Supporting Information for

Rh(III)-catalyzed oxidative C-H annulation of 6-arylpyridazin-3(2*H*)-ones: Direct access to diarylpyridazino[6,1-*a*]isoquinolin-5-ium-3-olates

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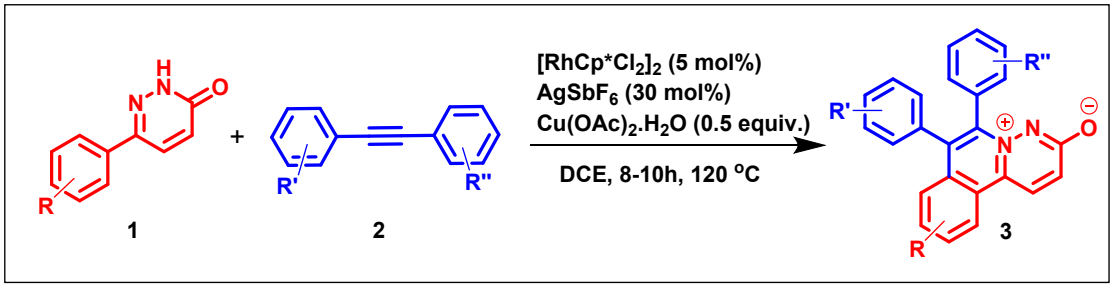

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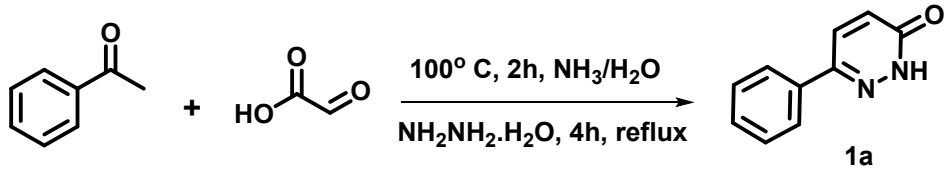
1. General procedures

All solvents were dried by a standard literature procedure. Crude products were purified by column chromatography on silica gel of 60–120 or 100-200 mesh. Thin layer chromatography (**TLC**) plates were visualized by exposure to ultraviolet light at 254 nm, and by exposure to iodine vapors and/or by exposure to methanolic acidic solution of *p*-anisaldehyde followed by heating (<1 min) on a hot plate (~250°C). Organic solvents were concentrated on rotary evaporator at 35–40 °C. Melting points (**mp**) were measured on Buchi B-540. **^{1}H** and **^{13}C NMR** (proton-decoupled) spectra were recorded in $CDCl_3$ solvent on 300, 400 or 500 MHz NMR spectrometer. Chemical shifts (δ) were reported in parts per million (ppm) with respect to TMS as an internal standard. Coupling constants (*J*) are quoted in hertz (Hz). ORBITRAP and ESI mass spectrometer were used for recording the HRMS.

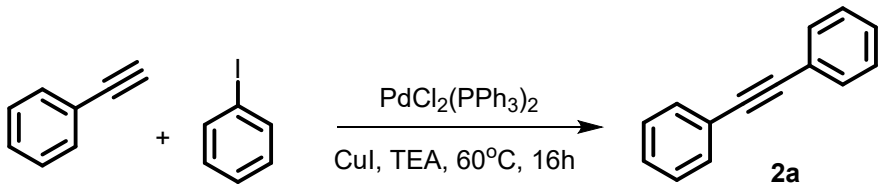
Experimental procedure for the synthesis of 1a:



1a

A mixture of acetophenone (1g, 1.0 equiv.) and glyoxylic acid hydrate (0.205 g, 0.33 equiv.) were heated at 100 °C for 2 h. After it was cooled at 40 °C, water (20 mL) and ammonia (4 mL) were added. The aqueous phase was extracted 3times with DCM. Hydrazine hydrate (0.2mL, 0.5equiv.) was added in the aqueous phase and the resulting solution was heated at reflux four 4 h. After cooling, the solid was filtered and washed with water, to afford **1a** as white solid (1.1g, 72%)

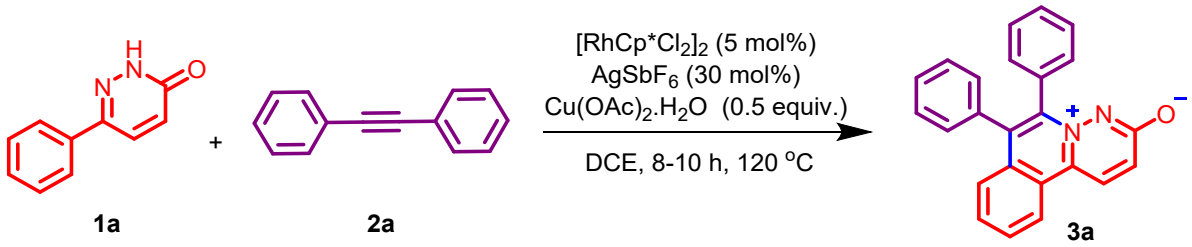
Experimental procedure for the synthesis of 2a:



2a

The iodobenzene (1.1 equiv.) copper iodide (2mol%) and $PdCl_2(PPh_3)_2$ (4mol%) were dissolved in TEA under argon atm. The mixture was degassed with argon and heated up to 60° C. Thenphenylacetylene (1.0 equiv.) was added to the reaction mixture and stirred for 16h. at 60° C, an aq. sat.NH_4Cl solution was added and the mixture was extracted with ethyl acetate and the residue was purified on flash chromatography.

Experimental procedure for the synthesis of 3a:

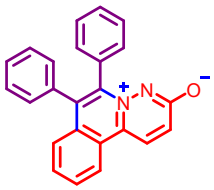


1a **2a** **3a**

To an oven dried sealed tube was equipped with a stir bar were charged with 6-phenylpyridazin-3(2*H*)-one (**1a**, 150 mg,1.0equiv), diphenylacetylene (**2a**,186mg,1.2equiv) in 3 mL of DCE, followed by addition of $[Cp^*RhCl_2]_2$catalyst (5 mol%), $AgSbF_6$(30 mol%) and $Cu(OAc)_2.H_2O$(0.5 equiv.) at room temperature. The resulting mixture was stirred at 120 °C for 8-10h and then concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (MeOH/Chloroform) to afford pure product **3a**.

2. Characterization of products

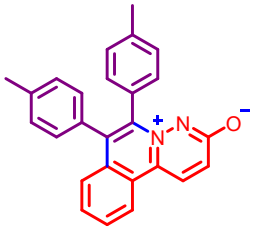
6,7-Diphenylpyridazino[6,1-*a*]isoquinolin-5-ium-3-olate (3a):



Isolated as a colourless solid, yield 88% (267 mg), m.p. 326-328°C, ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (d, J = 9.3 Hz, 1H), 8.46 (d, J = 8.4 Hz, 1H), 7.83 (t, J = 7.3 Hz, 1H), 7.68 (t, J = 7.6 Hz,

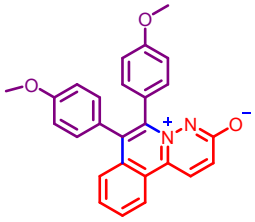
1H), 7.56 (d, J = 8.3 Hz, 1H), 7.29 (dt, J = 3.3, 2.7 Hz, 4H), 7.21 – 7.11 (m, 7H) ppm, ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 142.1, 136.3, 134.8, 134.7, 133.2, 132.9, 130.7, 130.3, 130, 129.8, 128.2, 128.1, 128, 127.3, 126, 125.1, 122.5 ppm, ESI-MS: *m/z* 349 $[M+H]^+$, HRMS (ESI) calcd. for $C_{24}H_{17}N_2O$ *m/z* 349.1355 $[M+H]^+$, found 349.1346.

6,7-Di-*p*-Tolylpyridazino[6,1-*a*]isoquinolin-5-ium-3-olate (3b):



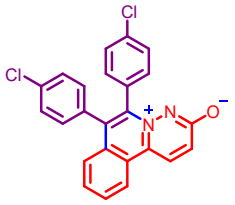
Isolated as a brownish solid, yield 87%(285 mg), m.p318-320^{o}C, ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, J = 9.7 Hz, 1H), 8.43 (d, J = 8.4 Hz, 1H), 7.81 (t, J = 7.3 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.58 – 7.54 (m, 1H), 7.32 – 7.27 (m, 1H), 7.10 (d, J = 7.9 Hz, 2H), 7.02 (dd, J = 6.2, 4.8 Hz, 6H), 2.33 (s, 3H), 2.25 (s, 3H)ppm,^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 142.3, 137.9, 137.7, 136.3, 134.8, 131.8, 131, 130.5, 130.1, 129.8, 129.4, 128.9, 128.7, 127.4, 126.2, 125, 122.5, 21.3, 21.3 ppm, ESI-MS: *m/z* 377 $[M+H]^+$, HRMS (ESI) calcd. for $C_{26}H_{21}N_2O$ *m/z* 377.1648 $[M+H]^+$, found 377.1654.

6,7-Bis(4-methoxyphenyl)pyridazino[6,1-a]isoquinolin-5-ium-3-olate (3c):



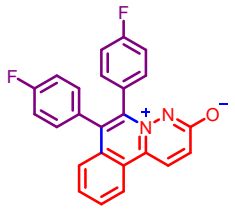
Isolated as a pale yellow solid, yield 85%(302 mg), m.p310-312^{o}C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (d, J = 9.7 Hz, 1H), 8.46 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 4.0 Hz, 1H), 7.69 (t, J = 7.5 Hz, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.33 – 7.30 (m, 1H), 7.08 (d, J = 8.7 Hz, 2H), 7.05 – 7.02 (m, 2H), 6.85 – 6.82 (m, 2H), 6.75 (d, J = 8.7 Hz, 2H), 3.80 (s, 3H), 3.74 (s, 3H)ppm, ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 159.2, 159.1, 142.3, 136.3, 134.9, 132.1, 131.5, 131.2, 130.7, 129.9, 129.6, 129.2, 127.8, 127.7, 127.4, 127, 126.3, 125.1, 125, 122.6 , 113.8, 113.6, 55.2, 55.1.ppm, ESI-MS: *m/z*409 $[M+H]^+$, HRMS (ESI) calcd. for $C_{26}H_{21}N_2O_3$ *m/z* 409.1547 $[M+H]^+$, found 409.1551.

6,7-Bis(4-chlorophenyl)pyridazino[6,1-a]isoquinolin-5-ium-3-olate (3d):



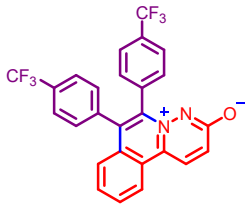
Isolated as a brick red solid, yield 90%(326 mg), m.p345-347°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, J = 9.9 Hz, 1H), 8.46 (d, J = 8.5 Hz, 1H), 7.89 – 7.83 (m, 1H), 7.74 – 7.69 (m, 1H), 7.52 (d, J = 8.3 Hz, 1H), 7.33 (t, J = 2.1 Hz, 1H), 7.31 (d, J = 1.9 Hz, 1H), 7.27 (s, 1H), 7.24 – 7.21 (m, 2H), 7.12 – 7.06 (m, 4H)ppm,^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 141, 135.2, 135, 134.6, 134.6, 132.9, 132, 131.5, 131.1, 131, 130.4, 130.3, 130.1, 128.9, 128.6, 127.1, 126, 125.2,122.6 ppm, ESI-MS: *m/z* 417 $[M+H]^+$, HRMS (ESI) calcd. for $C_{24}H_{15}Cl_2N_2O$ *m/z* 417.0556 $[M+H]^+$, found 417.0563.

6,7-Bis(4-fluorophenyl)pyridazino[6,1-a]isoquinolin-5-ium-3-olate (3e):



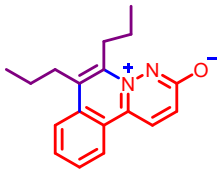
Isolated as a pale yellow solid, yield 92%(308 mg), m.p358-360°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 9.9 Hz, 1H), 8.47 (d, J = 8.5 Hz, 1H), 7.89 – 7.84 (m, 1H), 7.74 – 7.69 (m, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.29 (d, J = 9.8 Hz, 1H), 7.15 – 7.08 (m, 4H), 7.03 (dt, J = 8.7, 2.3 Hz, 2H), 6.95 – 6.90 (m, 2H)ppm,^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 162.3 (d, J = 248.9 Hz), 162.3 (d, J = 249.2 Hz), 141.3, 135.6, 135, 132.7, 132.6, 132.1, 132, 130.9, 130.5, 130.3, 129.9, 128.7, 127.1, 126, 125.2, 122.6, 115.8, 115.6, 115.5, 115.3ppm, ESI-MS: *m/z* 385 $[M+H]^+$, HRMS (ESI) calcd. for $C_{24}H_{15}F_2N_2O$ *m/z* 385.1147 $[M+H]^+$, found 385.1160.

6,7-Bis(4-(trifluoromethyl)phenyl)pyridazino[6,1-a]isoquinolin-5-ium-3-olate (3f):



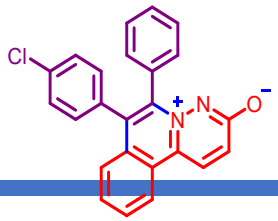
Isolated as a pale yellow solid, yield 80% (337 mg), m.p365-367°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 9.7 Hz, 1H), 8.51 (d, J = 8.5 Hz, 1H), 7.92 – 7.87 (m, 1H), 7.74 (t, J = 7.7 Hz, 1H), 7.60 (d, J = 8.1 Hz, 2H), 7.47 (d, 8.5 Hz, 3H), 7.31 (dd, J = 7.9, 4.3 Hz, 4H), 7.25 (d, J = 9.9 Hz, 1H)ppm,^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 140.4, 138, 136.2, 135.1 (d, J = 11.7 Hz), 131.3, 131.1, 130.9, 130.7, 130.6, 130.2, 130, 126, 126.1, 125.5, 125.5, 125.3, 125.2, 125.2, 125 (d, J = 9.6 Hz), 122.8, 121 (q, J = 272.4 Hz), 120.9 (q, J = 272.4 Hz) ppm, ESI-MS: *m/z* 485 $[M+H]^+$, HRMS (ESI) calcd. for $C_{26}H_{15}F_6N_2O$ *m/z* 485.1083 $[M+H]^+$, found 485.1100.

6,7-Dipropylpyridazino[6,1-a]isoquinolin-5-ium-3-olate (3g):



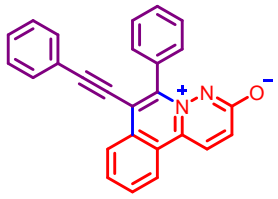
Isolated as a black solid, yield 80% (194 mg), m.p280-282°C, ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (d, J = 9.4 Hz, 1H), 8.34 (d, J = 8.1 Hz, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.81 – 7.68 (m, 2H), 7.22 (s, 1H), 3.40 – 3.29 (m, 2H), 3.10 – 3.00 (m, 2H), 1.79 – 1.63 (m, 4H), 1.07 (dt, J = 18.9, 7.3 Hz, 6H)ppm,^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 143.4, 134.4, 133, 131, 129.7, 129.2, 128.2, 126.7, 124.3, 124.2, 123.1, 31.2, 30.7, 23.6, 20.7, 14.6, 14.4 ppm, ESI-MS: *m/z* 281 $[M+H]^+$, HRMS (ESI) calcd. for $C_{18}H_{21}N_2OS$ *m/z* 281.1648 $[M+H]^+$, found 281.1657.

6-(4-Chlorophenyl)-7-phenylpyridazino[6,1-a]isoquinolin-5-ium-3-olate (3h):



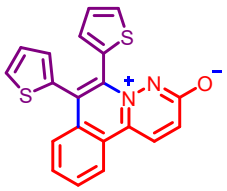
Isolated as a white solid, yield 82% (273mg), m.p338-340°C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 7.6 Hz, 1H), 8.48 (d, *J* = 8.4 Hz, 1H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.69 (td, *J* = 7.6, 3.9 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.33 – 7.29 (m, 2H), 7.27 (dd, *J* = 2.3, 1.7 Hz, 1H), 7.25 (s, 1H), 7.22 (d, *J* = 7.4 Hz, 1H), 7.15 – 7.06 (m, 5H) ppm,^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 142.2, 140.8, 136.5, 135.1, 134.4, 134.2, 133.2, 132.6, 132.2, 131.6, 131.4, 130.9, 130.6, 130.2, 128.6, 128.4, 128.3, 128.2, 127.4, 127, 126.3, 125.2, 122.7 ppm. ESI-MS: *m/z*383 $[M+H]^+$, HRMS (ESI) calcd. for $C_{24}H_{16}ClN_2O$ *m/z* 383.0946 $[M+H]^+$, found 383.0959.

6-Phenyl-7-(phenylethynyl)pyridazino[6,1-a]isoquinolin-5-ium-3-olate (3i):



Isolated as a white solid, yield 82% (266mg), m.p315-317°C, ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 8.62 (d, *J* = 9.2 Hz, 1H), 8.55 – 8.51 (m, 1H), 8.48 (d, *J* = 8.6 Hz, 1H), 7.95 – 7.90 (m, 2H), 7.56 – 7.49 (m, 5H), 7.35 – 7.33 (m, 2H), 7.31 (s, 1H), 7.30 – 7.28 (m, 1H), 7.24 (d, *J* = 1.4 Hz, 1H), 7.21 (d, *J* = 1.8 Hz, 1H) ppm,^{13}C NMR (125 MHz, $CDCl_3$) *δ* 168.1, 155.3, 152.4, 145.7, 135.5, 133.8, 133, 131.9, 131.7, 130.8, 130.3, 129.7, 129.2, 128.5, 128.1, 126.9, 125.8, 125.2, 124.7, 123.1, 121.5, 119.9, 118.2, 113, 103.3, 83.0ppm, ESI-MS: *m/z* 373 $[M+H]^+$, HRMS (ESI) calcd. for $C_{26}H_{17}N_2O$ *m/z* 373.1335 $[M+H]^+$, found 373.1339.

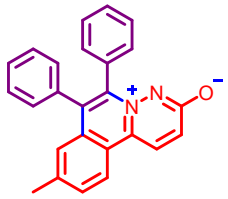
6,7-Di(thiophen-2-yl)pyridazino[6,1-a]isoquinolin-5-ium-3-olate (3j):



Isolated as a brownish solid, yield 85% (266mg), m.p 302-304 °C, ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.58 (d, *J* = 9.9 Hz, 1H), 8.46 (d, *J* = 8.5 Hz, 1H), 7.89 – 7.83 (m, 1H), 7.74 – 7.69 (m, 1H), 7.52

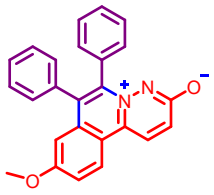
(d, J = 8.3 Hz, 1H), 7.33 (t, J = 2.1 Hz, 1H), 7.31 (d, J = 1.9 Hz, 1H), 7.27 (s, 1H), 7.24 – 7.21 (m, 2H), 7.12 – 7.06 (m, 4H) ppm,^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 141, 135.2, 135, 134.6, 134.6, 132.9, 132, 131.5, 131.1, 131, 130.4, 130.3, 130.1, 128.9, 128.6, 127.1, 126, 125.2,122.6 ppm, ESI-MS: *m/z*361 $[M+H]^+$, HRMS (ESI) calcd. for $C_{20}H_{13}N_2OS_2$ *m/z* 361.0464 $[M+H]^+$, found 361.0474.

9-Methyl-6,7-diphenylpyridazino[6,1-a]isoquinolin-5-ium-3-olate (3k):



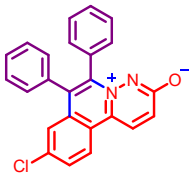
Isolated as a whitesolid, yield 92% (268mg), m.p326-328°C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, J = 9.8 Hz, 1H), 8.34 (d, J = 8.7 Hz, 1H), 7.66 (dd, J = 8.6, 1.4 Hz, 1H), 7.29 (dd, J = 7.9, 5.1 Hz, 5H), 7.22 – 7.16 (m, 3H), 7.16 – 7.14 (m, 2H), 7.13 – 7.10 (m, 2H), 2.47 (s, 3H)ppm, ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 142.1, 141.7, 135.8, 134.8, 133, 131.9, 130.9, 130.7, 130.3, 129.7, 128.2, 128.1, 128, 127.9, 126.5, 125.9, 123.2, 122.5, 22.0 ppm, ESI-MS: *m/z*363 $[M+H]^+$, HRMS (ESI) calcd. for $C_{25}H_{19}N_2O$ *m/z* 363.1492 $[M+H]^+$, found 363.1509.

9-Methoxy-6,7-diphenylpyridazino[6,1-a]isoquinolin-5-ium-3-olate (3l):



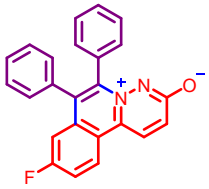
Isolated as a white solid, yield 91% (255mg), m.p330-332 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, J = 9.8 Hz, 1H), 8.36 (d, J = 9.3 Hz, 1H), 7.42 (dd, J = 9.2, 2.6 Hz, 1H), 7.28 – 7.23 (m, 4H), 7.20 – 7.09 (m, 7H), 6.82 (d, J = 2.5 Hz, 1H), 3.73 (s, 3H) ppm,^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 161.4, 142.5, 135.3, 134.9, 134.9, 133, 130.6, 130.2, 130, 128.3, 128.1, 128.1, 127.9, 125.7, 124.6, 121.1, 119.7, 107, 55.5 ppm, ESI-MS: *m/z* 379 $[M+H]^+$, HRMS (ESI) calcd. for $C_{25}H_{19}N_2O_2$ *m/z* 379.1441 $[M+H]^+$, found 379.1453.

9-Chloro-6,7-diphenylpyridazino[6,1-a]isoquinolin-5-ium-3-olate (3m):



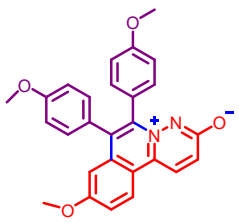
Isolated as a white solid, yield 88% (244mg), m.p.336-338°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 7.4 Hz, 1H), 8.43 (d, J = 8.1 Hz, 1H), 7.77 (d, J = 7.6 Hz, 1H), 7.50 (d, J = 1.7 Hz, 1H), 7.31 (dd, J = 4.4, 3.0 Hz, 2H), 7.30 (d, J = 2.1 Hz, 2H), 7.13 (dd, J = 9.5, 5.6 Hz, 7H)ppm,^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 143.2, 137.4, 135.4, 134.8, 134, 132.5, 131.8, 130.8, 130.5, 130.2, 129.9, 128.4, 128.4, 128, 126.4, 126.2, 124.4, 123.5ppm, ESI-MS: *m/z* 383 $[M+H]^+$, HRMS (ESI) calcd. for $C_{24}H_{16}ClN_2O$ *m/z* 383.0946 $[M+H]^+$, found 383.0949.

9-Fluoro-6,7-diphenylpyridazino[6,1-a]isoquinolin-5-ium-3-olate (3n):



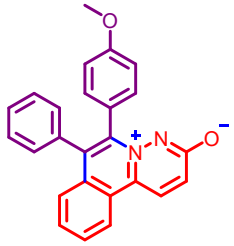
Isolated as a white solid, yield 90% (260mg), m.p.340-342°C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, J = 9.1 Hz, 1H), 8.52 (dd, J = 9.2, 5.0 Hz, 1H), 7.59 – 7.55 (m, 1H), 7.31 – 7.28 (m, 4H), 7.16 (t, J = 5.1 Hz, 6H), 7.12 – 7.10 (m, 2H)ppm,^{13}C NMR (125 MHz, $CDCl_3$) δ 168.18, 163.47 (d, J = 254.9 Hz), 143.18, 135.69, 134.84, 134.30, 132.90, 132.83, 132.65, 130.58, 130.15, 128.48, 128.38, 128.02, 126.13, 125.82, 125.75, 122.09, 119.77 (d, J = 24.9 Hz), 112.06 (d, J = 23.3 Hz) ppm, ESI-MS: *m/z* 367 $[M+H]^+$, HRMS (ESI) calcd. for $C_{24}H_{16}FN_2O$ *m/z* 367.1241 $[M+H]^+$, found 367.1249.

9-Methoxy-6,7-bis(4-methoxyphenyl)pyridazino[6,1-a]isoquinolin-5-ium-3-olate (3o):



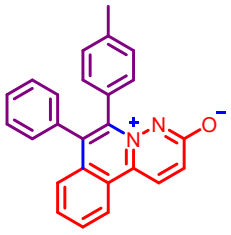
Isolated as a white solid, yield 88% (286mg), m.p.320-322°C, ^{1}H NMR (500 MHz, CD_3OD) δ 9.07 (d, *J* = 9.0 Hz, 1H), 8.72 (d, *J* = 9.3 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.32 (d, *J* = 9.4 Hz, 1H), 7.06 (t, *J* = 8.8 Hz, 4H), 6.88 (d, *J* = 2.5 Hz, 1H), 6.81 (d, *J* = 8.7 Hz, 2H), 6.73 (d, *J* = 8.7 Hz, 2H), 3.70 (d, *J*= 1.0 Hz, 6H), 3.66 (s, 3H) ppm,^{13}C NMR (126 MHz, CD_3OD+CF_3COOD) δ 164.1, 162.6, 160, 159.7, 143.3, 139.2, 137.9, 136.6, 132, 131.2, 127.1, 126.3, 124.8, 122.5, 122.1, 113.6, 113.4, 113.3, 111.2, 106.5, 55, 54.3, 54.3 ppm, ESI-MS: *m/z*439 $[M+H]^+$, HRMS (ESI) calcd. for $C_{27}H_{23}N_2O_4$ *m/z* 439.1652 $[M+H]^+$, found 439.1672.

6-(4-Methoxyphenyl)-7-phenylpyridazino[6,1-a]isoquinolin-5-ium-3-olate(3r):



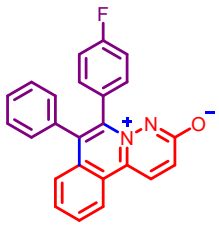
Isolated as a brownish solid, yield 85% (280mg), m.p 318-320 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (dd, *J* = 9.5, 7.9 Hz, 2H), 8.52 (dd, *J* = 8.4, 3.0 Hz, 2H), 7.84 (dd, *J* = 10.3, 4.3 Hz, 2H), 7.72 – 7.67 (m, 2H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 7.7 Hz, 1H), 7.31 (dd, *J* = 5.9, 5.0 Hz, 4H), 7.22 (ddd, *J* = 13.1, 5.9, 1.7 Hz, 3H), 7.19 – 7.11 (m, 5H), 7.10 – 7.07 (m, 2H), 7.06 – 7.02 (m, 2H), 6.83 – 6.79 (m, 2H), 6.73 – 6.69 (m, 2H), 3.78 (s, 3H), 3.69 (s, 3H) ppm, ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 159.2, 159.1, 142.2, 142. 136.5, 136.2, 135.2, 135,134.9, 133.1, 132.2, 131.5, 131.2, 130.9, 130.7, 130.3, 130, 130.05, 128.3, 128, 127.4, 127.3, 126.7, 126.6, 126.4, 125.1, 125, 124.9, 122.7, 113.7, 113.5, 55.2, 55.1 ppm, ESI-MS: *m/z* 379 $[M+H]^+$, HRMS (ESI) calcd. for $C_{25}H_{19}N_2O_2$ *m/z* 379.1441 $[M+H]^+$, found 379.1457.

7-Phenyl-6-(p-tolyl)pyridazino[6,1-a]isoquinolin-5-ium-3-olate (3s):



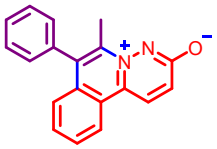
Isolated as a white solid, yield 80% (252 mg), m.p 322-324 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (dd, *J* = 9.8, 2.2 Hz, 1H), 8.55 (d, *J* = 8.5 Hz, 1H), 7.86 (tdd, *J* = 8.3, 3.8, 1.1 Hz, 1H), 7.70 (dt, *J* = 8.0, 4.1 Hz, 1H), 7.40 – 7.32 (m, 3H), 7.24 – 7.13 (m, 8H), 7.12 – 7.07 (m, 2H), 7.04 – 6.93 (m, 3H), 2.07 (s, 1H), 1.99 (s, 3H) ppm, ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 168.1, 142.2, 141.9, 137.1, 136.3, 136, 135.4, 135.1, 134.5, 133.9, 132.7, 131.3, 131, 130.8, 130.6, 130.5, 130.4, 130.3, 130.1, 129.7, 129.3, 129.2, 128.8, 128.7, 128.5, 128.4, 128.4, 128.3, 128.1, 128, 127.9, 127.3, 126.9, 126.7, 125.7, 125.4, 125.19, 124.9, 123, 122.8, 20, 19.8, ESI-MS: m/z 363 $[M+H]^+$, HRMS (ESI) calcd. for $C_{25}H_{19}N_2O$ *m/z* 363.1492 $[M+H]^+$, found 363.1488.

6-(4-Fluorophenyl)-7-phenylpyridazino[6,1-a]isoquinolin-5-ium-3-olate (3t):



Isolated as a pale yellow solid, yield 88% (280 mg), m.p 3418-350 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 8.9 Hz, 1H), 8.49 (d, *J* = 8.1 Hz, 1H), 7.85 (t, *J* = 7.5 Hz, 1H), 7.70 (dd, *J* = 14.7, 6.7 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.33 – 7.29 (m, 2H), 7.27 – 7.20 (m, 2H), 7.13 (ddd, *J* = 9.5, 6.6, 3.3 Hz, 4H), 6.99 (t, *J* = 8.6 Hz, 1H), 6.89 (t, *J* = 8.6 Hz, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 162.3 (d, *J* = 248.3 Hz), 142.4, 141.1, 136.6, 135.3, 134.9, 134.6, 132.7 (d, *J* = 8.5 Hz), 132.1 (d, *J* = 8.2 Hz), 130.8, 130.6, 130.2, 128.4, 128.1, 127.4, 127.1, 126.1, 125.2, 122.6, 115.6, 115.4, 115.3, 115.1 ppm, ESI-MS: *m/z* 367 $[M+H]^+$, HRMS (ESI) calcd. for $C_{24}H_{16}FN_2O$ *m/z* 367.1241 $[M+H]^+$, found 367.1250.

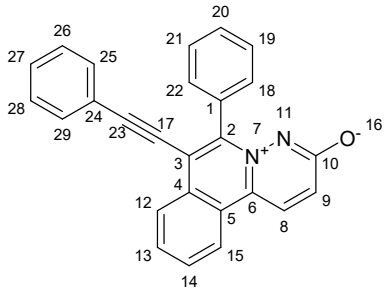
6-Methyl-7-phenylpyrido[2,1-a]isoquinolin-5-ium-3-olate (3u):



Isolated as a white solid, yield 80% (199mg), m.p 318-320 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 9.5 Hz, 1H), 8.55 (d, *J* = 3.2 Hz, 1H), 8.15 (dd, *J* = 6.2, 3.2 Hz, 1H), 7.91 (dd, *J* = 6.3, 3.1 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.37 (t, *J* = 7.1 Hz, 1H), 7.30 (d, *J* = 7.0 Hz, 2H),

2.47 (s, 3H) ppm, ^{13}C NMR 100 MHz, $CDCl_3$) δ 167.8, 141.8, 135, 133.5, 131.6, 130.9, 130.7, 129.8, 129.5, 129.4, 128.9, 128.1, 127, 124.9, 124.6, 123.4, 17ppm, ESI-MS: m/z 287 $[M+H]^+$, HRMS (ESI) calcd. for $C_{19}H_{15}N_2O$ *m/z* 287.1179 $[M+H]^+$, found 287.1182.

3. NOE studies of 3i & 3u



compound **3i**

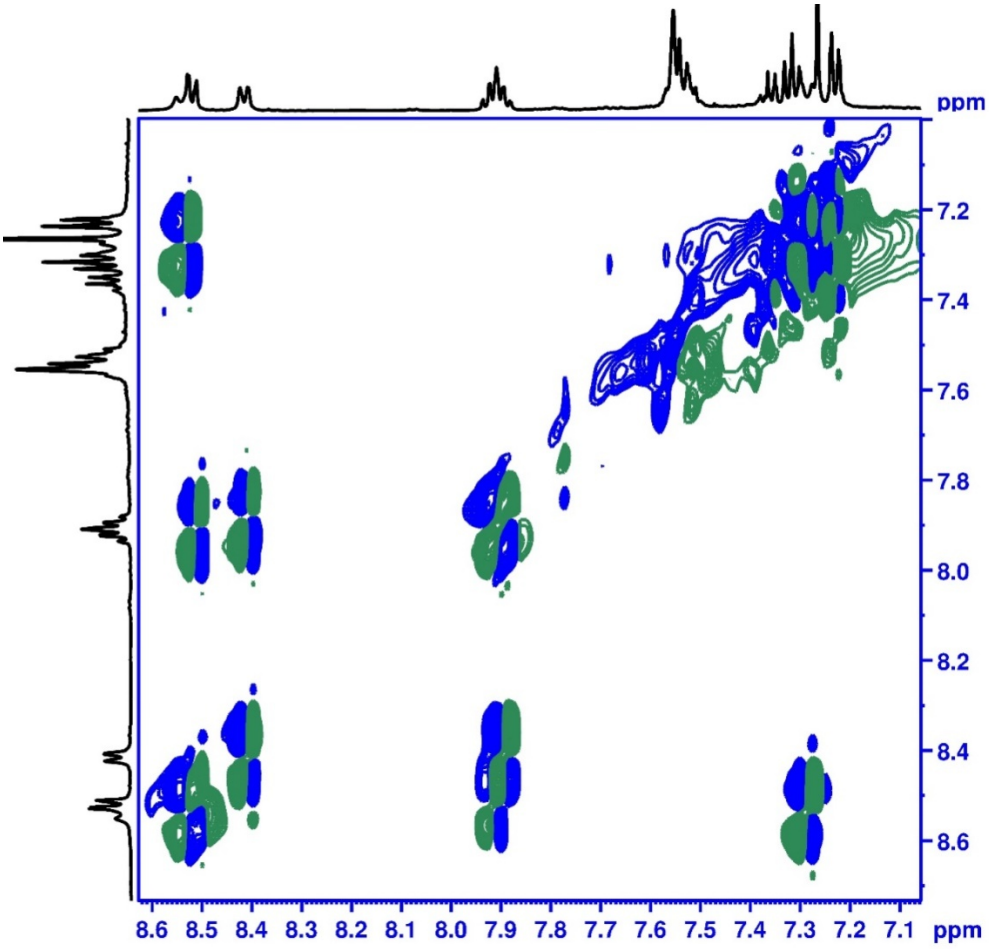


Figure Sx: ^{1}H-^{1}H COSY spectrum of **3i**. ^{1}H chemical shift assignments were annotated. ^{1}H chemical shift of protons is annotated on the proton projection on the top

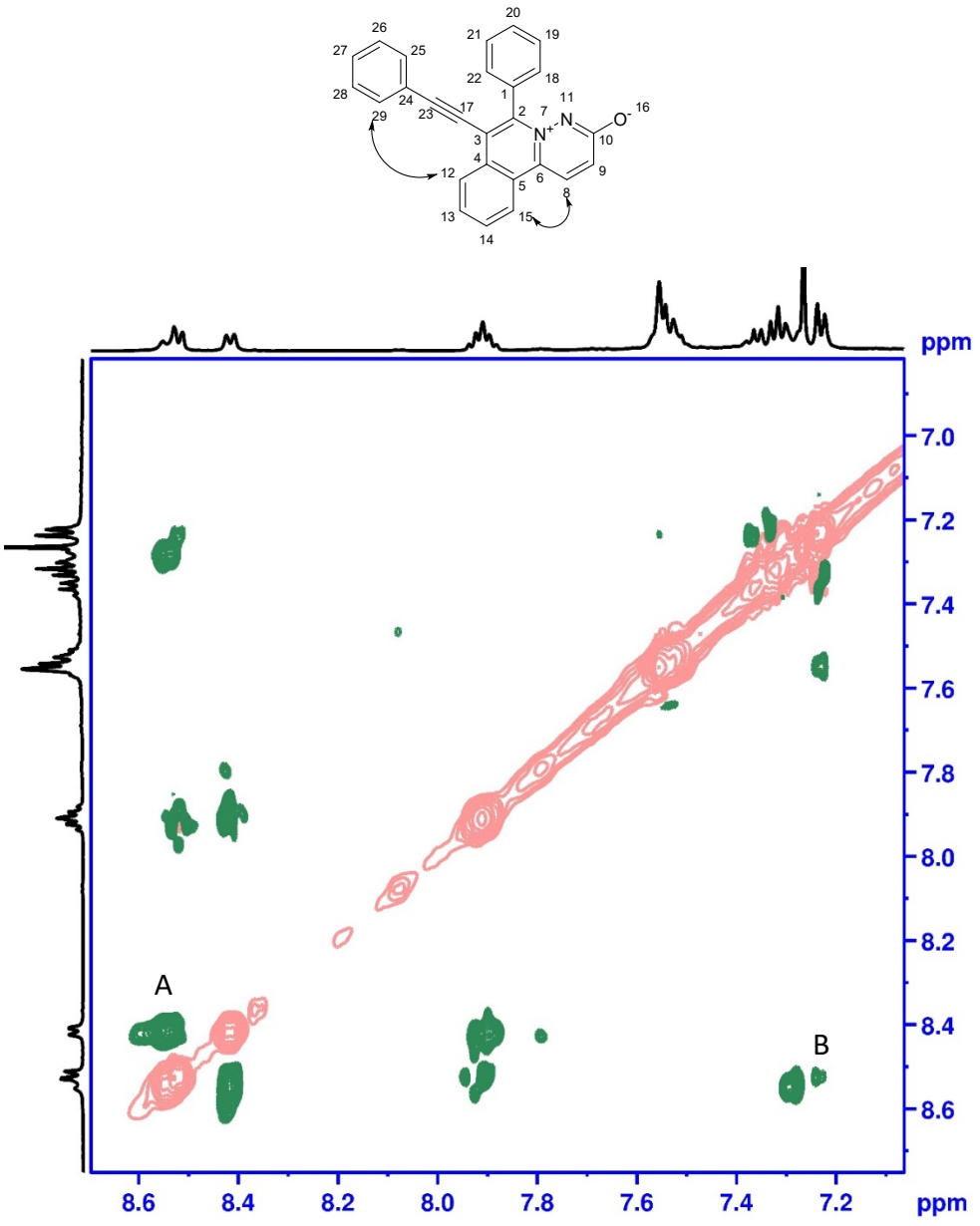


Figure SI: ^{1}H-^{1}H NOESY spectrum of compound **3i**; nOes between H12 ↔ H25,29; and H15 ↔H8 are depicted as A, and B respectively and are shown with double headed arrows on the chemical structure.

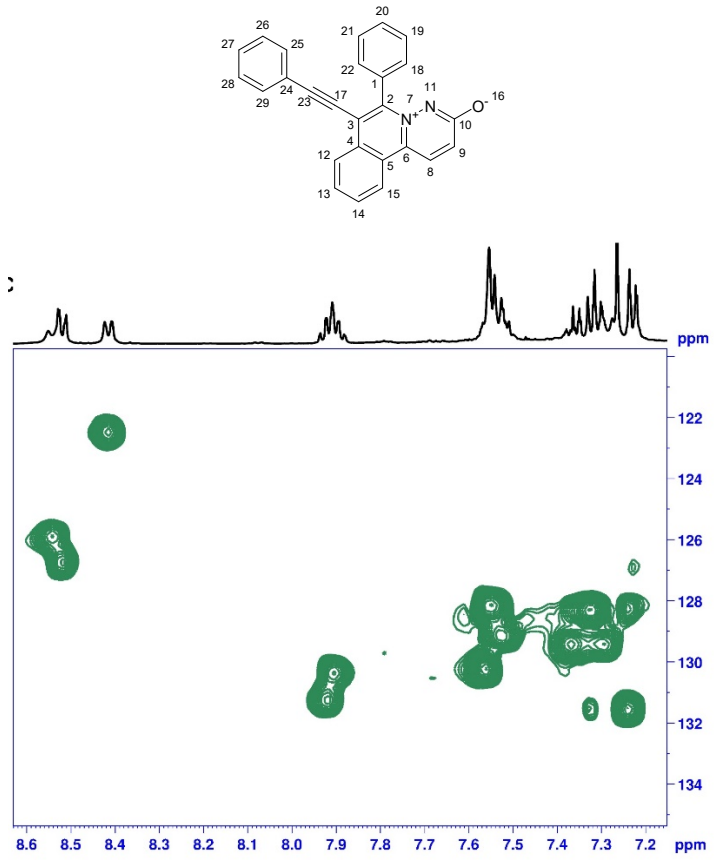
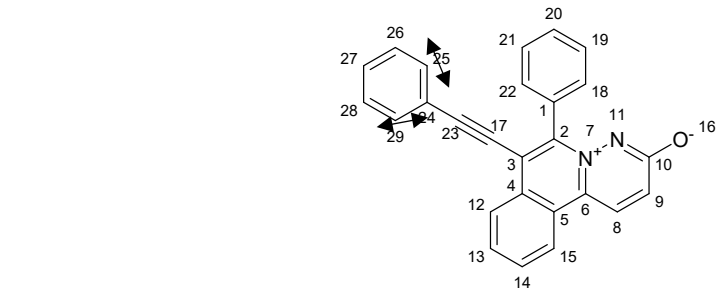


Figure Sb: ^{1}H-^{13}C HSQC spectrum of Compound **3i**. Carbon and proton chemical shift positions of the protonated carbons are given as table 2, below.

Atom No	^{1}H	^{13}C
12	8.52	126.7
13	7.92	131.2
14	7.90	130.3
15	8.41	122.4
8	8.54	126.1
9	7.29	129.4
25, 29	7.24	131.5

26,28	7.32	128.2
27	7.36	129.4
18,22	7.56	130.2
19,21	7.55	128.1
20	7.52	129.1
23	-	102.9
17	-	83.1



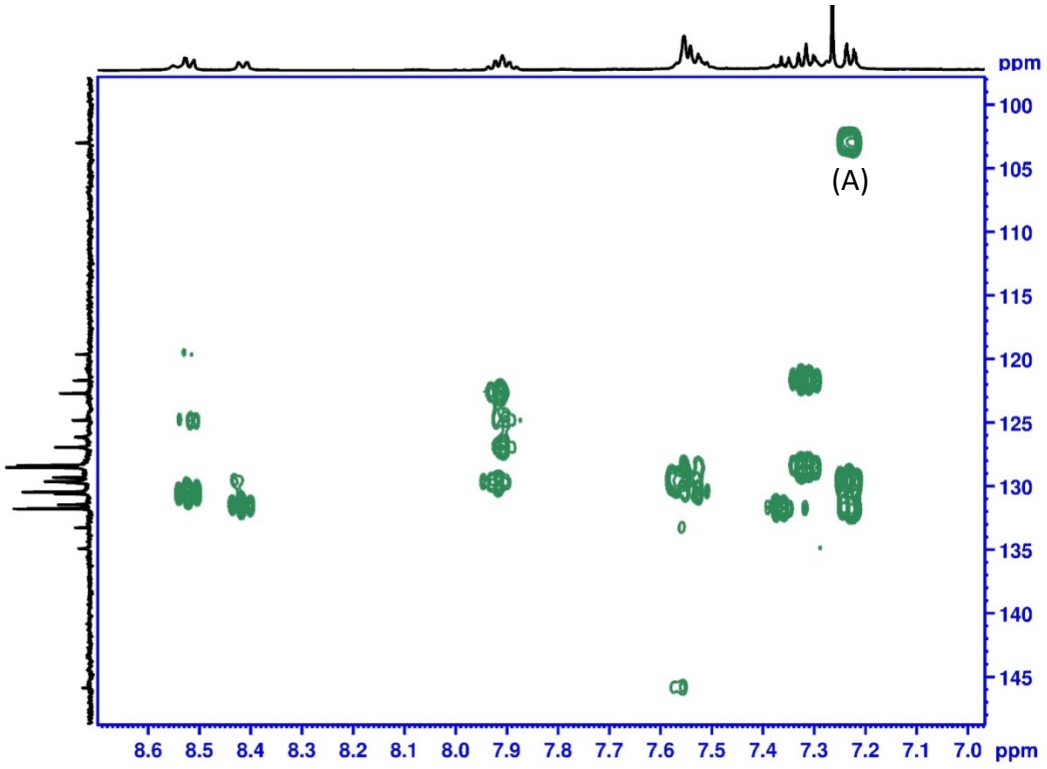


Figure Su: HMBC spectrum of the Compound **3i**; HMBC correlation between H25,29 ↔ C23 is depicted as A.

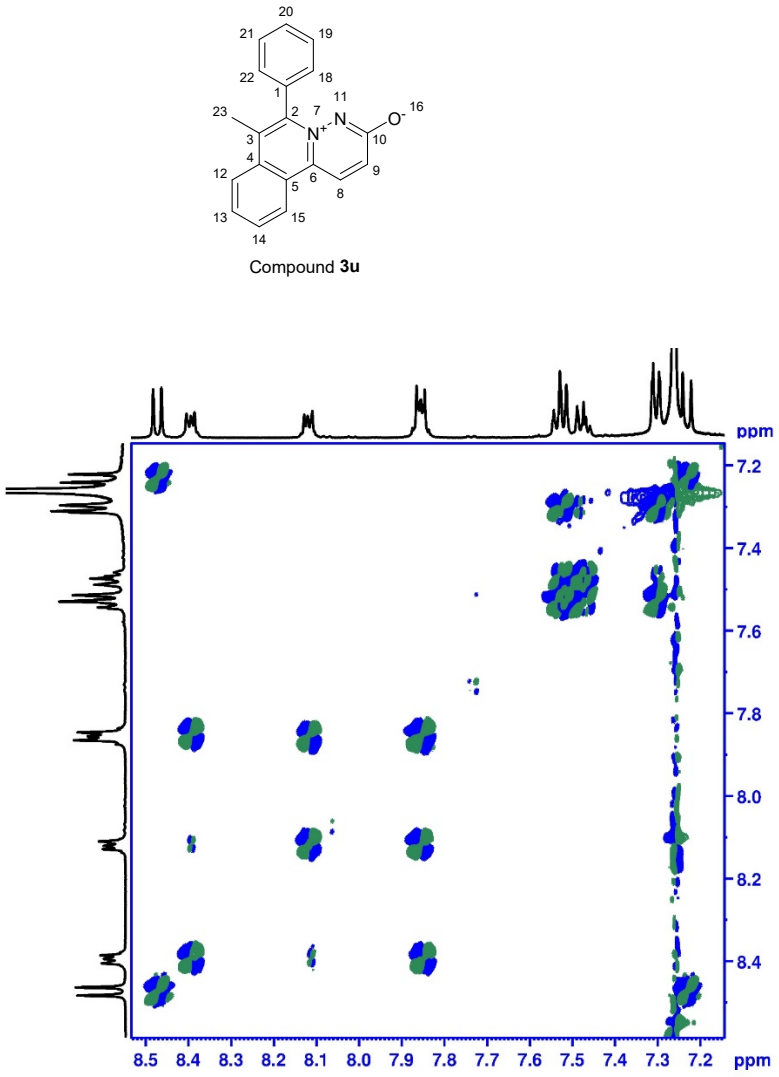


Figure S<u>x</u>: ^{1}H-^{1}H COSY spectrum of **3u**.^{1}H chemical shift of individual protons is annotated on the proton projection on the top.

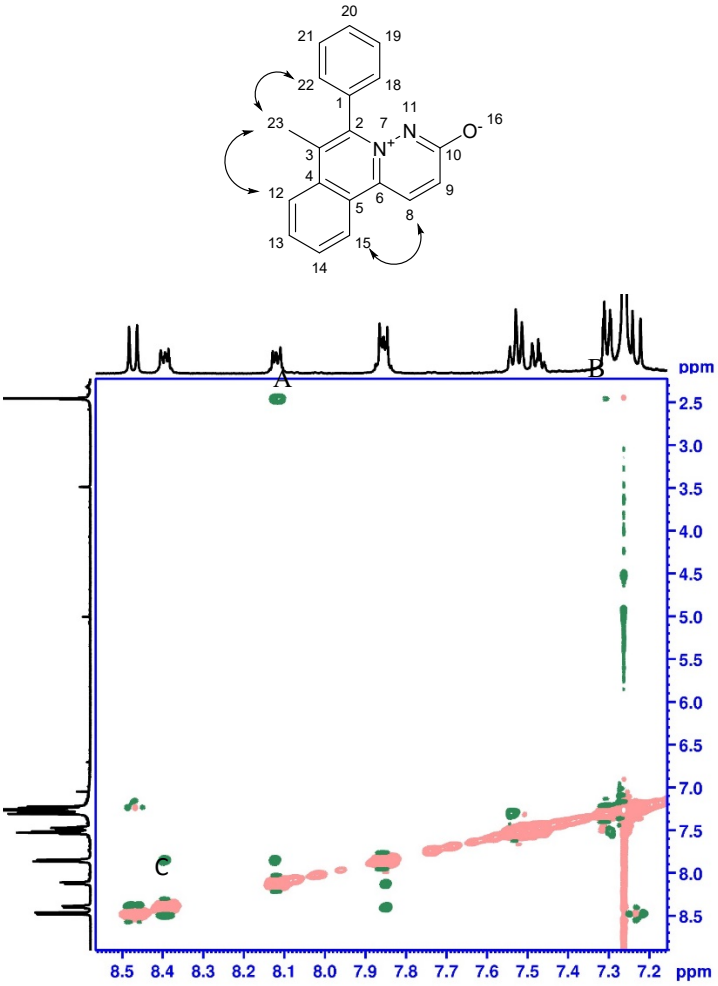


Figure Sa: ^{1}H-^{1}H NOESY spectrum of compound **3u**. nOes between 23(Methyl) ↔ H12, 23(Methyl) ↔ H18,22; and H15 ↔H8 are depicted as A, B and C respectively and are shown with double headed arrows on the chemical structure.

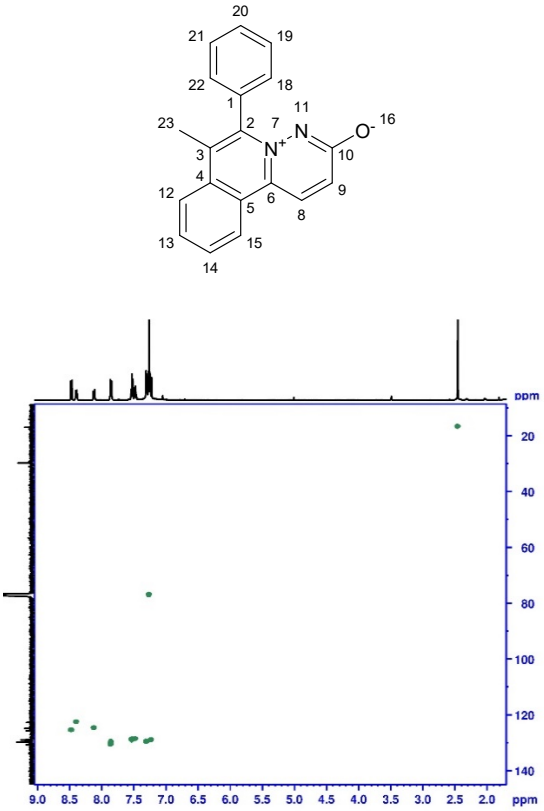


Figure Sb: ^{1}H-^{13}C HSQC spectrum of Compound **3u**. Carbon and proton chemical shift positions of the protonated carbons are given as Table 1, below.

Atom No	1H	^{13}C
12	8.12	124.6
13	7.86	130.5
14	7.85	129.6
15	8.48	125.4
23	2.45	16.74
18,22	7.30	129.5
19,21	7.53	128.74
20	7.48	128.6
8	8.47	125.4
9	7.23	128.9

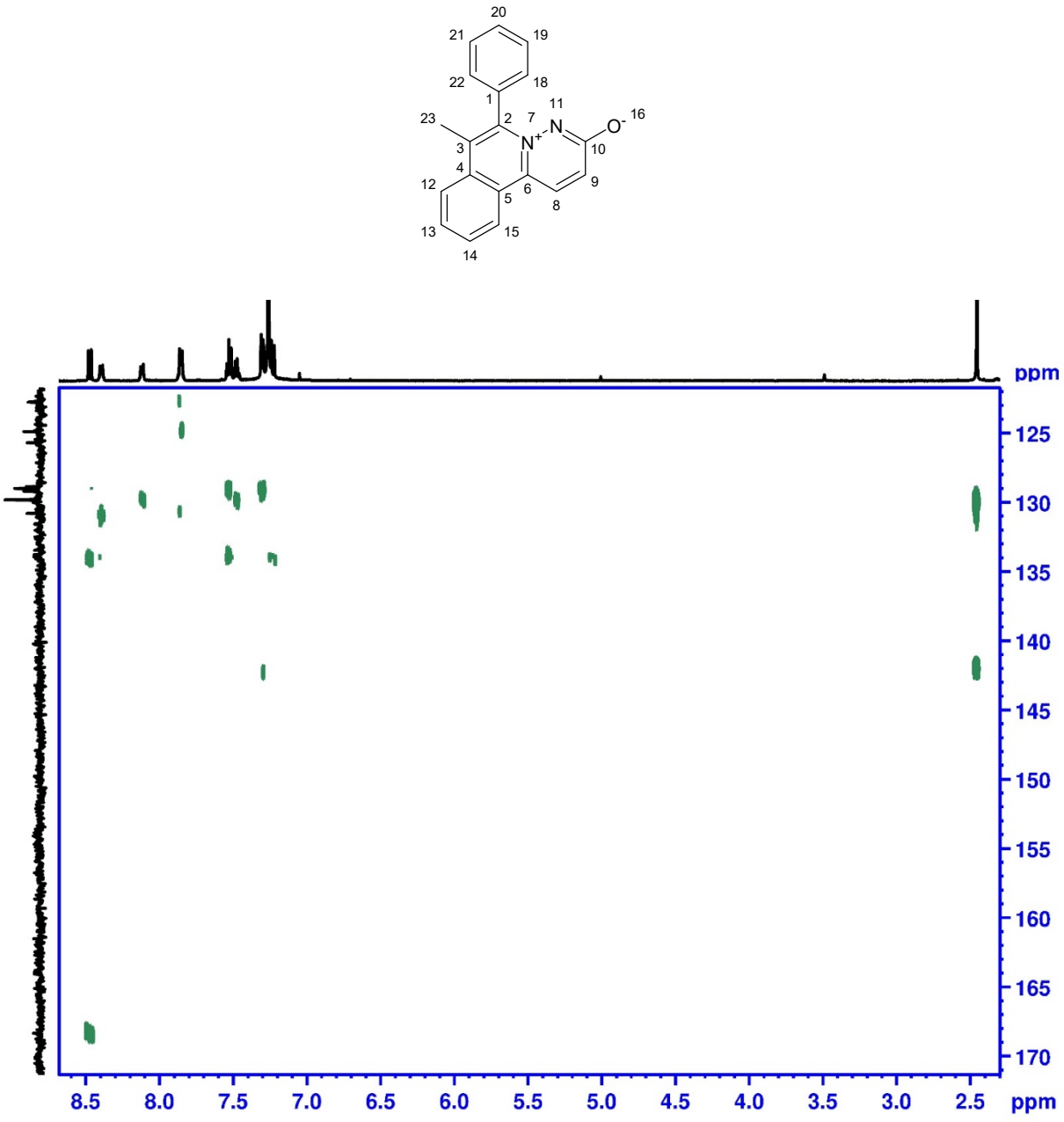
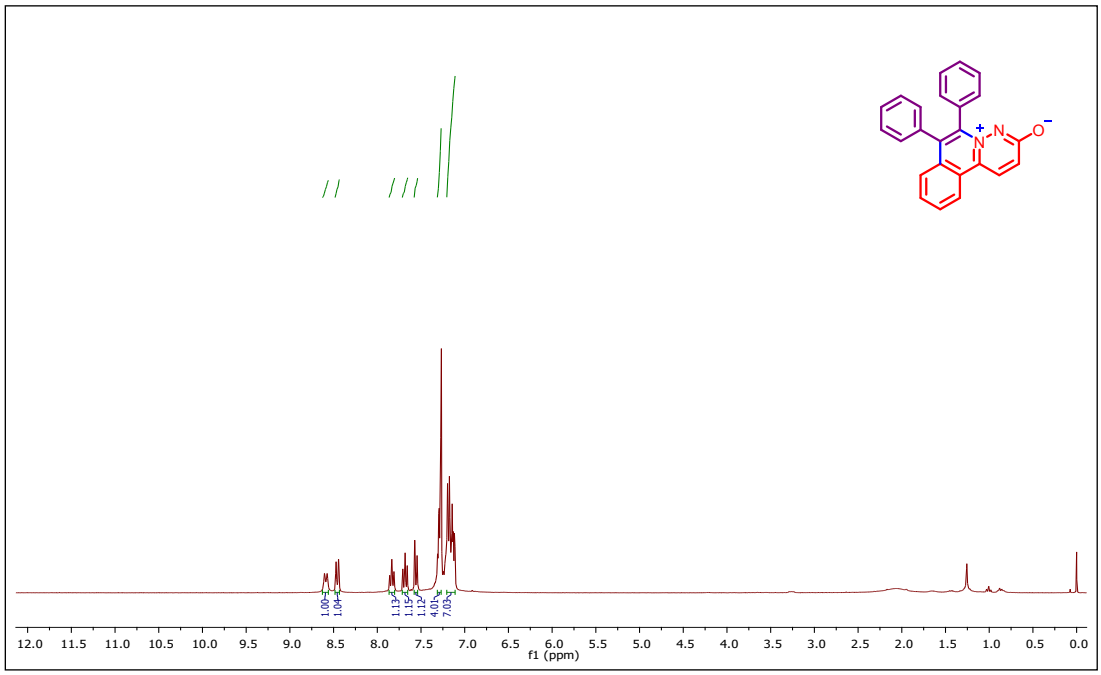
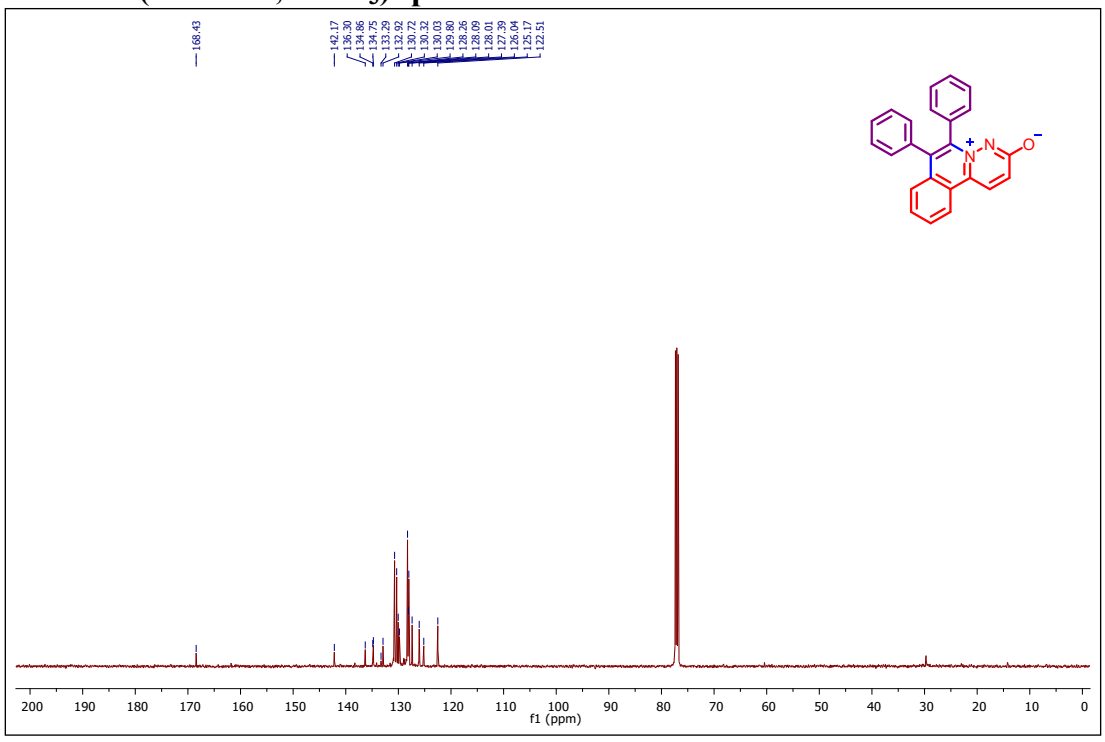


Figure Sc: HMBC spectrum of Compound **3u**.

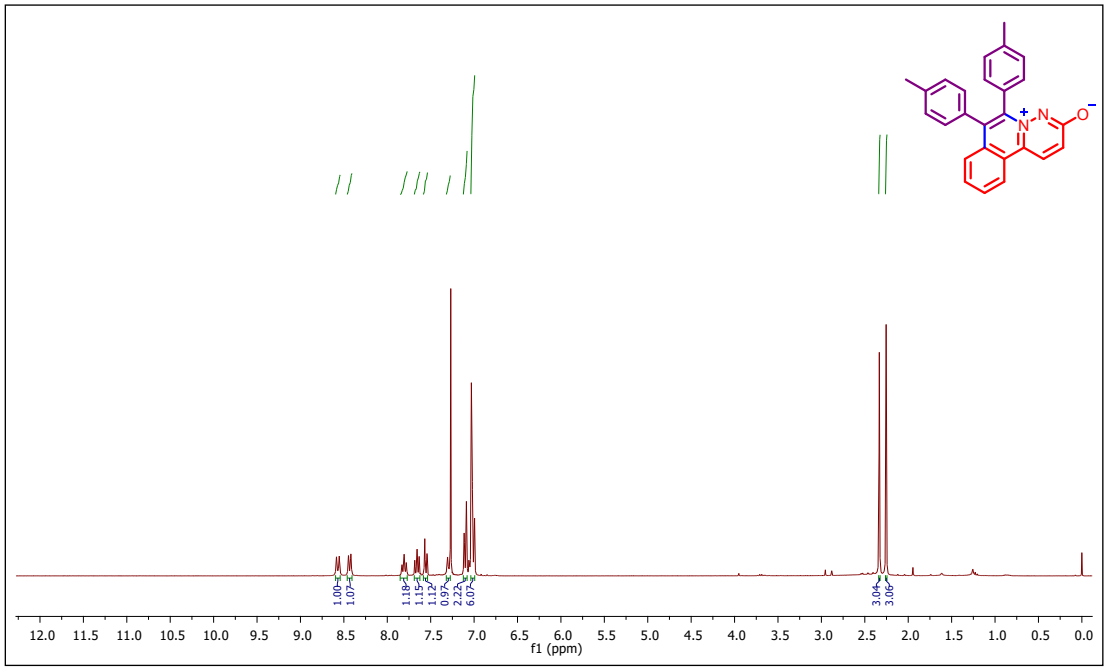
4. Copies of ^{1}H &^{13}C NMR spectra: ^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 3a:



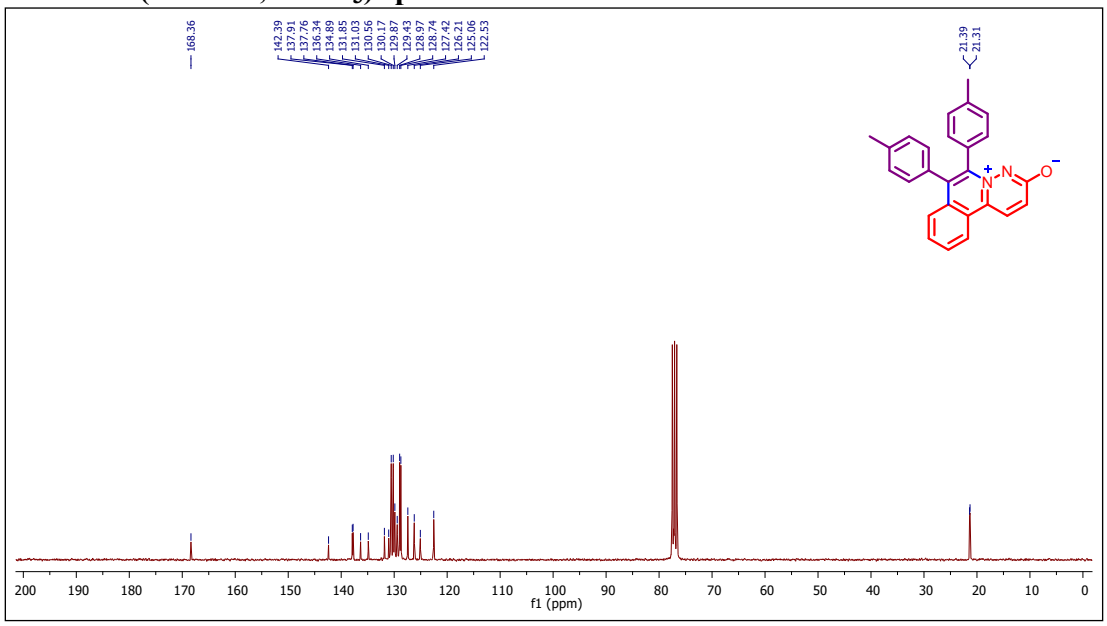
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3a:



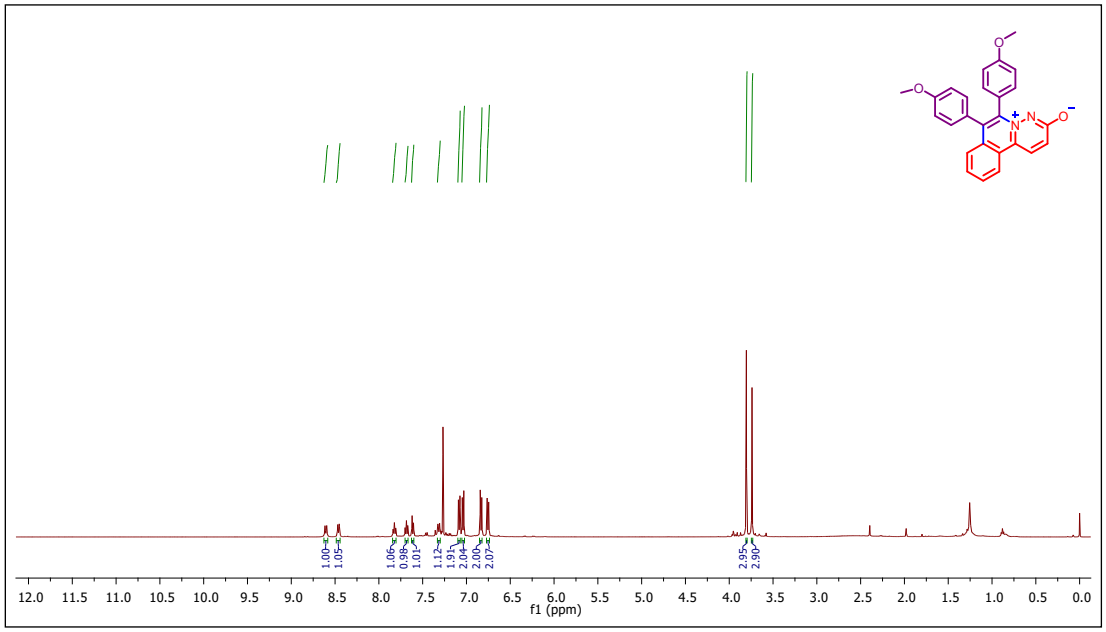
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 3b:



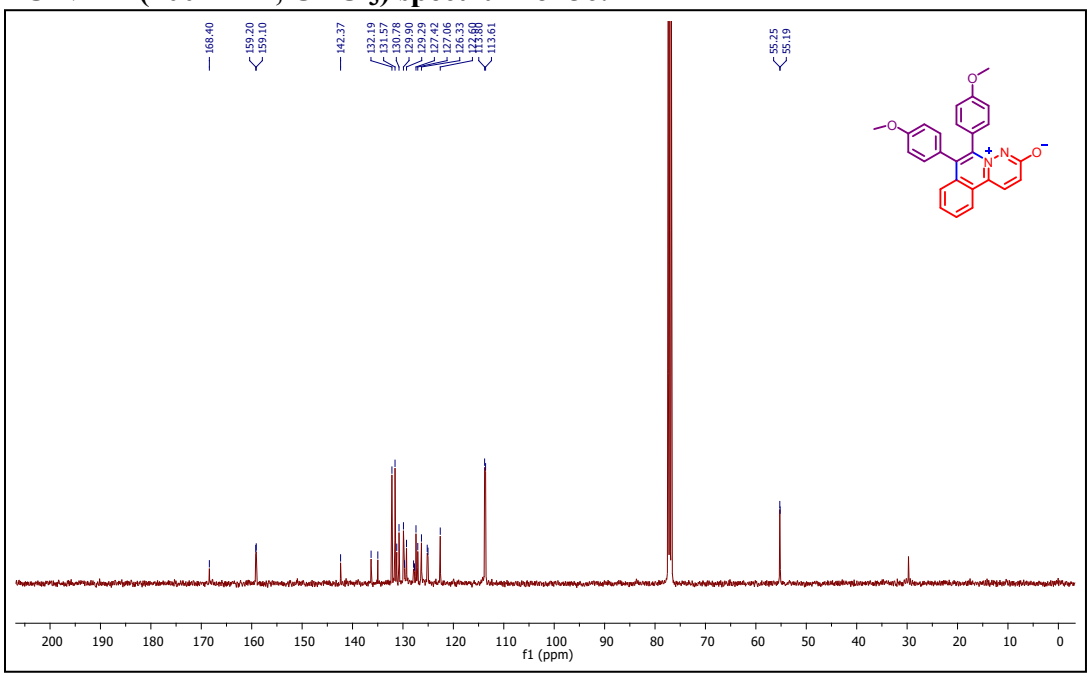
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of 3b:



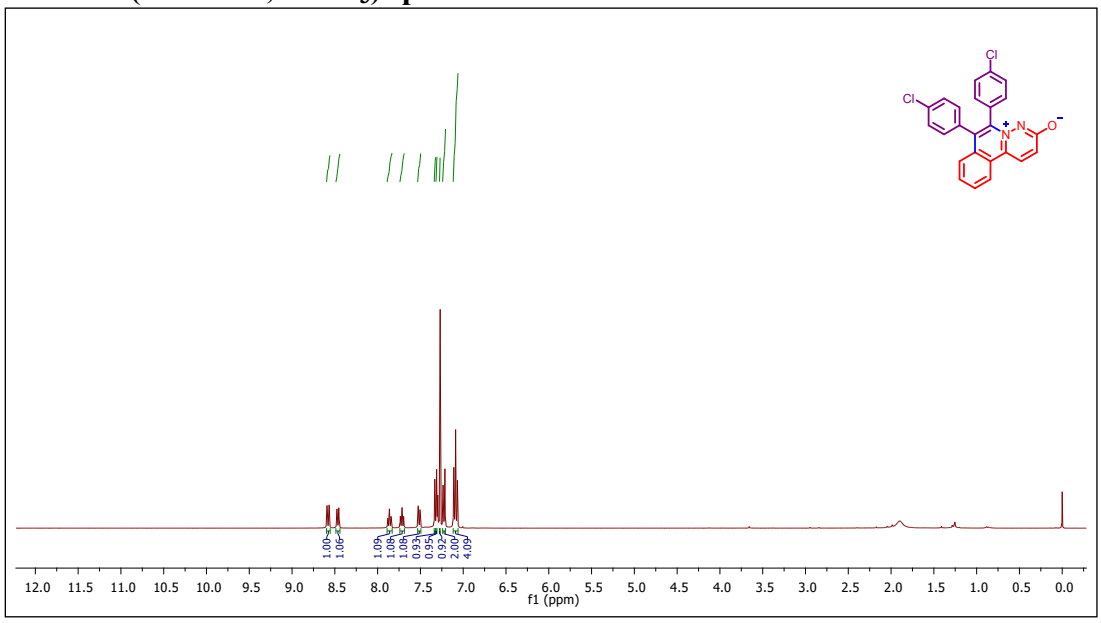
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3c:



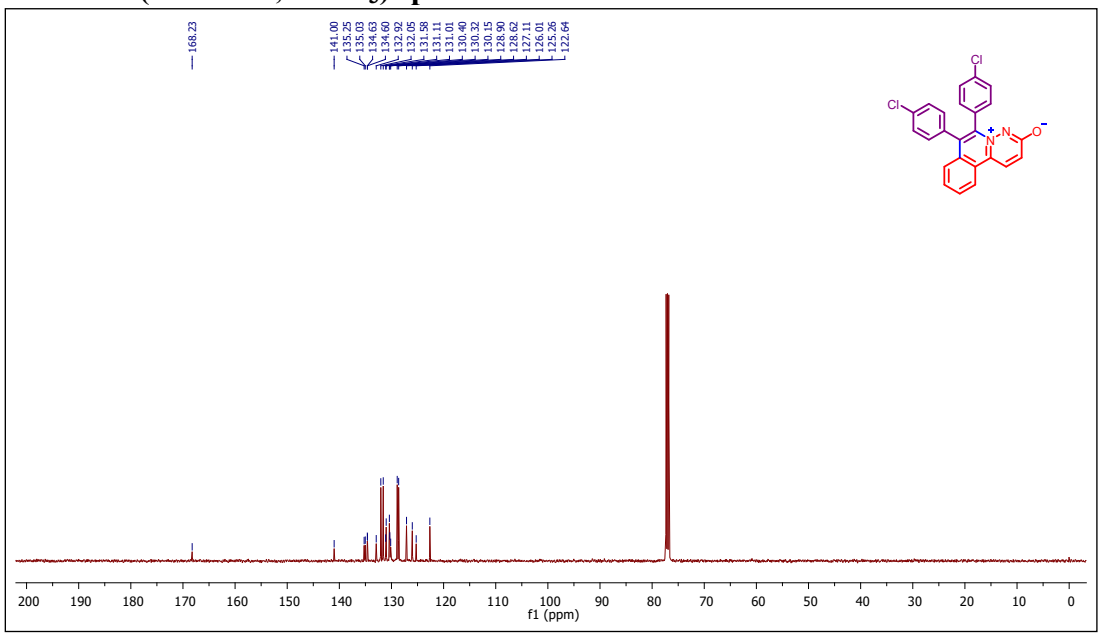
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3c:



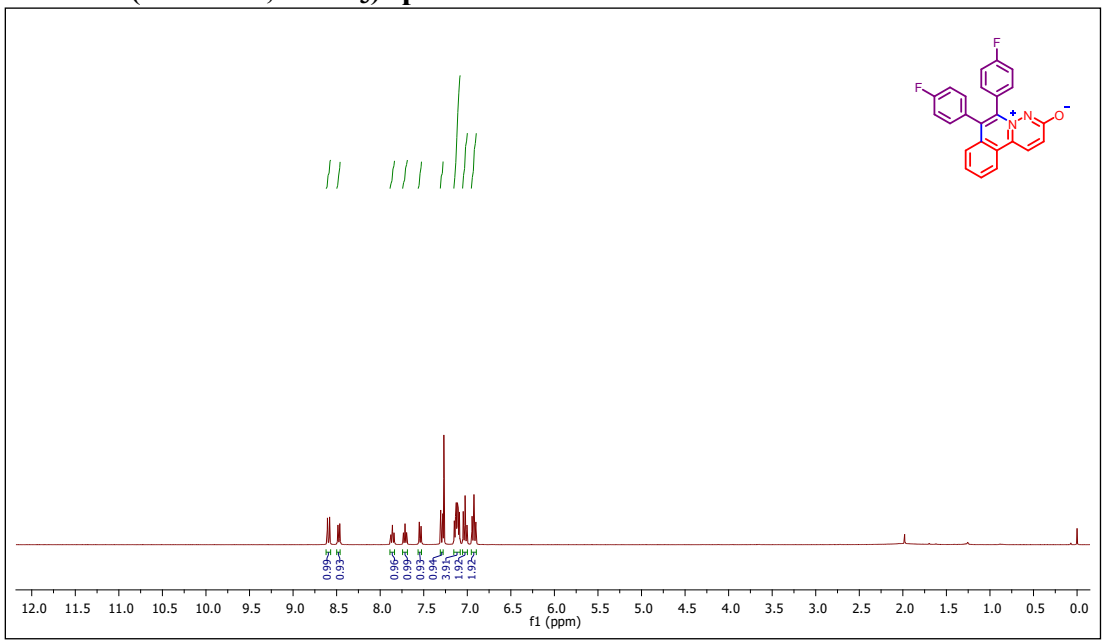
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3d:



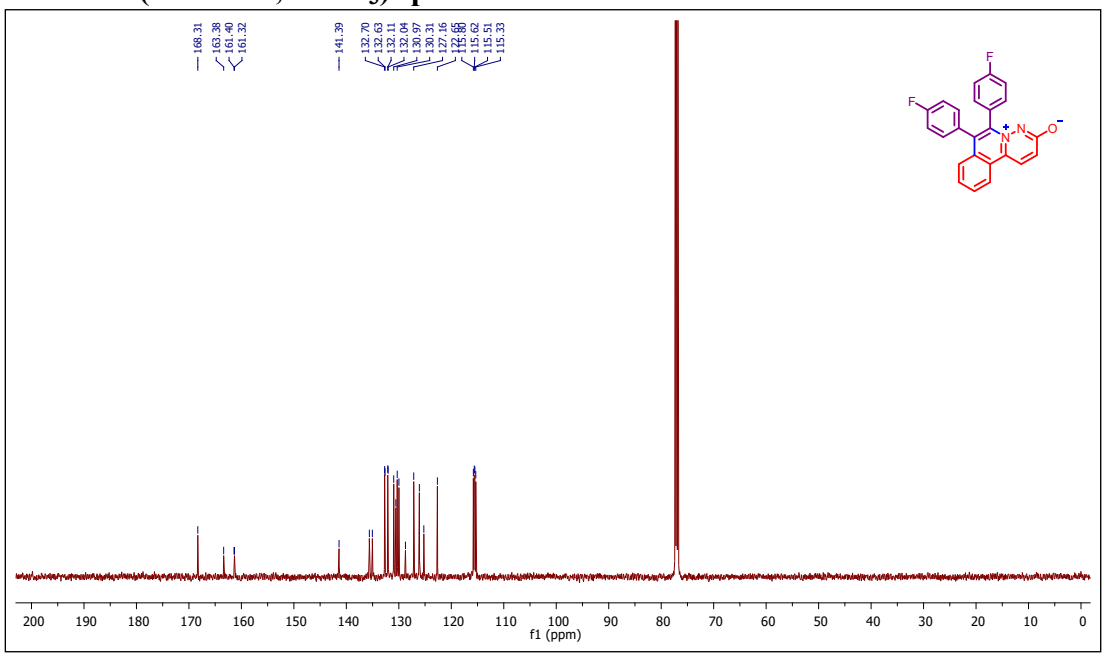
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3d:



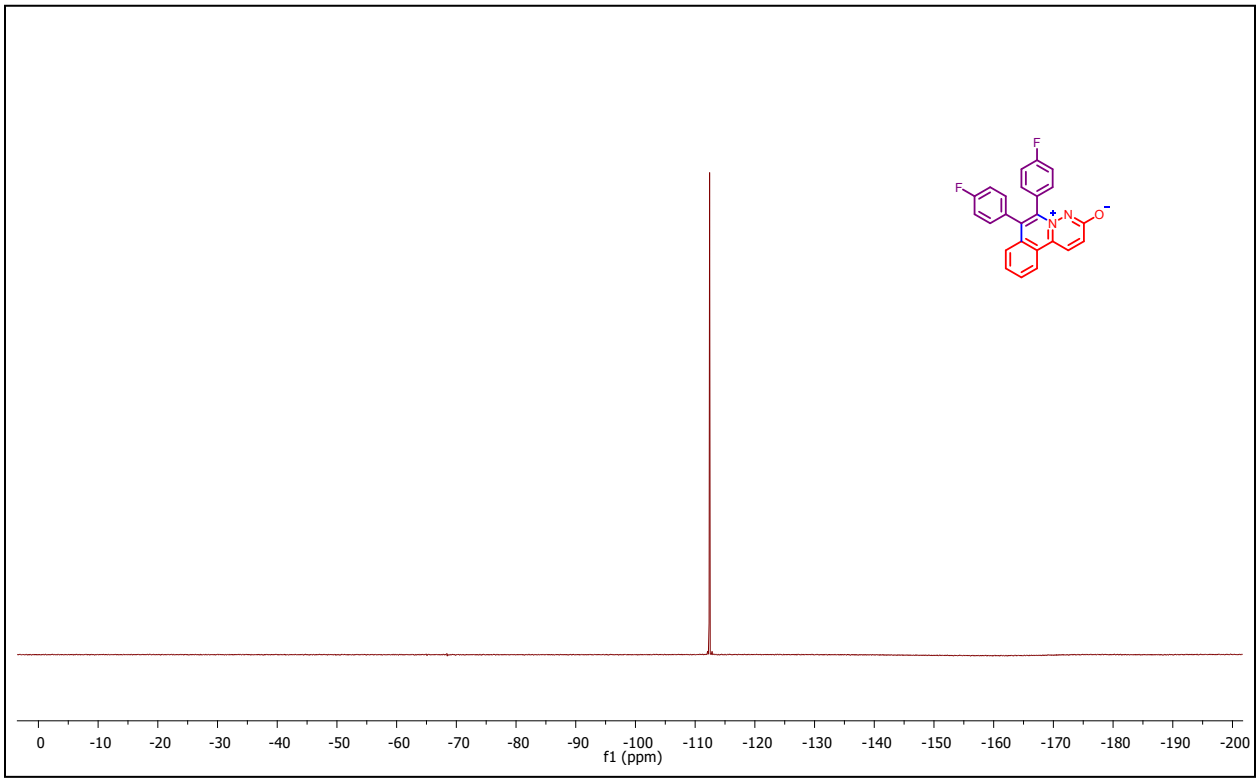
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3e:



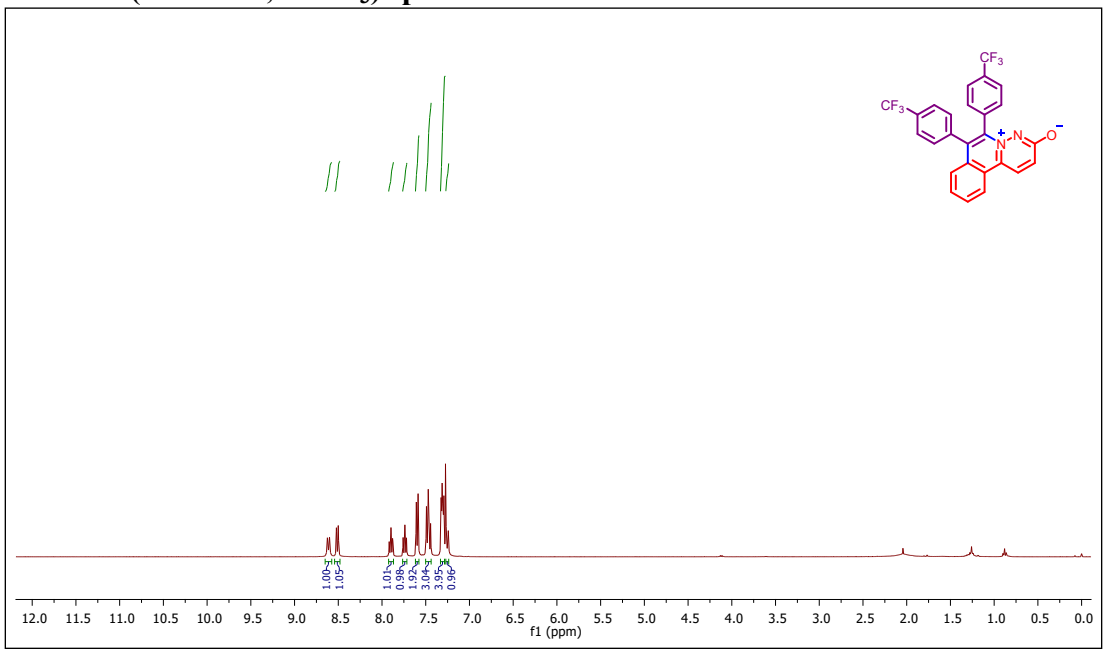
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3e:



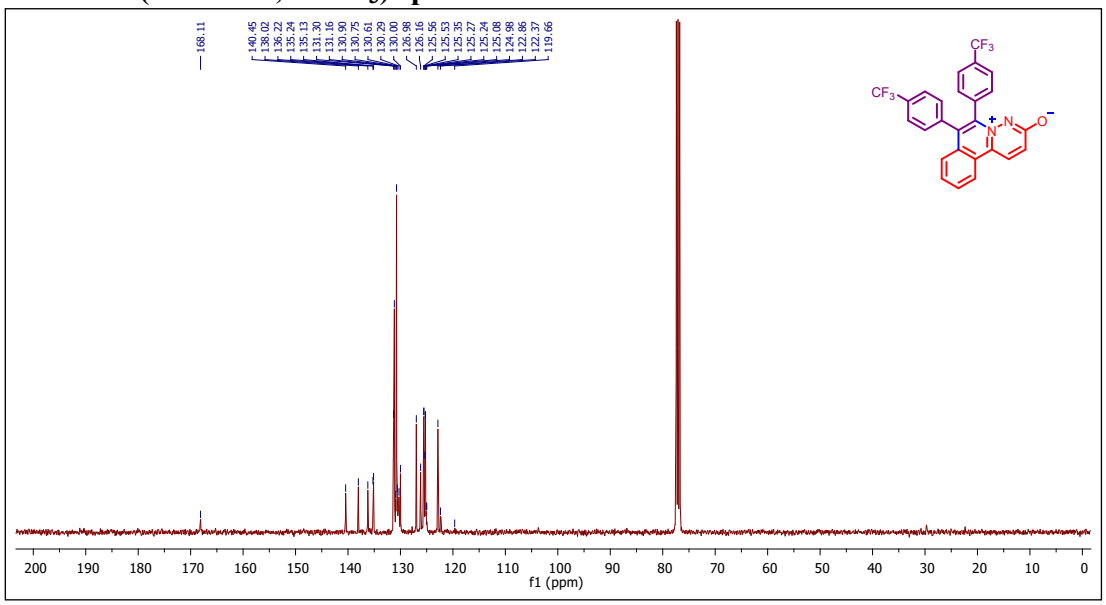
^{19}Fspectrum of 3e:



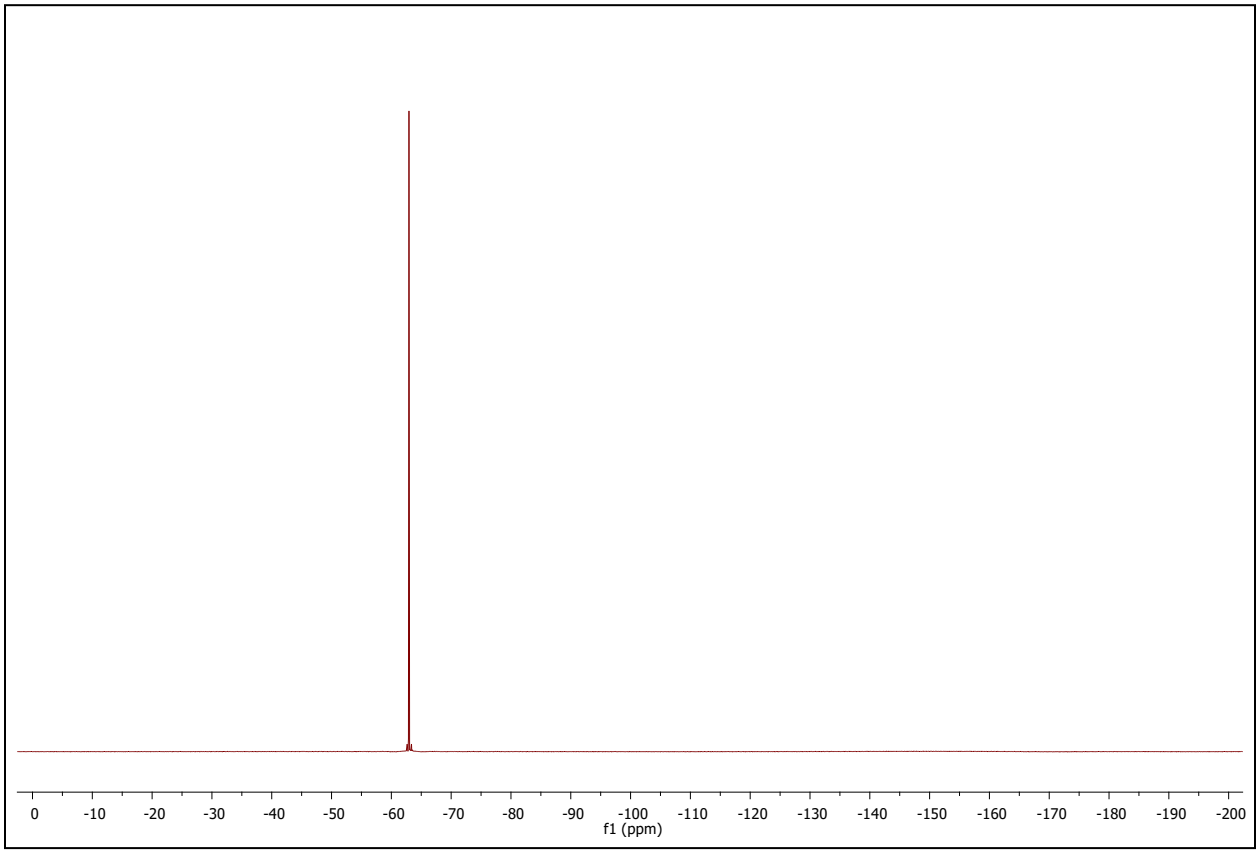
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3f:



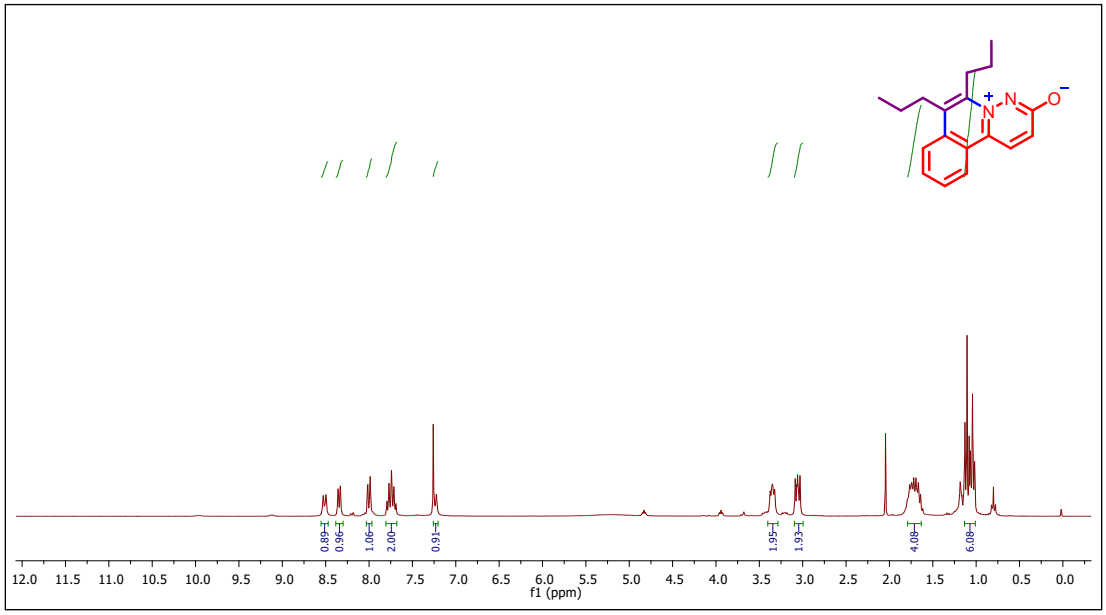
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3f:



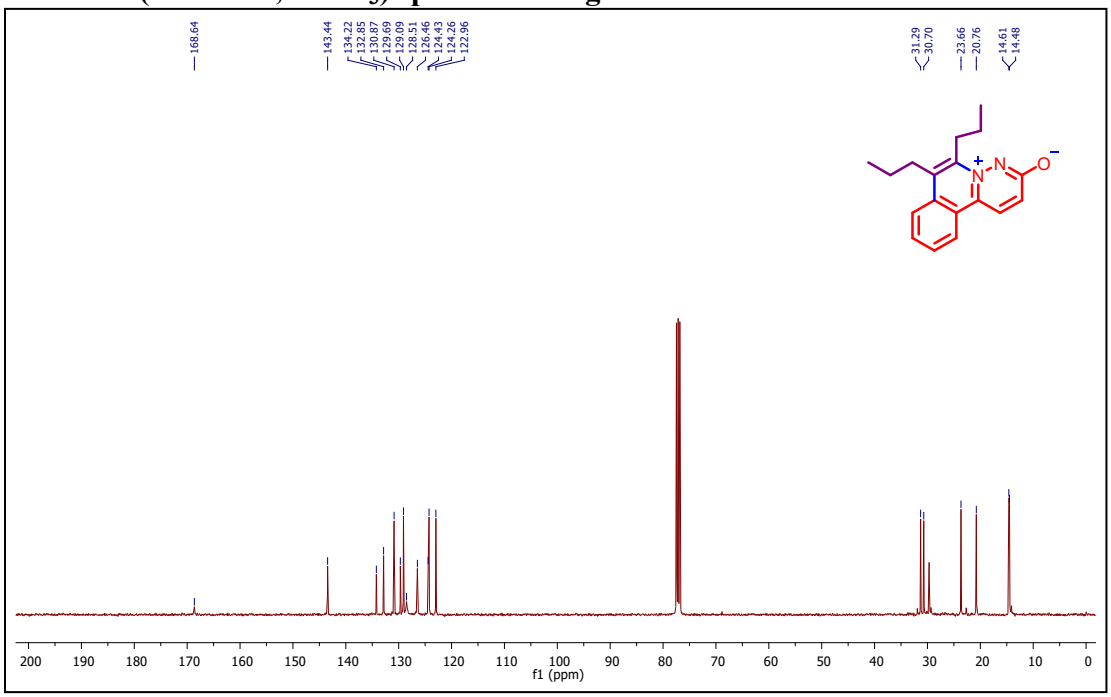
^{19}F spectrum of 3f:



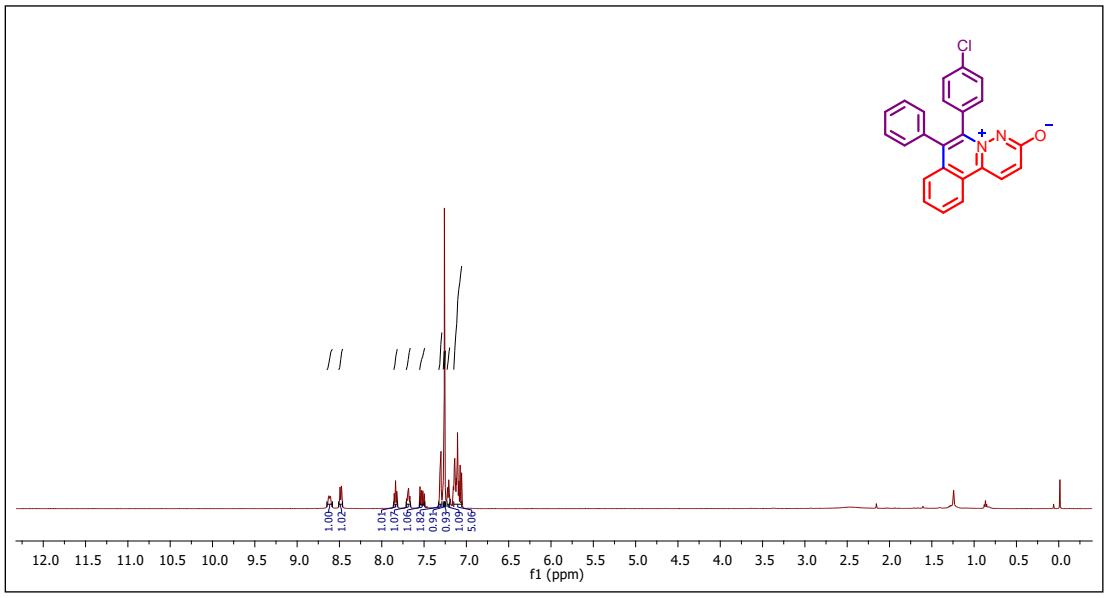
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 3g:



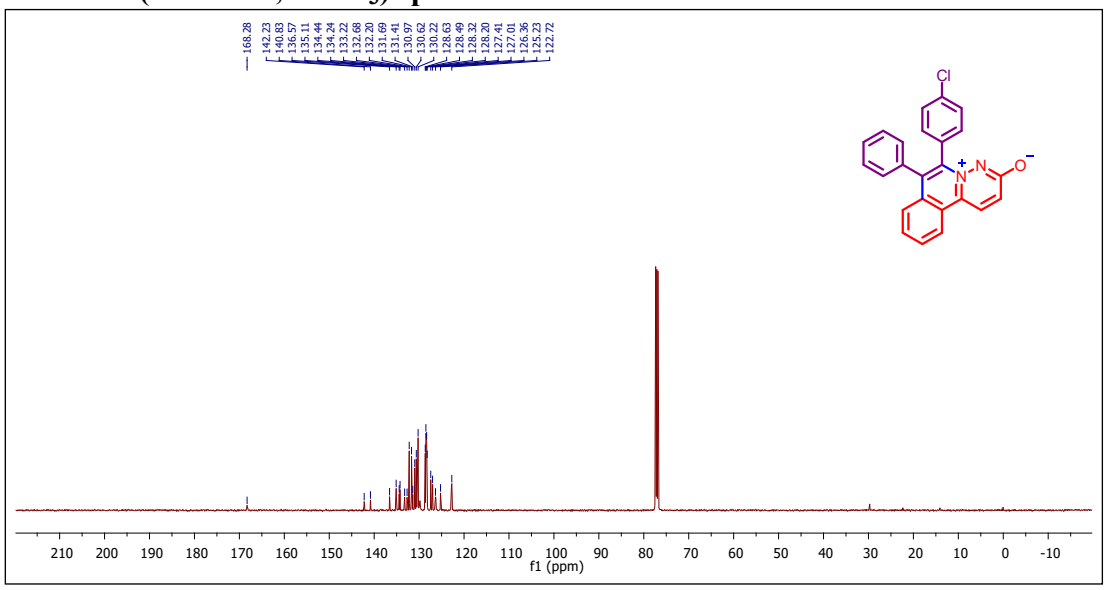
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3g:



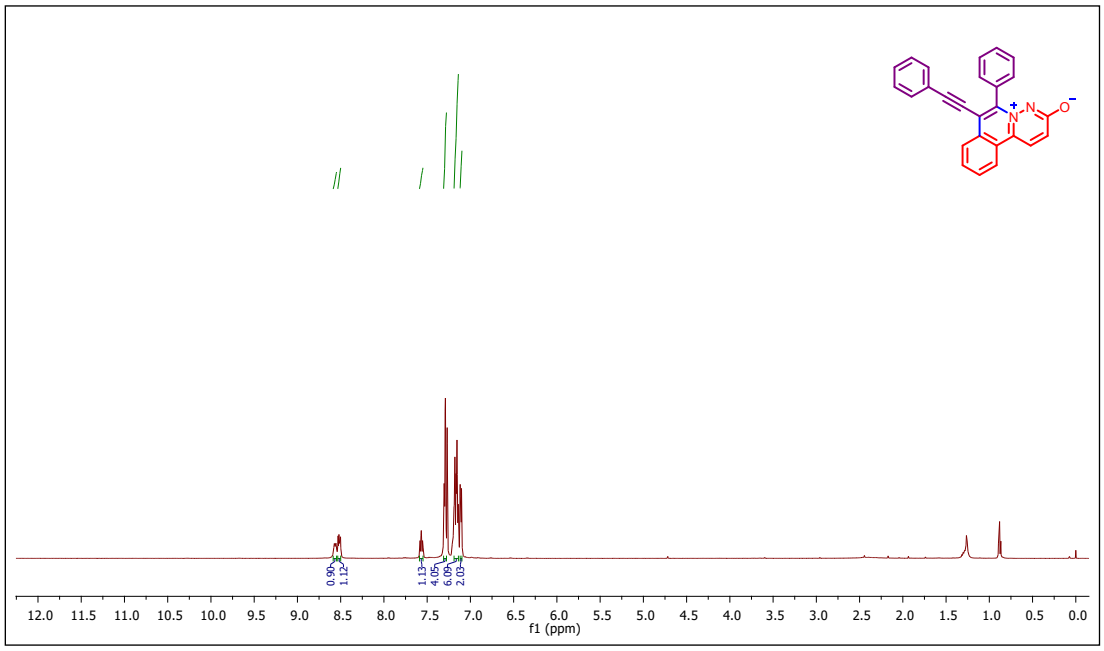
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3h:



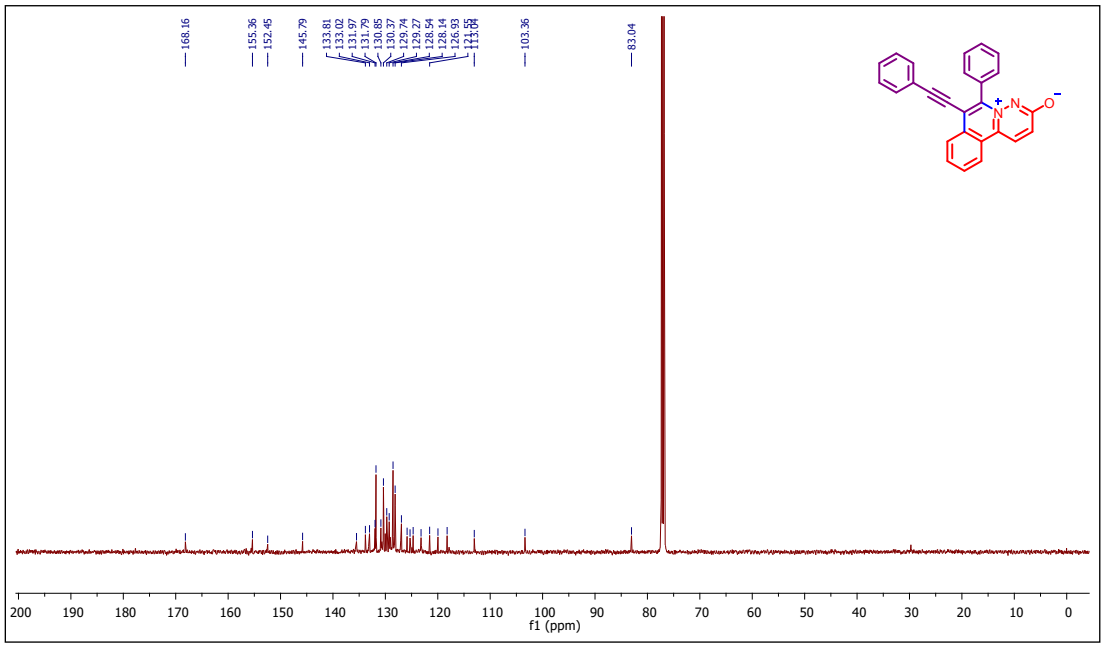
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3h:



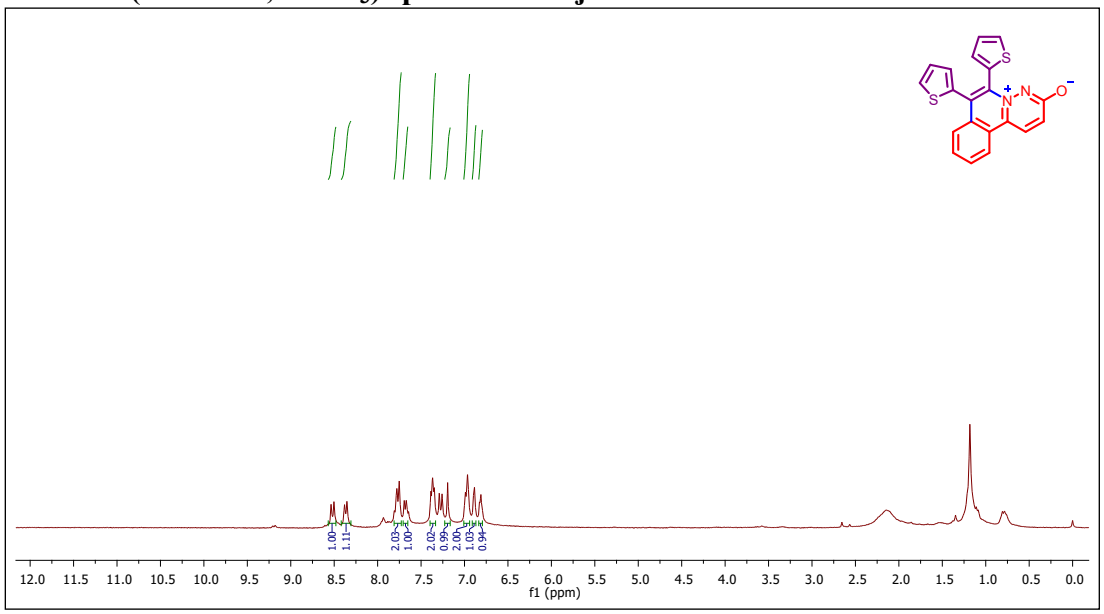
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 3i:



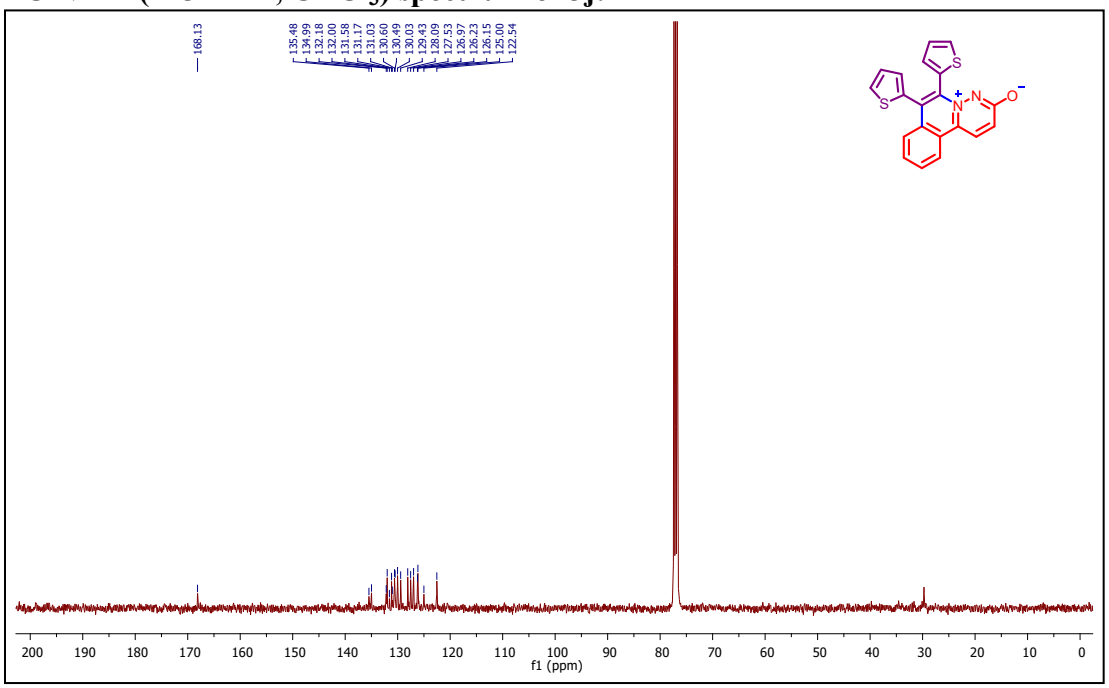
^{13}CNMR (125 MHz, $CDCl_3$) spectrum of 3i:



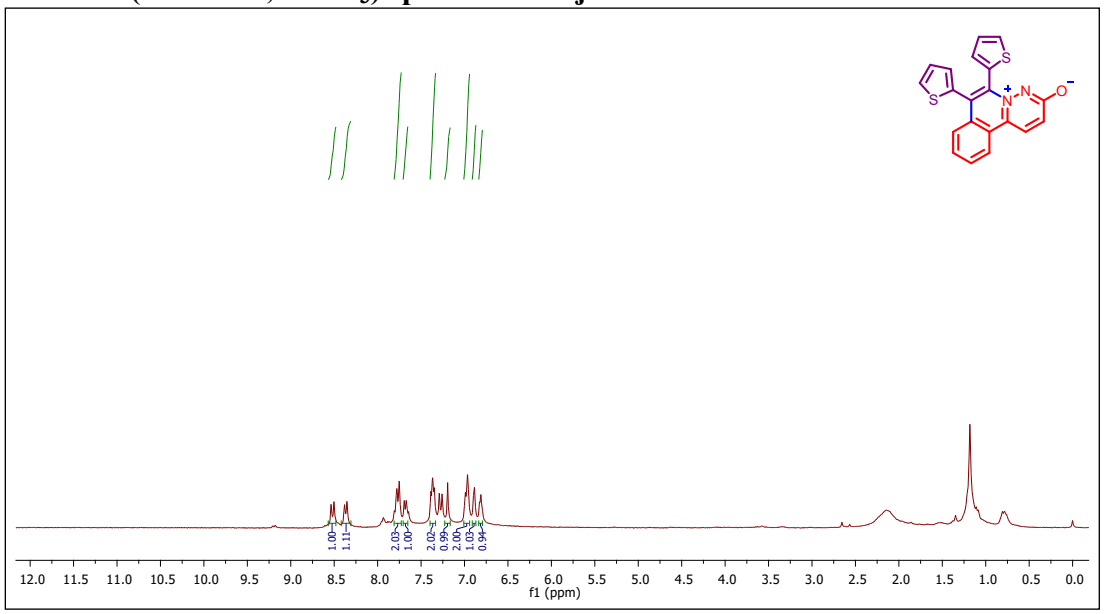
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3j:



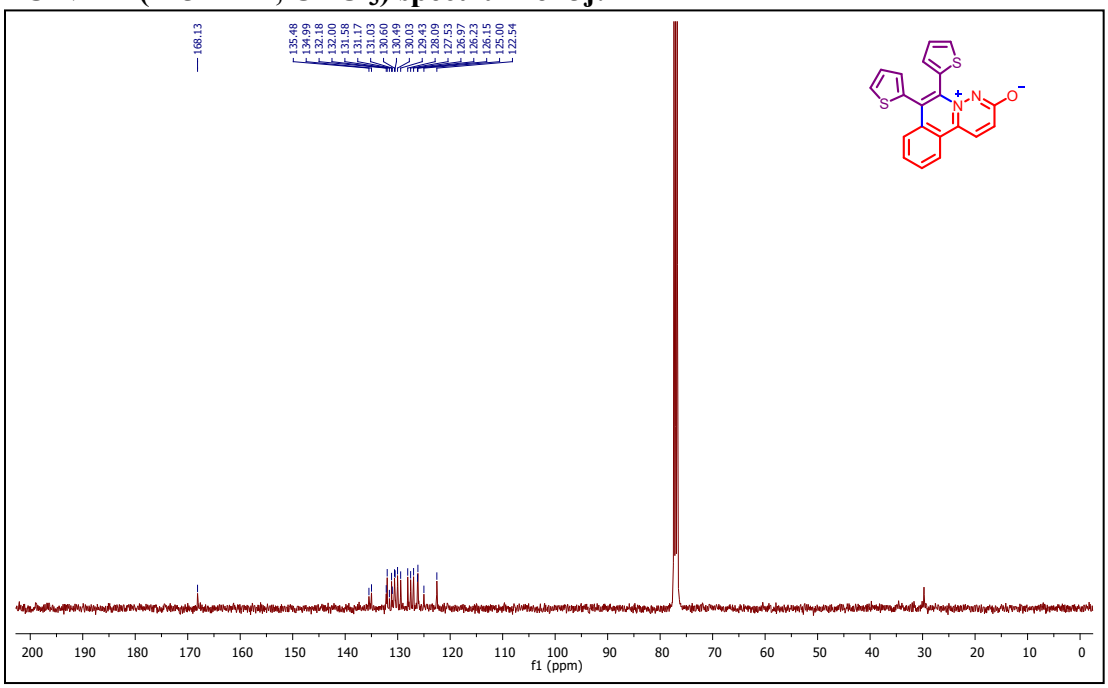
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3j:



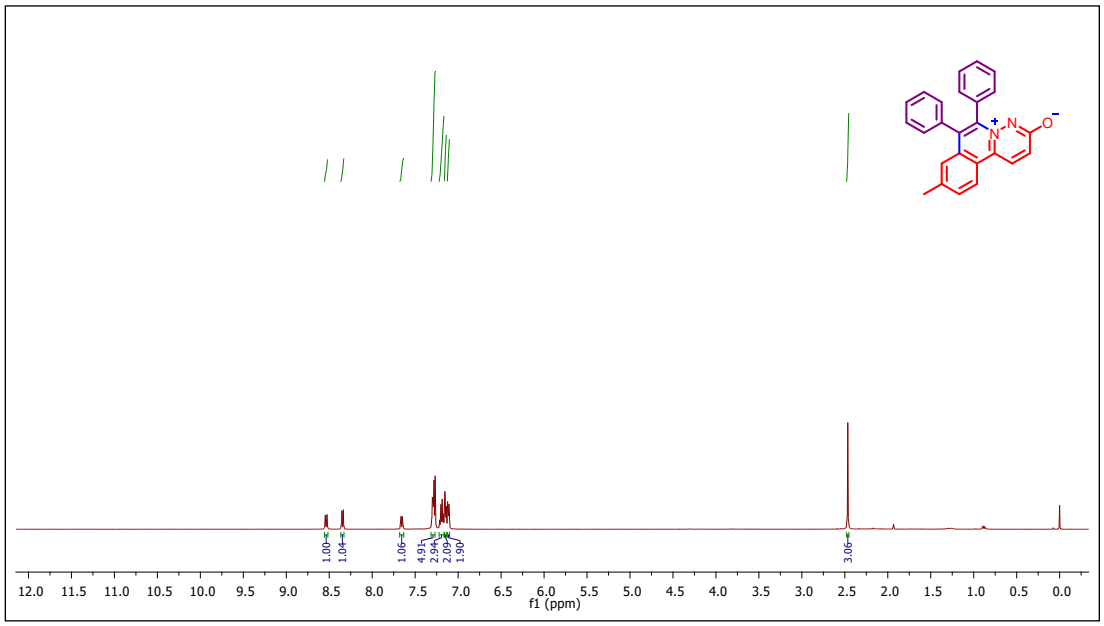
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3j:



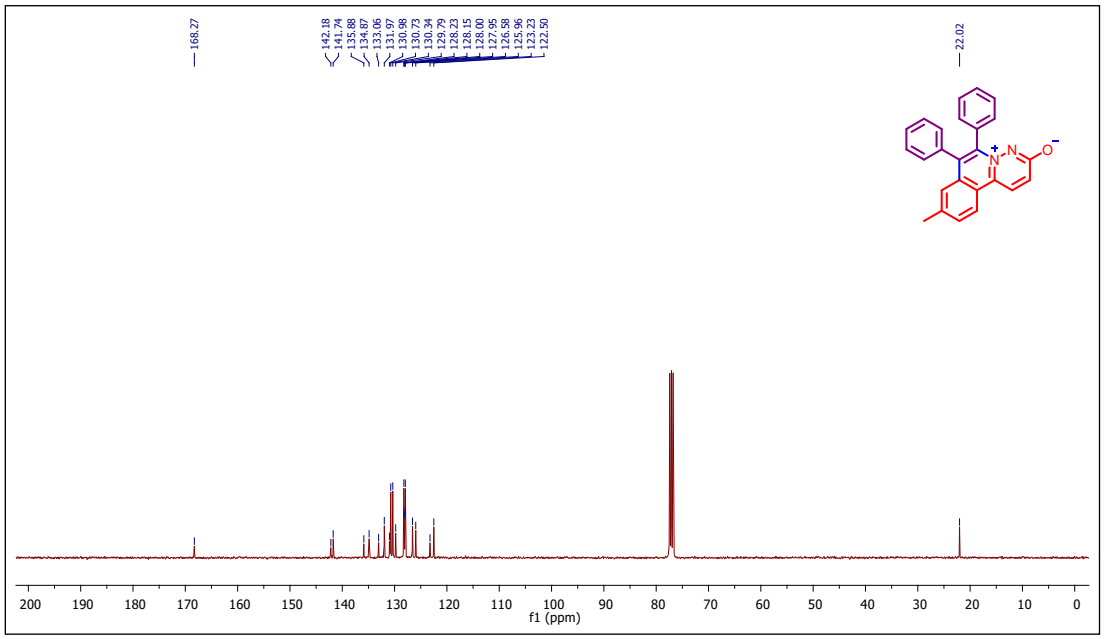
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3j:



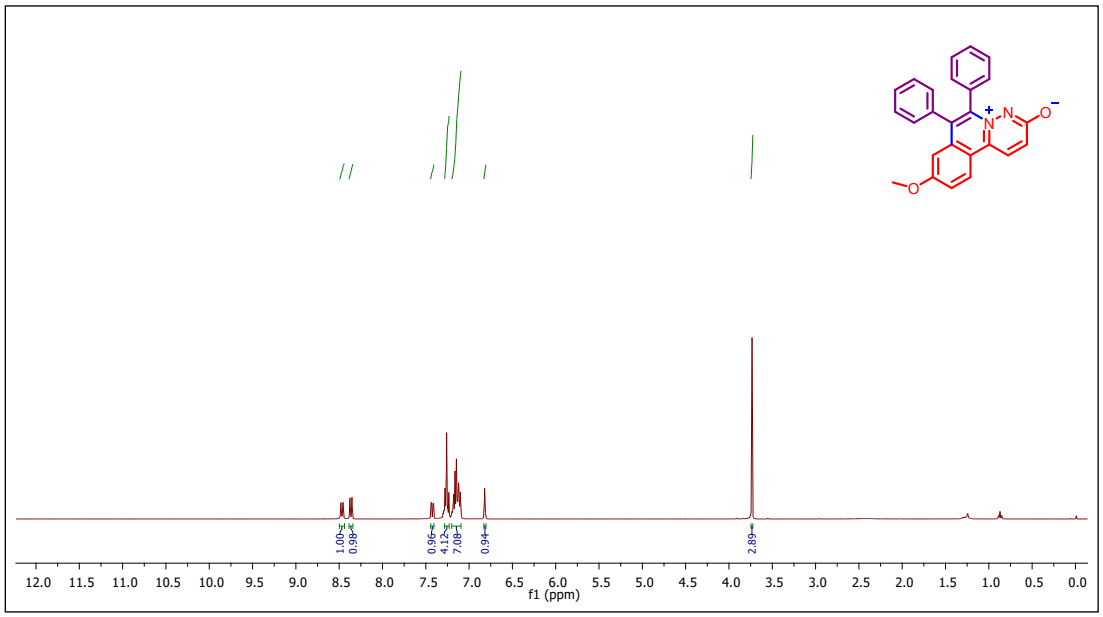
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3k:



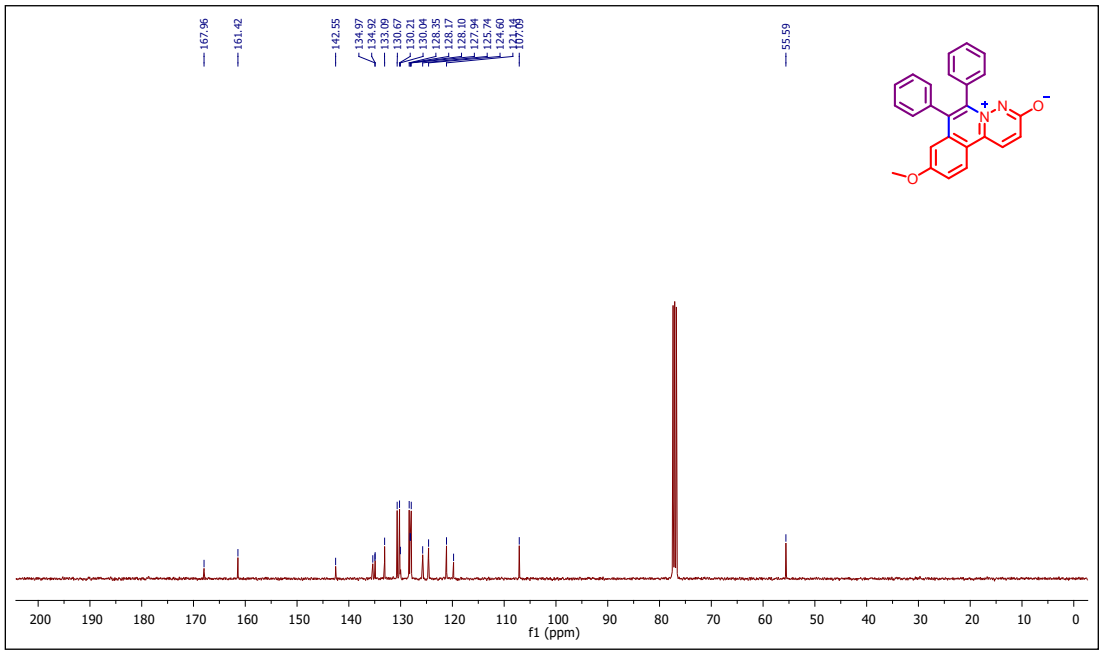
^{13}CNMR (100 MHz, $CDCl_3$) spectrum of 3k:



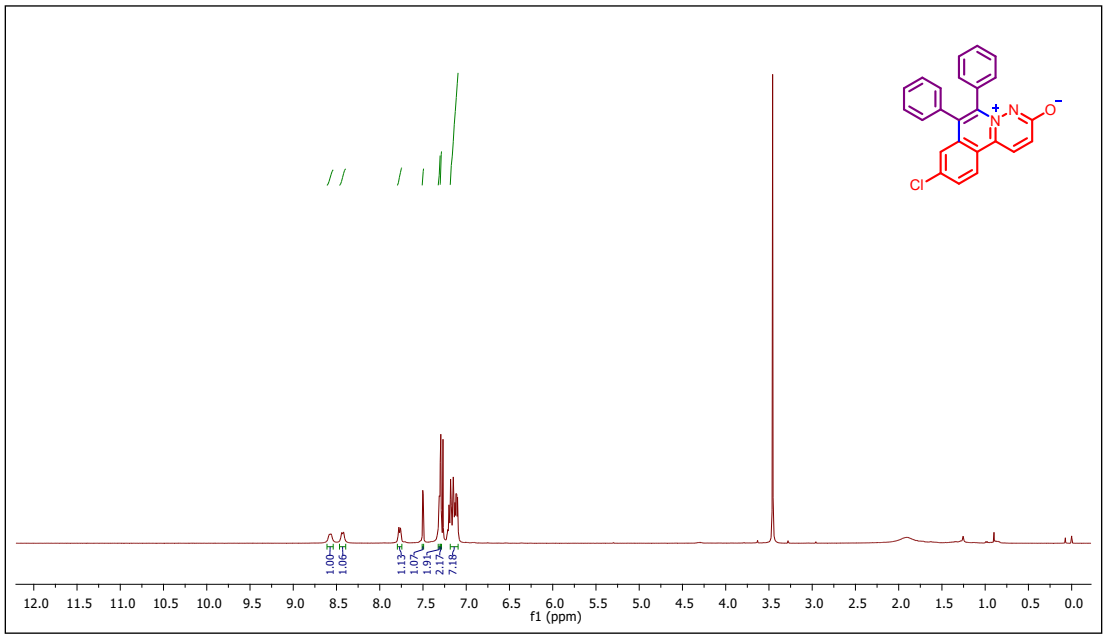
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3l:



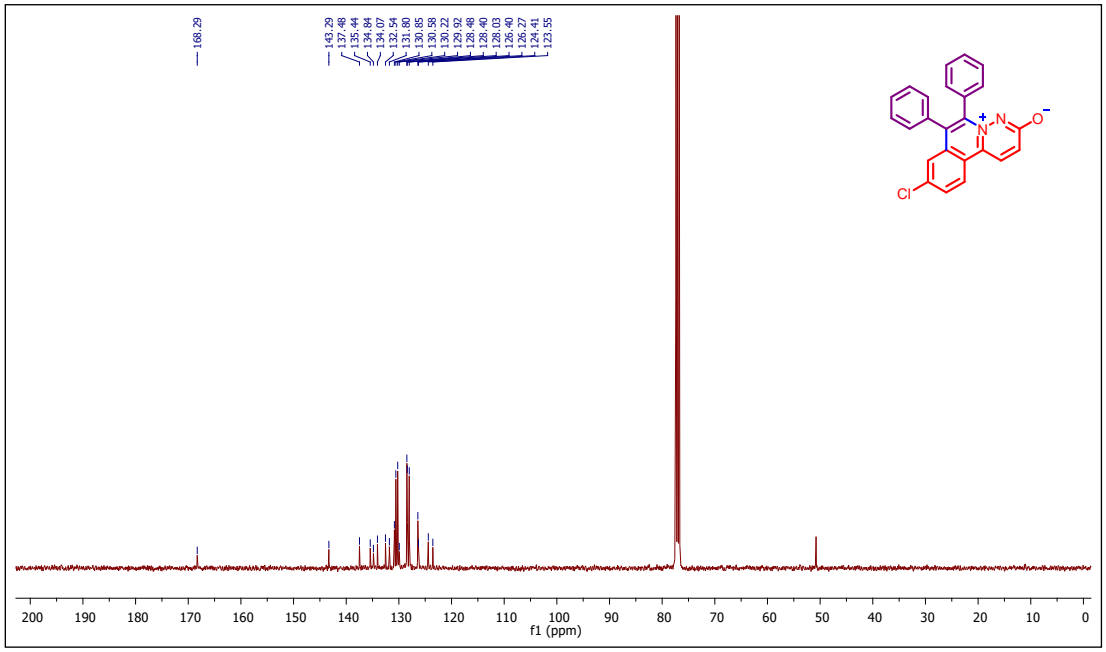
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3l:



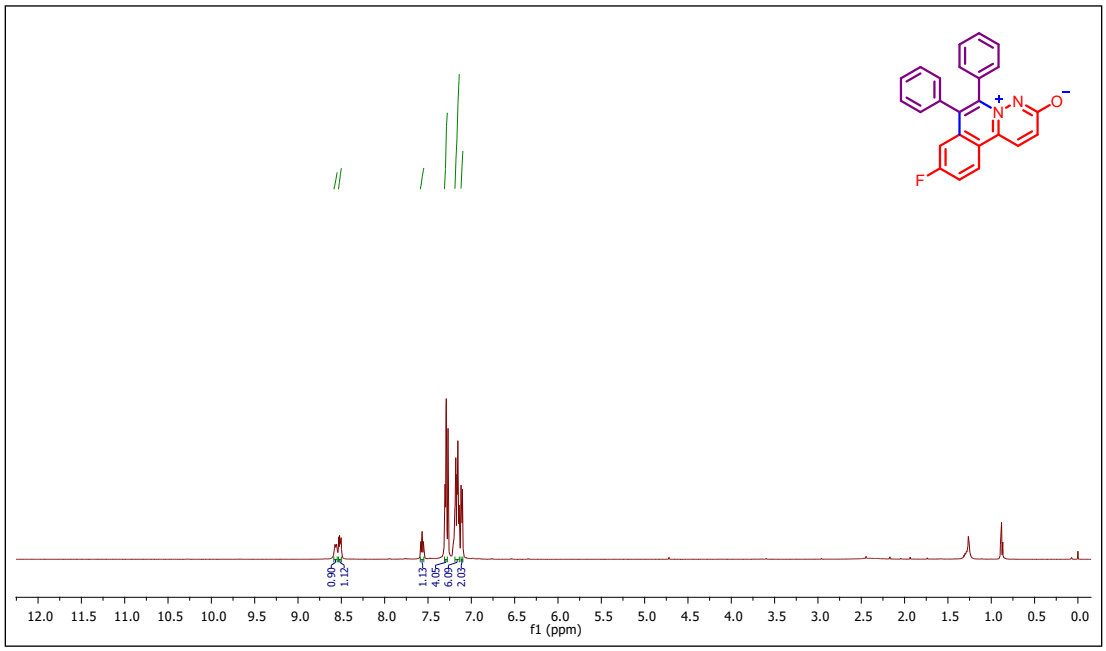
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3m:



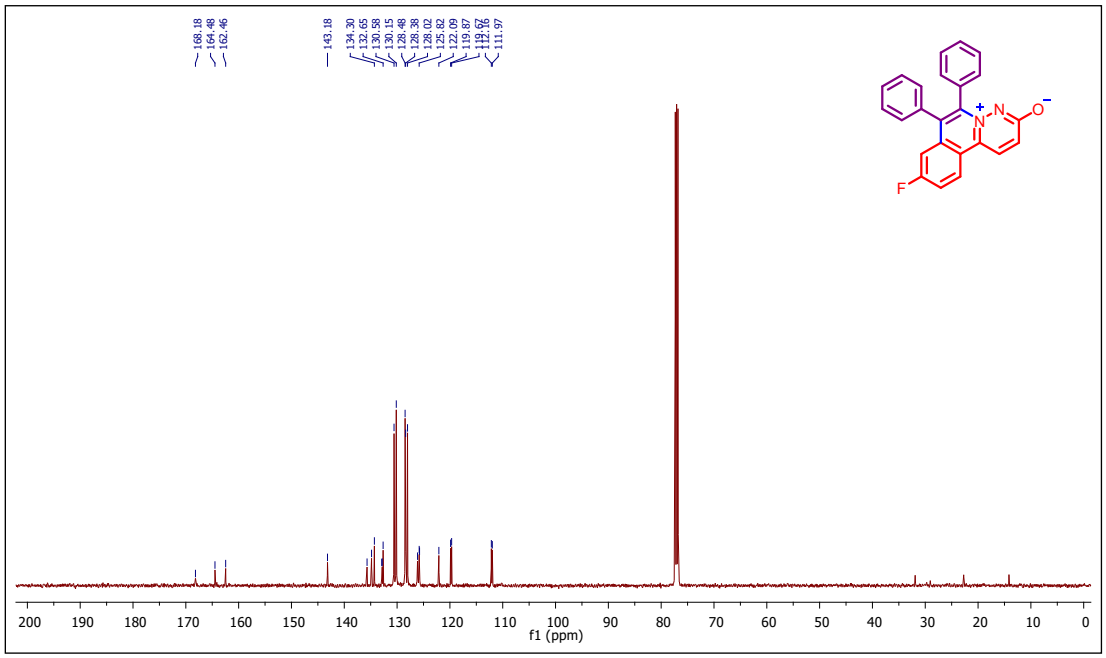
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3m:



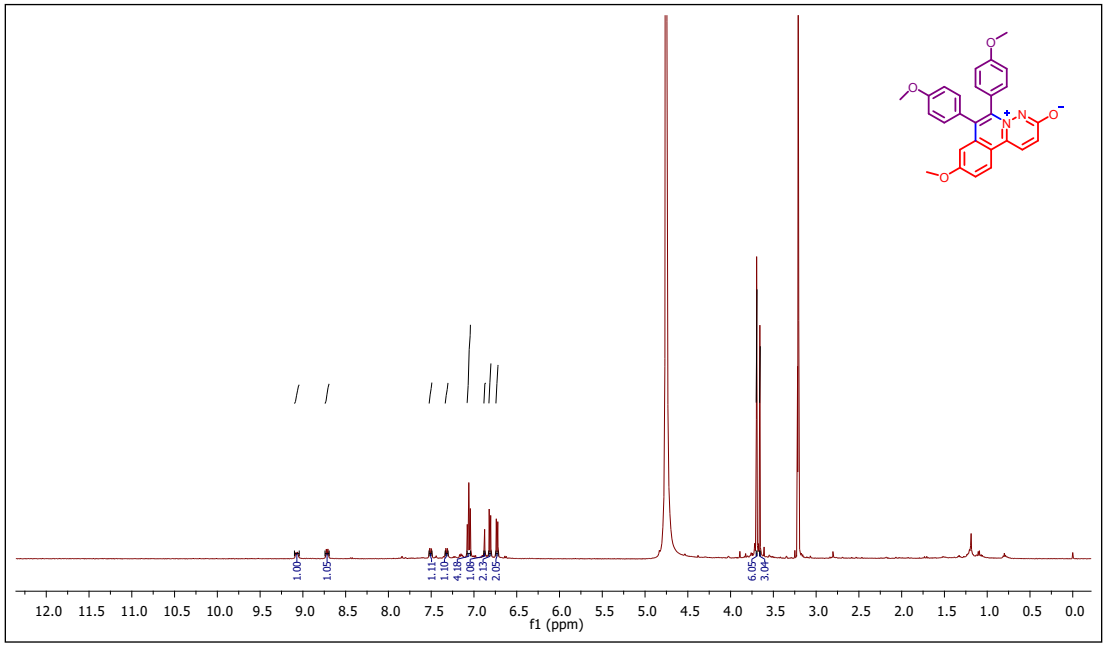
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3n:



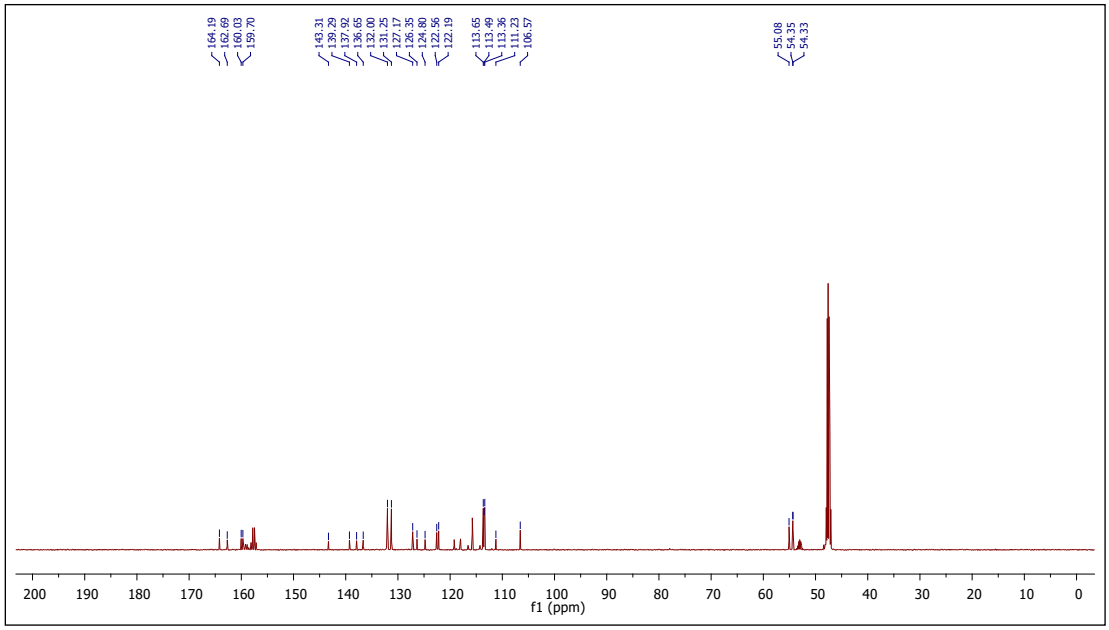
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3n:



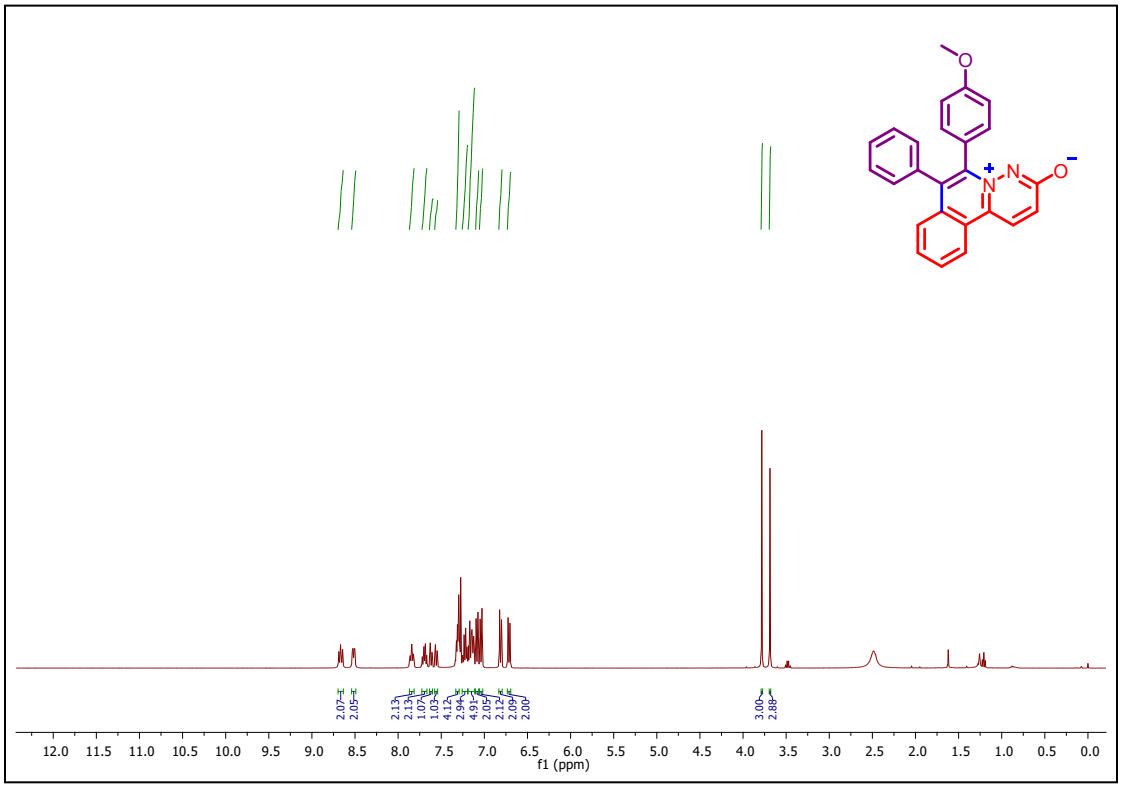
^{1}H NMR (500 MHz, CD_3OD) spectrum of 3o:



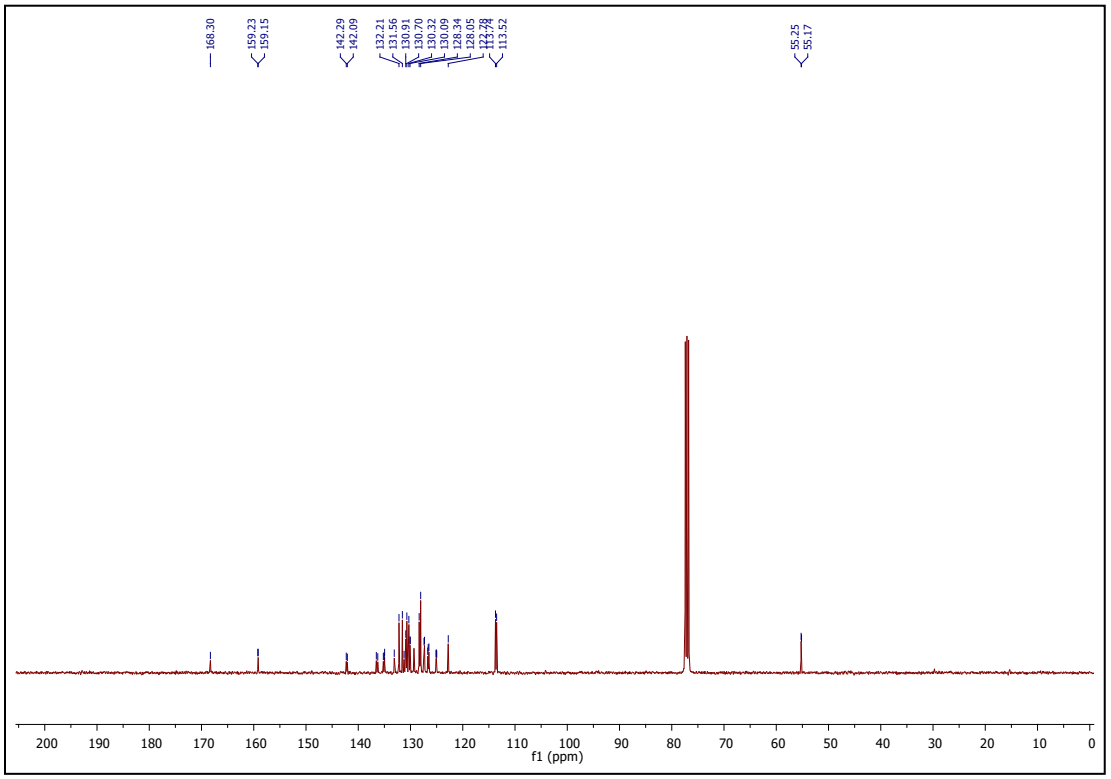
^{13}C NMR (125 MHz, CD_3OD) spectrum of 3o:



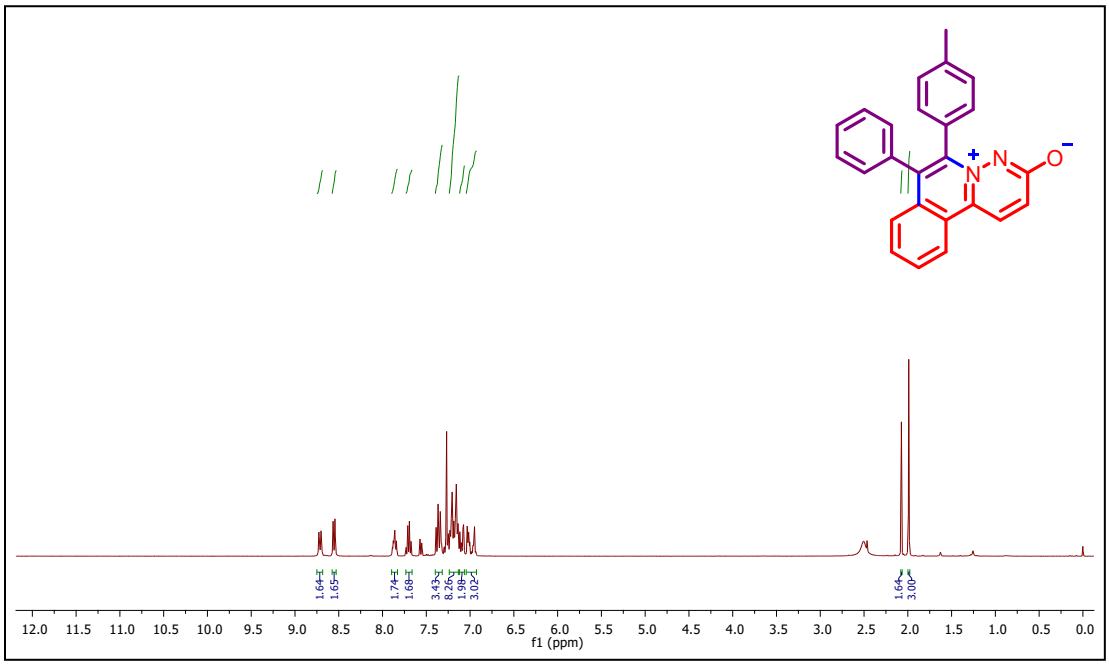
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3r:



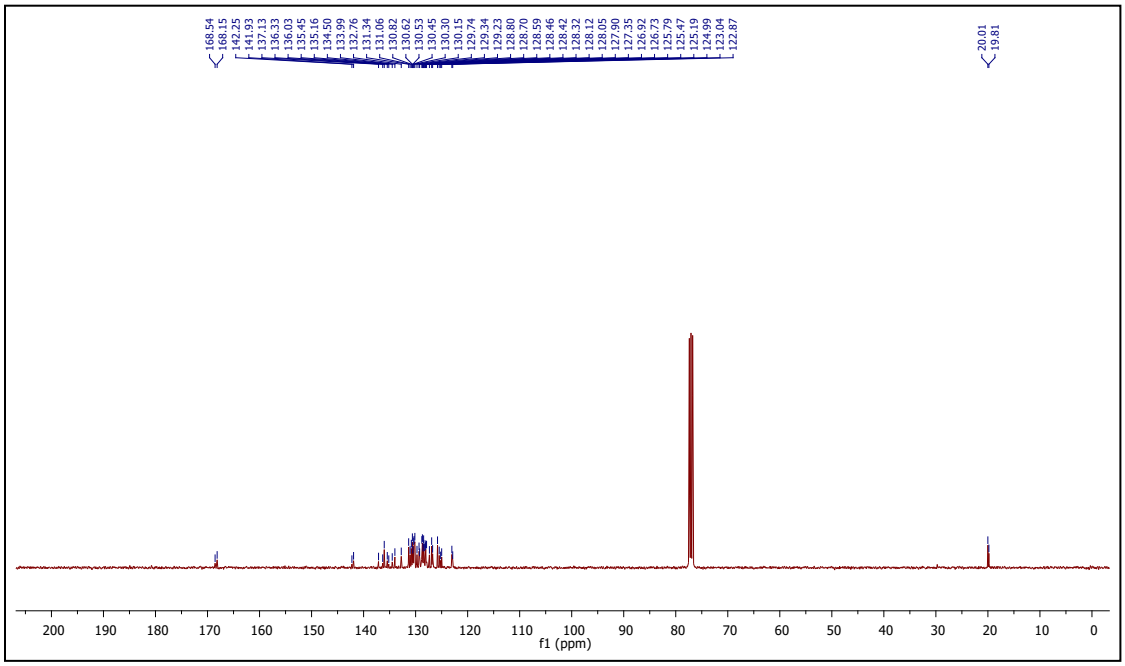
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3r:



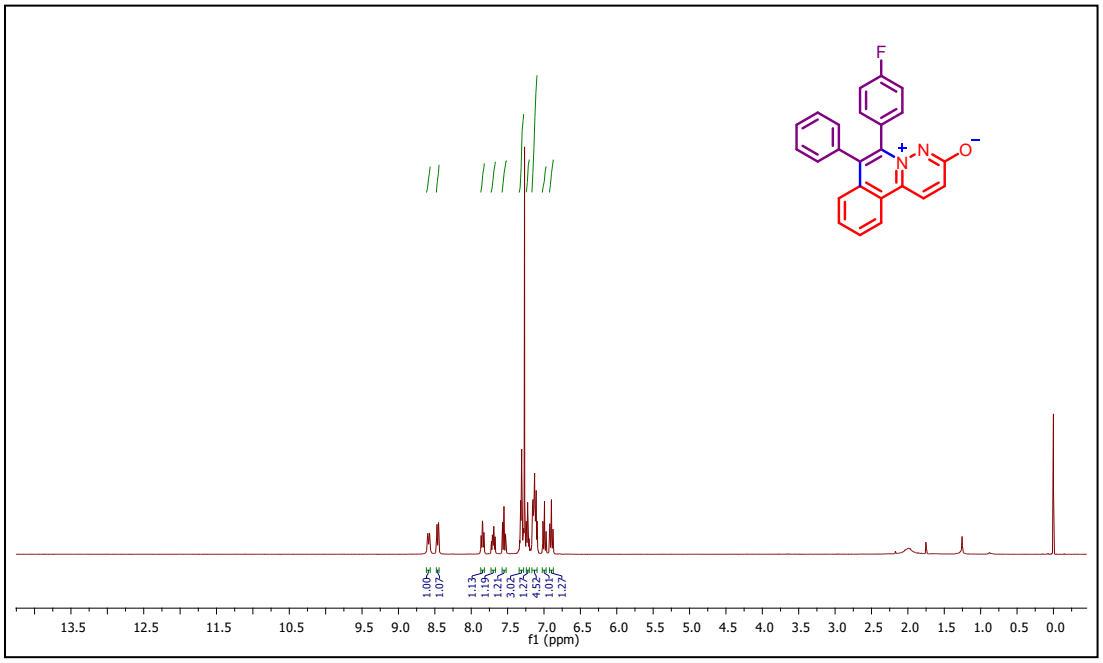
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3s:



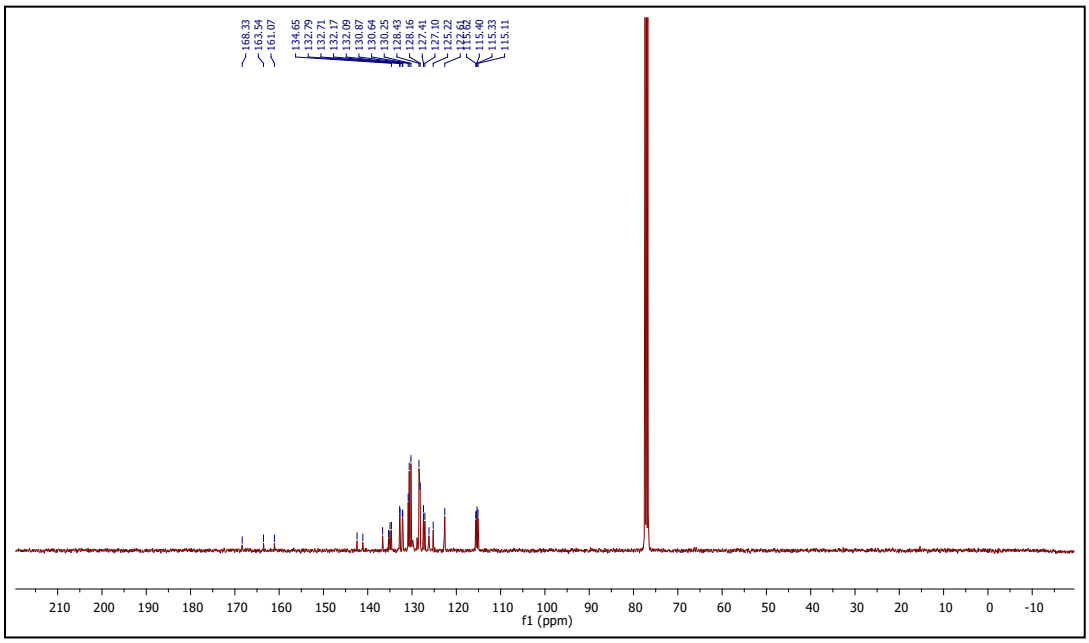
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3s:



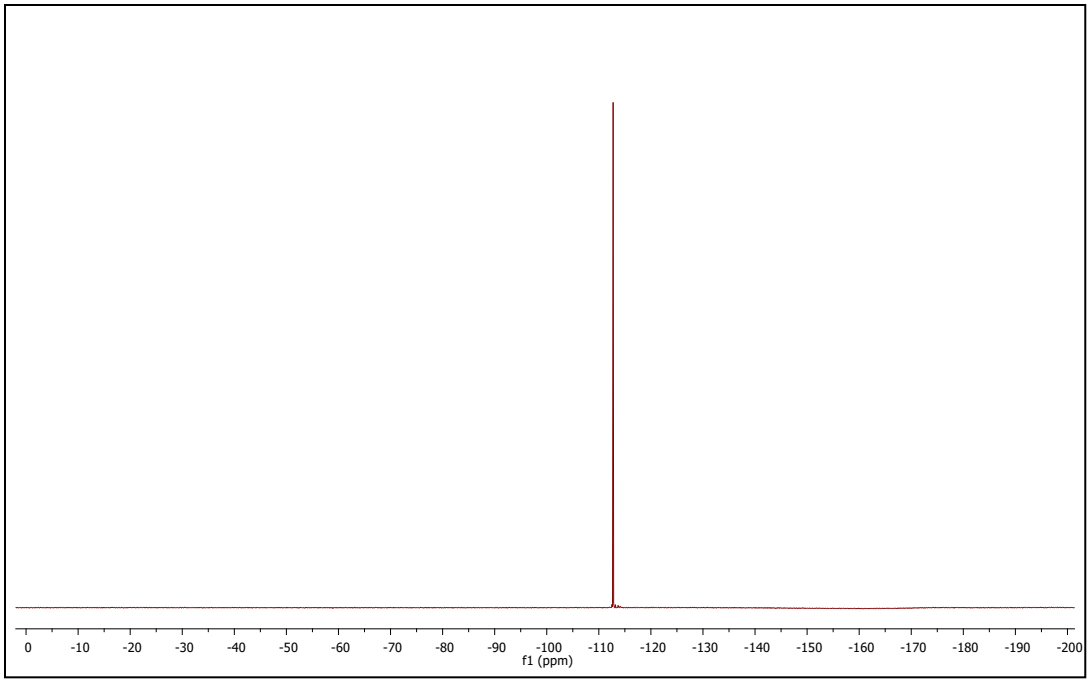
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3t:



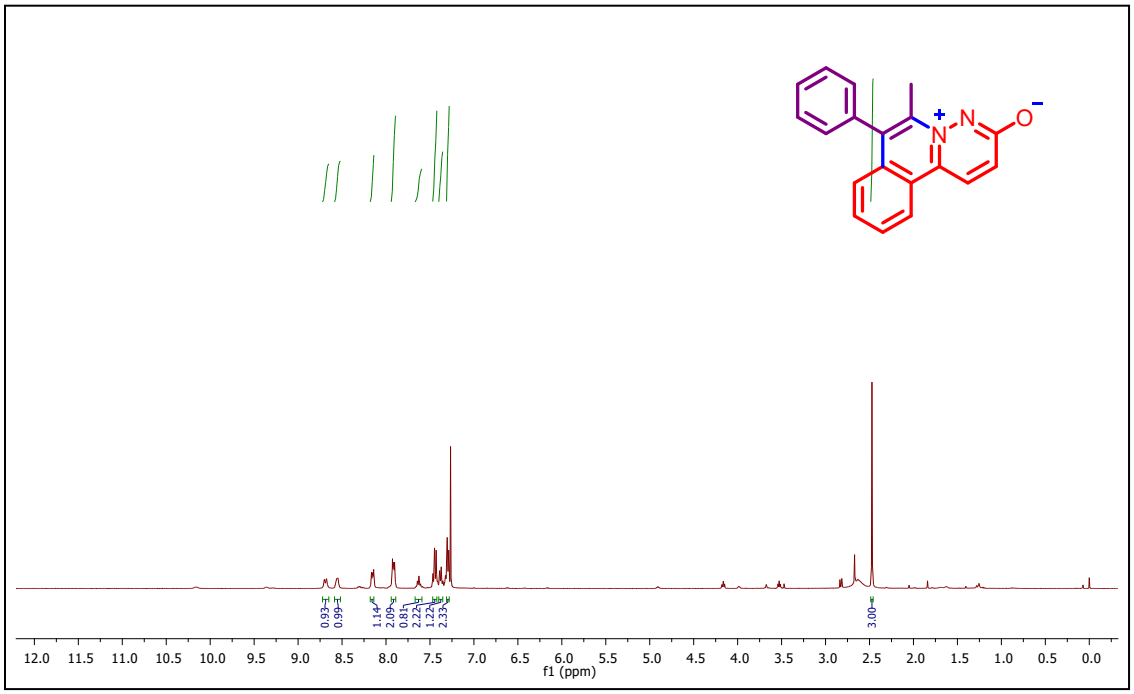
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3t:



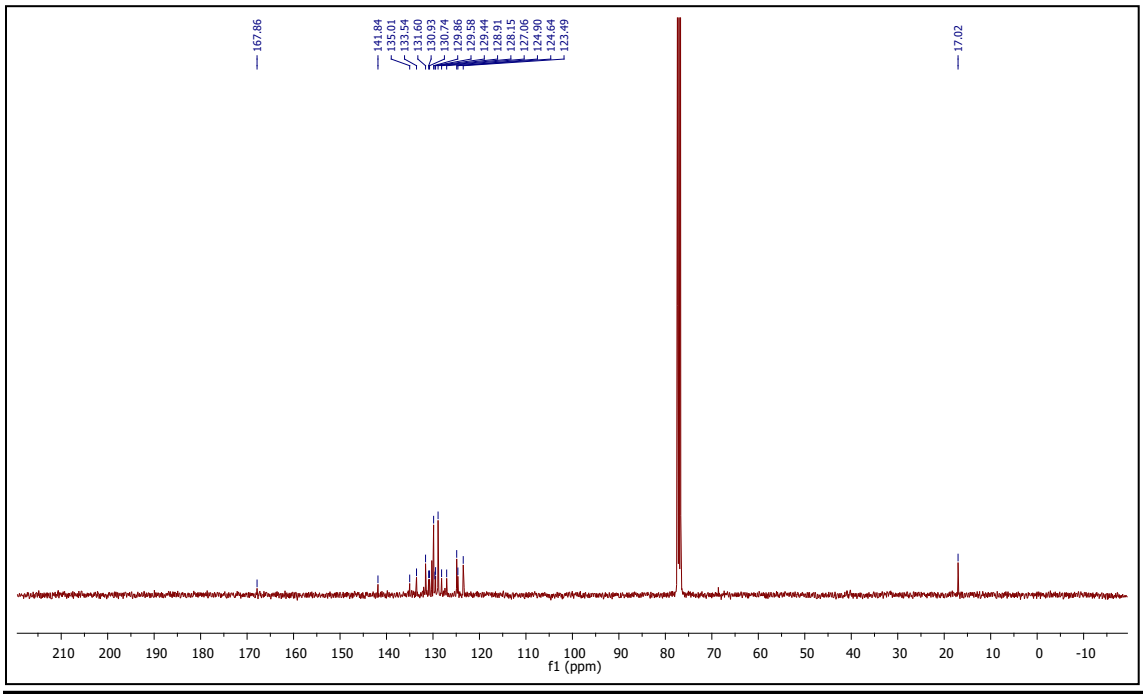
^{19}F spectrum of 3t:



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3u:



^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3u:



5. X-ray Crystallography:

X-ray data for the compound was collected at room temperature on a Bruker D8 VENTURE instrument with an IμSMomicrosource (λ = 0.7107 Å) and a Bruker PHOTON III C14 detector. The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 5 software suite programs [1]. The structure was solved using intrinsic phasing method [2] and further refined with the SHELXL [2] program and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. Atoms CL1/CL2/CL3of chloroform solvent were disordered over two positions and their site occupational factors were refined to 0.57(3) and 0.43(3) respectively. All C bound H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and Uiso(H) = 1.5Ueq(C) for methyl H or 1.2Ueq(C) for other H atoms].

Crystal structure determination of VA 214 (3d)

Crystal Data for $C_{25}H_{15}N_2OCl_3F_2$ (M =503.74 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 13.474(4) Å, b = 13.727(4) Å, c = 12.998(5) Å, β = 109.823(12)°, V = 2261.6(13) Å^3, Z = 4, T = 100.15 K, μ(MoKα) = 0.443 mm^{-1}, $Dcalc$ = 1.479 g/cm^3, 28966 reflections measured (4.374° ≤ 2Θ ≤ 56.592°), 5595 unique (R_{int} = 0.0627, R_{sigma} = 0.0469) which were used in all calculations. The final R_1 was 0.0453 (I > 2σ(I)) and wR_2 was 0.1302 (all

data). **CCDC 2480463**deposition number contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Crystal structure determination of [mo_VA771_0m_a] (3h)

Crystal Data for $C_{25}H_{16}Cl_4N_2O$ (M =502.20 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 13.6258(17) Å, b = 14.1135(16) Å, c = 12.9741(17) Å, β = 109.818(4)°, V = 2347.2(5) Å^3, Z = 4, T = 294.15 K, μ(MoKα) = 0.525 mm^{-1}, $Dcalc$ = 1.421 g/cm^3, 26455 reflections measured (4.292° ≤ 2Θ ≤ 56.76°), 5853 unique (R_{int} = 0.0486, R_{sigma} = 0.0493) which were used in all calculations. The final R_1 was 0.0705 (I > 2σ(I)) and wR_2 was 0.2471 (all data). **CCDC 2548013** deposition number contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Crystal structure determination of [mo_VA759_0m] (3t)

Crystal Data for $C_{24}H_{15.708425}N_2O_{1.35421}F$ (M =372.76 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 9.1194(17) Å, b = 16.274(4) Å, c = 12.513(3) Å, β = 101.163(7)°, V = 1822.0(7) Å^3, Z = 4, T = 294.15 K, μ(MoKα) = 0.092 mm^{-1}, $Dcalc$ = 1.359 g/cm^3, 17005 reflections measured (5.196° ≤ 2Θ ≤ 49.982°), 3196 unique (R_{int} = 0.0456, R_{sigma} = 0.0271) which were used in all calculations. The final R_1 was 0.0366 (I > 2σ(I)) and wR_2 was 0.1047 (all data). **CCDC 2548012** deposition number contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

1. Bruker (2023). APEX5, SAINT and SADABS. Bruker AXS, Inc., Madison, Wisconsin, USA.
2. Sheldrick G. M. (2019)ActaCrystallogr C71: 3-8.

Figure: ORTEP diagram of VA214 compound with the atom-numbering. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radius. The minor component of the disordered atoms was omitted for clarity.