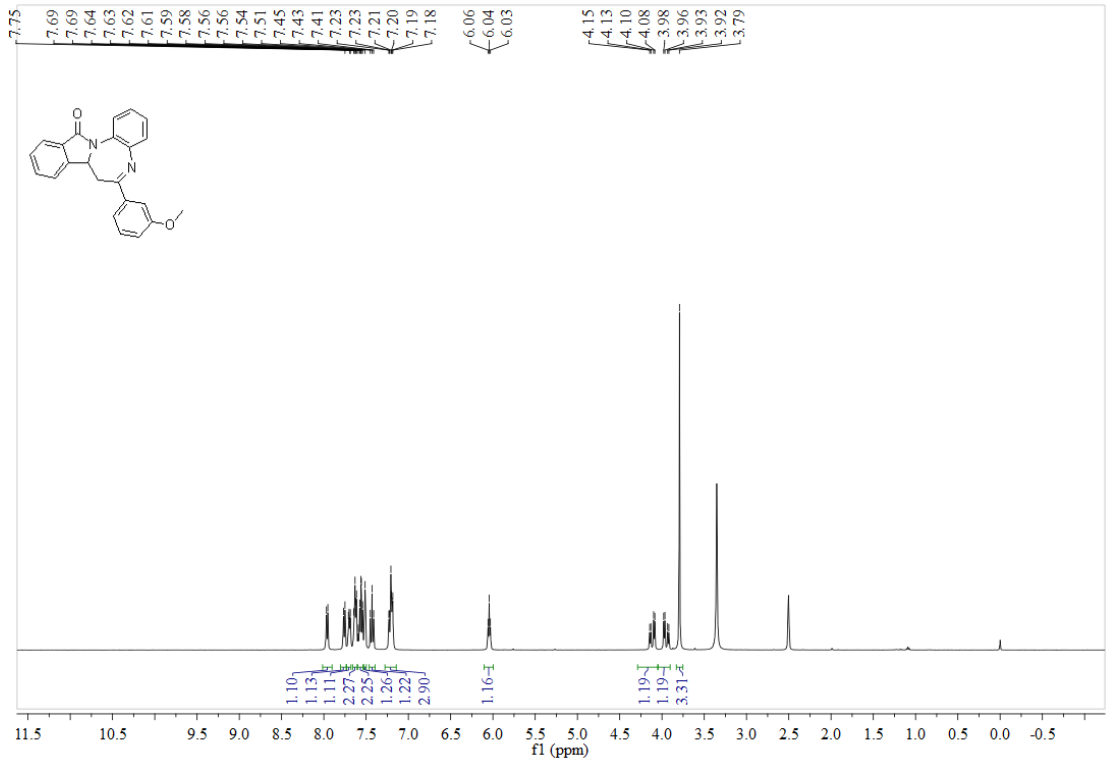
^{1}H NMR spectrum of compound 4i



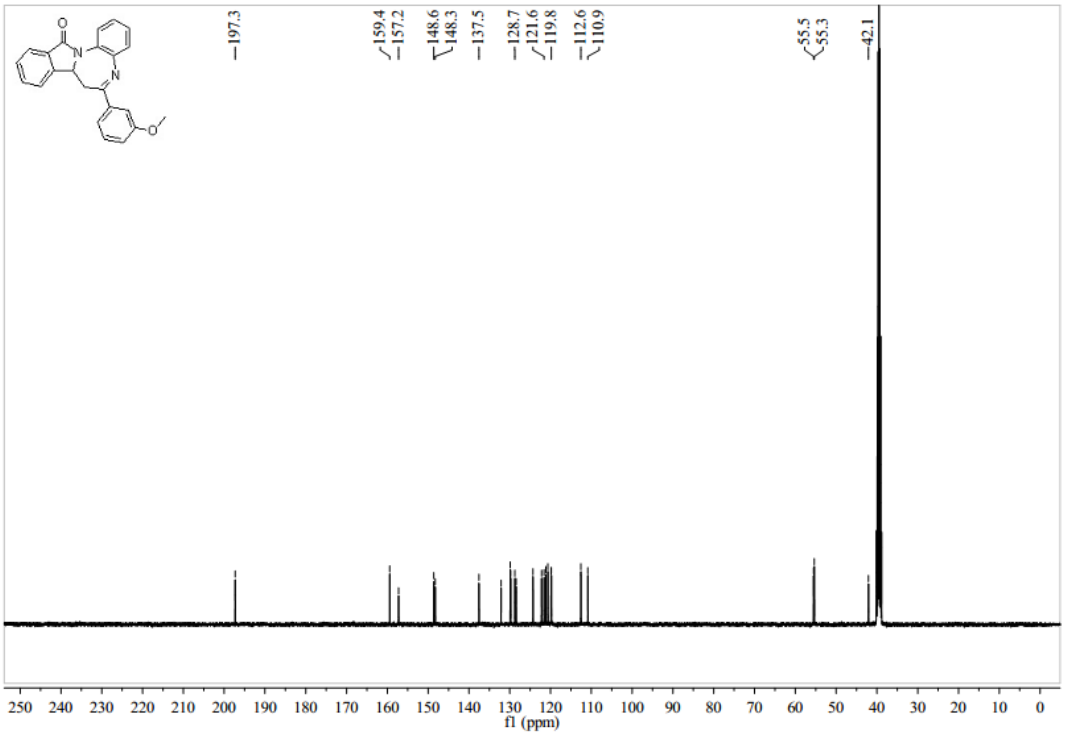
^{13}C NMR spectrum of compound 4i



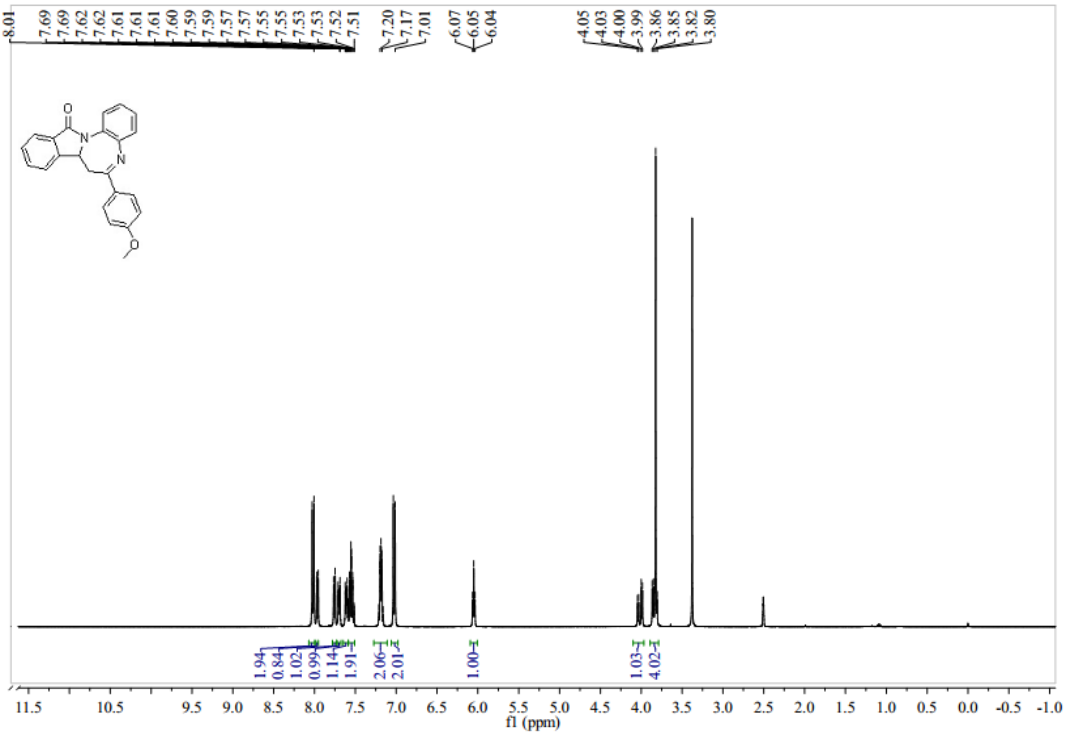
^{1}H NMR spectrum of compound 4j



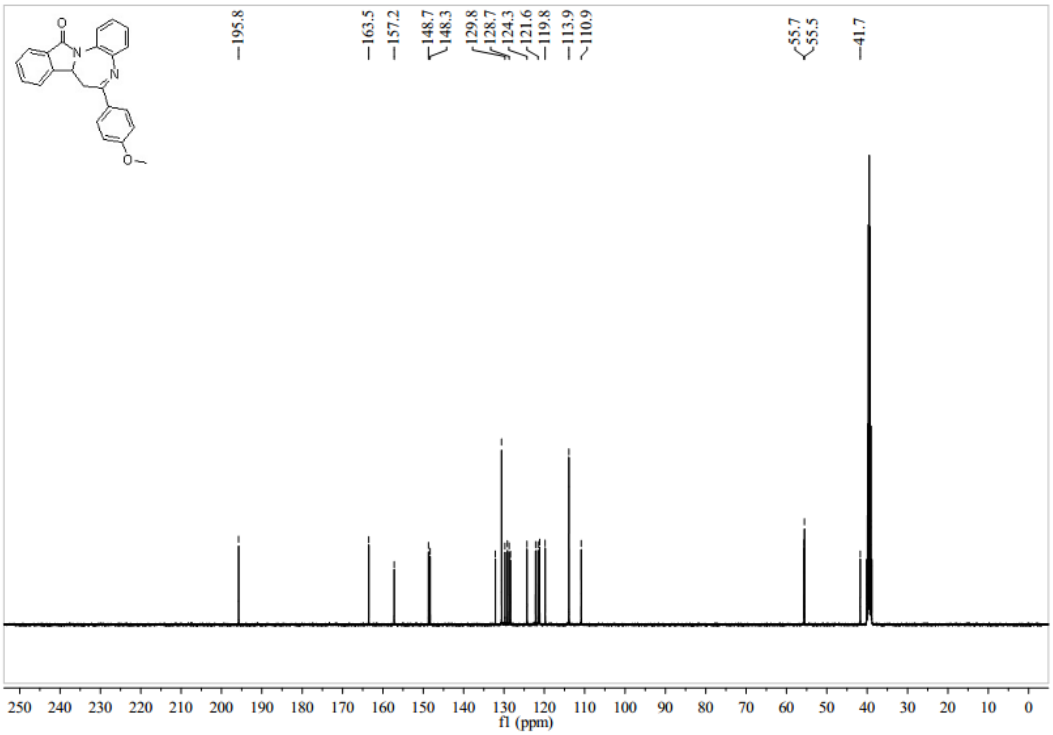
^{13}C NMR spectrum of compound 4j



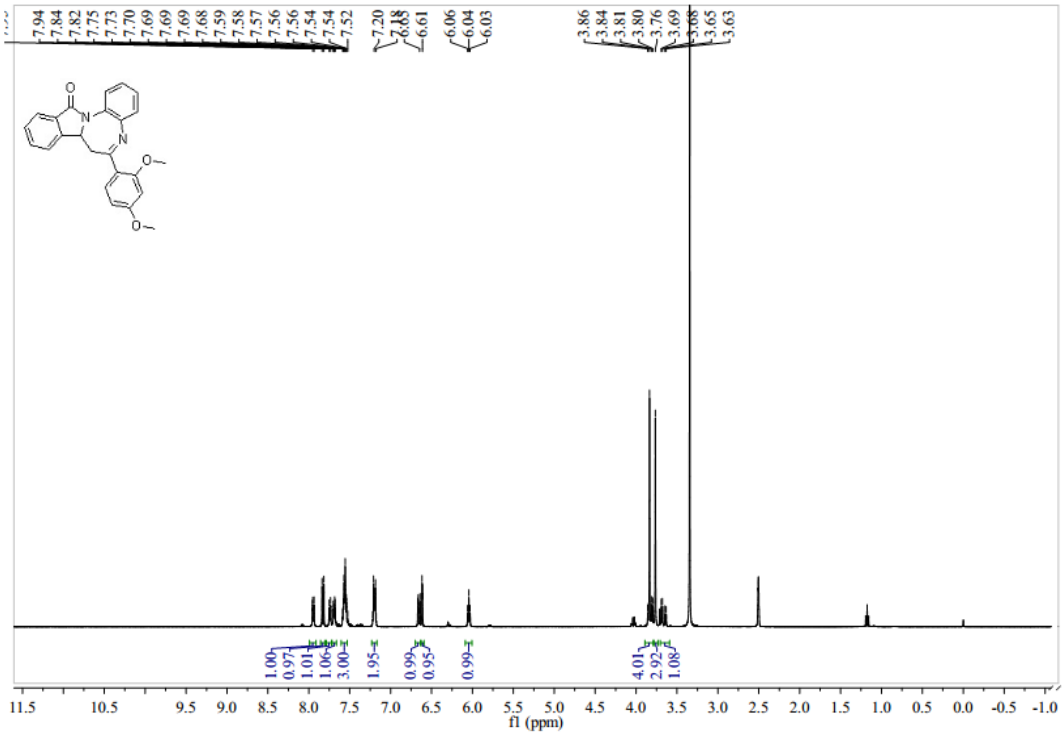
^{1}H NMR spectrum of compound 4k



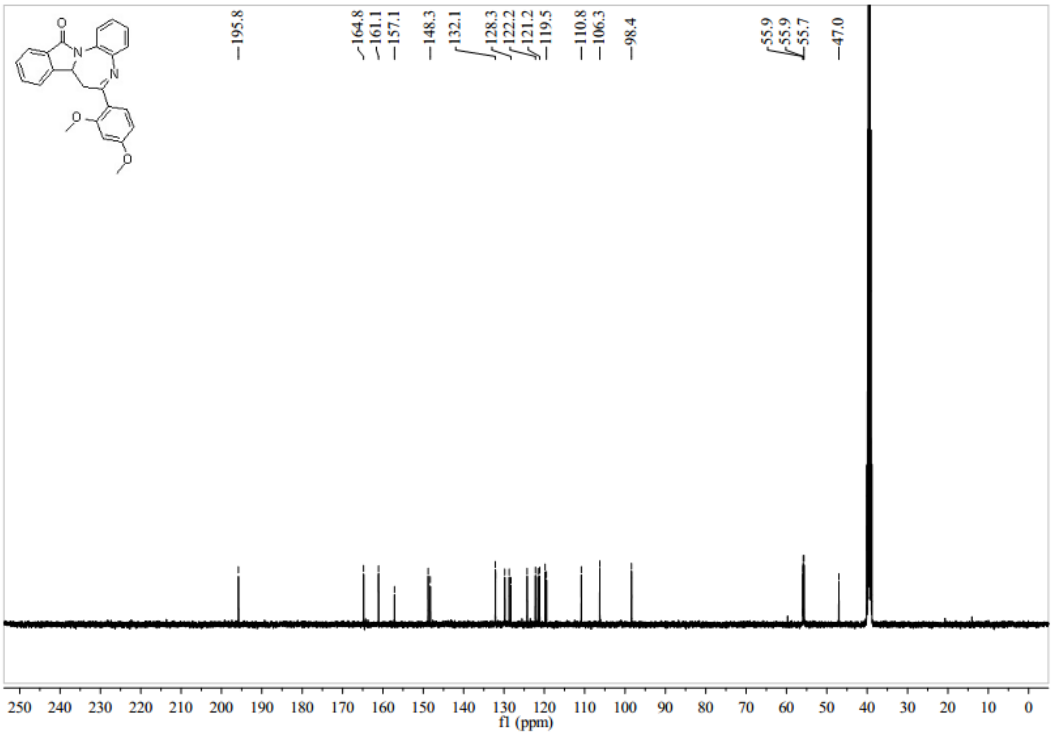
^{13}C NMR spectrum of compound 4k



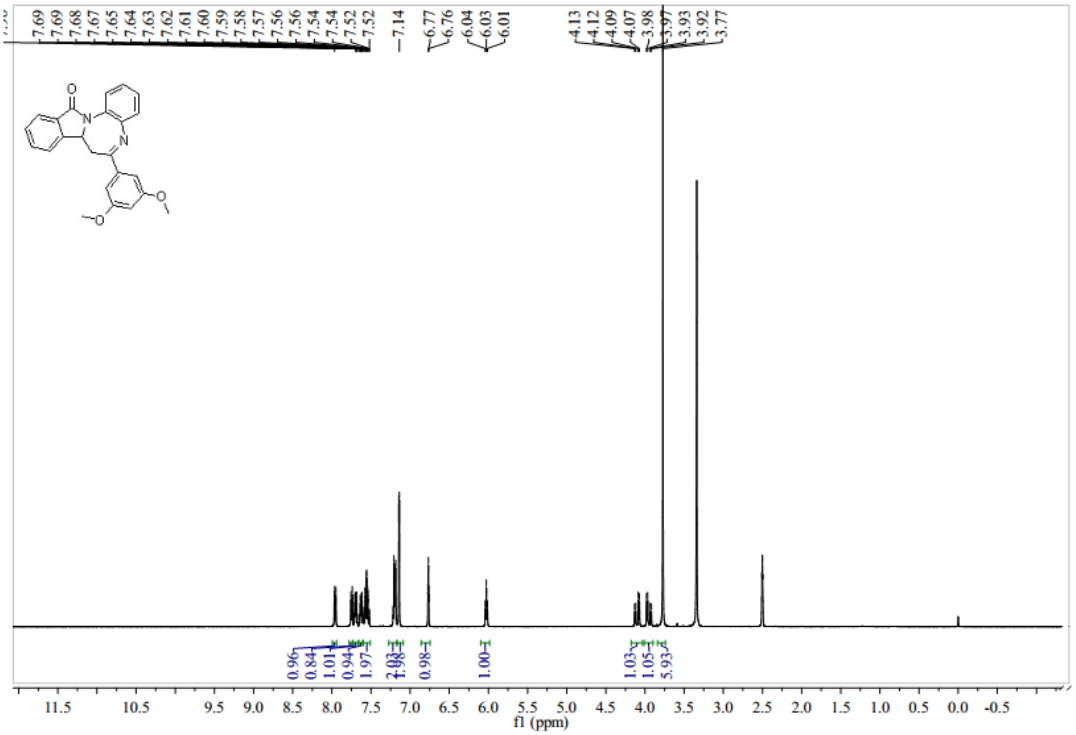
^{1}H NMR spectrum of compound 4l



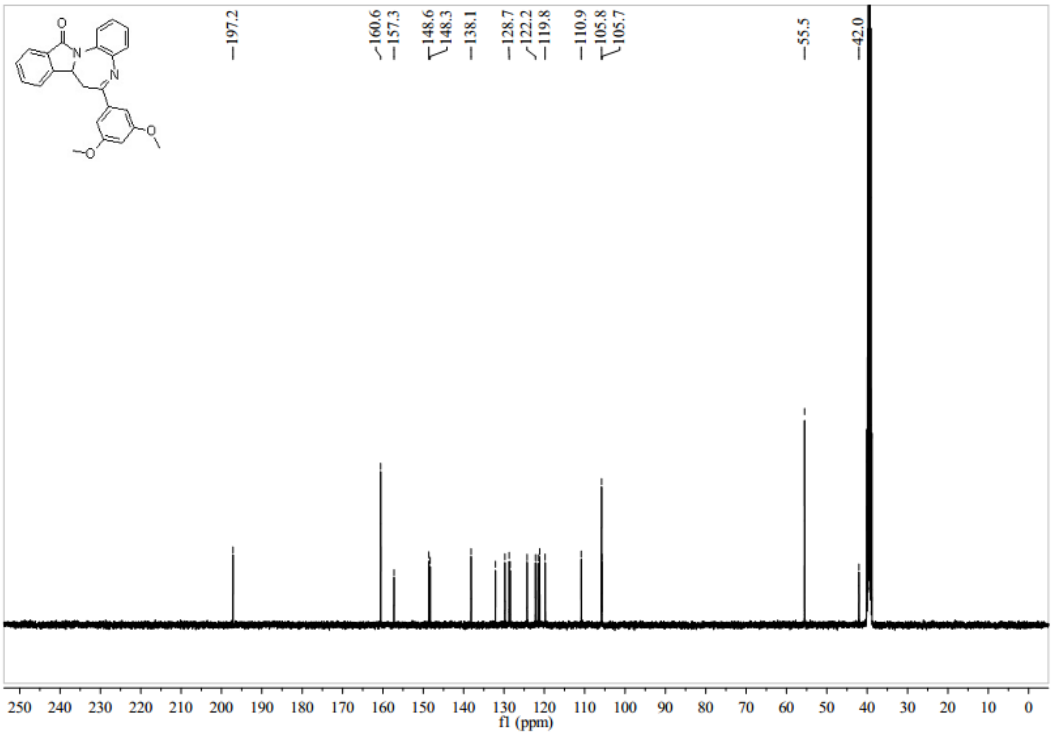
^{13}C NMR spectrum of compound 4l



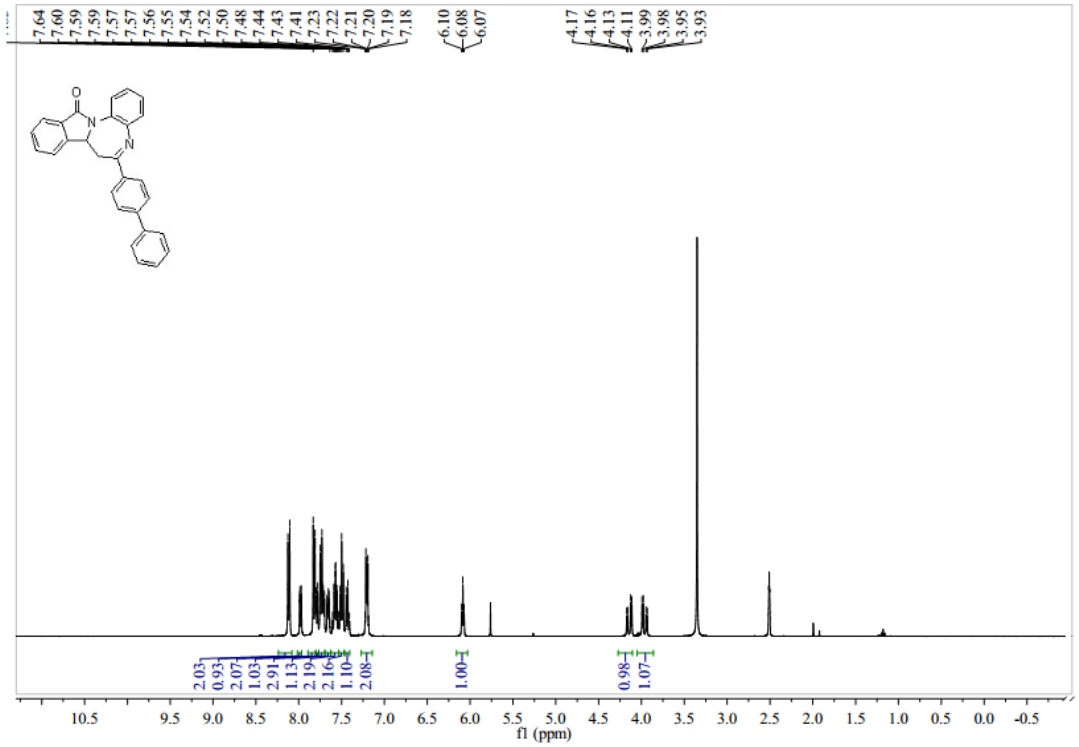
^{1}H NMR spectrum of compound 4m



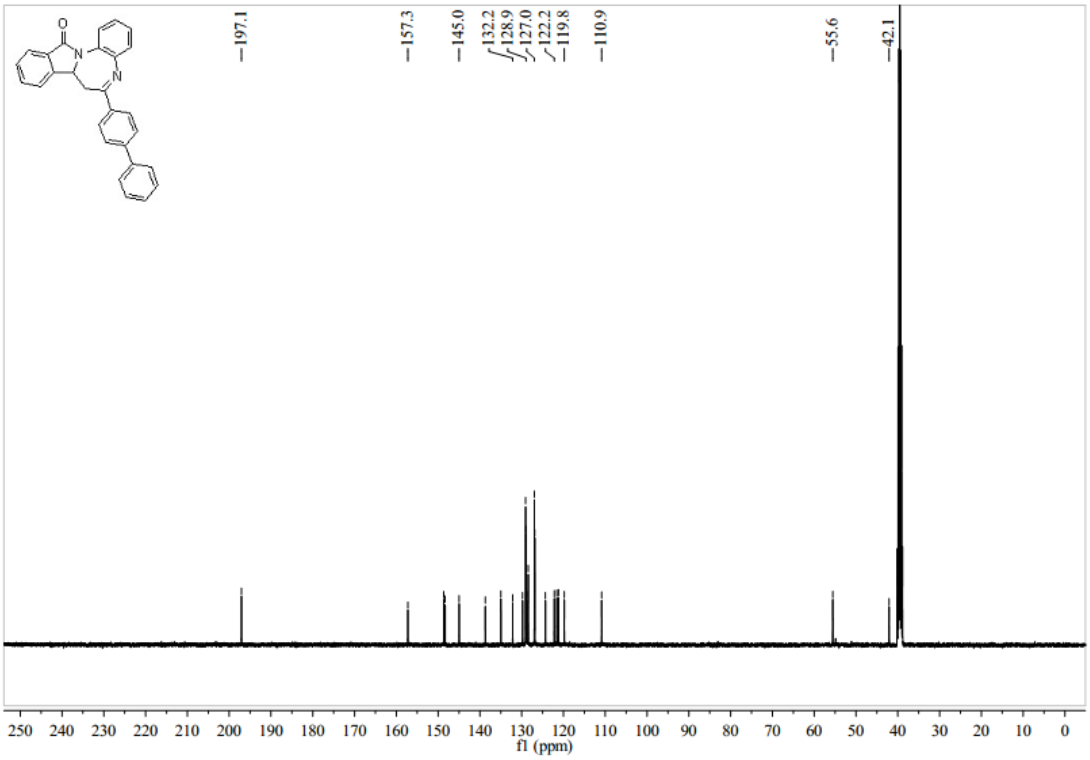
^{13}C NMR spectrum of compound 4m



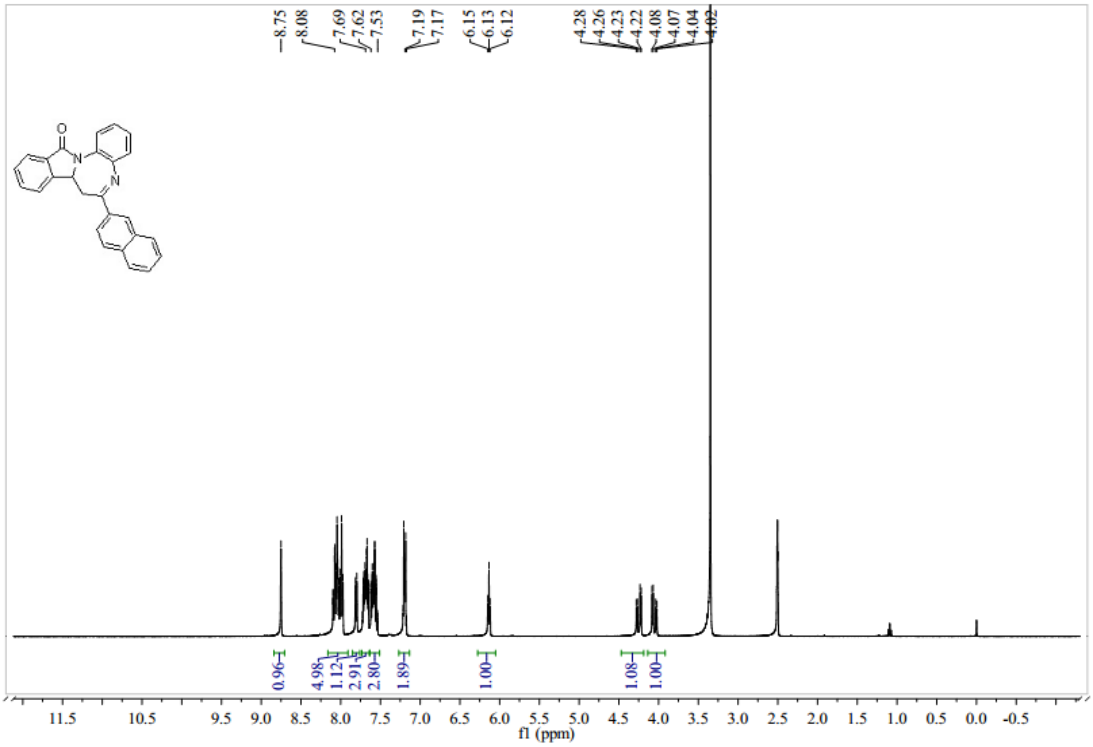
^{1}H NMR spectrum of compound 4n



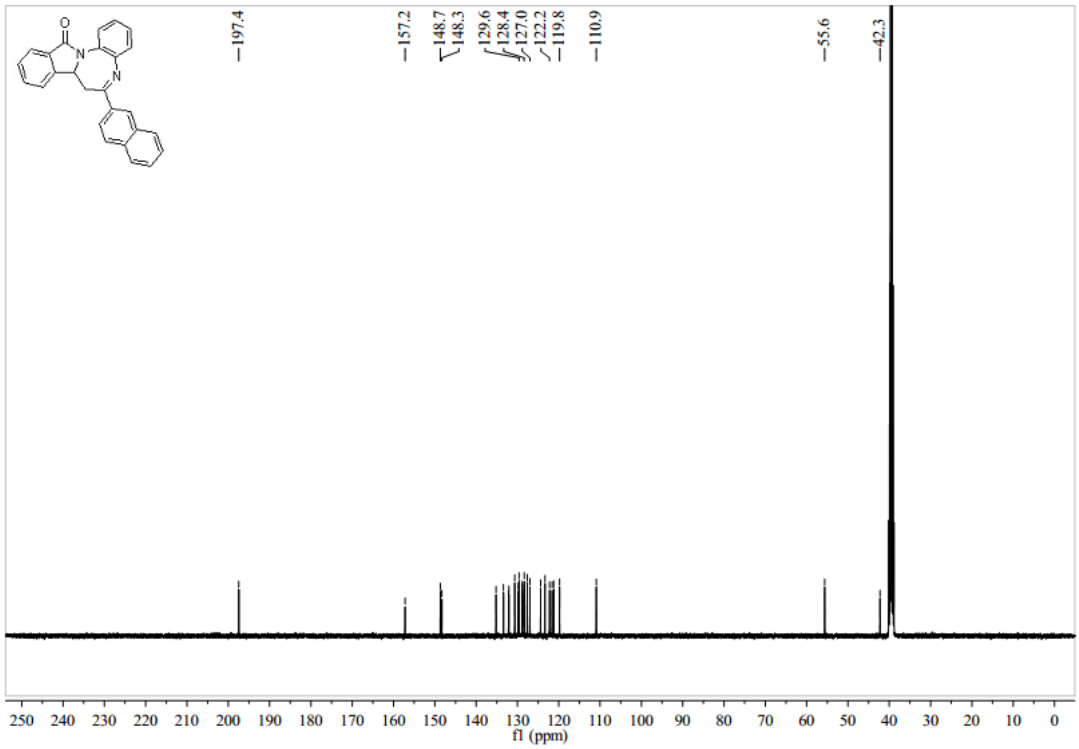
^{13}C NMR spectrum of compound 4n



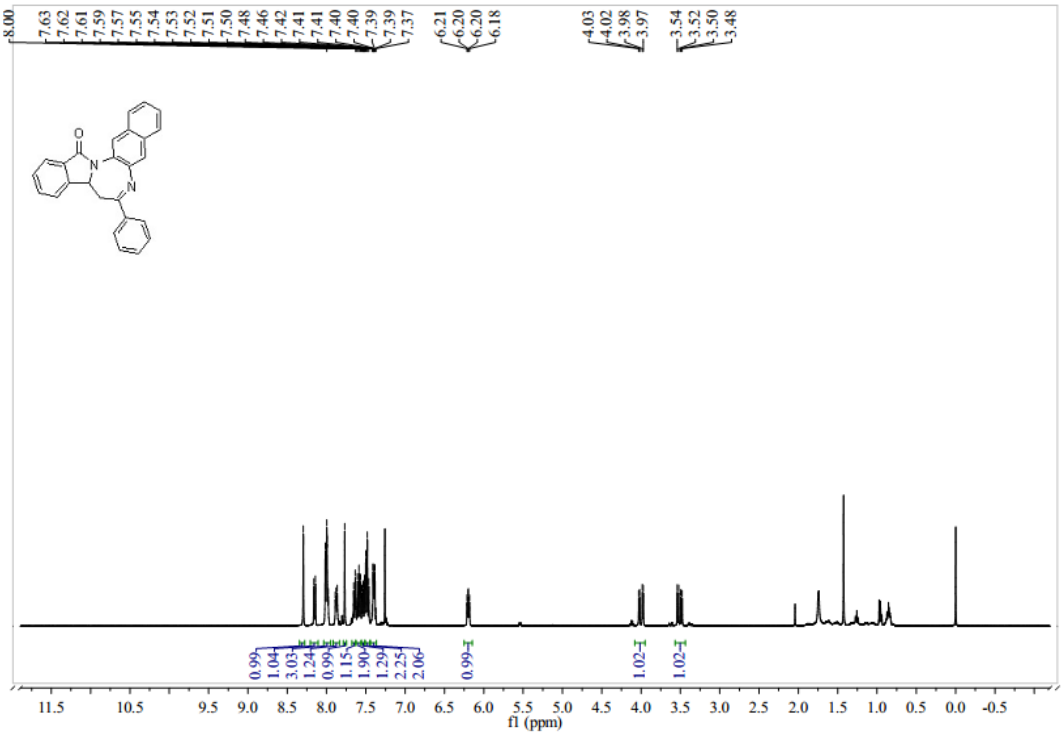
^{1}H NMR spectrum of compound 4o



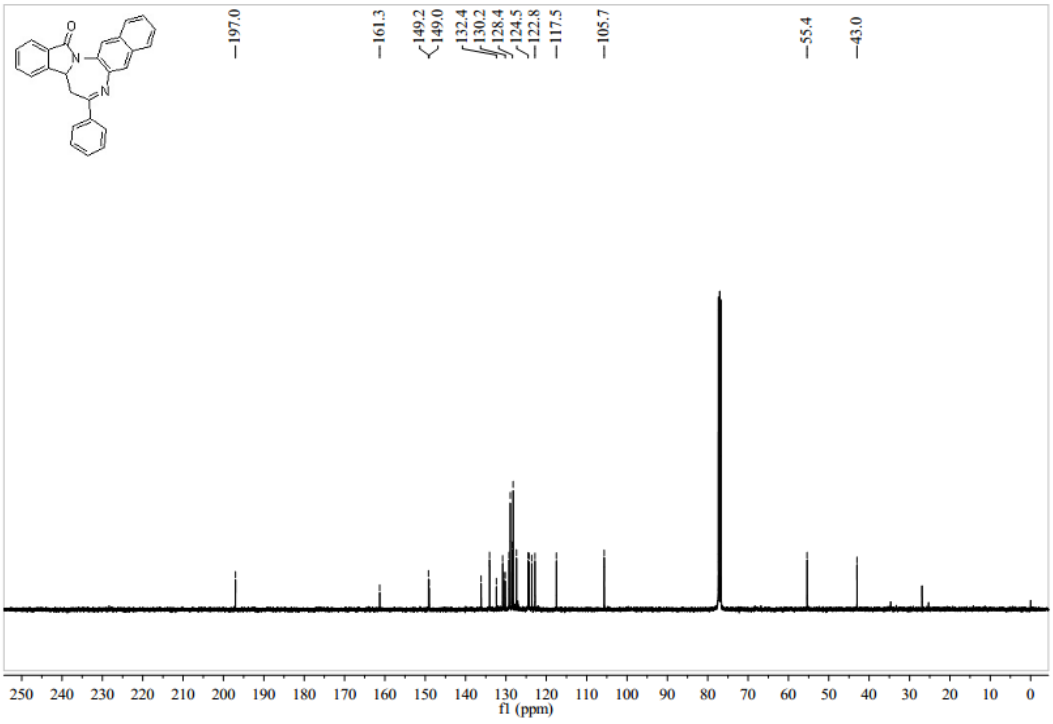
^{13}C NMR spectrum of compound 4o



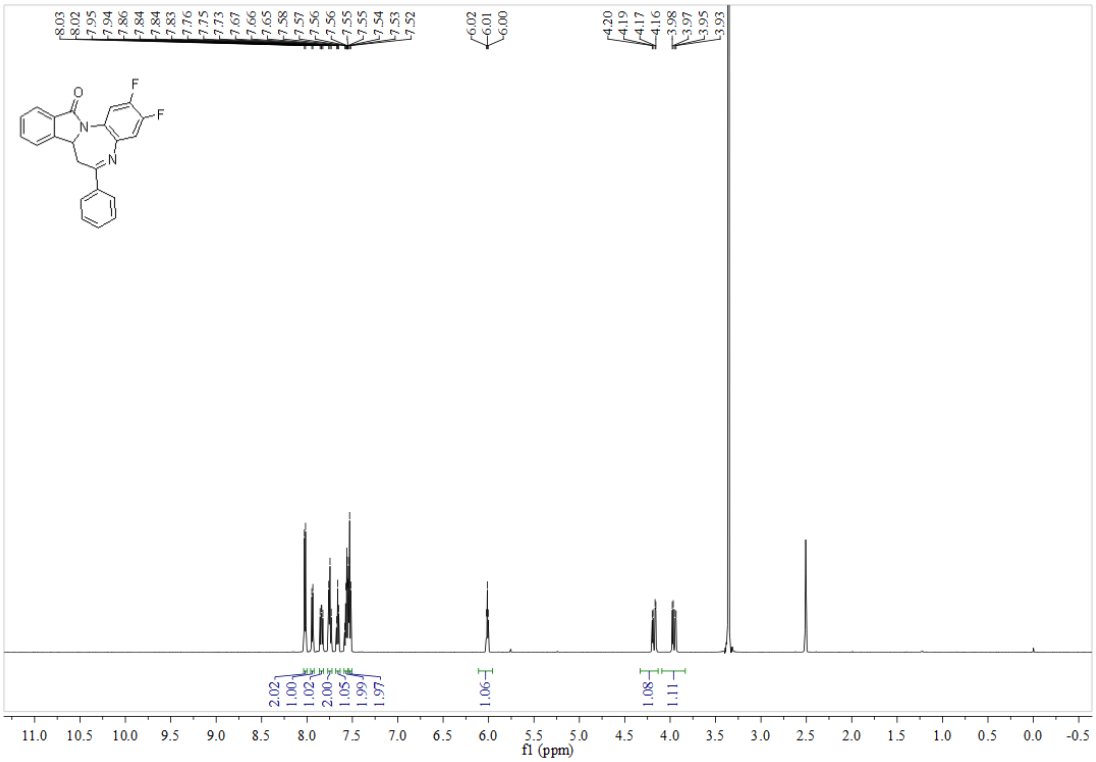
^{1}H NMR spectrum of compound 4p



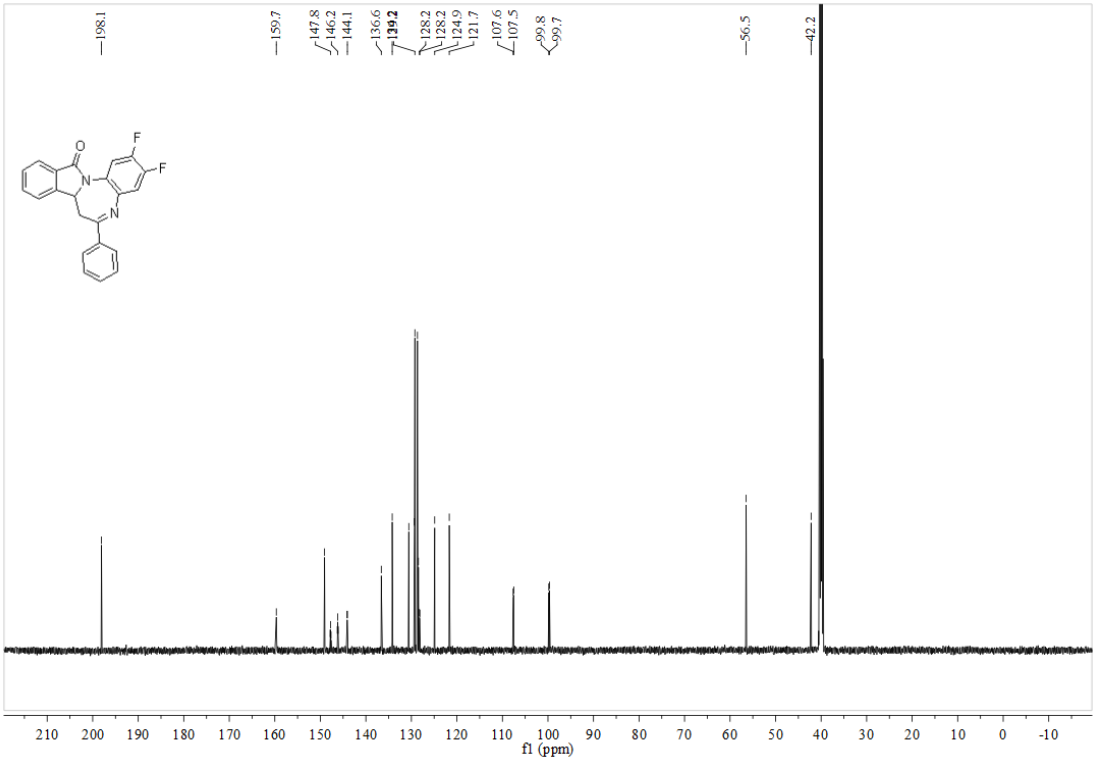
^{13}C NMR spectrum of compound 4p



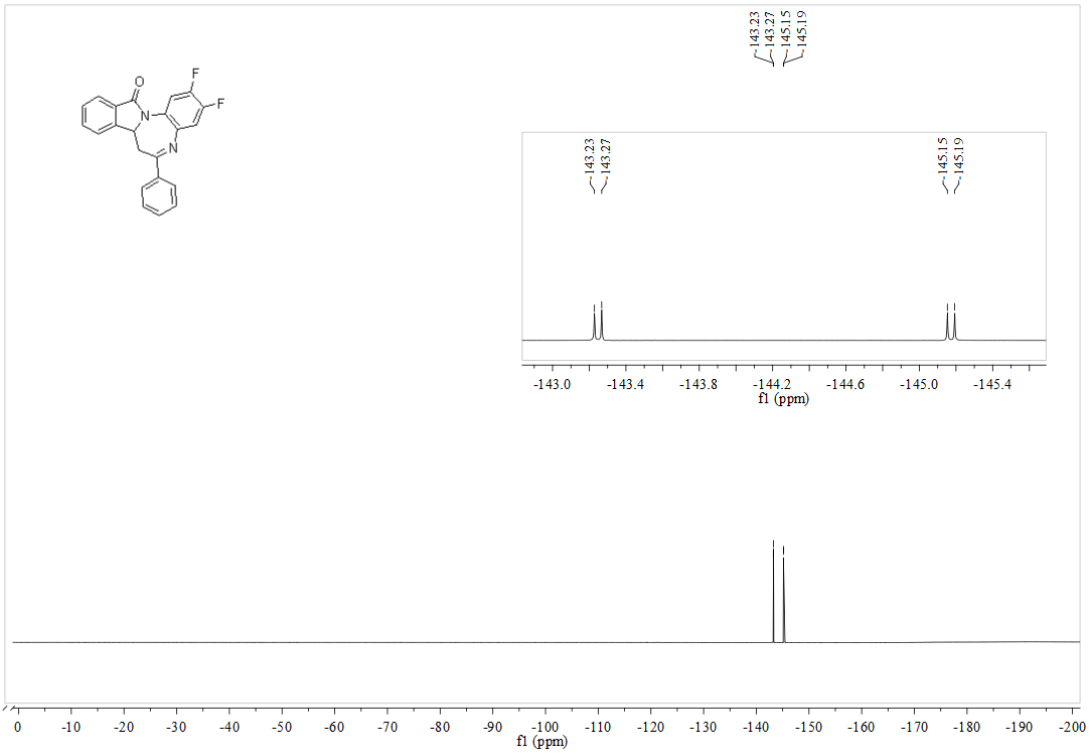
^{1}H NMR spectrum of compound 4q



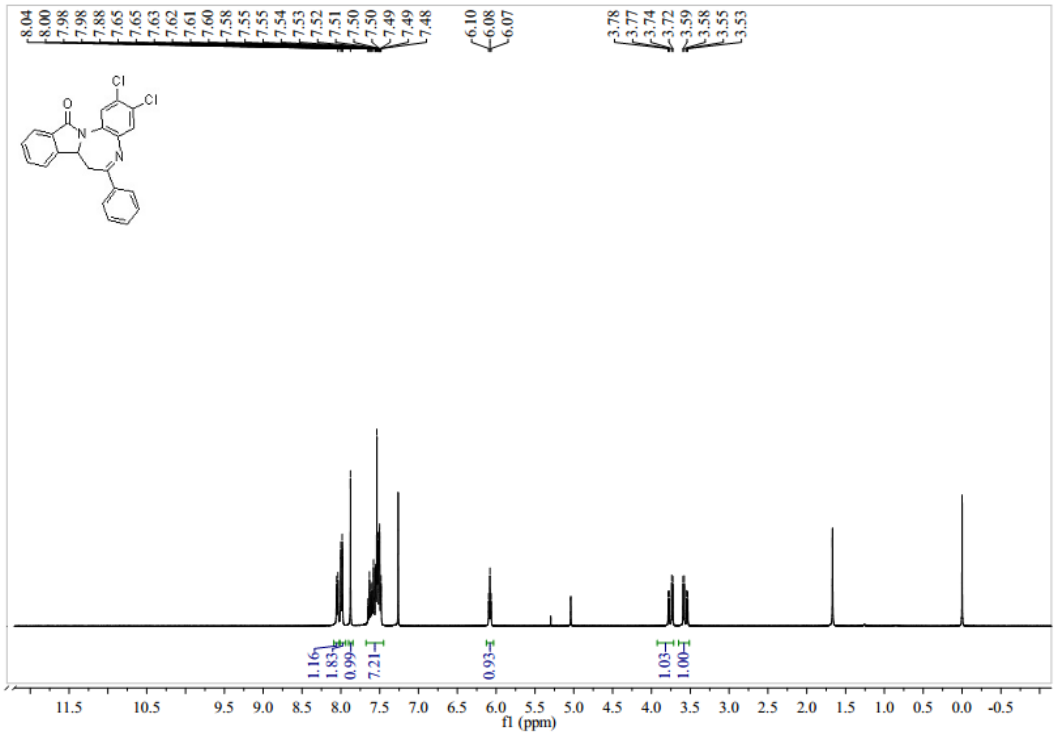
^{13}C NMR spectrum of compound 4q



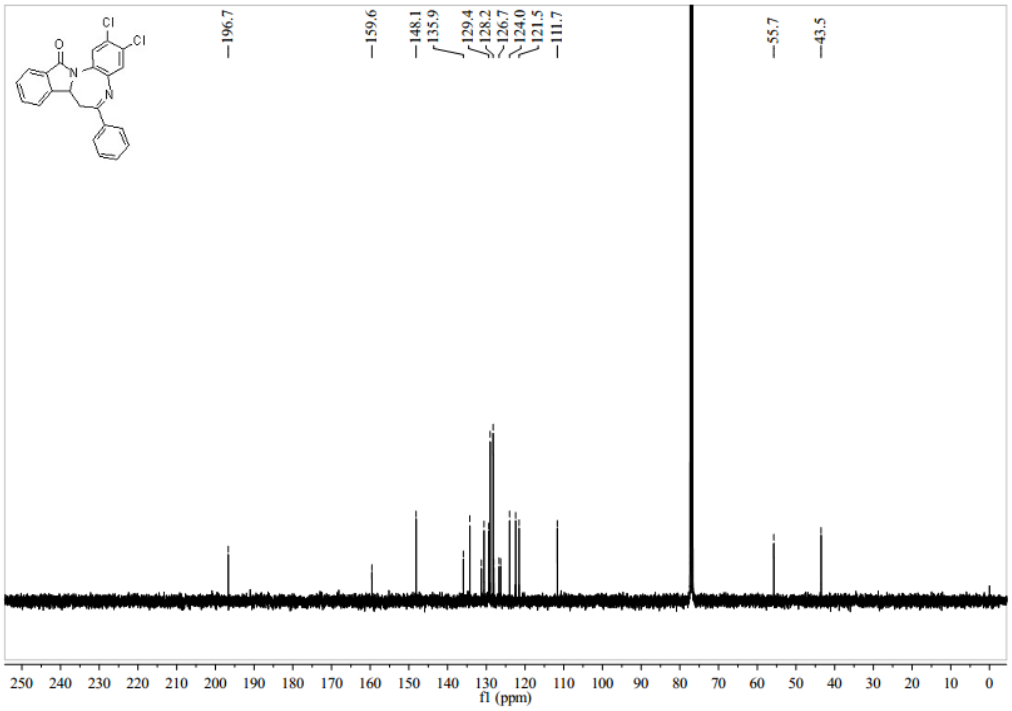
^{19}F NMR spectrum of compound 4q



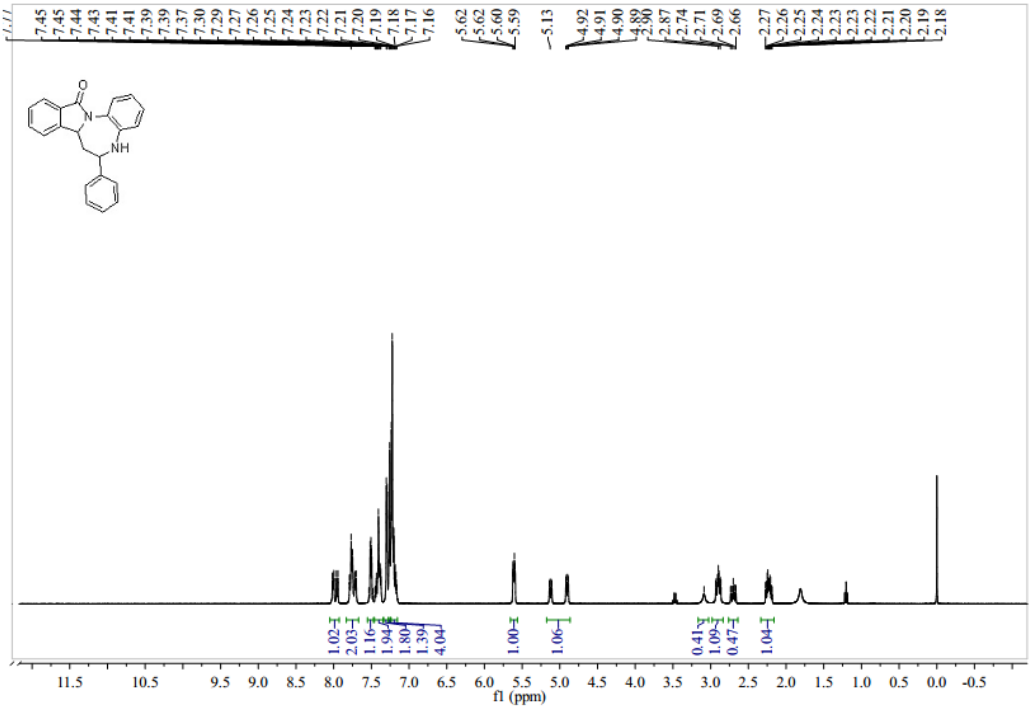
^{1}H NMR spectrum of compound 4r



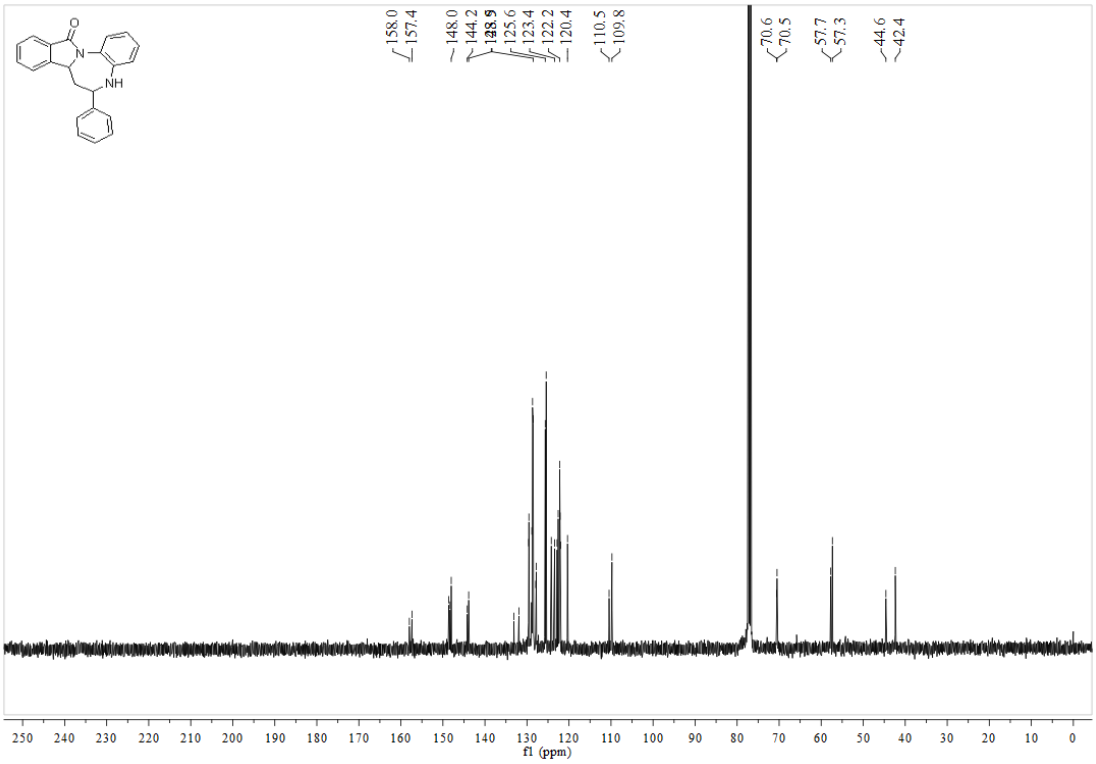
^{13}C NMR spectrum of compound 4r



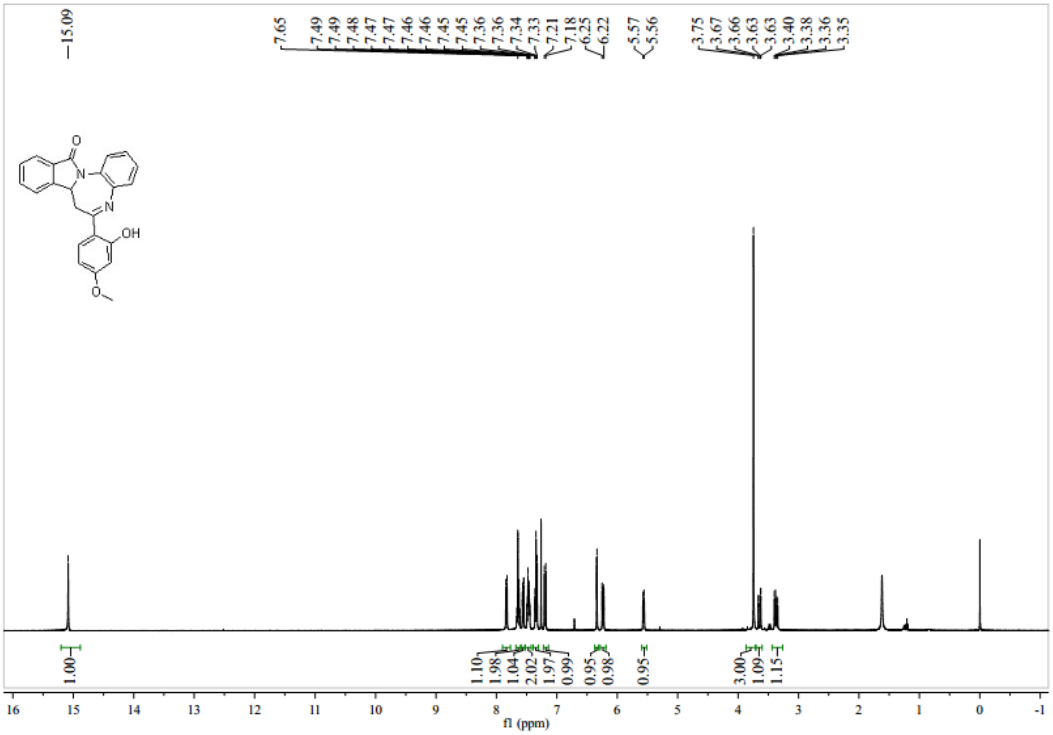
^{1}H NMR spectrum of compound 5



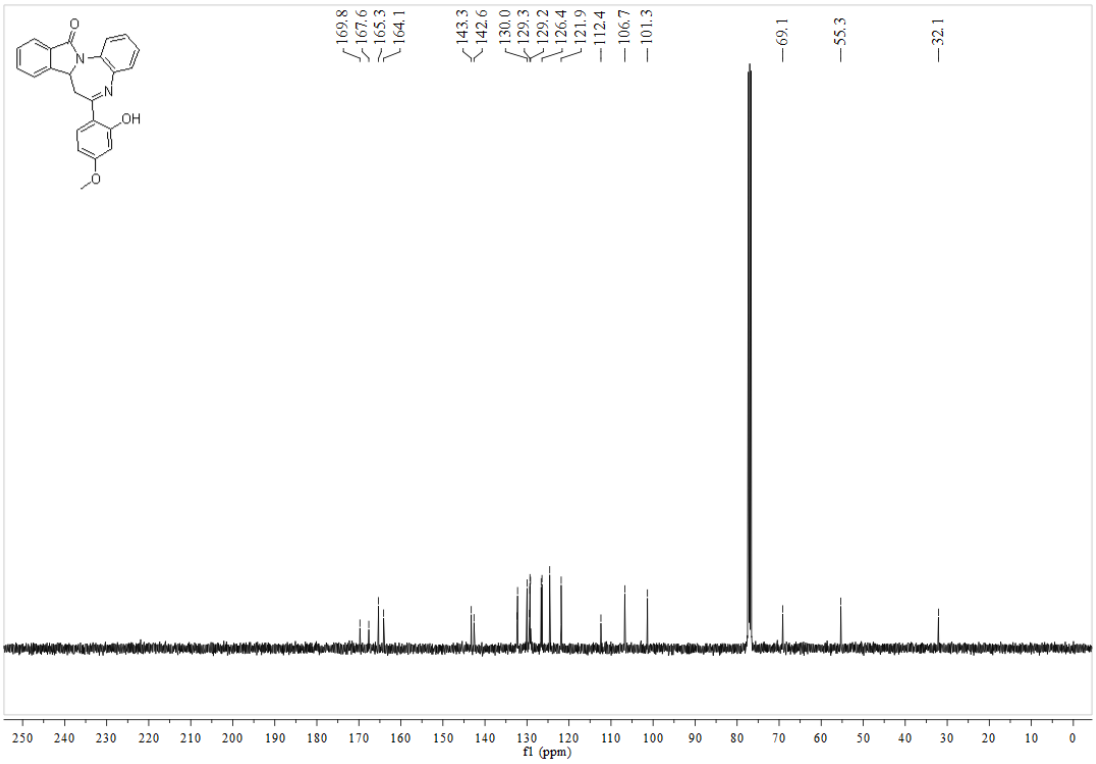
^{13}C NMR spectrum of compound 5



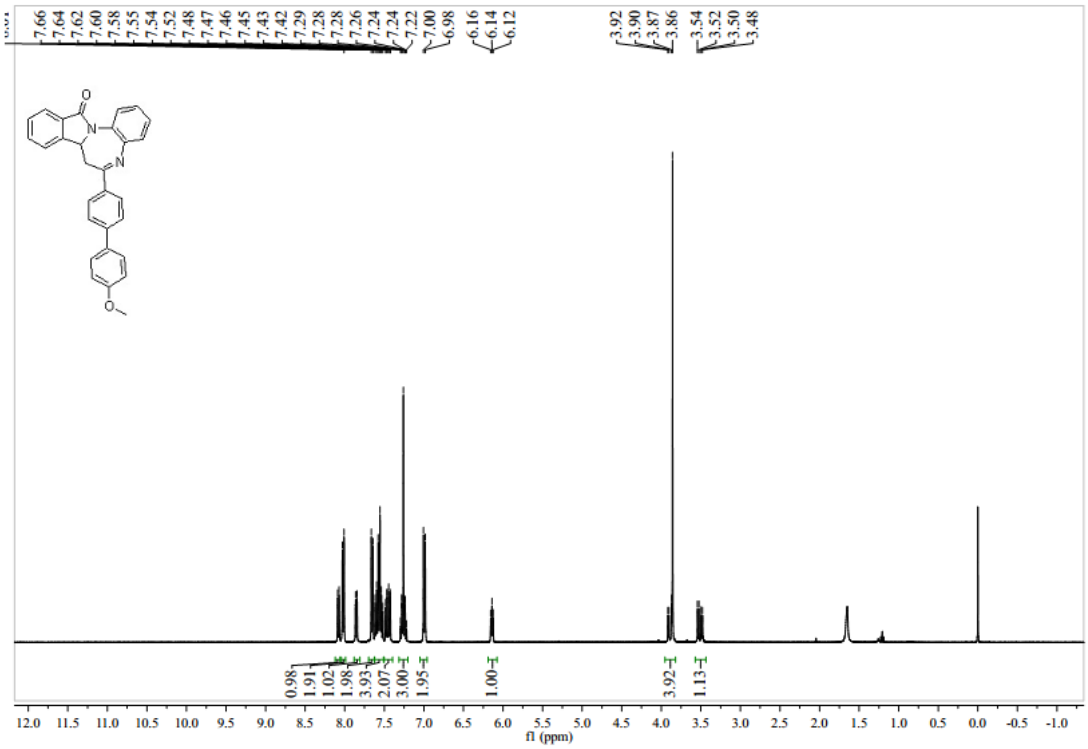
^{1}H NMR spectrum of compound 6



^{13}C NMR spectrum of compound 6



^{1}H NMR spectrum of compound 7



^{13}C NMR spectrum of compound 7