Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Electrosynthesis of (Hetero)aryl Nitriles from *α*-Imino-oxy Acids via Oxidative Decarboxylation/N-O Cleavage

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Table of Contents

1. General Information

Commercial solvents and reagents were used without further purification unless otherwise noted.

Electrolysis reactions were conducted using a Model QJ3005T (32.0 V) DC power supply purchased from Ningbo Jiuyuan Electronic Co., Ltd., China.

Analytical thin layer chromatography (TLC) plates and the silica gel (200 – 300 mesh) for column chromatography were phased from Qingdao Haiyang Chemical and Special Silica Gel Co, Ltd.

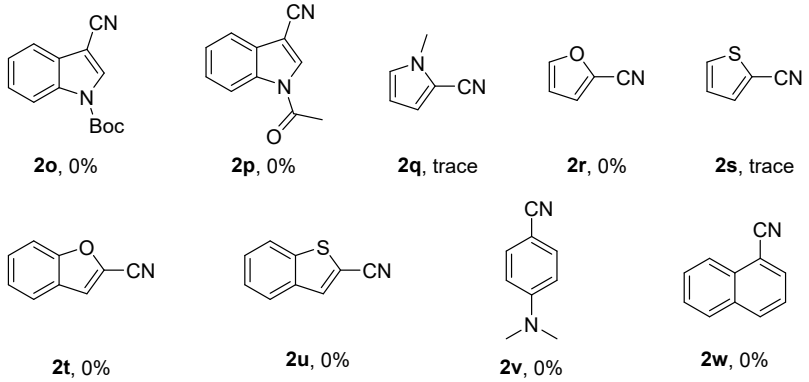
Proton nuclear magnetic resonance (^{1}H NMR), carbon nuclear magnetic resonance (^{13}C NMR) and fluorine nuclear magnetic resonance (^{19}F NMR) spectroscopy were performed on Bruker Advance III-400 spectrometers (400 MHz for ^{1}H NMR, 101 MHz for ^{13}C NMR, 377 MHz for ^{19}F NMR) and Bruker AscendTM 500 spectrometers (500 MHz for ^{1}H NMR, 126 MHz for ^{13}C NMR, 471 MHz for ^{19}F NMR). Chemical shifts of ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were reported as in units of parts per million (ppm) downfield from TMS (δ 0.0 ppm) and relative to the signal of $CDCl_3$ (δ 7.26 ppm for ^{1}H NMR and δ 77.2 ppm for ^{13}C NMR) and DMSO-d_6 (δ 2.50 ppm for ^{1}H NMR and δ 39.5 ppm for ^{13}C NMR). Multiplicities were given as: s (singlet); br s (broad singlet); d (doublet); t (triplet); q (quartet); m (multiplets), etc. The number of protons (n) for a given resonance was indicated by nH.

HR-MS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF and LCMS-Q Exactive).

Cyclic voltammetry (CV) analysis was performed on Ingsens IGS-1030 electrochemical workstation (Ingsens Instruments (Guangzhou) Co., Ltd., China) with a conventional three electrode cell, using a glassy carbon electrode (GCE) (d = 3.0 mm) as working electrode, a Pt wire as counter electrode and saturated calomel electrode (SCE) as a reference electrode. Cyclic voltammograms were recorded at 100.0 mV/s scan rate.

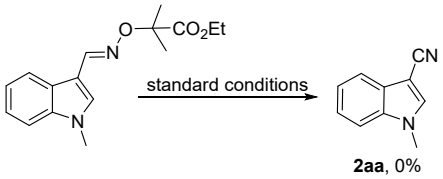
2. Additional Results of Substrate Scope and Control Experiments

Scheme S1. Unsuccessful or low yield examples for electrosynthesis of (hetero)aryl nitriles



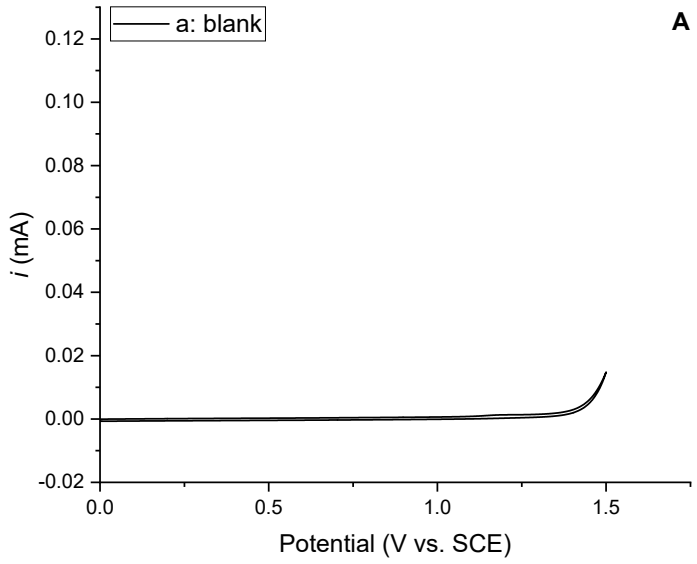
[a]Standard conditions: **1** (0.25 mmol), TBAOAc (0.1 M), MeOH (4.0 mL), MeCN (1.0 mL), undivided cell, RVC (100.0 PPI, 1.0 cm × 1.0 cm × 0.5 cm) anode, Pt cathode (1.0 cm × 1.5 cm), I = 4.0 mA, 3.5 h (2.1 F mol^{-1}), room temperature. [b]Isolated yield.

Scheme S2. Transformation from ester of **1aa** to **2aa**



The ester of **1aa** failed to obtain the desired product, indicating that only free carboxylic acid could participate in this reaction.

3. Cyclic Voltammetry Studies



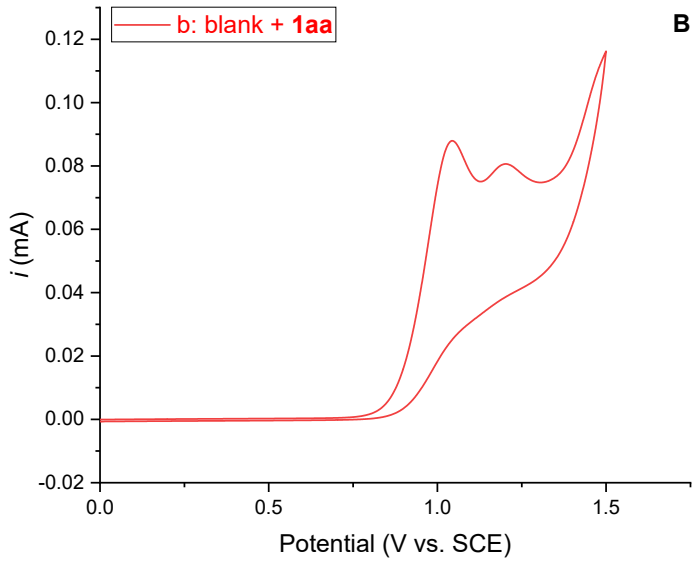
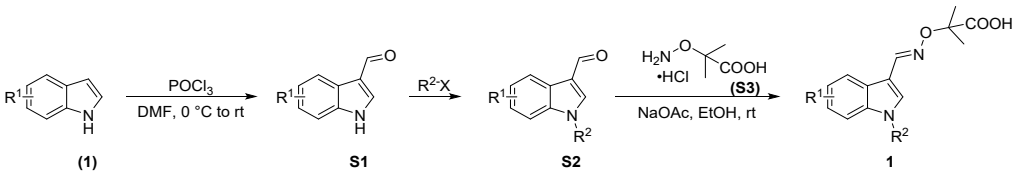


Figure S1. Cyclic voltammograms of 0.1 M TBAOAc solution in a mixed solvent of MeOH/MeCN (4:1) at room temperature. (a) None; (b) **1aa** (5.0 mM). The voltammogram was obtained with Pt wire as an auxiliary electrode and a saturated calomel electrode (SCE) as a reference electrode. The scan rate was 0.05 V s^{-1} on a glassy carbon electrode (GCE) (d = 3.0 mm).

4. Synthesis and Characterization of Starting Substrates

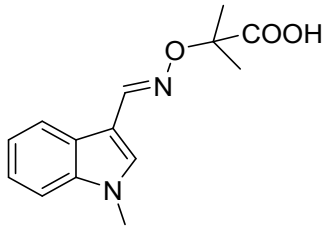


1*H*-indole-3-carbaldehyde **S1** were prepared according to reported method[1]: *N,N*-dimethylformamide (DMF, 10.0 equiv.) was cooled to 0 °C. Then, $POCl_3$ (5.0 equiv.) was added dropwise and stirred for 0.5 h. The reaction mixture was then warmed to room temperature and the intermediates **1** (1.0 equiv.) in DMF were added dropwise via syringe for 2.0 h. Once reaction was determined to be completed via TLC analysis, the mixture was quenched with water and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was purified by flash column chromatography to give the intermediates **S1**.

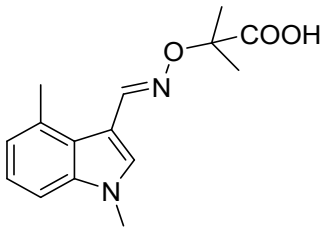
The different N-protected 1*H*-indole-3-carbaldehyde **S2** were prepared according to reported method[2]; and 2-(aminooxy)-2-methylpropanoic acid hydrochloride **S3** were prepared according to previous report[3].

The starting substrates **1aa-1ba**, **1ca-1d** and **1fa-1k** were synthesized according to the following procedures[4]: 2-(aminooxy)-2-methylpropanoic acid hydrochloride **(S3)**

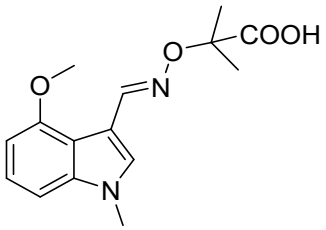
(1.5 equiv.) and NaOAc (3.0 equiv.) were added to a stirred solution of the intermediates **S2** (1.0 equiv.) in EtOH (0.2 M) at room temperature overnight. Once reaction was determined to be completed via TLC analysis, the mixture was quenched with H_2O and extracted with ethyl acetate. The combined organic extracts were then washed with H_2O and brine, then dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to give desired products **1aa-1ba**, **1ca-1d** and **1fa-1k**.



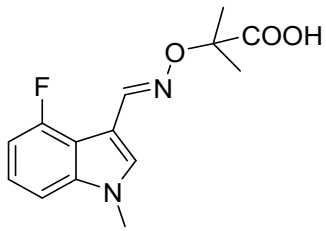
2-methyl-2-((((1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)propanoic acid (1aa): Yield = 82% (**1aa**);white solid; *E*:*Z* =4 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1H, *E*-isomers), 8.08 (s, 0.25H, *Z*-isomers), 8.00 (d, *J* = 7.9 Hz, 1H), 7.81 (s, 0.25H, *Z*-isomers), 7.73 (d, *J* = 7.9 Hz, 0.25H), 7.34 – 7.29 (m, 0.5H), 7.28 (d, *J* = 3.8 Hz, 2H), 7.26 – 7.23 (m, 0.25H), 7.22 – 7.19 (m, 1H), 7.17 (s, 1H, *E*-isomers), 3.81 (s, 0.75H, *Z*-isomers), 3.72 (s, 3H, *E*-isomers), 1.68 (s, 1.5H, *Z*-isomers), 1.63 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.52, 178.38, 145.99, 140.23, 137.73, 135.99, 135.38, 132.44, 127.40, 125.00, 123.24, 122.75, 122.26, 121.43, 121.13, 118.17, 109.82, 109.55, 108.31, 105.19, 81.69, 81.39, 33.40, 33.12, 24.43, 24.24.



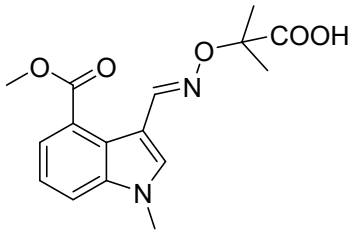
2-((((1,4-dimethyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1ab): Yield = 65% (**1ab**);white solid; *E*:*Z* =2 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (s, 0.5H, *Z*-isomers), 8.21 (d, *J* = 20.1 Hz, 2H), 7.51 (s, 0.5H, *Z*-isomers), 7.23 – 7.19 (m, 2H), 7.17– 7.13 (m, 1H), 7.00 (d, *J* = 6.8 Hz, 1H), 6.95 (d, *J* = 6.3 Hz, 0.5H), 3.83 (s, 3H, *E*-isomers), 3.77 (s, 1.5H, *Z*-isomers), 2.74 (s, 3H, *E*-isomers), 2.70 (s, 1.5H, *Z*-isomers), 1.69 (s, 6H, *E*-isomers), 1.60 (s, 3H, *Z*-isomers).^{13}C NMR (126 MHz, $CDCl_3$) δ 177.95, 177.46, 146.83, 142.12, 137.47, 136.25, 136.12, 130.90, 130.52, 129.41, 125.66, 125.22, 123.53, 122.69, 122.57, 107.91, 107.88, 107.79, 106.52, 81.72, 81.34, 33.60, 33.30, 24.49, 24.32, 21.73, 21.57.



2-((((4-methoxy-1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1ac): Yield = 76% (**1ac**);white solid; *E*:*Z* =5 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (s, 0.2H, *Z*-isomers), 8.52 (s, 1H, *E*-isomers), 8.04 (s, 1H, *E*-isomers), 7.45 (s, 0.2H, *Z*-isomers), 7.20 (t, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 8.1 Hz, 0.2H), 6.96 (d, *J* = 8.2 Hz, 1H), 6.93 (d, *J* = 8.3 Hz, 0.2H), 6.64 (d, *J* = 7.9 Hz, 1H), 6.60 (d, *J* = 7.9 Hz, 0.2H), 3.95 (s, 3H, *E*-isomers), 3.94 (s, 0.6H, *Z*-isomers), 3.80 (s, 3H, *E*-isomers), 3.76 (s, 0.6H, *Z*-isomers), 1.68 (s, 6H, *E*-isomers), 1.59 (s, 1H, *Z*-isomers). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.37, 177.27, 154.53, 154.37, 147.50, 143.08, 138.69, 137.55, 134.71, 127.76, 123.58, 123.49, 116.72, 116.26, 106.95, 105.74, 103.13, 103.02, 101.55, 101.14, 81.58, 81.31, 55.29, 55.23, 33.67, 33.46, 24.55, 24.40.

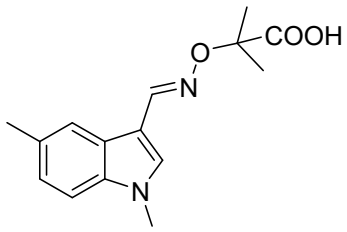


(*E*)-2-((((4-fluoro-1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1ad): Yield = 76% (**1ad**): ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.53 (s).^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, *J* = 6.5 Hz, 2H), 7.21 – 7.17 (m, 1H), 7.12 (d, *J* = 8.2 Hz, 1H), 6.88 (dd, *J* = 11.2, 7.8 Hz, 1H), 3.83 (s, 3H), 1.69 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.26, 155.03 (d, $J_{C\text{-}F}$ = 247.0 Hz), 139.40 (d, $J_{C\text{-}F}$ = 7.6 Hz), 136.60 (d, $J_{C\text{-}F}$ =11.3 Hz), 133.69, 121.29 (d, $J_{C\text{-}F}$ = 8.8 Hz), 113.81 (d, $J_{C\text{-}F}$ = 18.9 Hz), 104.66 (d, $J_{C\text{-}F}$ = 20.2Hz), 104.03 (d, $J_{C\text{-}F}$ = 3.8 Hz), 102.42 (d, $J_{C\text{-}F}$ = 3.8 Hz), 79.78, 31.83, 22.49.

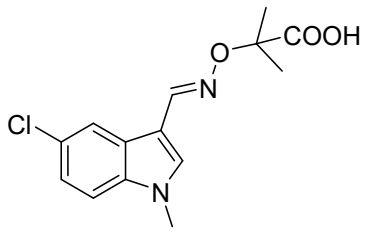


2-((((4-(methoxycarbonyl)-1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1ae): Yield = 76% (**1ae**);white solid; *E*:*Z* =1 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.79 (s, 1H, *Z*-isomers), 8.51 (s, 1H, *E*-isomers), 8.11 (s, 1H, *Z*-isomers), 7.88 (s, 1H, *E*-isomers), 7.80 (t, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 7.1 Hz, 1H), 7.68 (d, *J* = 7.0 Hz, 1H), 7.35 – 7.29 (m, 2H),

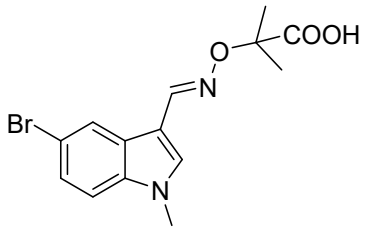
3.92 (d, *J* = 5.2 Hz, 6H), 3.89 (d, *J* = 8.2 Hz, 6H), 2.55 (s, 6H, *E*- and *Z*-isomers), 1.55 (s, 6H, *Z*-isomers), 1.48 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, DMSO-d_6) δ 175.66, 175.59, 168.82, 168.09, 146.66, 140.48, 138.38, 138.17, 137.14, 131.93, 124.28, 124.18, 123.88, 123.83, 123.72, 122.77, 121.71, 121.33, 115.99, 115.44, 107.22, 105.30, 81.23, 80.66, 52.69, 52.53, 40.87, 33.75, 33.39, 24.54, 24.51.



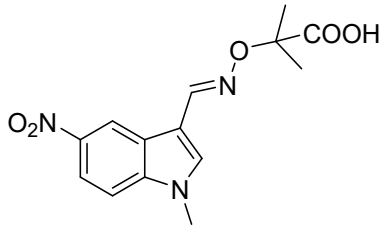
2-((((1,5-dimethyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1af): Yield = 69% (**1af**);white solid; *E*:*Z* =4 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (s, 1H, *E*-isomers), 8.03 (s, 0.25H, *Z*-isomers), 7.77 (d, *J* = 6.1 Hz, 1.3H), 7.51 (s, 0.25H, *Z*-isomers), 7.24 – 7.21 (m, 0.5H), 7.17 (d, *J* = 10.0 Hz, 2H), 7.11 (d, *J* = 8.2 Hz, 1.3H), 3.79 (s, 0.75H, *Z*-isomers), 3.72 (s, 3H, *E*-isomers), 2.48 (s, 0.75H, *Z*-isomers), 2.46 (s, 3H, *E*-isomers), 1.68 (s, 1.5H, *Z*-isomers), 1.63 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.14, 178.02, 146.33, 140.42, 136.17, 135.41, 134.43, 132.61, 130.99, 130.64, 127.67, 125.20, 124.84, 124.37, 121.86, 117.88, 109.51, 109.29, 107.66, 104.68, 81.65, 81.42, 33.42, 33.17, 24.45, 24.28, 21.65, 21.59.



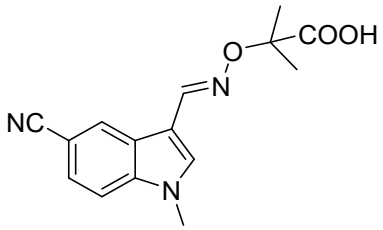
2-((((5-chloro-1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1ag): Yield = 76% (**1ag**);white solid; *E*:*Z* =7.6 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.31 (s, 1H, *E*-isomers), 8.23 (s, 0.13H, *Z*-isomers), 8.05 (d, *J* = 1.9 Hz, 0.13H), 7.90 (d, *J* = 2.1 Hz, 1H), 7.89 (s, 0.13H, *Z*-isomers), 7.74 (s, 1H, *E*-isomers), 7.55 (d, *J* = 8.9 Hz, 0.13H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.27 – 7.24 (m, 1.1H), 3.87 (s, 0.39H, *Z*-isomers), 3.81 (s, 3H, *E*-isomers), 1.56 (s, 0.79H, *Z*-isomers), 1.50 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, DMSO-d_6) δ 174.47, 143.69, 137.82, 135.79, 135.32, 134.00, 133.58, 127.27, 124.82, 124.73, 121.92, 121.53, 120.21, 117.54, 111.39, 106.91, 104.33, 80.27, 79.95, 32.58, 32.38, 23.50, 23.30.



2-((((5-bromo-1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1ah): Yield = 68% (**1ah**);white solid; *E*:*Z* =6 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.31 (s, 1H, *E*-isomers), 8.21 (s, 0.17H, *Z*-isomers), 8.19 (d, *J* = 1.8 Hz, 0.17H), 8.05 (d, *J* = 1.9 Hz, 1H), 7.89 (s, 0.17H, *Z*-isomers), 7.72 (s, 1H, *E*-isomers), 7.50 (d, *J* = 8.9 Hz, 0.17 H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.39 – 7.36 (m, 1.2H), 3.87 (s, 0.51H, *Z*-isomers), 3.80 (s, 3H, *E*-isomers), 1.55 (s, 1H, *Z*-isomers), 1.50 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, DMSO-d_6) δ 175.52, 144.75, 138.87, 136.69, 136.61, 134.91, 128.92, 126.51, 125.54, 125.14, 124.34, 121.64, 113.87, 113.81, 112.90, 107.86, 105.30, 81.32, 80.99, 33.62, 33.42, 24.56, 24.35.

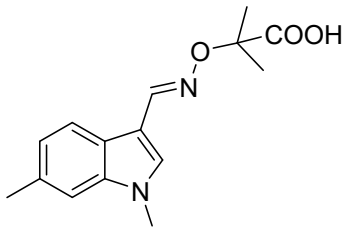


2-methyl-2-((((1-methyl-5-nitro-1*H*-indol-3-yl)methylene)amino)oxy)propanoic acid (1ai): Yield = 59% (**1ai**);white solid; *E*:*Z* =7 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.00 (d, *J* = 1.8 Hz, 0.14H), 8.85 (d, *J* = 2.1 Hz, 1H), 8.48 (s, 0.14H, *Z*-isomers), 8.39 (s, 1H, *E*-isomers), 8.13 (dd, *J* = 9.0, 2.1 Hz, 1.1H), 8.04 (s, 0.14H, *Z*-isomers), 7.92 (s, 1H, *E*-isomers), 7.74 – 7.70 (m, 1.1H), 3.95 (s, 0.42H, *Z*-isomers), 3.89 (s, 3H, *E*-isomers), 1.54 (s, 0.84H, *Z*-isomers), 1.52 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, DMSO-d_6) δ 175.57, 144.11, 142.14, 140.60, 138.94, 138.86, 138.23, 136.72, 126.28, 124.01, 118.77, 118.21, 117.73, 116.73, 111.41, 110.68, 108.05, 81.77, 81.30, 33.89, 33.71, 24.70, 24.51.

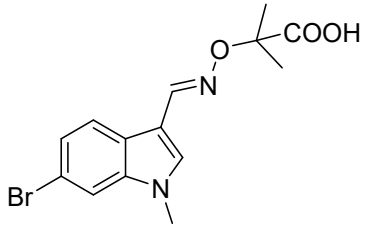


2-((((5-cyano-1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1aj): Yield = 71% (**1aj**);white solid; *E*:*Z* =5 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 0.2H, *Z*-isomers), 8.37 (s, 1H, *E*-isomers), 8.34 (s, 0.2H, *Z*-isomers), 8.26 (s, 1H, *E*-isomers), 7.97 (s, 0.2H, *Z*-isomers), 7.87 (s, 1H, *E*-isomers), 7.73 – 7.70 (m, 1.2H), 7.63 (d, *J* = 8.4 Hz, 1.2H), 3.93 (s, 0.6H, *Z*-isomers), 3.87 (s, 3H, *E*-isomers), 1.57 (s, 1.2H, *Z*-isomers), 1.51 (s, 6H, *E*-isomers).

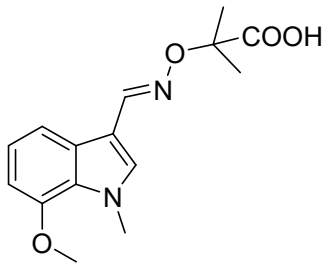
^{13}C NMR (126 MHz, DMSO-d_6) δ 175.47, 144.38, 139.41, 138.47, 137.64, 135.83, 127.07, 126.89, 125.83, 125.31, 124.97, 124.61, 120.87, 112.33, 112.22, 109.08, 106.31, 103.17, 103.00, 81.52, 81.26, 33.70, 33.51, 24.54, 24.33.



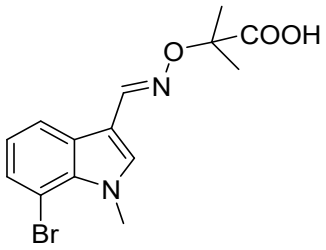
2-((((1,6-dimethyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1ak): Yield = 69% (**1ak**);white solid; *E*:*Z* =2 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (s, 1H, *E*-isomers), 8.00 (s, 0.5H, *Z*-isomers), 7.86 (d, *J* = 8.1 Hz, 1H), 7.80 (s, 0.5H, *Z*-isomers), 7.61 (d, *J* = 8.1 Hz, 1H), 7.16 (s, 1H, *E*-isomers), 7.13 (s, 0.5H, *Z*-isomers), 7.09 – 7.05 (m, 3H), 3.79 (s, 1.5H, *Z*-isomers), 3.73 (s, 3H, *E*-isomers)), 2.50 (s, 1.5H, *Z*-isomers), 2.49 (s, 3H, *E*-isomers), 1.68 (s, 3H, *Z*-isomers), 1.62 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.76, 177.70, 146.34, 140.54, 138.18, 136.40, 134.94, 133.33, 132.77, 132.22, 125.25, 123.24, 122.93, 122.74, 121.82, 117.84, 109.80, 109.59, 108.09, 105.01, 81.69, 81.44, 33.33, 33.08, 24.47, 24.28, 21.89, 21.84.



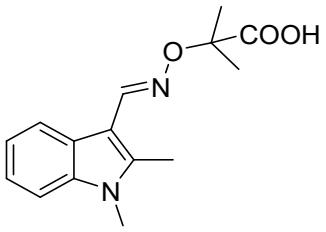
2-((((6-bromo-1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1al): Yield = 74% (**1al**);white solid; *E*:*Z* =3 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (s, 1H, *E*-isomers), 8.05 (s, 0.33H, *Z*-isomers), 7.82 (d, *J* = 8.5 Hz, 1H), 7.74 (s, 0.33H, *Z*-isomers), 7.58 (d, *J* = 8.5 Hz, 0.33H), 7.49 (d, *J* = 1.2 Hz, 0.33H), 7.40 (s, 1H, *E*-isomers), 7.32 (dd, *J* = 8.5, 1.5 Hz, 0.33H), 7.26 – 7.24 (m, 1H), 7.16 (s, 1H, *E*-isomers), 3.79 (s, 1H, *Z*-isomers), 3.71 (s, 3H, *E*-isomers), 1.68 (s, 2H, *Z*-isomers), 1.63 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.54, 178.25, 145.27, 139.59, 138.41, 136.76, 135.71, 132.57, 126.16, 124.51, 124.30, 123.79, 123.57, 119.57, 116.81, 116.30, 112.91, 112.55, 108.72, 105.47, 81.80, 81.47, 33.48, 33.21, 24.38, 24.13.



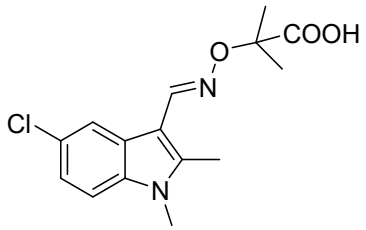
2-((((7-methoxy-1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1am): Yield = 73% (**1am**);white solid; *E*:*Z* =7.7 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.19 (s, 1H, *E*-isomers), 7.97 (s, 0.13H, *Z*-isomers), 7.72 (s, 0.13H, *Z*-isomers), 7.44 (d, *J* = 8.0 Hz, 1H), 7.42 (s, 1H, *E*-isomers), 7.36 (d, *J* = 8.0 Hz, 0.13H), 6.98 – 6.92 (m, 1.1H), 6.65 (d, *J* = 7.8 Hz, 1.1H), 3.97 (s, 0.39H, *Z*-isomers), 3.90 (s, 3H, *E*-isomers), 3.80 (d, *J* = 4.9 Hz, 3.4H), 1.47 (s, 0.78H, *Z*-isomers), 1.41 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, DMSO-d_6) δ 175.62, 148.04, 147.83, 144.97, 139.17, 136.19, 134.39, 129.74, 127.28, 127.14, 125.38, 121.88, 121.76, 115.05, 111.42, 108.39, 105.55, 104.50, 103.95, 81.23, 80.86, 56.03, 37.23, 37.01, 24.55, 24.38.



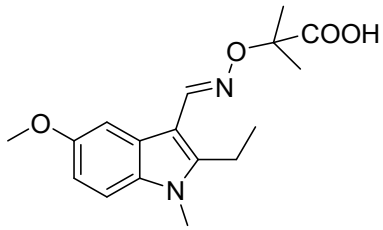
2-((((7-bromo-1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1an): Yield = 67% (**1an**);white solid; *E*:*Z* =2.3 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (s, 1H, *E*-isomers), 8.03 (s, 0.43H, *Z*-isomers), 7.95 (d, *J* = 7.9 Hz, 1H), 7.71 (s, 0.43H, *Z*-isomers), 7.62 (d, *J* = 7.9 Hz, 0.43H), 7.38 (d, *J* = 7.6 Hz, 0.43H), 7.34 (d, *J* = 7.7 Hz, 1H), 7.10 (s, 1H, *E*-isomers), 7.01 (t, *J* = 7.8 Hz, 0.43H),6.95 (t, *J* = 7.8 Hz, 1H), 4.15 (s, 1.3H, *Z*-isomers), 4.07 (s, 3H, *E*-isomers), 1.68 (s, 2.6H, *Z*-isomers), 1.63 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.01, 178.70, 144.97, 139.25, 137.95, 134.78, 134.04, 132.42, 130.35, 128.17, 128.09, 127.75, 122.41, 122.06, 121.73, 117.47, 108.23, 105.01, 104.46, 103.94, 81.75, 81.41, 37.60, 37.35, 24.34, 24.13.



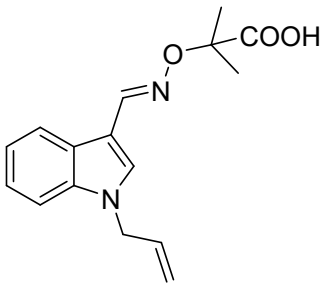
2-((((1,2-dimethyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1ba):^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.91 (d, *J* = 7.5 Hz, 1H), 7.20 – 7.15 (m, 3H), 3.53 (s, 3H), 2.34 (s, 3H), 1.64 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.16, 146.15, 140.49, 137.17, 124.84, 122.33, 121.41, 121.11, 108.93, 104.75, 81.35, 29.60, 24.27, 10.46.



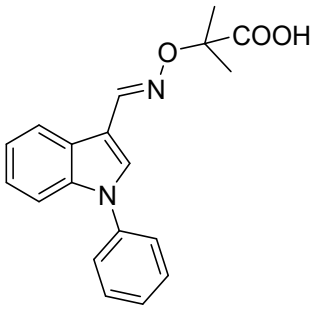
(*E*)-2-((((5-chloro-1,2-dimethyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1c): Yield = 68% (**1c**):^{1}H NMR (500 MHz, DMSO-d_6) δ 8.41 (s, 1H), 7.86 (d, J = 2.1 Hz, 1H), 7.46 (d, J = 8.7 Hz, 1H), 7.17 (dd, J = 8.7, 2.1 Hz, 1H), 3.66 (s, 3H), 2.46 (s, 3H), 1.50 (s, 6H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 175.61, 144.59, 142.50, 135.88, 125.83, 125.50, 121.94, 120.44, 111.59, 104.80, 80.92, 30.22, 24.37, 10.54.



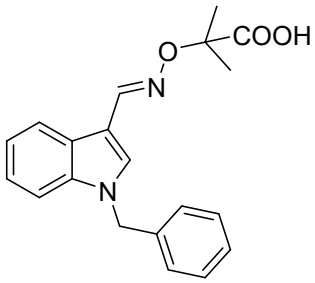
(*E*)-2-((((2-ethyl-5-methoxy-1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1d): Yield = 56% (**1d**):^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.48 (d, J = 2.4 Hz, 1H), 7.14 (d, J = 8.8 Hz, 1H), 6.86 (dd, J = 8.9, 2.5 Hz, 1H), 3.82 (s, 3H), 3.63 (s, 3H), 2.82 (q, J = 7.6 Hz, 2H), 1.63 (s, 6H), 1.21 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.43, 155.48, 146.13, 145.73, 132.25, 125.42, 112.33, 109.84, 103.82, 103.14, 81.41, 55.65, 29.71, 24.18, 18.03, 14.54.



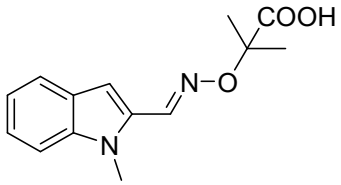
2-((((1-allyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1fa): Yield = 71% (**1fa**);white solid; *E*:*Z* =5 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (s, 1H, *E*-isomers), 8.14 (s, 0.2H, *Z*-isomers), 8.03 (d, J = 7.8 Hz, 1H), 7.83 (s, 0.2H, *Z*-isomers), 7.75 (d, J = 7.7 Hz, 0.2H), 7.36 – 7.19 (m, 5H), 6.03 – 5.91 (m, 1H), 5.27 –5.21 (m, 1.2H), 5.17 – 5.08 (m, 1.2H), 4.75 (d, J = 5.5 Hz, 0.4H), 4.69 – 4.68 (m, 2H), 1.68 (s, 1.2H, *Z*-isomers), 1.64 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.46, 145.94, 140.23, 137.15, 135.39, 134.45, 132.52, 132.38, 131.44, 127.60, 125.20, 123.29, 122.76, 122.42, 121.55, 121.21, 118.33, 118.29, 118.13, 110.31, 109.95, 108.83, 105.56, 81.68, 81.41, 49.40, 49.05, 24.40, 24.23.



2-methyl-2-((((1-phenyl-1*H*-indol-3-yl)methylene)amino)oxy)propanoic acid (1fb): Yield = 38% (**1fb**);white solid; *E*:*Z* =4 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.48 (s, 0.25H, *Z*-isomers), 8.41 (s, 1H, *E*-isomers), 8.07 (d, *J* = 7.7 Hz, 1H), 8.04 (s, 0.25H, *Z*-isomers), 8.01 (s, 1H, *E*-isomers), 7.64 (d, *J* = 4.3 Hz, 1H), 7.61 (d, *J* = 4.3 Hz, 4H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.50 – 7.44 (m, 1.3H), 7.32 – 7.24 (m, 2.5H), 1.56 (s, 1.5H, *Z*-isomers), 1.54 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, DMSO-d_6) δ 175.53, 175.44, 144.86, 139.02, 138.76, 138.73, 136.68, 135.06, 133.81, 132.55, 130.55, 130.43, 127.94, 127.66, 125.78, 124.77, 124.56, 124.24, 123.87, 122.80, 122.16, 121.95, 119.55, 111.22, 111.12, 107.93, 81.50, 81.16, 40.89, 24.47, 24.38.

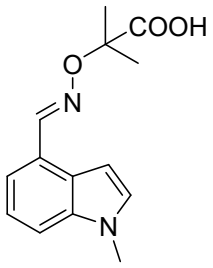


2-((((1-benzyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1fc): Yield = 59% (**1fc**);white solid; *E*:*Z* =4 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (s, 1H, *E*-isomers), 8.14 (s, 0.25H, *Z*-isomers), 8.06 – 8.04 (m, 1H), 7.84 (s, 0.25H, *Z*-isomers), 7.76 – 7.75 (m, 0.25H), 7.36 – 7.19 (m, 8.8H), 7.15 (d, *J* = 7.0 Hz, 0.5H), 7.10 – 7.09 (m, 2H), 5.32 (s, 0.5H, *Z*-isomers), 5.26 (s, 2H, *E*-isomers), 1.63 (s, 6H, *E*-isomers), 1.62 (s, 1.5H, *Z*-isomers). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.40, 178.16, 145.93, 140.27, 137.37, 136.40, 136.04, 134.86, 131.81, 128.96, 128.09, 128.03, 127.68, 127.16, 126.90, 125.27, 123.48, 122.93, 122.51, 121.68, 121.34, 118.35, 110.44, 110.08, 109.11, 105.71, 81.70, 81.45, 50.79, 50.38, 24.37, 24.25.

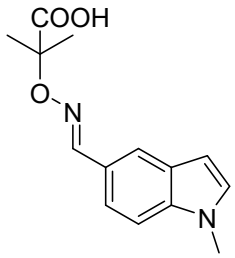


(*E*)-2-methyl-2-((((1-methyl-1*H*-indol-2-yl)methylene)amino)oxy)propanoic acid (1g): Yield = 65% (**1g**):^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.63 (d, *J* = 8.0 Hz,

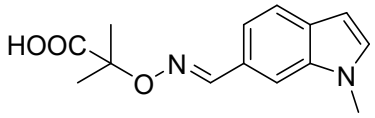
1H), 7.32 – 7.25 (m, 2H), 7.16 – 7.12 (m, 1H), 6.75 (s, 1H), 3.93 (s, 3H), 1.68 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.72, 143.60, 139.79, 130.96, 127.19, 123.93, 121.41, 120.10, 109.58, 108.62, 81.81, 32.25, 24.02.



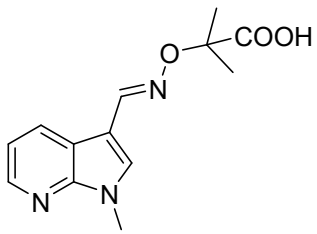
(*E*)-2-methyl-2-((((1-methyl-1*H*-indol-4-yl)methylene)amino)oxy)propanoic acid (1h): Yield = 56% (**1h**);white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.35 (dd, *J* = 7.1, 1.4 Hz, 1H), 7.21 – 7.17 (m, 2H), 7.04 (d, *J* = 3.1 Hz, 1H), 6.89 (d, *J* = 2.9 Hz, 1H), 3.75 (s, 3H), 1.66 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.77, 151.35, 137.00, 130.34, 125.18, 123.52, 122.37, 121.11, 111.63, 102.19, 81.72, 32.94, 24.18.



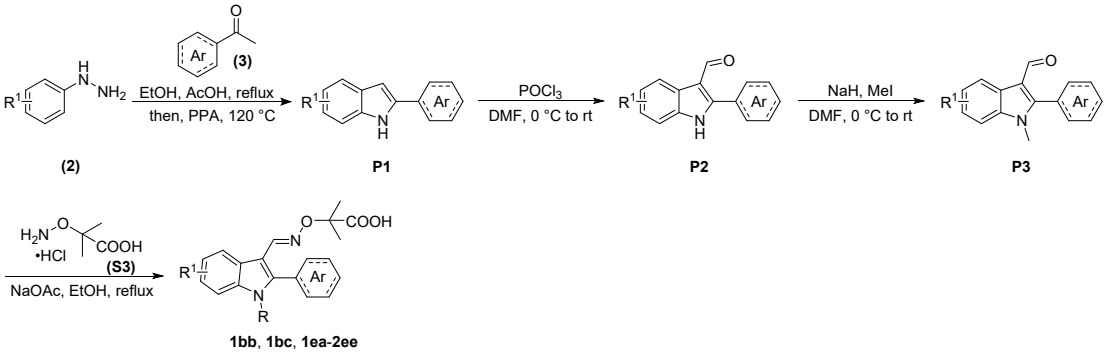
(*E*)-2-methyl-2-((((1-methyl-1*H*-indol-5-yl)methylene)amino)oxy)propanoic acid (2i): Yield = 53% (**2i**);white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.74 (s, 1H), 7.53 (dd, *J* = 8.6, 1.2 Hz, 1H), 7.25 – 7.23 (m, 1H), 7.04 (d, *J* = 3.1 Hz, 1H), 6.49 (d, *J* = 3.0 Hz, 1H), 3.76 (s, 3H), 1.62 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.79, 151.70, 137.78, 129.88, 128.37, 122.99, 121.81, 120.21, 109.74, 101.90, 81.47, 32.99, 24.28.



(*E*)-2-methyl-2-((((1-methyl-1*H*-indol-6-yl)methylene)amino)oxy)propanoic acid (1j): Yield = 51% (**1j**);white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.48 (s, 1H), 7.35 (dd, *J* = 8.3 , 1.1 Hz, 1H), 7.08 (d, *J* = 3.1 Hz, 1H), 6.46 (d, *J* = 2.7 Hz, 1H), 3.76 (s, 3H), 1.63 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.77, 151.62, 136.56, 130.87, 130.39, 125.00, 121.11, 118.73, 108.82, 101.40, 81.55, 32.97, 24.26.



2-methyl-2-((((1-methyl-1*H*-pyrrolo[2,3-b]pyridin-3-yl)methylene)amino)oxy)propanoic acid (1k): Yield = 63% (**1k**);white solid; *E*:*Z* =4.5 :1; Data of the mixture of *E*- and *Z*-isomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (dd, *J* = 4.8, 1.2 Hz, 0.22H), 8.35 (dd, *J* = 4.9, 1.4 Hz, 1H), 8.28 (dd, *J* = 7.8, 1.5 Hz, 1H), 8.21 (s, 1H, *E*-isomers), 8.18 (s, 0.22H, *Z*-isomers), 8.05 (dd, *J* = 7.9, 1.3 Hz, 0.22H), 7.67 (s, 0.22H, *Z*-isomers), 7.24 (s, 1H, *E*-isomers), 7.16 (dd, *J* = 7.9, 4.8 Hz, 0.22H), 7.06 (dd, *J* = 7.9, 4.8 Hz, 1H), 3.89 (s, 0.66H, *Z*-isomers), 3.81 (s, 3H, *E*-isomers), 1.71 (s, 1.3H, *Z*-isomers), 1.65 (s, 6H, *E*-isomers). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.02, 177.88, 147.79, 146.55, 144.51, 143.66, 143.39, 138.73, 135.27, 131.65, 131.48, 127.45, 119.80, 117.94, 117.08, 116.85, 107.55, 104.22, 81.87, 81.58, 32.04, 31.81, 24.37, 24.10.



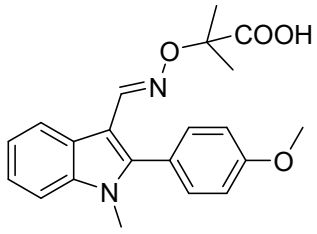
The various 2-aryl-1*H*-indoles **P1** were prepared according to reported method[5]: Appropriate amounts of substituted acetophenone **3** and phenyl hydrazine **2** (1.0 equiv.) were mixed in ethanol, and a few drops of glacial acetic acid was added. The solution was heated under reflux at 80 °C for 1.0–2.0 h. The solvent was evaporated in vacuum to give a solid that was added to polyphosphoric acid, and the mixture was slowly heated to 120 °C and kept at this temperature for a few hours until the reaction was complete. Once reaction was determined to be completed via TLC analysis, the mixture was allowed to cool and then poured into cold water. The acidic solution was neutralized by the slow addition of NaOH (1.0 M), and the solid precipitate of the crude product was collected. Purification by column chromatography gave the intermediates **P1**.

2-aryl-1*H*-indole-3-carbaldehyde **P2** were prepared according to reported method[1]: *N,N*-dimethylformamide (DMF, 10.0 equiv.) was cooled to 0 °C. Then, $POCl_3$ (5.0 equiv.) was added dropwise and stirred for 0.5 h. The reaction mixture was then warmed to room temperature and the intermediates **P1** (1.0 equiv.) in DMF were added dropwise via syringe for 2.0 h. Once reaction was determined to be

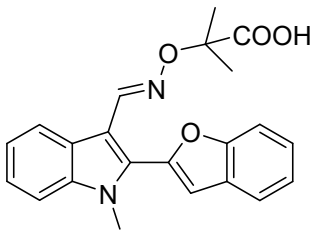
completed via TLC analysis, the mixture was quenched with water and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was purified by flash column chromatography to give the intermediates **P2**.

1-methyl-2-phenyl-1*H*-indole-3-carbaldehyde **P3** were prepared according to reported method[2a]: To a stirred solution of NaH (60% suspension in mineral oil, 1.5 equiv.) in dry *N,N*-dimethylformamide (DMF, 10.0 equiv.), the intermediates **P2** (1.0 equiv.) in DMF was added slowly at 0 ºC. The reaction mixture was then warmed to room temperature and stirred for 0.5 h. After cooling to 0 ºC again, iodomethane (2.0 equiv.) was added dropwise. The reaction mixture was warmed to room temperature again and stirred overnight. Once reaction was determined to be completed via TLC analysis, the mixture was quenched with water and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was purified by flash column chromatography to give the corresponding the intermediates **P3**.

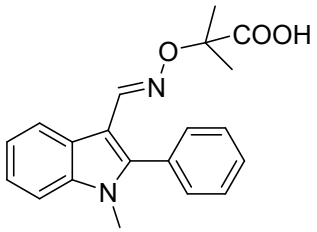
The starting substrates **1bb**, **1bc** and **1ea-1ee** were synthesized according to the following procedures[4]: 2-(aminooxy)-2-methylpropanoic acid hydrochloride**(S3)** (1.5 equiv.) and NaOAc (3.0 equiv.) were added to a stirred solution of the intermediates **P3** (1.0 equiv.) in EtOH (0.2 M) at room temperature overnight. Once reaction was determined to be completed via TLC analysis, the mixture was quenched with H_2O and extracted with ethyl acetate. The combined organic extracts were then washed with H_2O and brine, then dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to give desired products **1bb**, **1bc** and **1ea-1ee**.



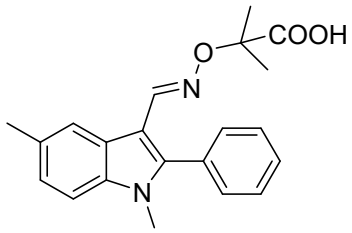
(*E*)-2-((((2-(4-methoxyphenyl)-1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1bb): Yield = 53% (**1bb**):^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.36 – 7.25 (m, 5H), 7.05 – 7.02 (m, 2H), 3.88 (s, 3H), 3.61 (s, 3H), 1.60 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.63, 160.39, 147.45, 144.82, 137.62, 132.06, 124.63, 123.29, 122.22, 121.96, 121.68, 114.22, 109.62, 106.48, 81.41, 55.47, 30.96, 24.25.



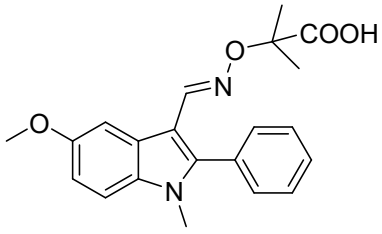
(*E*)-2-((((2-(benzofuran-2-yl)-1-methyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1bc): Yield = 49% (**1bc**):^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.57 (d, *J* = 8.2 Hz, 1H), 7.39 – 7.29 (m, 4H), 7.26 – 7.23 (m, 1H), 7.00 (s, 1H), 3.86 (s, 3H), 1.65 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.13, 155.46, 146.50, 145.77, 138.39, 132.41, 128.03, 125.48, 124.58, 124.41, 123.53, 123.04, 122.14, 121.51, 111.54, 109.96, 109.67, 109.32, 81.61, 31.80, 24.22.



(*E*)-2-methyl-2-((((1-methyl-2-phenyl-1*H*-indol-3-yl)methylene)amino)oxy)propanoic acid (1ea): Yield = 69% (**1ea**):^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 8.11 (d, *J* = 7.9 Hz, 1H), 7.53 – 7.47 (m, 3H), 7.39 – 7.37 (m, 2H), 7.35 – 7.31 (m, 2H), 7.28 – 7.24 (m, 1H), 3.61 (s, 3H), 1.60 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.49, 147.35, 144.76, 137.69, 130.78, 129.64, 129.31, 128.73, 124.61, 123.47, 122.32, 122.08, 109.68, 106.63, 81.47, 31.05, 24.25.

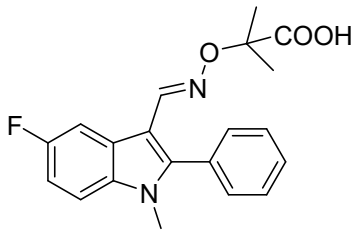


(*E*)-2-((((1,5-dimethyl-2-phenyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1eb): Yield = 52% (**1eb**):^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.87 (s, 1H), 7.53 – 7.48 (m, 3H), 7.37 (dd, *J* = 7.4, 1.9 Hz, 2H),7.25 (d, *J* = 8.3 Hz, 1H), 7.15 (dd, *J* = 8.4, 1.0 Hz, 1H), 3.59 (s, 3H), 2.49 (s, 3H), 1.60 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.90, 147.46, 144.79, 136.10, 131.56, 130.78, 129.76, 129.23, 128.70, 124.94, 124.79, 122.03, 109.39, 106.11, 81.43, 31.08, 24.26, 21.76.

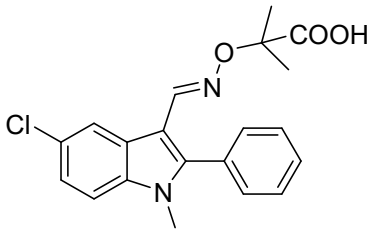


(*E*)-2-((((5-methoxy-1-methyl-2-phenyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1ec): Yield = 49% (**1ec**):^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.60 (d, *J* = 2.5 Hz, 1H), 7.54 – 7.48 (m, 3H), 7.40 – 7.37 (m, 2H), 7.25 (d, *J* = 9.3 Hz, 1H), 6.95 (dd, *J* = 8.9, 2.5 Hz, 1H), 3.86 (s, 3H), 3.61 (s, 3H), 1.60 (s, 6H). ^{13}C

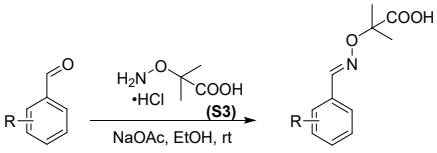
NMR (126 MHz, $CDCl_3$) δ 177.68, 155.83, 147.28, 144.79, 132.66, 130.73, 129.72, 129.21, 128.70, 125.08, 113.63, 110.49, 106.34, 103.60, 81.51, 55.67, 31.16, 24.14.



(*E*)-2-((((5-fluoro-1-methyl-2-phenyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1ed): Yield = 51% (**1ed**):^{19}F NMR (471 MHz, $CDCl_3$) δ -120.22 (s).;^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.76 (dd, J = 9.5, 2.5 Hz, 1H), 7.53 – 7.49 (m, 3H), 7.38 – 7.36 (m, 2H), 7.27 – 7.24 (m, 1H), 7.06 – 7.02 (m, 1H), 3.60 (s, 3H), 1.61 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.47, 159.05 (d, J_{C-F} = 236.9 Hz), 146.47, 145.48, 134.20, 130.69, 129.48, 129.37, 128.75, 125.06 (d, J_{C-F} = 10.1 Hz), 111.50 (d, J_{C-F} = 26.5 Hz), 110.31 (d, J_{C-F} = 8.8 Hz), 107.71 (d, J_{C-F} = 25.2 Hz), 106.91 (d, J_{C-F} = 3.8 Hz), 81.37, 31.20, 24.14.

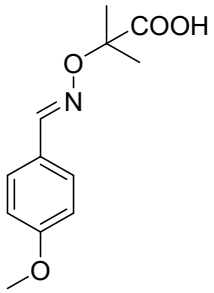


(*E*)-2-((((5-chloro-1-methyl-2-phenyl-1*H*-indol-3-yl)methylene)amino)oxy)-2-methylpropanoic acid (1ee): Yield = 52% (**1ee**):^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 8.06 (s, 1H), 7.54 – 7.49 (m, 3H), 7.39 – 7.37 (m, 2H), 7.26 (s, 2H), 3.60 (s, 3H), 1.61 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.76, 146.47, 145.25, 136.05, 130.70, 129.46, 129.31, 128.79, 127.51, 125.62, 123.59, 121.93, 110.60, 106.51, 81.47, 31.17, 24.19.

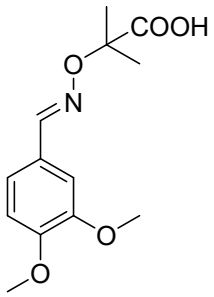


(4) **1l-1n**

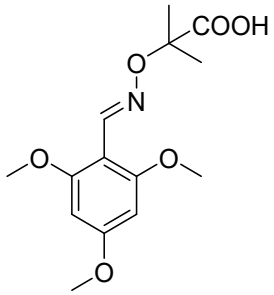
The starting substrates **1l-1n** were synthesized according to the following procedures[4]: 2-(aminooxy)-2-methylpropanoic acid hydrochloride **S3** (1.5 equiv.) and NaOAc (3.0 equiv.) were added to a stirred solution of benzaldehyde **4** (1.0 equiv.) in EtOH (0.2 M) at room temperature overnight. Once reaction was determined to be completed via TLC analysis, the mixture was quenched with H_2O and extracted with ethyl acetate. The combined organic extracts were then washed with H_2O and brine, then dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to give desired products **1l-1n**.



(*E*)-2-(((4-methoxybenzylidene)amino)oxy)-2-methylpropanoic acid (1l): Yield = 92% (**1l**):^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.53 – 7.50 (m, 2H), 6.89 – 6.87 (m, 2H), 3.82 (s, 3H), 1.60 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.26, 161.24, 149.54, 128.87, 124.44, 114.18, 81.48, 55.36, 24.15.



(*E*)-2-(((3,4-dimethoxybenzylidene)amino)oxy)-2-methylpropanoic acid (1m): Yield = 82% (**1m**):^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.17 (d, *J* = 1.8 Hz, 1H), 7.03 (dd, *J* = 8.3, 1.8 Hz, 1H), 6.83 (d, *J* = 8.3 Hz, 1H), 3.89 (d, *J* = 1.1 Hz, 6H), 1.61 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.19, 151.01, 149.79, 149.24, 124.67, 121.97, 110.75, 108.39, 81.46, 55.93, 55.92, 24.16.



(*E*)-2-methyl-2-(((2,4,6-trimethoxybenzylidene)amino)oxy)propanoic acid (1n): Yield = 86% (**1n**):^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48 (s, 1H), 6.13 (s, 2H), 3.87 (s, 6H), 3.86 (s, 3H), 1.55 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.83, 163.73, 160.64, 144.81, 100.96, 90.59, 81.79, 55.81, 55.50, 24.66.

5. General Procedure and Characterization of the Electrolysis Products

Into a round bottom flask, the substrate (0.25 mmol) and MeOH/MeCN (4.0 mL/1.0 mL) with TBAOAc (0.1 M) as an electrolyte was added. The flask was equipped with a reticulated vitreous carbon anode (100.0 PPI, 1.0 cm × 1.0 cm × 0.5 cm) and a platinum plate (1.0 cm × 1.5 cm) cathode. The constant current (4.0 mA) electrolysis was carried out at room temperature until complete consumption of the substrate (monitored by TLC). Water (10.0 mL) was added to the reaction solution and MeOH/MeCN was then removed under reduced pressure. The resulting suspension was extracted with ethyl acetate (3 × 10.0 mL). The combined organic solution was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed through silica gel eluting with ethyl acetate/petroleum ether to give the desired product.

The sequential one pot electrochemical gram scale electrolysis of compound **1aa** according to the following procedures: into a 100.0 mL three-necked flask,2-(aminooxy)-2-methylpropanoic acid hydrochloride **S3** (1.5 equiv.) and NaOAc (3.0 equiv.) were added to a stirred solution of 1-methyl-1*H*-indole-3-carbaldehyde (1.0 g, 6.3 mmol) in MeOH/MeCN (40.0 mL/10.0 mL) at 60 ℃ for 1.5 h. Once reaction was determined to be completed via TLC analysis, the mixture was equipped with TBAOAc (0.1 M) as an electrolyte for 22.5 h using a RVC plate (100.0PPI, 3.5 cm × 2.0 cm × 0.5 cm) as anode, a Pt plate cathode (3.0 cm × 2.0 cm) and a constant current of 28.0 mA. The RVC was fixed on a sharpened graphite rod (d = 5.0 mm). Water (50.0 mL) was added to the reaction solution and MeOH/MeCN was then removed under reduced pressure. The resulting suspension was extracted with ethyl acetate (3 × 50.0 mL). The combined organic solution was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed through silica gel eluting with ethyl acetate/petroleum ether to give the desired product **2aa** (83% yield).

The general procedure for radical trap experiment according to the following procedures: into a round bottom flask, the substrate (0.25 mmol) and MeOH/MeCN (4.0 mL/1.0 mL) with TBAOAc (0.1 M) as an electrolyte was added. 2.0 equiv of radical scavenger butylated hydroxytoluene (BHT) was then added into the reaction mixture. The flask was equipped with a reticulated vitreous carbon anode (100.0 PPI, 1.0 cm × 1.0 cm × 0.5 cm) and a platinum plate (1.0 cm × 1.5 cm) cathode. The constant current (4.0 mA) electrolysis was carried out at room temperature for 3.5 hours. After the electrolysis, 100.0 μL of the reaction mixture was extracted and filtered by syringe filter nylon membrane (PRECLEANTM 13.0 mm Syringe Filter Nylon membrane, 0.2 μm) and then detected by HR-MS. Water (10.0 mL) was added to the remaining reaction solution and MeOH/MeCN was then removed under reduced pressure. The resulting suspension was extracted with ethyl acetate (3 × 10.0 mL). The combined organic solution was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The yield of the desired product was determined by crude NMR using $MeNO_2$ as internal standard.

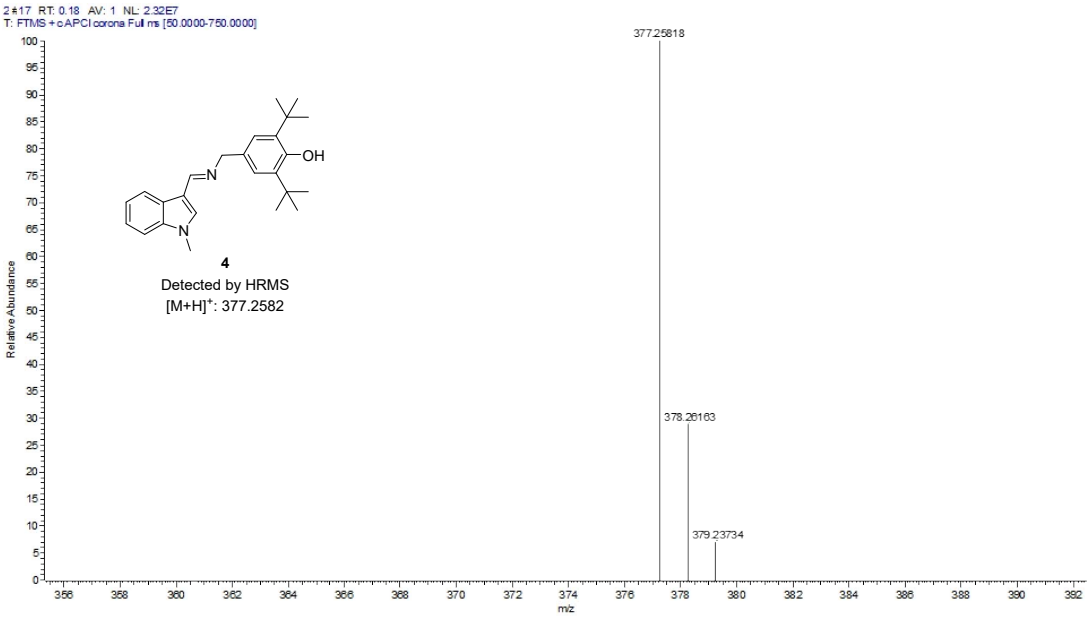
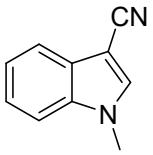
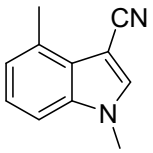


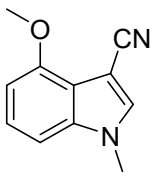
Figure S2. HR-MS result for **4**



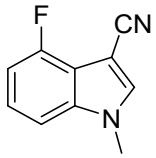
1-methyl-1*H*-indole-3-carbonitrile (2aa)[6]: The crude product was purified by column chromatography on silica gel to give **2aa** as colorless oil (35.9 mg, 92%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 7.9 Hz, 1H), 7.53 (s, 1H), 7.38 (d, J = 8.1 Hz, 1H), 7.36 – 7.33 (m, 1H), 7.30 – 7.27 (m, 1H), 3.83 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.03, 135.59, 127.80, 123.88, 122.14, 119.81, 115.99, 110.39, 85.43, 33.64; HRMS (m/z) calcd. for $C_{10}H_8N_2$ $[M+H]^+$: 157.0760; found: 157.0758.



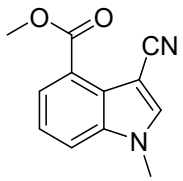
1,4-dimethyl-1*H*-indole-3-carbonitrile (2ab)[7]: **T**he crude product was purified by column chromatography on silica gel to give **2ab** as colorless oil (36.6 mg, 86%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.25 – 7.21 (m, 2H), 7.02 – 7.00 (m, 1H), 3.80 (s, 3H), 2.76 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.12, 131.33, 126.29, 123.99, 123.07, 117.63, 108.05, 84.69, 33.72, 18.45; HRMS (m/z) calcd. for $C_{11}H_{10}N_2$ $[M+H]^+$: 171.0917; found: 171.0913.



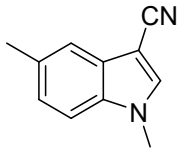
4-methoxy-1-methyl-1*H*-indole-3-carbonitrile (2ac)[8]: The crude product was purified by column chromatography on silica gel to give **2ac** as colorless oil (42.8 mg, 92%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.24 (t, *J* = 8.1 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 6.64 (d, *J* = 7.9 Hz, 1H), 3.97 (s, 3H), 3.79 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.64, 137.55, 135.13, 124.91, 117.46, 116.82, 103.21, 101.84, 83.94, 55.65, 33.80; HRMS (m/z) calcd. for $C_{11}H_{10}N_2O$ $[M+H]^+$: 187.0866; found: 187.0660.



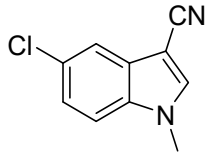
4-fluoro-1-methyl-1*H*-indole-3-carbonitrile (2ad): The crude product was purified by column chromatography on silica gel to give **2ad** as colorless oil (34.0 mg, 78%); ^{19}F NMR (471 MHz, $CDCl_3$) δ -122.30 (s).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.28 – 7.24 (m, 1H), 7.17 (d, *J* = 8.3 Hz, 1H), 6.92 (dd, *J* = 10.1, 7.9 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.88 (d, *J* = 250.7 Hz), 138.53 (d, *J* = 8.8 Hz), 136.27, 124.65 (d, *J* = 7.6 Hz), 116.35 (d, *J* = 20.2 Hz),115.63, 107.28 (d, *J* = 17.6 Hz), 106.59 (d, *J* = 3.8 Hz), 82.71, 34.03; HRMS (m/z) calcd. for $C_{10}H_7FN_2$ $[M+H]^+$: 175.0666; found: 175.0664.



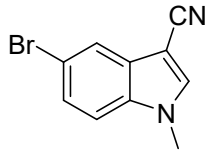
methyl 3-cyano-1-methyl-1*H*-indole-4-carboxylate (2ae): The crude product was purified by column chromatography on silica gel to give **2ae** as colorless oil (36.4 mg, 68%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 7.5, 0.7 Hz, 1H), 7.72 (s, 1H), 7.58 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 4.04 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.98, 139.57, 137.08, 125.68, 124.27, 123.06, 123.06,116.78, 115.03, 86.84, 51.25, 33.90; HRMS (m/z) calcd. for $C_{12}H_{10}N_2O_2$ $[M+H]^+$: 215.0815; found: 215.0813.



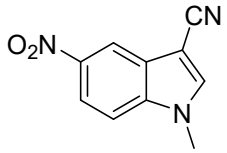
1,5-dimethyl-1*H*-indole-3-carbonitrile (2af)[6]: The crude product was purified by column chromatography on silica gel to give **2af** as colorless oil (34.5 mg, 81%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.47 (s, 1H), 7.26 (d, *J* = 8.3 Hz, 1H), 7.16 (dd, *J* = 8.4, 0.6 Hz, 1H), 3.80 (s, 3H), 2.47 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.41, 134.44, 131.84, 128.10, 125.51, 119.42, 116.19, 110.03, 84.74, 33.64, 21.41; HRMS (m/z) calcd. for $C_{11}H_{10}N_2$ $[M+H]^+$: 171.0917; found: 171.0913.



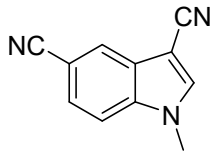
5-chloro-1-methyl-1*H*-indole-3-carbonitrile (2ag)[6]: The crude product was purified by column chromatography on silica gel to give **2ag** as colorless oil (34.8 mg, 73%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 1.1 Hz, 1H), 7.54 (s, 1H), 7.30 – 7.26 (m, 2H), 3.84 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.55, 134.45, 128.69, 128.32, 124.42, 119.27, 115.21, 111.52, 85.25, 33.89; HRMS (m/z) calcd. for $C_{10}H_7ClN_2$ $[M+H]^+$: 191.0371; found: 191.0367.



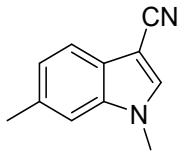
5-bromo-1-methyl-1*H*-indole-3-carbonitrile (2ah)[6]: The crude product was purified by column chromatography on silica gel to give **2ah** as colorless oil (47.6 mg, 81%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.0 Hz, 1H), 7.51 (s, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 7.8 Hz, 1H), 4.20 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.02, 132.58, 130.71, 128.93, 123.24, 119.32, 115.05, 104.79, 85.88, 37.97; HRMS (m/z) calcd. for $C_{10}H_7BrN_2$ $[M+H]^+$: 232.9720; found: 232.9716.



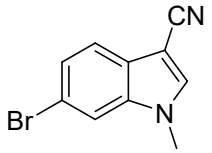
1-methyl-5-nitro-1*H*-indole-3-carbonitrile (2ai)[6]: The crude product was purified by column chromatography on silica gel to give **2ai** as colorless oil (34.2 mg, 68%); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.57 (s, 1H), 8.53 (d, *J* = 2.2 Hz, 1H), 8.25 (dd, *J* = 9.1, 2.2 Hz, 1H), 7.92 (d, *J* = 9.2 Hz, 1H), 4.00 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 143.18, 142.06, 139.20, 126.68, 118.96, 115.68, 115.07, 113.03, 86.27, 34.45; HRMS (m/z) calcd. for $C_{10}H_7N_3O_2$ $[M+H]^+$: 200.0465; found: 200.0459.



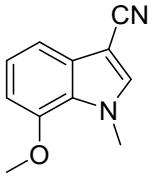
1-methyl-1*H*-indole-3,5-dicarbonitrile (2aj)[6]: The crude product was purified by column chromatography on silica gel to give **2aj** as colorless oil (29.0 mg, 64%);^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.74 (s, 1H), 7.59 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.51 (d, *J* = 8.6 Hz, 1H), 3.94 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.81, 137.53, 127.45, 126.84, 125.15, 119.34, 114.32, 111.59, 105.83, 87.01, 34.04; HRMS (m/z) calcd. for $C_{11}H_7N_3$ $[M+H]^+$: 180.0567; found: 180.0559.



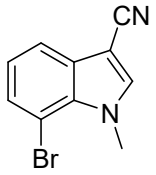
1,6-dimethyl-1*H*-indole-3-carbonitrile (2ak)[6]: The crude product was purified by column chromatography on silica gel to give **2ak** as colorless oil (38.3 mg, 90%);^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.1 Hz, 1H), 7.44 (s, 1H), 7.16 (s, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 3.77 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.42, 135.12, 134.01, 125.57, 123.91, 119.38, 116.22, 110.27, 85.12, 33.52, 21.85; HRMS (m/z) calcd. for $C_{11}H_{10}N_2$ $[M+H]^+$: 171.0917; found: 171.0913.



6-bromo-1-methyl-1*H*-indole-3-carbonitrile (2al)[6]: The crude product was purified by column chromatography on silica gel to give **2al** as colorless oil (44.1 mg, 75%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.5 Hz, 1H), 7.54 – 7.53 (m, 2H), 7.37 (dd, *J* = 8.5, 1.6 Hz, 1H), 3.81 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.77, 136.14, 126.54, 125.50, 121.04, 117.53, 115.31, 113.55, 85.96, 33.80; HRMS (m/z) calcd. for $C_{10}H_7BrN_2$ $[M+H]^+$: 234.9865; found: 234.9863.

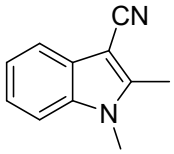


7-methoxy-1-methyl-1*H*-indole-3-carbonitrile (2am): The crude product was purified by column chromatography on silica gel to give **2am** as colorless oil (39.6 mg, 85%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (s, 1H), 7.30 – 7.28 (m, 1H), 7.14 (t, *J* = 8.0 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 4.05 (s, 3H), 3.92 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.22, 136.14, 130.23, 125.83, 122.83, 116.10, 112.15, 104.15, 85.24, 55.53, 37.58; HRMS (m/z) calcd. for $C_{11}H_{10}N_2O$ $[M+H]^+$: 187.0866; found: 187.0863.

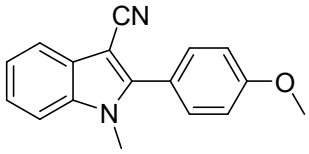


7-bromo-1-methyl-1*H*-indole-3-carbonitrile (2an)[9]: The crude product was purified by column chromatography on silica gel to give **2an** as colorless oil (39.4 mg, 67%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 1.7 Hz, 1H), 7.52 (s, 1H), 7.40 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.24 (d, *J* = 8.8 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ

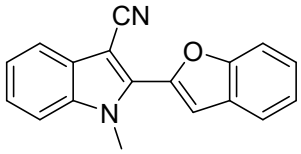
136.44, 134.72, 129.22, 126.96, 122.29, 115.76, 115.20, 111.91, 85.09, 33.89; HRMS (m/z) calcd. for $C_{10}H_7BrN_2$ $[M+H]^+$: 234.9865; found: 234.9862.



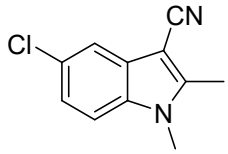
1,2-dimethyl-1*H*-indole-3-carbonitrile (2ba)[8]: The crude product was purified by column chromatography on silica gel to give **2ba** as colorless oil (34.9 mg, 82%);^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.4 Hz, 1H), 7.29 – 7.20 (m, 3H), 3.65 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.76, 136.28, 126.99, 122.99, 121.92, 118.89, 116.66, 109.82, 84.68, 30.18, 11.99; HRMS (m/z) calcd. for $C_{11}H_{10}N_2$ $[M+H]^+$: 171.0917; found: 171.0914.



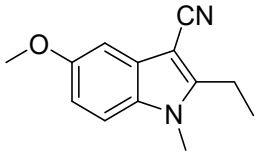
2-(4-methoxyphenyl)-1-methyl-1*H*-indole-3-carbonitrile (2bb)[10]: The crude product was purified by column chromatography on silica gel to give **2bb** as colorless oil (48.5 mg, 74%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.39 – 7.28(m, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 3.87 (s, 3H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.84, 148.27, 136.82, 131.26, 127.63, 123.68, 122.34, 120.88, 119.38, 117.01, 114.55, 110.51, 85.00, 55.48, 31.72; HRMS (m/z) calcd. for $C_{17}H_{14}N_2O$ $[M+H]^+$: 263.1179; found: 263.1175.



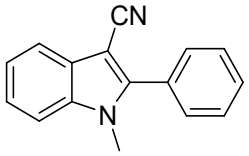
2-(benzofuran-2-yl)-1-methyl-1*H*-indole-3-carbonitrile (2bc): The crude product was purified by column chromatography on silica gel to give **2bc** as colorless oil (39.5 mg, 58%);^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.9 Hz, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.49 (s, 1H), 7.40 – 7.33 (m, 3H), 7.30 – 7.26 (m, 2H), 4.04 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.96, 145.21, 137.33, 136.16, 127.83, 127.73, 126.04, 124.70, 123.80, 122.74, 121.92, 119.67, 116.33, 111.50, 110.46, 109.51, 85.64, 32.79; HRMS (m/z) calcd. for $C_{18}H_{12}N_2O$ $[M+H]^+$: 273.1022; found: 273.1019.



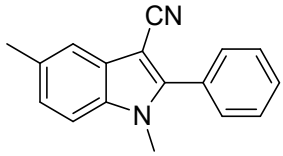
5-chloro-1,2-dimethyl-1*H*-indole-3-carbonitrile (2c): The crude product was purified by column chromatography on silica gel to give **2cb** as colorless oil (47.1 mg, 92%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.17 (d, *J* = 1.1 Hz, 2H), 3.66 (s, 3H), 2.53 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.88, 134.66, 127.85, 127.80, 123.31, 118.28, 110.86, 84.48, 30.43, 12.09; HRMS (m/z) calcd. for $C_{11}H_9ClN_2$ $[M+H]^+$: 205.0527; found: 205.0523.



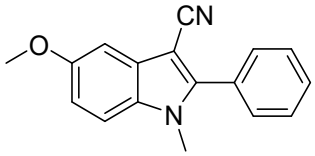
2-ethyl-5-methoxy-1-methyl-1*H*-indole-3-carbonitrile (2d): The crude product was purified by column chromatography on silica gel to give **2d** as colorless oil (35.9 mg, 67%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.9 Hz, 1H), 7.10 (d, *J* = 2.4 Hz, 1H), 6.90 (dd, *J* = 8.9, 2.4 Hz, 1H), 3.86 (s, 3H), 3.69 (s, 3H), 2.94 (q, *J* = 7.6 Hz, 2H), 1.34 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.88, 150.96, 131.26, 127.96, 116.84, 113.26, 110.74, 100.64, 83.37, 55.84, 30.25, 19.73, 13.67; HRMS (m/z) calcd. for $C_{13}H_{14}N_2O$ $[M+H]^+$: 215.1179; found: 215.1176.



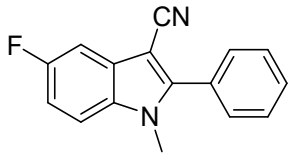
1-methyl-2-phenyl-1*H*-indole-3-carbonitrile (2ea)[6]: The crude product was purified by column chromatography on silica gel to give **2ea** as colorless oil (56.9 mg, 98%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.8 Hz, 1H), 7.56 – 7.49 (m, 5H), 7.41 (d, *J* = 8.1 Hz, 1H), 7.37 – 7.34 (m, 1H), 7.32 – 7.29 (m, 1H), 3.73 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.12, 136.89, 129.94, 129.87, 129.06, 128.75, 127.62, 123.93, 122.46, 119.54, 116.71, 110.61, 85.53, 31.77; HRMS (m/z) calcd. for $C_{16}H_{12}N_2$ $[M+H]^+$: 233.1073; found: 233.1068.



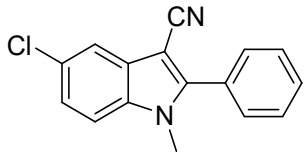
1,5-dimethyl-2-phenyl-1*H*-indole-3-carbonitrile (2eb)[11]: The crude product was purified by column chromatography on silica gel to give **2eb** as colorless oil (52.3 mg, 85%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.52 (m, 6H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.22 (dd, *J* = 8.4, 1.2 Hz, 1H), 3.75 (s, 3H), 2.54 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.91, 135.32, 132.14, 129.84, 129.82, 129.01, 128.89, 127.88, 125.51, 119.19, 116.91, 110.26, 84.89, 31.78, 21.50; HRMS (m/z) calcd. for $C_{17}H_{14}N_2$ $[M+H]^+$: 247.1230; found: 247.1227.



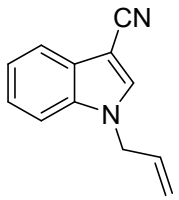
5-methoxy-1-methyl-2-phenyl-1*H*-indole-3-carbonitrile (2ec)[12]: The crude product was purified by column chromatography on silica gel to give **2ec** as colorless oil (60.3 mg, 92%);^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 – 7.47 (m, 5H), 7.28 (d, *J* = 9.0 Hz, 1H), 7.17 (d, *J* = 2.3 Hz, 1H), 6.97 (dd, *J* = 8.9, 2.4 Hz, 1H), 3.87 (s, 3H), 3.70 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.19, 147.91, 131.89, 129.82, 129.79, 129.01, 128.85, 128.43, 116.97, 114.43, 111.51, 100.66, 85.05, 55.84, 31.85; HRMS (m/z) calcd. for $C_{17}H_{14}N_2O$ $[M+H]^+$: 263.1179; found: 263.1174.



5-fluoro-1-methyl-2-phenyl-1*H*-indole-3-carbonitrile (2ed): The crude product was purified by column chromatography on silica gel to give **2ed** as colorless oil (49.4 mg, 79%); ^{19}F NMR (471 MHz, $CDCl_3$) δ -120.22 (s).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 – 7.52 (m, 5H), 7.38 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.34 (dd, *J* = 9.0, 4.1 Hz, 1H), 7.08 (td, *J* = 9.0, 2.5 Hz, 1H), 3.74 (s, 3H).;^{13}C NMR (126 MHz, $CDCl_3$) δ 159.32 (d, $J_{C\text{-}F}$= 239.4 Hz), 149.31, 133.42, 130.14, 129.78, 129.11, 128.44, 128.21, 128.12, 116.21, 112.42 (d, $J_{C\text{-}F}$= 26.5 Hz), 104.78 (d, $J_{C\text{-}F}$= 10.1 Hz), 104.78 (d, $J_{C\text{-}F}$= 25.2 Hz), 85.57 (d, $J_{C\text{-}F}$= 5.0 Hz), 32.00; HRMS (m/z) calcd. for $C_{16}H_{11}FN_2$ $[M+H]^+$: 251.0979; found: 251.0975.

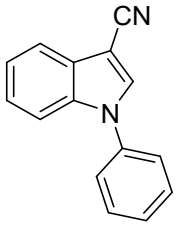


5-chloro-1-methyl-2-phenyl-1*H*-indole-3-carbonitrile (2ee): The crude product was purified by column chromatography on silica gel to give **2ee** as colorless oil (64.7 mg, 97%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 1.8 Hz, 1H), 7.56 – 7.52 (m, 5H), 7.32 (d, *J* = 8.7 Hz, 1H), 7.28 (dd, *J* = 8.7, 1.9 Hz, 1H), 3.73 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.06, 135.23, 130.17, 129.75, 129.09, 128.45, 128.32, 128.21, 124.27, 118.91, 115.96, 111.66, 85.12, 31.94; HRMS (m/z) calcd. for $C_{16}H_{11}ClN_2$ $[M+H]^+$: 267.0684; found: 267.0680.

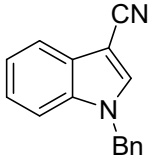


1-allyl-1*H*-indole-3-carbonitrile (2fa)[12]: The crude product was purified by column chromatography on silica gel to give **2fa** as colorless oil (39.6mg, 87%); ^{1}H NMR (500

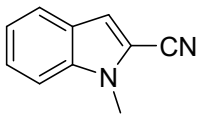
MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.8 Hz, 1H), 7.59 (s, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.34 – 7.27 (m, 2H), 6.01 – 5.93 (m, 1H), 5.30 (d, *J* = 10.3 Hz, 1H), 5.15 (d, *J* = 17.1 Hz, 1H), 4.75 (d, *J* = 5.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.45, 134.73, 131.68, 127.94, 123.91, 122.24, 119.92, 119.03, 115.92, 110.80, 85.98, 49.50; HRMS (m/z) calcd. for $C_{12}H_{10}N_2$ $[M+H]^+$: 183.0917; found: 183.0914.



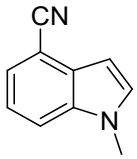
1-phenyl-1*H*-indole-3-carbonitrile (2fb)[12]: The crude product was purified by column chromatography on silica gel to give **2fb** as colorless oil (52.9 mg, 97%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.80 (m, 1H), 7.78 (s, 1H), 7.58 – 7.55 (m, 2H), 7.52 – 7.46 (m, 4H), 7.35 – 7.32 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.08, 130.86, 129.94, 125.32, 123.68, 123.23, 120.14, 119.83, 118.09, 115.30, 110.82, 106.83, 83.36; HRMS (m/z) calcd. for $C_{15}H_{10}N_2$ $[M+H]^+$: 219.0917; found: 219.0913.



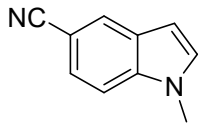
1-benzyl-1*H*-indole-3-carbonitrile (2fc)[12]: The crude product was purified by column chromatography on silica gel to give **2fc** as colorless oil (53.4 mg, 92%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.73 (m, 1H), 7.56 (s, 1H), 7.36 – 7.25 (m, 6H), 7.13 – 7.12 (m, 2H), 5.30 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.64, 135.31, 135.08, 129.17, 128.47, 128.02, 127.17, 124.07, 122.35, 119.98, 115.90, 110.95, 86.22, 50.92; HRMS (m/z) calcd. for $C_{16}H_{12}N_2$ $[M+H]^+$: 233.1073; found: 233.1069.



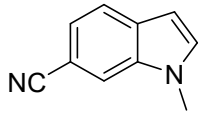
1-methyl-1*H*-indole-2-carbonitrile (2g)[13]: The crude product was purified by column chromatography on silica gel to give **2g** as colorless oil (32.4 mg, 83%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.1 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.15 (s, 1H), 3.89 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.00, 126.13, 125.84, 122.36, 121.39, 113.69, 112.68, 110.24, 110.14, 31.53; HRMS (m/z) calcd. for $C_{10}H_8N_2$ $[M+H]^+$: 157.0760; found: 157.0759.



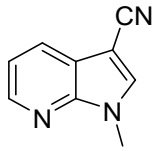
1-methyl-1*H*-indole-4-carbonitrile (2h)[14]: The crude product was purified by column chromatography on silica gel to give **2h** as colorless oil (14.5 mg, 37%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.3 Hz, 1H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.25 (d, *J* = 7.5 Hz, 1H), 7.23 – 7.22 (m, 1H), 6.69 (dd, *J* = 3.1, 0.6 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.38, 131.46, 129.70, 124.86, 121.09, 118.81, 114.00, 103.11, 100.14, 33.13; HRMS (m/z) calcd. for $C_{10}H_8N_2$ $[M+H]^+$: 157.0760; found: 157.0759.



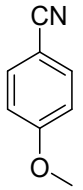
1-methyl-1*H*-indole-5-carbonitrile (2i)[15]: The crude product was purified by column chromatography on silica gel to give **2i** as colorless oil (16.4 mg, 42%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.44 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.36 (d, *J* = 8.6 Hz, 1H), 7.17 (d, *J* = 3.2 Hz, 1H), 6.56 (d, *J* = 3.1 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.16, 131.14, 128.16, 126.49, 124.46, 120.90, 110.08, 102.36, 102.16, 33.09; HRMS (m/z) calcd. for $C_{10}H_8N_2$ $[M+H]^+$: 157.0760; found: 157.0758.



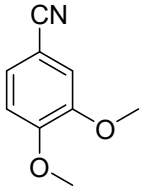
1-methyl-1*H*-indole-6-carbonitrile (2j)[15]: The crude product was purified by column chromatography on silica gel to give **2j** as colorless oil (13.7 mg, 35%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.8 Hz, 2H), 7.33 (dd, *J* = 8.5, 0.9 Hz, 1H), 7.25 (d, *J* = 3.1 Hz, 1H), 6.55 (d, *J* = 2.8 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.55, 132.58, 131.63, 122.20, 121.65, 120.81, 114.21, 103.95, 101.99, 33.11; HRMS (m/z) calcd. for $C_{10}H_8N_2$ $[M+H]^+$: 157.0760; found: 157.0758.



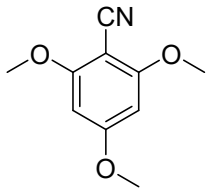
1-methyl-1*H*-pyrrolo[2,3-b]pyridine-3-carbonitrile (2k)[6]: The crude product was purified by column chromatography on silica gel to give **2k** as colorless oil (36.3 mg, 67%);^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.07 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.75 (s, 1H), 7.27 (dd, *J* = 7.9, 4.6 Hz, 1H), 3.96 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.84, 145.30, 135.90, 128.25, 120.03, 118.10, 115.13, 84.22, 32.06; HRMS (m/z) calcd. for $C_9H_7N_3$ $[M+H]^+$: 158.0713; found: 158.0710.



4-methoxybenzonitrile (2l)[16]: The crude product was purified by column chromatography on silica gel to give **2l** as colorless oil (25.5 mg, 65%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 – 7.57 (m, 2H), 6.97 – 6.94 (m, 2H), 3.86 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.86, 134.00, 119.26, 114.7, 103.95, 55.57; HRMS (m/z) calcd. for C_8H_7NO $[M+H]^+$: 134.0600; found: 134.0598.



3,4-dimethoxybenzonitrile (2m)[16]: The crude product was purified by column chromatography on silica gel to give **2m** as colorless oil (21.6 mg, 55%);^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (dd, J = 8.3, 1.9 Hz, 1H), 7.08 (d, J = 1.8 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 3.94 (s, 3H), 3.91 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.86, 149.18, 126.47, 119.24, 113.91, 111.25, 103.86, 56.14, 56.10; HRMS (m/z) calcd. for $C_9H_9NO_2$ $[M+H]^+$: 164.0706; found: 164.0704.



2,4,6-trimethoxybenzonitrile (2n)[16]: The crude product was purified by column chromatography on silica gel to give **2n** as colorless oil (33.4 mg, 85%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.07 (s, 2H), 3.88 (s, 6H), 3.86 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.38, 163.78, 114.67, 90.38, 83.97, 56.11, 55.73; HRMS (m/z) calcd. for $C_{10}H_{11}NO_3$ $[M+H]^+$: 194.0812; found: 194.0810.

6. Reference

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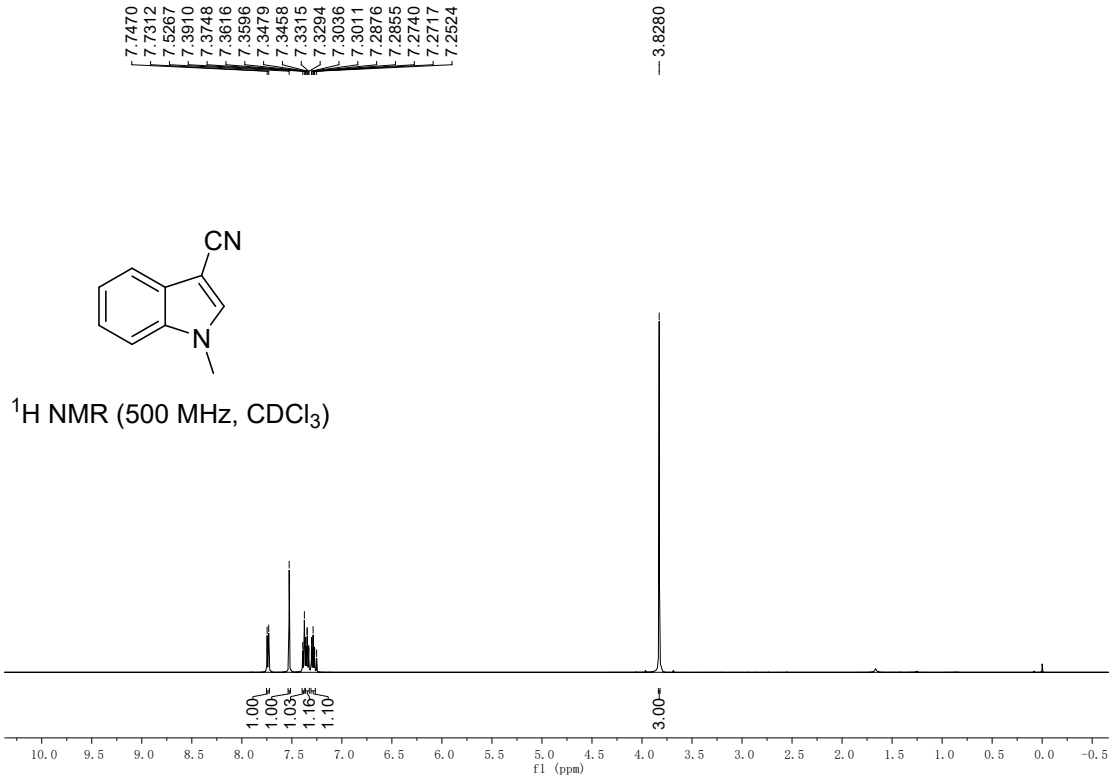
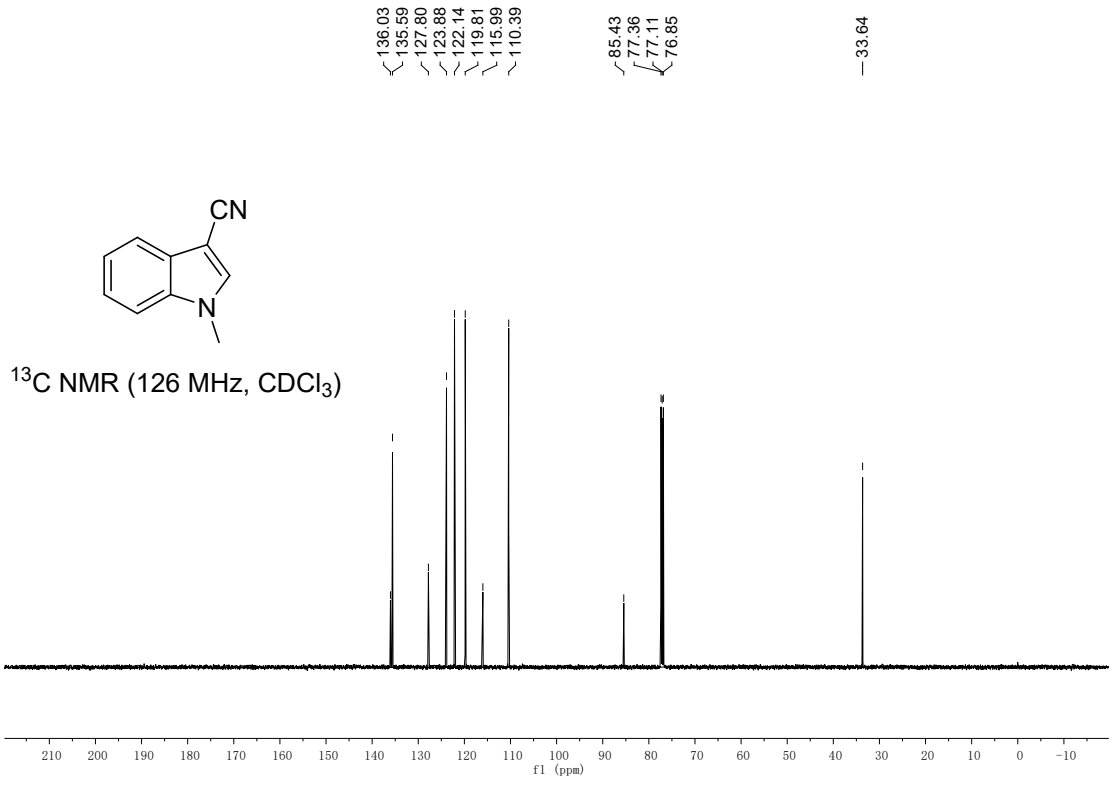
7. NMR Spectra for products

Compound 2aa

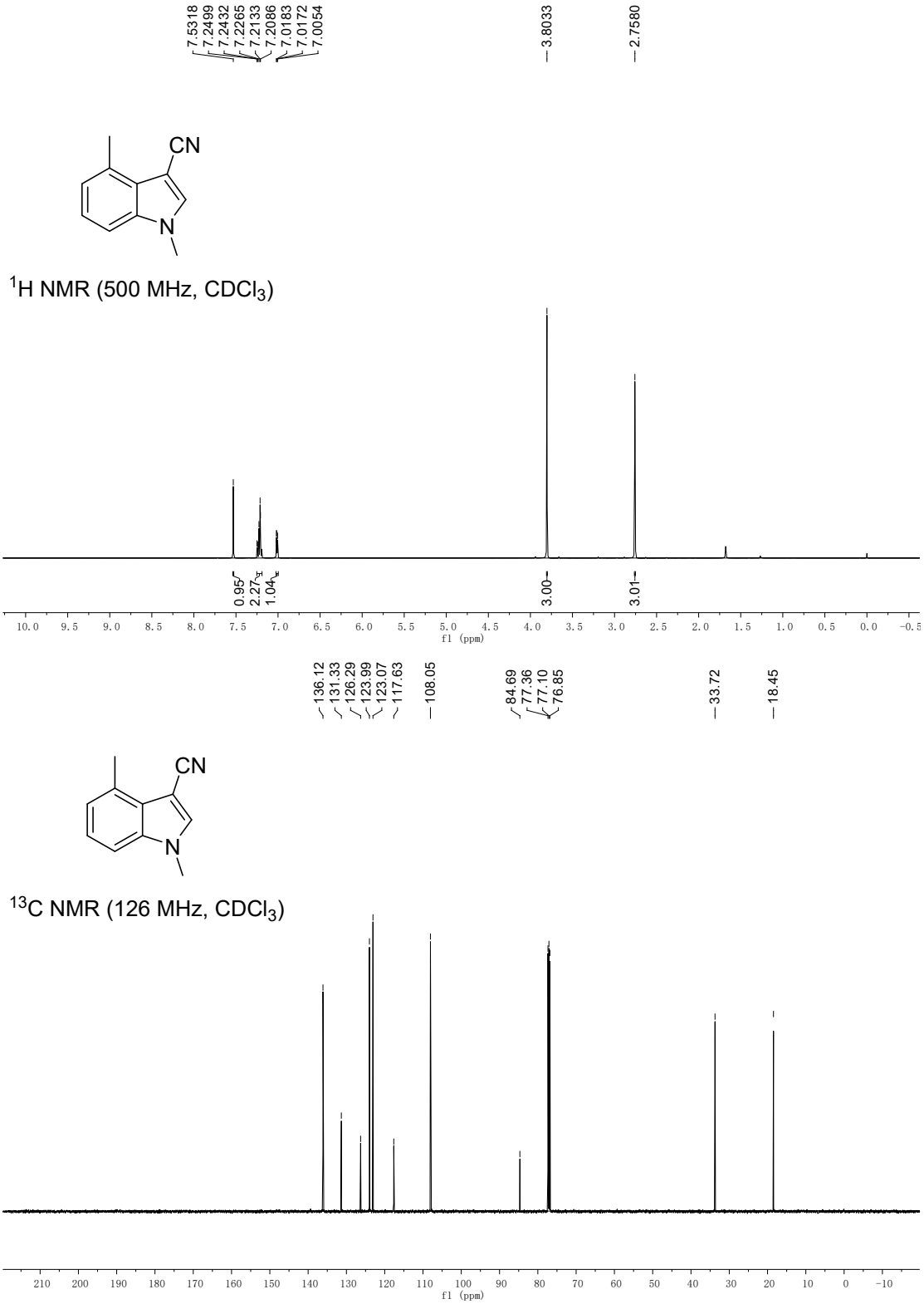


^{1}H NMR (500 MHz, $CDCl_3$)



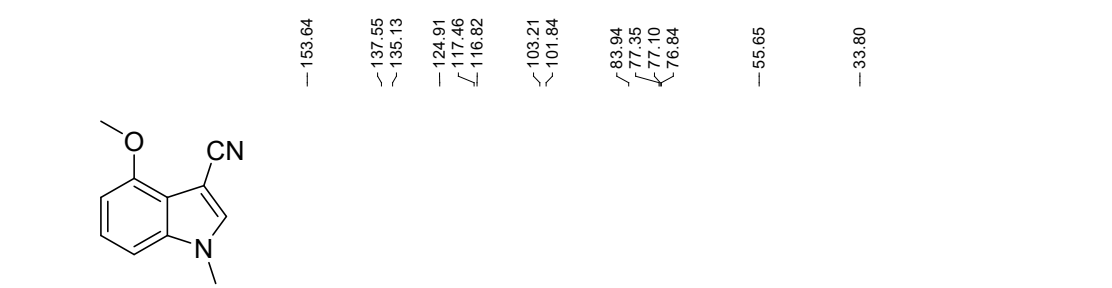
^{13}C NMR (126 MHz, $CDCl_3$)

Compound 2ab



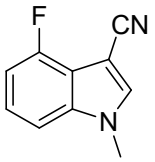
Compound 2ac

^{1}H NMR (500 MHz, $CDCl_3$)

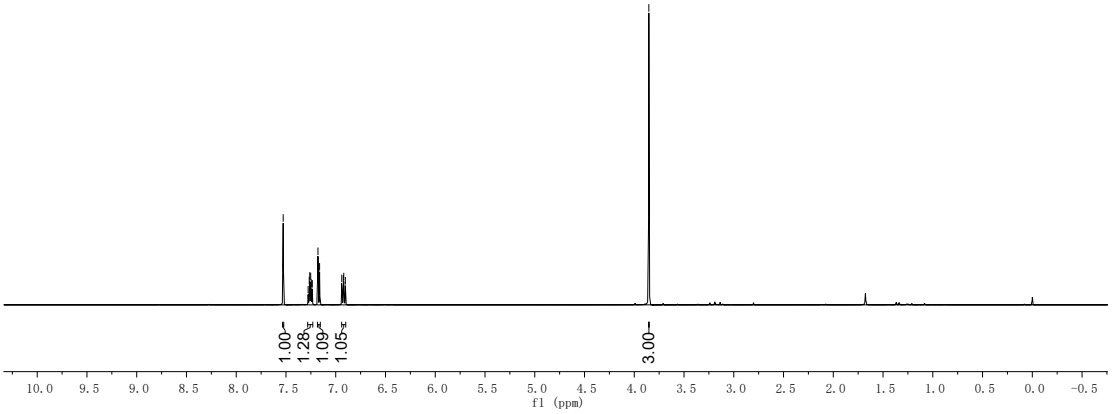


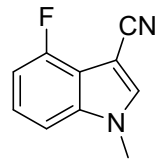
^{13}C NMR (126 MHz, $CDCl_3$)

Compound 2ad

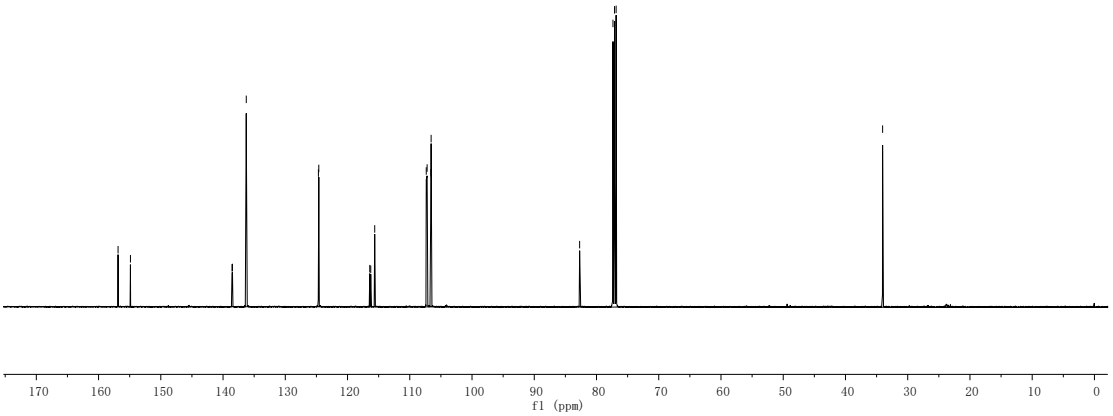


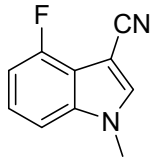
^{1}H NMR (500 MHz, $CDCl_3$)





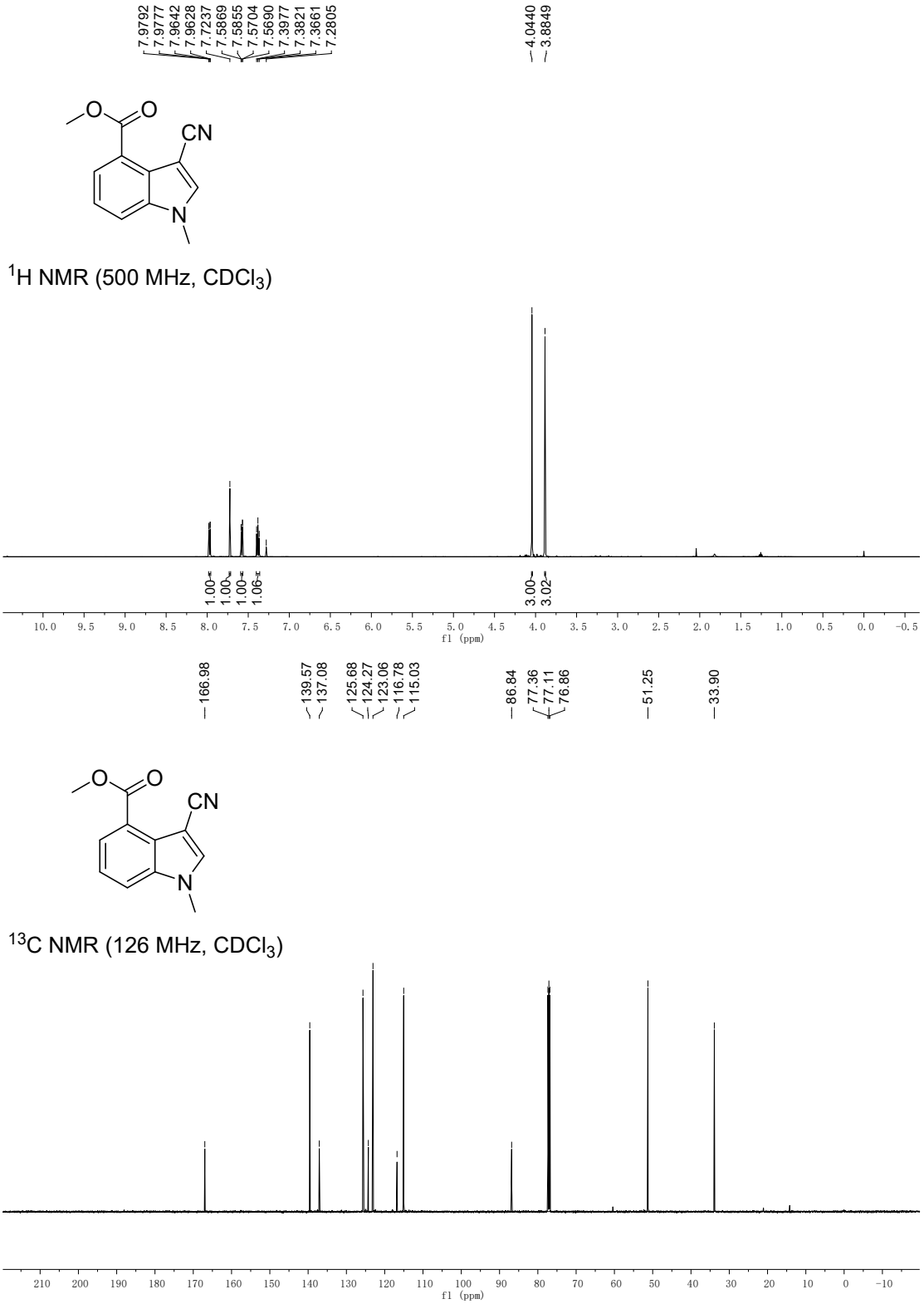
^{13}C NMR (126 MHz, $CDCl_3$)



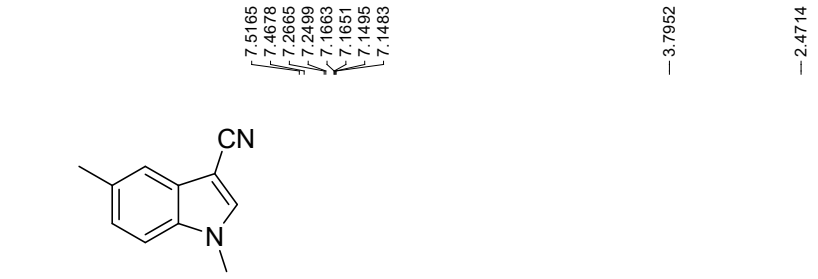


^{19}F NMR (471 MHz, $CDCl_3$)

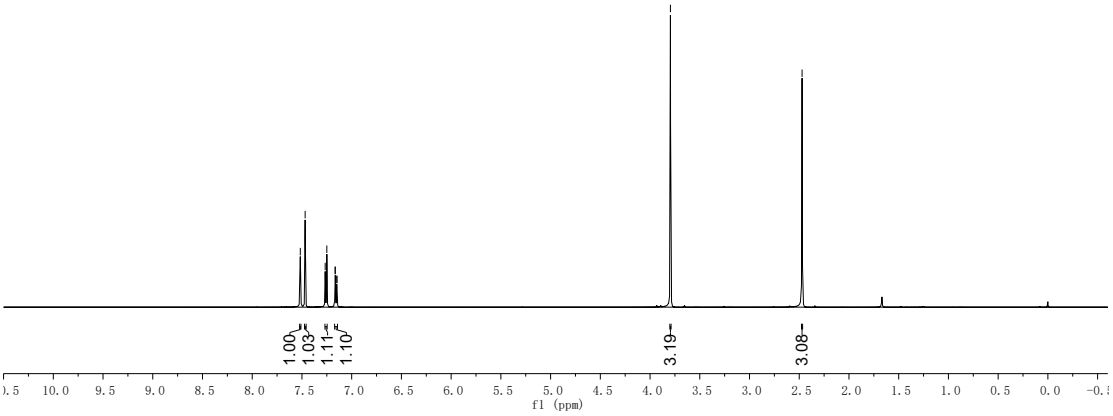
Compound 2ae

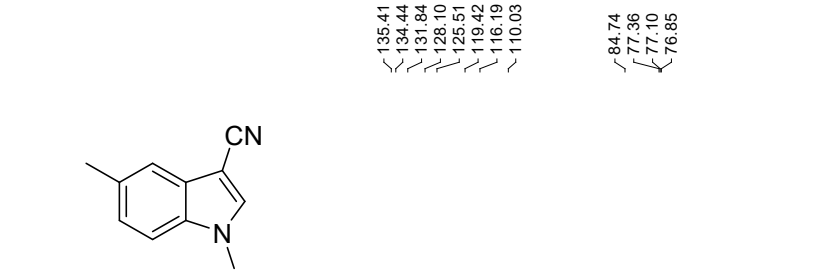


Compound 2af

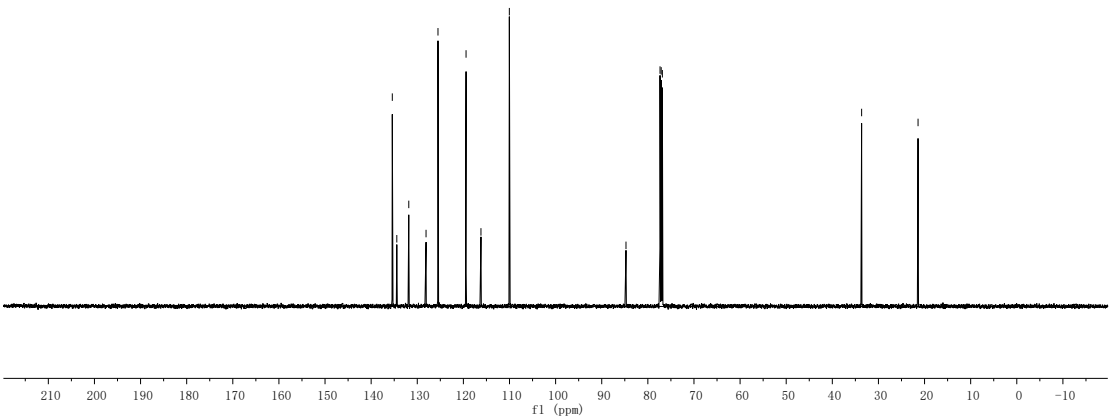


^{1}H NMR (500 MHz, $CDCl_3$)

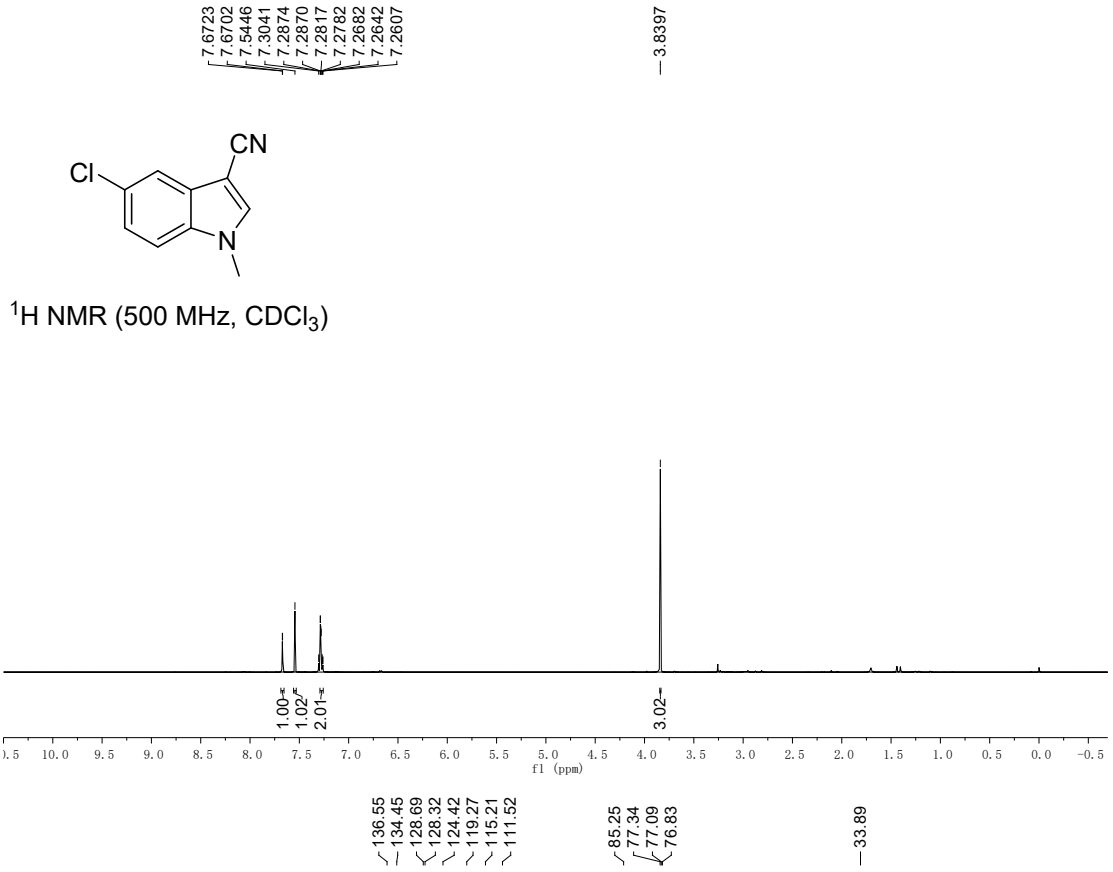




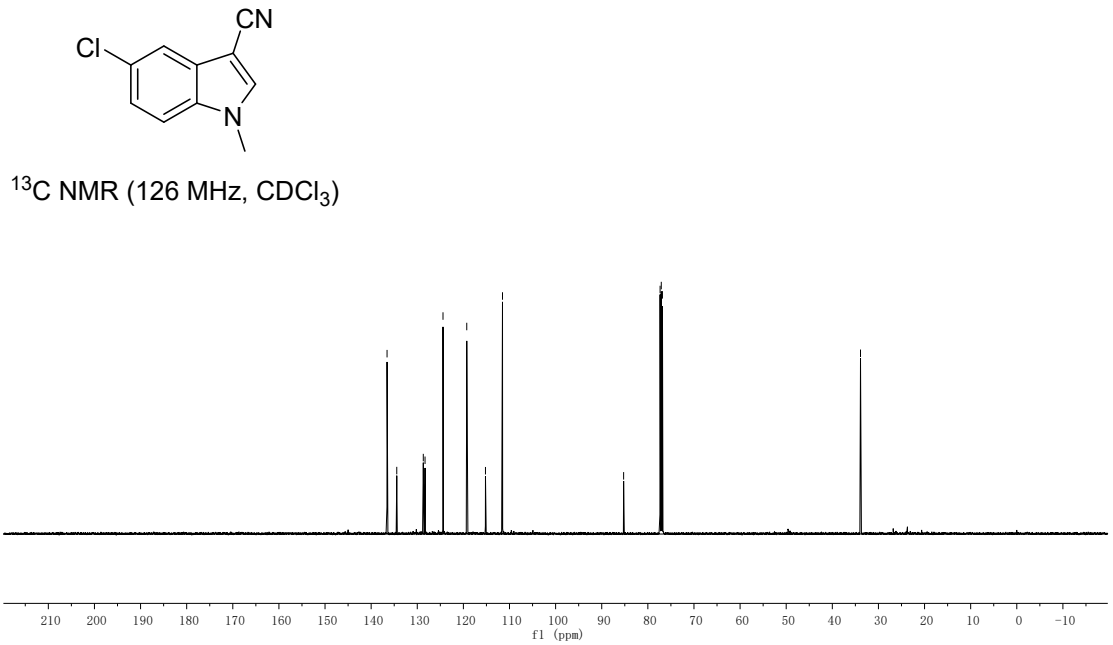
^{13}C NMR (126 MHz, $CDCl_3$)



Compound 2ag

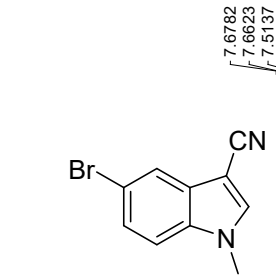


^{1}H NMR (500 MHz, $CDCl_3$)

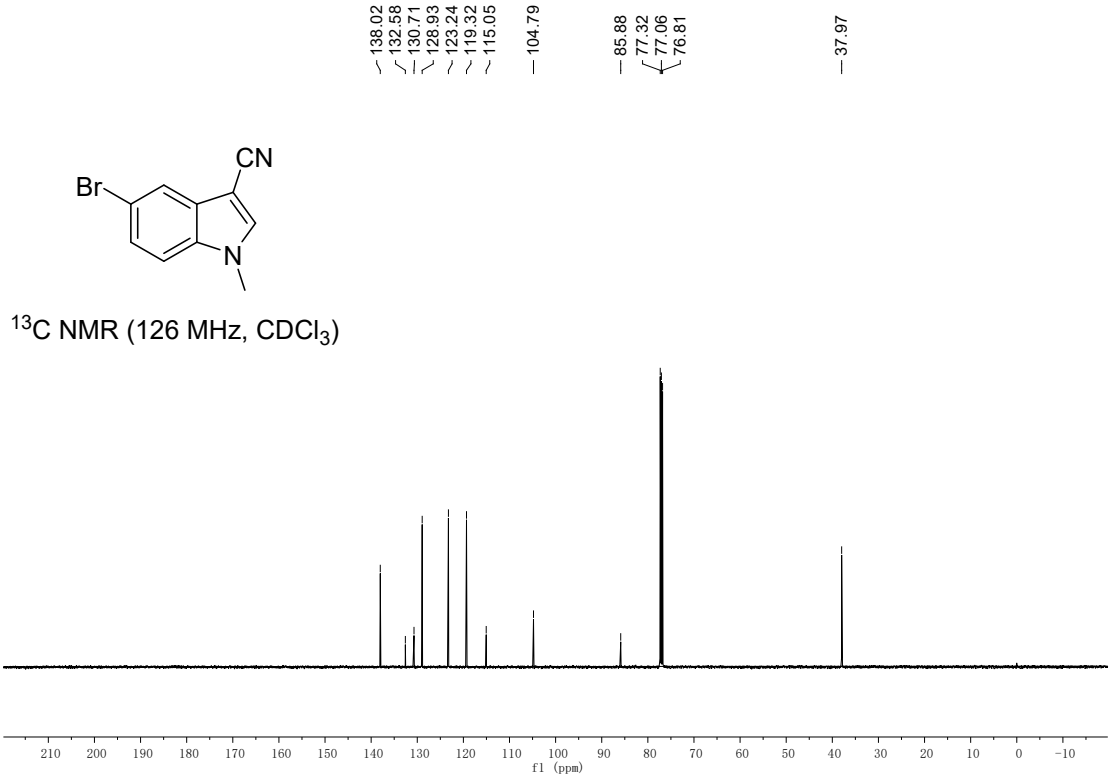


^{13}C NMR (126 MHz, $CDCl_3$)

Compound 2ah

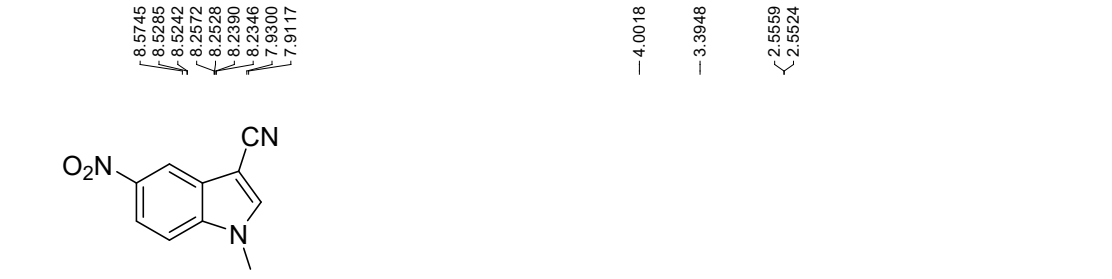


^{1}H NMR (500 MHz, $CDCl_3$)

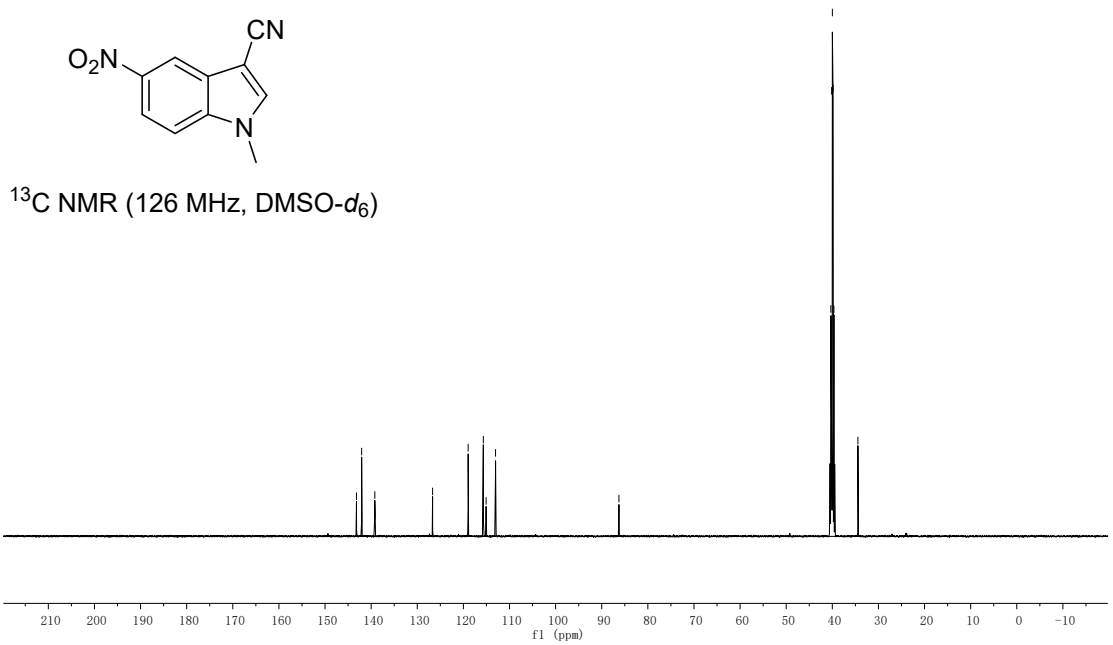


^{13}C NMR (126 MHz, $CDCl_3$)

Compound 2ai

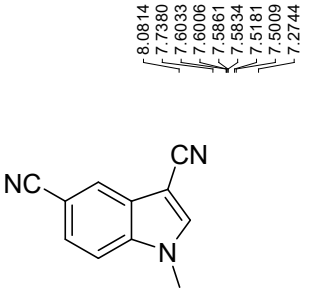


^{1}H NMR (500 MHz, DMSO-d_6)

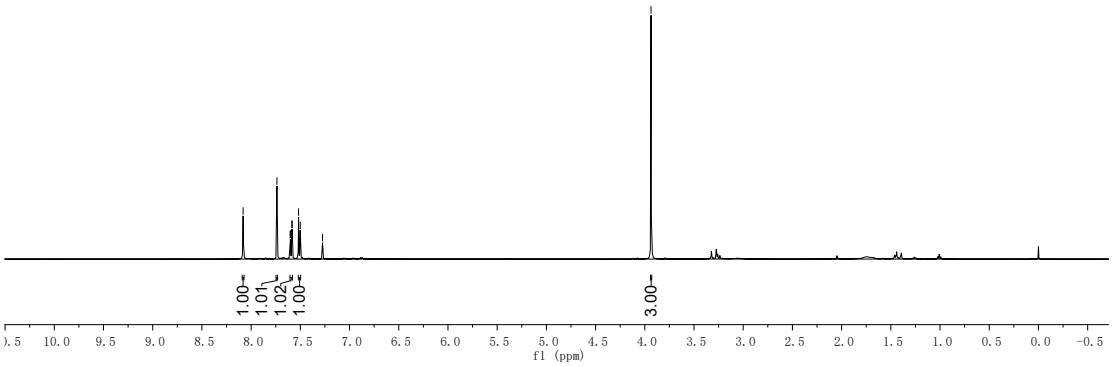


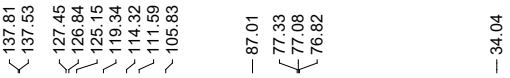
^{13}C NMR (126 MHz, DMSO-d_6)

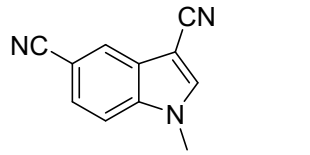
Compound 2aj



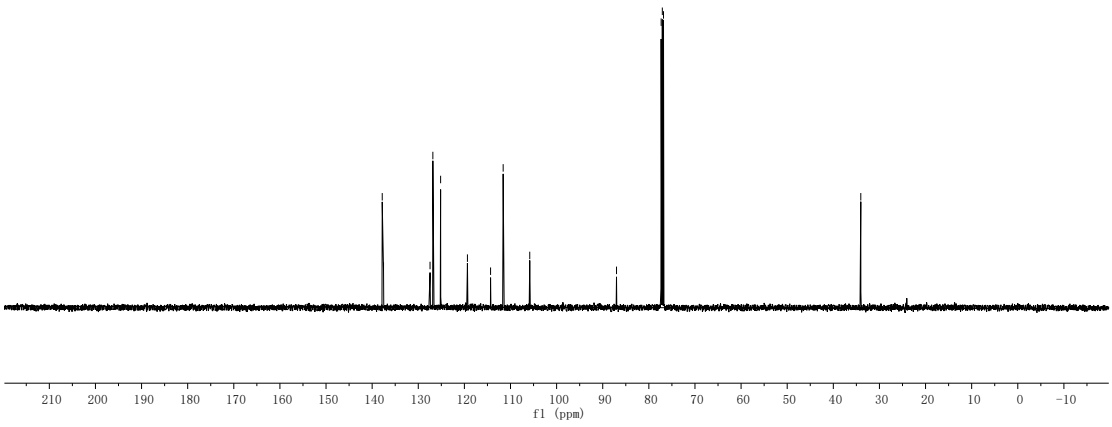
^{1}H NMR (500 MHz, $CDCl_3$)



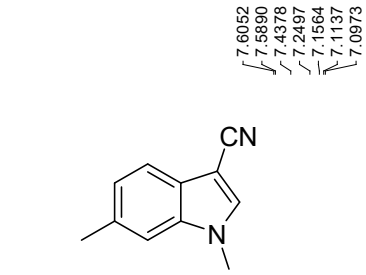




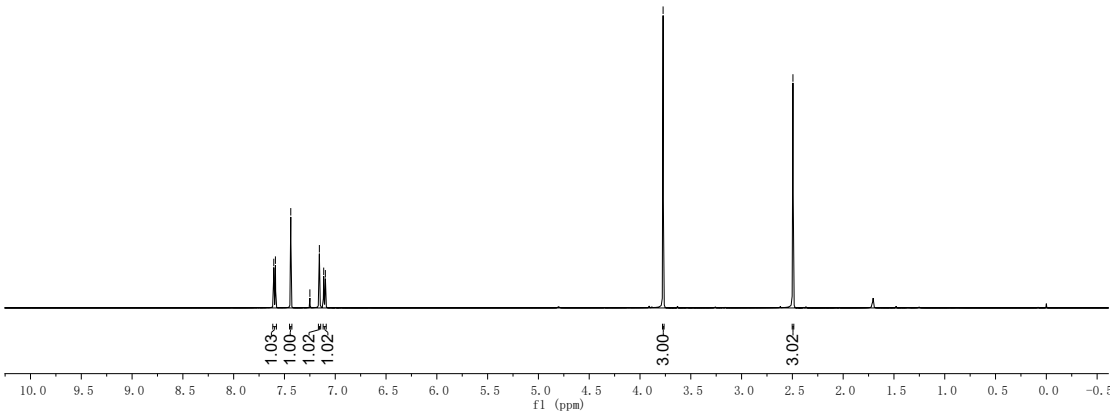
^{13}C NMR (126 MHz, $CDCl_3$)

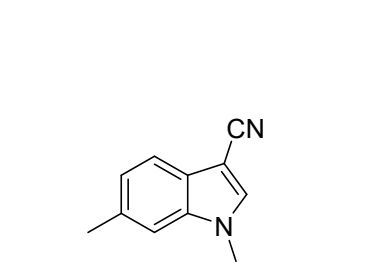


Compound 2ak

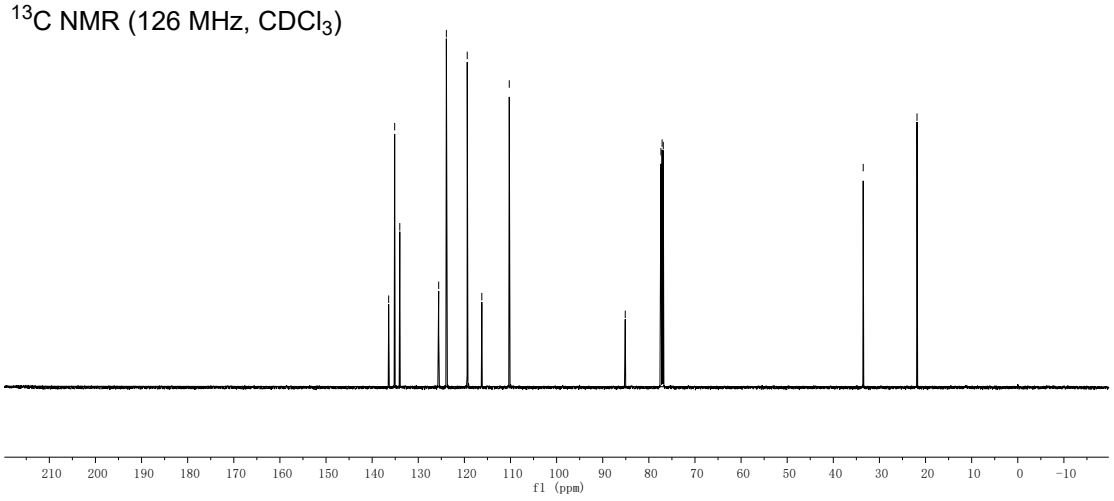


^{1}H NMR (500 MHz, $CDCl_3$)

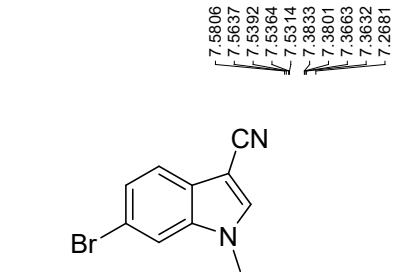




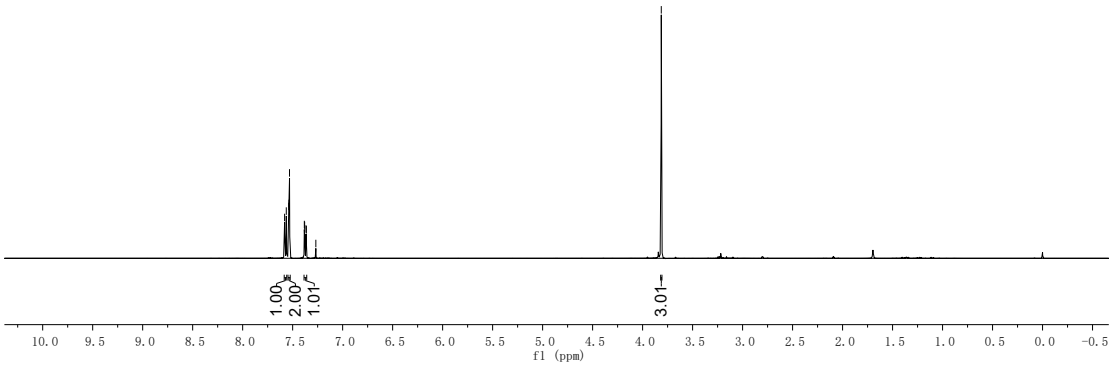
^{13}C NMR (126 MHz, $CDCl_3$)

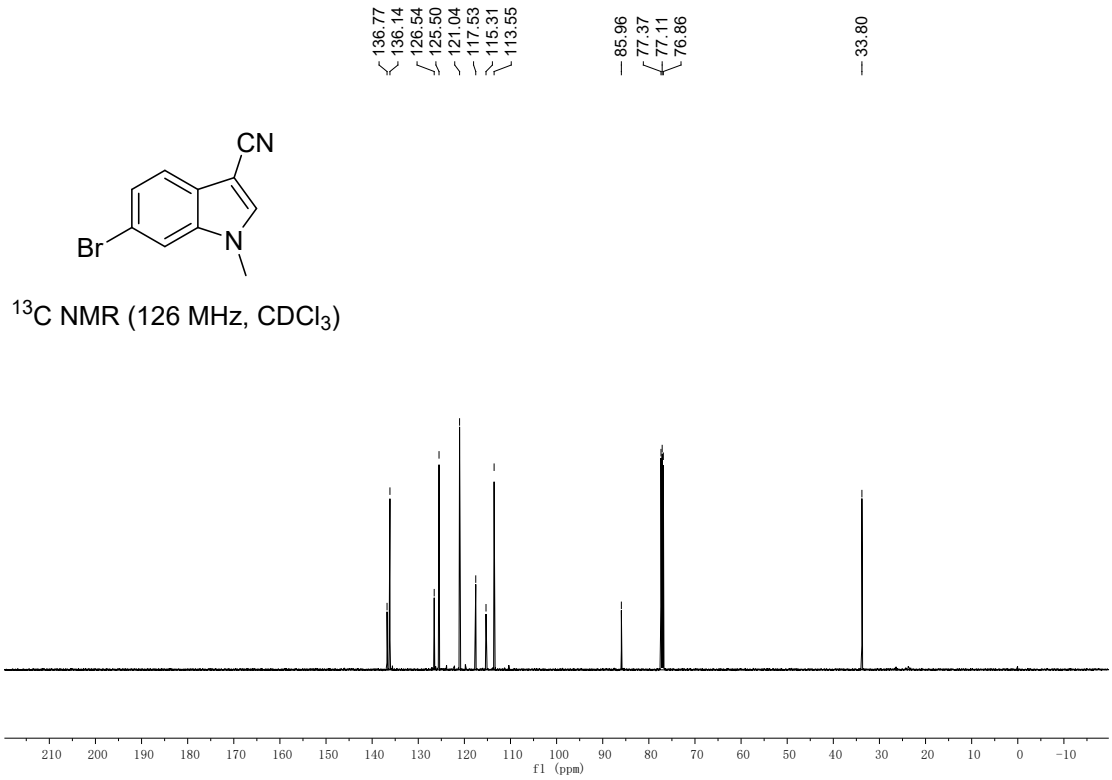


Compound 2al



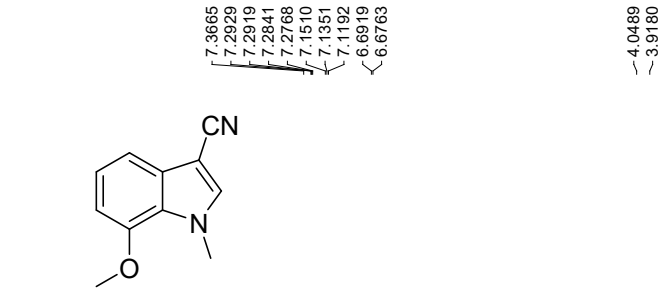
^{1}H NMR (500 MHz, $CDCl_3$)



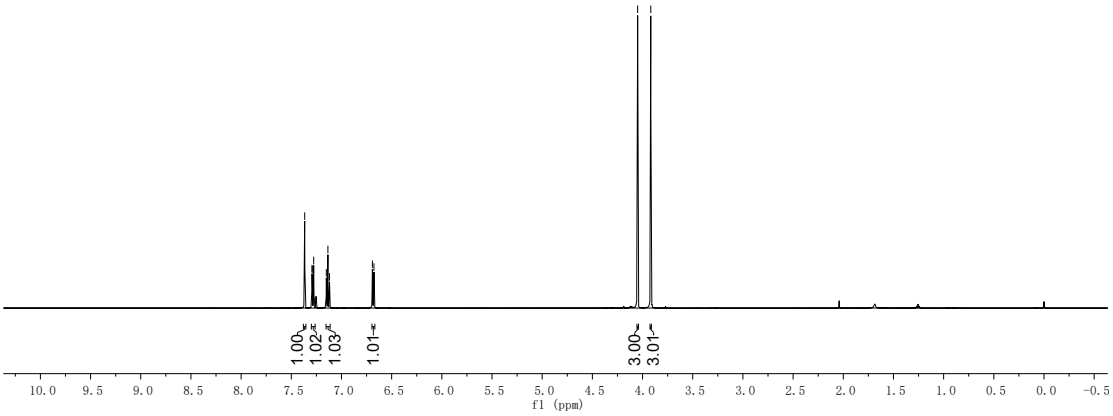


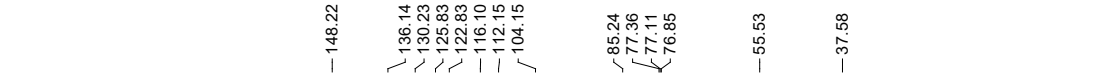
^{13}C NMR (126 MHz, $CDCl_3$)

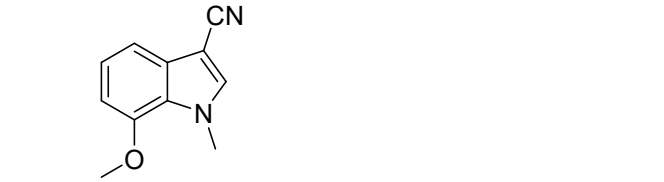
Compound 2am



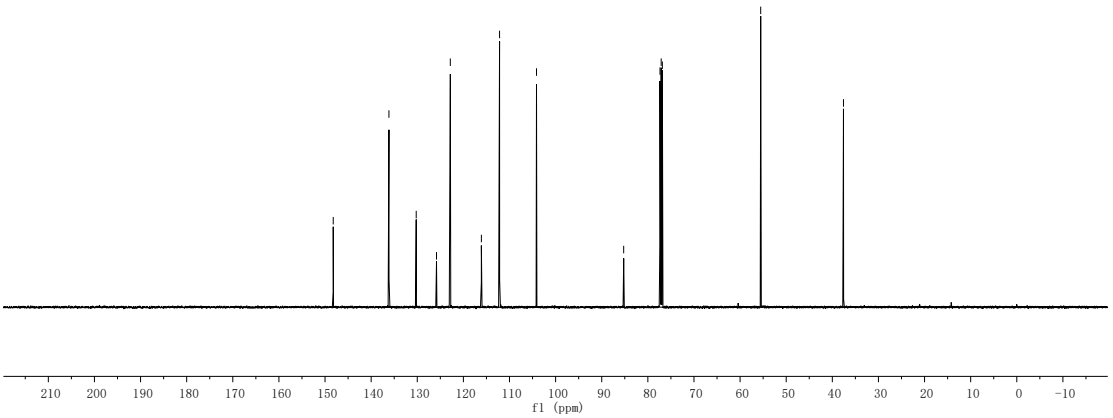
^{1}H NMR (500 MHz, $CDCl_3$)



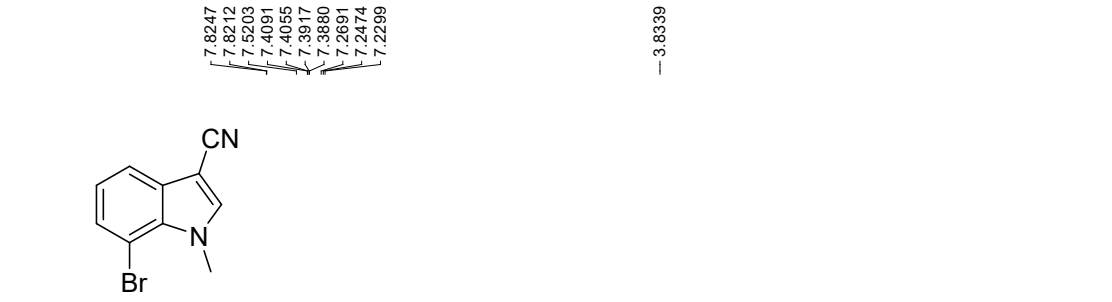




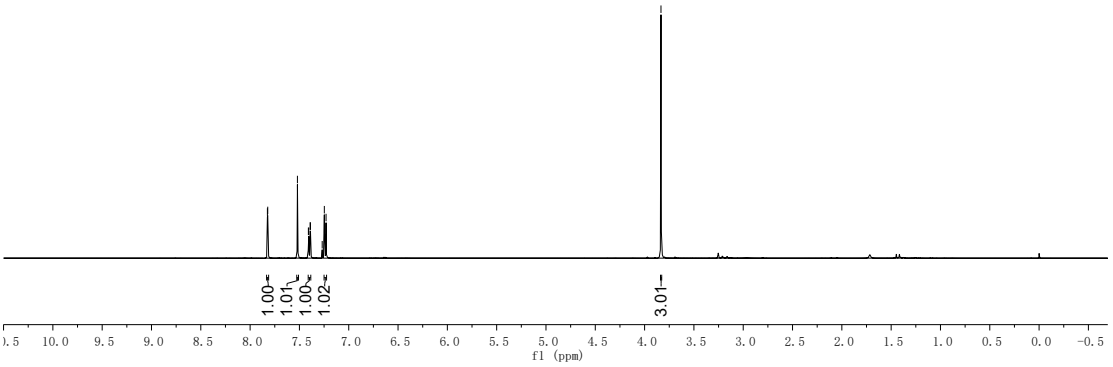
^{13}C NMR (126 MHz, $CDCl_3$)

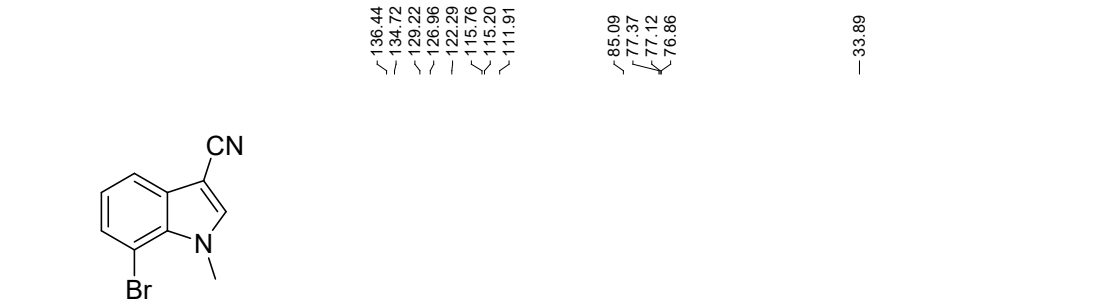


Compound 2an

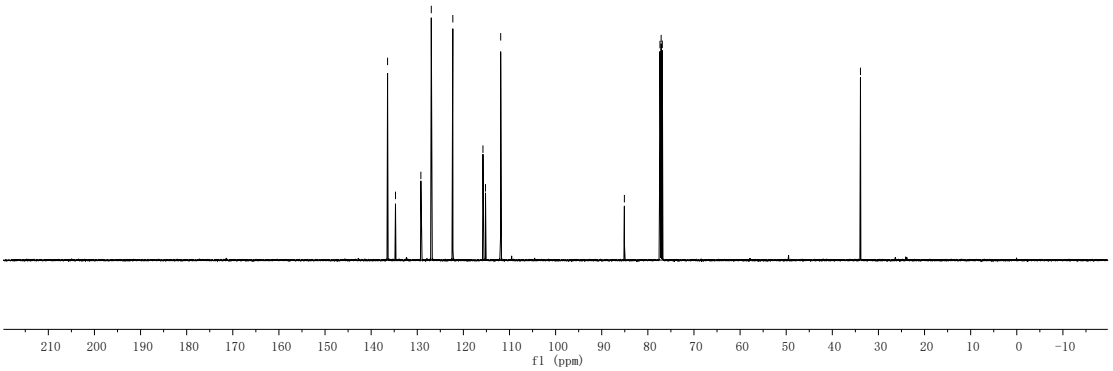


^{1}H NMR (500 MHz, $CDCl_3$)

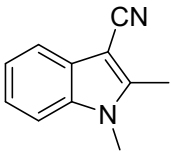




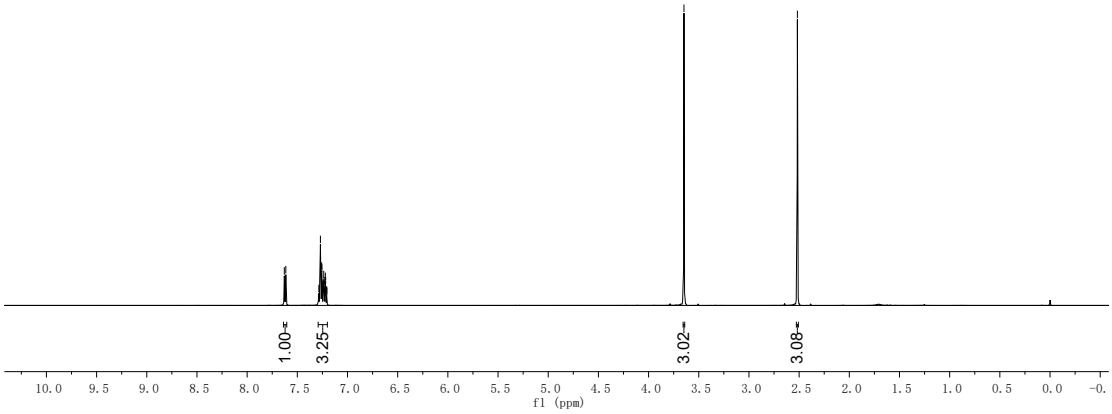
^{13}C NMR (126 MHz, $CDCl_3$)

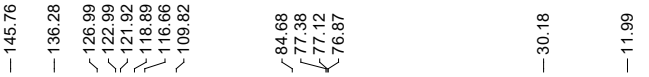


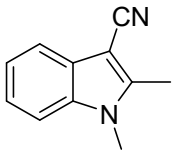
Compound 2ba



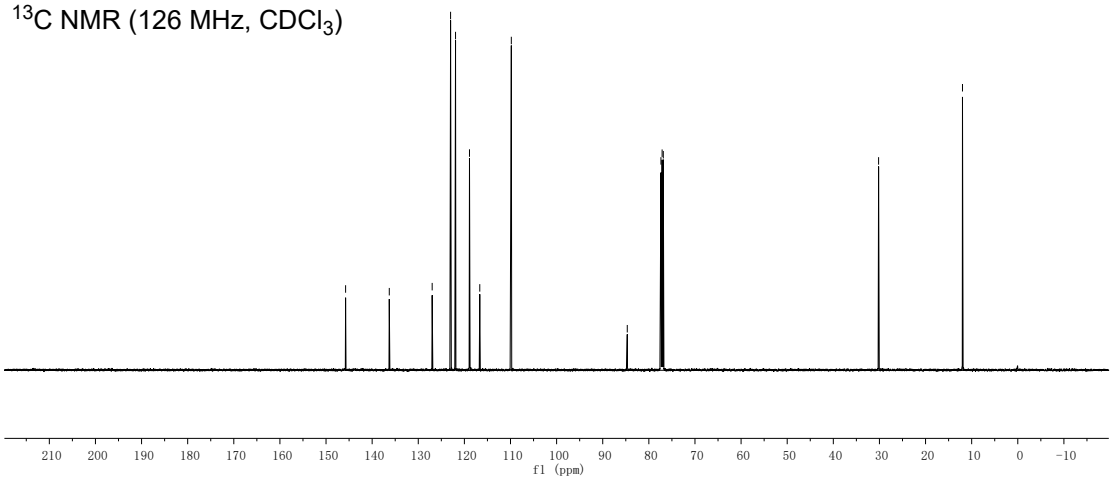
^{1}H NMR (500 MHz, $CDCl_3$)



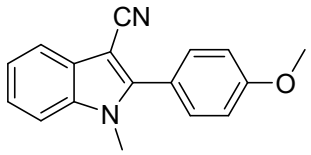




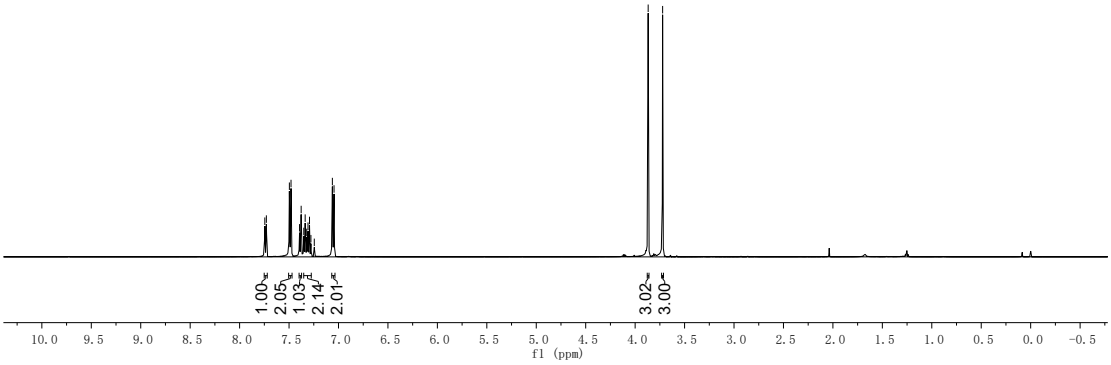
^{13}C NMR (126 MHz, $CDCl_3$)

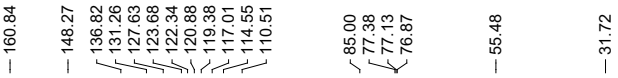


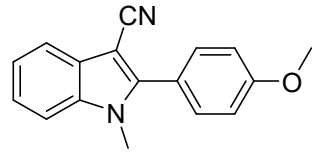
Compound 2bb



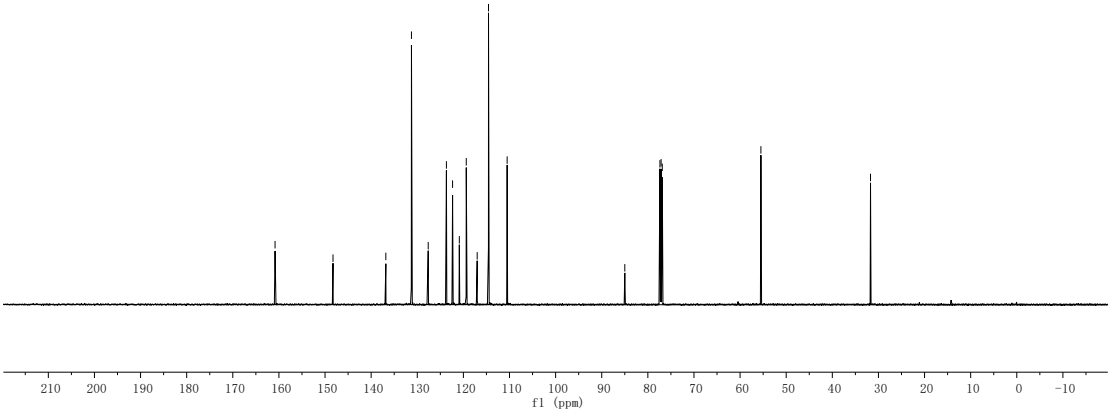
^{1}H NMR (500 MHz, $CDCl_3$)



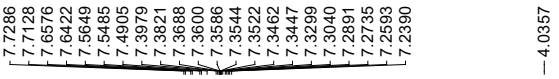


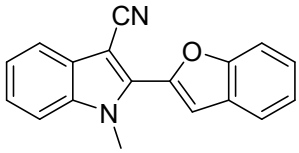


^{13}C NMR (126 MHz, $CDCl_3$)

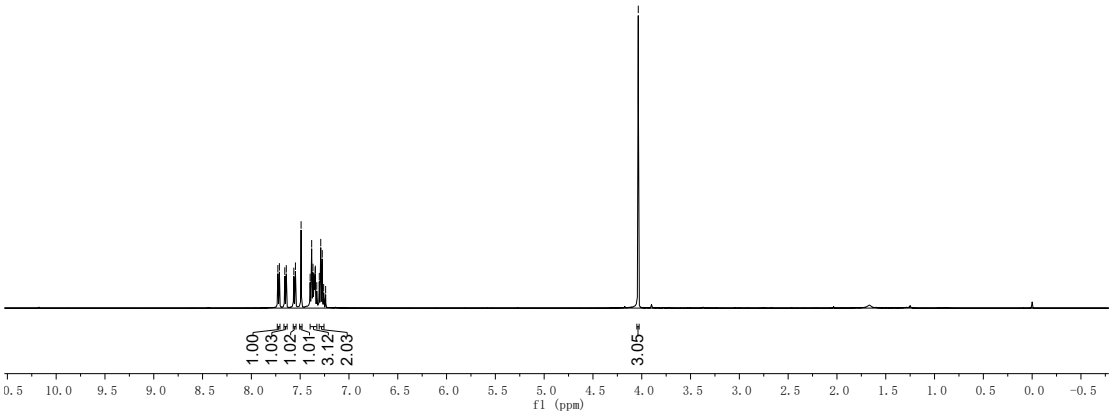


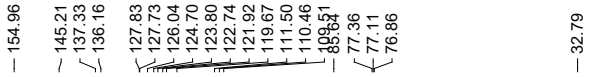
Compound 2bc

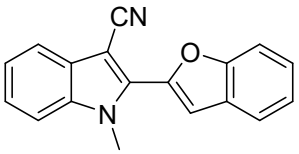




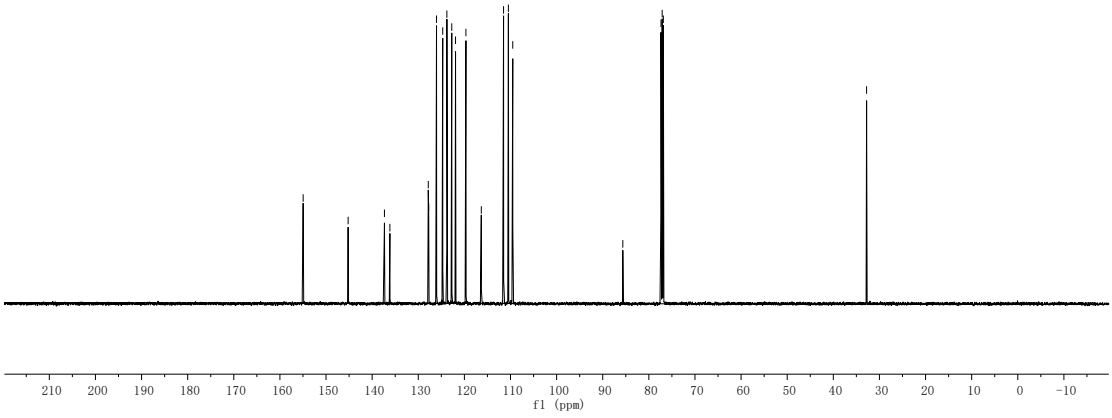
^{1}H NMR (500 MHz, $CDCl_3$)



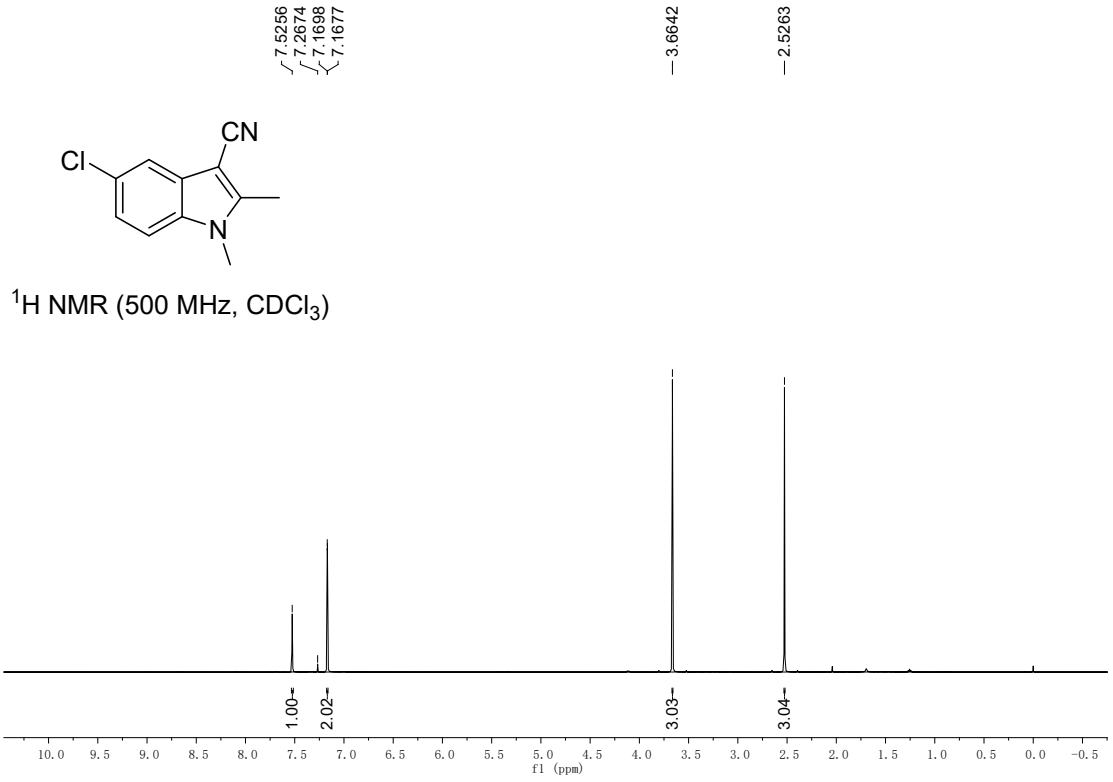




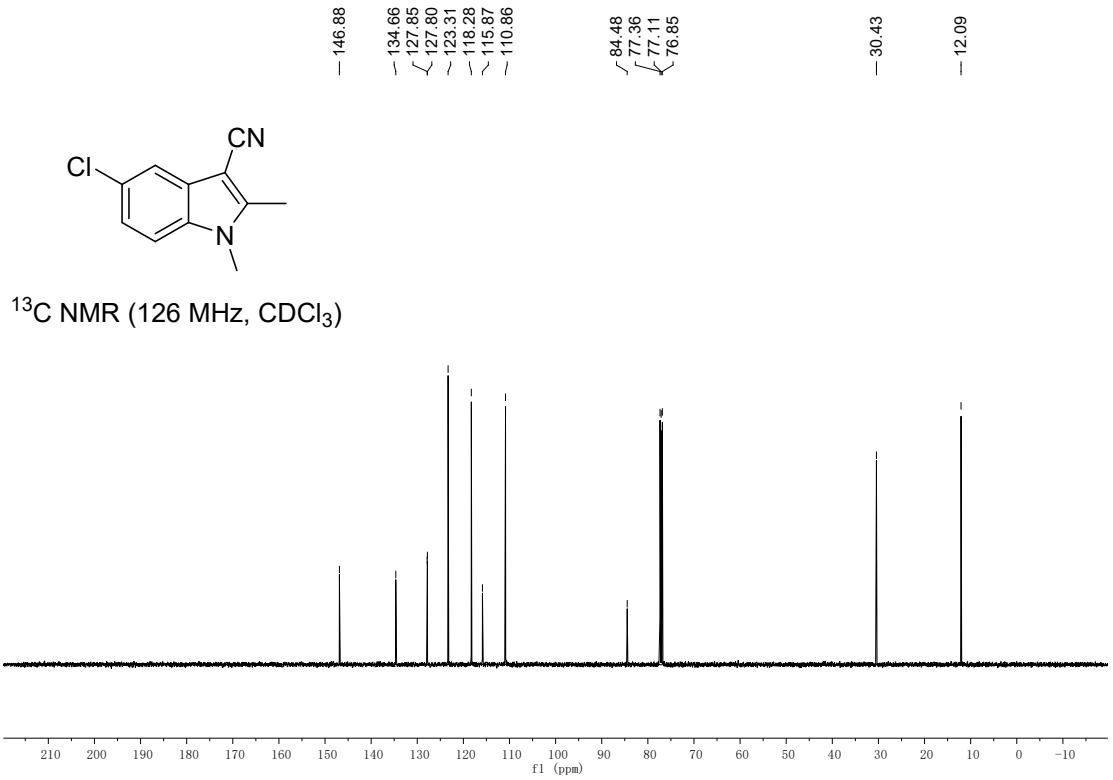
^{13}C NMR (126 MHz, $CDCl_3$)



Compound 2c



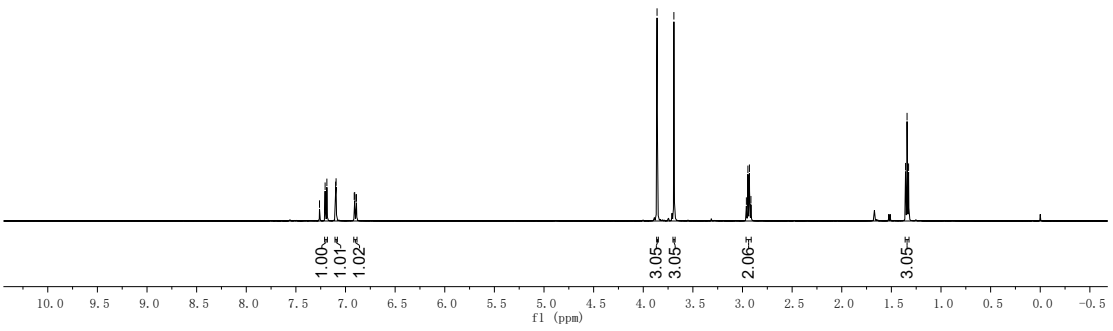
^{1}H NMR (500 MHz, $CDCl_3$)

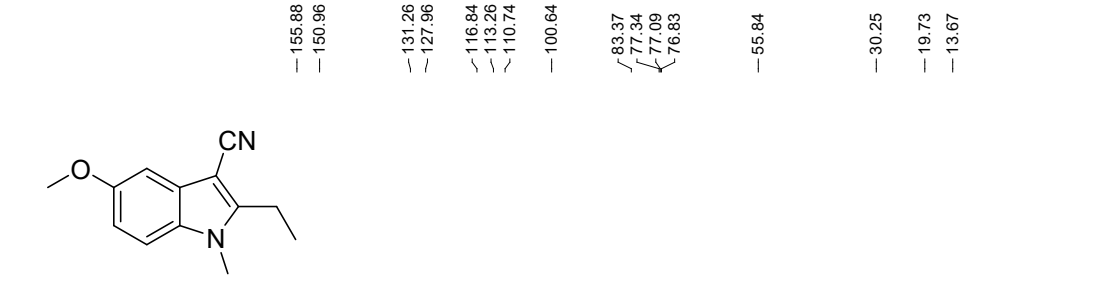


^{13}C NMR (126 MHz, $CDCl_3$)

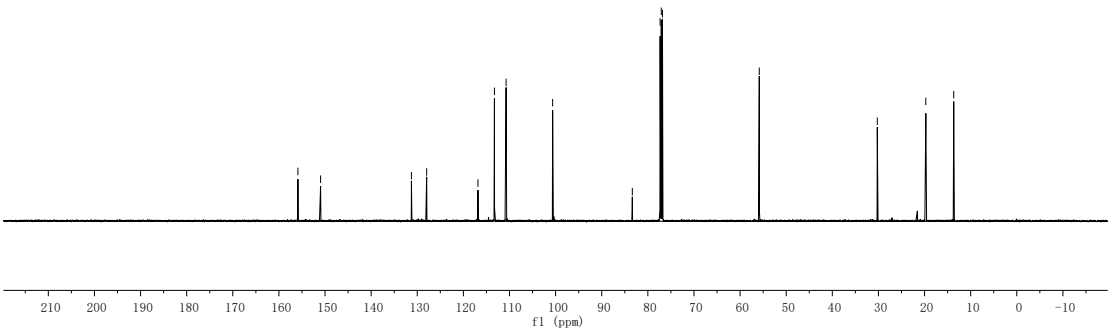
Compound 2d

^{1}H NMR (500 MHz, $CDCl_3$)

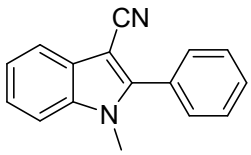




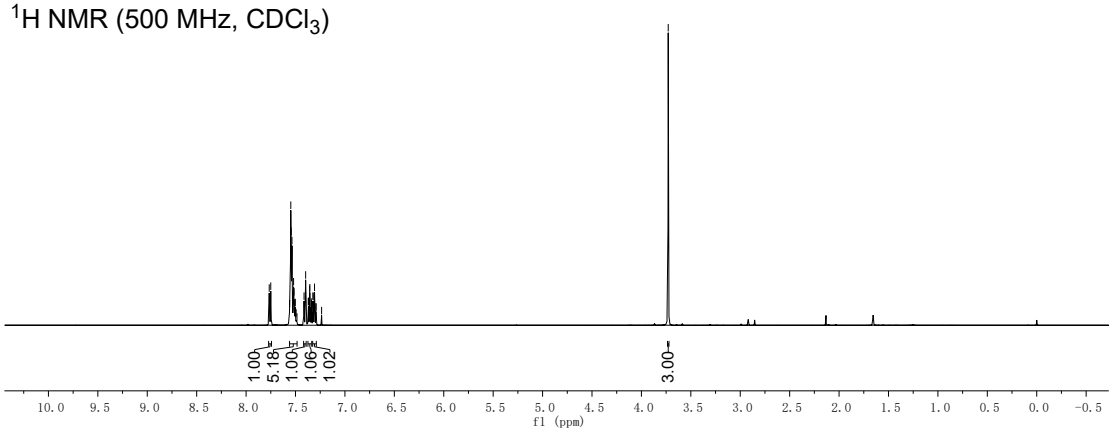
^{13}C NMR (126 MHz, $CDCl_3$)

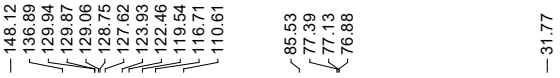


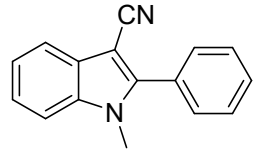
Compound 2ea



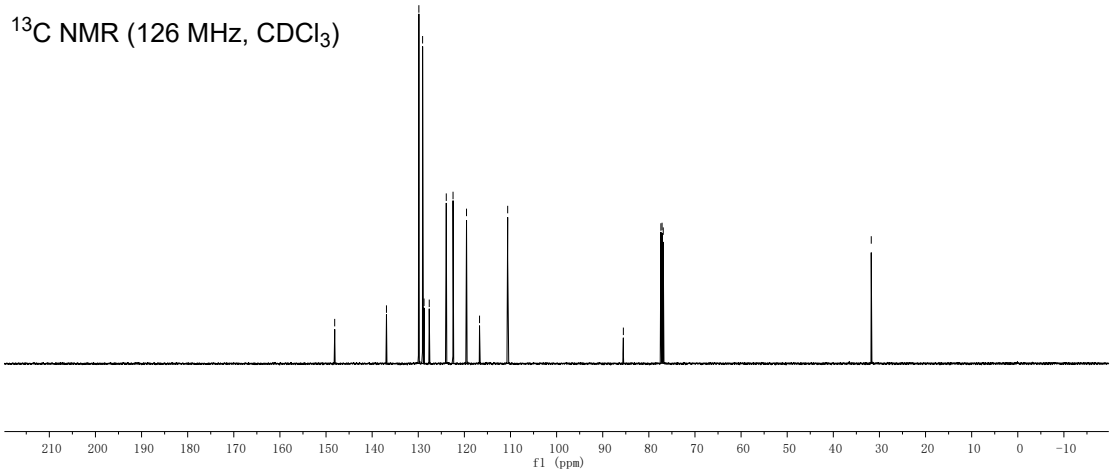
^{1}H NMR (500 MHz, $CDCl_3$)



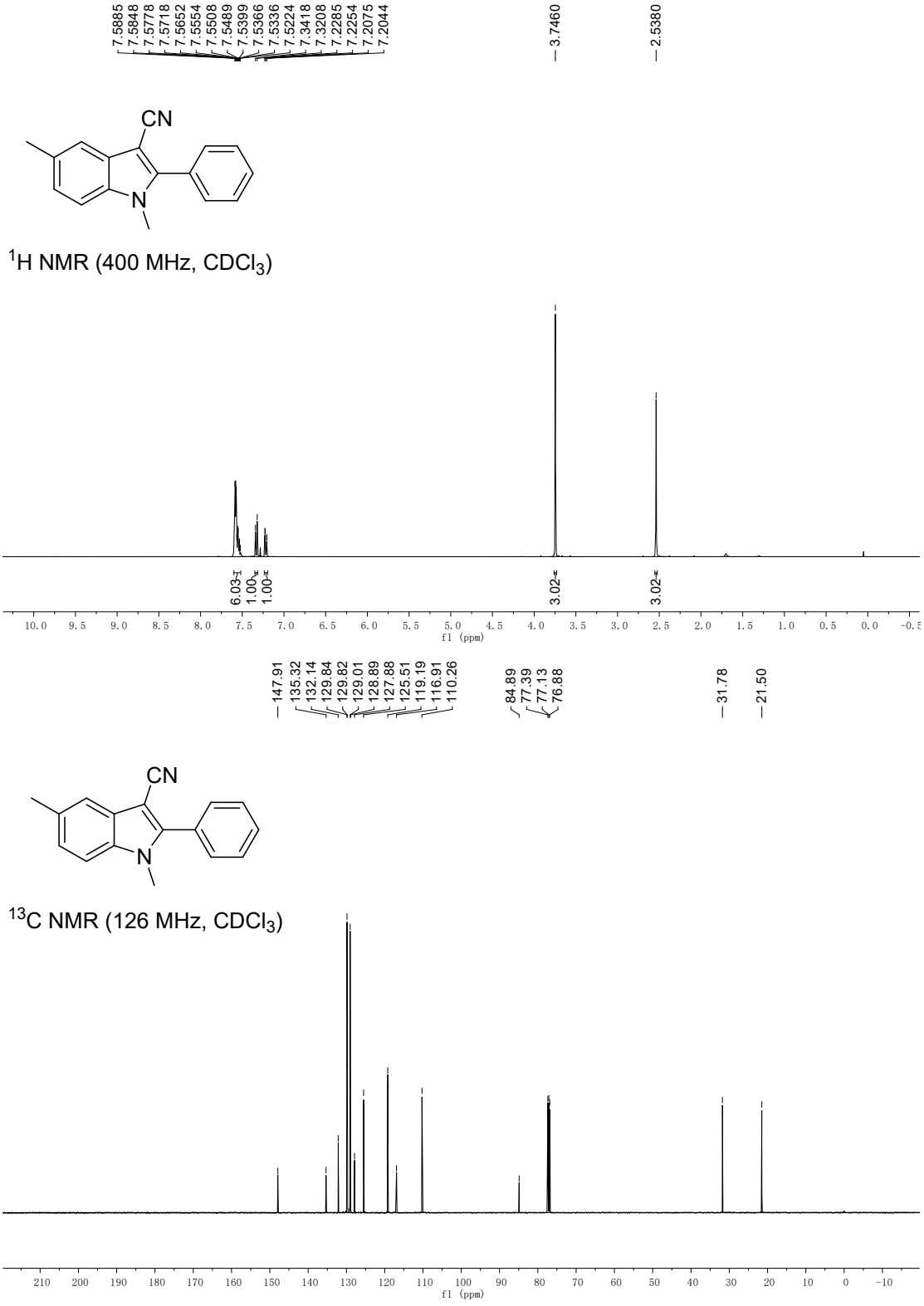




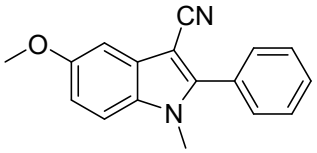
^{13}C NMR (126 MHz, $CDCl_3$)



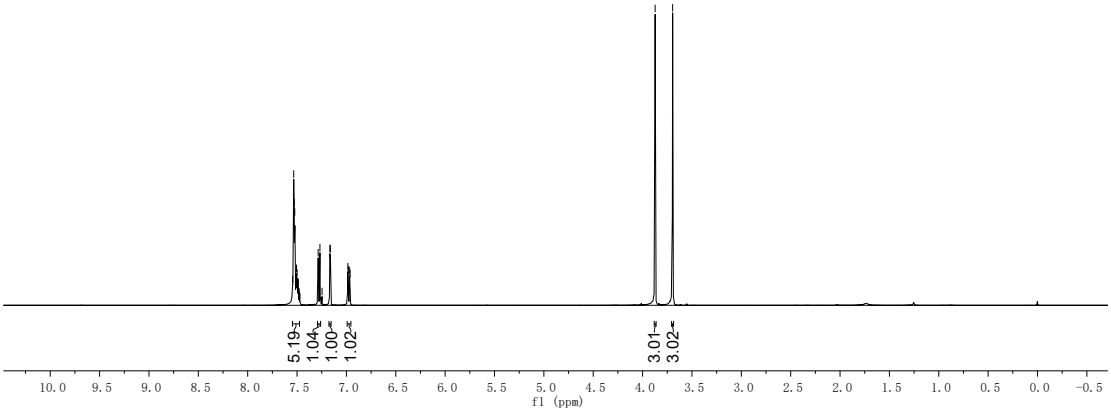
Compound 2eb

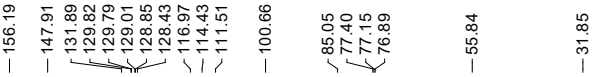


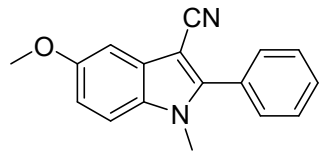
Compound 2ec



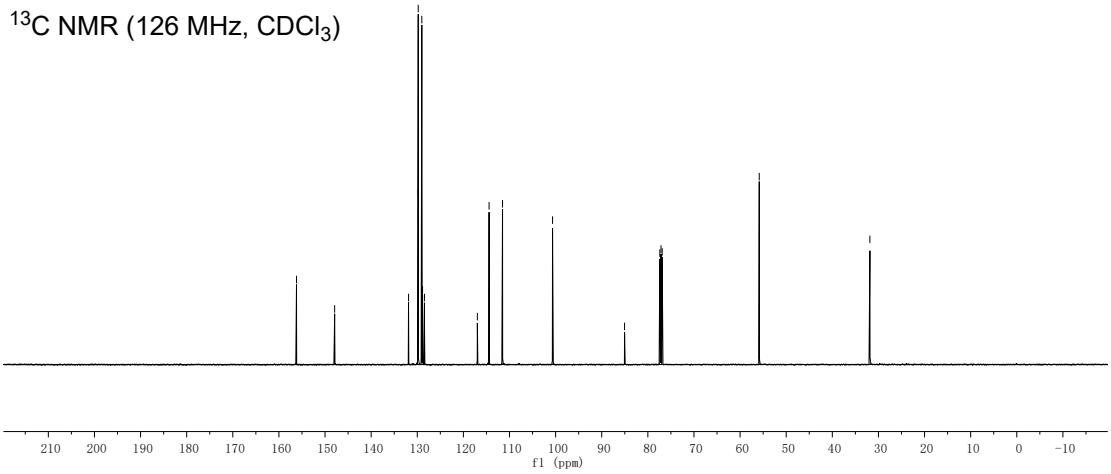
^{1}H NMR (500 MHz, $CDCl_3$)



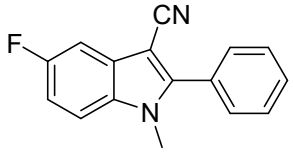




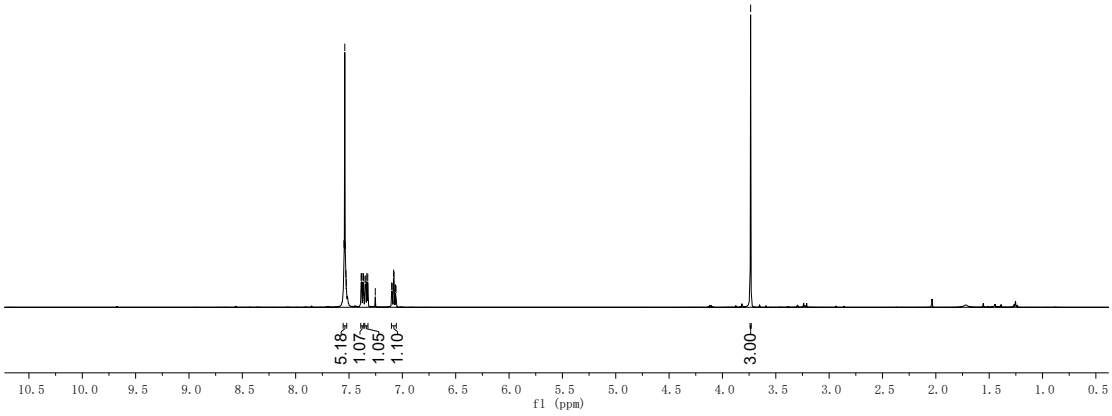
^{13}C NMR (126 MHz, $CDCl_3$)

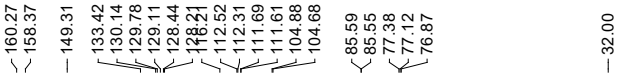


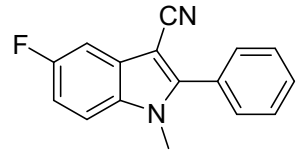
Compound 2ed



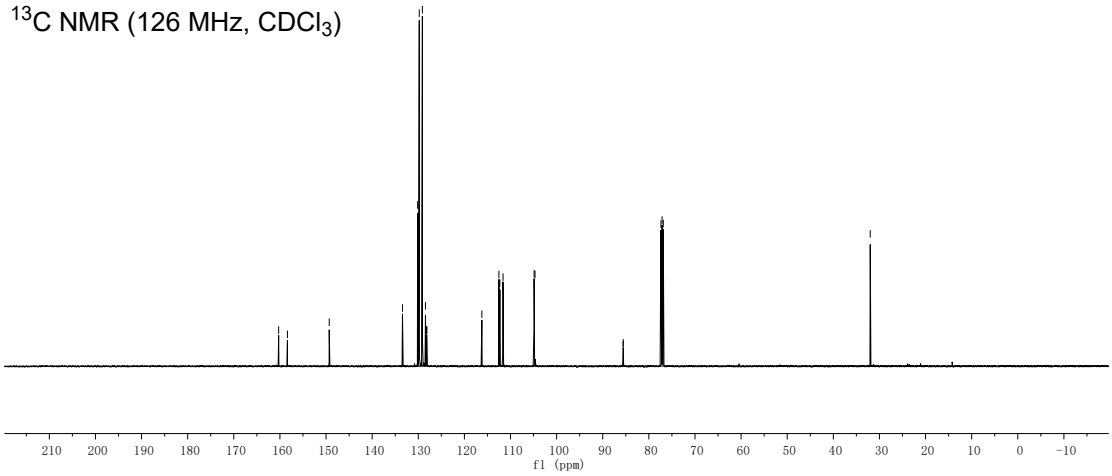
^{1}H NMR (500 MHz, $CDCl_3$)

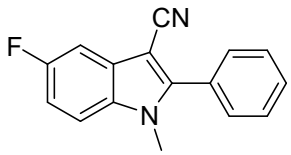






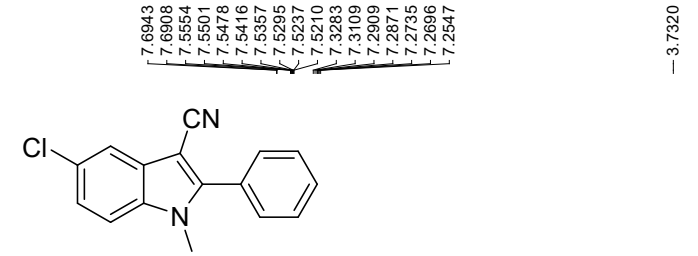
^{13}C NMR (126 MHz, $CDCl_3$)



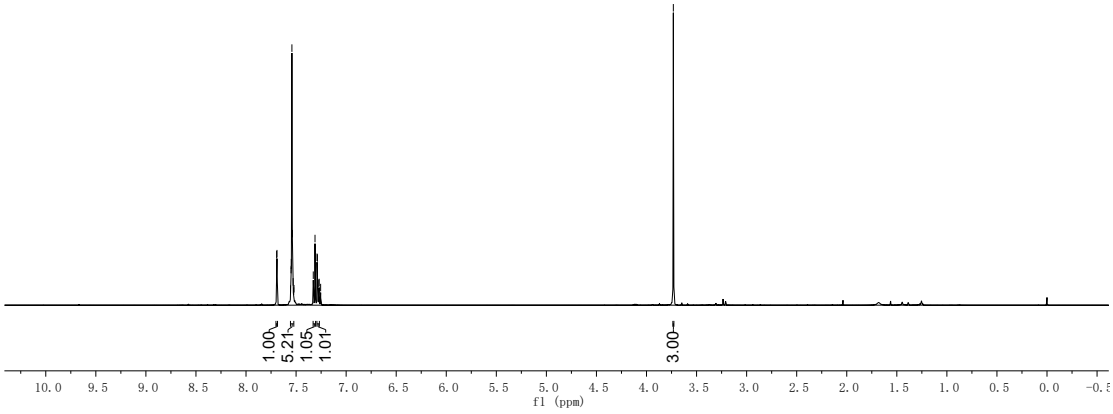


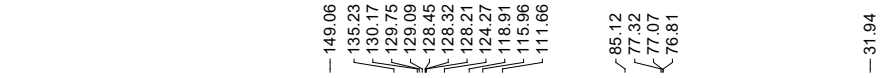
^{19}F NMR (471 MHz, $CDCl_3$)

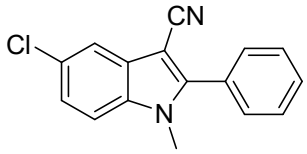
Compound 2ee



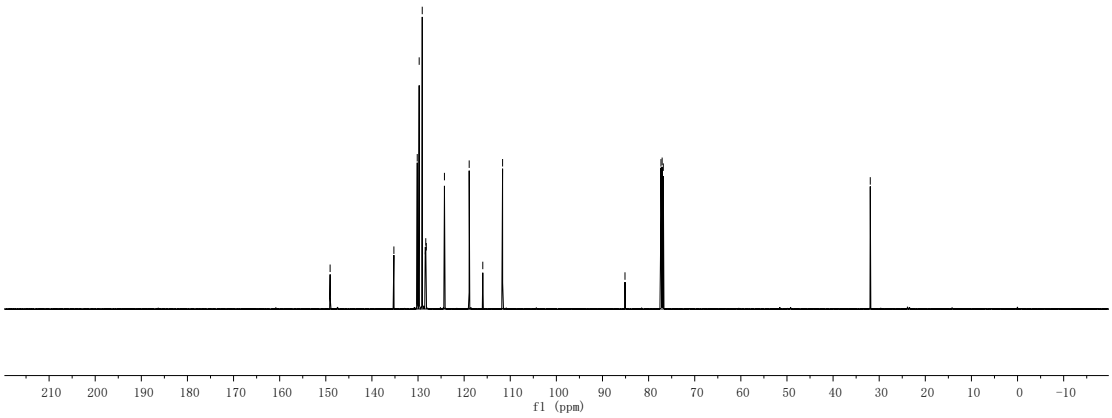
^{1}H NMR (500 MHz, $CDCl_3$)



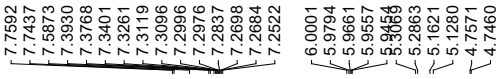


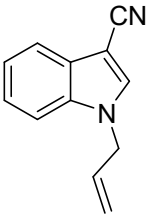


^{13}C NMR (126 MHz, $CDCl_3$)

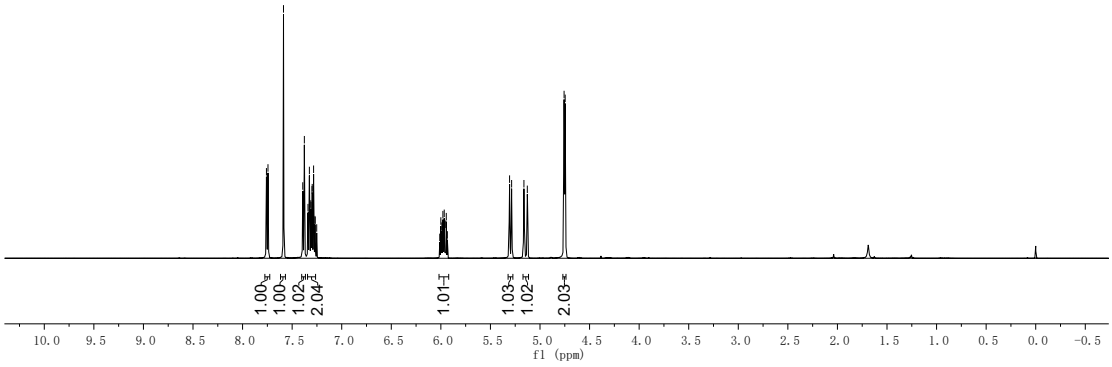


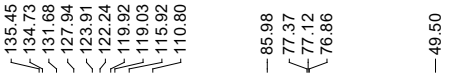
Compound 2fa

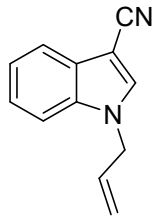




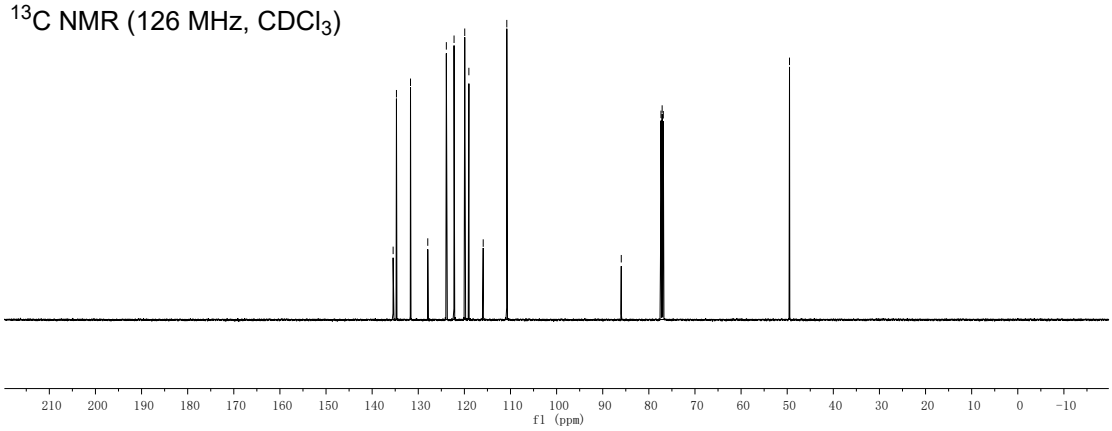
^{1}H NMR (500 MHz, $CDCl_3$)



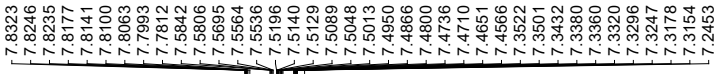


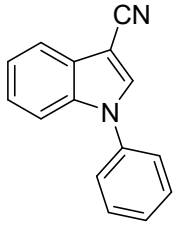


^{13}C NMR (126 MHz, $CDCl_3$)

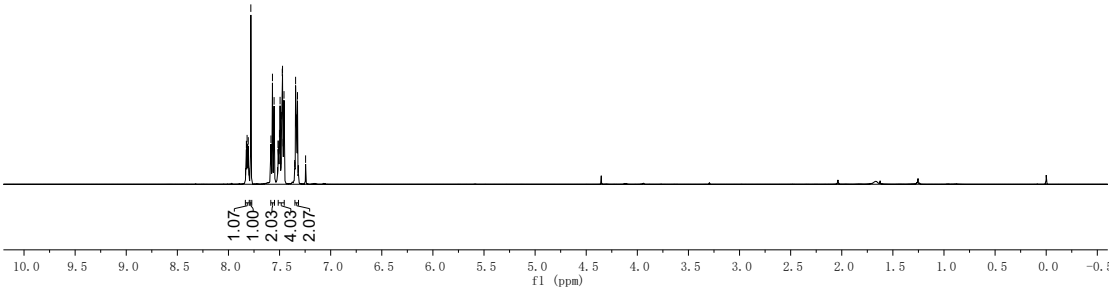


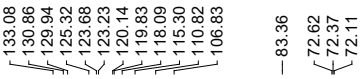
Compound 2fb

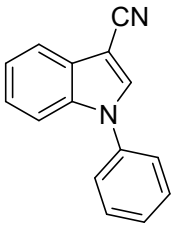




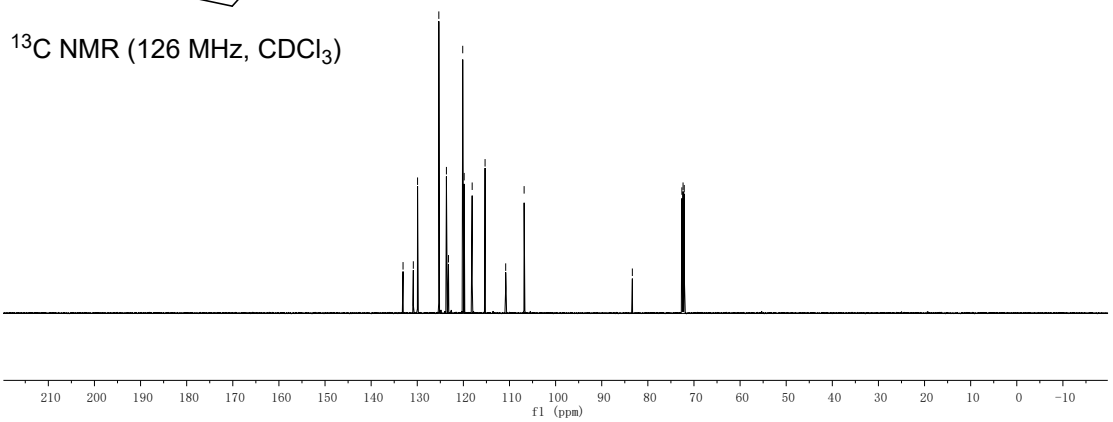
^{1}H NMR (500 MHz, $CDCl_3$)



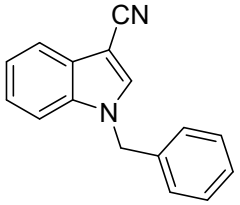




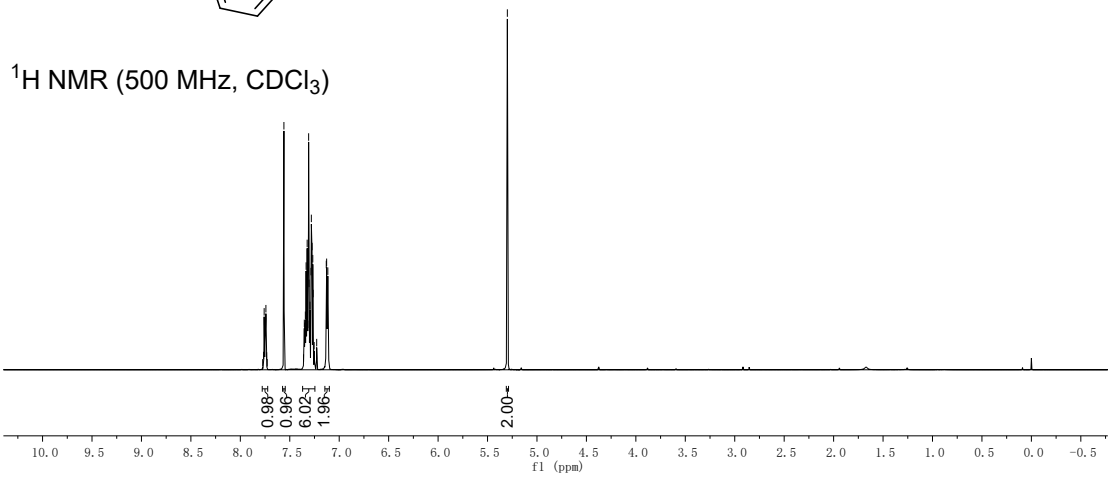
^{13}C NMR (126 MHz, $CDCl_3$)

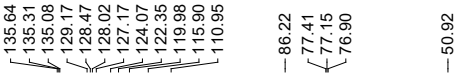


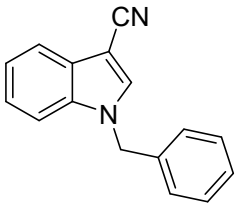
Compound 2fc



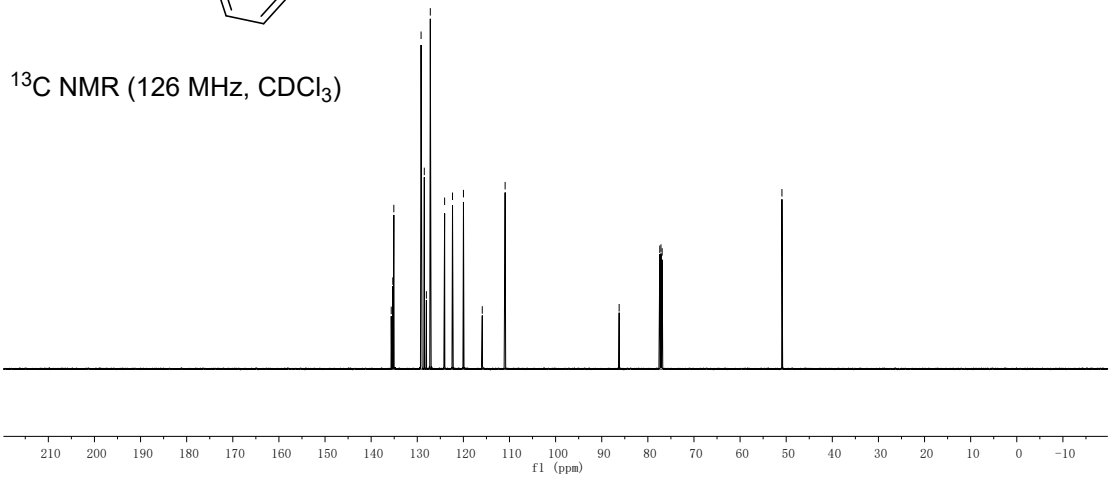
^{1}H NMR (500 MHz, $CDCl_3$)



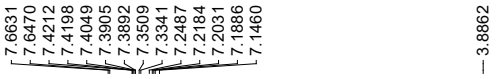


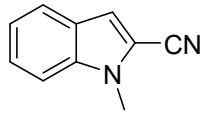


^{13}C NMR (126 MHz, $CDCl_3$)

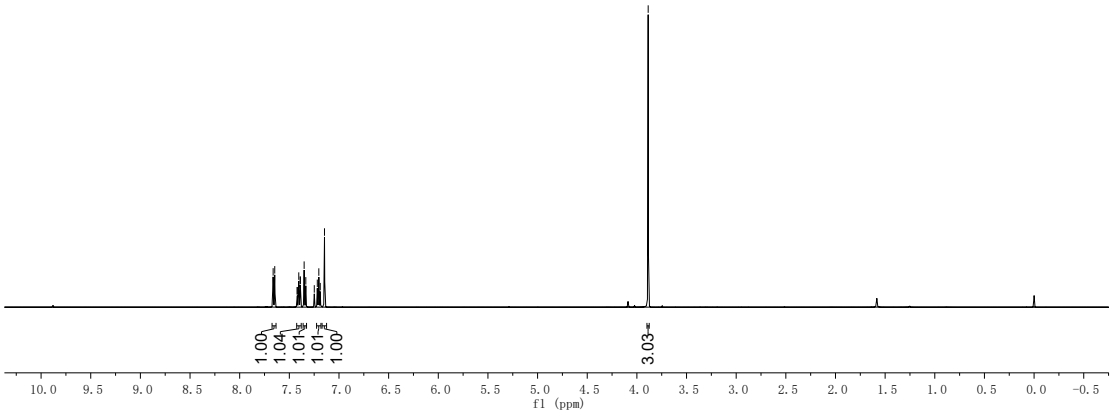


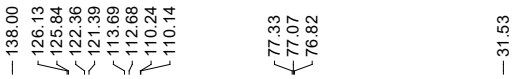
Compound 2g

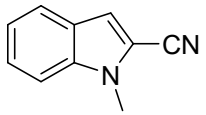




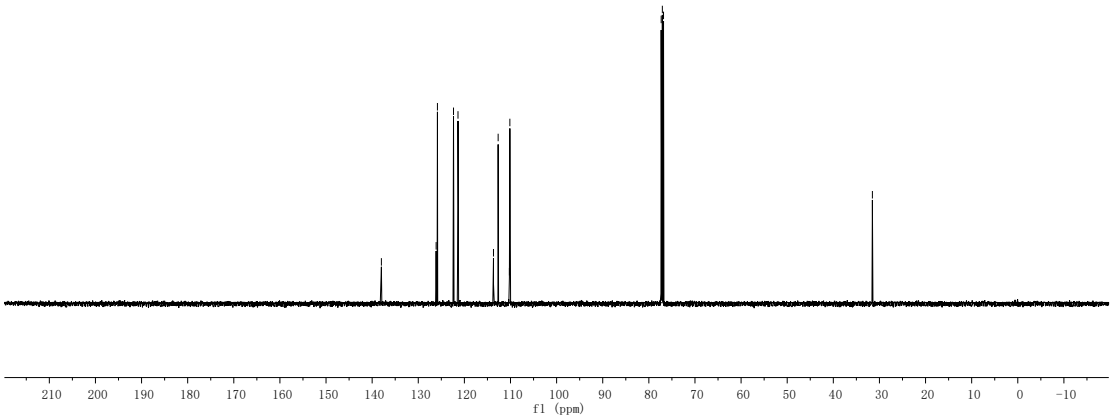
^{1}H NMR (500 MHz, $CDCl_3$)



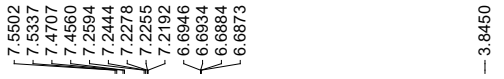


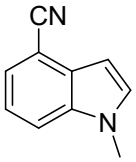


^{13}C NMR (126 MHz, $CDCl_3$)

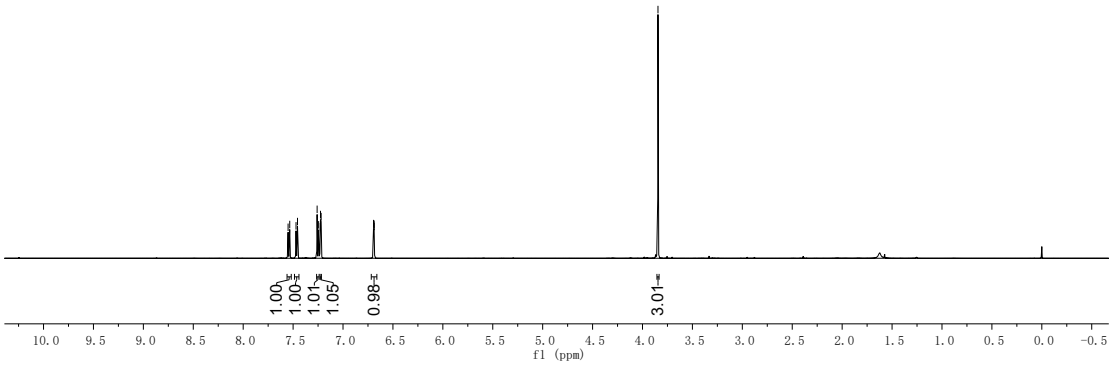


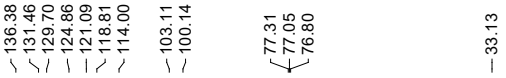
Compound 2h

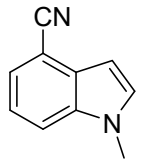




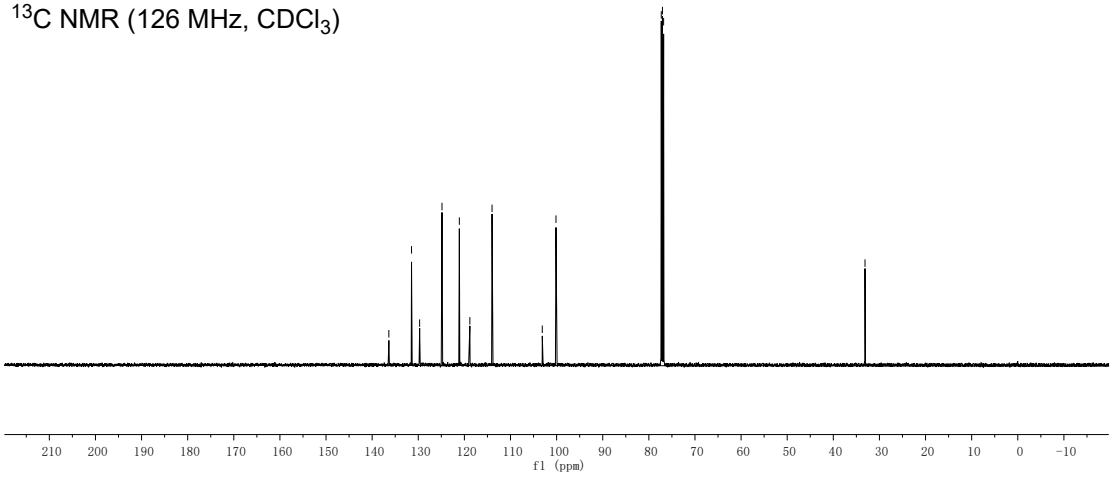
^{1}H NMR (500 MHz, $CDCl_3$)



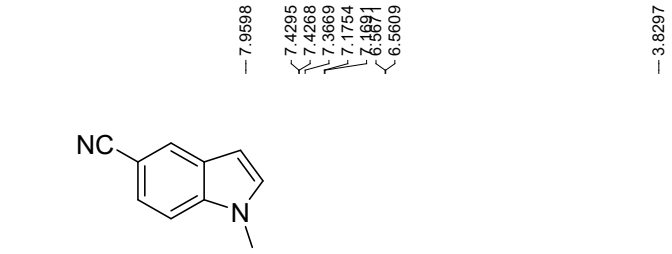




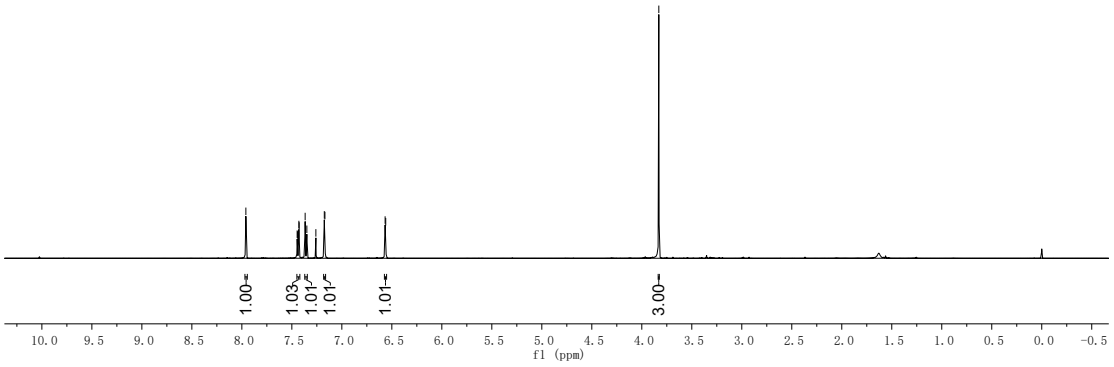
^{13}C NMR (126 MHz, $CDCl_3$)



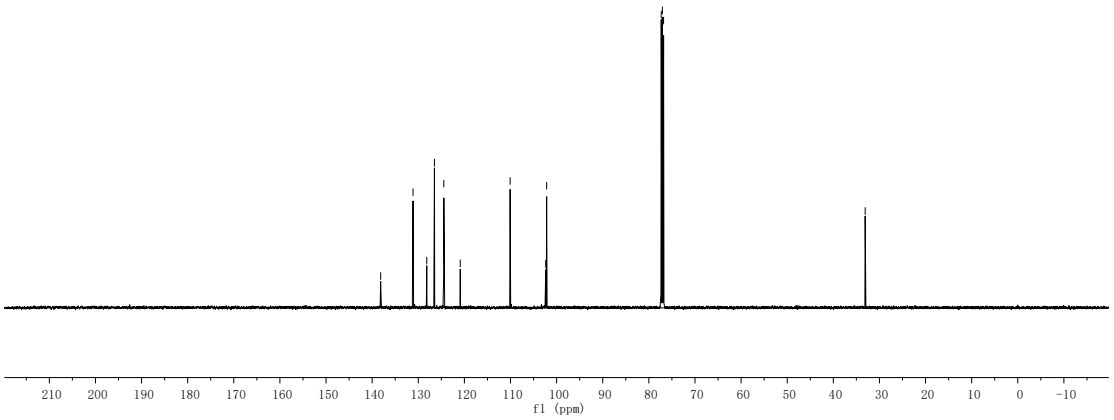
Compound 2i



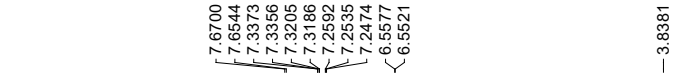
^{1}H NMR (500 MHz, $CDCl_3$)

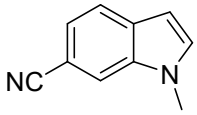


^{13}C NMR (126 MHz, $CDCl_3$)

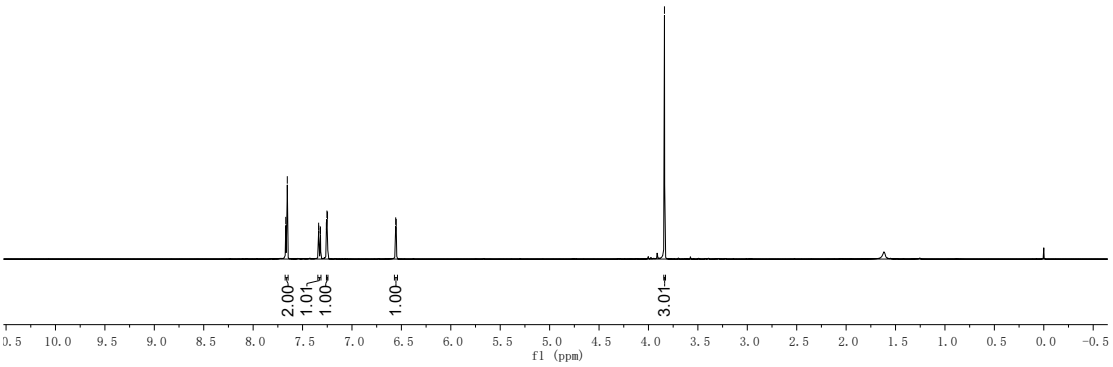


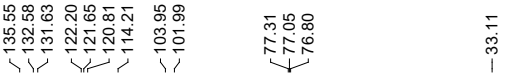
Compound 2j

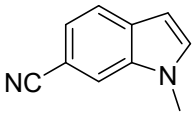




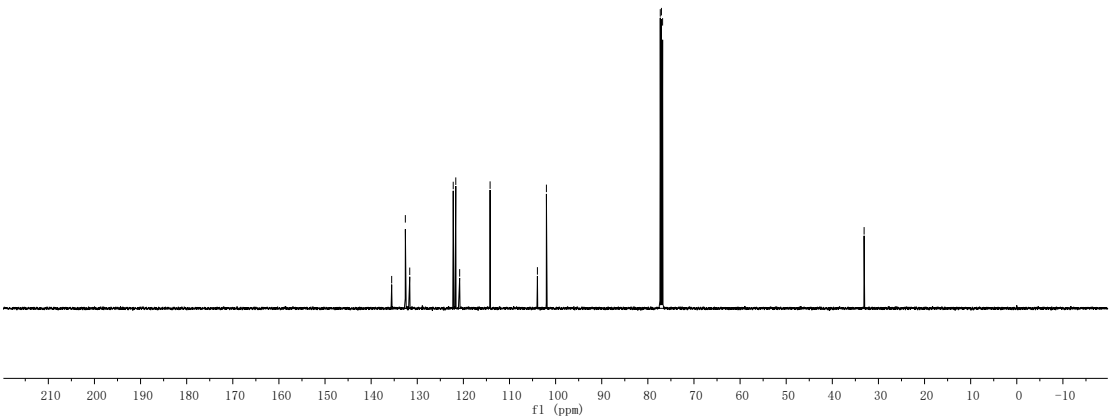
^{1}H NMR (500 MHz, $CDCl_3$)



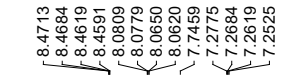


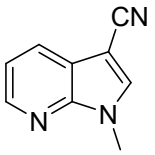


^{13}C NMR (126 MHz, $CDCl_3$)

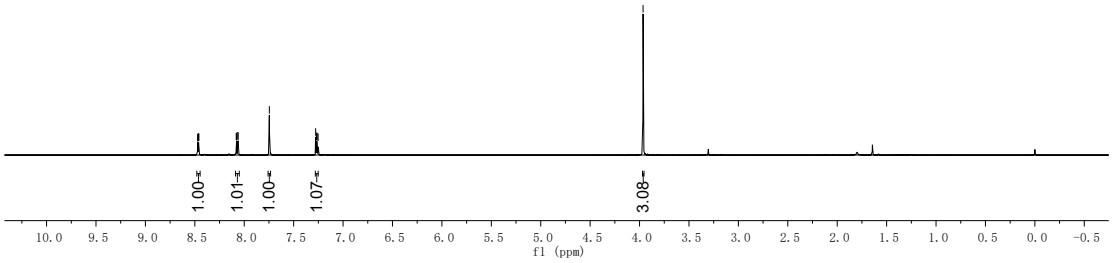


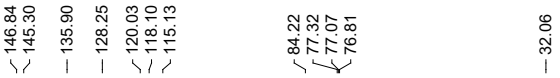
Compound 2k

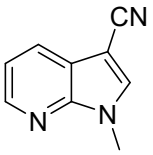




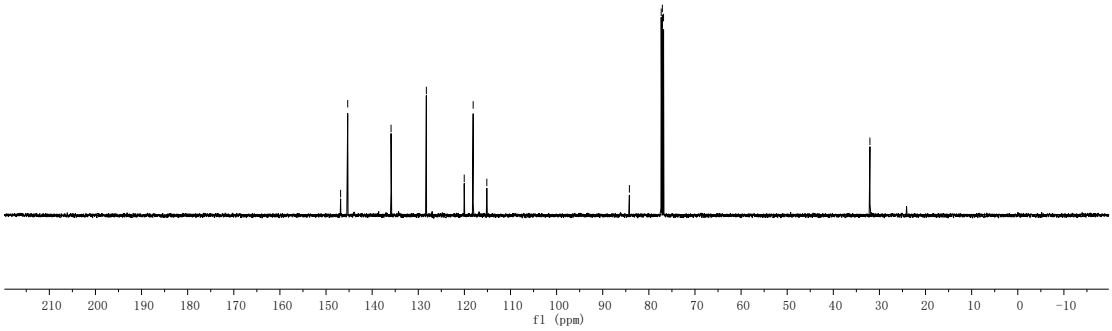
^{1}H NMR (500 MHz, $CDCl_3$)



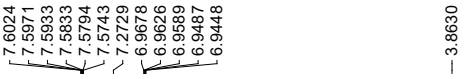


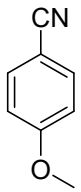


^{13}C NMR (126 MHz, $CDCl_3$)

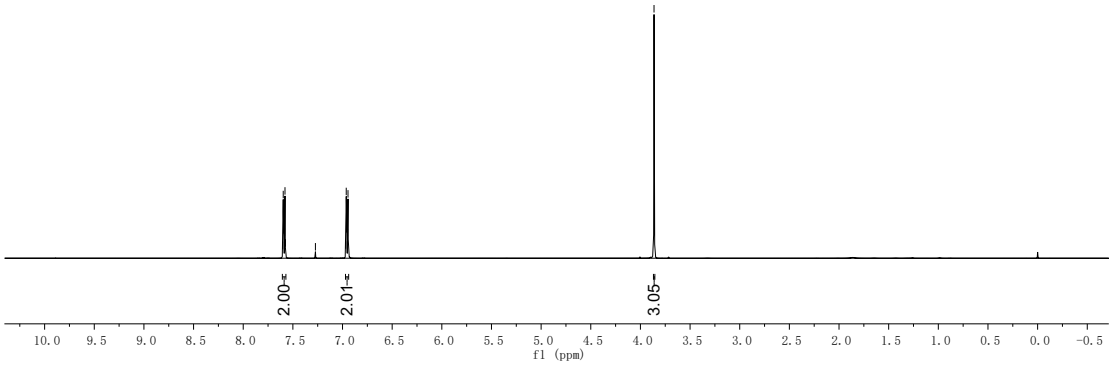


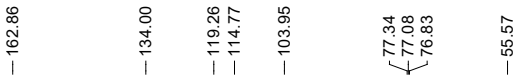
Compound 2l

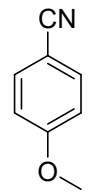




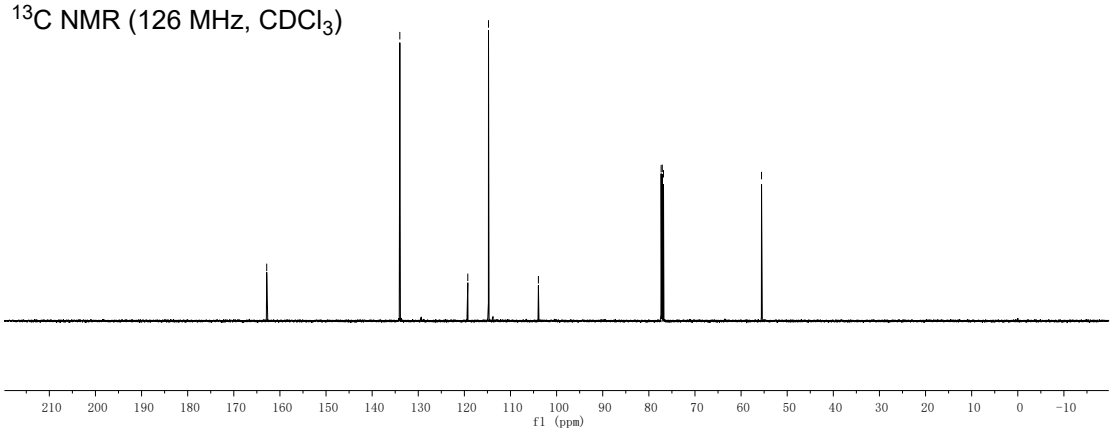
^{1}H NMR (500 MHz, $CDCl_3$)



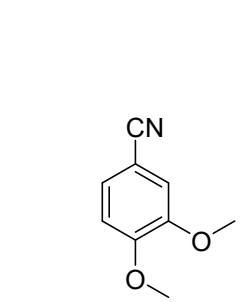




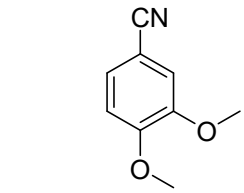
^{13}C NMR (126 MHz, $CDCl_3$)



Compound 2m

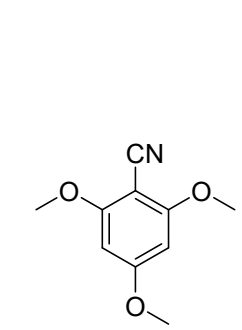


^{1}H NMR (500 MHz, $CDCl_3$)

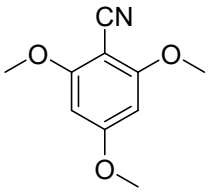


^{13}C NMR (126 MHz, $CDCl_3$)

Compound 2n



^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)