Electronic Supplementary Information (ESI)

Hypervalent Iodine(III) Catalyzed Oxidative C-N Bond Formation in Water: Synthesis of Benzimidazole-Fused Heterocycles

D Nageshwar Rao,[a,b] Sk. Rasheed,[a,b] Ram A Vishwakarma,[b] Parthasarathi Das[a,b] *

[a] *Academy of Scientific and Innovative Research (AcSIR)*

[b] *Medicinal Chemistry Division, Indian Institute of Integrative Medicine(CSIR), Jammu 180001, India*

Email: partha@iiim.ac.in

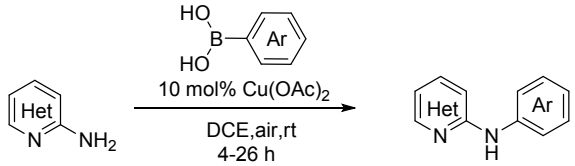
Table of Contents

1. General information

All purchased chemicals were used without further purification. All reactions were performed under open air. Analytical thin layer chromatography was performed using TLC pre-coated silica gel 60 F254 MERCK (20x20 cm). TLC plates were visualized by exposing UV light or by iodine vapors. Organic solutions were concentrated by rotary evaporation on BUCHI-Switzerland; R-120 rotary evaporator and vacuum pump V-710. Flash column chromatography was performed on Merck flash silica gel 100-200 mesh size. Melting points of solid compounds were determined on BUCHI-B-545-Switzerland melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded with BRUKER 500 and 400 MHz NMR instruments. Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded using tetramethylsilane (TMS) in the solvent of $CDCl_3$ as the internal standard (^{1}H NMR: TMS at 0.00 ppm, $CHCl_3$ at 7.24 ppm; ^{13}C NMR: $CDCl_3$ at 77.0 ppm) or were recorded using tetramethylsilane (TMS) in the solvent of Acetone-d_6 as the internal standard (^{1}H NMR: TMS at 0.00 ppm, Acetone at 2.09 ppm;^{13}C NMR: Acetone at 29.9 ppm, 206.7 ppm). All the NMR spectra were processed in MestReNova. HRMS spectra were recorded with LCMS-QTOF Module No. G6540 A (UHD) instrument.

2. Synthesis of substrates

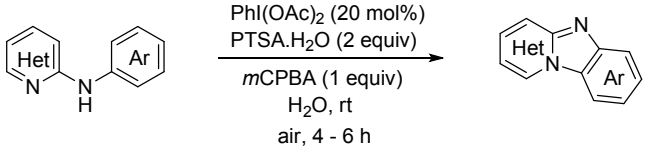
Synthesis of substrates **1a-**s and 1aa**-ak** were prepared according to the general procedure [1]



A round bottom flask equipped with a magnetic stirrer bar was charged with cyclic amidines (1 eq), boronic acids (1.1 eq), copper acetate (10 mol %) and dichloroethane (2 mL), was added into the flask. The flask was kept open and the reaction mixture was stirred for 4-26 h in air at room temperature. The progress of the reaction was monitored by TLC and after completion of the reaction the solvent was removed with aid of a rotatory evaporator. The crude reaction mixture was diluted with 20 mL of water and extracted with ethyl acetate (3x15 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by column chromatography (hexane/ EtOAc) to provide the desired products.

3. General procedure and characterization of products

3.1 General procedure

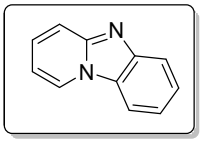


To a solution of *N*-aryl-2-aminopyridine (0.29 mmol, 1 equiv) in water 1 mL and $PhI(OAc)_2$ (0.058 mmol, 20 mol%) and *m*CPBA (0.29 mmol, 1 equiv) and $PTSA.H_2O$ (0.588 mmol, 2 equiv) were sequentially added to the reaction mixture with vigorous stirring at room temperature. The resulting mixture was stirred at room temperature for 4 to 6 h under air. The progress of the reaction was monitored by TLC until the starting material was completely consumed. The reaction mixture was diluted with EtOAc (10 mL). The organic layer was separated, and the aqueous phase was further extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine solution

and dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude reaction mixture was purified by column chromatography (Hexane/EtOAc) to give the corresponding heterocycles.

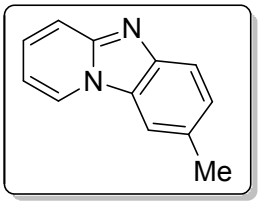
3.2 Characterization of products

Pyrido[1,2-*a*]benzimidazole (2a) [2]



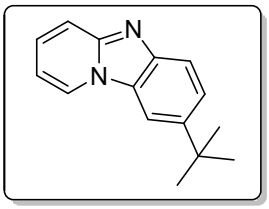
Yield: 90%. purification: hexane/ EtOAc (5:5); white solid, mp 181-182 °C; ^{1}H NMR (500 MHz, Acetone-d_6) δ 8.91 (d, *J* = 6.0 Hz, 1H), 8.20 (d, *J* = 7.9 Hz, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 1H), 7.58 – 7.46 (m, 2H), 7.37 (t, *J* = 7.6 Hz, 1H), 6.97 (t, *J* = 6.6 Hz, 1H); ^{13}C NMR (125 MHz, Acetone-d_6) δ 149.2, 145.6, 130.4, 129.8, 127.2, 126.1, 121.4, 120.3, 118.3, 112.1, 110.9; HRMS (ESI): calcd. for $C_{11}H_9N_2$ $[M+H]^+$, 169.0760; found: 169.0766.

8-Methylpyrido[1,2-*a*]benzimidazole (2b) [2]



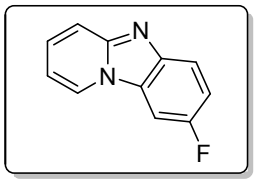
Yield: 99%. purification: hexane/ EtOAc (5:5); off white solid, mp 83-85 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.69 (d, *J* = 6.8 Hz, 1H), 7.84 (s, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 9.3 Hz, 1H), 7.38 – 7.28 (m, 1H), 7.21 (d, *J* = 8.3 Hz, 1H), 6.78 (t, *J* = 6.7 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 142.3, 131.2, 128.8, 128.7, 127.5, 124.9, 119.9, 119.3, 117.9, 110.1, 21.8; HRMS (ESI): calcd. for $C_{12}H_{11}N_2$ $[M+H]^+$, 183.0917; found: 183.0916.

8-(tert-butyl)Pyrido[1,2-*a*]benzimidazole (2c) [2]



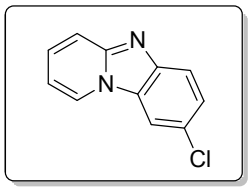
Yield: 98%. purification: hexane/ EtOAc (5:5); pale yellow solid, mp 90-92 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.81 (d, *J* = 6.9 Hz, 1H), 8.08 (d, *J* = 1.1 Hz, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.54 – 7.41 (m, 2H), 7.37 – 7.27 (m, 1H), 6.78 (t, *J* = 6.6 Hz, 1H), 1.31 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.7, 144.3, 139.7, 128.7, 127.1, 124.1, 123.6, 117.5, 116.3, 109.7, 105.5, 34.1, 30.7; HRMS (ESI): calcd. for $C_{15}H_{17}N_2$ $[M+H]^+$, 225.1386; found: 225.1380.

8-fluoropyrido[1,2-*a*]benzimidazole (2d) [2]



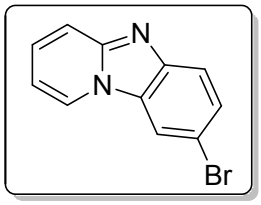
Yield: 98%. purification: hexane/ EtOAc (5:5). white solid, mp 181-182 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.88 (d, *J* = 6.9 Hz, 1H), 8.05 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.84 (dd, *J* = 9.0, 4.8 Hz, 1H), 7.64 (d, *J* = 9.3 Hz, 1H), 7.54 (ddd, *J* = 9.3, 6.5, 1.1 Hz, 1H), 7.35 (td, *J* = 9.4, 2.5 Hz, 1H), 6.99 (t, *J* = 6.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 157.0, 149.0, 140.7, 129.2, 125.0, 120.7 (d, *J* = 9.7 Hz), 118.2, 114.5 (d, *J* = 25.2 Hz), 110.6, 97.0 (d, *J* = 27.6 Hz); HRMS (ESI): calcd. for $C_{11}H_8FN_2$ $[M+H]^+$, 187.0666; found: 187.0663.

8-Chloropyrido[1,2-*a*]benzimidazole (2e) [2]



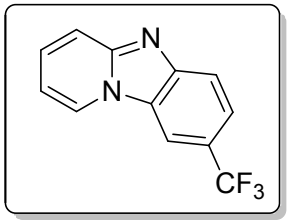
Yield: 99%. purification: hexane/ EtOAc (6:4); white solid, mp 110-111 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.95 (d, *J* = 6.9 Hz, 1H), 8.33 (d, *J* = 1.9 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 1H), 7.66 (d, *J* = 9.3 Hz, 1H), 7.62 – 7.55 (m, 1H), 7.52 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.03 (t, *J* = 6.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.3, 145.1, 131.3, 129.9, 127.2, 125.2, 121.5, 119.4, 118.0, 111.2, 110.9; HRMS (ESI): calcd. for $C_{11}H_8ClN_2$ $[M+H]^+$, 203.0371; found: 203.0367.

8-Bromopyrido[1,2-*a*]benzimidazole (2f) [2]



Yield: 98%. purification: hexane/ EtOAc (6:4); off white solid, mp 150-151 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.81 (d, *J* = 6.9 Hz, 1H), 8.33 (d, *J* = 1.7 Hz, 1H), 7.63 (d, *J* = 8.7 Hz, 1H), 7.57 – 7.36 (m, 3H), 6.88 (t, *J* = 6.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.7, 142.9, 130.0, 129.4, 129.1, 125.1, 121.0, 118.1, 113.9, 113.6, 111.0; HRMS (ESI): calcd. for $C_{11}H_8BrN_2$ $[M+H]^+$, 246.9866; found: 246.9863.

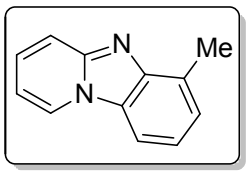
8-Trifluoromethylpyrido[1,2-*a*]benzimidazole (2g) [3]



Yield: 96%. purification: hexane/ EtOAc (4:6); pale yellow solid, mp 158-159 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 9.00 (d, *J* = 6.9 Hz, 1H), 8.53 (s, 1H), 7.84 (d, *J* = 8.6 Hz, 1H), 7.67 (d, *J* = 8.6 Hz, 1H), 7.61 – 7.51 (m, 2H), 6.97 (t, *J* = 7.1 Hz, 1H); ^{13}C NMR (125 MHz, Acetone) δ 149.9, 145.6, 132.0, 128.3, 127.2, 126.2, 124.1, 122.1 (q, *J* =

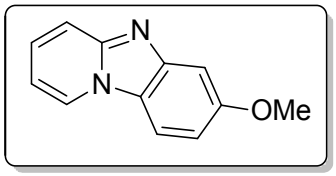
3.5 Hz), 119.5, 117.1, 111.6, 110.0 (q, J = 4.4 Hz); HRMS (ESI): calcd. for $C_{12}H_8F_3N_2$ $[M+H]^+$, 237.0634; found: 237.0629.

6-Methylpyrido[1,2-*a*]benzimidazole (2h) [2]



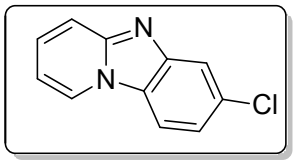
Yield: 89%. purification: hexane/ EtOAc (4:6); white solid, mp 140-142 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.72 (d, J = 6.8 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 9.3 Hz, 1H), 7.40 – 7.34 (m, 1H), 7.18 (d, J = 7.0 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 6.81 (t, J = 6.7 Hz, 1H), 2.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.7, 143.2, 129.7, 129.3, 128.0, 125.8, 125.3, 121.2, 117.9, 110.5, 107.9, 17.2; HRMS (ESI): calcd. for $C_{12}H_{11}N_2$ $[M+H]^+$, 183.0927; found: 183.0913.

7-Methoxypyrido[1,2-*a*]benzimidazole (2i) [2]



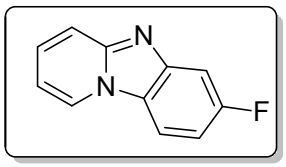
Yield: 85%. purification: hexane/ EtOAc (5:5). white solid, mp 146-147 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.71 (d, J = 6.8 Hz, 1H), 7.93 (d, J = 8.9 Hz, 1H), 7.45 (d, J = 9.3 Hz, 1H), 7.39 – 7.31 (m, 1H), 7.14 (d, J = 2.3 Hz, 1H), 6.89 – 6.73 (m, 2H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 148.3, 144.7, 129.1, 124.9, 122.9, 117.0, 112.2, 111.0, 110.7, 100.3, 55.7; HRMS (ESI): calcd. for $C_{12}H_{11}N_2O$ $[M+H]^+$, 199.0866; found: 199.0860.

7-Chloropyrido[1,2-*a*]benzimidazole (2j)[2]



Yield: 81%. purification: hexane/ EtOAc (5:5); off white solid, mp 209-211 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.80 (d, J = 6.9 Hz, 1H), 8.09 (d, J = 8.7 Hz, 1H), 7.68 (d, J = 1.9 Hz, 1H), 7.52 (d, J = 9.3 Hz, 1H), 7.49 – 7.44 (m, 1H), 7.23 (dd, J = 8.7, 1.9 Hz, 1H), 6.94 – 6.86 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.3, 145.1, 131.3, 129.9, 127.2, 125.2, 121.5, 119.4, 118.0, 111.2, 110.9; HRMS (ESI): calcd. for $C_{11}H_8ClN_2$ $[M+H]^+$, 203.0371; found: 203.0366.

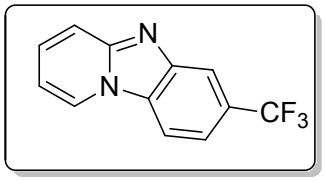
7-Fluoropyrido[1,2-*a*]benzimidazole (2k)[2]



Yield: 80%. purification: hexane/ EtOAc (5:5); white solid, mp 156-157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, J = 6.8 Hz, 1H), 7.83 (dd, J = 8.9, 4.6 Hz, 1H), 7.73 (d, J = 9.3 Hz, 1H), 7.59 (dd, J = 9.6, 2.3 Hz, 1H), 7.50 – 7.44 (m, 1H), 7.18 – 7.11 (m, 1H), 6.91 (t, J = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.3, 160.4, 149.6, 148.8

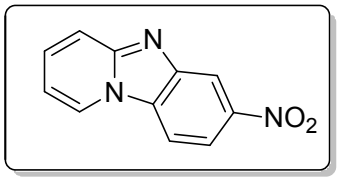
145.0 (d, *J* = 13.1 Hz), 129.7, 125.1, 117.7, 111.1 (d, *J* = 10.9 Hz), 109.9 (d, *J* = 27.1 Hz), 105.1 (d, *J* = 24.2 Hz); HRMS (ESI): calcd. for $C_{11}H_8FN_2$ $[M+H]^+$, 187.0666; found: 187.0664.

7-Trifluoromethylpyrido[1,2-*a*]benzimidazole (2l)



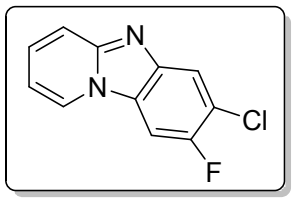
Yield: 88%. purification: hexane/EtOAc (4:6), brown solid, mp 89-90 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.65 (d, *J* = 7.2 Hz, 1H), 8.02 (d, *J* = 8.2 Hz, 1H), 7.64 (t, *J* = 8.2 Hz, 2H), 7.58 – 7.48 (m, 2H), 6.98 (t, *J* = 6.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.1, 144.9, 130.3, 129.8, 127.8 (d, *J* = 6.1 Hz), 124.8 (d, *J* = 11.1 Hz), 124.2, 122.7, 119.6 (q, *J* = 6.2 Hz), 118.0, 115.3, 111.8; FT-IR (KBr) 3438, 2919, 2850, 1647, 1509, 1324, 1115, 1020 cm^{-1}HRMS (ESI): calcd. for $C_{12}H_8F_3N_2$ $[M+H]^+$, 237.0634; found: 237.0632.

7-Nitropyrido[1,2-*a*]benzimidazole (2m)



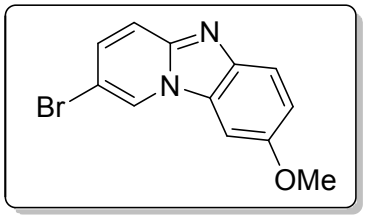
Yeild: 86%; purification: hexane/ EtOAc (3:7); yellow solid, mp 115-116 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.86 (d, *J* = 7.3 Hz, 1H), 8.10 (d, *J* = 8.2 Hz, 1H), 7.98 (d, *J* = 7.9 Hz, 1H), 7.59 (dd, *J* = 15.9, 8.7 Hz, 2H), 7.55 – 7.50 (m, 1H), 6.93 (t, *J* = 6.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 147.0, 137.6, 130.6, 129.6, 126.9, 124.5, 120.3, 119.3, 118.1, 111.4; FT-IR (KBr) 3395, 2916, 2849, 1648, 1520, 1505, 1403, 1365, 1019 cm $^{-1}$;HRMS (ESI): calcd. for $C_{11}H_8N_3O_2$ $[M+H]^+$, 214.0611; found: 214.0609.

7-chloro-8-fluorobenzo[4,5]imidazo[1,2-a]pyridine(2n)



Yeild: 82%; purification: Hexane/ EtOAc (4:6); brown solid, mp 222-223 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 6.9 Hz, 1H), 7.96 (d, *J* = 6.6 Hz, 1H), 7.68 (dd, *J* = 8.7, 6.7 Hz, 2H), 7.45 (ddd, *J* = 9.2, 6.7, 1.1 Hz, 1H), 6.89 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9, 151.4, 148.8, 139.5, 129.8, 125.0, 120.8, 119.7 (d, *J* = 54.9 Hz), 118.2, 111.1, 98.1 (d, *J* = 27.3 Hz); FT-IR (KBr) 3438, 2955, 2916, 2850, 1645, 1507, 1463, 1044, 1021 cm $^{-1}$; HRMS (ESI): calcd. for $C_{11}H_7ClFN_2$ $[M+H]^+$, 221.0277; found: 221.0280.

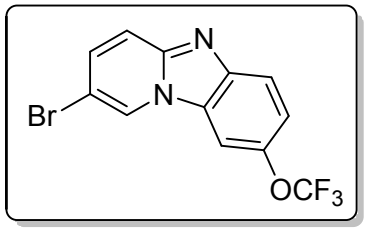
2-Bromo 8-methoxypyrido[1,2-*a*]benzimidazole (2o)



Yeild: 94%. purification: hexane/ EtOAc (6:4); brown solid, mp 150-151 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 9.00 (s, 1H), 7.73 (d, *J* = 2.2 Hz, 1H), 7.61 (d, *J* = 9.0 Hz, 1H), 7.47 (d, *J* = 9.7 Hz, 1H), 7.40 (dd, *J* = 9.7, 1.6 Hz, 1H), 7.06 (dd, *J* = 9.0, 2.3 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 144.4, 136.7, 131.0, 127.2,

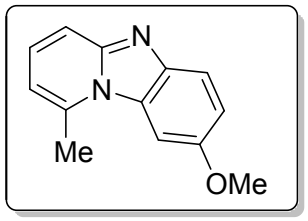
123.9, 119.4, 117.3, 116.1, 104.0, 91.9, 55.0; FT-IR (KBr) 3436, 2917, 2850, 1640, 1491, 1403, 1220, 1019, 771 cm^{-1}; HRMS (ESI): calcd. for $C_{12}H_{10}BrN_2O$ $[M+H]^+$, 278.9951; found: 278.9985.

2-Bromo 8-trifluoromethoxypyrido[1,2-*a*]benzimidazole (2p)



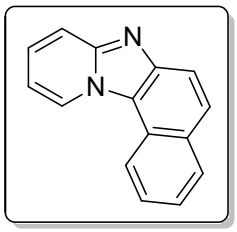
Yeild: 93%. purification: hexane/ EtOAc (5:5); , brown solid, mp 147-148 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 9.15 (d, *J* = 0.9 Hz, 1H), 8.23 (s, 1H), 7.78 (d, *J* = 8.9 Hz, 1H), 7.52 (s, 2H), 7.37 (d, *J* = 8.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.7, 143.8, 142.8, 133.3, 127.8, 125.3, 121.6, 121.1, 120.4, 119.6, 118.9, 105.2, 103.9; FT-IR (KBr) 3435, 2955, 2918, 2850, 1642, 1501, 1456, 1254, 1218, 1146, 1054, 1019, 800 cm^{-1}; HRMS (ESI): calcd. for $C_{12}H_7BrF_3N_2O$ $[M+H]^+$, 330.9689; found: 330.9691.

1-Methyl 8-methoxypyrido[1,2-*a*]benzimidazole (2q)



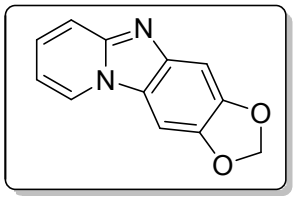
Yeild: 90%. purification: hexane/ EtOAc (4:6); white solid, mp 104-105 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.79 (d, *J* = 2.1 Hz, 1H), 7.74 (d, *J* = 8.9 Hz, 1H), 7.45 (d, *J* = 9.2 Hz, 1H), 7.34 (dd, *J* = 9.1, 6.8 Hz, 1H), 7.20 (dd, *J* = 8.9, 2.2 Hz, 1H), 6.66 (d, *J* = 6.6 Hz, 1H), 3.95 (s, 3H), 3.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.7, 149.3, 139.4, 138.4, 130.0, 128.5, 119.8, 115.5, 114.4, 110.7, 98.9, 56.2, 21.2; FT-IR (KBr) 3436, 2955, 2916, 2850, 1647, 1516, 1485, 1436, 1288, 1219, 1209, 1031, 819, 780 cm^{-1}; HRMS (ESI): calcd. for $C_{13}H_{13}N_2O$ $[M+H]^+$, 213.1023; found: 213.1018.

Naphthopyrido[1,2-*a*]benzimidazole (2r)



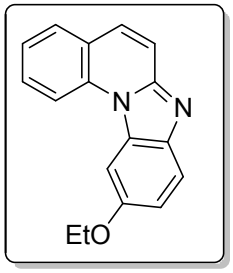
Yeild: 82%. purification: hexane/ EtOAc (5:5); pale yellw solid, mp 142-143 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 9.41 (d, *J* = 7.0 Hz, 1H), 8.69 (d, *J* = 8.4 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.85 (dd, *J* = 19.7, 8.9 Hz, 2H), 7.72 (d, *J* = 9.2 Hz, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 2H), 7.08 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 142.9, 130.3, 130.0, 127.8, 127.1, 126.9, 124.0, 122.9, 121.5, 119.9, 119.1, 118.2, 117.0, 112.0; FT-IR (KBr) 3401, 2955, 2917, 2850, 1734, 1648, 1403, 1385, 1219, 1156, 1019, 772 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{11}N_2$ $[M+H]^+$, 219.0917; found: 219.0912.

[1,3]dioxolo[4'',5'':4',5']benzo[1',2':4,5]imidazo[1,2-a]pyridine (2s)



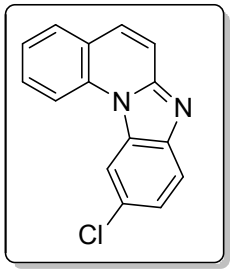
Yeild: 94%; purification: Hexane/ EtOAc (4:6); white solid, mp 236-237 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.61 (d, *J* = 6.9 Hz, 1H), 7.55 (s, 1H), 7.41 (d, *J* = 9.3 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.06 (s, 1H), 6.77 (t, *J* = 6.7 Hz, 1H), 5.96 (s, 2H); ^{13}C NMR (125 MHz, Acetone-d_6) δ 147.6, 147.4, 144.0, 127.1, 125.3, 123.0, 117.0, 110.0, 101.5, 98.0, 91.2, 78.3; FT-IR (KBr) 3435, 2955, 2917, 2850, 1737, 1643, 1512, 1466, 1384, 1287, 1180, 1019,752, 610 cm^{-1}; HRMS (ESI): calcd. for $C_{12}H_9N_2O_2$ $[M+H]^+$, 213.0659; found: 213.0656.

10-ethoxybenzo[4,5]imidazo[1,2-a]quinoline(3a)



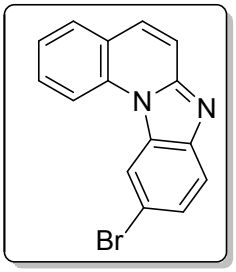
Yeild: 95%. purification: hexane/EtOAc (6:4); pale yellow solid, mp 119-120 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 8.9 Hz, 1H), 7.80 (d, *J* = 1.6 Hz, 1H), 7.75 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.66 (ddd, *J* = 8.6, 7.4, 1.5 Hz, 1H), 7.55 (s, 2H), 7.43 – 7.37 (m, 1H), 7.13 (dd, *J* = 8.8, 2.1 Hz, 1H), 4.16 (q, *J* = 7.0 Hz, 2H), 1.46 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.7, 145.9, 137.2, 133.7, 129.3, 128.3, 127.5, 127.4, 122.1, 121.6, 118.7, 115.9, 113.1, 111.7, 97.5, 62.7, 13.1; FT-IR (KBr) 3435, 2921, 2850, 1638, 1542, 1446, 1398, 1384, 1222, 1020, 814, 668 cm^{-1}; HRMS (ESI): calcd. for $C_{17}H_{15}N_2O$ $[M+H]^+$, 263.1179; found: 263.1176.

10-chlorobenzo[4,5]imidazo[1,2-a]quinoline(3b)



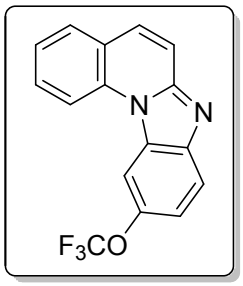
Yeild: 94%. purification: hexane/EtOAc (6:4); pale yellow solid, mp 136-137 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.5 Hz, 1H), 8.31 (s, 1H), 7.85 (d, *J* = 8.7 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.71 (t, *J* = 7.9 Hz, 1H), 7.64 (d, *J* = 9.4 Hz, 1H), 7.53 (d, *J* = 9.4 Hz, 1H), 7.48 – 7.41 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.8, 143.1, 135.3, 131.7, 131.1, 129.9, 129.7, 128.1, 125.1, 124.6, 123.4, 121.1, 117.6, 115.1, 114.0; FT-IR (KBr) 3400, 2917, 2850, 1735, 1634, 1543, 1459, 1439, 1396, 1279, 1018, 815, 759, 738, 668, 593 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{10}ClN_2$ $[M+H]^+$, 253.0527; found: 253.0522.

10-Bromobenzimidazo[1,2-*a*]quinoline (3c)



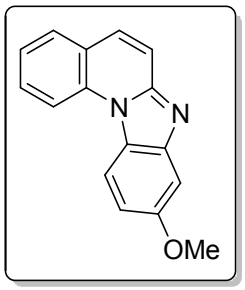
Yeild: 92%. purification: hexane/ EtOAc (6:4); white solid, mp 181-85 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.68 (d, *J* = 5.5 Hz, 2H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 9.5 Hz, 1H), 7.75 (dd, *J* = 15.2, 8.3 Hz, 2H), 7.55 (d, *J* = 8.6 Hz, 1H), 7.47 (dd, *J* = 8.4, 5.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 142.4, 134.1, 130.6, 130.5, 128.8, 128.6, 126.6, 123.5, 122.3, 120.4, 116.5, 115.8, 114.5, 114.0; FT-IR (KBr) 3435, 2954, 2917, 2850, 1734, 1632, 1542, 1457, 1396, 1020, 813, 770, 739 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{10}BrN_2$ $[M+H]^+$, 297.0022; found: 297.0021.

10-Trifluoromethoxybenzimidazo[1,2-*a*]quinoline (3d)



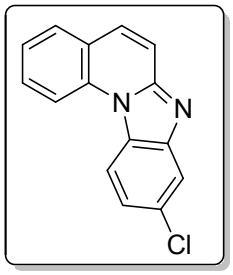
Yeild: 92%. purification: hexane/EtOAc (5:5); white solid, mp 149-150 °C, ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.67 (d, *J* = 8.5 Hz, 1H), 8.51 (s, 1H), 7.91 (t, *J* = 6.3 Hz, 1H), 7.87 (t, *J* = 7.1 Hz, 1H), 7.83 (d, *J* = 9.5 Hz, 1H), 7.79 – 7.71 (m, 1H), 7.53 – 7.44 (m, 2H), 7.47 – 7.37 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.4, 143.3, 142.2, 134.2, 130.7, 129.3, 128.9, 128.6, 123.6, 122.3, 121.0, 119.9, 118.5, 117.3, 116.6, 113.8, 106.7; FT-IR (KBr) 3388, 2954, 2916, 2849, 1730, 1641, 1545, 1448, 1398, 1307, 1261, 1197, 1148, 1019, 801, 772, 758, 743cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{10}F_3N_2O$ $[M+H]^+$, 303.0740; found: 303.0739.

9-methoxybenzo[4,5]imidazo[1,2-a]quinoline(3e)



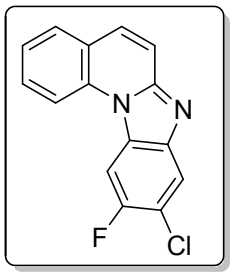
Yeild: 72%. purification: hexane/ EtOAc (6:4); brown solid, mp 121-122 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.5 Hz, 1H), 8.25 (d, *J* = 9.1 Hz, 1H), 7.85 (d, *J* = 6.9 Hz, 1H), 7.75 (t, *J* = 7.8 Hz, 1H), 7.66 (dd, *J* = 20.9, 9.5 Hz, 2H), 7.51 – 7.43 (m, 2H), 7.11 (dd, *J* = 9.1, 2.5 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.4, 148.5, 135.3, 130.8, 129.7, 129.5, 125.3, 124.1, 123.3, 123.2, 117.3, 115.0, 114.5, 112.9, 101.5, 55.7; FT-IR (KBr) 3439, 2954, 2918, 2850, 1735, 1606, 1539, 1487, 1450, 1393, 1285, 1205, 1162, 1021, 808, 772 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{13}N_2O$ $[M+H]^+$, 249.1023; found: 249.1013.

9-chlorobenzo[4,5]imidazo[1,2-a]quinoline(3f)



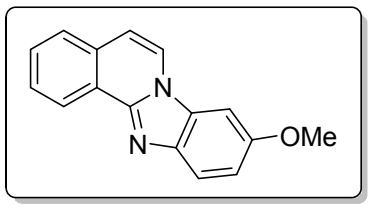
Yeild: 73%. purification: hexane/EtOAc (6:4); pale yellow solid, mp 174-175 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.5 Hz, 1H), 8.27 (d, *J* = 8.9 Hz, 1H), 7.96 (d, *J* = 2.0 Hz, 1H), 7.85 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.79 – 7.69 (m, 2H), 7.60 (d, *J* = 9.5 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.43 (dd, *J* = 8.9, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 145.6, 135.3, 131.8, 130.1, 129.9, 129.7, 124.5, 123.4, 123.2, 122.9, 120.0, 117.5, 115.1, 114.6;
FT-IR (KBr) 3435, 2916, 2849, 1632, 1539, 1450, 1020, 809 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{10}ClN_2$ $[M+H]^+$, 253.0527; found: 253.0536.

9-chloro-10-fluorobenzo[4,5]imidazo[1,2-a]quinoline(3g)



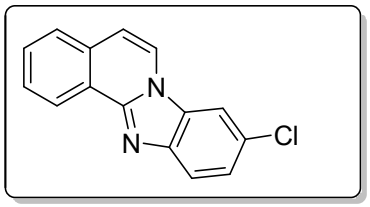
Yeild: 75%. purification: hexane/EtOAc (5:5); pale yellow solid, mp 205-206 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.5 Hz, 1H), 8.18 (d, *J* = 9.8 Hz, 1H), 8.01 (d, *J* = 7.0 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.82 – 7.75 (m, 1H), 7.72 (d, *J* = 9.5 Hz, 1H), 7.58 (d, *J* = 9.5 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.0, 153.1, 149.5 (d, *J* = 2.6 Hz), 141.2, 135.0, 131.8, 129.9 (d, *J* = 21.9 Hz), 128.6, 124.8, 123.4, 121.0, 118.4, 117.5, 114.7, 101.8 (d, *J* = 28.9 Hz); FT-IR (KBr) 3373, 2955, 2917, 2850, 1736, 1613, 1542, 1459, 1399, 1158, 1019, 815, 759 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_9ClFN_2$ $[M+H]^+$, 271.0433; found: 271.0439.

9-methoxybenzo[4,5]imidazo[2,1-a]isoquinoline(3h)



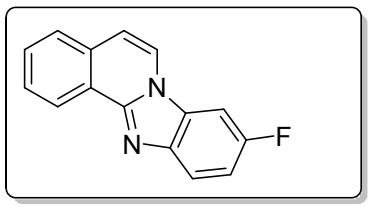
Yeild: 85%. purification: hexane/EtOAc (6:4); brown solid, mp 107-108 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 – 8.65 (m, 1H), 7.96 (d, *J* = 7.3 Hz, 1H), 7.83 (d, *J* = 8.9 Hz, 1H), 7.59 (ddd, *J* = 12.5, 9.7, 6.2 Hz, 3H), 7.14 (d, *J* = 2.2 Hz, 1H), 7.06 (dd, *J* = 8.9, 2.3 Hz, 1H), 6.94 (d, *J* = 7.3 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.1, 146.4, 137.5, 131.2, 130.2, 129.7, 128.3, 127.0, 124.6, 123.5, 121.1, 120.2, 114.6, 111.4, 93.1, 56.0; FT-IR (KBr) 3206, 2959, 2918, 2850, 1733, 1642, 1487, 1456, 1260, 1213, 1177, 1095, 1020, 799, 763 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{13}N_2O$ $[M+H]^+$, 249.1023; found: 249.1018.

9-chlorobenzo[4,5]imidazo[2,1-a]isoquinoline(3i)



Yeild: 85%. purification: hexane/EtOAc (6:4); brown solid, mp 149-150 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (br, 1H), 8.04 (d, *J* = 7.3 Hz, 1H), 7.85 (d, *J* = 8.7 Hz, 1H), 7.78 (d, *J* = 1.8 Hz, 1H), 7.70 (d, *J* = 4.0 Hz, 1H), 7.67 – 7.62 (m, 2H), 7.40 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.09 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.0, 130.3, 129.3, 128.7, 127.4, 126.6, 125.8, 124.4, 123.8, 119.4, 118.8, 114.2, 113.9, 111.1, 108.8; FT-IR (KBr) 3435, 2955, 2917, 2850, 1732, 1643, 1458, 1377, 1019, 760 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{10}ClN_2$ $[M+H]^+$, 253.0527; found: 253.0522.

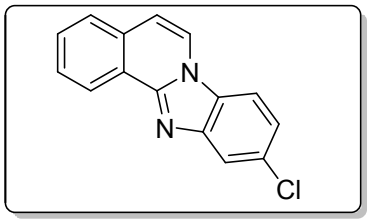
9-fluorobenzo[4,5]imidazo[2,1-a]isoquinoline(3j)



Yeild: 84%. purification: hexane/EtOAc (6:4); brown solid, mp 142-143 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (br, 1H), 7.98 (d, *J* = 7.1 Hz, 1H), 7.87 (dd, *J* = 8.6, 4.6 Hz, 1H), 7.67 (br, 1H), 7.62 (d, *J* = 3.3 Hz, 2H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.18 (d, *J* = 7.1 Hz, 1H), 7.01 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 156.6, 146.8, 138.8, 130.3, 129.1, 127.4, 126.1, 123.8, 122.5, 120.0, 119.5 (d, *J* = 9.8 Hz), 112.3 (d, *J* = 25.1 Hz), 110.8, 95.6 (d, *J*

= 27.7 Hz); FT-IR (KBr) 3439, 2955, 2917, 2850, 1736, 1641, 1619, 1521, 1489, 1384, 1214, 1022, 814 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{10}FN_2$ $[M+H]^+$, 237.0823; found: 237.0828.

10-chlorobenzo[4,5]imidazo[2,1-a]isoquinoline(3k)



Yeild: 72%. purification: hexane/EtOAc (6:4); brown solid, mp 170-171 °C, ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (br, 1H), 8.14 (d, *J* = 7.2 Hz, 1H), 7.99 (s, 1H), 7.77 (br, 2H), 7.71 (d, *J* = 4.2 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 1H), 7.13 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.1, 143.3, 130.6, 129.4, 129.3, 127.4, 126.1, 124.1, 124.0, 121.3, 120.1, 118.5, 118.1, 111.0, 109.5; FT-IR (KBr) 3435, 2955, 2918, 2850, 1733, 1643, 1465, 1402, 1384, 1271, 1019, 785, 668 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{10}ClN_2$ $[M+H]^+$, 253.0527; found: 253.0526.

4. References

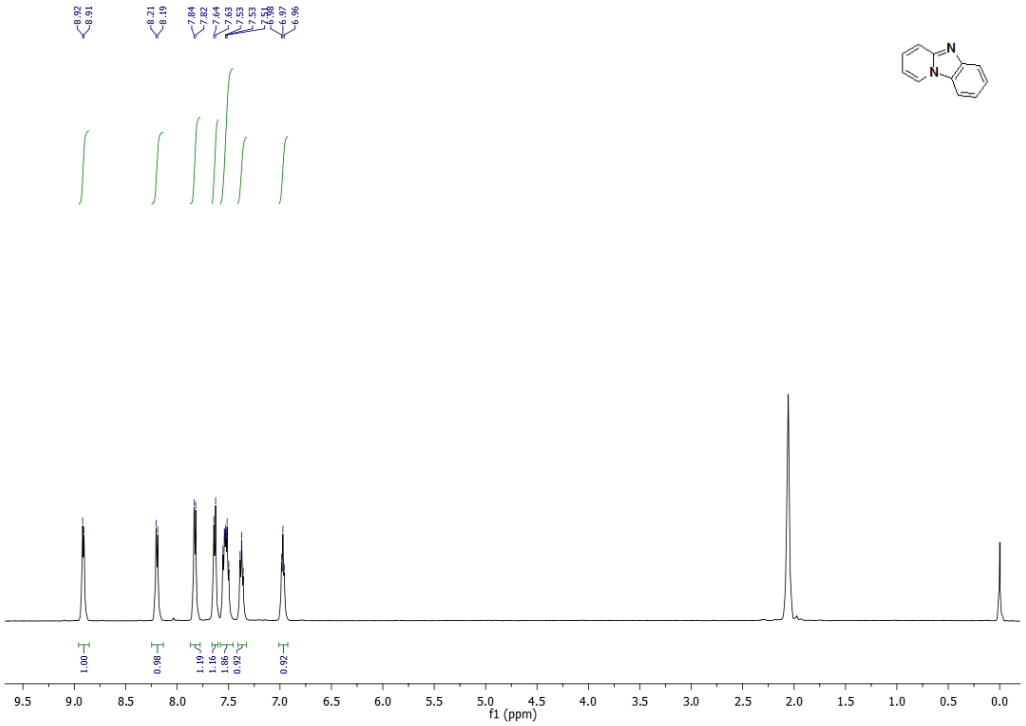
(1) D. N. Rao, Sk. Rasheed, S. Aravinda, R. A. Vishwakarma and P. Das, *RSC Adv.*, 2013, **3**, 11472.

(2) H. Wang, Y. Wang, C. Peng, J. Zhang and Q. Zhu, *J. Am.Chem. Soc.*, 2010, **132**, 13217.

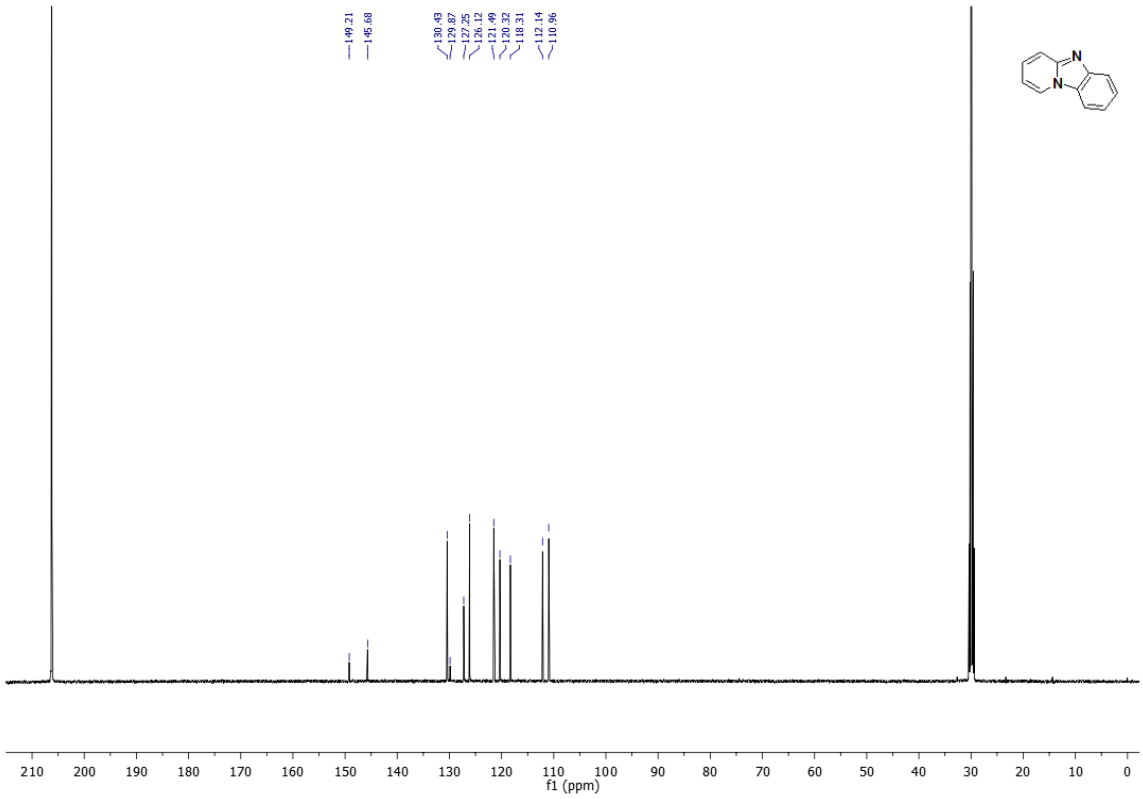
(3) K.-S. Masters, T. R. M. Rauws, A. K. Yadav, W. A. Herrebout, B. Van der Veken and B. U. W. Maes, *Chem.-Eur. J.*, 2011, **17**, 6315.

5. Copies of ^{1}H NMR and ^{13}C NMR Spectra

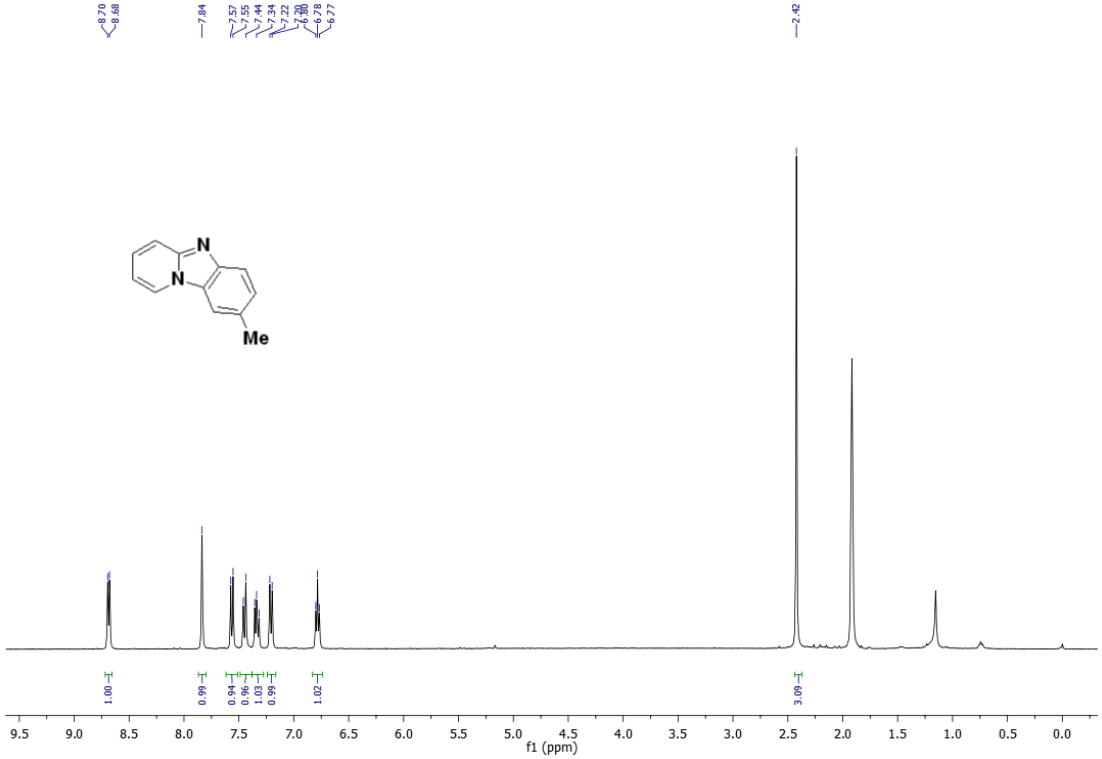
^{1}H-NMR spectra of pyrido[1,2-*a*]benzimidazole (2a)



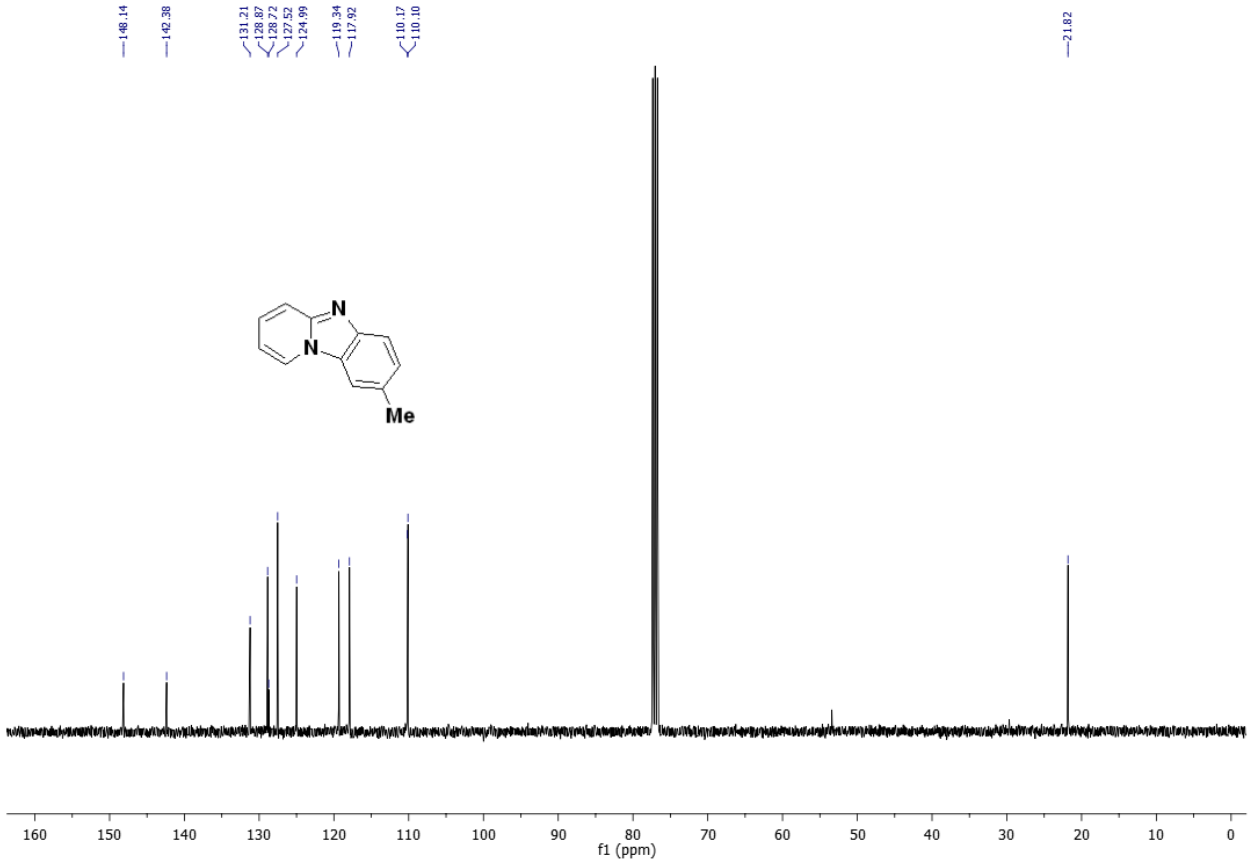
^{13}C-NMR spectra of pyrido[1,2-*a*]benzimidazole (2a)



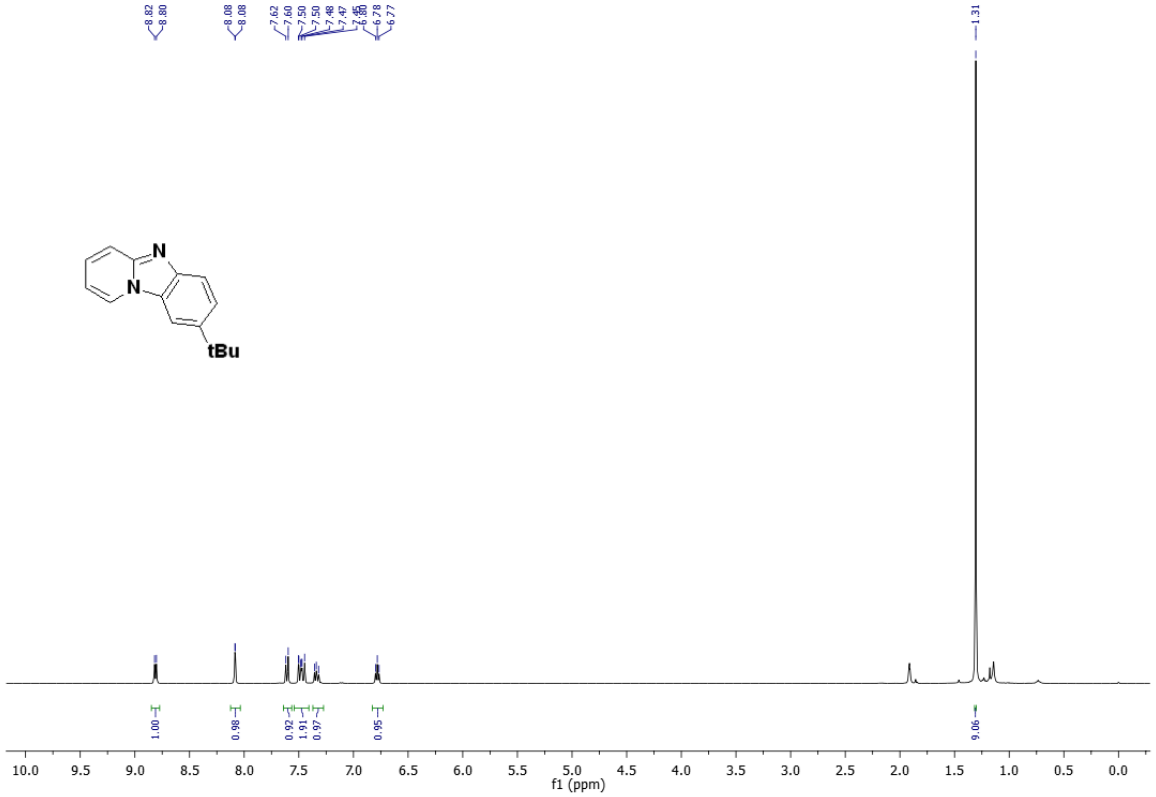
[1]H-NMR spectra of 8-methylpyrido[1,2-*a*]benzimidazole (2b)



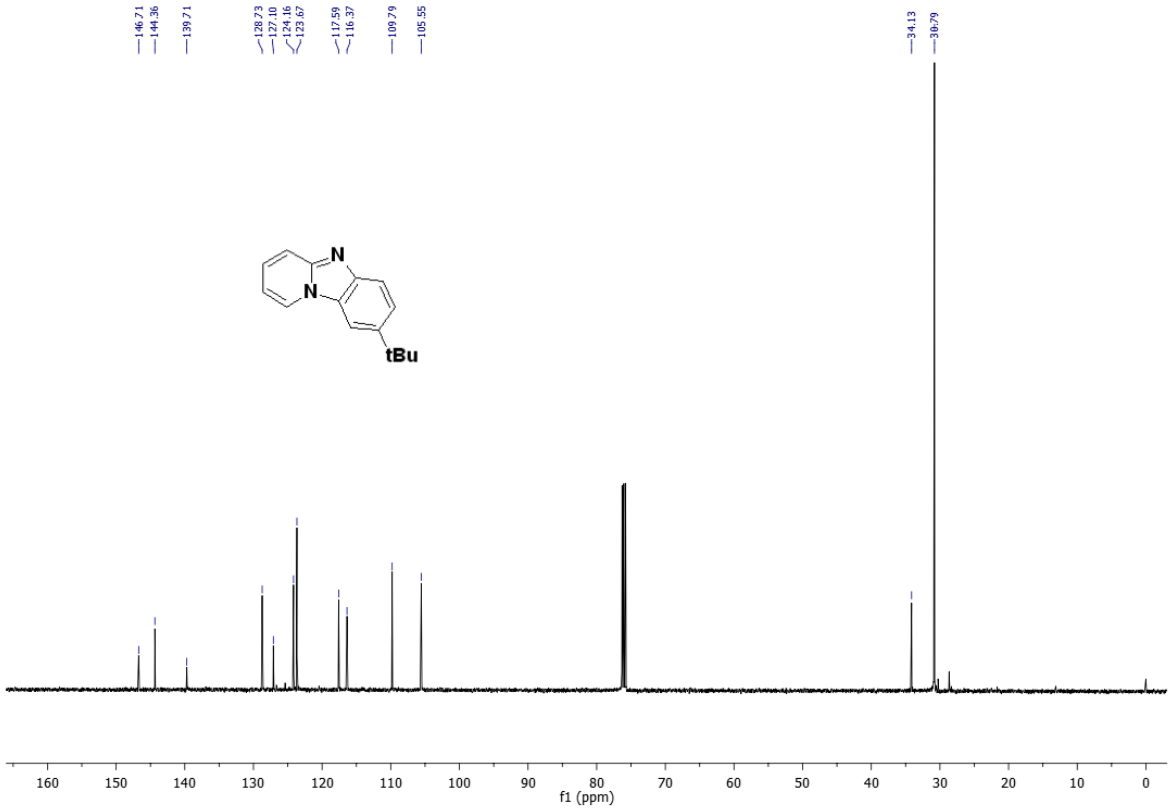
[13]C-NMR spectra of 8-methylpyrido[1,2-*a*]benzimidazole (2b)



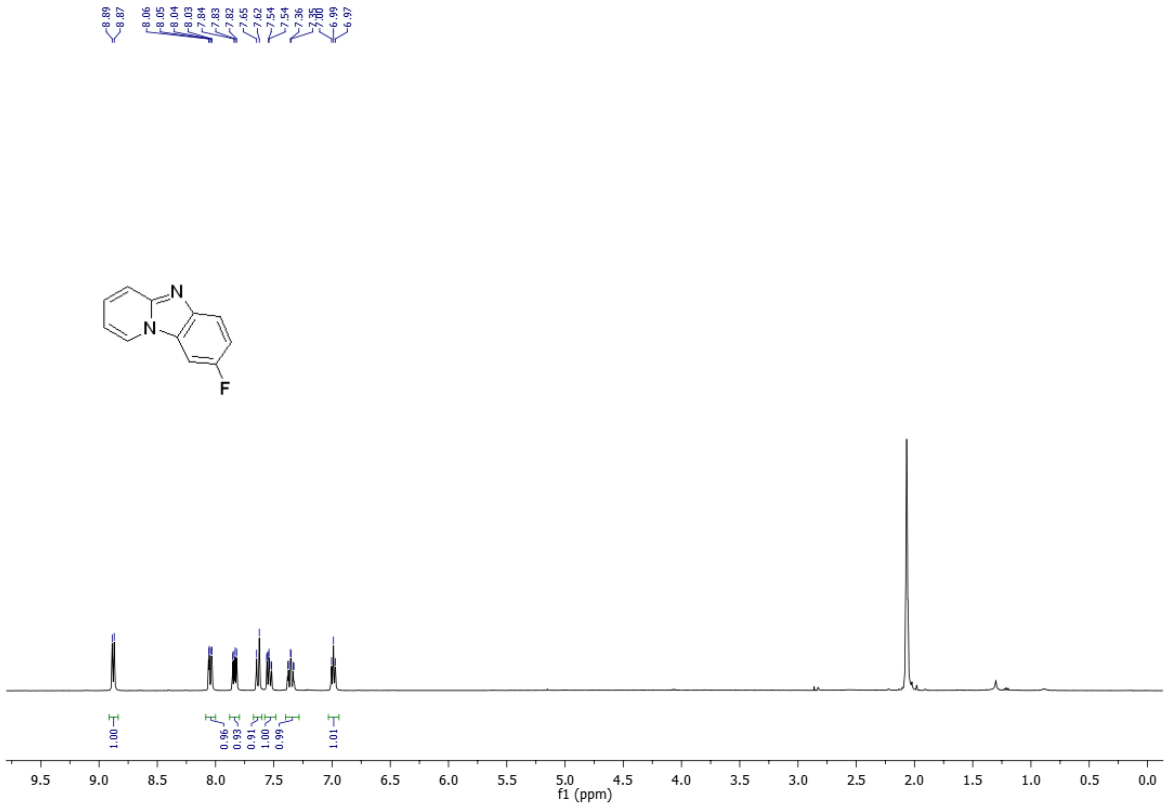
[1]H-NMR spectra of 8-(tert- butyl)pyrido[1,2-*a*]benzimidazole (2c)



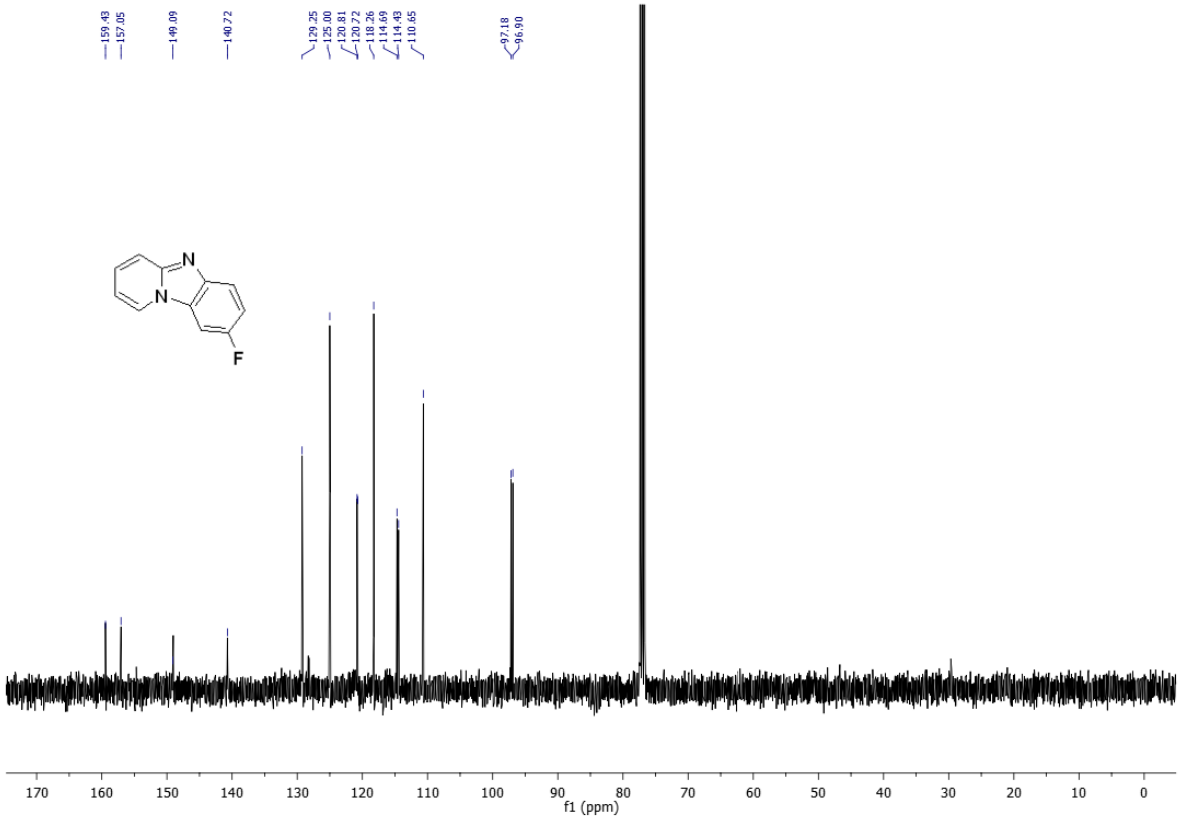
[13]C-NMR spectra of 8-(tert- butyl)pyrido[1,2-*a*]benzimidazole (2c)



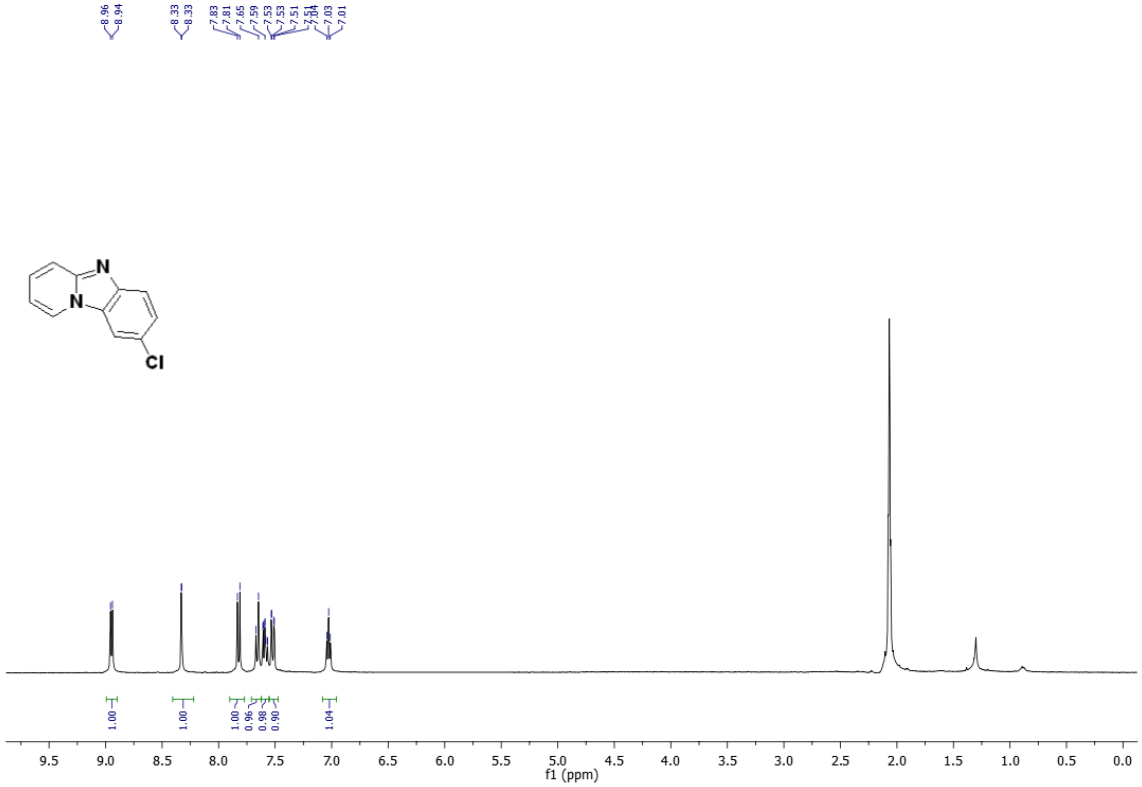
[1]H-NMR spectra of 8-fluoropyrido[1,2-*a*]benzimidazole (2d)



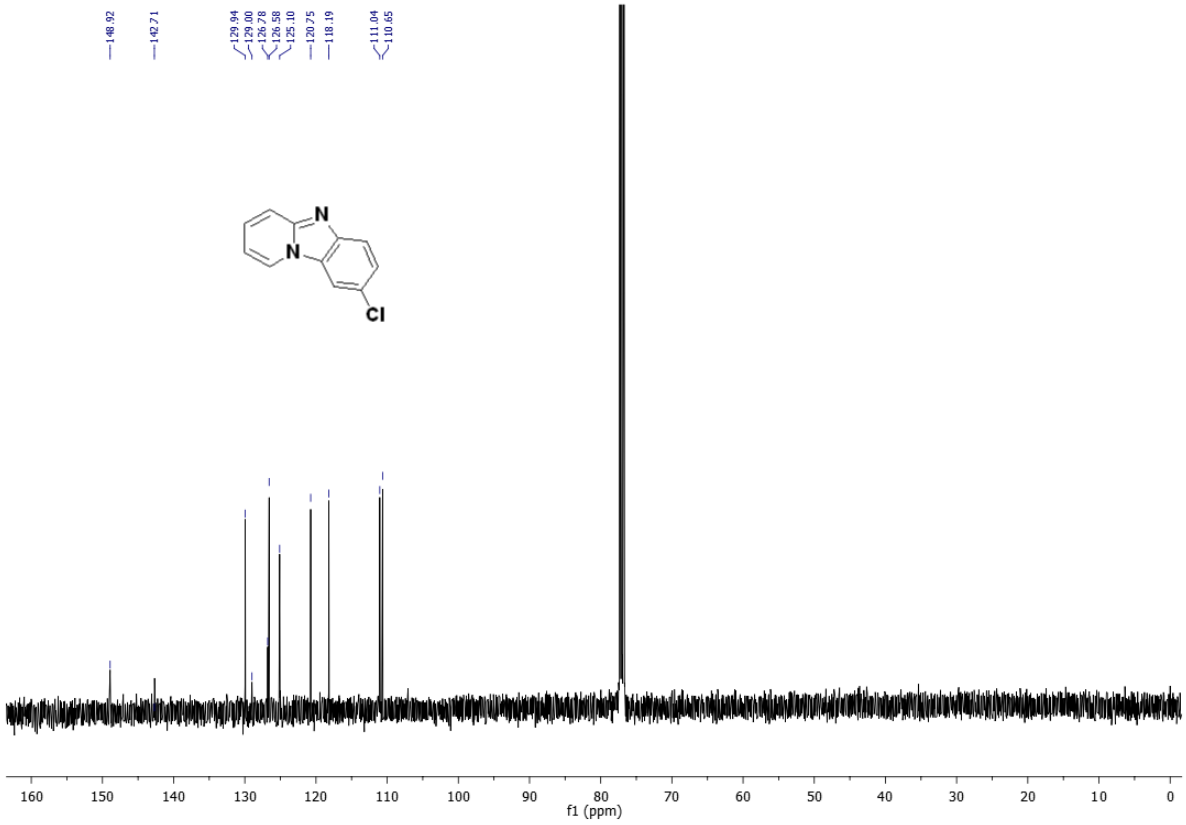
[13]C-NMR spectra of 8-fluoropyrido[1,2-*a*]benzimidazole (2d)



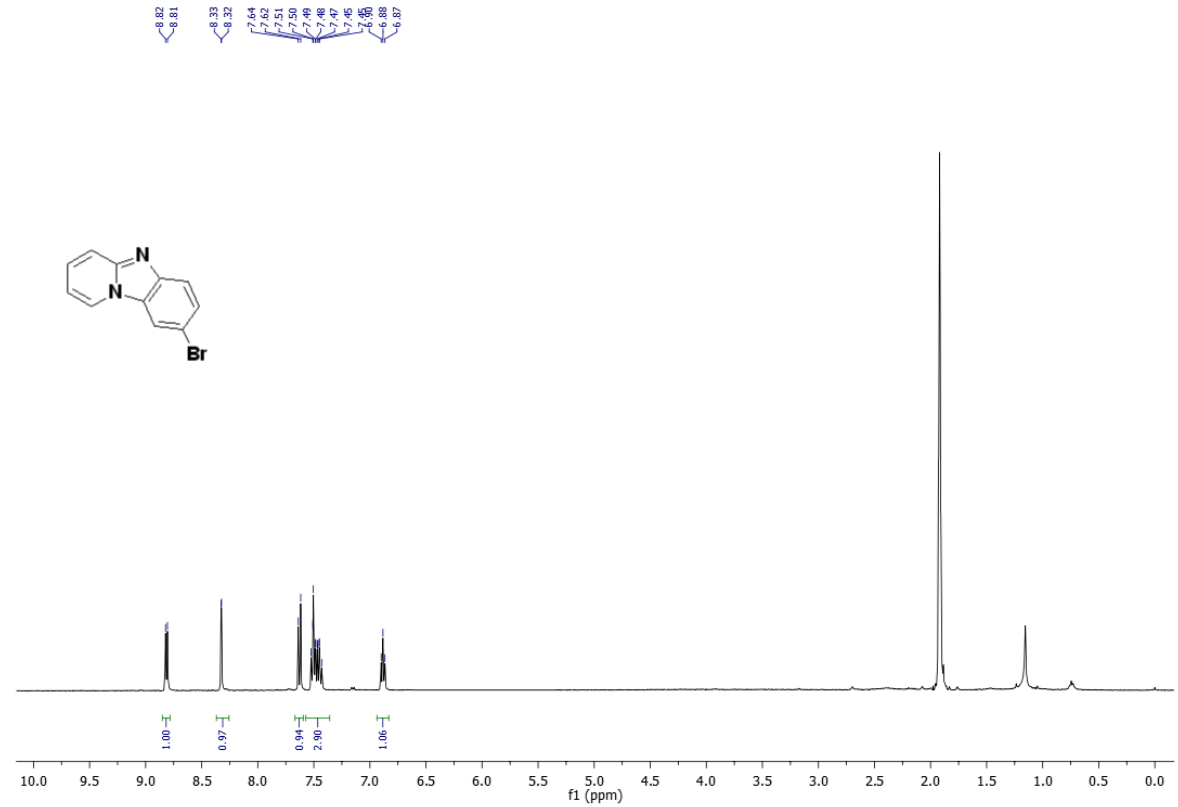
[1]H-NMR spectra of 8-chloropyrido[1,2-*a*]benzimidazole (2e)



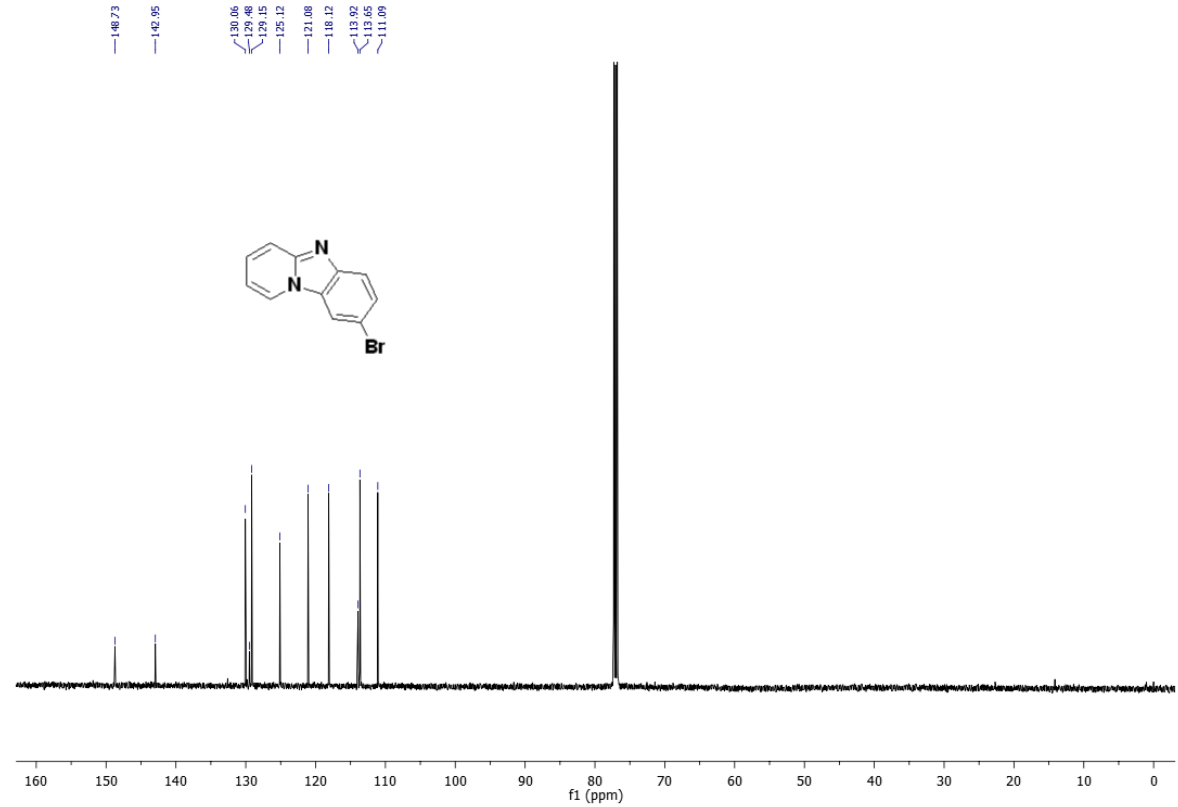
[13]C-NMR spectra of 8-chloropyrido[1,2-*a*]benzimidazole (2e)



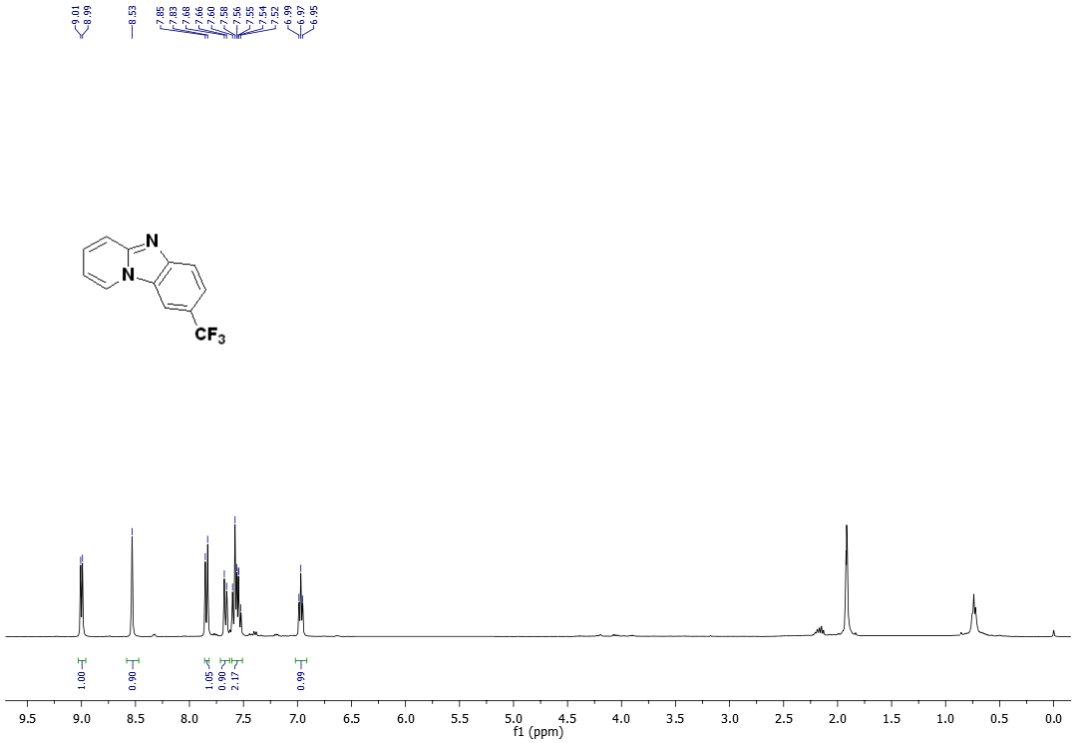
[1]H-NMR spectra of 8-Bromopyrido[1,2-*a*]benzimidazole (2f)



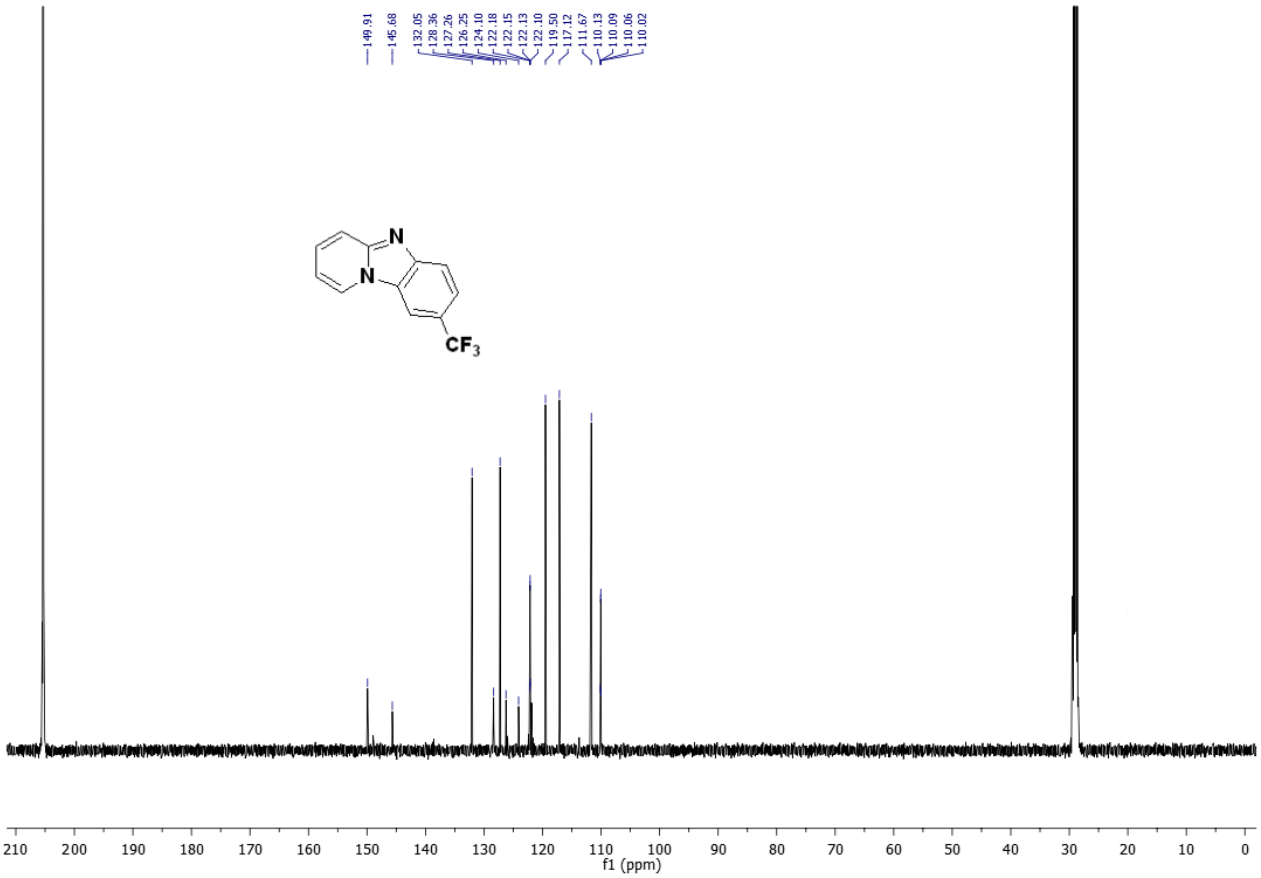
[13]C-NMR spectra of 8-Bromopyrido[1,2-*a*]benzimidazole (2f)



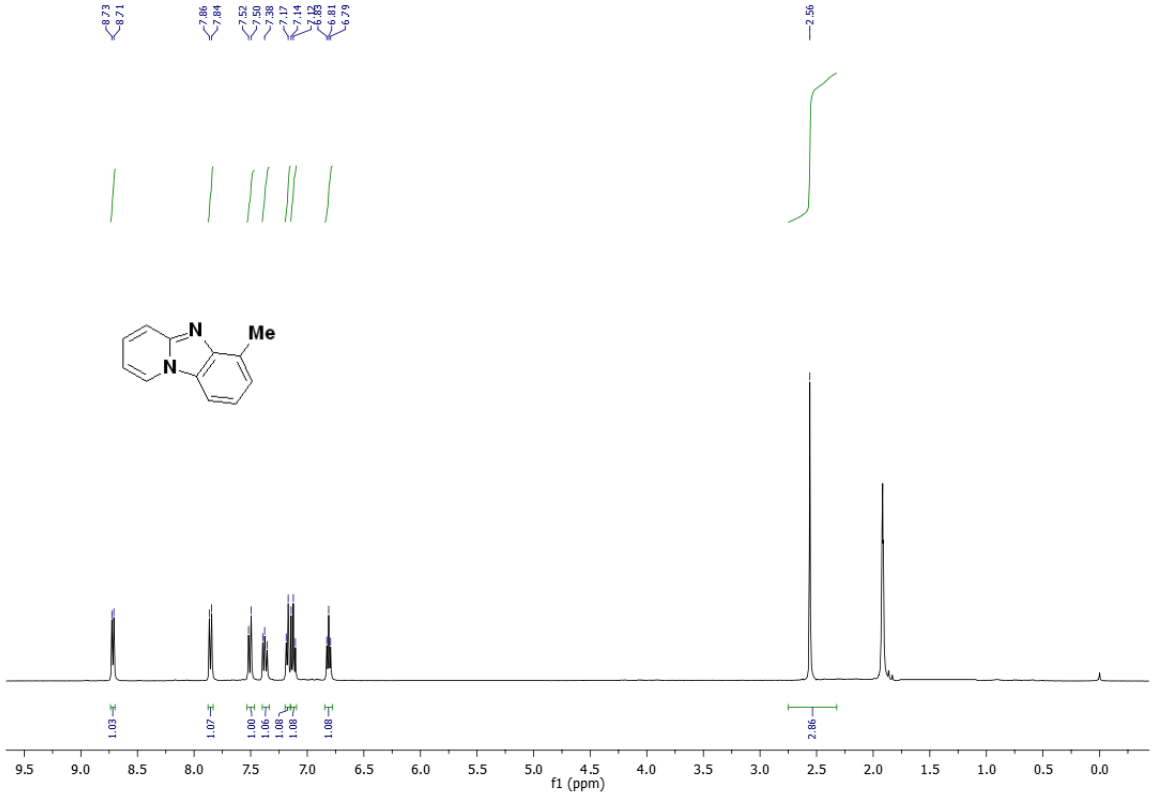
[1]H-NMR spectra of 8-trifluoromethylpyrido[1,2-*a*]benzimidazole (2g)



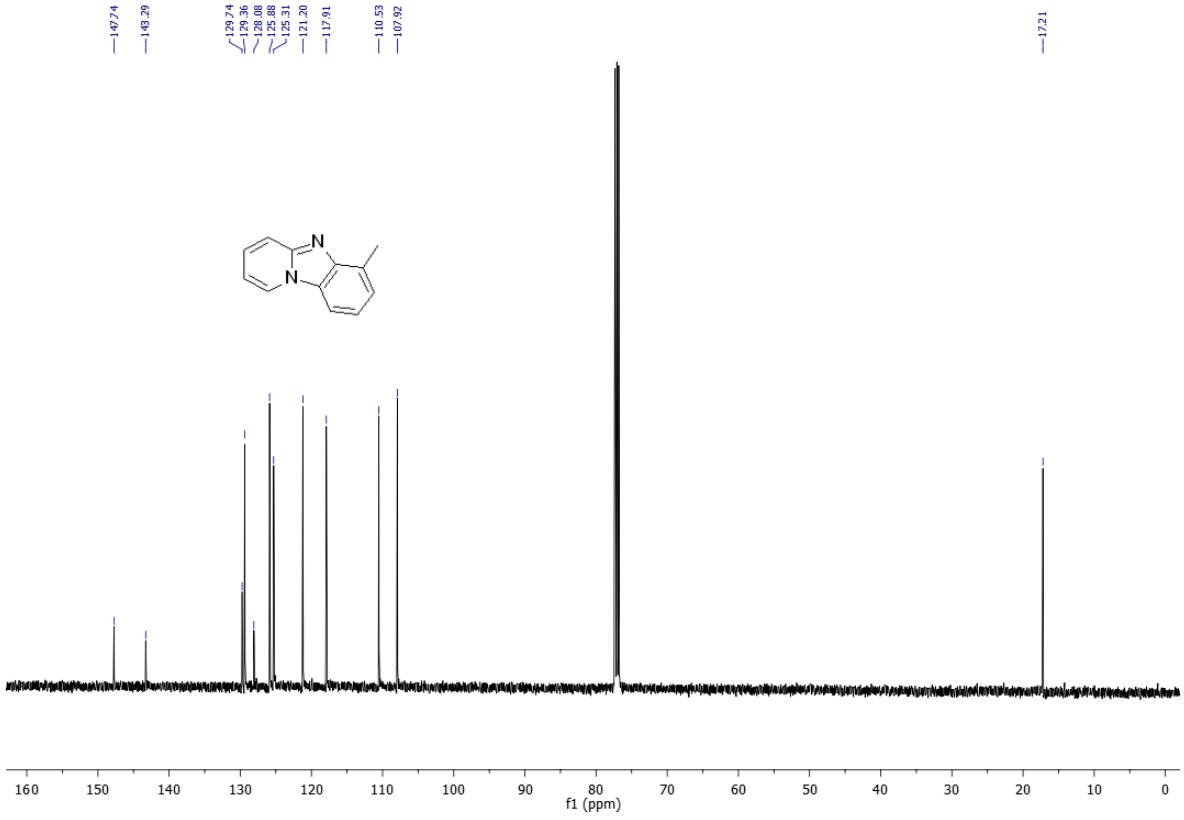
[13]C-NMR spectra of 8-trifluoromethylpyrido[1,2-*a*]benzimidazole (2g)



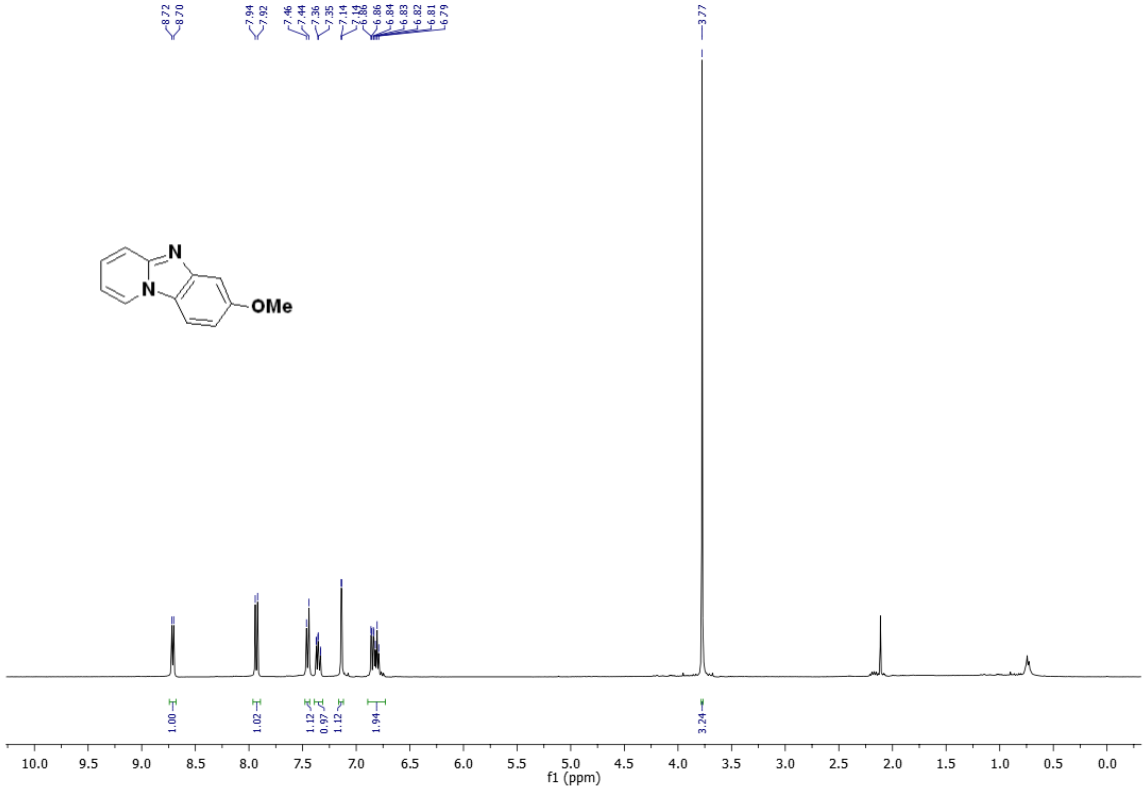
^{1}H-NMR spectra of 6-methylpyrido[1,2-*a*]benzimidazole (2h)



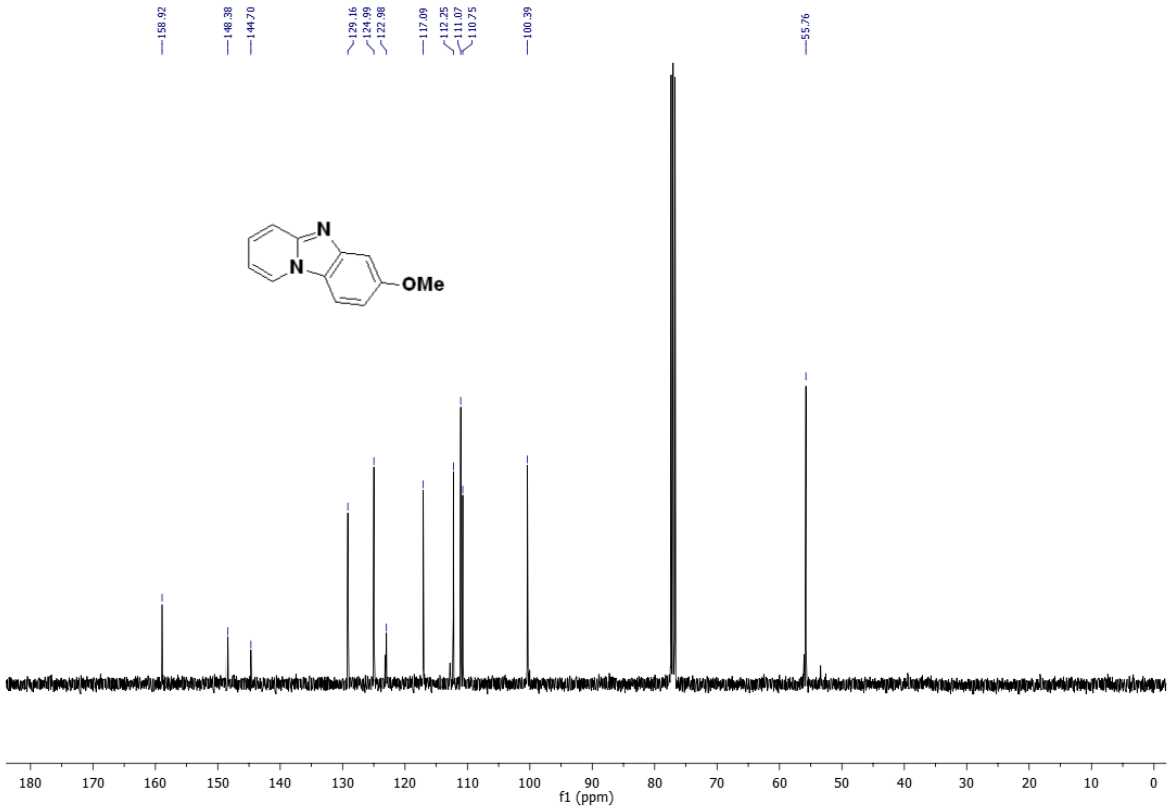
^{13}C-NMR spectra of 6-methylpyrido[1,2-*a*]benzimidazole (2h)



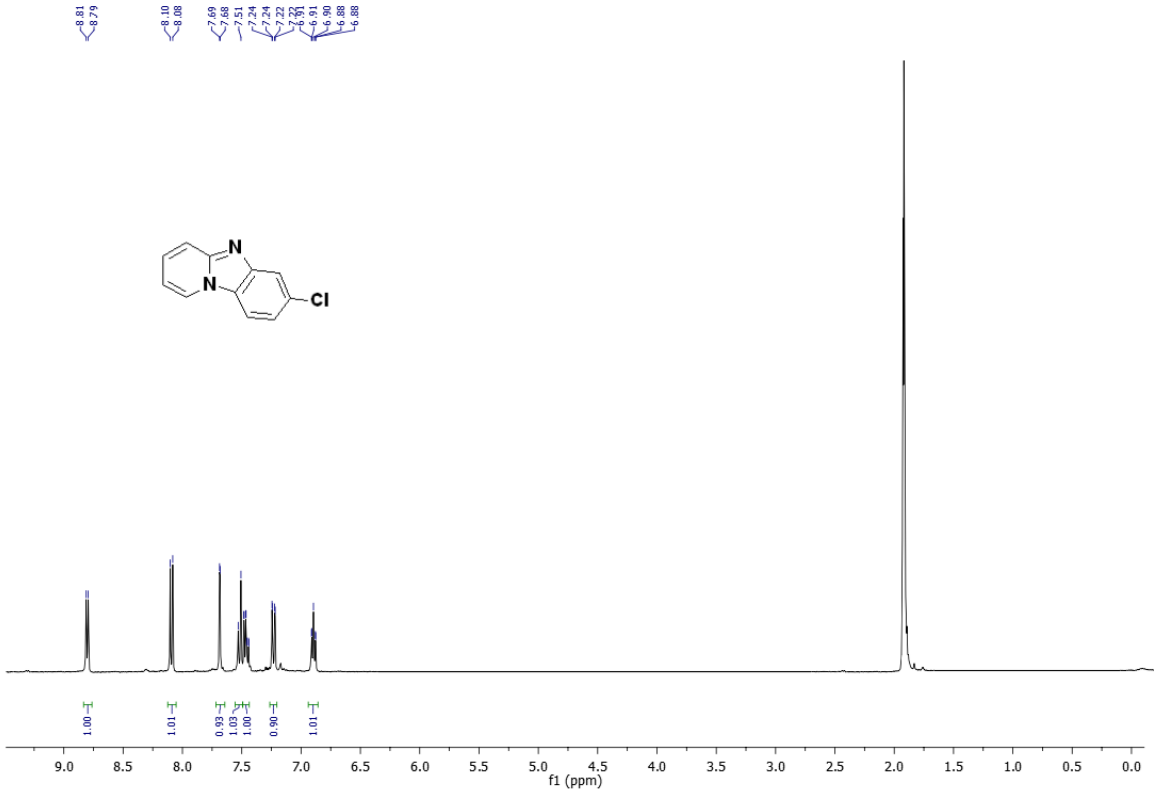
[1]H-NMR spectra of 7-methoxypyrido[1,2-*a*]benzimidazole (2i)



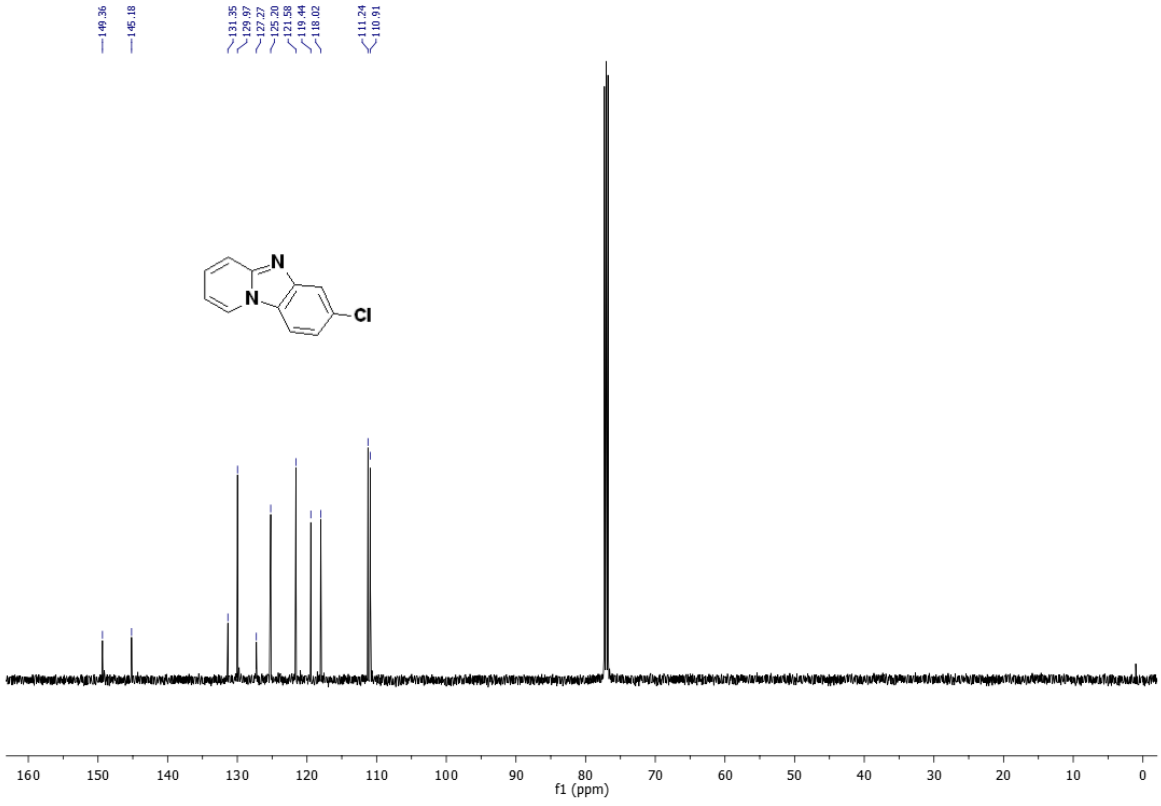
[13]C-NMR spectra of 7-methoxypyrido[1,2-*a*]benzimidazole (2i)



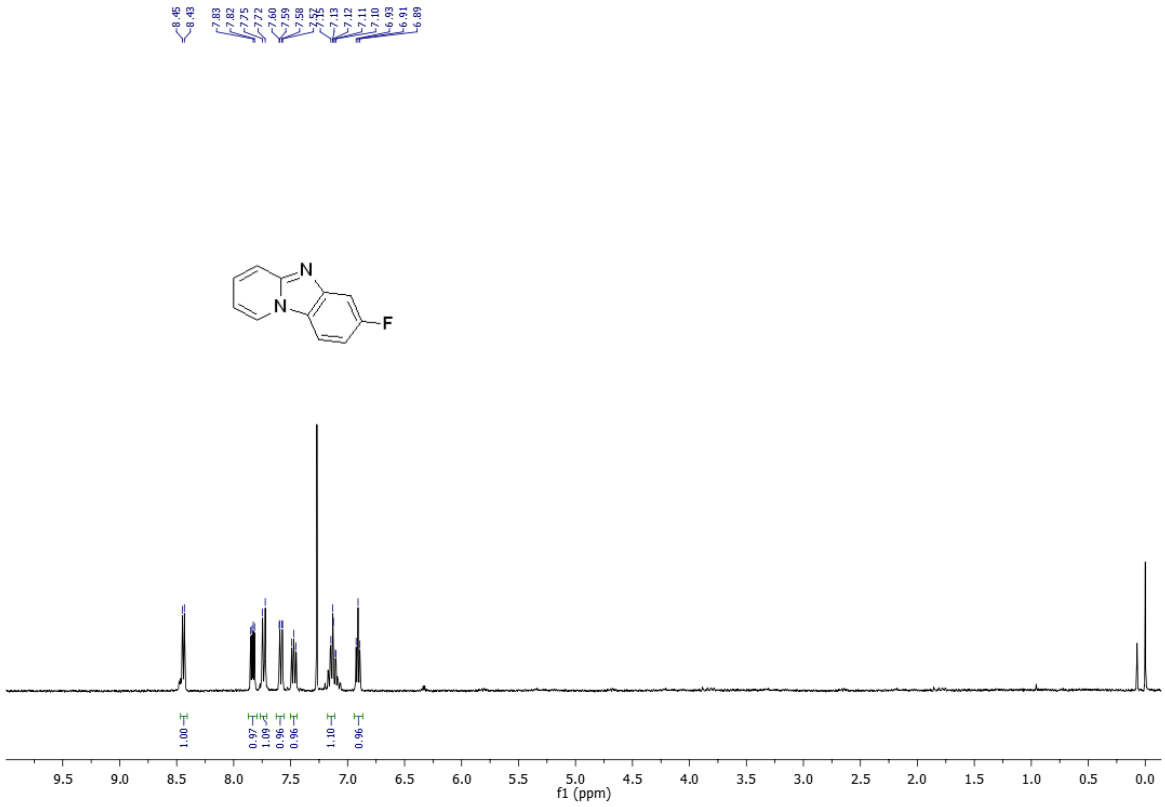
^{1}H-NMR spectra of 7-chloropyrido[1,2-*a*]benzimidazole (2j)



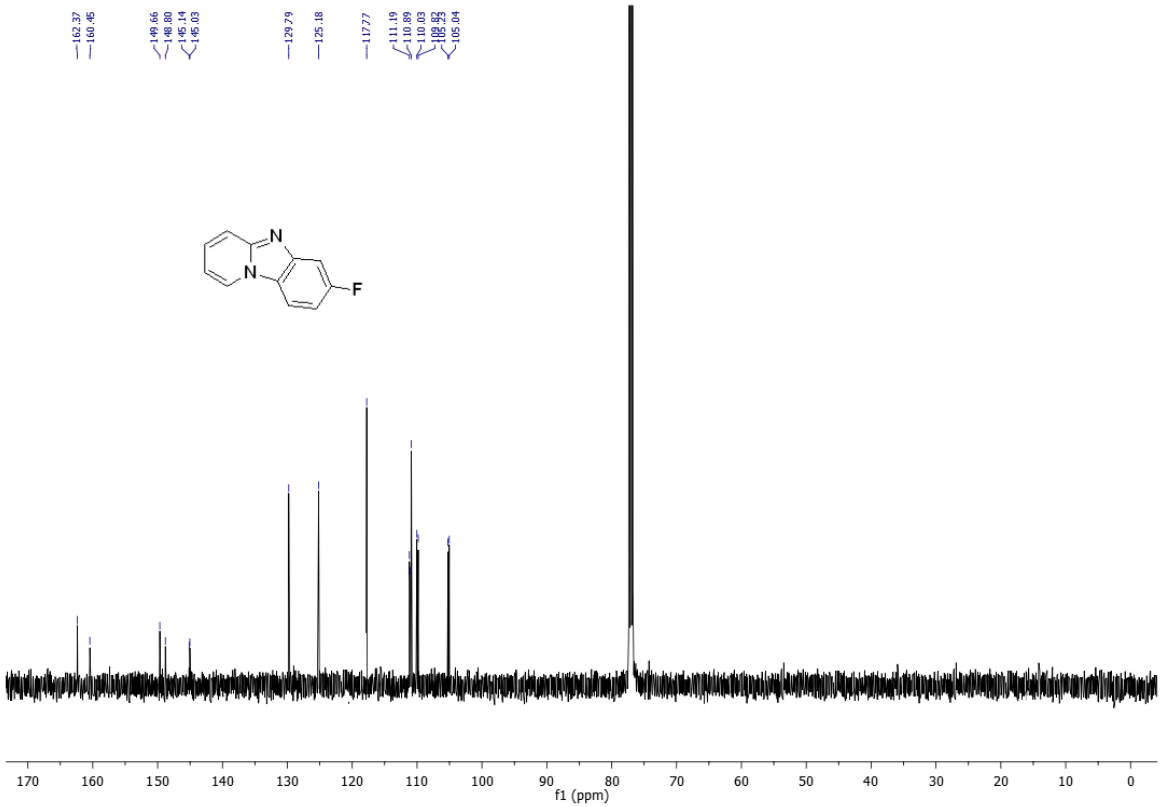
^{13}C-NMR spectra of 7-chloropyrido[1,2-*a*]benzimidazole (2j)



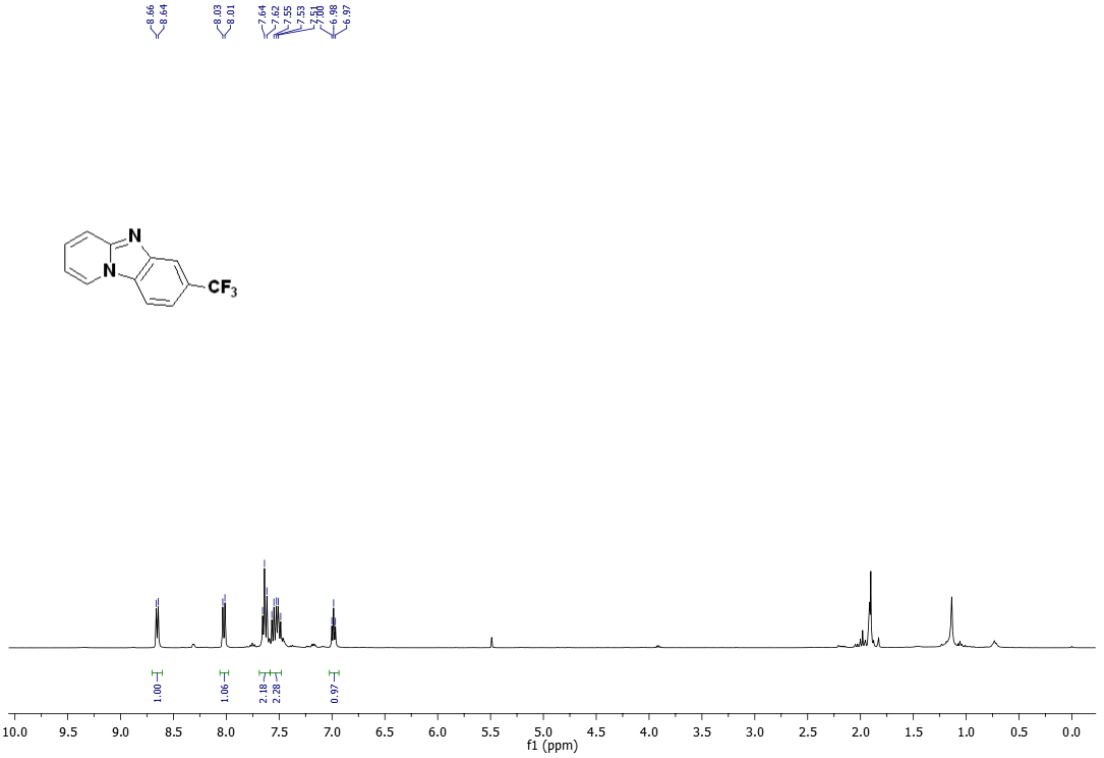
[1]H-NMR spectra of 7-fluoropyrido[1,2-*a*]benzimidazole (2k)



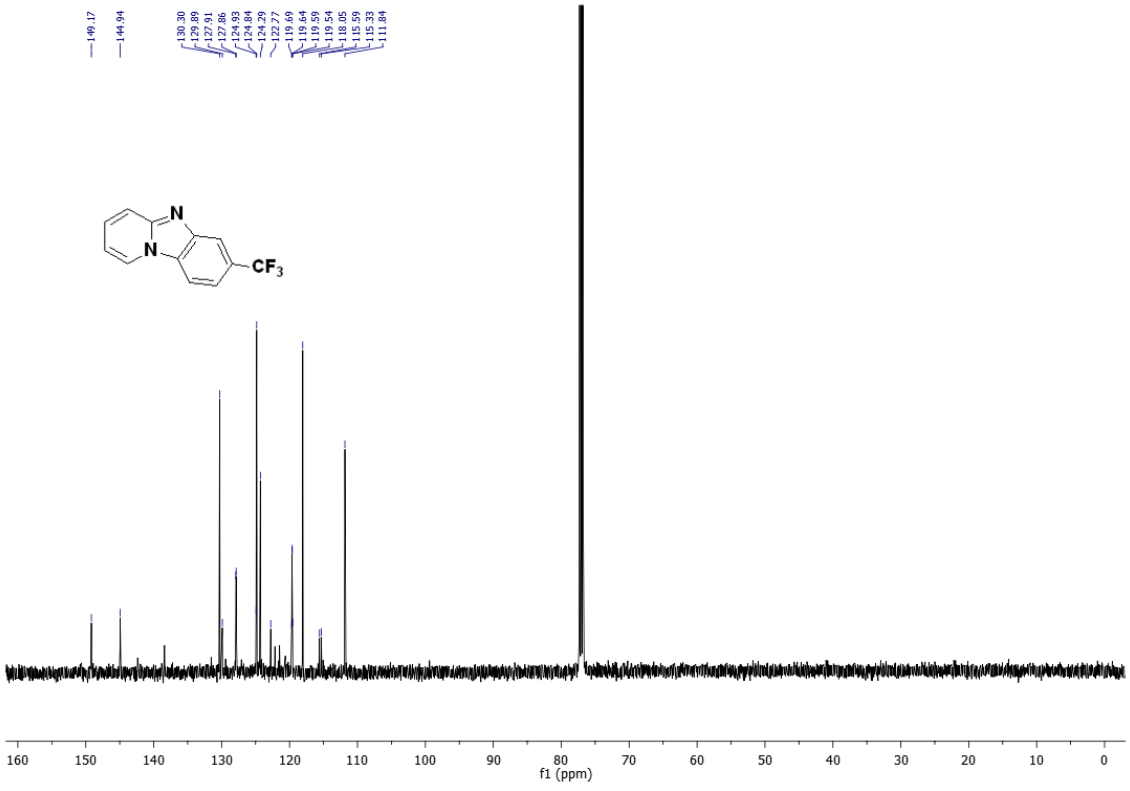
[13]C-NMR spectra of 7-fluoropyrido[1,2-*a*]benzimidazole (2k)



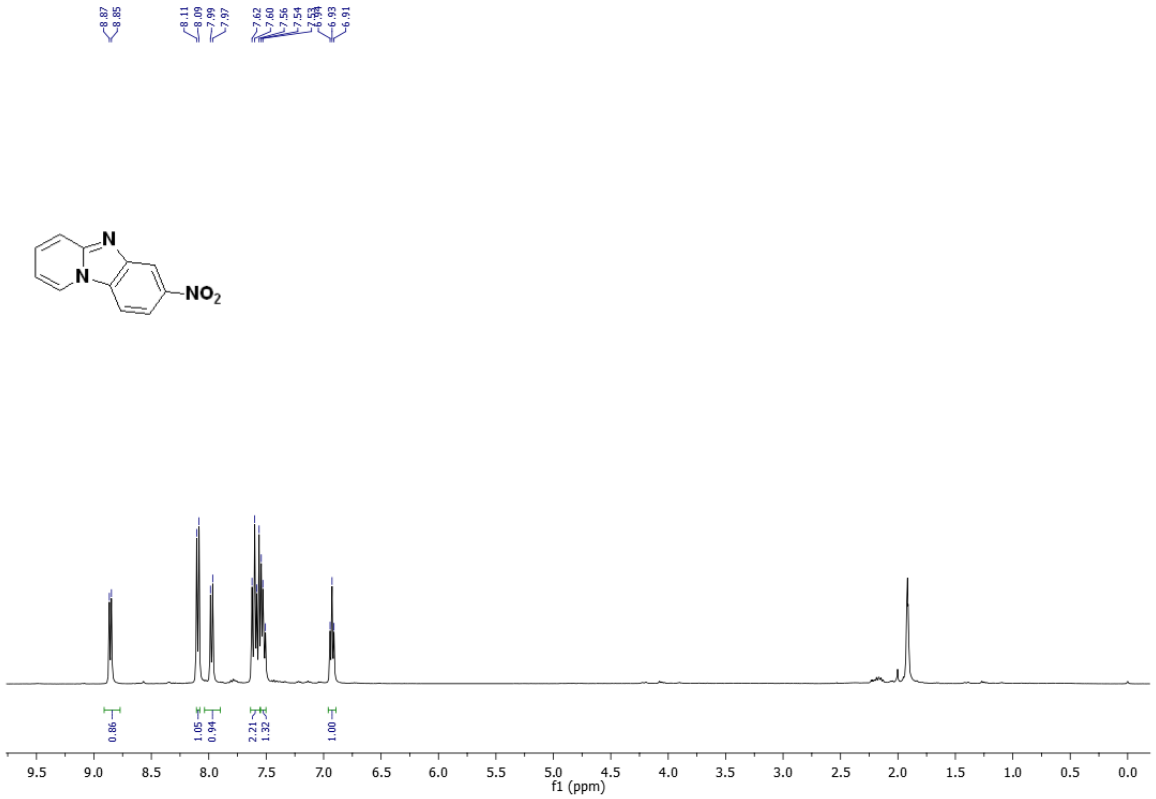
[1]H-NMR spectra of 7-trifluoromethylpyrido[1,2-*a*]benzimidazole (2l)



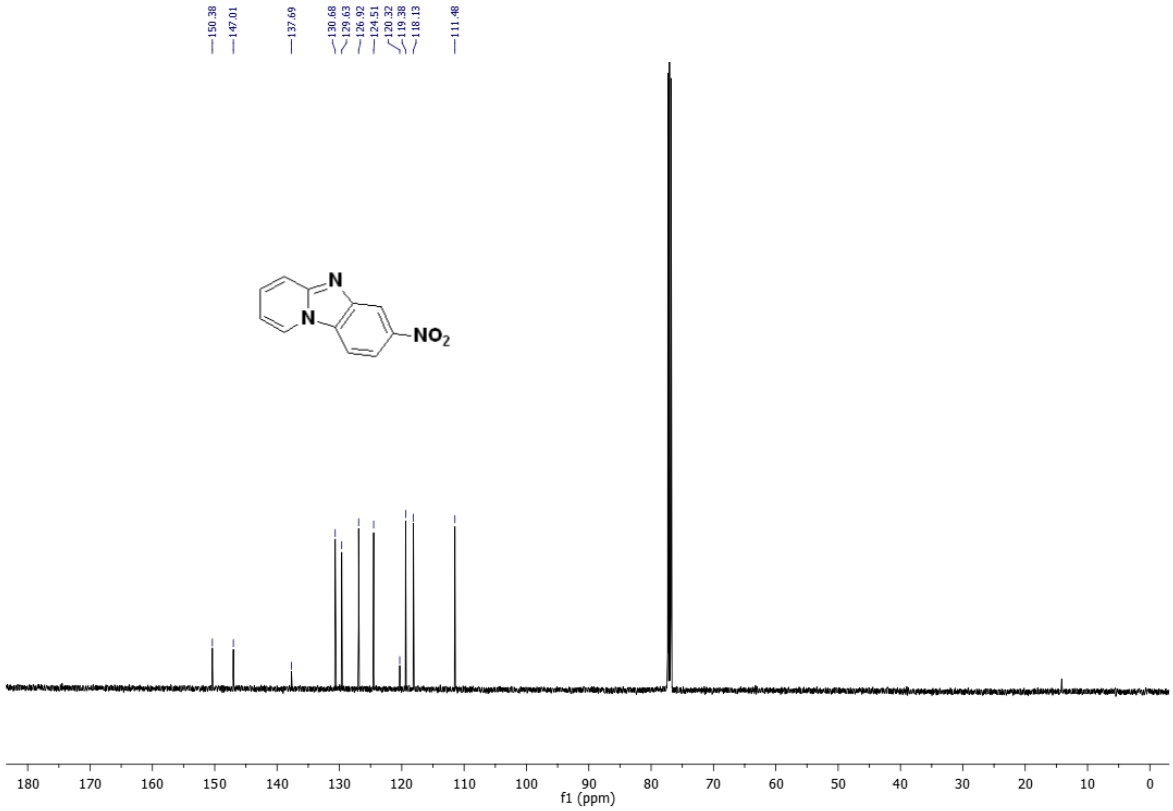
[1]H-NMR spectra of 7-trifluoromethylpyrido[1,2-*a*]benzimidazole (2l)



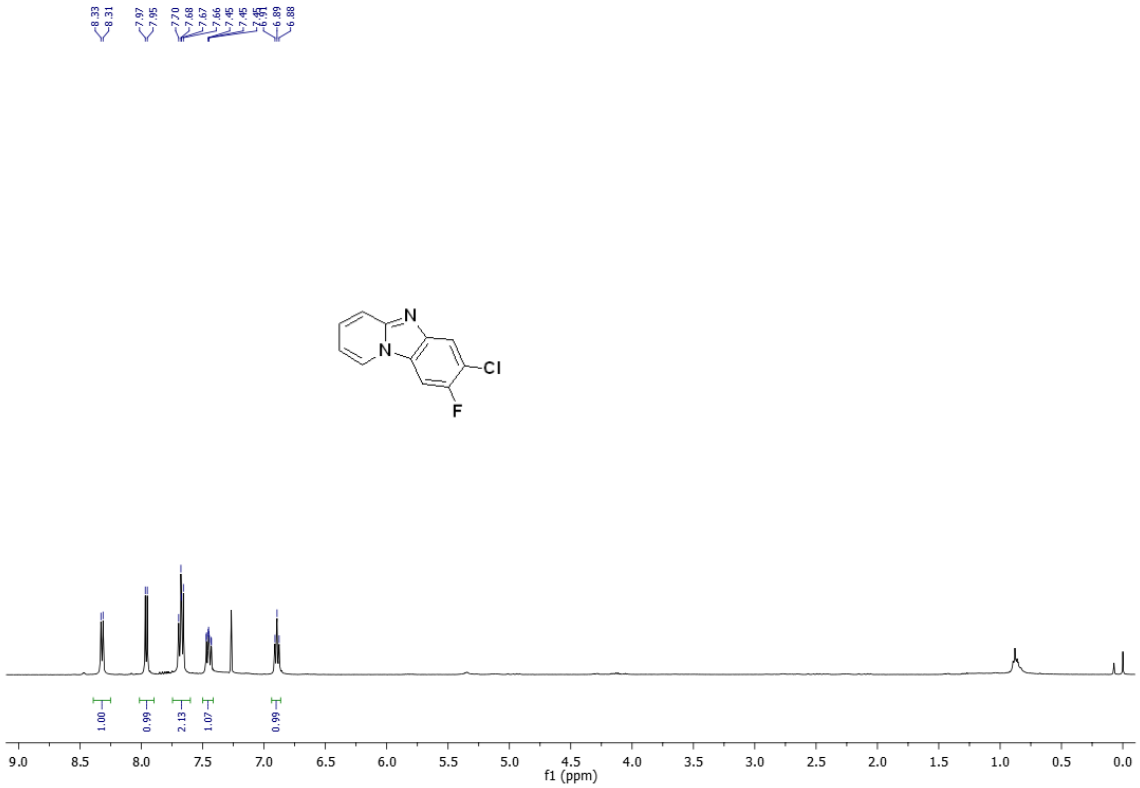
[1]H-NMR spectra of 7-nitropyrido[1,2-*a*]benzimidazole (2m)



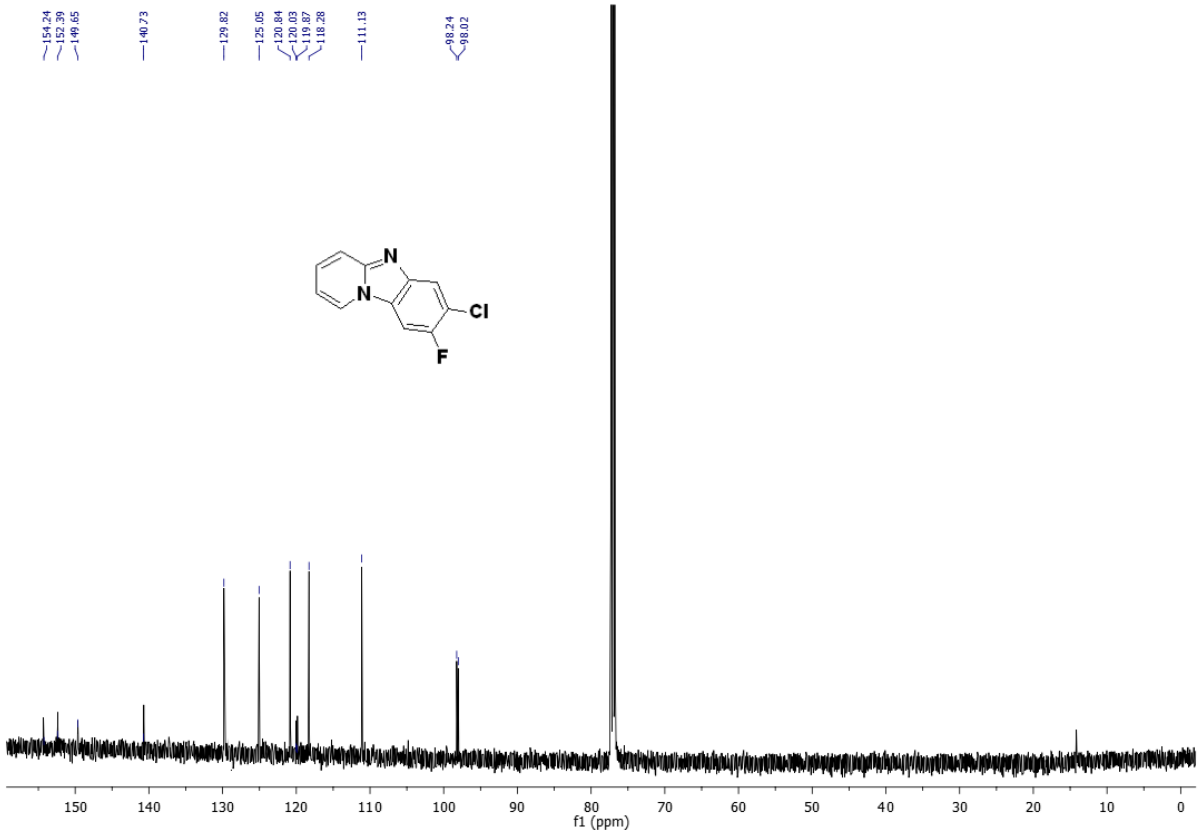
[13]C-NMR spectra of 7-nitropyrido[1,2-*a*]benzimidazole (2m)



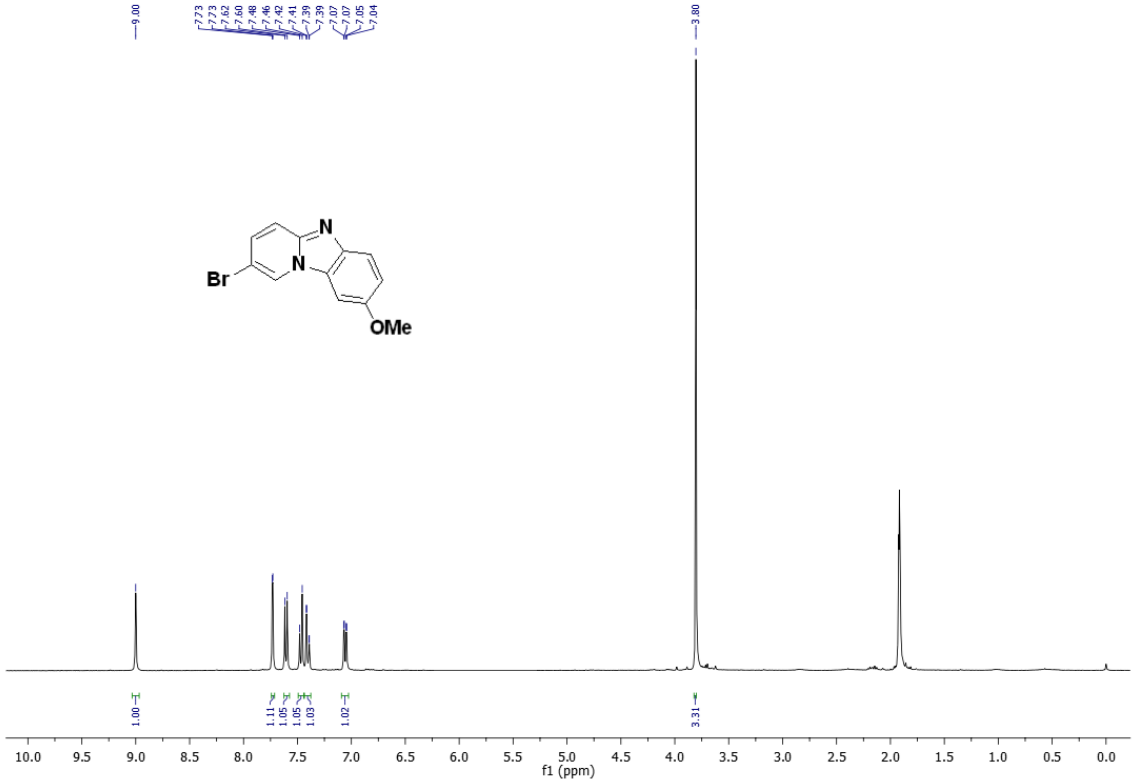
[1]H-NMR spectra of 7-chloro-8-fluorobenzo[4,5]imidazo[1,2-a]pyridine(2n)



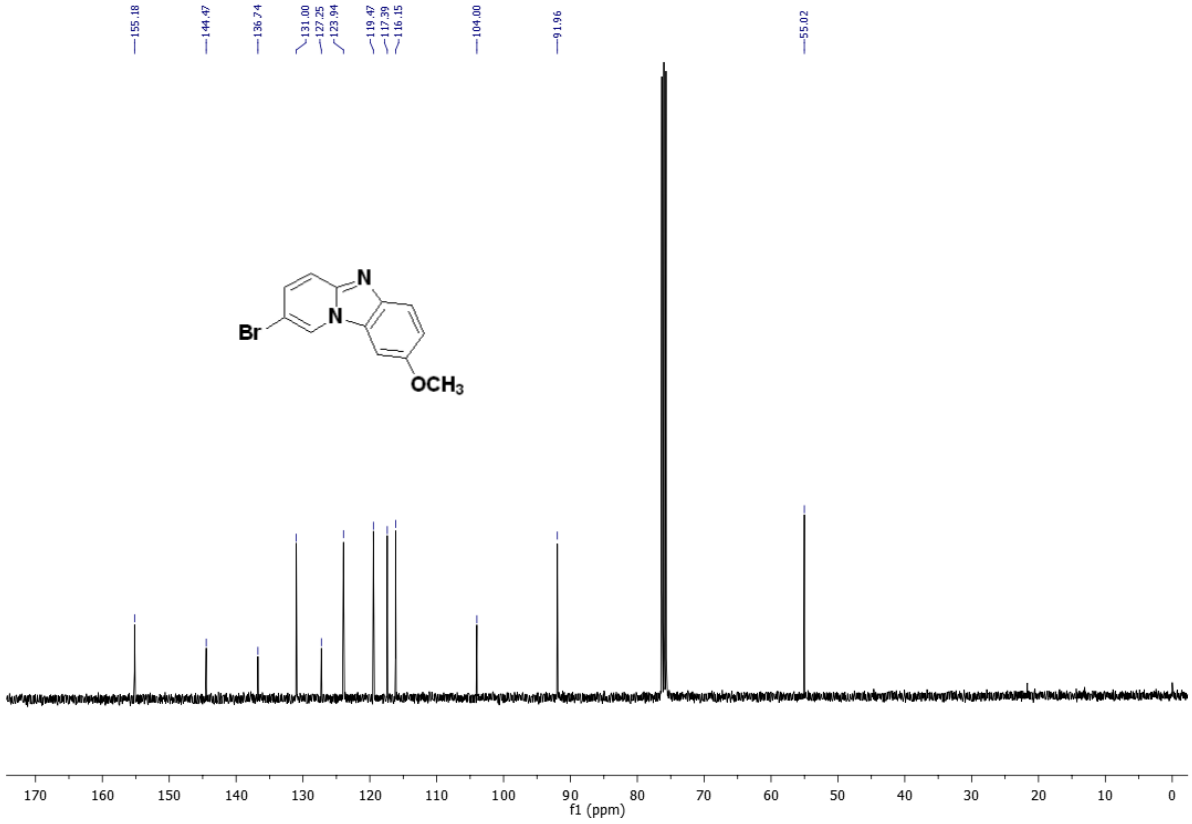
[13]C-NMR spectra of 7-chloro-8-fluorobenzo[4,5]imidazo[1,2-a]pyridine(2n)



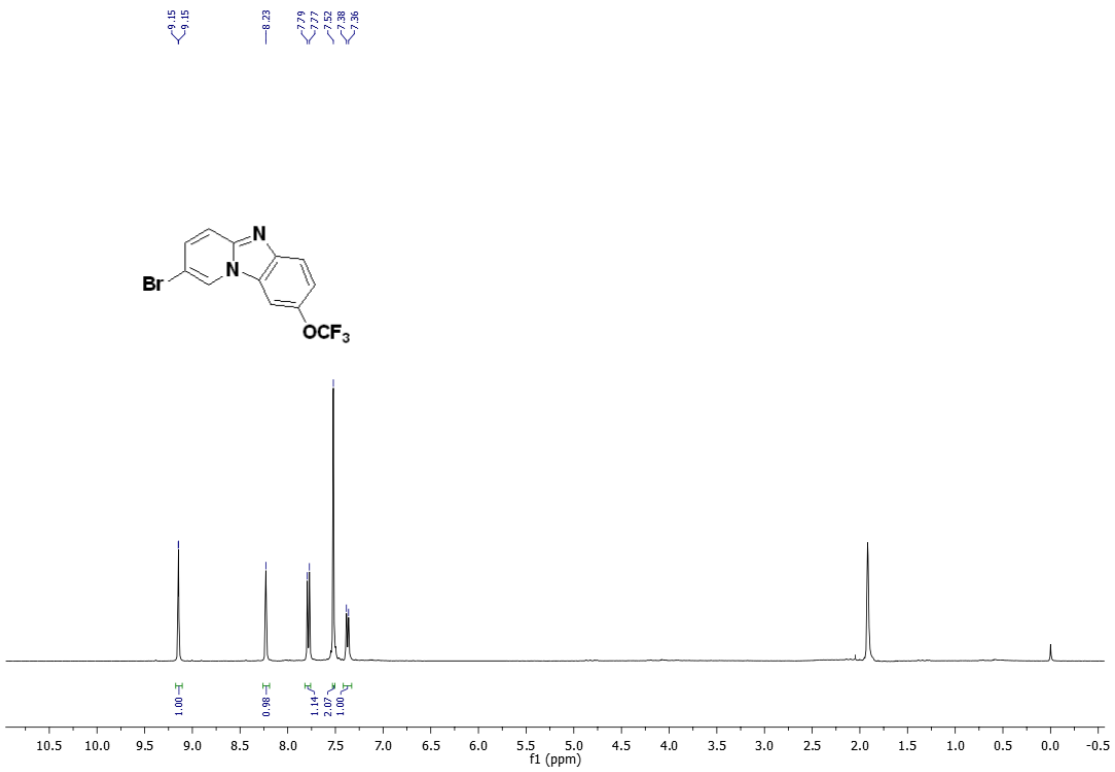
[1]H-NMR spectra of 2-bromo 8-methoxypyrido[1,2-*a*]benzimidazole (2o)



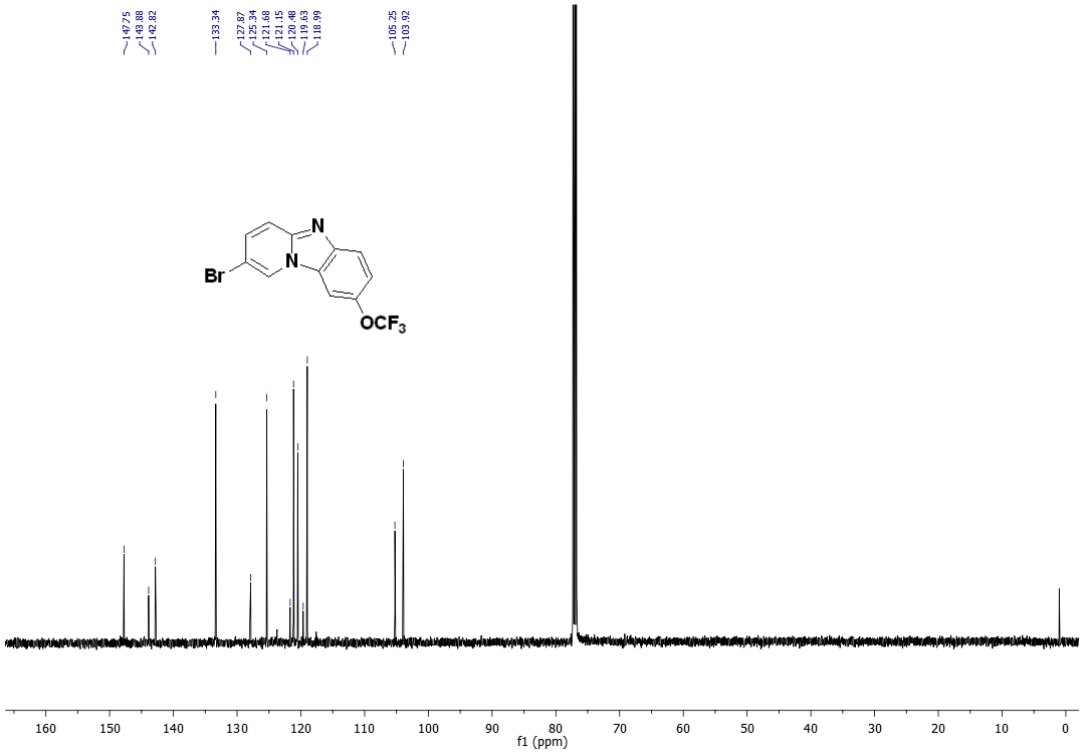
[13]C-NMR spectra of 2-bromo 8-methoxypyrido[1,2-*a*]benzimidazole (2o)



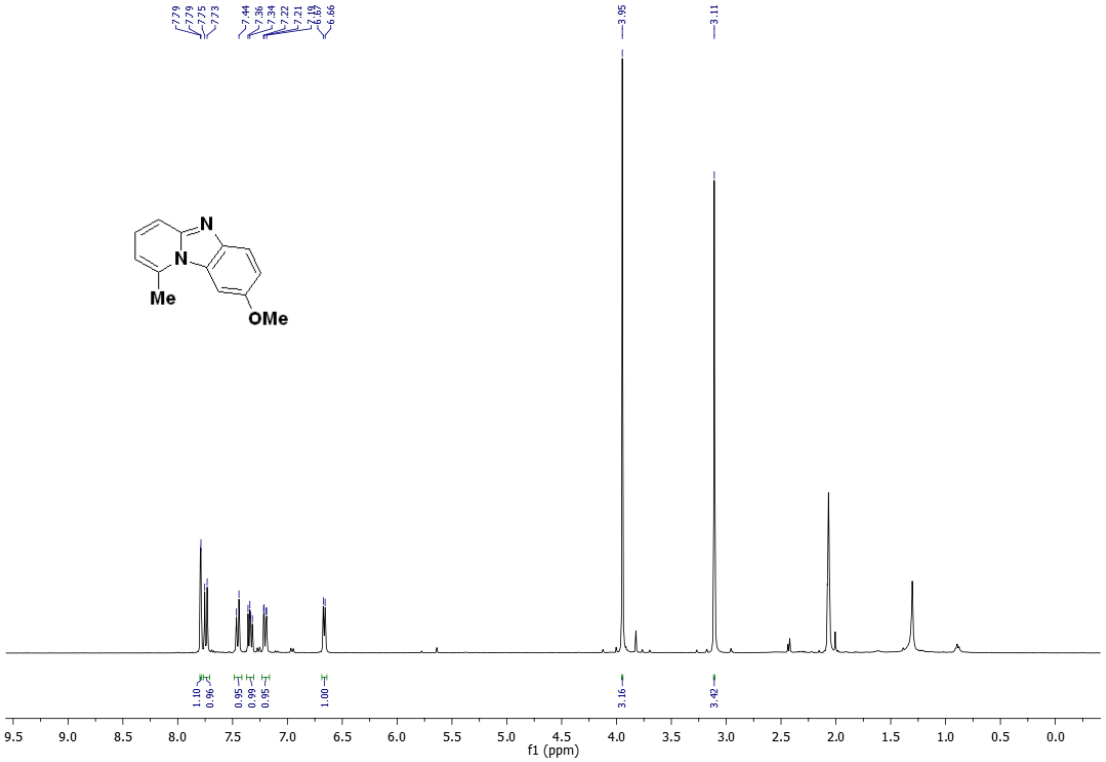
[1]H-NMR spectra of 2-bromo 8-trifluoromethoxypyrido[1,2-*a*]benzimidazole (2p)



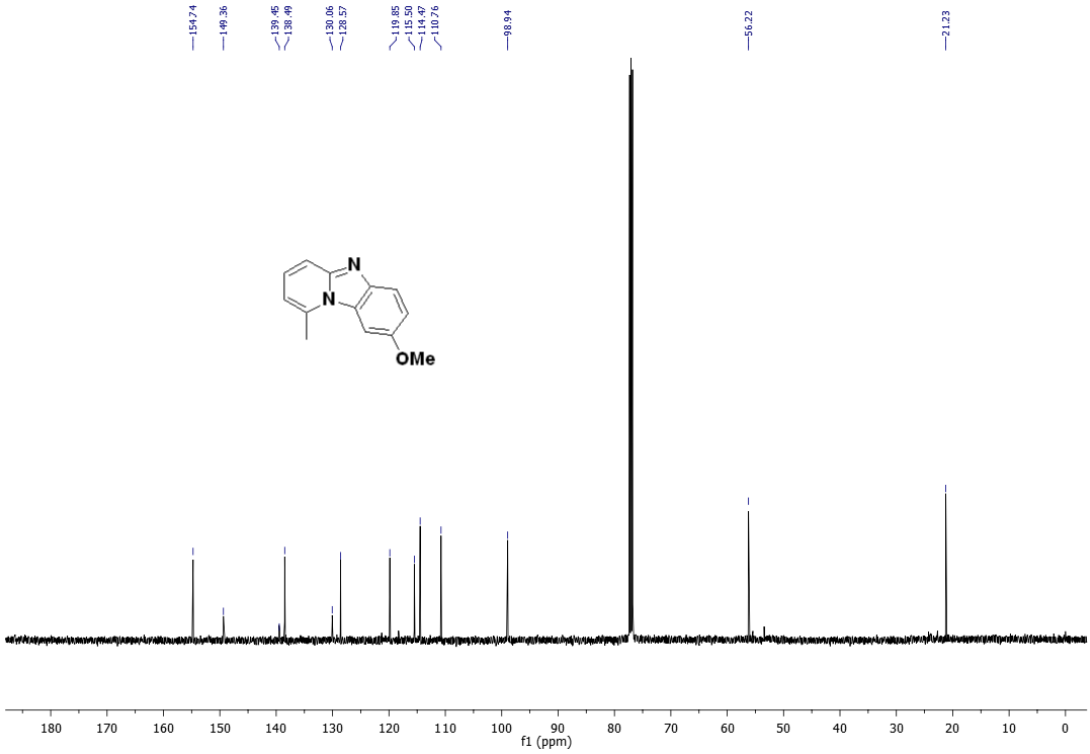
[13]C-NMR spectra of 2-bromo 8-trifluoromethoxypyrido[1,2-*a*]benzimidazole (2p)



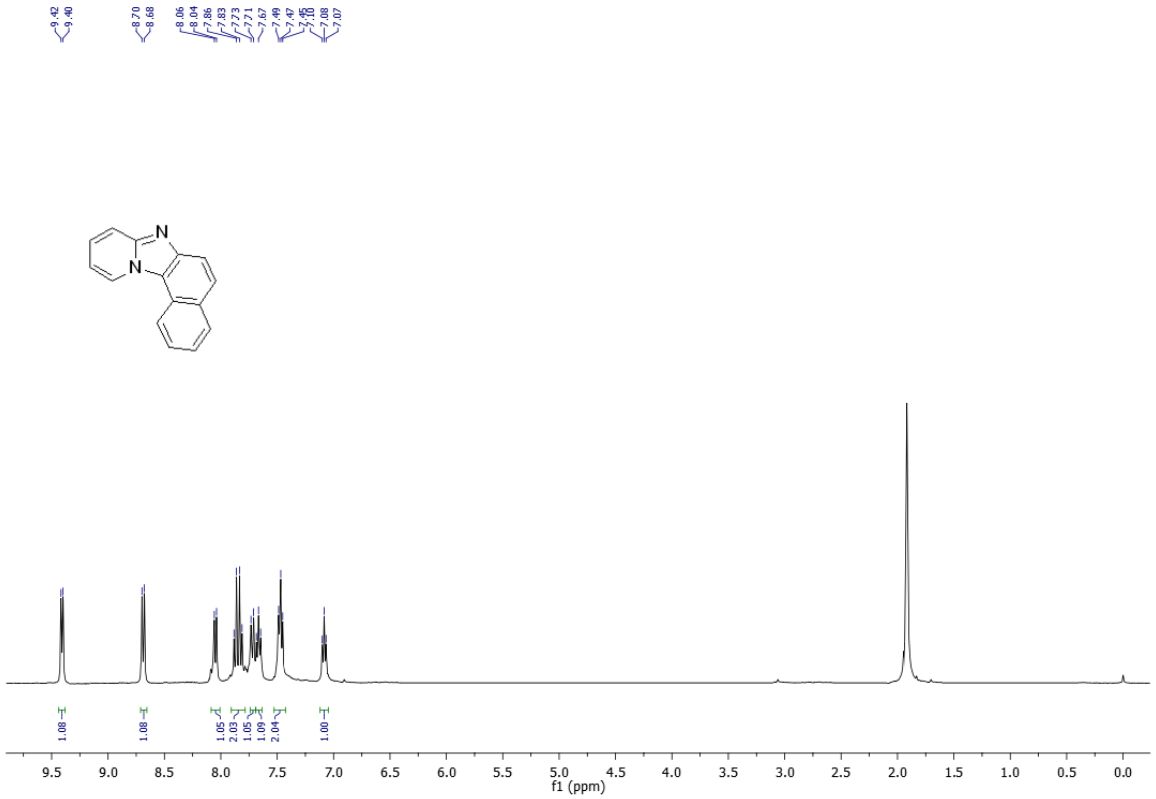
[1]H-NMR spectra of 1-methyl 8-methoxypyrido[1,2-*a*]benzimidazole (2q)



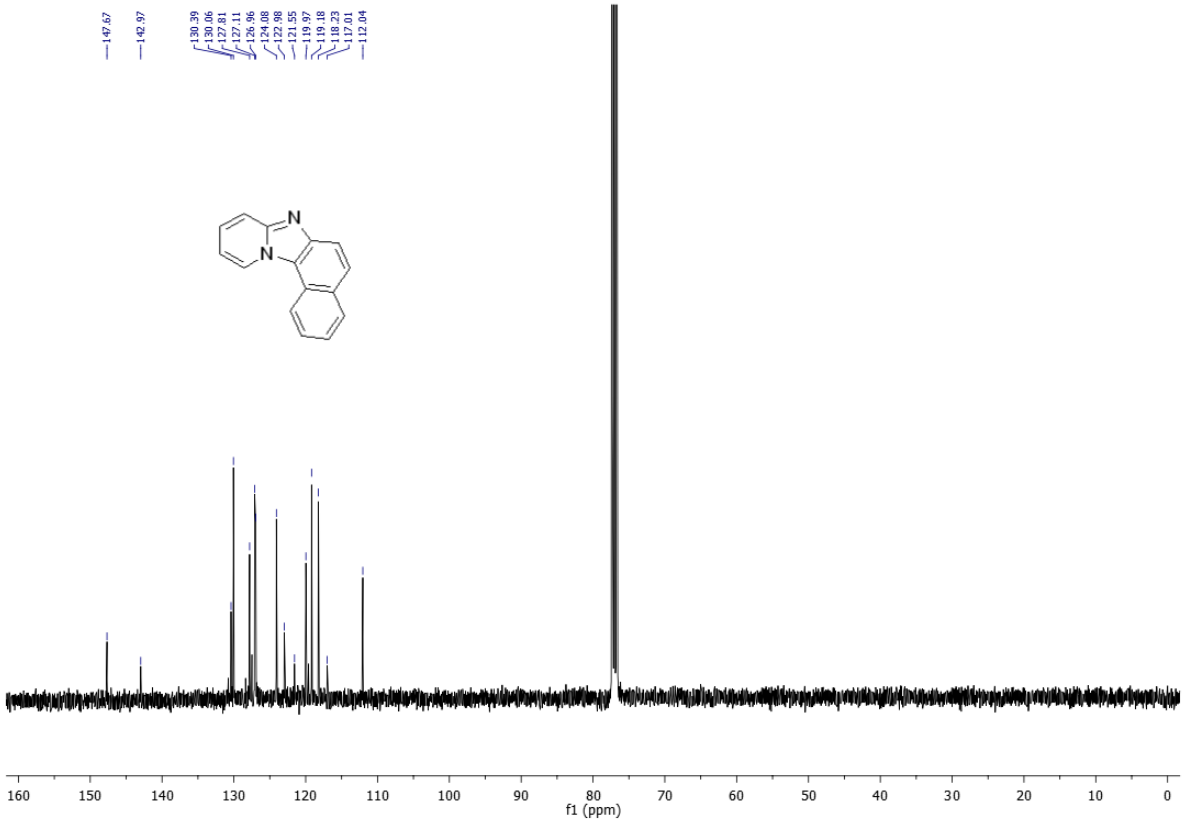
[13]C-NMR spectra of 1-methyl 8-methoxypyrido[1,2-*a*]benzimidazole (2q)



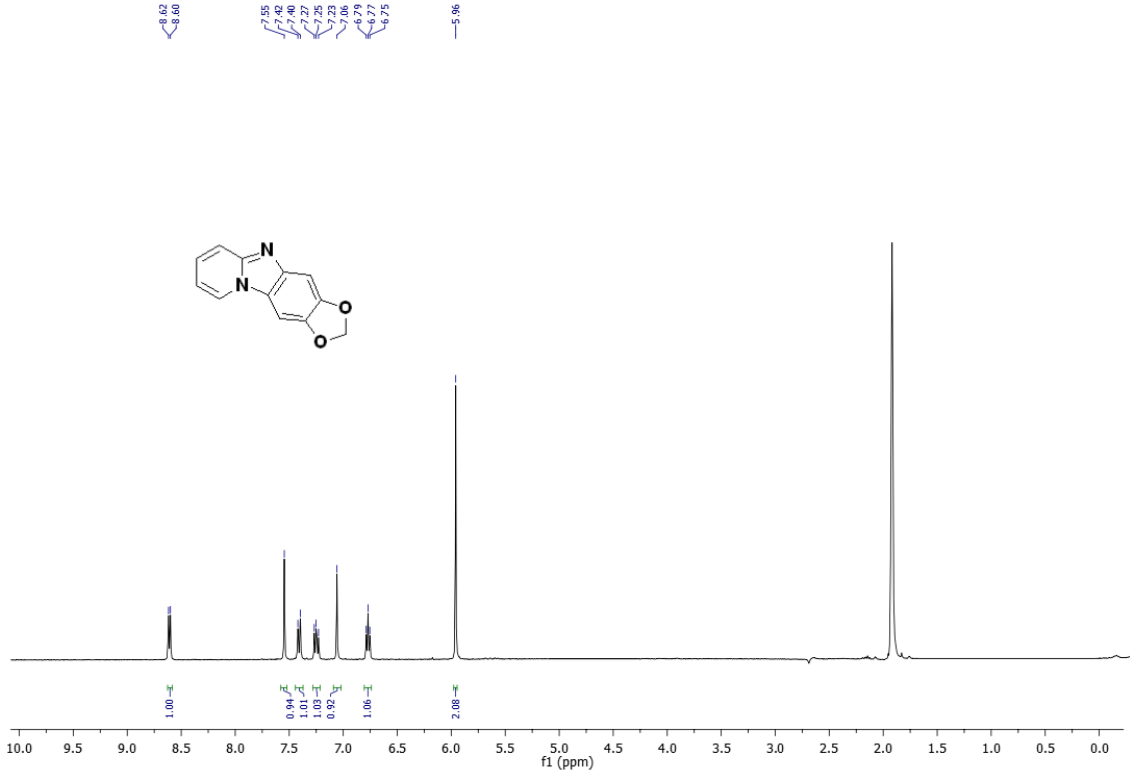
[1]H-NMR spectra of Naphthopyrido[1,2-*a*]benzimidazole (2r)



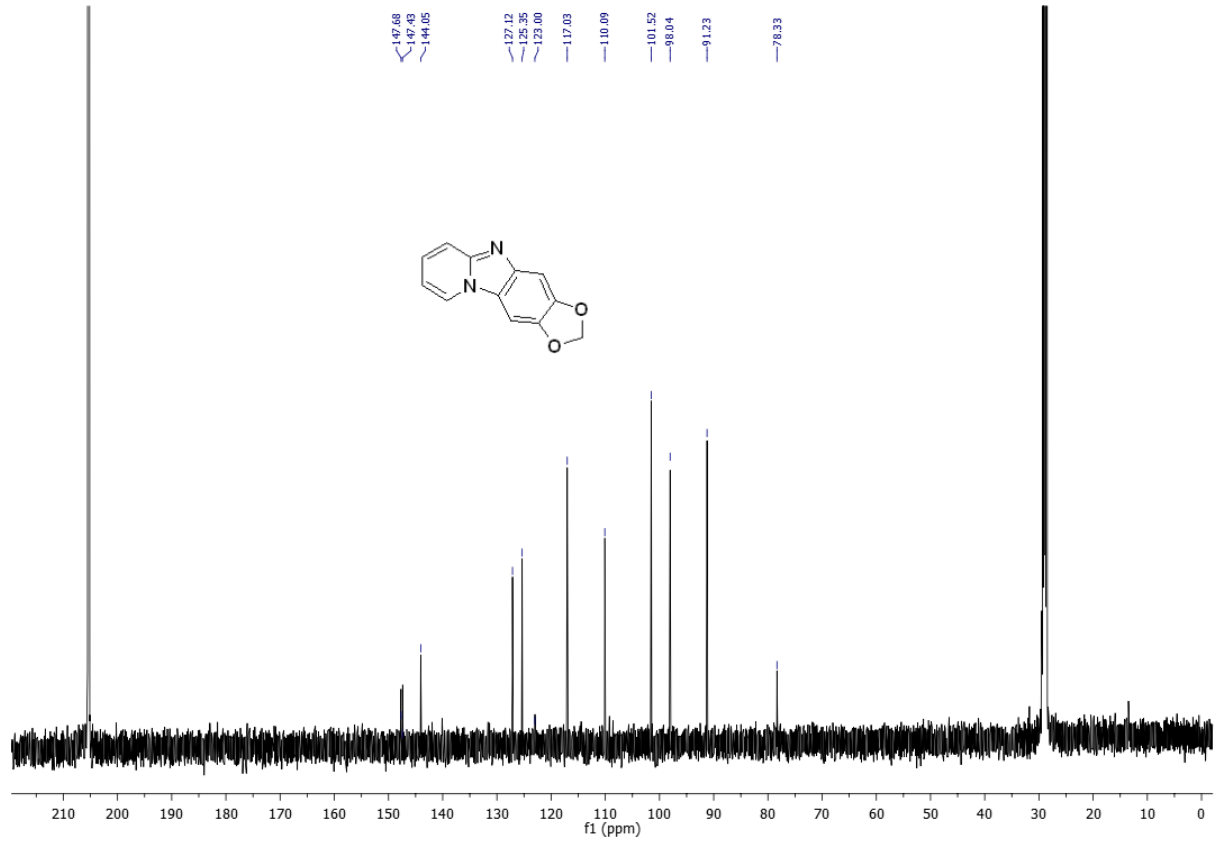
[13]C-NMR spectra of Naphthopyrido[1,2-*a*]benzimidazole (2r)



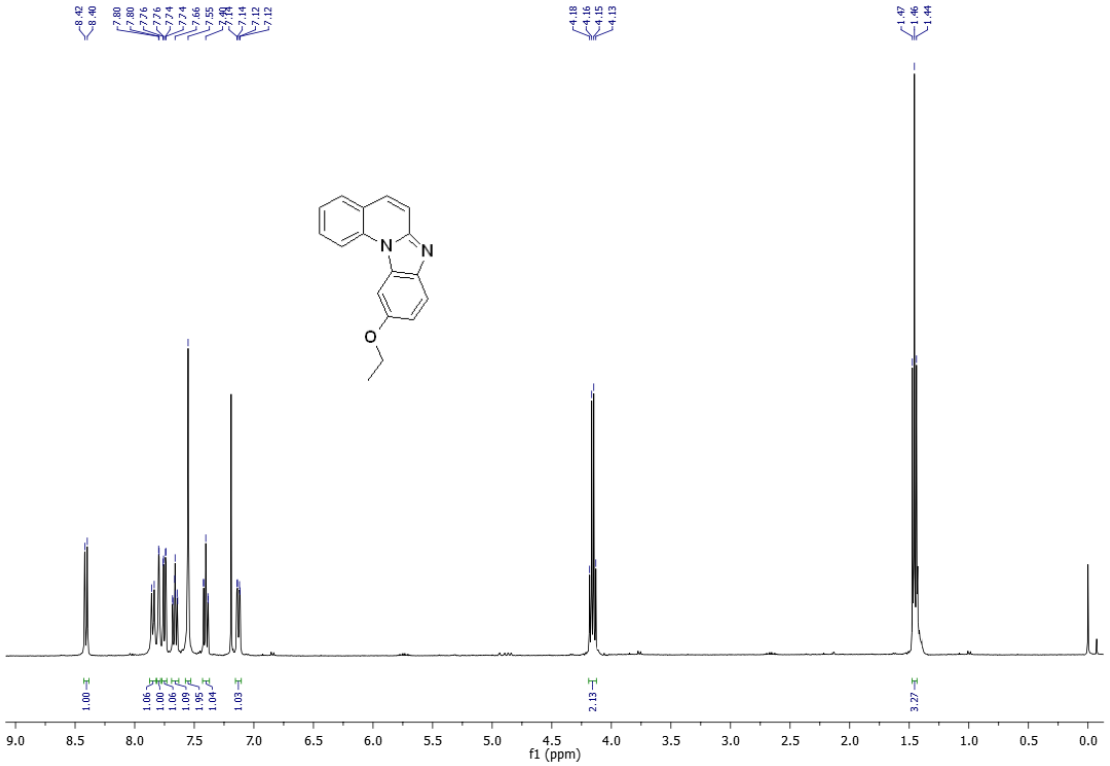
[1]H-NMR spectra of [1,3]dioxolo[4'',5'':4',5']benzo[1',2':4,5]imidazo[1,2-a]pyridine (2s)



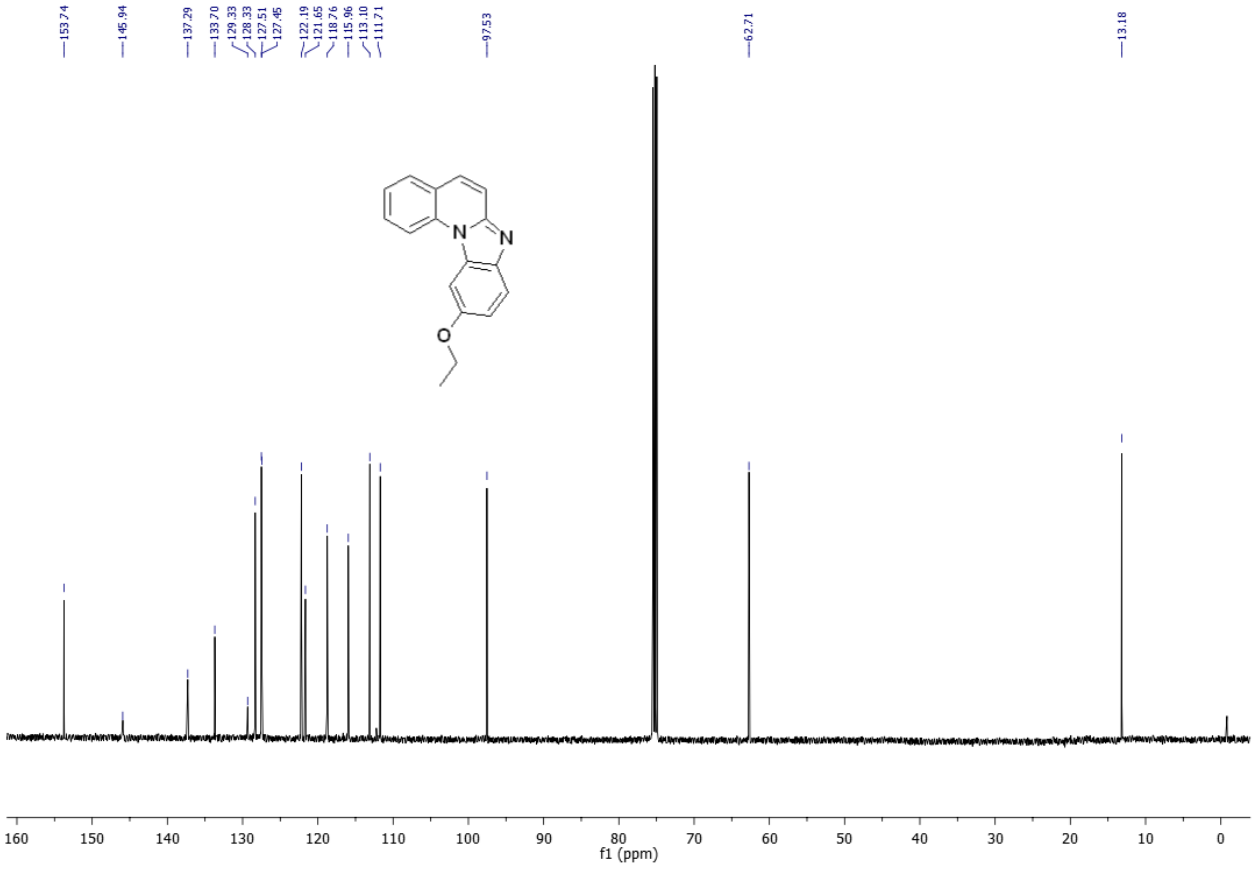
[13]C-NMR spectra of [1,3]dioxolo[4'',5'':4',5']benzo[1',2':4,5]imidazo[1,2-a]pyridine (2s)



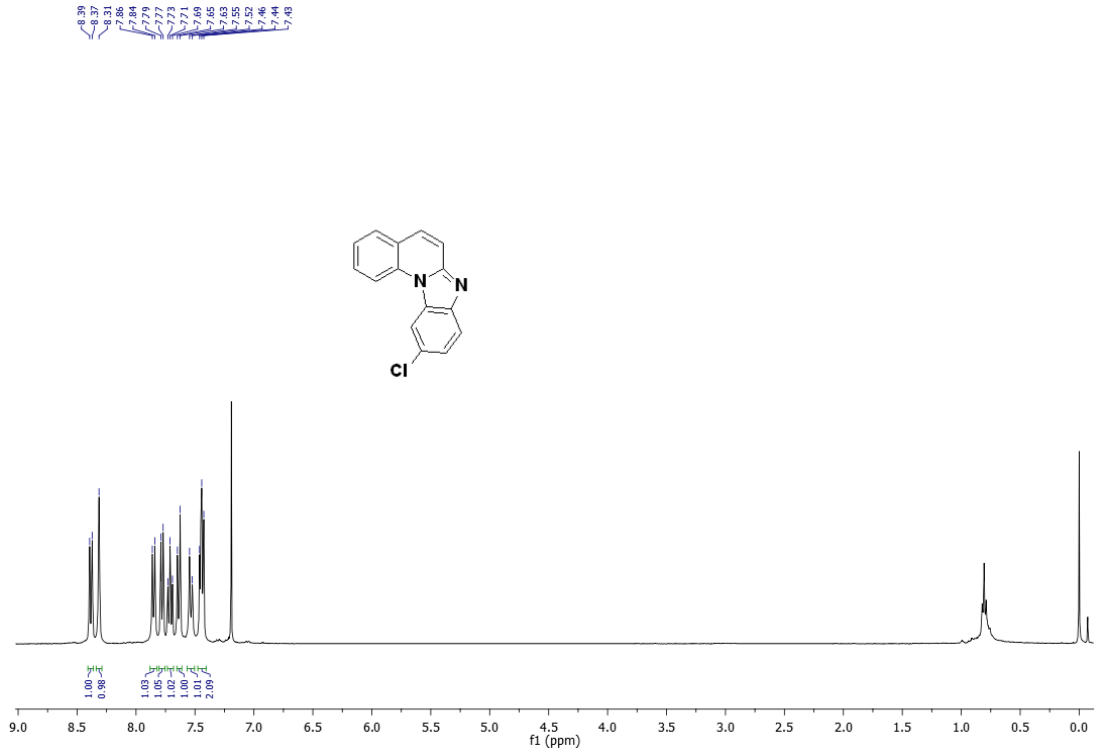
[1]H-NMR spectra of 10-ethoxybenzo[4,5]imidazo[1,2-a]quinoline(3a)



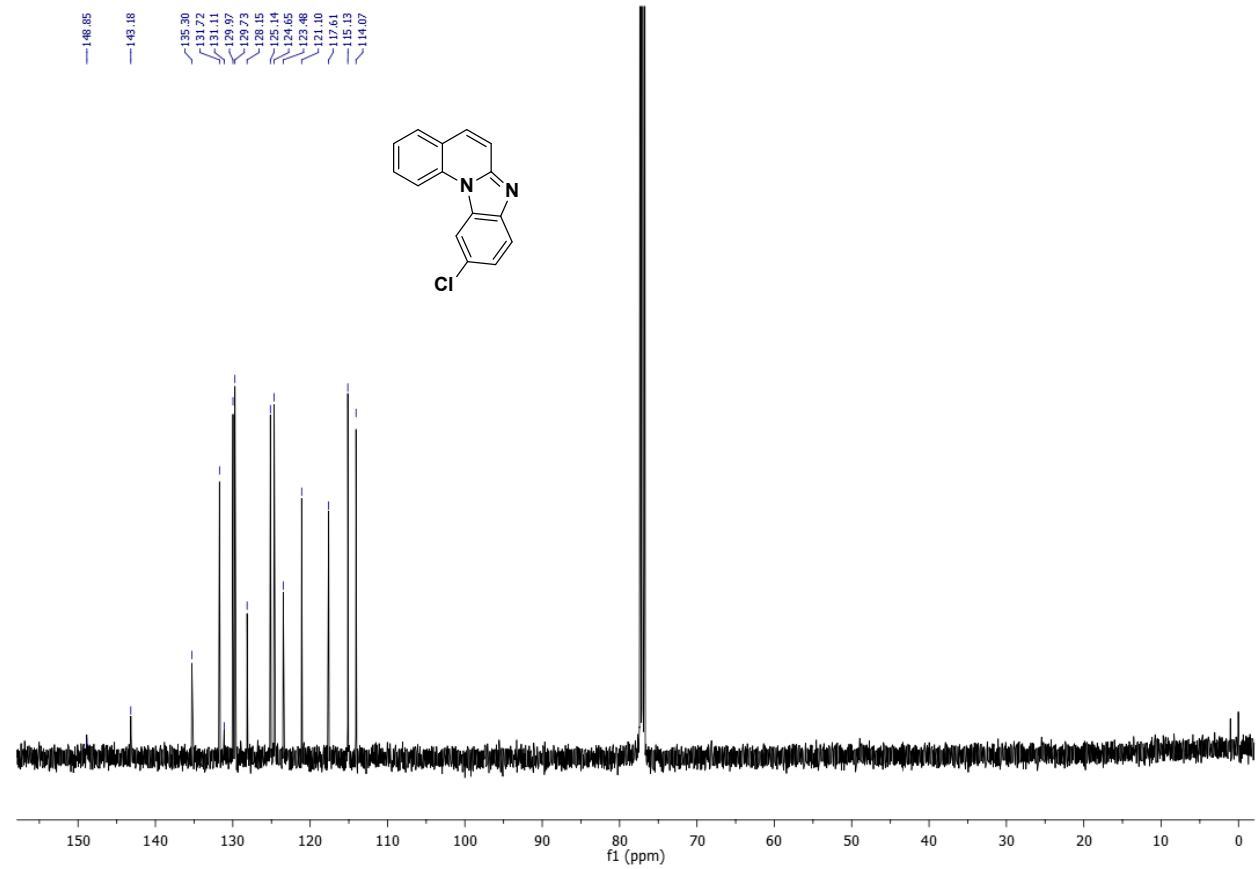
[13]C-NMR spectra of 10-ethoxybenzo[4,5]imidazo[1,2-a]quinoline(3a)



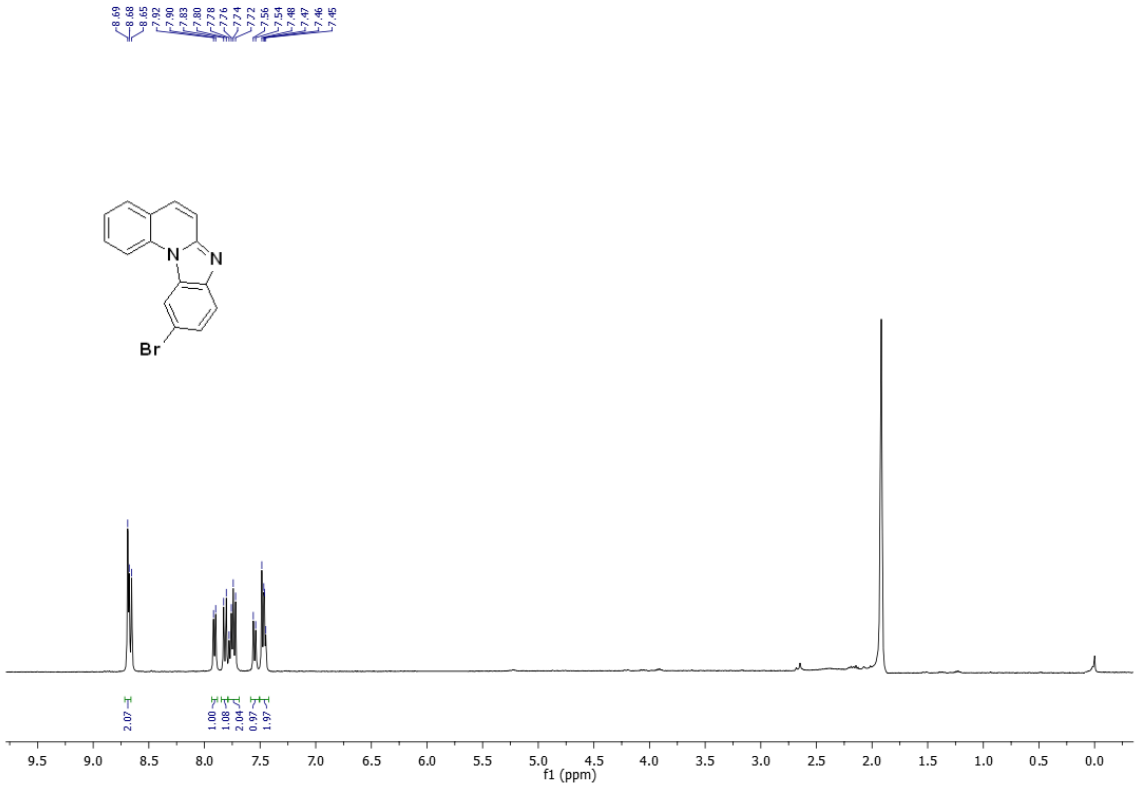
[1]H-NMR spectra of 10-chlorobenzo[4,5]imidazo[1,2-a]quinoline(3b)



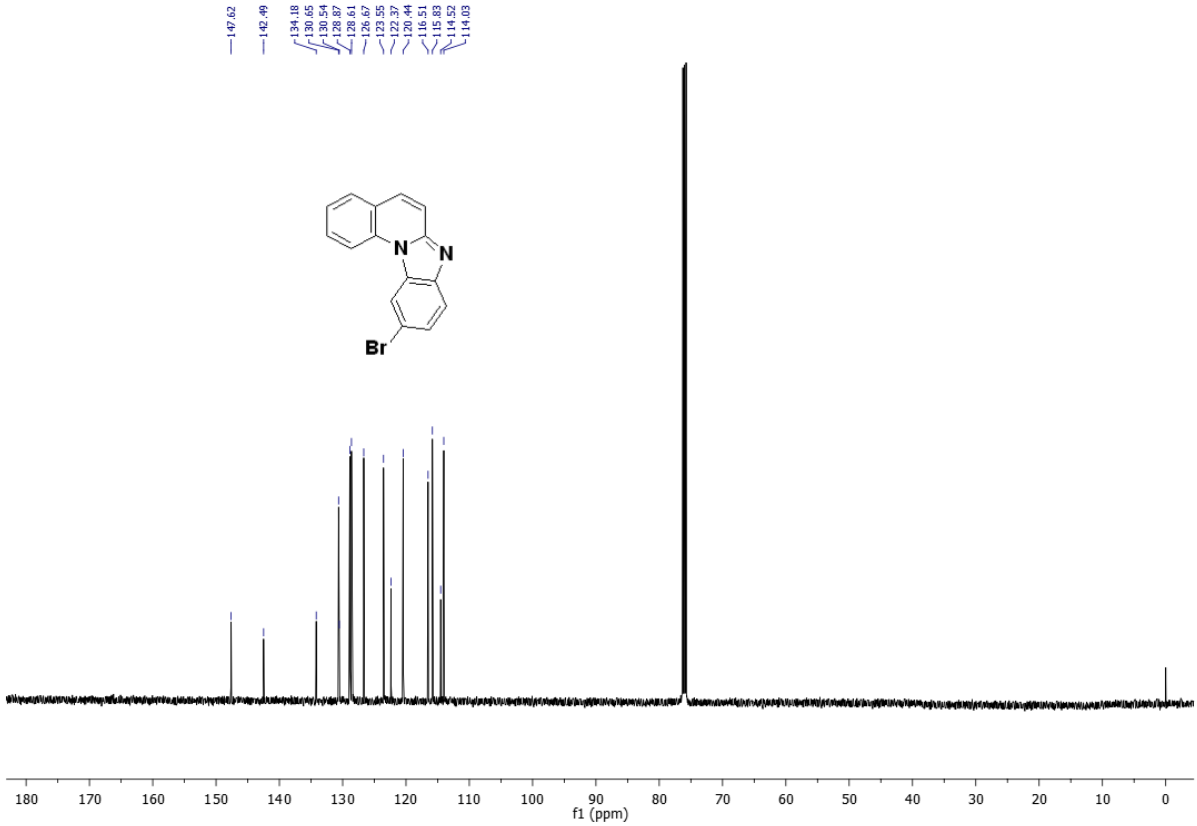
[13]C-NMR spectra of 10-chlorobenzo[4,5]imidazo[1,2-a]quinoline(3b)



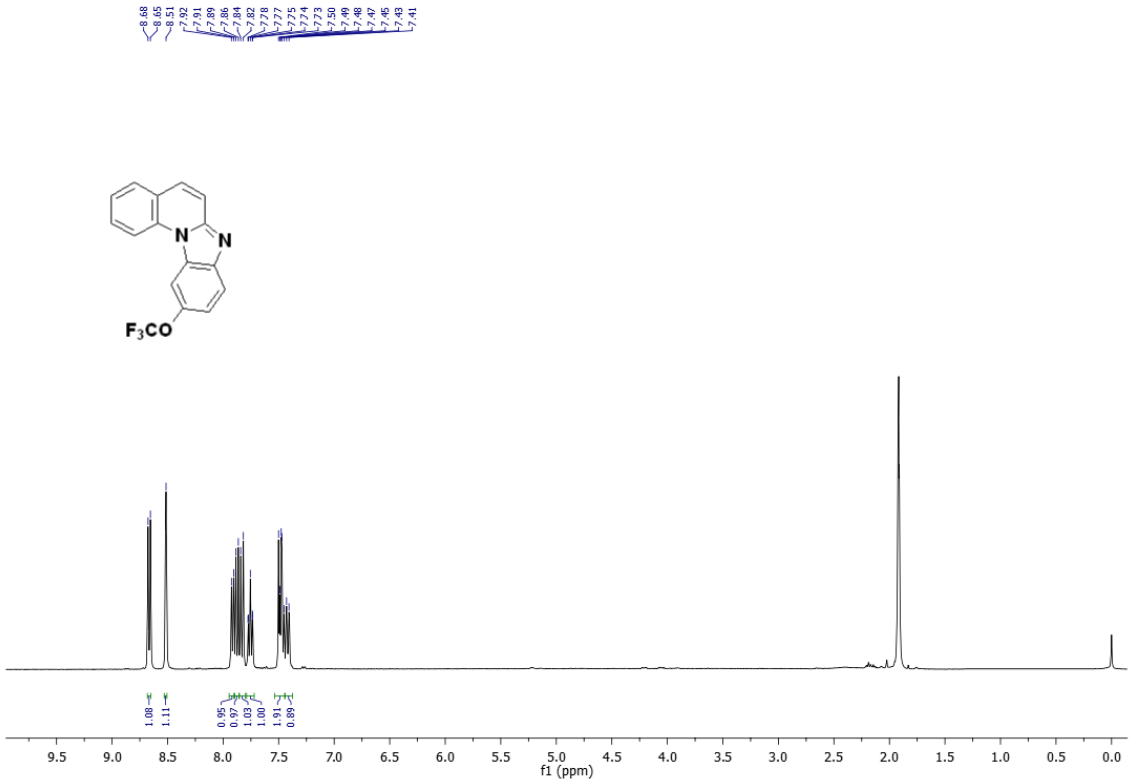
[1]H-NMR spectra of 10-bromobenzimidazo[1,2-*a*]quinoline (3c)



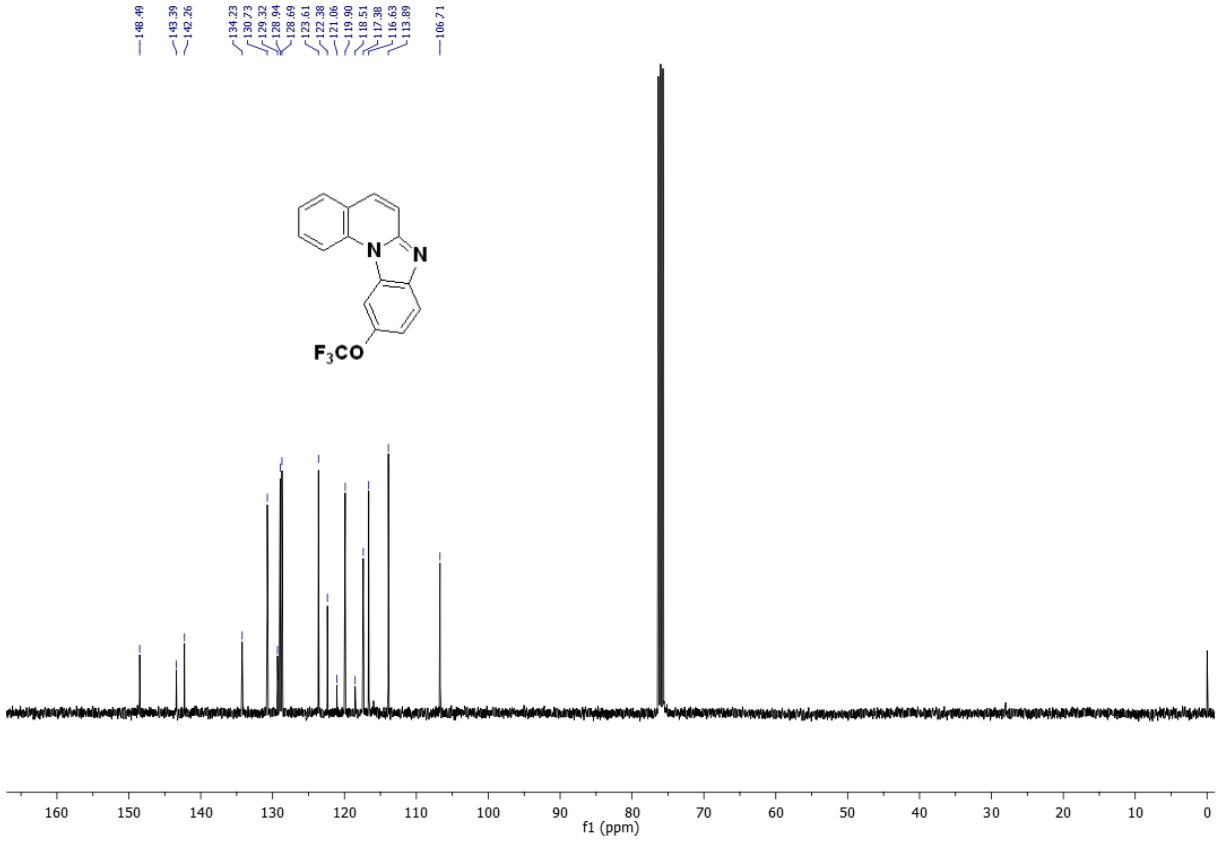
[13]C-NMR spectra of 10-bromobenzimidazo[1,2-*a*]quinoline (3c)



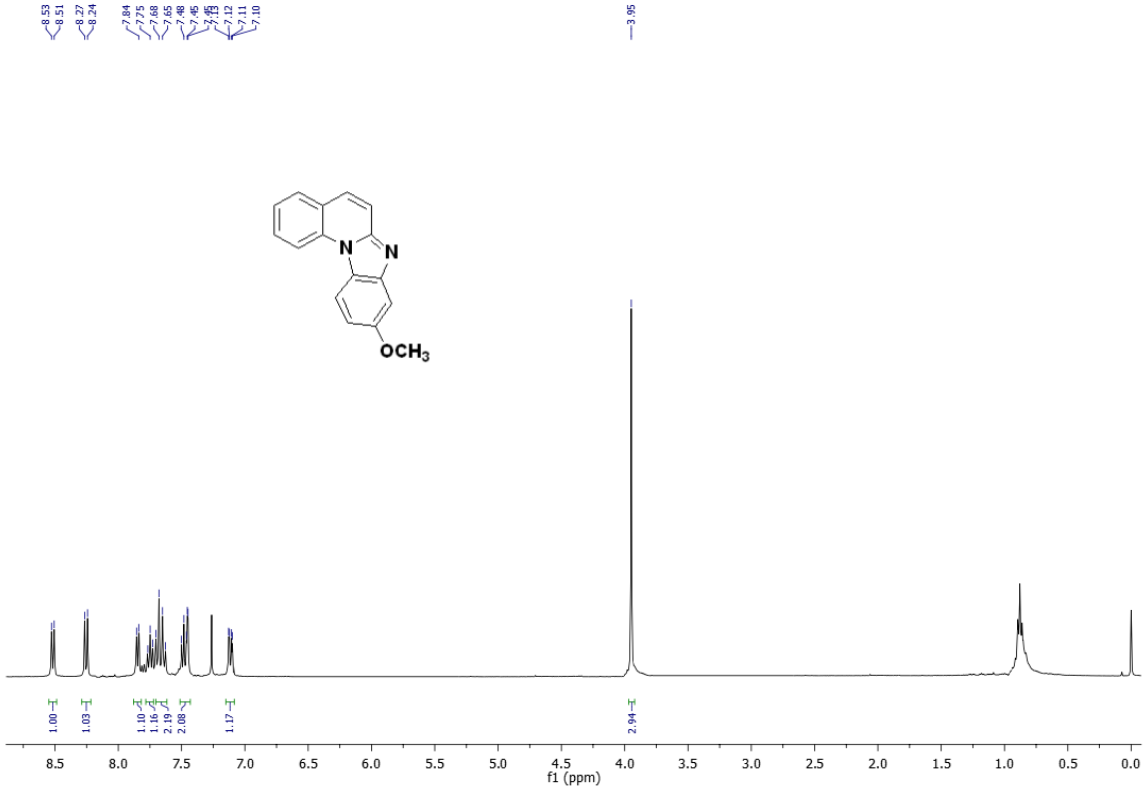
[1]H-NMR spectra of 10-trifluoromethoxybenzimidazo[1,2-*a*]quinoline (3d)



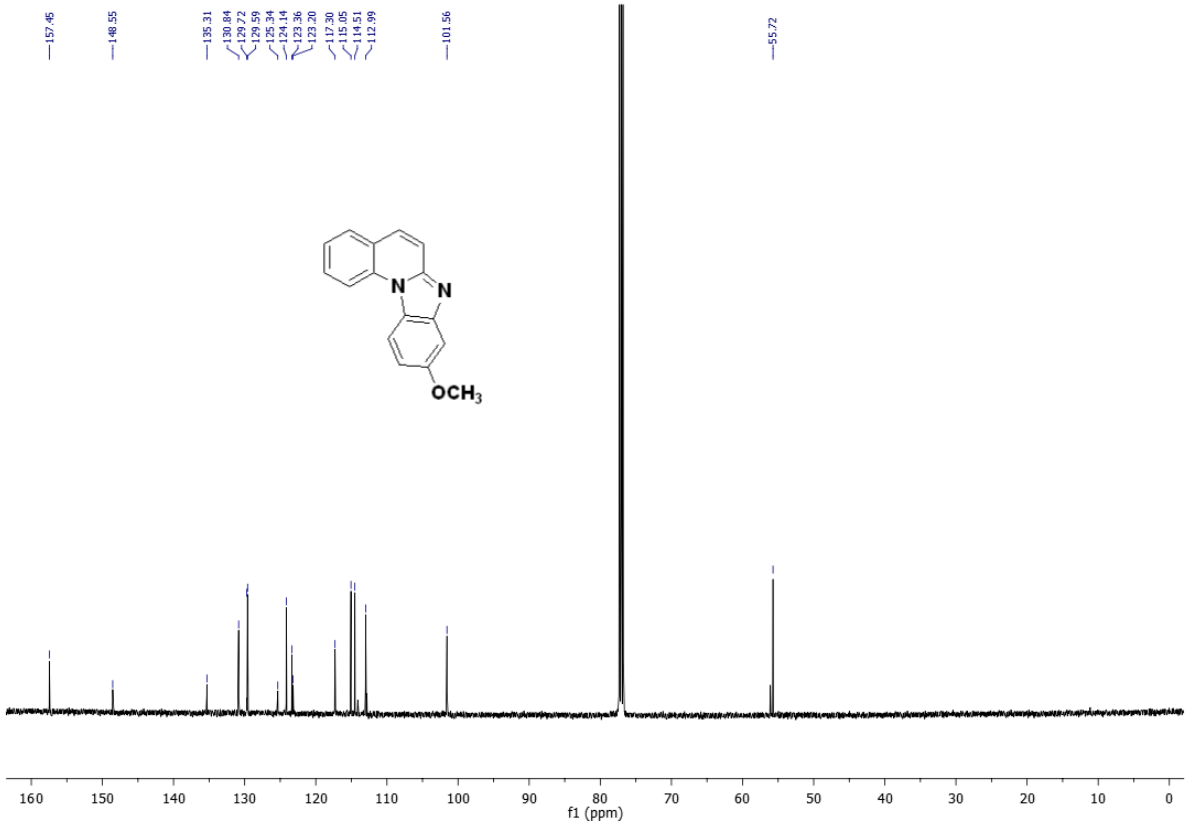
[13]C-NMR spectra of 10-trifluoromethoxybenzimidazo[1,2-*a*]quinoline (3d)



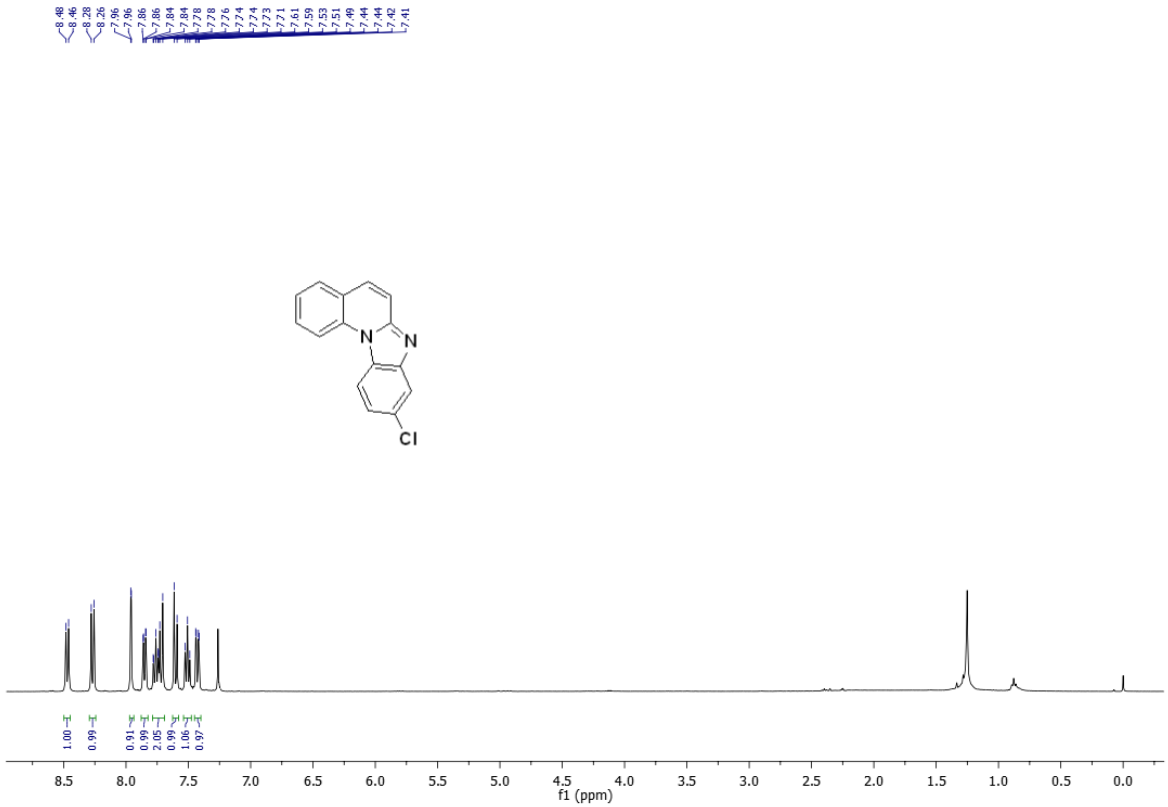
[1]H-NMR spectra of 9-methoxybenzo[4,5]imidazo[1,2-a]quinoline(3e)



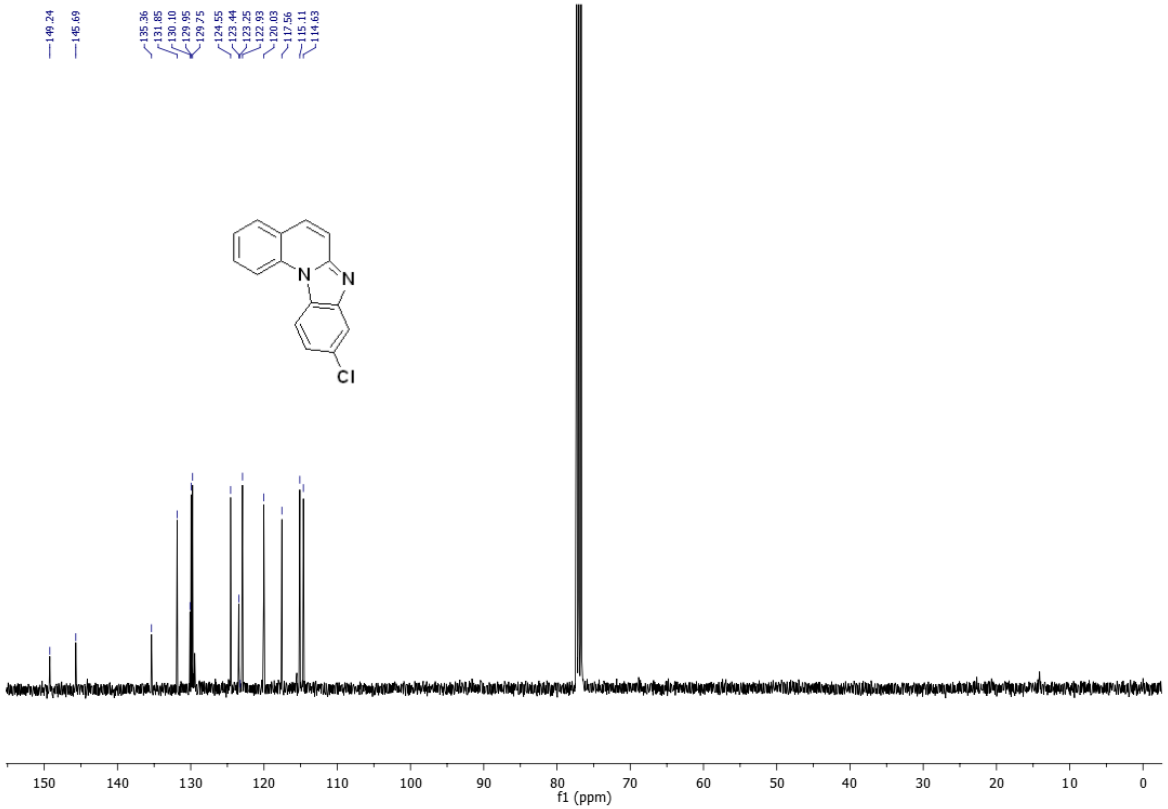
[13]C-NMR spectra of 9-methoxybenzo[4,5]imidazo[1,2-a]quinoline(3e)



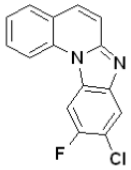
[1]H-NMR spectra of 9-chlorobenzo[4,5][1,2-a]quinoline(3f)

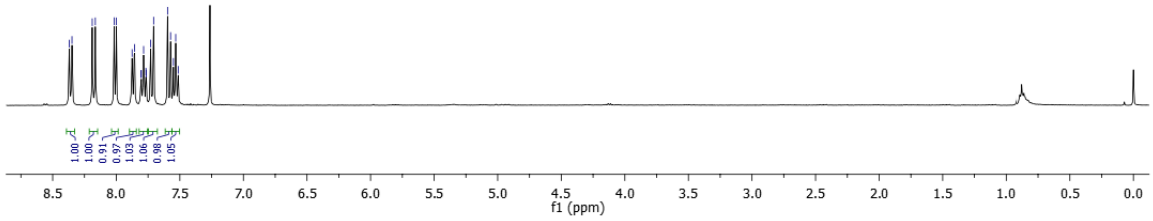


[13]C-NMR spectra of 9-chlorobenzo[4,5][1,2-a]quinoline(3f)

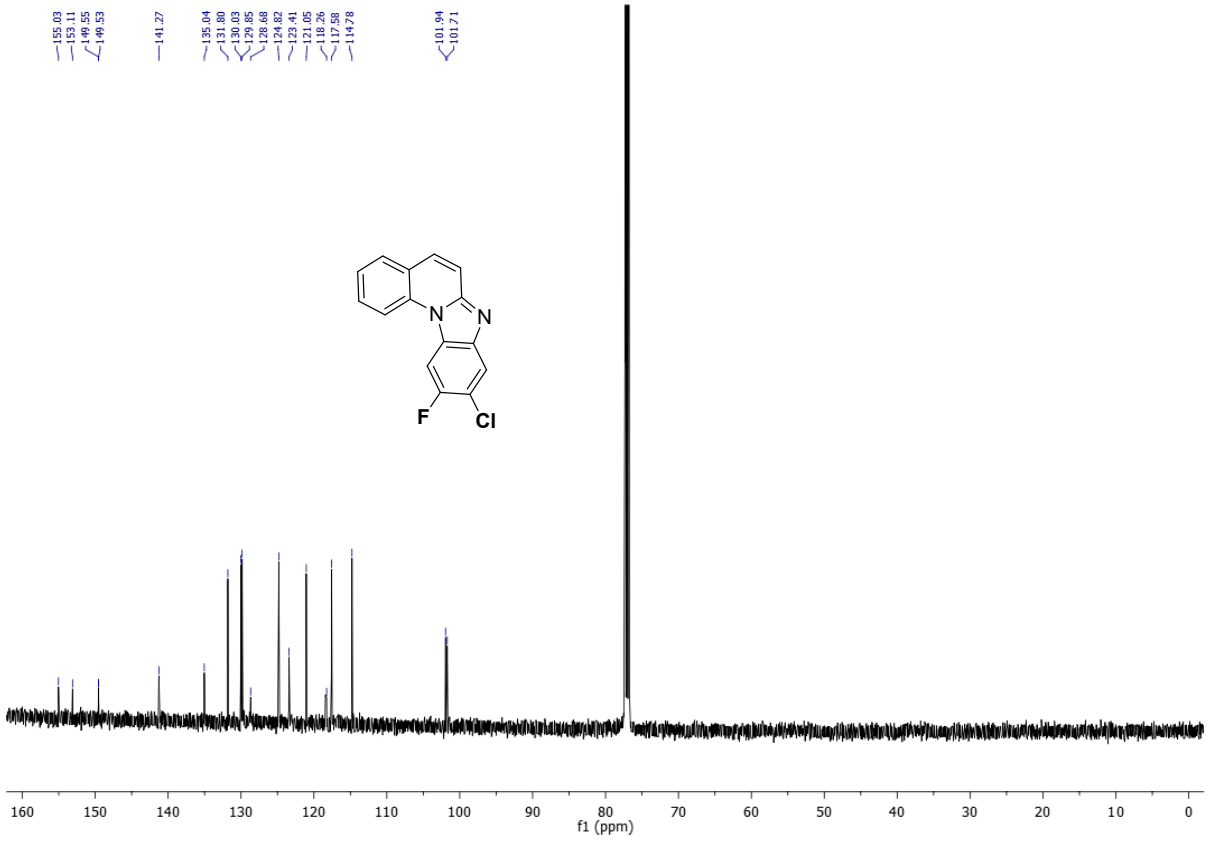


[1]H-NMR spectra of 9-chloro-10-fluorobenzo[4,5]imidazo[1,2-a]quinoline(3g)

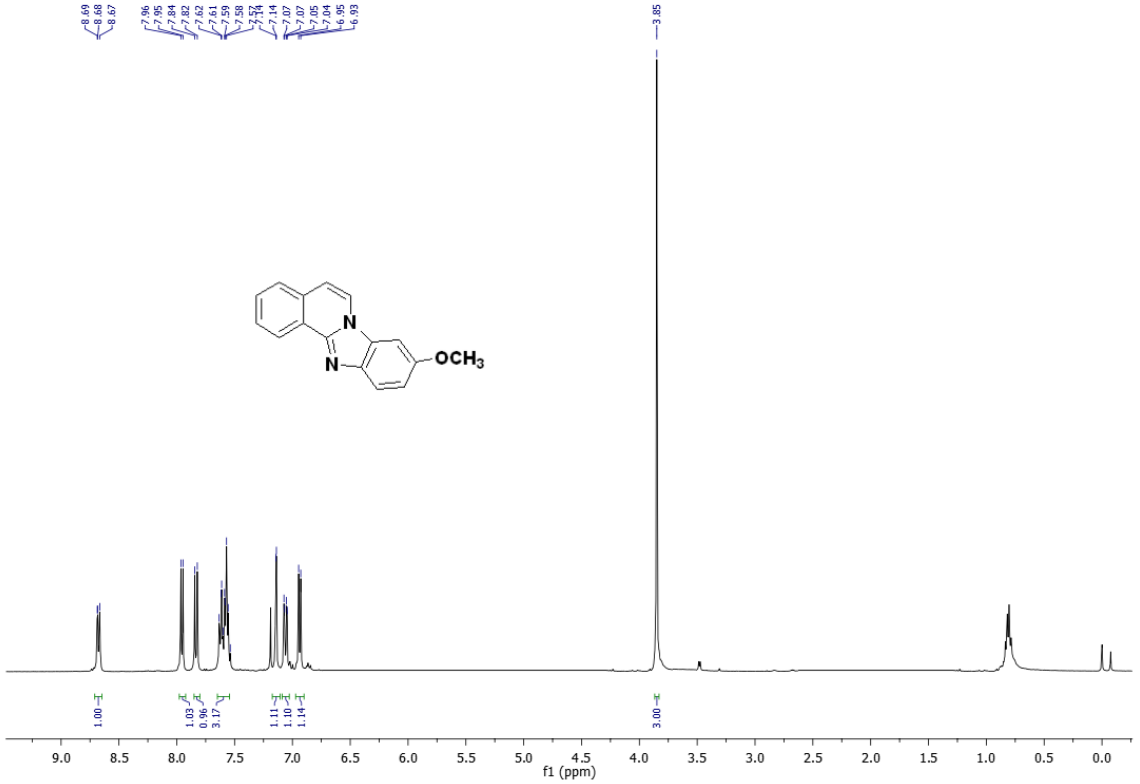




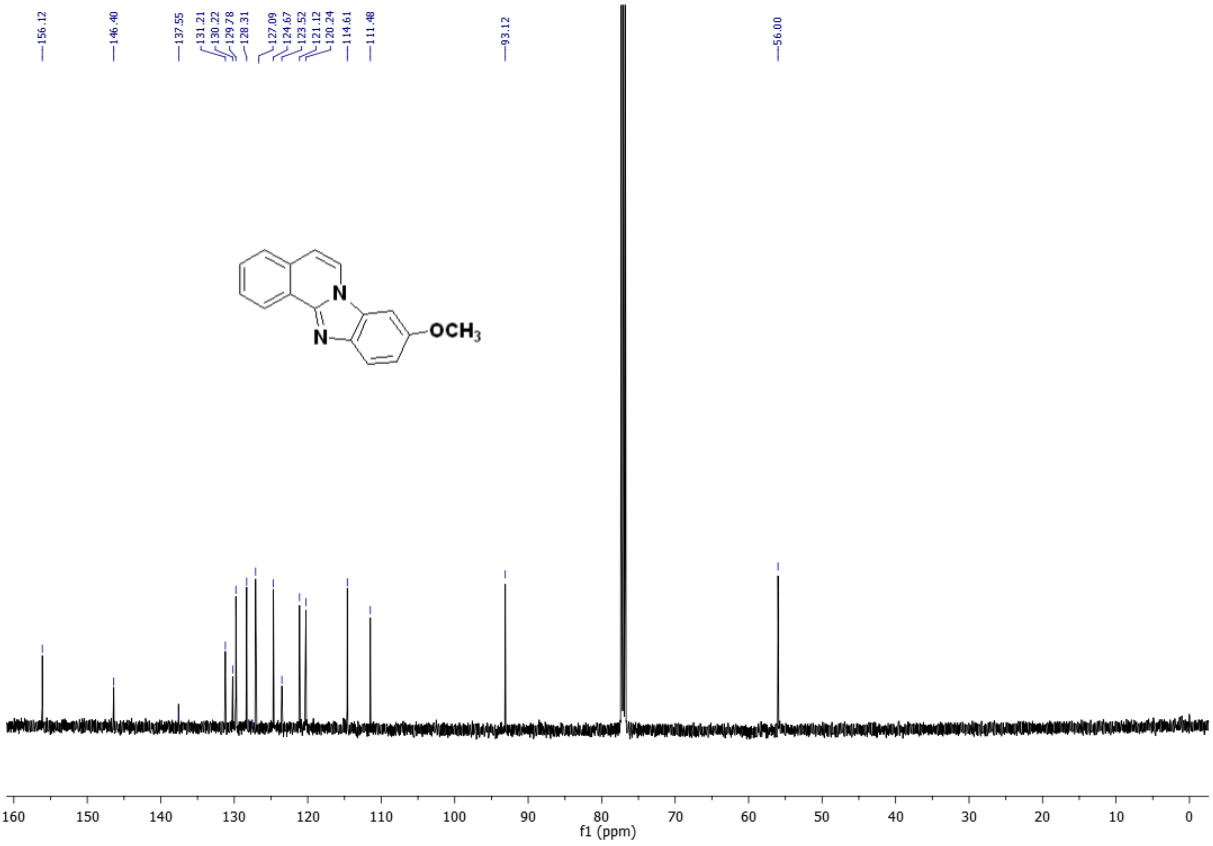
[13]C-NMR spectra of 9-chloro-10-fluorobenzo[4,5]imidazo[1,2-a]quinoline(3g)



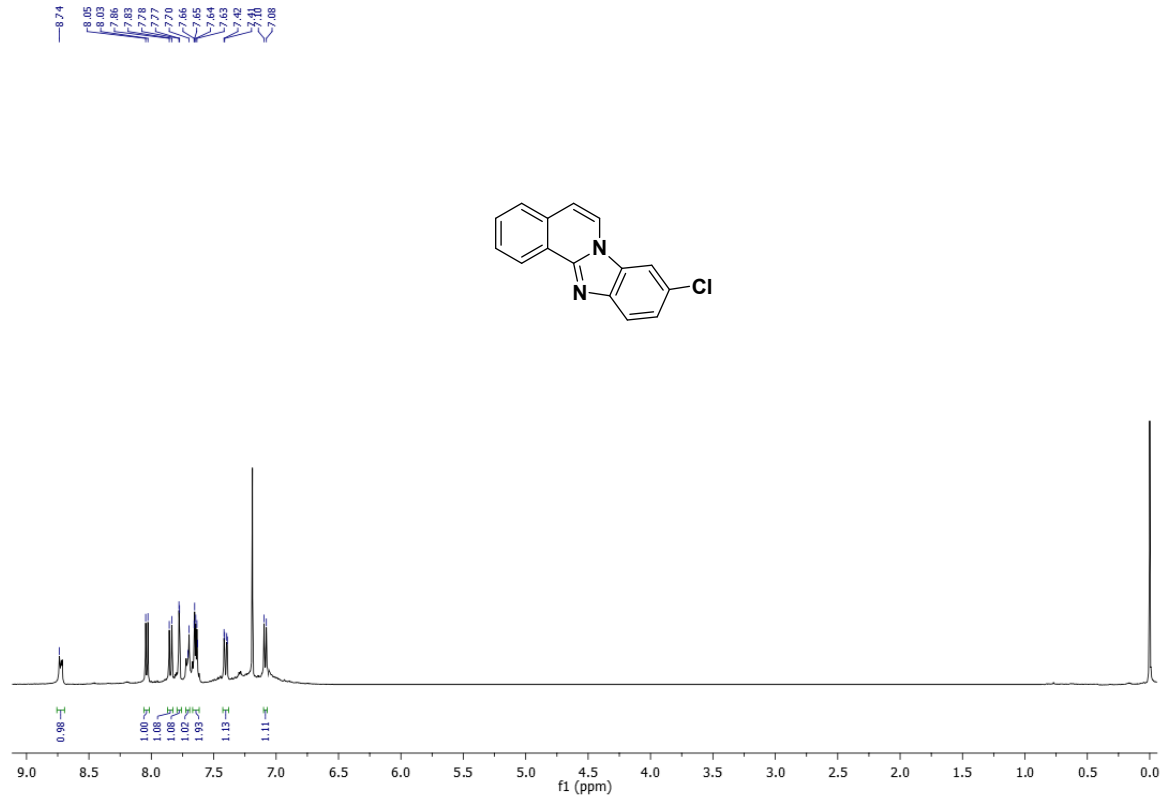
[1]H-NMR spectra of 9-methoxybenzo[4,5]imidazo[2,1-a]isoquinoline(3h)



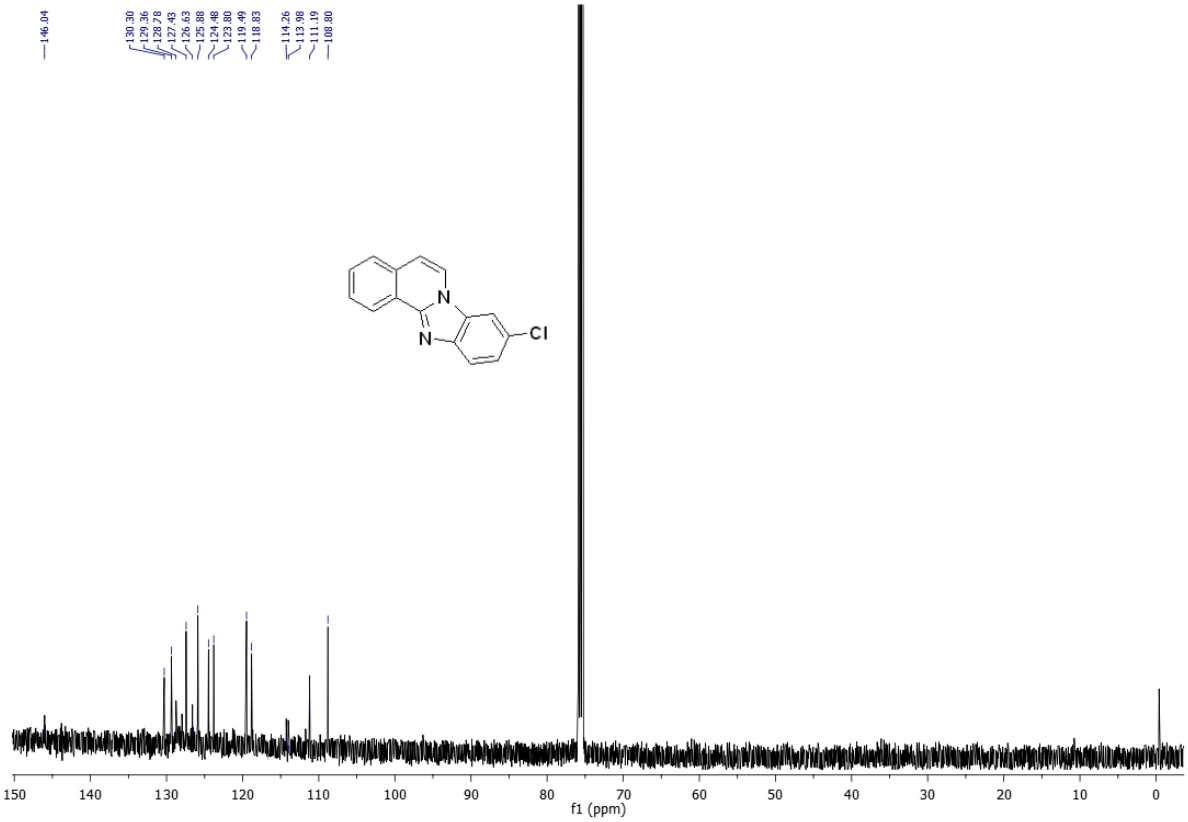
[13]C-NMR spectra of 9-methoxybenzo[4,5]imidazo[2,1-a]isoquinoline(3h)



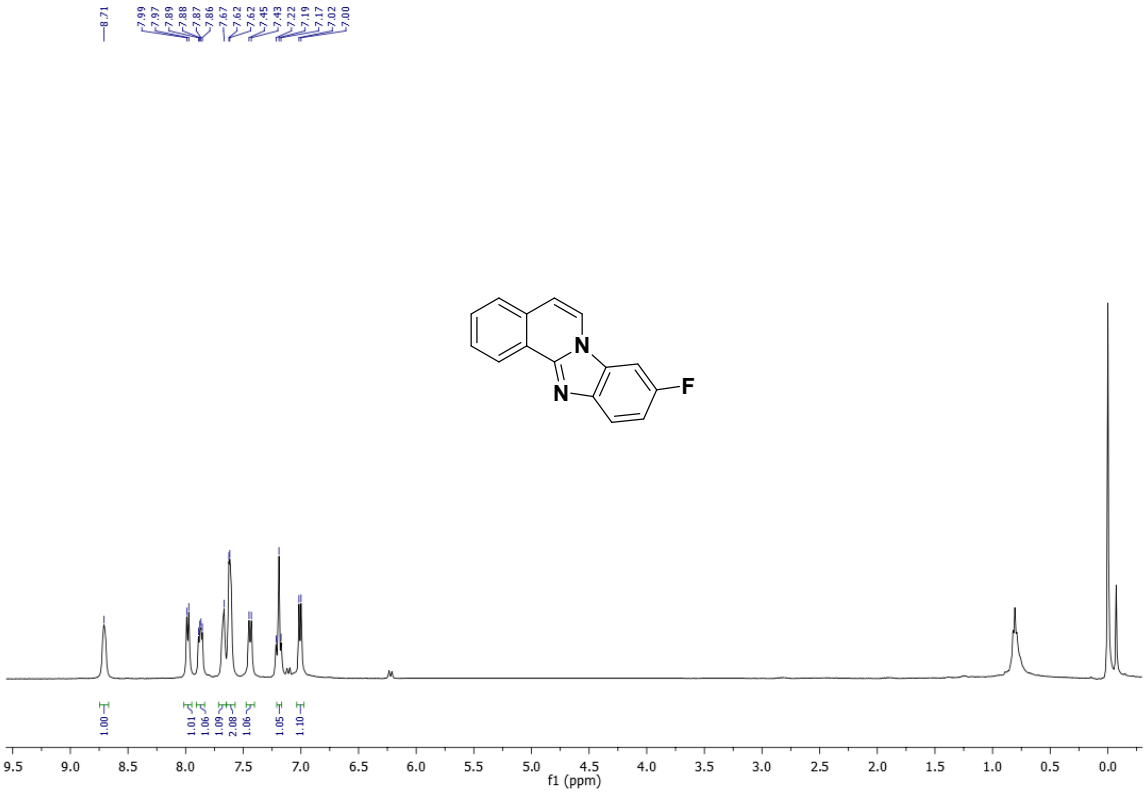
[1]H-NMR spectra of 9-chlorobenzo[4,5]imidazo[2,1-a]isoquinoline(3i)



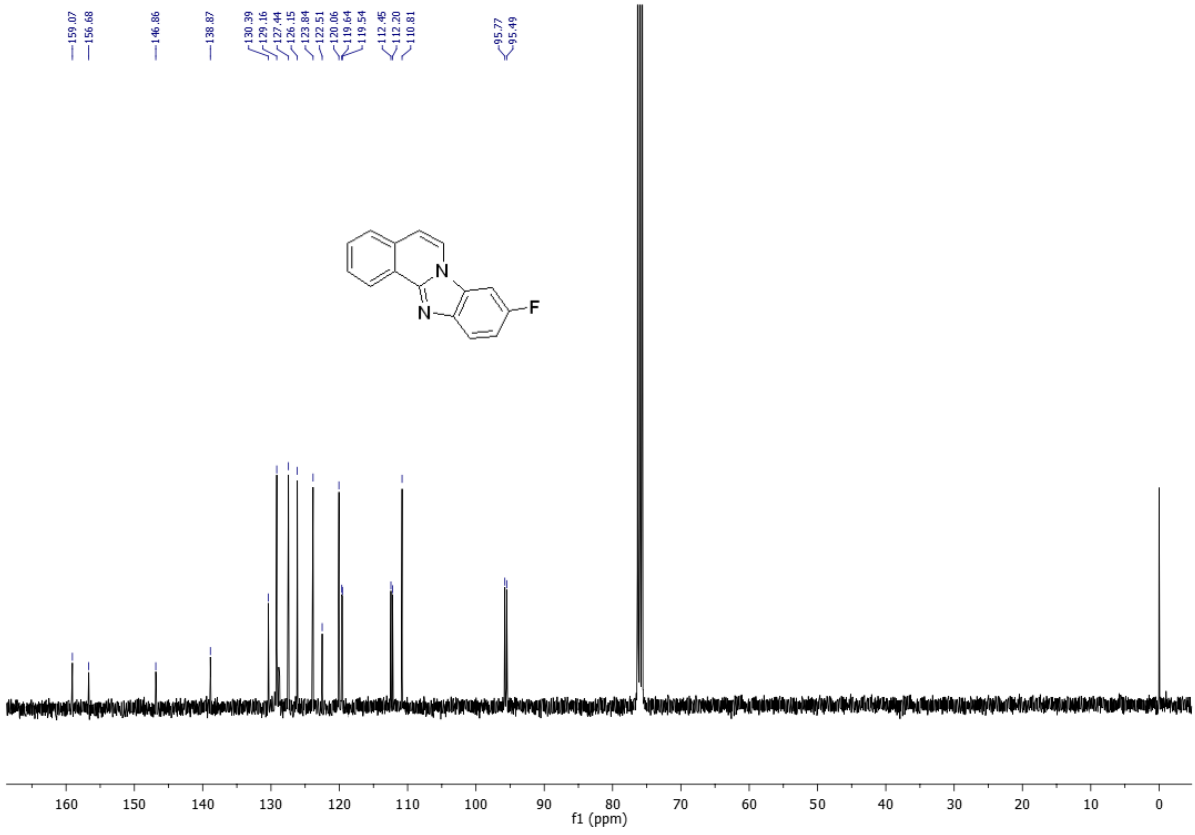
[13]C-NMR spectra of 9-chlorobenzo[4,5]imidazo[2,1-a]isoquinoline(3i)



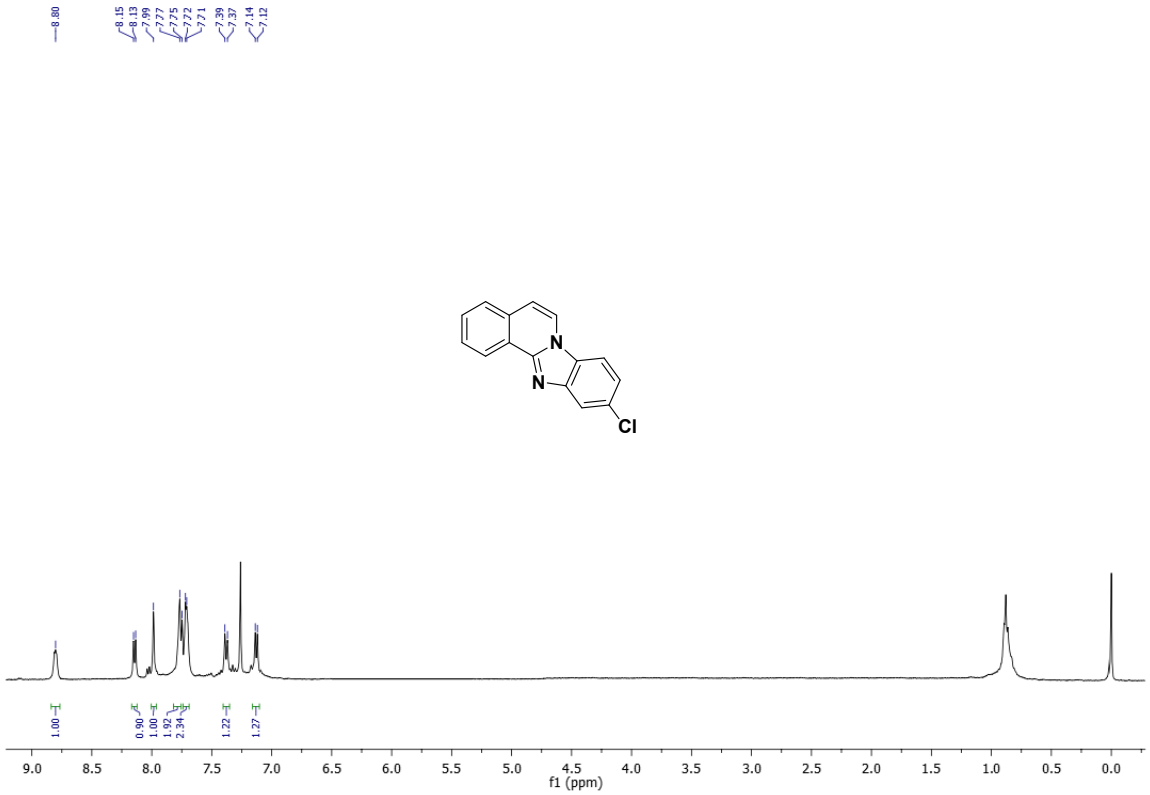
[1]H-NMR spectra of 9-fluorobenzo[4,5]imidazo[2,1-a]isoquinoline(3j)



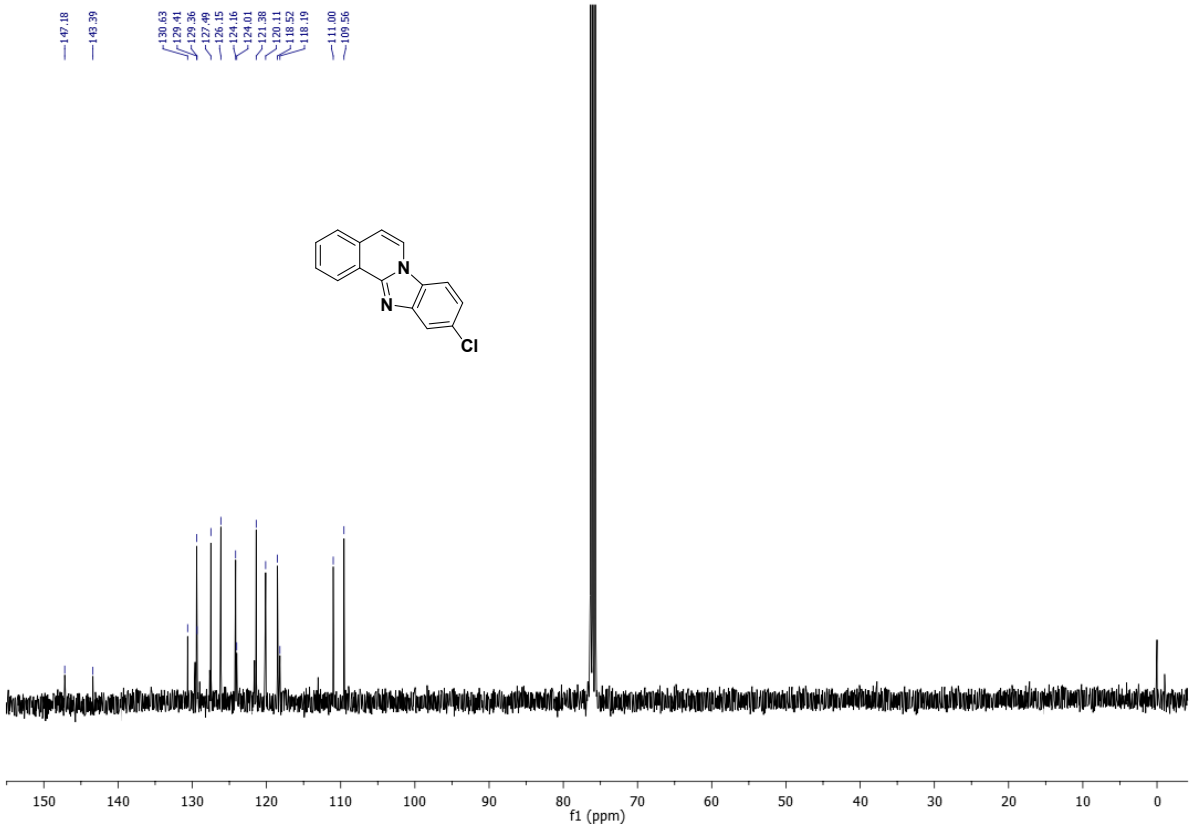
[13]C-NMR spectra of 9-fluorobenzo[4,5]imidazo[2,1-a]isoquinoline(3j)



[1]H-NMR spectra of 10-chlorobenzo[4,5]imidazo[2,1-a]isoquinoline(3k)



[13]C-NMR spectra of 10-chlorobenzo[4,5]imidazo[2,1-a]isoquinoline(3k)



6. **crude 1H-NMR of 7-Methoxypyrido[1,2-*a*]benzimidazole (2i)**