Clean Preparation of Multisubstituted Pyrroles under Metal and Solvent-free Conditions

Qing-Wen Gui[a], Xiaoli He[a], Wenjing Wang[a], Huilin Zhou[a], Yumei Dong[a], Nengqing Wang[a], Jia-Xi Tang[c], Zhong Cao[b] and Wei-Min He*[b]

[a]College of Science, Hunan Agricultural University, Changsha 410128, People's Republic of China

[b]Hunan Provincial Key Laboratory of Materials Protection for Electric Power and Transportation, Changsha University of Science and Technology, Changsha, 410114, China

[c]School of Chemistry and Chemical Engineering, Hunan University of Science and Technology, Xiangtan 411201, China

E-mail: weiminhe2016@yeah.net

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1. General Information

All reactions were carried out in anhydrous solvent and commercially available reagents were used as received unless otherwise stated. Analytical thin layer chromatography (TLC) was performed on precoated aluminum-backed silica gel 60 F254 plates (EMD Millipore, 200 μm thickness). TLC plates were visualized with ultraviolet light and treatment with KMnO4 or vanillin stains followed by heating. Flash column chromatography was performed using Tsingdao silica gel (200-300). Melting points (uncorrected) were obtained from a Büchi M-560 melting point instrument. ^{1}H and ^{13}CNMR spectra were recorded on a Bruker Avance DRX-500 or 400 spectrometers; chemical shifts (δ) are given in ppm and calibrated using the signal of residual undeuterated solvent as internal reference ($CHCl_3$: δH = 7.26 ppm and δC = 77.16 ppm). Data for 1H NMR and 13C NMR are reported as follows: chemical shift (δ, ppm), multiplicity, integration, and coupling constant (Hz). IR spectra were recorded on an Agilent Cary 630 FTIR spectrometer; wavenumbers (ν) are given in cm^{-1}.

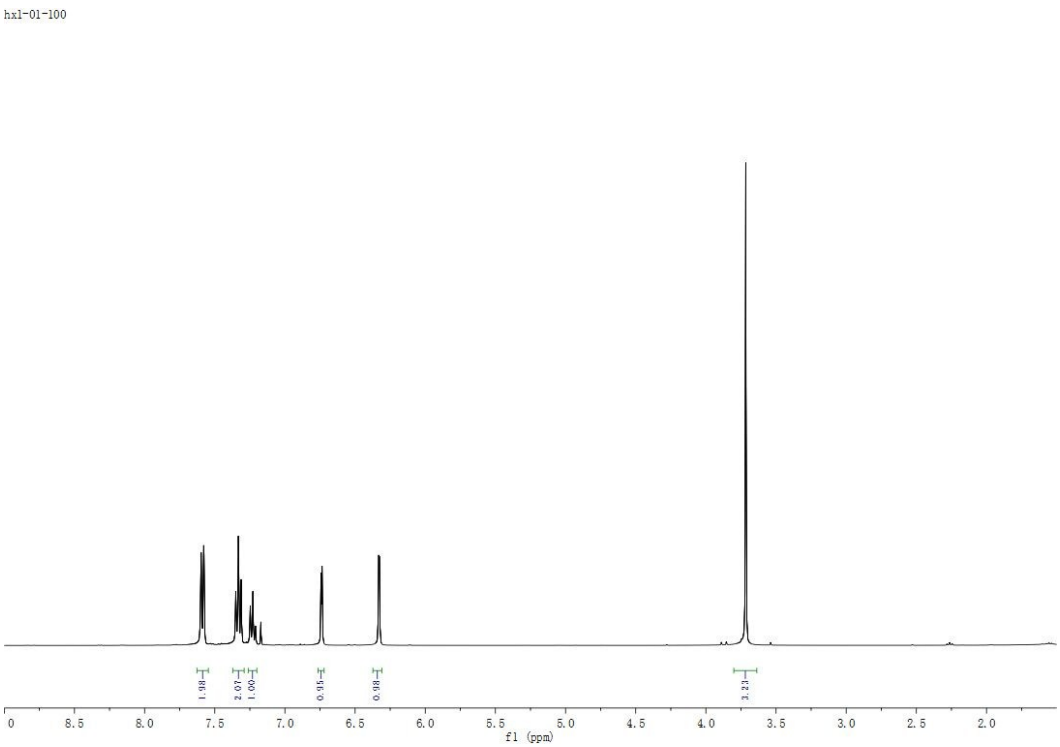
2. Experimental Section

2.1 General procedures for 0.3 mmol scale synthesis of **4aa-4ae.**

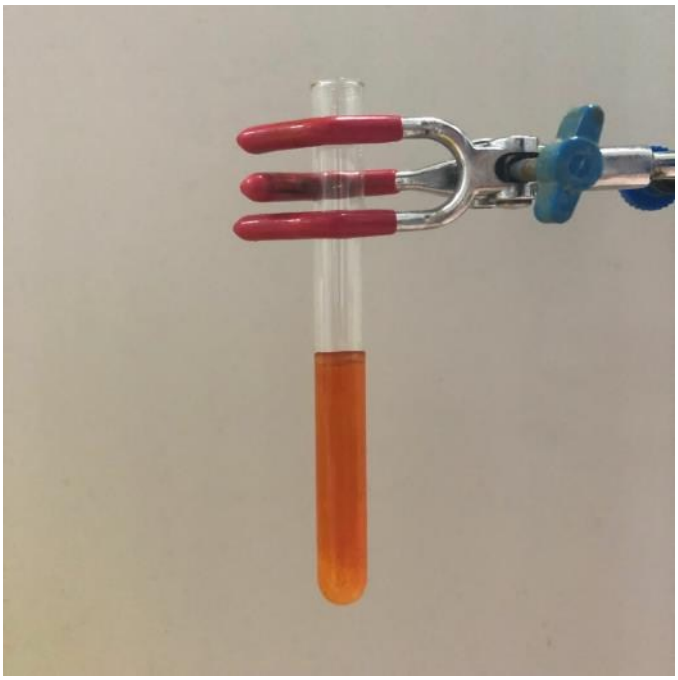
Iodine (0.06 mmol), alkyne (0.3 mmol), TMSCN (0.3 mmol) and DMF (0.3 mmol) were added to a 10 mL Schlenk tube. The mixture was stirred at 80 °C, and the progress of the reaction was monitored by TLC. Upon the completion of the reaction, the mixture was purified by column chromatography directly, and afforded the desired products.

2.2 General procedures for 7 mmol and 30 mmol scale synthesis of **4aa-4ha.**

Iodine (6 mmol), alkyne (30 mmol), TMSCN (30 mmol) and DMF (30 mmol) were added to a 150 mL flask. The mixture was stirred at 80 °C, and the progress of the reaction was monitored by TLC. Upon the completion of the reaction, the mixture was quenched by addition of 30 mL of water. The aqueous layer was extracted three times with EtOAc (30 mL × 3), and the combined organic layers were dried over sodium sulfate, evaporated to dryness, and to afford desired products.

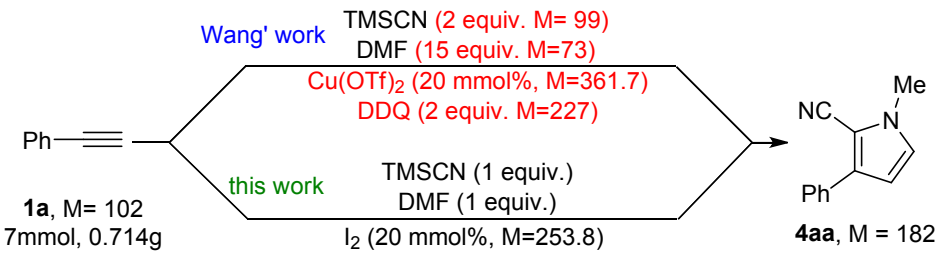


Fiure S1 NMR spectra of the extraction product **4aa**



Fiure S2 photo of the extraction product **4aa**

3. Calculation of green chemistry metrics



Entry	TMSCN	DMF	Catalyst	Oxidant	Extraction	Chromatography	4aa 182
Ref. 1	14 mmol 1.38 g	105 mmol 7.673 g	0.14 mmol 0.05 g	14 mmol 3.178 g	60 mL 54 g	SiO_2 100 g Eluent 4L, 3200 g	76% 0.96 g
This work	7 mmol 0.694 g	7 mmol 0.511 g	0.14 mmol 0.035 g	-	45 mL 40.5 g	-	84% 1.07 g

$$\text{Mol.E\%} = \frac{\text{moles product}}{\text{moles starting material + catalysts + additives + solvents}} \times 100\%$$

$$= \frac{5.32}{(7+14+105)+0.14+14} \times 100\% = 3.7\%$$

$$= \frac{5.88}{(7+7+7)+0.14} \times 100\% = \mathbf{27.8\%}$$

$$\text{PMI} = \frac{\text{total mass (kg) used in the process}}{\text{mass of product (kg)}}$$

$$= \frac{0.714+1.38g+7.673g+0.05g+3.178g+54g+3200g}{0.96g} = 3403$$

$$= \frac{0.714+0.694+0.511+0.035+40.5}{1.07g} = \mathbf{39.7}$$

$$\text{AE} = \frac{\text{molecular mass of desired product}}{\text{molecular mass of all reactants}} \times 100\%$$

$$= \frac{182}{102+99X2+73X15+361.7X0.2+227X2} \times 100\% = 9.3\%$$

$$= \frac{182}{102+99+73+50.7} \times 100\% = \mathbf{56.2\%}$$

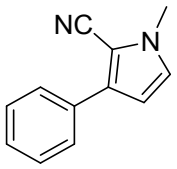
Previous' work

Parameter	Detail of parameters	Penalty points
1. Yield	76%	12
2. Cost of reactants to obtain	10 mmol of product	
	Phenylacetylene	0
	TMSCN	3
	DMF	0
	DDQ	3
	$Cu(OTf)_2$	0
3. Safety	TMSCN	5 (T)
	DDQ	15 (N,T, F)
	$Cu(OTf)_2$	5 (N)
4. Technical setup	Instruments for controlled addition of chemicals	1
	Gas atmosphere	1
5. Temperature/time	Heating > 1 h (14h)	3
6. Workup and purification	Liquid-liquid extraction	3
	Filtration	1
	Classical chromatography	10
Eco-scale score		**38**

This' work

Parameter	Detail of parameters	Penalty points
1. Yield	84%	8
2. Cost of reactants to obtain	10 mmol of product	
	Phenylacetylene	0
	TMSCN	0
	DMF	0
	I_2	0
3. Safety	TMSCN	5 (T)
4. Technical setup	Common setup	0
5. Temperature/time	Heating > 1 h (2h)	3
6. Workup and purification	Liquid-liquid extraction	3
Eco-scale score		**81**

4. Characterization data of products

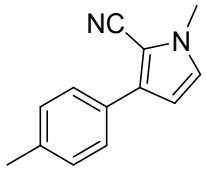


4aa

1-methyl-3-phenyl-1H-pyrrole-2-carbonitrile **(4aa)**[1]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 – 7.65 (m, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 6.83 (d, *J* = 2.6 Hz, 1H), 6.41 (d, *J* = 2.7 Hz, 1H), 3.81 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 135.44, 132.97, 128.79, 127.96, 127.77, 126.66, 114.66, 108.34, 101.43, 35.65.

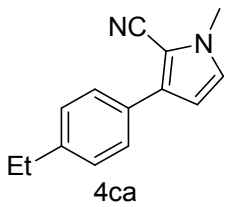


4ba

1-methyl-3-(p-tolyl)-1H-pyrrole-2-carbonitrile (**4ba**)[1]

[1]**H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 6.82 (d, *J* = 2.4 Hz, 1H), 6.39 (d, *J* = 2.5 Hz, 1H), 3.80 (s, 3H), 2.37 (s, 3H).

[13]**C NMR** (126 MHz, $CDCl_3$) δ 137.65, 135.56, 130.13, 129.69, 127.89, 126.56, 114.78, 108.18, 101.25, 35.61, 21.35.



4ca

4-(4-ethylphenyl)-1-methyl-1H-pyrrole-2-carbonitrile (**4ca**)

Tawny oil;

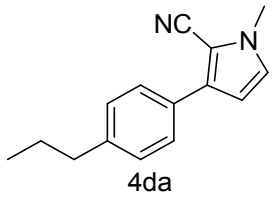
[1]**H NMR** (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.8 Hz, 2H), 7.59 (d, *J* = 7.7 Hz, 2H), 6.81 (d, *J* = 2.4 Hz, 1H), 6.39 (d, *J* = 2.4 Hz, 1H), 3.79 (s, 3H), 2.72-2.66 (m, 2H), 1.26 (t, *J* = 8.0 Hz, 3H).

[13]**C NMR** (101 MHz, $CDCl_3$) δ 144.00, 135.59, 130.37, 128.68, 128.50, 128.20, 127.89, 126.64,

114.80, 108.21, 101.24, 35.61, 28.74, 15.66.

IR (neat, cm $^{-1}$) *v* 2964, 2210, 1681, 1507, 1418, 1353, 1258, 835, 757, 489;

HRMS (ESI) calcd for $C_{14}H_{15}N_2$ [M+H] $^+$: 211.1230, found 211.1234.



4da

1-methyl-3-(4-propylphenyl)-1H-pyrrole-2-carbonitrile (**4da**)

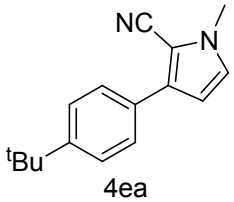
Rueest solid; MP: 59-61 °C;

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.9 Hz, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 6.81 (d, *J* = 2.4 Hz, 1H), 6.39 (d, *J* = 2.3 Hz, 1H), 3.80 (s, 3H), 2.64-2.57 (m, 2H), 1.69- 1.61 (m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 142.46, 135.61, 130.37, 129.10, 127.90, 126.53, 114.83, 108.20, 101.23, 37.91, 35.62, 24.63, 13.99.

IR (neat, cm $^{-1}$) *v* 2929, 2210, 1709, 1507, 1418, 1354, 1258, 1221, 1090, 804, 757, 529, 490;

HRMS (ESI) calcd for $C_{15}H_{17}N_2$ [M+H] $^+$: 225.1386, found 225.1390.



4ea

3-(4-(tert-butyl)phenyl)-1-methyl-1H-pyrrole-2-carbonitrile (**4ea**)

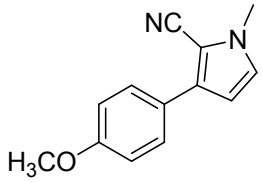
Pale yellow solid; MP: 123-125 °C;

^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 6.81 (d, *J* = 2.7 Hz, 1H), 6.39 (d, *J* = 2.7 Hz, 1H), 3.80 (s, 3H), 1.34 (s, 9H).

^{13}**C NMR** (126 MHz, $CDCl_3$) δ 137.35, 133.89, 130.29, 129.05, 128.21, 126.34, 114.25, 108.62, 101.96, 52.24, 35.73.

IR (neat, cm $^{-1}$) *v* 2960, 2209, 1506, 1417, 1353, 1256, 1019, 936, 761, 738, 554, 493.

HRMS (ESI) calcd for $C_{16}H_{19}N_2$ [M+H] $^+$: 239.1543, found 239.1545.



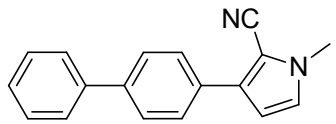
4fa

3-(4-methoxyphenyl)-1-methyl-1H-pyrrole-2-carbonitrile (**4fa**)[1]

Pale yellow solid, MP: 116-118 °C

^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 2.6 Hz, 1H), 6.35 (d, *J* = 2.7 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H).

^{13}**C NMR** (126 MHz, $CDCl_3$) δ 159.30, 135.39, 127.91, 127.88, 125.63, 114.93, 114.39, 107.95, 100.90, 55.46, 35.61.



4ga

3-([1,1'-biphenyl]-4-yl)-1-methyl-1H-pyrrole-2-carbonitrile (**4ga**)

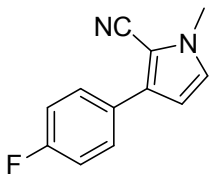
Yellow-white solid; MP: 158-160 °C;

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.78-7.72 (m, 2H), 7.67-7.61 (m, 4H), 7.47-7.43 (m， 2H), 7.40-7.31 (m, 1H), 6.84 (d, *J* = 2.7 Hz, 1H), 6.45 (d, *J* = 2.7 Hz, 1H), 3.82 (s, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 140.71, 140.53, 135.00, 131.95, 128.95, 128.05, 127.68, 127.53, 127.12, 127.01, 114.71, 108.33, 101.48, 35.68.

IR (neat, cm^{-1}) *v* 2202, 1496, 1256, 754, 479;

HRMS (ESI) calcd for $C_{18}H_{15}N_2$ $[M+H]^+$: 259.1230, found 259.1234.

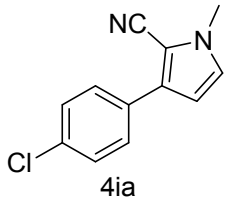


4ha

3-(4-fluorophenyl)-1-methyl-1H-pyrrole-2-carbonitrile (**4ha**)[1]

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 8.0, 4.0 Hz, 2H), 7.03 (t, *J* = 8.7 Hz, 2H), 6.76 (d, *J* = 2.7 Hz, 1H), 6.29 (d, *J* = 2.7 Hz, 1H), 3.74 (s, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 163.43 (d, *J* = 196 Hz), 134.30, 129.20 (d, *J* = 3Hz), 128.42 (d, *J* = 7 Hz), 128.02, 116.04 (d, *J* = 15 Hz), 114.53, 108.31, 101.41, 35.68.



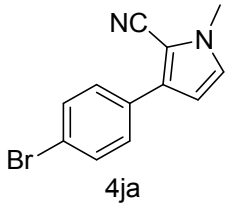
4ia

3-(4-chlorophenyl)-1-methyl-1H-pyrrole-2-carbonitrile (**4ia**)[1]

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 2.4 Hz, 1H), 6.43 (d, *J* = 2.4 Hz, 1H), 3.85 (s, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 134.15, 133.54, 131.47, 129.16, 128.08, 127.88, 114.39, 108.31, 101.53, 35.71.

IR (neat, cm^{-1}) ν 3130, 2924, 2208, 1502, 1422, 1258, 1090, 836, 755, 630, 607.



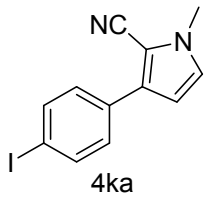
4ja

3-(4-bromophenyl)-1-methyl-1H-pyrrole-2-carbonitrile (**4ja**)[1]

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.55-7.53 (m, 4H), 6.83 (d, *J* = 2.4 Hz, 1H), 6.39 (d, *J* = 2.4 Hz, 1H), 3.81 (s, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 134.17, 132.13, 131.93, 128.20, 128.11, 121.70, 114.37, 108.29, 101.55, 35.73.

IR (neat, cm^{-1}) *v* 3119, 2923, 2203, 1501, 1420, 1353, 1257, 1072, 825, 761.



4ka

3-(4-iodophenyl)-1-methyl-1H-pyrrole-2-carbonitrile (**4ka**)

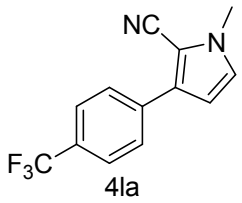
Yellow solid; MP: 76-78 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 6.84 (d, *J* = 2.4 Hz, 1H), 6.39 (d, *J* = 2.4 Hz, 1H), 3.82 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 138.11, 134.24, 132.51, 128.40, 128.11, 114.35, 108.26, 100.13, 35.75.

IR (neat, cm^{-1}) *v* 2924, 2209, 1679, 1499, 1413, 1355, 1253, 1221, 1061, 1005, 823, 758, 530, 481.

HRMS (ESI) calcd for $C_{12}H_{10}IN_2$ $[M+H]^+$: 308.9883, found 308.9886.

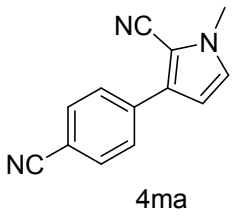


4la

1-methyl-3-(4-(trifluoromethyl)phenyl)-1H-pyrrole-2-carbonitrile (**4la**)[1]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 8.5 Hz, 2H), 6.90 (d, *J* = 2.7 Hz, 1H), 6.48 (d, *J* = 2.7 Hz, 1H), 3.86 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 136.50, 133.70, 129.46 (d, *J* = 26 Hz), 128.23, 126.83, 126.01, 125.98 (d, *J* = 216 Hz), 114.16, 108.67, 102.08, 35.80.



4ma

4-(4-cyanophenyl)-1-methyl-1H-pyrrole-2-carbonitrile (**4ma**)

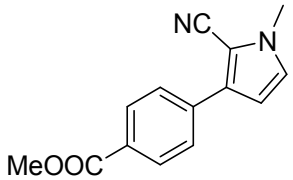
Yellow-white solid; MP: 172-174 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.1 Hz, 2H), 7.69 (d, *J* = 8.1 Hz, 2H), 6.89 (d, *J* = 2.7 Hz, 1H), 6.47 (d, *J* = 2.7 Hz, 1H), 3.85 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 137.46, 133.02, 132.86, 128.42, 127.02, 118.96, 113.95, 111.05, 108.72, 102.31, 35.88.

IR (neat, cm^{-1}) *v* 2210, 1709, 1357, 1220, 1092, 765, 529.

HRMS (ESI) calcd for $C_{13}H_{10}N_3$ $[M+H]^+$: 208.0869. found 208.0870.



4na

methyl 4-(2-cyano-1-methyl-1H-pyrrol-3-yl)benzoate (**4na**)

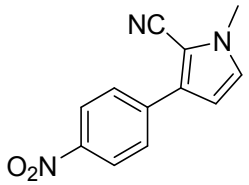
Yellow-white solid; MP: 118-120 °C;

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.9 Hz, 2H), 7.74 (d, *J* = 7.9 Hz, 2H), 6.87 (d, *J* = 2.0 Hz, 1H), 6.47 (d, *J* = 2.0 Hz, 1H), 3.93 (s, 3H), 3.83 (s, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 166.88, 137.35, 133.89, 130.29, 129.06, 128.21, 126.34, 114.24, 108.62, 101.97, 52.24, 35.73.

IR (neat, cm^{-1}) *v* 2205, 1711, 1610, 1435, 1353, 1278, 1257, 1187, 1105, 1017, 947, 853, 755, 704, 479.

HRMS (ESI) calcd for $C_{14}H_{13}N_2O_2$ $[M+H]^+$: 241.0972, found 241.0973.



4oa

1-methyl-3-(4-nitrophenyl)-1H-pyrrole-2-carbonitrile (**4oa**)

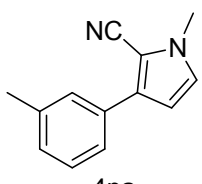
Pale yellow solid; MP: 146-148 °C;

1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.9 Hz, 2H), 7.81 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 2.8 Hz, 1H), 6.50 (d, *J* = 2.8 Hz, 1H), 3.86 (s, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 146.79, 139.38, 132.36, 128.55, 126.94, 124.30, 113.84, 108.85, 102.44, 35.84.

IR (neat, cm^{-1}) *v* 2923, 2210, 1709, 1599, 1514, 1341, 1258, 1220, 1082, 850, 768, 749, 529, 472.

HRMS (ESI) calcd for $C_{12}H_{10}N_3O_2$ $[M+H]^+$: 228.0768, found 228.0770.

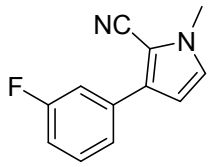


4pa

1-methyl-3-(m-tolyl)-1H-pyrrole-2-carbonitrile (**4pa**)[1]

[1]**H NMR** (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 5.6 Hz, 2H), 7.30 (t, *J* = 7.9 Hz, 1H), 7.13 (d, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 2.0 Hz, 1H), 6.40 (d, *J* = 2.2 Hz, 1H), 3.81 (s, 3H), 2.40 (s, 3H).

[13]**C NMR** (101 MHz, $CDCl_3$) δ 138.51, 135.44, 132.85, 128.82, 128.48, 127.88, 127.28, 123.71, 114.62, 108.27, 101.28, 35.51, 21.54.

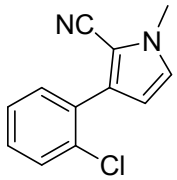


4qa

3-(3-fluorophenyl)-1-methyl-1H-pyrrole-2-carbonitrile (**4qa**)[1]

[1]**H NMR** (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.8 Hz, 1H), 7.43-7.30 (m, 2H), 7.00 (td, *J* = 8.4, 2.0 Hz, 1H), 6.84 (d, *J* = 2.5 Hz, 1H), 6.40 (d, *J* = 2.5 Hz, 1H), 3.81 (s, 3H).

[13]**C NMR** (101 MHz, $CDCl_3$) δ 164.17 (d, *J* = 195 Hz), 135.14 (d, *J* = 7 Hz), 134.01, 130.56(d, *J* = 6 Hz), 128.07, 122.28 (d, *J* = 2 Hz), 114.64, 114.47 (d, *J* = 20 Hz), 113.61 (d, *J* = 18 Hz), 108.47, 101.70, 35.70.



4ra

4-(2-chlorophenyl)-1-methyl-1H-pyrrole-2-carbonitrile (**4ra**)

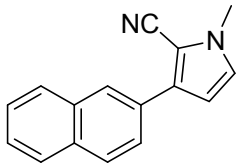
Pale yellow solid; MP: 107-108 °C;

[1]**H NMR** (500 MHz, $CDCl_3$) δ 7.52-7.43 (m, 2H), 7.31 (dd, *J* = 16.0, 8.3 Hz, 2H), 6.86 (d, *J* = 2.5 Hz, 1H), 6.45 (d, *J* = 2.5 Hz, 1H), 3.84 (s, 3H).

[13]**C NMR** (126 MHz, $CDCl_3$) δ 133.01, 132.87, 132.08, 131.39, 130.35, 129.23, 127.12, 127.03, 113.74, 111.46, 103.86, 35.77.

IR (neat, cm^{-1}) *v* 3130, 2927, 2211, 1501, 1354, 1264, 1250, 1090, 1028, 832, 739.

HRMS (ESI) calcd for $C_{12}H_{10}ClN_2$ $[M+H]^+$: 217.0527, found 217.0528.

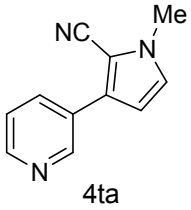


4sa

1-methyl-4-(naphthalen-2-yl)-1H-pyrrole-2-carbonitrile (**4sa**)[1]

[1]**H NMR** (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.88 (d, *J* = 8.2 Hz, 2H), 7.81 (dd, *J* = 15.5, 8.1 Hz, 2H), 7.48 (t, *J* = 8.1 Hz, 2H), 6.85 (s, 1H), 6.52 (s, 1H), 3.81 (s, 3H).

[13]**C NMR** (101 MHz, $CDCl_3$) δ 135.32, 133.68, 132.86, 130.37, 128.66, 128.28, 128.08, 127.78, 126.50, 126.20, 125.29, 124.90, 114.74, 108.59, 101.70, 35.67.



4ta

1-methyl-3-(pyridin-3-yl)-1H-pyrrole-2-carbonitrile (**4ta**)

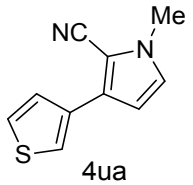
White solid; MP: 84-89 °C;

[1]**H NMR** (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.49 (s, 1H), 7.97-7.91 (m, 1H), 7.28 (dd, *J* = 7.8, 4.9 Hz, 1H), 6.82 (d, *J* = 2.7 Hz, 1H), 6.39 (d, *J* = 2.7 Hz, 1H), 3.77 (s, 3H).

[13]**C NMR** (101 MHz, $CDCl_3$) δ 148.71, 147.87, 133.74, 131.71, 128.34, 123.86, 114.01, 111.91, 108.37, 102.02, 35.81.

IR (neat, cm^{-1}) *v* 3127, 2920, 1625, 1520, 1414, 787.

HRMS (ESI) calcd for $C_{11}H_{10}N_3$ $[M+H]^+$: 184.0869, found 184.0872.

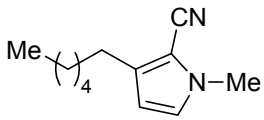


4ua

1-methyl-3-(thiophen-3-yl)-1H-pyrrole-2-carbonitrile (**4ua**)[1]

[1]**H NMR** (400 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 2.8, 1.3 Hz, 1H), 7.36 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.29 (dd, *J* = 5.0, 2.9 Hz, 1H), 6.71 (d, *J* = 2.6 Hz, 1H), 6.29 (d, *J* = 2.7 Hz, 1H), 3.71 (s, 3H).

[13]**C NMR** (101 MHz, $CDCl_3$) δ 133.78, 130.61, 127.87, 126.21, 126.18, 120.85, 114.72, 108.11, 101.14, 35.58.



4va

1-methyl-3-propyl-1H-pyrrole-2-carbonitrile (**4va**)

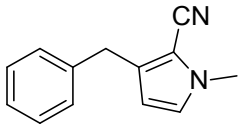
Yellowish green oil;

^{1}**H NMR** (500 MHz, $CDCl_3$) δ 6.68 (d, *J* = 2.5 Hz, 1H), 5.99 (d, *J* = 2.5 Hz, 1H), 3.71 (s, 3H), 2.56 (t, *J* = 7.7 Hz, 2H), 1.59-1.50 (m, 4H), 1.31-1.30 (m, 2H), 1.30-1.29 (m, 2H), 0.89 (t, *J* = 6.7 Hz, 3H).

^{13}**C NMR** (126 MHz, $CDCl_3$) δ 137.61, 127.19, 114.09, 109.26, 103.05, 35.37, 31.73, 30.65, 29.01, 26.85, 22.74, 14.23.

IR (neat, cm^{-1}) *v* 2970, 2260, 1555, 1320, 1041, 886, 761, 738.

HRMS (ESI) calcd for $C_9H_{19}N_2$ $[M+H]^+$: 191.1543, found 191.1546.

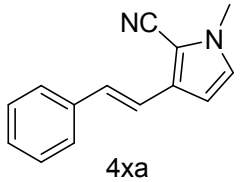


4wa

3-benzyl-1-methyl-1H-pyrrole-2-carbonitrile (**4wa**)[1]

^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.5 Hz, 2H), 7.25-7.19 (m, 3H), 6.69 (d, *J* = 2.4 Hz, 1H), 5.96 (d, *J* = 2.4 Hz, 1H), 3.91 (s, 2H), 3.73 (s, 3H).

^{13}**C NMR (**126 MHz, $CDCl_3$) δ 140.23, 135.72, 128.67, 128.64, 127.49, 126.41, 113.81, 109.81, 103.30, 35.46, 33.16.



4xa

(*E*)-1-methyl-3-styryl-1H-pyrrole-2-carbonitrile (**4xa**)

Orange solid; MP: 55-57 °C;

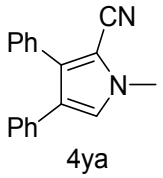
^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 12.0 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 3H), 7.04 (d, *J* = 4.0 Hz, 2H), 6.77 (d, *J* = 2.5 Hz, 1H), 6.41 (d, *J* = 2.6 Hz, 1H), 3.76 (s, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 137.08, 133.68, 129.68, 128.83, 128.21, 127.90, 126.56, 118.97,

113.69, 106.47, 100.12, 35.54.

IR (neat, cm $^{-1}$) *v* 2924, 2359, 2208, 1725, 1492, 1451, 1359, 1250, 1179, 966, 755, 696.

HRMS (ESI) calcd for $C_{14}H_{13}N_2$ [M+H] $^+$: 209.1073, found 209.1076.

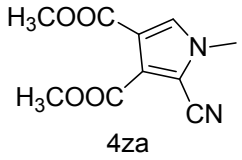


4ya

1-methyl-3,4-diphenyl-1H-pyrrole-2-carbonitrile (**4ya**)[1]

[1]**H NMR** (500 MHz, $CDCl_3$) δ 7.36-7.27 (m, 5H), 7.26-7.23 (m, 3H), 7.17-7.13 (m, 2H), 6.93 (s, 1H), 3.85 (s, 3H).

[13]**C NMR** (126 MHz, $CDCl_3$) δ 133.67, 133.37, 132.37, 129.32, 128.66, 128.55, 128.53, 127.73, 126.76, 126.40, 124.47, 114.14, 104.19, 35.72.



4za

dimethyl 2-cyano-1-methyl-1H-pyrrole-3,4-dicarboxylate (**4za**)

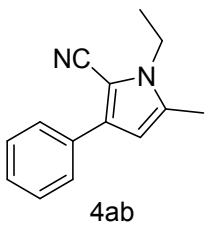
Dark yellow solid; MP: 56-58 °C;

[1]**H NMR** (400 MHz, $CDCl_3$) δ 7.37 (s, 1H), 3.92 (s, 3H), 3.85 (s, 3H), 3.83 (s, 3H).

[13]**C NMR** (101 MHz, $CDCl_3$) δ 162.27, 161.67, 131.78, 124.74, 116.67, 111.02, 109.17, 52.49, 52.04, 36.28.

IR (neat, cm $^{-1}$) *v* 2962, 1707, 1360, 1260, 1221, 1019, 798, 529.

HRMS (ESI) calcd for $C_{10}H_{11}N_2O_4$ [M+H] $^+$: 223.0713, found 223.0716.

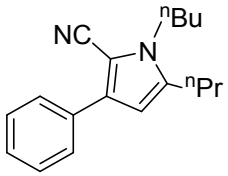


4ab

1-ethyl-5-methyl-3-phenyl-1H-pyrrole-2-carbonitrile (**4ab**)[1]

[1]**H NMR** (400 MHz, $CDCl_3$) δ 7.68-7.63 (m, 2H), 7.39 (dd, *J* = 15.9, 8.1 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 6.18 (s, 1H), 4.06 (q, *J* = 7.3 Hz, 2H), 2.30 (s, 3H), 1.41 (t, *J* = 7.3 Hz, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 135.07, 134.63, 133.17, 128.94, 128.62, 128.56, 127.59, 126.64, 115.37, 107.81, 99.15, 40.97, 16.31, 12.39.



4ac

butyl-3-phenyl-5-propyl-1H-pyrrole-2-carbonitrile (**4ac**)

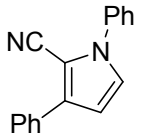
Yellow oil;

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 8.1, 0.9 Hz, 2H), 7.39 (dd, *J* = 10.5, 4.8 Hz, 2H), 7.33-7.24 (m, 1H), 6.19 (s, 1H), 3.99 (t, 7.6 Hz, 2H), 2.54 (t, *J* = 7.6 Hz, 2H), 1.80-1.66 (m, 4H), 1.45-1.36 (m, 2H), 1.03 (t, *J* = 7.3 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 134.49, 133.25, 128.92, 128.55, 127.54, 126.64, 115.60, 106.52, 99.55, 45.83, 33.37, 28.56, 21.88, 20.09, 14.12, 13.87.

IR (neat, cm $^{-1}$) *v* 2960, 2204, 1508, 1471, 1360, 1261, 1020, 798, 763, 695, 598.

HRMS (ESI) calcd for $C_{18}H_{23}N_2$ $[M+H]^+$: 267.1856, found 267.1860.



4ad

1,3-diphenyl-1H-pyrrole-2-carbonitrile (**4ad**)

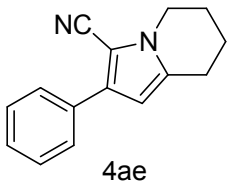
Yellow oil;

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.68(d, *J* = 8.0 Hz, 2H), 7.47-7.44 (m, 5H), 7.38 (t, *J* = 8.0 Hz, 2H), 7.28 (t, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 2.5 Hz, 1H); 6.54 (d, *J* = 2.5 Hz, 1H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 137.43, 132.89, 130.02, 129.84, 129.07, 128.59, 128.13, 127.50, 124.48, 123.00, 114.73, 109.94, 100.95.

IR (neat, cm $^{-1}$) *v* 2920, 2150, 1600, 1496, 1320, 1311, 1120, 858, 788, 655.

HRMS (ESI) calcd for $C_{17}H_{13}N_2$ $[M+H]^+$: 245.1073, found 245.1076.



4ae

2-phenyl-5,6,7,8-tetrahydroindolizine (**4ae**)

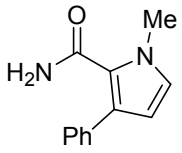
Yellowish-brown oil;

^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.72-7.61 (m, 2H), 7.39 (t, *J* = 7.7 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 6.13 (s, 1H), 4.04 (t, *J* = 6.1 Hz, 2H), 2.79 (t, *J* = 6.4 Hz, 2H), 2.10 – 1.96 (m, 2H), 1.95 – 1.76 (m, 2H).

^{13}**C NMR** (126 MHz, $CDCl_3$) δ 136.38, 134.88, 133.22, 128.91, 127.58, 126.63, 115.22, 105.47, 98.59, 44.63, 23.56, 22.98, 20.41.

IR (neat, cm $^{-1}$) *v* 2948, 2201, 1709, 1509, 1425, 1358, 1220, 760, 694, 529, 481;

HRMS (ESI) calcd for $C_{15}H_{15}N_2$ $[M+H]^+$: 223.1230, found 223.1234.



5aa

1-methyl-3-phenyl-1H-pyrrole-2-carboxamide (**5aa**)

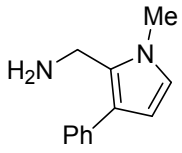
White solid; MP: 148-149 °C;

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.42 (t, *J* = 6.3 Hz, 4H), 7.39-7.33 (m, 1H), 6.75 (d, *J* = 2.4 Hz, 1H), 6.11 (d, *J* = 2.4 Hz, 1H), 5.34 (s, 2H), 3.96 (s, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 163.83, 136.35, 129.84, 129.70, 128.87, 127.59, 127.32, 121.38, 109.69, 37.63.

IR (neat, cm $^{-1}$) *v* 3390, 3192, 1634, 1610, 1503, 1441, 1342, 1091, 833.

MS (ESI) calcd for $C_{12}H_{13}N_2O$ $[M+H]^+$: 201.1022, found 201.1025.



5ab

(1-methyl-3-phenyl-1H-pyrrol-2-yl)methanamine (**5ab**)

Colorless oil;

^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.34-7.26 (m, 4H), 7.18-7.14 (m, 1H), 6.55 (d, *J* = 2.7 Hz, 1H), 6.15 (d, *J* = 2.7 Hz, 1H), 3.87 (s, 2H), 3.65 (s, 3H), 2.53 (s, 2H).

^{13}**C NMR** (126 MHz, $CDCl_3$) δ 136.96, 128.64, 128.51, 128.22, 125.86, 124.16, 122.35, 107.68, 35.40, 34.16.

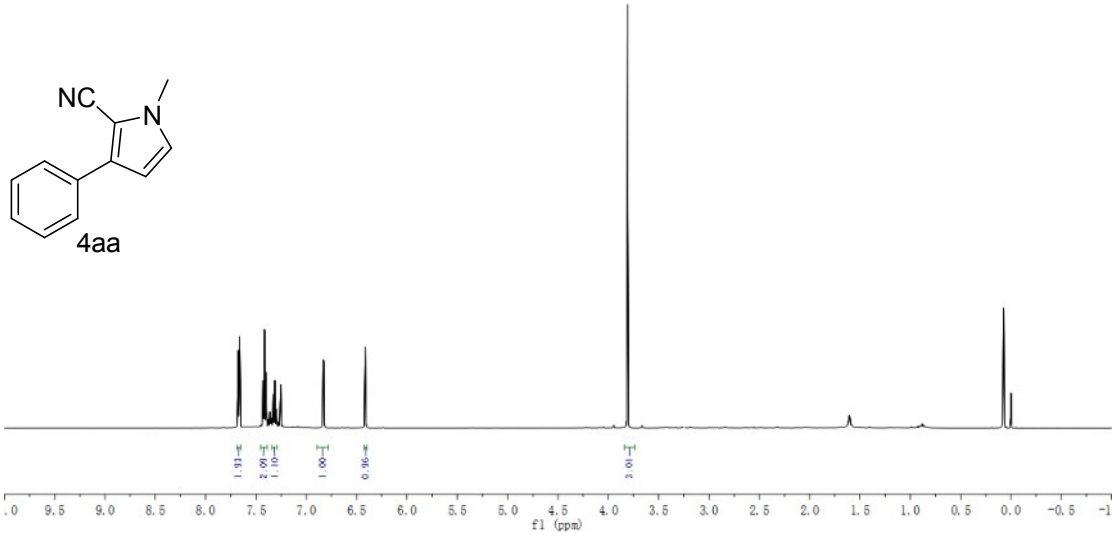
IR (neat, cm^{-1}) *v* 3374, 3052, 2927, 2854, 1736, 1504, 1266, 1246, 1092, 1046, 738.

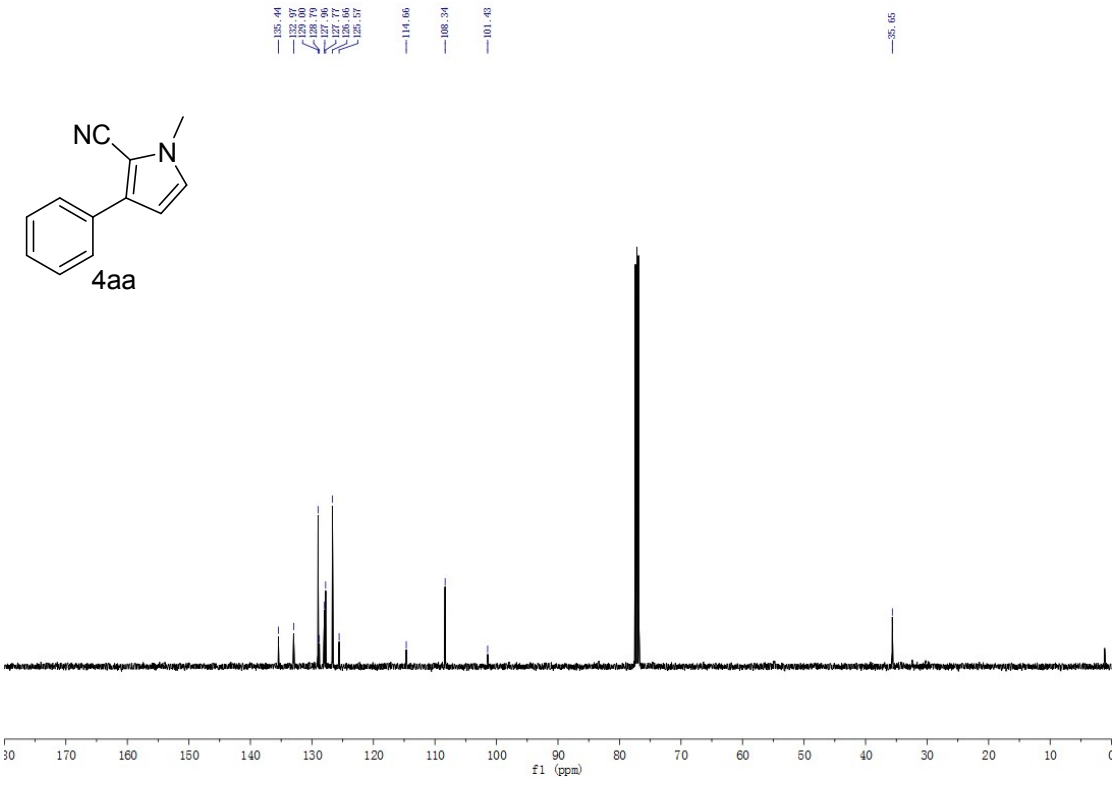
MS (ESI) calcd for $C_{12}H_{15}N_2$ $[M+H]^+$: 187.1230, found 187.1334.

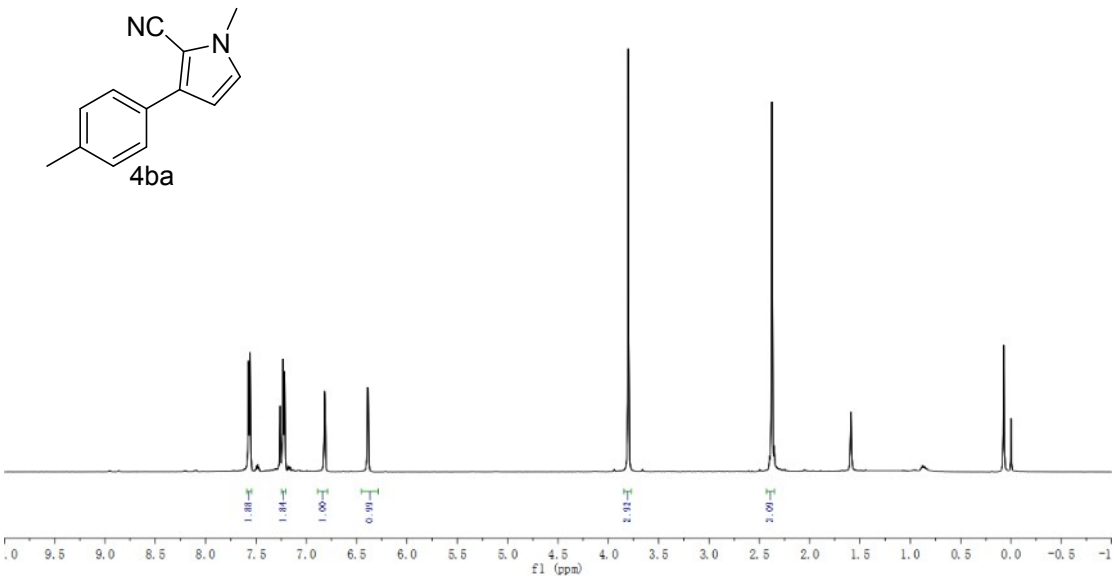
4. Reference

1. X.-Q. Mou, Z.-L. Xu, L. Xu, S.-H. Wang, B.-H. Zhang, D. Zhang, J. Wang, W.-T. Liu, W. Bao, Org. Lett. 2016, 18, 4032.

5. ^{1}H and ^{13}C NMR spectra of products



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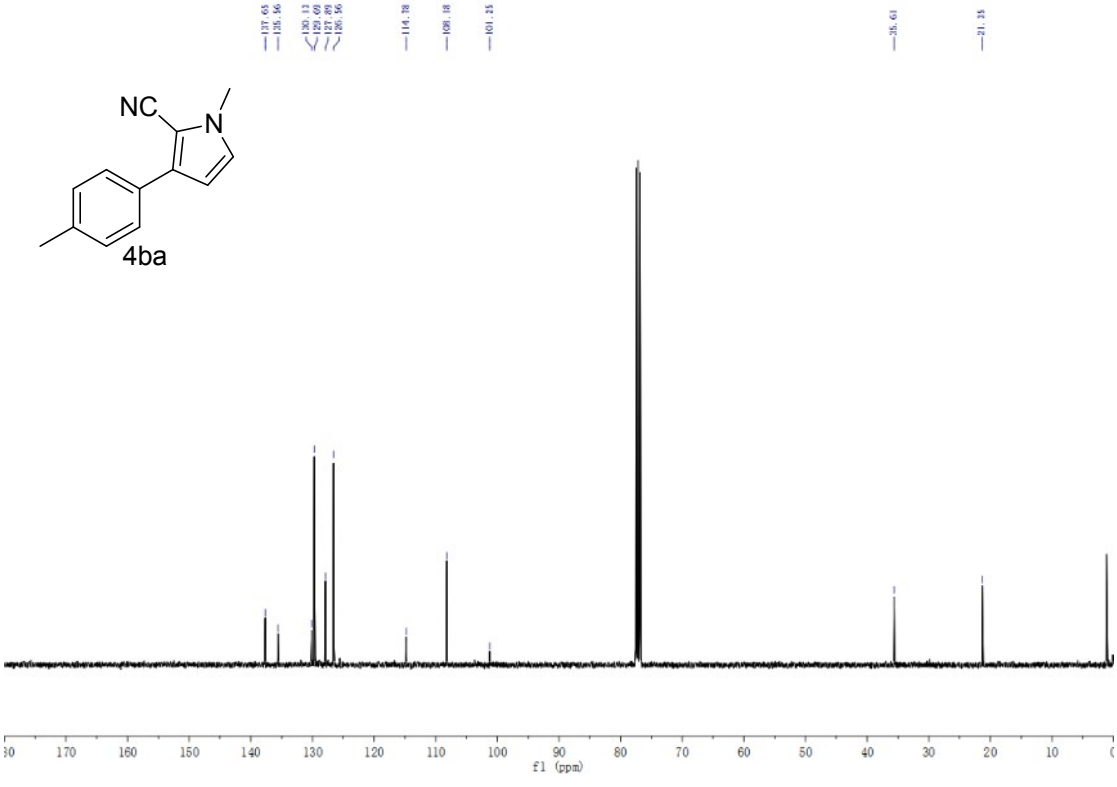
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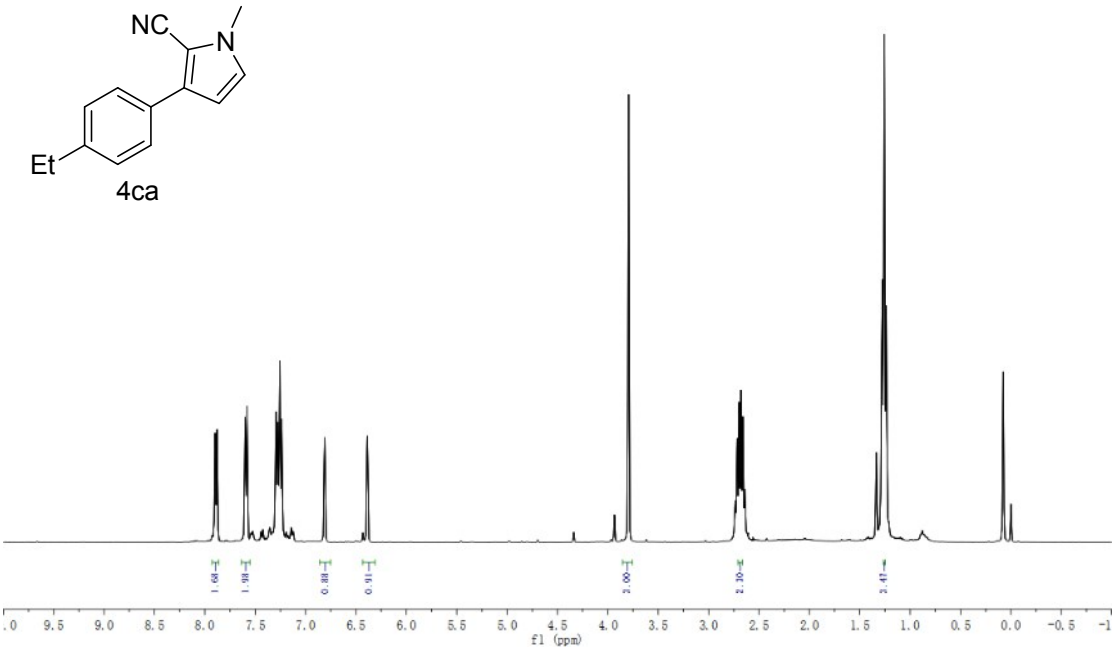
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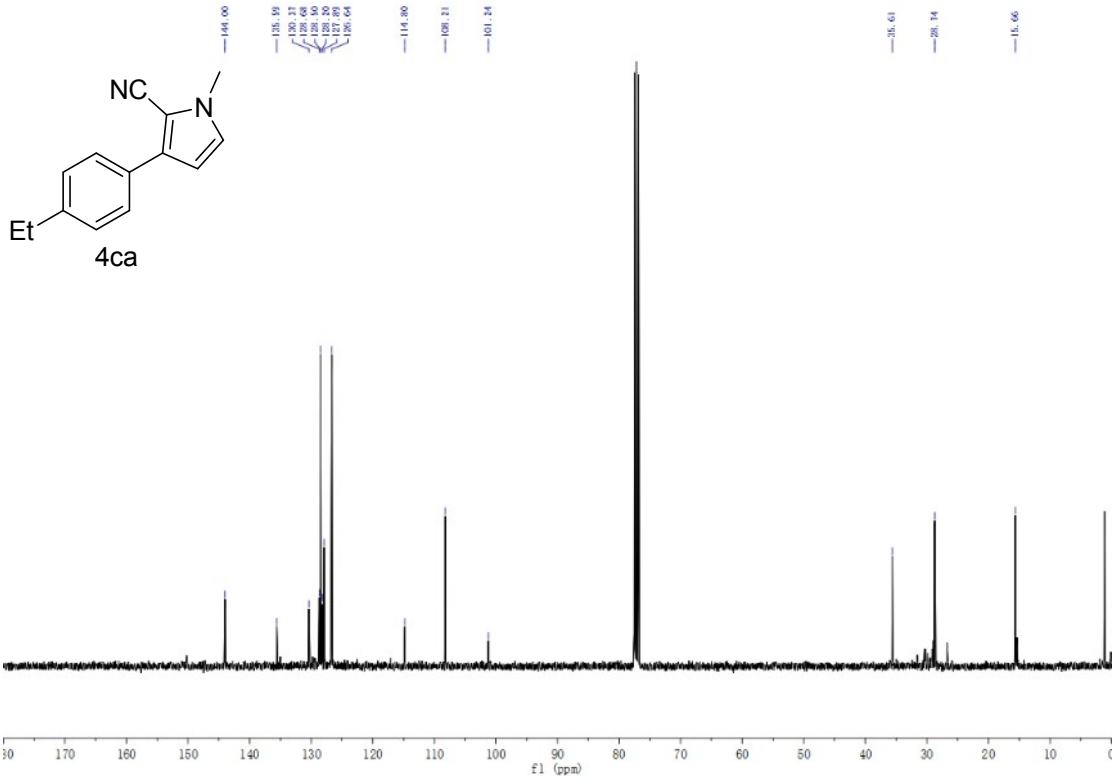
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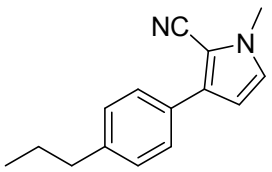
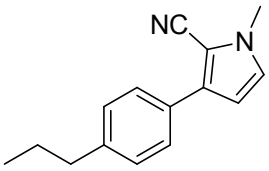
101.24
35.61
28.74
15.66
NC
N
Et
4ca
f1 (ppm)


NC
N

4da

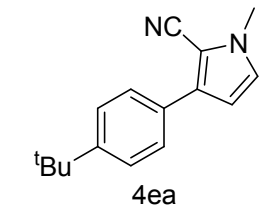
2.00
1.96
0.84
0.84
2.99
2.33
2.45
3.49
f1 (ppm)


142.46
135.61
130.37
129.95
127.99
126.53
114.83
108.20
101.23
37.91
35.62
24.63
13.99

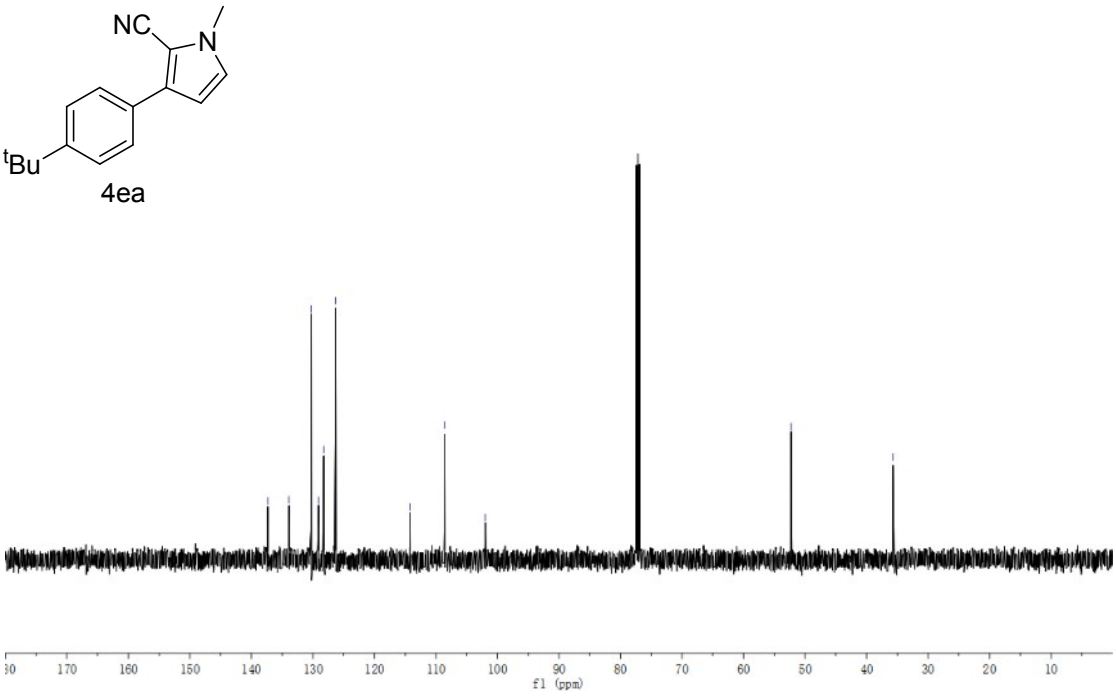

NC
N

4da

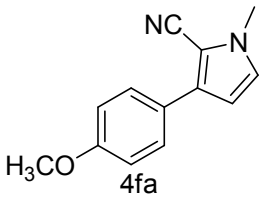
f1 (ppm)

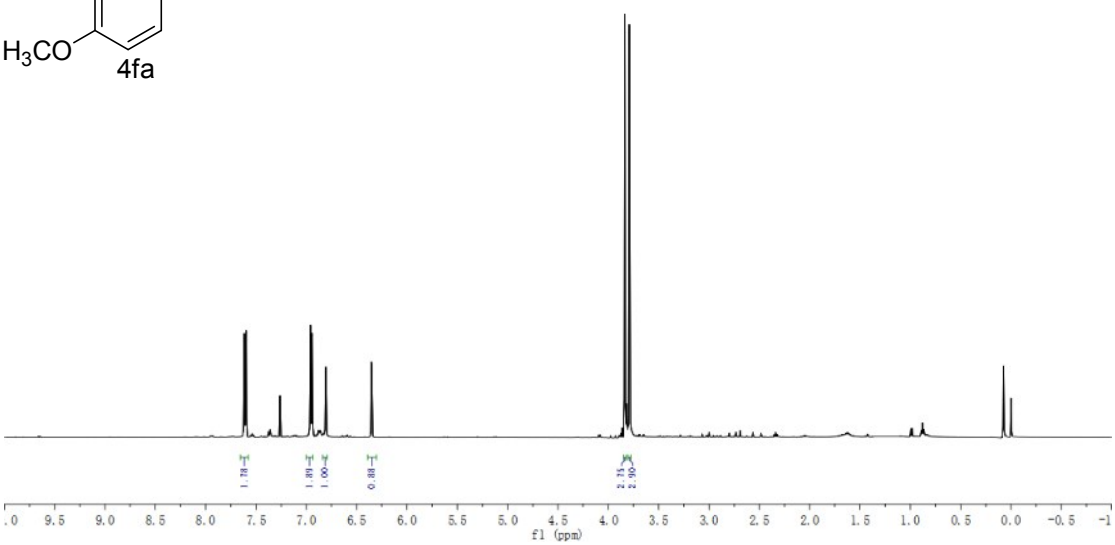


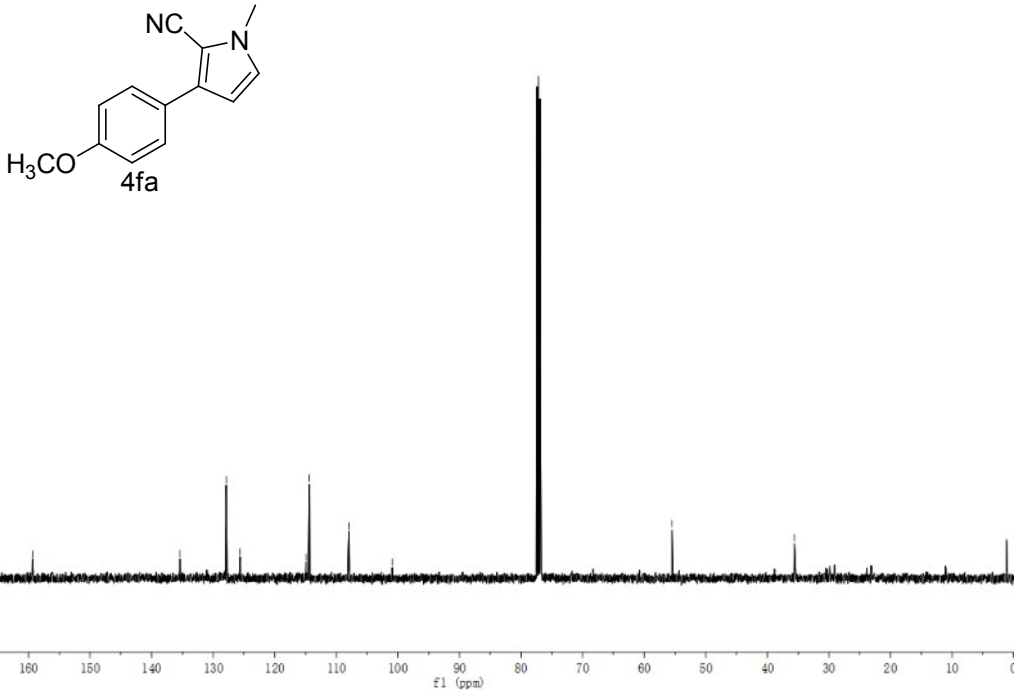
4ea

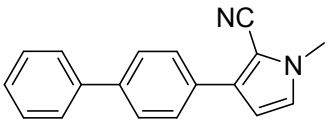


4ea


NC
N
H3CO
4fa


1.78
1.89
1.00
0.88
2.75
2.90
f1 (ppm)

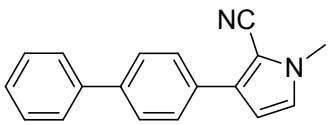

159.30
135.39
127.91
127.88
125.63
114.93
114.29
107.95
100.90
55.46
35.61
f1 (ppm)


NC
N

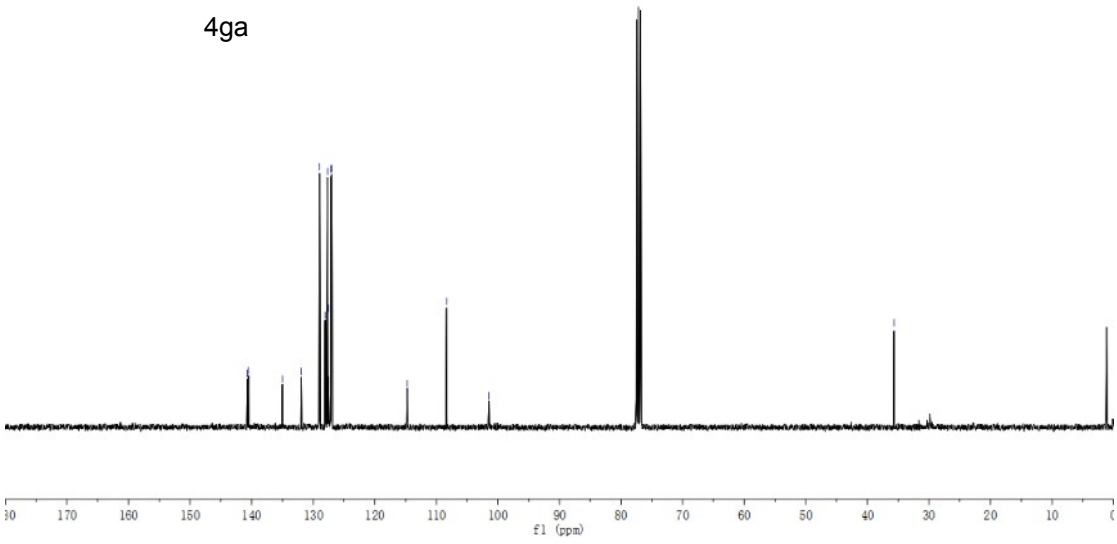
4ga

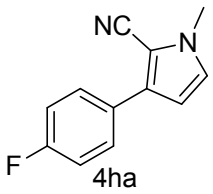
2.00
2.95
2.08
1.10
1.00
1.00
2.21
f1 (ppm)

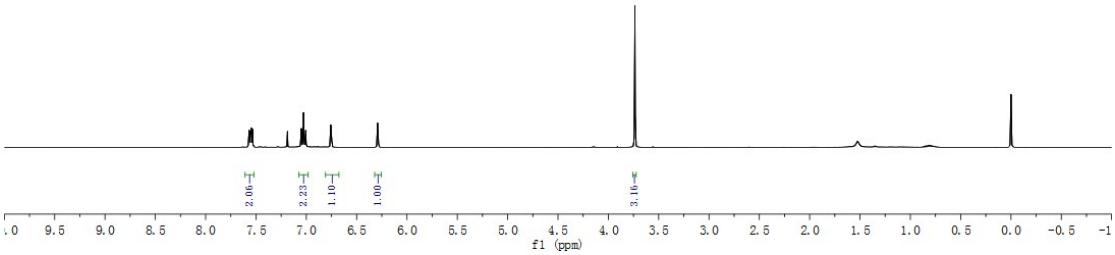

140.11
140.53
135.00
131.95
129.95
128.05
127.68
127.53
127.11
127.01
114.11
108.23
101.48
35.68


NC
N

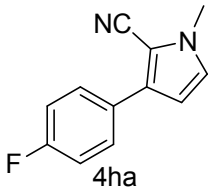
4ga

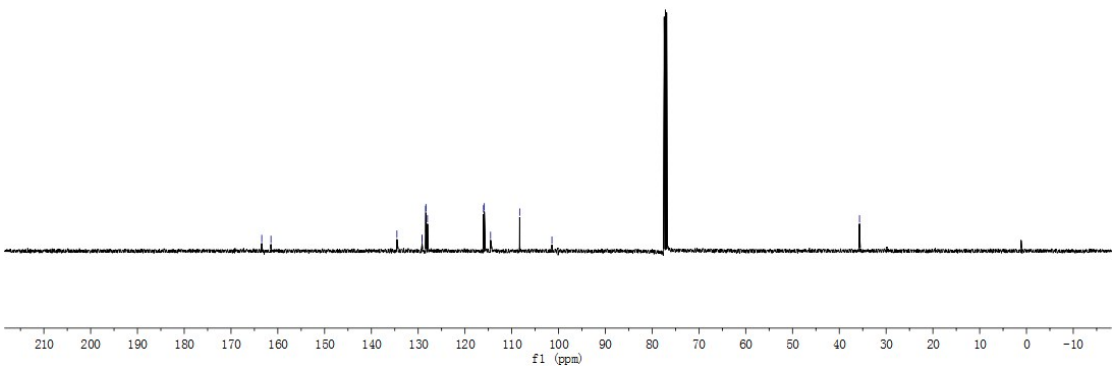

f1 (ppm)

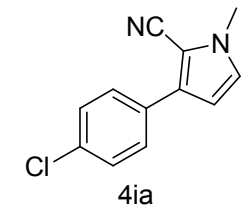

NC
N
F
4ha


2.06
2.23
1.10
1.00
3.16
f1 (ppm)

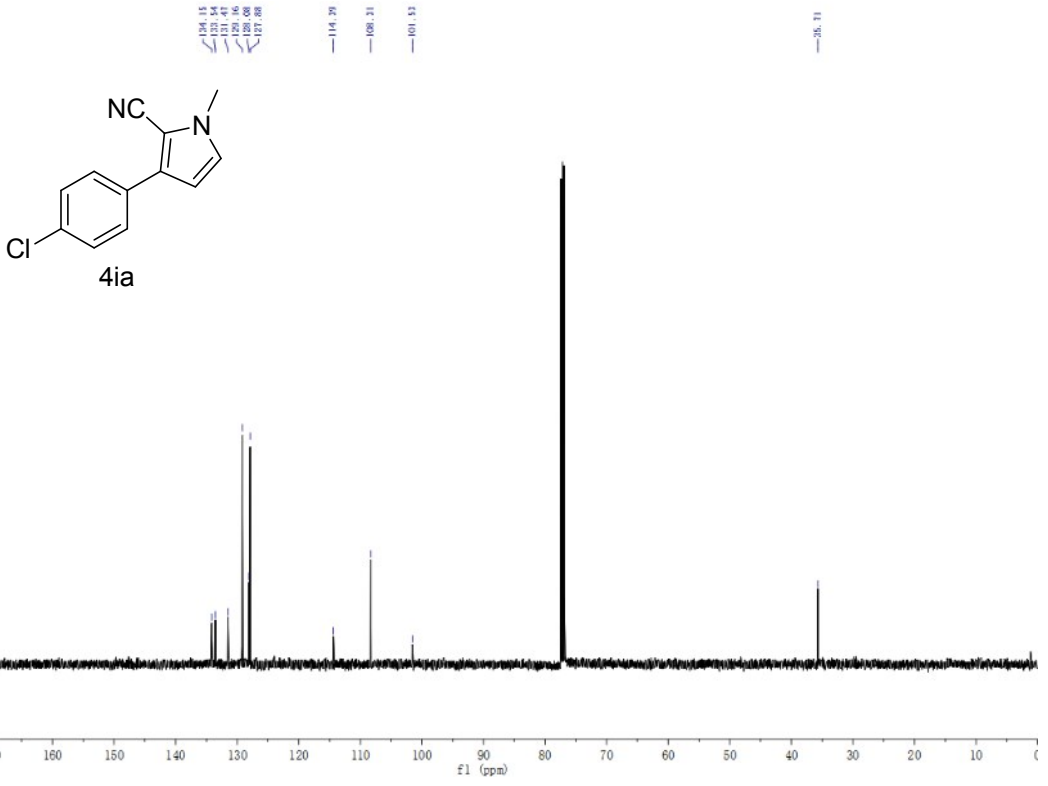

163.43
161.47
134.54
129.20
129.17
128.42
128.35
128.02
116.04
115.87
114.53
108.31
101.41
35.68


NC
N
F
4ha

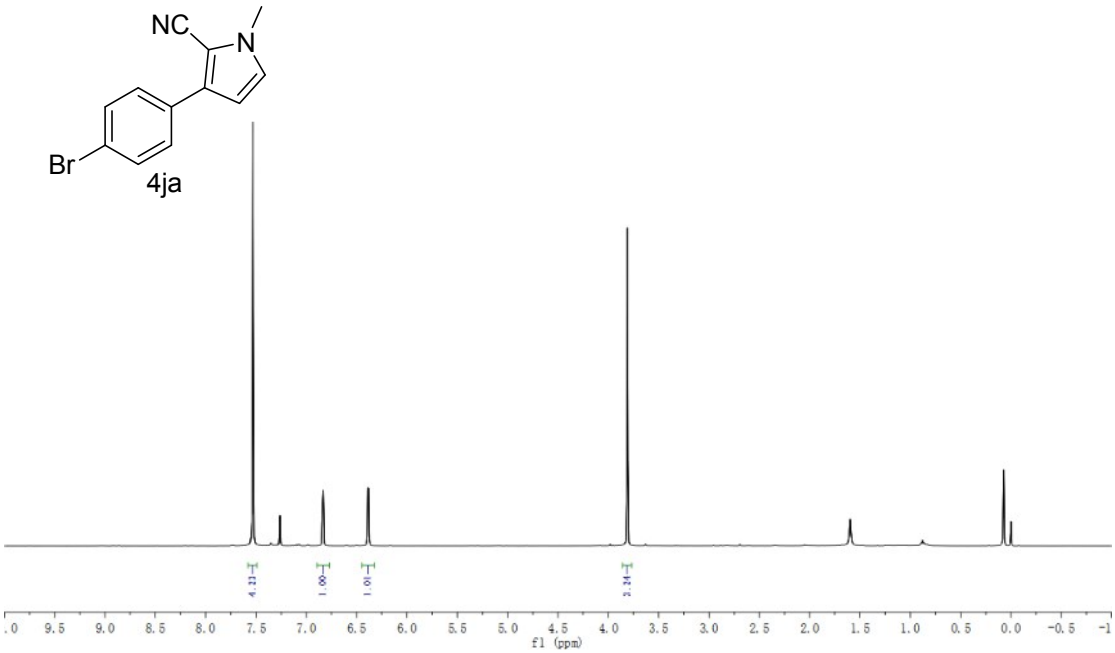

f1 (ppm)

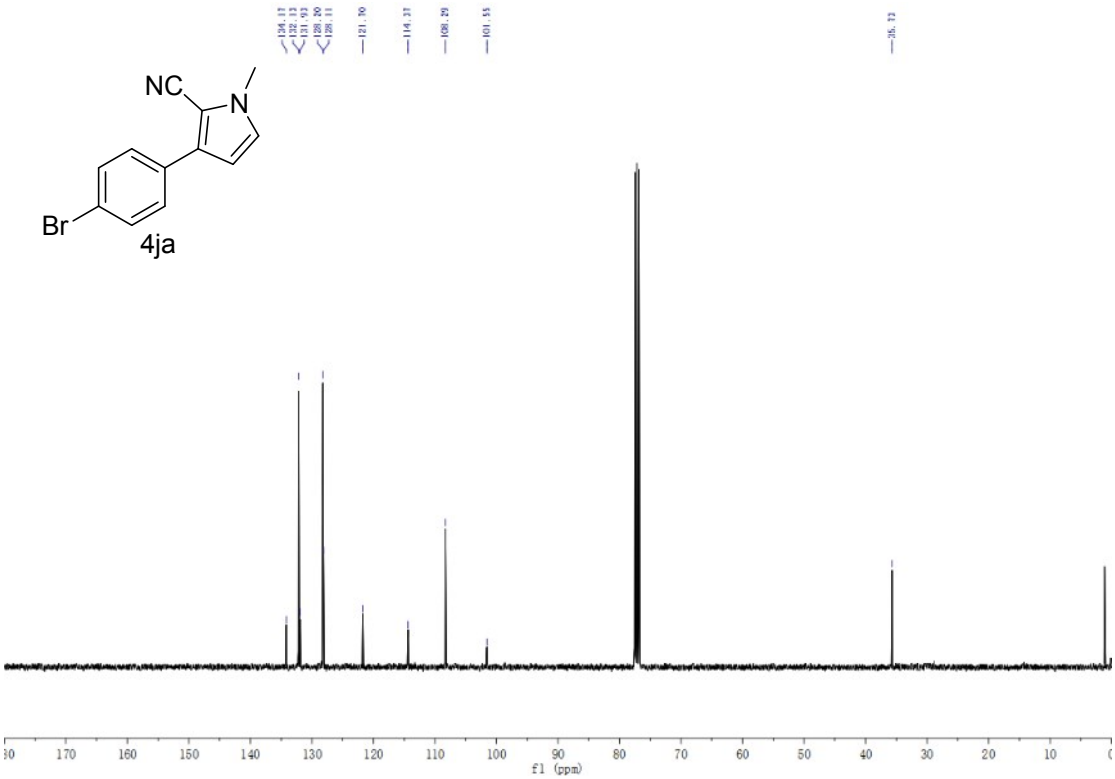


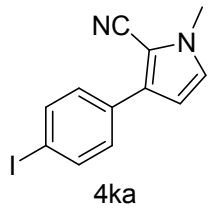
4ia



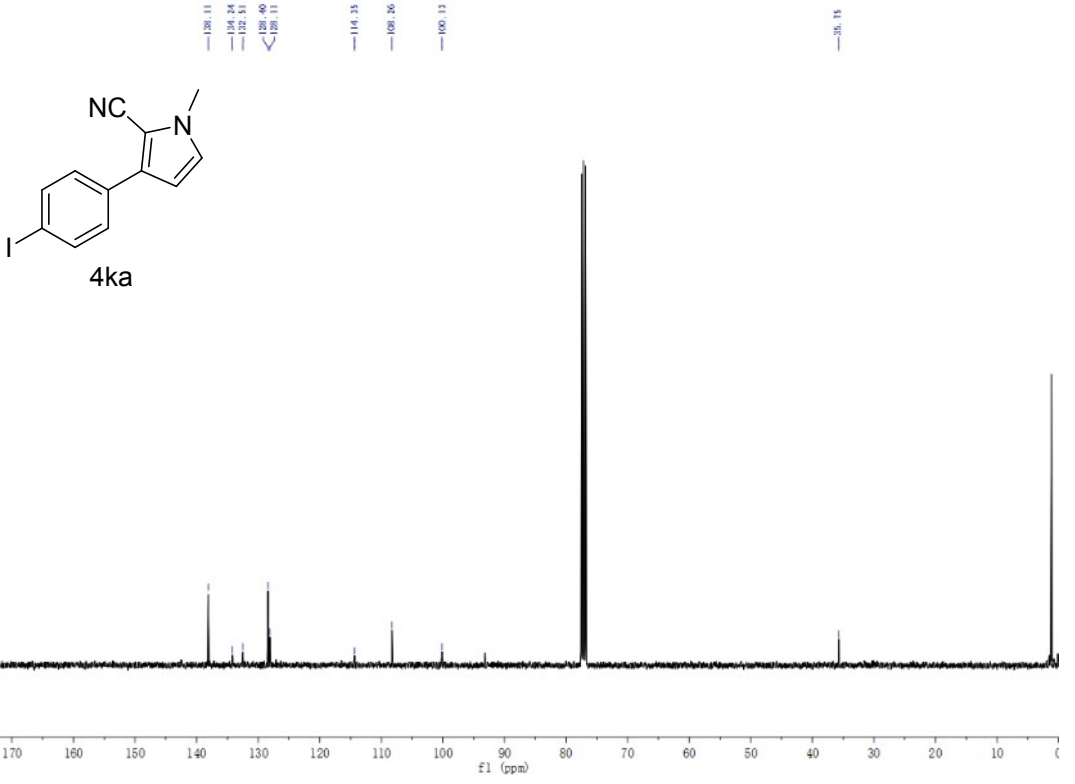
4ia


NC
N
Br
4ja
4.23
1.00
1.01
2.24
f1 (ppm)

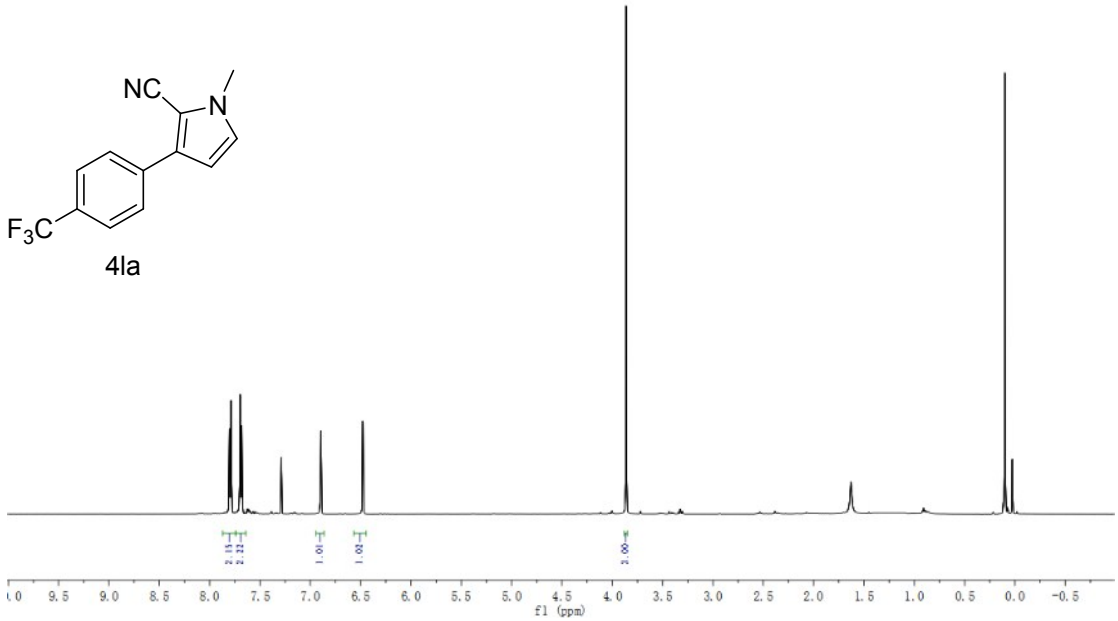

NC
N
Br
4ja
f1 (ppm)

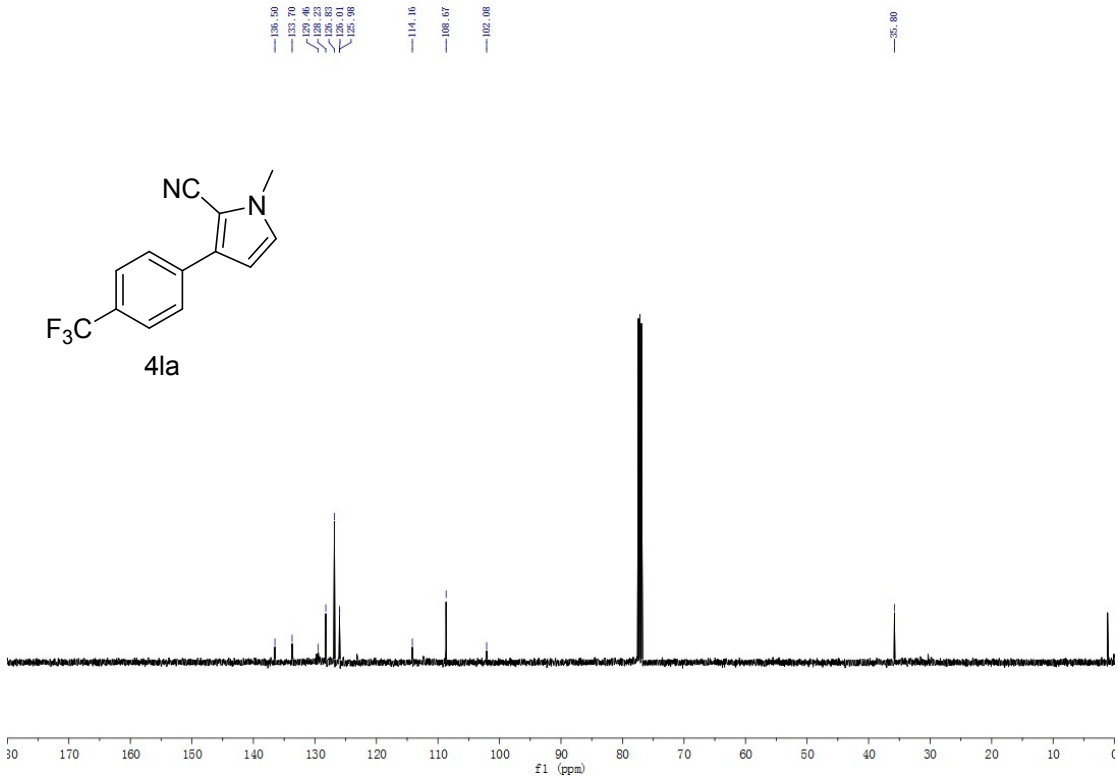


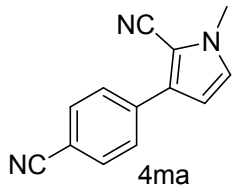
4ka



4ka


NC
N
F3C
4la
2.15
2.12
1.01
1.02
2.00
f1 (ppm)

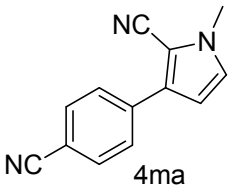

136.50
133.70
129.46
128.23
126.83
126.01
125.98
114.16
108.67
102.08
35.80
NC
N
F3C
4la
f1 (ppm)


NC
N
NC

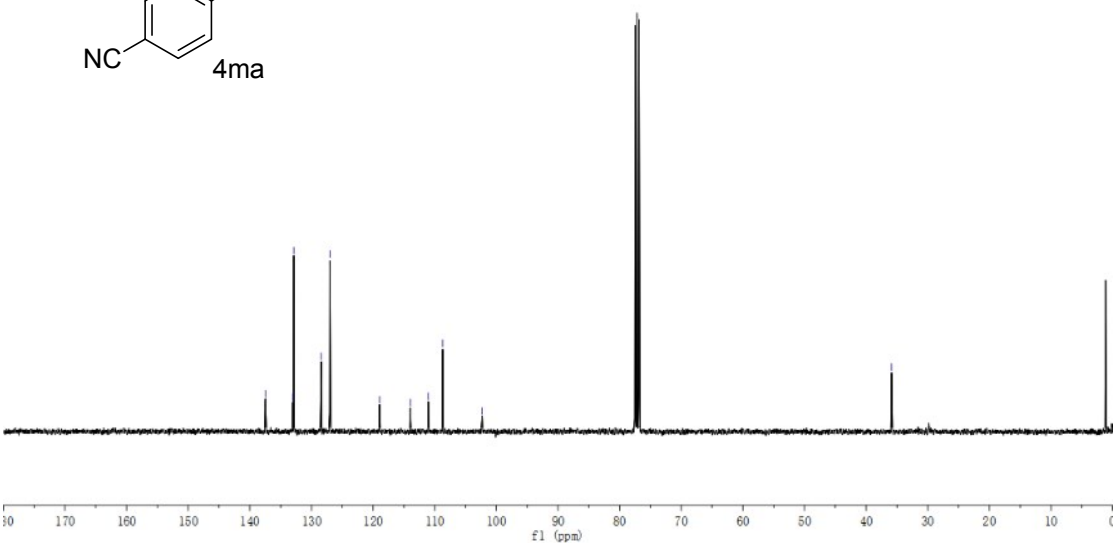
4ma

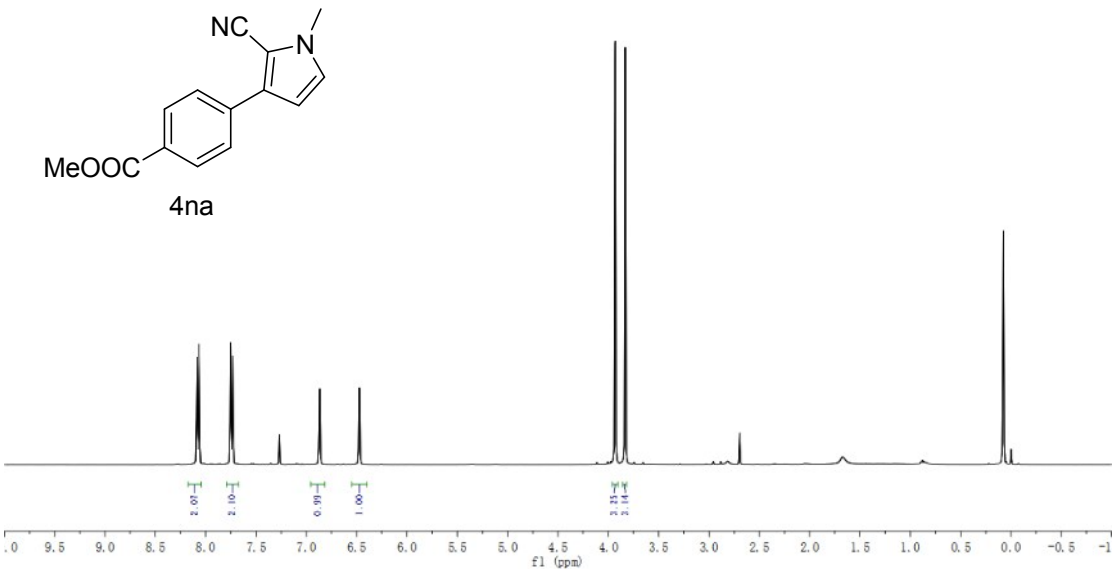
2.10
2.08
0.99
1.00
3.16
f1 (ppm)

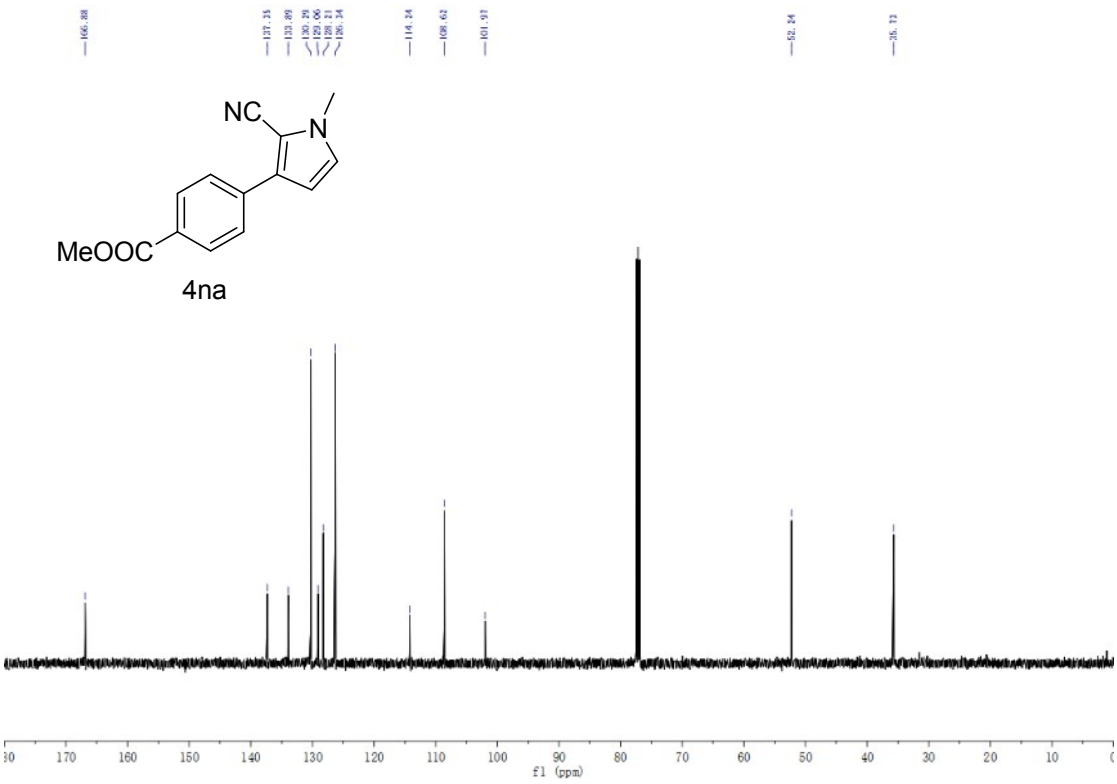

137.46
133.03
132.86
128.42
127.03
118.96
113.95
111.05
108.72
102.31
35.88

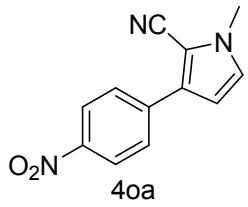

NC
N
NC

4ma

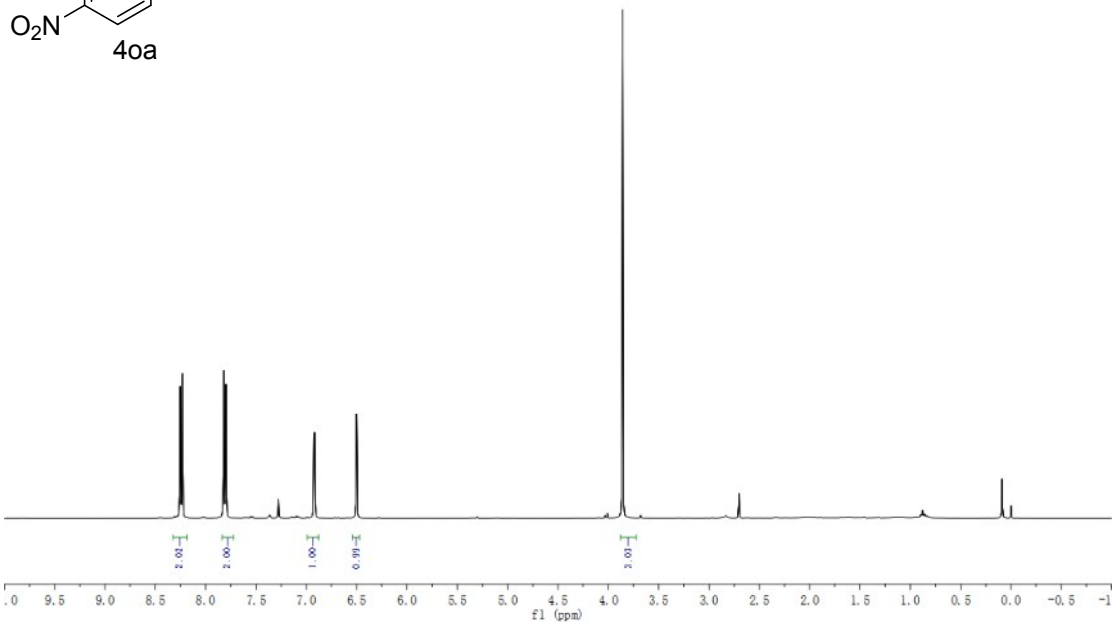

f1 (ppm)


NC
N
MeOOC
4na
2.07
2.10
0.99
1.00
2.25
3.14
f1 (ppm)

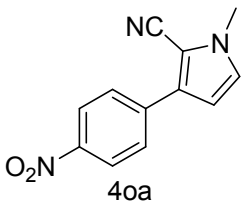

166.88
137.35
133.89
130.29
129.06
128.21
126.34
114.24
108.62
101.91
52.24
26.73
NC
N
MeOOC
4na
f1 (ppm)


NC
N
O_2N

4oa

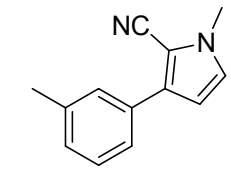

2.03
2.00
1.00
0.99
2.03
f1 (ppm)


146.79
139.38
132.36
128.55
126.94
124.30
113.84
108.65
102.44
35.84


NC
N
O_2N

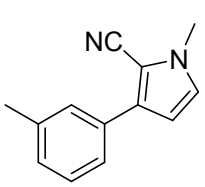
4oa

f1 (ppm)


NC
N

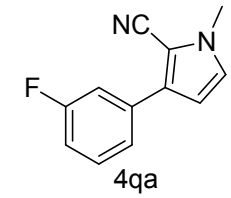
4pa

2.03
1.11
1.03
1.00
1.00
3.15
2.35
f1 (ppm)


NC
N

4pa

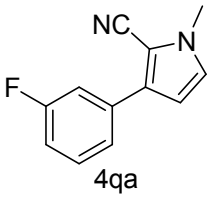
138.51
135.44
132.85
129.83
128.49
127.88
127.28
123.71
114.62
108.27
101.28
35.51
21.54
f1 (ppm)


NC
N
F

4qa

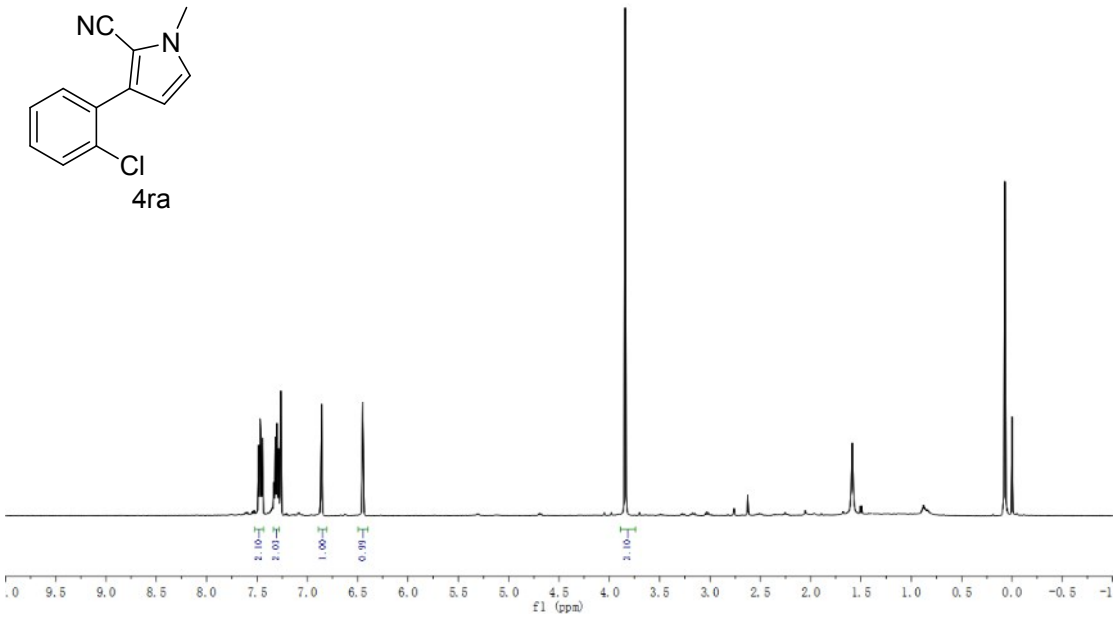
0.99
2.04
1.00
0.93
0.91
2.09
f1 (ppm)

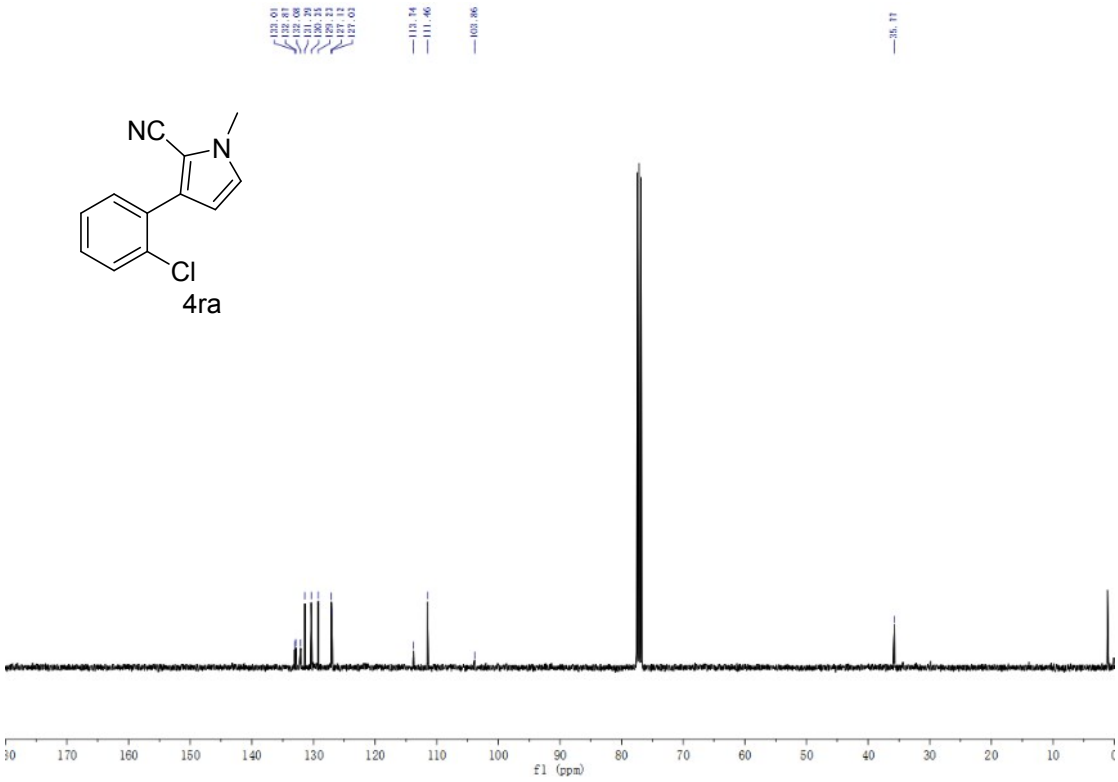

164.17
162.22
135.14
135.07
134.01
130.56
130.50
128.07
122.28
122.26
114.64
114.41
114.21
113.61
113.43
108.41
101.30
35.30

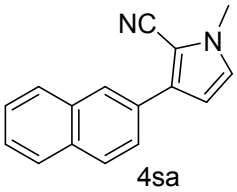

NC
N
F

4qa

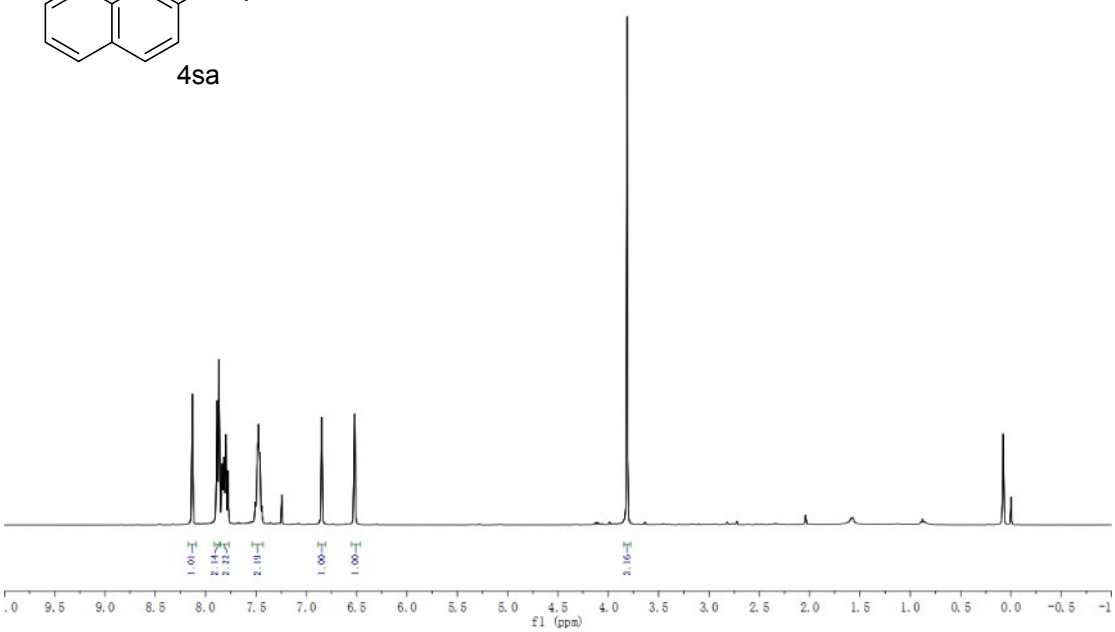
f1 (ppm)

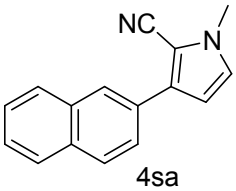

NC
N
Cl
4ra
2.10
2.03
1.00
0.99
2.10
f1 (ppm)


NC
N
Cl
4ra
f1 (ppm)

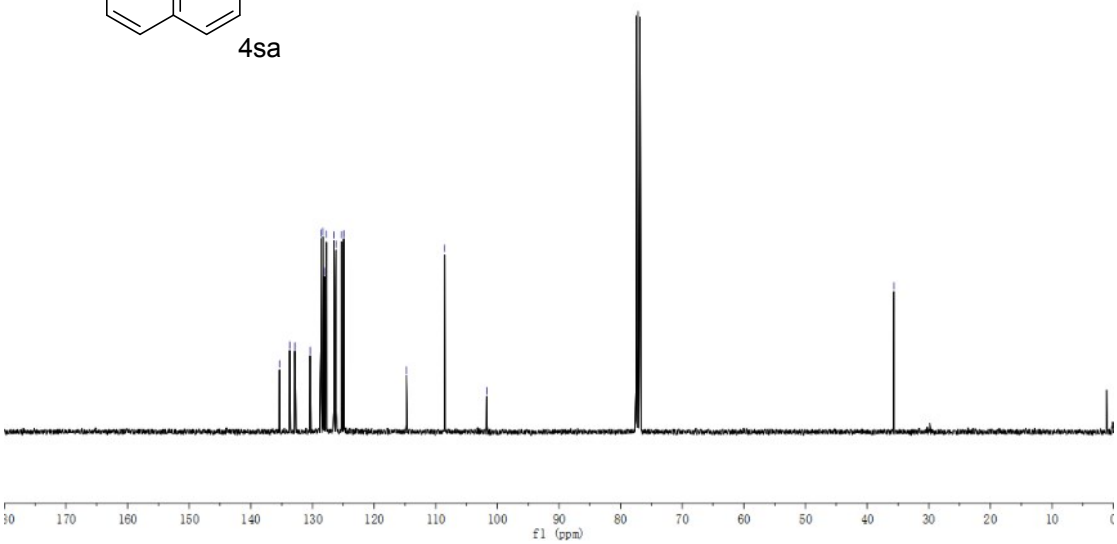


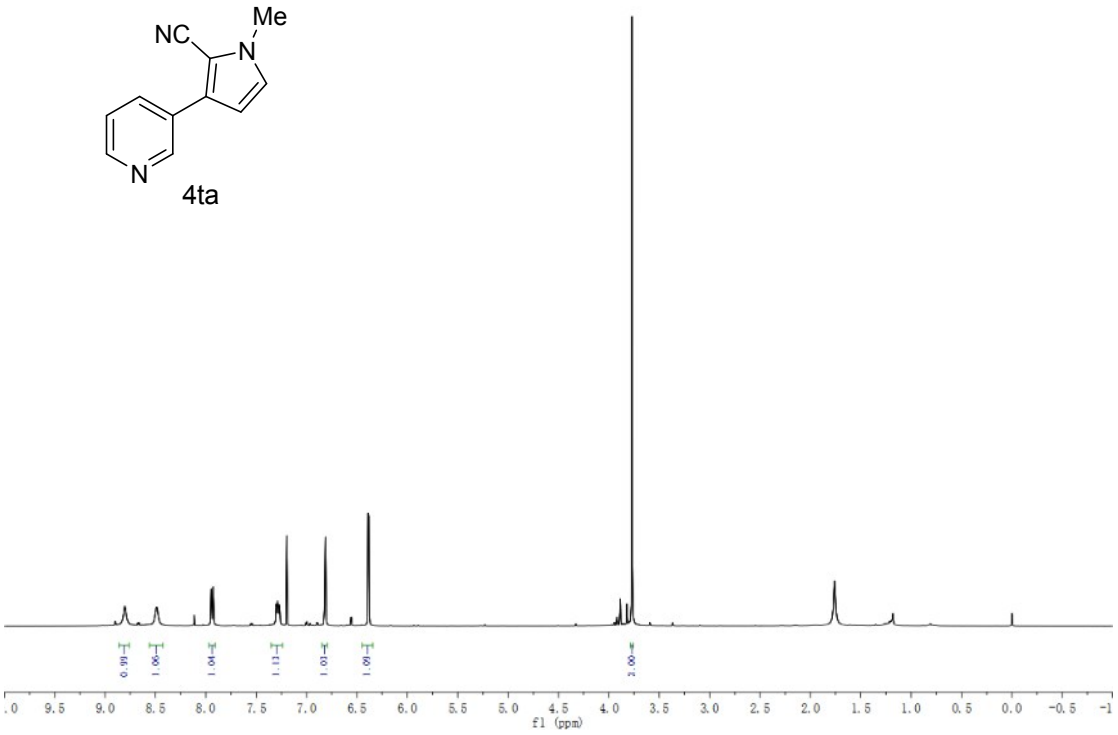
4sa

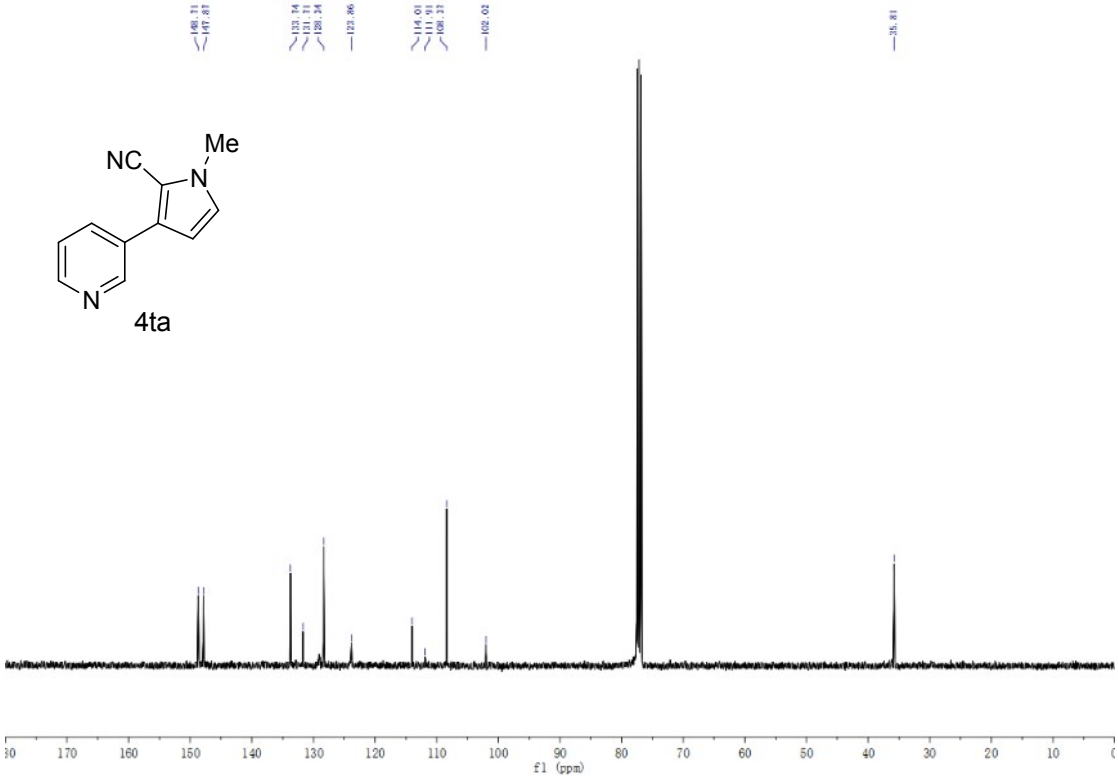


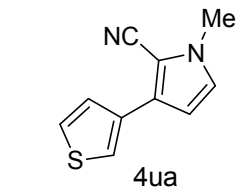


4sa

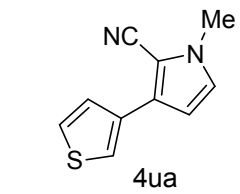



NC
Me
N
N
4ta
0.99
1.06
1.04
1.13
1.03
1.09
2.00
f1 (ppm)

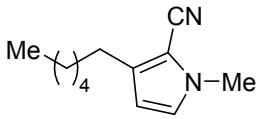

148.31
147.83
133.14
131.71
128.24
123.86
114.01
111.91
108.23
102.02
35.81
NC
Me
N
N
4ta
f1 (ppm)



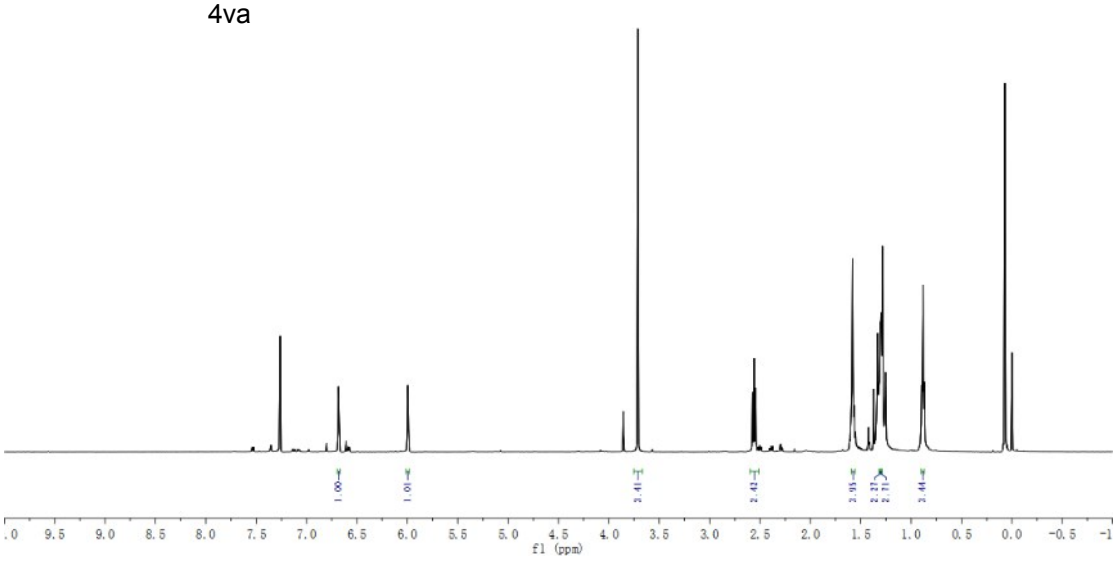
4ua

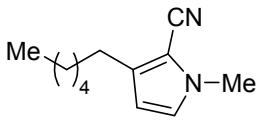


4ua

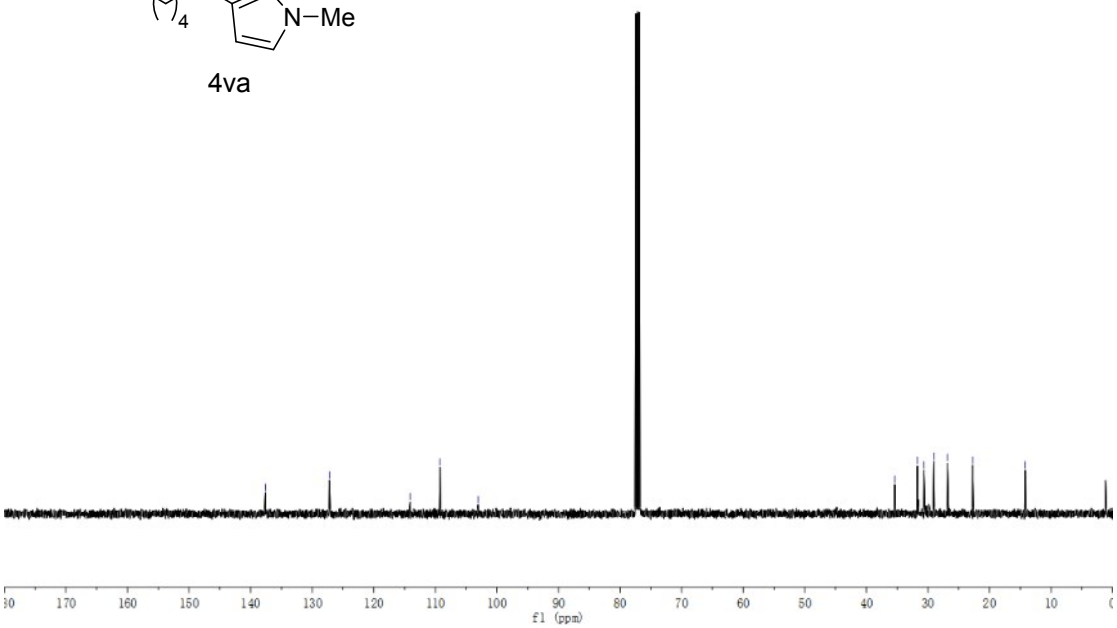


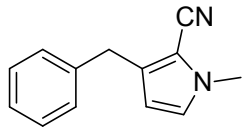
4va



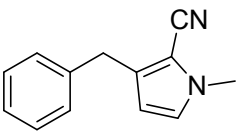


4va

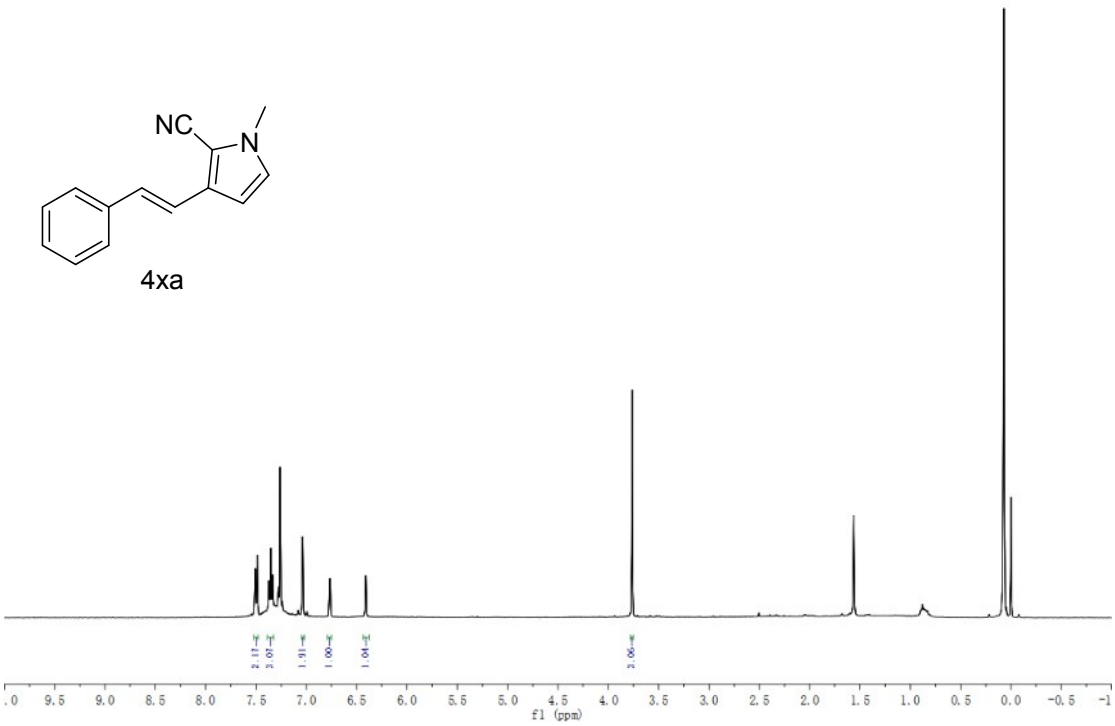


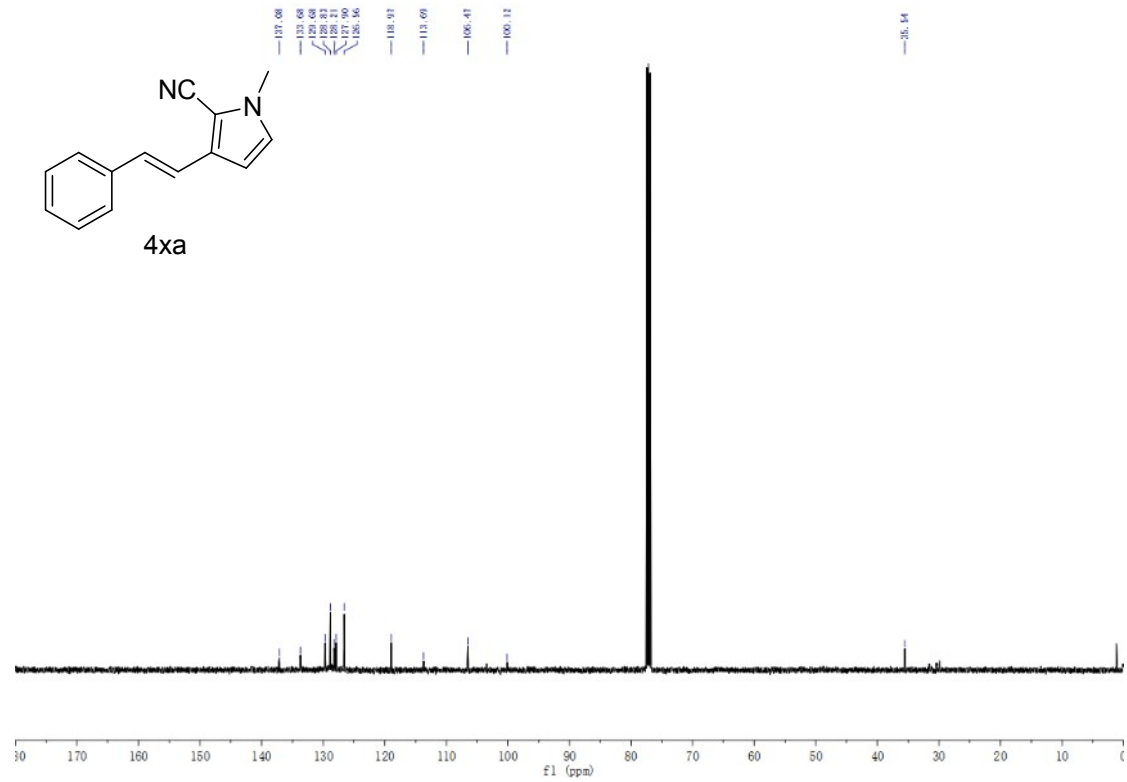


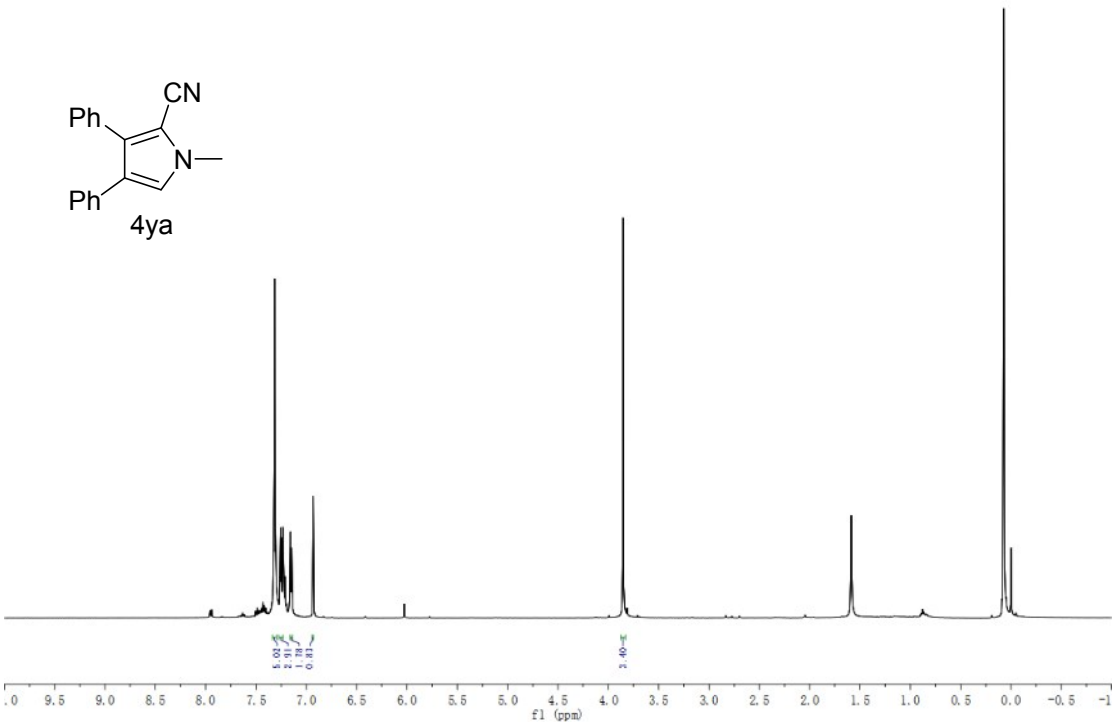
4wa

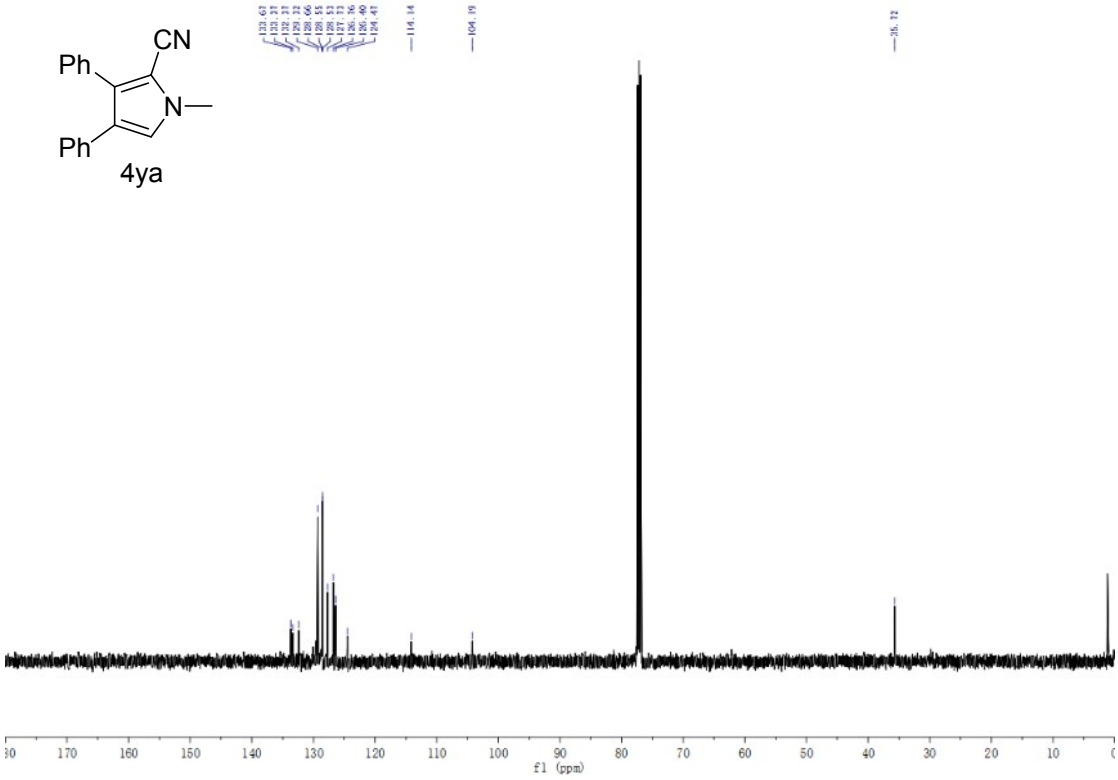


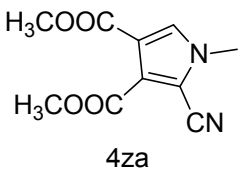
4wa


NC
N
4xa
2.17
3.05
1.91
1.00
1.04
2.06
f1 (ppm)

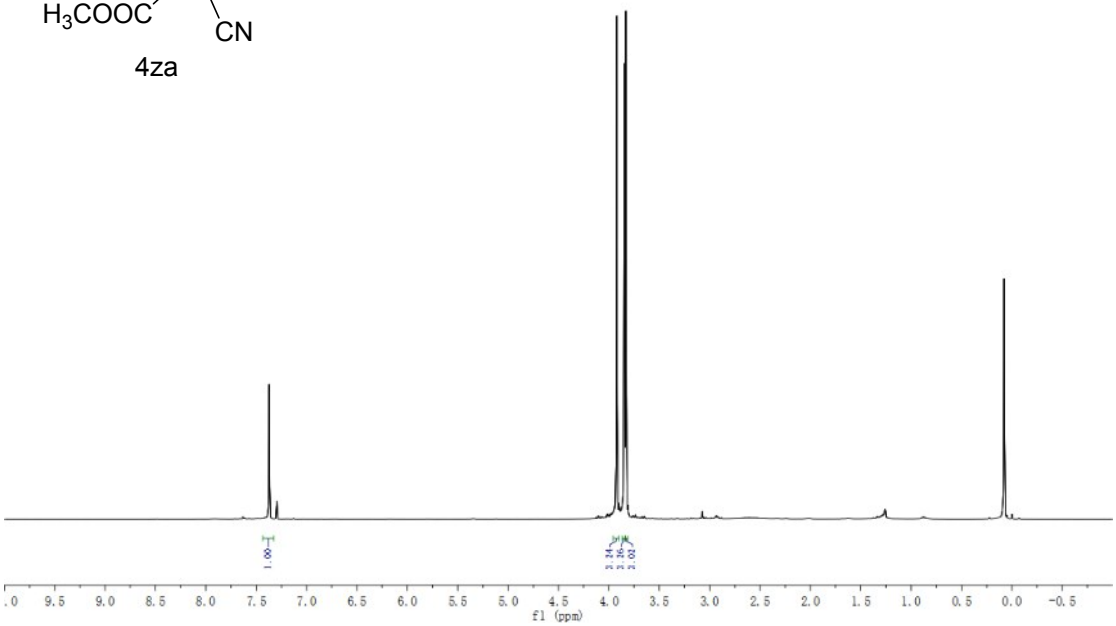

137.08
133.68
129.68
128.33
128.21
127.90
126.16
118.93
113.69
106.43
100.12
35.54
NC
N
4xa
f1 (ppm)

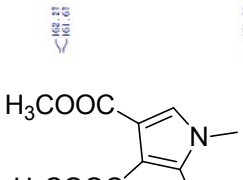

CN
Ph
N
Ph
4ya
f1 (ppm)


CN
Ph
N
Ph
4ya
f1 (ppm)


H3COOC
N
H3COOC
CN

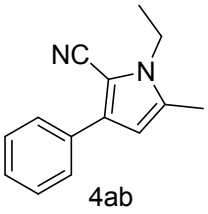
4za


1.00
2.24
2.36
2.03
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 -0.5
f1 (ppm)

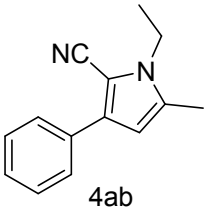

H3COOC
N
H3COOC
CN

4za

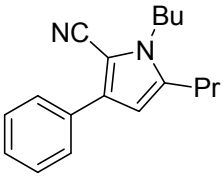
162.27
161.67
131.78
124.74
116.61
111.02
109.17
52.49
52.04
36.28
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



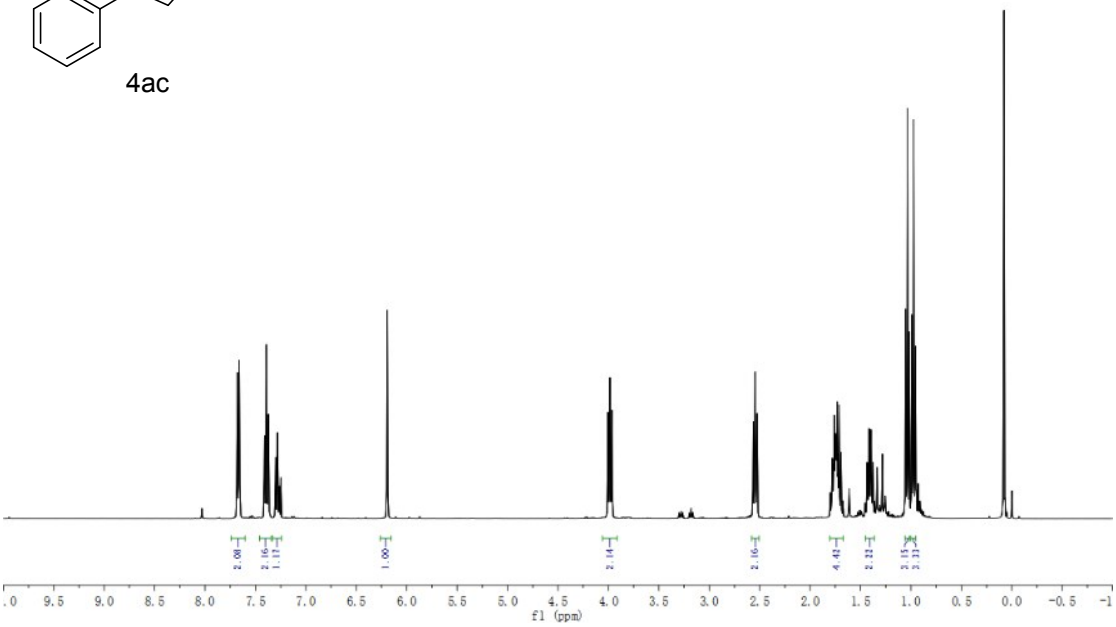
4ab

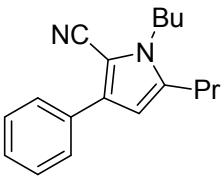


4ab

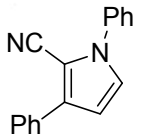


4ac

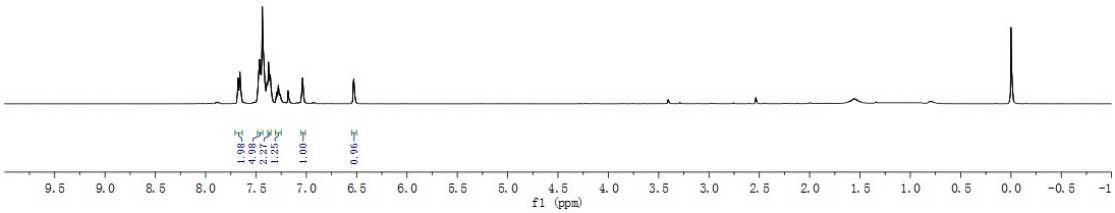


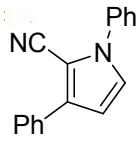


4ac


Ph
NC
N
Ph

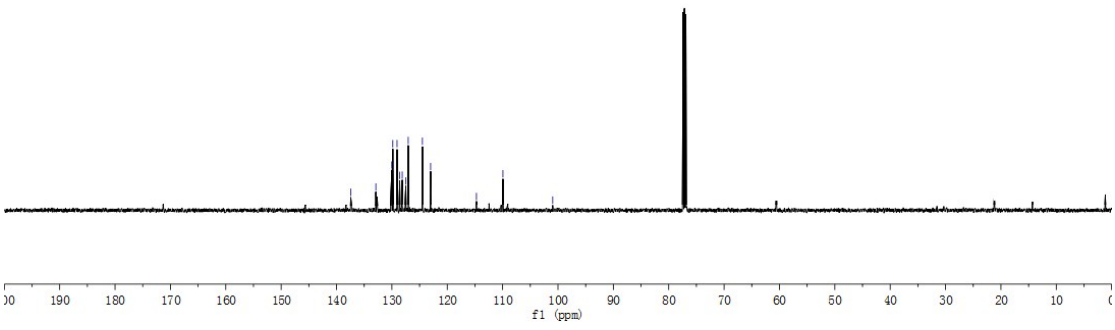
4ad

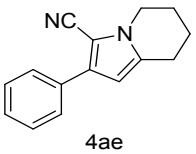

1.98
4.98
2.27
1.25
1.00
0.96
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


Ph
NC
N
Ph

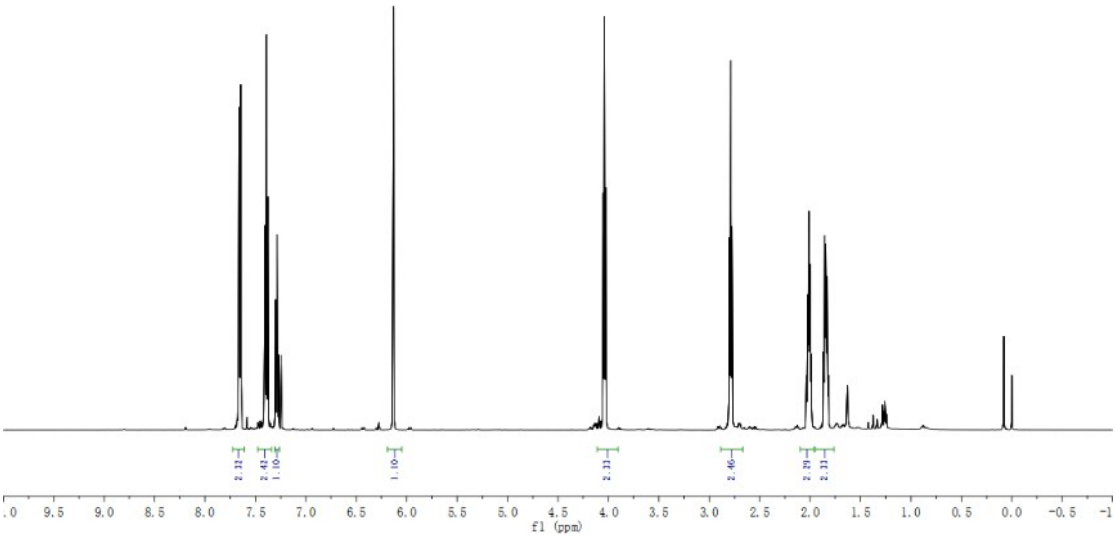
4ad


137.43
132.89
130.02
129.84
129.07
128.59
128.11
127.50
127.05
124.48
123.00
114.73
109.94
100.95

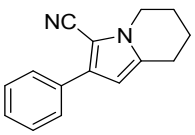

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


NC
N

4ae

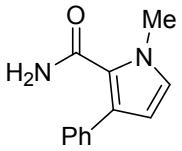

2.32
2.43
1.10
1.10
2.33
2.46
2.29
2.33
f1 (ppm)


136.38
134.88
133.22
128.91
127.84
126.63
115.22
105.47
98.99
44.63
23.56
22.98
20.41


NC
N

4ae

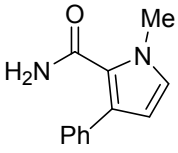
f1 (ppm)


O
Me
H2N
N
Ph

5aa

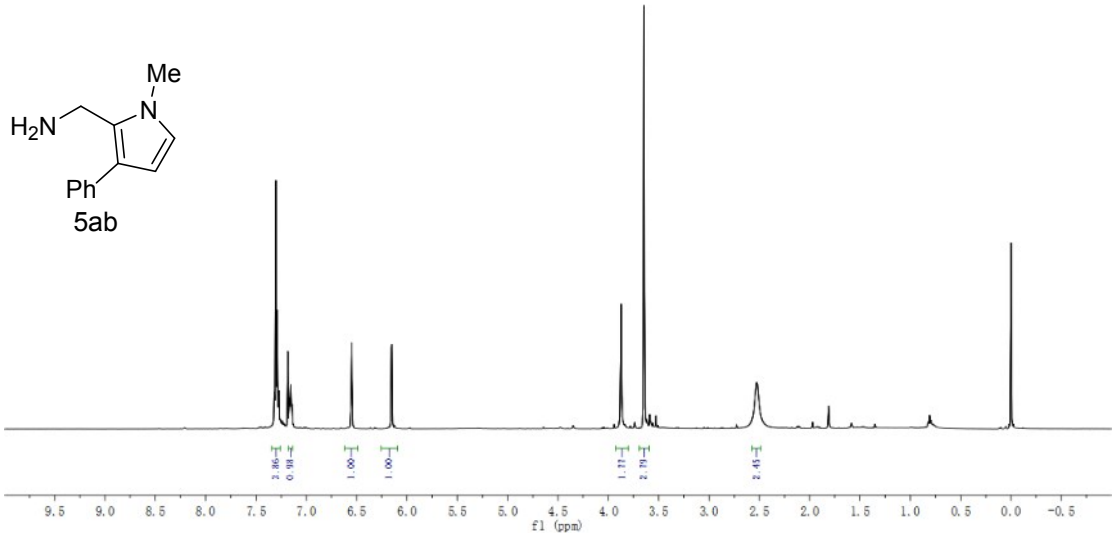
4.29
1.43
1.03
1.00
1.91
2.41
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

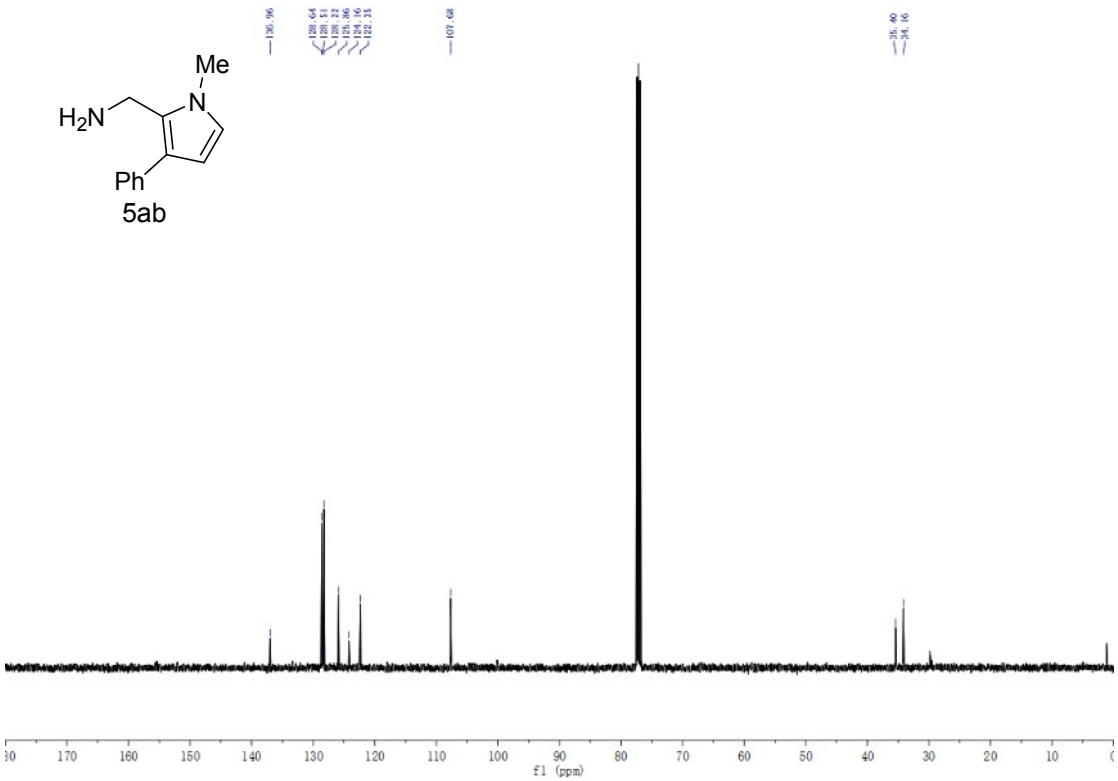
163.81
130.35
129.84
129.70
128.83
127.59
127.32
121.28
109.69
37.63


O
Me
H2N
N
Ph

5aa

170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


Me
N
H2N
Ph
5ab
f1 (ppm)


Me
N
H2N
Ph
5ab
f1 (ppm)