Lewis Acid Catalyzed Decarboxylative Annulation of 2-Aminoindole-3-Carboxylate with ynals involving [3+2] spirocycloaddition and 2,3-Aza Migration.

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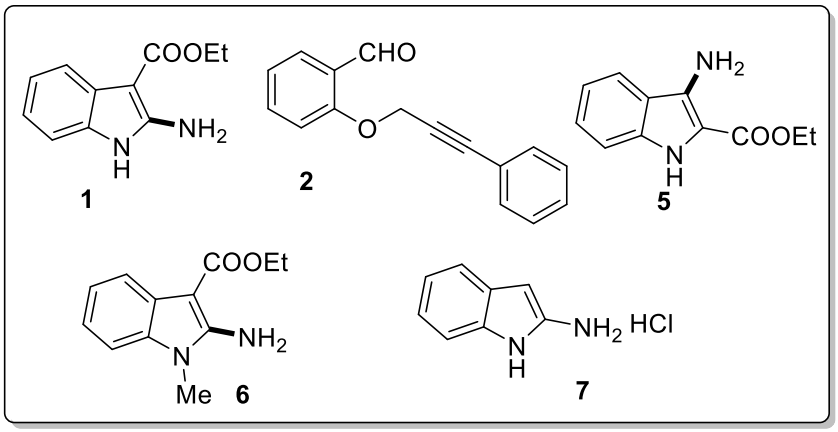
I. General Information and methods:

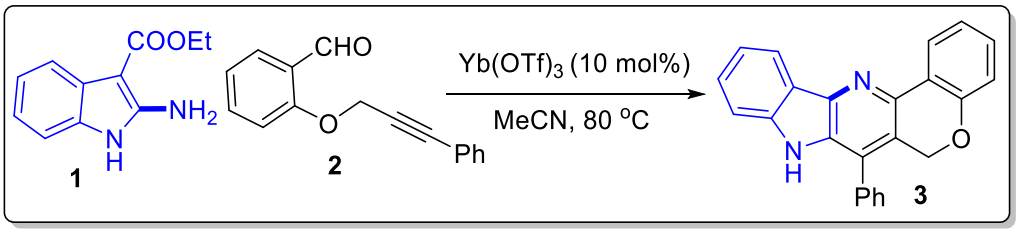
All reagents and solvents were purchased from commercial sources and used without purification. NMR spectra were recorded with a 300, 400 MHz spectrometers for ^{1}H NMR, 75, 100 MHz for ^{13}C NMR, NMR Chemical shifts δ are given in ppm relative to the residual signals of tetramethylsilane in $CDCl_3$ or deuterated solvent DMSO-d_6 for ^{1}H and ^{13}C NMR. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), multiplet (m), broad singlet (bs). HRMS were obtained using the electro spray ionization (ESI) technique and a time-of-flight (TOF) analyzer. Column chromatography was performed using silica gel (100-200 mesh) as the stationary phase. All reactions were monitored by thin layer chromatography (TLC). The purity and characterization of these compounds were further established using HRMS/ESI Mass spectroscopy. Melting points were measured on a capillary melting point apparatus and are uncorrected.

II. General Procedure for the preparation of starting materials and final compounds and chareteristic data of compounds:

Starting materials **1**,[1] **2**,[2] **5**[3], **6**[4] and **7**[5] were prepared following the literature procedures.

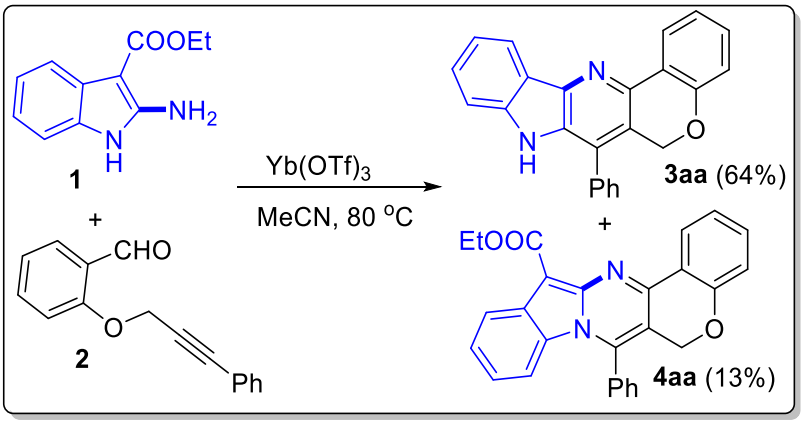


General Procedure A for the synthesis of dihydrochromeno δ-carbolines (3aa-3ja and 3ab-3at) taking Synthesis of 3aa as an example.



To a 15 mL Schlenk tube was added ethyl 2-amino-1*H*-indole-3-carboxylate (**1a**) (102 mg, 0.5 mmol), 2-((3-phenylprop-2-yn-1-yl)oxy) benzaldehyde (**2a**) (118 mg, 0.5 mmol) and $Yb(OTf)_3$ (31 mg, 10 mol%) in anhydrous MeCN (3 mL) and the reaction mixture was stirred at 80 °C (oil bath temperature) until complete conversion of starting material (monitored by TLC, 14 h for **3aa−3da**, 16 h for **3ea−3ja** 14 h for **3ag−3aj** and 18 h for **3ak-3at**). After completion of the reaction, the solvent was removed under reduced pressure, the crude material was purified on silica gel using 20% EtOAc/hexane to get **3aa** (118 mg, 68%) as off-colorless solid.

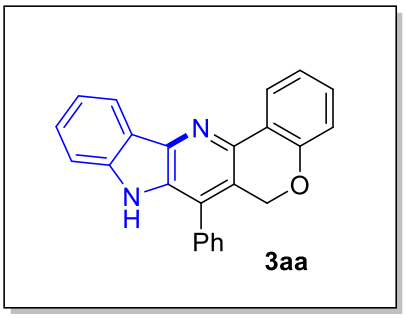
Synthesis of dihydrochromeno δ-carboline 3aa in 2 mmol Scale.



To a 25 mL round bottom flask was added ethyl 2-amino-1*H*-indole-3-carboxylate (**1a**) (410 mg, 2 mmol), 2-((3-phenylprop-2-yn-1-yl)oxy) benzaldehyde (**2a**) (472 mg, 2 mmol) and $Yb(OTf)_3$ (124 mg, 10 mol%) in anhydrous MeCN (12 mL) and the reaction mixture was stirred at 80 °C (oil bath temperature) until complete conversion of starting material (monitored by TLC, 15 h). After completion of the reaction, the solvent was removed under reduced pressure, the crude material was purified on silica gel using 20%

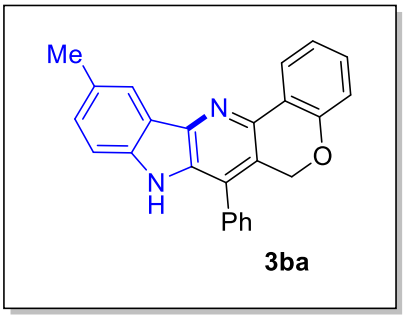
EtOAc/hexane to get **3aa** (446 mg, 64%) as off-colorless solid along with minor amount of **4aa** (112 mg 13%).

7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3aa):



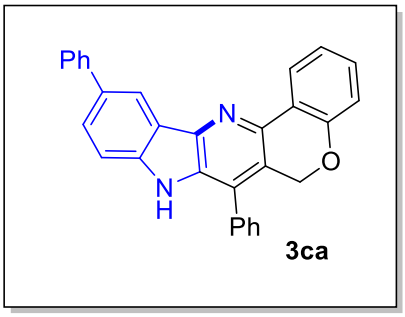
3aa (118 mg) was obtained from **1a** (102 mg) following general procedure **A**; Off-colorless solid; R_f = 0.30 (20% EtOAc/Hexanes); mp: 304-306 °C; Yield (68%); ^{1}H NMR (400 MHz, DMSO) δ 11.19 (s, 1H), 8.42 (d, *J* = 7.6 Hz, 1H), 8.29 (d, *J* = 7.8 Hz, 1H), 7.69 – 7.61 (m, 3H), 7.58 (d, *J* = 7.5 Hz, 2H), 7.52 (dd, *J* = 15.5, 8.5 Hz, 2H), 7.36 – 7.27 (m, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 5.25 (s, 2H); ^{13}C NMR (101 MHz, DMSO) δ 155.6, 141.9, 141.3, 140.9, 133.3, 131.4, 130.4, 129.7, 129.6, 129.3, 129.0, 128.0, 124.8, 124.7, 122.7, 121.9, 121.3, 120.6, 120.2, 117.0, 112.7, 66.5; IR (KBr) υ 3178, 2966, 1545, 1446, 1239, 848, 652 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{17}N_2O$ [M + H]$^+$ 349.1341 found 349.1325.

11-methyl-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ba)



3ba (107 mg) was obtained from **1b** (109 mg) following general procedure **A**; Off-colorless solid; R_f = 0.32 (20% EtOAc/Hexanes); mp: 274-276 °C; Yield (59%); ^{1}H NMR (400 MHz, DMSO) δ 11.06 (s, 2H), 8.40 (dd, *J* = 7.7, 1.6 Hz, 2H), 8.09 (s, 2H), 7.68 – 7.60 (m, 6H), 7.58 – 7.55 (m, 4H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.35 – 7.30 (m, 4H), 7.21 – 7.17 (m, 2H), 7.00 (d, *J* = 7.9 Hz, 2H), 5.24 (s, 4H), 2.51 – 2.50 (m, 9H); ^{13}C NMR (100 MHz, DMSO): δ 155.7, 141.2, 140.6, 140.3, 133.5, 131.7, 130.3, 129.8, 129.6, 129.4, 129.2, 128.9, 128.8, 125.0, 124.7, 122.7, 122.2, 121.1, 120.3, 117.0, 112.4, 66.5, 21.5; IR (KBr) υ 3169, 2943, 1554, 1439, 1231, 867, 638 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{19}N_2O$ [M + H]$^+$ 363.1497 found 363.1499.

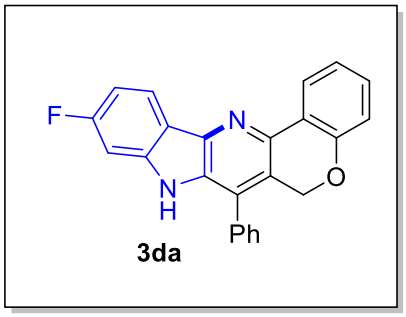
7,11-diphenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ca)



3ca (140 mg) was obtained from **1c** (140 mg) following general procedure **A**; Colorless solid; R_f = 0.26 (20% EtOAc/Hexanes); mp: 256-258 °C; Yield (66%); ^{1}H NMR (400 MHz, DMSO) δ 11.27 (s, 1H), 8.43 (d, *J* = 6.7 Hz, 1H), 8.36 (d, *J* = 8.1 Hz, 1H), 7.79 – 7.65 (m, 5H), 7.58 (ddd, *J* = 29.8, 13.9, 7.4 Hz, 6H), 7.43 – 7.32 (m, 2H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 5.27 (s, 2H). ^{13}C NMR (101 MHz, DMSO) δ

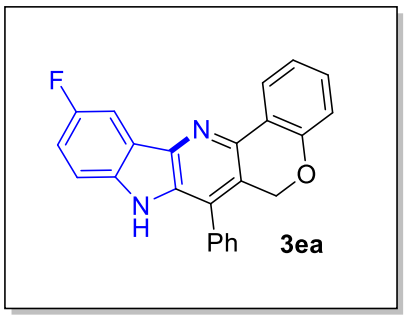
155.7, 142.5, 141.4, 141.1, 140.3, 133.4, 132.1, 130.4, 129.8, 129.6, 129.5, 129.3, 128.9, 127.9, 127.5, 124.9, 124.7, 122.7, 121.4, 121.3, 121.1, 119.5, 117.1, 110.5, 66.5; IR (KBr) υ 3163, 2964, 1554, 1424, 1214, 837, 637 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{21}N_2O$ $[M + H]^+$ 425.1654 found 425.1672.

10-fluoro-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3da)



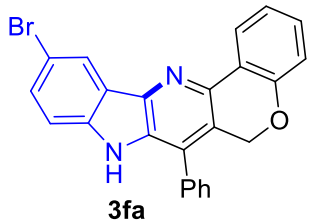
3da (93 mg) was obtained from **1d** (111 mg) following general procedure **A**; Off-colorless solid; R_f = 0.34 (20% EtOAc/Hexanes); mp: 271-273 °C; Yield (51%); ^{1}H NMR (300 MHz, DMSO) δ 11.24 (s, 1H), 8.33 (dd, *J* = 7.7, 1.4 Hz, 1H), 8.22 (dd, *J* = 8.6, 5.6 Hz, 1H), 7.63 – 7.54 (m, 3H), 7.53 – 7.47 (m, 2H), 7.30 – 7.23 (m, 1H), 7.19 (dd, *J* = 9.9, 2.1 Hz, 1H), 7.15 – 7.01 (m, 2H), 6.93 (d, *J* = 7.9 Hz, 1H), 5.17 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ 162.5 (d, *J* = 242.4 Hz), 155.7, 142.5 (d, *J* = 13.2 Hz), 141.3, 140.9, 133.2, 131.9, 130.6, 129.8, 129.6, 129.4, 129.0, 124.7, 122.7, 122.3, 122.2, 121.1, 118.8, 117.1, 108.6 (d, *J* = 24.5 Hz), 98.8 (d, *J* = 26.2 Hz), 66.4; ^{19}F NMR (376 MHz, DMSO) δ -112.90 (s, 1F); IR (KBr) υ 3126, 2971, 1544, 1426, 1241, 865, 631 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{16}N_2OF$ $[M + H]^+$ 367.1247 found 367.1236.

11-fluoro-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ea)



3ea (106 mg) was obtained from **1e** (111 mg) following general procedure **A**; Off-colorless solid; R_f = 0.34 (20% EtOAc/Hexanes); mp: 215-217 °C; Yield (58%); ^{1}H NMR (400 MHz, DMSO) δ 11.30 (s, 1H), 8.40 (dd, *J* = 7.7, 1.4 Hz, 1H), 8.29 (dd, *J* = 8.5, 5.6 Hz, 1H), 7.72 – 7.55 (m, 5H), 7.38 – 7.31 (m, 1H), 7.26 (dd, *J* = 9.9, 2.1 Hz, 1H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.16 – 7.09 (m, 1H), 7.00 (d, *J* = 7.9 Hz, 1H), 5.24 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ 162.4 (d, *J* = 241.7 Hz), 155.7, 142.6 (d, *J* = 13.4 Hz), 141.3, 140.9, 133.2, 131.9, 130.5, 129.7, 129.6, 129.3, 129.0, 124.7, 122.7, 122.3, 122.2, 121.1, 118.8, 117.0, 108.6 (d, *J* = 24.5 Hz), 98.8 (d, *J* = 24.6 Hz), 66.4; ^{19}F NMR (376 MHz, DMSO) δ -112.86 (s, 1F); IR (KBr) υ 3154, 2939, 1544, 1456, 1236, 842, 629 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{16}N_2OF$ $[M + H]^+$ 367.1247 found 367.1279.

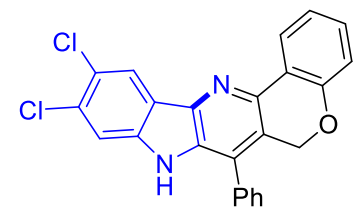
11-bromo-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3fa)



3fa

3fa (126 mg) was obtained from **1f** (141 mg) following general procedure **A**; Off-colorless solid; R_f = 0.32 (20% EtOAc/Hexanes); mp: 293-295 °C; Yield (59%); ^{1}H NMR (400 MHz, DMSO) δ 11.30 (s, 1H), 8.40 (dd, *J* = 7.7, 1.2 Hz, 1H), 8.22 (d, *J* = 8.3 Hz, 1H), 7.71 – 7.60 (m, 4H), 7.57 (d, *J* = 6.8 Hz, 2H), 7.41 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.37 – 7.31 (m, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 5.23 (s, 2H). ^{13}C NMR (100 MHz, DMSO) δ 155.7, 142.5, 141.5, 140.6, 133.1, 131.6, 130.6, 129.7, 129.6, 129.4, 129.3, 124.7, 124.6, 123.1, 122.7, 122.3, 121.8, 121.1, 120.7, 117.0, 115.2, 66.4; IR (KBr) υ 3156, 2988, 1562, 1447, 1265, 858, 662 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{16}N_2OBr$ [M + H]$^+$ 427.0446 found 427.0453.

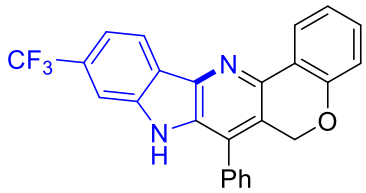
10,11-dichloro-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ga)



3ga

3ga (100 mg) was obtained from **1g** (136 mg) following general procedure **A**; Off-colorless solid; R_f = 0.34 (20% EtOAc/Hexanes); mp: 229-231°C; Yield (48%); ^{1}H NMR (400 MHz, DMSO) δ 11.41 (s, 1H), 8.48 – 8.35 (m, 2H), 7.71 – 7.61 (m, 4H), 7.56 (d, *J* = 6.8 Hz, 2H), 7.35 (t, *J* = 7.0 Hz, 1H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 5.23 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ 155.7, 141.9, 140.4, 139.6, 132.9, 132.4, 131.9, 130.81, 129.93, 129.75, 129.68, 129.54, 128.75, 124.87, 124.4, 122.7, 122.4, 122.0, 121.6, 117.1, 114.1, 66.3; IR (KBr) υ 3191, 2974, 1555, 1459, 1246, 837, 645 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{15}N_2OCl_2$ [M + H]$^+$ 417.0561 found 417.0551.

7-phenyl-10-(trifluoromethyl)-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ha)

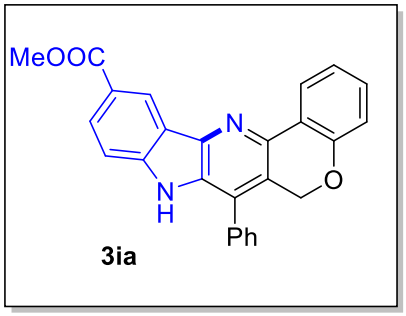


3ha

3ha (98 mg) was obtained from **1h** (136 mg) following general procedure **A**; Off-colorless solid; R_f = 0.28 (20% EtOAc/Hexanes); mp: 148-150 °C; Yield (47%); ^{1}H NMR (400 MHz, DMSO) δ 11.55 (s, 1H), 8.49 (d, *J* = 8.2 Hz, 1H), 8.43 (d, *J* = 7.4 Hz, 1H), 7.85 (s, 1H), 7.71 – 7.67 (m, 2H), 7.61 (dt, *J* = 14.6, 7.3 Hz, 4H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 5.28 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ 155.8, 142.0, 140.7, 140.0, 133.0, 132.7, 130.8, 129.8, 129.7, 129.5, 129.2, 127.9, 127.6, 126.5 (q, *J* = 256.7

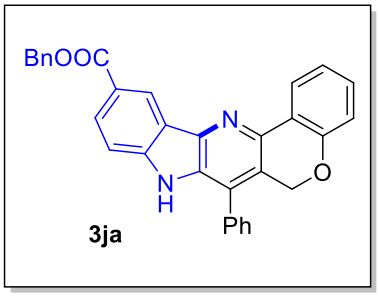
Hz), 124.8, 124.5, 123.9, 122.8 (d, J = 4.1 Hz), 121.6, 117.1, 116.3, 109.7 (d, J = 4.2 Hz), 66.4; ^{19}F NMR (376 MHz, DMSO) δ -59.76 (s, 3F); IR (KBr) υ 3146, 2949, 1558, 1459, 1239, 846, 651 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{16}N_2OCF_3$ [M + H]$^+$ 417.1215 found 417.1232.

Methyl 7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole-11-carboxylate (3ia)



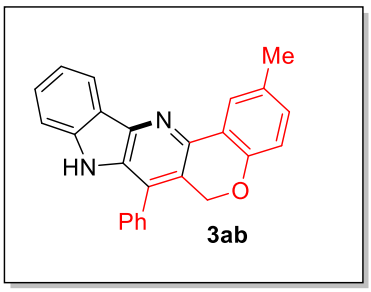
3ia (107 mg) was obtained from **1i** (131 mg) following general procedure **A**; Off-colorless solid; R_f = 0.32 (30% EtOAc/Hexanes); mp: 290-292 °C; Yield (53%); ^{1}H NMR (400 MHz, DMSO) δ 11.47 (s, 1H), 8.47 – 8.33 (m, 2H), 8.19 (s, 1H), 7.88 (d, J = 7.7 Hz, 1H), 7.73 – 7.56 (m, 5H), 7.41 – 7.33 (m, 1H), 7.24 – 7.17 (m, 1H), 7.01 (d, J = 7.6 Hz, 1H), 5.27 (s, 2H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 167.1, 155.8, 141.8, 141.02, 140.18, 133.11, 133.06, 130.79, 129.82, 129.70, 129.6, 129.5, 128.8, 128.5, 125.5, 124.8, 124.6, 122.7, 120.6, 117.1, 114.2, 66.4, 52.6; IR (KBr) υ 3171, 2978, 1567, 1449, 1254, 857, 659 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{19}N_2O_3$ [M + H]$^+$ 407.1396 found 407.1395.

benzyl 7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole-11-carboxylate (3ja)



3ja (149 mg) was obtained from **1j** (169 mg) following general procedure **A**; Off-colorless solid; R_f = 0.34 (30% EtOAc/Hexanes); mp: 222-224 °C; Yield (62%); ^{1}H NMR (400 MHz, DMSO) δ 11.46 (s, 1H), 8.41 (t, J = 7.6 Hz, 2H), 8.24 (s, 1H), 7.91 (d, J = 9.0 Hz, 1H), 7.70 – 7.62 (m, 3H), 7.59 (d, J = 6.8 Hz, 2H), 7.53 (d, J = 7.1 Hz, 2H), 7.44 (t, J = 7.3 Hz, 2H), 7.37 (dd, J = 17.6, 7.3 Hz, 2H), 7.20 (t, J = 7.3 Hz, 1H), 7.02 (d, J = 8.0 Hz, 1H), 5.41 (s, 2H), 5.28 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ 166.4, 155.8, 141.9, 141.0, 140.1, 136.6, 133.0, 133.0, 130.7, 129.8, 129.6, 129.5, 129.5, 129.03, 128.6, 128.5, 128.4, 125.6, 124.8, 124.6, 122.7, 120.7, 120.7, 117.1, 117.0, 114.3, 66.7, 66.4; IR (KBr) υ 3192, 2971, 1714, 1546, 1443, 1245, 886, 649 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{23}N_2O_3$ [M + H]$^+$ 483.1709 found 483.1699.

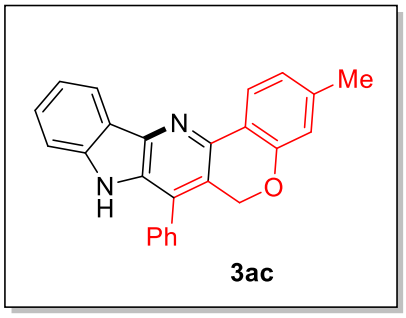
2-methyl-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ab)



3ab (101 mg) was obtained from **1a** (102 mg) following general procedure **A**; Off-colorless solid; R_f = 0.32 (20% EtOAc/Hexanes); mp: 272-274 °C; Yield (56%); ^{1}H NMR (400 MHz, DMSO) δ 11.17 (s, 1H), 8.31 (d, J = 7.8 Hz, 1H), 8.22 (d, J = 1.8 Hz, 1H), 7.68 – 7.60 (m, 3H),

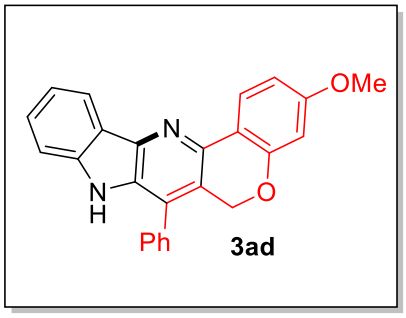
7.58 – 7.54 (m, 3H), 7.53 – 7.48 (m, 1H), 7.31 – 7.26 (m, 1H), 7.13 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.89 (d, *J* = 8.1 Hz, 1H), 5.20 (s, 2H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 153.6, 141.9, 141.2, 141.0, 133.5, 131.4, 130.9, 129.8, 129.5, 129.2, 128.9, 127.9, 124.8, 124.6, 122.0, 121.50, 120.6, 120.1, 116.8, 112.7, 66.4, 21.0; IR (KBr) υ 3178, 2956, 1559, 1452, 1242, 856, 658 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{19}N_2O$ [M + H]$^+$ 363.1497 found 363.1506.

3-methyl-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ac)



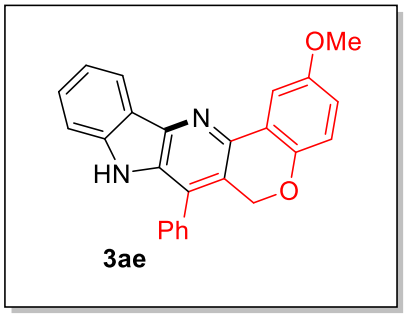
3ac (107 mg) was obtained from **1a** (102 mg) following general procedure **A**; Off-colorless solid; R_f = 0.32 (20% EtOAc/Hexanes); mp: 306-308 °C; Yield (59%); ^{1}H NMR (400 MHz, DMSO) δ 11.16 (s, 1H), 8.29 (d, *J* = 7.8 Hz, 2H), 7.68 – 7.47 (m, 7H), 7.28 (t, *J* = 7.2 Hz, 1H), 7.01 (d, *J* = 7.7 Hz, 1H), 6.83 (s, 1H), 5.22 (s, 2H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 155.65, 141.90, 141.20, 140.35, 133.54, 131.28, 129.82, 129.57, 129.26, 128.93, 127.90, 124.59, 123.56, 122.29, 122.06, 120.98, 120.63, 120.08, 117.36, 112.70, 21.50; IR (KBr) υ 3178, 2944, 1535, 1428, 1251, 845, 637 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{19}N_2O$ [M + H] 363.1497 found 363.1505.

3-methoxy-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ad)



3ad (119 mg) was obtained from **1a** (102 mg) following general procedure **A**; Colorless solid; R_f = 0.28 (20% EtOAc/Hexanes); mp: 258-260 °C; Yield (63%); ^{1}H NMR (400 MHz, DMSO) δ 11.11 (s, 1H), 8.29 (dd, *J* = 17.3, 8.1 Hz, 2H), 7.72 – 7.44 (m, 7H), 7.27 (t, *J* = 7.1 Hz, 1H), 6.79 (d, *J* = 6.7 Hz, 1H), 6.59 (s, 1H), 5.24 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 161.5, 157.0, 141.8, 141.3, 141.1, 133.5, 130.9, 129.8, 129.5, 129.25, 129.01, 127.81, 125.82, 122.04, 120.59, 120.16, 120.0, 117.8, 112.6, 109.5, 101.9, 66.8, 55.8; IR (KBr) υ 3154, 2942, 1513, 1472, 1256, 84, 684 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{19}N_2O_2$ [M + H]$^+$ 379.1447 found 379.1440.

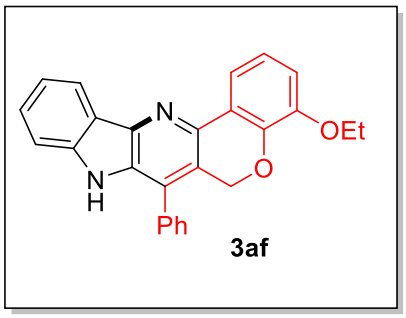
2-methoxy-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ae)



3ae (115 mg) was obtained from **1a** (102 mg) following general procedure **A**; Off-colorless solid; R_f = 0.28 (30% EtOAc/Hexanes); mp: 190-192 °C; Yield (61%); ^{1}H NMR (400 MHz, DMSO): δ 11.21 (s, 1H), 8.31 (d, *J* = 7.8 Hz, 1H), 7.93 (d, *J* = 2.8 Hz, 1H), 7.70-7.48 (m, 7H), 7.29 (t, *J* = 7.3 Hz, 1H), 6.99-6.88 (m,

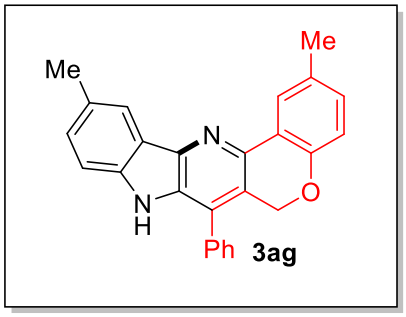
2H), 5.19 (s, 2H), 3.88 (s, 3H);^{13}C NMR (100 MHz, DMSO) δ ^{13}C NMR (100 MHz, DMSO) δ 155.0, 149.6, 141.9, 141.2, 140.9, 133.4, 131.5, 129.8, 129.5, 129.3, 128.9, 128.0, 125.5, 121.9, 121.7, 120.7, 120.1, 117.9, 116.5, 112.7, 108.6, 66.5, 56; IR (KBr) υ 3178, 2937, 1544, 1435, 1229, 857, 643 cm^{-1} HRMS (ESI) calcd for $C_{25}H_{19}N_2O_2$ [M + H]$^+$ 379.1447 found 379.1428.

4-ethoxy-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3af)



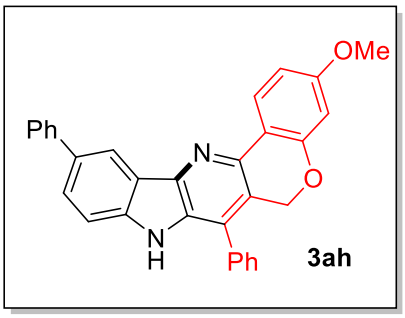
3af (131 mg) was obtained from **1a** (102 mg) following general procedure **A**; Off-colorless solid; R_f = 0.26 (20% EtOAc/Hexanes); mp: 202-204 °C; Yield (67%); ^{1}H NMR (400 MHz, DMSO) δ 11.19 (s, 1H), 8.28 (d, *J* = 7.8 Hz, 1H), 8.00 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.69 – 7.65 (m, 2H), 7.63 – 7.54 (m, 4H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.28 (t, *J* = 7.3 Hz, 1H), 7.10 (t, *J* = 7.9 Hz, 1H), 7.05 – 7.01 (m, 1H), 5.24 (s, 2H), 4.07 (dd, *J* = 13.7, 6.8 Hz, 2H), 1.34 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ 148.0, 145.2, 141.8, 141.2, 141.1, 133.2, 131.4, 129.7, 129.6, 129.3, 128.9, 128.0, 125.7, 122.3, 121.9, 121.3, 120.6, 120.2, 116.6, 114.6, 112.7, 66.4, 64.5, 15.1; IR (KBr) υ 3166, 2972, 1558, 1454, 1234, 878, 653 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{21}N_2O_2$ [M + H]$^+$ 393.1603 found 393.1601.

2,11-dimethyl-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ag)



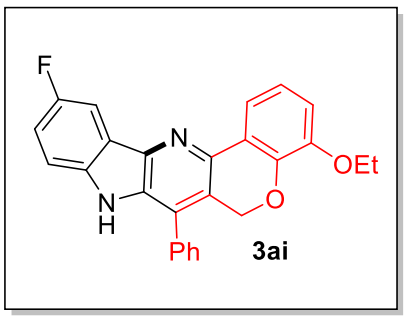
3ag (105 mg) was obtained from **1b** (109 mg) following general procedure **A**; Off-colorless solid; R_f = 0.32 (20% EtOAc/Hexanes); mp: 314-316 °C; Yield (56%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.01 (s, 1H), 8.19 (d, *J* = 1.4 Hz, 1H), 8.09 (s, 1H), 7.66 – 7.57 (m, 3H), 7.54 (dd, *J* = 7.4, 6.0 Hz, 2H), 7.42 (d, *J* = 8.3 Hz, 1H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.10 (dd, *J* = 8.1, 1.7 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 5.16 (s, 2H), 2.50 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 153.5, 141.0, 140.8, 140.2, 133.5, 131.6, 131.4, 130.9, 129.8, 129.5, 129.4, 129.2, 129.0, 128.8, 124.7, 124.6, 122.1, 121.2, 120.3, 116.8, 112.4, 66.4, 21.4, 21.0; IR (KBr) υ 3148, 2932, 1559, 1445, 1248, 840, 655 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{21}N_2O$ [M + H]$^+$ 377.1654 found 377.1646.

3-methoxy-7,11-diphenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ah)



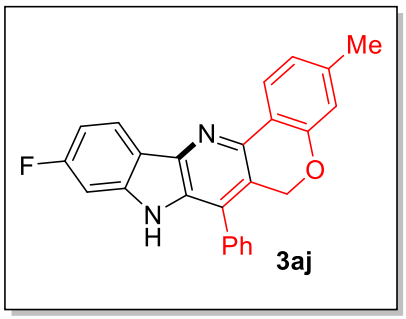
3ah (157 mg) was obtained from **1c** (140 mg) following general procedure **A**; Off-colorless solid; R_f = 0.30 (30% EtOAc/Hexanes); mp: 289-291°C; Yield (69%); ^{1}H NMR (400 MHz, DMSO) δ 11.20 (s, 1H), 8.33 (dd, *J* = 8.4, 3.3 Hz, 2H), 7.74 (dd, *J* = 6.0, 4.9 Hz, 3H), 7.70 – 7.65 (m, 2H), 7.63 (d, *J* = 7.1 Hz, 1H), 7.59 (dd, *J* = 12.5, 4.9 Hz, 3H), 7.52 (t, *J* = 7.7 Hz, 2H), 7.41 (d, *J* = 7.3 Hz, 1H), 6.80 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.60 (d, *J* = 2.4 Hz, 1H), 5.25 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 161.6, 157.0, 142.4, 141.6, 141.4, 140.9, 140.1, 133.5, 131.6, 129.8, 129.6, 129.5, 129.3, 129.0, 127.8, 127.4, 125.8, 121.3, 121.1, 120.2, 119.4, 117.8, 110.5, 109.5, 101.9, 66.8, 55.8; IR (KBr) υ 3198, 2963, 1527, 1443, 1231, 839, 625 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{23}N_2O_2$ [M + H]$^+$ 455.1760 found 455.1737.

4-ethoxy-11-fluoro-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ai)



3ai (129 mg) was obtained from **1e** (111 mg) following general procedure **A**; Off-colorless solid; R_f = 0.28 (20% EtOAc/Hexanes); mp: 226-228 °C; Yield (63%); ^{1}H NMR (300 MHz, DMSO) δ 11.30 (s, 1H), 8.27 (dd, *J* = 8.5, 5.6 Hz, 1H), 7.97 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.70 – 7.59 (m, 3H), 7.59 – 7.53 (m, 2H), 7.25 (dd, *J* = 9.9, 2.0 Hz, 1H), 7.07 (ddd, *J* = 16.0, 9.4, 4.4 Hz, 3H), 5.22 (s, 2H), 4.09 – 4.00 (m, 2H), 1.32 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ 162.5 (d, *J* = 241.6 Hz), 148.0, 145.3, 142.5 (d, *J* = 13.6 Hz), 141.6, 140.8, 133.2, 131.9, 129.8, 129.6, 129.4, 128.9, 125.6, 122.3, 122.2, 121.1, 118.8, 116.6, 114.7, 108.6 (d, *J* = 24.2 Hz), 98.9 (d, *J* = 26.2 Hz), 66.4, 64.5, 15.2; ^{19}F NMR (376 MHz, DMSO) δ -112.84 (s, 1F); IR (KBr) υ 3159, 2974, 1556, 1460, 1238, 847, 634 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{20}N_2O_2F$ [M + H]$^+$ 411.1509 found 411.1506.

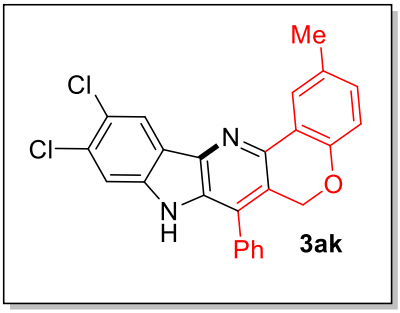
10-fluoro-3-methyl-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3aj)



3aj (125 mg) was obtained from **1d** (111 mg) following general procedure **A**; Off-colorless solid; R_f = 0.30 (20% EtOAc/Hexanes); mp: 292-294 °C; Yield = 125 mg (66%); ^{1}H NMR (400 MHz, DMSO) δ 11.26 (s, 1H), 8.28 (t, *J* = 6.9 Hz, 2H), 7.62 (ddd, *J* = 23.1, 14.9,

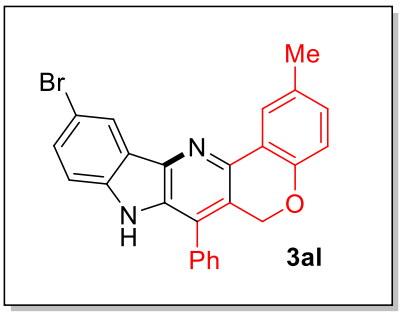
6.8 Hz, 5H), 7.25 (dd, J = 9.9, 1.9 Hz, 1H), 7.15 – 7.08 (m, 1H), 7.00 (d, J = 7.9 Hz, 1H), 6.82 (s, 1H), 5.21 (s, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 162.7 (d, J = 240.2 Hz), 155.6, 142.5 (d, J = 12.7 Hz), 141.6, 140.8, 140.4, 133.3, 131.7, 129.7, 129.5, 129.3, 128.9, 124.6, 123.5, 122.2, 122.1, 120.7, 118.8, 117.3, 108.4 (d, J = 24.4 Hz), 98.8 (d, J = 25.9 Hz), 66.4, 21.4; ^{19}F NMR (376 MHz, DMSO) δ -113.02 (s, 1F); IR (KBr) υ 3189, 2971, 1549, 1444, 1236, 857, 652 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{18}N_2OF$ [M + H]$^+$ 381.1403 found 381.1414.

10,11-dichloro-2-methyl-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ak)



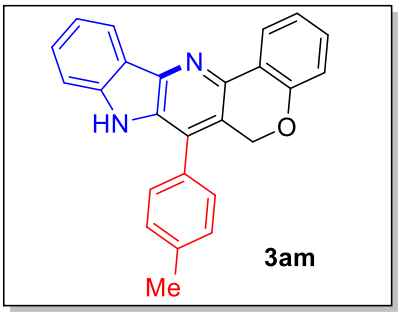
3ak (112 mg) was obtained from **1g** (136 mg) following general procedure **A**; Off-colorless solid; R_f = 0.36 (20% EtOAc/Hexanes); mp: 205-207 °C; Yield (52%); ^{1}H NMR (400 MHz, DMSO) δ 11.53 (s, 1H), 8.50 (d, J = 7.9 Hz, 1H), 8.23 (s, 1H), 7.84 (s, 1H), 7.71 – 7.56 (m, 6H), 7.16 (d, J = 7.8 Hz, 1H), 6.90 (d, J = 8.1 Hz, 1H), 5.22 (s, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 154.7, 142.0, 141.4, 139.2, 133.1, 132.7, 131.8, 129.8, 129.6, 129.4, 129.0, 128.3, 127.0, 126.7, 121.8, 121.2, 120.8, 120.3, 119.6, 114.5, 112.7, 66.6, 27.4; IR (KBr) υ 3145, 2972, 1544, 1446, 1265, 845, 639 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{17}N_2OCl_2$ [M + H]$^+$ 431.0718 found 431.0711.

11-bromo-2-methyl-7-phenyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3al)



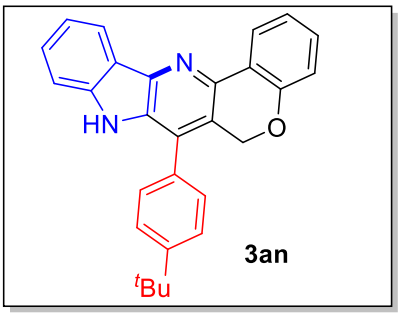
3al (123 mg) was obtained from **1f** (141 mg) following general procedure **A**; Off-colorless solid; R_f = 0.30 (20% EtOAc/Hexanes); mp: 218-220 °C; Yield (56%); ^{1}H NMR (400 MHz, DMSO) δ 11.28 (s, 1H), 8.26 – 8.18 (m, 2H), 7.70 – 7.60 (m, 4H), 7.58 – 7.53 (m, 2H), 7.41 (dd, J = 8.3, 1.5 Hz, 1H), 7.16 – 7.10 (m, 1H), 6.88 (d, J = 8.1 Hz, 1H), 5.17 (s, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 153.6, 142.5, 141.7, 140.5, 133.2, 131.6, 131.4, 131.1, 129.7, 129.6, 129.4, 129.3, 124.8, 124.3, 123.1, 122.3, 122.0, 121.1, 120.6, 116.8, 115.2, 66.3, 21.0; IR (KBr) υ 3171, 2946, 1546, 1437, 1244, 856, 644 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{18}N_2OBr$ [M + H]$^+$ 441.0606 found 441.0600.

7-(p-tolyl)-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3am)



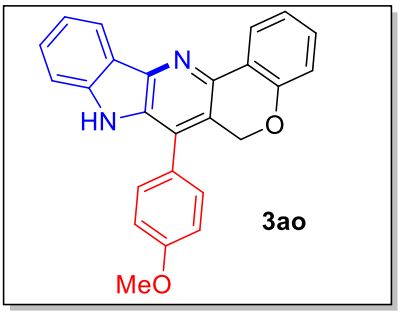
3am (85 mg) was obtained from **1a** (102 mg) following general procedure **A**; Off-colorless solid; R_f = 0.30 (20% EtOAc/Hexanes); mp: 248-250 °C; Yield (47%); ^{1}H NMR (400 MHz, DMSO) δ 11.16 (s, 1H), 8.42 (d, *J* = 7.6 Hz, 1H), 8.29 (d, *J* = 7.8 Hz, 1H), 7.57 – 7.44 (m, 6H), 7.36 – 7.26 (m, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 5.26 (s, 2H), 2.47 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 155.6, 141.9, 141.2, 140.8, 138.7, 131.6, 130.4, 130.3, 130.1, 129.7, 128.9, 127.9, 124.9, 124.7, 122.6, 122.0, 121.3, 120.6, 120.1, 117.0, 112.7, 66.5, 21.4; IR (KBr) υ 3168, 2945, 1554, 1459, 1266, 847, 614 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{19}N_2O$ [M + H]$^+$ 363.1497 found 363.1493.

7-(4-(tert-butyl)phenyl)-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3an)



3an (107 mg) was obtained from **1a** (102 mg) following general procedure **A**; Off-colorless solid; R_f = 0.34 (30% EtOAc/Hexanes); mp: 234-236 °C; Yield (53%); ^{1}H NMR (400 MHz, DMSO) δ 11.18 (s, 1H), 8.41 (dd, *J* = 7.7, 1.4 Hz, 1H), 8.29 (d, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.50 (dd, *J* = 7.5, 5.8 Hz, 3H), 7.35 – 7.26 (m, 2H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 7.9 Hz, 1H), 5.25 (s, 2H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ 155.6, 151.6, 141.9, 141.3, 140.9, 131.5, 130.5, 130.3, 129.5, 128.8, 127.9, 126.3, 124.9, 124.7, 122.6, 122.0, 121.4, 120.6, 120.1, 117.0, 112.7, 66.5, 35.0, 31.5; IR (KBr) υ 3172, 2944, 1555, 1456, 1244, 857, 643 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{25}N_2O$ [M + H]$^+$ 405.1967 found 405.1989.

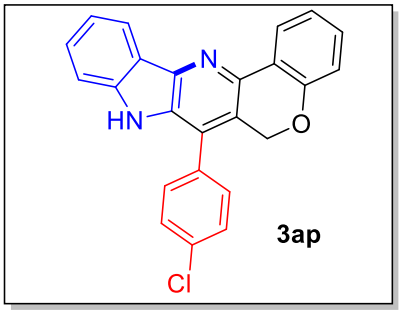
7-(4-methoxyphenyl)-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ao)



3ao (104 mg) was obtained from **1a** (102 mg) following general procedure **A**; Off-colorless solid; R_f = 0.28 (30% EtOAc/Hexanes); mp: 215-217 °C; Yield (55%); ^{1}H NMR (400 MHz, DMSO) δ 11.17 (s, 1H), 8.40 (dd, *J* = 7.7, 1.5 Hz, 1H), 8.28 (d, *J* = 7.8 Hz, 1H), 7.58 – 7.45 (m, 4H), 7.31 (ddd, *J* = 18.0, 11.3, 4.3 Hz, 2H), 7.20 (dd, *J* = 13.3, 8.0 Hz, 3H), 7.00 (d, *J* = 8.0 Hz, 1H), 5.27 (s, 2H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 160.0, 155.7, 141.8, 141.2, 140.9, 131.7, 131.1, 130.3, 128.8, 127.9, 125.4, 125.0, 124.7, 122.6, 122.1, 121.4, 120.6, 120.1, 117.0, 115.0, 112.7, 66.5, 55.7; IR (KBr)

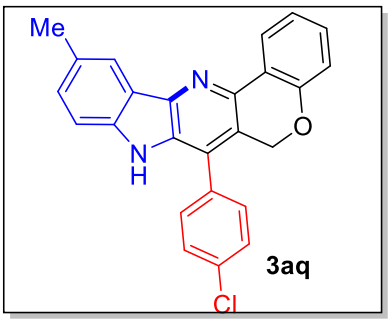
υ 3182, 2949, 1551, 1442, 1229, 836, 648 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{19}N_2O_2$ [M + H]$^+$ 379.1447 found 379.1450.

7-(4-chlorophenyl)-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3ap)



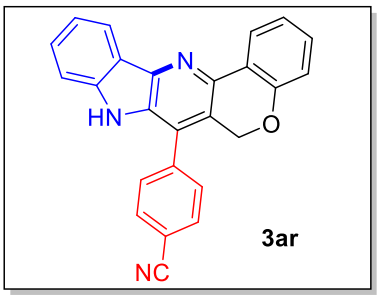
3ap (97 mg) was obtained from **1a** (102 mg) following general procedure **A**; Off-colorless solid; R_f = 0.28 (20% EtOAc/Hexanes); mp: 264-268 °C; Yield = 97 mg (51%); ^{1}H NMR (400 MHz, DMSO) δ 11.23 (s, 1H), 8.41 (dd, *J* = 7.7, 1.4 Hz, 1H), 8.29 (d, *J* = 7.8 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.56 – 7.48 (m, 2H), 7.37 – 7.26 (m, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 5.25 (s, 2H); ^{13}C NMR (101 MHz, DMSO) δ 155.6, 141.9, 141.3, 140.8, 134.1, 132.3, 131.8, 131.4, 130.4, 129.6, 128.1, 127.7, 124.8, 124.7, 122.7, 122.0, 121.3, 120.7, 120.2, 117.0, 112.6, 66.3; IR (KBr) υ 3176, 2976, 1554, 1451, 1247, 837, 661 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{16}N_2OCl$ [M + H]$^+$ 383.0951 found 383.0942.

7-(4-chlorophenyl)-11-methyl-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3aq)



3aq (107 mg) was obtained from **1a** (102 mg) following general procedure **A**; Off-colorless solid; R_f = 0.32 (30% EtOAc/Hexanes); mp: 209-211 °C; Yield (54%); ^{1}H NMR (400 MHz, DMSO) δ 11.10 (s, 1H), 8.40 (d, *J* = 7.4 Hz, 1H), 8.09 (s, 1H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.48 – 7.40 (m, 1H), 7.38 – 7.29 (m, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.00 (d, *J* = 7.9 Hz, 1H), 5.24 (s, 2H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 155.6, 141.2, 140.5, 140.2, 134.1, 133.7, 132.3, 131.7, 131.6, 130.3, 129.6, 129.0, 127.5, 124.9, 124.6, 122.6, 122.1, 121.1, 120.3, 117.0, 112.3, 66.4, 21.5; IR (KBr) υ 3172, 2941, 1560, 1442, 1235, 849, 644 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{18}N_2OCl$ [M + H]$^+$ 397.1108 found 397.1122.

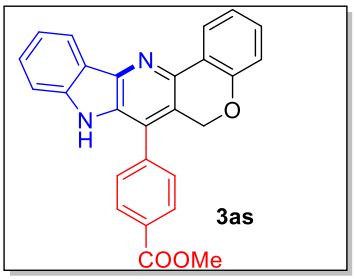
4-(6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indol-7-yl)benzonitrile (3ar)



3ar (108 mg) was obtained from **1a** (102 mg) following general procedure **A**; Light pink solid; R_f = 0.32 (20% EtOAc/Hexanes); mp: 212-214 °C; Yield (58%); ^{1}H NMR (400 MHz, DMSO) δ 11.26 (s, 1H), 8.42 (dd, *J* = 7.7, 1.5 Hz, 1H), 8.30 (d, *J* = 7.8 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 2H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.55 – 7.51 (m, 2H), 7.36 – 7.29 (m, 2H), 7.20 (t, *J* = 7.1 Hz, 1H), 7.01 (d, *J* = 7.7 Hz, 1H), 5.25 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ

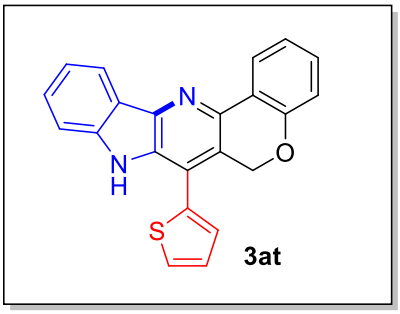
155.6, 141.9, 141.5, 140.8, 136.7, 132.7, 131.3, 130.9, 130.5, 128.2, 127.4, 126.4, 124.7, 122.7, 122.1, 121.9, 121.2, 120.7, 120.3, 117.1, 114.9, 112.6, 66.3; IR (KBr) υ 3165, 2938, 1537, 1428, 1251, 845, 637 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{16}N_3O$ $[M + H]^+$ 374.1293 found 374.1294.

Methyl 4-(6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indol-7-yl)benzoate (3as)



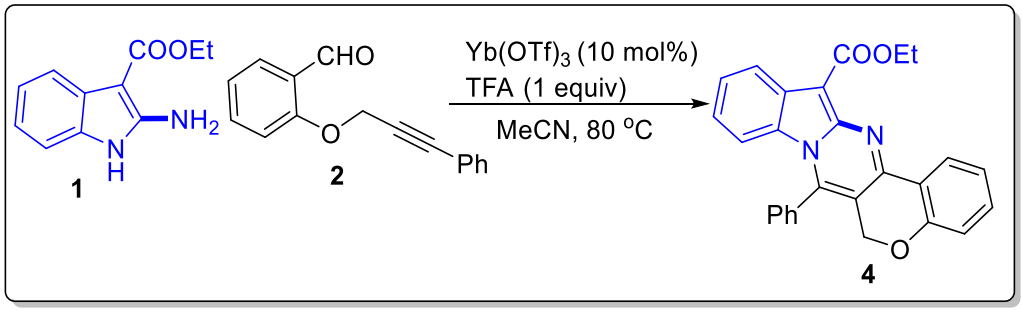
3as (132 mg) was obtained from **1a** (102 mg) following general procedure **A**; Off-colorless solid; R_f = 0.28 (20% EtOAc/Hexanes); mp: 224-226 °C; Yield (65%); ^{1}H NMR (400 MHz, DMSO) δ 11.27 (s, 1H), 8.39 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.28 (d, *J* = 7.9 Hz, 1H), 8.20 (d, *J* = 8.3 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.52 – 7.50 (m, 2H), 7.35 – 7.26 (m, 2H), 7.18 (td, *J* = 7.6, 1.1 Hz, 1H), 7.02 – 6.98 (m, 1H), 5.24 (s, 2H), 3.94 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 166.5, 155.6, 141.9, 141.4, 140.8, 138.3, 131.1, 130.6, 130.4, 130.3, 128.2, 127.8, 124.7, 122.8, 121.8, 121.2, 120.7, 120.3, 117.1, 112.6, 66.3, 52.9; IR (KBr) υ 3157, 2987,1682, 1578, 1436, 1211, 842, 652 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{19}N_2O_3$ $[M + H]^+$ 407.1396 found 407.1393.

7-(thiophen-2-yl)-6,8-dihydrochromeno[3',4':5,6]pyrido[3,2-b]indole (3at)



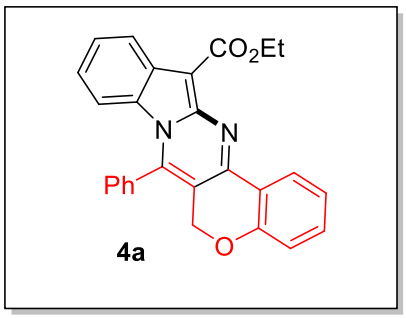
3at (103 mg) was obtained from **1a** (102 mg) following general procedure **A**; Off-colorless solid; R_f = 0.28 (20% EtOAc/Hexanes); mp: 307-309 °C; Yield (58%); ^{1}H NMR (400 MHz, DMSO) δ 11.34 (s, 1H), 8.34 (dd, *J* = 44.1, 7.6 Hz, 2H), 7.98 (d, *J* = 4.6 Hz, 1H), 7.63 – 7.51 (m, 2H), 7.36 (ddd, *J* = 22.3, 15.5, 9.8 Hz, 4H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.02 (d, *J* = 7.8 Hz, 1H), 5.40 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ 155.6, 141.9, 141.4, 140.8, 132.8, 131.8, 130.5, 130.3, 129.2, 128.7, 128.2, 124.7, 122.7, 122.0, 121.8, 120.7, 120.4, 117.0, 112.9, 66.5; IR (KBr) υ 3178, 2966, 1558, 1436, 1246, 838, 657 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{15}N_2OS$ $[M + H]^+$ 355.0905 found 355.0907.

General Procedure B for the synthesis of annelated pyrimidines (4a-c) Taking Synthesis of 4a as an Example.



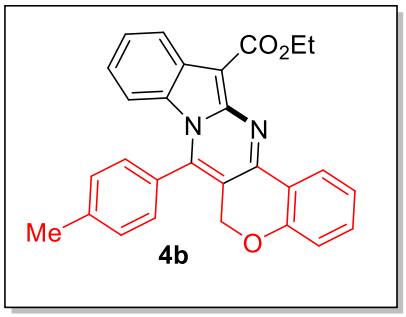
Ethyl 2-amino-1*H*-indole-3-carboxylate (**1a**) (102 mg, 0.5 mmol), 2-((3-phenylprop-2-yn-1-yl)oxy) benzaldehyde (**2a**) (118 mg, 0.5 mmol) and $Yb(OTf)_3$ (31 mg, 10 mol%) in anhydrous MeCN (3 mL) in a 15 mL Schlenk tube were added TFA (Triflouro acetic acid) (0.04 mL, 1 equiv) and the reaction mixture was stirred at 80 °C (oil bath temperature) until complete conversion of starting material (monitored by TLC, 20 h). After completion of the reaction, the solvent removed under reduced pressure and the crude material was purified on silica gel using 40% EtOAc/hexane to get **4a** (136 mg, 65%) as a dark brick red solid.

ethyl 7-phenyl-6H-chromeno[4',3':4,5]pyrimido[1,2-a]indole-13-carboxylate (4a)



Brick red solid; R_f = 0.28 (20% EtOAc/Hexanes); mp: 198-200 °C; Yield = 136 mg (65%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 – 8.47 (m, 2H), 7.77 – 7.68 (m, 3H), 7.51 – 7.34 (m, 4H), 7.19 (t, *J* = 7.1 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 6.91 (dd, *J* = 11.5, 4.2 Hz, 1H), 6.21 (d, *J* = 8.7 Hz, 1H), 4.95 (s, 2H), 4.57 (q, *J* = 7.1 Hz, 2H), 1.59 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ δ 165.1, 158.1, 151.1, 146.5, 142.7, 133.6, 131.1, 130.4, 130.2, 128.5, 128.4, 126.6, 125.1, 122.8, 121.9, 121.7, 121.5, 117.4, 114.3, 110.23, 95.2, 64.8, 59.7, 14.8; IR (KBr) υ 2933, 1667, 1378, 1219, 770 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{27}H_{21}N_2O_3$ $[M + H]^+$ 421.1552 found 421.1560.

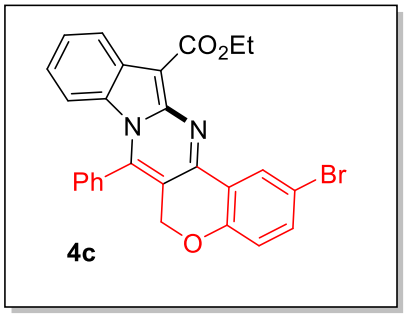
ethyl 7-(p-tolyl)-6H-chromeno[4',3':4,5]pyrimido[1,2-a]indole-13-carboxylate (4b)



4b (137 mg) was obtained from **1a** (102 mg) following general procedure **B**; Brick red solid; R_f = 0.34 (30% EtOAc/Hexanes); mp: 203-205 °C; Yield (63%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 7.8, 1.6 Hz,

1H), 8.51 (d, J = 8.1 Hz, 1H), 7.50 (d, J = 7.8 Hz, 2H), 7.44 – 7.37 (m, 2H), 7.36 (dd, J = 7.0, 4.5 Hz, 2H), 7.21 – 7.16 (m, 1H), 6.98 – 6.95 (m, 1H), 6.92 (ddd, J = 8.5, 7.1, 1.2 Hz, 1H), 6.30 (d, J = 8.7 Hz, 1H), 4.95 (s, 2H), 4.57 (q, J = 7.1 Hz, 2H), 2.58 (s, 3H), 1.58 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, CDCl3) δ 165.1, 158.1, 151.1, 146.6, 143.0, 141.4, 133.6, 130.8, 130.2, 128.6, 128.2, 127.4, 126.6, 125.0, 122.7, 121.8, 121.7, 121.4, 117.3, 114.5, 110.3, 95.0, 64.8, 59.7, 21.7, 14.8; IR (KBr) υ 2933, 1732, 1436, 1220, 770 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{28}H_{23}N_2O_3$ [M + H]$^+$ 435.1709 found 435.1707.

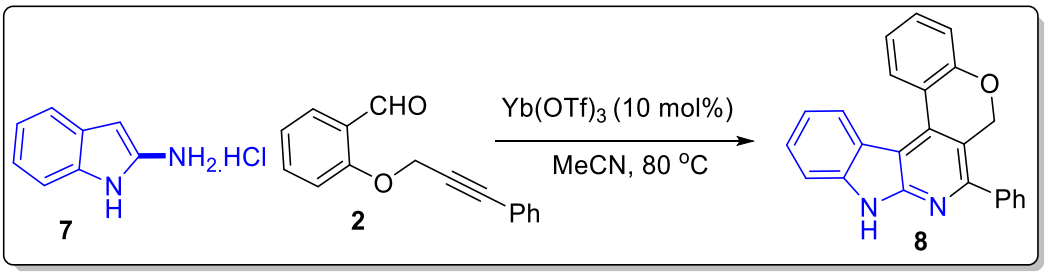
ethyl 2-bromo-7-phenyl-6H-chromeno[4',3':4,5]pyrimido[1,2-a]indole-13-carboxylate (4c):



4c (169 mg) was obtained from **1a** (102 mg) following general procedure **B**; Brick red solid; R_f = 0.28 (20% EtOAc/Hexanes); mp: 221-223 °C; Yield (68%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, J = 2.5 Hz, 1H), 8.51 (d, J = 8.1 Hz, 1H), 7.77 – 7.69 (m, 3H), 7.49 (ddd, J = 8.1, 4.5, 2.1 Hz, 3H), 7.39 (t, J = 7.3 Hz, 1H), 6.92 (ddd, J = 8.5, 7.1, 1.2 Hz, 1H), 6.86 (d, J = 8.7 Hz, 1H), 6.21 (d, J = 8.7 Hz, 1H), 4.94 (s, 2H), 4.57 (q, J = 7.1 Hz, 2H), 1.61 (d, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl3) δ 165.0, 156.9, 149.6, 146.0, 143.0, 136.1, 131.31, 130.3, 129.01, 128.5, 128.3, 125.3, 123.2, 122.0, 121.8, 119.3, 115.4, 114.4, 109.6, 95.5, 64.9, 59.9, 14.6; IR (KBr) υ 2972, 1616, 1496, 1229, 667 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{27}H_{20}N_2O_3Br$ [M + H]$^+$ 499.0657 found 499.0671.

General Procedure C for the synthesis dihydrochromeno α-carbolines of (7a-c)

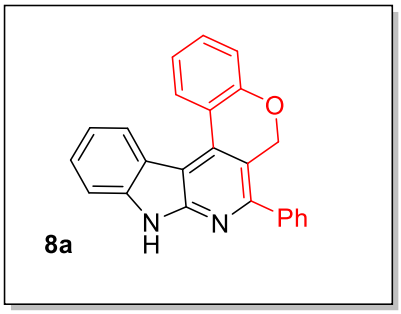
Taking Synthesis of 7a as an Example.



To a 15 mL Schlenk tube was added ethyl 1H-indol-2-amine hydrochloride (**7**) (84 mg, 0.5 mmol), 2-((3-phenylprop-2-yn-1-yl)oxy) benzaldehyde (**2a**) (118 mg, 0.5 mmol) and $Yb(OTf)_3$ (31 mg, 10 mol%) in anhydrous MeCN (3 mL) and the reaction mixture was stirred at 80 °C (oil bath temperature) until complete conversion of starting material (monitored by TLC, 18 h). After completion of the reaction, solvent was removed under

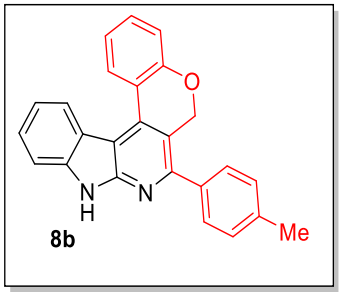
reduced pressure and the crude material purified on silica gel using 30% EtOAc/hexane to get **4a** (107 mg, 62%) as a off-colorless solid

7-phenyl-6,9-dihydrochromeno[4',3':4,5]pyrido[2,3-b]indole (8a)



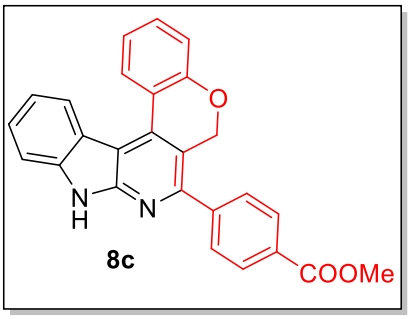
Off-colorless solid; R_f = 0.28 (20% EtOAc/Hexanes); mp: 195-198 °C; Yield = 107 mg (62%); ^{1}H NMR (400 MHz, DMSO) δ 12.11 (s, 1H), 8.34 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.71 (dd, *J* = 5.8, 4.4 Hz, 3H), 7.59 – 7.54 (m, 3H), 7.45 – 7.40 (m, 2H), 7.24 (d, *J* = 1.1 Hz, 1H), 7.06 (dd, *J* = 8.1, 0.9 Hz, 1H), 6.99 (dd, *J* = 7.8, 1.3 Hz, 2H), 5.19 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ 156.4, 152.0, 145.1, 141.3, 139.9, 135.7, 131.5, 129.6, 129.4, 128.8, 127.0, 125.0, 124.3, 122.7, 121.7, 120.0, 119.8, 117.2, 116.3, 113.2, 111.8, 66.2; IR (KBr) υ 3090, 2966, 1592, 1460, 1222, 839, 769 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{17}N_2O$ [M + H]$^+$ 349.1341 found 349.1339.

7-(p-tolyl)-6,9-dihydrochromeno[4',3':4,5]pyrido[2,3-b]indole (8b)



8b (107 mg) was obtained from **7** (84 mg) following general procedure **C**; Off- colorless solid; R_f = 0.28 (20% EtOAc/Hexanes); mp: 209-211 °C; Yield (59%); ^{1}H NMR (300 MHz, DMSO) δ 12.11 (s, 1H), 8.36 (d, *J* = 8.1 Hz, 2H), 7.58 – 7.47 (m, 5H), 7.38 (dd, *J* = 13.4, 7.5 Hz, 3H), 7.20 (t, *J* = 7.8 Hz, 2H), 5.19 (s, 2H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 156.4, 152.1, 145.1, 141.4, 139.8, 138.7, 132.7, 131.4, 130.1, 128.81, 126.9, 125.0, 124.3, 122.6, 121.8, 120.7, 119.8, 117.2, 116.47, 113.3, 111.8, 66.2, 21.5; IR (KBr) υ 2934, 1678, 1484, 1216, 827, 769 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{19}N_2O$ [M + H]$^+$ 363.1497 found 363.1497.

methyl 4-(6,9-dihydrochromeno[4',3':4,5]pyrido[2,3-b]indol-7-yl)benzoate (8c)



8c (118 mg) mg was obtained from **7** (84 mg) following general procedure **C**; Off-colorless solid; R_f = 0.28 (20% EtOAc/Hexanes); mp: 204-206 °C; Yield (58%); ^{1}H NMR (400 MHz, DMSO) δ 12.22 (s, 1H), 8.41 – 8.33 (m, 2H), 8.12 (d, *J* = 8.4 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.59 – 7.50 (m, 3H), 7.39 (td, *J* = 7.6, 1.1 Hz, 1H), 7.21 (dd, *J* = 10.7, 4.6 Hz, 2H), 5.20 (s, 2H), 3.91 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 166.5, 157.1, 152.8, 150.7, 143.9, 140.5, 134.6, 132.0, 130.1, 129.9, 129.60, 128.5, 127.7, 123.0, 122.9, 122.6, 120.3, 119.9, 119.6, 118.06, 112.1, 109.3, 67.3, 52.7; IR (KBr) υ

2924, 1725, 1460, 1278, 872, 761 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{19}N_2O_3$ $[M + H]^+$ 407.1396 found 407.1397.

III. References

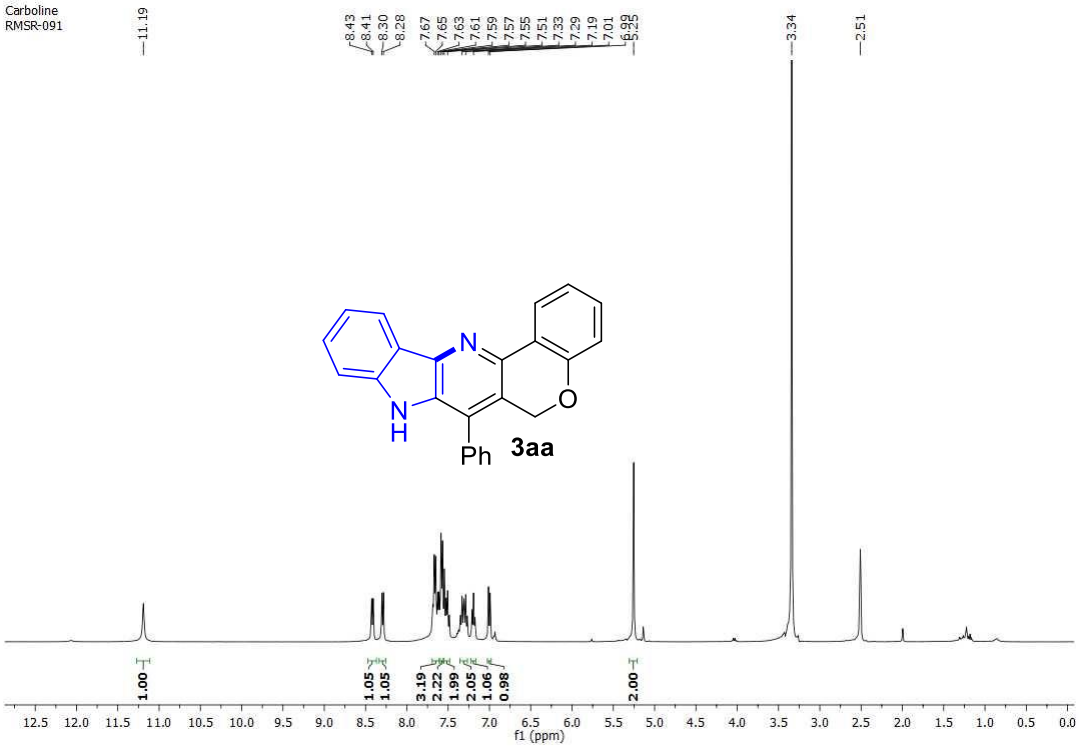
1. *For 2-Amino-1Hindole-3-carboxylate Derivatives (**1**) see:* (a) Yang, X.; Fu, H.; Qiao, R.; Jiang, Y.; Zhao, Y. A Simple Copper-Catalyzed Cascade Synthesis of 2-Amino-1Hindole-3-carboxylate Derivatives. *Adv. Synth. Catal*. **2010**, *352*, 1033–1038. Arigela, R. K.; Kumar, R.; Samala, S.; Gupta, S.; Kundu, B. Diversity-Oriented Synthesis of Polycyclic Indoles: Brønsted or Lewis Acid Catalyzed Three-Component Reaction for the Synthesis of α-Carbolines and Pyrimidoindoles. *Eur. J. Org. Chem.* **2014**, 6057–6066.

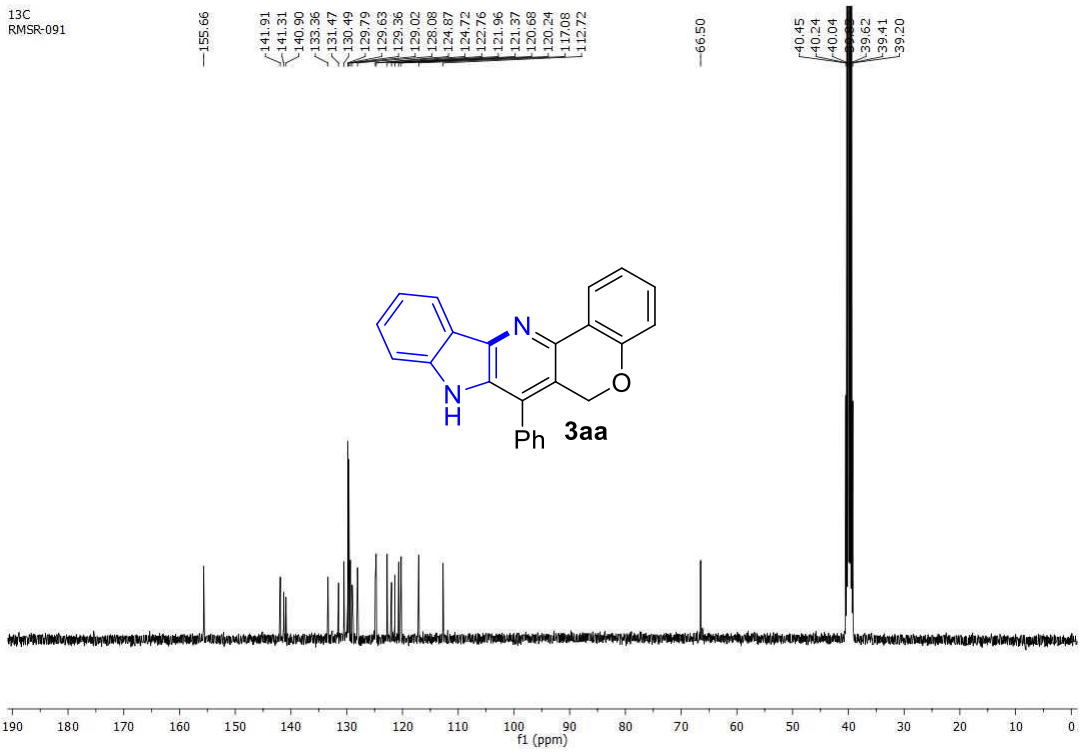
2. *For O-(Arylpropynyloxy) Salicylaldehydes (**2**) see:* Acosta, P.; Feresin, G.; Tapia, A.; Estévez-Braun, A. Microwave-Assisted Organocatalytic Intramolecular Knoevenagel/Hetero Diels−Alder Reaction with O-(Arylpropynyloxy) Salicylaldehydes: Synthesis of Polycyclic Embelin Derivatives. *J. Org. Chem*. **2016**, *81*, 9738−9756.

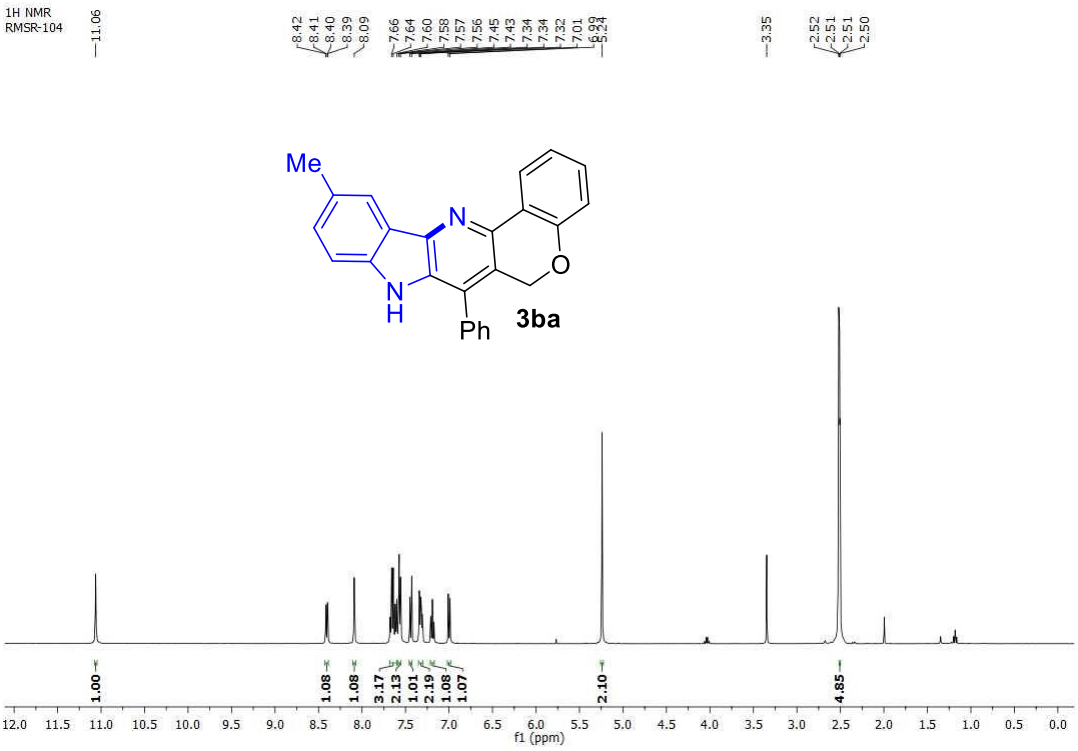
3. *For 3-amino-1H-indole-2-carboxylates (**5**) see:* Harajani, J.; Tang, A. X.; Norton, R. S.; Baell, J. B. A new methodology for the synthesis of 3-amino-1H-indole-2-carboxylates. *Tetrahedron* **2014**, *70*, 8047-8055.

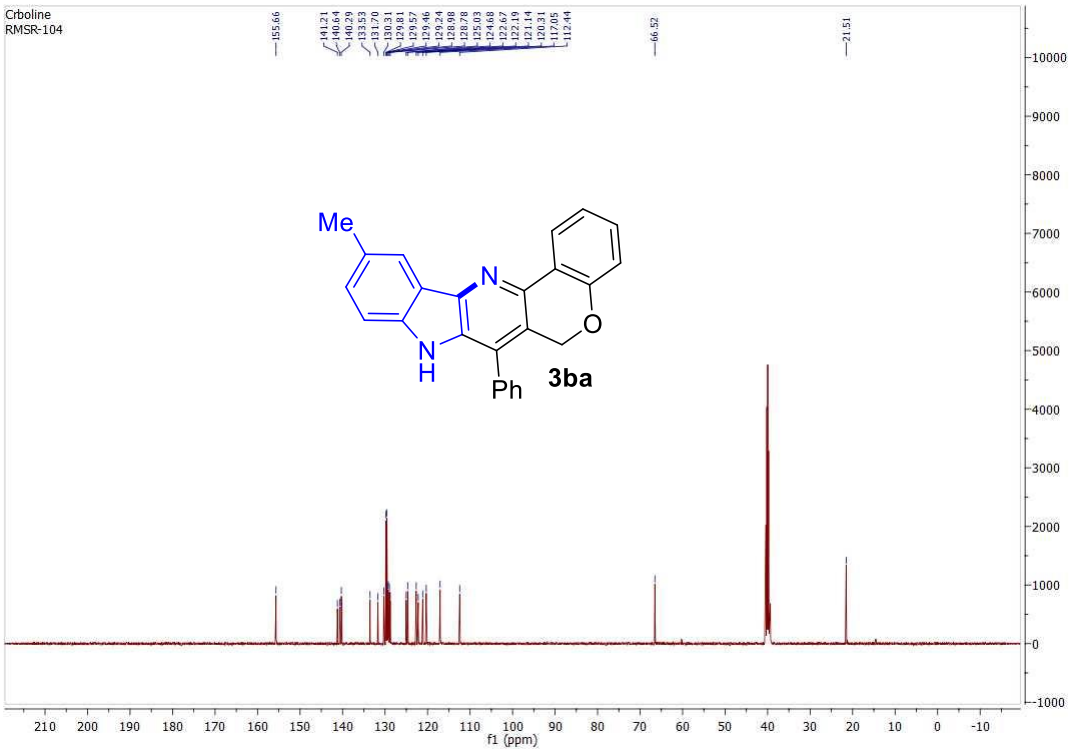
4. *For Ethyl 2-Amino-1-methyl-1H-indole-3-carboxylate (**6**) see:* Lauria, A.; Patella, C.; Diana, P.; Barraja, P.; Montalbano, A.; Cirrincione, G.; Dattolo, G.; Almerico, A. M. A New Tetracyclic Ring System of Biological Interest. Indolo[3,2-e][1,2,3]triazolo[1,5-a]pyrimidines Through Domino Reactions of 2-Azidoindole. *Heterocycles*, **2003**, 60, 2669−2675.
5. *For 2-Aminoindole Hydrochlorides (**7**) see*: (a) Gupta, S.; Kumar, B.; Kundu, B. Three-Component Tandem Reaction Involving Acid Chlorides, Terminal Alkynes, and 2-Aminoindole Hydrochlorides: Synthesis of ***α***-Carboline Derivatives in Aqueous Conditions via Regioselective [3 + 3] Cyclocondensation. *J. Org. Chem.* **2011**, *76*, 10154−10162. (b) Forbes, I. T.; Johnson, C. N.; Thompson, M. *J.* Syntheses of Functionalised Pyrido[2,3-b]indoles. *Chem. Soc., Perkin Trans. 1* **1992**, 275−281.

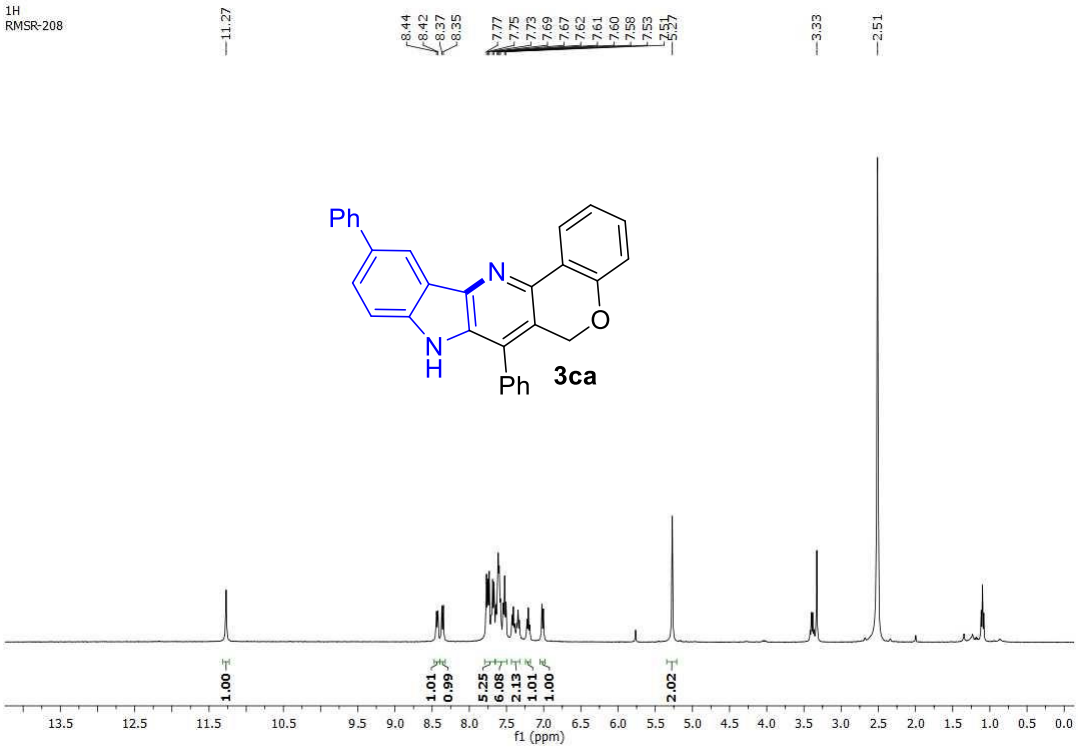
IV. Spectral data of 3aa-ja, 3ab-3au, 4a-c and 8a-c.

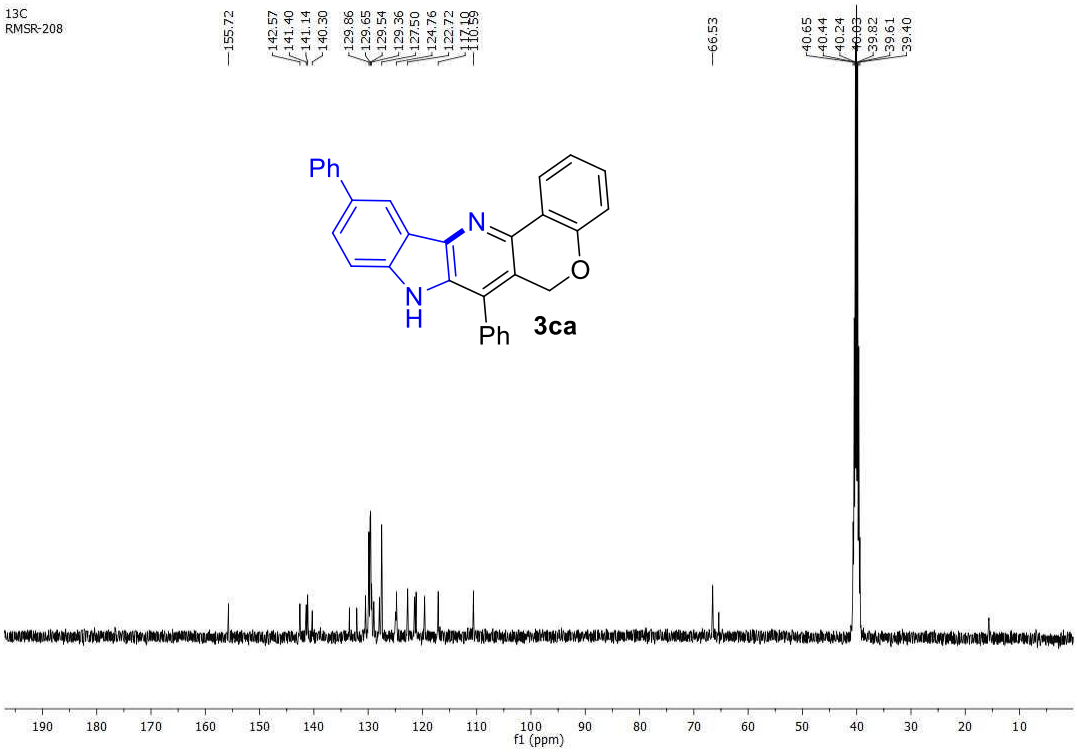


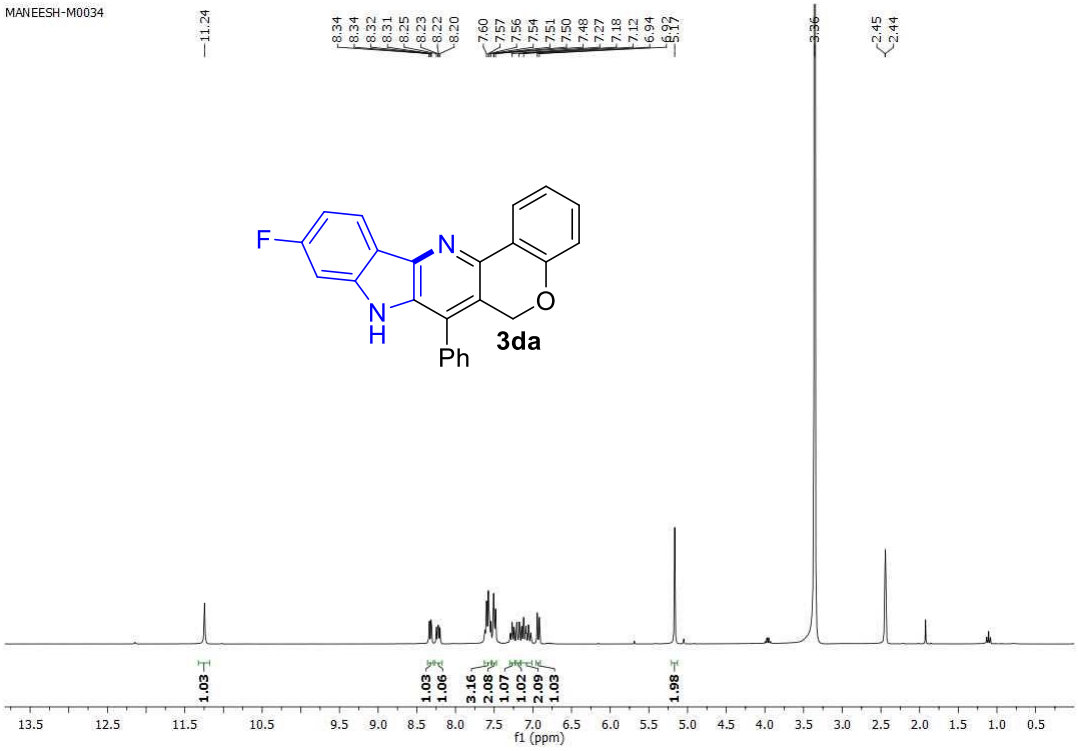


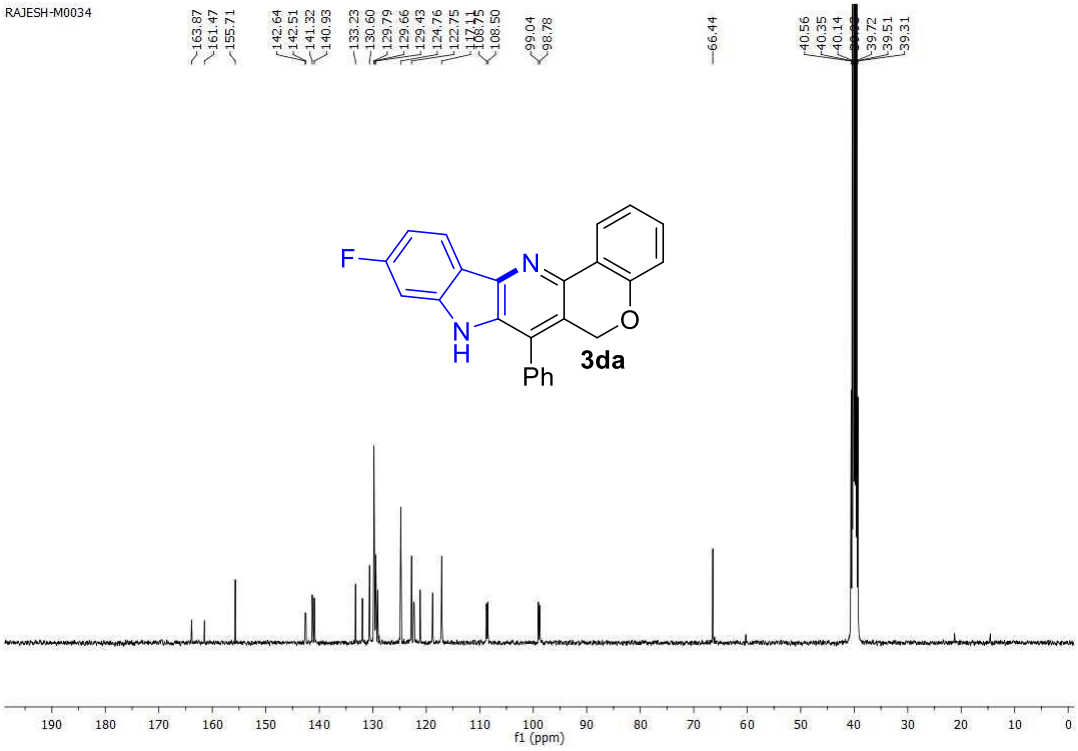

1H NMR
RMSR-104
Me
N
O
N
H
Ph
3ba
f1 (ppm)

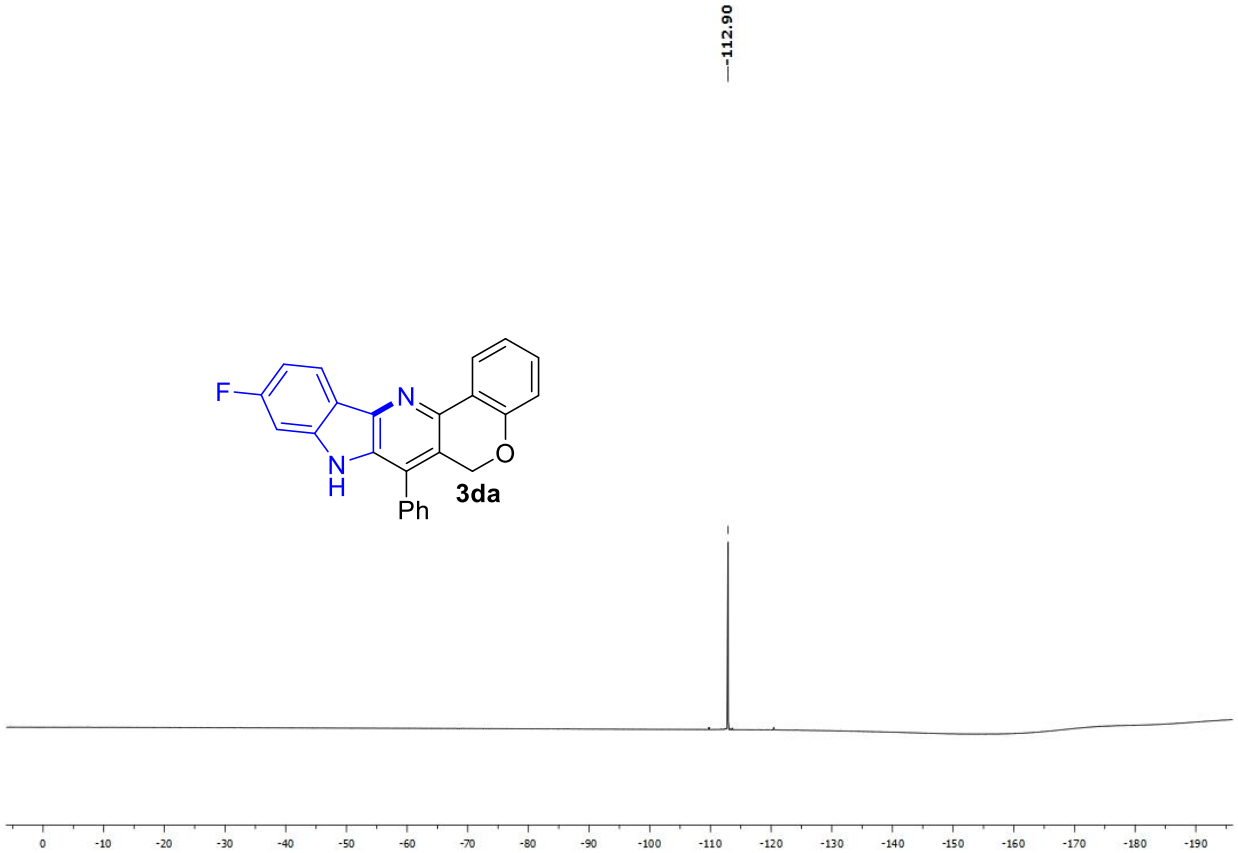

Crboline
RMSR-104
Me
N
O
N
H
Ph
3ba
f1 (ppm)

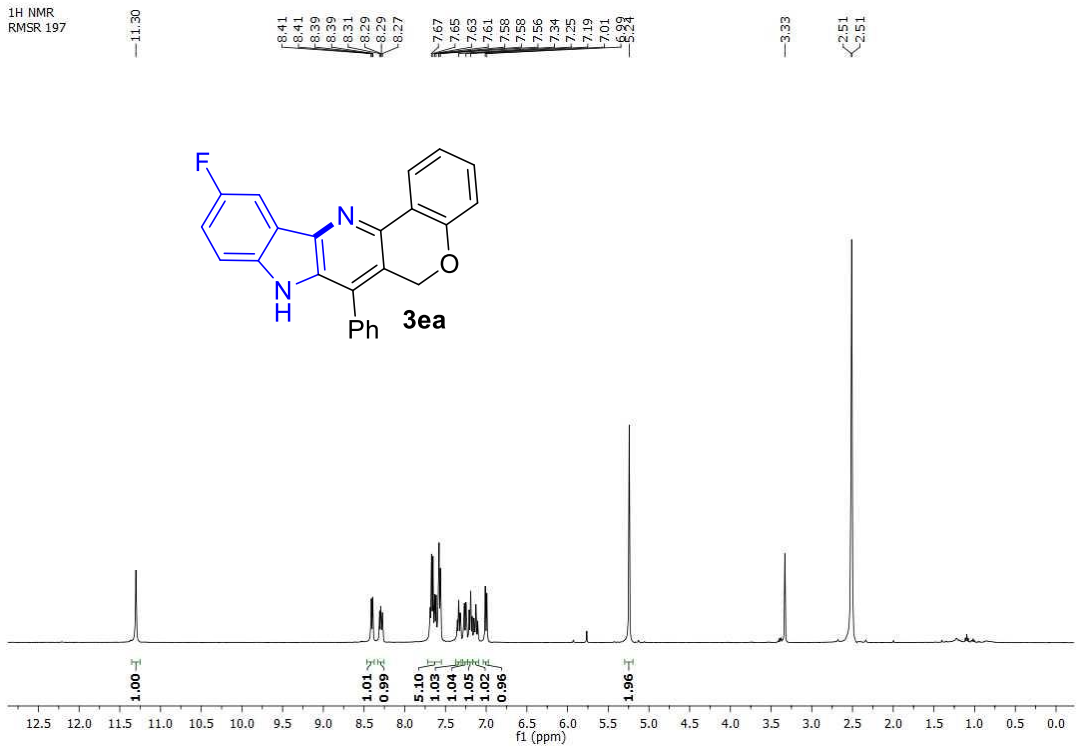

1H
RMSR-208
11.27
8.44
8.42
8.37
8.35
7.77
7.75
7.73
7.69
7.67
7.62
7.61
7.60
7.58
7.53
7.51
7.27
3.33
2.51
Ph
N
O
N
H
Ph
3ca
1.00
1.01
0.99
5.25
6.08
2.13
1.01
1.00
2.02
f1 (ppm)

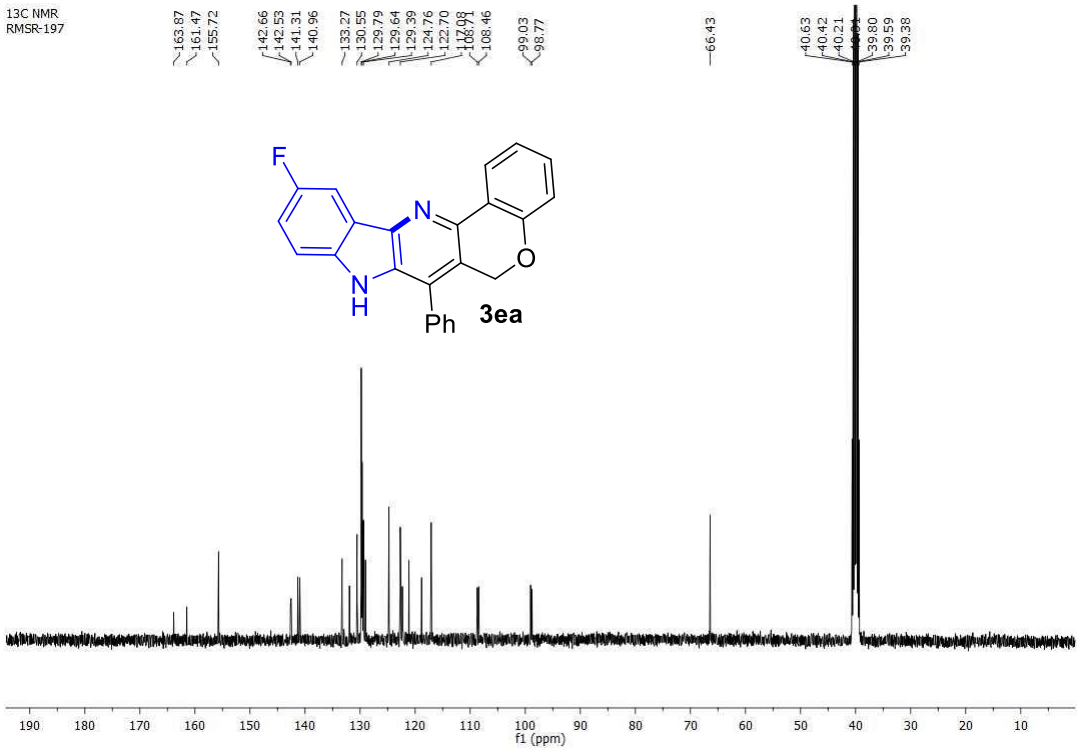

13C
RMSR-208
155.72
142.57
141.40
141.14
140.30
129.86
129.65
129.54
129.36
127.50
124.76
122.72
117.10
110.59
66.53
40.65
40.44
40.24
40.03
39.82
39.61
39.40
Ph
N
O
N
H
Ph
3ca
f1 (ppm)

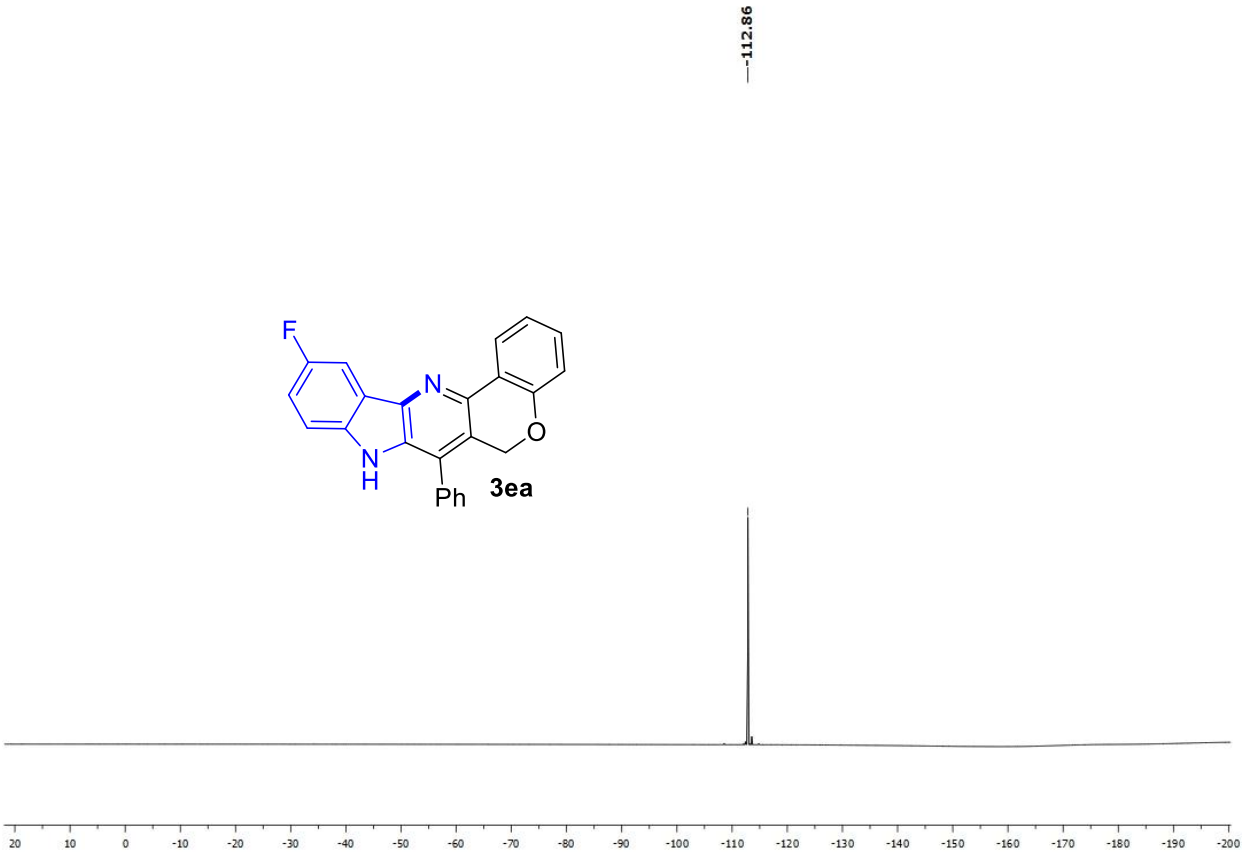

MANEESH-M0034
11.24
8.34
8.34
8.32
8.31
8.25
8.23
8.22
8.20
7.60
7.57
7.56
7.54
7.51
7.50
7.48
7.27
7.18
7.12
6.94
6.92
5.17
3.36
2.45
2.44
F
N
N
H
O
Ph
3da
1.03
1.03
1.06
3.16
2.08
1.07
1.02
2.09
1.03
1.98
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

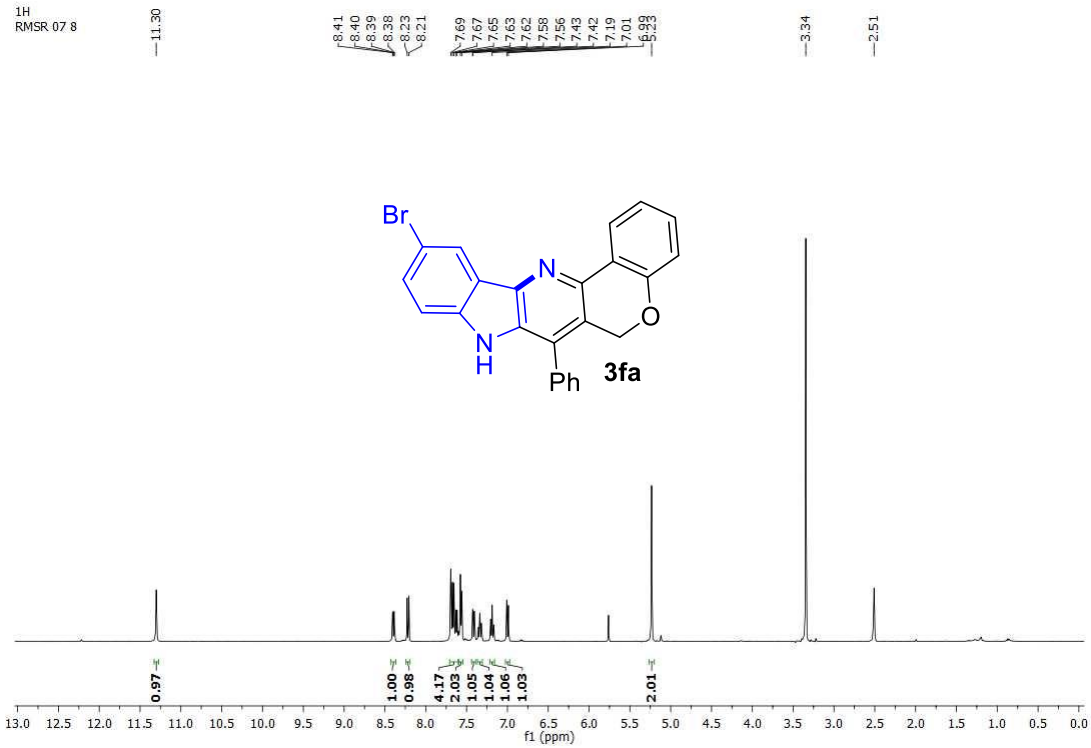

RAJESH-M0034
163.87
161.47
155.71
142.64
142.51
141.32
140.93
133.23
130.60
129.79
129.66
129.43
124.76
122.75
117.11
108.75
108.50
99.04
98.78
66.44
40.56
40.35
40.14
39.72
39.51
39.31
F
N
N
H
O
Ph
3da
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

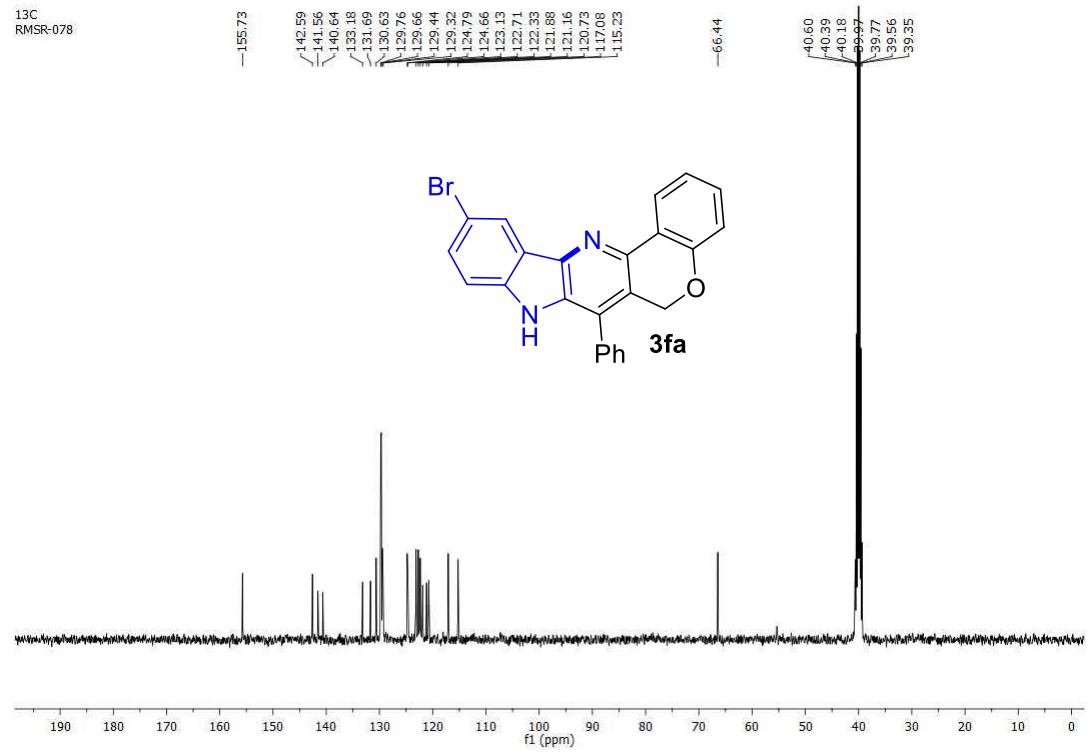

-112.90
F
N
N
H
O
Ph
3da
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190

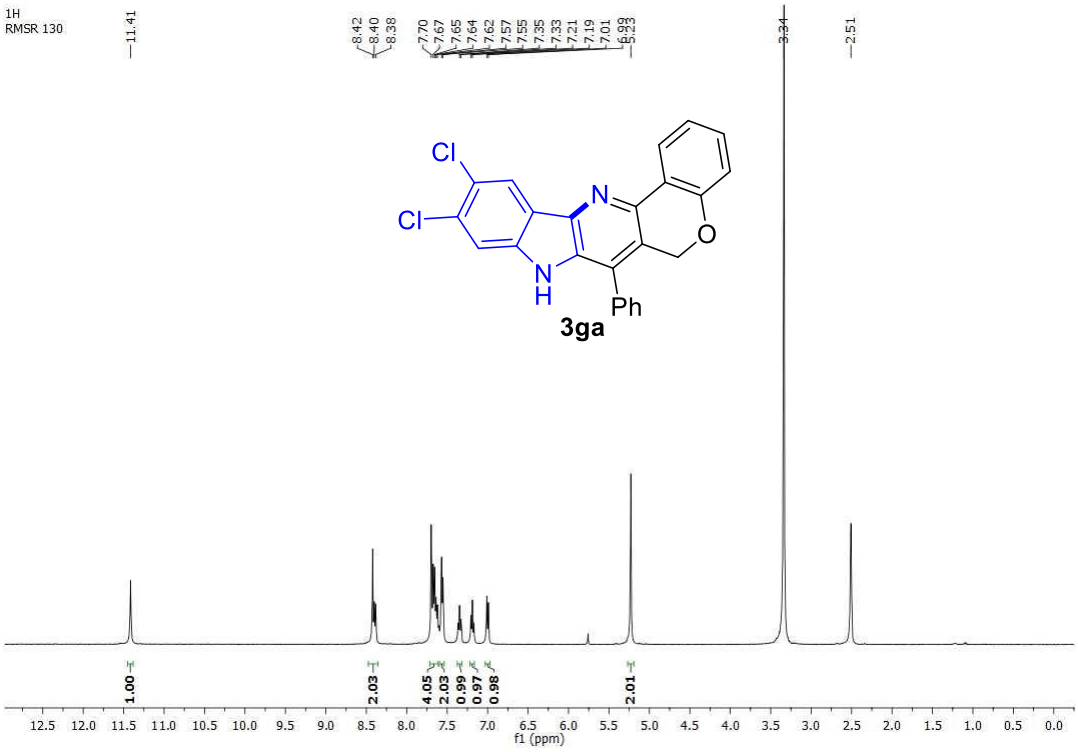

1H NMR
RMSR 197
11.30
8.41
8.41
8.39
8.39
8.31
8.29
8.29
8.27
7.67
7.65
7.63
7.61
7.58
7.58
7.56
7.34
7.25
7.19
7.01
6.99
5.24
3.33
2.51
2.51
F
N
O
N
H
Ph
3ea
1.00
1.01
0.99
5.10
1.03
1.04
1.05
1.02
0.96
1.96
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

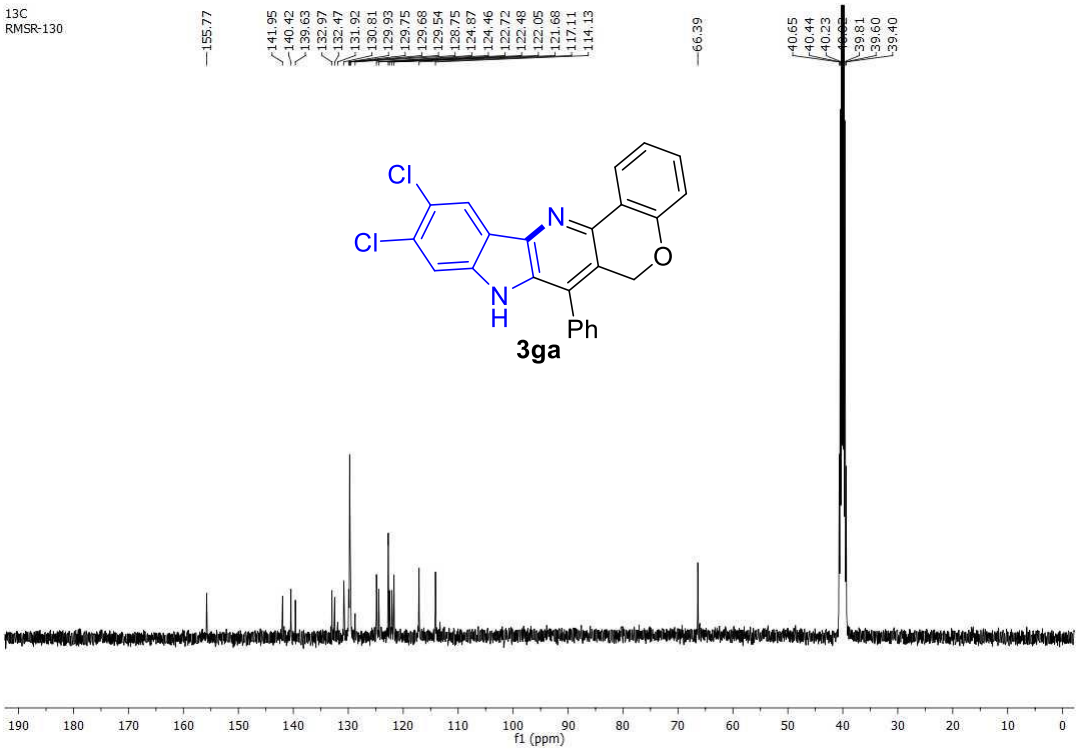

13C NMR
RMSR-197
163.87
161.47
155.72
142.66
142.53
141.31
140.96
133.27
130.55
129.79
129.64
129.39
124.76
122.70
117.08
108.71
108.46
99.03
98.77
66.43
40.63
40.42
40.21
39.80
39.59
39.38
F
N
O
N
H
Ph
3ea
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

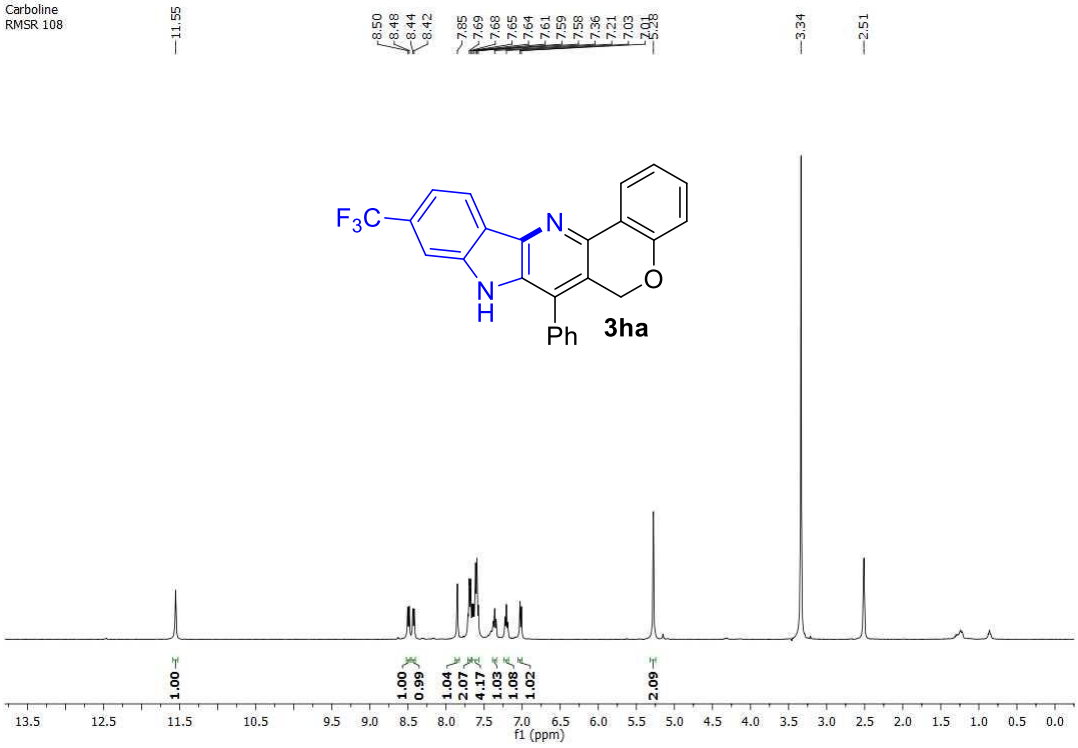

-112.86
F
N
O
N
H
Ph
3ea
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

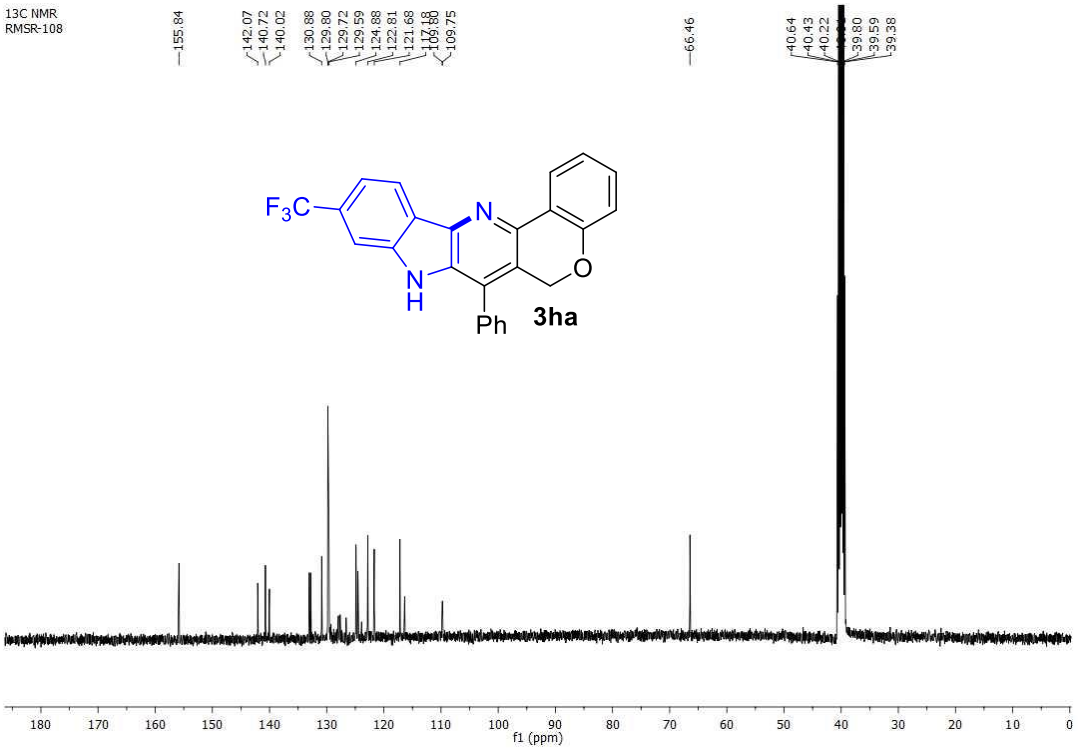

1H
RMSR 07 8
11.30
8.41
8.40
8.39
8.38
8.23
8.21
7.69
7.67
7.65
7.63
7.62
7.58
7.56
7.43
7.42
7.19
7.01
6.99
6.33
3.34
2.51
Br
N
O
N
H
Ph
3fa
0.97
1.00
0.98
4.17
2.03
1.05
1.04
1.06
1.03
2.01
f1 (ppm)


13C
RMSR-078
155.73
142.59
141.56
140.64
133.18
131.69
130.63
129.76
129.66
129.44
129.32
124.79
124.66
123.13
122.71
122.33
121.88
121.16
120.73
117.08
115.23
66.44
40.60
40.39
40.18
39.97
39.77
39.56
39.35
Br
N
O
N
H
Ph
3fa
f1 (ppm)


1H
RMSR 130
11.41
8.42
8.40
8.38
7.70
7.67
7.65
7.64
7.62
7.57
7.55
7.35
7.33
7.21
7.19
7.01
6.99
5.23
3.34
2.51
Cl
Cl
N
O
N
H
Ph
3ga
1.00
2.03
4.05
2.03
0.99
0.97
0.98
2.01
f1 (ppm)

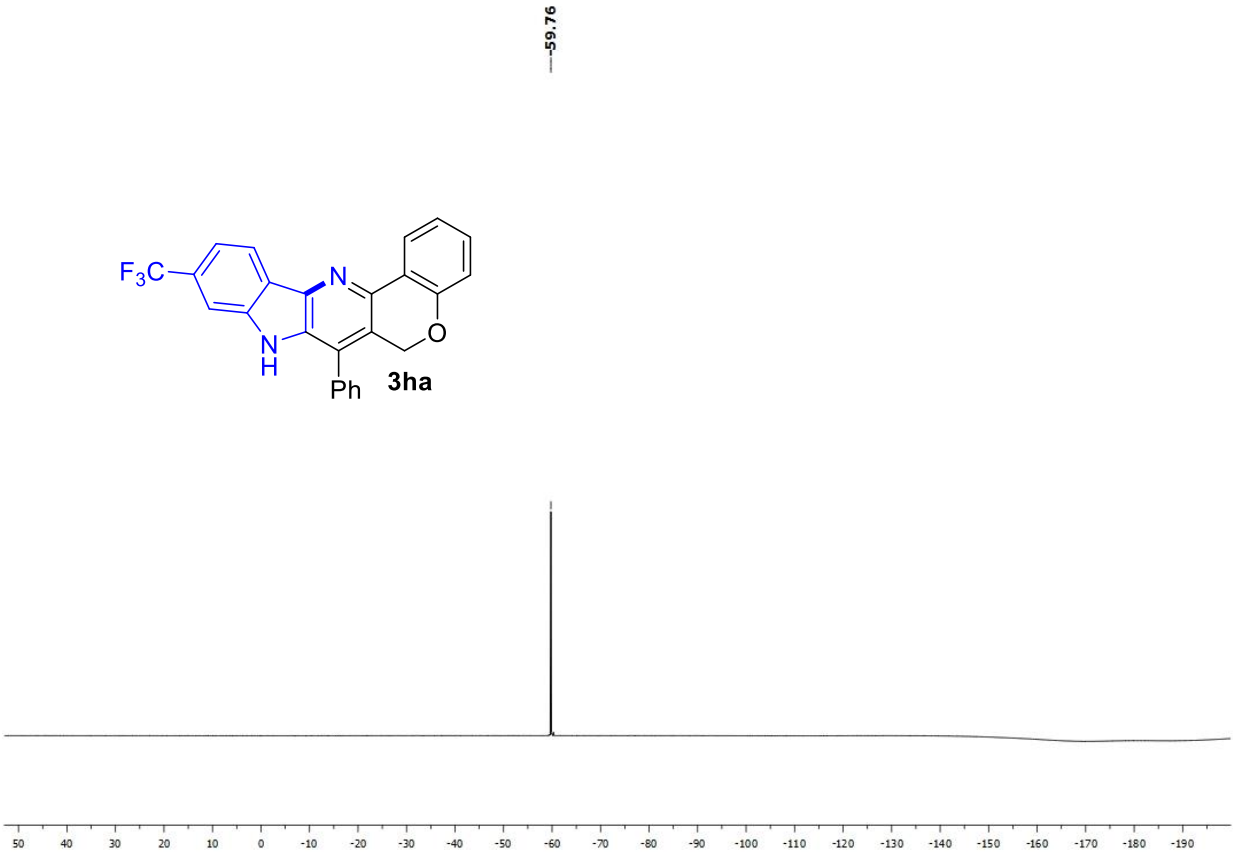

13C
RMSR-130
155.77
141.95
140.42
139.63
132.97
132.47
131.92
130.81
129.93
129.75
129.68
129.54
128.75
124.87
124.46
122.72
122.48
122.05
121.68
117.11
114.13
66.39
40.65
40.44
40.23
39.81
39.60
39.40
Cl
Cl
N
O
N
H
Ph
3ga
f1 (ppm)

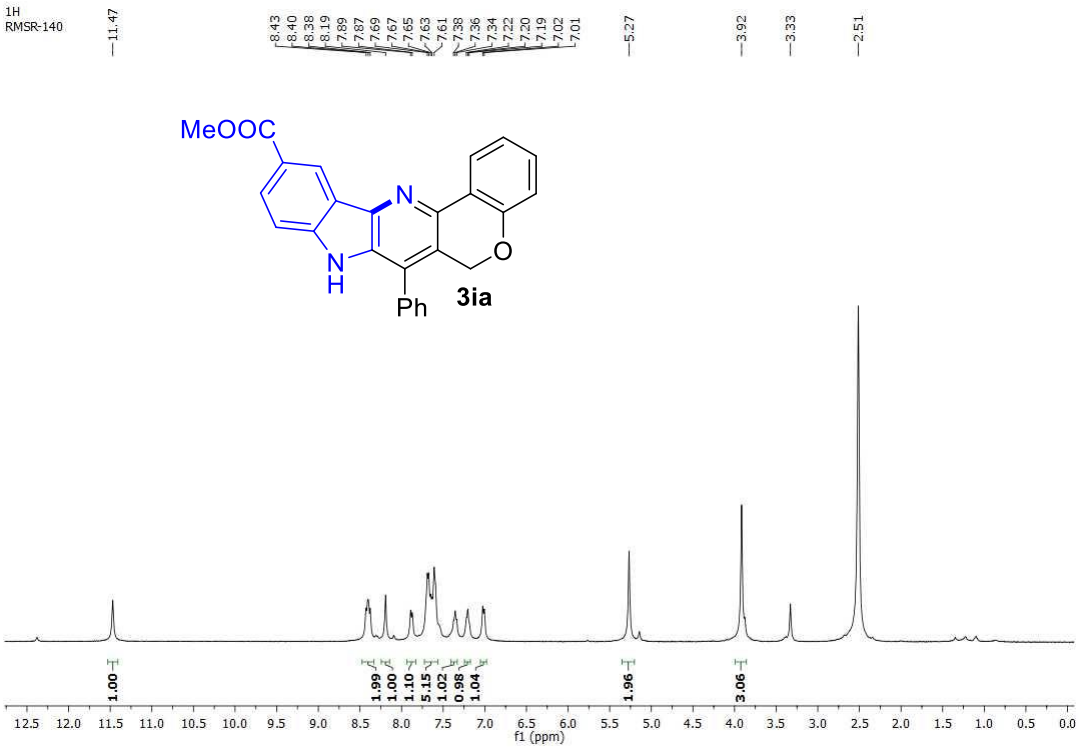

Carboline
RMSR 108
11.55
8.50
8.48
8.44
8.42
7.85
7.69
7.68
7.65
7.64
7.61
7.59
7.58
7.36
7.21
7.03
7.01
5.28
3.34
2.51
F3C
N
N
H
O
Ph
3ha
1.00
1.00
0.99
1.04
2.07
4.17
1.03
1.08
1.02
2.09
f1 (ppm)

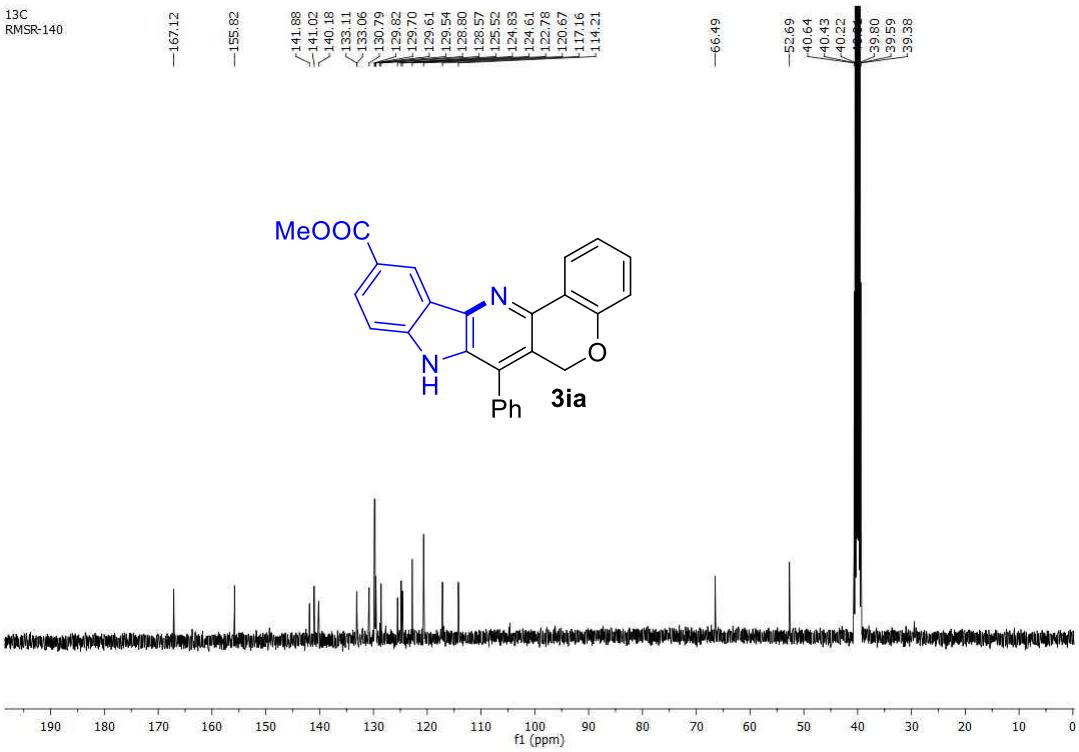

13C NMR
RMSR-108
155.84
142.07
140.72
140.02
130.88
129.80
129.72
129.59
124.88
122.81
121.68
117.80
109.75
66.46
40.64
40.43
40.22
39.80
39.59
39.38
F3C
N
N
H
O
Ph
3ha
f1 (ppm)

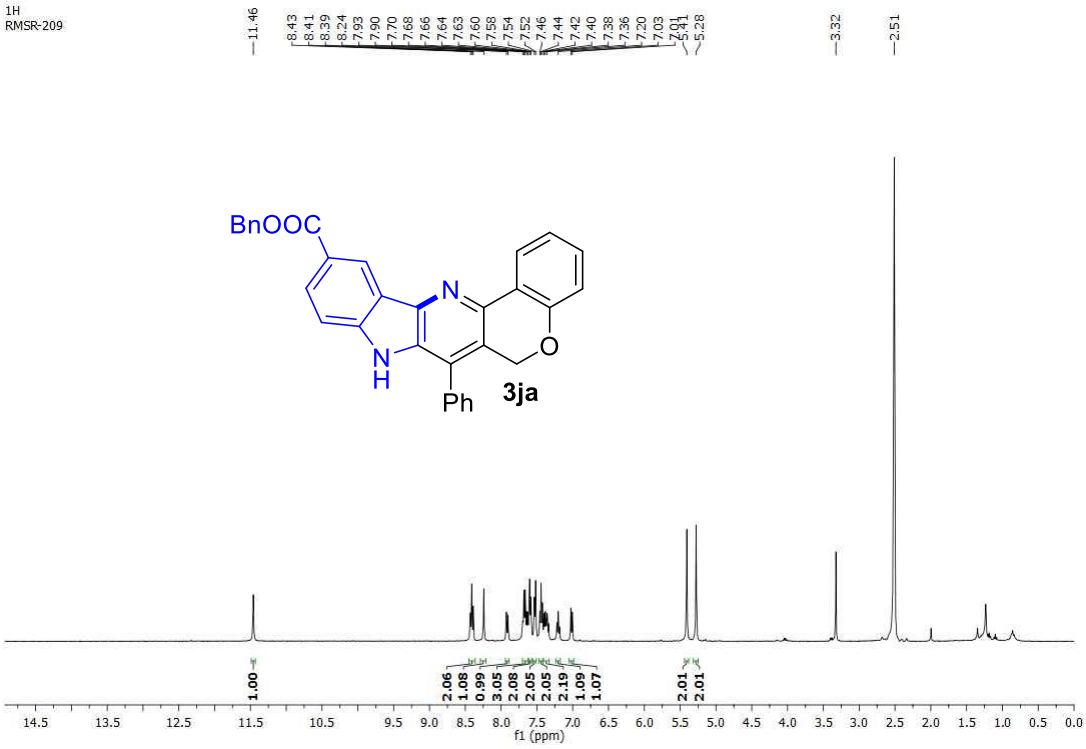
F3C
N
N
H
O
Ph

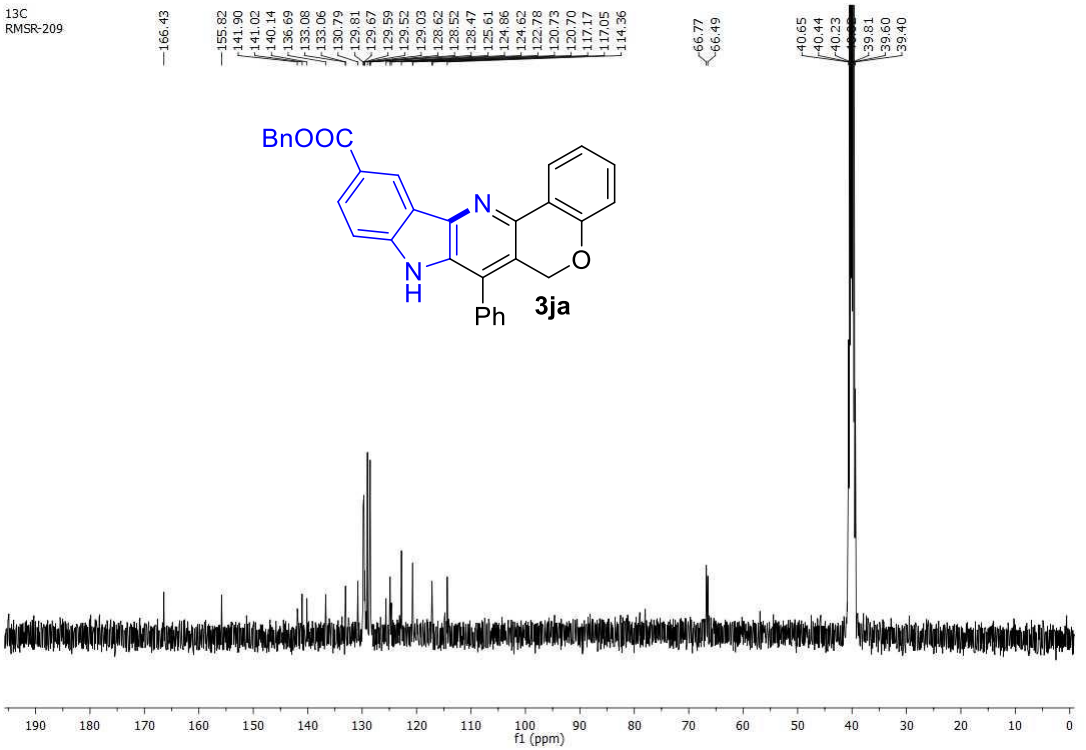
3ha

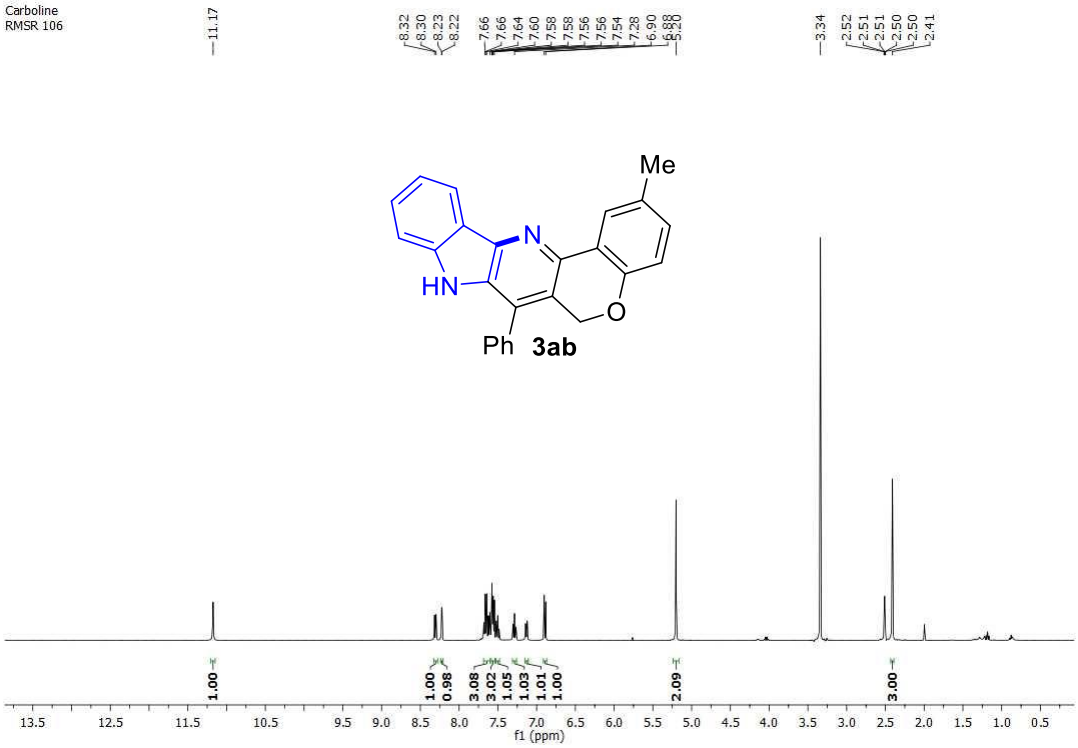

-59.76
50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190

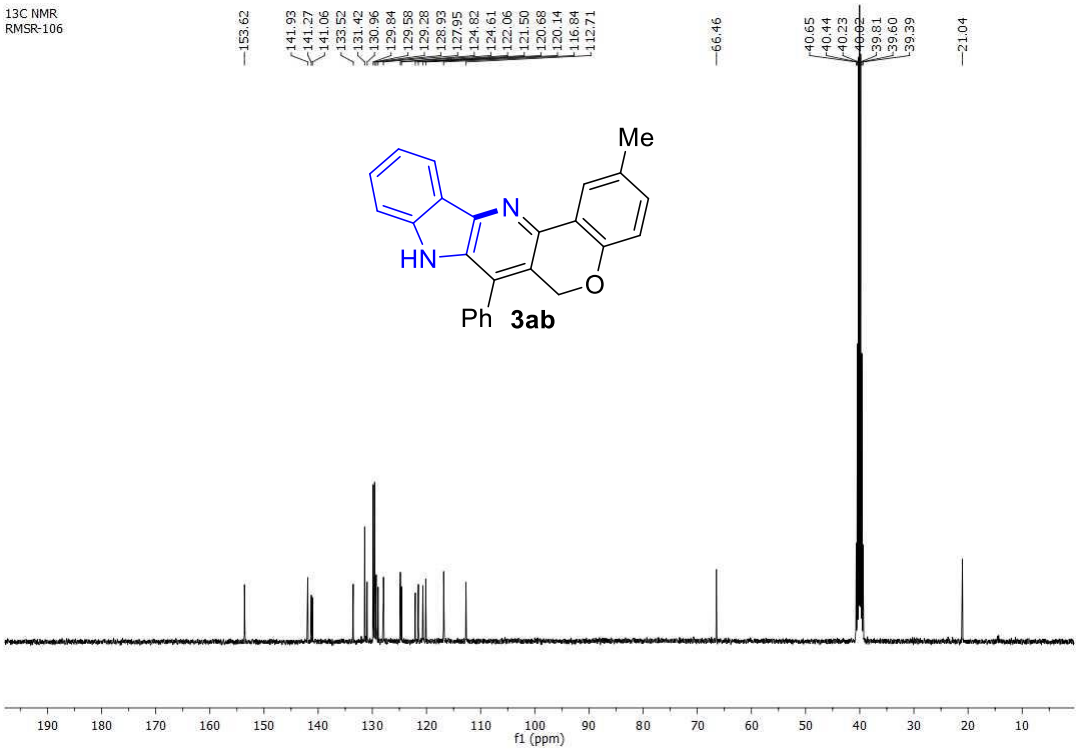

1H
RMSR-140
11.47
8.43
8.40
8.38
8.19
7.89
7.87
7.69
7.67
7.65
7.63
7.61
7.38
7.36
7.34
7.22
7.20
7.19
7.02
7.01
5.27
3.92
3.33
2.51
MeOOC
N
N
H
O
Ph
3ia
1.00
1.99
1.00
1.10
5.15
1.02
0.98
1.04
1.96
3.06
f1 (ppm)

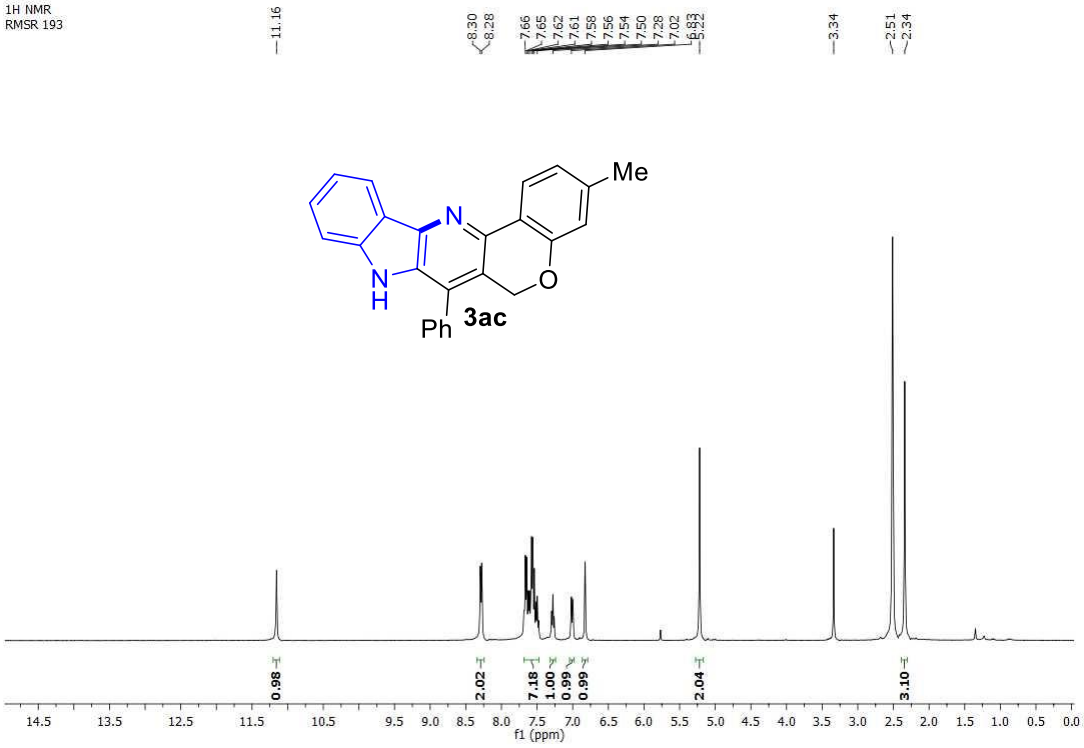

13C
RMSR-140
167.12
155.82
141.88
141.02
140.18
133.11
133.06
130.79
129.82
129.70
129.61
129.54
128.80
128.57
125.52
124.83
124.61
122.78
120.67
117.16
114.21
66.49
52.69
40.64
40.43
40.22
39.80
39.59
39.38
MeOOC
N
N
H
O
Ph
3ia
f1 (ppm)

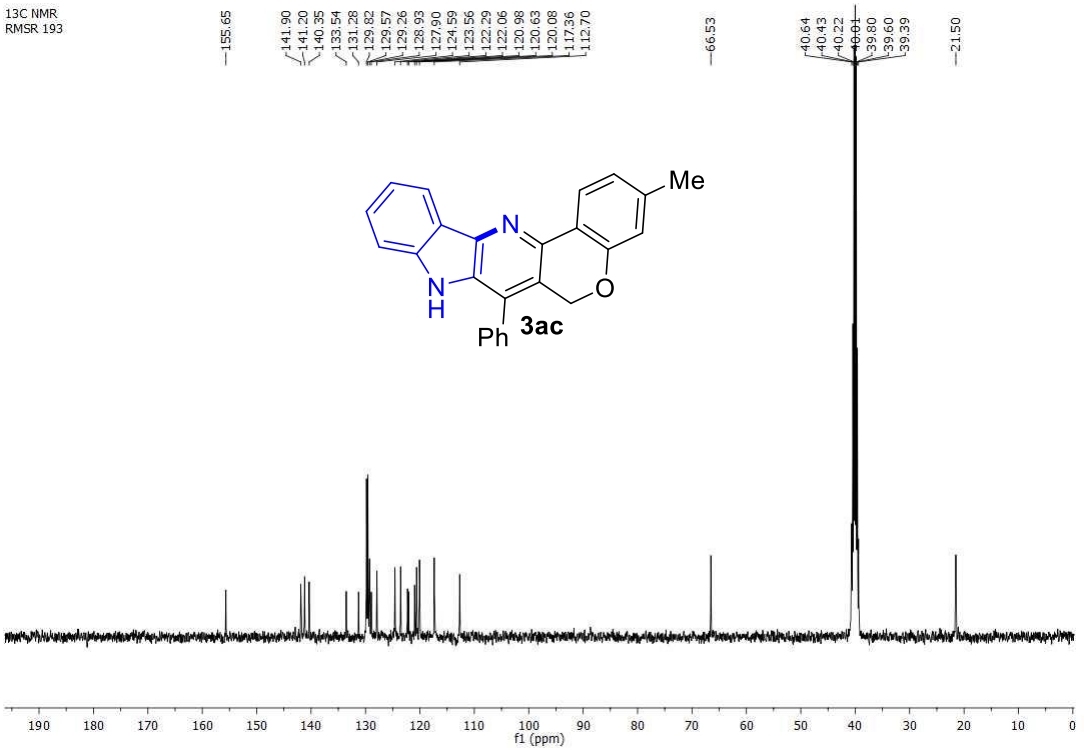

1H
RMSR-209
BnOOC
N
N
H
O
Ph
3ja
f1 (ppm)

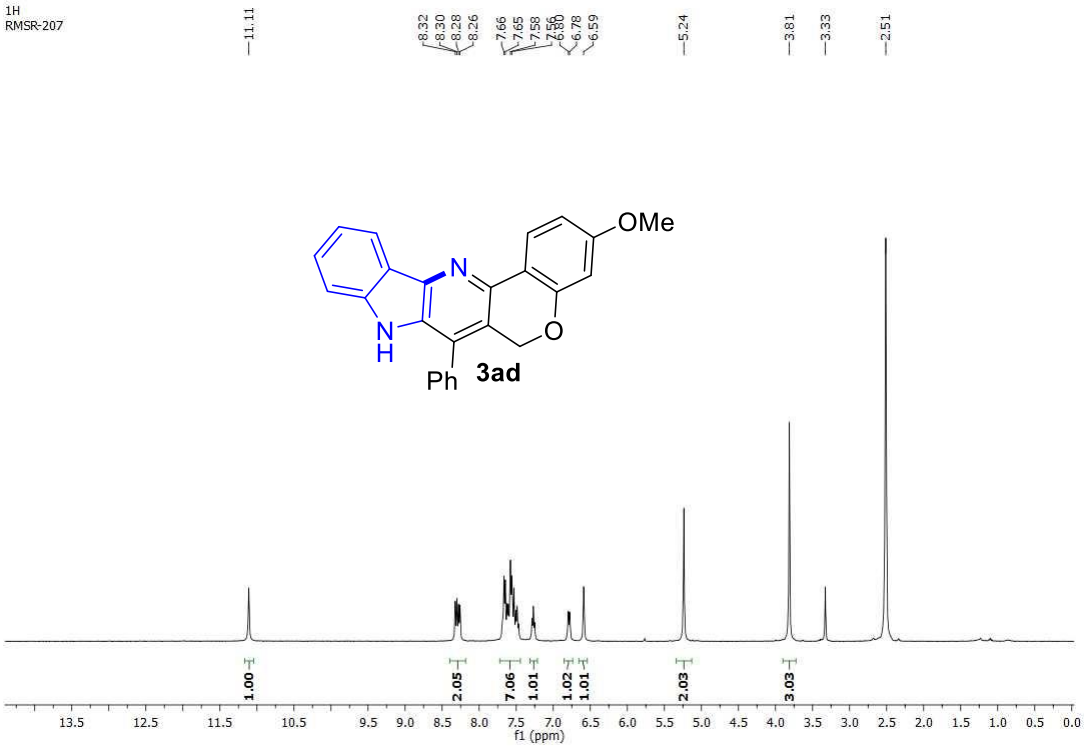

13C
RMSR-209
BnOOC
N
N
H
O
Ph
3ja
f1 (ppm)

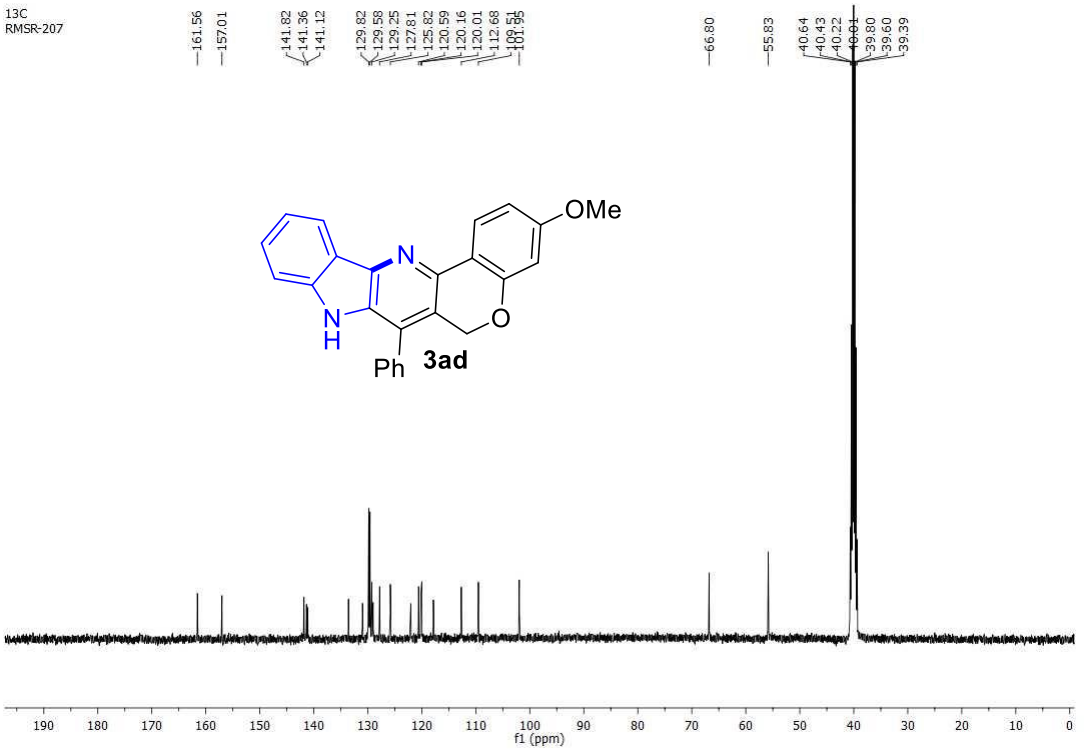

Carboline
RMSR 106
11.17
8.32
8.30
8.23
8.22
7.66
7.66
7.64
7.60
7.58
7.58
7.56
7.56
7.54
7.28
6.90
6.88
5.20
3.34
2.52
2.51
2.51
2.50
2.50
2.41
Me
N
HN
O
Ph 3ab
1.00
1.00
0.98
3.08
3.02
1.05
1.03
1.01
1.00
2.09
3.00
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

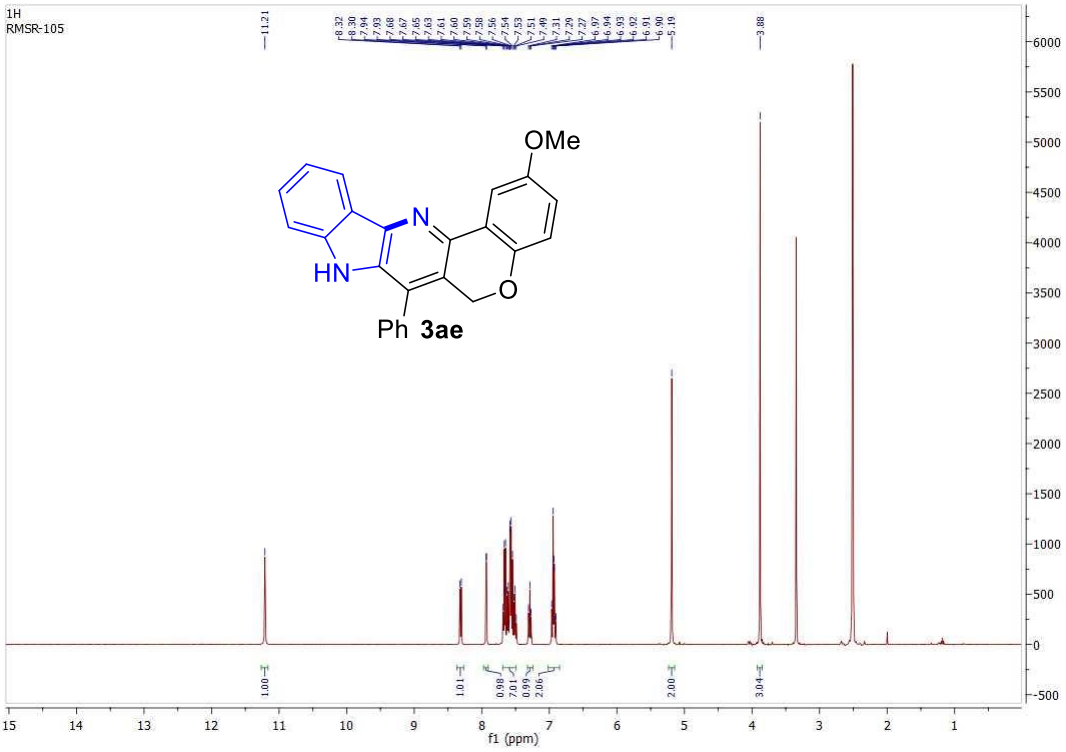

13C NMR
RMSR-106
153.62
141.93
141.27
141.06
133.52
131.42
130.96
129.84
129.58
129.28
128.93
127.95
124.82
124.61
122.06
121.50
120.68
120.14
116.84
112.71
66.46
40.65
40.44
40.23
39.81
39.60
39.39
21.04
Me
N
HN
O
Ph 3ab
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

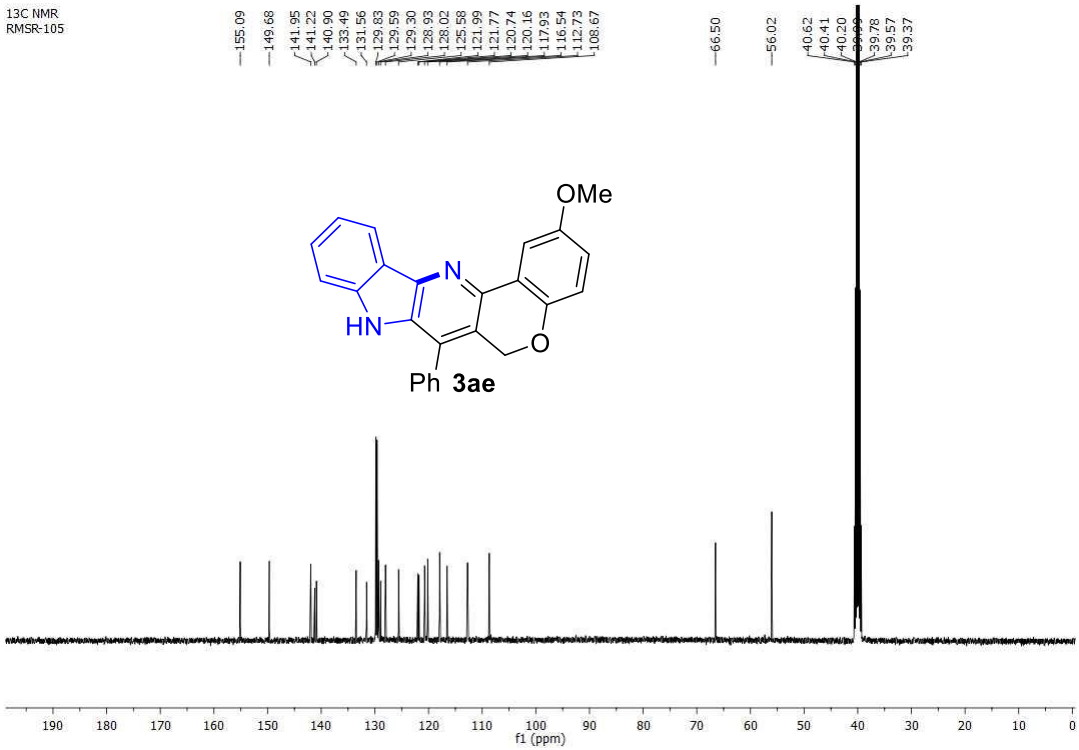

1H NMR
RMSR 193
11.16
8.30
8.28
7.66
7.65
7.62
7.61
7.58
7.56
7.54
7.50
7.28
7.02
6.83
6.82
3.34
2.51
2.34
Me
N
N
H
O
Ph
3ac
0.98
2.02
7.18
1.00
0.99
0.99
2.04
3.10
f1 (ppm)

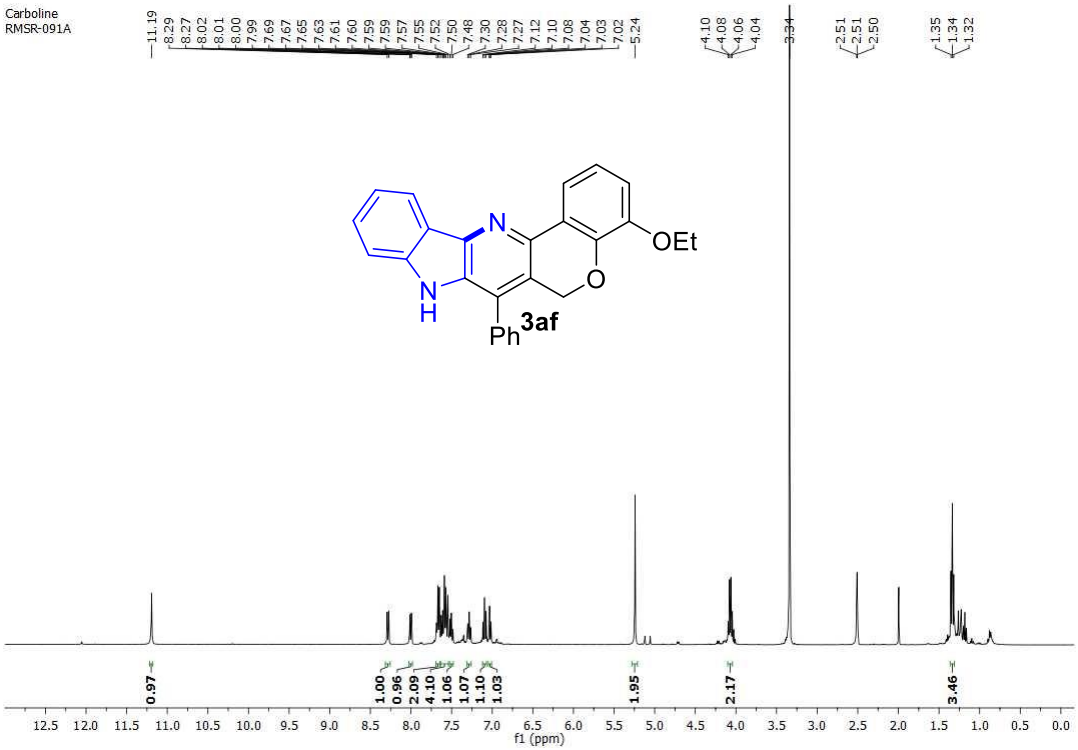

13C NMR
RMSR 193
155.65
141.90
141.20
140.35
133.54
131.28
129.82
129.57
129.26
128.93
127.90
124.59
123.56
122.29
122.06
120.98
120.63
120.08
117.36
112.70
66.53
40.64
40.43
40.22
40.01
39.80
39.60
39.39
21.50
Me
N
N
H
O
Ph
3ac
f1 (ppm)

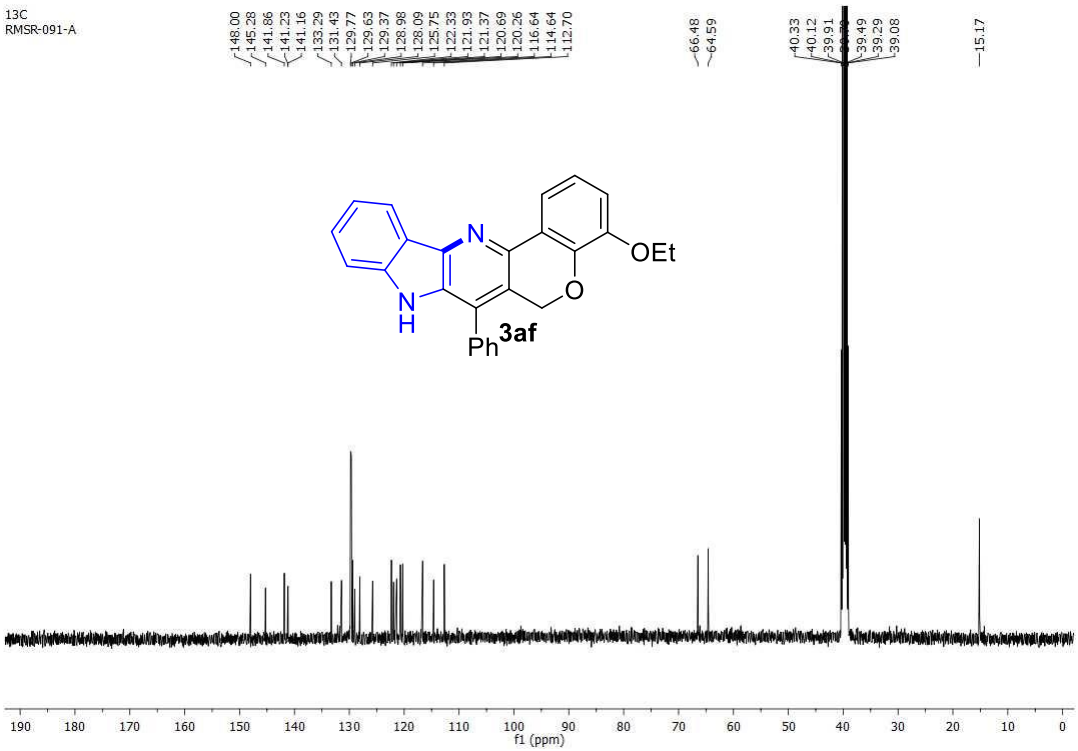

1H
RMSR-207
11.11
8.32
8.30
8.28
8.26
7.66
7.65
7.58
6.78
6.59
5.24
3.81
3.33
2.51
OMe
N
N
H
O
Ph
3ad
1.00
2.05
7.06
1.01
1.02
1.01
2.03
3.03
f1 (ppm)

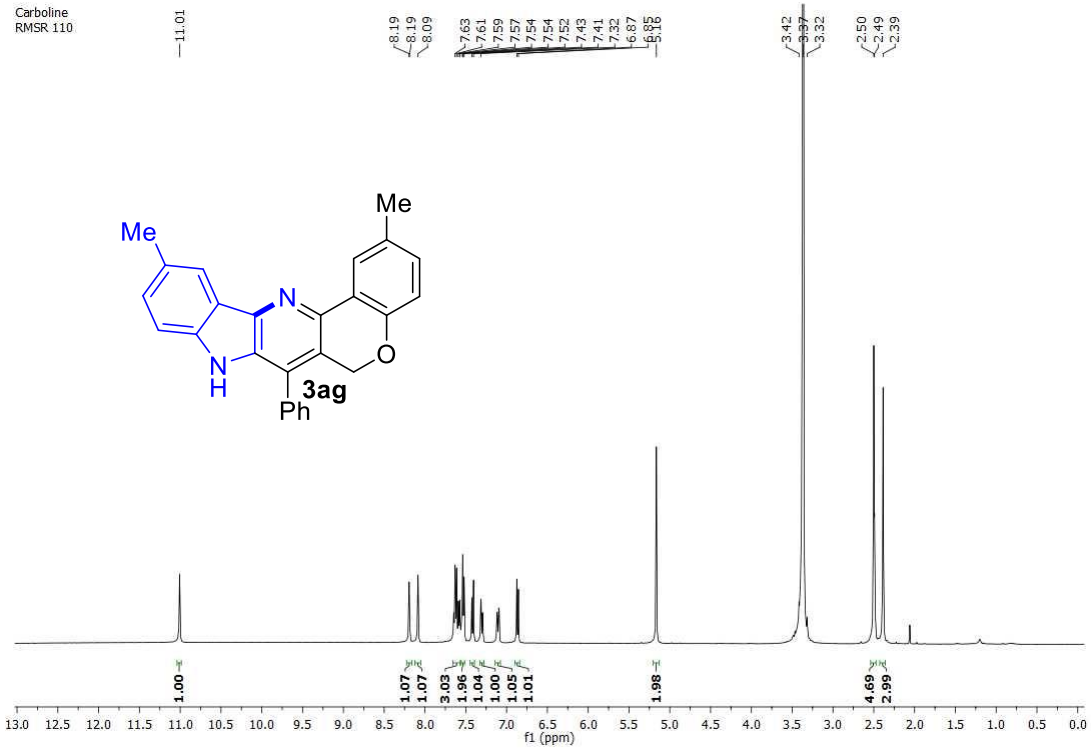

13C
RMSR-207
161.56
157.01
141.82
141.36
141.12
129.82
129.58
129.25
127.81
125.82
120.59
120.16
120.01
112.68
66.80
55.83
40.64
40.43
40.22
39.80
39.60
39.39
OMe
N
N
H
O
Ph
3ad
f1 (ppm)

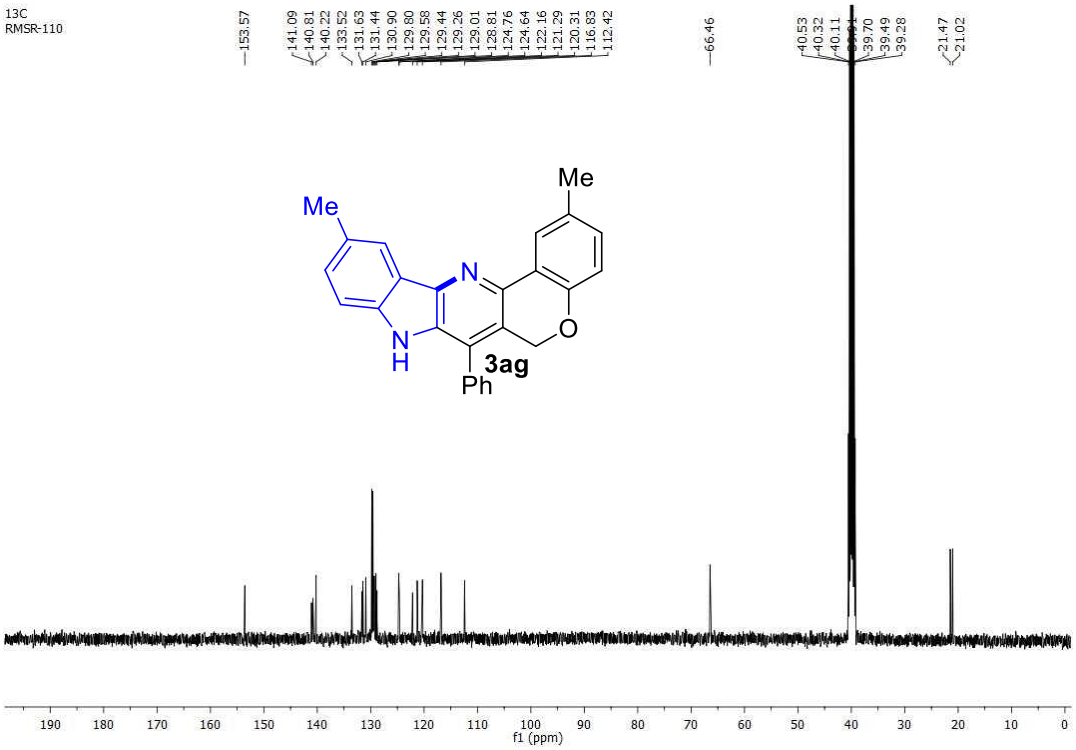

1H
RMSR-105
OMe
N
HN
O
Ph 3ae
f1 (ppm)

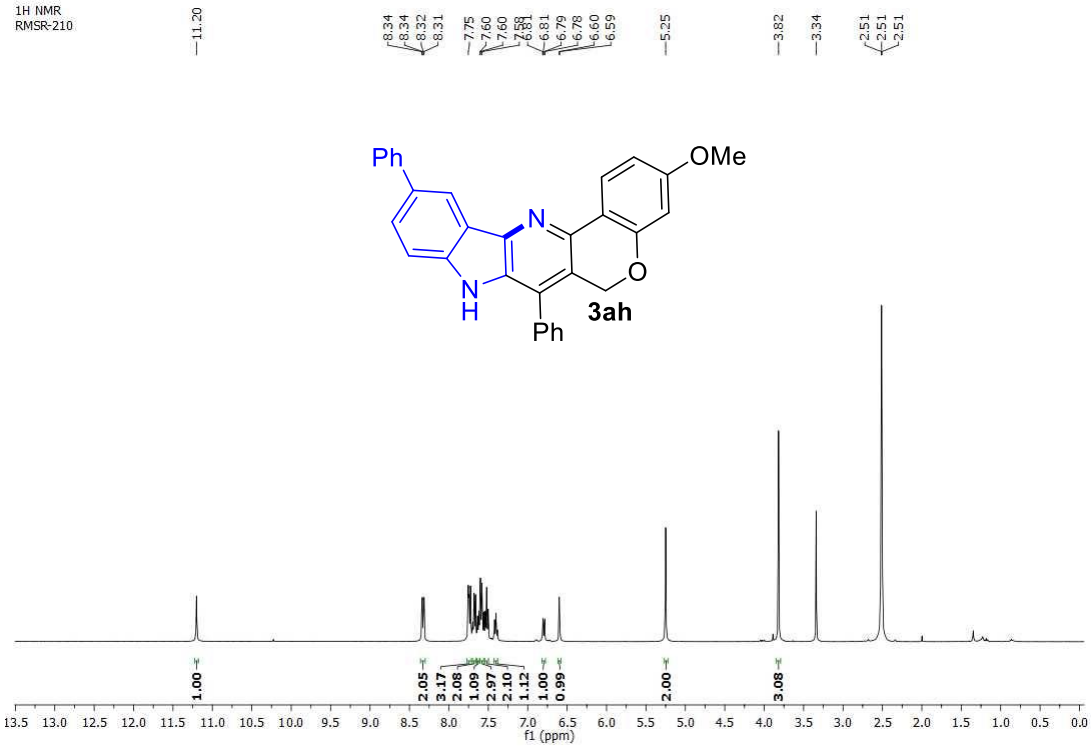

13C NMR
RMSR-105
OMe
N
HN
O
Ph 3ae
f1 (ppm)

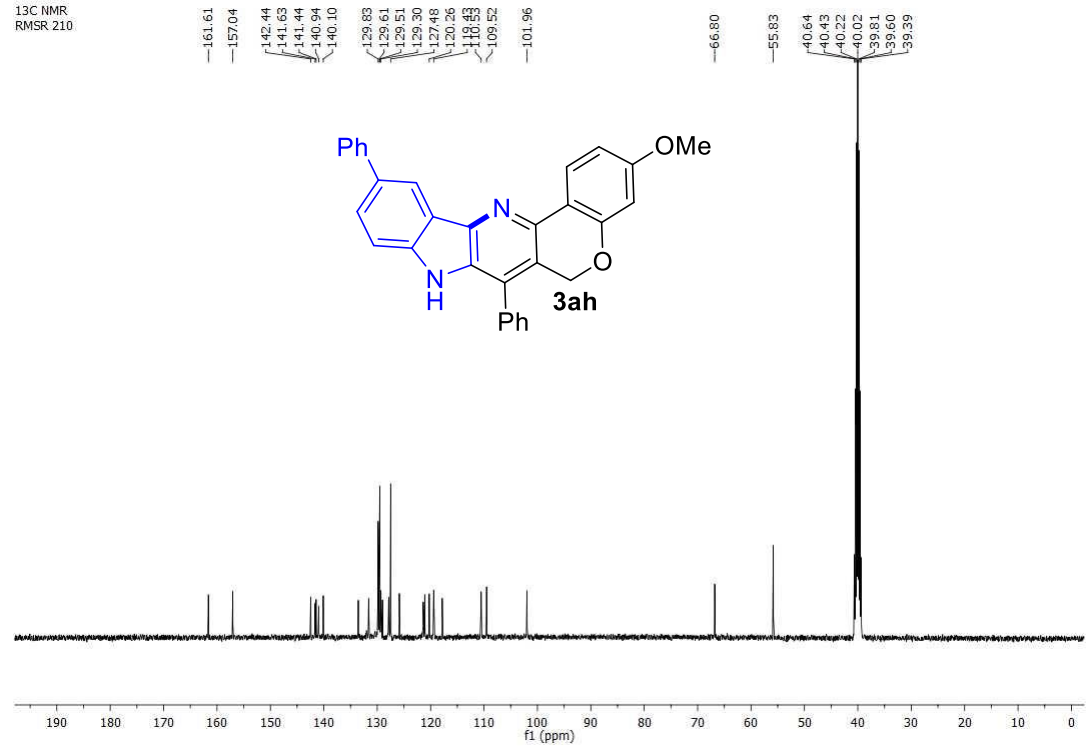

Carboline
RMSR-091A
OEt
N
H
O
Ph
3af
f1 (ppm)

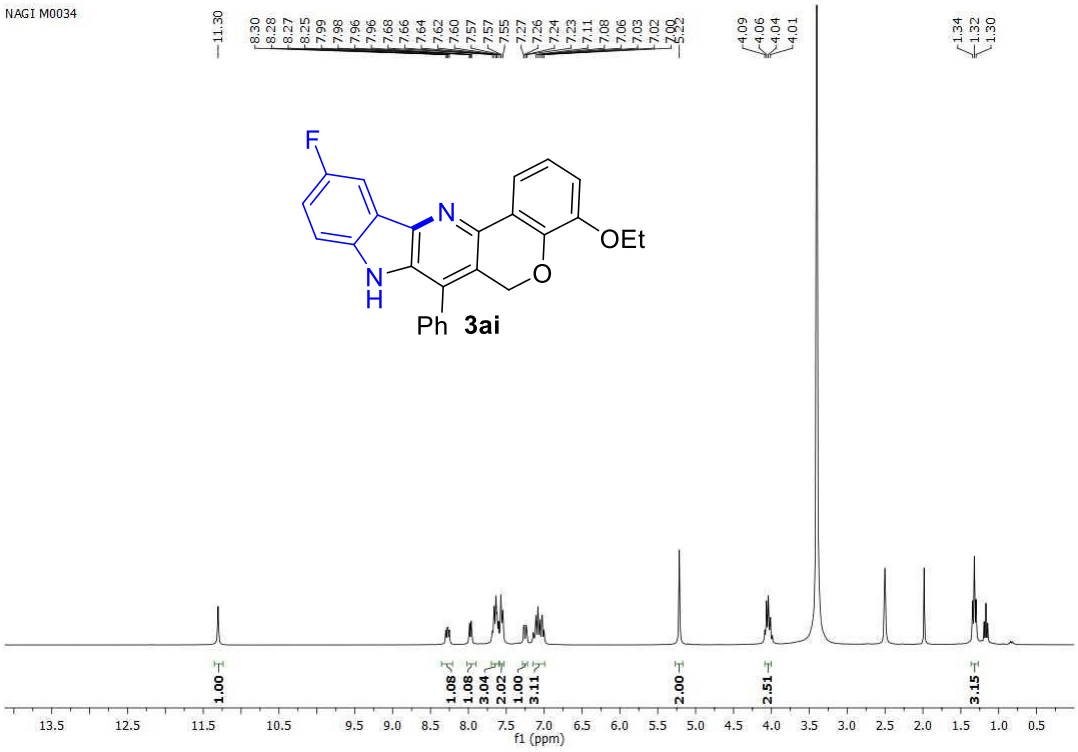

13C
RMSR-091-A
OEt
N
H
O
Ph
3af
f1 (ppm)

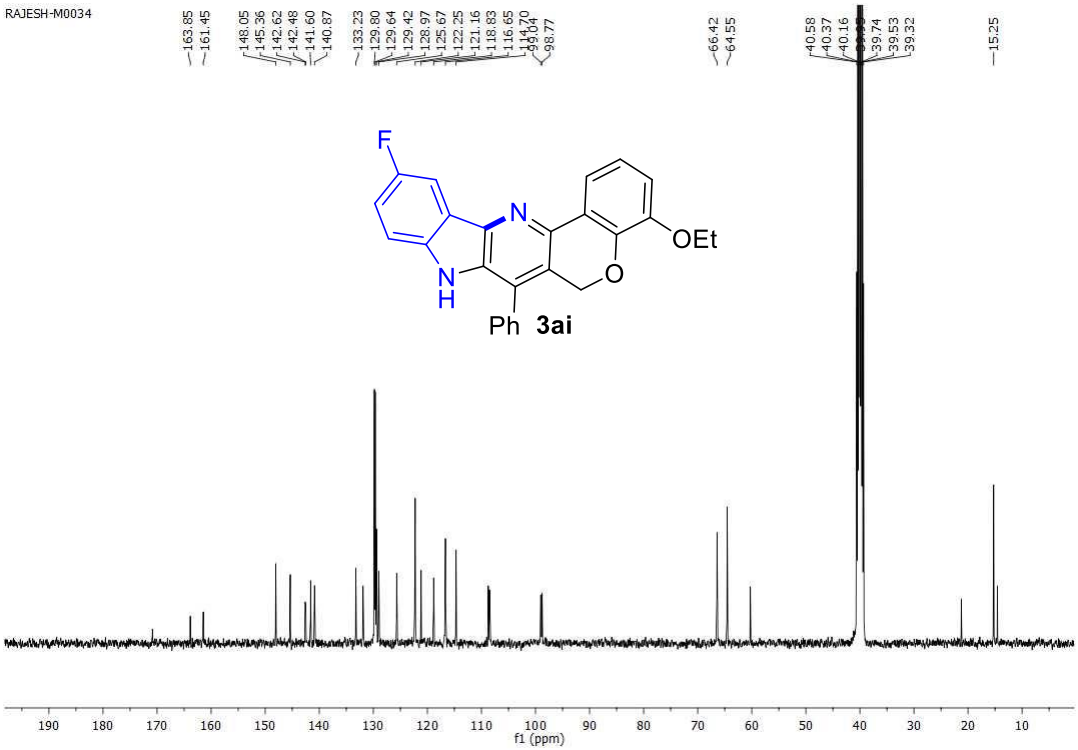

Carboline
RMSR 110
Me
Me
N
N
H
O
3ag
Ph
f1 (ppm)

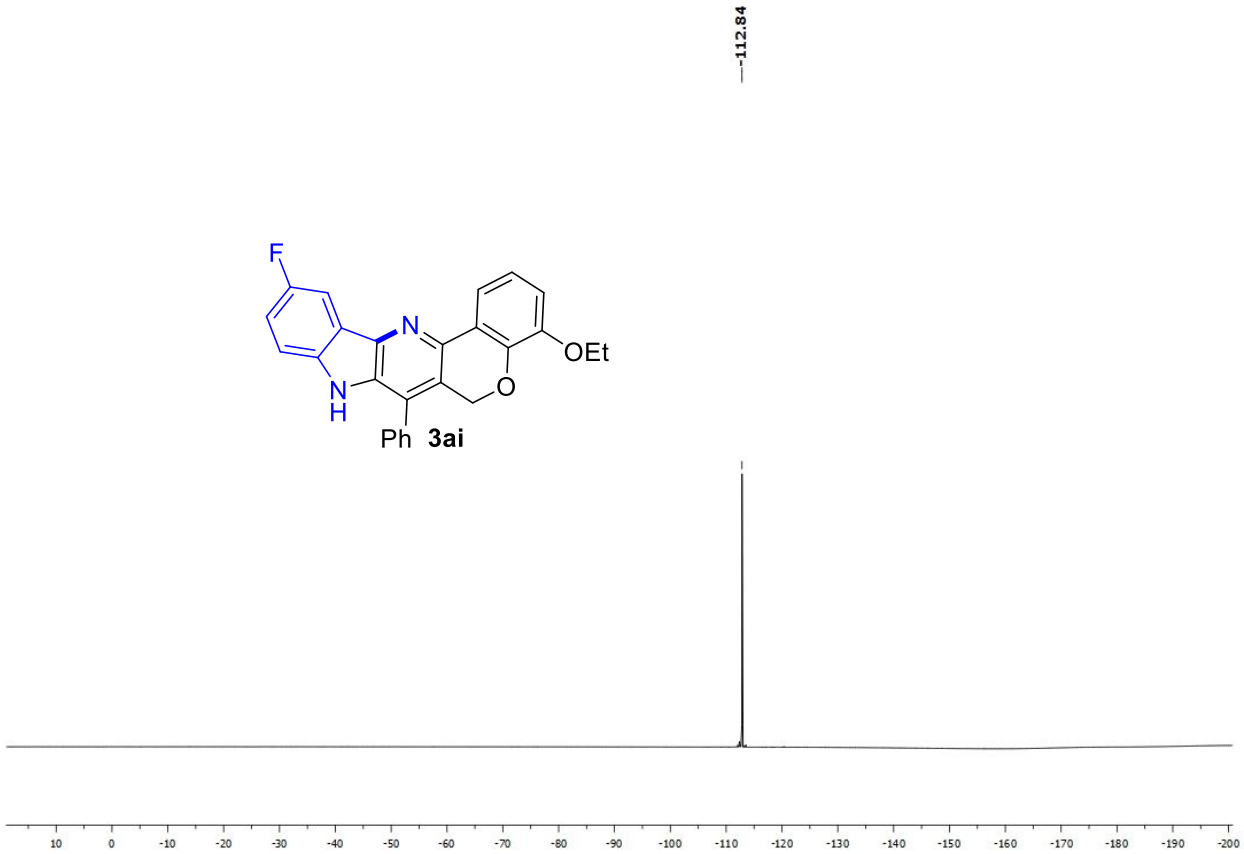

13C
RMSR-110
Me
Me
N
N
H
O
3ag
Ph
f1 (ppm)

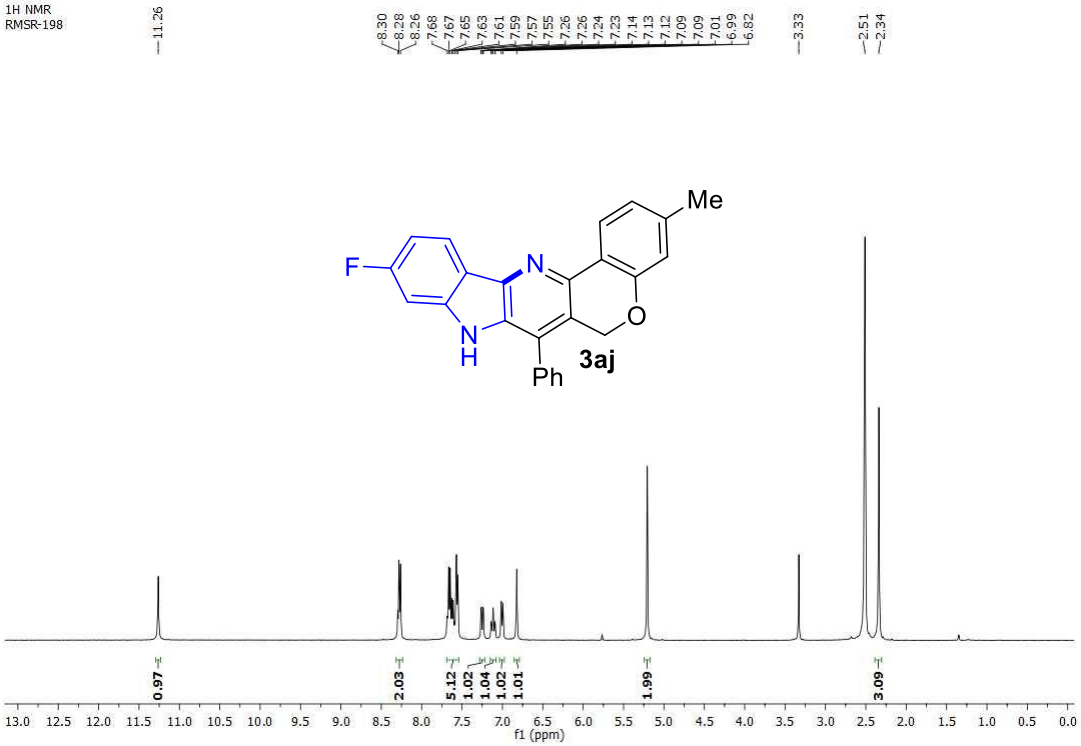

1H NMR
RMSR-210
11.20
8.34
8.34
8.32
8.31
7.75
7.60
7.60
7.59
7.58
6.81
6.79
6.78
6.60
6.59
5.25
3.82
3.34
2.51
2.51
2.51
Ph
OMe
N
O
N
H
Ph
3ah
1.00
2.05
3.17
2.08
1.09
2.97
2.10
1.12
1.00
0.99
2.00
3.08
f1 (ppm)

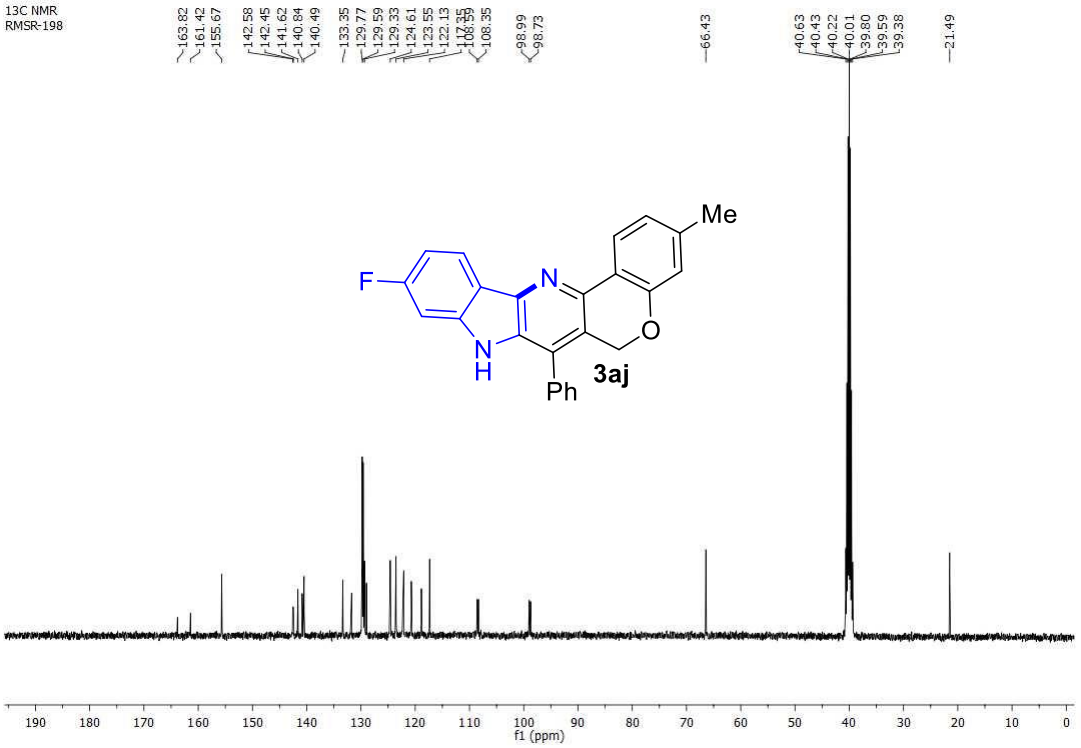

13C NMR
RMSR 210
161.61
157.04
142.44
141.63
141.44
140.94
140.10
129.83
129.61
129.51
129.30
127.48
120.26
119.43
110.53
109.52
101.96
66.80
55.83
40.64
40.43
40.22
40.02
39.81
39.60
39.39
Ph
OMe
N
O
N
H
Ph
3ah
f1 (ppm)

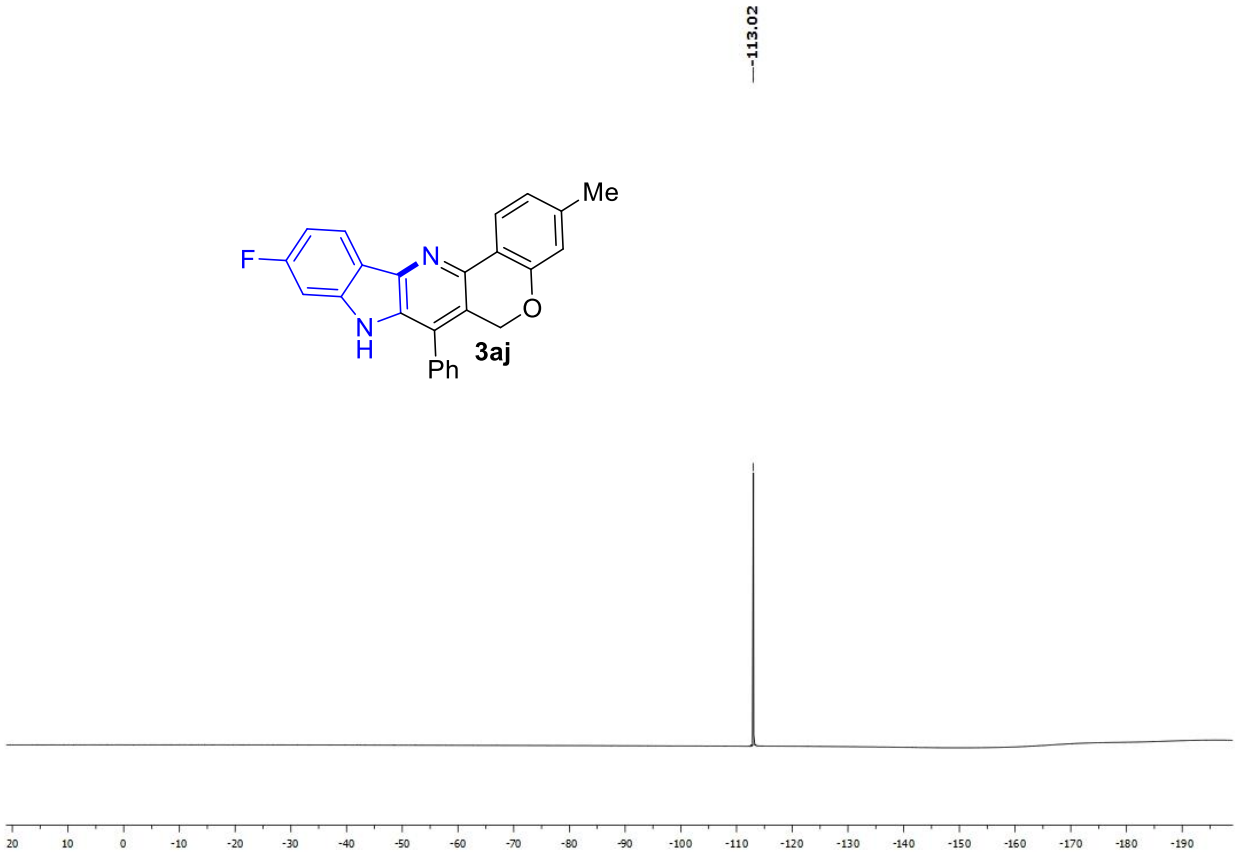

NAGI M0034
F
N
OEt
N
H
O
Ph 3ai
f1 (ppm)

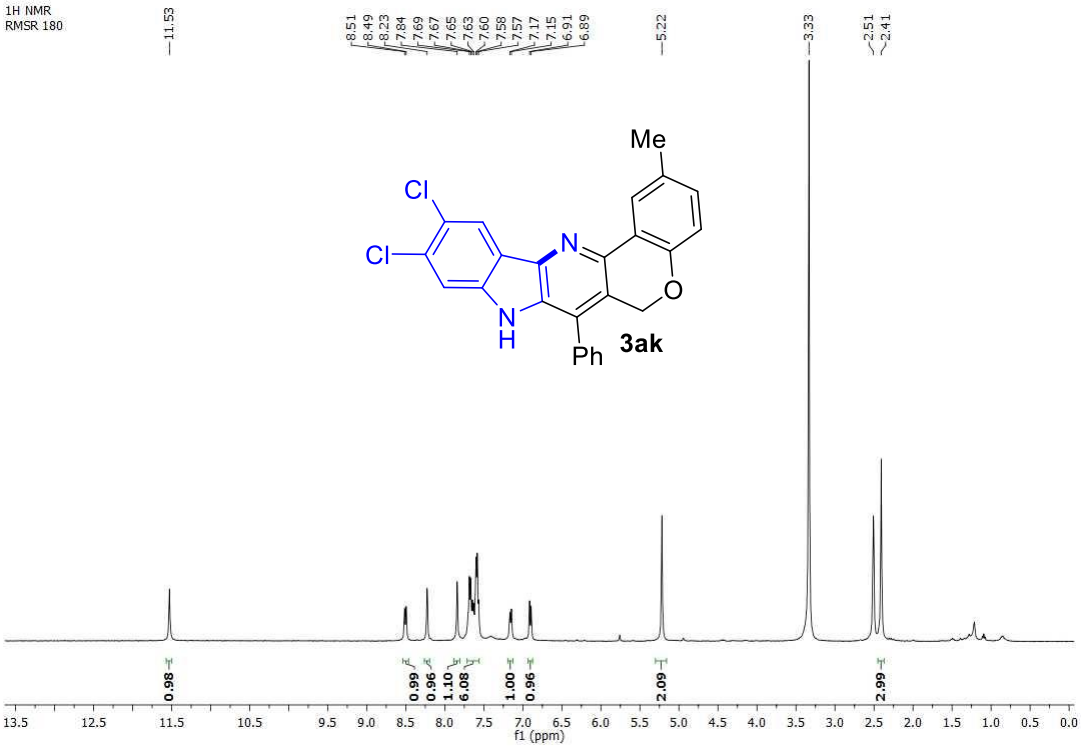

RAJESH-M0034
F
N
OEt
N
H
O
Ph 3ai
f1 (ppm)

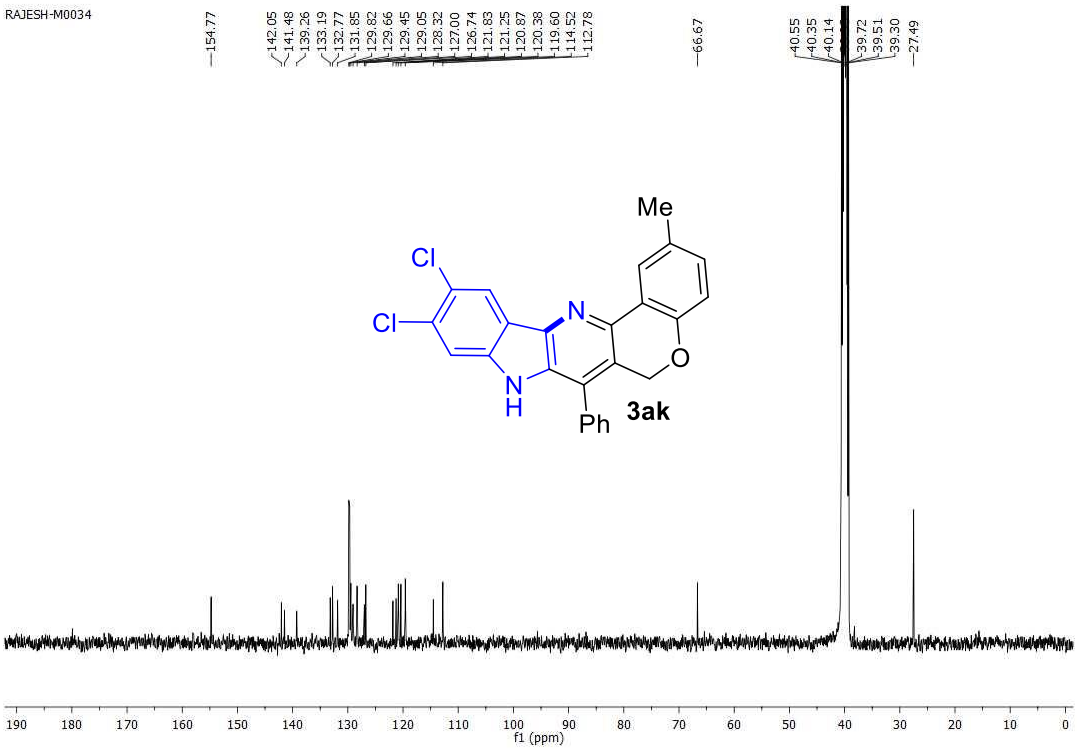

-112.84
F
N
OEt
N
H
O
Ph
3ai
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

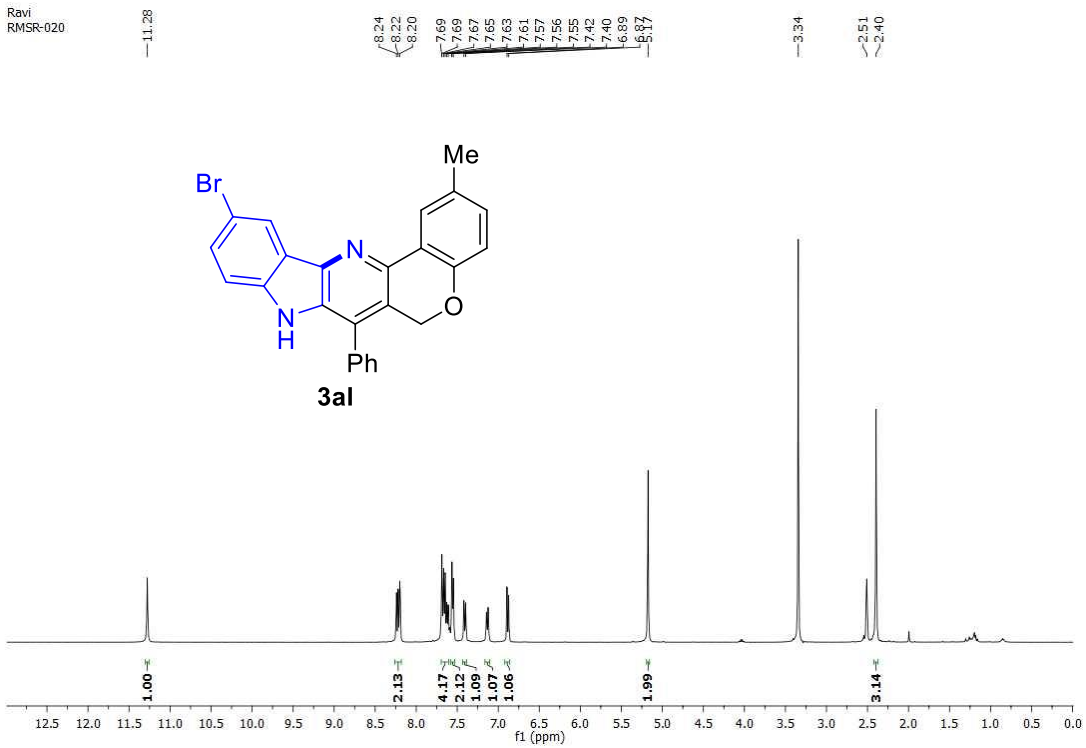

1H NMR
RMSR-198
11.26
8.30
8.28
8.26
7.68
7.67
7.65
7.63
7.61
7.59
7.57
7.55
7.26
7.26
7.24
7.23
7.14
7.13
7.12
7.09
7.09
7.01
6.99
6.82
3.33
2.51
2.34
Me
F
N
O
N
H
Ph
3aj
0.97
2.03
5.12
1.02
1.04
1.02
1.01
1.99
3.09
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

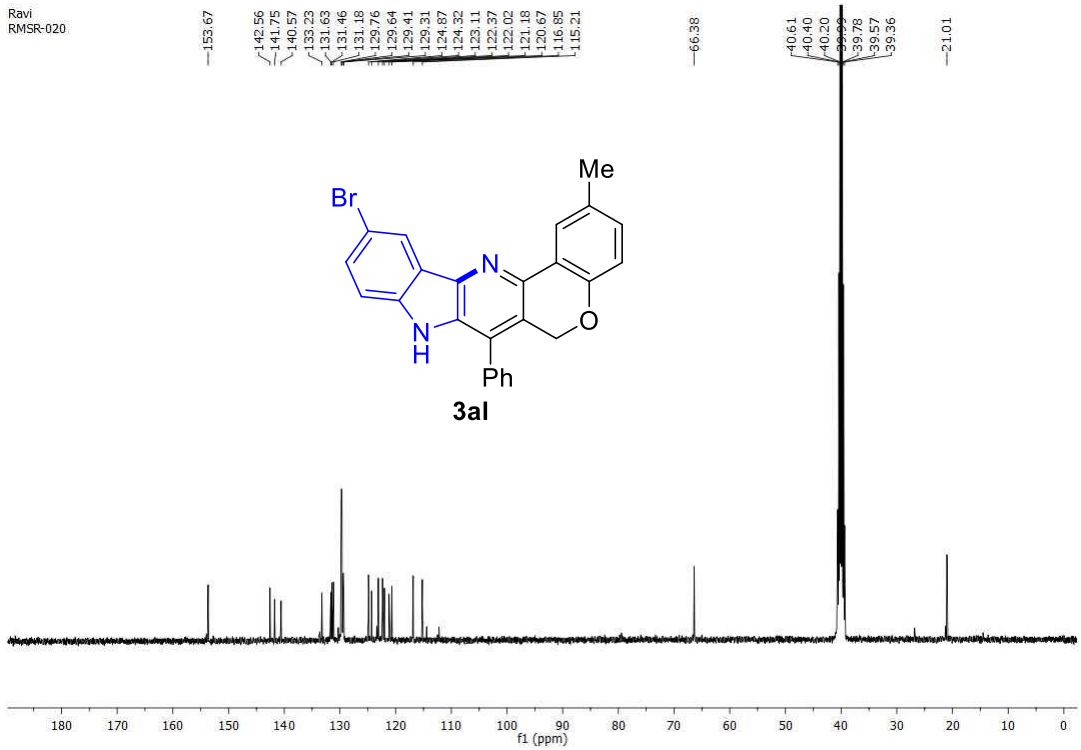

13C NMR
RMSR-198
163.82
161.42
155.67
142.58
142.45
141.62
140.84
140.49
133.35
129.77
129.59
129.33
124.61
123.55
122.13
117.35
108.59
108.35
98.99
98.73
66.43
40.63
40.43
40.22
40.01
39.80
39.59
39.38
21.49
Me
F
N
O
N
H
Ph
3aj
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

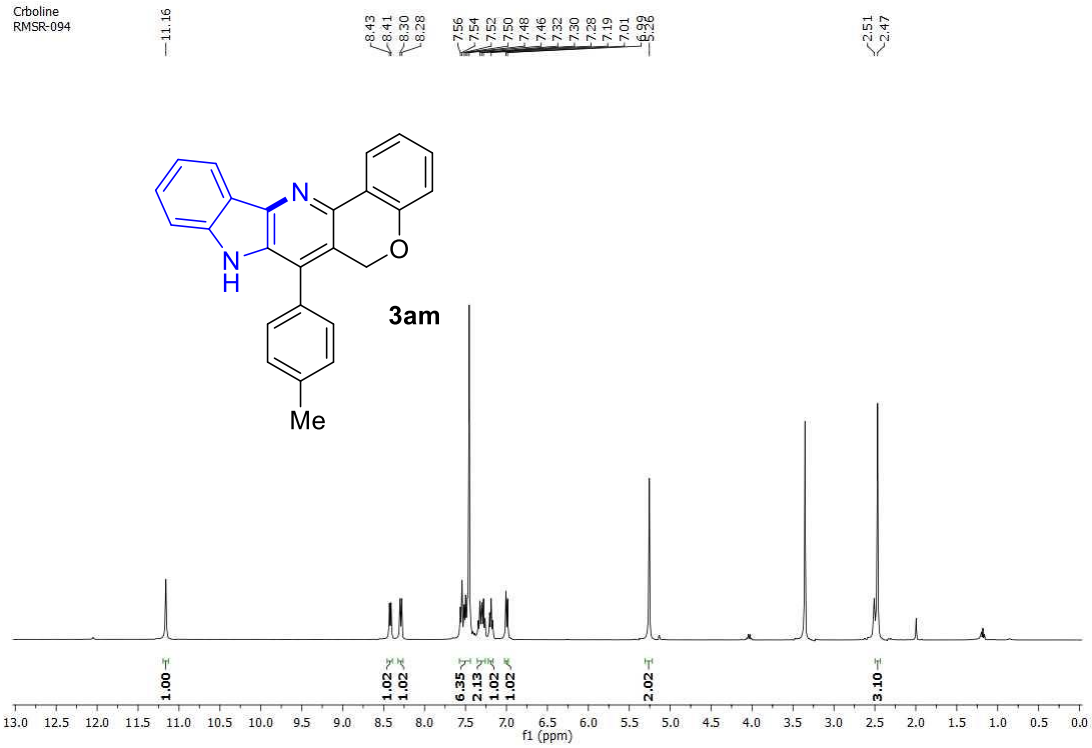

-113.02
Me
F
N
O
N
H
Ph
3aj
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190

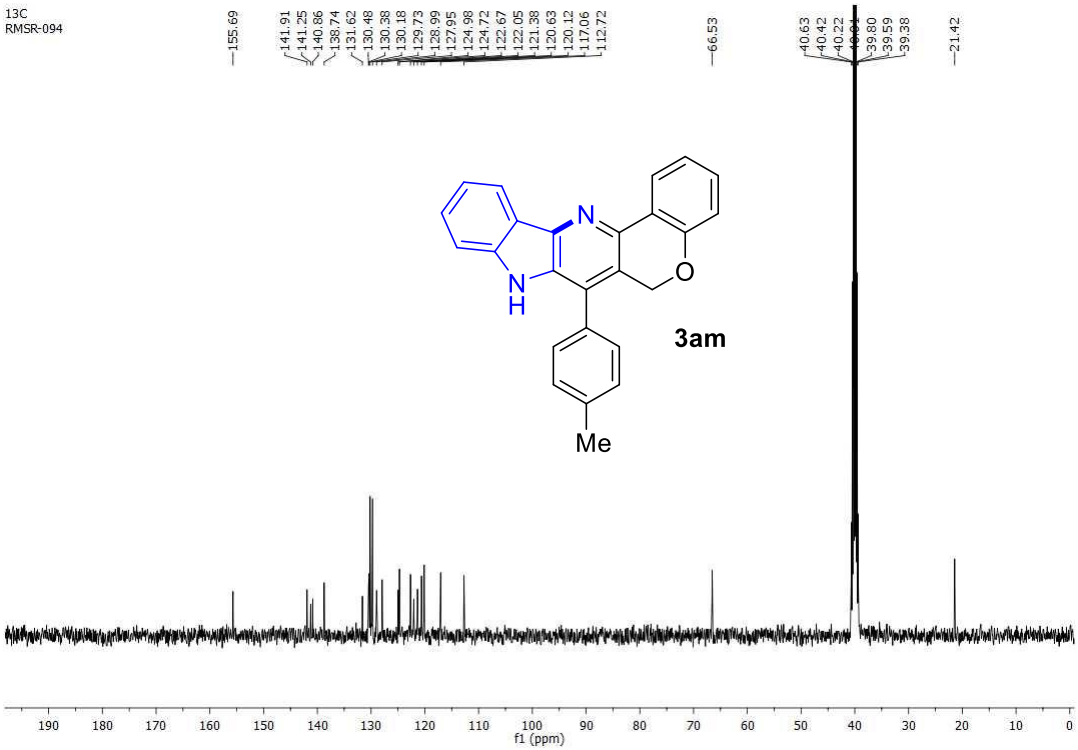

1H NMR
RMSR 180
11.53
8.51
8.49
8.23
7.84
7.69
7.67
7.65
7.63
7.60
7.58
7.57
7.17
7.15
6.91
6.89
5.22
3.33
2.51
2.41
Me
Cl
Cl
N
O
N
H
Ph
3ak
0.98
0.99
0.96
1.10
6.08
1.00
0.96
2.09
2.99
f1 (ppm)

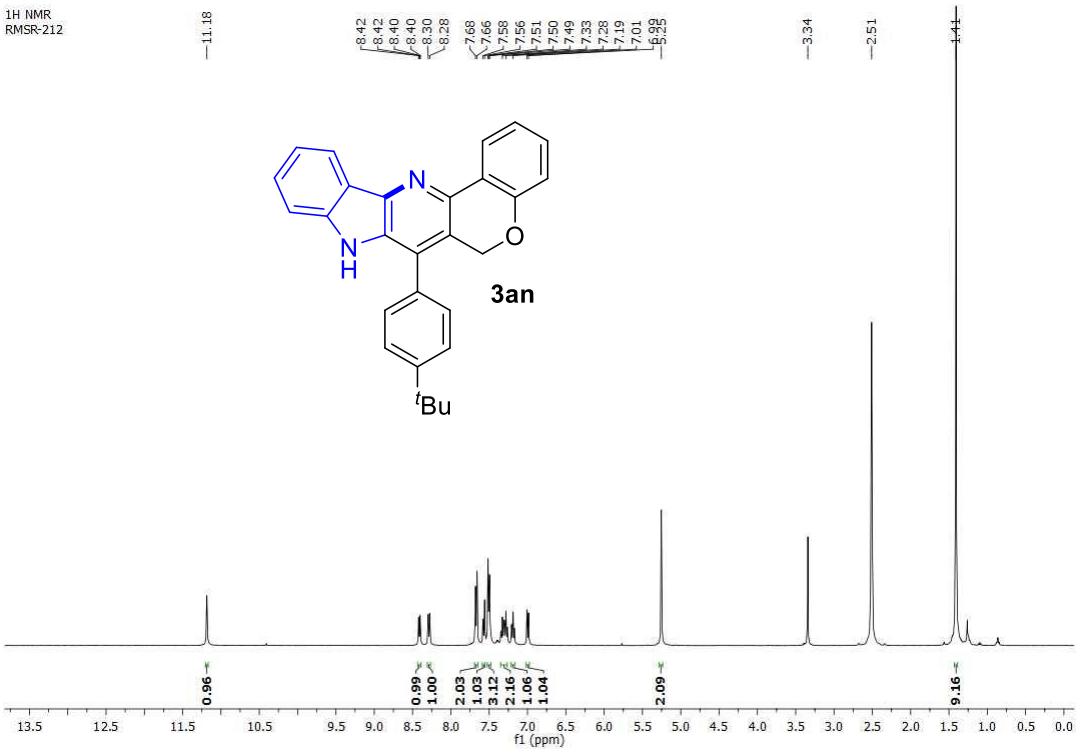

RAJESH-M0034
154.77
142.05
141.48
139.26
133.19
132.77
131.85
129.82
129.66
129.45
129.05
128.32
127.00
126.74
121.83
121.25
120.87
120.38
119.60
114.52
112.78
66.67
40.55
40.35
40.14
39.72
39.51
39.30
27.49
Me
Cl
Cl
N
O
N
H
Ph
3ak
f1 (ppm)

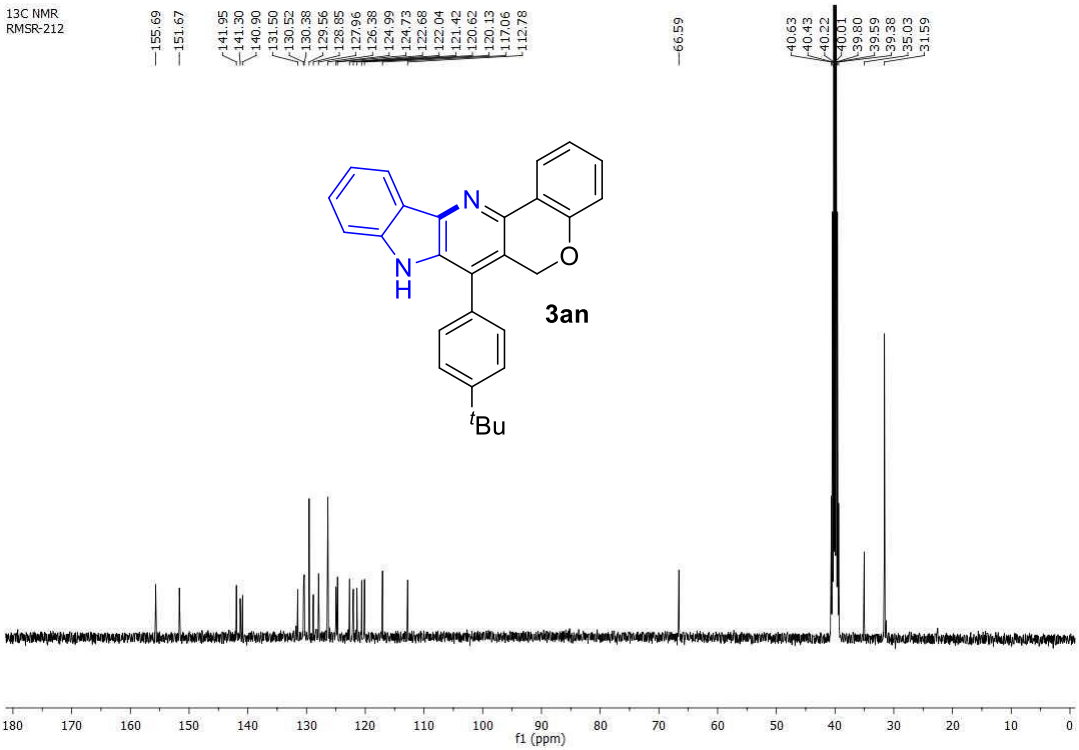

Ravi
RMSR-020
Me
Br
N
N
H
O
Ph
3al
f1 (ppm)

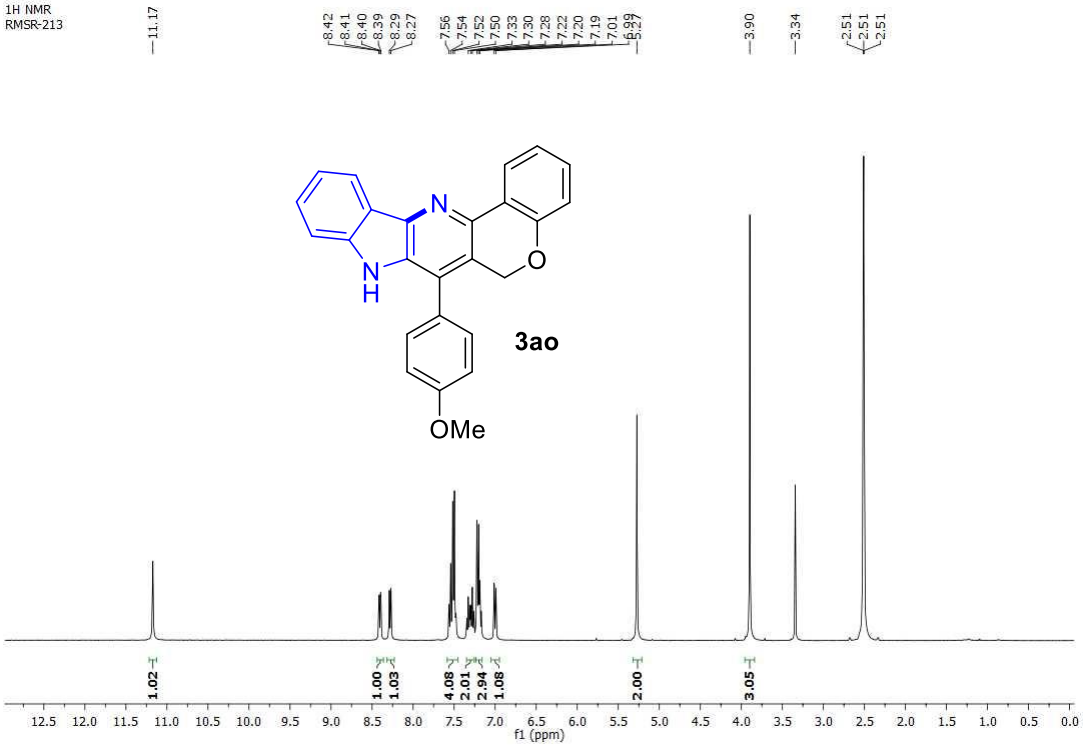

Ravi
RMSR-020
Me
Br
N
N
H
O
Ph
3al
f1 (ppm)

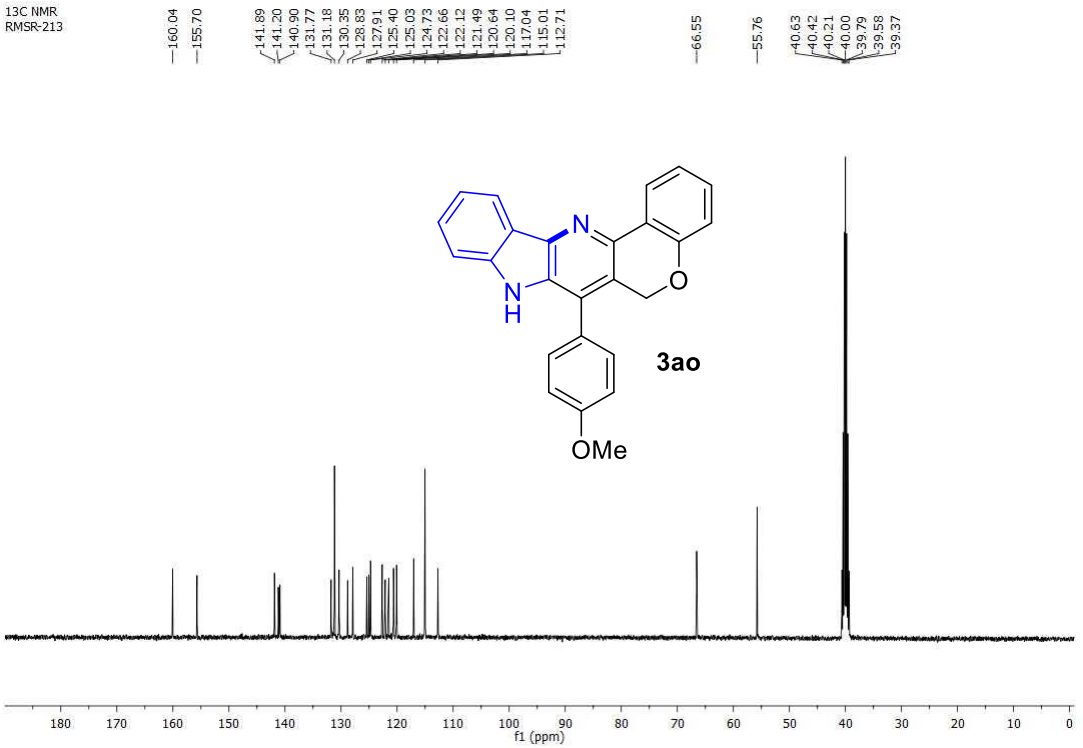

Crboline
RMSR-094
11.16
8.43
8.41
8.30
8.28
7.56
7.54
7.52
7.50
7.48
7.46
7.32
7.30
7.28
7.19
7.01
6.99
6.98
5.29
2.51
2.47
N
N
H
O
3am
Me
1.00
1.02
1.02
6.35
2.13
1.02
1.02
2.02
3.10
f1 (ppm)

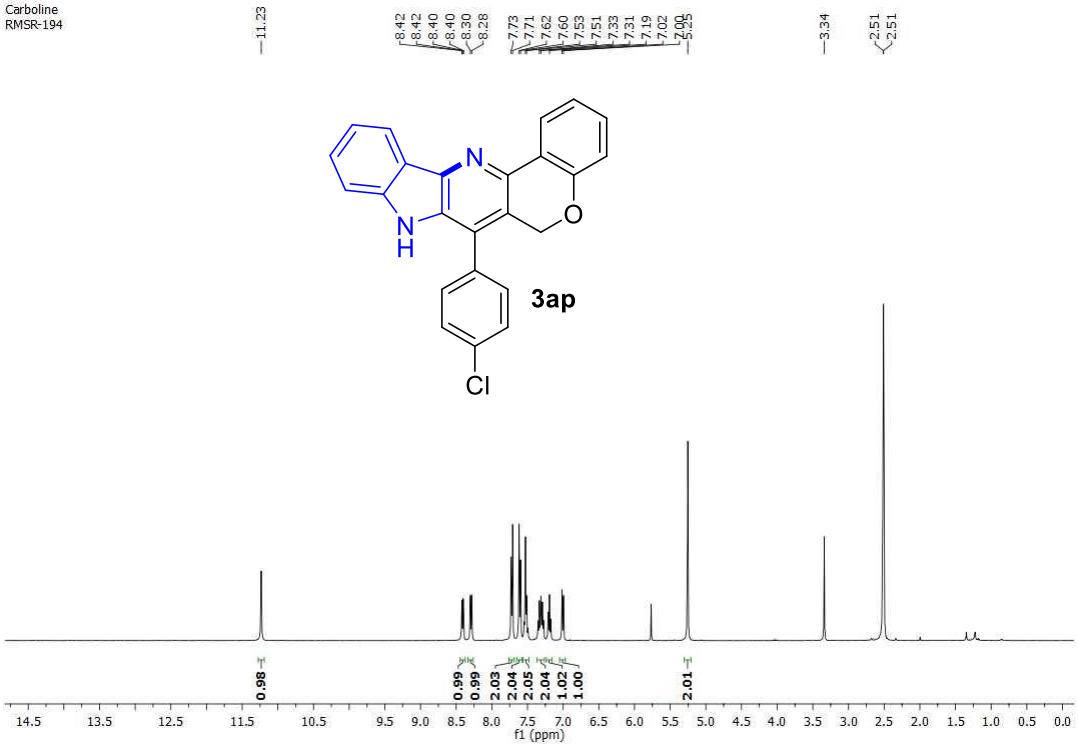

13C
RMSR-094
155.69
141.91
141.25
140.86
138.74
131.62
130.48
130.38
130.18
129.73
128.99
127.95
124.98
124.72
122.67
122.05
121.38
120.63
120.12
117.06
112.72
66.53
40.63
40.42
40.22
39.80
39.59
39.38
21.42
N
N
H
O
3am
Me
f1 (ppm)

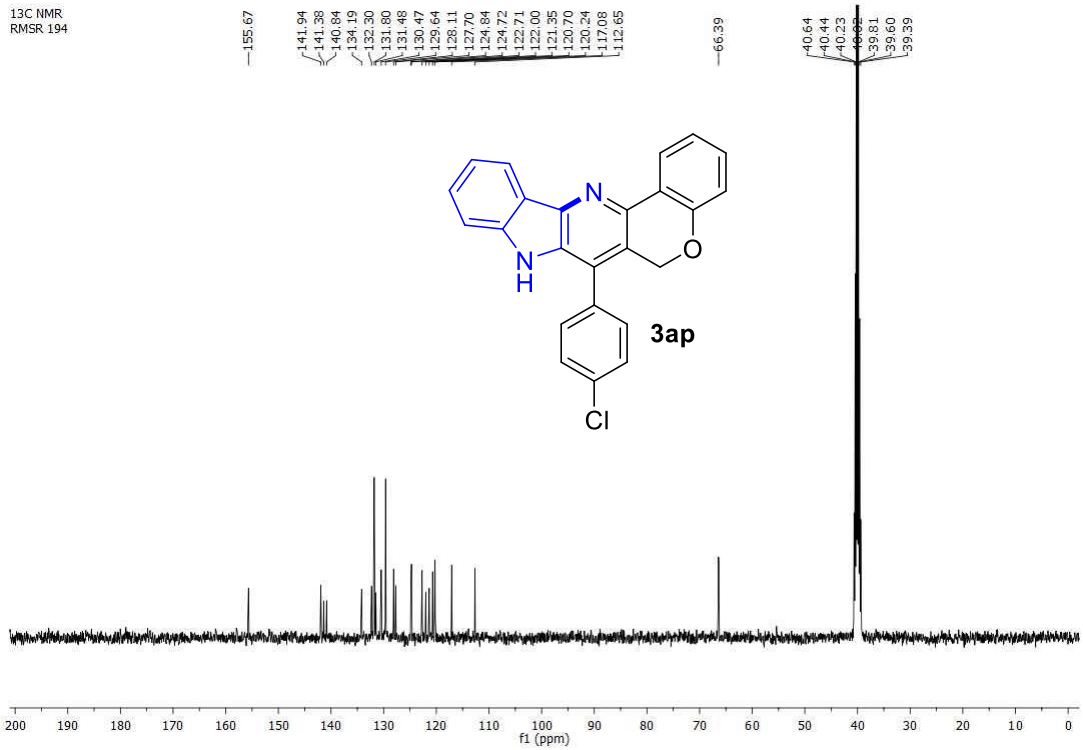

1H NMR
RMSR-212
11.18
8.42
8.42
8.40
8.40
8.30
8.28
7.68
7.66
7.58
7.56
7.51
7.50
7.49
7.33
7.28
7.19
7.01
6.99
5.25
3.34
2.51
1.41
N
N
H
O
3an
tBu
0.96
0.99
1.00
2.03
1.03
3.12
2.16
1.06
1.04
2.09
9.16
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

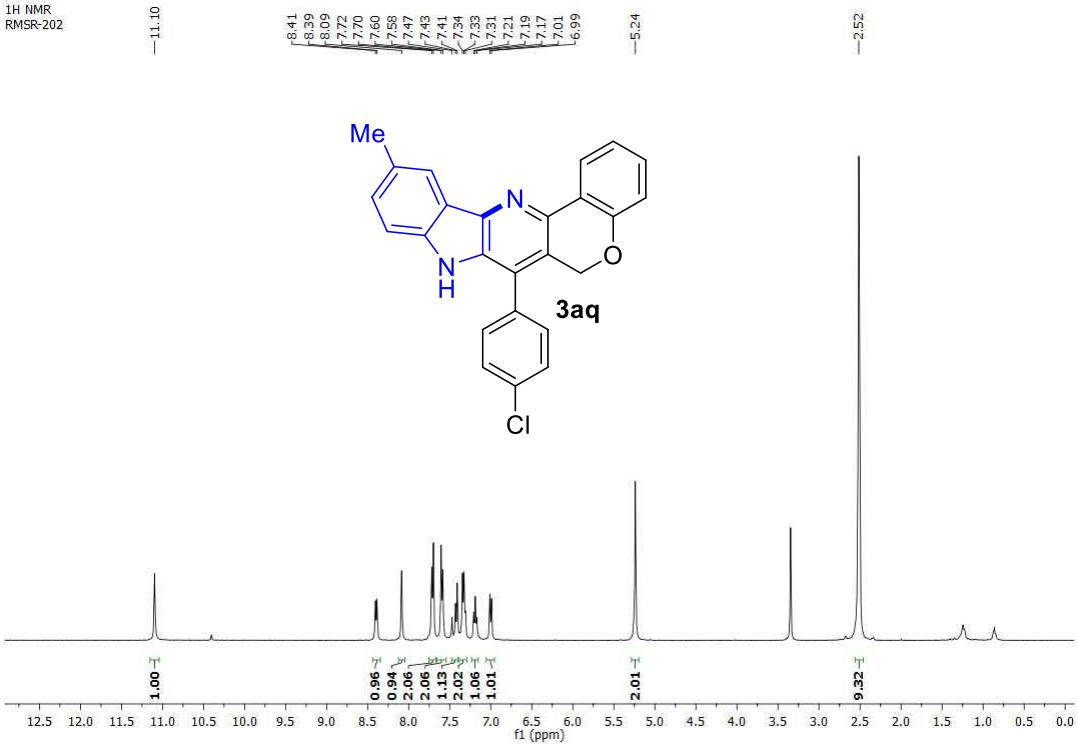

13C NMR
RMSR-212
155.69
151.67
141.95
141.30
140.90
131.50
130.52
130.38
129.56
128.85
127.96
126.38
124.99
124.73
122.68
122.04
121.42
120.62
120.13
117.06
112.78
66.59
40.63
40.43
40.22
40.01
39.80
39.59
39.38
35.03
31.59
N
N
H
O
3an
tBu
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

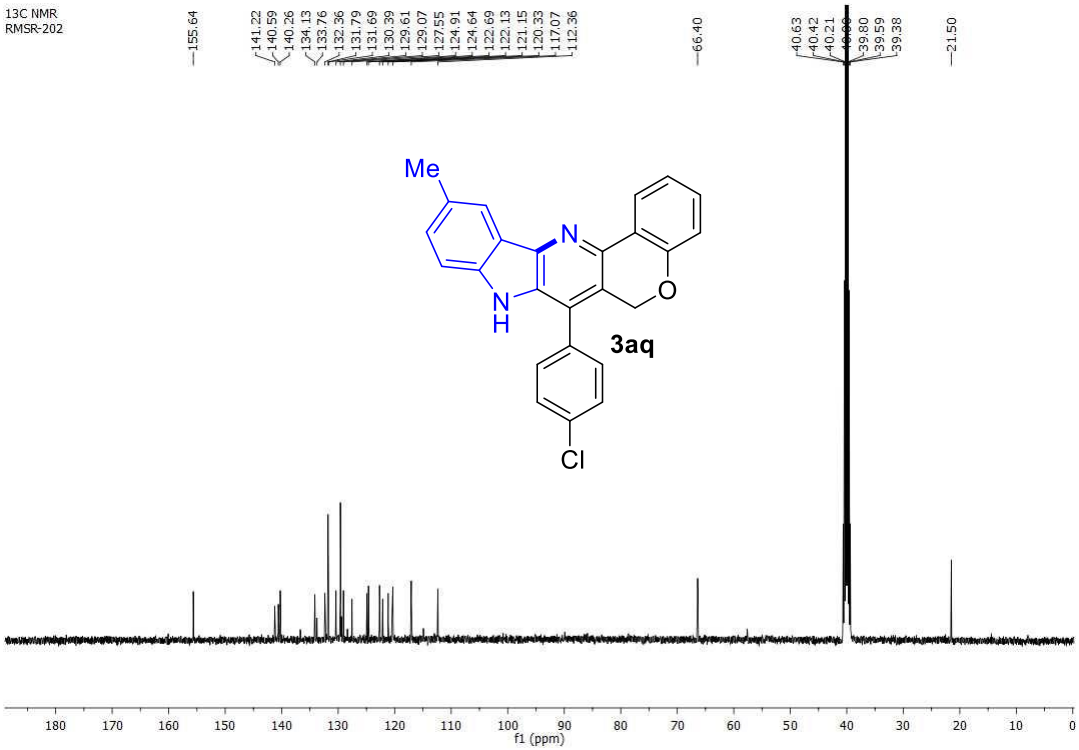

1H NMR
RMSR-213
11.17
8.42
8.41
8.40
8.39
8.29
8.27
7.56
7.54
7.52
7.50
7.33
7.30
7.28
7.22
7.20
7.19
7.01
6.99
5.27
3.90
3.34
2.51
2.51
2.51
N
N
H
O
OMe
3ao
1.02
1.00
1.03
4.08
2.01
2.94
1.08
2.00
3.05
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

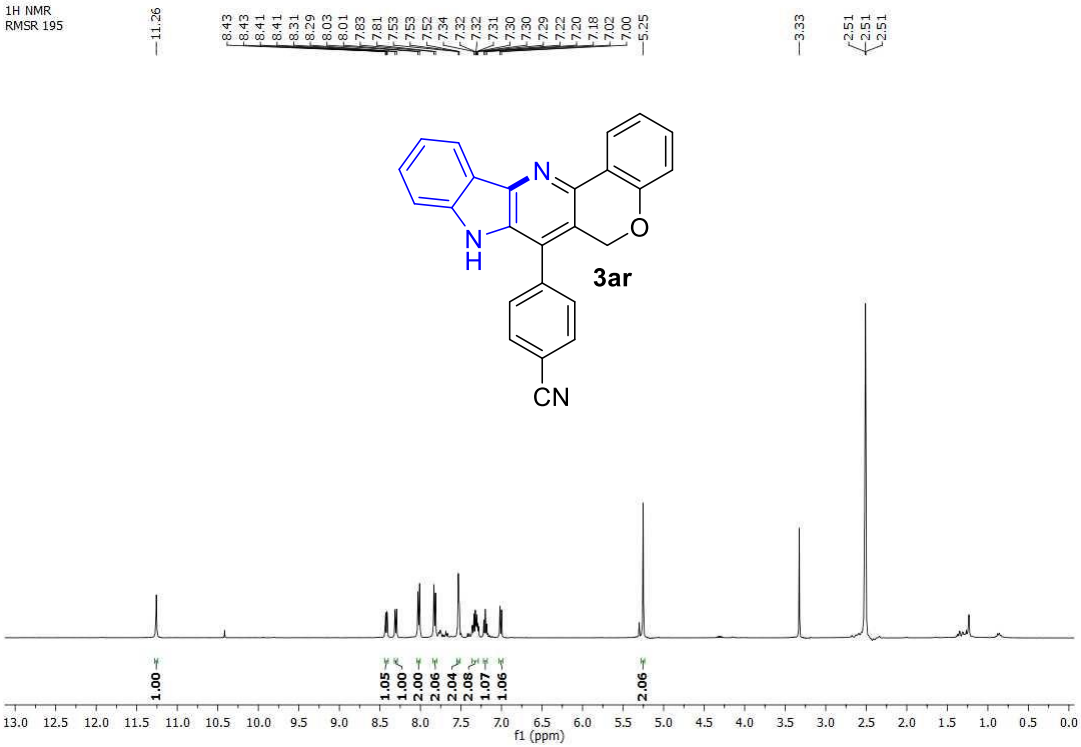

13C NMR
RMSR-213
160.04
155.70
141.89
141.20
140.90
131.77
131.18
130.35
128.83
127.91
125.40
125.03
124.73
122.66
122.12
121.49
120.64
120.10
117.04
115.01
112.71
66.55
55.76
40.63
40.42
40.21
40.00
39.79
39.58
39.37
N
N
H
O
OMe
3ao
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

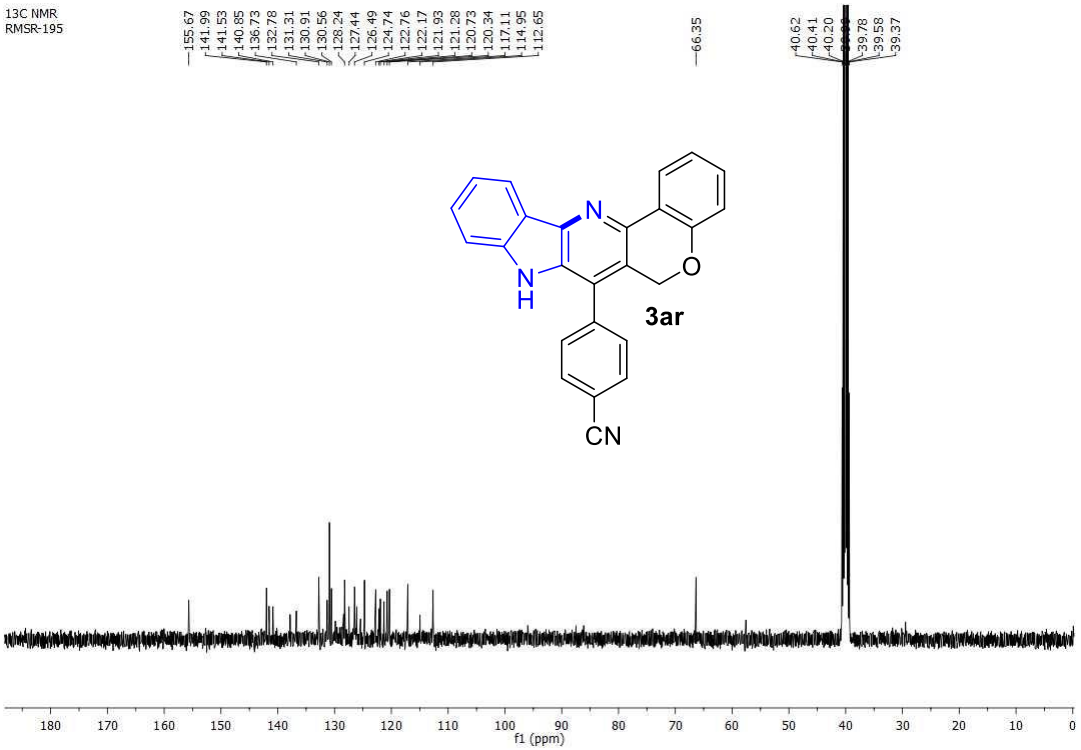

Carboline
RMSR-194
11.23
8.42
8.42
8.40
8.40
8.30
8.28
7.73
7.71
7.62
7.60
7.53
7.51
7.33
7.31
7.19
7.02
7.00
5.25
3.34
2.51
2.51
N
N
H
O
Cl
3ap
0.98
0.99
0.99
2.03
2.04
2.05
2.04
1.02
1.00
2.01
14.5
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

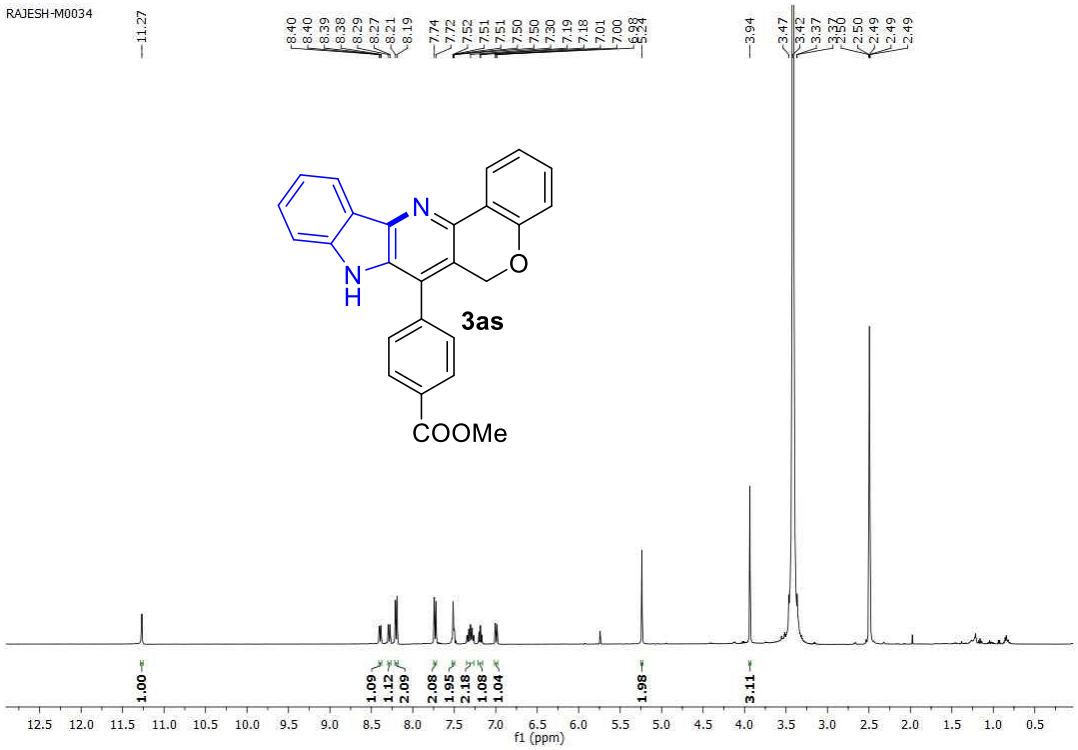

13C NMR
RMSR 194
155.67
141.94
141.38
140.84
134.19
132.30
131.80
131.48
130.47
129.64
128.11
127.70
124.84
124.72
122.71
122.00
121.35
120.70
120.24
117.08
112.65
66.39
40.64
40.44
40.23
39.81
39.60
39.39
N
N
H
O
Cl
3ap
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

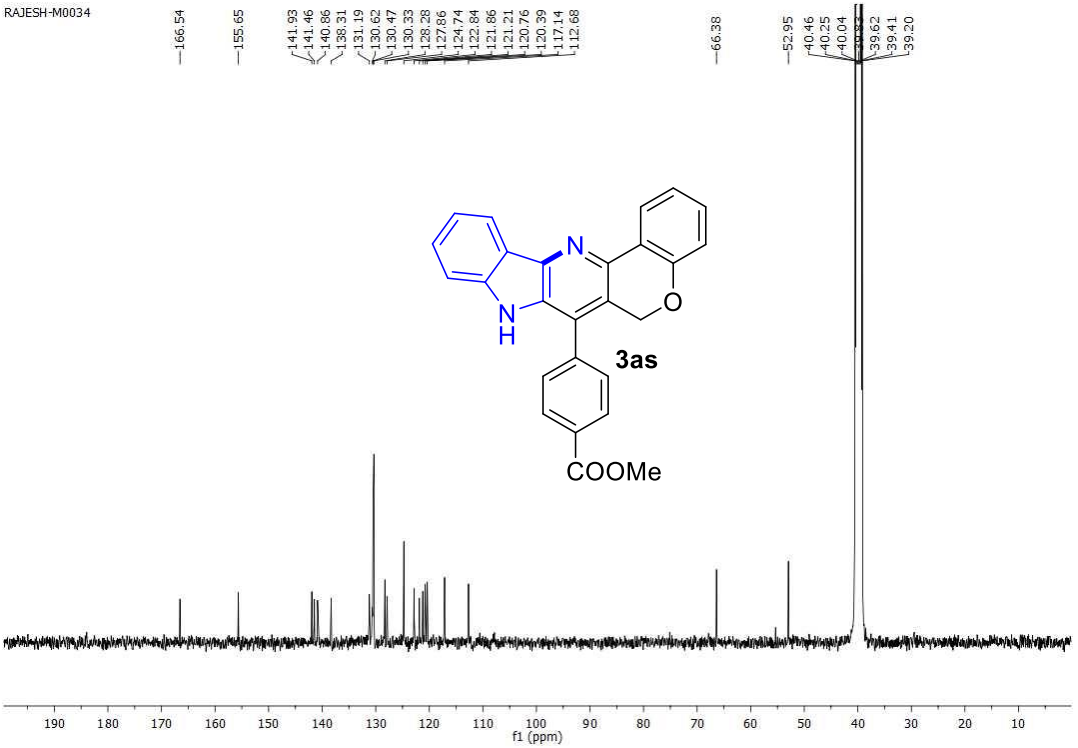

1H NMR
RMSR-202
11.10
8.41
8.39
8.09
7.72
7.70
7.60
7.58
7.47
7.43
7.41
7.34
7.33
7.31
7.21
7.19
7.17
7.01
6.99
5.24
2.52
Me
N
N
H
O
3aq
Cl
1.00
0.96
0.94
2.06
2.06
1.13
2.02
1.06
1.01
2.01
9.32
f1 (ppm)

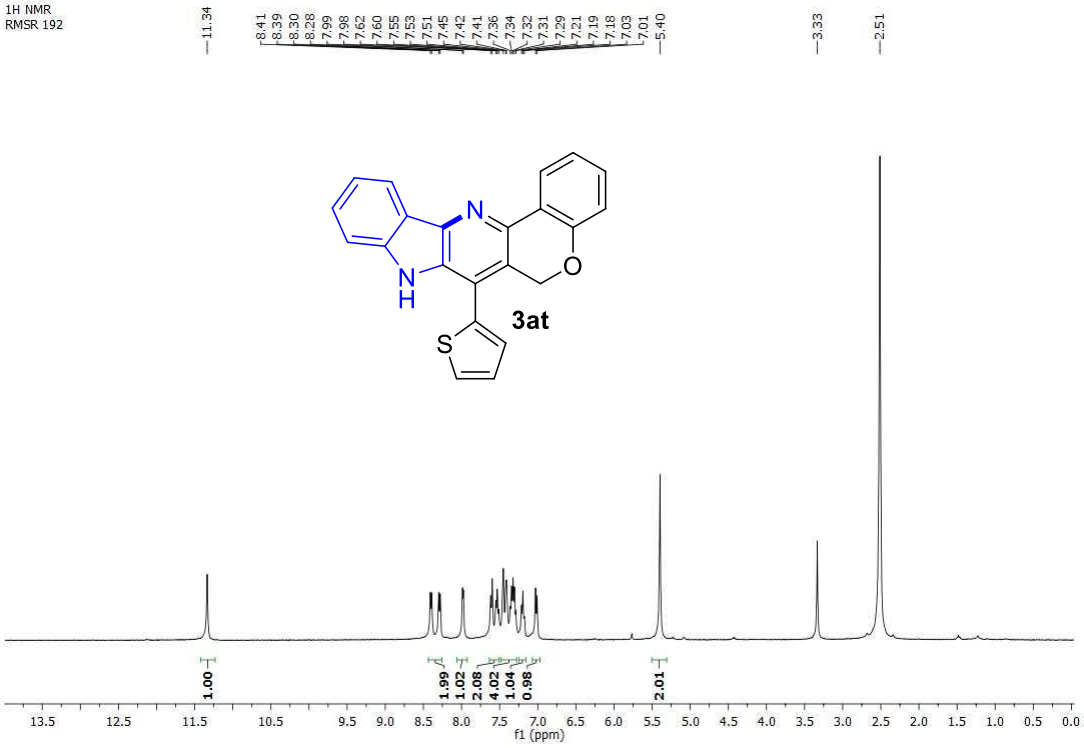

13C NMR
RMSR-202
155.64
141.22
140.59
140.26
134.13
133.76
132.36
131.79
131.69
130.39
129.61
129.07
127.55
124.91
124.64
122.69
122.13
121.15
120.33
117.07
112.36
66.40
40.63
40.42
40.21
39.80
39.59
39.38
21.50
Me
N
N
H
O
3aq
Cl
f1 (ppm)

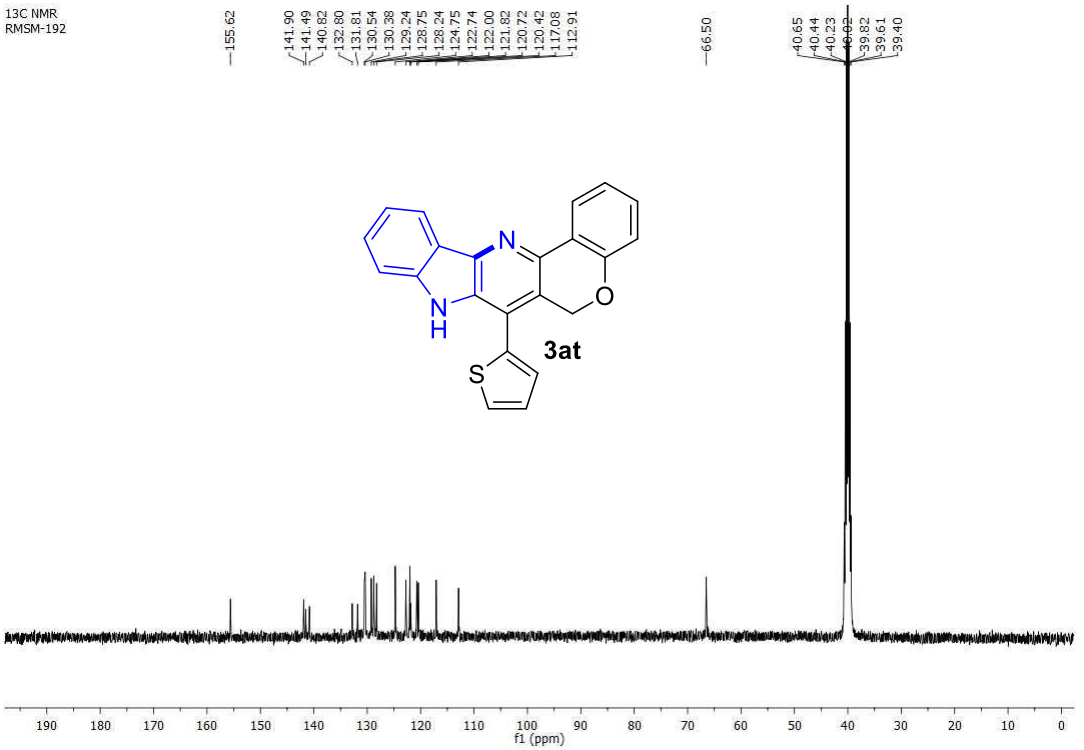

1H NMR
RMSR 195
11.26
8.43
8.43
8.41
8.41
8.31
8.29
8.03
8.01
7.83
7.81
7.53
7.53
7.52
7.34
7.32
7.32
7.31
7.30
7.30
7.29
7.22
7.20
7.18
7.02
7.00
5.25
3.33
2.51
2.51
2.51
N
N
H
O
3ar
CN
1.00
1.05
1.00
2.00
2.06
2.04
2.08
1.07
1.06
2.06
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


13C NMR
RMSR-195
155.67
141.99
141.53
140.85
136.73
132.78
131.31
130.91
130.56
128.24
127.44
126.49
124.74
122.76
122.17
121.93
121.28
120.73
120.34
117.11
114.95
112.65
66.35
40.62
40.41
40.20
39.78
39.58
39.37
N
N
H
O
3ar
CN
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


RAJESH-M0034
11.27
8.40
8.40
8.39
8.38
8.29
8.27
8.21
8.19
7.74
7.72
7.52
7.51
7.51
7.50
7.50
7.30
7.19
7.18
7.01
7.00
5.98
5.24
3.94
3.47
3.42
3.37
3.37
3.50
2.50
2.49
2.49
2.49
N
N
H
O
3as
COOMe
1.00
1.09
1.12
2.09
2.08
1.95
2.18
1.08
1.04
1.98
3.11
12.5 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
f1 (ppm)


RAJESH-M0034
166.54
155.65
141.93
141.46
140.86
138.31
131.19
130.62
130.47
130.33
128.28
127.86
124.74
122.84
121.86
121.21
120.76
120.39
117.14
112.68
66.38
52.95
40.46
40.25
40.04
39.83
39.62
39.41
39.20
N
N
H
O
3as
COOMe
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


1H NMR
RMSR 192
11.34
8.41
8.39
8.30
8.28
7.99
7.98
7.62
7.60
7.55
7.53
7.51
7.45
7.42
7.41
7.36
7.34
7.32
7.31
7.29
7.21
7.19
7.18
7.03
7.01
5.40
3.33
2.51
N
N
H
O
S
3at
1.00
1.99
1.02
2.08
4.02
1.04
0.98
2.01
f1 (ppm)


13C NMR
RMSM-192
155.62
141.90
141.49
140.82
132.80
131.81
130.54
130.38
129.24
128.75
128.24
124.75
122.74
122.00
121.82
120.72
120.42
117.08
112.91
66.50
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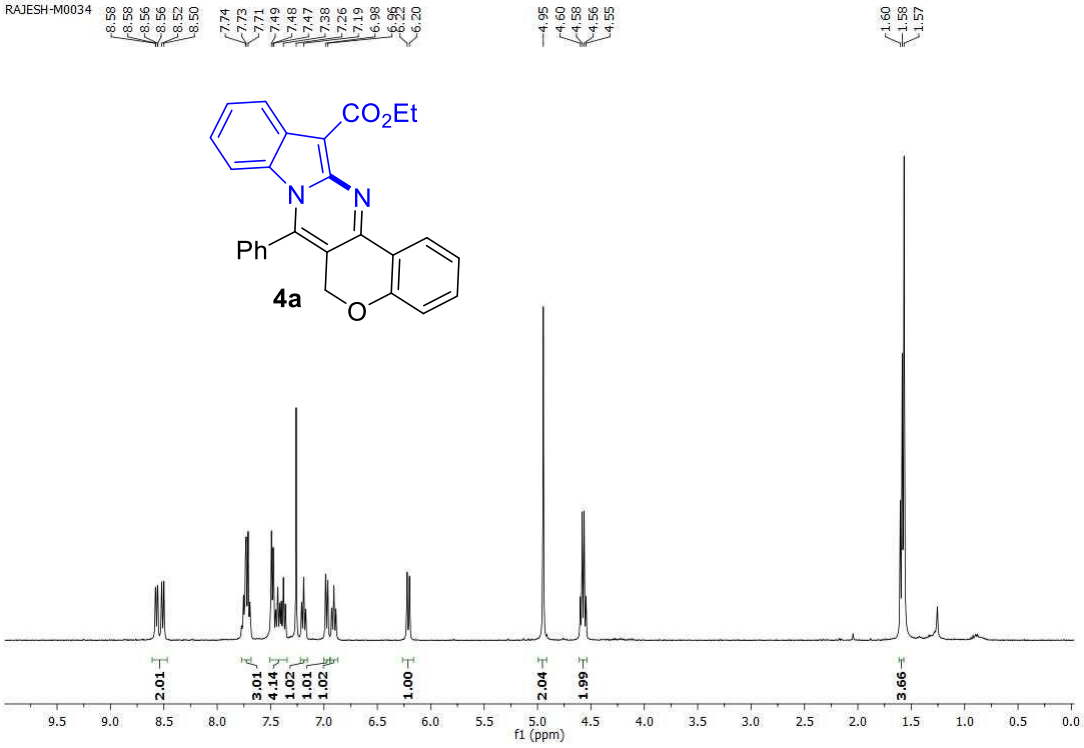
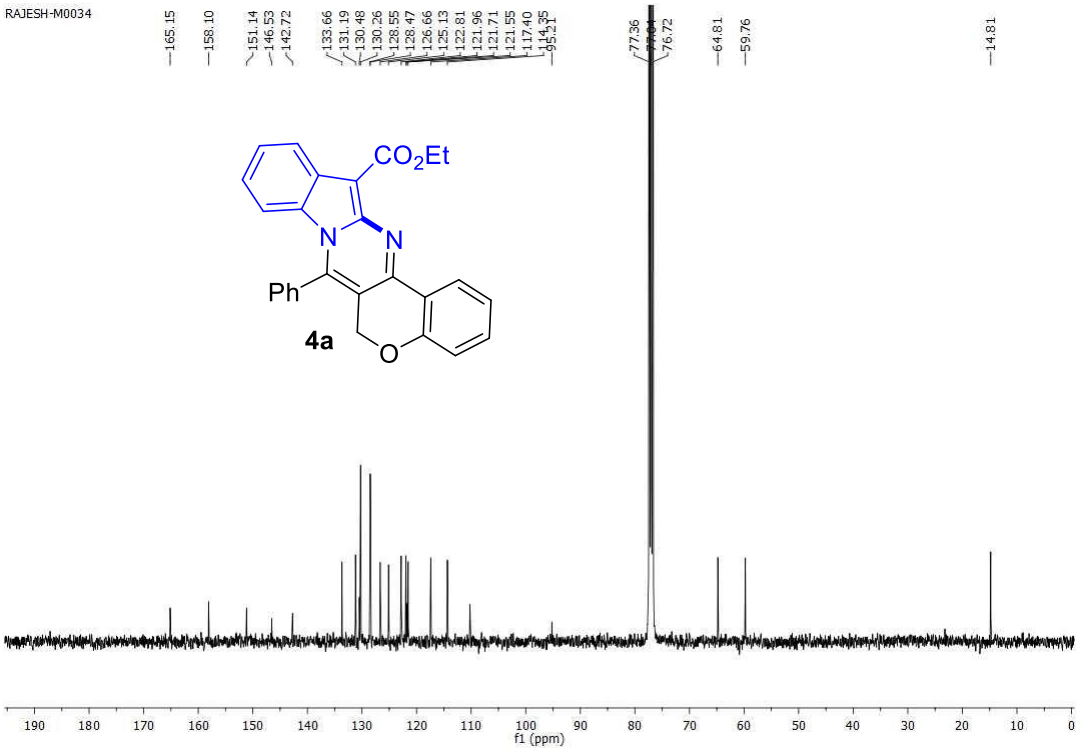
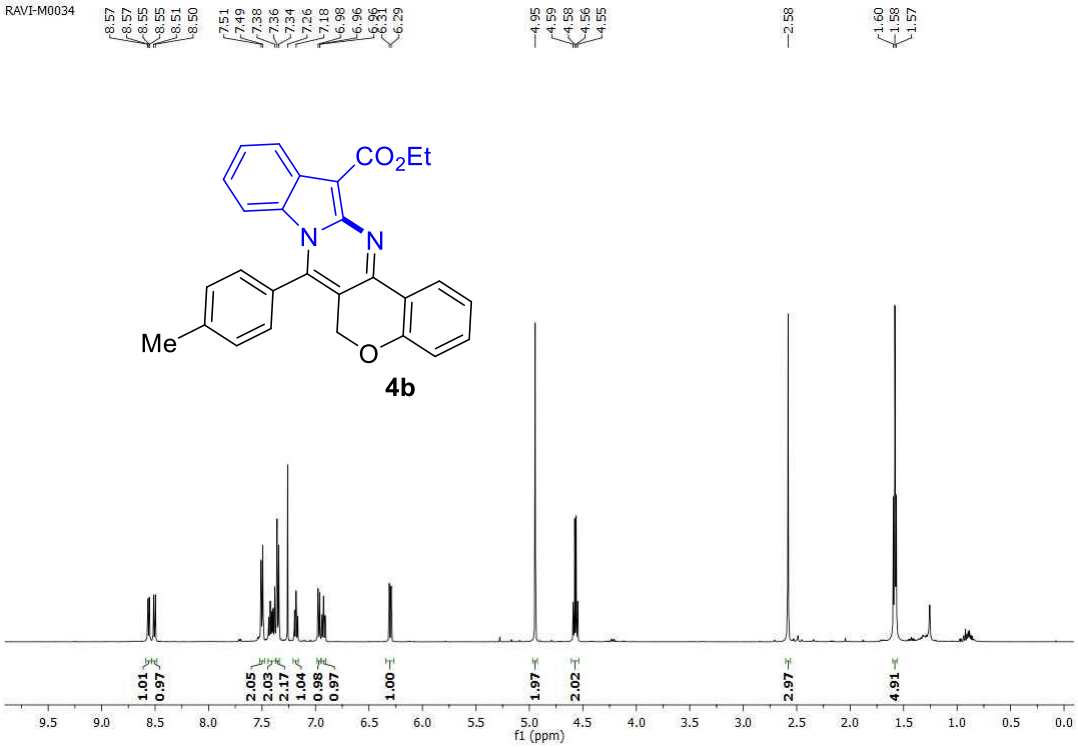
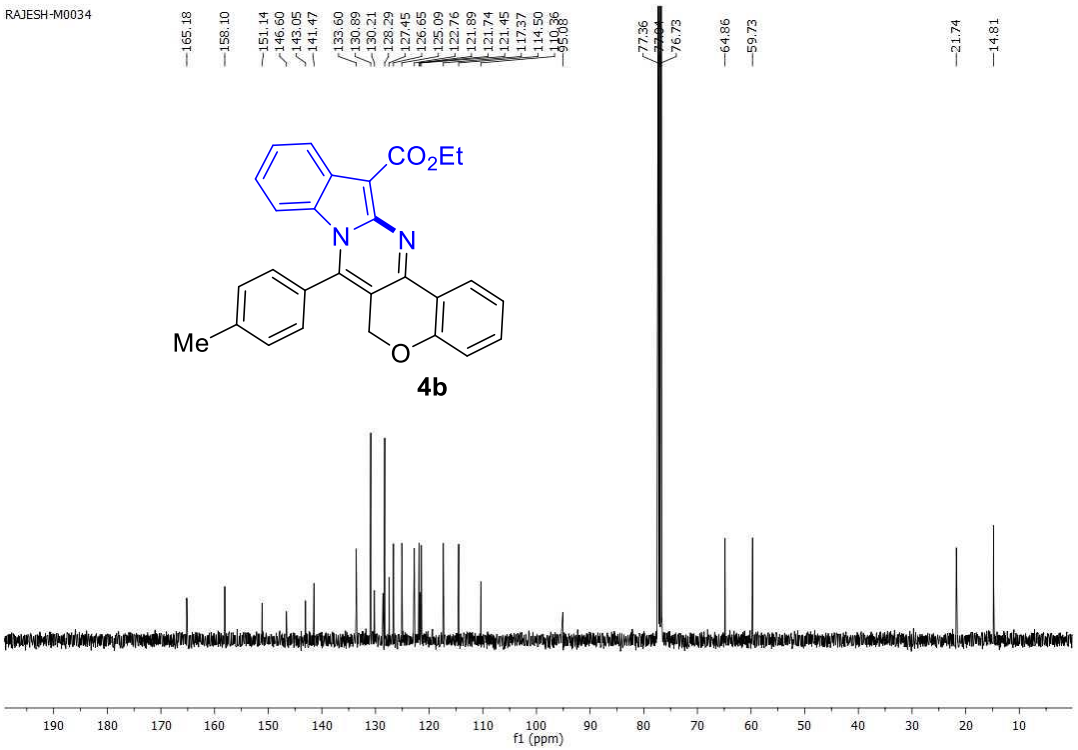
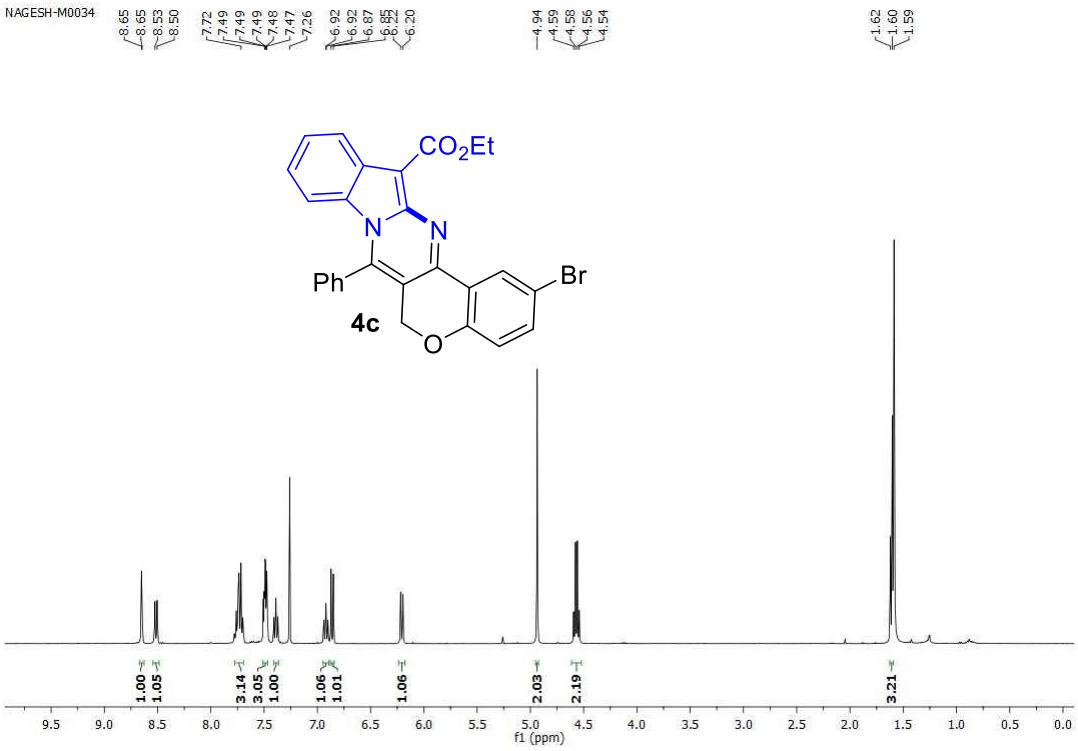
39.40
N
N
H
O
S
3at
f1 (ppm)

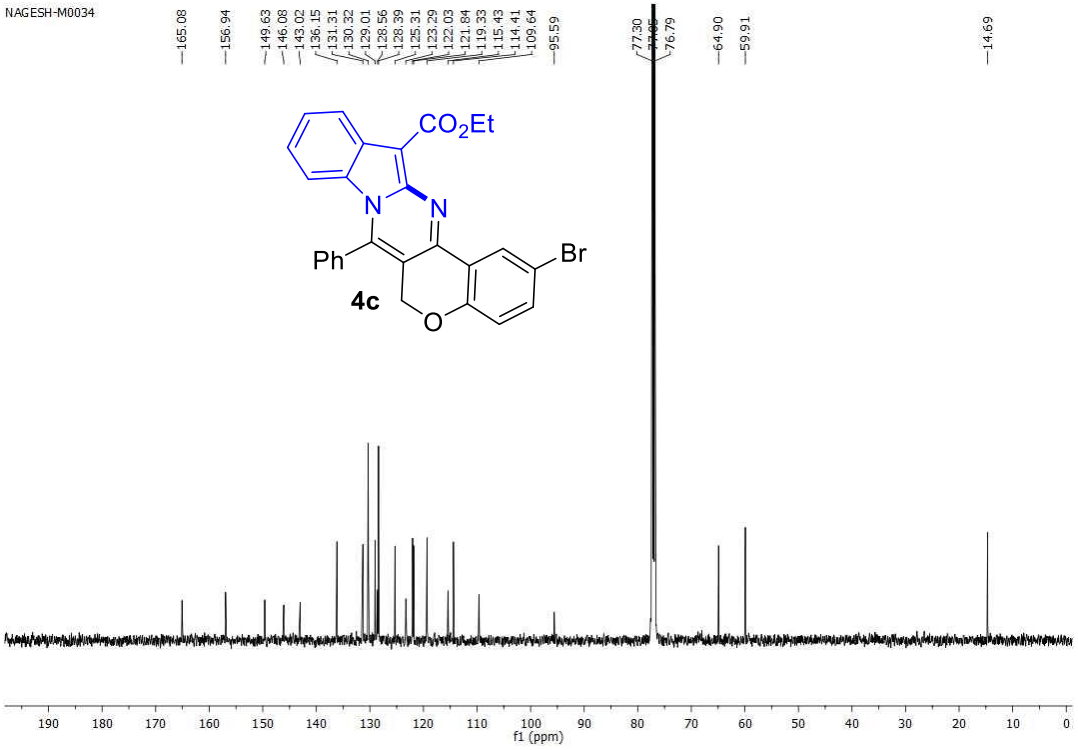

RAJESH-M0034
8.58
8.58
8.56
8.56
8.52
8.50
7.74
7.73
7.71
7.49
7.48
7.47
7.38
7.26
7.19
6.98
6.96
6.22
6.20
4.95
4.60
4.58
4.56
4.55
1.60
1.58
1.57
CO2Et
N
N
Ph
O
4a
2.01
3.01
4.14
1.02
1.01
1.02
1.00
2.04
1.99
3.66
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

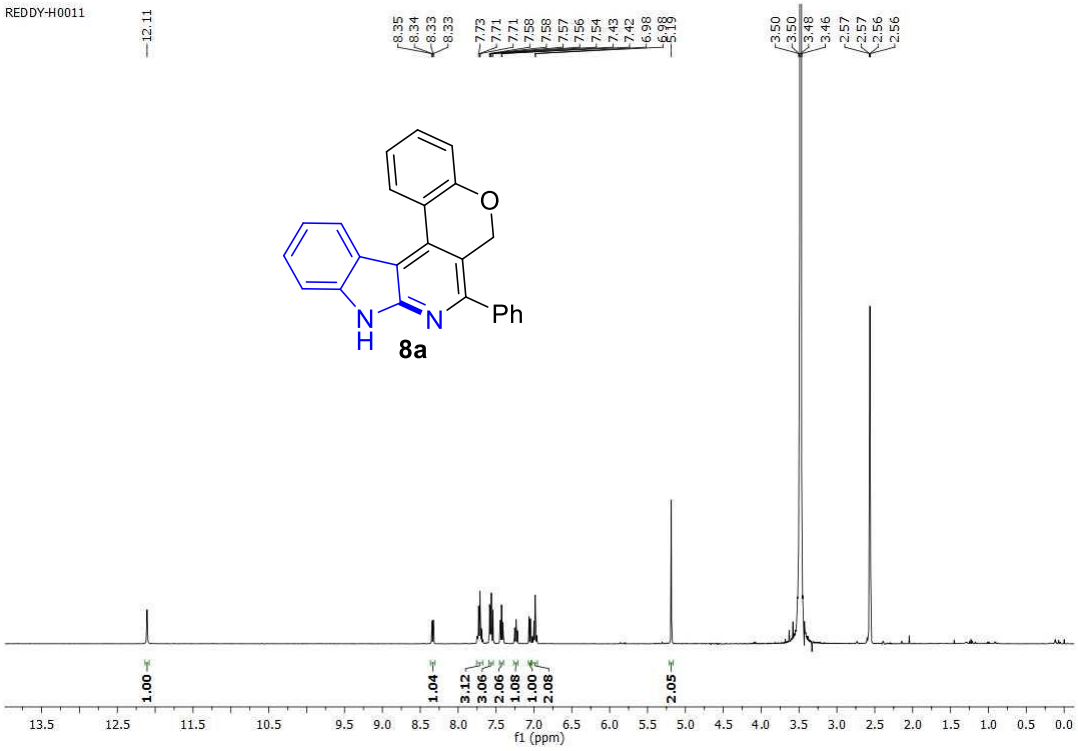

RAJESH-M0034
165.15
158.10
151.14
146.53
142.72
133.66
131.19
130.48
130.26
128.55
128.47
126.66
125.13
122.81
121.96
121.71
121.55
117.40
114.35
95.21
77.36
77.04
76.72
64.81
59.76
14.81
CO2Et
N
N
Ph
O
4a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

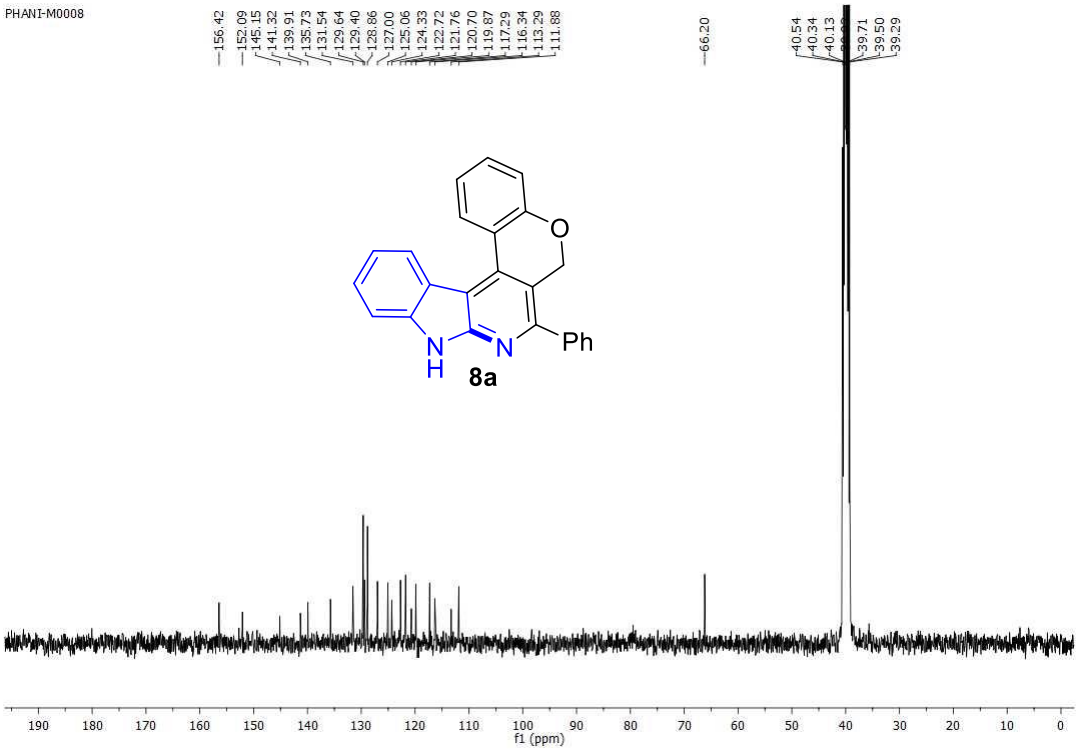

RAVI-M0034
8.57
8.57
8.55
8.55
8.51
8.50
7.51
7.49
7.38
7.36
7.34
7.26
7.18
6.98
6.96
6.96
6.31
6.29
4.95
4.59
4.58
4.56
4.55
2.58
1.60
1.58
1.57
CO2Et
N
N
Me
O
4b
1.01
0.97
2.05
2.03
2.17
1.04
0.98
0.97
1.00
1.97
2.02
2.97
4.91
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

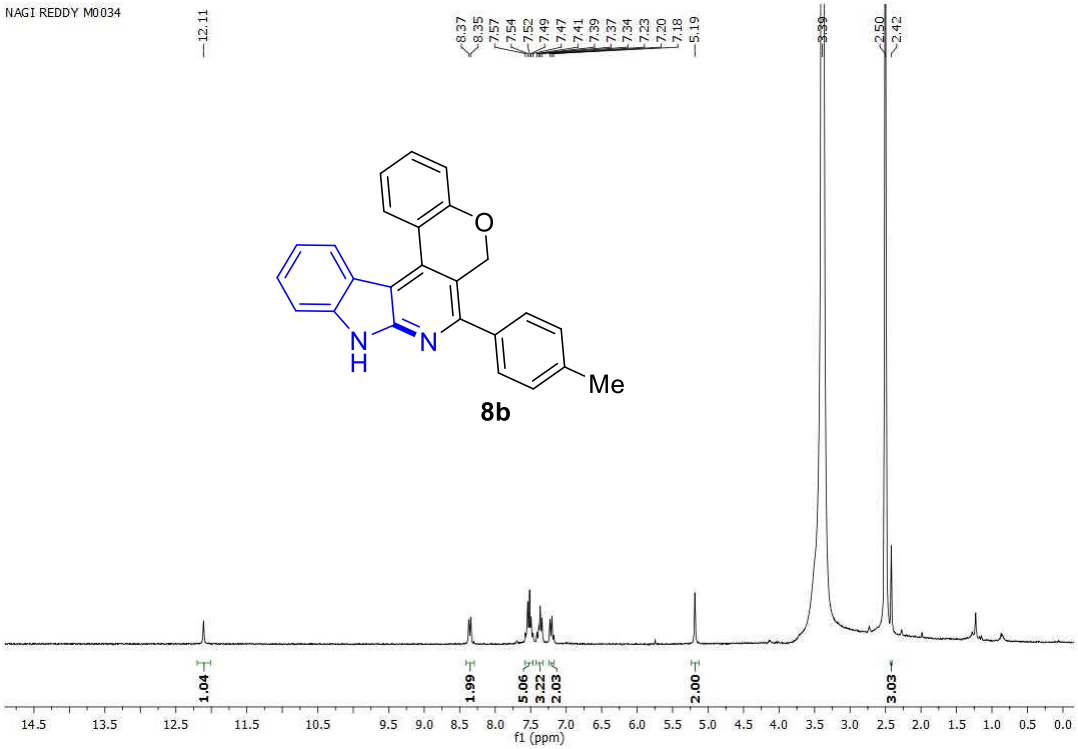

RAJESH-M0034
165.18
158.10
151.14
146.60
143.05
141.47
133.60
130.89
130.21
128.29
127.45
126.65
125.09
122.76
121.89
121.74
121.45
117.37
114.50
110.36
95.08
77.36
77.04
76.73
64.86
59.73
21.74
14.81
CO2Et
N
N
Me
O
4b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


NAGESH-M0034
8.65
8.65
8.53
8.50
7.72
7.49
7.49
7.49
7.48
7.47
7.26
6.92
6.92
6.87
6.85
6.82
6.20
4.94
4.59
4.58
4.56
4.54
1.62
1.60
1.59
CO2Et
N
N
Ph
Br
4c
O
1.00
1.05
3.14
3.05
1.00
1.06
1.01
1.06
2.03
2.19
3.21
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
f1 (ppm)


NAGESH-M0034
165.08
156.94
149.63
146.08
143.02
136.15
131.31
130.32
129.01
128.56
128.39
125.31
123.29
122.03
121.84
119.33
115.43
114.41
109.64
95.59
77.30
77.06
76.79
64.90
59.91
14.69
CO2Et
N
N
Ph
Br
4c
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


REDDY-H0011
12.11
8.35
8.34
8.33
8.33
7.73
7.71
7.71
7.58
7.58
7.57
7.56
7.54
7.43
7.42
6.98
6.98
5.19
3.50
3.50
3.48
3.46
2.57
2.57
2.56
2.56
O
N
H
N
Ph
8a
1.00
1.04
3.12
3.06
2.06
1.08
1.00
2.08
2.05
13.5
12.5
11.5
10.5
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
f1 (ppm)


PHANI-M0008
156.42
152.09
145.15
141.32
139.91
135.73
131.54
129.64
129.40
128.86
127.00
125.06
124.33
122.72
121.76
120.70
119.87
117.29
116.34
113.29
111.88
66.20
40.54
40.34
40.13
39.71
39.50
39.29
O
N
H
N
Ph
8a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


NAGI REDDY M0034
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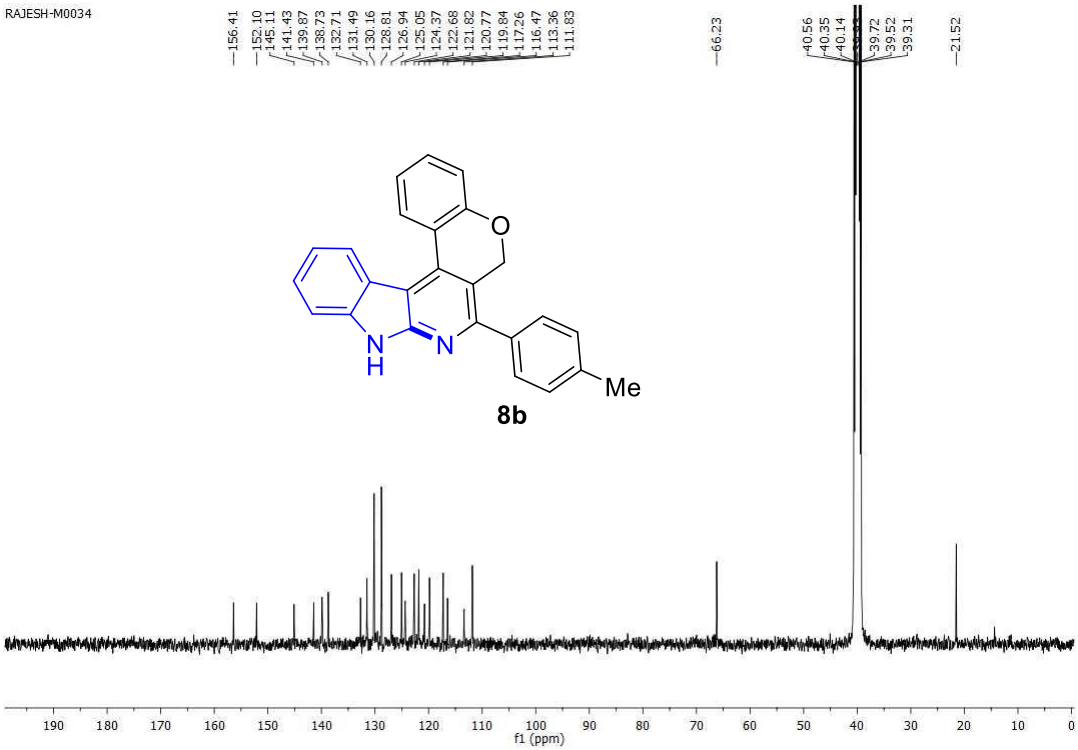
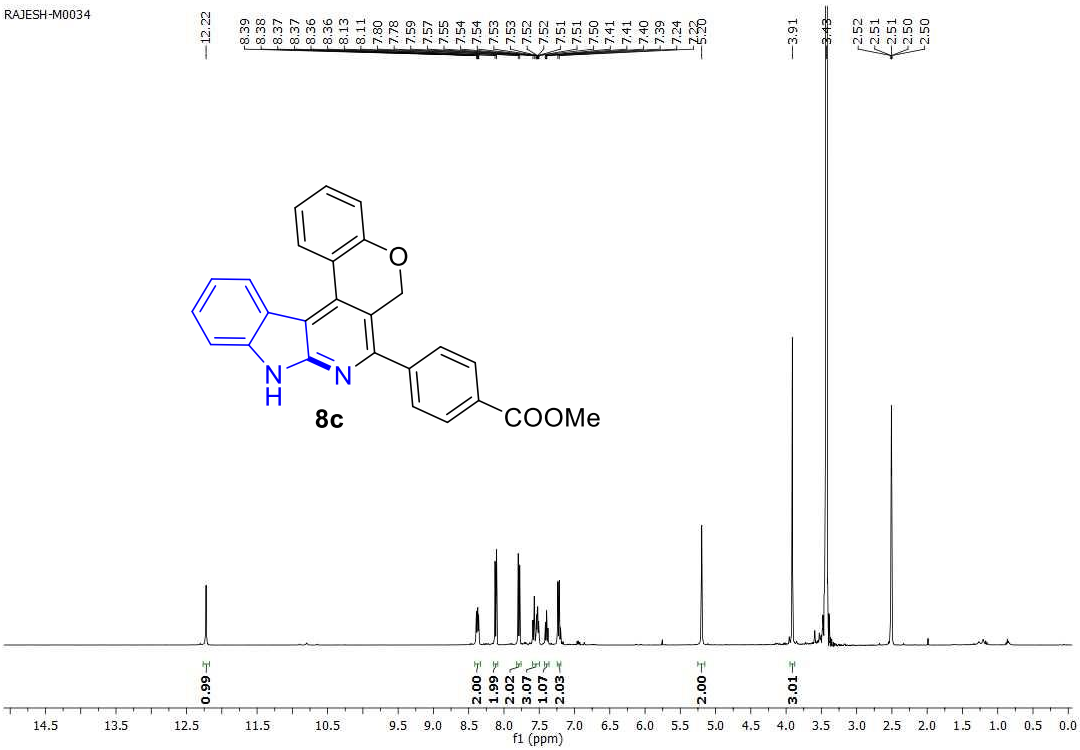
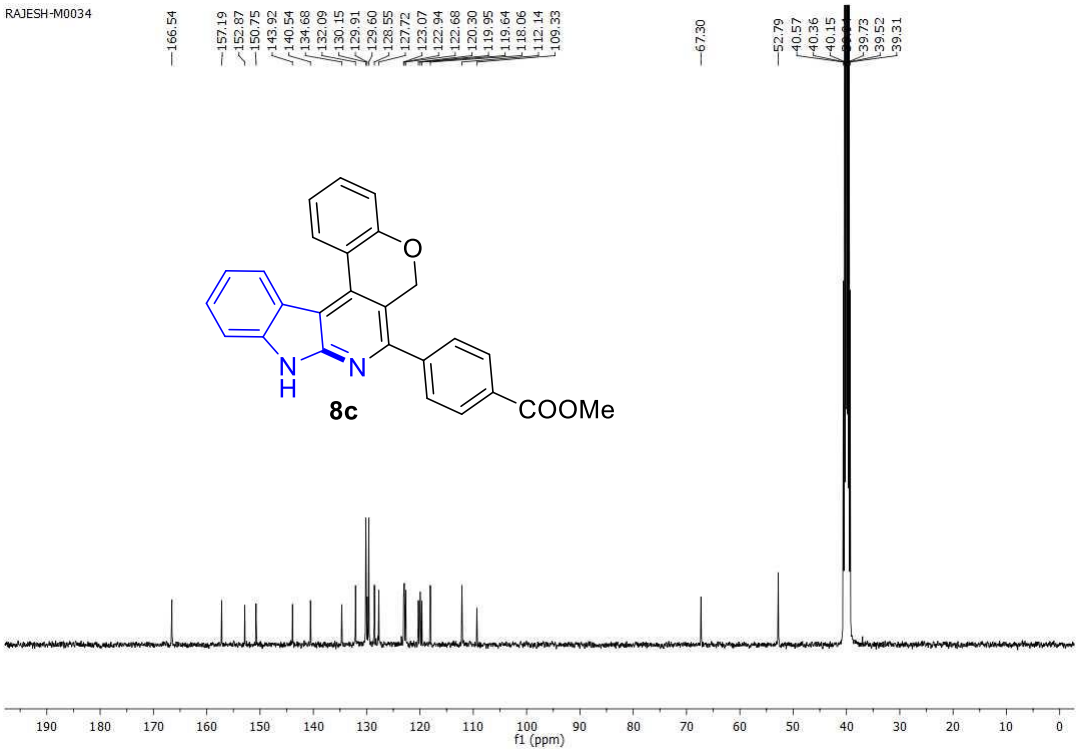
7.47
7.41
7.39
7.37
7.34
7.23
7.20
7.18
5.19
3.39
2.50
2.42
O
N
H
N
Me
8b
1.04
1.99
5.06
3.22
2.03
2.00
3.03
f1 (ppm)


RAJESH-M0034
156.41
152.10
145.11
141.43
139.87
138.73
132.71
131.49
130.16
128.81
126.94
125.05
124.37
122.68
121.82
120.77
119.84
117.26
116.47
113.36
111.83
66.23
40.56
40.35
40.14
39.72
39.52
39.31
21.52
O
N
H
N
Me
8b
f1 (ppm)


RAJESH-M0034
12.22
8.39
8.38
8.37
8.37
8.36
8.36
8.13
8.11
7.80
7.78
7.59
7.57
7.55
7.54
7.54
7.53
7.53
7.52
7.52
7.51
7.51
7.51
7.50
7.41
7.41
7.40
7.39
7.24
7.22
5.20
3.91
3.43
2.52
2.51
2.51
2.50
2.50
O
N
H
N
8c
COOMe
0.99
2.00
1.99
2.02
3.07
1.07
2.03
2.00
3.01
14.5
13.5
12.5
11.5
10.5
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
f1 (ppm)


RAJESH-M0034
166.54
157.19
152.87
150.75
143.92
140.54
134.68
132.09
130.15
129.91
129.60
128.55
127.72
123.07
122.94
122.68
120.30
119.95
119.64
118.06
112.14
109.33
67.30
52.79
40.57
40.36
40.15
39.73
39.52
39.31
O
N
H
N
8c
COOMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

V. X-ray crystallographic data.

Crystallographic data

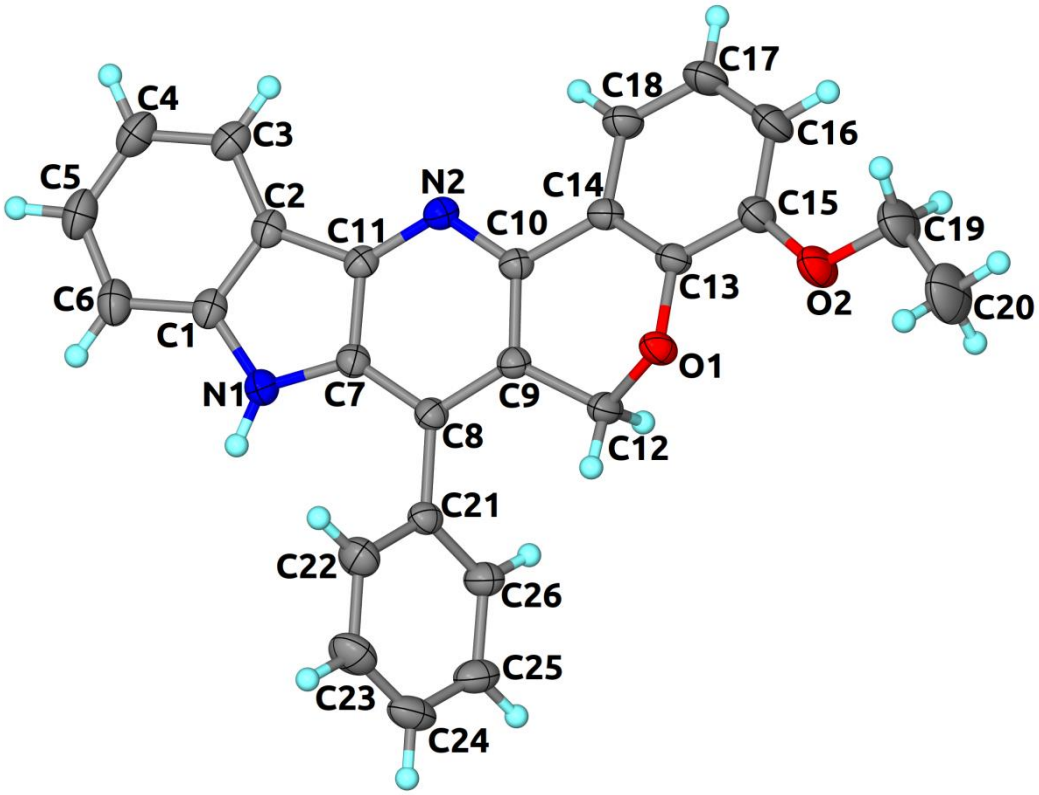


Figure caption: ORTEP diagram of **3af** compound with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius. CCDC 1970227 contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

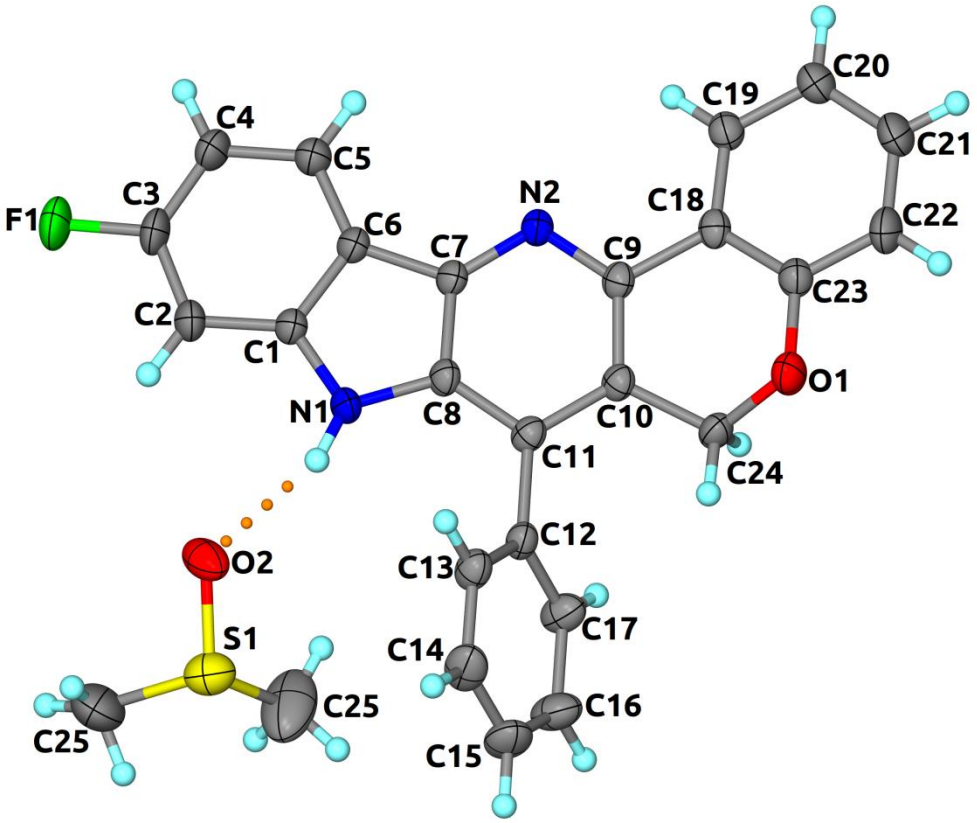
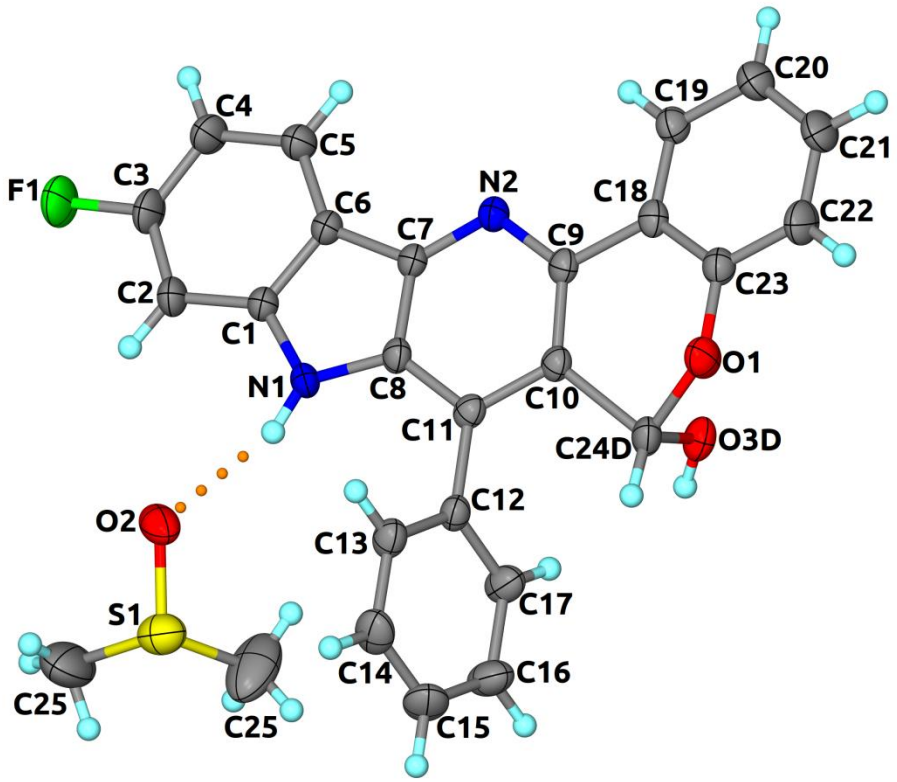
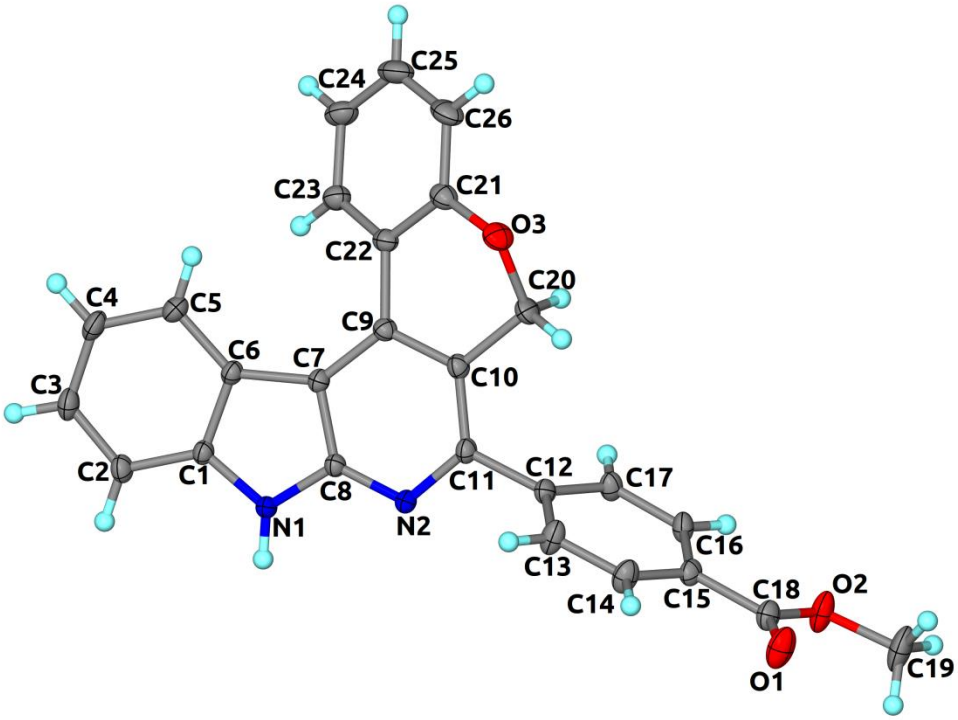


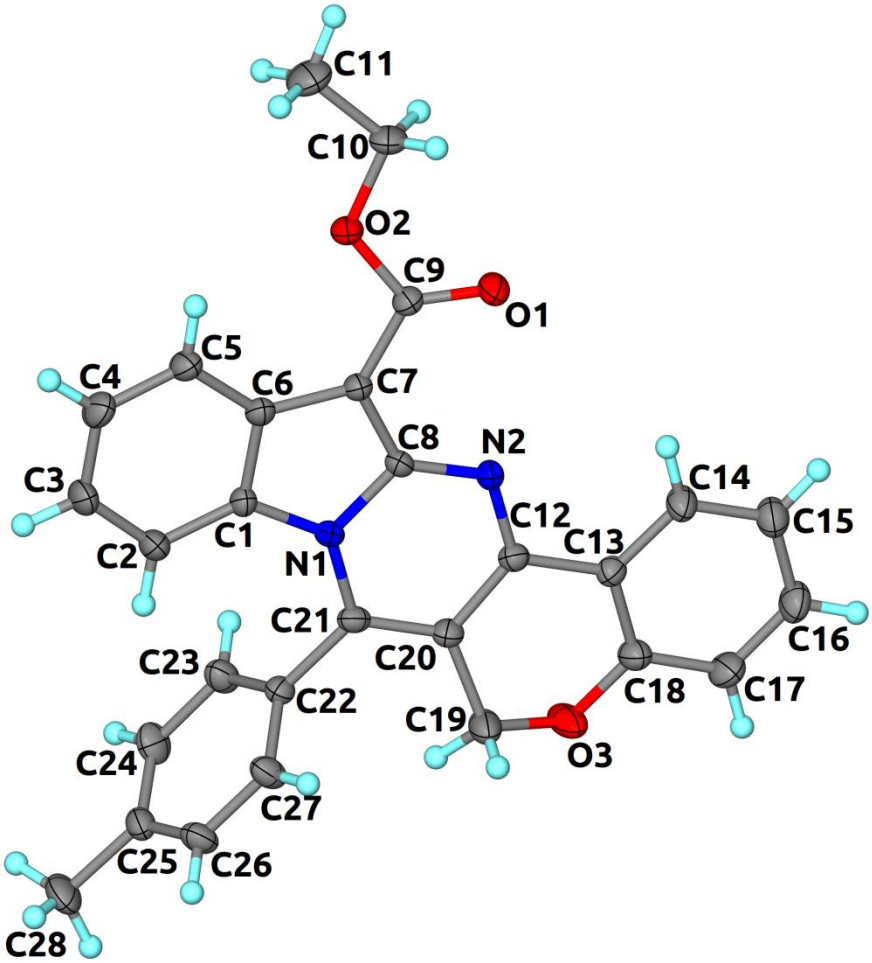
Figure caption: ORTEP diagram of **3da** compound (major component) with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius. The asymmetric unit contains compound and DMSO solvent in 1:0.5 ratio. DMSO interacts with the molecule by N-H...O hydrogen bond, indicated by a dotted line. The symmetry related second half of DMSO is shown for clarity purpose. The -CH_2 group at carbon C24 atom was found to be partially oxidized to -CHOH and found as a disordered site in the crystal lattice. The disorder model refinement suggested that the unoxidized product is the major component with site occupancy of 0.905(5) for C24/H24A/H24B atoms and the oxidized product is the minor component with site occupancy of 0.095(5) for C24D/H24D/O3D/H3D atoms. CCDC 1970228 contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/.



ORTEP diagram of **3da** compound (minor component) with the atom-numbering.



ORTEP diagram of **8c** compound with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius. CCDC 1970229 contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/



ORTEP diagram of **4b** compound with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius. CCDC 1970230 contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Table S1. Crystal Data Collection and Refinement Parameters for 3af.

	3af
chemical formula	$C_{26}H_{20}N_2O_2,C_4H_8O_2$
***Fw*; *F*(000)**	480.54; 4572
***T* (K)**	293(2)
wavelength (Å)	0.71073
space group	R-3
***a* (Å)**	26.635(19)
***b* (Å)**	26.635
***c* (Å)**	16.714(14)
α (deg)	90
β (deg)	90
γ (deg)	120
Z	18
***V* (Å^3)**	10269(17)
ρ_{calcd} (g·cm^{-3})	1.399
μ (mm^{-1})	0.093
θ range (deg); completeness	2.635 − 30.632; 0.998
collected reflections; R_σ	28339; 0.0433
unique reflections; R_{int}	28339; 0.0400
R1[a]; wR2[b] [I > 2σ(I)]	0.0561; 0.1542
R1; wR2 [all data]	0.1016; 0.1776
GOF	1.007
largest diff peak and hole	0.184 and -0.213

[a] $R_1=\Sigma(||F_o|-|F_c||)/\Sigma|F_o|$

[b] $wR_2=\{\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$

Table S2. Crystal Data Collection and Refinement Parameters for 3da.

	3da
chemical formula	$2(C_{24}H_{15}FN_2O_{1.10}),C_2H_6OS$
***Fw*; *F*(000)**	813.92; 1694
***T* (K)**	293(2)
wavelength (Å)	0.71073
space group	C2/c
***a* (Å)**	22.70(2)
***b* (Å)**	7.518(7)
***c* (Å)**	24.71(2)
α (deg)	90
β (deg)	109.661(16)
γ (deg)	90
Z	4
***V* (Å^3)**	3972(6)
ρ_{calcd} (g·cm^{-3})	1.361
μ (mm^{-1})	0.142
θ range (deg); completeness	2.109 − 24.998; 0.999
collected reflections; R_σ	17034; 0.0535
unique reflections; R_{int}	17034; 0.0545
R1[a]; wR2[b] [I > 2σ(I)]	0.0579; 0.1456
R1; wR2 [all data]	0.1079; 0.1723
GOF	1.051
largest diff peak and hole	0.212 and -0.267

[a] $R_1=\Sigma(||F_o|-|F_c||)/\Sigma|F_o|$

[b] $wR_2=\{\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$

Table S3. Crystal Data Collection and Refinement Parameters for 8c.

	8c
chemical formula	$C_{26}H_{18}N_2O3$
***Fw*; *F*(000)**	406.42; 424
***T* (K)**	293(2)
wavelength (Å)	0.71073
space group	P-1
***a* (Å)**	8.031(3)
***b* (Å)**	10.670(5)
***c* (Å)**	12.569(5)
α (deg)	93.207(12)
β (deg)	102.784(9)
γ (deg)	108.553(11)
Z	2
***V* (Å^3)**	986.4(7)
ρ_{calcd} (g·cm^{-3})	1.368
μ (mm^{-1})	0.091
θ range (deg); completeness	2.452 − 30.555; 0.998
collected reflections; R_σ	25056; 0.0533
unique reflections; R_{int}	25056; 0.0543
R1[a]; wR2[b] [I > 2σ(I)]	0.0540; 0.1576
R1; wR2 [all data]	0.0837; 0.1770
GOF	1.155
largest diff peak and hole	0.385 and -0.255

[a] $R_1=\Sigma(||F_o|-|F_c||)/\Sigma|F_o|$

[b] $wR_2=\{\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$

Table S4. Crystal Data Collection and Refinement Parameters for 4b.

	4b
chemical formula	$C_{28}H_{22}N_2O_3$
***Fw*; *F*(000)**	434.47; 456
***T* (K)**	293(2)
wavelength (Å)	0.71073
space group	P-1
***a* (Å)**	9.503(7)
***b* (Å)**	9.907(8)
***c* (Å)**	12.446(10)
α (deg)	96.68(2)
β (deg)	99.585(17)
γ (deg)	103.549(19)
Z	2
***V* (Å^3)**	1108.4(15)
ρ_{calcd} (g·cm^{-3})	1.302
μ (mm^{-1})	0.085
θ range (deg); completeness	2.143 − 24.998; 0.999
collected reflections; R_σ	21141; 0.0925
unique reflections; R_{int}	21141; 0.1256
R1[a]; wR2[b] [I > 2σ(I)]	0.0635; 0.1489
R1; wR2 [all data]	0.1346; 0.1815
GOF	0.997
largest diff peak and hole	0.243 and -0.196

[a] $R_1=\Sigma(||F_o|-|F_c||)/\Sigma|F_o|$

[b] $wR_2=\{\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$

Data collection and Structure solution details: Single crystal X-ray data for **3af**, **3da**, **8c**, **4b** compounds were collected at room temperature on a Bruker D8 QUEST equipped with a four-circle kappa diffractometer and Photon 100 detector. An Iμs microfocus Mo source (□=0.71073Å) supplied the multi-mirror monochromated incident beam. A combination of Phi and Omega scans were used to collect the necessary data and unit cell dimensions were determined using 9904 reflections for **3af**, 5015 reflections for **3da**, 9956 reflections for **8c** and 3949 reflections for **4b** data sets. Integration and scaling of intensity data were accomplished using SAINT program.[1] The structures were solved by Direct Methods using SHELXS97[2] and refinement was carried out by full-matrix least-squares technique using SHELXL-2014/7.[2-3] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with U_{iso}(H) = 1.2U_{eq} (C) or 1.5U_{eq} for methyl atoms. The N bound H atoms were located from the difference Fourier map.

In KA422, the solvent of crystallization ethyl acetate was trapped inside the crystal lattice; however, the ethyl acetate solvent molecule showed extensive disorder and could not be resolved well. PLATON SQUEEZE module[4] was employed to remove the solvent contribution from the overall scattering during the final cycle of refinement. In KA844 also, the solvent of crystallization DMSO was trapped inside the crystal lattice and was found to be disordered over a two fold axis with 50% site occupancy. The -CH_2 group at carbon C24 atom was found to be partially oxidized to -CHOH and found as a disordered site in the crystal lattice. The disorder model refinement suggested that the unoxidized product is the major component with site occupancy of 0.905(5) for C24/H24A/H24B atoms and the oxidized product is the minor component with site occupancy of 0.095(5) for C24D/H24D/O3D/H3D atoms. The disorder model structural refinement was performed with DELU and SIMU instructions. Structures with CCDC Deposition Numbers 1970227-1970230 contain the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

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