Supporting Information

β-Carboline directed regioselective hydroxylation by employing $Cu(OAc)_2$ and mechanistic investigation by ESI-MS

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1. General Information

Commercially available reagents and solvents were used without further purification. ^{1}H NMR spectra were recorded on an NMR instrument operated at 500 MHz. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (DMSO-d_6: δ = 2.50 ppm). ^{13}C NMR spectra were recorded on an NMR instrument operated at 125 MHz with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (DMSO-d_6: δ = 39.52 ppm). The following abbreviations were used for ^{1}H NMR spectra to indicate the signal multiplicity: s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). HRMS was measured in ESI-MS mass spectrophotometer. Thin layer chromatography was performed on MERCK precoated silica gel 60F-254 (0.5 mm) aluminum plates and visualized under UV light at 254 nm. Column chromatography was performed using silica gel 60-120.

2. Experimental Procedure

(a) Microwave Irradiation Experiments

Microwave irradiation experiments were performed in a monowave 300 single-mode microwave reactor. The reaction temperature is monitored by an external infrared (IR) sensor housed in the side-walls of the microwave cavity measuring the surface temperature of the reaction vessel. Reaction times refer to hold time at the desired set temperature and not to the total radiation time. Pressure sensing is achieved by a hydraulic sensor integrated in the swivelling cover of the instrument. The reusable 10 mL G10 Pyrex vial is sealed with PEEK snap caps and standard PTFE coated silicone septa. Reaction cooling is performed by compressed air automatically after the heating period has elapsed. The required force of 6-8 bar is also used to pneumatically seal the vials tightly at the beginning to withstand 30 bar and to ensure smooth release of potentially remaining pressure before the cover is opened.

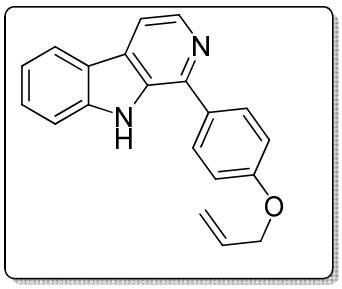
All the β-carboline derivatives **1a-f, 1i-t** and **4** were synthesized by the reported procedures.[39-42]

(b) General Procedure for the Synthesis of β-Carbolines 1g and 1h

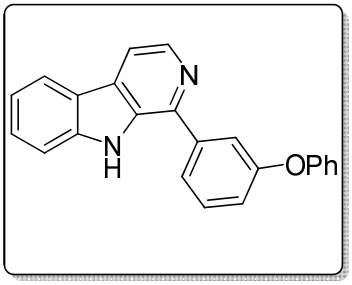
To a stirred solution of L-tryptophan (1 mmol) in acetic acid was added aldehyde (1.1 mmol). The mixture was stirred in a pre-heated oil bath at a temperature of 80 °C for 1 h and then acetic acid was removed under reduced pressure and dried well. This residue was

taken in dimethylformamide (DMF), and triethylamine (3 mmol) and solution of NCS (2 mmol) in DMF were added at 0 °C. Then, the reaction mixture was stirred for 30 min at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with water, extracted with ethyl acetate, and washed with saturated Na_2CO_3 solution. The combined organic layers were washed with water and brine solution, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue obtained was purified by column chromatography by using 20-40% of ethyl acetate and hexane to afford the desired β-carbolines.

1-(4-(Allyloxy)phenyl)-9H-pyrido[3,4-b]indole (1g). (355.9 mg), 82% yield; yellow solid; mp: 198-202 °C; FT-IR $(cm)^{-1}$: 3251, 2945, 2867, 1664, 1519; ^1H NMR (500 MHz, DMSO-d_6): δ 11.47 (s, 1H), 8.42 (d, *J* = 5.1 Hz, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 8.07 (d, *J* = 5.1 Hz, 1H), 7.96-8.03 (m, 2H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.52-7.58 (m, 1H), 7.26 (t, *J* = 7.2 Hz, 1H), 7.18 (dt, *J* = 1.9, 8.7 Hz, 2H), 6.04-6.19 (m, 1H), 5.47 (dd, *J* = 1.6, 15.5 Hz, 1H), 5.32 (dd, *J* = 1.5, 8.9 Hz, 1H), 4.7 (dt, *J* = 1.3, 5.1 Hz, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 159.0, 142.5, 141.5, 138.7, 134.1, 133.1, 131.4, 130.1, 129.4, 128.4, 122.0, 121.3, 119.9, 118.0, 115.3, 112.8, 68.7 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{20}H_{16}N_2O$ 301.1341 found 301.1331.



1-(3-Phenoxyphenyl)-9H-pyrido[3,4-b]indole (1h). (378.1 mg), 86% yield; light yellow solid; mp: 189-193 °C; FT-IR $(cm)^{-1}$: 3269, 2981, 1562, 1626, 1450; ^1H NMR (500 MHz, DMSO-d_6): δ 11.84 (s, 1H), 8.48 (d, *J* = 5.3 Hz, 1H), 8.34 (d, *J* = 7.8 Hz, 1H), 8.30 (d, *J* = 5.3 Hz, 1H), 7.80-7.85 (m, 1H), 7.60-7.72 (m, 4H), 7.42-7.46 (m, 2H), 7.30-7.35 (m, 1H), 7.14-7.23 (m, 4H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 157.7, 156.8, 142.4, 140.5, 136.6, 133.3, 131.0, 130.6, 129.6, 124.3, 124.1, 122.5, 121.0, 120.5, 119.7, 119.5, 118.9, 115.2, 113.1 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{23}H_{16}N_2O$ 337.1341 found 337.1360.

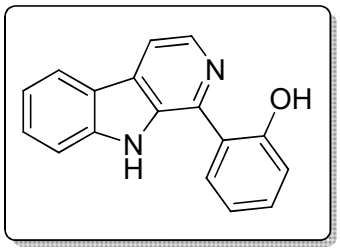


(c) General procedure for hydroxylation of β-carbolines 2a-t

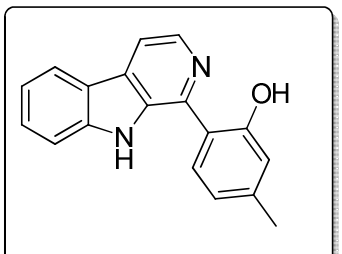
A mixture of β-carboline (1 equiv.), copper(II) acetate (1 equiv.), silver(I) acetate (1 equiv.) and 10 equiv. of water in acetonitrile:acetic acid (1;1) were heated through

microwave irradiation at 150 °C for 30-40 min. After completion of the reaction, the reaction mixture was allowed to cool to room temperature, then neutralized with sodium bicarbonate solution and extracted with ethyl acetate, followed by flash column to afford pure compounds **2a–t** in 55-85% yields. All the synthesized compounds were thoroughly characterized by IR, ^{1}H NMR, ^{13}C NMR and HRMS (ESI).

2-(9H-Pyrido[3,4-b]indol-1-yl)phenol (2a). (174.7 mg), 82% yield; yellow solid; mp: 192-195 °C; FT-IR (cm)$^{-1}$: 3293, 3051, 2922, 2852, 1887, 1602; ^{1}H NMR (500 MHz, DMSO-d_6): δ 13.37 (s, 1H), 11.62 (s, 1H), 8.44 (d, *J* = 5.9 Hz, 1H), 8.32 (d, *J* = 7.9 Hz, 1H), 8.23 (d, *J* = 5.2 Hz, 1H), 8.07 (dd, *J* = 1.5, 6.2 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.58-7.62 (m, 1H), 7.22-7.36 (m, 2H), 7.01-7.12 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.2, 142.2, 141.8, 136.0, 132.6, 130.8, 130.4, 129.4, 129.0, 122.1, 121.2, 121.0, 120.3, 119.3, 117.7, 114.5, 113.0 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{17}H_{12}N_2O$ 216.1028 found 261.1035.



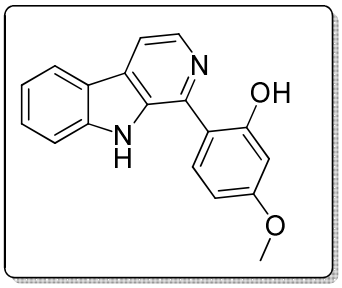
5-Methyl-2-(9H-pyrido[3,4-b]indol-1-yl)phenol (2b). (169.9 mg), 80% yield; yellow solid; mp: 172-180 °C; FT-IR (cm)$^{-1}$: 3399, 3015, 2920, 2851, 2732, 2622; ^{1}H NMR (500 MHz, DMSO-d_6): δ 13.65 (s, 1H), 11.62 (s, 1H), 8.37-8.45 (m, 1H), 8.31 (d, *J* = 7.6 Hz, 1H), 8.18-8.22 (m, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.60 (t, *J* = 7.1 Hz, 1H), 7.31 (t, *J* = 7.5Hz, 1H), 6.84-6.95 (m, 2H), 2.37 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.4, 142.5, 141.8, 140.8, 135.7, 132.3, 130.4, 129.0, 122.1, 121.0, 120.3, 120.2, 118.2, 114.2, 113.1, 21.5 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{18}H_{14}N_2O$ 275.1184 found 275.1188.



5-Isopropyl-2-(9H-pyrido[3,4-b]indol-1-yl)phenol (2c). (177.3 mg), 84% yield; yellow solid; mp: 191-195 °C; FT-IR (cm)$^{-1}$: 3294, 2969, 2983, 2815, 1835, 1632; ^{1}H NMR (500 MHz, DMSO-d_6): δ 13.58 (s, 1H), 11.63 (s, 1H), 8.41 (d, *J* = 5.2 Hz, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 8.19 (d, *J* = 5.3 Hz, 1H), 8.04 (d, *J* = 8.1 Hz, 1H), 7.73 (dt, *J* = 0.8, 8.2 Hz, 1H), 7.56-7.63 (m, 1H), 7.26-7.35 (m, 1H), 6.96 (dd, *J* = 1.7, 6.3 Hz, 1H), 6.92 (d, *J* = 1.6 Hz, 1H), 2.93 (qui, *J* = 0.7, 6.3 Hz, 1H), 1.28

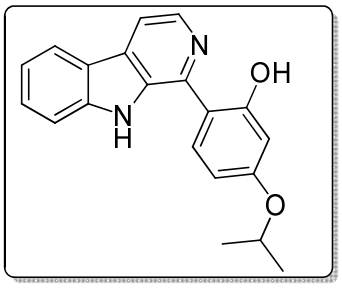
(s, 3H), 1.28 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.5, 151.7, 142.4, 141.8, 135.8, 132.3, 130.4, 129.1, 129.0, 122.0, 121.0, 120.3, 118.6, 117.6, 115.5, 114.2, 113.1, 33.8, 24.1 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{20}H_{18}N_2O$ 303.1497 found 303.1508.

5-Methoxy-2-(9H-pyrido[3,4-b]indol-1-yl)phenol (2d). (171.4 mg), 81% yield; yellow solid;



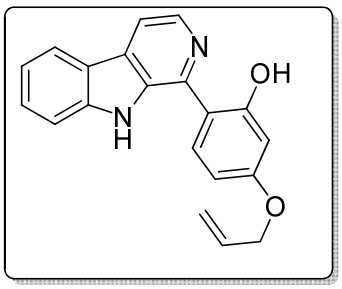
mp: 230-234 °C; FT-IR $(cm)^{-1}$: 3326, 3039, 2917, 2849, 1872, 1738; ^{1}H NMR (500 MHz, DMSO-d_6): δ 14.31 (s, 1H), 11.65 (s, 1H), 8.37 (d, *J* = 5.3 Hz, 1H), 8.30 (d, *J* = 7.8 Hz, 1H), 8.17 (d, *J* = 5.2 Hz, 1H), 8.09 (d, *J* = 8.6 Hz, 1H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.54-7.64 (m, 1H), 7.31 (t, *J* = 7.0 Hz, 1H), 6.66 (dd, *J* = 2.5 Hz, 1H), 6.59 (d, *J* = 2.5 Hz, 1H), 3.84 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 161.6, 160.8, 142.6, 141.8, ,135.3, 131.8, 130.5, 130.0, 129.0, 122.0, 121.0, 120.4, 113.8, 113.5, 113.1, 106.0, 102.5, 55.7 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{18}H_{14}N_2O_2$ 291.1134 found 291.1177.

5-Isopropoxy-2-(9H-pyrido[3,4-b]indol-1-yl)phenol (2f). (178.9 mg), 85% yield; yellow solid;



mp: 176-180 °C; FT-IR $(cm)^{-1}$: 3291, 2971, 2936, 2828, 1853, 1610; ^{1}H NMR (500 MHz, DMSO-d_6): δ 14.11 (s, 1H), 11.73 (s, 1H), 8.39 (d, *J* = 5.4 Hz, 1H), 8.33 (d, *J* = 7.8 Hz, 1H), 8.22 (d, *J* = 5.1 Hz, 1H), 8.0 (d, *J* = 8.7 Hz, 1H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.32 (t, *J* = 7.3 Hz, 1H), 6.63 (dd, *J* = 6.6, 8.6 Hz, 1H), 6.54-6.60 (m, 1H), 4.72 (qui, *J* = 6.1, 12.0 Hz, 1H), 1.33 (d, J = 5.9 Hz, 6H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.5, 160.0, 142.0, 134.7, 131.9, 130.7, 130.3, 129.2, 122.2, 120.9, 120.5, 114.0, 113.1, 112.9, 107.3, 103.9, 69.7, 22.3 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{20}H_{18}N_2O_2$ 319.1447 found 319.1450.

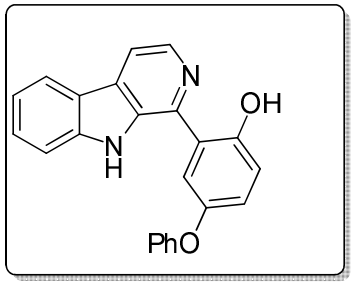
5-(Allyloxy)-2-(9H-pyrido[3,4-b]indol-1-yl)phenol (2g). (149.5 mg), 71% yield; yellow solid;



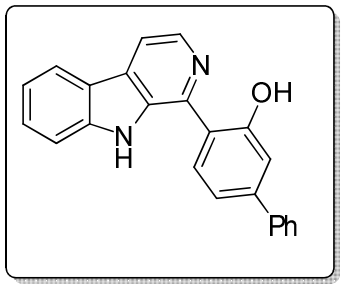
mp: 192-195 °C; FT-IR $(cm)^{-1}$: 3398, 3053, 2854, 2769, 1865, 1628; ^{1}H NMR (500 MHz, DMSO-d_6): δ 14.43 (s, 1H), 11.66 (s, 1H), 8.37 (d, *J* = 5.3 Hz, 1H), 8.30 (d, *J* = 7.9 Hz, 1H), 8.17 (d, *J* = 5.2 Hz, 1H), 8.09 (d, *J* = 8.7 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.57-7.63 (m, 1H), 7.28-7.34 (m, 1H), 6.67 (dd, J = 2.5, 6.1 Hz, 1H), 6.61 (d, *J* = 2.5 Hz, 1H), 6.04-6.16 (m, 1H), 5.41-5.50 (m, 1H),

5.27-5.35 (m, 1H), 4.67 (dt, *J* = 1.4, 5.1 Hz, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.8, 160.5, 142.5, 141.8, 135.3, 134.1, 131.8, 130.5, 130.0, 129.0, 122.0, 121.0, 120.4, 118.0, 113.8, 113.6, 113.1, 106.5, 103.3, 68.7 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{20}H_{16}N_2O_2$ 317.1290 found 317.1292.

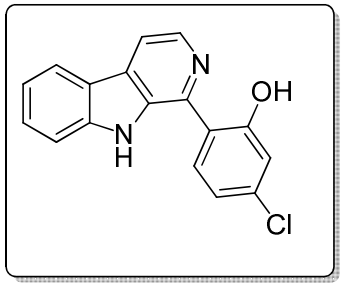
4-Phenoxy-2-(9H-pyrido[3,4-b]indol-1-yl)phenol (2h). (144.4 mg), 69% yield; yellow solid; mp: 235-240 °C; FT-IR (cm)$^{-1}$: 3351, 3132, 2917, 1752, 1481, 1033; ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.74 (s, 1H), 11.54 (s, 1H), 8.44 (d, *J* = 5.2 Hz, 1H), 8.29 (d, *J* = 7.8 Hz, 1H), 8.22 (d, *J* = 5.1 Hz, 1H), 7.67-7.75 (m, 2H), 7.53-7.63 (m, 1H), 7.33-7.39 (m 2H), 7.25-7.32 (m, 1H), 6.98-7.12 (m, 5H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.7, 154.3, 148.2, 141.7, 141.3, 136.4, 132.9, 130.4, 130.3, 129.0, 122.8, 122.7, 122.4, 122.1, 121.0, 121.0, 118.7, 117.6, 114.7, 113.0 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{23}H_{16}N_2O_2$ 353.1290 found 353.1289.



4-(9H-Pyrido[3,4-b]indol-1-yl)-[1,1'-biphenyl]-3-ol (2i). (161.6 mg), 77% yield; yellow solid; mp: 269-275 °C; FT-IR (cm)$^{-1}$: 3376, 3083, 2850, 1864, 1792, 1644; ^{1}H NMR (500 MHz, DMSO-d_6): δ 13.72 (s, 1H), 11.73 (s, 1H), 8.46 (d, *J* = 5.3Hz, 1H), 8.33 (d, *J* = 5.2 Hz, 1H), 8.25 (d, *J* = 5.2 Hz, 1H), 8.20 (d, *J* = 8.1 Hz, 1H), 7.73-7.80 (m, 3H), 7.59-7.64 (m, 1H), 7.50-7.55 (m, 2H), 7.37-7.45 (m, 2H), 7.30-7.36 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.9, 142.5, 141.9, 141.8, 139.9, 135.9, 132.6, 129.8, 129.5, 129.1, 128.3, 127.0, 122.1, 121.0, 120.4, 120.1, 117.7, 115.6, 114.6, 113.1 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{23}H_{16}N_2O$ 337.1341 found 337.1390.

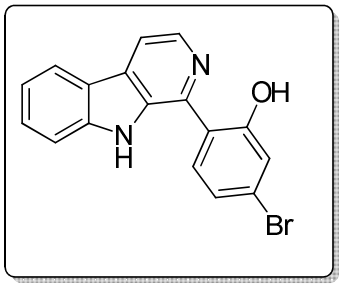


5-Chloro-2-(9H-pyrido[3,4-b]indol-1-yl)phenol (2k). (167.0 mg), 79% yield; yellow solid; mp: 269-275 °C; FT-IR (cm)$^{-1}$: 3350, 3018, 2970, 1894, 1738, 1626; ^{1}H NMR (500 MHz, DMSO-d_6): δ 13.72 (s, 1H), 11.59 (s, 1H), 8.41 (d, *J* = 5.3Hz, 1H), 8.30 (d, *J* = 7.8 Hz, 1H), 8.23 (d, *J* = 5.2 Hz 1H), 7.93-8.00 (m, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.54-7.64 (m, 1H), 7.23-7.35 (m, 1H), 7.03-7.15 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 159.3, 141.7, 141.1, 136.1, 134.6, 132.7,

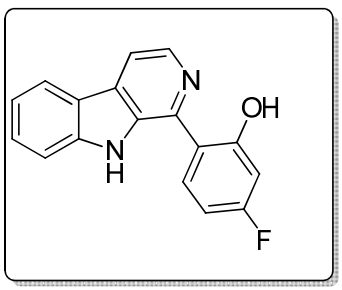


131.0, 130.4, 129.1, 122.2, 120.9, 120.6, 120.3, 119.2, 117.3, 114.8, 112.9 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{17}H_{11}ClN_2O$ 295.0638 found 295.0246.

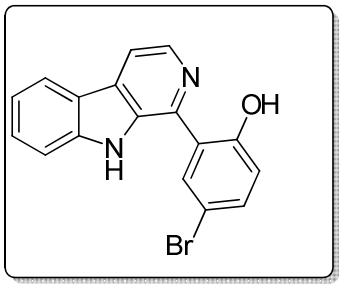
5-Bromo-2-(9H-pyrido[3,4-b]indol-1-yl)phenol (2l). (157.4 mg), 75% yield; yellow solid; mp: 256-260 °C; FT-IR $(cm)^{-1}$: 3327, 2975, 2923, 2854, 1738, 1625; ^1H NMR (500 MHz, DMSO-d_6): δ 13.62 (s, 1H), 11.60 (s, 1H), 8.43 (d, *J* = 5.2Hz, 1H), 8.32 (d, *J* = 7.8 Hz, 1H), 8.25 (d, *J* = 5.2 Hz 1H), 7.95 (d, *J* = 8.1 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.31 (t, *J* = 7.7Hz, 1H), 7.20-7.27 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 159.2, 141.7, 141.2, 136.1, 132.7, 131.2, 130.4, 129.1, 123.1, 122.2, 122.1, 121.0, 120.9, 120.3, 120.2, 114.8, 112.9 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{17}H_{11}BrN_2O$ 339.0133 $[M+H]^+$ found 339.0115.



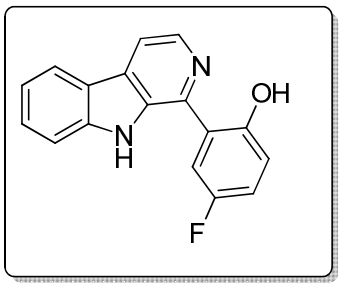
5-Fluoro-2-(9H-pyrido[3,4-b]indol-1-yl)phenol (2m). (152.7 mg), 72% yield; yellow solid; mp: 214-216 °C; FT-IR $(cm)^{-1}$: 3281, 3054, 2970, 1738, 1626, 1603; ^1H NMR (500 MHz, DMSO-d_6): δ 13.73 (s, 1H), 11.61 (s, 1H), 8.43 (dd, *J* = 0.7, 4.5 Hz, 1H), 8.32 (d, *J* = 7.8 Hz, 1H), 8.25 (d, *J* = 4.7 Hz 1H), 8.03 (d, *J* = 8.9 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.57-7.63 (m, 1H), 7.26-7.34 (m, 1H), 7.05-7.14 (m, 2H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 161.76 (d, J_{C-F} = 284.9 Hz), 159.3, 141.8, 141.1, 136.1, 134.6, 132.7, 131.0, 130.49 (d, J_{C-F} = 5.7 Hz), 122.2, 120.9, 120.6, 120.4, 119.2, 117.3, 114.8, 112.9 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -108.8 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{17}H_{11}FN_2O$ 279.0934 found 279.0690.



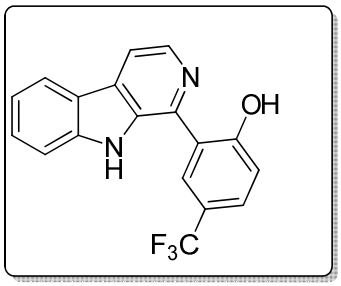
4-bromo-2-(9H-pyrido[3,4-b]indol-1-yl)phenol (2n). (159.5 mg), 76% yield; yellow solid; mp: 210-214°C; FT-IR $(cm)^{-1}$: 3341, 2852, 2812, 1751, 1621; ^1H NMR (500 MHz, DMSO-d_6): δ 12.69 (s, 1H), 11.56 (s, 1H), 8.44 (d, *J* = 5.3 Hz, 1H), 8.31 (d, *J* = 7.8 Hz, 1H), 8.23 (d, *J* = 5.2 Hz, 1H), 7.98 (d, *J* = 2.4 Hz, 1H), 7.70 (d, *J* = 8.23 Hz, 1H), 7.56-7.63 (m, 1H), 7.52 (dd, *J* = 2.4, 6.2 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 156.9, 141.7, 140.6, 136.7, 133.2, 131.9, 130.2, 129.0, 124.6, 122.2, 121.0, 120.2, 119.6, 114.9, 112.9, 110.5 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{17}H_{11}BrN_2O$ 339.0133 found 339.0190.



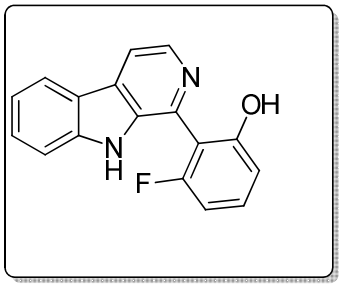
4-fluoro-2-(9H-pyrido[3,4-b]indol-1-yl)phenol (2o). (157.0 mg), 74% yield; yellow solid; mp: 199-203 °C; FT-IR (cm)$^{-1}$: 3251, 3062, 2965, 1751, 1692, 1612; ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.91 (s, 1H), 11.63 (s, 1H), 8.45 (d, J = 5.1 Hz, 1H), 8.32 (d, J = 7.8 Hz, 1H), 8.26 (d, J = 5.2 Hz, 1H), 7.80 (dd, J = 3.1, 6.7 Hz, 1H), 7.69-7.74 (m, 1H), 7.58-7.64 (m, 1H), 7.29-7.35 (m, 1H), 7.19-7.26 (m, 1H), 7.05 (q, J = 3.9, 5.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 155.5 (d, $J_{C\text{-}F}$ = 233.8 Hz), 154.2, 141.8, 140.9, 136.3, 132.8, 130.5, 129.1, 122.2, 122.0 (d, $J_{C\text{-}F}$ = 7.4 Hz), 120.9, 120.3, 118.5 (d, $J_{C\text{-}F}$ = 8.07 Hz), 117.3 (d, $J_{C\text{-}F}$ = 22.7 Hz) , 115.6, 115.4, 115.07, 113.0 ppm; ^{19}F NMR (470 MHz, DMSO-d_6): δ -124.8 ppm; HRMS (ESI-QTOF): m/z $[M+H]^+$ calcd. for $C_{17}H_{11}FN_2O$ 279.0934 found 279.0937.



2-(9H-pyrido[3,4-b]indol-1-yl)-4-(trifluoromethyl)phenol (2p). (151.3 mg), 72% yield; yellow solid; mp: 147-150 °C; FT-IR (cm)$^{-1}$: 3460, 2993, 2952, 2830, 1638, 1614; ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.60 (s, 1H), 11.45 (s, 1H), 8.45 (d, J = 5.1 Hz, 1H), 8.30 (d, J = 7.8 Hz, 1H), 8.22 (d, J = 5.2 Hz, 1H), 7.06 (d, J = 1.9 Hz, 1H), 7.71 (dd, J = 2.1, 6.5 Hz, 1H), 7.66 (d, J = 8.1 Hz, 1H), 7.55-7.60 (m, 1H), 7.26-7.31 (m, 1H), 7.24 (d, J = 8.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.2, 141.6, 140.5, 137.1, 133.6, 129.8, 128.9, 127.7, 127.32 (q, $J_{C\text{-}CF3}$ = 278.2 Hz), 127.5,.122.2, 120.06 (q, $J_{C\text{-}CF3}$= 32.0 Hz), 117.9, 114.9, 112.8 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -60.9 ppm; HRMS (ESI-QTOF): m/z $[M+H]^+$ calcd. for $C_{18}H_{11}F_3N_2O$ 329.0902 found 329.0960.

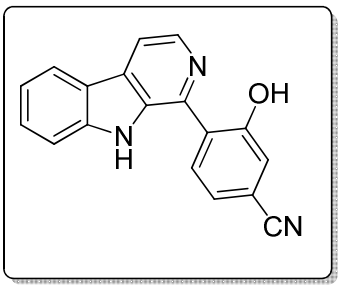


3-Fluoro-2-(9H-pyrido[3,4-b]indol-1-yl)phenol (2q). (135.8 mg), 64% yield; yellow solid; mp: 205-209 °C; FT-IR (cm)$^{-1}$: 3298, 3045, 2969, 1754, 1701, 1662; ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.21 (s, 1H), 10.31 (s, 1H), 8.41 (d, J = 5.2 Hz, 1H), 8.27 (d, J = 7.9 Hz, 1H), 8.14 (d, J = 5.1 Hz, 1H), 7.49-7.61 (m, *2*H), 7.32-7.42 (m, 1H), 7.21-7.30 (m, 1H), 6.90 (d, J = 8.3 Hz, 1H), 6.80-6.86 (m, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 161.3 (d, $J_{C\text{-}F}$ = 243.1 Hz), 157.8, 157.7, 141.2, 137.7, 135.2, 130.9 (d, $J_{C\text{-}F}$ = 10.06 Hz), 128.7, 122.1, 121.0, 119.7, 114.6, 112.5, 112.5,



106.6, 106.4 ppm; ^{19}F NMR (470 MHz, $CDCl_3$): δ -113. ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{17}H_{11}FN_2O$ 279.0934 found 279.0925.

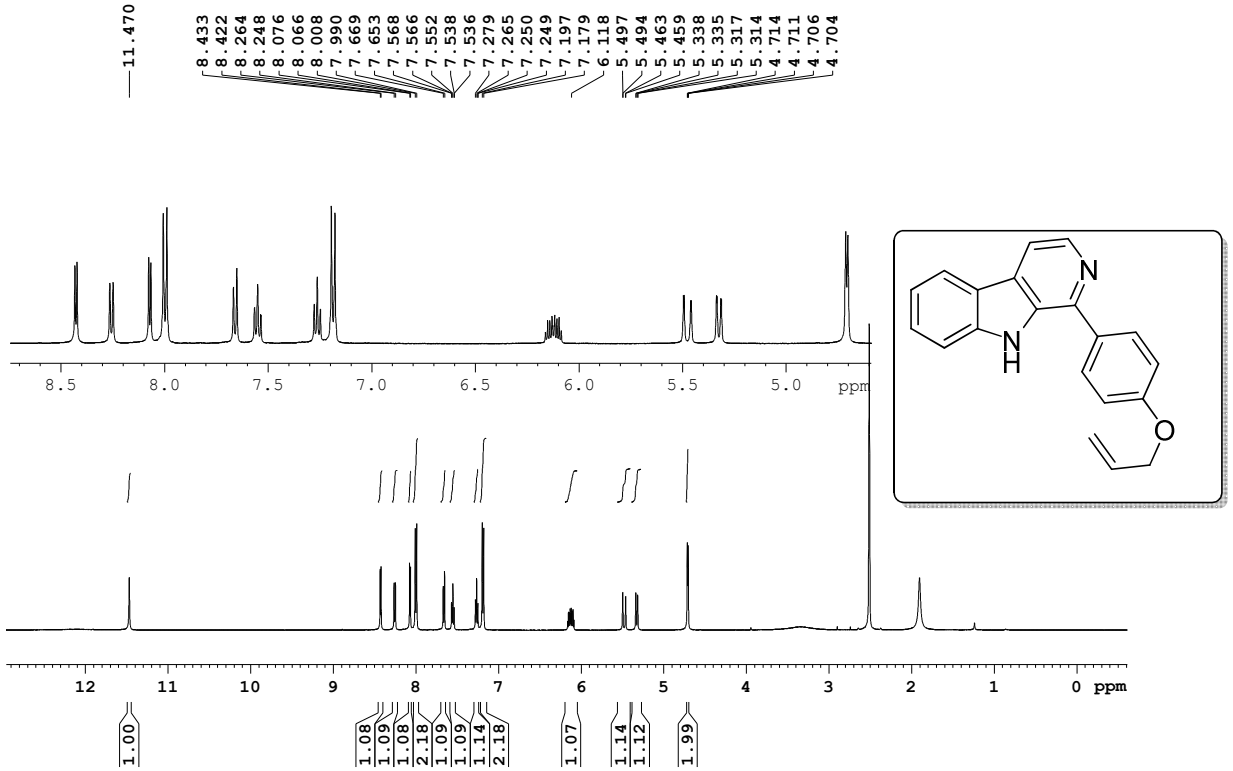
3-Hydroxy-4-(9H-pyrido[3,4-b]indol-1-yl)benzonitrile (2r). (116.5 mg), 55% yield; yellow solid; mp: 159-162 °C; FT-IR $(cm)^{-1}$: 3295, 2951, 2842, 2219, 1851, 1732; ^{1}H NMR (500 MHz, DMSO-d_6): δ 13.54 (s, 1H), 11.65 (s, 1H), 8.48 (d, *J* = 5.1 Hz, 1H), 8.28-8.36 (m, 2H), 8.13 (d, *J* = 7.9 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.48 (dd, *J* = 1.4, 6.5 Hz, 1H), 7.42-7.47 (m, 1H), 7.32 (t, *J* = 7.6 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.2, 141.8, 140.2, 136.5, 133.1, 130.9, 130.6, 129.3, 126.7, 122.8, 122.2, 120.9, 120.6, 120.4, 119.1, 115.6, 112.9, 112.5 ppm; HRMS (ESI-QTOF): *m/z* $[M+H]^+$ calcd. for $C_{18}H_{11}N_3O$ 286.0980 found 286.0977.



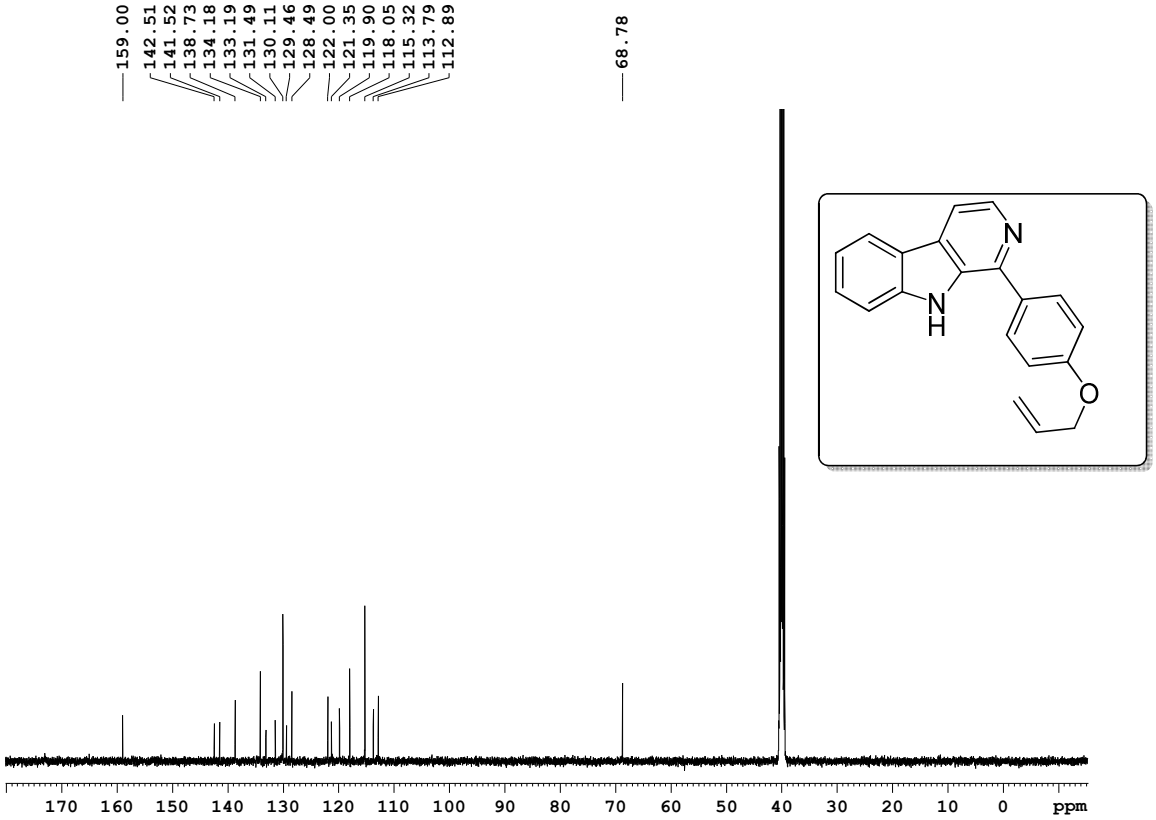
(d) Gram scale reaction

To demonstrate the scalability of this regioselective hydroxylation, a gram-scale synthesis was performed by using **1a** (1.5 g) under the optimized conditions, discussed in the general procedure. The reaction proceeded efficiently to give the desired product **2a** (1.2 g) in 80% yield.

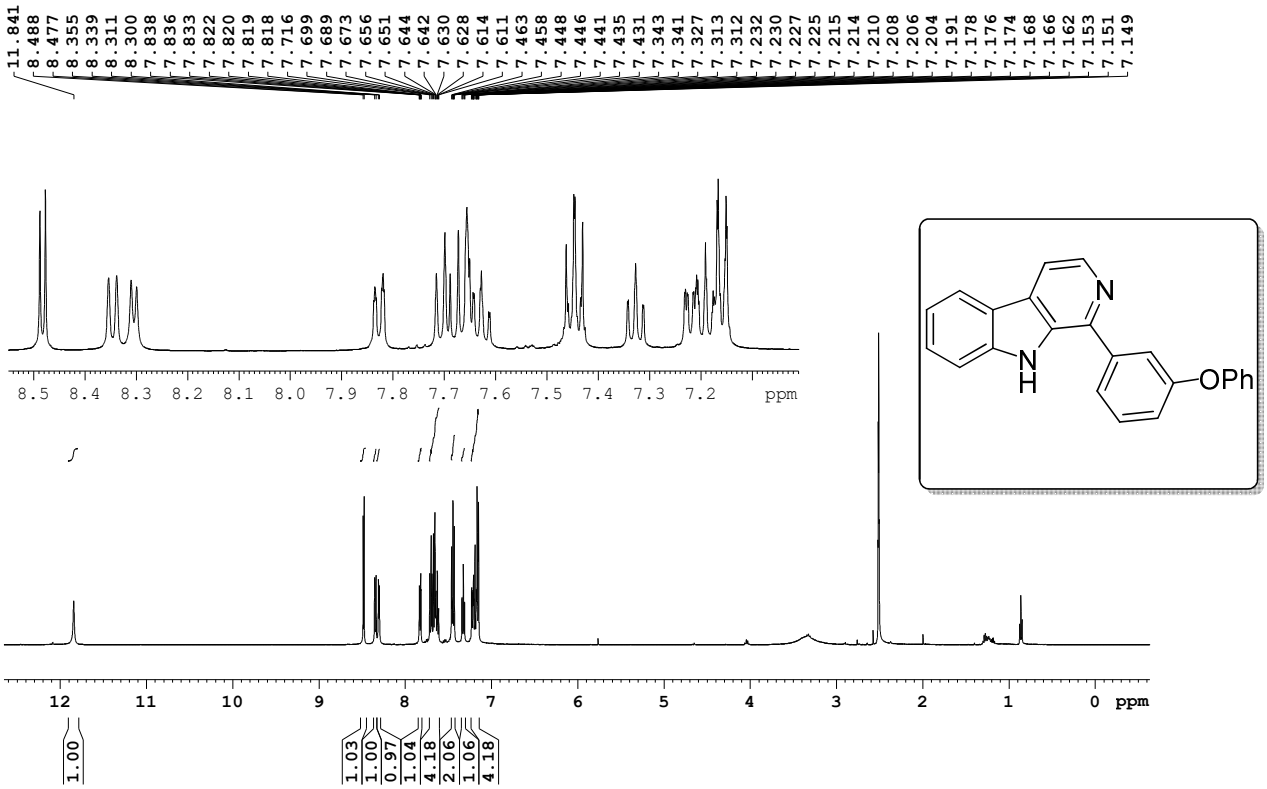
2. NMR Spectra



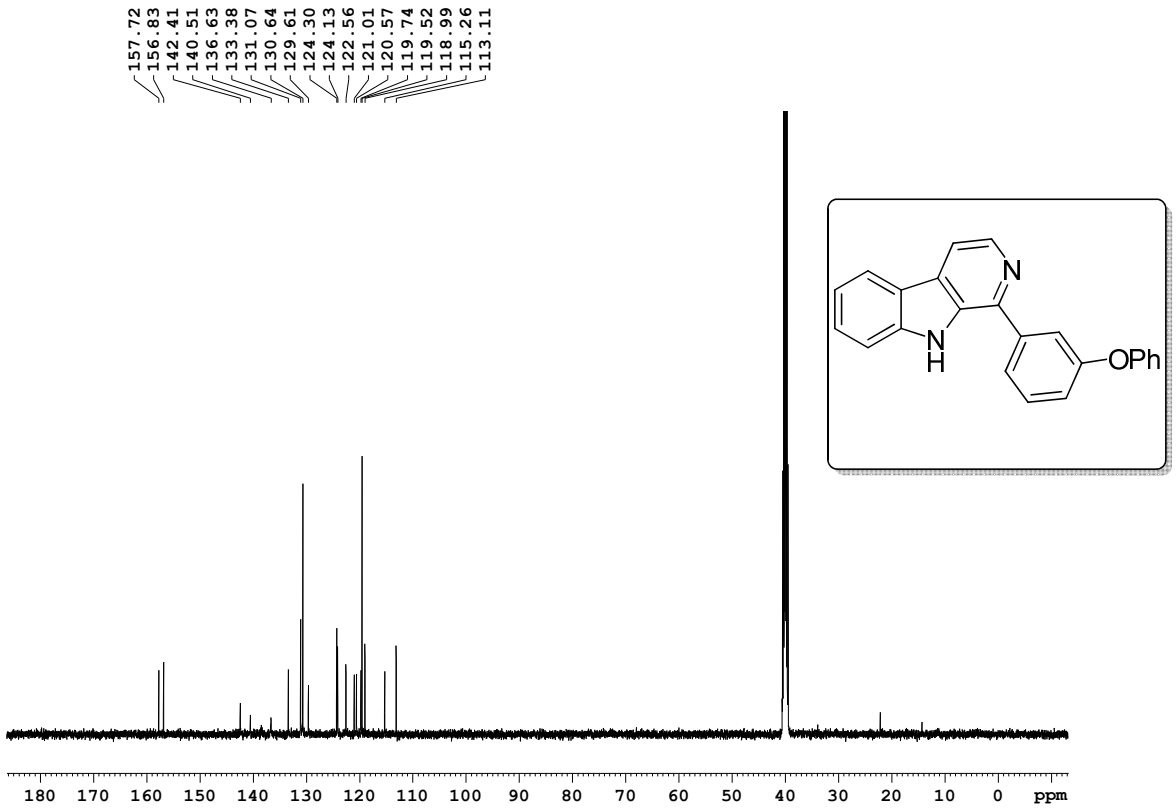
Compound **1g**: ^{1}H NMR (500 MHz, DMSO–d_6)



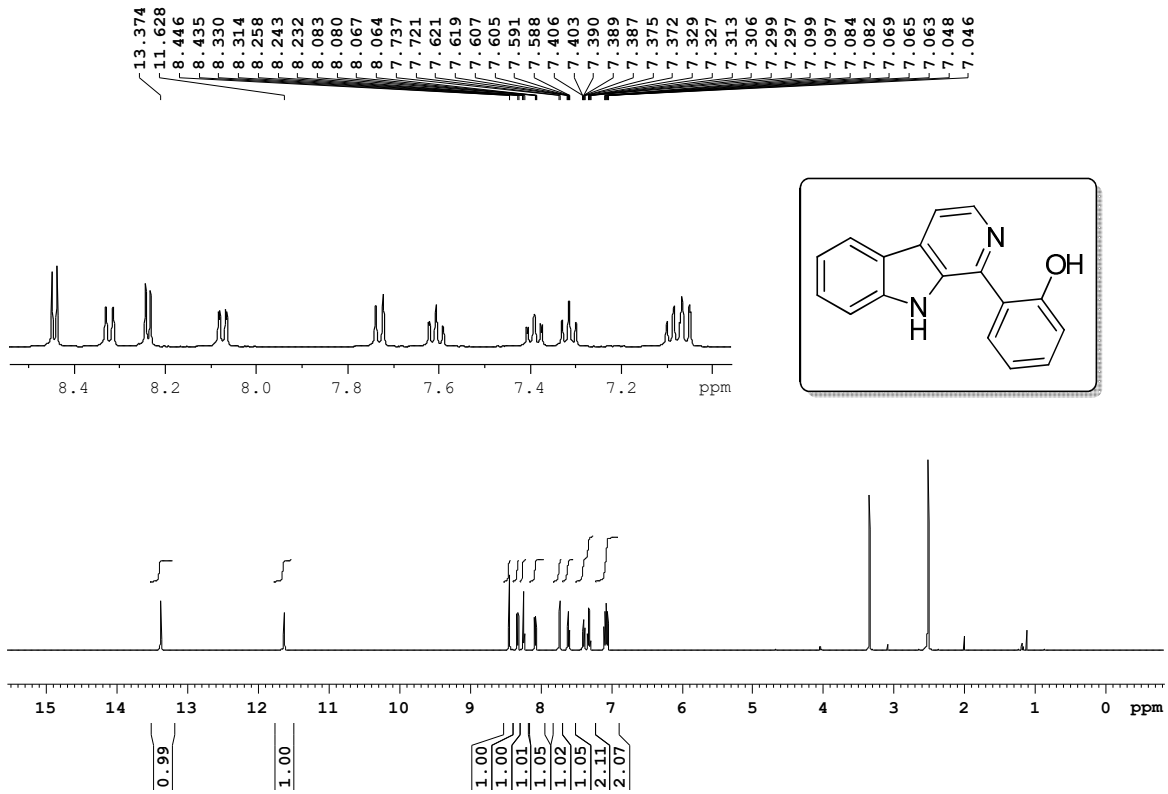
Compound **1g**: ^{13}C NMR (125 MHz, DMSO–d_6)



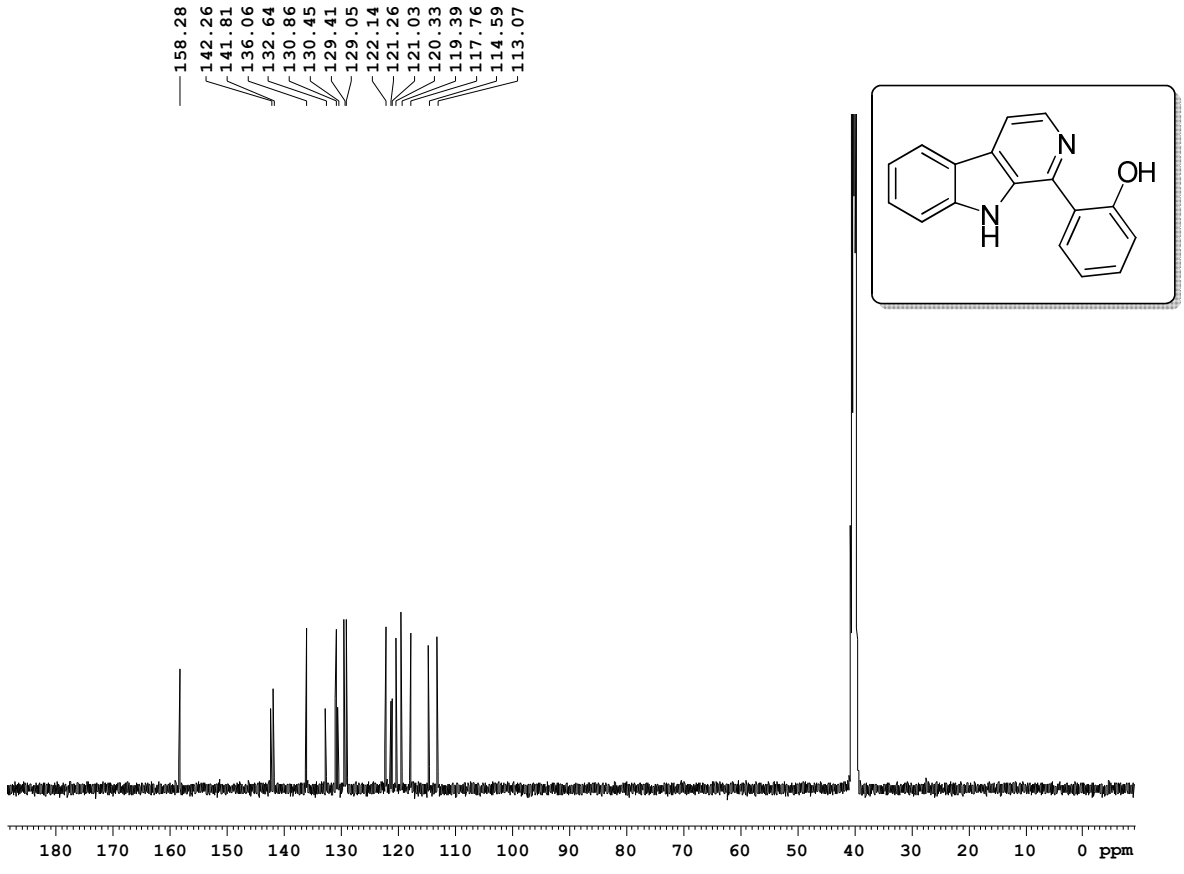
Compound **1h**: ^{1}H NMR (500 MHz, DMSO–d_6)



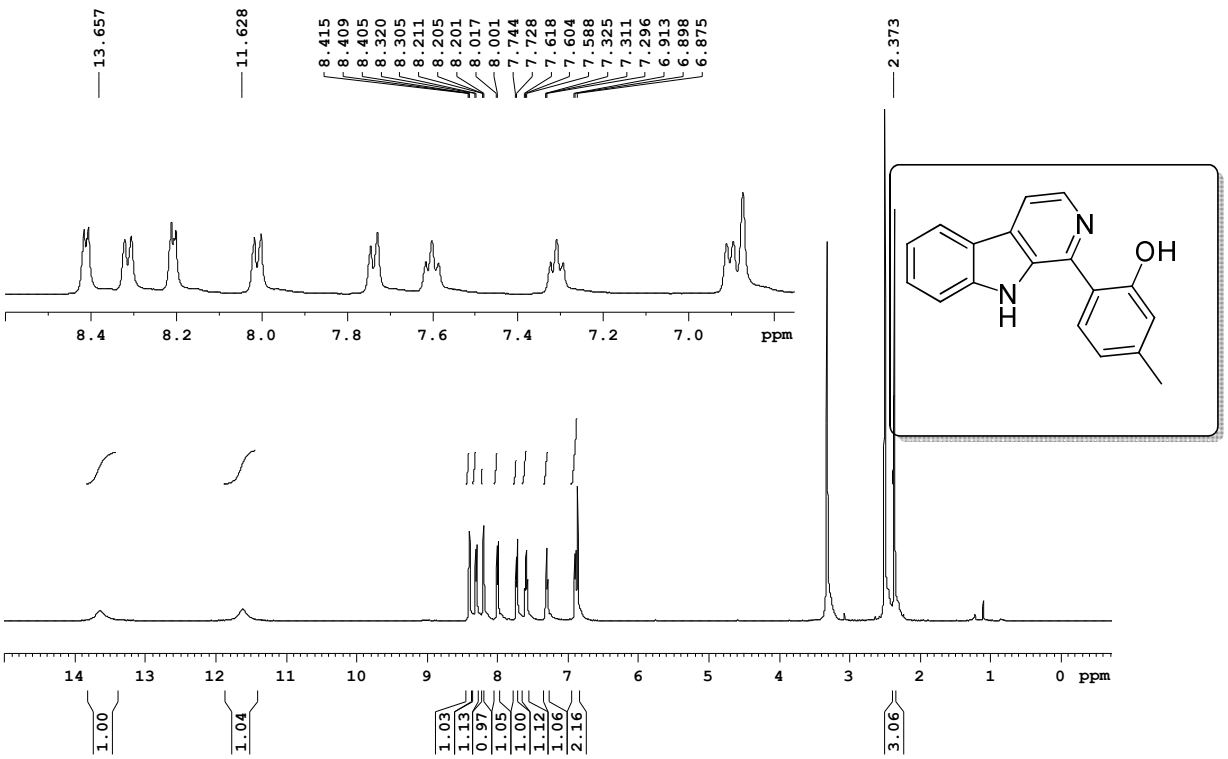
Compound **1h**: ^{13}C NMR (125 MHz, DMSO–d_6)



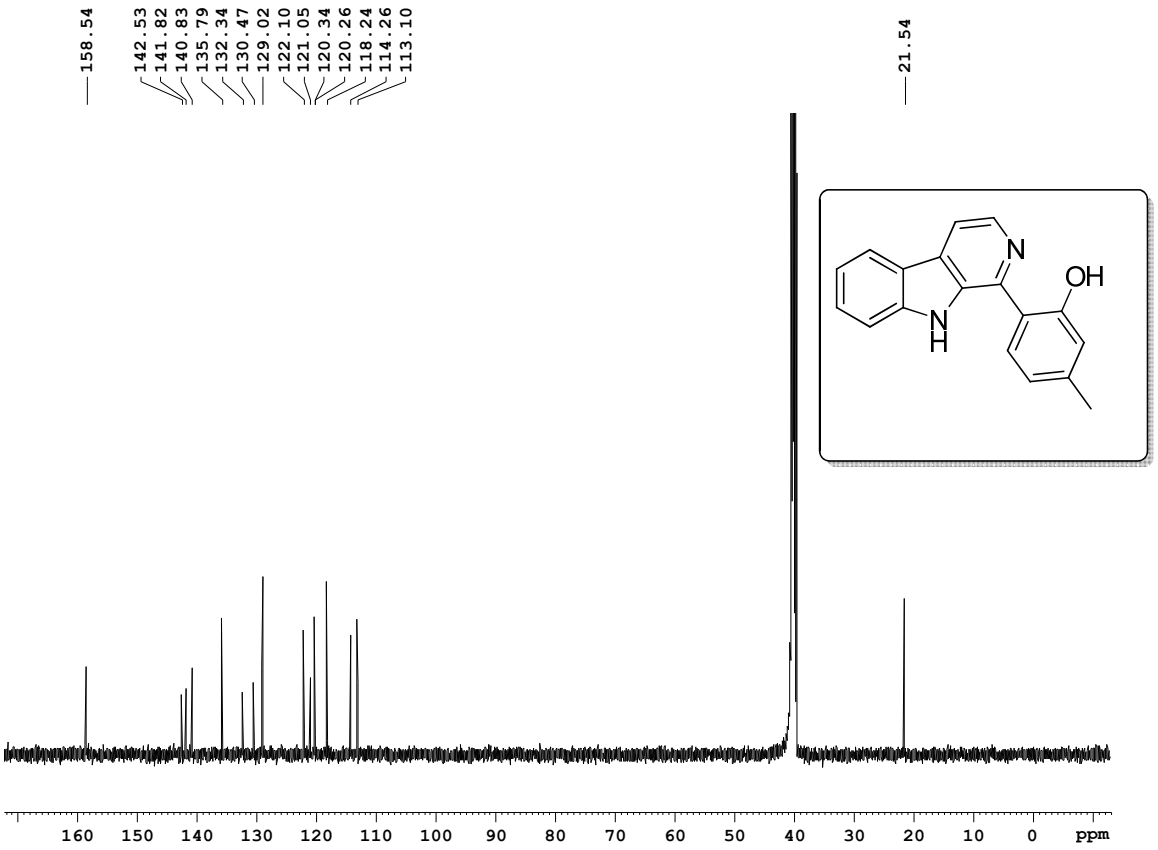
Compound **2a**: ^{1}H NMR (500 MHz, DMSO–d_6)



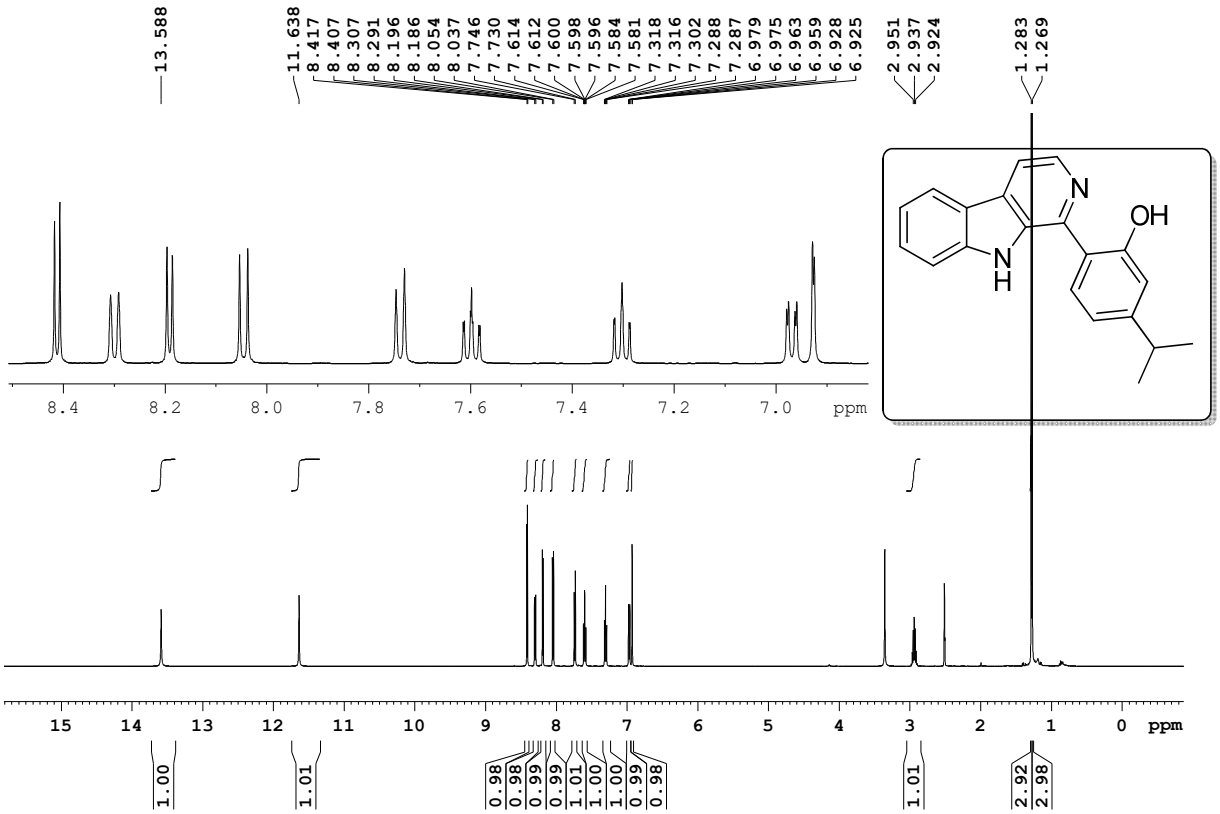
Compound **2a**: ^{13}C NMR (125 MHz, DMSO–d_6)



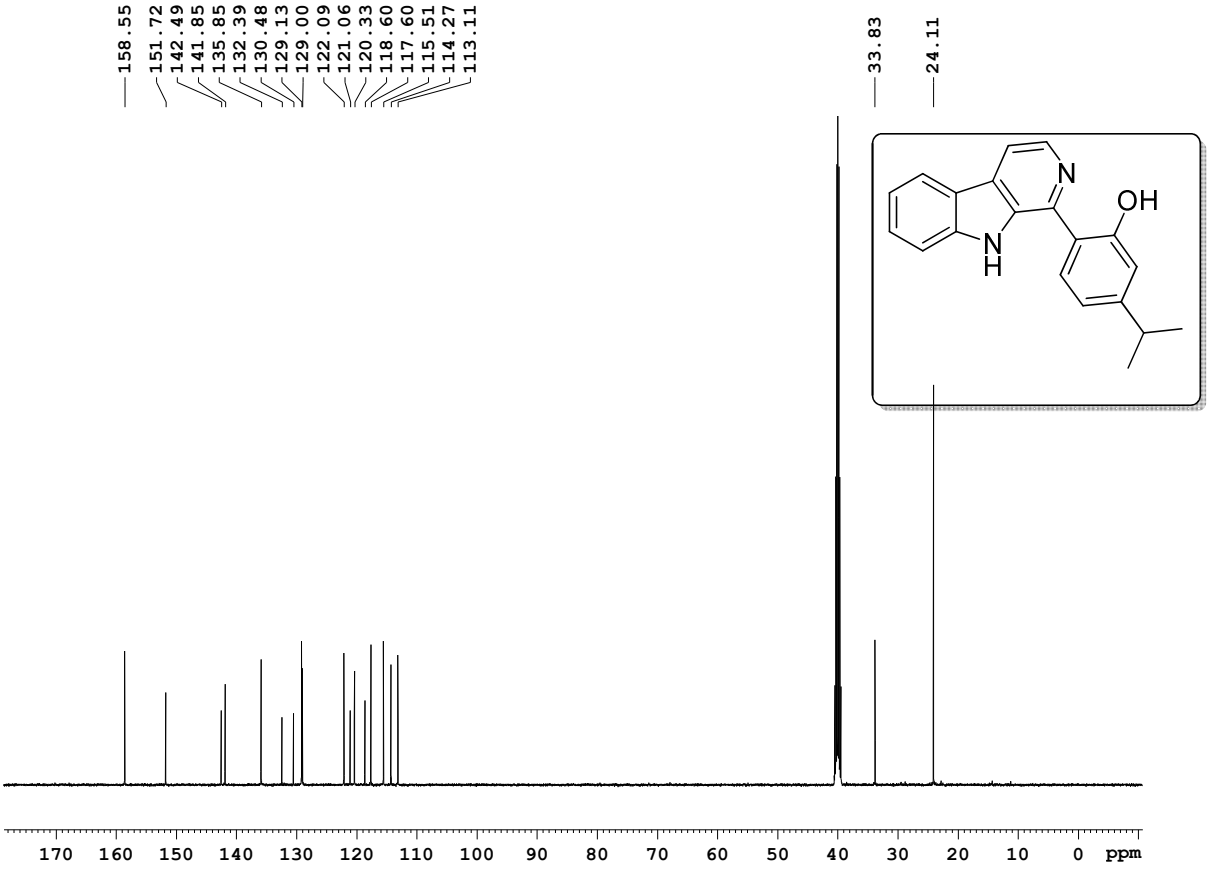
Compound **2b**: ^{1}H NMR (500 MHz, DMSO–d_6)



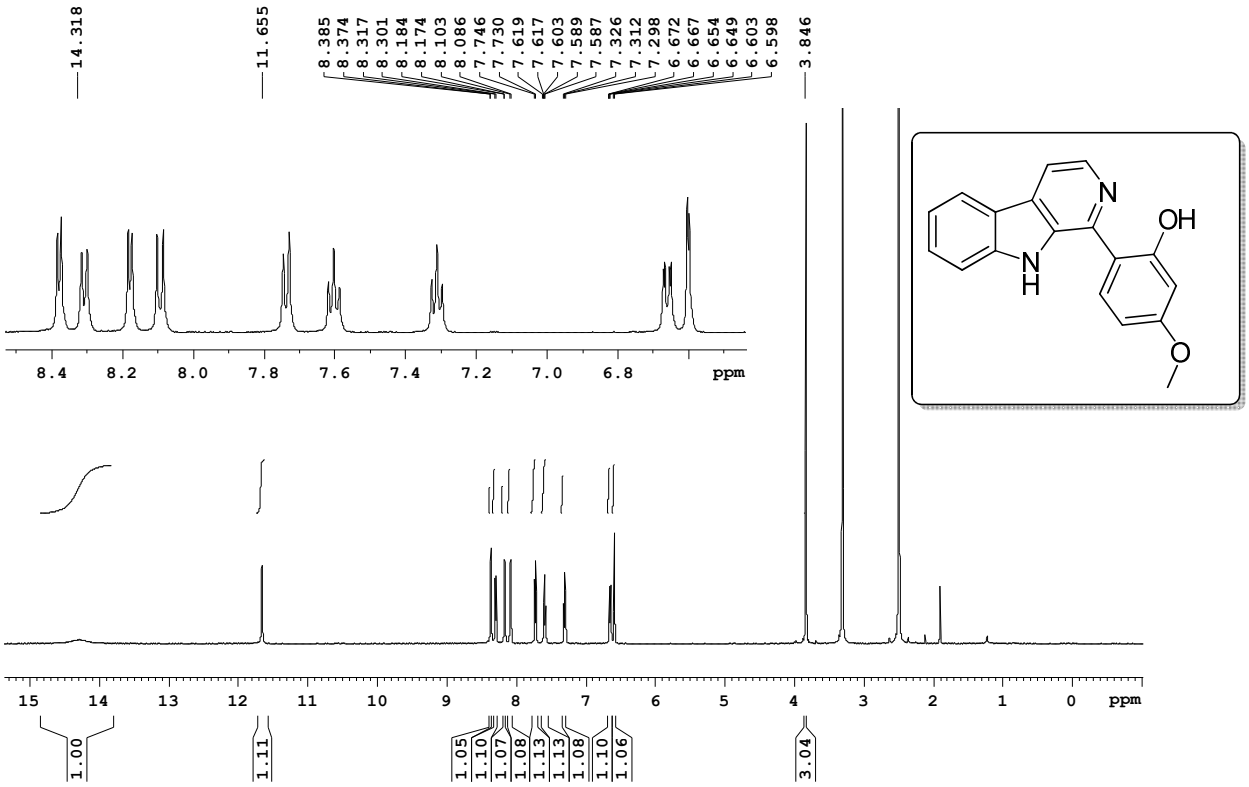
Compound **2b**: ^{13}C NMR (125 MHz, DMSO–d_6)



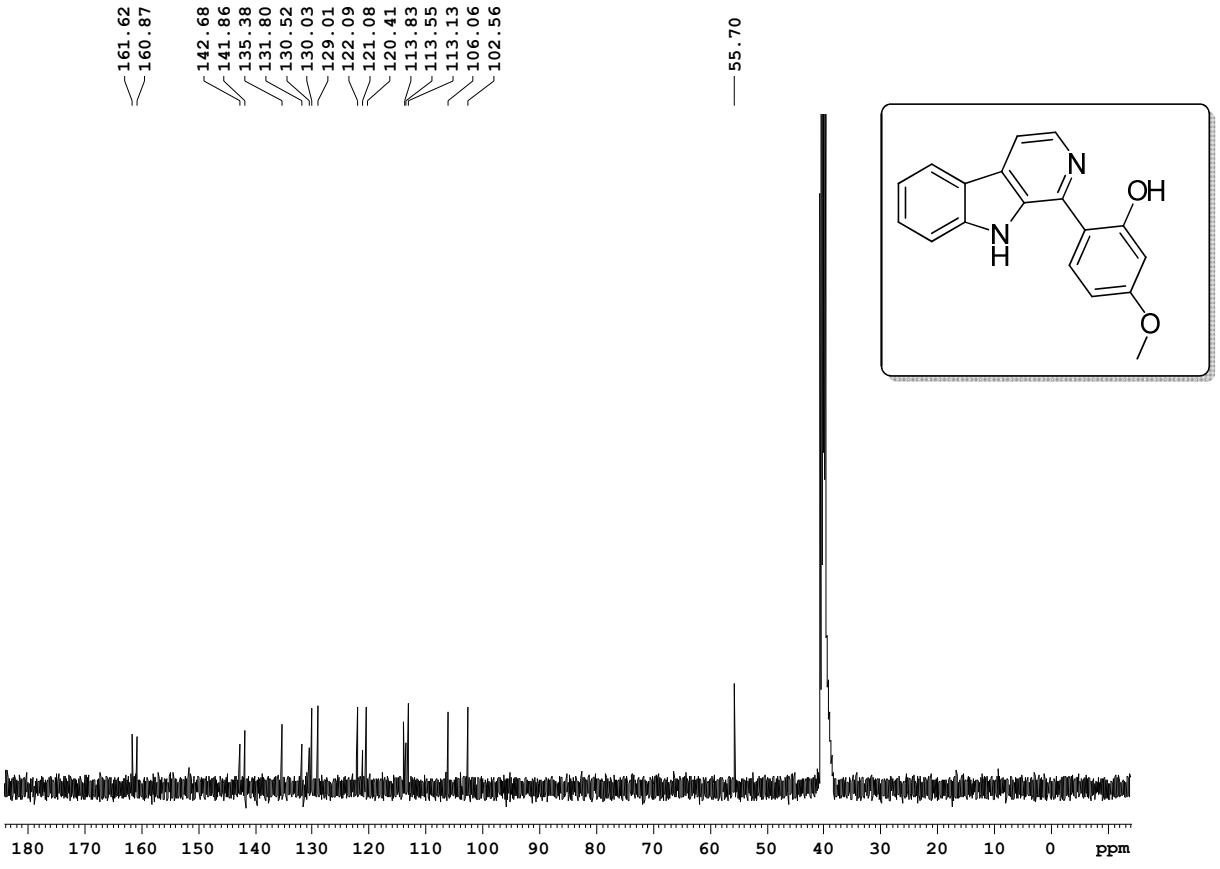
Compound **2c**: ^{1}H NMR (500 MHz, DMSO–d_6)



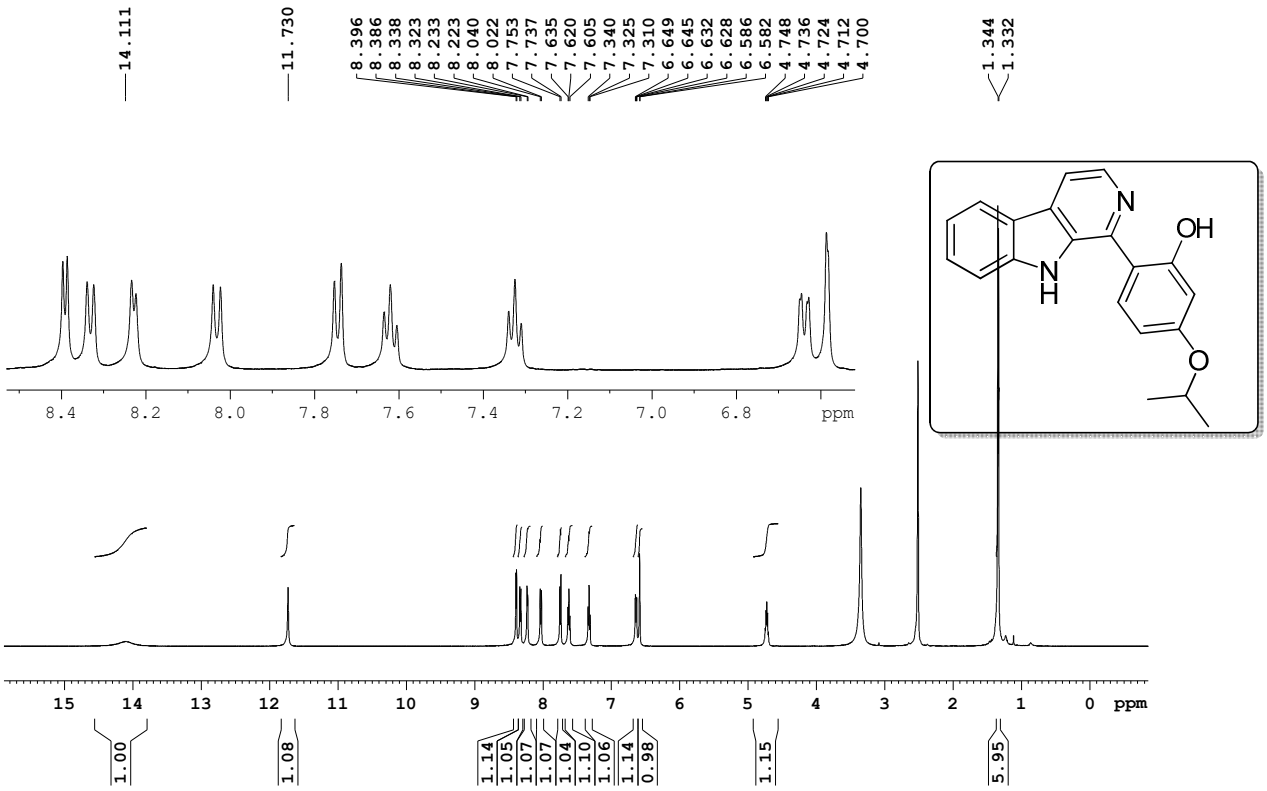
Compound **2c**: ^{13}C NMR (125 MHz, DMSO–d_6)



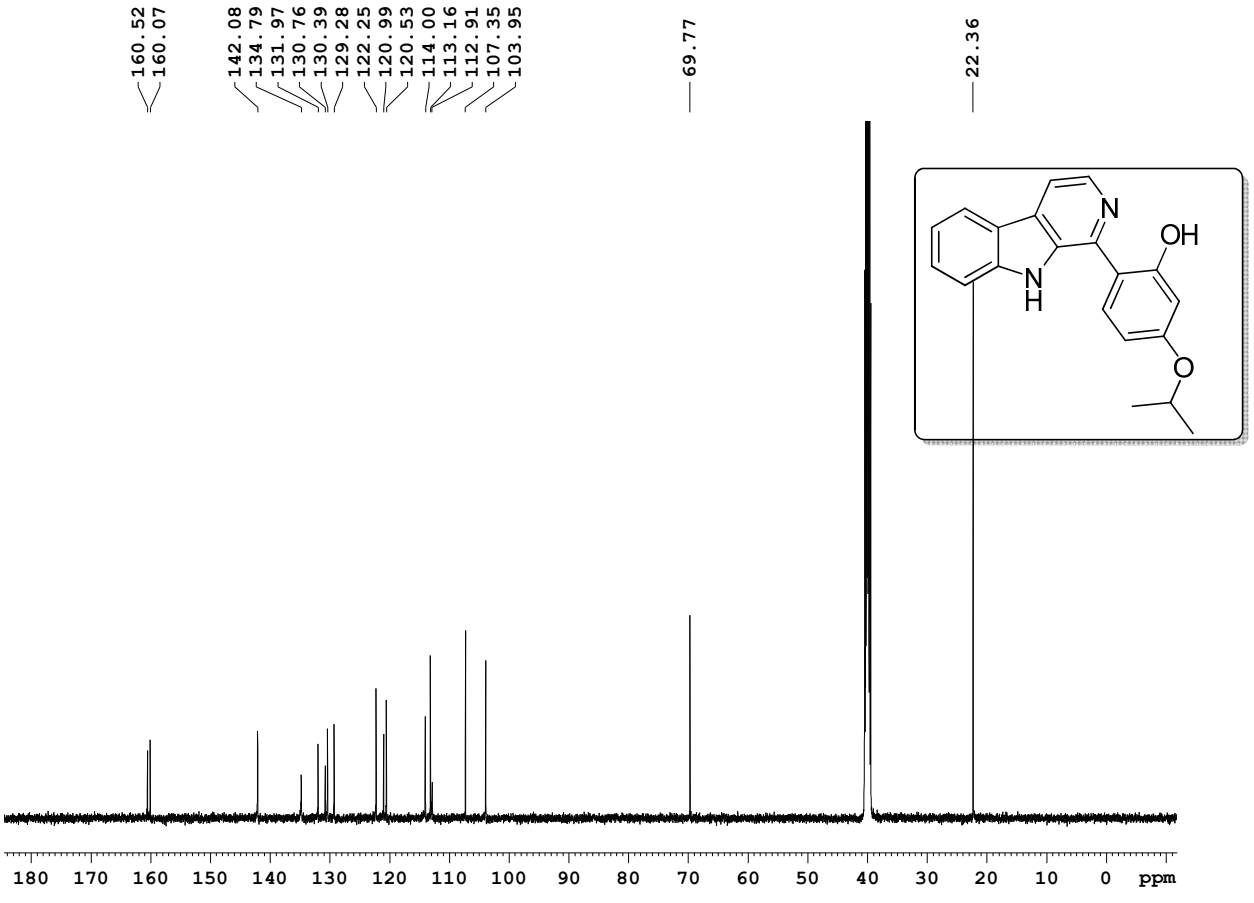
Compound **2d**: ^{1}H NMR (500 MHz, DMSO–d_6)



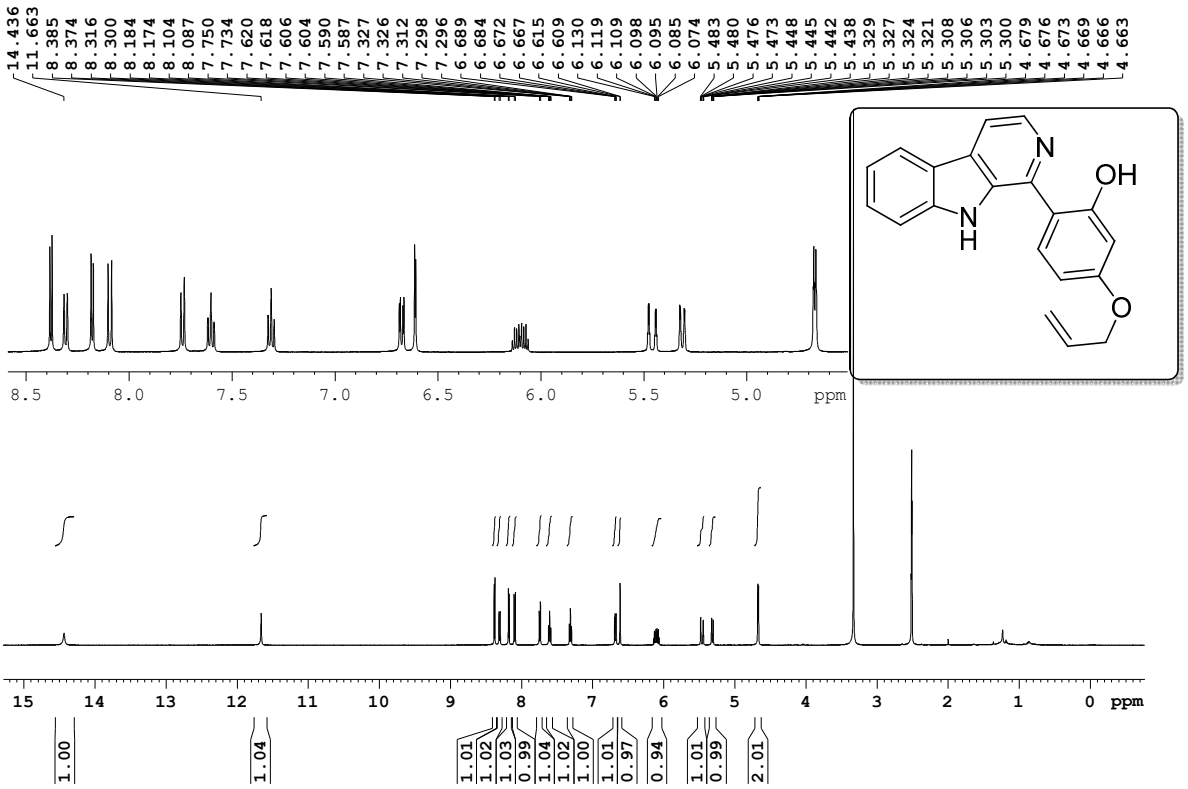
Compound **2d**: ^{13}C NMR (125 MHz, DMSO–d_6)



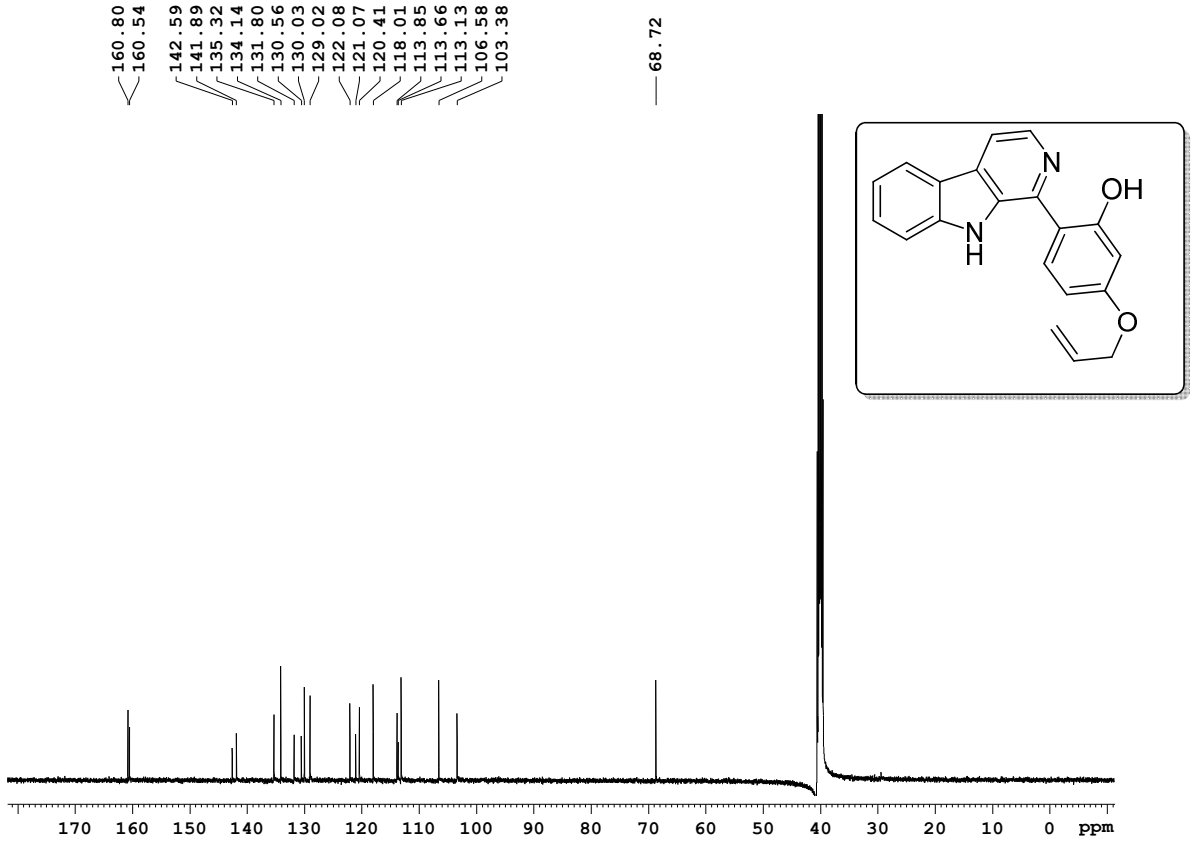
` Compound **2f**: ^{1}H NMR (500 MHz, DMSO–d_6)



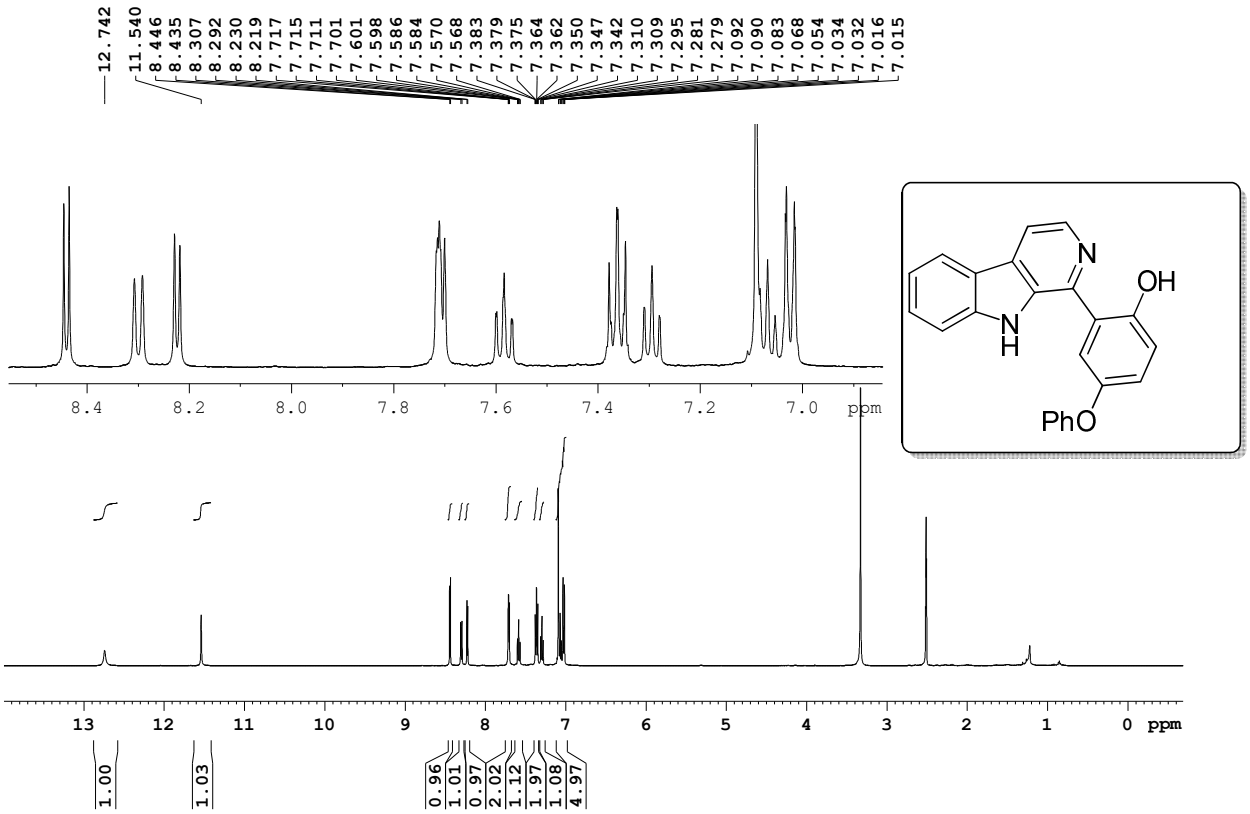
Compound **2f**: ^{13}C NMR (125 MHz, DMSO–d_6)



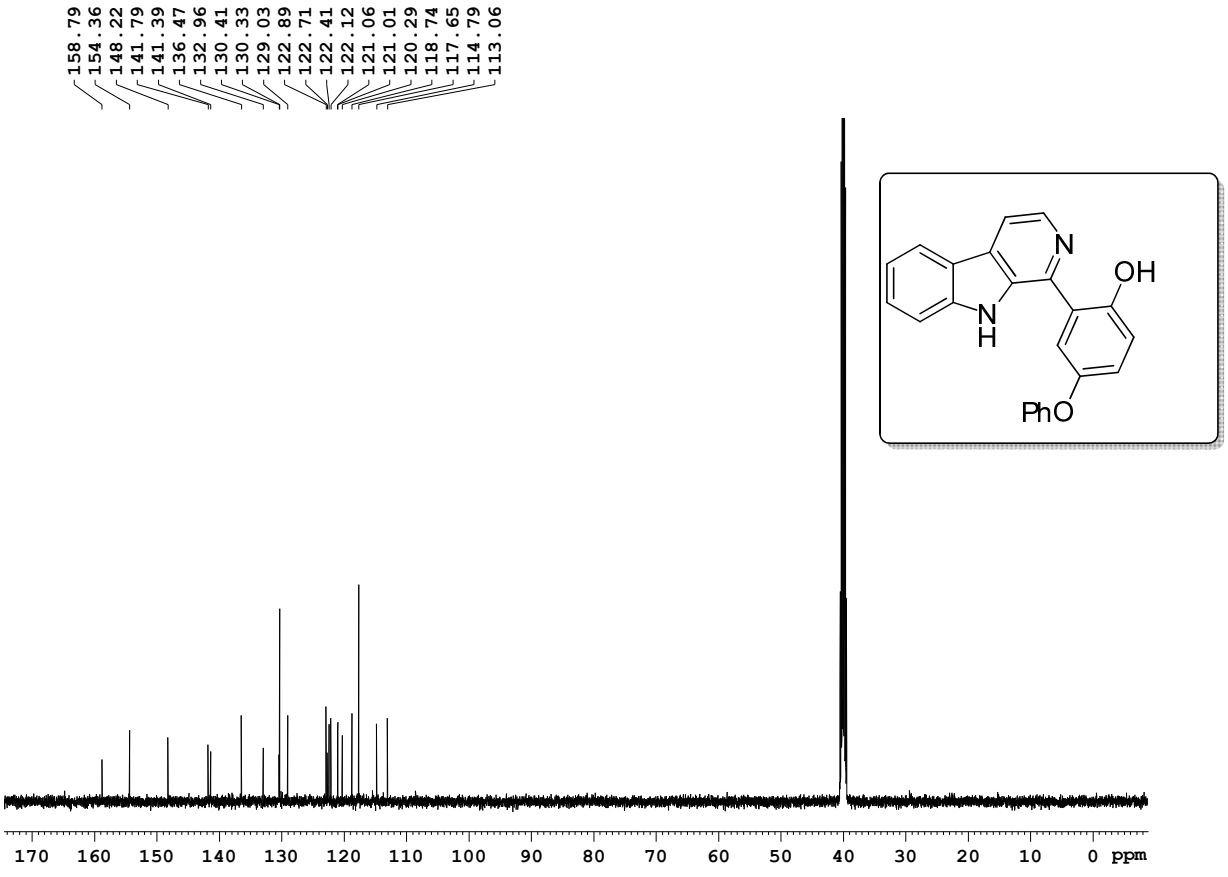
` Compound **2g**: ^{1}H NMR (500 MHz, DMSO–d_6)



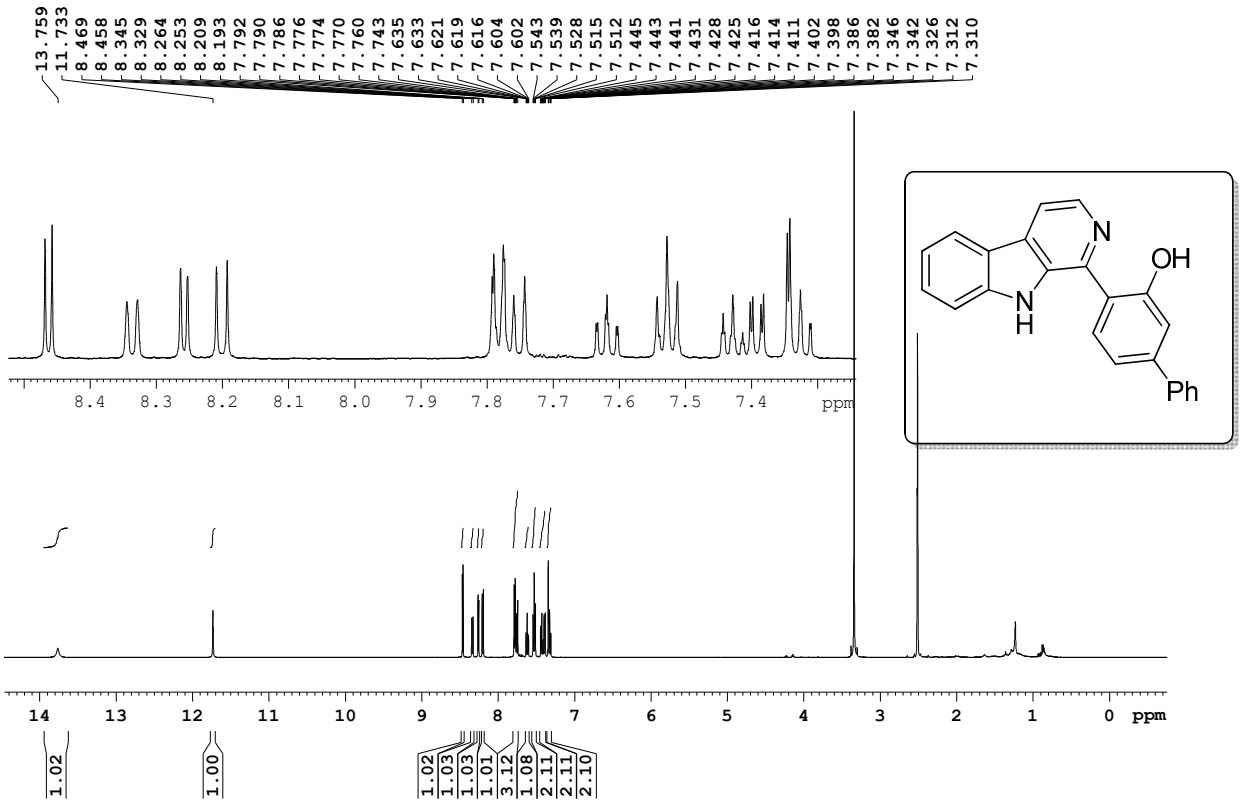
Compound **2g**: ^{13}C NMR (125 MHz, DMSO–d_6)



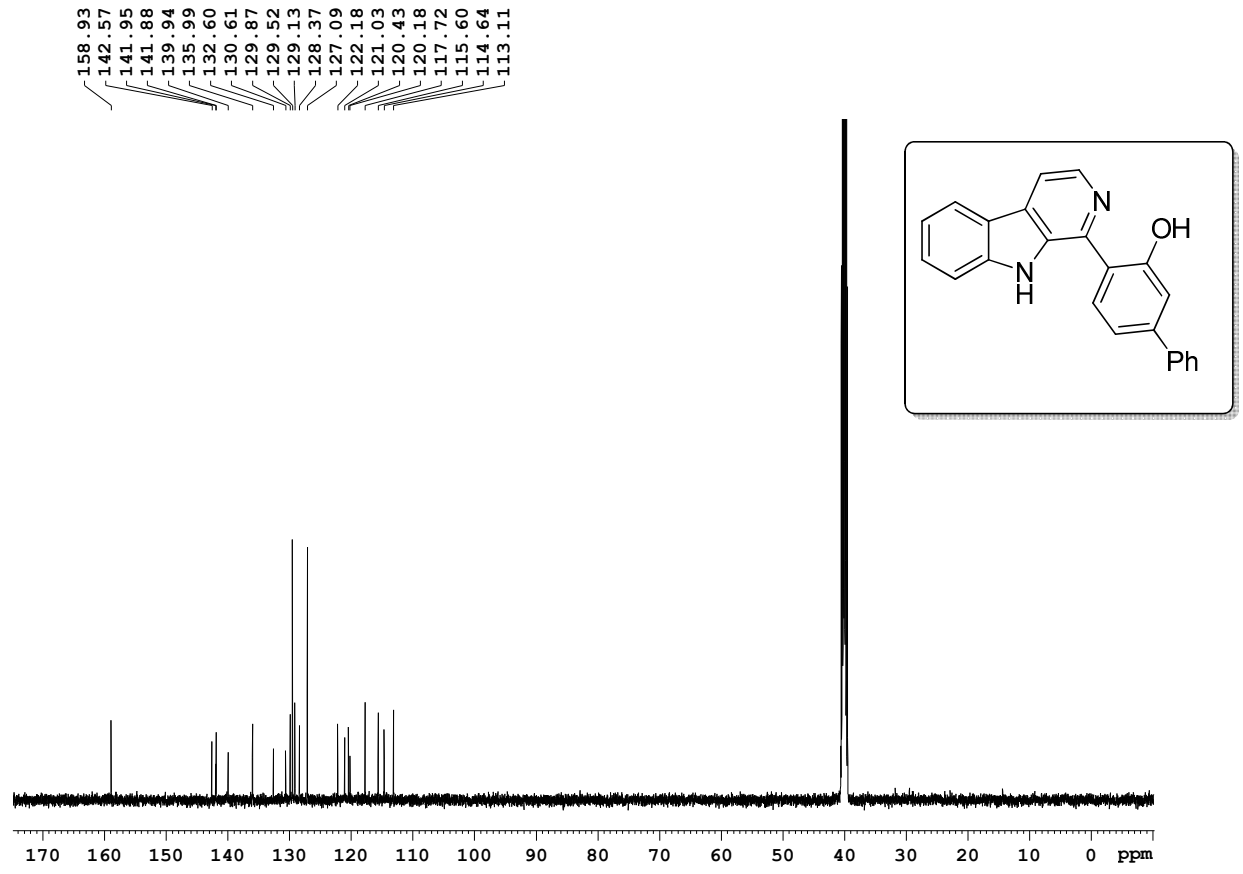
Compound **2h**: ^{1}H NMR (500 MHz, DMSO–d_6)



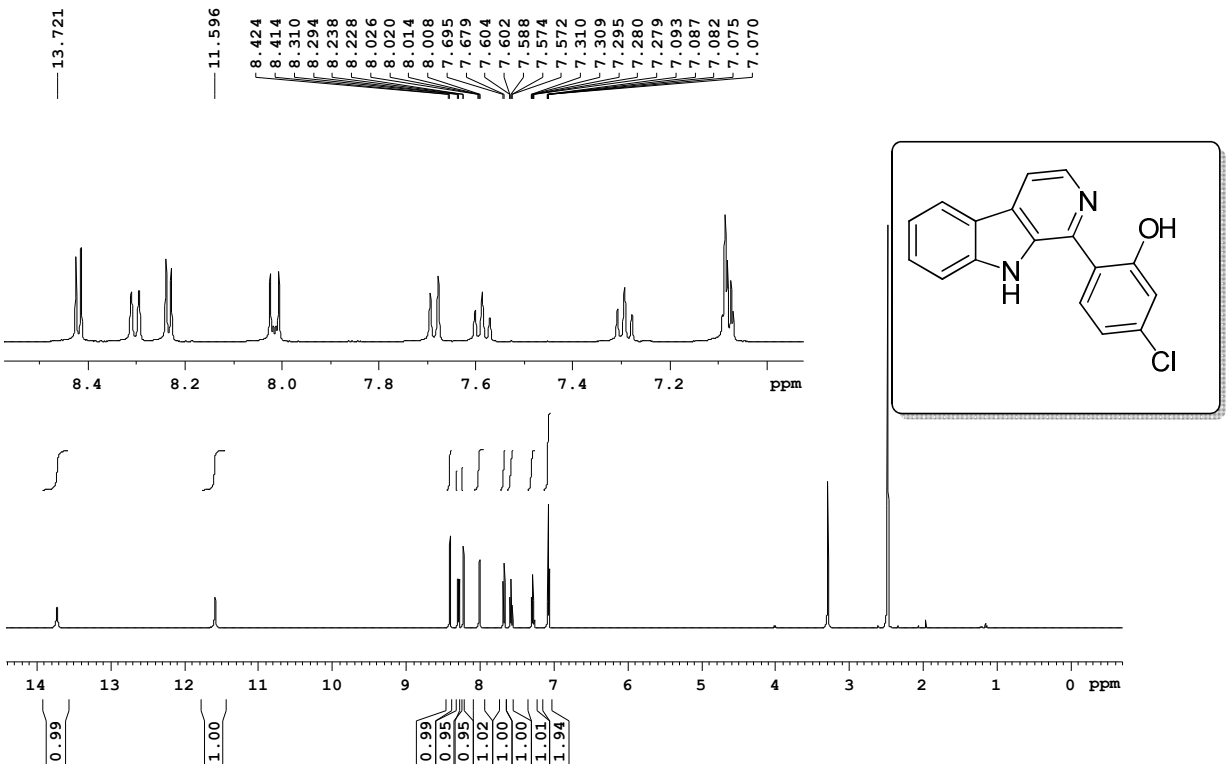
Compound **2h**: ^{13}C NMR (125 MHz, DMSO–d_6)



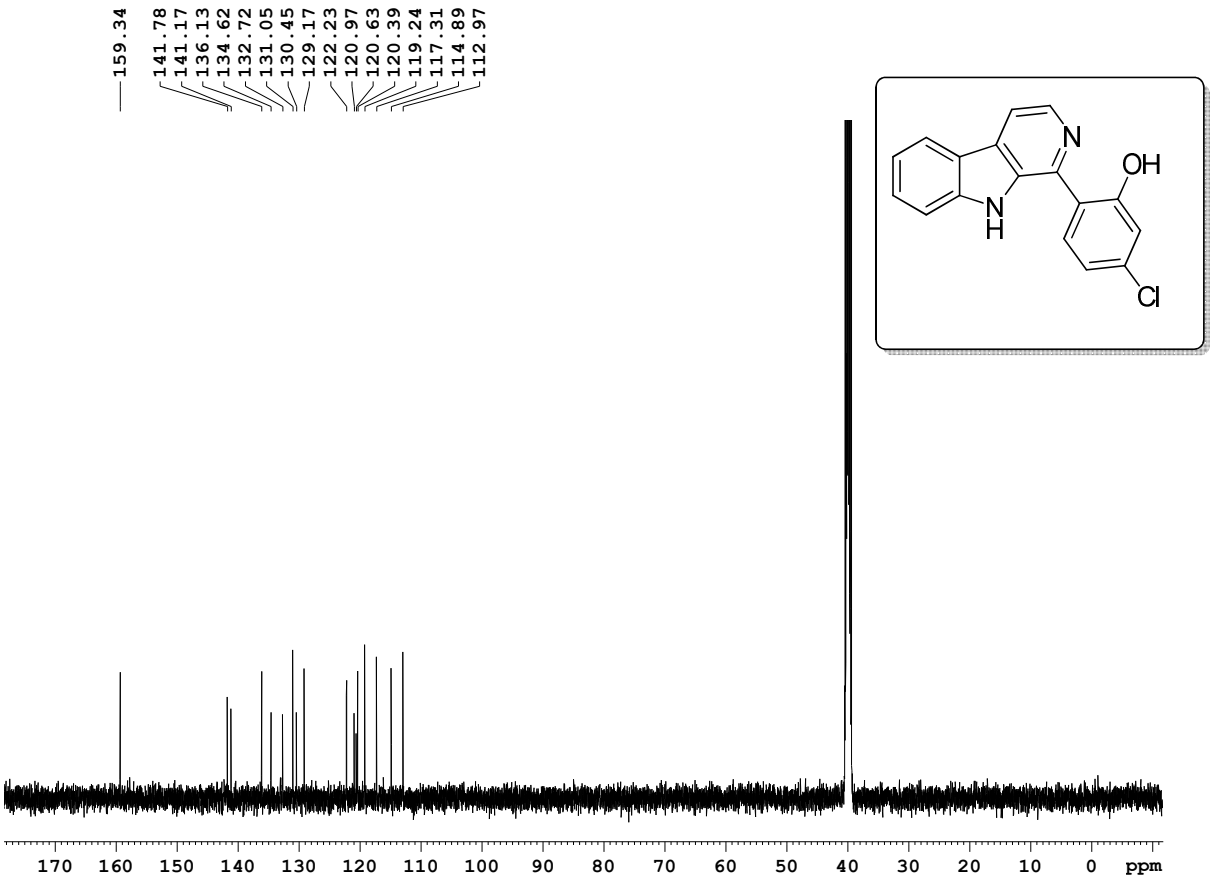
Compound **2i**: ^{1}H NMR (500 MHz, DMSO–d_6)



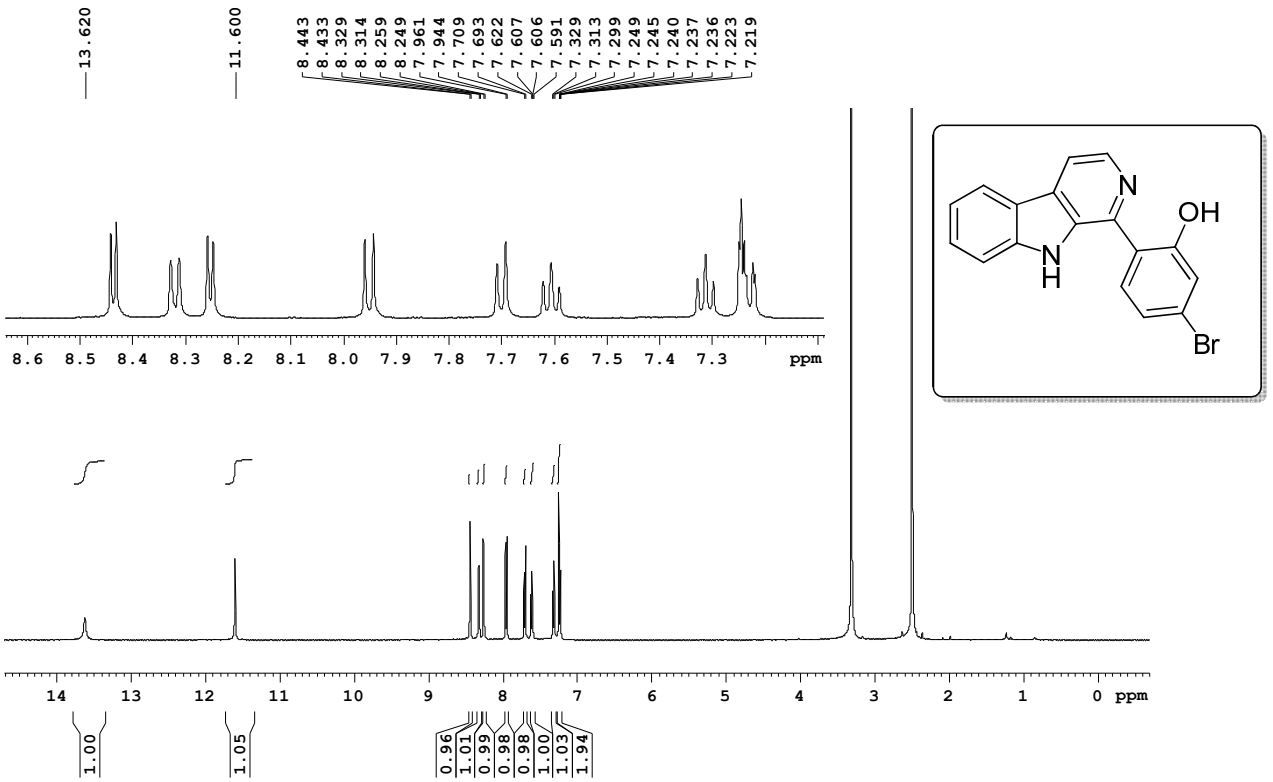
Compound **2i**: ^{13}C NMR (125 MHz, DMSO–d_6)



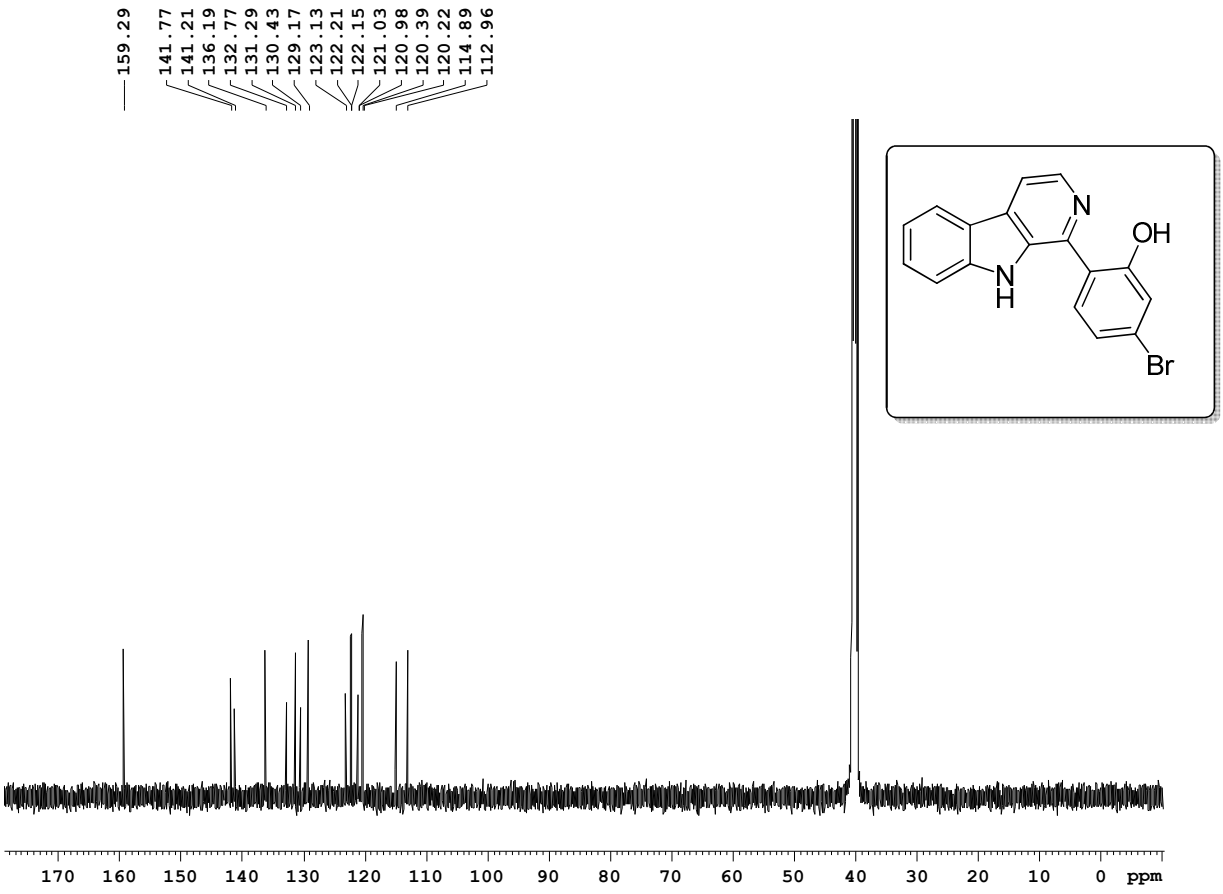
Compound **2k**: ^{1}H NMR (500 MHz, DMSO–d_6)



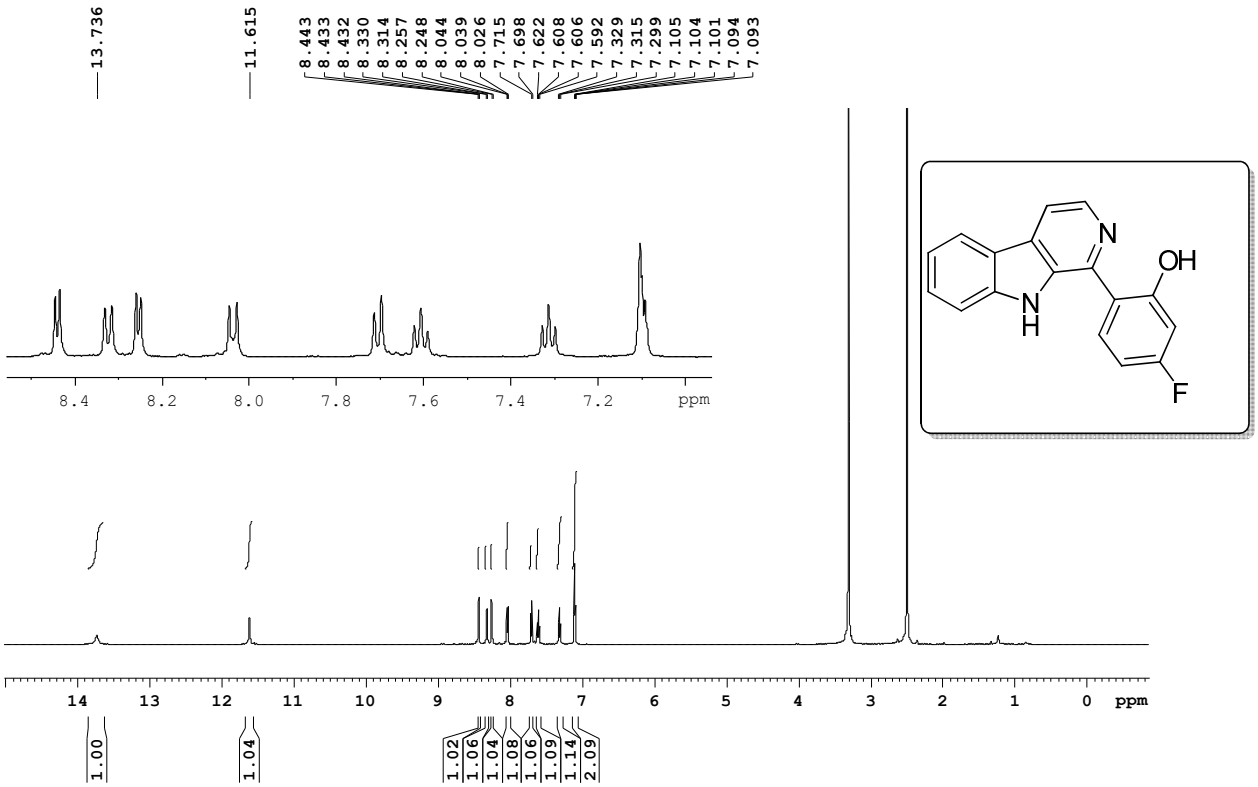
Compound **2k**: ^{13}C NMR (125 MHz, DMSO–d_6)



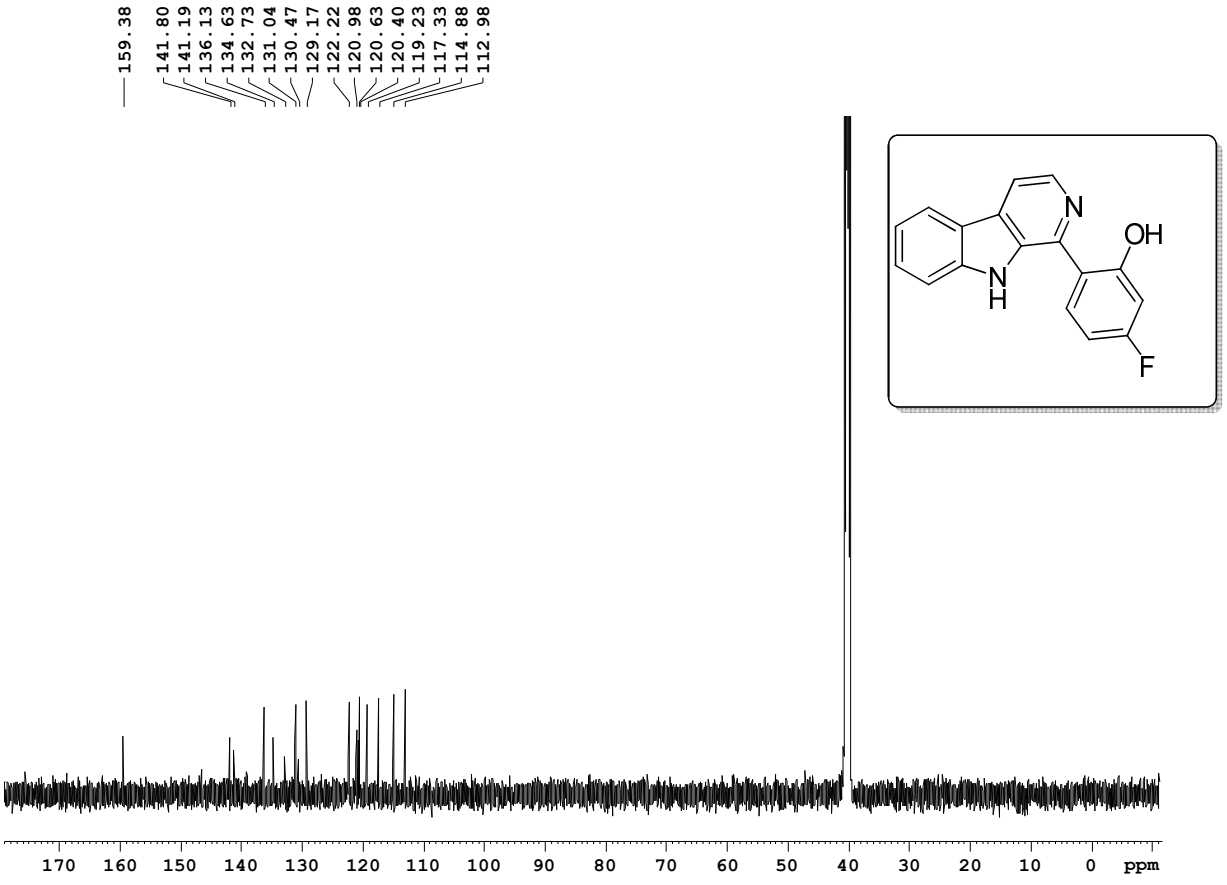
Compound **2l**: ^{1}H NMR (500 MHz, DMSO–d_6)



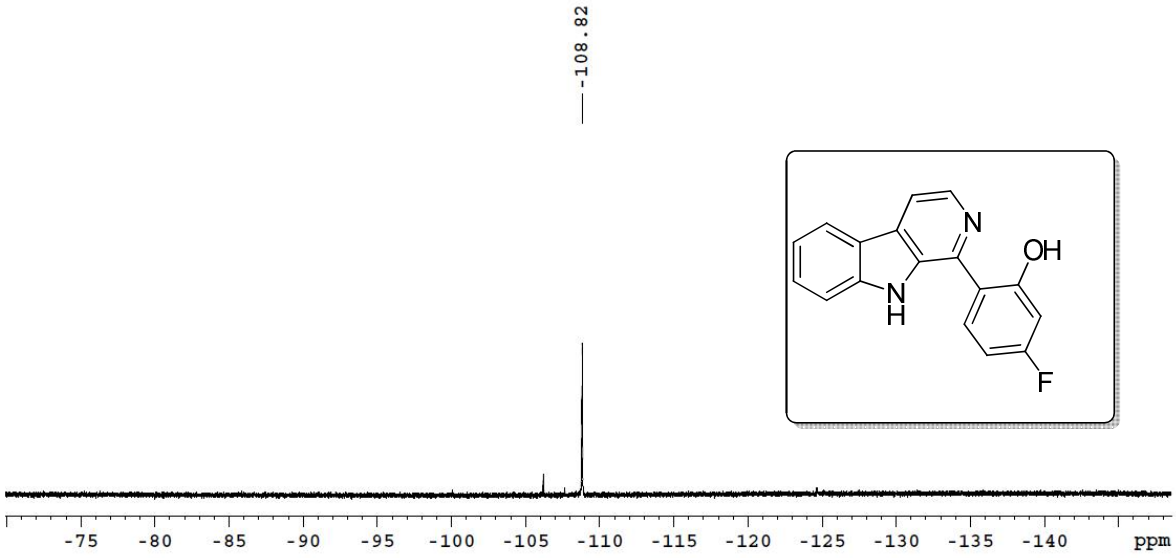
Compound **2l**: ^{13}C NMR (125 MHz, DMSO–d_6)



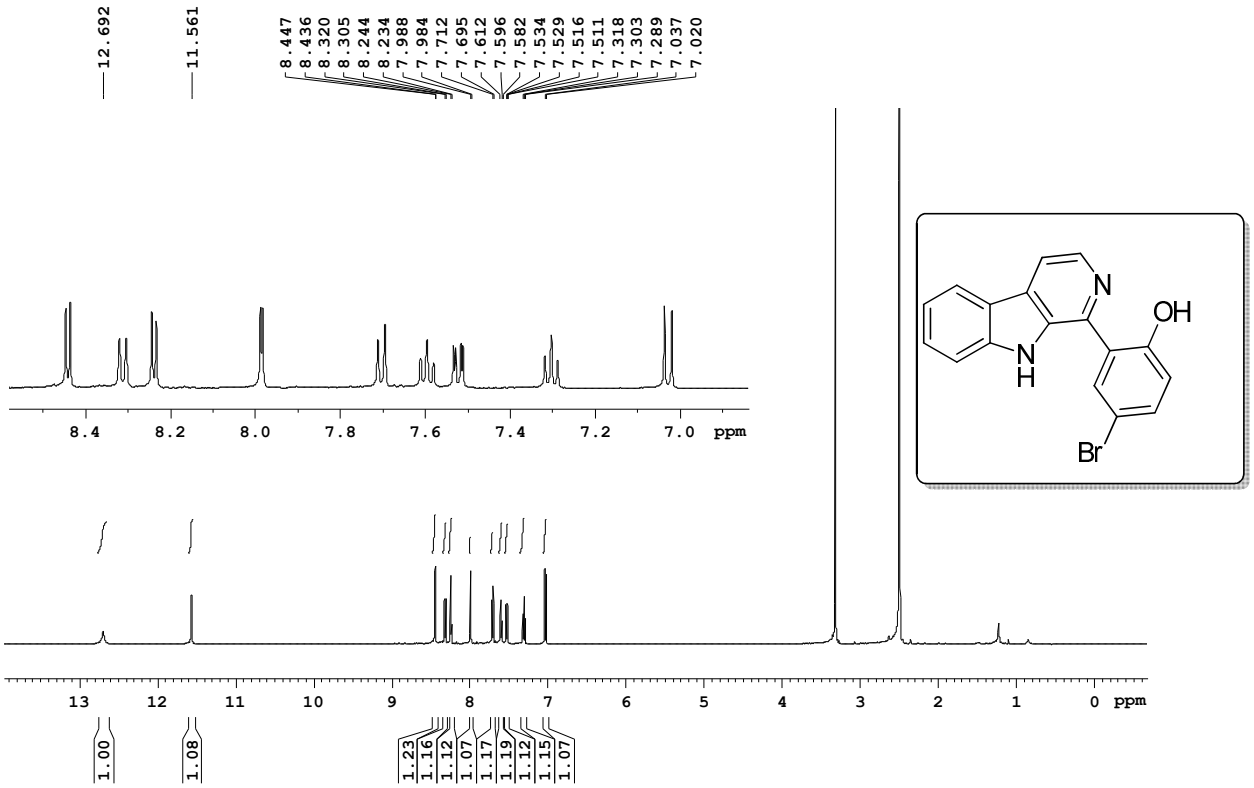
Compound **2m**: ^{1}H NMR (500 MHz, DMSO–d_6)



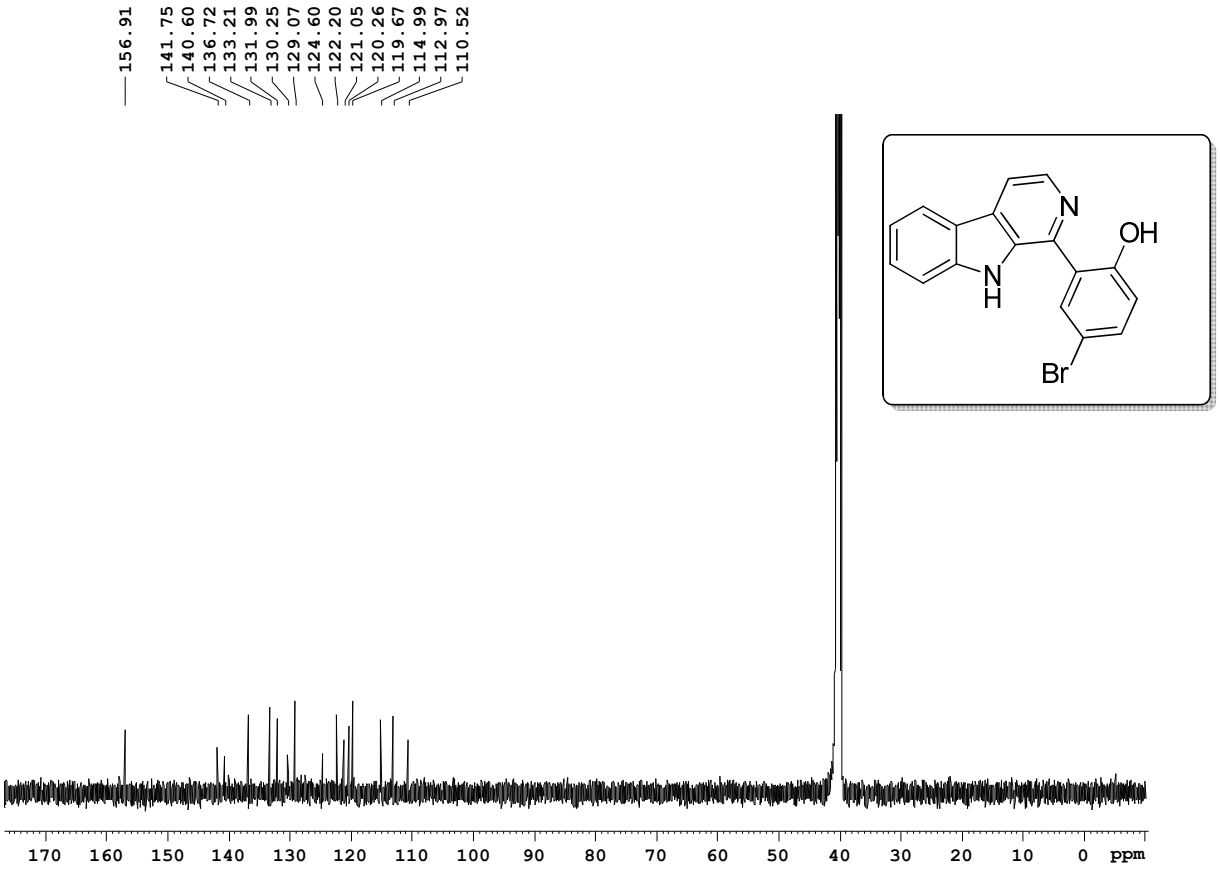
Compound **2m**: ^{13}C NMR (125 MHz, DMSO–d_6)



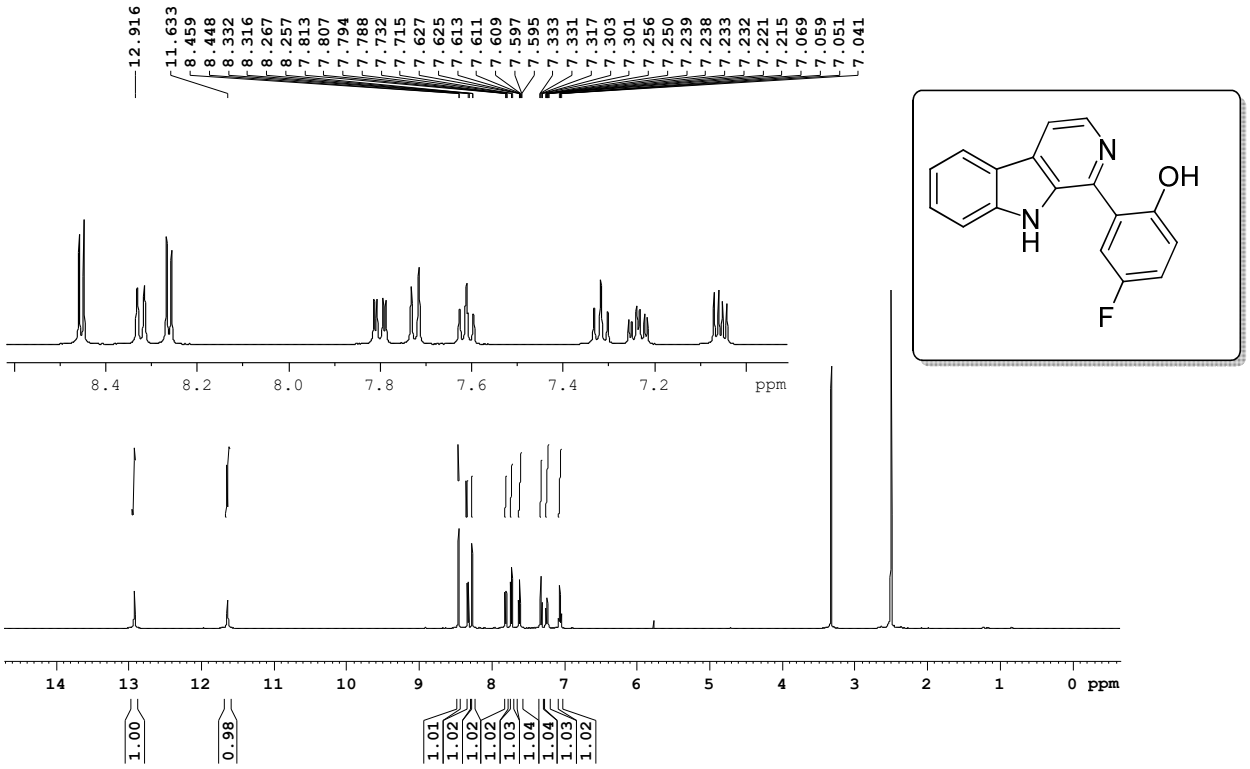
Compound **2m**: ^{19}F NMR (470 MHz, $CDCl_3$)



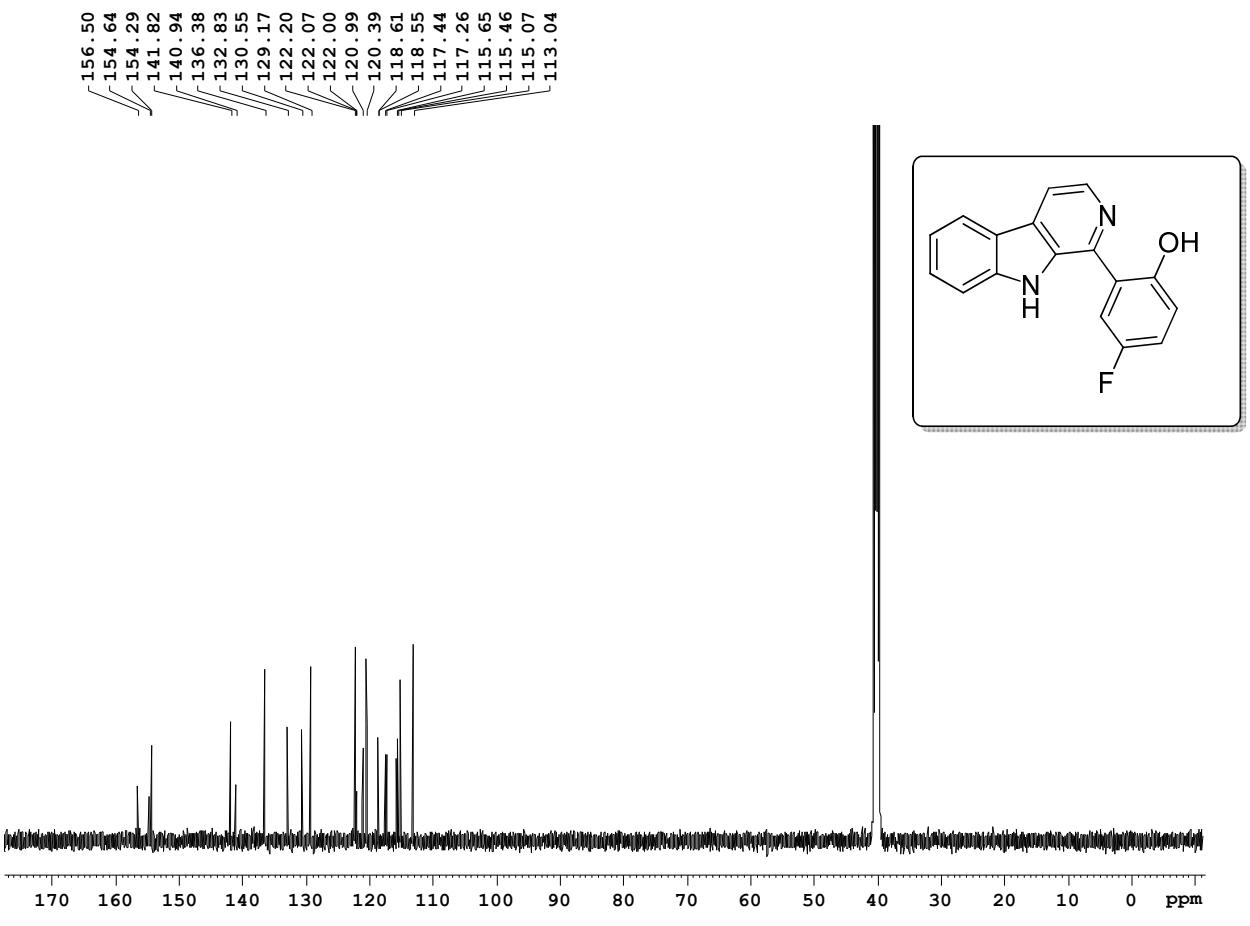
Compound **2n**: ^{1}H NMR (500 MHz, DMSO–d_6)



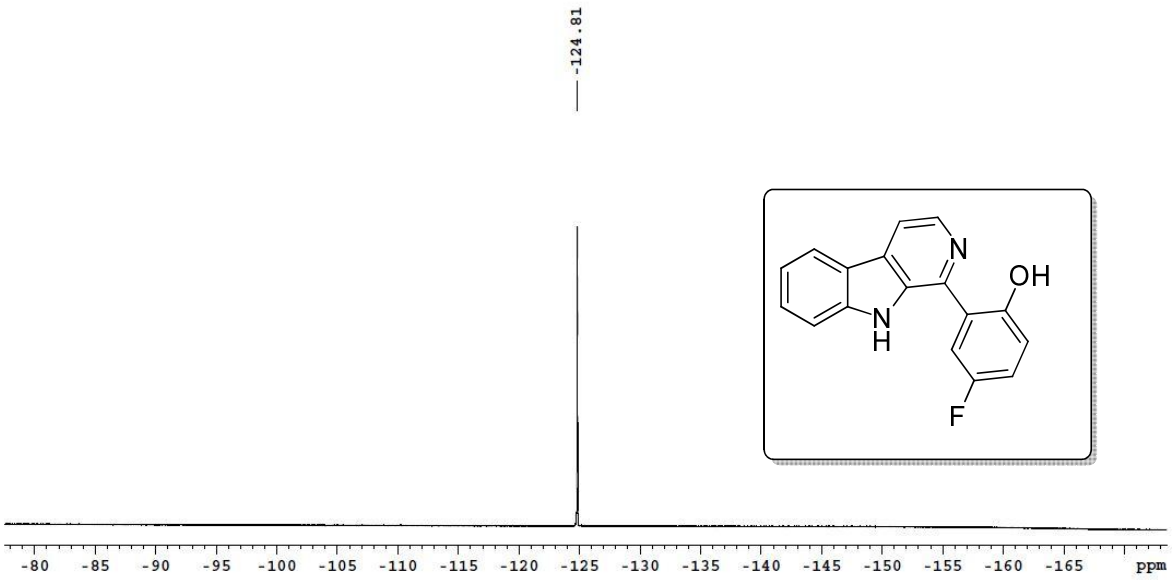
Compound **2n**: ^{13}C NMR (125 MHz, DMSO–d_6)



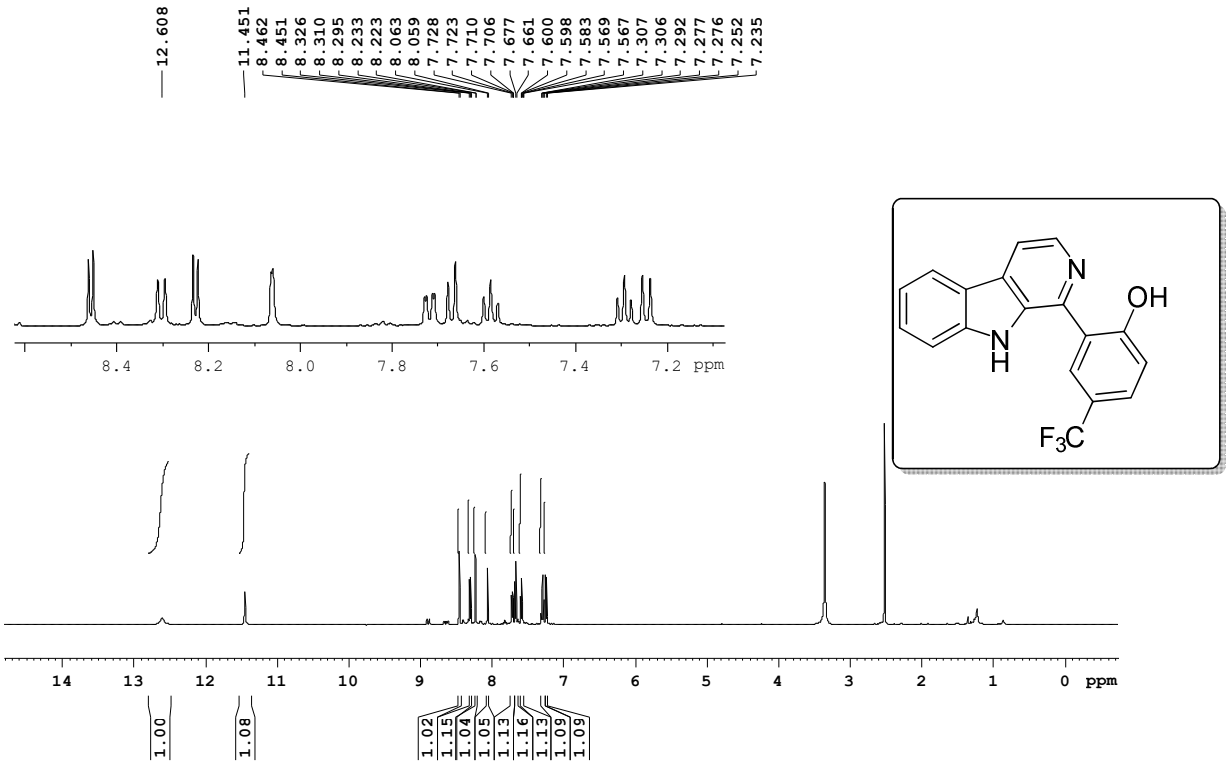
Compound **2o**: ^{1}H NMR (500 MHz, DMSO–d_6)



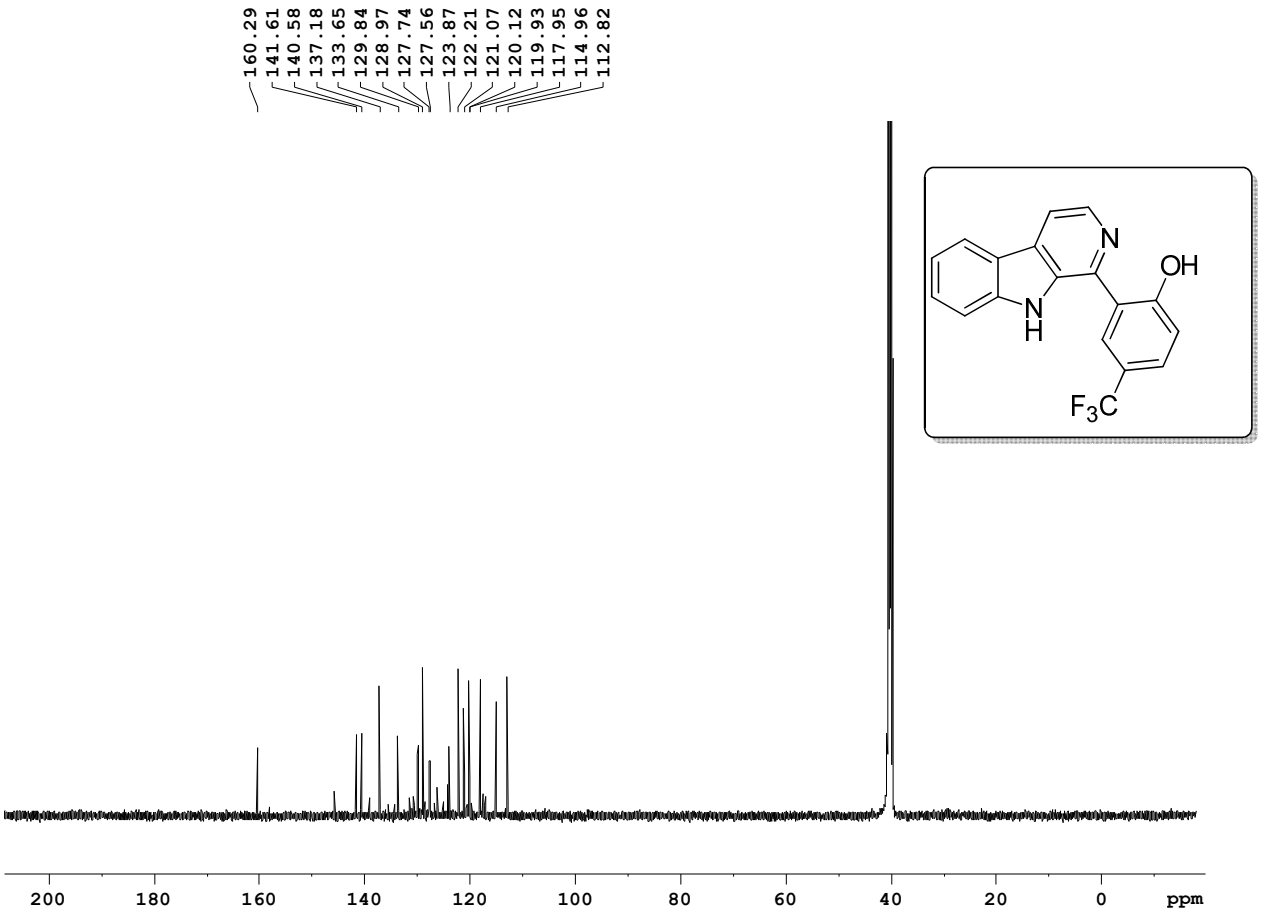
Compound **2o**: ^{13}C NMR (125 MHz, DMSO–d_6)



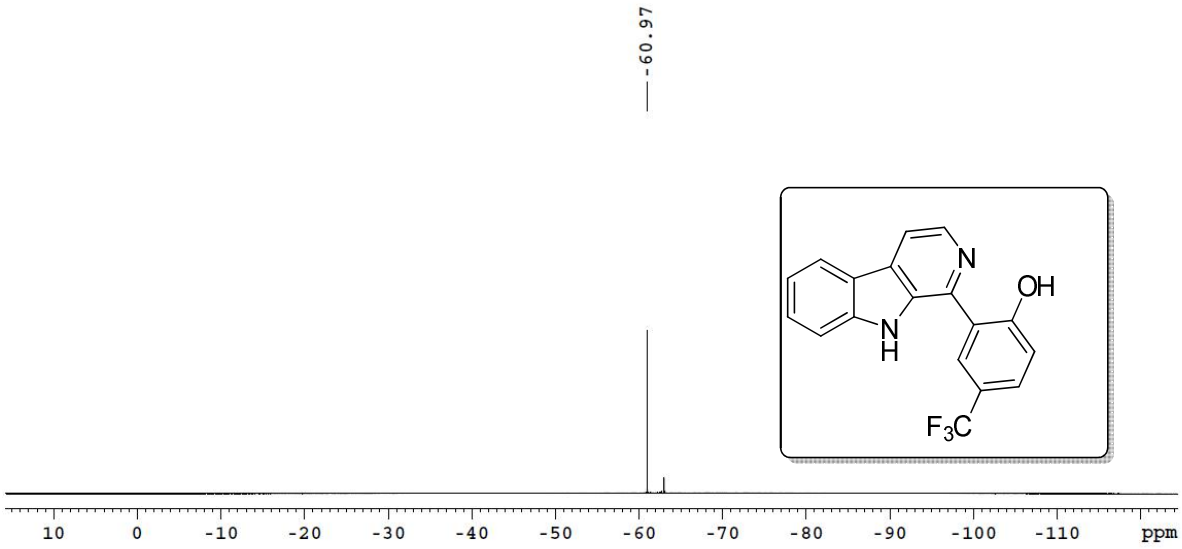
Compound **2o**: ^{19}F NMR (470 MHz, DMSO-d_6)



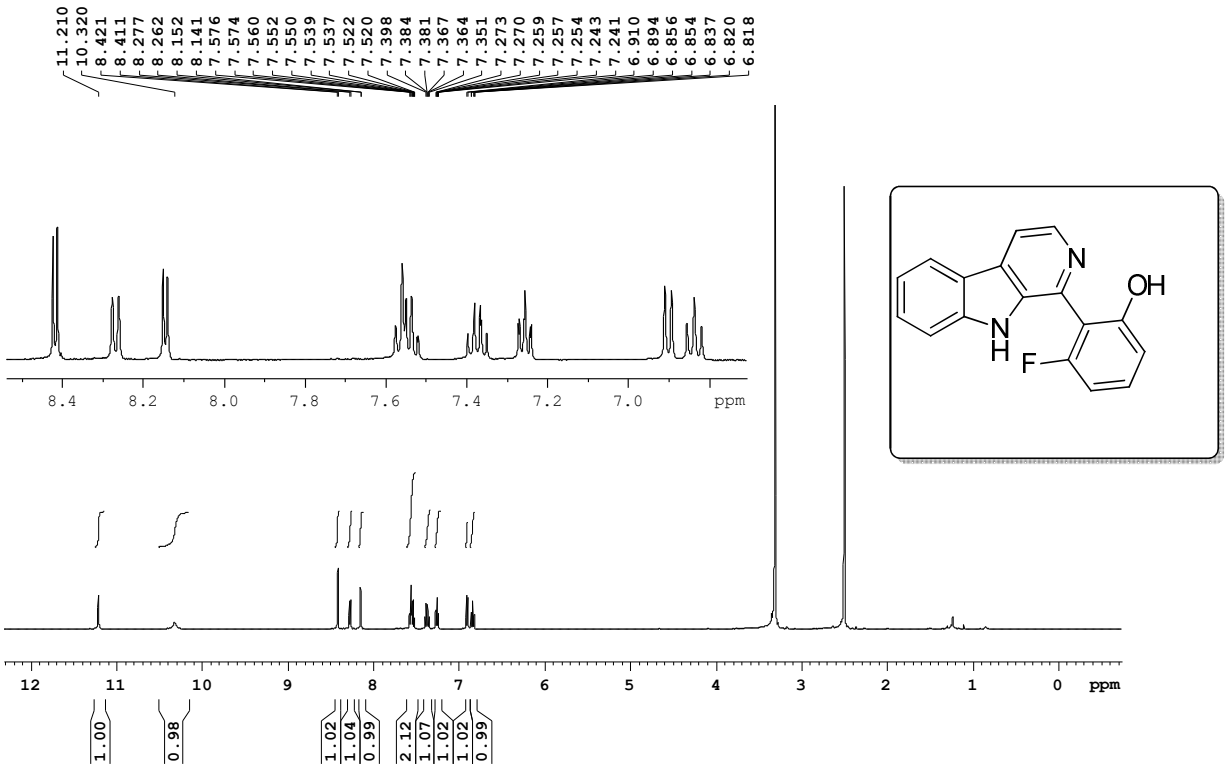
Compound **2p**: ^{1}H NMR (500 MHz, DMSO–d_6)



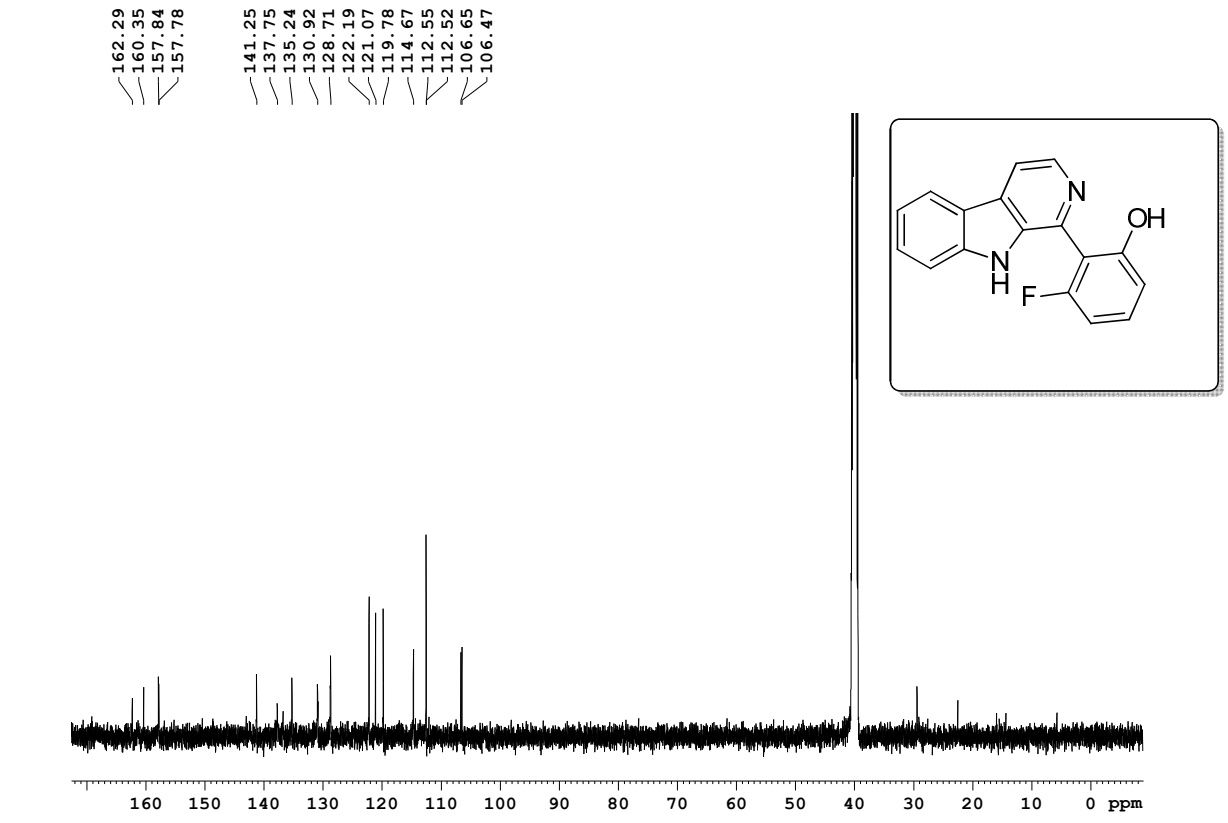
Compound **2p**: ^{13}C NMR (125 MHz, DMSO–d_6)



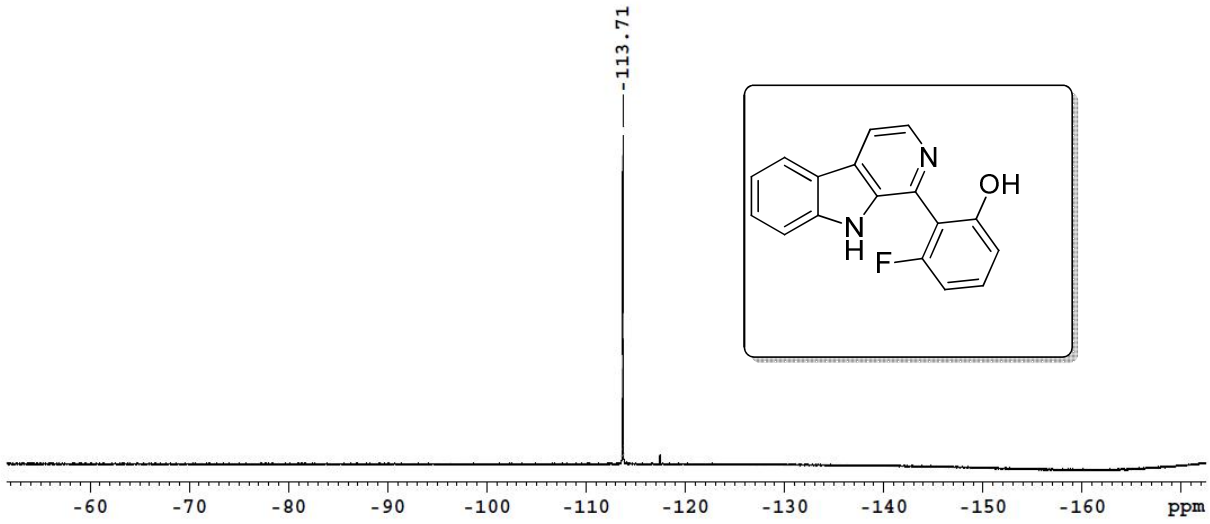
Compound **2p**: ^{19}F NMR (470 MHz, $CDCl_3$)



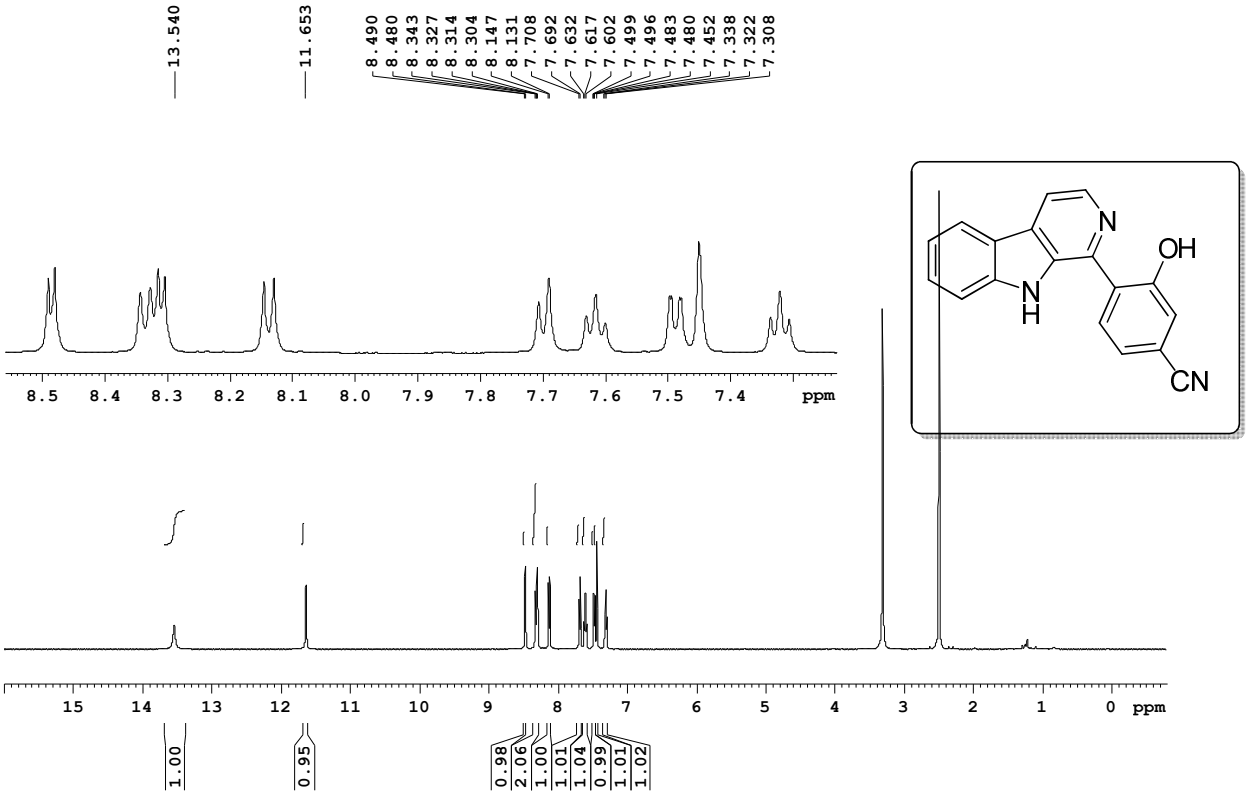
Compound **2q**: ^{1}H NMR (500 MHz, DMSO–d_6)



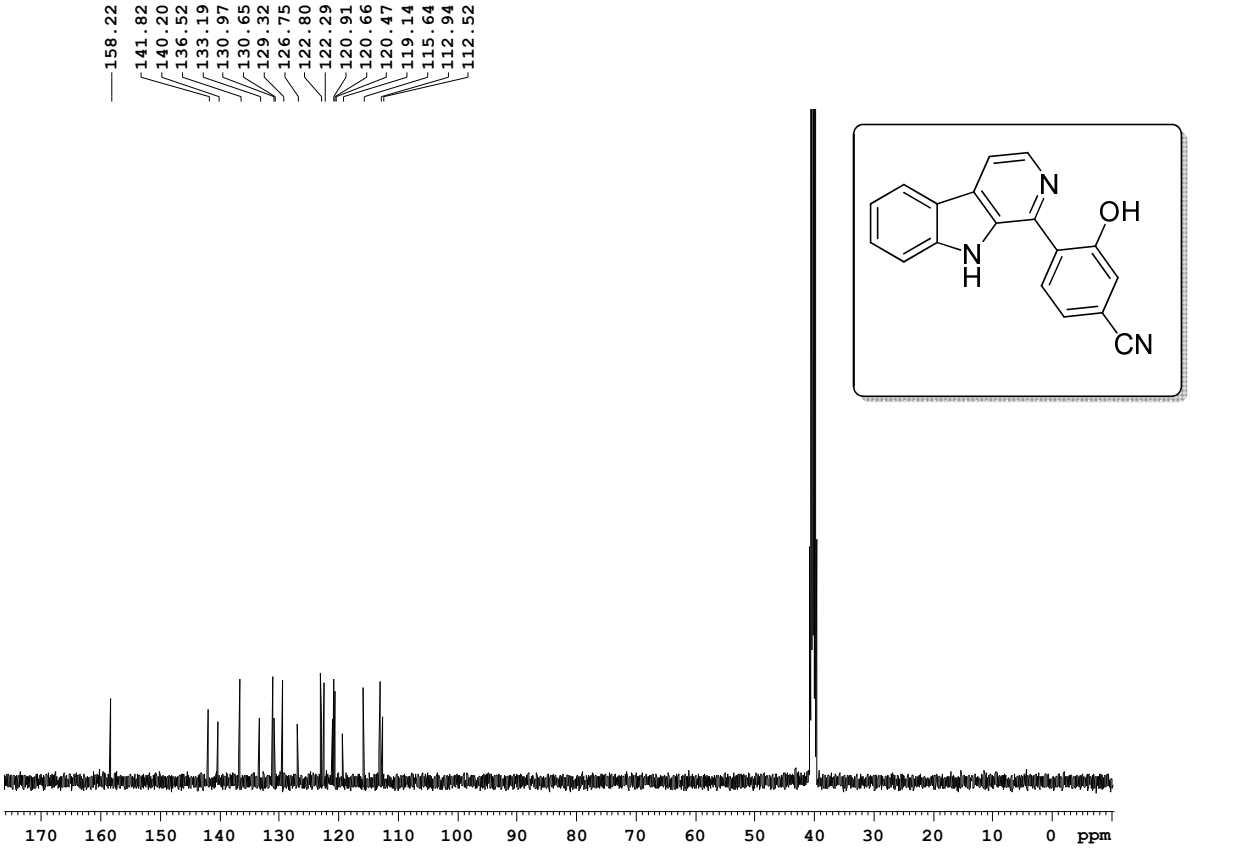
Compound **2q**: ^{13}C NMR (125 MHz, DMSO–d_6)



Compound **2q**: ^{19}F NMR (470 MHz, $CDCl_3$)



Compound **2r**: ^{1}H NMR (500 MHz, DMSO–d_6)



Compound **2r**: ^{13}C NMR (125 MHz, DMSO-d_6)