Supporting Information

Copper(I)-Catalyzed Synthesis of Natural Alkaloid Tryptanthrin and Its Derivatives

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1. General information

All reagents, unless otherwise specified, were purchased from commercial sources and were used without further purification. Other isatins were synthesized according to the corresponding literature procedures. Column chromatographic purification was generally performed on silica gel (200-300 mesh) and reactions were monitored by thin layer chromatography (TLC) under UV light to visualize the course of the reactions. The ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) data were recorded on a Bruker AVANCE II 400MHz spectrometer using $CDCl_3$ or DMSO-d_6 as solvent. The chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. ^{1}H NMR spectra were recorded with tetramethylsilane (δ = 0.00 ppm) as an internal reference; ^{13}C NMR spectra were recorded with $CDCl_3$ (δ = 77.06 ppm) or DMSO-d_6 (δ = 39.53 ppm) as an internal reference.

2. Gas chromatograms

This reaction was performed by replacing the small test tube with a Schlenk tube, displacing air three times with N_2, inserting a balloon and closing the reaction hermetically. The reaction was carried out for 24 h under optimal reaction conditions. Immediately after the reaction, the gas in the closed system was extracted with a syringe and analyzed with gas chromatograph (the gas chromatograph (GC) was measured on Agilent 7890A with thermal conductivity (TCD) and flame ionization detector (FID). The injection temperature was set at 280 ℃. Nitrogen was used as the carrier gas at 1.5 mL·min^{-1}. All reported date were averages of experiments performed at least thrice). The reaction for O_2 replacement was performed as described above. As shown in figures S1 and S2.

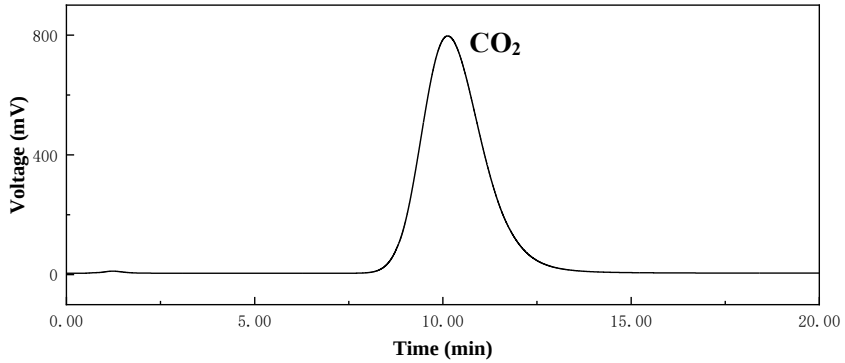


Figure S1. Gas chromatogram of carbon dioxide emitted from the reaction under N_2 atmosphere

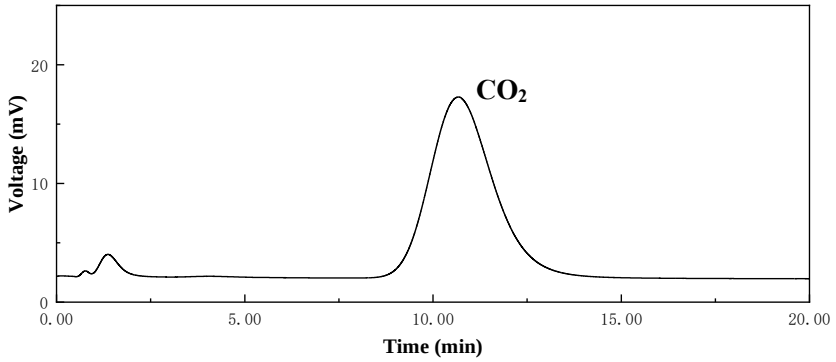
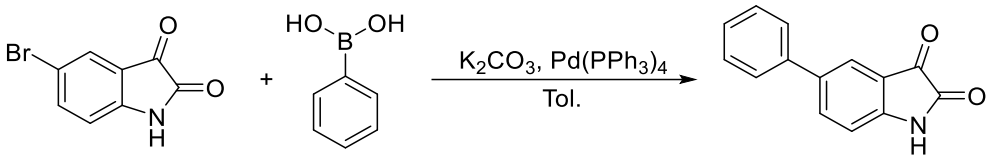
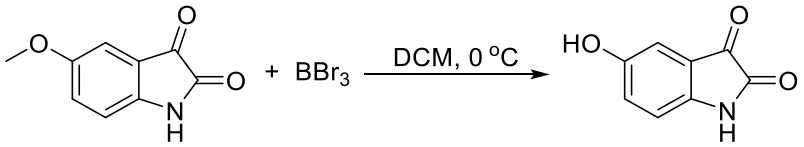


Figure S2. Gas chromatogram of carbon dioxide emitted from the reaction under in O_2 atmosphere

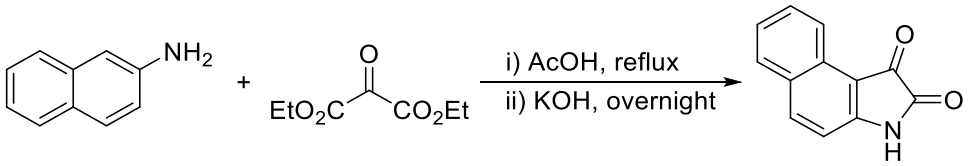
3. General procedure for synthesizing substrates 1j, 1k, 1p and 3a



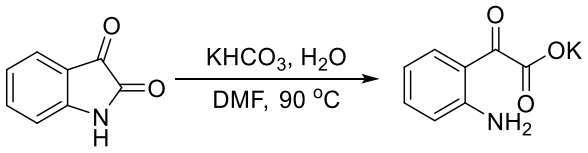
5-Phenylindoline-2,3-dione (1j)[1]**:** 5-Bromoisatin (452 mg, 2.0 mmol), phenylboronic acid (268 mg, 2.2 mmol), and $Pd(PPh_3)_4$ (46 mg, 0.04 mmol) were added to a 25 mL Schlenk tube and replaced three times with N_2. The reaction mixture was injected toluene (10 mL) and K_2CO_3 solution (4.0 mmol, 2 M in water) with a syringe and stirred at 90 ℃ for 48 h. After the completion of the reaction which was indicated by TLC, and the crude residue was obtained by removing the solvent, which was purified by column chromatography to afford the desired product **1j**. The product was obtained as a red solid (397 mg, 89%), m.p. 249-250 ℃.



5-Hydroxyindoline-2,3-dione (1k)[2]**:** Under nitrogen atmosphere, 5-methoxyisatin (354 mg, 2.0 mmol), DCM (20 mL) were added to a 100 mL flask, and BBr_3 (0.48 mL, 5.0 mmol) was slowly added to the flask at 0 ℃. The reaction mixture was stirred overnight at room temperature. The reaction was monitored by TLC and quenched by adding MeOH (20 mL). The solvent was evaporated and the residue was recrystallized in AcOH. The product **1k** was obtained as an oxblood red solid (300 mg, 92%).



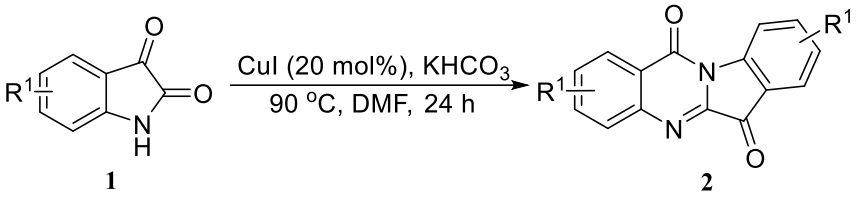
1*H*-benzo[*e*]indole-1,2(3*H*)-dione (1p)[3]**:** 2-Naphthylamine (286 mg, 2.0 mmol), diethyl keto-malonate (0.326 mL, 2.2 mmol), and AcOH (20 mL) were added to a 100 mL flask. The reaction mixture was refluxed for 4 h. After the reaction, the solvent was evaporated. KOH solution (30 mL, 1 M in water) was added and stirred at room temperature overnight. Hydrochloric acid (12 M) was added to the reaction system to pH = 4 to give a red solid. The solid was filtered and recrystallized with 30 mL of MeOH. The product **1p** was obtained as a red solid (272 mg, 69%), m.p. 250-251 ℃.



Potassium 2-(2-aminophenyl)-2-oxoacetate (3a): Isatin (147 mg, 1.0 mmol), $KHCO_3$ (100 mg, 1.0 mmol), DMF (2 mL) and water (20 μL) were added to a 10 mL reaction tube. The reaction mixture was stirred at 90 ℃ for 24 h. The reaction was quenched and the solvent was evaporated. The crude residue was purified by column chromatography to afford the product **3a**. The product

3a was obtained as a yellow solid (203 mg, 100%); ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.52 (dd, J = 7.9, 1.7 Hz, 1H), 7.15 (ddd, J = 8.4, 6.9, 1.7 Hz, 1H), 7.03 (s, 2H), 6.68 (d, J = 8.3 Hz, 1H), 6.45 (t, J = 7.5 Hz, 1H).

4. General procedure for the synthesis of 2a-2u

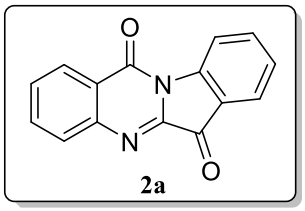


1 **2**

Isatin derivative (1.0 mmol), CuI (0.2 mmol), $KHCO_3$ (1.0 mmol), and DMF (2 mL) were added to a 10 mL reaction tube. The reaction mixture was stirred at 90 ℃ for 24 h. The reaction mixture was quenched, filtered to remove the insoluble residue, and washed 3 times with ethyl acetate (250 mL) and saturated NaCl solution (250 mL), respectively. The organic phase was dried with $MgSO_4$. The crude residue was obtained by removing the solvent, which was purified by column chromatography to afford the desired product **2**.

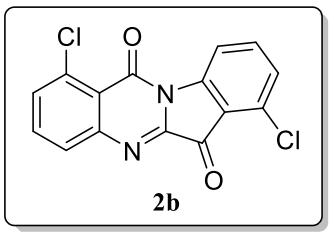
Characterization data:

Tryptanthrin, indolo[2,1-*b*]quinazoline-6,12-dione (2a):


2a

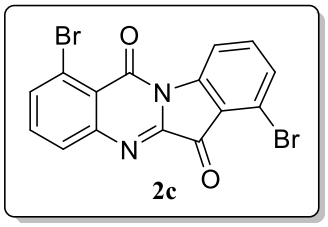
The title compound was prepared according to the general procedure described above using isatin (147 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a dark yellow solid (121.2 mg, 98%), m.p. 249-250 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.47 (d, J = 8.0 Hz, 1H), 8.31 (d, J = 7.9 Hz, 1H), 7.94 (d, J = 4.0 Hz, 2H), 7.86 (dd, J = 9.0, 7.4 Hz, 2H), 7.73 (dt, J = 8.2, 4.2 Hz, 1H), 7.47 (t, J = 7.5 Hz, 1H); ^{13}C NMR (101 MHz, DMSO) δ: 182.9, 158.2, 146.9, 146.5, 145.5, 138.2, 135.6, 130.4, 130.3, 127.40, 127.36, 125.2, 123.8, 122.7, 117.5. Anal. Calcd for $C_{15}H_8N_2O_2$; C, 72.58; H, 3.25; N, 11.29. Found: C, 72.35; H, 3.08; N, 11.48.

1,7-Dichloroindolo[2,1-*b*]quinazoline-6,12-dione (2b):


2b

The title compound was prepared according to the general procedure described above using 4-chloroisatin (182 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 5:1) as an orange solid (131.1 mg, 83%), m.p. > 300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.63 (dd, J = 8.1, 0.8 Hz, 1H), 7.97 (d, J = 7.3 Hz, 1H), 7.75-7.64 (m, 3H), 7.41-7.36 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.2, 156.2, 149.0, 147.1, 143.9, 138.5, 135.9, 134.7, 134.1, 133.2, 130.1, 128.9, 120.6, 118.9, 116.3. Anal. Calcd for $C_{15}H_6Cl_2N_2O_2$; C, 56.81; H, 1.91; N, 8.83. Found: C, 56.60; H, 2.13; N, 8.62.

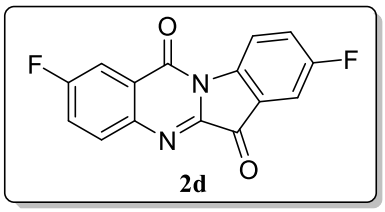
1,7-Dibromoindolo[2,1-*b*]quinazoline-6,12-dione (2c):



2c

The title compound was prepared according to the general procedure described above using 4-bromo-1*H*-indole-2,3-dione (226 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 8:1) as a yellow solid (151.5 mg, 75%), m.p. > 300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.70 (dd, *J* = 7.1, 1.8 Hz, 1H), 8.01 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.91 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.66-7.57 (m, 3H). Anal. Calcd for $C_{15}H_6Br_2N_2O_2$; C, 44.37; H, 1.49; N, 6.90. Found: C, 44.65; H, 1.72; N, 6.88.

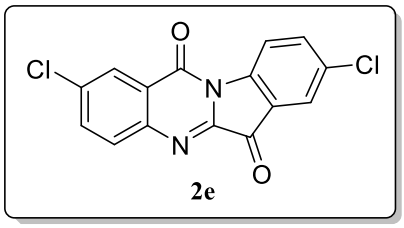
2,8-Difluoroindolo[2,1-*b*]quinazoline-6,12-dione (2d):



2d

The title compound was prepared according to the general procedure described above using 5-fluoroisatin (165 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a dark yellow solid (86.8 mg, 70%), m.p. > 300 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.49 (dd, *J* = 8.8, 4.2 Hz, 1H), 8.05 (ddd, *J* = 8.5, 6.8, 4.0 Hz, 2H), 7.89-7.78 (m, 2H), 7.74 (td, *J* = 9.0, 2.8 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 181.8 (d, *J* = 3.2 Hz), 162.6 (d, *J* = 250.9 Hz), 160.9 (d, *J* = 246.8 Hz), 157.2 (d, *J* = 3.1 Hz), 151.2, 143.7 (d, *J* = 1.9 Hz), 142.6 (d, *J* = 1.9 Hz), 133.3 (d, *J* = 8.8 Hz), 125.5 (d, *J* = 9.1 Hz), 124.6 (d, *J* = 7.9 Hz), 124.5 (d, *J* = 24.0 Hz), 123.9 (d, *J* = 24.1 Hz), 119.4 (d, *J* = 8.0 Hz), 112.8 (d, *J* = 24.5 Hz), 112.1 (d, *J* = 25.0 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ: -111.93 (s, 1F), -106.15 (s, 1F). Anal. Calcd for $C_{15}H_6F_2N_2O_2$; C, 63.39; H, 2.13; N, 9.86. Found: C, 63.19; H, 2.45; N, 9.65.

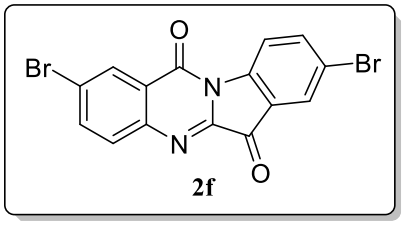
2,8-Dichloroindolo[2,1-*b*]quinazoline-6,12-dione (2e):



2e

The title compound was prepared according to the general procedure described above using 5-chloroisatin (182 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a yellow solid (123.2 mg, 78%), m.p. > 300 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.46 (d, *J* = 8.5 Hz, 1H), 8.28 (dd, *J* = 2.1, 0.8 Hz, 1H), 8.04-7.97 (m, 3H), 7.94 (dd, *J* = 8.6, 2.3 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 181.5, 157.1, 145.67, 145.68, 144.7, 137.4, 135.6, 135.0, 132.4, 132.0, 126.6, 125.0, 124.9, 124.5, 119.1. Anal. Calcd for $C_{15}H_6Cl_2N_2O_2$; C, 56.81; H, 1.91; N, 8.83. Found: C, 56.99; H, 1.62; N, 8.60.

2,8-Dibromoindolo[2,1-*b*]quinazoline-6,12-dione (2f):

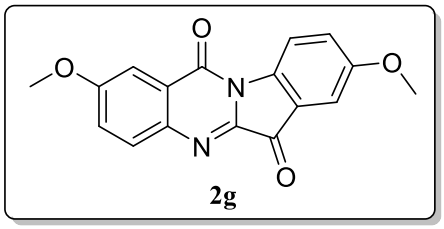


2f

The title compound was prepared according to the general procedure described above using 5-bromoisatin (226 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a yellow solid (139.3 mg, 69%), m.p. > 300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.56 (d, *J* =

2.2 Hz, 1H), 8.52 (d, *J* = 8.6 Hz, 1H), 8.03 (d, *J* = 2.1 Hz, 1H), 7.98-7.86 (m, 3H). Anal. Calcd for $C_{15}H_6Br_2N_2O_2$; C, 44.37; H, 1.49; N, 6.90. Found: C, 44.55; H, 1.21; N, 6.67.

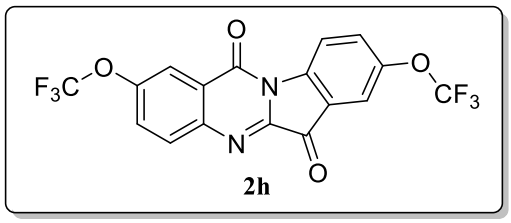
2,8-Dimethoxyindolo[2,1-*b*]quinazoline-6,12-dione (2g):



2g

The title compound was prepared according to the general procedure described above using 5-methoxyisatin (177 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as an orange solid (97.0 mg, 63%), m.p. > 300 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.50 (d, *J* = 8.8 Hz, 1H), 7.93 (d, *J* = 8.9 Hz, 1H), 7.81 (d, *J* = 2.9 Hz, 1H), 7.38 (dd, *J* = 10.5, 2.8 Hz, 2H), 7.29 (dd, *J* = 8.8, 2.8 Hz, 1H), 3.98 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 182.5, 161.3, 158.7, 157.5, 142.99, 143.01, 140.8, 140.2, 132.4, 124.8, 124.1, 123.4, 119.1, 108.3, 108.1, 56.1, 56.0. Anal. Calcd for $C_{17}H_{13}N_2O_4$; C, 66.23; H, 3.92; N, 9.09. Found: C, 66.00; H, 3.75; N, 9.26.

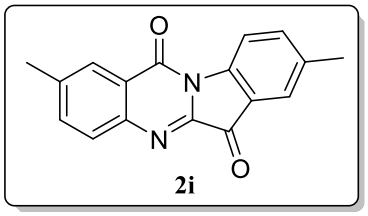
2,8-Bis(trifluoromethoxy)indolo[2,1-*b*]quinazoline-6,12-dione (2h):



2h

The title compound was prepared according to the general procedure described above using 5-(trifluoromethoxy)isatin (231 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 3:1) as an orange red solid (183.0 mg, 88%), m.p. > 300 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.69 (d, *J* = 8.8 Hz, 1H), 8.25 (dd, *J* = 2.9, 1.3 Hz, 1H), 8.09 (d, *J* = 8.8 Hz, 1H), 7.80-7.75 (m, 1H), 7.73-7.61 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.0, 156.9, 150.3, 148.0, 144.7, 144.3, 144.0, 133.0, 130.6, 127.92, 127.87 (q, *J* = 235.7 Hz), 125.1, 123.1, 120.3 (q, *J* = 257.5 Hz), 119.6, 118.6, 117.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -58.19 (s, 3F), -57.79 (s, 3F). Anal. Calcd for $C_{17}H_6F_6N_2O_4$; C, 49.06; H, 1.45; N, 6.73. Found: C, 49.33; H, 1.69; N, 6.50.

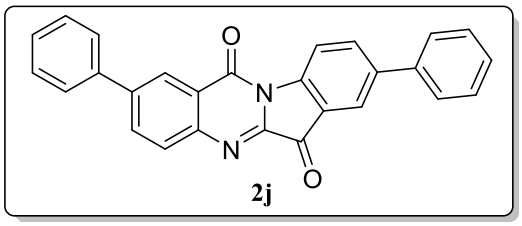
2,8-Dimethylindolo[2,1-*b*]quinazoline-6,12-dione (2i):



2i

The title compound was prepared according to the general procedure described above using 5-methylisatin (161 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as an orange solid (85.6 mg, 62%), m.p. > 300 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.41 (d, *J* = 8.2 Hz, 1H), 8.15 (s, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.74-7.41 (m, 3H), 2.52 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 182.6, 157.9, 144.6, 144.2, 144.0, 141.1, 138.7, 137.3, 136.2, 130.5, 127.2, 125.4, 123.5, 122.1, 117.6, 21.6, 21.1. Anal. Calcd for $C_{17}H_{12}N_2O_2$; C, 73.90; H, 4.38; N, 10.14. Found: C, 73.68; H, 4.71; N, 10.41.

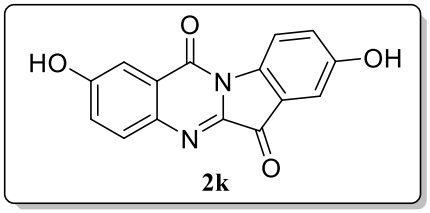
2,8-Diphenylindolo[2,1-*b*]quinazoline-6,12-dione (2j):



2j

The title compound was prepared according to the general procedure described above using 5-phenylindoline-2,3-dione (223 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) as a yellow solid (166.0 mg, 83%), m.p. > 300 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.71-8.63 (m, 2H), 8.13 (d, *J* = 1.4 Hz, 1H), 8.09 (d, *J* = 1.1 Hz, 2H), 8.01 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.77-7.71 (m, 2H), 7.65-7.60 (m, 2H), 7.55-7.39 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 182.5, 158.1, 145.7, 145.2, 144.4, 143.3, 140.7, 138.8, 138.7, 136.7, 133.8, 131.3, 129.2, 128.7, 128.4, 127.3, 126.9, 125.5, 124.1, 123.6, 122.6, 118.3. Anal. Calcd for $C_{27}H_{16}N_2O_2$; C, 80.99; H, 4.03; N, 7.00. Found: C, 80.76; H, 4.25; N, 6.85.

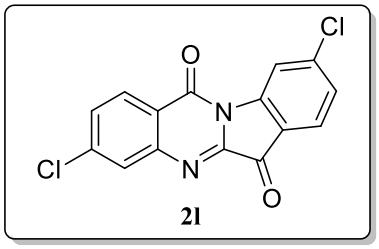
2,8-Dihydroxyindolo[2,1-*b*]quinazoline-6,12-dione (2k):



2k

The title compound was prepared according to the general procedure described above using 5-hydroxyindoline-2,3-dione (163 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 3:1) as a brown solid (9.8 mg, 7%), m.p. > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.67 (s, 1H), 10.17 (s, 1H), 8.25 (d, *J* = 8.6 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.56 (d, *J* = 2.8 Hz, 1H), 7.31 (dd, *J* = 8.8, 2.9 Hz, 1H), 7.19 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.11 (d, *J* = 2.7 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 182.7, 159.6, 157.2, 156.7, 143.2, 139.6, 138.8, 132.4, 125.4, 124.4, 124.1, 124.0, 118.8, 111.1, 110.4. Anal. Calcd for $C_{15}H_8N_2O_4$; C, 64.29; H, 2.88; N, 10.00. Found: C, 64.46; H, 2.53; N, 9.77.

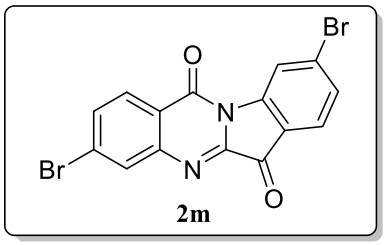
3,9-Dichloroindolo[2,1-*b*]quinazoline-6,12-dione (2l):



2l

The title compound was prepared according to the general procedure described above using 6-chloroisatin (182 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 5:1) as a yellow solid (107.4 mg, 68%), m.p. > 300 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.67 (d, *J* = 1.8 Hz, 1H), 8.37 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 2.0 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.64 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.43 (dd, *J* = 8.1, 1.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.8, 157.3, 153.1, 147.6, 146.7, 144.9, 141.8, 130.9, 130.3, 128.9, 127.9, 126.4, 121.9, 120.2, 118.6. Anal. Calcd for $C_{15}H_6Cl_2N_2O_2$; C, 56.81; H, 1.91; N, 8.83. Found: C, 56.97; H, 2.15; N, 8.80.

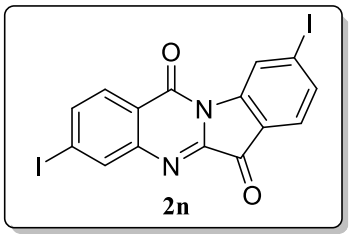
3,9-Dibromoindolo[2,1-*b*]quinazoline-6,12-dione (2m):



2m

The title compound was prepared according to the general procedure described above using 6-bromoisatin (226 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 5:1) as a yellow solid (107.0 mg, 53%), m.p. > 300 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.85 (d, *J* = 1.5 Hz, 1H), 8.29 (d, *J* = 8.5 Hz, 1H), 8.19 (d, *J* = 1.9 Hz, 1H), 7.82-7.76 (m, 2H), 7.61 (dd, *J* = 8.1, 1.6 Hz, 1H). Anal. Calcd for $C_{15}H_6Br_2N_2O_2$; C, 44.37; H, 1.49; N, 6.90. Found: C, 44.15; H, 1.74; N, 6.67.

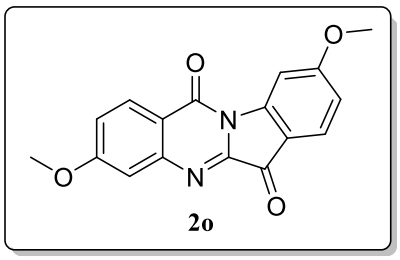
3,9-Diiodoindolo[2,1-*b*]quinazoline-6,12-dione (2n):



2n

The title compound was prepared according to the general procedure described above using 6-iodo-1*H*-indole-2,3-dione (273 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) as a yellow solid (120.0 mg, 48%), m.p. > 300 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.07 (d, *J* = 1.4 Hz, 1H), 8.41 (d, *J* = 1.6 Hz, 1H), 8.10 (d, *J* = 8.3 Hz, 1H), 8.00 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.84 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.60 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 196.7, 157.6, 147.2, 146.0, 144.8, 139.6, 139.5, 136.9, 128.6, 127.1, 126.0, 122.8, 121.0, 107.1, 102.6. Anal. Calcd for $C_{15}H_6I_2N_2O_2$; C, 36.03; H, 1.21; N, 5.60. Found: C, 36.28; H, 1.00; N, 5.36.

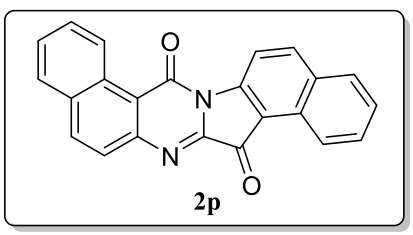
3,9-Dimethoxyindolo[2,1-*b*]quinazoline-6,12-dione (2o):



2o

The title compound was prepared according to the general procedure described above using 6-methoxy-1*H*-indole-2,3-dione (177 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a yellow solid (72.4 mg, 47%), m.p. > 300 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.30 (d, *J* = 8.9 Hz, 1H), 8.16 (d, *J* = 2.3 Hz, 1H), 7.82 (d, *J* = 8.5 Hz, 1H), 7.43 (d, *J* = 2.6 Hz, 1H), 7.19 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.86 (dd, *J* = 8.5, 2.3 Hz, 1H), 4.01 (s, 3H), 3.95 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.4, 168.0, 165.1, 149.2, 149.0, 141.0, 128.8, 127.3, 119.1, 116.7, 115.1, 114.5, 113.8, 111.9, 102.9, 56.4, 55.9. Anal. Calcd for $C_{17}H_{12}N_2O_4$; C, 66.23; H, 3.92; N, 9.09. Found: C, 66.50; H, 3.66; N, 9.24.

Benzo[*f*]benzo[4,5]indolo[2,1-*b*]quinazoline-8,16-dione (2p):

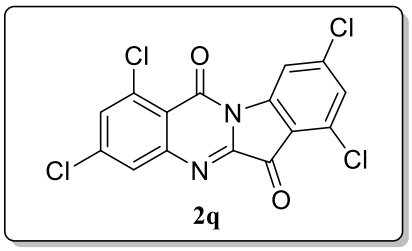


2p

The title compound was prepared according to the general procedure described above using 1*H*-benzo[*e*]indole-1,2(3*H*)-dione (197 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) as a brick red solid (83.5 mg, 48%), m.p. > 300 °C. ^{1}H NMR (400 MHz, CF_3COOD) δ: 8.36 (d, *J* = 8.4 Hz, 1H), 8.12 (d, *J* = 8.6 Hz, 1H), 7.88 – 7.77 (m, 2H), 7.77 –

7.69 (m, 2H), 7.62 (q, J = 8.0 Hz, 2H), 7.56 – 7.35 (m, 3H), 7.19 (d, J = 8.6 Hz, 1H). Anal. Calcd for $C_{23}H_{12}N_2O_2$; C, 79.30; H, 3.47; N, 8.04. Found: C, 79.55; H, 3.72; N, 8.00.

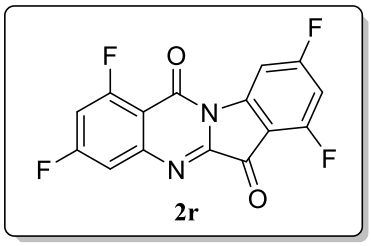
1,3,7,9-Tetrachloroindolo[2,1-*b*]quinazoline-6,12-dione (2q):



2q

The title compound was prepared according to the general procedure described above using 4,6-dichloro-1*H*-indole-2,3-dione (216 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) as a brown solid (105.6 mg, 55%), m.p. > 300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.65 (d, J = 1.6 Hz, 1H), 7.92 (d, J = 2.1 Hz, 1H), 7.65 (d, J = 2.1 Hz, 1H), 7.40 (d, J = 1.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 177.6, 155.5, 149.4, 147.1, 144.9, 144.6, 141.1, 136.9, 134.9, 133.2, 129.7, 129.0, 118.8, 117.3, 117.1. Anal. Calcd for $C_{15}H_4Cl_4N_2O_2$; C, 46.67; H, 1.04; N, 7.26. Found: C, 46.47; H, 1.35; N, 7.50.

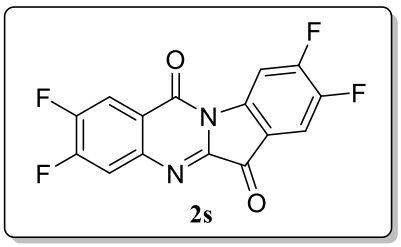
1,3,7,9-Tetrafluoroindolo[2,1-*b*]quinazoline-6,12-dione (2r):



2r

The title compound was prepared according to the general procedure described above using 4,6-difluoro-1*H*-indole-2,3-dione (183 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) as a brown solid (110.4 mg, 69%), m.p. > 300 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.07 (dd, J = 9.0, 2.1 Hz, 1H), 7.78-7.65 (m, 2H), 7.47 (td, J = 9.8, 2.1 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 177.2, 167.21, 167.19, 162.9, 159.4, 154.8, 150.2, 147.6, 146.6, 112.9, 109.7, 108.0, 107.0, 103.7, 102.6; ^{19}F NMR (376 MHz, DMSO-d_6) δ: -91.79 (d, J = 14.9 Hz, 1F), -98.99 (d, J = 13.0 Hz, 1F), -104.88 (d, J = 13.1 Hz, 1F), -106.78 (d, J = 14.9 Hz, 1F). Anal. Calcd for $C_{15}H_4F_4N_2O_2$; C, 56.27; H, 1.26; N, 8.75. Found: C, 56.07; H, 1.53; N, 8.51.

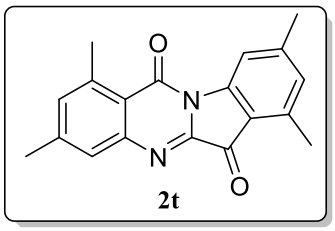
2,3,8,9-Tetrafluoroindolo[2,1-*b*]quinazoline-6,12-dione (2s):



2s

The title compound was prepared according to the general procedure described above using 5,6-difluoroisatin (183 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 8:1) as a dark yellow solid (86,4 mg, 54%), m.p. > 300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.50 (dd, J = 9.8, 6.3 Hz, 1H), 8.20 (dd, J = 9.6, 8.1 Hz, 1H), 7.82 (dd, J = 9.9, 7.0 Hz, 1H), 7.74 (t, J = 7.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 185.7, 179.7, 157.0, 156.2, 154.9, 153.8, 153.2, 150.9, 148.6, 144.3, 142.8, 119.4, 119.0, 115.0, 108.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -115.62 (d, J = 19.5 Hz, 1F), -123.38 (d, J = 21.1 Hz, 1F), -129.31 (d, J = 21.2 Hz, 1F), -135.12 (d, J = 19.2 Hz, 1F). Anal. Calcd for $C_{15}H_4F_4N_2O_2$; C, 56.27; H, 1.26; N, 8.75. Found: C, 56.49; H, 1.56; N, 8.79.

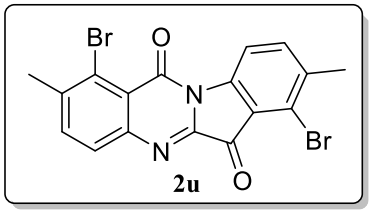
1,3,7,9-Tetramethylindolo[2,1-*b*]quinazoline-6,12-dione (2t):



2t

The title compound was prepared according to the general procedure described above using 4,6-dimethylisatin (175 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 6:1) as a yellow solid (117.1 mg, 77%), m.p. > 300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.20 (s, 1H), 7.58 (s, 1H), 7.14 (s, 1H), 6.87 (s, 1H), 2.85 (s, 3H), 2.62 (s, 3H), 2.43 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 182.4, 158.9, 149.4, 148.3, 146.9, 144.9, 144.7, 142.1, 140.9, 134.1, 129.5, 128.9, 119.3, 117.8, 115.8, 22.9, 22.7, 21.5, 18.3. Anal. Calcd for $C_{19}H_{16}N_2O_2$; C, 74.98; H, 5.30; N, 9.20. Found: C, 74.77; H, 5.52; N, 9.39.

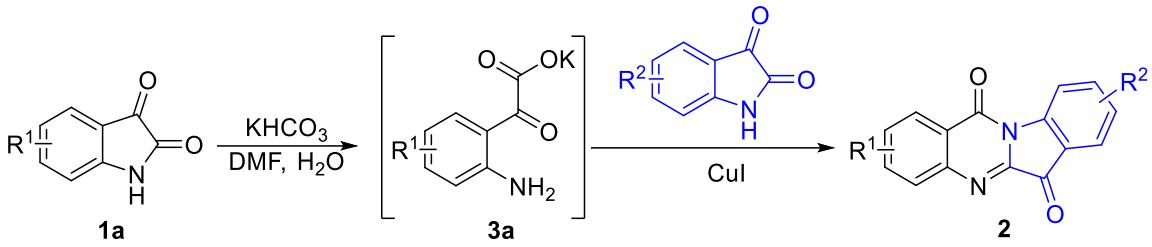
1,7-Dibromo-2,8-dimethylindolo[2,1-*b*]quinazoline-6,12-dione (2u):



2u

The title compound was prepared according to the general procedure described above using 4-bromo-5-methylisatin (240 mg, 1.0 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a yellow solid (164.1 mg, 76%), m.p. > 300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.58 (d, J = 8.2 Hz, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.70 (d, J = 8.2 Hz, 1H), 7.61 (dd, J = 8.2, 0.8 Hz, 1H), 2.62 (s, 3H), 2.50 (s, 3H). Anal. Calcd for $C_{17}H_{10}Br_2N_2O_2$; C, 47.04; H, 2.32; N, 6.45. Found: C, 46.77; H, 2.63; N, 6.21.

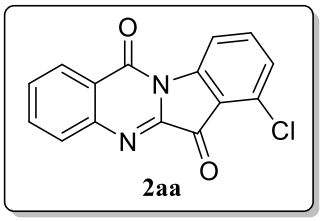
5. General procedure for the synthesis of 2aa-2am



Isatin derivative (0.5 mmol), $KHCO_3$ (1.0 mmol), DMF (2 mL), and water (20 μL) were added to a 10 mL reaction tube. The reaction mixture was stirred at 90 ℃ for 12 h. Then CuI (0.2 mmol) and another isatin derivative (0.5 mmol) were added to the reaction tube, which was continuously stirred at 90 ℃ for 12 h. The reaction mixture was quenched, filtered to remove the insoluble residue, and washed 3 times with ethyl acetate (250 mL) and saturated NaCl solution (250 mL), respectively. The organic phase was dried with $MgSO_4$. The crude residue was obtained by removing the solvent, which was purified by column chromatography to afford the desired product **2**.

Characterization data:

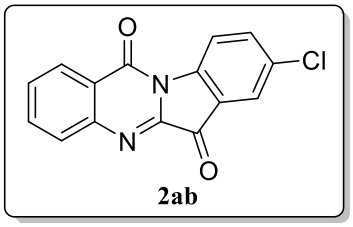
7-Chloroindolo[2,1-*b*]quinazoline-6,12-dione (2aa):



2aa

The title compound was prepared according to the general procedure described above using isatin (74 mg, 0.5 mmol), 4-chloroisatin (91 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a yellow solid (114.5 mg, 81%), m.p. >300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.60 (d, J = 8.0 Hz, 1H), 8.43 (d, J = 7.9 Hz, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.87 (t, J = 7.8 Hz, 1H), 7.69 (t, J = 8.1 Hz, 2H), 7.37 (d, J = 8.1 Hz, 1H). Anal. Calcd for $C_{15}H_7ClN_2O_2$; C, 63.73; H, 2.50; N, 9.91. Found: C, 63.99; H, 2.24; N, 9.69.

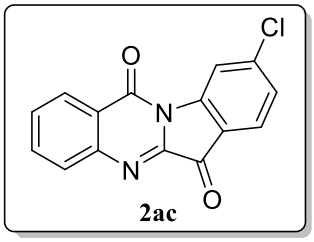
8-Chloroindolo[2,1-*b*]quinazoline-6,12-dione (2ab):



2ab

The title compound was prepared according to the general procedure described above using isatin (74 mg, 0.5 mmol), 5-chloroisatin (91 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a brown solid (117.3 mg, 83%), m.p. >300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.59 (d, J = 8.5 Hz, 1H), 8.43 (ddd, J = 8.0, 1.6, 0.5 Hz, 1H), 8.03 (dd, J = 8.0, 1.0 Hz, 1H), 7.92-7.82 (m, 2H), 7.74 (dd, J = 8.6, 2.2 Hz, 1H), 7.69 (ddd, J = 8.4, 7.3, 1.2 Hz, 1H). Anal. Calcd for $C_{15}H_7ClN_2O_2$; C, 63.73; H, 2.50; N, 9.91. Found: C, 63.87; H, 2.76; N, 9.97.

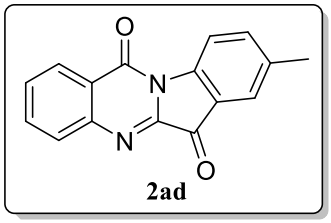
9-Chloroindolo[2,1-*b*]quinazoline-6,12-dione (2ac):



2ac

The title compound was prepared according to the general procedure described above using isatin (74 mg, 0.5 mmol), 6-chloroisatin (91 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a dark yellow solid (108.8 mg, 77%), m.p. >300 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.48 (d, J = 1.8 Hz, 1H), 8.34 (dt, J = 7.9, 1.1 Hz, 1H), 7.97 (dd, J = 3.7, 1.0 Hz, 2H), 7.93 (d, J = 8.1 Hz, 1H), 7.76 (ddd, J = 8.2, 4.8, 3.6 Hz, 1H), 7.57 (dd, J = 8.1, 1.9 Hz, 1H). Anal. Calcd for $C_{15}H_7ClN_2O_2$; C, 63.73; H, 2.50; N, 9.91. Found: C, 63.50; H, 2.26; N, 10.18.

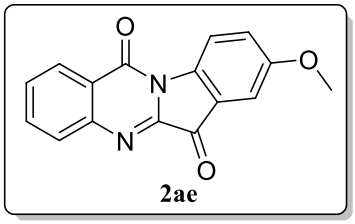
8-Methylindolo[2,1-*b*]quinazoline-6,12-dione (2ad):



2ad

The title compound was prepared according to the general procedure described above using isatin (74 mg, 0.5 mmol), 5-methylisatin (81 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a dark yellow solid (112.8 mg, 86%), m.p. >300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.44 (d, J = 8.2 Hz, 1H), 8.39 (dd, J = 7.9, 1.5 Hz, 1H), 8.00 (dd, J = 8.2, 1.1 Hz, 1H), 7.82 (ddd, J = 8.1, 7.2, 1.5 Hz, 1H), 7.68 (dt, J = 1.7, 0.8 Hz, 1H), 7.64 (ddd, J = 8.2, 7.2, 1.2 Hz, 1H), 7.55 (ddd, J = 8.3, 1.9, 0.8 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 182.7, 157.9, 146.7, 144.6, 144.3, 138.7, 137.5, 135.0, 130.7, 130.1, 127.5, 125.5, 123.8, 122.0, 117.7, 21.1. Anal. Calcd for $C_{16}H_{10}N_2O_2$; C, 73.27; H, 3.84; N, 10.68. Found: C, 73.55; H, 3.58; N, 10.87.

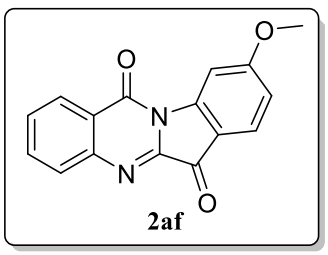
8-Methoxyindolo[2,1-*b*]quinazoline-6,12-dione (2ae):



2ae

The title compound was prepared according to the general procedure described above using isatin (74 mg, 0.5 mmol), 5-methoxyisatin (89 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as an orange solid (123.8 mg, 89%), m.p. >300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.47 (d, J = 8.8 Hz, 1H), 8.39 (dd, J = 7.9, 1.6 Hz, 1H), 7.99 (d, J = 8.2 Hz, 1H), 7.82 (td, J = 8.1, 7.7, 1.6 Hz, 1H), 7.69-7.59 (m, 1H), 7.34 (d, J = 2.7 Hz, 1H), 7.30-7.26 (m, 1H), 3.87 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 182.6, 158.7, 157.7, 146.6, 144.7, 140.4, 134.9, 130.7, 130.2, 127.4, 125.0, 123.9, 123.0, 119.1, 108.4, 56.0. Anal. Calcd for $C_{16}H_{10}N_2O_3$; C, 69.06; H, 3.62; N, 10.07. Found: C, 69.22; H, 3.86; N, 10.01.

9-Methoxyindolo[2,1-*b*]quinazoline-6,12-dione (2af):

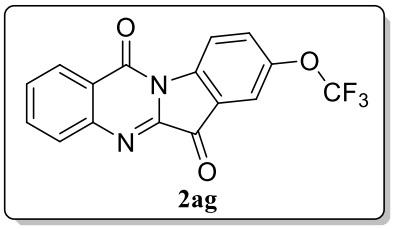


2af

The title compound was prepared according to the general procedure described above using isatin (74 mg, 0.5 mmol), 6-methoxyisatin (89 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a yellow solid (116.9 mg, 84%), m.p. >300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39 (ddd, J =

7.9, 1.6, 0.5 Hz, 1H), 8.15 (d, *J* = 2.2 Hz, 1H), 8.01 (dd, *J* = 8.4, 0.9 Hz, 1H), 7.88-7.78 (m, 2H), 7.65 (ddd, *J* = 8.4, 7.3, 1.2 Hz, 1H), 6.86 (dd, *J* = 8.5, 2.3 Hz, 1H), 4.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.2, 168.0, 158.2, 148.9, 146.7, 145.4, 135.1, 130.6, 130.0, 127.4, 127.3, 123.5, 115.3, 113.9, 103.0, 56.4. Anal. Calcd for $C_{16}H_{10}N_2O_3$; C, 69.06; H, 3.62; N, 10.07. Found: C, 69.01; H, 3.38; N, 9.84.

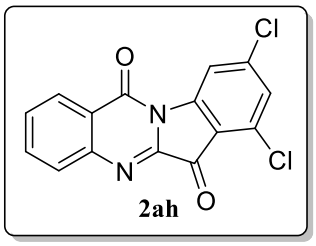
8-(Trifluoromethoxy)indolo[2,1-*b*]quinazoline-6,12-dione (2ag):



2ag

The title compound was prepared according to the general procedure described above using isatin (74 mg, 0.5 mmol), 5-(trifluoromethoxy)isatin (116 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a brick red solid (149.5 mg, 89%), m.p. >300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.65 (d, *J* = 8.8 Hz, 1H), 8.39 (dd, *J* = 7.9, 1.5 Hz, 1H), 8.00 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.89-7.80 (m, 1H), 7.74 (dd, *J* = 2.4, 1.2 Hz, 1H), 7.67 (ddd, *J* = 8.3, 7.3, 1.2 Hz, 1H), 7.60 (ddd, *J* = 8.8, 2.6, 0.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.4, 157.9, 147.7 (q, *J* = 1.9 Hz), 146.4, 144.3, 144.1, 135.4, 130.9, 130.6, 130.5, 127.6, 123.5, 123.1, 120.3 (q, *J* = 259.2 Hz), 119.4, 117.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -58.21 (s, 3F). Anal. Calcd for $C_{16}H_7F_3N_2O_3$; C, 57.84; H, 2.12; N, 8.43. Found: C, 57.60; H, 2.46; N, 8.61.

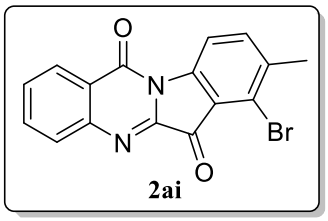
7,9-Dichloroindolo[2,1-*b*]quinazoline-6,12-dione (2ah):



2ah

The title compound was prepared according to the general procedure described above using isatin (74 mg, 0.5 mmol), 4,6-dichloro-1*H*-indole-2,3-dione (108 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a dark yellow solid (106.2 mg, 67%), m.p. >300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.65 (d, *J* = 1.6 Hz, 1H), 8.42 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.04 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.88 (ddd, *J* = 8.1, 7.3, 1.6 Hz, 1H), 7.70 (ddd, *J* = 8.4, 7.3, 1.2 Hz, 1H), 7.38 (d, *J* = 1.7 Hz, 1H). Anal. Calcd for $C_{15}H_6Cl_2N_2O_2$; C, 56.81; H, 1.91; N, 8.83. Found: C, 56.97; H, 1.66; N, 8.61.

7-Bromo-8-methylindolo[2,1-*b*]quinazoline-6,12-dione (2ai):

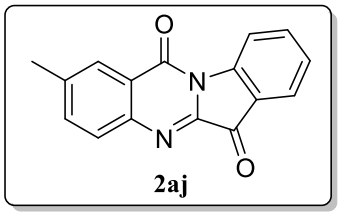


2ai

The title compound was prepared according to the general procedure described above using isatin (74 mg, 0.5 mmol), 4-bromo-5-methylisatin (120 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a yellow solid (138.2 mg, 81%), m.p. >300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.51 (d, *J* = 8.1 Hz, 1H), 8.41 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.04 (d, *J* = 8.2 Hz, 1H), 7.85 (td, *J* = 8.2, 7.7, 1.6 Hz, 1H), 7.71-7.63 (m, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 2.50 (s, 3H). Anal. Calcd for $C_{16}H_9BrN_2O_2$; C, 56.33; H, 2.66; N, 8.21. Found: C, 56.09; H, 2.48; N, 8.48.

2-Methylindolo[2,1-*b*]quinazoline-6,12-dione (2aj):

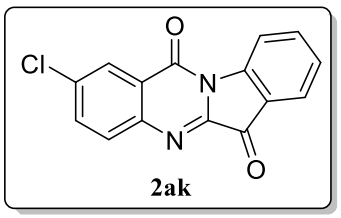
The title compound was prepared according to the general procedure described above using 5-



2aj

methylisatin (81 mg, 0.5 mmol), isatin (74 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a yellow solid (241.3 mg, 92%), m.p. >300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.57 (d, *J* = 8.1 Hz, 1H), 8.20-8.13 (m, 1H), 7.87 (d, *J* = 8.2 Hz, 2H), 7.75 (td, *J* = 7.8, 1.4 Hz, 1H), 7.62 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.39 (td, *J* = 7.5, 0.9 Hz, 1H), 2.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 182.5, 158.1, 146.3, 144.5, 143.7, 141.2, 138.1, 136.4, 130.5, 127.3, 127.1, 125.3, 123.5, 122.1, 117.9, 21.6. Anal. Calcd for $C_{16}H_{10}N_2O_2$; C, 73.27; H, 3.84; N, 10.68. Found: C, 73.42; H, 3.58; N, 10.83.

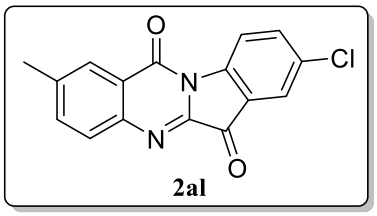
2-Chloroindolo[2,1-*b*]quinazoline-6,12-dione (2ak):



2ak

The title compound was prepared according to the general procedure described above using 5-chloroisatin (91 mg, 0.5 mmol), isatin (74 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 8:1) as a yellow solid (127.2 mg, 45%), m.p. >300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.62 (d, *J* = 8.1 Hz, 1H), 8.40 (d, *J* = 2.5 Hz, 1H), 7.97 (d, *J* = 8.6 Hz, 1H), 7.93 (d, *J* = 7.5 Hz, 1H), 7.86-7.73 (m, 2H), 7.45 (t, *J* = 7.6 Hz, 1H). Anal. Calcd for $C_{15}H_7ClN_2O_2$; C, 63.73; H, 2.50; N, 9.91. Found: C, 63.51; H, 2.76; N, 9.67.

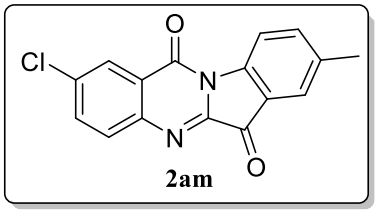
8-Chloro-2-methylindolo[2,1-*b*]quinazoline-6,12-dione (2al):



2al

The title compound was prepared according to the general procedure described above using 5-methylisatin (81 mg, 0.5 mmol), 5-chloroisatin (91 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 4:1) as a yellow solid (210.7 mg, 71%), m.p. >300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.56 (d, *J* = 8.6 Hz, 1H), 8.22-8.15 (m, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 2.2 Hz, 1H), 7.71 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.65 (dd, *J* = 8.3, 2.1 Hz, 1H), 2.55 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.4, 157.9, 144.5, 144.4, 143.4, 141.6, 137.6, 136.6, 133.2, 130.7, 127.4, 125.1, 123.4, 123.3, 119.2, 21.7. Anal. Calcd for $C_{16}H_9ClN_2O_2$; C, 64.77; H, 3.06; N, 9.44. Found: C, 64.97; H, 3.37; N, 9.19.

2-Chloro-8-methylindolo[2,1-*b*]quinazoline-6,12-dione (2am):



2am

The title compound was prepared according to the general procedure described above using 5-chloroisatin (91 mg, 0.5 mmol), 5-methylisatin (81 mg, 0.5 mmol), CuI (38 mg, 0.2 mmol), $KHCO_3$ (100 mg, 1.0 mmol), and purified by column chromatography (petroleum ether/ethyl acetate = 8:1) as a yellow solid (157.3 mg, 53%), m.p. >300 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.47 (d, *J* = 8.2 Hz, 1H), 8.39 (d, *J* = 2.5 Hz, 1H), 7.96 (d, *J* = 8.6 Hz, 1H), 7.77 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.71 (s, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 2.46 (s, 3H). Anal. Calcd for $C_{16}H_9ClN_2O_2$; C, 64.77; H, 3.06; N, 9.44. Found: C, 64.91; H, 3.32; N, 9.46.

6. X-ray analysis

X-Ray Crystal-Structure Determination of 2a (CCDC 2149708). The single crystal X-ray structure of **2a** was determined (Figure S3). The crystal data and structure refinement of specific compound **2a** were shown in Table S1. Single crystals of compound **2a** were obtained by slow evaporation of ethyl acetate/cyclohexane solution at room temperature over a period of two weeks. Compound **2a** was obtained as yellow acicular crystals with monoclinic crystal system and P 21/n space group.

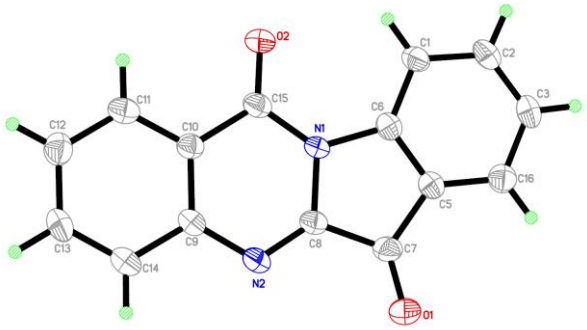


Figure S3. X-ray structure of **2a** (displacement ellipsoids were drawn at the 30% probability level).

Table S1. Crystal data and structure refinement for compound **2a**.

Empirical formula	C_{15} H_8 N_2 O_2
Formula weight	248.23
Temperature/K	293(2)
Wavelength/Å	0.71073
Crystal system	Monoclinic
Space group	P 21/n
a/Å	7.4100(15)
b/Å	7.6000(15)
c/Å	19.460(4)
α/deg	90
β/deg	91.52(3)
γ/deg	90
V/ $Å^3$	1095.5(4)
Z	4
ρ_{calc}/g·cm^{-3}	1.505
μ/mm^{-1}	0.103
F(000)	512
Crystal size (mm^3)	0.2×0.2×0.2
θ range for entire data collection	3.402 to 25.349°
Index ranges	-8<=h<=8, -8<=k<=9, -23<=l<=16
Reflections collected	4715
Independent reflections	1989 [R(int) = 0.0516]
Completeness to theta = 25.242°	99.2%
Refinement method	Full-matrix least-squares on F^2
Date / restraints / parameters	1989 / 0 / 172

Goodness-of-fit on F^2	1.207
Final R indices [I>2σ(I)]	R_1 = 0.0829, wR_2 = 0.1748
R indices (all data)	R_1 = 0.1316, wR_2 = 0.2018
Largest peak and hole /e $Å^{-3}$	0.204 and -0.277

References

1. T. T.Yu, R. Kuppusamy, M. Yasir, M. M. Hassan, A. Alghalayini, S. Gadde, E. Deplazes, C. Cranfield, M. D. P. Willcox, D. S. Black and N. Kumar, Design, synthesis and biological evaluation of biphenylglyoxamide-based small molecular antimicrobial peptide mimics as antibacterial agents, *Int. J. Mol. Sci.,* 2020, **21**, 6789-6827.
2. K. C. Nicolaou, Y.-P. Wang, M. Lu, D. Mandal, M. R. Pattanayak, R.-C. Yu, A. A. Shah, J.-S. Chen, H.-J. Zhang, J. J. Crawford, L. Pasunoori, Y. B. Poudel, N. S. Chowdari, C. Pan, A. Nazeer, S. Gangwar, G. Vite and E. N. Pitsinos, Streamlined total synthesis of uncialamycin and its application to the synthesis of designed analogues for biological investigations, *J. Am. Chem. Soc.,* 2016, **138**, 8235-8246.
3. B. M. Trost, C. A. Kalnmals, D. Ramakrishnan, M. C. Ryan, R. W. Smaha and S. Parkin, Ruthenium-catalyzed asymmetric allylic alkylation of isatins, *Org. Lett.,* 2020, **22**, 2584-2589.

7. Spectroscopic Data for Products

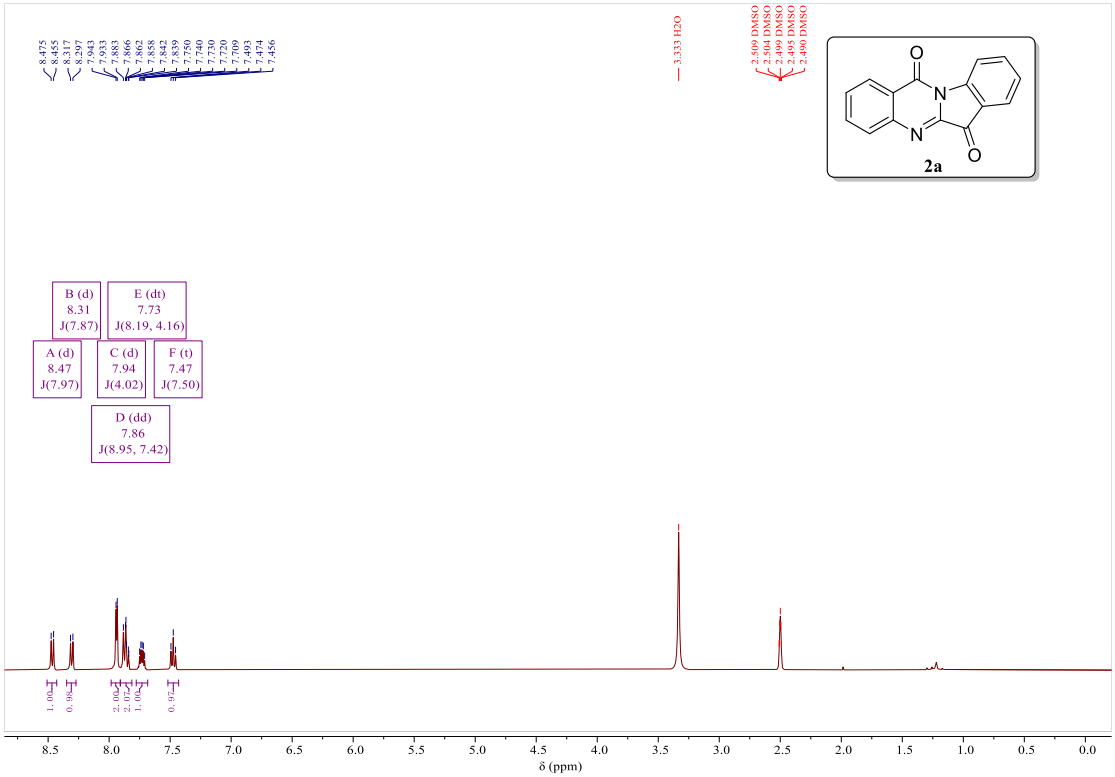


Figure S4. ^{1}H NMR (400 MHz, DMSO-d_6) of compound **2a**

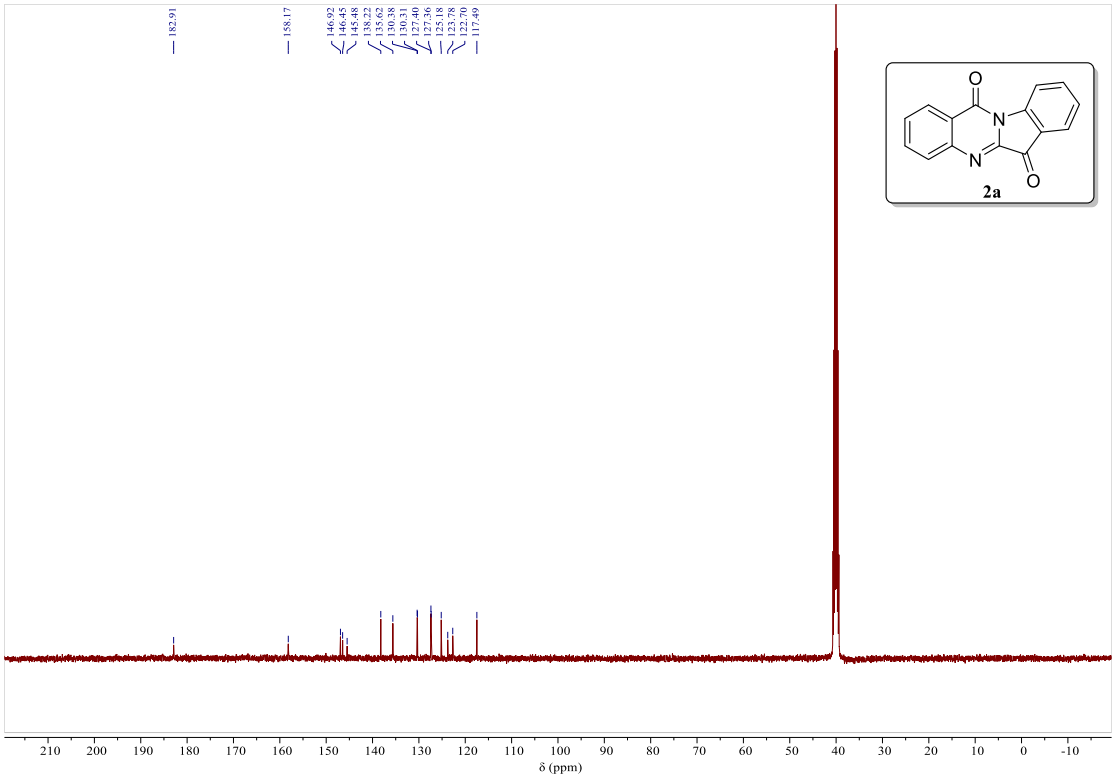


Figure S5. ^{13}C NMR (101 MHz, DMSO-d_6) of compound **2a**

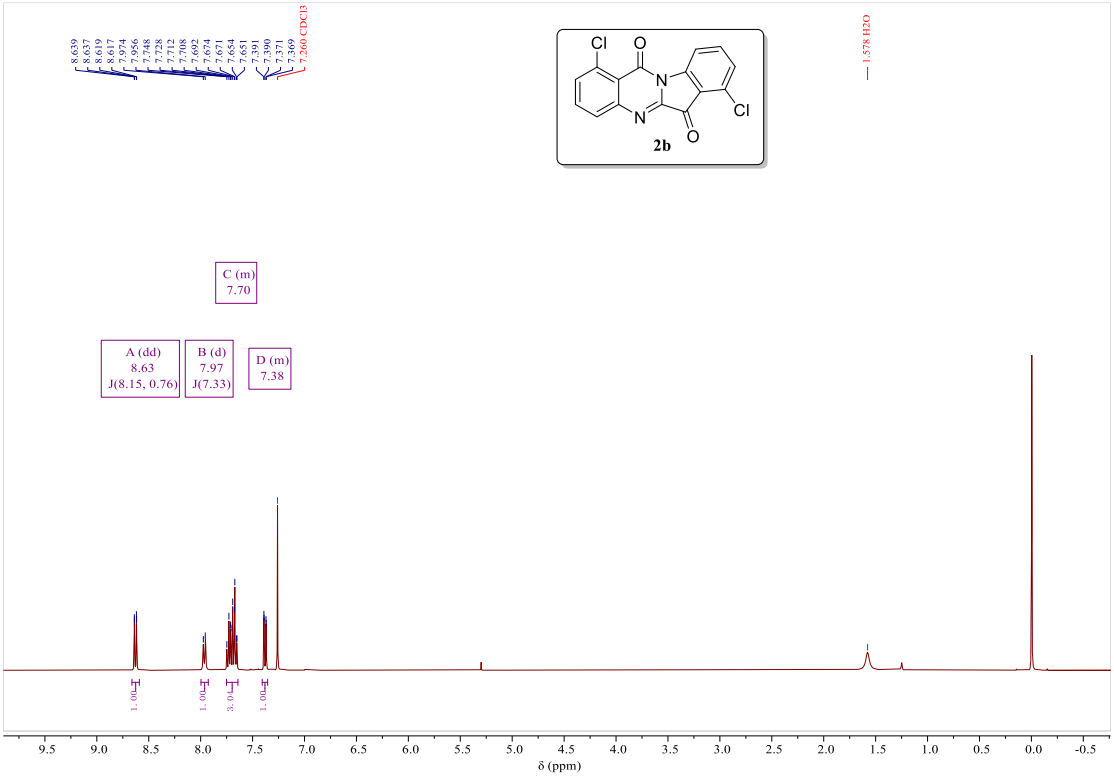


Figure S6. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2b**

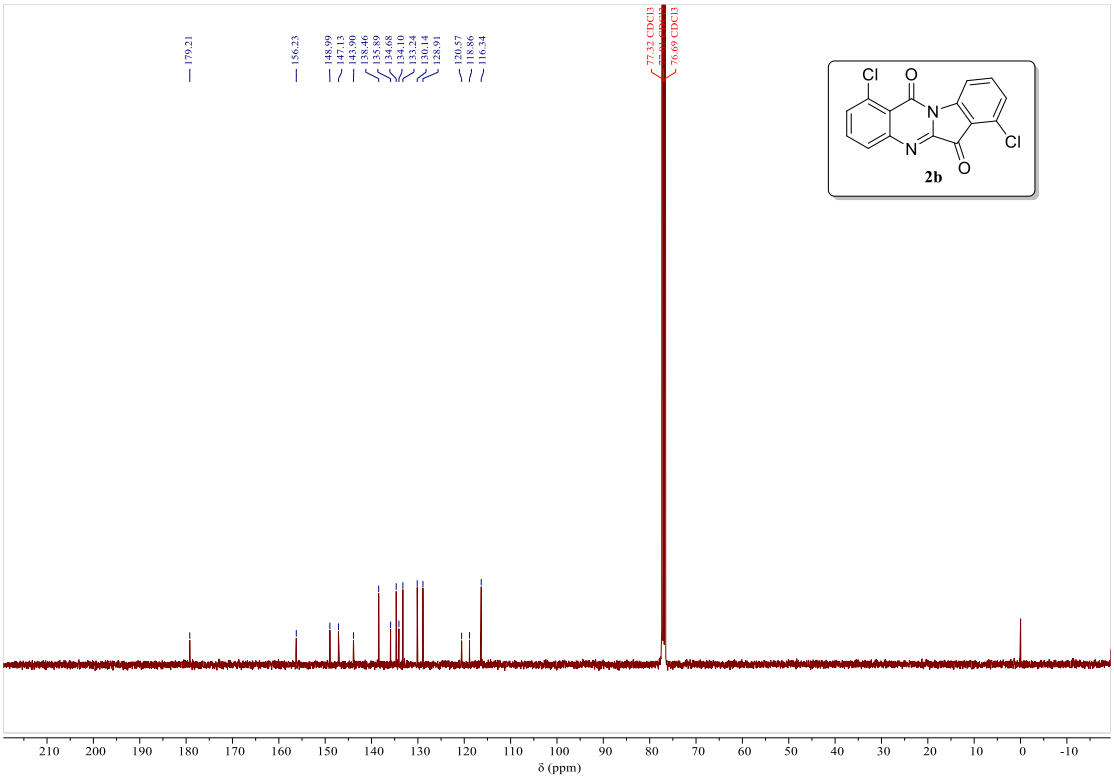


Figure S7. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2b**

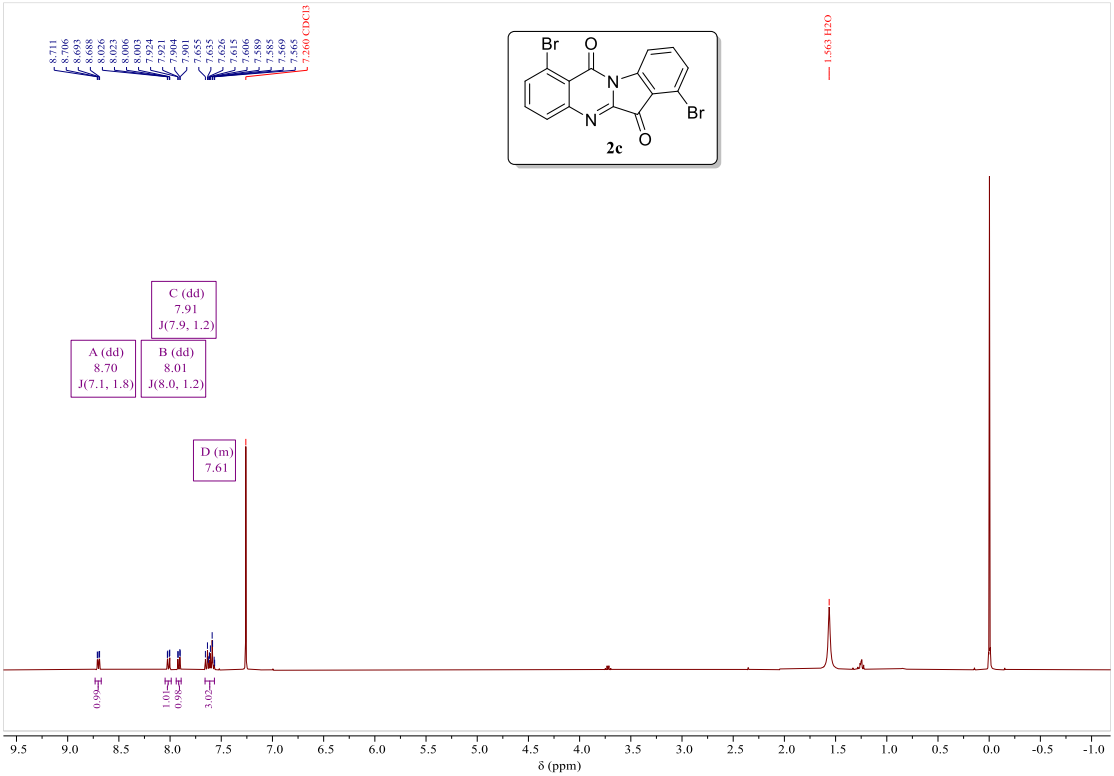


Figure S8. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2c**

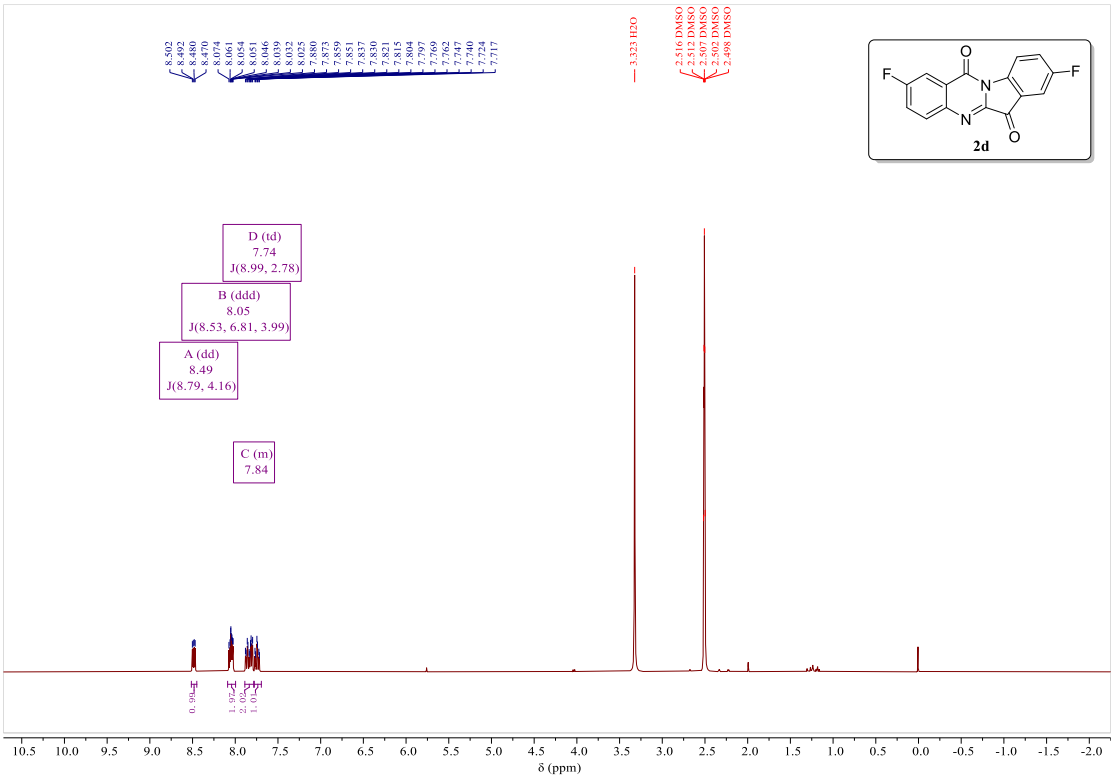


Figure S9. ^{1}H NMR (400 MHz, DMSO-d_6) of compound **2d**

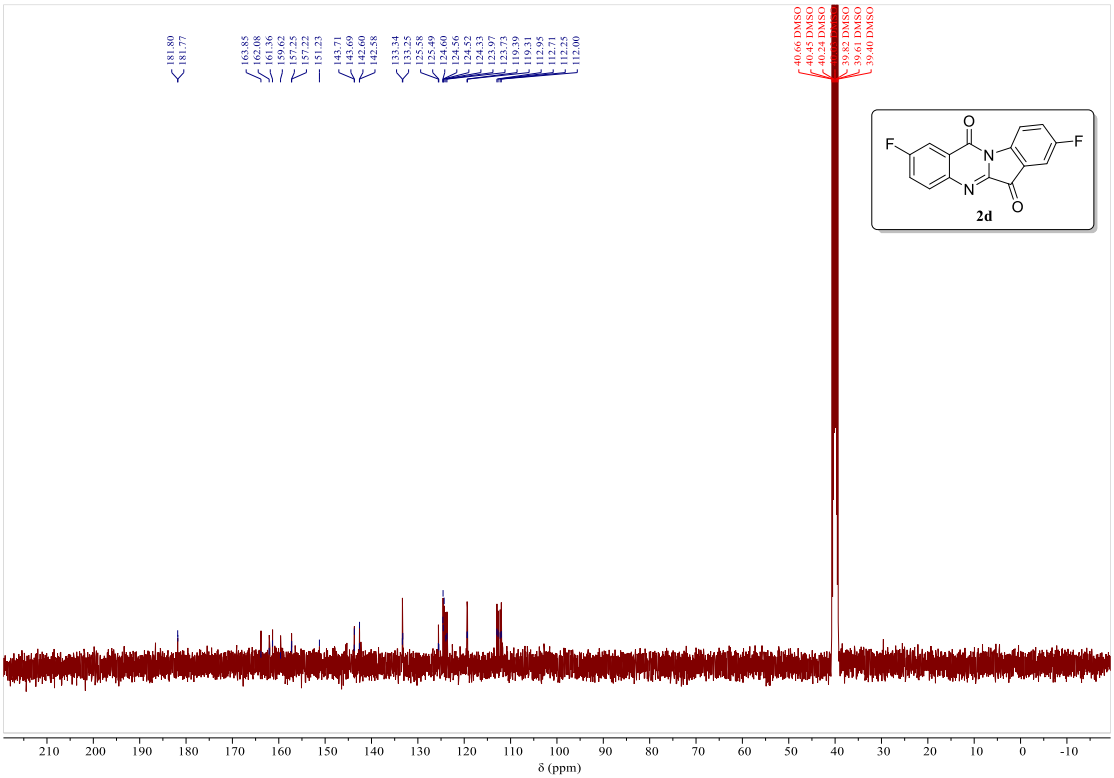


Figure S10. ^{13}C NMR (101 MHz, DMSO-d_6) of compound **2d**

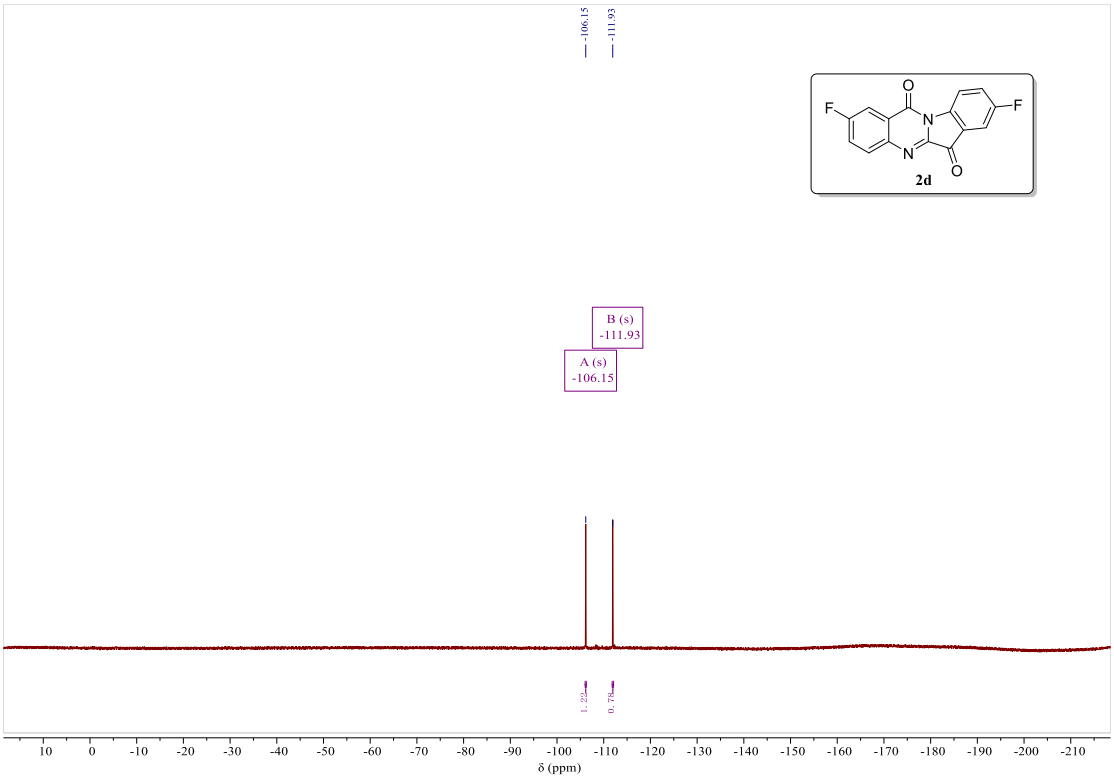


Figure S11. ^{19}F NMR (376 MHz, DMSO-d_6) of compound **2d**

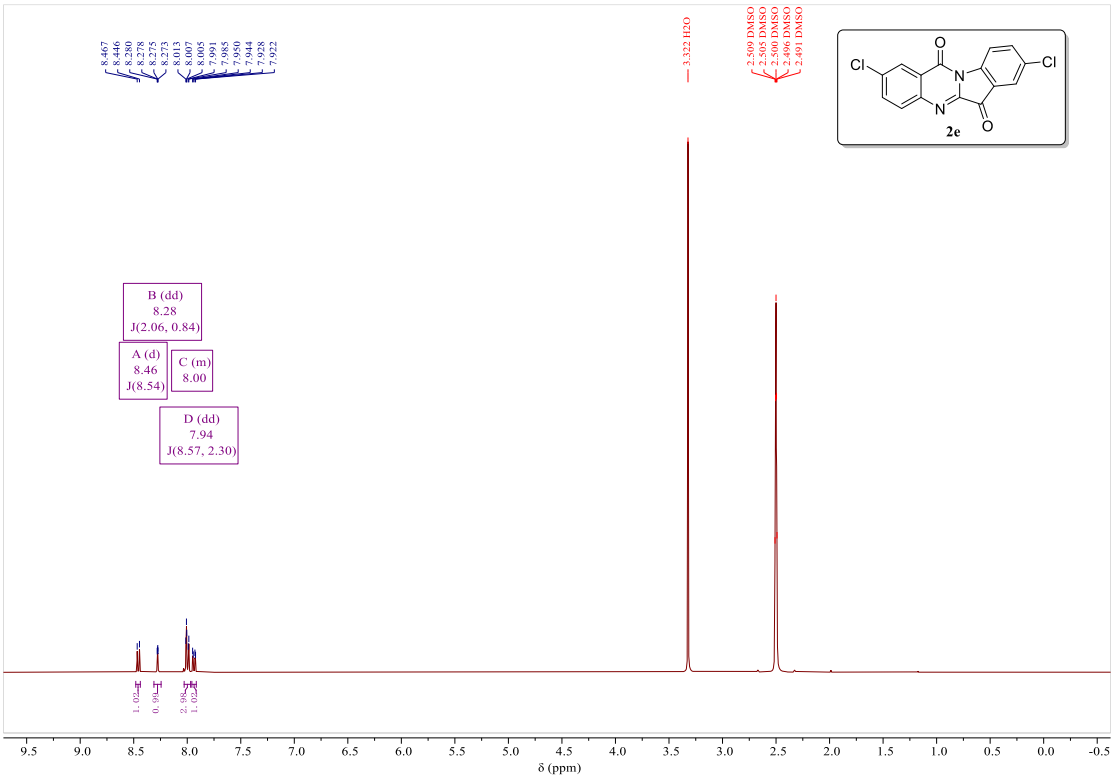


Figure S12. ^{1}H NMR (400 MHz, DMSO-d_6) of compound **2e**

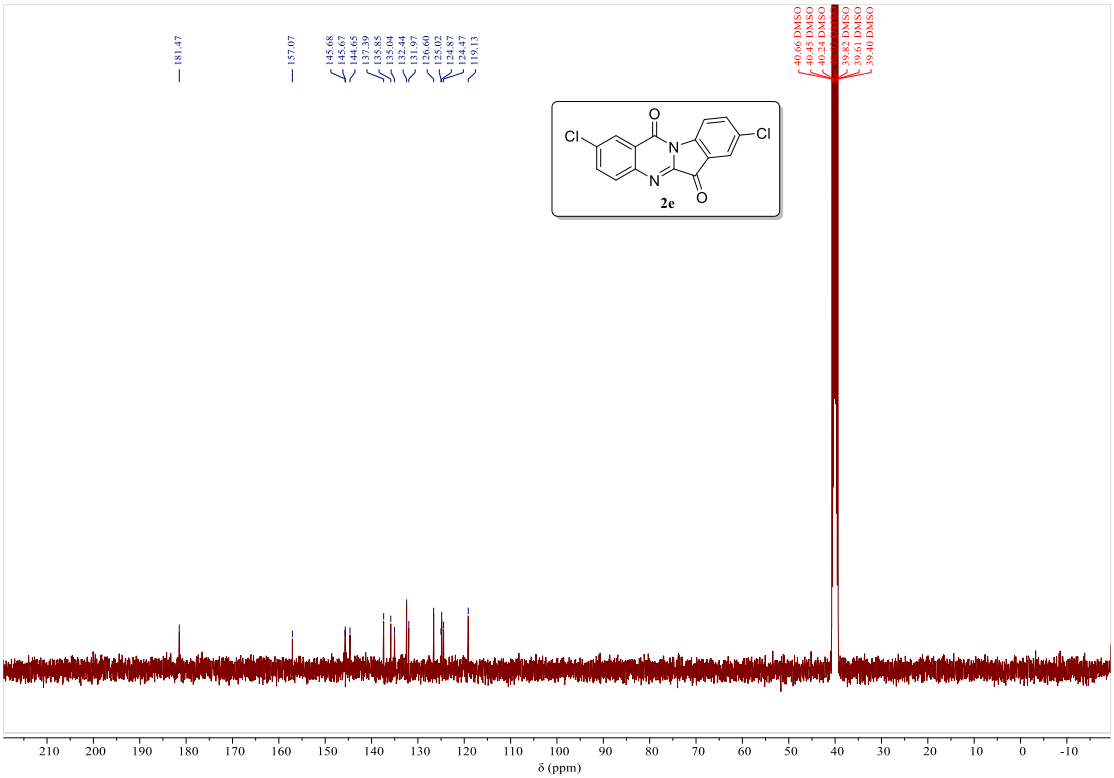


Figure S13. ^{13}C NMR (101 MHz, DMSO-d_6) of compound **2e**

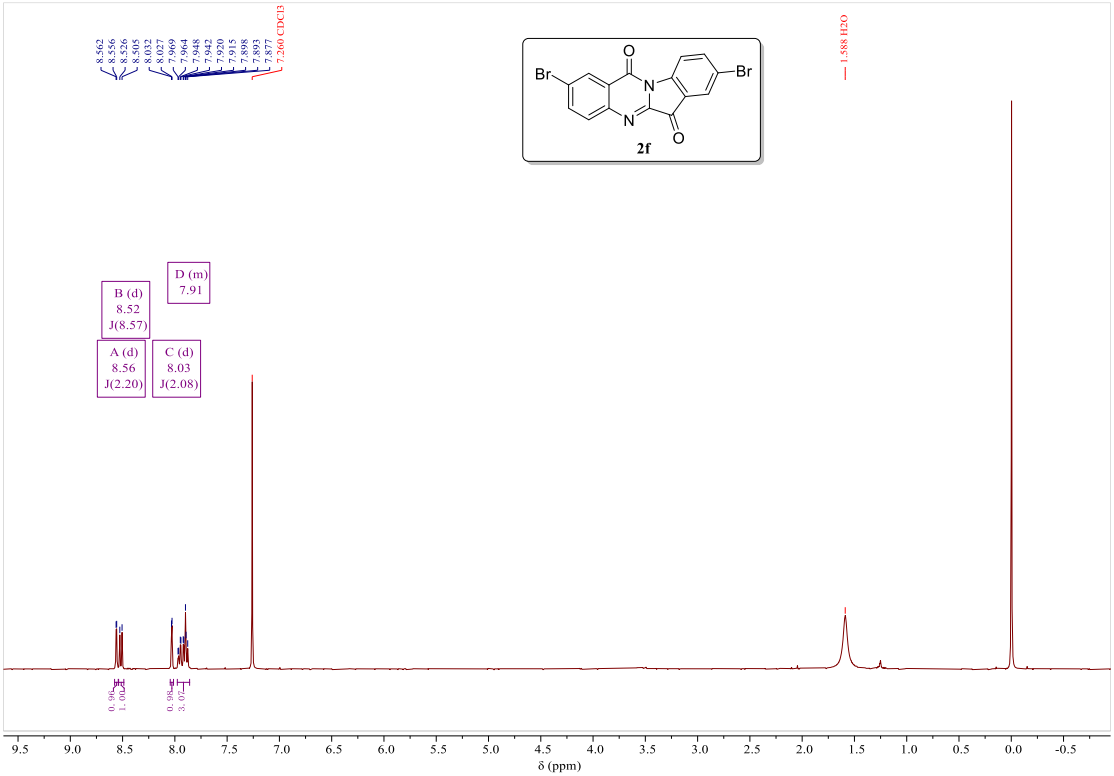


Figure S14. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2f**

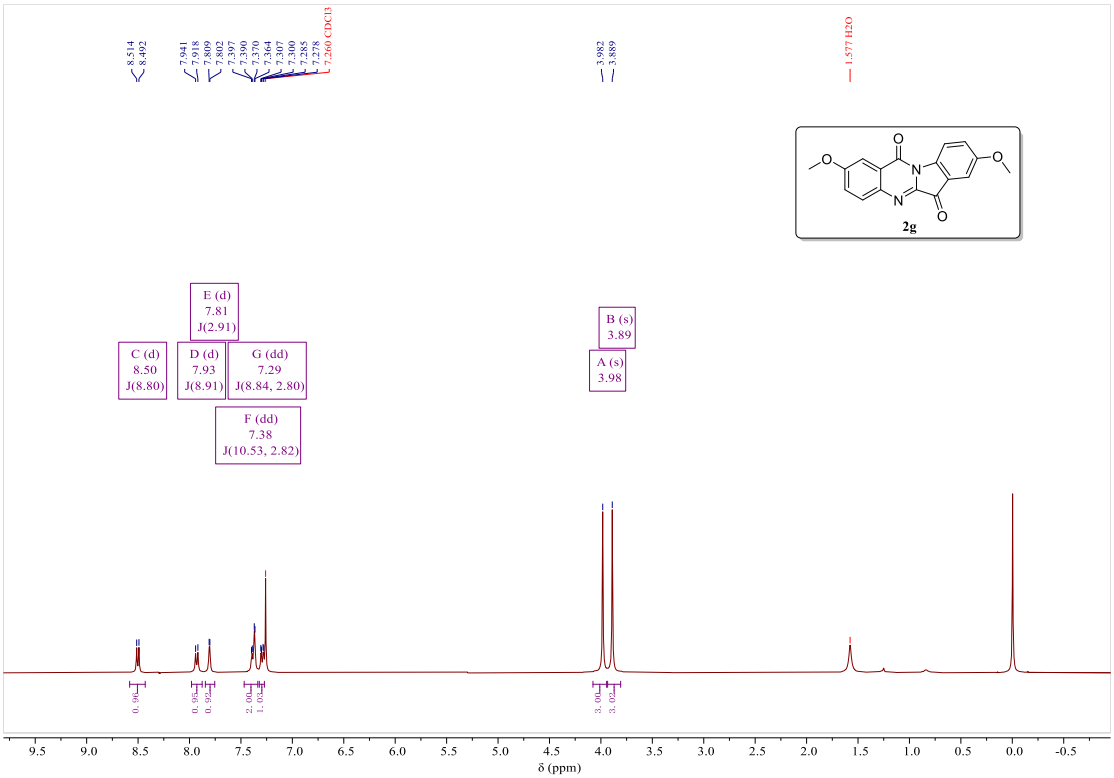


Figure S15. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2g**

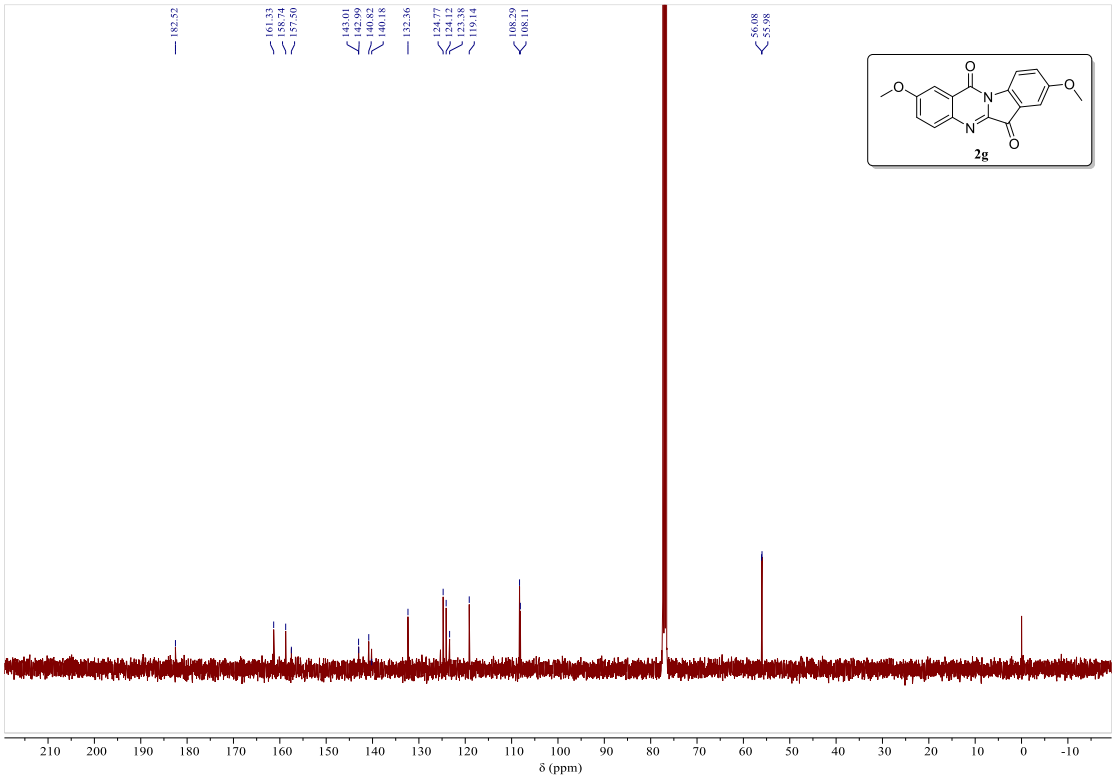


Figure S16. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2g**

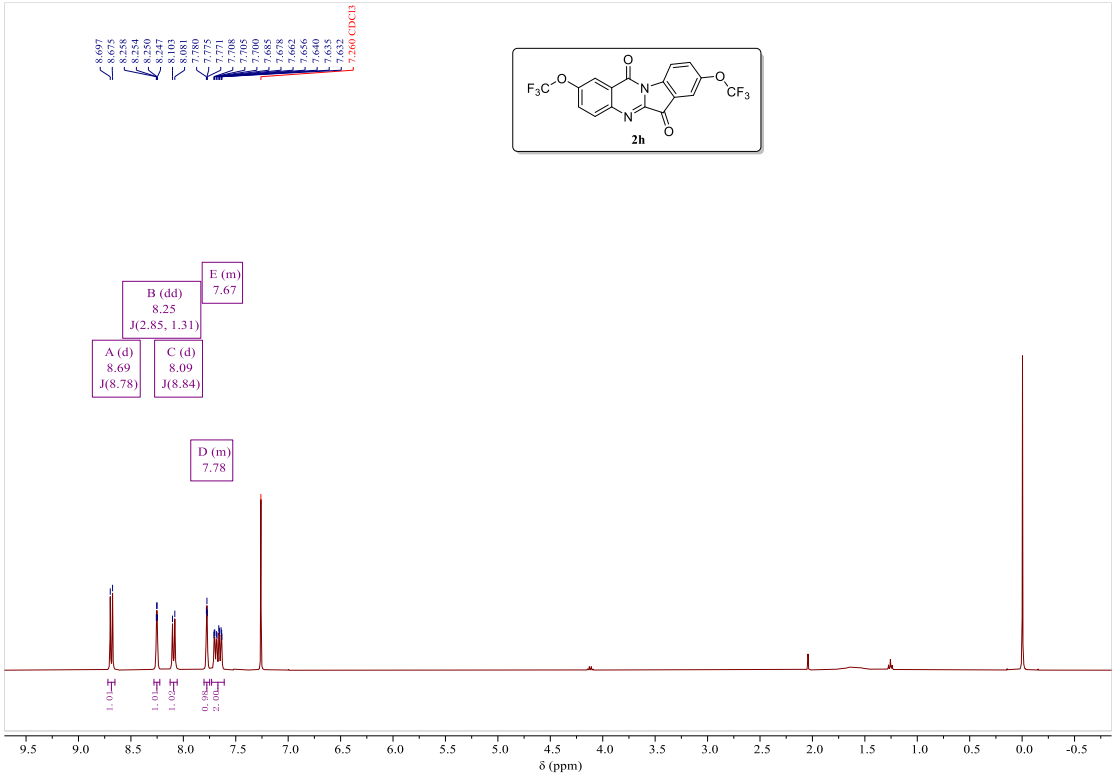


Figure S17. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2h**

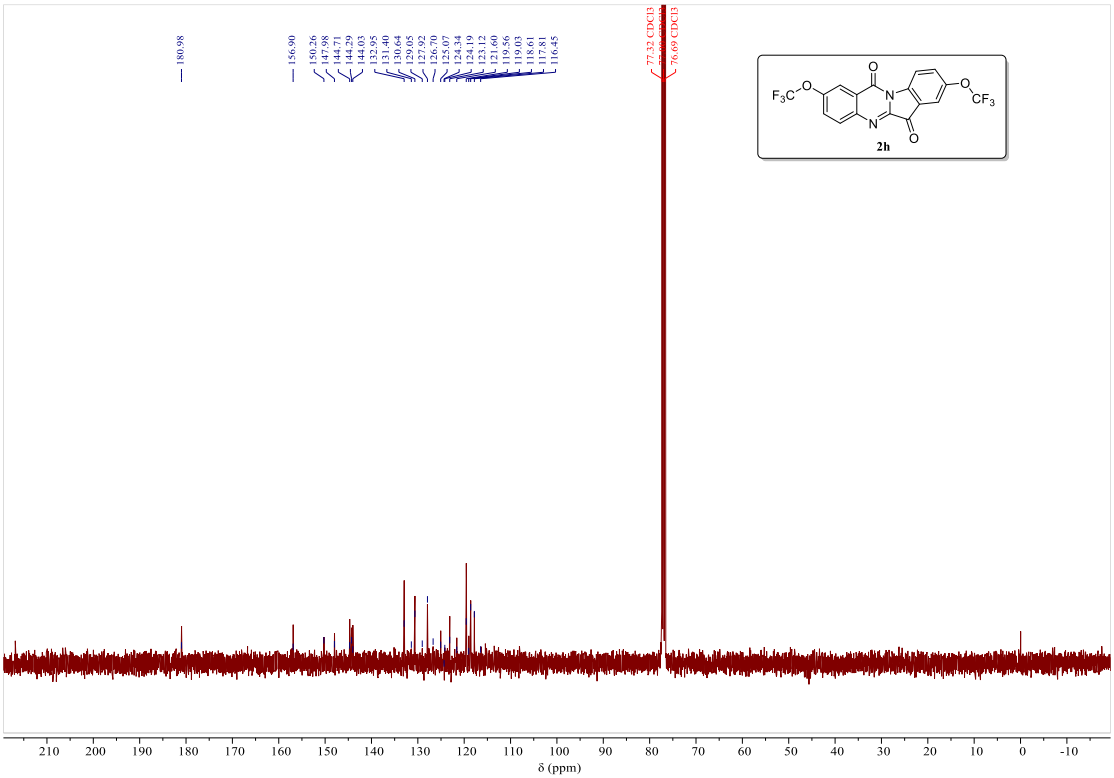


Figure S18. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2h**

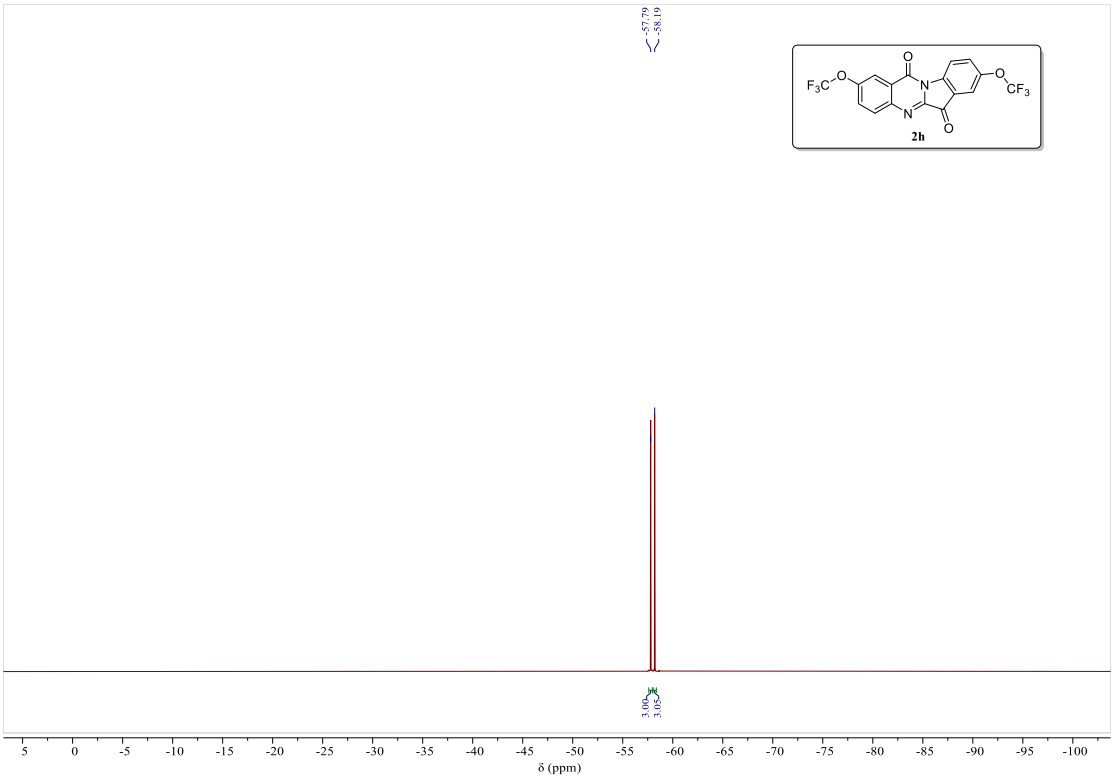


Figure S19. ^{19}F NMR (376 MHz, $CDCl_3$) of compound **2h**

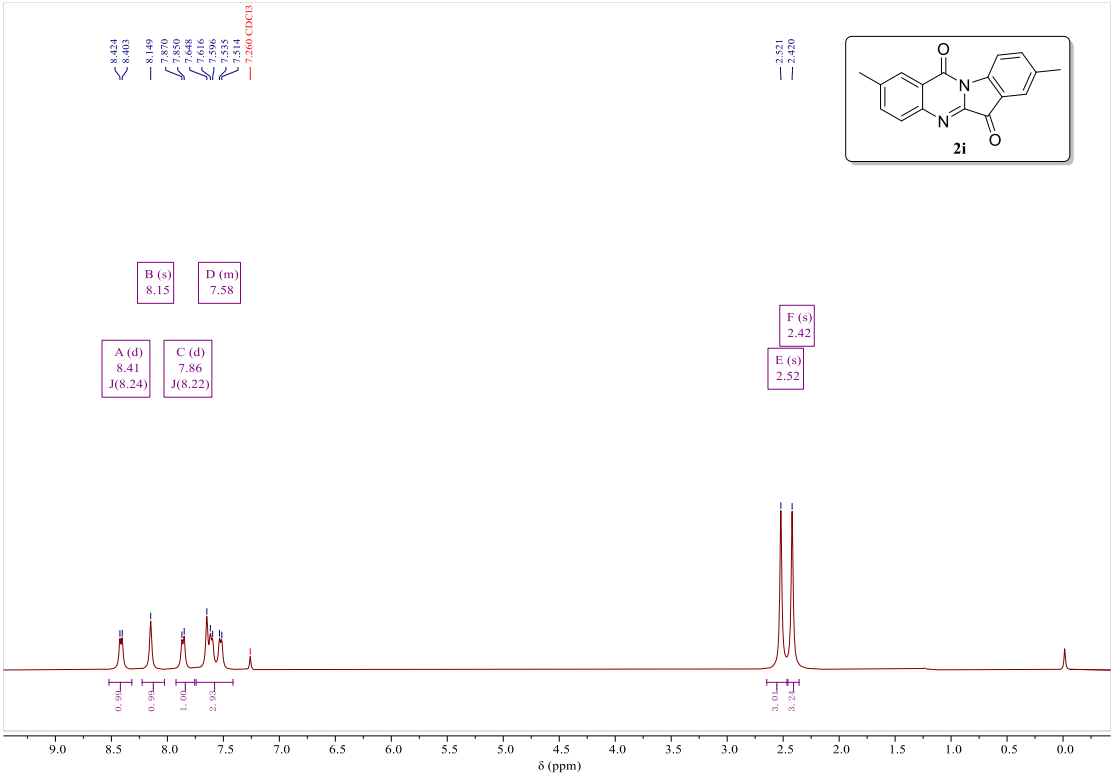


Figure S20. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2i**

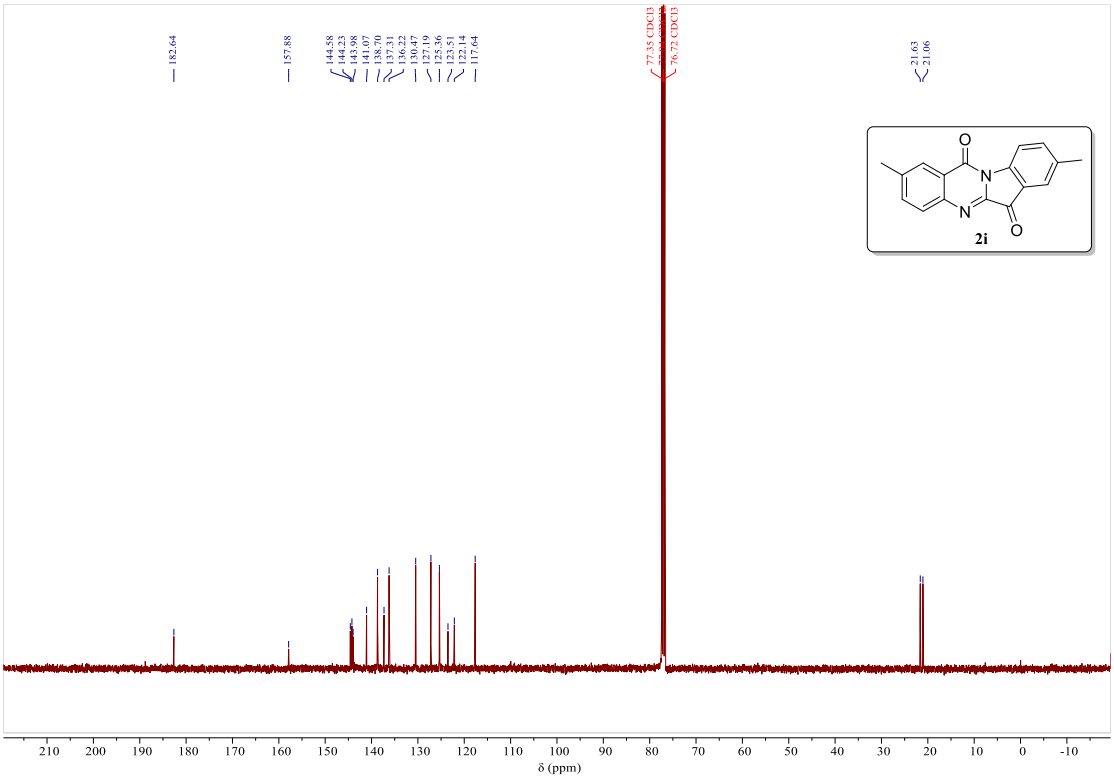


Figure S21. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2i**

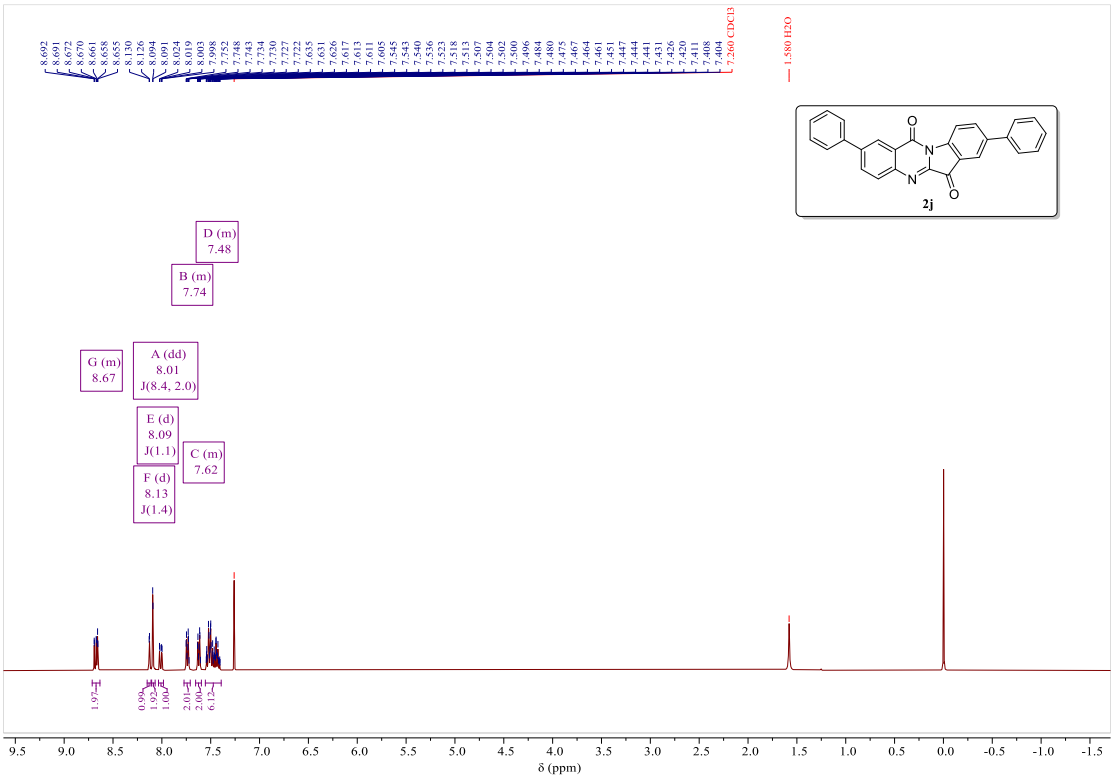


Figure S22. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2j**

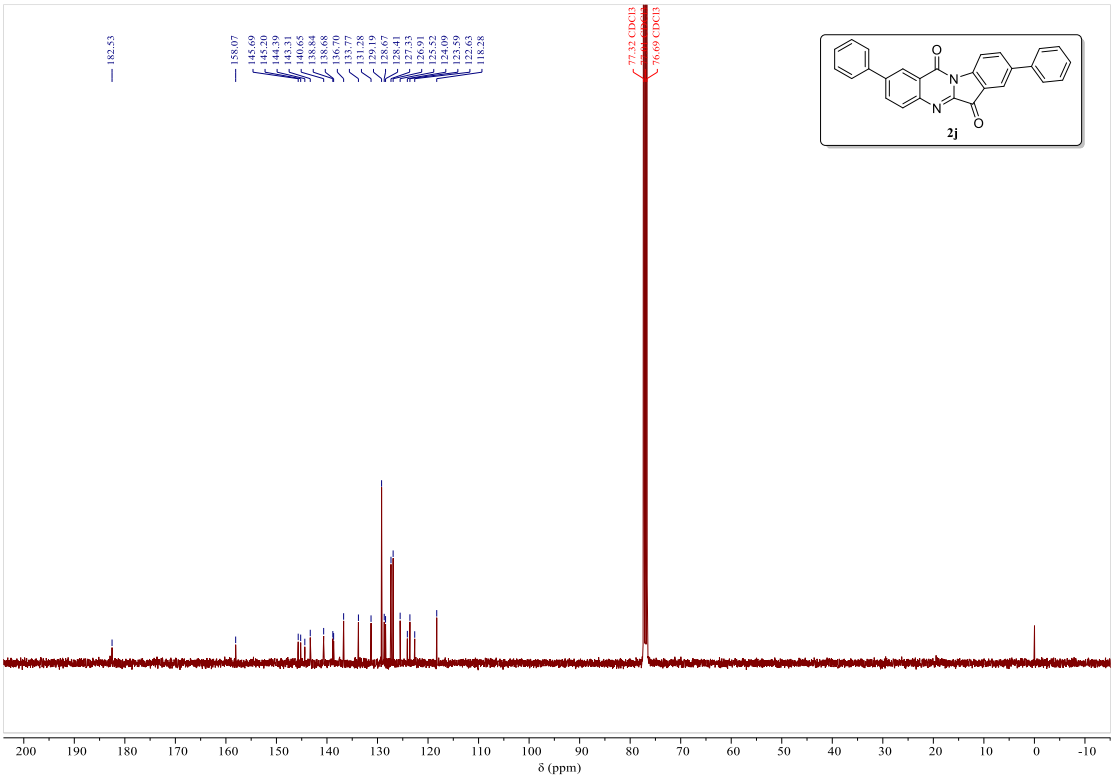


Figure S23. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2j**

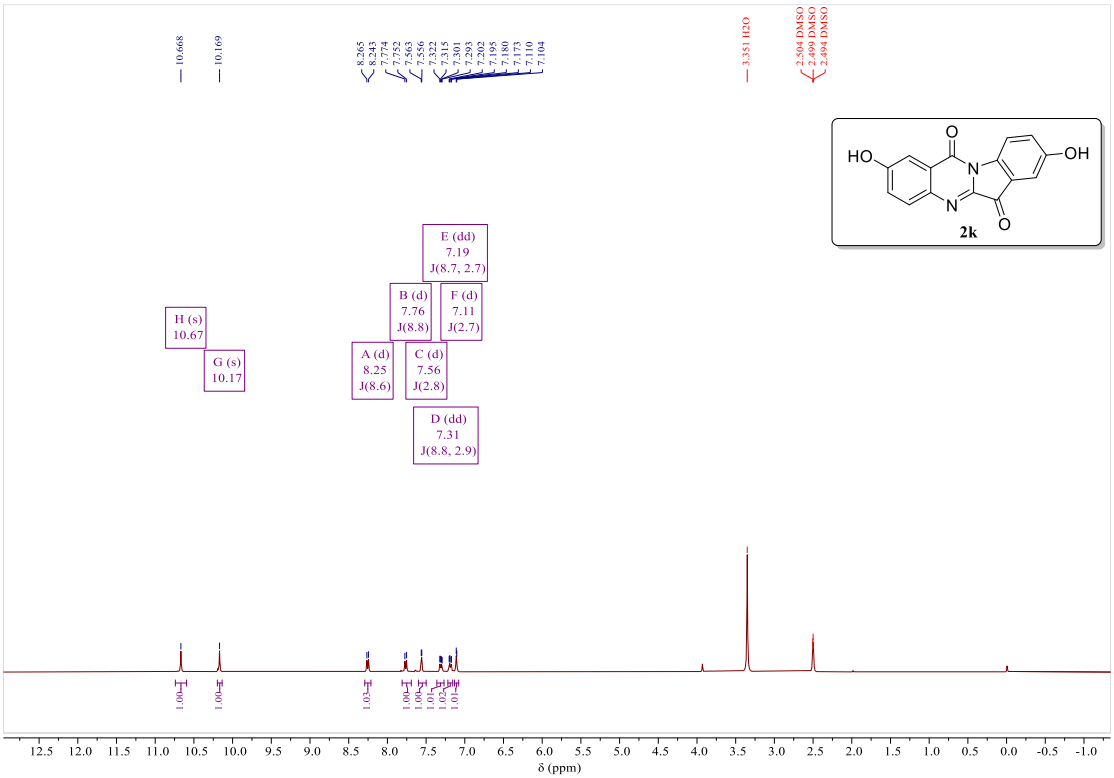


Figure S24. ^{1}H NMR (400 MHz, DMSO-d_6) of compound **2k**

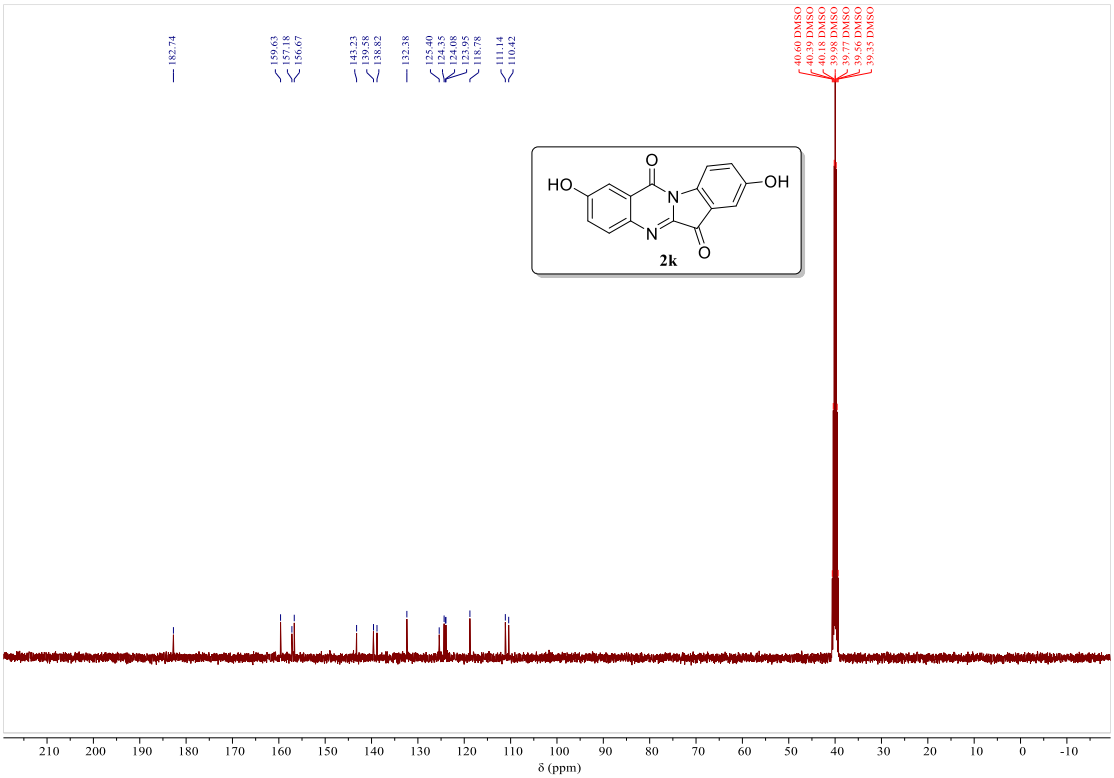


Figure S25. ^{13}C NMR (101 MHz, DMSO-d_6) of compound **2k**

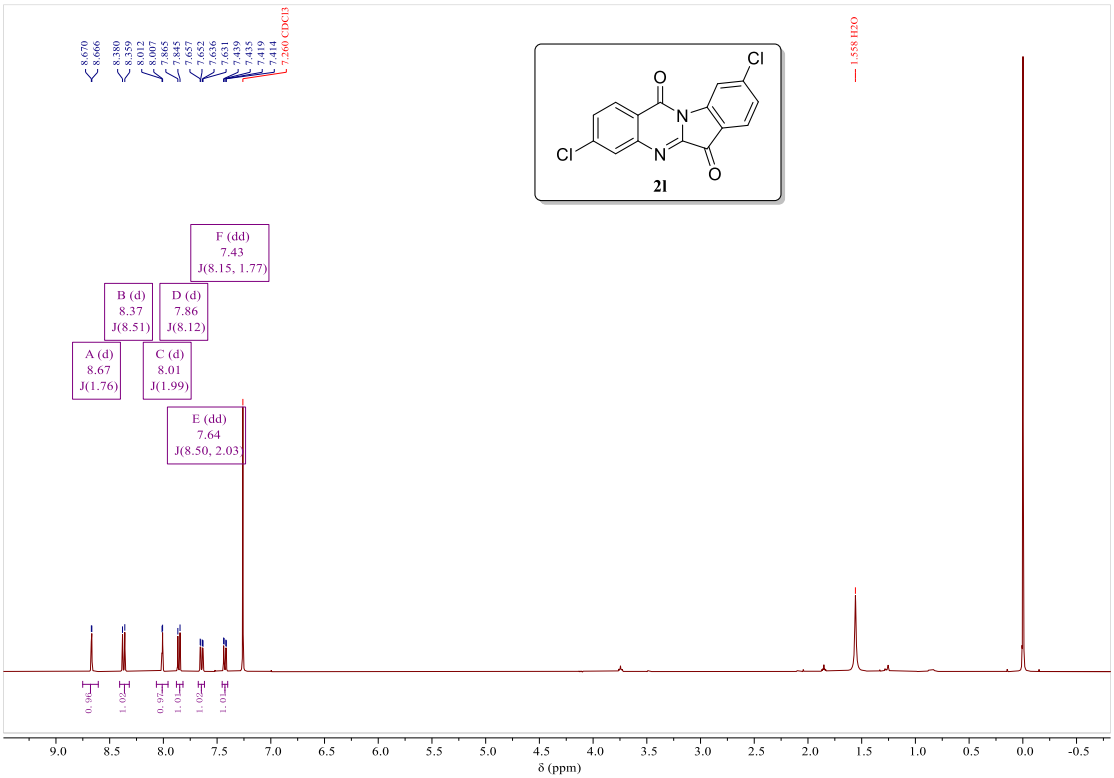


Figure S26. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2l**

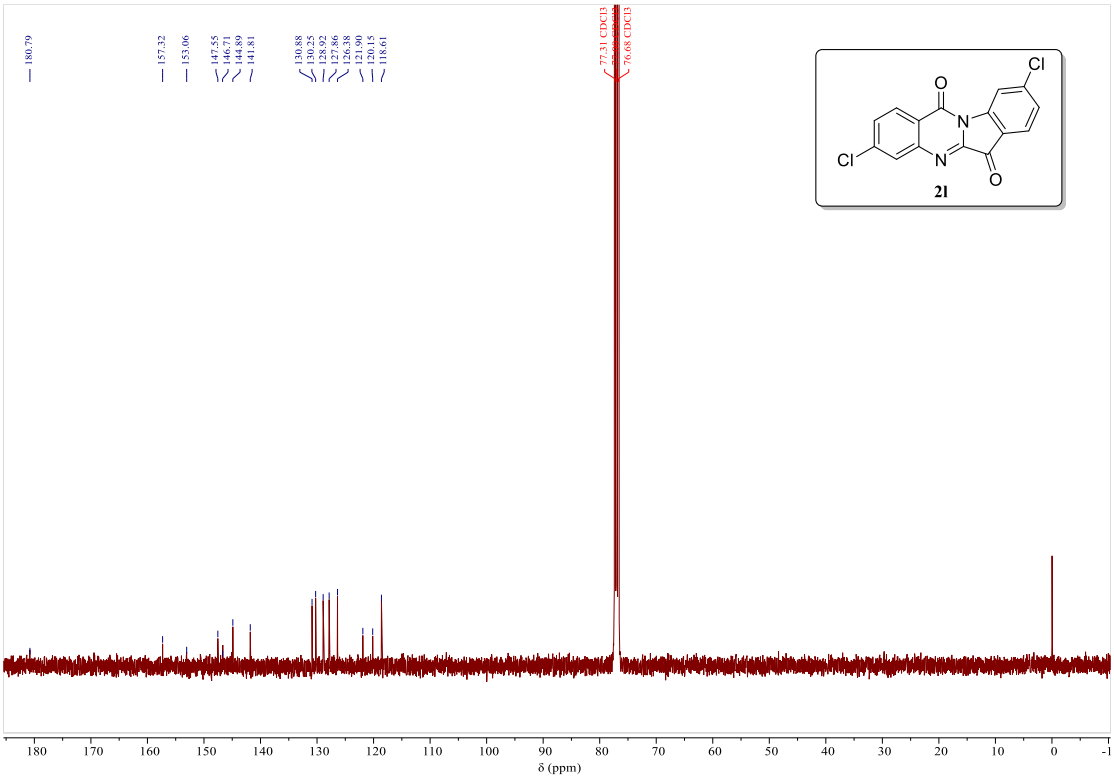


Figure S27. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2l**

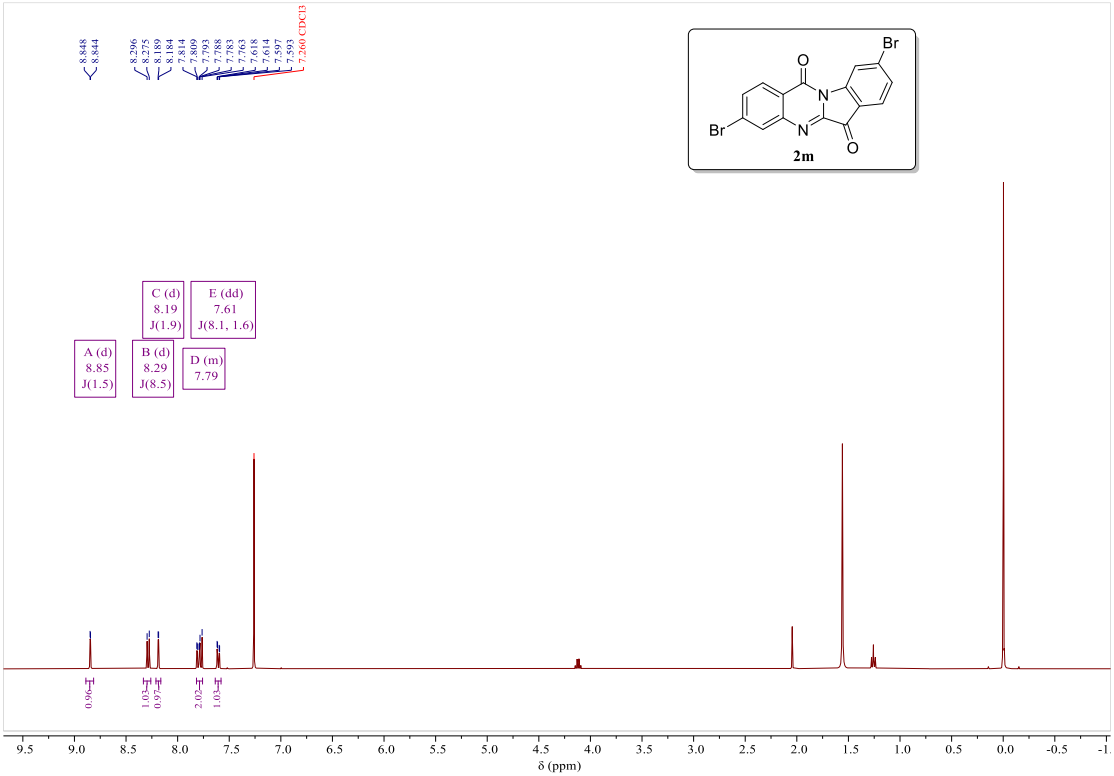


Figure S28. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2m**

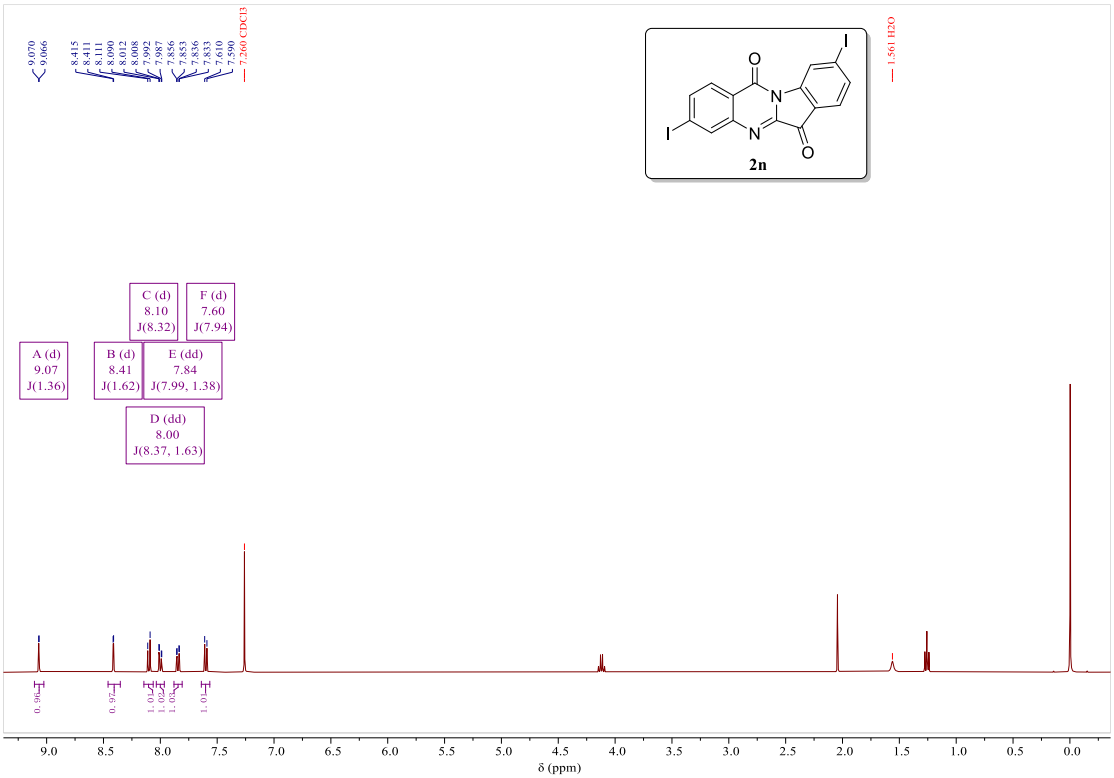


Figure S29. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2n**

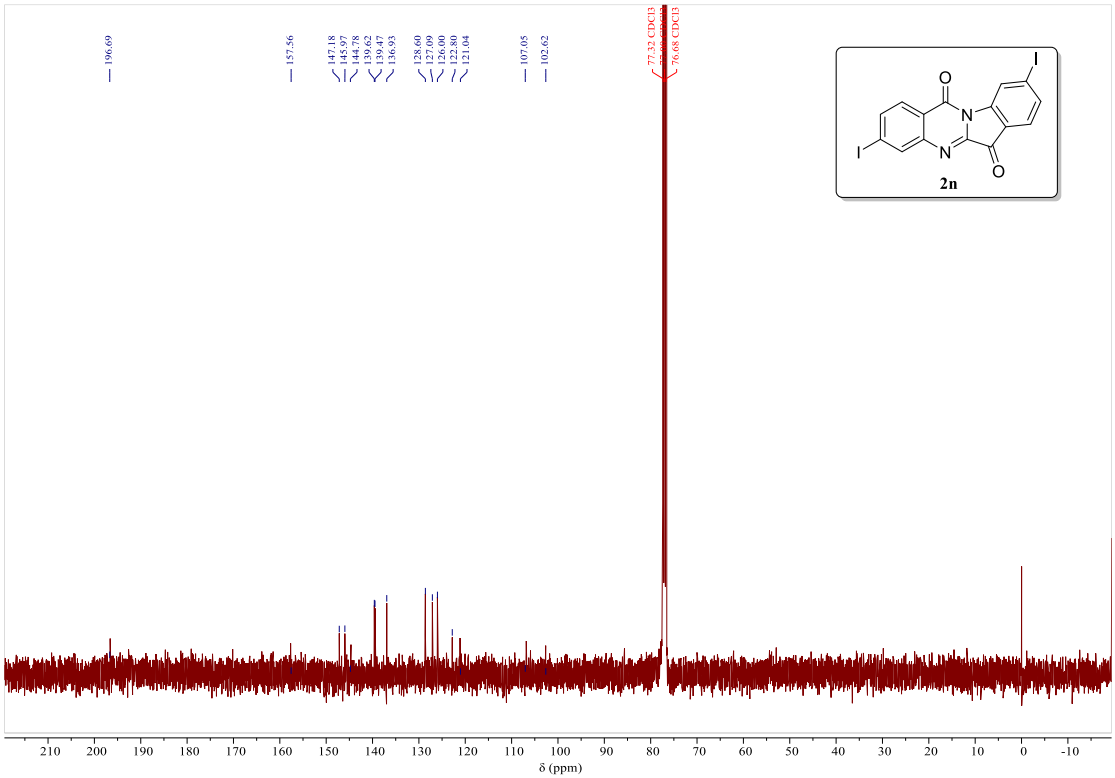


Figure S30. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2n**

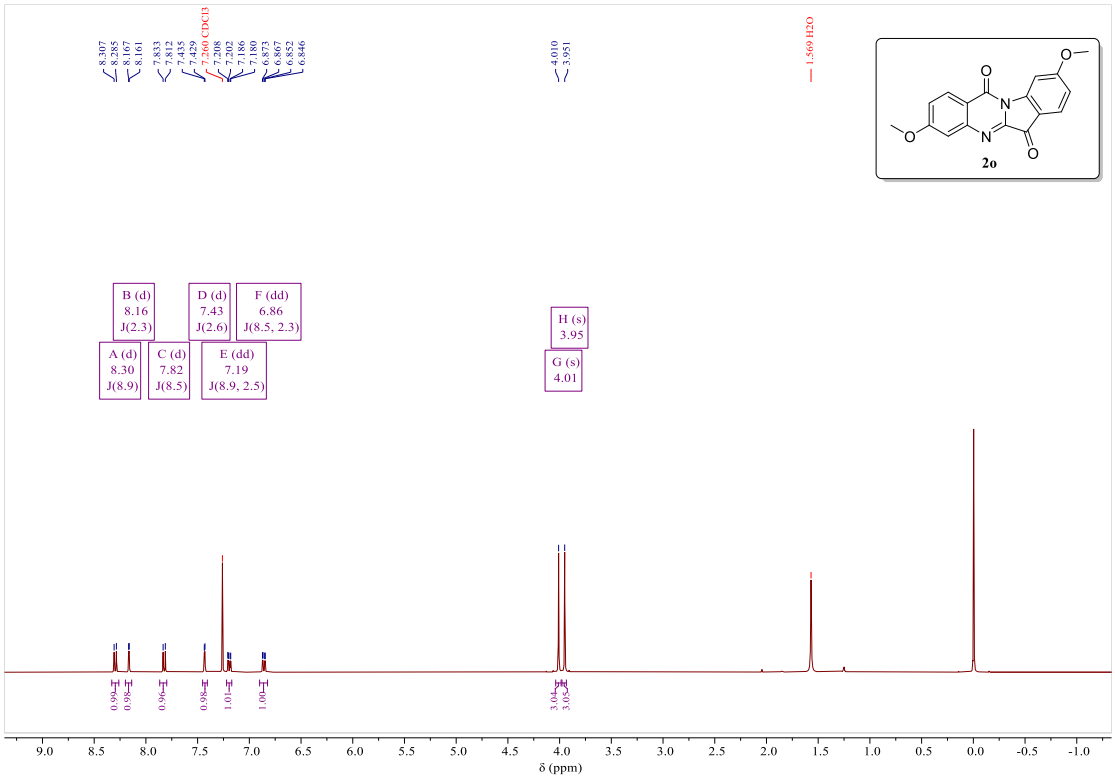


Figure S31. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2o**

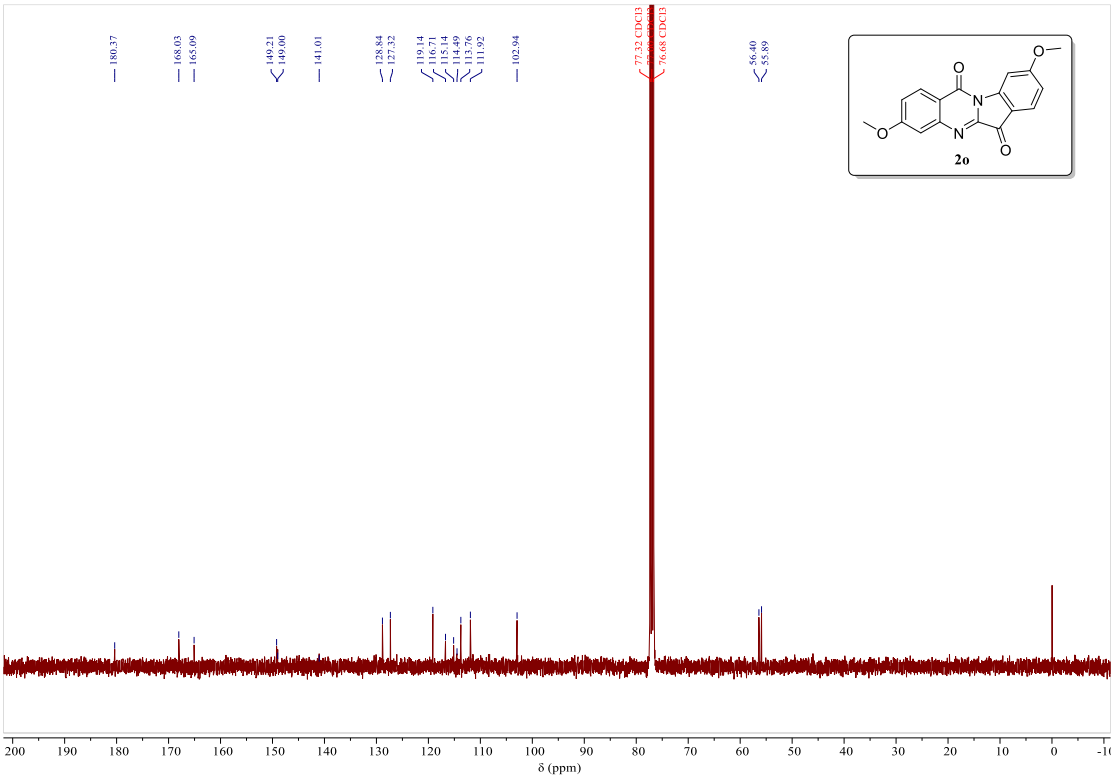


Figure S32. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2o**

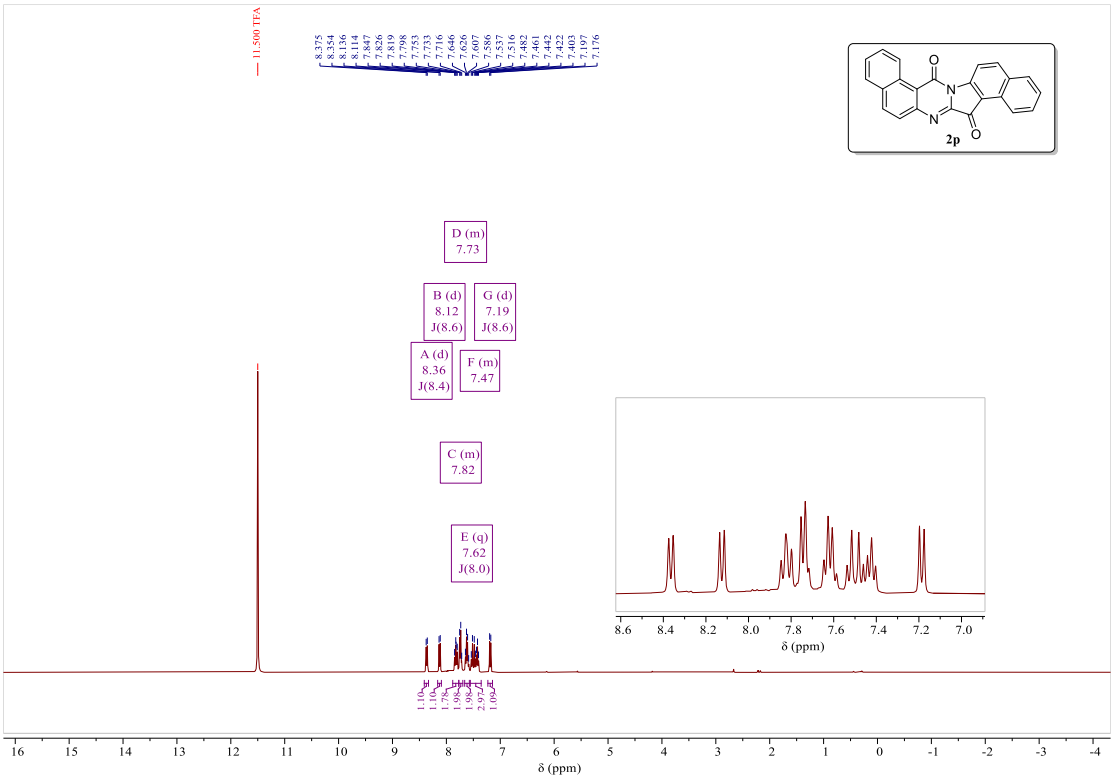


Figure S33. ^{1}H NMR (400 MHz, CF_3COOD) of compound **2p**

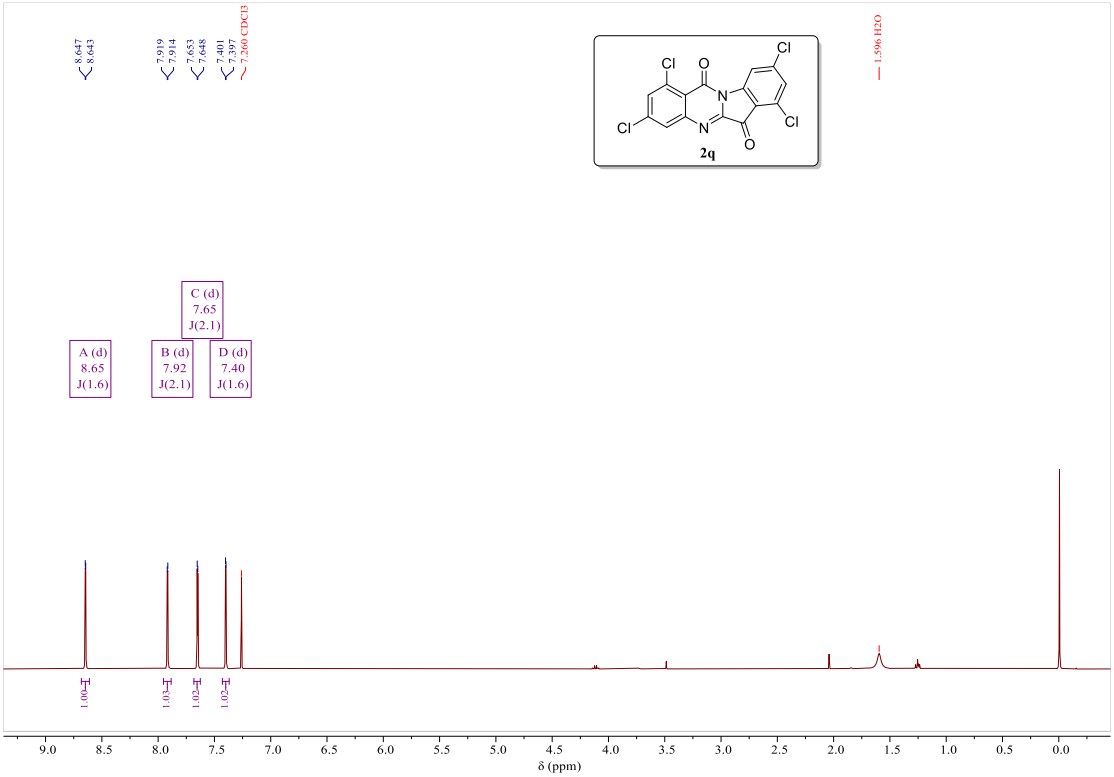


Figure S34. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2q**

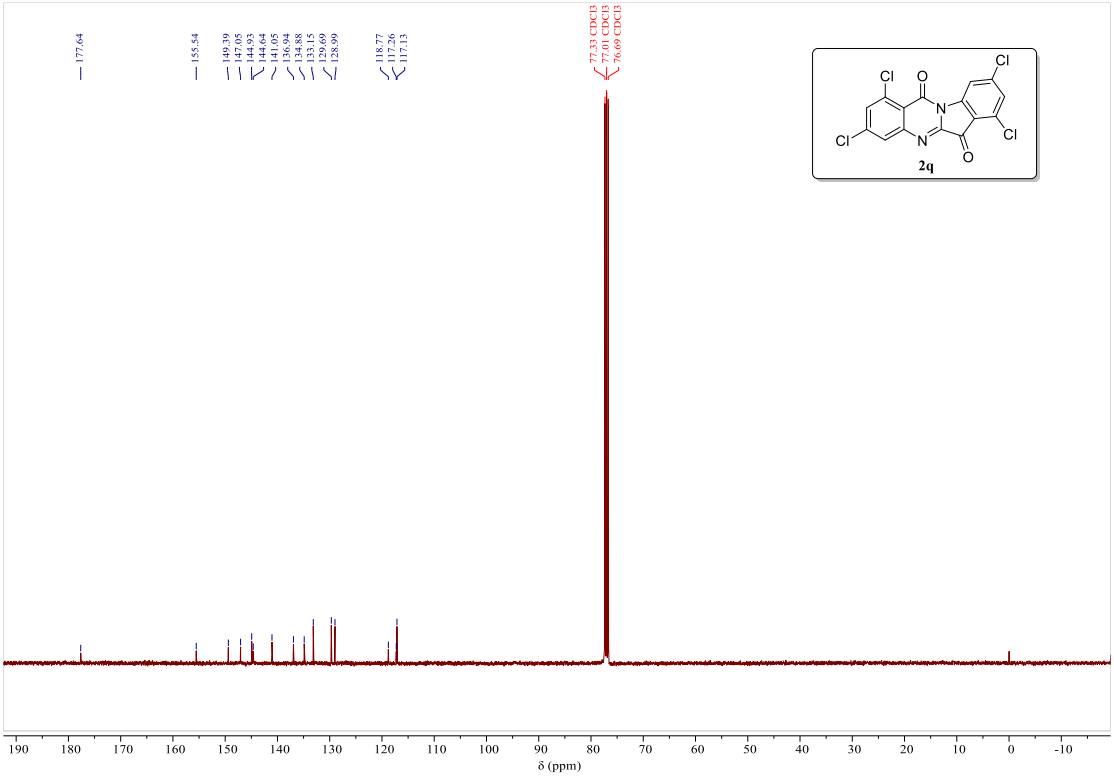


Figure S35. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2q**

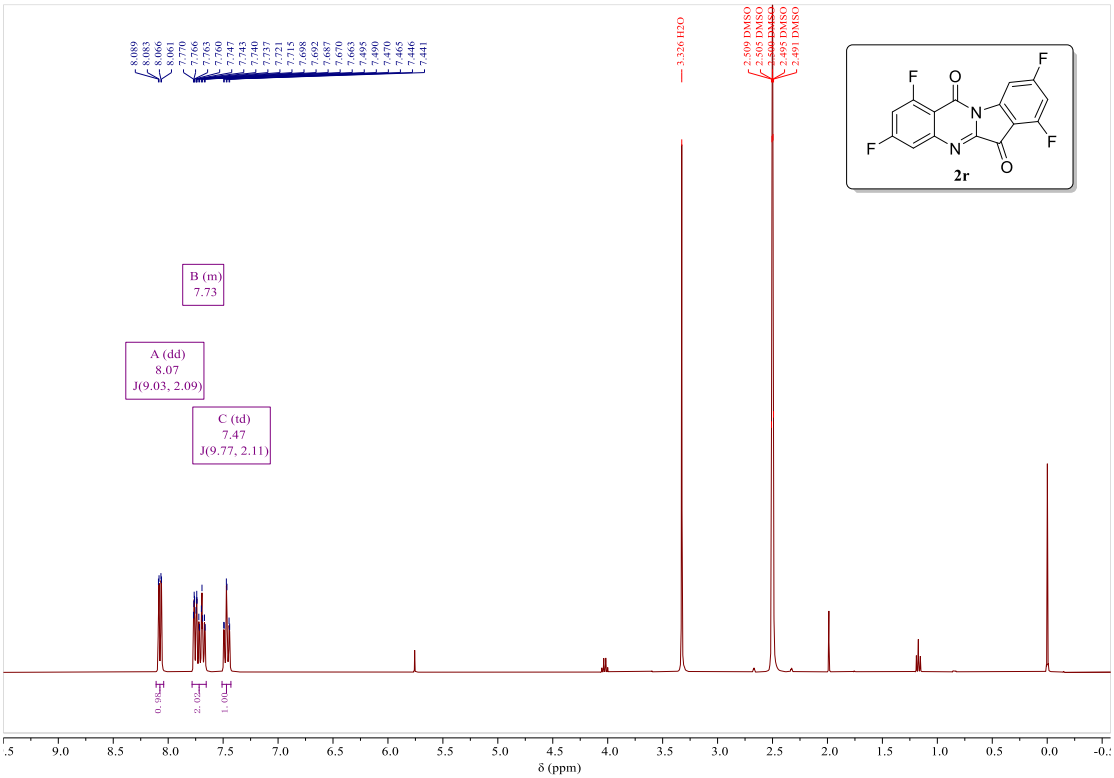


Figure S36. ^{1}H NMR (400 MHz, DMSO-d_6) of compound **2r**

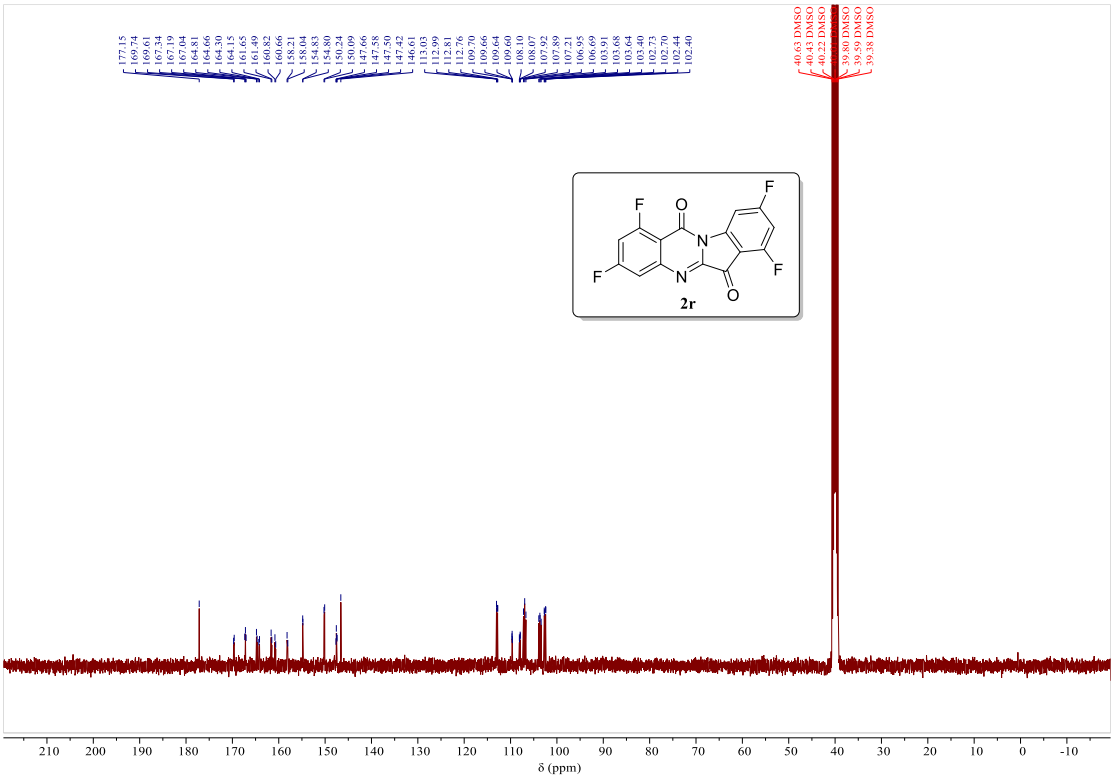


Figure S37. ^{13}C NMR (101 MHz, DMSO-d_6) of compound **2r**

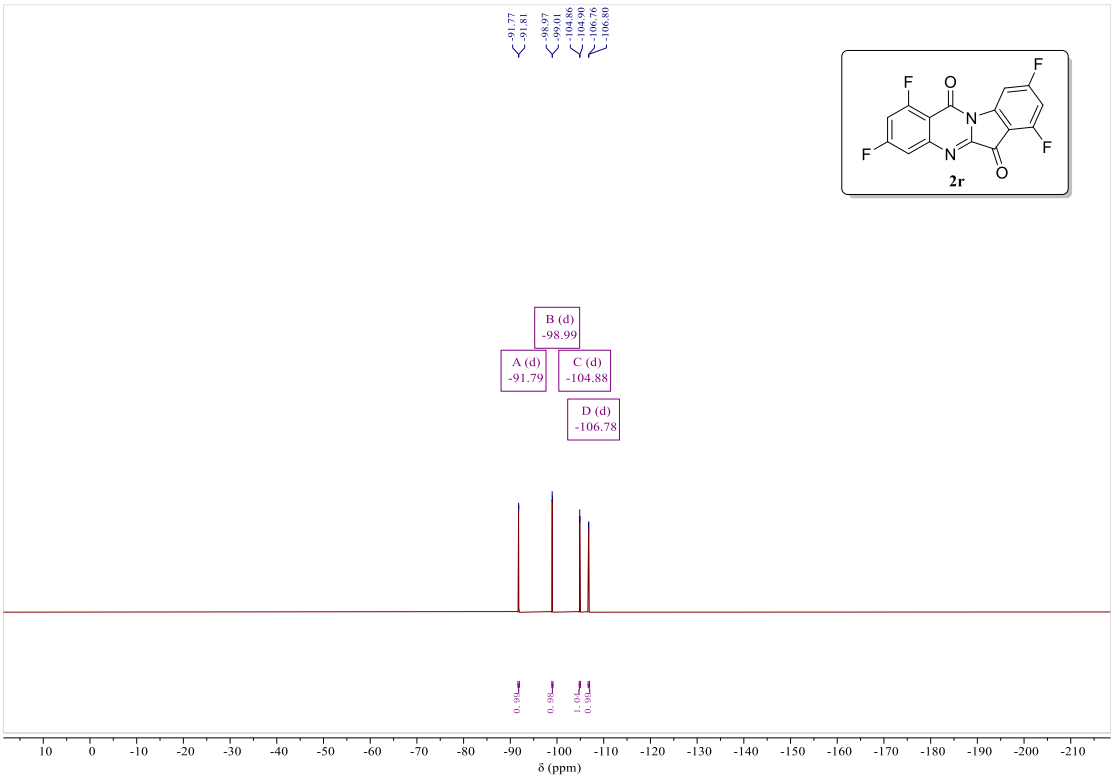


Figure S38. ^{19}F NMR (376 MHz, DMSO-d_6) of compound **2r**

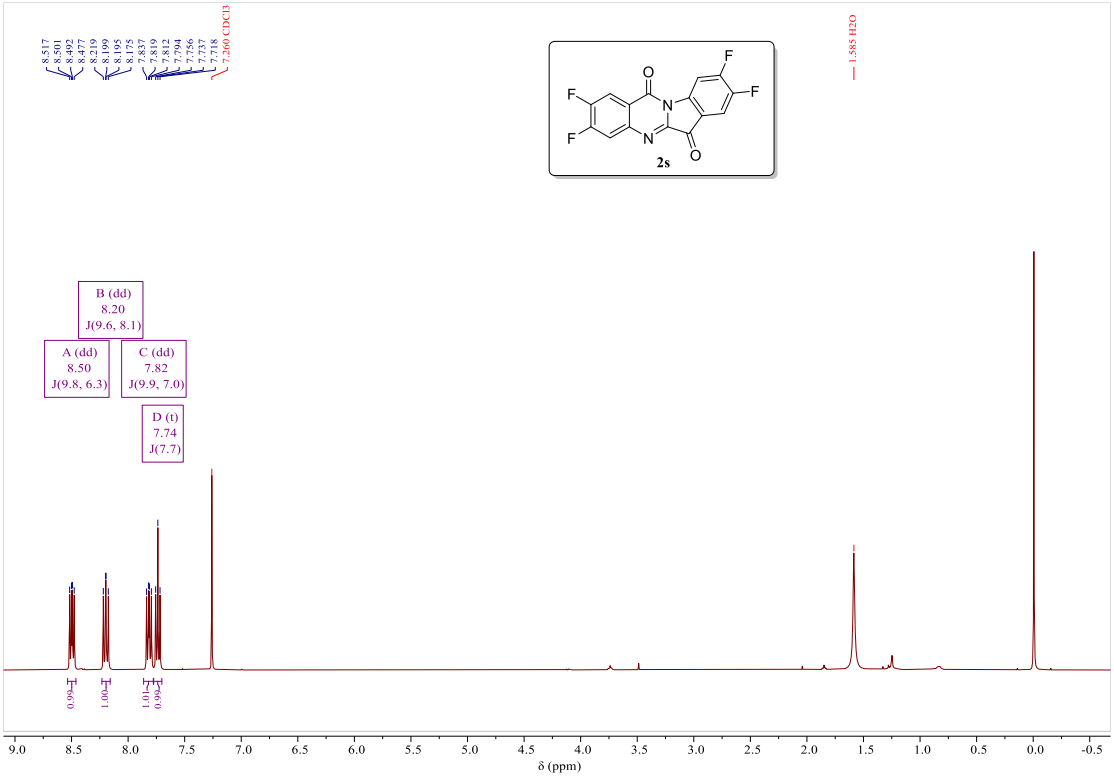


Figure S39. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2s**

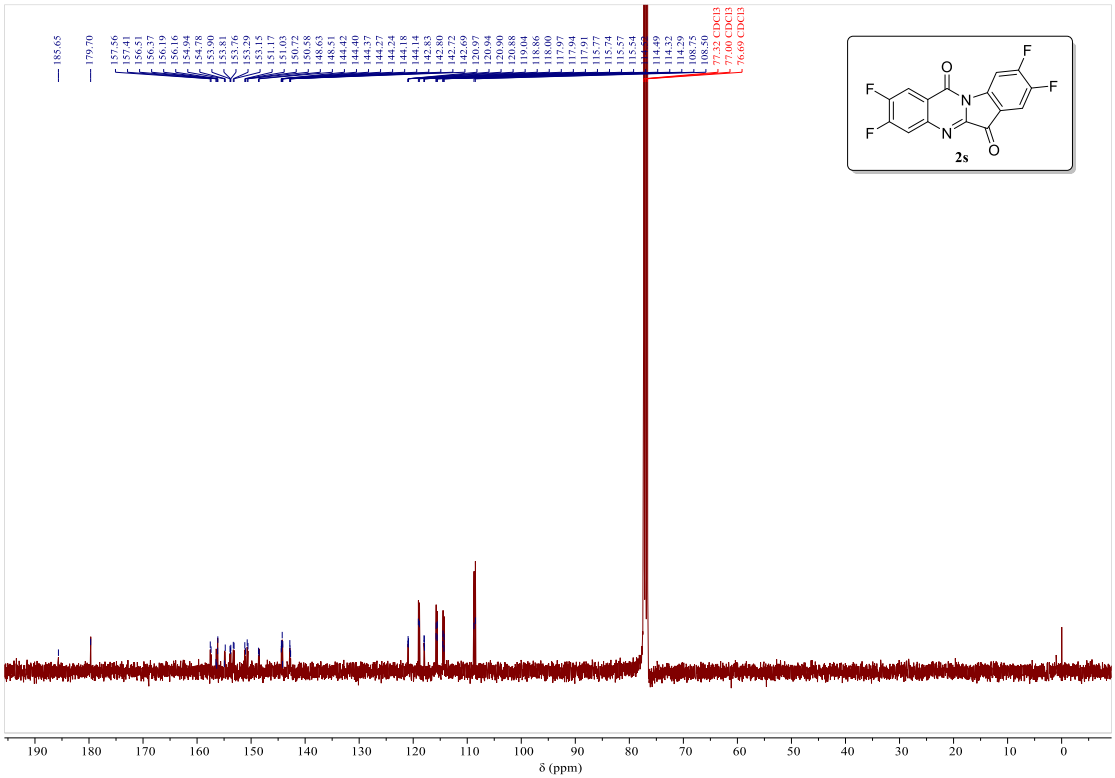


Figure S40. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2s**

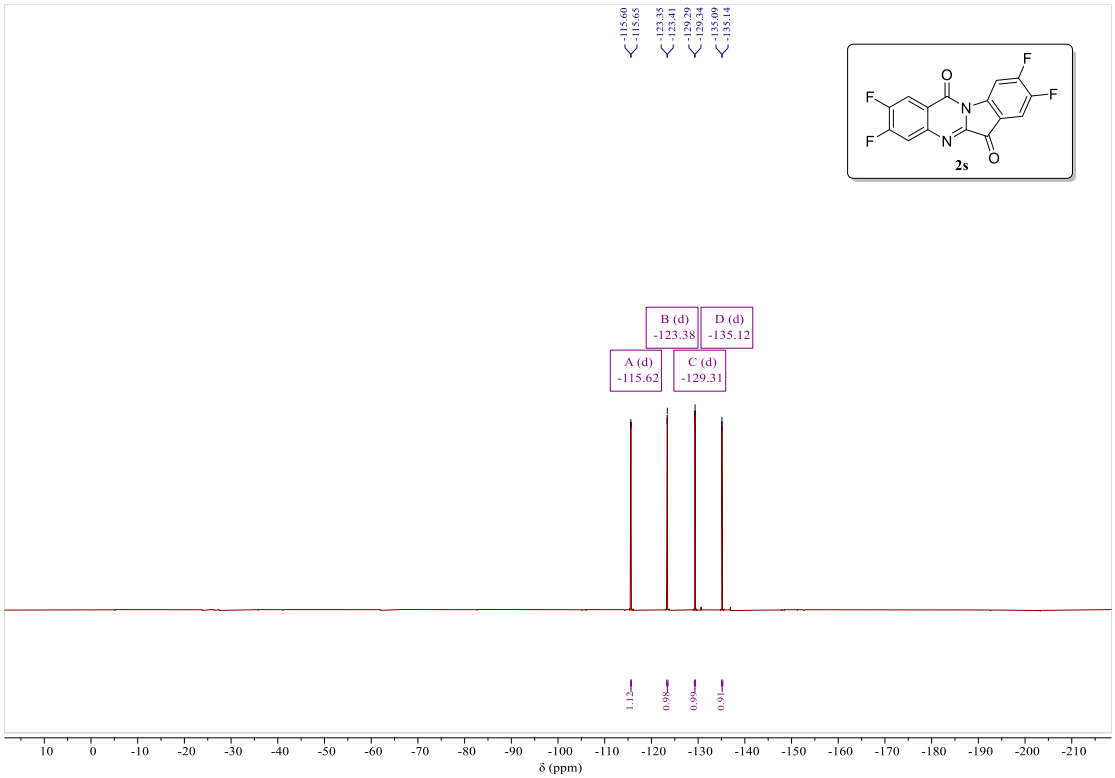


Figure S41. ^{19}F NMR (376 MHz, $CDCl_3$) of compound **2s**

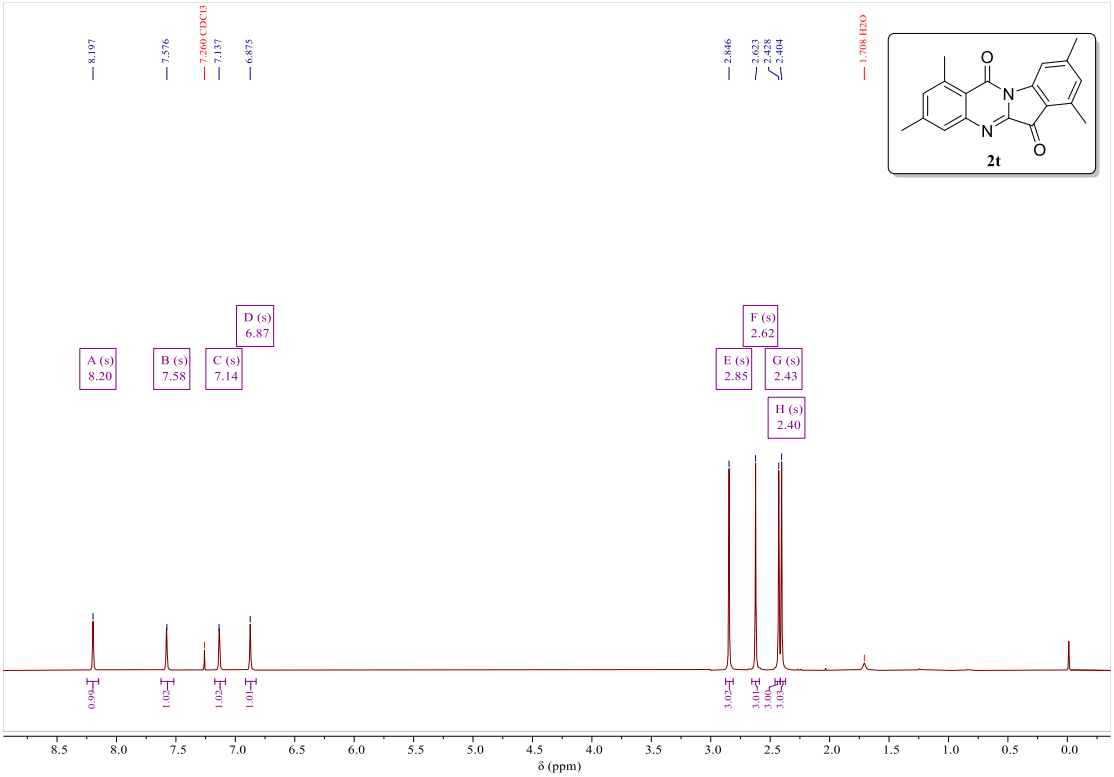


Figure S42. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2t**

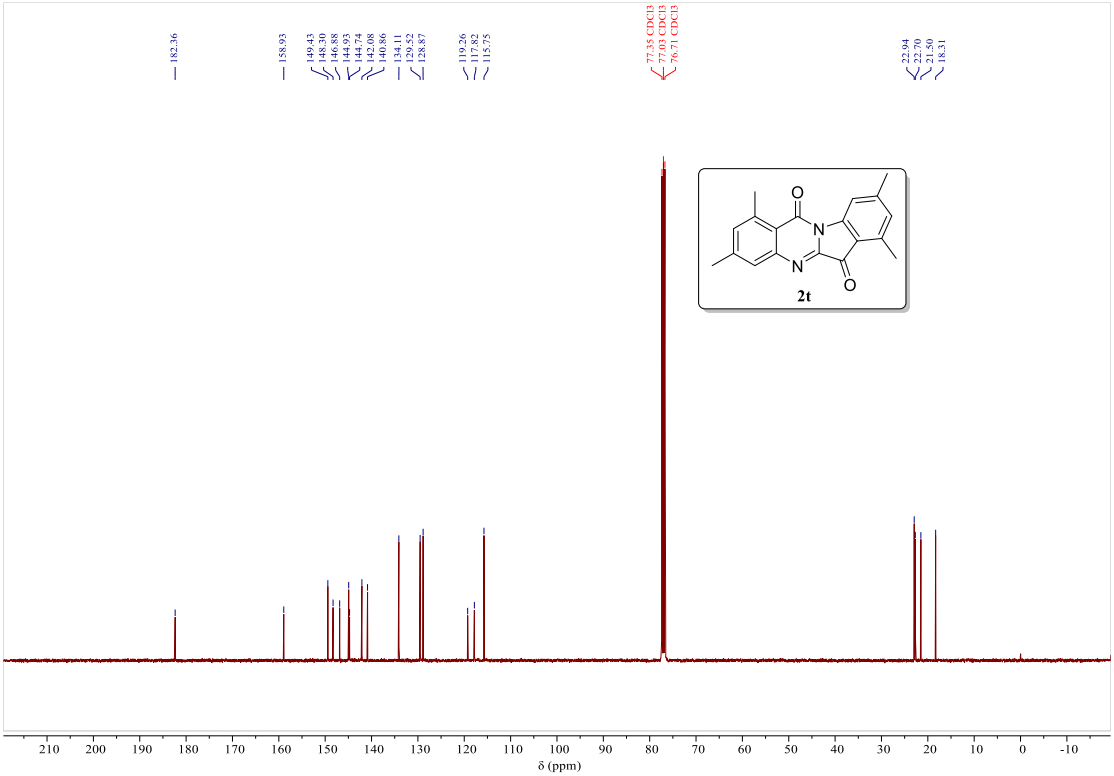


Figure S43. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2t**

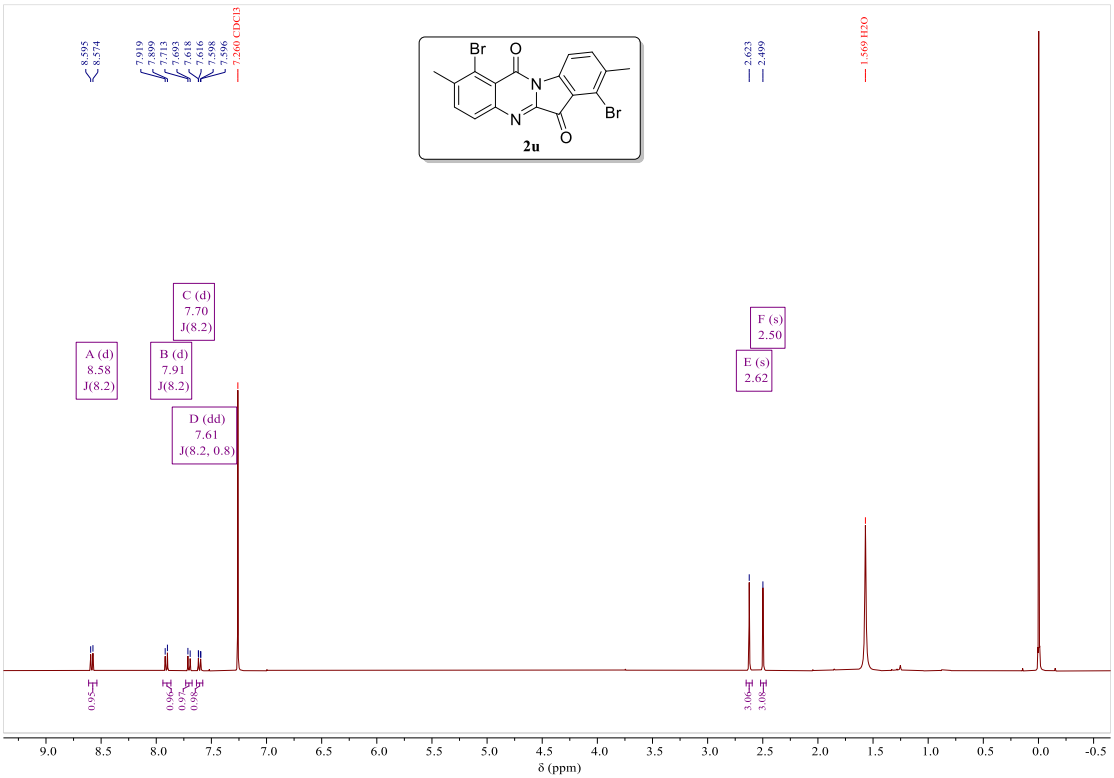


Figure S44. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2u**

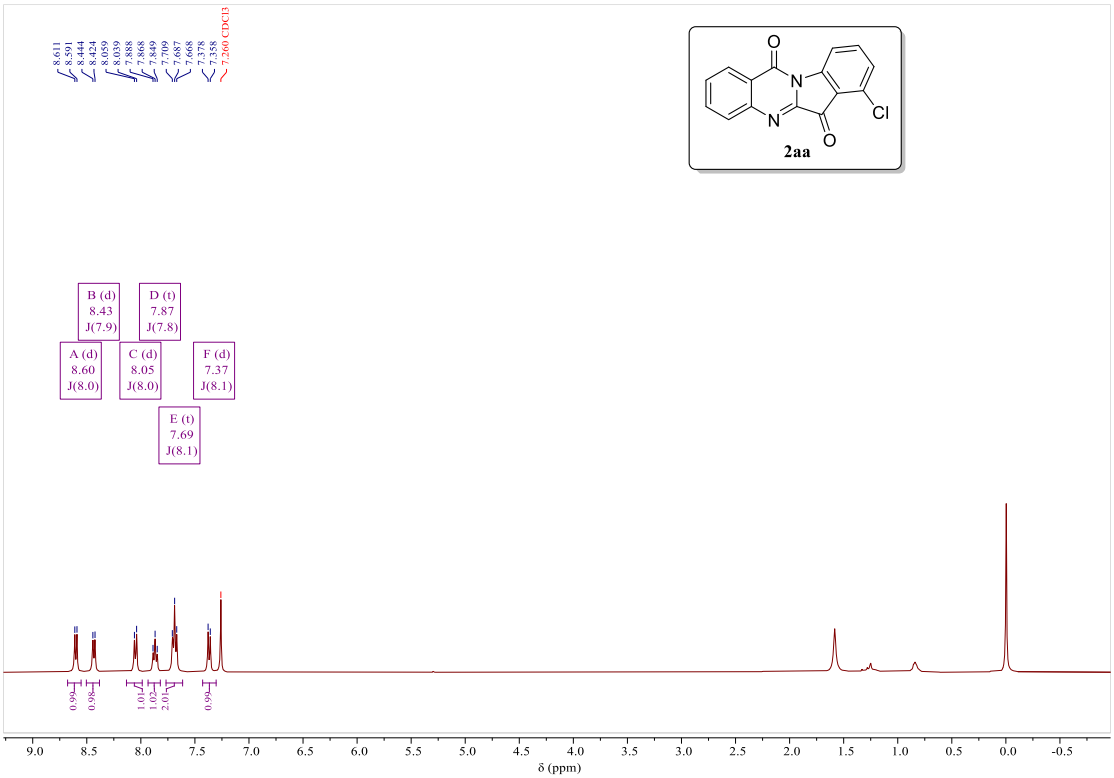


Figure S45. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2aa**

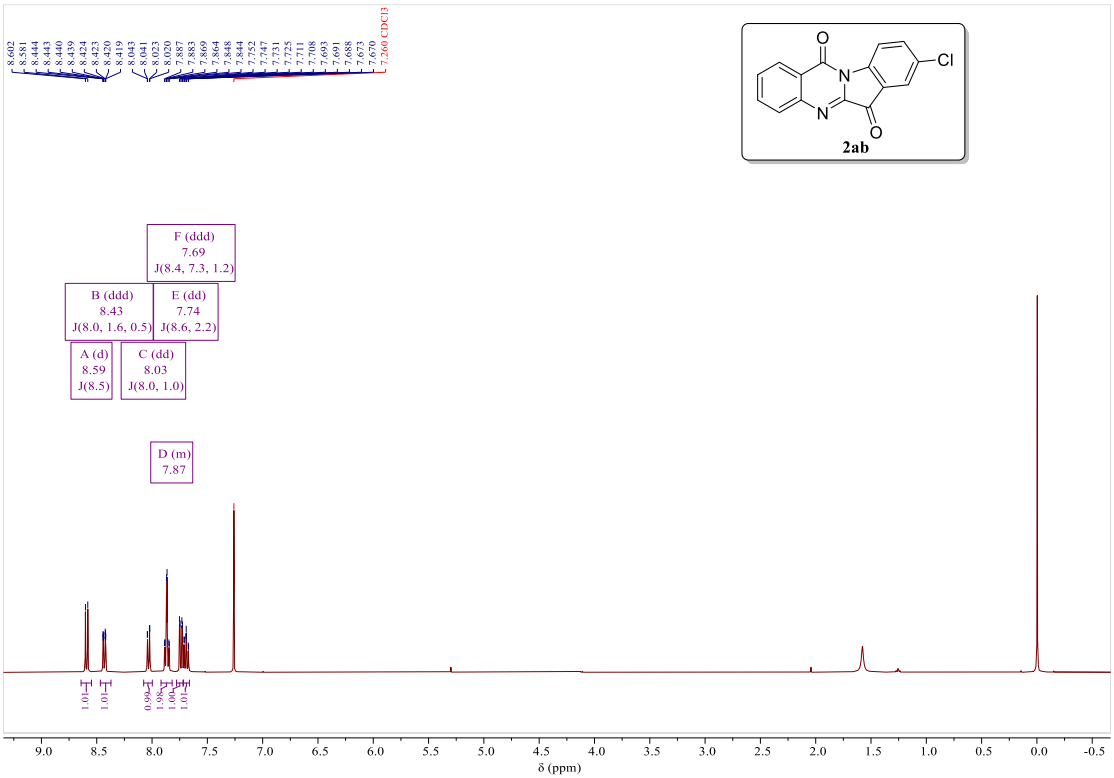


Figure S46. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2ab**

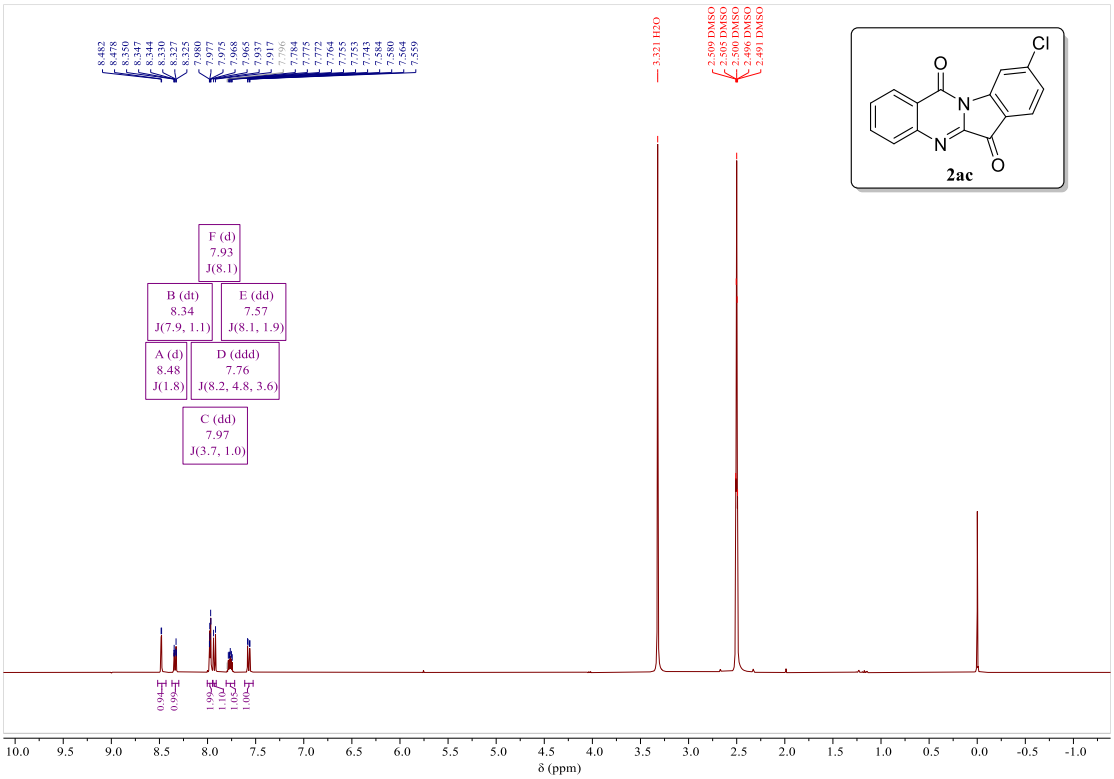


Figure S47. ^{1}H NMR (400 MHz, DMSO-d_6) of compound **2ac**

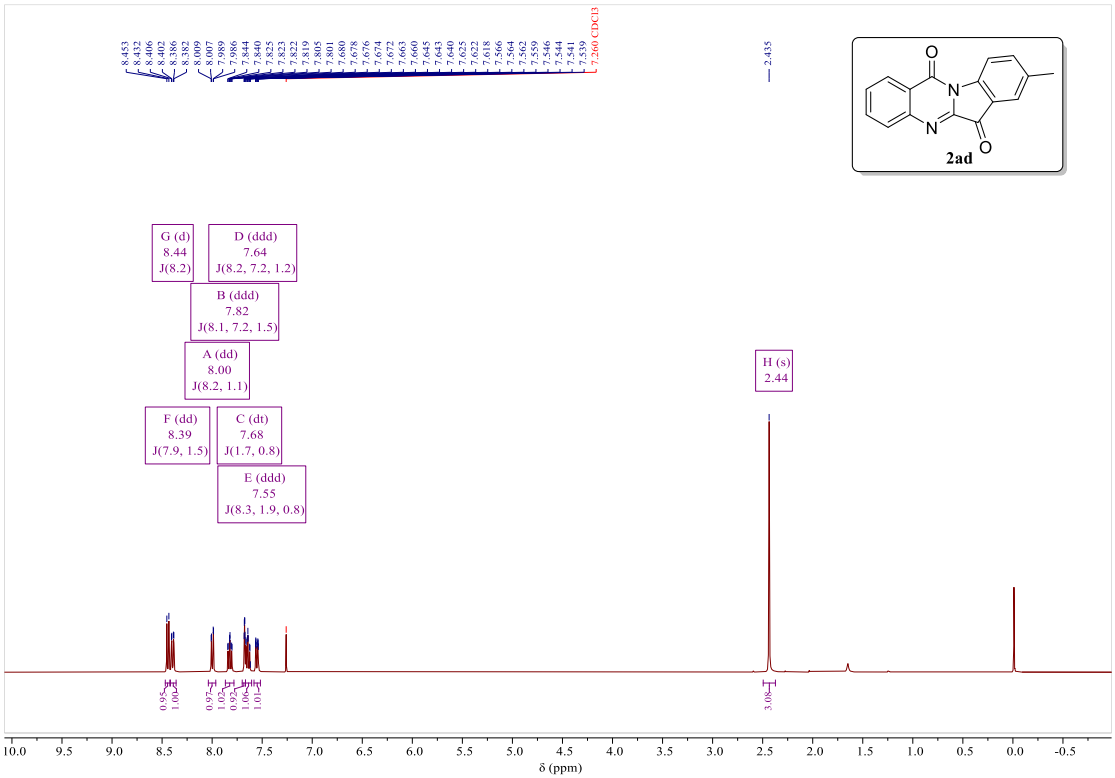


Figure S48. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2ad**

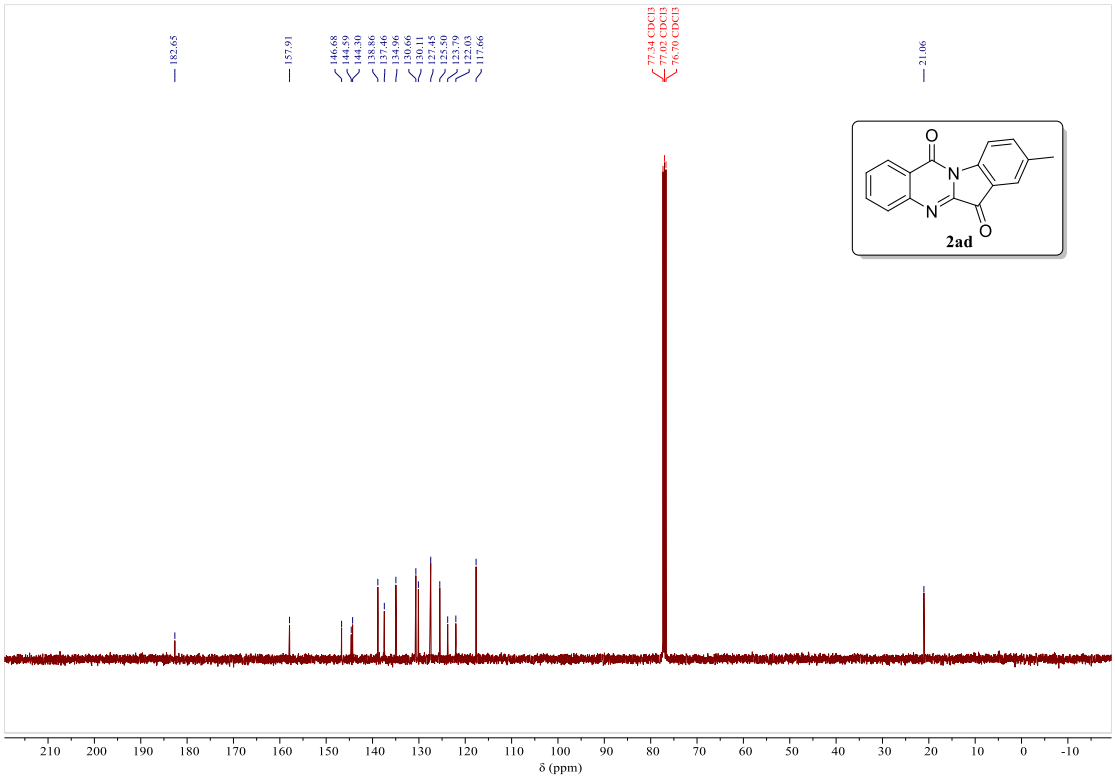


Figure S49. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2ad**

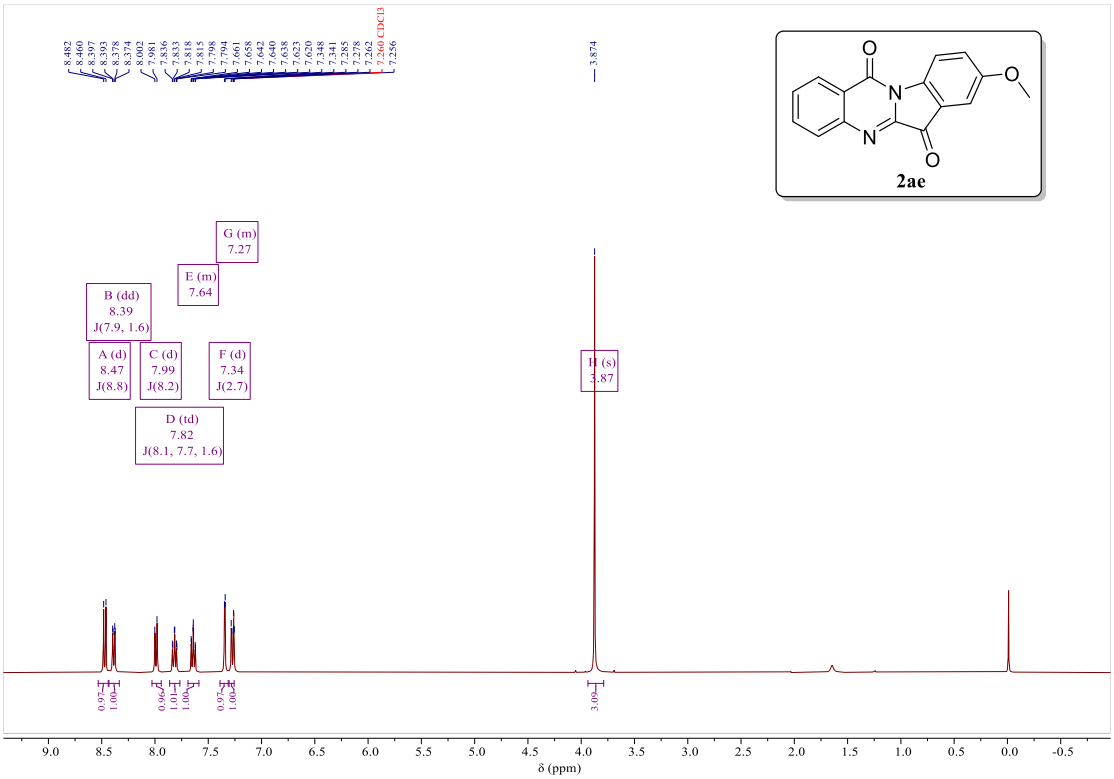


Figure S50. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2ae**

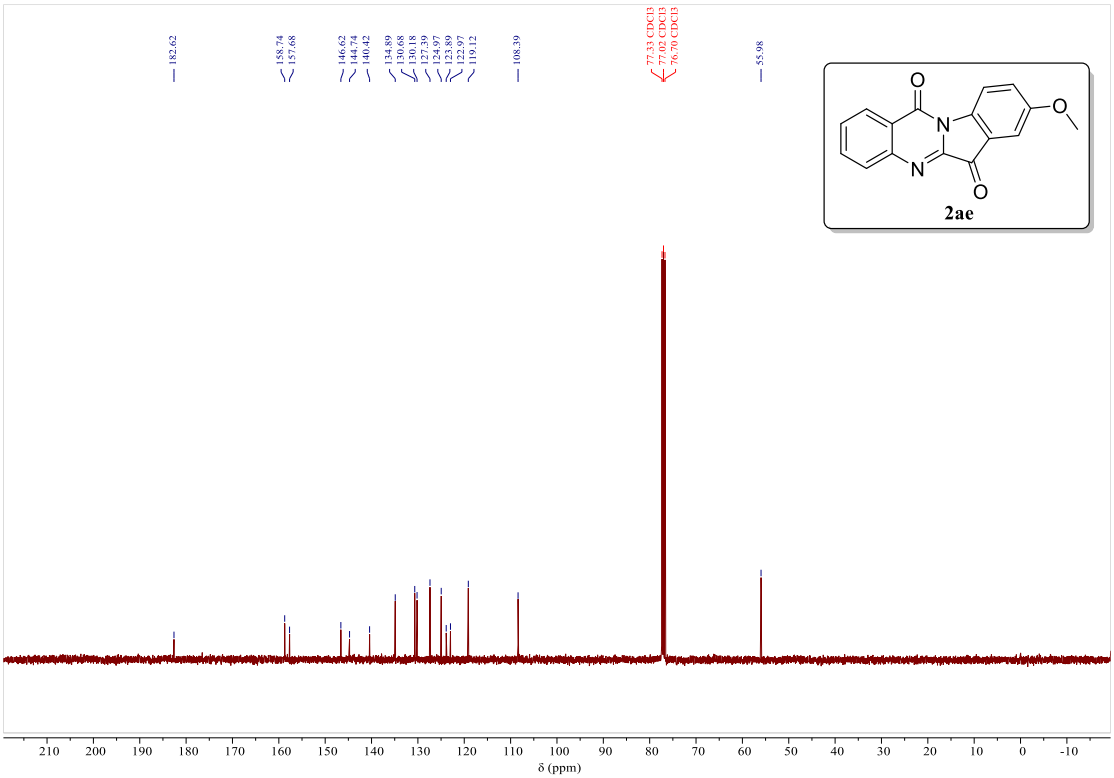


Figure S51. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2ae**

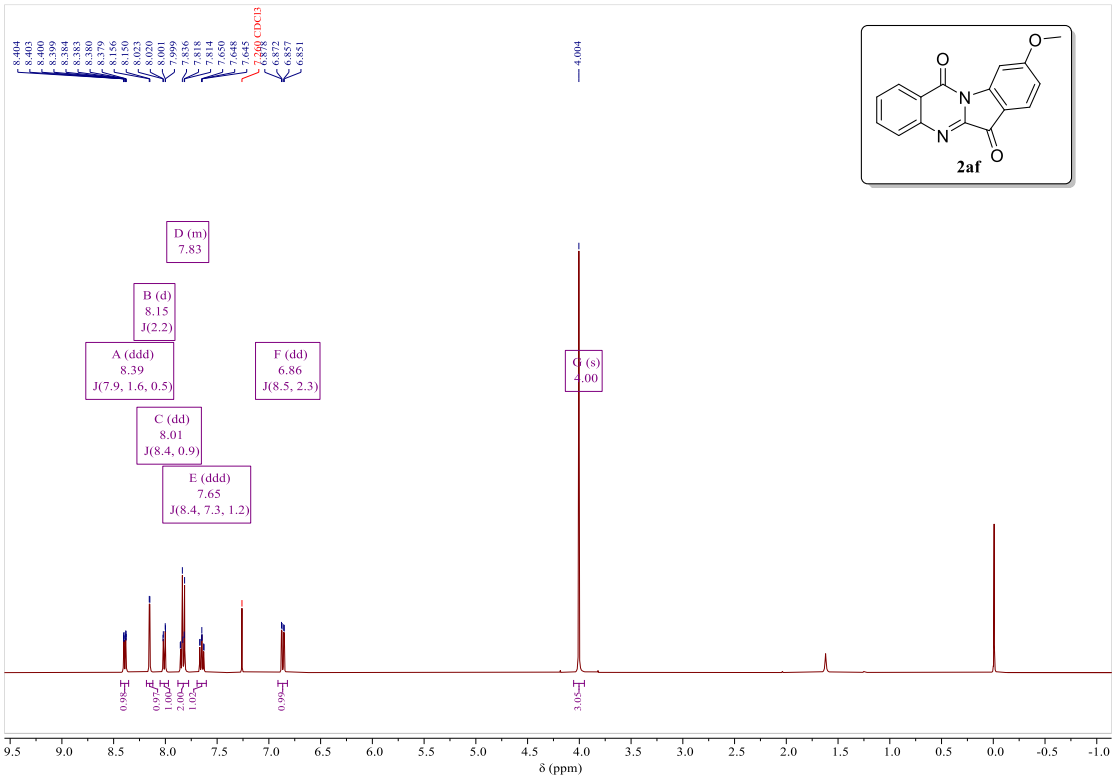


Figure S52. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2af**

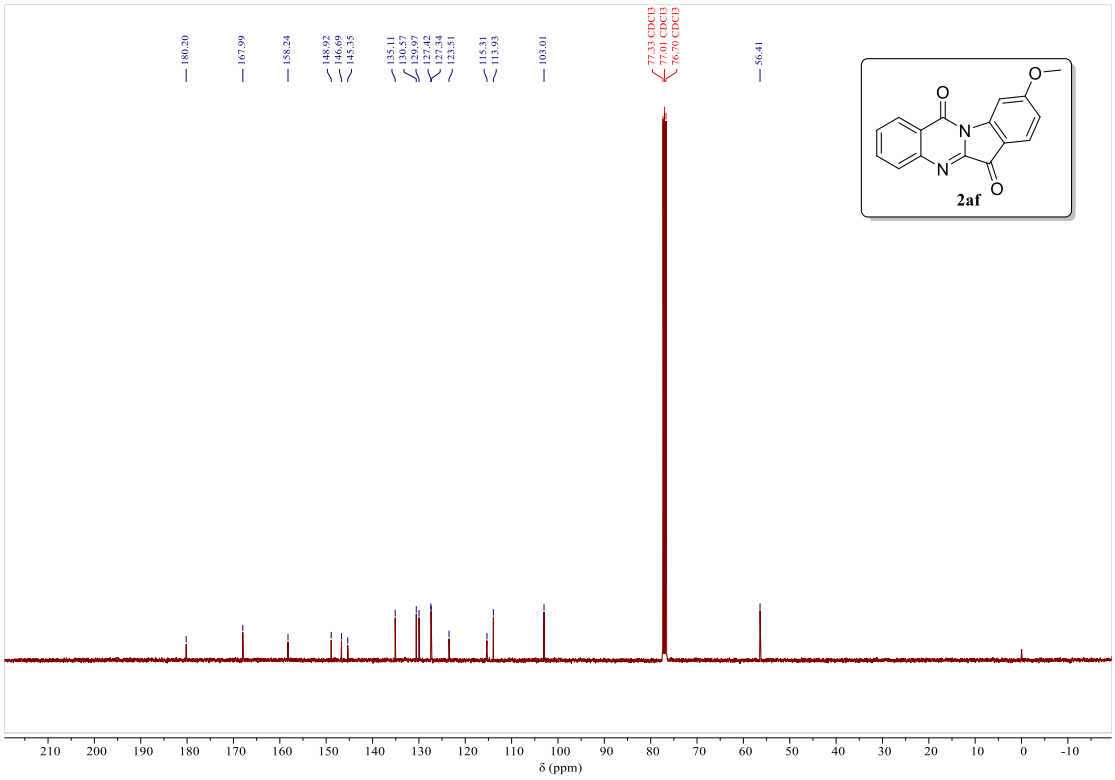


Figure S53. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2af**

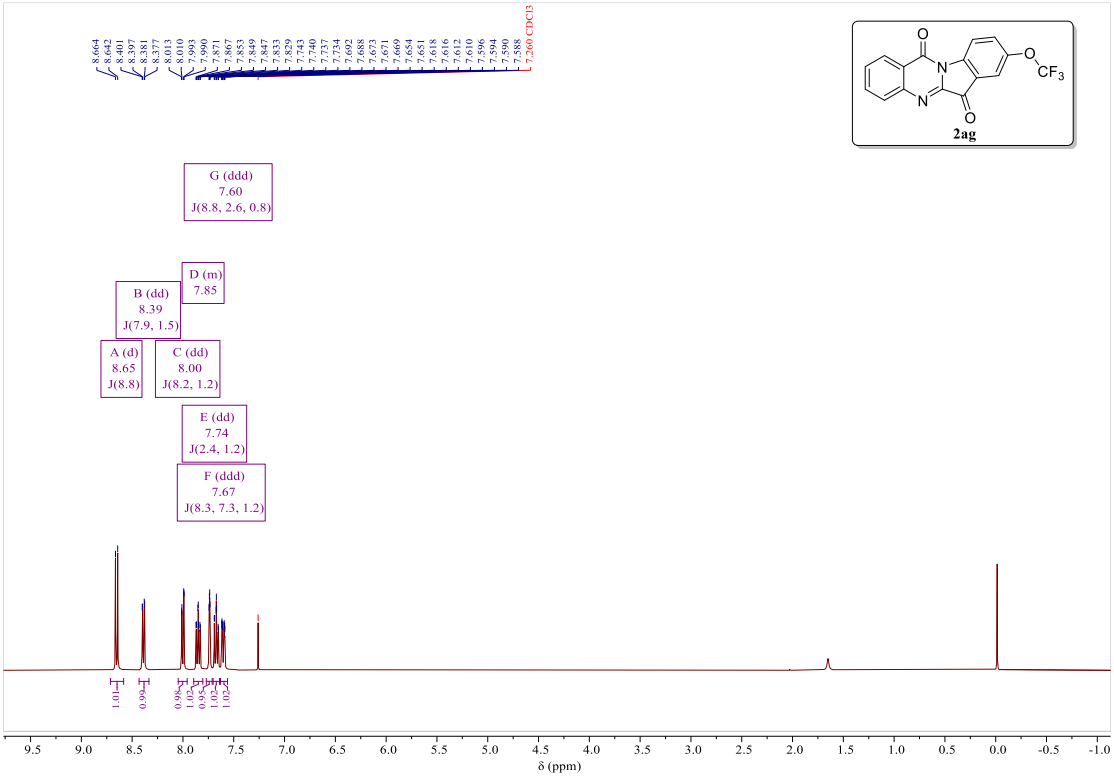


Figure S54. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2ag**

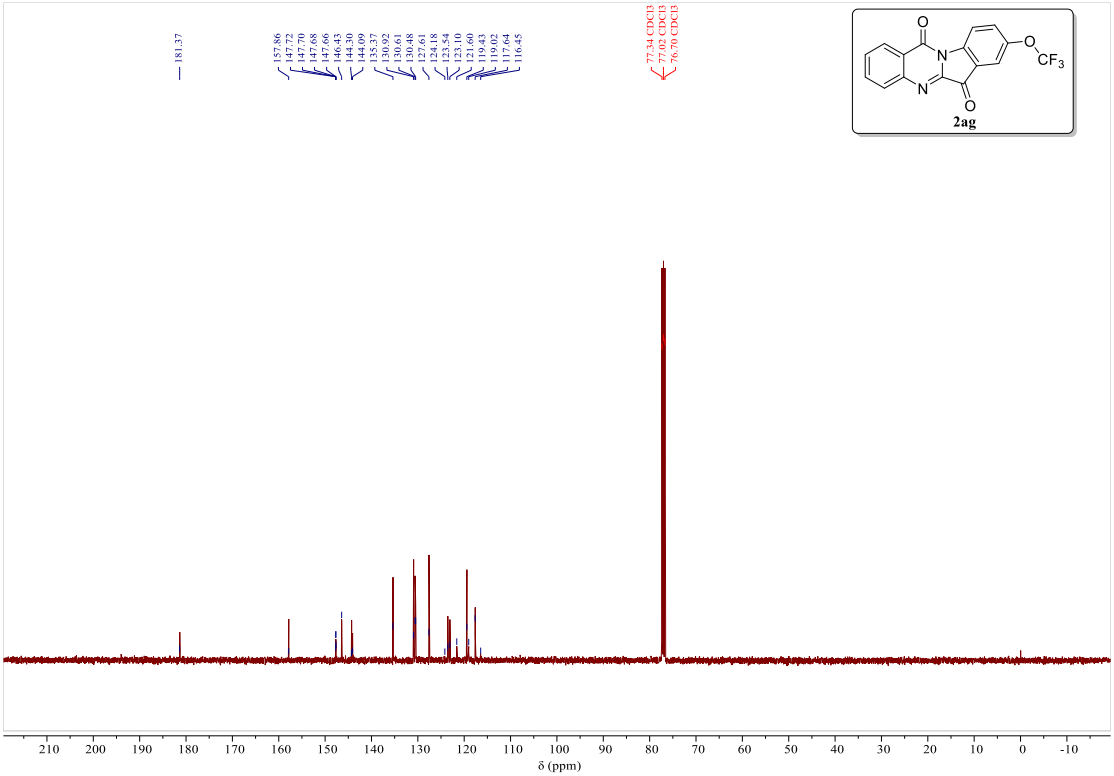


Figure S55. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2ag**

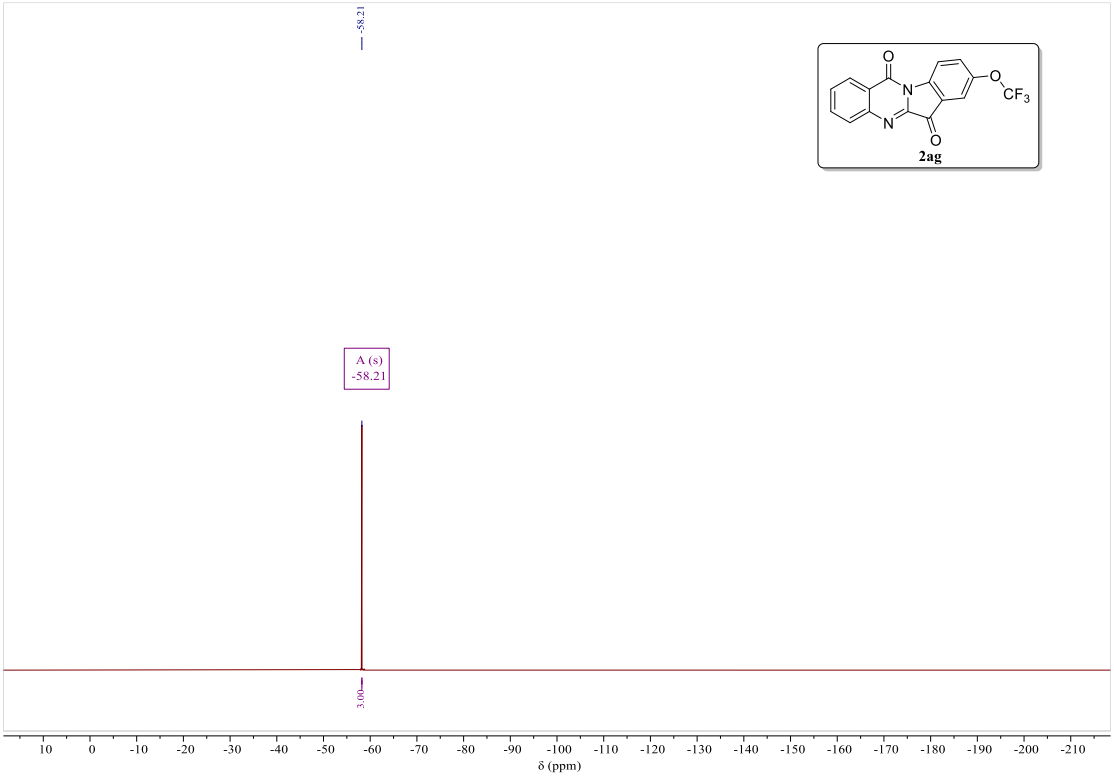


Figure S56. ^{19}F NMR (376 MHz, $CDCl_3$) of compound **2ag**

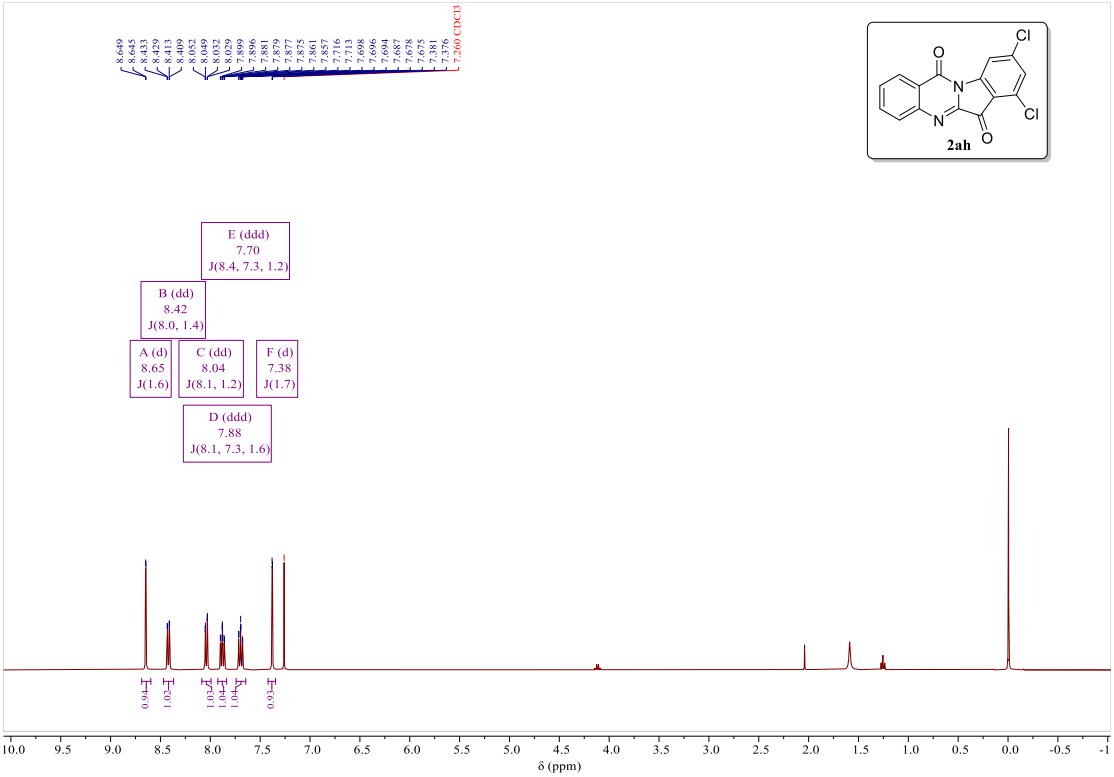


Figure S57. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2ah**

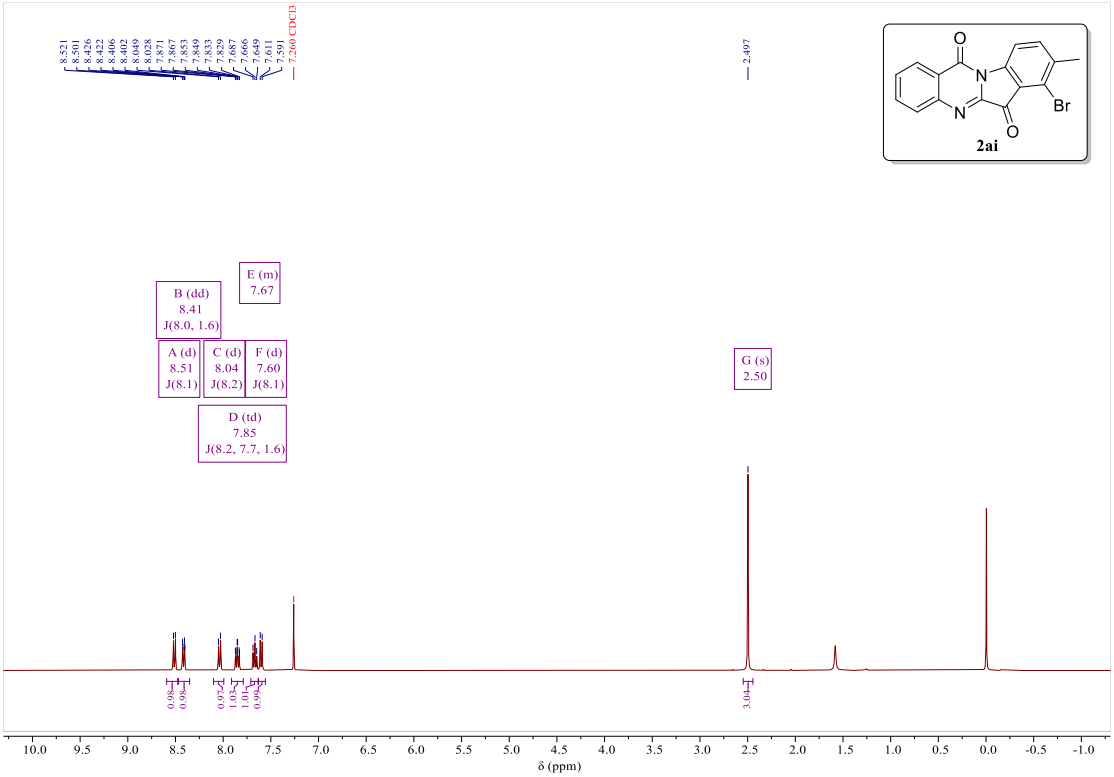


Figure S58. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2ai**

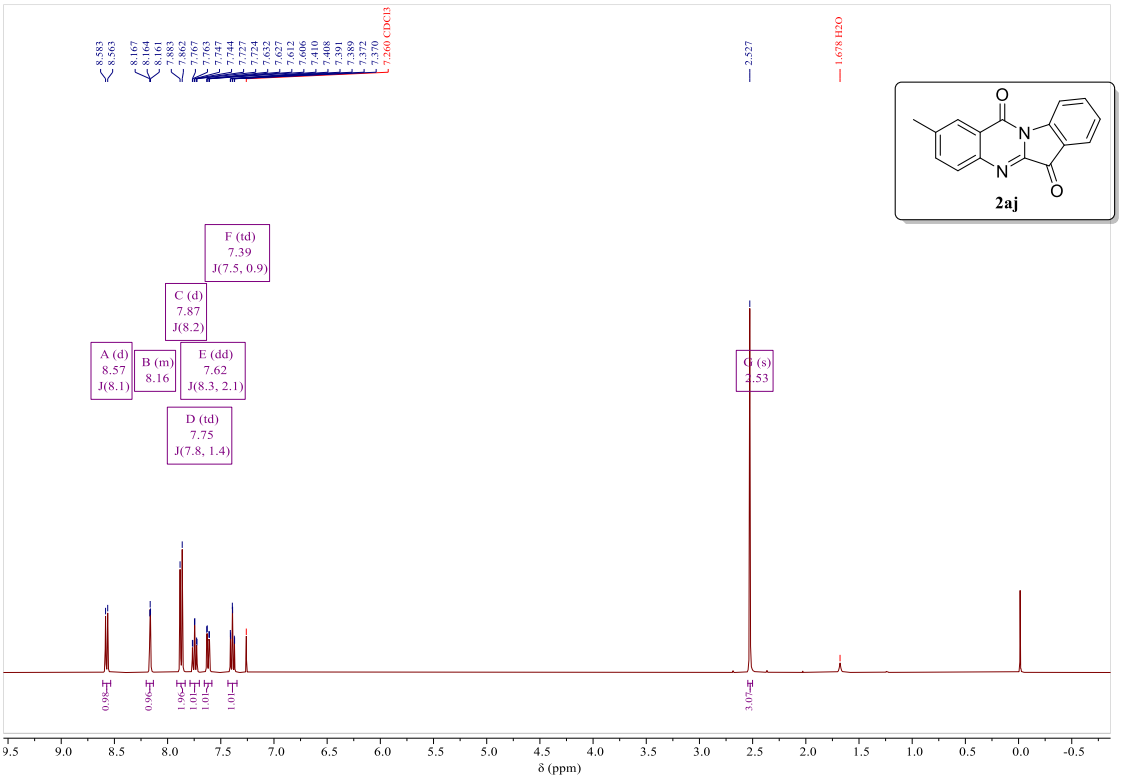


Figure S59. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2aj**

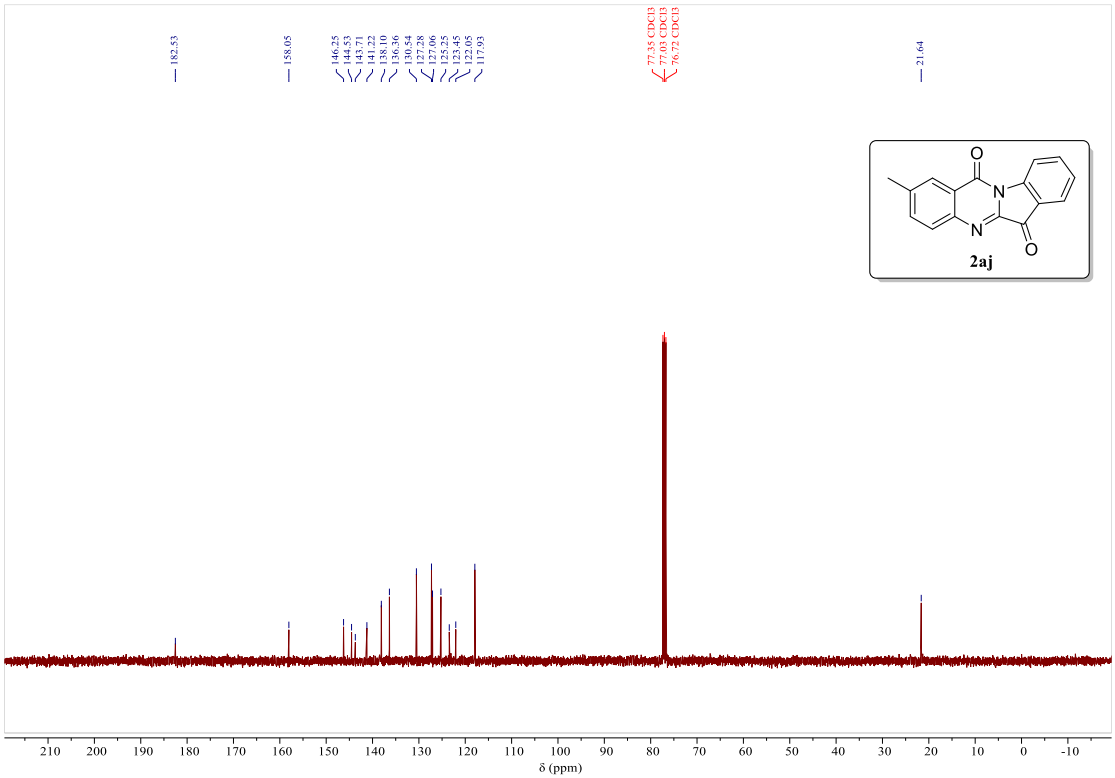


Figure S60. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2aj**

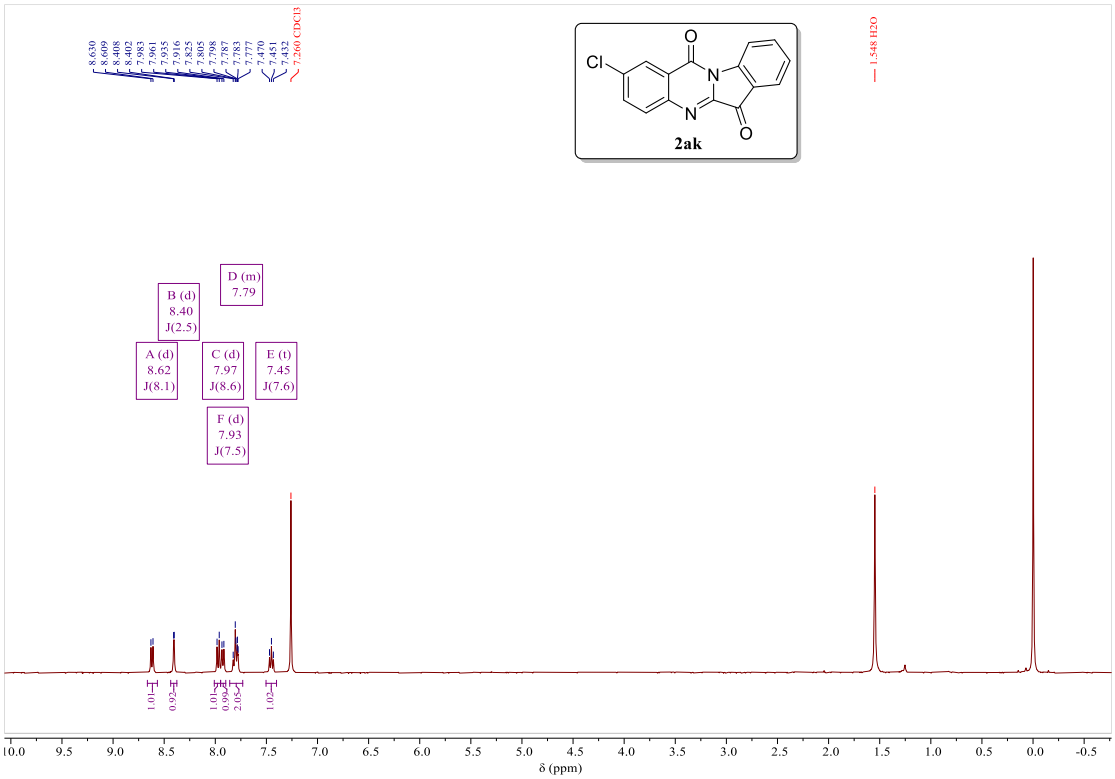


Figure S61. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2ak**

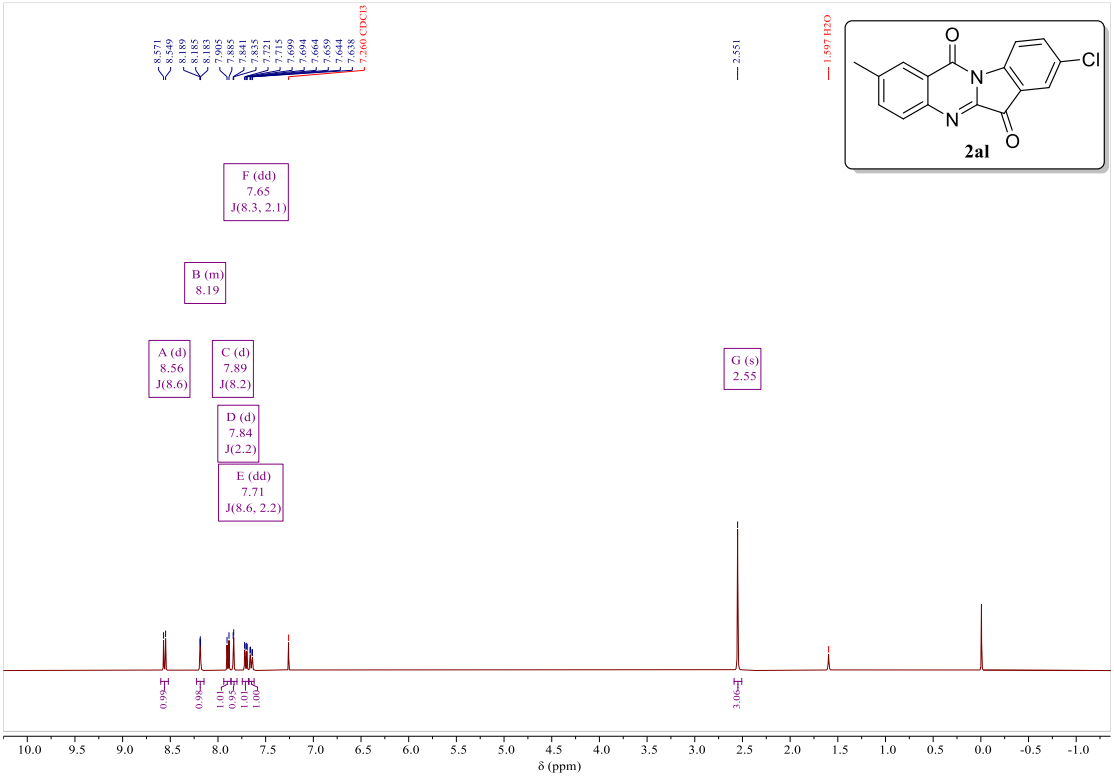


Figure S62. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2al**

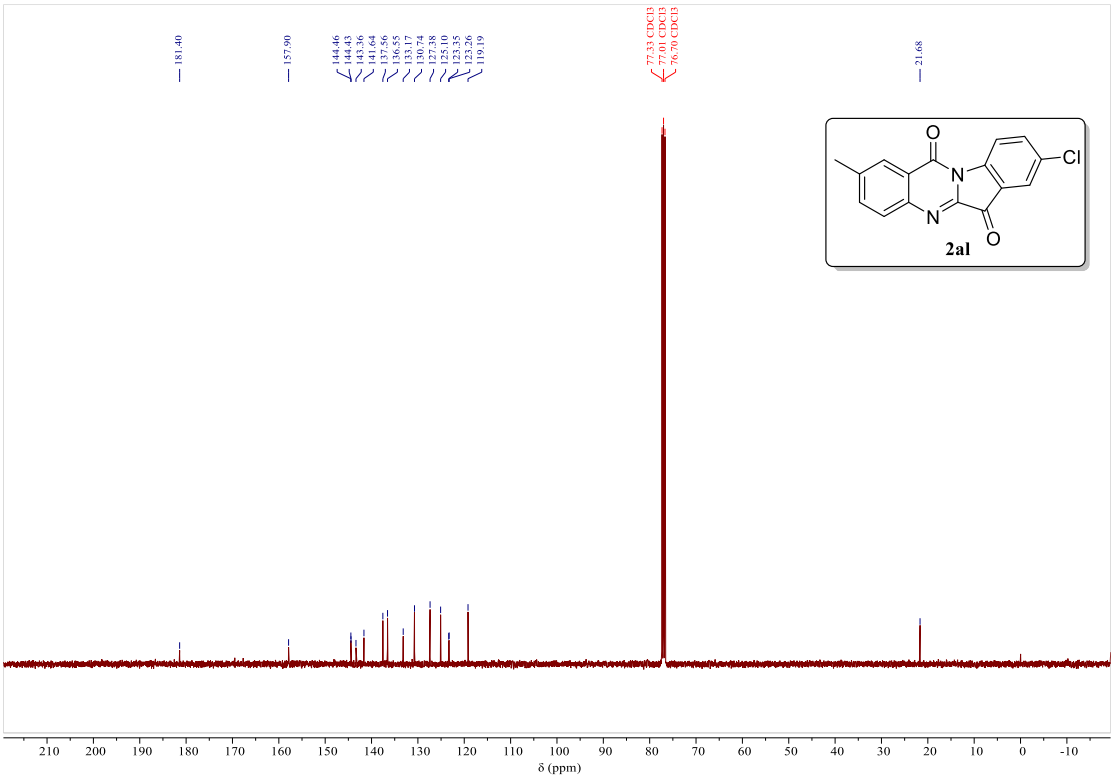


Figure S63. ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2al**

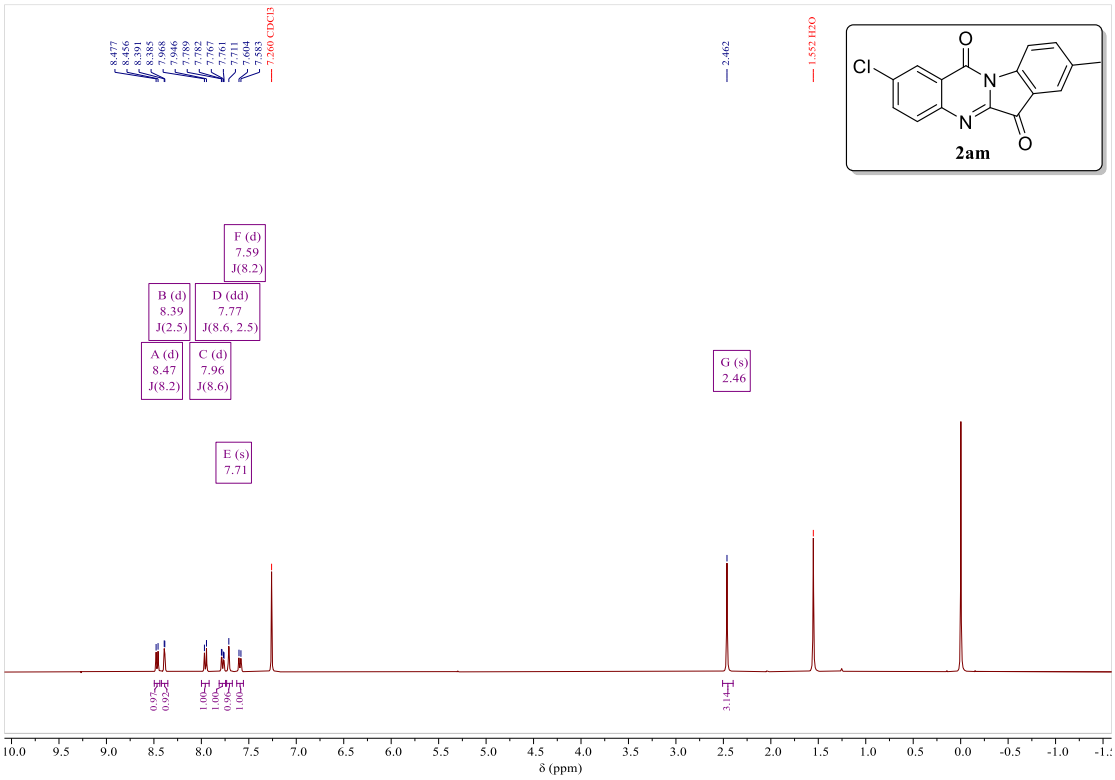


Figure S64. ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2am**

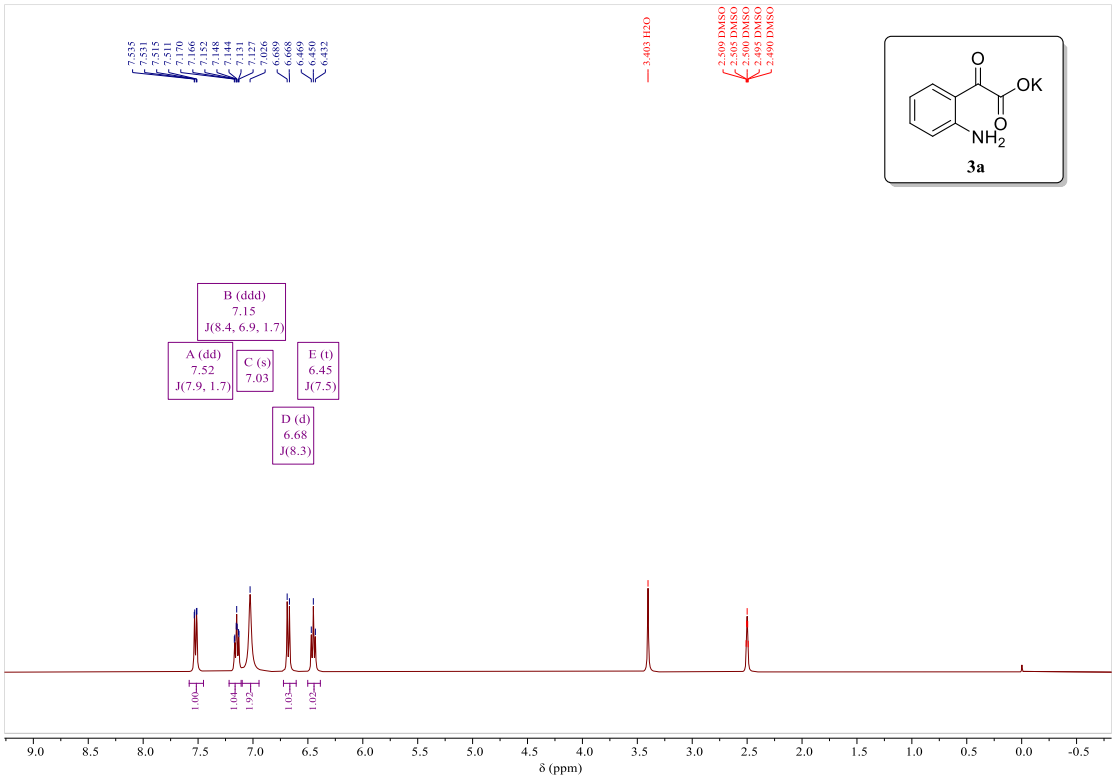


Figure S65. ^{1}H NMR (400 MHz, DMSO-d_6) of compound **3a**