Supporting Information

Copper-mediated C-H cyanation of (hetero)arenes with ethyl (ethoxymethylene)cyanoacetate as a cyanating agent

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A. General remarks

^{1}H and ^{13}C NMR spectra were recorded using a Bruker DRX-400 spectrometer using $CDCl_3$ as solvent and TMS as an internal standard. The chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively. GC analyses were performed on a GC-7900 chromatograph with an FID and equipped with an AT.SE-30 capillary column (internal diameter: 0.32 mm, length: 30 m). Mass spectra were recorded on a Thermo Scientific ISQ gas chromatograph-mass spectrometer at an ionization voltage of 70 eV and equipped with a DB-WAX capillary column (internal diameter: 0.25 mm, length: 30 m). The data of HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with a TENSOR 27 spectrometer. Melting points were determined with a Büchi Melting Point B-545 instrument. Compound **1a**, **1b**, **1e**, **4i** and **4j** were commercially purchased and used without further purification. Other pyridine or pyrimidine derivatives were prepared via Suzuki coupling of the corresponding boronic acid and 2-bromopyridine or 2-chloropyrimidine according to a reported procedure.[1]

B. General Procedure for the copper-mediated C–H cyanation of (hetero)arene with ethyl (ethoxymethylene)cyanoacetate

To a 25 mL round flask was added the mixture of (hetero)arene (**1** or **4**, 0.3 mmol), ethyl 2-cyano-3-ethoxyacrylate (**2a**, 0.36 mmol), $Cu(OAc)_2$ (0.3 mmol) in DMF (2 mL) successively. The mixture was stirred at 130 °C for 12 h under 1 atm of O_2. After the reaction was completed, the mixture was cooled to the room temperature, diluted with water (15 mL) and then extracted with dichloromethanethe (3 × 5 mL). The organic layers were combined, washed with brine and dried over anhydrous $MgSO_4$. After removal of the solvent in vacuum, the crude product thus obtained was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as eluent to give the desired cyanated product **3** or **5**.

C. Detection of cyanide anion (CN^-) by indicator paper

(i) The representative procedure for the detection of cyanide anion[2]

Picrate paper was prepared by wetting filter paper with a solution of sodium bicarbonate (5.0 g) and picric acid (0.5 g) in water (100 mL). After drying the paper, it was cut into strips for use. To a 25 mL round flask

was added the mixture of ethyl (ethoxymethylene)cyanoacetate (**2a**, 0.36 mmol), $Cu(OAc)_2$ (0.3 mmol), in DMF (2 mL) successively. The mixture was stirred at 130 °C for 3 h under O_2 (1 atm), and then cooled to 80 °C. Subsequently, tartaric acid (0.5 mmol) was added to the reaction mixture. A 2 mL plastic vial with a number of holes and a strip inside was placed above the reaction mixture. The round flask was sealed and heated at 80 °C for 1 h. The test paper in the plastic vial turned rose-red indicating the existence of cyanide anion.

(ii) Detection of cyanide anion under different conditions

Table S1 Detection of CN^- by indicator paper under different conditions[a]

Entry	**2a**	$Cu(OAc)_2$	O_2	Rose-red
1	√	√	√	+
2[b]	√	√	-	−
3	√	-	√	−
4	-	√	√	−

[a] Conditions: **2a** (0.36 mmol), $Cu(OAc)_2$ (0.3 mmol), O_2 (1 atm), DMF (2 mL). The mixture was heated at 130 °C for 3 h before test. "−" means negative result; "+" means positive result. [b] Under 1 atm of N_2.

D. H/D exchange experiment

To a 25 mL round flask was added the mixture of 2-(4-methoxyphenyl)pyridine (**1e**) (0.3 mmol), $Cu(OAc)_2$ (0.3 mmol), CD_3OD (1.2 mmol) in DMF (2 mL) successively. The mixture was stirred at 130 °C (oil bath) for 12 h under O_2 (1 atm). After the reaction was completed, the mixture was cooled to the room temperature, diluted with water (15 mL) and then extracted with dichloromethane (3 × 5 mL). The organic layers were combined, washed with brine and dried over anhydrous $MgSO_4$. After removal of the volatile compounds in vacuum, the extent of deuterium incorporation was measured by ^1H NMR analysis of the crude mixture.

E. Kinetic Isotope Effect study

(i) Parallel Experiments: 2-Phenylpyridine (**1a**) (0.3 mmol) or [D_5]-2-phenylpyridine ([D_5]-**1a**) (0.3 mmol) were added to two separate dried 25 mL round flasks equipped with a magnetic stirbar along with ethyl 2-cyano-3-ethoxyacrylate (**2a**) (0.36 mmol), $Cu(OAc)_2$ (0.3 mmol) and DMF (2 mL). Each of the reaction was stirred at 130 °C under 1 atm of O_2 for a selected period of time. Then, the reaction mixture was cooled to the

room temperature, diluted with water (15 mL) and extracted with dichloromethane (3 × 5 mL). The combined organic layers were washed with brine, dried over anhydrou $MgSO_4$ and then analyzed by GC-MS using *n*-dodecane as internal standard. The reaction profile and initial rate constants (Kobs) with 4 hours were obtained (Figure S1-S4). The value of intermolecular kinetic isotope effect in paraller reaction could be determined by the ratio of Kobs(**1a**) to Kobs([D_5]-**1a**) (Table S2).

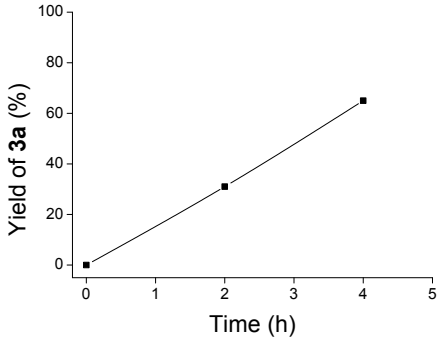


Figure S1 Reaction profile of **1a**

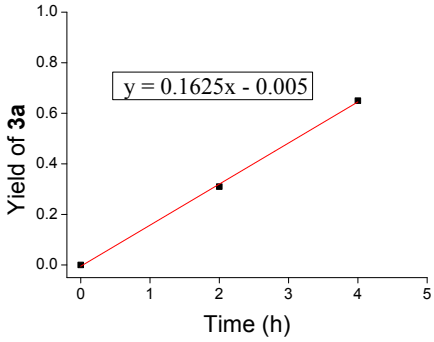


Figure S2 Initial rate of **1a**

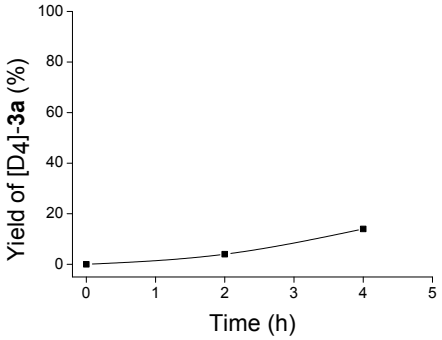


Figure S3 Reaction profile of [D_5]-**1a**

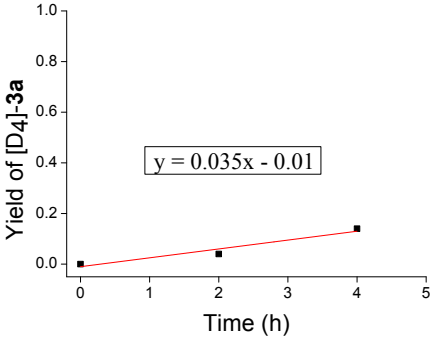


Figure S4 Initial rate of [D_5]-**1a**

Table S2 KIE studies for copper-mediated cyanation of **1a** and [D_5]-**1a** [a]

	Kobs(h^{-1})	Kobs(**1a**)/Kobs([D_5]-**1a**)
1a	0.1625	4.6
[D_4]-**1a**	0.035	

[a]Reaction condition: substrate (0.3 mmol), **2a** (0.36 mmol), $Cu(OAc)_2$ (0.3 mmol), O_2 (1 atm), DMF (2 mL), 130 °C.

(ii) Competitive experiment: To a 25 mL round flask was added the mixture of 2-phenylpyridine (**1a**) (0.3 mmol), [D_5]-2-phenylpyridine ([D_5]-**1a**) (0.3 mmol), ethyl 2-cyano-3-ethoxyacrylate (**2a**) (0.36 mmol), $Cu(OAc)_2$ (0.3 mmol) in DMF (2 mL) successively. The mixture was stirred at 130 °C for 12 h under 1 atm of O_2. After the reaction was completed, the mixture was cooled to the room temperature, diluted with water

(15 mL) and then extracted with dichloromethanethe (3 × 5 mL). The organic extract was combined, washed with brine, and dried over anhydrous $MgSO_4$. After removal of the volatile compounds under reduced pressure, the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 1:10) to give a mixture of desired products **3a**/[D_4]-**3a**. The ratio of **3a**/[D_4]-**3a** was determined by ^{1}H NMR analysis to give a KIE value of 4.0 (Figure S5).

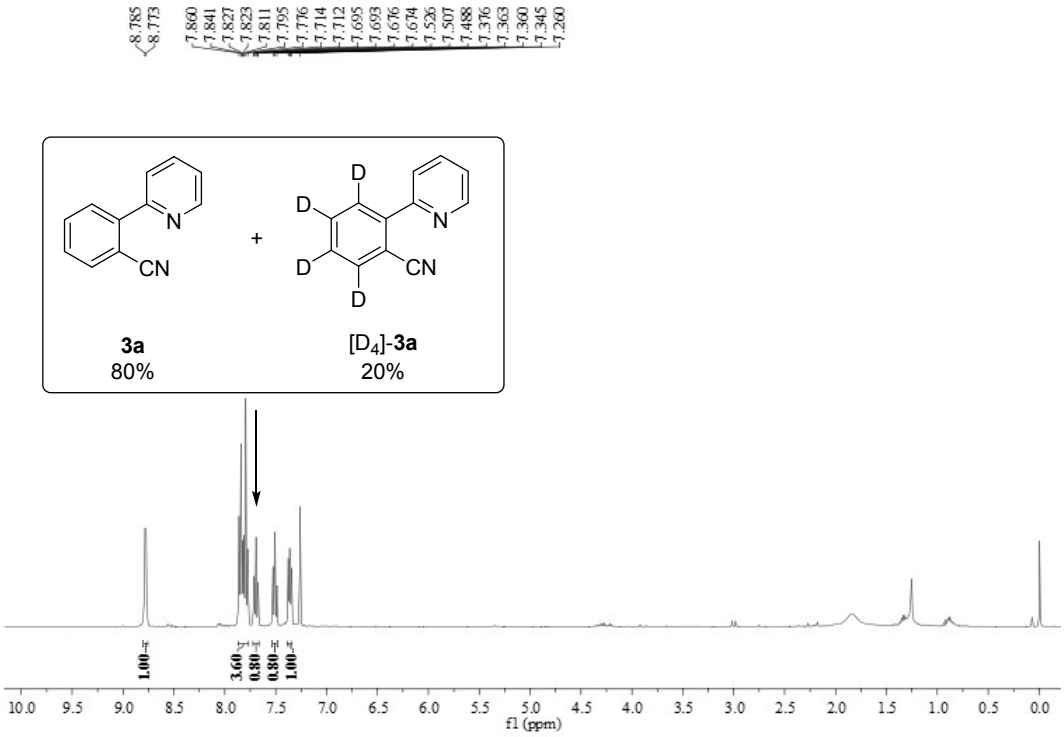
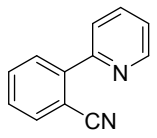


Figure S5 ^{1}H NMR of a mixture of **3a** and [D_4]-**3a** in one vessel

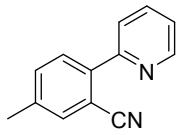
F. Analytical data

2-(Pyridin-2-yl)benzonitrile (3a)[3]



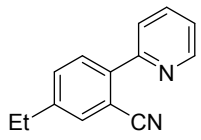
White solid (43 mg, 81 %), mp: 49 - 50 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.78 (d, J = 4.4 Hz, 1 H), 7.88 - 7.77 (m, 4 H), 7.70 (t, J = 7.6 Hz, 1 H), 7.51 (t, J = 7.6 Hz, 1 H), 7.39 - 7.34 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.2, 149.8, 143.4, 136.8, 134.1, 132.8, 129.9, 128.7, 123.3, 123.2, 118.6, 111.0. IR (KBr): 3066, 2225, 1587, 1467, 1440, 1426, 762, 720 cm^{-1}. MS (EI) *m/z*: 180 [M$^+$] (100), 168, 153, 128, 123, 101, 96, 76.

5-Methyl-2-(pyridin-2-yl)benzonitrile (3b)[3]



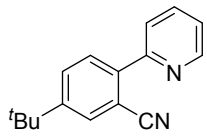
White solid (40 mg, 70 %), mp: 73 - 74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.73 (d, J = 4.8 Hz, 1 H), 7.79 (t, J = 7.6 Hz, 1 H), 7.73 (t, J = 7.8 Hz, 2 H), 7.57 (s, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.30 (t, J = 6.0 Hz, 1 H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.1, 149.7, 140.6, 139.0, 136.7, 134.3, 133.6, 129.7, 123.0, 129.9, 118.8, 110.7, 20.7. IR (KBr): 3026, 2919, 2226, 1587, 1465, 1428, 830, 784, 731 cm^{-1}. MS (EI) *m/z*: 194 [M$^+$] (100), 179, 167, 164, 140, 114, 96, 91.

5-Ethyl-2-(pyridin-2-yl)benzonitrile (3c)



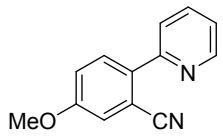
Yellow oil (53 mg, 85 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.75 (d, J = 4.8 Hz, 1 H), 7.83 - 7.78 (m, 1 H), 7.75 (d, J = 8.0 Hz, 2 H), 7.61 (s, 1 H), 7.50 (dd, J = 8.0, 1.2 Hz, 1 H), 7.34 - 7.30 (m, 1 H), 2.72 (q, J = 7.6 Hz, 2 H), 1.28 (t, J = 7.6 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.3, 149.8, 145.3, 140.9, 136.7, 133.3, 132.6, 129.9, 123.0, 118.9, 110.8, 28.1, 15.0. IR (KBr): 3056, 2966, 2223, 1641, 1584, 1461, 1429, 1263, 1023, 793, 739 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{14}H_{12}N_2Na$ [M+Na]$^+$: 231.0893; found: 231.0899.

5-(Tert-butyl)-2-(pyridin-2-yl)benzonitrile (3d)[3]



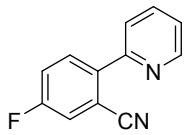
Yellow oil (51 mg, 73 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (d, J = 4.8 Hz, 1 H), 7.86 - 7.76 (m, 4.0 H), 7.71 (d, J = 8.4 Hz, 1 H), 7.36 - 7.30 (m, 1 H), 1.37 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.2, 152.3, 149.9, 140.6, 136.7, 131.1, 130.2, 129.7, 123.1, 123.0, 119.2, 110.6, 34.79, 30.97. IR (KBr): 3070, 2964, 2869, 2224, 1585, 1462, 1437, 790 cm^{-1}. MS (EI) *m/z*: 236 [M$^+$], 221 (100), 205, 193, 181, 179, 152, 140, 113, 96, 82.

5-Methoxy-2-(pyridin-2-yl)benzonitrile (3e)[3]



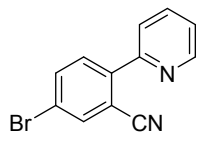
White solid (50 mg, 80 %), mp: 104 - 105 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.74 (d, J = 4.8 Hz, 1 H), 7.83 - 7.73 (m, 3 H), 7.33 - 7.28 (m, 1 H), 7.27 (d, J = 2.0 Hz, 1 H), 7.21 (dd, J = 8.8, 2.8 Hz, 1 H), 3.88 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.5, 155.0, 149.8, 136.7, 136.0, 131.3, 122.8, 122.7, 119.4, 118.6, 118.5, 111.7, 55.7. IR (KBr): 3076, 3002, 2225, 1607, 1509, 1468, 1324, 1290, 1243, 1040, 785 cm^{-1}. MS (EI) *m/z*: 210 [M$^+$] (100), 195, 180, 167, 152, 140, 113, 89, 78.

5-Fluoro-2-(pyridin-2-yl)benzonitrile (3f)[3]



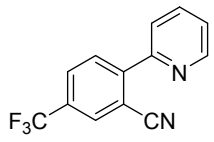
White solid (49 mg, 83 %), mp: 127 - 128 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (d, J = 4.4 Hz, 1 H), 7.89 - 7.82 (m, 2 H), 7.77 (d, J = 7.6 Hz, 1 H), 7.50 (d, J = 8.0 Hz, 1 H), 7.44 - 7.35 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.0 (d, $J_{C\text{-}F}$ = 251.8 Hz), 154.2, 149.9, 139.9, 136.9, 132.1 (d, $J_{C\text{-}F}$ = 8.3 Hz), 123.4, 123.1, 120.7 (d, $J_{C\text{-}F}$ = 22.4 Hz), 120.5 (d, $J_{C\text{-}F}$ = 18.9 Hz), 117.4 (d, $J_{C\text{-}F}$ = 2.7 Hz), 112.4 (d, $J_{C\text{-}F}$ = 9.5 Hz). IR (KBr): 3065, 3029, 2926, 2232, 1606, 1589, 1467, 1278, 1264, 1224, 1153, 843, 784, 748 cm^{-1}. MS (EI) *m/z*: 198 [M$^+$] (100), 171, 151, 145, 120, 99, 83.

5-Bromo-2-(pyridin-2-yl)benzonitrile (3g)[4]



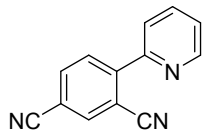
White solid (54 mg, 70 %), mp: 145 - 146 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.78 (s, 1 H), 7.93 (d, J = 2.0 Hz, 1 H), 7.88 - 7.73 (m, 4 H), 7.39 (t, J = 5.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.1, 150.0, 142.2, 137.0, 136.5, 136.1, 131.4, 123.6, 123.1, 122.6, 117.3, 112.7. IR (KBr): 3050, 2961, 2921, 2851, 2228, 1567, 1461, 840, 785, 745 cm^{-1}. MS (EI) *m/z*: 258 [M$^+$], 205, 179 (100), 152, 125, 100, 89, 76.

2-(Pyridin-2-yl)-5-(trifluoromethyl)benzonitrile (3h)[3]



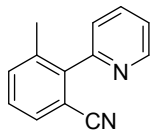
White solid (60 mg, 81 %), mp: 65 - 66 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.81 (d, J = 4.6 Hz, 1 H), 8.06 (s, 1 H), 8.02 (d, J = 8.0 Hz, 1 H), 7.93 (d, J = 8.4 Hz, 1 H), 7.88 (td, J = 7.6, 1.6 Hz, 1 H), 7.83 (d, J = 7.8 Hz, 1 H), 7.44 - 7.39 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8, 150.2, 146.5, 137.1, 131.0 (q, $J_{C\text{-}F}$ = 3.8 Hz), 130.7, 129.4 (q, $J_{C\text{-}F}$ = 3.4 Hz), 124.1, 123.3, 122.9 (d, $J_{C\text{-}F}$ = 271.2 Hz), 117.4, 111.9. IR (KBr): 3045, 2928, 2232, 1677, 1592, 1475, 1335, 1305, 1155, 1129, 1090, 797 cm^{-1}. MS (EI) *m/z*: 248 [M$^+$] (100), 229, 200, 179, 171, 152, 125, 99, 87, 78.

4-(Pyridin-2-yl)isophthalonitrile (3i)[5]



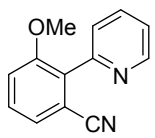
White solid (37 mg, 60 %), mp: 155 - 156 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (d, J = 3.6 Hz, 1 H), 8.08 (d, J = 1.2 Hz, 1 H), 8.03 (d, J = 8.2 Hz, 1 H), 7.96 (dd, J = 8.2, 1.4 Hz, 1 H), 7.93 - 7.87 (m, 1 H), 7.85 (d, J = 7.6 Hz, 1 H), 7.46 - 7.42 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.2, 150.3, 147.0, 137.4, 137.2, 135.7, 131.0, 124.4, 123.4, 116.7, 116.6, 113.3, 112.6. IR (KBr): 3070, 2921, 2851, 2236, 1649, 1583, 1462, 1268, 911, 852, 791 cm^{-1}. MS (EI) *m/z*: 205 [M$^+$] (100), 178, 151, 125, 102, 75.

3-Methyl-2-(pyridin-2-yl)benzonitrile (3j)[5]



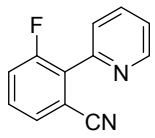
Yellow oil (47 mg, 81 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.74 (d, J = 4.4 Hz, 1 H), 7.85 - 7.80 (m, 1 H), 7.58 (d, J = 7.6 Hz, 1 H), 7.49 (d, J = 8.0 Hz, 1 H), 7.43 - 7.32 (m, 3 H), 2.21 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 149.7, 143.5, 137.7, 136.6, 134.7, 130.5, 128.4, 124.5, 123.0, 118.1, 112.68, 20.0. IR (KBr): 2926, 2226, 1593, 1567, 1457, 1423, 791, 749 cm^{-1}. MS (EI) *m/z*: 194 [M$^+$] (100), 166, 140, 126, 114, 96, 83, 63.

3-Methoxy-2-(pyridin-2-yl)benzonitrile (3k)[6]



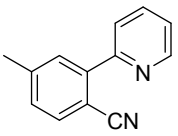
Yellow oil (52 mg, 83 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (dd, J = 4.2, 0.6 Hz, 1 H), 7.78 (td, J = 7.8, 1.8 Hz, 1 H), 7.51 (d, J = 7.6 Hz, 1 H), 7.46 - 7.42 (m, 1 H), 7.37 (dd, J = 7.8, 1.0 Hz, 2 H), 7.35 - 7.30 (m, 1 H), 7.20 (dd, J = 8.4, 0.8 Hz, 1 H), 3.80 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 153.0, 149.5, 136.1, 133.1, 130.0, 125.5, 125.3, 123.1, 117.8, 115.6, 114.0, 56.0. IR (KBr): 3008, 2939, 2843, 2229, 1591, 1464, 1431, 1068, 801, 747 cm^{-1}. MS (EI) *m/z*: 210 [M$^+$], 192, 179, 166, 153, 140, 127, 113, 101, 90, 80 (100).

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



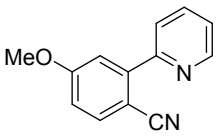
Yellow solid (38 mg, 65 %), mp: 41 - 43 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.81 (d, J = 3.8 Hz, 1 H), 7.84 (td, J = 7.8, 1.6 Hz, 1 H), 7.61 (t, J = 6.6 Hz, 2 H), 7.53 - 7.45 (m, 1 H), 7.45 - 7.37 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.8 (d, $J_{C\text{-}F}$ = 249.6 Hz), 150.3, 149.9, 136.5, 130.4 (d, $J_{C\text{-}F}$ = 8.9 Hz), 129.9 (d, $J_{C\text{-}F}$ = 3.8 Hz), 125.3 (d, $J_{C\text{-}F}$ = 3.8 Hz), 123.8, 120.8 (d, $J_{C\text{-}F}$ = 22.7 Hz), 114.4 (d, $J_{C\text{-}F}$ = 4.5 Hz), 103.7. IR (KBr): 3081, 2922, 2850, 2229, 1644, 1585, 1450, 1427, 1256, 800, 748, 728 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{12}H_8FN_2$ [M+H]$^+$: 199.0666; found: 199.0675.

4-Methyl-2-(pyridin-2-yl)benzonitrile (3m)[3]



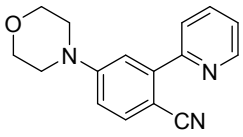
Yellow oil (48 mg, 83 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.74 (d, J = 4.6 Hz, 1 H), 7.84 - 7.74 (m, 2 H), 7.66 (d, J = 8.2 Hz, 2 H), 7.35 - 7.27 (m, 2 H), 2.46 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.3, 149.8, 143.8, 143.2, 136.7, 133.9, 130.6, 129.5, 123.2, 123.1, 118.9, 107.9, 21.71. IR (KBr): 3046, 3002, 2218, 1607, 1588, 1570, 1464, 822, 792, 750 cm^{-1}. MS (EI) *m/z*: 194 [M$^+$] (100), 179, 167, 152, 140, 114, 96, 83, 78.

4-Methoxy-2-(pyridin-2-yl)benzonitrile (3n)[3]



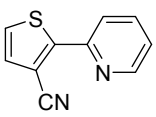
White solid (54 mg, 86 %), mp: 67 - 68 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (d, J = 4.4 Hz, 1 H), 7.86 - 7.79 (m, 2 H), 7.71 (d, J = 8.8 Hz, 1 H), 7.38 - 7.33 (m, 2 H), 7.00 (dd, J = 8.6, 2.6 Hz, 1 H), 3.92 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.8, 155.1, 149.9, 145.5, 136.8, 135.7, 123.4, 123.3, 119.1, 115.1, 115.0, 102.7, 55.7. IR (KBr): 2938, 2212, 1599, 1561, 1475, 1431, 1334, 1302, 1232, 1023, 833, 791 cm^{-1}. MS (EI) *m/z*: 210 [M$^+$] (100), 195, 179, 166, 153, 140, 127, 113, 105, 88, 78.

4-Morpholino-2-(pyridin-2-yl)benzonitrile (3o)



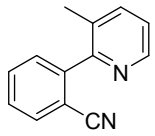
White solid (67 mg, 85 %), mp: 119 - 120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 - 8.72 (m, 1 H), 7.84 - 7.79 (m, 2 H), 7.63 (d, J = 8.4 Hz, 1 H), 7.36 - 7.32 (m, 1 H), 7.27 (d, J = 2.6 Hz, 1 H), 6.90 (dd, J = 8.8, 2.7 Hz, 1 H), 3.85 (t, J = 4.8 Hz, 4 H), 3.36 (t, J = 4.8 Hz, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.7, 153.4, 149.8, 144.7, 136.8, 135.3, 123.5, 123.3, 119.7, 115.0, 113.8, 99.5, 66.4, 47.3. IR (KBr): 3056, 2963, 2921, 2851, 2213, 1644, 1600, 1504, 1259, 793, 748 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{16}H_{15}N_3NaO$ [M+Na]$^+$: 288.1107; found: 288.1098.

2-(Pyridin-2-yl)thiophene-3-carbonitrile (3p)[4]



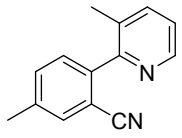
White solid (46 mg, 82 %), mp: 72 - 73 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.64 (d, J = 4.0 Hz, 1 H), 8.24 (d, J = 8.0 Hz, 1 H), 7.82 (td, J = 7.8, 1.8 Hz, 1 H), 7.42 (d, J = 5.2 Hz, 1 H), 7.34 - 7.28 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.6, 149.8, 149.6, 137.3, 130.8, 127.7, 123.9, 120.1, 115.9, 105.9. IR (KBr): 3110, 2921, 2851, 2224, 1578, 1462, 947, 782 cm^{-1}. MS (EI) *m/z*: 186 [M$^+$] (100), 159, 142, 114, 108, 93, 78.

2-(3-Methylpyridin-2-yl)benzonitrile (5a)[3]



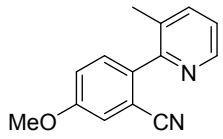
Yellow oil (48 mg, 82 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.56 (d, J = 4.4 Hz, 1 H), 7.79 - 7.76 (m, 1 H), 7.70 - 7.64 (m, 2 H), 7.53 - 7.48 (m, 2 H), 7.29 (dd, J = 7.8, 4.8 Hz, 1 H), 2.27 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.5, 147.1, 144.3, 138.5, 133.0, 132.6, 131.7, 129.9, 128.4, 123.5, 117.8, 112.5, 19.0. IR (KBr): 3055, 2222, 1562, 1438, 1417, 807, 757 cm^{-1}. MS (EI) *m/z*: 194 [M^{+}] (100), 168, 140, 113, 102, 83.

5-Methyl-2-(3-methylpyridin-2-yl)benzonitrile (5b)[3]



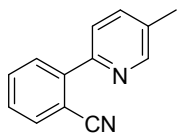
White solid (51 mg, 83 %), mp: 90 - 91 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.56 (s, 1 H), 7.64 (d, J = 8.0 Hz, 1 H), 7.57 (s, 1 H), 7.48 (d, J = 8.0 Hz, 1 H), 7.38 (d, J = 8.0 Hz, 1 H), 7.31 - 7.26 (m, 1 H), 2.44 (s, 3 H), 2.26 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.5, 147.0, 138.6, 138.5, 133.4, 133.3, 129.8, 123.4, 118.0, 112.2, 20.9, 19.1. IR (KBr): 3053, 2924, 2225, 1607, 1572, 1444, 1422, 1386, 843, 804 cm^{-1}. MS (EI) *m/z*: 208 [M^{+}], 207 (100), 192, 182, 167, 152, 140, 103, 89.

5-Methoxy-2-(3-methylpyridin-2-yl)benzonitrile (5c)[3]



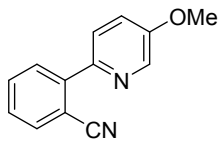
Yellow oil (58 mg, 87 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.55 (d, J = 4.0 Hz, 1 H), 7.63 (d, J = 8.0 Hz, 1 H), 7.41 (d, J = 8.6 Hz, 1 H), 7.28 - 7.24 (m, 2 H), 7.20 (dd, J = 8.6, 2.6 Hz, 1 H), 3.88 (s, 3 H), 2.27 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 155.3, 147.0, 138.4, 136.8, 131.8, 131.3, 123.3, 119.1, 117.8, 117.4, 113.2, 55.7, 19.1. IR (KBr): 3060, 3001, 2964, 2934, 2839, 2228, 1611, 1572, 1503, 1446, 1413, 1296, 1278, 1242, 1116, 1051, 890, 814 cm^{-1}. MS (EI) *m/z*: 224 [M^{+}] (100), 209, 197, 180, 159, 154, 140, 114, 102, 77, 63.

2-(5-Methylpyridin-2-yl)benzonitrile (5d)[4]



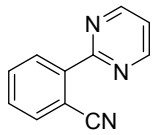
White solid (49 mg, 85 %), mp: 79 - 80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.61 (s, 1 H), 7.83 (d, J = 8 Hz, 1 H), 7.79 (d, J = 8 Hz, 1 H), 7.72 - 7.62 (m, 3 H), 7.48 (t, J = 7.6 Hz, 1 H), 2.42 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.3, 141.7, 137.4, 134.1, 133.2, 132.8, 129.8, 128.5, 122.7, 118.8, 111.0, 18.3. IR (KBr): 3070, 2923, 2851, 2223, 1595, 1497, 1470, 834, 748 cm^{-1}. MS (EI) *m/z*: 194 [M^{+}] (100), 179, 166, 151, 140, 128, 113, 100, 87, 75, 63.

2-(5-Methoxypyridin-2-yl)benzonitrile (5e)



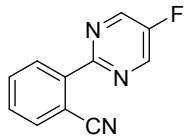
White solid (52 mg, 83 %), mp: 54 - 56 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.47 (d, J = 2.8 Hz, 1 H), 7.82 (d, J = 7.8 Hz, 1 H), 7.76 (t, J = 8.2 Hz, 2 H), 7.66 (t, J = 7.7 Hz, 1 H), 7.46 (t, J = 7.6 Hz, 1 H), 7.33 (dd, J = 8.6, 3.0 Hz, 1 H), 3.93 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 147.4, 143.2, 137.7, 134.1, 132.8, 129.7, 128.1, 123.6, 120.9, 119.0, 110.7, 55.7. IR (KBr): 3067, 2921, 2848, 2222, 1645, 1573, 1471, 1439, 1267, 1222, 1013, 731 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{13}H_{10}N_2NaO$ $[M+Na]^+$: 233.0685; found: 233.0688.

2-(Pyrimidin-2-yl)benzonitrile (5g)[4]



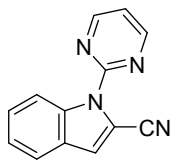
White solid (28 mg, 52 %), mp: 138 - 139 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.92 (d, J = 4.8 Hz, 2 H), 8.37 (dd, J = 8.0, 1.0 Hz, 1 H), 7.85 (dd, J = 7.6, 1.0 Hz, 1 H), 7.72 (td, J = 7.8, 1.2 Hz, 1 H), 7.57 (td, J = 7.6, 1.6 Hz, 1 H), 7.33 (t, J = 4.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.9, 157.3, 140.3, 135.1, 132.5, 130.4, 130.2, 120.1, 118.9, 111.9. IR (KBr): 3412, 2225, 1577, 1566, 1555, 1428, 1411, 818, 757 cm^{-1}. MS (EI) *m/z*: 181 [M^+] (100), 172, 154, 144, 128, 123, 101, 90, 75.

2-(5-Fluoropyrimidin-2-yl)benzonitrile (5h)



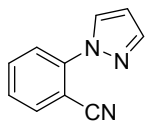
Light yellow solid (36 mg, 60 %), mp: 122 - 123 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (s, , 2 H), 8.33 (dd, J = 8.0, 0.8 Hz, 1 H), 7.85 (dd, J = 7.6, 0.8 Hz, 1 H), 7.71 (td, J = 7.8, 1.6 Hz, 1 H), 7.57 (td, J = 7.6, 1.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0 (d, $J_{C\text{-}F}$ = 5.7 Hz), 158.3, 155.7, 145.2 (d, $J_{C\text{-}F}$ = 20.4 Hz), 139.2, 133.8 (d, $J_{C\text{-}F}$ = 249.1 Hz), 130.4, 130.2, 118.7, 111.8. IR (KBr): 3045, 2923, 2854, 2220, 1655, 1554, 1430, 1260, 803, 749, 717 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{11}H_6FN_3Na$ $[M+Na]^+$: 222.0438; found: 222.0437.

1-(Pyrimidin-2-yl)-1H-indole-2-carbonitrile (5i)[3]



White solid (55 mg, 84 %), mp: 121 - 122 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.84 (d, J = 4.8 Hz, 2 H), 8.70 (dd, J = 8.6, 0.6 Hz, 1 H), 7.69 (d, J = 8.0 Hz, 1 H), 7.53 - 7.48 (m, 1 H), 7.48 (s, 1 H), 7.36 - 7.31 (m, 1 H), 7.24 (t, J = 4.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.3, 153.3, 136.6, 127.8, 127.5, 123.5, 122.0, 121.0, 118.0, 116.1, 114.2, 109.0. IR (KBr): 3102, 2227, 1568, 1532, 1449, 1428, 1333, 1257, 814, 731 cm^{-1}. MS (EI) *m/z*: 220 [M^+] (100), 207, 194, 169, 141, 114, 110, 88, 79.

2-(1*H*-pyrazol-1-yl)benzonitrile (5j)[4]



Colorless oil (22 mg, 45 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, J = 2.4 Hz, 1 H), 7.82 - 7.75 (m, 3 H), 7.70 (td, J = 7.6, 1.2 Hz, 1 H), 7.42 (td, J = 7.6, 0.8 Hz, 1 H), 6.54 (t, J = 2.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.2, 142.0, 134.4, 134.0, 129.5, 127.2, 124.3, 116.9, 108.4, 105.3. IR (KBr): 3059, 2963, 2922, 2856, 2228, 1657, 1515, 1459, 803, 760, 675 cm^{-1}. MS (EI) *m/z*: 169 [M$^+$] (100), 142, 129, 115, 102, 88, 75.

Reference

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2. (a) G. Zhang, X. Ren, J. Chen and M. Hu, J. Cheng, *Org. Lett.* 2011, **13**, 5004.

   (b) J. Kim, J. Choi, K. Shin and S. Chang, *J. Am. Chem. Soc.* 2012, **134**, 2528.

   (c) L. Zhang, P. Lu and Y. Wang, *Chem. Commun.* 2014, **51**, 2840.

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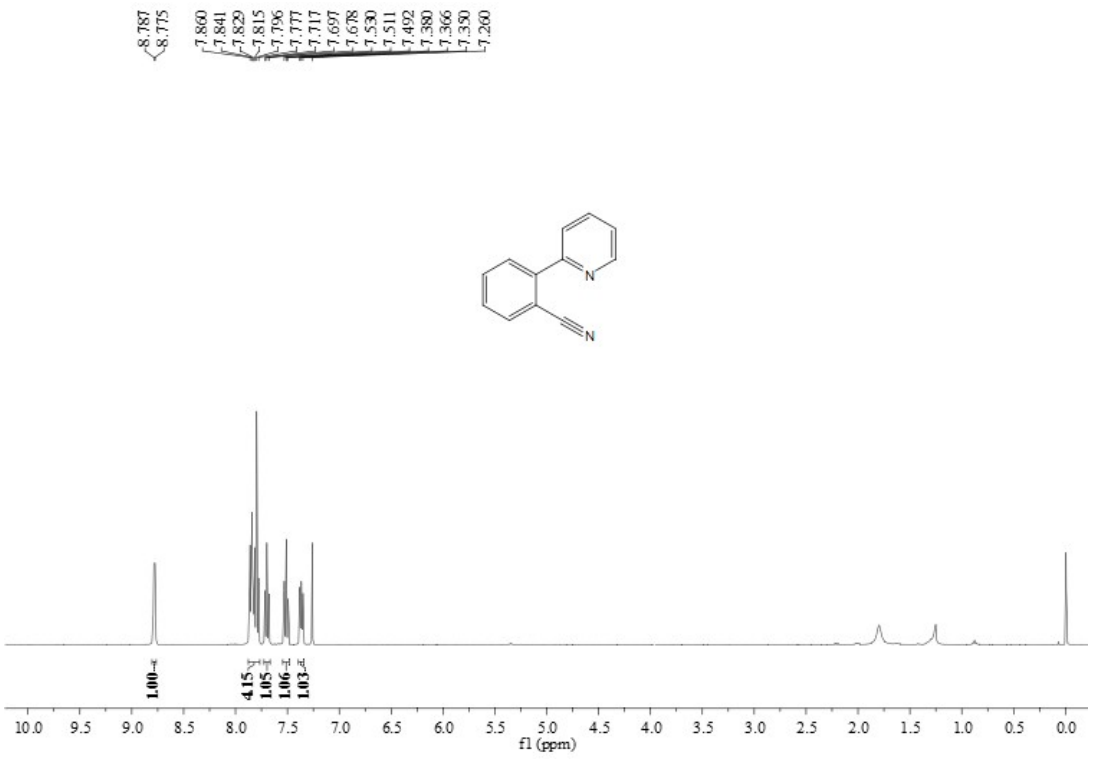
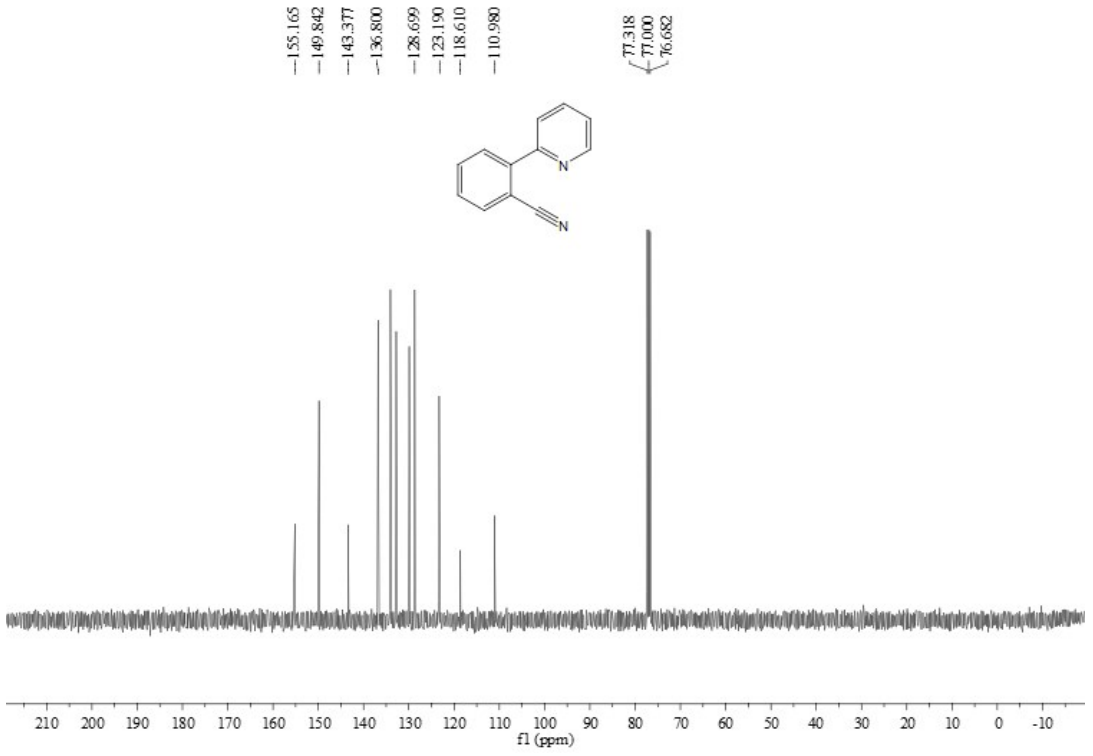
6. H. Xu, P.-T. Liu, Y.-H. Li and F.-S.Han, *Org. Lett.* 2013, **15**, 3354.

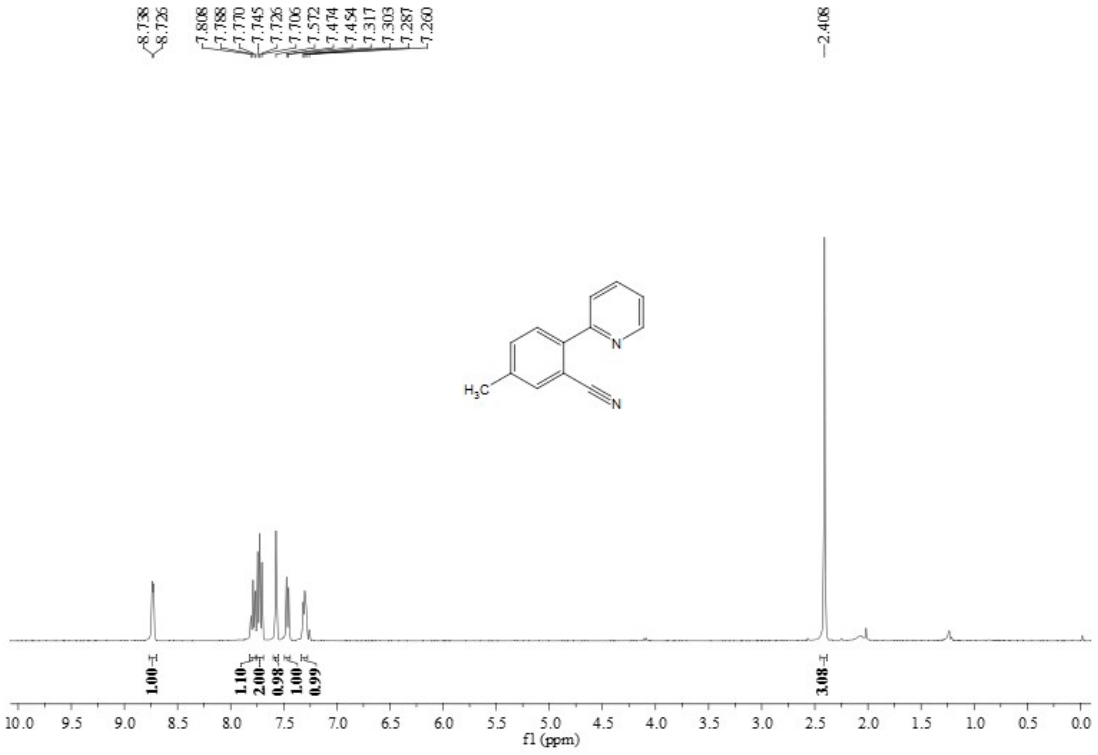
G. NMR spectra

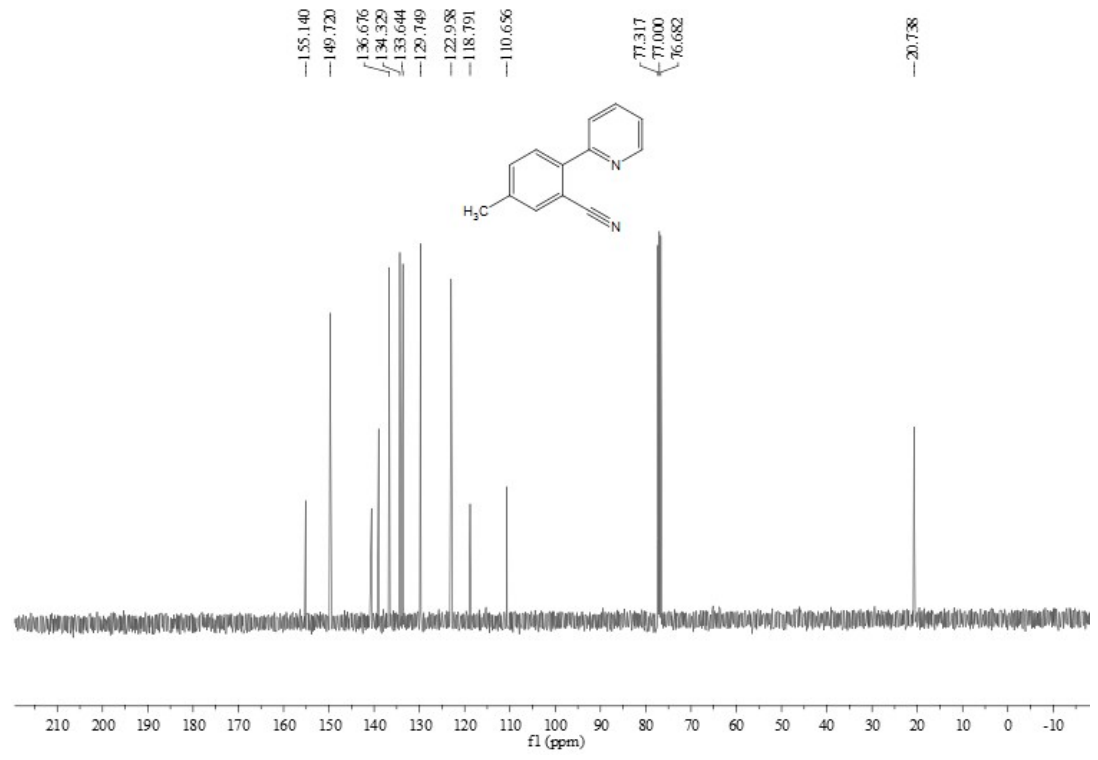
2-(Pyridin-2-yl)benzonitrile (3a)



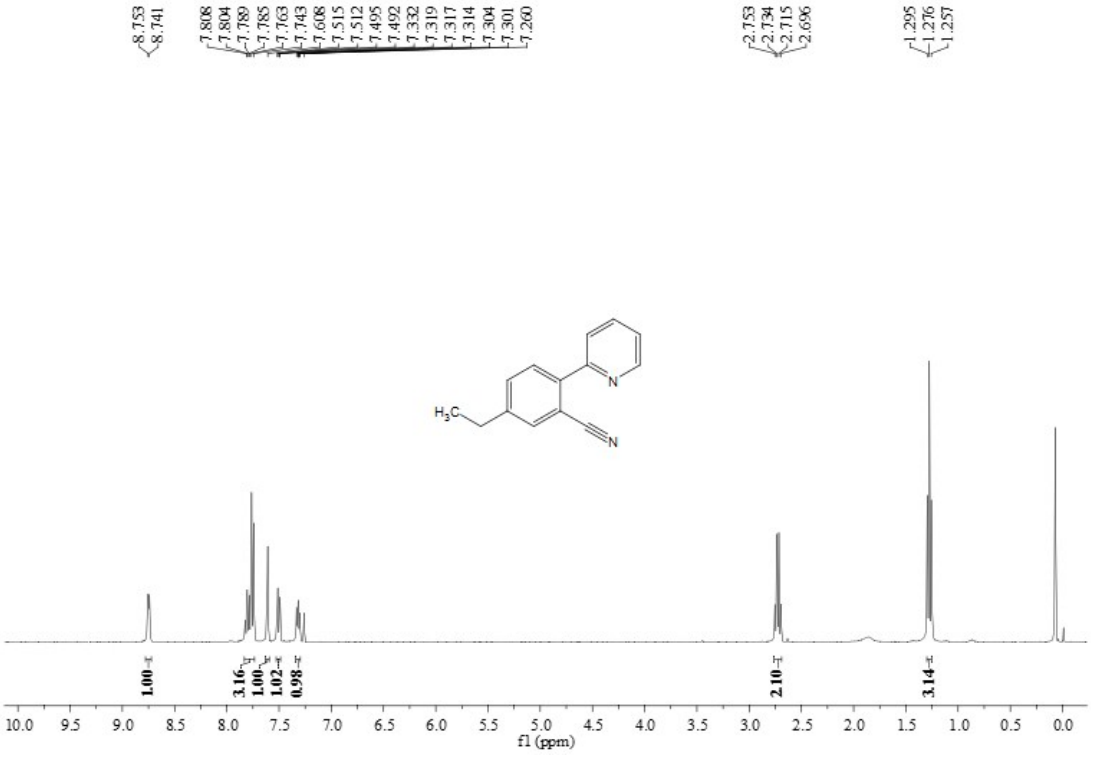


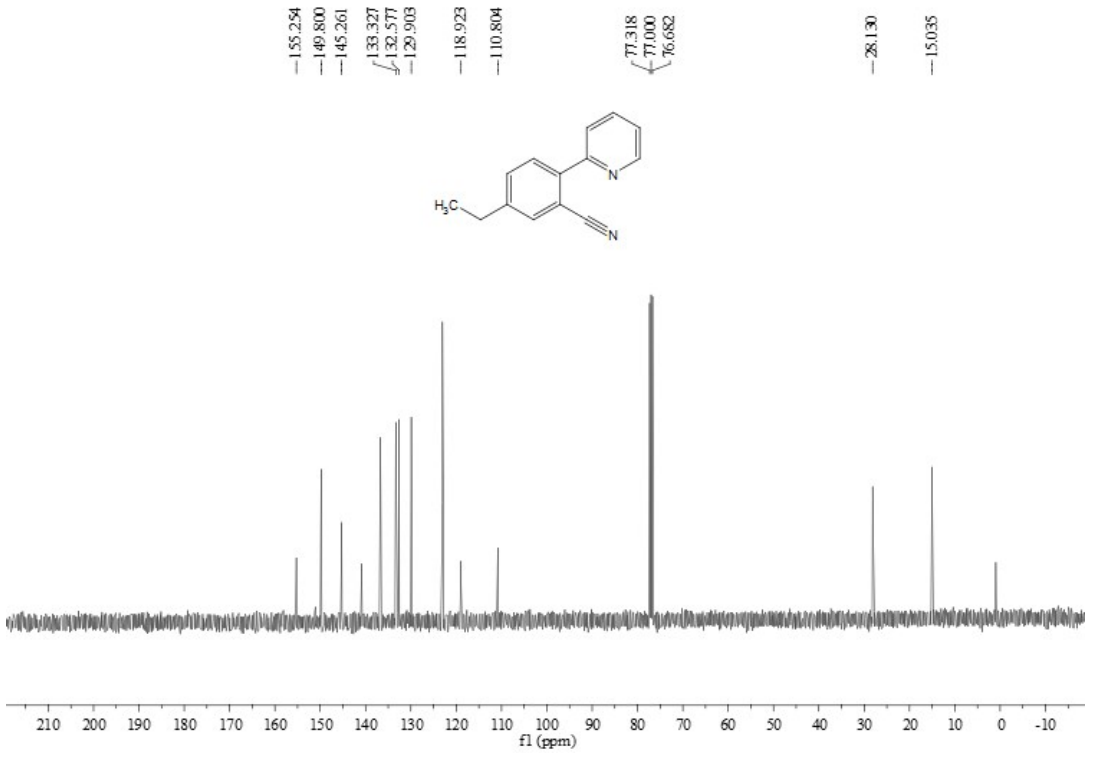
5-Methyl-2-(pyridin-2-yl)benzonitrile (3b)



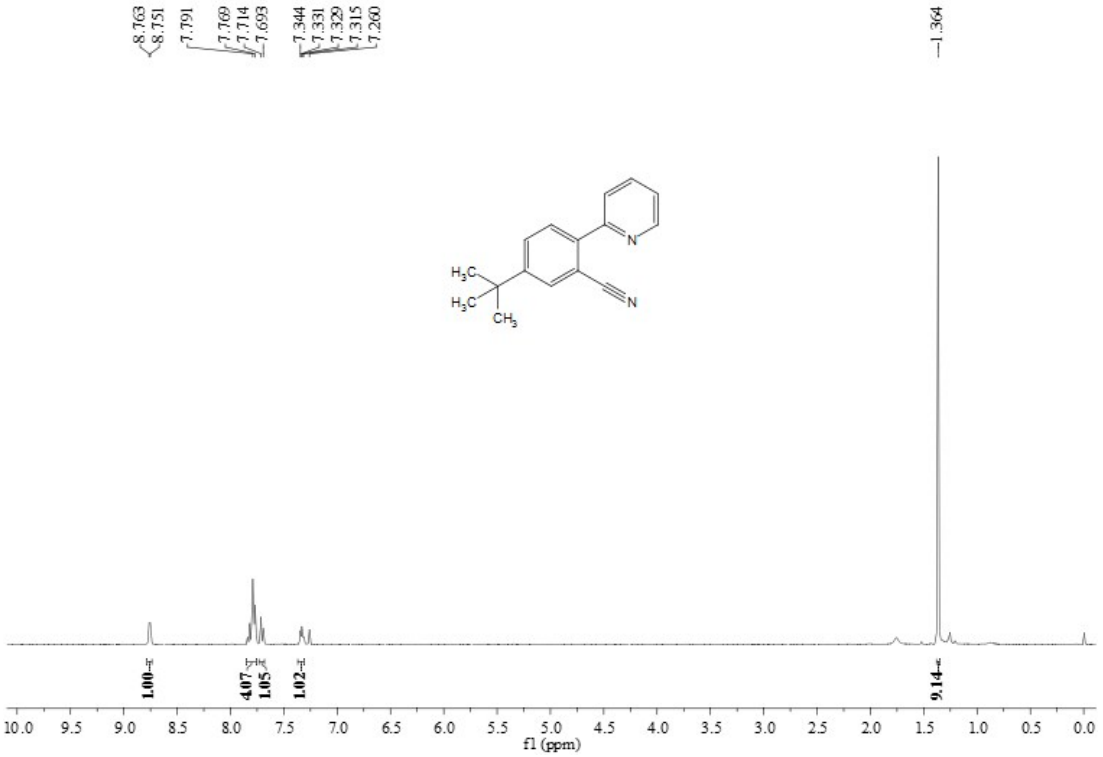


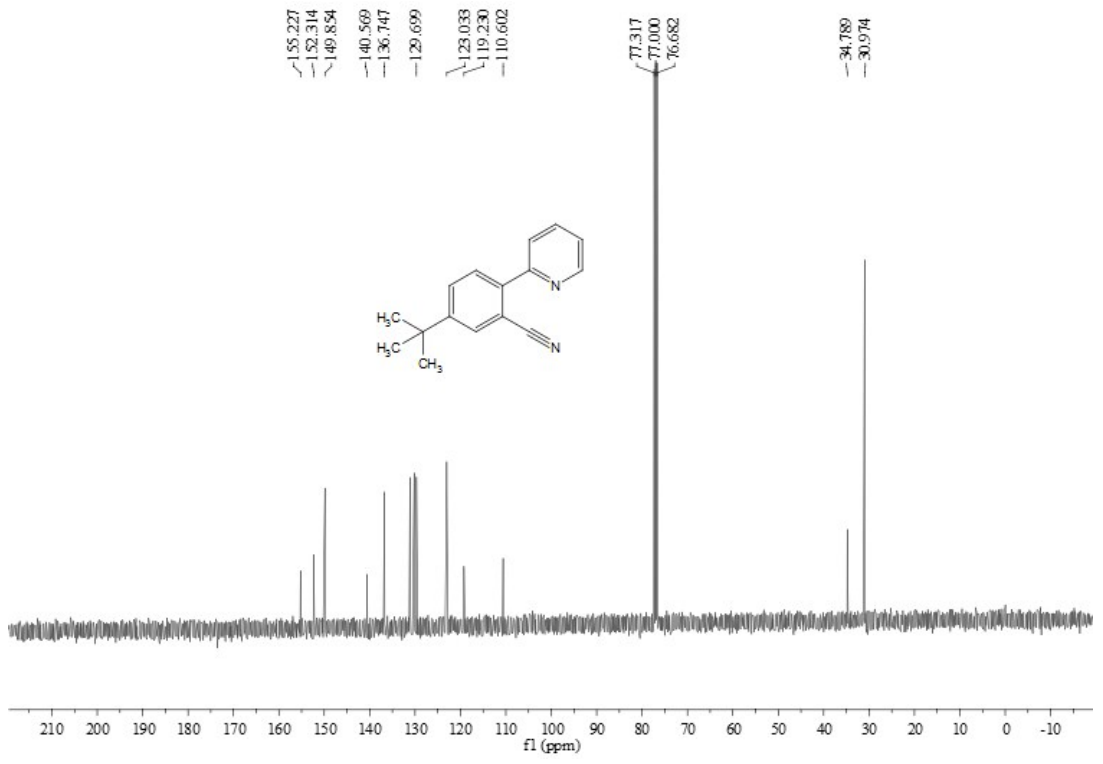
5-Ethyl-2-(pyridin-2-yl)benzonitrile (3c)



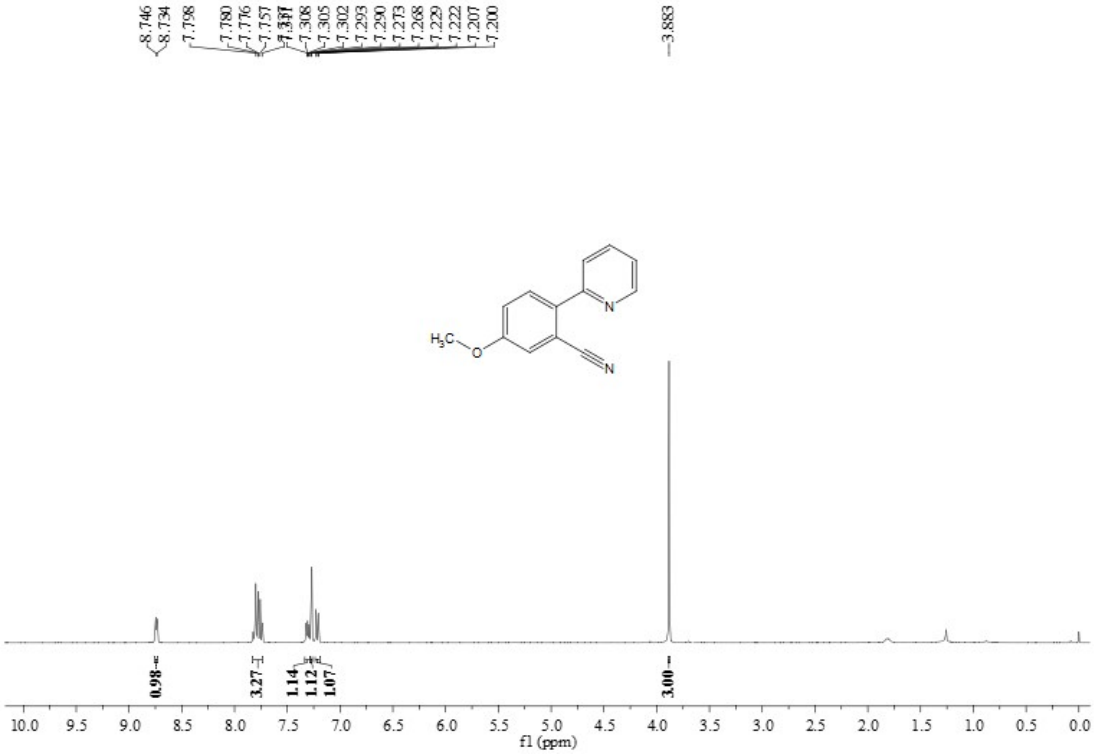


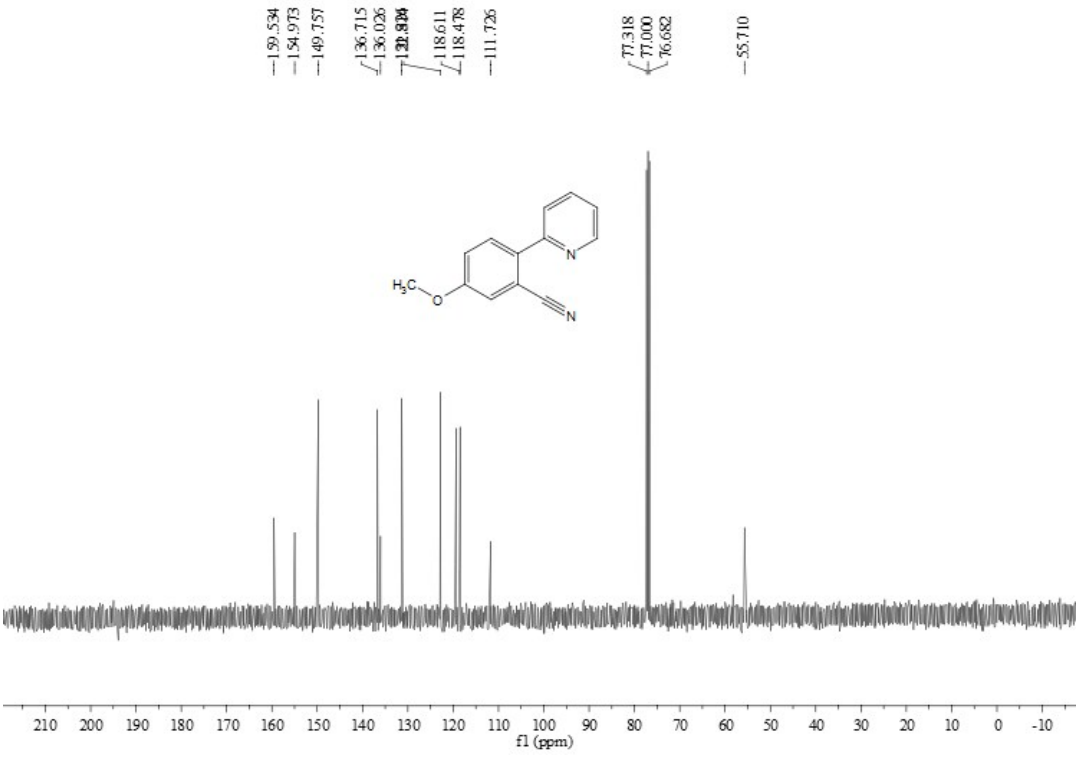
5-(Tert-butyl)-2-(pyridin-2-yl)benzonitrile (3d)



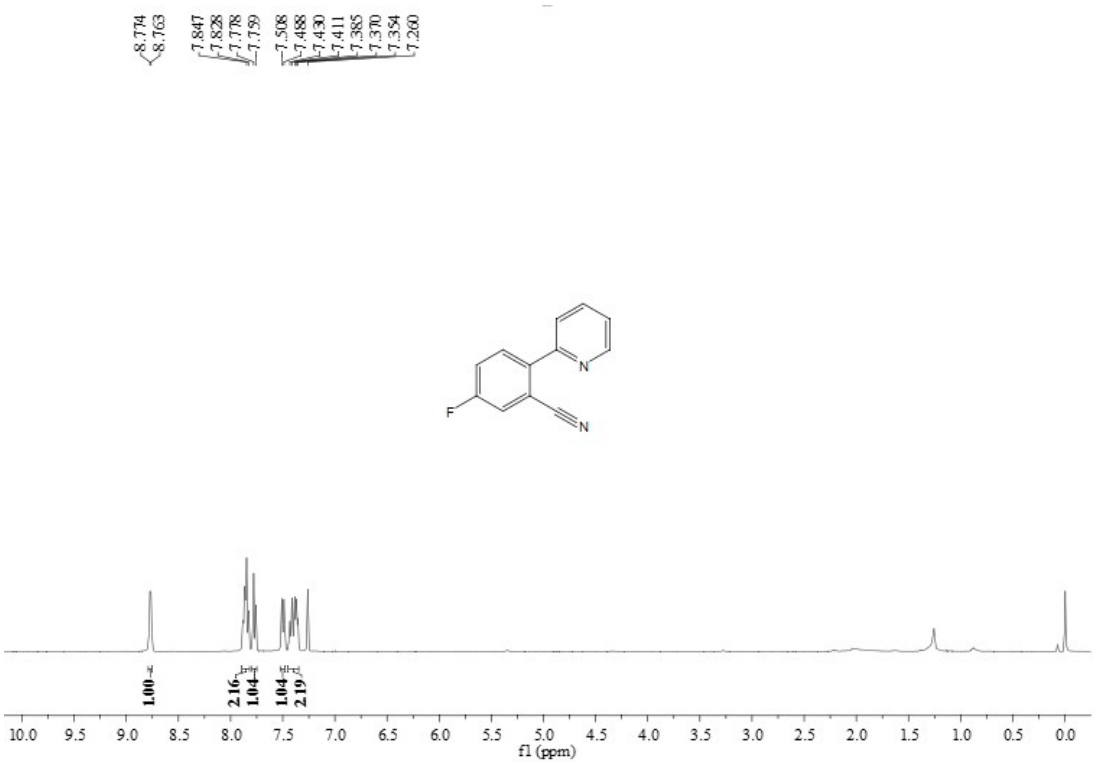


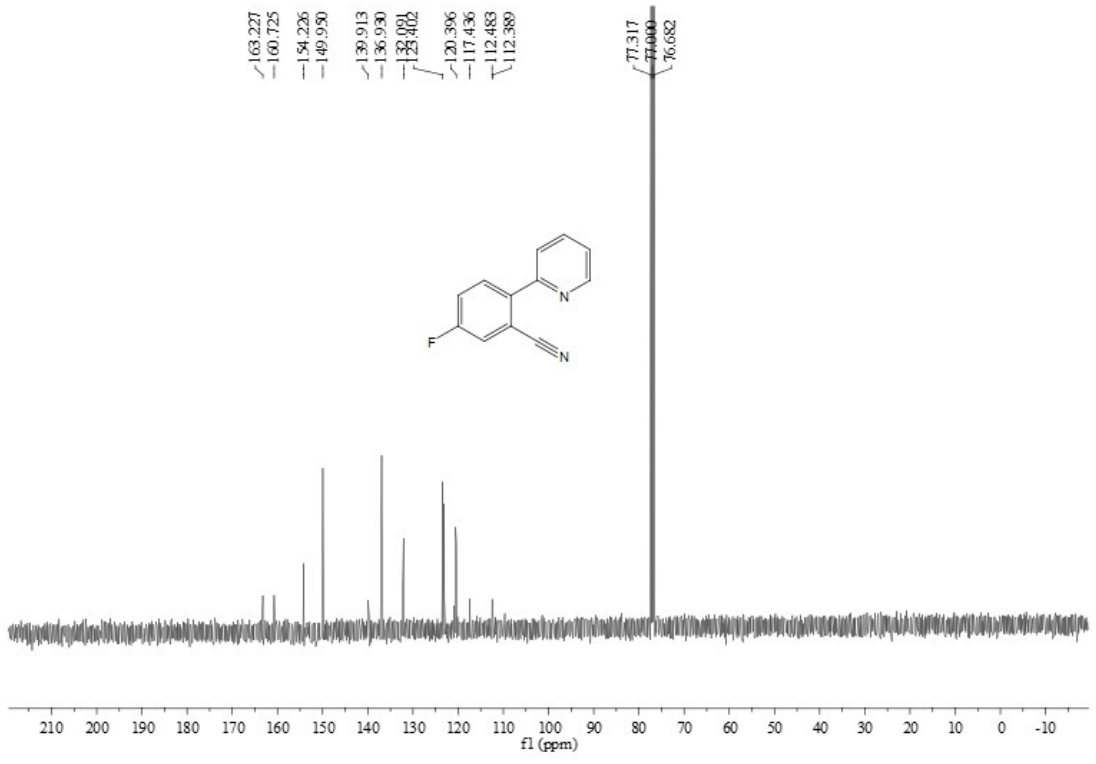
5-Methoxy-2-(pyridin-2-yl)benzonitrile (3e)



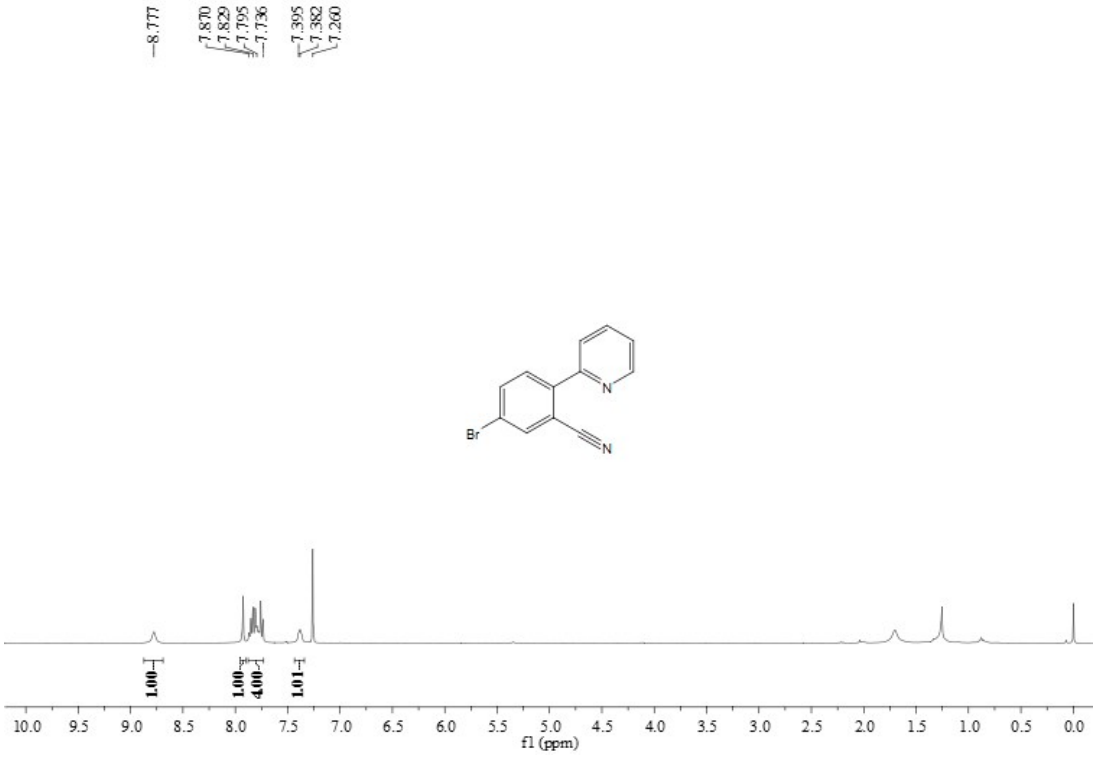


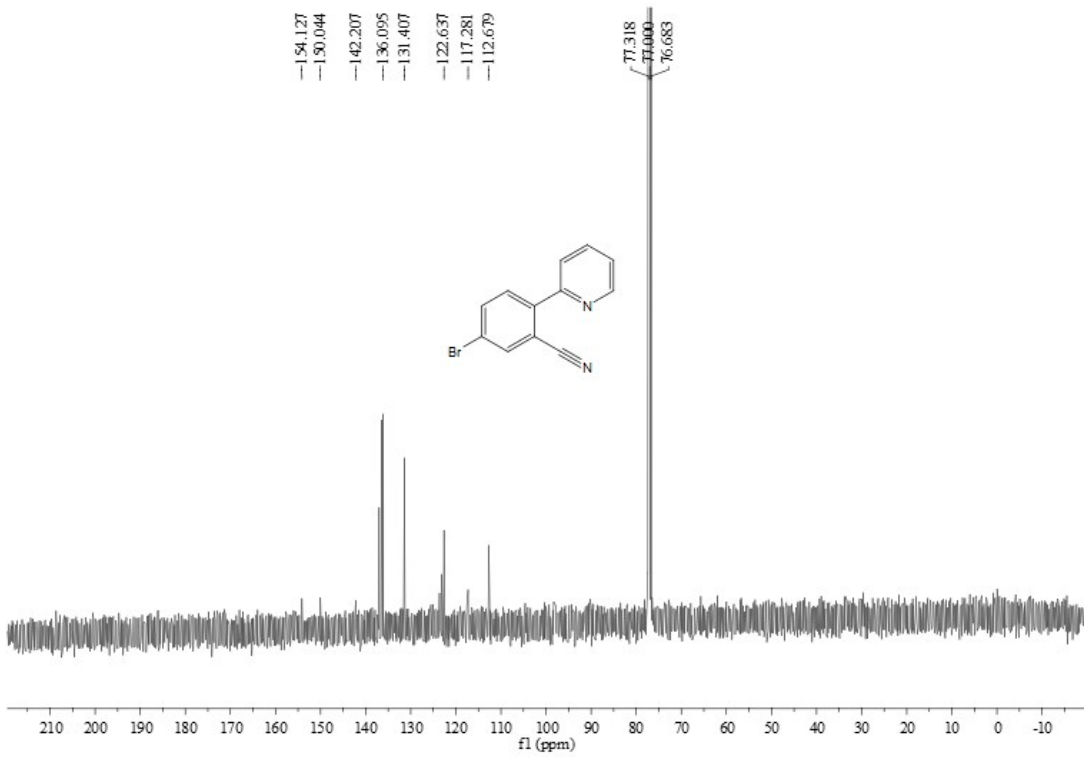
5-Fluoro-2-(pyridin-2-yl)benzonitrile (3f)



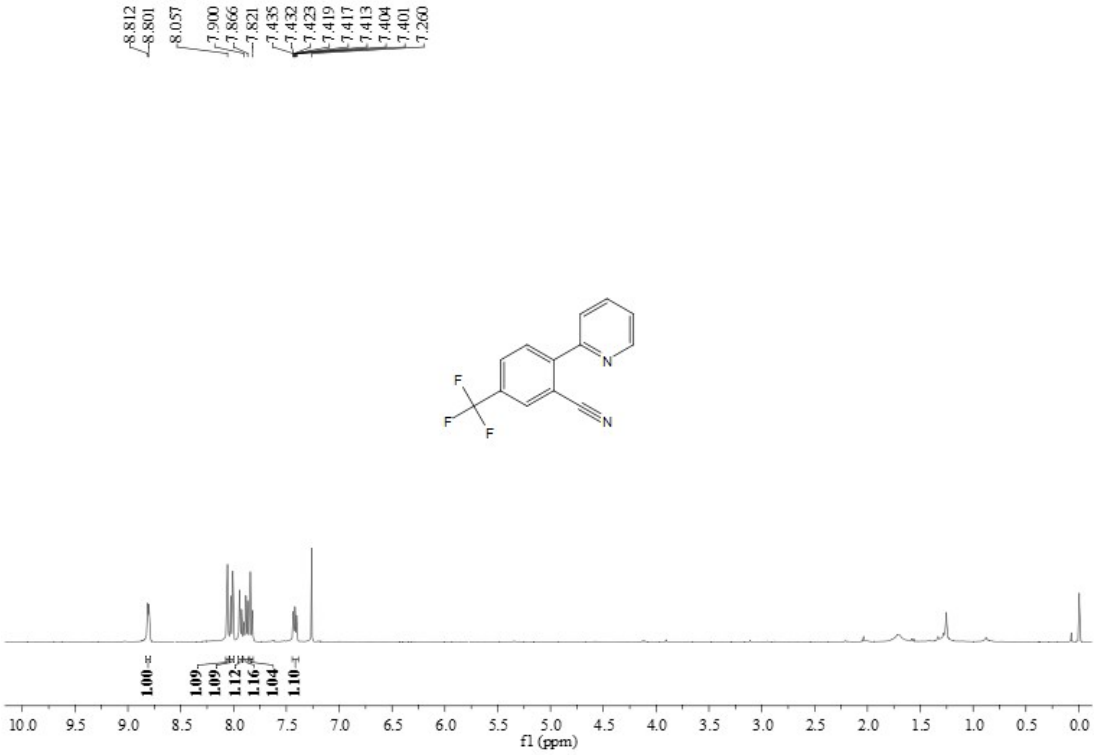


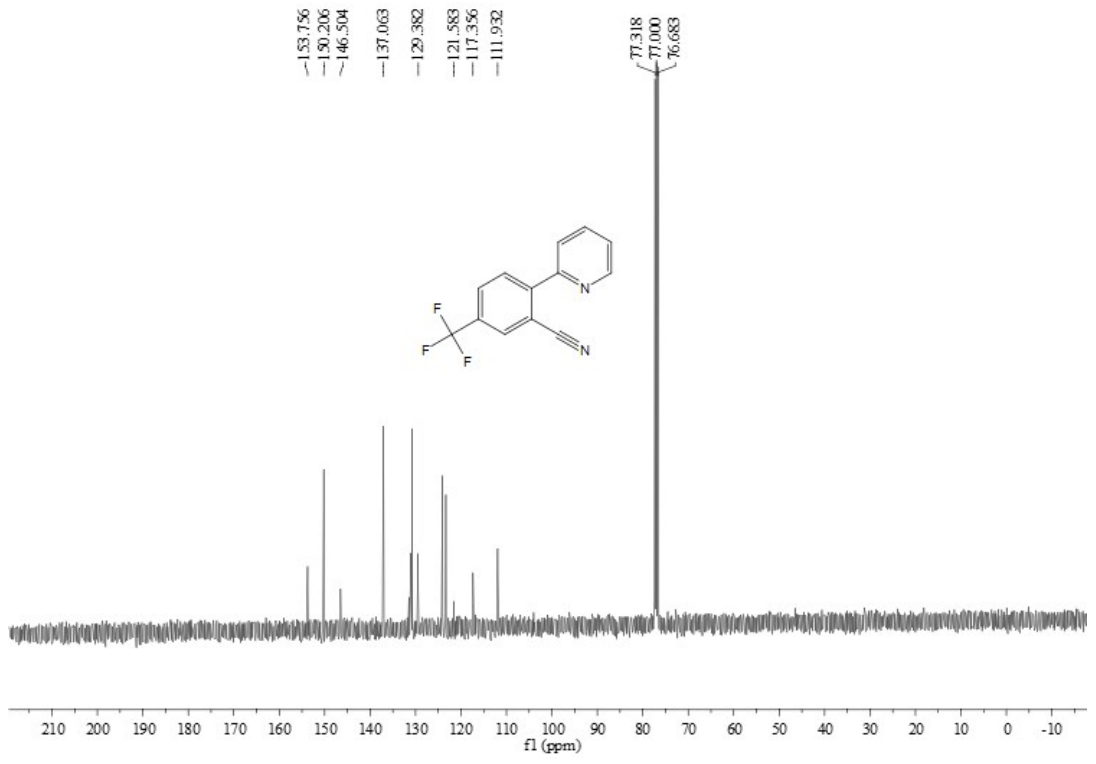
5-Bromo-2-(pyridin-2-yl)benzonitrile (3g)



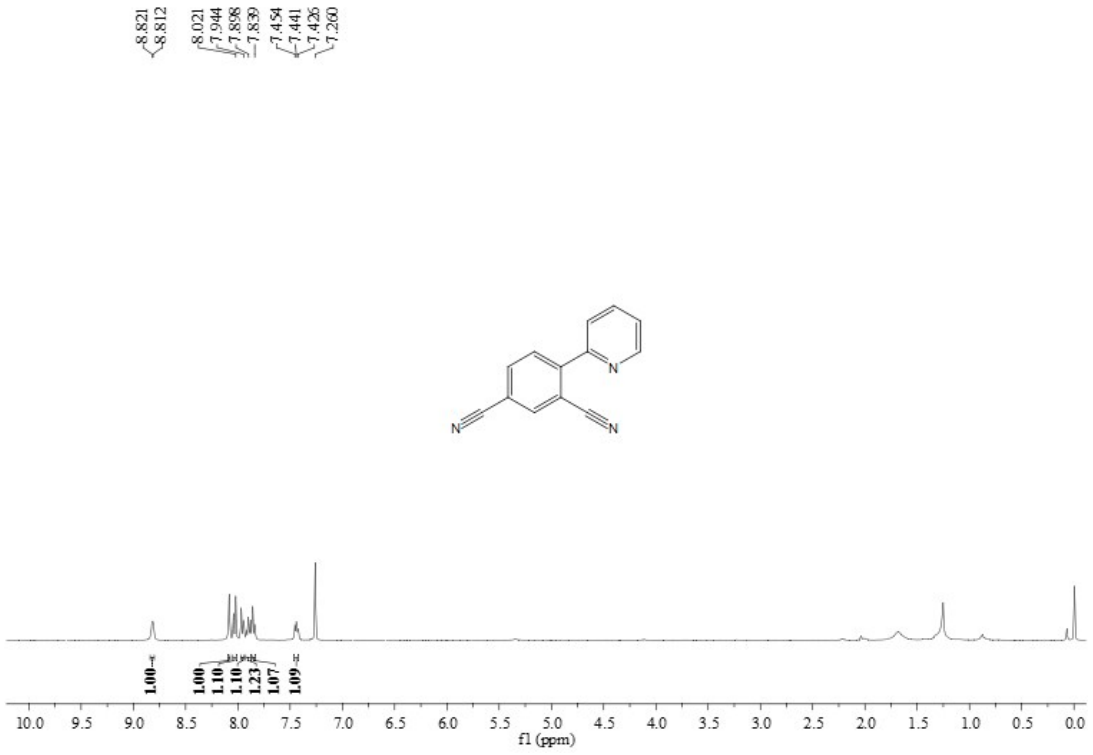


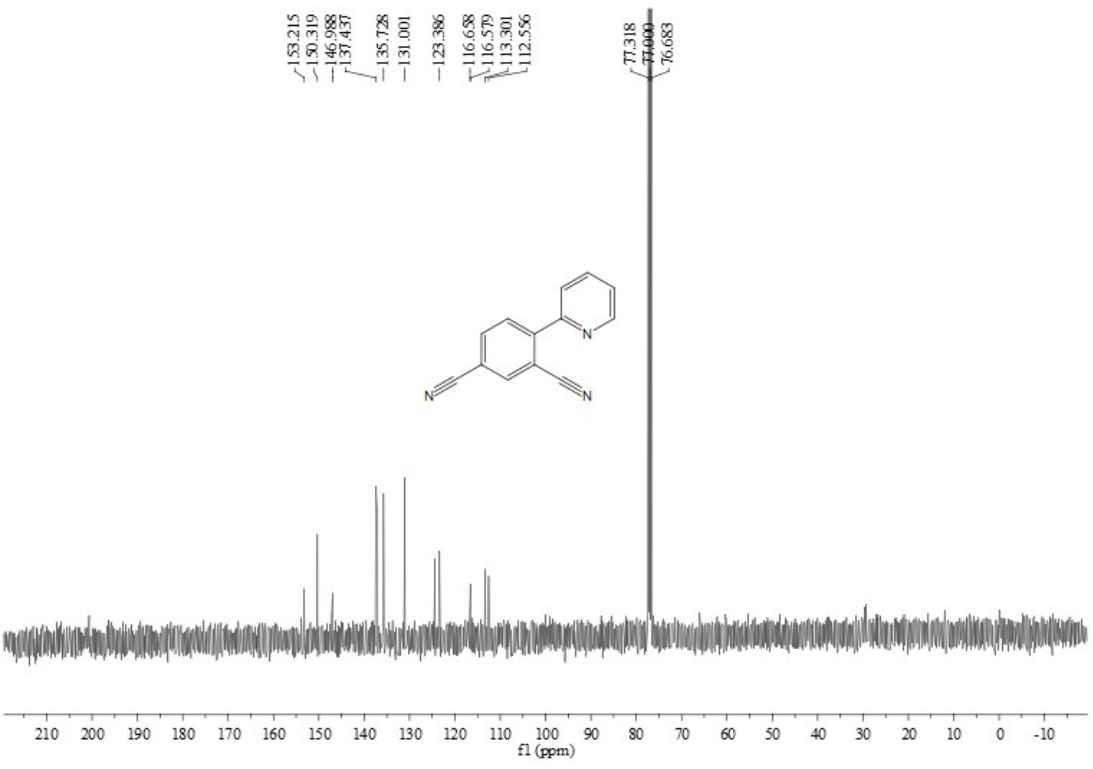
2-(Pyridin-2-yl)-5-(trifluoromethyl)benzonitrile (3h)



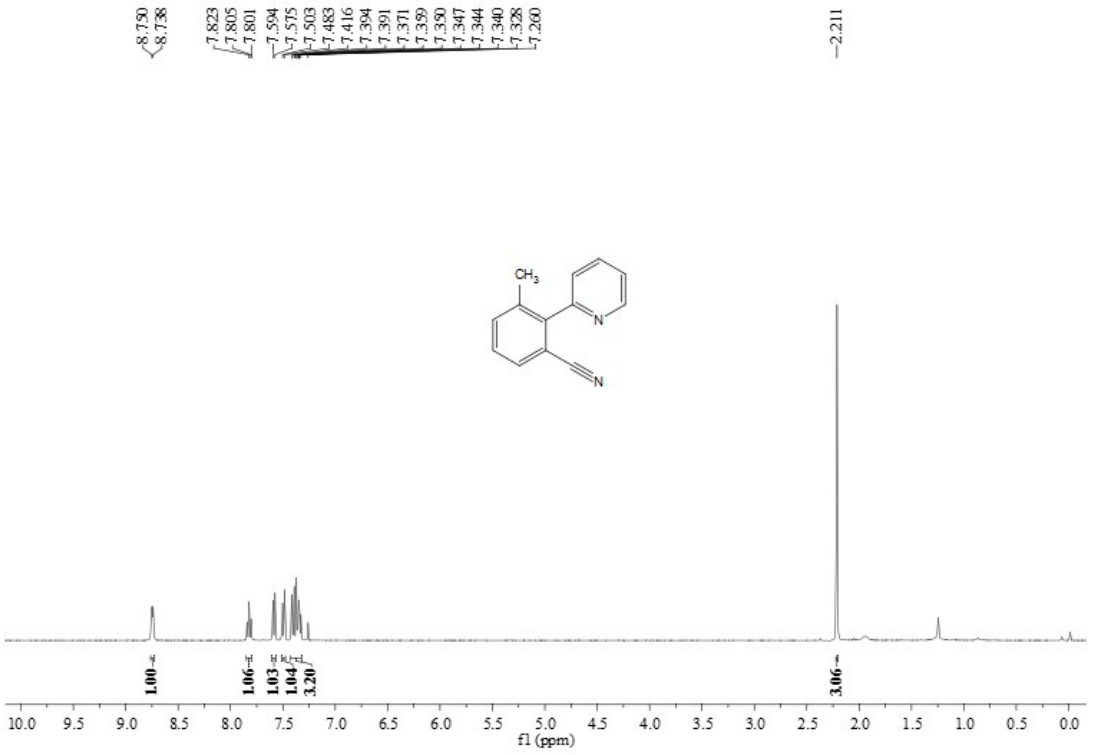


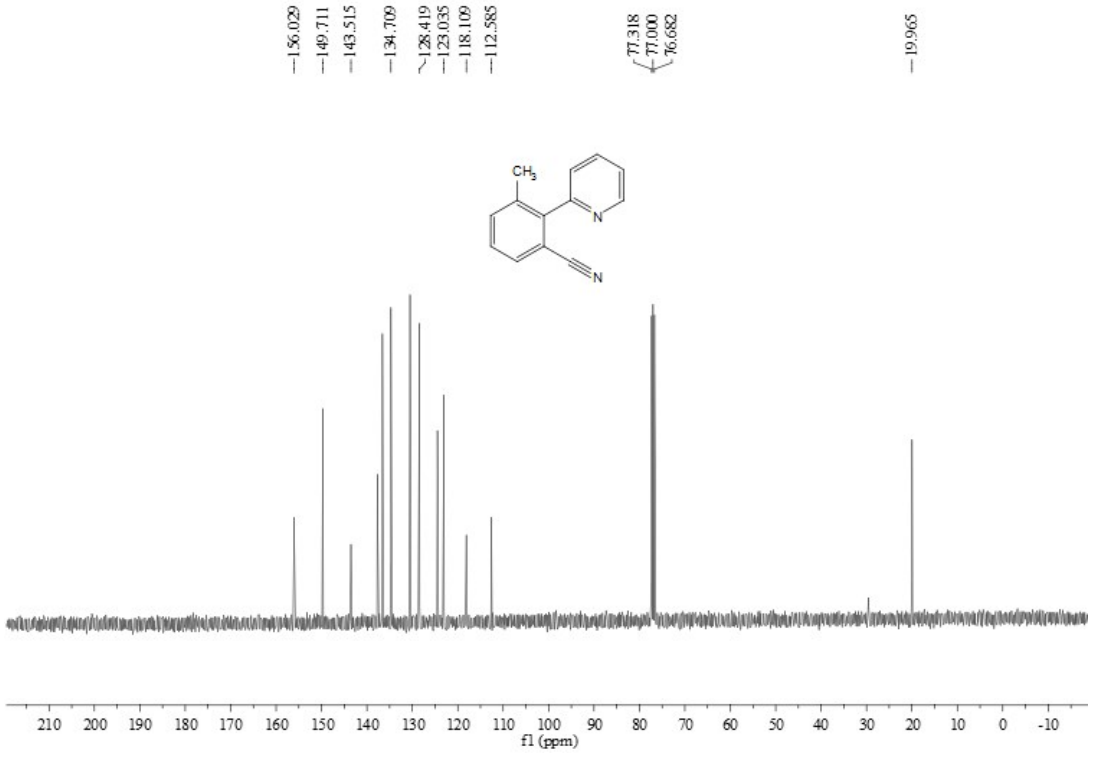
4-(Pyridin-2-yl)isophthalonitrile (3i)



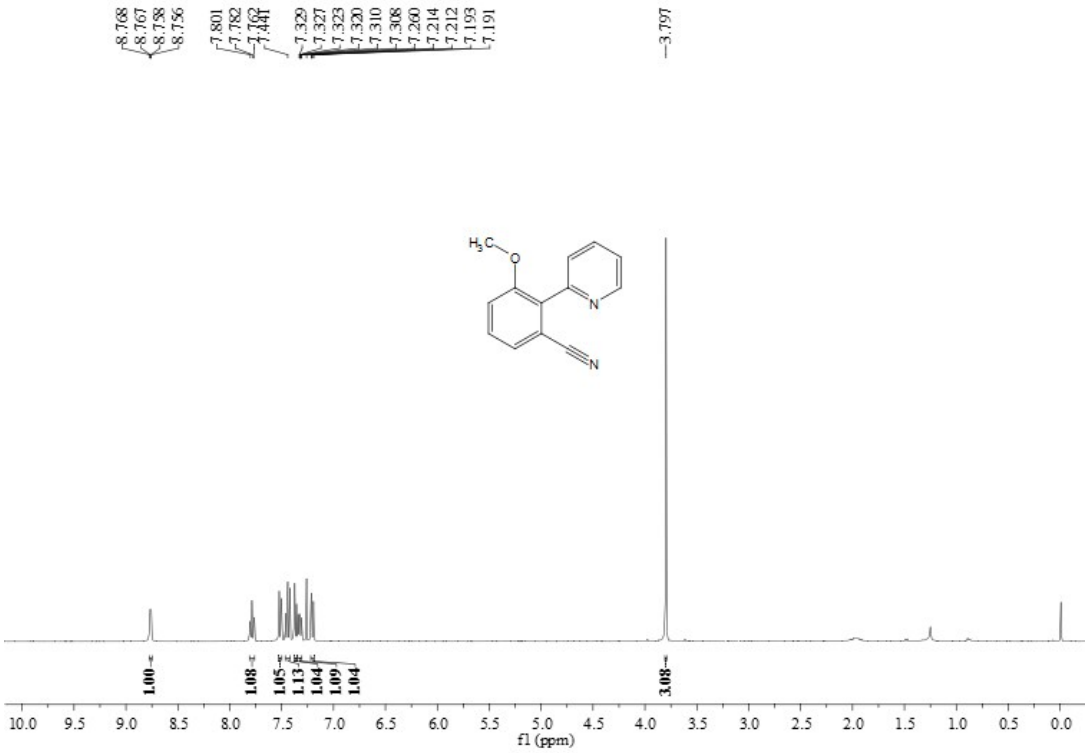


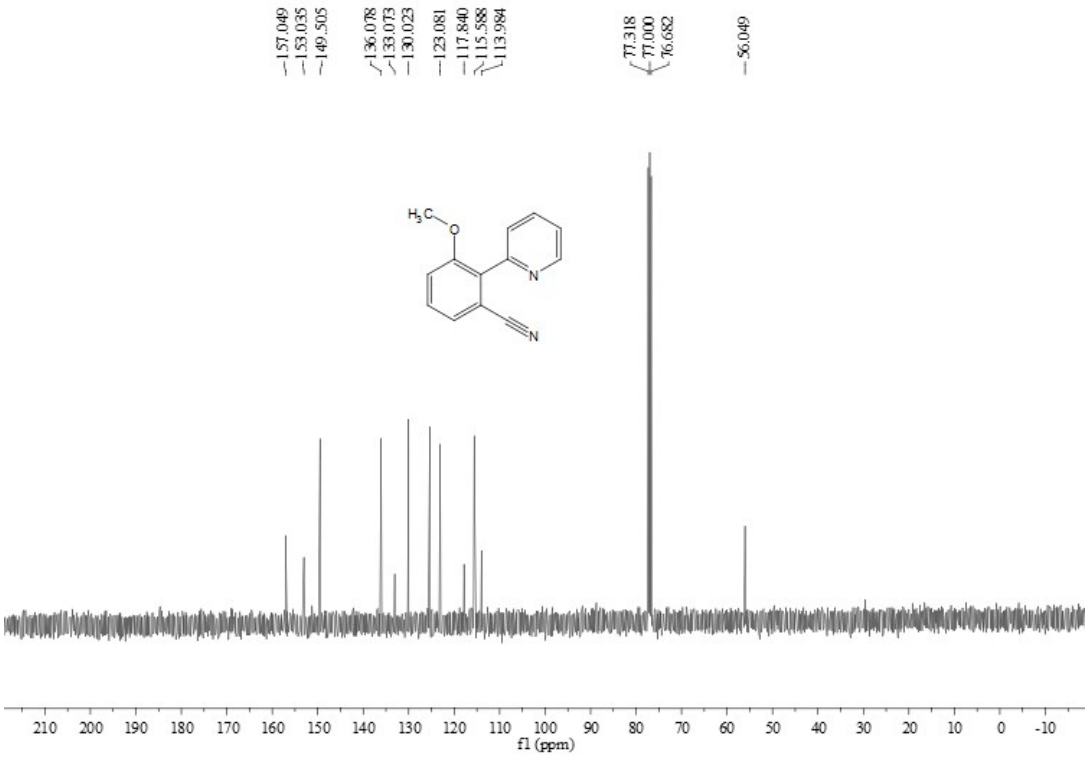
3-Methyl-2-(pyridin-2-yl)benzonitrile (3j)



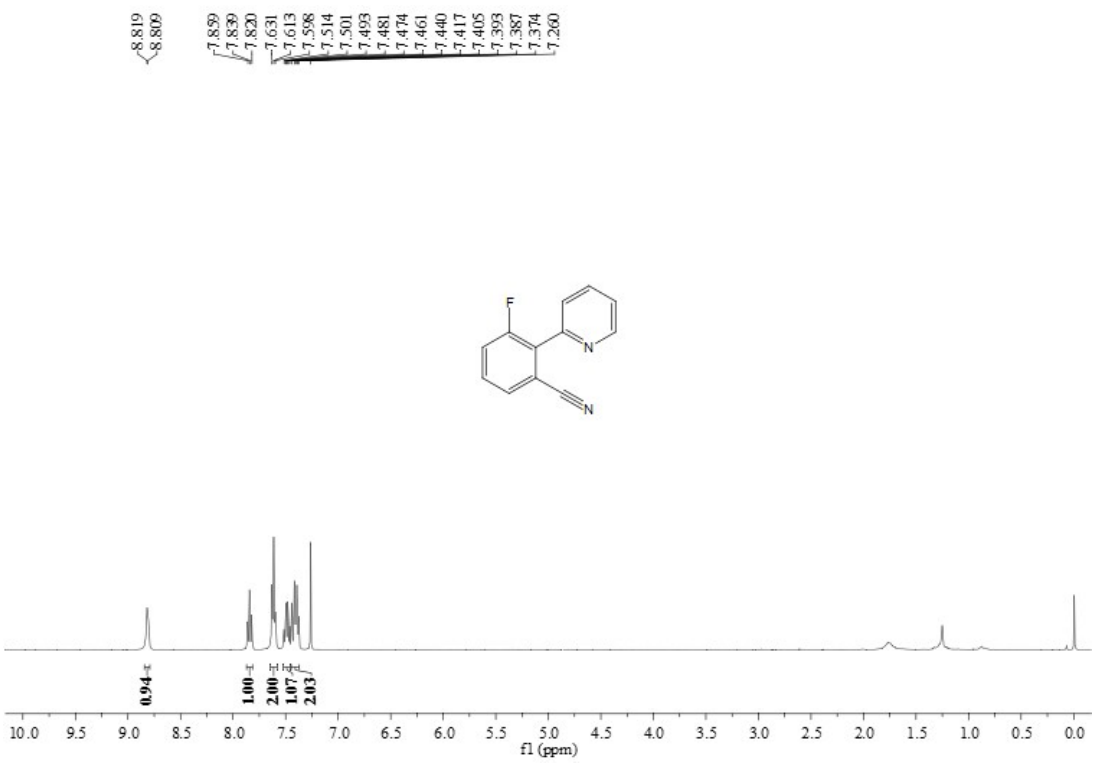


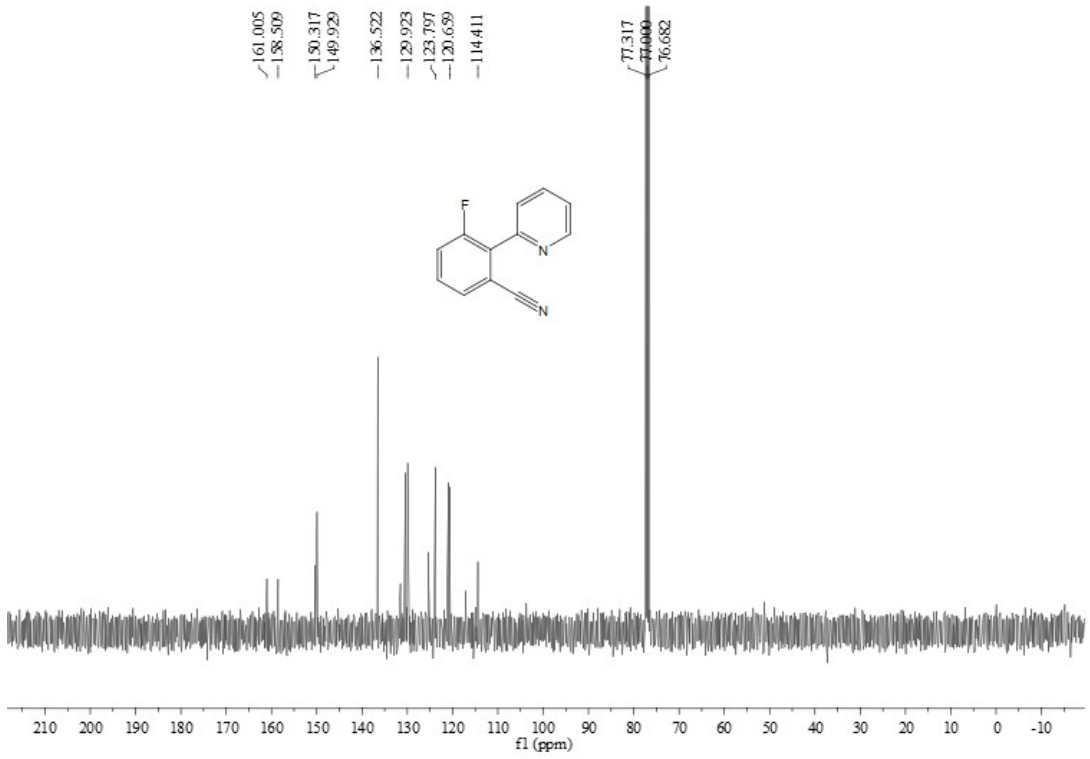
3-Methoxy-2-(pyridin-2-yl)benzonitrile (3k)



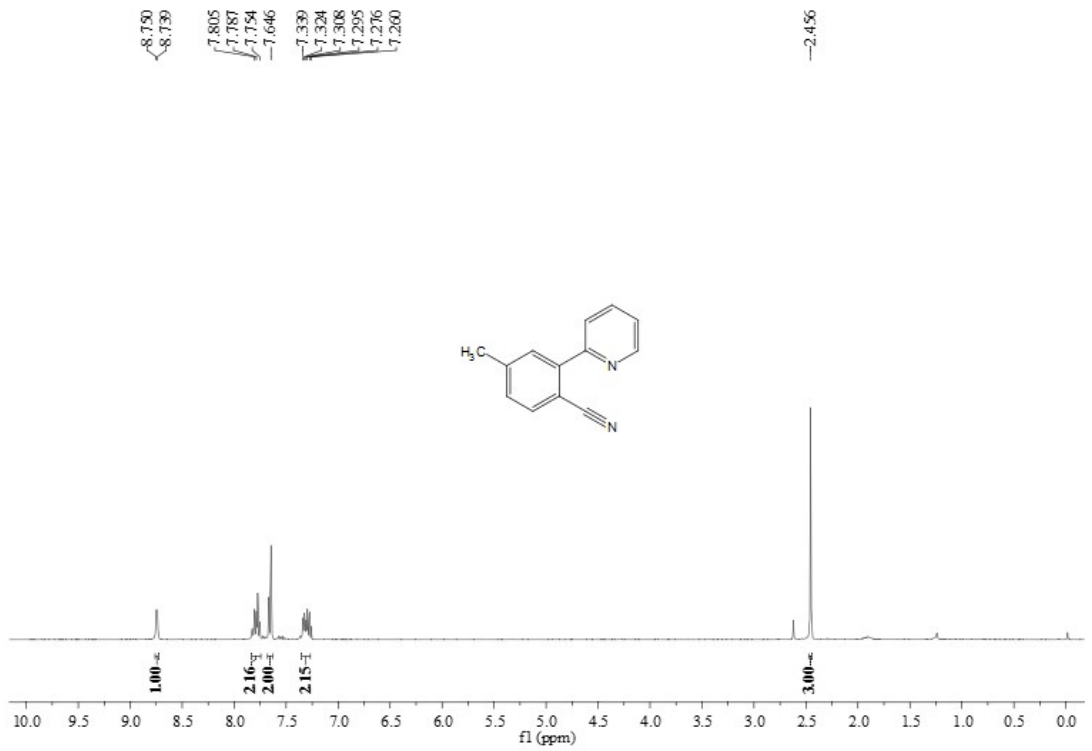


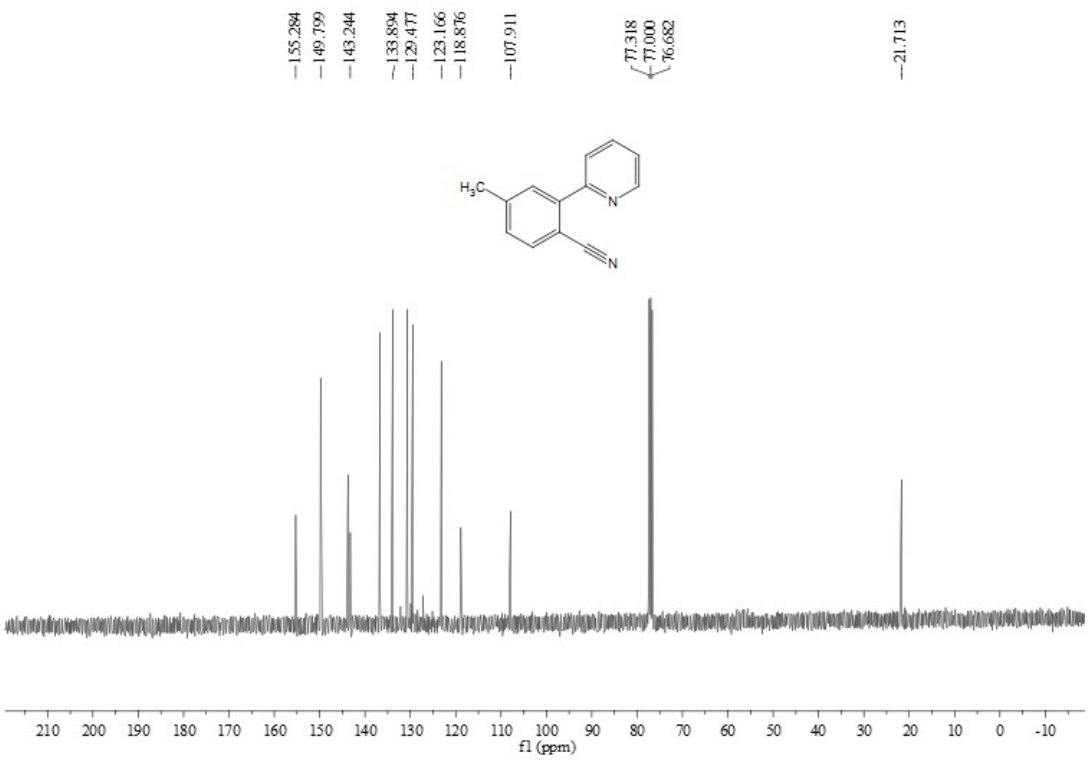
3-Fluoro-2-(pyridin-2-yl)benzonitrile (3l)



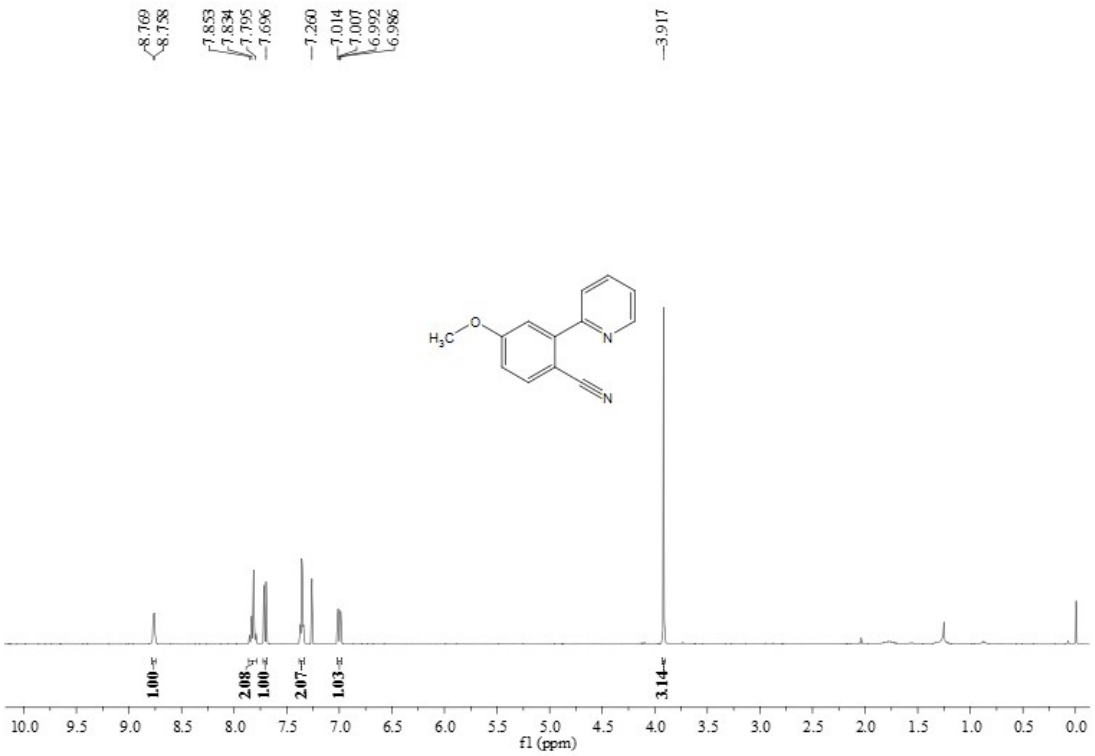


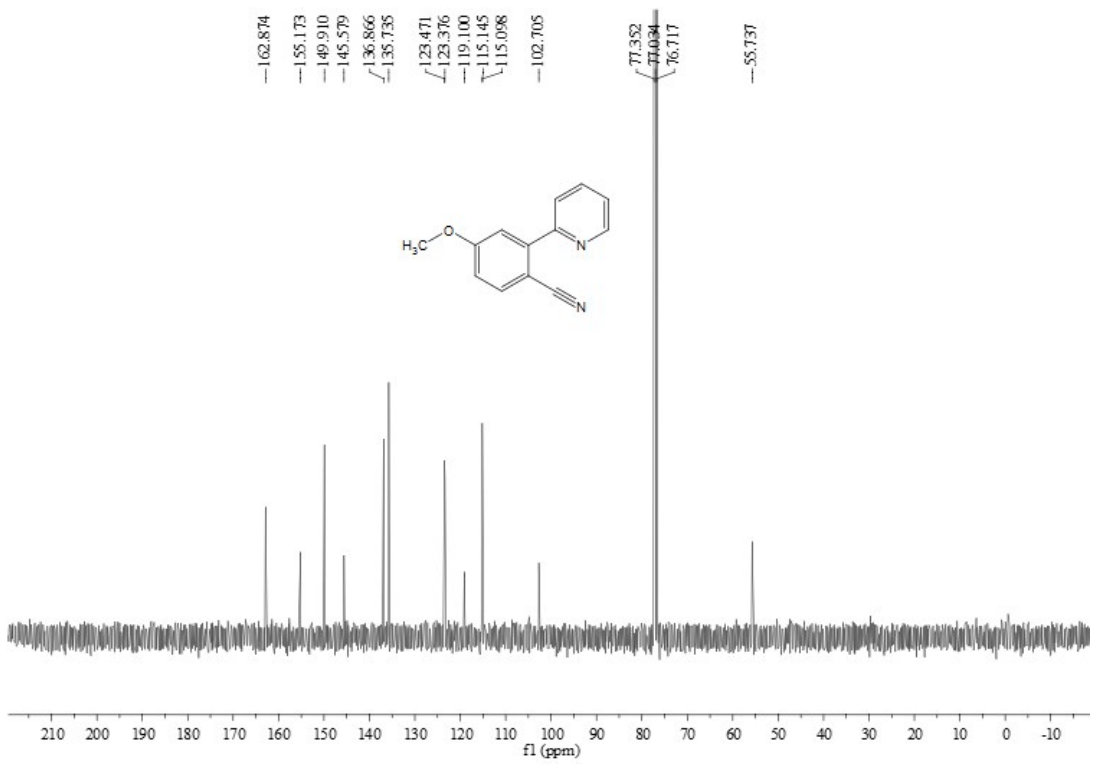
4-Methyl-2-(pyridin-2-yl)benzonitrile (3m)



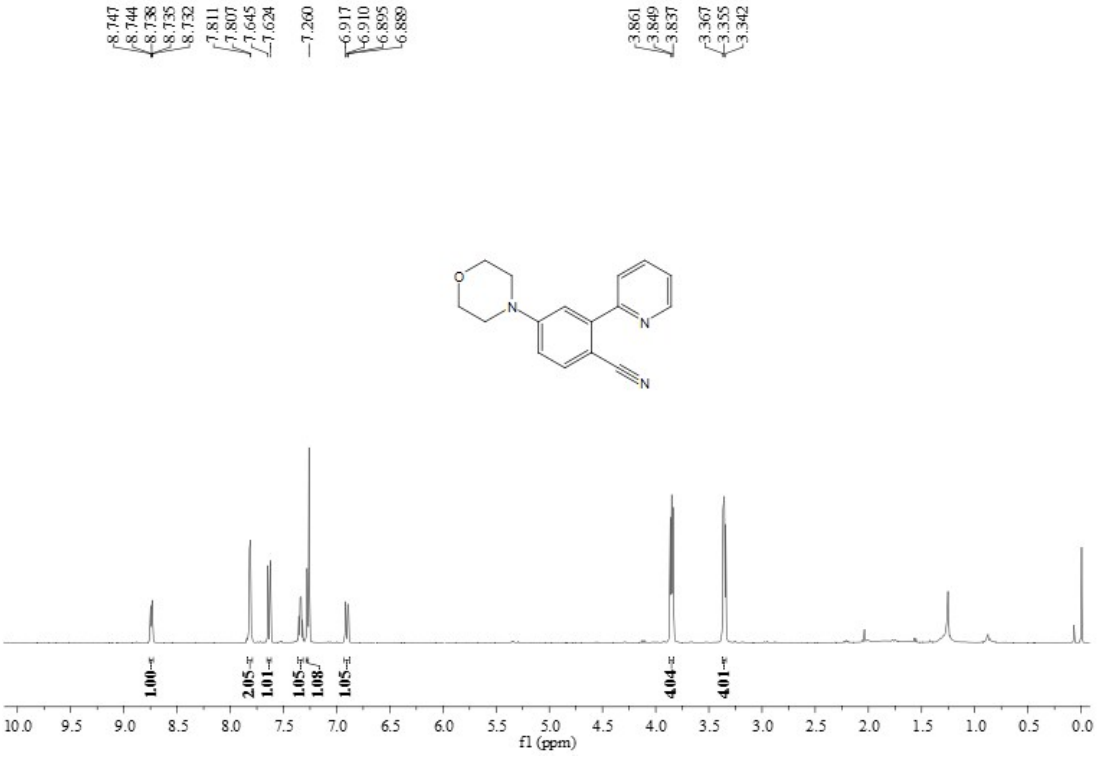


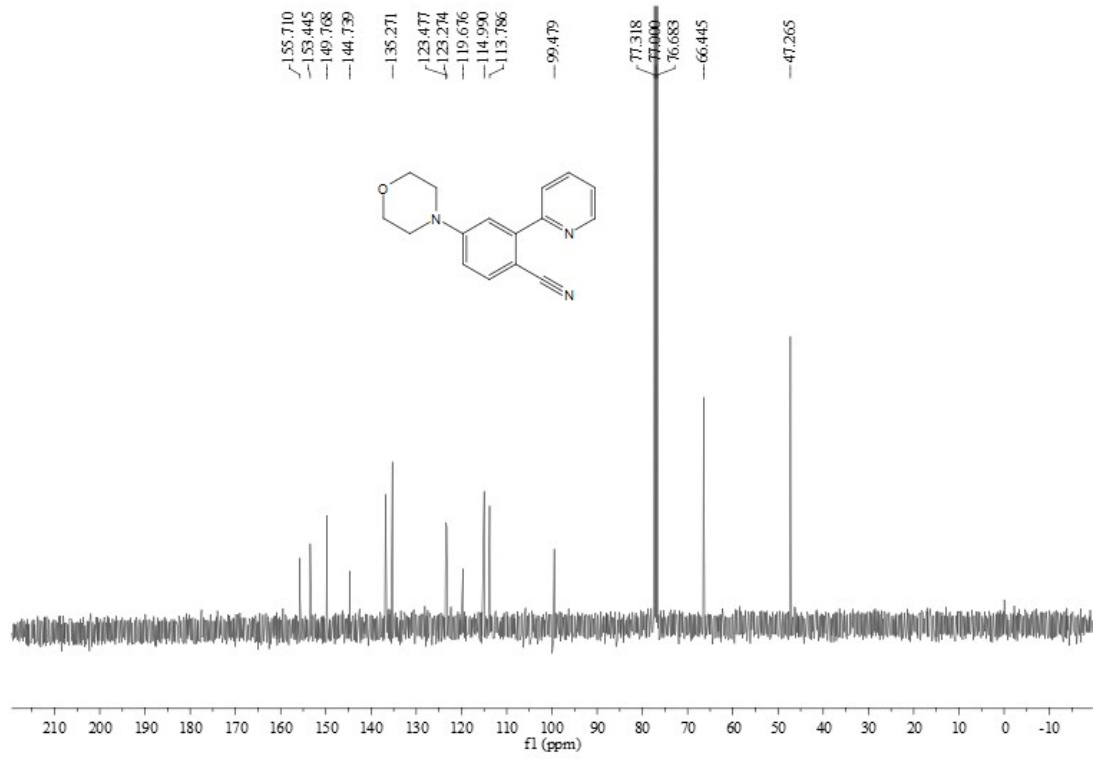
4-Methoxy-2-(pyridin-2-yl)benzonitrile (3n)



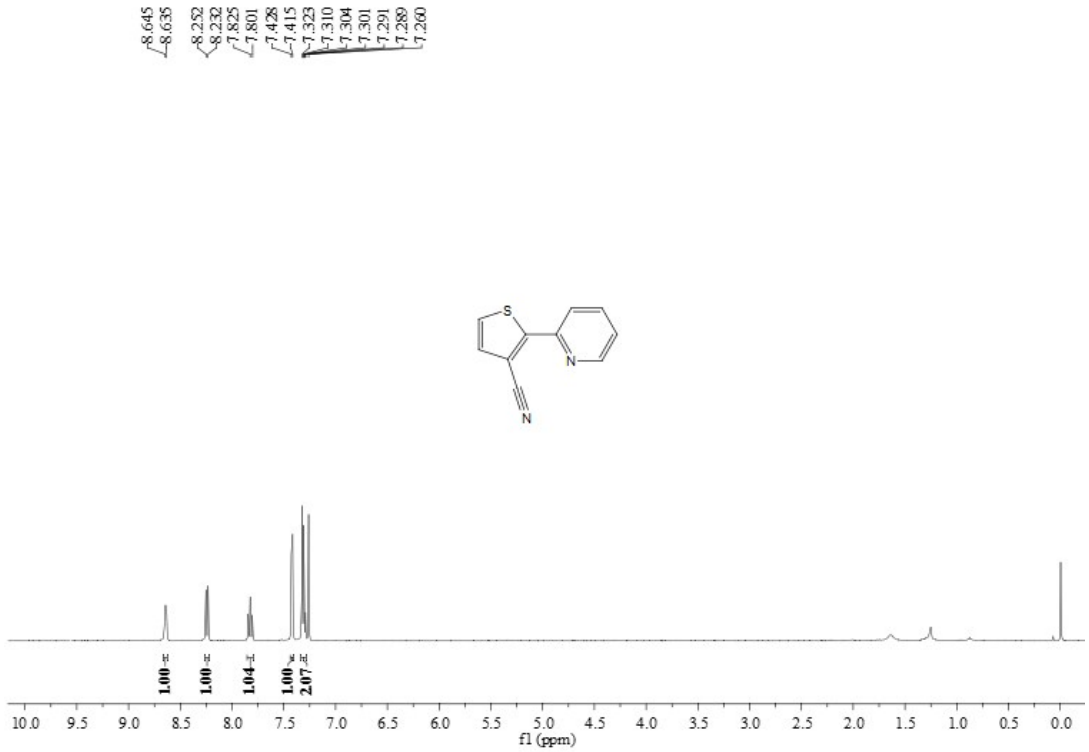


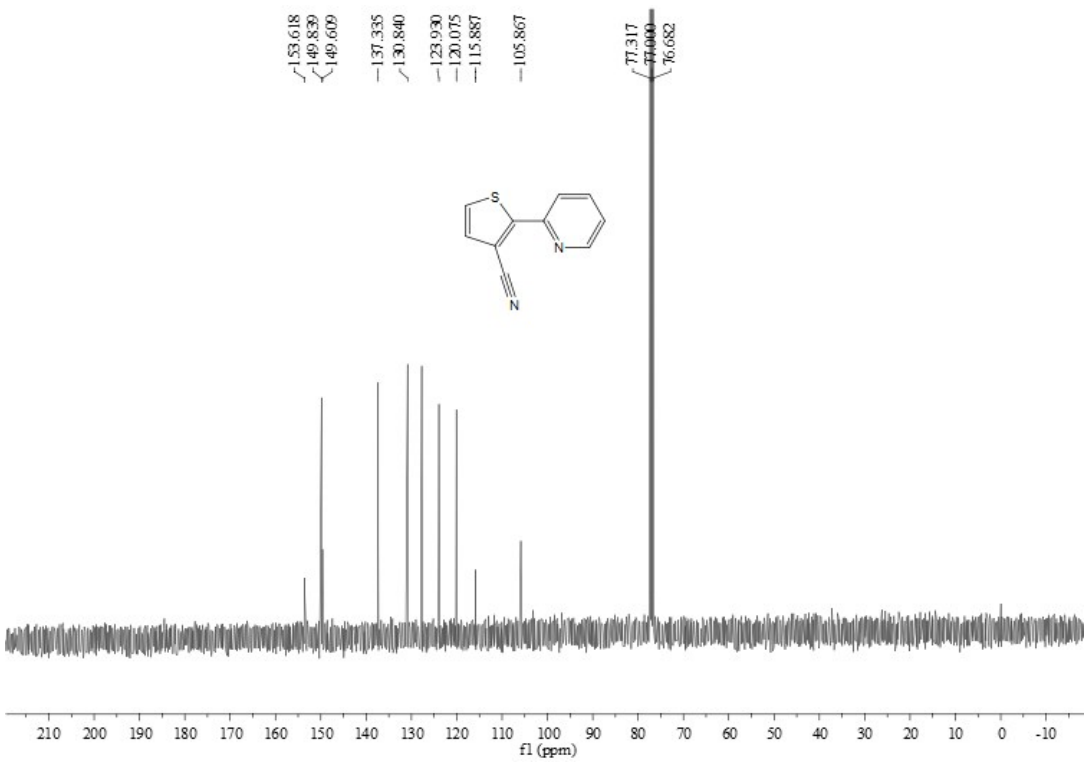
4-Morpholino-2-(pyridin-2-yl)benzonitrile (3o)



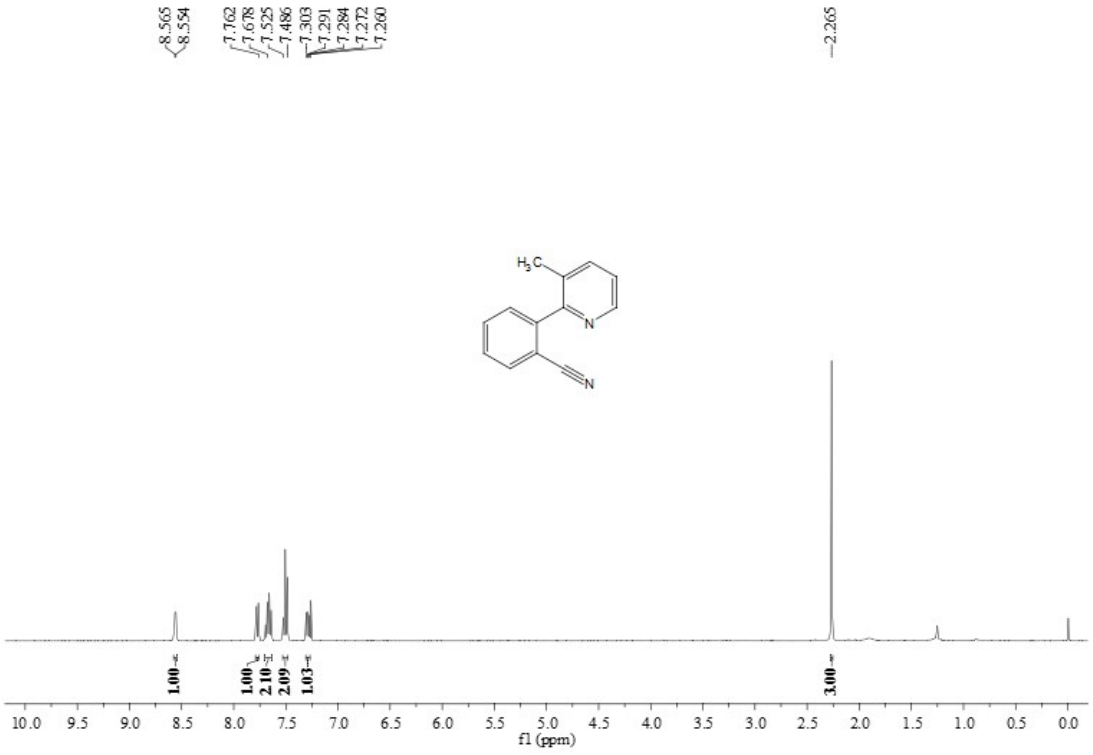


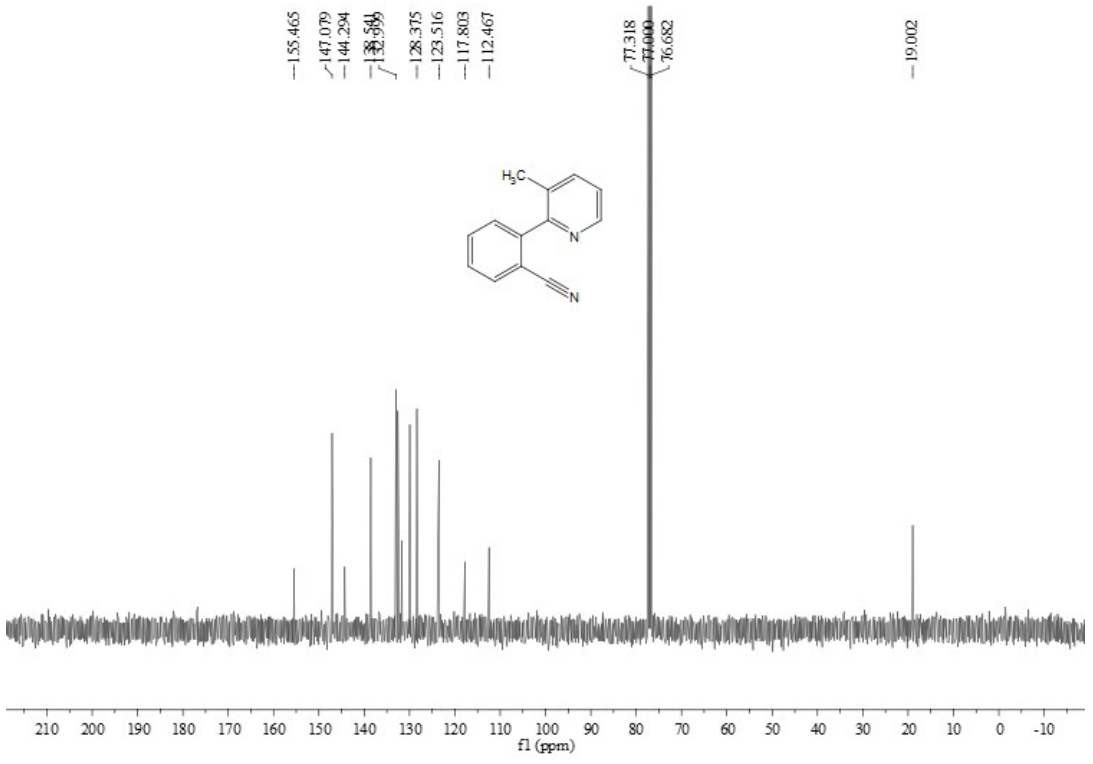
2-(Pyridin-2-yl)thiophene-3-carbonitrile (3p)



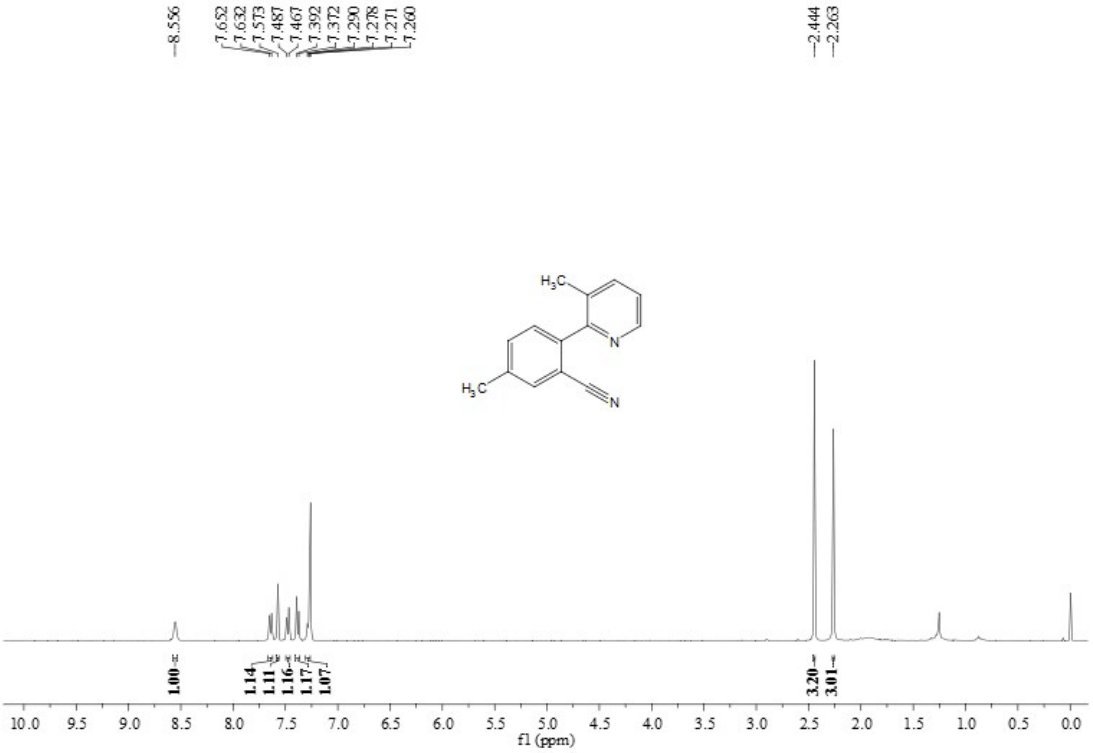


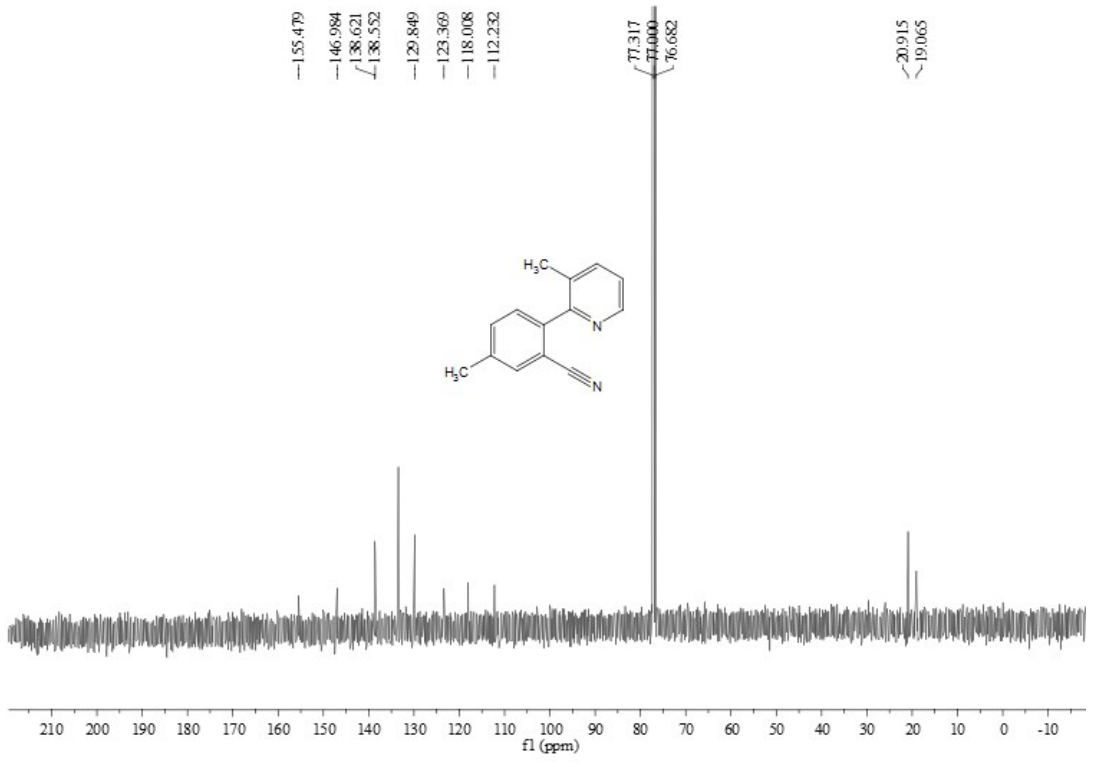
2-(3-Methylpyridin-2-yl)benzonitrile (5a)



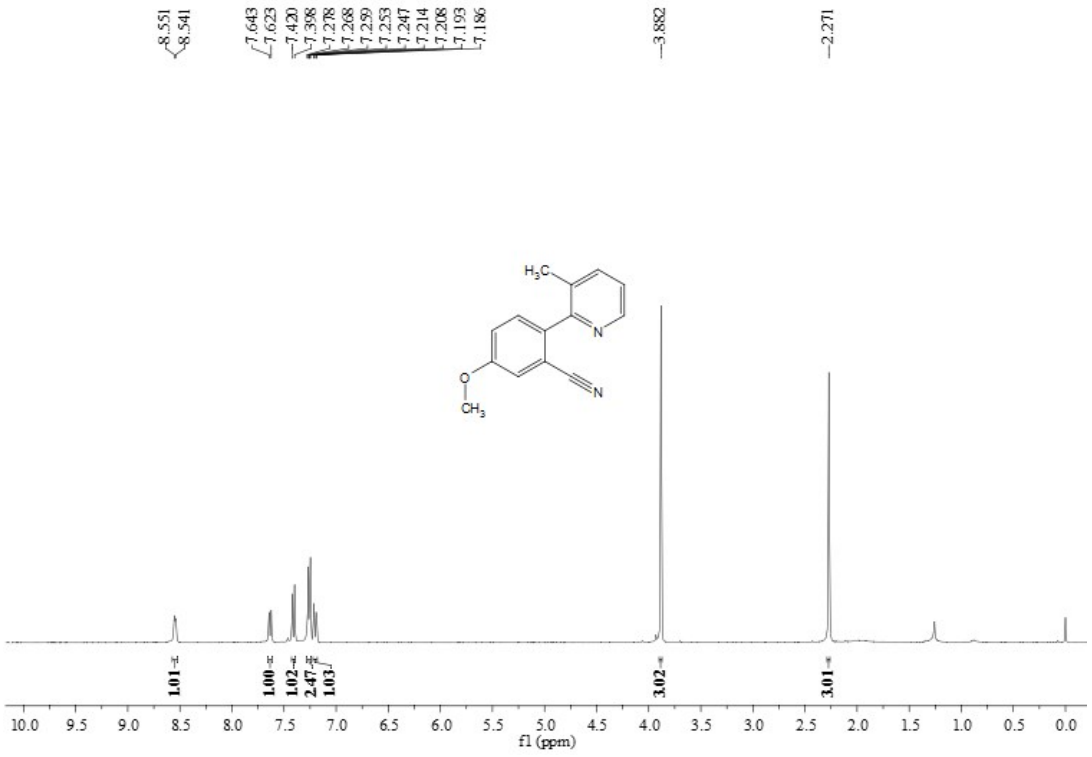


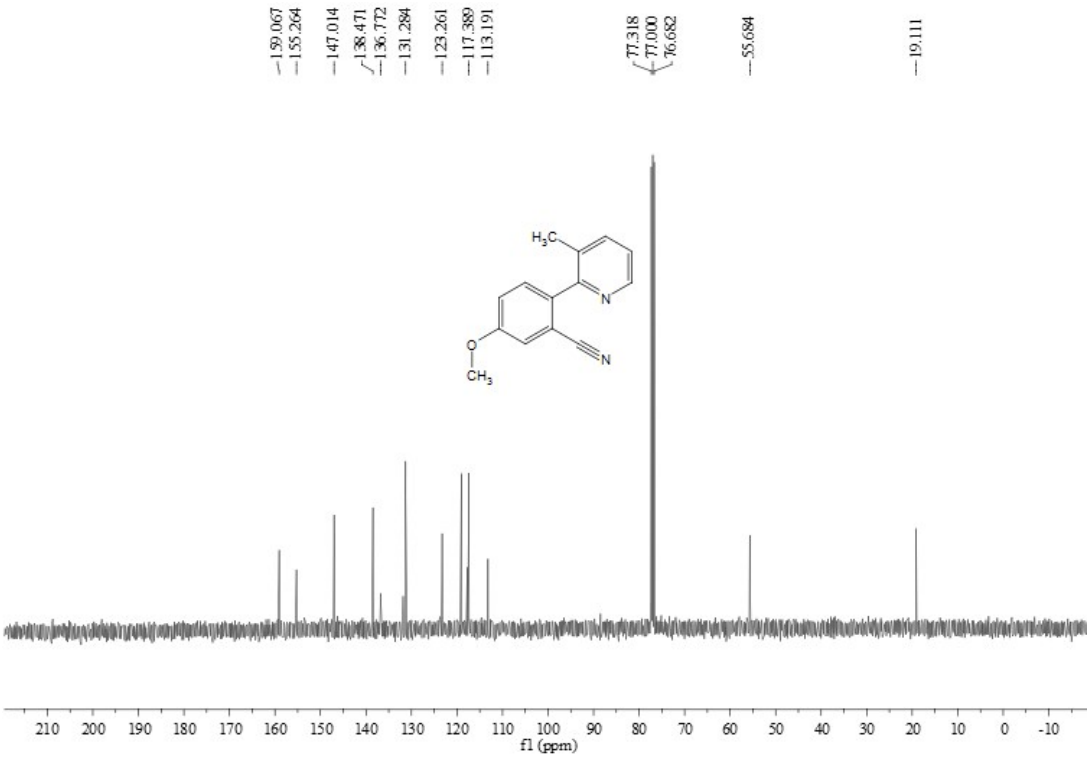
5-Methyl-2-(3-methylpyridin-2-yl)benzonitrile (5b)



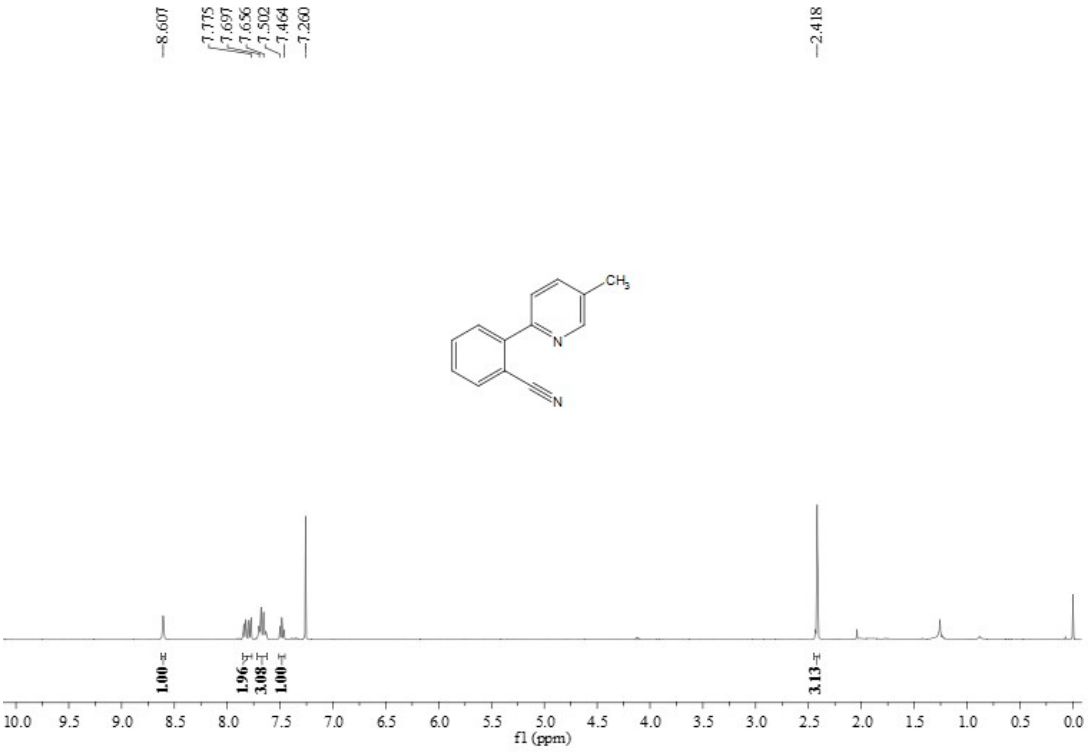


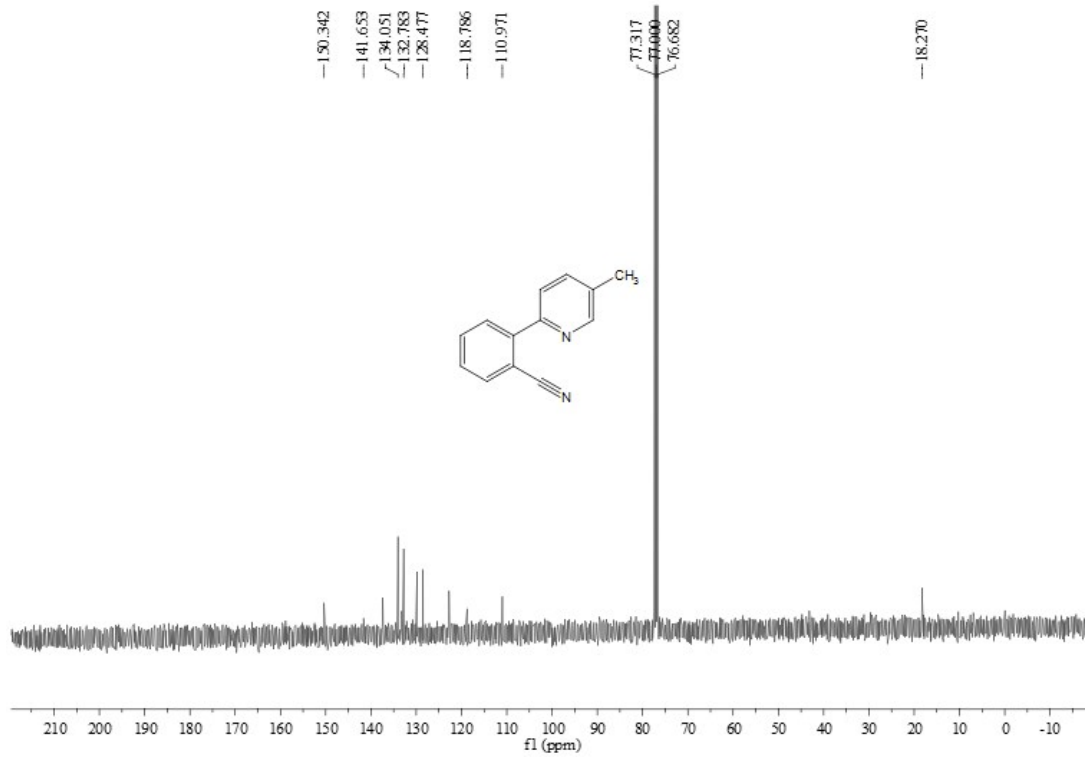
5-Methoxy-2-(3-methylpyridin-2-yl)benzonitrile (5c)



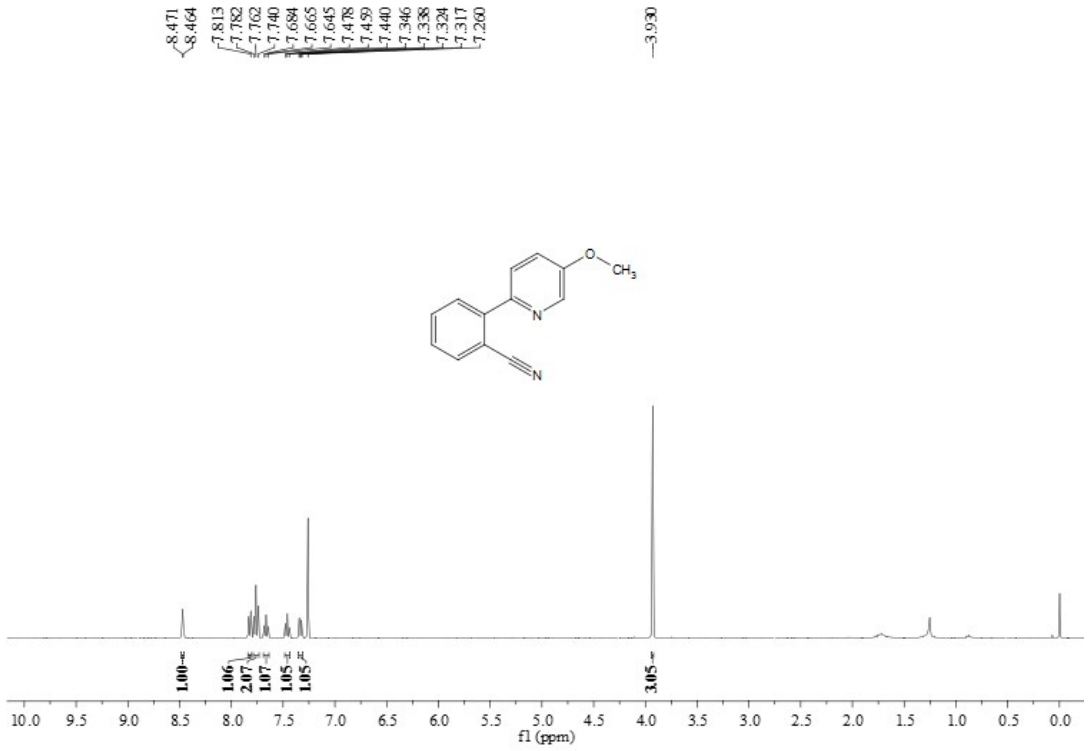


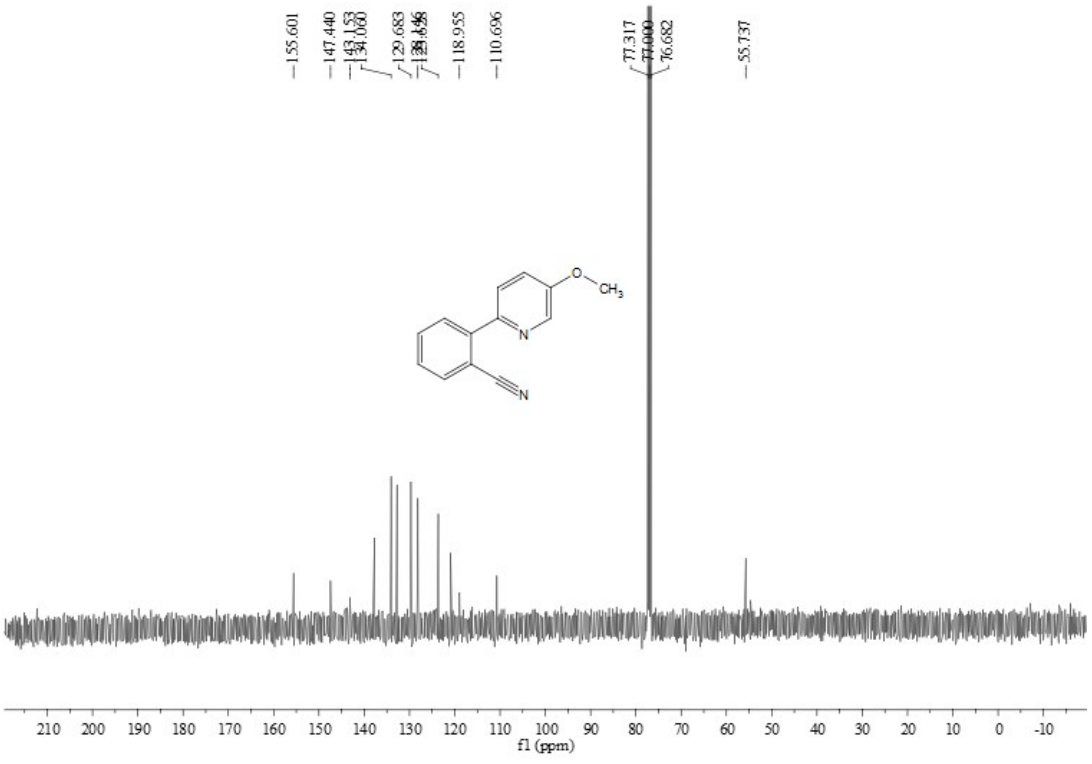
2-(5-Methylpyridin-2-yl)benzonitrile (5d)



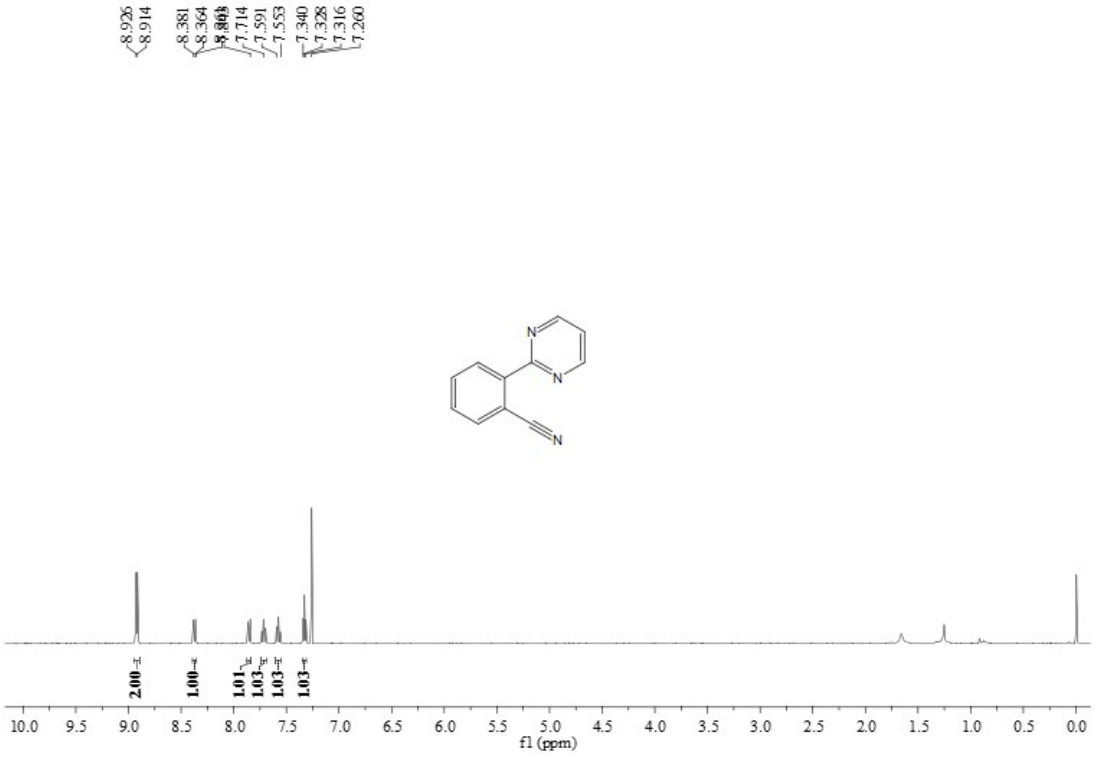


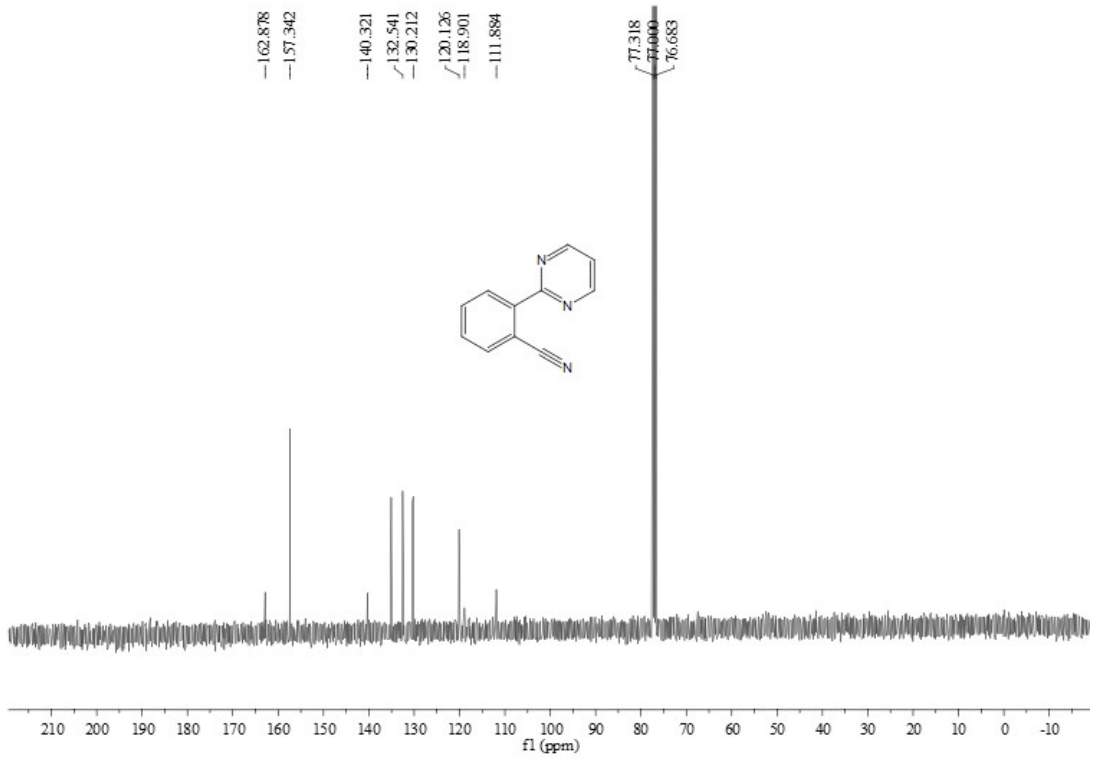
2-(5-Methoxypyridin-2-yl)benzonitrile (5e)



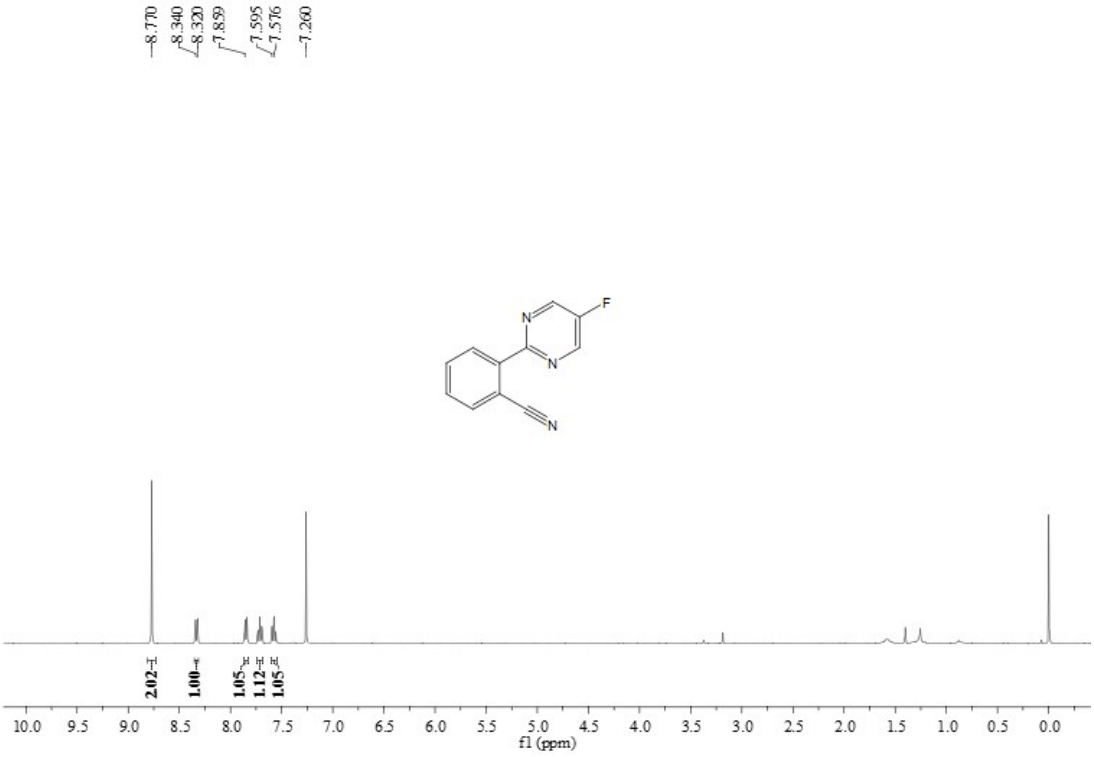


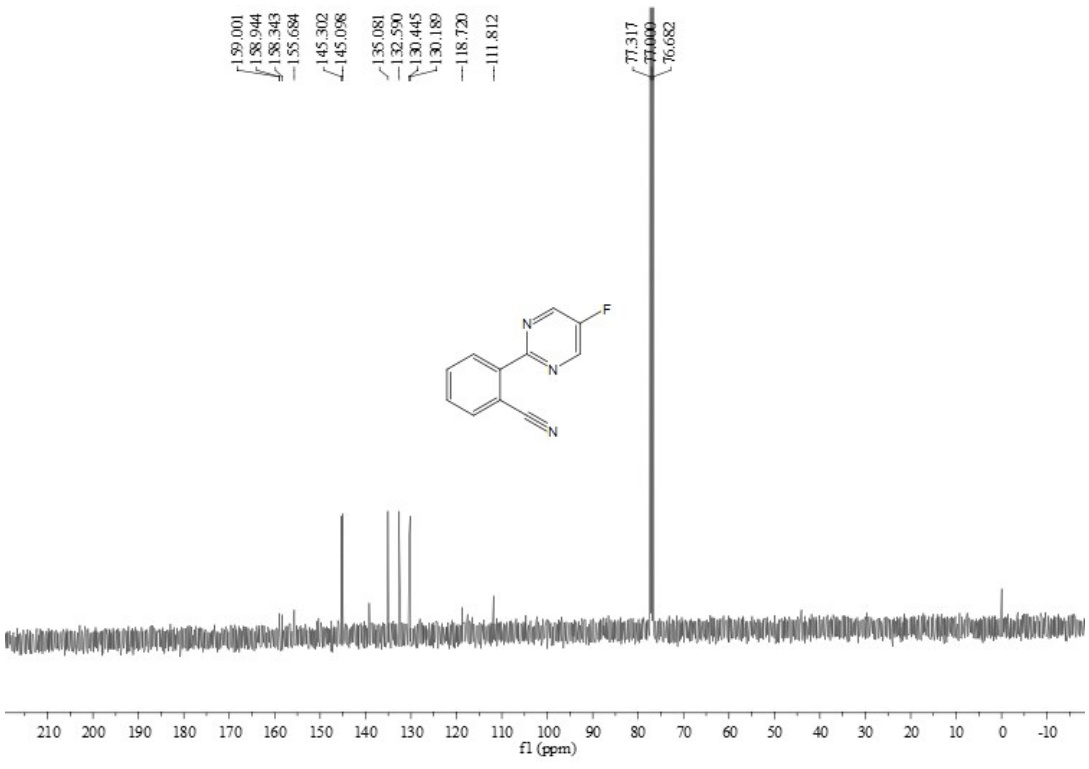
2-(Pyrimidin-2-yl)benzonitrile (5g)



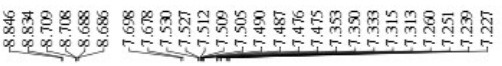


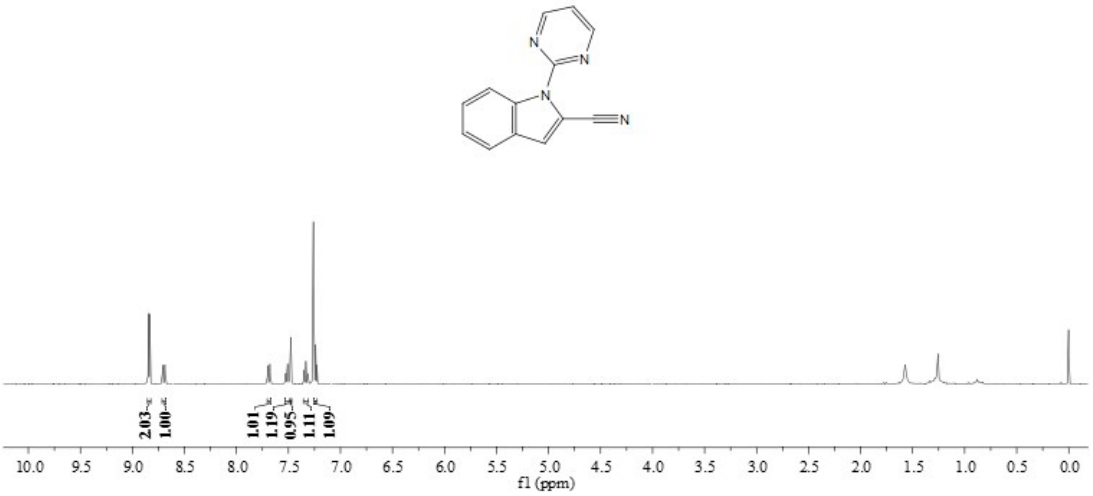
2-(5-Fluoropyrimidin-2-yl)benzonitrile (5h)

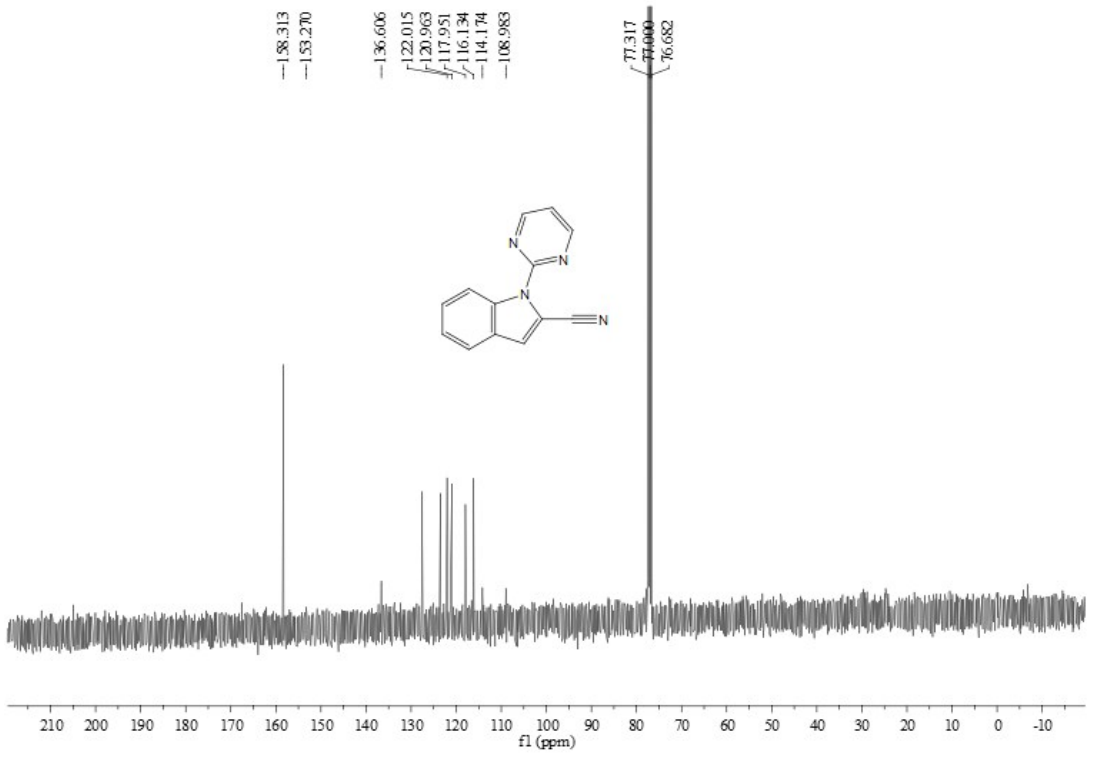




1-(Pyrimidin-2-yl)-1*H*-indole-2-carbonitrile (5i)







2-(1*H*-pyrazol-1-yl)benzonitrile (5j)