Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

for

Palladium-Catalyzed Cyanation of Aryl Halides with *in situ* Generated CN^- from $ClCF_2H$ and $NaNH_2$

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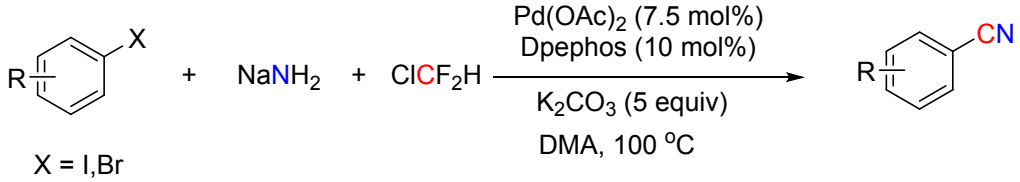
1. General information

All chemicals were purchased from Adamas Reagent, Sigma -Aldrich, J&K Scientific Ltd, Alfa Aesar and Tansoole. Unless otherwise stated, all solvents and reagents were used as purchased without further purification. All reactions were generally accomplished in dried Schlenk tubes under an atmosphere of N_2. Reactions were monitored by thin layer chromatography (TLC). Flash column chromatography was performed on silica gel (200-300 mesh). ^{1}H-NMR, ^{13}C-NMR spectra were recorded on Bruker 500 (500 MHz ^{1}H, 125 MHz ^{13}C). NMR spectra were calibrated by $CDCl_3$ (δ = 7.26 for ^{1}H-NMR, δ = 77.00 for ^{13}C-NMR) as an internal reference. Chemical shifts were quoted in parts per million (ppm). The following abbreviations are used to describe multiplets: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, br = broad. Coupling constants (*J*) were reported in Hertz (Hz). The products were purified from the reaction mixture by column chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

2. Experimental procedures



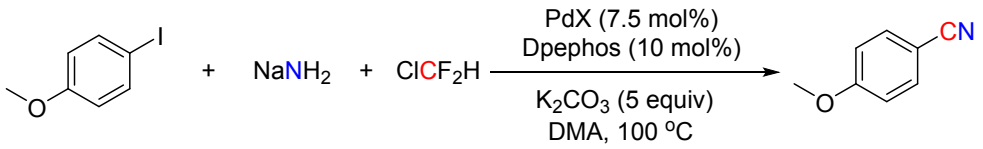
X = I,Br

1a **2a**

A Schlenk tube was charged with aryl halides **1** or **3** (0.2 mmol, 1 equiv), $Pd(OAc)_2$ (7.5 mol%), Dpephos (10 mol%), K_2CO_3 (5 equiv), $NaNH_2$ (5 equiv) under $ClCF_2H$ atmosphere with a balloon. Subsequently, DMA (2.0 mL) were added with injector. The mixture was stirred at 100 °C in oil bath for 20 h. After that, the reaction mixture was concentrated in vacuo and the desired product was obtained by flash column chromatography on silica gel.

3. Optimization of the reaction conditions for the synthesis of 2a

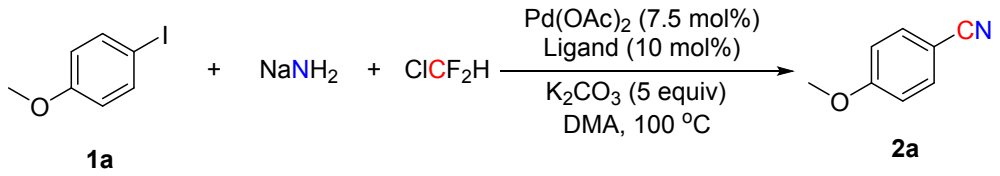
Table S1. Optimization of the reaction with different catalysts.



1a **2a**

entry[a]	cataiyst	Ligand	base	solvent (2 mL)	T (°C)	time (h)	yield (%)[b]
1	$PdCl_2$	Dpephos	K_2CO_3	DMA	100	20	71
2	$Pd_2(dba)_3$	Dpephos	K_2CO_3	DMA	100	20	60
3	$Pd(PhCN)2Cl_2$	Dpephos	K_2CO_3	DMA	100	20	43
4	$Pd(PPh_3)_2Cl_2$	Dpephos	K_2CO_3	DMA	100	20	50
5	$Pd(PPh_3)_4$	Dpephos	K_2CO_3	DMA	100	20	64
6	$Pd(TFA)_2$	Dpephos	K_2CO_3	DMA	100	20	42

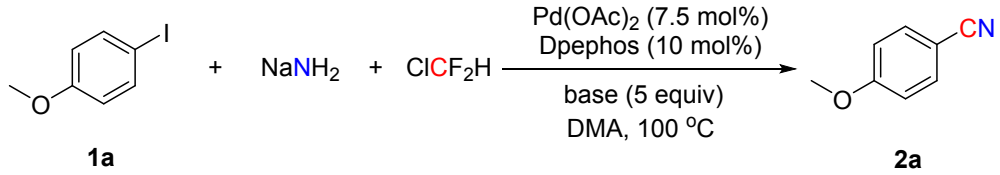
Table S2. Optimization of the reaction with different ligands.



1a **2a**

entry	cataiyst	Ligand	base	solvent (2 mL)	T (°C)	time (h)	yield (%)
1	$Pd(OAc)_2$	Xantphos	K_2CO_3	DMA	100	20	60
2	$Pd(OAc)_2$	S-phos	K_2CO_3	DMA	100	20	31
3	$Pd(OAc)_2$	dppf	K_2CO_3	DMA	100	20	33
4	$Pd(OAc)_2$	PPh_3	K_2CO_3	DMA	100	20	58
5	$Pd(OAc)_2$	dppb	K_2CO_3	DMA	100	20	20

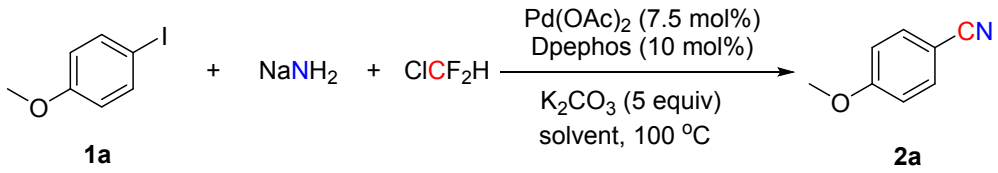
Table S3. Optimization of the reaction with different bases.



1a **2a**

entry	cataiyst	Ligand	base	solvent (2 mL)	T (°C)	time (h)	yield (%)
1	$Pd(OAc)_2$	Dpephos	Na_2CO_3	DMA	100	20	27
2	$Pd(OAc)_2$	Dpephos	CS_2CO_3	DMA	100	20	13
3	$Pd(OAc)_2$	Dpephos	$NaHCO_3$	DMA	100	20	44
4	$Pd(OAc)_2$	Dpephos	K_3PO_4	DMA	100	20	41
5	$Pd(OAc)_2$	Dpephos	DBU	DMA	100	20	NR

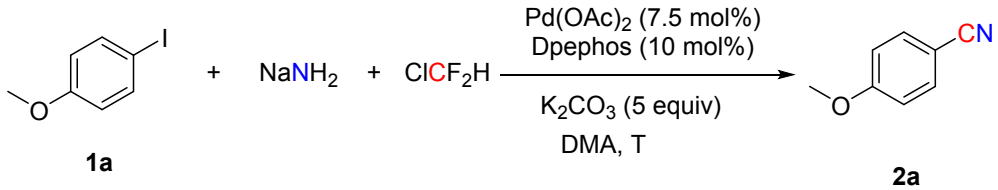
Table S4. Optimization of the reaction solvents.



1a **2a**

entry	cataiyst	Ligand	base	solvent (2 mL)	T (°C)	time (h)	yield (%)
1	$Pd(OAc)_2$	Dpephos	K_2CO_3	dioxane	100	20	NR
2	$Pd(OAc)_2$	Dpephos	K_2CO_3	toluene	100	20	20
3	$Pd(OAc)_2$	Dpephos	K_2CO_3	DMF	100	20	78
4	$Pd(OAc)_2$	Dpephos	K_2CO_3	CH_3CN	100	20	55
5	$Pd(OAc)_2$	Dpephos	K_2CO_3	CH_3OH	100	20	80
6	$Pd(OAc)_2$	Dpephos	K_2CO_3	THF	100	20	NR

Table S5. Optimization of the reaction temperature.

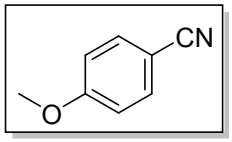


1a **2a**

entry	cataiyst	Ligand	base	solvent (2 mL)	T (°C)	time (h)	yield (%)
1	$Pd(OAc)_2$	Dpephos	K_2CO_3	DMA	120	20	trace
2	$Pd(OAc)_2$	Dpephos	K_2CO_3	DMA	110	20	59
3	$Pd(OAc)_2$	Dpephos	K_2CO_3	DMA	90	20	66
4	$Pd(OAc)_2$	Dpephos	K_2CO_3	DMA	80	20	47
5	$Pd(OAc)_2$	Dpephos	K_2CO_3	DMA	70	20	31

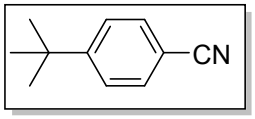
4. Characterization data for products

4-methoxybenzonitrile (2a)[1]



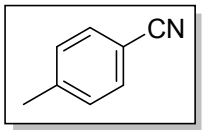
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (22.1 mg, 82%). m.p. 57-58. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 8.9 Hz, 2H), 6.95 (d, *J* = 8.9 Hz, 2H), 3.86 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 162.9, 134.0, 119.3, 114.8, 104.0, 55.6.

4-(tert-Butyl)benzonitrile (2b)[2]



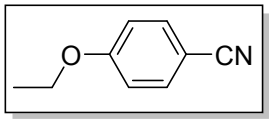
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a colorless oil (25.4 mg, 80%). m.p. 110-112. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 8.5 Hz, 2H), 7.48 (d, *J* = 8.5 Hz, 2H), 1.32 (s, 9H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 156.6, 132.0, 126.2, 119.2, 109.3, 35.3, 31.0.

4-methylbenzonitrile (2c)[1]



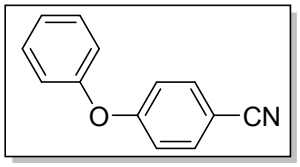
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (16.8 mg, 72%). m.p. 27-29. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.56 – 7.52 (m, 2H), 7.27 (d, *J* = 8.6 Hz, 2H), 2.42 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 143.7, 132.1, 129.8, 119.2, 109.3, 21.9.

4-ethoxybenzonitrile (2d)[10]



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (23.8 mg, 81%). m.p. 58-60. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.60 – 7.54 (m, 2H), 6.95 – 6.90 (m, 2H), 4.07 (q, *J* = 7.0 Hz, 2H), 1.44 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 162.3, 134.0, 119.3, 115.2, 103.7, 63.9, 14.7. HRMS (ESI, m/z) calcd for C_9H_9NO $[M+H]^+$: 147.0684; found: 147.0683.

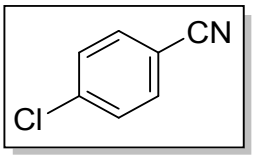
4-phenoxybenzonitrile (2e)[2]



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as white powder as colorless oil (28.8 mg, 74%). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.62 – 7.58 (m, 2H), 7.46 – 7.38 (m, 2H), 7.26 – 7.21 (m, 1H), 7.08 – 7.05 (m, 2H), 7.02 – 6.99 (m, 2H).

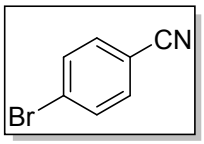
^{13}C NMR (125 MHz, Chloroform-*d*) δ 161.7, 154.9, 134.1, 130.3, 125.3, 120.4, 118.9, 118.8, 118.0, 105.9.

4-chlorobenzonitrile (2f)[1]



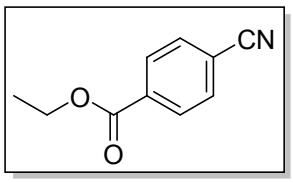
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a yellow solid (17.5 mg, 64%). m.p. 85-86. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 8.6 Hz, 2H), 7.46 (d, *J* = 8.6 Hz, 2H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 139.6, 133.4, 129.7, 118.0, 110.8.

4-bromobenzonitrile (2g)[5]



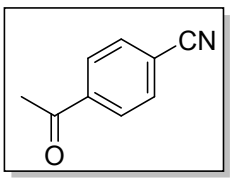
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (22.4 mg, 62%). m.p. 110-112. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.66 – 7.60 (m, 2H), 7.55 – 7.43 (m, 2H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 133.4, 132.7, 132.3, 118.1, 111.3.
HRMS (ESI, m/z) calcd for C_7H_4BrN $[M+H]^+$: 180.9527; found: 180.9529.

Ethyl 4-cyanobenzoate (2h)[2]



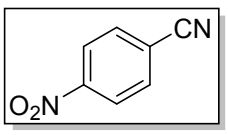
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (22.4 mg, 64%). m.p. 72-73. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.17 – 8.08 (m, 2H), 7.77 – 7.66 (m, 2H), 4.41 (s, 2H), 1.41 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 164.9, 132.2, 130.1, 127.2, 118.0, 116.3, 61.8, 14.2.

4-acetylbenzonitrile (2i)[1]



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (19.4 mg, 67%). m.p. 57-58. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.06 – 8.01 (m, 2H), 7.80 – 7.75 (m, 2H), 2.64 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 196.5, 140.0, 132.5, 128.7, 117.9, 116.5, 26.7.

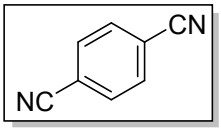
4-nitrobenzonitrile (2j)[1]



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a yellow solid (19.5 mg, 66%). m.p. 140-141. **^{1}H NMR** (500 MHz,

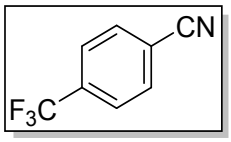
Chloroform-*d*) δ 8.36 (d, *J* = 8.9 Hz, 2H), 7.89 (d, *J* = 8.8 Hz, 2H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 133.5, 133.5, 124.3, 124.3, 118.4, 116.8.

Terephthalonitrile (2k)[2]



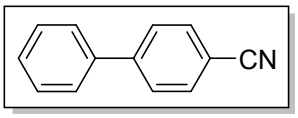
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (13.3mg, 52%). m.p. 213-214. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.80 (s, 4H). **^{13}C NMR** (126 MHz, Chloroform-*d*) δ 132.9, 132.9, 118.4, 112.5. HRMS (ESI, m/z) calcd for $C_8H_4N_2$ $[M+H]^+$: 128.0374; found: 128.0377.

4-(trifluoromethyl)benzonitrile (2l)[1]



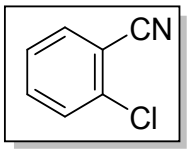
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (14.4 mg, 42%). m.p. 35-36. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.76 (d, *J* = 8.3 Hz, 2H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 134.7, 134.4, 132.7, 126.2, 126.2, 126.2, 126.15, 124.1, 122.0, 117.5, 116.1. **^{19}F NMR** (470 MHz, Chloroform-*d*) δ -63.6.

[1,1'-biphenyl]-4-carbonitrile (2m)[2]



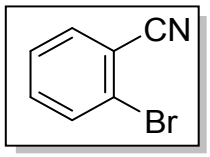
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a yellow solid (27.9 mg, 78%). m.p. 83-84. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.75 – 7.71 (m, 2H), 7.71 – 7.67 (m, 2H), 7.61 – 7.58 (m, 2H), 7.51 – 7.46 (m, 2H), 7.45 – 7.41 (m, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 145.7, 139.2, 132.6, 129.1, 128.7, 127.8, 127.3, 119.0, 110.9.

2-Chlorobenzonitrile (2n)[3]



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (15.3 mg, 56%). m.p. 44-45. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.68 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.38 (dt, *J* = 7.4, 1.6 Hz, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 136.9, 134.0, 133.9, 130.1, 127.2, 113.4.

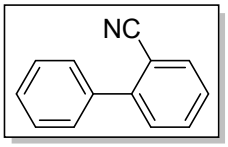
Bromobenzonitrile (2o)[6]



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a yellow solid (14.4 mg, 40%). m.p.52-54. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.68 (dd, *J* = 14.2, 7.7, 1.7 Hz, 2H), 7.45 (dt, *J* = 19.2, 7.6, 1.6 Hz,

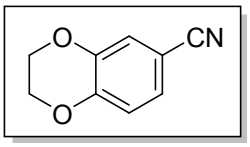
2H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 134.3, 133.9, 133.2, 127.6, 125.4, 117.1, 116.0.HRMS (ESI, m/z) calcd for C_7H_4BrN $[M+H]^+$: 180.9527; found: 180.9525.

[1,1'-biphenyl]-2-carbonitrile (2p)[4]



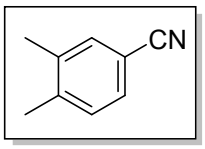
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a yellow solid (23.6 mg, 66%). m.p. 38- 39. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.80 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.67 (td, *J* = 7.7, 1.4 Hz, 1H), 7.61 – 7.57 (m, 2H), 7.56 – 7.50 (m, 3H), 7.49 (dt, *J* = 3.3, 1.2 Hz, 1H), 7.48 – 7.46 (m, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 145.5, 138.2, 133.8, 132.8, 130.1, 128.8, 128.7, 128.7, 127.6, 118.7, 111.3.

2,3-dihydrobenzo[b][1,4]dioxine-6-carbonitrile (2q)[7]



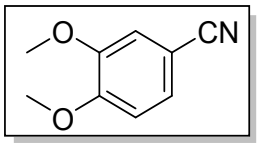
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (23.8 mg, 74%). m.p. 91-92. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.16 – 7.11 (m, 2H), 6.91 (d, *J* = 8.1 Hz, 1H), 4.33 – 4.30 (m, 2H), 4.29 – 4.26 (m, 2H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 147.7, 143.8, 125.9, 121.3, 118.9, 118.3, 104.5, 64.6, 64.1. HRMS (ESI, m/z) calcd for $C_9H_7NO_2$ $[M+H]^+$: 161.0477; found: 164.0475.

3,4-dimethylbenzonitrile (2r)[2]



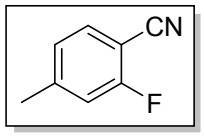
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (19.1 mg, 73%). m.p 63-64. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.43 – 7.35 (m, 2H), 7.21 (d, *J* = 7.8 Hz, 1H), 2.32 (s, 3H), 2.29 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 142.5, 137.9, 132.9, 130.3, 129.7,119.3, 109.6, 20.2, 19.6.

3,4-dimethoxybenzonitrile (2s)[8]



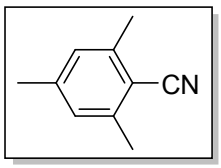
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a yellow solid (24.8 mg, 76%). m.p. 64-65. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.29 (ddd, *J* = 8.4, 2.0, 0.8 Hz, 1H), 7.08 (d, *J* = 2.0 Hz, 1H), 6.90 (dd, *J* = 8.5, 1.8 Hz, 1H), 3.94 – 3.92 (m, 3H), 3.91 – 3.89 (m, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 152.9, 149.3, 126.5, 119.2, 114.1, 111.3, 104.0, 56.2, 56.1. HRMS (ESI, m/z) calcd for $C_9H_9NO_2$ $[M+H]^+$: 163.0633; found: 163.0636.

2-fluoro-4-methylbenzonitrile (2t)[11]



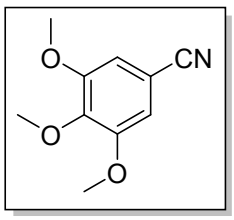
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white powder (12.7 mg, 47%). m.p. 47-49. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.49 (dd, *J* = 7.9, 6.7 Hz, 1H), 7.06 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.02 (d, *J* = 9.9 Hz, 1H), 2.43 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 164.2, 162.1, 146.9, 133.1, 117.0, 116.9, 114.2, 98.51, 98.4, 21.9. **^{19}F NMR** (471 MHz, Chloroform-*d*) δ -107.43. HRMS (ESI, m/z) calcd for C_8H_6FN $[M+H]^+$: 135.0484; found: 135.0481.

2,4,6-trimethylbenzonitrile (2u)[5]



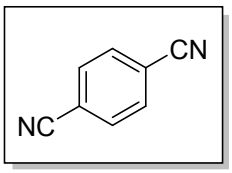
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a yellow solid (20.3 mg, 70%). m.p. 42–43. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 6.96 – 6.90 (m, 2H), 2.48 (s, 6H), 2.32 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 142.8, 142.0, 128.2, 117.7, 110.3, 21.6, 20.6. HRMS (ESI, m/z) calcd for $C_{10}H_{11}N$ $[M+H]^+$: 145.0891; found: 145.0894.

3,4,5-trimethoxybenzonitrile (2v)[9]



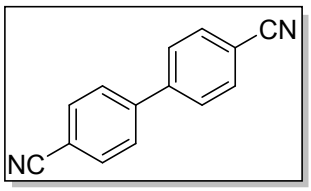
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as white powder (10.5 mg, 41%). m.p. 92-94. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 6.86 (s, 2H), 3.89 (d, *J* = 11.0 Hz, 9H).**^{13}C NMR** (125 MHz, Chloroform-*d*) δ 153.6, 119.0, 109.6, 106.7, 61.1, 56.4. HRMS (ESI, m/z) calcd for $C_{10}H_{11}NO_3$ $[M+H]^+$: 193.0739; found: 193.073.

Terephthalonitrile (2w)[2]



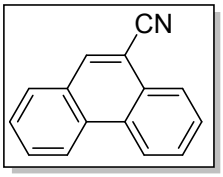
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (10.5 mg, 41%). m.p. 213-214. **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.78 (d, J = 8.5 Hz, 2H), 7.69 (d, J = 8.6 Hz, 2H). **^{13}C NMR** (125 MHz, Chloroform-d) δ 132.8, 117.0, 116.7. HRMS (ESI, m/z) calcd for C8H4N2 [M+H]+: 128.0374; found: 128.0377.

[1,1'-biphenyl]-4,4'-dicarbonitrile (2x)[2]



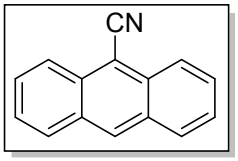
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (15.9 mg, 39%). m.p. 232-234. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.82 – 7.79 (m, 4H), 7.74 – 7.70 (m, 4H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 143.5, 132.9, 127.9, 118.4, 112.5.

Phenanthrene-9-carbonitrile (2y)[3]



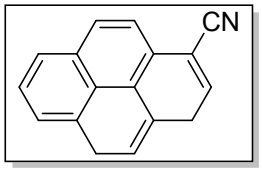
The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (30.0 mg, 47%). m.p. 108-109. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.71 – 8.66 (m, 2H), 8.34 – 8.19 (m, 2H), 7.92 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.80 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.78 – 7.76 (m, 1H), 7.76 – 7.73 (m, 1H), 7.68 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 135.6, 131.8, 130.1, 129.8, 129.5, 128.9, 128.2, 128.1, 127.6, 126.1, 123.1, 122.9, 117.9, 109.5.

Anthracene-9-carbonitrile (2z)[3]



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (25.6 mg, 63%). m.p. 177-178. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.80 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.67 (td, *J* = 7.7, 1.4 Hz, 1H), 7.61 – 7.57 (m, 2H), 7.56 – 7.50 (m, 3H), 7.49 (dt, *J* = 3.3, 1.2 Hz, 1H), 7.48 – 7.46 (m, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 145.5, 138.2, 133.8, 132.8, 130.1, 128.8, 128.8, 128.7, 127.6, 118.7, 111.3.

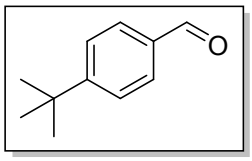
3,5-dihydropyrene-1-carbonitrile (2aa)[3]



The reaction was performed following the general procedure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:AcOEt = 30:1, v/v) to give the product as a white solid (20.2 mg, 44%). m.p. 152-154. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.41 (d, *J* = 9.0 Hz, 1H), 8.30 (ddd, *J* = 7.9, 4.8, 1.2 Hz, 2H), 8.27 – 8.23 (m, 2H), 8.22 (d, *J* = 1.7 Hz, 2H), 8.14 (s, 1H), 8.06 (d, *J* = 8.9 Hz, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 134.2, 133.0, 130.8, 130.5, 130.5, 129.5, 127.0, 127.0, 126.9, 126.8, 124.4, 124.0, 123.9, 123.5, 118.8, 105.6.

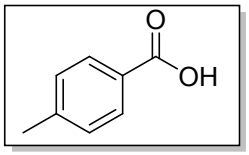
4 4-(*tert*-butyl)benzaldehyde

To a solution of 4-tert-Butylbenzonitrile (32.0 mg, 0.2 mmol) in toluene (2 mL) was added DIBAL–H (159 μL, 1.2 equiv) at –78 °C. The reaction mixture was stirred at –78 °C for 2.5 h and then quenched with aqueous HCl solution (1 M) at 0 °C. The aqueous phase was extracted with Et_2O. The combined organic layers were dried over



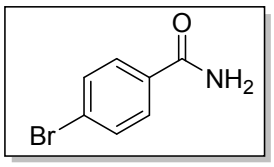
Na_2SO_4 and evaporated under reduced pressure. The residue was subjected to flash column chromatography to give the desired product (21 mg, 65%). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 9.99 (s, 1H), 7.83 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 8.3 Hz, 2H), 1.37 (d, *J* = 1.2 Hz, 9H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 192.0, 158.4, 134.1, 129.7, 126.0, 35.4, 31.1.

5 4-methylbenzoic acid



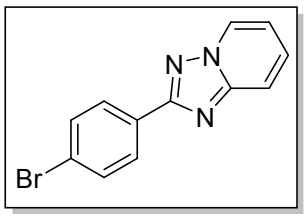
A 25 mL round bottom flask equipped with a magnetic stirring bar was charged with p-Tolunitrile (58.5 mg, 0.5 mmol) and 1M HCl. The reaction mixture was stirred at 100 °C under nitrogen atmosphere for 8 h. After being cooled to room temperature, the reaction mixture was quenched with aqueous $NaHCO_3$ (3 mL) and extracted with CH_2Cl_2. The organic solution was washed with brine, dried over Na_2SO_4, and filtered. After the solvent was removed under reduced pressure, the residue was subjected to flash column chromatography (to afford the desired product (42 mg, 62%). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.04 – 7.99 (m, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 2.43 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 172.4, 144.7, 130.3, 129.2, 126.7, 21.8.

6 4-bromobenzamide



A flame-dried flask fitted with magnetic stir bar was charged with 4-bromobenzonitrile (36.4 mg, 0.2 mmol, 1.0 equiv) and KO^{t}Bu (67.2 mg, 0.6 mmol, 3.0 equiv), and dry tert-butyl alcohol (4 mL/mmol) was added. The reaction mixture was stirred at room temperature for 12 h under nitrogen atmosphere, and progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was treated with water (10 mL). The solid amide product was filtered, washed with water, and dried under vacuum to provide the corresponding amide (36 mg, 90%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 7.00 – 6.92 (m, 2H), 6.85 – 6.78 (m, 2H). **^{13}C NMR** (125 MHz, DMSO-d_6) δ 167.4, 133.9, 131.7, 131.7, 130.1, 125.5.

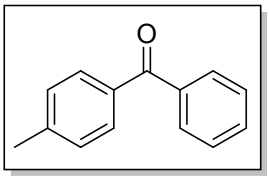
9 2-(4-bromophenyl)-[1,2,4]triazolo[1,5-*a*]pyridine



To a dried screw-cap vial was added 4-bromobenzonitrile (0.30 mmol), 2-aminopyridine (0.36 mmol), CuBr (2.2 mg, 0.015 mmol), 1,10-phenanthroline (2.7 mg, 0.015 mmol, 5 mol%) and ZnI_2 (9.6 mg, 0.03 mmol, 10 mol%). 1,2-Dichlorobenzene (0.6 ml) was then added and the vial was sealed under atmospheric air. The reaction mixture was stirred at 130 °C for 24 h in pre-heated oil bath. After cooling to room temperature, the reaction was diluted with EtOAc and filtered over glass filter. The filtrate was concentrated and purified by column chromatography on silica gel (64 mg, 78%). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.56 (d, *J* = 6.8 Hz, 1H), 8.14 (d, *J* = 8.1 Hz, 2H),

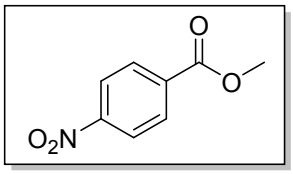
7.73 (d, *J* = 8.9 Hz, 1H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.00 (t, *J* = 6.8 Hz, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 163.3, 151.7, 137.9, 131.9, 129.8, 129.7, 128.9, 128.8, 128.4, 124.5, 116.5, 113.8.

10 phenyl(*p*-tolyl)methanone



A 25 mL round-bottom Schlenk bottle was charged with p-Tolunitrile (58.5 mg, 0.5 mmol) and 0.5 mL of THF. The bottle was evacuated and backfilled with N_2 for three times and placed in an ice bath. Grignard reagent (1.5 mmol, freshly prepared) was added dropwise to the solution at 0 °C. The resulting mixture was allowed to warm to room temperature and was stirred for 6 h. Upon the completion of the reaction, 1 M HCl was added dropwise to the mixture with stirring, followed by addition of solid NaOH to make the solution basic. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 30 mL). The combined organic solutions were washed with brine, dried over Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography to yield the corresponding ketone (80 mg, 82%). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.81 – 7.76 (m, 2H), 7.74 – 7.70 (m, 2H), 7.57 (s, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.28 (d, *J* = 7.9 Hz, 2H), 2.44 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 196.5, 143.3, 138.0, 134.9, 132.2, 130.3, 129.9, 129.0, 128.2, 21.7.

11 methyl 4-nitrobenzoate



To a stirring solution of 4-nitrobenzonitrile (29.6 mg, 0.2 mmol) in MeOH (0.45 mL) was added H_2SO_4 (0.18 mL) at room temperature. The resulting mixture was stirred at 110 °C for 24 h. After being cooled to room temperature, the reaction mixture was quenched with aqueous $NaHCO_3$ (3 mL) and extracted with CH_2Cl_2. The organic solution was washed with brine, dried over Na_2SO_4, and filtered. After the solvent was removed under reduced pressure, the residue was subjected to flash column chromatography to afford the desired product (30.2 mg, 83% yield).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.31 – 8.25 (m, 2H), 8.23 – 8.18 (m, 2H), 3.97 (d, *J* = 0.9 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 165.2, 150.6, 135.5, 130.7, 123.6, 52.8.

5. References

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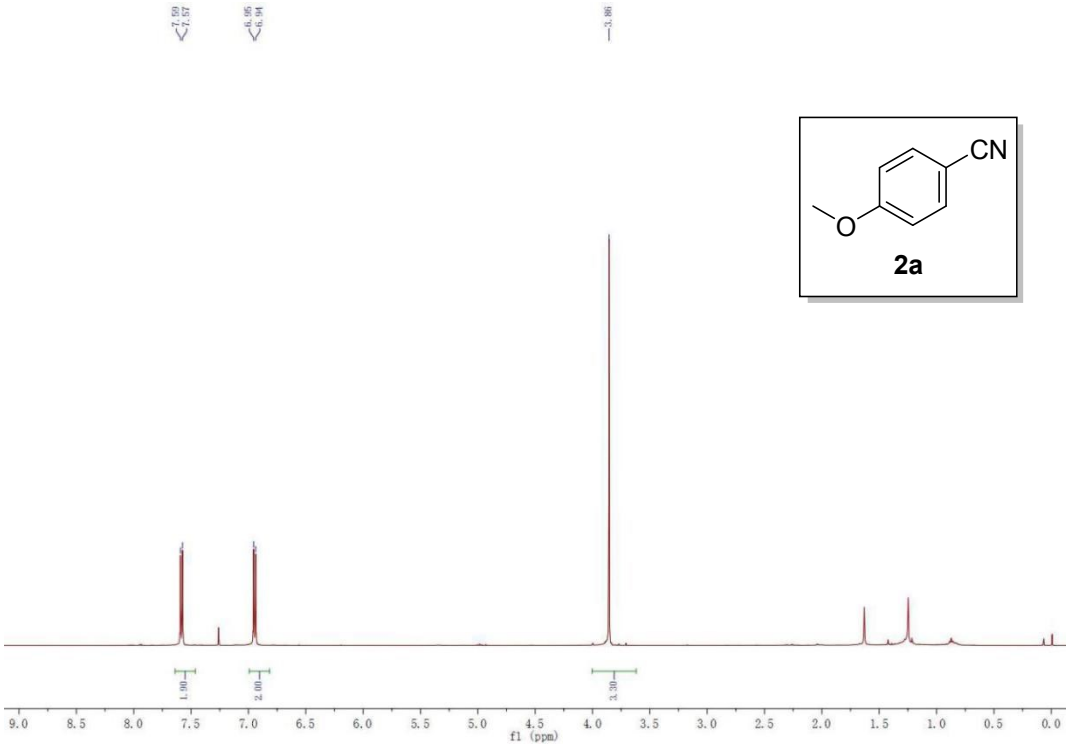
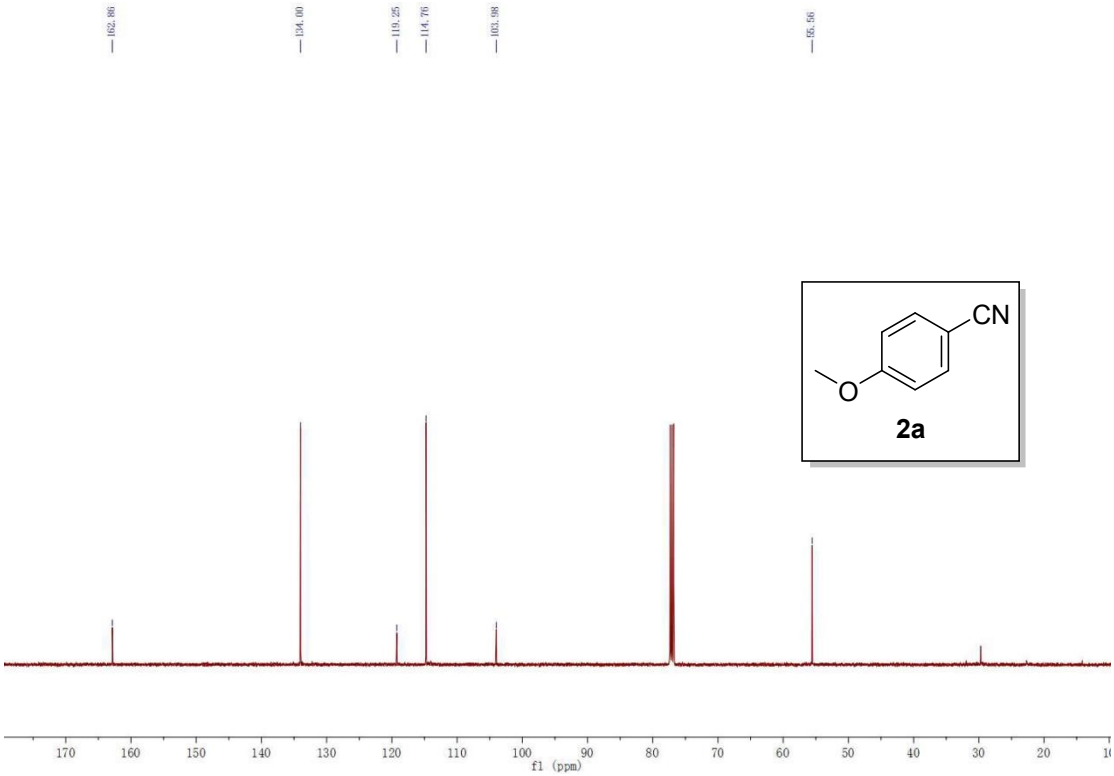
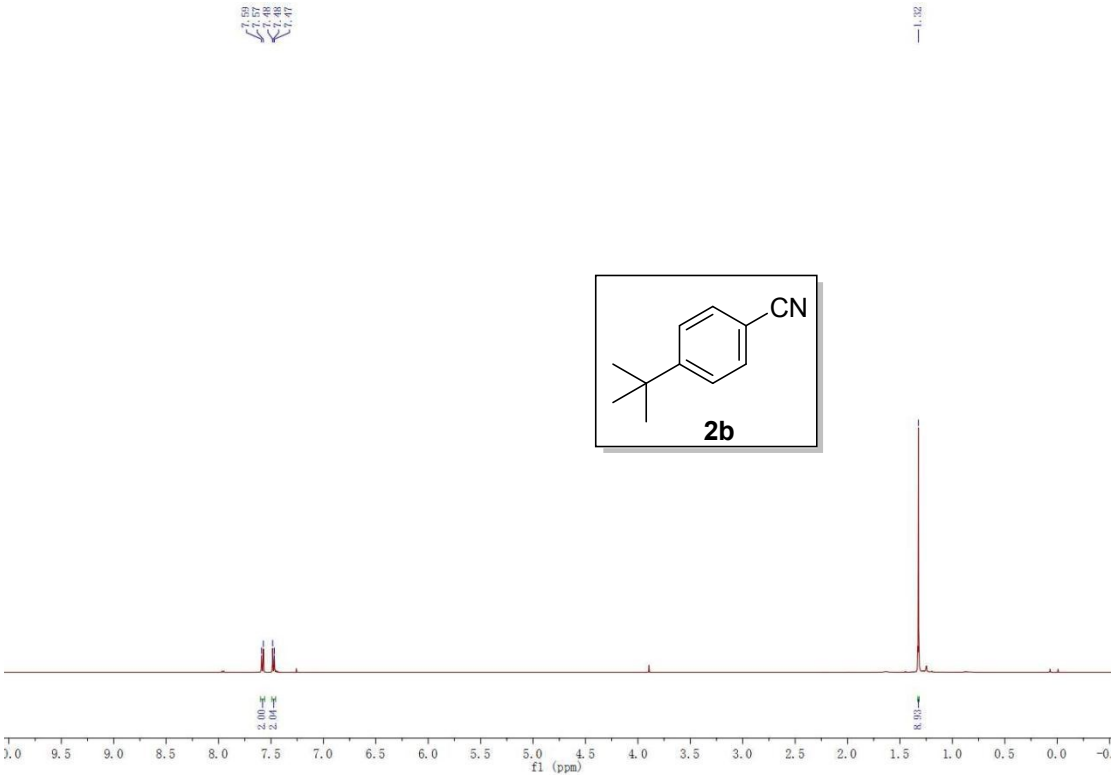
6.NMR Spectra

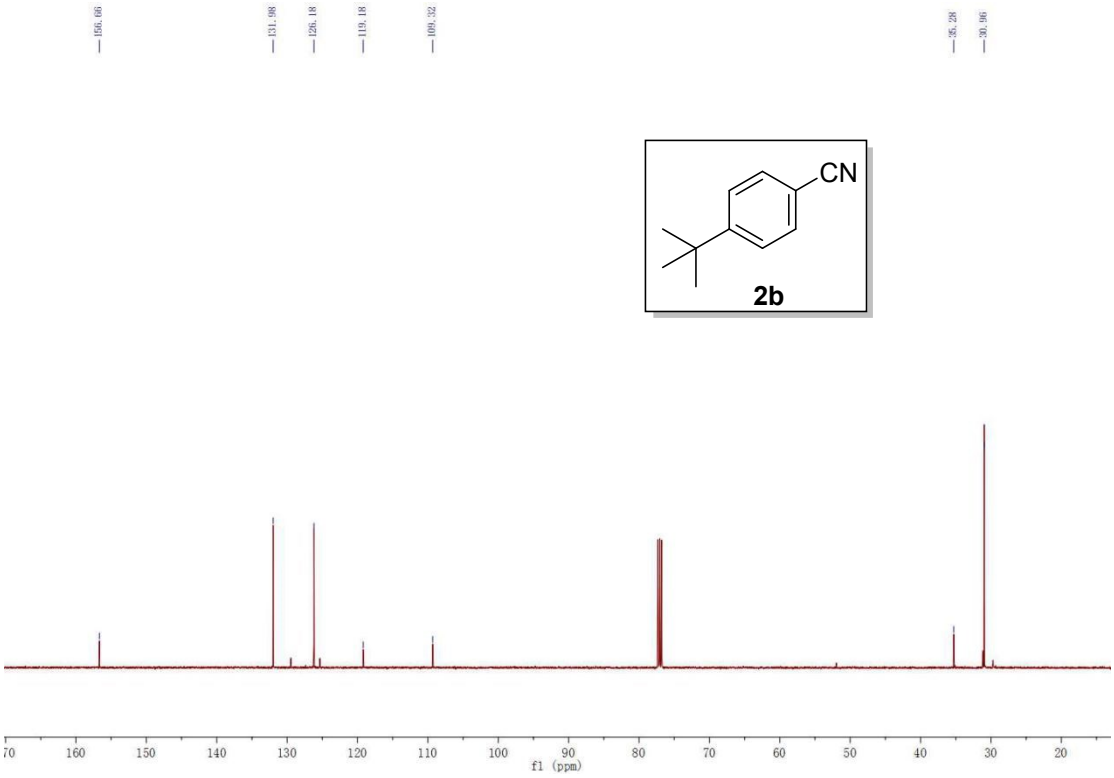
4-methoxybenzonitrile (2a)



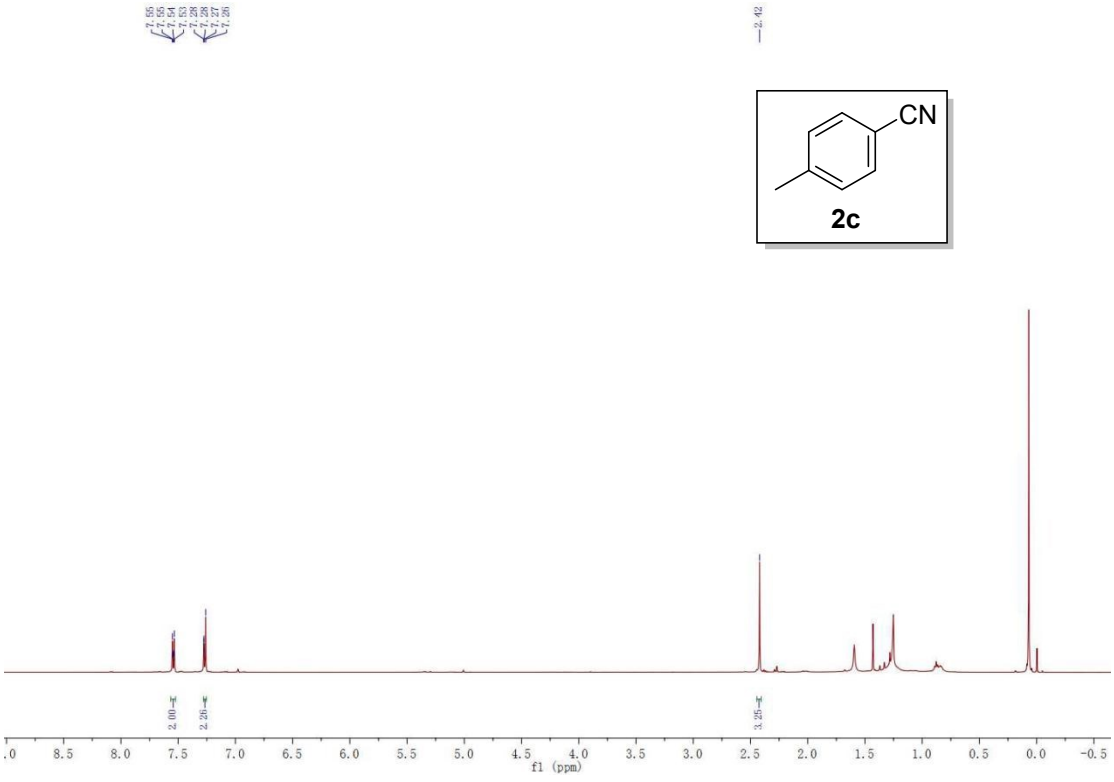


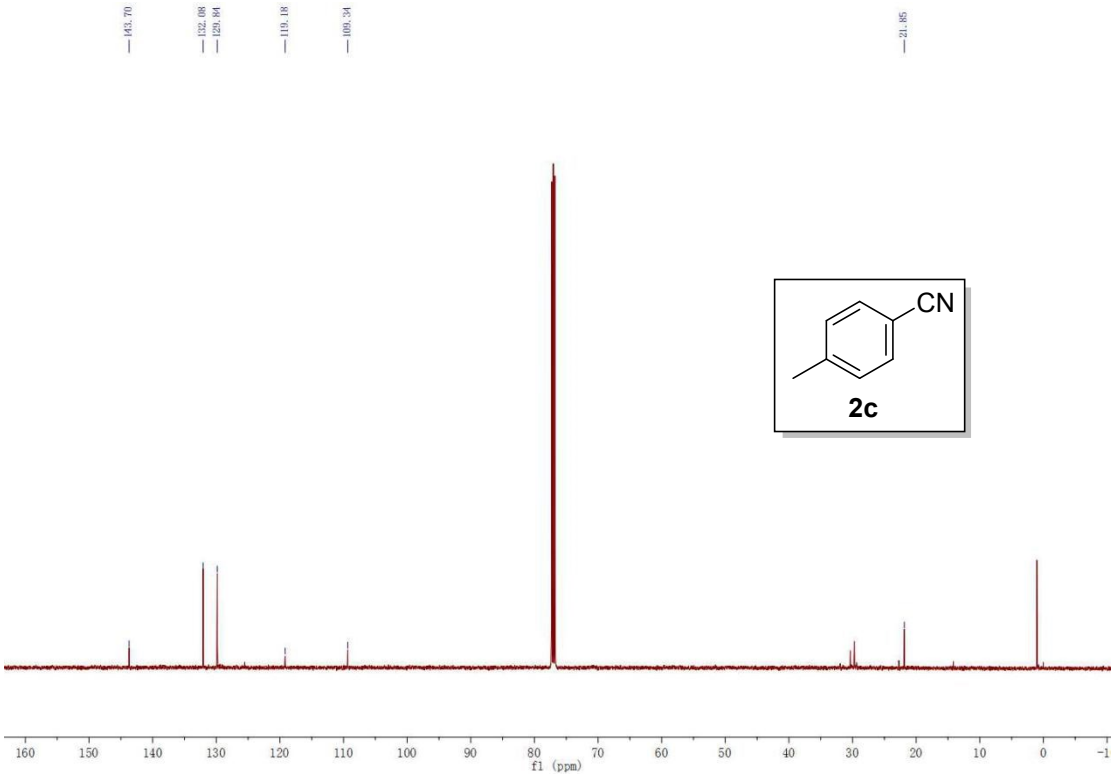
4-(tert-Butyl)benzonitrile (2b)



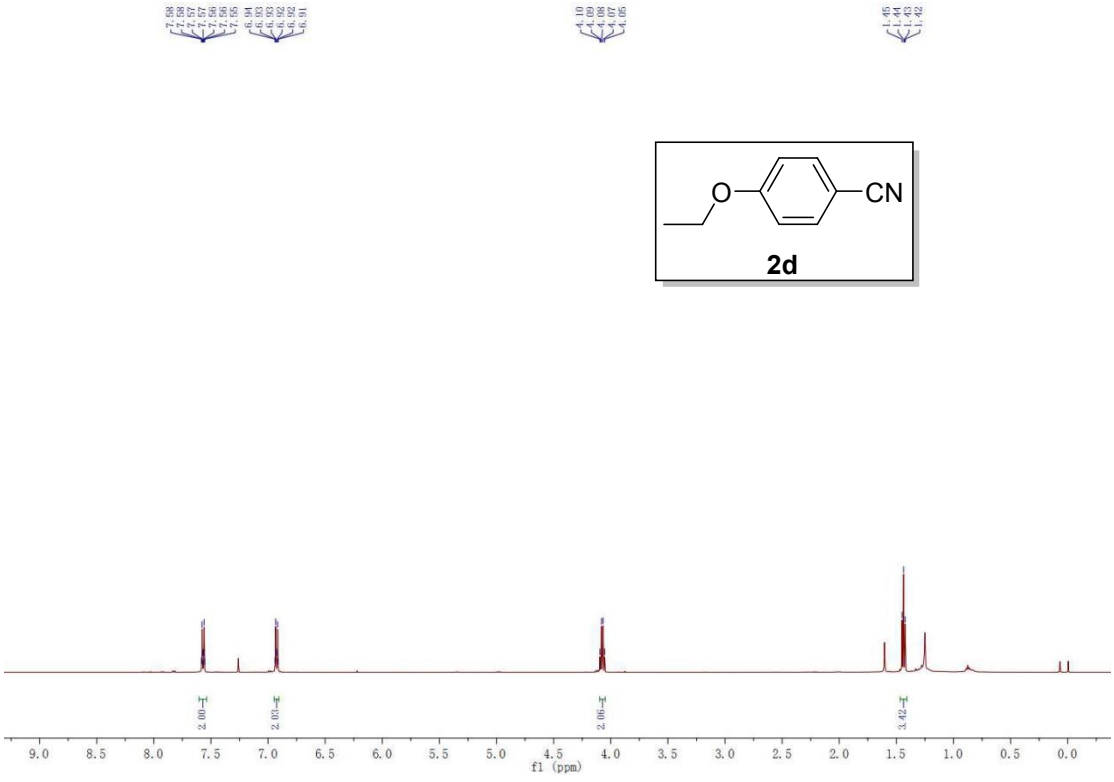


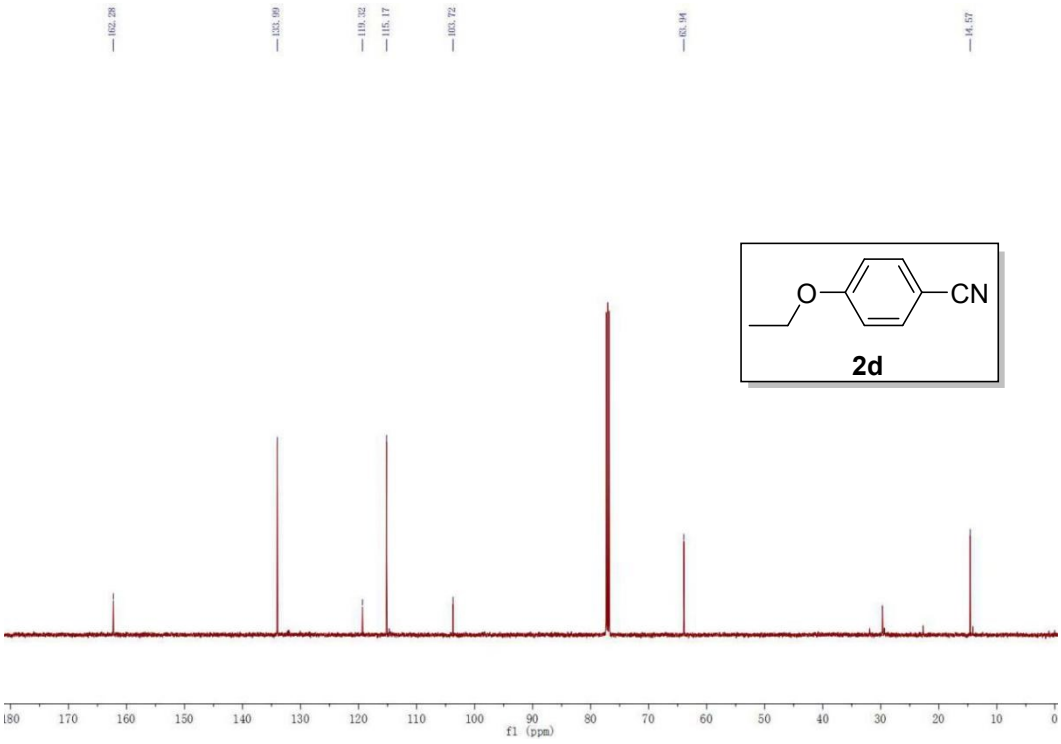
4-methylbenzonitrile (2c)



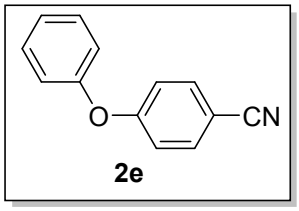


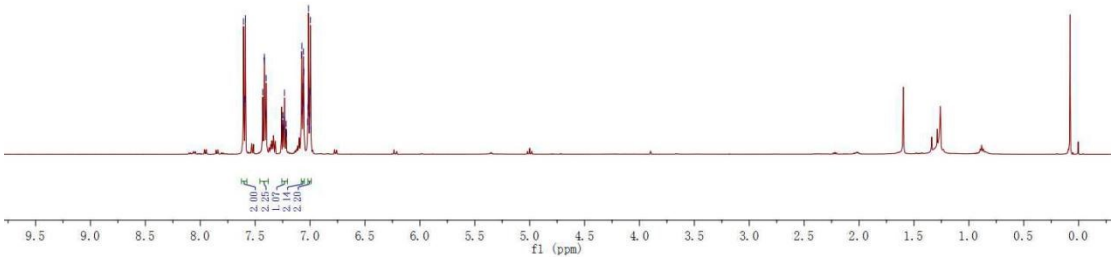
4-ethoxybenzonitrile (2d)

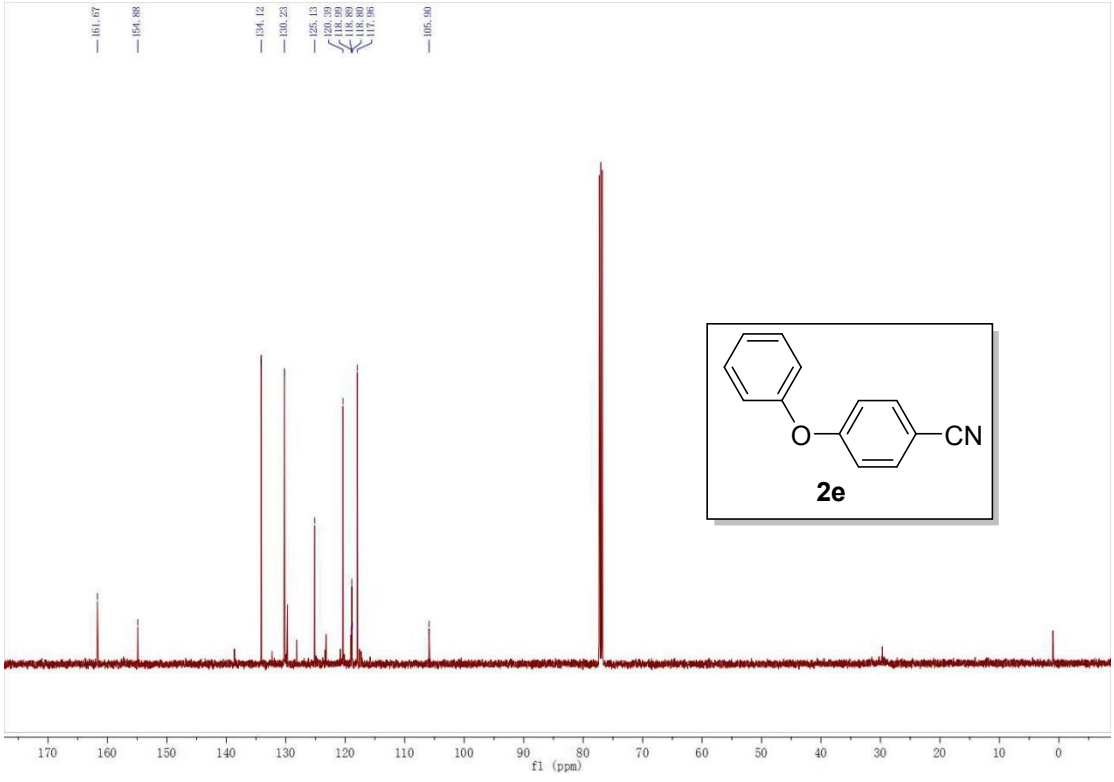




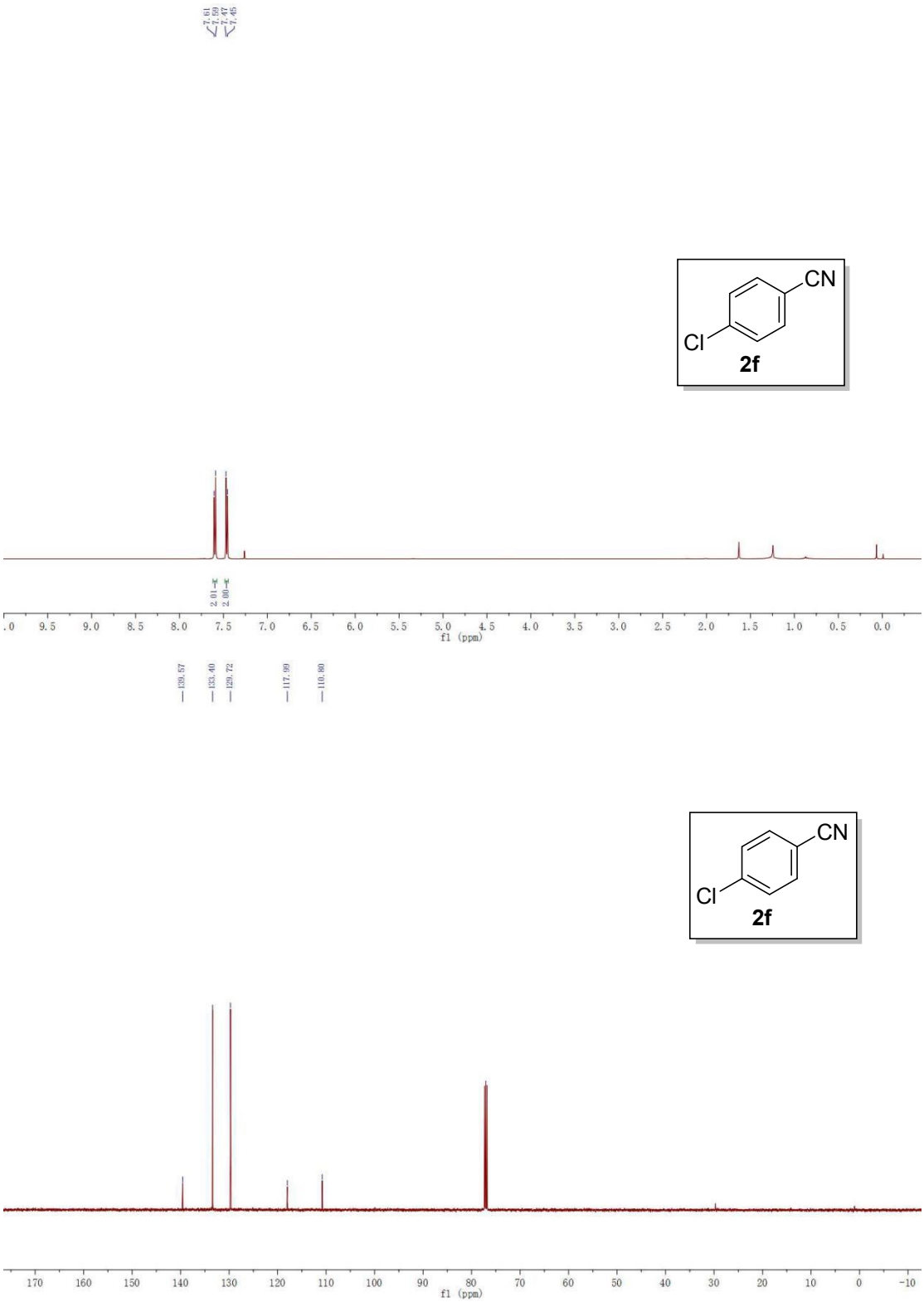
4-phenoxybenzonitrile (2e)



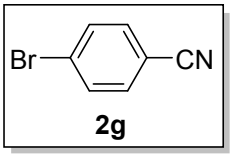


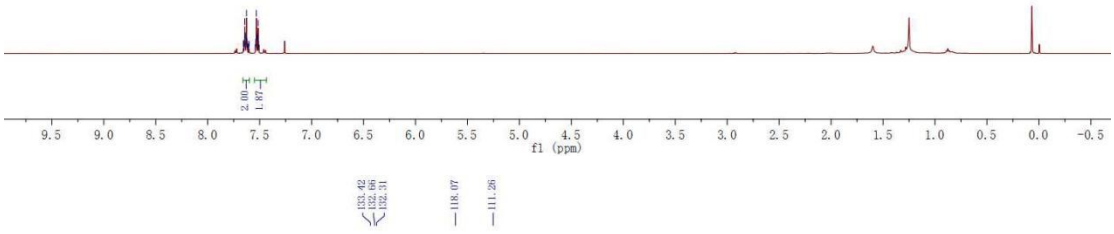


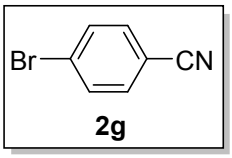
4-chlorobenzonitrile (2f)



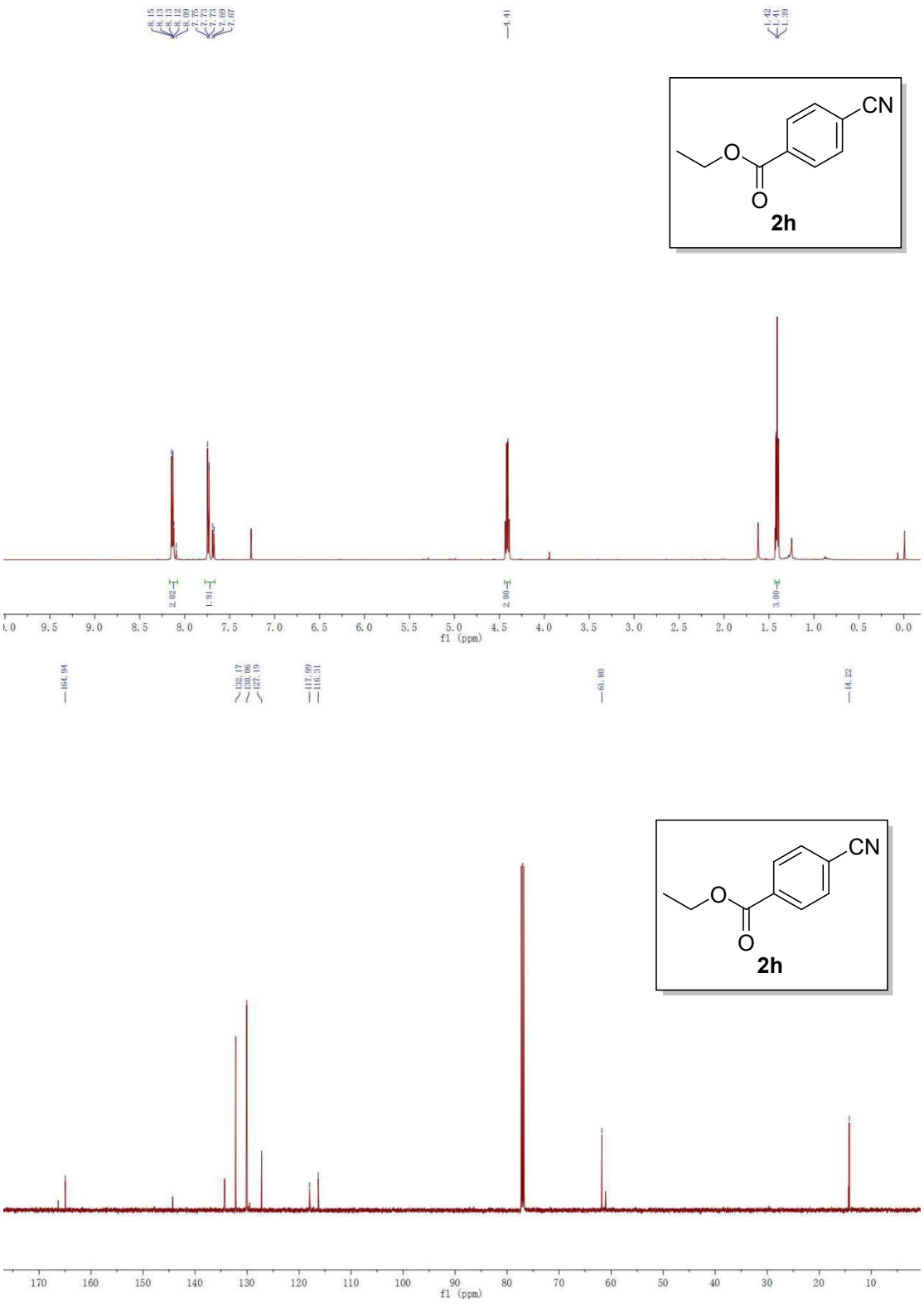
4-bromobenzonitrile (2g)



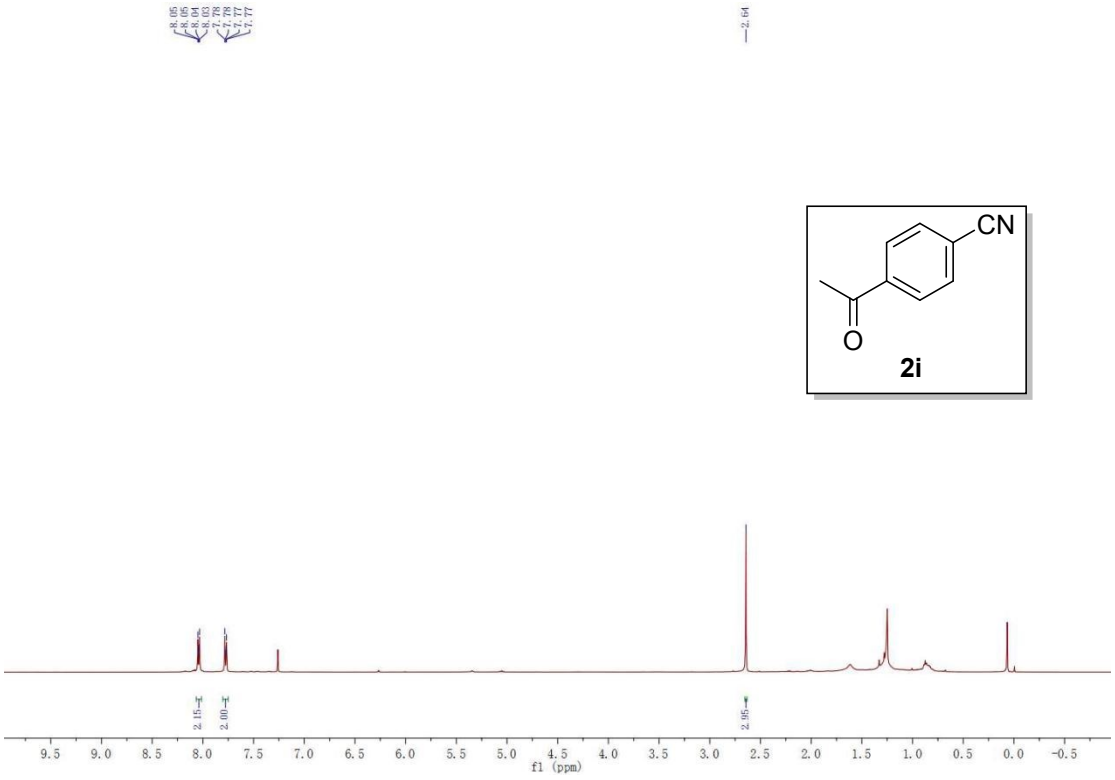


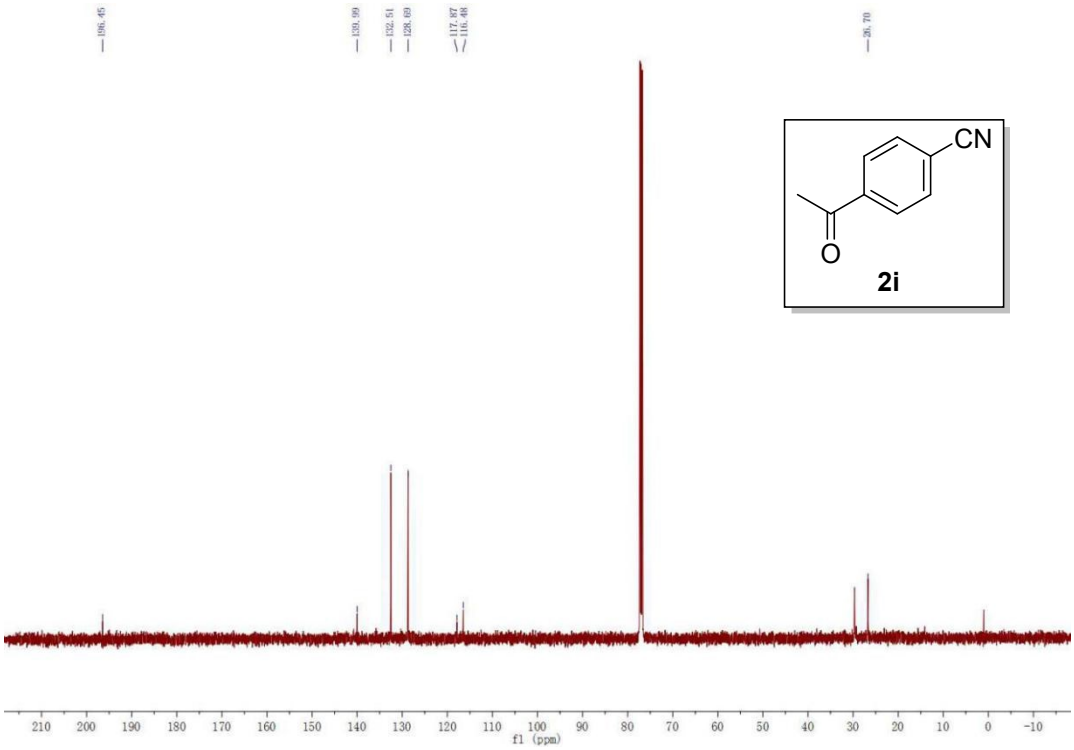


Ethyl 4-cyanobenzoate (2h)

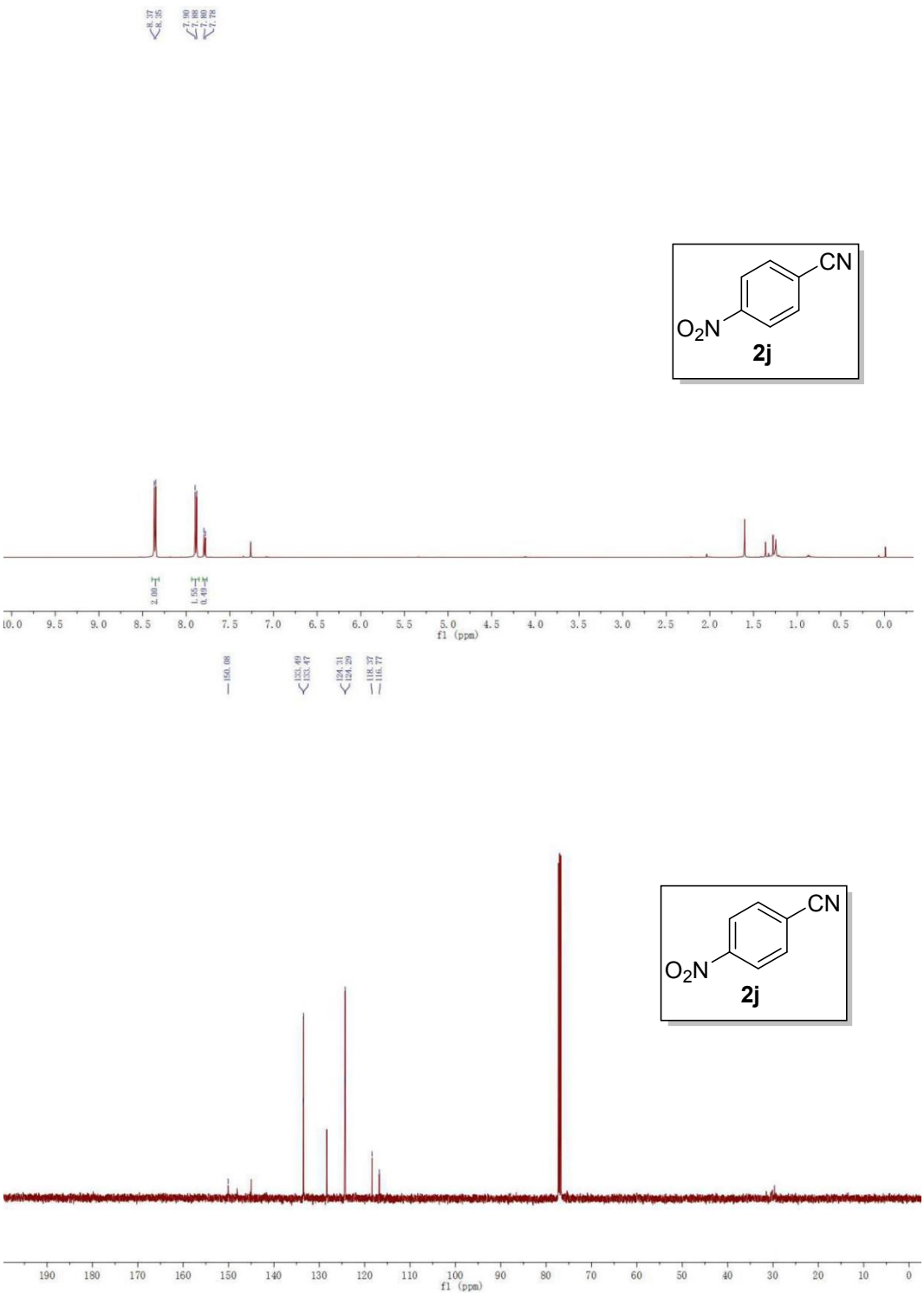


4-acetylbenzonitrile (2i)

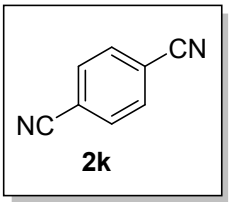




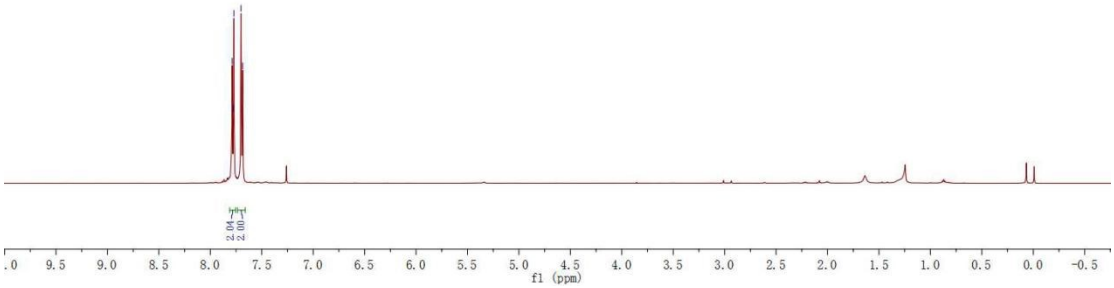
4-nitrobenzonitrile (2j)

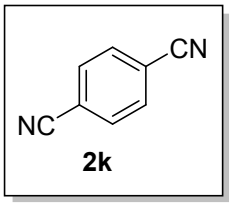


Terephthalonitrile (2k)

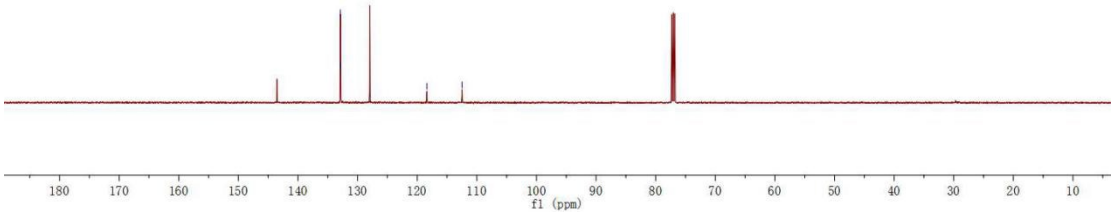


2k

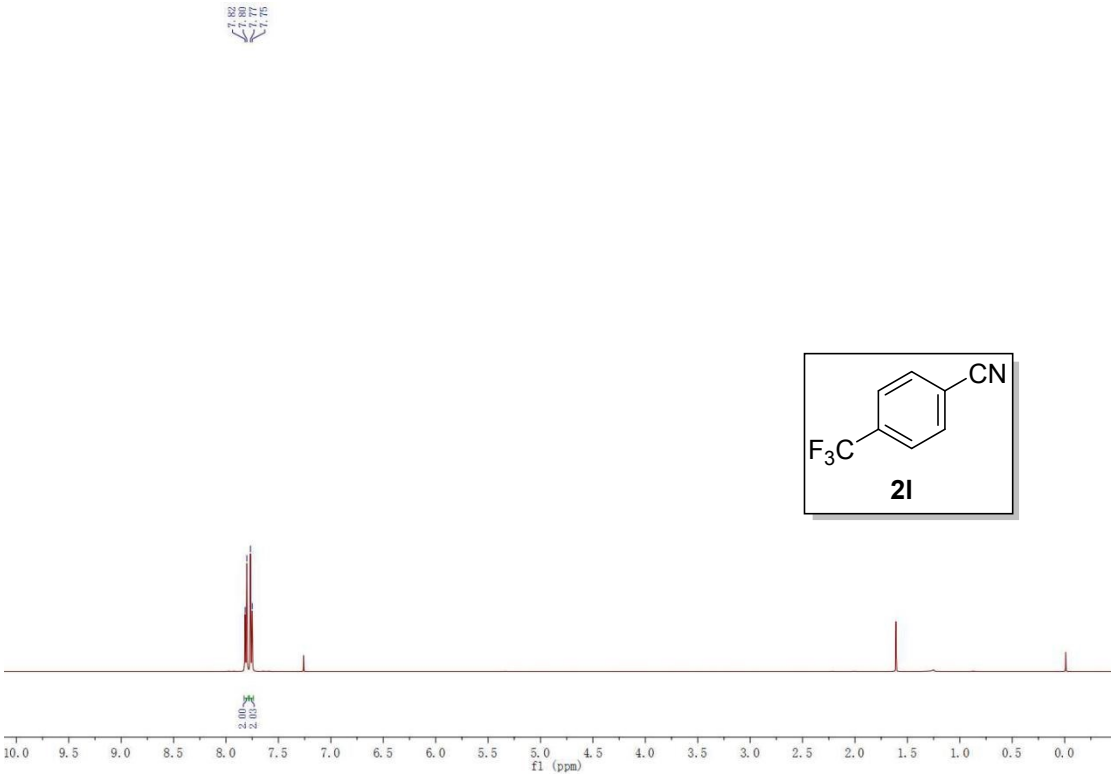


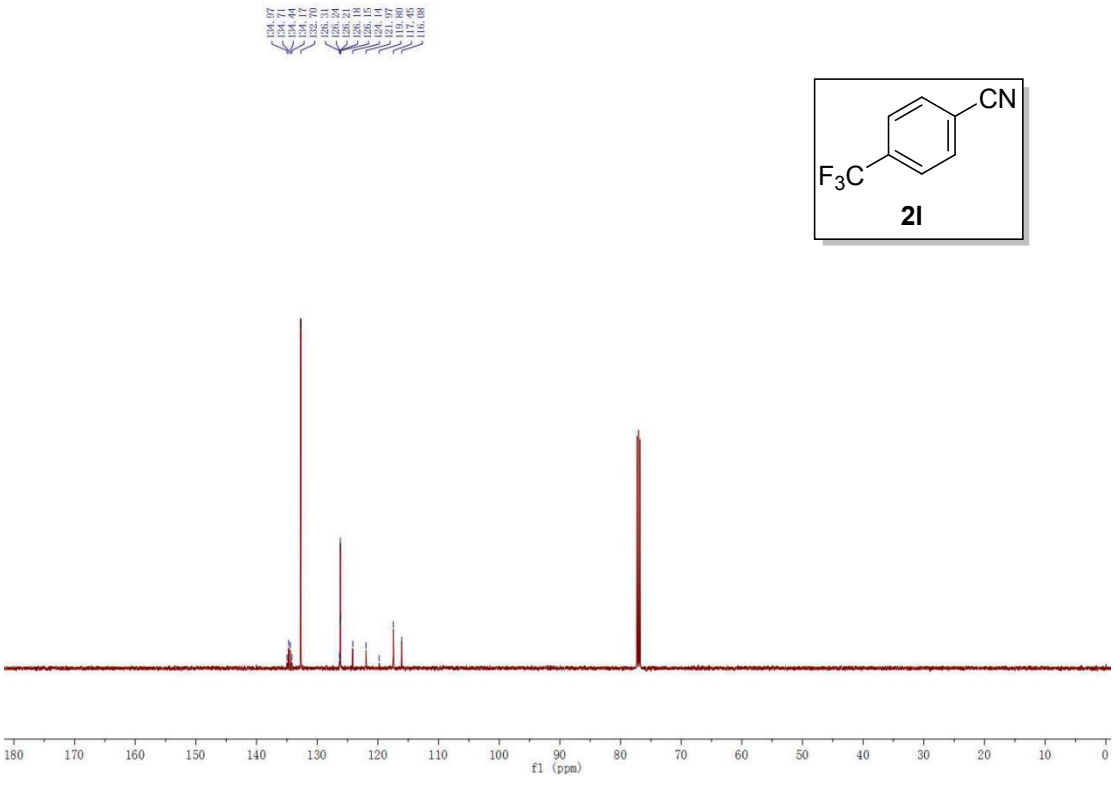


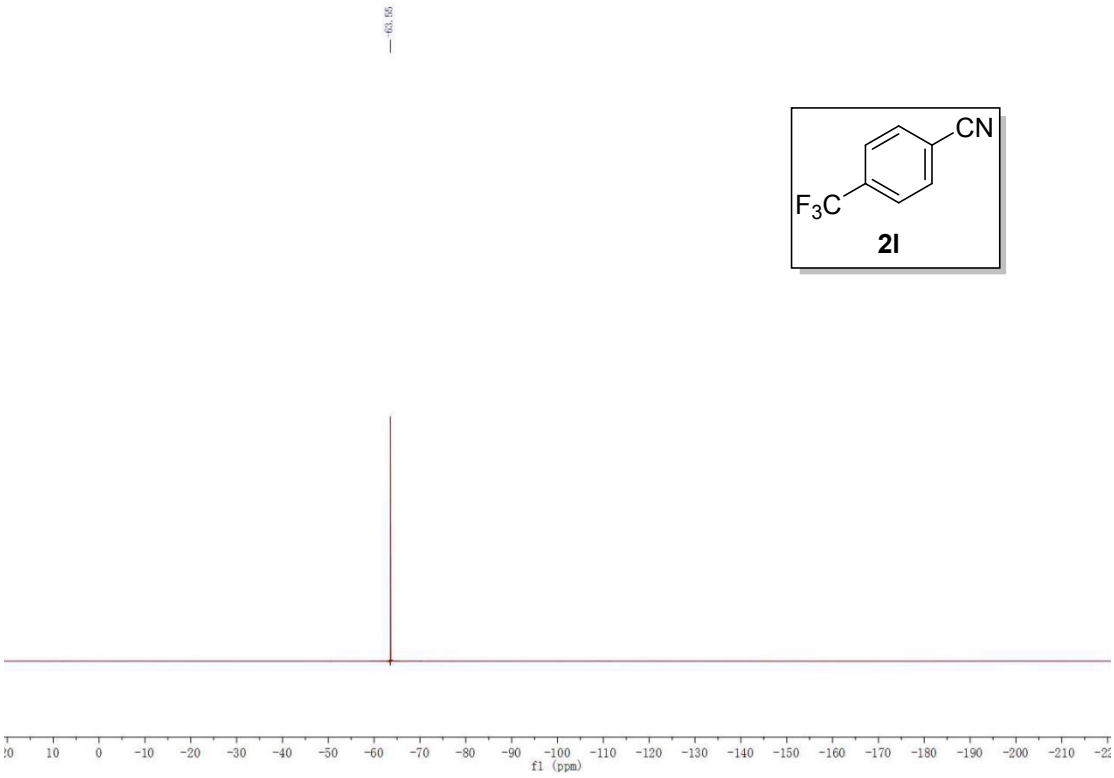
2k



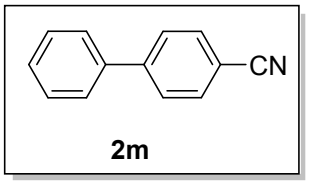
4-(trifluoromethyl)benzonitrile (2l)

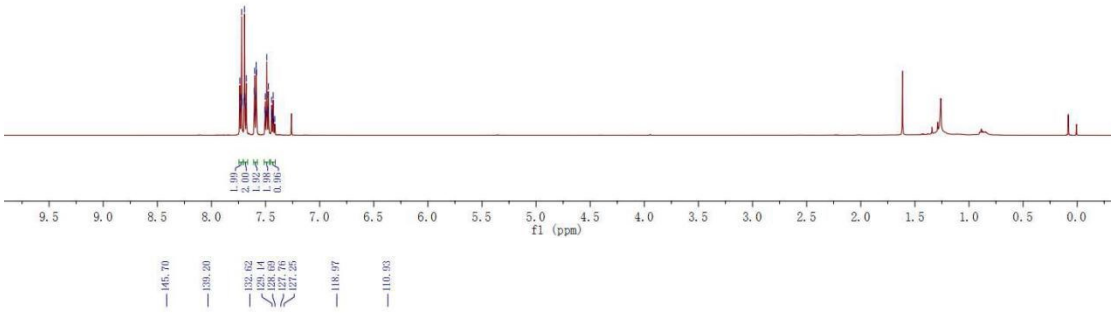

7.82
7.80
7.77
7.75
CN
F3C
2l
2.00
2.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

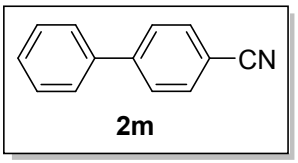

134.97
134.71
134.44
134.17
132.70
126.34
126.21
126.18
126.15
124.14
121.97
119.80
117.45
116.98
CN
F3C
2l
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

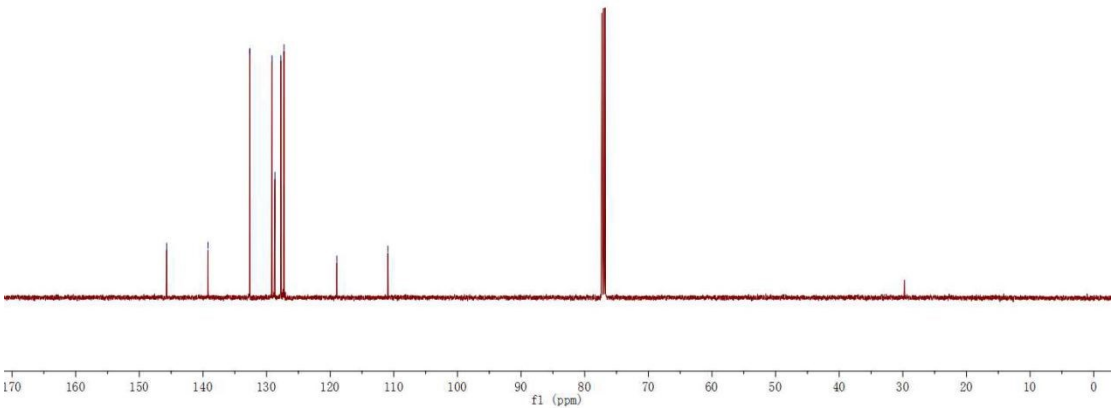

-63.55
CN
F3C
2l
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

[1,1'-biphenyl]-4-carbonitrile (2m)

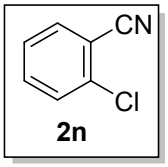


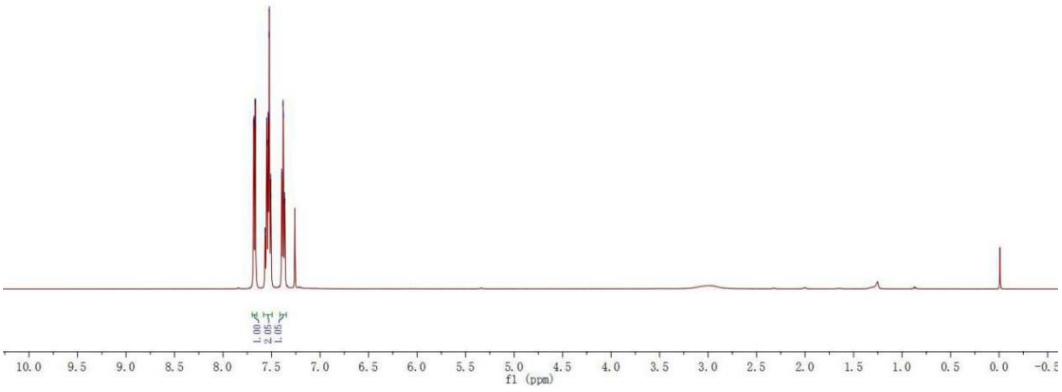


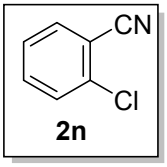


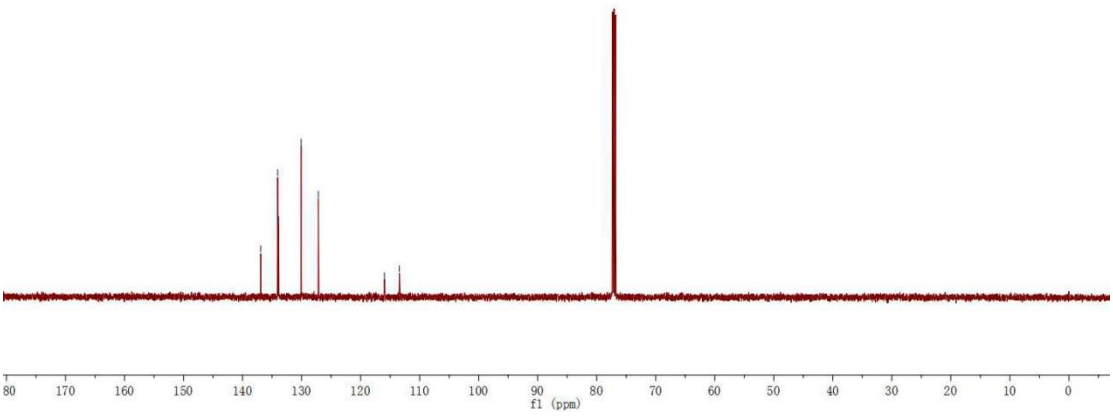


2-Chlorobenzonitrile (2n)

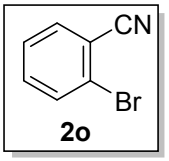


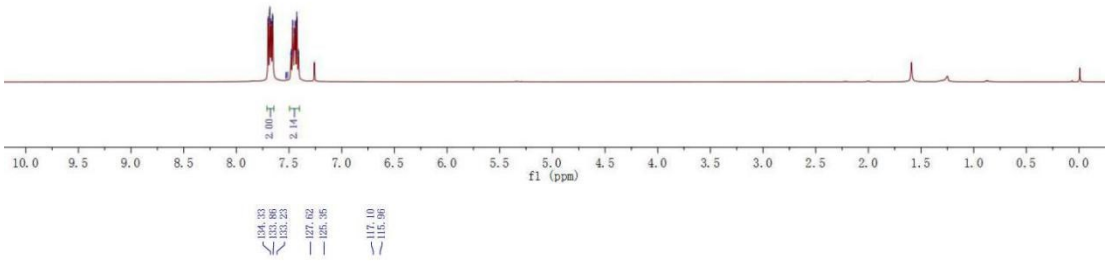


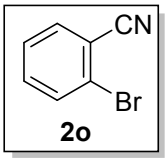


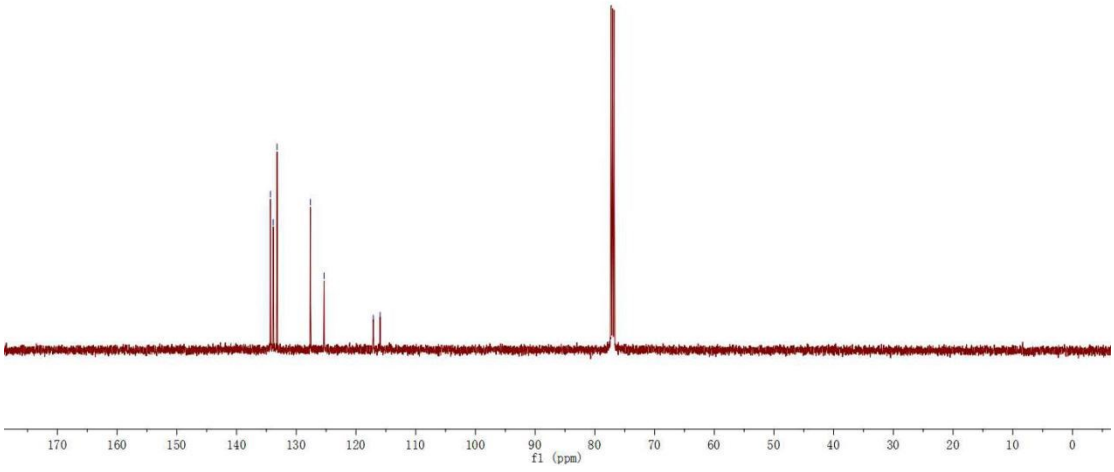


Bromobenzonitrile (2o)

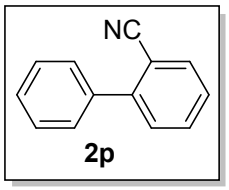


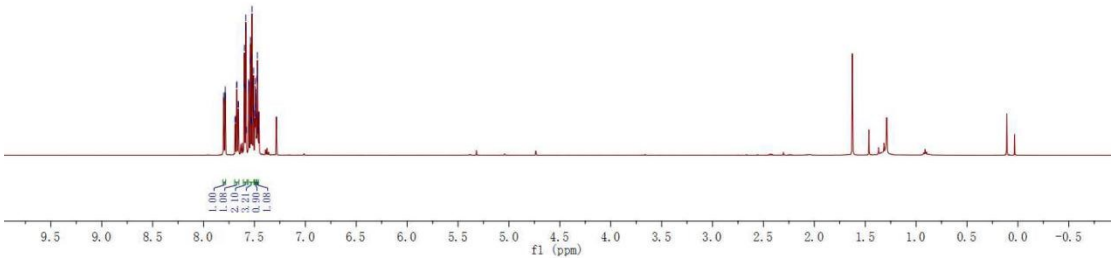


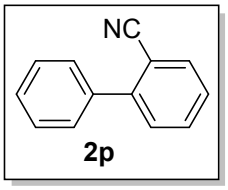




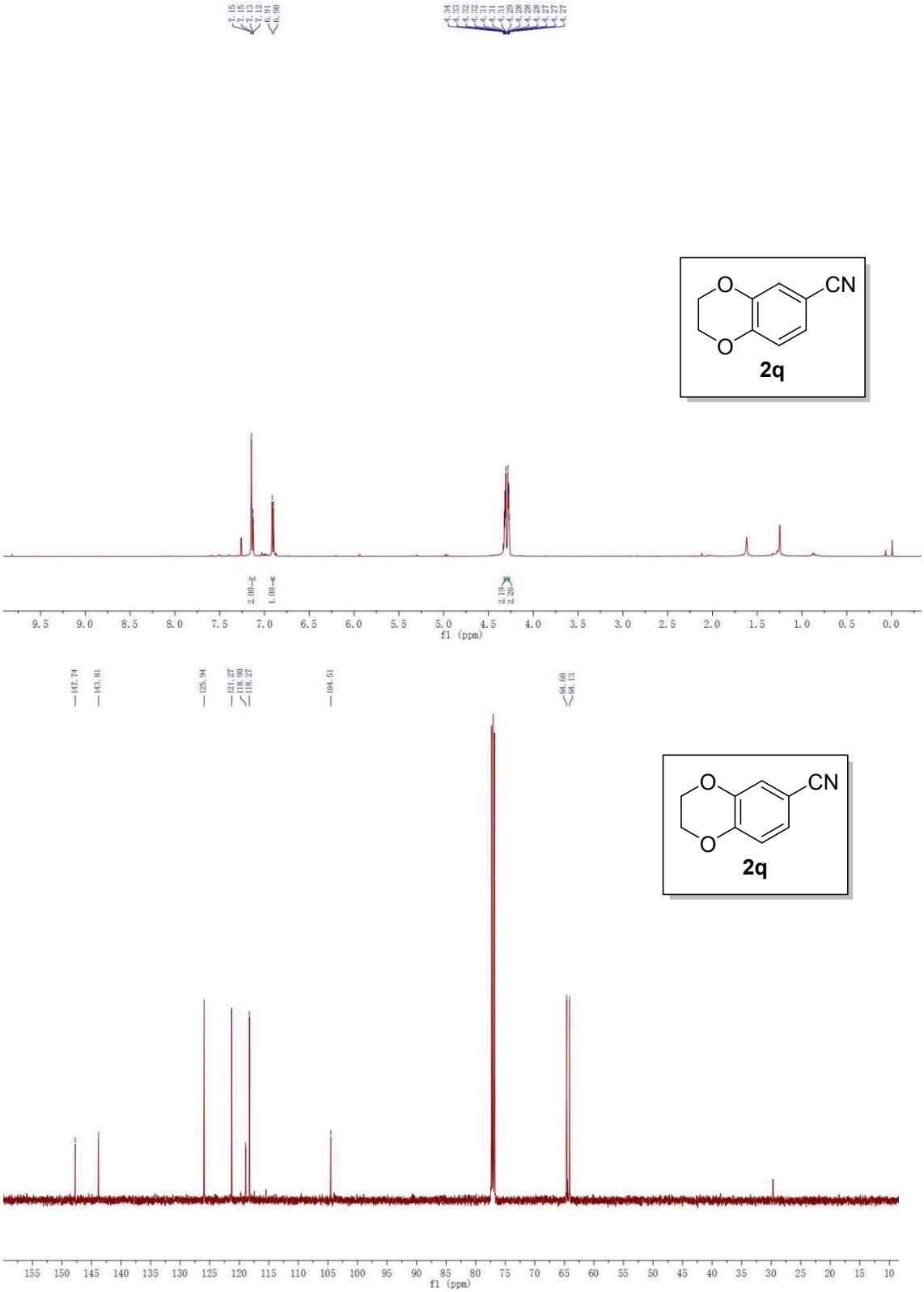
[1,1'-biphenyl]-2-carbonitrile (2p)



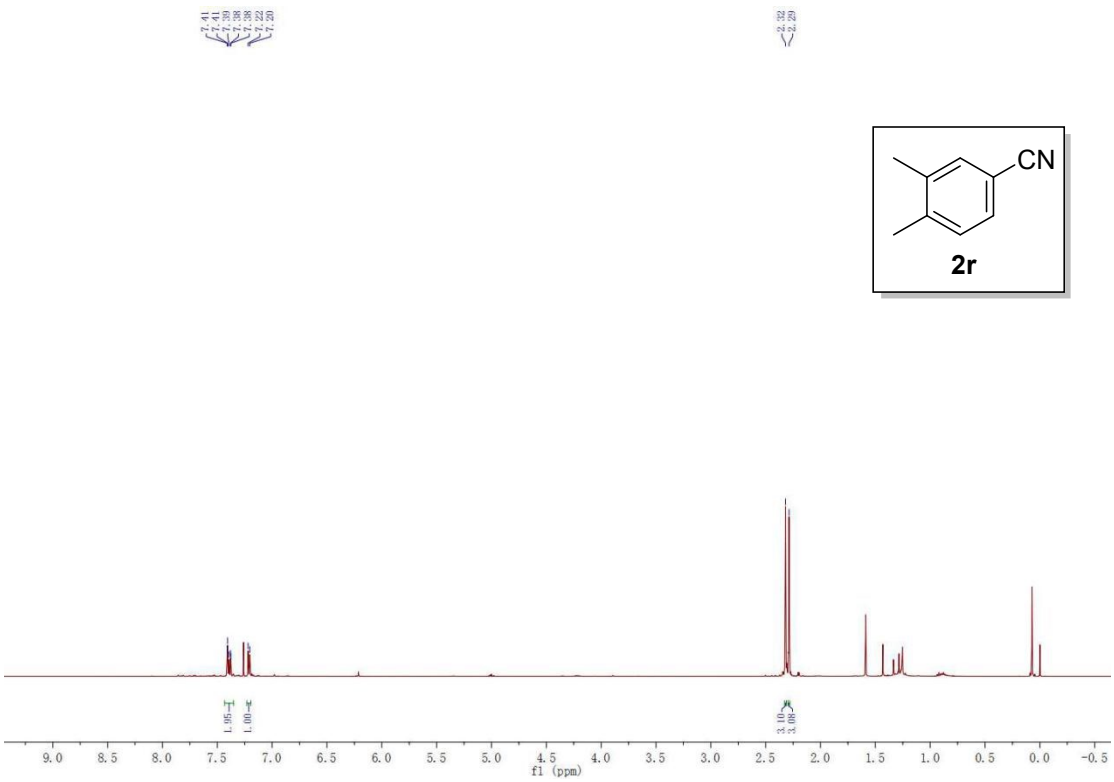


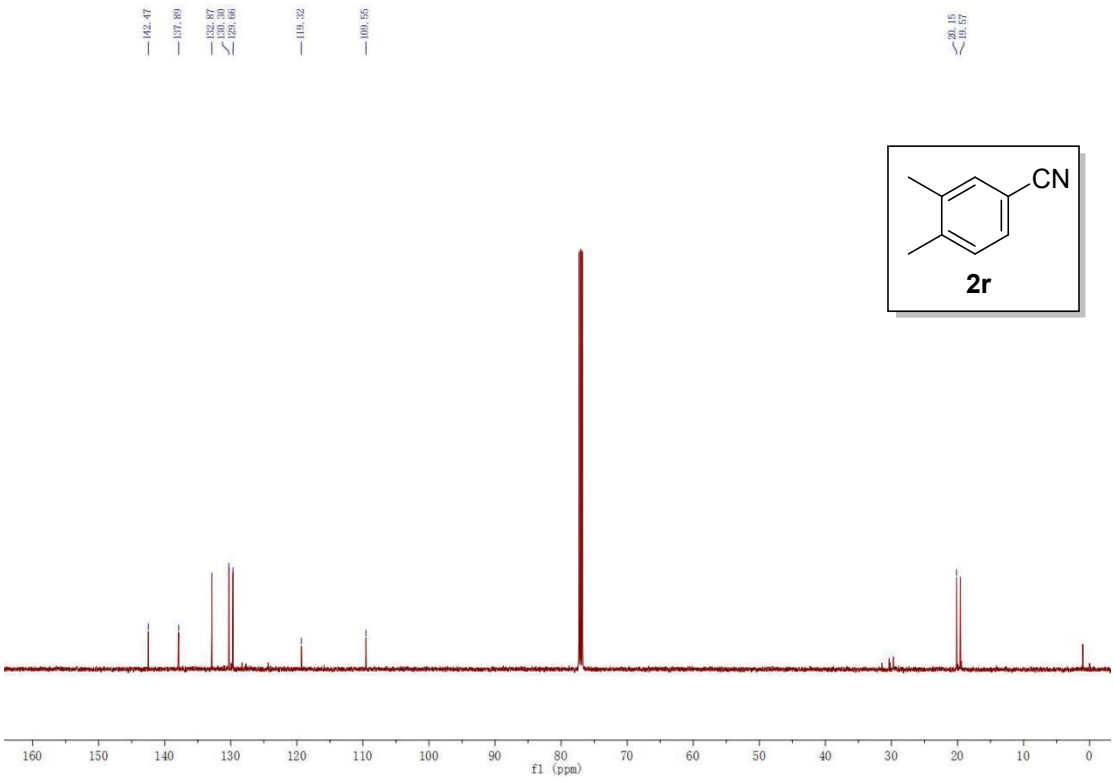


2,3-dihydrobenzo[b][1,4]dioxine-6-carbonitrile(2q)

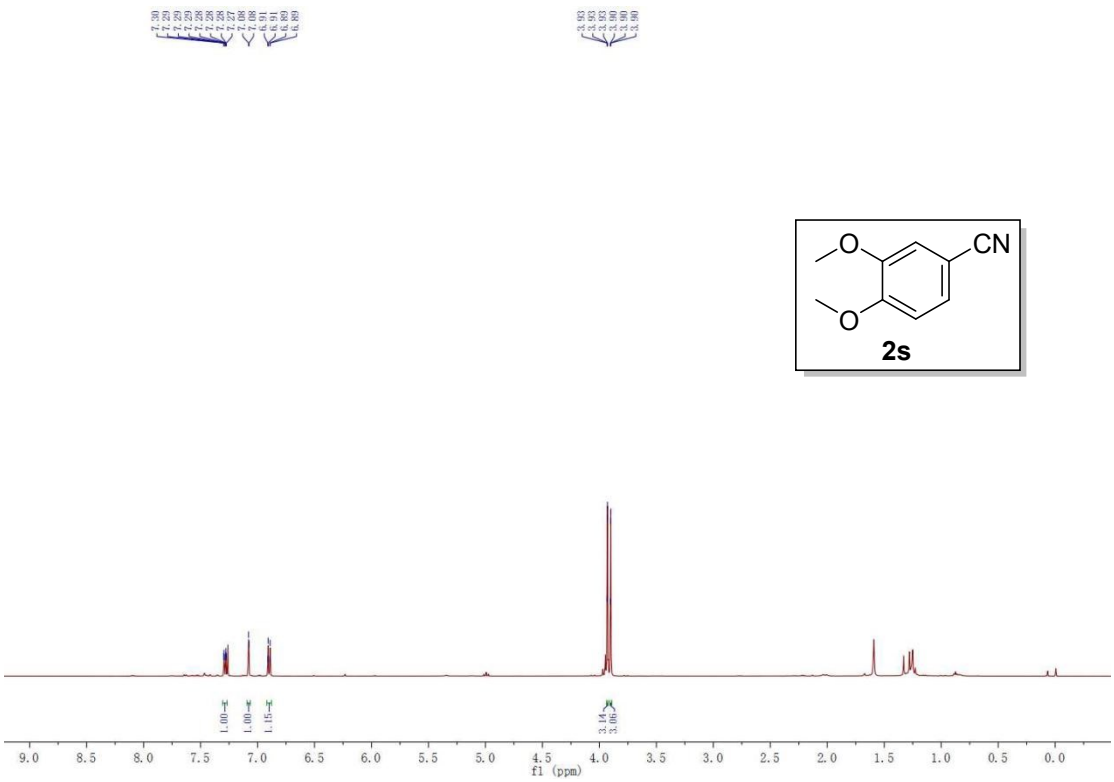


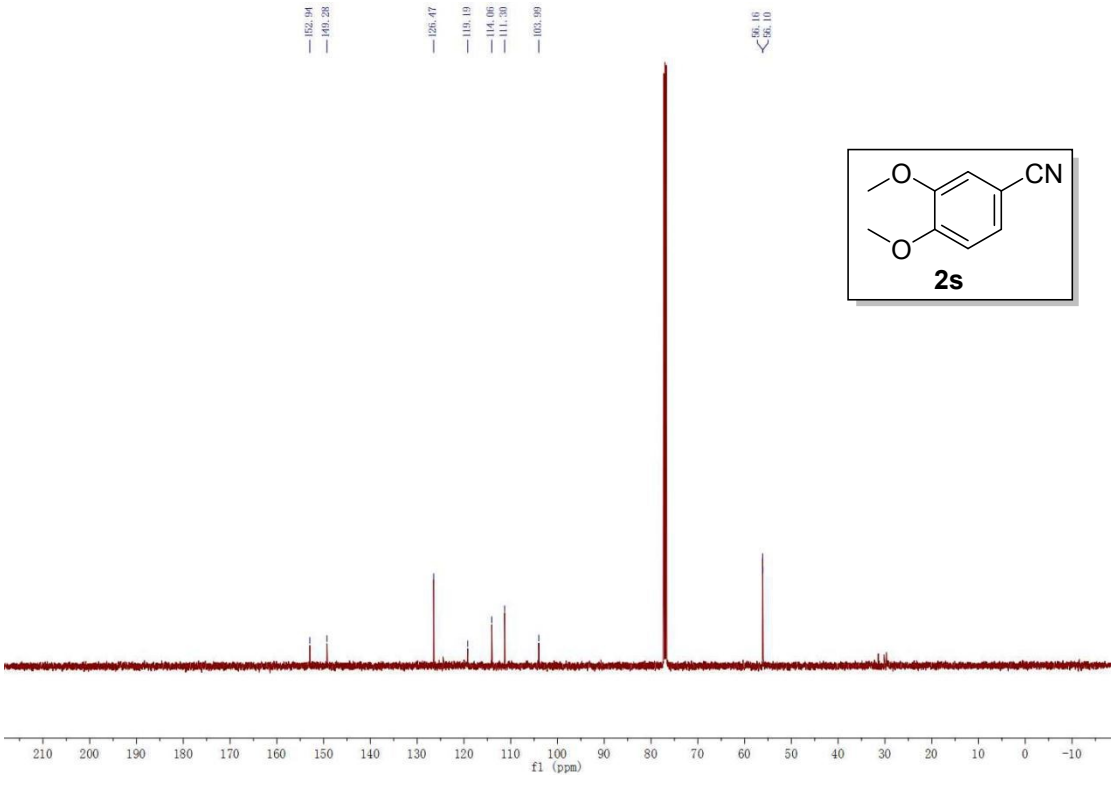
3,4-dimethylbenzonitrile (2r)



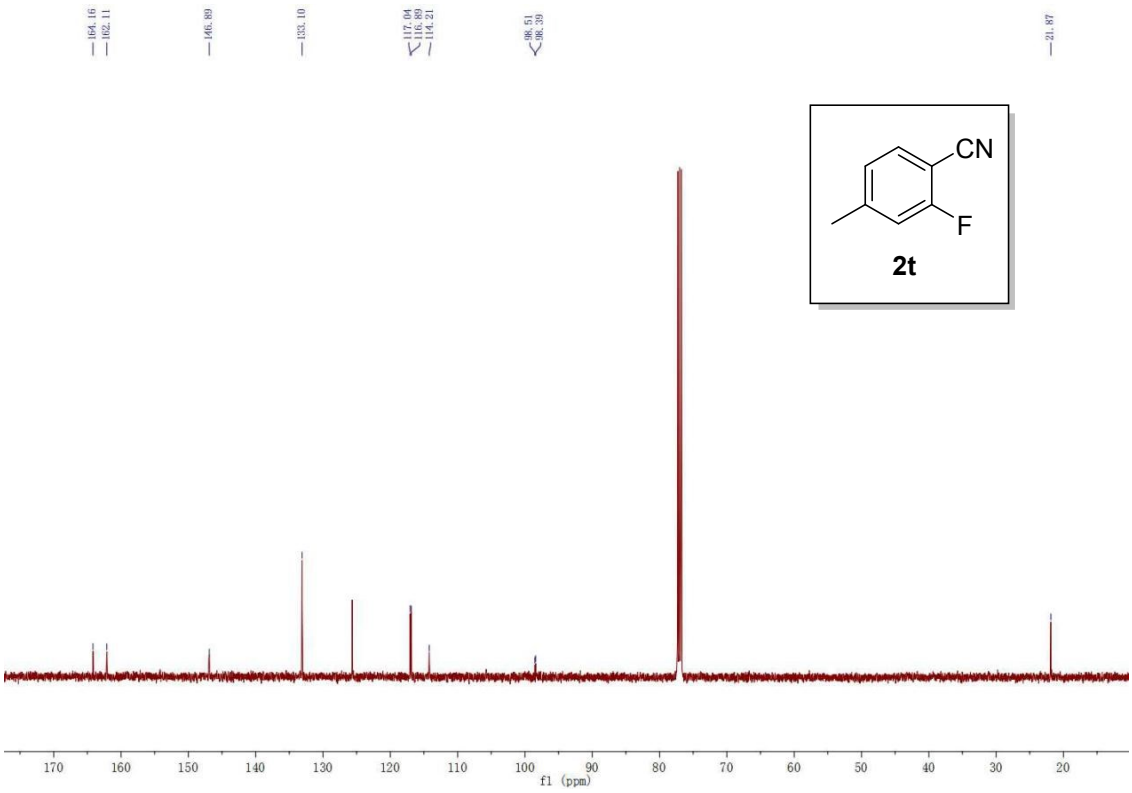


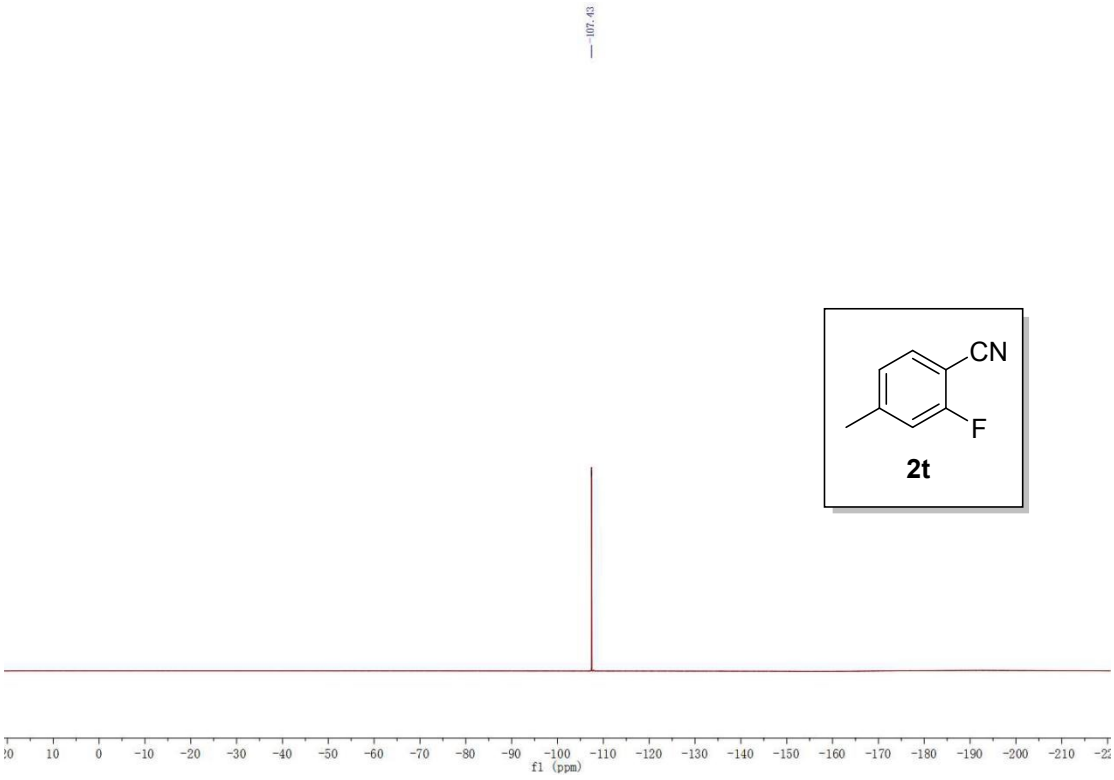
3,4-dimethoxybenzonitrile (2s)



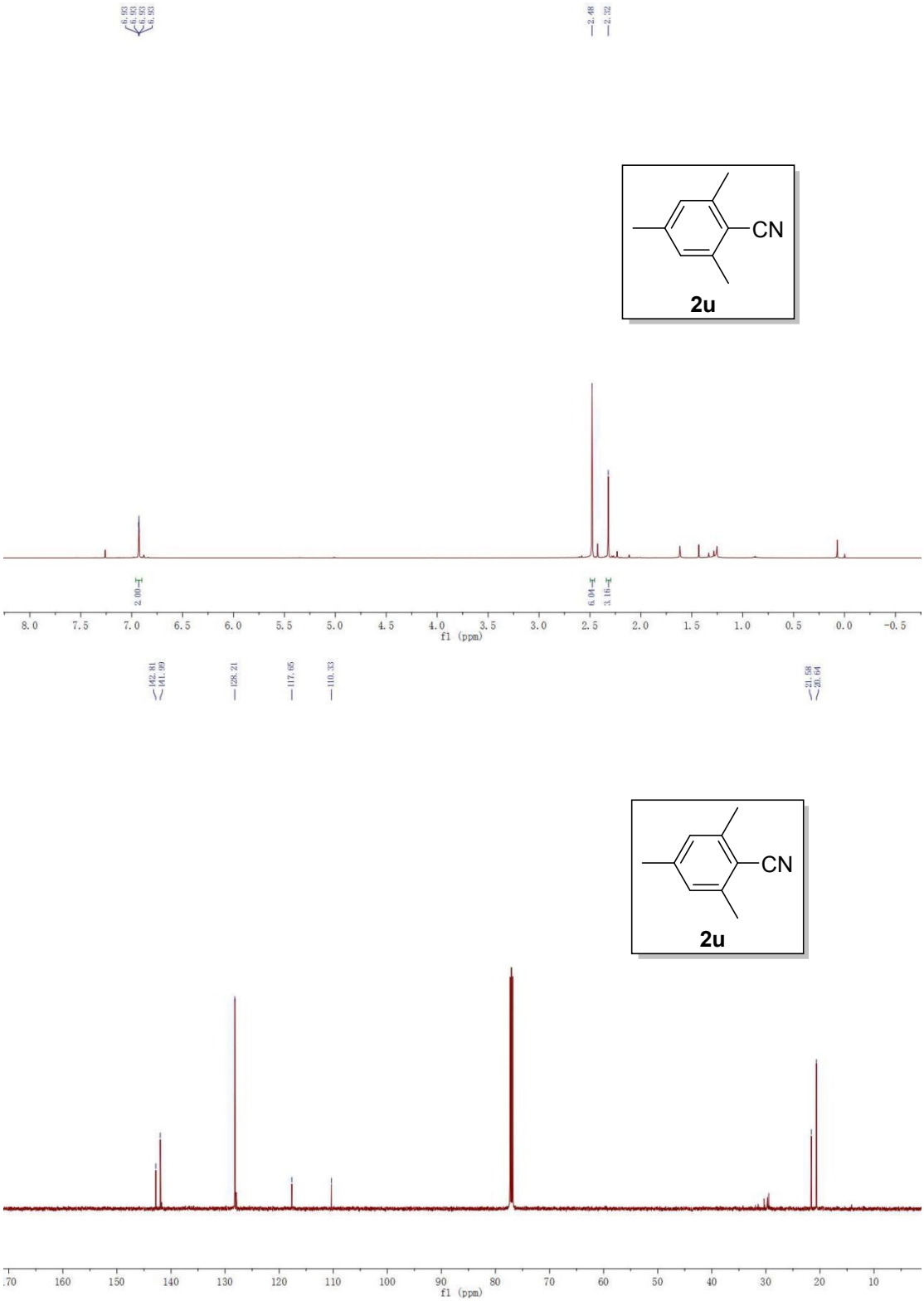


2-fluoro-4-methylbenzonitrile (2t)

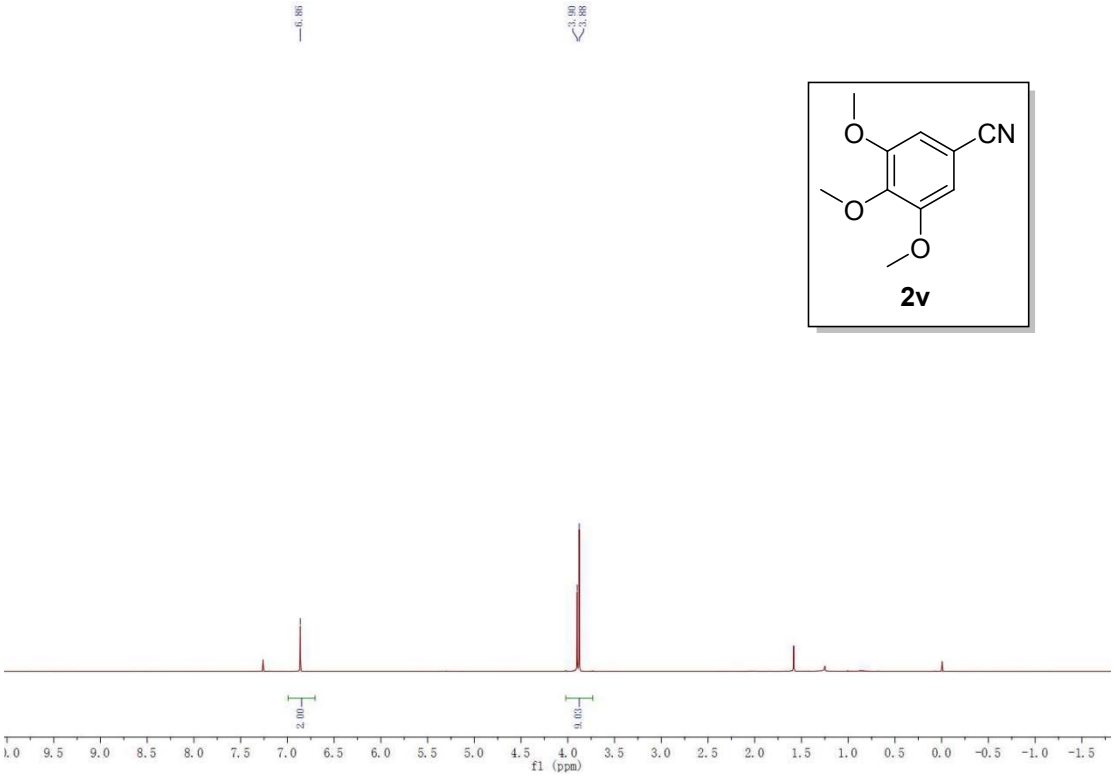


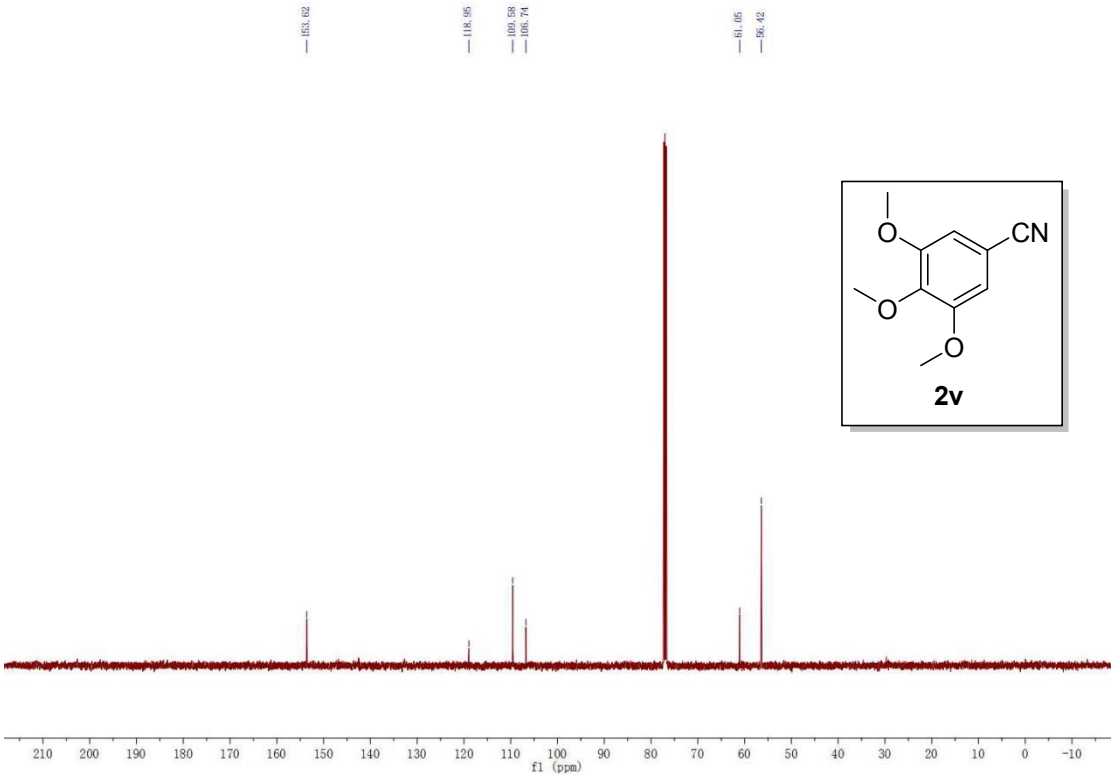

-107.43
CN
F
2t
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

2,4,6-trimethylbenzonitrile (2u)

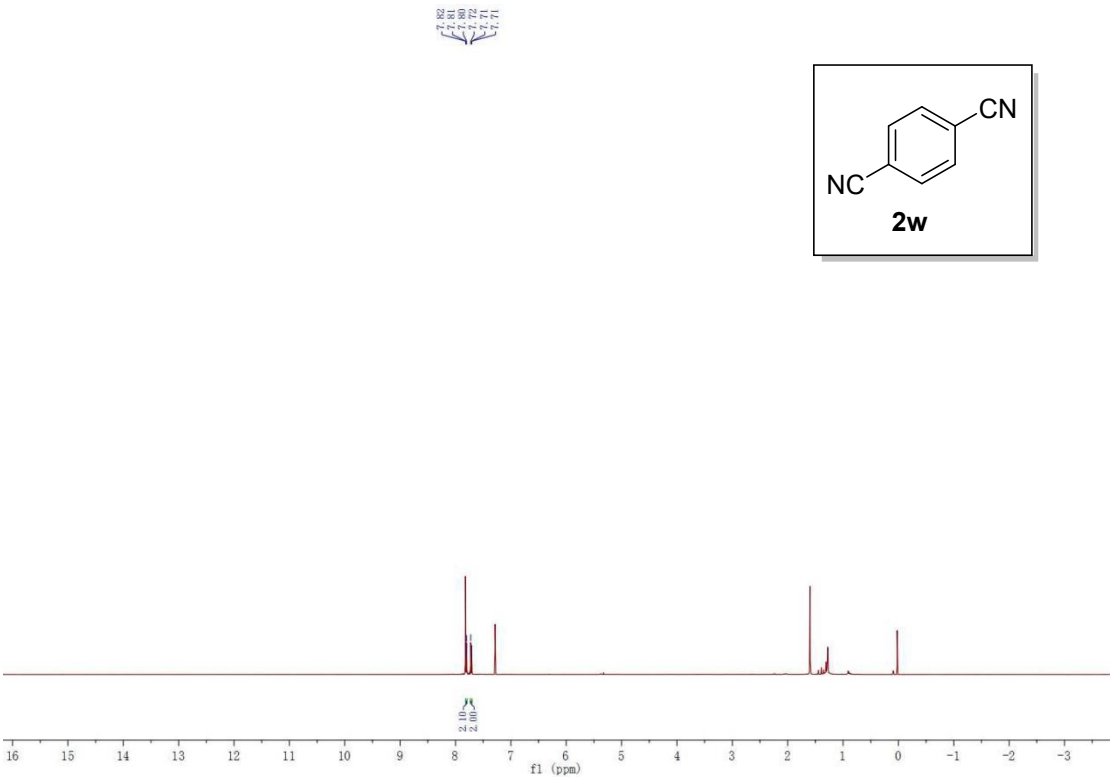


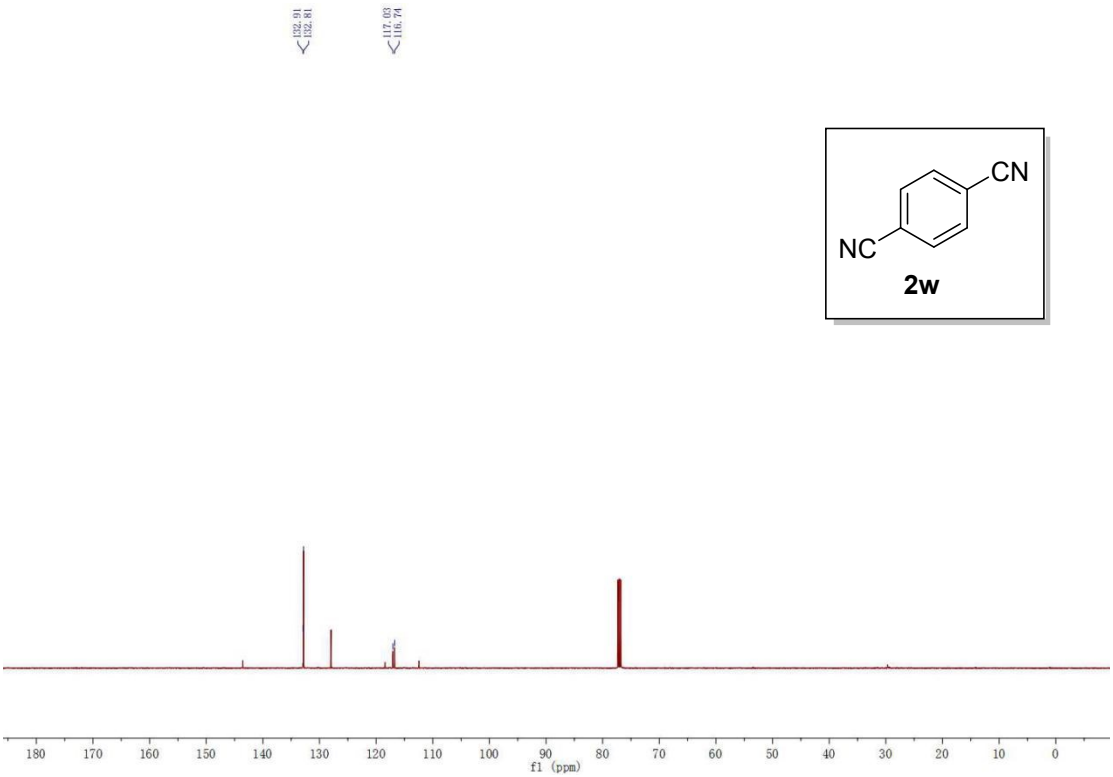
3,4,5-trimethoxybenzonitrile (2v)



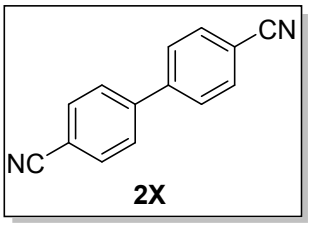


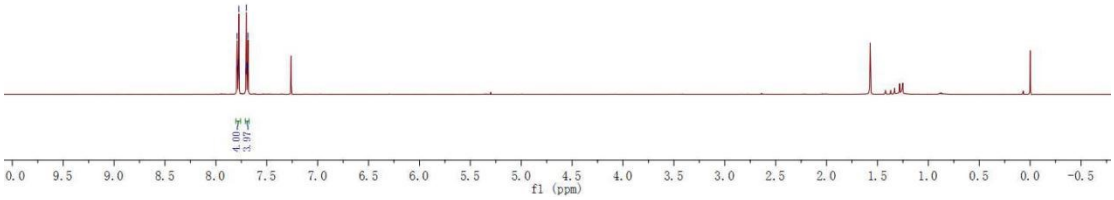
Terephthalonitrile (2w)

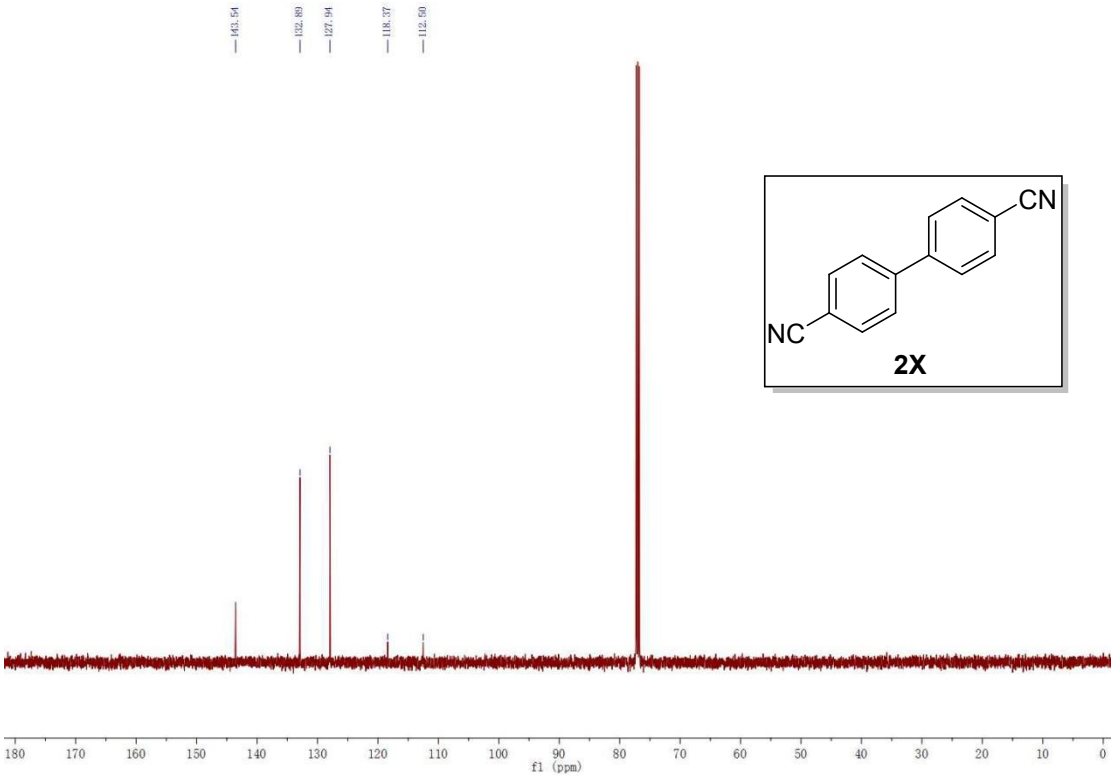




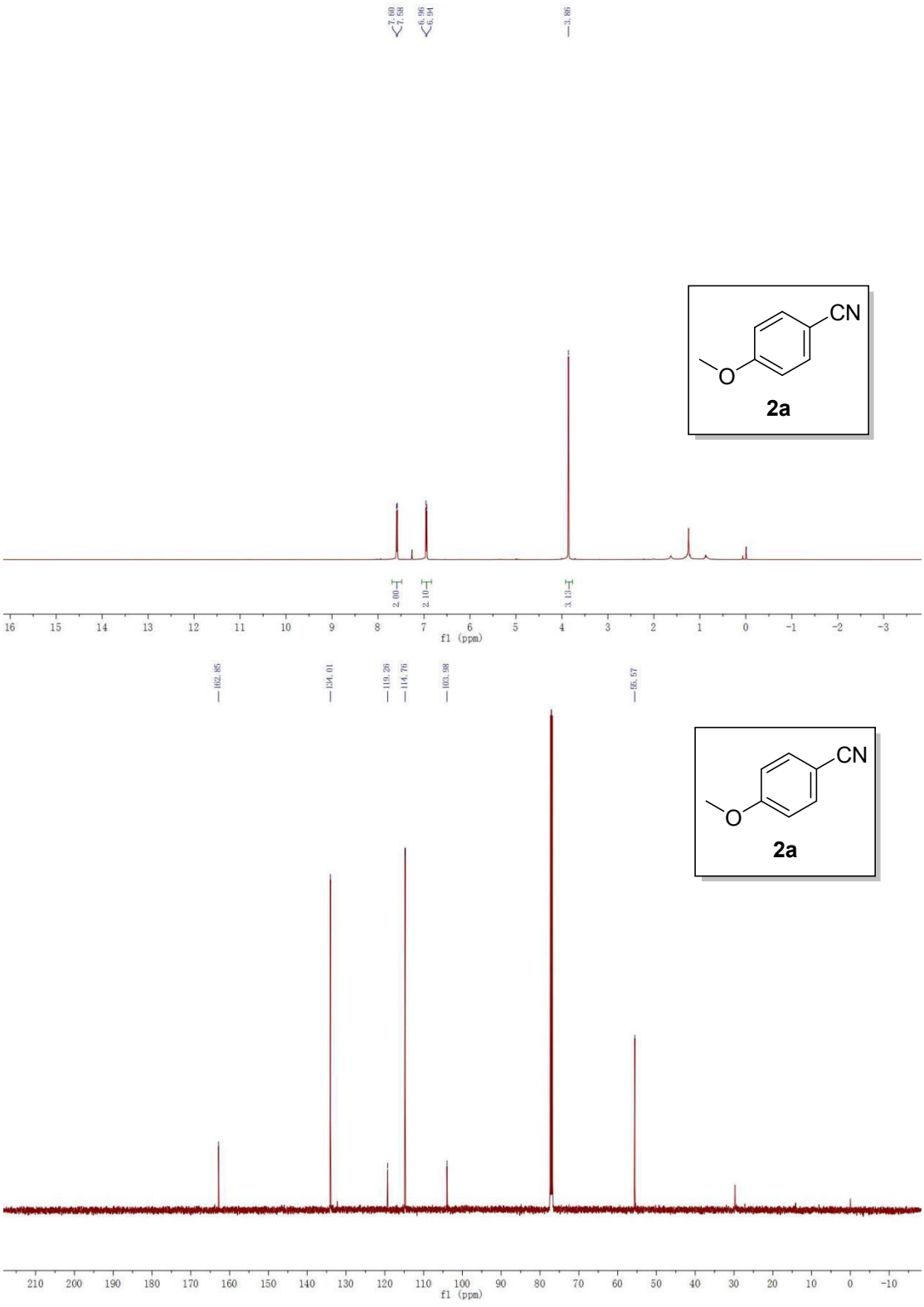
[1,1'-biphenyl]-4,4'-dicarbonitrile (2x)



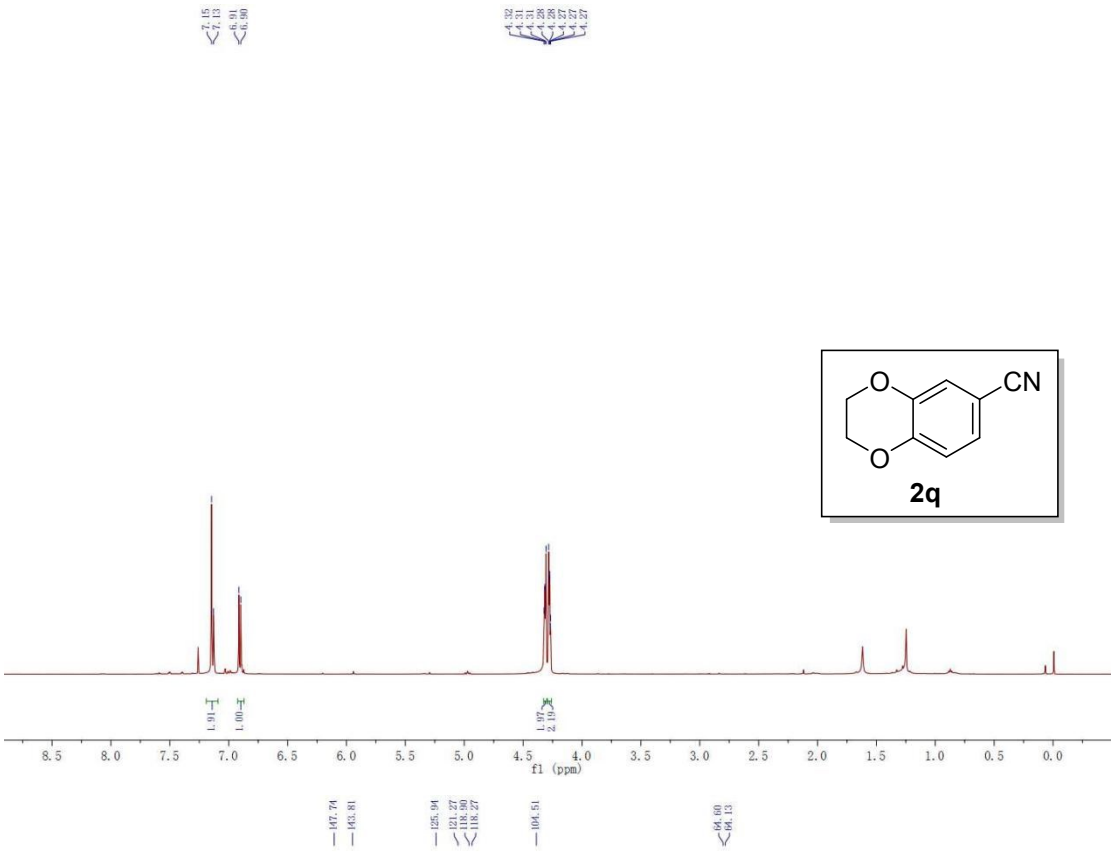


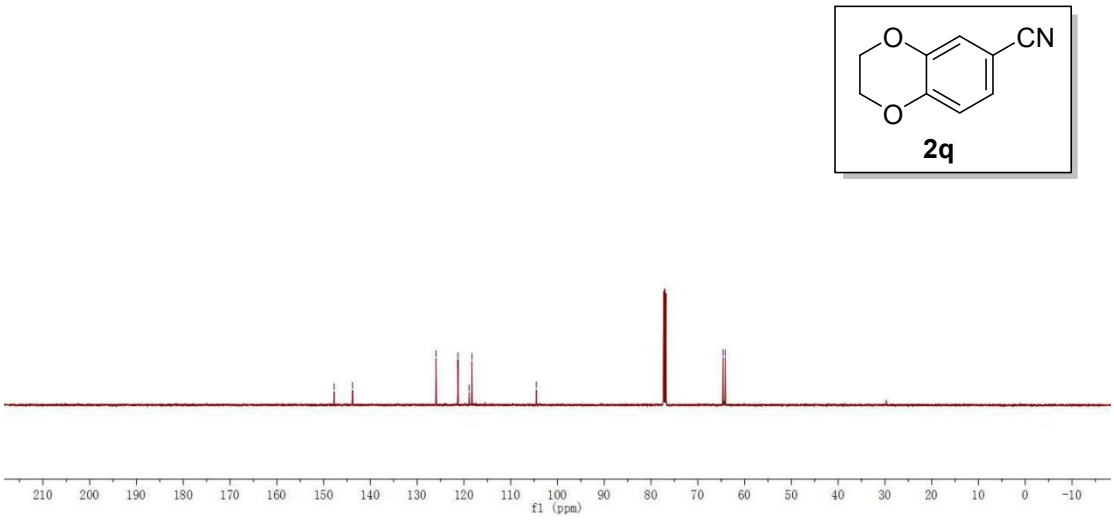


4-methoxybenzonitrile (2a)

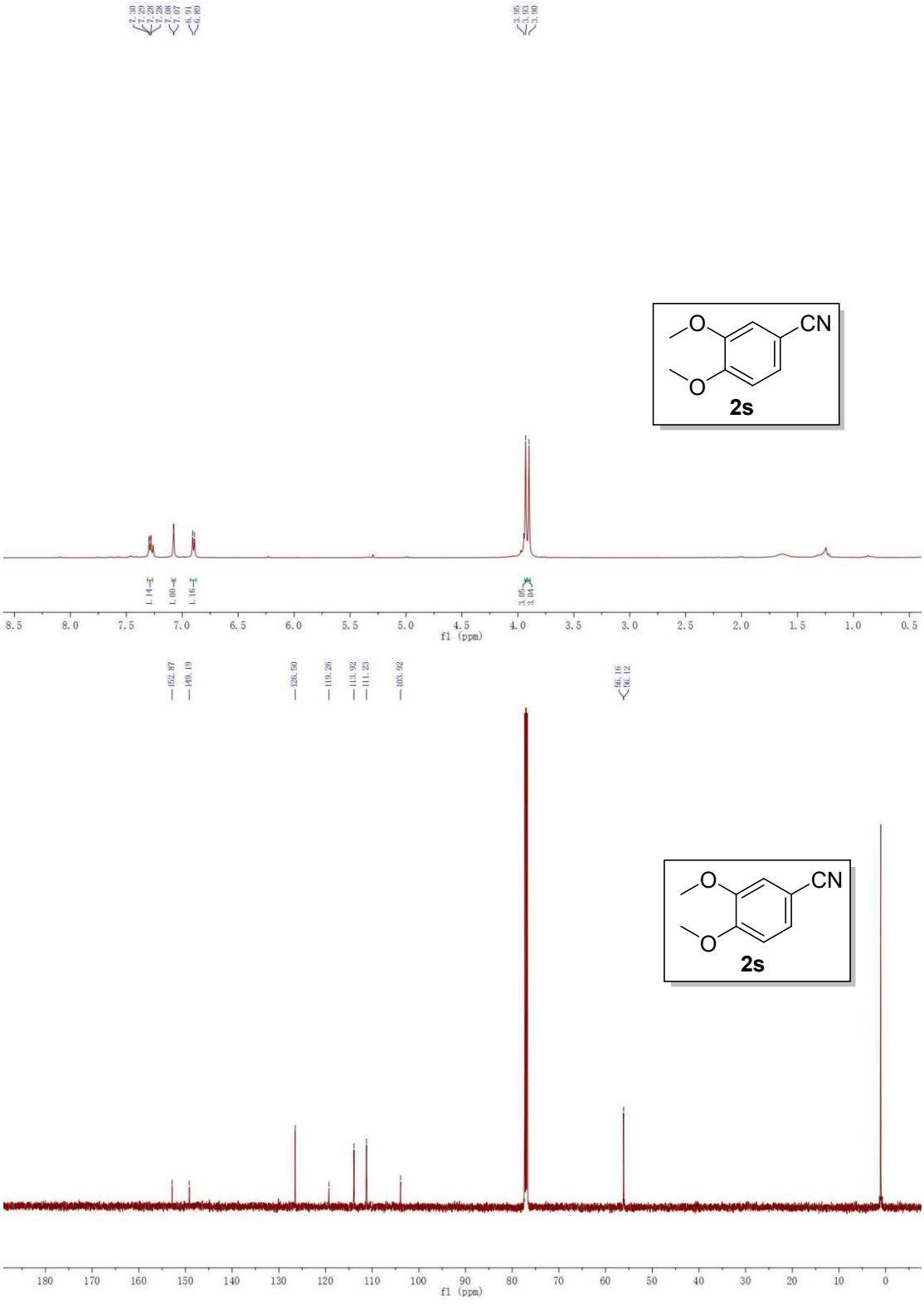


2,3-dihydrobenzo[b][1,4]dioxine-6-carbonitrile (2q)

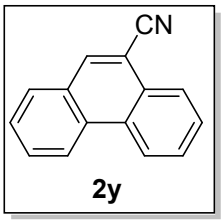


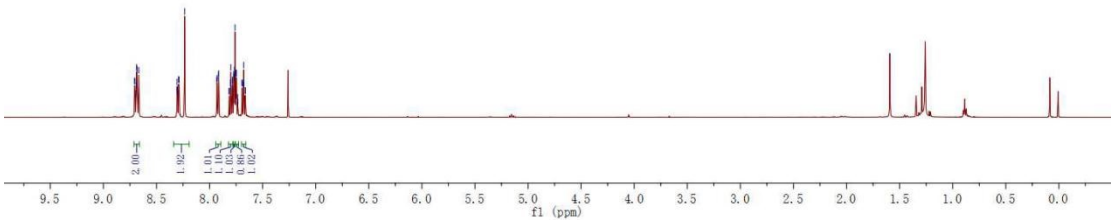


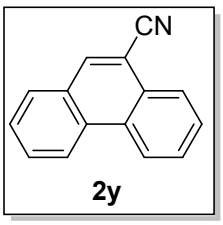
3,4-dimethoxybenzonitrile (2s)

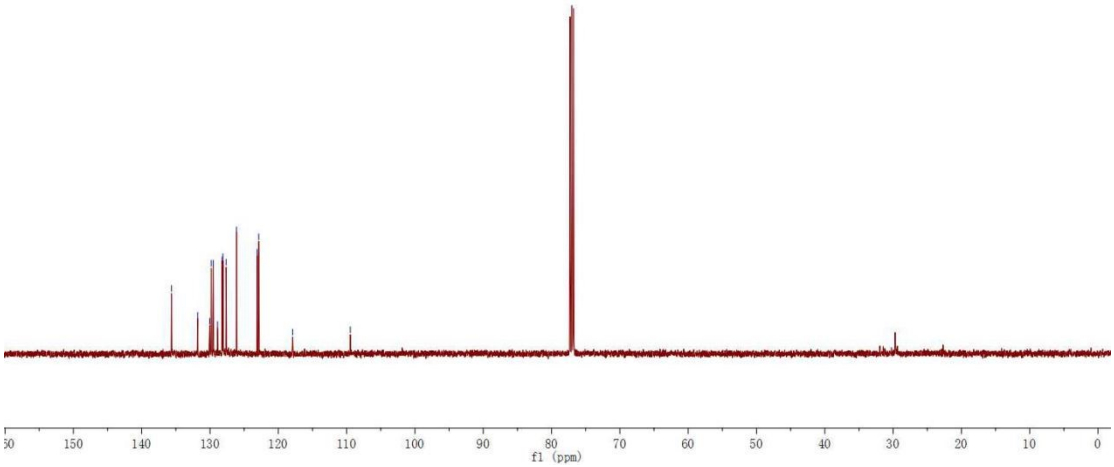


Phenanthrene-9-carbonitrile (2y)

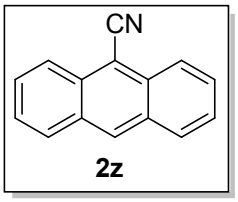


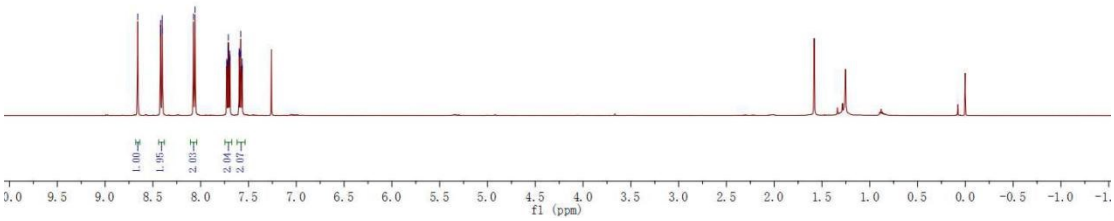


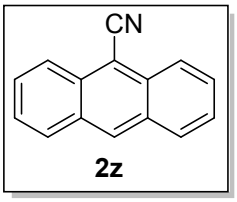




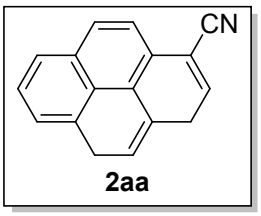
Anthracene-9-carbonitrile (2z)

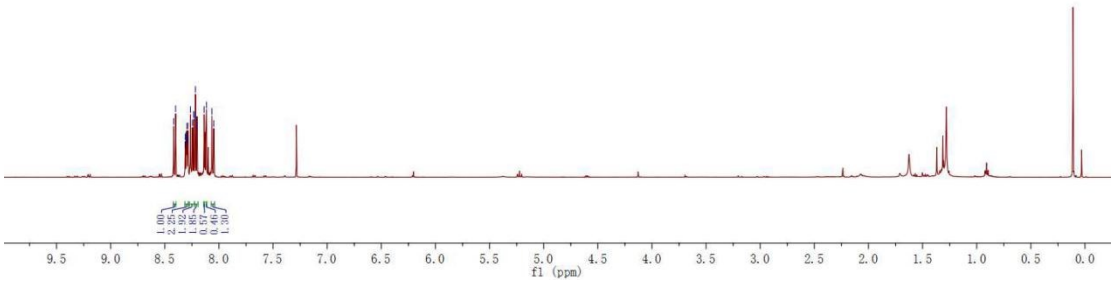


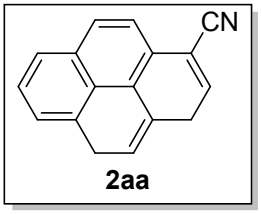




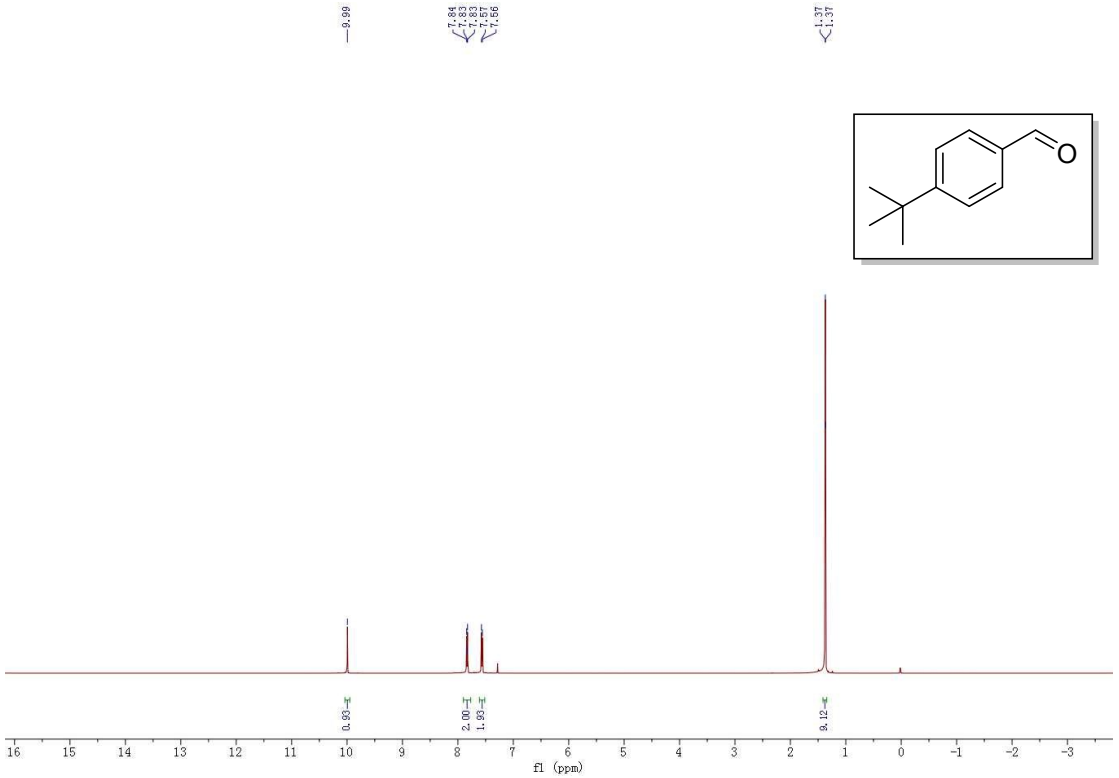
3,5-dihydropyrene-1-carbonitrile (2aa)

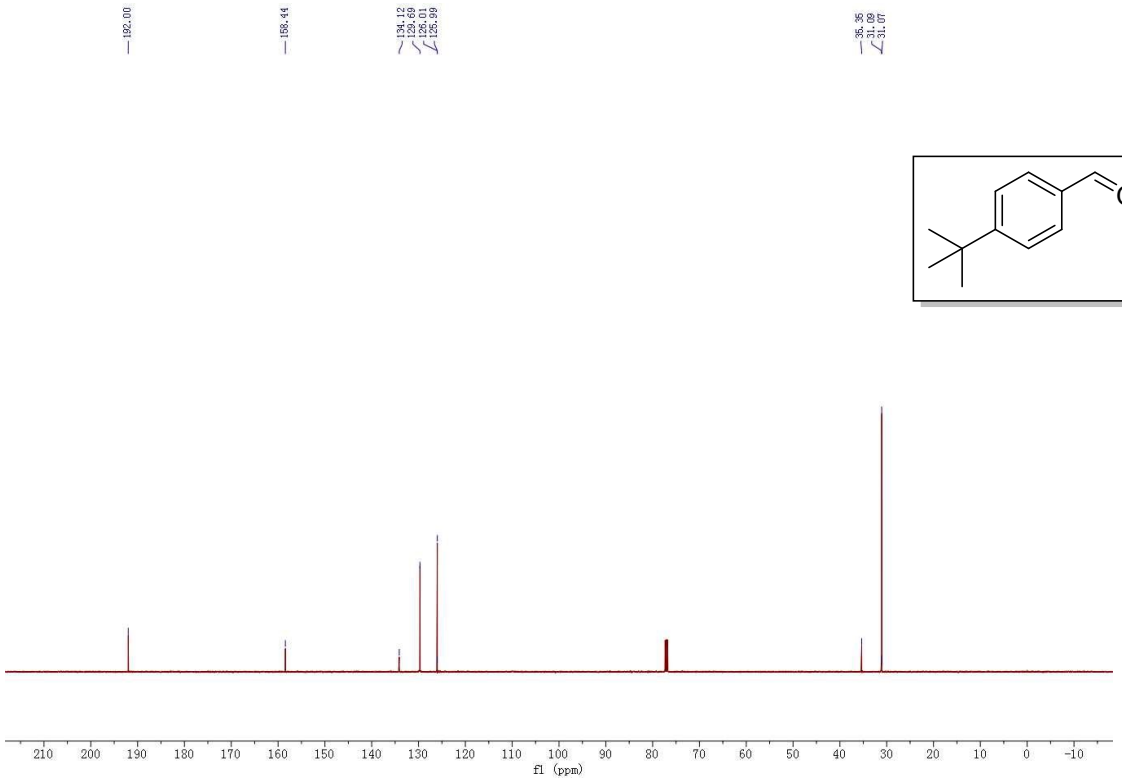




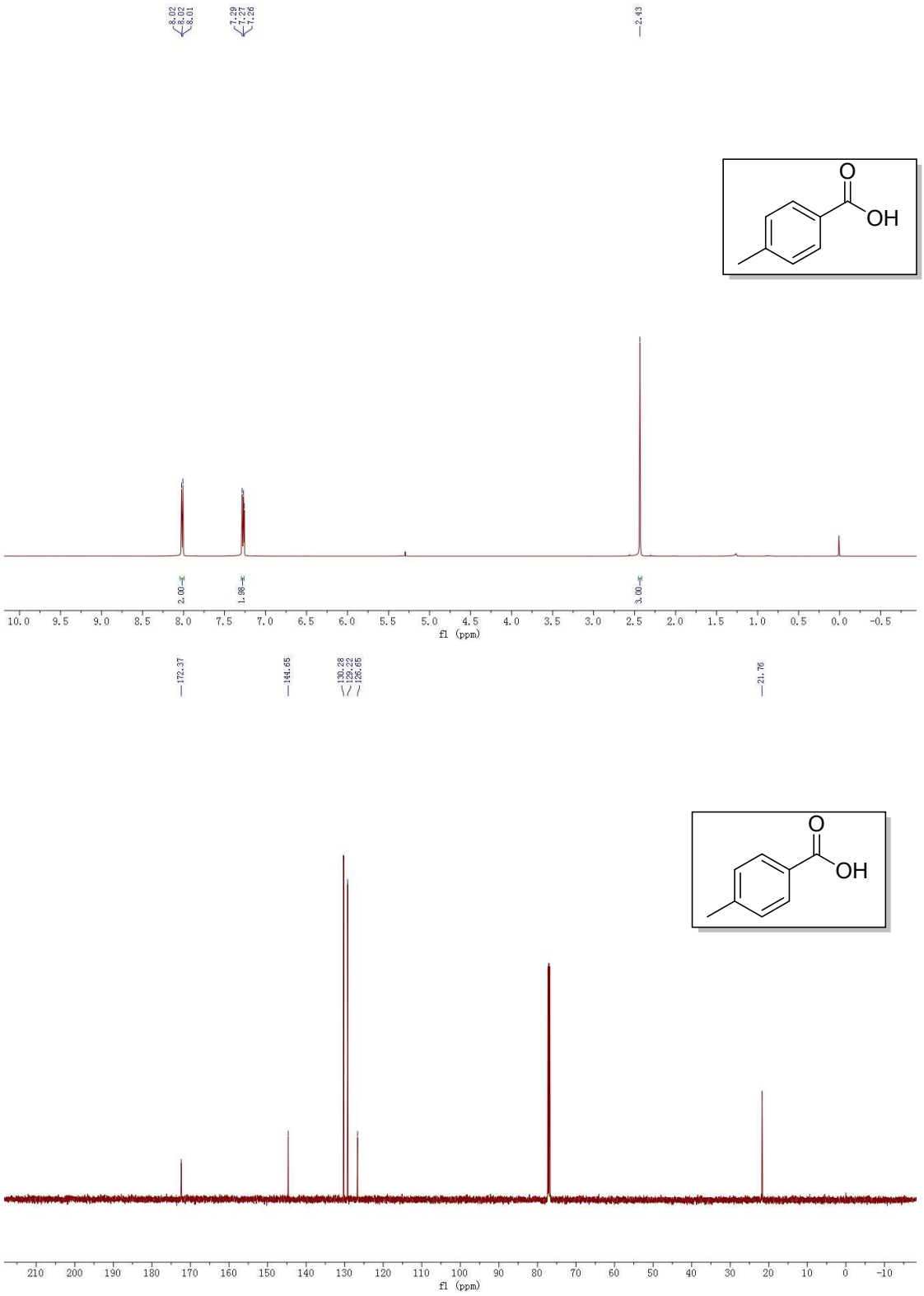


4 4-(*tert*-butyl)benzonitrile

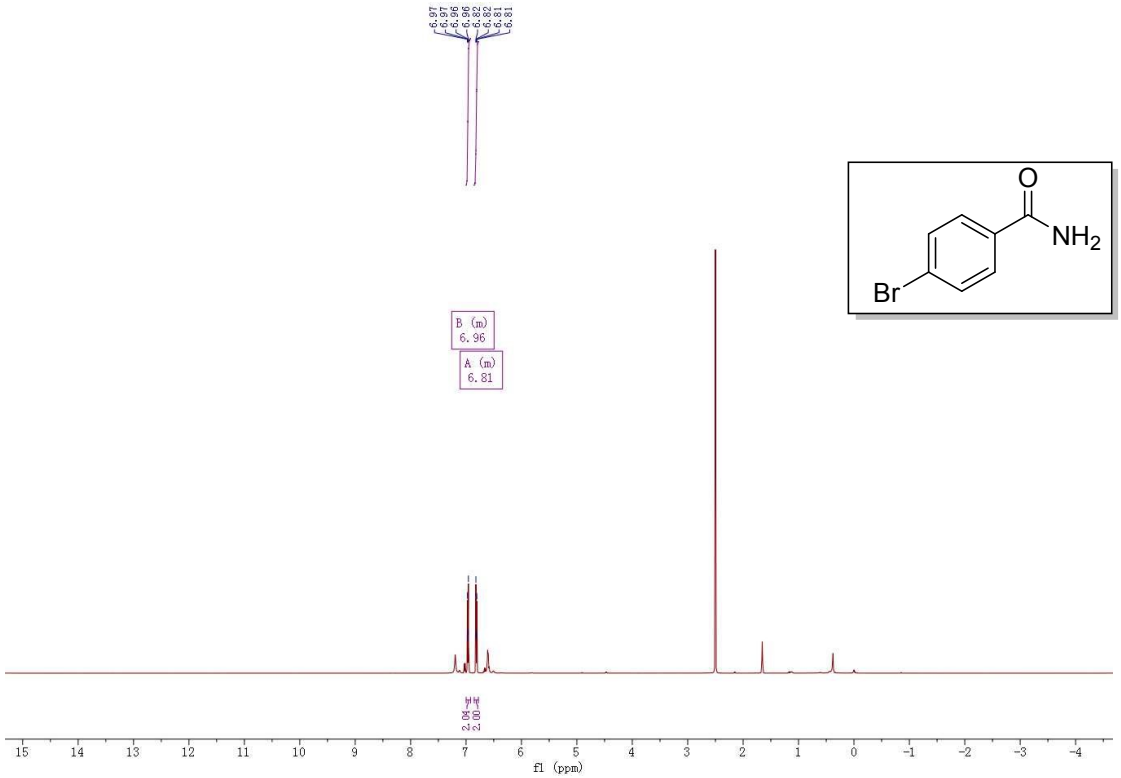


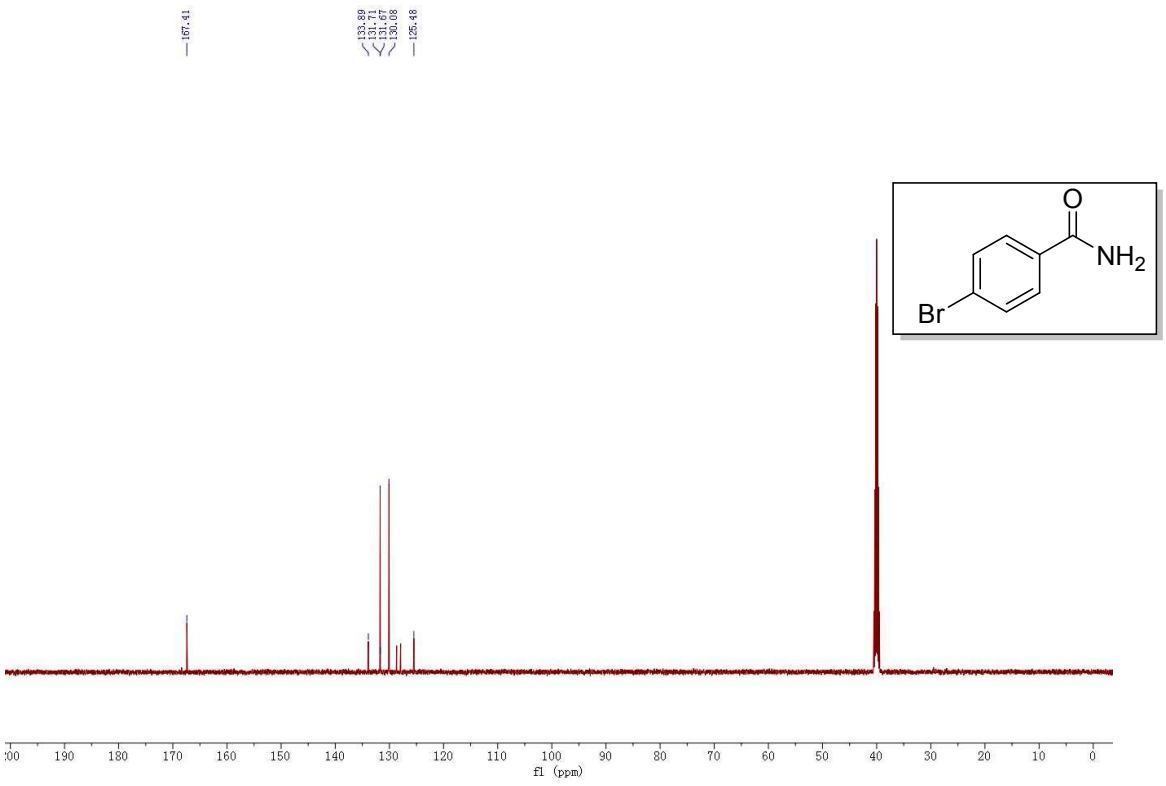


5 4-methylbenzoic acid

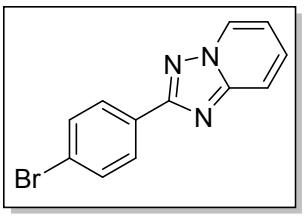


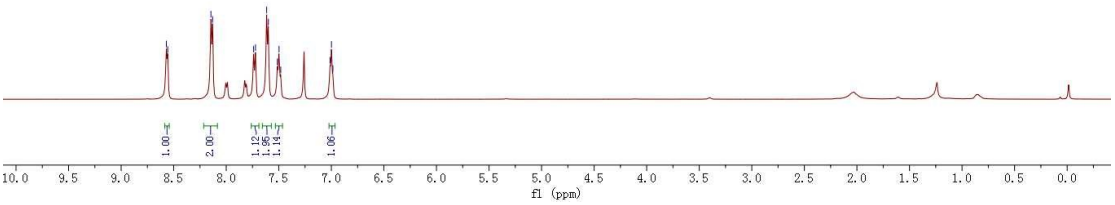
6 4-bromobenzamide

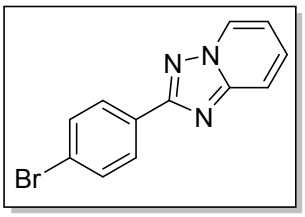


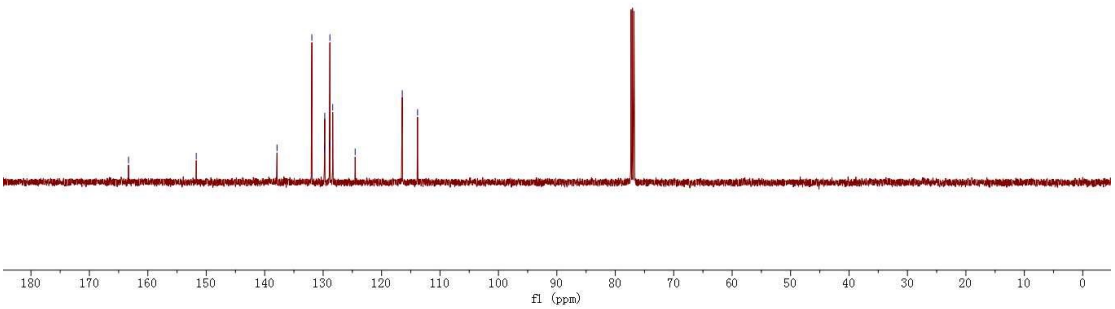


9 2-(4-bromophenyl)-[1,2,4]triazolo[1,5-*a*]pyridine

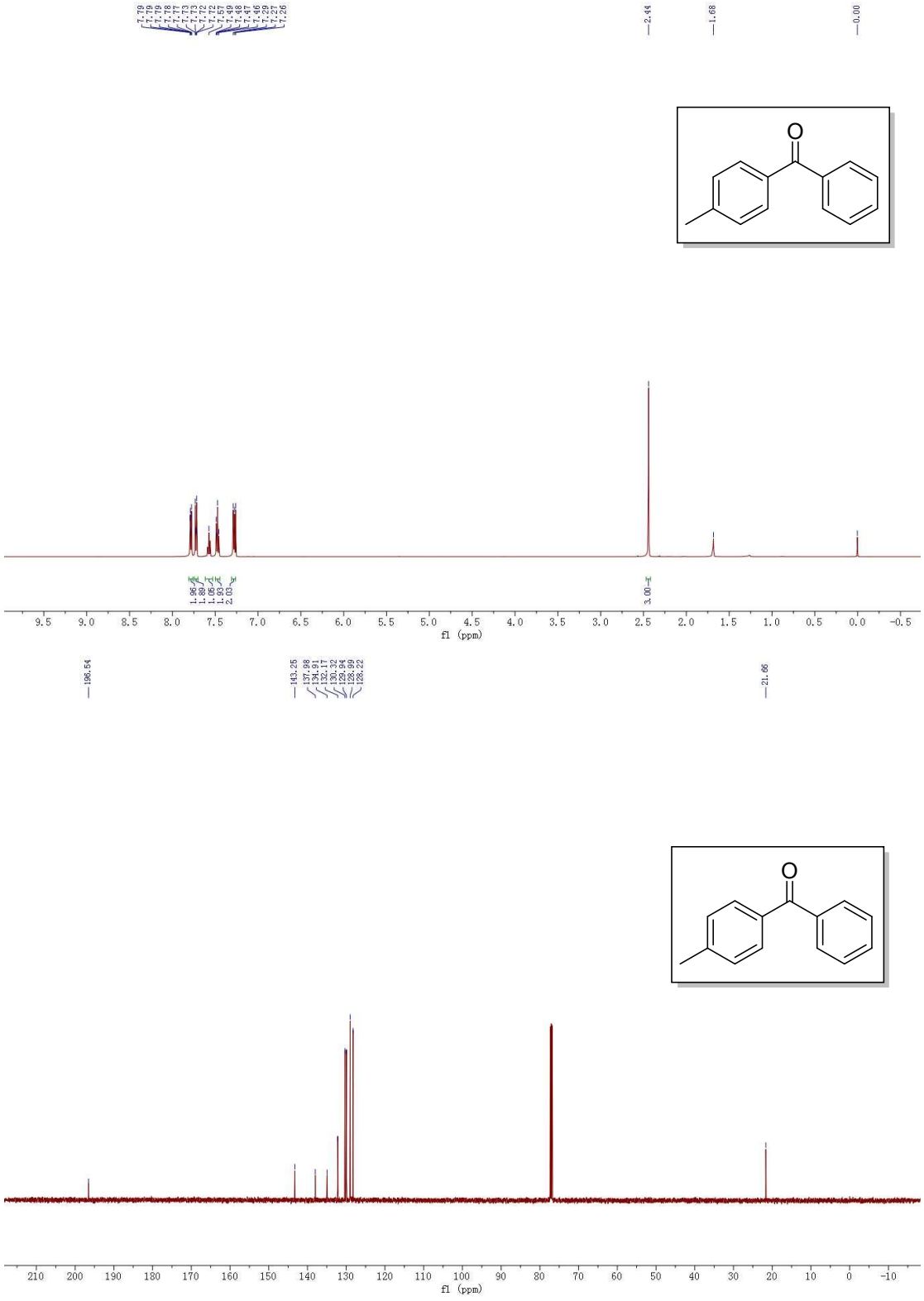








10 phenyl(*p*-tolyl)methanone



11 methyl 4-nitrobenzoate