Supporting Information

Ni-Catalyzed C-H Cyanation of (Hetero)arenes with 2-Cyanoisothiazolidine 1,1-Dioxide as a Cyanation Reagent

Junjie Ma, Hao Liu, Xin He, Zhicheng Chen, Yue Liu, Chuanfu Hou, Zhizhong Sun and Wenyi Chu*

School of Chemistry and Materials Science, Heilongjiang University, Harbin 150080, P. R. China (E-mail: wenyichu@hlju.edu.cn; Fax: +86-451-86609135; Tel: +86-451-86609135)

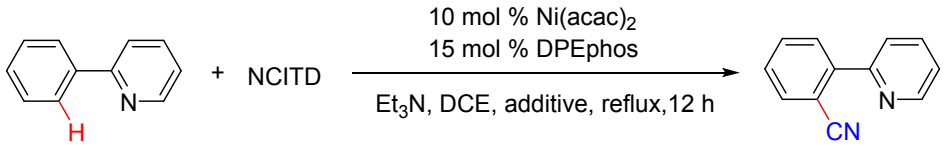
Table of Contents

1. Materials and measurements

All starting materials and the reagents were purchased from TCI or J&K Chemical Company and used without further purification unless specified. The cyanation reactions were monitored by thin layer chromatography (TLC), and column chromatography were carried out on silica gel (300 ~ 400 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Ultrashield™ 400 spectrometer operating at 400 MHz and 100 MHz in $CDCl_3$ or DMSO. ^{1}H NMR and ^{13}C NMR were reported in ppm with tetramethylsilane (TMS) as internal standard. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, m = multiple. Coupling constants (*J*) are reported in Hertz (Hz). Melting points were recorded on a WRR melting point apparatus. Infrared spectra were recorded with Shimadzu IRAffinity-1S Fourier transform infrared spectrophotometer. UV-visible spectra were measured by Shimadzu UV-2501PC UV-visible spectrophotometer. Elemental analyses of C, H, N were performed on a Elementar Vario MICRO cube. High-resolution mass spectrometry is performed on an Agilent 1100 (VL) mass spectrometer with a mass analyzer type ion trap.

2. Parameter optimization.

Table S1. Screening of additive



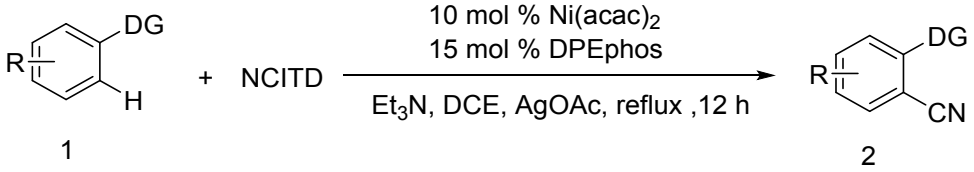
1a 2a

entry	Additive	Amount (mmol)	Yield [b] (%)
1	$ZnCl_2$	0.20	52
2	AgCl	0.20	63
3	AgOTf	0.20	68
4	AgOAc	0.20	85
5	-	-	46
6	AgOAc	0.25	84
7	AgOAc	0.15	70

Reaction conditions: 2-phenylpyridine (1a, 0.10 mmol), NCITD (0.20 mmol), $Ni(acac)_2$ (10 mol%), DPEphos (15 mol%), additive, Et_3N (0.025 mmol), in solvent (1.0 mL), refluxing for 12 h.

In order to study the influence of additives, we screened the additives, and the results were shown in **Table S1**. It was found that silver salt was more effective as the additive (**Table S1**, entries 1-2). For silver salts, it was found that the effect of AgOAc was significantly better than other silver salts (**Table S1**, entries 2-4). The yield of the product decreased significantly without the additive (**Table S1**, entry 5). In addition, increasing the amount of AgOAc had little effect on the yield (**Table S1**, entry 6). However, reducing the amount of AgOAc, the yield decreased significantly to 70% (**Table S1**, entry 7). The results showed that a key role of AgOAc is likely to exist in the form of Ni-Ag heterobimetallic species, thereby promoting the electron transport between metals, which is conducive to the formation of stable metal ring intermediates, making the reaction easier to occur.[1]

3. General experimental procedure

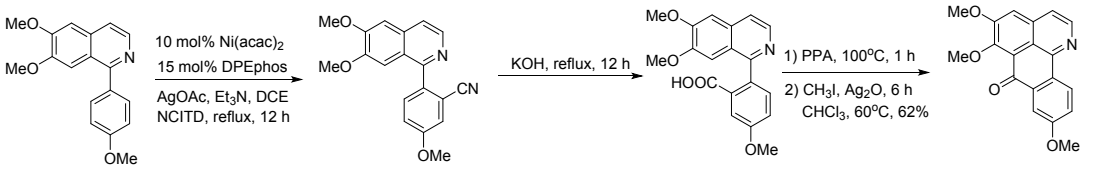


1 2

DG=2-pyridyl, 2-quinolinyl, 1-isoquinolinyl, 2-benzimidazolyl

To an ovendried 25 mL vial containing a magnetic stirring bar and a condenser, 1 (0.1 mmol), NCITD (0.2 mmol), AgOAc (0.2 mmol), DPEphos (15 mol%), $Ni(acac)_2$ (10 mol%) and Et_3N (0.025 mmol) were added followed by dichloroethane (DCE) (1 mL). Then, the reaction vessel was placed into an oil bath and stirred at reflux for 12 h (monitored by TLC). After the reaction was cooled to room temperature, a saturated aqueous NaCl solution (20 mL) was added to the reaction mixture and extracted with CH_2Cl_2 (20 mL × 3). The organic extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The solvent was then removed under reduced pressure, and the product was purified by flash column chromatography (eluent: EA : PE : Et_3N = 1 : 5 : 0.04).

4. Preparation of natural alkaloid Menisporphine



2af, 82% **3,** 92% menisporphine

Preparation of compound 2af

Compound **2af** was obtained by using general experimental procedure, a white solid, Yield: 640.25 mg (82%).

Preparation of compound 3[2]

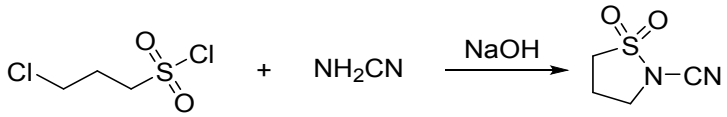
To a 50 mL vial containing a magnetic stirring bar and a condenser，a mixture of the compound 2af (600 mg，3.33 mmol) and 4N KOH (15 mL) was heated to reflux into an oil bath for 12 h. After completion of the reaction, the reaction mixture was neutralized by 2N HCl (24 mL). Then the reaction mixture was extracted with CH_2Cl_2 (30 mL × 3). The combined organic phases were dried over Na_2SO_4 and filtered. The solvent was concentrated in vacuo and the solid was washed with Et_2O (10 mL× 3) to afford product 3 (567 mg, 92%) as a white solid.

Preparation of Menisporphine[3]

To an ovendried 25 mL vial containing a magnetic stirring bar and a condenser, the compound 3（530 mg，1.57mmol） was added followed by Polyphosphoric acid (PPA) (5 mL). The reaction vessel was placed into an oil bath at 100 °C and stirred at this temperature for 1 h. After the mixture was cooled to room temperature, CH_3I (444 mg, 3.13 mmol), Ag_2O (725 mg, 3.13 mmol) and $CHCl_3$ (3 mL) were added, and the mixture was heated into an oil bath at 60 ℃ for 6 h (monitored by TLC). Next, the mixture was poured into ice water, adjusted pH=8 with Na_2CO_3, and extracted with CH_2Cl_2 (30 mL × 3). The organic extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography using ethyl acetate: hexane (ratio: 1:2) as solvent system for elution, and a yellow needle-like solid product (302 mg) was obtained with a yield of

62%.

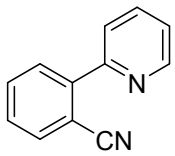
5. Preparation of 2-cyanoisothiazolidine 1,1-dioxide (NCITD)



To a 25 mL vial containing a magnetic stirring bar and a condenser, NaOH (451.84 mg, 11.30 mmol) was dissolved in 6 mL of water and cooled the solution to 0 °C, then cyanamide (237.47 mg, 5.56 mmol) was added to the solution in batches. Next, 3-chloropropanesulfonyl chloride (1.00 g, 5.56 mmol) was slowly added dropwise to the clear and colorless cyanamide solution within 1 h at 0-5 °C. After completion of the dropwise addition, the mixture was stirred at the same temperature for 1 h. Finally, 12 mL of dichloromethane was added, and the reaction mixture was heated to reflux into an oil bath for 1 h. After the reaction was cooled to room temperature, water was added to the mixture and extracted with dichloromethane (10 mL×3), the organic phases were combined. The organic phases were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Then the solvent was removed under reduced pressure to obtain a pure white solid product (725 mg) with a yield of 91%.

6. Structures and data of target compounds

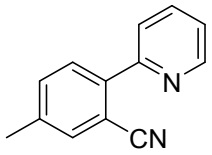
2-(Pyridin-2-yl)benzonitrile (2a)



The pure product was obtained as a white solid; m.p: 85.3~87.1°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.78 (d, *J* = 4.4 Hz, 1H), 7.90 – 7.75 (m, 4H), 7.74 – 7.66 (m, 1H), 7.51 (td, *J* = 7.6, 1.3 Hz, 1H), 7.36 (d, *J* = 6.4 ， 1.3 Hz, 1H). **(Figure S1)**. ^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.2, 149.9, 143.4, 136.9, 134.1, 132.9, 130.0, 128.8, 123.4, 123.3, 118.7, 111.1. **(Figure S2)**. HRMS: $C_{12}H_8N_2$ for $[M+H]^+$: 181.0766. Found: 181.0770. Anal.calcd for: $C_{12}H_8N_2$: C 79.54, H 5.01, N 15.46; Found: C 79.55, H 5.04, N 15.43. FT-IR (KBr disc): *v*= 2918, 2222, 1585, 1560,

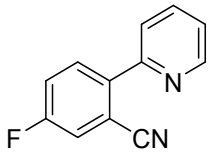
1467, 1423, 1276, 759 cm^{-1}.

5-Methyl-2-(pyridin-2-yl)benzonitrile (2b)[4]



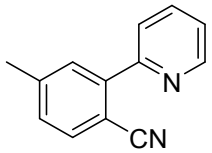
The pure product was obtained as a white solid; m.p: 83.2~84.7°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.84 – 8.68 (m, 1H), 7.86 – 7.71 (m, 3H), 7.60 (s, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.34 (s, 1H), 2.44 (s, 3H). **(Figure S3).** HRMS: $C_{13}H_{10}N_2$ for $[M+H]^+$: 195.0922. Found: 195.0917. Anal.calcd for: $C_{13}H_{10}N_2$: C 80.39, H 5.19, N 14.42; Found: C 80.42, H 5.20, N 14.40. FT-IR (KBr disc): *v*= 2924, 2225, 1680, 1587, 1464, 1423, 1276cm^{-1}.

5-Fluoro-2-(pyridin-2-yl)benzonitrile (2c)



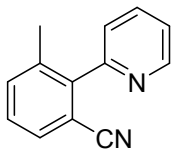
The pure product was obtained as a white solid; m.p: 130.5~131.8°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.77 (d, *J* = 4.7 Hz, 1H), 7.90 – 7.80 (m, 2H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.46 (m, 1H), 7.46 – 7.33 (m, 2H). **(Figure S4).** ^{13}C NMR (100 MHz, Chloroform-d) δ 163.2, 160.7, 154.3, 150.0, 136.9, 132.2 (C-F, $^2J_{C\text{-}F}$ =44.0 Hz), 123.3, 123.1, 120.8, 120.4 (C-F, $^2J_{C\text{-}F}$ =13.0 Hz), 117.5, 112.4 (C-F, $^2J_{C\text{-}F}$ =92.0 Hz). **(Figure S5).** HRMS: $C_{12}H_7FN_2$ for $[M+H]^+$: 199.0672. Found: 199.0670. Anal.calcd for: $C_{12}H_7FN_2$: C 72.72, H 3.56, F 9.59, N 14.13; Found: C 72.77, H 3.59, F 9.57, N 14.10. FT-IR (KBr disc): *v*= 3024, 2225, 1604, 1577, 1467, 1467, 1274 cm^{-1}.

4-Methyl-2-(pyridin-2-yl)benzonitrile (2d)



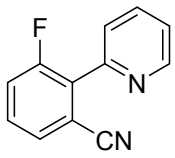
The pure product was obtained as a white solid; m.p: 79.1~80.4°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 (d, *J* = 5.0 Hz, 1H), 7.81 (t, *J* = 8.6 Hz, 2H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.59 (s, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 4.7 Hz, 1H), 2.46 (s, 3H). **(Figure S6).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.3, 149.9, 143.9, 143.3, 136.8, 134.0, 130.7, 129.6, 123.4, 123.3, 119.0, 108.0, 21.8. **(Figure S7).** HRMS: $C_{13}H_{10}N_2$ for $[M+H]^+$: 195.0922. Found: 195.0927. Anal.calcd for: $C_{13}H_{10}N_2$: C 80.39, H 5.19, N 14.42; Found: C 80.37, H 5.22, N 14.44. FT-IR (KBr disc): *v*= 2962, 2221, 1656, 1560, 1458, 1469, 1257 cm^{-1}.

3-Methyl-2-(pyridin-2-yl)benzonitrile (2e)



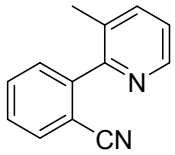
The pure product was obtained as a white solid; m.p: 83.7~85.2°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 (d, *J* = 5.0 Hz, 1H), 7.81 (t, *J* = 8.6 Hz, 2H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.59 (s, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 4.7 Hz, 1H), 2.46 (s, 3H). **(Figure S8).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.3, 149.9, 140.7, 139.1, 136.8, 134.4, 133.8, 129.9, 123.1, 118.9, 110.8, 20.9. **(Figure S9).** HRMS: $C_{13}H_{10}N_2$ for $[M+H]^+$: 195.0922. Found: 195.0920. Anal.calcd for: $C_{13}H_{10}N_2$: C 80.39, H 5.19, N 14.42; Found: C 80.40, H 5.23 N 14.45. FT-IR (KBr disc): *v*= 2966, 2223, 1658, 1569, 1466, 1469, 1257 cm^{-1}.

3-Fluoro-2-(pyridin-2-yl)benzonitrile (2f)



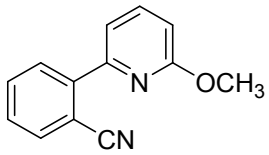
The pure product was obtained as a yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.81 (d, *J* = 4.4 Hz, 1H), 7.84 (t, *J* = 7.7 Hz, 1H), 7.61 (t, *J* = 6.8 Hz, 2H), 7.49 (td, *J* = 8.0, 5.2 Hz, 1H), 7.45 – 7.35 (m, 2H). **(Figure S10).** ^{13}C NMR (100 MHz, Chloroform-d) δ 161.0, 158.5, 150.3, 150.0, 136.56, 131.7, 130.5, 130.0 (C-F, $^2J_{C\text{-}F}$ =38.0 Hz), 125.3 (C-F, $^2J_{C\text{-}F}$ =37.0 Hz), 123.8, 120.9, 114.4 (C-F, $^2J_{C\text{-}F}$ =46.0 Hz). **(Figure S11).** HRMS: $C_{12}H_7FN_2$ for $[M+H]^+$: 199.0672. Found: 199.0670. Anal.calcd for: $C_{12}H_7FN_2$: C 72.72, H 3.56, F 9.59, N 14.13; Found: C 72.75, H 3.58, F 9.61, N 14.14. FT-IR (KBr disc): *v*= 3024, 2223, 1607, 1580, 1459, 1467, 1269 cm^{-1}.

2-(3-Methylpyridin-2-yl)benzonitrile (2g)



The pure product was obtained as a light yellow solid; m.p: 81.6~83.5°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.57 (d, *J* = 4.3 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 8.5 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 2H), 7.31 (dd, *J* = 7.7, 4.8 Hz, 1H), 2.28 (s, 3H). **(Figure S12).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.8, 152.5, 143.0, 139.2, 134.8, 132.52, 129.4, 128.5, 119.2, 115.3, 111.1, 103.3, 22.6. **(Figure S13).** HRMS: $C_{13}H_{10}N_2$ for $[M+H]^+$: 195.0922. Found: 195.0930. Anal.calcd for: $C_{13}H_{10}N_2$: C 80.39, H 5.19, N 14.42; Found: C 80.44, H 5.21, N 14.46. FT-IR (KBr disc): *v*= 2956, 2225, 1657, 1563, 1470, 1473, 1250 cm^{-1}.

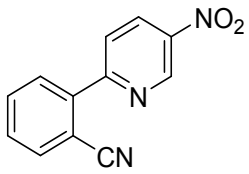
2-(6-Methoxypyridin-2-yl)benzonitrile (2h)[5]



The pure product was obtained as a yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (t, *J* = 8.0 Hz, 2H), 7.76 (dd, *J* = 15.0, 7.6 Hz, 2H), 7.56 (t, *J* = 7.0 Hz, 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 4.17 (s, 3H). **(Figure S14).** HRMS: $C_{13}H_{10}N_2O$ for $[M+H]^+$: 211.0871. Found: 211.0869. Anal.calcd for: $C_{13}H_{10}N_2O$: C

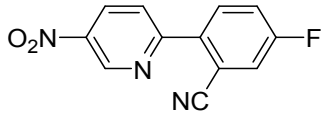
74.27, H 4.79, N 13.33; Found: C 74.30, H 4.81, N 13.36. FT-IR (KBr disc): *v*= 2966, 2221, 1660, 1563, 1470, 1469, 1246 cm^{-1}.

2-(5-Nitropyridin-2-yl)benzonitrile (2i)



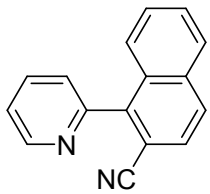
The pure product was obtained as a light yellow solid; m.p: 97.1~98.4°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.60 (d, *J* = 2.5 Hz, 1H), 8.65 (dd, *J* = 8.7, 2.6 Hz, 1H), 8.03 (d, *J* = 8.7 Hz, 1H), 7.91 (dd, *J* = 22.2, 7.7 Hz, 2H), 7.79 (t, *J* = 7.7 Hz, 1H), 7.64 (t, *J* = 7.7 Hz, 1H). **(Figure S15).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 160.2, 152.1, 151.7, 145.3, 134.5, 133.1, 132.1, 130.3, 130.2, 123.3, 118.0, 111.4. **(Figure S16).** HRMS: $C_{12}H_{10}N_3O_2$ for $[M+H]^+$: 226.0617. Found: 226.0620. Anal.calcd for: $C_{12}H_{10}N_3O_2$: C 64.00, H 3.13, N 18.66; Found: C 64.03, H 3.16, N 18.68. FT-IR (KBr disc): *v*= 3028, 2226, 1607, 1580, 1469, 1278 cm^{-1}.

5-Fluoro-2-(5-nitropyridin-2-yl)benzonitrile (2j)



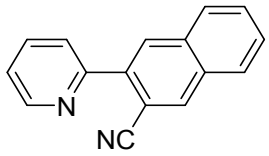
The pure product was obtained as a yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (s, 1H), 7.70 (d, *J* = 7.5 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 1H). **(Figure S17).** ^{13}C NMR (100 MHz, Chloroform-d) δ 160.7, 154.2, 150.0, 139.9, 137.0, 132.2 (C-F, $^2J_{C\text{-}F}$ =83.0 Hz), 132.1, 123.4, 123.1, 120.9, 120.6 (C-F, $^2J_{C\text{-}F}$ =41.0 Hz), 112.4(C-F, $^2J_{C\text{-}F}$ =83.0 Hz). **(Figure S18).** HRMS: $C_{12}H_6FN_3O_2$ for $[M+H]^+$: 244.0522. Found: 244.0519. Anal.calcd for: $C_{12}H_6FN_3O_2$: C 59.27, H 2.49, F 7.81, N 17.28; Found: C 59.29, H 2.51, F 7.83, N 17.30. FT-IR (KBr disc): *v*= 3024, 2225, 1604, 1577, 1467, 1273 cm^{-1}.

1-(Pyridin-2-yl)-2-naphthonitrile (2k)[6]



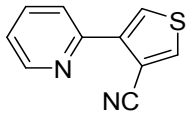
The pure product was obtained as a white solid; m.p: 156.1~157.2°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.04 (d, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 7.0 Hz, 1H), 7.63 – 7.50 (m, 4H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.16 (dd, *J* = 15.9, 11.2 Hz, 1H), 7.03 (d, *J* = 15.5 Hz, 1H), 6.77 – 6.59 (m, 1H). **(Figure S19).** HRMS: $C_{16}H_{10}N_2$ for $[M+H]^+$: 231.0922. Found: 231.0927. Anal.calcd for: $C_{16}H_{10}N_2$: C 83.46, H 4.38, N 12.17; Found: C 83.50, H 4.40, N 12.20. FT-IR (KBr disc): *v*= 2933, 2221, 1584, 1475, 1447, 1384cm^{-1}.

3-(Pyridin-2-yl)-2-naphthonitrile (2l)



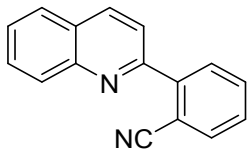
The pure product was obtained as a white solid; m.p: 158.8~160.5°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.83 (d, *J* = 4.5 Hz, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 7.92 (dt, *J* = 25.4, 7.2 Hz, 4H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.45 – 7.35 (m, 1H). **(Figure S20).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.7, 150.1, 143.8， 136.8, 133.1, 133.0, 132.5, 129.0, 128.5, 127.8, 126.6, 125.9, 124.1, 123.4, 117.4, 108.2. **(Figure S21).** HRMS: $C_{16}H_{10}N_2$ for $[M+H]^+$: 231.0922. Found: 231.0920. Anal.calcd for: $C_{16}H_{10}N_2$: C 83.46, H 4.38, N 12.17; Found: C 83.42, H 4.36, N 12.20. FT-IR (KBr disc): *v*= 2924, 2219, 1584, 1477, 1450, 1379 cm^{-1}.

4-(Pyridin-2-yl)thiophene-3-carbonitrile (2m)



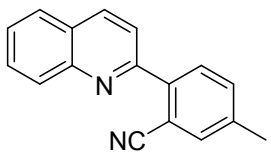
The pure product was obtained as a white solid; m.p: 75.2~77.6°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 (d, *J* = 4.6 Hz, 1H), 7.95 (d, *J* = 7.9 Hz, 1H), 7.86 – 7.78 (m, 1H), 7.69 (d, *J* = 5.2 Hz, 1H), 7.61 (d, *J* = 5.2 Hz, 1H), 7.36 – 7.28 (m, 1H). **(Figure S22).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 151.0, 150.0, 137.1, 131.8, 128.4, 123.6, 121.9, 114.7, 106.2. **(Figure S23).** HRMS: $C_{10}H_6N_2S$ for $[M+H]^+$: 187.0330. Found: 187.0333. Anal.calcd for: $C_{10}H_6N_2S$: C 64.49, H 3.25, N 15.94, S 17.22; Found: C 64.52, H 3.27, N 15.92, S 17.20. FT-IR (KBr disc): *v*= 3103, 2212, 1585, 1465, 1429, 1382 cm^{-1}.

2-(Quinolin-2-yl)benzonitrile (2n)



The pure product was obtained as a white solid; m.p: 111.2~112.9°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 8.5 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.87 (q, *J* = 6.6, 5.5 Hz, 3H), 7.76 (dt, *J* = 15.4, 7.4 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H). **(Figure S24).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.4, 148.3, 139.7, 136.8, 129.8, 129.7, 129.3, 128.9, 127.6, 127.5, 127.2, 126.3, 119.0. **(Figure S25).** HRMS: $C_{16}H_{10}N_2$ for $[M+H]^+$: 231.0922. Found: 231.0918. Anal.calcd for: $C_{16}H_{10}N_2$: C 83.46, H 4.38, N 12.17; Found: C 83.42, H 4.35, N 12.13. FT-IR (KBr disc): *v*= 3153, 2222, 1597, 1504, 1485, 1446, 1417, 1319, 1290 cm^{-1}.

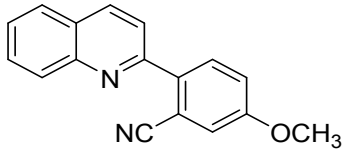
5-Methyl-2-(quinolin-2-yl)benzonitrile (2o)



The pure product was obtained as a white solid; m.p: 116.8~118.4°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.29 (d, *J* = 8.5 Hz, 1H), 8.21 (d, *J* = 8.5 Hz, 1H), 7.87 (dt, *J* =

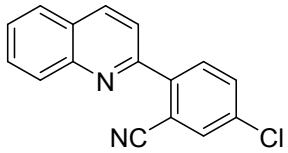
8.5, 3.7 Hz, 3H), 7.81 – 7.73 (m, 1H), 7.65 (s, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 2.47 (s, 3H). **(Figure S26).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.3, 146.7, 143.9, 137.3, 136.4, 134.3, 132.8, 132.5, 130.2, 129.5, 128.8, 127.5, 126.4, 120.6, 118.8, 111.5, 21.7. **(Figure S27).** HRMS: $C_{17}H_{12}N_2$ for $[M+H]^+$: 245.1079. Found: 245.1083. Anal.calcd for: $C_{17}H_{12}N_2$: C 83.58, H 4.95, N 11.47; Found: C 83.60, H 4.99, N 11.50. FT-IR (KBr disc): *v*= 3053, 2225, 1597, 1504, 1487, 1444, 1421, 1319, 1290 cm^{-1}.

5-Methoxy-2-(quinolin-2-yl)benzonitrile (2p)



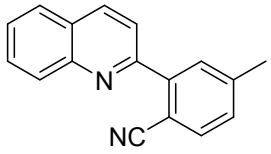
The pure product was obtained as a white solid; m.p: 115.5~116.7°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.28 (d, *J* = 8.5 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 8.7 Hz, 1H), 7.86 (t, *J* = 8.2 Hz, 2H), 7.76 (t, *J* = 7.0 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.33 (d, *J* = 2.6 Hz, 1H), 7.26 (dd, *J* = 8.7, 2.7 Hz, 1H), 3.91 (s, 3H). **(Figure S28).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 159.8, 154.9, 148.1, 137.0, 136.2, 131.6, 130.1, 129.7, 127.5, 127.2, 127.0, 120.4, 119.4, 118.8, 112.4, 55.8. **(Figure S29).** HRMS: $C_{17}H_{12}N_2O$ for $[M+H]^+$: 261.1028. Found: 261.1031. Anal.calcd for: $C_{17}H_{12}N_2O$: C 78.44, H 4.65, N 10.76; Found: C 78.40, H 4.62, N 10.74. FT-IR (KBr disc): *v*= 3153, 2226, 1597, 1508, 1496, 1425, 1228, 819 cm^{-1}.

5-Chloro-2-(quinolin-2-yl)benzonitrile (2q)



The pure product was obtained as a white solid; m.p: 110.7~111.9°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (d, *J* = 8.5 Hz, 1H), 8.21 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.91 – 7.74 (m, 4H), 7.70 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.61 (t, *J* = 7.1 Hz, 1H). **(Figure S30).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.0, 148.1, 142.0, 137.3, 135.2, 133.9, 133.2, 131.5, 130.3, 129.8, 127.6, 127.5, 120.2, 117.5, 113.0. **(Figure S31).** HRMS: $C_{17}H_9ClN_2$ for $[M+H]^+$: 265.7200. Found: 265.7204. Anal.calcd for: $C_{17}H_9ClN_2$: C 72.60, H 3.43, Cl 13.39 N 10.58; Found: C 72.58, H 3.40, Cl 13.41 N 10.62. FT-IR (KBr disc): *v*= 3070, 2225, 1591, 1558, 1483, 1446, 1427, 1319, 1211, 821 cm^{-1}.

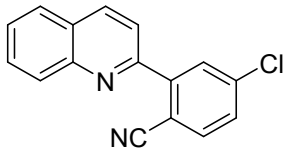
4-Methyl-2-(quinolin-2-yl)benzonitrile (2r)



The pure product was obtained as a white solid; m.p: 108.1~110.9°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (d, *J* = 8.5 Hz, 1H), 8.22 (d, *J* = 8.5 Hz, 1H), 7.88 (t, *J* = 7.1 Hz, 2H), 7.82 – 7.70 (m, 3H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 7.9 Hz, 1H), 2.52 (s, 3H). **(Figure S32).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.5,148.1, 143.9, 143.7,

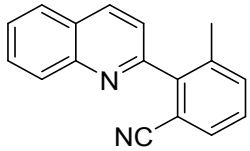
137.0, 134.2, 130.1, 129.8, 129.8, 127.6, 127.4, 127.2, 120.7, 118.9, 108.6, 21.9. **(Figure S33).** HRMS: $C_{17}H_{12}N_2$ for $[M+H]^+$: 245.1079. Found: 245.1081. Anal.calcd for: $C_{17}H_{12}N_2$: C 83.58, H 4.95, N 11.47; Found: C 83.56, H 4.93, N 11.49. FT-IR (KBr disc): *v*= 3059, 2224, 1590, 1560, 1480, 1427, 1319, 1211 cm^{-1}.

4-Chloro-2-(quinolin-2-yl)benzonitrile (2s)



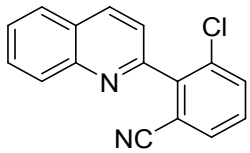
The pure product was obtained as a yellow solid; m.p: 112.1~113.2°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.33 (d, *J* = 8.5 Hz, 1H), 8.22 (d, *J* = 8.5 Hz, 1H), 7.99 (s, 1H), 7.84 (dt, *J* = 38.8, 8.2 Hz, 4H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 8.3 Hz, 1H). **(Figure S34).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.8, 148.1, 145.3, 145.2, 139.6, 137.3, 135.3, 130.6, 130.4, 129.8, 129.3, 127.6, 127.6, 120.3, 118.0, 109.9. **(Figure S35).** HRMS: $C_{17}H_9ClN_2$ for $[M+H]^+$: 265.7200 Found: 265.7198. Anal.calcd for: $C_{17}H_9ClN_2$: C 72.60, H 3.43, Cl 13.39, N 10.58; Found: C 72.62, H 3.46, Cl 13.43, N 10.63. FT-IR (KBr disc): *v*= 3074, 2225, 1591, 1554, 1477, 1450, 1429, 1290, 1211, 823 cm^{-1}.

3-Methyl-2-(quinolin-2-yl)benzonitrile (2t)



The pure product was obtained as a yellow solid; m.p: 119.0~ 120.4°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.44 (d, *J* = 6.4 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 7.3 Hz, 1H), 7.72(ddd, *J* = 12.5, 7.3, 2.4 Hz, 4H), 7.58-7.51 (m, 2H), 2.23 (s, 3H). **(Figure S36).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.7, 147.3, 143.1, 142.9, 136.2, 134.7, 133.4, 130.2, 129.3, 129.0, 126.8, 126.6, 126.4, 120.0, 118.2, 107.8, 21.1. **(Figure S37).** HRMS: $C_{17}H_{12}N_2$ for $[M+H]^+$: 245.1079 Found: 245.1083. Anal.calcd for: $C_{17}H_{12}N_2$: C 83.58, H 4.95, N 11.47; Found: C 83.60, H 4.98, N 11.52. FT-IR (KBr disc): *v*= 3077, 2222, 1590, 1550, 1470, 1449, 1429, 1288, 1216, 825 cm^{-1}.

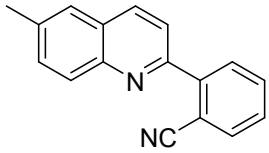
3-Chloro-2-(quinolin-2-yl)benzonitrile (2u)



The pure product was obtained as a white solid; m.p: 117.2~119.1°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.44 (d, *J* = 7.6 Hz, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 7.91 (d, *J* = 7.3 Hz, 1H), 7.85(dd, *J* = 7.4, 2.0 Hz, 1H), 7.78-7.70 (m, 3H), 7.54 (q, *J* = 7.8 Hz, 2H). **(Figure S38).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.7, 148.6, 138.9, 138.0, 132.9, 131.3, 130.6, 130.5, 128.4, 127.9, 126.4, 125.7, 119.1, 117.0, 116.2. **(Figure S39).** HRMS: $C_{17}H_9ClN_2$ for $[M+H]^+$: 265.7200. Found: 265.7196. Anal.calcd for: $C_{17}H_9ClN_2$: C 72.60, H 3.43, Cl 13.39, N 10.58; Found: C 72.58, H 3.41, Cl 13.36, N

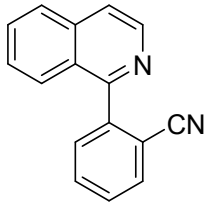
10.56. FT-IR (KBr disc): *v*= 3071, 2221, 1593, 1548, 1472, 1451, 1433, 1290, 1216 cm^{-1}.

2-(6-Methylquinolin-2-yl)benzonitrile (2v)



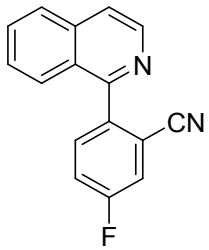
The pure product was obtained as a white solid; m.p: 113.1~114.5°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 (d, *J* = 8.5 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.83 (t, *J* = 7.3 Hz, 2H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.67 – 7.58 (m, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 2.57 (s, 3H). **(Figure S40).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.3, 146.7, 143.9, 137.3, 136.4, 134.3, 132.8, 132.5, 130.2, 129.5, 128.8, 127.5, 126.4, 120.6, 118.8, 111.5, 21.7. **(Figure S41).** HRMS: $C_{17}H_{12}N_2$ for $[M+H]^+$: 245.1079. Found: 245.1085. Anal.calcd for: $C_{17}H_{12}N_2$: C 83.58, H 4.95, N 11.47; Found: C 83.62, H 4.92, N 11.50. FT-IR (KBr disc): *v*= 2914, 2222, 1597, 1550, 1487, 1444, 1373, 1284, 1244, 835 cm^{-1}.

2-(Isoquinolin-1-yl)benzonitrile (2w)



The pure product was obtained as a yellow solid; m.p: 126.1~127.3°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.68 (d, *J* = 5.6 Hz, 1H), 7.95 (d, *J* = 8.2 Hz, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.81 – 7.72 (m, 4H), 7.68 (d, *J* = 7.4 Hz, 1H), 7.60 (dt, *J* = 14.5, 7.6 Hz, 2H). **(Figure S42).** ^{13}C NMR (100MHz, Chloroform-*d*) δ 156.8, 142.5, 141.8, 136.8, 133.5, 132.4, 131.0, 1308, 129.1, 128.0, 127.3, 126.8, 126.6, 121.6, 117.7, 113.2. **(Figure S43).** HRMS: $C_{16}H_{10}N_2$ for $[M+H]^+$: 231.0922. Found: 231.0918. Anal.calcd for: $C_{16}H_{10}N_2$: C 83.46, H 4.38, N 12.17; Found: C 83.44, H 4.36, N 12.20. FT-IR (KBr disc): *v*= 3053, 2230, 1606, 1577, 1496, 1462, 1386, 1352, 1323, 1253 cm^{-1}.

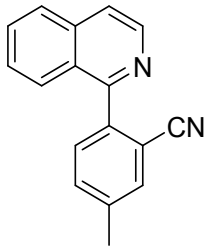
5-Fluoro-2-(isoquinolin-1-yl)benzonitrile (2x)



The pure product was obtained as a yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 (d, *J* = 5.7 Hz, 1H), 7.93 (d, *J* = 8.5 Hz, 1H), 7.74 (dd, *J* = 13.5, 4.6 Hz, 3H), 7.65 (dd, *J* = 8.6, 5.3 Hz, 1H), 7.57 (dd, *J* = 9.8, 4.4 Hz, 2H), 7.45 (td, *J* = 8.3, 2.6 Hz, 1H). **(Figure S44).** ^{13}C NMR (100 MHz, Chloroform-d) δ 163.2, 160.7, 155.9, 142.2, 139.4(C-F, $^2J_{C\text{-}F}$ =38.0 Hz), 136.7, 133.1(C-F, $^2J_{C\text{-}F}$ =84.0 Hz), 130.6, 128.0, 127.4,

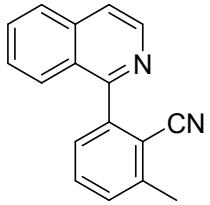
126.8, 126.2, 121.5, 120.3(C-F, $^{2}J_{C\text{-}F}$ =65.0 Hz), 116.6, 114,7(C-F, $^{3}J_{C\text{-}F}$ =6.0 Hz). **(Figure S45).** HRMS: $C_{16}H_9FN_2$ for $[M+H]^+$: 249.0828. Found: 249.0831. Anal.calcd for: $C_{16}H_9FN_2$: C 77.41, H 3.65, F 7.65, N 11.28; Found: C 77.44, H 3.69, F 7.61 N, 11.24. FT-IR (KBr disc): *v*= 3061, 2229, 1608, 1575, 1494, 1383, 1354, 1263 cm^{-1}.

5-Methyl -2-(isoquinolin-1-yl)benzonitrile (2y)



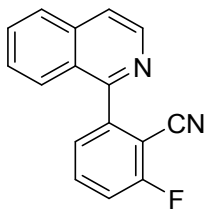
The pure product was obtained as a yellow solid; m.p: 125.2~126.3°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.59 (d, *J* = 5.6 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.72 – 7.58 (m, 4H), 7.49 (d, *J* = 12.7 Hz, 3H), 2.43 (s, 3H). **(Figure S46).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.0, 142.1, 140.0, 139.3, 136.8, 133.8, 133.2, 130.9, 130.5, 127.8, 127.2, 126.9, 126.7, 121.2, 117.9, 113.0, 21.1. **(Figure S47).** HRMS: $C_{17}H_{12}N_2$ for $[M+H]^+$: 245.3050. Found: 245.3046. Anal.calcd for: $C_{17}H_{12}N_2$: C 83.58, H 4.95, N 11.47; Found: C 83.55, H 4.97, N 11.50. FT-IR (KBr disc): *v*= 3016, 2225, 1616, 1581, 1554, 1494, 1382, 1355, 1323 cm^{-1}.

2-(Isoquinolin-1-yl)-6-methylbenzonitrile (2z)



The pure product was obtained as a white solid; m.p: 120.2~122.1°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 (d, *J* = 5.0 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.74 (t, *J* = 10.1 Hz, 4H), 7.60 – 7.53 (m, 1H), 7.47 (s, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 2.50 (s, 3H). **(Figure S48).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 143.5, 142.9, 142.2, 136.7, 133.3, 131.9, 131.6, 130.5, 129.7, 127.8, 127.2, 126.9, 126.6, 121.3, 118.0, 110.2, 21.9. **(Figure S49).** HRMS: $C_{17}H_{12}N_2$ for $[M+H]^+$: 245.3050. Found: 245.3043. Anal.calcd for: $C_{17}H_{12}N_2$: C 83.58, H 4.95, N 11.47; Found: C 83.60, H 4.92, N 11.44. FT-IR (KBr disc): *v*= 3019, 2223, 1619, 1582, 1557, 1494, 1387, 1355, 1321 cm^{-1}.

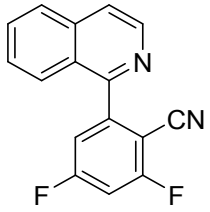
2-Fluoro-6-(isoquinolin-1-yl)benzonitrile (2aa)



The pure product was obtained as a colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.67 (d, *J* = 5.7 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.74 (d, *J* = 14.3, 7.6, 6.4 Hz, 4H),

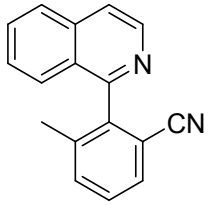
7.58 (t, J = 7.6 Hz, 1H), 7.46 (d, J = 7.7 Hz, 1H), 7.35 (t, J = 8.6 Hz, 1H). **(Figure S50).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ, 162.6, 155.6(C-F, $^{2}J_{C\text{-}F}$ =25.0 Hz), 144.8, 142.2, 136.8, 134.1(C-F, $^{2}J_{C\text{-}F}$ =90.0 Hz), 130.7, 128.1, 127.4, 126.7, 126.6(C-F, $^{2}J_{C\text{-}F}$ =33.0 Hz), 126.2, 121.7, 116.1(C-F, $^{1}J_{C\text{-}F}$ =197.0 Hz), 112.7, 102.6. **(Figure S51).** HRMS: $C_{16}H_9FN_2$ for $[M+H]^+$: 249.0828. Found: 249.0833. Anal.calcd for: $C_{16}H_9FN_2$: C 77.41, H 3.65, F 7.65, N 11.28; Found: C 77.39, H 3.61, F 7.61, N 11.31. FT-IR (KBr disc): v= 3045, 2227, 1608, 1575, 1554, 1494, 1382, 1354, 1263 cm^{-1}.

2,4-Difluoro-6-(isoquinolin-1-yl)benzonitrile (2ab)



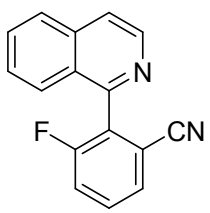
The pure product was obtained as a colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.69 (s, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.76 (dd, J = 16.6, 9.1 Hz, 3H), 7.57 (s, 2H), 6.73 (t, J = 13.1 Hz, 1H). **(Figure S52).** HRMS: $C_{16}H_8F_2N_2$ for $[M+H]^+$: 267.0734. Found: 267.0729. Anal.calcd for: $C_{16}H_8F_2N_2$: C 72.18, H 3.03, F 14.27, N 10.52; Found: C 72.21, H 3.00, F 14.24, N 10.50. FT-IR (KBr disc): v= 3044, 2225, 1606, 1578, 1554, 1494, 1382, 1355, 1327 cm^{-1}.

2-(Isoquinolin-1-yl)-3-methylbenzonitrile (2ac)



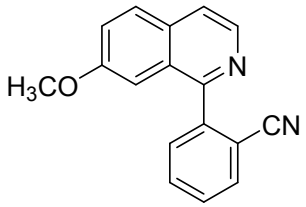
The pure product was obtained as a white solid; m.p: 126.9~127.8°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.29 (d, J = 8.5 Hz, 1H), 8.21 (d, J = 8.5 Hz, 1H), 7.87 (dt, J = 8.5, 3.7 Hz, 3H), 7.81 – 7.73 (m, 1H), 7.65 (s, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 2.47 (s, 3H). **(Figure S53).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.3, 146.7, 143.9, 137.3, 136.4, 134.3, 132.8, 132.5, 130.2, 129.5, 128.8, 127.5, 126.4, 120.6, 118.8, 111.5, 21.7. **(Figure S54).** HRMS: $C_{17}H_{12}N_2$ for $[M+H]^+$: 245.3050. Found: 245.3053. Anal.calcd for: $C_{17}H_{12}N_2$: C 83.58, H 4.95, N 11.47; Found: C 83.55, H 4.98, N 11.50. FT-IR (KBr disc): v= 3019, 2225, 1611, 1587, 1554, 1494, 1382, 1350, 1261 cm^{-1}.

3-Fluoro-2-(isoquinolin-1-yl)benzonitrile (2ad)



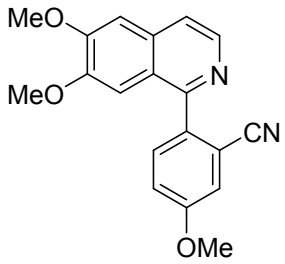
The pure product was obtained as a colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.71 (d, *J* = 5.7 Hz, 1H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.80 (d, *J* = 5.7 Hz, 1H), 7.76 – 7.70 (m, 1H), 7.68 (d, *J* = 7.2 Hz, 1H), 7.58 (dq, *J* = 11.2, 4.1, 3.3 Hz, 3H), 7.51 – 7.44 (m, 1H). **(Figure S55).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 161.2, 158.7, 151.9, 142.6, 136.4, 131.1(C-F, $^{2}J_{C\text{-}F}$ =86.0 Hz), 130.7, 129.4(C-F, $^{2}J_{C\text{-}F}$ =38.0 Hz), 128.1, 127.4, 126.0, 122.0, 120.8, 120.6, 116.4(C-F, $^{2}J_{C\text{-}F}$ =39.0 Hz), 115.4(C-F, $^{2}J_{C\text{-}F}$ =52.0 Hz). **(Figure S56).** HRMS: $C_{16}H_9FN_2$ for $[M+H]^+$: 249.0828. Found: 249.0822. Anal.calcd for: $C_{16}H_9FN_2$: C 77.41, H 3.65, F 7.65, N 11.28; Found: C 77.44, H 3.68, F 7.67, N 11.24. FT-IR (KBr disc): *v*= 3049, 2230, 1606, 1577, 1554, 1496, 1462, 1386, 1352, 1323 cm^{-1}.

2-(7-Methoxyisoquinolin-1-yl)benzonitrile (2ae)



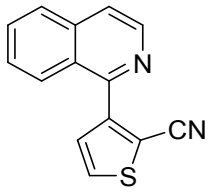
The pure product was obtained as a yellow solid; m.p: 122.1~123.5°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.28 (d, *J* = 8.5 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 7.94 – 7.82 (m, 3H), 7.76 (t, *J* = 7.7 Hz, 1H), 7.61 – 7.55 (m, 1H), 7.33 (d, *J* = 2.6 Hz, 1H), 7.26 (dd, *J* = 8.7, 2.7 Hz, 2H), 3.91 (s, 3H). **(Figure S57).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 159.8, 154.9, 148.1, 137.0, 136.2, 131.6, 130.1, 129.7, 127.5, 127.2, 127.0, 120.4, 119.4, 118.8, 112.4, 55.8. **(Figure S58).** HRMS: $C_{17}H_{12}N_2O$ for $[M+H]^+$: 261.1028. Found: 261.1033. Anal.calcd for: $C_{17}H_{12}N_2O$: C 78.44, H 4.65, N 10.76; Found: C 78.49, H 4.67, N 10.74. FT-IR (KBr disc): *v*= 3009, 2225, 1621, 1576, 1550, 1497, 1385, 1352, 1323 cm^{-1}.

2-(6,7-Dimethoxyisoquinolin-1-yl)-5-methoxybenzonitrile (2af)



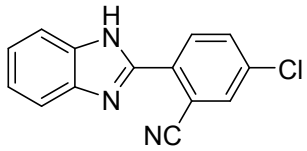
The pure product was obtained as a white solid; m.p: 202.3~204.1 ℃. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.46 (d, *J* = 5.4 Hz, 1H), 7.67 (d, *J* = 8.6 Hz, 2H), 7.48 (d, *J* = 5.5 Hz, 1H), 7.41 (s, 1H), 7.14 – 7.03 (m, 3H), 4.05 (s, 3H), 3.89 (d, *J* = 7.1 Hz, 6H). **(Figure S59).** ^{13}C NMR (100 MHz, Chloroform-*d*) δ 159.9, 157.9, 152.7, 150.0, 141.1, 133.9, 132.3, 130.9, 122.5, 119.0, 118.5, 117.8, 117.5, 113.9, 105.7, 105.0, 56.1, 55.9, 55.4. **(Figure S60).** HRMS: $C_{19}H_{16}N_2O_3$ for $[M+H]^+$: 321.1239. Found: 321.1244. Anal.calcd for: $C_{19}H_{16}N_2O_3$: C 71.24, H 5.03, N 8.74; Found: C 71.20, H 5.01, N 8.77. FT-IR (KBr disc): *v*= 2923, 2228, 1669, 1606, 1563, 1509, 1425 cm^{-1}.

3-(Isoquinolin-1-yl)thiophene-2-carbonitrile (2ag)



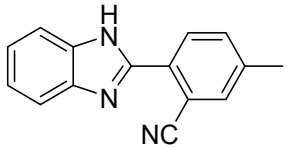
The pure product was obtained as a yellow solid; m.p: 129.5~130.8°C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 (d, *J* = 5.4 Hz, 1H), 8.00 – 7.90 (m, 2H), 7.81 – 7.71 (m, 3H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 4.9 Hz, 1H). **(Figure S61).** HRMS: $C_{17}H_{12}N_2S$ for [M+H]+: 237.0486. Found: 237.0490. Anal.calcd for: $C_{17}H_{12}N_2S$: C 71.16, H 3.41, N 11.86, S 13.57; Found: C 71.19, H 3.44, N 11.83, S 13.60. FT-IR (KBr disc): *v*= 3045, 2222, 1784, 1718, 1558, 1448, 1211 cm^{-1}.

2-(1H-benzo[d]imidazol-2-yl)-5-chlorobenzonitrile (2ah)



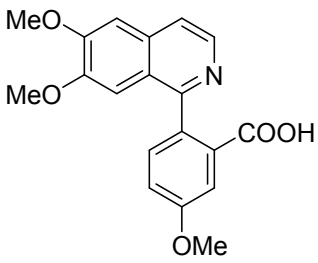
The pure product was obtained as a yellow solid; m.p: 249.4~250.7 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.29 (s, 1H), 8.57 (d, *J* = 8.6 Hz, 1H), 7.89 – 7.52 (m, 4H), 7.36 (dd, *J* = 6.0, 3.0 Hz, 2H). **(Figure S62).** ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 149.7, 148.5, 143.4, 137.4, 127.5, 127.5, 126.6, 122.6, 100.1. **(Figure S63).** HRMS: $C_{14}H_8ClN_3$ for [M+H]+: 254.6970. Found: 254.6966. Anal.calcd for: $C_{14}H_8ClN_3$: C 66.28, H 3.18, Cl 13.97, N 16.56; Found: C 66.24, H 3.20, Cl 13.93, N 16.59. FT-IR (KBr disc): *v*= 2924, 2222, 1587, 1509, 1485, 1448, 1209 cm^{-1}.

2-(1H-benzo[d]imidazol-2-yl)-5-methylbenzonitrile (2ai)



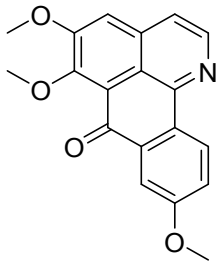
The pure product was obtained as a yellow solid; m.p: >280 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.01 (s, 1H), 7.98 (d, *J* = 7.7 Hz, 1H), 7.86 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 2H), 7.58 (d, *J* = 6.9 Hz, 1H), 7.28 (d, *J* = 8.8 Hz, 2H), 2.44 (s, 3H). **(Figure S64).** ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.0, 144.0, 140.9, 135.8, 135.3, 134.5, 130.4, 129.5, 123.7, 122.5, 119.9, 118.8, 112.1, 110.4, 20.8. **(Figure S65).** HRMS: $C_{15}H_{11}N_3$ for [M+H]$^+$: 234.1031. Found: 234.1028. Anal.calcd for: $C_{15}H_{11}N_3$: C 77.23, H 4.75, N 18.01; Found: C 77.20, H 4.79, N 18.05. FT-IR (KBr disc): *v*= 2939, 2223, 1581, 1503, 1490, 1448, 1209, 817 cm^{-1}.

2-(6,7-Dimethoxyisoquinolin-1-yl)-5-methoxybenzoic acid (3)



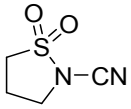
The pure product was obtained as a white solid; m.p: 253.1~254.8 ℃. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.1 (s, 1H), 8.34 (d, *J*=1.9 Hz, 1H), 8.06 (d, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 7.6, 1.6 Hz, 1H), 7.39 (d, *J* = 7.3 Hz, 1H), 7.14 (s, 1H), 7.08 (dd, *J* = 7.4, 2.0 Hz, 1H), 3.94 (s, 6H), 3.97 (s, 3H). **(Figure S66).** HRMS: $C_{19}H_{17}NO_5$ for $[M+H]^+$: 340.1185. Found: 340.1190. Anal.calcd for: $C_{19}H_{17}NO_5$: C 67.25, H 5.05, N 4.13; Found: C 67.27, H 5.03, N 4.15. FT-IR (KBr disc): *v*= 2927, 1890, 1677, 1612, 1558, 1509, 1423 cm^{-1}.

Menisporphine[7]



The pure product was obtained as a yellow needle-like solid；m.p: 119.5~200.5 ℃. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.74 (d, *J*=7.6 Hz, 1H), 8.44 (d, *J* = 7.4 Hz, 1H), 8.10 (dd, *J* = 7.5, 1.6 Hz, 1H), 8.04 (d, *J* = 2.1 Hz, 1H), 7.82 (d, *J* = 1.7 Hz, 1H), 7.52 (dd, *J* = 7.6, 2.0 Hz, 1H), 4.13 (s, 3H), 4.06 (s, 3H), 3.97 (s, 3H). **(Figure S67).** HRMS: $C_{19}H_{15}NO_4$ for $[M+H]^+$: 322.1079. Found: 322.1086. Anal.calcd for: $C_{19}H_{15}NO_4$: C 71.02, H 4.71, N 4.36; Found: C 77.08, H 4.73, N 4.38. FT-IR (KBr disc): *v*= 3422, 2965, 2361, 1656, 1604, 1474, 1413, 1349, 1279, 1242, 1140, 1027, 1013, 992, 864, 843, 628, 607 cm^{-1}.

2-Cyanoisothiazolidine 1,1-dioxide



The pure product was obtained as a white solid; m.p: 201.3-203.1℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.74 (t, *J* = 6.5 Hz, 2H), 3.00 – 2.88 (m, 2H), 2.09 (p, *J* = 6.8 Hz, 2H). **(Figure S68).** ^{13}C NMR (100 MHz, DMSO-d_6) δ 51.0, 44.3, 28.2, 20.2. **(Figure S69).** HRMS: $C_4H_6N_2O_2S$ for $[M+H]^+$: 147.0228. Found: 147.0230. Anal.calcd for: $C_4H_6N_2O_2S$: C 32.87, H 4.14, N 19.17, S 21.93; Found: C 32.89, H 4.10, N 19.14, S 21.96. FT-IR (KBr disc): *v*= 3016, 2223, 1451, 1250, 910 cm^{-1}.

7. References

(1) Aihara, Y.; Chatani, N. The Nickel-Catalyzed Reaction of C-H Bonds in Amides with I_2: ortho-Iodination via the Cleavage of C(sp^2)-H Bonds and Oxidative Cyclization to β-Lactams via the Cleavage of C(sp^3)-H Bonds. *Acs. Catal.* **2016**, *6*, 4323-4329.

(2) Li, J.; Ackermann, L. Cobalt(III)-Catalyzed Aryl and Alkenyl CH Aminocarbonylation with Isocyanates and Acyl Azides. *Angew. Chem. Int. Edit.* **2015,** *54,* 3635-3638.

(3) Kunitomo, J.; Satoh, M.; Shingu, T. Structure and synthesis of menisporphine, a new type of isoquinoline alkaloid: Alkaloids of menispermum dauricum dc. (9)1. *Tetrahedron.* **1983,** *39,* 3261-3265.

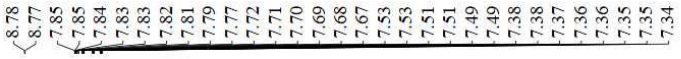
(4) Jia, X. F.; Yang, D. P.; Zhang, S. H.; Cheng, J. Chelation-Assisted Palladium-Catalyzed Direct Cyanation of 2-Arylpyridine C−H Bonds. *Org. Lett.* **2009,** *11,* 4716-4719.

(5) Chaitanya, M.; Yadagiri, D.; Anbarasan, P. Rhodium Catalyzed Cyanation of Chelation Assisted C–H Bonds. *Org. Lett.* **2013,** *15,* 4960-4963.

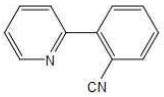
(6) Jin, J. S.; Wen, Q. D.; Lu, P.; Wang, Y. G. Copper-catalyzed cyanation of arenes using benzyl nitrile as a cyanide anion surrogate. *Chen. Commun.* **2012,** *48,* 9933-9935.

(7) Melzer, B. C.; Bracher, F. A novel approach to oxoisoaporphine alkaloids via regioselective metalation of alkoxy isoquinolines. *Beilstein. J. Org. Chem.* **2017**, *13,* 1564-1571.

8. NMR spectra for target compounds.



^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.78 (d, *J* = 4.4 Hz, 1H), 7.90 – 7.75 (m, 4H), 7.74 – 7.66 (m, 1H), 7.51 (td, *J* = 7.6, 1.3 Hz, 1H), 7.36 (d, *J* = 6.4, 1.3 Hz, 1H).



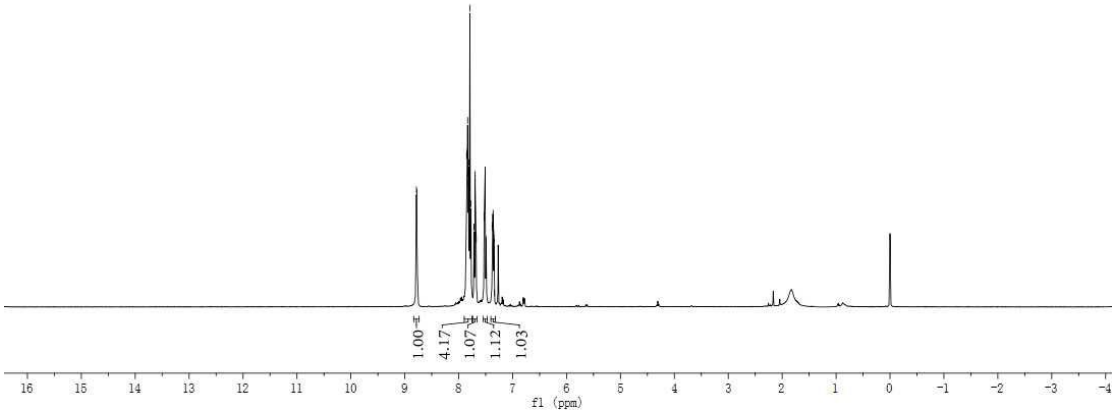
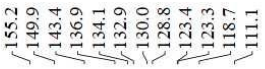
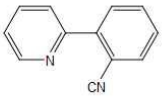


Figure S1. ^{1}H NMR of 2-(Pyridin-2-yl)benzonitrile **(2a)**



^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.2 , 149.9 , 143.4 , 136.9 , 134.1 , 132.9 , 130.0 , 128.8 , 123.4 , 123.3 , 118.7 , 111.1 .



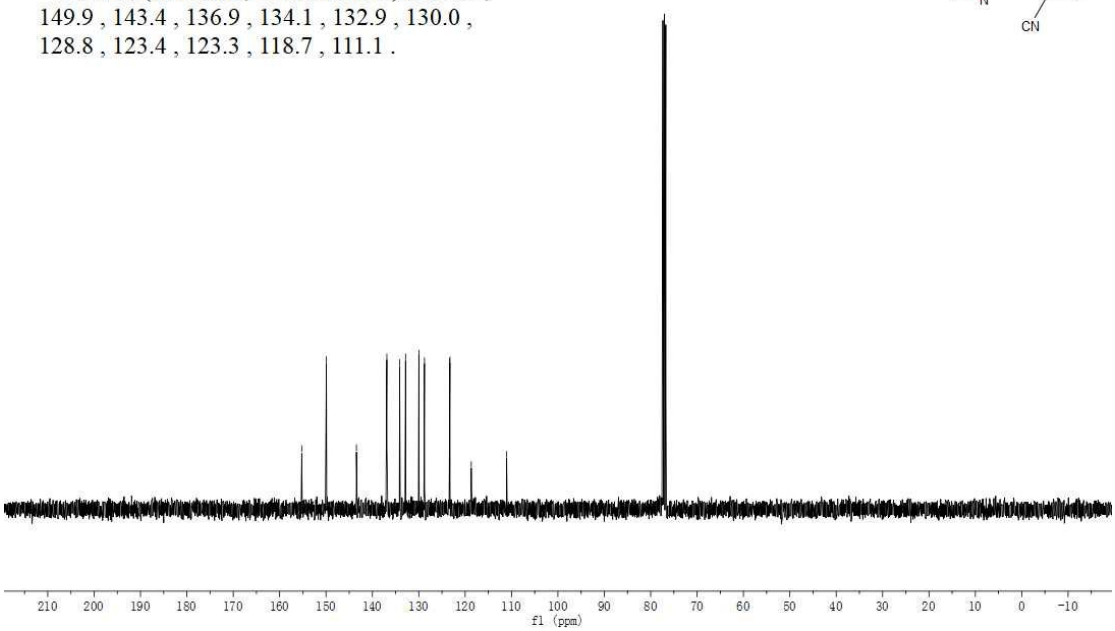
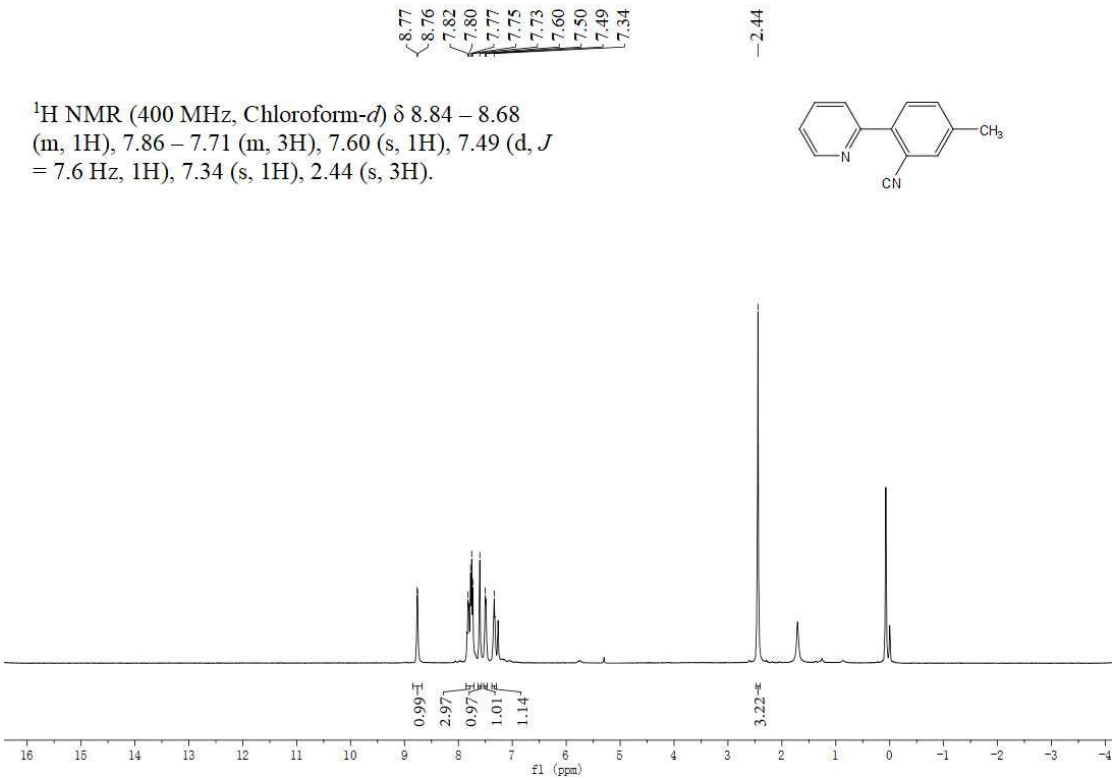
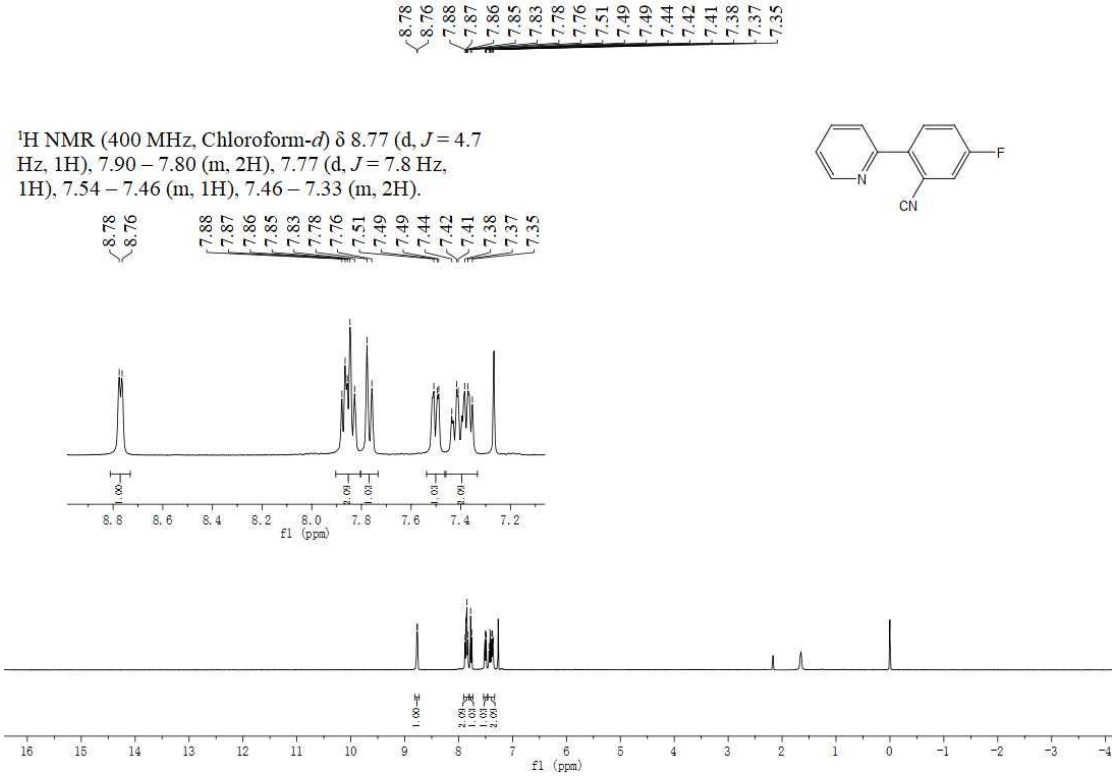


Figure S2. ^{13}C NMR of 2-(Pyridin-2-yl)benzonitrile **(2a)**



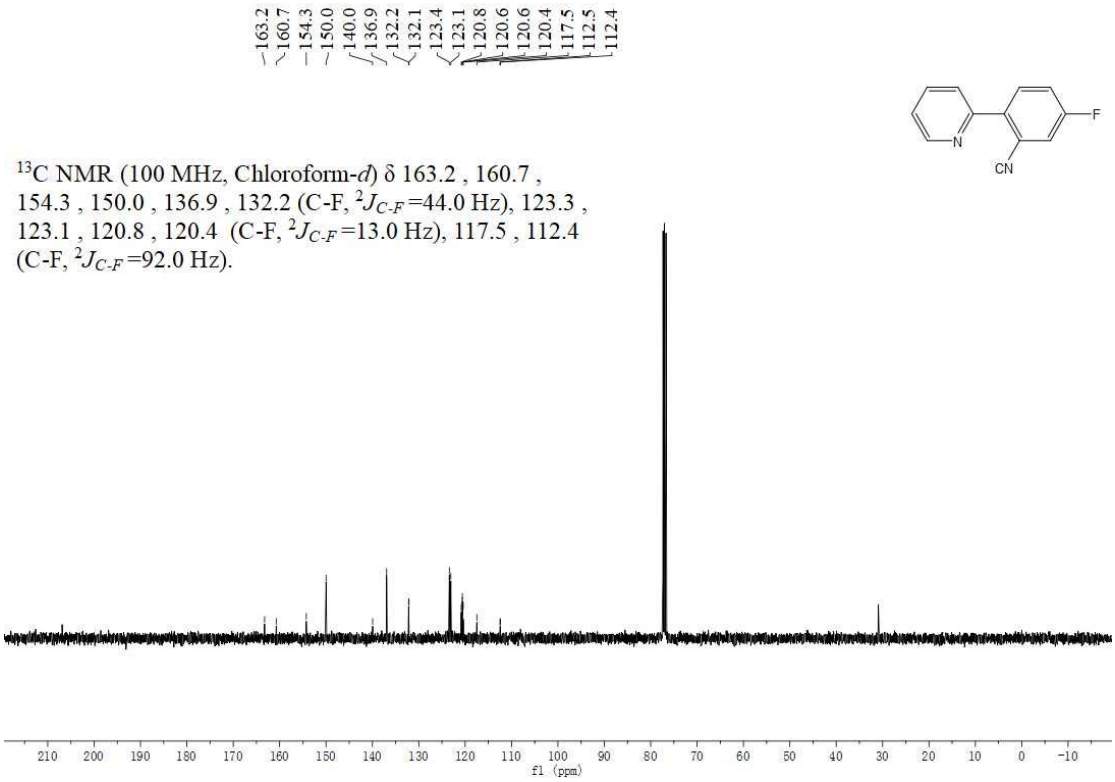
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.84 – 8.68 (m, 1H), 7.86 – 7.71 (m, 3H), 7.60 (s, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.34 (s, 1H), 2.44 (s, 3H).

Figure S3. ^{1}H NMR of 5-Methyl-2-(pyridin-2-yl)benzonitrile (**2b**)



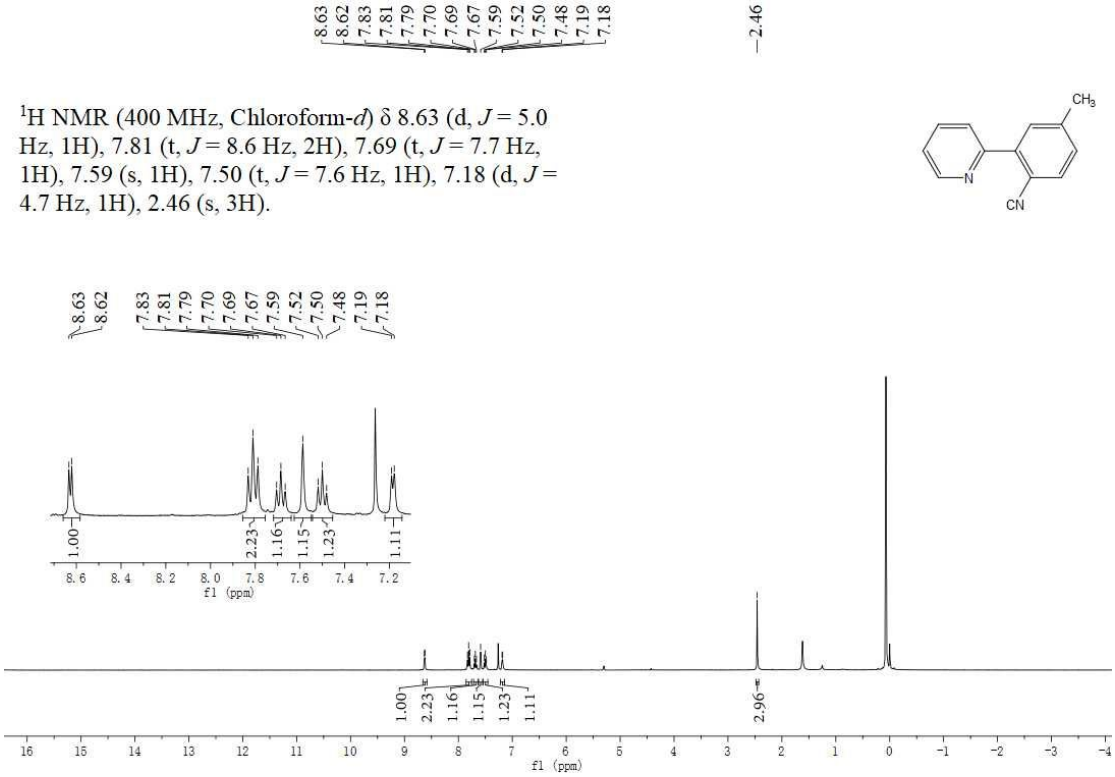
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.77 (d, *J* = 4.7 Hz, 1H), 7.90 – 7.80 (m, 2H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.46 (m, 1H), 7.46 – 7.33 (m, 2H).

Figure S4. ^{1}H NMR of 5-Fluoro-2-(pyridin-2-yl)benzonitrile (**2c**)



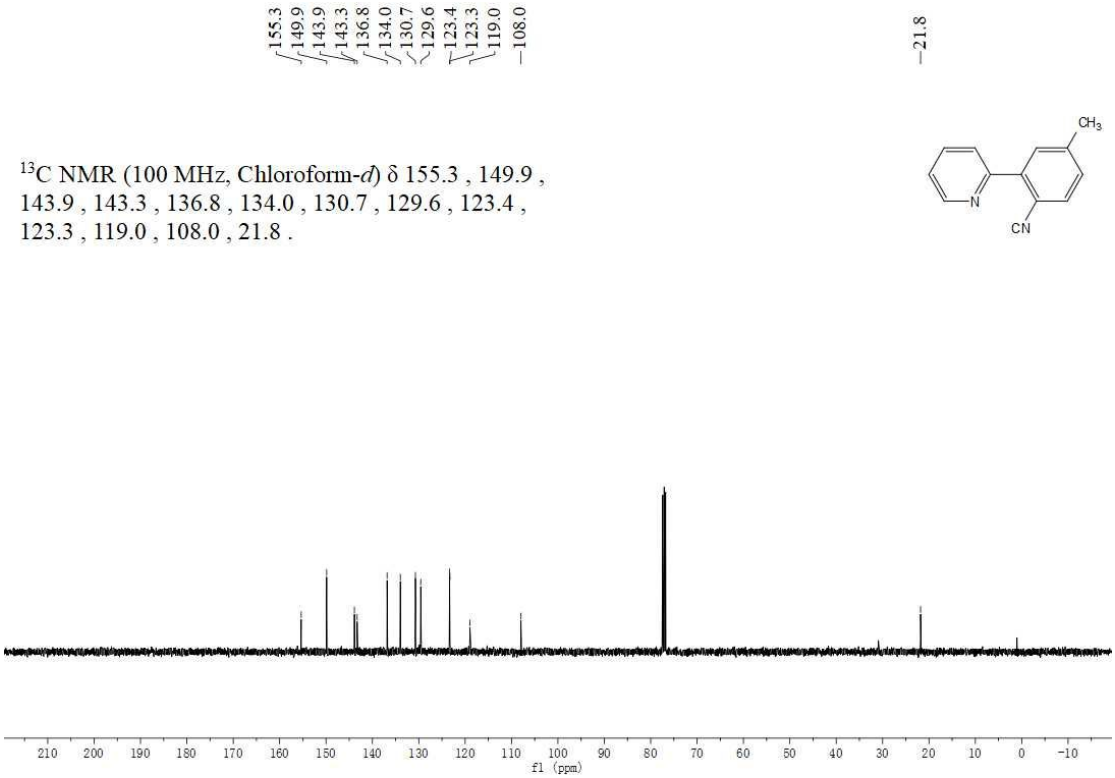
^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.2 , 160.7 , 154.3 , 150.0 , 136.9 , 132.2 (C-F, $^{2}J_{C\text{-}F}$ =44.0 Hz), 123.3 , 123.1 , 120.8 , 120.4 (C-F, $^{2}J_{C\text{-}F}$ =13.0 Hz), 117.5 , 112.4 (C-F, $^{2}J_{C\text{-}F}$ =92.0 Hz).

Figure S5. ^{13}C NMR of 5-Fluoro-2-(pyridin-2-yl)benzonitrile (**2c**)



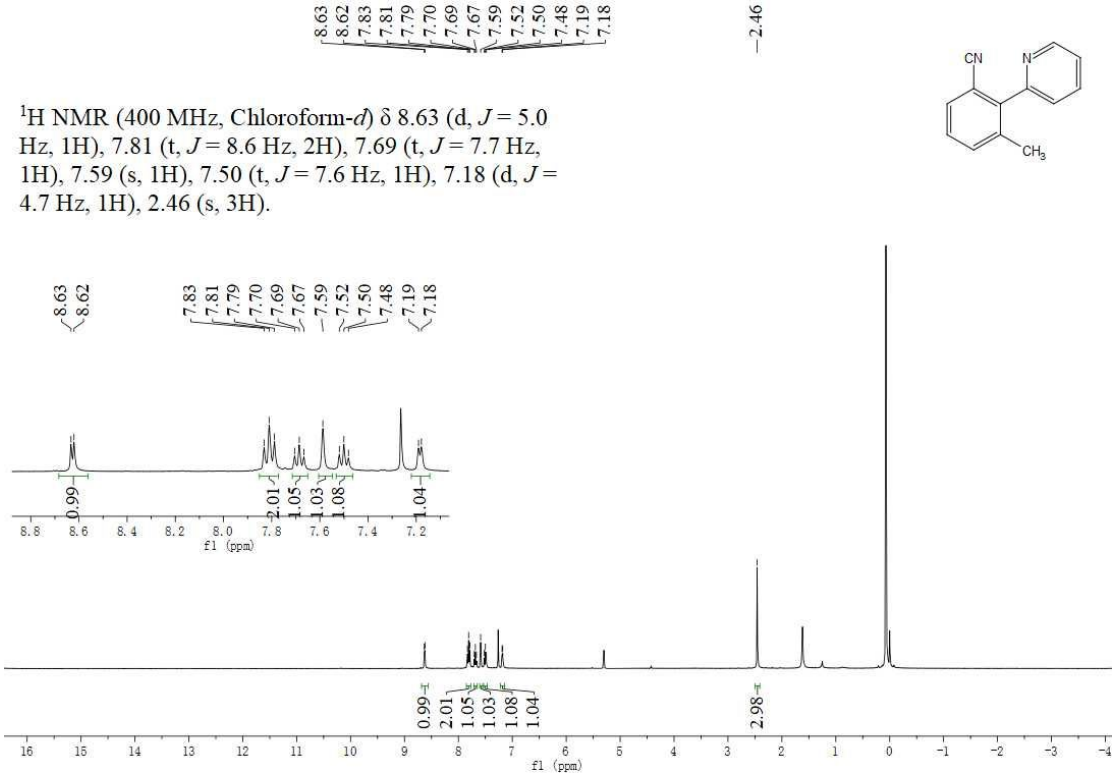
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 (d, *J* = 5.0 Hz, 1H), 7.81 (t, *J* = 8.6 Hz, 2H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.59 (s, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 4.7 Hz, 1H), 2.46 (s, 3H).

Figure S6. ^{1}H NMR of 4-Methyl-2-(pyridin-2-yl)benzonitrile **(2d)**



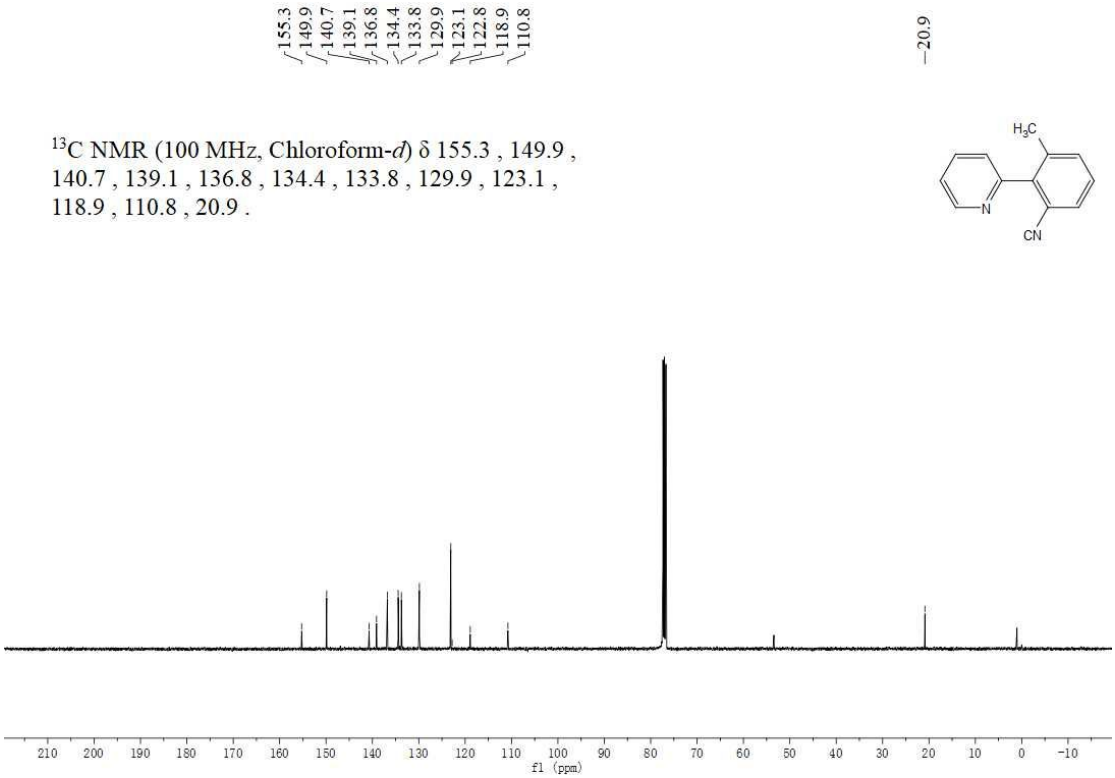
^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.3 , 149.9 , 143.9 , 143.3 , 136.8 , 134.0 , 130.7 , 129.6 , 123.4 , 123.3 , 119.0 , 108.0 , 21.8 .

Figure S7. ^{13}C NMR of 4-Methyl-2-(pyridin-2-yl)benzonitrile **(2d)**



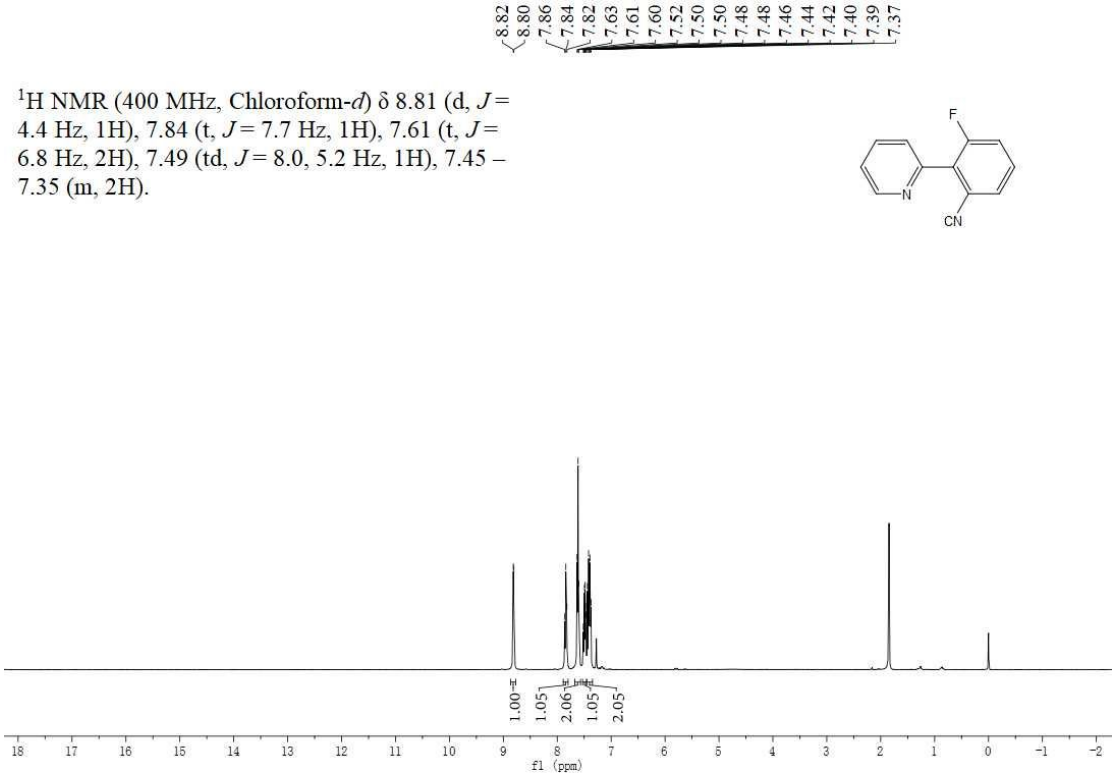
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 (d, *J* = 5.0 Hz, 1H), 7.81 (t, *J* = 8.6 Hz, 2H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.59 (s, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 4.7 Hz, 1H), 2.46 (s, 3H).

Figure S8. ^{1}H NMR of 3-Methyl-2-(pyridin-2-yl)benzonitrile **(2e)**



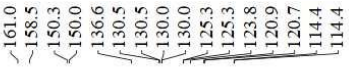
^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.3 , 149.9 , 140.7 , 139.1 , 136.8 , 134.4 , 133.8 , 129.9 , 123.1 , 118.9 , 110.8 , 20.9 .

Figure S9. ^{13}C NMR of 3-Methyl-2-(pyridin-2-yl)benzonitrile **(2e)**

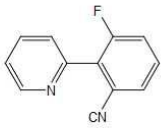


^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.81 (d, *J* = 4.4 Hz, 1H), 7.84 (t, *J* = 7.7 Hz, 1H), 7.61 (t, *J* = 6.8 Hz, 2H), 7.49 (td, *J* = 8.0, 5.2 Hz, 1H), 7.45 – 7.35 (m, 2H).

Figure S10. ^{1}H NMR of 3-Fluoro-2-(pyridin-2-yl)benzonitrile (**2f**)



^{13}C NMR (100 MHz, Chloroform-*d*) δ 161.0 , 158.5 , 150.3 , 150.0 , 136.56 , 131.7 , 130.5 , 130.0 (C-F, $^{2}J_{C\text{-}F}$ =38.0 Hz) , 125.3 (C-F, $^{2}J_{C\text{-}F}$ =37.0 Hz) , 123.8 , 120.9 , 114.4 (C-F, $^{2}J_{C\text{-}F}$ =46.0 Hz) .



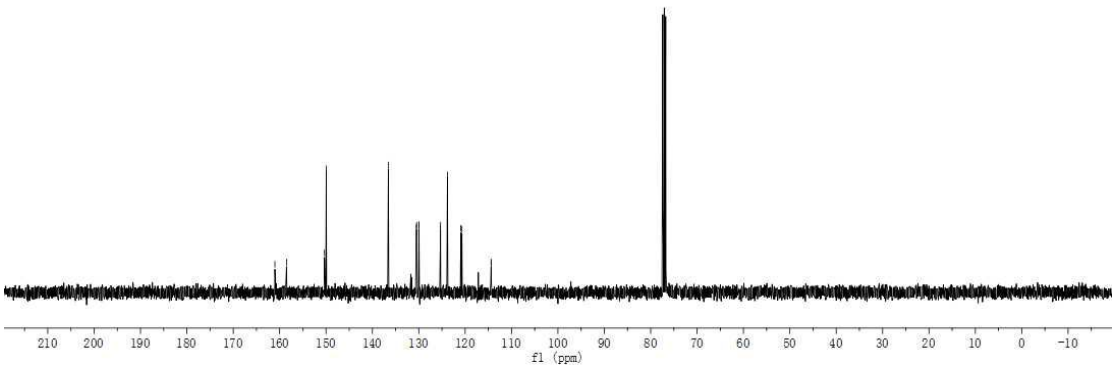
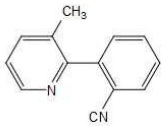


Figure S11. ^{13}C NMR of 3-Fluoro-2-(pyridin-2-yl)benzonitrile (**2f**)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.57 (d, *J* = 4.3 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 8.5 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 2H), 7.31 (dd, *J* = 7.7, 4.8 Hz, 1H), 2.28 (s, 3H).



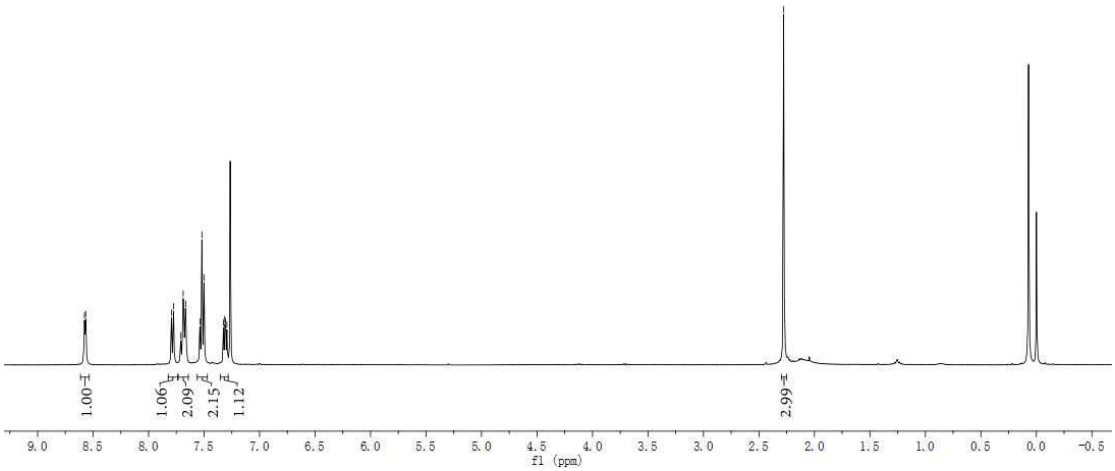
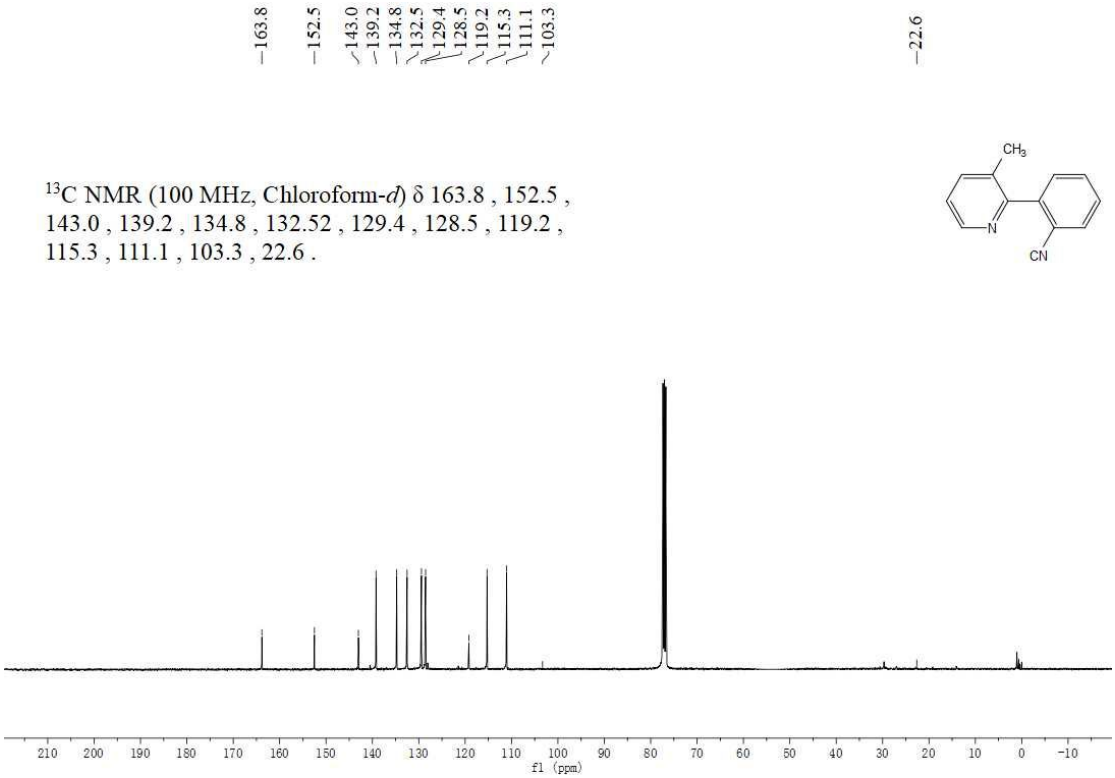
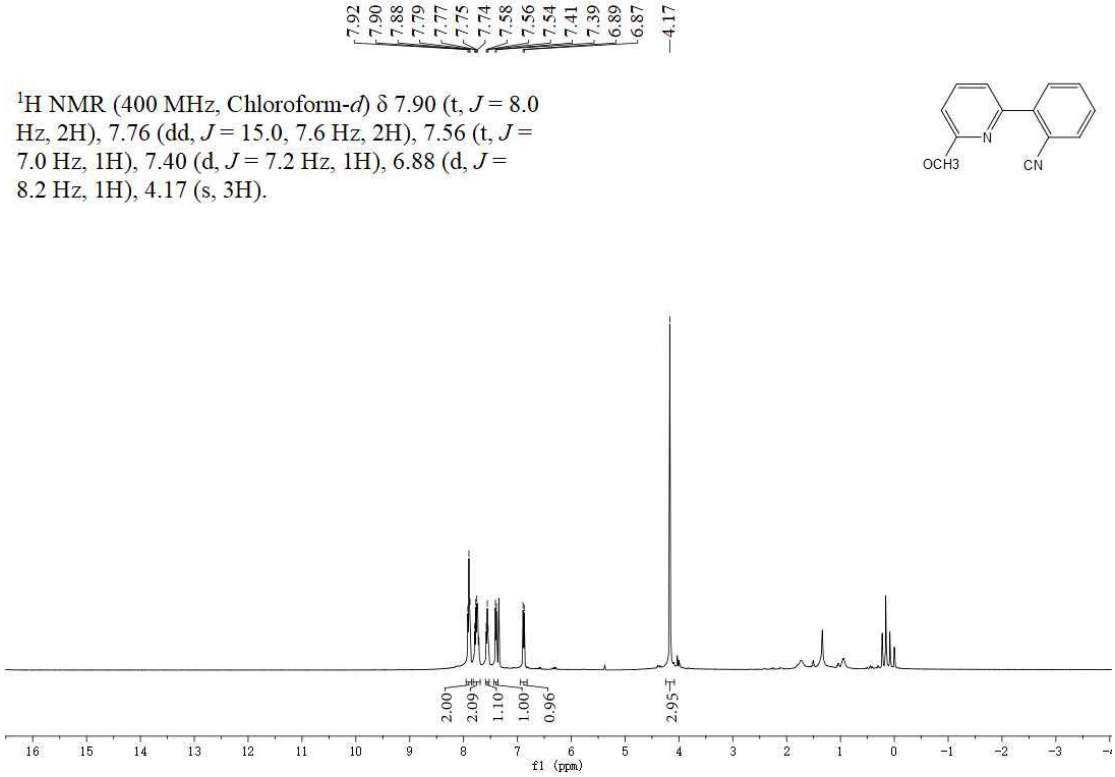


Figure S12. ^{1}H NMR of 2-(3-Methylpyridin-2-yl)benzonitrile **(2g)**



^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.8 , 152.5 , 143.0 , 139.2 , 134.8 , 132.52 , 129.4 , 128.5 , 119.2 , 115.3 , 111.1 , 103.3 , 22.6 .

Figure S13. ^{13}C NMR of 2-(3-Methylpyridin-2-yl)benzonitrile **(2g)**



^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (t, *J* = 8.0 Hz, 2H), 7.76 (dd, *J* = 15.0, 7.6 Hz, 2H), 7.56 (t, *J* = 7.0 Hz, 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 4.17 (s, 3H).

Figure S14. ^{1}H NMR of 2-(6-Methoxypyridin-2-yl)benzonitrile **(2h)**

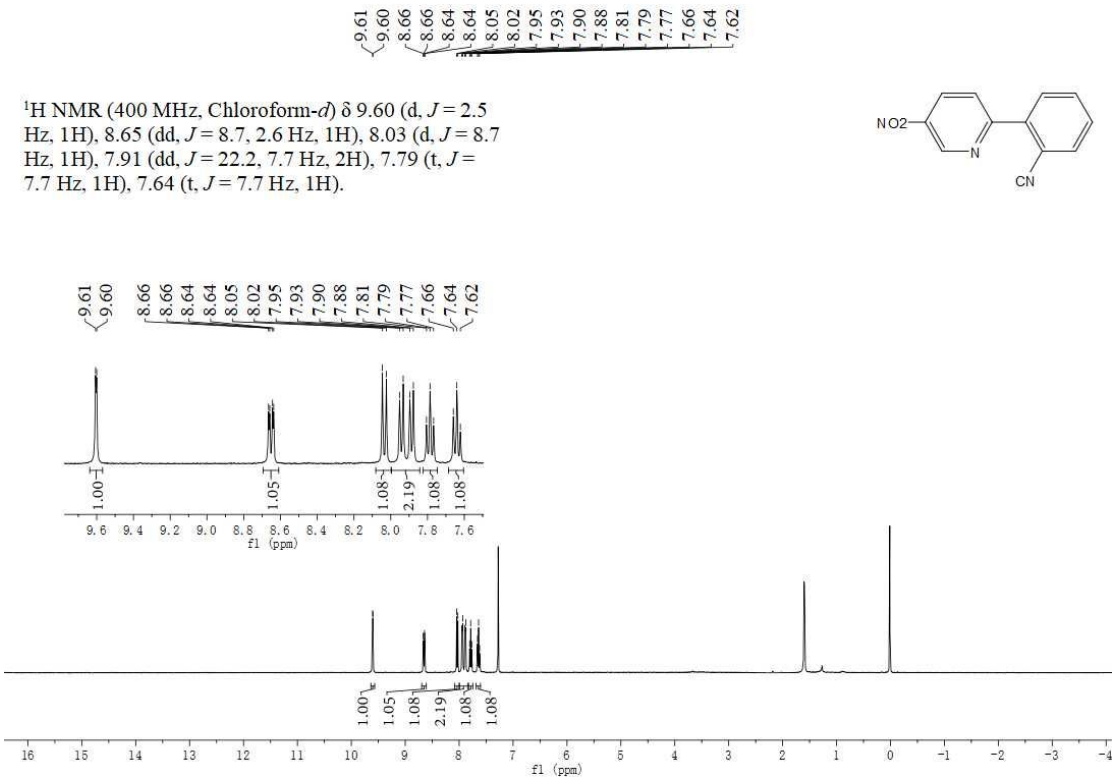


Figure S15. [1]H NMR of 2-(5-Nitropyridin-2-yl)benzonitrile **(2i)**

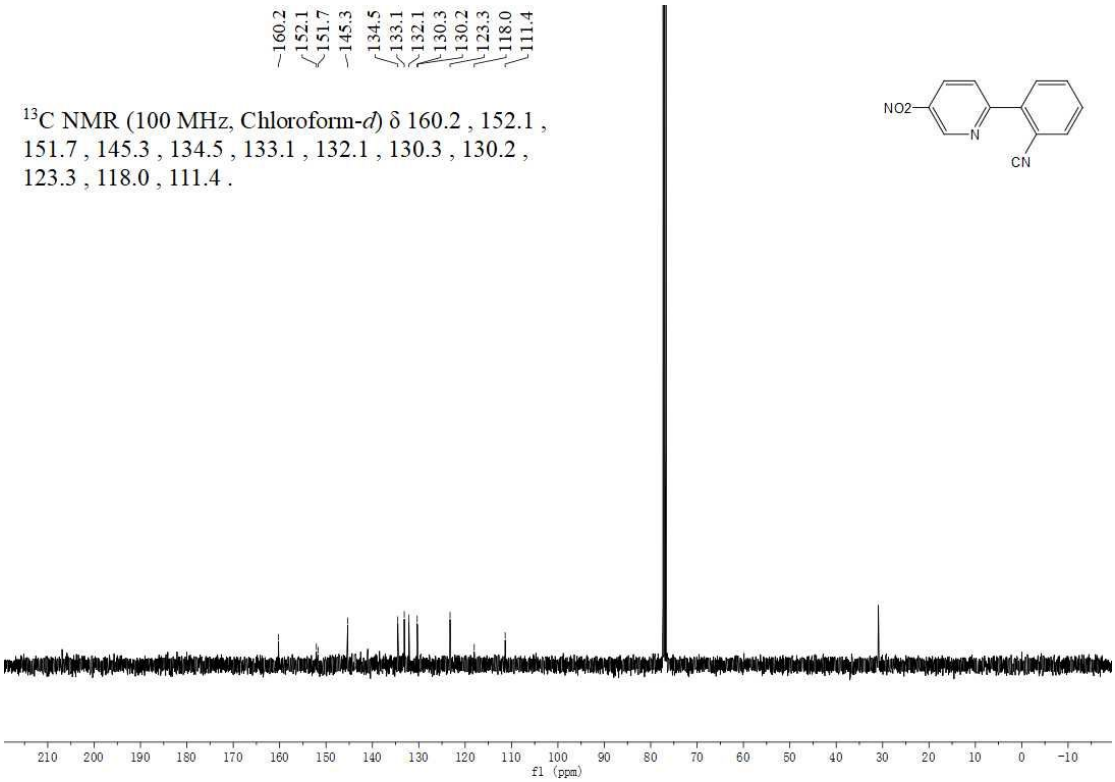


Figure S16. [13]C NMR of 2-(5-Nitropyridin-2-yl)benzonitrile **(2i)**

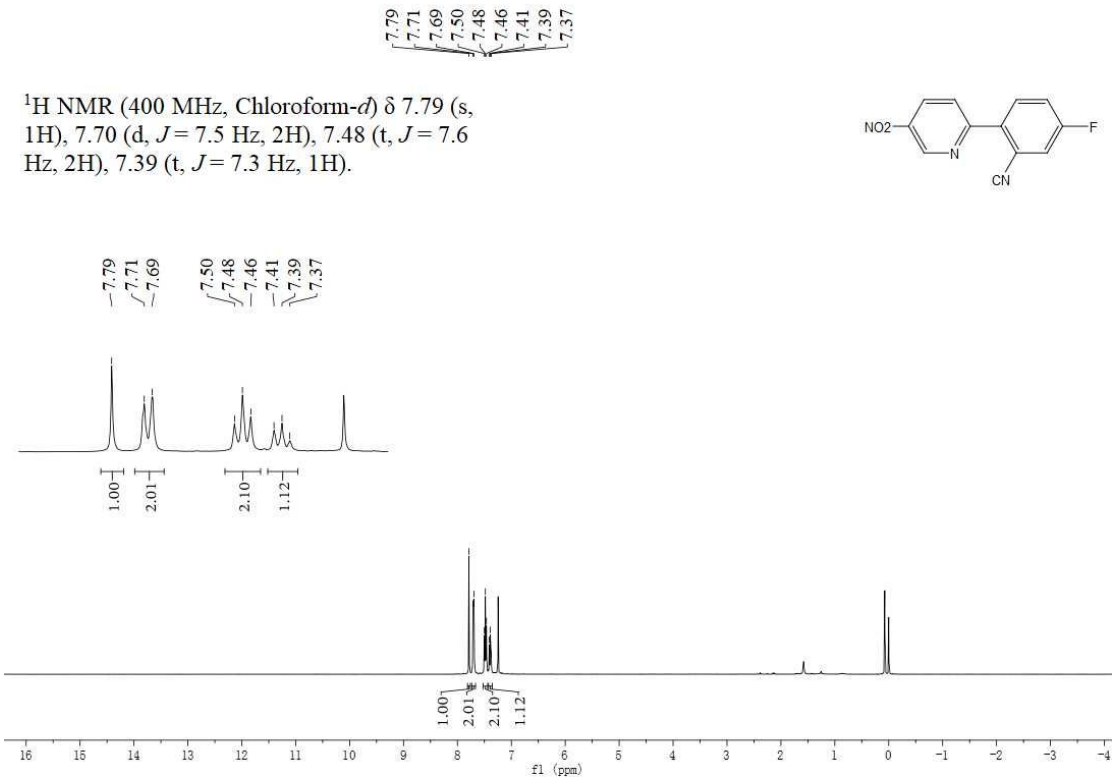


Figure S17. ^{1}H NMR of 5-Fluoro-2-(5-nitropyridin-2-yl)benzonitrile **(2j)**

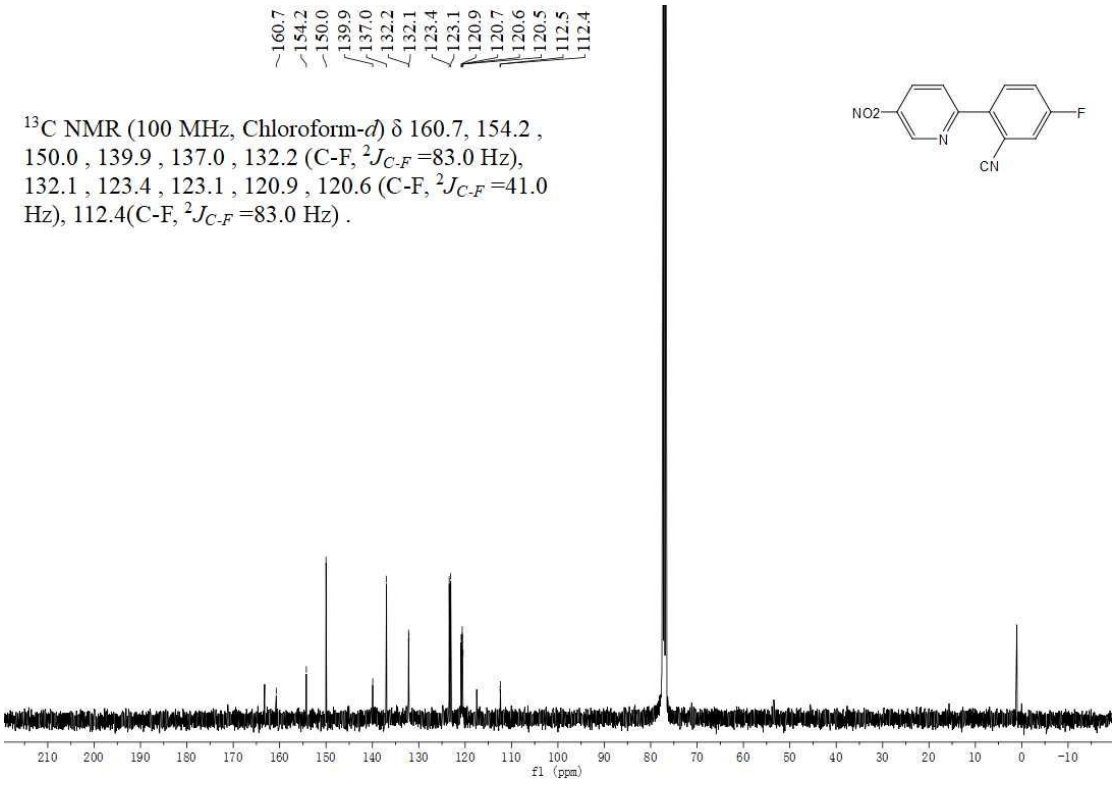
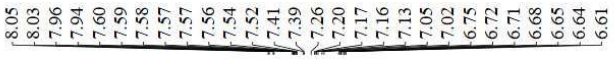
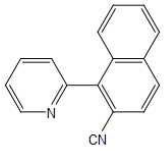


Figure S18. ^{13}C NMR of 5-Fluoro-2-(5-nitropyridin-2-yl)benzonitrile **(2j)**



^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.04 (d, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 7.0 Hz, 1H), 7.63 – 7.50 (m, 4H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.16 (dd, *J* = 15.9, 11.2 Hz, 1H), 7.03 (d, *J* = 15.5 Hz, 1H), 6.77 – 6.59 (m, 1H).



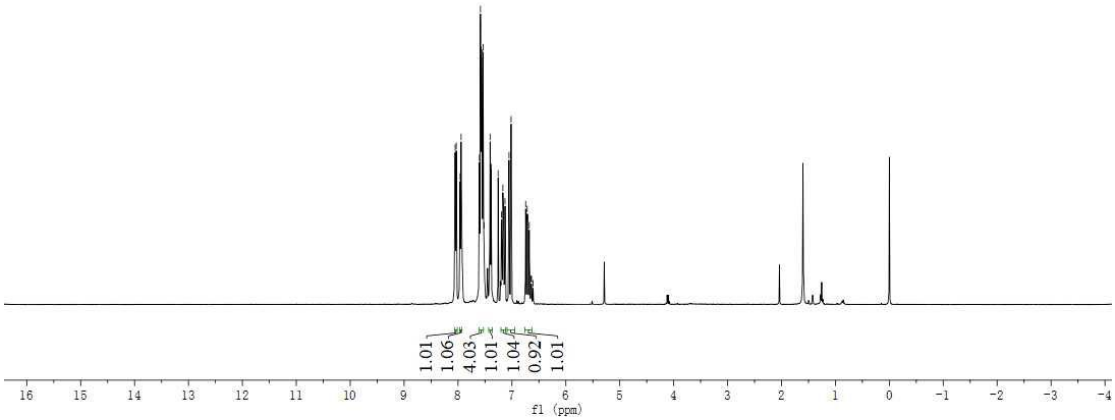
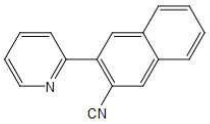


Figure S19. ^{1}H NMR of 1-(Pyridin-2-yl)-2-naphthonitrile **(2k)**



^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.83 (d, *J* = 4.5 Hz, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 7.92 (dt, *J* = 25.4, 7.2 Hz, 4H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.45 – 7.35 (m, 1H).

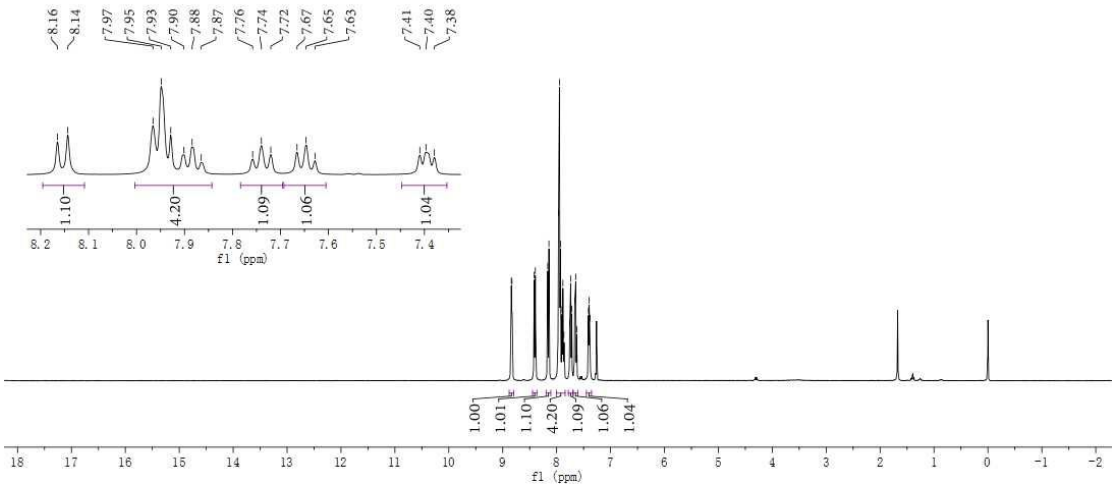
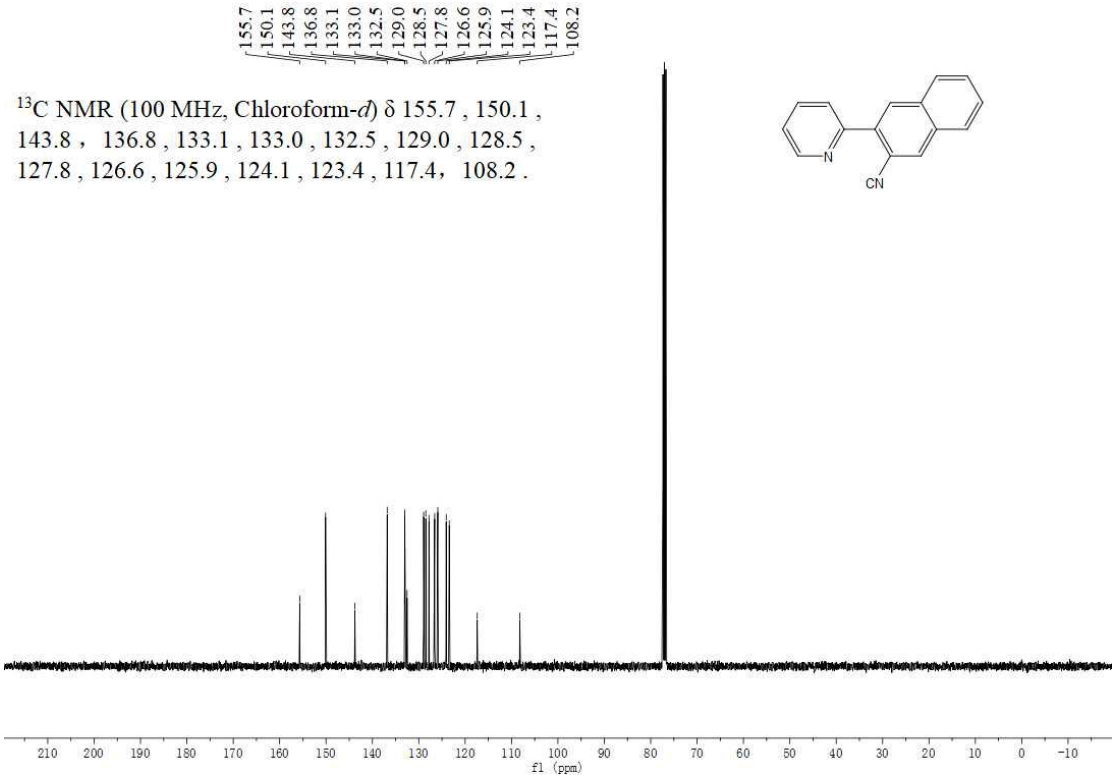
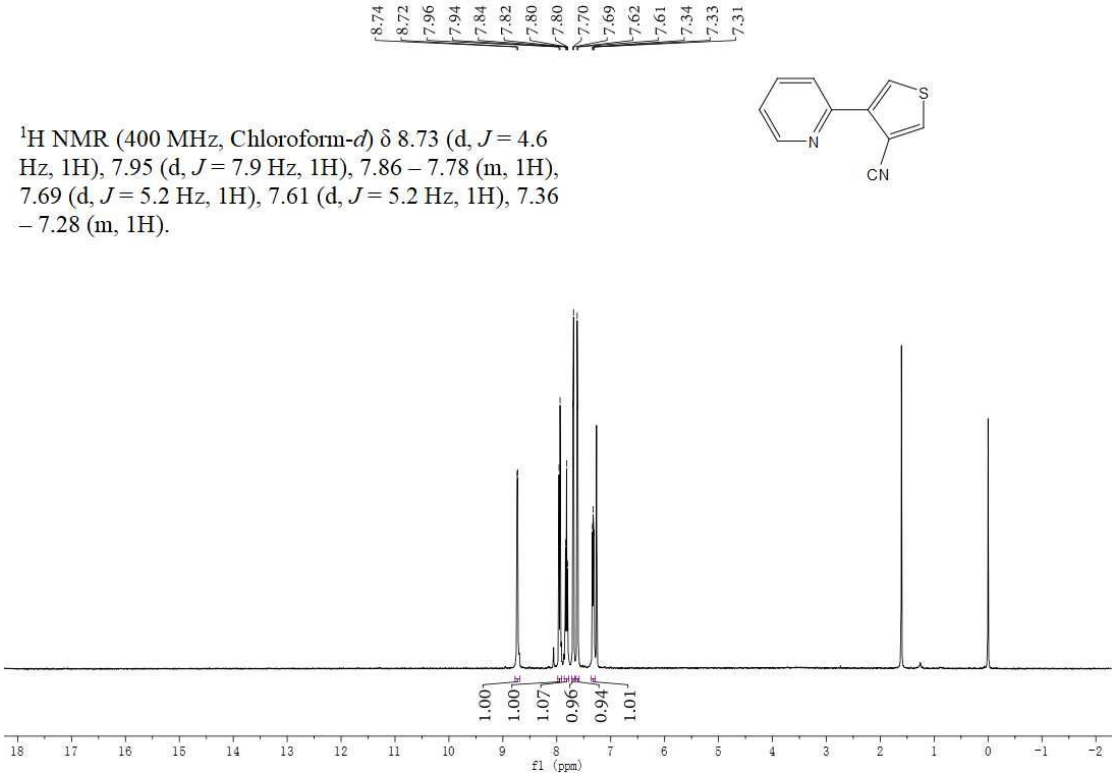


Figure S20. ^{1}H NMR of 3-(Pyridin-2-yl)-2-naphthonitrile **(2l)**



^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.7 , 150.1 , 143.8 ， 136.8 , 133.1 , 133.0 , 132.5 , 129.0 , 128.5 , 127.8 , 126.6 , 125.9 , 124.1 , 123.4 , 117.4， 108.2 .

Figure S21. ^{13}C NMR of 3-(Pyridin-2-yl)-2-naphthonitrile **(2l)**



^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 (d, *J* = 4.6 Hz, 1H), 7.95 (d, *J* = 7.9 Hz, 1H), 7.86 – 7.78 (m, 1H), 7.69 (d, *J* = 5.2 Hz, 1H), 7.61 (d, *J* = 5.2 Hz, 1H), 7.36 – 7.28 (m, 1H).

Figure S22. ^{1}H NMR of 4-(Pyridin-2-yl)thiophene-3-carbonitrile **(2m)**

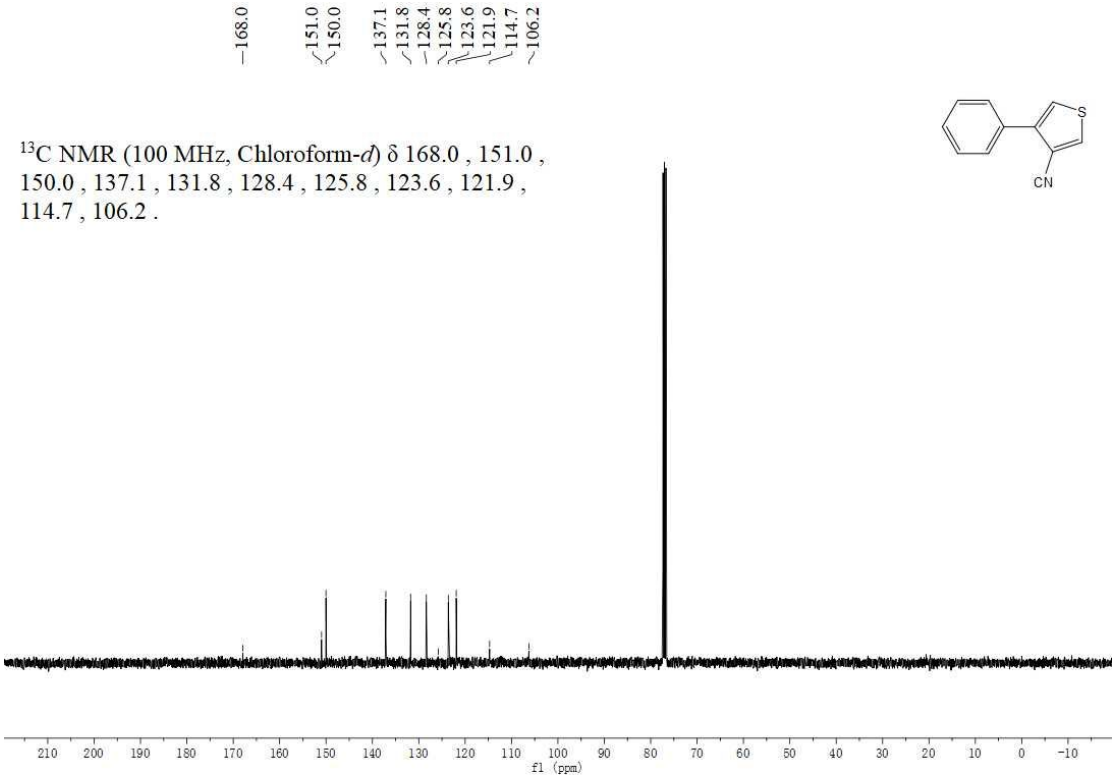


Figure S23. ^{13}C NMR of 4-(Pyridin-2-yl)thiophene-3-carbonitrile **(2m)**

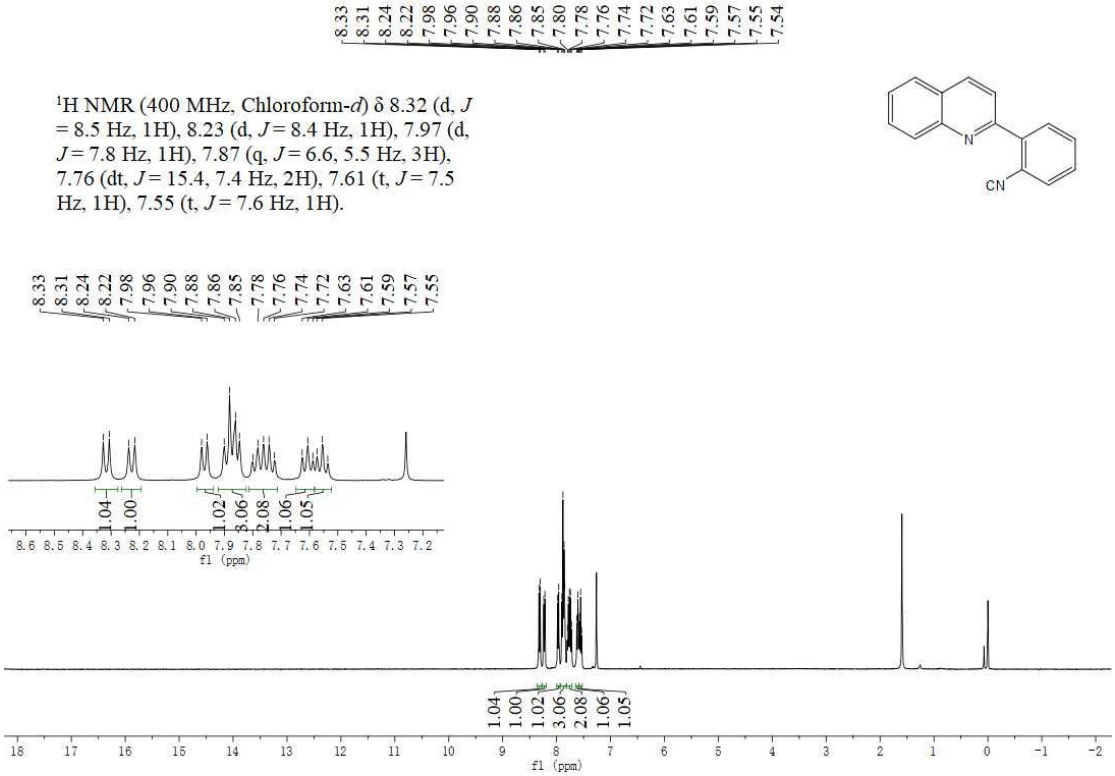


Figure S24. ^{1}H NMR of 2-(Quinolin-2-yl)benzonitrile **(2n)**

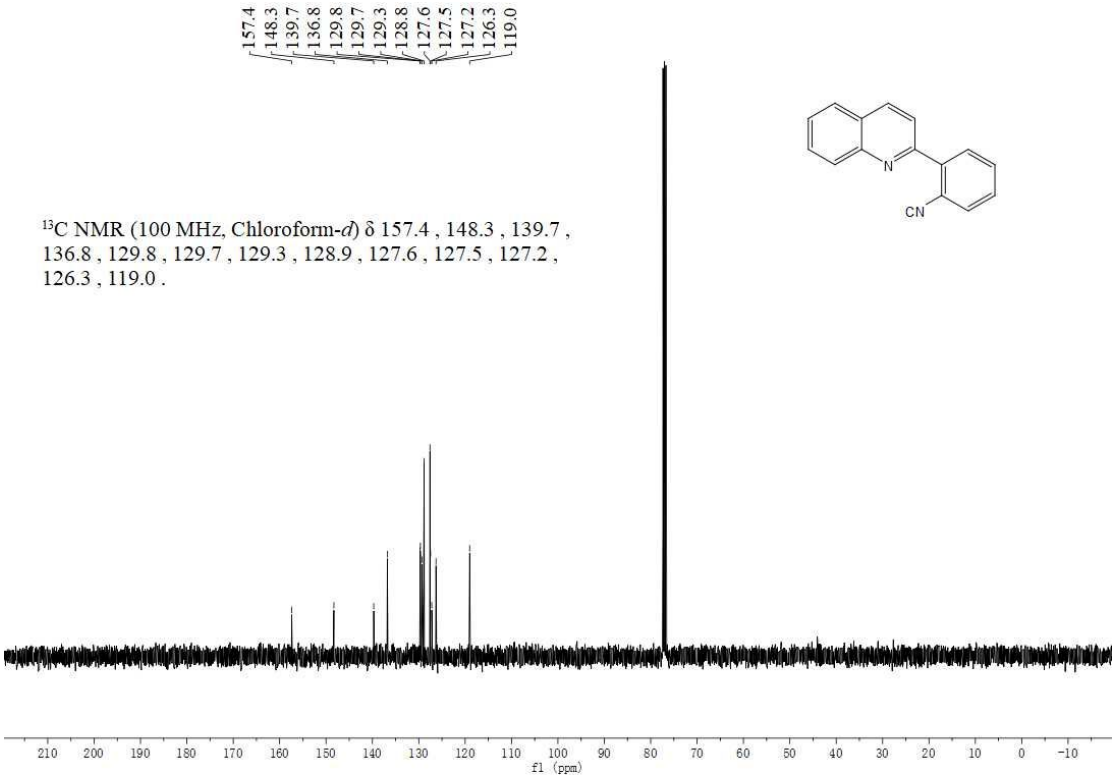


Figure S25. ^{13}C NMR of 2-(Quinolin-2-yl)benzonitrile **(2n)**

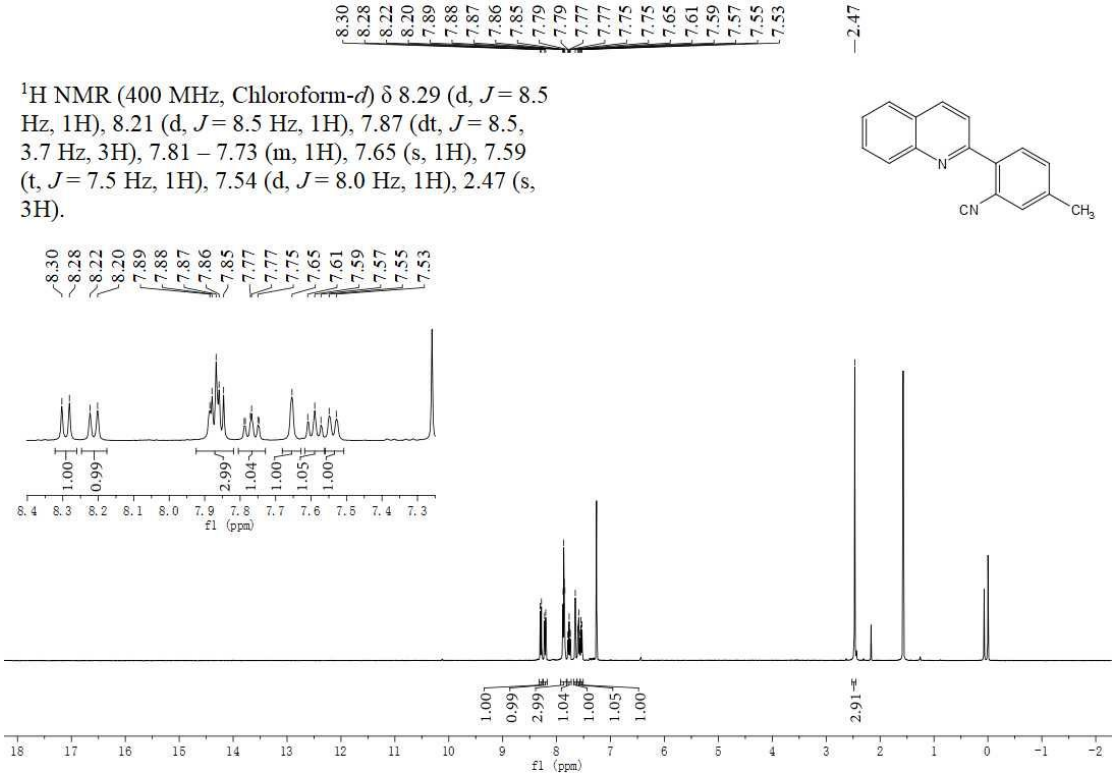
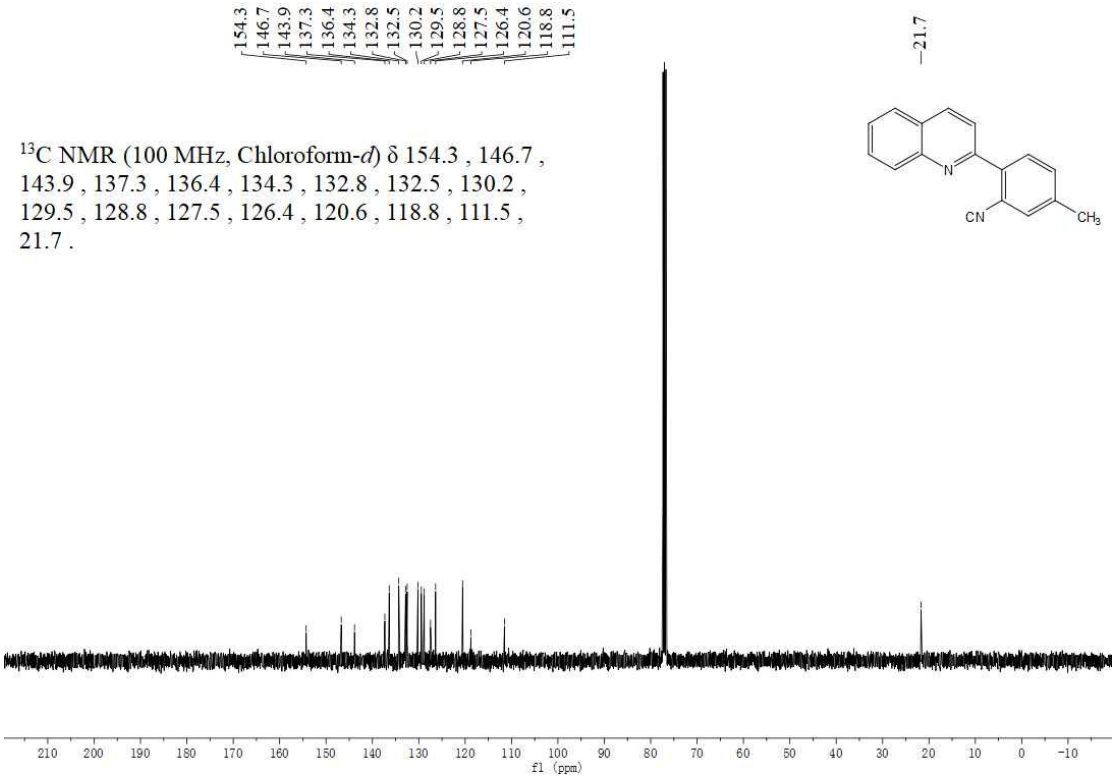
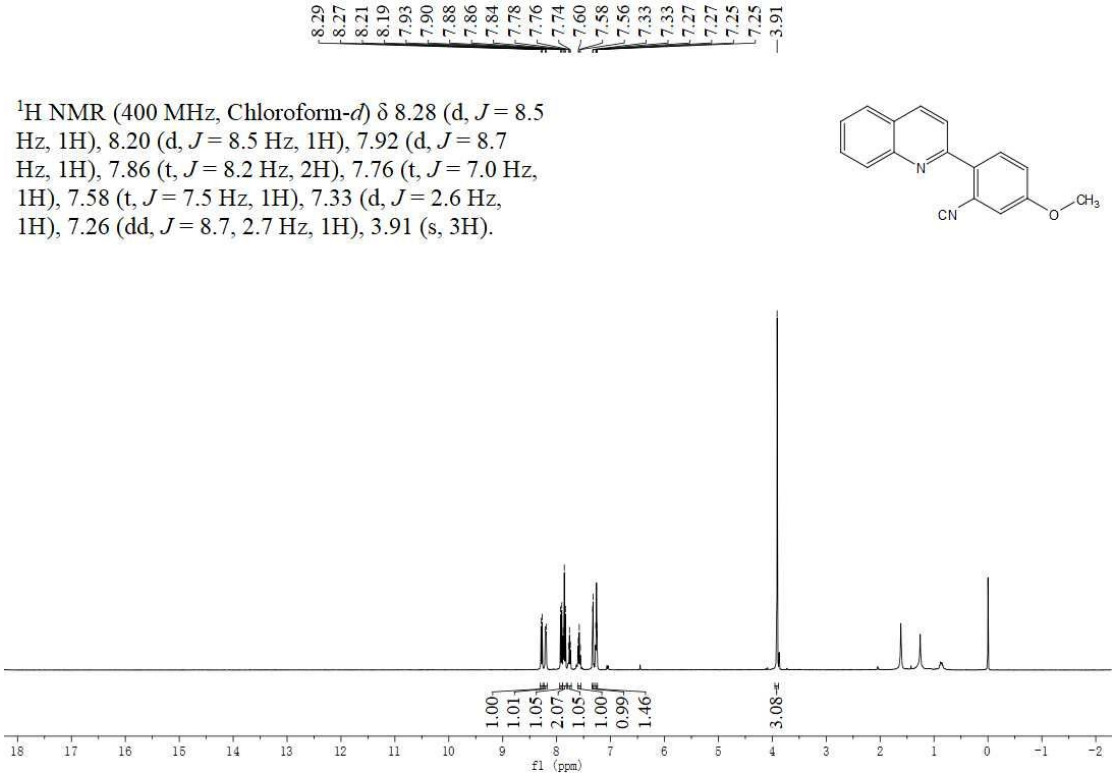


Figure S26. ^{1}H NMR of 5-Methyl-2-(quinolin-2-yl)benzonitrile **(2o)**



^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.3 , 146.7 , 143.9 , 137.3 , 136.4 , 134.3 , 132.8 , 132.5 , 130.2 , 129.5 , 128.8 , 127.5 , 126.4 , 120.6 , 118.8 , 111.5 , 21.7 .

Figure S27. ^{13}C NMR of 5-Methyl-2-(quinolin-2-yl)benzonitrile **(2o)**



^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.28 (d, *J* = 8.5 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 8.7 Hz, 1H), 7.86 (t, *J* = 8.2 Hz, 2H), 7.76 (t, *J* = 7.0 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.33 (d, *J* = 2.6 Hz, 1H), 7.26 (dd, *J* = 8.7, 2.7 Hz, 1H), 3.91 (s, 3H).

Figure S28. ^{1}H NMR of 5-Methoxy-2-(quinolin-2-yl)benzonitrile **(2p)**

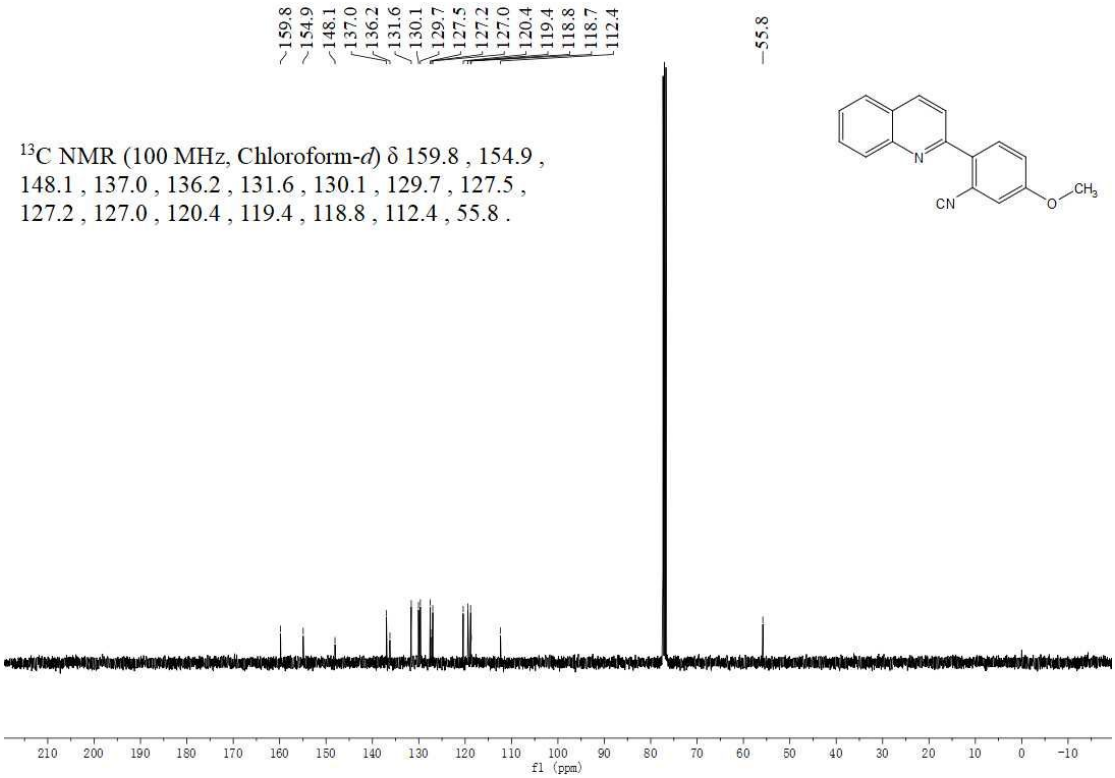


Figure S29. ^{13}C NMR of 5-Methoxy-2-(quinolin-2-yl)benzonitrile **(2p)**

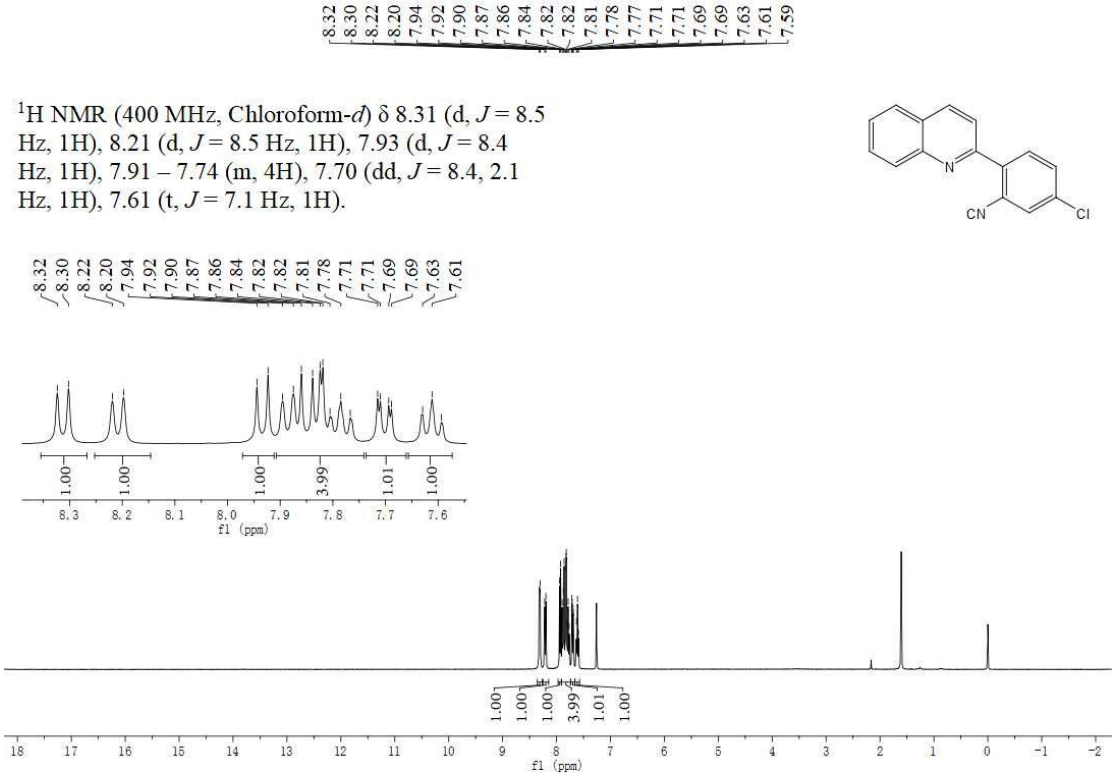


Figure S30. ^{1}H NMR of 5-Chloro-2-(quinolin-2-yl)benzonitrile **(2q)**

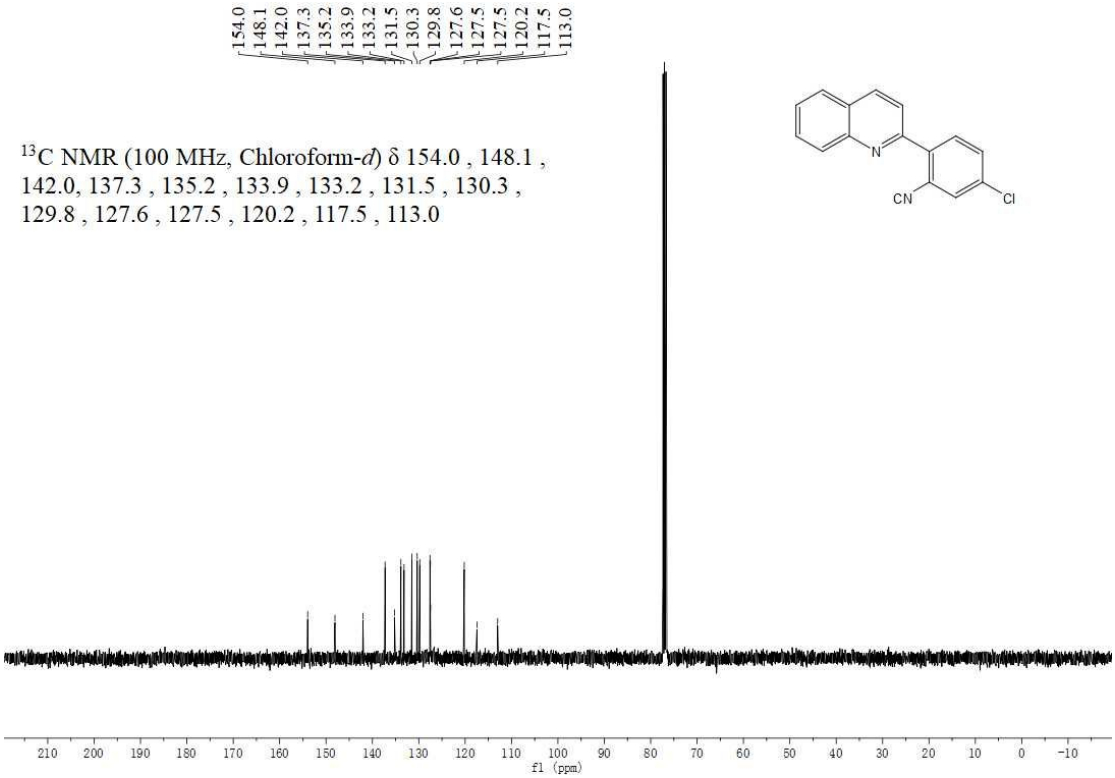


Figure S31. ^{13}C NMR of 5-Chloro-2-(quinolin-2-yl)benzonitrile **(2q)**

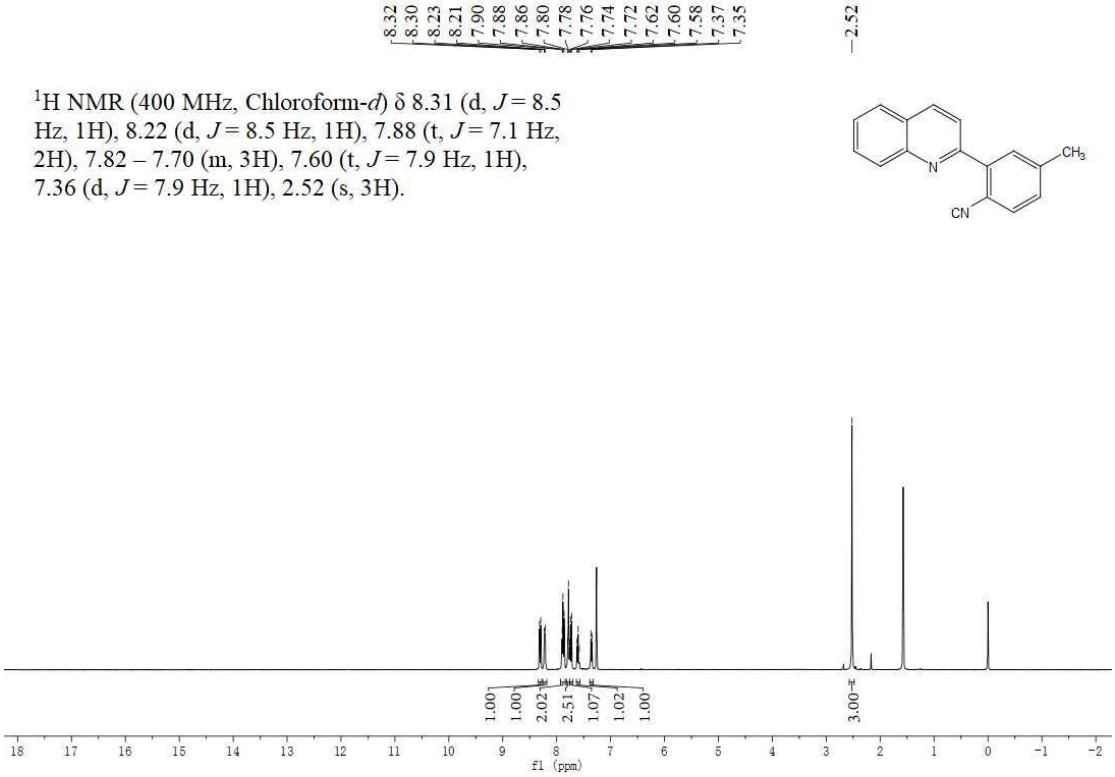


Figure S32. ^{1}H NMR of 4-Methyl-2-(quinolin-2-yl)benzonitrile **(2r)**

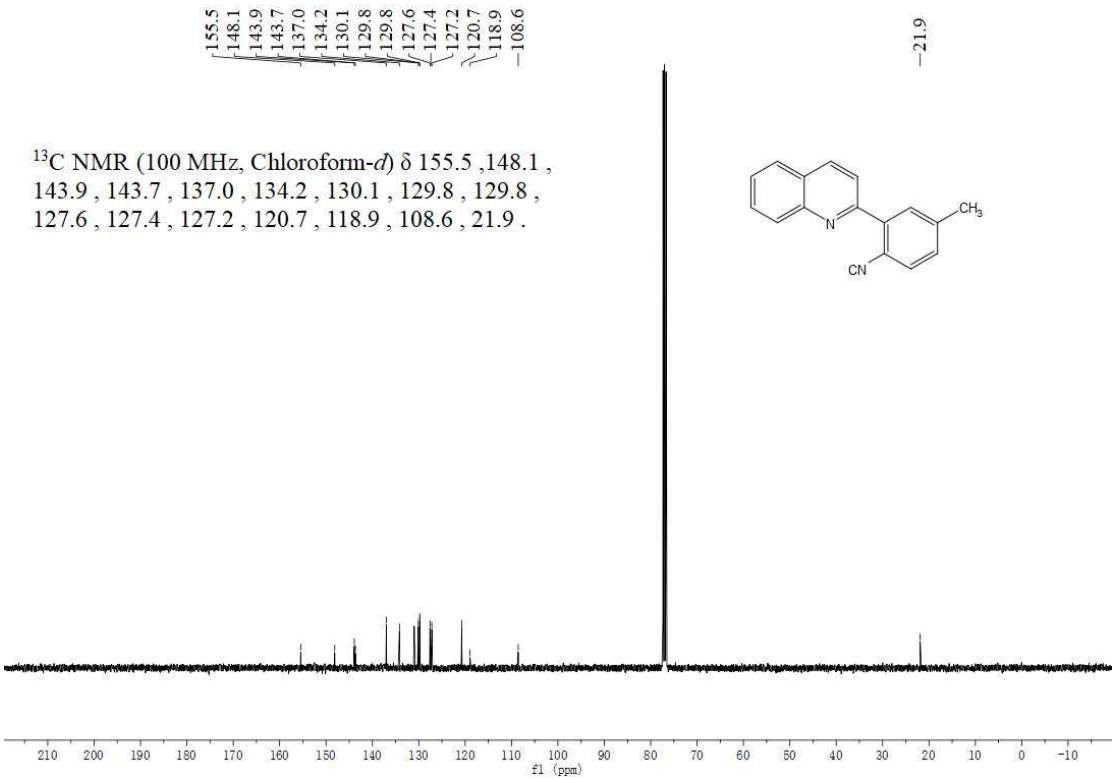


Figure S33. ^{13}C NMR of 4-Methyl-2-(quinolin-2-yl)benzonitrile **(2r)**

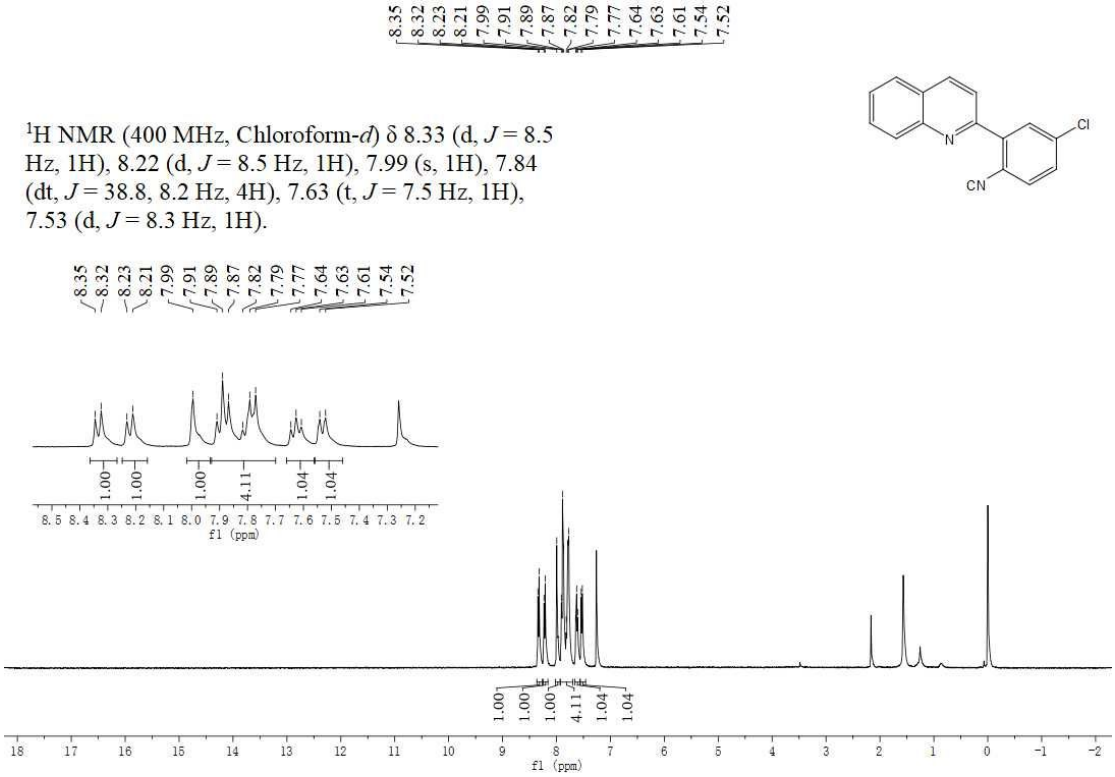


Figure S34. ^{1}H NMR of 4-Chloro-2-(quinolin-2-yl)benzonitrile **(2s)**

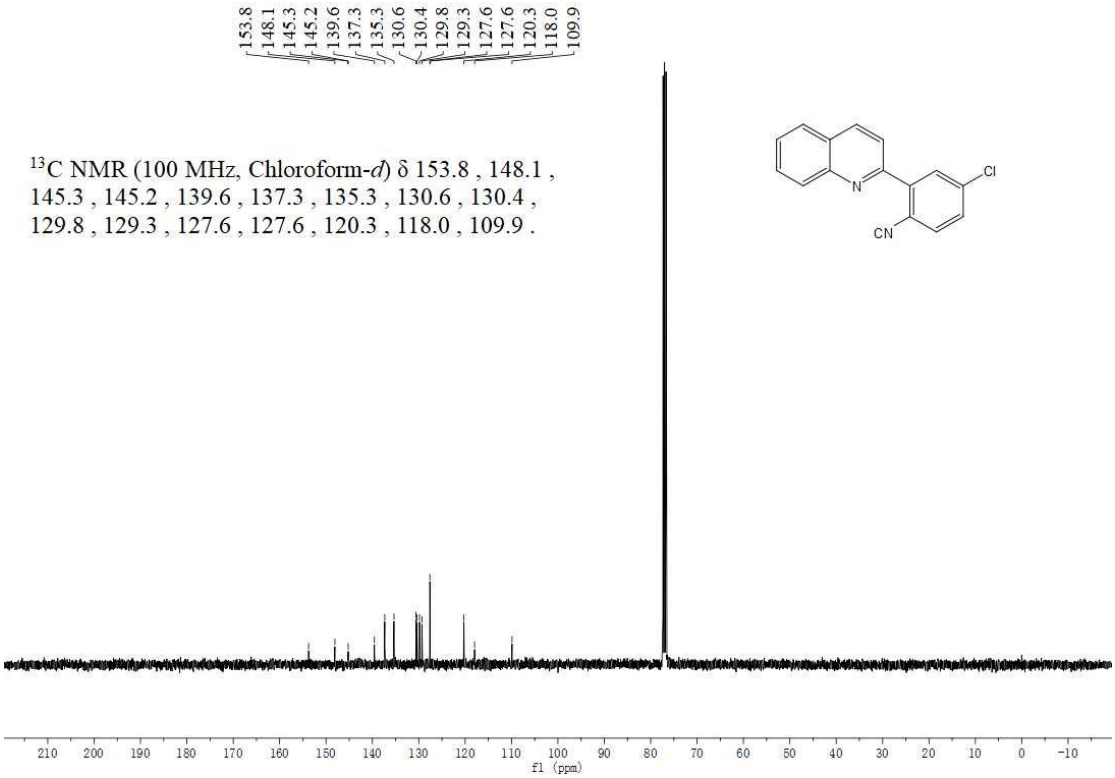


Figure S35. ^{13}C NMR of 4-Chloro-2-(quinolin-2-yl)benzonitrile **(2s)**

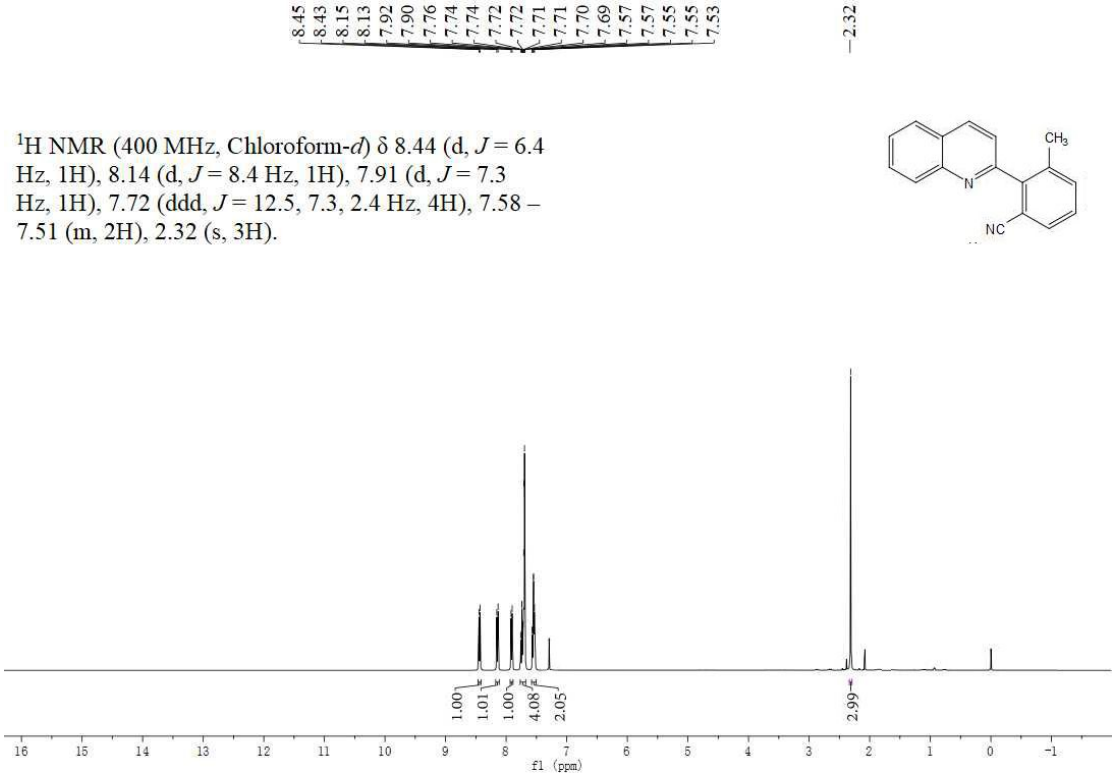


Figure S36. ^{1}H NMR of 3-Methyl-2-(quinolin-2-yl)benzonitrile **(2t)**

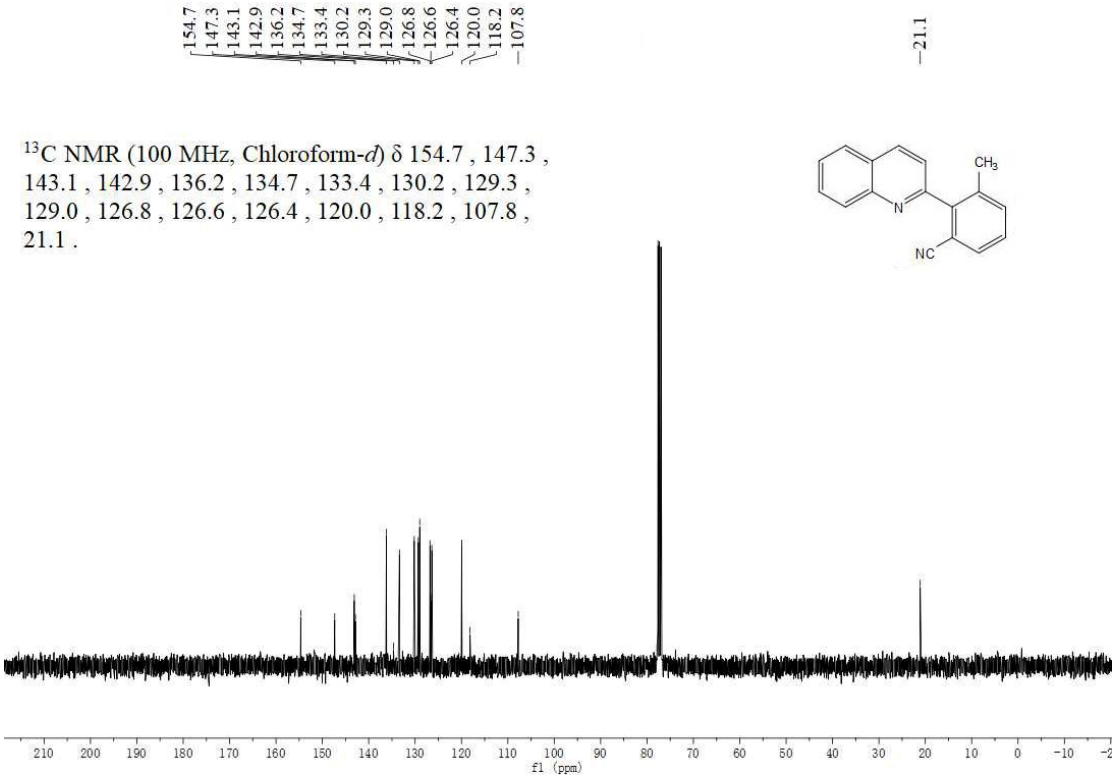


Figure S37. ^{13}C NMR of 3-Methyl-2-(quinolin-2-yl)benzonitrile **(2t)**

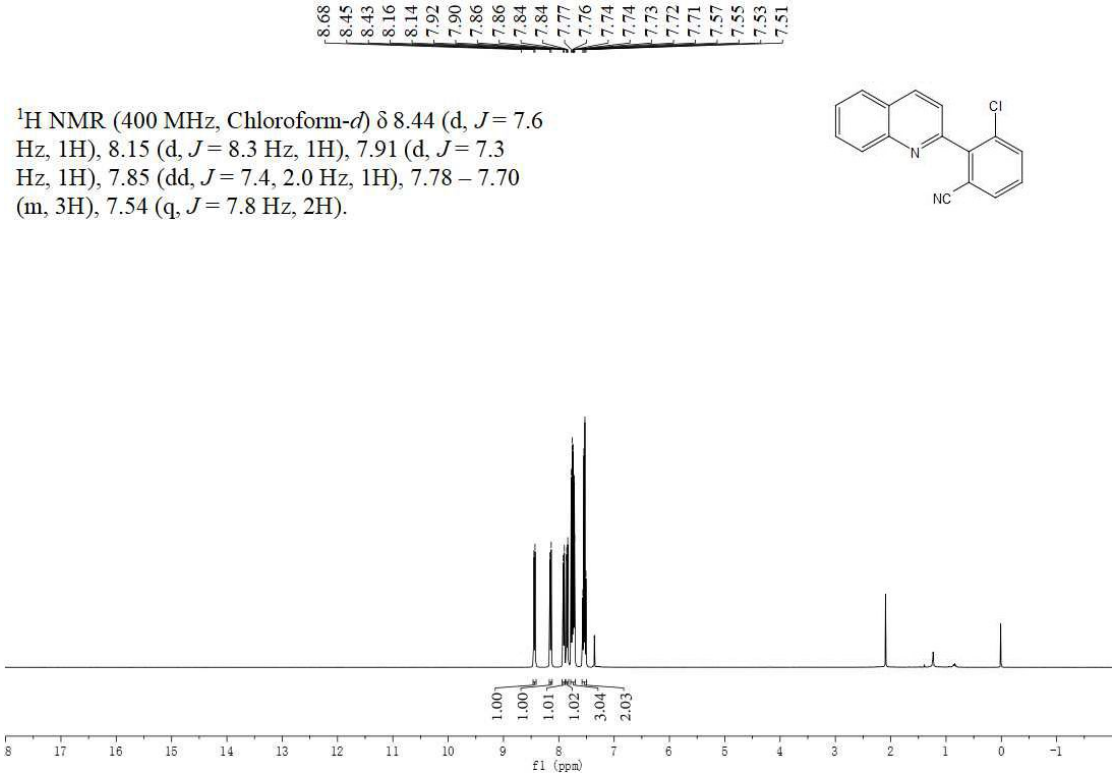


Figure S38. ^{1}H NMR of 3-Chloro-2-(quinolin-2-yl)benzonitrile **(2u)**

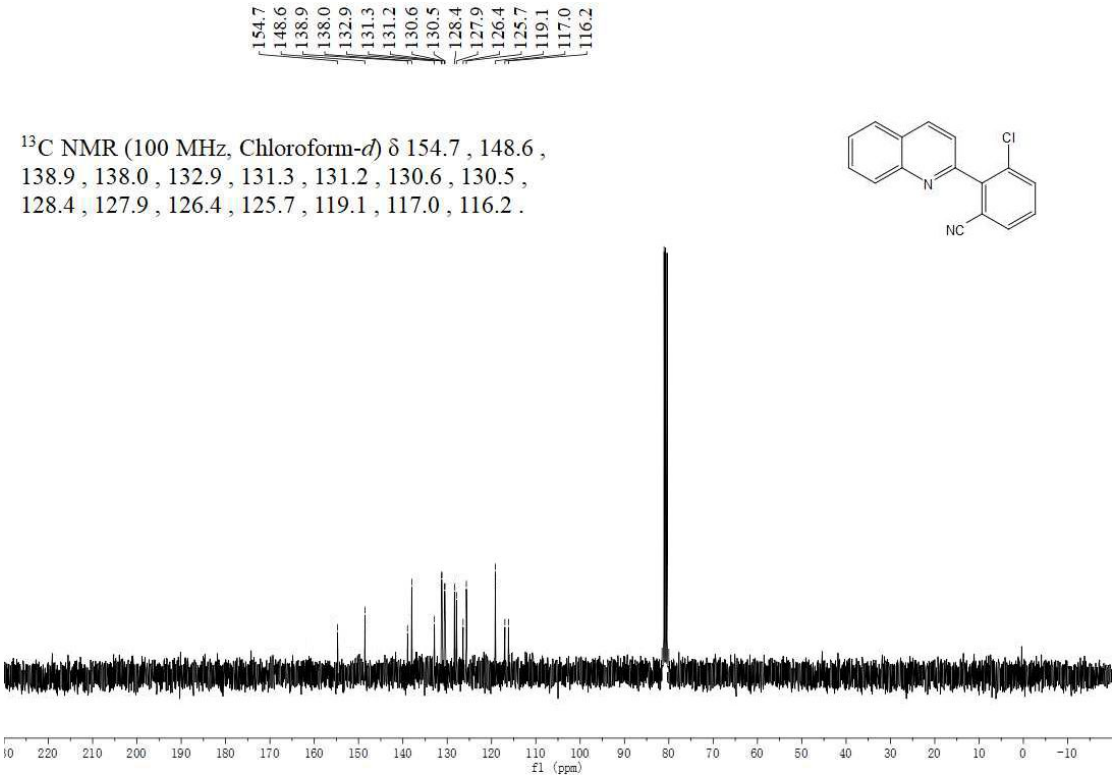


Figure S39. ^{13}C NMR of 3-Chloro-2-(quinolin-2-yl)benzonitrile **(2u)**

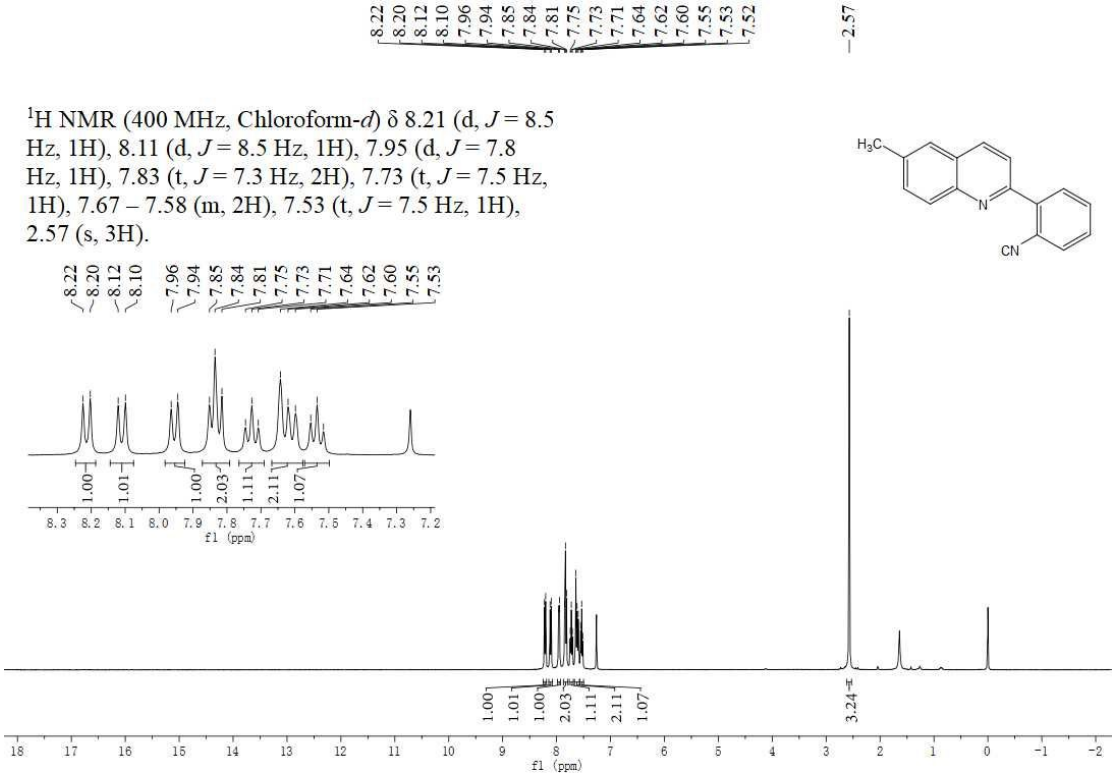


Figure S40. ^{1}H NMR of 2-(6-Methylquinolin-2-yl)benzonitrile **(2v)**

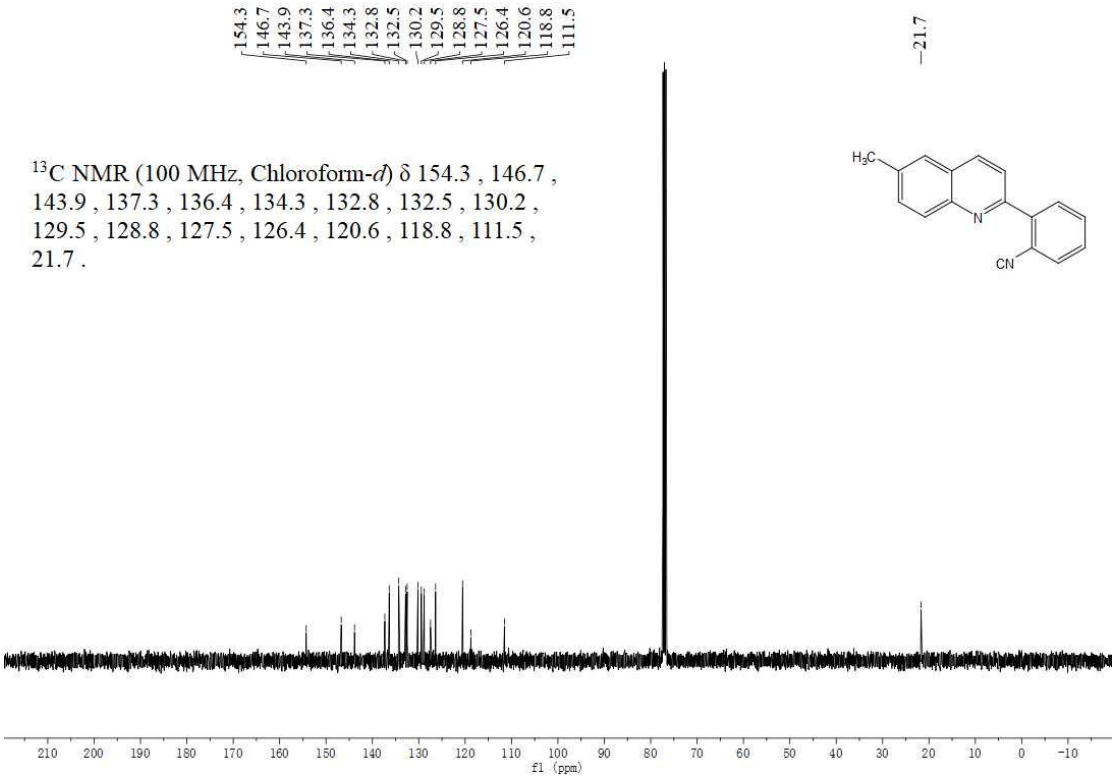


Figure S41. ^{13}C NMR of 2-(6-Methylquinolin-2-yl)benzonitrile **(2v)**

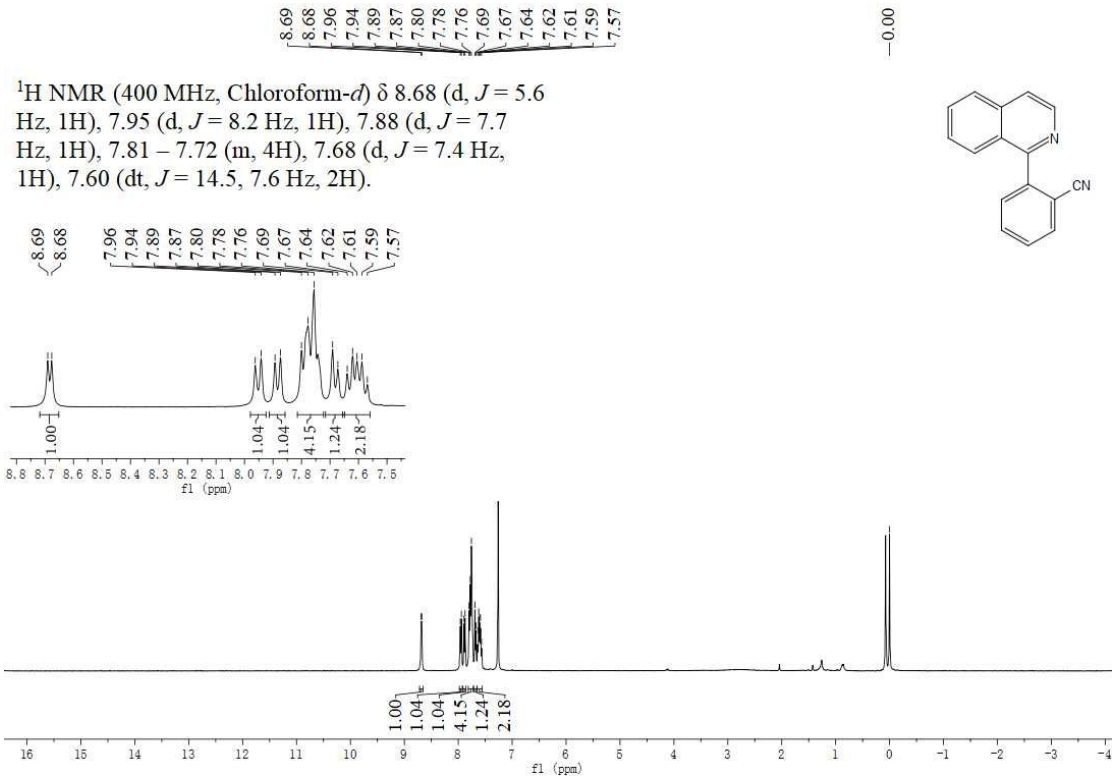


Figure S42. ^{1}H NMR of 2-(Isoquinolin-1-yl)benzonitrile **(2w)**

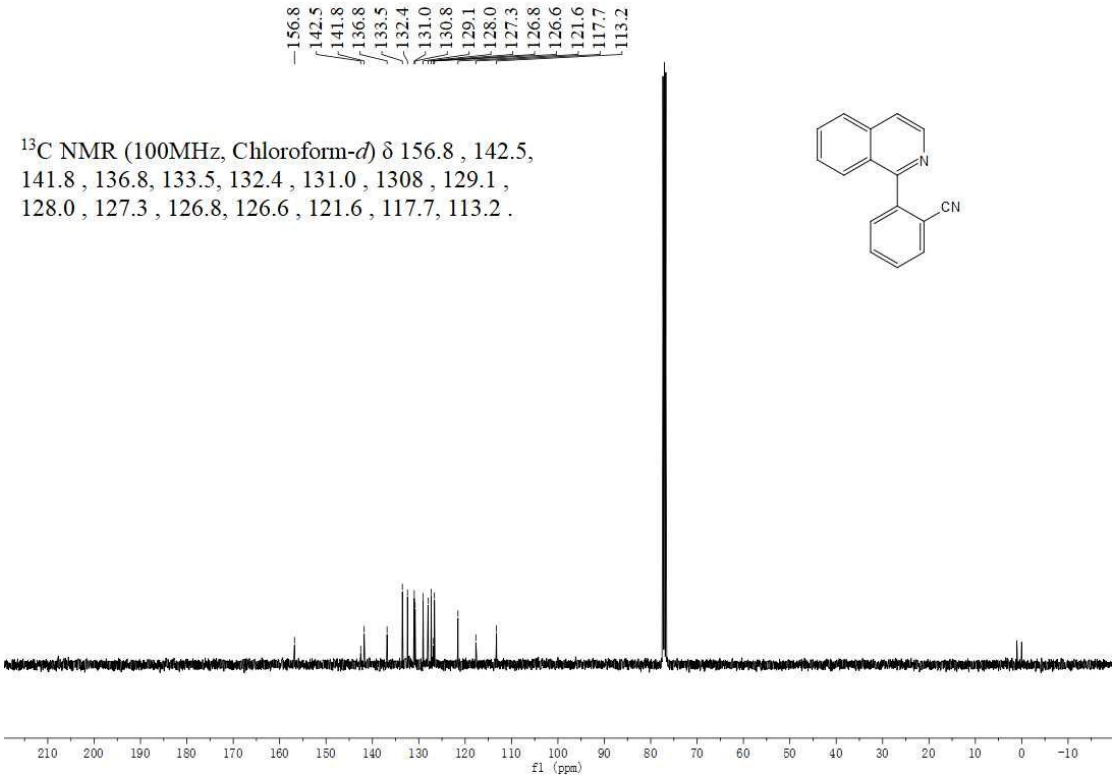


Figure S43. ^{13}C NMR of 2-(Isoquinolin-1-yl)benzonitrile **(2w)**

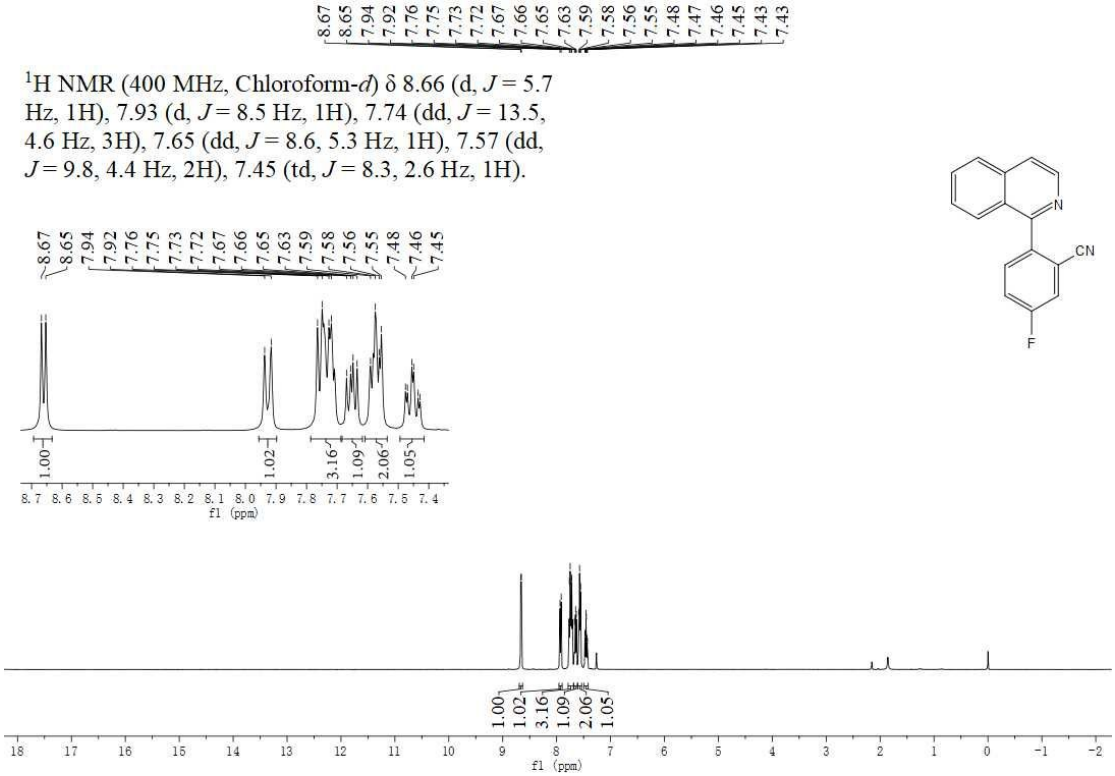


Figure S44. ^{1}H NMR of 5-Fluoro-2-(isoquinolin-1-yl)benzonitrile **(2x)**

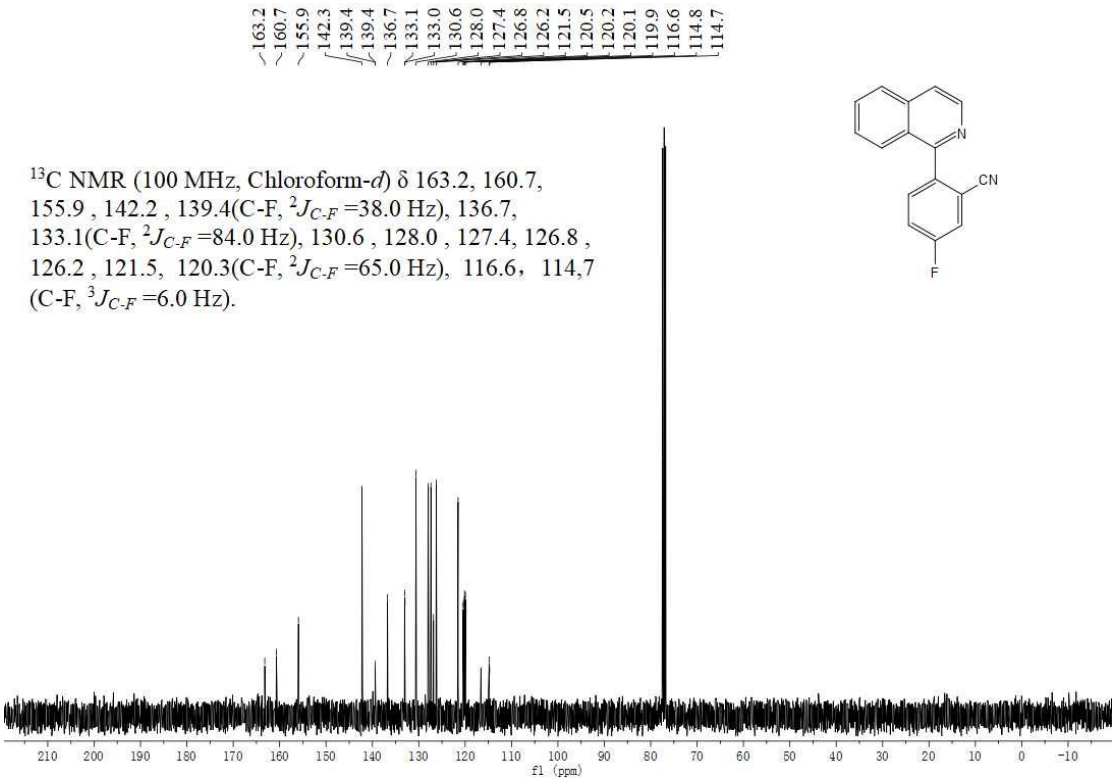


Figure S45. ^{13}C NMR of 5-Fluoro-2-(isoquinolin-1-yl)benzonitrile **(2x)**

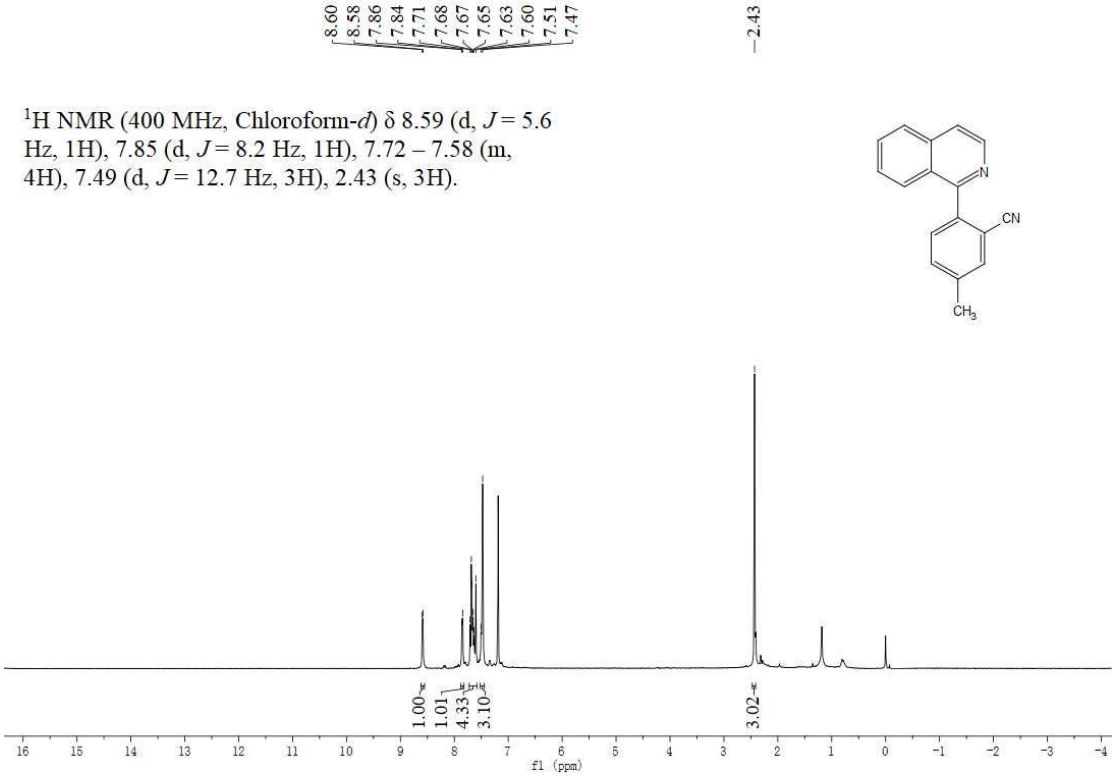


Figure S46. ^{1}H NMR of 5-Methyl -2-(isoquinolin-1-yl)benzonitrile **(2y)**

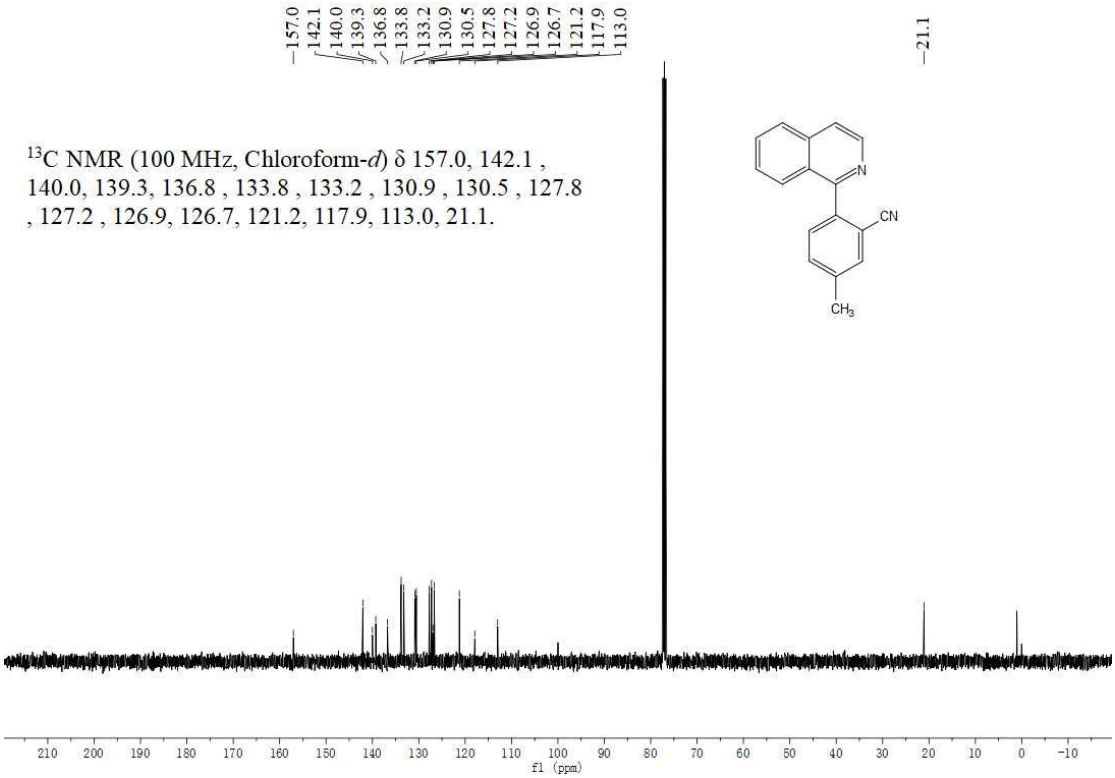


Figure S47. ^{13}C NMR of 5-Methyl -2-(isoquinolin-1-yl)benzonitrile **(2y)**

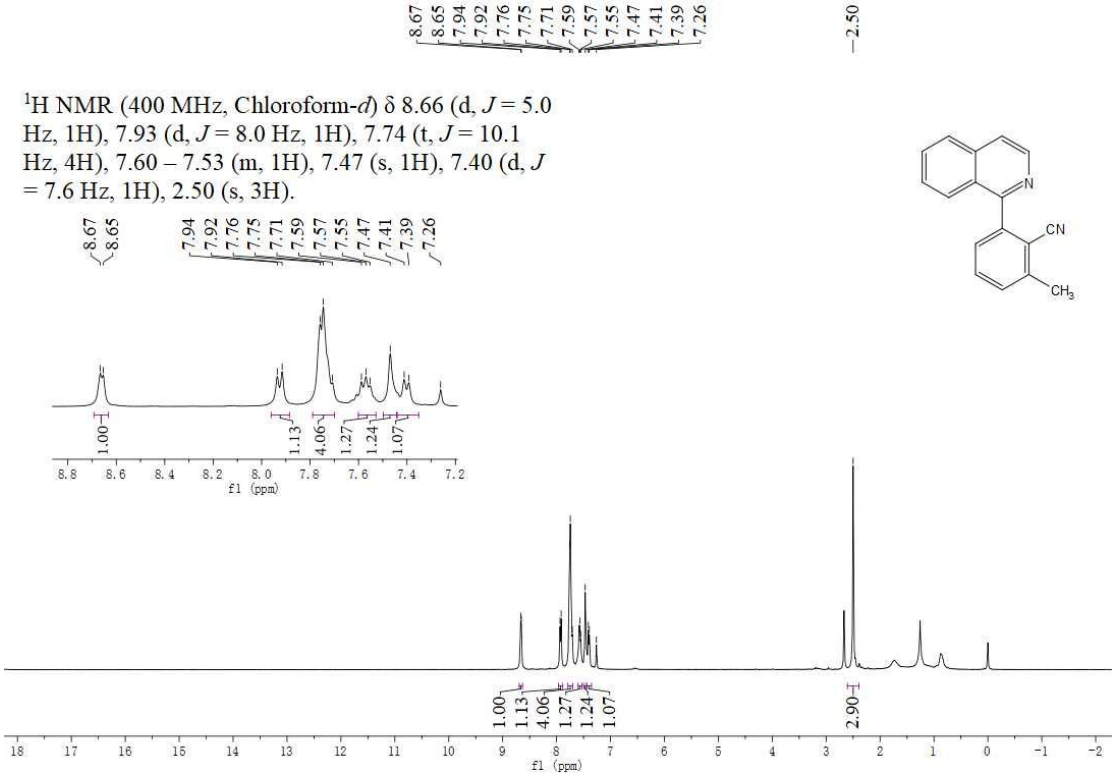


Figure S48. ^{1}H NMR of 2-(Isoquinolin-1-yl)-6-methylbenzonitrile **(2z)**

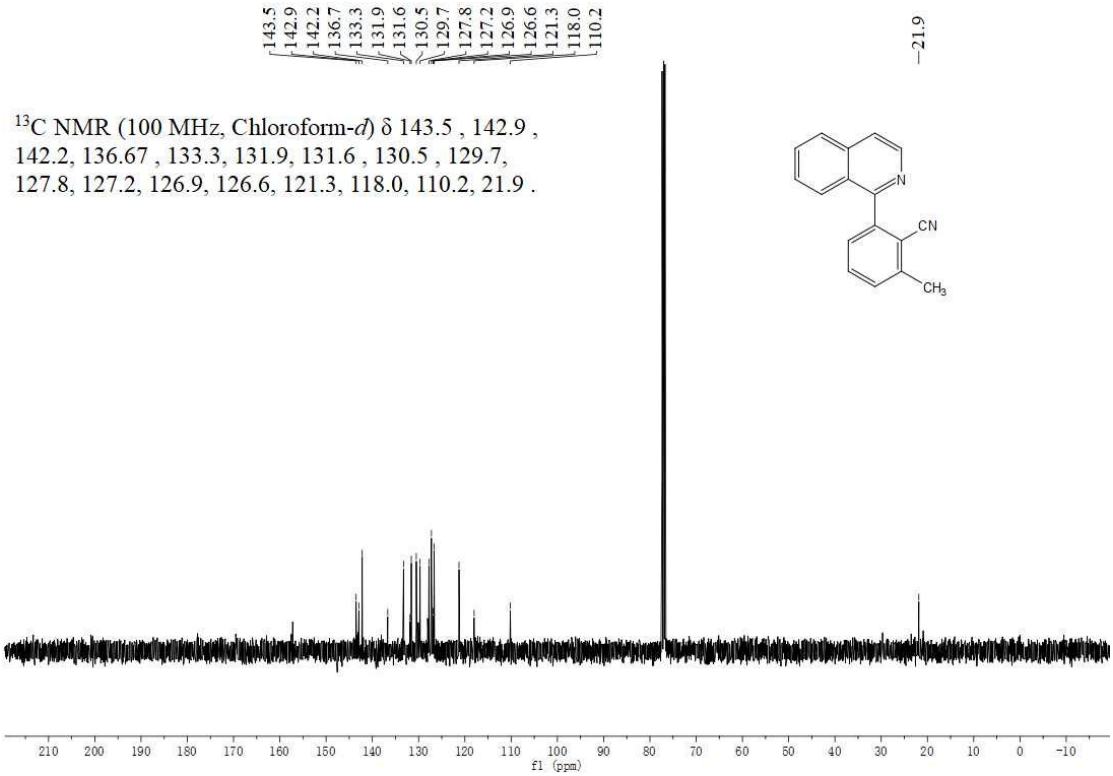


Figure S49. ^{13}C NMR of 2-(Isoquinolin-1-yl)-6-methylbenzonitrile **(2z)**

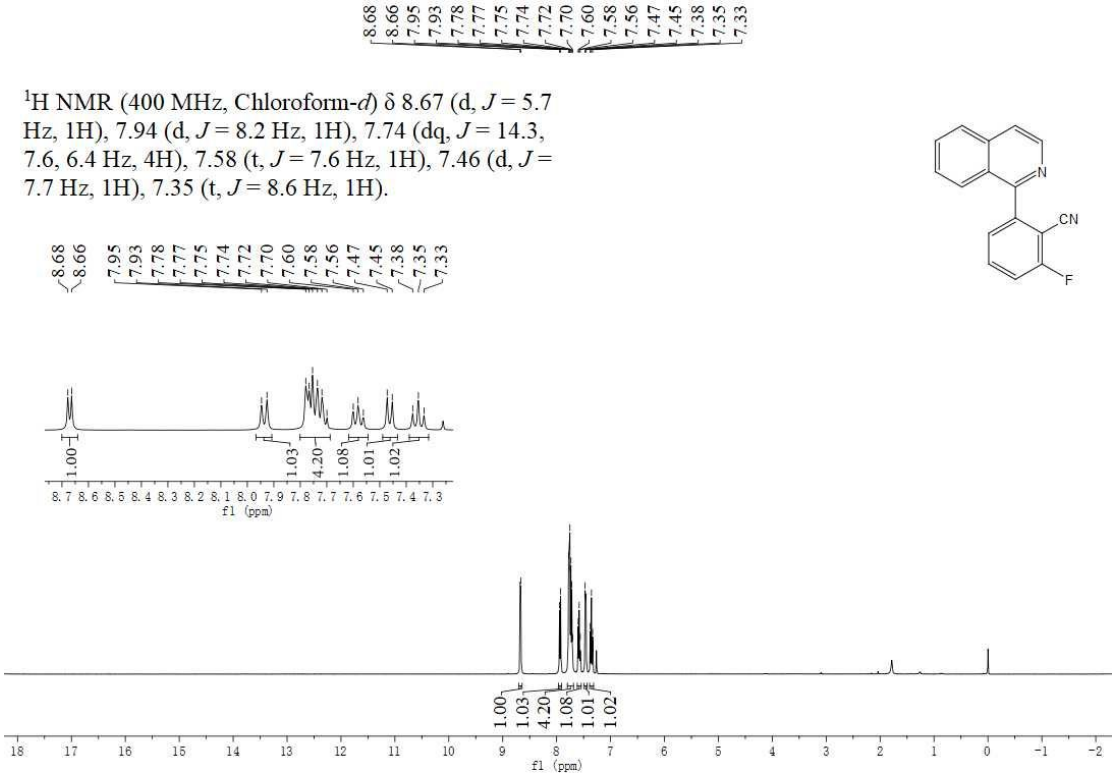


Figure S50. ^{1}H NMR of 2-Fluoro-6-(isoquinolin-1-yl)benzonitrile **(2aa)**

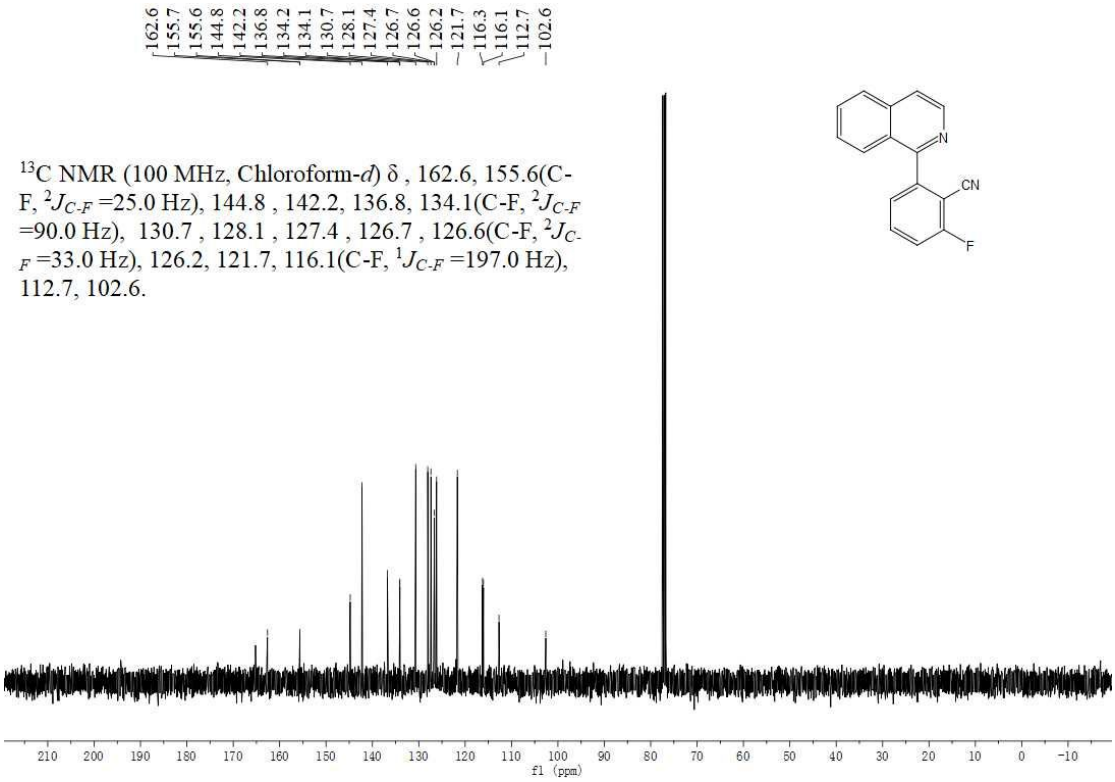


Figure S51. ^{13}C NMR of 2-Fluoro-6-(isoquinolin-1-yl)benzonitrile **(2aa)**

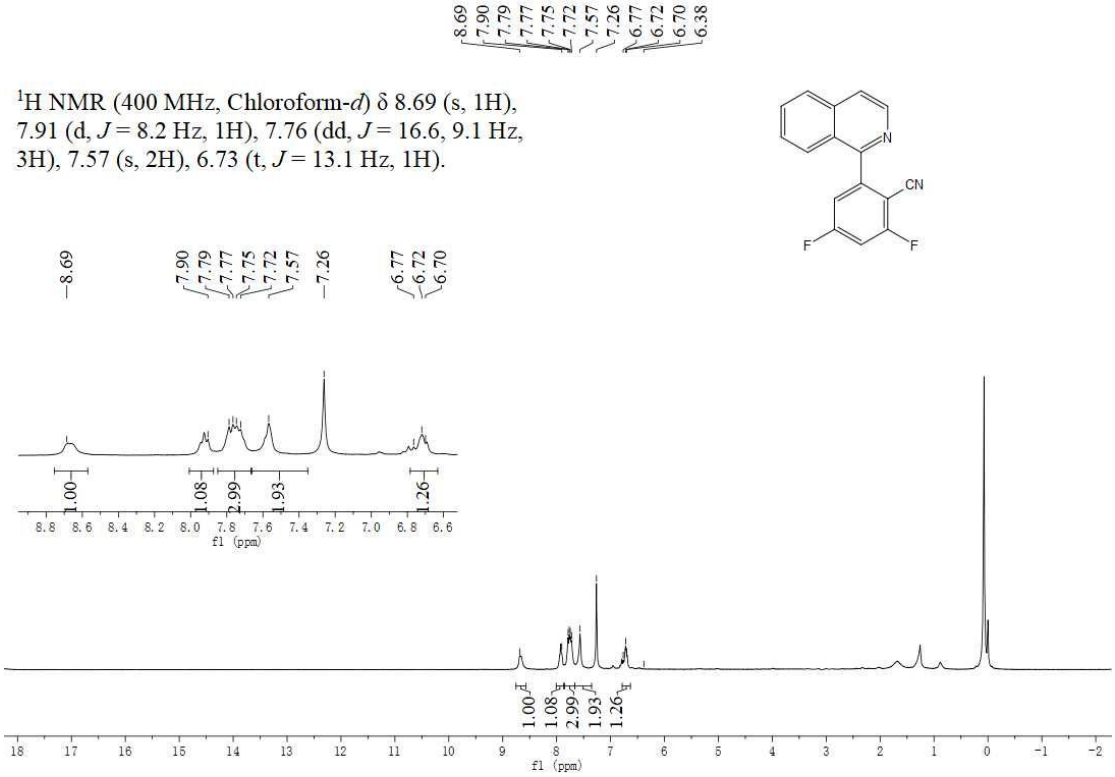


Figure S52. ^{1}H NMR of 2,4-Difluoro-6-(isoquinolin-1-yl)benzonitrile **(2ab)**

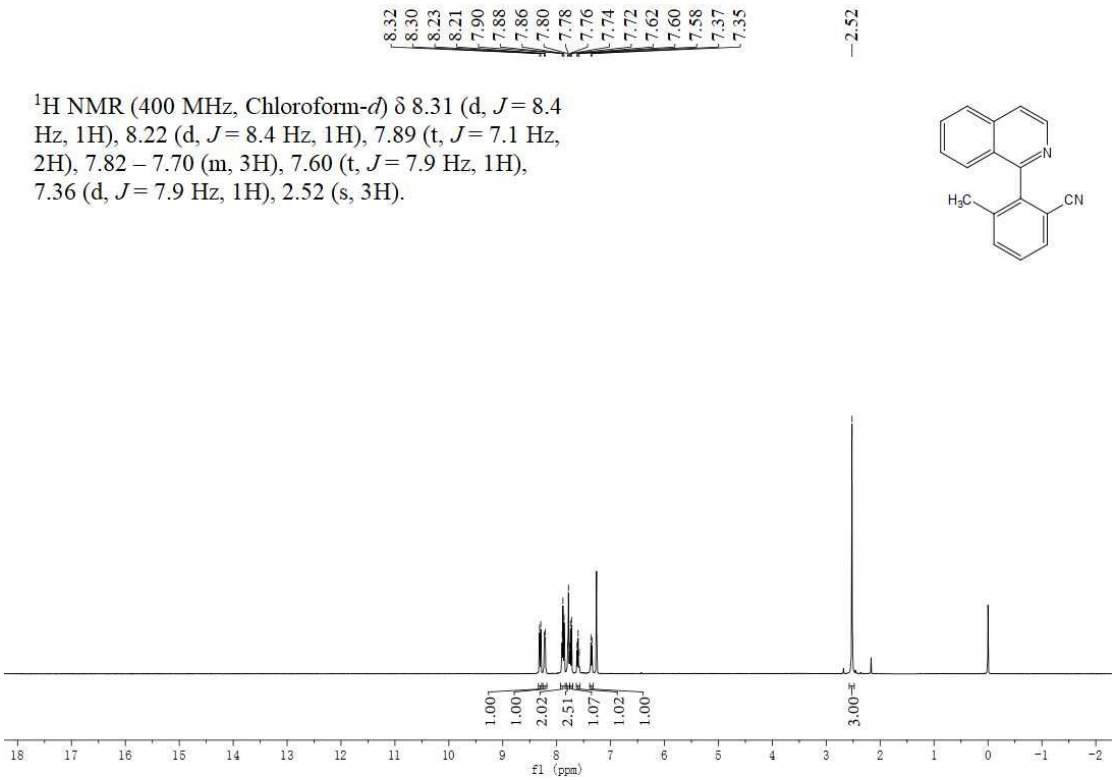


Figure S53. ^{13}C NMR of 2-(Isoquinolin-1-yl)-3-methylbenzonitrile **(2ac)**

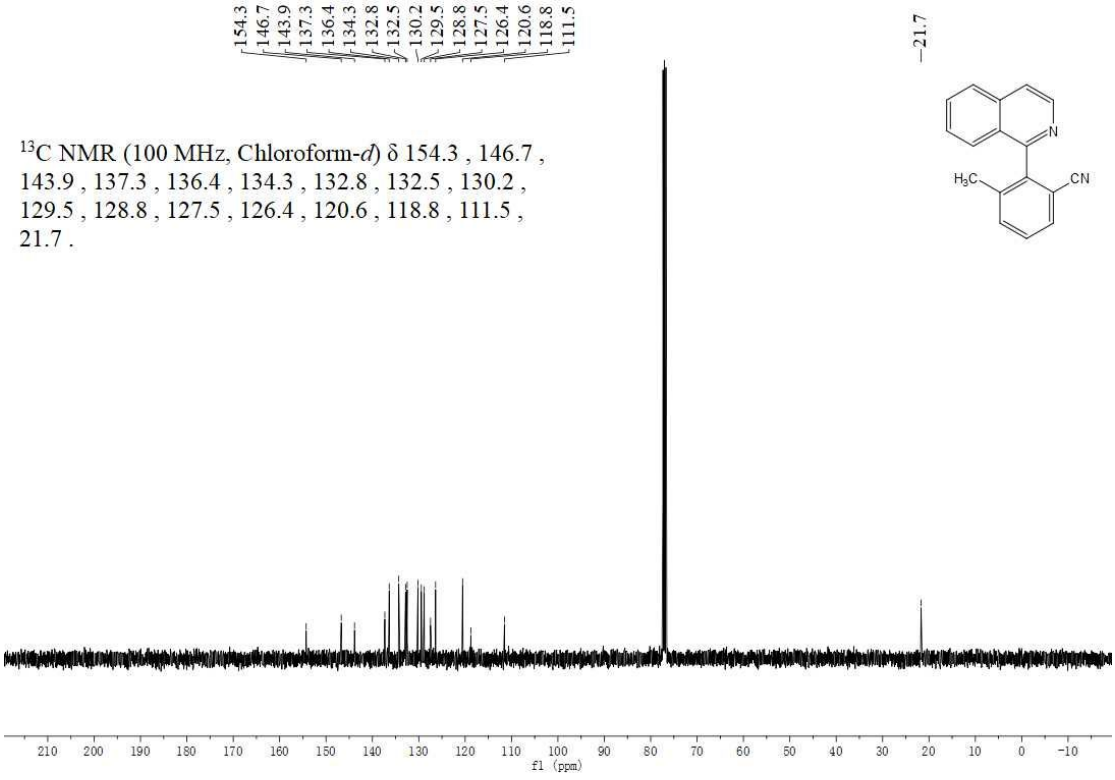


Figure S54. ^{13}C NMR of 2-(Isoquinolin-1-yl)-3-methylbenzonitrile **(2ac)**

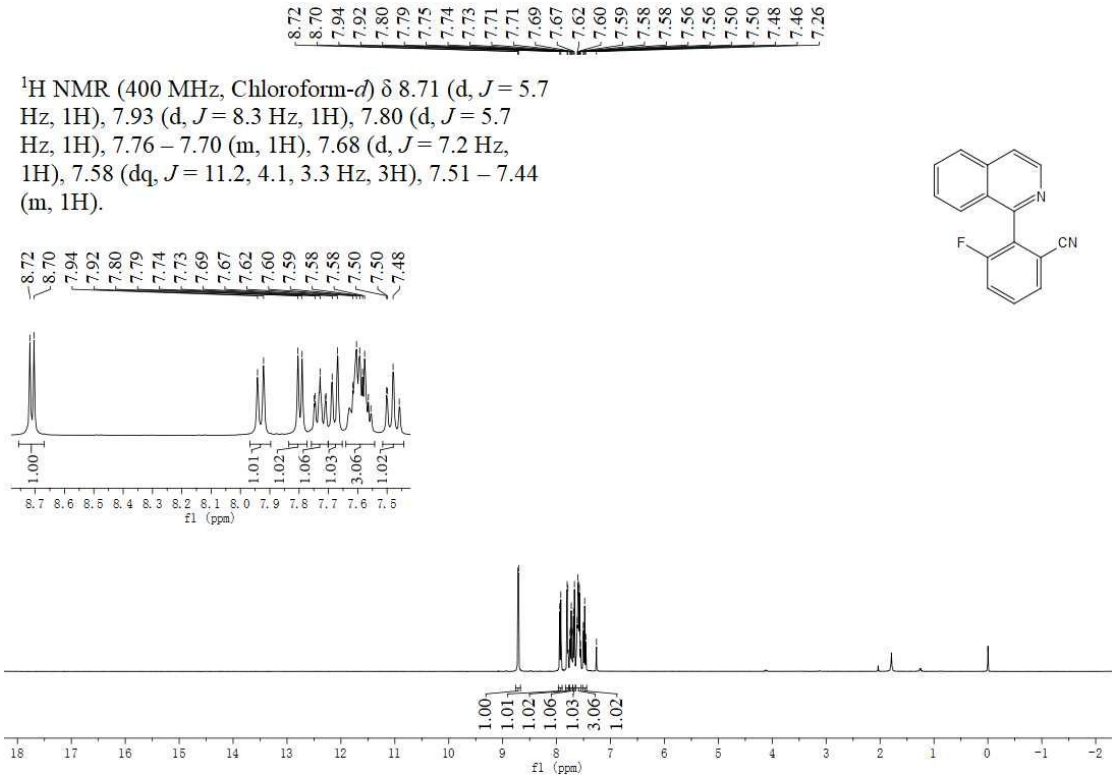


Figure S55. ^{1}H NMR of 3-Fluoro-2-(isoquinolin-1-yl)benzonitrile **(2ad)**

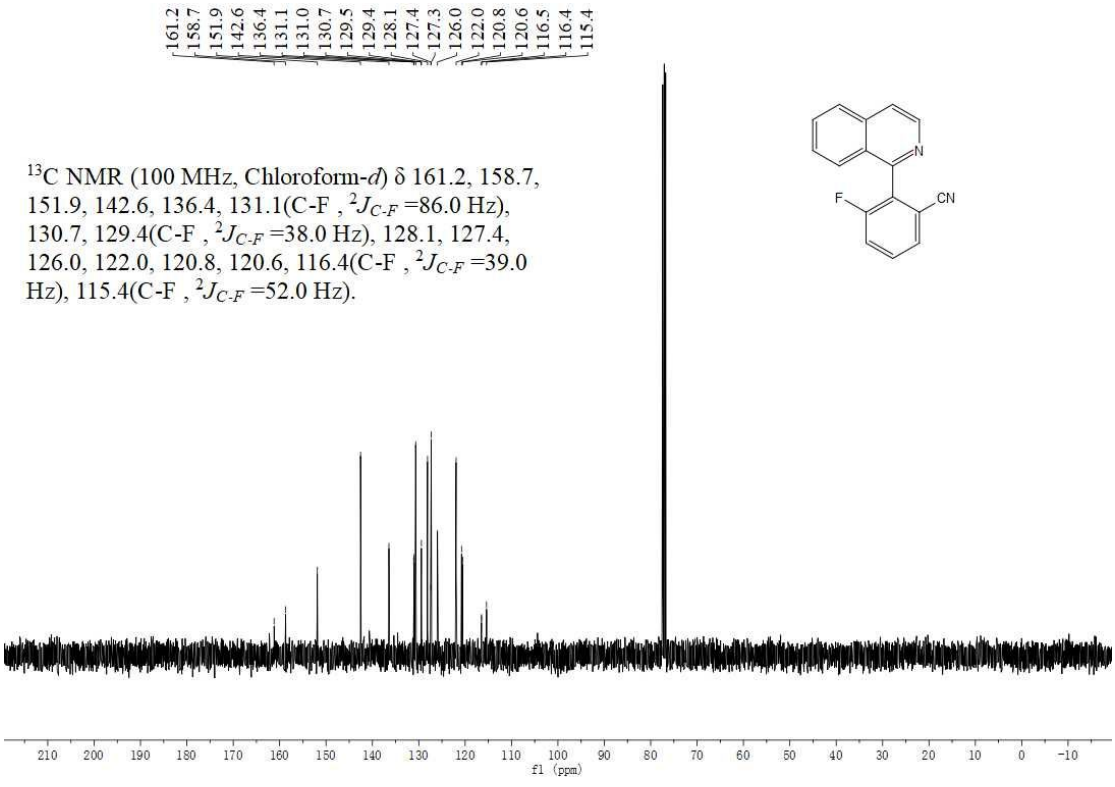


Figure S56. ^{13}C NMR of 3-Fluoro-2-(isoquinolin-1-yl)benzonitrile **(2ad)**

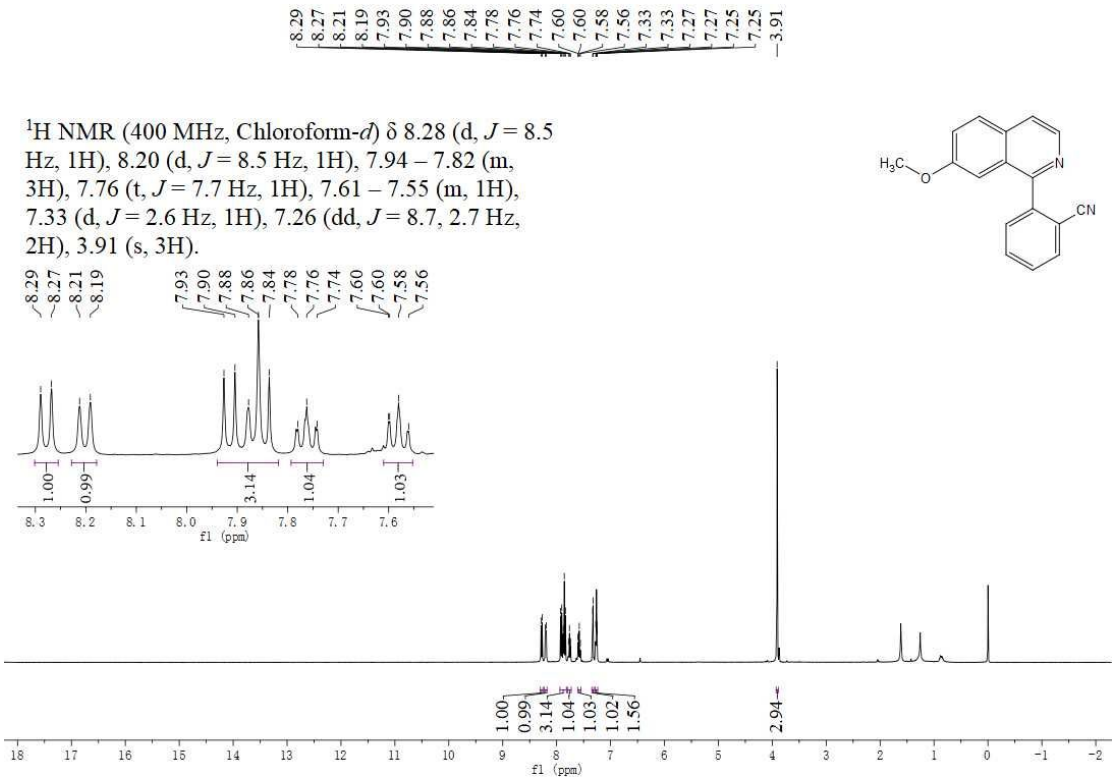


Figure S57. [1]H NMR of 2-(7-Methoxyisoquinolin-1-yl)benzonitrile **(2ae)**

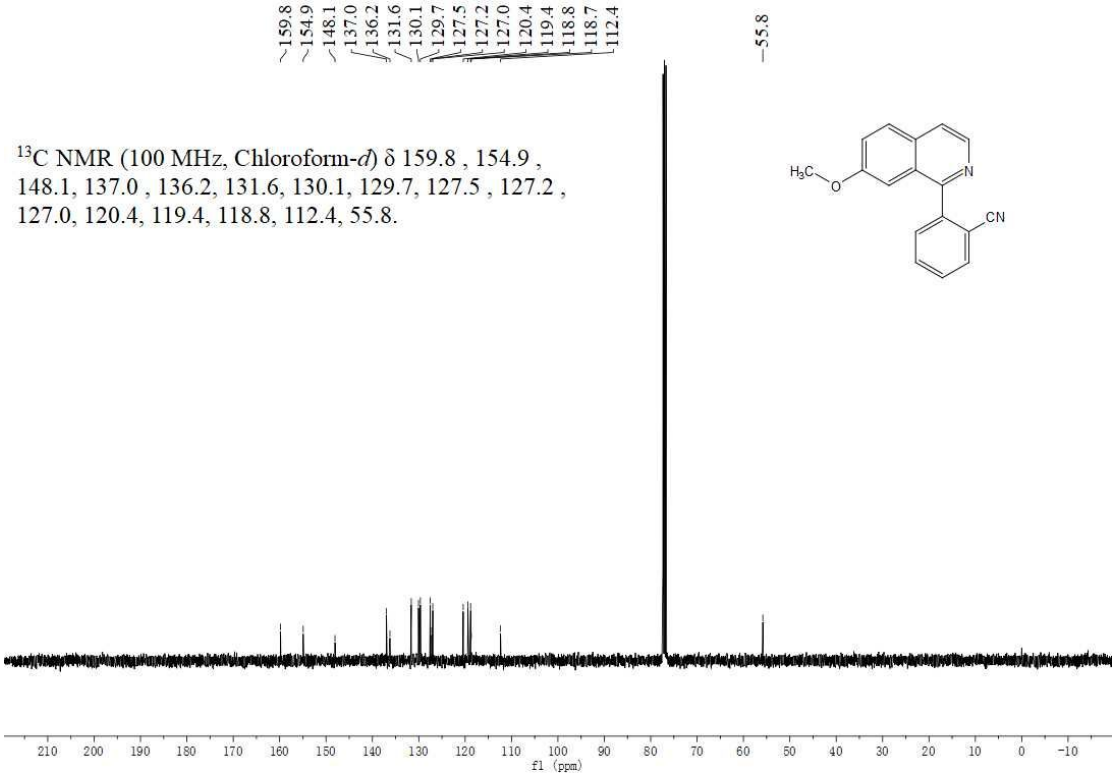


Figure S58. [13]C NMR of 2-(7-Methoxyisoquinolin-1-yl)benzonitrile **(2ae)**

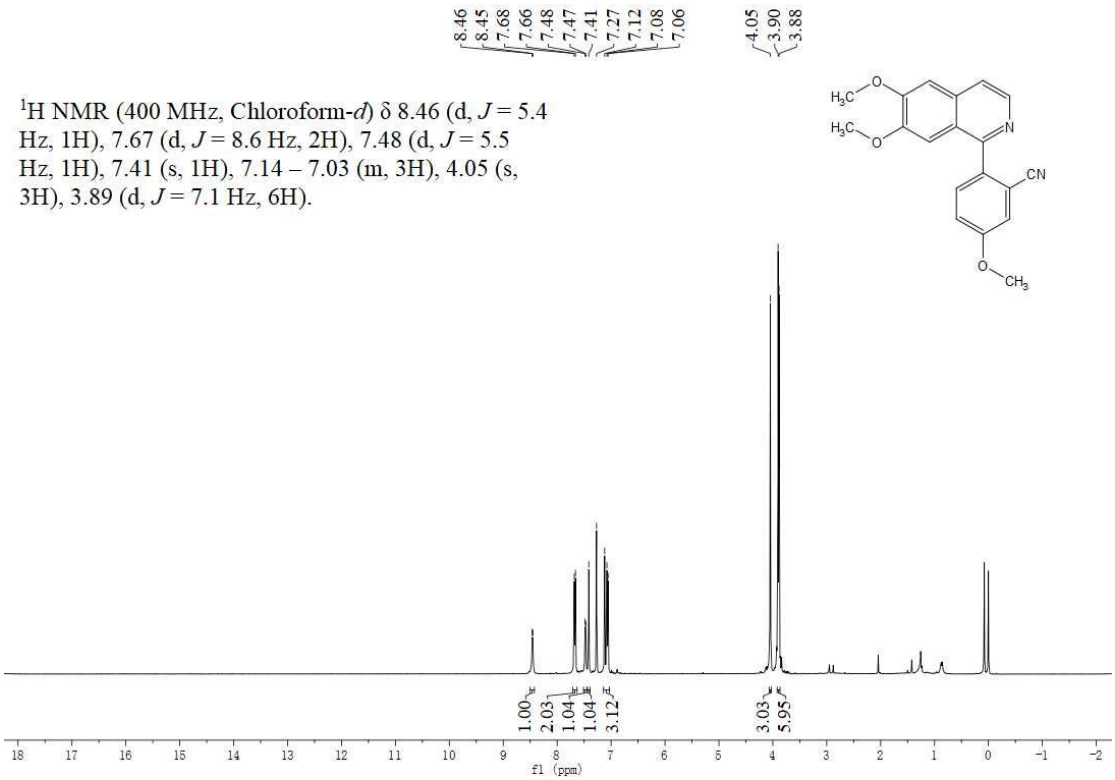


Figure S59. [1]H NMR of 2-(6,7-Dimethoxyisoquinolin-1-yl)-5-methoxybenzonitrile **(2af)**

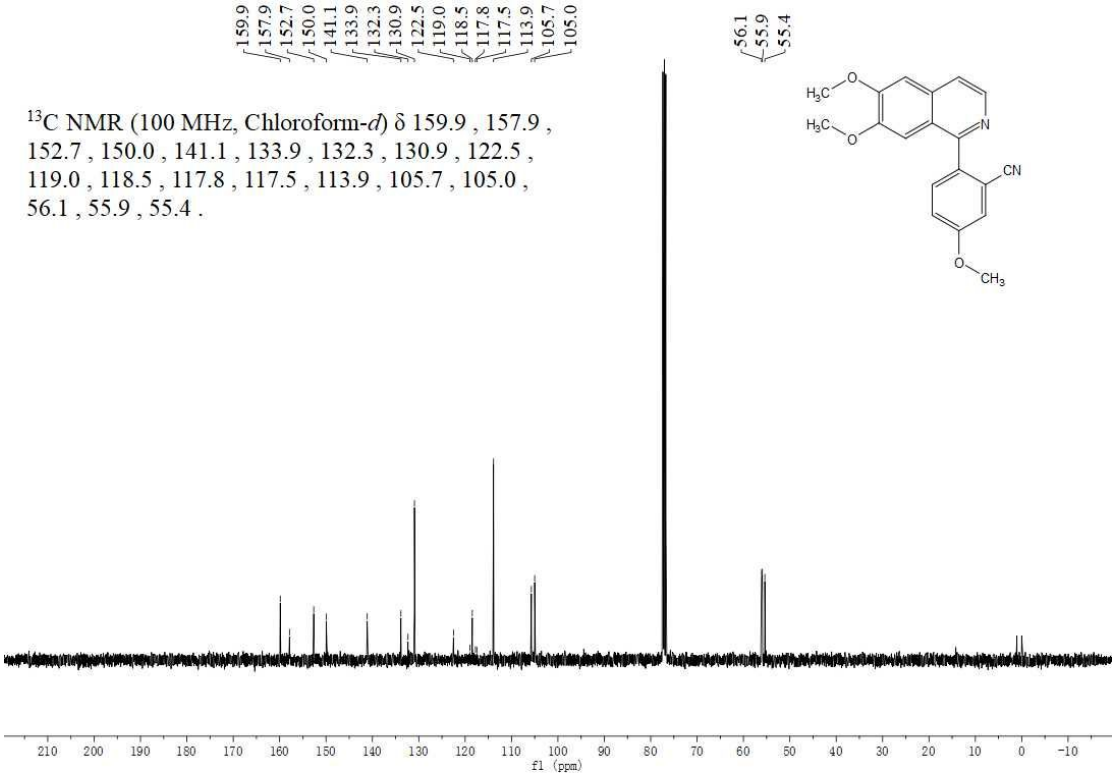
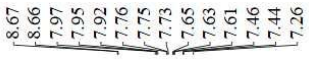
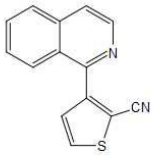


Figure S60. [13]C NMR of 2-(6,7-Dimethoxyisoquinolin-1-yl)-5-methoxybenzonitrile **(2af)**



^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 (d, *J* = 5.4 Hz, 1H), 8.00 – 7.90 (m, 2H), 7.81 – 7.71 (m, 3H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 4.9 Hz, 1H).



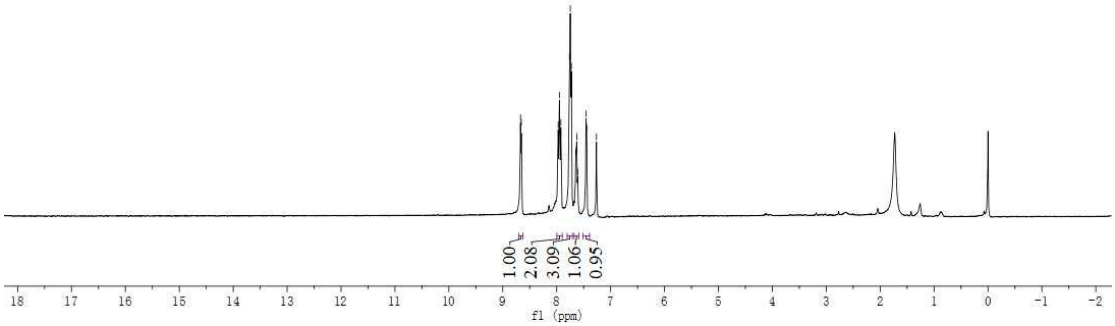


Figure S61. ^{1}H NMR of 3-(Isoquinolin-1-yl)thiophene-2-carbonitrile **(2ag)**

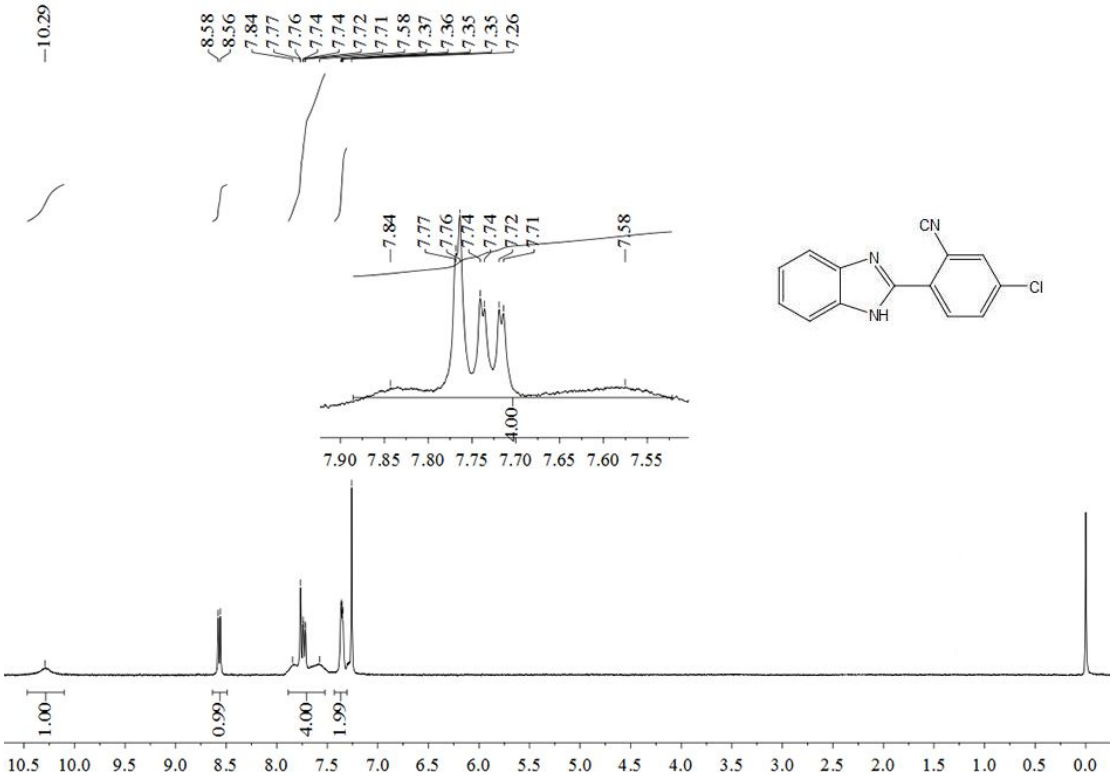


Figure S62. ^{1}H NMR of 2-(1H-benzo[d]imidazol-2-yl)-5-chlorobenzonitrile **(2ah)**

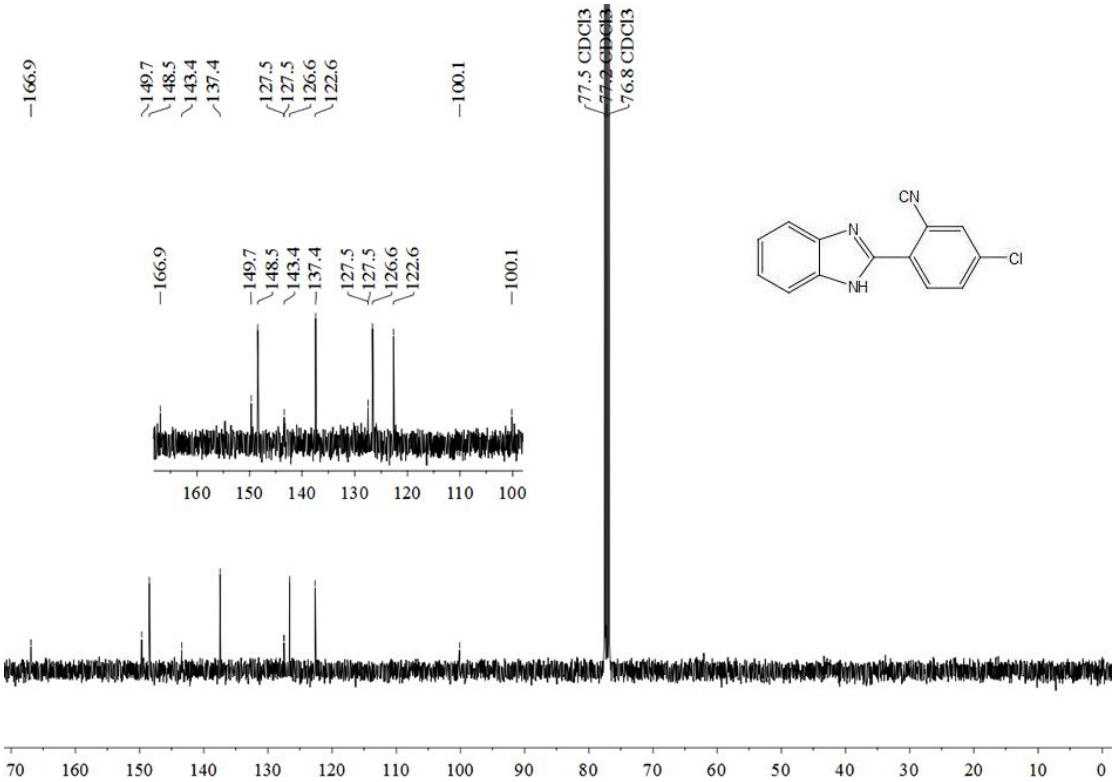


Figure S63. ^{13}C NMR of 2-(1H-benzo[d]imidazol-2-yl)-5-chlorobenzonitrile **(2ah)**

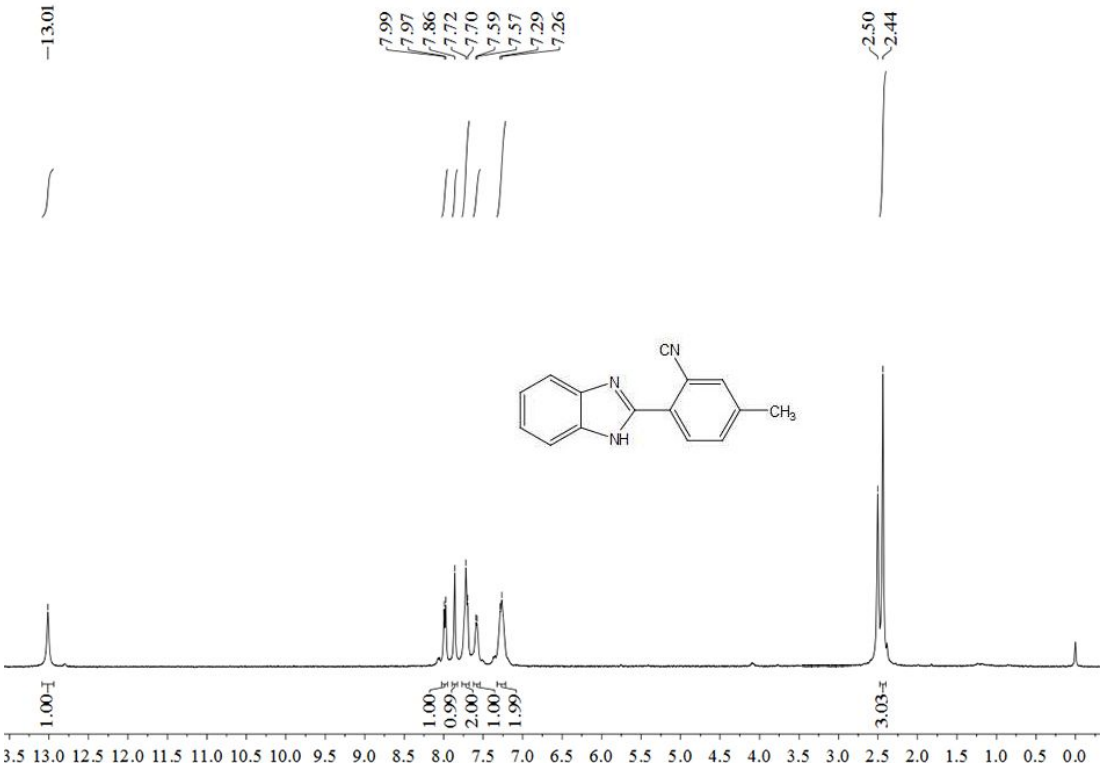


Figure S64. ^{1}H NMR of 2-(1H-benzo[d]imidazol-2-yl)-5-methylbenzonitrile **(2ai)**

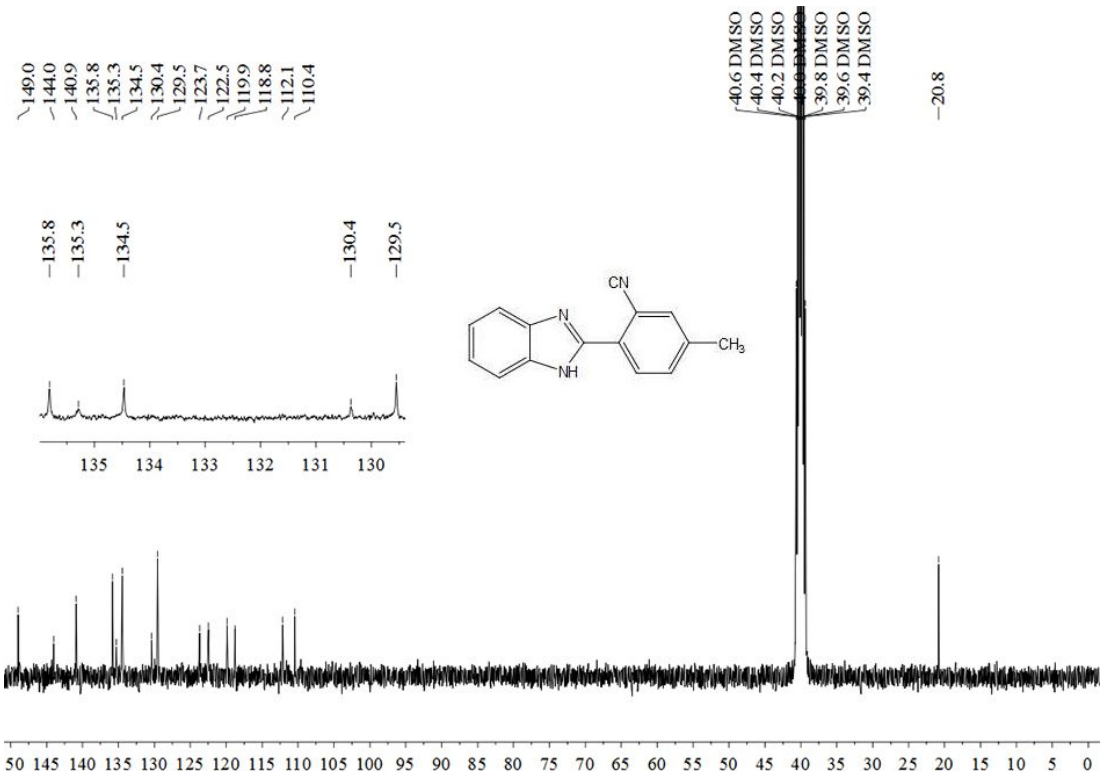


Figure S65. ^{13}C NMR of 2-(1H-benzo[d]imidazol-2-yl)-5-methylbenzonitrile **(2ai)**

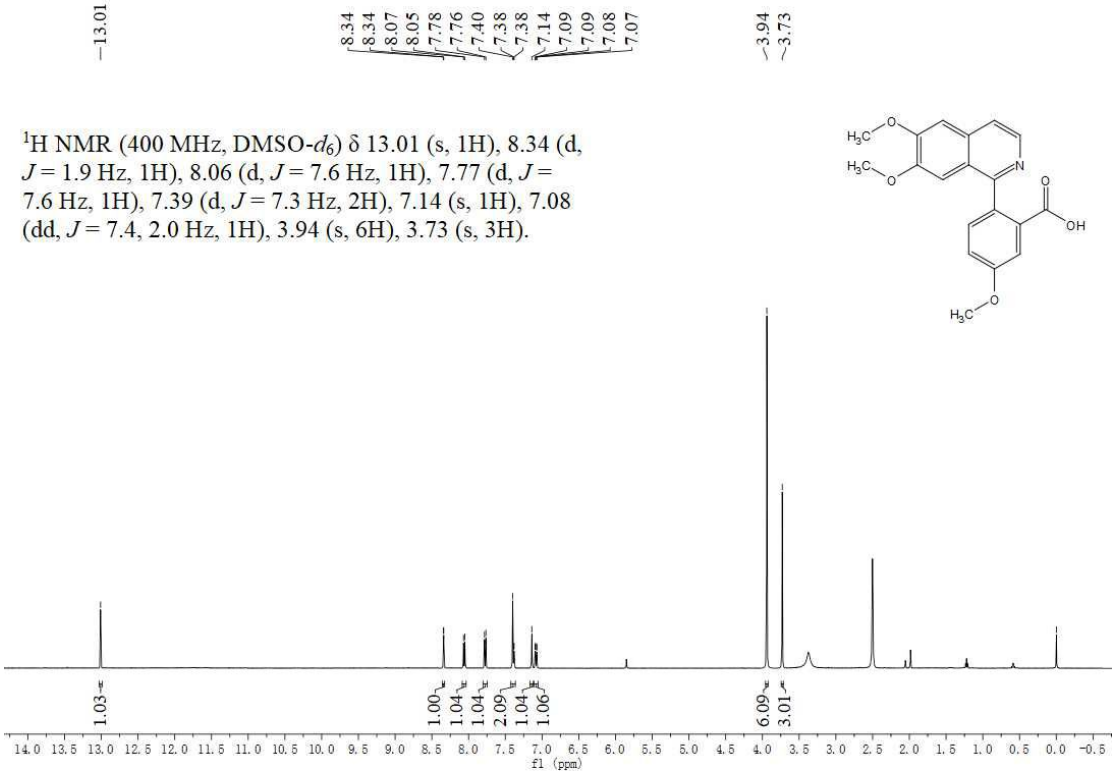


Figure S66. ^{1}H NMR of 2-(6,7-Dimethoxyisoquinolin-1-yl)-5-methoxybenzoic acid **(3)**

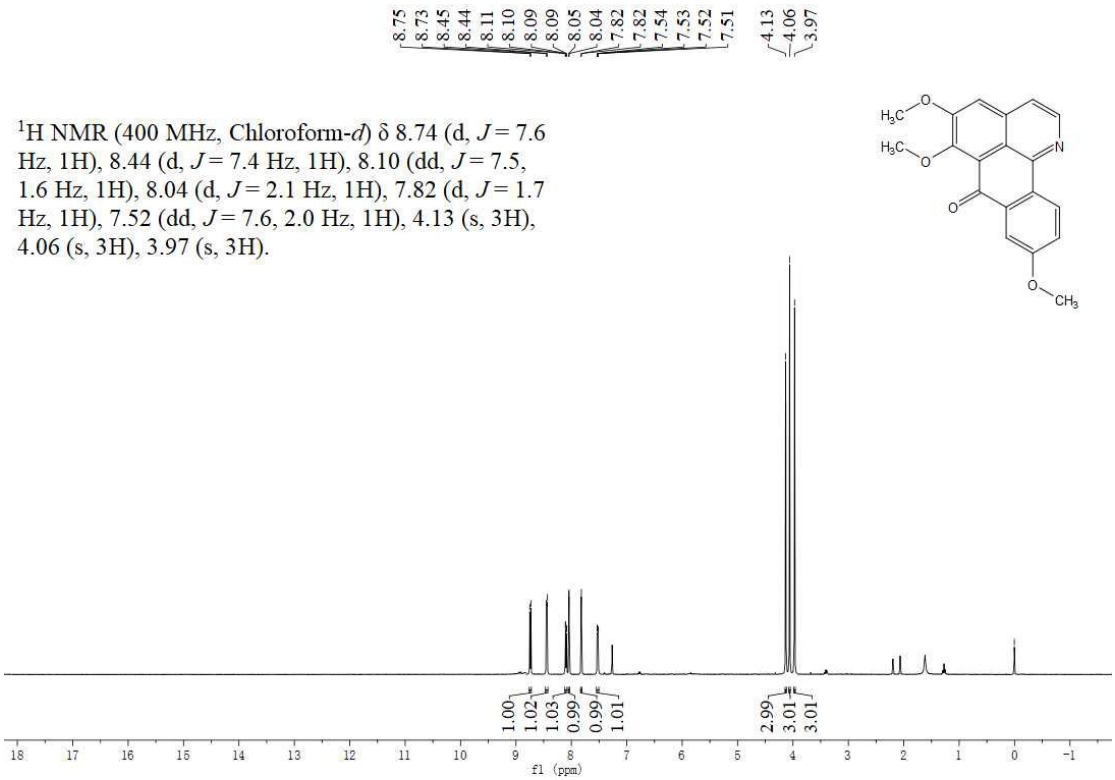


Figure S67. [1]H NMR of Menisporphine

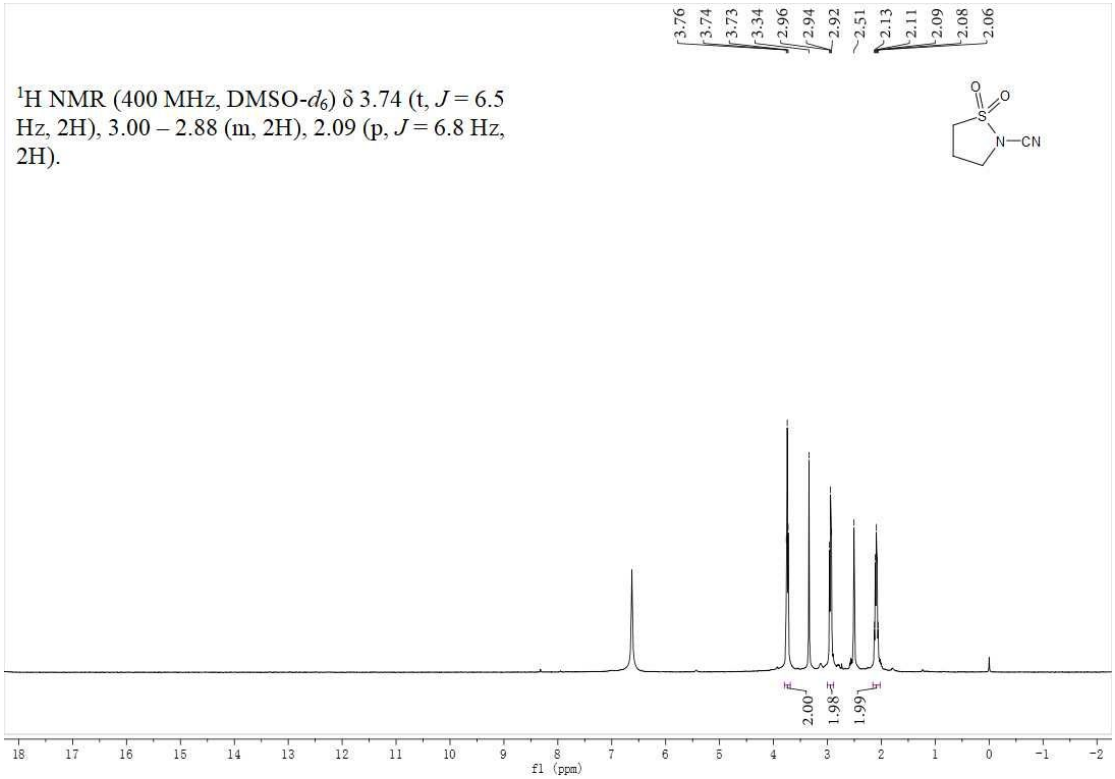


Figure S68. [1]H NMR of 2-Cyanoisothiazolidine 1,1-dioxide

^{13}C NMR (100 MHz, DMSO-d_6) δ 51.0 , 44.3 , 28.2 , 20.2

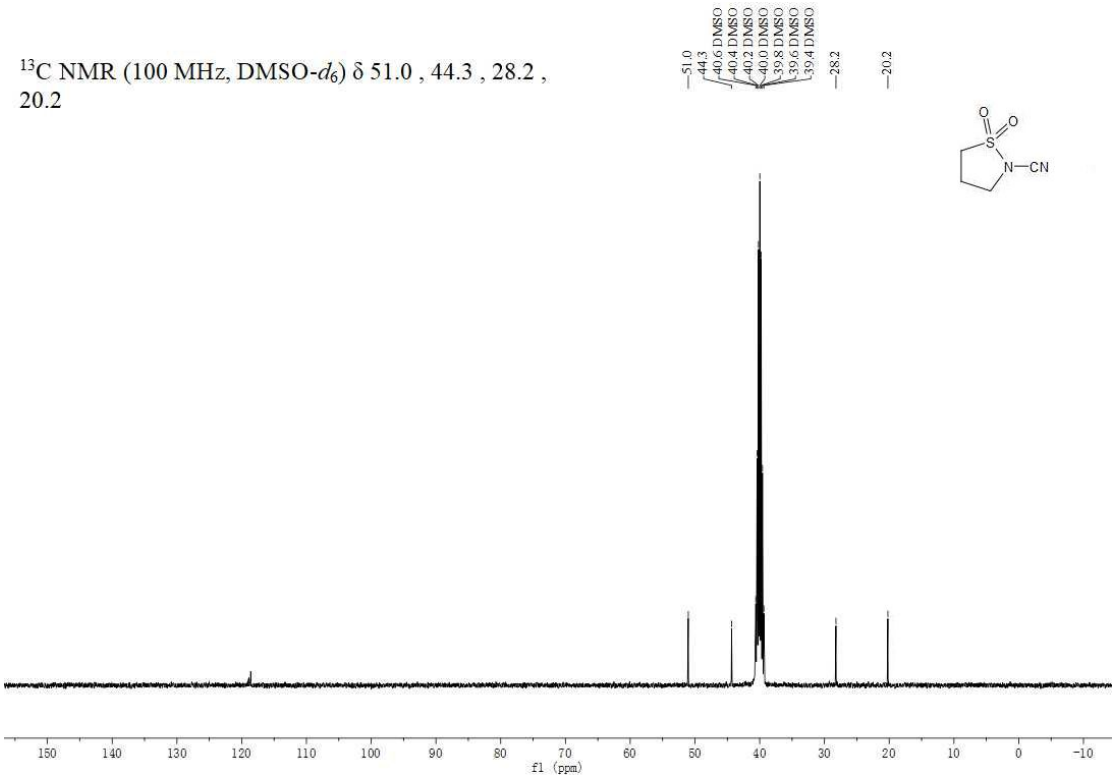


Figure S69. ^{13}C NMR of 2-Cyanoisothiazolidine 1,1-dioxide