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α-Iminonitrile: a new cyanating agent for the palladium catalyzed C-H cyanation of arenes

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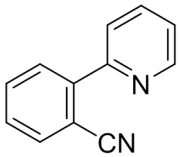
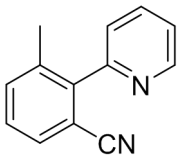
1. General Information. Unless otherwise noted, all solvents were dried and freshly distilled. TLC was performed on silica HSGF254 plates. Melting points were determined with a digital melting-point apparatus. NMR spectra were run in a solution of deuterated chloroform ($CDCl_3$) with tetramethylsilane (TMS) as internal standard and were reported in parts per million (ppm). ^{1}H and ^{13}C NMR spectra were obtained at 400/101 MHz ($^{1}H/^{13}C$), respectively. High-resolution mass spectra (HRMS) analyses were carried out on a chemical ionization (CI) apparatus using time-of-flight (TOF) mass spectrometry. Starting materials **1a**, **1d**, **1o**, **1e** were purchased from commercial suppliers and used without further purification. Other starting materials phenylpyridines **1b**, **1c**, **1e-1n**, **1p**, phenylpyrimidine **4a-4d**, phenylpyrazoles **4e-4h** and cyanating agents **2a-2g** were prepared by the reported procedures.[1-3]

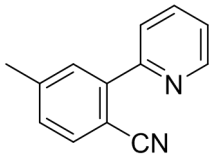
2. General procedure for the C-H cyanation. To a solution of **1** or **4** (0.50 mmol), α-iminonitrile (**2a**) (139.5 mg, 0.75 mmol), $Pd(OAc)_2$ (5.6 mg, 5 mol %), $Cu(TFA)_2$ (289 mg, 1.0 mmol) in THF (2.0 mL), the mixture was stirred at 120 °C for 24 h. At ambient temperature, the solvent was evaporated in vacuo and the remaining residue was purified by column chromatography on silica gel (petroleum ether/EtOAc 9/1) to yield products **3** or **5**.



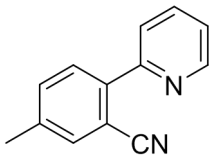
2-(pyridin-2-yl)benzonitrile (3a).[4c] Yellow solid (81 mg, 90% yield). Mp:64-65°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.7 Hz, 1H), 7.82 (ddd, *J* = 19.1, 12.0, 6.5 Hz, 4H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.52 (d, *J* = 6.6 Hz, 1H), 7.39 – 7.34 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2 (s), 149.9 (s), 143.4 (s), 136.9 (s), 134.2 (s), 132.9 (s), 130.0 (s), 128.8 (s), 123.4 (s), 123.3 (s), 118.7 (s), 111.0 (s). LRMS (CI): *m/z* calcd for $C_{12}H_8N_2Na$ $[M+Na]^+$, 180.1 ; found, 180.0.



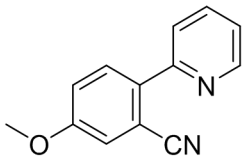
3-methyl-2-(pyridin-2-yl)benzonitrile (3b).[4b] Yellow oil (47 mg, 49% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.7 Hz, 1H), 7.84 (td, *J* = 7.7, 1.5 Hz, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.39 (ddd, *J* = 12.5, 8.5, 6.5 Hz, 3H), 2.23 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2 (s), 149.9 (s), 143.7 (s), 137.9 (s), 136.8 (s), 134.9 (s), 130.7 (s), 128.6 (s), 124.6 (s), 123.2 (s), 118.3 (s), 112.8 (s), 20.1 (s). LRMS (CI): *m/z* calcd for $C_{13}H_{10}N_2Na$ $[M+Na]^+$, 217.1 ; found, 217.0.



4-methyl-2-(pyridin-2-yl)benzonitrile (3c).[4c] White solid (67 mg, 69% yield). Mp: 63-65°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.3 Hz, 1H), 7.85 – 7.76 (m, 2H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.36 – 7.27 (m, 2H), 2.47 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4 (s), 149.9 (s), 143.9 (s), 143.3 (s), 136.9 (s), 134.0 (s), 130.8 (s), 129.6 (s), 123.4 (s), 123.3 (s), 119.0 (s), 108.0 (s), 21.9 (s). LRMS (CI): *m/z* calcd for $C_{13}H_{10}N_2Na$ $[M+Na]^+$, 217.1 ; found, 217.0.

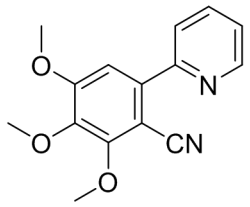


5-methyl-2-(pyridin-2-yl)benzonitrile (3d).[4d] White solid (82 mg, 85% yield). Mp: 76-78°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.2 Hz, 1H), 7.82 (t, *J* = 7.7 Hz, 1H), 7.78 – 7.72 (m, 2H), 7.60 (s, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.37 – 7.31 (m, 1H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2 (s), 149.8 (s), 140.6 (s), 139.2 (s), 136.9 (s), 134.5 (s), 133.8 (s), 129.9 (s), 128.3 (s), 123.2 (s), 118.9 (s), 110.8 (s), 20.9 (s). LRMS (CI): *m/z* calcd for $C_{13}H_{10}N_2Na$ $[M+Na]^+$, 217.1 ; found, 217.0.

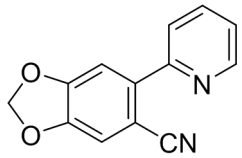


5-methoxy-2-(pyridin-2-yl)benzonitrile (3e).[4c] White solid (94 mg, 90% yield). Mp: 105-107°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.11 (t, *J* = 7.3 Hz, 1H), 7.94 (d, *J* = 6.0 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 1H), 7.61 (s, 1H), 7.32 (t, *J* = 6.9 Hz, 2H), 3.92 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8 (s), 153.2 (s), 147.2 (s), 140.4

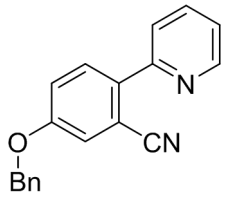
(s), 132.2 (s), 131.8 (s), 125.2 (s), 124.2 (s), 119.5 (s), 119.4 (s), 117.9 (s), 112.4 (s), 56.1 (s). LRMS (CI): *m/z* calcd for $C_{13}H_{10}N_2ONa$ $[M+Na]^+$, 233.1 ; found, 233.0.



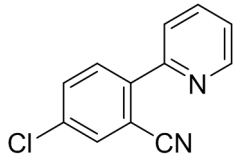
2,3,4-trimethoxy-6-(pyridin-2-yl)benzonitrile (3f). White solid (90 mg, 67% yield). Mp: 147-149°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.7 Hz, 1H), 7.84 – 7.78 (m, 2H), 7.35 (dd, *J* = 8.8, 4.6 Hz, 1H), 7.15 (s, 1H), 4.09 (s, 3H), 3.99 (s, 3H), 3.92 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4 (s), 156.6 (s), 155.0 (s), 149.9 (s), 142.0 (s), 140.5 (s), 136.9 (s), 123.6 (s), 123.4 (s), 116.1 (s), 108.9 (s), 98.5 (s), 62.1 (s), 61.3 (s), 56.5 (s). HRMS (CI): *m/z* calcd for $C_{15}H_{15}N_2O_3$ $[M+H]^+$, 271.1083 ; found, 271.1075.



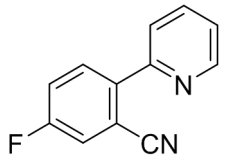
6-(pyridin-2-yl)benzo[d][1,3]dioxole-5-carbonitrile (3g). White solid (76 mg, 68% yield). Mp: 97-99°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.84 – 7.65 (m, 2H), 7.36 – 7.26 (m, 2H), 7.16 – 7.02 (m, 1H), 6.19 (s, 1H), 6.12 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.94 (d, *J* = 2.7 Hz), 152.43 (s), 151.82 (s), 149.83 (d, *J* = 15.9 Hz), 148.37 (s), 148.07 (s), 140.49 (s), 136.90 (d, *J* = 3.0 Hz), 135.87 (s), 123.42 (d, *J* = 26.5 Hz), 122.83 (d, *J* = 37.6 Hz), 118.91 (s), 114.26 (s), 112.55 (s), 112.00 (s), 110.29 (s), 103.72 (s), 103.16 (s), 102.75 (s), 92.91 (s). HRMS (CI): *m/z* calcd for $C_{13}H_9N_2O_2$ $[M+H]^+$, 225.0664 ; found, 225.0663.



5-(benzyloxy)-2-(pyridin-2-yl)benzonitrile (3h).[4d] White solid (132 mg, 92% yield). Mp: 84-85°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.9 Hz, 1H), 7.84 – 7.74 (m, 3H), 7.42 (q, *J* = 7.4 Hz, 4H), 7.39 – 7.27 (m, 4H), 5.14 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8 (s), 155.0 (s), 149.8 (s), 137.1(s), 136.2 (s), 135.8 (s), 131.6 (s), 128.9 (s), 128.6 (s), 127.6 (s), 123.1 (s), 123.0 (s), 120.3 (s), 119.7 (s), 118.7 (s), 111.9 (s), 70.6 (s). LRMS (CI): *m/z* calcd for $C_{19}H_{14}N_2ONa$ $[M+Na]^+$, 309.1 ; found, 308.9.

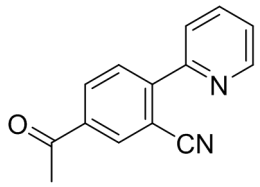


5-chloro-2-(pyridin-2-yl)benzonitrile (3i).[4d] White solid (74 mg, 69% yield). Mp: 165-166°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.3 Hz, 1H), 7.90 – 7.74 (m, 4H), 7.67 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.42 – 7.36 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.2 (s), 150.1 (s), 141.8 (s), 137.2 (s), 135.2 (s), 133.8 (s), 133.3 (s), 131.5 (s), 123.8 (s), 123.3 (s), 117.6 (s), 112.6 (s). LRMS (CI): *m/z* calcd for $C_{12}H_7ClN_2Na$ $[M+Na]^+$, 237.0 ; found, 236.9.

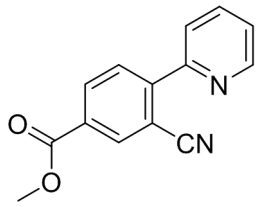


5-fluoro-2-(pyridin-2-yl)benzonitrile (3j).[4d] White solid (55 mg, 56% yield). Mp: 133-134°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.7 Hz, 1H), 7.88 – 7.82 (m, 2H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.50 (dd, *J* = 8.0, 2.5 Hz, 1H), 7.45 – 7.34 (m, 2H). ^{13}C

NMR (101 MHz, $CDCl_3$) δ 163.73 (s), 160.39 (s), 154.29 (s), 150.03 (s), 139.98 (s), 137.08 (s), 132.25 (d, *J* = 8.4 Hz), 123.53 (s), 123.20 (s), 120.73 (dd, *J* = 23.0, 14.4 Hz), 117.59 (d, *J* = 1.2 Hz), 112.51 (d, *J* = 9.4 Hz). LRMS (CI): *m/z* calcd for $C_{12}H_7FN_2Na$ $[M+Na]^+$, 221.1 ; found, 220.9.

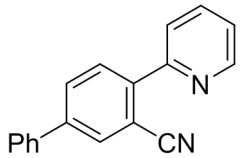


5-acetyl-2-(pyridin-2-yl)benzonitrile (3k).[4d] White solid (54 mg, 49% yield). Mp: 102-104°C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.38 (d, *J* = 1.6 Hz, 1H), 8.25 (d, *J* = 9.8 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.91 – 7.84 (m, 2H), 7.45 – 7.40 (m, 1H), 2.68 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.7 (s), 154.2 (s), 150.3 (s), 147.0 (s), 137.2 (s), 137.1 (s), 134.4 (s), 132.3 (s), 130.6 (s), 124.2 (s), 123.6 (s), 118.1 (s), 111.8 (s), 26.8 (s). LRMS (CI): *m/z* calcd for $C_{14}H_{10}N_2ONa$ $[M+Na]^+$, 245.1 ; found, 244.9.

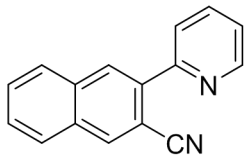


methyl 3-cyano-4-(pyridin-2-yl)benzoate (3l).[4d] White solid (101 mg, 85% yield). Mp: 91-92°C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 4.3 Hz, 1H), 8.47 (d, *J* = 1.3 Hz, 1H), 8.33 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.93 (dd, *J* = 13.8, 8.6 Hz, 2H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.47 – 7.43 (m, 1H), 3.99 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1 (s), 154.1 (s), 150.0 (s), 146.7 (s), 137.4 (s), 135.5 (s), 133.7 (s), 130.9 (s), 130.4 (s), 124.2 (s), 123.7 (s), 117.9 (s), 111.6 (s), 52.9 (s). LRMS (CI): *m/z* calcd for

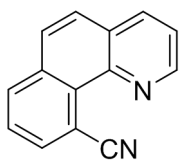
$C_{14}H_{10}N_2O_2Na$ $[M+Na]^+$, 261.1 ; found, 260.9.



4-(pyridin-2-yl)-[1,1'-biphenyl]-3-carbonitrile (3m).[4d] White solid (82 mg, 63% yield). Mp: 68-69°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.01 (s, 1H), 7.91 (q, *J* = 8.1 Hz, 2H), 7.84 (s, 2H), 7.62 (d, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.1 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.36 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.0 (s), 150.1 (s), 142.1 (s), 142.0 (s), 138.5 (s), 137.1 (s), 132.8 (s), 131.6 (s), 130.6 (s), 129.3 (s), 128.7 (s), 127.2 (s), 123.5 (s), 123.3 (s), 118.9 (s), 111.6 (s). LRMS (CI): *m/z* calcd for $C_{18}H_{12}N_2Na$ $[M+Na]^+$, 279.1 ; found, 279.0.

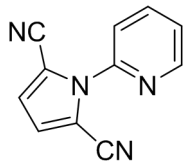


3-(pyridin-2-yl)-2-naphthonitrile (3n).[4d] White solid (100 mg, 87% yield). Mp: 154-156°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, *J* = 4.5 Hz, 1H), 8.43 (s, 1H), 8.33 (s, 1H), 8.09 (td, *J* = 7.9, 1.2 Hz, 1H), 7.98 (dd, *J* = 15.2, 8.0 Hz, 3H), 7.75 – 7.66 (m, 2H), 7.59 (dd, *J* = 6.6, 5.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1 (s), 147.9 (s), 139.6 (s), 136.9 (s), 134.5 (s), 134.4 (s), 132.3 (s), 130.9 (s), 130.1 (s), 129.0 (s), 128.9 (s), 128.3 (s), 125.1 (s), 124.2 (s), 118.5 (s), 108.3 (s). LRMS (CI): *m/z* calcd for $C_{16}H_{10}N_2Na$ $[M+Na]^+$, 253.1 ; found, 253.0.

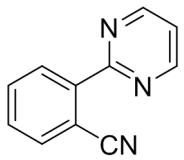


benzo[h]quinoline-10-carbonitrile (3o).[4d] White solid (79 mg, 77% yield). Mp:

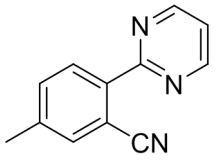
139-141°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 – 9.09 (m, 1H), 8.19 (d, *J* = 8.1 Hz, 1H), 8.10 (dd, *J* = 16.1, 7.7 Hz, 2H), 7.80 – 7.68 (m, 3H), 7.60 (dd, *J* = 8.0, 4.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.6 (s), 144.5 (s), 136.3 (s), 135.8 (s), 134.1 (s), 132.8 (s), 127.5 (s), 127.3 (s), 127.2 (s), 127.0 (s), 123.2 (s), 120.9 (s), 109.0 (s). LRMS (CI): *m/z* calcd for $C_{14}H_8N_2Na$ $[M+Na]^+$, 227.1 ; found, 227.0.



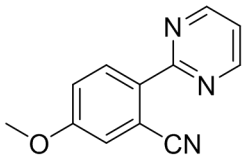
1-(pyridin-2-yl)-1H-pyrrole-2,5-dicarbonitrile (**3p**). White solid (39 mg, 40% yield). Mp: 165-167°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (dd, *J* = 4.8, 1.0 Hz, 1H), 8.00 (td, *J* = 8.0, 1.8 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.51 (ddd, *J* = 7.5, 4.9, 0.7 Hz, 1H), 7.03 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.0 (s), 147.7 (s), 139.6 (s), 125.0 (s), 121.7 (s), 118.6 (s), 111.7 (s), 108.9 (s). HRMS (CI): *m/z* calcd for $C_{11}H_7N_4$ $[M+H]^+$, 195.0671 ; found, 195.0667.



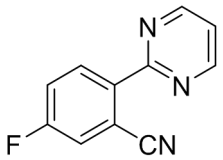
2-(pyrimidin-2-yl)benzonitrile (5a).[4d] White solid (61 mg, 67% yield). Mp: 138-139°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, *J* = 4.9 Hz, 2H), 8.37 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 7.7 Hz, 1H), 7.72 (t, *J* = 7.7 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 4.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9 (s), 157.5 (s), 140.4 (s), 135.2 (s), 132.7 (s), 130.6 (s), 130.4 (s), 120.3 (s), 119.0 (s), 111.9 (s), 91.5 (s). LRMS (CI): *m/z* calcd for $C_{11}H_7N_3Na$ $[M+Na]^+$, 204.1 ; found, 204.0.



5-methyl-2-(pyrimidin-2-yl)benzonitrile (5b).[4e] White solid (70 mg, 72% yield). Mp: 172-174°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, *J* = 4.8 Hz, 2H), 8.27 (d, *J* = 8.1 Hz, 1H), 7.66 (s, 1H), 7.51 (d, *J* = 8.1 Hz, 1H), 7.30 (t, *J* = 4.9 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0 (s), 157.3 (s), 141.2 (s), 135.0 (s), 130.2 (s), 129.5 (s), 128.2 (s), 118.9 (s), 115.3 (s), 21.6 (s). LRMS (CI): *m/z* calcd for $C_{12}H_9N_3Na$ $[M+Na]^+$, 218.1 ; found, 218.0.

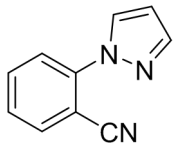


5-methoxy-2-(pyrimidin-2-yl)benzonitrile (5c).[4e] White solid (36 mg, 34% yield). Mp: 127-129°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, *J* = 2.2 Hz, 2H), 8.35 (d, *J* = 8.9 Hz, 1H), 7.33 (d, *J* = 2.6 Hz, 1H), 7.27 (t, *J* = 4.8 Hz, 1H), 7.22 (dd, *J* = 8.9, 2.6 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7 (s), 160.9 (s), 157.3 (s), 132.8 (s), 132.1 (s), 119.9 (s), 119.7 (s), 118.9 (s), 113.0 (s), 55.9 (s). LRMS (CI): *m/z* calcd for $C_{12}H_9N_3Na$ $[M+Na]^+$, 234.1 ; found, 233.9.

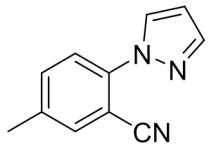


5-fluoro-2-(pyrimidin-2-yl)benzonitrile (5d).[4e] White solid (46 mg, 46% yield). Mp: 170-172°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, *J* = 4.9 Hz, 2H), 8.43 (dd, *J* = 8.9, 5.6 Hz, 1H), 7.55 (dd, *J* = 8.1, 2.6 Hz, 1H), 7.42 (td, *J* = 8.8, 2.6 Hz, 1H), 7.33 (t, *J* = 4.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.96 (s), 162.28 (s), 162.02 (s),

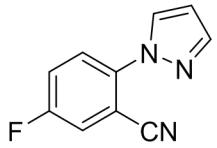
157.46 (s), 136.74 (d, J = 3.4 Hz), 132.88 (d, J = 8.7 Hz), 122.05 (s), 121.88 (s), 120.24 (t, J = 10.6 Hz), 117.80 (s), 113.65 (d, J = 9.4 Hz). LRMS (CI): *m/z* calcd for $C_{11}H_6FN_3Na$ $[M+Na]^+$, 222.1 ; found, 221.9.



2-(1H-pyrazol-1-yl)benzonitrile (5e).[4d] Yellow oil (62 mg, 73% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 – 8.16 (m, 1H), 7.87 (dd, J = 13.8, 6.2 Hz, 3H), 7.80 (s, 1H), 7.51 (dd, J = 15.4, 7.8 Hz, 1H), 6.62 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.4 (s), 142.1 (s), 134.6 (s), 134.1 (s), 129.6 (s), 127.3 (s), 124.4 (s), 117.1 (s), 108.6 (s), 105.4 (s). LRMS (CI): *m/z* calcd for $C_{10}H_7N_3Na$ $[M+Na]^+$, 192.1 ; found, 192.0.

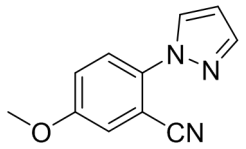


5-methyl-2-(1H-pyrazol-1-yl)benzonitrile (5f).[4f] White solid (59 mg, 65% yield). Mp: 64-66°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 2.2 Hz, 1H), 7.80 (s, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.57 (s, 1H), 7.50 (d, J = 8.3 Hz, 1H), 6.53 (s, 1H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9 (s), 138.1 (s), 136.3 (s), 130.0 (s), 126.8 (s), 119.3 (s), 107.4 (s), 21.0 (s). LRMS (CI): *m/z* calcd for $C_{11}H_9N_3Na$ $[M+Na]^+$, 206.1 ; found, 206.0.



5-fluoro-2-(1H-pyrazol-1-yl)benzonitrile (5g).[4f] White solid (53 mg, 57% yield). Mp: 99-101°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 2.3 Hz, 1H), 7.83 – 7.75

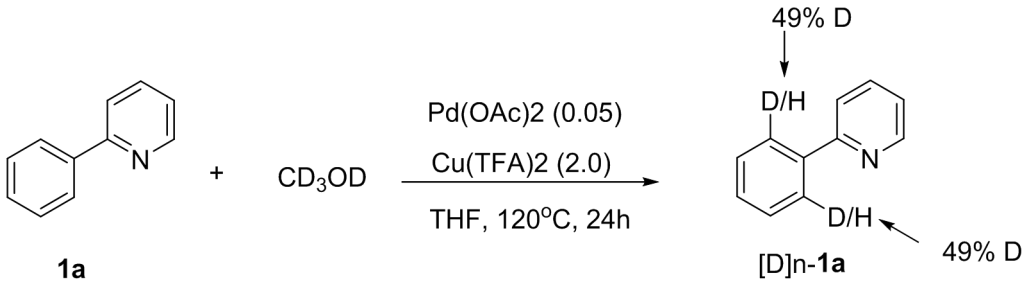
(m, 2H), 7.51 – 7.41 (m, 2H), 6.56 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.68 (s), 159.18 (s), 142.48 (s), 138.87 (s), 129.79 (s), 126.74 (d, *J* = 8.5 Hz), 121.89 (s), 121.67 (s), 120.93 (s), 120.68 (s), 115.78 (s), 108.73 (s), 106.93 (d, *J* = 9.5 Hz). LRMS (CI): *m/z* calcd for $C_{10}H_6FN_3Na$ $[M+Na]^+$, 210.1 ; found, 209.9.



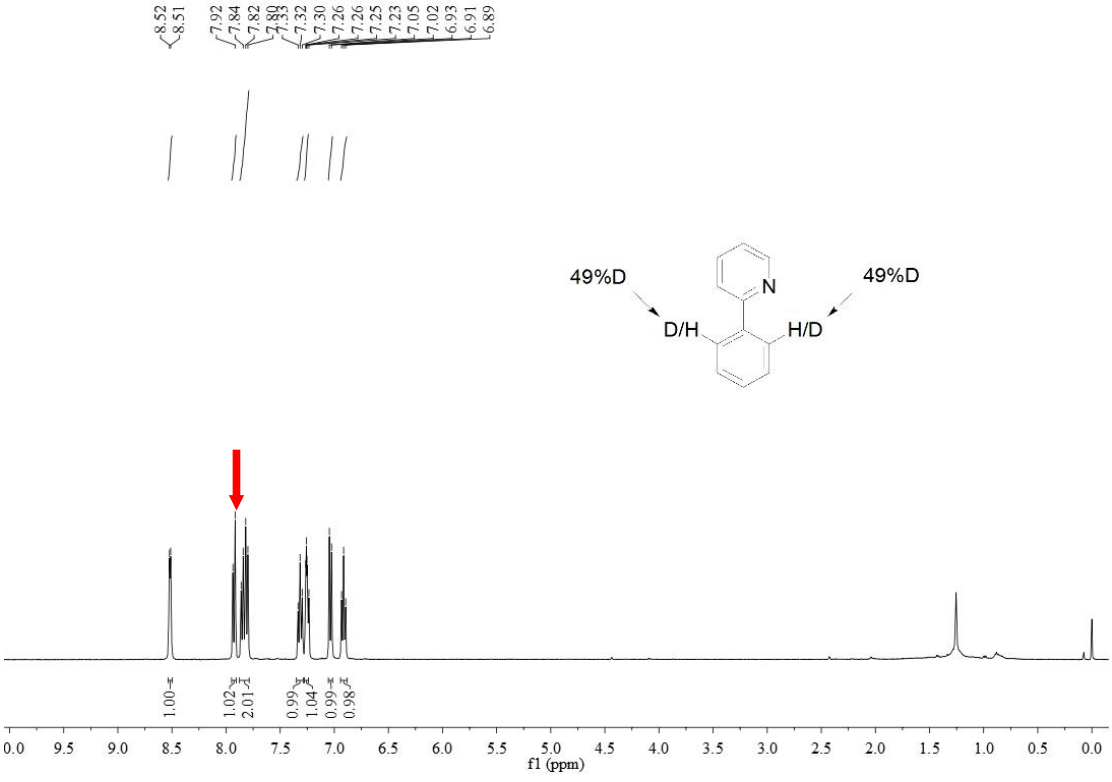
5-methoxy-2-(1H-pyrazol-1-yl)benzonitrile (5h). White solid (61 mg, 61% yield). Mp: 92-94°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 2.3 Hz, 1H), 7.78 (s, 1H), 7.67 – 7.62 (m, 1H), 7.25 – 7.20 (m, 2H), 6.53 – 6.50 (m, 1H), 3.88 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4 (s), 141.9 (s), 135.9 (s), 129.8 (s), 126.4 (s), 118.0 (s), 116.7 (s), 108.1 (s), 106.9 (s), 56.1 (s). HRMS (CI): *m/z* calcd for $C_{11}H_{10}N_3O$ $[M+H]^+$, 200.0824 ; found, 200.0817.

3. H/D Exchange Experiment: [4d]

A suspension of 2-phenylpyridine (**1a**) (78 mg, 0.50 mmol), $Pd(OAc)_2$ (5.6 mg, 5 mol %), $Cu(TFA)_2$ (289 mg, 1.0 mmol), CD_3OD (72 mg, 2.0 mmol) in THF (2.0 ml) was stirred at 120 °C for 24 h. At ambient temperature, the reaction mixture was evaporated in vacuo and the remaining residue was purified by column chromatography on silica gel to afford [D]n-**1a** as a slight yellow oil. The D-incorporation in [D]-**1a** was estimated by ^{1}H-NMR spectroscopy.



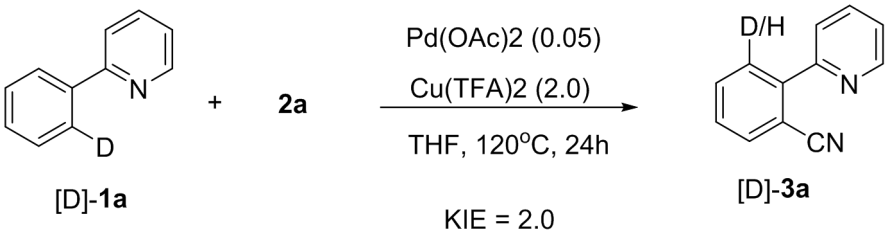
^{1}H NMR spectra of compound [D]n-**1a**



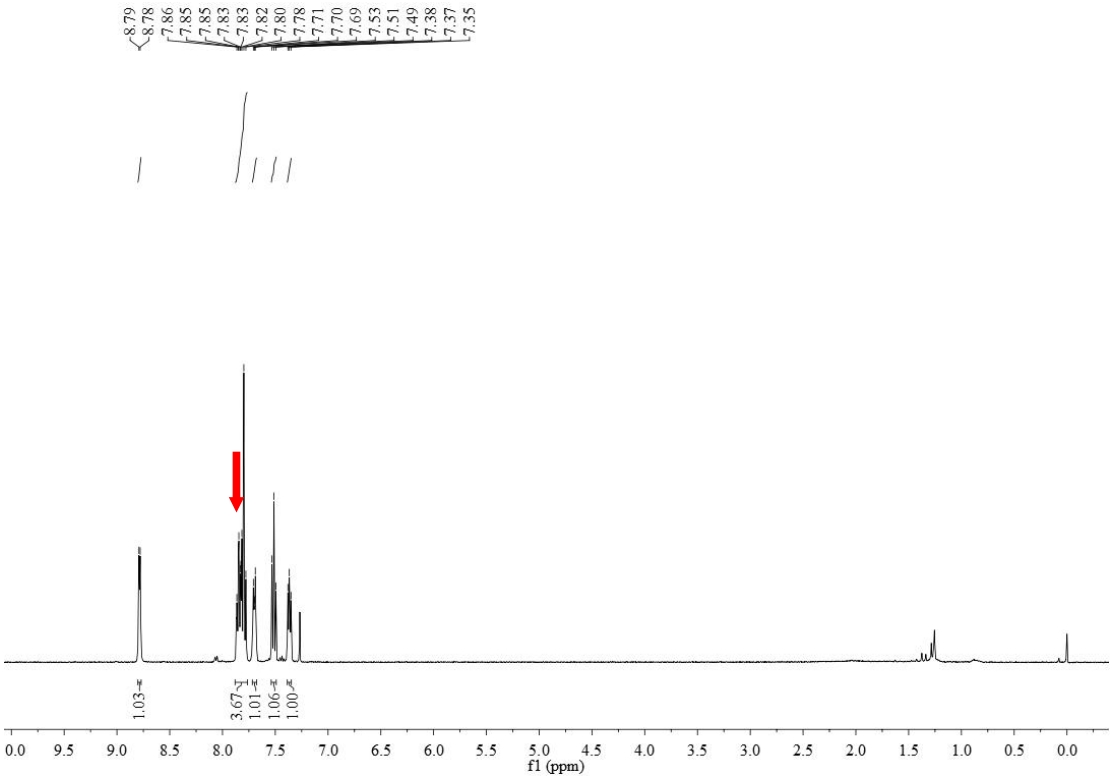
4. Kinetic isotope effect (KIE) Experiments: [4c]

4.1 Intramolecular competition experiment:

A suspension of 2-[D]-phenylpyridine ([D]-**1a**) (46.8 mg, 0.3 mmol), **2a** (83 mg, 0.45 mmol), $Pd(OAc)_2$ (3.4mg, 5 mol %), $Cu(TFA)_2$ (173 mg, 0.6 mmol) in THF (1.0 mL) was stirred at 120 °C for 150 min. At ambient temperature, the reaction mixture was evaporated in vacuo and the remaining residue was purified by column chromatography on silica gel to afford [D]-**3a** (10 mg, 18%) as a solid. The D-incorporation in [D]-**3a** was estimated by ^{1}H-NMR spectroscopy.

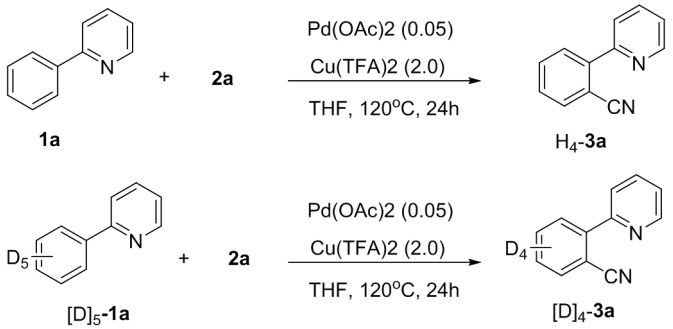


^{1}H NMR spectra of compound [D]-**3a**



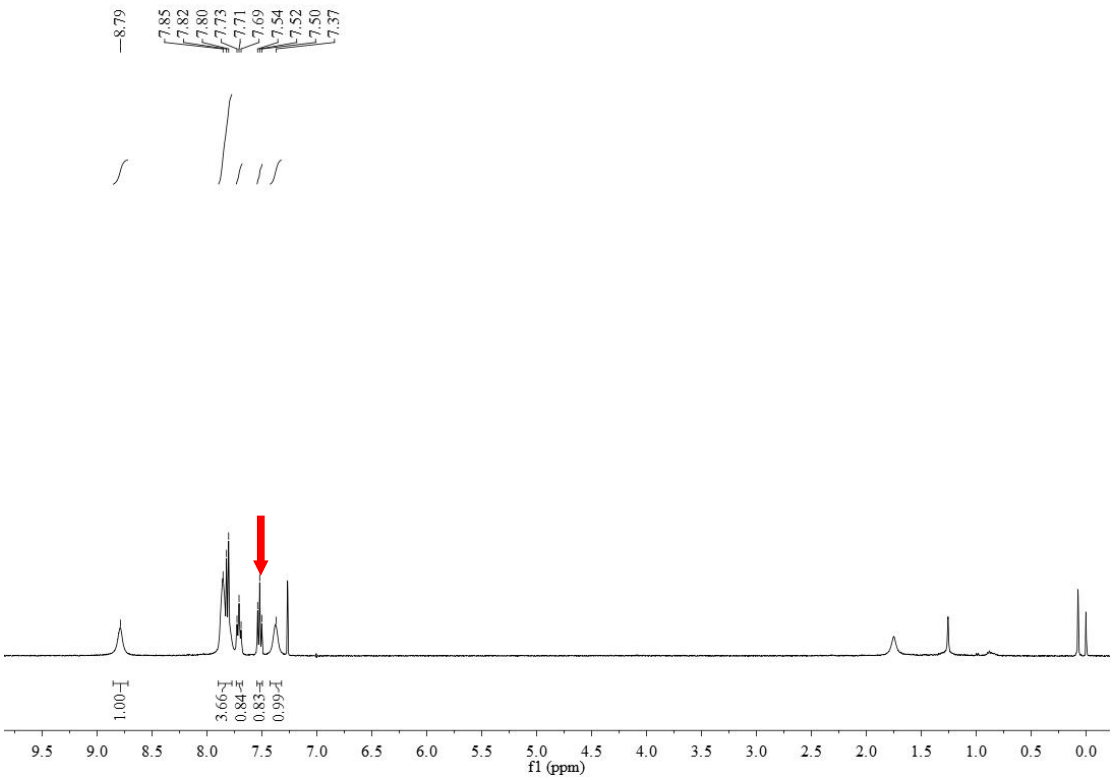
4.2 Parallel experiments:

Two parallel reactions with **1a** and deuterate substrate $[D]_5$-**1a** under the standard conditions proceeded: A suspension of substrates **1a** (46.8 mg, 0.3 mmol) or $[D]_5$-**1a** (48 mg, 0.3 mmol), **2a** (83 mg, 0.45 mmol), $Pd(OAc)_2$ (3.4mg, 5 mol %), $Cu(TFA)_2$ (173 mg, 0.6 mmol) in THF (1.0 mL) was stirred at 120 °C for 150 min, respectively. At ambient temperature, the reaction mixture was evaporated in vacuo and the remaining residue was purified by column chromatography on silica gel to afford $H_4/[D]_4$-**3a** (8 mg, 15%) as a solid. The H/D-incorporation in $H_4/[D]_4$-**3a** was estimated by ^{1}H-NMR spectroscopy.



KIE = 4.8

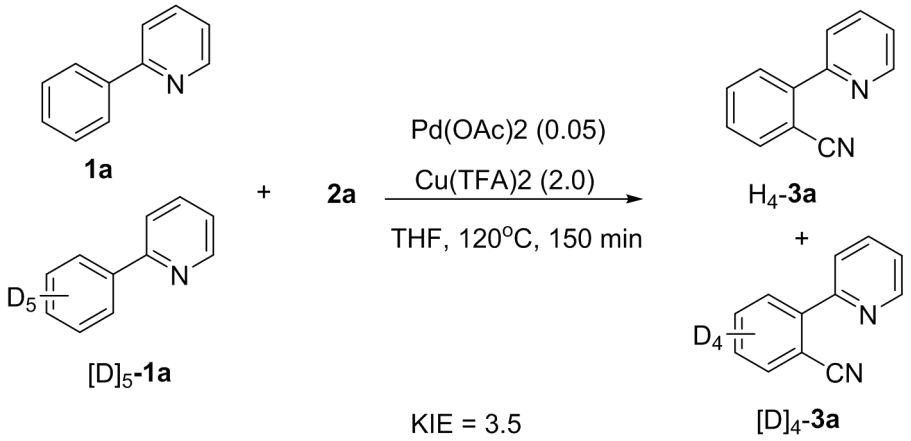
^{1}H NMR spectra of compound $H_4/[D]_4$-**3a**



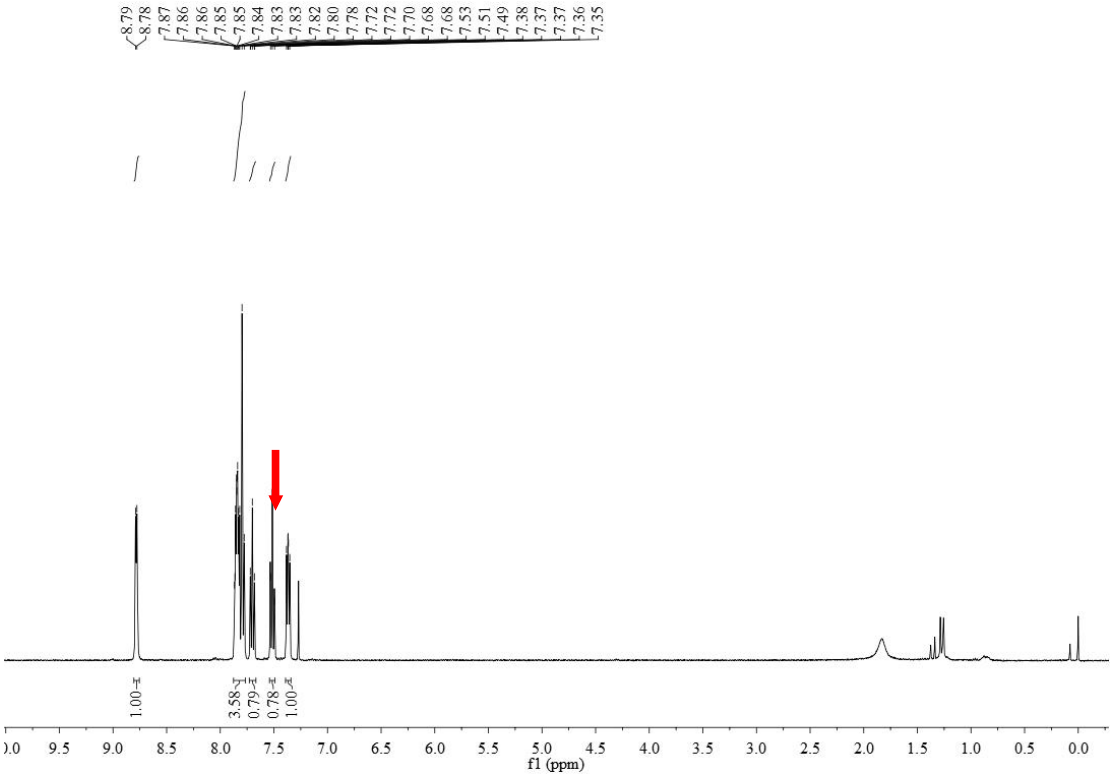
4.3 Intermolecular competition experiment:

A sealed tube with **1a** and deuterate substrate $[D]_5$-**1a** under the standard conditions proceeded:

To a sealed tube, **1a** (23.4 mg, 0.15 mmol) and $[D]_5$-**1a** (24 mg, 0.15 mmol), **2a** (83 mg, 0.45 mmol), $Pd(OAc)_2$ (3.4mg, 5 mol %), $Cu(TFA)_2$ (173 mg, 0.6 mmol) THF (1.0 mL) were added and stirred at 120 °C for 150 min. At ambient temperature, the reaction mixture was evaporated in vacuo and the remaining residue was purified by column chromatography on silica gel to afford $H_4/[D]_4$-**3a** (9 mg, 17%) as a solid. The H/D-incorporation in $H_4/[D]_4$-**3a** was estimated by ^{1}H-NMR spectroscopy.



^{1}H NMR spectra of compound H$_4$/[D]$_4$-**3a**



Refreences:

(1) X.-Z. Kou, M.-D. Zhao, X.-X. Qiao, Y.-M. Zhu, X.-F. Tong and Z.-M. Shen *Chem. Eur. J.*, 2013, **19**, 16880.

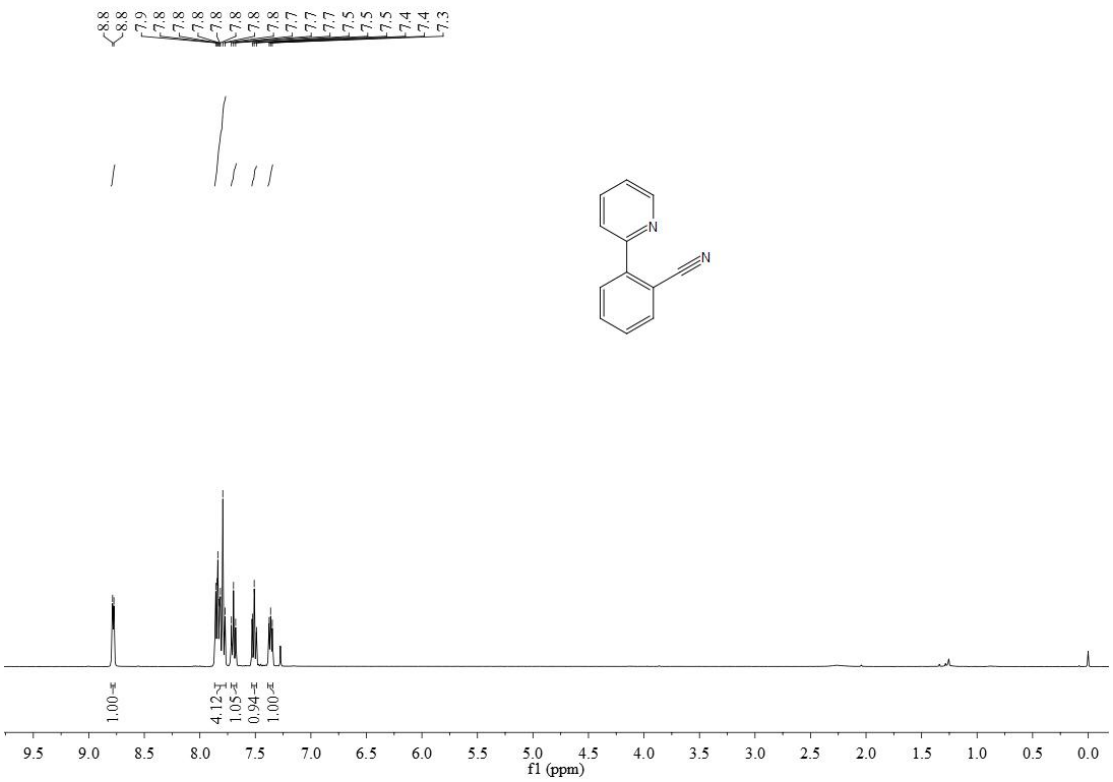
(2) A. F. de Brito, J. L. R. Martins, J. O. Fajemiroye, P. M. Galdino, T. C. M. De Lima,R. Menegatti and E. A. Costa, *Life Sciences,* 2012, **90**, 910.

(3) (a) Z.-B. Chen, Y. Zhang, Q. Yuan, F.-L. Zhang, Y.-M. Zhu and J.-K. Shen, *J. Org. Chem.*, 2016, **81**, 1610. (b) Fontaine, P.; Chiaroni, A. L.; Masson, G.; Zhu, J. P. *Org. Lett.* **2008**, *10,* 1509.

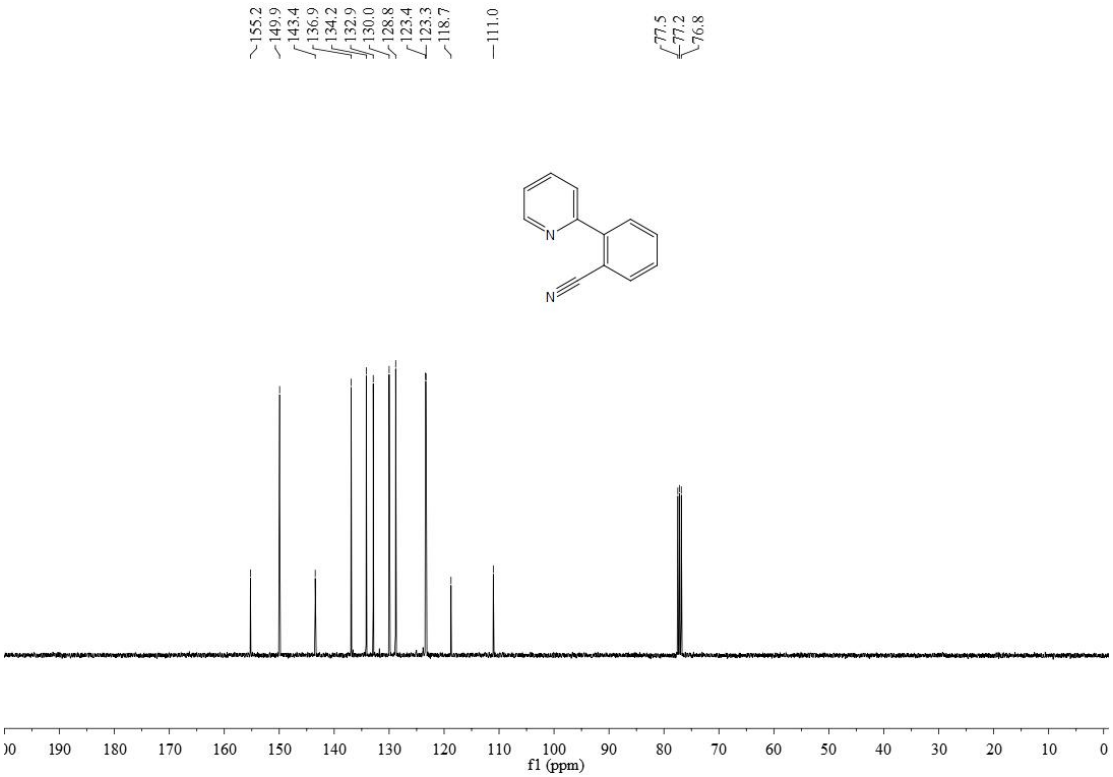
(4) (a) C. Liu, N. Han, X.-X. Song, and J.-S. Qiu *Eur. J. Org. Chem.* 2010, 5548. (b) J. Jin, Q. Wen, P. Lu and Y. Wang, *Chem. Commun.*, 2012, **48**, 9933. (c) J. Li, L. Ackermann, *Angew. Chem.* 2015, **127**, 3906; *Angew. Chem. Int. Ed.* 2015, **54**, 3635. (d) A. B. Pawar and S. Chang, *Org. Lett.*, 2015, **17**, 660. (e) X. Hong, H. Wang, G. Qian, Q. Tan and B. Xu, *J. Org. Chem.*, 2014, **79**, 3228. (f) X.-F. Jia, D.-P. Yang,W.-H Wang, F. Luo, and J. Cheng *J. Org. Chem.* 2009, **74**, 9470.

5. NMR spectra for the products

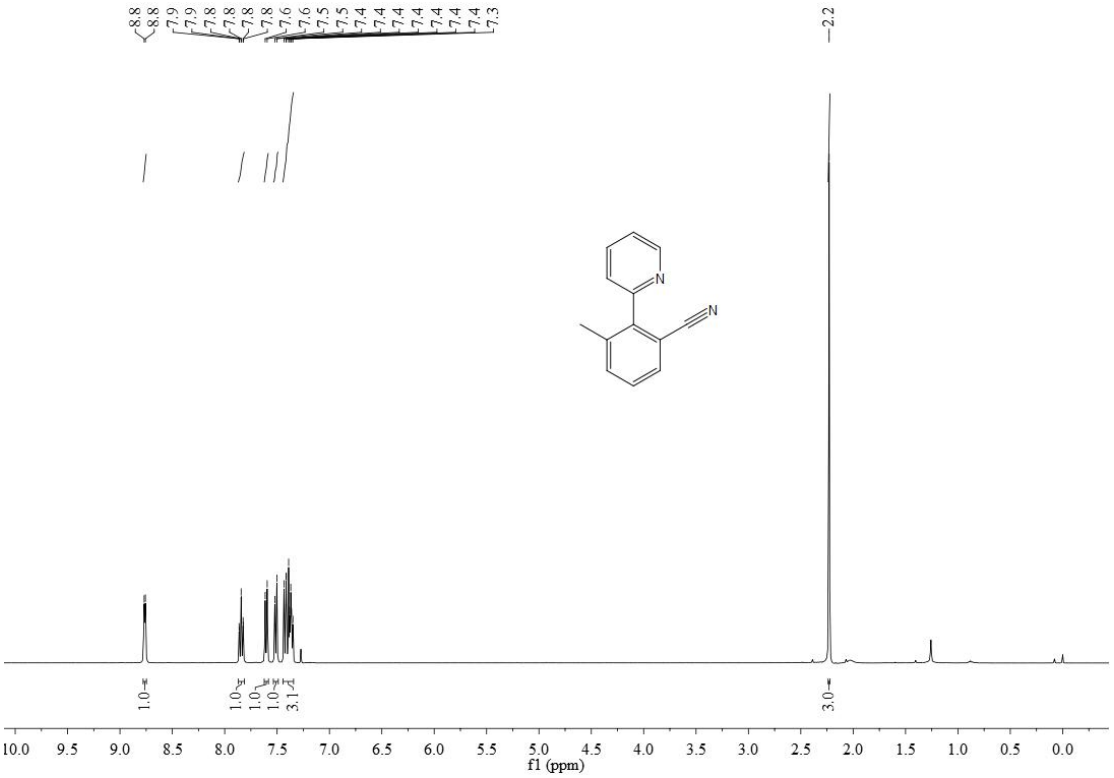
^{1}H NMR spectrum of compound **3a**



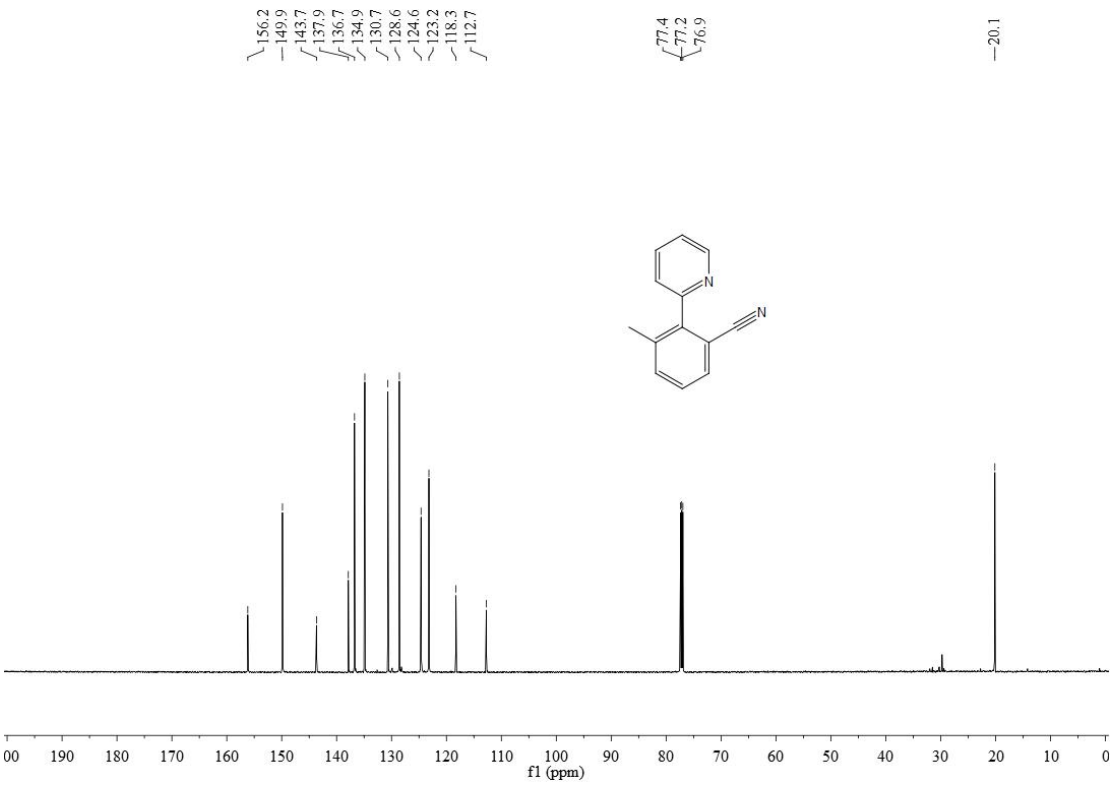
^{13}C NMR spectrum of compound **3a**



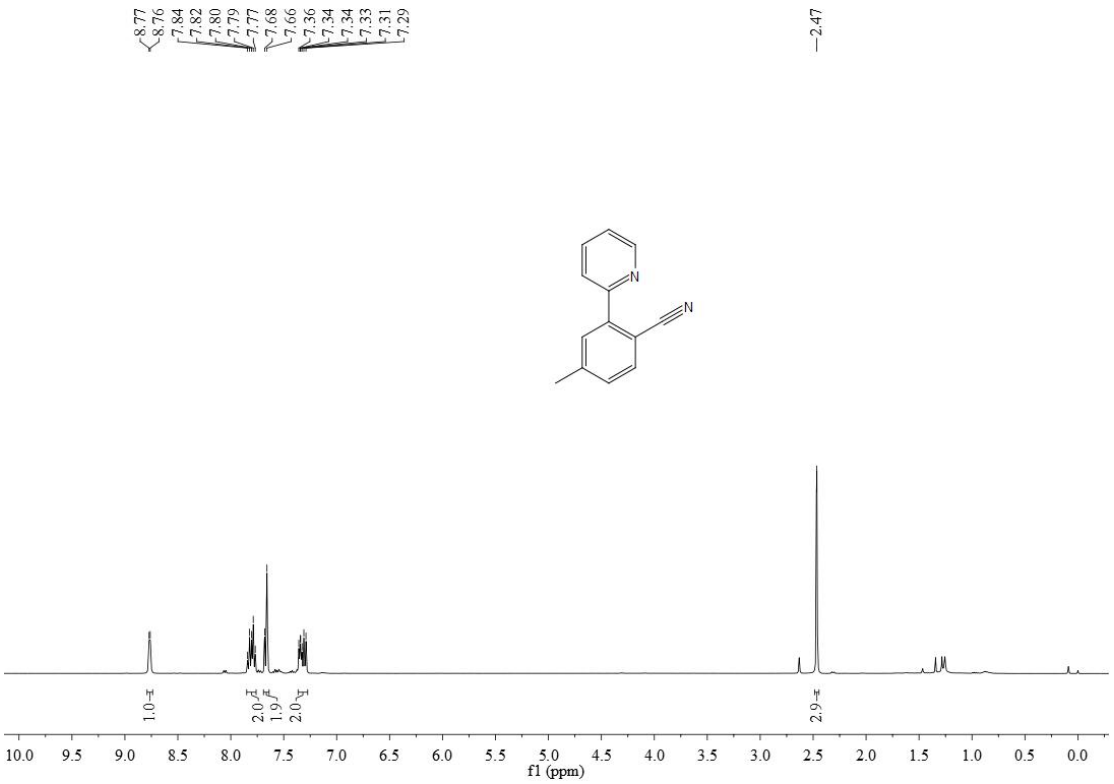
^{1}H NMR spectrum of compound **3b**



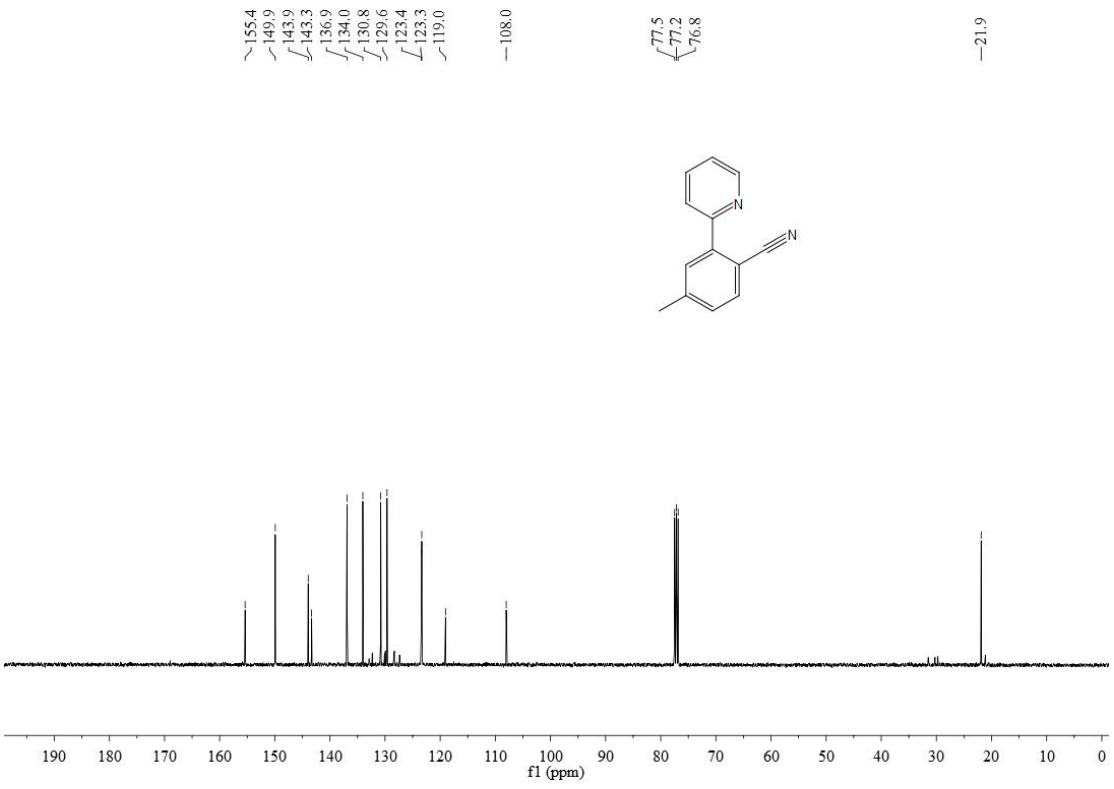
^{13}C NMR spectrum of compound **3b**



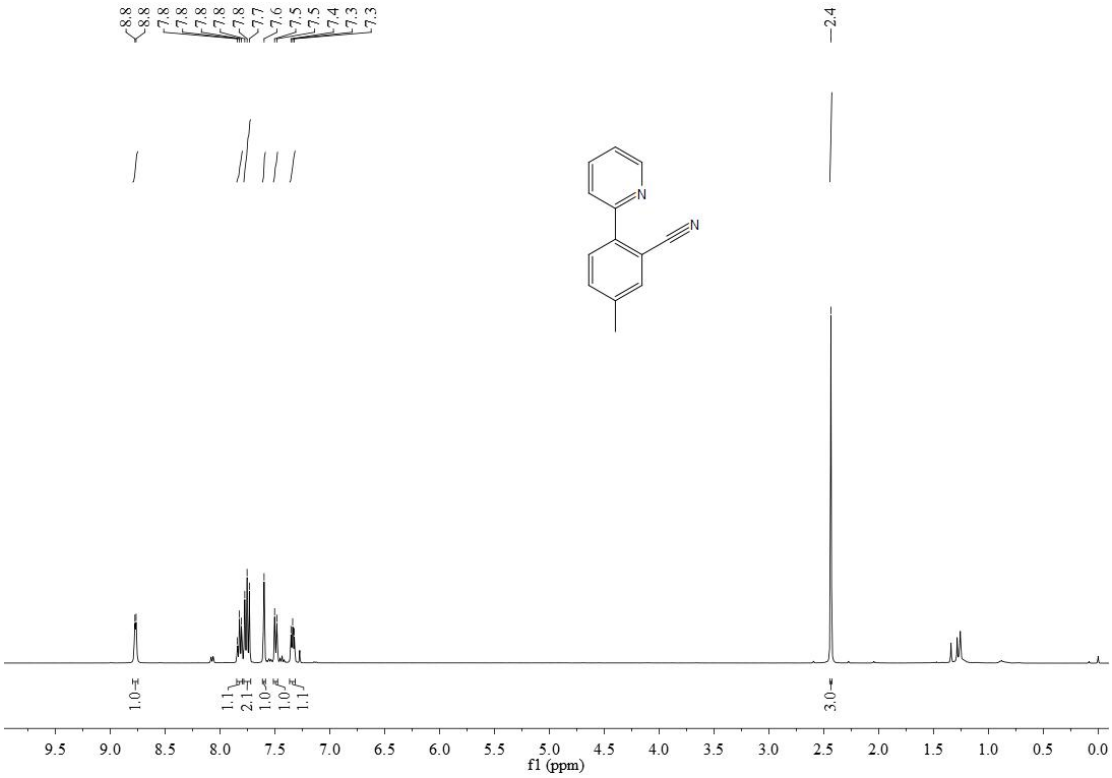
^{1}H NMR spectrum of compound **3c**



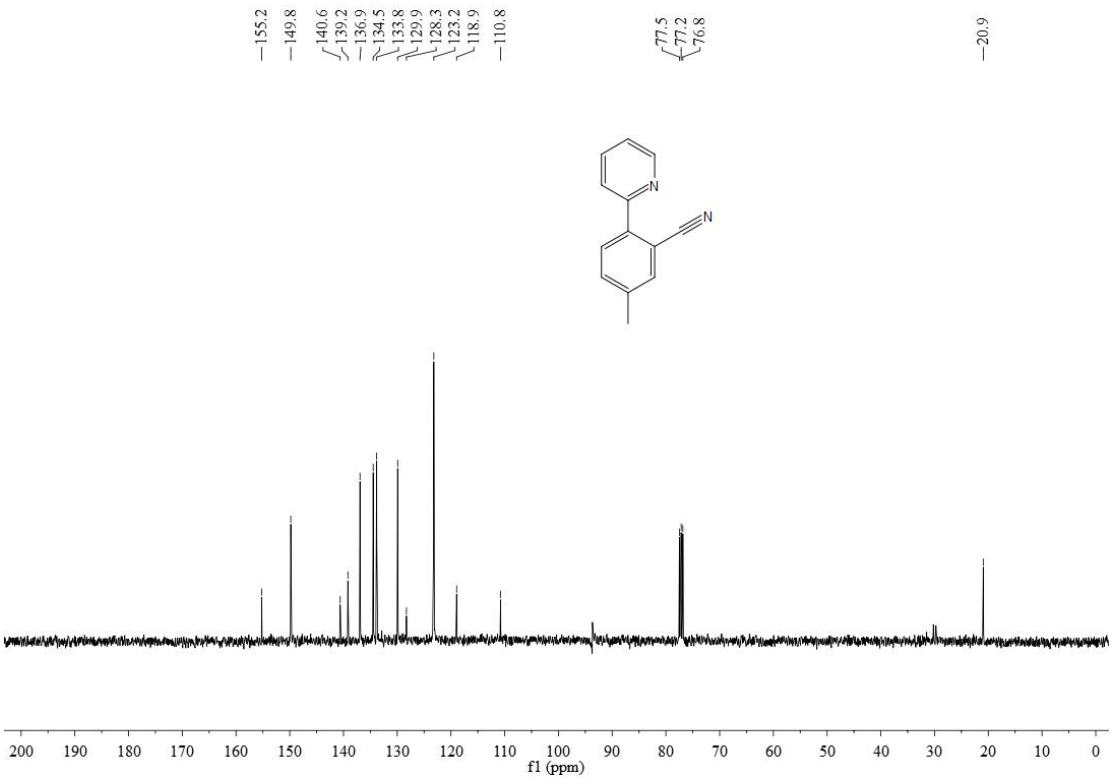
^{13}C NMR spectrum of compound **3c**



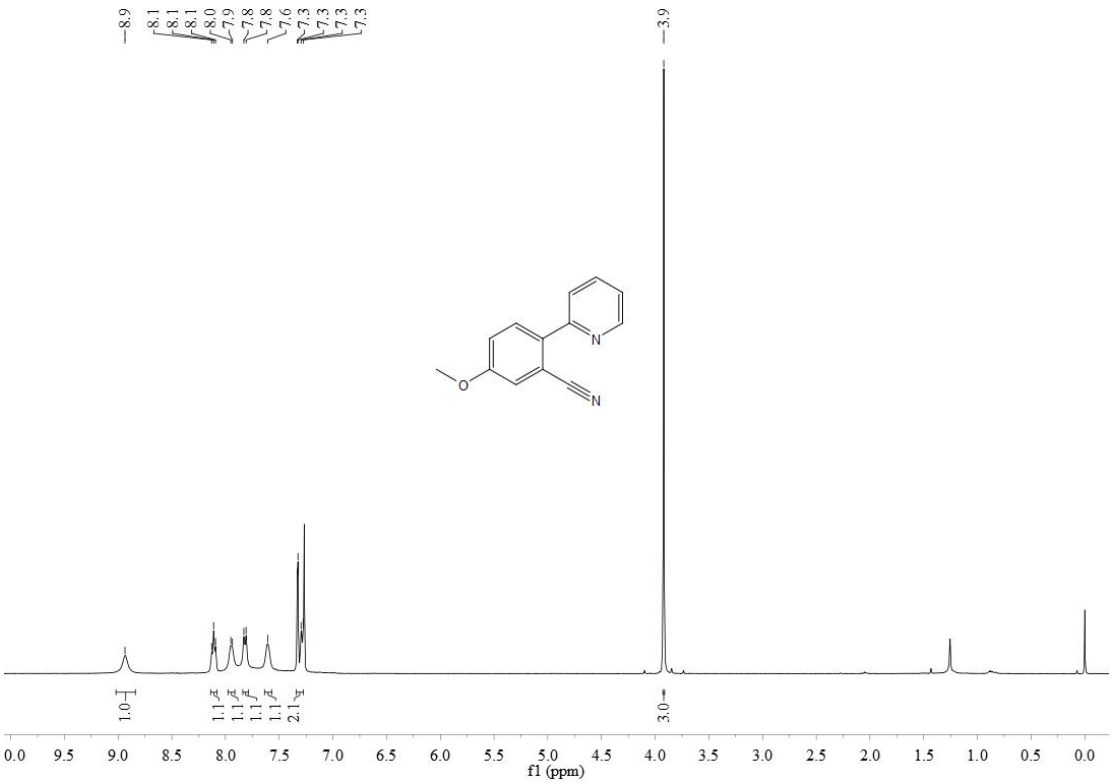
^{1}H NMR spectrum of compound **3d**



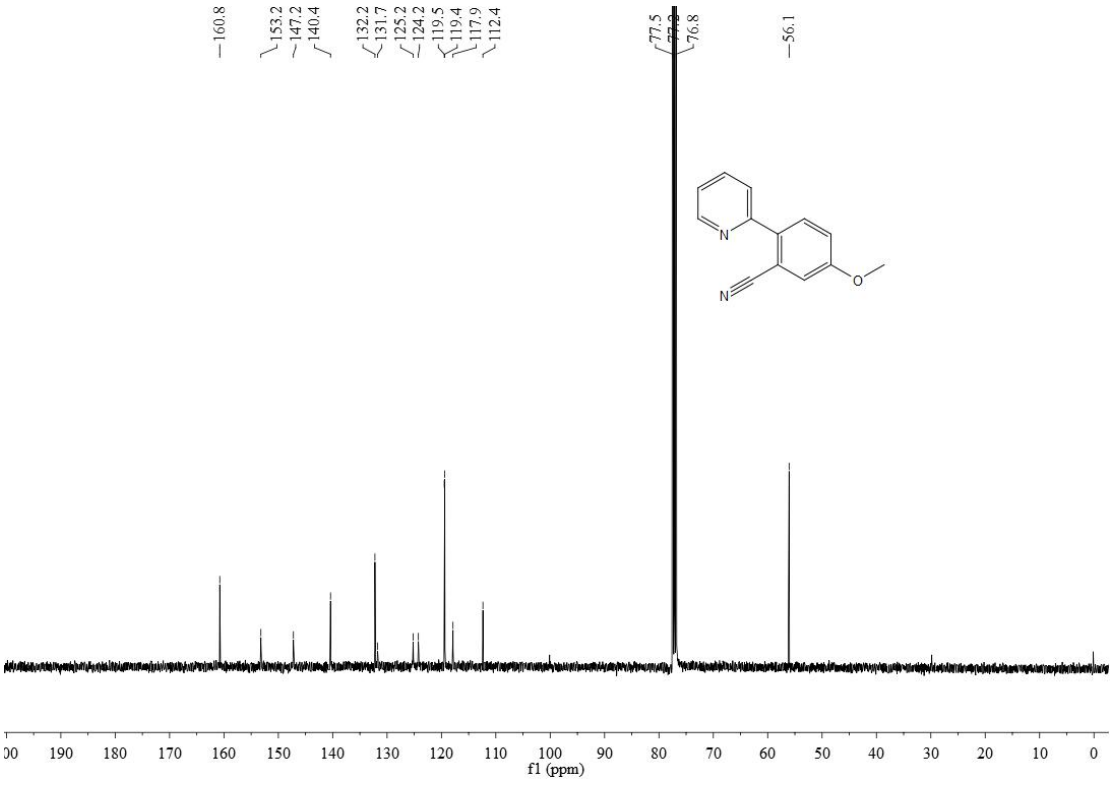
^{13}C NMR spectrum of compound **3d**



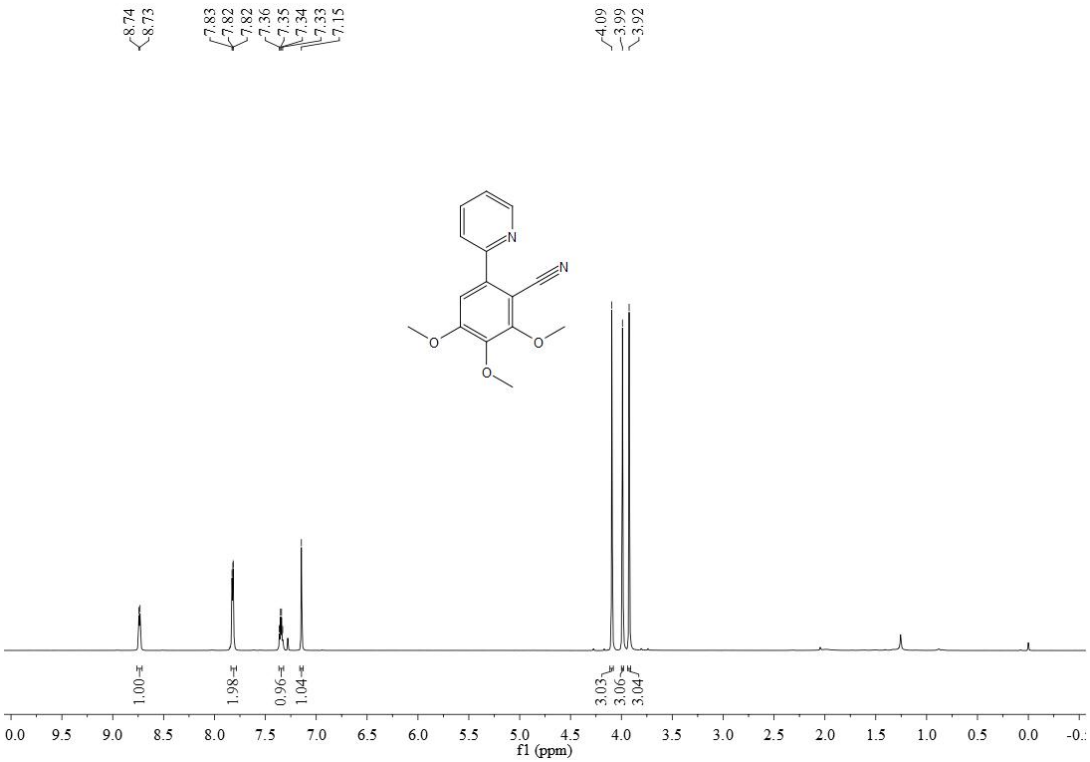
^{1}H NMR spectrum of compound **3e**



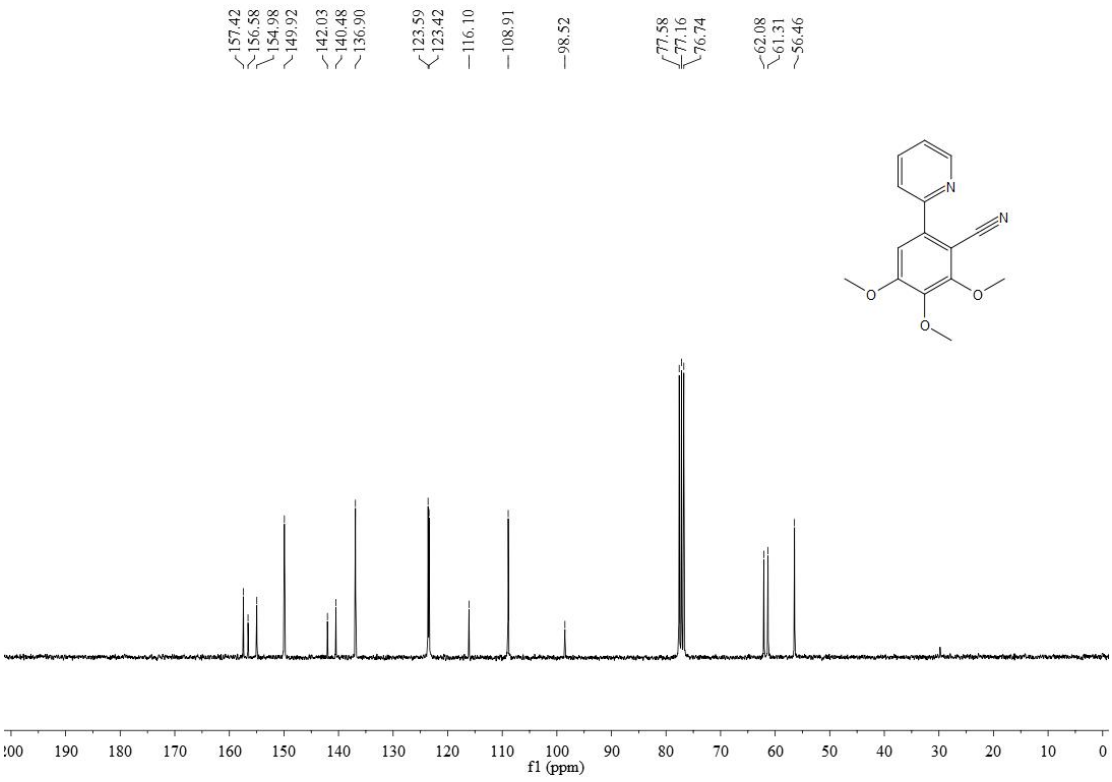
^{13}C NMR spectrum of compound **3e**



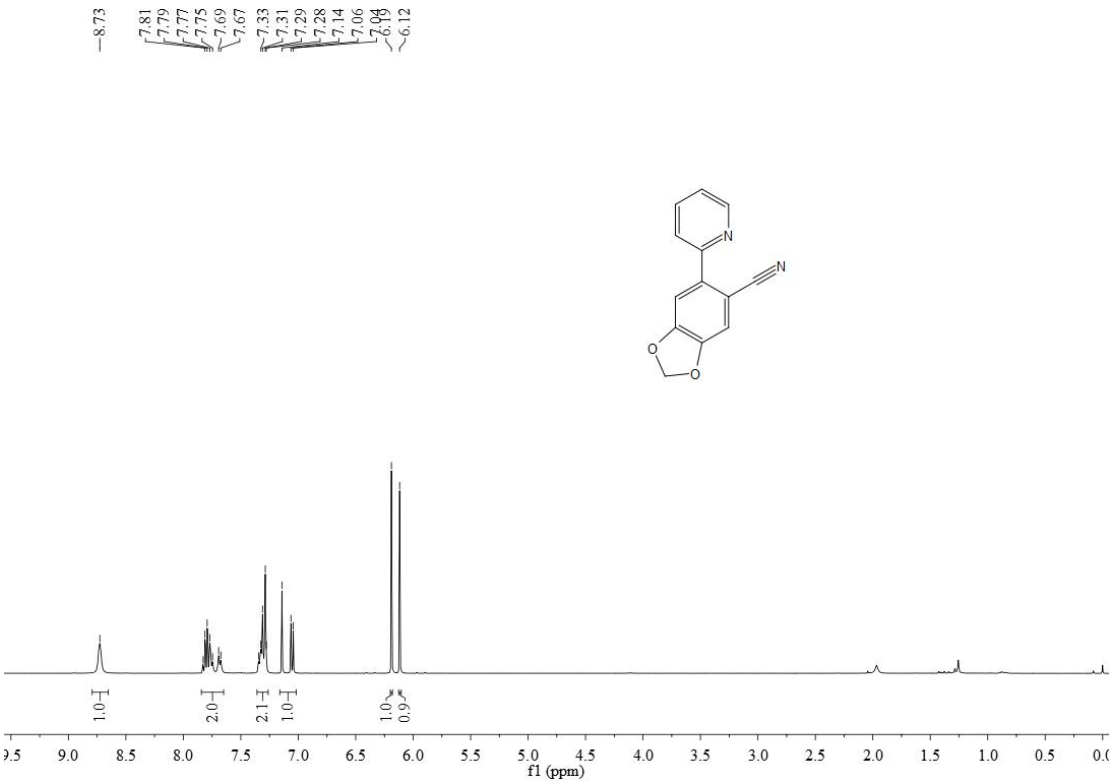
^{1}H NMR spectrum of compound **3f**



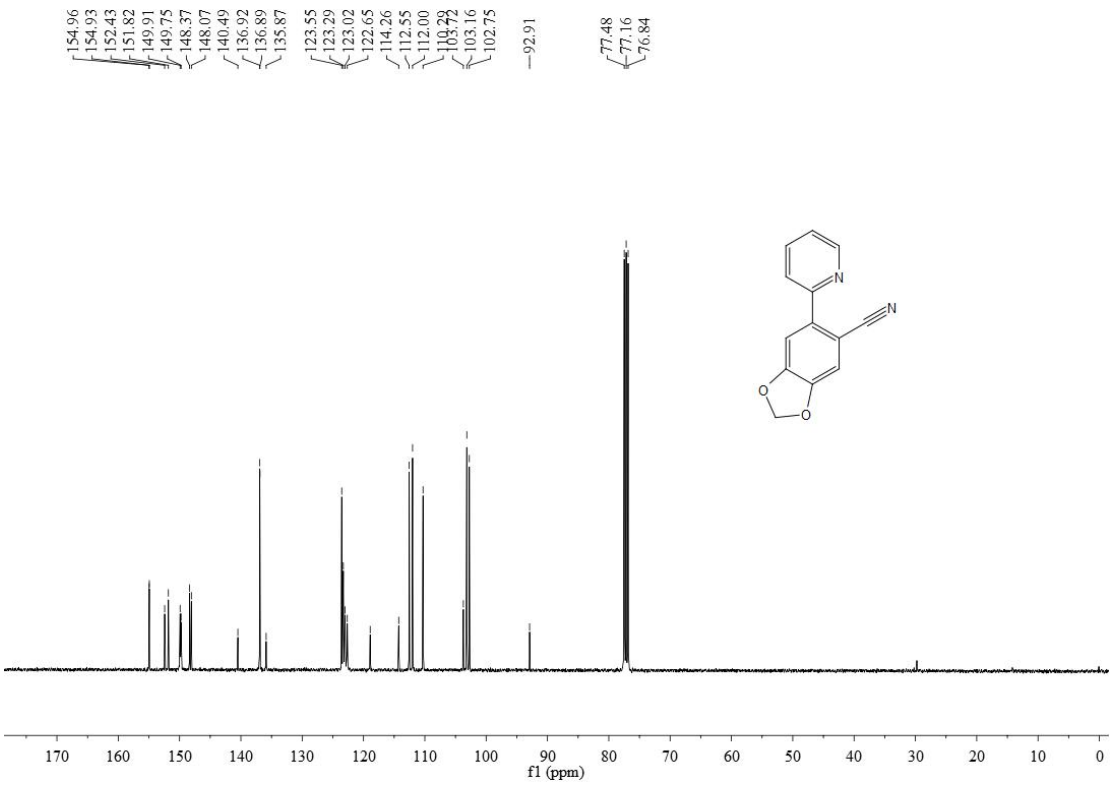
^{13}C NMR spectrum of compound **3f**



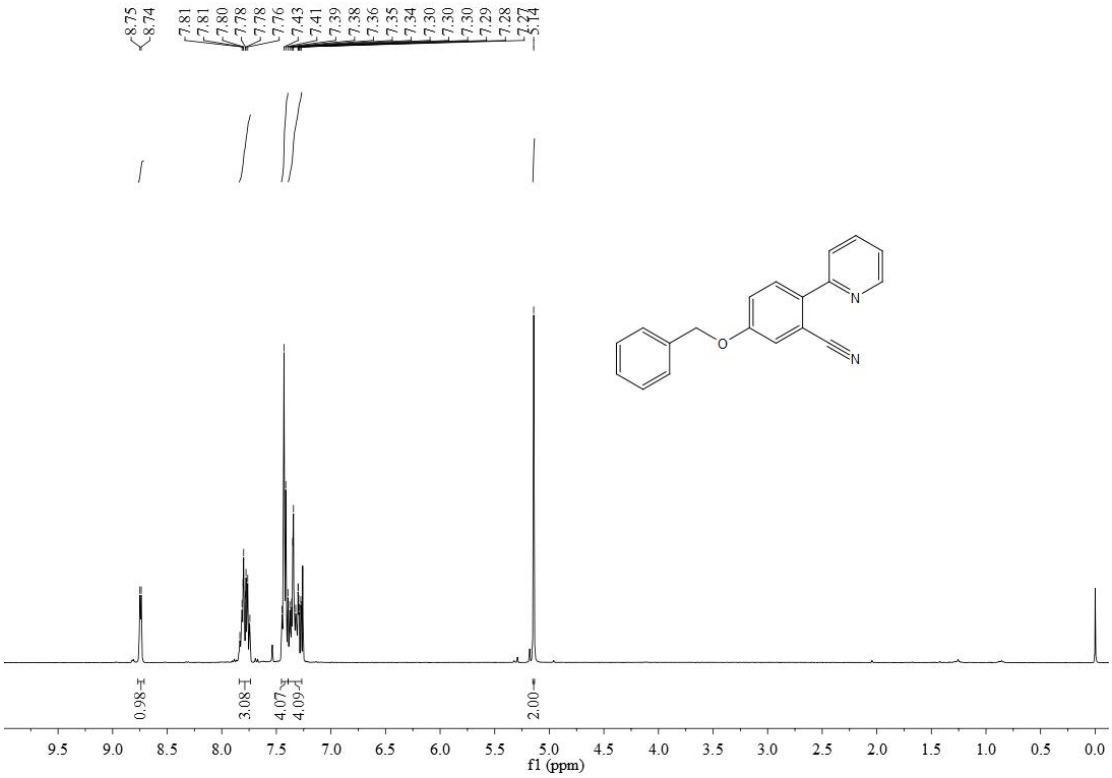
^{1}H NMR spectrum of compound **3g**



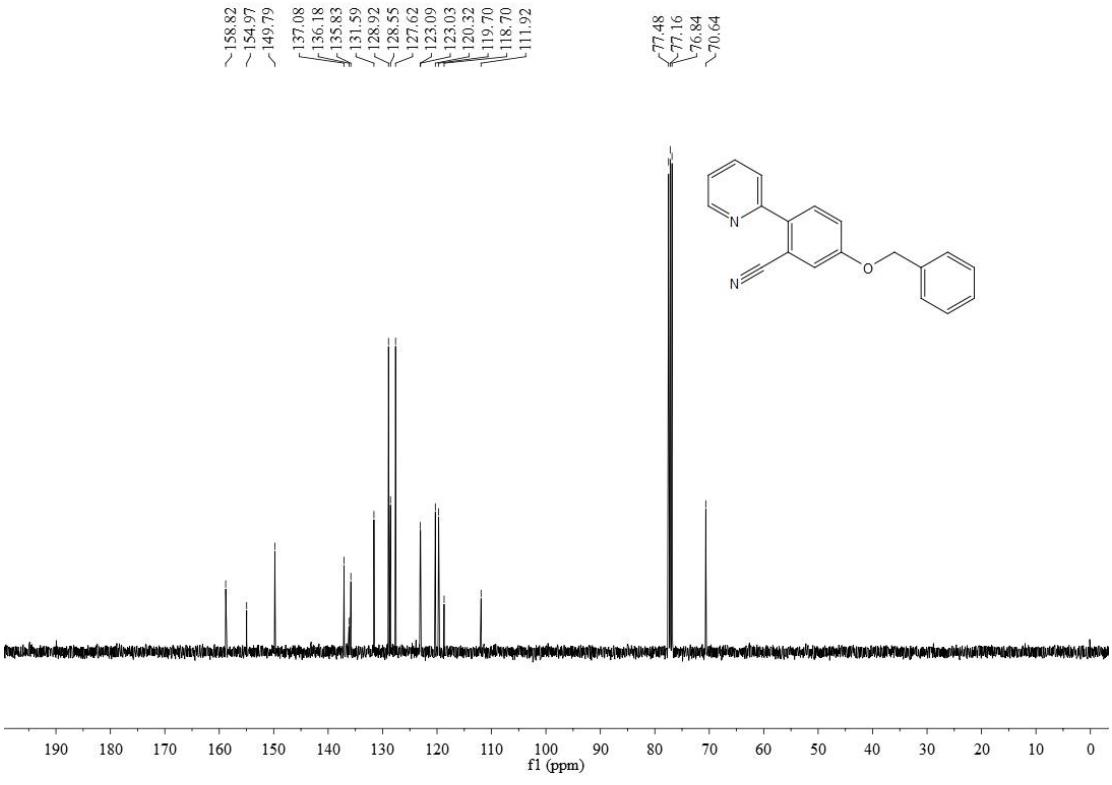
^{13}C NMR spectrum of compound **3g**



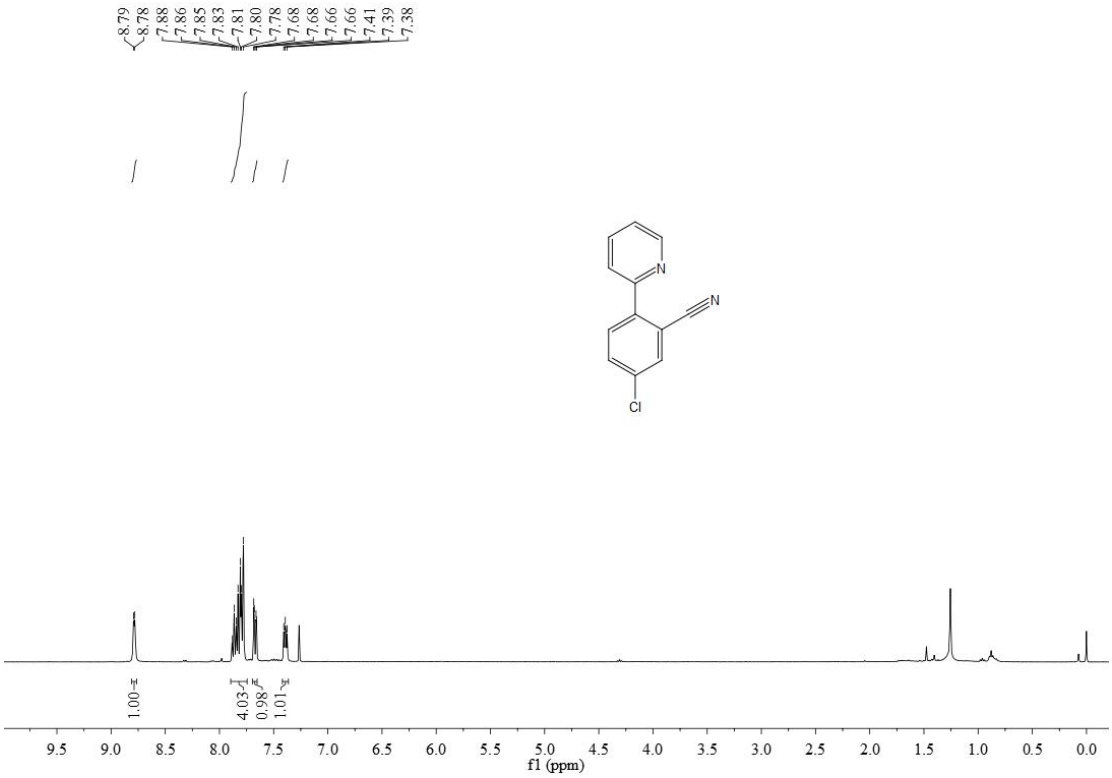
^{1}H NMR spectrum of compound **3h**



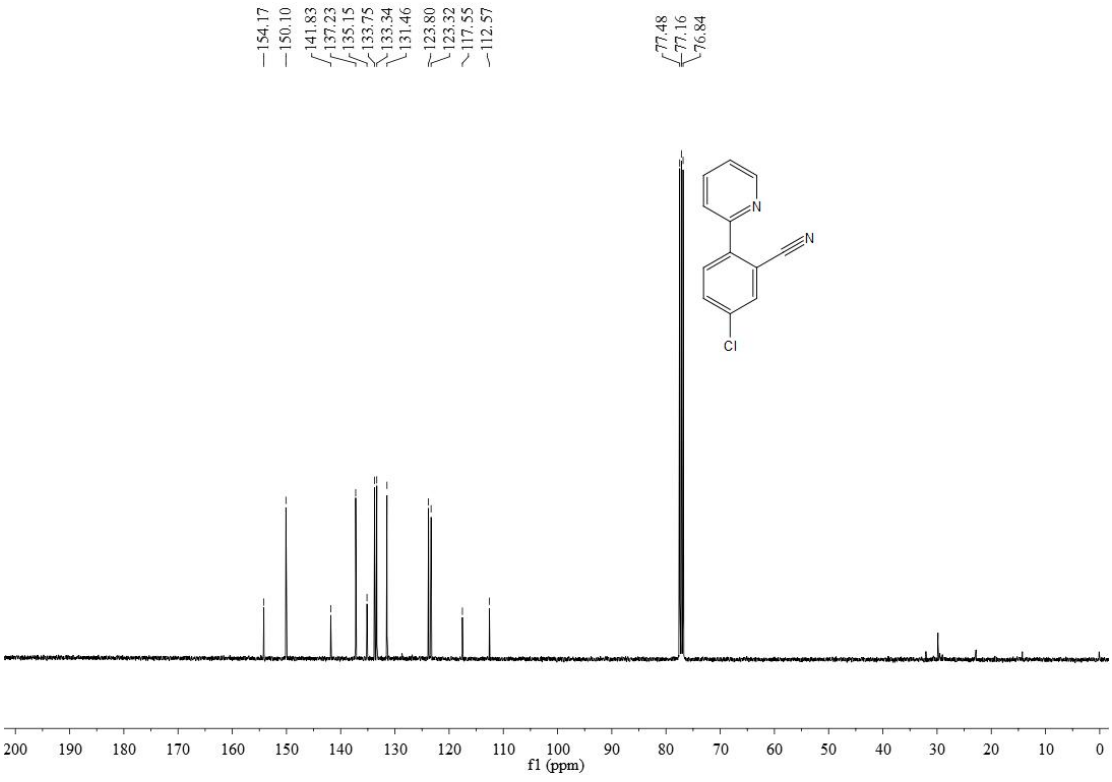
^{13}C NMR spectrum of compound **3h**



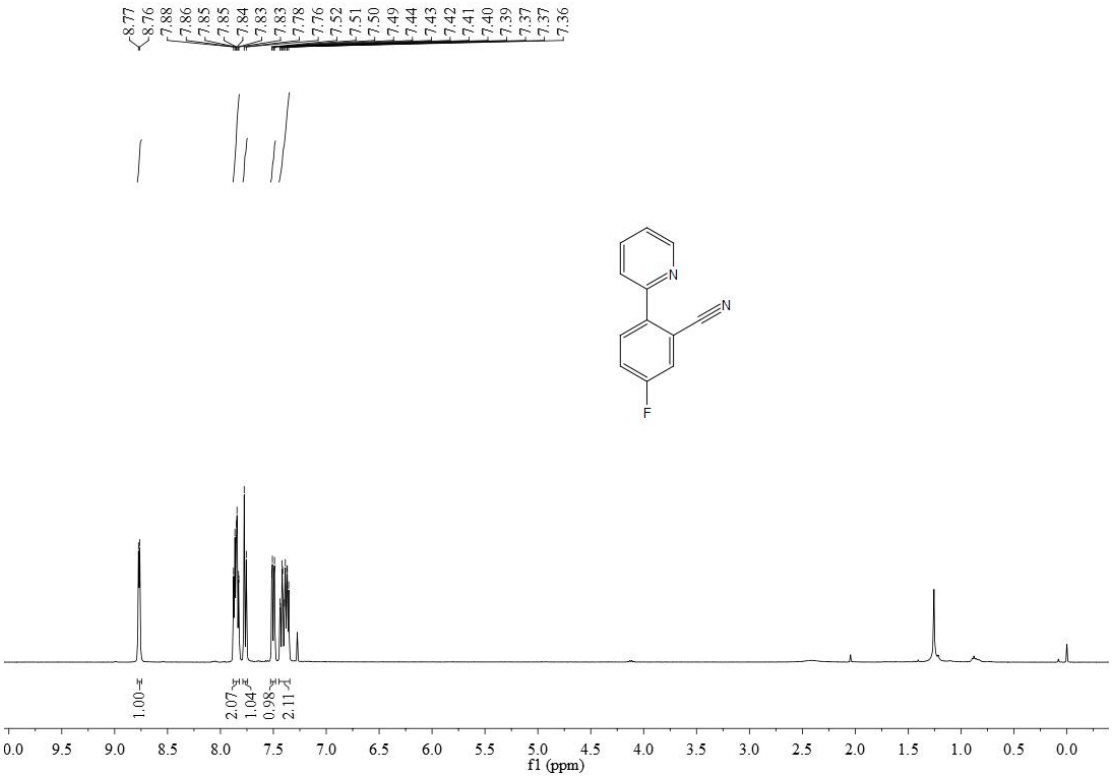
^{1}H NMR spectrum of compound **3i**



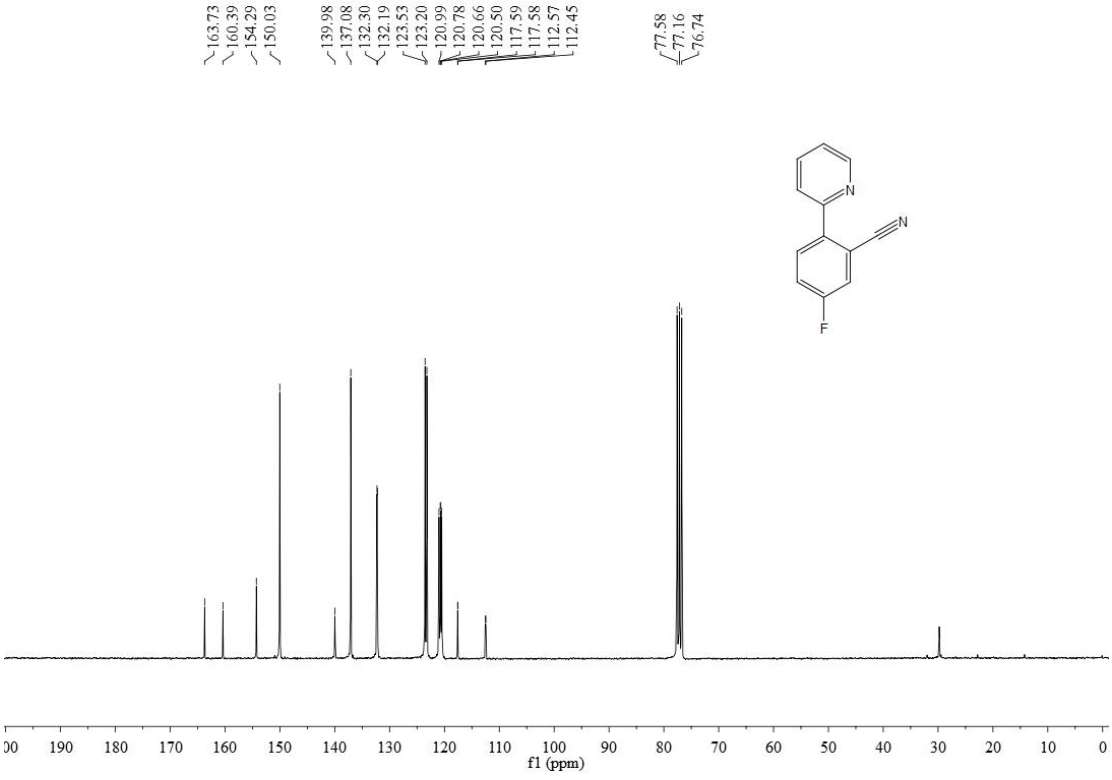
^{13}C NMR spectrum of compound **3i**



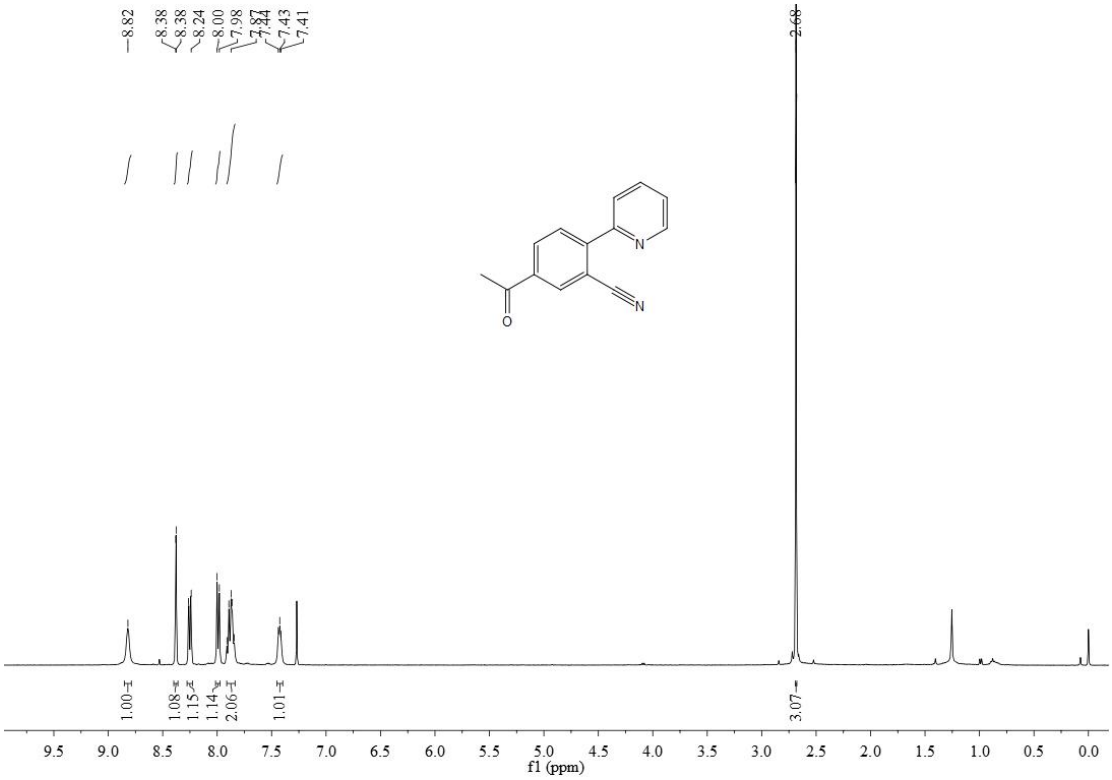
^{1}H NMR spectrum of compound **3j**



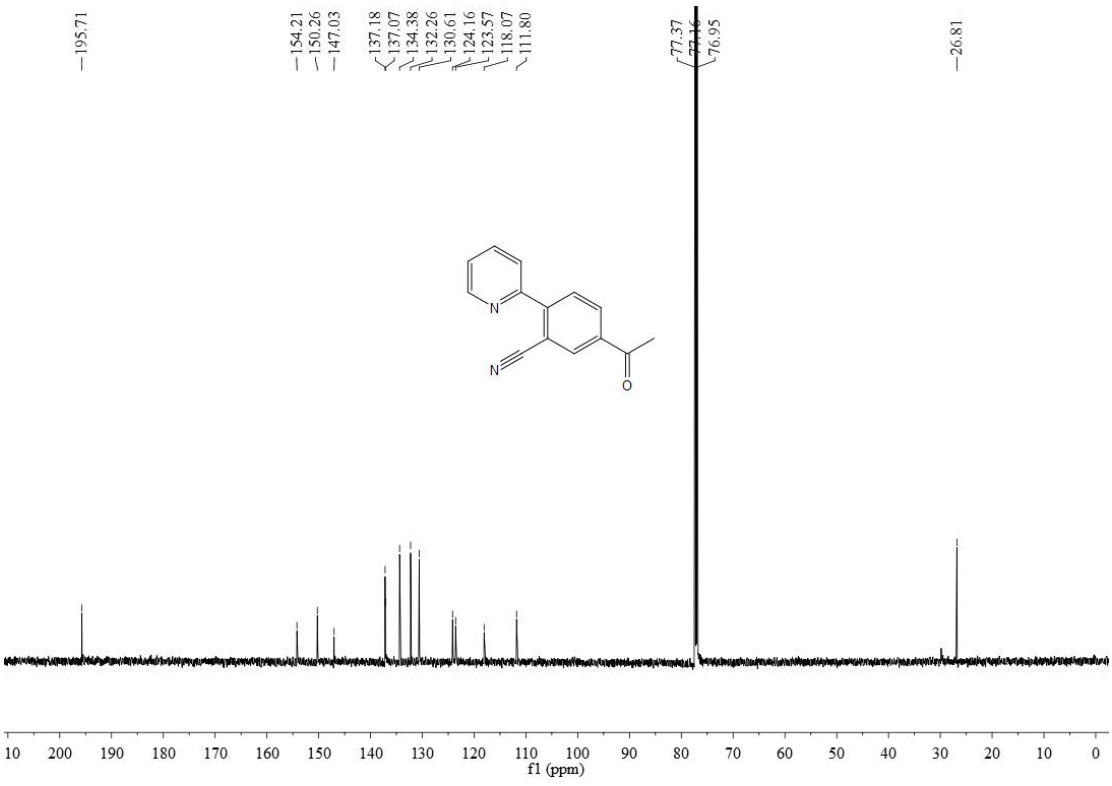
^{13}C NMR spectrum of compound **3j**



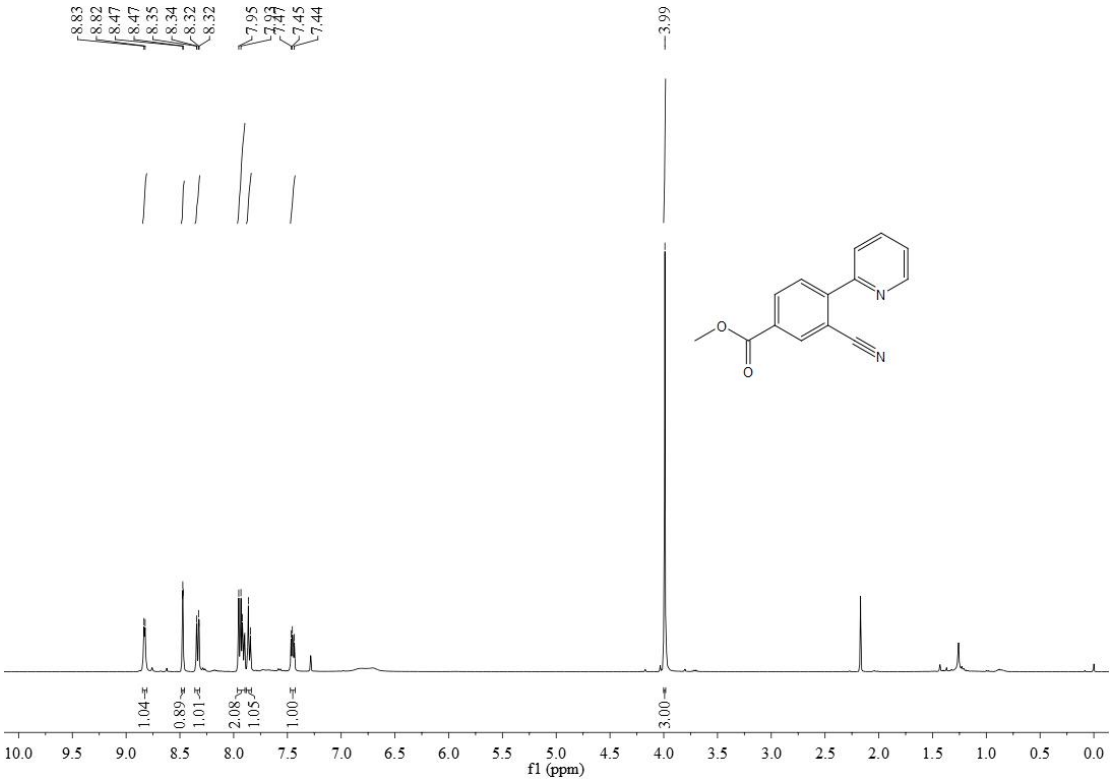
^{1}H NMR spectrum of compound **3k**



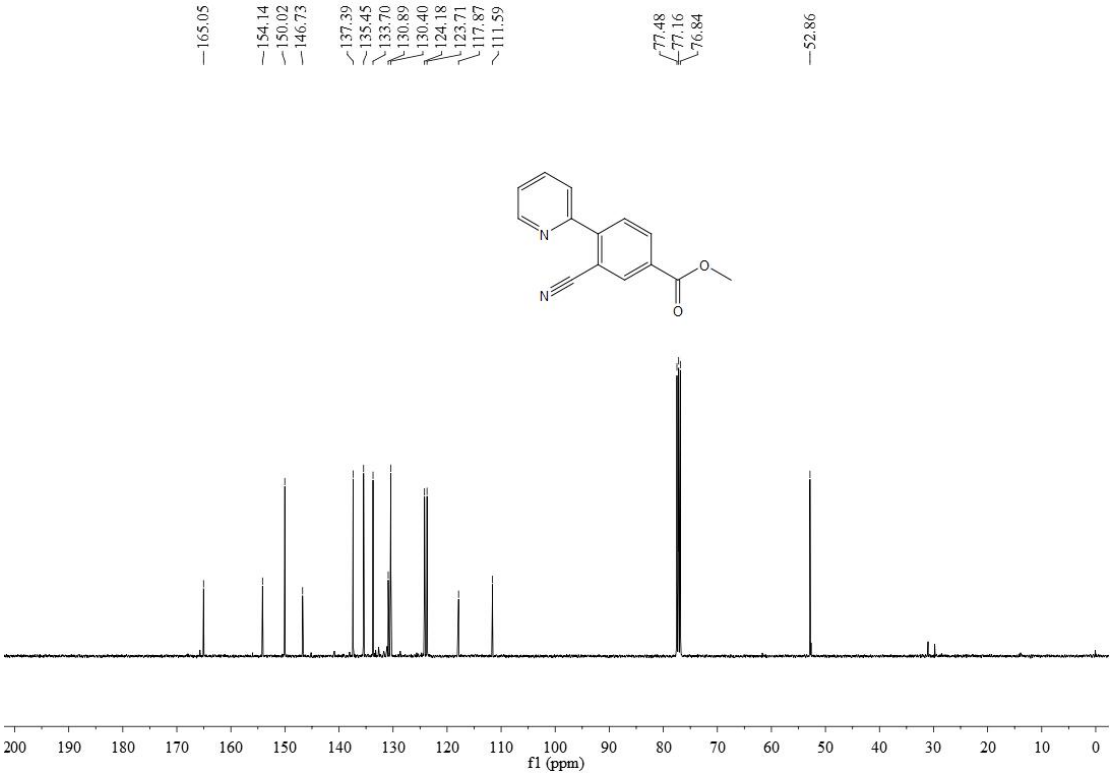
^{13}C NMR spectrum of compound **3k**



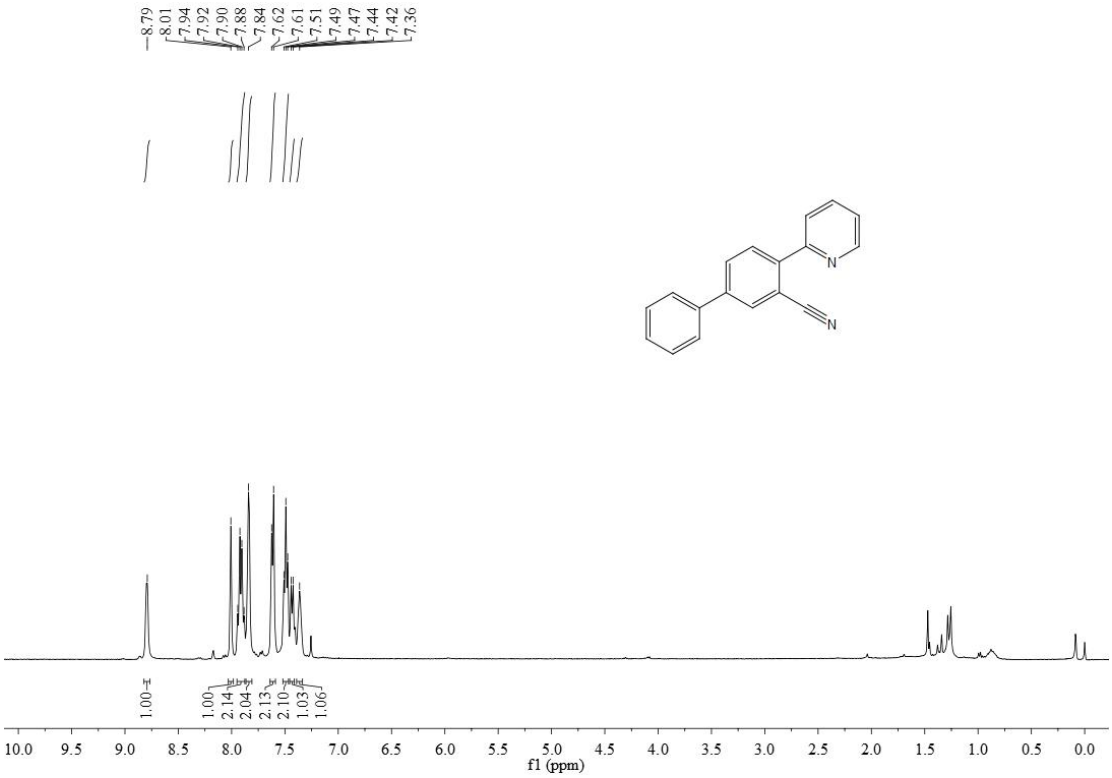
^{1}H NMR spectrum of compound **3l**



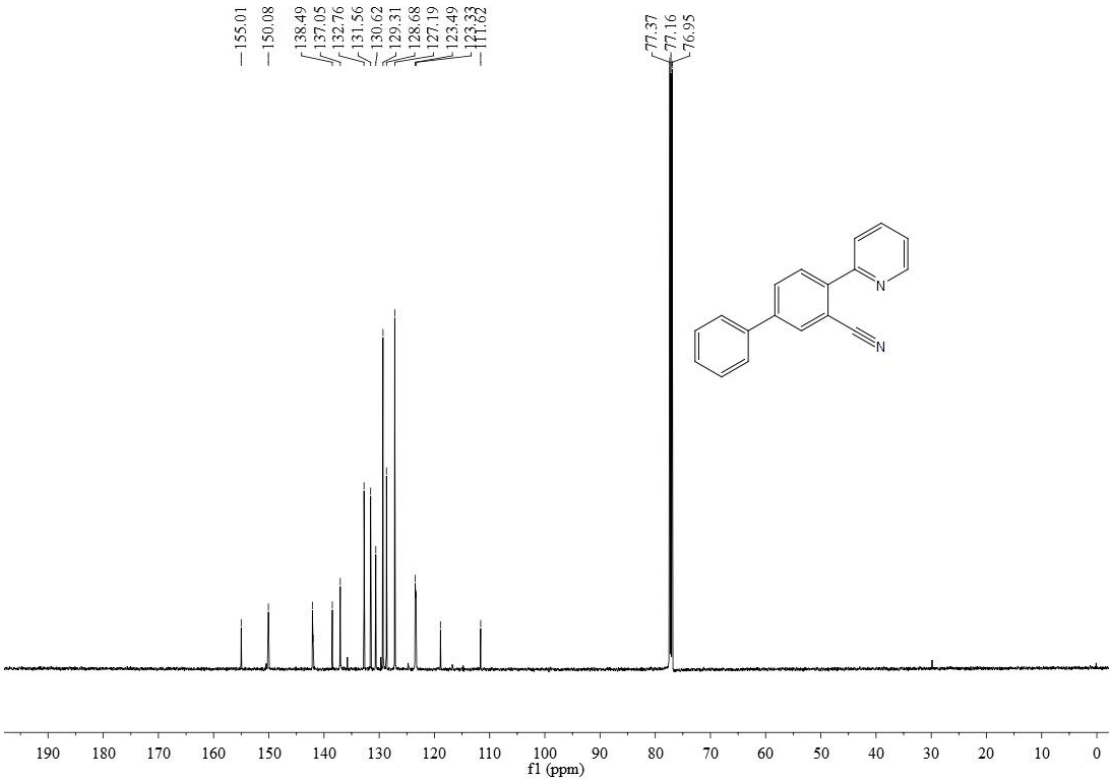
^{13}C NMR spectrum of compound **3l**



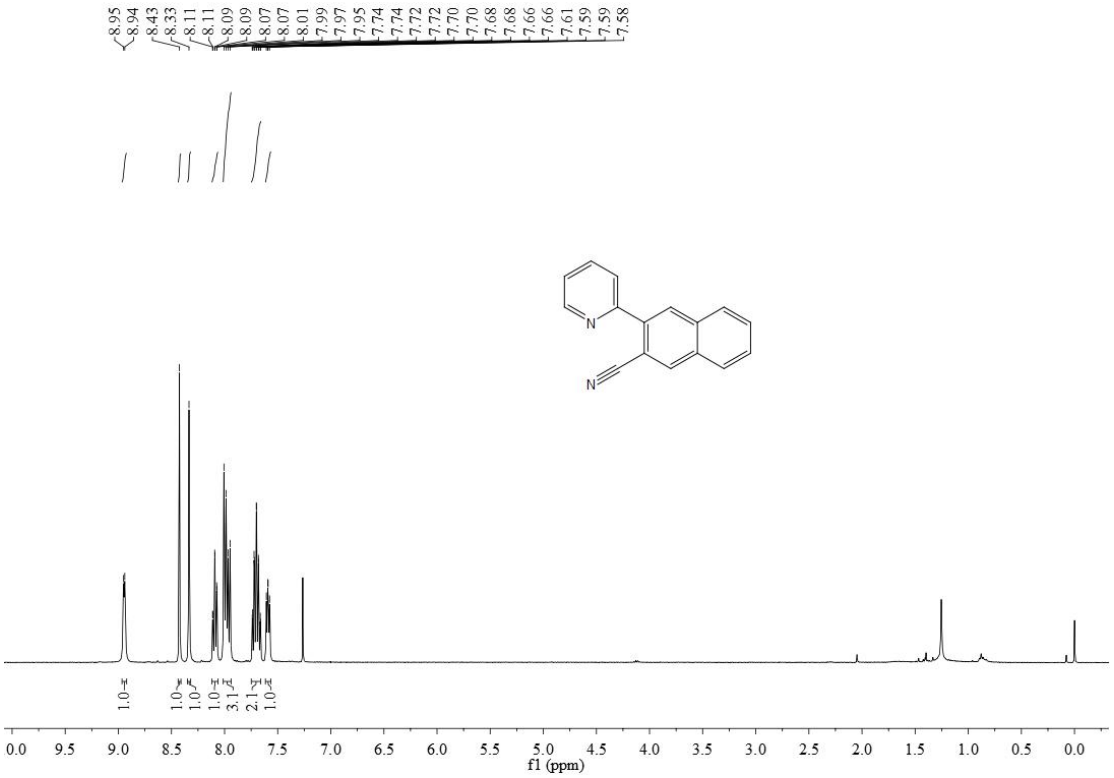
^{1}H NMR spectrum of compound **3m**



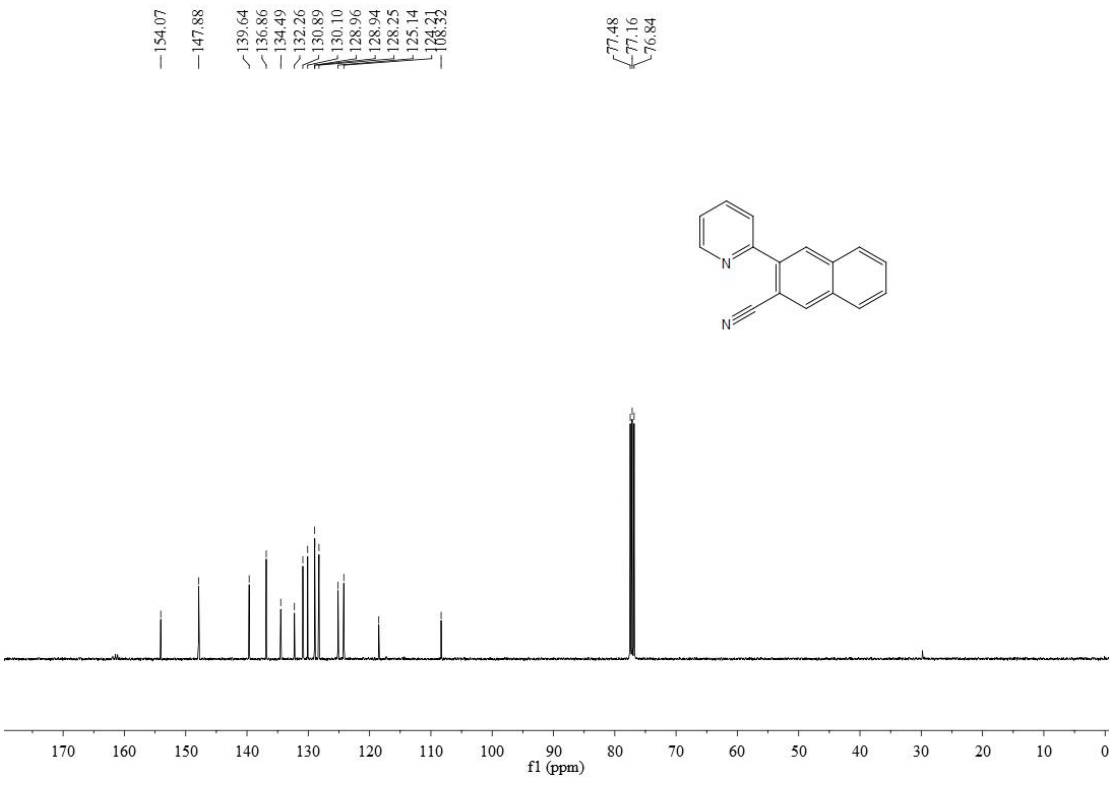
^{13}C NMR spectrum of compound **3m**



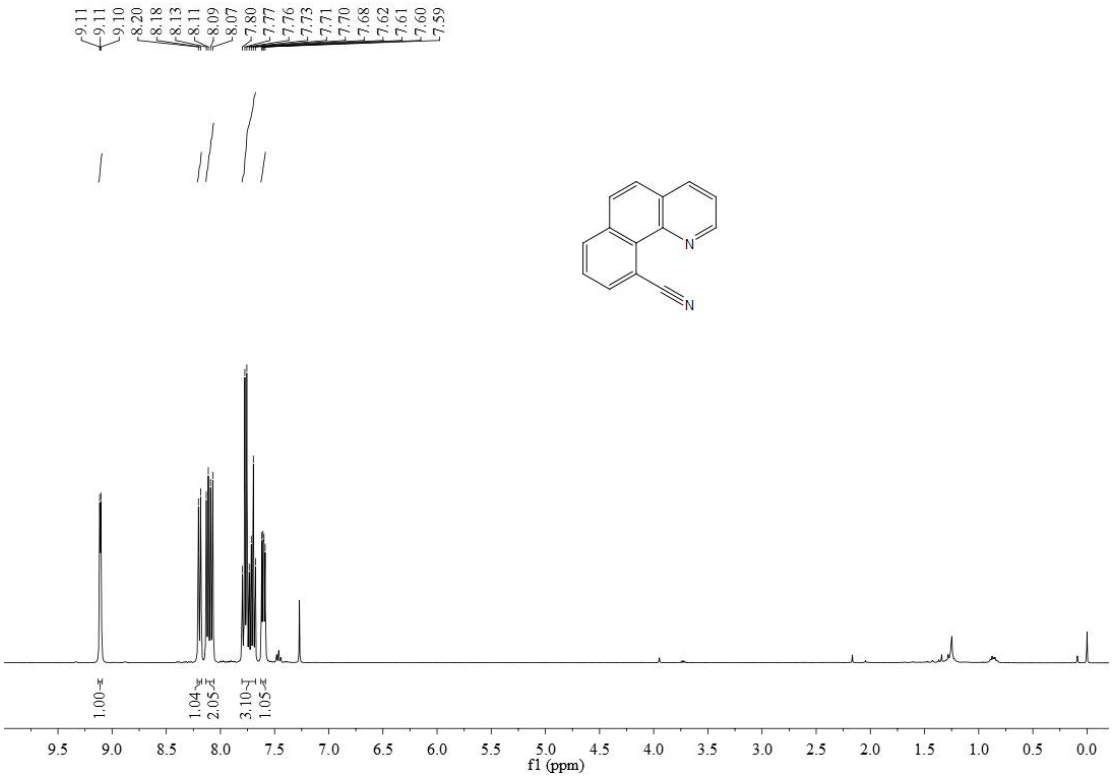
^{1}H NMR spectrum of compound **3n**



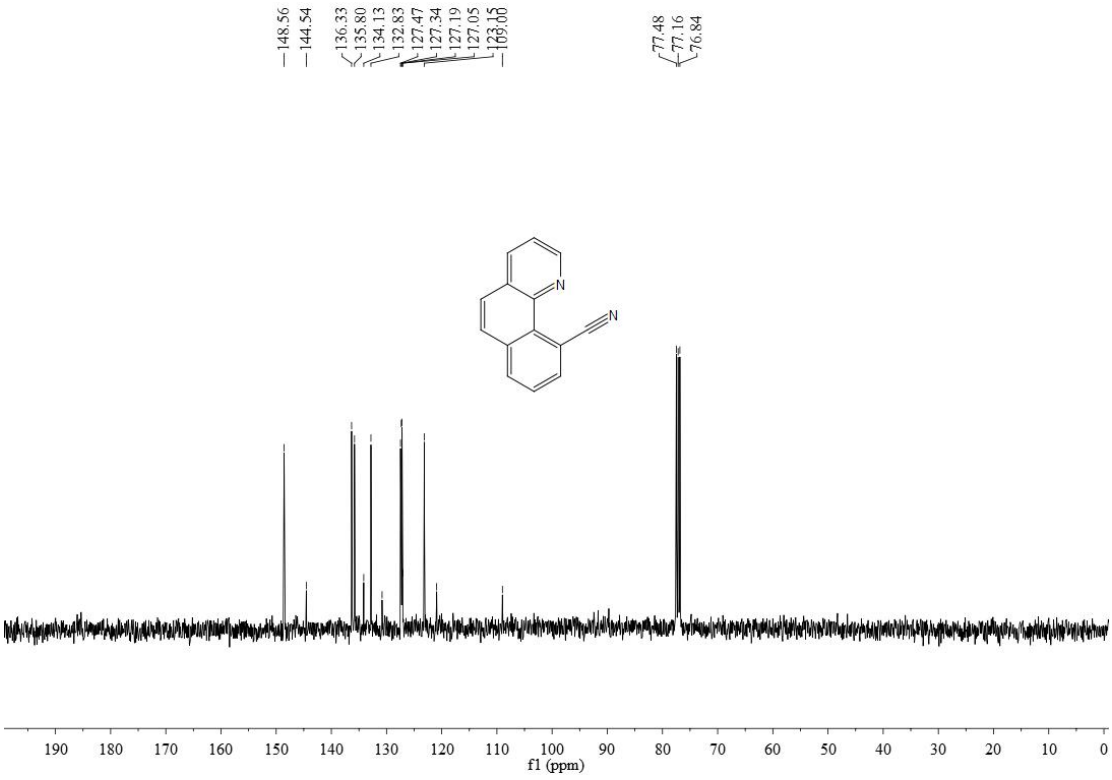
^{13}C NMR spectrum of compound **3n**



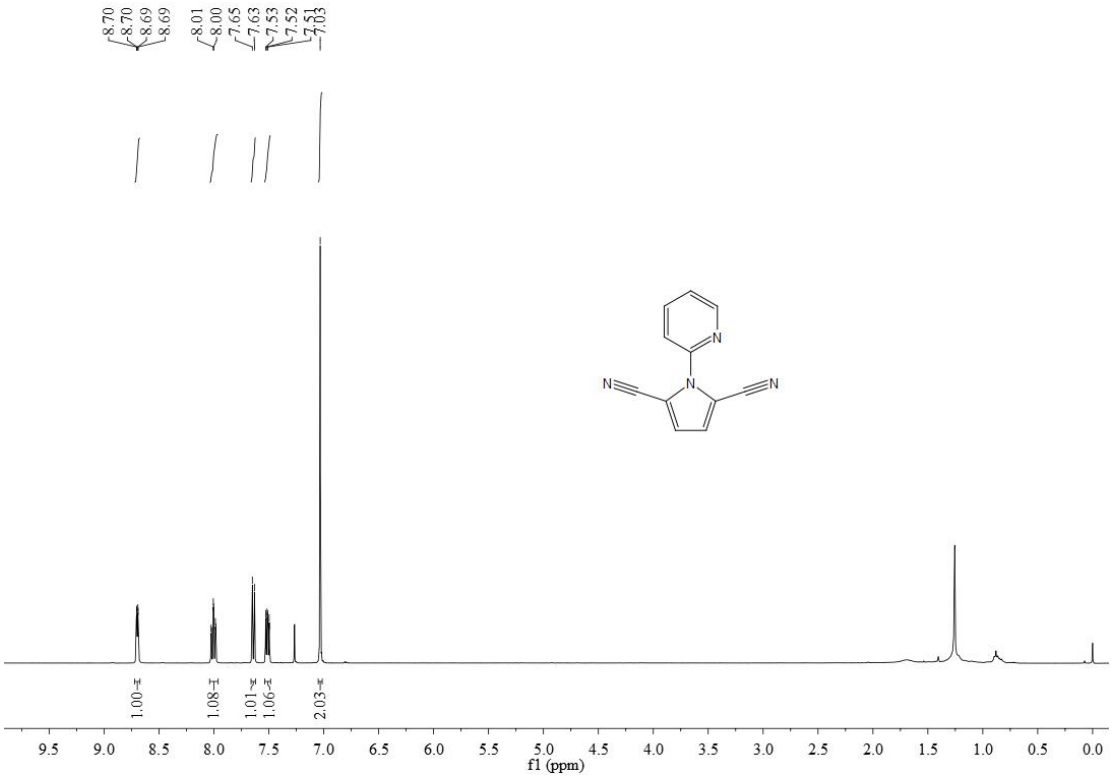
^{1}H NMR spectrum of compound **3o**



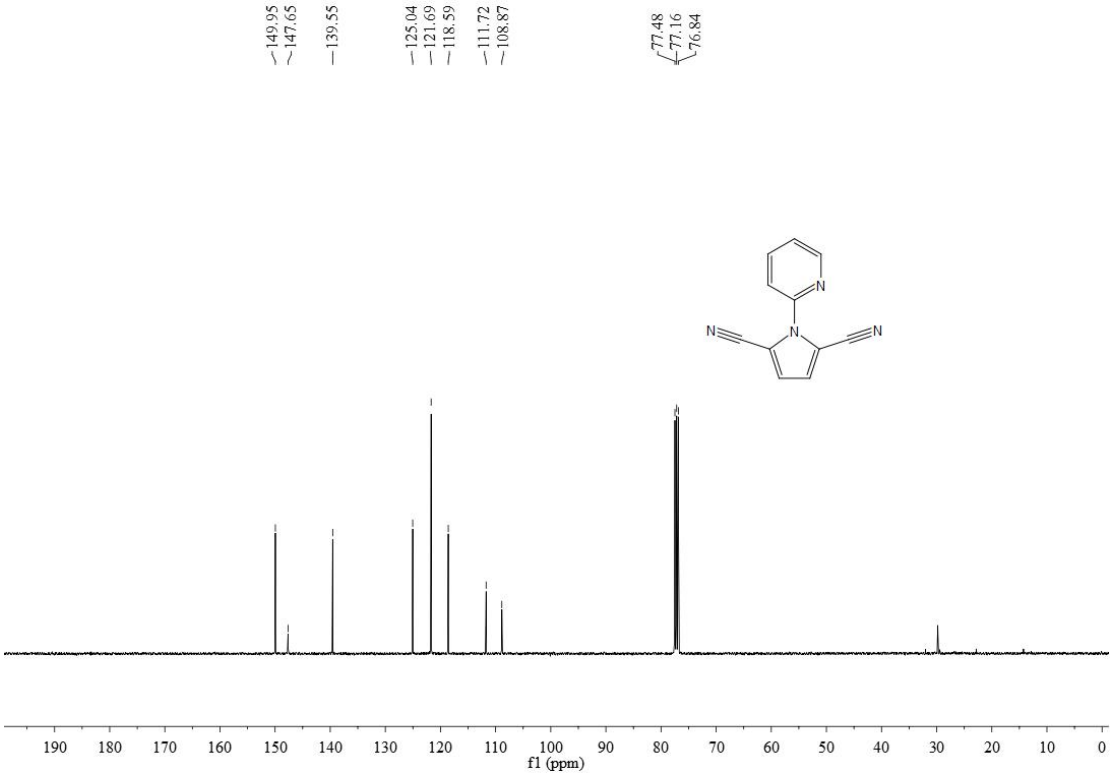
^{13}C NMR spectrum of compound **3o**



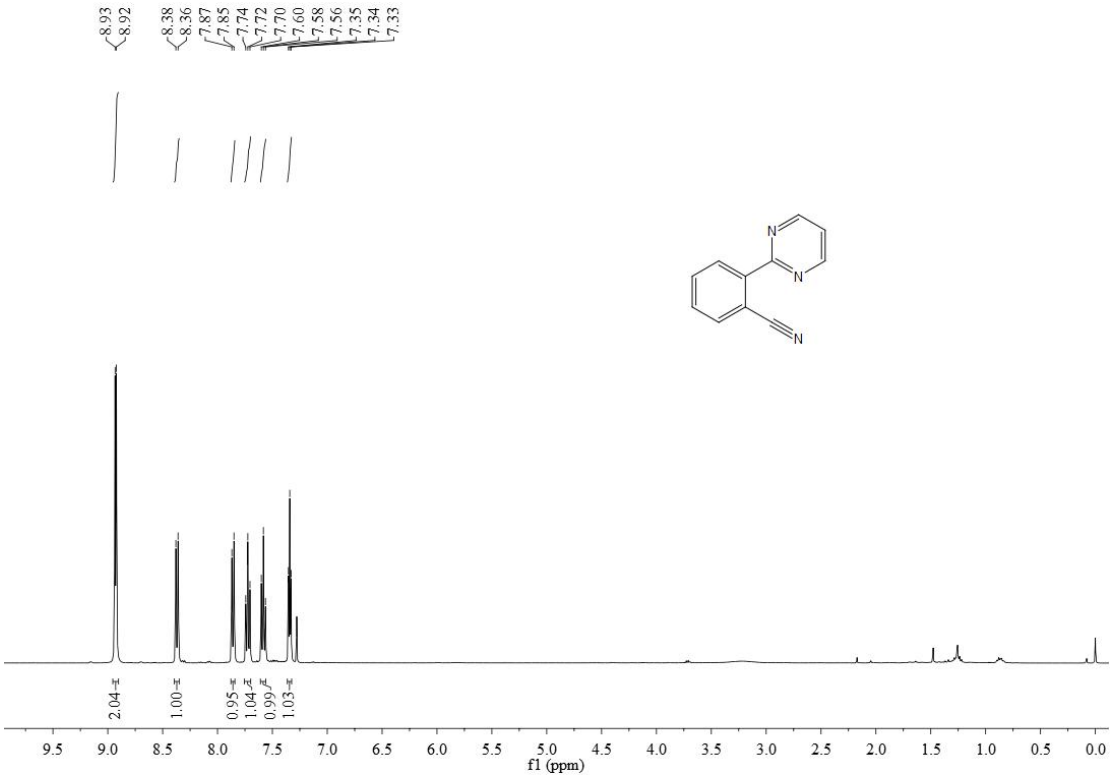
^{1}H NMR spectrum of compound **3p**



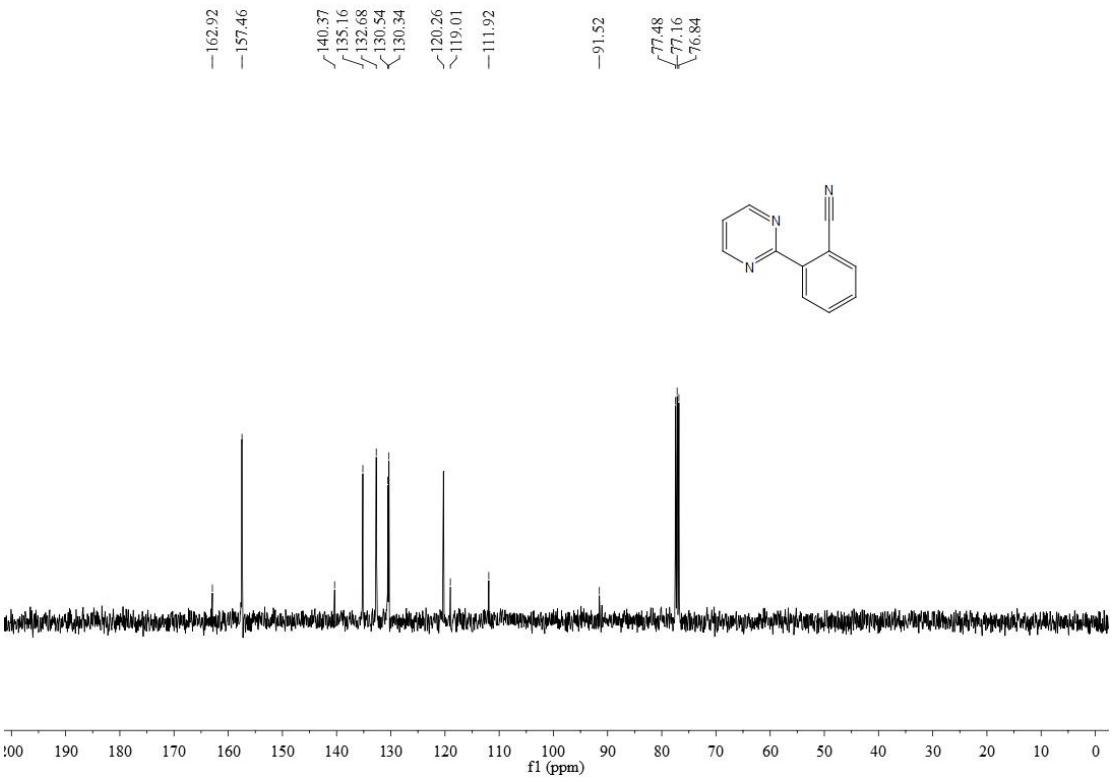
^{13}C NMR spectrum of compound **3p**



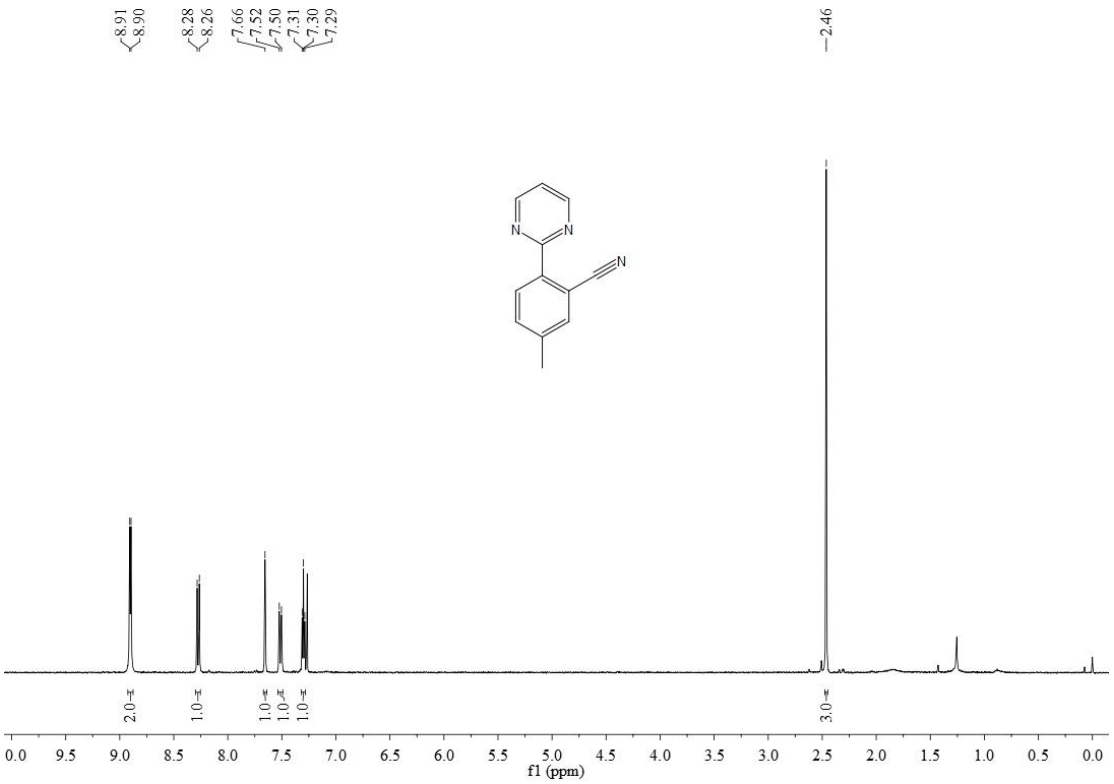
^{1}H NMR spectrum of compound **5a**



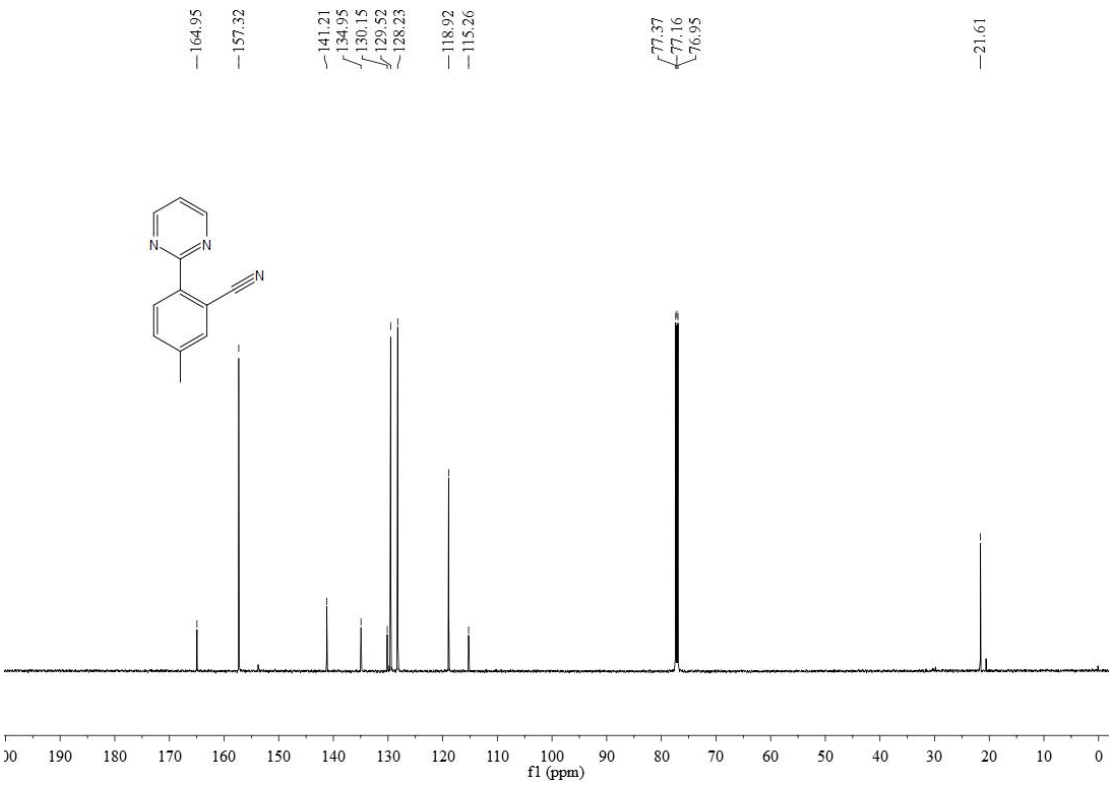
^{13}C NMR spectrum of compound **5a**



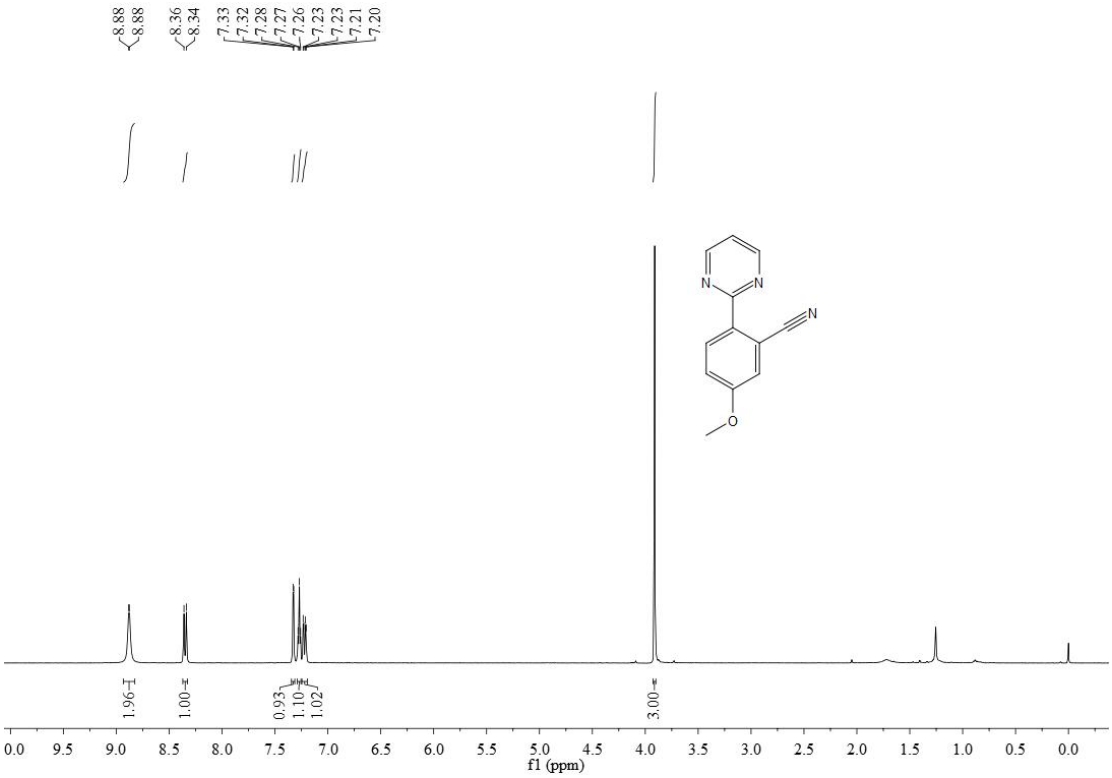
^{1}H NMR spectrum of compound **5b**



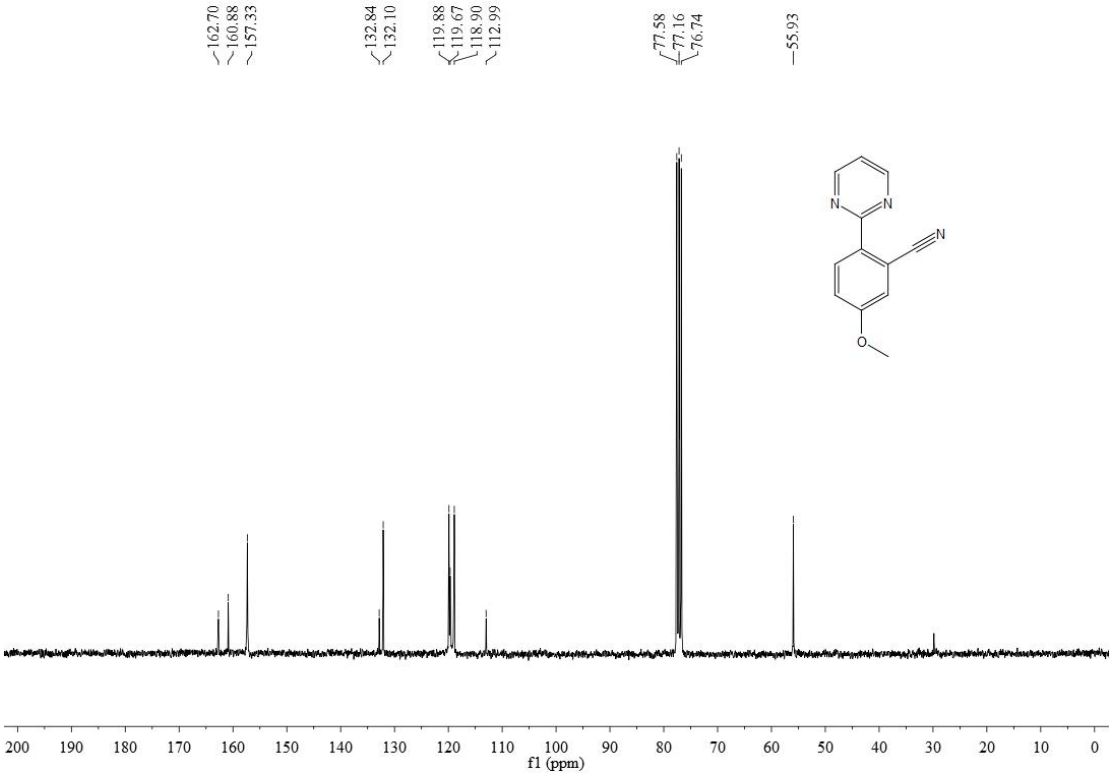
^{13}C NMR spectrum of compound **5b**



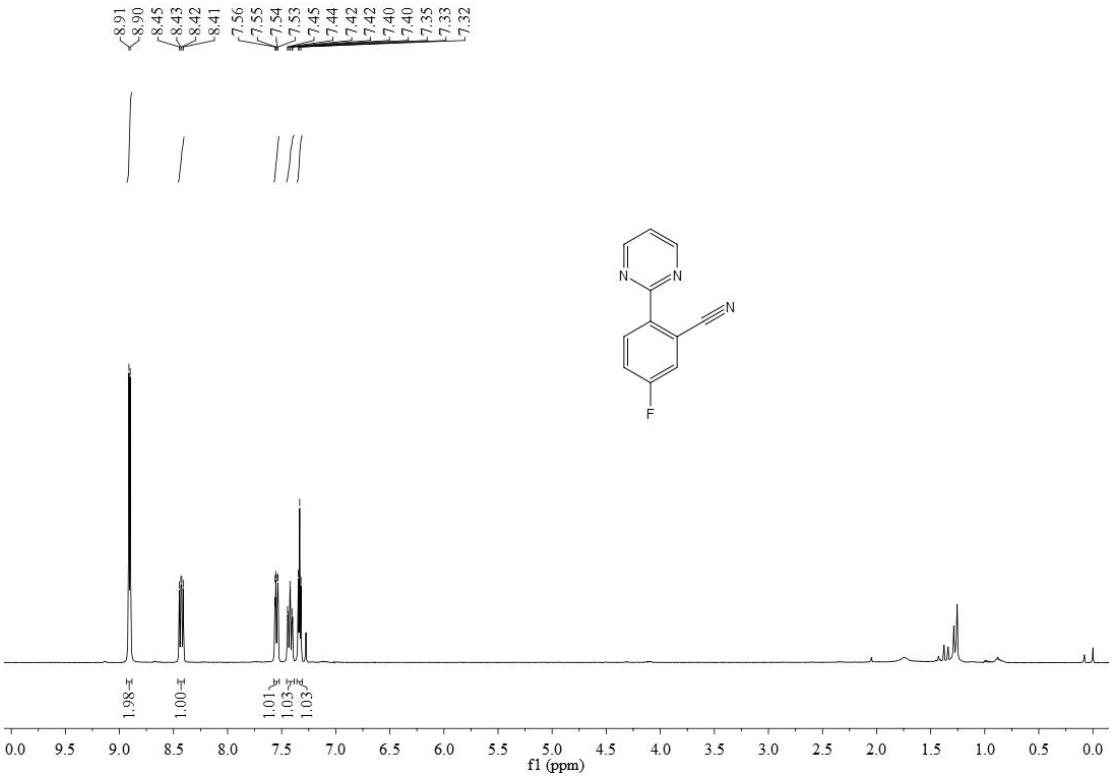
^{1}H NMR spectrum of compound **5c**



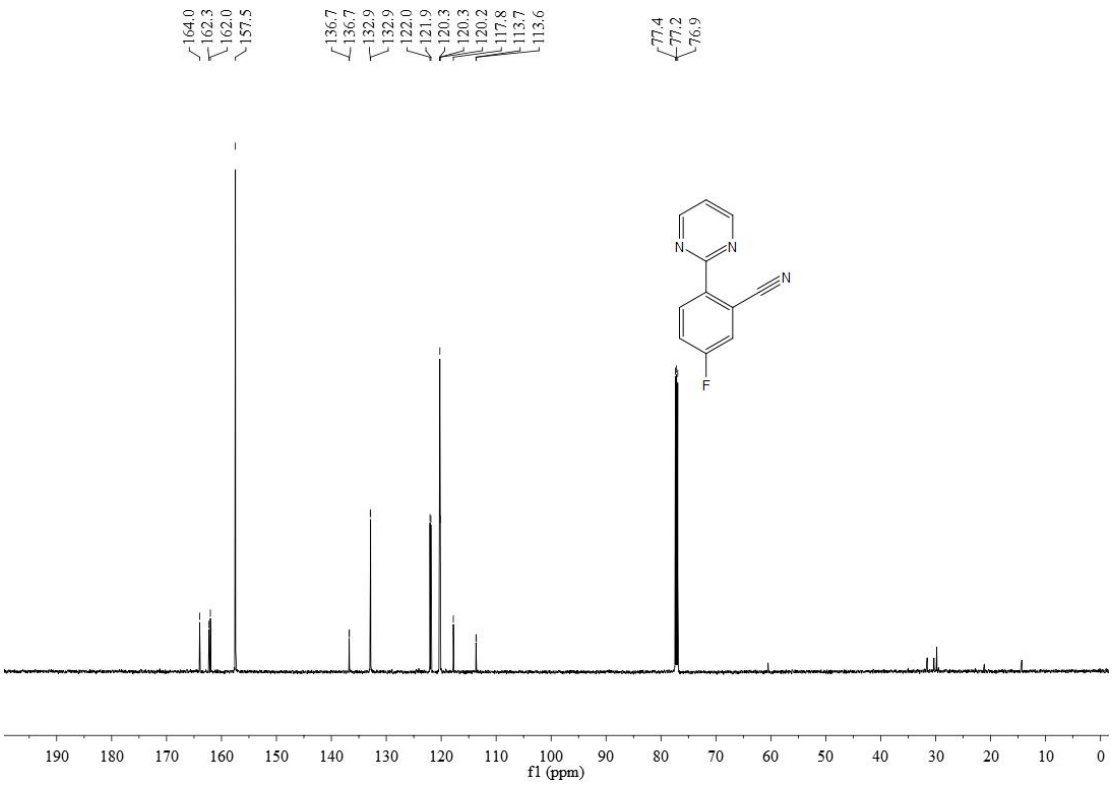
^{13}C NMR spectrum of compound **5c**



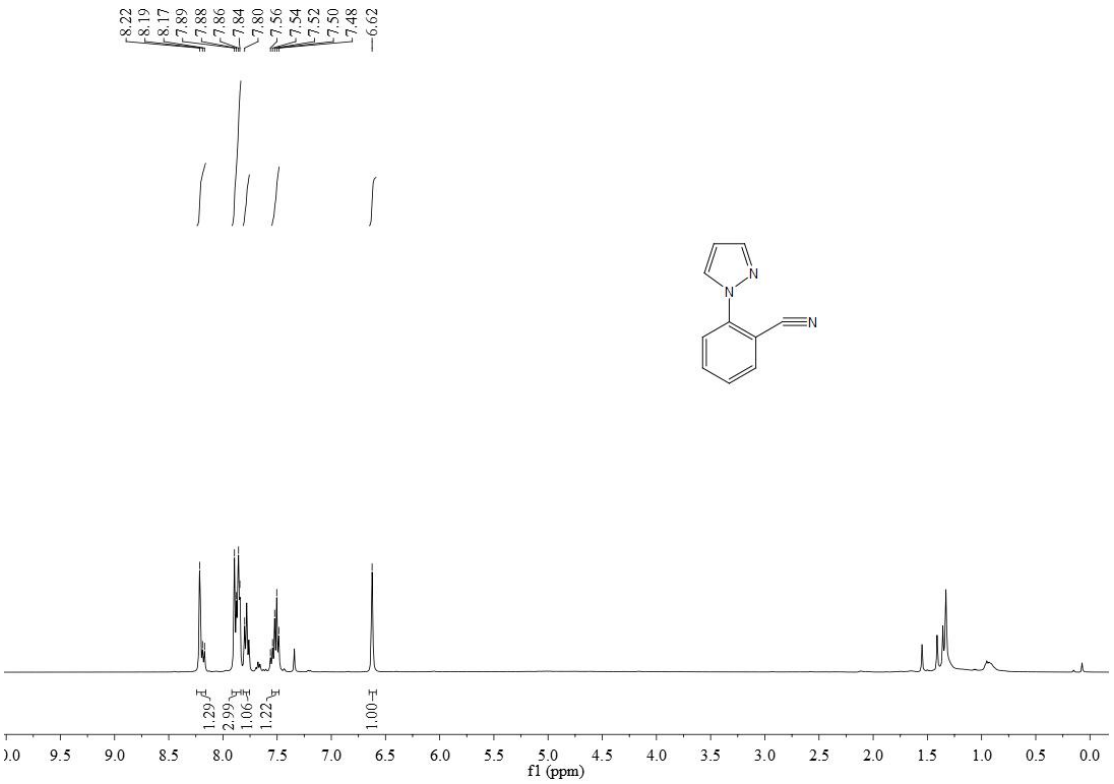
^{1}H NMR spectrum of compound **5d**



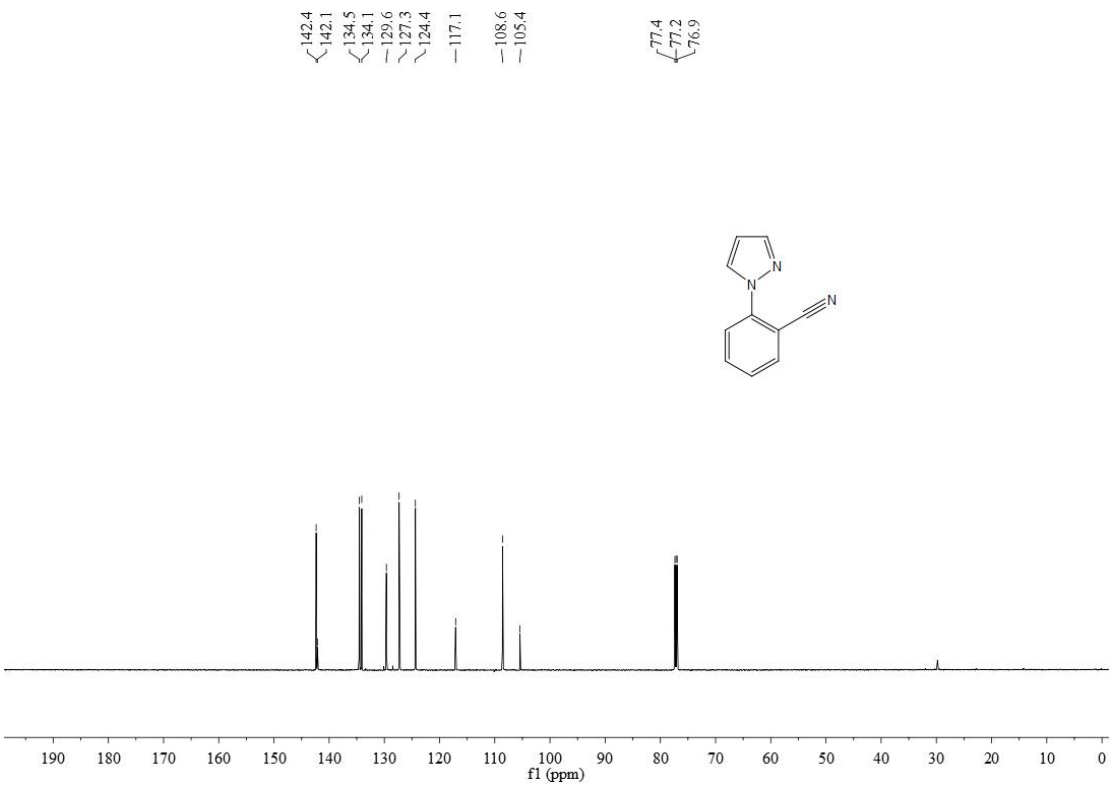
^{13}C NMR spectrum of compound **5d**



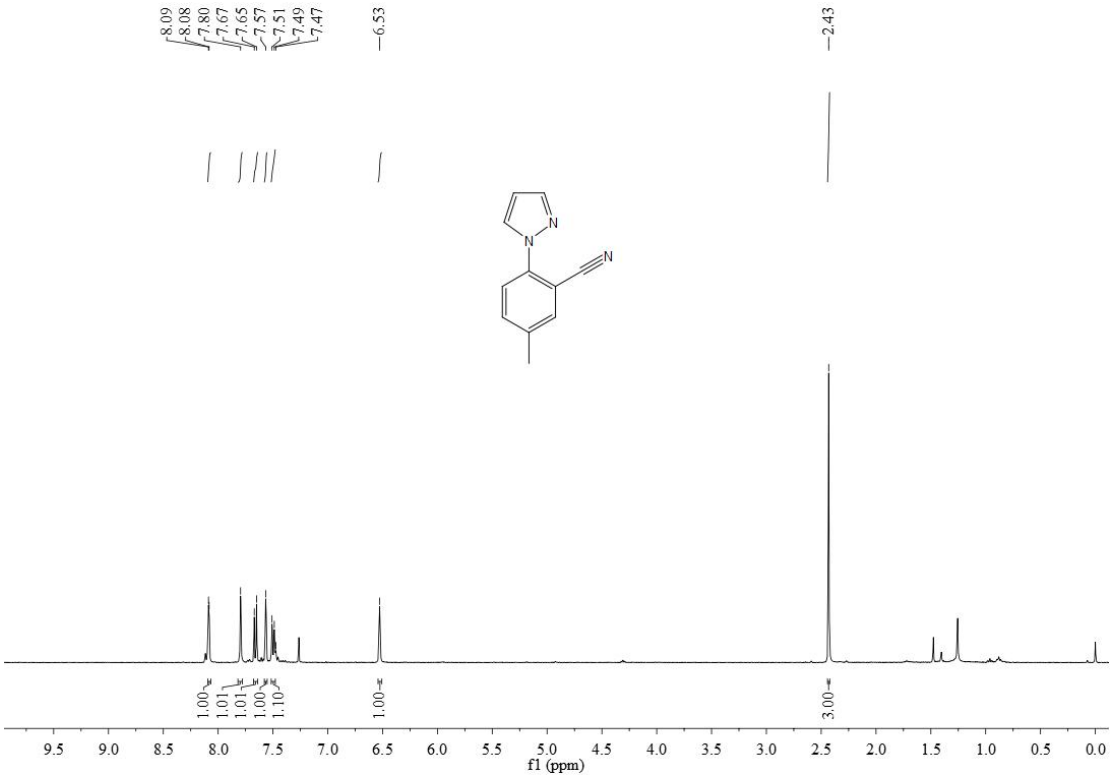
^{1}H NMR spectrum of compound **5e**



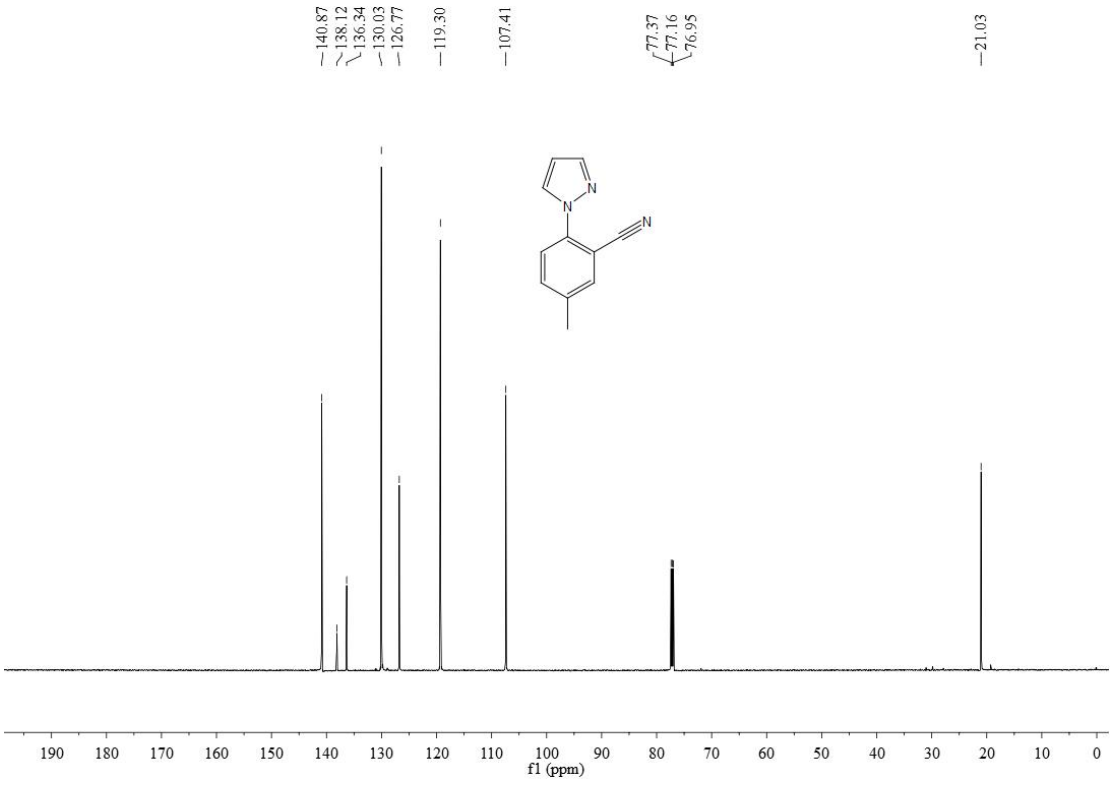
^{13}C NMR spectrum of compound **5e**



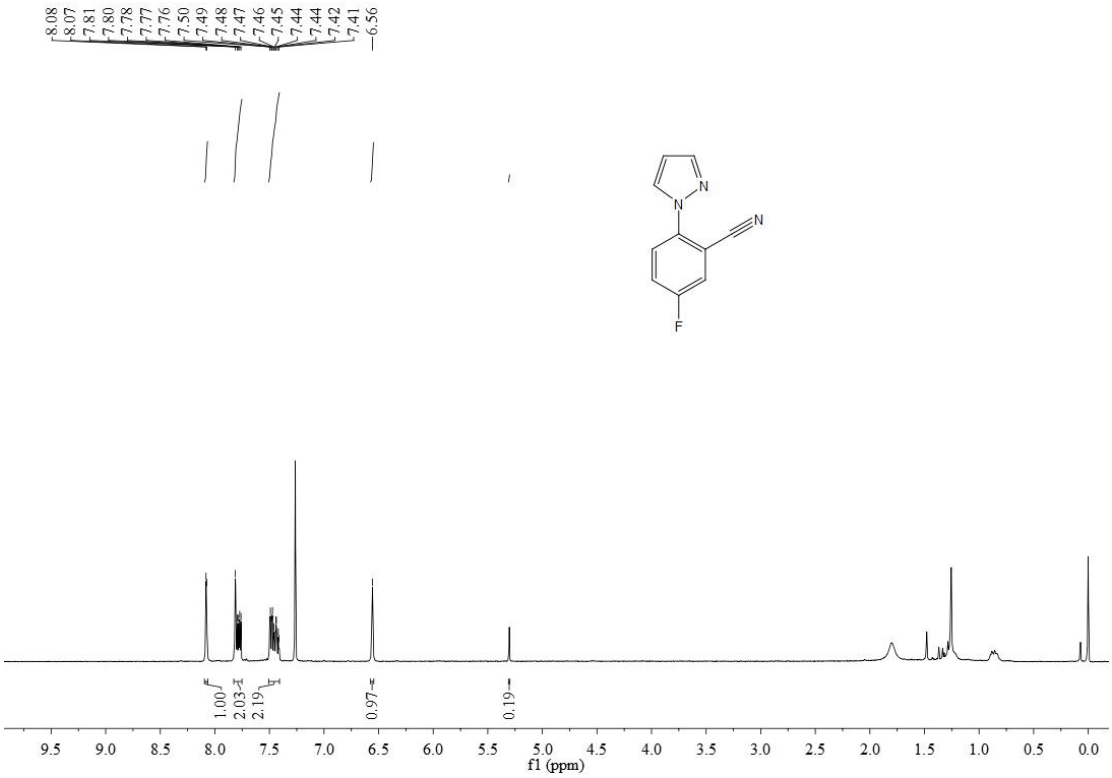
^{1}H NMR spectrum of compound **5f**



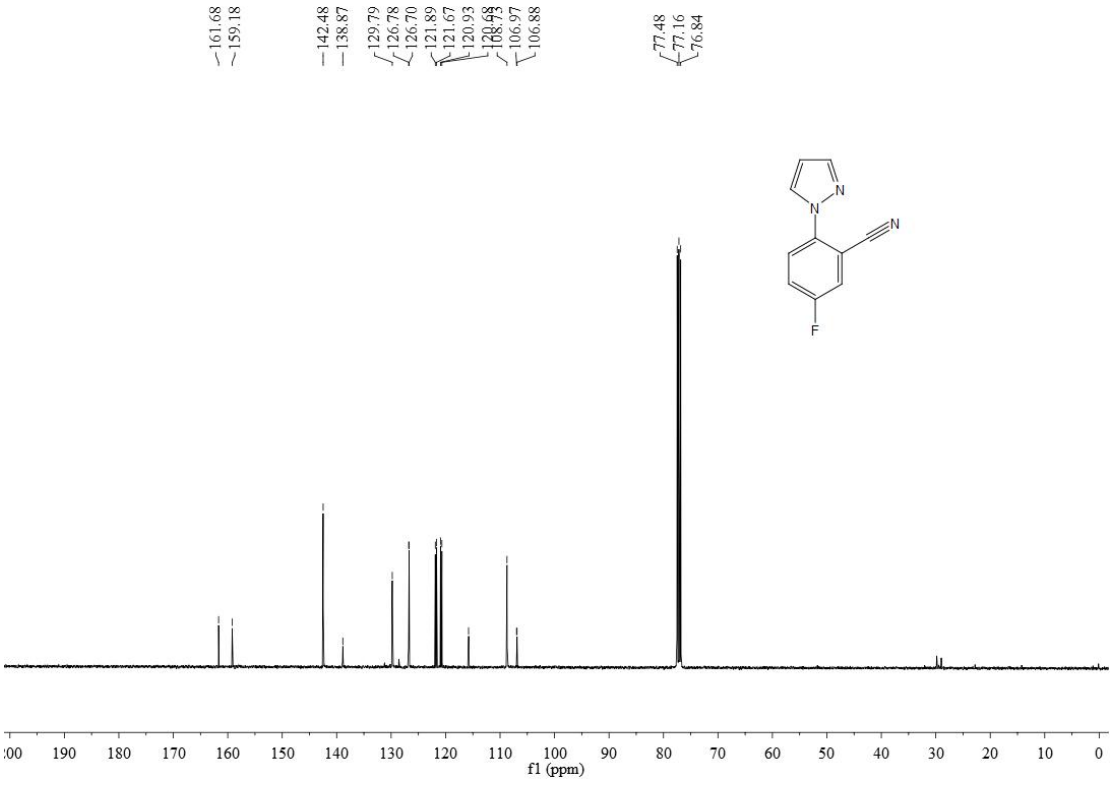
^{13}C NMR spectrum of compound **5f**



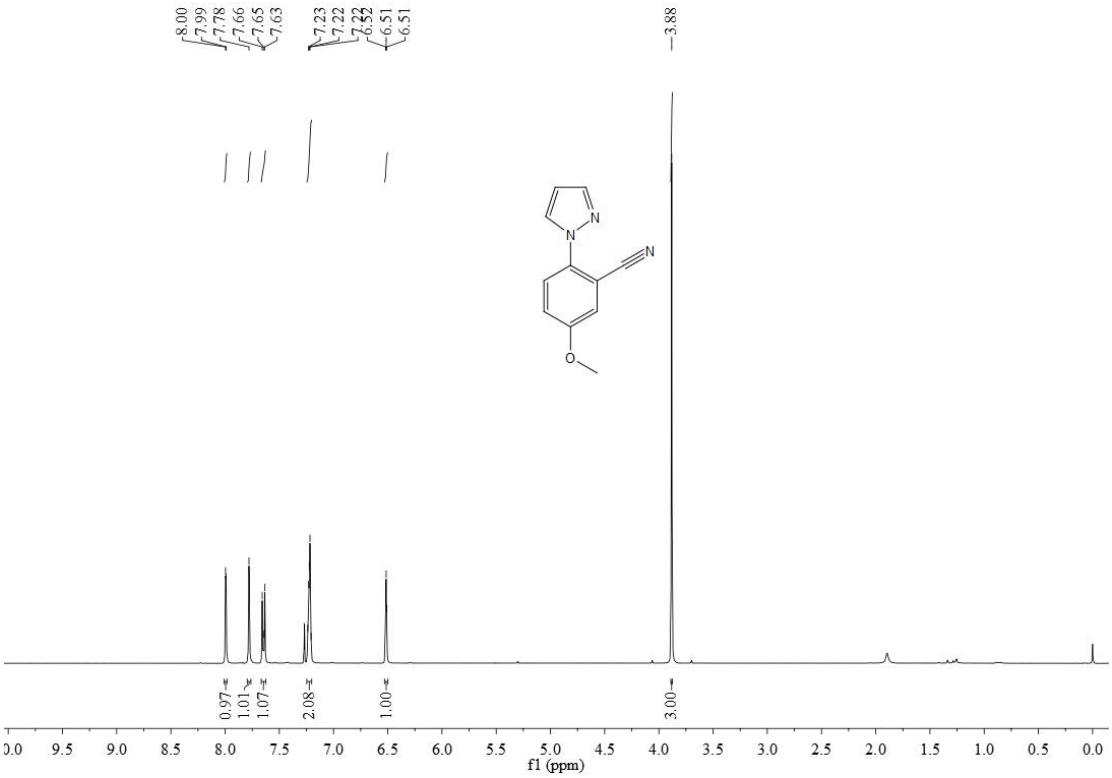
^{1}H NMR spectrum of compound **5g**



^{13}C NMR spectrum of compound **5g**



^{1}H NMR spectrum of compound **5h**



^{13}C NMR spectrum of compound **5h**