Synthesis of cinnolines *via* Rh(III)-catalysed dehydrogenative C-H/N-H functionalization: Aggregation induced emission and cell imaging

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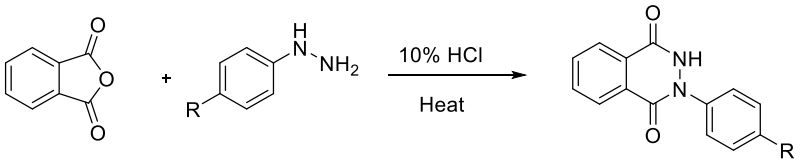
Electronic Supplementary Information

Contents

1. General information

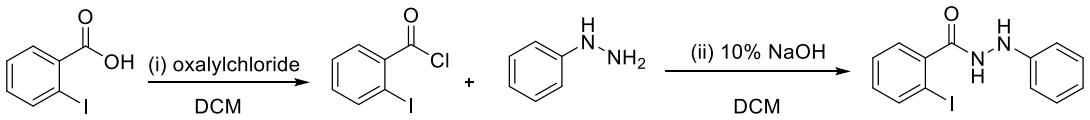
Reagents and solvents were purchased from commercial sources (Aldrich and Merck). Dry DCM were purchased sigma Aldrich, reagents were used without further purification unless otherwise noted. Column chromatography was performed on silica gel (100–200 mesh, SRL. India). Analytical TLC was performed on precoated aluminium sheets of silica gel 60F254 of 0.2 mm thickness (Merck, Germany). Melting points were determined in capillary tubes and are uncorrected. ^{1}H NMR (400 MHz) and ^{13}C (100 MHz) spectra were recorded in $CDCl_3$ solution with TMS as internal standard on a Bruker Avance III HD spectrometer. High resolution mass spectra (HRMS-ESI) were recorded using Thermo Scientific Exactive Orbitrap mass spectrometer. UV-visible absorption spectra were measured using Shimadzu UV-1800 spectrophotometer. The steady state fluorescence measurements were measured using Varian Cary Eclipse fluorescence spectrophotometer. Cell imaging was done using ZEISS-LSM 710/LSM 710 NLO and CONFOCOR 3 instrument.

2. General procedure for synthesis of *N*-phenyl phthalazines (1a-e)



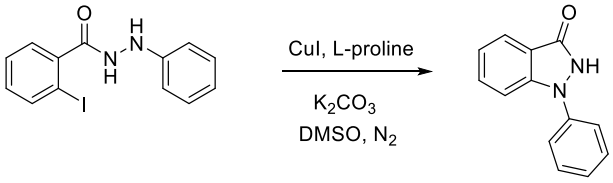
A mixture of phenyl hydrazine (1.equv) and phthalic anhydride (1.equv) in 10% HCl was heated at reflux for 9 h. Then the reaction was cooled, the resulting solid was collected for filtration, washed with water, and recrystallized from ethanol. The 2-phenyl-2,3-dihydrophthalazine-1,4-dione was obtained as colourless solid with the yield of 75%.

3. General procedure for the synthesis of *N-phenyl indazoles* (6)



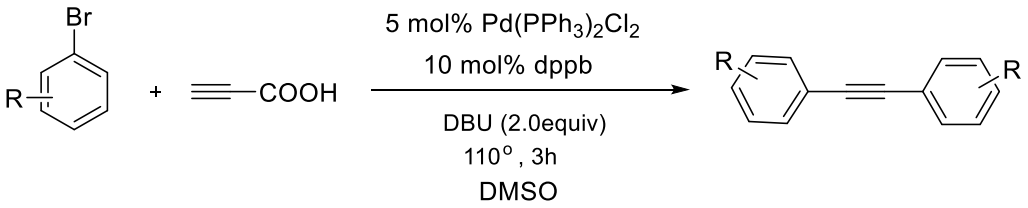
(i) Synthesis of 2-Iodobenzoyl chloride: 2-Iodobenzoic acid (10 mmol) was dissolved in anhydrous dichloromethane (25 mL) and cooled to 0^{o}C in ice bath. Oxalyl chlodide (30 mmol) was added drop-wise followed by the addition of a catalytic amount of DMF (0.01 mL) the reaction was allowed to warm to room temperature over the course of 1 h and after that time the solution was evaporated to rota evaporator for dryness. The dark brown viscous solid was formed. This was used as the without purification.

(ii) Synthesis of 2-iodo-*N*'-phenylbenzohydrazide: To a solution of phenylhydrazine (1.0 equv) dissolved in 10 mL of dichloromethane, 5 mL of 10% NaOH solution was added. Then the 2-iodobenzoyl chloride (1.2 equv) dissolved in 5ml of dichloromethane was added and stirred violently at room temperature for 1.5 h. Completion of the reaction was confirmed by TLC. The DCM layer was washed with water, saturated NaCl solution and dried with anhydrous Na_2SO_4. The Na_2SO_4 was filtered, after the solvent was evaporated under reduced pressure, the crude residue was purified by silica gel chromatography in ethyl acetate/petroleum ether 50%. 2-Iodo-*N*'-phenylbenzohydrazide was obtained as white solid.



The mixture of 2-iodo-*N*'-phenylbenzohydrazide (1.0 mmol), copper iodide (0.10 mmol, 10 mol%), L-proline (0.20 mmol, 20 mol%) and K_2CO_3 (2.0 mmol) in DMSO (10 mL) was stirred at room temperature for 3-4 h under nitrogen atmosphere. After the completion of reaction, the reaction mixture was treated with water and extracted with EtOAc. The combined organic layer washed with saturated sodium chloride solution (Brine solution) and dried over anhydrous sodium sulphate. After the filtration the solvent was evaporated in rota evaporator and purified by column chromatography (EtOAc: pet ether 50%). *N*-phenyl indazole was obtained as the white solid with the yield of 90%.

4. General procedure for synthesis of alkynes (2)

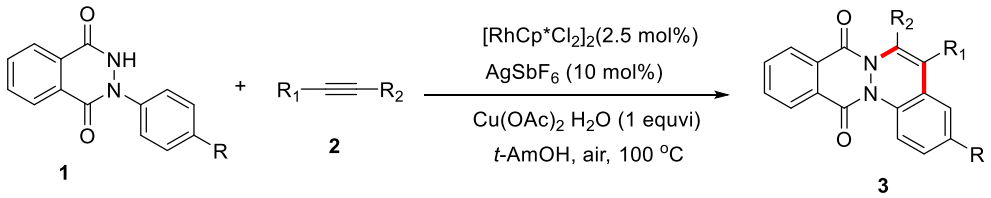


Following the literature procedure,[1] Pd $(PPh_3)_2Cl_2$ (105 mg, 0.15 mmol), 1,4- bis (diphenyl phosphino) butane (128 mg, 0.30 mmol), aryl halides (6.00 mmol), and propiolic acid (212 mg, 3.0 mmol) were combined with DBU (913 mg, 6.0 mmol) in a round bottom flask. DMSO (15.0 mL) was added and the reaction was maintained in the oxygen atmosphere. The resulting mixture was placed in an oil bath at 80 °C for 3 h. The reaction was poured in saturated ammonium chloride solution and extracted with ethyl acetate 3× 25 mL. The combined ethyl acetate layer was washed with brine solution, dried over anhydrous sodium sulphate, filtered, and the solvent were removed under

1). K. Park, G. Bae, J. Moon, J. Choe, K. H. Song, S. Lee, *J. Org. Chem.* **2010**, *75*, 6244.

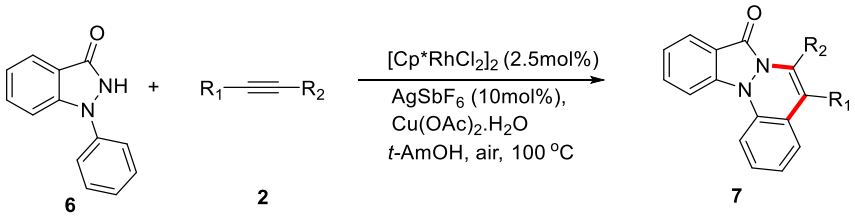
vacuum. The resulting crude product was purified using flash column chromatography in silica gel 100-200 mesh using 5% EtOAc in pet ether.

5. General procedure for synthesis of phthalazino[2,3-*a*]cinnolines



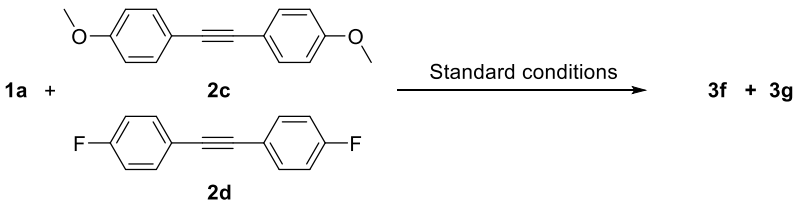
N-phenyl phthalazinone (**1**) (0.3 mmol) was treated with acetylene (**2**) (0.3 mmol) in the presence of $[RhCp^*Cl_2]_2$ (2.5 mol%), $Cu(OAc)_2 \cdot H_2O$ (1 equiv) and $AgSbF_6$ (10 mol%) in tert-amyl alcohol using a 15-mL screw cap pressure tube. The reaction mixture was heated at 100 °C for 6 h. After cooling to ambient temperature, the reaction mixture was diluted with CH_2Cl_2, filtered through Celite and the filtrate was concentrated. The crude residue was purified through a silica gel column using petroleum ether and ethyl acetate as eluent to afford pure desired product **3** in 60-98% yield.

6. General procedure for synthesis of indazolo[1,2-*a*]cinnolines

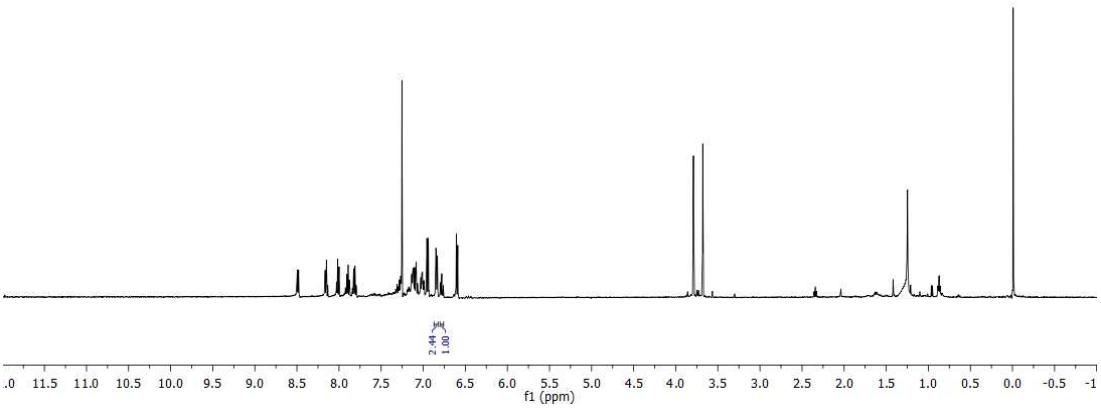


N-phenyl indazolone (**6**) (0.3 mmol) was treated with acetylene (**2**) (0.3 mmol) in the presence of $[RhCp^*Cl_2]_2$ (2.5 mol%), $Cu(OAc)_2 \cdot H_2O$ (1 equiv) and $AgSbF_6$ (10 mol%) in tert-amyl alcohol using a 15-mL screw cap pressure tube. The mixture was heated at 100 °C for 6 h. After cooling to ambient temperature, the reaction mixture was diluted with CH_2Cl_2, filtered through Celite and the filtrate was concentrated. The crude residue was purified through a silica gel column using petroleum ether and ethyl acetate as eluent. To give afford desired product **7** was obtained in 64-94% yield.

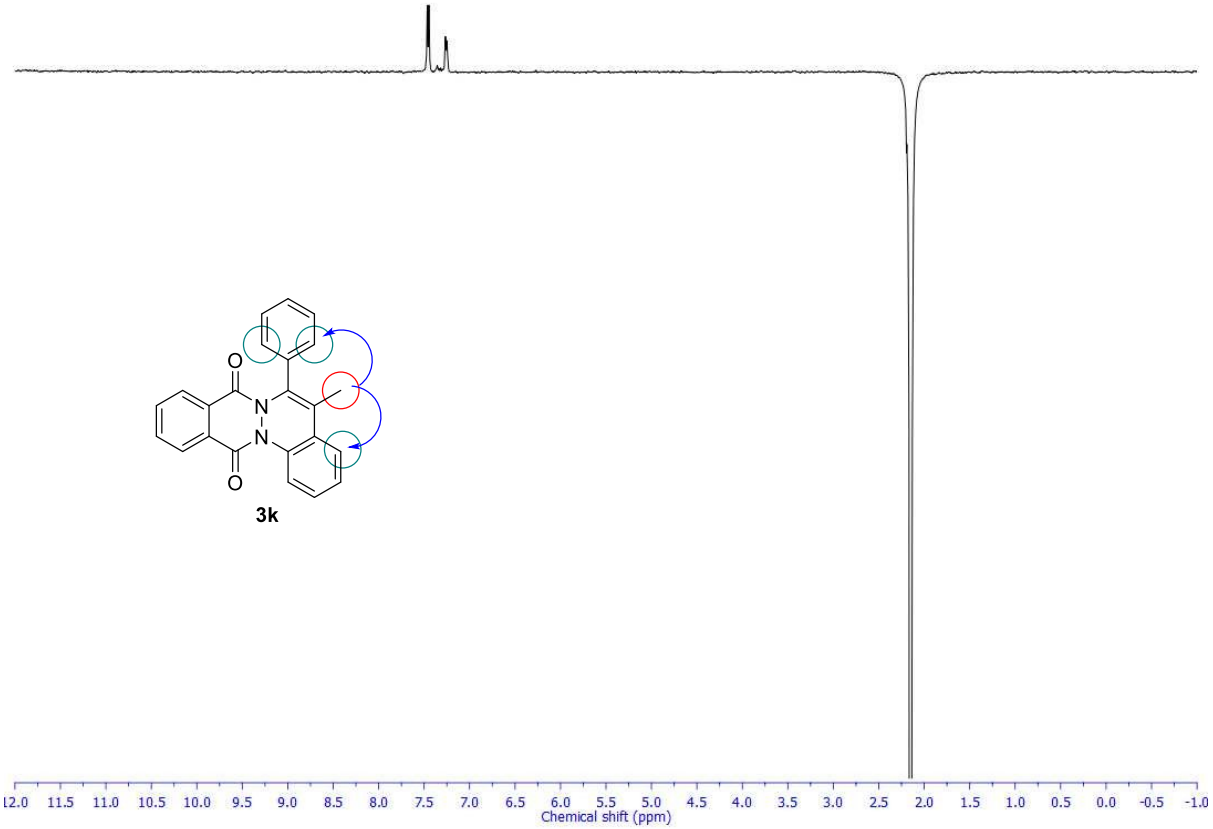
7. Competition experiment

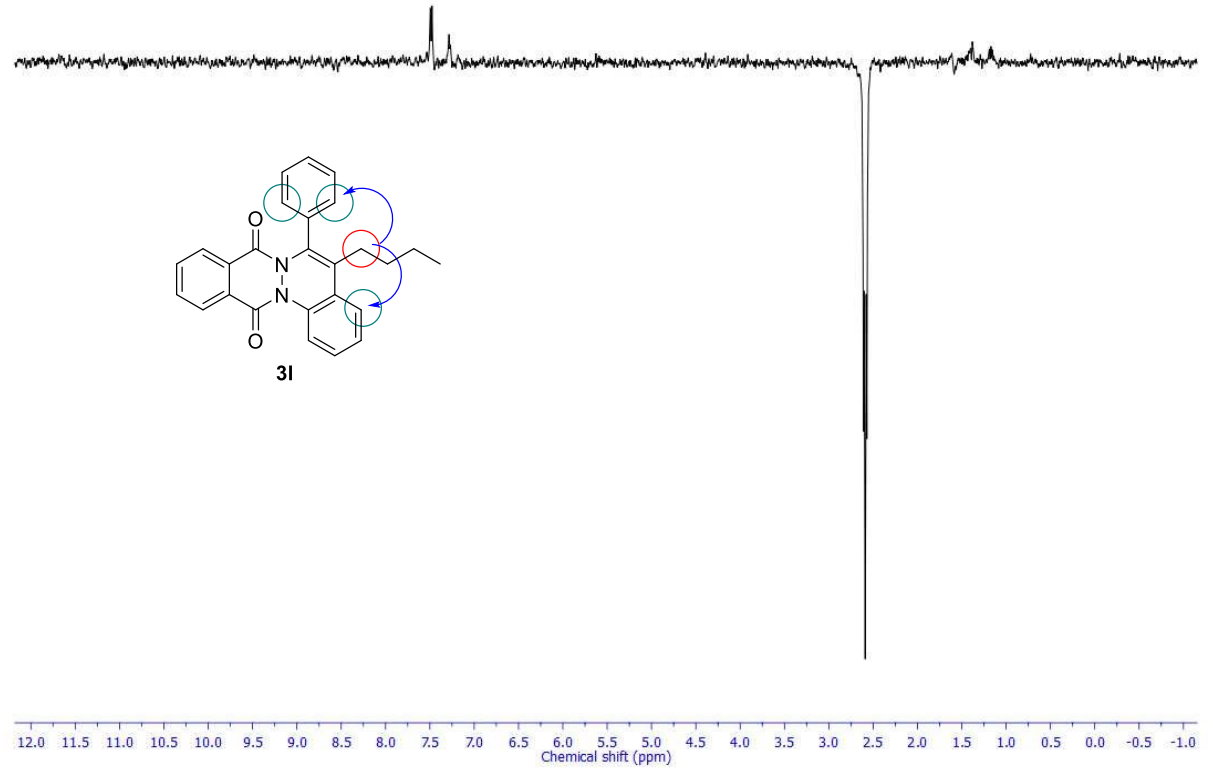


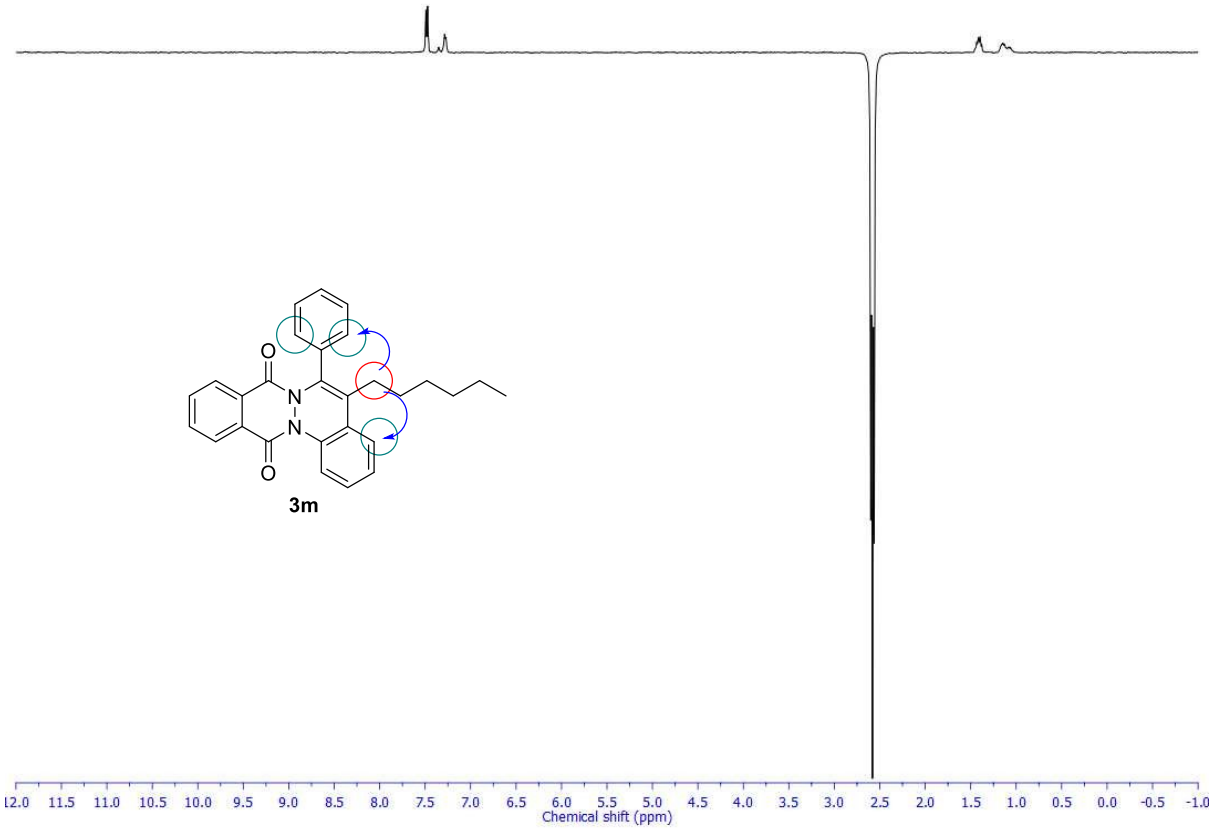
N-phenyl phthalazinone **1a** (0.2 mmol), alkyne **2c** (0.2 mmol), alkyne **2d** (0.2 mmol), $[RhCp^*Cl_2]_2$ (2.5 mol%), $AgSbF_6$ (10 mol%) and $Cu(OAc)_2 \cdot H_2O$ (1 equiv) in tert-amyl alcohol 3mL using a 15-mL screw cap pressure tube. The reaction mixture was heated at 100 ºC for 6 h. After cooling to ambient temperature, the reaction mixture was diluted with CH_2Cl_2, filtered through Celite and the filtrate was concentrated. The crude residue was purified through a silica gel column using petroleum ether and ethyl acetate as eluent to give pure desired product **3f** and **3g**. ^1H NMR analysis of the product mixture obtained revealed that **3f** and **3g** were obtained in 2.4:1.0 ratio, suggesting that more electron-rich alkyne is kinetically favoured.

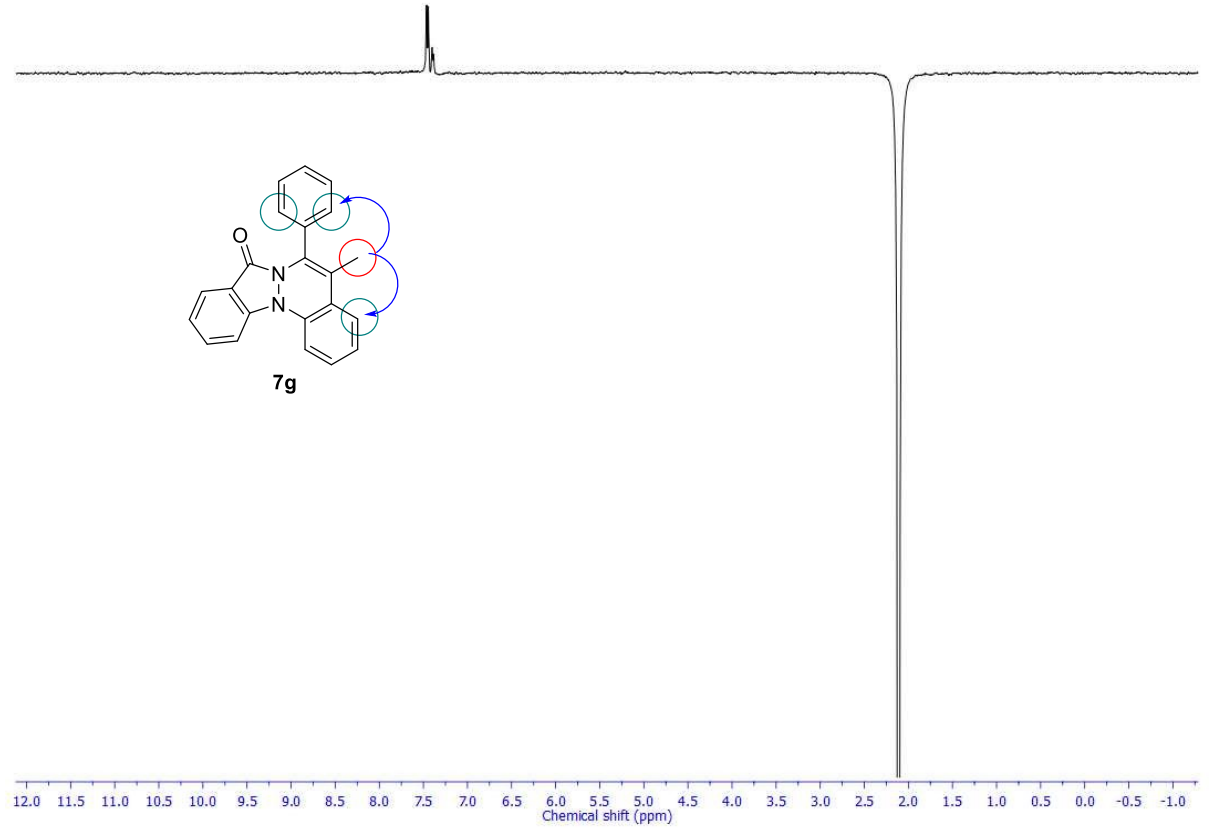


8. Regioselectivity of the reaction

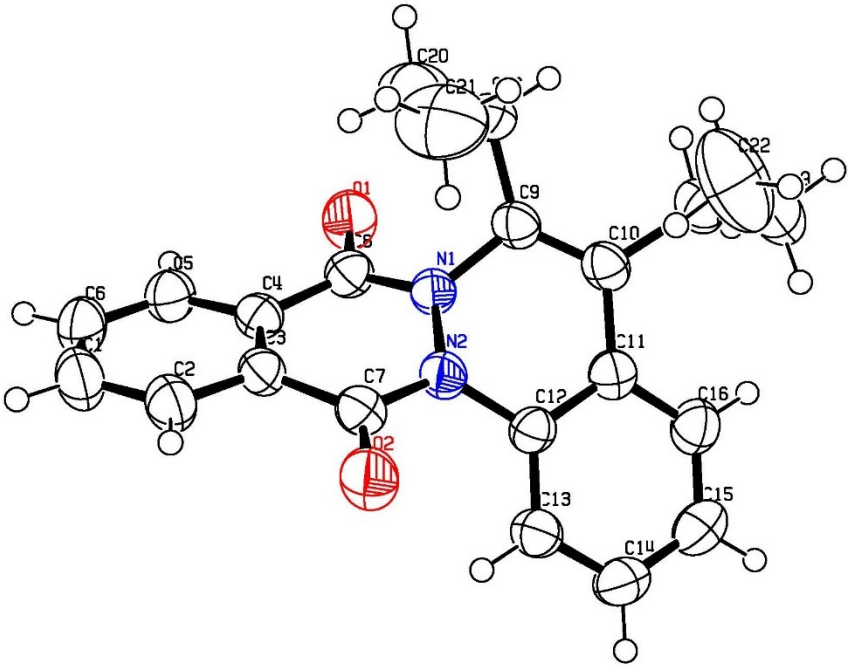





O
N
N
O
3m
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
Chemical shift (ppm)


O
N
N
7g
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
Chemical shift (ppm)

9. ORTEP of compound **3o**

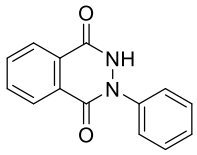


CCDC No: 1405249[2]

[2] Crystallographic data for the synthesised compound **3o** in this communication have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 1405249. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC),12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 (0)1223 336 033; email: deposit@ccdc.cam.ac.uk].

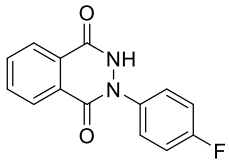
10. Spectral Data for synthesised compounds

2-phenyl-2,3-dihydrophthalazine-1,4-dione *(1a)*



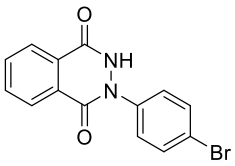
Yield: 72%, white solid. **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.86 (s, 1H), 8.31 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.03 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.99 – 7.90 (m, 2H), 7.68 – 7.62 (m, 2H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.41 – 7.34 (m, 1H) ppm; **^{13}C NMR (100 MHz, DMSO- *d*$_6$)** δ 157.79, 150.85, 142.21, 134.03, 132.95, 129.70, 128.88, 127.54, 127.33, 126.42, 124.66 ppm; **HRMS** m/z (ESI): calcd. for $C_{14}H_{10}N_2NaO_2$ $[M+Na]^+$ 261.0640, found 261.0641.

2-(4-fluorophenyl)-2,3-dihydrophthalazine-1,4-dione *(1b)*



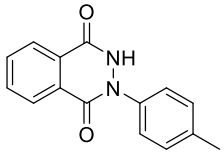
Yield: 72%, white solid. **^{1}H NMR (400 MHz, CDCl$_3$-DMSO-*d*$_6$)** δ 10.98 (s, 1H), 8.16 (t, *J* = 5.5 Hz, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.59 (dq, *J* = 13.4, 7.6 Hz, 2H), 7.45 – 7.35 (m, 2H), 6.89 (t, *J* = 8.6 Hz, 2H) ppm; **^{13}C NMR (100 MHz, CDCl$_3$-DMSO-*d*$_6$)** δ 158.16, 151.16, 137.80, 132.96, 131.93, 129.42, 127.56, 127.48, 127.02, 124.99, 124.32, 115.11, 114.89 ppm.

2-(4-bromophenyl)-2,3-dihydrophthalazine-1,4-dione (*1c*)



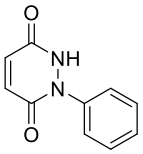
Yield: 73%, white solid. **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 11.94 (s, 1H), 8.32 (dd, *J* = 7.0, 1.2 Hz, 1H), 8.05 – 7.93 (m, 3H), 7.72 – 7.64 (m, 4H) ppm; **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.85, 151.08, 141.41, 134.20, 133.07, 131.77, 129.57, 128.25, 127.37, 124.72, 120.01 ppm.

2-(p-tolyl)-2,3-dihydrophthalazine-1,4-dione (*1d*)



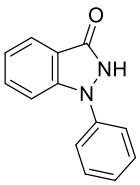
Yield: 74%, white solid. **^{1}H NMR (400 MHz, DMSO- *d*$_6$)** δ 11.86 (s, 1H), 8.30 (dd, *J* = 7.0, 1.3 Hz, 1H), 8.05 – 7.88 (m, 3H), 7.51 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 2.36 (s, 3H) ppm; **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 157.77, 150.78, 139.74, 136.85, 133.95, 132.92, 129.70, 129.31, 127.30, 126.18, 125.06, 124.63, 21.15 ppm.

1-phenyl-1,2-dihydropyridazine-3,6-dione *(1e)*



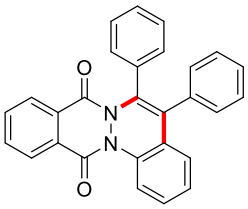
Yield: 74%, white solid. **^{1}H NMR (400 MHz, $CDCl_3$-DMSO-d_6)** δ 10.87 (s, 1H), 7.59 (d, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.07 – 6.95 (m, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$-DMSO-d_6)** δ 158.47, 153.16, 141.44, 133.83, 128.37, 127.49, 127.22, 125.39 ppm.

1-phenyl-1,2-dihydro-3H-indazol-3-one *(6)*



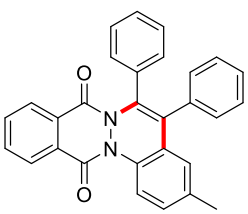
Yield: 80 %, white solid. **^{1}H NMR (400 MHz, $CDCl_3$-DMSO-d_6)** δ_H 11.29 (s, 1H), 7.77 (d, *J* = 9.1 Hz, 2H), 7.72 – 7.67 (m, 2H), 7.52 (t, *J* = 7.9 Hz, 2H), 7.49 – 7.42 (m, 1H), 7.29 – 7.24 (m, 1H), 7.20 – 7.13 (m, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$-DMSO-d_6)** δ_C 156.79, 140.70, 139.70, 129.94, 128.81, 125.22, 121.07, 120.97, 120.76, 115.26, 110.77.

5,6-diphenylphthalazino[2,3-a]cinnoline-8,13-dione (3a)



Yield: 92 %, Yellow Solid; mp: 228-230 °C; FT-IR (cm^{-1}) Neat; 3059, 2922, 1668, 1601, 1569, 1450, 1368, 1315, 1129, 693; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 8.50 (dd, *J* = 7.9, 0.9 Hz, 1H), 8.15 (dd, *J* = 7.7, 0.9 Hz, 1H), 8.04 (d, *J* = 8.1 Hz, 1H), 7.90 (td, *J* = 7.6, 1.3 Hz, 1H), 7.81 (td, *J* = 7.6, 1.3 Hz, 1H), 7.34 – 7.27 (m, 4H), 7.25 – 7.20 (m, 2H), 7.14 – 7.02 (m, 7H) ppm; **^{13}C(100 MHz, $CDCl_3$)** δ_C 157.90, 156.60, 136.02, 135.77, 134.47, 134.07, 133.88, 133.60, 130.83, 129.60, 129.49, 129.02, 128.51, 128.44, 128.27, 128.11, 127.93, 127.87, 127.64, 127.59, 126.79, 126.24, 126.07, 118.41, 0.02 ppm; **HRMS** m/z (ESI): calcd. for $C_{28}H_{19}N_2O_2$ $[M+H]^+$ 415.1447, found 415.1439; $C_{28}H_{18}N_2NaO_2$ $[M+Na]^+$ 437.1266; found 437.1258.

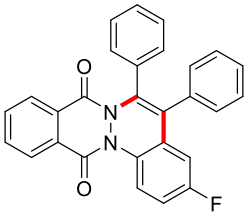
3-methyl-5,6-diphenylphthalazino[2,3-a]cinnoline-8,13-dione (3b)



Yield: 94 %, Yellow Solid; mp: 222-224 °C; **FT-IR (cm^{-1}) Neat;** 3055, 2922, 2856, 1667, 1606, 1488, 1316, 1266, 1142, 1019, 727, 691; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 8.49 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.14 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.89 (td, *J* = 7.6, 1.4 Hz, 1H),

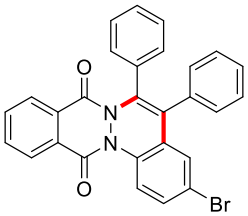
7.80 (td, *J* = 7.6, 1.3 Hz, 1H), 7.33 – 7.27 (m, 3H), 7.21 (dt, *J* = 5.9, 1.7 Hz, 2H), 7.13 – 7.00 (m, 6H), 6.87 (d, *J* = 2.0 Hz, 1H), 2.24 (s, 3H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 157.70, 156.61, 135.92, 134.57, 133.92, 133.83, 133.71, 133.34, 130.85, 129.56, 129.08, 129.04, 128.42, 128.22, 128.10, 127.88, 127.78, 127.59, 127.52, 126.55, 126.48, 118.32, 21.13 ppm; **HRMS** m/z (ESI): calcd. for $C_{29}H_{21}N_2O_2$ $[M+H]^+$ 429.1603, found 429.1296; $C_{29}H_{20}N_2NaO_2$ $[M+Na]^+$ 451.1422, found 451.1415.

3-fluoro-5,6-diphenylphthalazino[2,3-a]cinnoline-8,13-dione (3c)



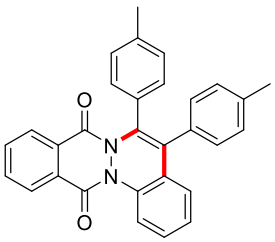
Yield: 85 %, Yellow Solid; mp: 224-226 °C; **FT-IR (cm^{-1}) Neat**; 3059, 2926, 2856, 1669, 1599, 1487, 1313, 1261, 1081, 691; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 8.49 (dd, *J* = 7.9, 1.3 Hz, 1H), 8.15 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.03 (dd, *J* = 9.1, 5.0 Hz, 1H), 7.91 (td, *J* = 7.6, 1.3 Hz, 1H), 7.82 (td, *J* = 7.6, 1.4 Hz, 1H), 7.34 – 7.27 (m, 3H), 7.20 (dd, *J* = 6.3, 1.9 Hz, 2H), 7.11 – 7.05 (m, 3H), 7.03 – 6.96 (m, 3H), 6.79 (dd, *J* = 9.4, 2.9 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 157.76, 156.67, 137.28, 134.77, 134.13, 134.04, 133.93, 133.24, 131.57, 131.54, 130.69, 129.52, 129.36, 128.97, 128.52, 128.47, 128.10, 127.97, 127.85, 127.71, 127.03, 120.54, 120.45, 115.11, 114.88, 112.84, 112.59 ppm; **HRMS** m/z (ESI): calcd. for $C_{28}H_{18}FN_2O_2$ $[M+H]^+$ 433.1352, found 433.1346; $C_{28}H_{17}FN_2NaO_2$ $[M+Na]^+$ 455.1172, found 455.1165.

3-bromo-5,6-diphenylphthalazino[2,3-a]cinnoline-8,13-dione (3d)



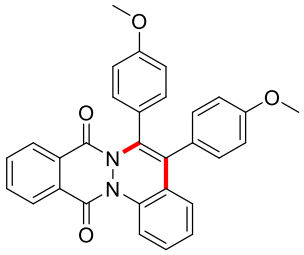
Yield: 92 %, Yellow Solid; mp: 222-224 °C; **FT-IR (cm^{-1}) Neat;** 3059, 2924, 2852, 1669, 1603, 1476, 1311, 1263, 1016, 683; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 8.49 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.18 – 8.12 (m, 1H), 7.95 – 7.88 (m, 2H), 7.82 (td, *J* = 7.5, 1.4 Hz, 1H), 7.40 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.35 – 7.27 (m, 3H), 7.19 (dd, *J* = 8.2, 2.1 Hz, 3H), 7.11 – 7.03 (m, 3H), 7.03 – 6.98 (m, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 157.84, 156.55, 137.31, 134.70, 134.24, 134.05, 133.73, 133.25, 131.14, 130.73, 129.53, 129.28, 128.96, 128.91, 128.71, 128.55, 128.51, 128.10, 128.01, 127.89, 127.70, 126.85, 120.18, 119.35 ppm; **HRMS** m/z (ESI): calcd. for $C_{28}H_{18}BrN_2O_2$ $[M+H]^+$ 493.0552, found 493.0546.

5,6-di-p-tolylphthalazino[2,3-a]cinnoline-8,13-dione (3e)



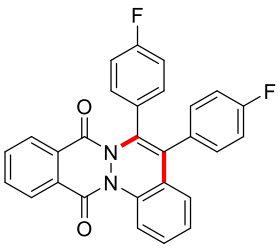
Yield: 89 %, Yellow Solid; mp: 222-224 °C; **FT-IR (cm^{-1}) Neat**; 3023, 2922, 2859, 1669, 1450, 1313, 1128, 816; **^{1}H NMR (400 MHz, CDCl$_3$)** δ_H 8.50 (dd, *J* = 7.7, 1.3 Hz, 1H), 8.16 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.02 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.89 (td, *J* = 7.6, 1.4 Hz, 1H), 7.81 (td, *J* = 7.6, 1.4 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.14 – 7.07 (m, 6H), 6.94 – 6.83 (m, 4H), 2.33 (s, 3H), 2.19 (s, 3H) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)** δ_C 157.94, 156.66, 137.50, 137.16, 135.97, 135.83, 134.02, 133.79, 131.57, 130.69, 130.65, 129.67, 129.50, 128.99, 128.85, 128.48, 128.46, 128.22, 127.89, 127.84, 127.17, 126.30, 125.98, 118.20, 21.34, 21.28 ppm; **HRMS** m/z (ESI): calcd. for $C_{30}H_{23}N_2O_2$ $[M+H]^+$ 443.1760, found 443.1754; $C_{30}H_{22}N_2NaO_2$ $[M+Na]^+$ 465.1579, found 465.1572.

5,6-bis(4-methoxyphenyl)phthalazino[2,3-a]cinnoline-8,13-dione (3f)



Yield: 85 %, Yellow Solid; mp: 200-202 °C; **FT-IR (cm^{-1}) Neat**; 3066, 2926, 2836, 1667, 1606, 1509, 1314, 1248, 1176, 1030, 828; **^{1}H NMR (400 MHz, CDCl$_3$)** δ_H 8.49 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.16 (dd, *J* = 7.9, 1.1 Hz, 1H), 8.01 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.89 (td, *J* = 7.6, 1.4 Hz, 1H), 7.81 (td, *J* = 7.5, 1.3 Hz, 1H), 7.32 – 7.24 (m, 1H), 7.16 – 7.08 (m, 4H), 6.98 – 6.93 (m, 2H), 6.88 – 6.82 (m, 2H), 6.63 – 6.58 (m, 2H), 3.80 (s, 3H), 3.68 (s, 3H) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)** δ_C 158.81, 158.75, 157.97, 156.68, 136.00, 135.84, 134.03, 133.79, 131.95, 130.35, 129.65, 129.48, 128.46, 128.15, 127.87, 127.34, 126.82, 126.21, 126.00, 125.95, 125.68, 118.23, 113.77, 113.17, 55.18, 54.96 ppm; **HRMS** m/z (ESI): calcd. for $C_{30}H_{23}N_2O_4$ $[M+H]^+$ 475.1658, found 475.1651; $C_{30}H_{22}N_2NaO_4$ $[M+Na]^+$ 497.1477, found 497.1470.

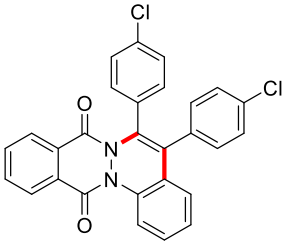
5,6-bis(4-fluorophenyl)phthalazino[2,3-a]cinnoline-8,13-dione (3g)



Yield: 70 %, Yellow Solid; mp: 236-238 °C; **FT-IR (cm^{-1}) Neat**; 3061, 2926, 2862, 1668, 1601, 1497, 1314, 1224, 1159, 834; **^{1}H NMR (400 MHz, CDCl$_3$)** δ_H 8.50 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.15 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.03 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.91 (td, *J* = 7.6, 1.4 Hz, 1H), 7.83

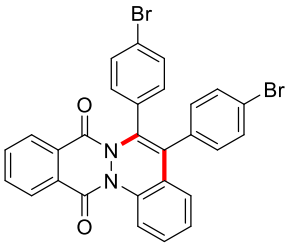
(td, *J* = 7.6, 1.3 Hz, 1H), 7.31 (ddd, *J* = 8.6, 7.3, 1.6 Hz, 1H), 7.17 (ddd, *J* = 10.3, 5.1, 1.6 Hz, 2H), 7.12 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.06 – 6.98 (m, 5H), 6.82 – 6.75 (m, 2H) ppm. **^{13}C NMR (100 MHz, CDCl3)** δ_C 163.39, 163.15, 160.93, 160.68, 157.86, 156.57, 135.79, 135.51, 134.20, 134.06, 132.49, 132.41, 130.95, 130.87, 130.21, 130.17, 129.49, 129.46, 129.44, 129.41, 128.72, 128.58, 127.88, 127.45, 126.54, 126.17, 126.06, 118.55, 115.66, 115.45, 115.11, 114.89 ppm; **HRMS** m/z (ESI): calcd. for $C_{28}H_{17}F_2N_2O_2$ $[M+H]^+$ 451.1258, found 451.1251; $C_{28}H_{16}F_2N_2NaO_2$ $[M+Na]^+$ 473.1078, found 473.1071.

5,6-bis(4-chlorophenyl)phthalazino[2,3-a]cinnoline-8,13-dione (3h)



Yield: 80 %, Yellow Solid; mp: 250-252 ^{o}C; **FT-IR (cm^{-1}) Neat**; 3074, 2926, 2848, 1668, 1486, 1314, 1091, 1015, 821; **^{1}H NMR (400 MHz, CDCl$_3$)** δ_H 8.50 (dd, J = 7.9, 1.3 Hz, 1H), 8.15 (dd, J = 7.7, 1.3 Hz, 1H), 8.03 (dd, J = 8.3, 1.1 Hz, 1H), 7.92 (td, J = 7.6, 1.4 Hz, 1H), 7.84 (td, J = 7.6, 1.3 Hz, 1H), 7.35 – 7.29 (m, 3H), 7.17 – 7.11 (m, 3H), 7.09 – 7.05 (m, 2H), 7.02 (dd, J = 7.9, 1.5 Hz, 1H), 6.98 – 6.94 (m, 2H) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)** δ_C 157.83, 156.57, 135.81, 135.19, 134.25, 134.13, 133.97, 133.95, 132.65, 132.05, 131.86, 130.30, 129.43, 129.33, 128.90, 128.81, 128.62, 128.22, 127.91, 127.52, 126.19, 126.18, 126.07, 118.54 ppm; **HRMS** m/z (ESI): calcd. for $C_{28}H_{17}Cl_2N_2O_2$ $[M+H]^+$ 483.0667, found 483.0664; $C_{28}H_{16}Cl_2N_2NaO_2$ $[M+Na]^+$ 505.0487, found 505.0484.

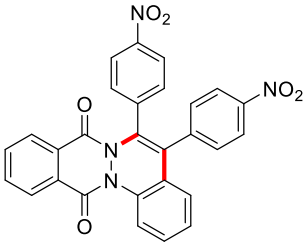
5,6-bis(4-bromophenyl)phthalazino[2,3-a]cinnoline-8,13-dione (3i)



Yield: 85 %, Yellow Solid; mp: 218-220 ^{o}C; **FT-IR (cm^{-1}) Neat**; 3070, 2924, 2856, 1669, 1486, 1313, 1070, 1011, 817; **^{1}H NMR (400 MHz, CDCl$_3$)** δ_H 8.49 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.14 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.03 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.92 (td, *J* = 7.6, 1.4 Hz, 1H), 7.83 (td, *J* = 7.5, 1.3 Hz, 1H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.32 (ddd, *J* = 8.5, 7.4, 1.6 Hz, 1H), 7.25 – 7.19 (m, 2H), 7.16 – 7.05 (m, 3H), 7.01 (dd, *J* = 7.9, 1.5 Hz, 1H), 6.93 – 6.87 (m, 2H) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)** δ_C 157.82, 156.57, 135.81, 135.14, 134.26, 134.17, 134.14, 133.12, 132.34, 131.77, 131.16, 130.55, 129.43, 129.31, 128.93, 128.63, 127.91,

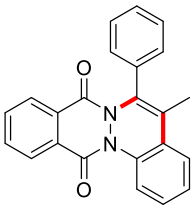
127.53, 126.19, 126.10, 126.08, 122.30, 122.18, 118.53 ppm; **HRMS** m/z (ESI): calcd. for $C_{28}H_{17}Br_2N_2O_2$ $[M+H]^+$ 570.9657, found 570.9657.

5,6-bis(4-nitrophenyl)phthalazino[2,3-a]cinnoline-8,13-dione (3j)



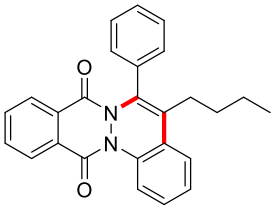
Yield: 60 %, Yellow Solid; mp: 240-242 °C; **FT-IR (cm^{-1}) Neat**; 3078, 2925, 2854, 1670, 1592, 1519, 1346, 1312, 1107, 696; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.22 (d, *J* = 8.8 Hz, 1H), 8.13 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.08 (dd, *J* = 8.3, 1.1 Hz, 1H), 8.00 – 7.96 (m, 2H), 7.89 – 7.85 (m, 1H), 7.65 – 7.59 (m, 1H), 7.53 – 7.35 (m, 5H), 7.23 – 7.15 (m, 2H), 6.97 (dd, *J* = 7.9, 1.5 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 157.71, 147.65, 140.65, 139.69, 135.79, 134.60, 134.56, 131.75, 129.88, 129.84, 129.39, 128.97, 128.88, 128.86, 128.02, 127.97, 127.89, 126.45, 125.87, 125.81, 124.95, 123.93, 123.41, 118.96.ppm; **HRMS** m/z (ESI): calcd. for $C_{28}H_{17}N_4O_6$ $[M+H]^+$ 505.1148, found 505.1140.

5-methyl-6-phenylphthalazino[2,3-a]cinnoline-8,13-dione (3k)



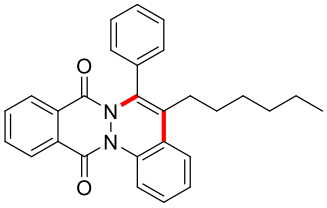
Yield: 85 %, Yellow Solid; mp: 206-208 °C; **FT-IR (cm^{-1}) Neat**; 3063, 2928, 2859, 1668, 1668, 1699, 1450, 1316, 1267, 1130, 755; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 8.46 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.12 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.03 – 7.97 (m, 1H), 7.87 (td, *J* = 7.6, 1.4 Hz, 1H), 7.79 (td, *J* = 7.6, 1.4 Hz, 1H), 7.45 – 7.41 (m, 1H), 7.38 – 7.27 (m, 5H), 7.23 (dd, *J* = 7.8, 1.8 Hz, 2H), 2.13 (s, 3H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 157.83, 156.22, 136.27, 135.00, 133.97, 133.95, 133.67, 129.72, 129.45, 128.90, 128.41, 128.26, 128.19, 127.85, 127.65, 126.23, 124.35, 121.04, 118.12, 14.56 ppm; **HRMS** m/z (ESI): calcd. for $C_{23}H_{17}N_2O_2$ $[M+H]^+$ 353.1290, found 353.1285; $C_{23}H_{16}N_2NaO_2$ $[M+Na]^+$ 375.1109, found 375.1105.

5-butyl-6-phenylphthalazino[2,3-a]cinnoline-8,13-dione (3l)



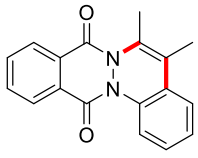
Yield: 78 %, Yellow Solid; mp:204-206 °C; **FT-IR (cm^{-1}) Neat**; 3070, 2927, 2863, 1686, 1601, 1452, 1328, 1291, 1180, 707; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 8.45 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.10 (dd, *J* = 7.8, 1.4 Hz, 1H), 8.01 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.86 (td, *J* = 7.6, 1.4 Hz, 1H), 7.77 (td, *J* = 7.6, 1.4 Hz, 1H), 7.46 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.35 – 7.28 (m, 4H), 7.25 (ddd, *J* = 9.3, 6.3, 1.5 Hz, 3H), 2.61 – 2.53 (m, 2H), 1.38 (td, *J* = 7.4, 6.8, 2.0 Hz, 2H), 1.14 (h, *J* = 7.4 Hz, 2H), 0.70 (t, *J* = 7.3 Hz, 3H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 157.71, 156.08, 136.84, 135.51, 133.97, 133.93, 133.64, 129.75, 129.44, 129.19, 128.37, 128.25, 128.22, 128.18, 127.80, 126.19, 126.09, 125.70, 124.39, 118.57, 31.00, 26.57, 22.24, 13.62; **HRMS** m/z (ESI): calcd. for $C_{26}H_{23}N_2O_2$ $[M+H]^+$ 395.1760, found 395.1755.

5-hexyl-6-phenylphthalazino[2,3-a]cinnoline-8,13-dione (3m)



Yield: 65 %, Yellow Solid; mp: 202-204 °C; **FT-IR (cm^{-1}) Neat**; 3063, 2928, 2871, 1667, 1601, 1451, 1317, 789; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 8.45 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.10 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.01 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.86 (td, *J* = 7.6, 1.4 Hz, 1H), 7.77 (td, *J* = 7.6, 1.4 Hz, 1H), 7.46 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.38 – 7.30 (m, 4H), 7.29 (dd, *J* = 4.3, 1.7 Hz, 1H), 7.27 (d, *J* = 1.6 Hz, 1H), 7.25 (dd, *J* = 2.6, 1.4 Hz, 1H), 2.59 – 2.51 (m, 2H), 1.44 – 1.33 (m, 2H), 1.19 – 1.00 (m, 6H), 0.77 (t, *J* = 7.1 Hz, 3H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 157.70, 156.08, 136.84, 135.47, 134.00, 133.92, 133.64, 129.75, 129.44, 129.17, 128.38, 128.21, 128.19, 127.80, 126.19, 126.10, 125.78, 124.38, 118.56, 31.23, 28.82, 28.80, 26.81, 22.45, 13.96 ppm; **HRMS** m/z (ESI): calcd. for $C_{28}H_{27}N_2O_2$ $[M+H]^+$ 423.2073, found 423.2068; $C_{28}H_{26}N_2NaO_2$ $[M+Na]^+$ 445.1892, found 445.1887.

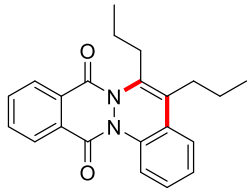
5,6-dimethylphthalazino[2,3-a]cinnoline-8,13-dione (3n)



Yield: 98 %, Yellow Solid**;** mp: 216-218 °C; **FT-IR (cm^{-1}) Neat**; 3076, 2926, 2852, 1662, 1599, 1490, 1333, 1319, 1097, 722; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 8.44 – 8.38 (m, 1H), 8.35 – 8.28 (m, 1H), 7.96 – 7.90

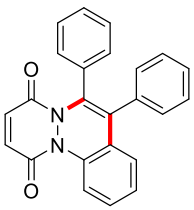
(m, 1H), 7.89 – 7.82 (m, 2H), 7.35 – 7.30 (m, 1H), 7.23 (ddd, *J* = 6.6, 4.4, 1.9 Hz, 2H), 2.27 (d, *J* = 1.0 Hz, 3H), 2.14 (d, *J* = 1.0 Hz, 3H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 157.73, 156.45, 135.69, 133.88, 133.63, 131.91, 129.64, 129.57, 128.23, 127.56, 127.49, 127.11, 126.09, 123.33, 119.77, 118.22, 15.73, 13.46 ppm; **HRMS** m/z (ESI): calcd. for $C_{18}H_{15}N_2O_2$ $[M+H]^+$ 291.1134, found 291.1128; $C_{18}H_{14}N_2NaO_2$ $[M+Na]^+$ 313.0953, found 313.0947.

5,6-dipropylphthalazino[2,3-a]cinnoline-8,13-dione (3o)



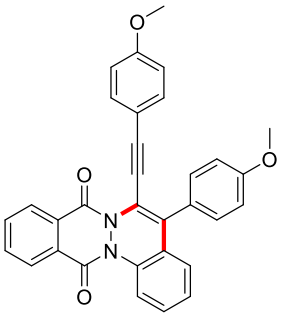
Yield: 96 %, Yellow Solid; mp: 148-150 °C; **FT-IR (cm^{-1}) Neat**; 3678, 2928, 2871, 1667, 1601, 1451, 1317, 789; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 8.44 – 8.39 (m, 1H), 8.34 – 8.29 (m, 1H), 7.94 – 7.90 (m, 1H), 7.89 – 7.82 (m, 2H), 7.36 (dd, *J* = 7.4, 2.1 Hz, 1H), 7.26 – 7.20 (m, 2H), 2.83 (s, 2H), 2.63 – 2.53 (m, 2H), 1.57 (dq, *J* = 14.8, 7.4 Hz, 2H), 1.29 (h, *J* = 7.4 Hz, 2H), 1.07 – 0.97 (m, 3H), 0.84 (t, *J* = 7.4 Hz, 3H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 157.73, 156.63, 136.91, 136.40, 133.95, 133.61, 129.54, 129.50, 128.30, 127.60, 127.54, 126.26, 126.02, 124.98, 123.61, 118.19, 29.58, 28.39, 22.61, 21.50, 14.33, 13.67 ppm; **HRMS** m/z (ESI): calcd. for $C_{22}H_{23}N_2O_2$ $[M+H]^+$ 347.1760, found 347.1757; $C_{22}H_{22}N_2NaO_2$ $[M+Na]^+$ 369.1579, found 369.1577.

6,7-diphenylpyridazino[1,2-a]cinnoline-1,4-dione (3p)



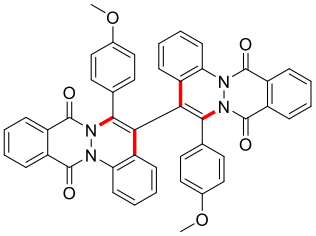
Yield: 98 %, Yellow Solid; mp: 160-162 °C; **FT-IR (cm^{-1}) Neat;** 3057, 2926, 1662, 1601, 1450, 1307, 1127, 830, 750**; ^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.18 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.35 – 7.25 (m, 4H), 7.20 – 7.09 (m, 7H), 7.09 – 7.03 (m, 3H), 6.86 (d, *J* = 10.0 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.71, 155.37, 135.61, 135.22, 135.18, 135.15, 134.11, 133.09, 130.72, 129.05, 128.51, 128.27, 128.12, 128.02, 127.69, 126.48, 126.32, 126.16, 117.77 ppm; **HRMS** m/z (ESI): calcd. for $C_{24}H_{17}N_2O_2$ $[M+H]^+$ 365.1290, found 365.1286.

6-(4-methoxyphenyl)-5-((4-methoxyphenyl)ethynyl)phthalazino[2,3-a]cinnoline-8,13-dione(5a)



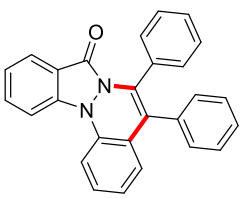
Yellow Solid; mp: 200-202 °C; **FT-IR (cm^{-1}) Neat**; 3070, 2930, 2836, 1667, 1609, 1485, 1509, 1314, 1247, 1176, 1030, 828, 689; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 8.49 (dd, *J* = 8.0, 1.0 Hz, 1H), 8.16 (dd, *J* = 7.5, 1.0 Hz, 1H), 8.01 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.89 (td, *J* = 7.6, 1.3 Hz, 1H), 7.84 – 7.79 (m, 1H), 7.30 – 7.26 (m, 1H), 7.18 – 7.06 (m, 4H), 6.98 – 6.93 (m, 2H), 6.85 (d, *J* = 8.9 Hz, 2H), 6.64 – 6.57 (m, 2H), 3.80 (s, 3H), 3.68 (s, 3H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 158.81, 158.75, 157.97, 156.68, 136.00, 135.84, 134.03, 133.80, 131.95, 130.35, 129.64, 129.48, 128.91, 128.46, 128.15, 127.87, 127.34, 126.82, 126.21, 126.00, 125.95, 125.70, 124.76, 118.23, 113.77, 113.17, 55.18, 54.96 ppm; **HRMS** m/z (ESI): calcd. for $C_{32}H_{21}N_2O_4$ $[M-H]^-$ 497.1496, found 497.1496.

6,6'-bis(4-methoxyphenyl)-[5,5'-biphthalazino[2,3-a]cinnoline]-8,8',13,13'-tetraone (5b)



Yellow Solid; mp: °C; **FT-IR (cm^{-1}) Neat**; 3098, 2899, 2876, 1657, 1609, 1588, 1485, 1509, 1314, 1247, 1176, 1030, 828, 726, 689; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.49 (dd, *J* = 7.8, 1.1 Hz, 1H), 8.37 (ddd, *J* = 15.7, 7.7, 0.7 Hz, 2H), 8.00 – 7.94 (m, 2H), 7.91 (dt, *J* = 7.5, 3.8 Hz, 1H), 7.83 (ddd, *J* = 14.4, 8.2, 6.7 Hz, 4H), 7.70 (dd, *J* = 7.4, 6.5 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.25 – 7.23 (m, 1H), 7.05 (dd, *J* = 11.3, 3.8 Hz, 1H), 6.85 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.72 (d, *J* = 8.8 Hz, 2H), 6.65 (d, *J* = 8.8 Hz, 2H), 6.58 (d, *J* = 8.7 Hz, 2H), 6.44 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H), 3.70 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 159.65, 159.32, 157.38, 156.71, 156.27, 155.91, 136.88, 135.91, 135.68, 135.28, 134.13, 133.78, 133.66, 131.96, 131.81, 130.73, 129.61, 129.46, 129.34, 129.19, 129.18, 128.51, 128.48, 128.46, 128.24, 128.20, 128.04, 127.92, 127.83, 127.46, 126.29, 125.83, 125.65, 125.48, 121.85, 120.13, 119.77, 118.44, 113.45, 113.42, 55.35, 55.09 ppm; **HRMS** m/z (ESI): calcd. for $C_{46}H_{31}N_4O_6$ $[M+H]^+$ 735.2244, found 735.2238.

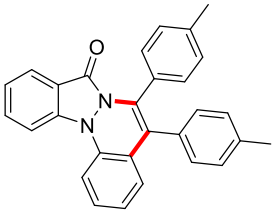
5,6-diphenyl-8H-indazolo[1,2-a]cinnolin-8-one (7a)



Yield: 89 %, Greenish yellow Solid; mp: 198-200 °C; **FT-IR (cm^{-1}) Neat**; 3056, 2829, 1687, 1588, 1463, 1453, 1356, 1356, 1352, 1142, 749,

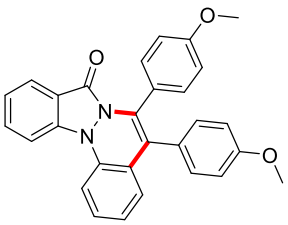
701, 669; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 7.96 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.76 (ddd, *J* = 8.5, 7.2, 1.3 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.38 – 7.32 (m, 1H), 7.32 – 7.26 (m, 4H), 7.25 – 7.16 (m, 7H), 7.02 (d, *J* = 4.3 Hz, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 156.13, 139.58, 137.94, 134.67, 134.41, 132.19, 131.23, 130.14, 128.88, 128.86, 128.52, 128.19, 128.13, 127.41, 127.36, 126.96, 125.22, 124.56, 123.97, 122.98, 118.84, 113.94, 111.05 ppm; **HRMS** m/z (ESI): calcd. for $C_{27}H_{19}N_2O$ $[M+H]^+$ 387.1497, found 387.1490.

5,6-di-p-tolyl-8H-indazolo[1,2-a]cinnolin-8-one (7b)



Yield: 94 %, Greenish yellow Solid; mp: 224-226 ^{o}C; **FT-IR (cm^{-1}) Neat**; 2926, 2881, 1691, 1610, 1463, 1351, 1294, 818, 741; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 7.96 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.75 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H), 7.69 (d, *J* = 8.2 Hz, 1H), 7.38 – 7.32 (m, 1H), 7.29 – 7.26 (m, 1H), 7.09 (d, *J* = 6.3 Hz, 6H), 7.04 – 6.95 (m, 4H), 2.32 (s, 3H), 2.26 (s, 3H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 156.15, 139.68, 138.04, 137.77, 136.94, 134.68, 132.05, 131.48, 131.04, 129.98, 128.93, 128.65, 128.55, 128.18, 126.99, 125.58, 124.52, 123.90, 123.20, 122.96, 119.07, 114.04, 110.93, 21.42, 21.28 ppm; **HRMS** m/z (ESI): calcd. for $C_{29}H_{22}N_2NaO$ $[M+Na]^+$ 437.1630, found 437.1587.

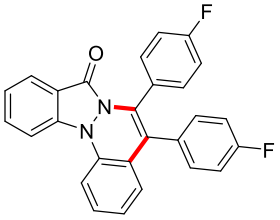
5,6-bis(4-methoxyphenyl)-8H-indazolo[1,2-a]cinnolin-8-one (7c)



Yield: 85 %, Greenish yellow Solid; mp: 216-218 ^{o}C; **FT-IR (cm^{-1}) Neat**; 2925, 2856, 1682, 1643, 1463, 1293, 1177, 1033, 830, 746; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 7.96 (d, *J* = 7.9 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 8.2 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.28 (s, 1H), 7.13 (d, *J* = 8.3 Hz, 4H), 7.02 (d, *J* = 6.8 Hz, 2H), 6.83 (d, *J* = 7.3 Hz, 2H), 6.73 (d, *J* = 7.4 Hz, 2H), 3.79 (s, 3H), 3.75 (s, 3H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 159.12, 158.68, 156.17, 139.68, 138.03, 134.72, 132.32, 132.03, 131.47, 128.59, 126.88, 126.77, 125.73,

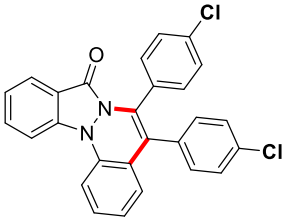
124.50, 123.91, 123.88, 122.95, 122.78, 119.08, 114.03, 113.71, 112.91, 110.95, 55.16, 55.04 ppm; **HRMS** m/z (ESI): calcd. for $C_{29}H_{23}N_2O_3$ $[M+H]^+$ 447.1709, found 447.2716.

5,6-bis(4-fluorophenyl)-8H-indazolo[1,2-a]cinnolin-8-one (7d)



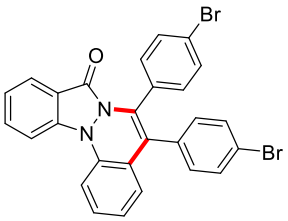
Yield: 75 %, Greenish yellow Solid; mp: 218-220 °C; **FT-IR (cm^{-1}) Neat**; 2930, 2858, 1638, 1506, 1353, 1297, 1223, 834, 745; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 7.96 (d, *J* = 7.8 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.77 (ddd, *J* = 8.5, 7.1, 1.3 Hz, 1H), 7.71 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.39 – 7.34 (m, 1H), 7.34 – 7.28 (m, 1H), 7.20 – 7.14 (m, 4H), 7.07 – 6.95 (m, 4H), 6.93 – 6.87 (m, 2H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 179.99, 156.17, 139.58, 132.87, 132.78, 132.38, 132.01, 131.93, 129.14, 126.76, 125.01, 124.55, 124.07, 123.10, 122.62, 122.62, 118.66, 115.57, 115.35, 114.79, 114.58, 113.88, 111.17 ppm; **HRMS** m/z (ESI): calcd. for $C_{27}H_{17}F_2N_2O$ $[M+H]^+$ 423.1309, found 423.1271.

5,6-bis(4-chlorophenyl)-8H-indazolo[1,2-a]cinnolin-8-one (7e)



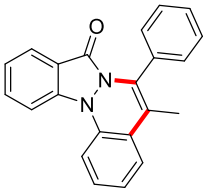
Yield: 78 %, Greenish yellow Solid; mp: 202-204 °C; **FT-IR (cm^{-1}) Neat**; 2925, 2856, 1688, 1614, 1487, 1352, 1294, 1251, 1089, 1016, 821, 750; **^{1}H NMR (400 MHz, $CDCl_3$)** δ_H 7.89 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.70 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.29 (ddd, *J* = 7.9, 7.1, 0.8 Hz, 1H), 7.26 – 7.20 (m, 3H), 7.14 – 7.09 (m, 2H), 7.06 (dq, *J* = 8.5, 2.2 Hz, 4H), 6.96 (td, *J* = 7.6, 1.1 Hz, 1H), 6.88 (dd, *J* = 7.8, 1.6 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ_C 156.20, 139.65, 137.94, 134.36, 133.82, 133.74, 132.61, 132.47, 132.46, 131.39, 129.68, 129.32, 128.74, 127.93, 126.78, 124.70, 124.56, 124.11, 123.21, 122.66, 118.60, 113.94, 111.20 ppm; **HRMS** m/z (ESI): calcd. for $C_{27}H_{17}Cl_2N_2O$ $[M+H]^+$ 455.0718, found 455.0708.

5,6-bis(4-bromophenyl)-8H-indazolo[1,2-a]cinnolin-8-one (7f)



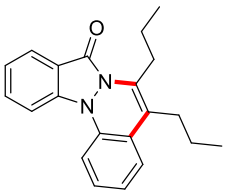
Yield: 85 %, Greenish yellow Solid; mp: 254-256 °C; **FT-IR (cm^{-1}) Neat**; 2922, 2712, 2079, 1649, 1633, 1486, 1463, 1012, 749; **^{1}H NMR (400 MHz, CDCl$_3$)** δ_H 7.99 – 7.93 (m, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.77 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H), 7.70 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.40 – 7.28 (m, 4H), 7.07 (dt, *J* = 8.9, 2.7 Hz, 4H), 7.02 (dd, *J* = 7.5, 1.1 Hz, 1H), 6.95 (dd, *J* = 7.8, 1.5 Hz, 1H) ppm; **^{13}C NMR (101 MHz, CDCl$_3$)** δ_C 156.20, 139.67, 137.95, 133.75, 133.07, 132.75, 132.49, 131.71, 131.62, 130.88, 130.12, 129.36, 126.80, 124.61, 124.57, 124.13, 123.24, 122.76, 122.66, 121.96, 118.59, 113.96, 111.20 ppm; **HRMS** m/z (ESI): calcd. for $C_{27}H_{17}Br_2N_2O$ $[M+H]^+$ 542.9708, found 542.9702.

5-methyl-6-phenyl-8H-indazolo[1,2-a]cinnolin-8-one (7g)



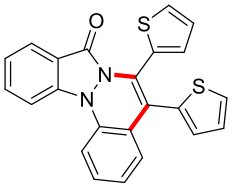
Yield: 87 %, Greenish yellow Solid; mp: 180-182 °C; **FT-IR (cm^{-1}) Neat**; 2926, 2856, 2063, 1681, 1633, 1488, 1452, 1284, 1144, 749; **^{1}H NMR (400 MHz, CDCl$_3$)** δ_H 7.93 (d, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 1H), 7.75 – 7.69 (m, 1H), 7.66 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.46 – 7.40 (m, 4H), 7.38 – 7.35 (m, 2H), 7.31 (dd, *J* = 7.7, 6.6 Hz, 2H), 7.18 (td, *J* = 7.6, 1.1 Hz, 1H), 2.09 (s, 3H) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)** δ_C 155.77, 139.78, 138.47, 133.58, 131.90, 131.87, 129.84, 128.71, 128.55, 127.97, 125.69, 124.91, 124.43, 124.13, 123.02, 119.25, 116.23, 114.14, 110.87, 13.75 ppm; **HRMS** m/z (ESI): calcd. for $C_{22}H_{16}N_2O$ $[M+H]^+$ 325.1341, found 325.1335.

5,6-dipropyl-8H-indazolo[1,2-a]cinnolin-8-one (7h)



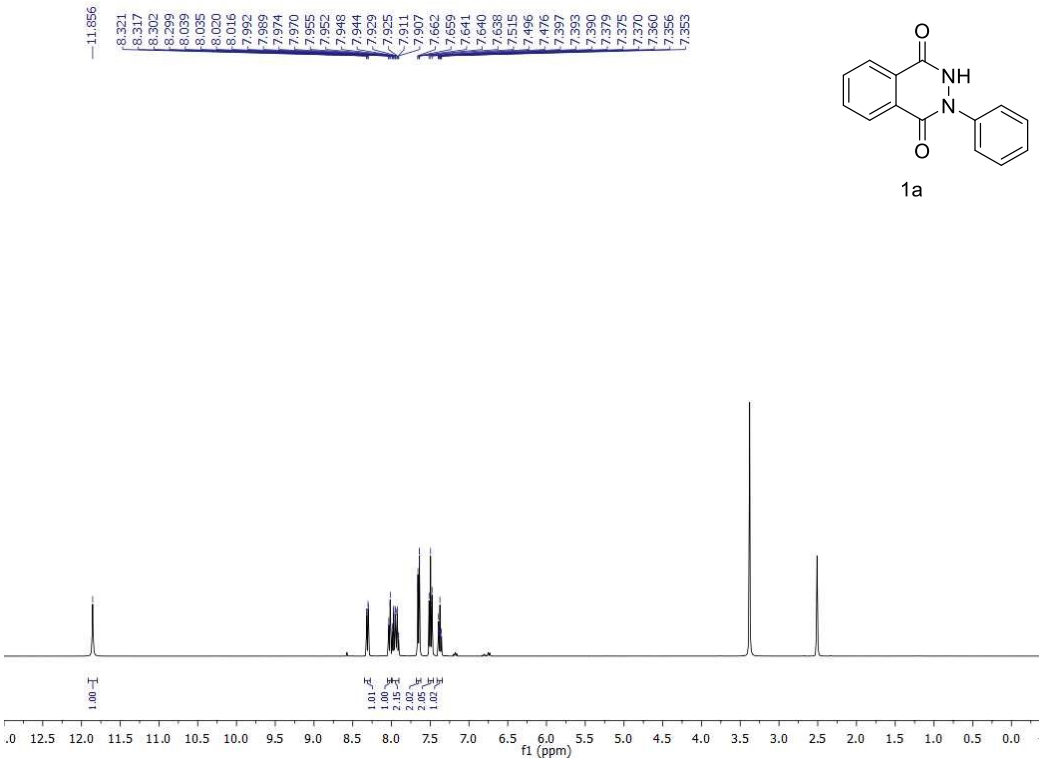
Yield: 80 %, Greenish yellow Solid; mp: 192-194 °C; **FT-IR (cm^{-1}) Neat**; 2922, 2132, 2079, 1638, 1630, 1482, 1456, 1010, 748; **^{1}H NMR (400 MHz, CDCl$_3$)** δ_H 8.04 – 7.98 (m, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.68 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H), 7.60 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.36 – 7.29 (m, 2H), 7.21 (td, *J* = 7.8, 1.5 Hz, 1H), 7.12 (td, *J* = 7.6, 1.2 Hz, 1H), 3.20 – 3.11 (m, 2H), 2.62 – 2.52 (m, 2H), 1.64 (dq, *J* = 15.9, 7.6 Hz, 4H), 1.04 (dt, *J* = 11.8, 7.3 Hz, 6H) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)** δ_C 156.81, 139.06, 137.95, 136.67, 131.76, 127.75, 124.48, 124.16, 124.06, 123.95, 122.70, 118.98, 118.21, 113.84, 111.21, 28.36, 28.05, 22.79, 22.71, 14.32, 13.80 ppm; **HRMS** m/z (ESI): calcd. for $C_{21}H_{23}N_2O$ $[M+H]^+$ 319.1810, found 319.1801.

5,6-di(thiophen-2-yl)-8H-indazolo[1,2-a]cinnolin-8-one (7i)

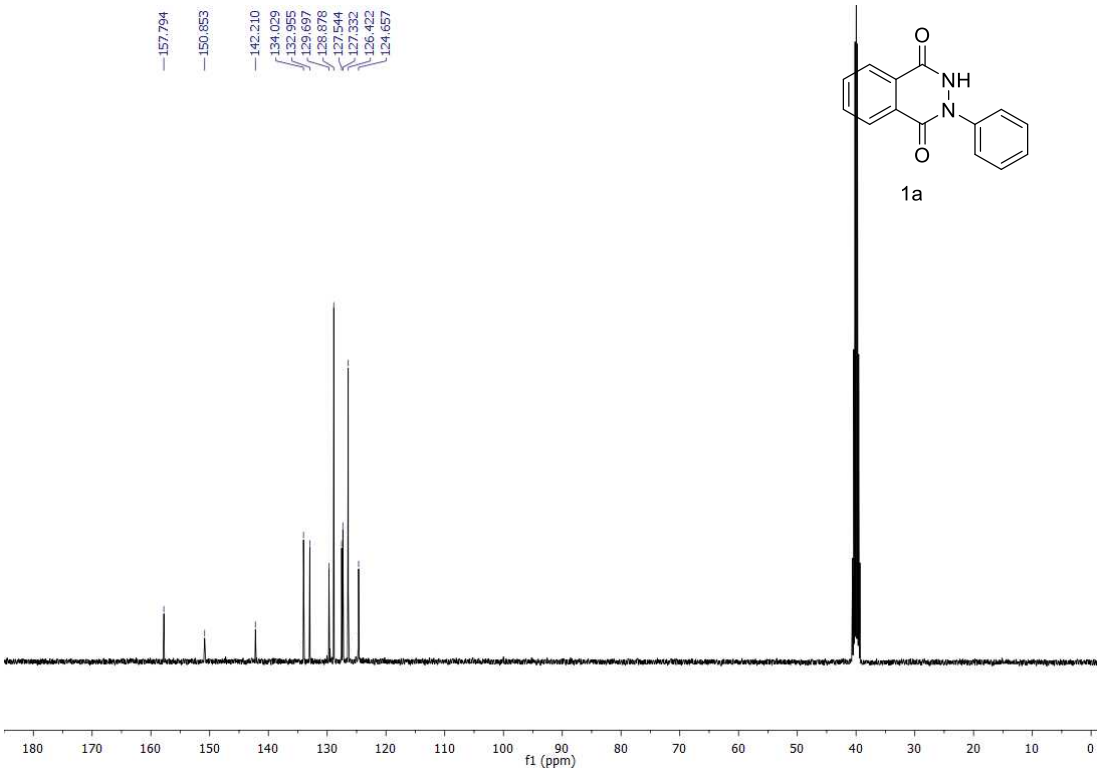


Yield: 94 %, Greenish yellow Solid; mp: 238-240 ^{o}C; **FT-IR (cm^{-1}) Neat**; 2922, 2856, 1691, 1691, 1628, 1483, 1462, 1359, 1275, 1231, 1117, 748; **^{1}H NMR (400 MHz, CDCl$_3$)** δ_H 7.99 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 1H), 7.81 – 7.74 (m, 1H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.42 – 7.32 (m, 3H), 7.30 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.20 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.13 – 7.03 (m, 4H), 6.94 (dd, *J* = 5.0, 3.5 Hz, 1H) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)** δ_C 156.62, 140.60, 138.70, 134.74, 132.37, 131.66, 130.97, 130.61, 129.37, 127.97, 127.41, 127.16, 126.83, 126.17, 125.36, 124.62, 124.62, 12 4.26, 123.58, 119.37, 118.60, 114.64, 110.90 ppm; **HRMS** m/z (ESI): calcd. for $C_{23}H_{15}N_2OS_2$ $[M+H]^+$ 399.0626, found 399.0621.

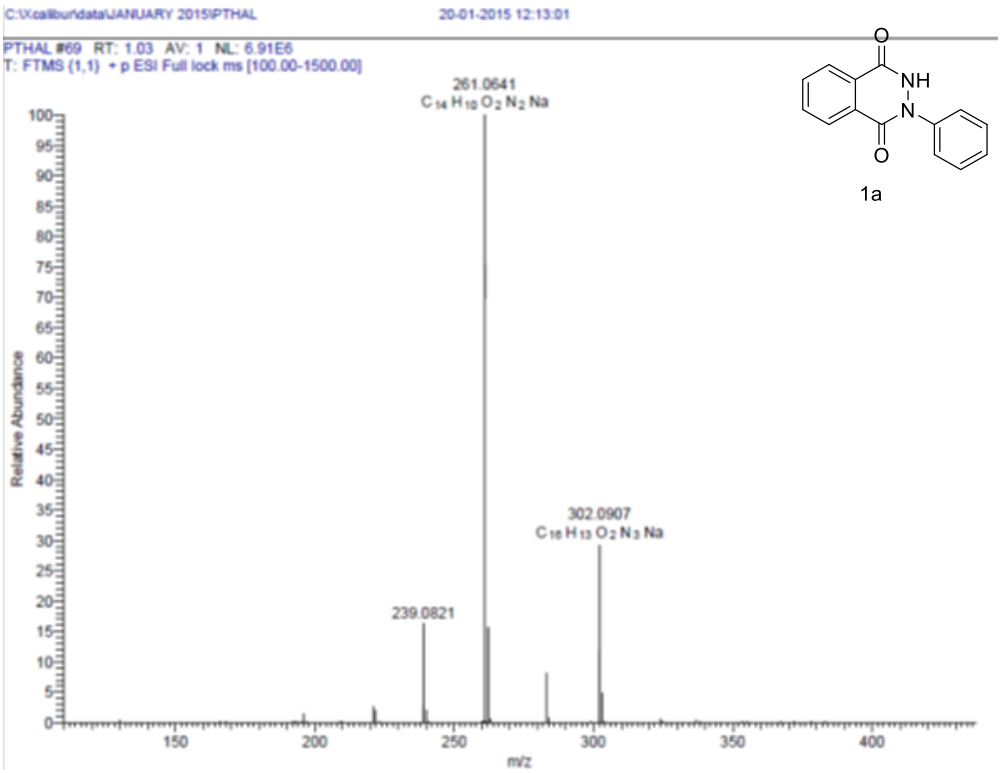
11. Copies of ^{1}H, ^{13}C NMR and HRMS spectrum of synthesized compounds



^{1}H NMR Spectrum of Compound 1a in DMSO-d_6

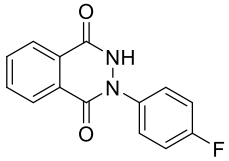


^{13}C NMR Spectrum of *Compound* 1a in DMSO-d_6

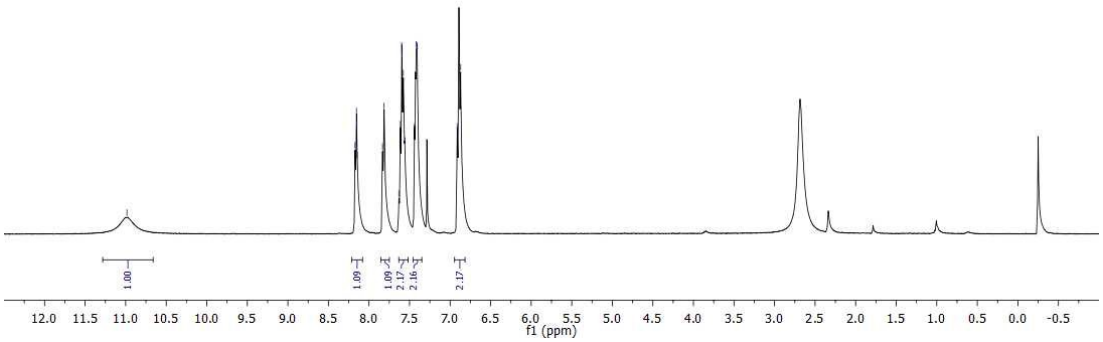


1a

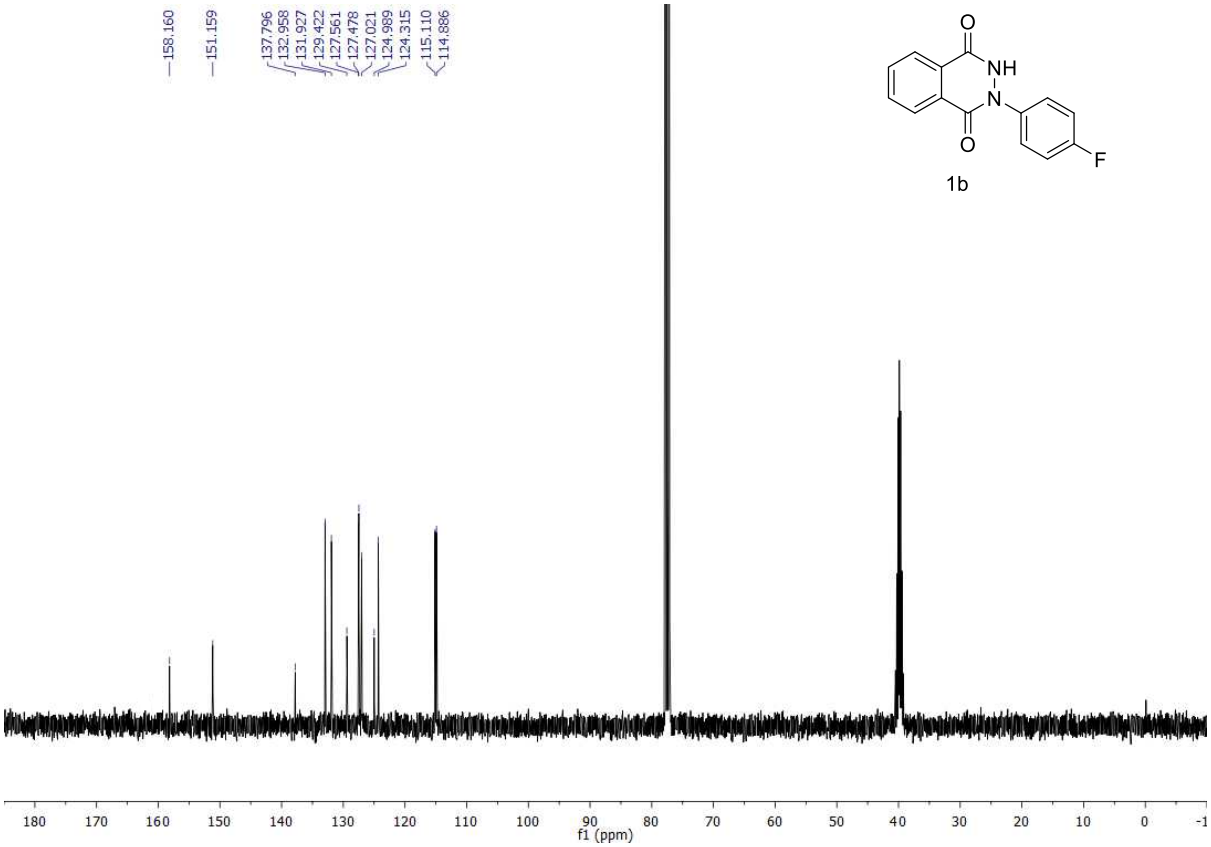
HRMS Spectrum of *Compound* 1a



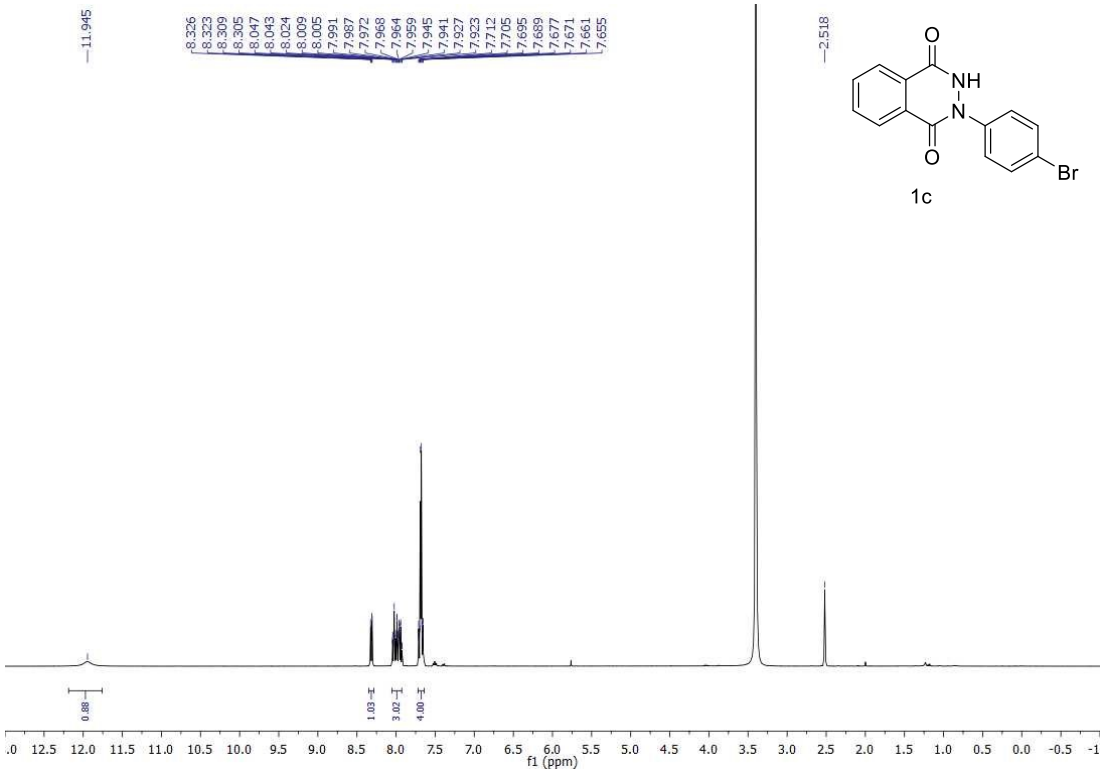
1b



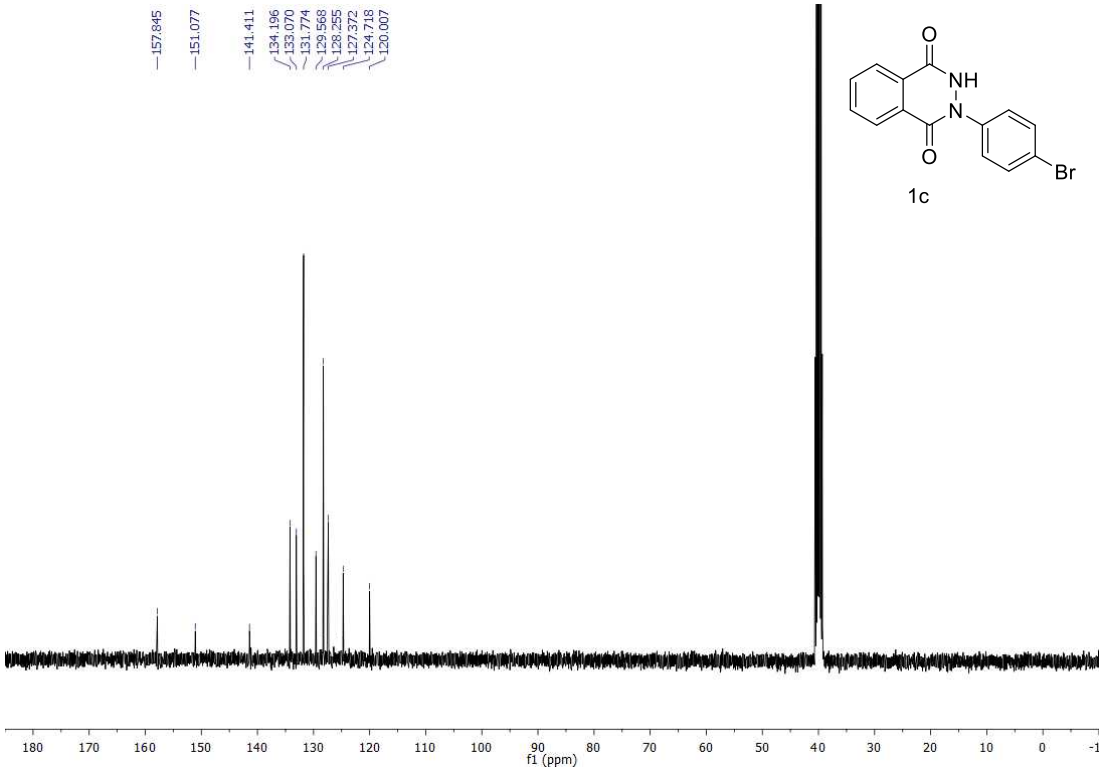
[1]H NMR Spectrum of Compound 1b in $CDCl_3$-DMSO-d_6



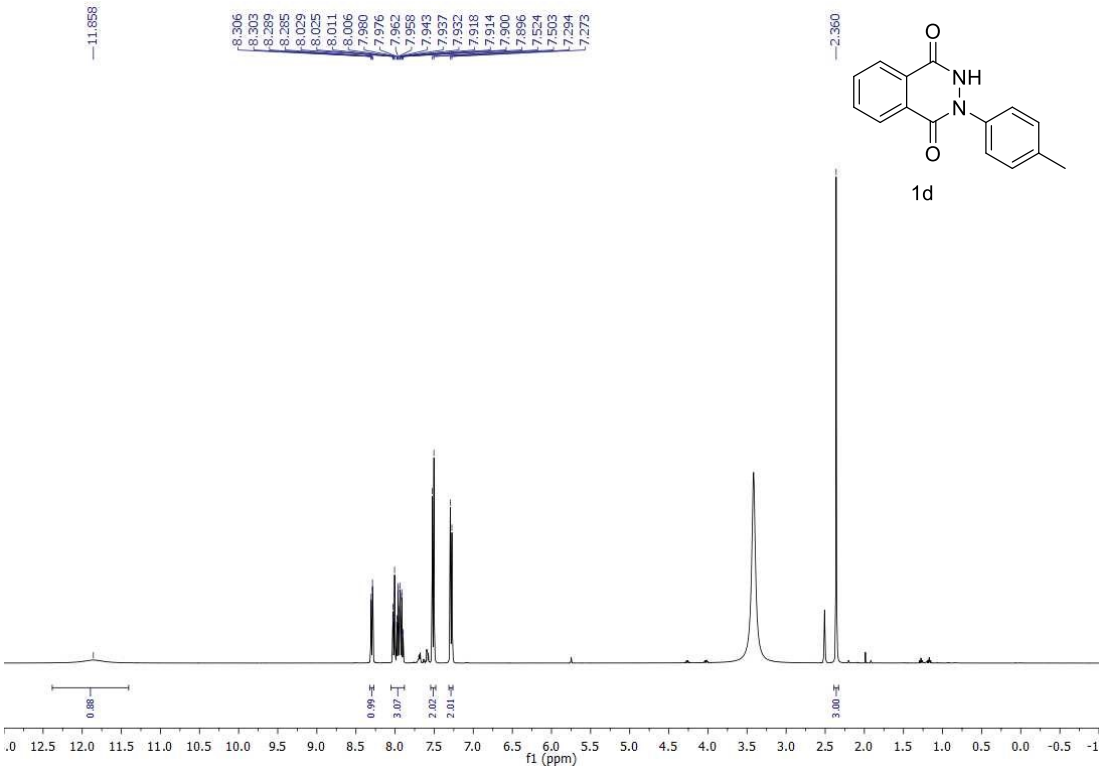
^{13}C NMR Spectrum of Compound 1b in $CDCl_3$-DMSO-d_6



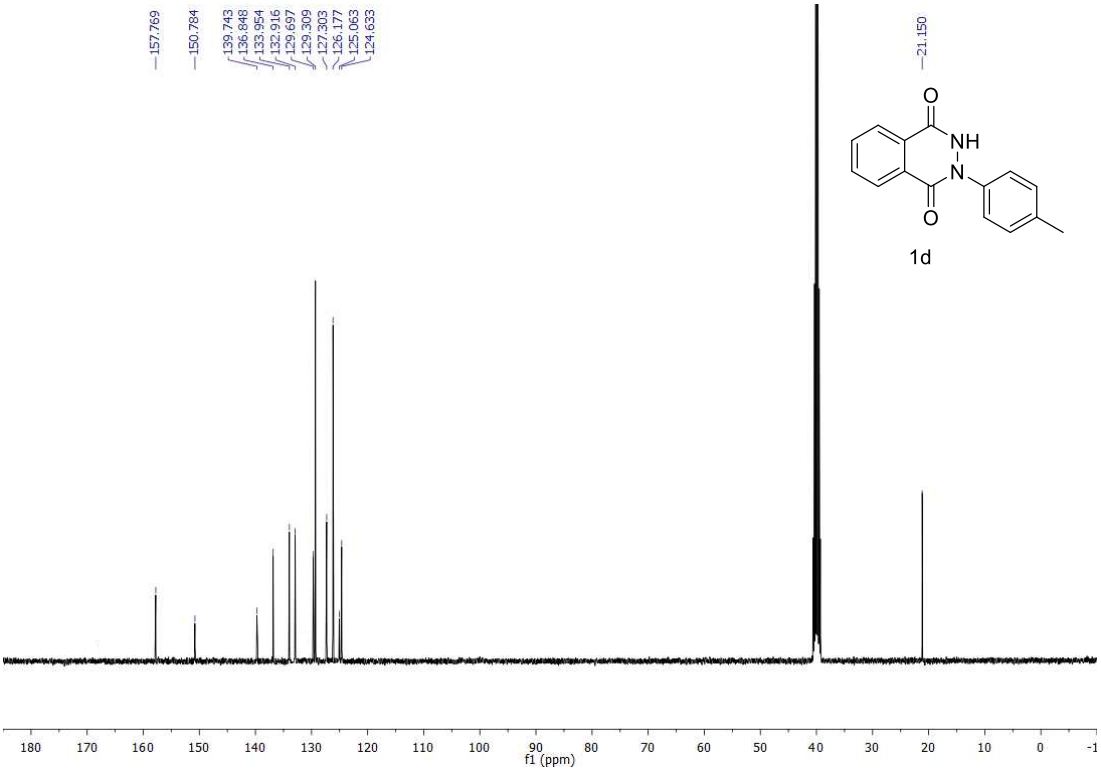
^{1}H NMR Spectrum of Compound 1c in DMSO-d_6



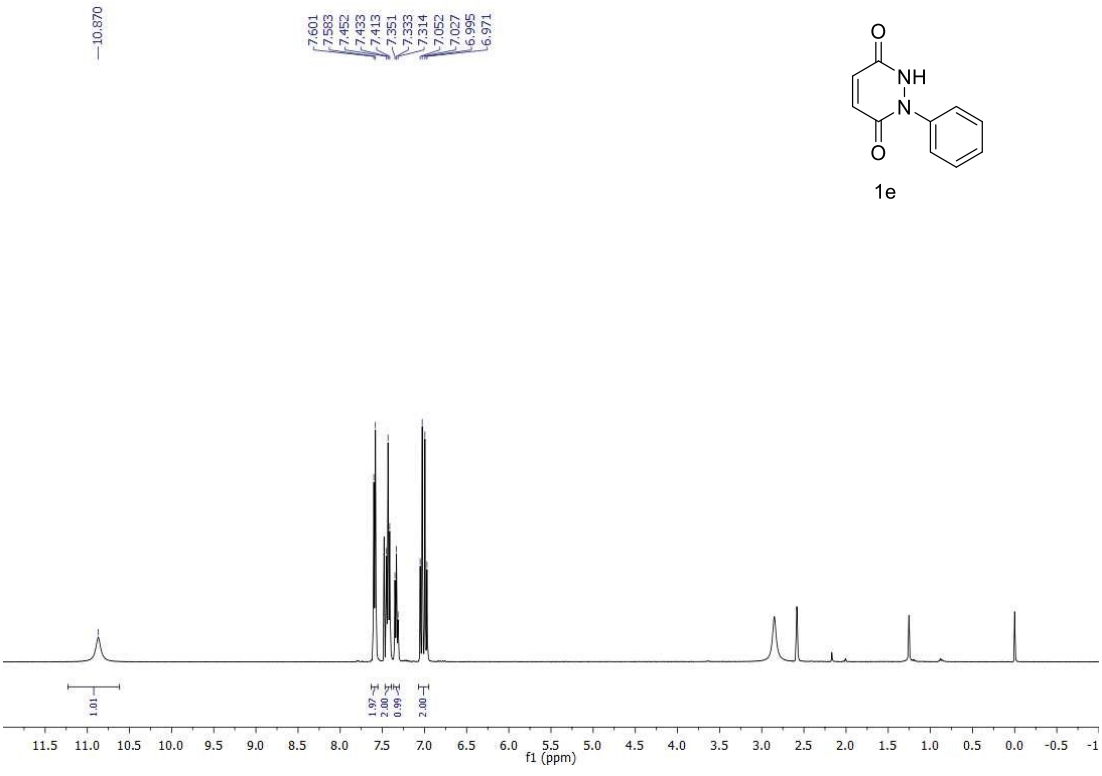
^{13}C NMR Spectrum of Compound 1c in DMSO-d_6



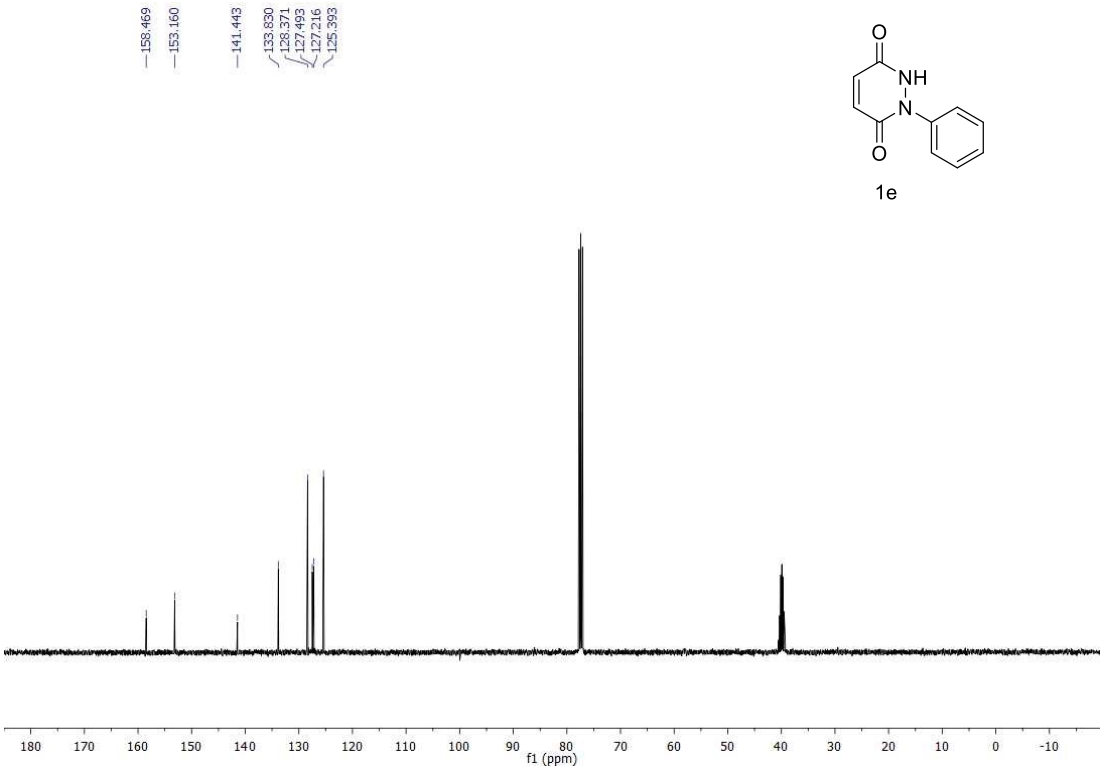
^{1}H NMR Spectrum of Compound 1d in DMSO-d_6



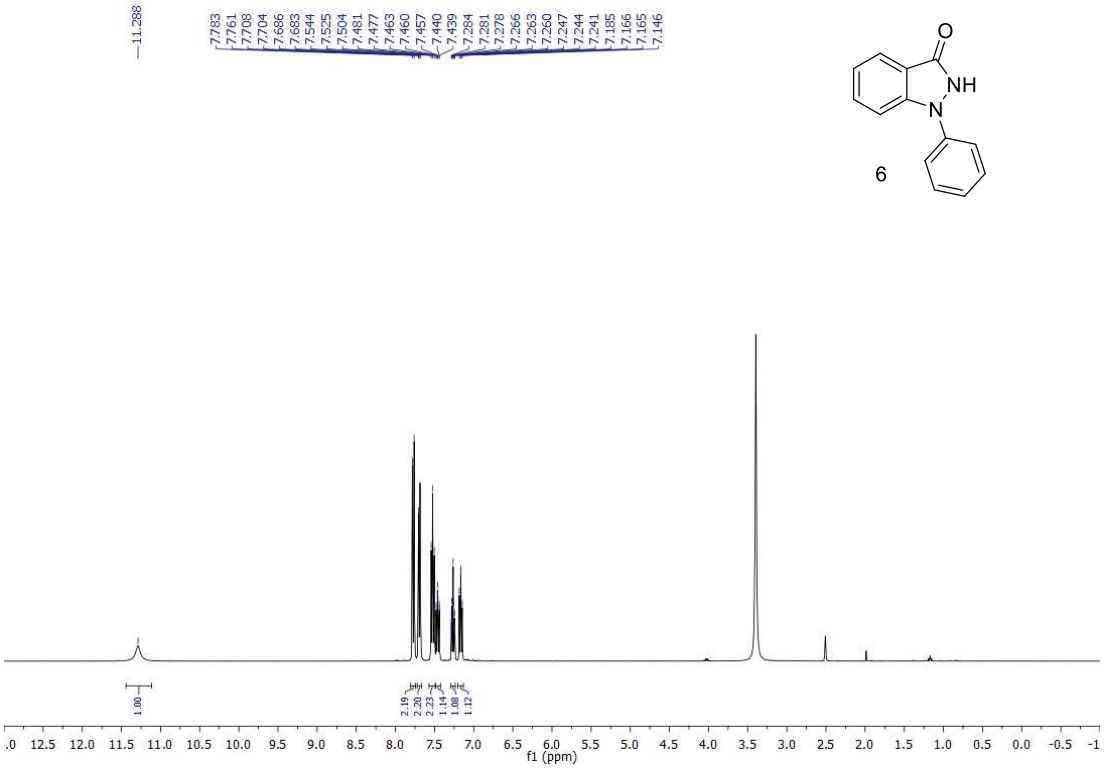
^{13}C NMR Spectrum of Compound 1d in DMSO-d_6



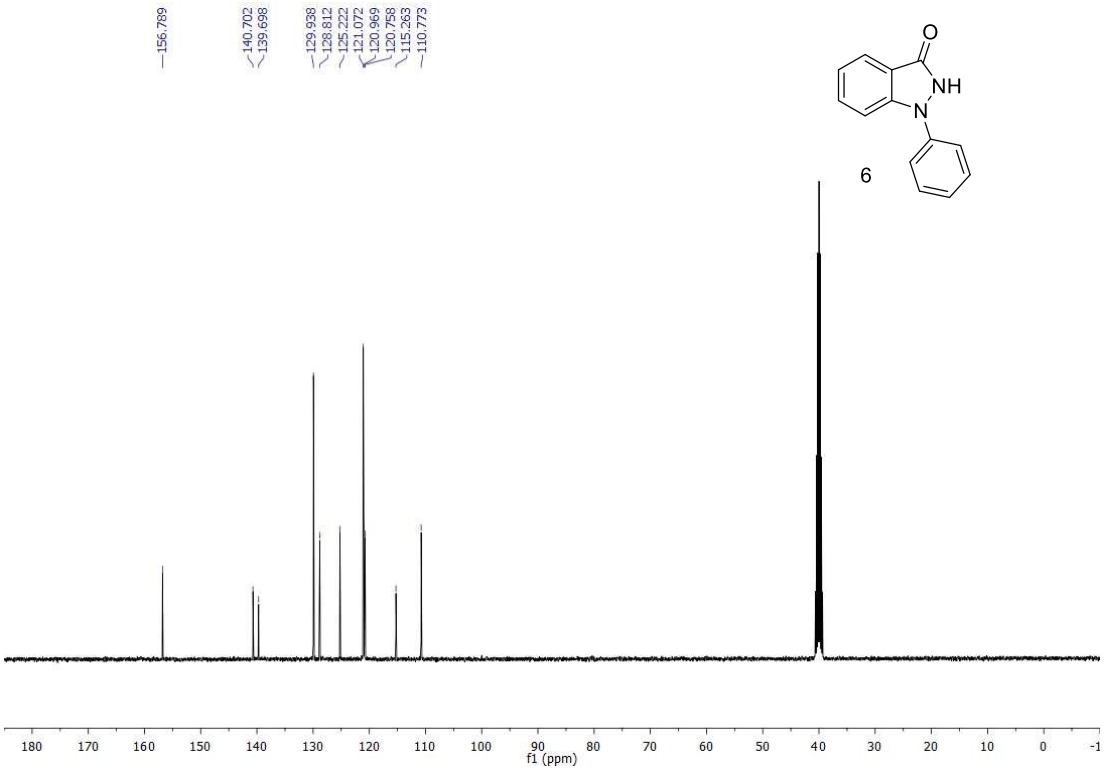
^{1}H NMR Spectrum of Compound 1e in $CDCl_3$-DMSO-d_6



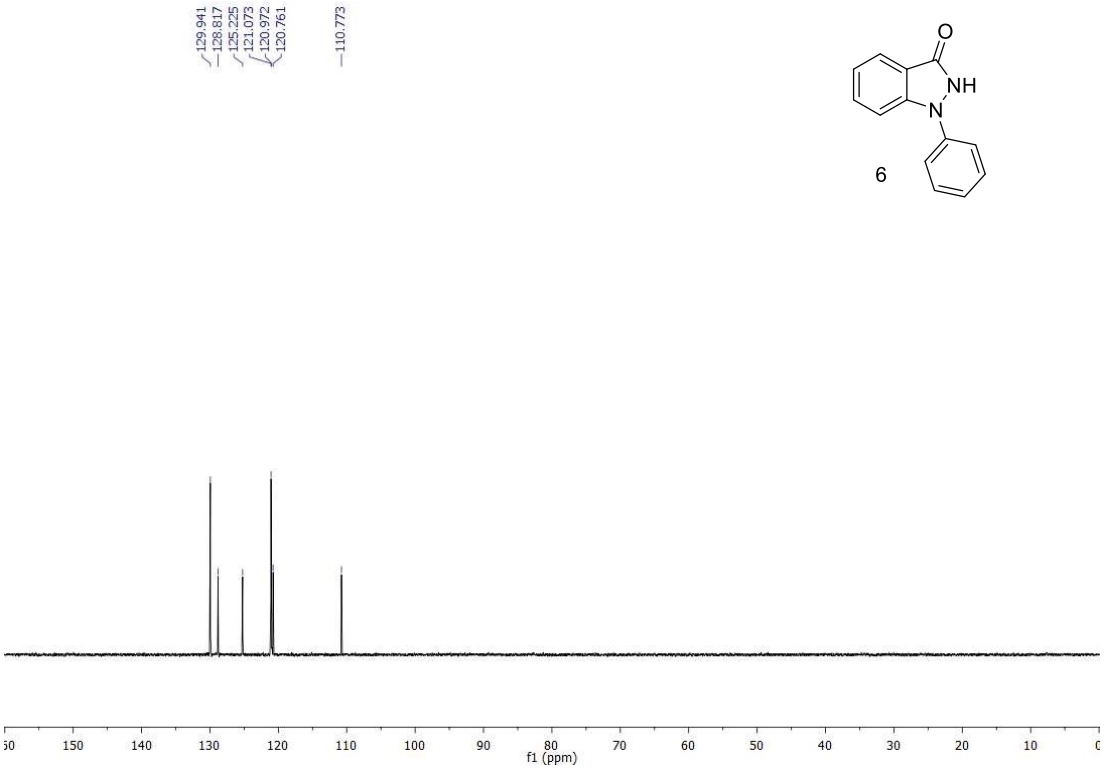
^{13}C NMR Spectrum of Compound 1e in $CDCl_3$-DMSO-d_6



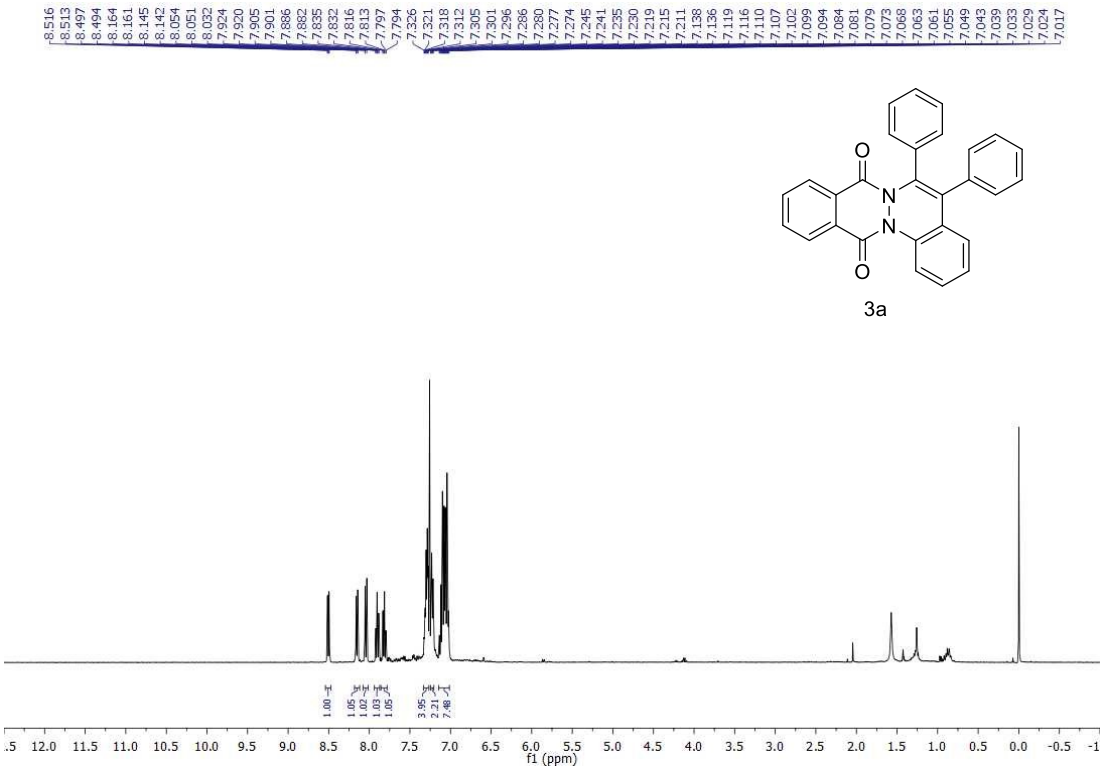
^{1}H NMR Spectrum of Compound 6 in DMSO-d_6



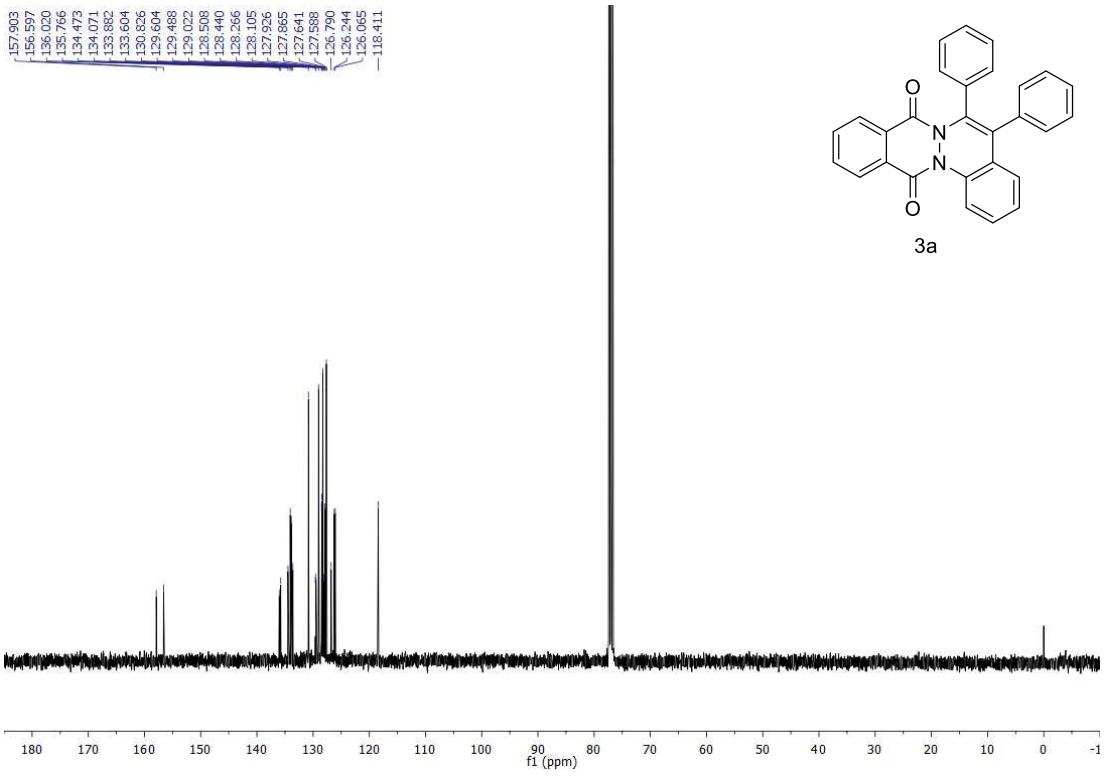
[13] C NMR Spectrum of Compound 6 in DMSO-d_6



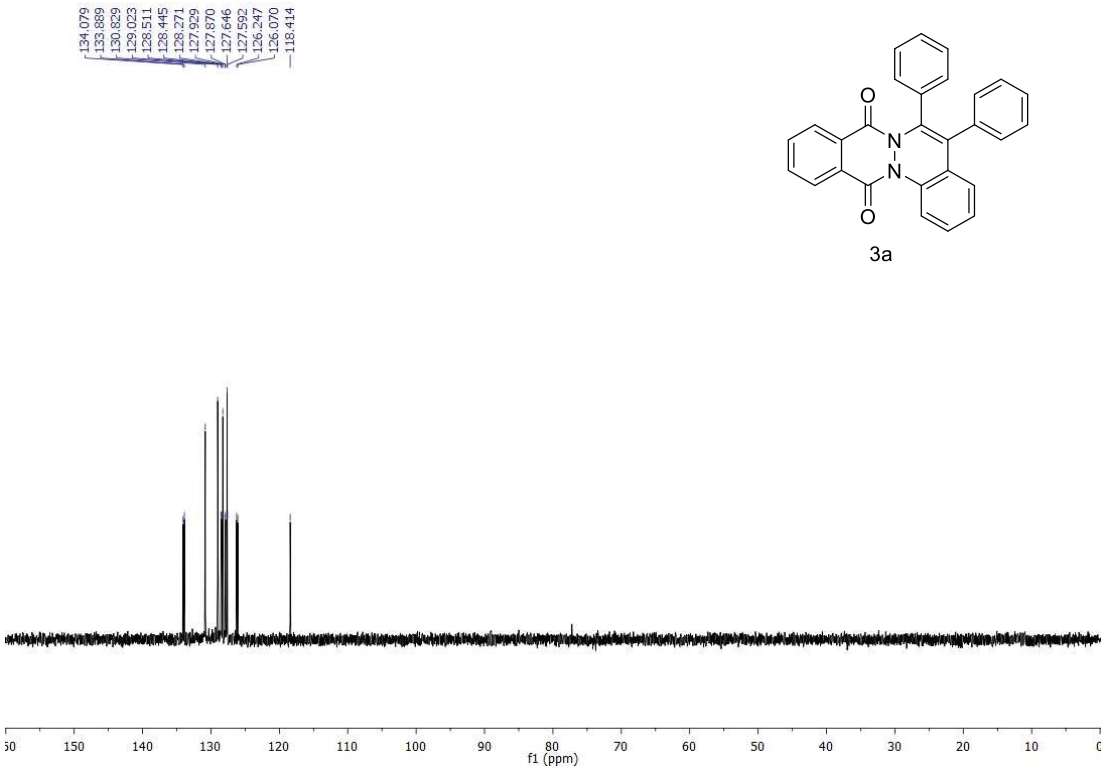
DEPT-135 NMR Spectrum of Compound 6 in DMSO-d_6



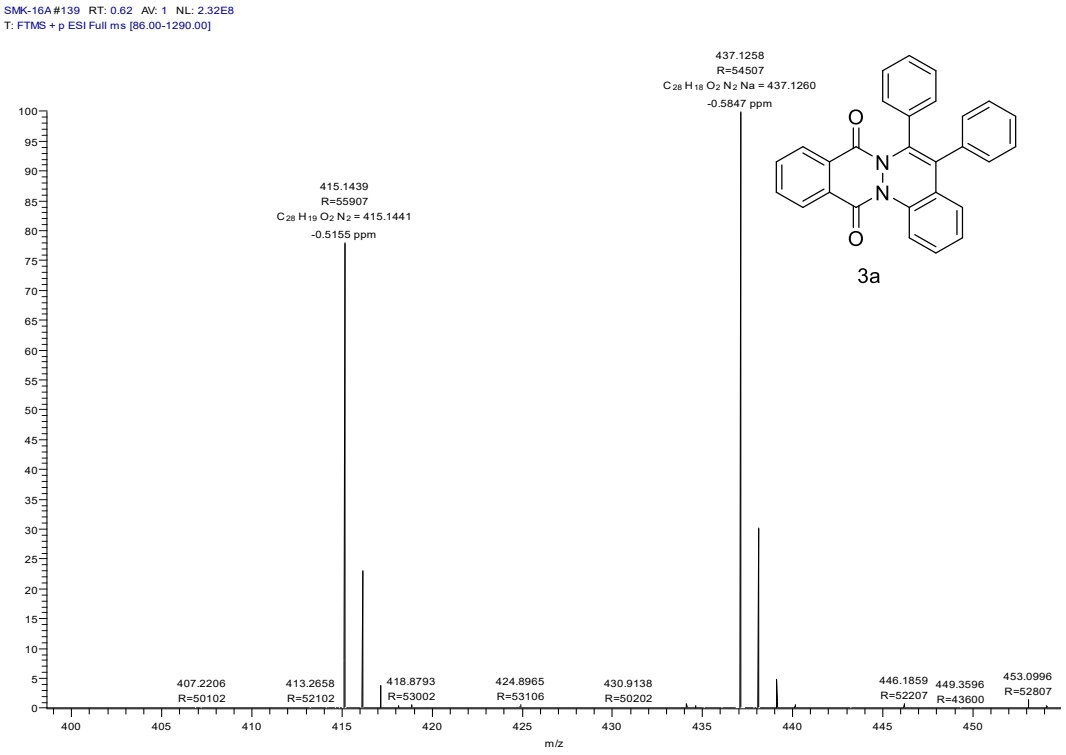
^{1}H NMR Spectrum of Compound 3a in $CDCl_3$



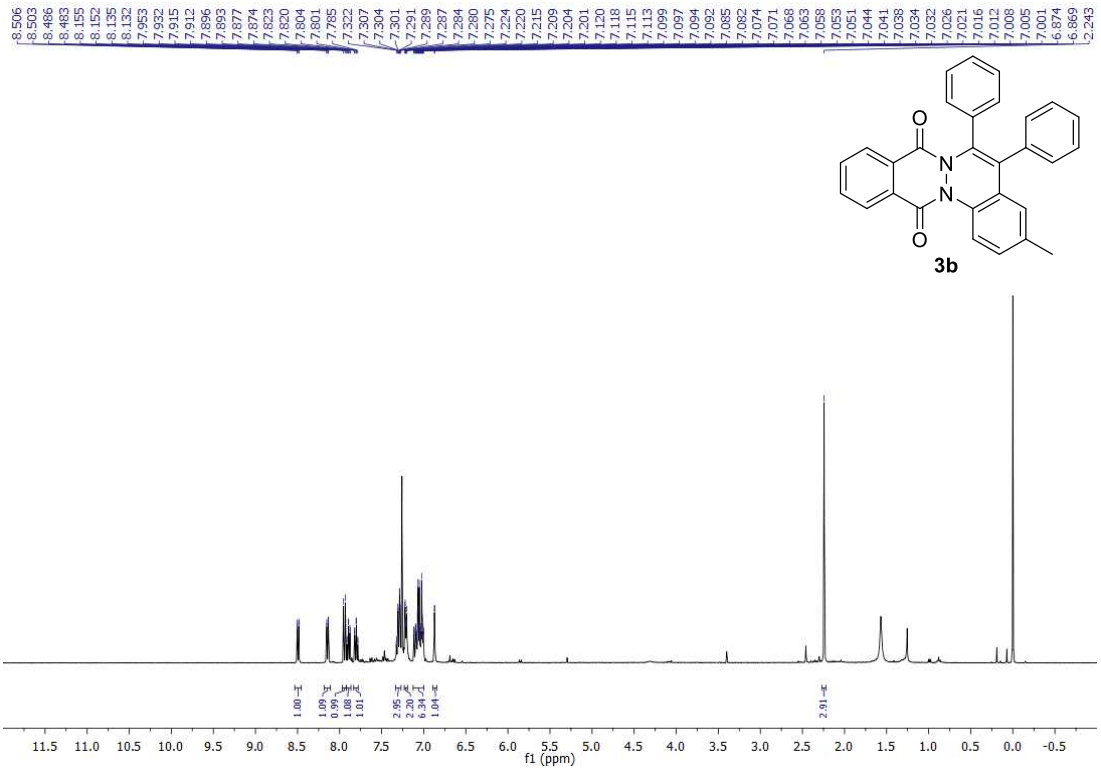
^{13}C NMR Spectrum of Compound 3a in $CDCl_3$



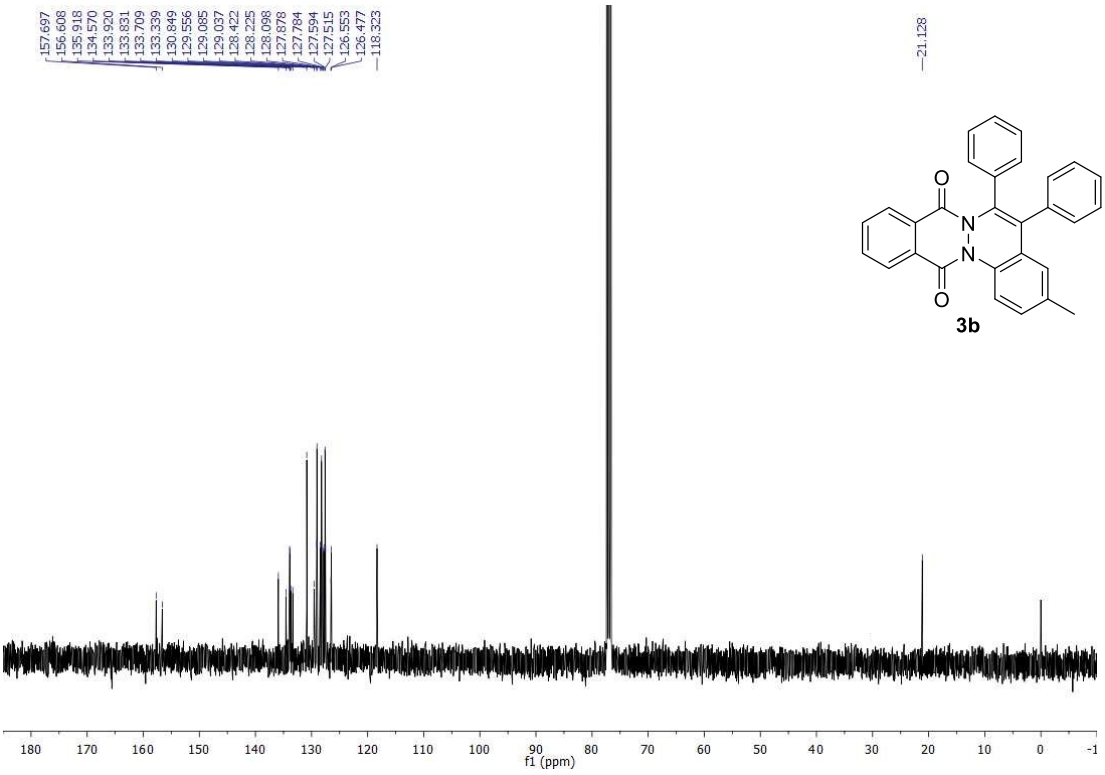
DEPT-135 NMR Spectrum of Compound 3a in $CDCl_3$



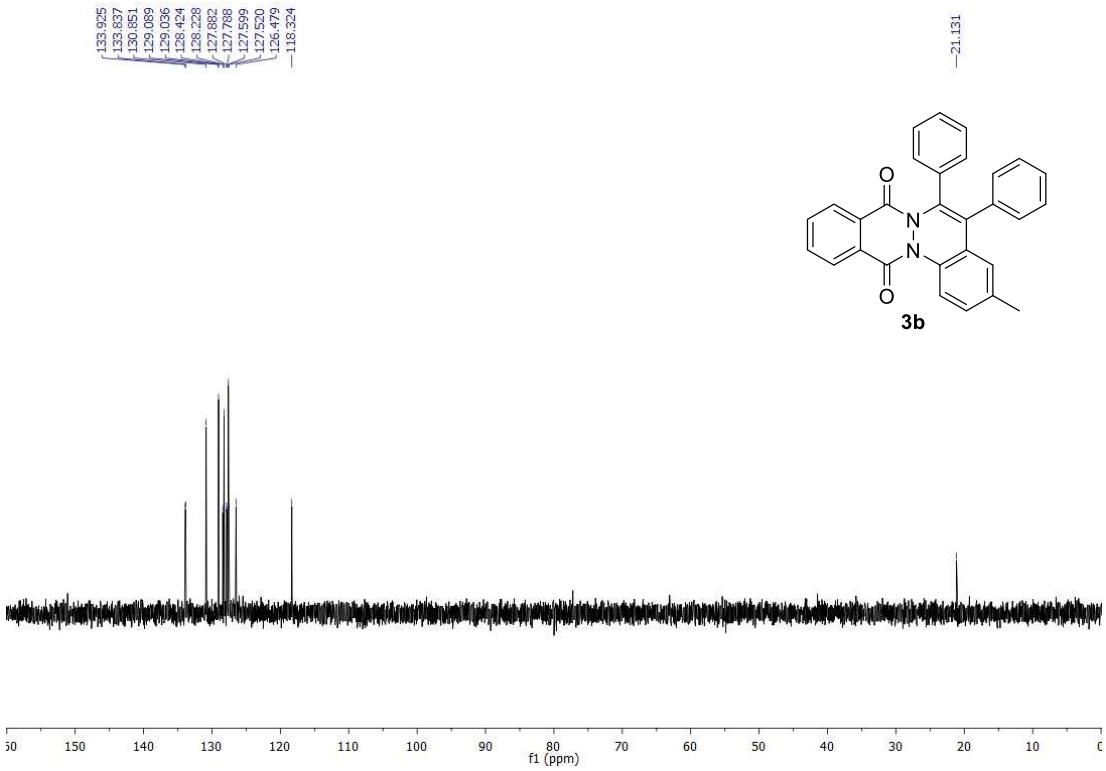
HRMS Spectrum of Compound 3a



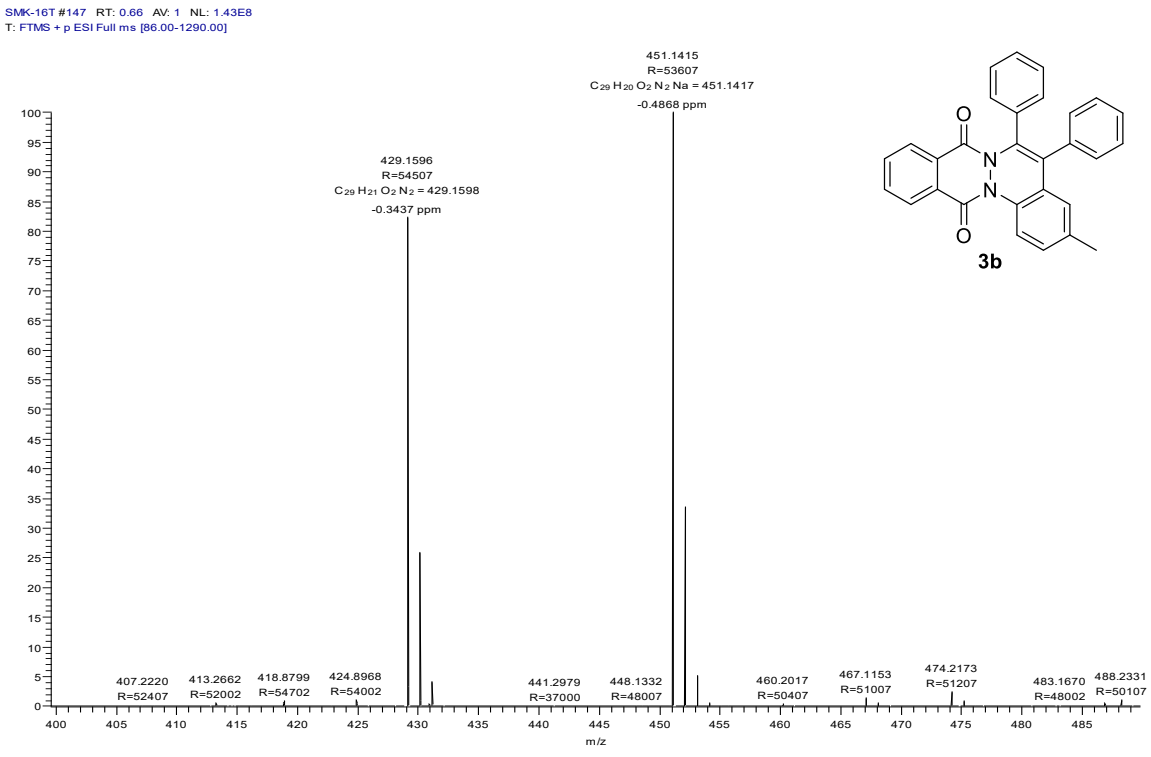
^{1}H NMR Spectrum of Compound 3p in $CDCl_3$



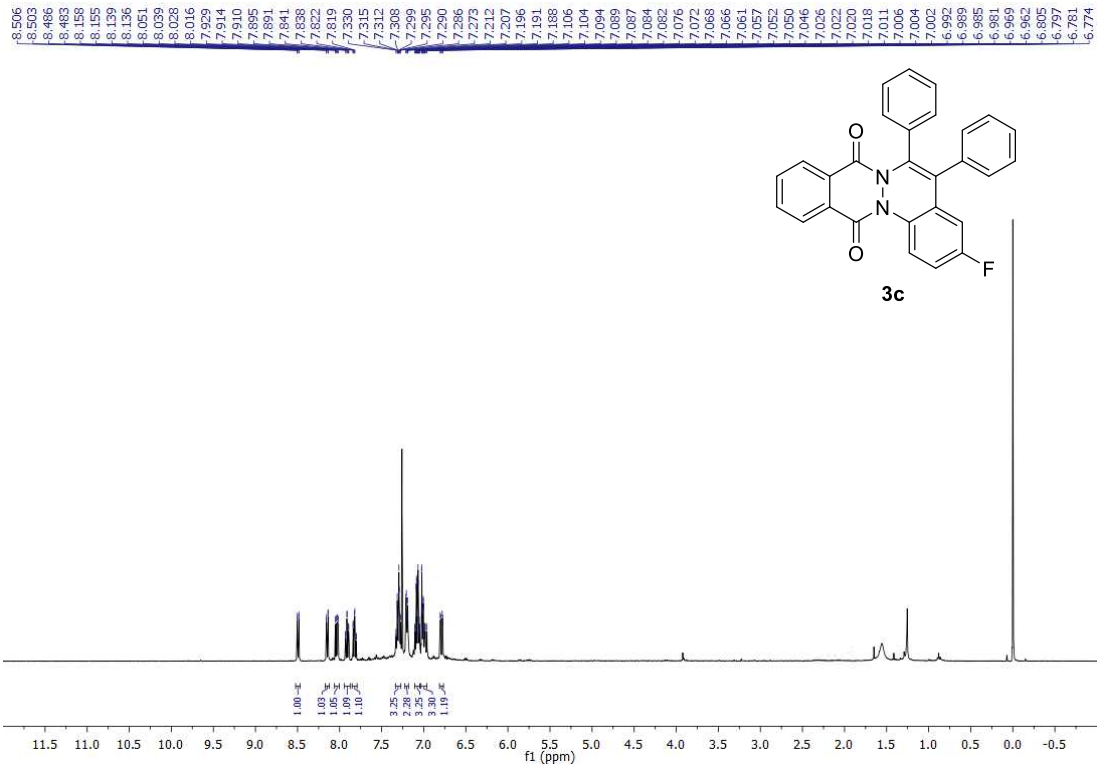
^{13}C NMR Spectrum of Compound 3p in $CDCl_3$



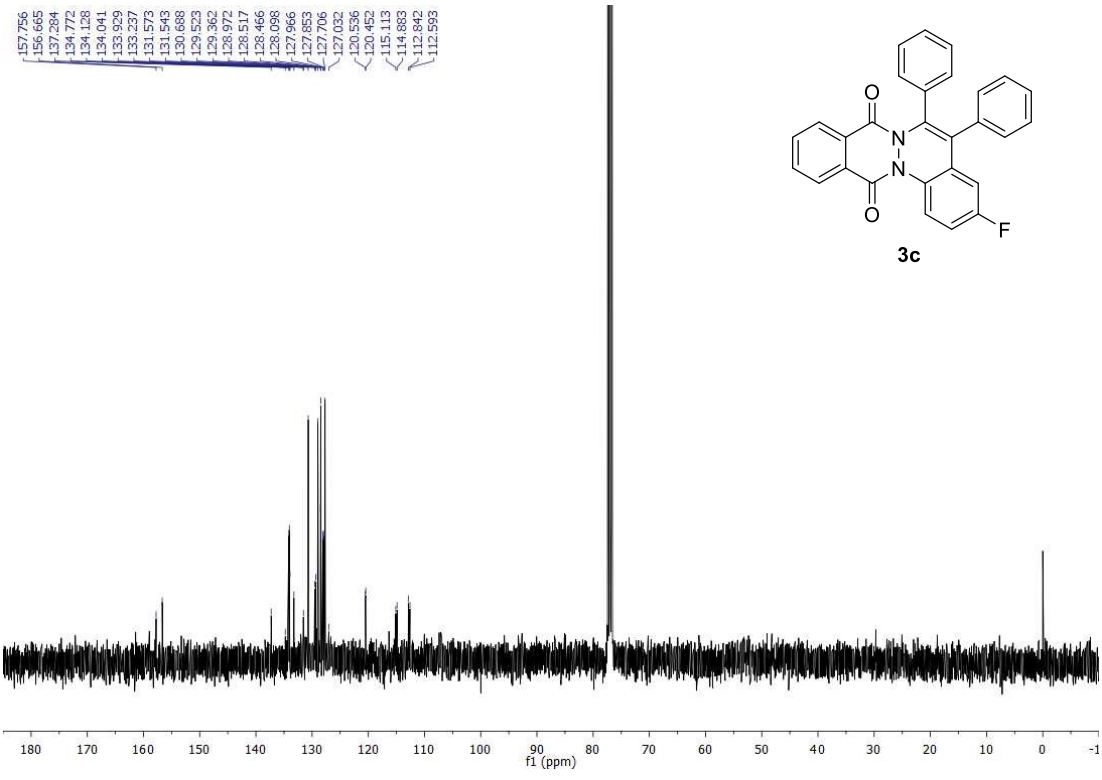
DEPT-135 NMR Spectrum of Compound 3p in $CDCl_3$



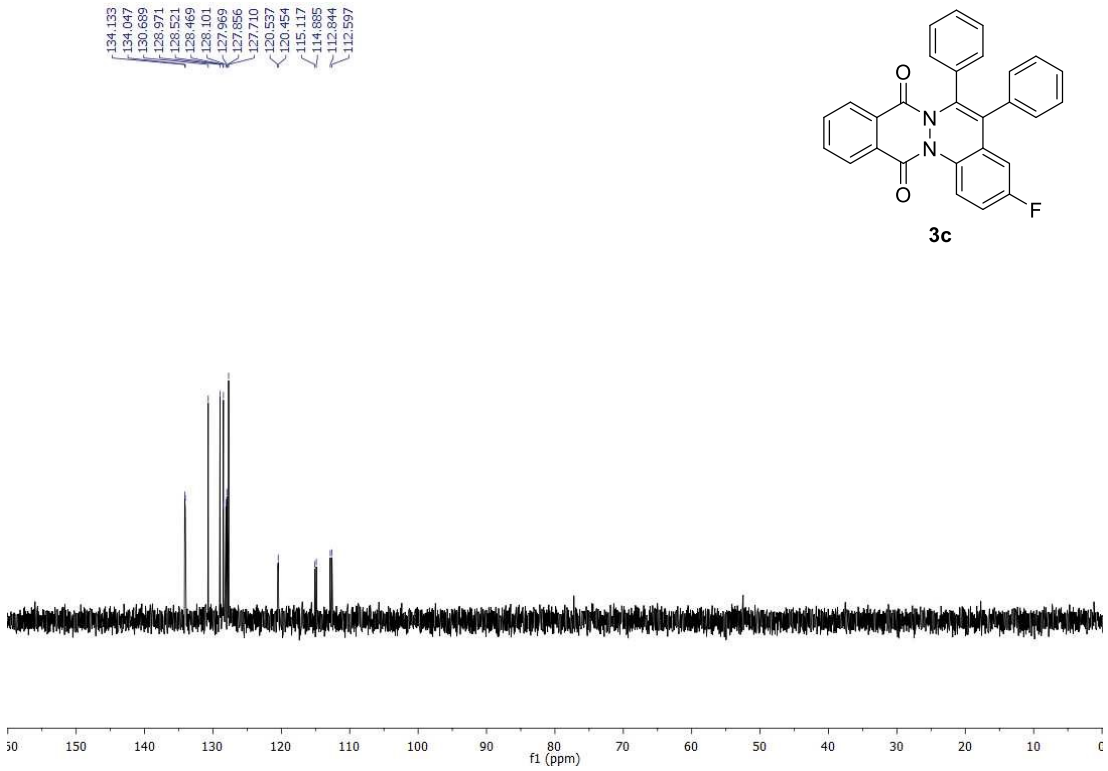
HRMS Spectrum of Compound 3b



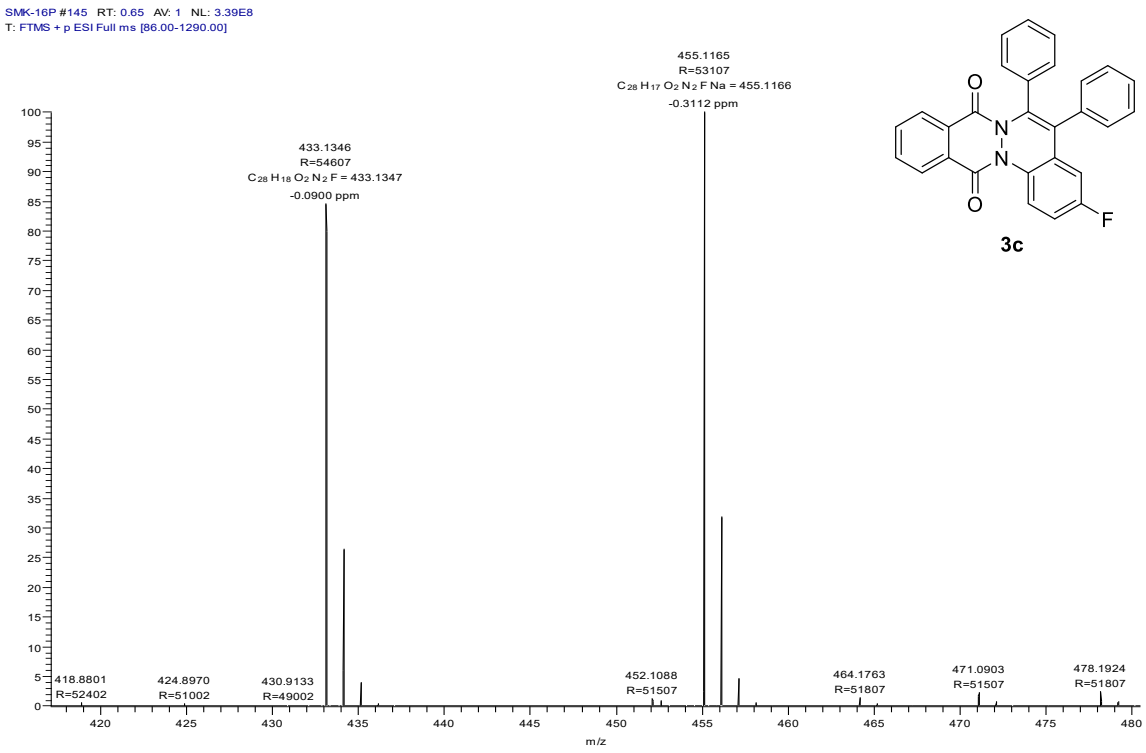
^{1}H NMR Spectrum of Compound 3c in $CDCl_3$



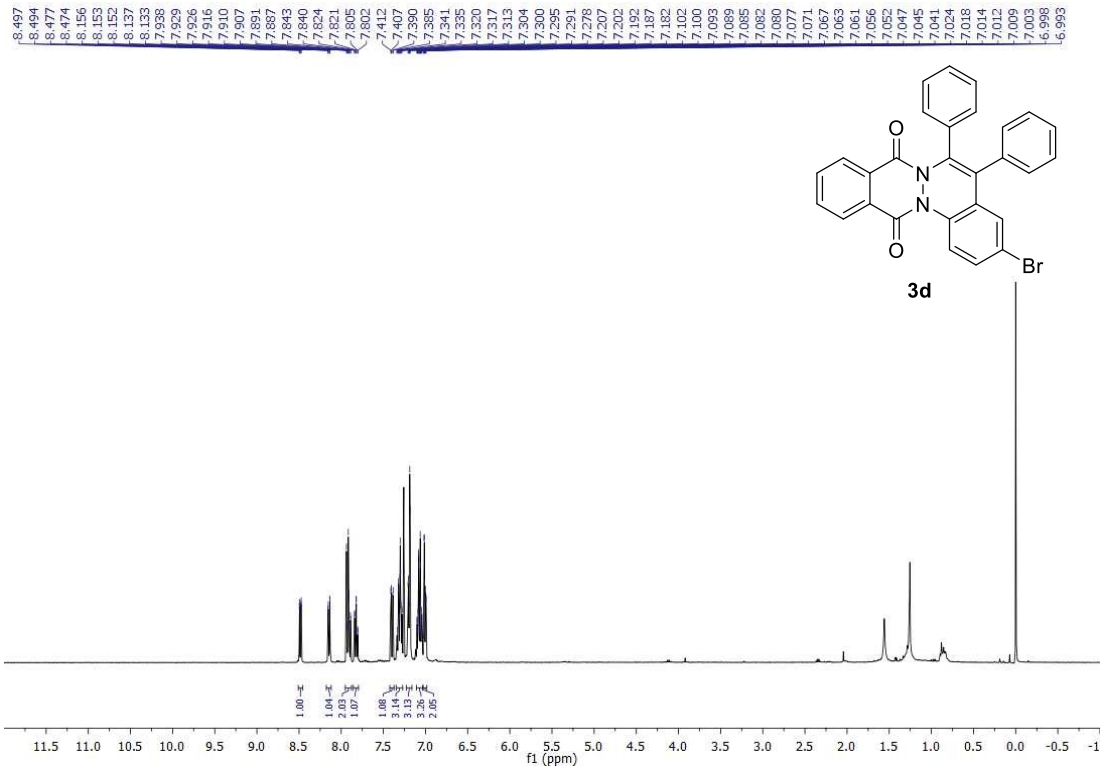
^{13}C NMR Spectrum of Compound 3c in $CDCl_3$



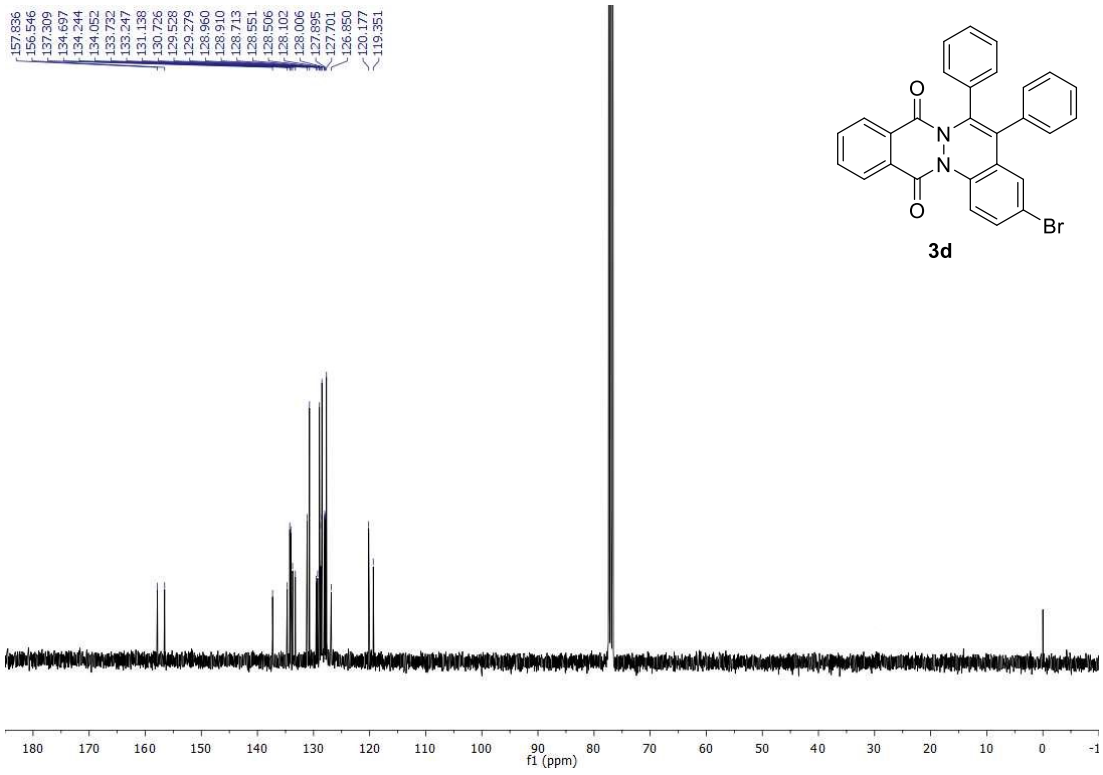
DEPT-135 NMR Spectrum of Compound 3c in $CDCl_3$



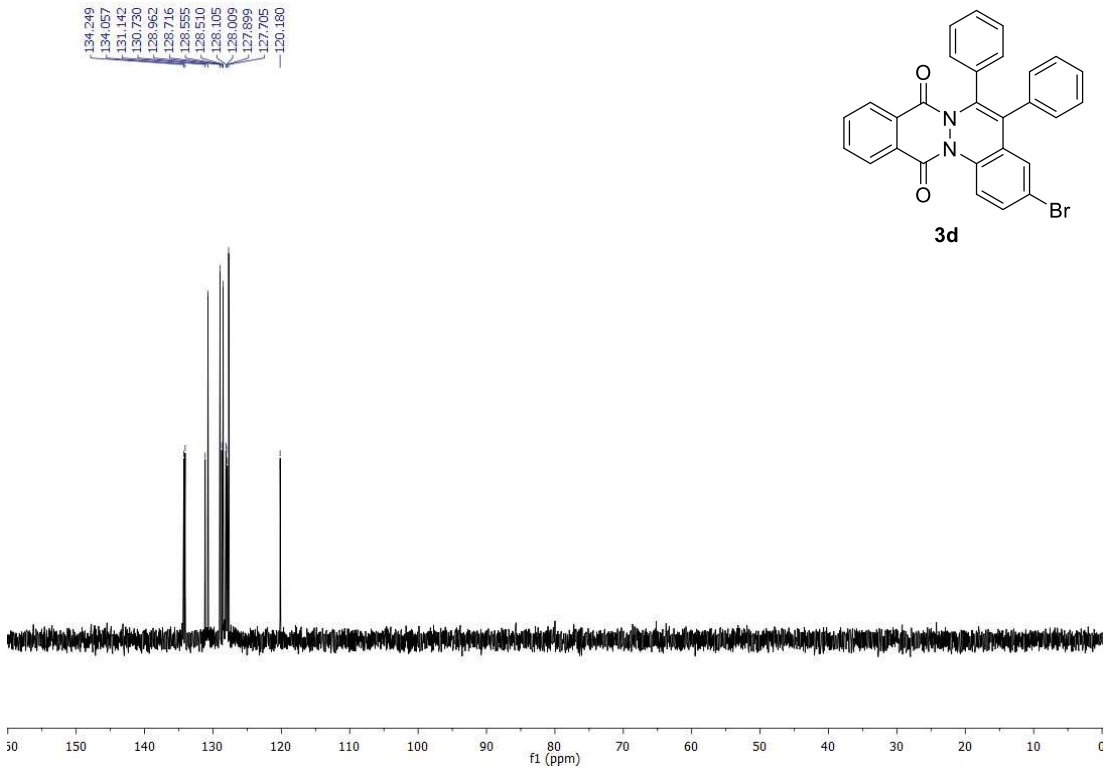
HRMS Spectrum of Compound 3c



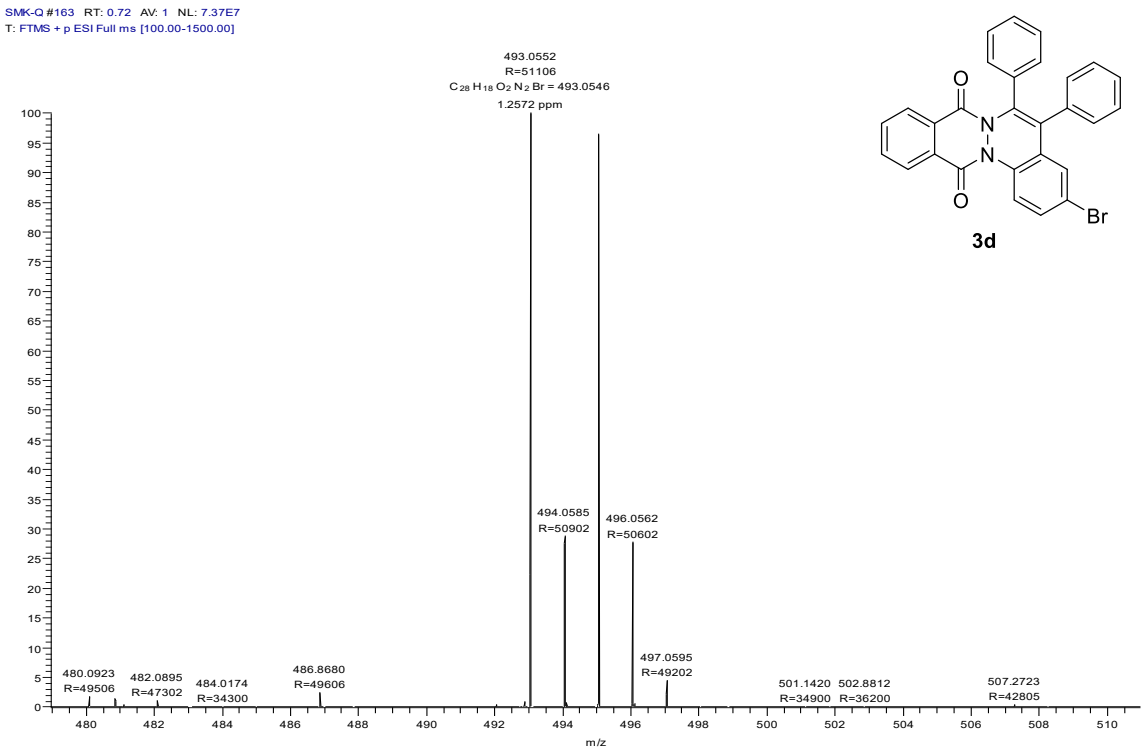
^{1}H NMR Spectrum of Compound 3d in $CDCl_3$



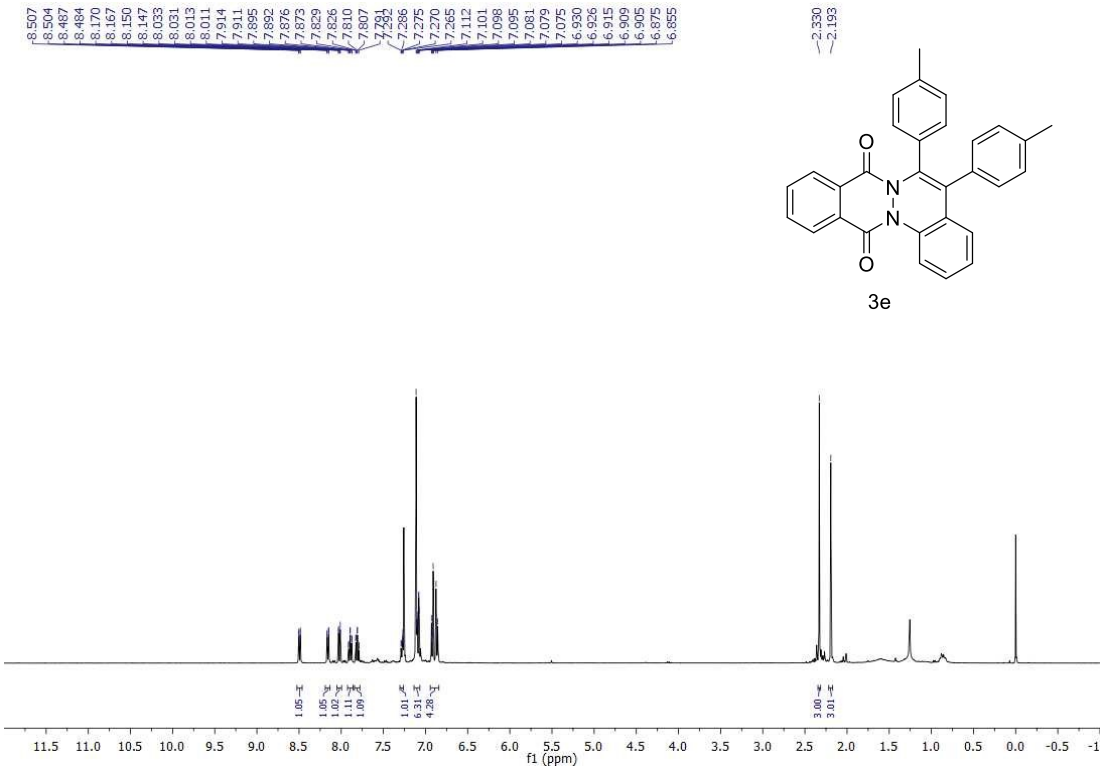
^{13}C NMR Spectrum of Compound 3d in $CDCl_3$



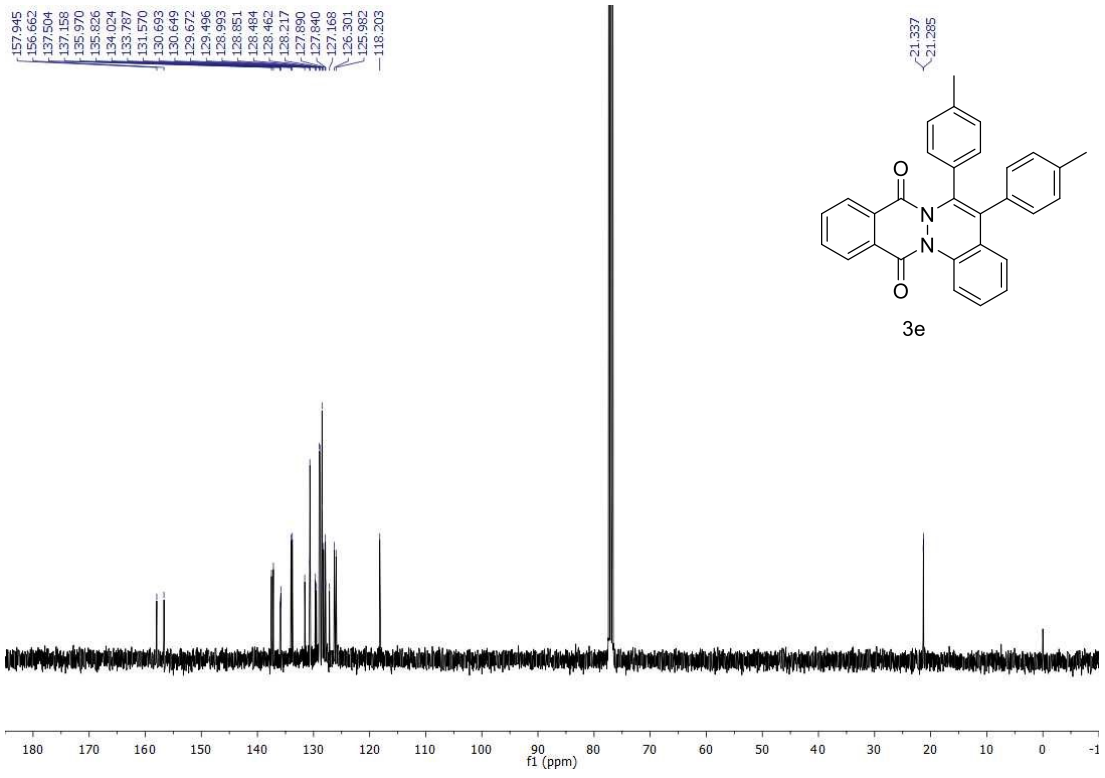
DEPT-135 NMR Spectrum of Compound 3d in $CDCl_3$



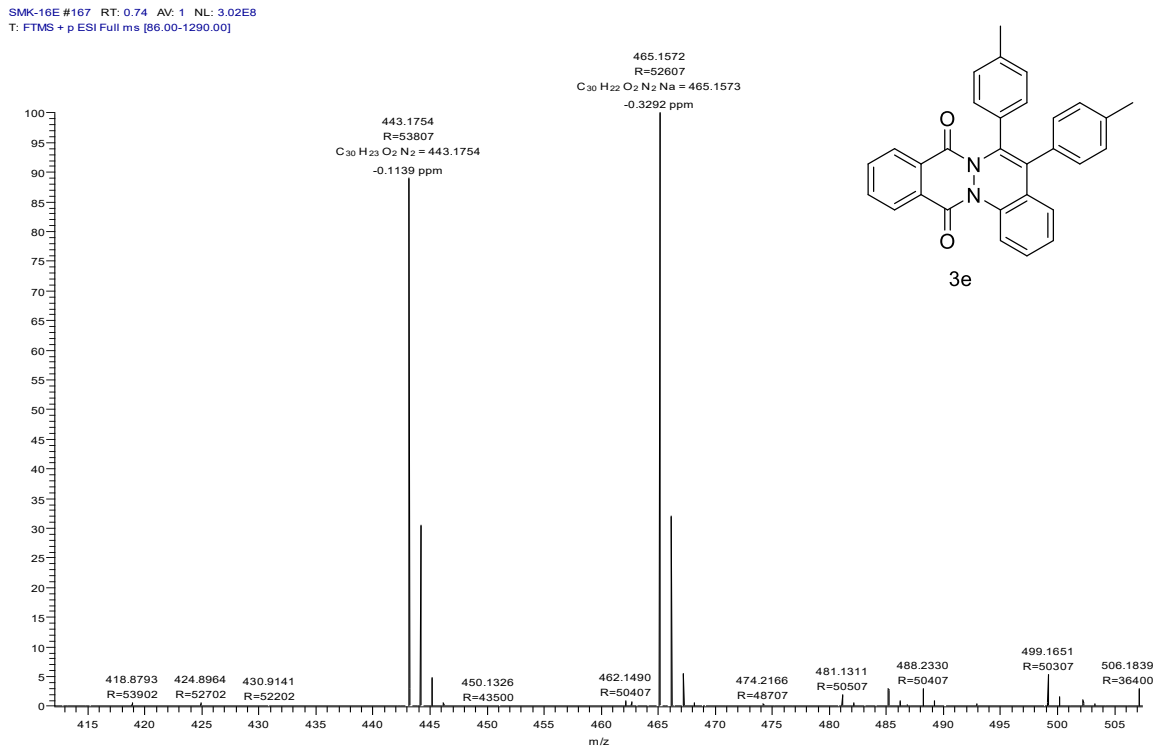
HRMS Spectrum of Compound 3d



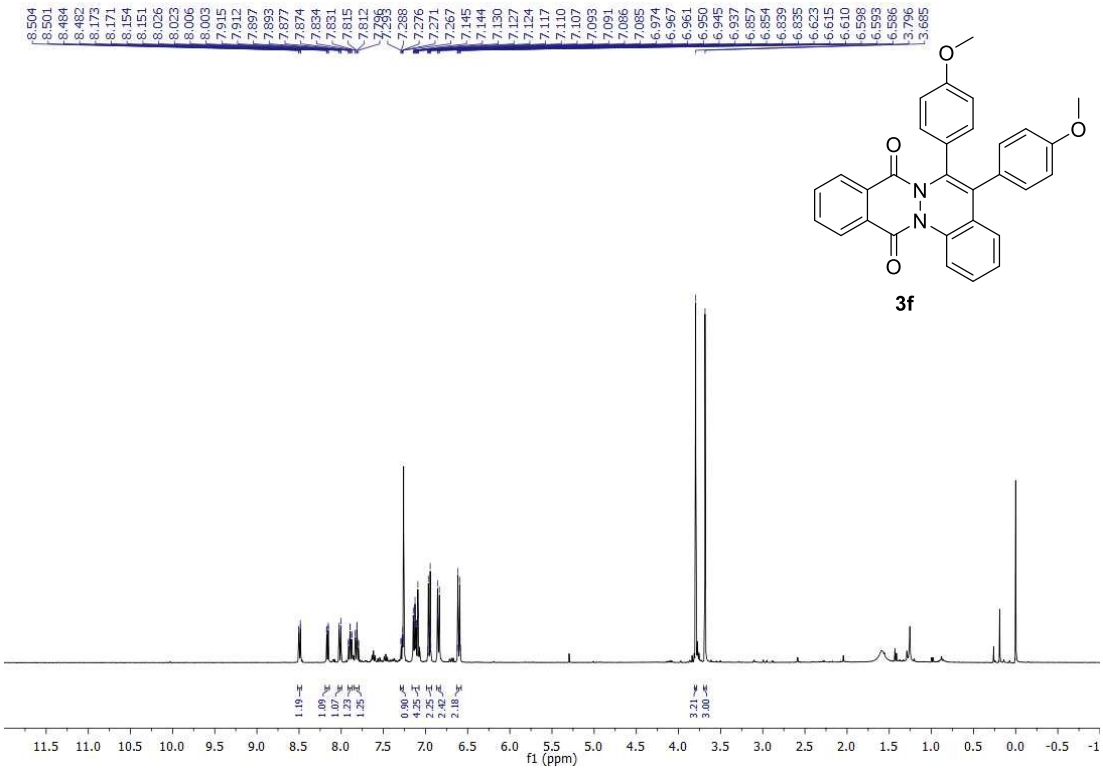
^{1}H NMR Spectrum of Compound 3e in $CDCl_3$



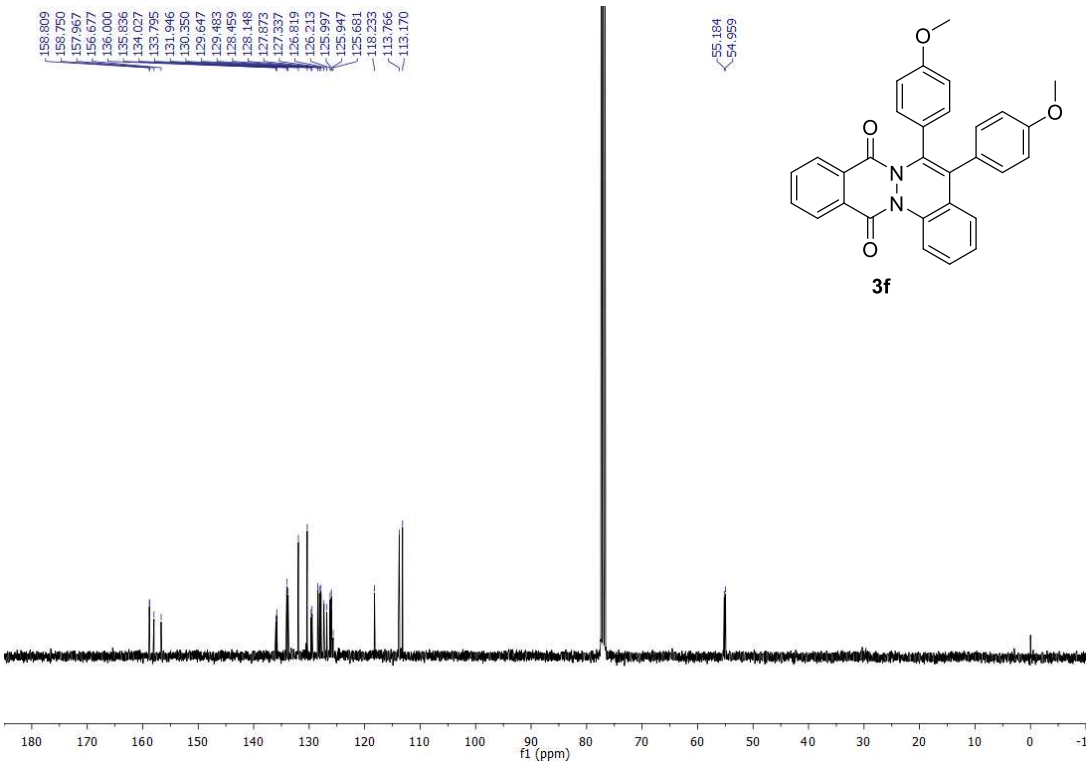
^{13}C NMR Spectrum of Compound 3e in $CDCl_3$



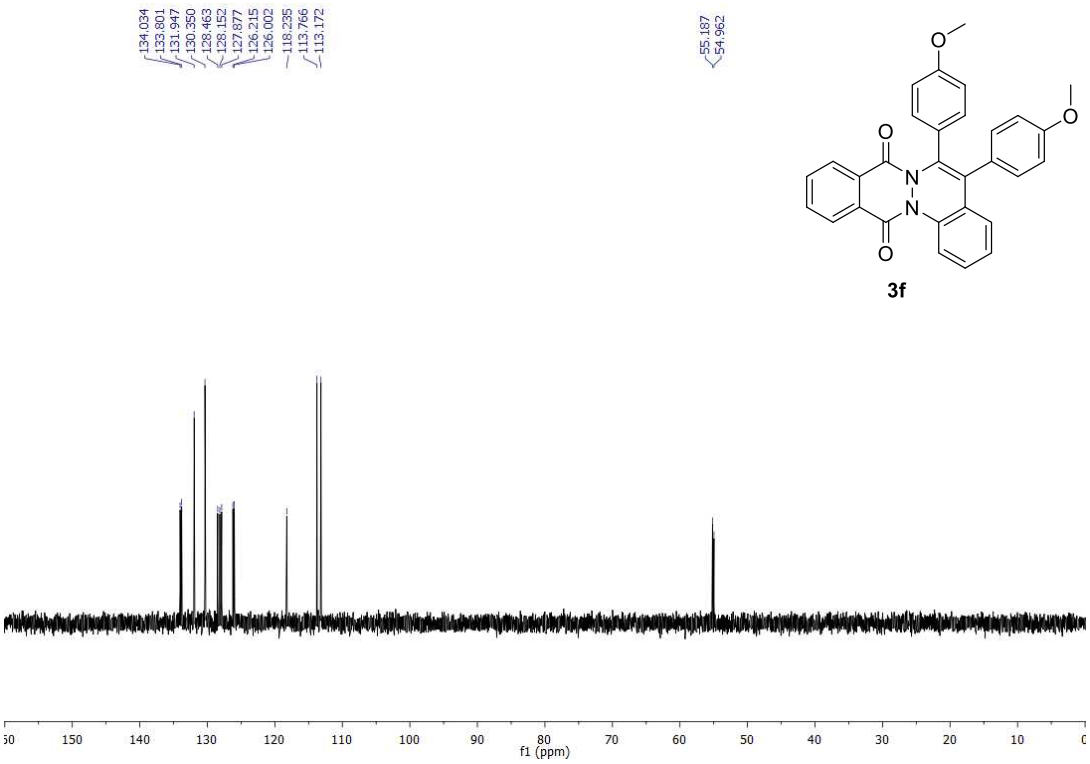
HRMS Spectrum of Compound 3e



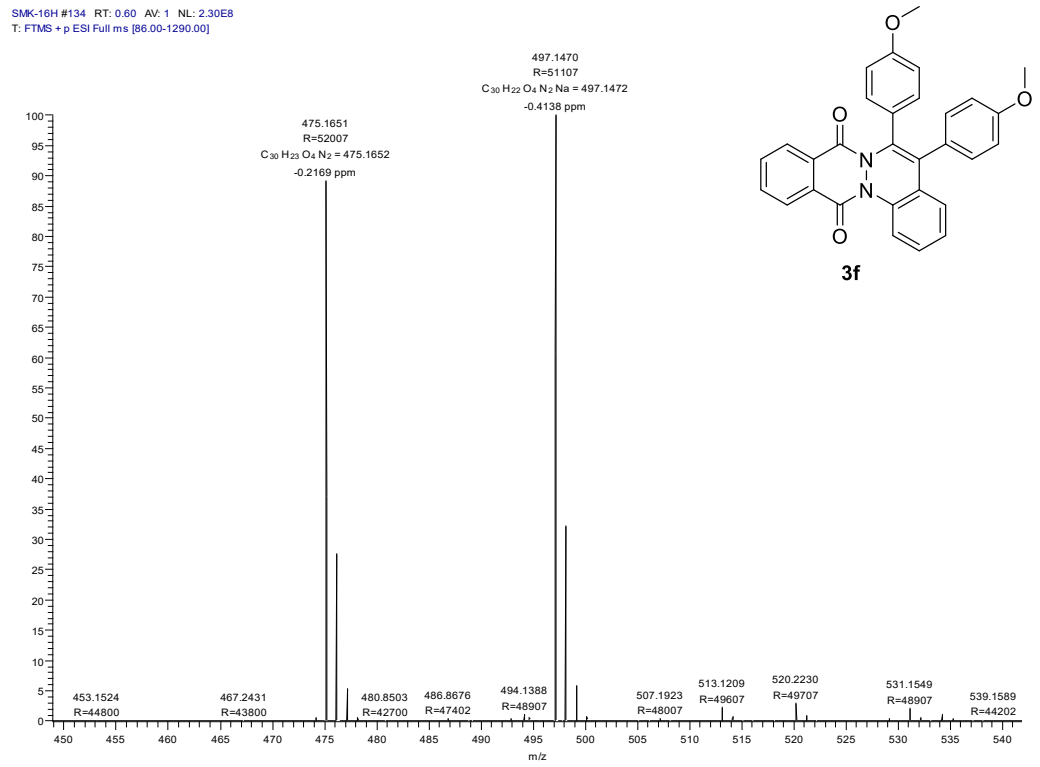
^{1}H NMR Spectrum of Compound 3f in $CDCl_3$



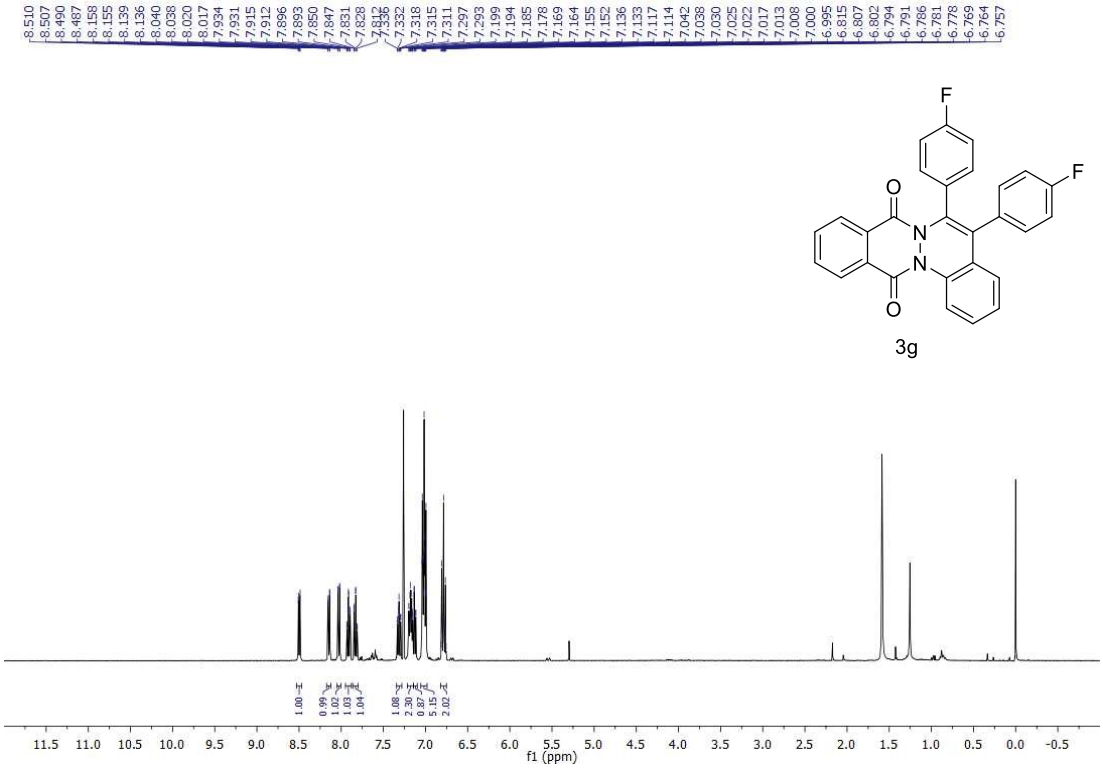
^{13}C NMR Spectrum of Compound 3f in $CDCl_3$



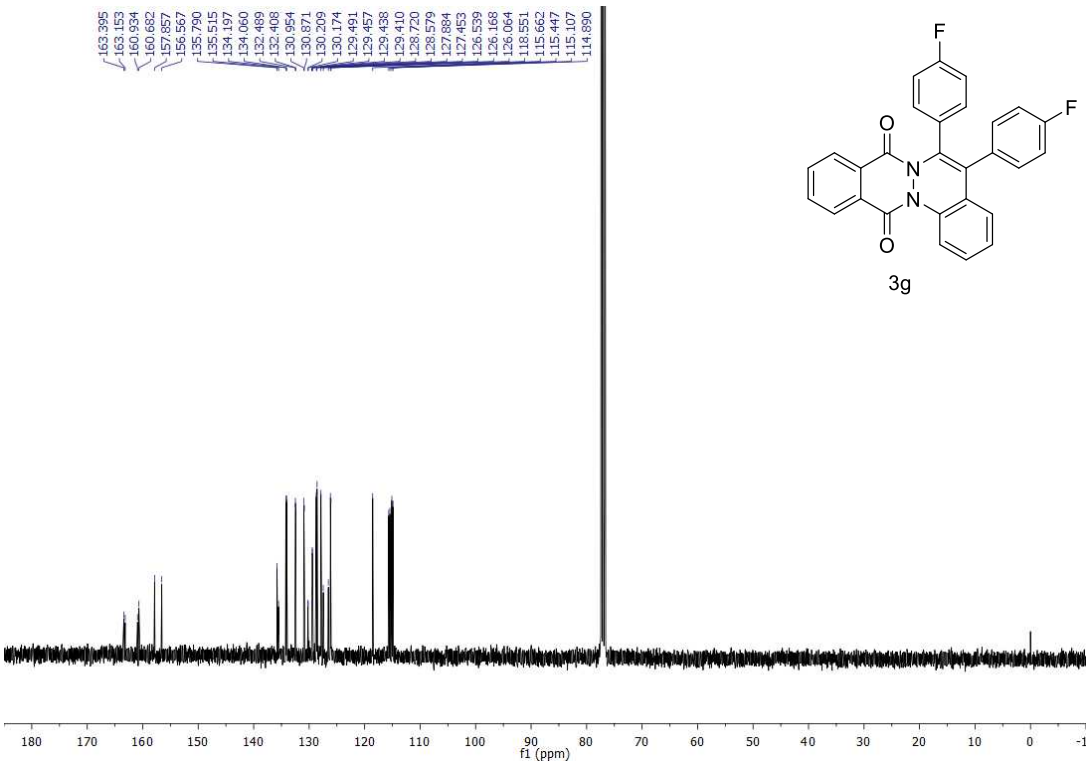
DEPT-135 NMR Spectrum of Compound 3f in $CDCl_3$



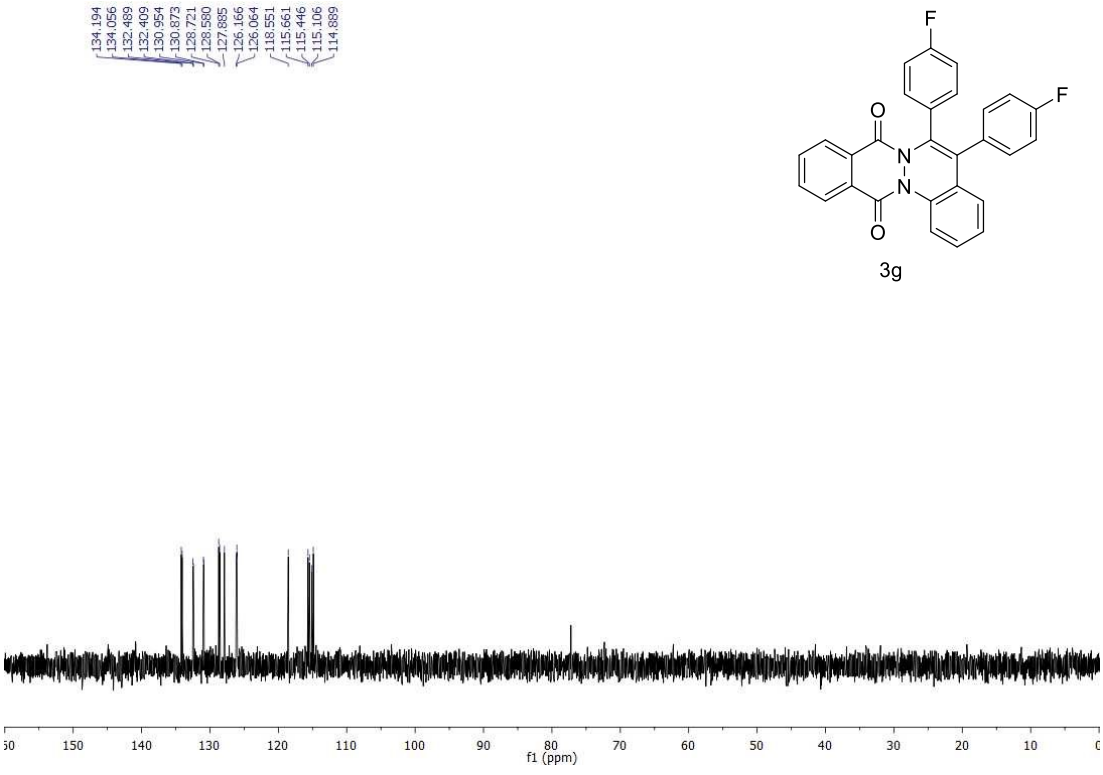
HRMS Spectrum of Compound 3f



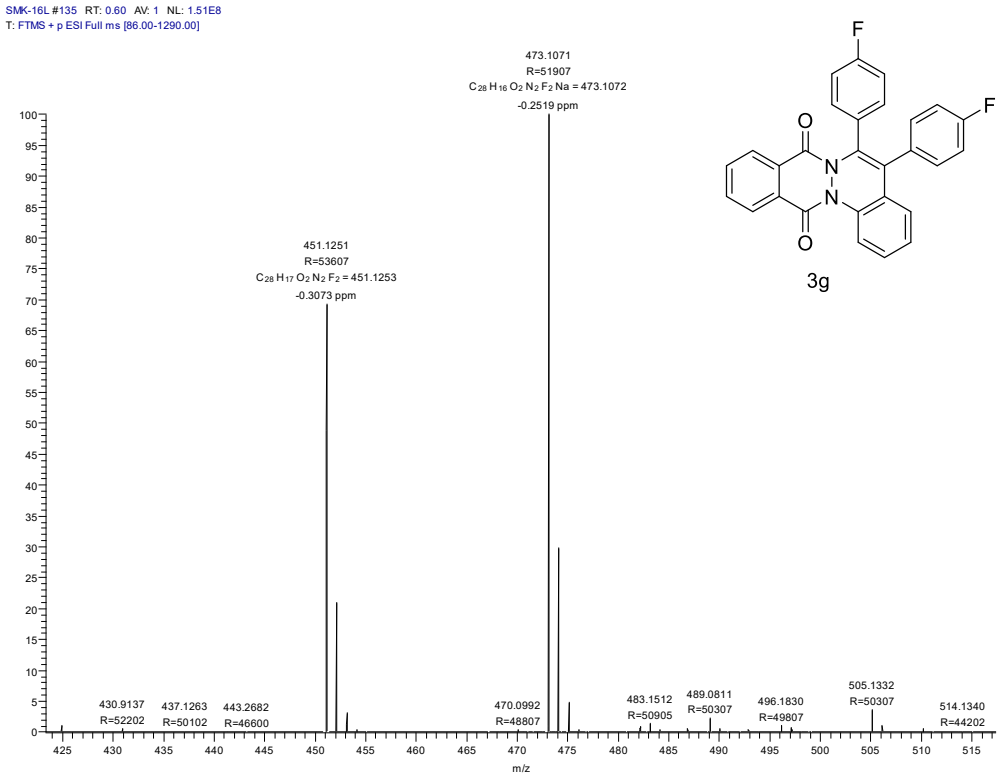
^{1}H NMR Spectrum of Compound 3g in $CDCl_3$



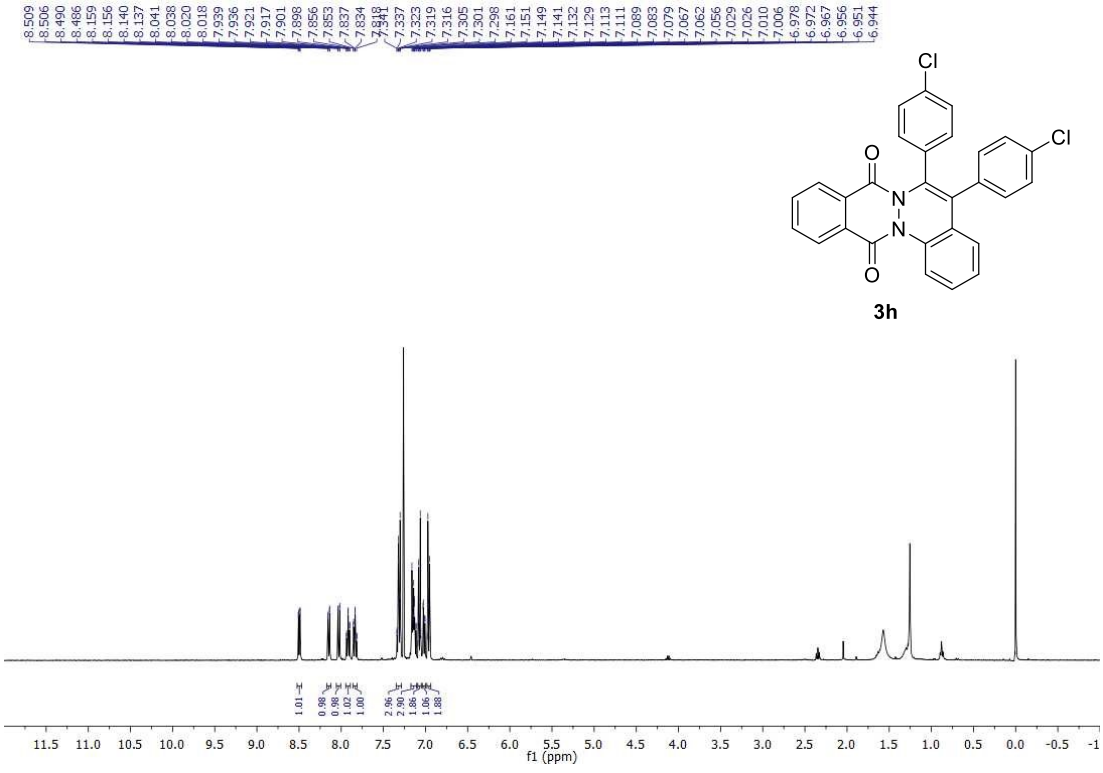
^{13}C NMR Spectrum of Compound 3g in $CDCl_3$



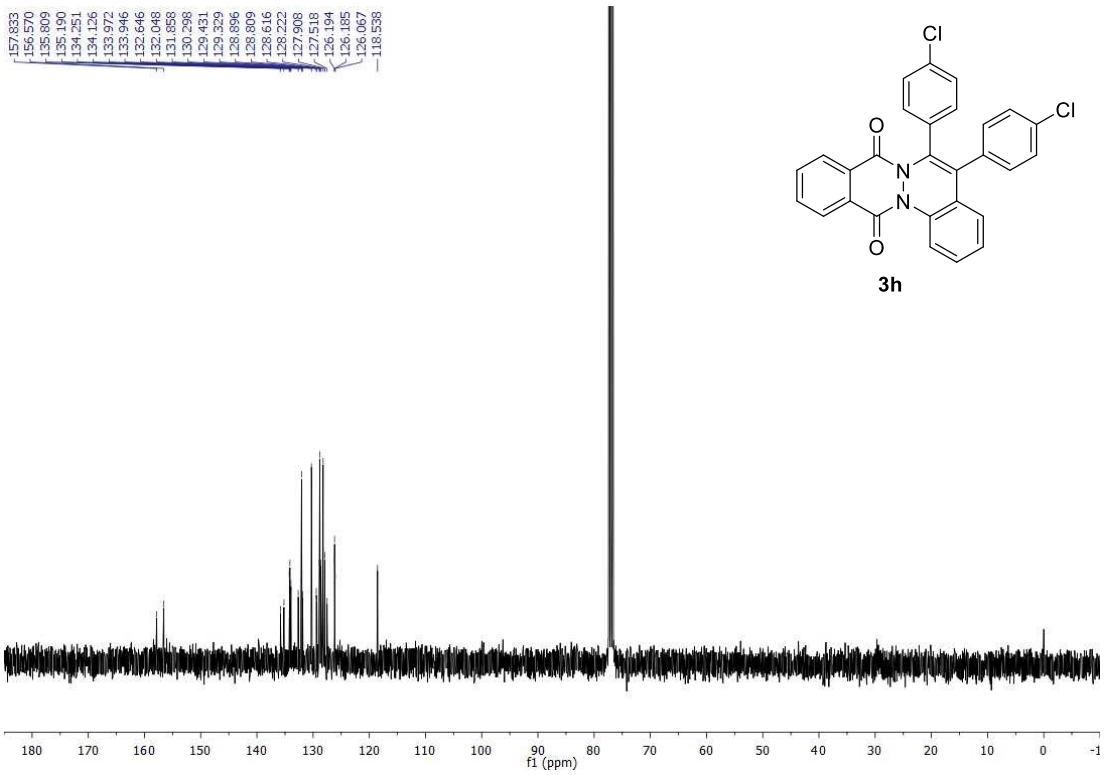
DEPT-135 NMR Spectrum of Compound 3g in $CDCl_3$



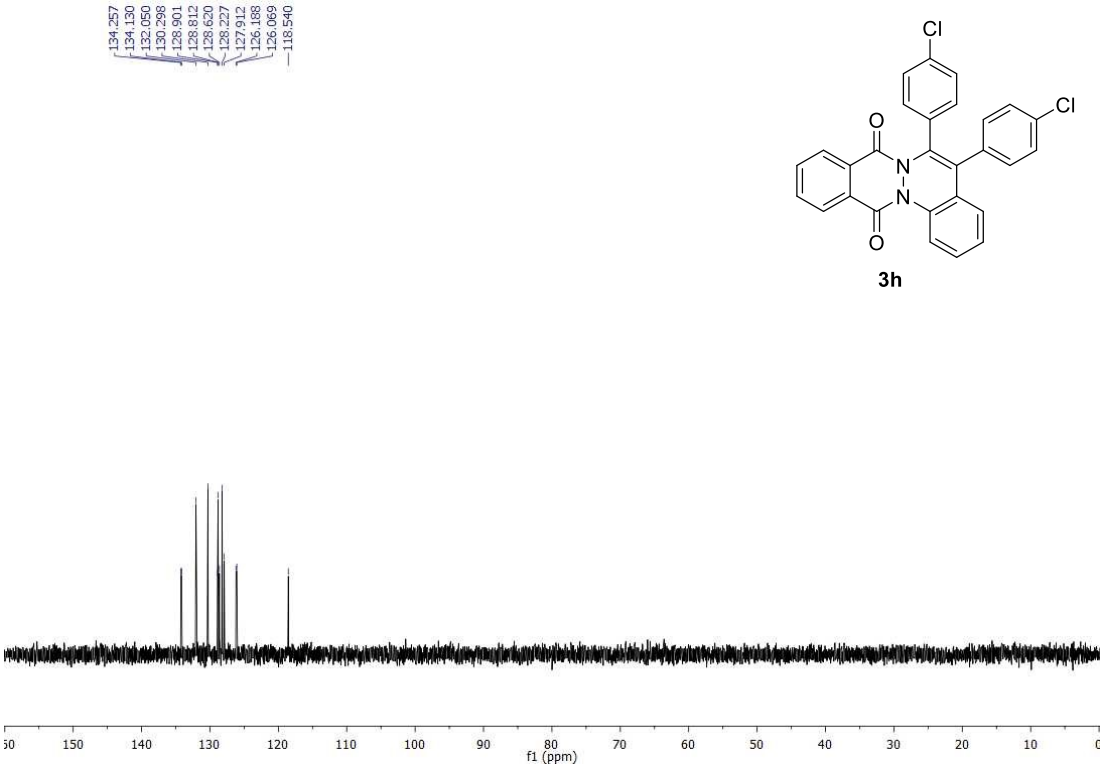
HRMS Spectrum of Compound 3g



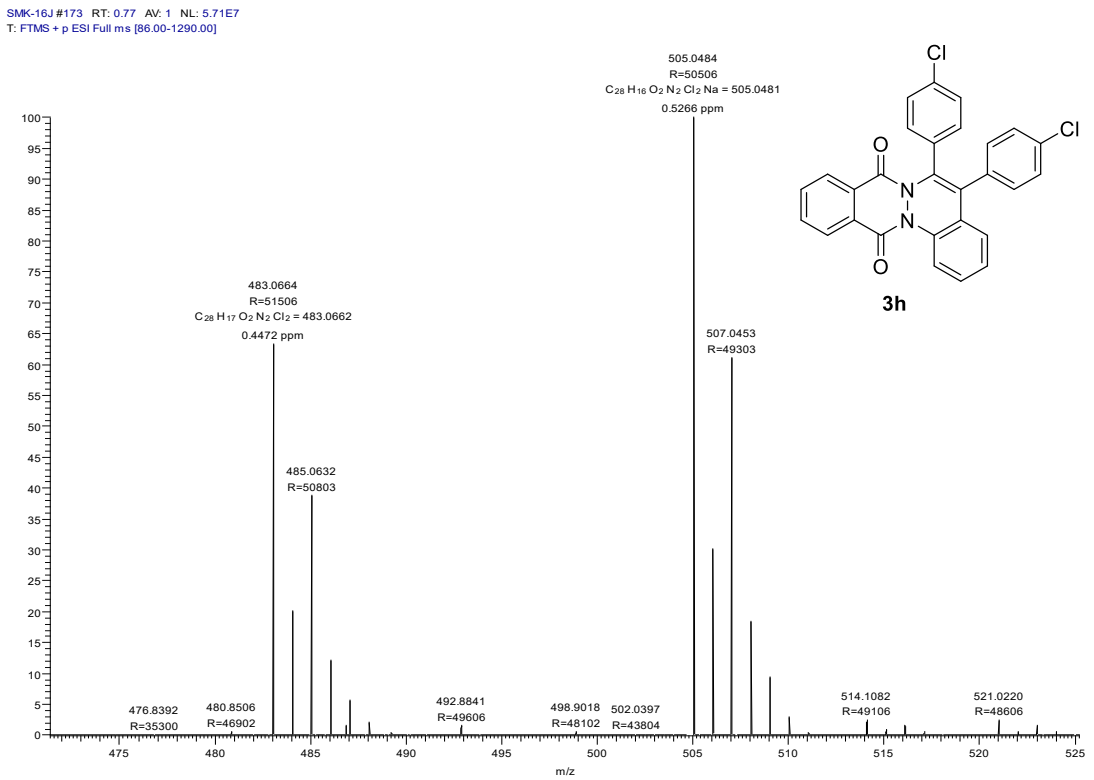
^{1}H NMR Spectrum of Compound 3h in $CDCl_3$



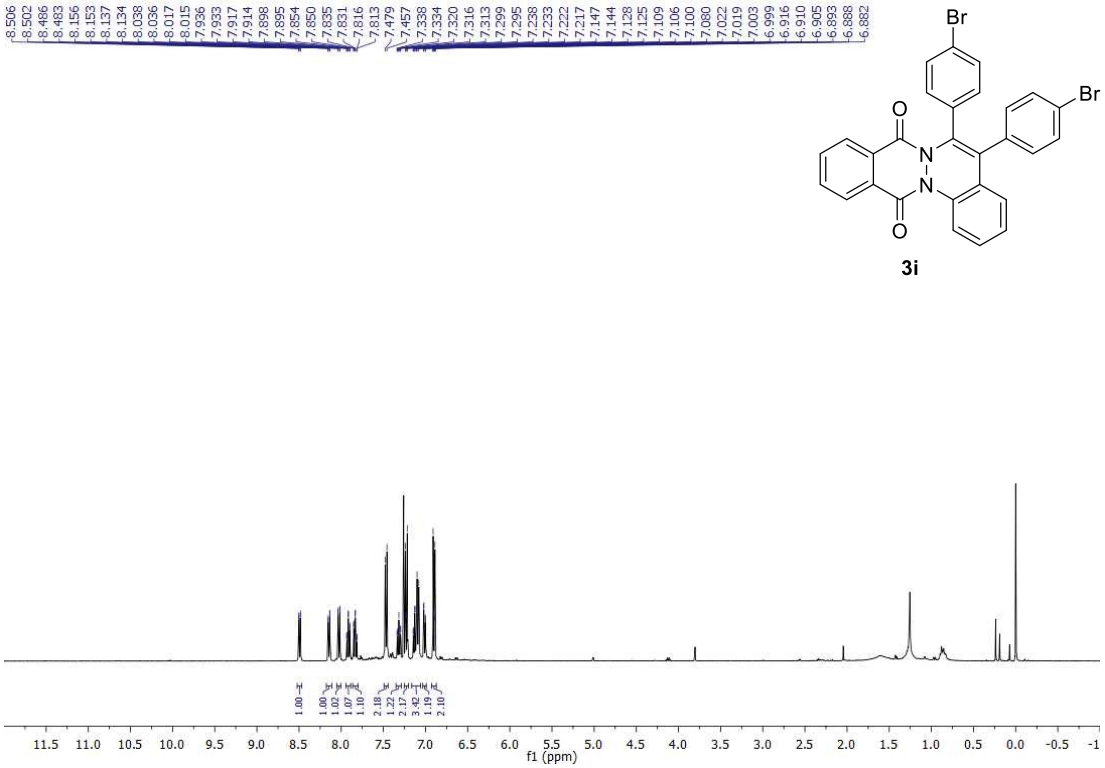
^{13}C NMR Spectrum of Compound 3h in $CDCl_3$



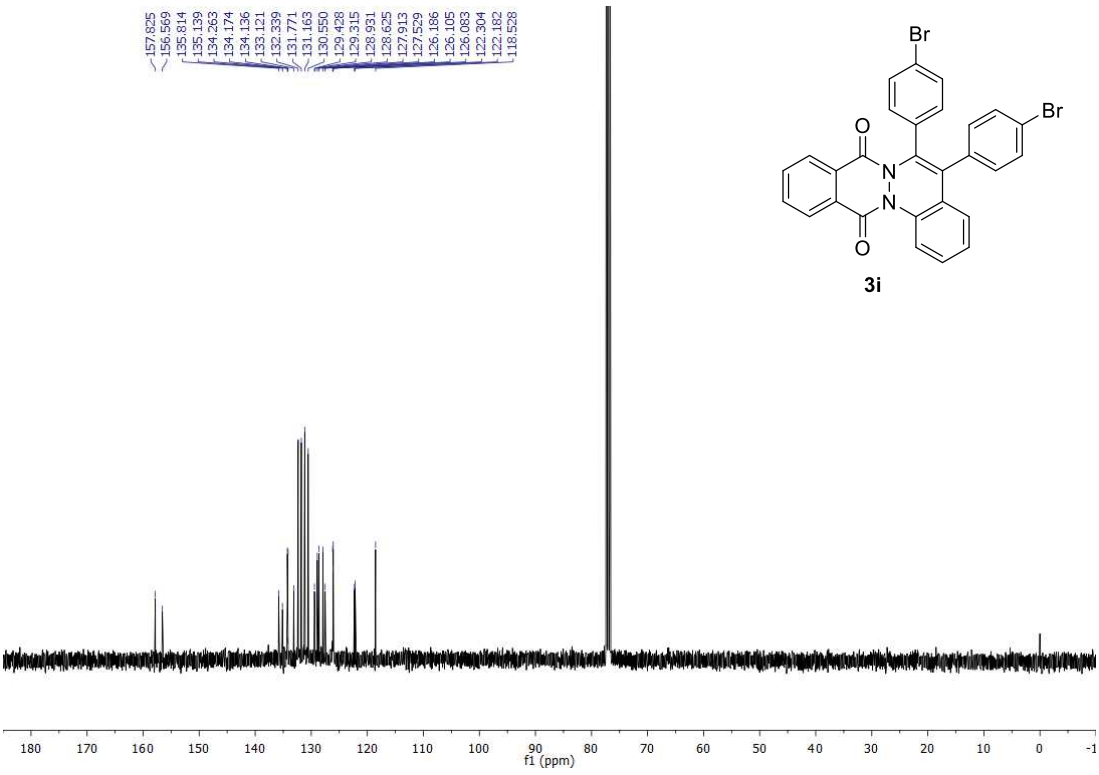
DEPT-135 NMR Spectrum of Compound 3h in $CDCl_3$



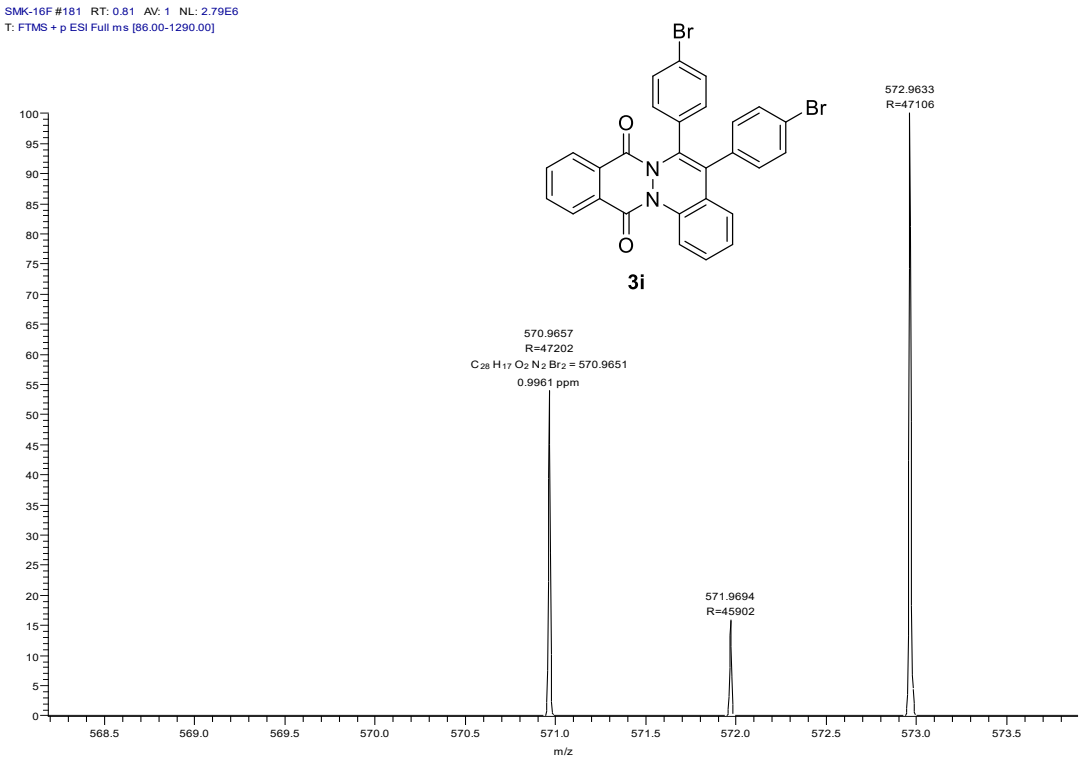
HRMS Spectrum of Compound 3h



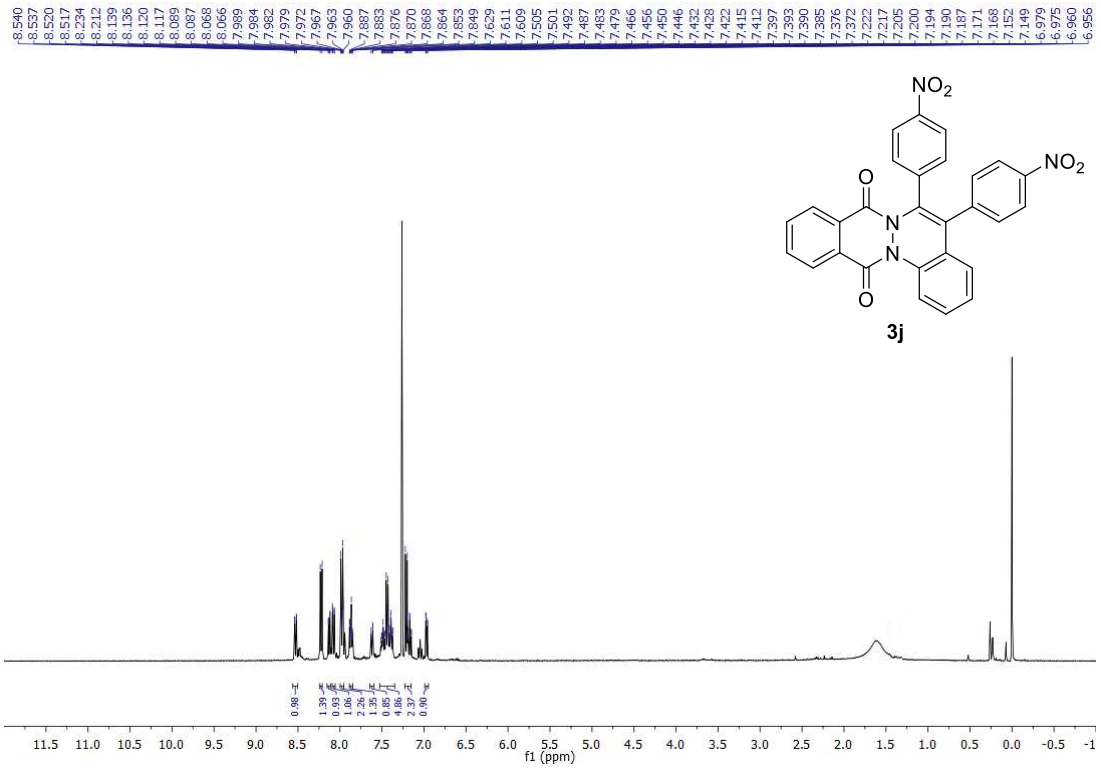
^{1}H NMR Spectrum of Compound 3i in $CDCl_3$



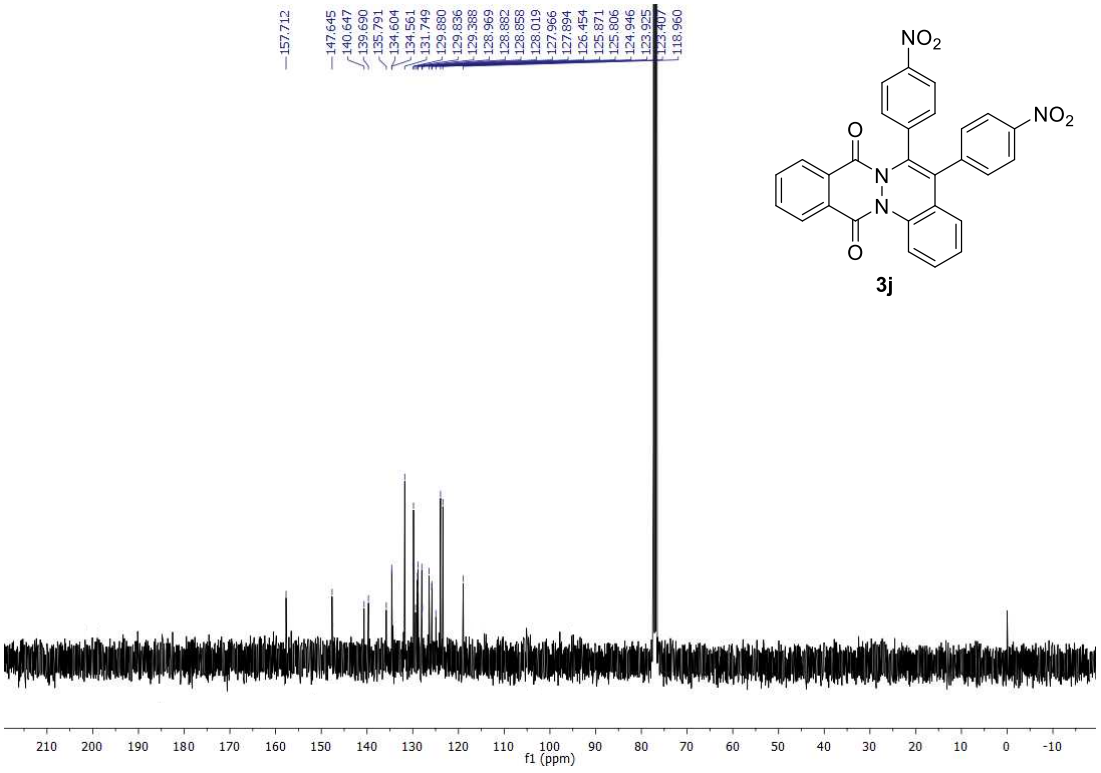
^{13}C NMR Spectrum of Compound 3i in $CDCl_3$



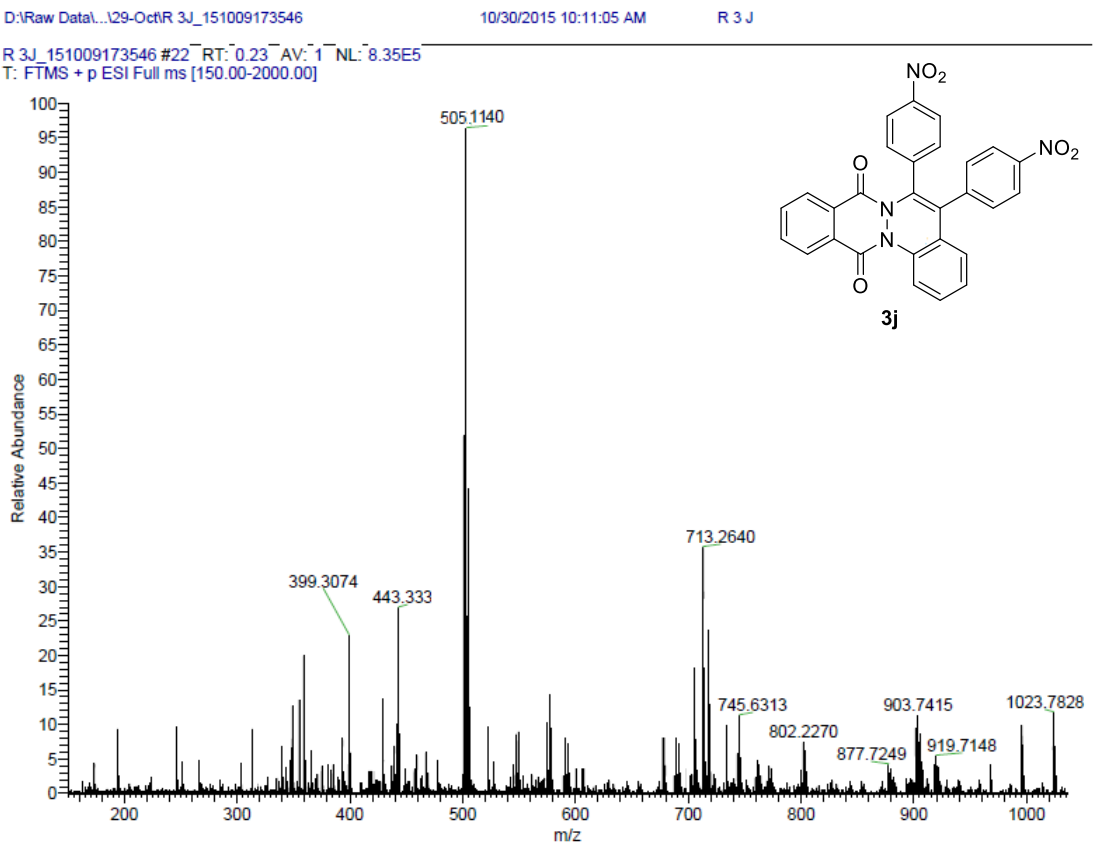
HRMS Spectrum of Compound 3i



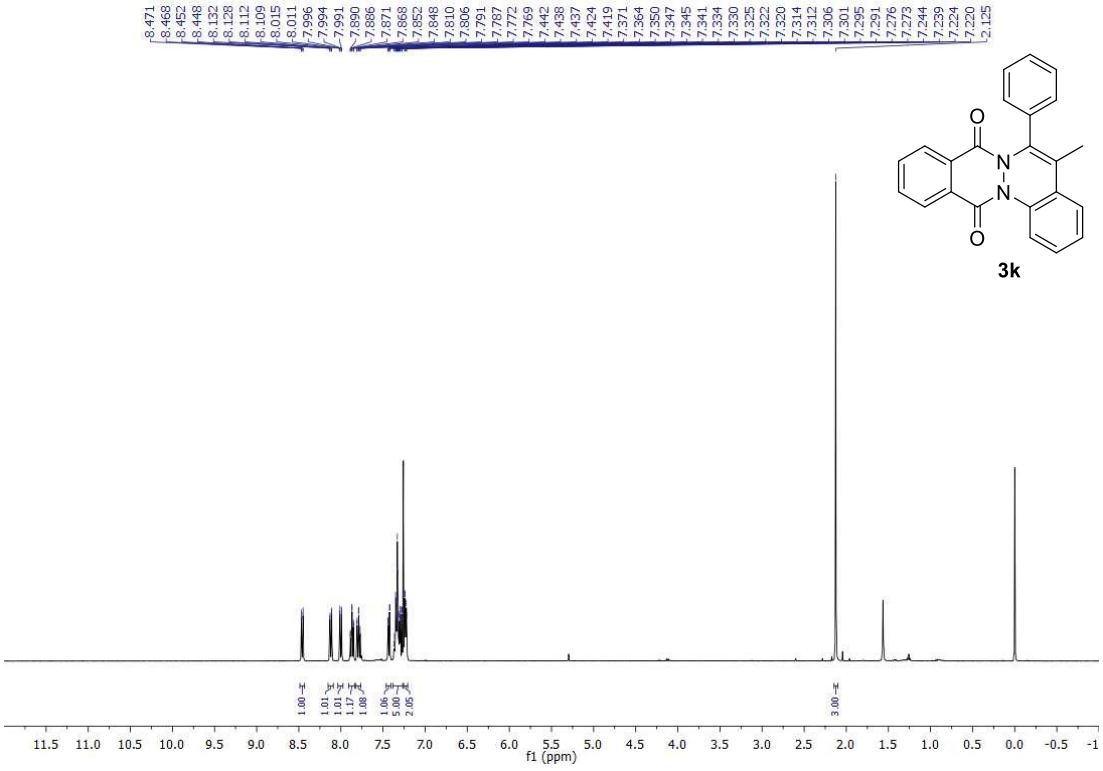
^{1}H NMR Spectrum of Compound 3j in $CDCl_3$



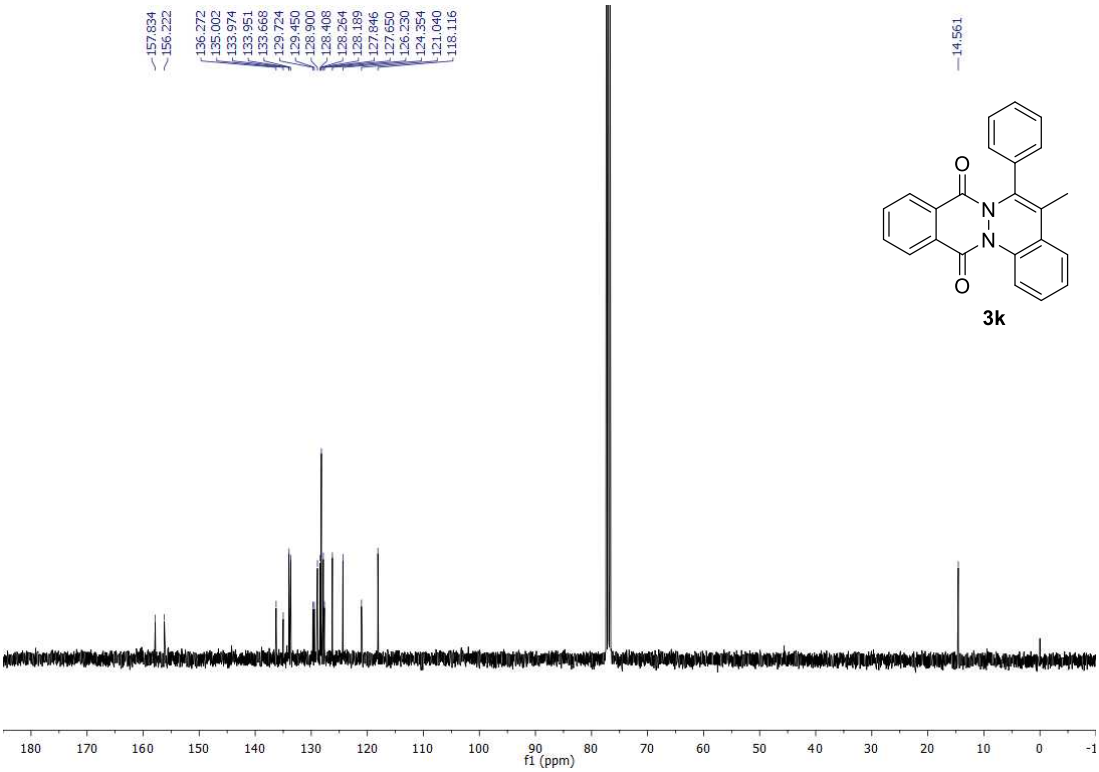
^{13}C NMR Spectrum of Compound 3j in $CDCl_3$



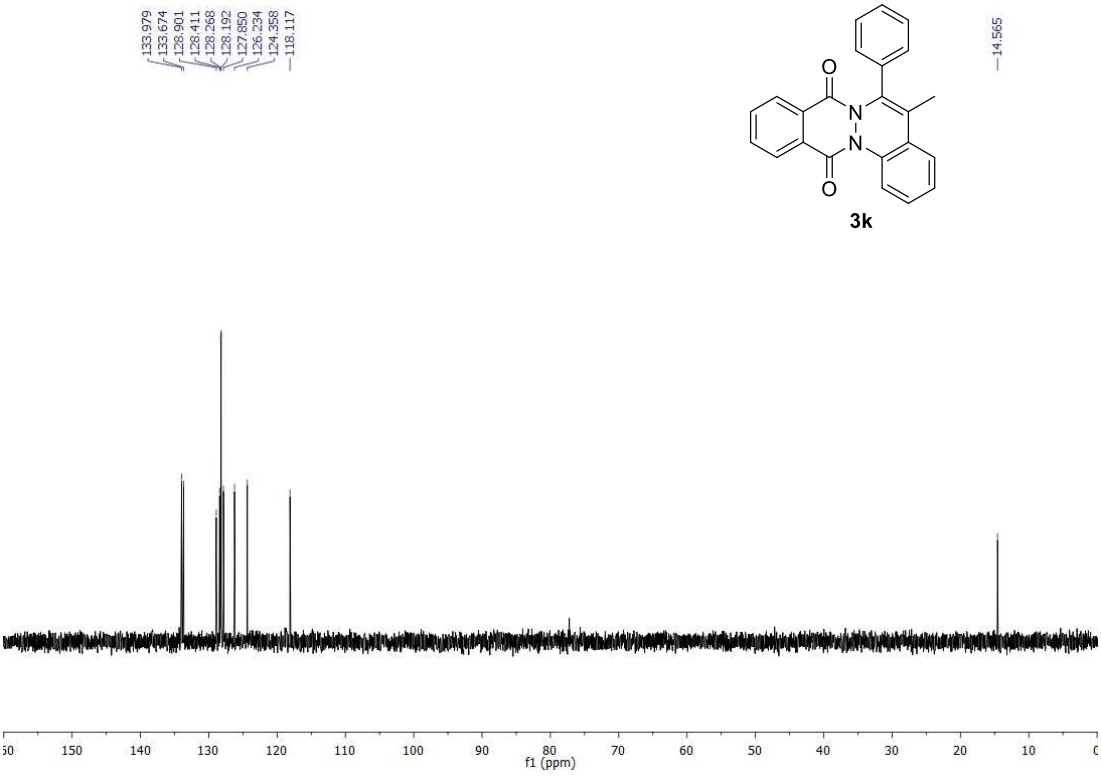
HRMS Spectrum of Compound 3j



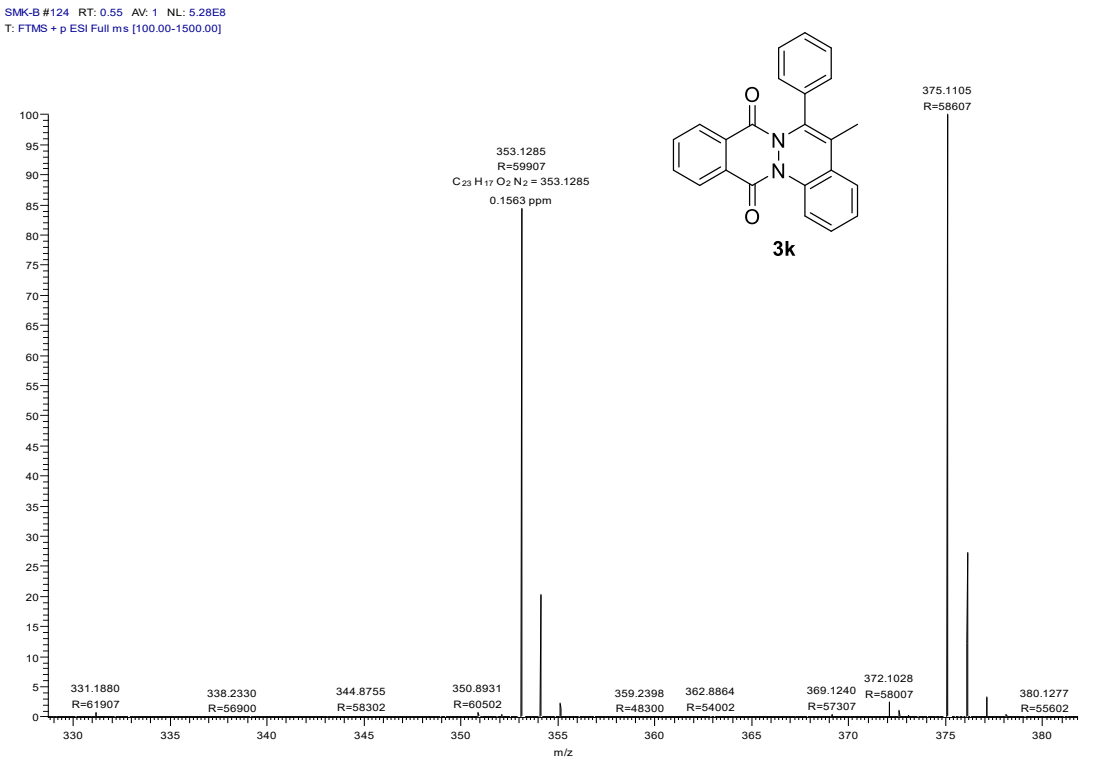
^{1}H NMR Spectrum of Compound 3k in $CDCl_3$



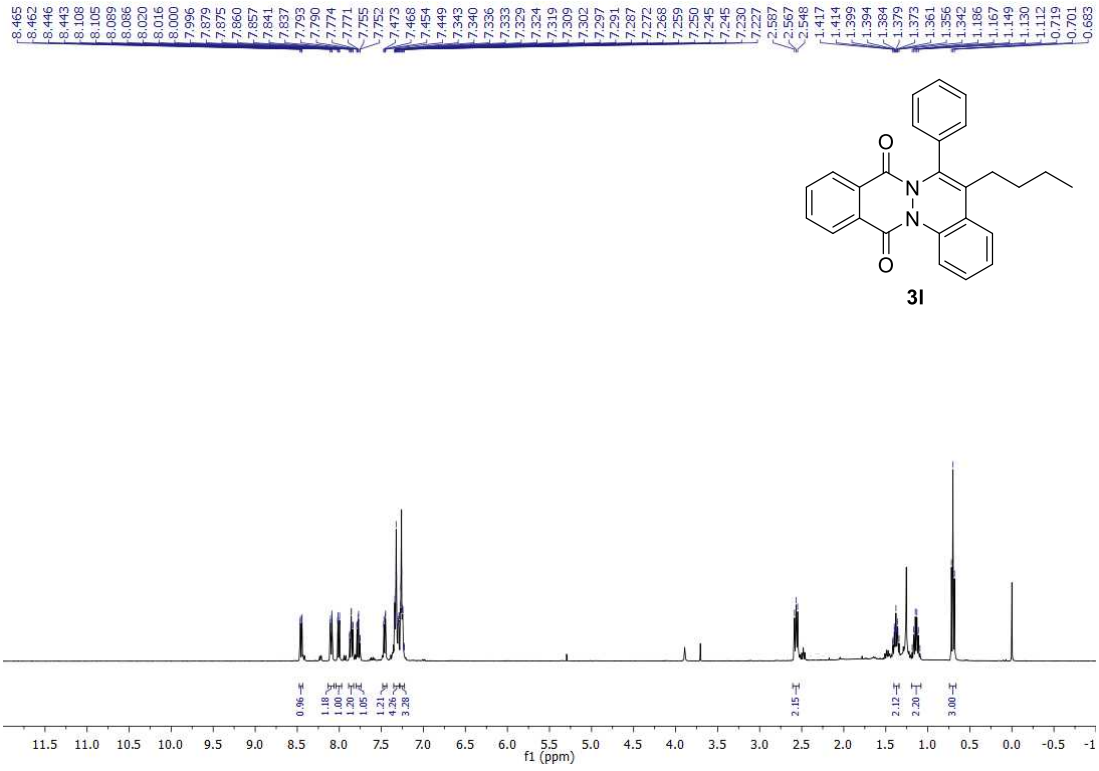
^{13}C NMR Spectrum of Compound 3k in $CDCl_3$



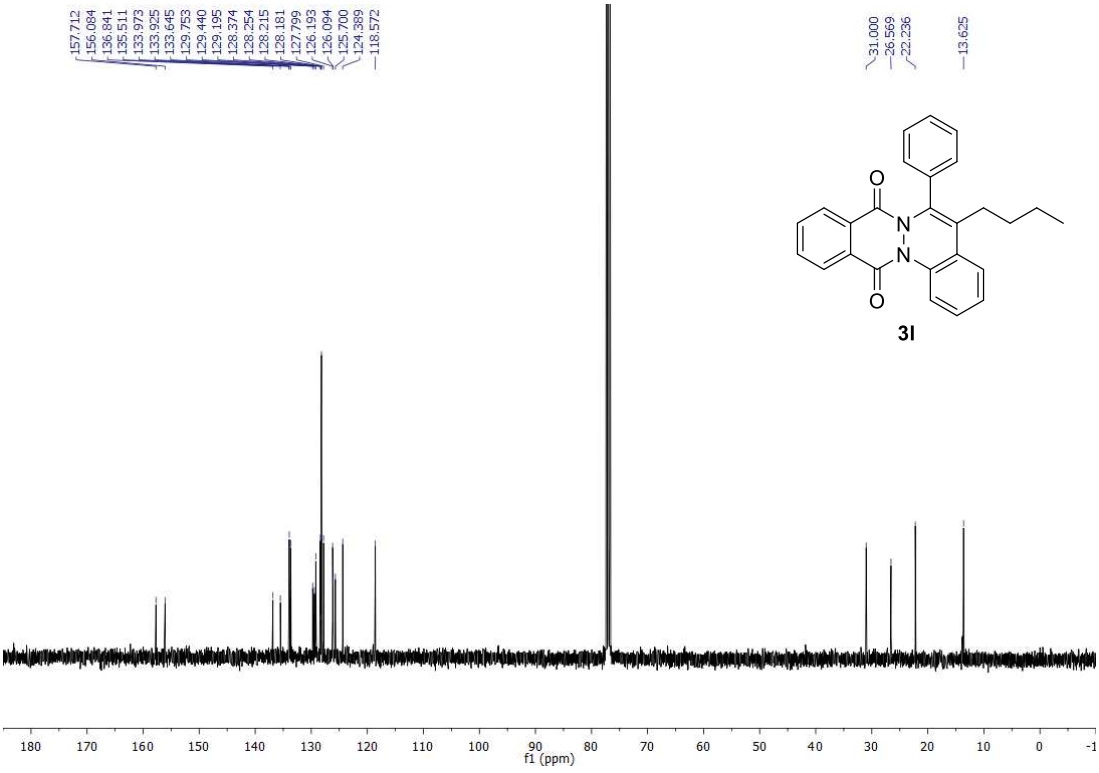
DEPT-135 NMR Spectrum of Compound 3k in $CDCl_3$



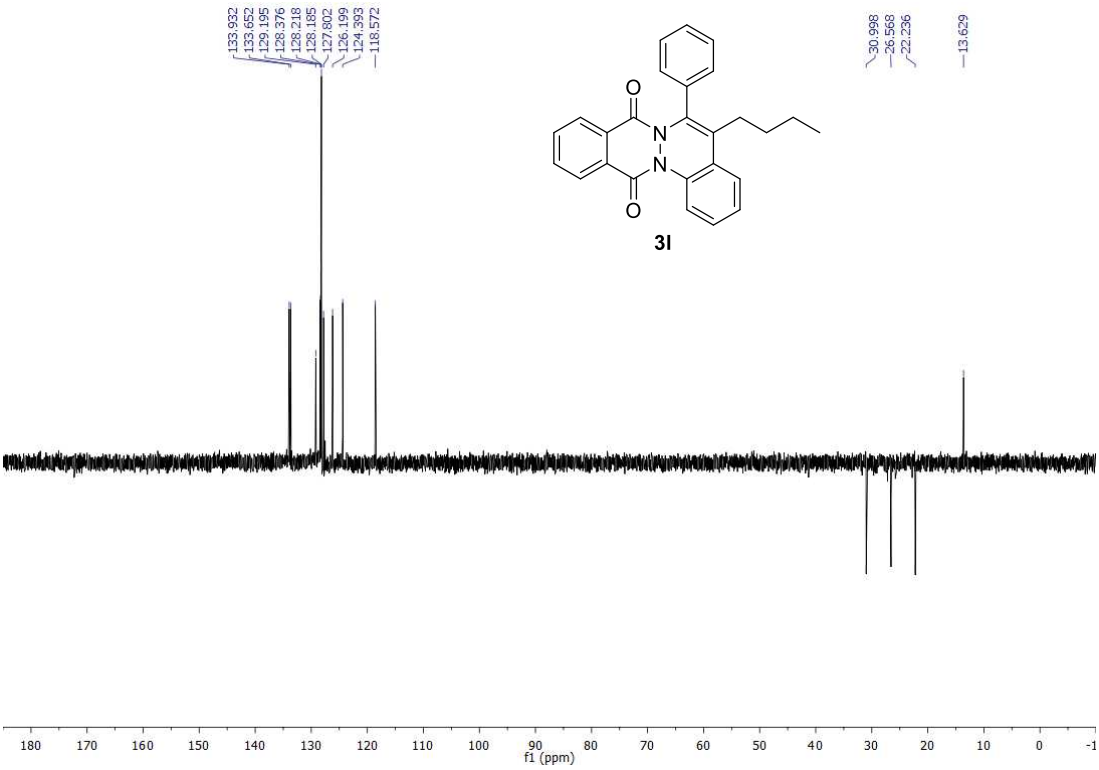
HRMS Spectrum of Compound 3k



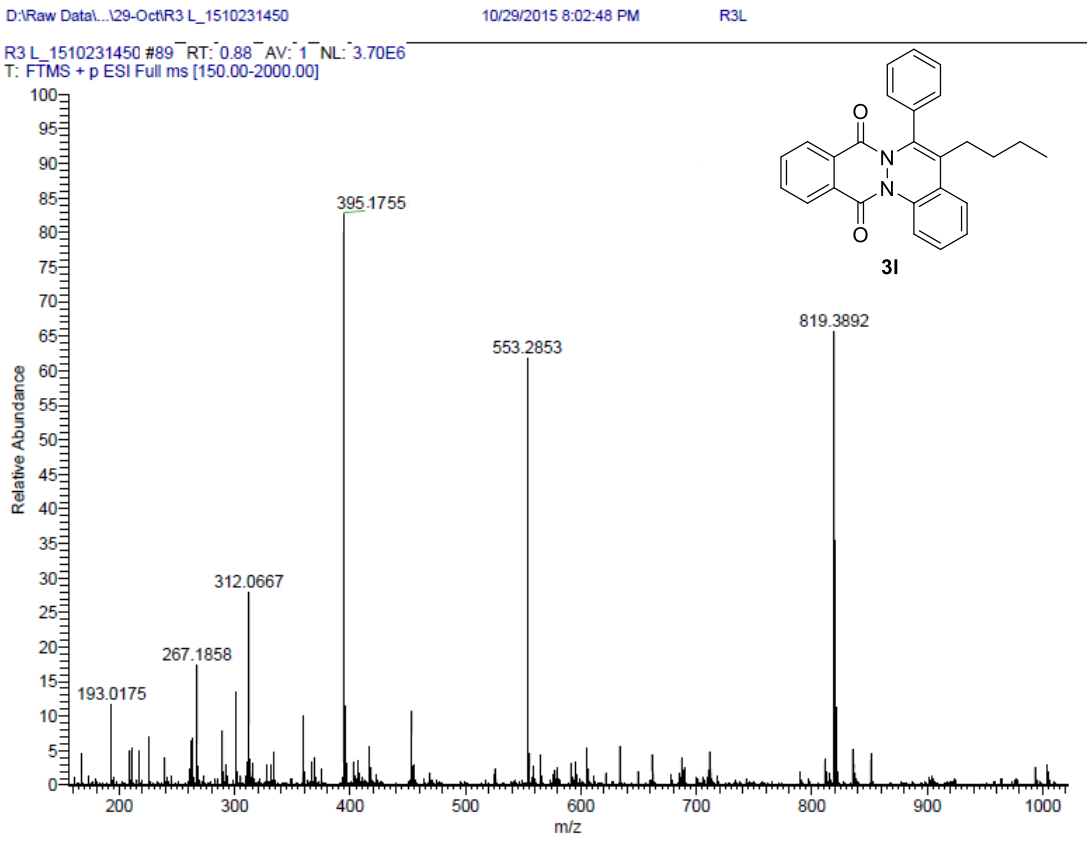
^{1}H NMR Spectrum of Compound 3l in $CDCl_3$



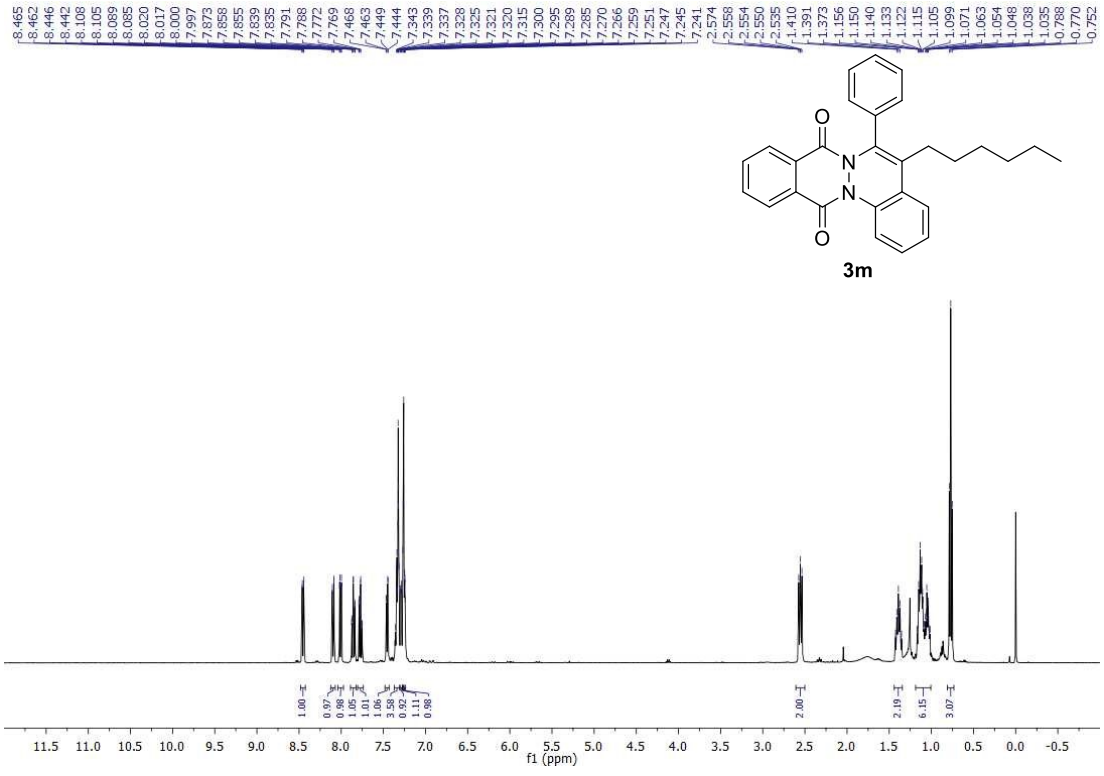
^{13}C NMR Spectrum of Compound 3l in $CDCl_3$



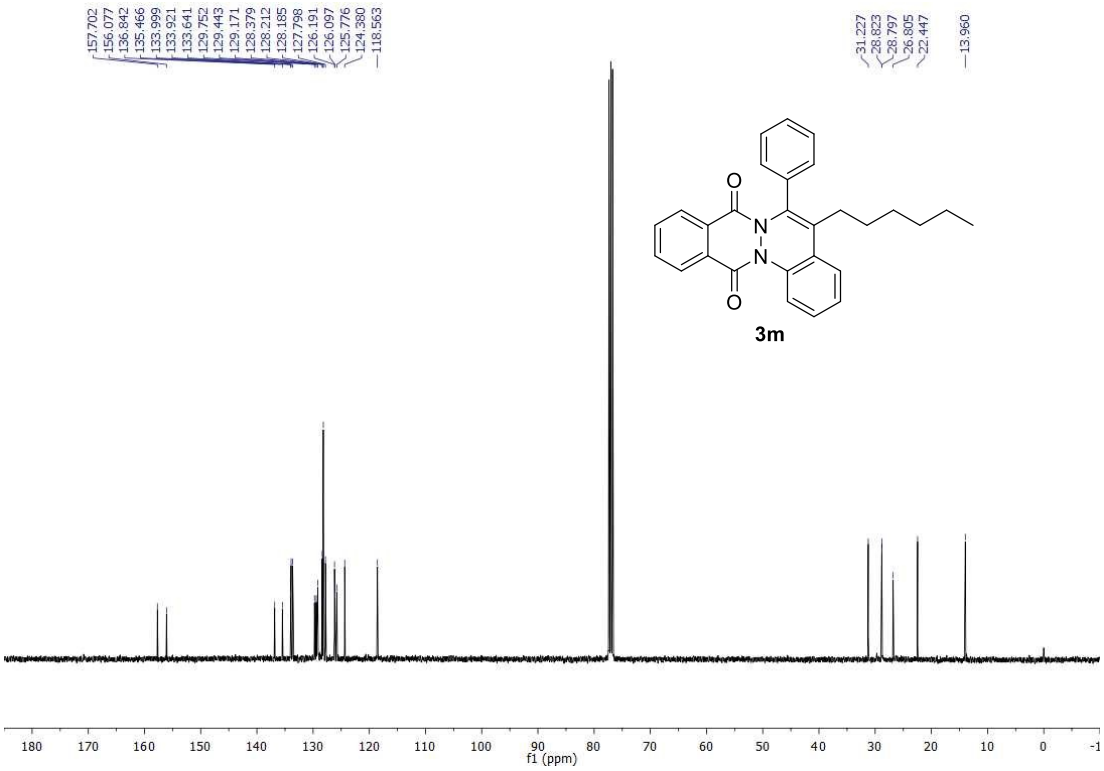
DEPT-135 NMR Spectrum of Compound 3l in $CDCl_3$



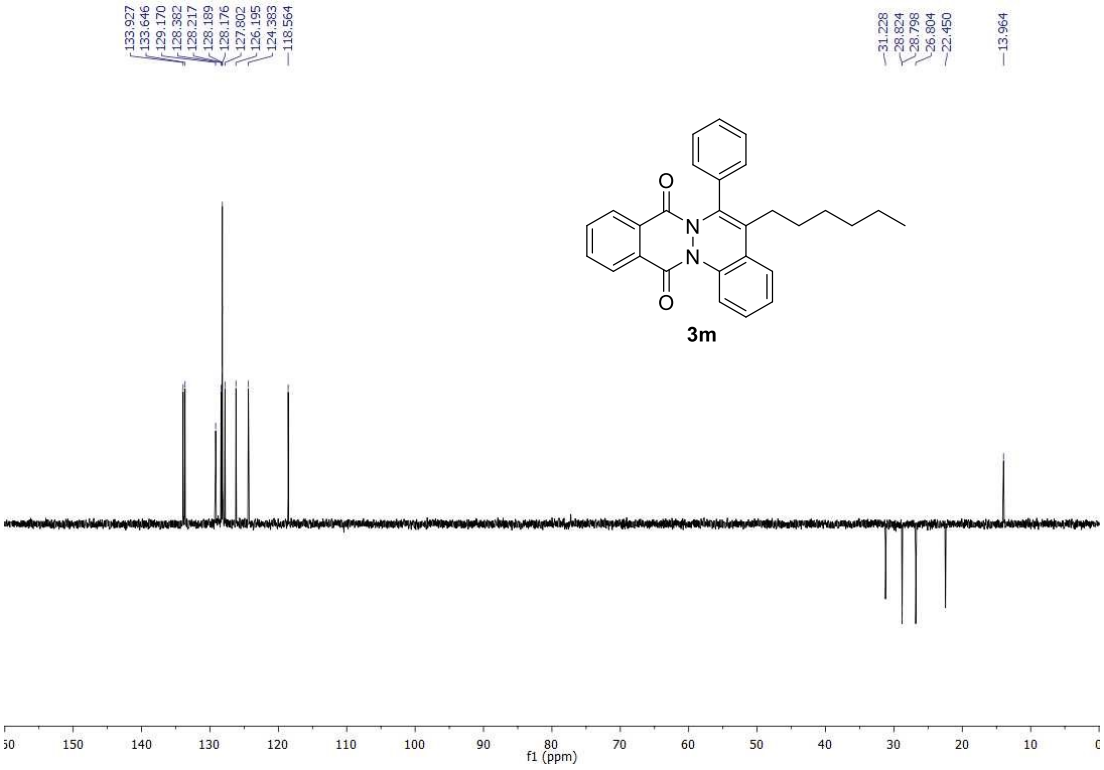
HRMS Spectrum of Compound 3l



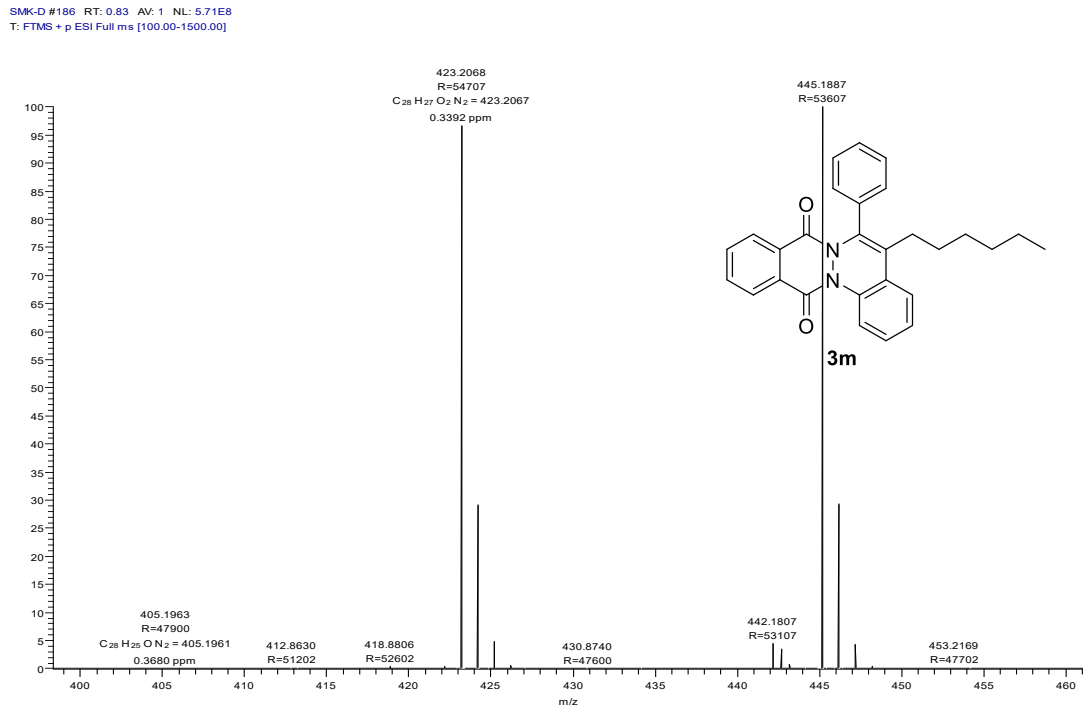
^{1}H NMR Spectrum of Compound 3m in $CDCl_3$



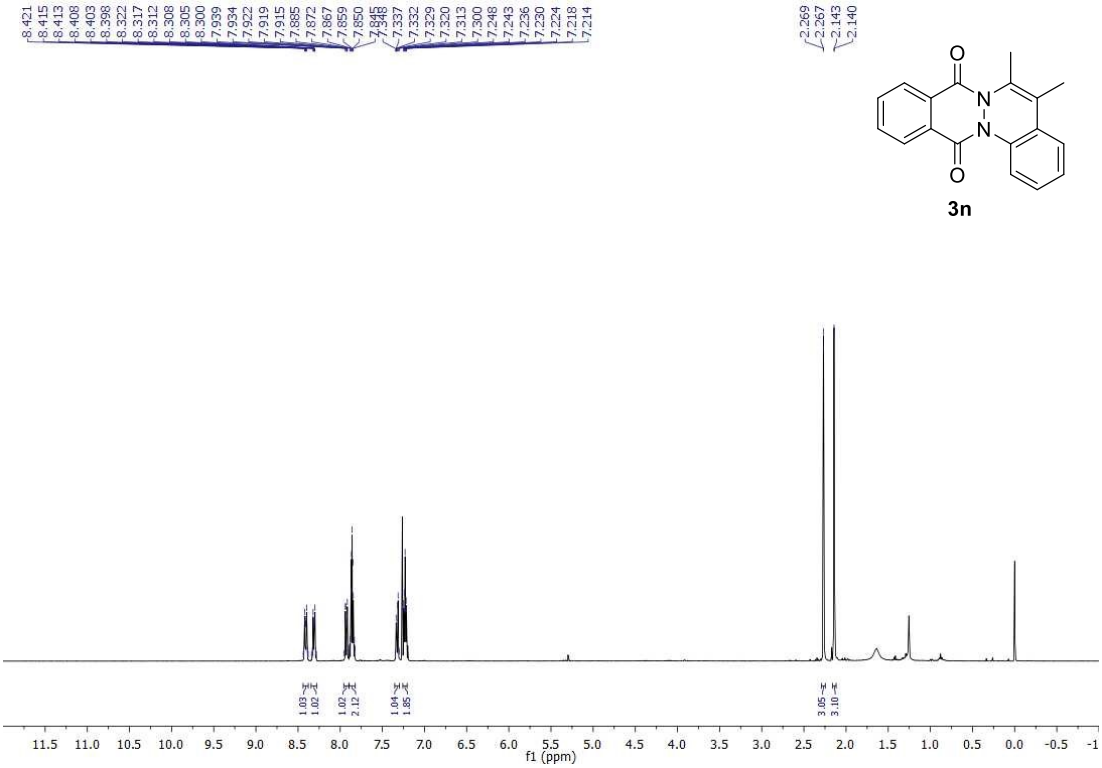
^{13}C NMR Spectrum of Compound 3m in $CDCl_3$



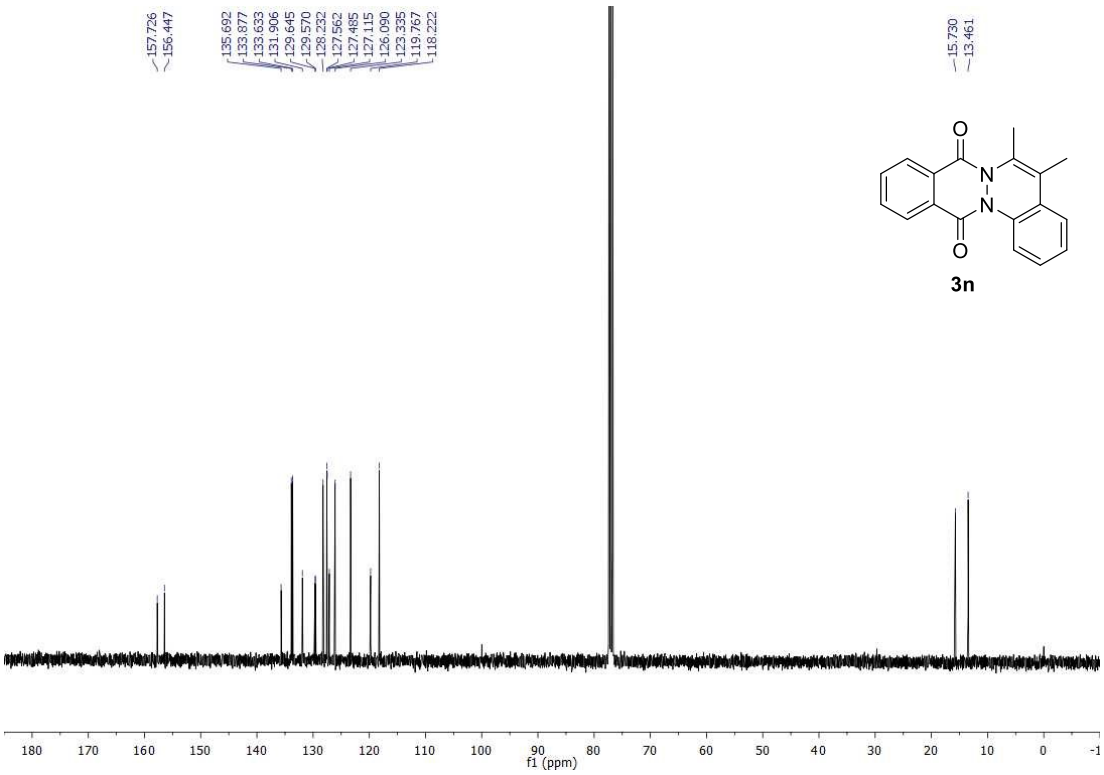
DEPT-135 NMR Spectrum of Compound 3m in $CDCl_3$



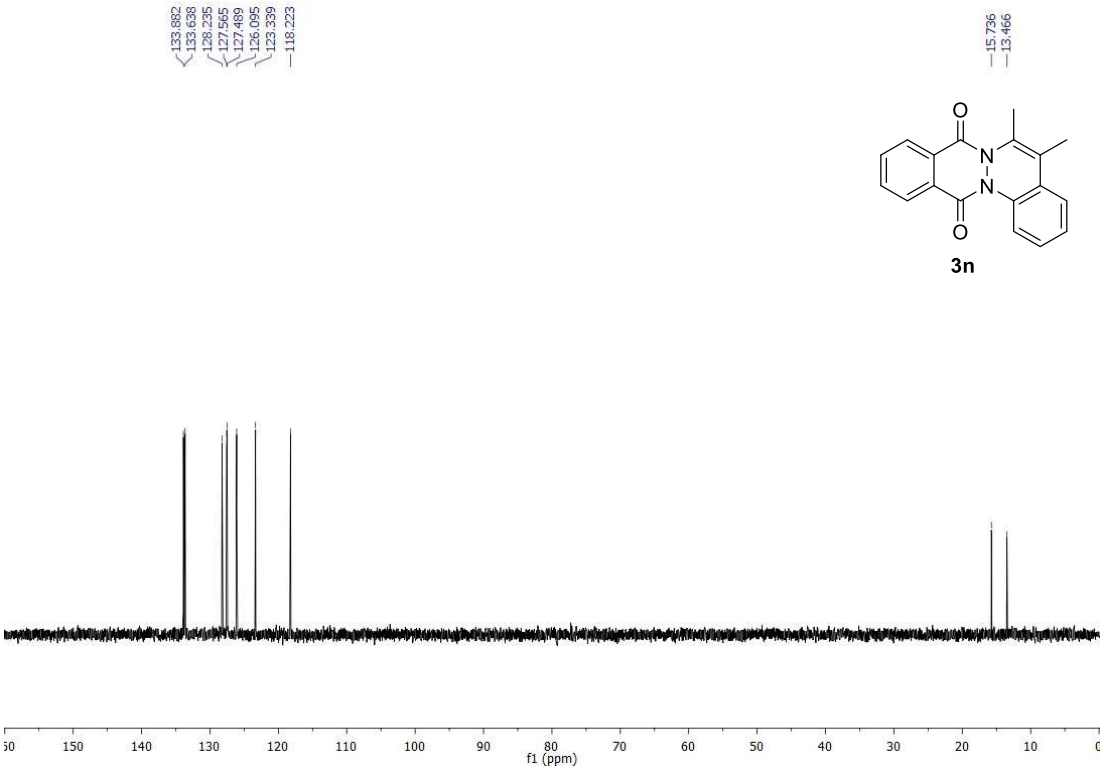
HRMS Spectrum of Compound 3m



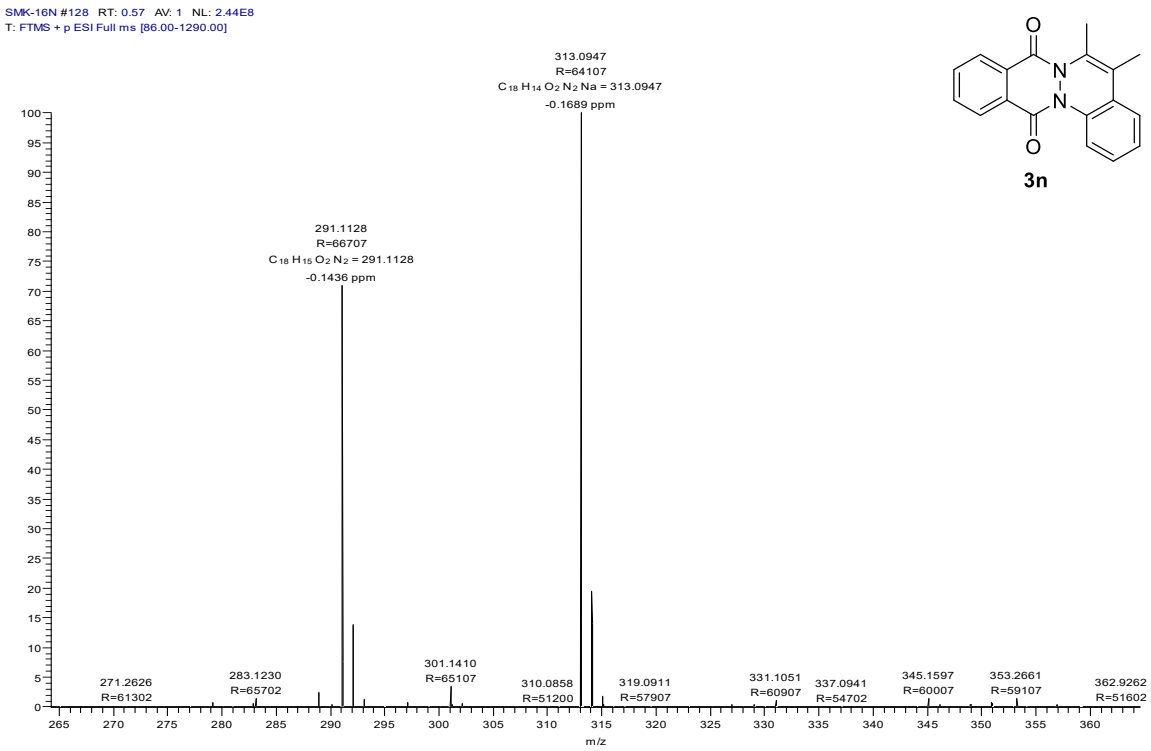
^{1}H NMR Spectrum of Compound 3n in $CDCl_3$



^{13}C NMR Spectrum of Compound 3n in $CDCl_3$

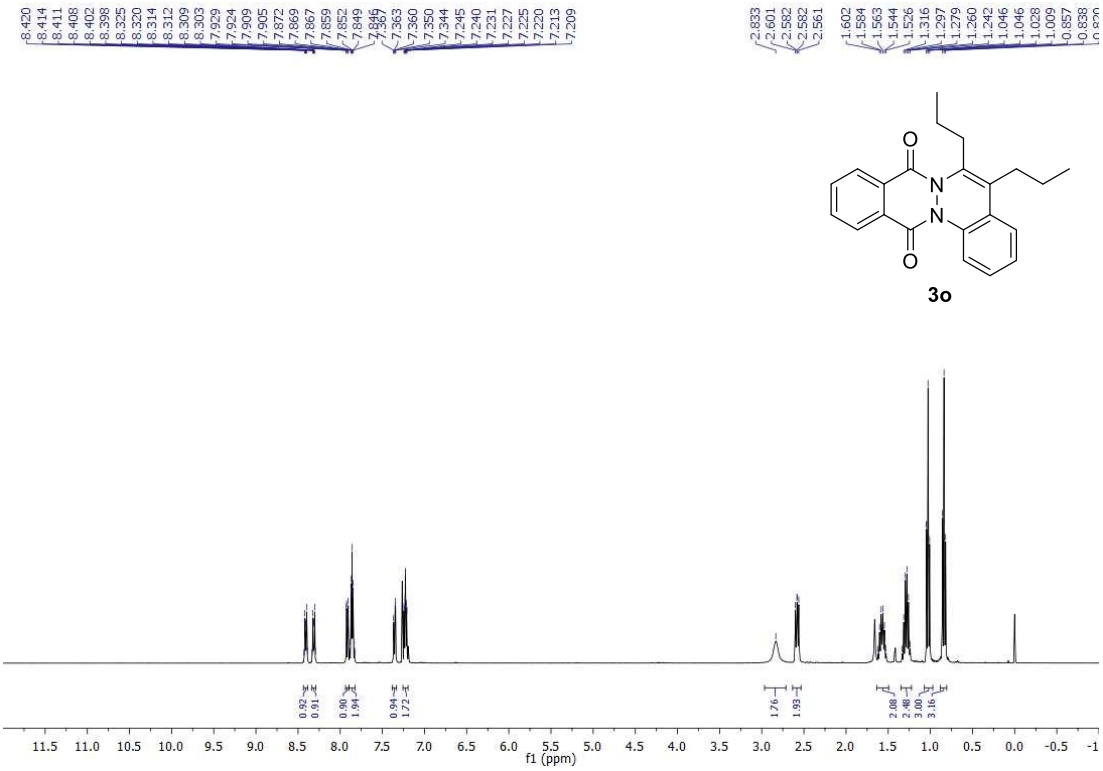


DEPT-135 NMR Spectrum of Compound 3n in $CDCl_3$



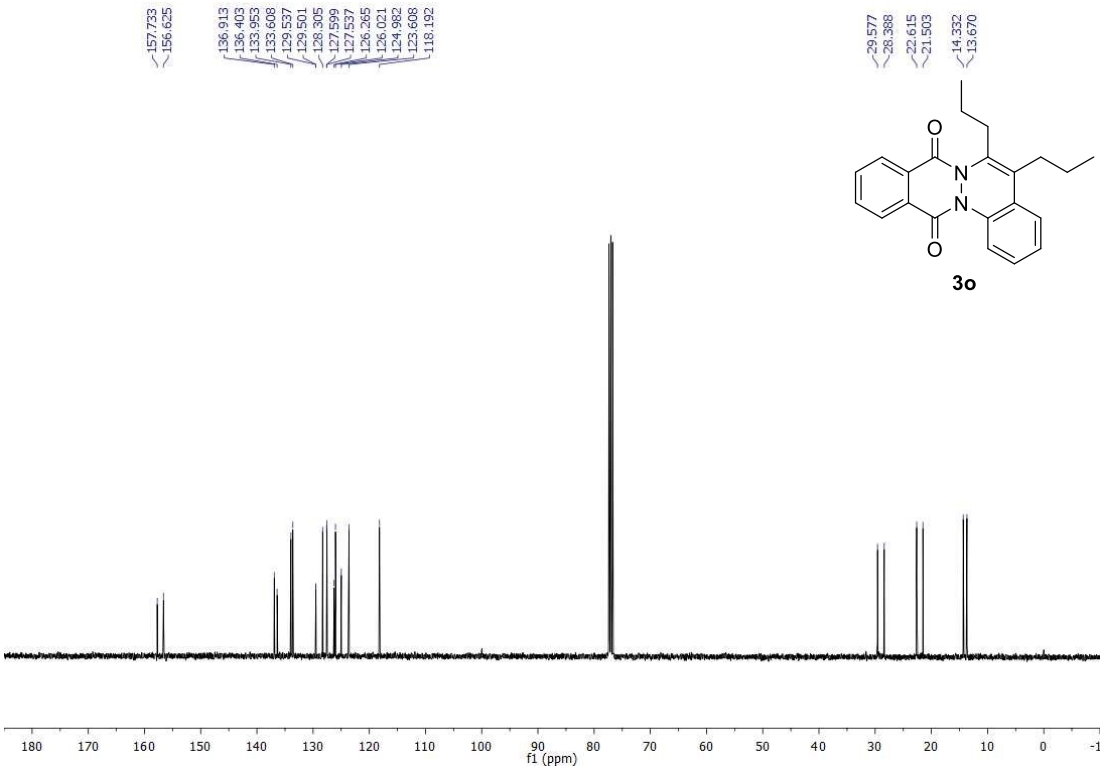
3n

HRMS Spectrum of Compound 3n

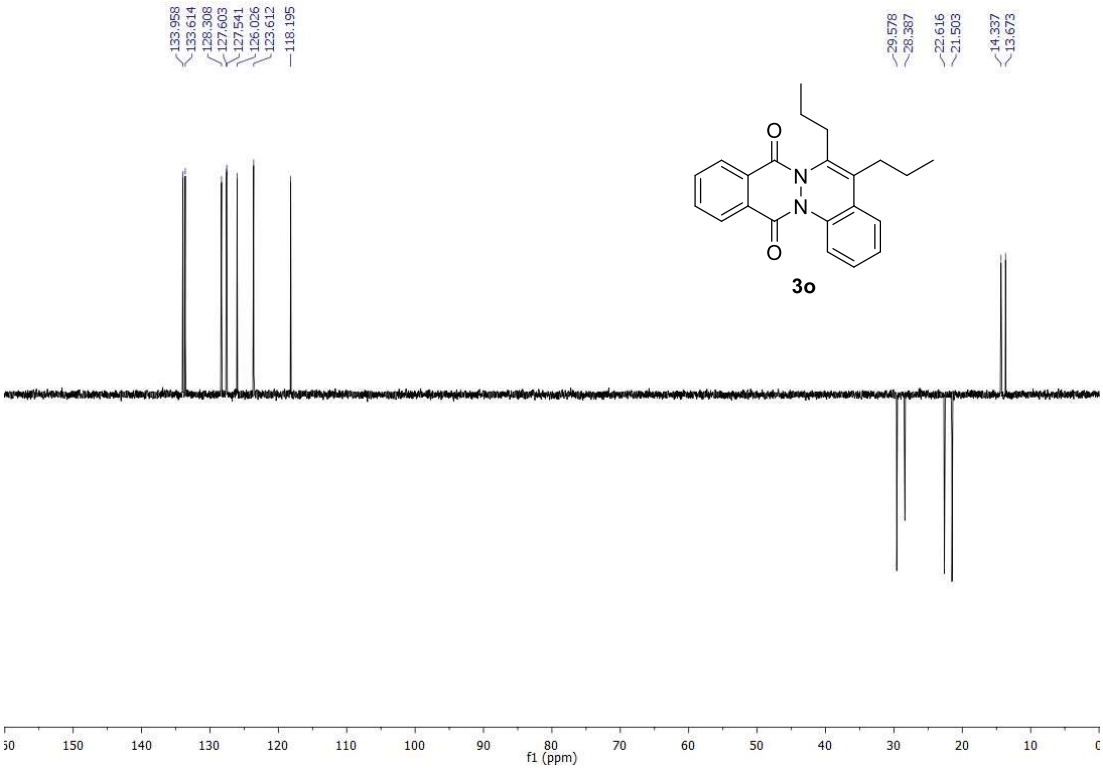


3o

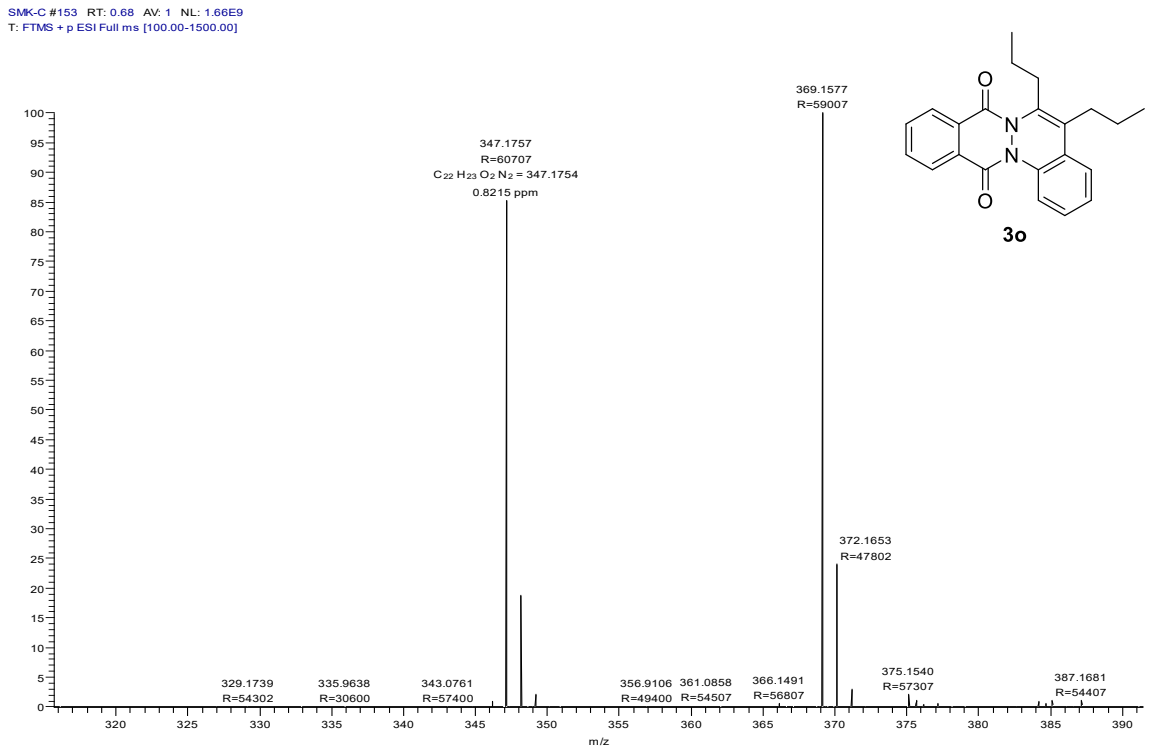
^{1}H NMR Spectrum of Compound 3o in $CDCl_3$



^{13}C NMR Spectrum of Compound 3o in $CDCl_3$

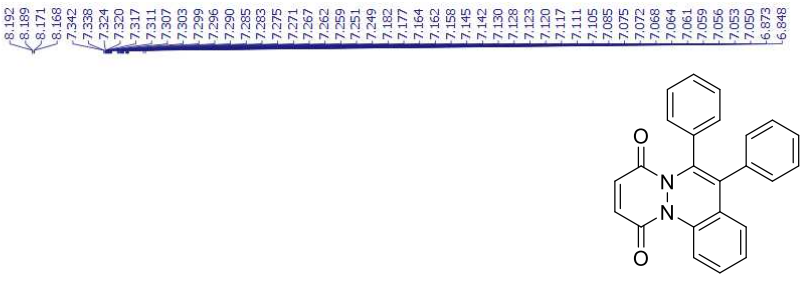


DEPT-135 NMR Spectrum of Compound 3o in $CDCl_3$

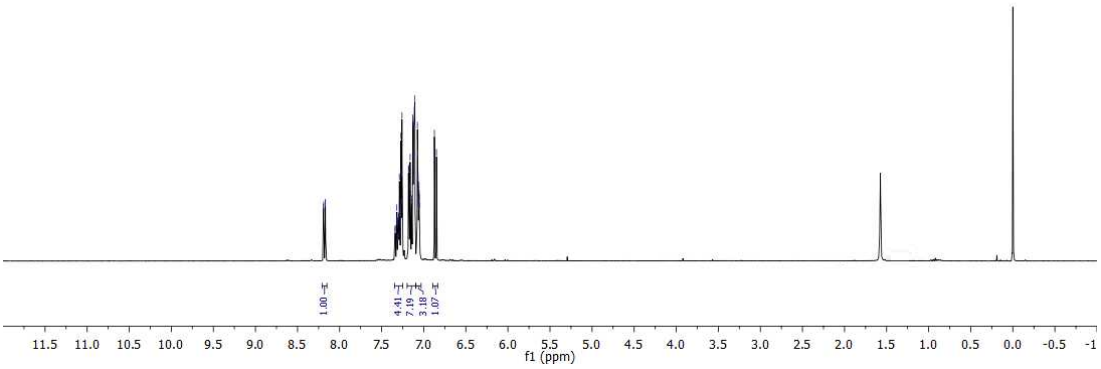


3o

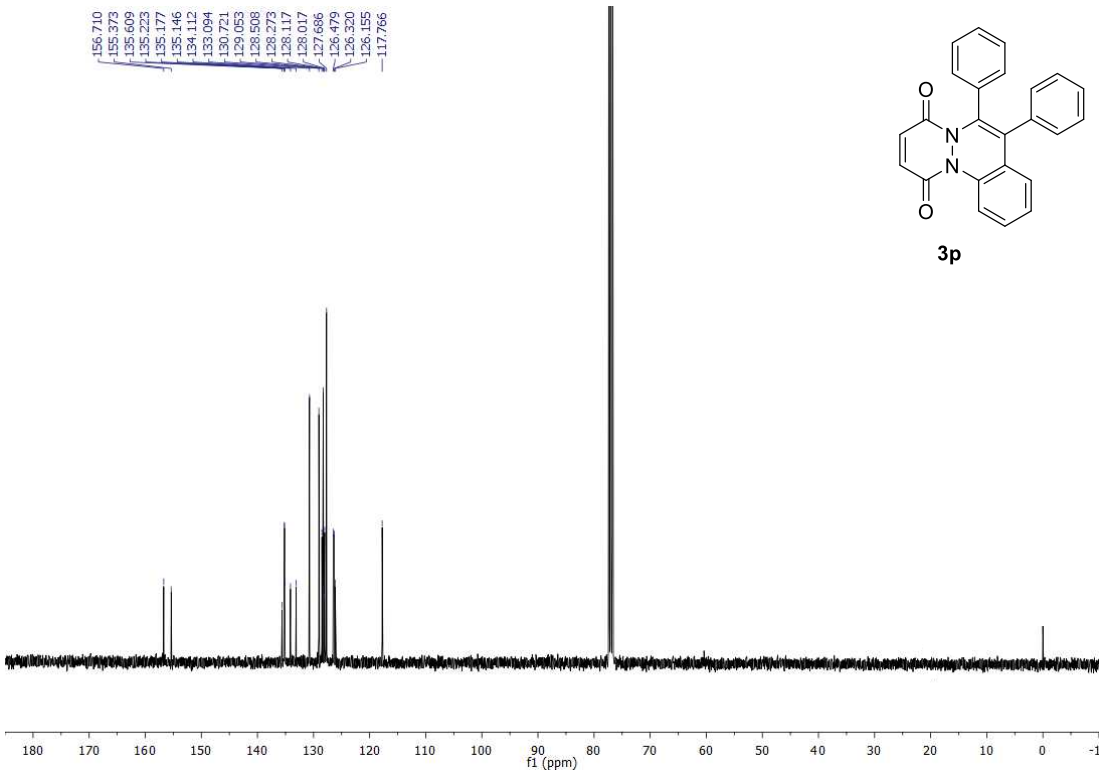
HRMS Spectrum of Compound 3o



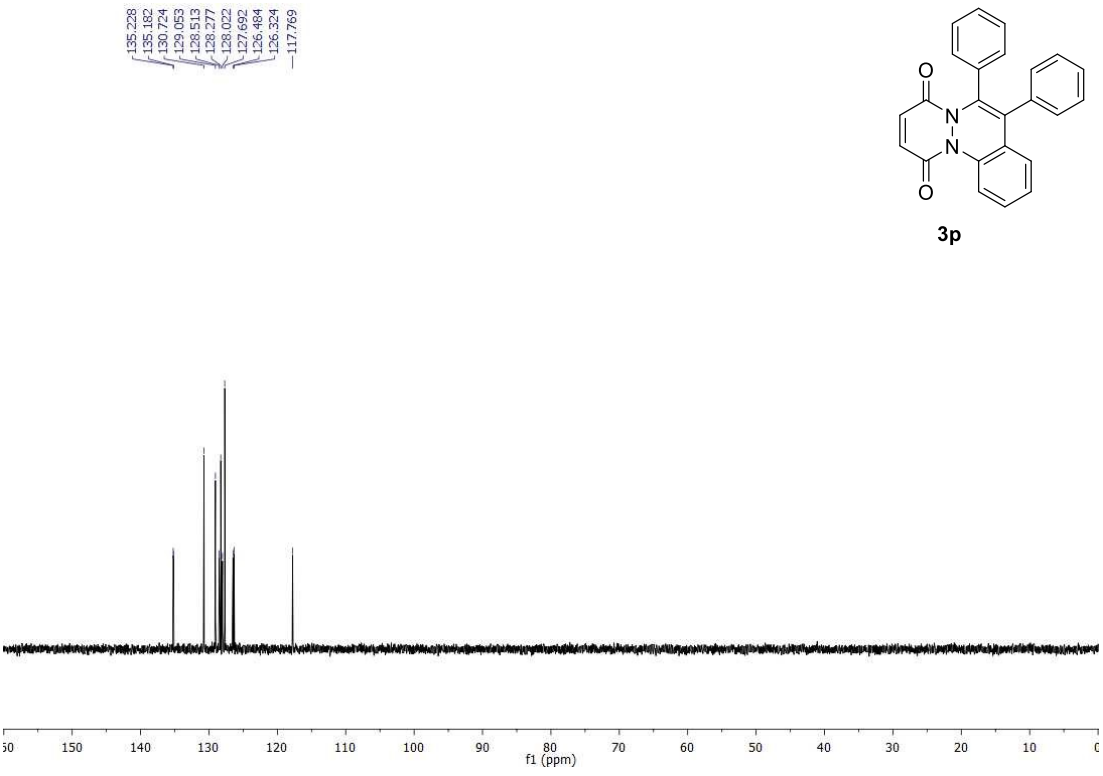
3p



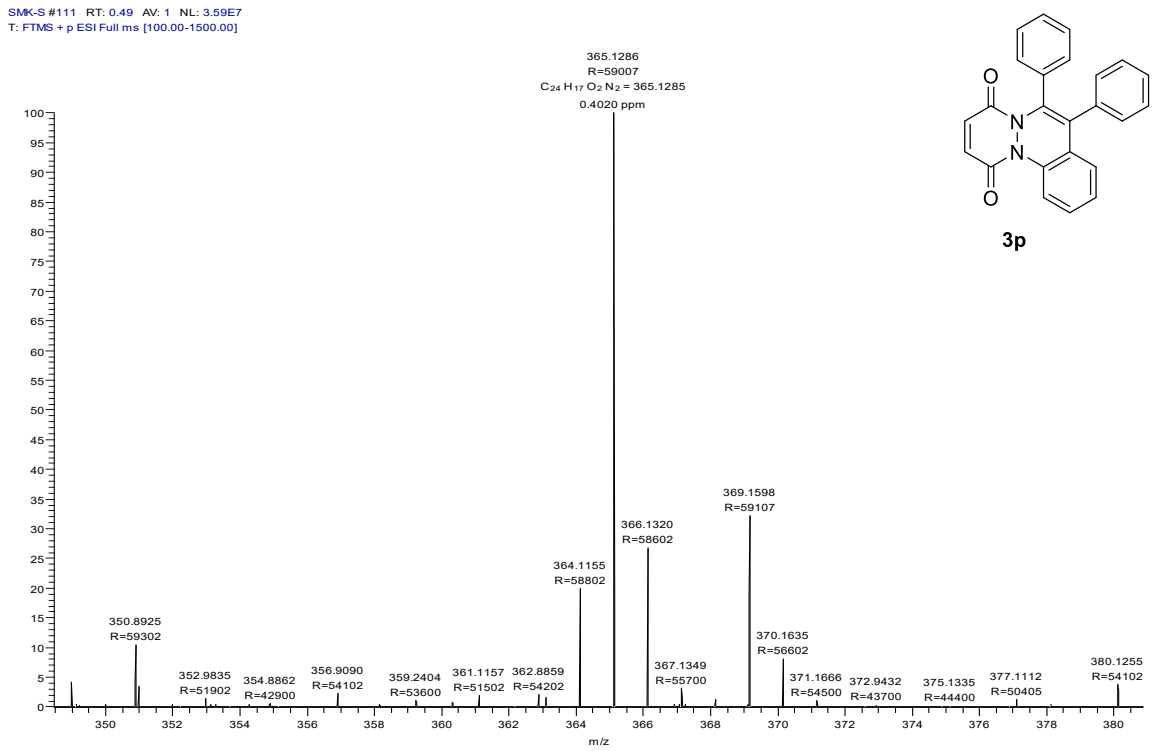
^{1}H NMR Spectrum of Compound 3p in $CDCl_3$



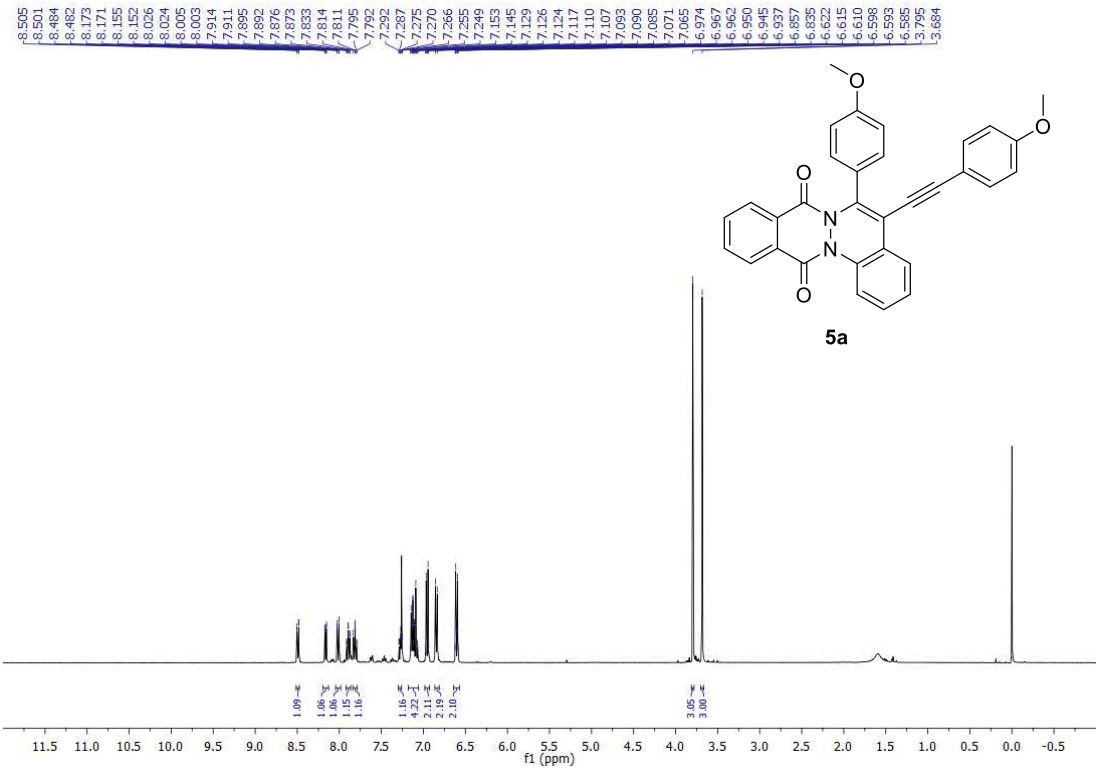
^{13}C NMR Spectrum of Compound 3p in $CDCl_3$



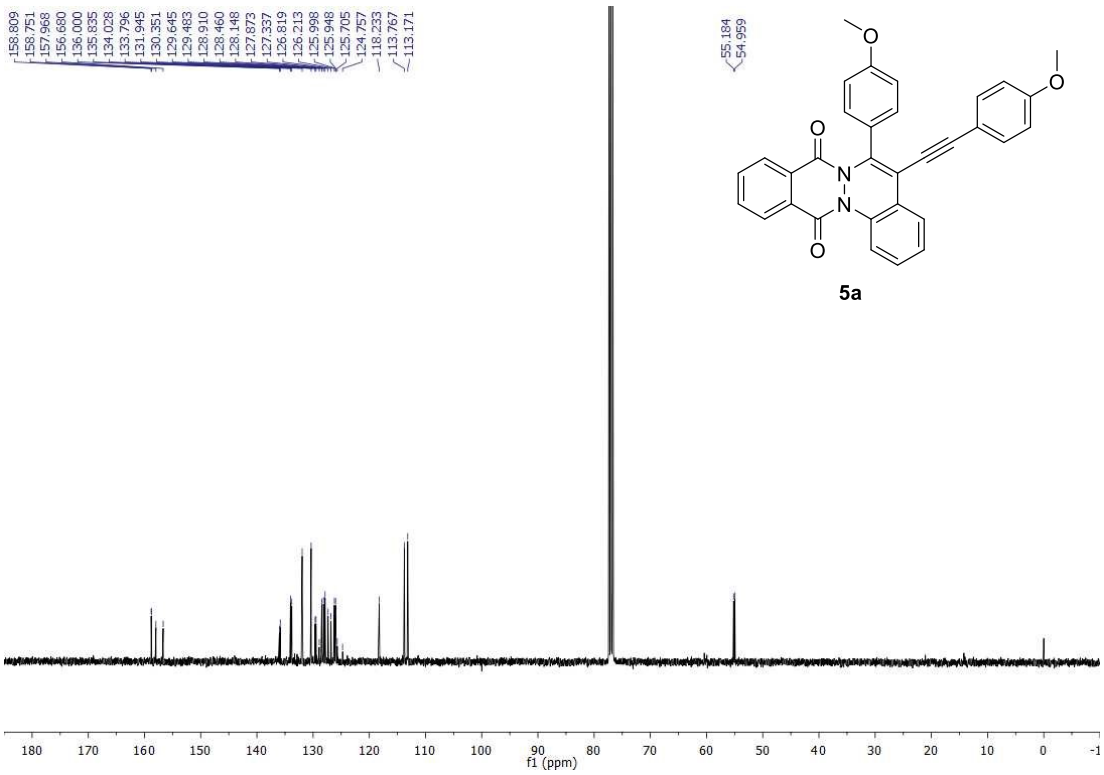
DEPT-135 NMR Spectrum of Compound 3p in $CDCl_3$



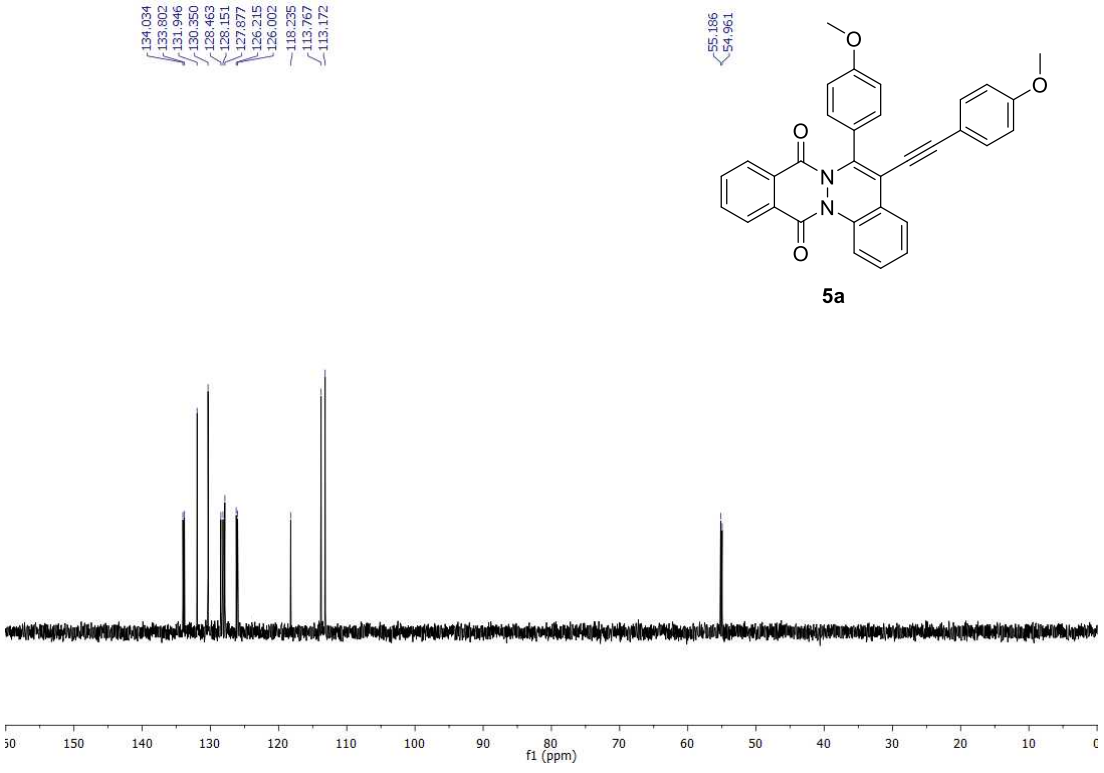
HRMS Spectrum of Compound 3p



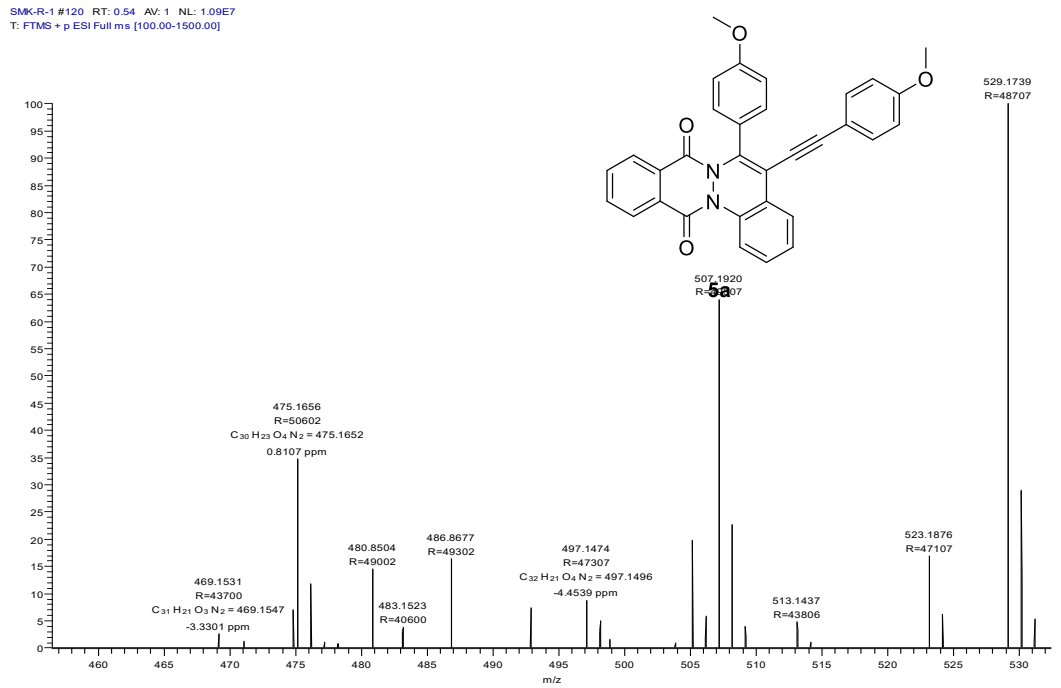
^{1}H NMR Spectrum of Compound 5a in $CDCl_3$



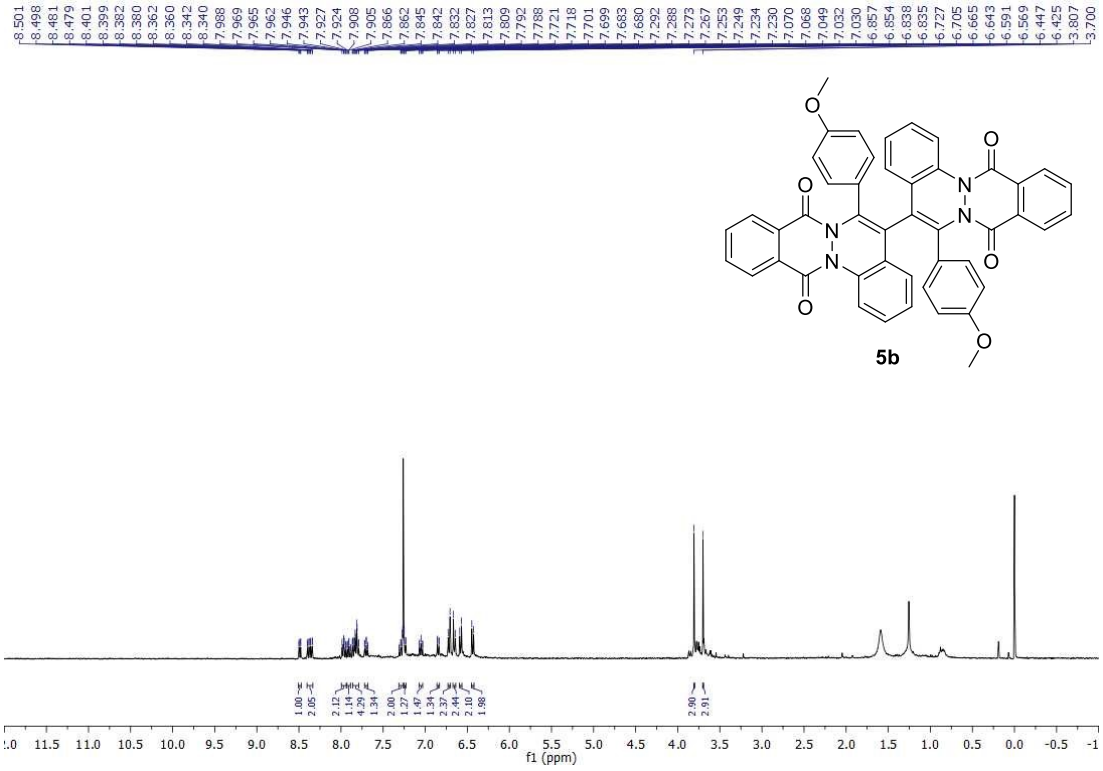
^{13}C NMR Spectrum of Compound 5a in $CDCl_3$



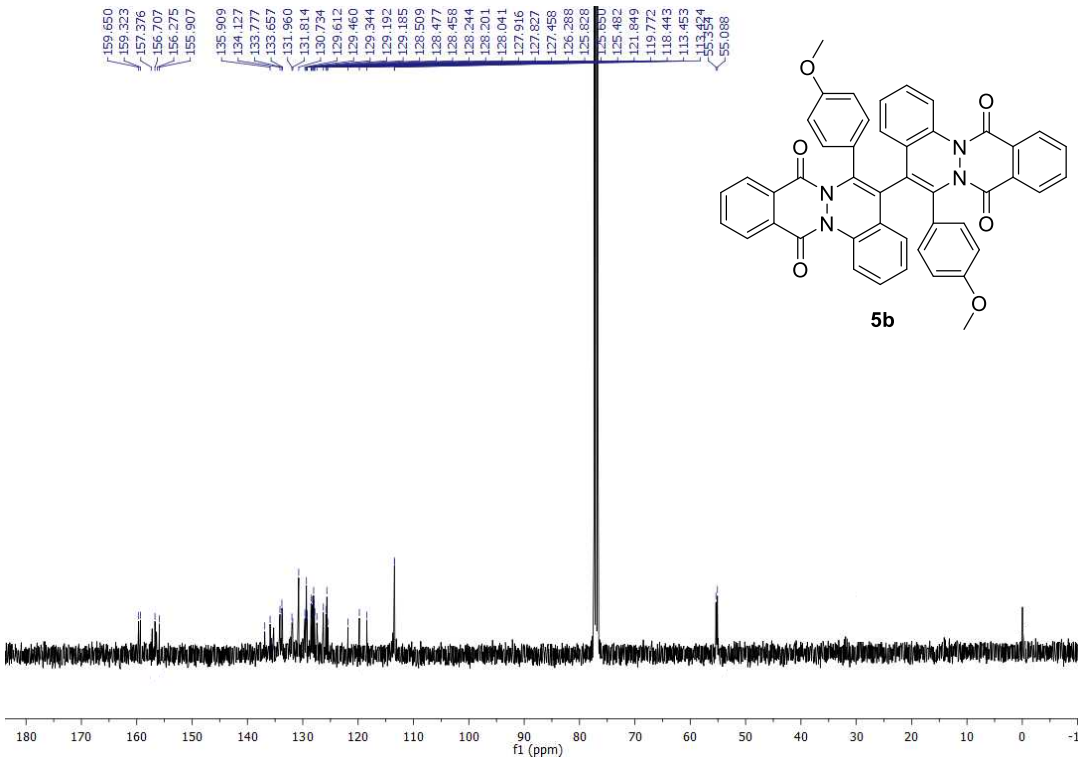
DEPT-135 NMR Spectrum of Compound 5a in $CDCl_3$



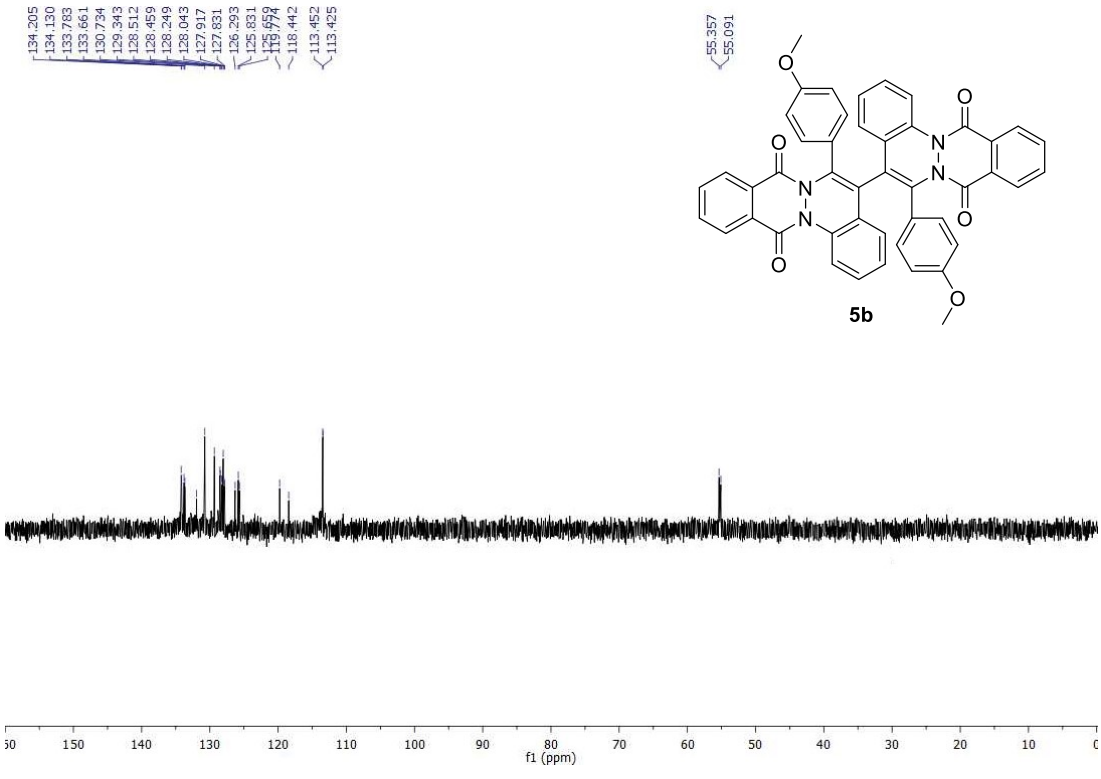
HRMS Spectrum of Compound 5a



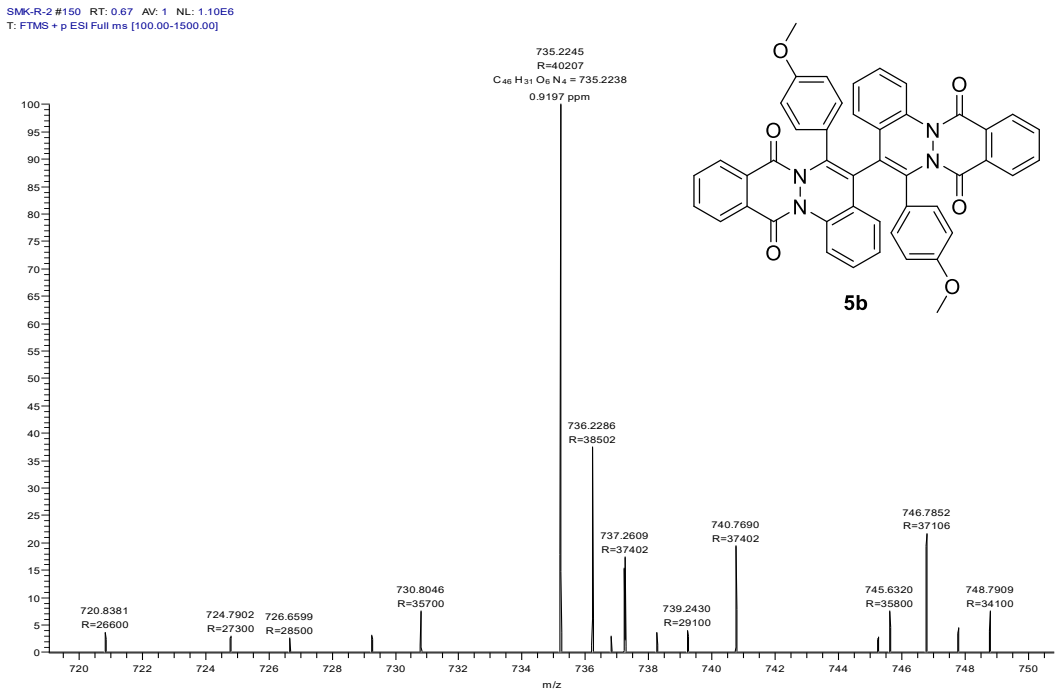
^{1}H NMR Spectrum of Compound 5b in $CDCl_3$



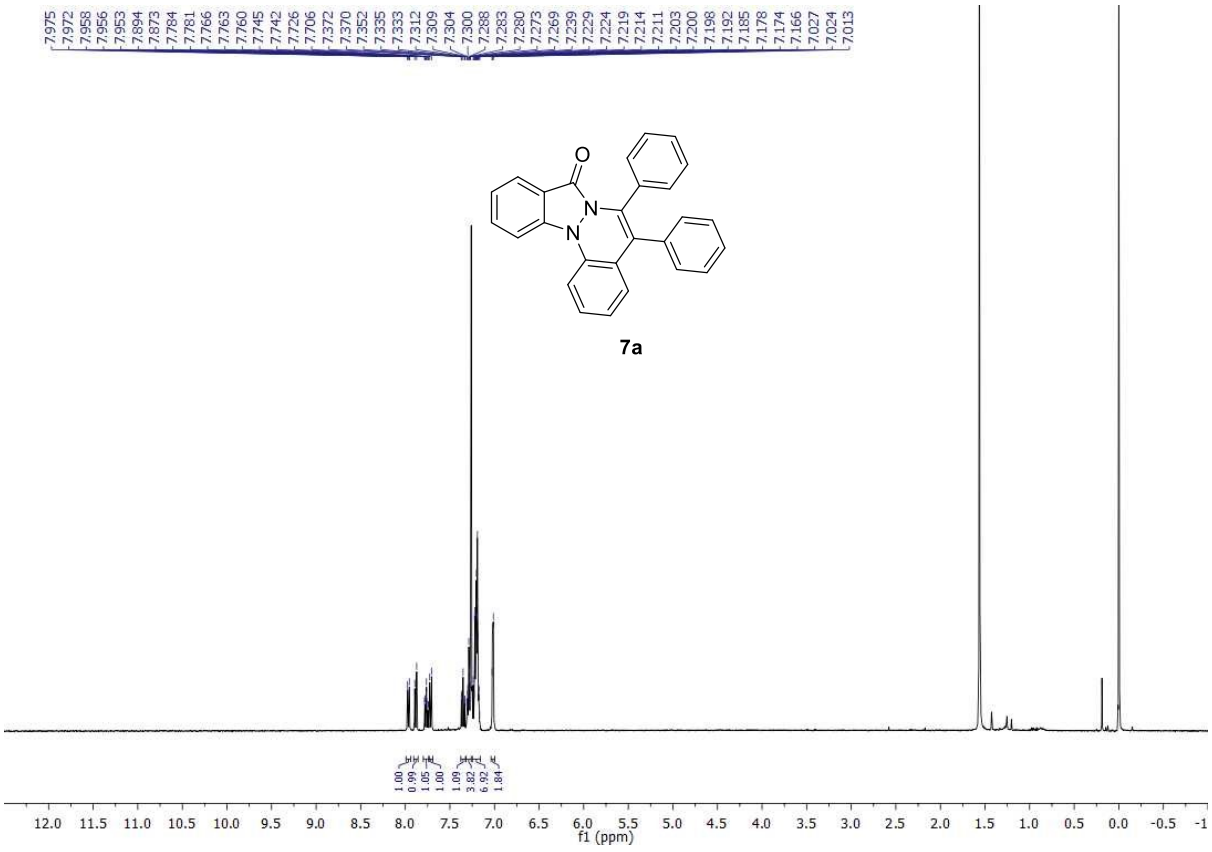
^{13}C NMR Spectrum of Compound 5b in $CDCl_3$



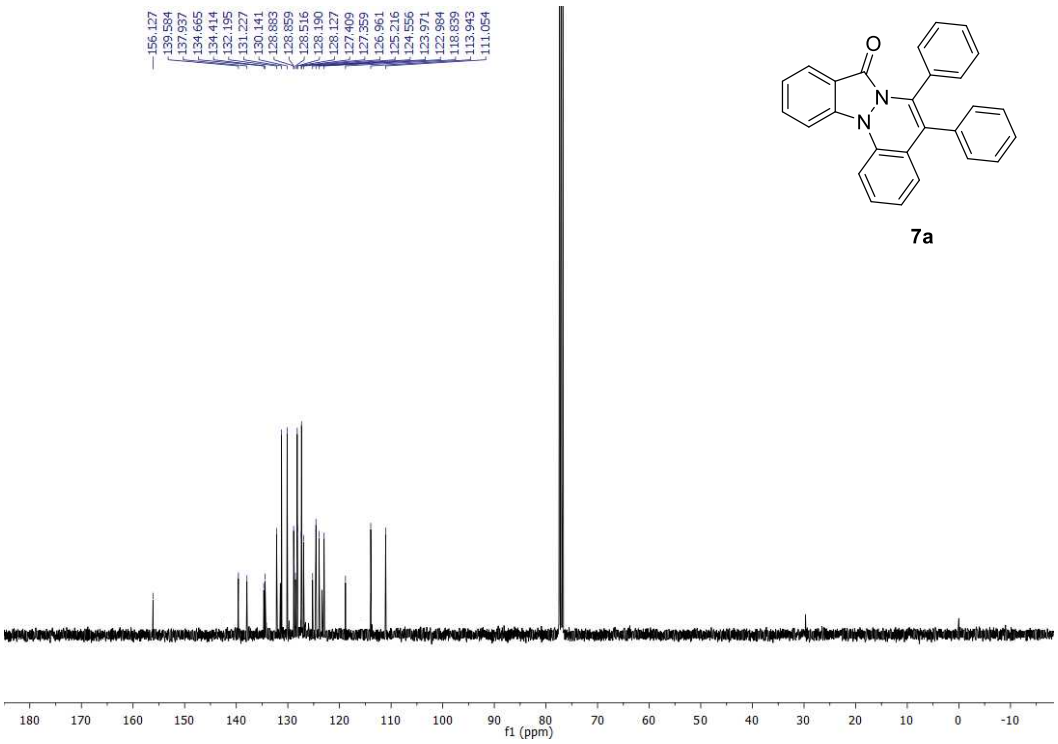
DEPT-135 NMR Spectrum of Compound 5b in $CDCl_3$



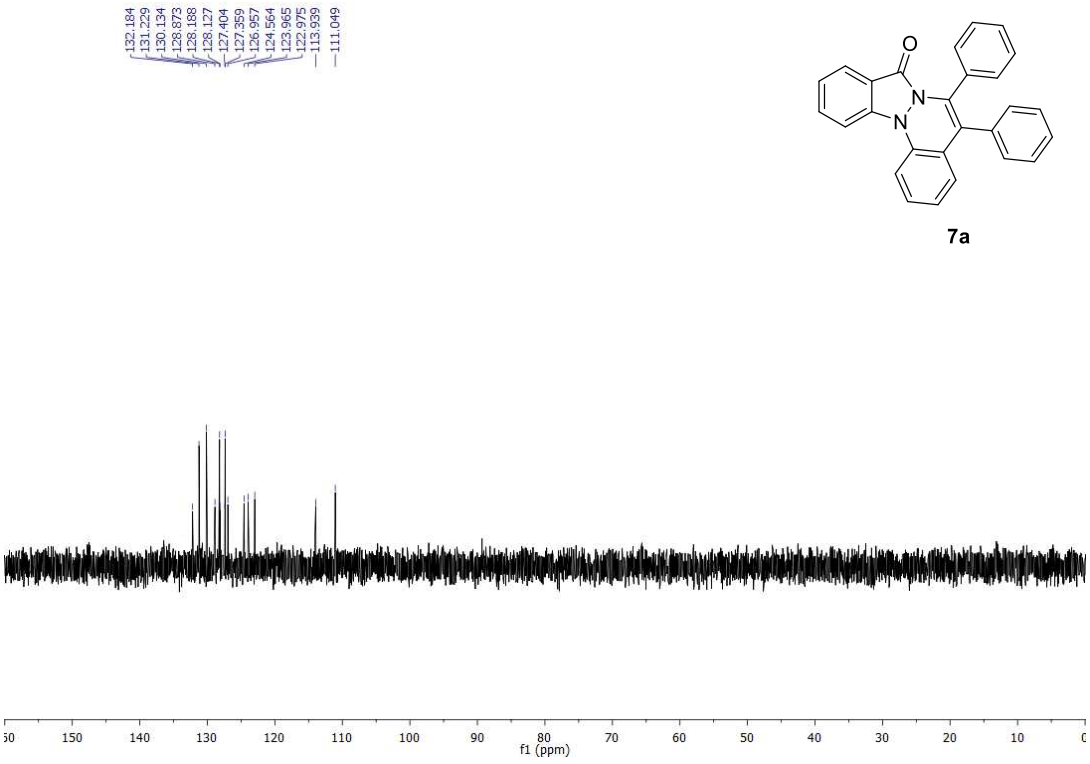
HRMS Spectrum of Compound 5b



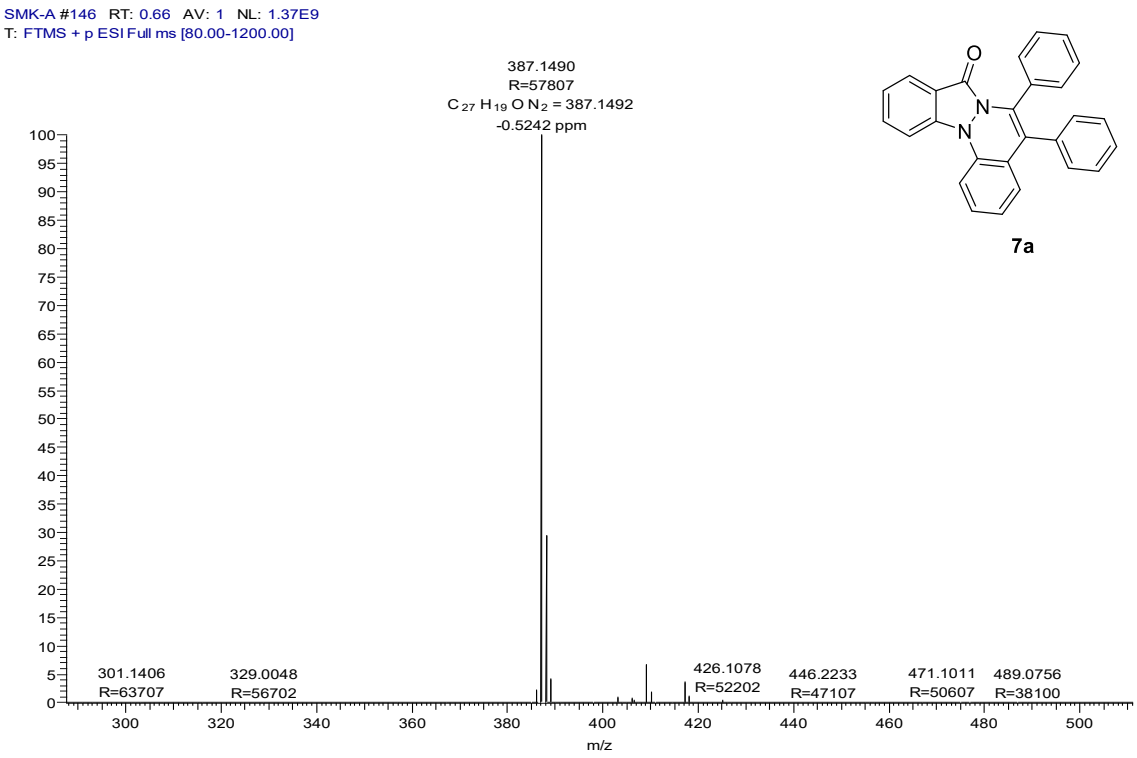
^{1}H NMR Spectrum of Compound 7a in $CDCl_3$



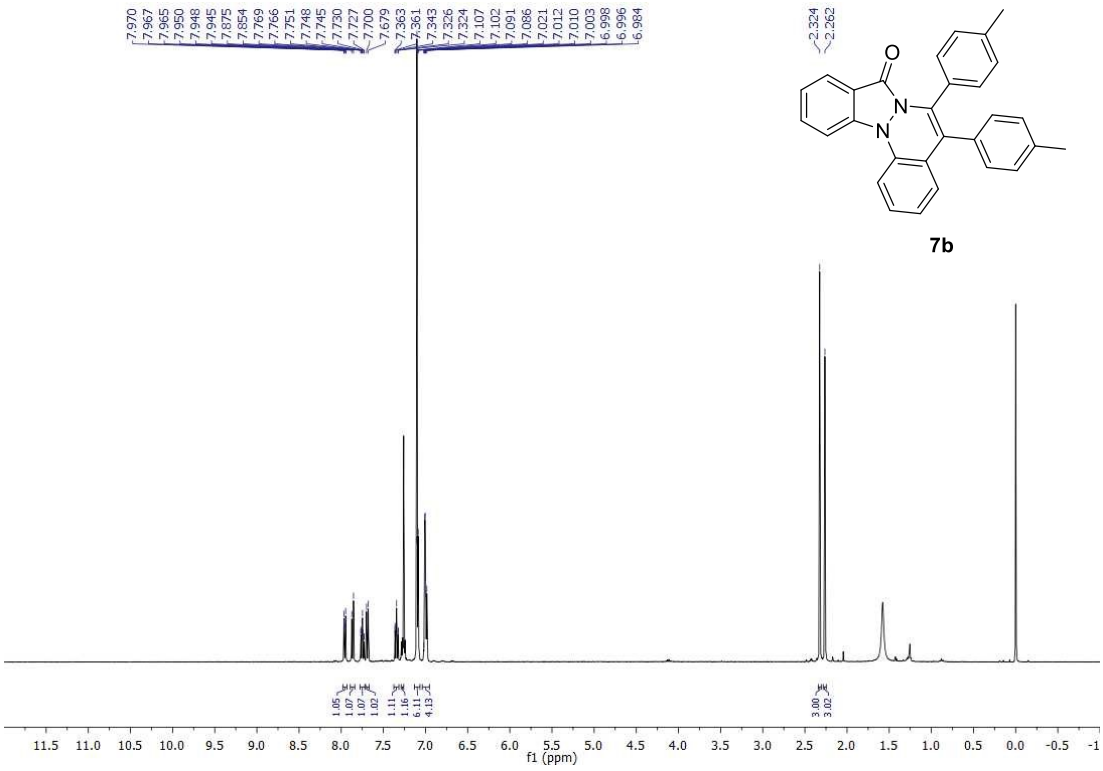
^{13}C NMR Spectrum of Compound 7a in $CDCl_3$



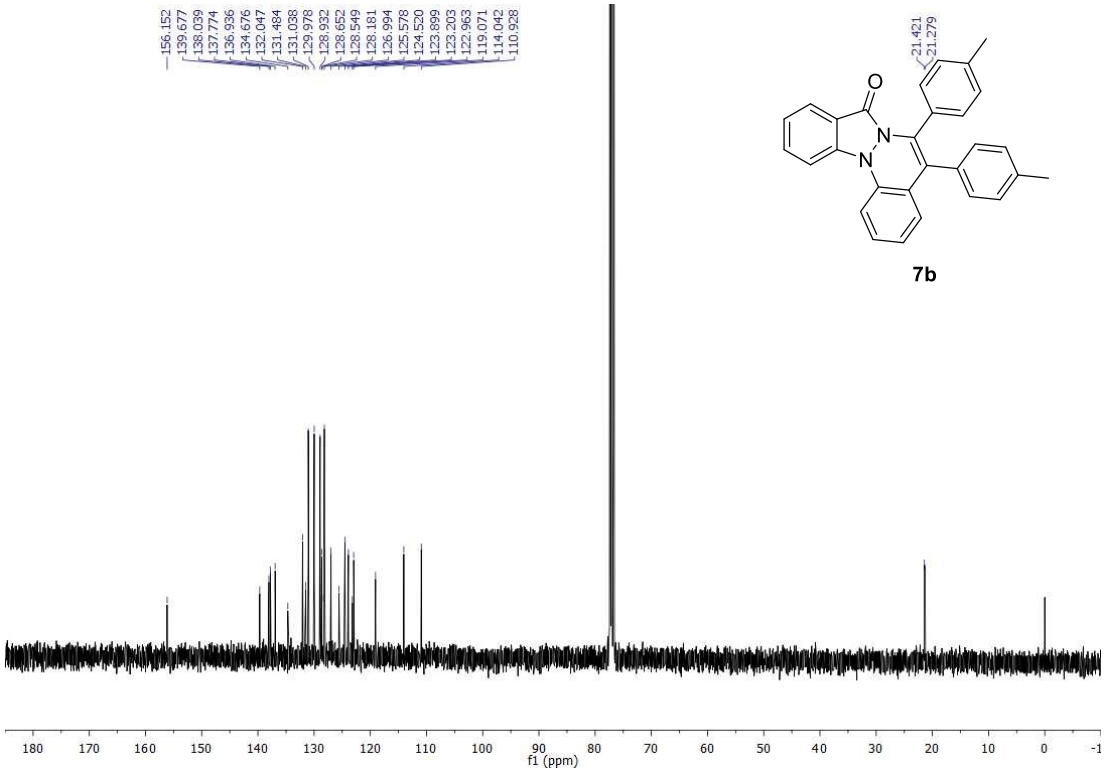
DEPT-135 NMR Spectrum of Compound 7a in $CDCl_3$



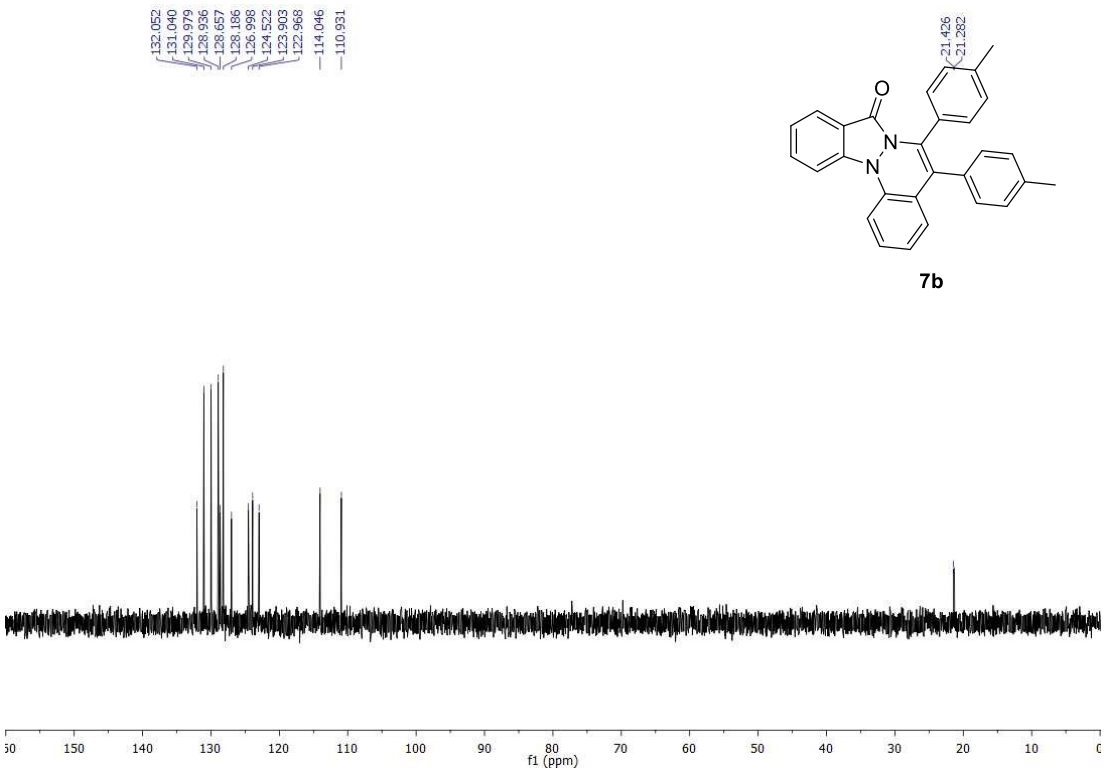
HRMS Spectrum of Compound 7a



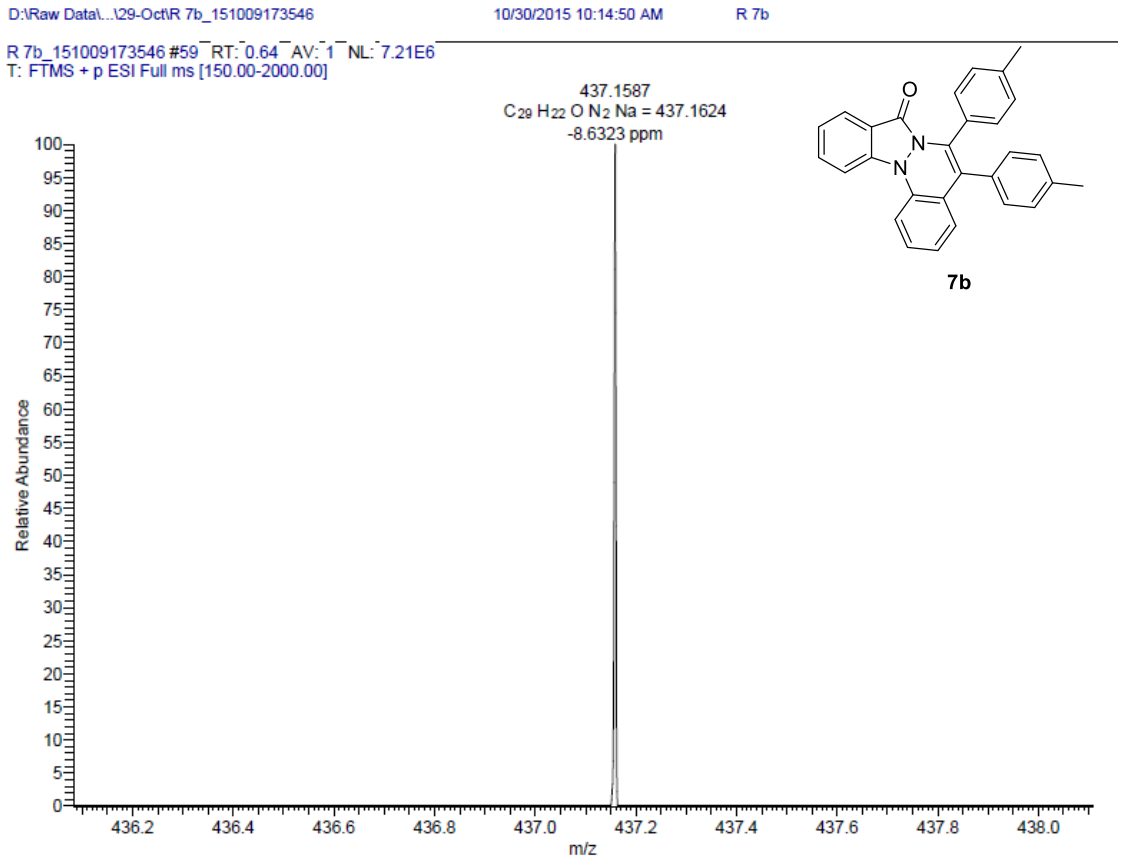
^{1}H NMR Spectrum of Compound 7b in $CDCl_3$



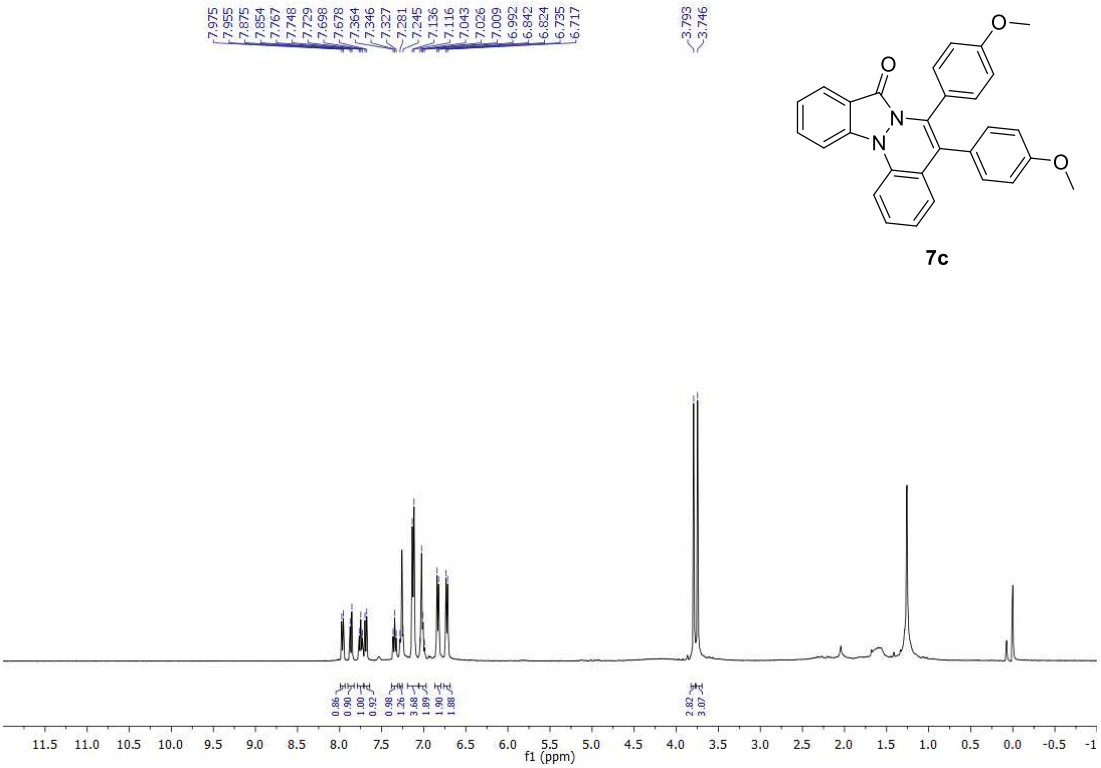
^{13}C NMR Spectrum of Compound 7b in $CDCl_3$



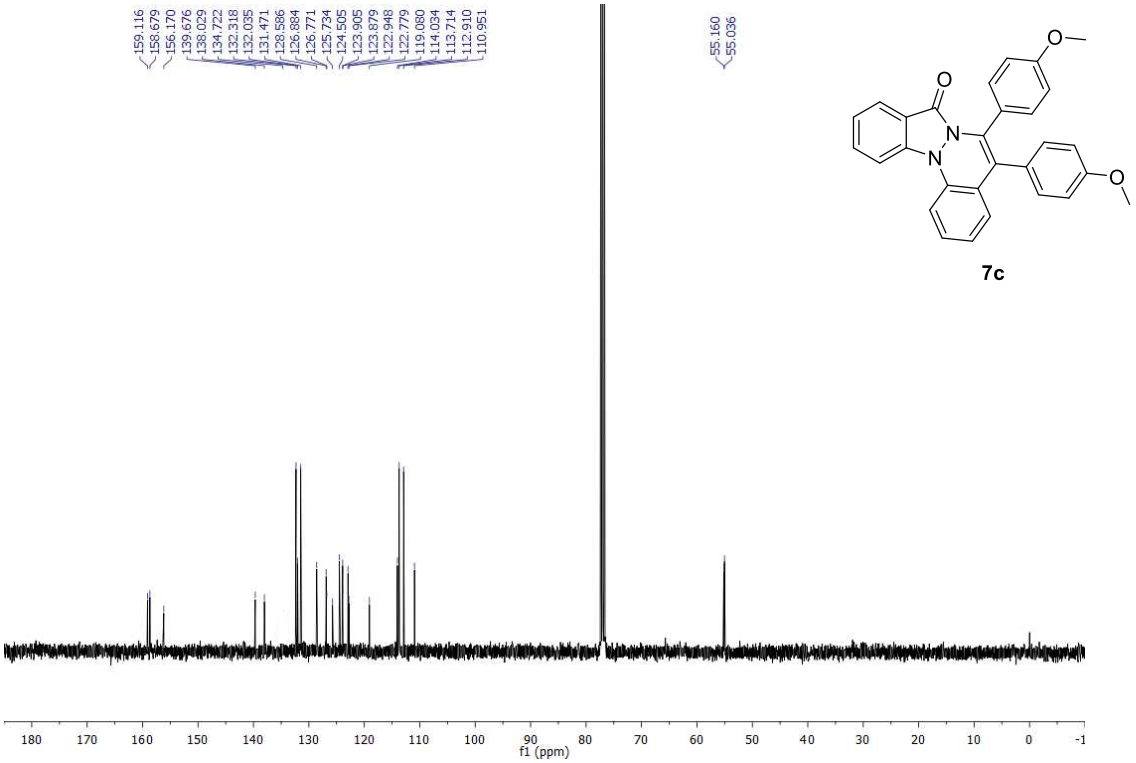
DEPT-135 NMR Spectrum of Compound 7b in $CDCl_3$



HRMS Spectrum of Compound 7b

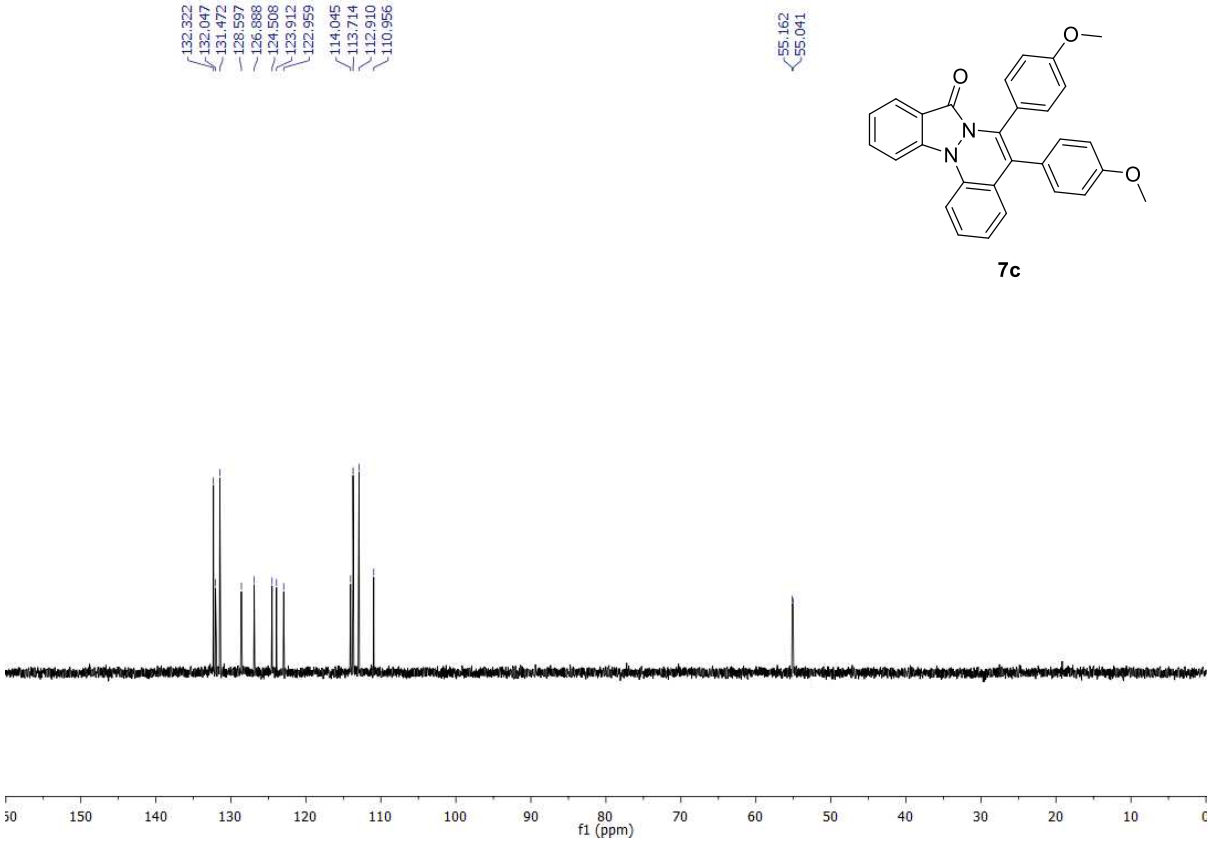


^{1}H NMR Spectrum of Compound 7c in $CDCl_3$



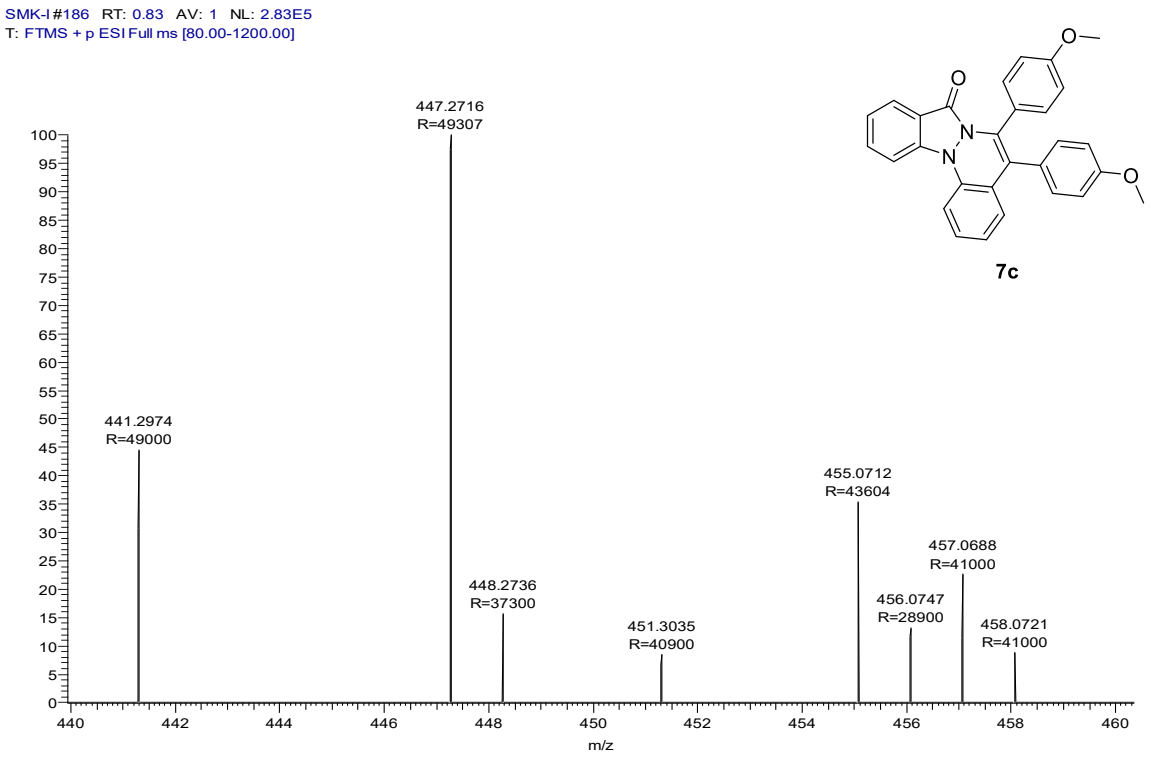
7c

^{13}C NMR Spectrum of Compound 7c in $CDCl_3$



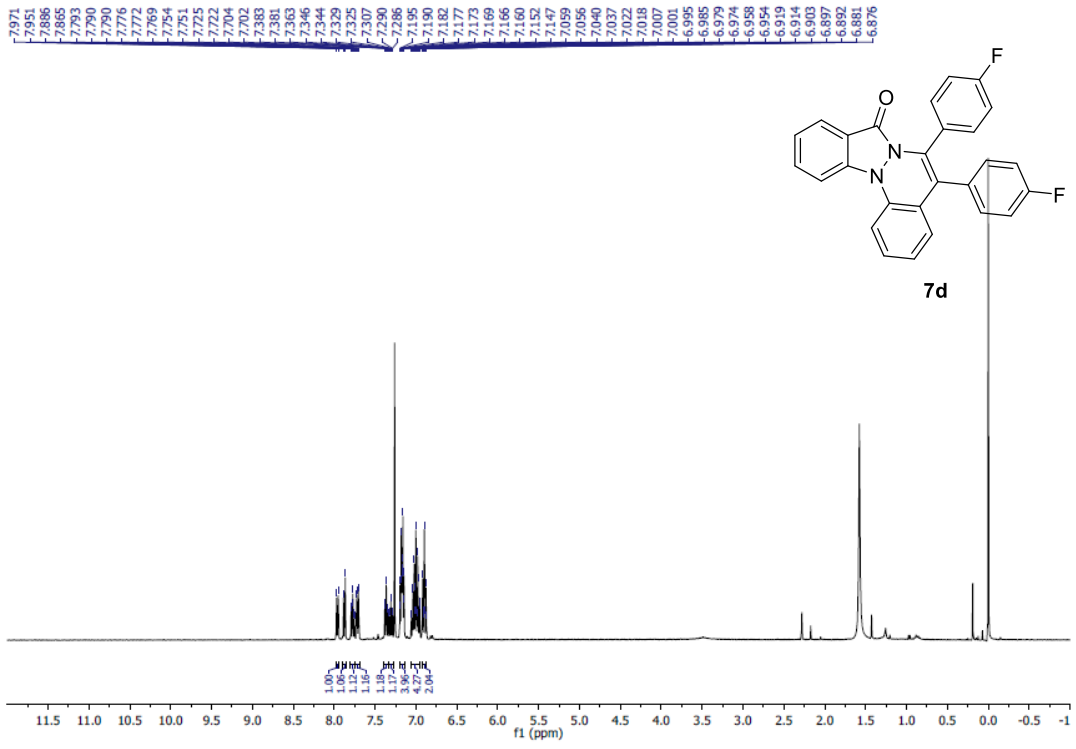
7c

DEPT-135 NMR Spectrum of Compound 7c in $CDCl_3$



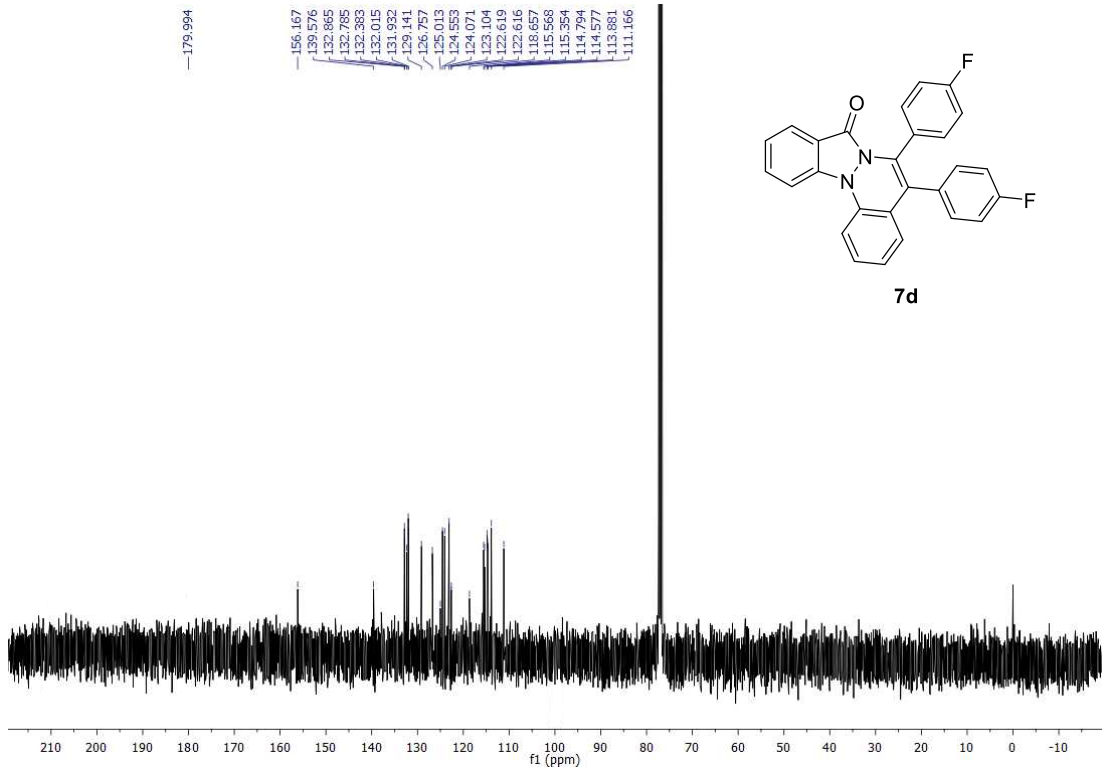
7c

HRMS Spectrum of Compound 7c

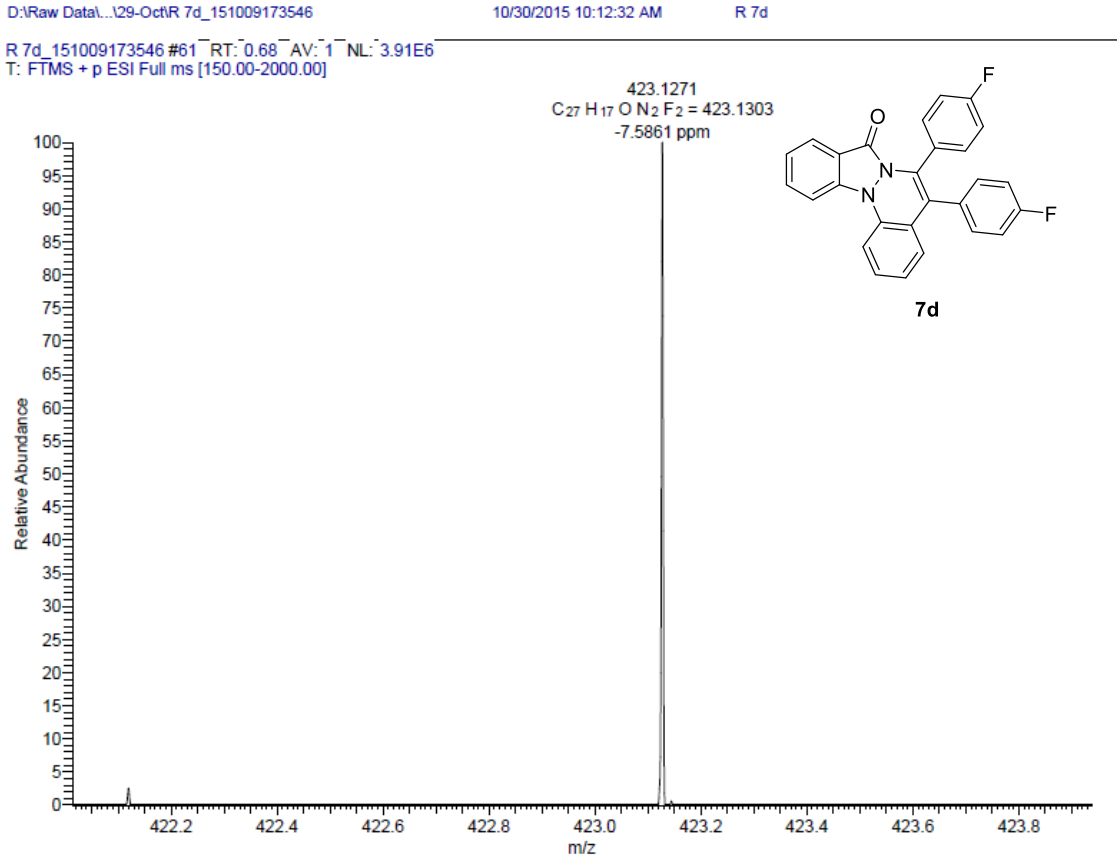


7d

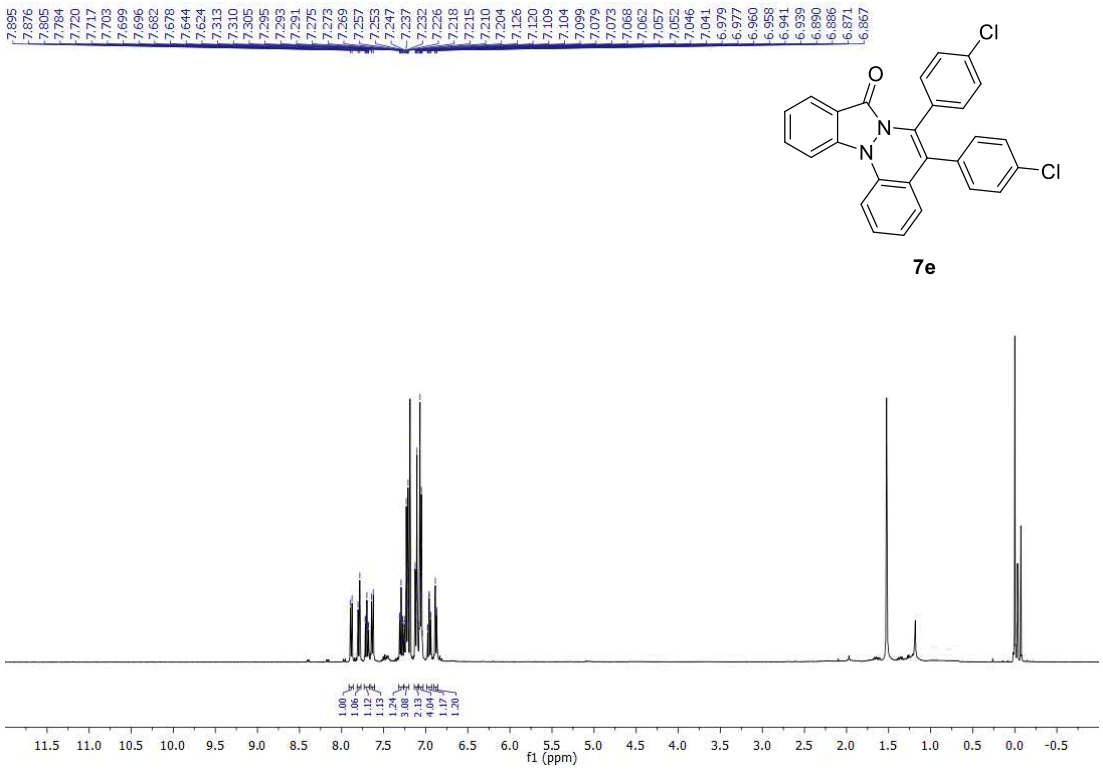
^{1}H NMR Spectrum of Compound 7d in $CDCl_3$



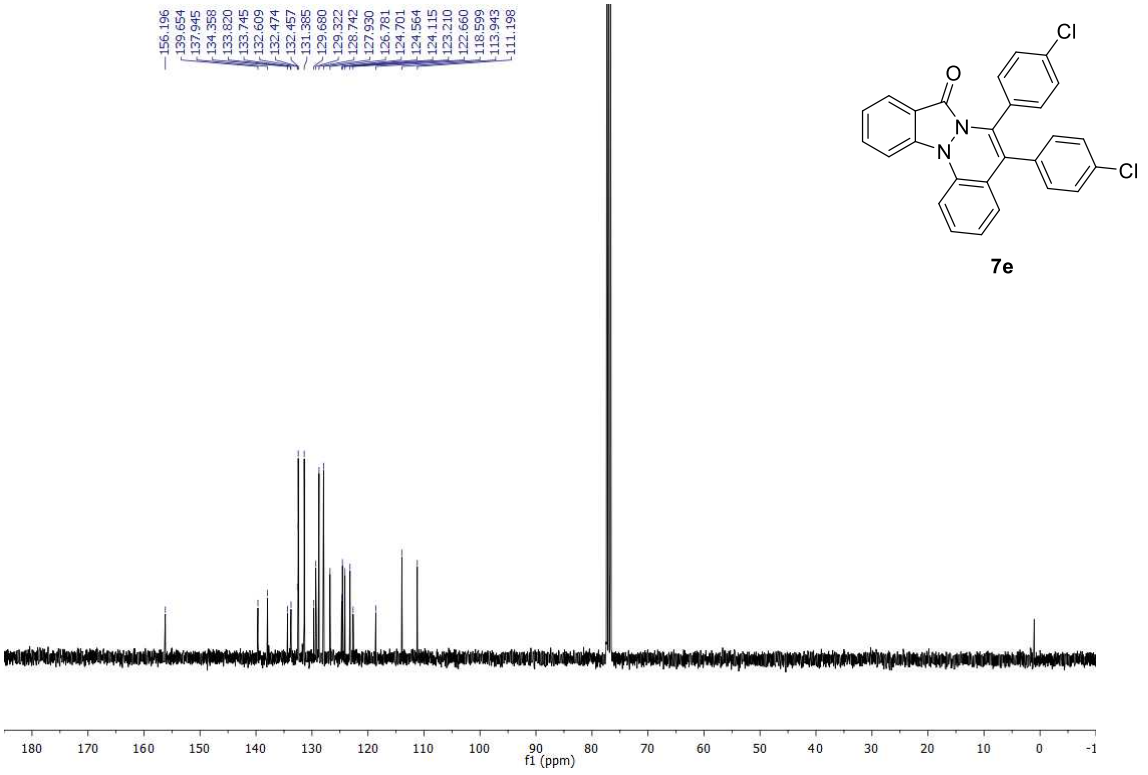
^{13}C NMR Spectrum of Compound 7d in $CDCl_3$



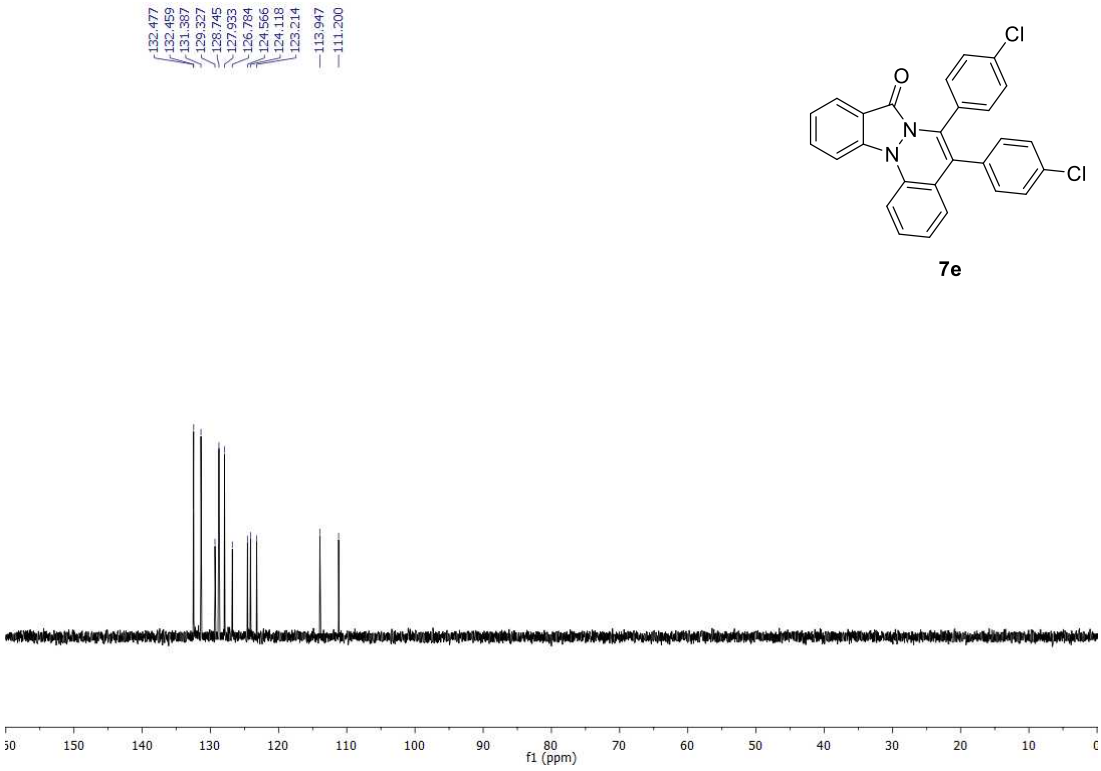
HRMS Spectrum of Compound 7d



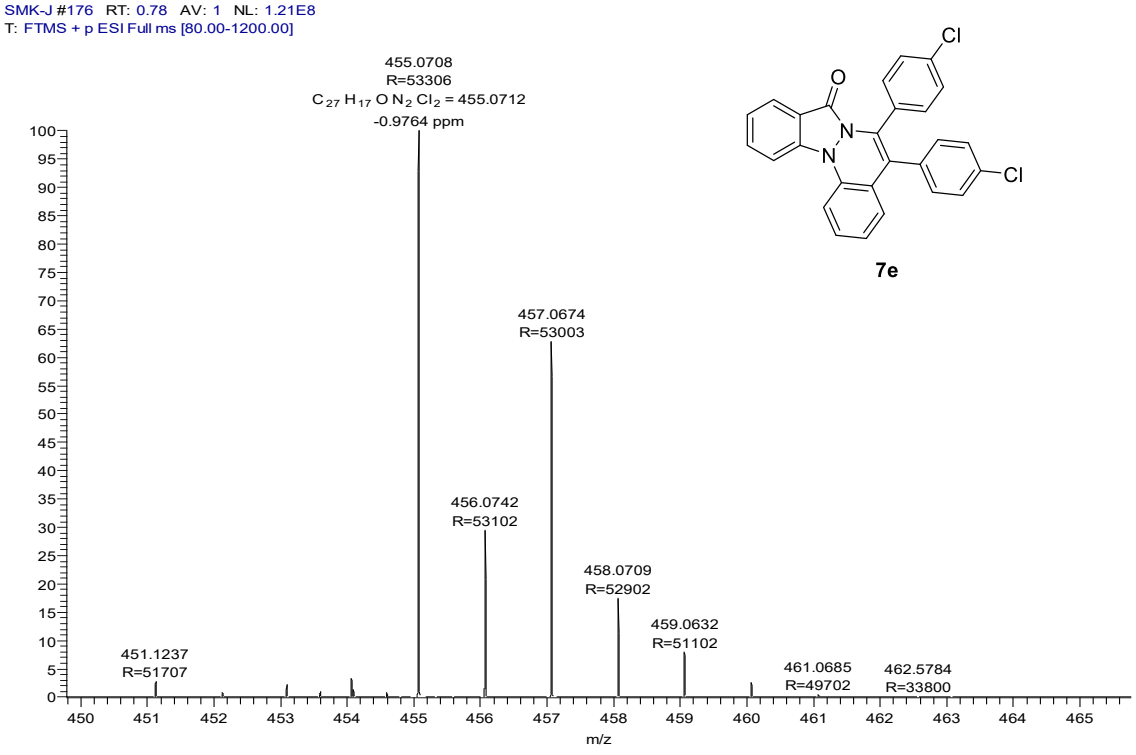
^{1}H NMR Spectrum of Compound 7e in $CDCl_3$



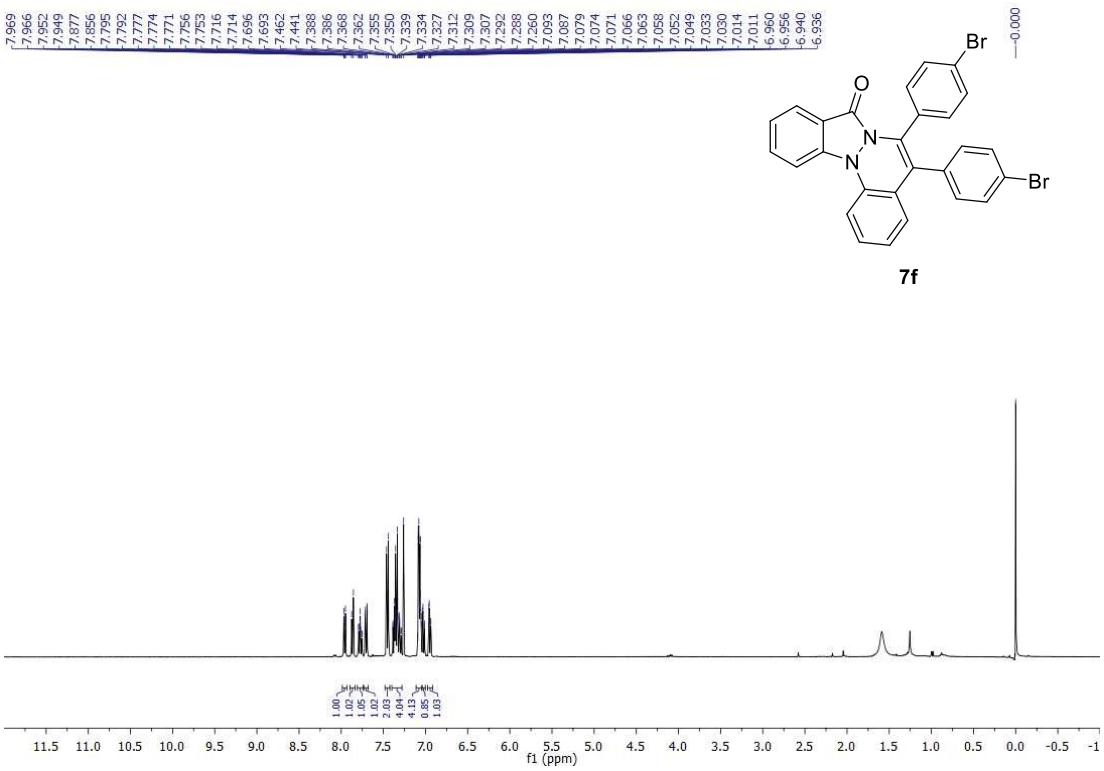
^{13}C NMR Spectrum of Compound 7e in $CDCl_3$



DEPT-135 NMR Spectrum of Compound 7e in $CDCl_3$

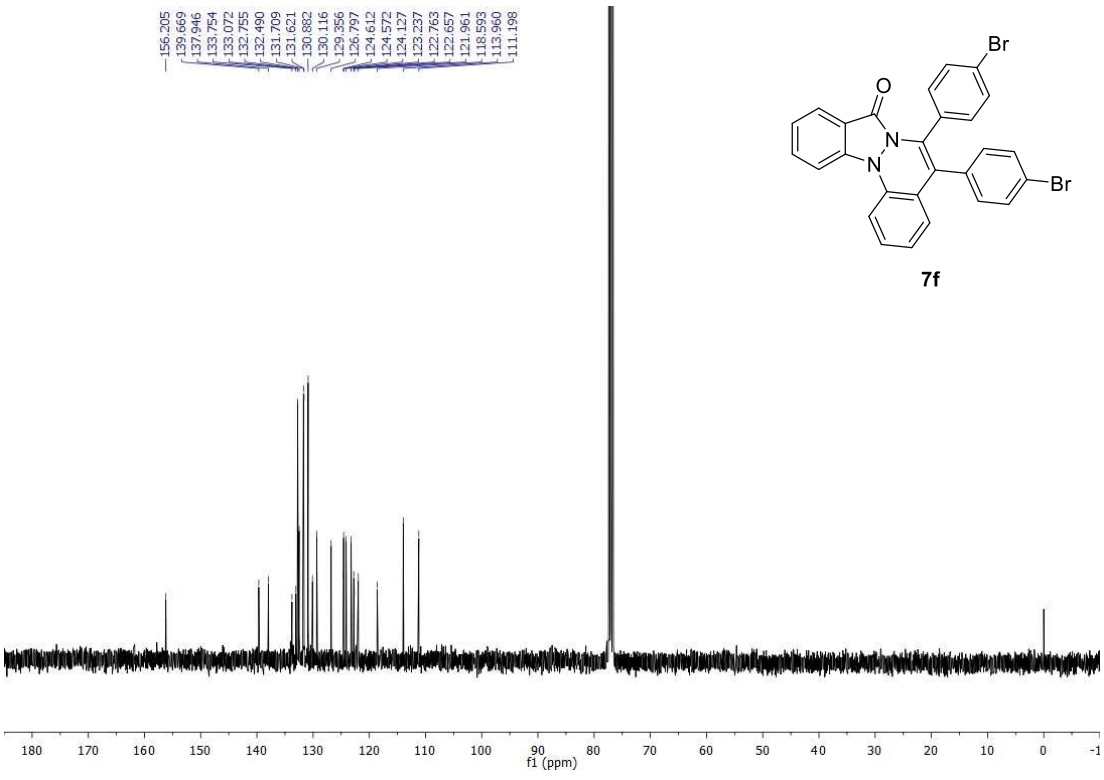


HRMS Spectrum of Compound 7e



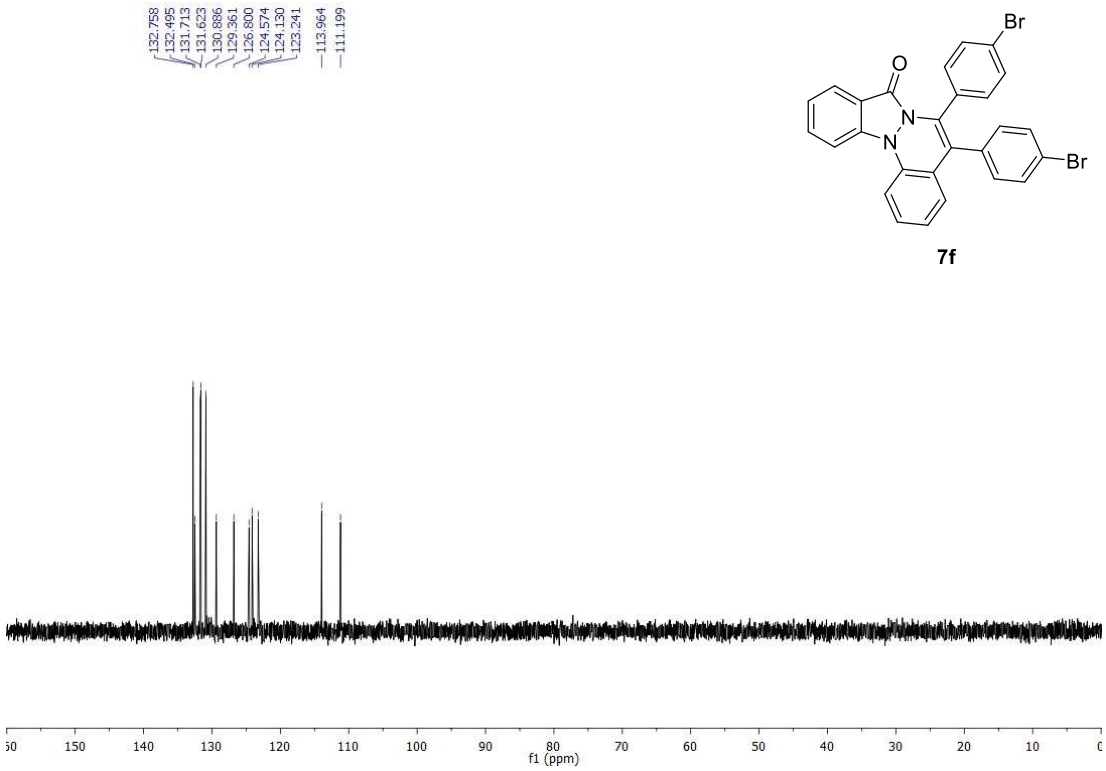
7f

^{1}H NMR Spectrum of Compound 7f in $CDCl_3$

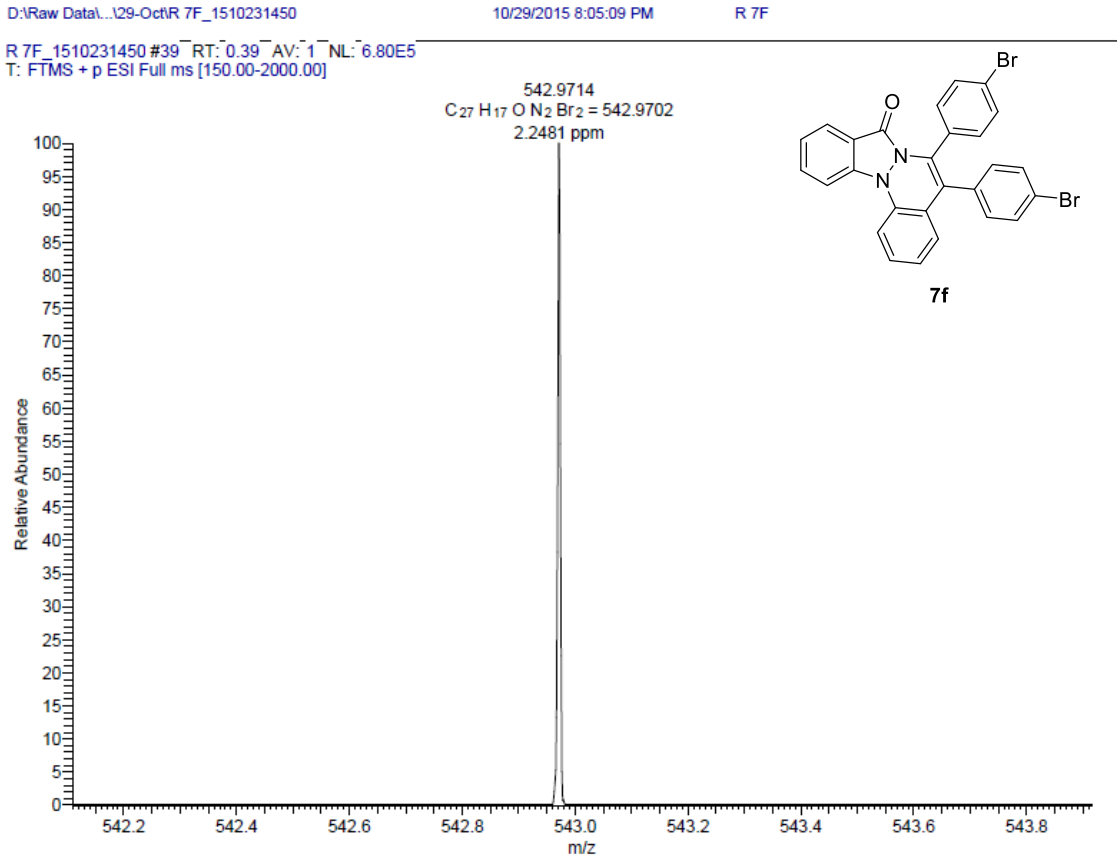


7f

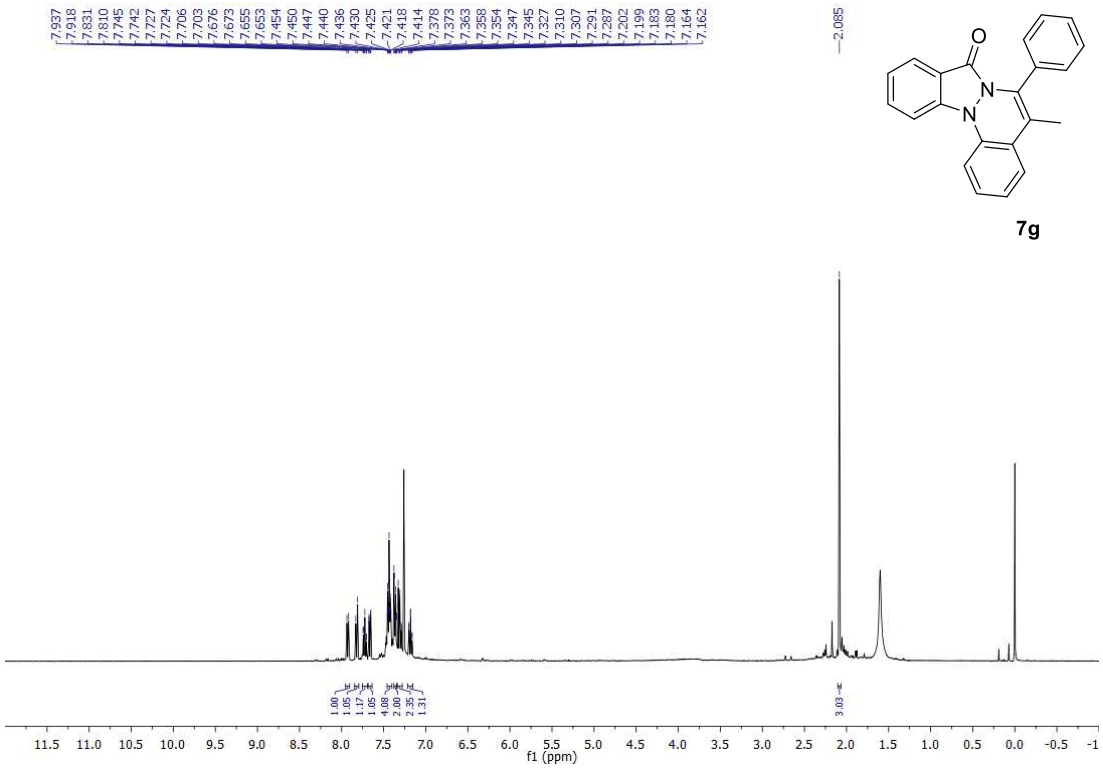
^{13}C NMR Spectrum of Compound 7f in $CDCl_3$



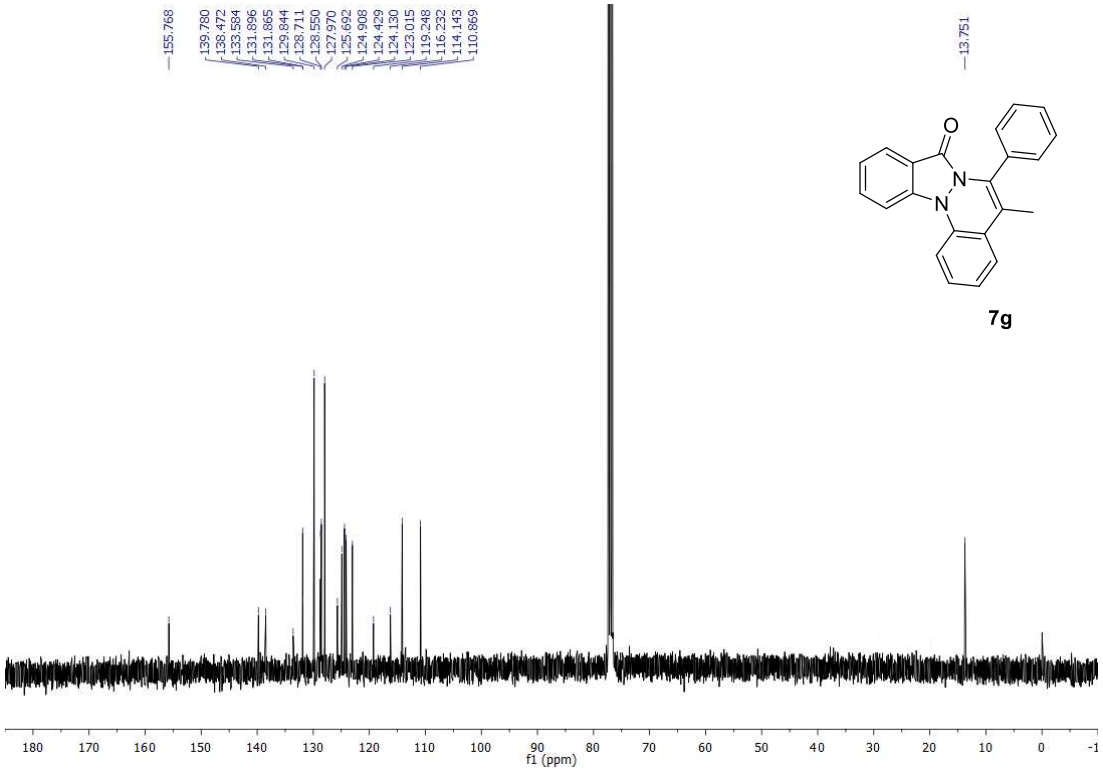
DEPT-135 NMR Spectrum of Compound 7f in $CDCl_3$



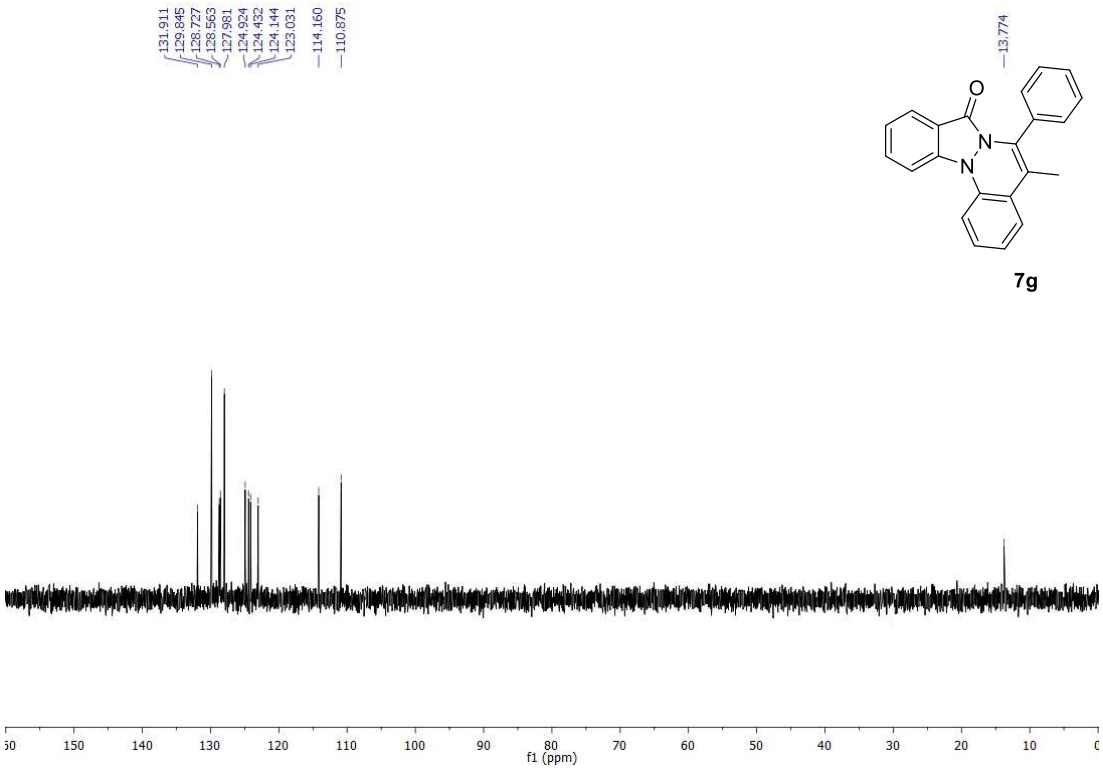
HRMS Spectrum of Compound 7f



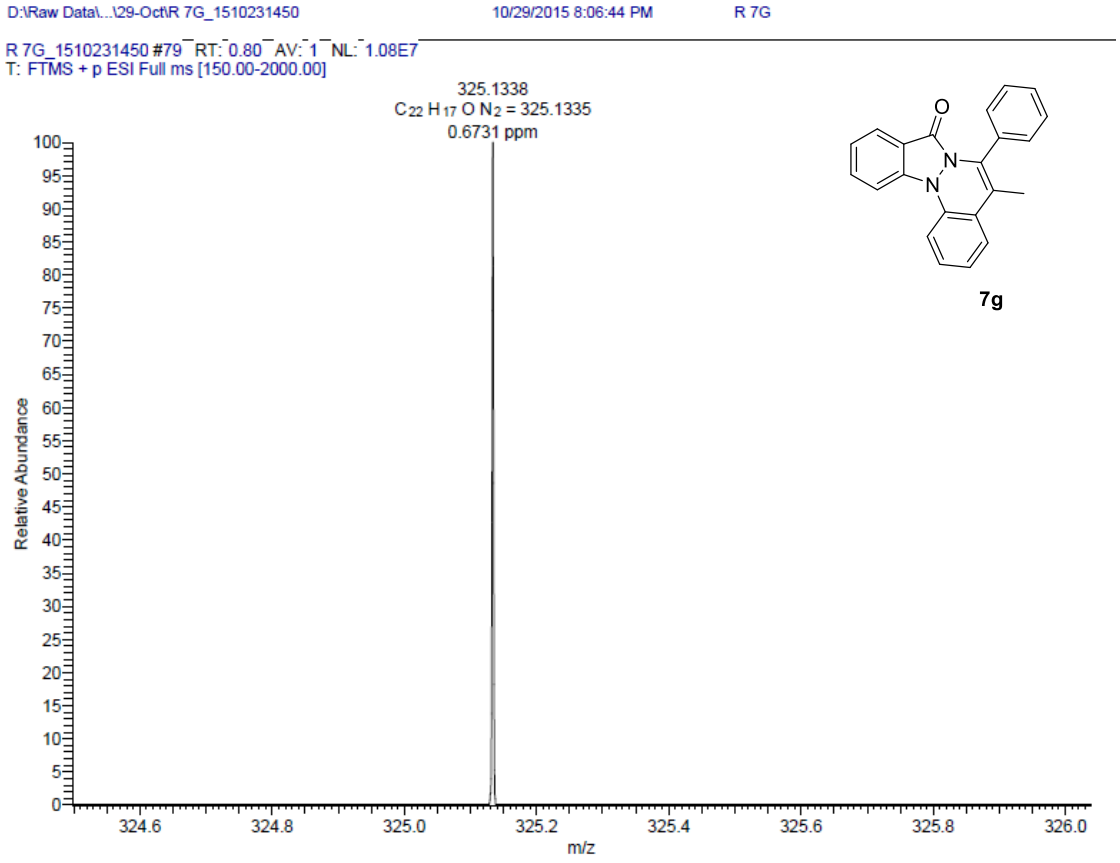
^{1}H NMR Spectrum of Compound 7g in $CDCl_3$



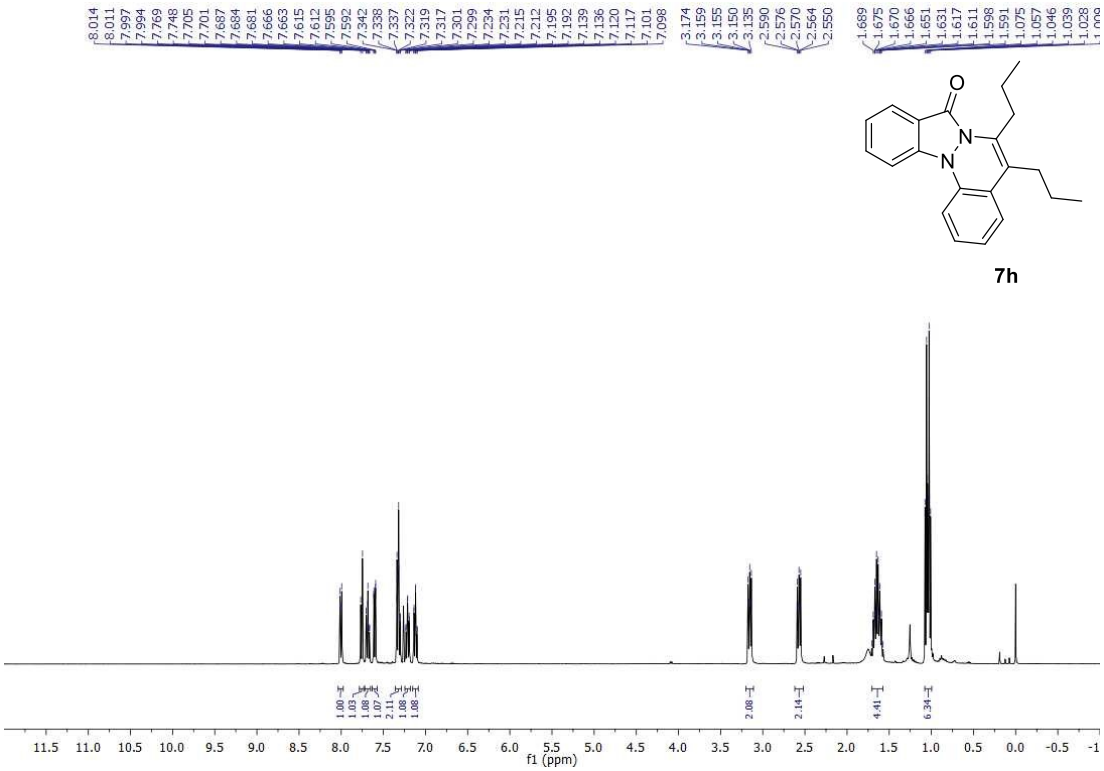
^{13}C NMR Spectrum of Compound 7g in $CDCl_3$



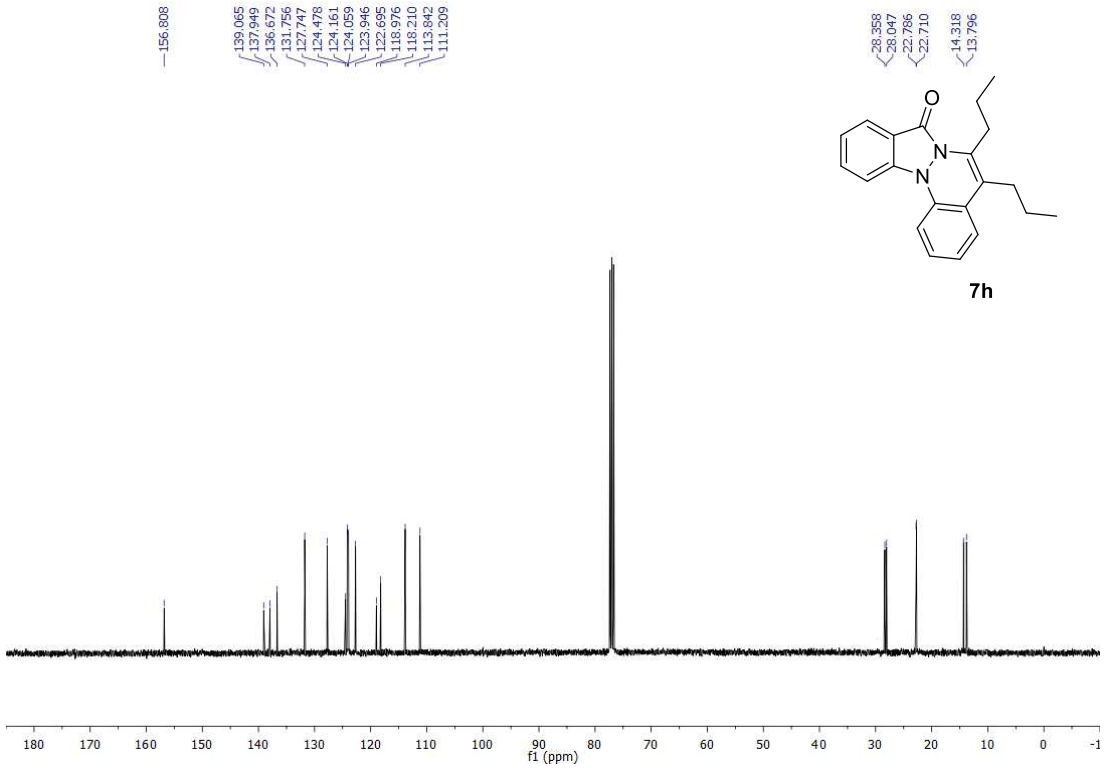
DEPT-135 NMR Spectrum of Compound 7g in $CDCl_3$



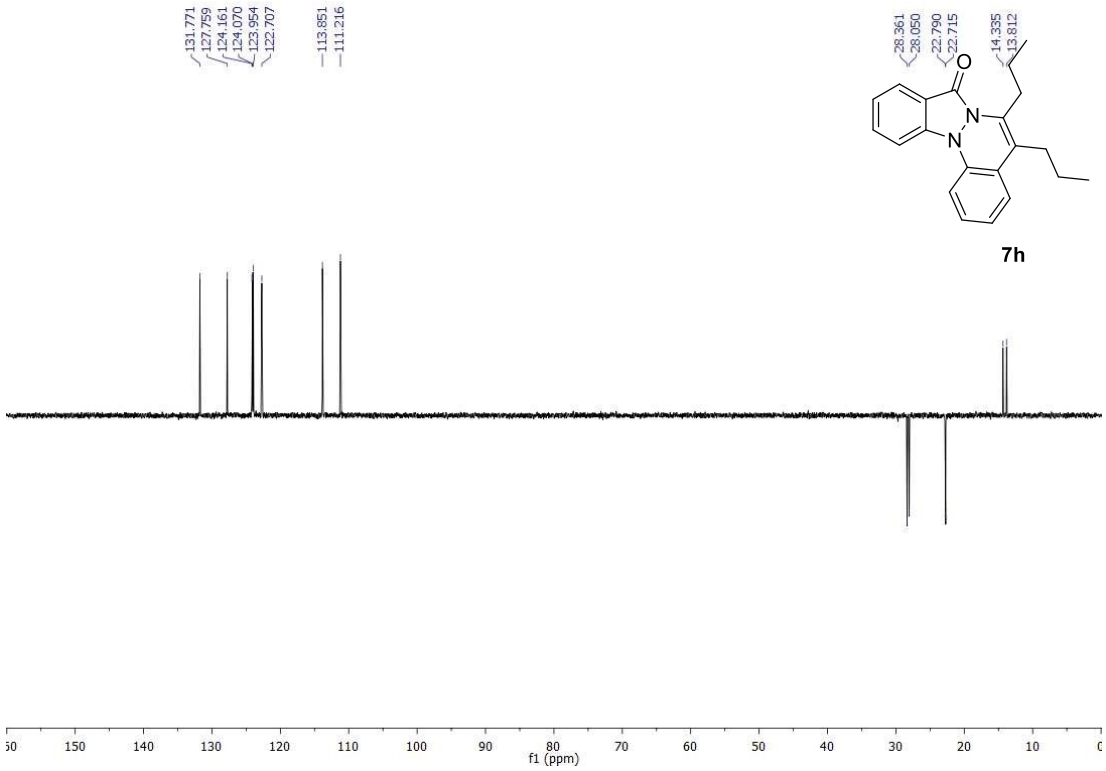
HRMS Spectrum of Compound 7g



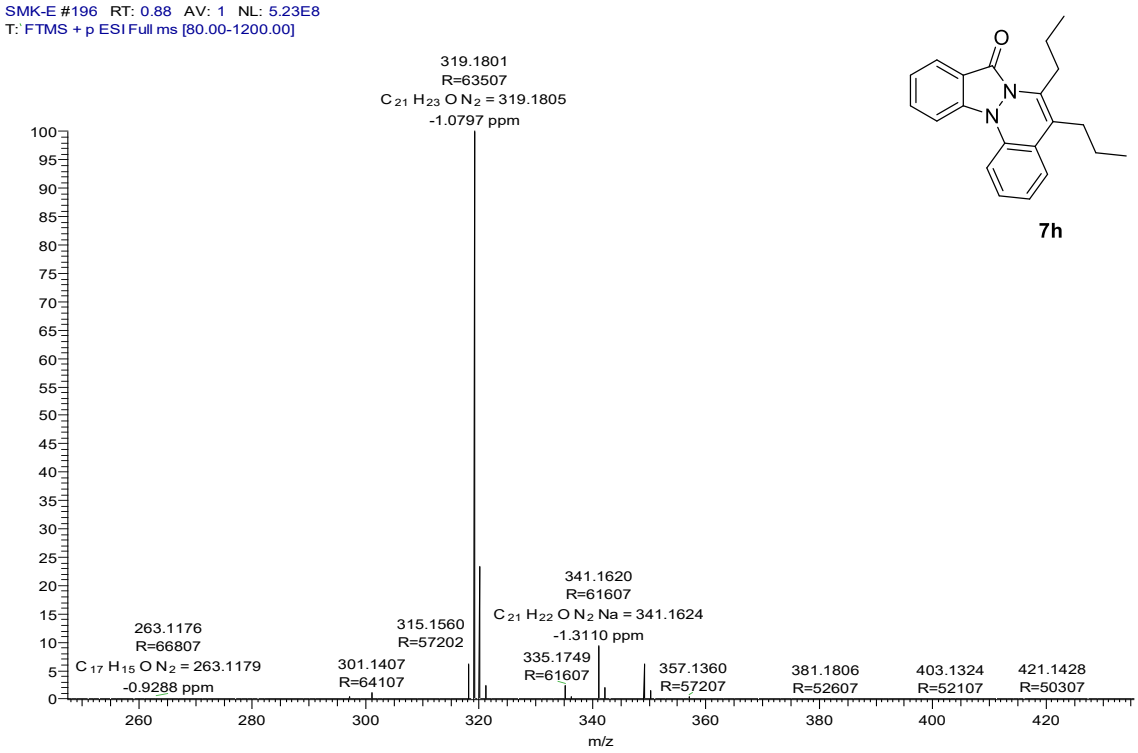
^{1}H NMR Spectrum of Compound 7h in $CDCl_3$



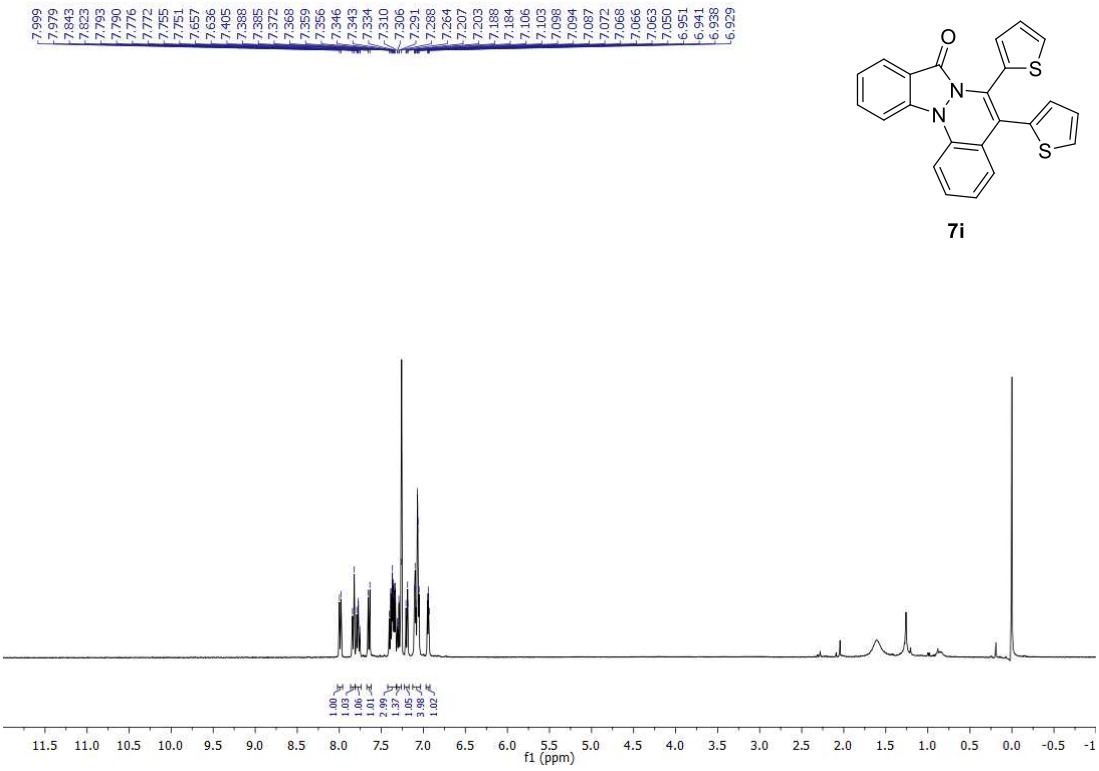
^{13}C NMR Spectrum of Compound 7h in $CDCl_3$



DEPT-135 NMR Spectrum of Compound 7h in $CDCl_3$

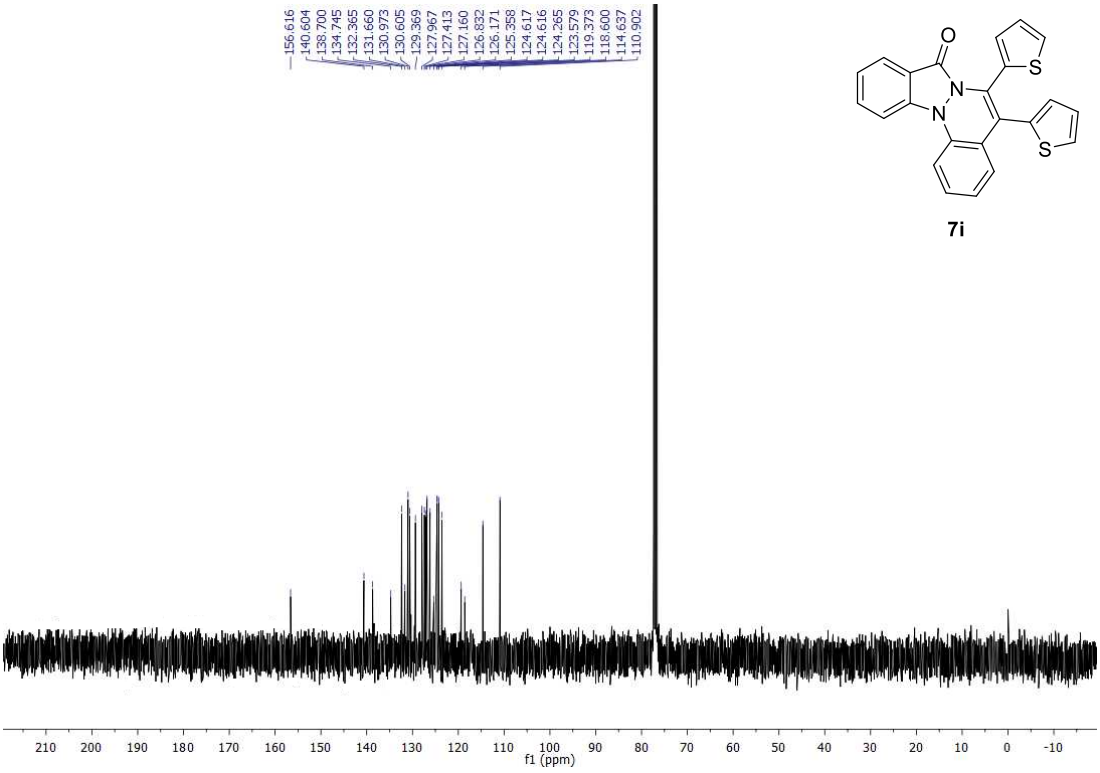


HRMS Spectrum of Compound 7h



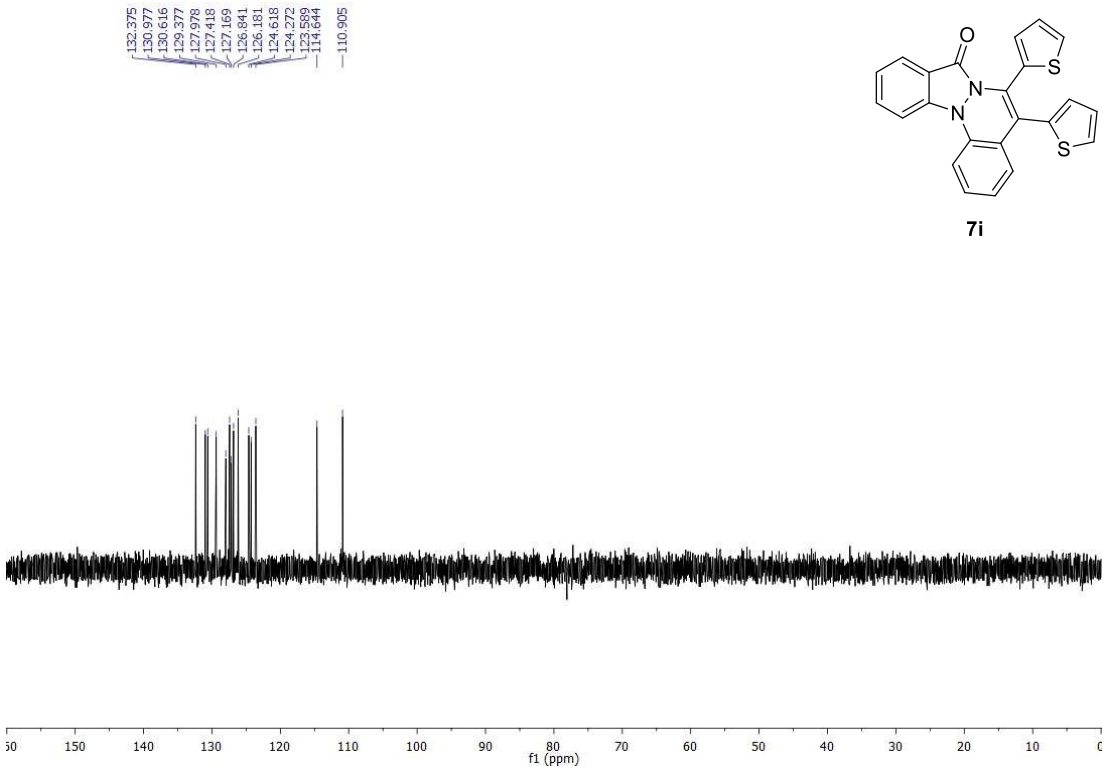
7i

^{1}H NMR Spectrum of Compound 7i in $CDCl_3$



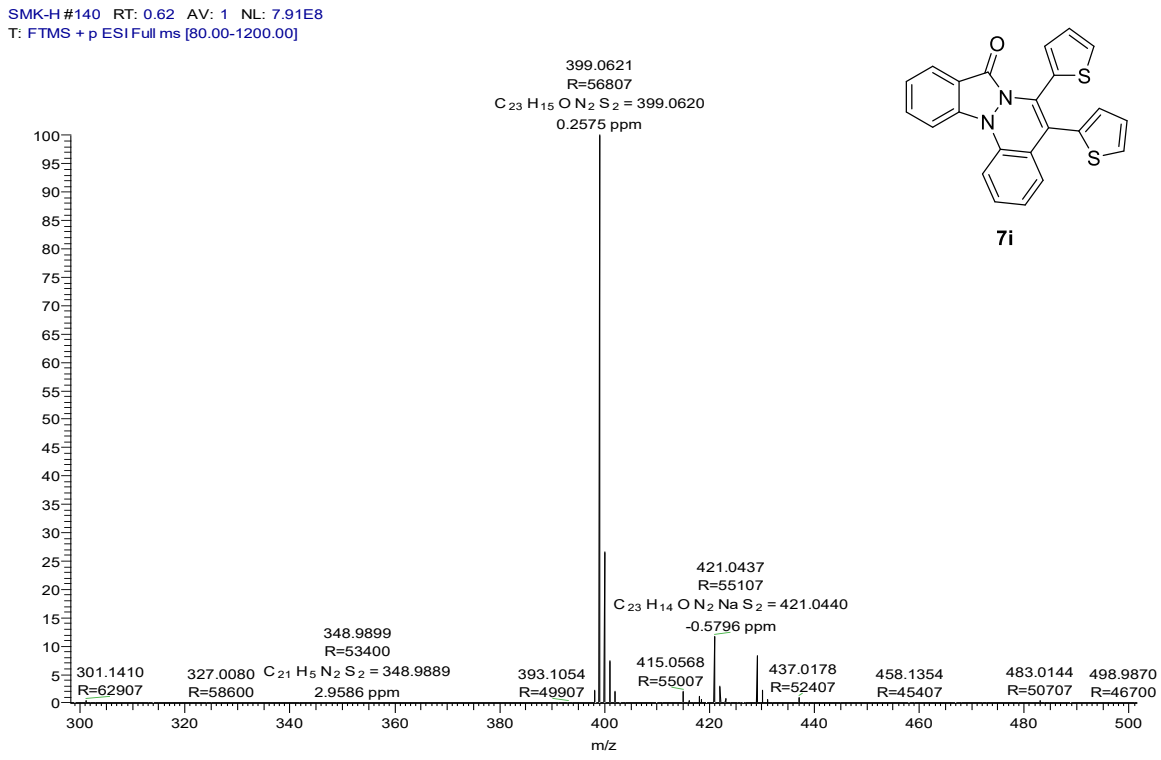
7i

^{13}C NMR Spectrum of Compound 7i in $CDCl_3$



7i

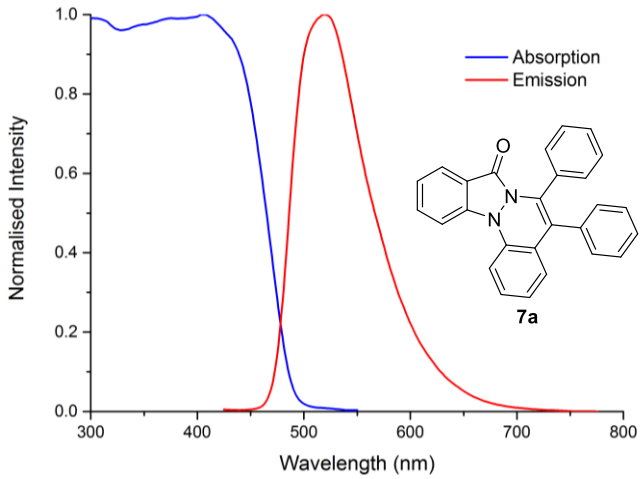
DEPT-135 NMR Spectrum of Compound 7i in $CDCl_3$



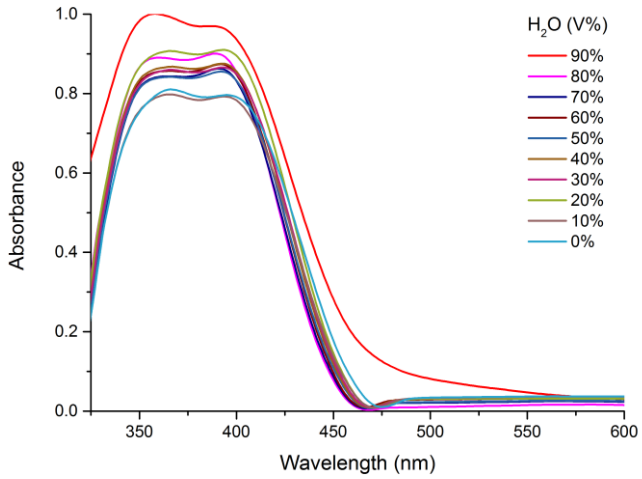
7i

HRMS Spectrum of Compound 7i

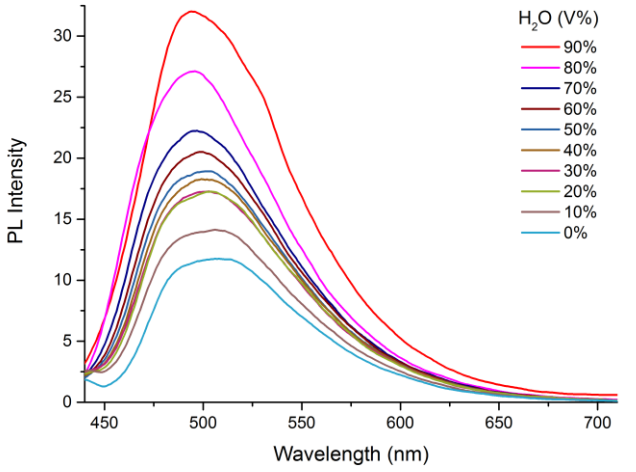
12. UV-vis absorption and PL spectra of 7a-i (in aggregation and thin film state)



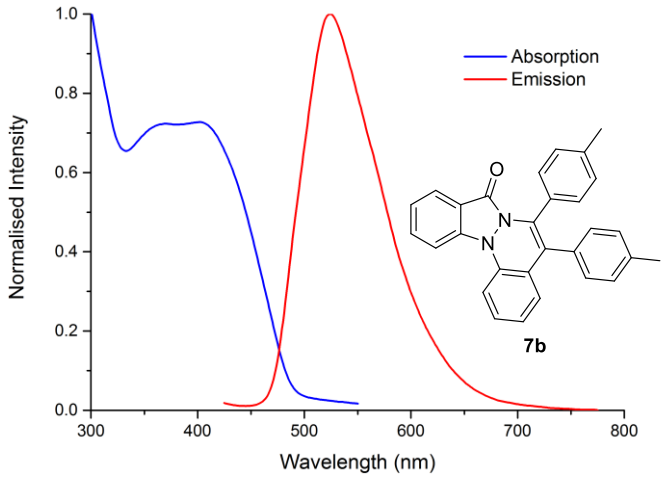
Normalized absorption (blue) and PL (red) spectra of compound **7a** in thin film. (Excitation wavelength: 400 nm)



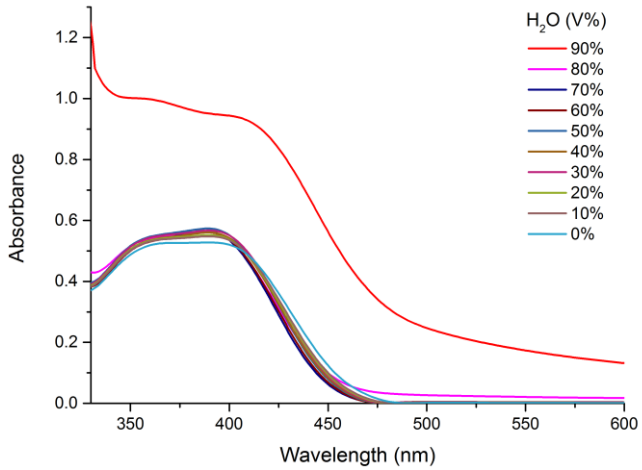
Absorption spectra of **7a** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM.



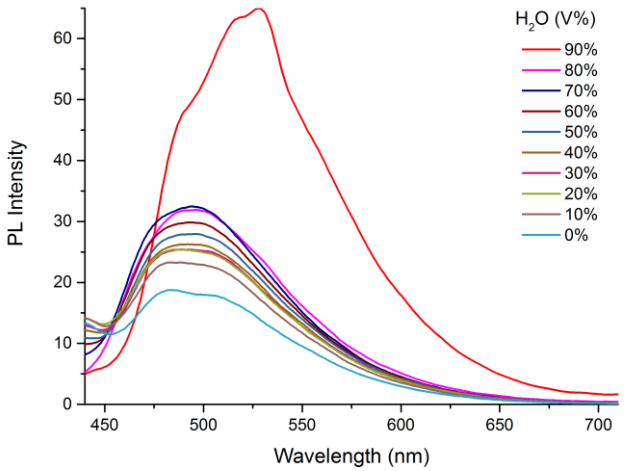
PL spectra of **7a** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM, excitation wavelength: 380 nm.



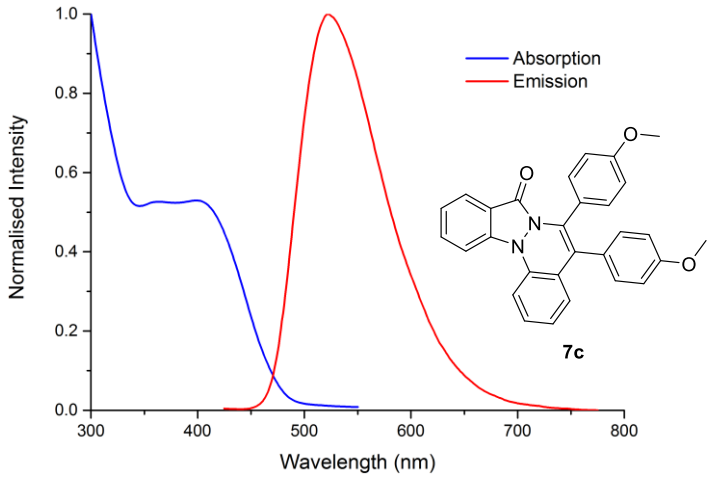
Normalized absorption (blue) and PL (red) spectra of compound **7b** in thin film. (Excitation wavelength: 400 nm)



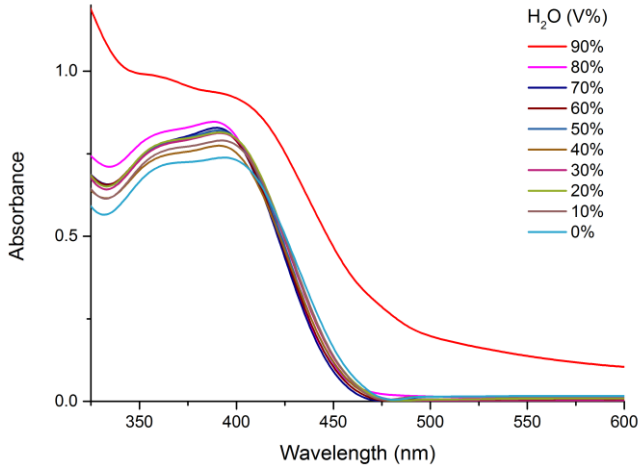
Absorption spectra of **7b** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM.



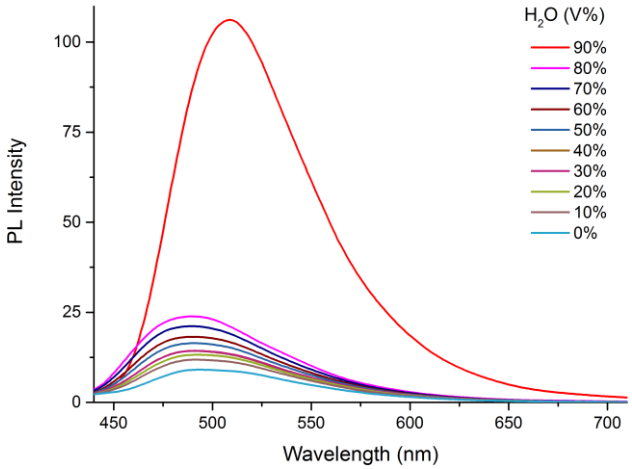
PL spectra of **7b** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM, excitation wavelength: 400 nm.



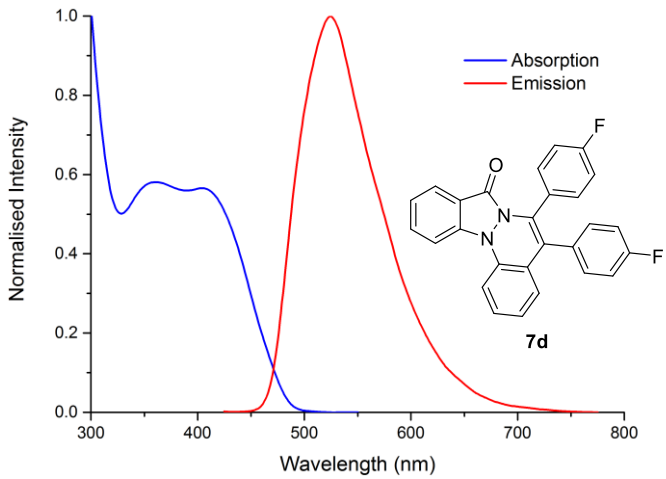
Normalized absorption (blue) and PL (red) spectra of compound **7c** in thin film. (Excitation wavelength: 400 nm)



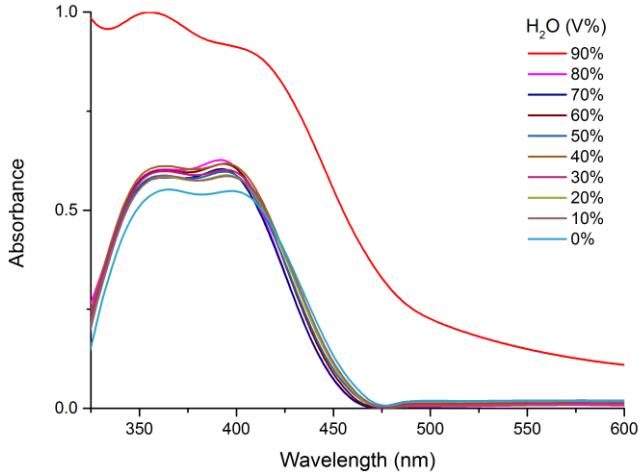
Absorption spectra of **7c** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM.



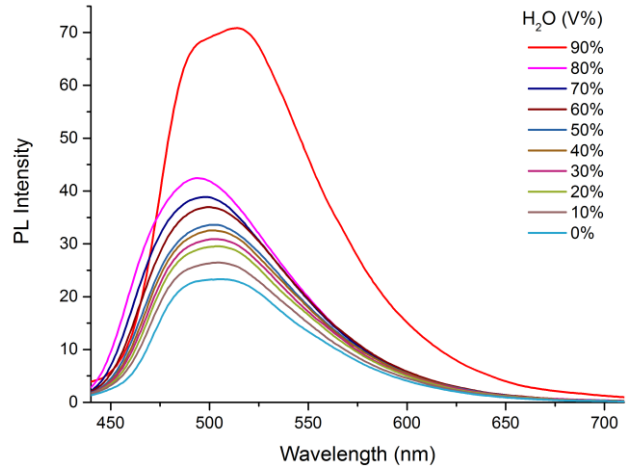
PL spectra of **7c** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM, excitation wavelength: 400 nm.



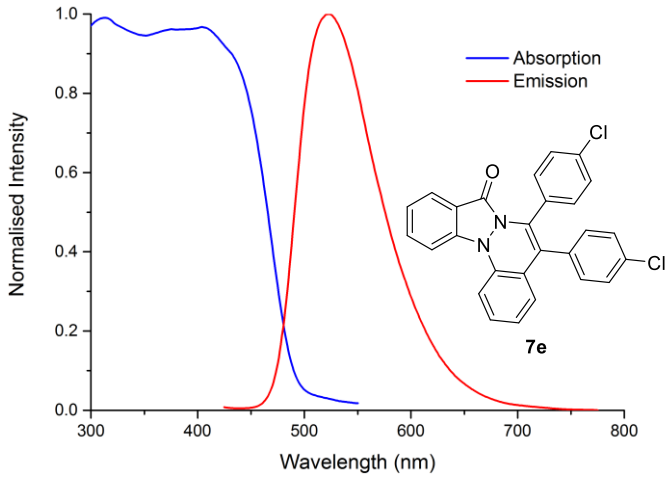
Normalized absorption (blue) and PL (red) spectra of compound **7d** in thin film. (Excitation wavelength: 400 nm)



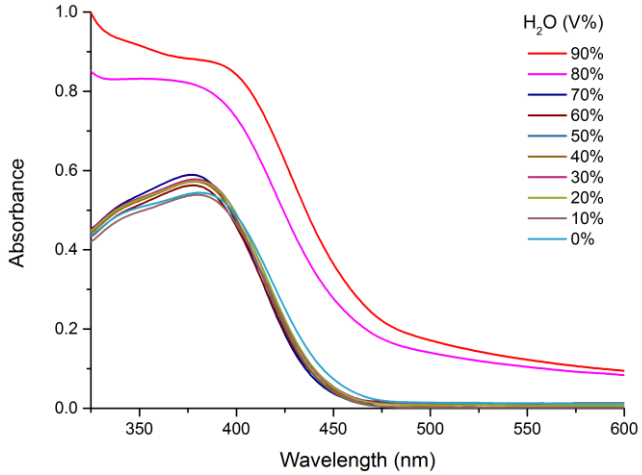
Absorption spectra of **7d** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM.



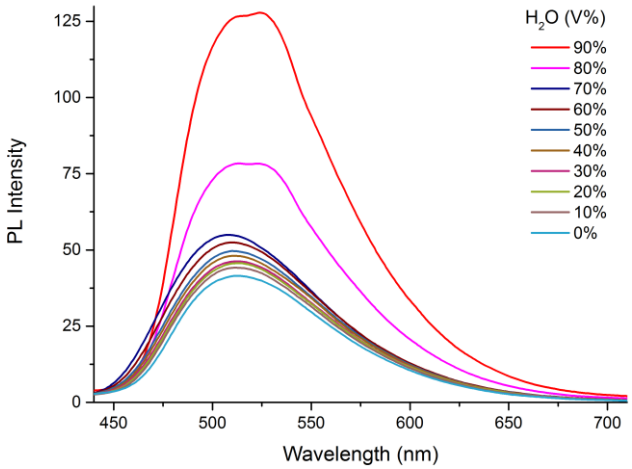
PL spectra of **7d** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM, excitation wavelength: 400 nm.



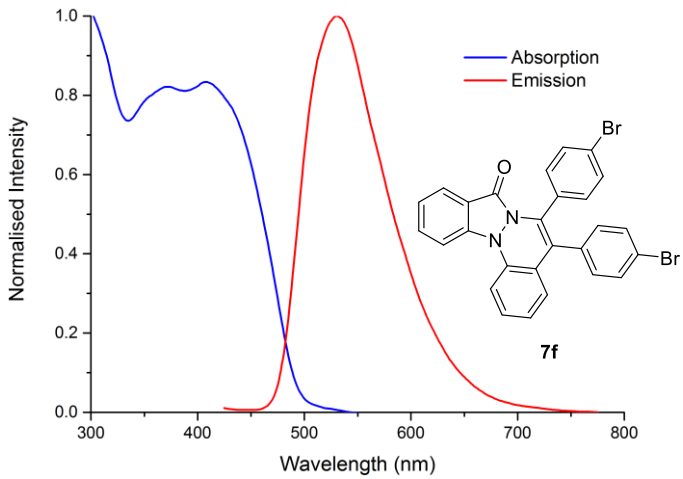
Normalized absorption (blue) and PL (red) spectra of compound **7e** in thin film. (Excitation wavelength: 400 nm)



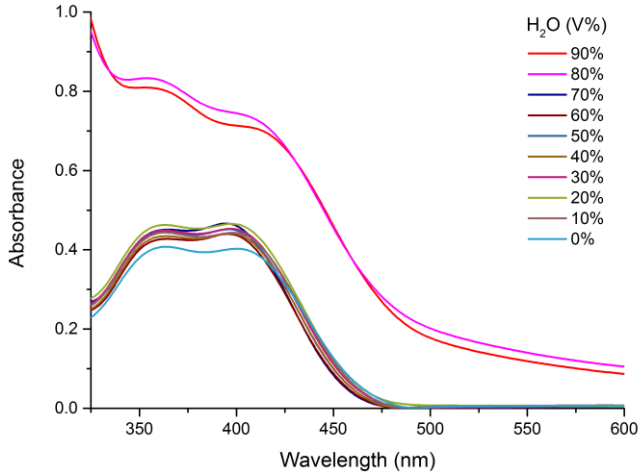
Absorption spectra of **7e** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM.



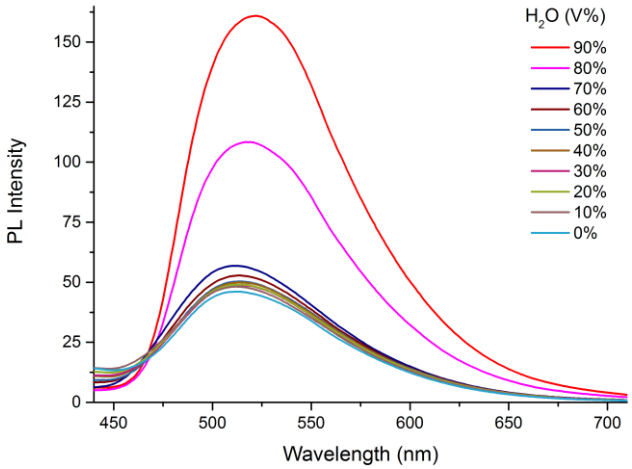
PL spectra of **7e** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM, excitation wavelength: 380 nm.



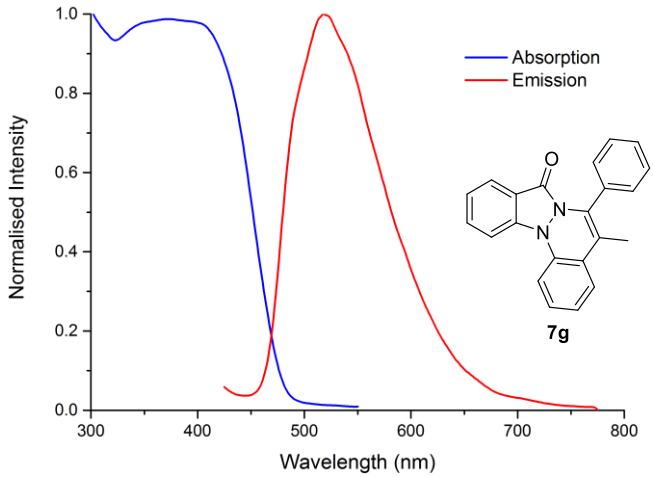
Normalized absorption (blue) and PL (red) spectra of compound **7f** in thin film. (Excitation wavelength: 400 nm)



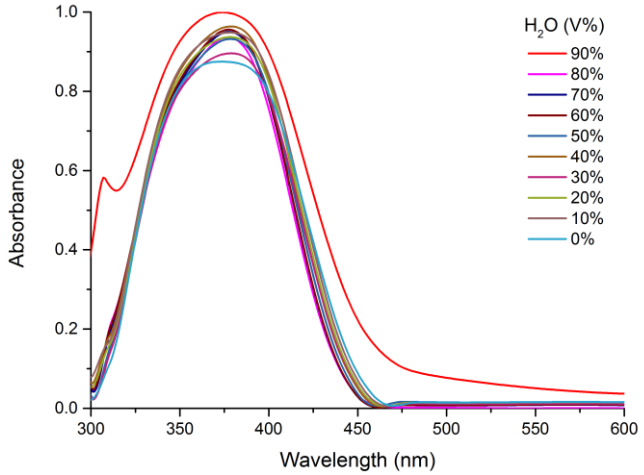
Absorption spectra of **7f** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM.



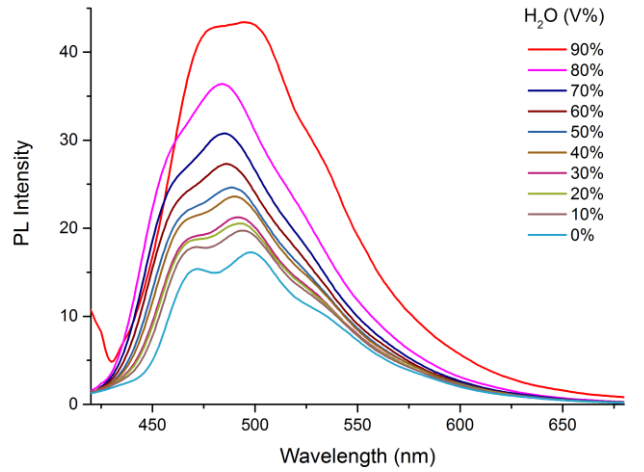
PL spectra of **7f** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM, excitation wavelength: 400 nm.



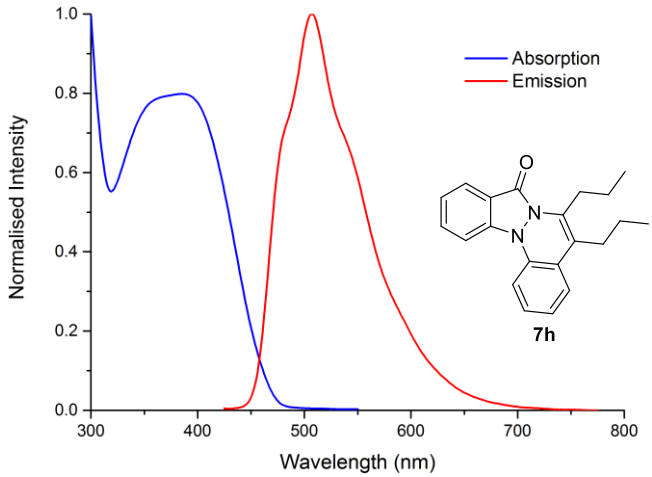
Normalized absorption (blue) and PL (red) spectra of compound **7g** in thin film. (Excitation wavelength: 400 nm)



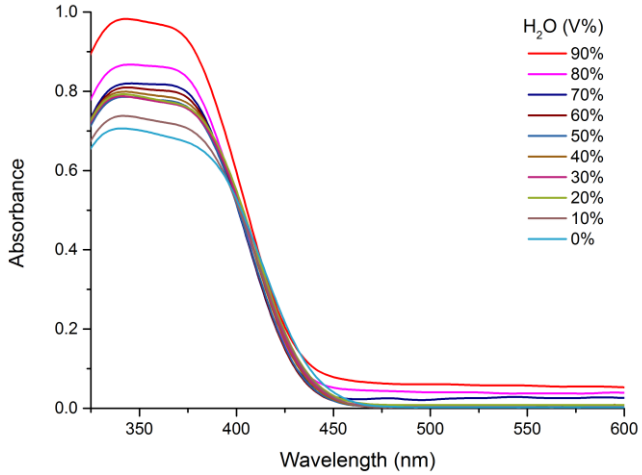
Absorption spectra of **7g** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM.



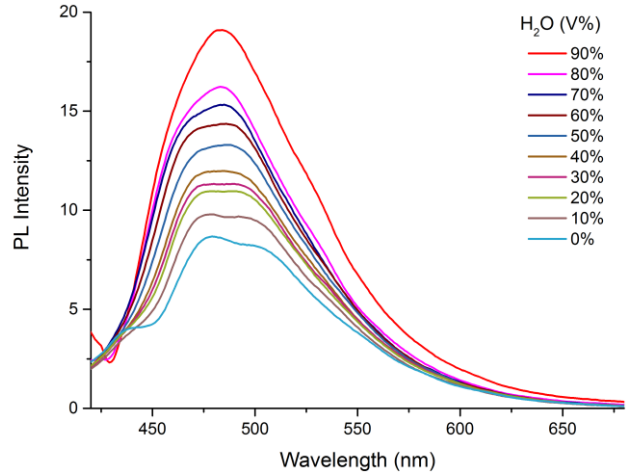
PL spectra of **7g** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM, excitation wavelength: 380 nm.



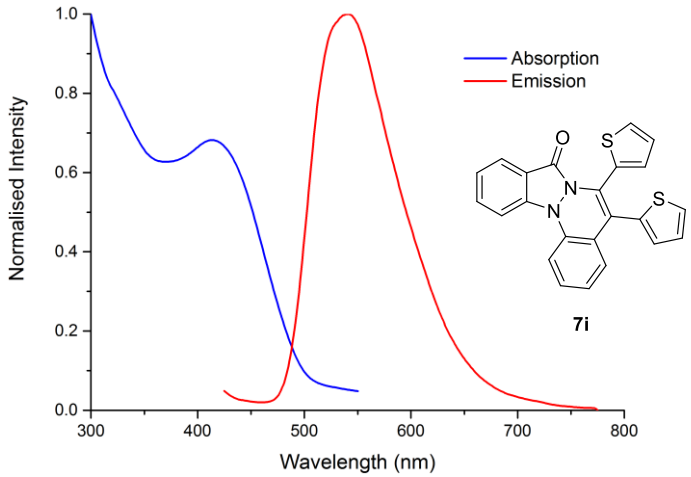
Normalized absorption (blue) and PL (red) spectra of compound **7h** in thin film. (Excitation wavelength: 400 nm)



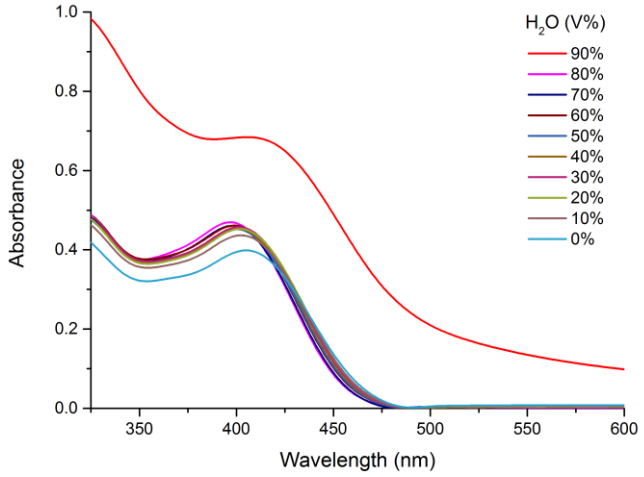
Absorption spectra of **7h** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM.



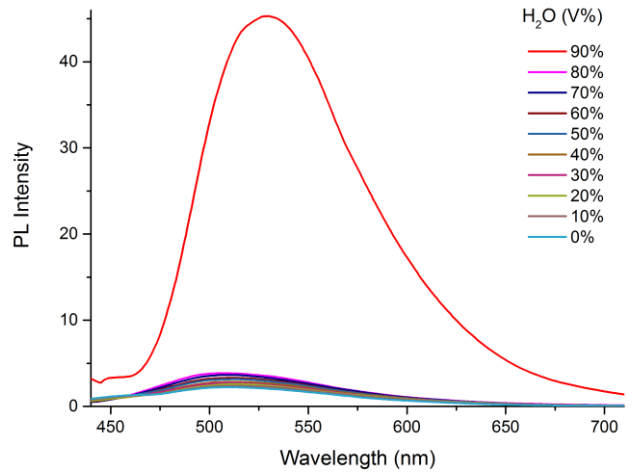
PL spectra of **7h** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM, excitation wavelength: 380 nm.



Normalized absorption (blue) and PL (red) spectra of compound **7i** in thin film. (Excitation wavelength: 400 nm)



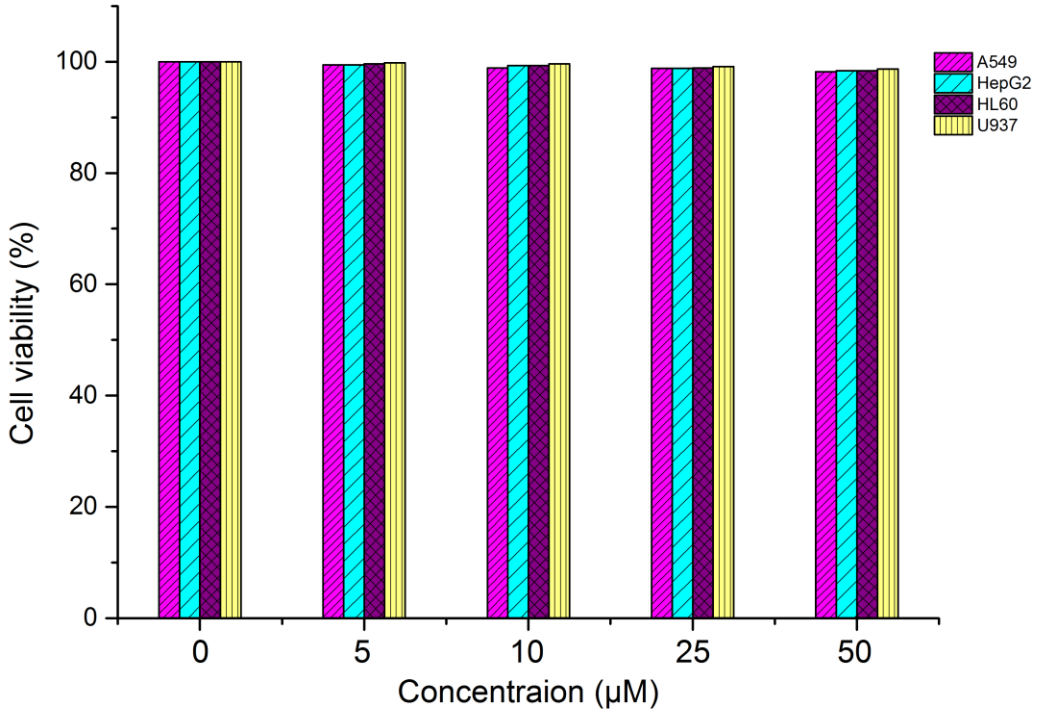
Absorption spectra of **7i** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM.



PL spectra of **7i** in THF/H_2O mixtures with different water fraction (fw), Concentration: 50 μM, excitation wavelength: 400 nm.

13. Cell viability assay

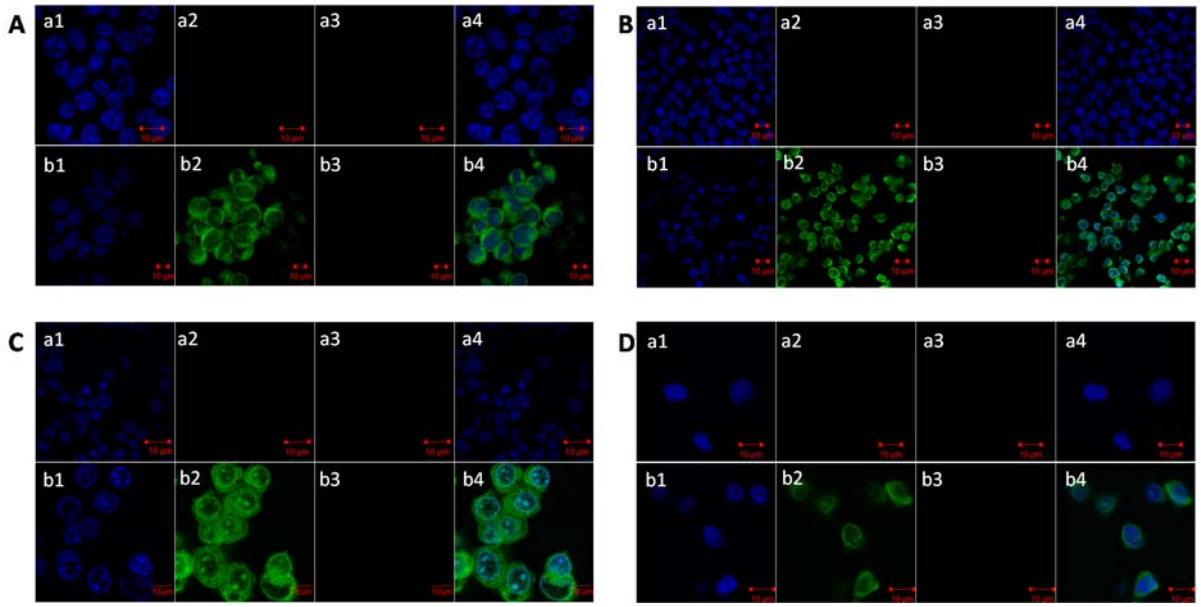
Cytotoxic properties of synthesized compounds were studied against A549, HepG2, HL60 and U937 cells. A549 and HepG2 cells were maintained in complete tissue culture medium DMEM and, HL60 and U937 cells were maintained in RPMI with 10% Fetal Bovine Serum and 2mM L-Glutamine, along with antibiotics (about 100 International Unit/mL of penicillin, 100 µg/mL of streptomycin) with the pH adjusted to 7.2. 50 µL medium containing 5000 cells/well and different concentrations of synthesized compound **7i** were seeded in 96 well plates. The cells were cultivated at 37°C with 5% CO_2 and 95% air in 100% relative humidity. 20µL AQueous one solution reagent was added per well of CellTiter 96® according to manufacture guidelines and incubated at 37°C for 1–4 h in a humidified, 5% CO_2 atmosphere. The cytotoxicity against cells was determined by measuring the absorbance of the converted dye at 490 nm in an ELISA reader. Cytotoxicity of each sample was expressed as IC_{50} value.



Cell viability assay in A549, HepG2, HL60 and U937 cells using MTS reagent. Cells have been incubated with Compound **7i** (0-50 µM) for 48 h.

14. Cell imaging

Compound **7i** was examined for intracellular imaging in A549, HepG2, HL60 and U937 cells. A549 and HepG2 cells were grown in DMEM and, HL60 and U937 cells were grown in RMPI media with 10% fetal bovine serum, 1% penicillin/streptomycin at 37 °C with 5% CO_2 atmosphere for 24 h. Then, all the cells were incubated at 37ºC first with 5 µM of compound for 30 min. After thorough washing with PBS, the cells were stained with 2 µM of staining dyes DAPI and PI at 37ºC for another 20 min. The cells were again washed thrice with PBS. Finally, the green fluorescence images of A549, HepG2, HL60 and U937 cells treated with **7i** and DAPI stained blue fluorescence images were captured using under confocal laser scanning microscope (ZEISS, LSM710).



In vitro imaging in U937, HepG2, A549 and HL60 cells. (**A**) Row 1 (a1–a4): untreated U937 cells; Row 2 (b1–b4): U937 cells treated with 5 µM **7i** for 30 min; (**B**) Row 1 (a1–a4): untreated HepG2cells; Row 2 (b1–b4): A549 cells treated with 5 µM **7i** for 30 min; (**C**) Row 1 (a1–a4): untreated A549 cells; Row 2 (b1–b4): HL60 cells treated with 5 µM **7i** for 30 min; (**D**) Row 1 (a1–a4): untreated HL60 cells; Row 2 (b1–b4): HepG2 cells treated with 5 µM **7i** for 30 min. For **A**, **B**, **C** and **D**, Column 1 (a1–b1): DAPI stained blue fluorescence images; Column 2 (a2–b2): green fluorescence images; Column 3 (a3–b3): PI stained red fluorescence images; Column 4 (a4–b4): merging of all fluorescence images. Scale bar = 10 µm. Excitation and emission wavelength: 405 nm and 488 nm for blue fluorescence images; 488 nm and 561 nm for green fluorescence images; 561 nm and 633 nm for red fluorescence images.