Supporting information

Iron(II)-Catalyzed C-2 cyanomethylation of the indoles and pyrroles *via* direct oxidative cross-dehydrogenative coupling with acetonitrile derivatives

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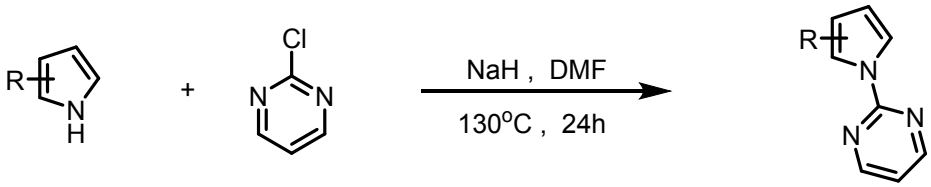
1. General Information

All reactions were carried out with magnetic stirring and in dried glassware. Standard syringe techniques were applied for transfer of dry solvents. All reagents and solvents were commercially available and used without any further purification unless specified. Proton (^{1}H NMR) and carbon (^{13}C NMR) nuclear magnetic resonance spectra were recorded at 400 MHz and 100MHz, respectively. The chemical shifts are given in parts per million (ppm) on the delta (δ) scale. The solvent peak was used as a reference value, for ^{1}H NMR: TMS = 0.00 ppm, for ^{13}C NMR: $CDCl_3$ = 77.00 ppm. The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, td = triplet of doublet, q = quartet, m = multiplet, and br = broad. Analytical TLC was performed on precoated silica gel plates. High-resolution mass spectra (HRMS) were obtained on an Agilent mass spectrometer using ESI-TOF (electrospray ionization-time of flight).

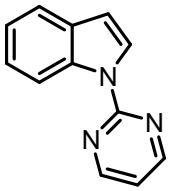
2. Experimental Section

2.1 General procedure for the synthesis of starting materials

2.1.1 Synthesis of 1-(Pyrimidin-2-yl)-1H-indoles and1-(Pyrimidin-2-yl) -1H-pyrroles [1]

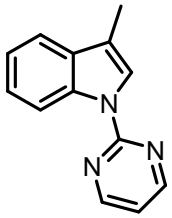


In an oven-dried flask (100 mL), NaH (60% dispersion in mineral oil, 11 mmol) was added in portions at 0 °C to a stirred solution of the corresponding indoles or pyrroles (10 mmol) in DMF (25 mL). After stirring for 30min at 0 °C, 2-chloropyrimidine (12 mmol) was added and the mixture was stirred at 130 °C for 24 h. Then, the reaction mixture was cooled to room temperature, poured into H_2O (300 mL) and extracted with EtOAc (4×75 mL). The combined organic phase was dried over Na_2SO_4. After filtration and evaporation of the solvents under reduced pressure, the crude product was purified by column chromatography on silica gel (n-hexane/EtOAc) to give the desired product.



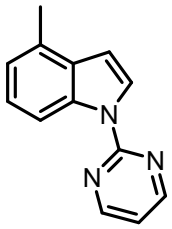
1-(pyrimidin-2-yl)-1H-indole (1a)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 9.1 Hz, 1H), 8.62 (d, *J* = 4.8 Hz, 2H), 8.26 (d, *J* = 3.7 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 8.4 Hz, 1H), 7.23 (t, *J* = 8.0 Hz, 1H), 6.94 (t, *J* = 4.8 Hz, 1H), 6.69 (d, *J* = 4.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.98, 157.67, 135.29, 131.24, 125.73, 123.56, 122.04, 120.75, 116.21, 116.01, 106.83; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_9N_3$ $[M+H]^+$: 196.0869, found: 196.0897.



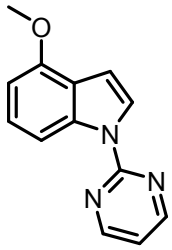
3-methyl-1-(pyrimidin-2-yl)-1H-indole (1b)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 8.3 Hz, 1H), 8.59 (d, *J* = 4.8 Hz, 2H), 8.01 (s, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 8.2 Hz, 1H), 7.24 (t, *J* = 7.4 Hz, 1H), 6.88 (t, *J* = 4.8 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.90, 157.52, 135.53, 131.96, 123.60, 122.81, 121.67, 118.70, 116.16, 115.98, 115.42, 9.75; HRMS (ESI-TOF) m/z Calcd for $C_{13}H_{11}N_3$ $[M+H]^+$: 210.1026, found: 210.1036.



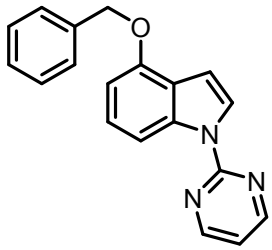
4-methyl-1-(pyrimidin-2-yl)-1H-indole (1c)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.8 Hz, 2H), 8.64 (d, *J* = 8.5 Hz, 1H), 8.26 (d, *J* = 3.7 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 7.2 Hz, 1H), 7.00 (t, *J* = 4.8 Hz, 1H), 6.73 (d, *J* = 3.7 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.03, 157.84, 135.16, 130.94, 130.01, 125.20, 123.65, 122.51, 116.00, 113.80, 105.24, 18.57; HRMS (ESI-TOF) m/z Calcd for $C_{13}H_{11}N_3$ $[M+H]^+$: 210.1026, found: 210.1011.



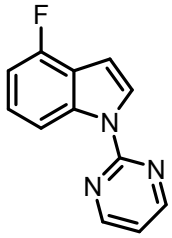
4-methoxy-1-(pyrimidin-2-yl)-1H-indole (1d)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 4.8 Hz, 2H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.17 (d, *J* = 3.6 Hz, 1H), 7.26 (t, *J* = 8.1 Hz, 1H), 7.00 (t, *J* = 4.8 Hz, 1H), 6.83 (d, *J* = 3.6 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 1H), 3.96 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.03, 157.87, 152.90, 136.65, 124.37, 124.32, 121.58, 116.12, 109.51, 103.84, 102.51, 55.38; HRMS (ESI-TOF) m/z Calcd for $C_{13}H_{11}N_3O$ $[M+H]^+$: 226.0975, found: 226.0962.



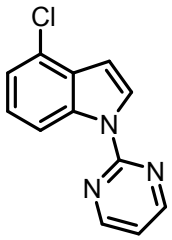
4-(benzyloxy)-1-(pyrimidin-2-yl)-1H-indole (1e)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 4.8 Hz, 2H), 8.41 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 3.7 Hz, 1H), 7.49 (d, J = 7.2 Hz, 2H), 7.37 (m, 2H), 7.30 (m, 1H), 7.23 (t, J = 8.2 Hz, 1H), 6.95 – 6.85 (m, 2H), 6.71 (d, J = 7.9 Hz, 1H), 5.20 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.91, 157.74, 151.99, 137.40, 136.69, 128.41, 127.70, 127.25, 124.32, 124.29, 121.95, 116.03, 109.80, 104.06, 104.01, 70.01; HRMS (ESI-TOF) m/z Calcd for $C_{19}H_{15}N_3O$ $[M+H]^+$: 302.1288, found: 302.1273.



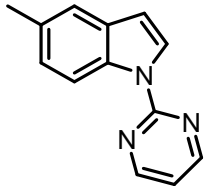
4-fluoro-1-(pyrimidin-2-yl)-1H-indole (1f)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 – 8.40 (m, 3H), 8.16 (d, J = 3.4 Hz, 1H), 7.24 – 7.16 (m, 1H), 6.94 – 6.81 (m, 2H), 6.75 (d, J = 3.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.79, 157.34, 155.71 (d, $J_{C\text{-}F}$ = 246.1 Hz), 137.37 (d, $J_{C\text{-}F}$ = 9.9 Hz), 125.71, 123.97 (d, $J_{C\text{-}F}$ = 7.5 Hz), 119.91 (d, $J_{C\text{-}F}$ = 22.1 Hz), 116.25, 112.40 (d, $J_{C\text{-}F}$ = 3.5 Hz), 107.00 (d, $J_{C\text{-}F}$ = 18.5 Hz), 102.03; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_8FN_3$ $[M+H]^+$: 214.0775, found: 214.0769.



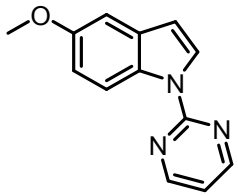
4-chloro-1-(pyrimidin-2-yl)-1H-indole (1g)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 – 8.64 (m, 1H), 8.60 (d, J = 4.7 Hz, 2H), 8.26 (d, J = 3.5 Hz, 1H), 7.24 – 7.15 (m, 2H), 6.96 (t, J = 4.6 Hz, 1H), 6.78 (d, J = 3.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.00, 157.43, 135.98, 129.89, 126.36, 125.77, 124.13, 121.77, 116.47, 114.87, 104.84; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_8ClN_3$ $[M+H]^+$: 230.0480, found: 230.0465.



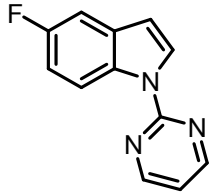
5-methyl-1-(pyrimidin-2-yl)-1H-indole (1h)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, J = 8.5 Hz, 1H), 8.61 (d, J = 4.8 Hz, 2H), 8.21 (d, J = 3.6 Hz, 1H), 7.39 (s, 1H), 7.15 (d, J = 8.5 Hz, 1H), 6.92 (t, J = 4.8 Hz, 1H), 6.61 (d, J = 3.6 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.92, 157.68, 133.61, 131.54, 131.38, 125.75, 124.96, 120.63, 115.90, 115.75, 106.56, 21.27; HRMS (ESI-TOF) m/z Calcd for $C_{13}H_{11}N_3$ $[M+H]^+$: 210.1026, found: 210.1019.



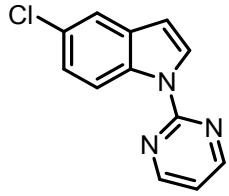
5-methoxy-1-(pyrimidin-2-yl)-1H-indole (1i)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.57 (m, 3H), 8.24 – 8.11 (m, 1H), 7.02 (d, J = 2.6 Hz, 1H), 6.96 (t, J = 4.8 Hz, 1H), 6.89 (dd, J = 9.1, 2.6 Hz, 1H), 6.57 (d, J = 3.6 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.05, 157.58, 155.43, 132.04, 130.23, 126.30, 117.02, 115.88, 112.55, 106.71, 103.08, 55.65; HRMS (ESI-TOF) m/z Calcd for $C_{13}H_{11}N_3O$ $[M+H]^+$: 226.0975, found: 226.0978.



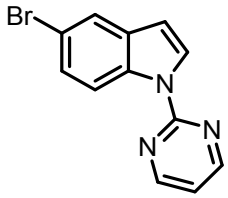
5-fluoro-1-(pyrimidin-2-yl)-1H-indole (1j)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (dd, J = 9.1, 4.8 Hz, 1H), 8.59 (d, J = 4.8 Hz, 2H), 8.21 (d, J = 3.7 Hz, 1H), 7.20 – 7.14 (m, 1H), 7.01 – 6.92 (m, 2H), 6.55 (d, J = 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.90 (d, $J_{C\text{-}F}$ = 237.9 Hz), 158.03 , 157.40 , 131.99 (d, $J_{C\text{-}F}$ = 10.0 Hz), 131.73 , 127.26 , 117.17 (d, $J_{C\text{-}F}$ = 9.0 Hz), 116.22 , 111.27 (d, $J_{C\text{-}F}$ = 24.8 Hz), 106.51 (d, $J_{C\text{-}F}$ = 4.1 Hz), 105.95 (d, $J_{C\text{-}F}$ = 23.5 Hz); HRMS (ESI-TOF) m/z Calcd for $C_{12}H_8FN_3$ $[M+H]^+$: 214.0775, found: 214.0775.



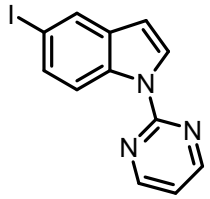
5-chloro-1-(pyrimidin-2-yl)-1H-indole (1k)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 8.9 Hz, 1H), 8.68 (d, J = 4.8 Hz, 2H), 8.30 (d, J = 3.7 Hz, 1H), 7.60 (d, J = 2.1 Hz, 1H), 7.30 (dd, J = 8.9, 2.1 Hz, 1H), 7.05 (t, J = 4.8 Hz, 1H), 6.65 (d, J = 3.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.13, 157.44, 133.66, 132.41, 127.61, 127.03, 123.68, 120.23, 117.29, 116.41, 106.17; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_8ClN_3$ $[M+H]^+$: 230.0480, found: 230.0479.



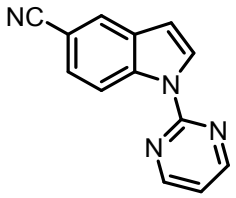
5-bromo-1-(pyrimidin-2-yl)-1H-indole (1l)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 – 8.62 (m, 3H), 8.25 (d, *J* = 3.7 Hz, 1H), 7.72 (d, *J* = 2.0 Hz, 1H), 7.40 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.03 (t, *J* = 4.8 Hz, 1H), 6.61 (d, *J* = 3.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.05, 157.33, 133.91, 132.92, 126.85, 126.26, 123.24, 117.70, 116.39, 115.31, 105.99; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_8BrN_3$ $[M+H]^+$: 273.9974, found: 273.9982.



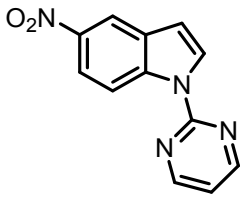
5-iodo-1-(pyrimidin-2-yl)-1H-indole (1m)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.8 Hz, 2H), 8.58 (d, *J* = 8.8 Hz, 1H), 8.24 (d, *J* = 3.7 Hz, 1H), 7.96 (d, *J* = 1.6 Hz, 1H), 7.60 (dd, *J* = 8.8, 1.7 Hz, 1H), 7.05 (t, *J* = 4.8 Hz, 1H), 6.62 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.98, 157.26, 134.39, 133.52, 131.83, 129.42, 126.46, 118.16, 116.34, 105.70, 86.08; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_8IN_3$ $[M+H]^+$: 321.9836, found: 321.9844.



1-(pyrimidin-2-yl)-1H-indole-5-carbonitrile (1n)

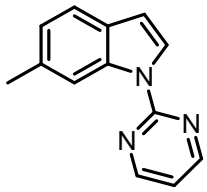
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (d, *J* = 8.7 Hz, 1H), 8.75 (d, *J* = 4.8 Hz, 2H), 8.40 (d, *J* = 3.7 Hz, 1H), 7.96 (s, 1H), 7.58 (d, *J* = 10.1 Hz, 1H), 7.16 (t, *J* = 4.8 Hz, 1H), 6.76 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.26, 157.18, 136.94, 131.07, 128.00, 126.58, 125.67, 120.20, 117.17, 117.03, 106.58, 105.10; HRMS (ESI-TOF) m/z Calcd for $C_{13}H_8N_4$ $[M+H]^+$: 221.0822, found: 221.0831.



5-nitro-1-(pyrimidin-2-yl)-1H-indole (1o)

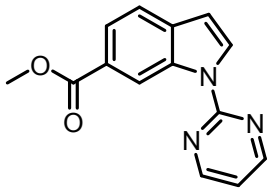
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.92 (d, *J* = 9.2 Hz, 1H), 8.76 (d, *J* = 4.7 Hz, 2H), 8.54 (s, 1H), 8.44 (d, *J* = 3.6 Hz, 1H), 8.21 (d, *J* = 10.6 Hz, 1H), 7.17 (t, *J* = 4.7 Hz, 1H), 6.84 (d, *J* = 3.6 Hz, 1H);^{13}C NMR (125 MHz, $CDCl_3$) δ 158.35, 157.23, 143.25, 138.28, 130.97, 128.89, 118.88,

117.37, 117.20, 116.34, 107.70; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_8N_4O_2$ $[M+H]^+$: 241.0720, found: 241.0712.



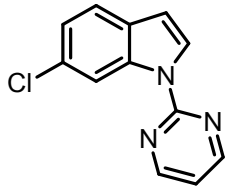
6-methyl-1-(pyrimidin-2-yl)-1H-indole (1p)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.8 Hz, 2H), 8.63 (s, 1H), 8.19 (d, *J* = 3.8 Hz, 1H),7.50 (d, *J* = 7.9 Hz, 1H), 7.07 (d, *J* = 7.9 Hz, 1H), 7.01 (t, *J* = 5.4 Hz, 1H), 6.65 (d, *J* = 3.7 Hz, 1H),2.54 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.93, 157.78, 135.72, 133.41, 129.05, 125.21, 123.57, 120.30, 116.30, 115.82, 106.73, 22.02; HRMS (ESI-TOF) m/z Calcd for $C_{13}H_{11}N_3$ $[M+H]^+$: 210.1026, found: 210.1012.



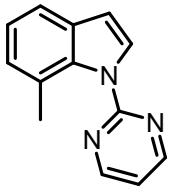
methyl 1-(pyrimidin-2-yl)-1H-indole-6-carboxylate (1q)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 (s, 1H), 8.68 (d, *J* = 4.8 Hz, 2H), 8.36 (d, *J* = 3.6 Hz, 1H),7.87 (d, *J* = 9.7 Hz, 1H), 7.58 (d, *J* = 8.2 Hz, 1H), 7.04 (t, *J* = 4.8 Hz, 1H), 6.67 (d, *J* = 3.6 Hz, 1H),3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.11, 158.27, 157.43, 134.98, 134.73, 128.82, 125.31, 123.24, 120.42, 118.28, 116.66, 106.72, 52.04; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{11}N_3O_2$ $[M+H]^+$: 254.0924, found: 254.0923.



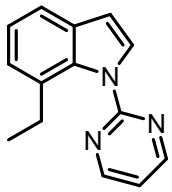
6-chloro-1-(pyrimidin-2-yl)-1H-indole (1r)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, *J* = 1.9 Hz, 1H), 8.67 (d, *J* = 4.8 Hz, 2H), 8.24 (d, *J* = 3.7 Hz, 1H), 7.50 (d, *J* = 8.3 Hz, 1H), 7.20 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.03 (t, *J* = 4.8 Hz, 1H), 6.65 (d, *J* = 3.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.00, 157.26, 135.46, 129.65, 129.32, 126.30, 122.49, 121.33, 116.38, 106.50; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_8ClN_3$ $[M+H]^+$: 230.0480, found: 230.0497.



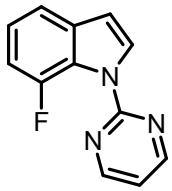
7-methyl-1-(pyrimidin-2-yl)-1H-indole (1s)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.8 Hz, 2H), 7.92 (d, *J* = 3.5 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.35 – 7.21 (m, 2H), 7.02 (t, *J* = 4.8 Hz, 1H), 6.83 (d, *J* = 3.6 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.83, 157.57, 134.38, 131.46, 129.55, 126.36, 123.95, 121.97, 118.51, 117.06, 106.58, 22.09; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{17}NO$ $[M+H]^+$: 210.1026, found: 210.1027.



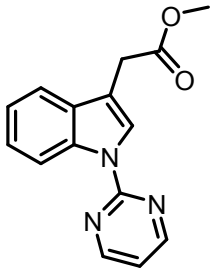
7-ethyl-1-(pyrimidin-2-yl)-1H-indole (1t)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 4.8 Hz, 2H), 7.76 (d, *J* = 3.6 Hz, 1H), 7.49 (dd, *J* = 6.8, 2.1 Hz, 1H), 7.22 – 7.15 (m, 2H), 7.03 (t, *J* = 4.8 Hz, 1H), 6.70 (d, *J* = 3.6 Hz, 1H), 2.87 (q, *J* = 7.5 Hz, 2H), 1.03 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.11, 158.07, 133.66, 131.86, 130.27, 129.91, 124.47, 122.25, 118.73, 117.29, 106.86, 27.60, 13.77; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{13}N_3$ $[M+H]^+$: 224.1182, found: 224.1190.



7-fluoro-1-(pyrimidin-2-yl)-1H-indole (1u)

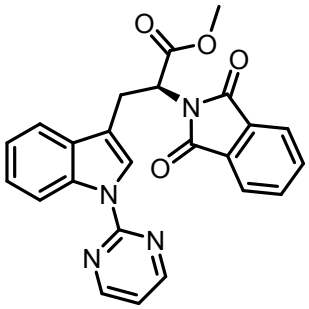
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.8 Hz, 2H), 7.94 (d, *J* = 3.5 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.21 – 7.10 (m, 2H), 7.04 (dd, *J* = 12.3, 7.9 Hz, 1H), 6.73 (dd, *J* = 3.5, 2.1 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$) δ 158.19, 156.86, 150.05 (d, $J_{C\text{-}F}$ = 250.5 Hz), 134.71 (d, $J_{C\text{-}F}$ = 4.0 Hz), 129.11, 122.47 (d, $J_{C\text{-}F}$ = 6.9 Hz), 122.22 (d, $J_{C\text{-}F}$ = 9.7 Hz), 117.35, 116.67 (d, $J_{C\text{-}F}$ = 3.6 Hz), 110.35 (d, $J_{C\text{-}F}$ = 20.6 Hz), 106.90 (d, $J_{C\text{-}F}$ = 1.7 Hz); HRMS (ESI-TOF) m/z Calcd for $C_{12}H_8FN_3$ $[M+H]^+$: 214.0775, found: 214.0784.



methyl 2-(1-(pyrimidin-2-yl)-1H-indol-3-yl)acetate (1y)

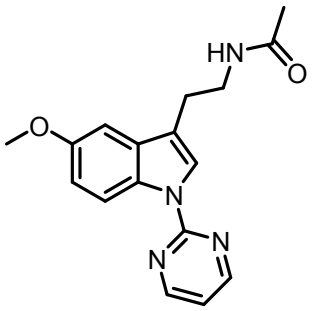
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 8.4 Hz, 1H), 8.59 (d, *J* = 4.8 Hz, 2H), 8.17 (s, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.28 (t, *J* = 7.7 Hz, 1H), 7.19 (t, *J* = 7.3 Hz, 1H), 6.93 (t, *J* = 4.8 Hz, 1H), 3.73 (s, 2H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.75, 158.02, 157.52, 135.50, 130.65,

124.49, 123.93, 122.06, 118.82, 116.33, 115.99, 112.63, 52.09, 31.14; HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{13}N_3O_2$ $[M+H]^+$: 268.1081, found: 268.1041.



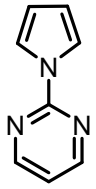
methyl (S)-2-(1,3-dioxoisoindolin-2-yl)-3-(1-(pyrimidin-2-yl)-1H-indol-3-yl)propanoate (1z)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 8.3 Hz, 1H), 8.63 (d, *J* = 4.8 Hz, 2H), 8.14 (s, 1H), 7.83 – 7.75 (m, 2H), 7.72 – 7.65 (m, 2H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.35 – 7.27 (m, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 6.99 (t, *J* = 4.7 Hz, 1H), 5.38 (dd, *J* = 8.8, 7.0 Hz, 1H), 3.88 – 3.77 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.46, 167.50, 157.95, 157.40, 135.48, 133.98, 131.64, 130.59, 124.04, 123.86, 123.45, 121.96, 118.46, 116.21, 115.85, 115.25, 52.92, 52.09, 24.82; HRMS (ESI-TOF) m/z Calcd for $C_{24}H_{18}N_4O_4$ $[M+H]^+$: 427.1401, found: 427.1393.



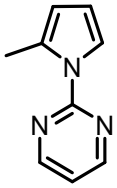
***N*-(2-(5-methoxy-1-(pyrimidin-2-yl)-1H-indol-3-yl)ethyl)acetamide (1za)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 9.1 Hz, 1H), 8.66 (d, *J* = 4.8 Hz, 2H), 8.08 (s, 1H), 7.04 (d, *J* = 2.5 Hz, 1H), 7.03 – 6.95 (m, 2H), 5.65 (brs, 1H), 3.89 (s, 3H), 3.64 (q, *J* = 6.6 Hz, 2H), 2.96 (t, *J* = 6.7 Hz, 2H), 1.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.09, 158.06, 157.37, 155.50, 131.73, 130.57, 123.71, 117.31, 117.04, 115.71, 112.82, 101.20, 55.73, 39.16, 25.24, 23.40; HRMS (ESI-TOF) m/z Calcd for $C_{17}H_{18}N_4O_2$ $[M+H]^+$: 311.1503, found: 311.1492.



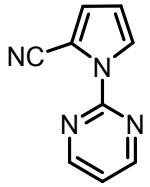
2-(1H-pyrrol-1-yl)pyrimidine (4a)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.8 Hz, 2H), 7.83 – 7.73 (m, 2H), 7.01 (t, *J* = 4.8 Hz, 1H), 6.40 – 6.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.27, 156.12, 118.95, 117.04, 111.93; HRMS (ESI-TOF) m/z Calcd for $C_8H_7N_3$ $[M+H]^+$: 146.0713, found: 146.0715.



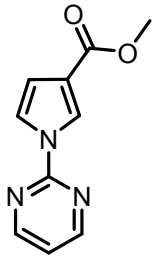
2-(2-methyl-1H-pyrrol-1-yl)pyrimidine (4b)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.8 Hz, 2H), 7.83 – 7.65 (m, 1H), 7.07 (t, *J* = 4.8 Hz, 1H), 6.23 (t, *J* = 3.2 Hz, 1H), 6.15 – 6.02 (m, 1H), 2.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.95, 157.81, 131.10, 120.28, 116.75, 112.04, 109.72, 16.61; HRMS (ESI-TOF) m/z Calcd for $C_9H_9N_3$ $[M+H]^+$: 160.0869, found: 160.0881.



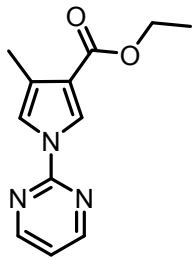
1-(pyrimidin-2-yl)-1H-pyrrole-2-carbonitrile (4c)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.8 Hz, 2H), 8.00 (dd, *J* = 3.0, 1.7 Hz, 1H), 7.25 (t, *J* = 4.8 Hz, 1H), 7.09 (dd, *J* = 3.7, 1.7 Hz, 1H), 6.38 (t, *J* = 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.52, 154.97, 126.09, 124.92, 118.84, 114.04, 111.71, 102.69; HRMS (ESI-TOF) m/z Calcd for $C_9H_6N_4$ $[M+H]^+$: 171.0665, found: 171.0678.



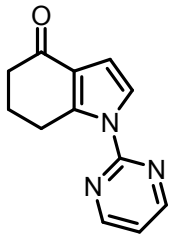
methyl 1-(pyrimidin-2-yl)-1H-pyrrole-3-carboxylate (4d)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.8 Hz, 2H), 8.38 – 8.27 (m, 1H), 7.72 – 7.60 (m, 1H), 7.07 (t, *J* = 4.8 Hz, 1H), 6.71 – 6.59 (m, 1H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.88, 158.51, 155.56, 123.97, 119.71, 119.04, 118.23, 112.18, 51.29; HRMS (ESI-TOF) m/z Calcd for $C_{10}H_9N_3O_2$ $[M+H]^+$: 204.0768, found: 204.0781.



ethyl 4-methyl-1-(pyrimidin-2-yl)-1H-pyrrole-3-carboxylate (4e)

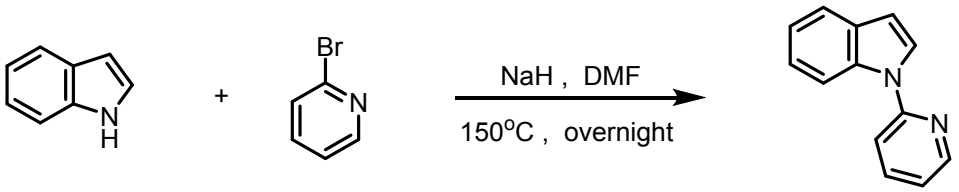
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.8 Hz, 2H), 8.26 (d, *J* = 2.3 Hz, 1H), 7.49 – 7.36 (m, 1H), 7.03 (t, *J* = 4.8 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.24 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.93, 158.42, 155.45, 124.57, 123.68, 118.21, 117.82, 117.79, 59.60, 14.40, 11.87; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_{13}N_3O_2$ $[M+H]^+$: 232.1081, found: 232.1092.



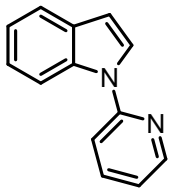
1-(pyrimidin-2-yl)-1,5,6,7-tetrahydro-4H-indol-4-one (4f)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 4.8 Hz, 2H), 7.74 (d, *J* = 3.5 Hz, 1H), 7.19 (t, *J* = 4.8 Hz, 1H), 6.69 (d, *J* = 3.5 Hz, 1H), 3.39 (t, *J* = 6.2 Hz, 2H), 2.56 – 2.50 (m, 2H), 2.23 – 2.13 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.16, 158.25, 157.02, 144.69, 124.35, 121.50, 118.03, 107.30, 37.66, 25.84, 23.82; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_{11}N_3O$ $[M+H]^+$: 214.0975, found: 214.0963.

2.1.2 Synthesis of 1-(pyridine-2-yl)-1H-indole[2]



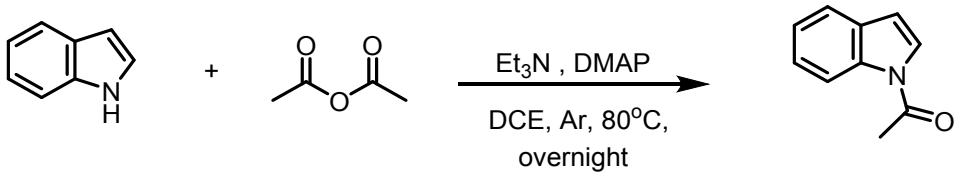
To a solution of indole (10 mmol) in DMF (25 mL) was added NaH (60% dispersion in mineral oil, 15 mmol) in portions. The reaction mixture was allowed to stir at room temperature for 1 hour. To the solution was added 2-bromopyridine (12 mmol) and the reaction mixture was heated to 150 °C overnight. The reaction mixture was allowed to return to room temperature before being poured into brine (100 mL) and EtOAc (100 mL). The organic layer was separated and the aqueous layer was re-extracted with EtOAc (2 × 100 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified via silica gel column chromatography (n-hexane/EtOAc) to give the desired product as a light brown oil.



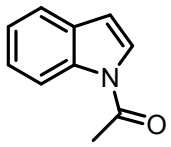
1-(pyridin-2-yl)-1H-indole (6)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 – 8.54 (m, 1H), 8.27 (d, *J* = 8.4 Hz, 1H), 7.83 (t, *J* = 8.8 Hz, 1H), 7.77 (d, *J* = 3.5 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 8.2 Hz, 1H), 7.36 (t, *J* = 7.7 Hz, 1H), 7.29 – 7.23 (m, 1H), 7.23 – 7.16 (m, 1H), 6.77 (d, *J* = 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.40, 148.89, 138.33, 134.98, 130.35, 125.92, 123.05, 121.19, 121.02, 119.99, 114.52, 112.90, 105.45; HRMS (ESI-TOF) m/z Calcd for $C_{13}H_{10}N_2$ $[M+H]^+$: 195.0917, found: 195.0937.

2.1.3 Synthesis of 1-(1H-indol-1-yl)ethan-1-one[3]



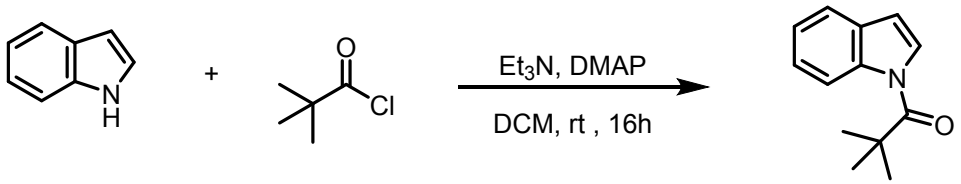
Indole (10 mmol), acetic anhydride (19 mmol), triethylamine (15mmol) and N,N-dimethyl -4 -aminopyridine (1.9 mmol) were dissolved in 1,2-dichlororoethane (25 mL). The reaction mixture was stirred at 80 °C overnight under Ar atmosphere. After the reaction, EtOAc and water were added to the reaction mixture. The organic phase was concentrated under reduced pressure and purified by column chromatography (n-hexane/EtOAc) to give the desired product as a yellow oil.



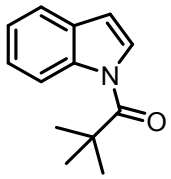
1-(1H-indol-1-yl)ethan-1-one (7)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.42 – 7.28 (m, 3H), 6.65 (d, *J* = 2.9 Hz, 1H), 2.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.51, 135.32, 130.24, 125.11, 124.89, 123.47, 120.67, 116.34, 108.90, 23.74; HRMS (ESI-TOF) m/z Calcd for $C_{10}H_9NO$ $[M+H]^+$: 160.0757, found: 160.0768.

2.1.4 Synthesis of 1-(1H-indol-1-yl)-2,2-dimethylpropan-1-one[4]



Pivaloyl chloride (11.7 mmol) was added dropwise to a solution of indole (10 mmol), DMAP (1 mmol) and triethylamine (14.8 mmol) in anhydrous CH_2Cl_2 (25 mL) at 0 ºC. The solution was stirred for 16 hours at room temperature. After this time, the reaction mixture was evaporated to dryness under reduced pressure. The crude was portioned between Et_2O and saturated aqueous NH_4Cl. The two layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and evaporated to dryness. The crude was purified by column chromatography to afford the desired N-pivaloyl indole.

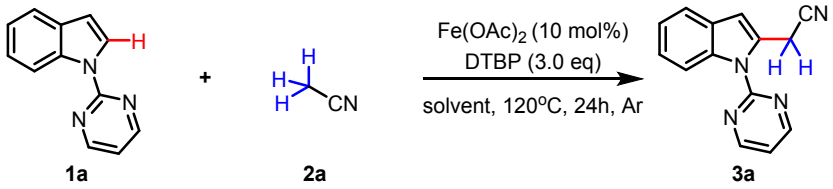


1-(1H-indol-1-yl)-2,2-dimethylpropan-1-one (9)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 8.3 Hz, 1H), 7.77 (d, *J* = 3.8 Hz, 1H), 7.59 (d, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.34 – 7.27 (m, 1H), 6.65 (d, *J* = 3.8 Hz, 1H), 1.55 (s, 9H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 177.07, 136.70, 129.33, 125.62, 125.07, 123.51, 120.44, 117.29, 108.21, 41.21, 28.67; HRMS (ESI-TOF) m/z Calcd for $C_{13}H_{15}NO$ $[M+H]^+$: 202.1226, found: 202.1228.

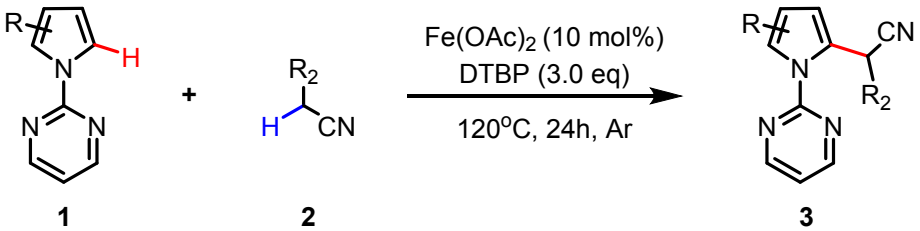
2.2 optimization of solvents



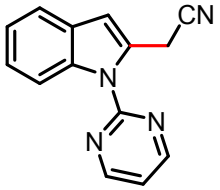
Entry	Solvent	Yield (%,**3a**)[b]
1	toluene	trace
2	chlorobenzene	trace
3	1,2-dichloroethane	trace
4	1,4-dioxane	0
5	tetrahydrofuran	0
6	N,N-Dimethylformamide	0
7	dimethyl sulfoxide	trace
8	ethanol	0

[a] Reaction conditions: **1a** (0.20 mmol), acetonitrile **2a** (10.0 equiv), $Fe(OAc)_2$ (10 mol%), DTBP (3.0 equiv), solvent (4 mL), stirred at 120 °C for 24 h under argon in a 15 mL schlenk tube. [b] Yield was determined by ^1H NMR analysis using CH_2Br_2 as internal standard.

2.3 General procedure for C2-cyanomethylation of indoles or pyrroles

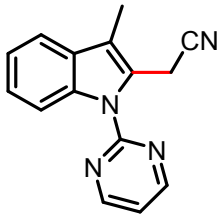


In a 15 mL schlenk tube, the corresponding indoles or pyrroles **1** (0.2 mmol, 1.0 eq), $Fe(OAc)_2$ (0.02 mmol, 10 mol%), DTBP (0.6 mmol, 3.0 eq) and acetonitrile or acetonitrile derivatives **2** (4 mL) was added under Ar atmosphere. The tube was sealed and the resulting solution was heated in a 120 °C oil bath with vigorous stirring for 24 h. Then the reaction mixture was cooled to room temperature. The mixture was poured into water (10 mL) and extracted with ethyl acetate (20 mL × 3), and the combined organic layer was dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under vacuum. The residue was purified by flash chromatography using EtOAc /*n*-hexene (1:4) as eluent to afford the products.



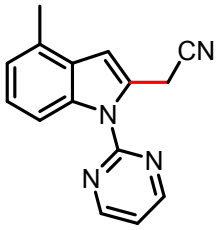
2-(1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3a)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, *J* = 4.7 Hz, 2H), 8.51 (d, *J* = 8.4 Hz, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.26 (t, *J* = 7.6 Hz, 1H), 7.20 – 7.15 (m, 1H), 7.08 (t, *J* = 4.7 Hz, 1H), 6.74 (s, 1H), 4.34 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.08, 157.91, 137.10, 128.98, 128.43, 124.14, 122.60, 120.43, 117.24, 117.09, 115.46, 109.55, 20.87; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{10}N_4$ $[M+H]^+$: 235.0978, found: 235.0966.



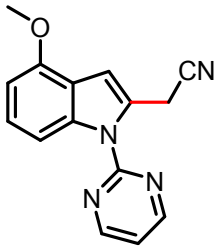
2-(3-methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3b)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.8 Hz, 2H), 8.56 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 8.4 Hz, 1H), 7.30 – 7.21 (m, 1H), 7.09 (t, *J* = 4.8 Hz, 1H), 4.31 (s, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.97, 157.77, 136.10, 129.54, 124.40, 123.95, 122.13, 118.54, 117.35, 116.72, 116.71, 115.21, 17.48, 8.80; HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{12}N_4$ $[M+H]^+$: 249.1135, found: 249.1149.



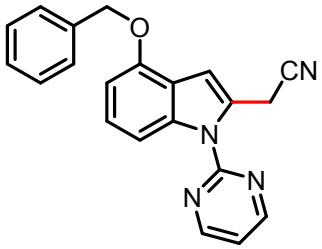
2-(4-methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3c)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.8 Hz, 2H), 8.39 (d, *J* = 8.4 Hz, 1H), 7.25 – 7.20 (m, 1H), 7.13 (t, *J* = 4.8 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 6.83 (s, 1H), 4.41 (s, 2H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.03, 157.88, 136.87, 129.80, 128.31, 128.04, 124.16, 122.93, 117.36, 117.04, 112.90, 107.89, 20.85, 18.49; HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{12}N_4$ $[M+H]^+$: 249.1135, found: 249.1125.



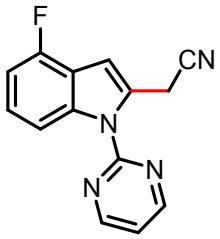
2-(4-methoxy-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3d)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 4.8 Hz, 2H), 8.15 (d, J = 8.5 Hz, 1H), 7.25 (t, J = 8.2 Hz, 1H), 7.15 (t, J = 4.8 Hz, 1H), 6.92 (s, 1H), 6.68 (d, J = 7.9 Hz, 1H), 4.38 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.06, 157.92, 152.60, 138.31, 127.29, 124.93, 118.89, 117.26, 117.15, 108.49, 106.58, 102.71, 55.39, 20.79; HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{12}N_4O$ $[M+H]^+$: 265.1084, found: 265.1075.



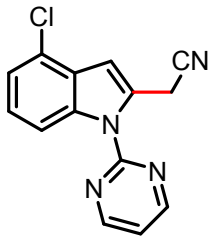
2-(4-(benzyloxy)-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3e)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, J = 4.8 Hz, 2H), 8.08 (d, J = 8.5 Hz, 1H), 7.42 (d, J = 7.2 Hz, 2H), 7.38 – 7.30 (m, 2H), 7.30 – 7.22 (m, 1H), 7.14 (t, J = 8.2 Hz, 1H), 7.05 (t, J = 4.8 Hz, 1H), 6.89 (s, 1H), 6.65 (d, J = 7.9 Hz, 1H), 5.13 (s, 2H), 4.29 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.04, 157.88, 151.68, 138.37, 137.08, 128.51, 127.85, 127.34, 127.31, 124.87, 119.22, 117.29, 117.14, 108.74, 106.73, 104.14, 69.96, 20.76; HRMS (ESI-TOF) m/z Calcd for $C_{21}H_{16}N_4O$ $[M+H]^+$: 341.1397, found: 341.1389.



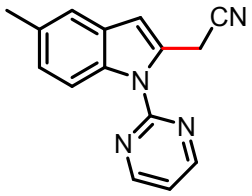
2-(4-fluoro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3f)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 4.8 Hz, 2H), 8.27 (d, J = 8.5 Hz, 1H), 7.23 – 7.09 (m, 2H), 6.91 – 6.79 (m, 2H), 4.32 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.16, 157.70, 155.43 (d, $J_{C\text{-}F}$ = 247.4 Hz), 139.15 (d, $J_{C\text{-}F}$ = 9.6 Hz), 129.08, 124.69 (d, $J_{C\text{-}F}$ = 7.5 Hz), 117.53, 117.32, 116.93, 111.53 (d, $J_{C\text{-}F}$ = 3.7 Hz), 107.64 (d, $J_{C\text{-}F}$ = 18.2 Hz), 104.92, 20.83; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_9FN_4$ $[M+H]^+$: 253.0884, found: 253.0872.



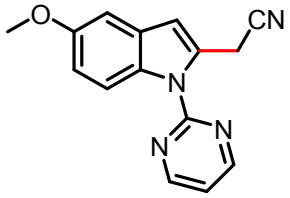
2-(4-chloro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3g)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.8 Hz, 2H), 8.49 – 8.44 (m, 1H), 7.26 – 7.22 (m, 2H), 7.19 (t, *J* = 4.8 Hz, 1H), 6.91 (s, 1H), 4.40 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.15, 157.57, 137.63, 129.74, 127.13, 125.56, 124.69, 122.28, 117.56, 116.89, 114.08, 107.50, 20.86; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_9ClN_4$ $[M+H]^+$: 269.0589, found: 269.0576.



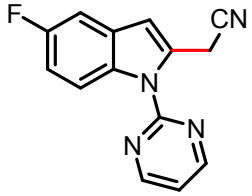
2-(5-methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3h)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.8 Hz, 2H), 8.45 (d, *J* = 8.6 Hz, 1H), 7.34 (s, 1H), 7.13 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.10 (t, *J* = 4.8 Hz, 1H), 6.70 (s, 1H), 4.38 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.94, 157.88, 135.30, 131.97, 128.90, 128.61, 125.49, 120.19, 117.35, 116.78, 115.25, 109.27, 21.23, 20.92; HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{12}N_4$ $[M+H]^+$: 249.1135, found: 249.1126.



2-(5-methoxy-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3i)

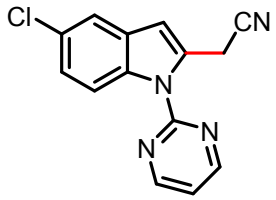
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.8 Hz, 2H), 8.52 (d, *J* = 9.2 Hz, 1H), 7.13 (t, *J* = 4.8 Hz, 1H), 7.04 (d, *J* = 2.6 Hz, 1H), 6.95 (dd, *J* = 9.2, 2.6 Hz, 1H), 6.74 (s, 1H), 4.42 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.00, 157.87, 155.71, 131.90, 129.47, 129.21, 117.32, 116.82, 116.64, 113.20, 109.46, 102.45, 55.63, 21.08; HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{12}N_4O$ $[M+H]^+$: 265.1084, found: 265.1083.



2-(5-fluoro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3j)

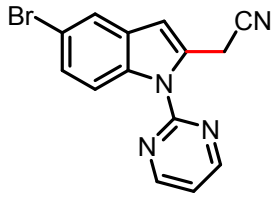
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.8 Hz, 2H), 8.57 (dd, *J* = 9.2, 4.7 Hz, 1H), 7.22 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.18 (t, *J* = 4.8 Hz, 1H), 7.05 (td, *J* = 9.2, 2.6 Hz, 1H), 6.77 (s, 1H), 4.42 (s,

2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.04 (d, J_{C-F} = 238.9 Hz), 158.09, 157.67, 133.44, 130.58, 129.12 (d, J_{C-F} = 10.2 Hz), 117.24, 117.05, 116.75 (d, J_{C-F} = 8.9 Hz), 111.95 (d, J_{C-F} = 24.8 Hz), 109.20 (d, J_{C-F} = 4.1 Hz), 105.61 (d, J_{C-F} = 23.7 Hz), 21.02; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_9FN_4$ $[M+H]^+$: 253.0884, found: 253.0881.



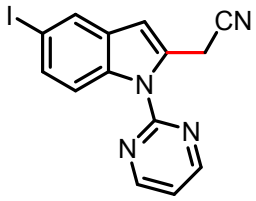
2-(5-chloro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3k)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.8 Hz, 2H), 8.54 (d, *J* = 9.0 Hz, 1H), 7.55 (d, *J* = 2.1 Hz, 1H), 7.29 – 7.26 (m, 1H), 7.20 (t, *J* = 4.8 Hz, 1H), 6.76 (s, 1H), 4.43 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.16, 157.66, 135.43, 130.41, 129.53, 128.12, 124.28, 119.87, 117.40, 116.99, 116.78, 108.82, 20.98; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_9ClN_4$ $[M+H]^+$: 269.0589, found: 269.0585.



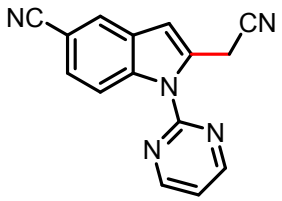
2-(5-bromo-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3l)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.8 Hz, 2H), 8.46 (d, *J* = 9.0 Hz, 1H), 7.68 (d, *J* = 1.9 Hz, 1H), 7.38 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.18 (t, *J* = 4.8 Hz, 1H), 6.72 (s, 1H), 4.40 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.11, 157.57, 135.71, 130.27, 130.03, 126.85, 122.87, 117.39, 117.15, 116.97, 115.74, 108.61, 20.92; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_9BrN_4$ $[M+H]^+$: 313.0083, found: 313.0095.



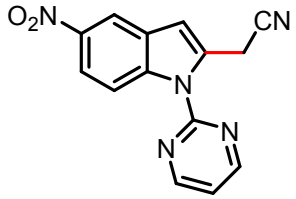
2-(5-iodo-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3m)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.8 Hz, 2H), 8.35 (d, *J* = 8.9 Hz, 1H), 7.89 (d, *J* = 1.7 Hz, 1H), 7.56 (dd, *J* = 8.9, 1.7 Hz, 1H), 7.19 (t, *J* = 4.8 Hz, 1H), 6.72 (s, 1H), 4.40 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.13, 157.60, 136.29, 132.48, 130.68, 129.91, 129.12, 117.56, 117.40, 116.97, 108.37, 86.46, 20.87; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_9IN_4$ $[M+H]^+$: 360.9945, found: 360.9955.



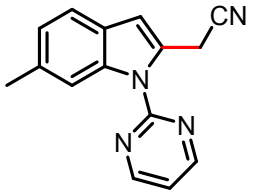
2-(cyanomethyl)-1-(pyrimidin-2-yl)-1H-indole-5-carbonitrile (3n)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J* = 4.7 Hz, 2H), 8.67 (d, *J* = 8.7 Hz, 1H), 7.93 (s, 1H), 7.57 (d, *J* = 8.7 Hz, 1H), 7.29 (t, *J* = 4.7 Hz, 1H), 6.89 (s, 1H), 4.45 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.39, 157.31, 138.73, 131.63, 128.23, 127.09, 125.39, 119.82, 118.17, 116.57, 116.39, 109.08, 105.85, 20.83; HRMS (ESI-TOF) m/z Calcd for $C_{15}H_9N_5$ $[M+H]^+$: 260.0931, found: 260.0938.



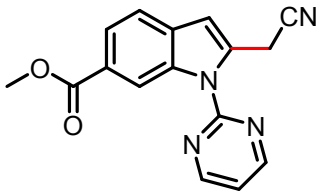
2-(5-nitro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3o)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.8 Hz, 2H), 8.60 (d, *J* = 9.3 Hz, 1H), 8.45 (d, *J* = 1.8 Hz, 1H), 8.14 (dd, *J* = 9.3, 2.0 Hz, 1H), 7.24 (t, *J* = 4.8 Hz, 1H), 6.91 (s, 1H), 4.39 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.44, 157.21, 143.43, 139.93, 132.45, 127.94, 119.28, 118.37, 116.84, 116.50, 115.72, 110.00, 20.86; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_9N_5O_2$ $[M+H]^+$: 280.0829, found: 280.0819.



2-(6-methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3p)

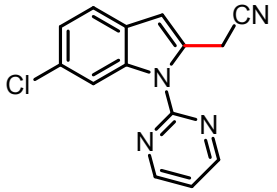
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.8 Hz, 2H), 8.37 (s, 1H), 7.45 (d, *J* = 7.9 Hz, 1H), 7.14 (t, *J* = 4.8 Hz, 1H), 7.08 (d, *J* = 7.9 Hz, 1H), 6.74 (s, 1H), 4.37 (s, 2H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.04, 157.88, 137.42, 134.07, 128.23, 126.15, 124.10, 119.99, 117.34, 116.95, 115.33, 109.39, 22.09, 20.79; HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{12}N_4$ $[M+H]^+$: 249.1135, found: 249.1123.



methyl 2-(cyanomethyl)-1-(pyrimidin-2-yl)-1H-indole-6-carboxylate (3q)

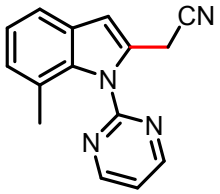
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (s, 1H), 8.84 (d, *J* = 4.8 Hz, 2H), 7.95 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.23 (t, *J* = 4.8 Hz, 1H), 6.87 (s, 1H), 4.45 (s, 2H), 3.96 (s, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 167.84, 158.34, 157.53, 136.49, 132.20, 132.03, 125.78, 123.68, 120.12, 117.64, 117.51, 116.80, 109.20, 52.11, 20.93; HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{12}N_4O_2$ $[M+H]^+$: 293.1033, found: 293.1035.



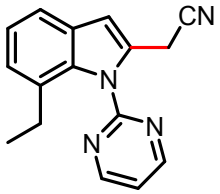
2-(6-chloro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3r)

^1H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, *J* = 4.8 Hz, 2H), 8.57 (s, 1H), 7.40 (d, *J* = 8.3 Hz, 1H), 7.14 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.11 (t, *J* = 4.8 Hz, 1H), 6.69 (s, 1H), 4.32 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.13, 157.59, 137.29, 129.98, 129.77, 126.87, 123.16, 121.07, 117.40, 117.02, 115.81, 109.23, 20.95; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_9ClN_4$ $[M+H]^+$: 269.0589, found: 269.0603.



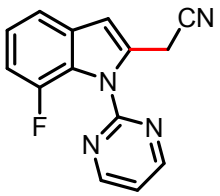
2-(7-methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3s)

^1H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, *J* = 4.9 Hz, 2H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.32 (t, *J* = 4.9 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.75 (s, 1H), 4.01 (s, 2H), 2.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.59, 157.47, 136.69, 129.06, 128.87, 126.67, 122.71, 122.17, 119.10, 118.59, 116.21, 107.17, 20.67, 18.29; HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{12}N_4$ $[M+H]^+$: 249.1135, found: 249.1134.



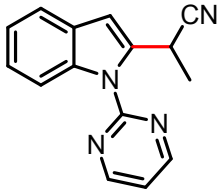
2-(7-ethyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3t)

^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 4.8 Hz, 2H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.27 (t, *J* = 4.8 Hz, 1H), 7.16 – 7.02 (m, 2H), 6.69 (s, 1H), 3.93 (s, 2H), 2.37 (q, *J* = 7.5 Hz, 2H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.65, 157.93, 136.00, 129.21, 129.13, 128.93, 124.49, 122.35, 119.24, 118.66, 116.18, 107.33, 26.28, 18.34, 13.58; HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{14}N_4$ $[M+H]^+$: 263.1291, found: 263.1305.



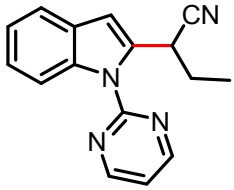
2-(7-fluoro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3u)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 4.8 Hz, 2H), 7.31 (d, J = 7.8 Hz, 1H), 7.24 (t, J = 4.8 Hz, 1H), 7.08 (td, J = 7.9, 4.3 Hz, 1H), 6.93 (dd, J = 12.2, 7.9 Hz, 1H), 6.74 (s, 1H), 4.09 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.45, 156.59, 149.65 (d, $J_{C\text{-}F}$ = 249.2 Hz), 131.76 (d, $J_{C\text{-}F}$ = 3.9 Hz), 129.96, 124.64 (d, $J_{C\text{-}F}$ = 9.4 Hz), 122.62 (d, $J_{C\text{-}F}$ = 7.0 Hz), 118.92, 116.50 (d, $J_{C\text{-}F}$ = 3.6 Hz), 116.19, 110.45 (d, $J_{C\text{-}F}$ = 19.4 Hz), 107.72 (d, $J_{C\text{-}F}$ = 1.9 Hz), 18.53; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_9FN_4$ $[M+H]^+$: 253.0884, found: 253.0894.



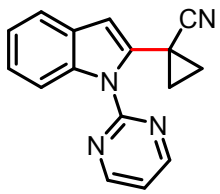
2-(1-(pyrimidin-2-yl)-1H-indol-2-yl)propanenitrile (3v)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 4.8 Hz, 2H), 8.48 (d, J = 8.5 Hz, 1H), 7.59 (d, J = 7.5 Hz, 1H), 7.32 (t, J = 8.4 Hz, 1H), 7.24 (t, J = 7.9 Hz, 1H), 7.15 (t, J = 4.8 Hz, 1H), 6.84 (s, 1H), 5.28 (q, J = 6.6 Hz, 1H), 1.72 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.13, 157.79, 137.24, 135.57, 128.34, 124.10, 122.49, 121.09, 120.52, 117.25, 115.04, 107.51, 26.28, 19.08; HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{12}N_4$ $[M+H]^+$: 249.1135, found: 249.1127.



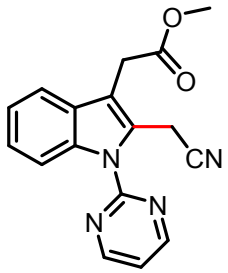
2-(1-(pyrimidin-2-yl)-1H-indol-2-yl)butanenitrile (3w)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 4.8 Hz, 2H), 8.50 (d, J = 8.4 Hz, 1H), 7.63 (d, J = 7.7 Hz, 1H), 7.35 (t, J = 7.8 Hz, 1H), 7.28 (t, J = 7.3 Hz, 1H), 7.20 (t, J = 4.8 Hz, 1H), 6.91 (s, 1H), 5.27 (dd, J = 8.7, 4.8 Hz, 1H), 2.21 – 1.84 (m, 2H), 1.18 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.16, 157.83, 137.21, 134.39, 128.35, 124.02, 122.51, 120.52, 120.30, 117.26, 114.96, 108.30, 33.54, 26.89, 11.51; HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{14}N_4$ $[M+H]^+$: 263.1291, found: 263.1310.



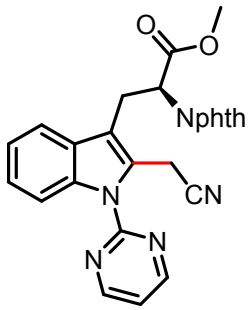
1-(1-(pyrimidin-2-yl)-1H-indol-2-yl)cyclopropane-1-carbonitrile (3x)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, *J* = 4.8 Hz, 2H), 8.49 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 1H), 7.30 – 7.24 (m, 1H), 7.22 (t, *J* = 4.8 Hz, 1H), 6.73 (s, 1H), 1.77 – 1.72 (m, 2H), 1.49 – 1.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.00, 157.49, 136.68, 135.02, 127.92, 124.41, 122.66, 122.35, 120.62, 117.34, 114.81, 110.02, 18.08, 10.81; HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{12}N_4$ $[M+H]^+$: 261.1135, found: 261.1154.



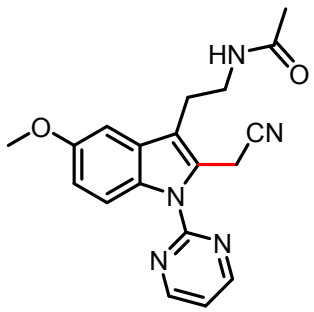
methyl 2-(2-(cyanomethyl)-1-(pyrimidin-2-yl)-1H-indol-3-yl)acetate (3y)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 4.8 Hz, 2H), 8.48 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.28 (t, *J* = 8.3 Hz, 1H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.08 (t, *J* = 4.8 Hz, 1H), 4.35 (s, 2H), 3.73 (s, 2H), 3.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.81, 158.10, 157.65, 136.05, 128.43, 126.08, 124.67, 122.56, 118.50, 117.24, 116.92, 115.31, 113.61, 52.31, 30.02, 17.75; HRMS (ESI-TOF) m/z Calcd for $C_{17}H_{14}N_4O_2$ $[M+H]^+$: 307.1190, found: 307.1175.



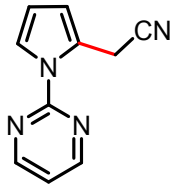
methyl(S)-3-(2-(cyanomethyl)-1-(pyrimidin-2-yl)-1H-indol-3-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (3z)

^{1}H NMR (400 MHz, CDCl3) δ 8.74 (d, *J* = 4.8 Hz, 2H), 8.49 (d, *J* = 8.2 Hz, 1H), 7.84 – 7.74 (m, 2H), 7.71 – 7.62 (m, 3H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.27 – 7.22 (m, 1H), 7.12 (t, *J* = 4.8 Hz, 1H), 5.35 (dd, *J* = 9.1, 6.4 Hz, 1H), 4.56 – 4.31 (m, 2H), 3.87 – 3.75 (m, 4H), 3.68 – 3.57 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.15, 167.53, 158.01, 157.57, 136.25, 134.16, 131.56, 128.11, 126.47, 124.60, 123.61, 122.53, 118.38, 117.15, 117.12, 115.46, 115.22, 53.01, 51.27, 24.68, 17.52; HRMS (ESI-TOF) m/z Calcd for $C_{26}H_{19}N_5O_4$ $[M+H]^+$: 466.1510, found: 466.1491.



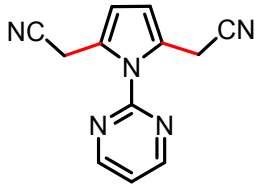
***N*-(2-(2-(cyanomethyl)-5-methoxy-1-(pyrimidin-2-yl)-1H-indol-3-yl)ethyl)acetamide (3za)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, *J* = 4.7 Hz, 2H), 8.44 (d, *J* = 9.1 Hz, 1H), 7.07 (t, *J* = 4.7 Hz, 1H), 6.95 (s, 1H), 6.90 (d, *J* = 9.1 Hz, 1H), 5.74 (brs, 1H), 4.27 (s, 2H), 3.81 (s, 3H), 3.48 (q, *J* = 6.0 Hz, 2H), 2.92 (t, *J* = 6.4 Hz, 2H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.71, 158.04, 157.68, 155.76, 131.12, 129.43, 125.94, 117.88, 117.70, 116.85, 116.69, 113.61, 100.73, 55.73, 39.44, 24.28, 23.39, 17.74; HRMS (ESI-TOF) m/z Calcd for $C_{19}H_{19}N_5O_2$ $[M+H]^+$: 350.1612, found: 350.1595.



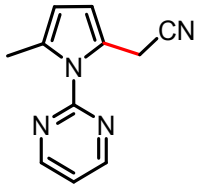
2-(1-(pyrimidin-2-yl)-1H-pyrrol-2-yl)acetonitrile (5a)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.8 Hz, 2H), 7.88 (dd, *J* = 3.3, 1.9 Hz, 1H), 7.12 (t, *J* = 4.8 Hz, 1H), 6.44 – 6.32 (m, 1H), 6.26 (t, *J* = 3.3 Hz, 1H), 4.28 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.18, 156.88, 122.10, 122.04, 117.81, 117.44, 114.61, 110.12, 20.16; HRMS (ESI-TOF) m/z Calcd for $C_{10}H_8N_4$ $[M+H]^+$: 185.0822, found: 185.0816.



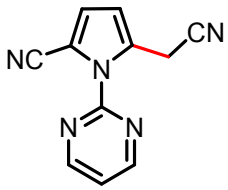
2,2'-(1-(pyrimidin-2-yl)-1H-pyrrole-2,5-diyl)diacetonitrile (5aa)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.8 Hz, 2H), 7.27 – 7.24 (m, 1H), 6.33 (s, 2H), 4.18 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.36, 156.72, 124.25, 118.46, 117.22, 112.55, 19.98; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_9N_5$ $[M+H]^+$: 224.0931, found: 224.0951.



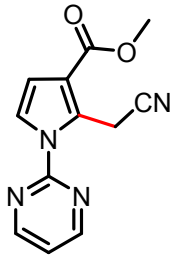
2-(5-methyl-1-(pyrimidin-2-yl)-1H-pyrrol-2-yl)acetonitrile (5b)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.8 Hz, 2H), 7.20 (t, *J* = 4.8 Hz, 1H), 6.22 (d, *J* = 3.1 Hz, 1H), 5.98 (d, *J* = 2.7 Hz, 1H), 4.05 (s, 2H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.21, 157.31, 132.75, 121.22, 118.09, 117.58, 111.69, 109.62, 19.11, 15.52; HRMS (ESI-TOF) m/z Calcd for $C_{11}H_{10}N_4$ $[M+H]^+$: 199.0978, found: 199.0973.



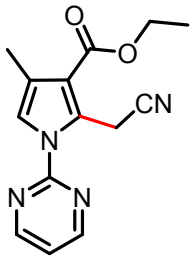
5-(cyanomethyl)-1-(pyrimidin-2-yl)-1H-pyrrole-2-carbonitrile (5c)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J* = 4.8 Hz, 2H), 7.35 (t, *J* = 4.8 Hz, 1H), 7.05 (d, *J* = 3.8 Hz, 1H), 6.49 (d, *J* = 3.8 Hz, 1H), 4.27 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.63, 155.31, 127.84, 123.95, 119.56, 116.13, 113.77, 113.44, 105.89, 19.79; HRMS (ESI-TOF) m/z Calcd for $C_{11}H_7N_5$ $[M+H]^+$: 210.0774, found: 210.0809.



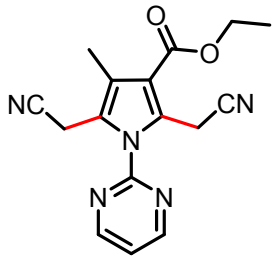
methyl 2-(cyanomethyl)-1-(pyrimidin-2-yl)-1H-pyrrole-3-carboxylate (5d)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.8 Hz, 2H), 7.77 (d, *J* = 3.5 Hz, 1H), 7.17 (t, *J* = 4.8 Hz, 1H), 6.62 (d, *J* = 3.5 Hz, 1H), 4.79 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.75, 158.39, 156.41, 127.15, 121.75, 118.69, 118.13, 117.16, 111.34, 51.49, 17.17; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_{10}N_4O_2$ $[M+H]^+$: 243.0877, found: 243.0895.



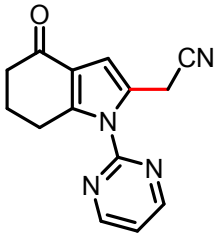
ethyl 2-(cyanomethyl)-4-methyl-1-(pyrimidin-2-yl)-1H-pyrrole-3-carboxylate (5e)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.8 Hz, 2H), 7.56 (s, 1H), 7.14 (t, *J* = 4.8 Hz, 1H), 4.76 (s, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.20 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.09, 158.34, 156.40, 127.44, 122.23, 120.24, 118.32, 118.04, 117.41, 60.22, 17.59, 14.29, 12.73; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{14}N_4O_2$ $[M+H]^+$: 271.1190, found: 271.1208.



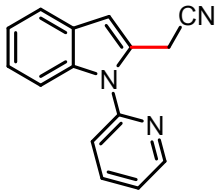
ethyl 2,5-bis(cyanomethyl)-4-methyl-1-(pyrimidin-2-yl)-1H-pyrrole-3-carboxylate (5ee)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, *J* = 4.9 Hz, 2H), 7.40 (t, *J* = 4.9 Hz, 1H), 4.58 (s, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 4.03 (s, 2H), 2.30 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.49, 158.91, 155.87, 128.39, 121.96, 120.12, 119.83, 116.49, 116.43, 116.12, 60.48, 16.61, 15.48, 14.26, 11.17; HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{15}N_5O_2$ $[M+H]^+$: 310.1299, found: 310.1320.



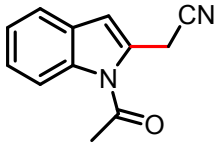
2-(4-oxo-1-(pyrimidin-2-yl)-4,5,6,7-tetrahydro-1H-indol-2-yl)acetonitrile (5f)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.8 Hz, 2H), 7.26 (t, *J* = 4.8 Hz, 1H), 6.65 (s, 1H), 4.05 (s, 2H), 3.09 (t, *J* = 6.2 Hz, 2H), 2.50 – 2.43 (m, 2H), 2.17 – 2.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.58, 158.51, 156.46, 146.66, 123.62, 121.92, 119.13, 116.75, 109.38, 37.64, 25.29, 23.75, 19.10; HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{12}N_4O$ $[M+H]^+$: 253.1084, found: 253.1076.



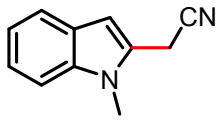
2-(1-(pyridin-2-yl)-1H-indol-2-yl)acetonitrile (6a)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 – 8.50 (m, 1H), 7.85 (td, *J* = 7.8, 1.9 Hz, 1H), 7.59 – 7.53 (m, 1H), 7.51 (d, *J* = 8.1 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.29 – 7.22 (m, 1H), 7.20 – 7.08 (m, 2H), 6.69 (s, 1H), 4.09 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.26, 149.53, 138.79, 136.84, 128.69, 127.87, 123.20, 122.18, 121.44, 120.91, 119.85, 116.57, 110.17, 105.65, 18.04; HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{11}N_3$ $[M+H]^+$: 234.1026, found: 234.1010.



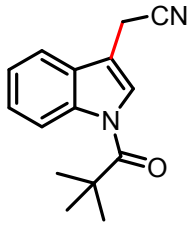
2-(1-acetyl-1H-indol-2-yl)acetonitrile (7a)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.39 – 7.33 (m, 1H), 7.33 – 7.27 (m, 1H), 6.83 (s, 1H), 4.23 (s, 2H), 2.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.35, 135.72, 130.69, 129.12, 124.82, 123.56, 121.50, 116.77, 114.05, 111.40, 27.47, 20.89; HRMS (ESI-TOF) m/z Calcd for $C_{12}H_{10}N_2O$ $[M+Na]^+$: 221.0685, found: 221.0671.



2-(1-methyl-1H-indol-2-yl)acetonitrile (8a)

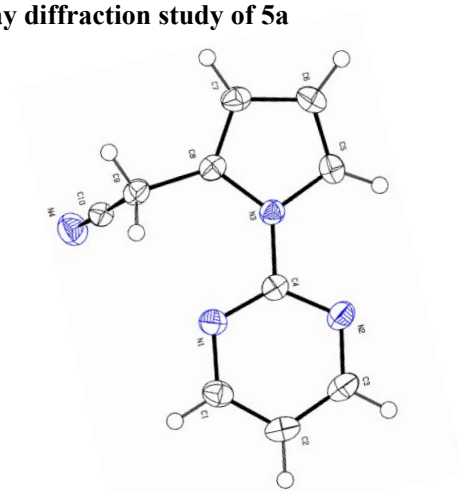
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.9 Hz, 1H), 7.32 – 7.20 (m, 2H), 7.18 – 7.09 (m, 1H), 6.50 (s, 1H), 3.79 (s, 2H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.76, 127.61, 126.98, 122.20, 120.58, 120.02, 115.99, 109.15, 102.08, 29.71, 16.58; HRMS (ESI-TOF) m/z Calcd for $C_{11}H_{10}N_2$ $[M+Na]^+$: 193.0736, found: 193.0729.



2-(1-pivaloyl-1H-indol-3-yl)acetonitrile (9a)

^{1}H NMR (400 MHz, CDCl3) δ 8.52 (d, *J* = 8.4 Hz, 1H), 7.78 (s, 1H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.41 (t, *J* = 8.3 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 3.80 (s, 2H), 1.52 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.74, 137.10, 127.32, 126.05, 123.80, 123.76, 117.67, 117.63, 116.98, 110.50, 41.19, 28.56, 14.41; HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{16}N_2O$ $[M+Na]^+$: 263.1155, found: 263.1138.

2.4 The single crystal X-ray diffraction study of 5a



X-ray structure of **5a**

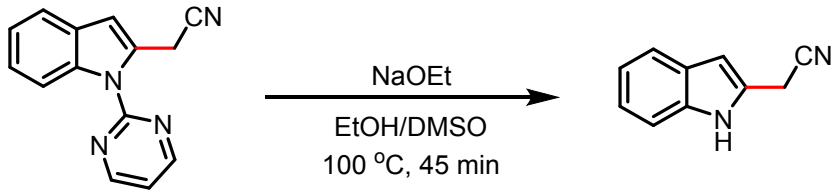
CCDC 1573954 (**5a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via https://www.ccdc.cam.ac.uk/structures/.

Crystal Data and Structure Refinement for **5a**

complex	**1**
Formula	$C_{10}H_8N_4$
Formula weight	184.20
Crystal system	Monoclinic
space group	P2(1)
a (Å)	4.3504(4)
b (Å)	24.437(2)

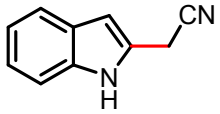
c (Å)	8.5476(7)
α (º)	90.00
β (º)	102.442(2)
γ (º)	90.00
Volume(Å^3)	887.35(13)
Z	4
T (K)	153(2)
D_{calcd} (g/m^3)	1.379
F(000)	384
Reflections collected	1551
Unique reflections	1419
Goof	1.058
R_1[I> 2σ(I)]	0.0449
wR_2[I>2σ(I)]	0.1151

2.5 Procedure for removal of the directing Group[5,6]



3a **3aa 45%**

To a solution of 2-(1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile **3a** (0.2 mmol, 1.0 eq) in DMSO (1.0 mL) was added NaOEt (0.6 mmol, 3.0 eq) (20% wt. in EtOH) at room temperature under Ar atmosphere. After the mixture was stirred at 100 °C for 45 min, saturated aq. NH_4Cl was added at room temperature. Then, the reaction mixture was diluted with EtOAc (10 mL) and washed with H_2O (2 × 25 mL). The aqueous layer was extracted with EtOAc (2 × 25 mL). The combined organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography using EtOAc/hexanes (1:4) as eluent to afford the desired product **3aa** in 45% yield.

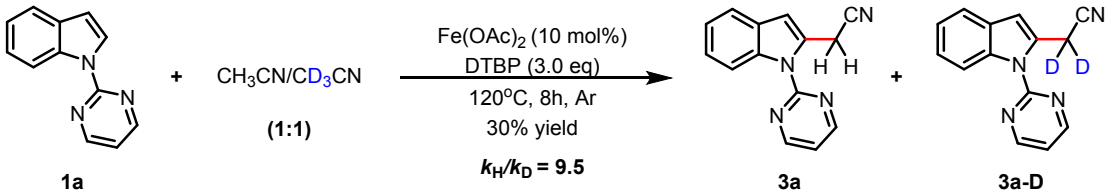


2-(1H-indol-2-yl)acetonitrile (3aa)

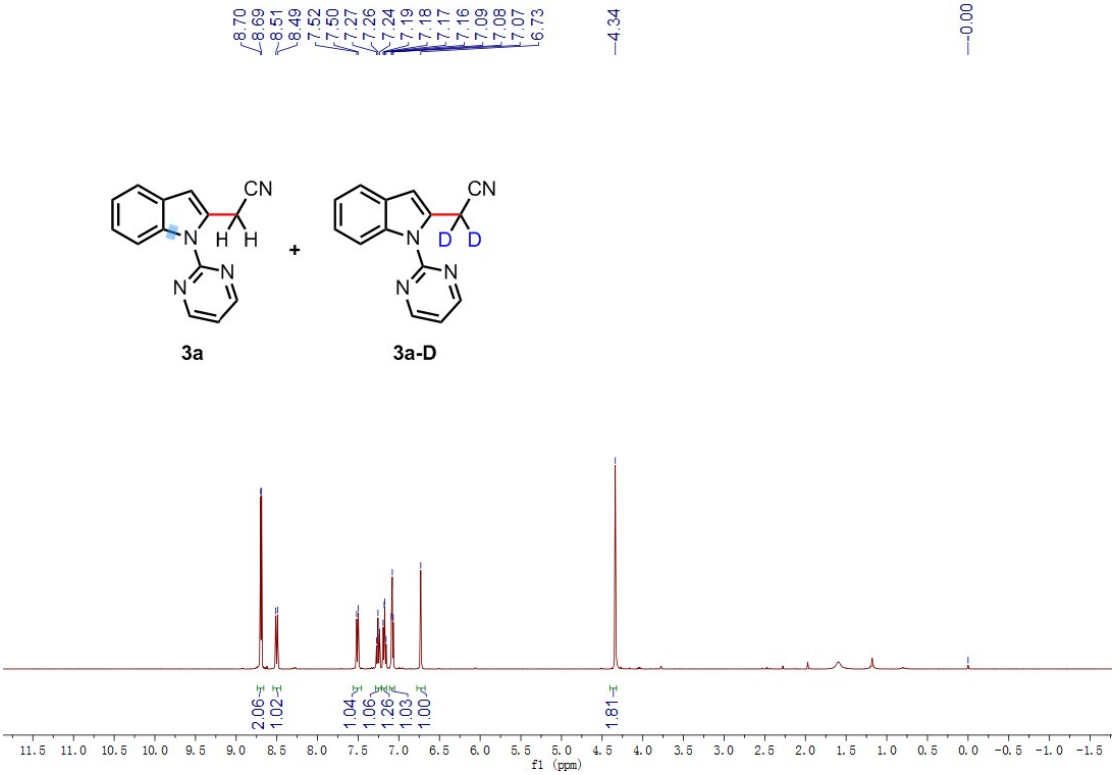
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.57 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 8.1 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 6.48 (s, 1H), 3.91 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.45, 128.02, 125.70, 122.69, 120.52, 120.46, 116.32, 110.91, 102.73, 17.59; HRMS (ESI-TOF) m/z Calcd for $C_{10}H_8N_2$ [M-H]$^-$:155.0615, found: 155.0608.

2.6 Kinetic isotope effect studies

2.6.1 The KIE studies on solvent (competition reaction)

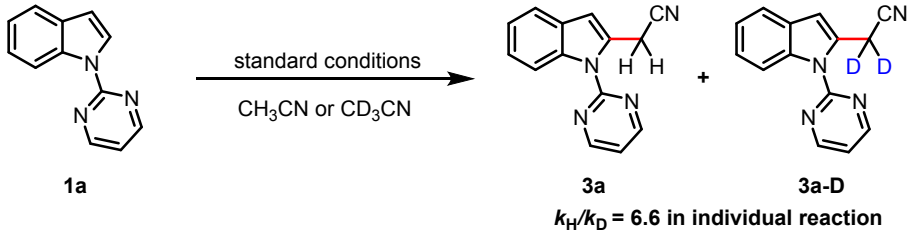


The KIE value was calculated as k_H/k_D = 9.5.



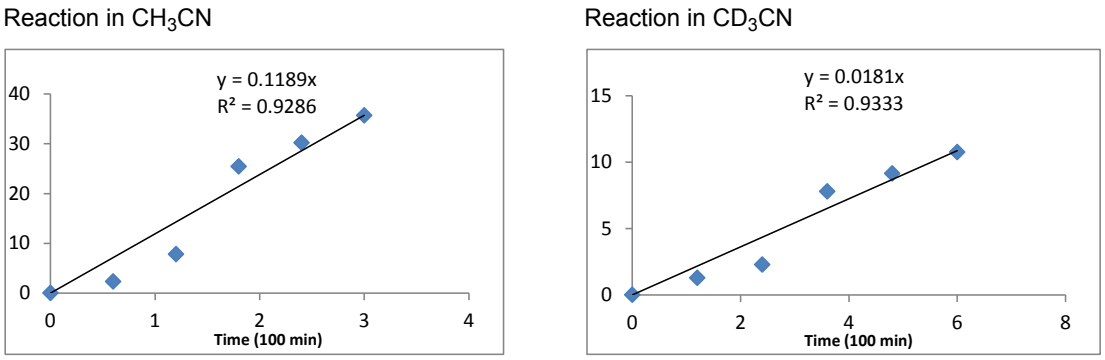
2.6.2 The Kinetic Isotopic Effect Studies on Solvent (parallel reaction) [7]

In ten parallel sealed tubes, *N*-pyrimidyl indole (**1a**, 0.2 mmol) was treated by standard condition in CH_3CN or D_3-CH_3CN (five experiments for each). Then the reactions were quenched by cooling to room temperature in specified time. The mixture was analyzed by ^1H NMR with CH_2Br_2 as inert standard to record the yield of products **3a** or **3a-D**. A significant intermolecular kinetic isotope effect (k_H/k_D = 6.6) was observed. The results were listed below:



2-(1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile-d_2 (3a-D)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, J = 4.8 Hz, 2H), 8.51 (d, J = 8.4 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.25 (t, J = 8.4 Hz, 1H), 7.20 – 7.14 (m, 1H), 7.07 (t, J = 4.8 Hz, 1H), 6.73 (s, 1H).



2.7 Electrospray Ionization-Time-of-Flight-Mass Spectrometry (ESI-TOF-MS) of compound 12

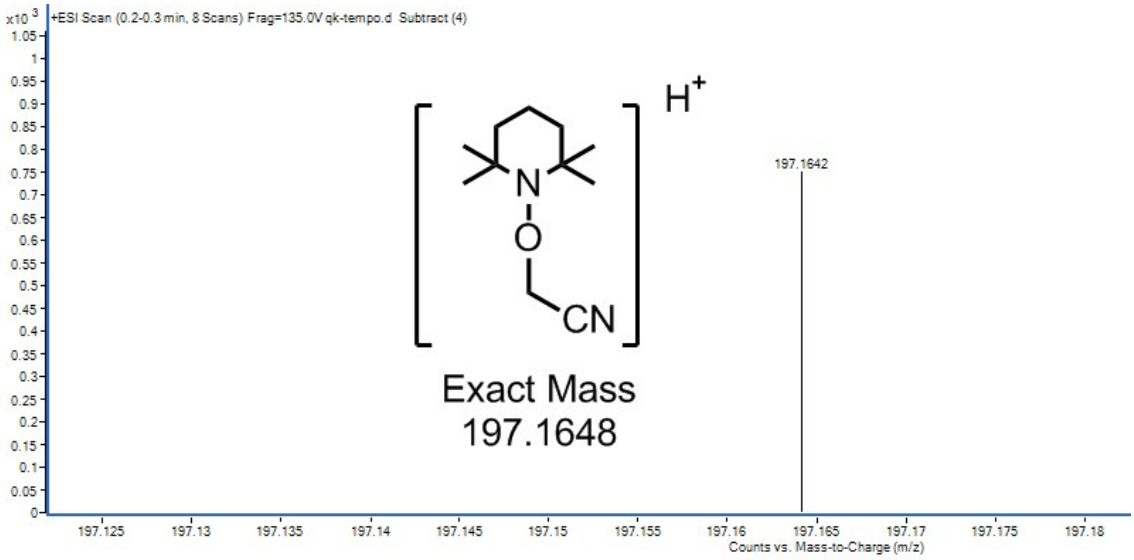


Figure1. HRMS spectrum of compound **12**

3. References

[1] L. Ackermann and A. V. Lygin, *Org. Lett.*, 2011, **13**, 3332-3335.

[2] J. A. Leitch, C. L. McMullin, M. F. Mahon, Y. Bhonoah, and C. G. Frost, *ACS Catal.*, 2017, **7**, 2616−2623.

[3] N. Morimoto, K. Morioku, H. Suzuki, Y. Takeuchi, and Y. Nishina, *Org. Lett.*, 2016, **18**, 2020−2023.

[4] J. Cornella, P. Lu, and I. Larrosa, *Org. Lett.*, 2009, **11**, 5506–5509.

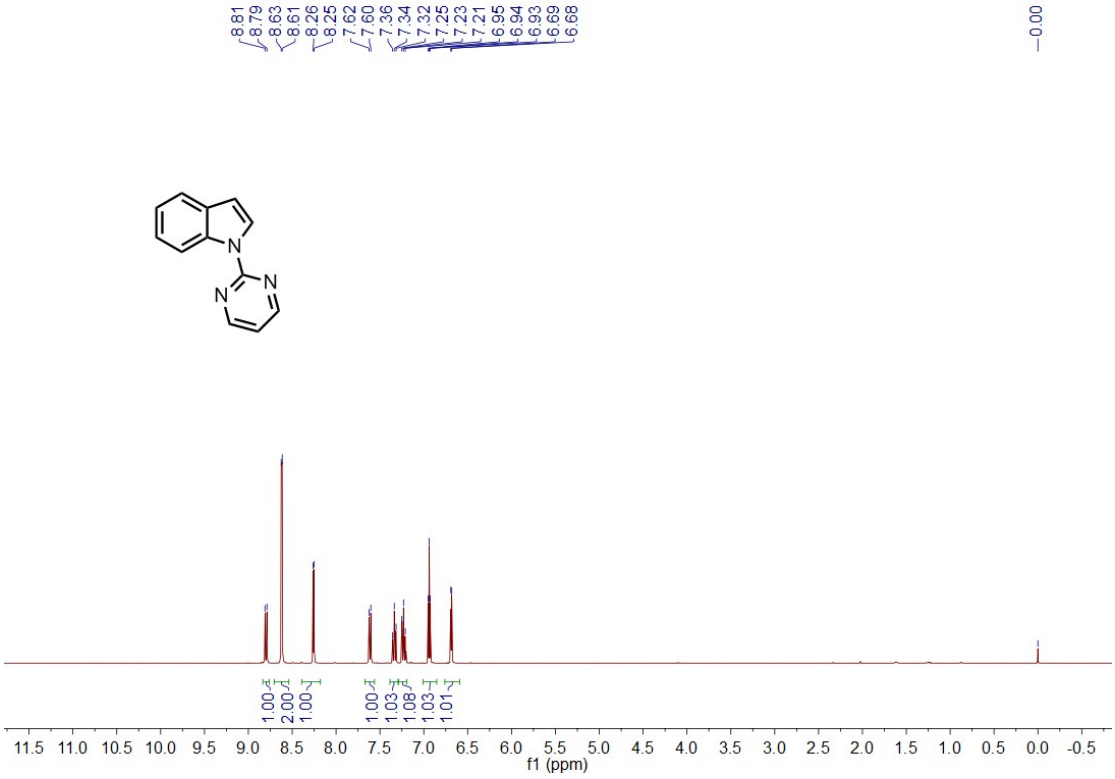
[5] T. Jeong, S. Han, N. K. Mishra, S. Sharma, S.-Y. Lee, J. S. Oh, J. H. Kwak, Y. H. Jung and I. S. Kim, *J. Org. Chem.*, 2015, **80**, 7243-7250.

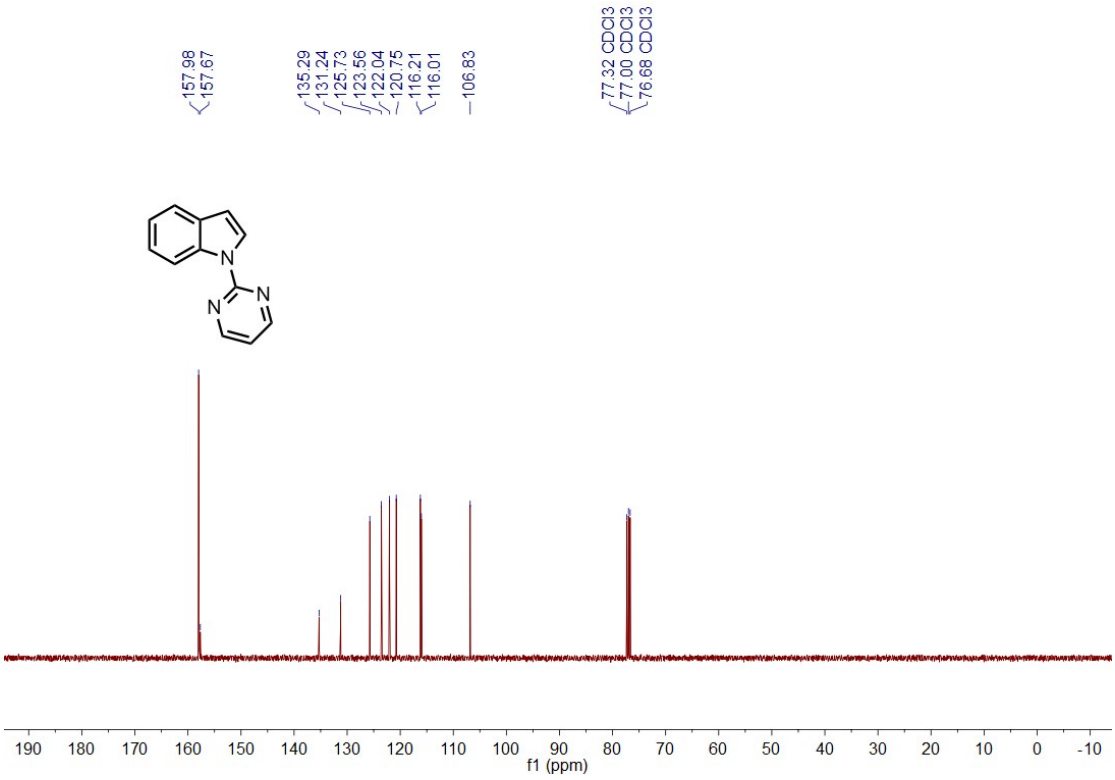
[6] T. Yoshino, H. Ikemoto, S. Matsunaga and M. Kanai, *Chem. Eur. J.*, 2013, **19**, 9142-9146.

[7] H. Zhang and C. Zhu, *Org. Chem. Front.*, 2017, **4**, 1272-1275.

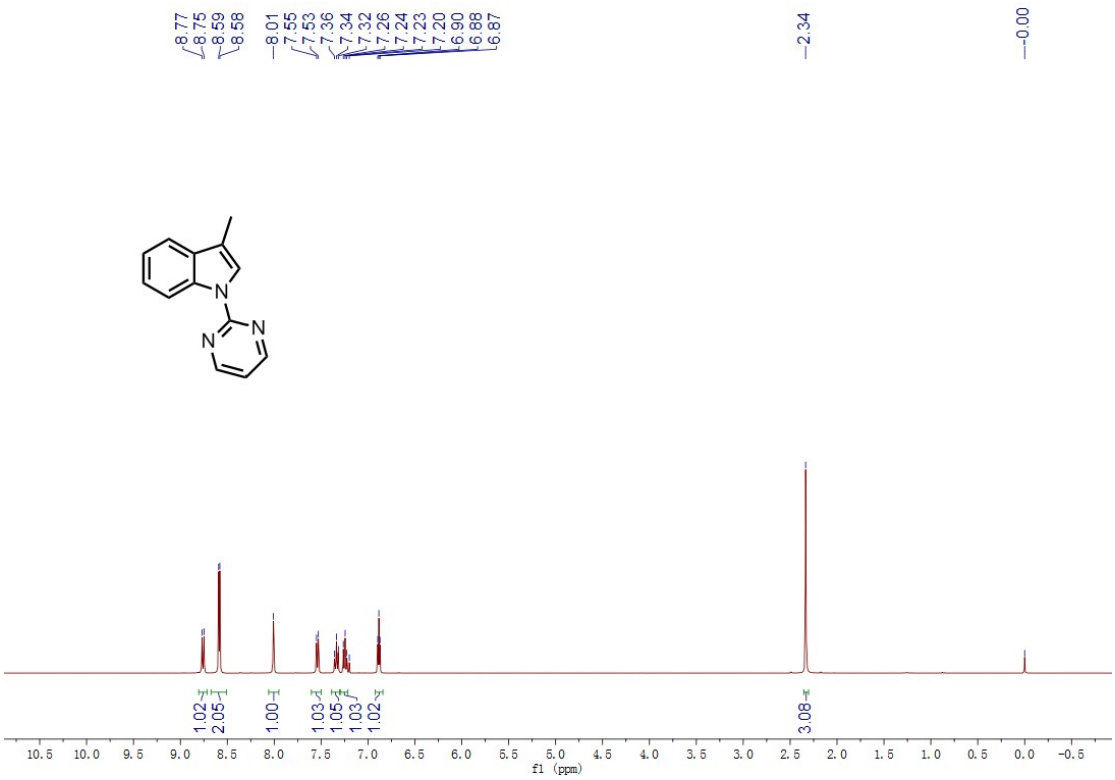
4. ^{1}H and ^{13}C NMR spectra

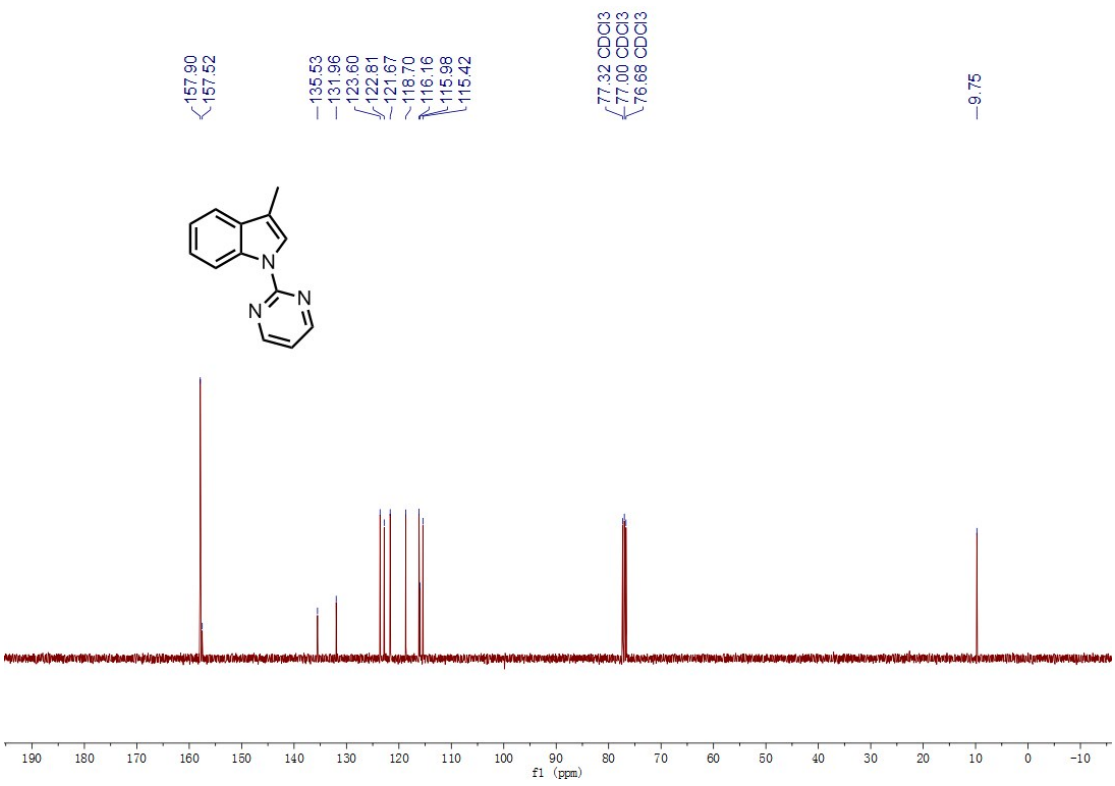
1-(pyrimidin-2-yl)-1H-indole (1a)



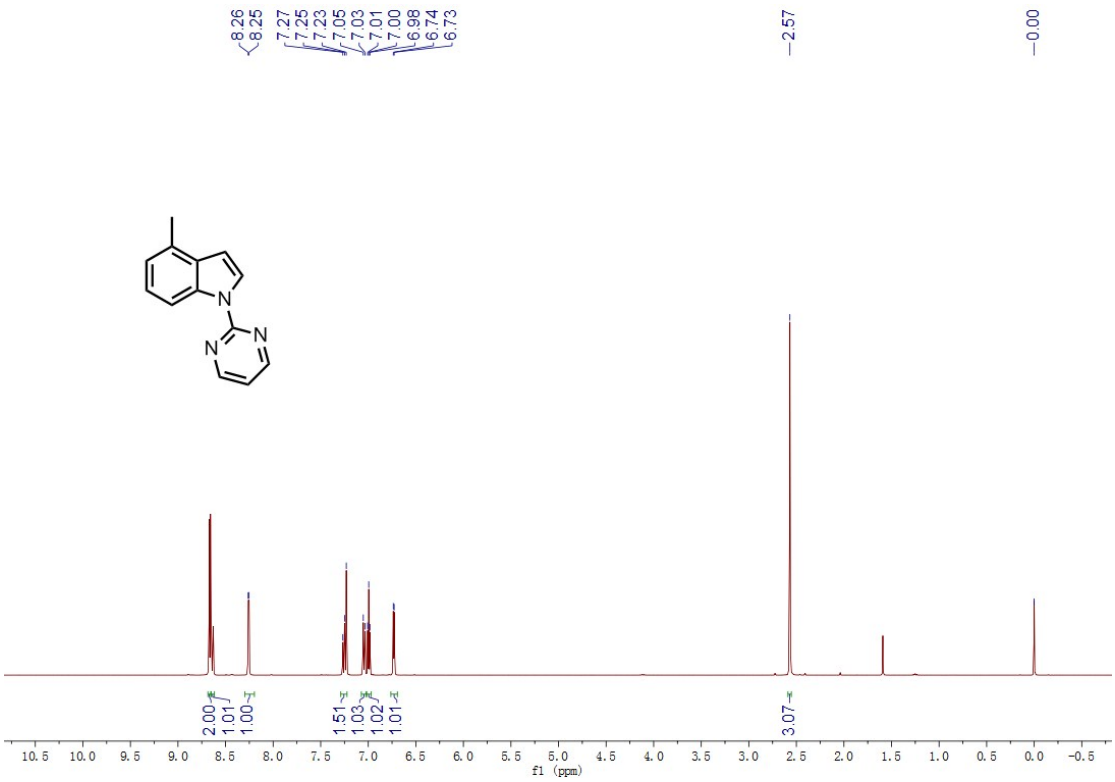


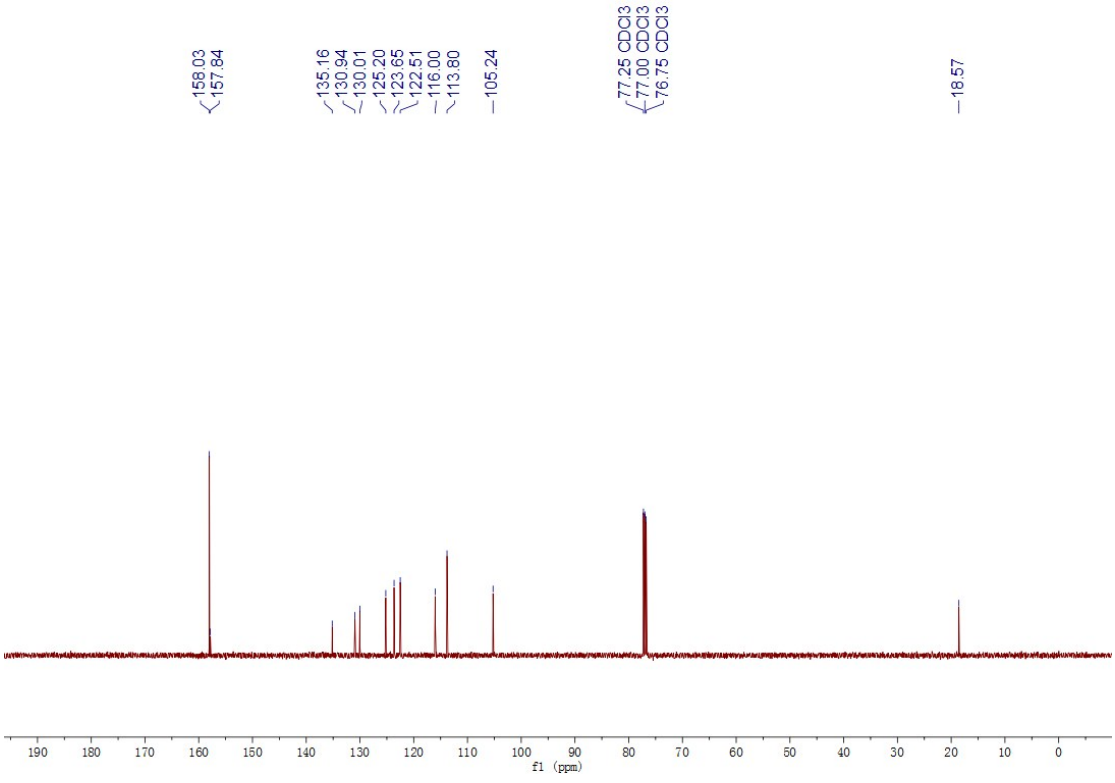
3-methyl-1-(pyrimidin-2-yl)-1H-indole (1b)



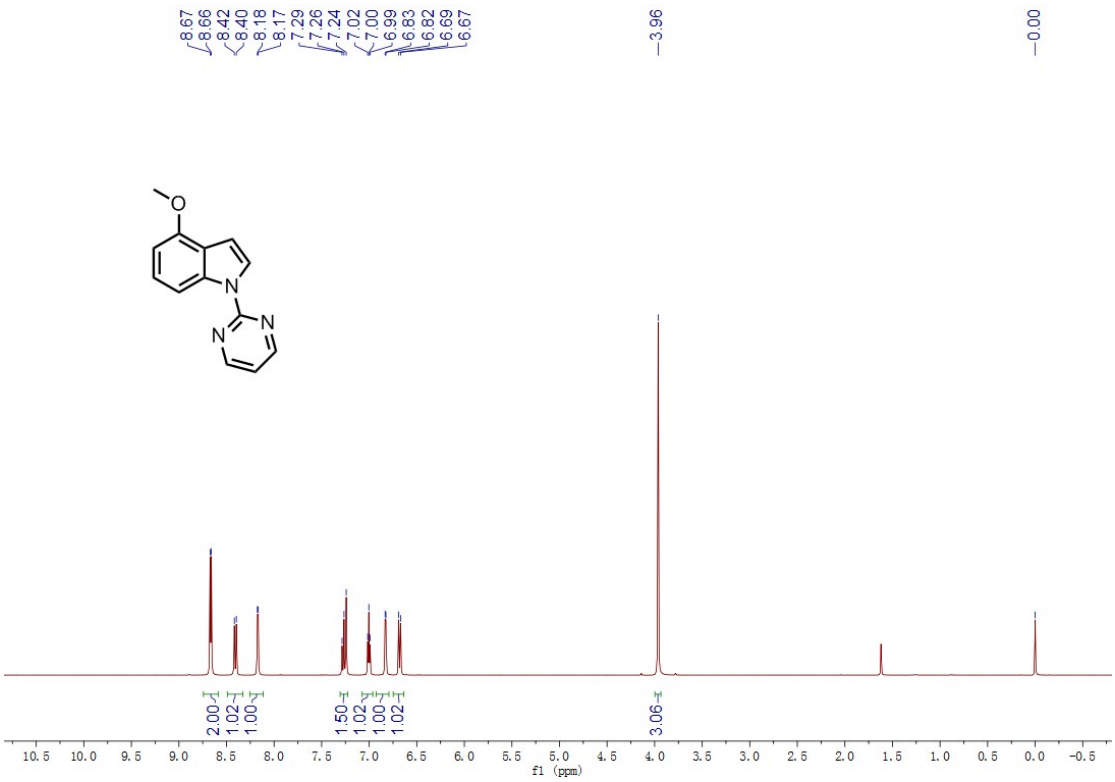


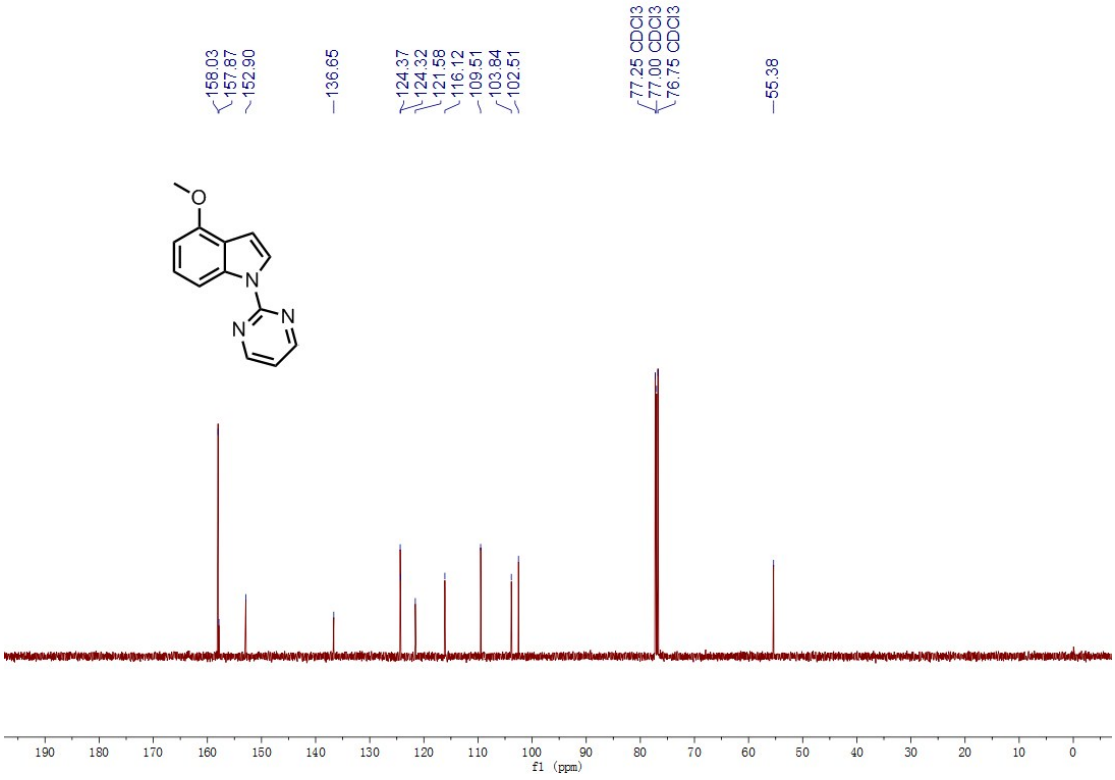
4-methyl-1-(pyrimidin-2-yl)-1H-indole (1c)



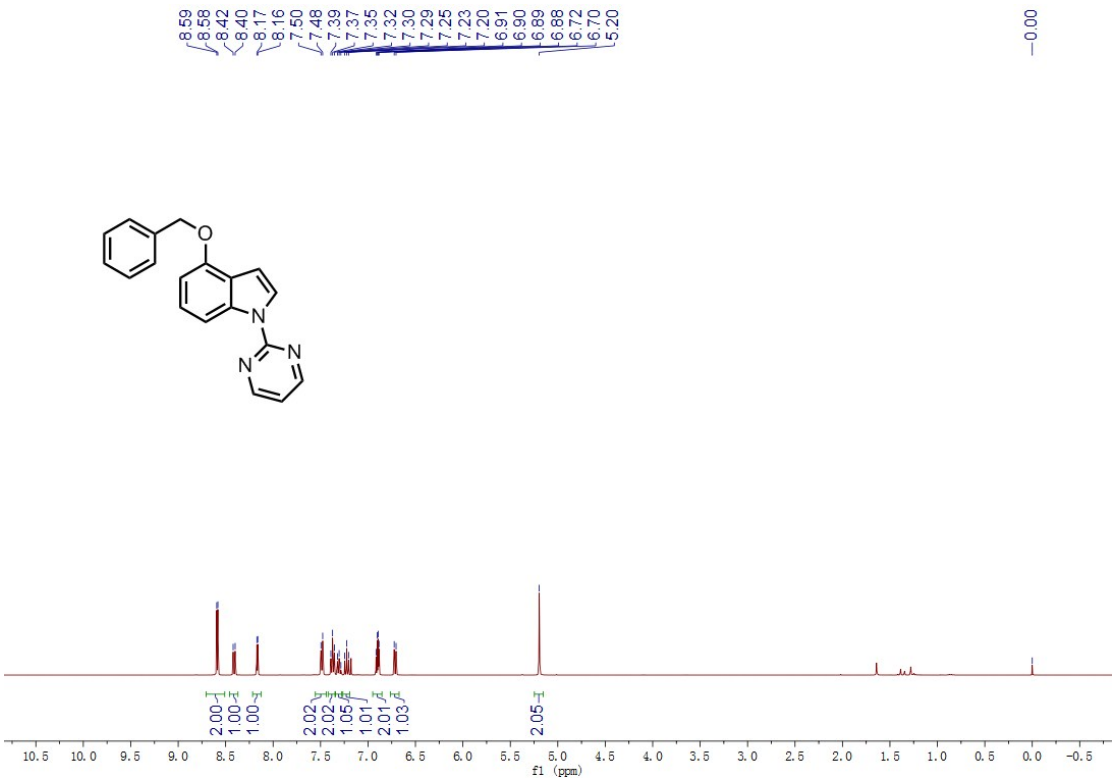


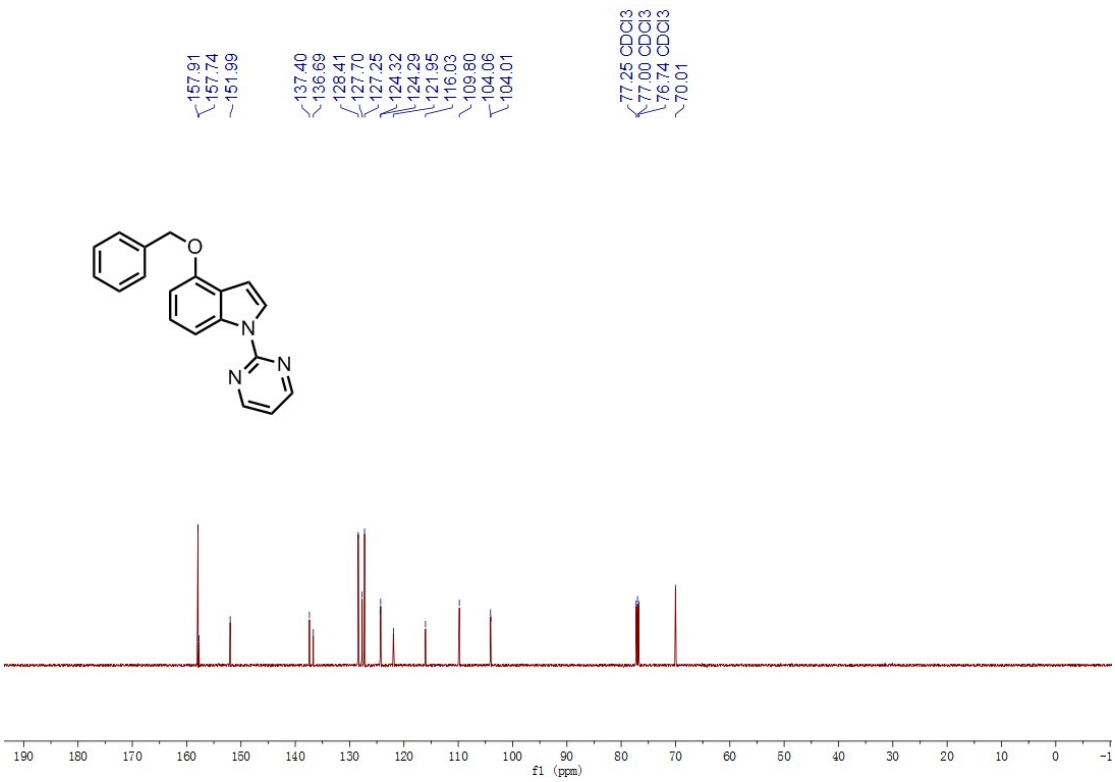
4-methoxy-1-(pyrimidin-2-yl)-1H-indole (1d)



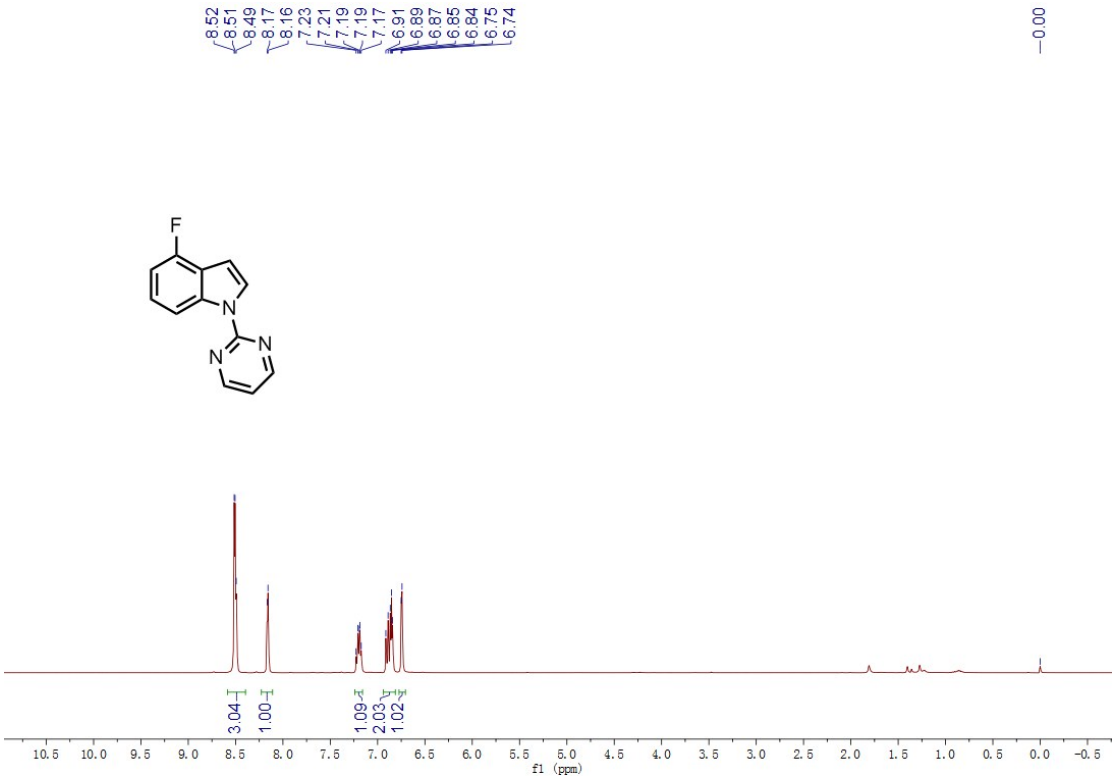


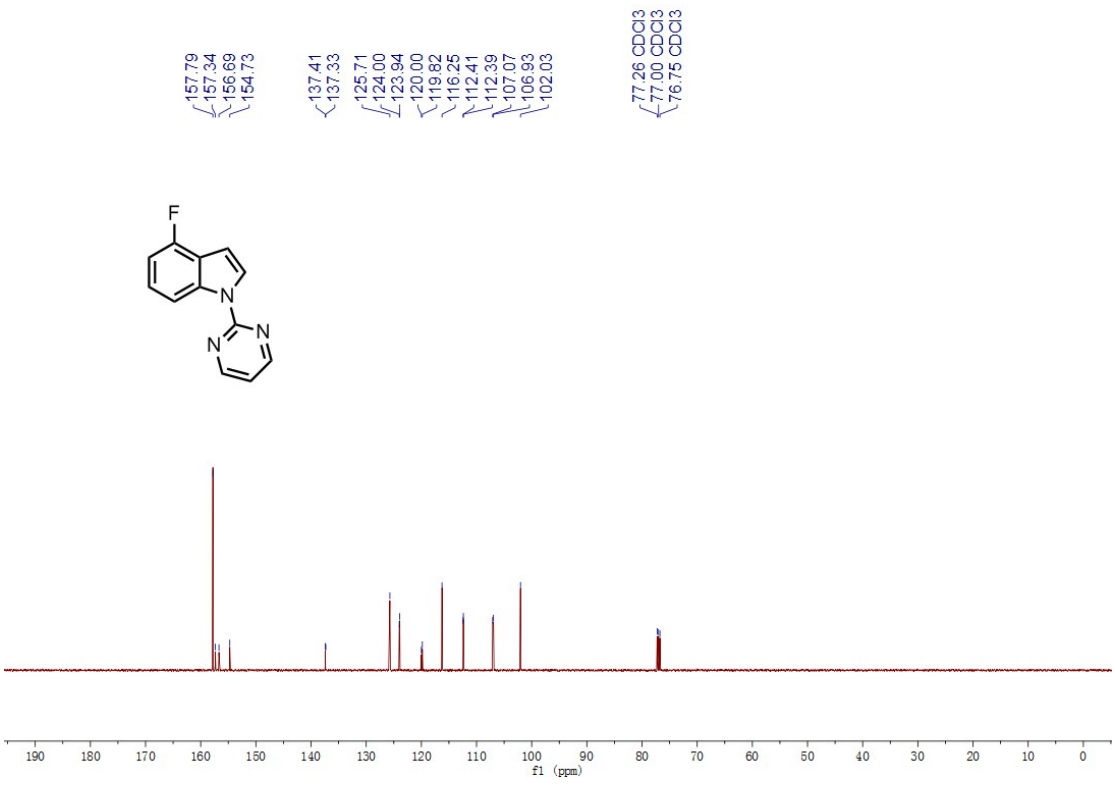
4-(benzyloxy)-1-(pyrimidin-2-yl)-1H-indole (1e)



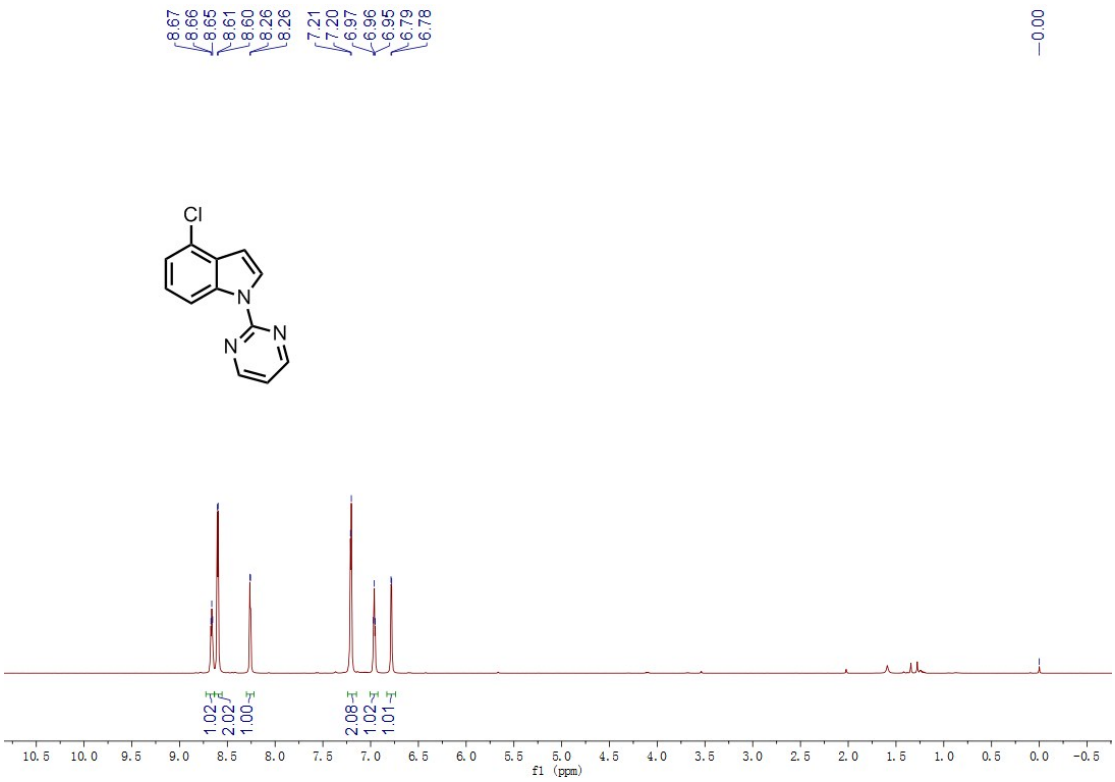


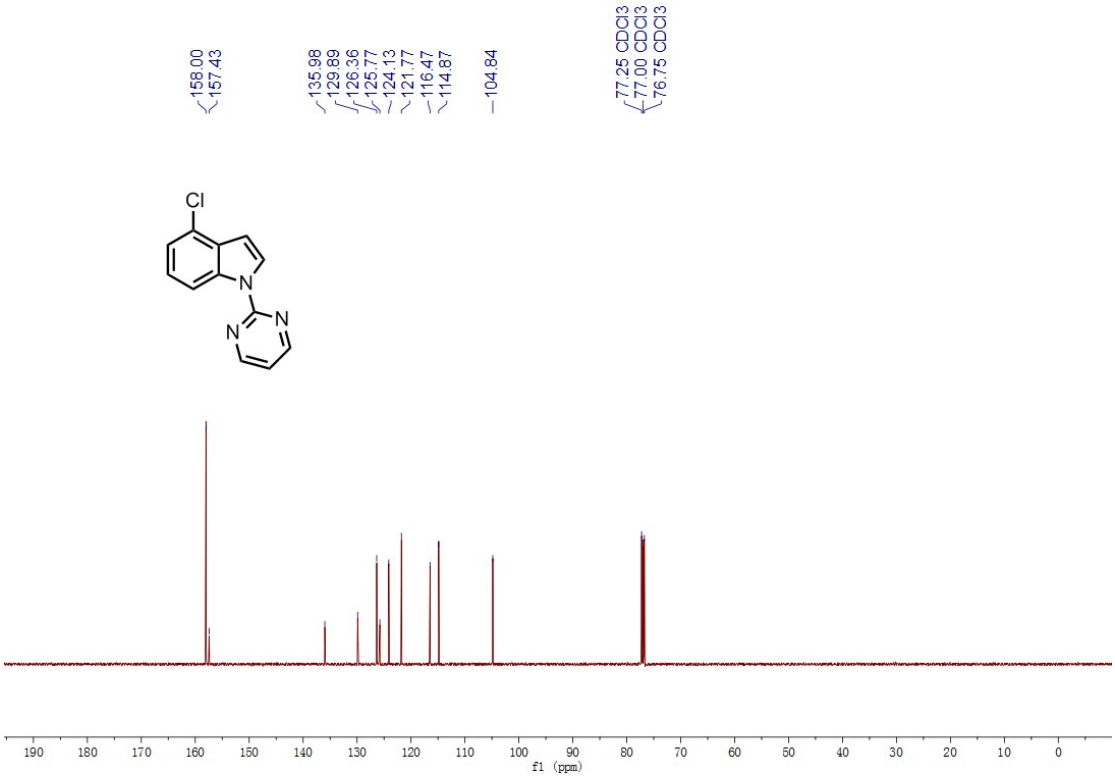
4-fluoro-1-(pyrimidin-2-yl)-1H-indole (1f)



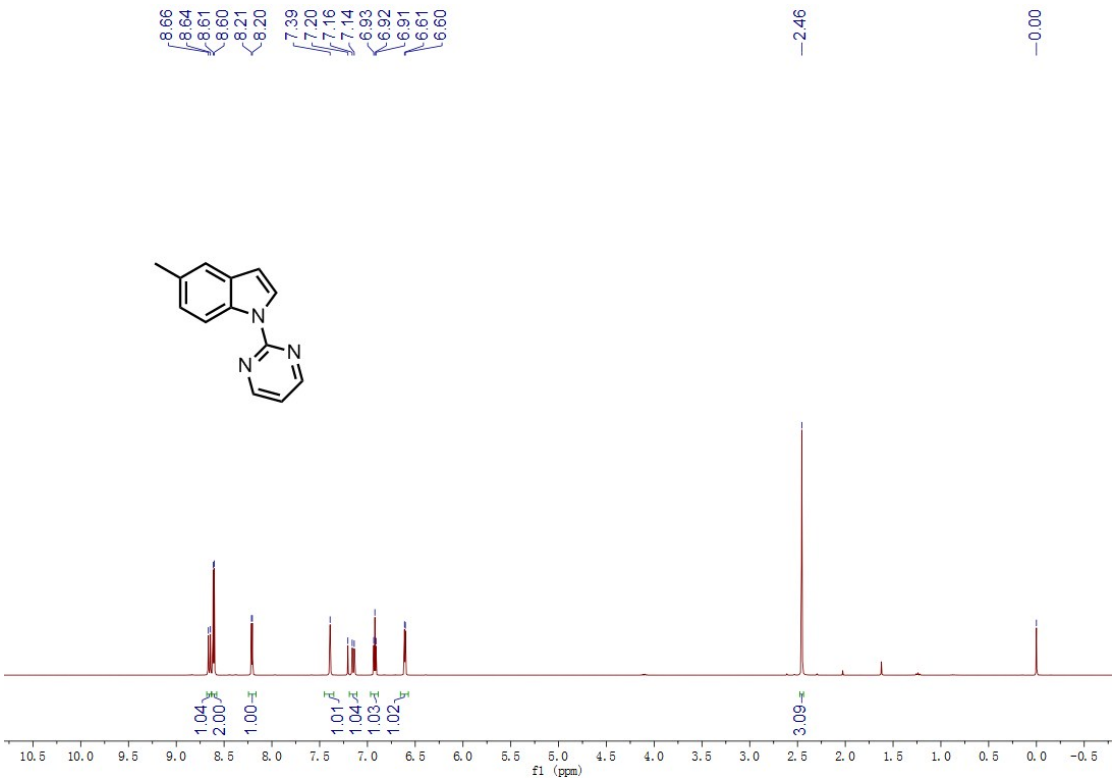


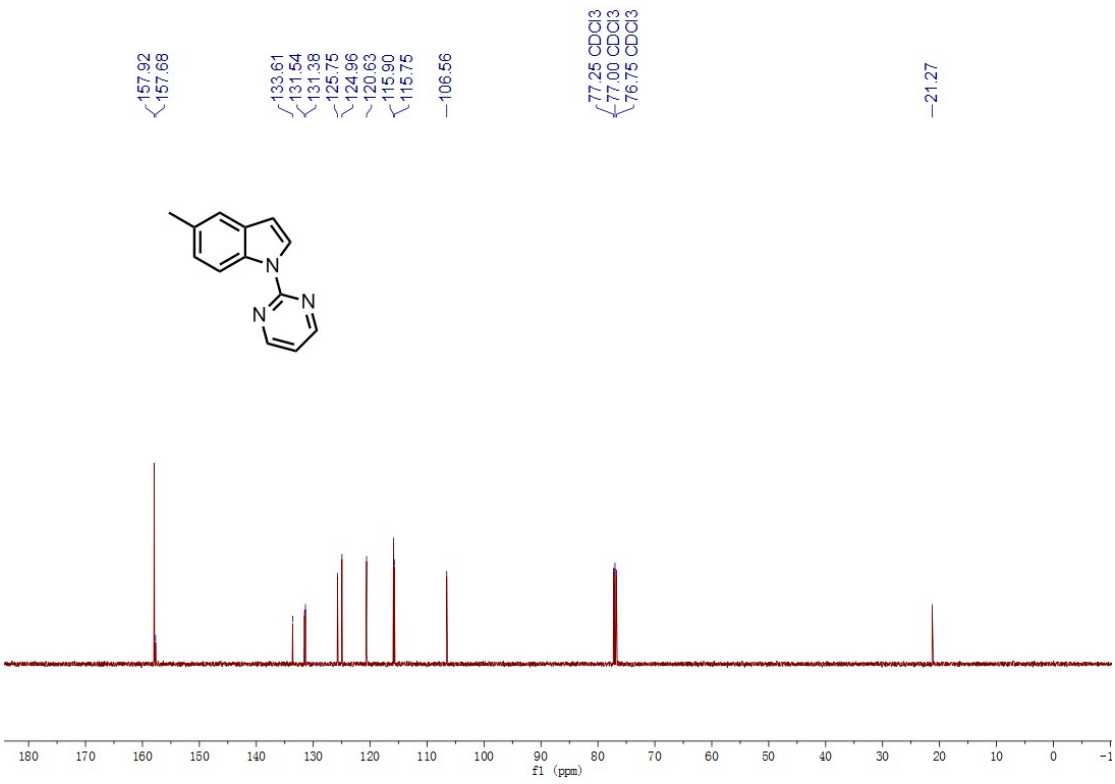
4-chloro-1-(pyrimidin-2-yl)-1H-indole (1g)



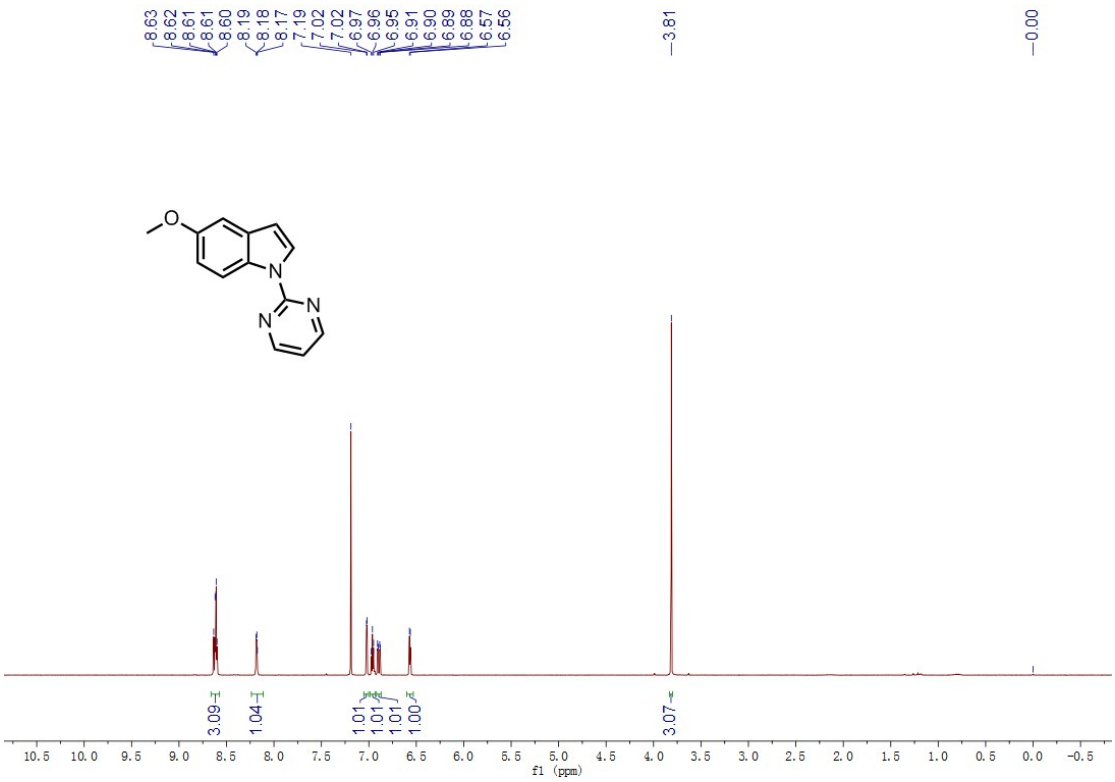


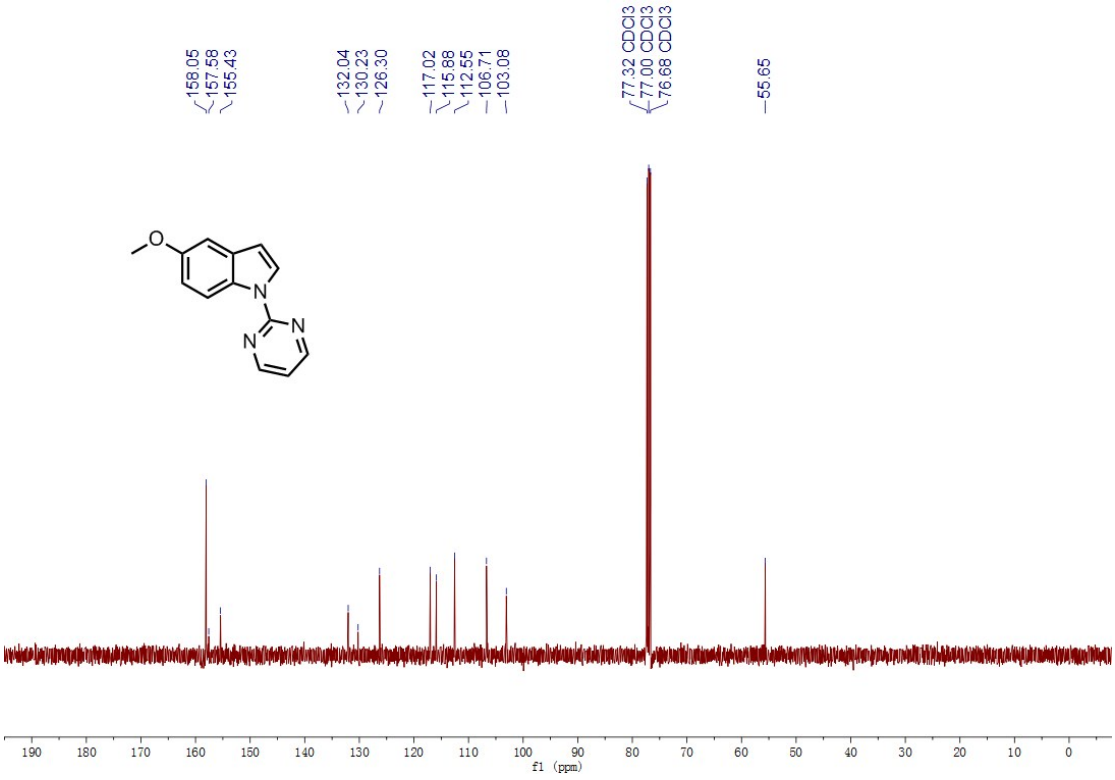
5-methyl-1-(pyrimidin-2-yl)-1H-indole (1h)



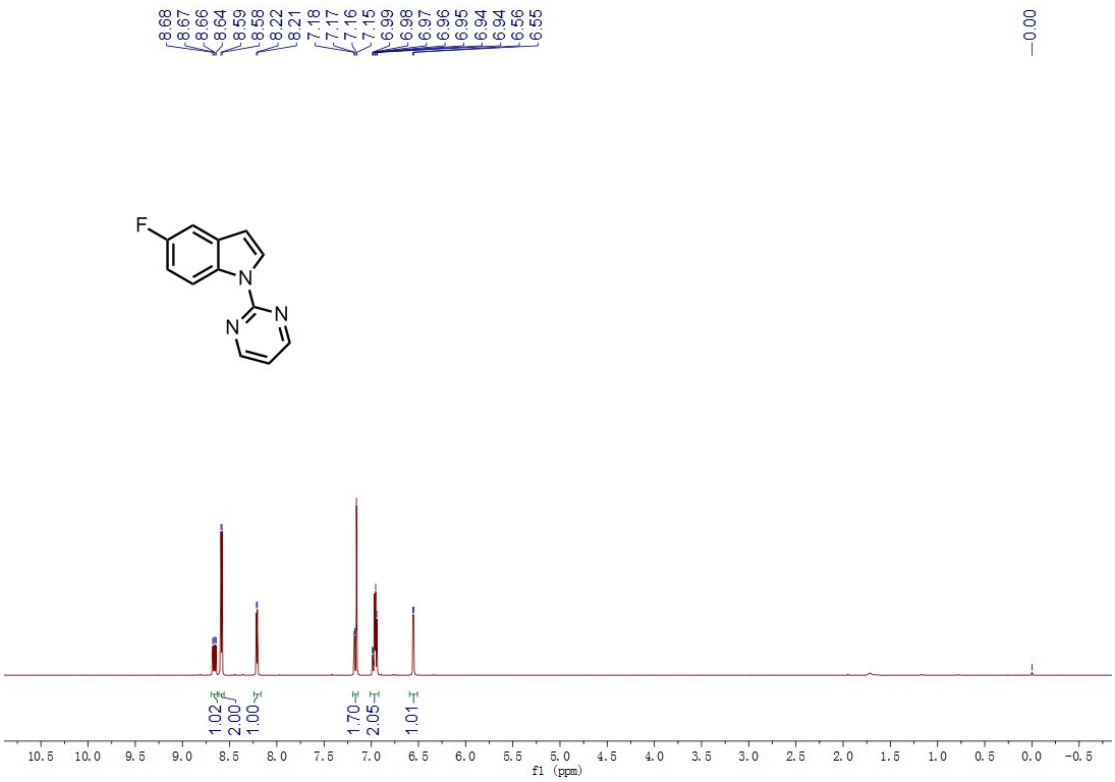


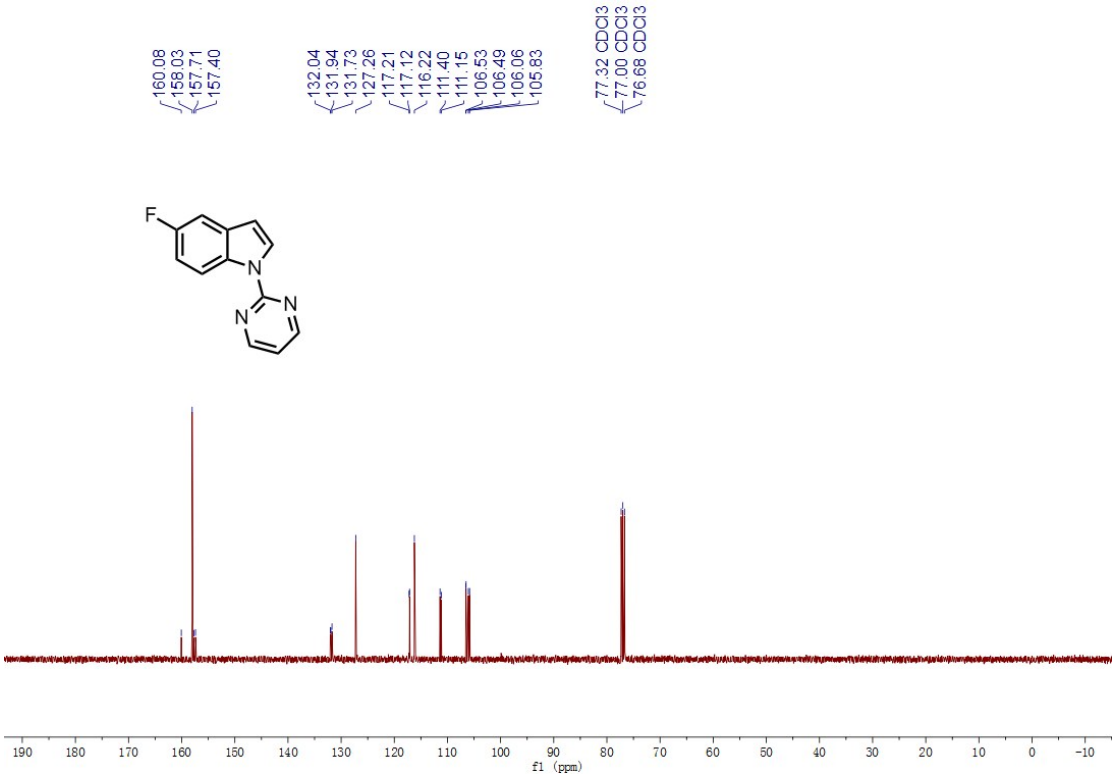
5-methoxy-1-(pyrimidin-2-yl)-1H-indole (1i)



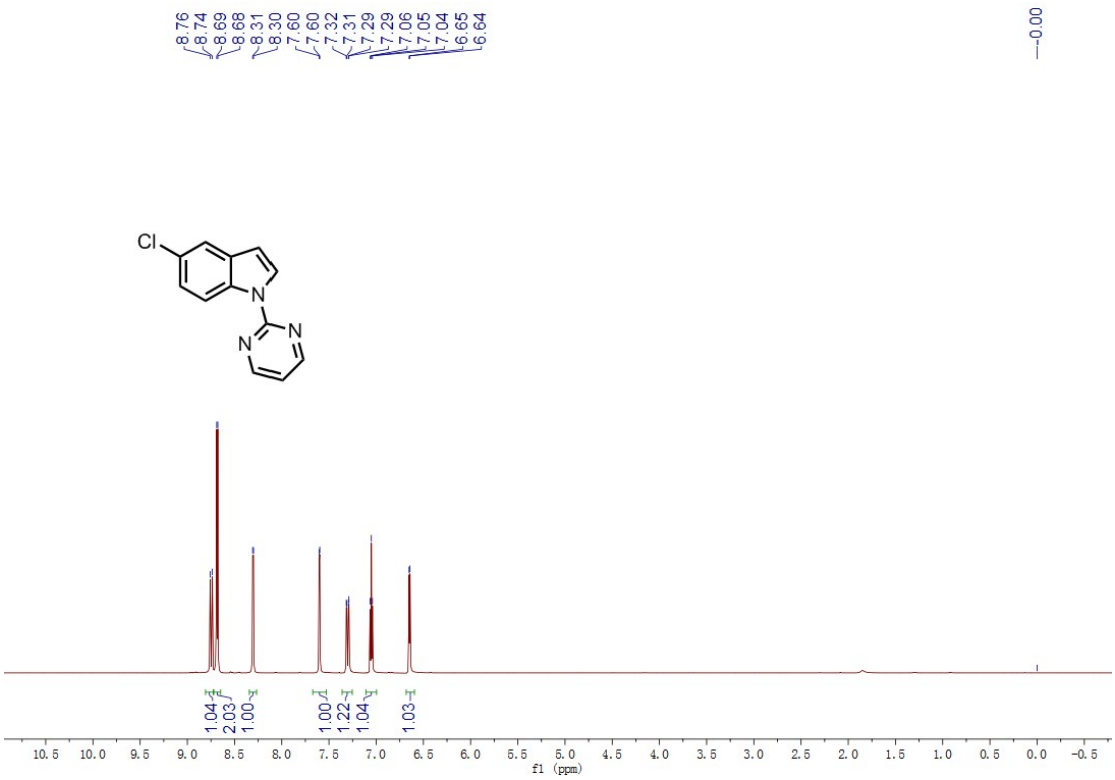


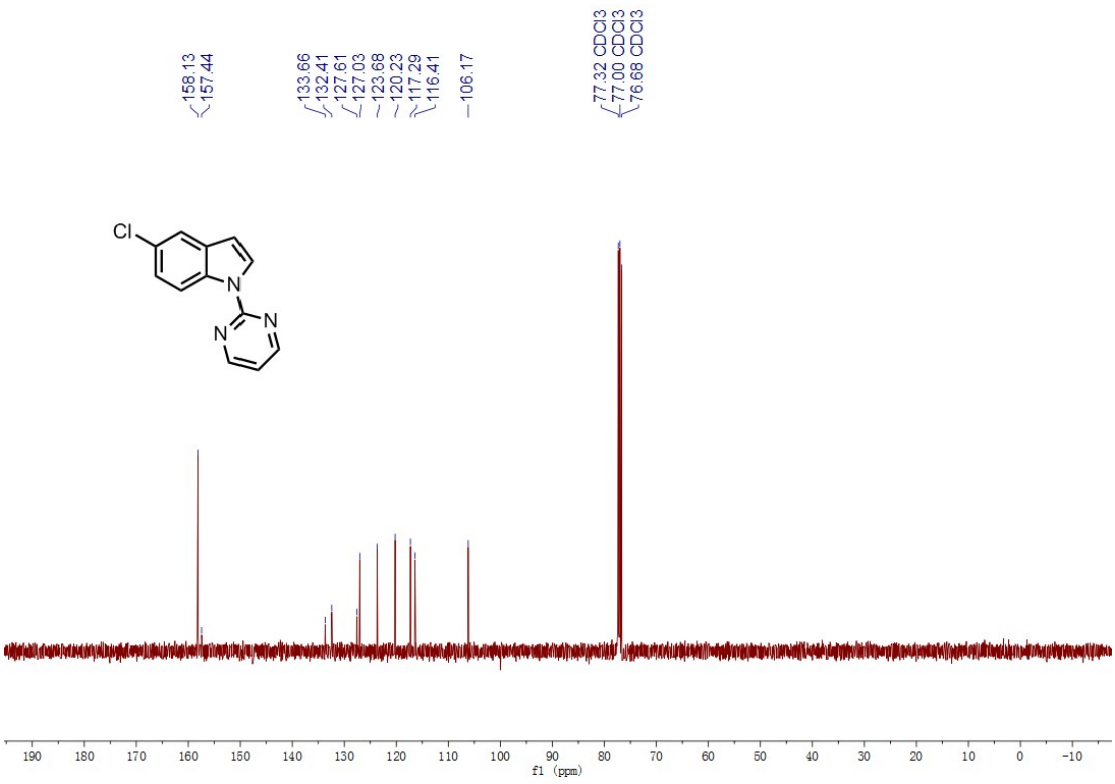
5-fluoro-1-(pyrimidin-2-yl)-1H-indole (1j)



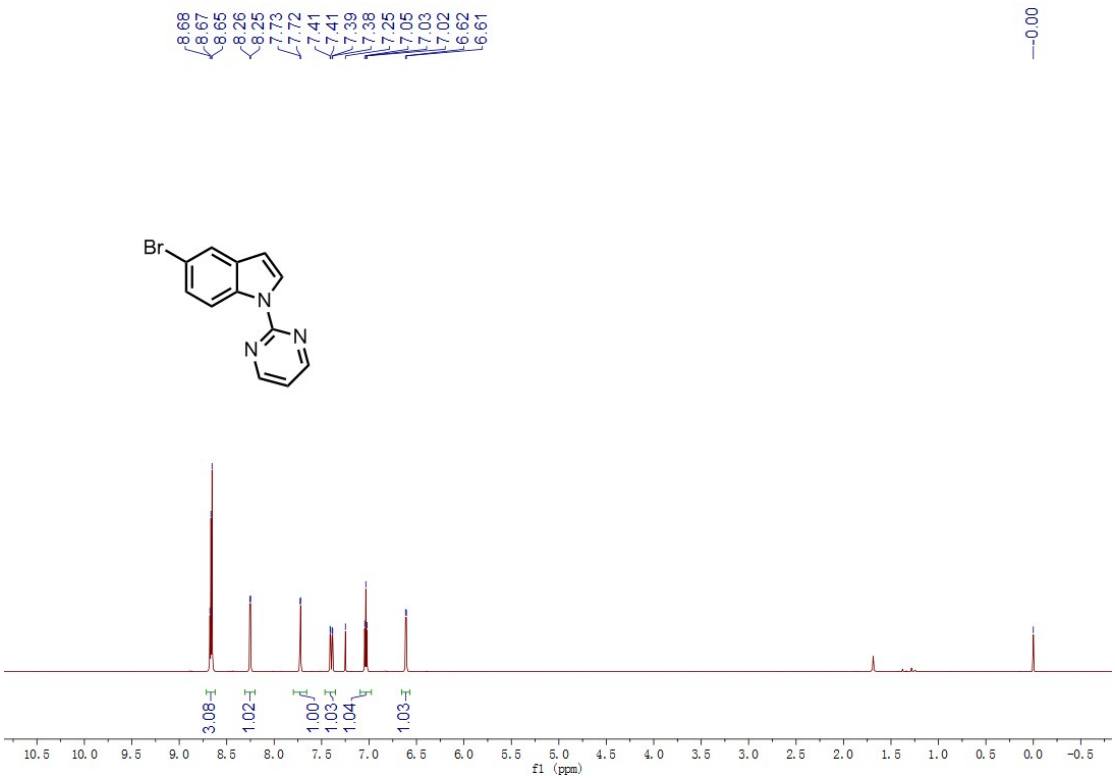


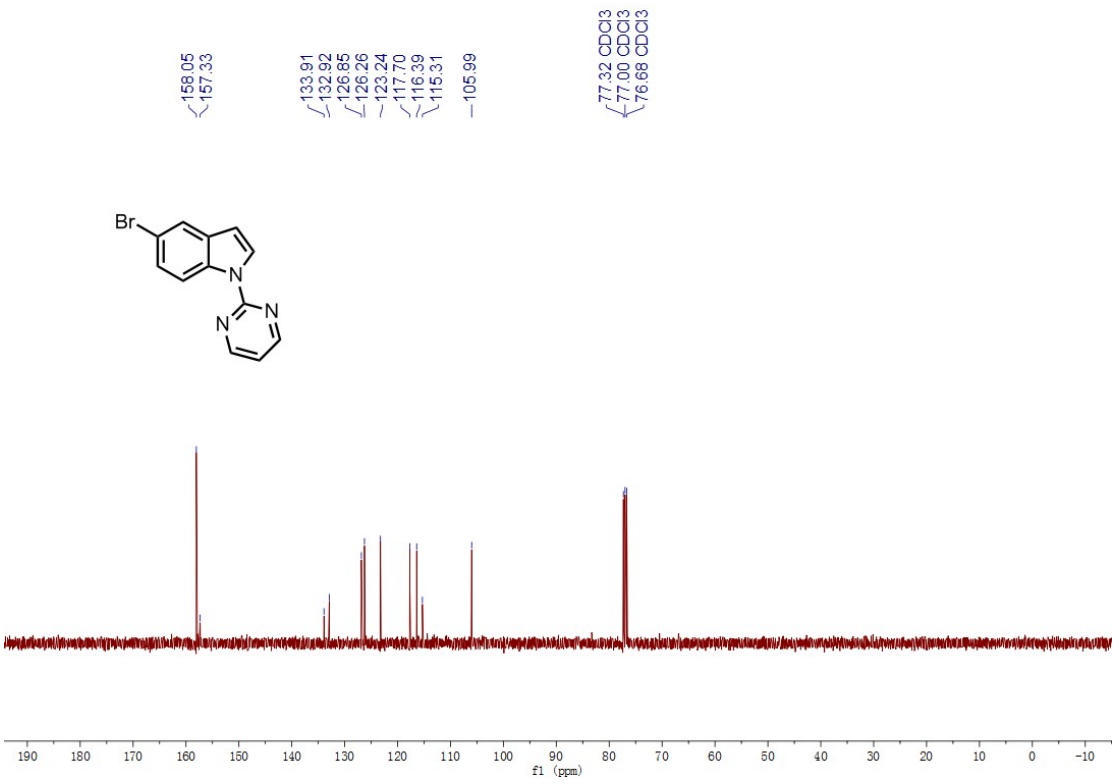
5-chloro-1-(pyrimidin-2-yl)-1H-indole (1k)



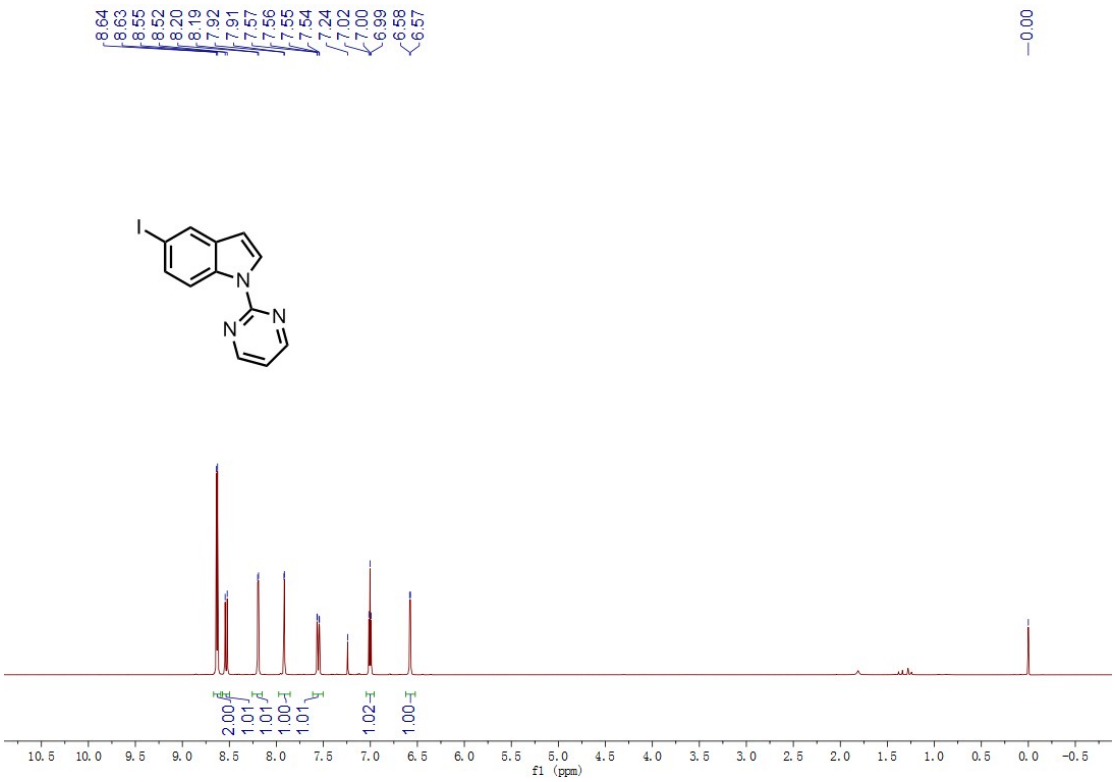


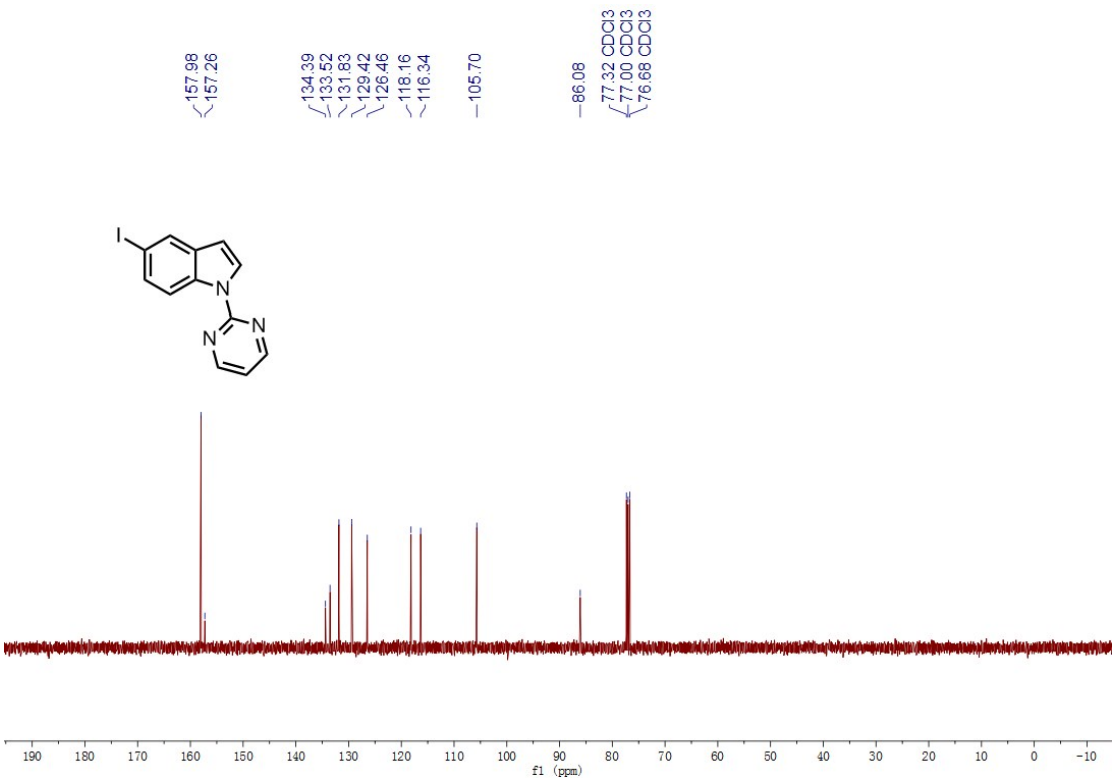
5-bromo-1-(pyrimidin-2-yl)-1H-indole (1l)



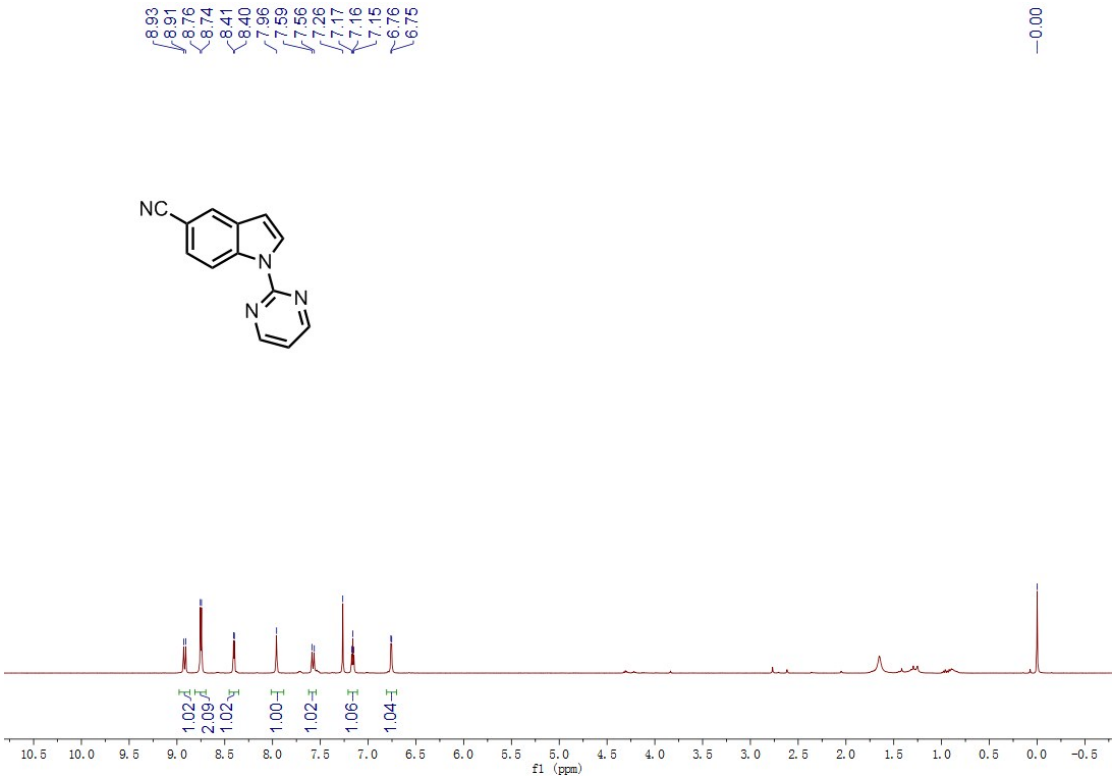


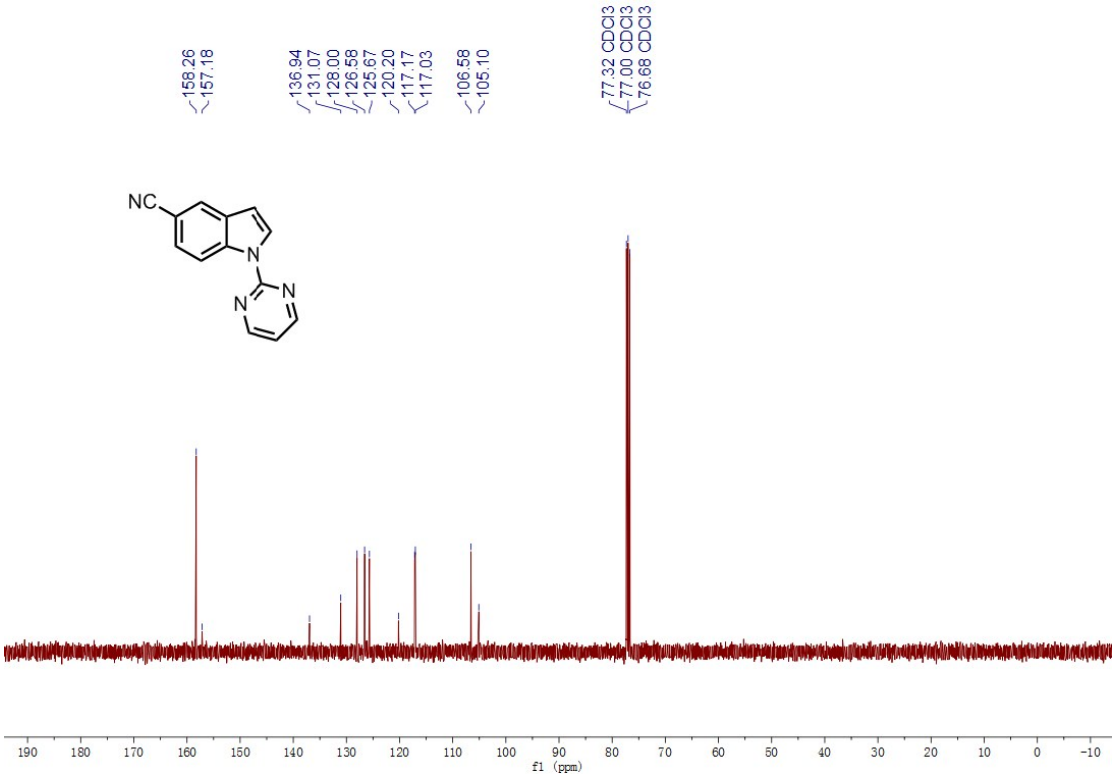
5-iodo-1-(pyrimidin-2-yl)-1H-indole (1m)



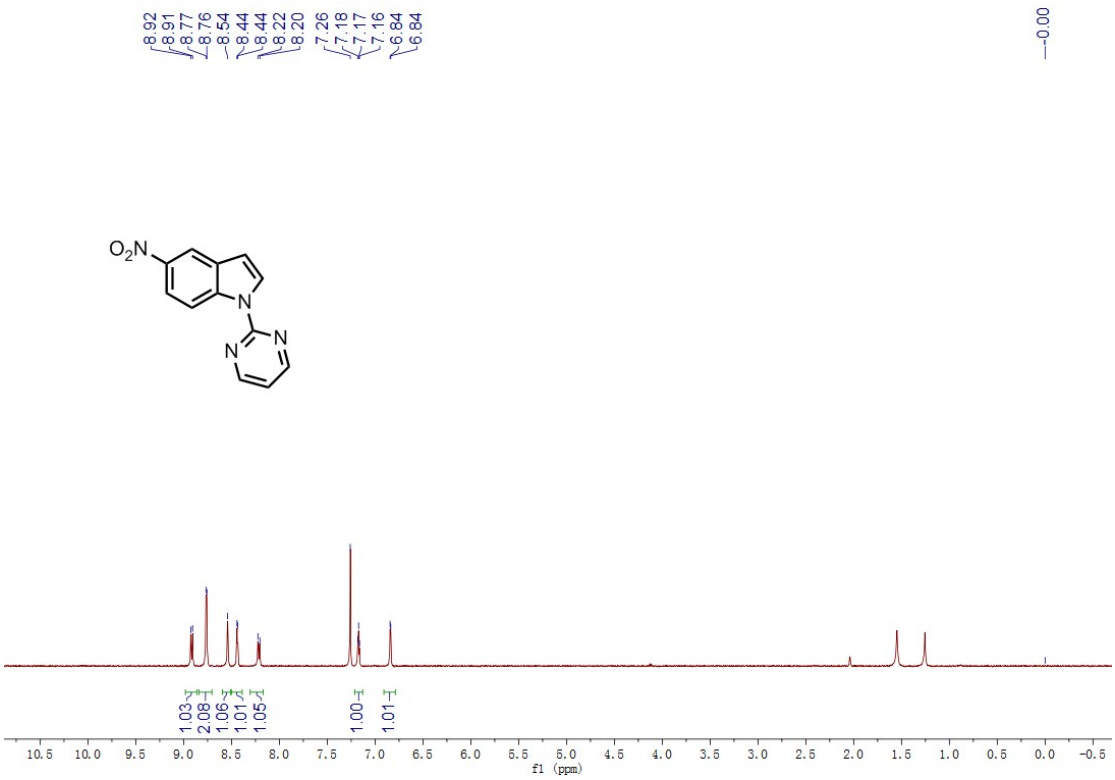


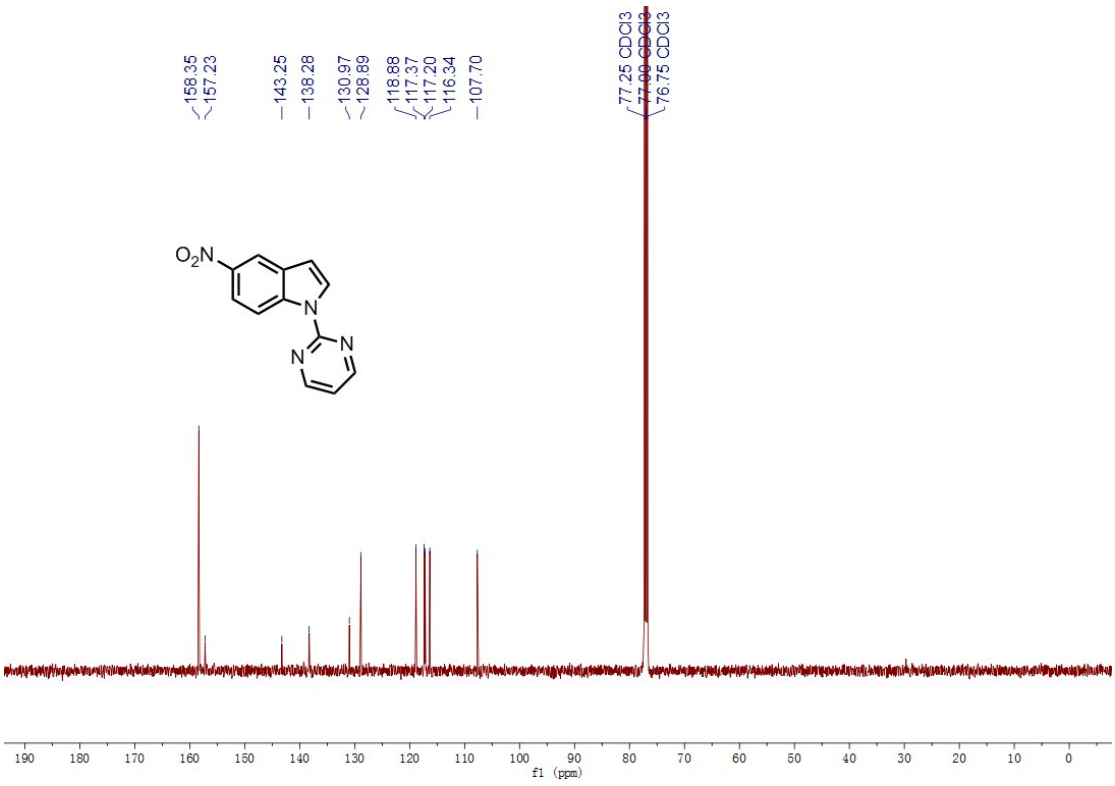
1-(pyrimidin-2-yl)-1H-indole-5-carbonitrile (1n)



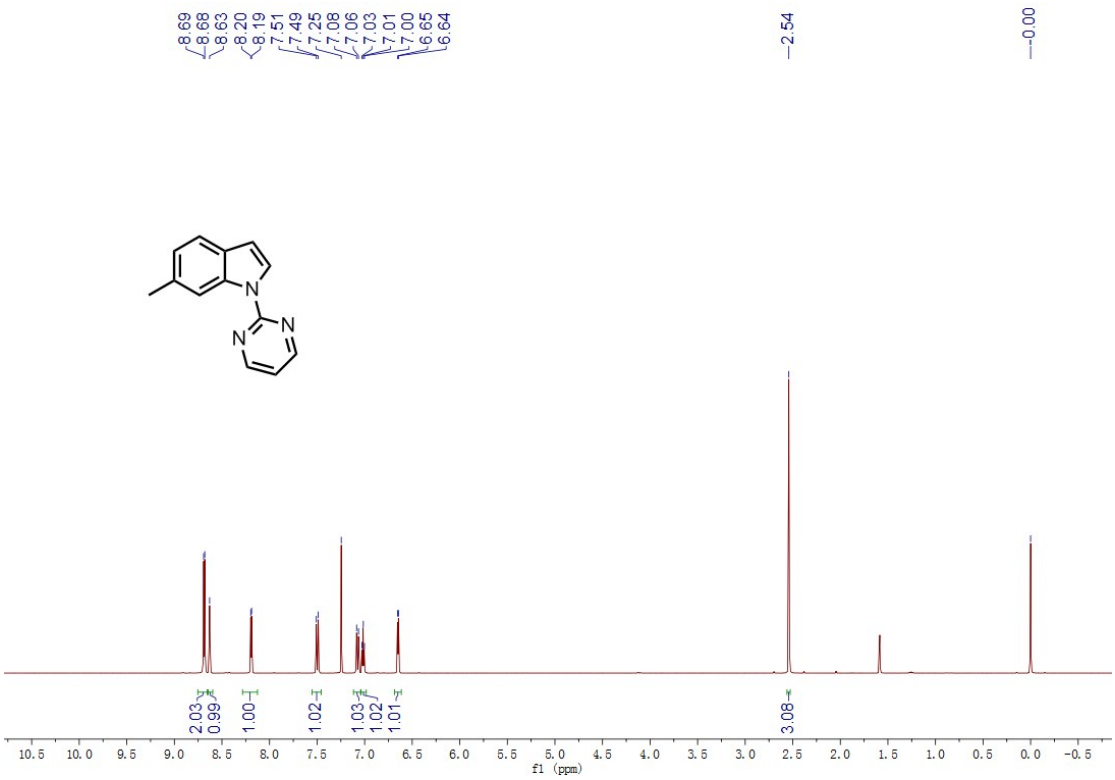


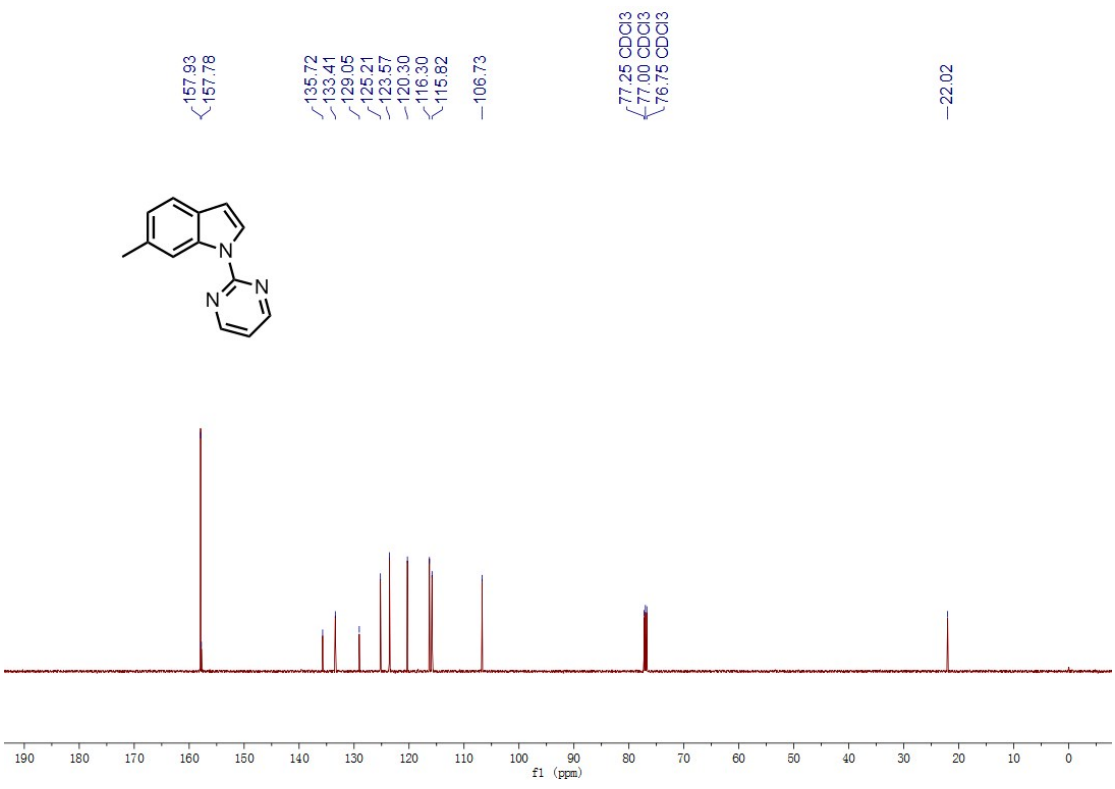
5-nitro-1-(pyrimidin-2-yl)-1H-indole (1o)



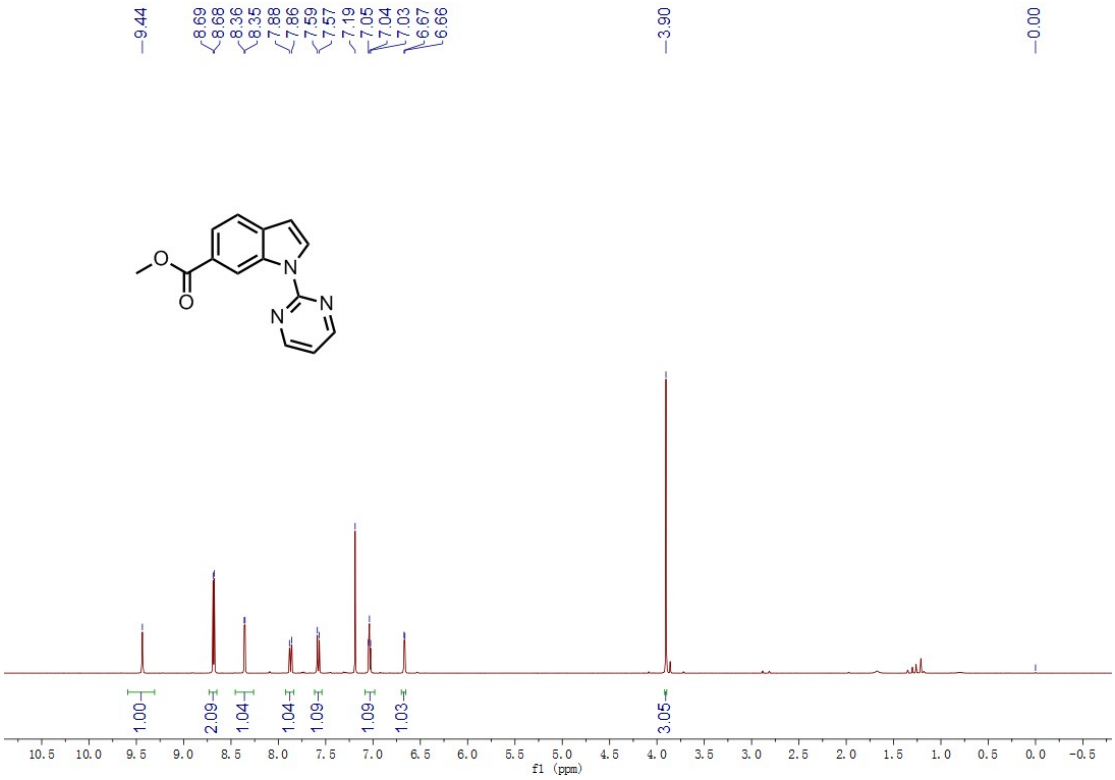


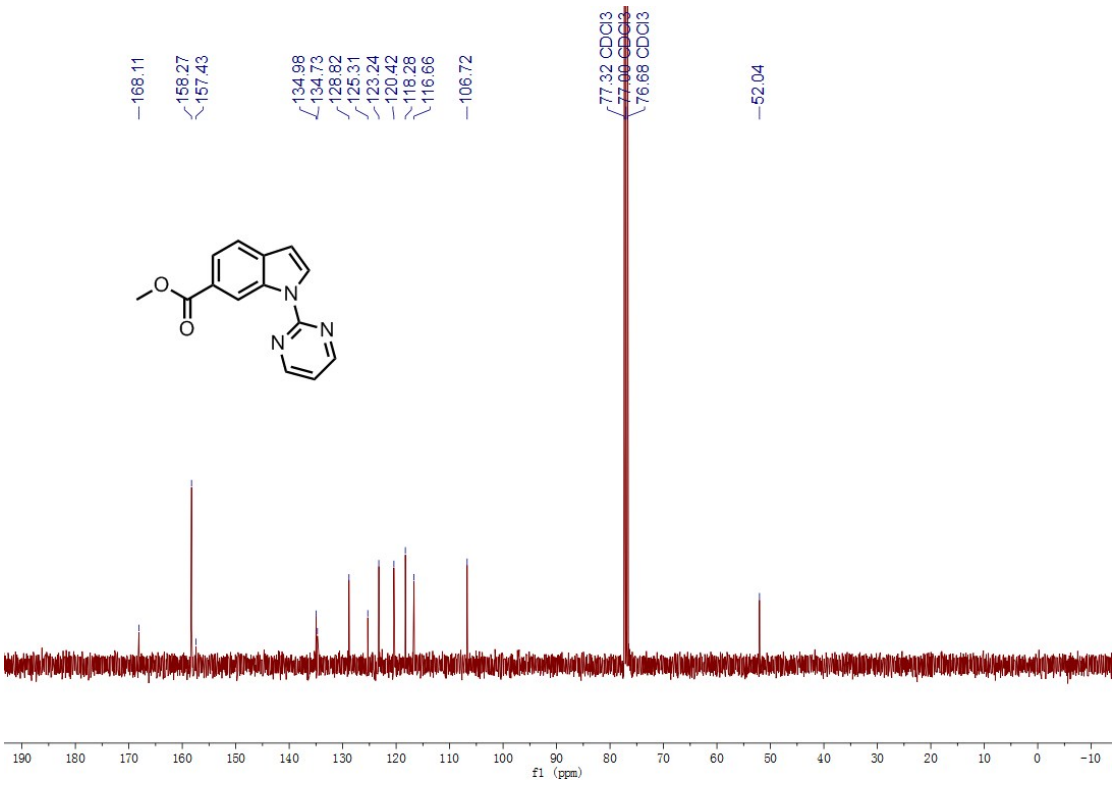
6-methyl-1-(pyrimidin-2-yl)-1H-indole (1p)



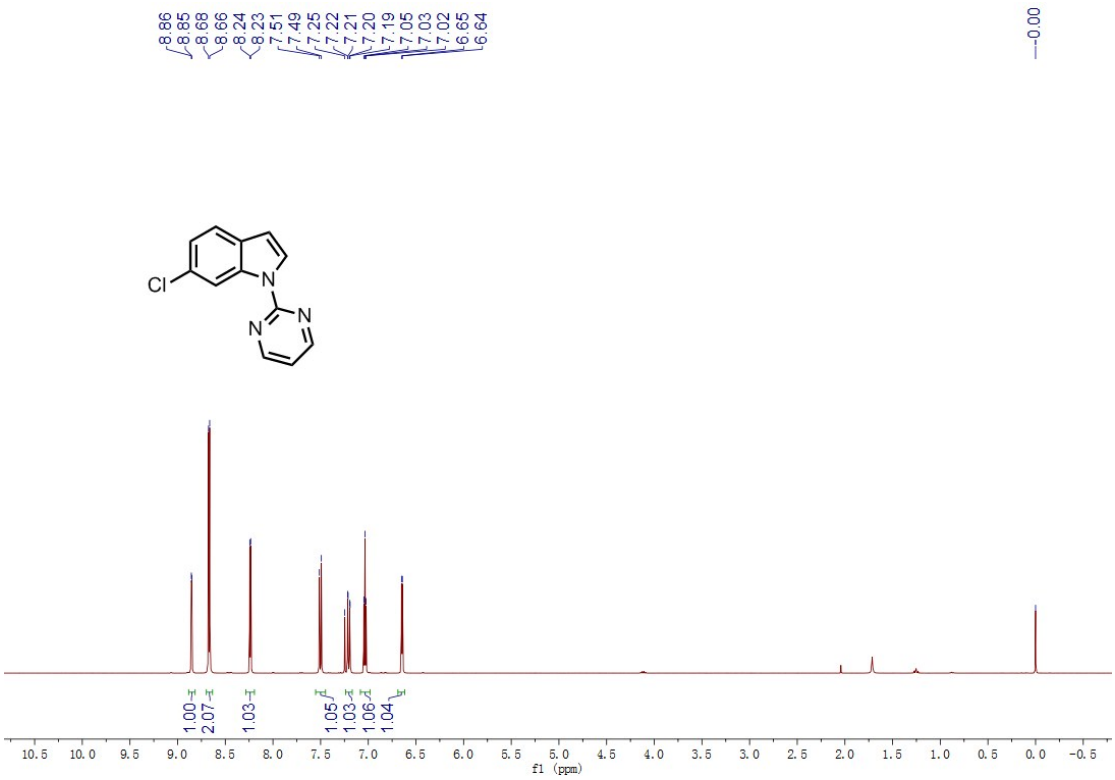


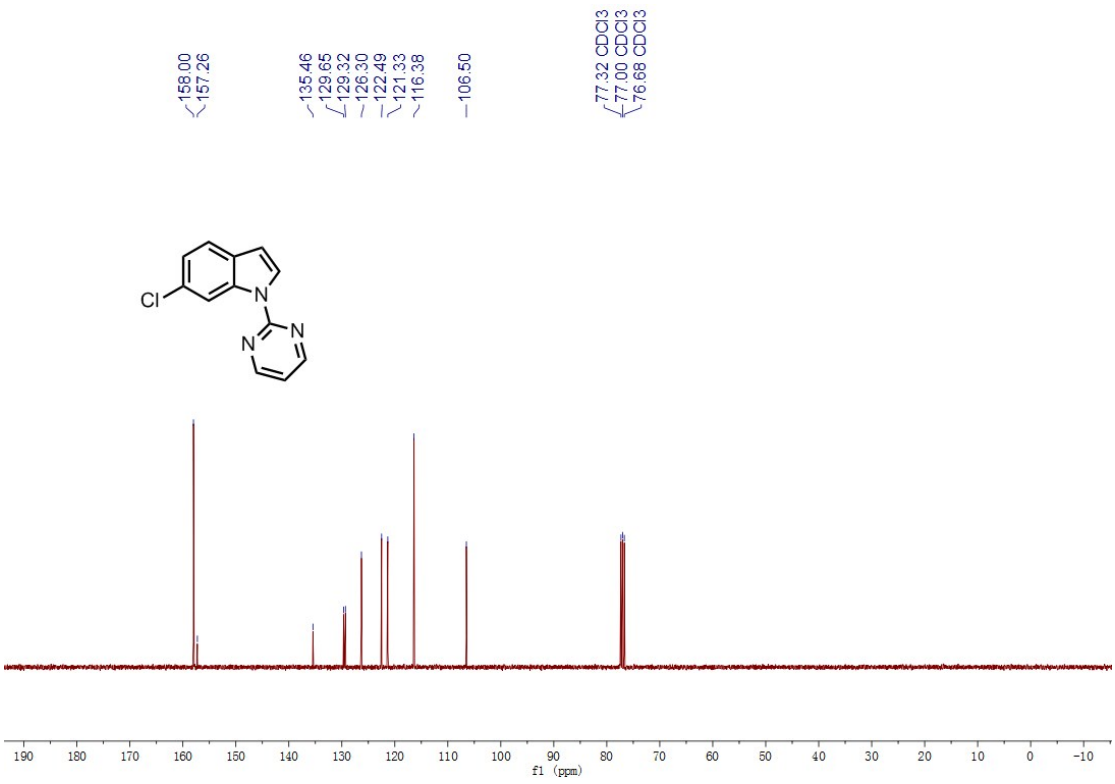
methyl 1-(pyrimidin-2-yl)-1H-indole-6-carboxylate (1q)



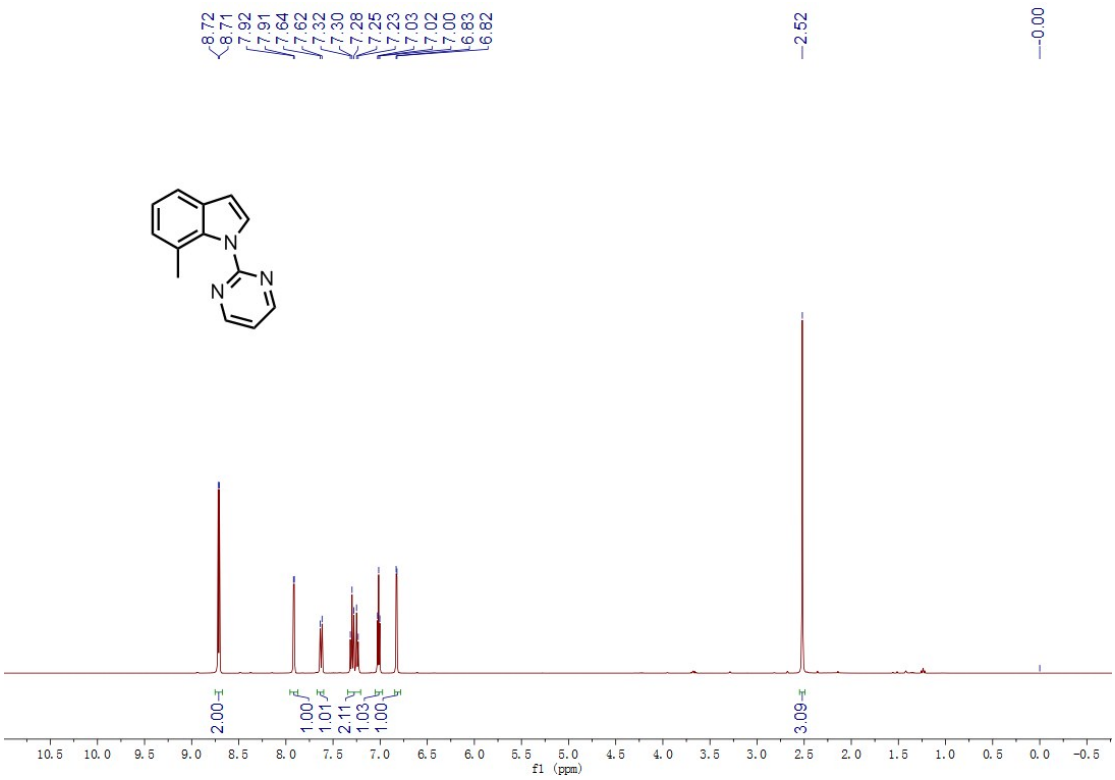


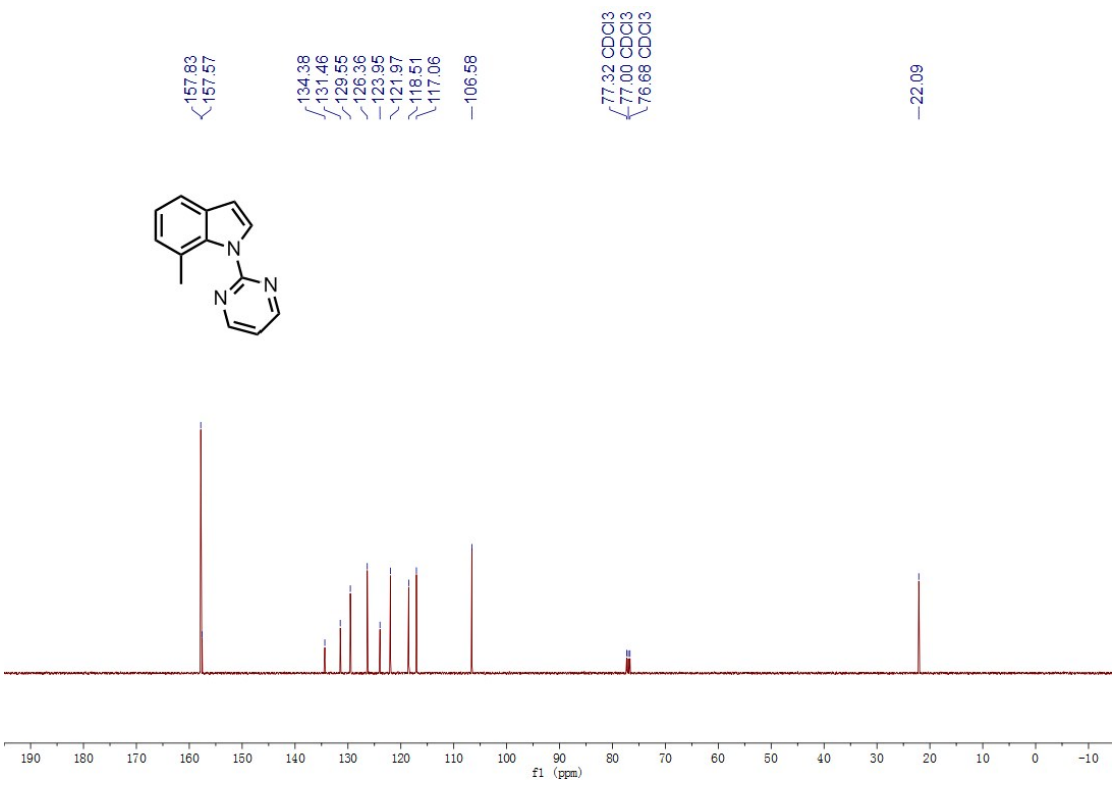
6-chloro-1-(pyrimidin-2-yl)-1H-indole (1r)



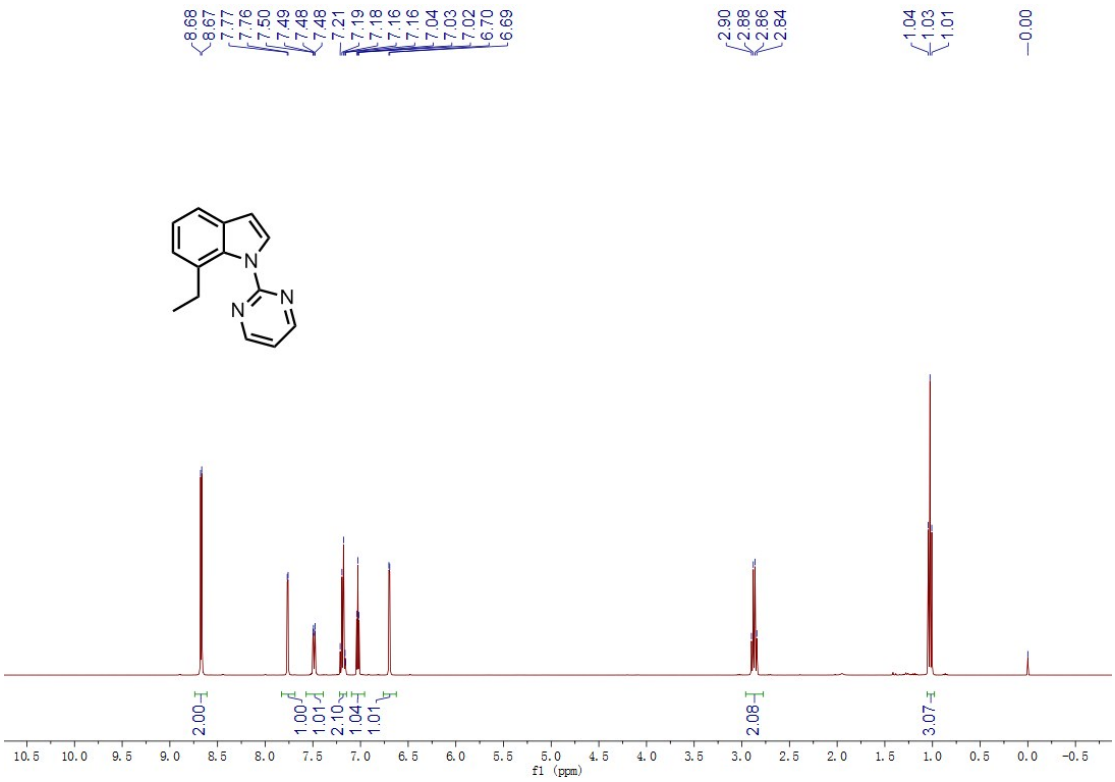


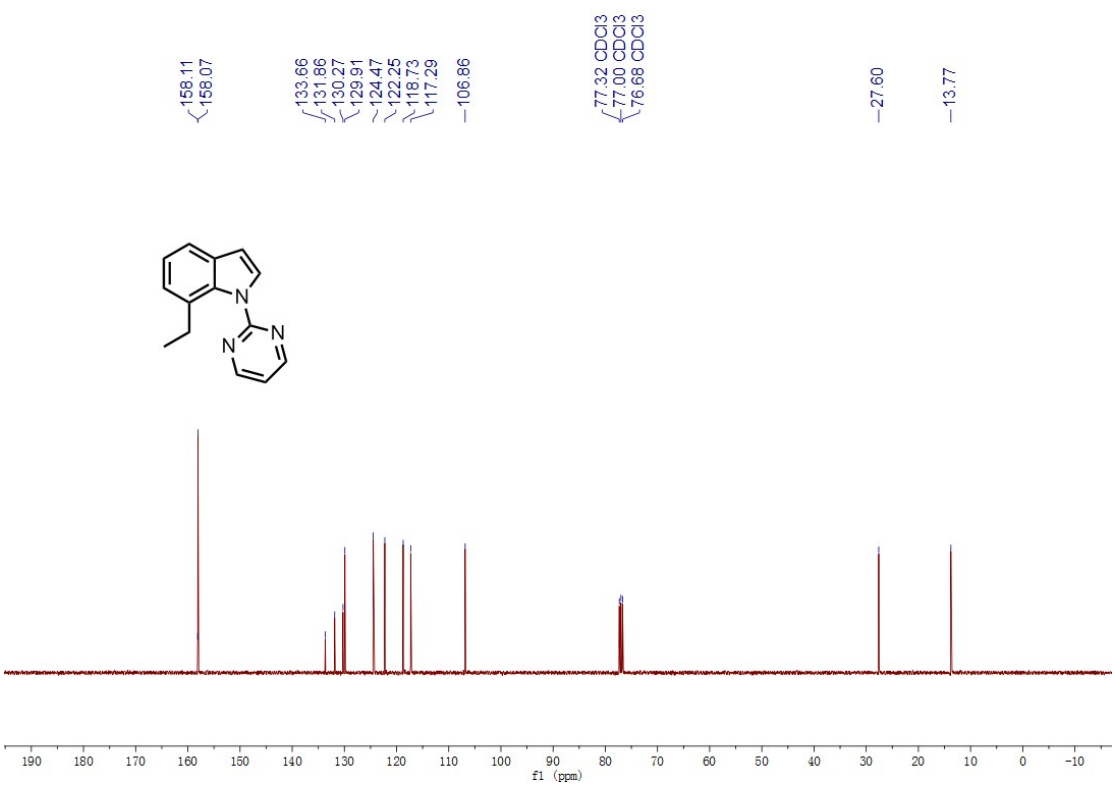
7-methyl-1-(pyrimidin-2-yl)-1H-indole (1s)



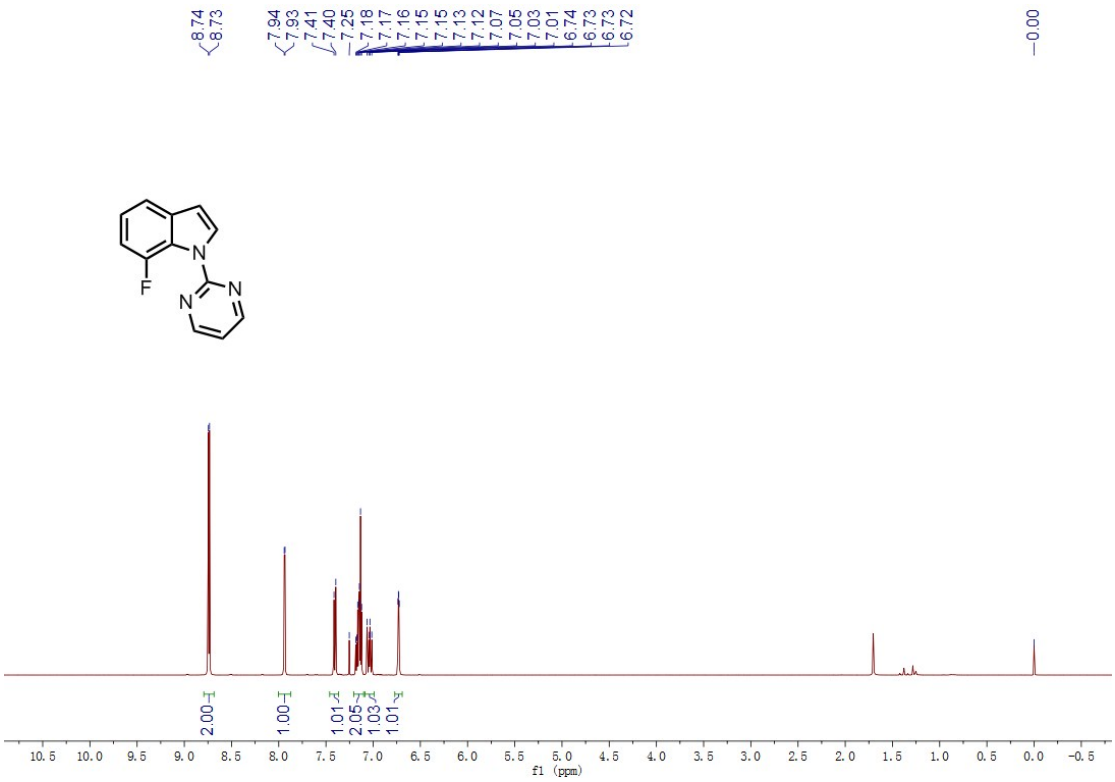


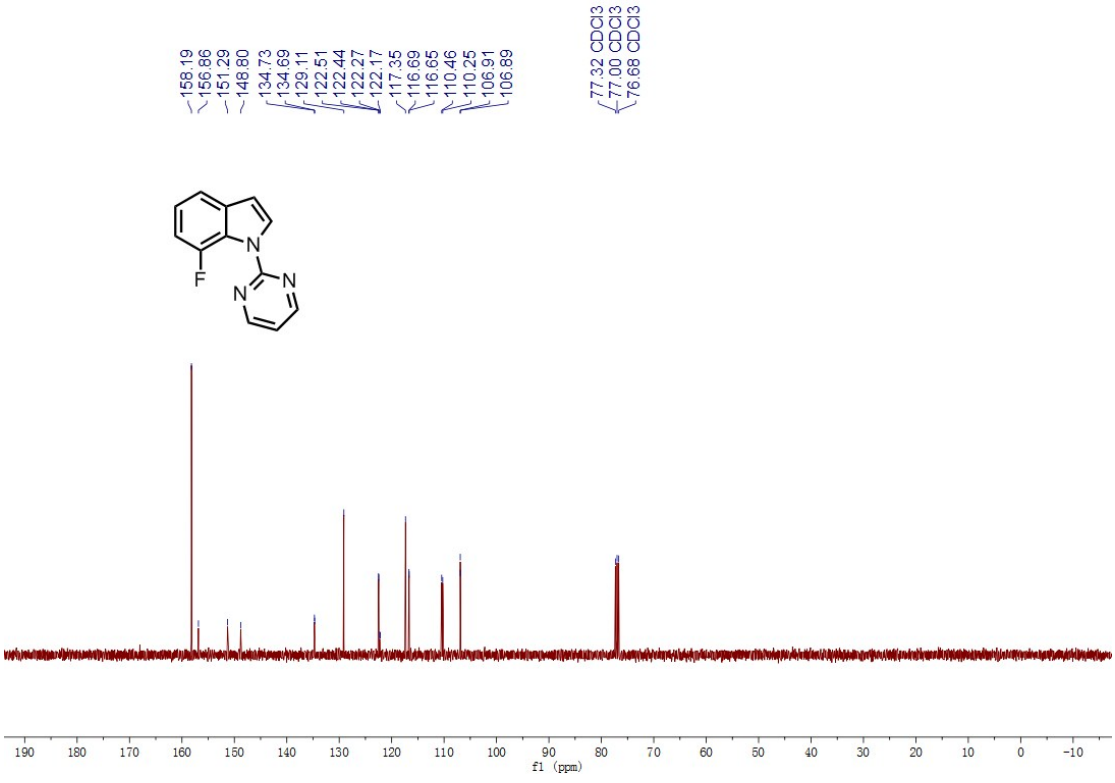
7-ethyl-1-(pyrimidin-2-yl)-1H-indole (1t)



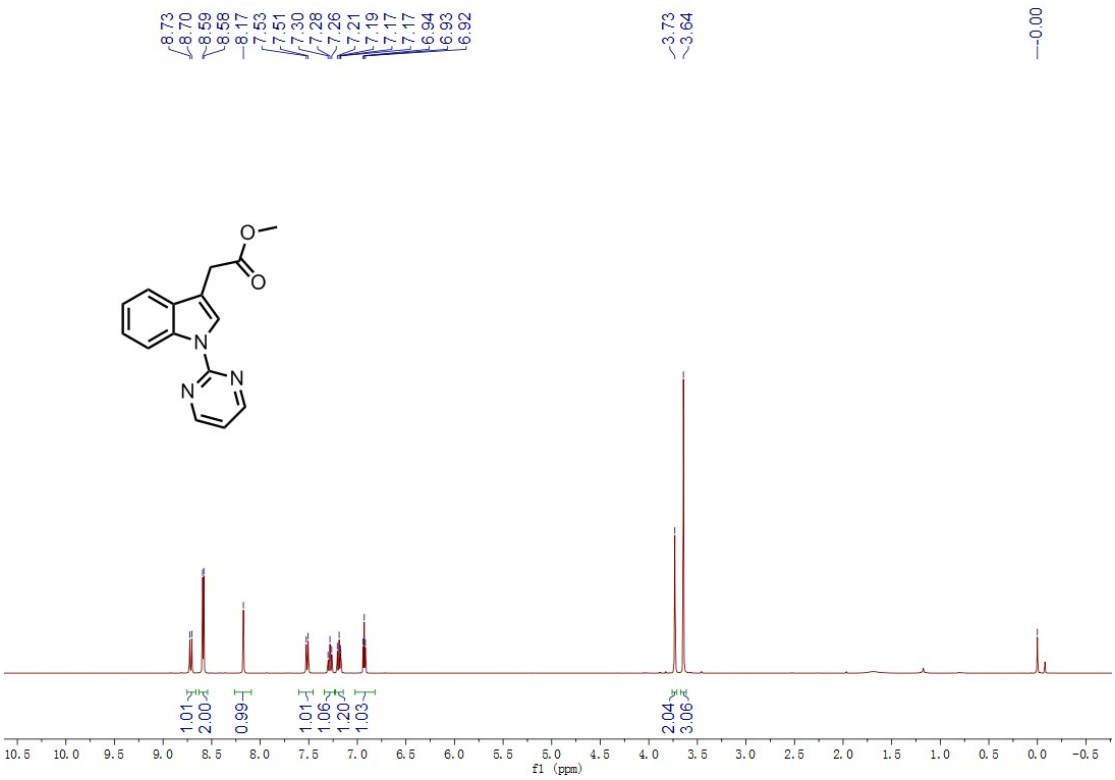


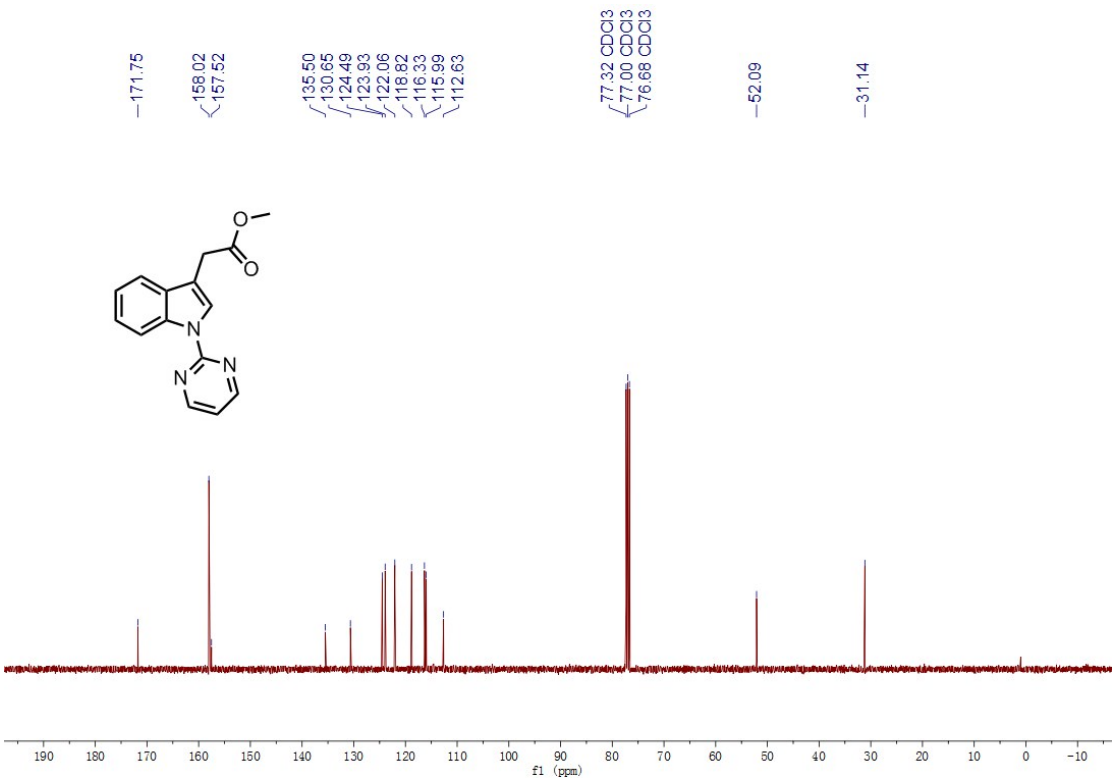
7-fluoro-1-(pyrimidin-2-yl)-1H-indole (1u)



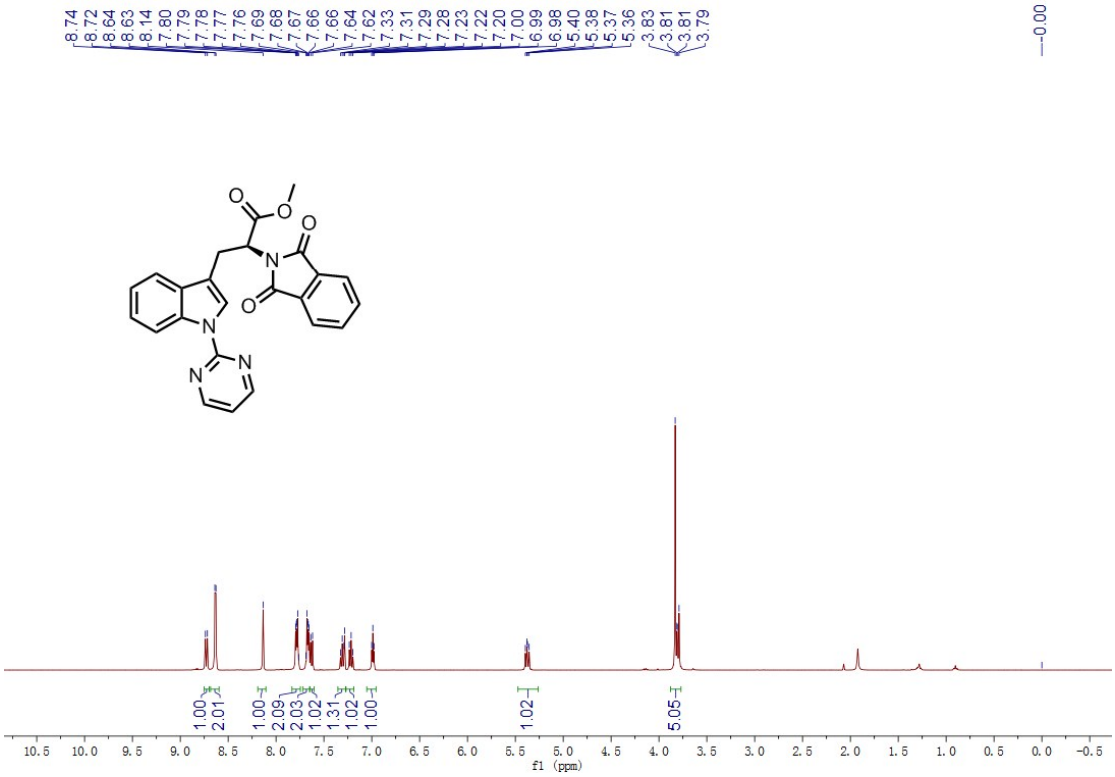


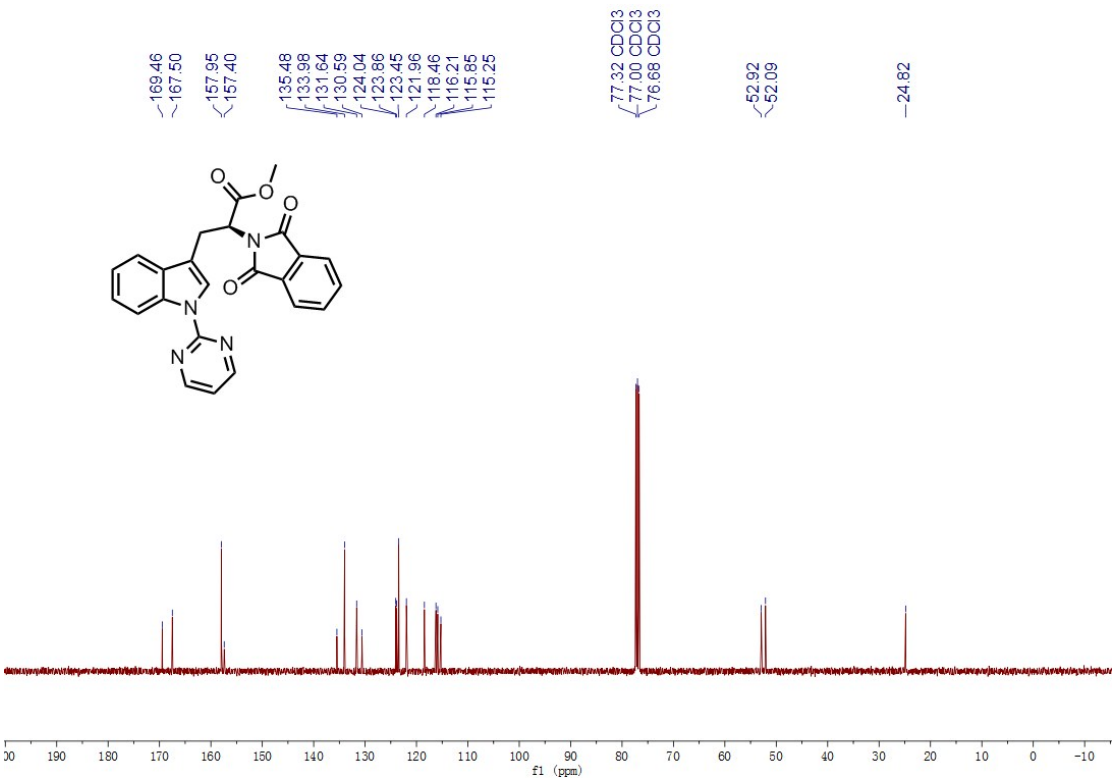
methyl 2-(1-(pyrimidin-2-yl)-1H-indol-3-yl)acetate (1y)



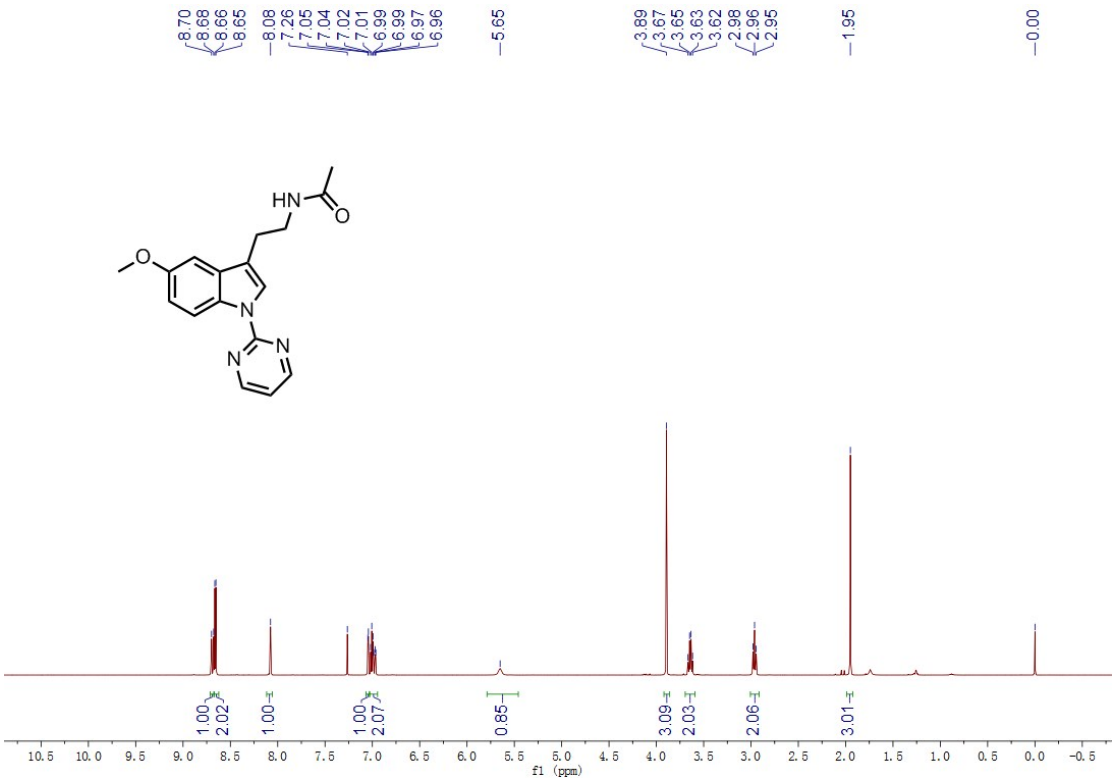


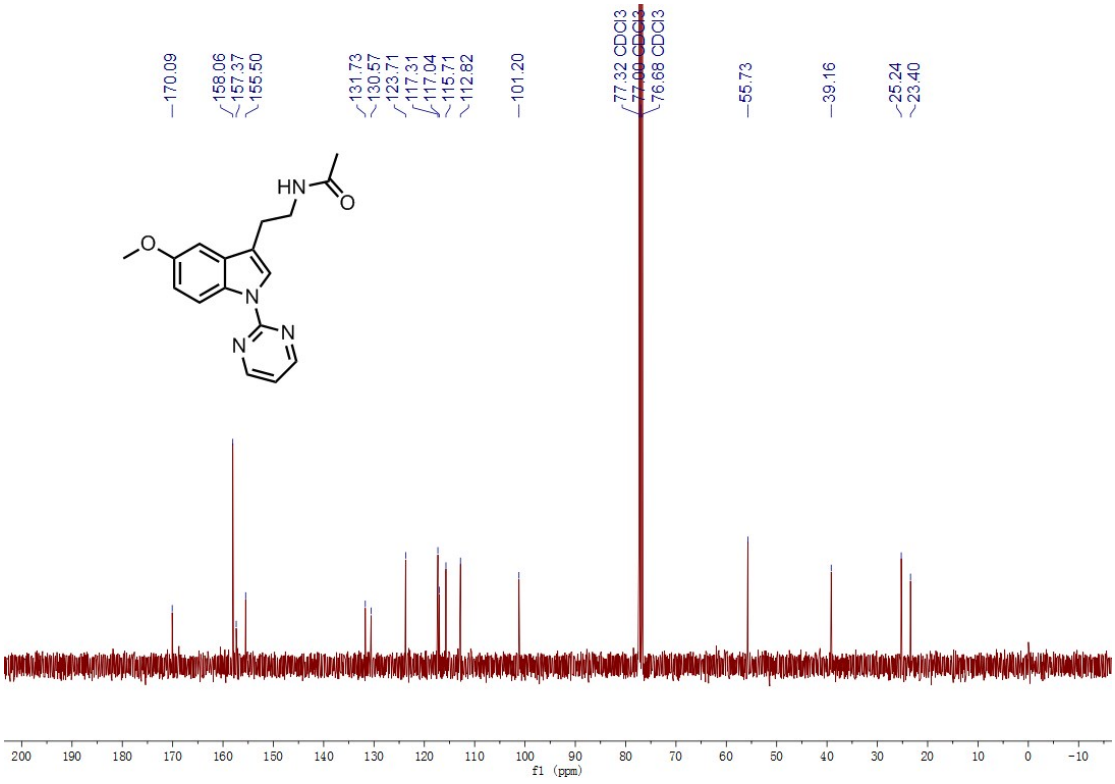
methyl (S)-2-(1,3-dioxoisoindolin-2-yl)-3-(1-(pyrimidin-2-yl)-1H-indol-3-yl)propanoate (1z)



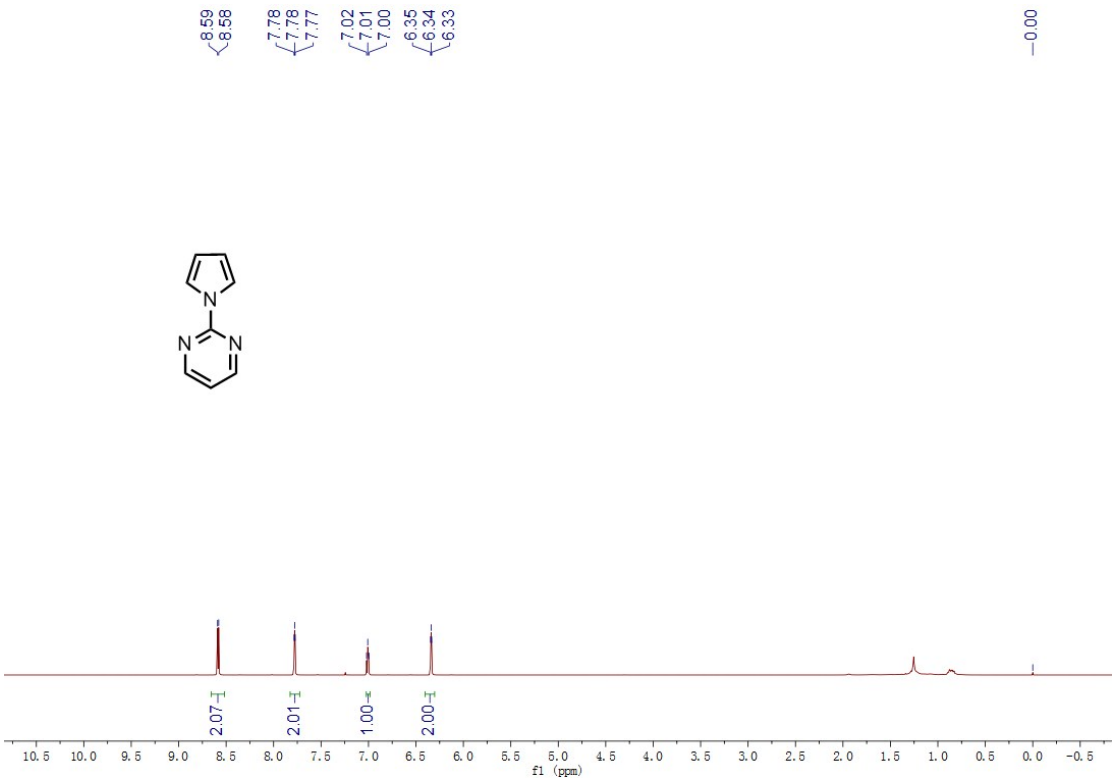


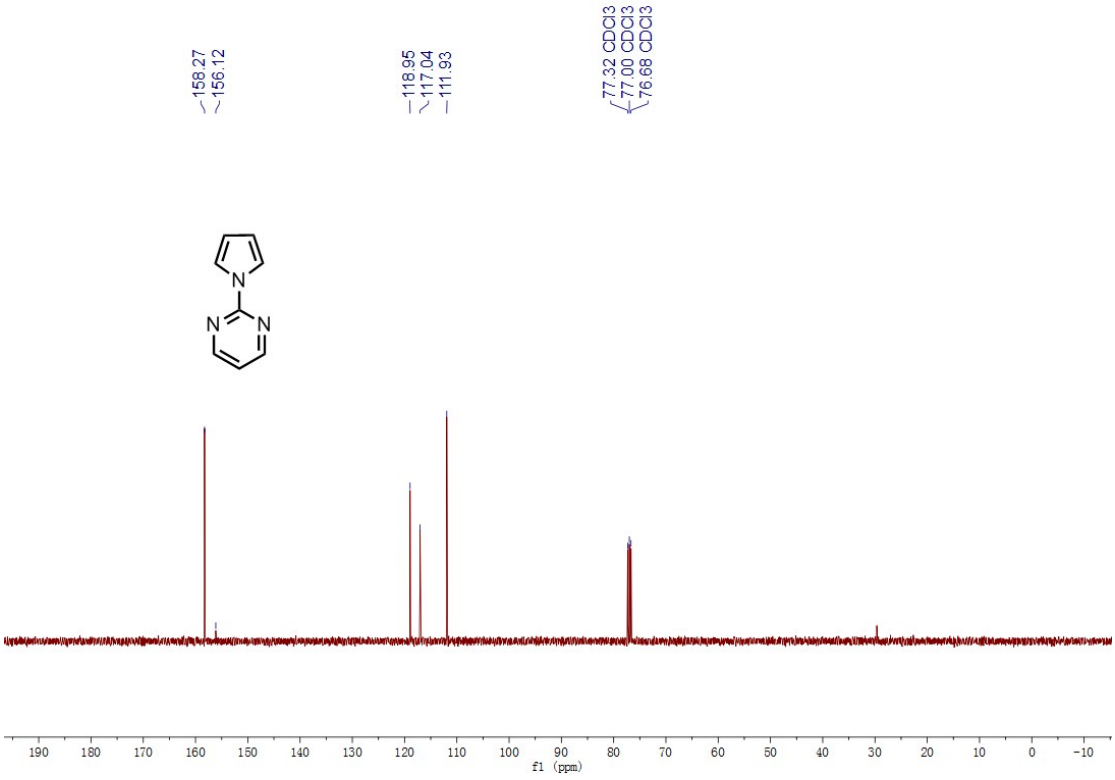
***N*-(2-(5-methoxy-1-(pyrimidin-2-yl)-1H-indol-3-yl)ethyl)acetamide (1za)**



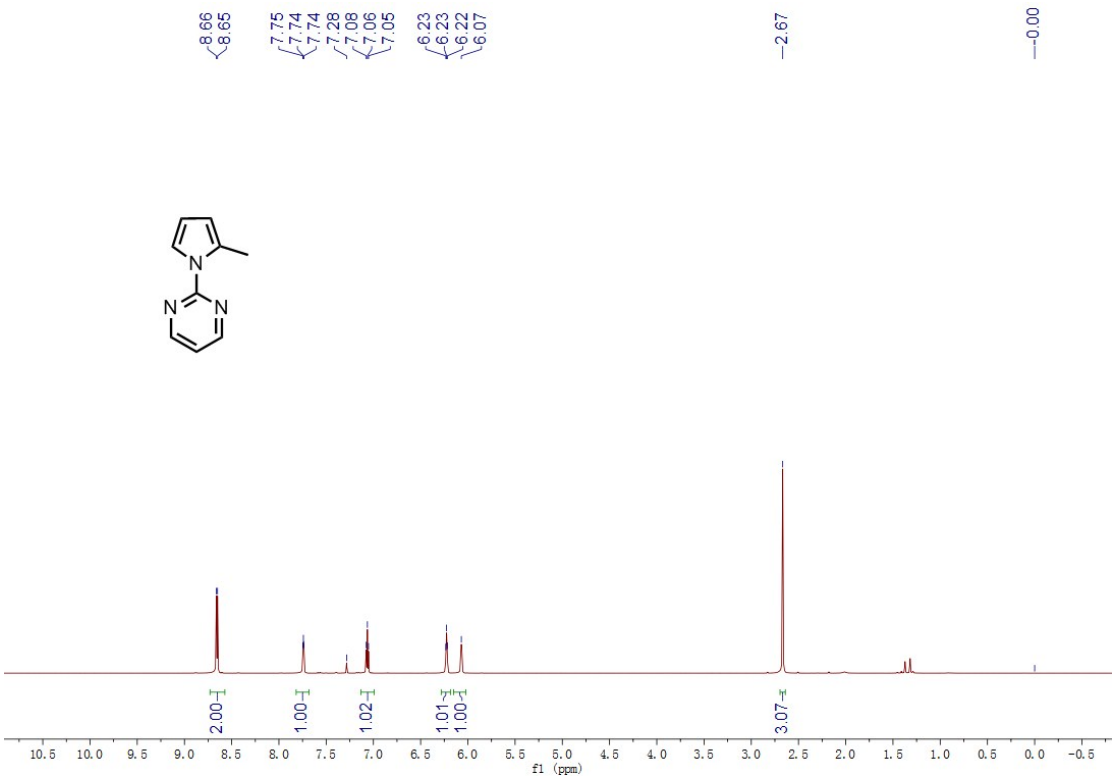


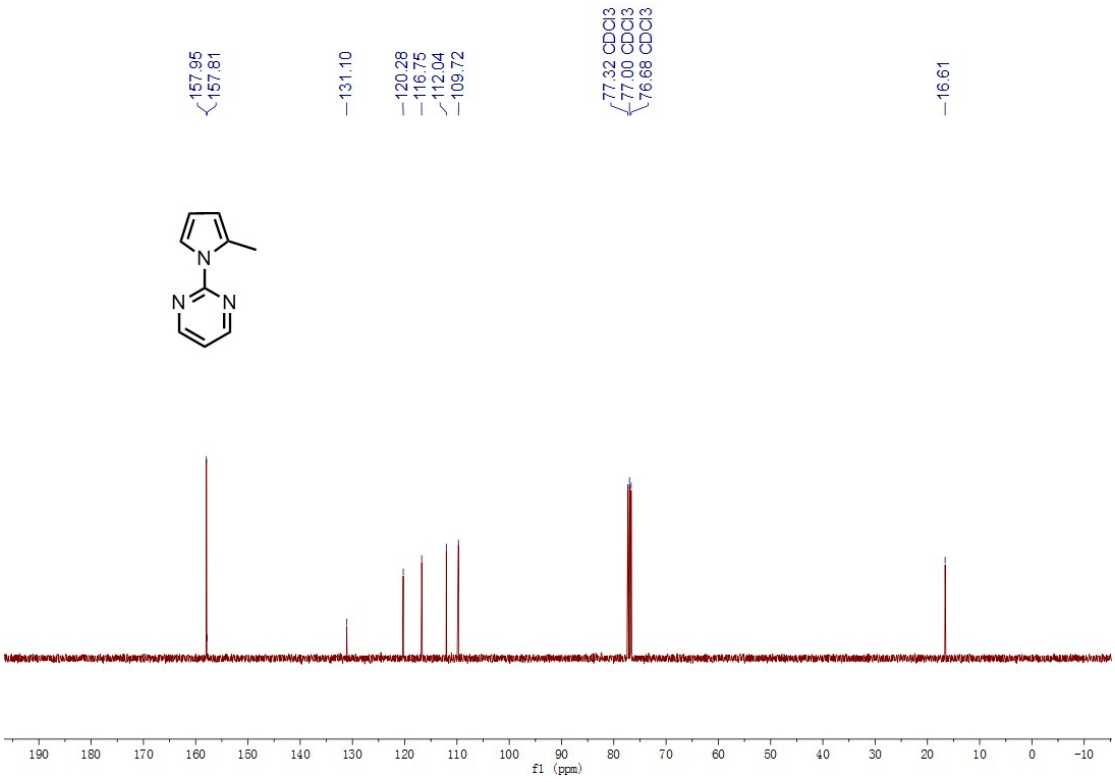
2-(1H-pyrrol-1-yl)pyrimidine (4a)



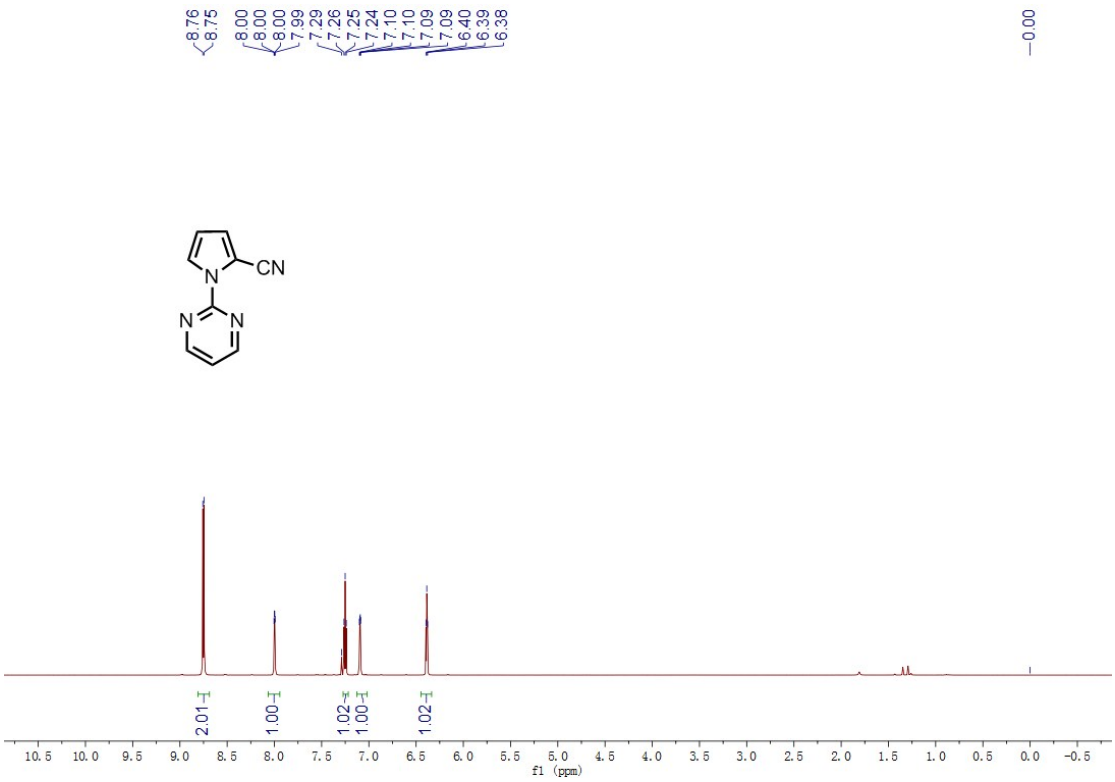


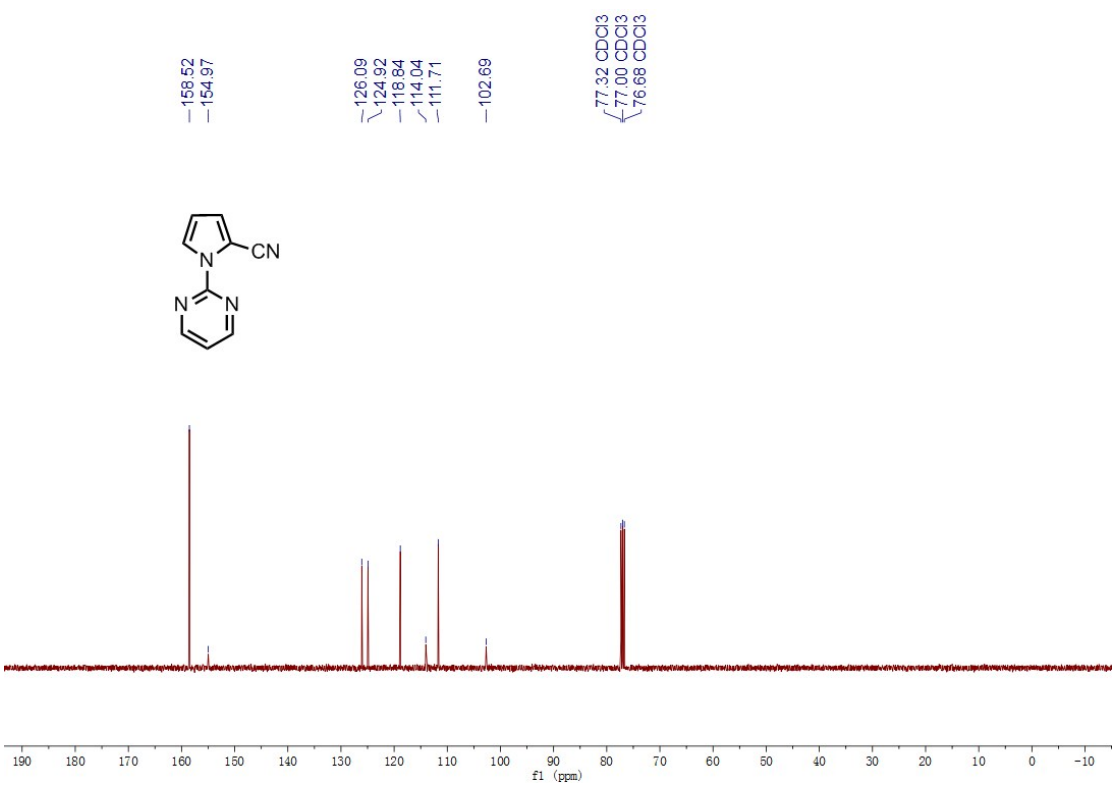
2-(2-methyl-1H-pyrrol-1-yl)pyrimidine (4b)



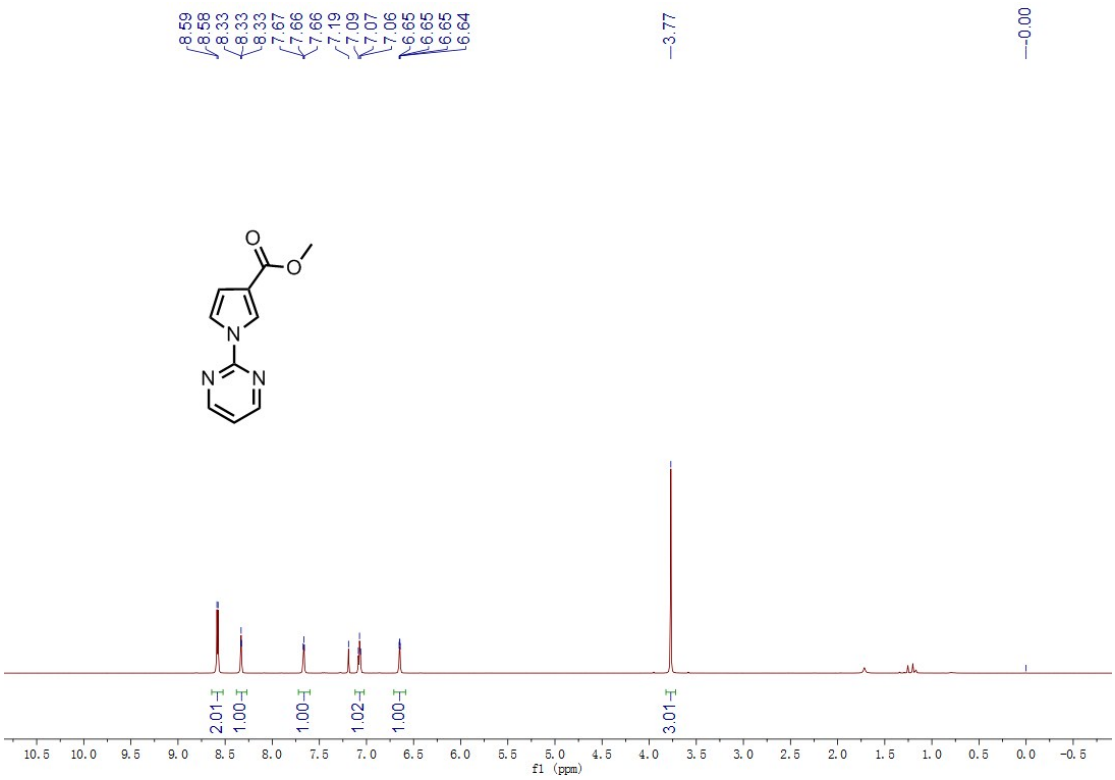


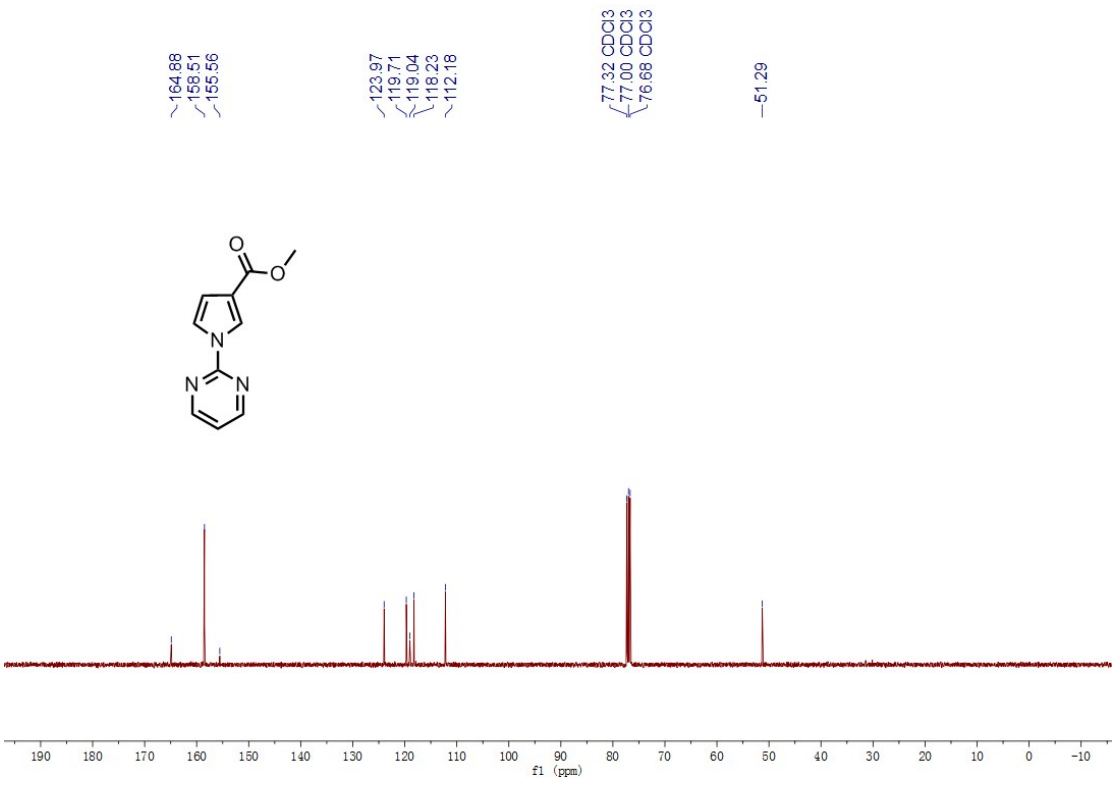
1-(pyrimidin-2-yl)-1H-pyrrole-2-carbonitrile (4c)



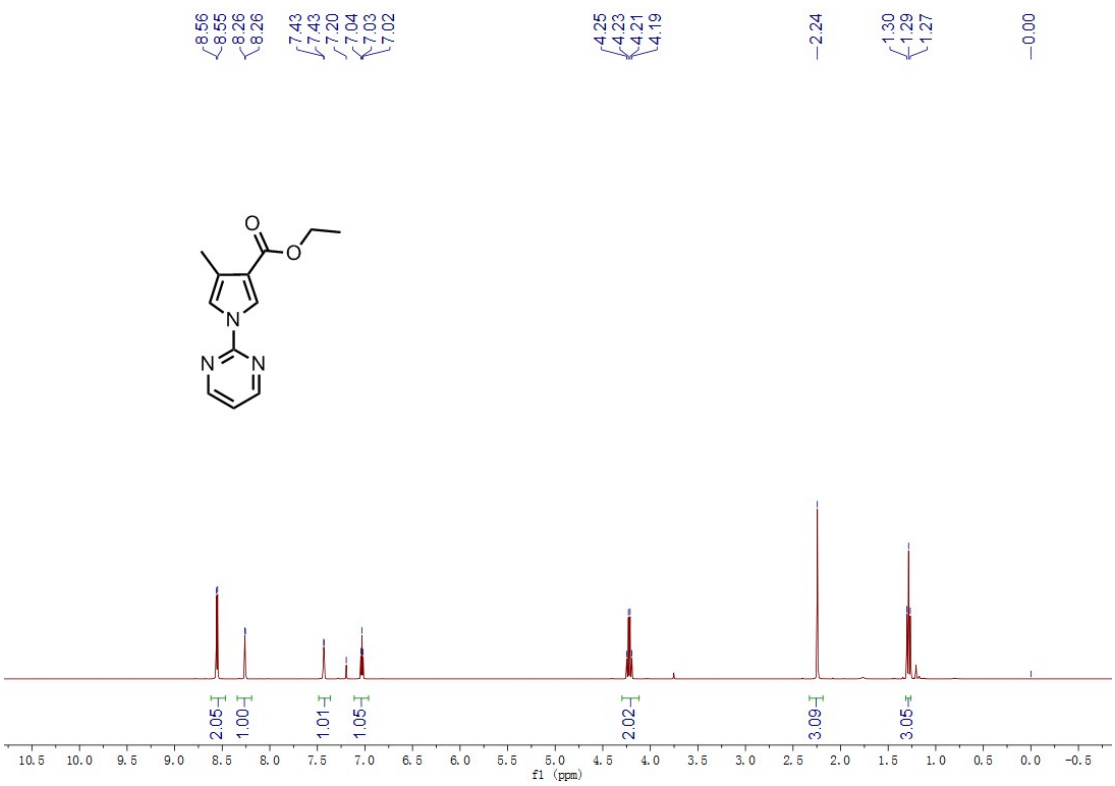


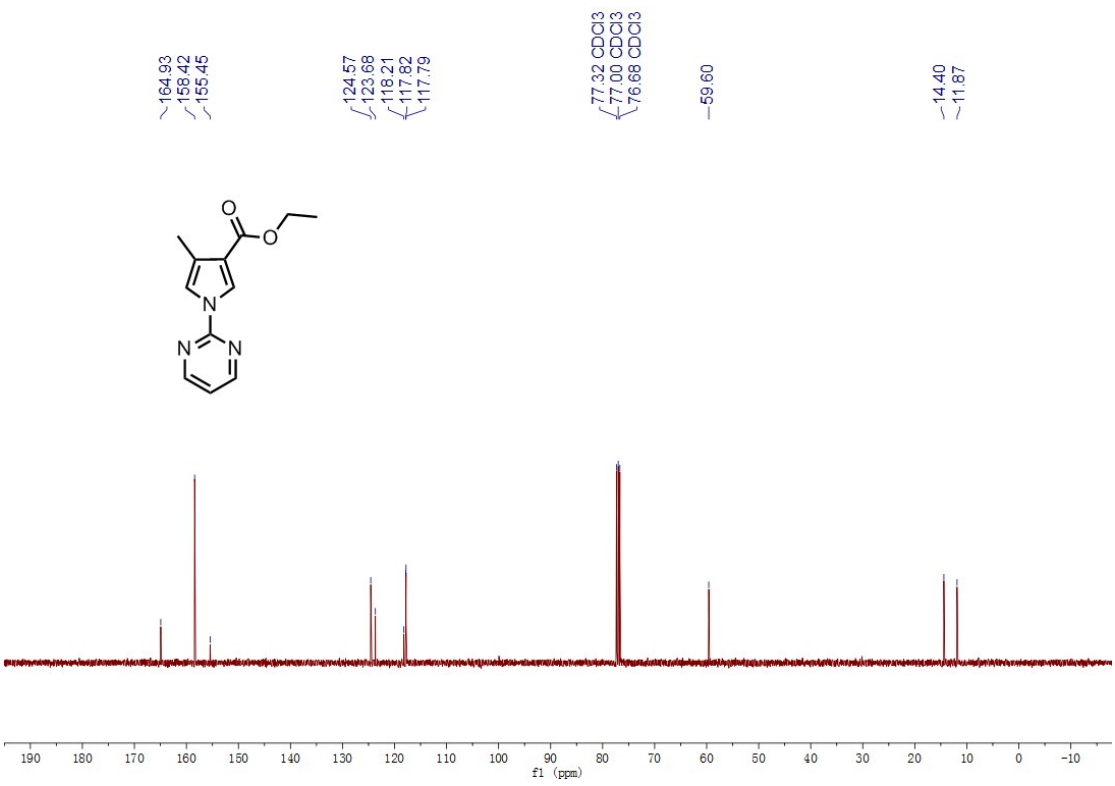
methyl 1-(pyrimidin-2-yl)-1H-pyrrole-3-carboxylate (4d)



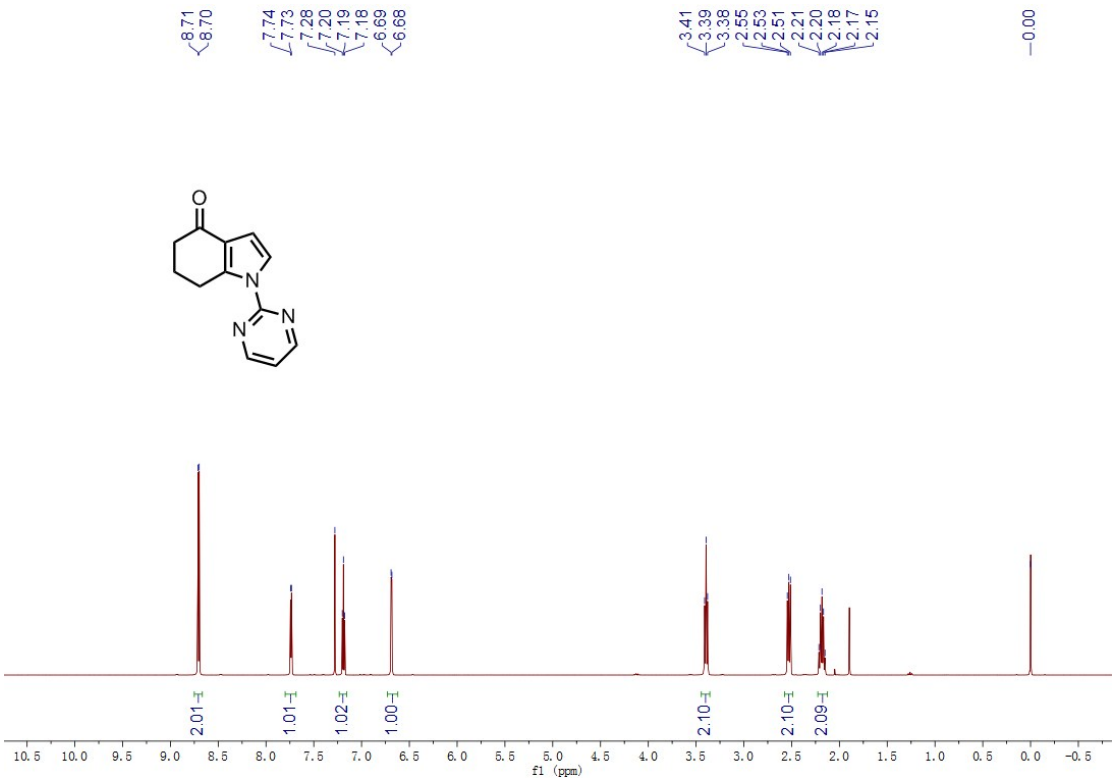


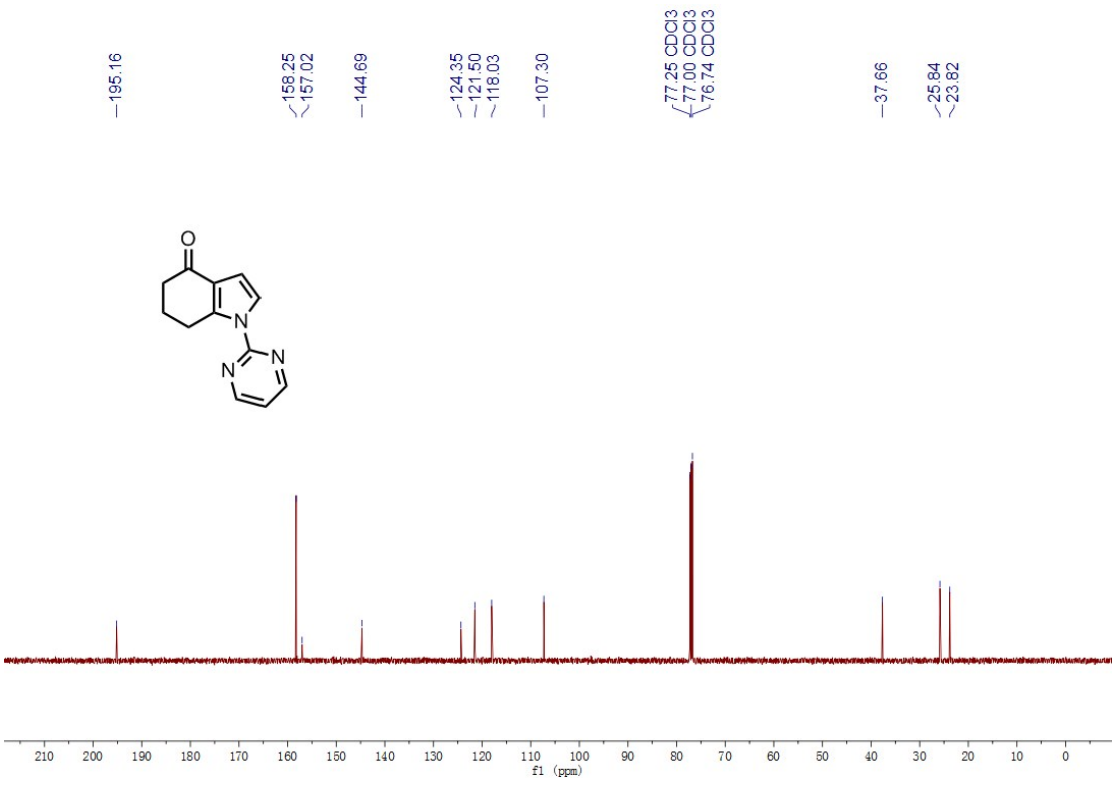
ethyl 4-methyl-1-(pyrimidin-2-yl)-1H-pyrrole-3-carboxylate (4e)



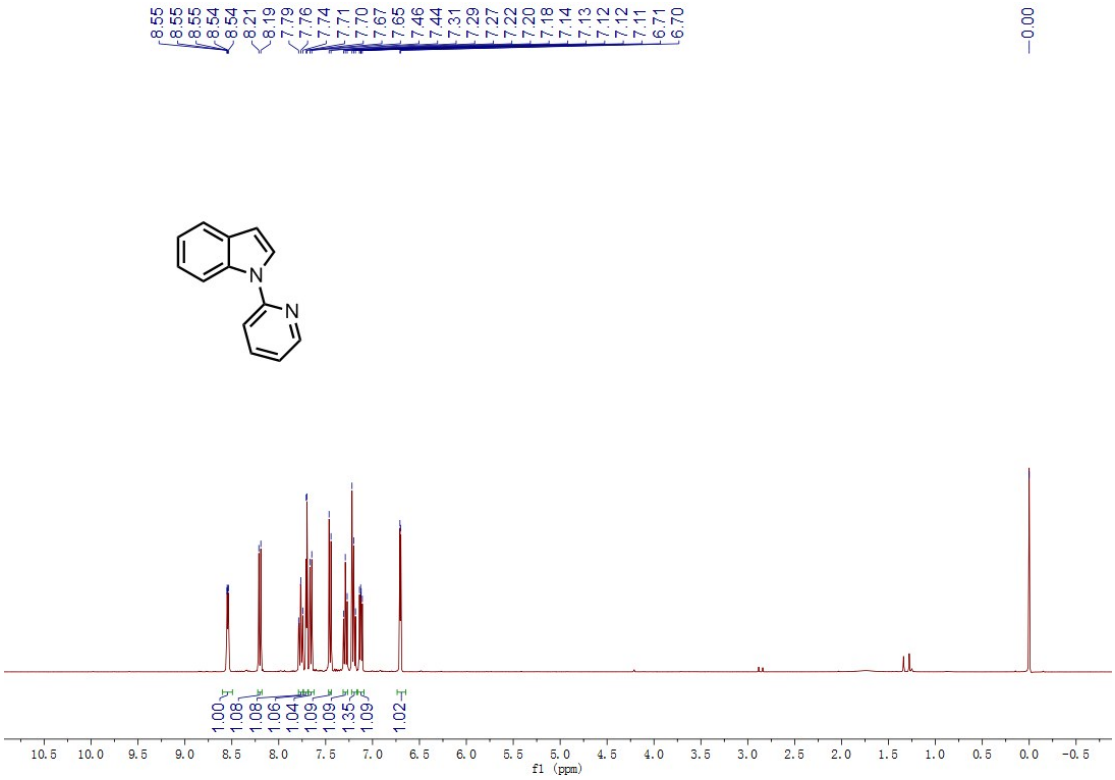


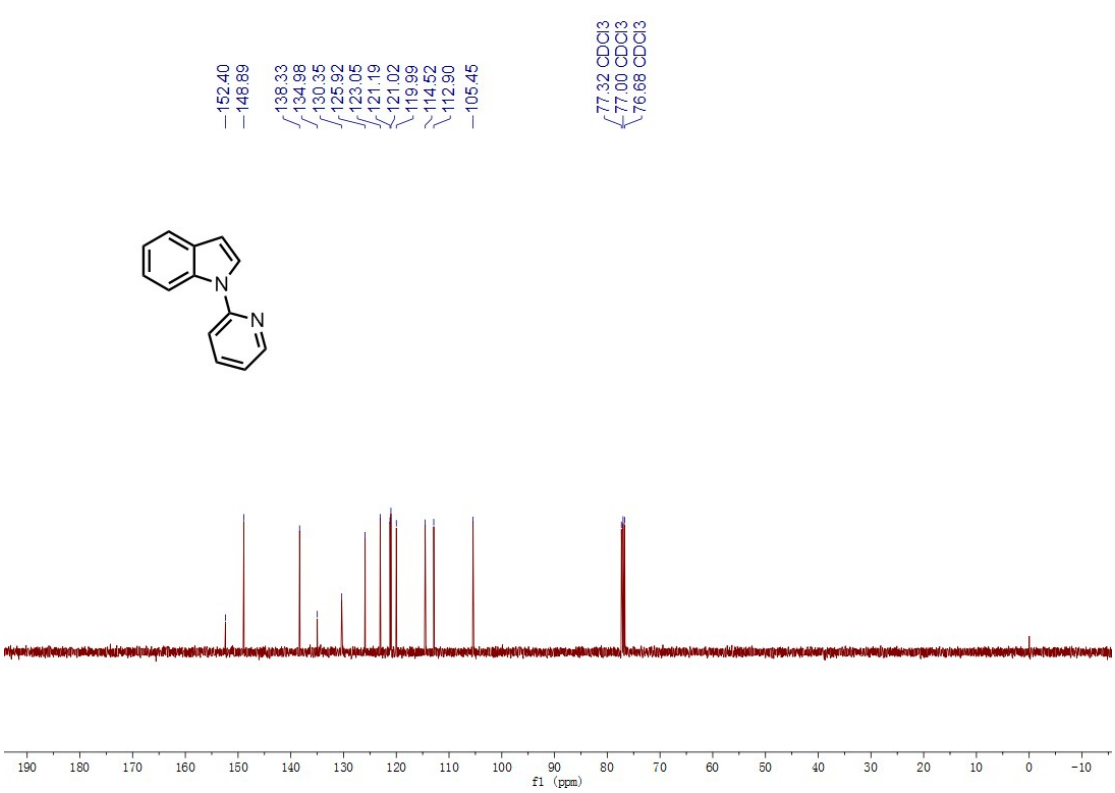
1-(pyrimidin-2-yl)-1,5,6,7-tetrahydro-4H-indol-4-one (4f)



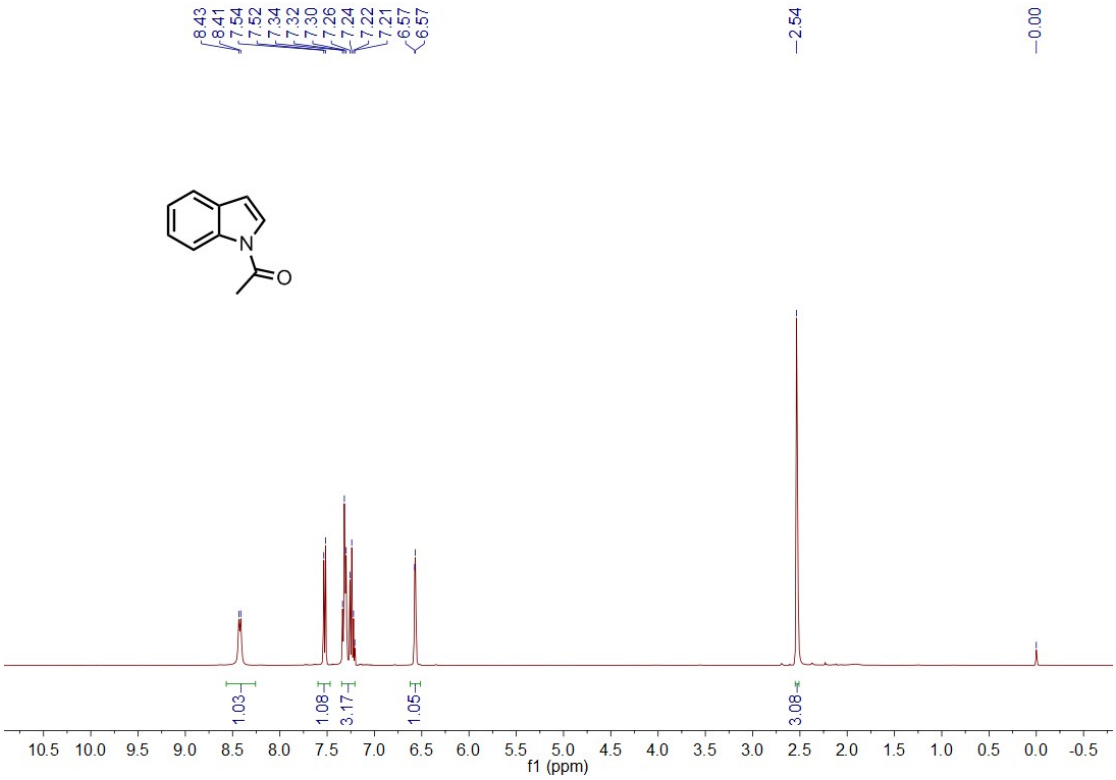


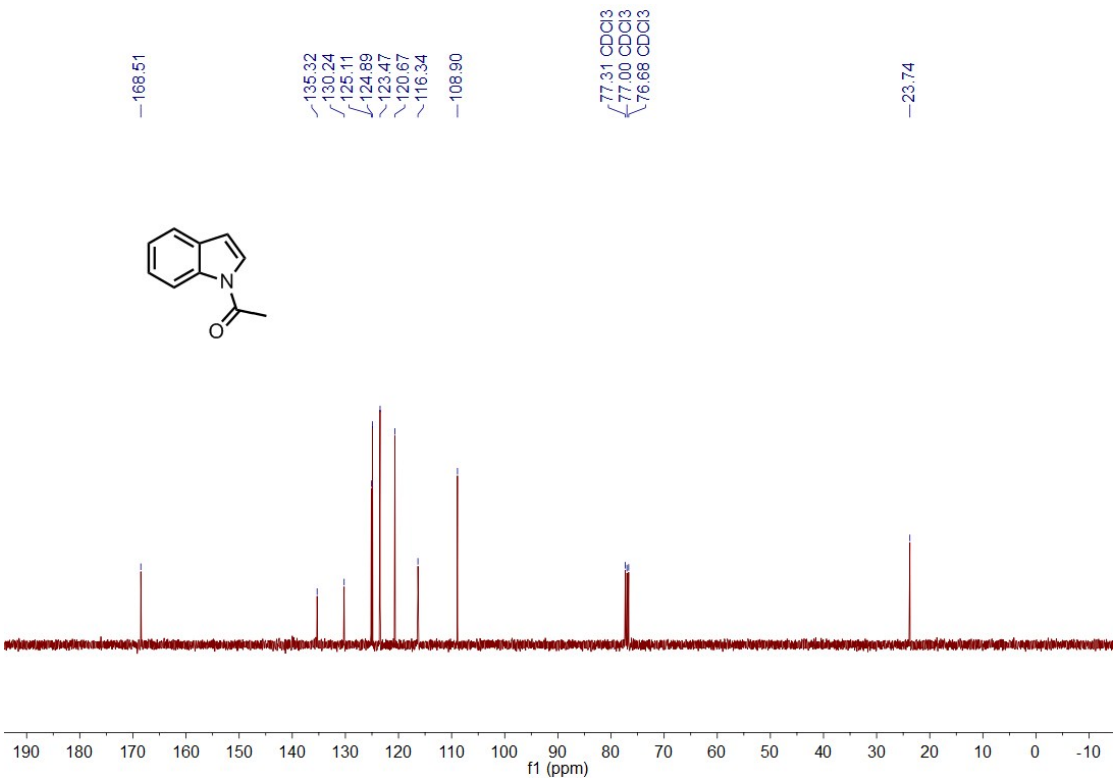
1-(pyridin-2-yl)-1H-indole (6)



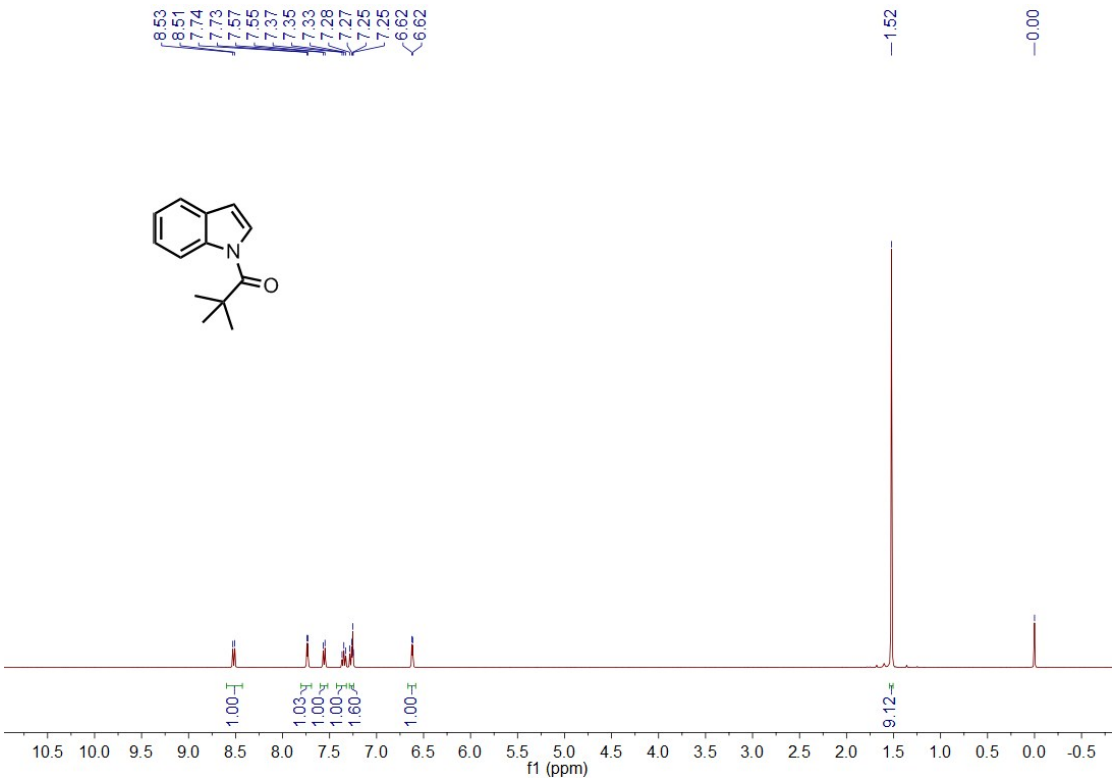


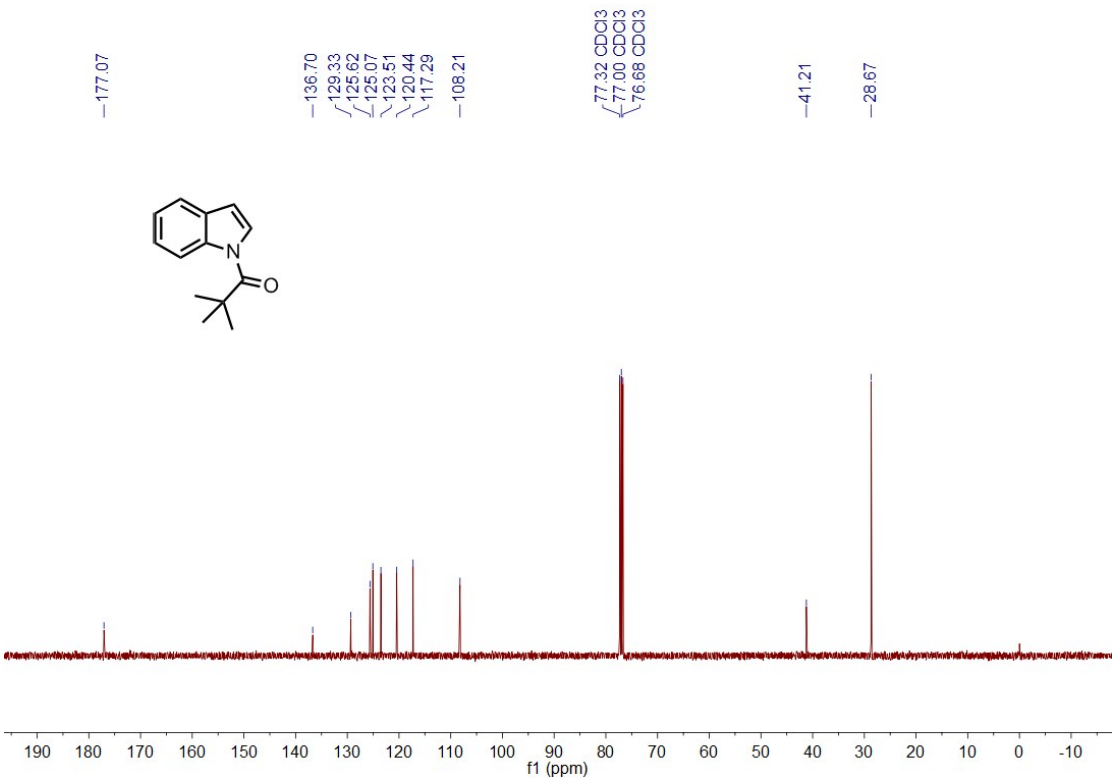
1-(1H-indol-1-yl)ethan-1-one (7)



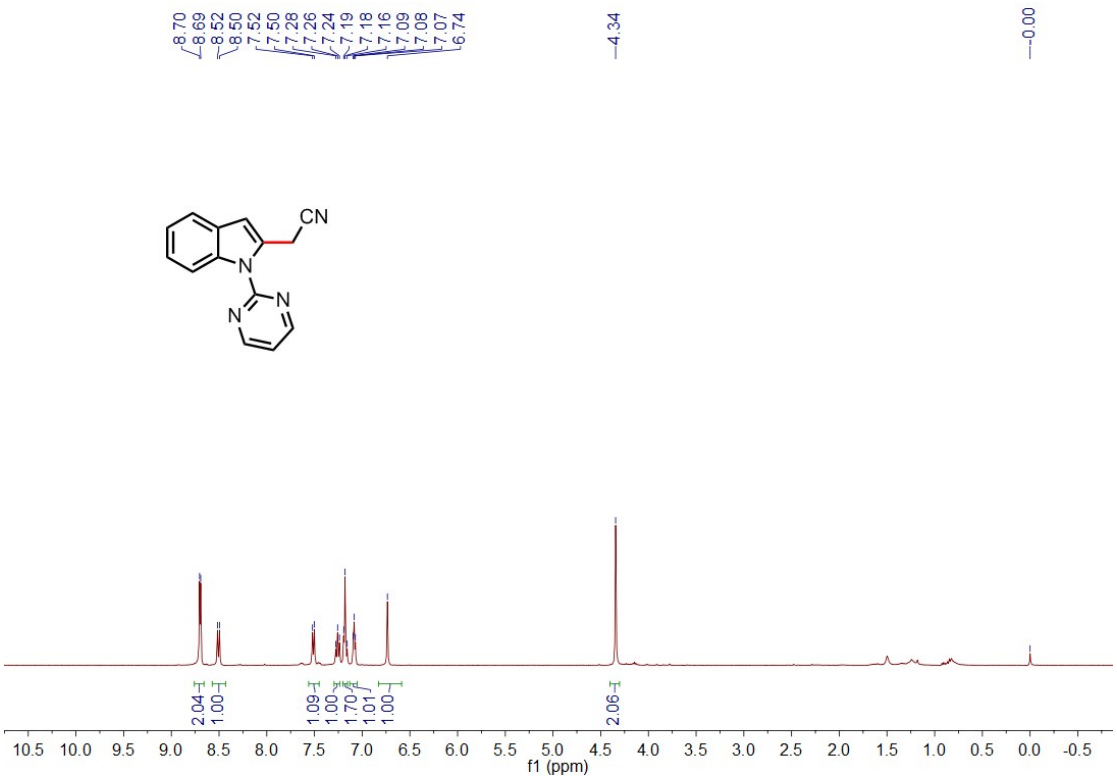


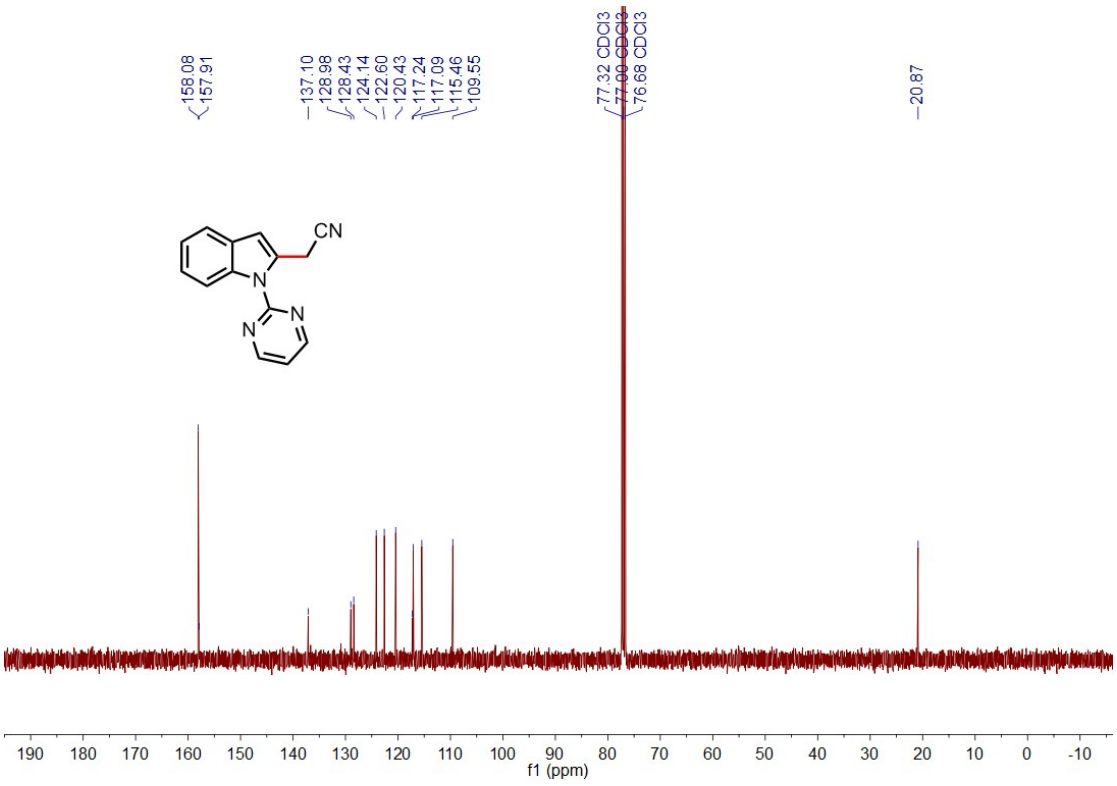
1-(1H-indol-1-yl)-2,2-dimethylpropan-1-one (9)



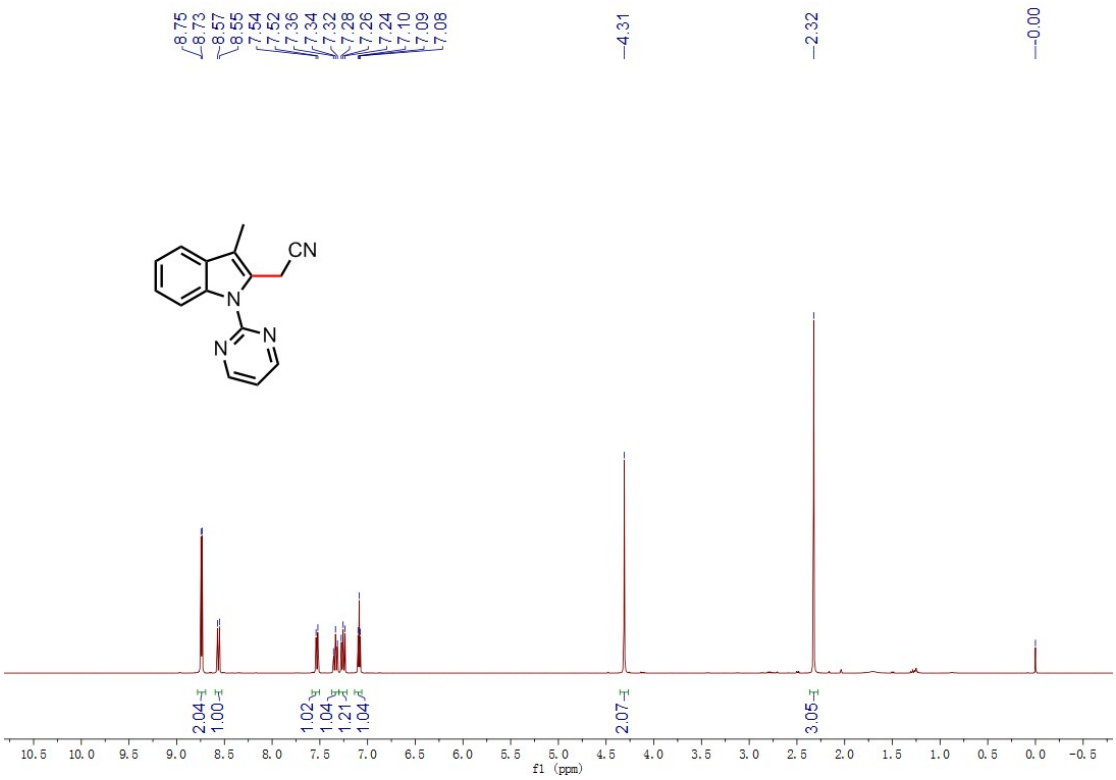


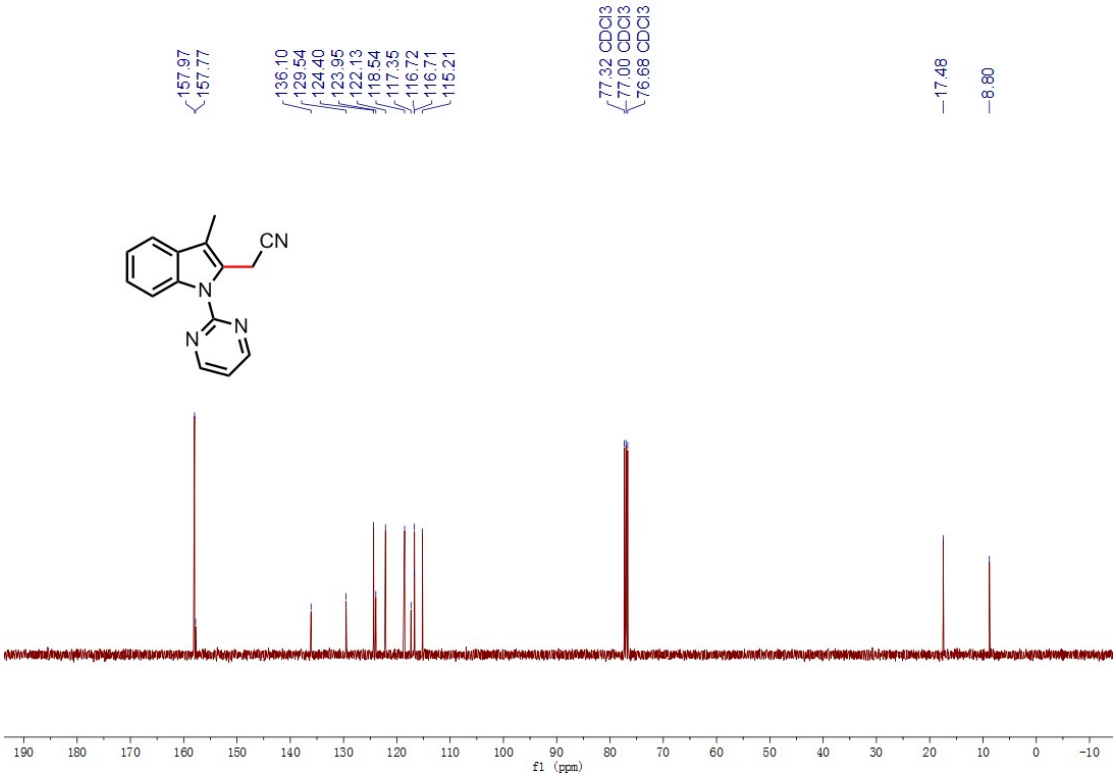
2-(1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3a)



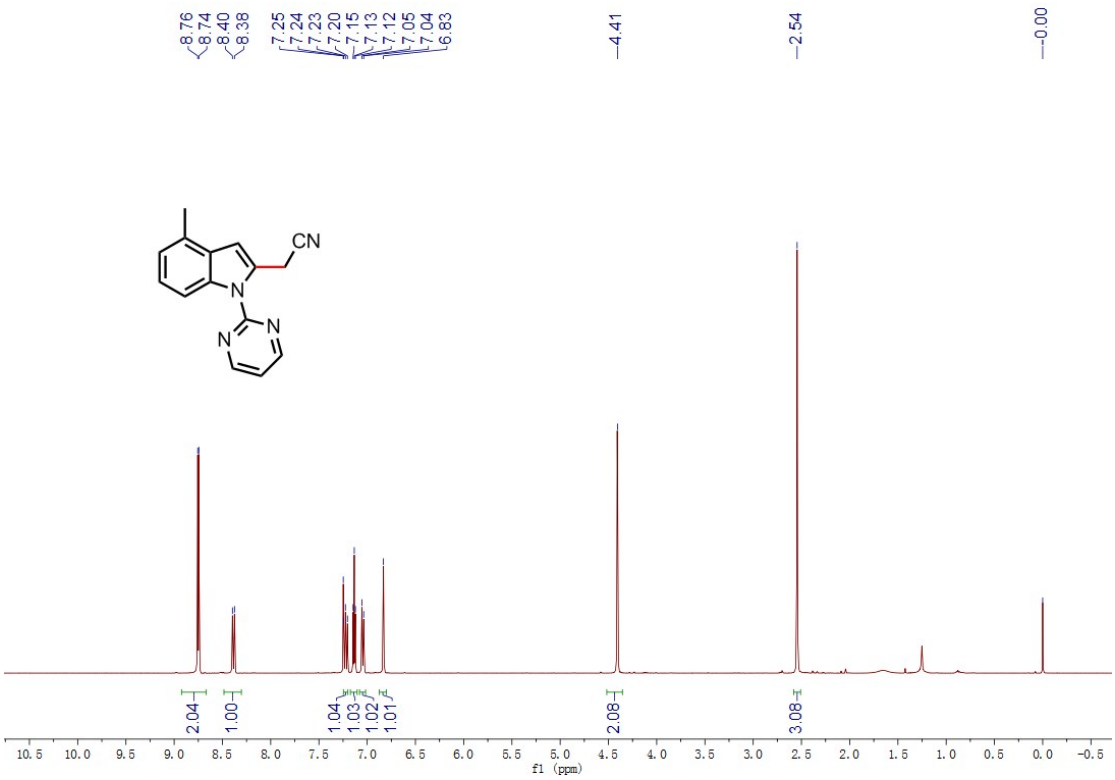


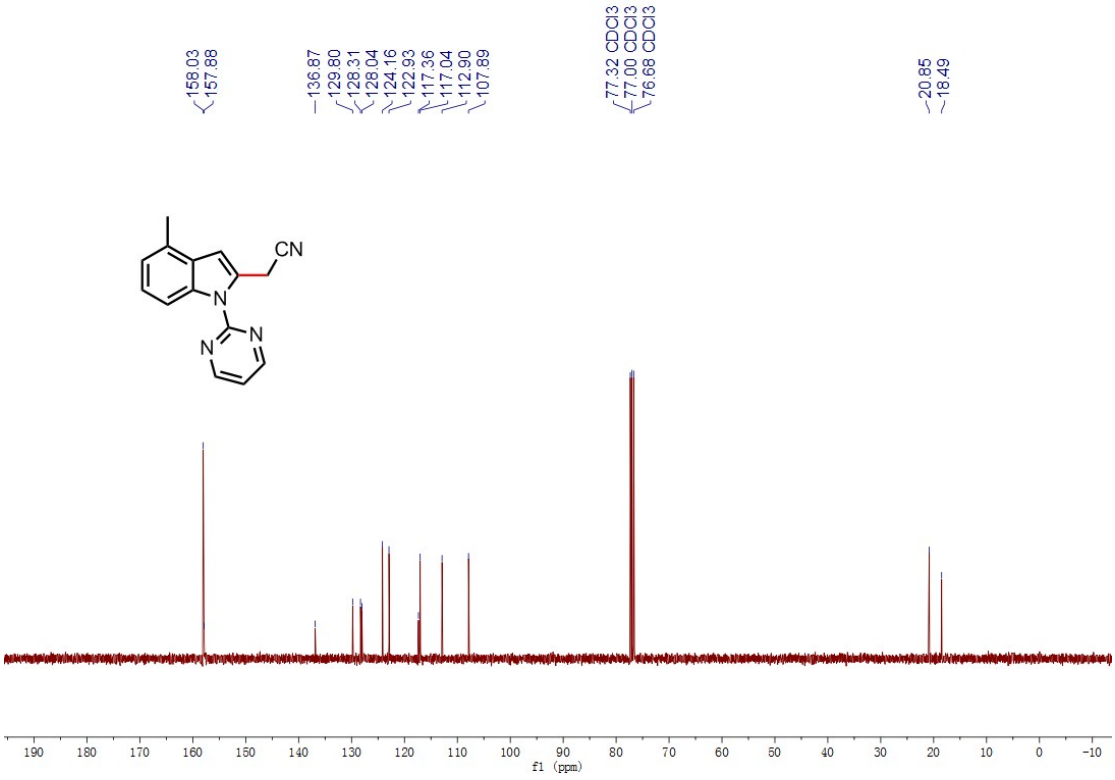
2-(3-methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3b)



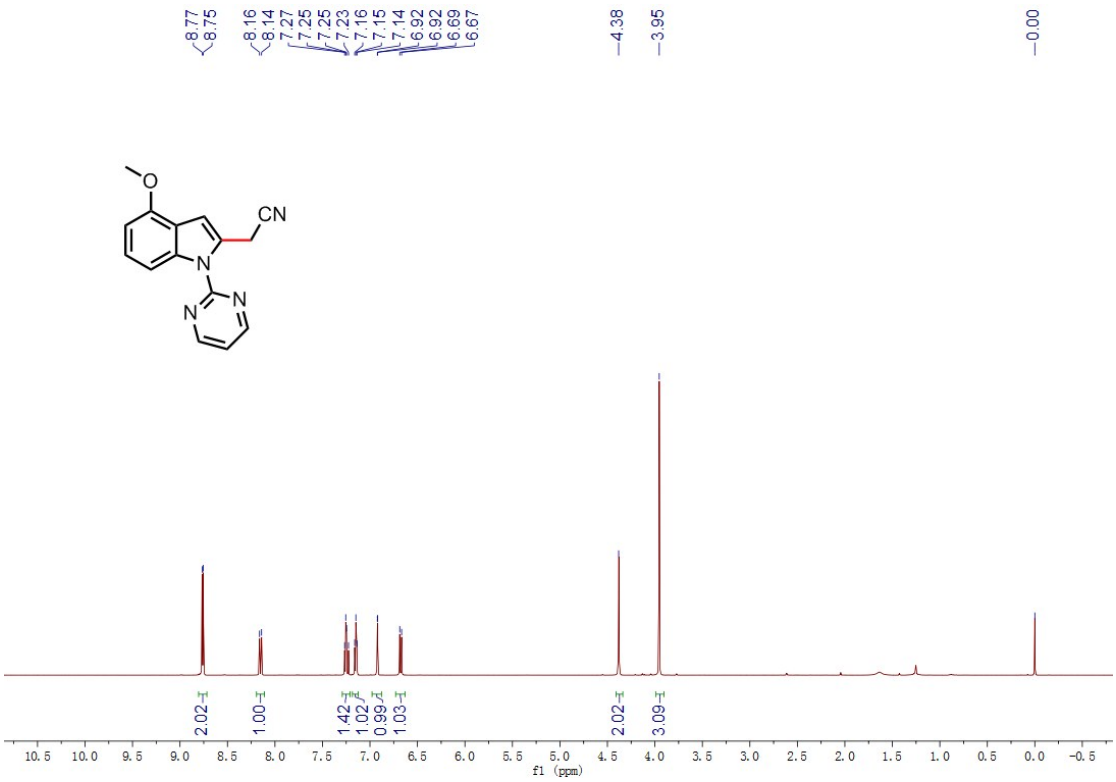


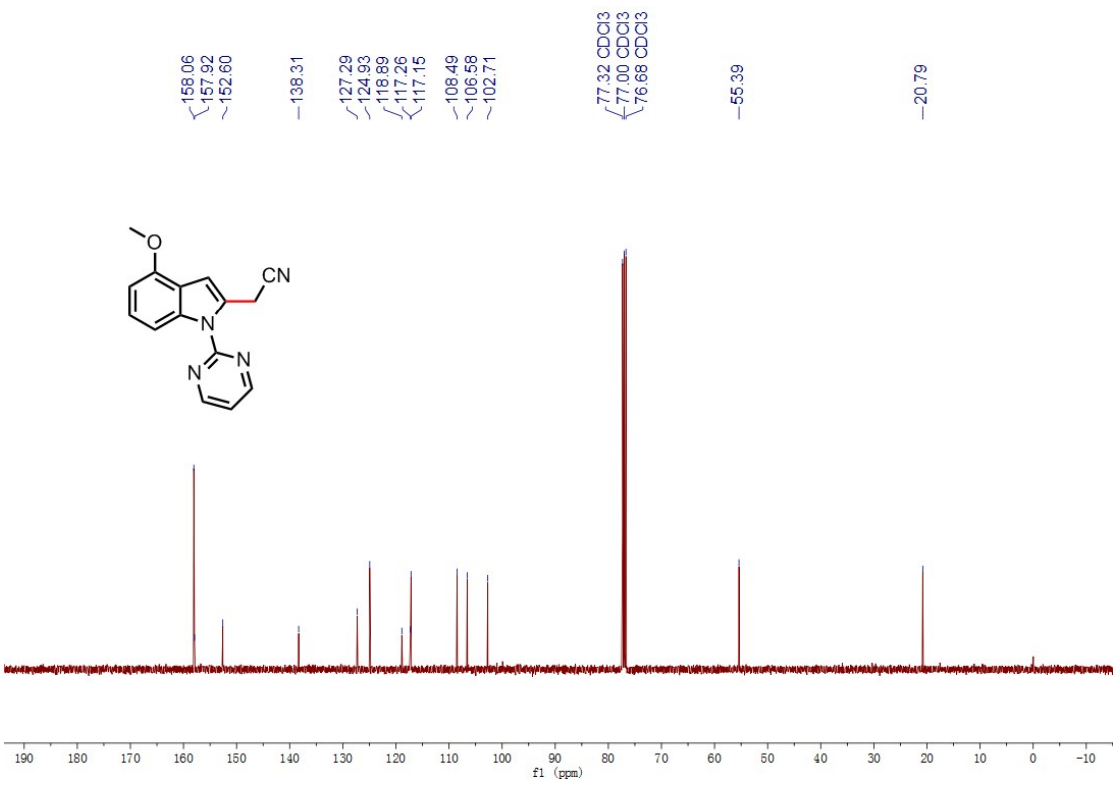
2-(4-methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3c)



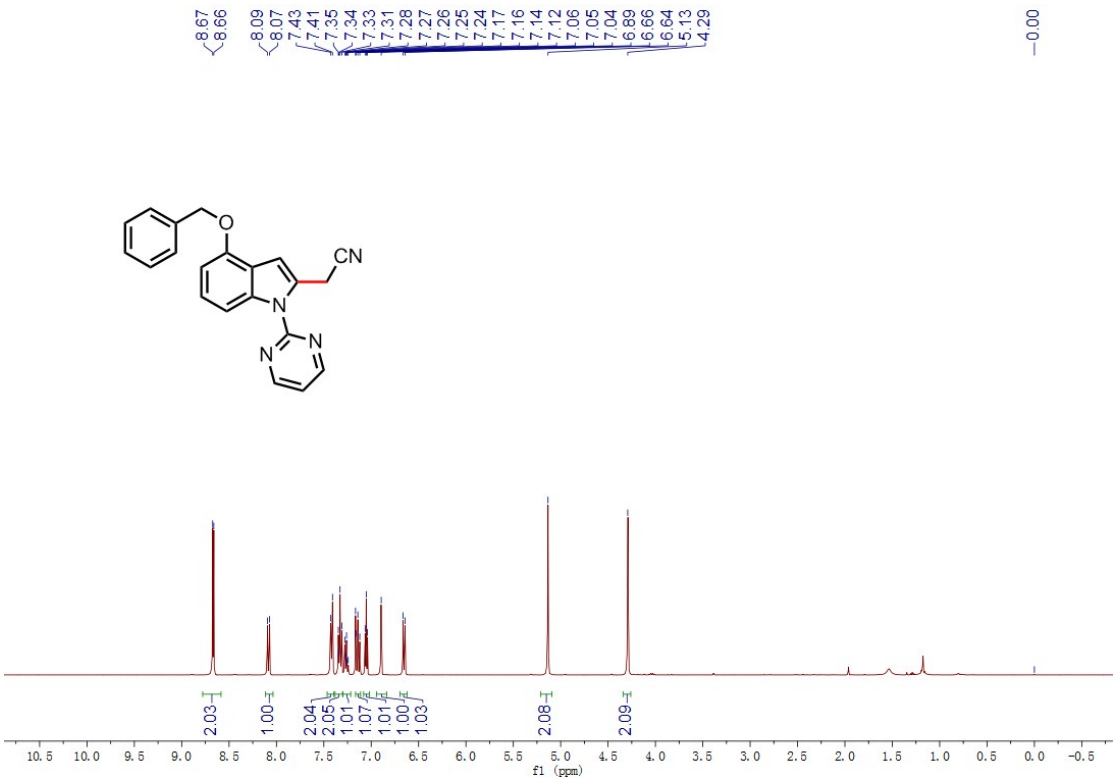


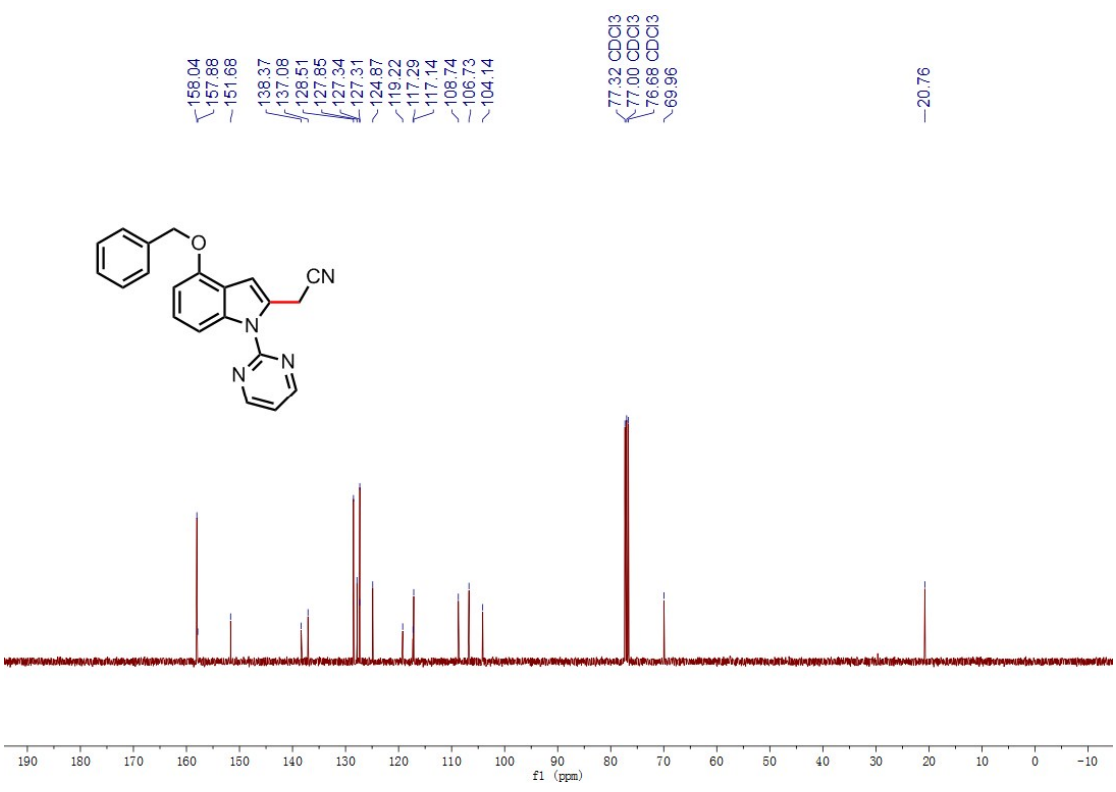
2-(4-methoxy-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3d)



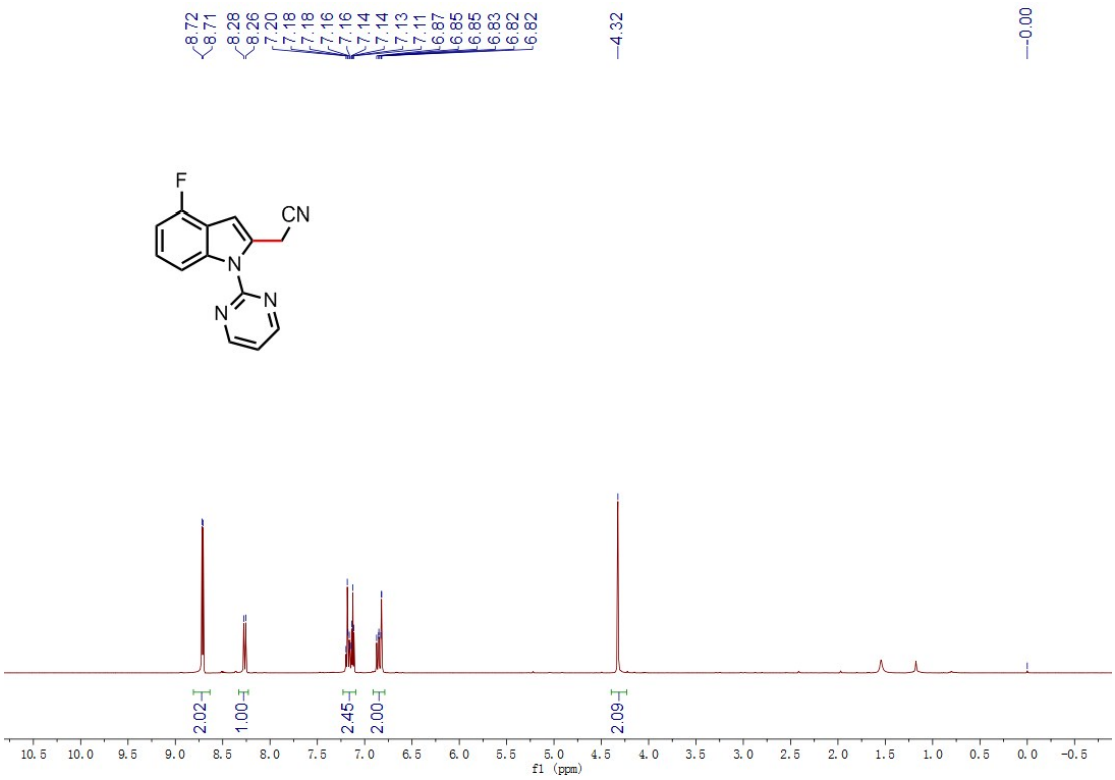


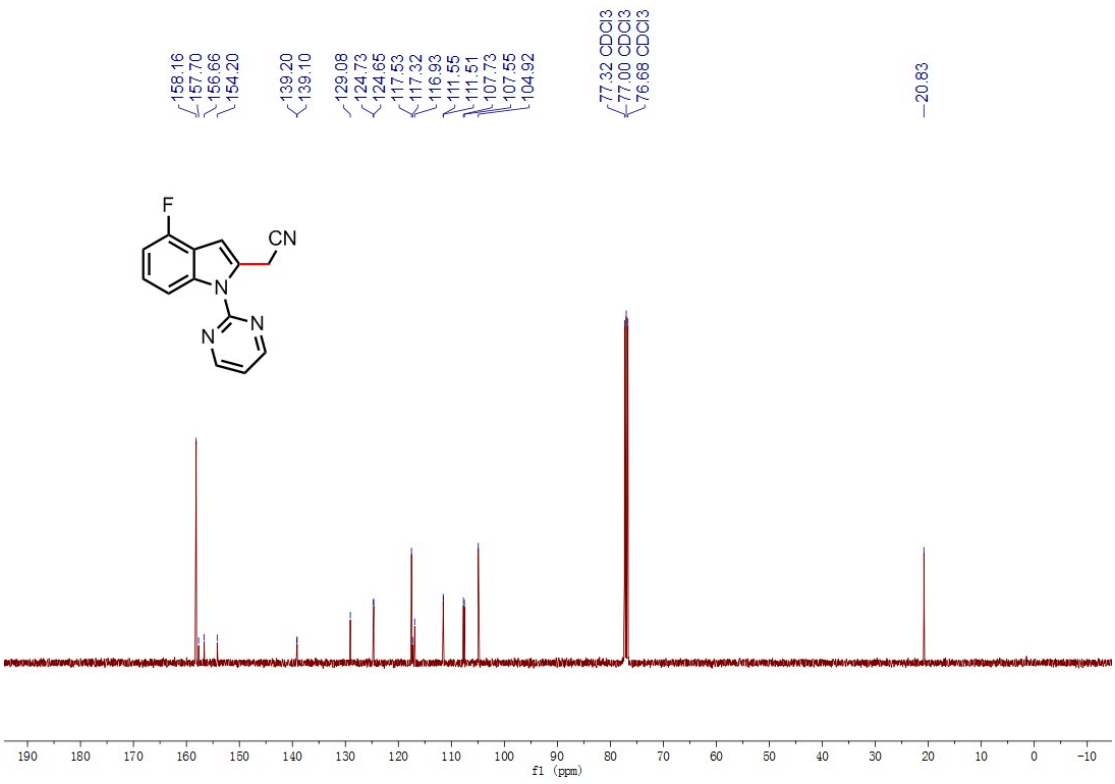
2-(4-(benzyloxy)-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3e)



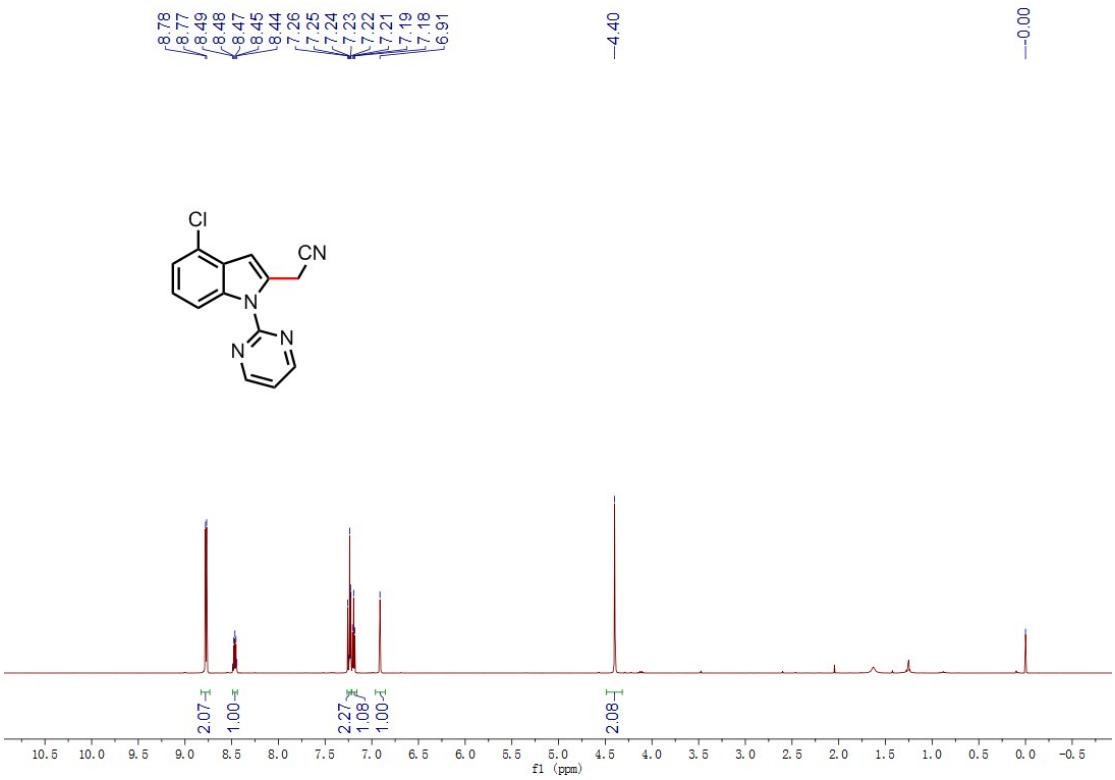


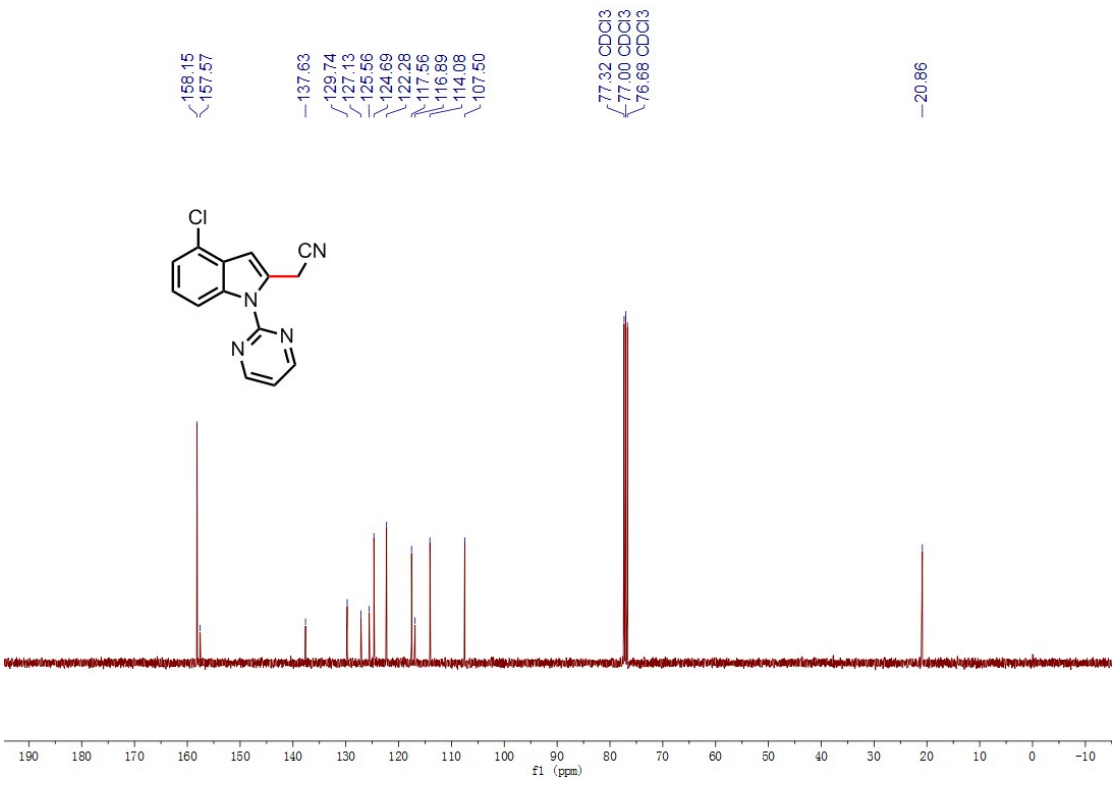
2-(4-fluoro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3f)



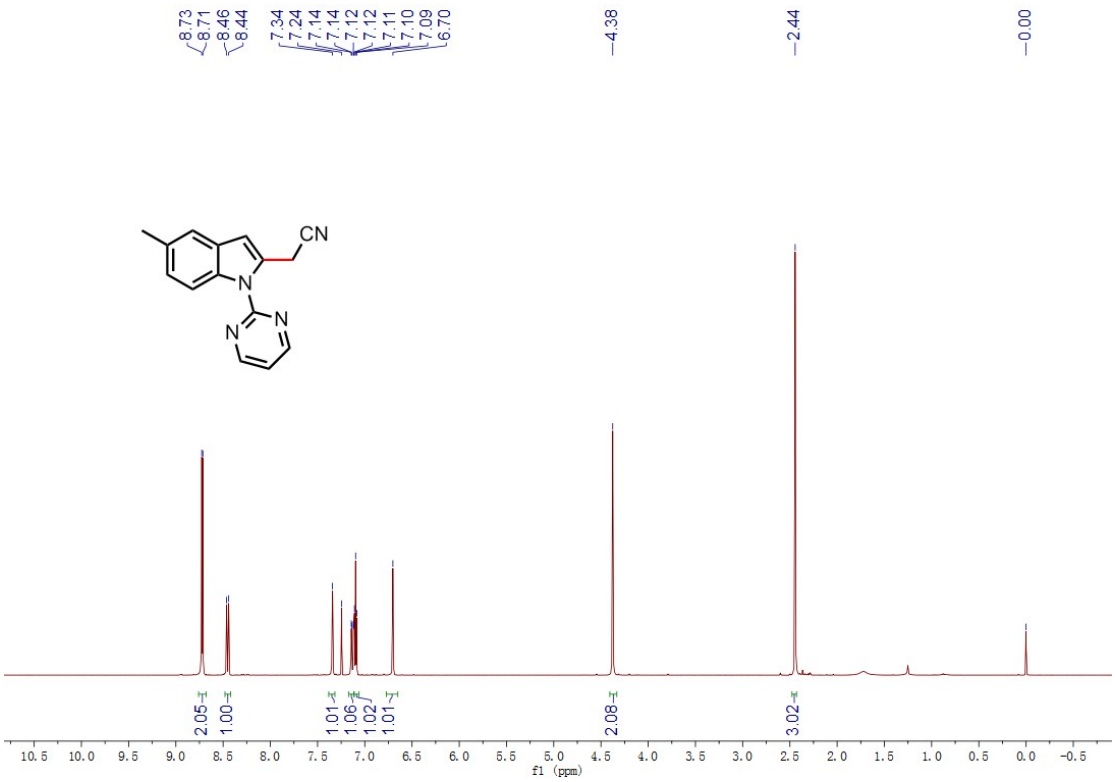


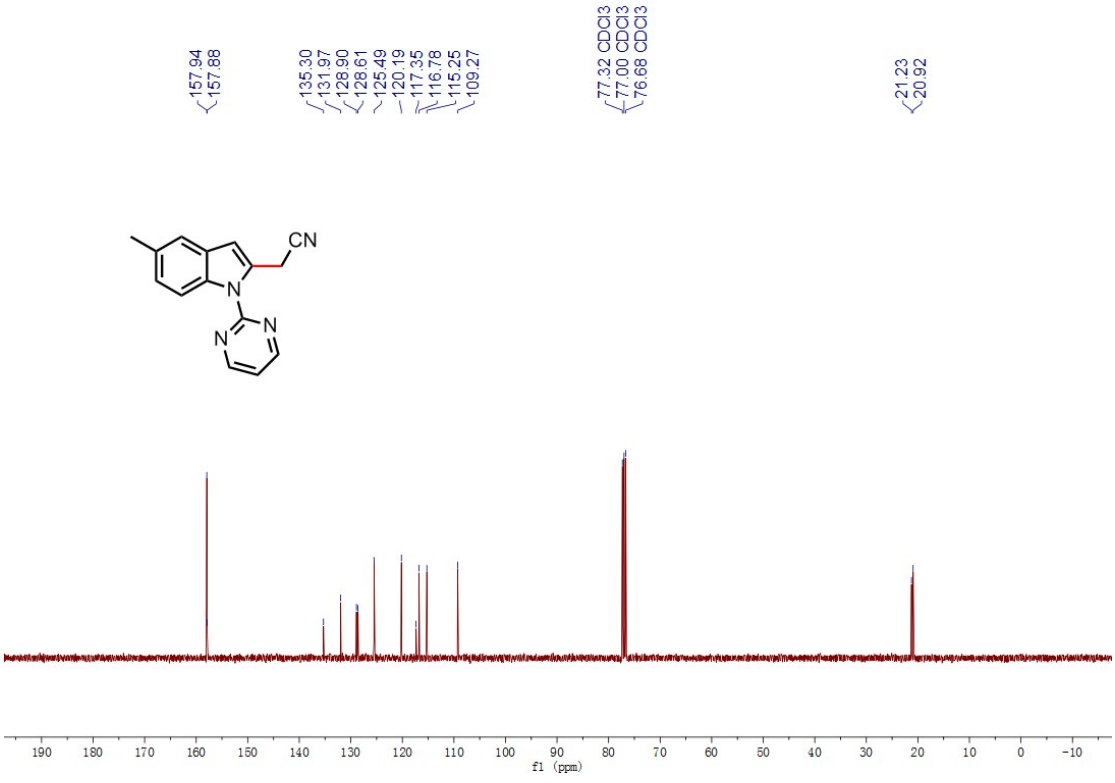
2-(4-chloro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3g)



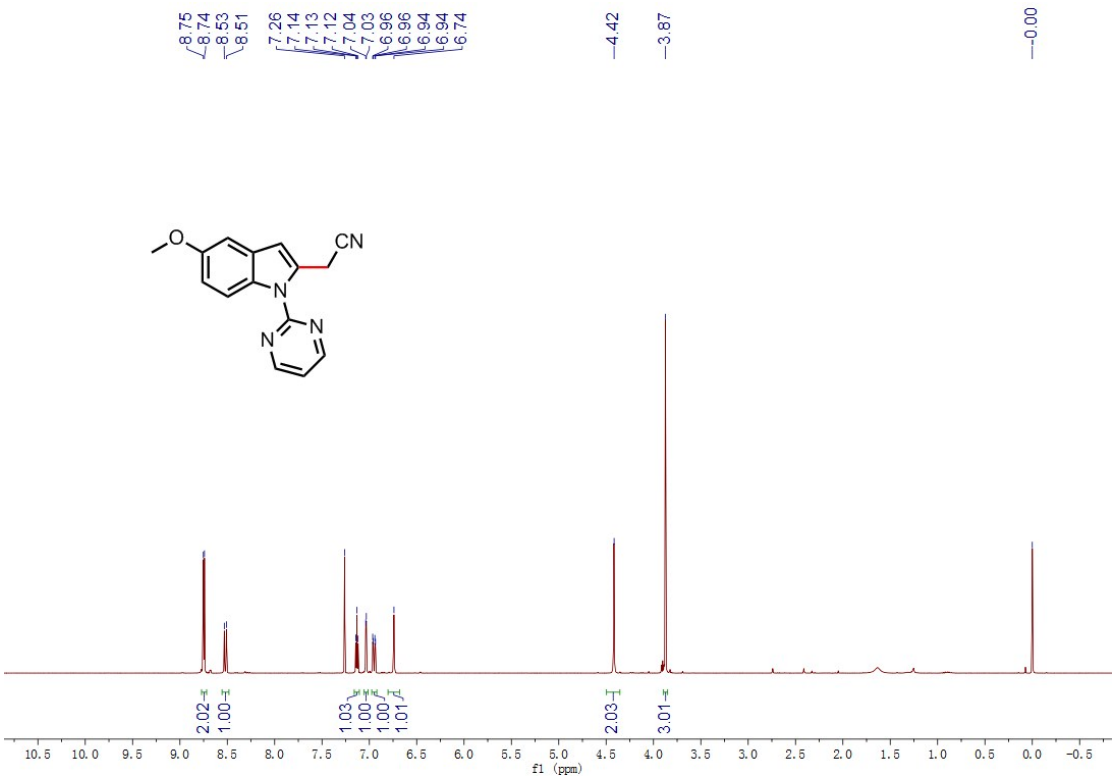


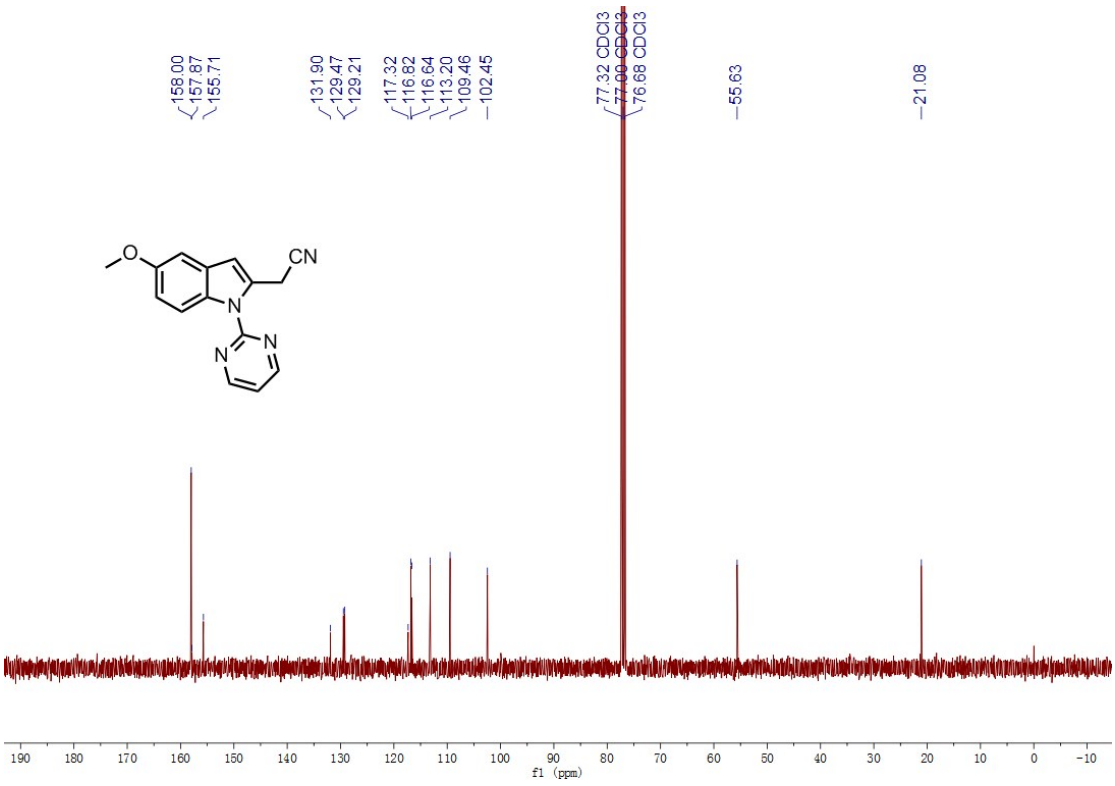
2-(5-methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3h)



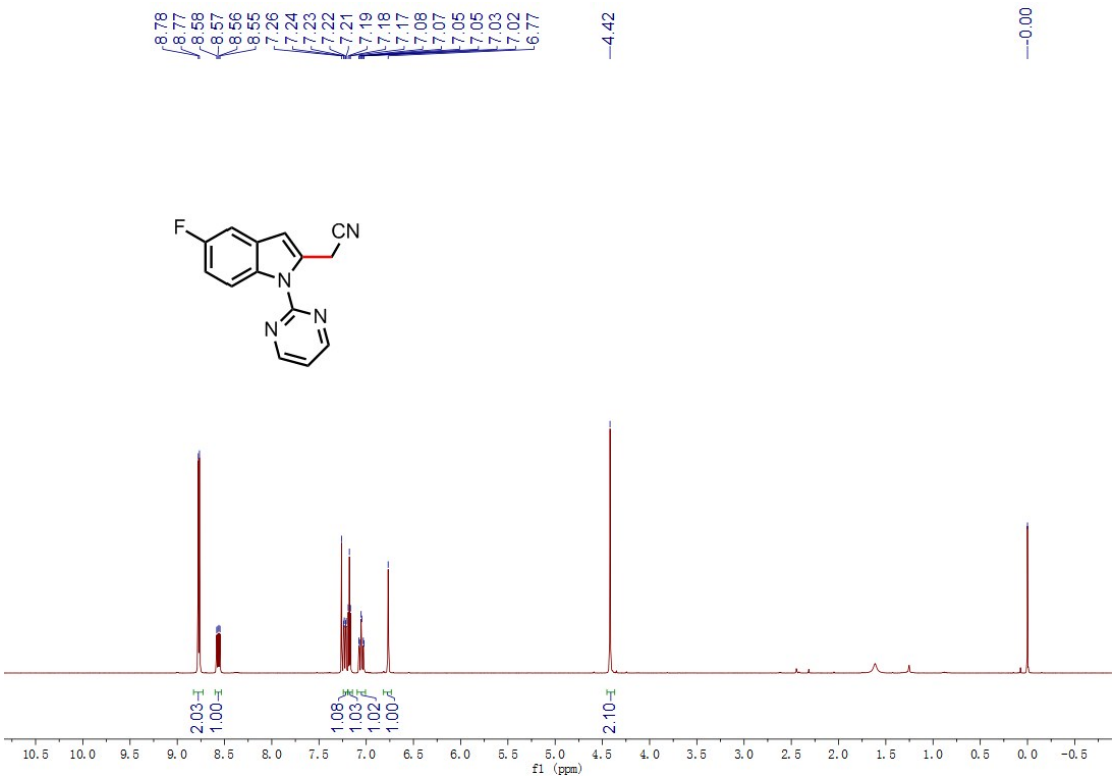


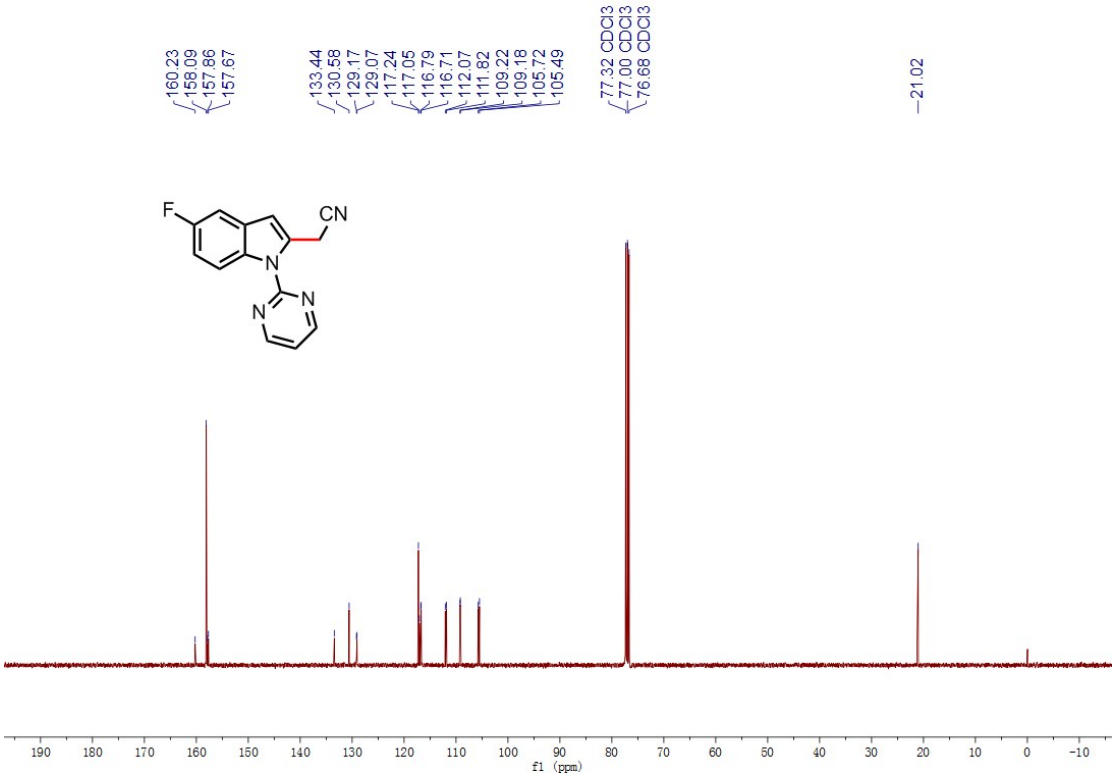
2-(5-methoxy-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3i)



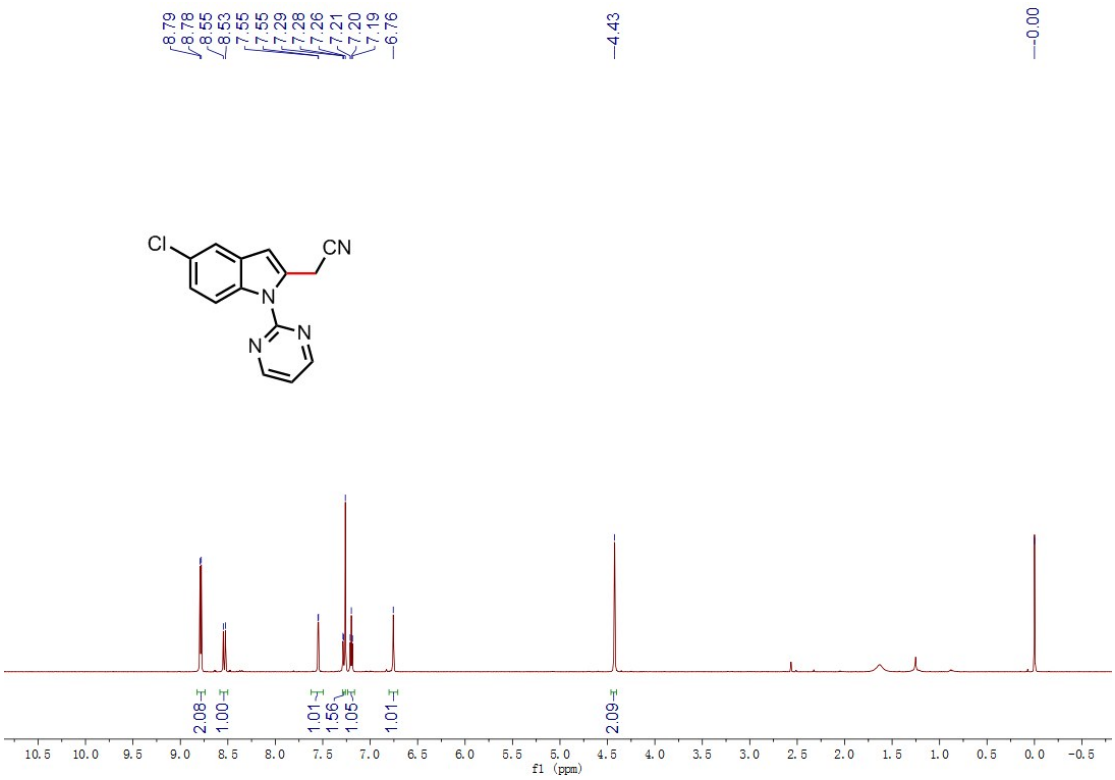


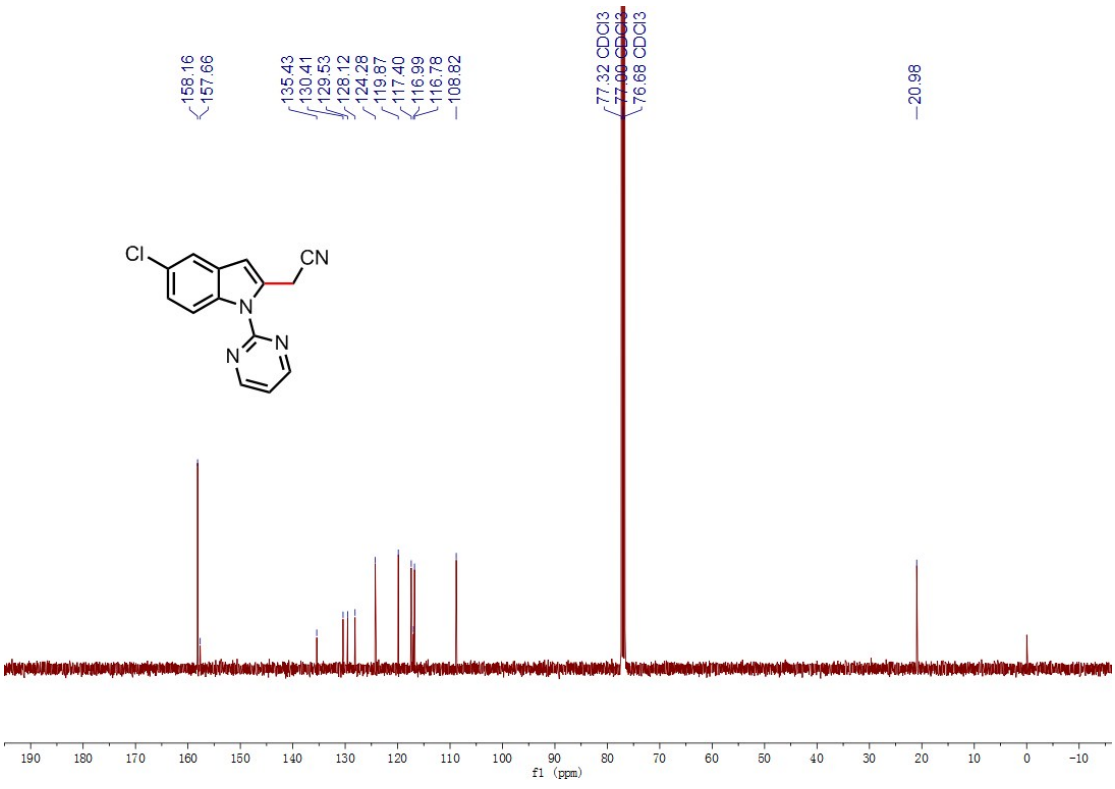
2-(5-fluoro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3j)



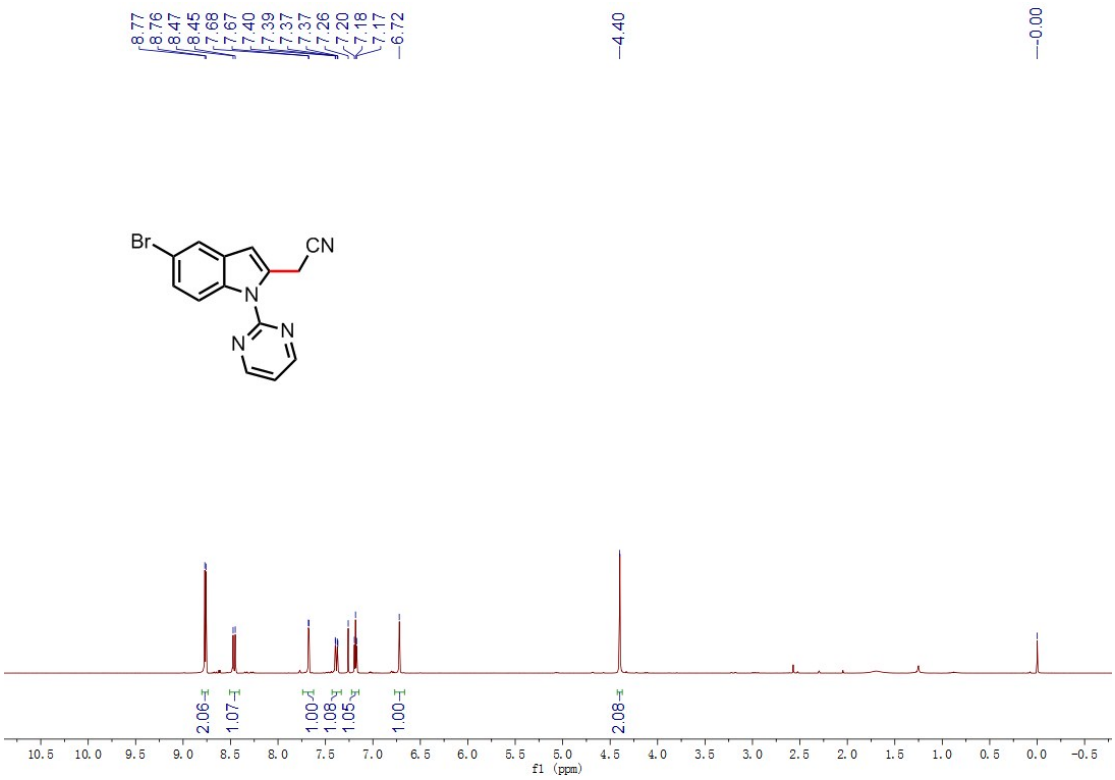


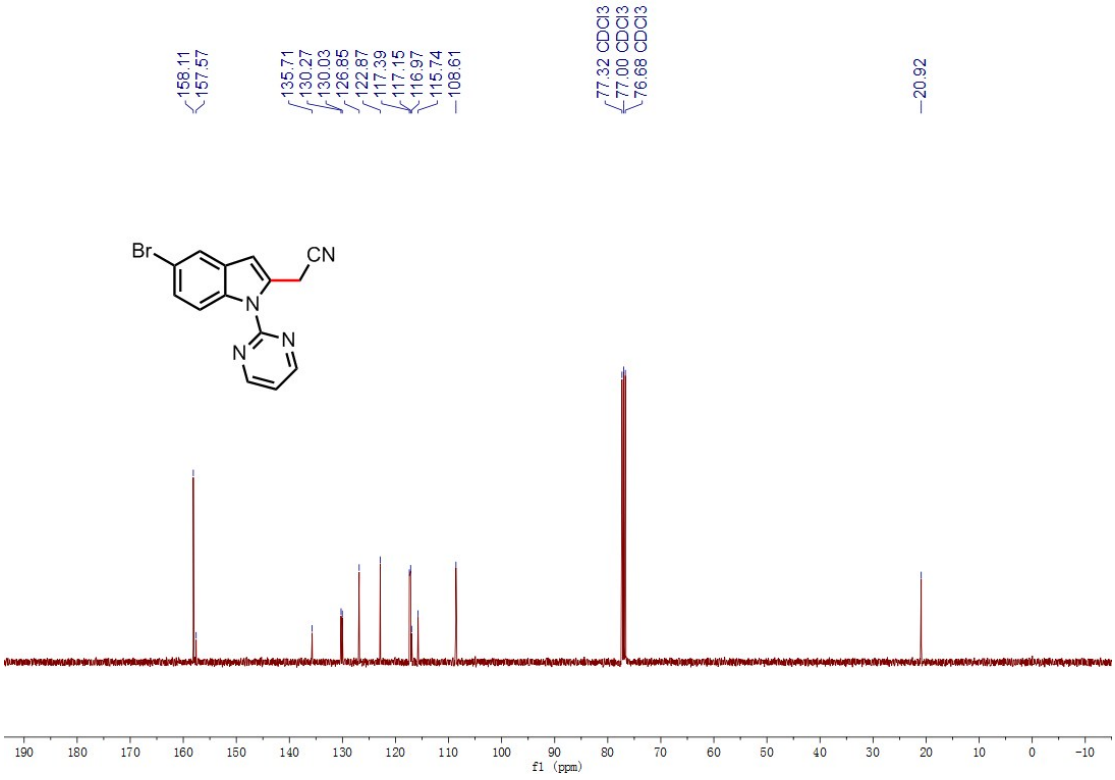
2-(5-chloro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3k)



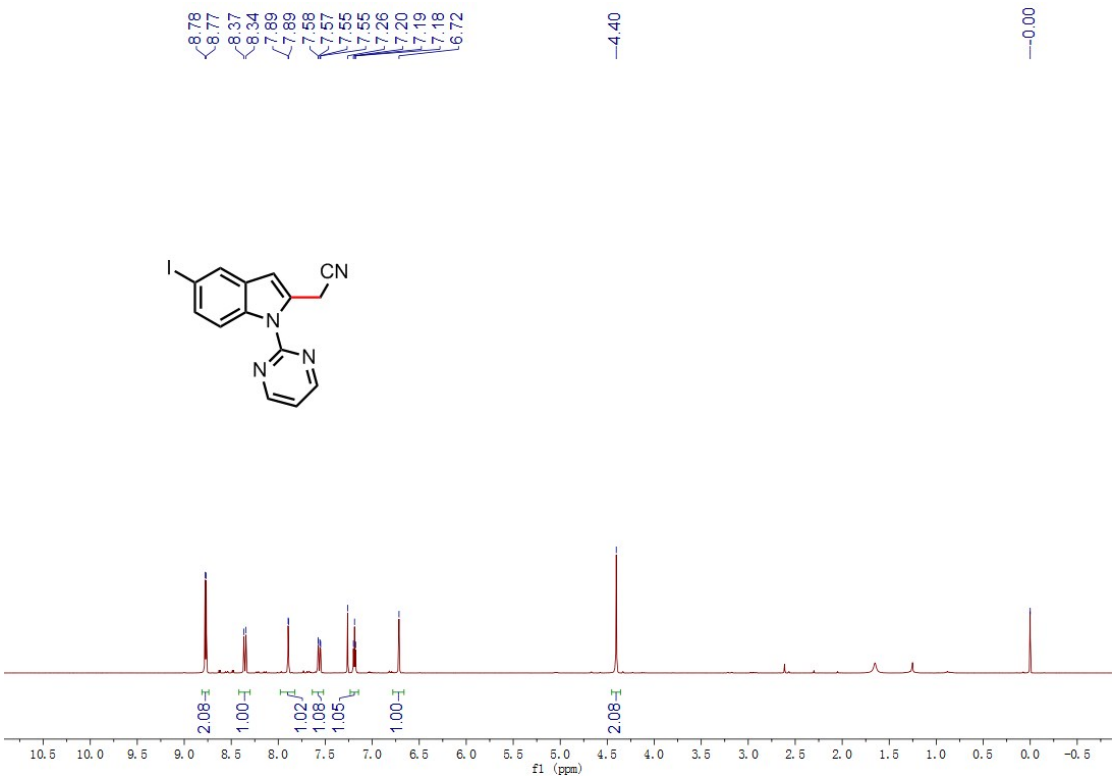


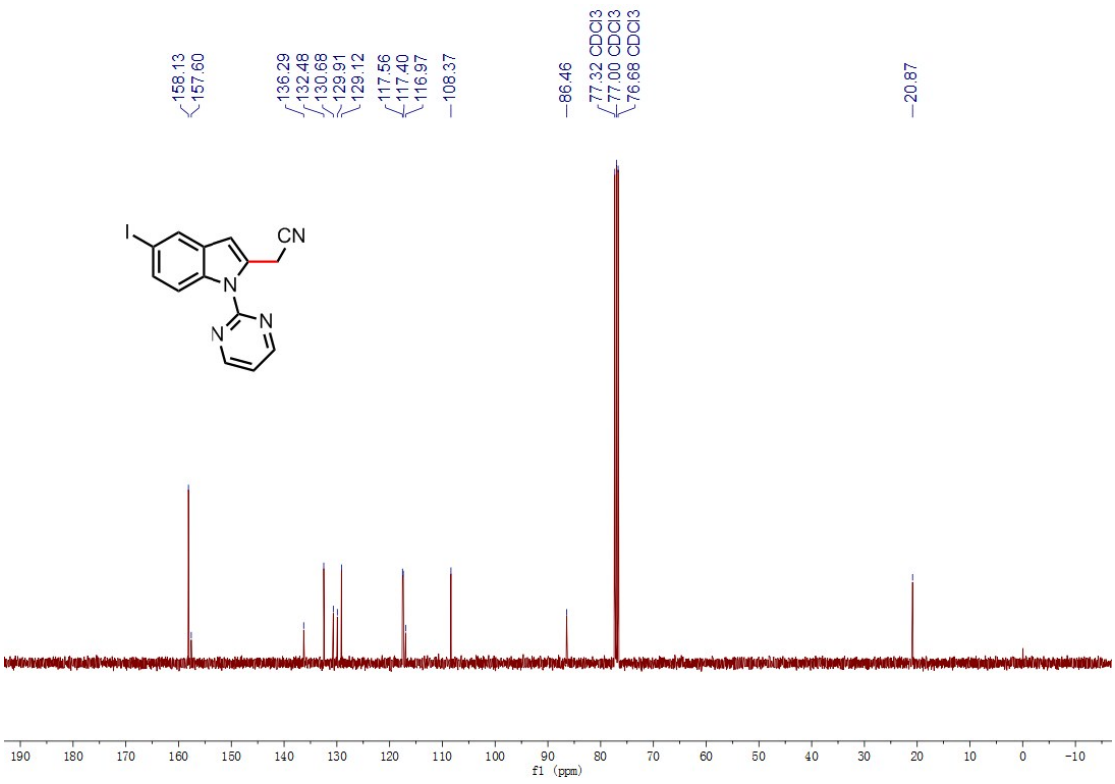
2-(5-bromo-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3l)



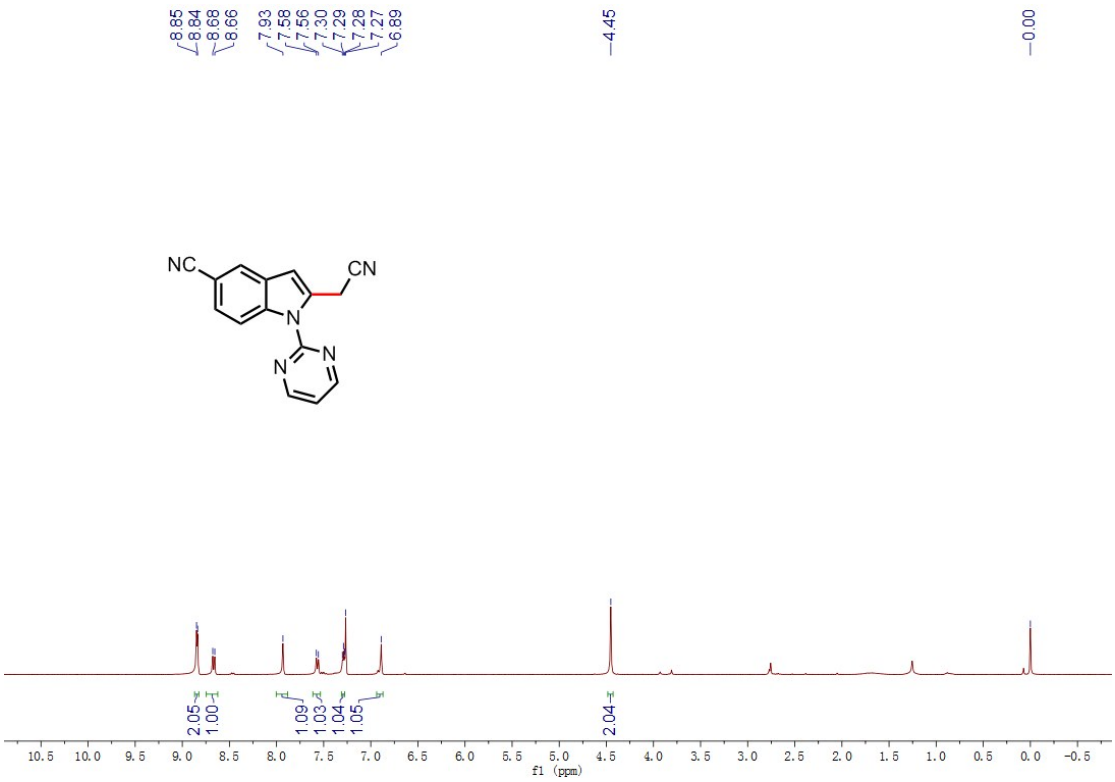


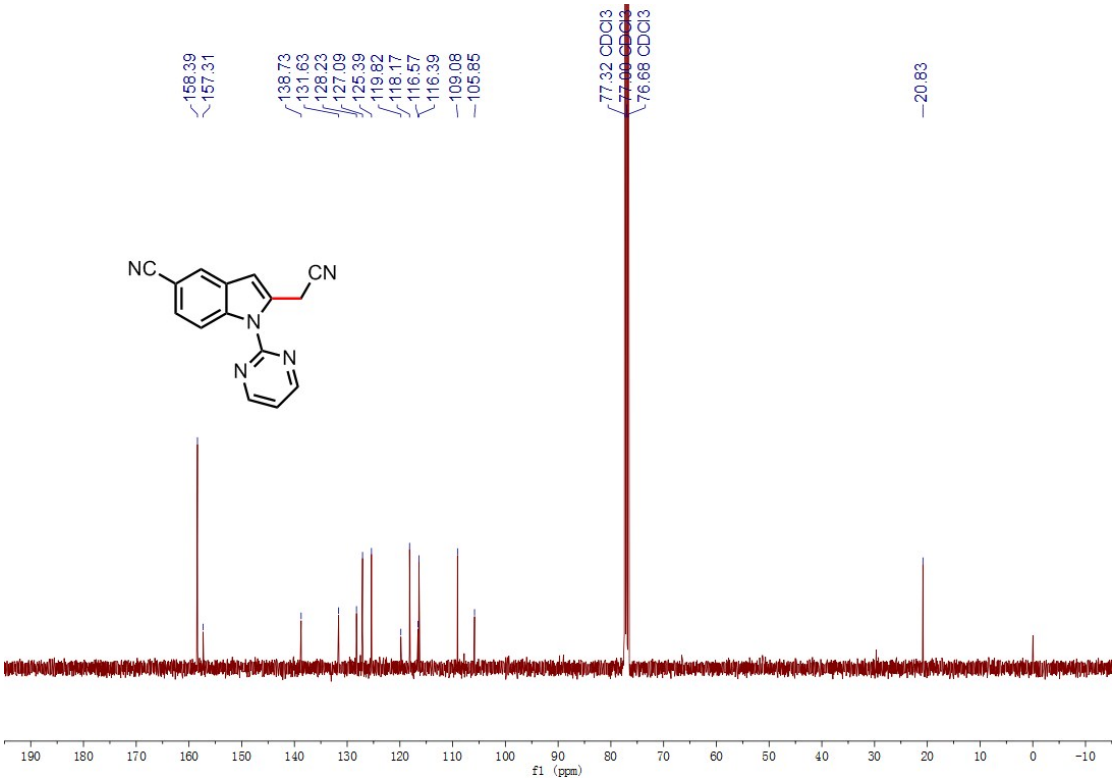
2-(5-iodo-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3m)



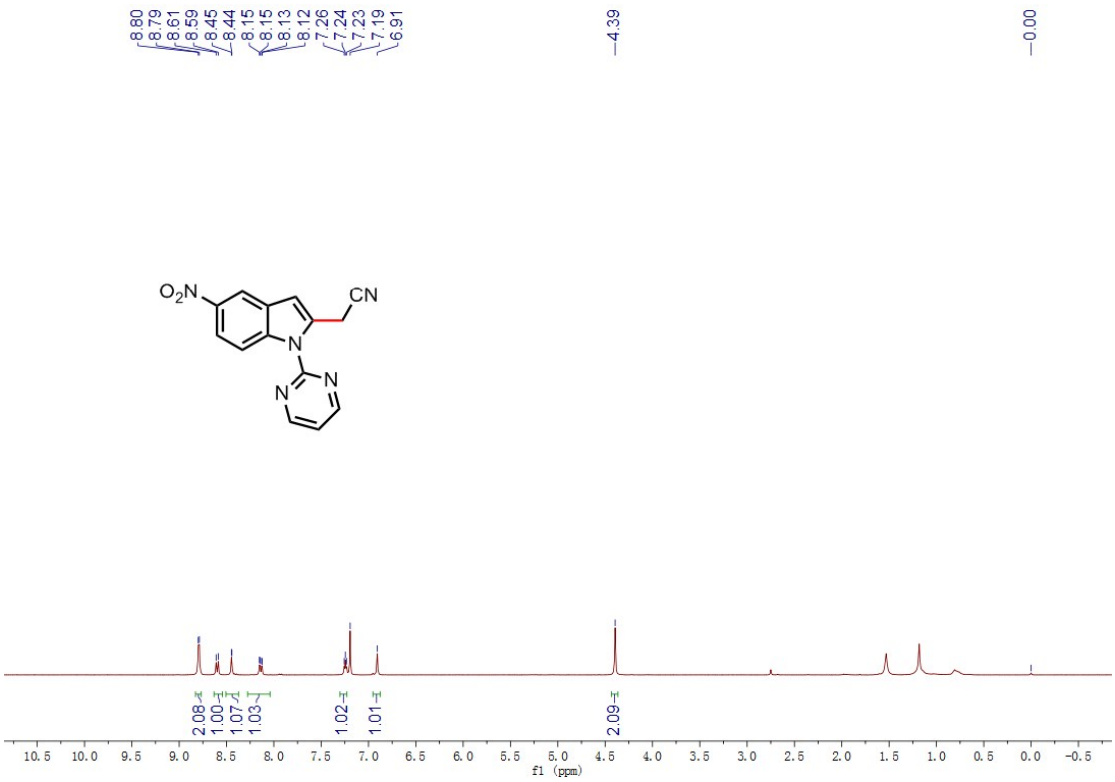


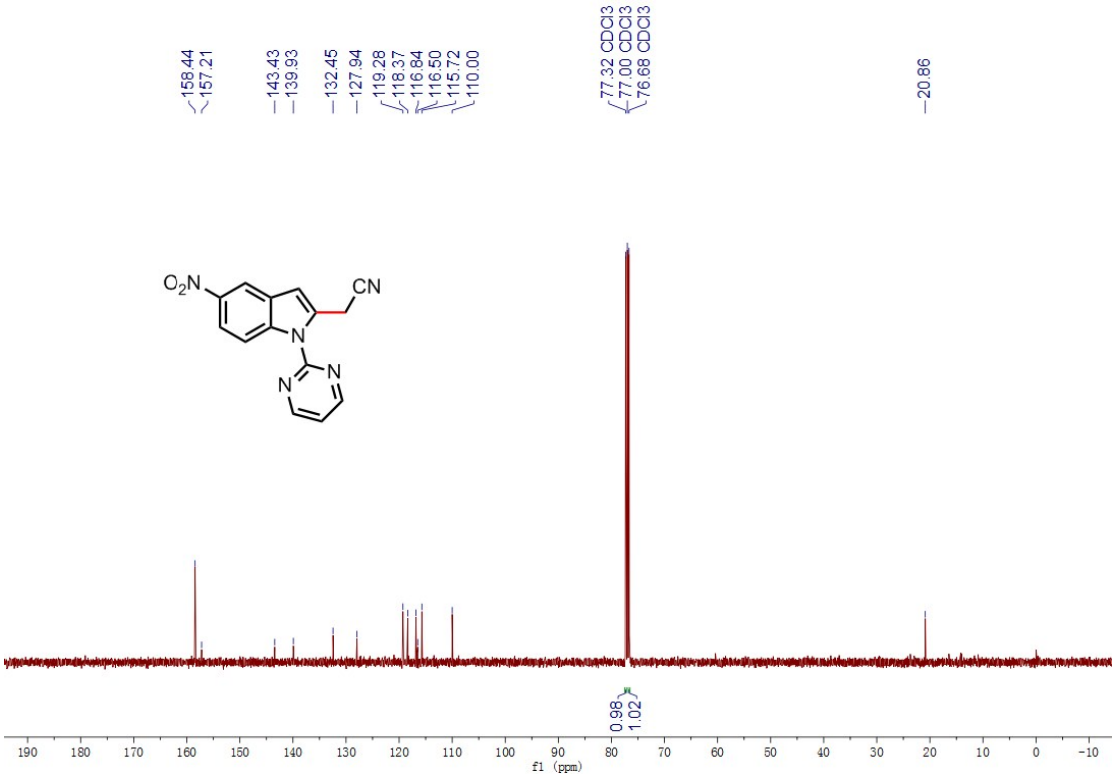
2-(cyanomethyl)-1-(pyrimidin-2-yl)-1H-indole-5-carbonitrile (3n)



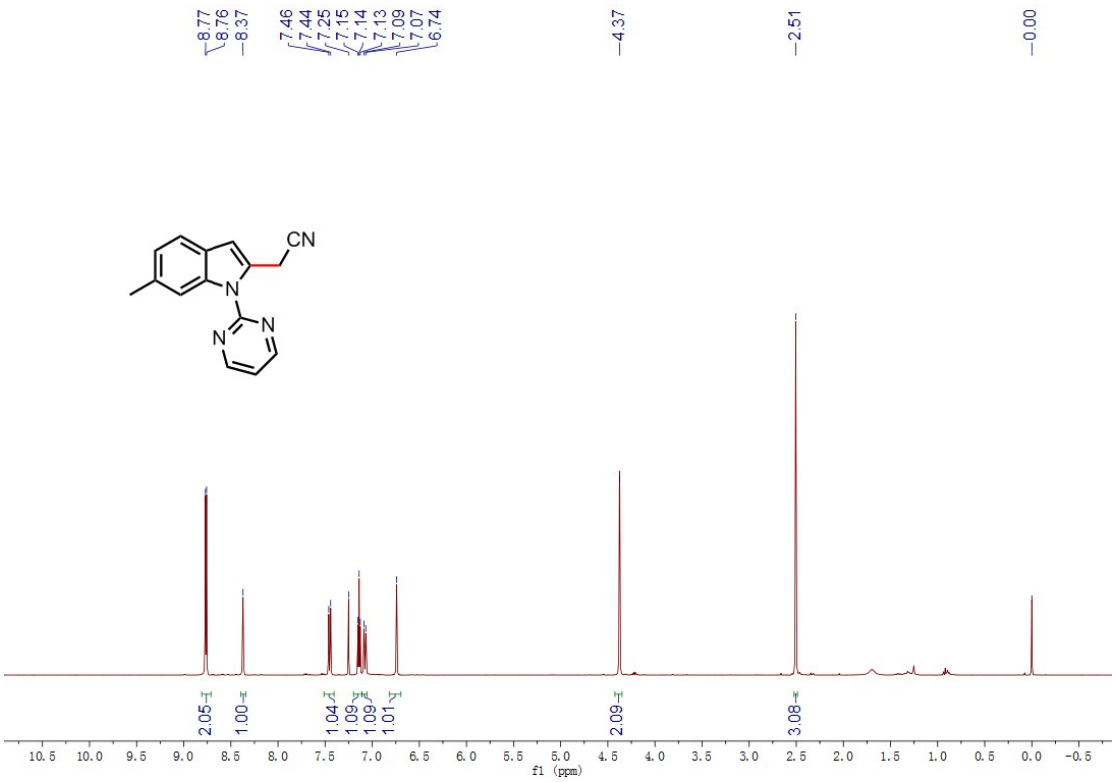


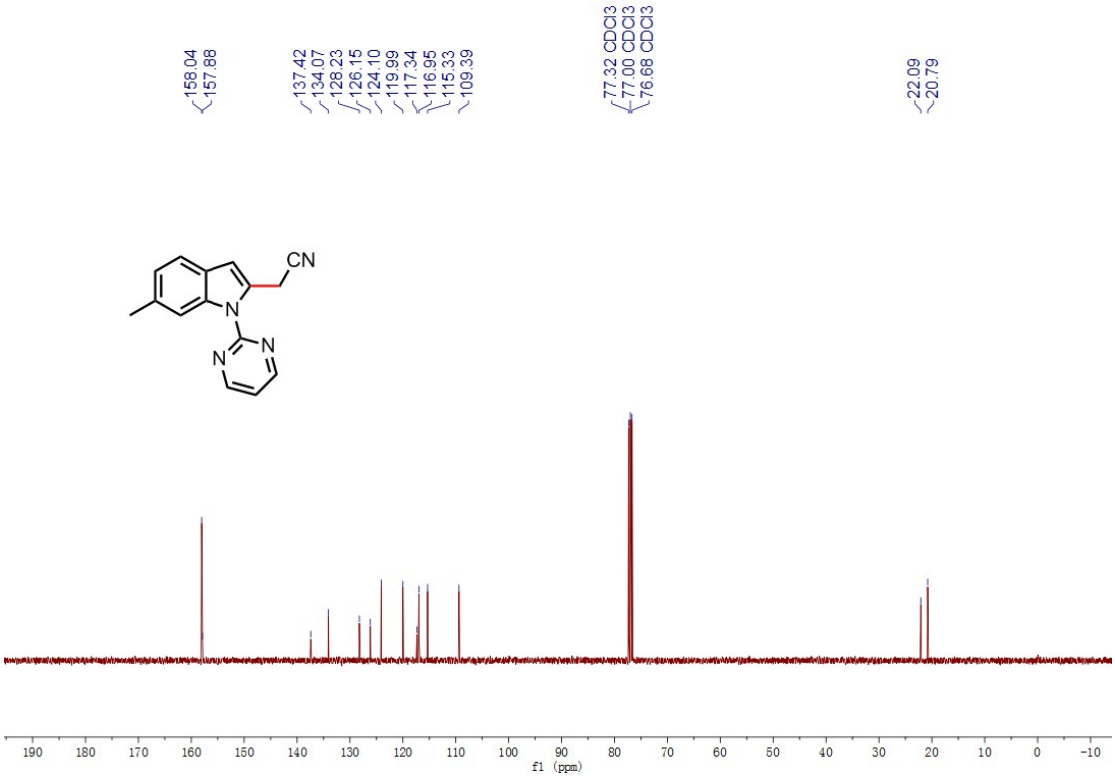
2-(5-nitro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3o)



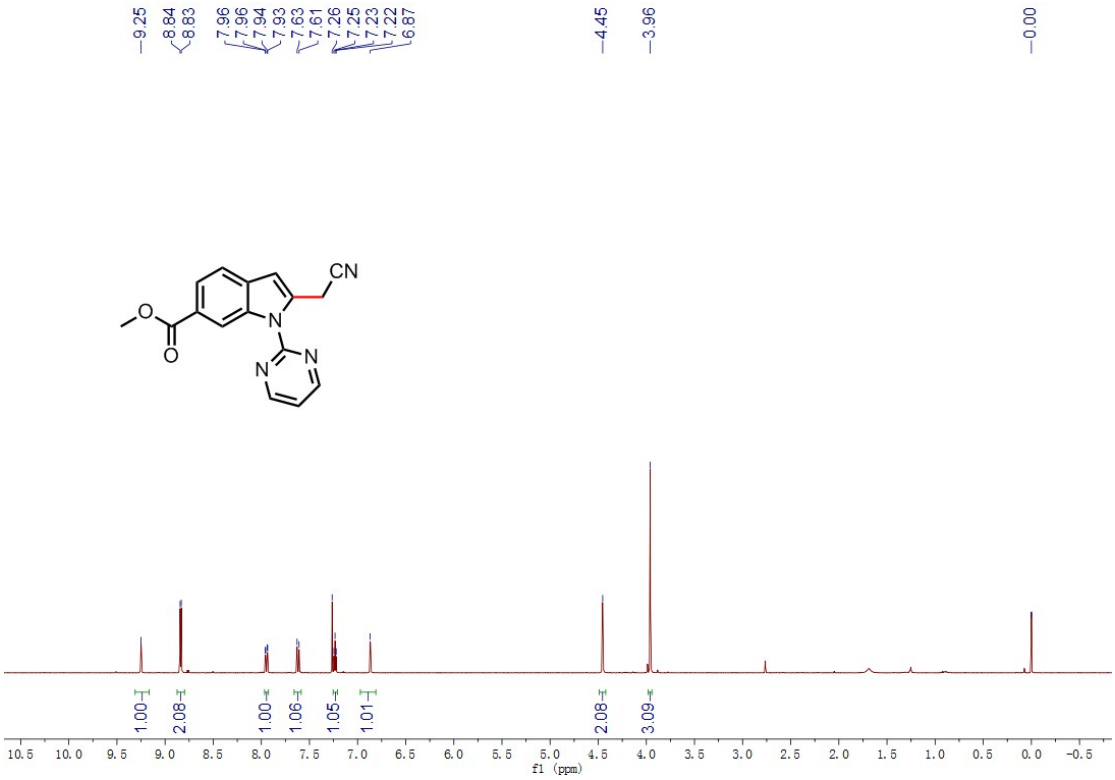


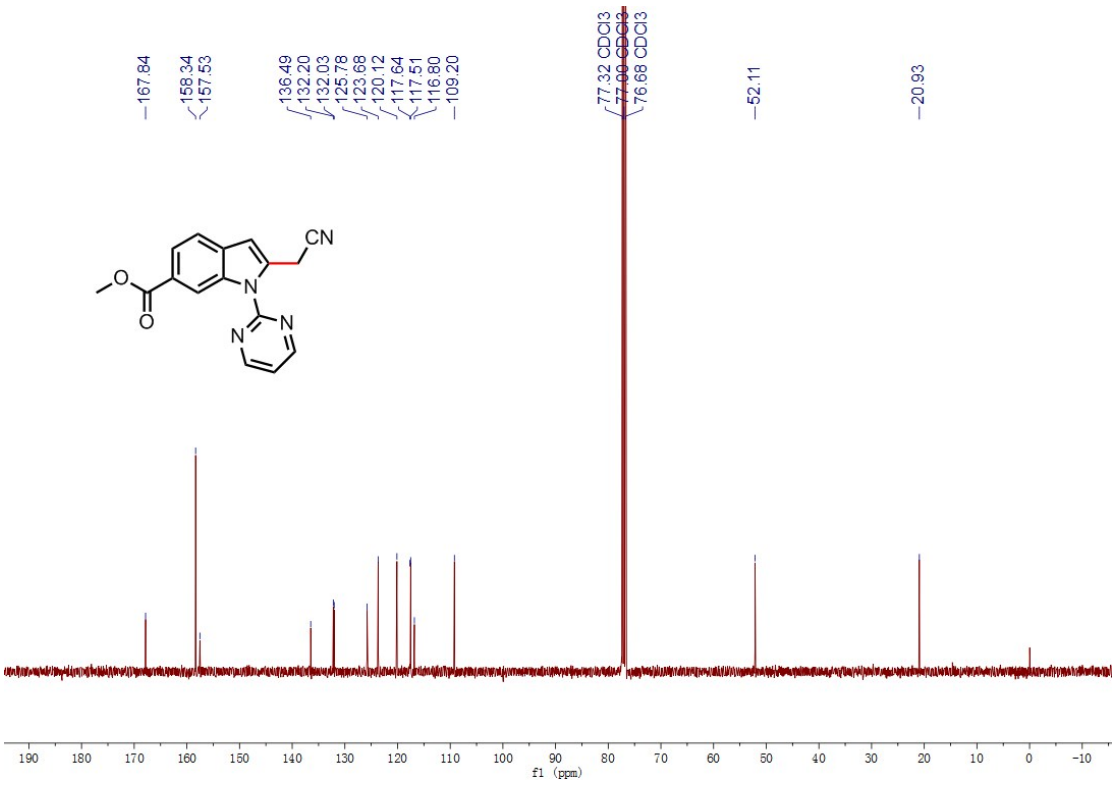
2-(6-methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3p)



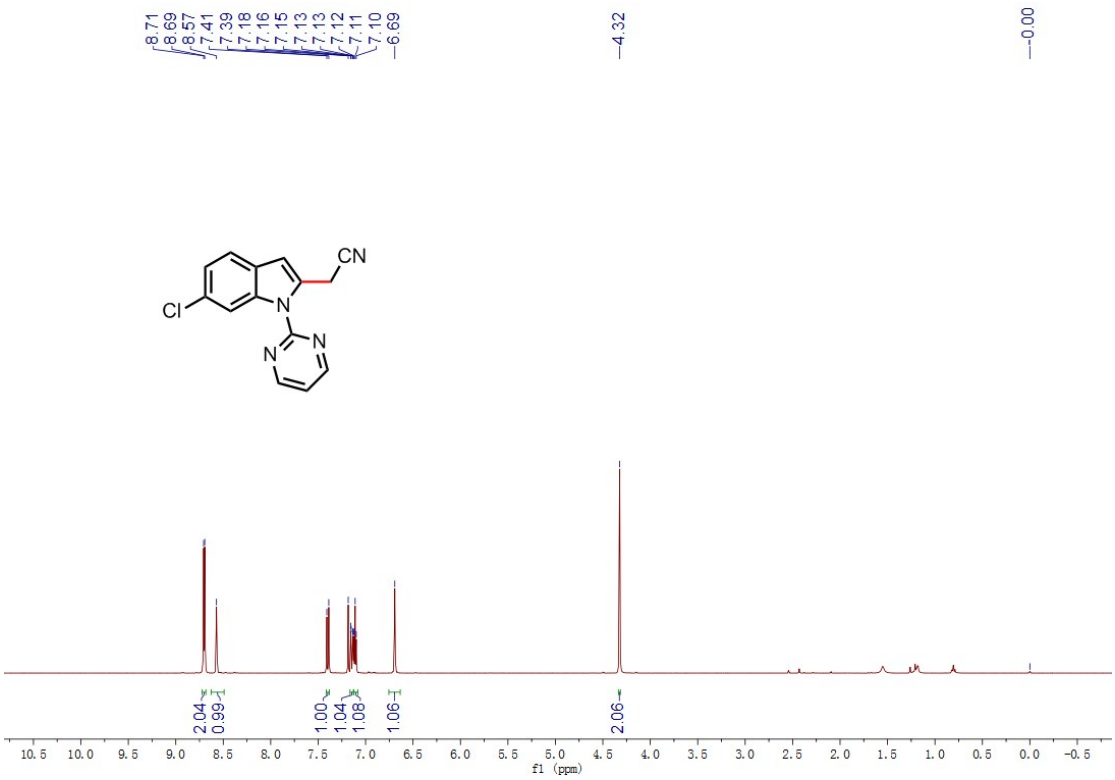


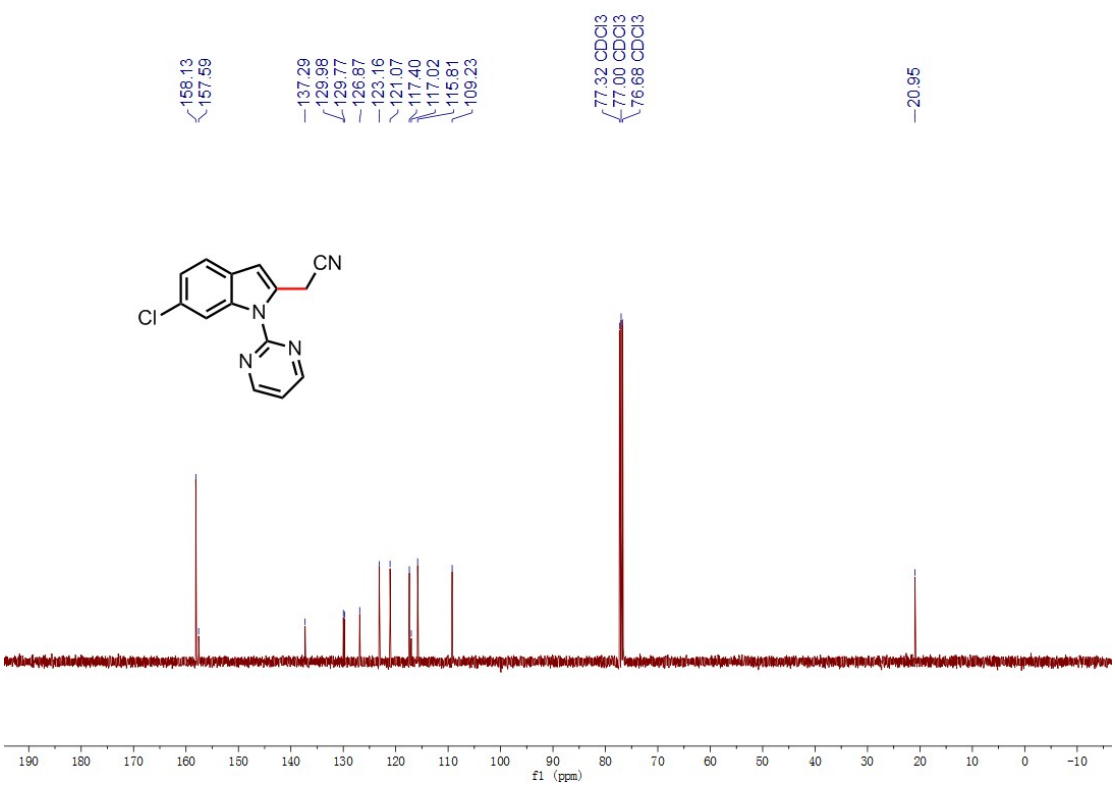
methyl 2-(cyanomethyl)-1-(pyrimidin-2-yl)-1H-indole-6-carboxylate (3q)



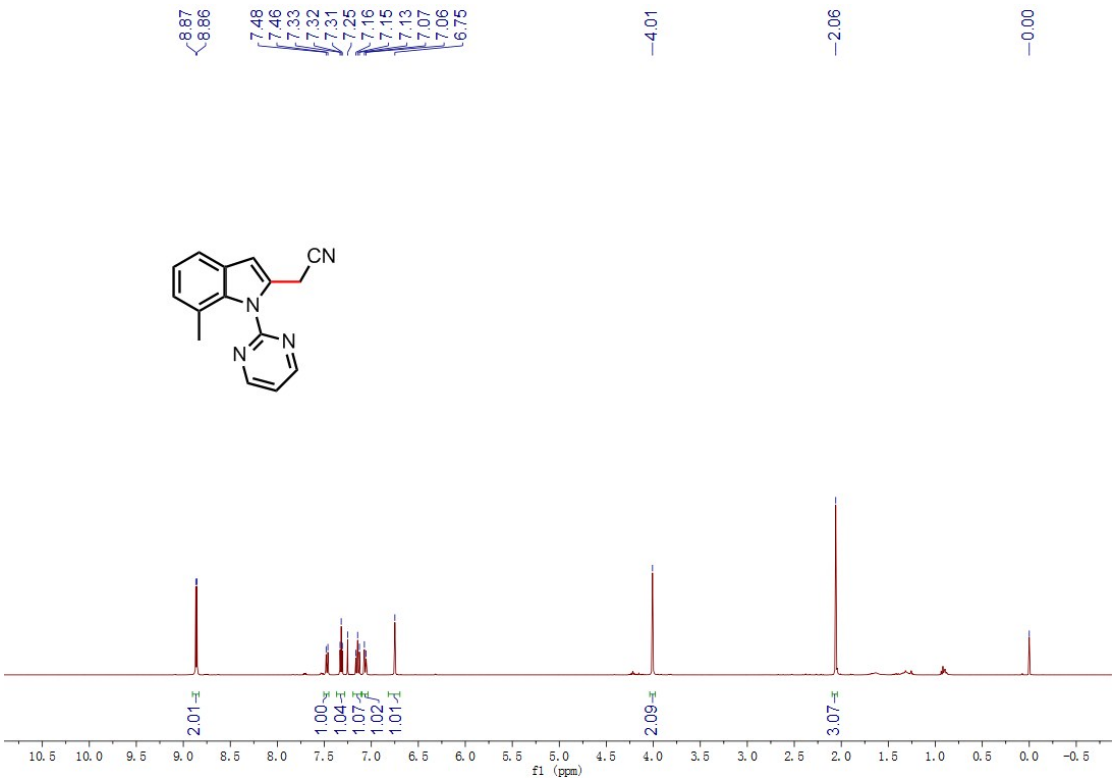


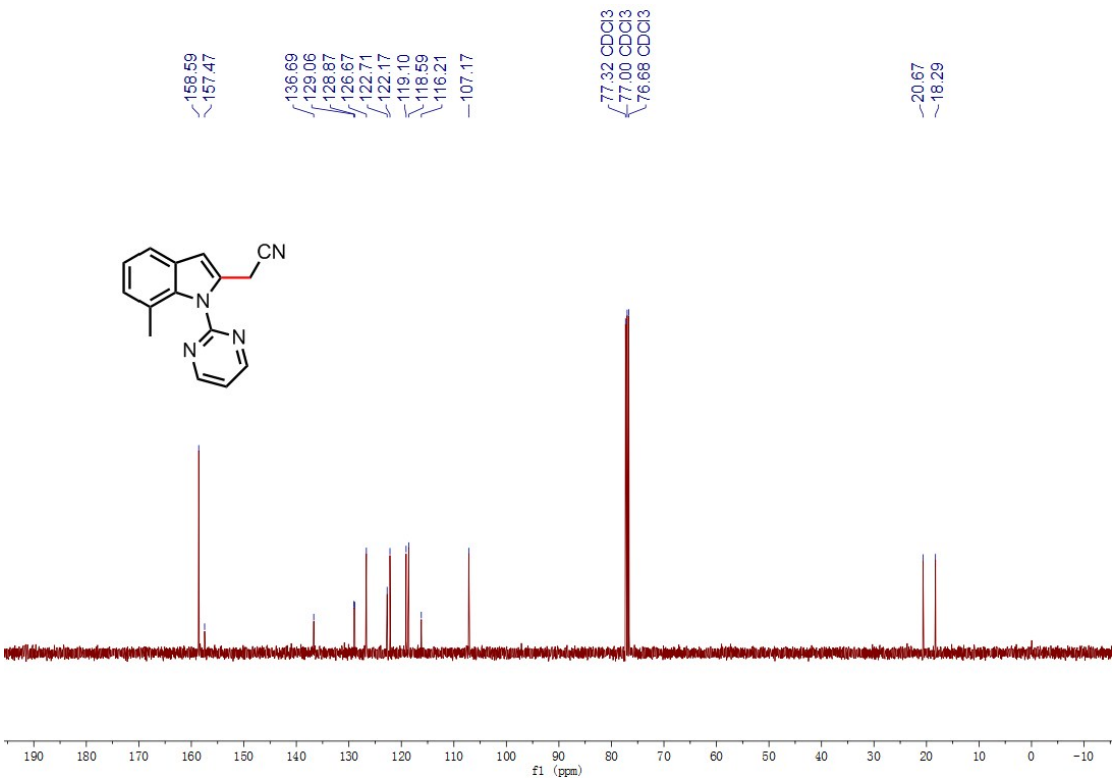
2-(6-chloro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3r)



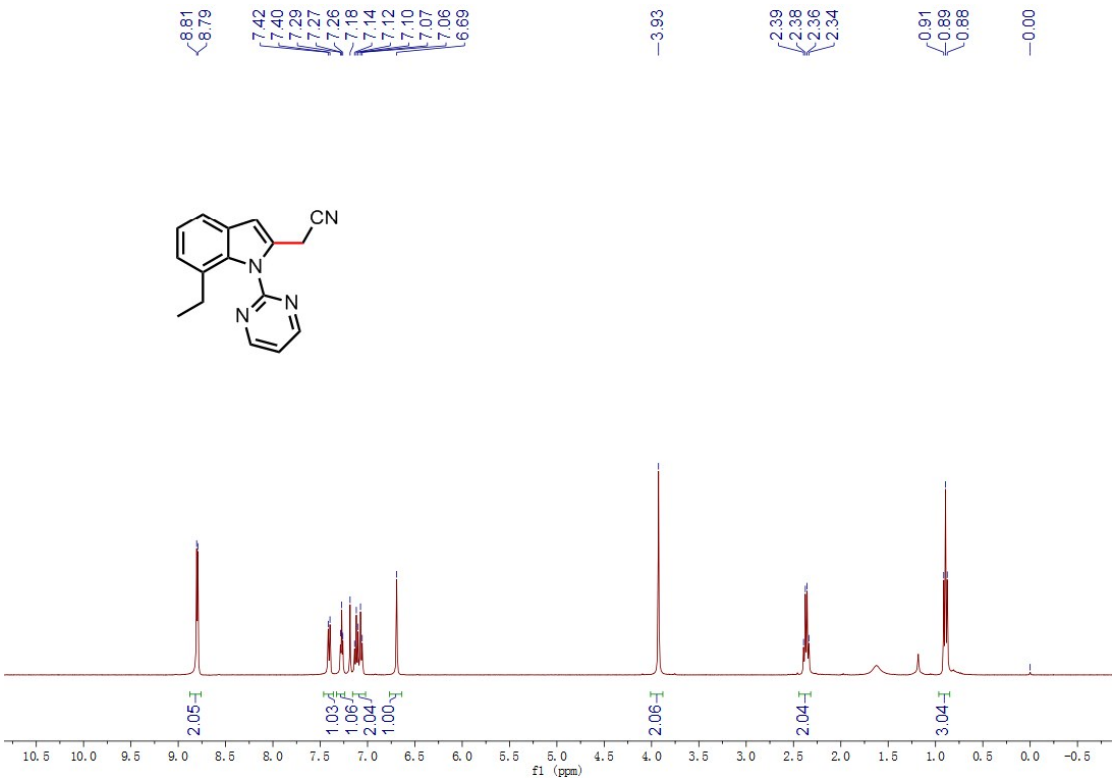


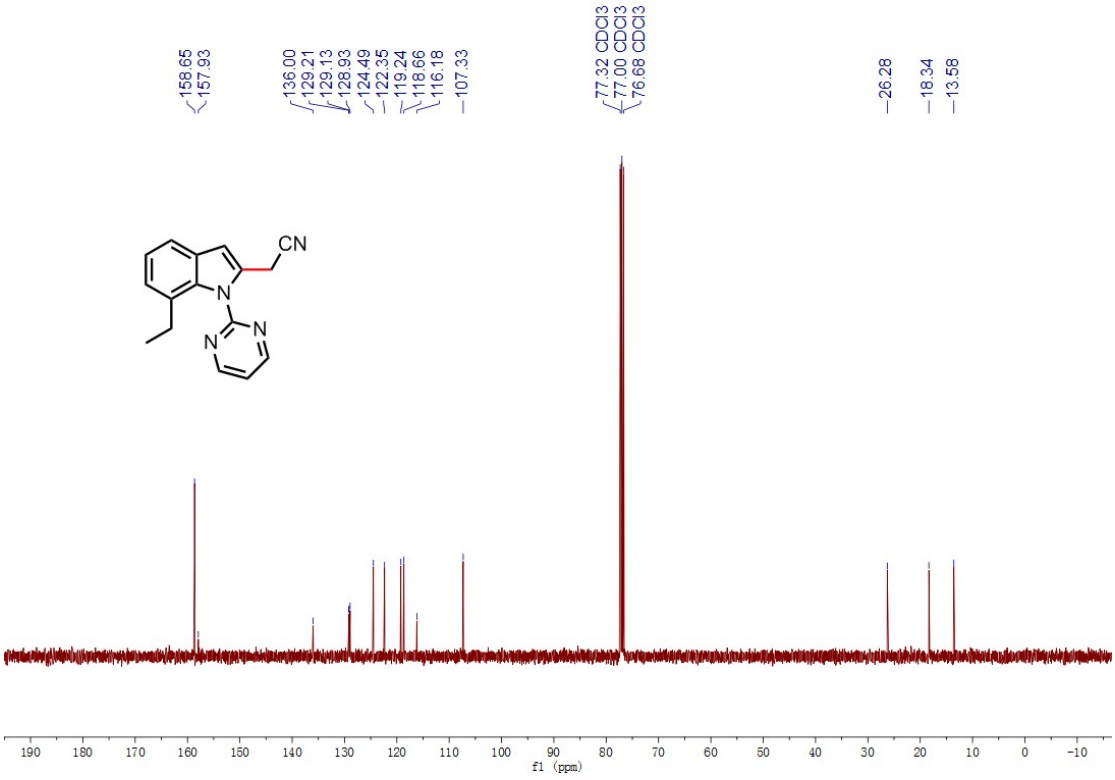
2-(7-methyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3s)



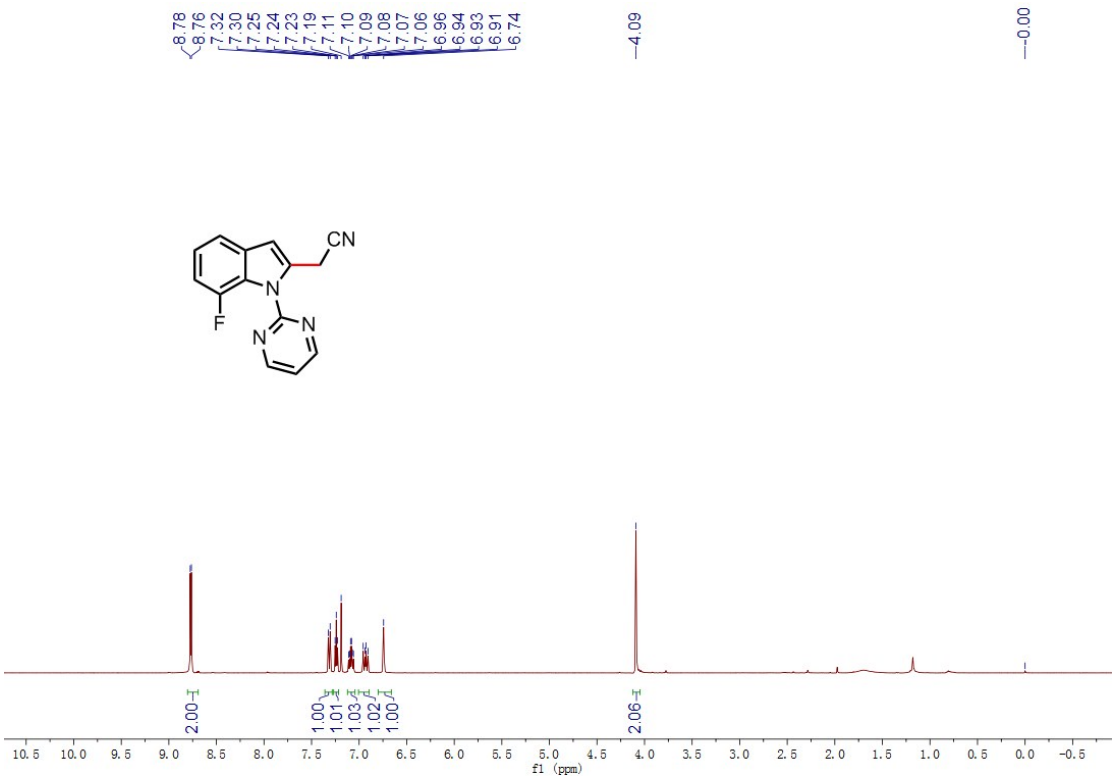


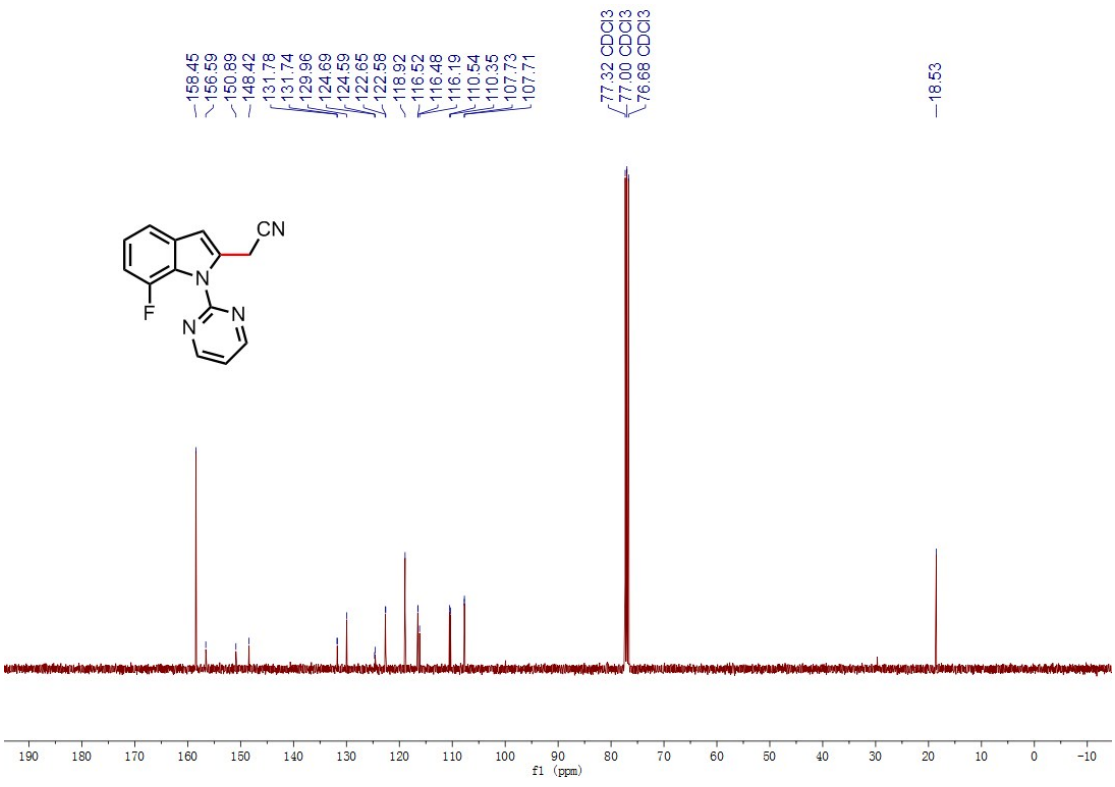
2-(7-ethyl-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3t)



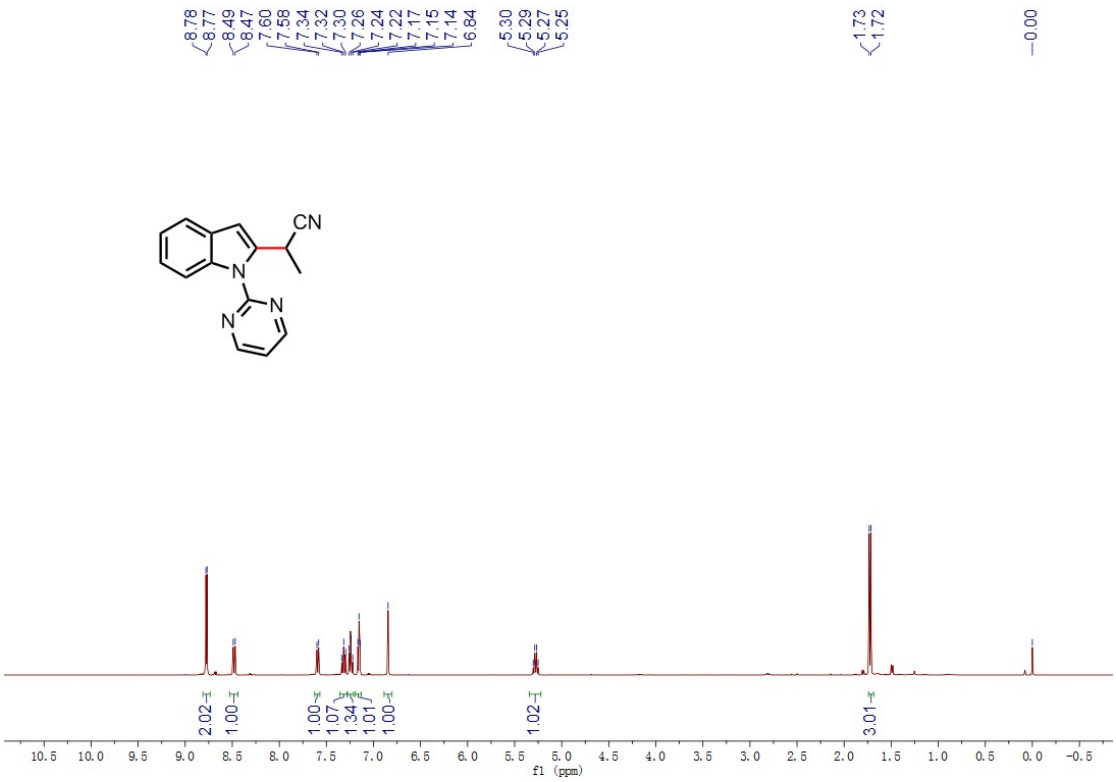


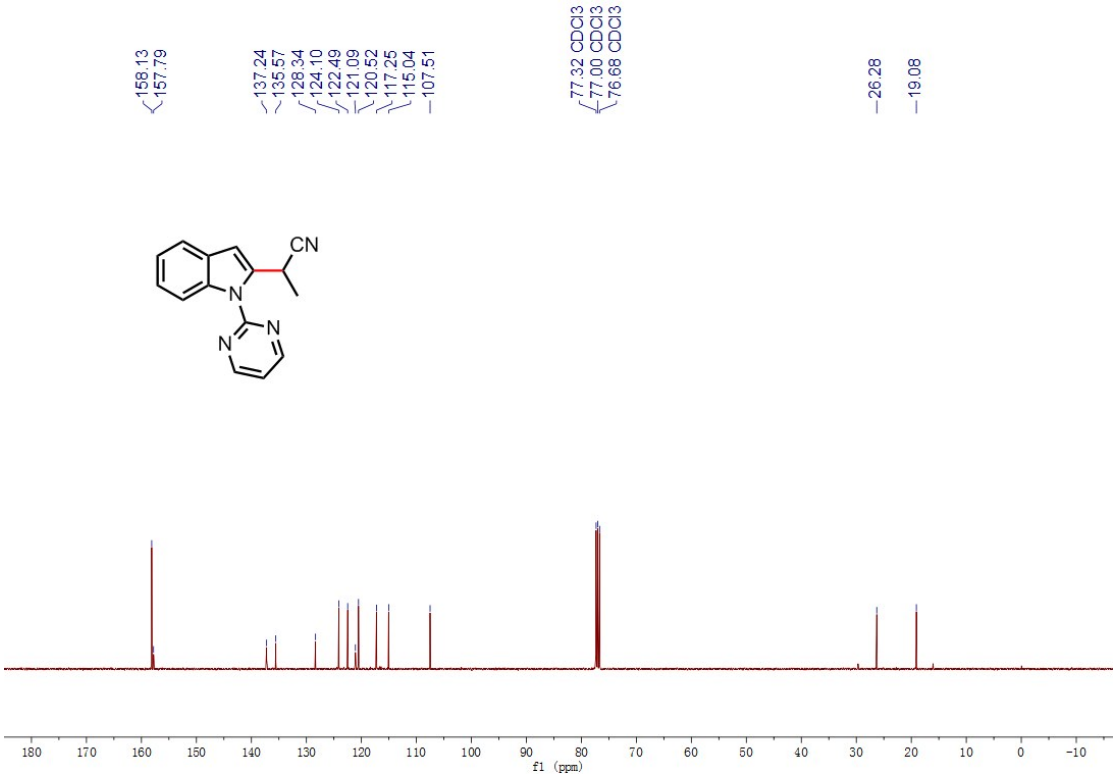
2-(7-fluoro-1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile (3u)



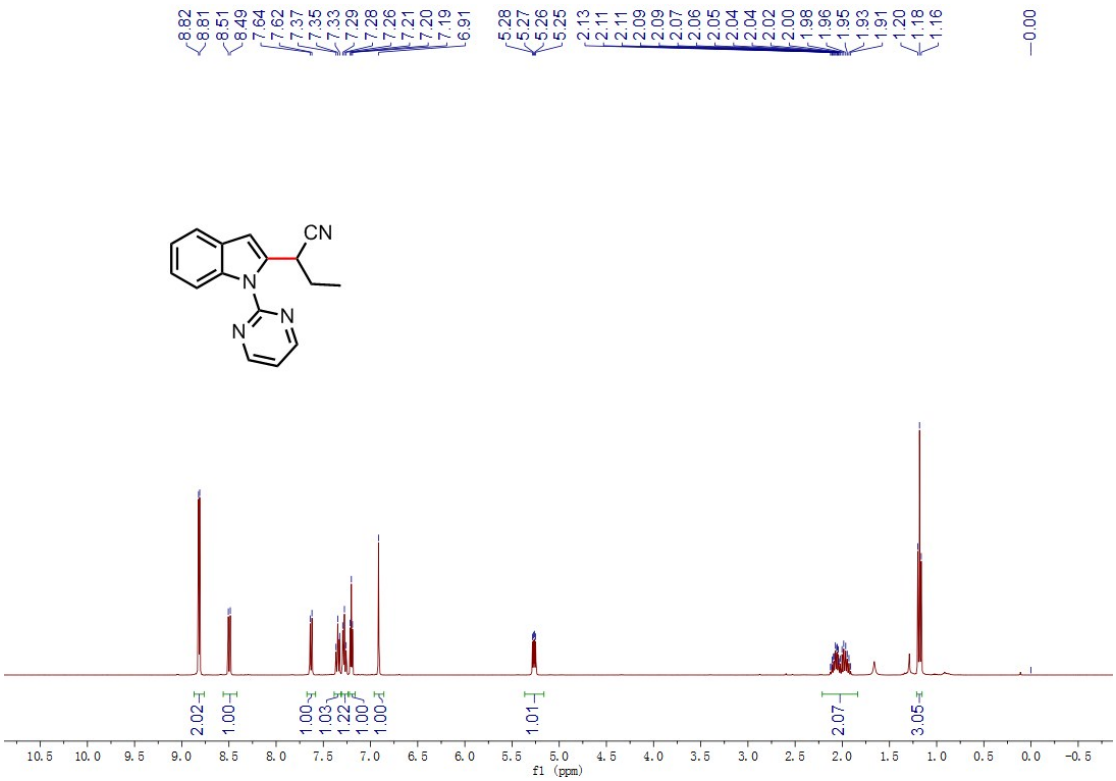


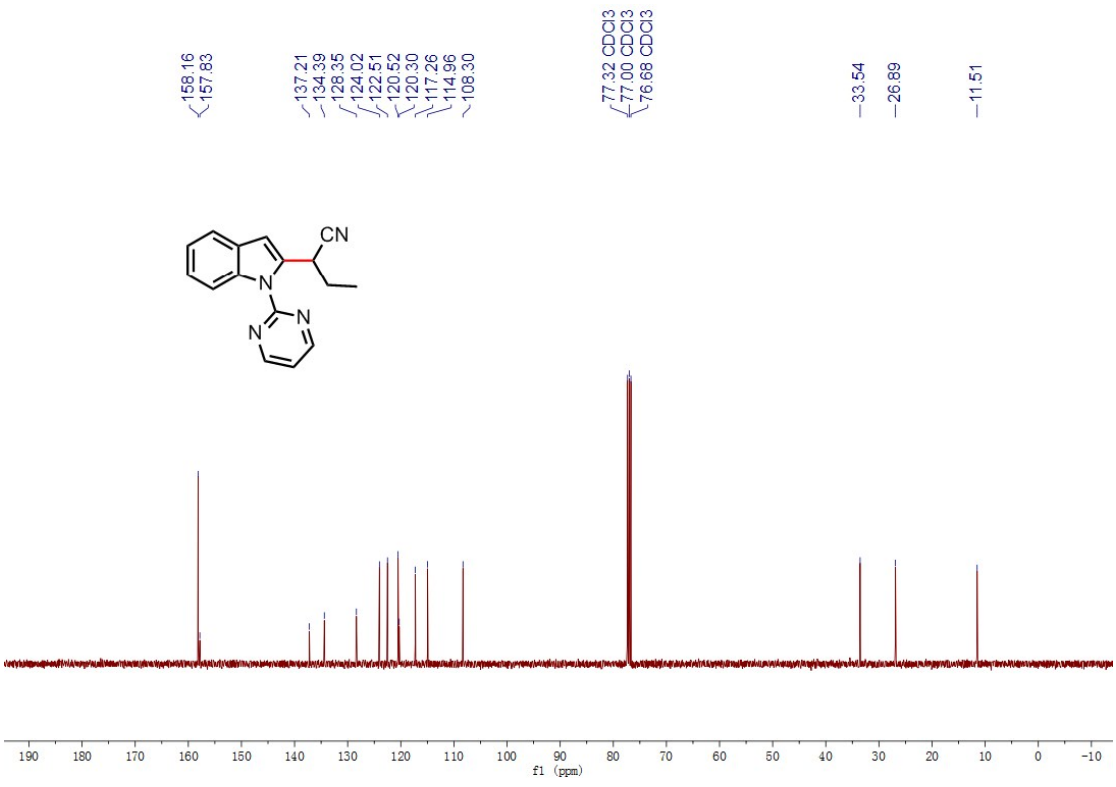
2-(1-(pyrimidin-2-yl)-1H-indol-2-yl)propanenitrile (3v)



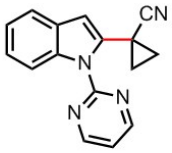


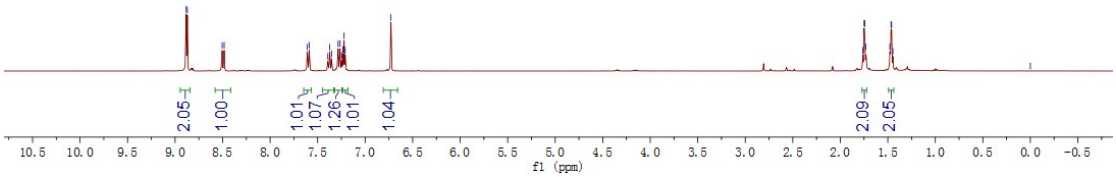
2-(1-(pyrimidin-2-yl)-1H-indol-2-yl)butanenitrile (3w)

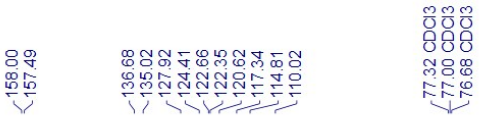


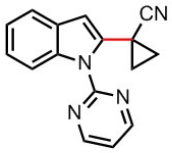


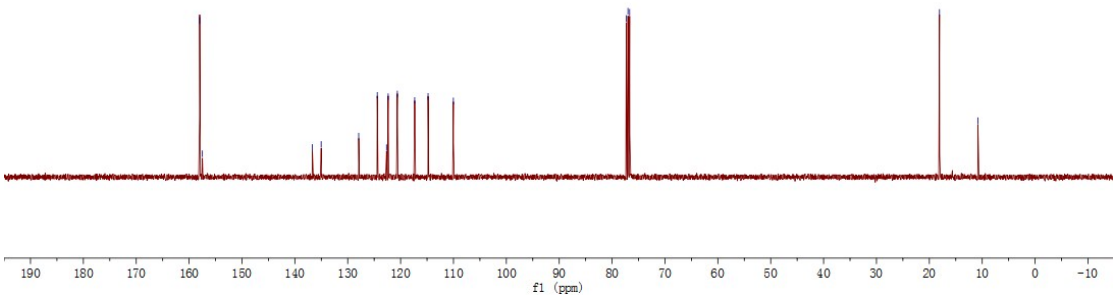
1-(1-(pyrimidin-2-yl)-1H-indol-2-yl)cyclopropane-1-carbonitrile (3x)



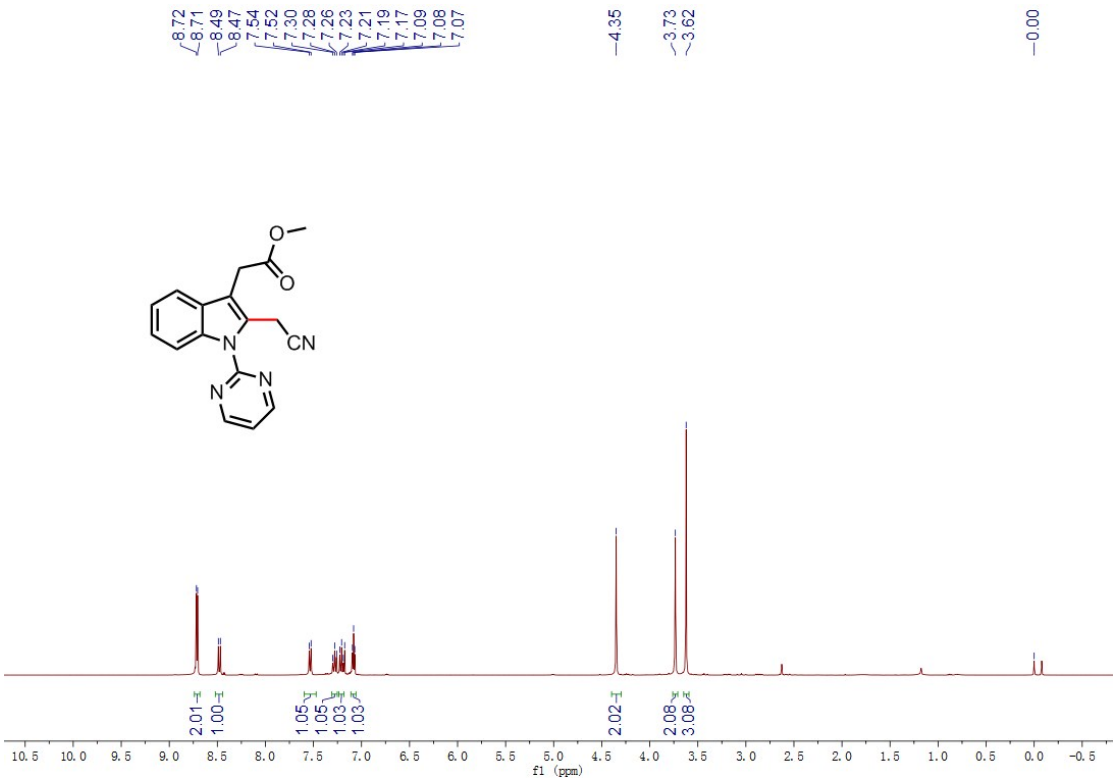


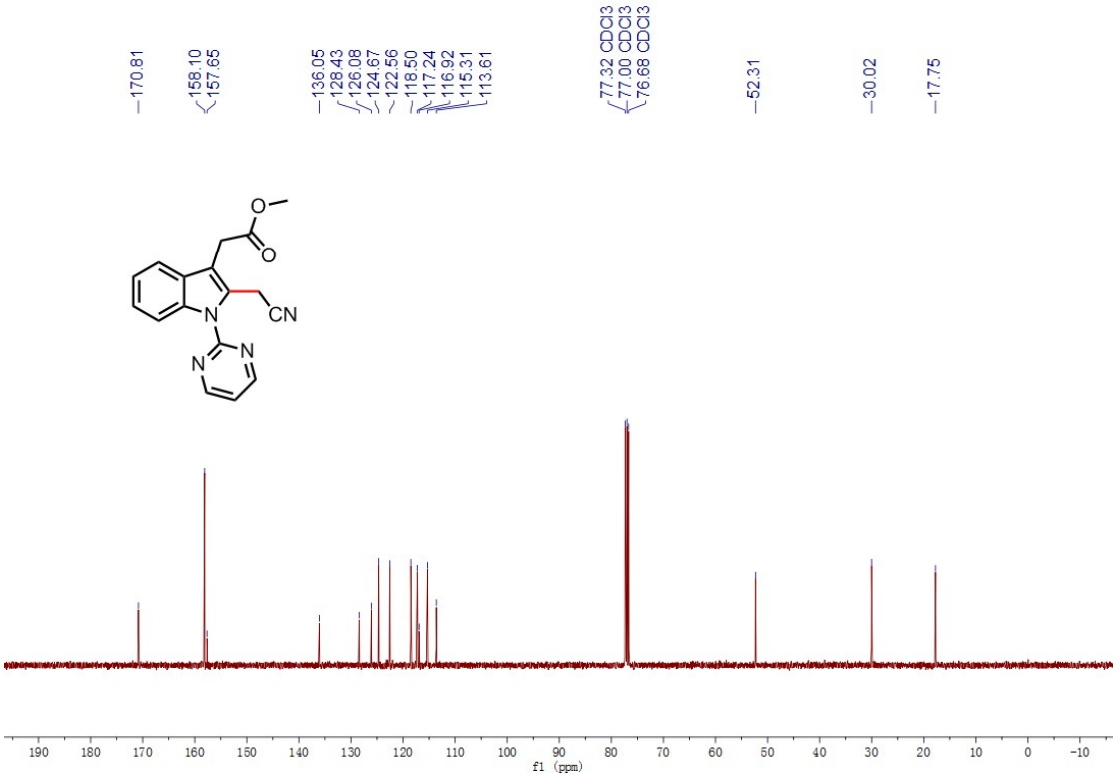




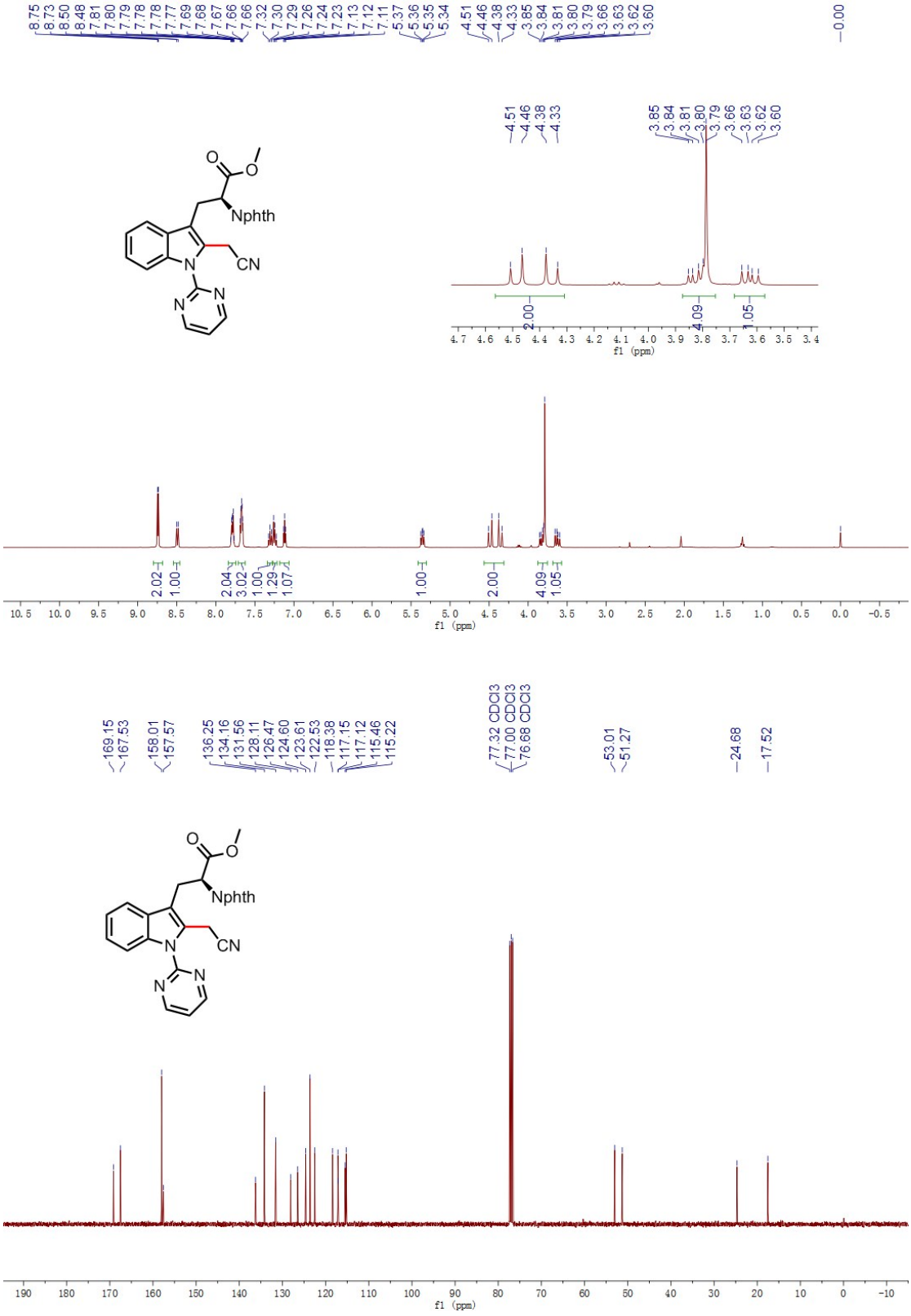


methyl 2-(2-(cyanomethyl)-1-(pyrimidin-2-yl)-1H-indol-3-yl)acetate (3y)

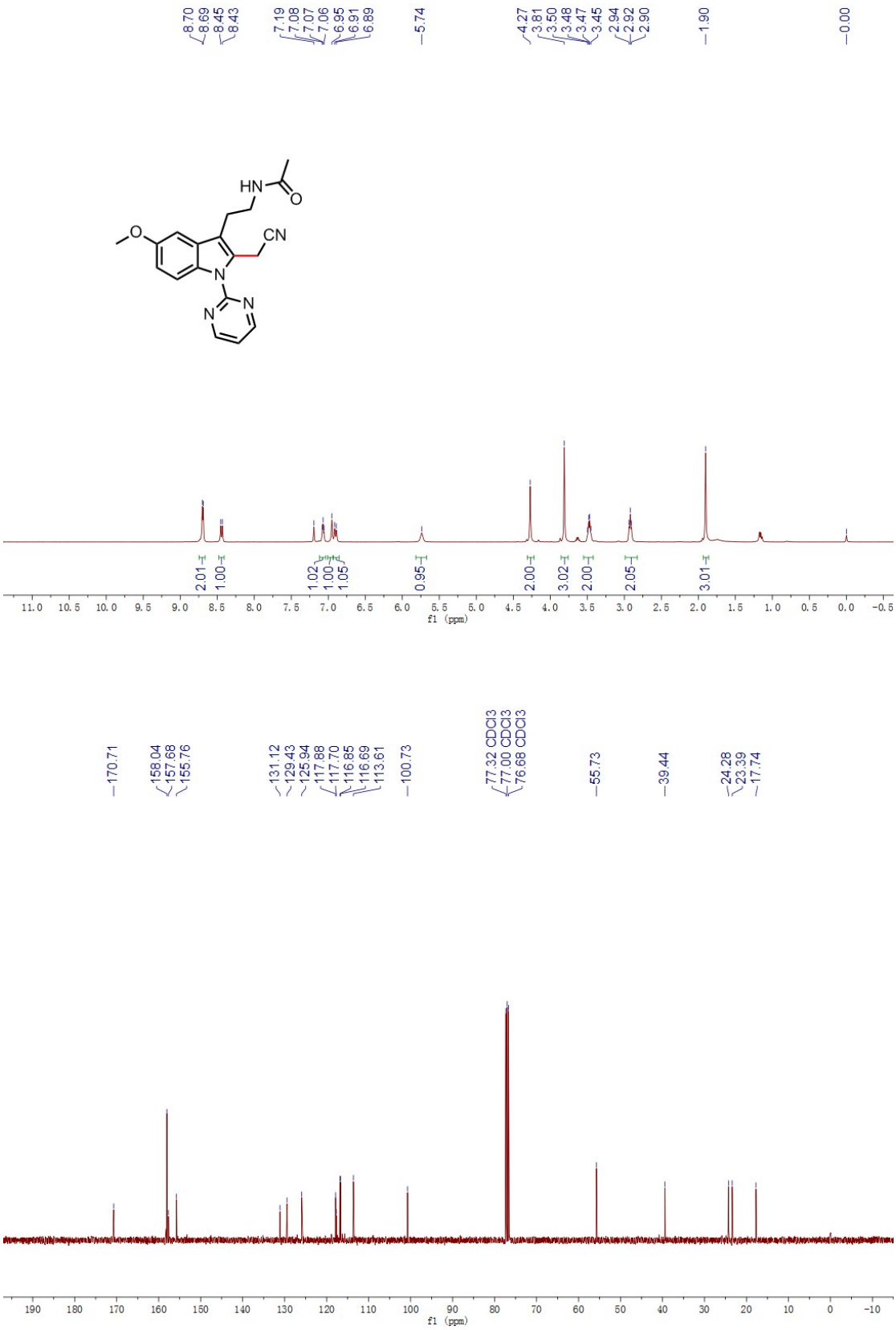




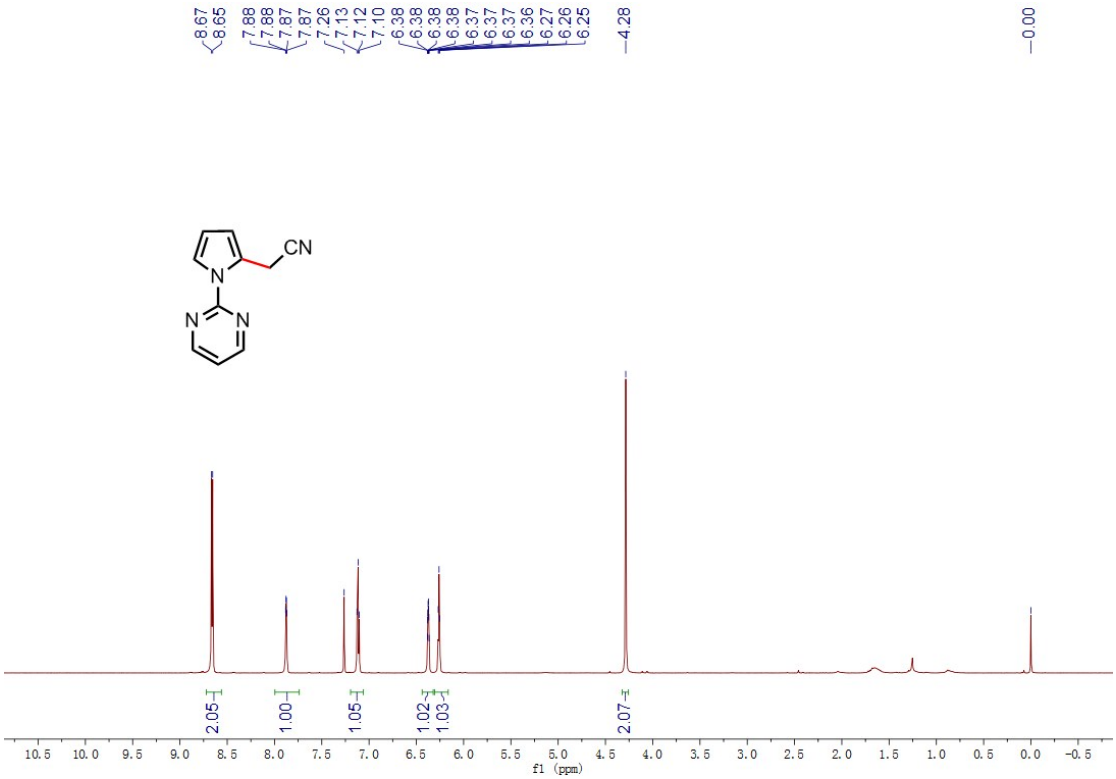
methyl(S)-3-(2-(cyanomethyl)-1-(pyrimidin-2-yl)-1H-indol-3-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (3z)

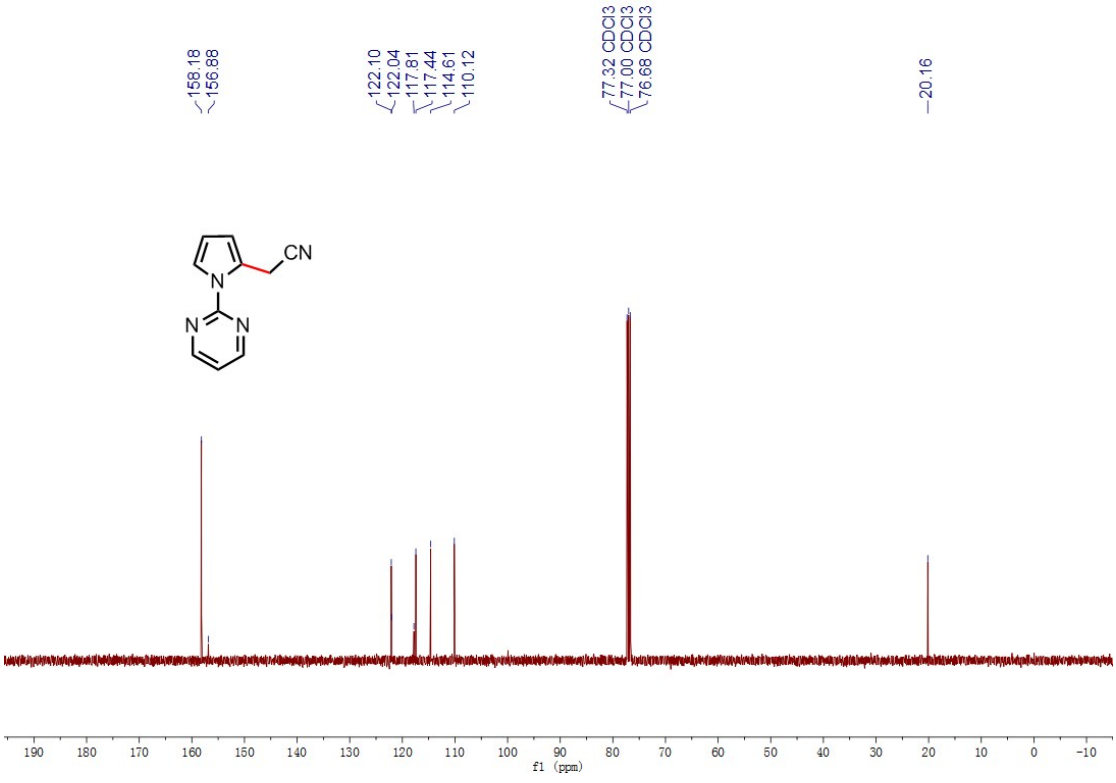


***N*-(2-(2-(cyanomethyl)-5-methoxy-1-(pyrimidin-2-yl)-1H-indol-3-yl)ethyl)acetamide (3za)**

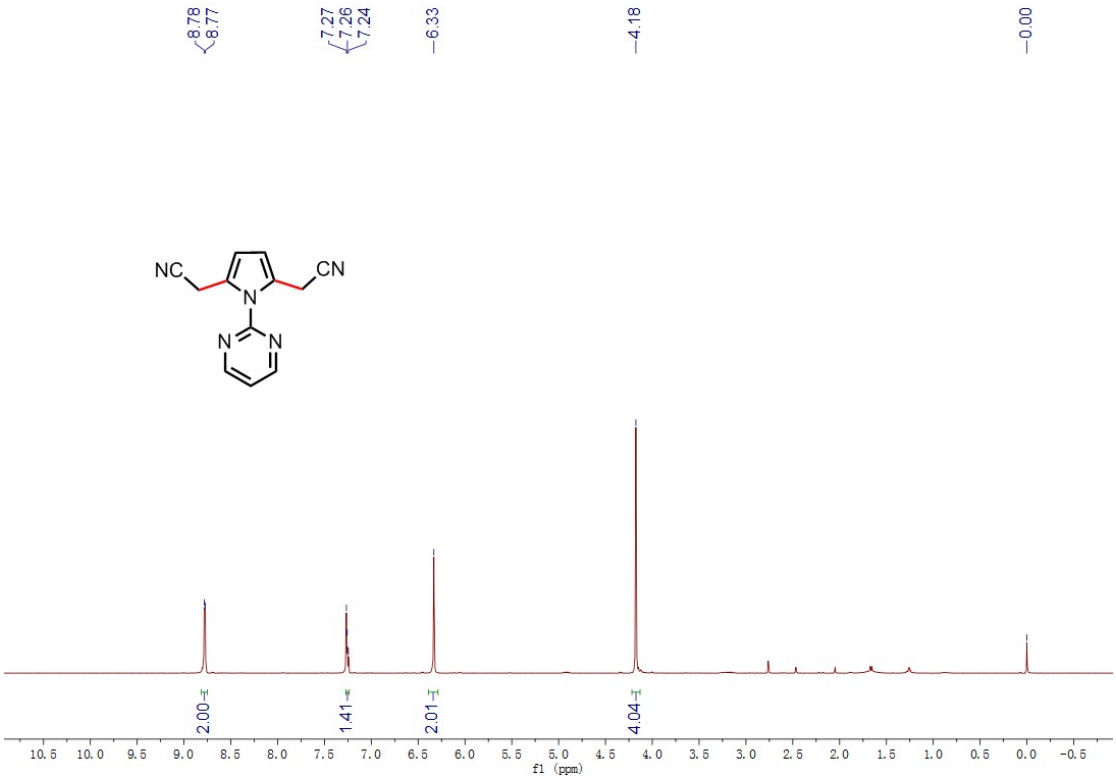


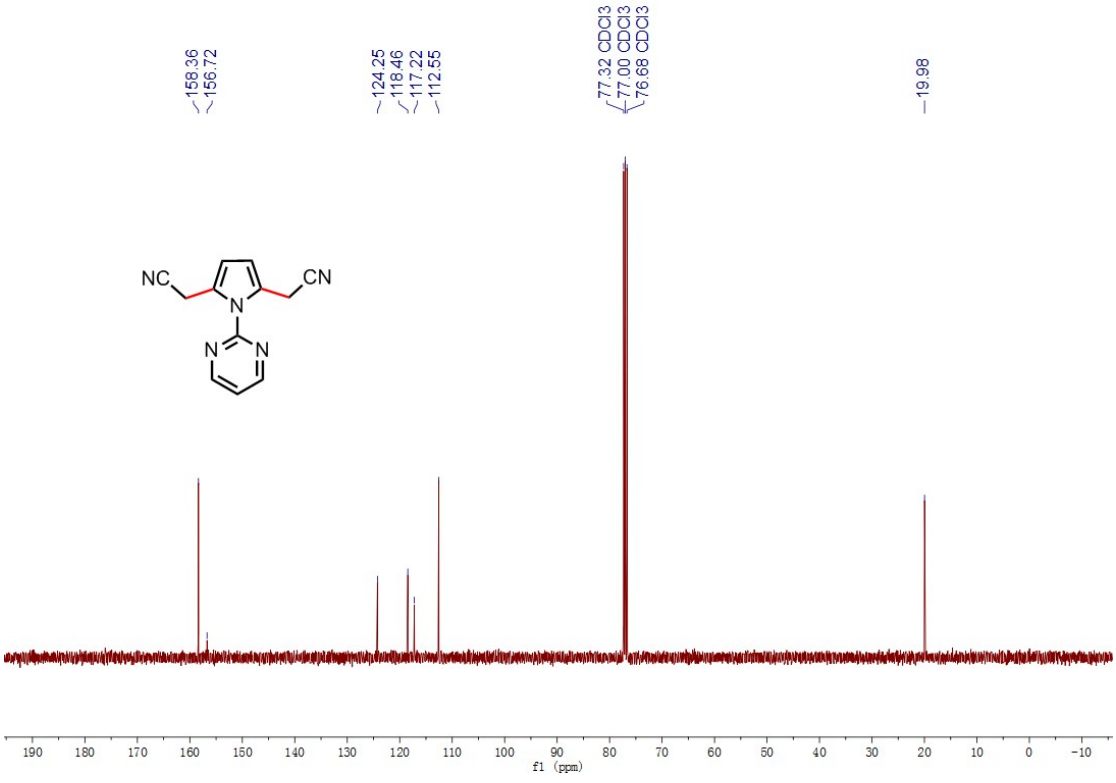
2-(1-(pyrimidin-2-yl)-1H-pyrrol-2-yl)acetonitrile (5a)



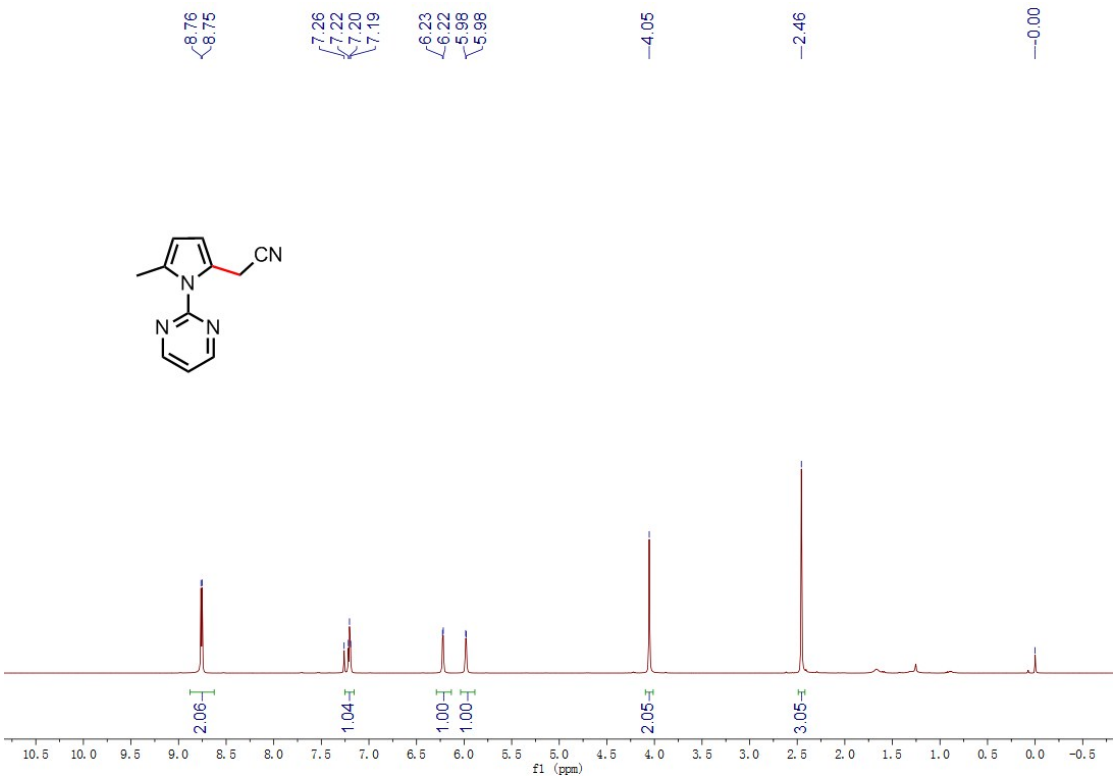


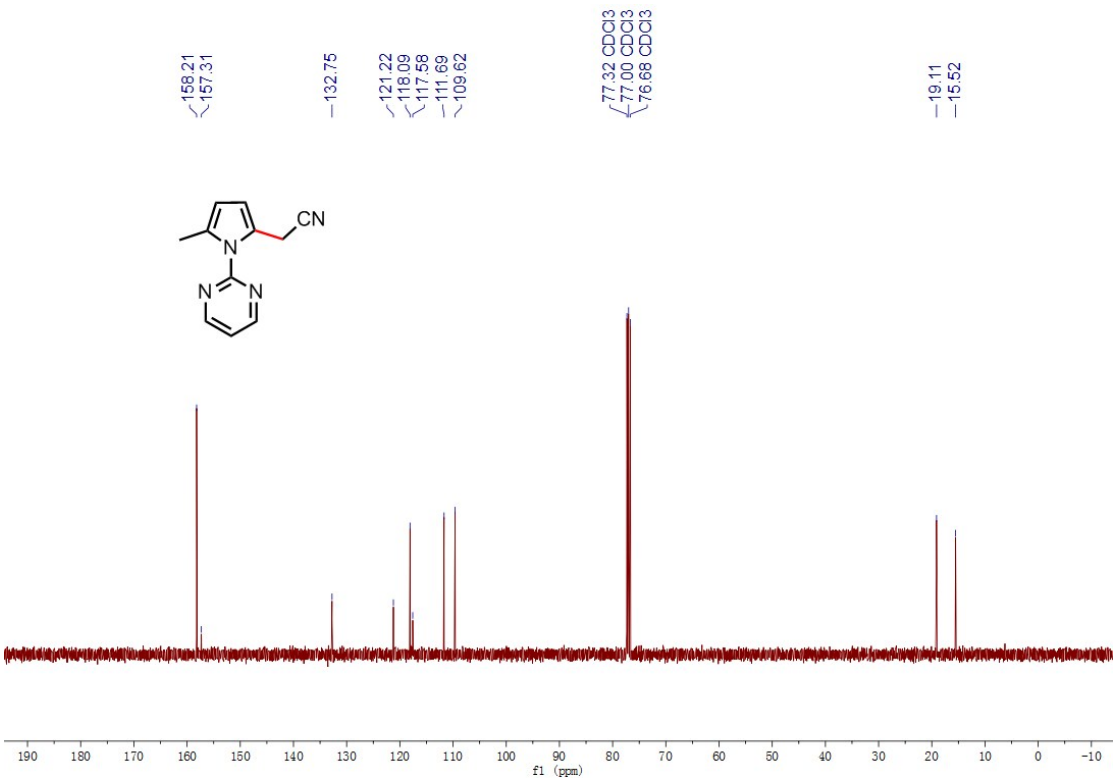
2,2'-(1-(pyrimidin-2-yl)-1H-pyrrole-2,5-diyl)diacetonitrile (5aa)



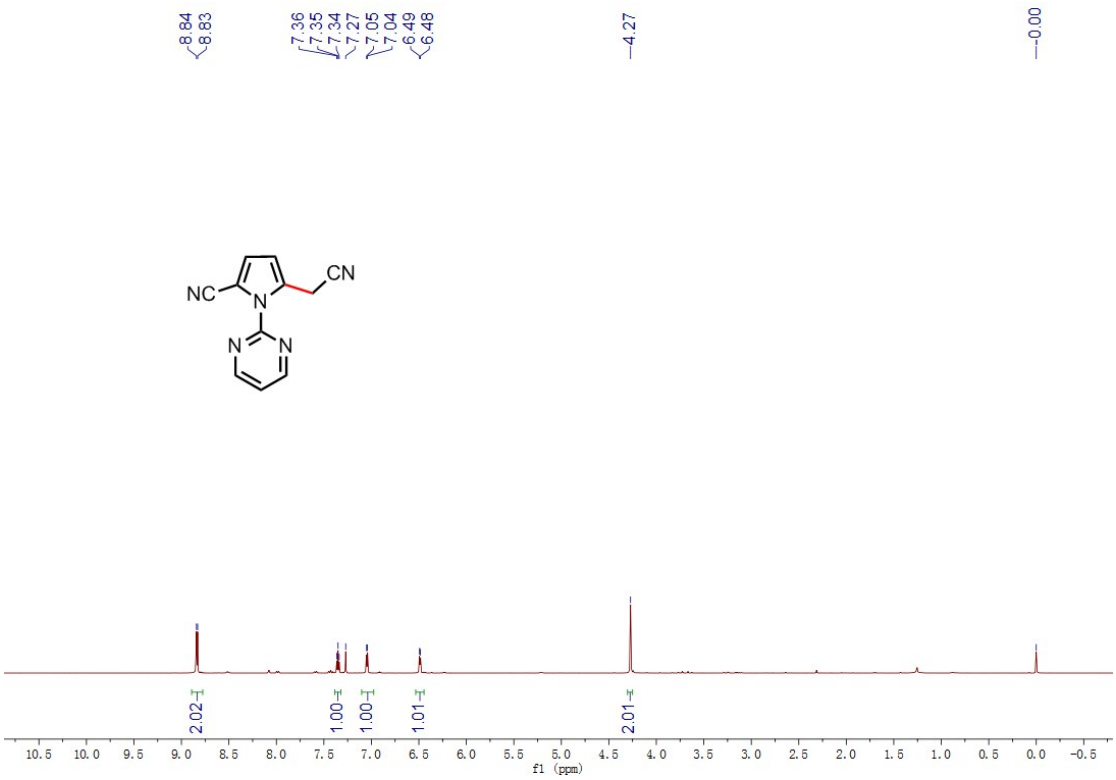


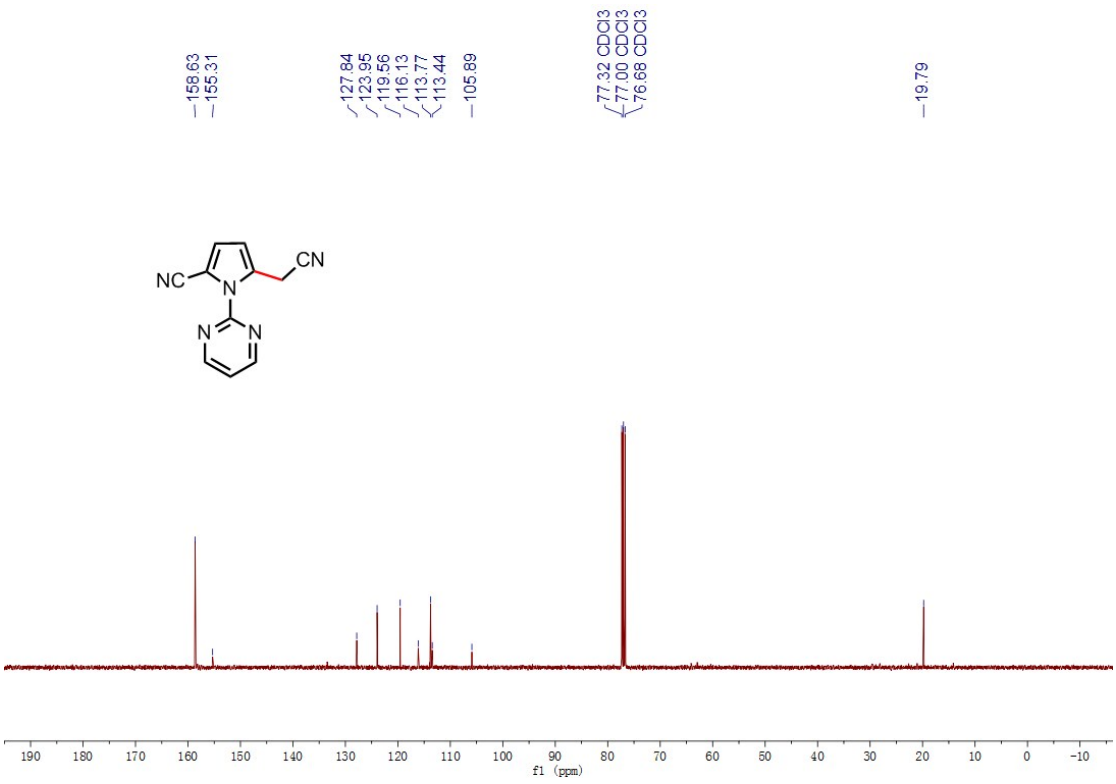
2-(5-methyl-1-(pyrimidin-2-yl)-1H-pyrrol-2-yl)acetonitrile (5b)



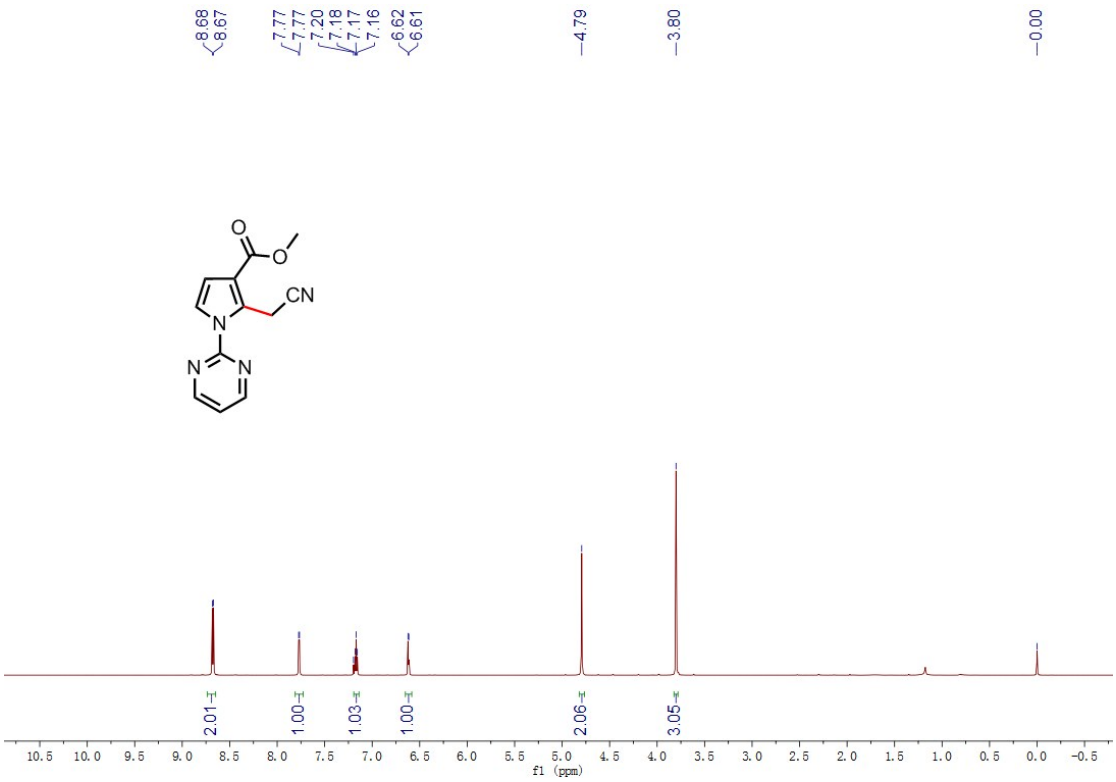


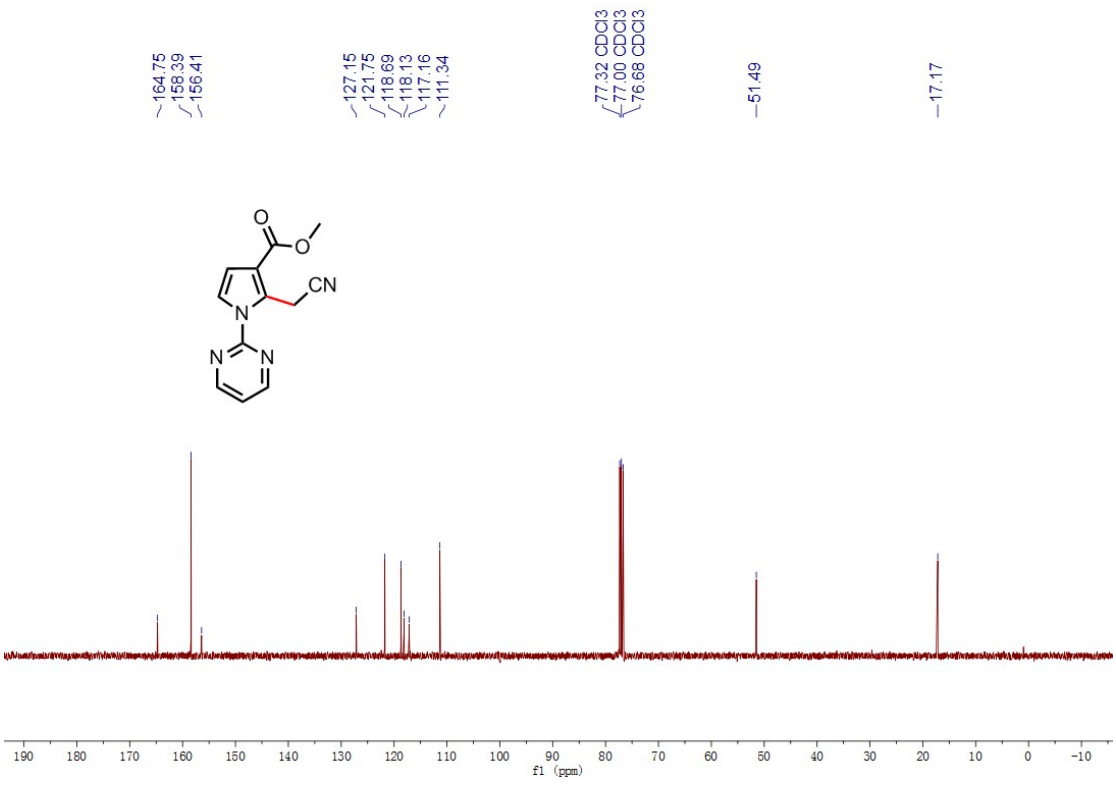
5-(cyanomethyl)-1-(pyrimidin-2-yl)-1H-pyrrole-2-carbonitrile (5c)



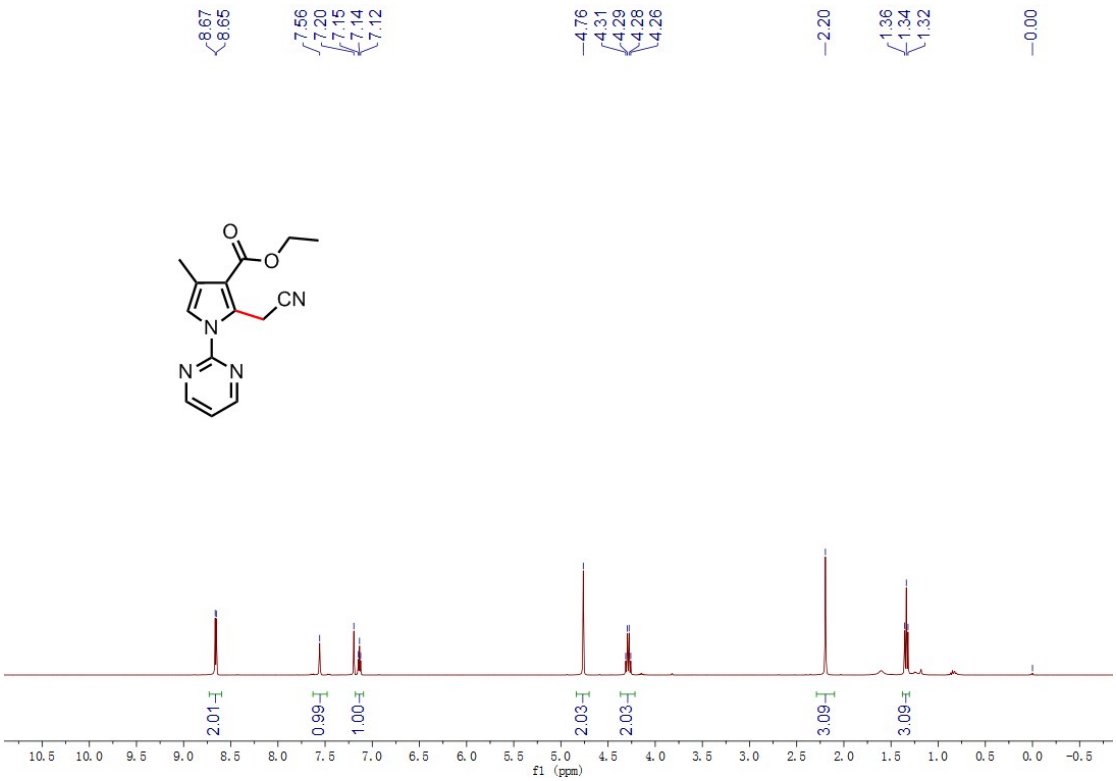


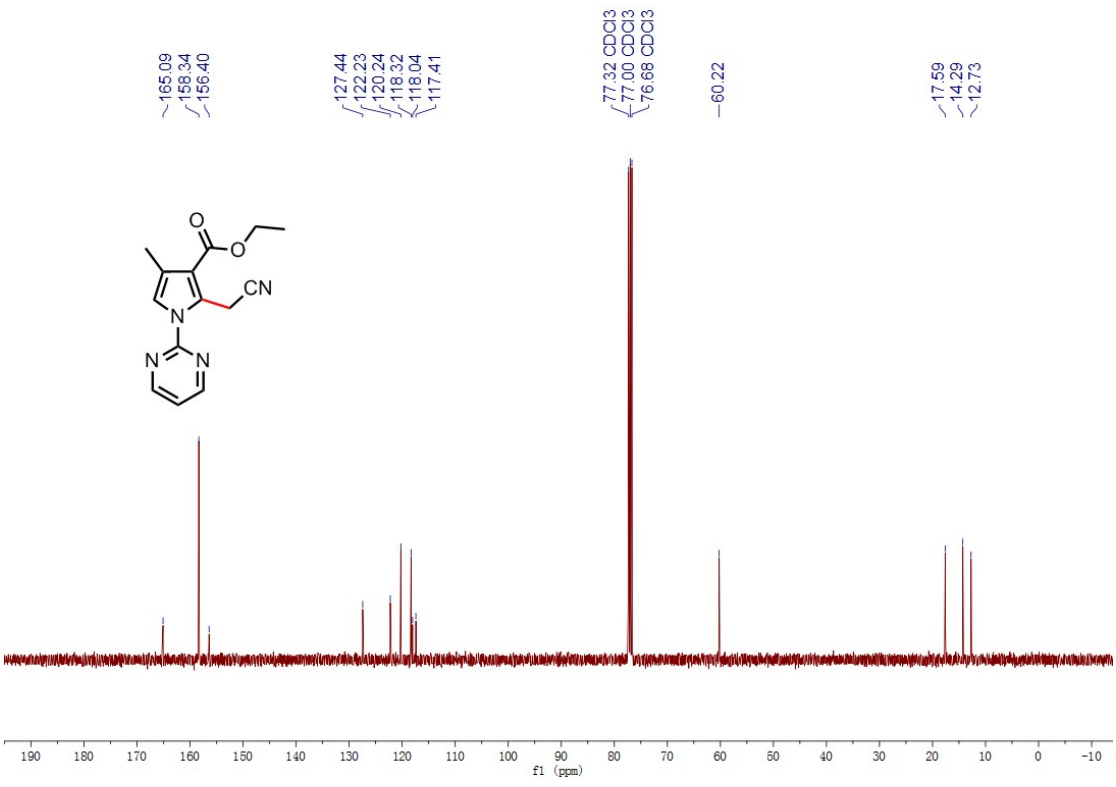
methyl 2-(cyanomethyl)-1-(pyrimidin-2-yl)-1H-pyrrole-3-carboxylate (5d)



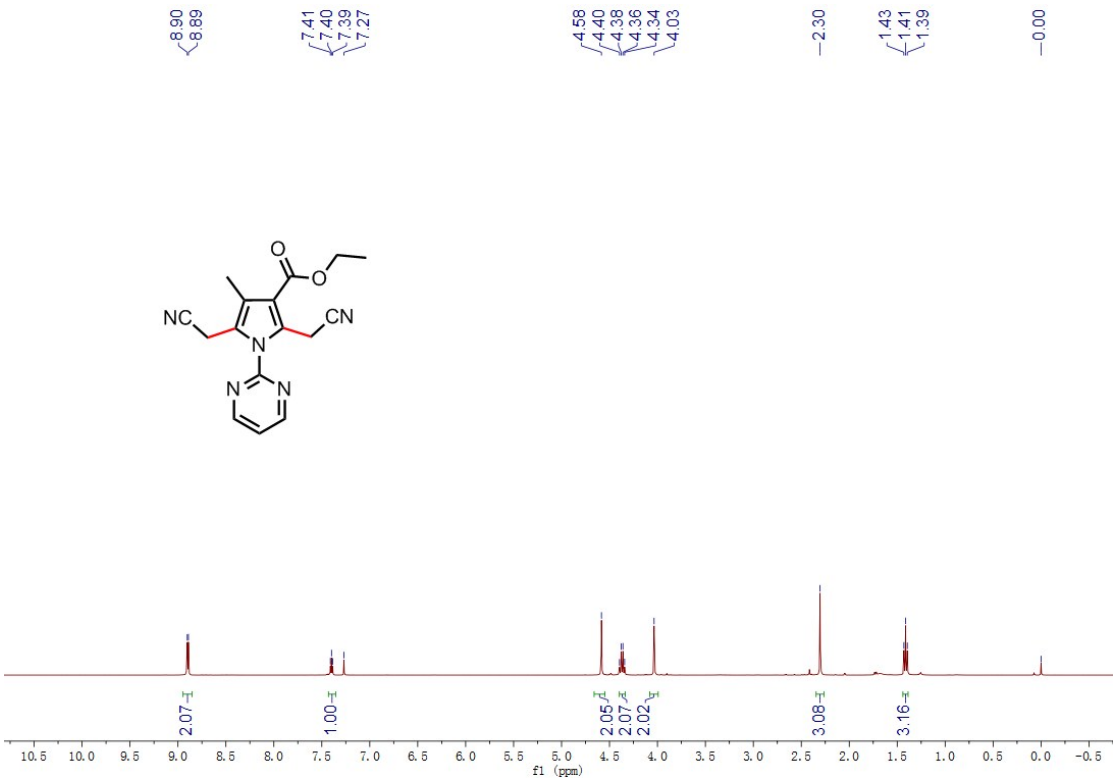


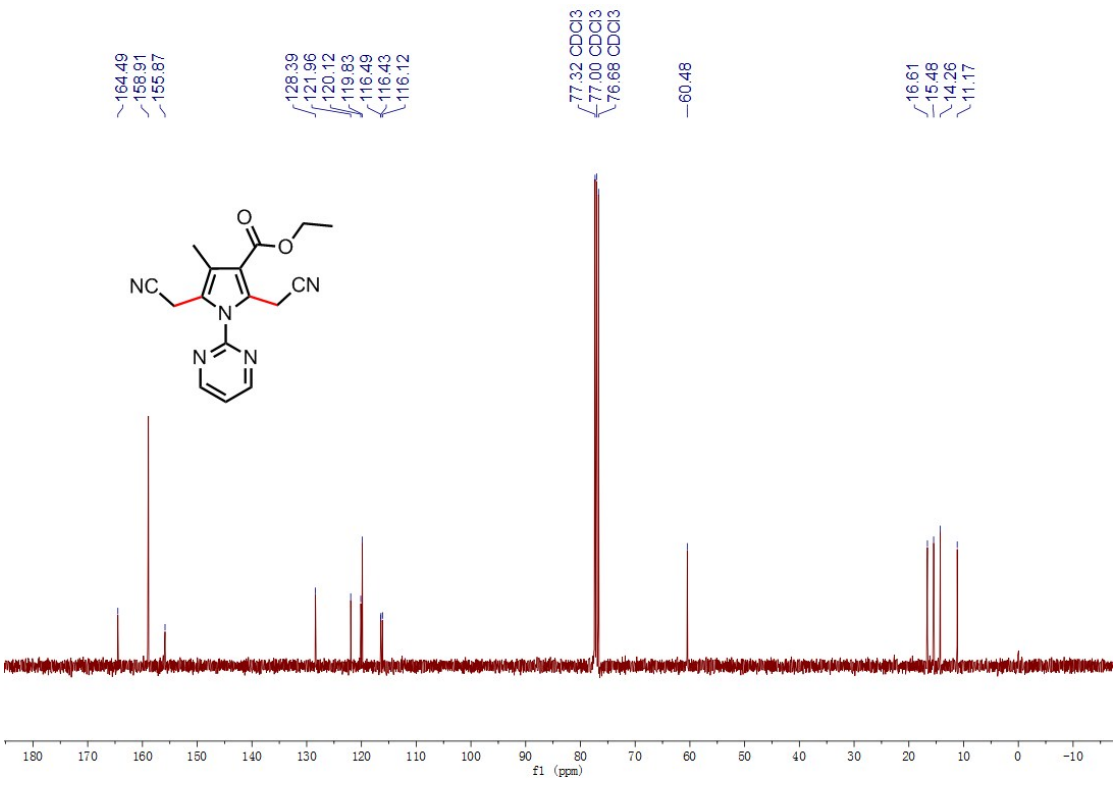
ethyl 2-(cyanomethyl)-4-methyl-1-(pyrimidin-2-yl)-1H-pyrrole-3-carboxylate (5e)



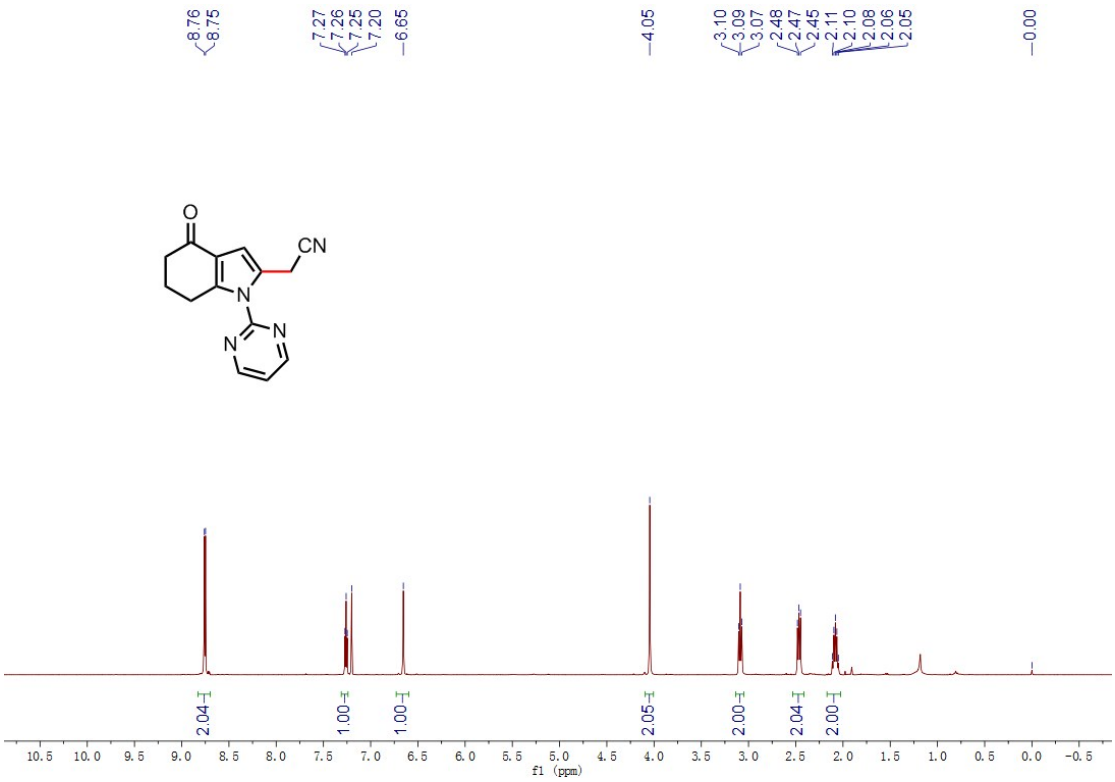


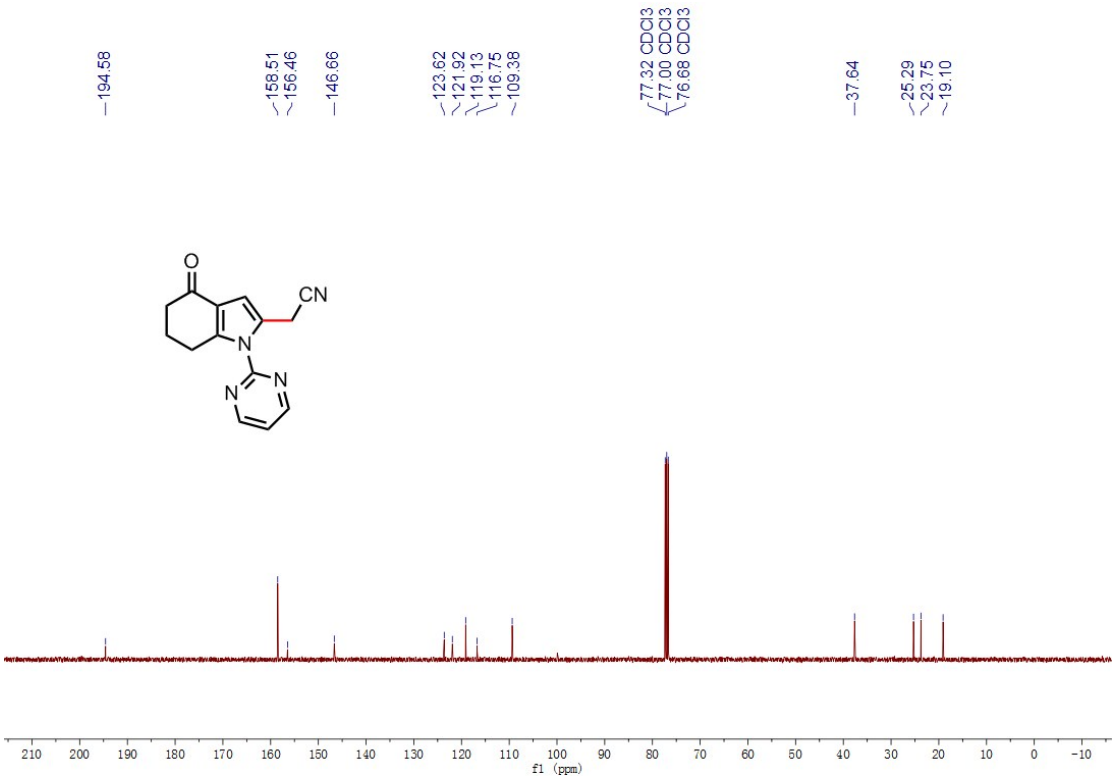
ethyl 2,5-bis(cyanomethyl)-4-methyl-1-(pyrimidin-2-yl)-1H-pyrrole-3-carboxylate (5ee)



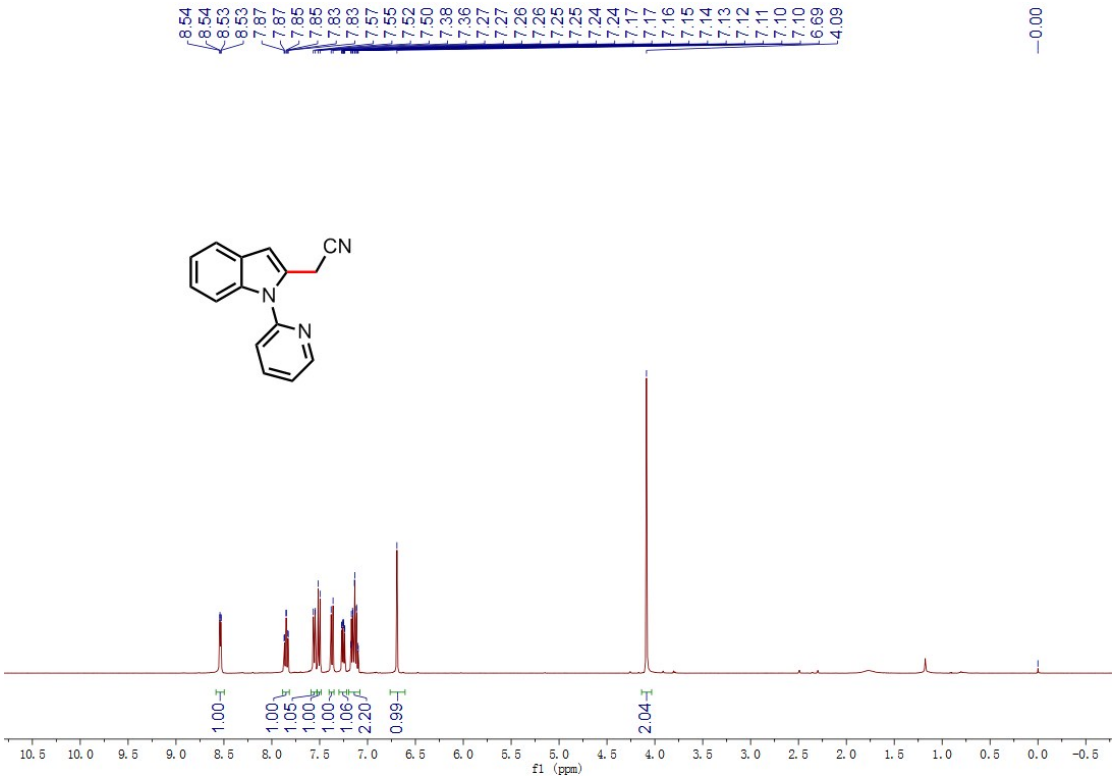


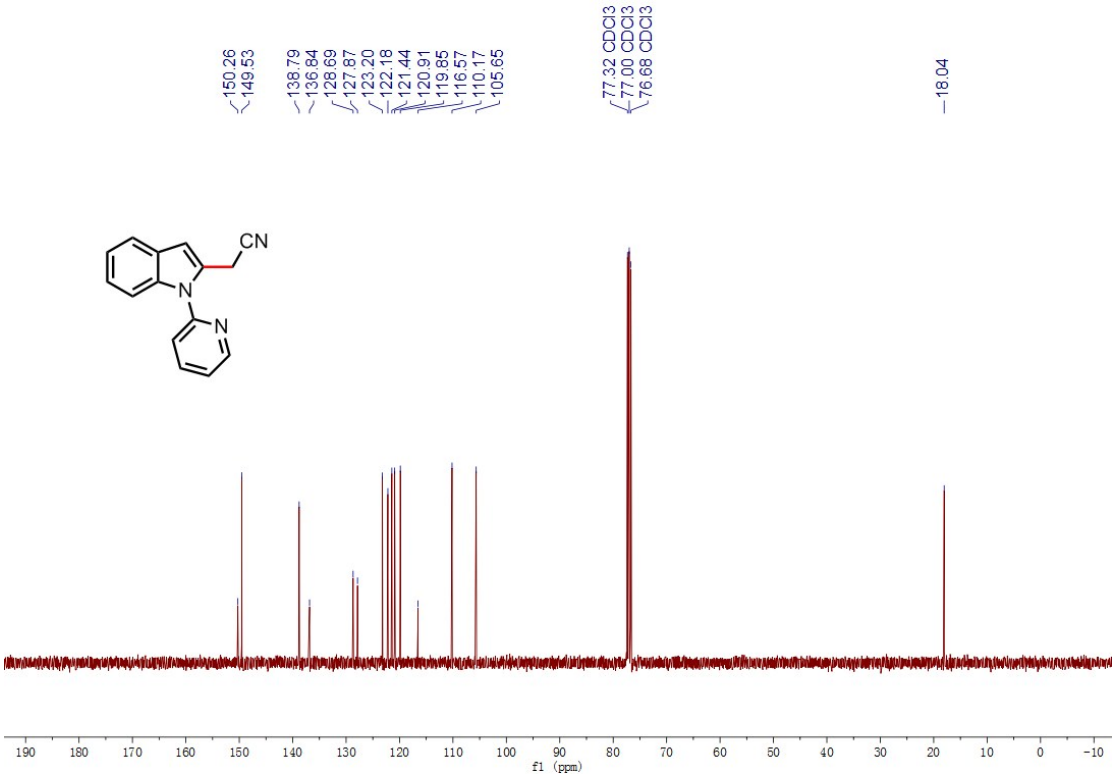
2-(4-oxo-1-(pyrimidin-2-yl)-4,5,6,7-tetrahydro-1H-indol-2-yl)acetonitrile (5f)



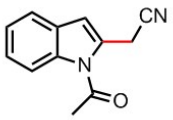


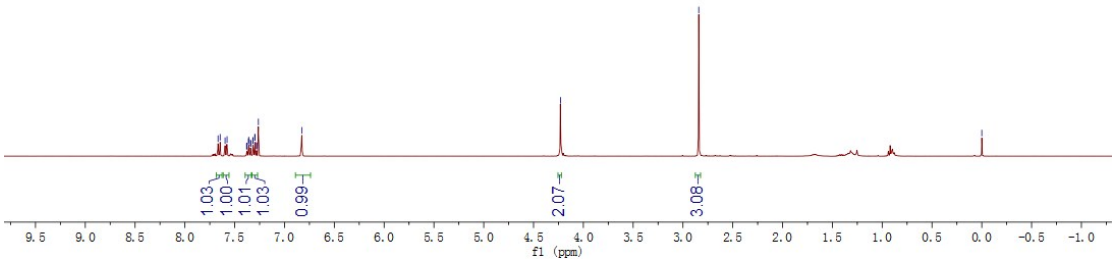
2-(1-(pyridin-2-yl)-1H-indol-2-yl)acetonitrile (6a)

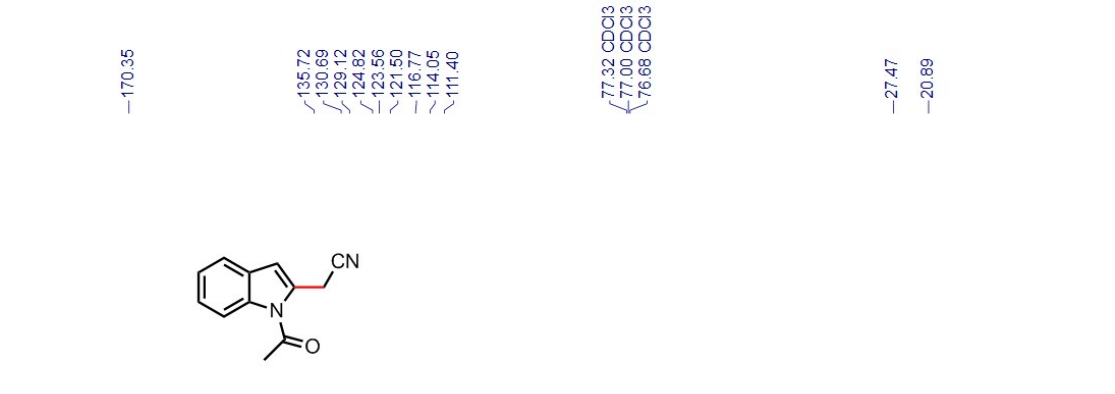


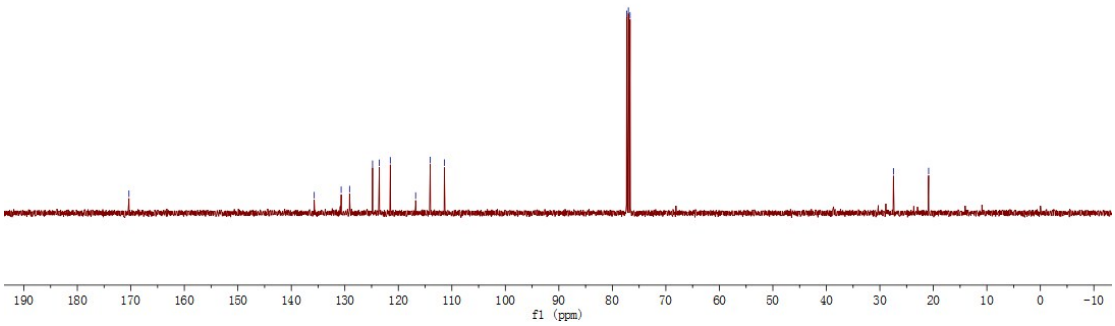


2-(1-acetyl-1H-indol-2-yl)acetonitrile (7a)

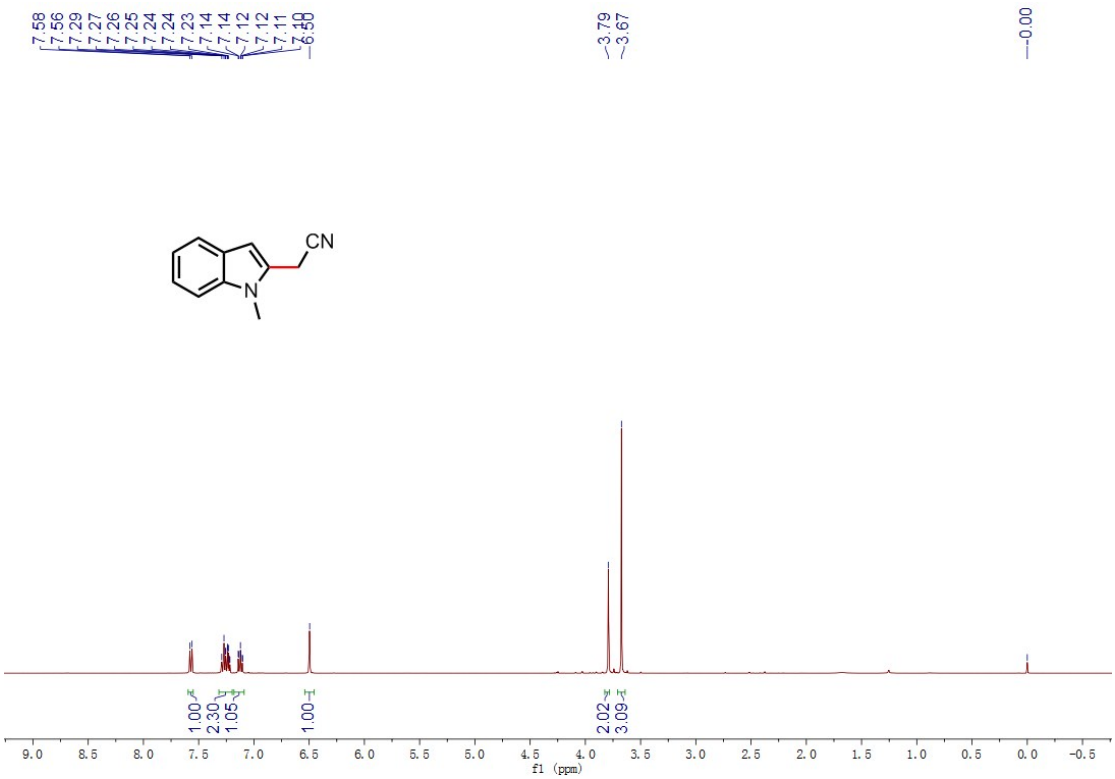


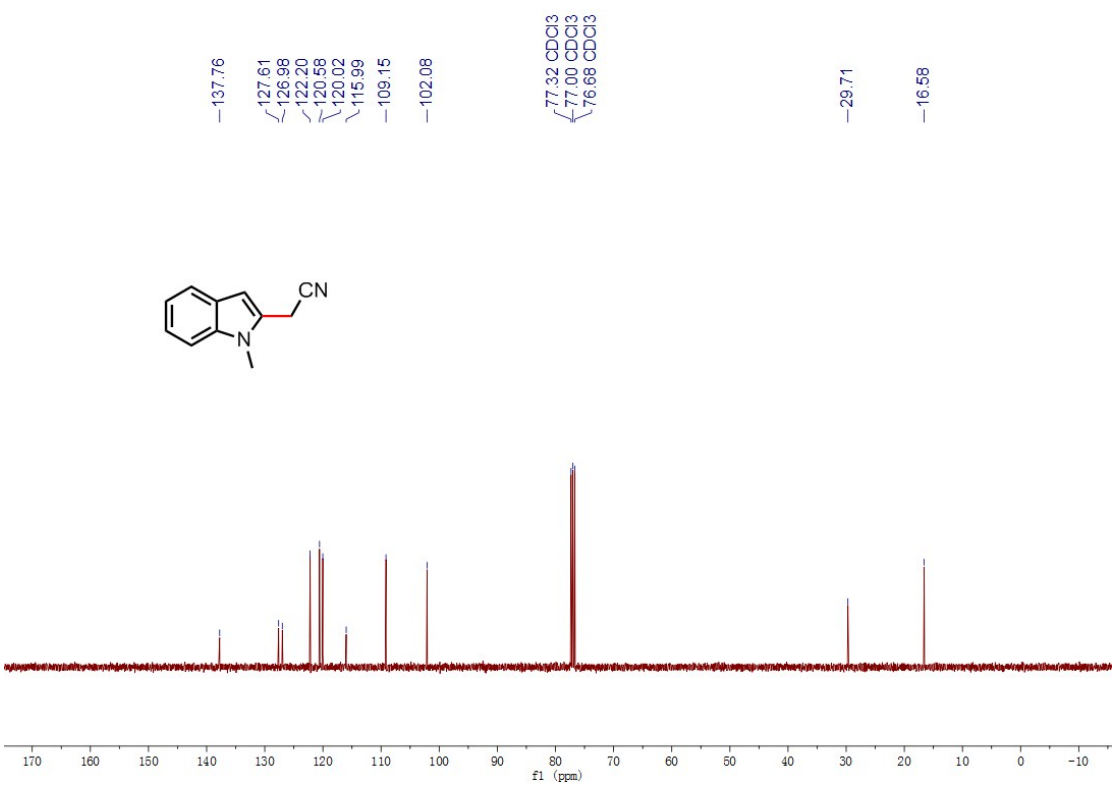




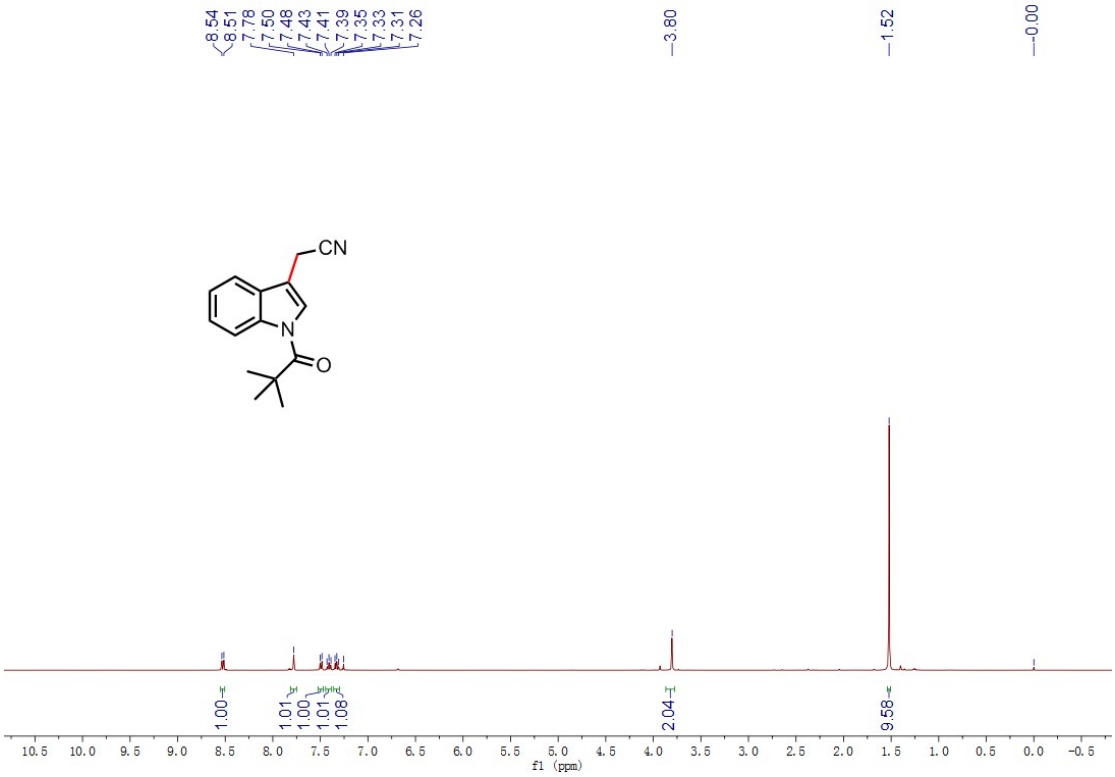


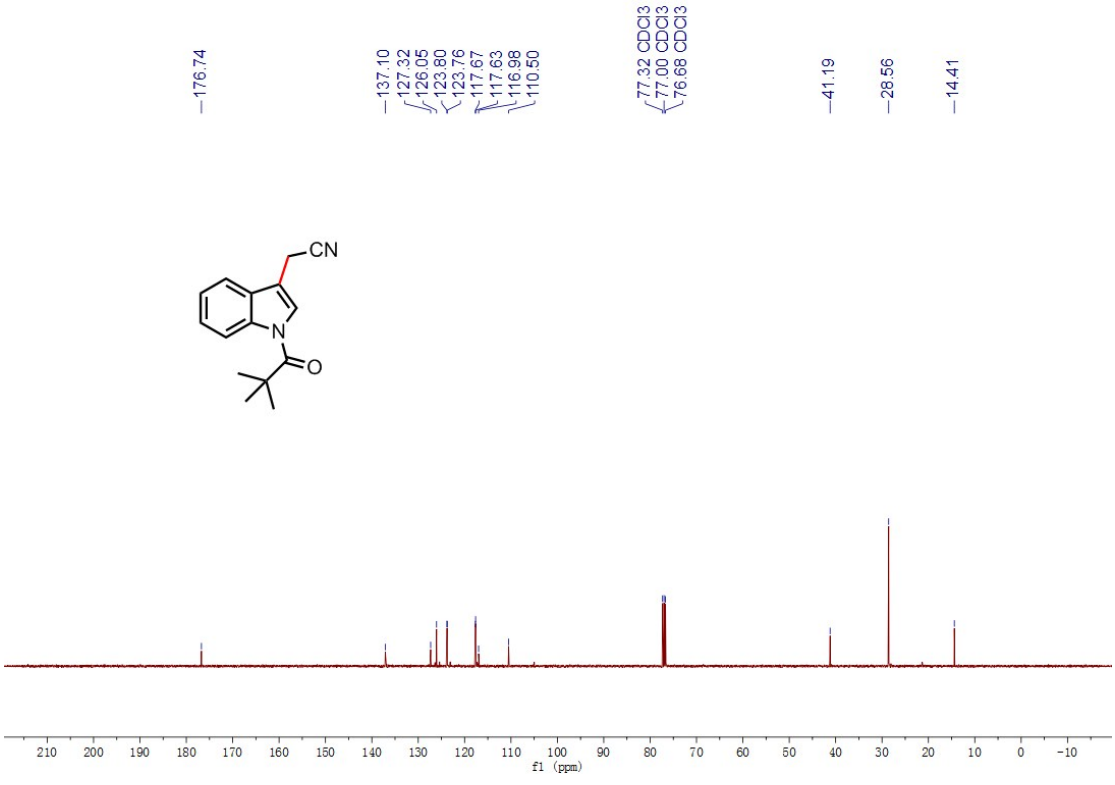
2-(1-methyl-1H-indol-2-yl)acetonitrile (8a)



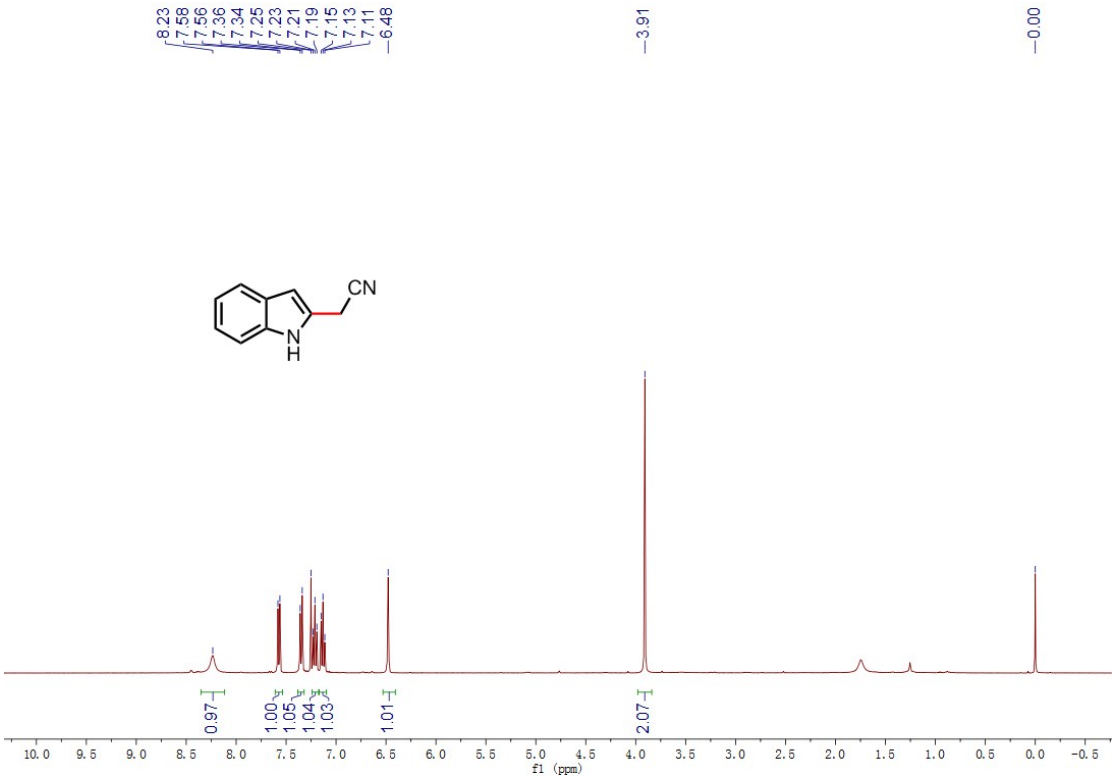


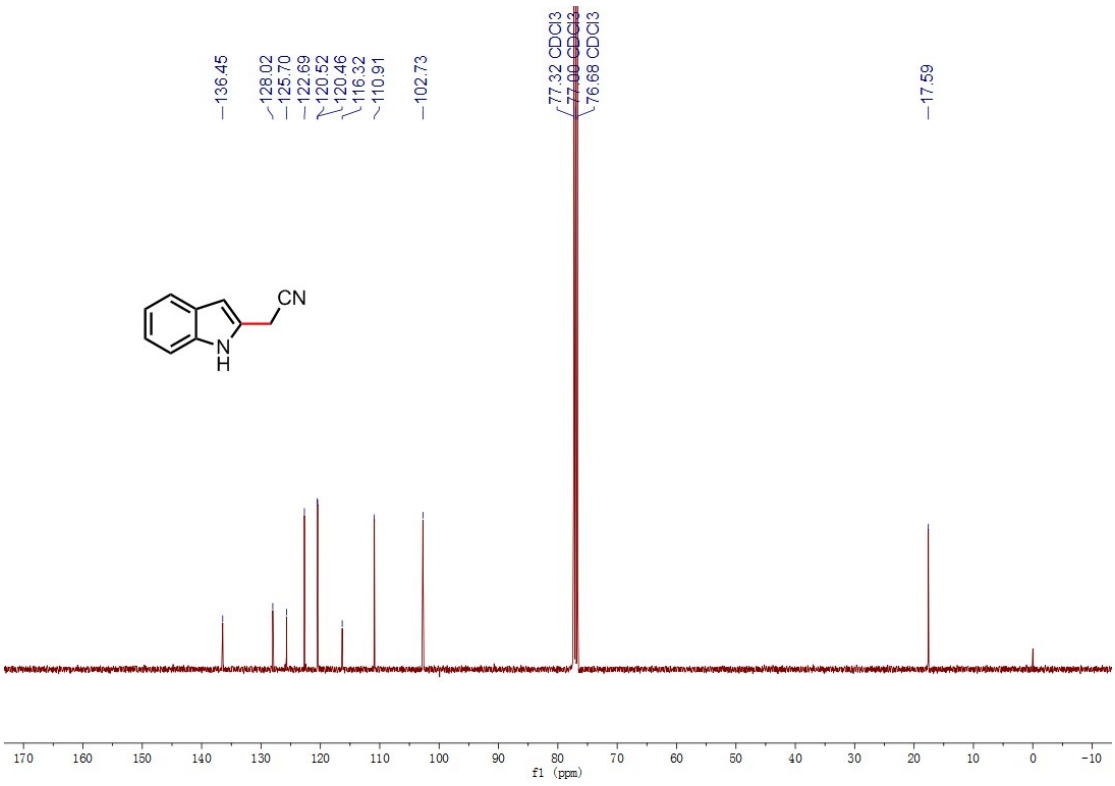
2-(1-pivaloyl-1H-indol-3-yl)acetonitrile (9a)





2-(1H-indol-2-yl)acetonitrile (3aa)





2-(1-(pyrimidin-2-yl)-1H-indol-2-yl)acetonitrile-d_2 (3a-D)