Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting information

A novel three-component coupling reaction of aryne, C=N derivatives, and acrylonitrile

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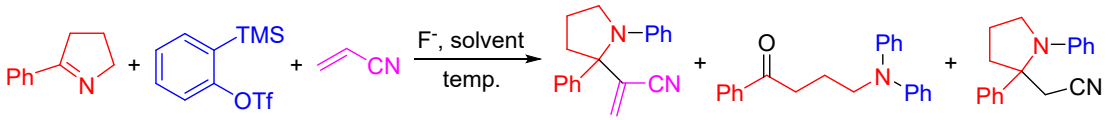
Part 1. General information

All reagents, if commercially available, were purchased from standard suppliers and were used without further purification unless otherwise stated. Melting points were determined on a XT4A hot-stage apparatus and are uncorrected. IR spectra were obtained using an PerkinElmer FT/IR spectrometer. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AV400 instrument. High-resolution mass spectra were recorded on a Micromass Q-TOF mass spectrometer. Flash column chromatography was performed over silica gel 200–300 mesh.

Part 2. Optimization of reaction conditions for the synthesis of 4a

Table S1. Optimization of the three-component reaction conditions for the synthesis of **4a**



1a **2a** **3** **4a** **4a'** **4a''**

Entry	F- source	Solvent	Temp. (°C)	Yield **4a** (%)[e]	Yield **4a′** (%)[e]	Yield **4a″** (%)[e]
1[a]	KF	THF	25	5	60	-
2[b]	KF	THF	25	27	35	-
3[b]	KF/18-crown-6	THF	25	54	27	-
4[b]	CsF	THF	25	59	5	-
5[b]	TBAF[f]	THF	25	25	45	-
6[b]	CsF	MeCN	25	28	-	50
7[b]	CsF	THF	60	61	-	-
8[b]	CsF	THF	70	66	-	-
9[b]	CsF	THF	80	62	-	-
10[c]	CsF	THF	70	77	-	-
11[d]	CsF	THF	70	77	-	-

[a] **1a** (0.2 mmol), **2a** (0.3 mmol), acrylonitrile (0.3 mmol), F- source (0.6 mmol), solvent (0.5 mL); [b] **1a** (0.2 mmol), **2a** (0.3 mmol), acrylonitrile (0.5 mL), F- source (0.6 mmol), solvent (0.5 mL); [c] **1a** (0.2 mmol), **2a** (0.4 mmol), acrylonitrile (0.5 mL), F- source (0.8 mmol), solvent (0.5 mL); [d] **1a** (0.2 mmol), **2a** (0.5 mmol), acrylonitrile (0.5 mL), F- source (1.0 mmol), solvent (0.5 mL); [e] Isolated yield; [f] 1 M in THF.

Part 3. Scope of substrates

Figure S1. Pyrroline/imine/dihydroisoquinoline substrates involved in the manuscript

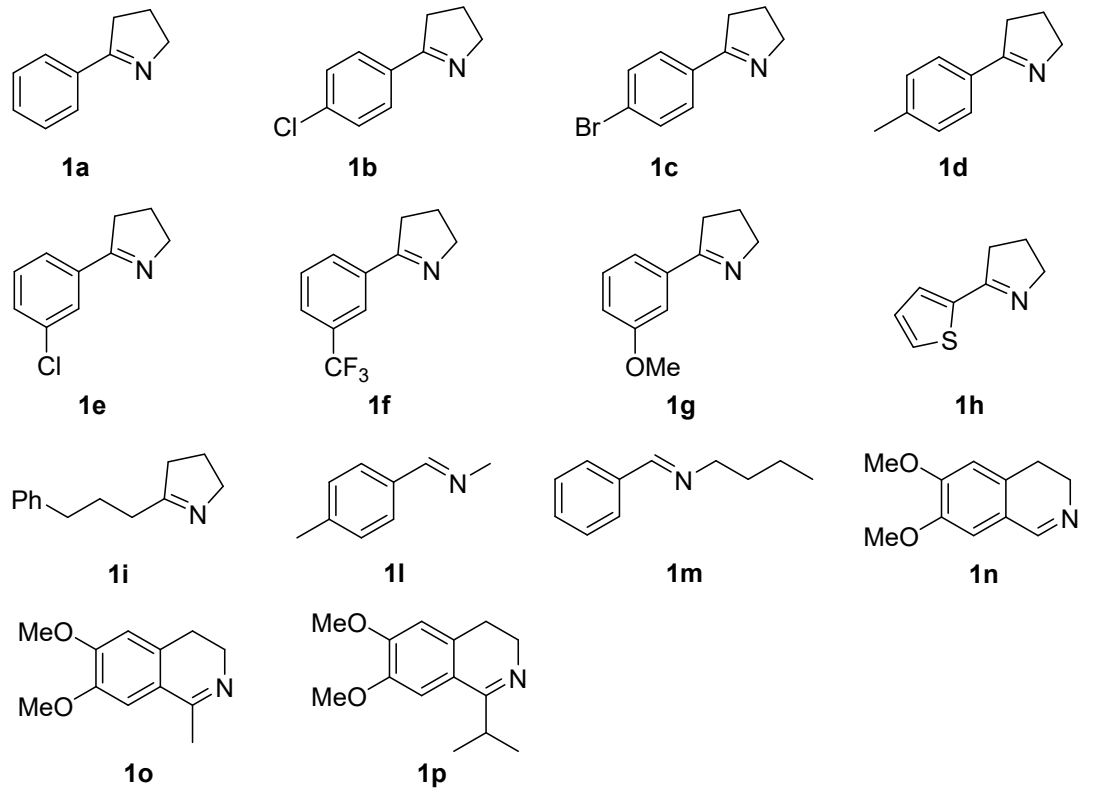


Figure S2. Imidazoline substrates involved in the manuscript

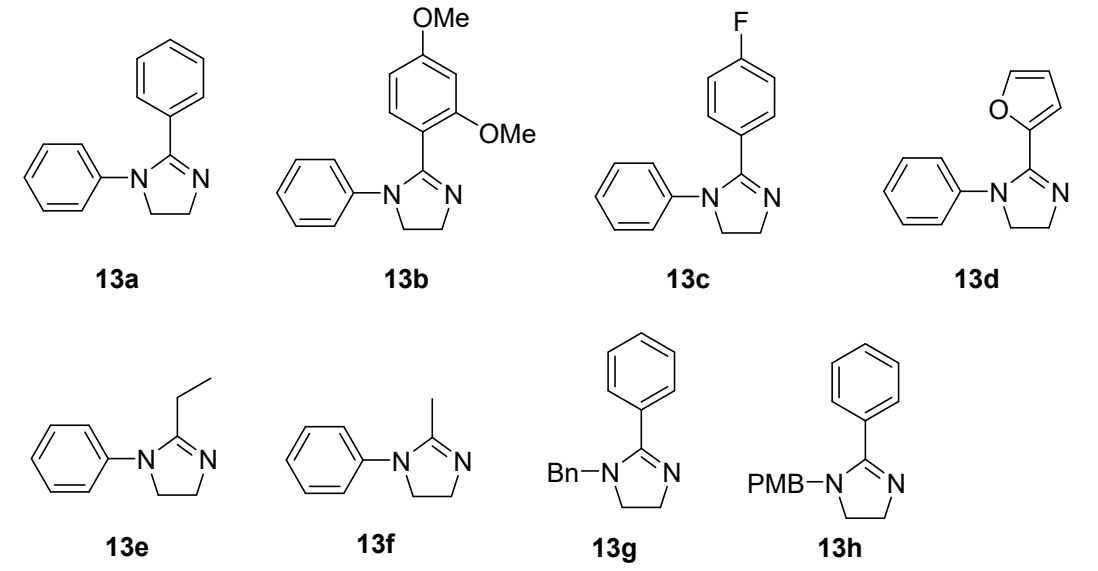


Figure S3. Oxazoline substrates involved in the manuscript

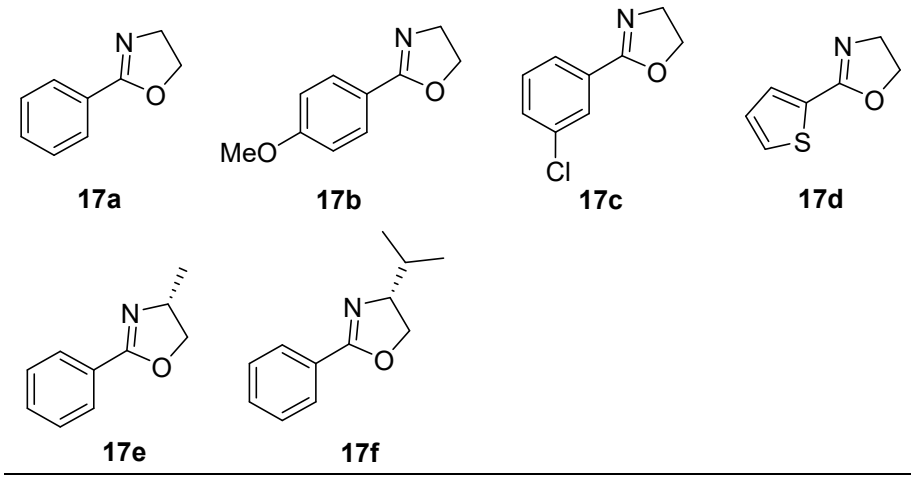
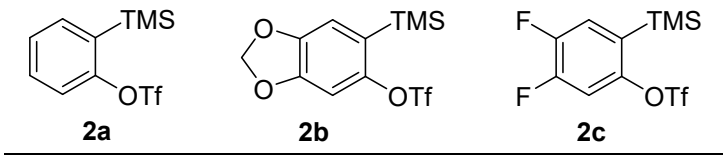


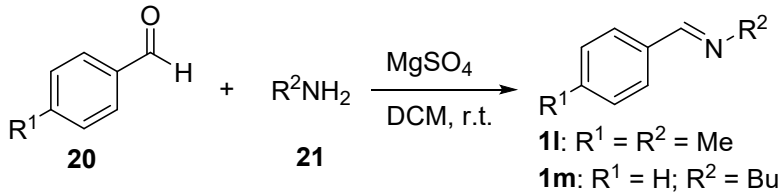
Figure S4. Aryne precursor substrates involved in the manuscript



Part 4. Preparation of substrates

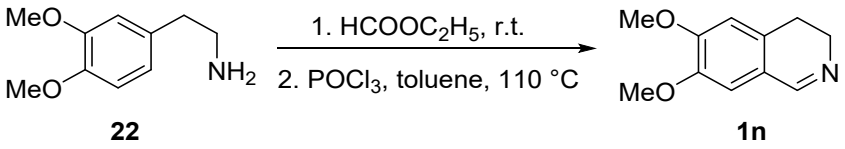
Pyrrolines **1a-1i** were prepared according to literature method,[1] and their characterization data match the reported data.

Synthesis of imines 1l and 1m



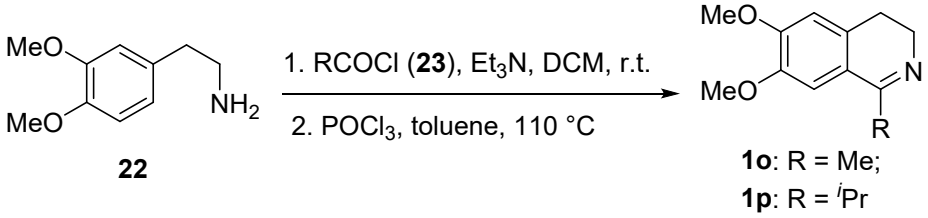
To a mixture of aldehyde **20** (2.0 mmol), magnesium sulfate (963 mg, 8.0 mmol) and DCM (10 mL), was added slowly amine **21** (8.0 mmol). After addition, the reaction was stirred at room temperature until completion according to TLC. Water (20 mL) was added, and the separated aqueous phase was extract with DCM (30 mL × 2). The combined organic extracts were washed with brine (15 mL × 2), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The crude product was used directly for the next step without further purification.

Synthesis of dihydroisoquinoline 1n



A mixture of (3,4-dimethoxyphenyl)ethanamine **22** (0.54 g, 3.0 mmol) and ethyl formate (10 mL) was stirred at room temperature for 12 h. The bulk of excess ethyl formate was evaporated in vacuo. The residue was dissolved in toluene (10 mL). The mixture was charged into a 30 mL sealed tube. Phosphorus oxychloride (1.12 mL, 12.0 mmol) was added slowly. The resulting mixture was heated at 110 ℃ in an oil bath for 5 hours, and then cooled. An aqueous solution of sodium hydroxide (2 M) was added dropwise until pH > 7. The mixture was extracted with ethyl acetate (30 mL x 3). The combined organic extracts were washed with brine (15 mL x 2), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate) to give **1n** (0.37 g, 65% over the two steps) as an orange oil.

Synthesis of dihydroisoquinolines 1o and 1p

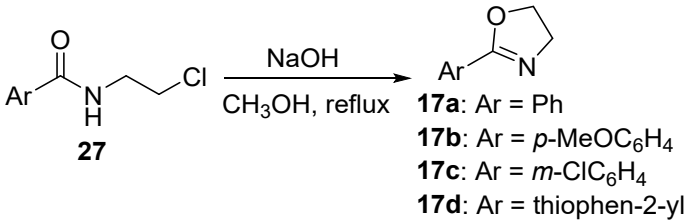


Acyl chloride **23** (3.6 mmol) was added dropwise to a mixture of (3,4-dimethoxyphenyl)ethanamine **22** (0.54 g, 3.0 mmol), triethylamine (0.5 mL, 3.6 mmol) and DCM (10 mL) at 0℃. After addition, the

resulting mixture was allowed to warm to ambient temperature and stirred for 1h. The bulk of solvent was evaporated in vacuo. The residue was dissolved in toluene (10 mL). The mixture was charged into a 30 mL sealed tube. Phosphorus oxychloride (1.12 mL, 12.0 mmol) was added slowly. The resulting mixture was heated at 110 ℃ in an oil bath for 5 hours, and then cooled. An aqueous solution of sodium hydroxide (2 M) was added dropwise until pH > 7. The mixture was extracted with ethyl acetate (30 mL x 3). The combined organic extracts were washed with brine (15 mL x 2), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give dihydroisoquinolines **1o** and **1p**.

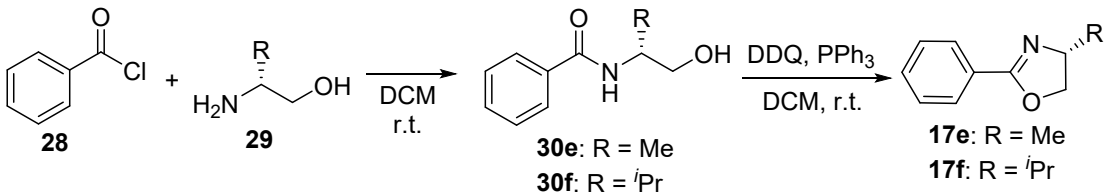
Imidazolines **13a-13h** were prepared according to literature method,[2] and their characterization data match the reported data.

Synthesis of oxazolines 17a-17d



A mixture of amide **27** (2.0 mmol), sodium hydroxide (104 mg, 2.6 mmol) and methanol (8mL) was heated at refluxed for 5 hours, and then cooled and concentrated in vacuo. The residue was partitioned between ethyl acetate (20 mL) and water (10 mL). The separated aqueous phase was extracted with ethyl acetate (20 mL x 2). The combined organic extracts were washed with brine (10 mL x 2), then dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography on silica gel to provide oxazolines **17a-17d**.

Synthesis of oxazolines 17e and 17f



Step1: To a solution of amino alcohol **29** (5.0 mmol) in DCM (20 mL) at 0℃, was added dropwise benzoyl chloride **28** (0.64 mL, 5.5 mmol). After addition, the resulting mixture was allowed to warm to ambient temperature and stirred for 3 hours. Water (15 mL) was added. The mixture was extract with DCM (30 mL × 3). The combined organic extracts were washed with brine (15 mL x 2), then dried over Na_2SO_4, filtered and evaporated. The residue was purified by flash chromatography on silica gel to yield amides **30e**, **30f**.

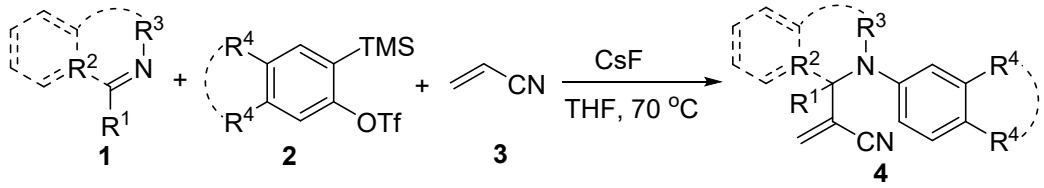
Step 2: DDQ (0.68 g, 3.0 mmol) was added to a solution of the amide **30e**/**30f** (2.0 mmol) and triphenylphosphine (0.78 g, 3.0 mmol) in DCM (20 mL). After addition, the reaction was stirred at

ambient temperature for 10 min before being quenched by the addition of saturated aqueous sodium carbonate (20 mL). The mixture was extract with DCM (30 mL × 3). The combined organic extracts were washed with brine (15 mL x 2), then dried over Na_2SO_4, filtered and evaporated. The residue was purified by column chromatography on silica gel to yield oxazolines **17e**, **17f**.

Compounds **2a-2c** were prepared according to literature method,[3] and their characterization data match the reported data.

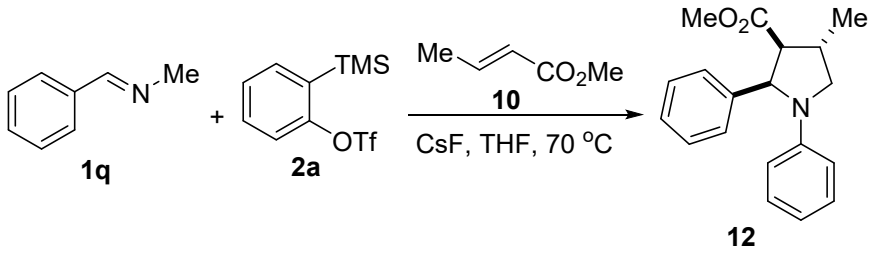
Part 5. Procedure for the three-component reactions

General procedure for the three-component coupling reaction of pyrroline/imine/dihydroisoquinoline, aryne, and acrylonitrile for the synthesis of 4a-4p



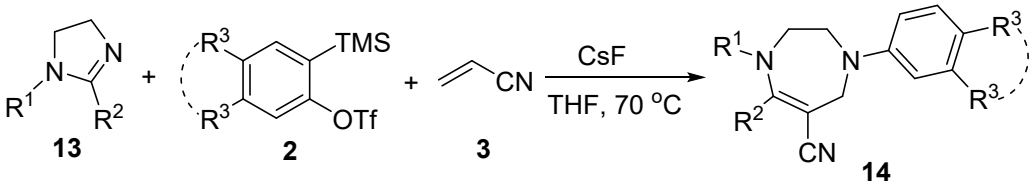
To a 15 mL Schlenk tube equipped with a stir bar, was charged imine **1** (0.2 mmol) and aryne precursor **2** (0.4 mmol). The system was degassed and refilled with nitrogen three times. Tetrahydrofuran (0.5 mL) and arcylonitrile **3** (0.5 mL) were added via syringe. Subsequently, CsF (0.12 g, 0.8 mmol) was added quickly. The tube was sealed and the mixture was heated at 70 ℃ for 10 hours before being cooled and evaporated. The residue was purified by column chromatography on silica gel to give the three-component coupling products **4a**-**4p**.

Procedure for the three-component coupling reaction of imine 1q, aryne, and methyl crotonate 10 for the synthesis of pyrrolidine-3-carboxylate 12



To a 15 mL Schlenk tube equipped with a stir bar, was charged imine **1q** (34 mg, 0.29 mmol) and aryne precursor **2a** (128 mg, 0.43 mmol). The system was degassed and refilled with nitrogen three times. Tetrahydrofuran (1.0 mL) and methyl crotonate **10** (1.0 mL) were added via syringe. Subsequently, CsF (130 mg, 0.86 mmol) was added quickly. The tube was sealed and the mixture was heated at 70 ℃ for 5 hours before being cooled and evaporated. The residue was purified by column chromatography on silica gel (0.5% ethyl acetate in petroleum ether) to give compound **12** (34 mg, 40%) as a white solid.

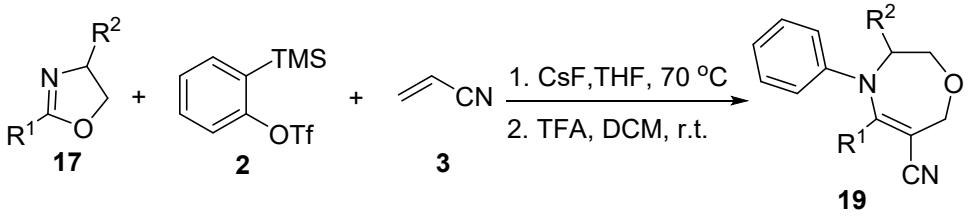
General procedure for the three-component coupling reaction of imidazoline, aryne, and acrylonitrile for the synthesis of 14a-14j



To a 15 mL Schlenk tube equipped with a stir bar, was charged imidazoline **13** (0.2 mmol) and aryne precursor **2** (0.4 mmol). The system was degassed and refilled with nitrogen three times. Tetrahydrofuran (0.5 mL) and arcylonitrile **3** (0.5 mL) were added via syringe. Subsequently, CsF (0.12 g, 0.8 mmol) was

added quickly. The tube was sealed and the mixture was heated at 70 ℃ for 4 hours before being cooled and evaporated. The residue was purified by column chromatography on silica gel to give the three-component coupling products **14a**-**14k**.

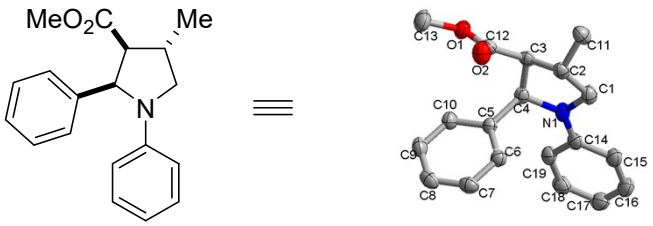
General procedure for the synthesis of tetrahydro-1,4-oxazepines 19a-19f



To a 15 mL Schlenk tube equipped with a stir bar, was charged oxazoline **17** (0.2 mmol) and aryne precursor **2** (0.4 mmol). The system was degassed and refilled with nitrogen three times. Tetrahydrofuran (0.5 mL) and arcylonitrile **3** (0.5 mL) were added via syringe. Subsequently, CsF (0.12 g, 0.8 mmol) was added quickly. The tube was sealed and the mixture was heated at 70 ℃ for 10 hours before being cooled and evaporated. The residue was partitioned between water (10 mL) and DCM (15 mL). The separated aqueous phase was extracted with DCM (15 mL × 2). The combined organic extracts were concentrated until ~5 mL of solvent left. TFA (15 μL, 0.2 mmol) was added. The mixture was stirred at ambient temperature for 10 mins, and then concentrated. The residue was purified by column chromatography on silica gel to give the title compounds **19a**-**19f**.

Part 6. Crystal data and structure refinement

Compound 12



X-ray structure

CCDC: 2189779

Bond precision: C-C = 0.0027Å Wavelength = 1.54184

Cell: a = 10.8216 (3) b = 6.14060(16) c = 24.5560 (5)

alpha = 90 beta = 98.460 (2) gamma = 90

Temperature: 293 K

	Calculated	Reported
Volume	1614.02 (7)	1614.02 (7)
Space group	P 21/n	P 21/n
Hall group	-P 2yn	-P 2yn
Moiety formula	C19 H21 N O2	C19 H21 N O2
Sum formula	C19 H21 N O2	C19 H21 N O2
Mr	295.37	295.37
Dx,g cm-3	1.215	1.216
Z	4	4
Mu (mm-1)	0.620	0.620
F000	632.0	632.0
F000'	633.80	
h, k, lmax	12, 7, 29	12, 7, 29
Nref	2882	2882
Tmin, Tmax	0.911, 0.940	
Tmin'	0.911	

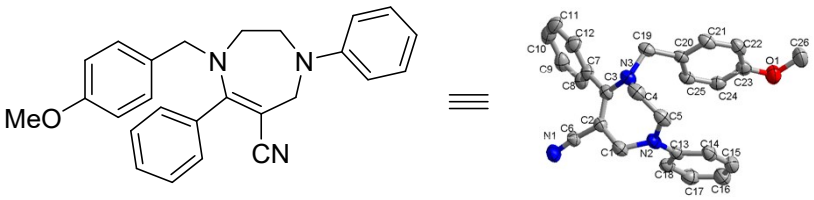
Correction method = Not given

Data completeness = 1.000 Theta(max) = 67.071

R(reflections) = 0.0439 (2224) wR2(reflections) = 0.1260(2882)

S = 1.031 Npar= 201

Compound 14h



X-ray structure

CCDC: 2190017

Bond precision:	C-C = 0.0046 A		Wavelength = 1.54184
Cell:	a=9.7602 (3)	b = 10.5608 (4)	c = 21.6908 (8)
	alpha = 84.366 (3)	beta = 81.071 (3)	gamma = 89.652 (3)
Temperature:	293 K		

	Calculated	Reported
Volume	2197.93 (14)	2197.93 (13)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C26 H25 N3 O	C26 H25 N3 O
Sum formula	C26 H25 N3 O	C26 H25 N3 O
Mr	395.49	395.49
Dx,g cm-3	1.195	1.195
Z	4	4
Mu (mm-1)	0.578	0.578
F000	840.0	840.0
F000'	842.30	
h, k, lmax	11, 12, 25	11, 12, 25
Nref	7865	7859
Tmin, Tmax	0.933, 0.966	
Tmin'	0.912	

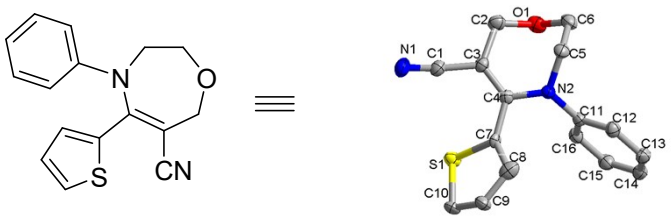
Correction method = Not given

Data completeness = 0.999 Theta(max) = 67.079

R(reflections) = 0.0538(4660) wR2(reflections) = 0.1695 (7859)

S = 1.015 Npar = 543

Compound 19d



X-ray structure

CCDC: 2190240

Bond precision: C-C = 0.0023 A Wavelength = 1.54184

Cell: a = 19.4233 (6) b = 5.92585 (16) c = 24.5767 (7)

alpha = 90 beta = 93.764 (3) gamma = 90

Temperature: 293 K

	Calculated	Reported
Volume	2822.67 (14)	2822.67 (14)
Space group	C 2/c	C 2/c
Hall group	-C 2yc	-C 2yc
Moiety formula	C16 H14 N2 O S	C16 H14 N2 O S
Sum formula	C16 H14 N2 O S	C16 H14 N2 O S
Mr	282.35	282.35
Dx,g cm-3	1.329	1.329
Z	8	8
Mu (mm-1)	2.003	2.003
F000	1184.0	1184.0
F000'	1189.69	
h, k, lmax	22, 7, 29	22, 7, 29
Nref	2512	2510
Tmin, Tmax	0.778, 0.835	
Tmin'	0.705	

Correction method = Not given

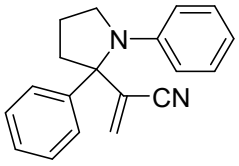
Data completeness = 0.999 Theta(max) = 67.076

R(reflections) = 0.0378(2138) wR2(reflections) = 0.1041(2510)

S = 1.046 Npar= 248

Part 7. Characterization data of the products

2-(1,2-Diphenylpyrrolidin-2-yl)acrylonitrile (4a)



The crude product was purified by column chromatography on silica gel (0.3% ethyl acetate in petroleum ether) to give **4a** (42 mg, 77% yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.25 (m, 5H, overlapped with the peak of chloroform), 7.10–7.05 (m, 2H), 6.69–6.65 (m, 1H), 6.50–6.48 (m, 2H), 6.21 (s, 1H), 6.01 (s, 1H), 3.78–3.66 (m, 2H), 2.81 (ddd, J = 12.8, 9.2, 6.4 Hz, 1H), 2.44–2.38 (m, 1H), 2.05–1.97 (m, 1H), 1.93–1.82 (m, 1H) ppm;

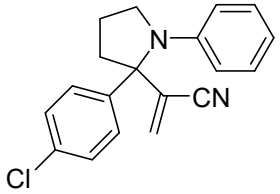
^{13}C NMR (100 MHz, $CDCl_3$): δ 144.7, 139.9, 133.6, 128.3, 128.24, 128.18, 127.4, 127.0, 118.6, 117.1,

114.7, 72.6, 50.5, 45.5, 22.2 ppm;

IR (neat): ν_{max} 3069, 2919, 2839, 2230, 1598, 1501, 1480 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{19}H_{19}N_2^+$ $[M + H]^+$ 275.1543, found 275.1544.

2-(2-(4-Chlorophenyl)-1-phenylpyrrolidin-2-yl)acrylonitrile (4b)



The crude product was purified by column chromatography on silica gel (1.2% ethyl acetate in petroleum ether) to give **4b** (37 mg, 60% yield) as a colorless oil.

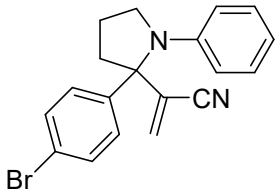
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.24 (m, 4H, overlapped with the peak of chloroform), 7.12–7.07 (m, 2H), 6.72–6.68 (m, 1H), 6.48–6.44 (m, 2H), 6.22 (s, 1H), 5.98 (s, 1H), 3.77–3.67 (m, 2H), 2.81 (ddd, J = 12.8, 9.2, 6.4 Hz, 1H), 2.38–2.32 (m, 1H), 2.06–1.98 (m, 1H), 1.92–1.82 (m, 1H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 144.4, 138.6, 133.7, 133.4, 129.6, 128.5, 128.4, 126.6, 118.3, 117.4, 114.7, 72.2, 50.5, 45.5, 22.2 ppm;

IR (neat): ν_{max} 2921, 2852, 2218, 1596, 1501 cm^{-1};

HRMS (ESI$^+$) calcd for $C_{19}H_{18}{}^{35}ClN_2^+$ $[M + H]^+$ 309.1153, found 309.1157.

2-(2-(4-Bromophenyl)-1-phenylpyrrolidin-2-yl)acrylonitrile (4c)



The crude product was purified by column chromatography on silica gel (0.5% ethyl acetate in petroleum ether) to give **4c** (53 mg, 76% yield) as a colorless oil.

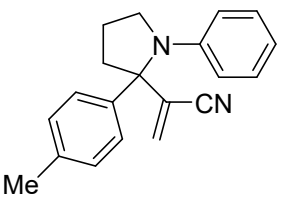
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.44 (m, 2H), 7.22–7.18 (m, 2H), 7.11–7.07 (m, 2H), 6.70 (t, J = 7.4 Hz, 1H), 6.46 (d, J = 8.0 Hz, 2H), 6.22 (s, 1H), 5.98 (s, 1H), 3.77–3.67 (m, 2H), 2.80 (ddd, J = 12.8, 9.2, 6.4 Hz, 1H), 2.38–2.32 (m, 1H), 2.07–1.98 (m, 1H), 1.93–1.82 (m, 1H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 144.4, 139.2, 133.7, 131.4, 130.0, 128.5, 126.5, 121.6, 118.3, 117.5, 114.7, 72.3, 50.6, 45.5, 22.2 ppm;

IR (neat): ν_{max} 2845, 2226, 1594, 1501, 1483 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{19}H_{18}{}^{79}BrN_2^+$ $[M + H]^+$ 353.0648, found 353.0650.

2-(1-Phenyl-2-(*p*-tolyl)pyrrolidin-2-yl)acrylonitrile (4d)



The crude product was purified by column chromatography on silica gel (1.0% ethyl acetate in petroleum ether) to give **4d** (47 mg, 82% yield) as a colorless oil.

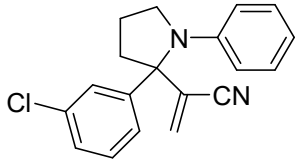
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20–7.18 (m, 2H), 7.14–7.05 (m, 4H), 6.69–6.65 (m, 1H), 6.51–6.48 (m, 2H), 6.19 (s, 1H), 6.00 (s, 1H), 3.77–3.66 (m, 2H), 2.78 (ddd, J = 12.8, 9.2, 6.4 Hz, 1H), 2.41–2.35 (m, 1H), 2.33 (s, 3H), 2.03–1.96 (m, 1H), 1.92–1.82 (m, 1H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 144.8, 137.2, 136.9, 133.5, 128.9, 128.3, 128.1, 127.2, 118.6, 117.0, 114.7, 72.4, 50.5, 45.4, 22.2, 21.0 ppm;

IR (neat): ν_{max} 2951, 2918, 2220, 1594, 1501, 1477 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{20}H_{21}N_2^+$ $[M + H]^+$ 289.1699, found 289.1700.

2-(2-(3-Chlorophenyl)-1-phenylpyrrolidin-2-yl)acrylonitrile (4e)



The crude product was purified by column chromatography on silica gel (1.2% ethyl acetate in petroleum ether) to give **4e** (40 mg, 65% yield) as a colorless oil.

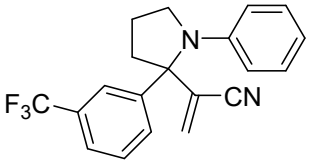
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.30 (m, 1H), 7.27–7.20 (m, 3H, overlapped with the peak of chloroform), 7.13–7.07 (m, 2H), 6.73–6.69 (m, 1H), 6.49–6.47 (m, 2H), 6.22 (s, 1H), 5.99 (s, 1H), 3.78–3.68 (m, 2H), 2.82 (ddd, J = 12.8, 9.2, 6.2 Hz, 1H), 2.41–2.35 (m, 1H), 2.07–1.98 (m, 1H), 1.93–1.83 (m, 1H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 144.4, 142.4, 134.4, 133.8, 129.5, 128.5, 128.3, 127.8, 126.46, 126.45, 118.2, 117.5, 114.8, 72.4, 50.6, 45.5, 22.2 ppm;

IR (neat): ν_{max} 3071, 2924, 2830, 2220, 1597, 1495, 1478, cm^{-1};

HRMS (ESI$^+$): calcd for $C_{19}H_{18}{}^{35}ClN_2^+$ $[M + H]^+$ 309.1153, found 309.1156.

2-(1-Phenyl-2-(3-(trifluoromethyl)phenyl)pyrrolidin-2-yl)acrylonitrile (4f)



The crude product was purified by column chromatography on silica gel (0.5% ethyl acetate in petroleum ether) to give **4f** (38 mg, 56% yield) as a colorless oil.

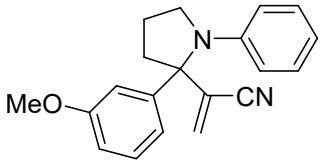
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58–7.52 (m, 3H), 7.48–7.44 (m, 1H), 7.12–7.07 (m, 2H), 6.73–6.69 (m, 1H), 6.48–6.45 (m, 2H), 6.24 (s, 1H), 5.96 (s, 1H), 3.81–3.71 (m, 2H), 2.87 (ddd, J = 12.8, 9.2, 6.4 Hz, 1H), 2.42–2.36 (m, 1H), 2.10–2.01 (m, 1H), 1.93–1.82 (m, 1H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 144.3, 141.4, 133.7, 131.7, 130.6 (q, $J_{F\text{-}C}$ = 31.2 Hz), 128.9, 128.5, 126.5, 124.9 (q, $J_{F\text{-}C}$ = 3.8 Hz), 124.5 (q, $J_{F\text{-}C}$ = 3.8 Hz), 123.9 (q, $J_{F\text{-}C}$ = 270.7 Hz), 118.2, 117.7, 114.9, 72.5, 50.6, 45.6, 22.3 ppm;

IR (neat): ν_{max} 3064, 2926, 2847, 2226, 1597, 1504, 1487 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{20}H_{18}F_3N_2^+$ $[M + H]^+$ 343.1417, found 343.1419.

2-(2-(3-Methoxyphenyl)-1-phenylpyrrolidin-2-yl)acrylonitrile (4g)



The crude product was purified by column chromatography on silica gel (0.8% ethyl acetate in petroleum ether) to give **4g** (47 mg, 78% yield) as a colorless oil.

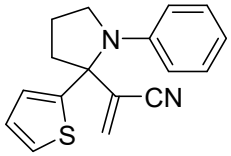
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.23 (m, 1H, overlapped with the peak of chloroform), 7.11–7.05 (m, 2H), 6.92–6.89 (m, 1H), 6.88–6.87 (m, 1H), 6.82–6.79 (m, 1H), 6.70–6.66 (m, 1H), 6.52–6.49 (m, 2H), 6.21 (s, 1H), 6.03 (s, 1H), 3.75 (s, 3H), 3.77–3.66 (m, 2H), 2.80 (ddd, J = 12.8, 9.2, 6.4 Hz, 1H), 2.44–2.38 (m, 1H), 2.04–1.96 (m, 1H), 1.95–1.84 (m, 1H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 144.7, 141.8, 133.7, 129.2, 128.3, 126.8, 120.6, 118.6, 117.2, 114.74, 114.68, 112.2, 72.6, 55.3, 50.6, 45.4, 22.3 ppm;

IR (neat): ν_{max} 2944, 2833, 2219, 1597, 1501, 1483, 1459 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{20}H_{21}N_2O^+$ $[M + H]^+$ 305.1649, found 305.1650.

2-(1-Phenyl-2-(thiophen-2-yl)pyrrolidin-2-yl)acrylonitrile (4h)



The crude product was purified by column chromatography on silica gel (0.3% ethyl acetate in petroleum ether) to give **4h** (45 mg, 81% yield) as a colorless oil.

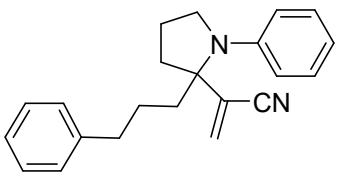
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (dd, J = 5.1, 1.2 Hz, 1H), 7.14 (dd, J = 3.6, 1.2 Hz, 1H), 7.11–7.07 (m, 2H), 6.94 (dd, J = 5.1, 3.6 Hz, 1H), 6.71–6.67 (m, 1H), 6.60–6.57 (m, 2H), 6.24 (s, 1H), 6.14 (s, 1H), 3.74–3.62 (m, 2H), 2.81–2.75 (m, 1H), 2.51–2.44 (m, 1H), 2.07–1.97 (m, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 145.7, 144.6, 133.4, 128.4, 126.8, 126.5, 126.2, 125.5, 118.2, 117.5, 114.6, 70.2, 50.2, 46.8, 22.3 ppm;

IR (neat): ν_{max} 3097, 2922, 2851, 2229, 1596, 1510 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{17}H_{17}N_2S^+$ $[M + H]^+$ 281.1097, found 281.1107.

2-(1-Phenyl-2-(3-phenylpropyl)pyrrolidin-2-yl)acrylonitrile (4i)



The crude product was purified by column chromatography on silica gel (0.7% ethyl acetate in petroleum

ether) to give **4i** (43 mg, 68% yield) as a colorless oil.

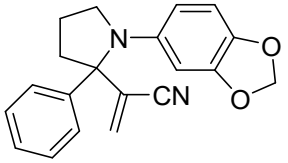
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22–7.11 (m, 5H), 6.95–6.92 (m, 2H), 6.76–6.72 (m, 1H), 6.59–6.57 (m, 2H), 6.00 (s, 1H), 5.74 (s, 1H), 3.49–3.46 (m, 2H), 2.45–2.35 (m, 3H), 2.26–2.18 (m, 1H), 2.07–1.97 (m, 2H), 1.95–1.81 (m, 2H), 1.60–1.47 (m, 1H), 1.27–1.17 (m, 1H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 145.1, 141.6, 130.2, 128.9, 128.24, 128.23, 128.0, 125.7, 118.3, 117.1, 113.9, 68.1, 51.5, 38.2, 35.6, 32.9, 24.1, 21.2 ppm;

IR (neat): ν_{max} 3030, 2944, 2214, 1594, 1501 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{22}H_{25}N_2^+$ $[M + H]^+$ 317.2012, found 317.2015.

2-(1-(Benzo[*d*][1,3]dioxol-5-yl)-2-phenylpyrrolidin-2-yl)acrylonitrile (4j)



The crude product was purified by column chromatography on silica gel (2.5% ethyl acetate in petroleum ether) to give **4j** (49 mg, 77% yield) as a colorless oil.

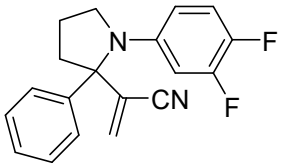
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.25 (m, 5H, overlapped with the peak of chloroform), 6.59 (d, J = 8.4 Hz, 1H), 6.21 (s, 1H), 6.09 (d, J = 2.4 Hz, 1H), 6.00 (s, 1H), 5.95 (dd, J = 8.4, 2.4 Hz, 1H), 5.82 (d, J = 1.6 Hz, 1H), 5.80 (d, J = 1.6 Hz, 1H), 3.73–3.61 (m, 2H), 2.79 (ddd, J = 12.8, 9.6, 6.4 Hz, 1H), 2.41–2.36 (m, 1H), 2.03–1.95 (m, 1H), 1.90–1.79 (m, 1H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 147.4, 140.5, 139.9, 139.2, 133.5, 128.3, 128.2, 127.5, 127.2, 118.6, 107.9, 106.6, 100.5, 97.5, 72.8, 51.2, 45.4, 22.3 ppm;

IR (neat): ν_{max} 2920, 2221, 1610, 1503, 1483, 1222, 1037 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{20}H_{19}N_2O_2^+$ $[M + H]^+$ 319.1441, found 319.1441.

2-(1-(3,4-Difluorophenyl)-2-phenylpyrrolidin-2-yl)acrylonitrile (4k)



The crude product was purified by column chromatography on silica gel (0.7% ethyl acetate in petroleum ether) to give **4k** (30 mg, 48% yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.25 (m, 5H, overlapped with the peak of chloroform), 6.86 (dt, J = 10.4, 9.2 Hz, 1H), 6.28 (ddd, J = 13.6, 6.8, 2.8 Hz, 1H), 6.24 (s, 1H), 6.14 (dtd, J = 9.2, 3.2, 1.6 Hz, 1H), 6.00 (s, 1H), 3.72–3.61 (m, 2H), 2.81 (ddd, J = 12.8, 9.6, 6.4 Hz, 1H), 2.45–2.39 (m, 1H), 2.06–1.98 (m, 1H), 1.93–1.82 (m, 1H) ppm;

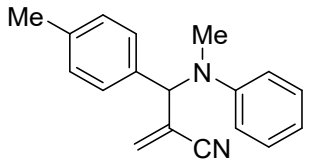
^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0 (dd, $J_{F\text{-}C}$ = 242.2, 13.0 Hz), 142.9 (dd, $J_{F\text{-}C}$ = 237.2, 13.2 Hz), 141.8 (dd, $J_{F\text{-}C}$ = 8.5, 2.0 Hz), 139.1, 133.7, 128.5, 128.1, 127.8, 126.8, 118.2, 116.6 (dd, $J_{F\text{-}C}$ = 17.6, 1.8

Hz), 109.6 (dd, $J_{F\text{-}C}$ = 5.2, 3.0 Hz), 103.4 (d, $J_{F\text{-}C}$ = 21.5 Hz), 72.9, 51.0, 45.3, 22.2 ppm;

IR (neat): ν_{max} 2952, 2222, 1598, 1516, 1490, 1240 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{19}H_{17}F_2N_2^+$ $[M + H]^+$ 311.1355, found 311.1357.

2-((Methyl(phenyl)amino)(p-tolyl)methyl)acrylonitrile (4l)



The crude product was purified by column chromatography on silica gel (1.0% ethyl acetate in petroleum ether) to give **4l** (21 mg, 40% yield) as a colorless oil.

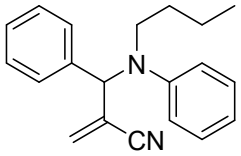
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.14 (m, 6H, overlapped with the peak of chloroform), 6.83 –6.79 (m, 3H), 6.20 (d, J = 1.4 Hz, 1H), 5.91 (d, J = 1.4 Hz, 1H), 5.59 (s, 1H), 2.73 (s, 3H), 2.36 (s, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1, 138.2, 133.0, 132.6, 129.6, 129.3, 128.3, 122.8, 118.14, 118.09, 113.5, 65.8, 33.9, 21.1 ppm;

IR (neat): ν_{max} 3024, 2920, 2220, 1594, 1501 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{18}H_{19}N_2^+$ $[M + H]^+$ 263.1543, found 263.1547.

2-((Butyl(phenyl)amino)(phenyl)methyl)acrylonitrile (4m)



The crude product was purified by column chromatography on silica gel (0.7% ethyl acetate in petroleum ether) to give **4m** (30 mg, 52% yield) as a colorless oil.

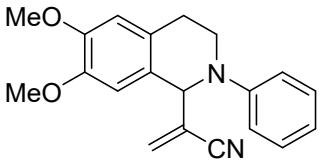
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.32 (m, 5H), 7.27–7.23 (m, 2H), 6.85–6.81 (m, 3H), 6.14 (d, J = 1.2 Hz, 1H), 5.86 (d, J = 1.2 Hz, 1H), 5.52 (s, 1H), 3.15–3.10 (m, 2H), 1.50–1.41 (m, 1H), 1.16–0.99 (m, 3H), 0.75 (t, J = 7.2 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 147.9, 136.4, 132.6, 129.2, 129.0, 128.8, 128.5, 123.0, 118.9, 118.1, 115.6, 66.6, 47.9, 30.0, 20.1, 13.7 ppm;

IR (neat): ν_{max} 2957, 2929, 2871, 2226, 1600, 1501 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{20}H_{23}N_2^+$ $[M + H]^+$ 291.1856, found 291.1857.

2-(6,7-Dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acrylonitrile (4n)



The crude product was purified by column chromatography on silica gel (5.0% ethyl acetate in petroleum ether) to give **4n** (49 mg, 76% yield) as a white solid.

m.p. 164–166 °C;

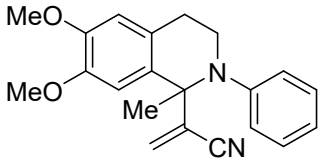
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.26 (m, 2H, overlapped with the peak of chloroform), 6.90–6.83 (m, 3H), 6.74 (s, 1H), 6.69 (s, 1H), 5.98 (d, J = 1.2 Hz, 1H), 5.83 (d, J = 1.2 Hz, 1H), 5.21 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.70 (ddd, J = 11.6, 6.4, 4.8 Hz, 1H), 3.51 (ddd, J = 12.0, 8.0, 4.8 Hz, 1H), 2.93 (ddd, J = 16.0, 6.4, 4.8 Hz, 1H), 2.83 (ddd, J = 16.0, 8.0, 4.8 Hz, 1H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 148.7, 148.6, 147.6, 130.2, 129.3, 128.1, 125.2, 124.2, 119.0, 118.1, 114.8, 111.1, 110.8, 62.2, 56.1, 55.9, 43.5, 27.2 ppm;

IR (neat): ν_{max} 2917, 2221, 1597, 1502, 1493 cm^{-1};

HRMS (ESI$^+$): calcd: for $C_{20}H_{21}N_2O_2^+$ $[M + H]^+$ 321.1598, found 321.1602.

2-(6,7-Dimethoxy-1-methyl-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acryl-onitrile (4o)



The crude product was purified by column chromatography on silica gel (10.0% ethyl acetate in petroleum ether) to give **4o** (35 mg, 52% yield) as a white solid.

m.p. 161–163 ℃;

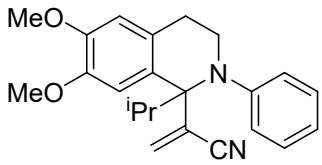
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.25 (m, 2H, overlapped with the peak of chloroform), 7.19 (d, J = 7.4 Hz, 2H), 7.13 (t, J = 7.4 Hz, 1H), 6.64 (s, 1H), 6.51 (s, 1H), 5.95 (s, 1H), 5.54 (s, 1H), 3.89 (s, 3H), 3.82 (s, 3H), 3.44–3.42 (m, 2H), 2.99 (dt, J = 16.0, 6.4 Hz, 1H), 2.81 (dt, J = 16.0, 4.8 Hz, 1H), 1.53 (s, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 148.8, 148.2, 147.4, 133.3, 129.6, 128.6, 128.4, 128.3, 127.6, 124.9, 118.6, 111.4, 110.3, 63.9, 56.1, 55.8, 46.5, 28.9, 22.5 ppm;

IR (neat): ν_{max} 2917, 2226, 1597, 1515, 1493, 1250 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{21}H_{23}N_2O_2^+$ $[M + H]^+$ 335.1754, found 335.1759.

2-(1-Isopropyl-6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acryl-onitrile (4p)



The crude product was purified by column chromatography on silica gel (10.0% ethyl acetate in petroleum ether) to give **4p** (48 mg, 67% yield) as a white solid.

m.p. 140–142 ℃;

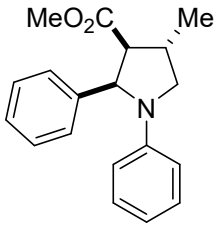
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.28 (m, 2H), 7.20–7.15 (m, 3H), 6.65 (s, 1H), 6.52 (s, 1H), 6.01 (s, 1H), 5.51 (s, 1H), 3.90 (s, 3H), 3.81 (s, 3H), 3.48 (td, J = 11.6, 2.4 Hz, 1H), 3.19 (ddd, J = 11.6, 4.4, 2.4 Hz, 1H), 3.09 (ddd, J = 15.6, 11.6, 4.4 Hz, 1H), 2.83–2.73 (m, 1H), 2.59 (dt, J = 15.6, 2.4 Hz, 1H), 1.06 (d, J = 6.8 Hz, 3H), 0.97 (d, J = 6.8 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 147.9, 145.9, 131.9, 131.8, 128.5, 127.7, 127.5, 125.6, 125.1, 118.7, 112.6, 110.9, 70.5, 56.0, 55.7, 48.4, 34.8, 31.3, 19.9, 17.6 ppm;

IR (neat): ν_{max} 2921, 2851, 2799, 2215, 1593, 1514, 1251, 1201, 1082, 1013 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{22}H_{27}N_2O_2^+$ $[M + H]^+$ 363.2067, found 363.2066.

***cis,trans*-Methyl 4-methyl-1,2-diphenylpyrrolidine-3-carboxylate (12)**



34 mg, 40% yield, white solid.

m.p. 91–93 °C;

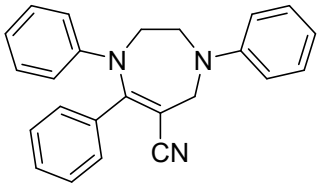
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.11 (m, 7H), 6.65 (t, J = 7.2 Hz, 1H), 6.45 (d, J = 8.0 Hz, 2H), 4.99 (d, J = 8.4 Hz, 1H), 3.92 (m, 1H), 3.41 (s, 3H), 3.12-3.06 (m, 2H), 3.01-2.89 (m, 1H), 1.15 (d, J = 6.4 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 146.4, 140.2, 129.2, 128.5, 127.8, 126.9, 116.5, 112.2, 65.7, 57.4, 55.3, 51.6, 32.5, 16.4 ppm;

IR (neat): ν_{max} 1739, 1504, 1259, 1077, 1019 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{19}H_{22}NO_2^+$ $[M + H]^+$ 296.1645, found 296.1648.

1,4,7-Triphenyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepine-6-carbonitrile (14a)



The crude product was purified by column chromatography on silica gel (10.0% ethyl acetate in petroleum ether) to give **14a** (56 mg, 80% yield) as a white solid.

m.p. 127–129 °C;

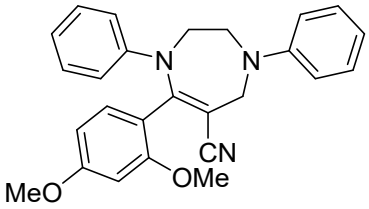
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.36 (m, 2H), 7.27–7.23 (m, 2H, overlapped with the peak of chloroform), 7.18–7.14 (m, 3H), 6.94–6.90 (m, 2H), 6.83–6.76 (m, 4H), 6.53–6.51 (m, 2H), 4.45 (s, 2H), 4.30 (t, J = 5.6 Hz, 2H), 3.64 (t, J = 5.6 Hz, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.3, 148.5, 144.0, 135.0, 130.3, 130.0, 129.3, 128.7, 128.1, 125.5, 124.5, 121.7, 117.9, 113.1, 86.8, 54.5, 49.2, 49.0 ppm;

IR (neat): ν_{max} 3053, 2876, 2177, 1557, 1494, 1377, 1219, 1164 cm^{-1};

HRMS (ESI): calcd for $C_{24}H_{21}N_3^+$ $(M+H)^+$ 352.1808, found 352.1812.

7-(2,4-Dimethoxyphenyl)-1,4-diphenyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepine-6-carbonitrile (14b)



The crude product was purified by column chromatography on silica gel (16.7% ethyl acetate in petroleum ether) to give **14b** (55 mg, 67% yield) as a white solid.

m.p. 74–77 °C;

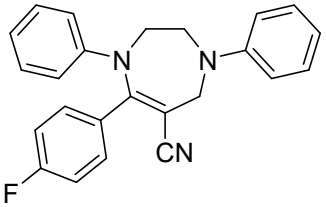
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.24 (m, 2H, overlapped with the peak of chloroform), 7.11 (d, J = 8.5 Hz, 1H), 6.95–6.90 (m, 2H), 6.87–6.77 (m, 4H), 6.57–6.53 (m, 2H), 6.29 (dd, J = 8.5, 2.3 Hz, 1H), 6.16 (d, J = 2.3 Hz, 1H), 4.40 (s, 2H), 4.24–4.21 (m, 2H), 3.72 (s, 3H), 3.69 (s, 3H), 3.68–3.65 (m, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 158.4, 158.3, 148.6, 144.5, 133.0, 129.1, 128.2, 125.3, 124.5, 122.2, 117.6, 116.9, 113.5, 104.2, 98.4, 85.4, 55.3, 55.2, 54.1, 49.8, 48.8 ppm;

IR (neat): ν_{max} 2928, 2184, 1597, 1578, 1506, 1493, 1211 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{26}H_{25}N_3O_2^+$ $[M + H]^+$ 412.2020, found 412.2024.

7-(4-Fluorophenyl)-1,4-diphenyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepine-6-carbonitrile (14c)



The crude product was purified by column chromatography on silica gel (10.0% ethyl acetate in petroleum ether) to give **14c** (53 mg, 72% yield) as a white solid.

m.p. 134–136 °C;

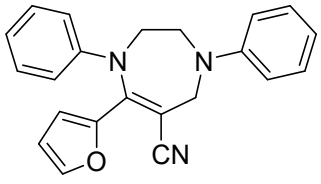
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.35 (m, 2H), 7.27–7.23 (m, 2H, overlapped with the peak of chloroform), 6.94 (t, J = 7.6 Hz, 2H), 6.88–6.77 (m, 6H), 6.50–6.48 (m, 2H), 4.44 (s, 2H), 4.28 (t, J = 5.6 Hz, 2H), 3.64 (t, J = 5.6 Hz, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 163.3 (d, $J_{F\text{-}C}$ = 249.3 Hz), 160.1, 148.4, 143.8, 132.2 (d, $J_{F\text{-}C}$ = 8.7 Hz), 131.0 (d, $J_{F\text{-}C}$ = 3.2 Hz), 129.3, 128.8, 125.6, 124.8, 121.6, 117.9, 115.4 (d, $J_{F\text{-}C}$ = 21.8 Hz), 113.0, 86.7, 54.5, 49.1, 48.9 ppm;

IR (neat): ν_{max} 2965, 2919, 2179, 1594, 1562, 1501, 1495, 1218 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{24}H_{21}FN_3^+$ $[M + H]^+$ 370.1714, found 370.1718.

7-(Furan-2-yl)-1,4-diphenyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepine-6-carbonitrile (14d)



The crude product was purified by column chromatography on silica gel (6.3% ethyl acetate in petroleum ether) to give **14d** (47 mg, 69% yield) as a white solid.

m.p. 120–122 ℃;

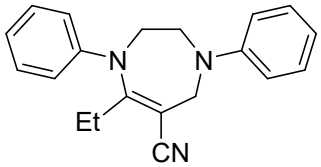
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24–7.20 (m, 3H), 7.02 (t, J = 7.8 Hz, 2H), 6.90 (t, J = 7.2 Hz, 1H), 6.78–6.75 (m, 3H), 6.69 (d, J = 3.6 Hz, 1H), 6.61 (d, J = 8.0 Hz, 2H), 6.26 (dd, J = 3.6, 1.8 Hz, 1H), 4.41 (s, 2H), 4.18 (t, J = 5.6 Hz, 2H), 3.58 (t, J = 5.6 Hz, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 149.5, 148.4, 147.3, 144.5, 143.8, 129.3, 128.9, 124.2, 123.5, 120.9, 118.1, 116.0, 113.5, 111.6, 86.4, 53.4, 49.6, 48.9 ppm;

IR (neat): ν_{max} 2939, 2184, 1596, 1555, 1489 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{22}H_{20}N_3O^+$ $[M + H]^+$ 342.1601, found 342.1605.

7-Ethyl-1,4-diphenyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepine-6-carbonitrile (14e)



The crude product was purified by column chromatography on silica gel (10.0% ethyl acetate in petroleum ether) to give **14e** (40 mg, 67% yield) as a white solid.

m.p. 68–70 ℃;

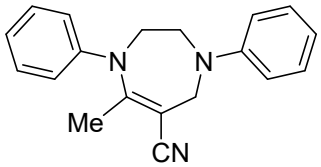
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25–7.17 (m, 4H), 7.14–7.10 (m, 1H), 6.77 (tt, J = 7.4, 1.0 Hz, 1H), 6.73–6.70 (m, 4H), 4.26 (s, 2H), 4.04–4.01 (m, 2H), 3.55 (t, J = 5.6 Hz, 2H), 2.28 (q, J = 7.5 Hz, 2H), 0.94 (t, J = 7.5 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 148.6, 143.9, 129.31, 129.27, 126.4, 126.0, 121.6, 117.6, 113.0, 83.6, 55.1, 49.4, 47.9, 26.7, 13.1 ppm;

IR (neat): ν_{max} 2961, 2176, 1575, 1493, 1394 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{20}H_{22}N_3^+$ $[M + H]^+$ 304.1808, found 304.1812.

7-Methyl-1,4-diphenyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepine-6-carbonitrile (14f)



The crude product was purified by column chromatography on silica gel (10.0% ethyl acetate in petroleum ether) to give **14f** (33 mg, 58% yield) as a white solid.

m.p. 106–108 ℃;

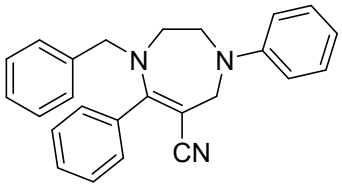
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.20 (m, 4H, overlapped with the peak of chloroform), 7.16–7.12 (m, 1H), 6.80–6.72 (m, 5H), 4.28 (s, 2H), 4.06 (t, J = 5.6 Hz, 2H), 3.59 (t, J = 5.6 Hz, 2H), 1.88 (s, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 148.6, 144.1, 129.4, 129.3, 126.4, 126.2, 122.1, 117.7, 113.0, 83.1, 54.6, 49.7, 47.8, 20.9 ppm;

IR (neat): ν_{max} 2919, 2180, 1578, 1490, 1398 cm^{-1};

HRMS (ESI^+): calcd for $C_{19}H_{20}N_3^+$ $[M + H]^+$ 290.1652, found 290.1657.

4-Benzyl-1,7-diphenyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepine-6-carbonitrile (14g)



The crude product was purified by column chromatography on silica gel (16.7% ethyl acetate in petroleum ether) to give **14g** (44 mg, 60% yield) as a colorless oil.

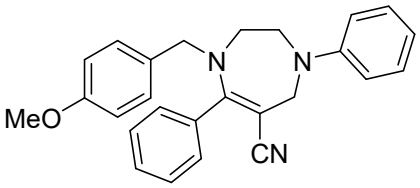
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.39 (m, 5H), 7.29–7.24 (m, 2H, overlapped with the peak of chloroform), 7.20–7.11 (m, 3H), 7.01–6.99 (m, 2H), 6.79 (t, J = 7.2 Hz, 1H), 6.75–6.73 (m, 2H), 4.35 (s, 2H), 3.97 (s, 2H), 3.77 (t, J = 5.6 Hz, 2H), 3.47 (t, J = 5.6 Hz, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8, 148.9, 137.1, 135.4, 130.3, 129.4, 129.3, 128.8, 128.7, 127.6, 127.5, 122.5, 117.7, 113.2, 81.1, 55.8, 51.0, 49.5, 48.6 ppm;

IR (neat): ν_{max} 2918, 2850, 2182, 1596, 1562, 1503, 1244 cm^{-1};

HRMS (ESI^+): calcd for $C_{25}H_{24}N_3^+$ $[M + H]^+$ 366.1965, found 366.1970.

4-(4-Methoxybenzyl)-1,7-diphenyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepine-6-carbonitrile (14h)



The crude product was purified by column chromatography on silica gel (16.7% ethyl acetate in petroleum ether) to give **14h** (55 mg, 70% yield) as a white solid.

m.p. 96–98°C;

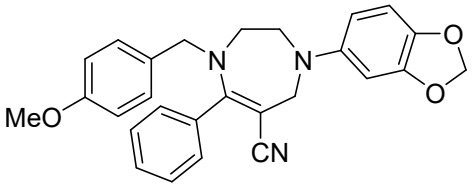
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.39 (m, 5H), 7.28–7.24 (m, 2H), 6.90–6.87 (m, 2H), 6.78 (t, J = 7.2 Hz, 1H), 6.71 (d, J = 8.0 Hz, 2H), 6.64–6.60 (m, 2H), 4.33 (s, 2H), 3.90 (s, 2H), 3.76 (t, J = 5.6 Hz, 2H), 3.73 (s, 3H), 3.42 (t, J = 5.6 Hz, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7, 159.0, 148.9, 135.4, 130.2, 129.5, 129.3, 129.0, 128.83, 128.80, 122.6, 117.6, 114.0, 113.1, 80.7, 55.3, 55.2, 51.1, 49.6, 48.6 ppm;

IR (neat): ν_{max} 2839, 2175, 1599, 1558, 1509, 1242 cm^{-1};

HRMS (ESI^+): calcd for $C_{26}H_{26}N_3O_2^+$ $[M + H]^+$ 396.2071, found 396.2077.

4-(Benzo[*d*][1,3]dioxol-5-yl)-1-(4-methoxybenzyl)-7-phenyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepine-6-carbonitrile (14i)



The crude product was purified by column chromatography on silica gel (20.0% ethyl acetate in petroleum ether) to give **14i** (71 mg, 81% yield) as a white solid.

m.p. 114–116 ℃;

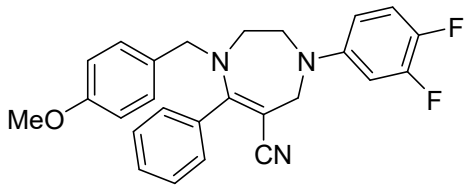
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.41 (m, 5H), 6.94–6.90 (m, 2H), 6.72 (d, J = 8.4 Hz, 1H), 6.68–6.65 (m, 2H), 6.29 (d, J = 2.4 Hz, 1H), 6.15 (dd, J = 8.4, 2.4 Hz, 1H), 5.91 (s, 2H), 4.25 (s, 2H), 3.93 (s, 2H), 3.75 (s, 3H), 3.73 (t, J = 5.6 Hz, 2H), 3.33 (t, J = 5.6 Hz, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 163.6, 159.0, 148.4, 145.3, 139.7, 135.4, 130.3, 129.5, 129.1, 128.9, 128.8, 122.6, 113.9, 108.4, 105.2, 100.7, 80.9, 55.5, 55.2, 51.3, 50.5, 49.7 ppm;

IR (neat): ν_{max} 2902, 2177, 1558, 1502, 1489, 1238, 1219, 1035 cm^{-1};

HRMS (ESI): calcd for $C_{27}H_{26}N_3O_3^+$ $(M+H)^+$ 440.1969, found 440.1969.

4-(3,4-Difluorophenyl)-1-(4-methoxybenzyl)-7-phenyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepine-6-carbonitrile (14j)



The crude product was purified by column chromatography on silica gel (20.0% ethyl acetate in petroleum ether) to give **14j** (40 mg, 46% yield) as a white solid.

m.p. 102–104 ℃;

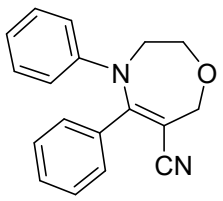
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.42 (m, 5H), 7.06–6.99 (m, 1H), 6.87–6.84 (m, 2H), 6.65–6.61 (m, 2H), 6.36–6.30 (m, 2H), 4.26 (s, 2H), 3.93 (s, 2H), 3.79 (t, J = 5.6 Hz, 2H), 3.74 (s, 3H), 3.30 (t, J = 5.6 Hz, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 163.6, 159.2, 150.7 (dd, $J_{F\text{-}C}$ = 243.3, 13.2 Hz), 146.1 (dd, $J_{F\text{-}C}$ = 8.4, 1.7 Hz), 143.0 (dd, $J_{F\text{-}C}$ = 237.2, 13.0 Hz), 135.1, 130.4, 129.5, 129.01, 128.96, 128.9, 122.3, 117.3 (dd, $J_{F\text{-}C}$ = 17.6, 1.7 Hz), 113.9, 107.9 (dd, $J_{F\text{-}C}$ = 5.3, 2.8 Hz), 102.0 (d, J = 20.9 Hz), 79.7, 55.8, 55.1, 51.5, 50.4, 48.7 ppm;

IR (neat): ν_{max} 2933, 2838, 2181, 1559, 1515, 1242 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{26}H_{24}F_2N_3O^+$ $[M + H]^+$ 432.1882, found 432.1885;

4,5-Diphenyl-2,3,4,7-tetrahydro-1,4-oxazepine-6-carbonitrile (19a)



The crude product was purified by column chromatography on silica gel (10.0% ethyl acetate in petroleum ether) to give **19a** (37 mg, 67% yield) as a white solid.

m.p. 170–172 ℃;

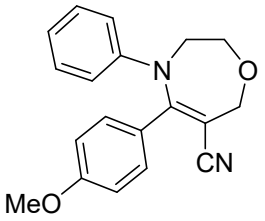
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.43 (m, 2H), 7.27–7.20 (m, 3H, overlapped with the peak of chloroform), 7.15–7.10 (m, 2H), 6.93–6.89 (m, 3H), 4.55 (s, 2H), 4.22–4.19 (m, 2H), 3.86–3.84 (m, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 144.6, 134.7, 130.4, 130.3, 129.0, 128.3, 124.4, 124.2, 120.8, 90.7, 68.4, 68.2, 55.0 ppm;

IR (neat): ν_{max} 2957, 2916, 2867, 2199, 1572, 1490, 1388, 1308, 1124 cm^{-1};

HRMS (ESI^+): calcd for $C_{18}H_{17}N_2O^+$ $[M + H]^+$ 277.1336, found 277.1338.

5-(4-Methoxyphenyl)-4-phenyl-2,3,4,7-tetrahydro-1,4-oxazepine-6-carbonitrile (19b)



The crude product was purified by column chromatography on silica gel (2.0% ethyl acetate in petroleum ether) to give **19b** (42 mg, 68% yield) as a white solid.

m.p. 136–138 ℃;

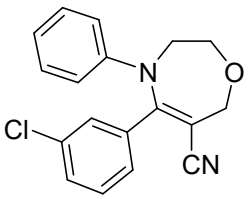
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.39 (m, 2H), 7.16–7.11 (m, 2H), 6.94–6.89 (m, 3H), 6.76–6.72 (m, 2H), 4.52 (s, 2H), 4.19–4.16 (m, 2H), 3.83–3.80 (m, 2H), 3.74 (s, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 161.1, 144.8, 132.0, 129.0, 126.8, 124.2, 123.9, 121.2, 113.7, 89.5, 68.6, 68.0, 55.2, 55.0 ppm;

IR (neat): ν_{max} 2967, 2842, 2189, 1606, 1554, 1511, 1348, 1258, 1171 cm^{-1};

HRMS (ESI^+): calcd for $C_{19}H_{19}N_2O_2^+$ $[M + H]^+$ 307.1441, found 307.1445.

5-(3-Chlorophenyl)-4-phenyl-2,3,4,7-tetrahydro-1,4-oxazepine-6-carbonitrile (19c)



The crude product was purified by column chromatography on silica gel (16.7% ethyl acetate in petroleum ether) to give **19c** (20 mg, 33% yield) as a white solid.

m.p. 154–156 ℃;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.38 (m, 2H), 7.24–7.14 (m, 4H), 6.99–6.92 (m, 3H), 4.55 (s, 2H), 4.21–4.18 (m, 2H), 3.87–3.84 (m, 2H) ppm;

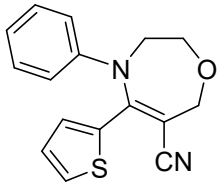
^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 144.2, 136.6, 134.3, 130.4, 130.1, 129.6, 129.3, 128.7, 124.7,

124.6, 120.2, 91.5, 68.2, 68.1, 55.1 ppm;

IR (neat): ν_{max} 2918, 2184, 1554, 1499, 1208, 1101 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{18}H_{16}ClN_2O^+$ $[M + H]^+$ 311.0946, found 311.0946.

4-Phenyl-5-(thiophen-2-yl)-2,3,4,7-tetrahydro-1,4-oxazepine-6-carbonitrile (19d)



The crude product was purified by column chromatography on silica gel (10.0% ethyl acetate in petroleum ether) to give **19d** (39 mg, 69% yield) as a white solid.

m.p. 178–180 °C;

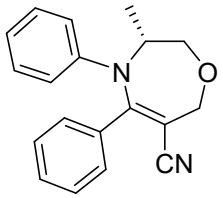
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (dd, J = 3.8, 1.2 Hz, 1H), 7.31 (dd, J = 5.1, 1.2 Hz, 1H), 7.22–7.17 (m, 2H), 7.00–6.96 (m, 3H), 6.94 (dd, J = 5.1, 3.8 Hz, 1H), 4.51 (s, 2H), 4.14–4.11 (m, 2H), 3.79–3.76 (m, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.3, 144.7, 137.6, 132.3, 130.2, 129.2, 127.3, 124.0, 123.4, 120.5, 91.1, 68.7, 67.8, 54.7 ppm;

IR (neat): ν_{max} 2923, 2186, 1566, 1493, 1380, 1120 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{16}H_{15}N_2OS^+$ $[M + H]^+$ 283.0900, found 283.0902.

(*R*)-3-Methyl-4,5-diphenyl-2,3,4,7-tetrahydro-1,4-oxazepine-6-carbonitrile (19e)



The crude product was purified by column chromatography on silica gel (7.7% ethyl acetate in petroleum ether) to give **19e** (39 mg, 67% yield) as a white solid.

m.p. 136–137 °C;

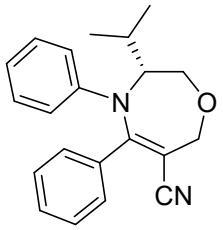
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.37 (m, 2H), 7.24–7.18 (m, 3H), 7.13–7.08 (m, 2H), 6.92–6.89 (m, 3H), 4.70 (d, J = 13.6 Hz, 1H), 4.57–4.50 (m, 1H), 4.34 (d, J = 13.6 Hz, 1H), 3.82 (dd, J = 12.2, 2.0 Hz, 1H), 3.57 (dd, J = 12.2, 2.0 Hz, 1H), 1.55 (d, J = 6.8 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1, 145.4, 135.3, 130.7, 130.1, 128.9, 128.1, 124.8, 124.4, 121.4, 90.5, 72.9, 71.1, 59.8, 15.9 ppm;

IR (neat): ν_{max} 2955, 2918, 2853, 2191, 1566, 1492, 1259 cm^{-1};

HRMS (ESI$^+$): calcd for $C_{19}H_{19}N_2O^+$ $[M + H]^+$ 291.1492, found 291.1497.

(*R*)-3-Isopropyl-4,5-diphenyl-2,3,4,7-tetrahydro-1,4-oxazepine-6-carbonitrile (19f)



The crude product was purified by column chromatography on silica gel (6.3% ethyl acetate in petroleum ether) to give **19f** (39 mg, 62% yield) as a white solid.

m.p. 146–148 °C;

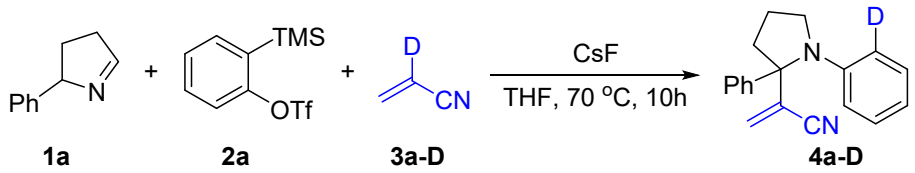
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55–7.50 (m, 2H), 7.25–7.19 (m, 3H), 7.14–7.10 (m, 2H), 7.02–6.99 (m, 2H), 6.97–6.93 (m, 1H), 4.67 (d, J = 14.4 Hz, 1H), 4.44 (d, J = 14.4 Hz, 1H), 4.00 (dd, J = 12.3, 5.3 Hz, 1H), 3.81 (ddd, J = 12.3, 5.3, 2.7 Hz, 1H), 3.52 (dd, J = 12.3, 2.7 Hz, 1H), 2.39–2.27 (m, 1H), 1.45 (d, J = 6.8 Hz, 3H), 1.06 (d, J = 6.8 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 145.3, 135.5, 131.1, 130.3, 128.9, 128.1, 126.5, 125.1, 121.4, 89.4, 72.3, 71.0, 69.7, 27.5, 22.5, 20.4 ppm;

IR (neat): ν_{max} 2963, 2919, 2850, 2189, 1552, 1493, 1272 cm^{-1};

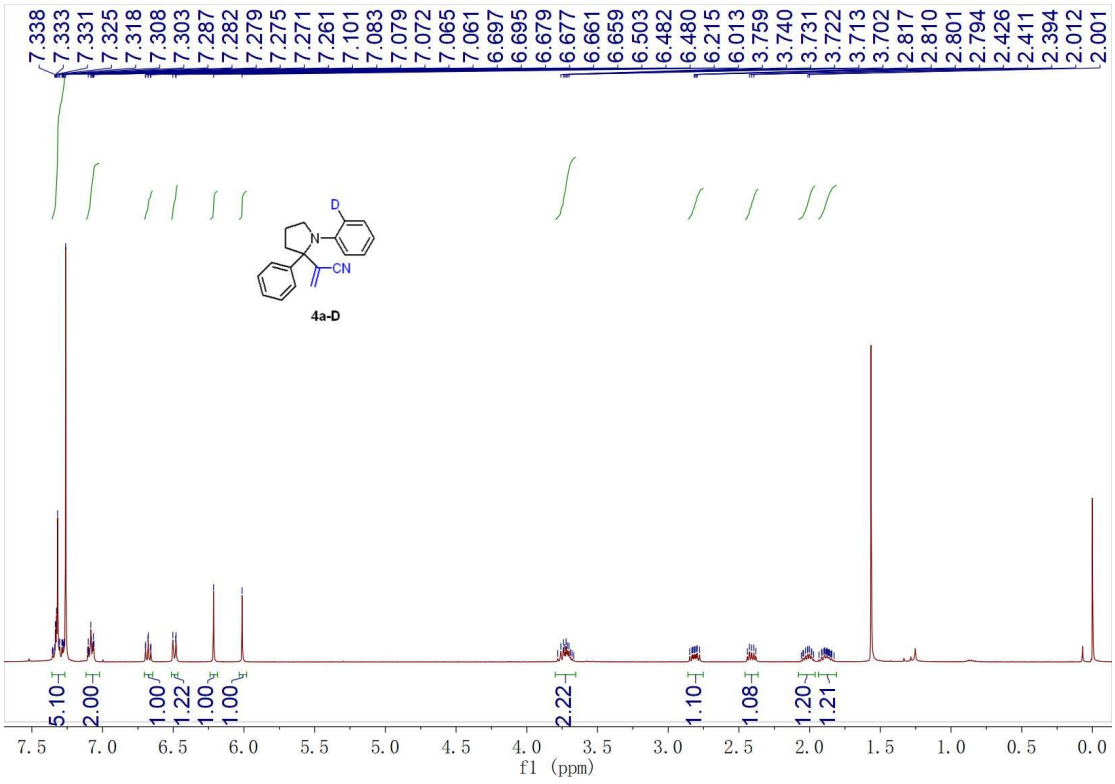
HRMS (ESI$^+$): calcd for $C_{21}H_{23}N_2O^+$ $[M + H]^+$ 319.1805, found 319.1809.

Part 8. Control Experiment.



1a **2a** **3a-D** **4a-D**

To a 15 mL Schlenk tube equipped with a stir bar, was charged imine **1a** (29.04 mg, 0.2 mmol) and aryne precursor **2a** (119.34 mg, 0.4 mmol). The system was degassed and refilled with nitrogen three times. Tetrahydrofuran (0.5 mL) and arcylonitrile **3-D** (0.5 mL) were added via syringe. Subsequently, CsF (0.12 g, 0.8 mmol) was added quickly. The tube was sealed and the mixture was heated at 70 ℃ for 10 hours before being cooled and evaporated. The residue was purified by column chromatography on silica gel to give the three-component coupling products **4a-D** in 69% isolated yield. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.36–7.27 (m, 5H), 7.11–7.06 (m, 2H), 6.68 (td, J = 7.3, 0.9 Hz, 1H), 6.51–6.48 (m, 1H), 6.22 (s, 1H), 6.01 (s, 1H), 3.80–3.65 (m, 2H), 2.81 (ddd, J = 12.6, 9.1, 6.3 Hz, 1H), 2.44–2.38 (m, 1H), 2.08–1.96 (m, 1H), 1.94–1.81 (m, 1H) ppm.



Part 9. References

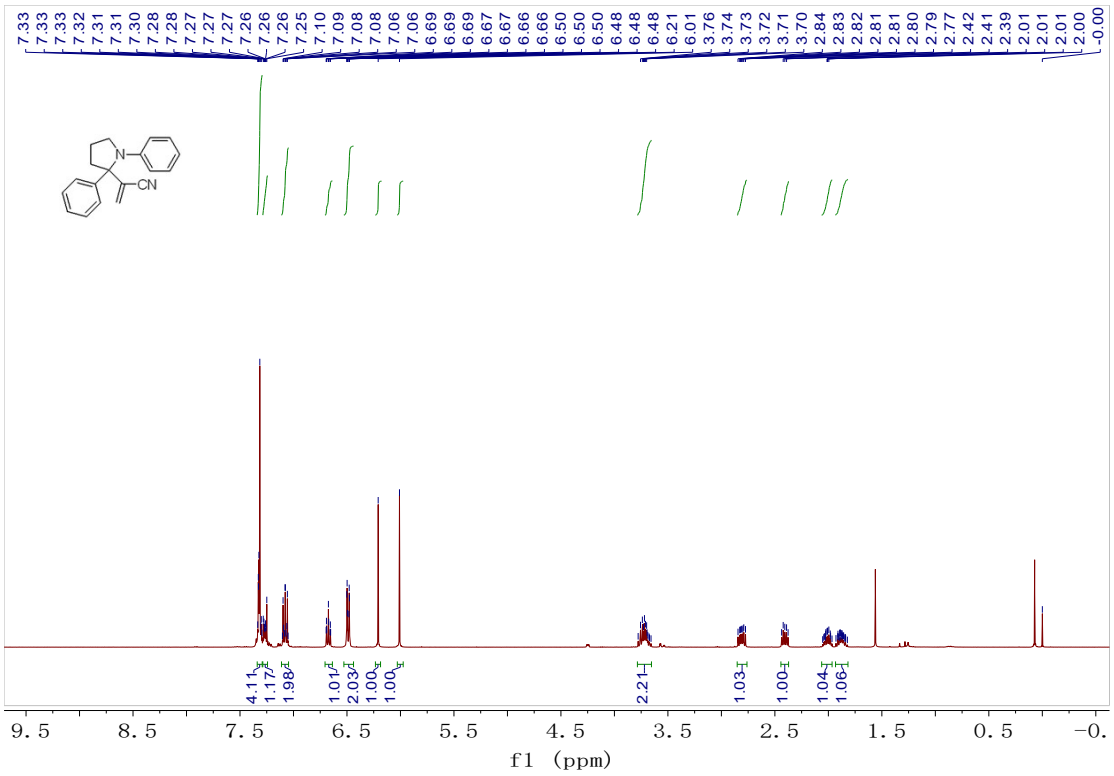
[1] H. Huang, Q. Yang, Q. Zhang, J. Wu, Y. Liu, C. Song, J. Chang, *Adv. Synth. Catal.* **2016**, *358*, 1130-1135

[2] A. A. Ellsworth, C. L. Magyar, G. E. Hubbell, C. C. Theisen, D. Holmes, R. A. Mosey, *Tetrahedron* **2016**, *72*, 6380-6389

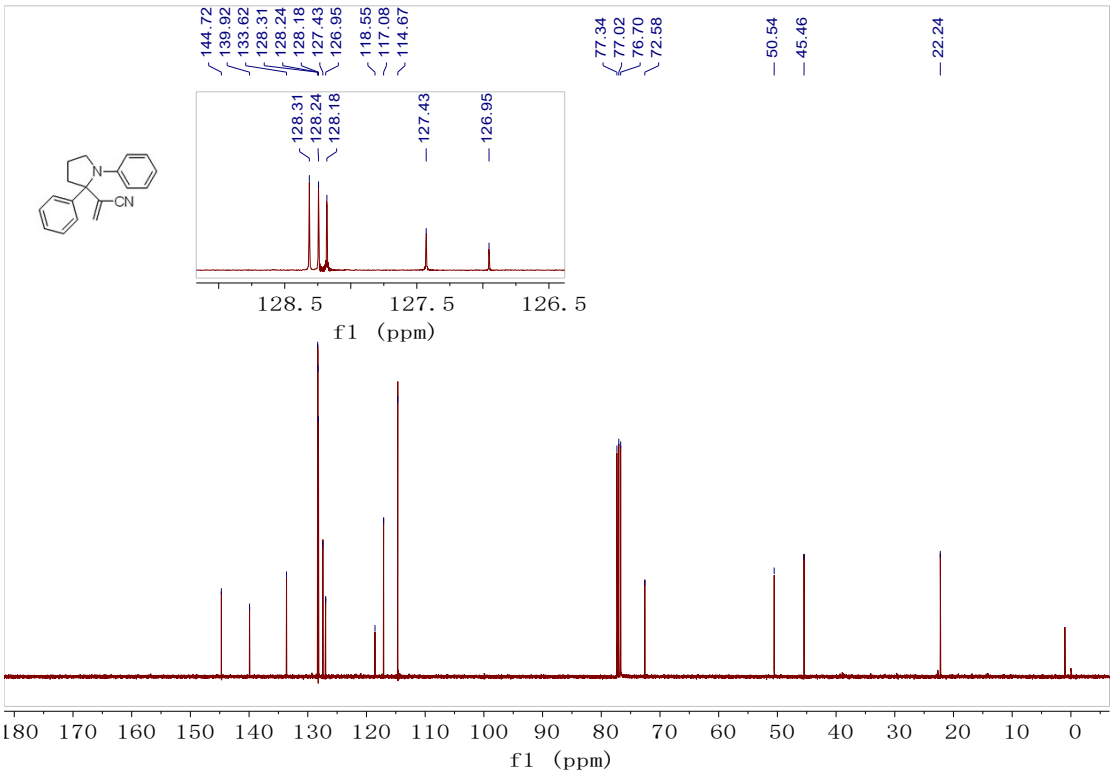
[3] X. Li, Y. Sun, X. Huang, L. Zhang, L. Kong, B. Peng, *Org. Lett.* **2017**, *19*, 838-841

Part 10. Copies of NMR Spectra

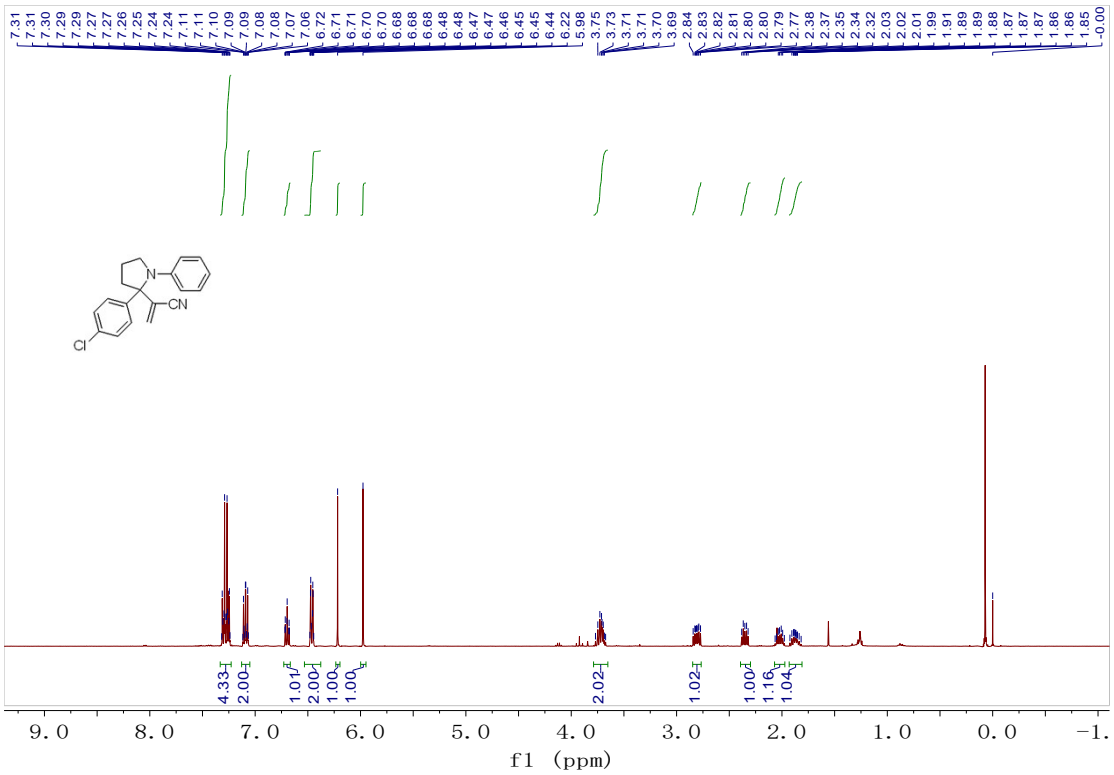
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4a



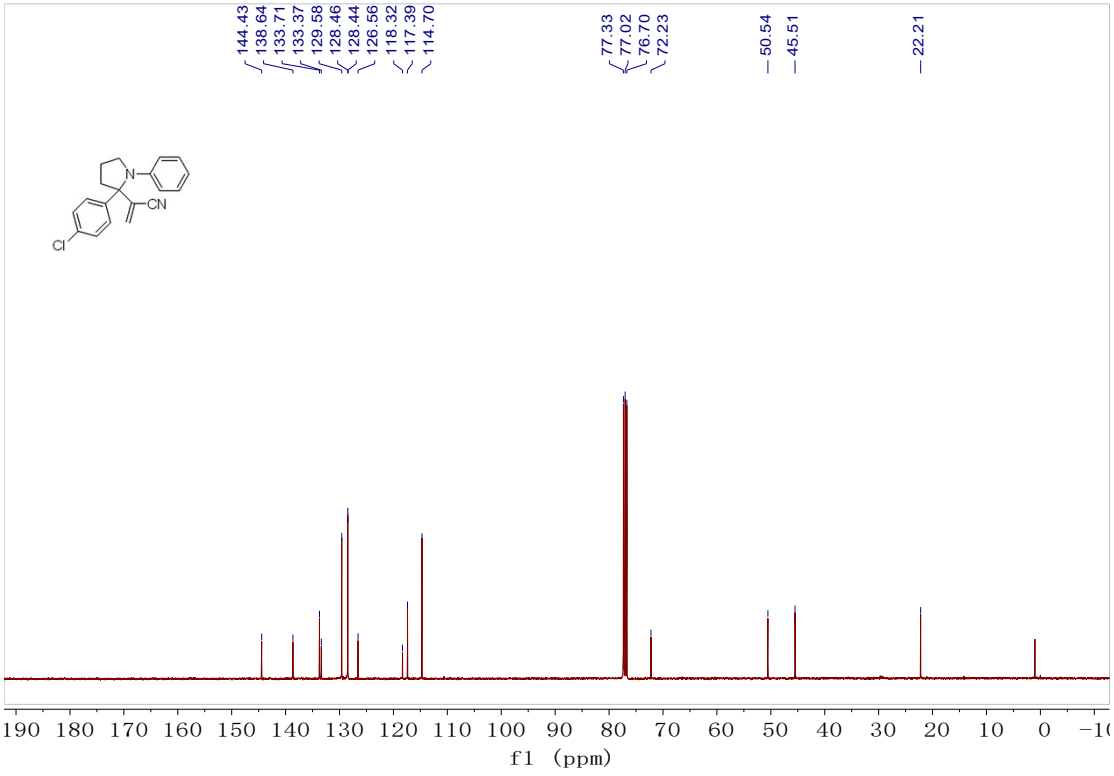
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4a



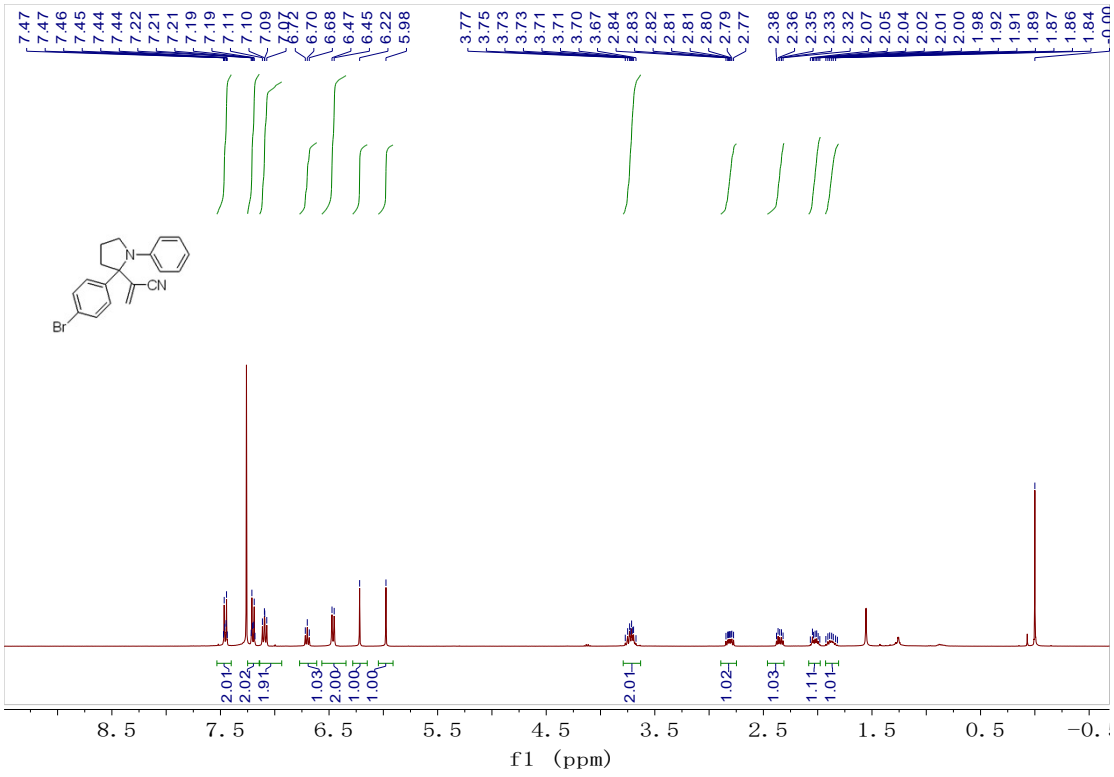
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4b



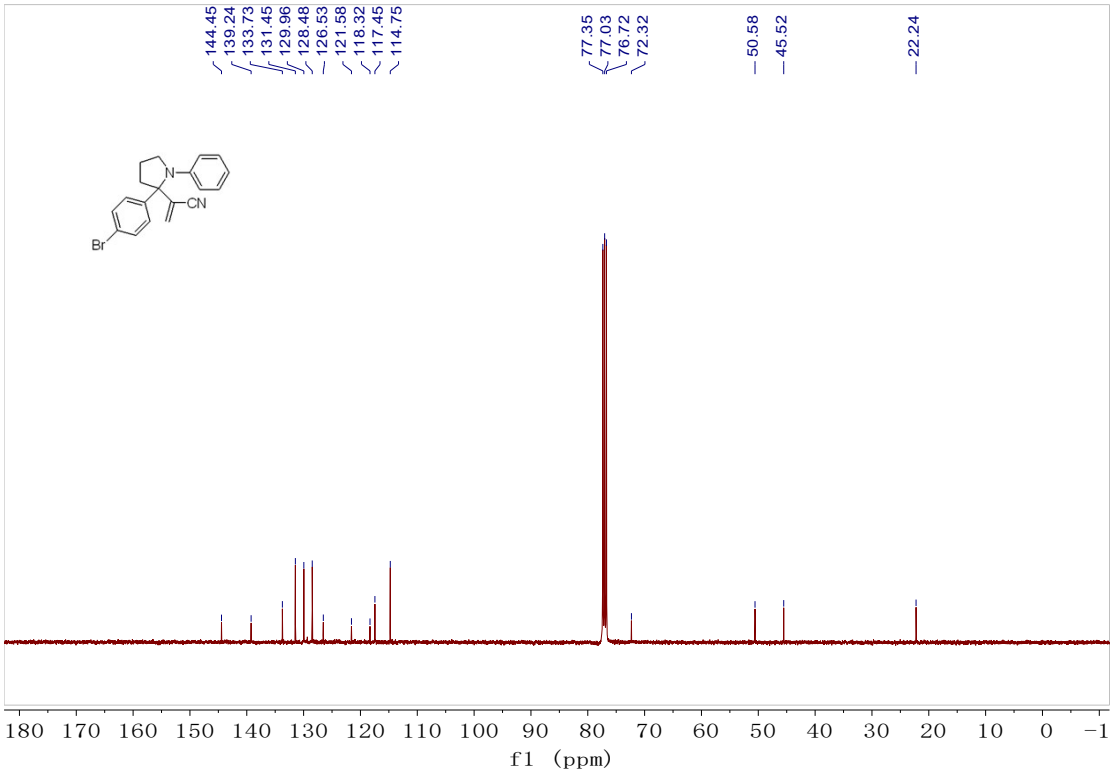
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4b



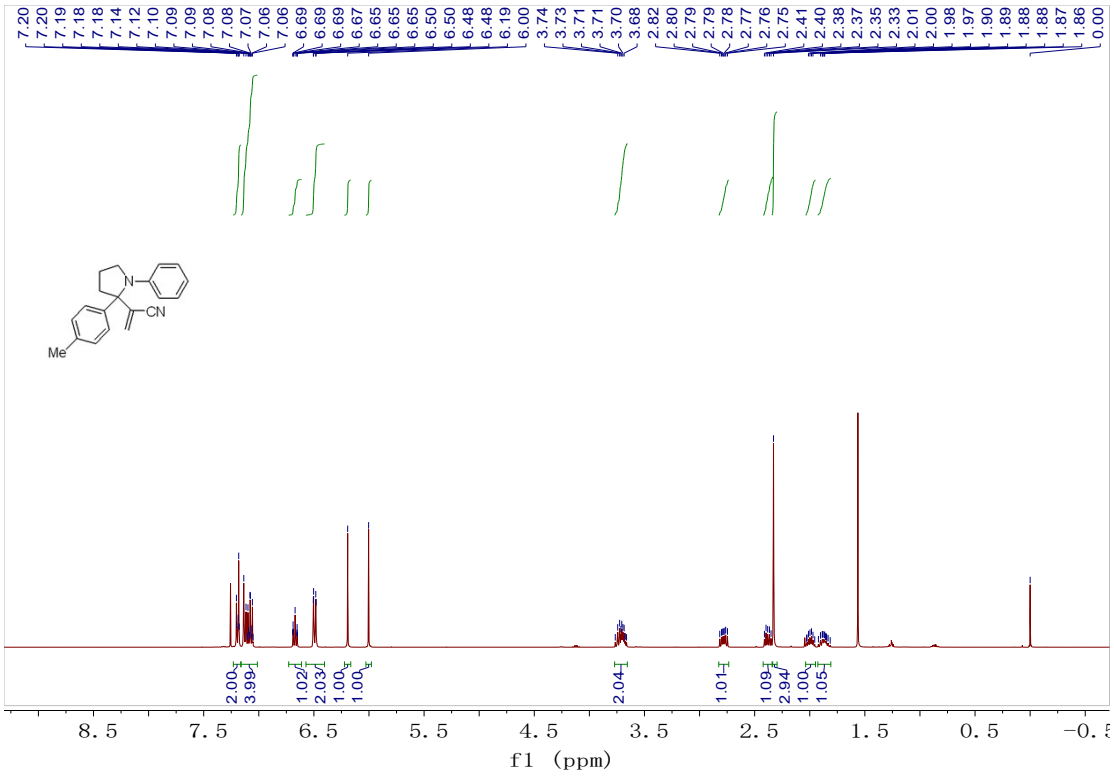
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4c



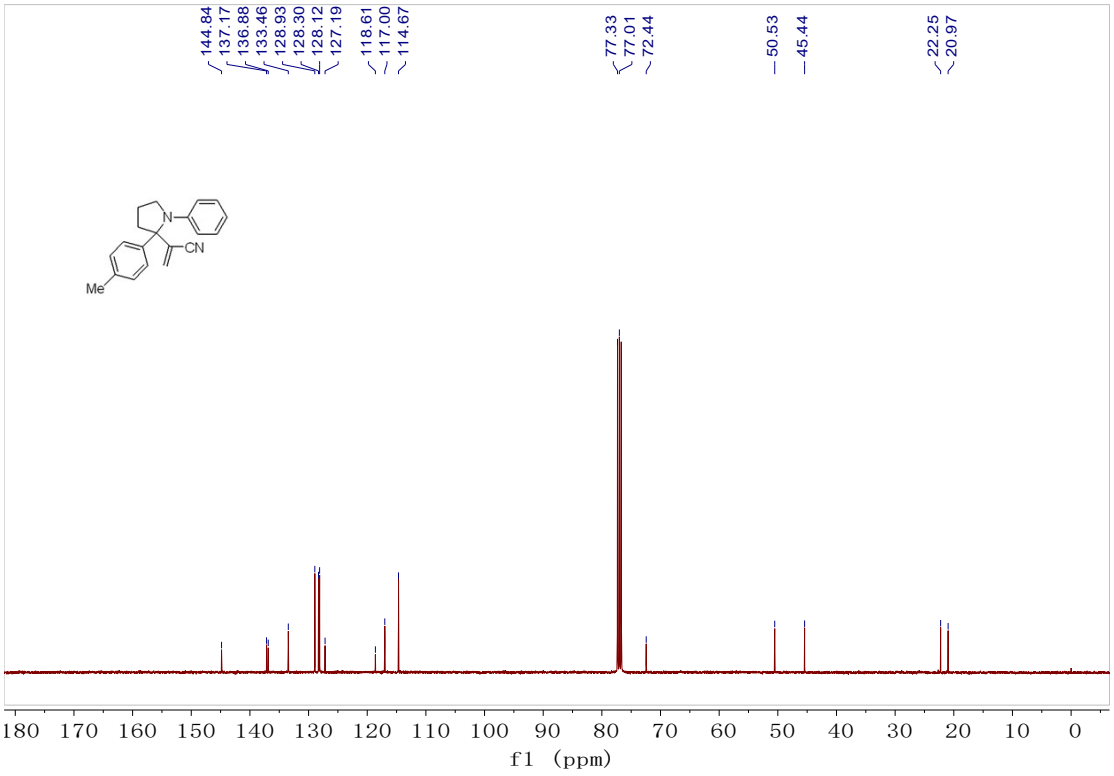
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4c



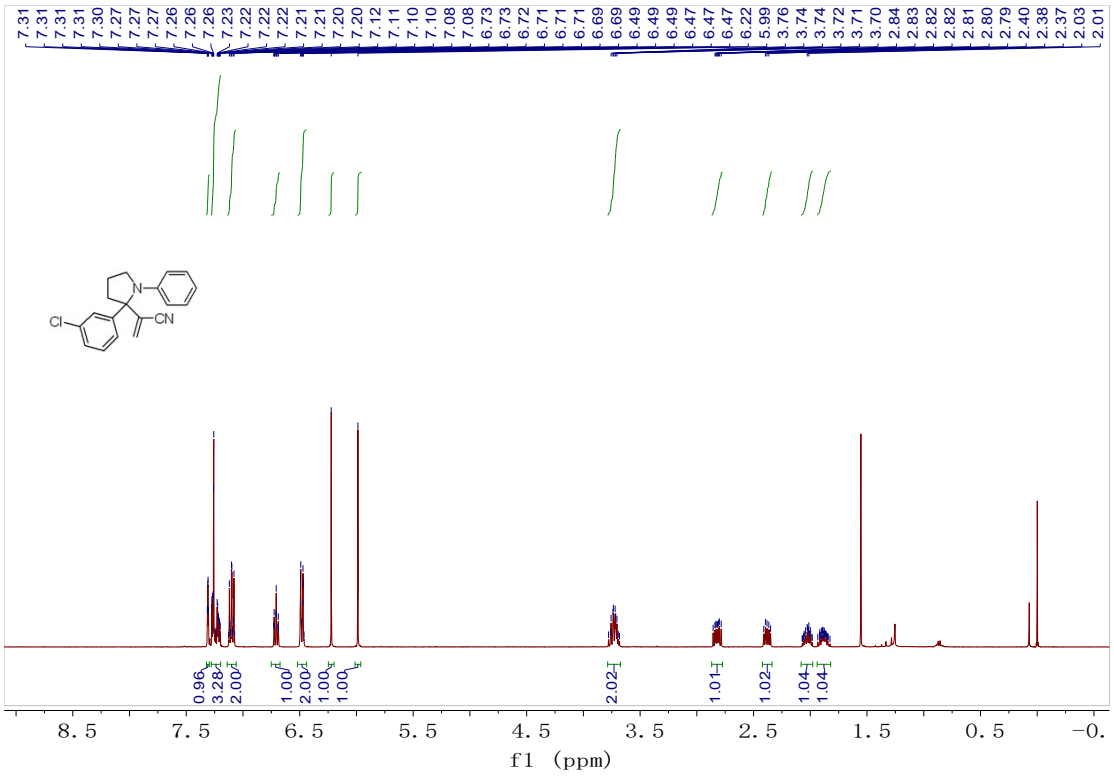
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4d



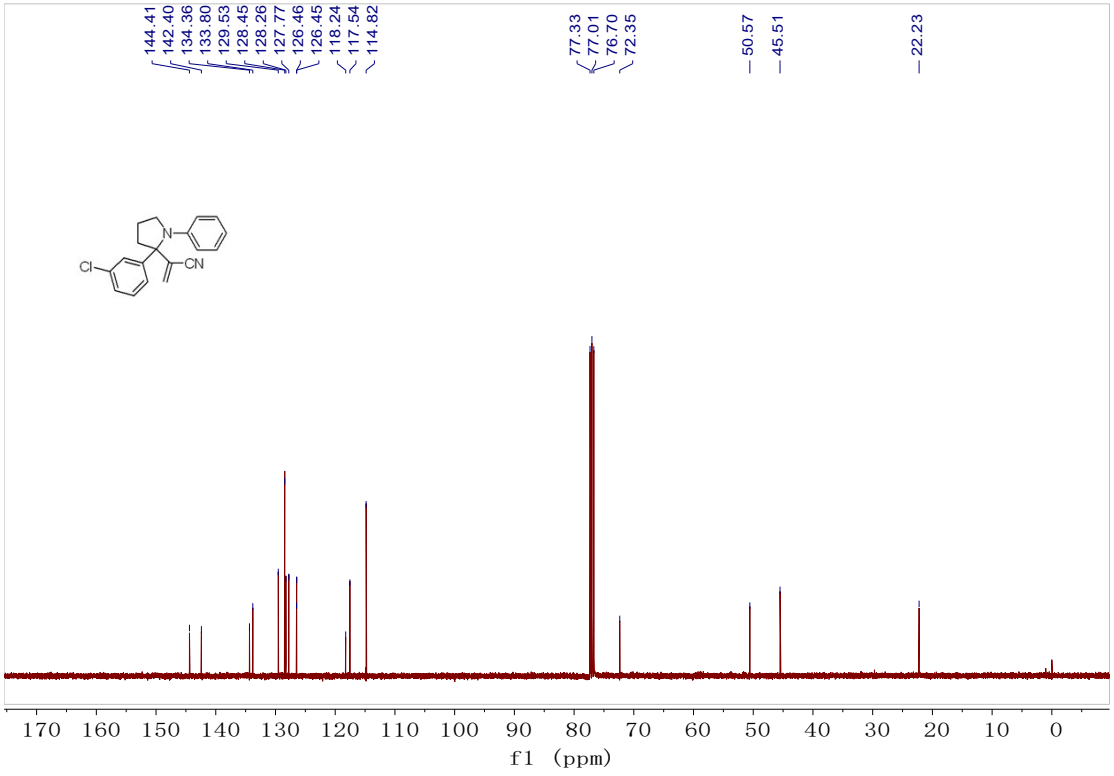
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4d



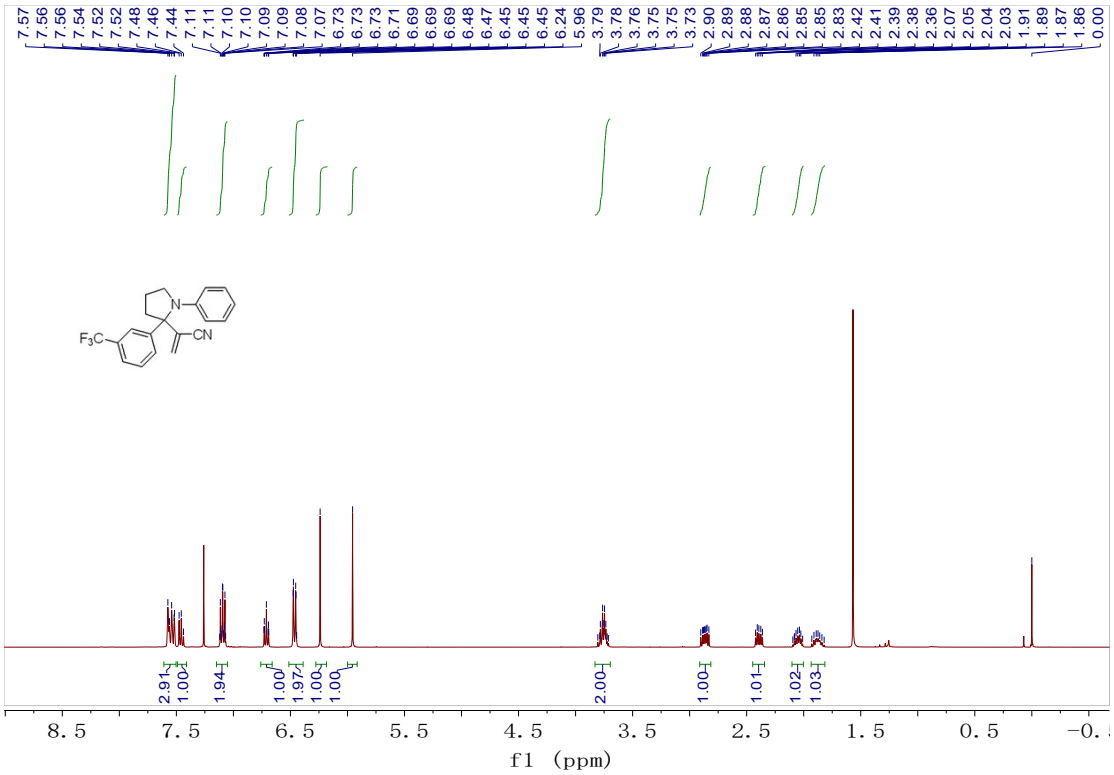
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4e



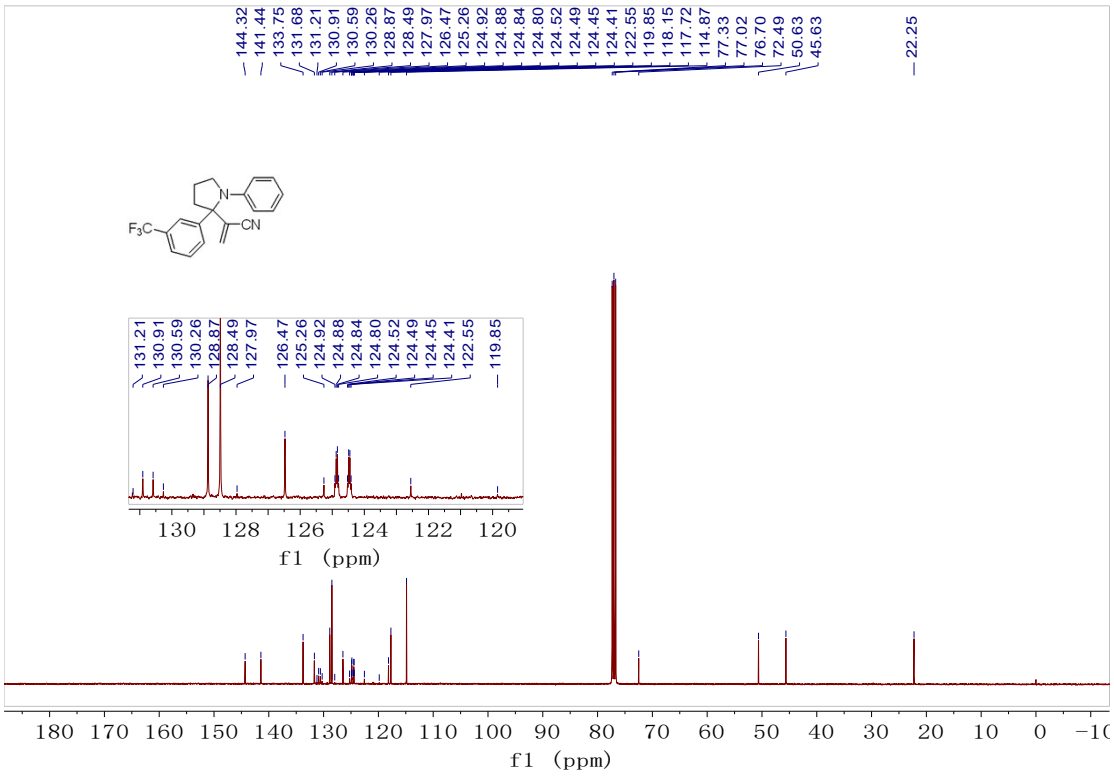
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4e



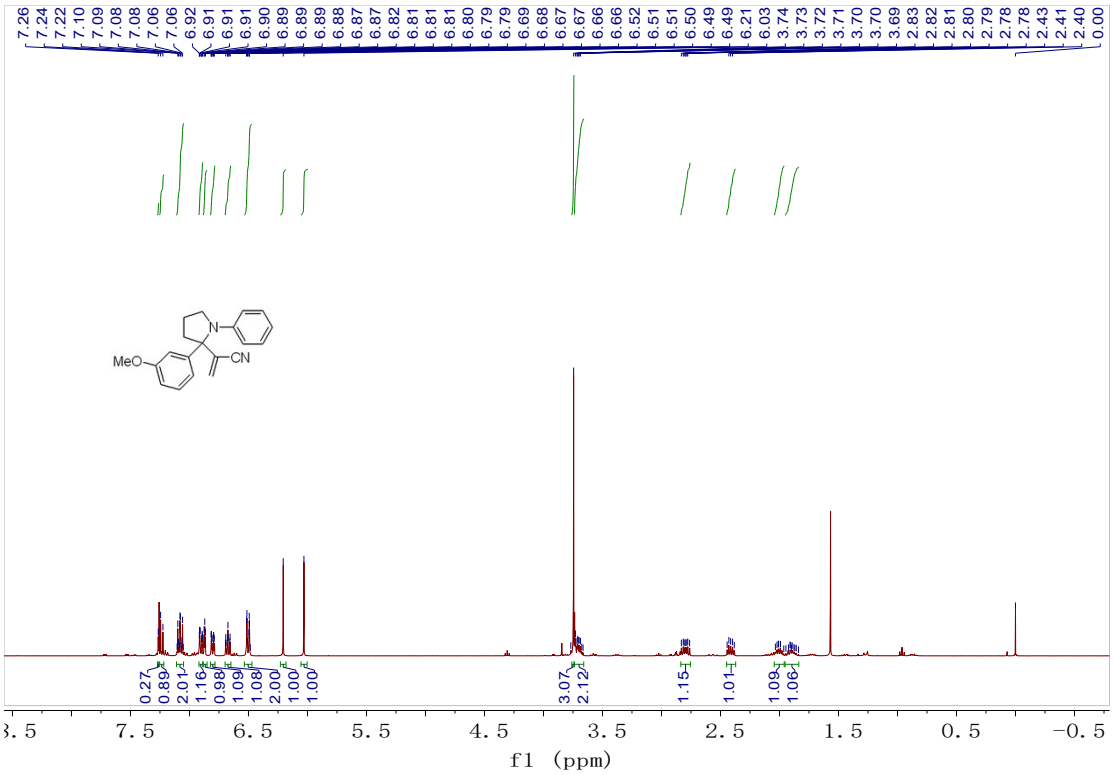
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4f



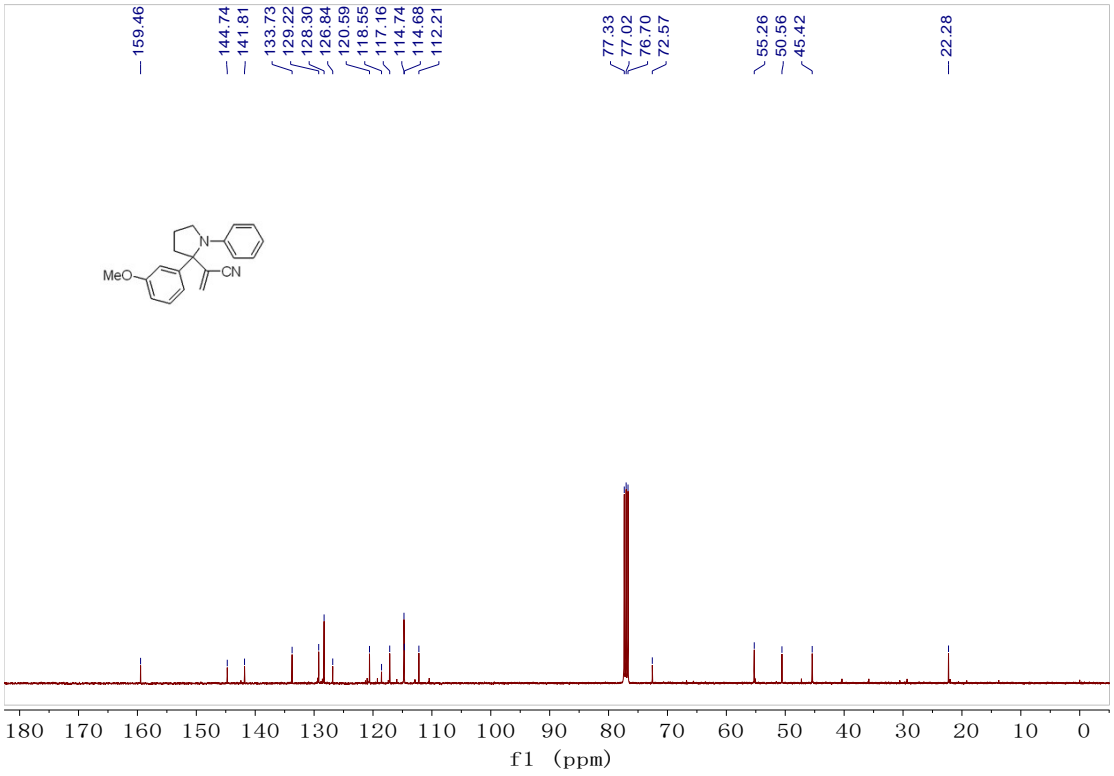
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4f



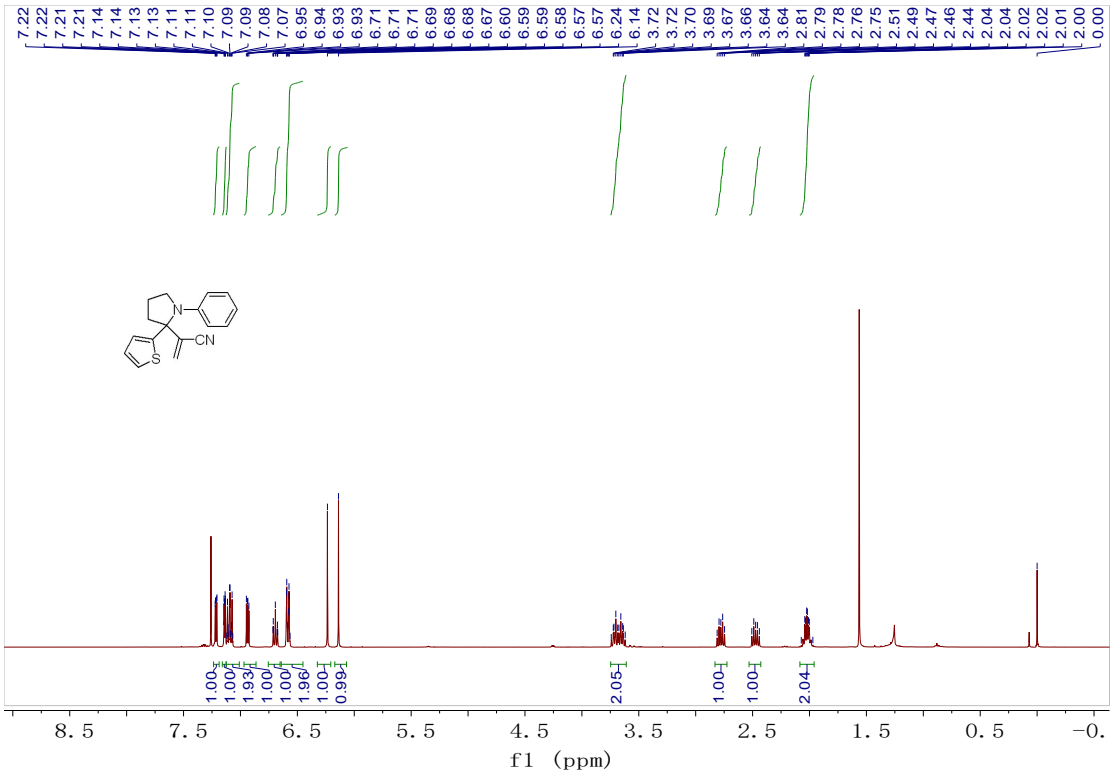
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4g



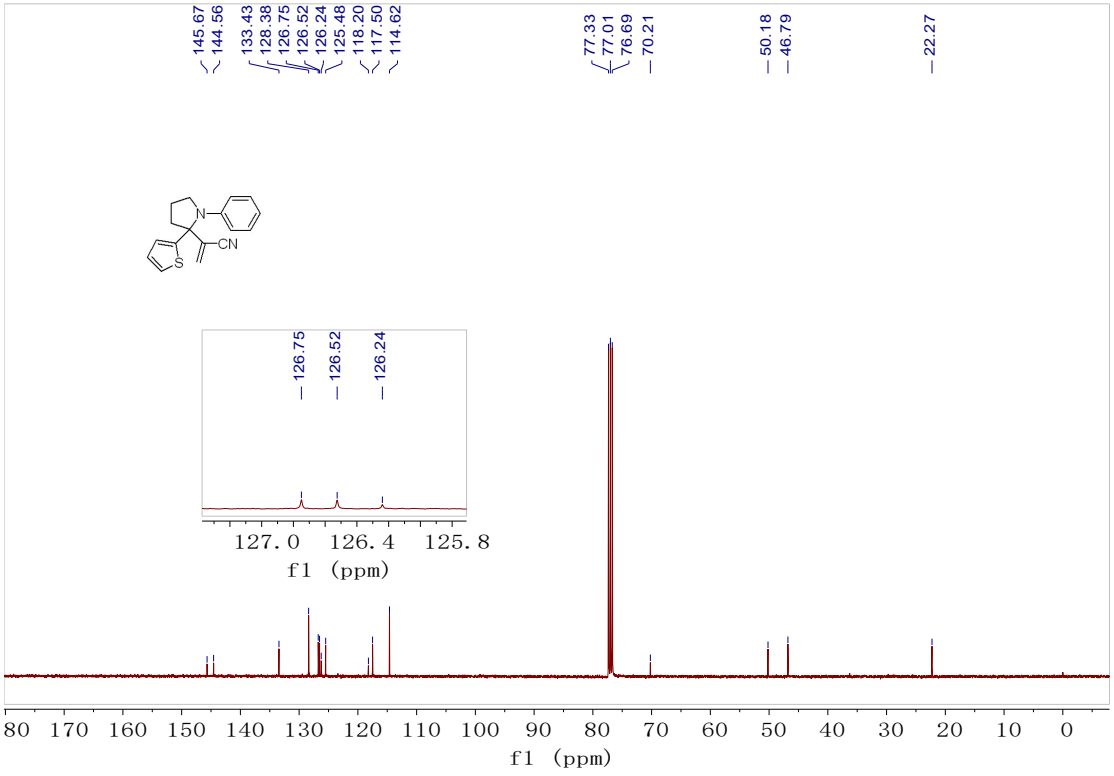
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4g



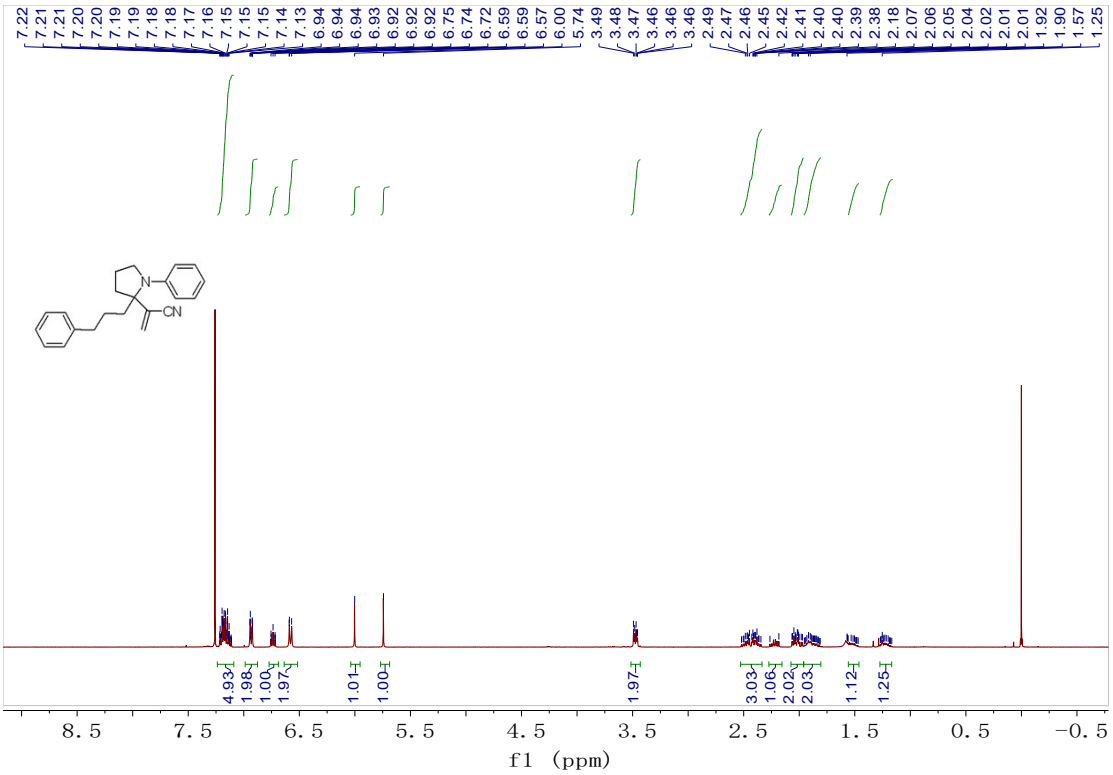
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4h



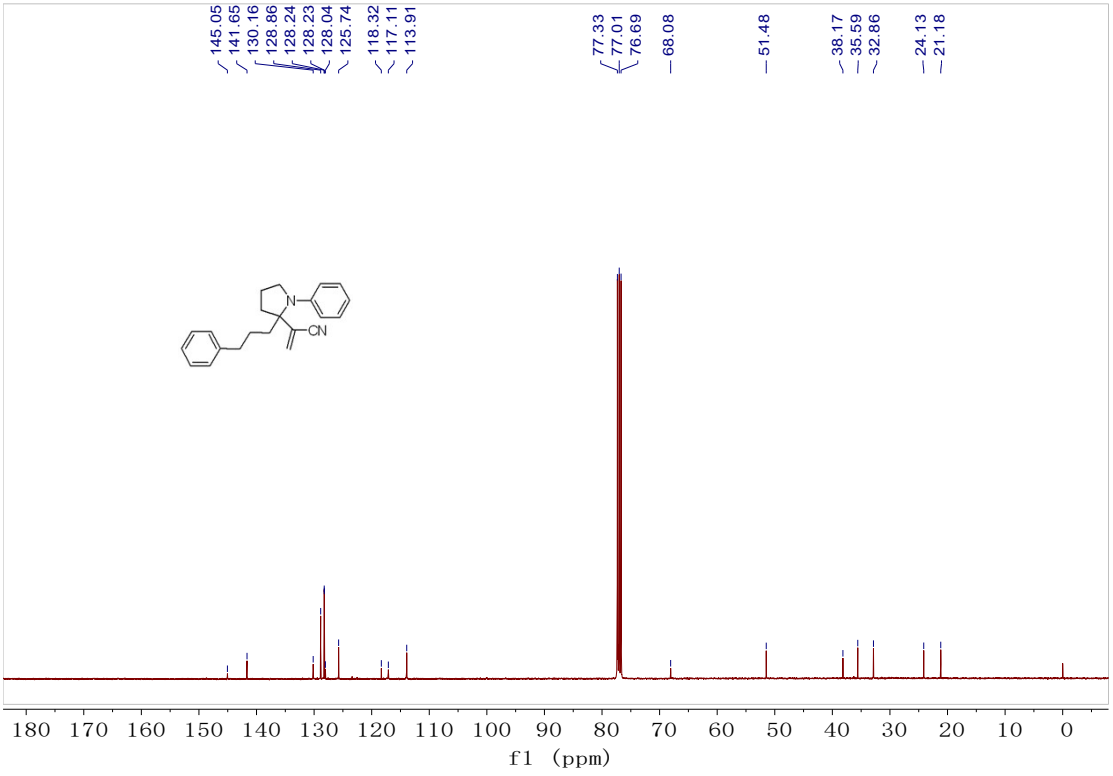
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4h



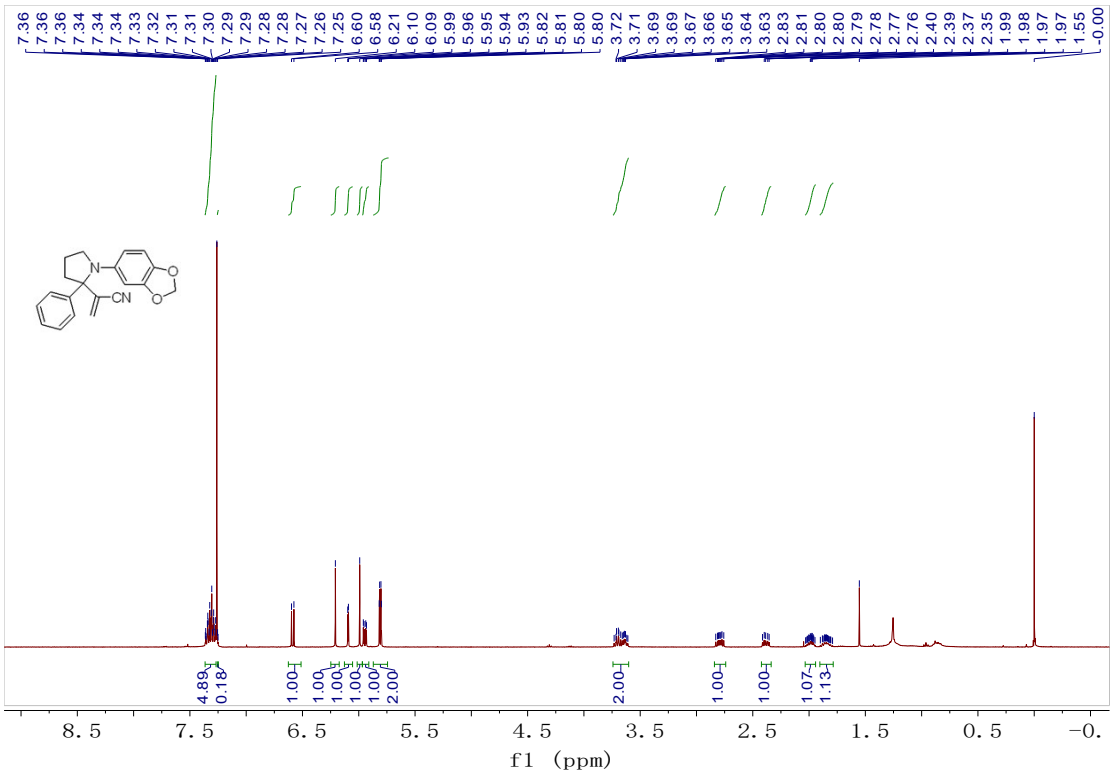
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4i



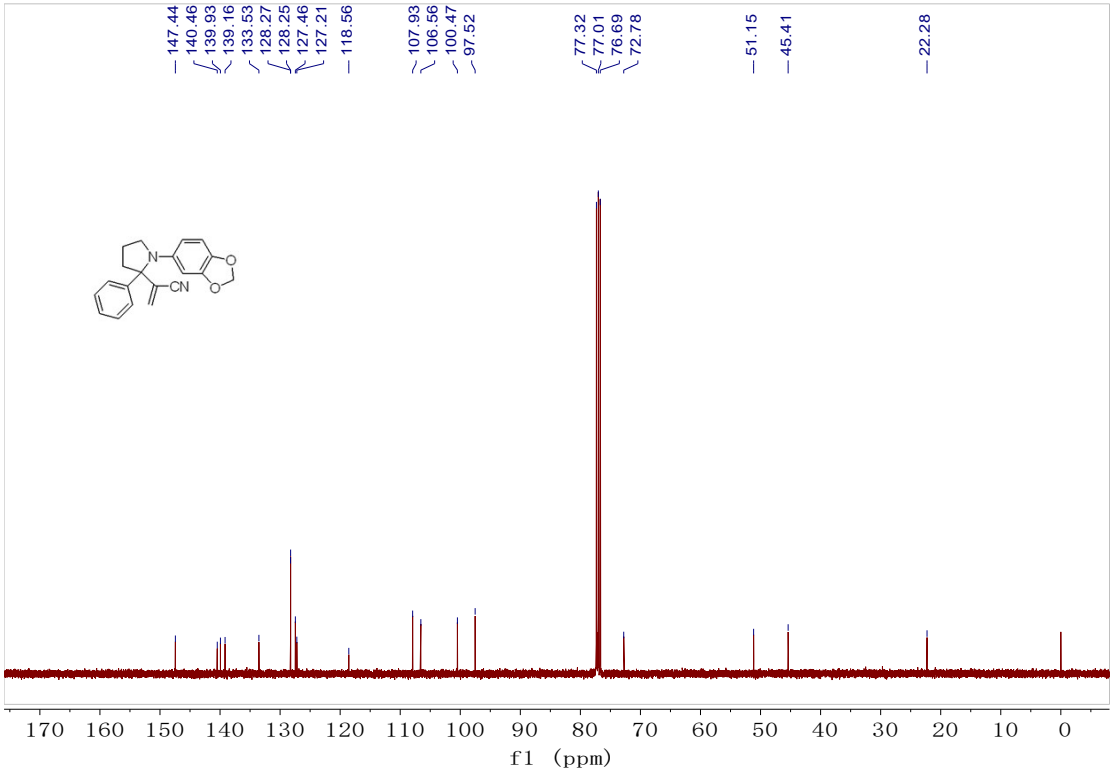
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4i



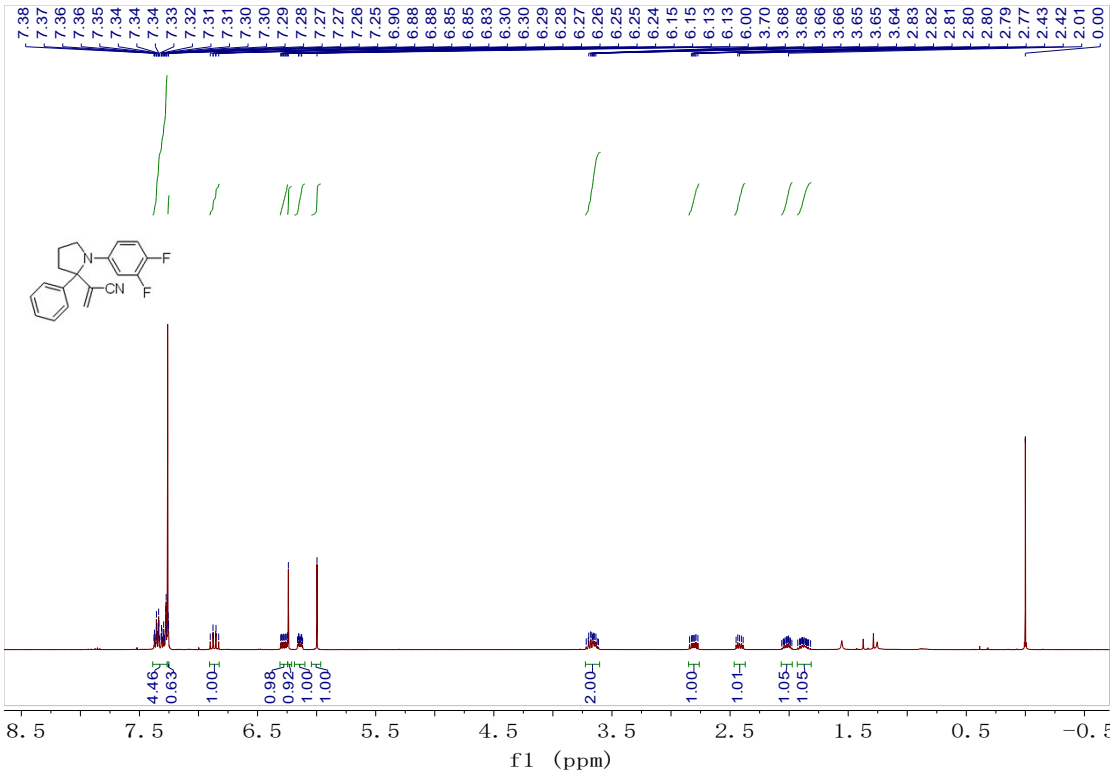
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4j



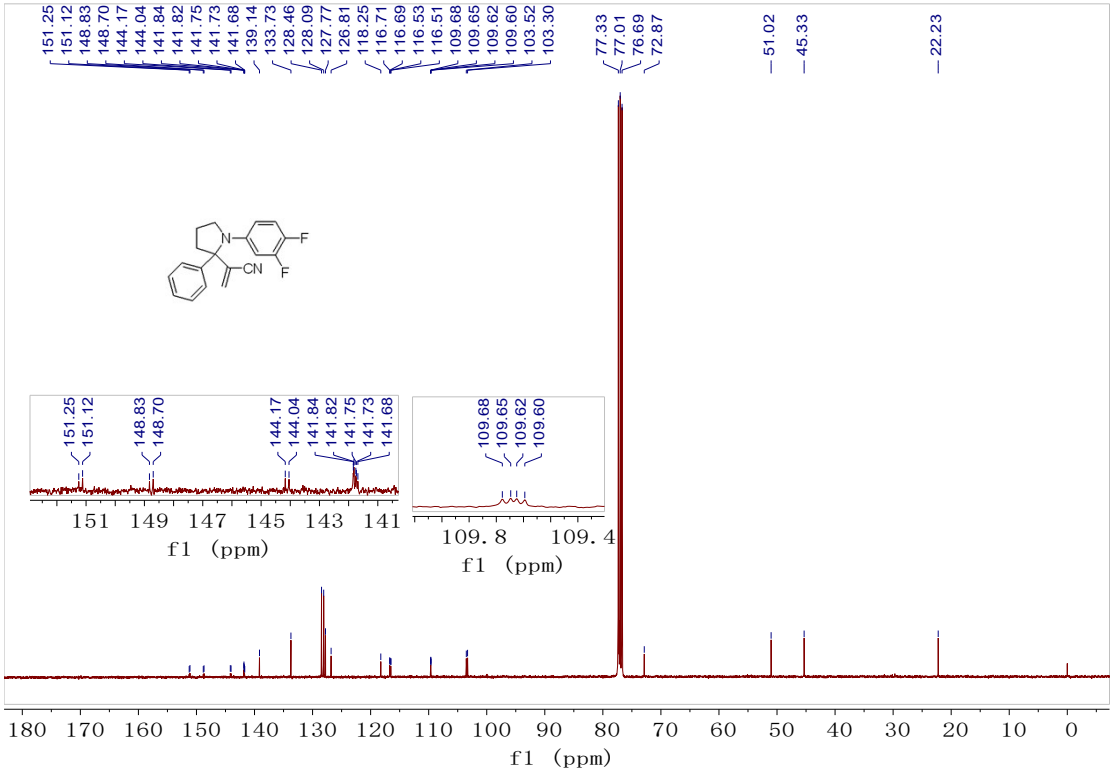
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4j



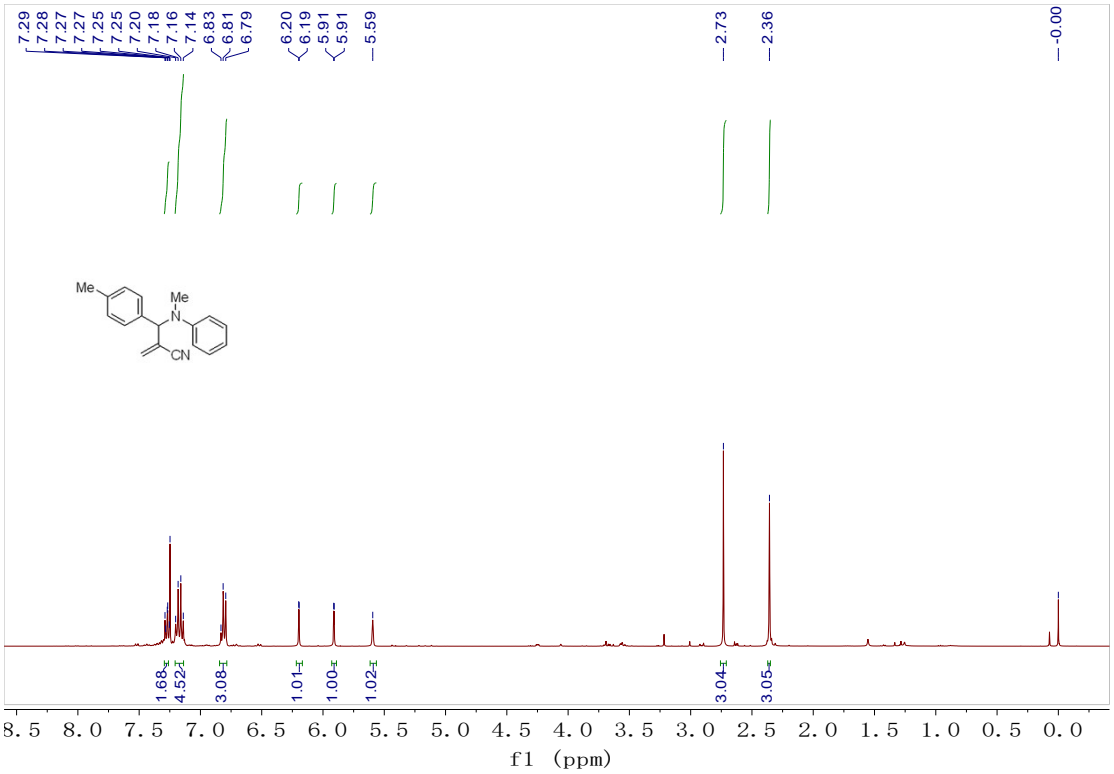
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4k



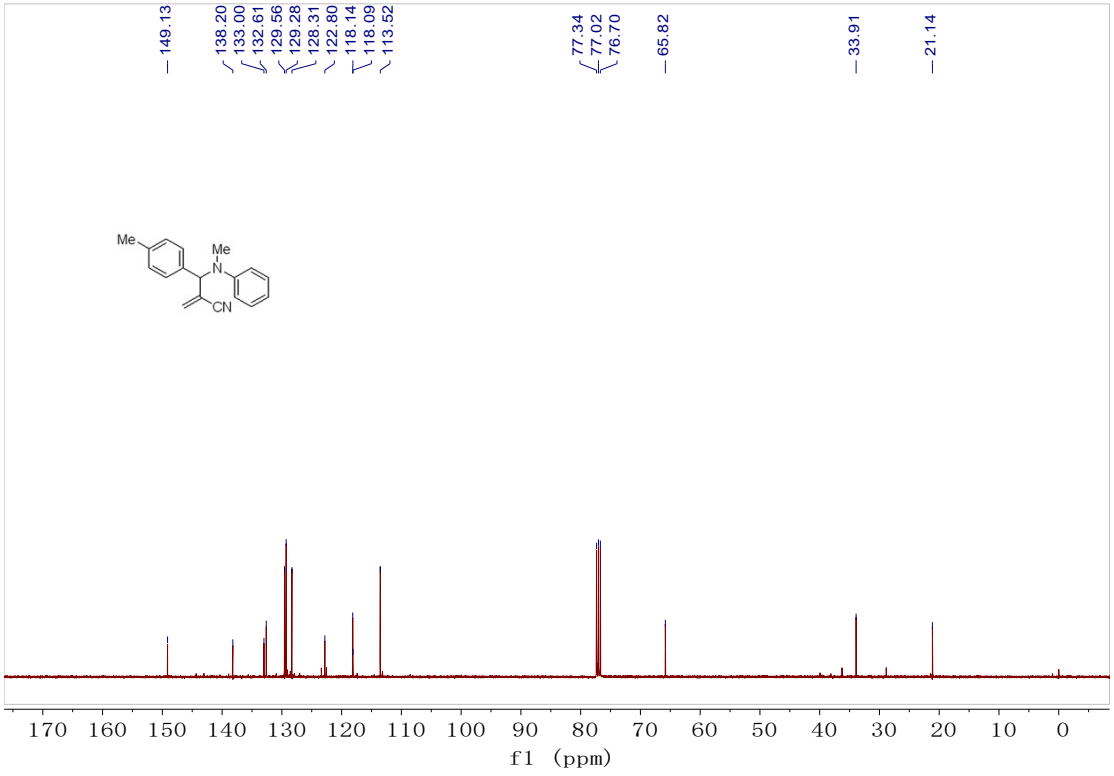
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4k



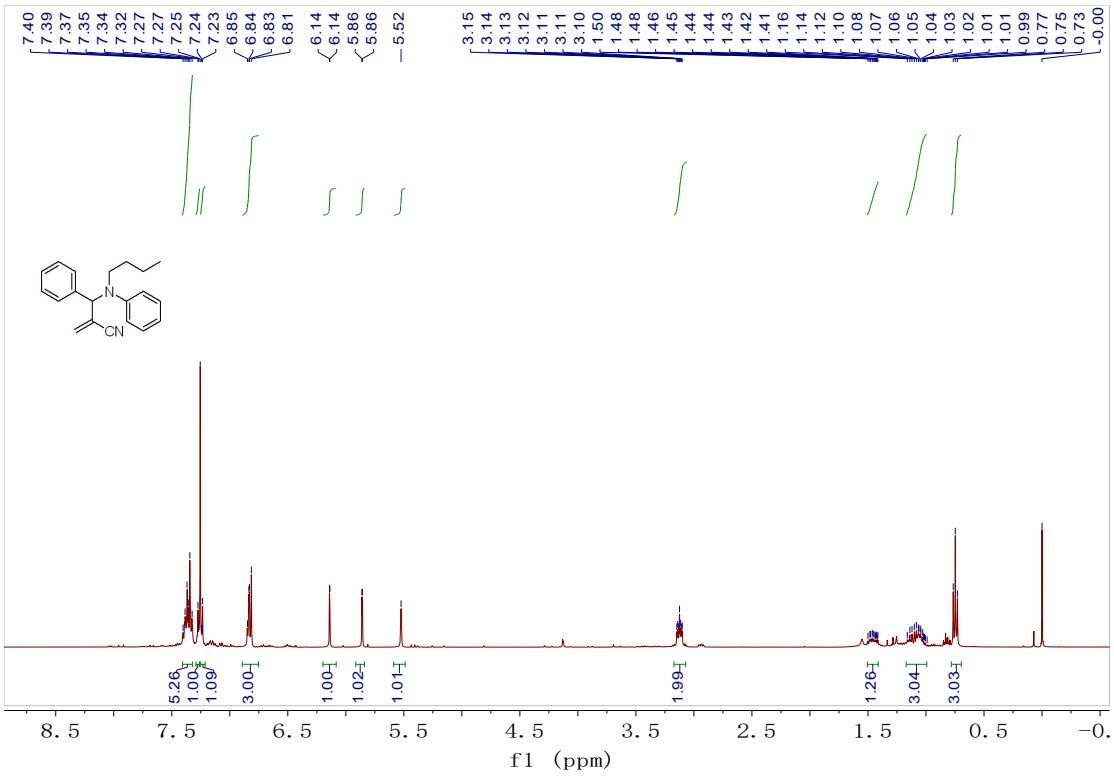
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4l



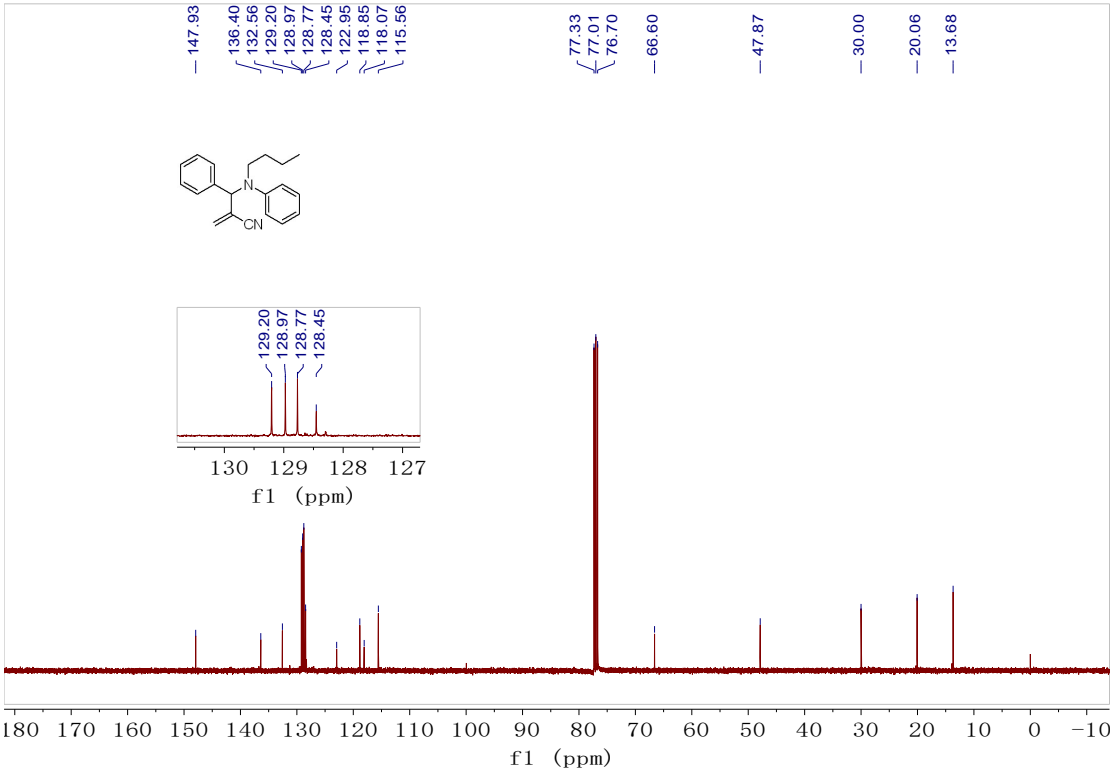
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4l



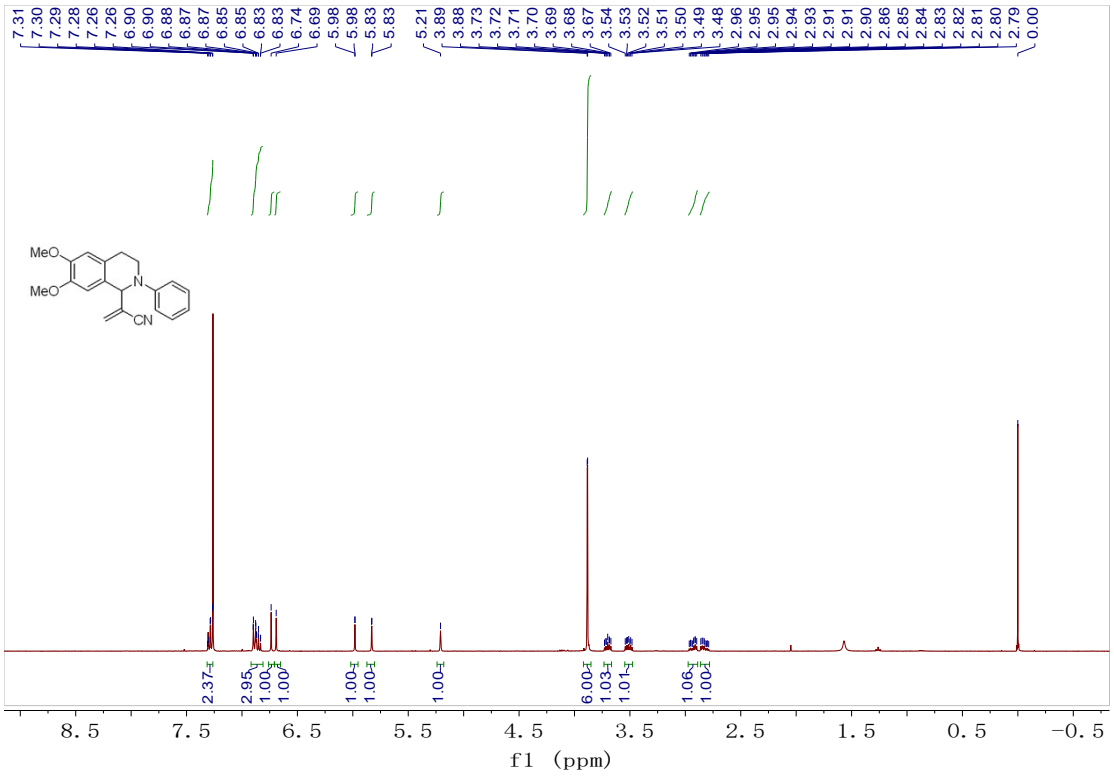
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4m



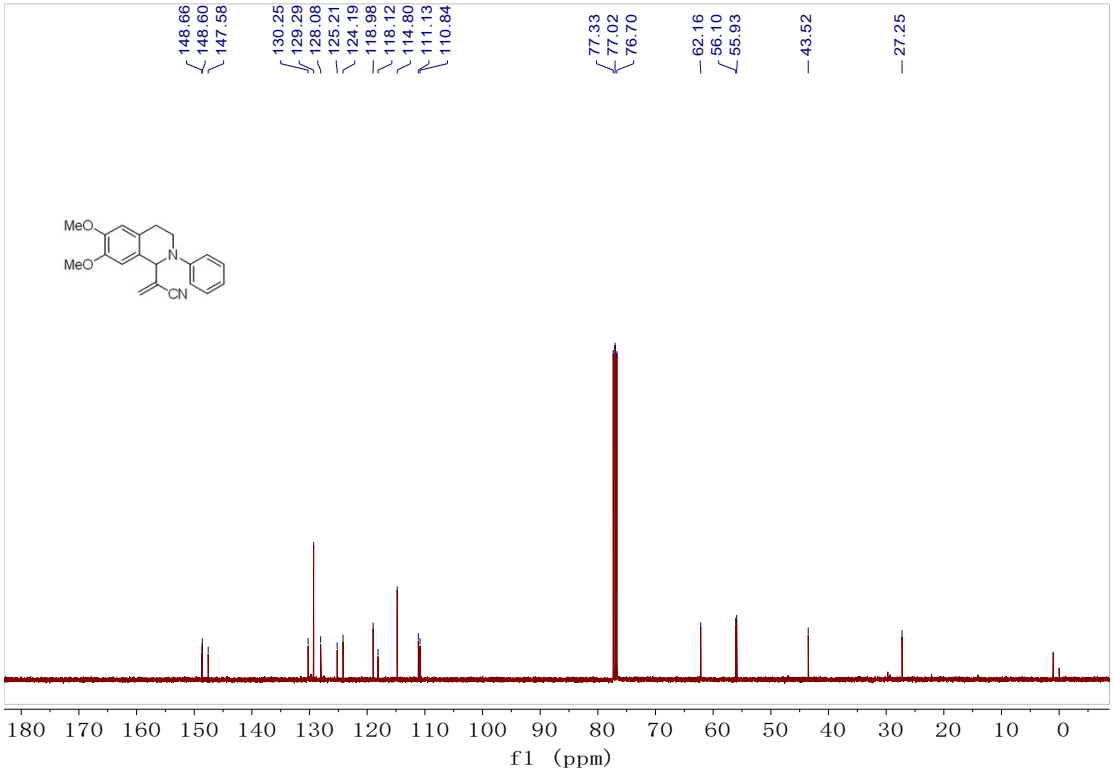
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4m



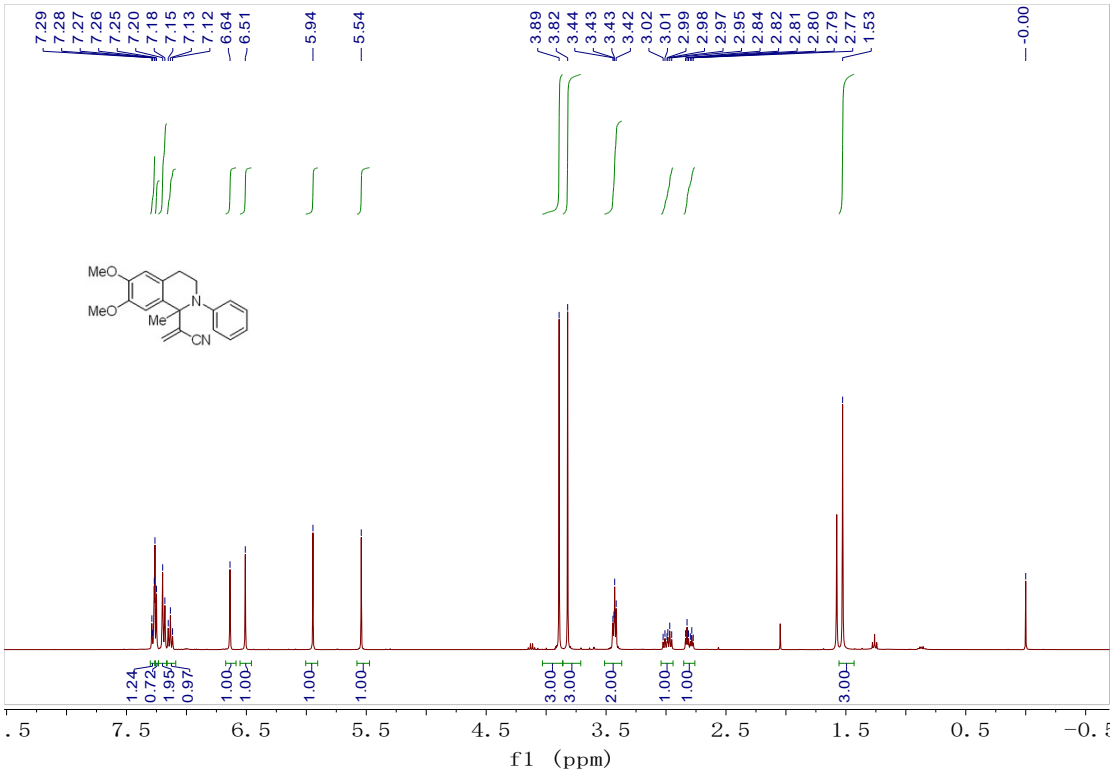
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4n



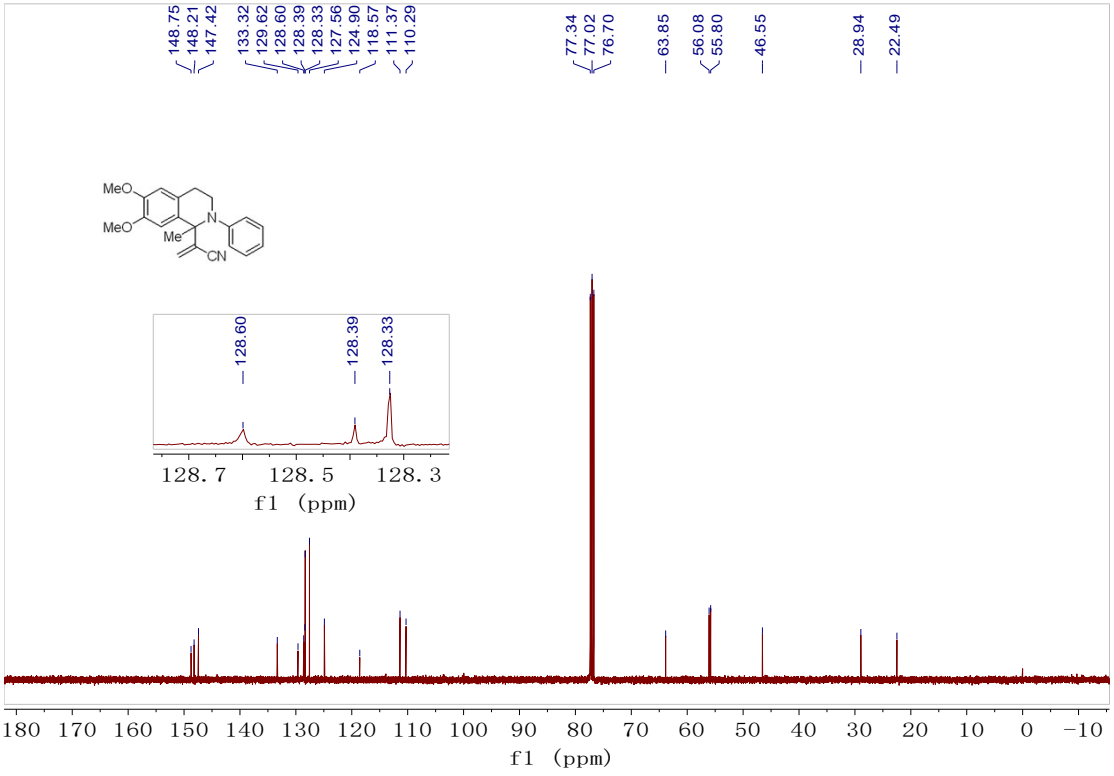
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4n



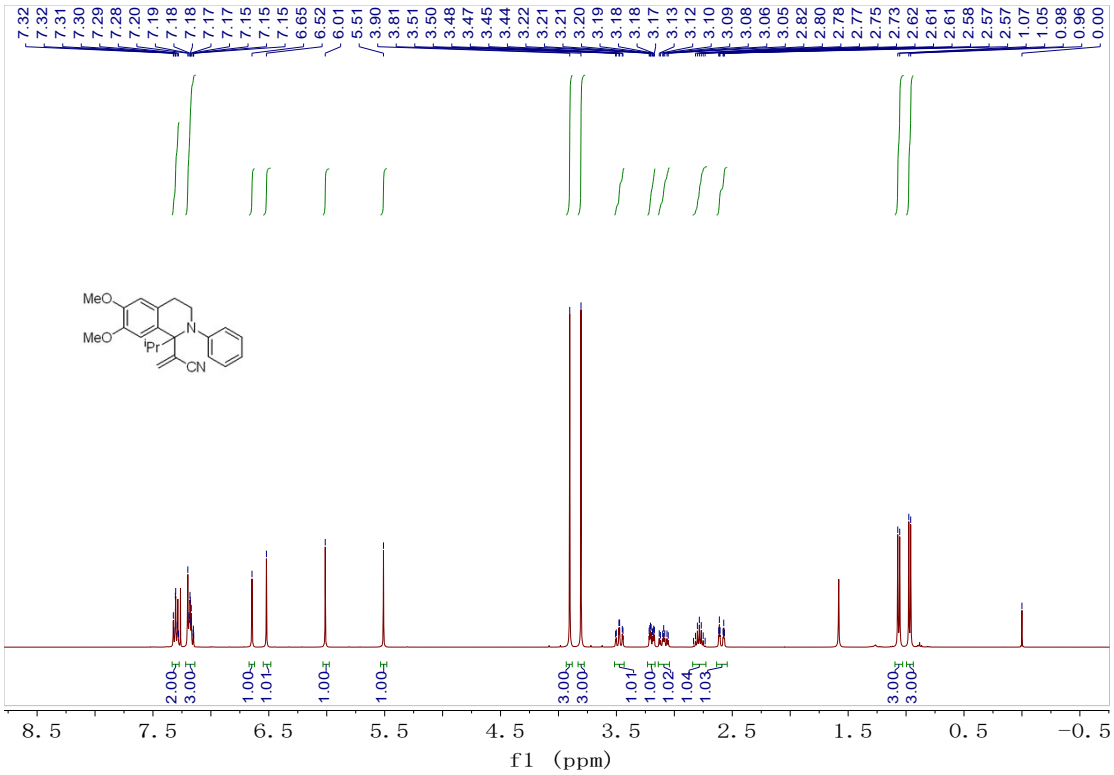
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4o



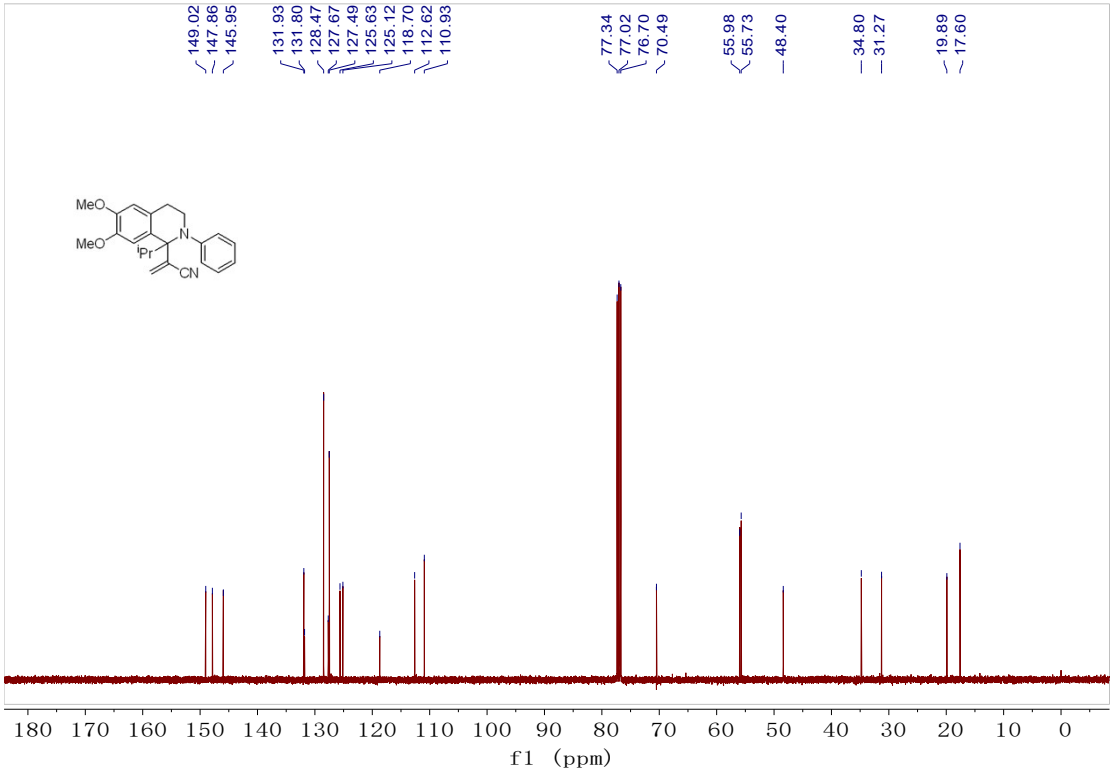
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4o



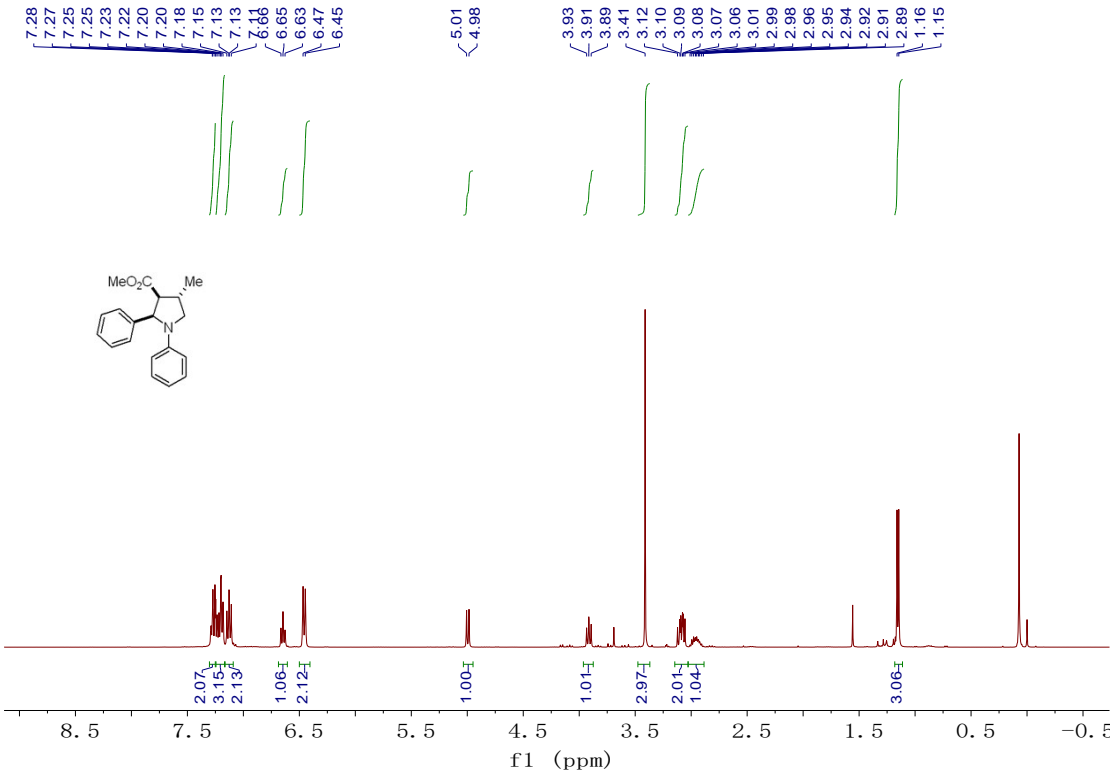
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4p



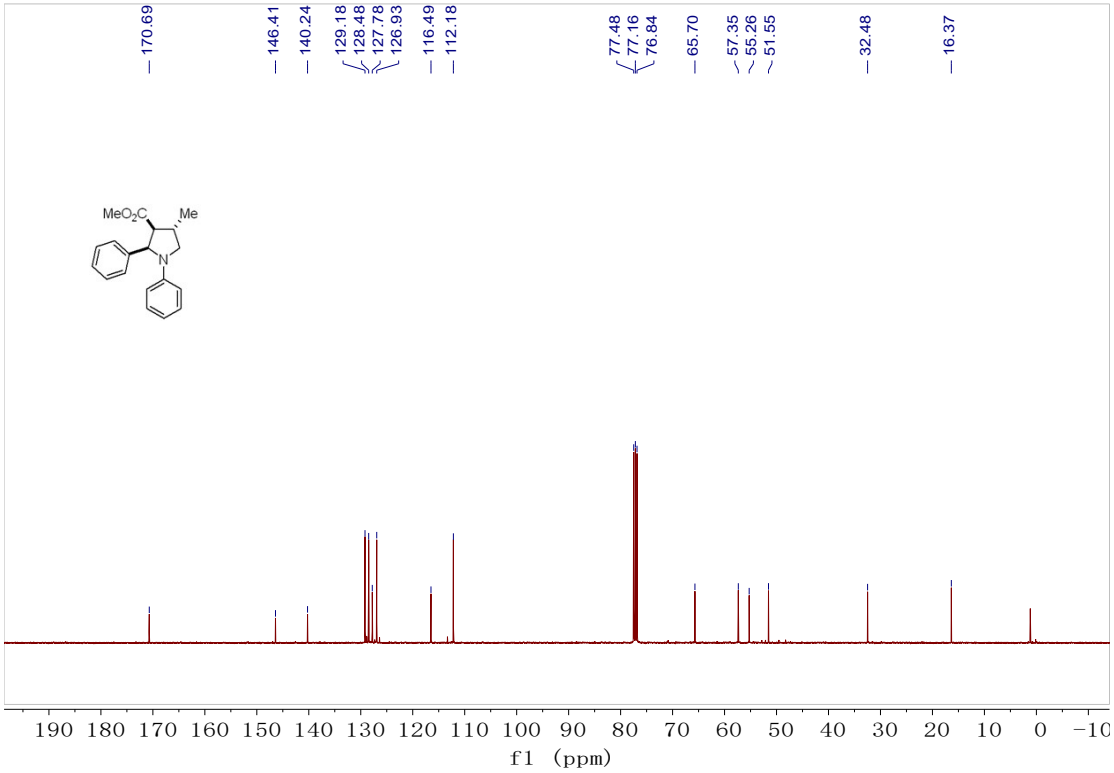
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4p



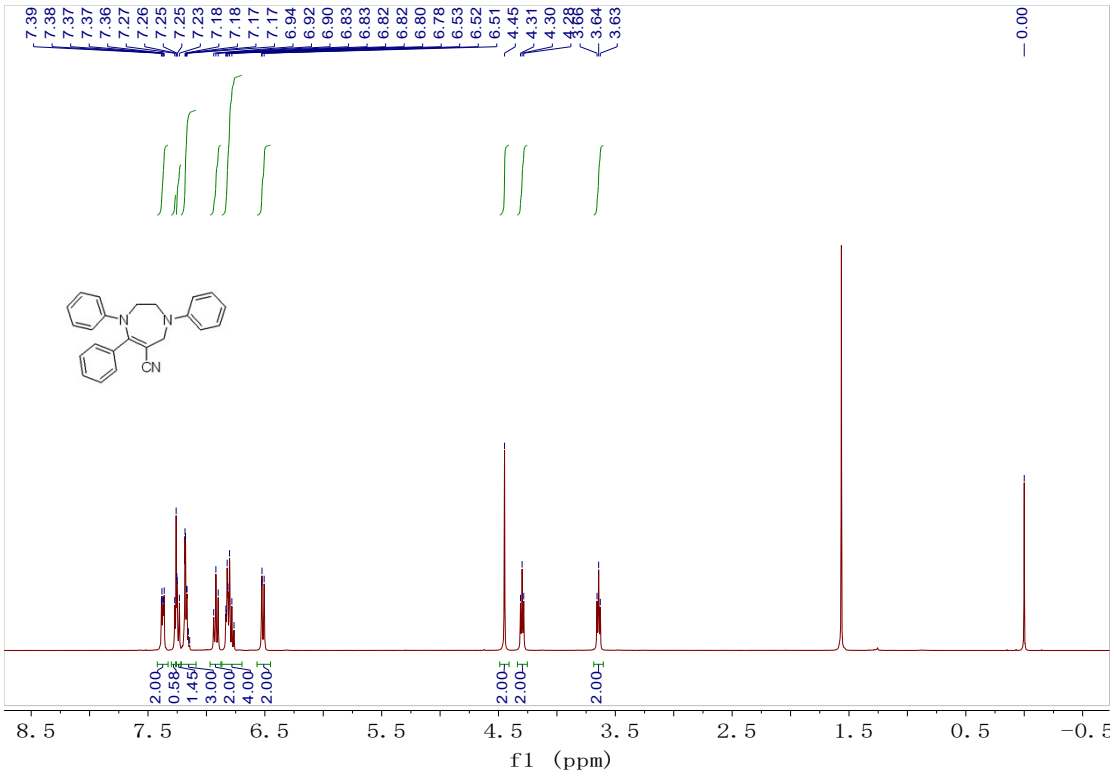
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 12



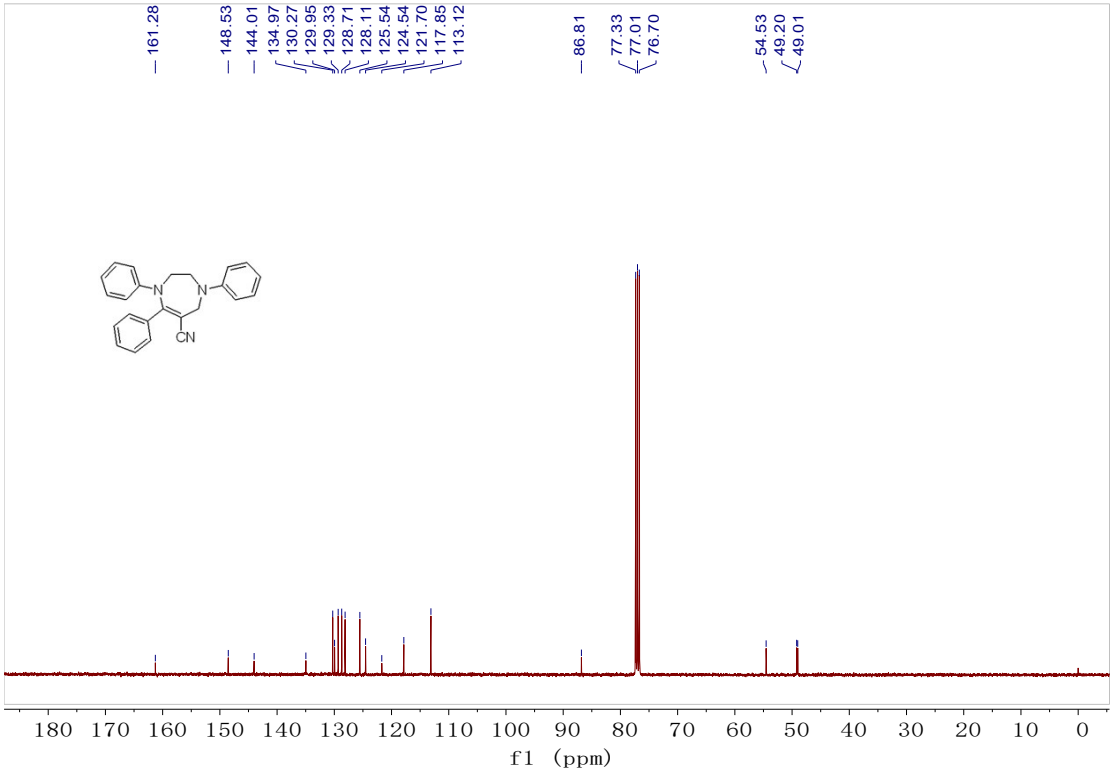
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 12



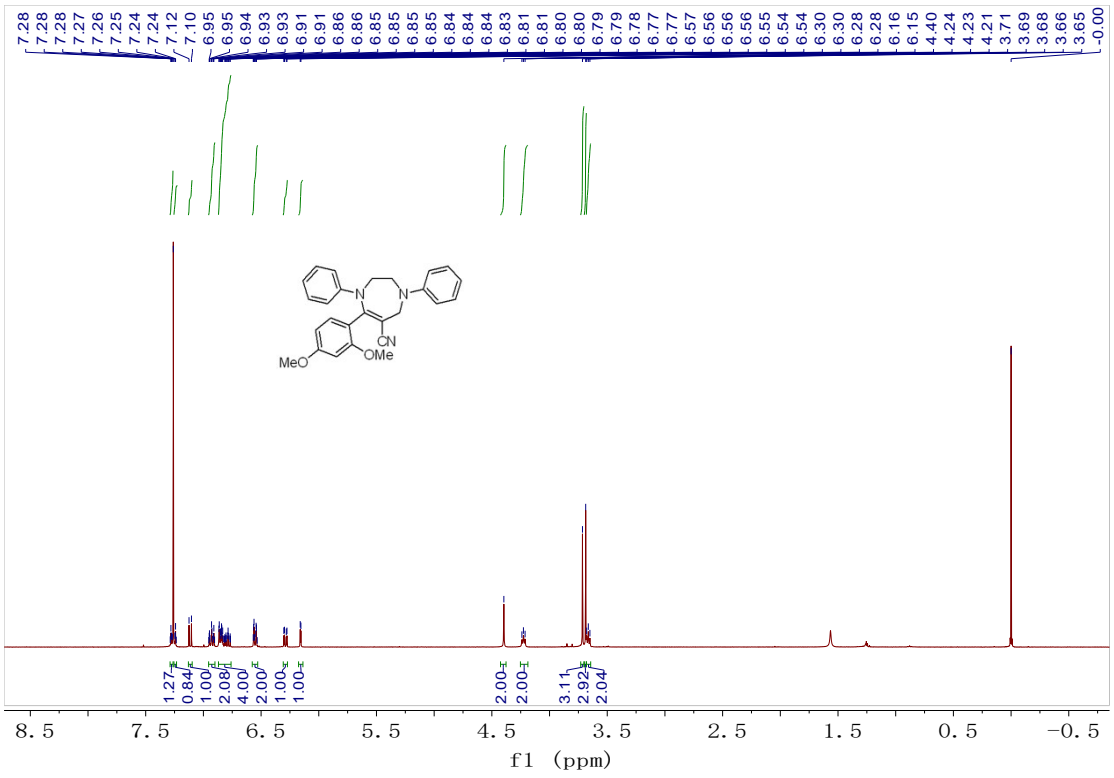
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 14a



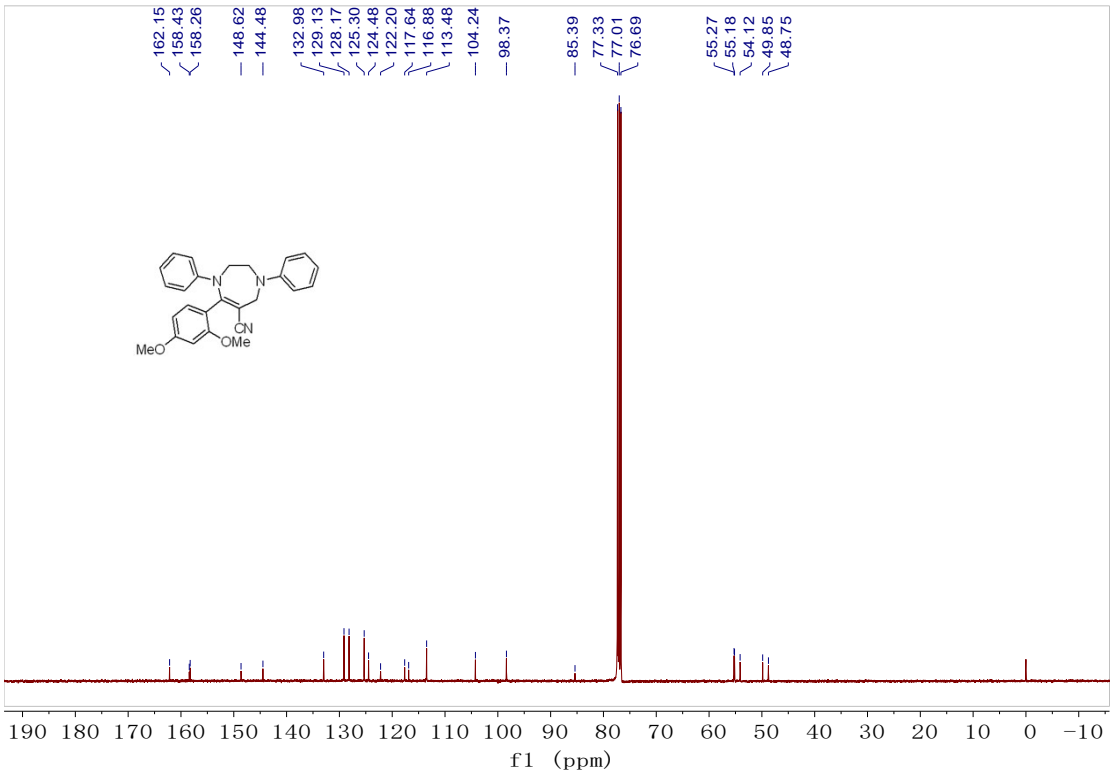
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 14a



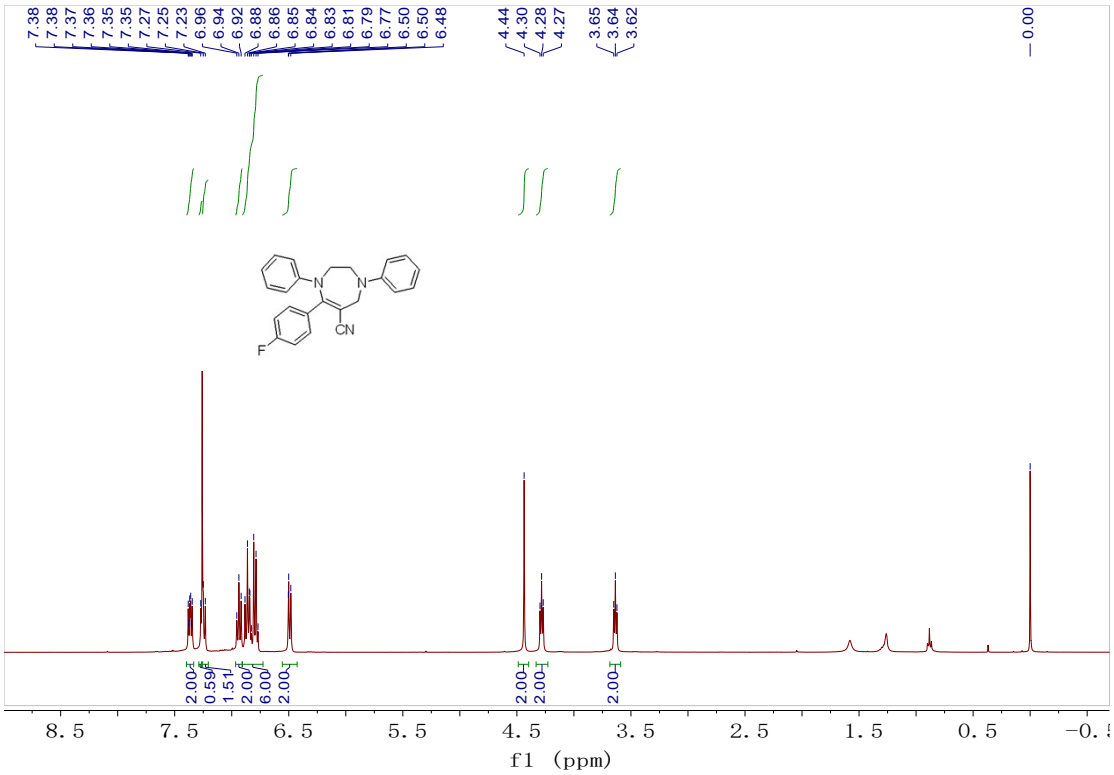
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 14b



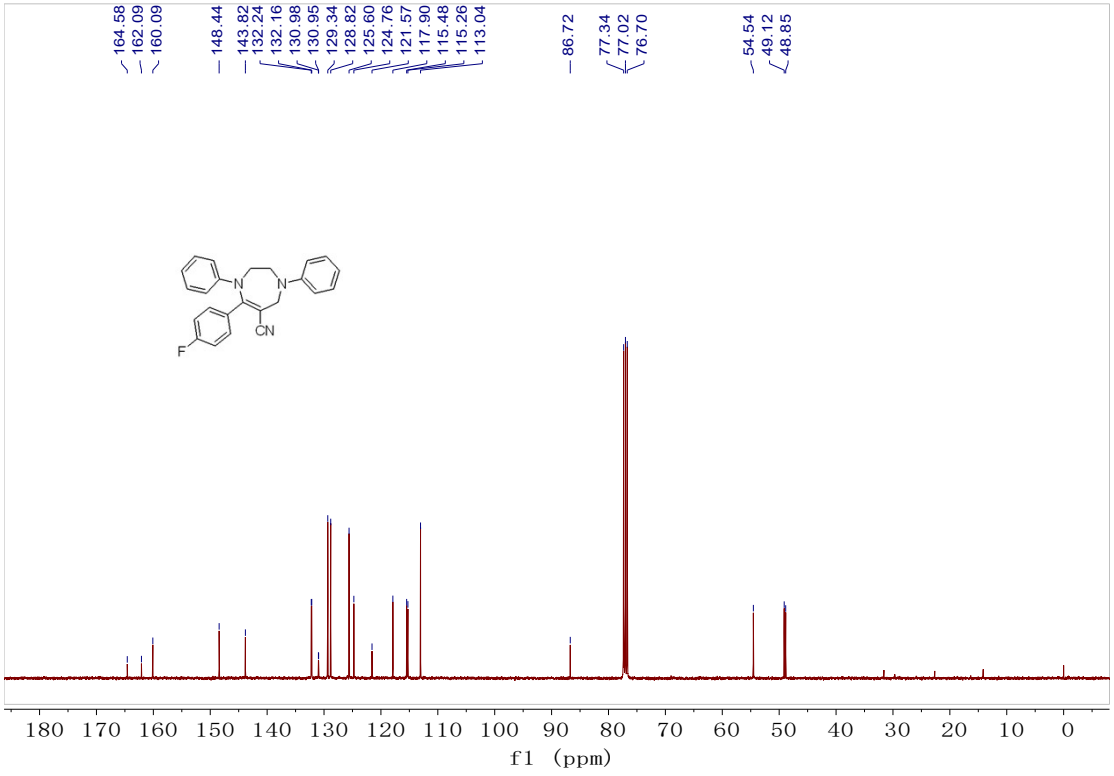
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 14b



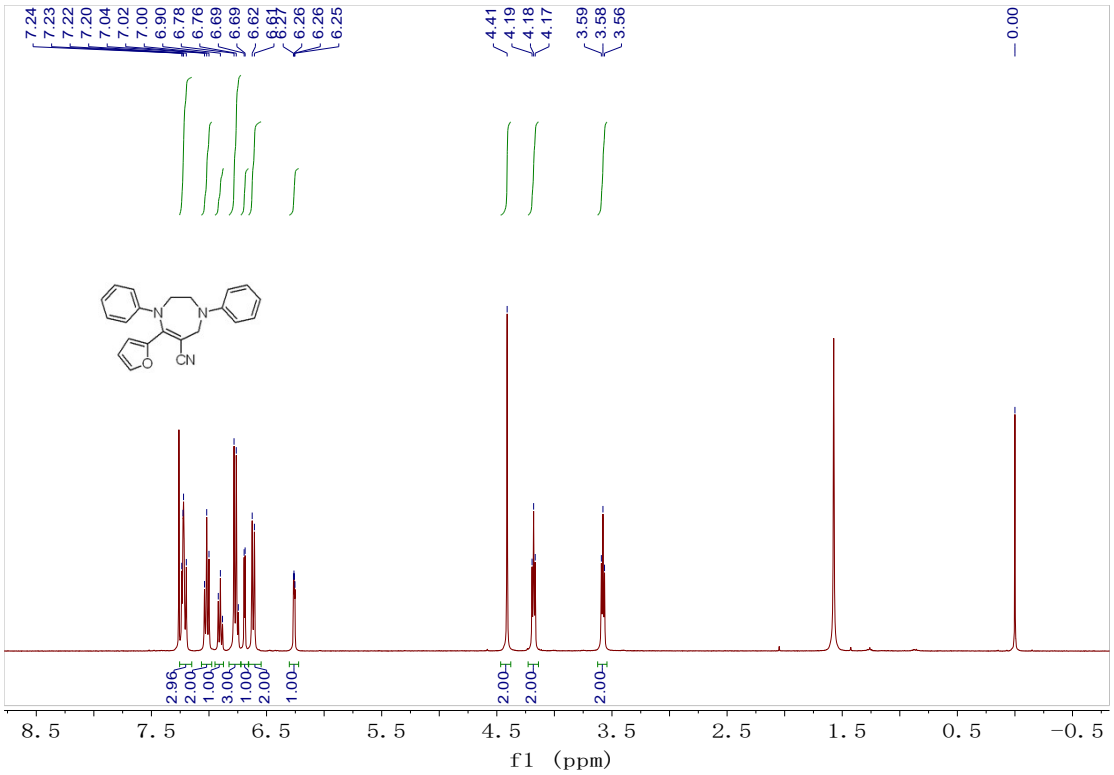
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 14c



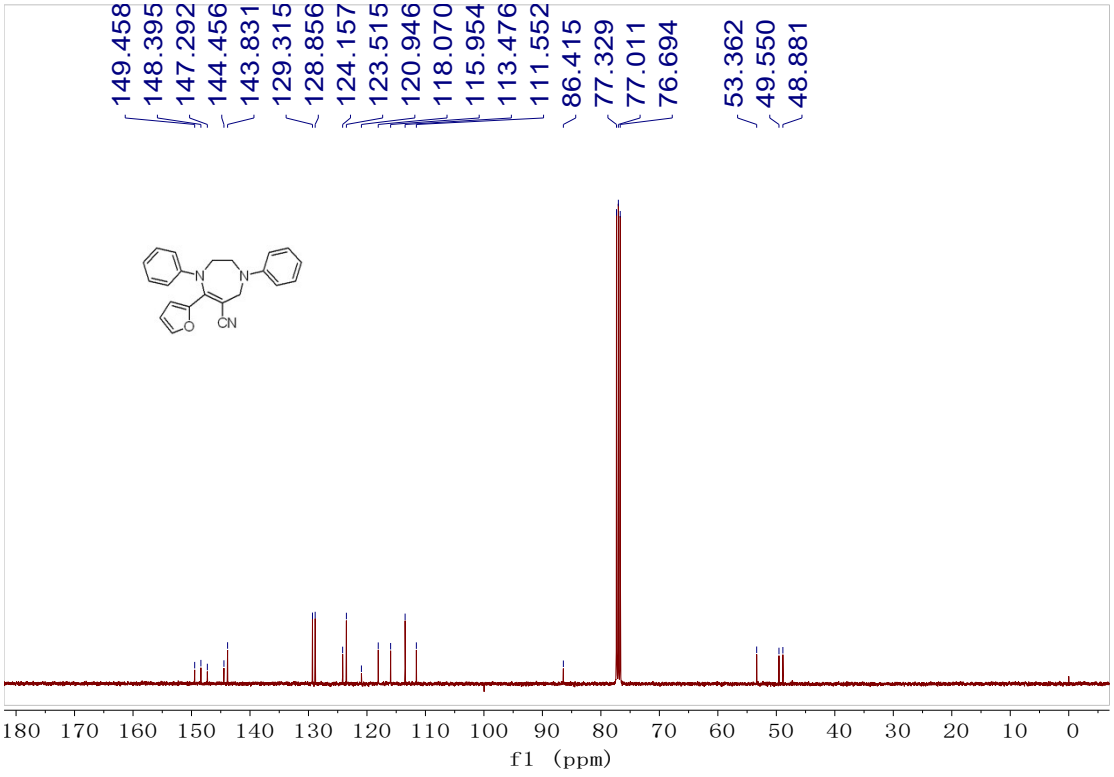
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 14c



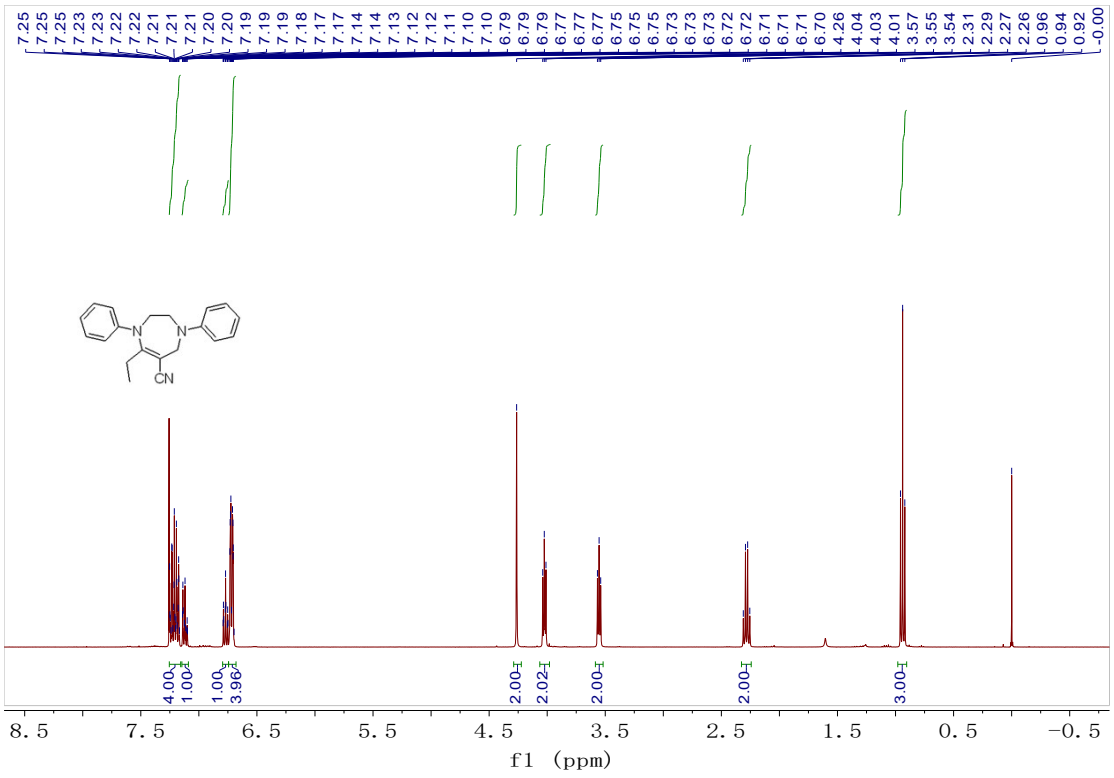
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 14d



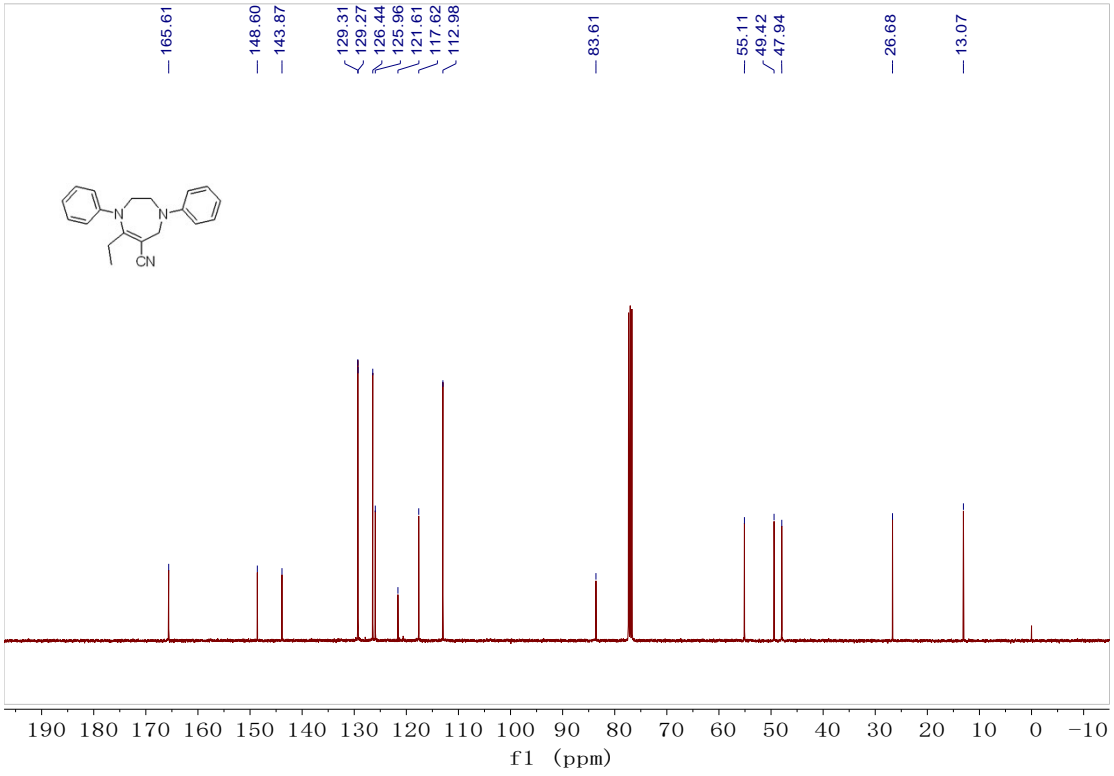
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 14d



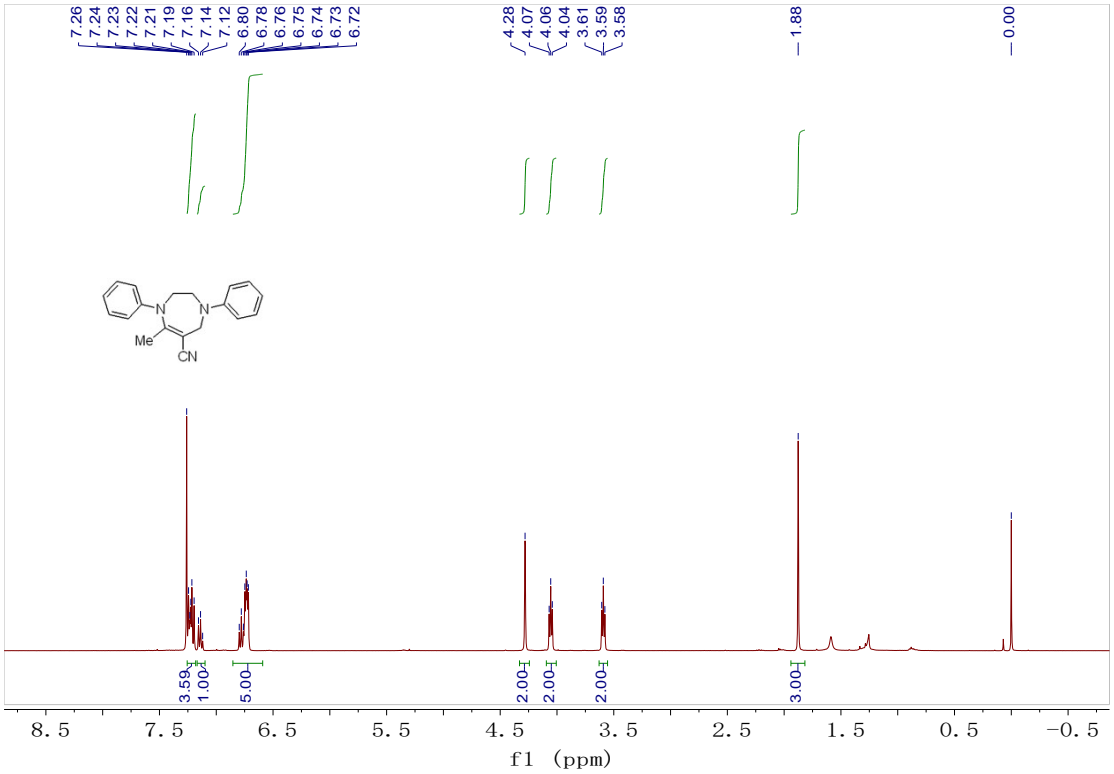
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 14e



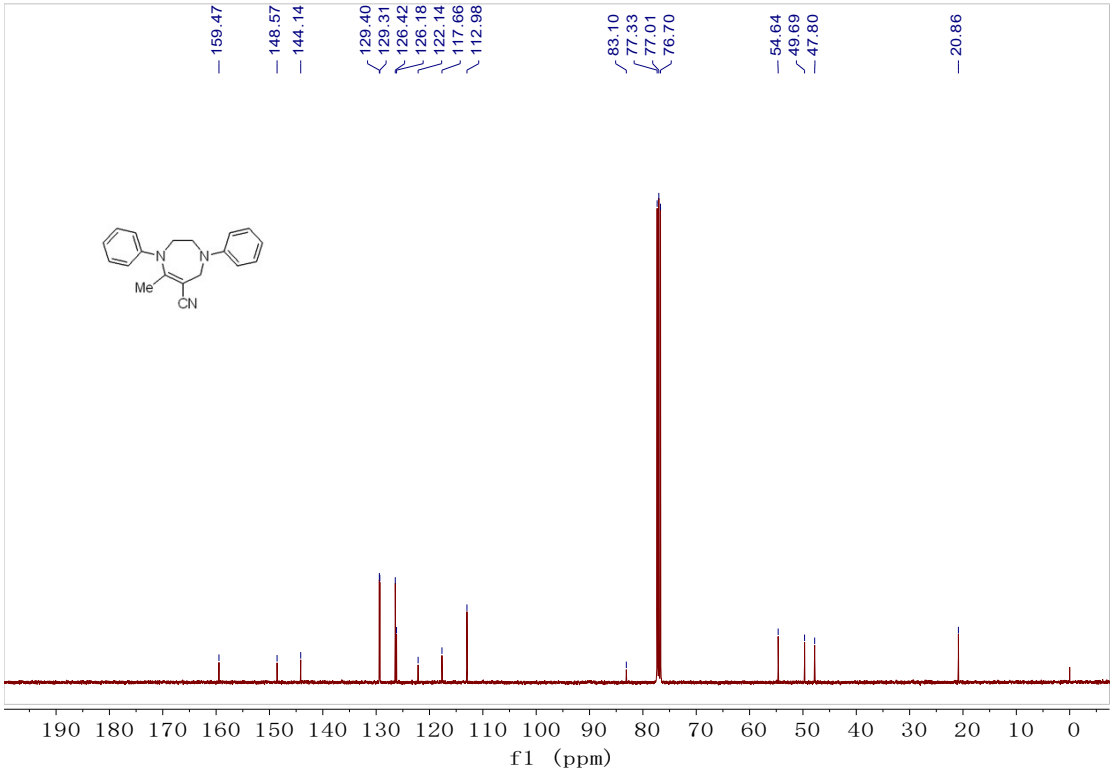
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 14e



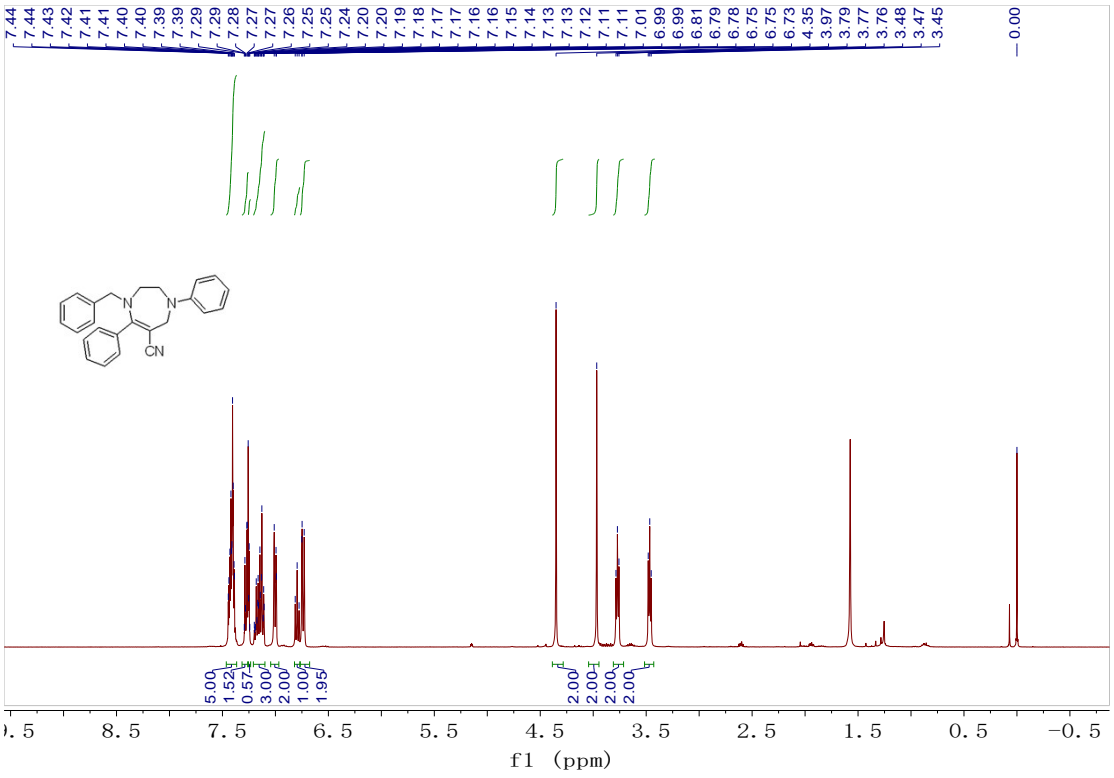
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 14f



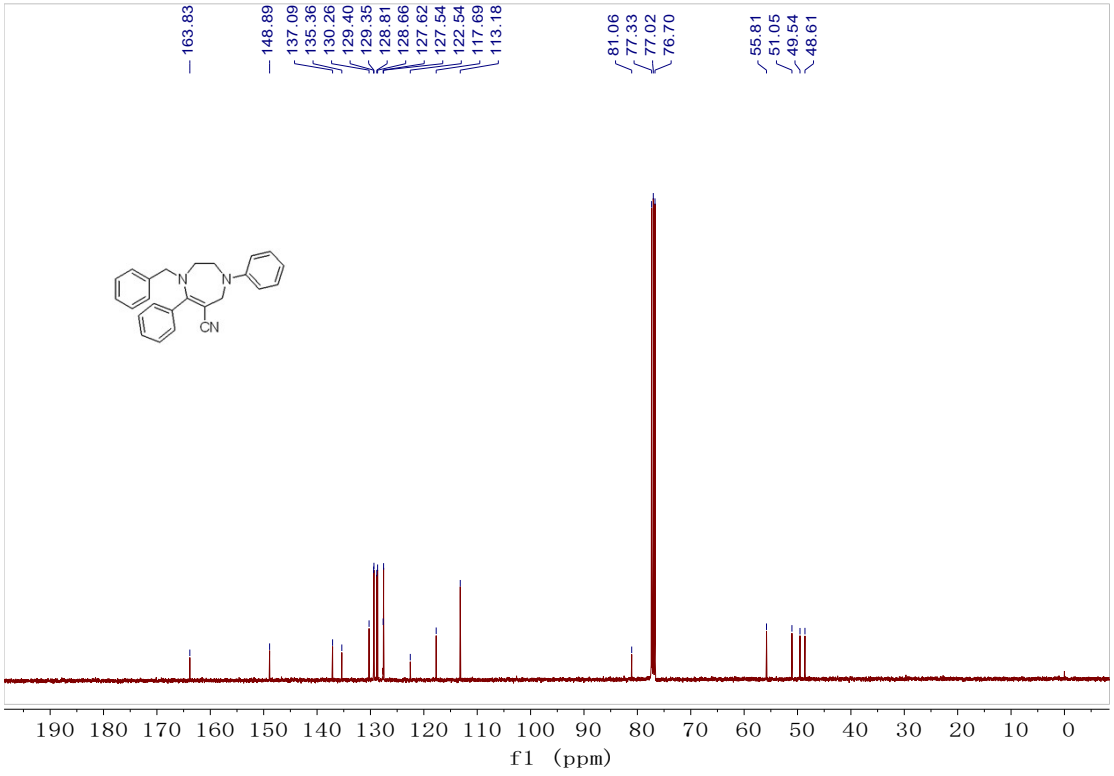
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 14f



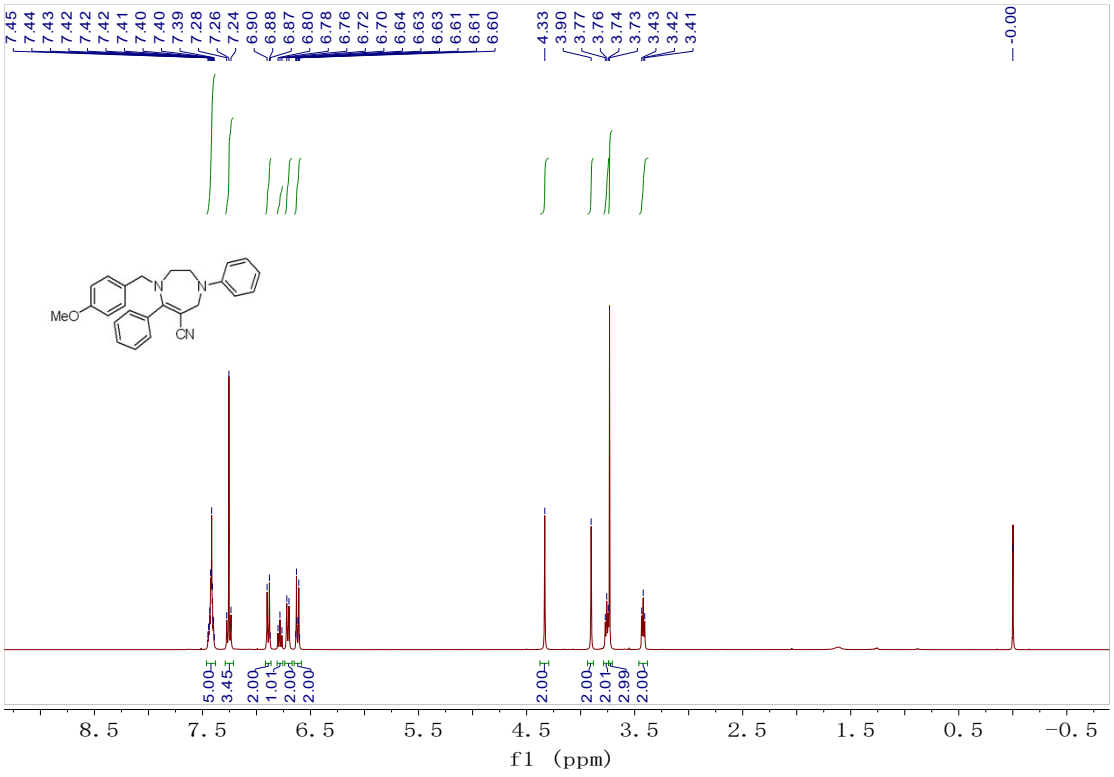
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 14g



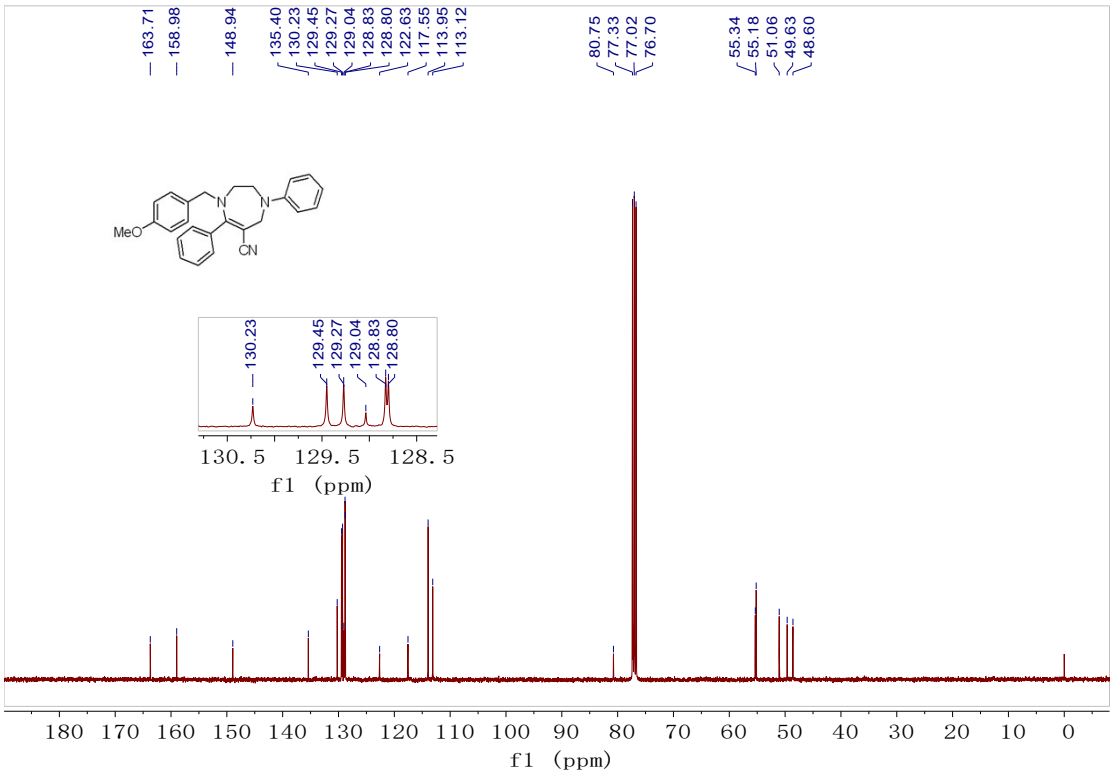
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 14g



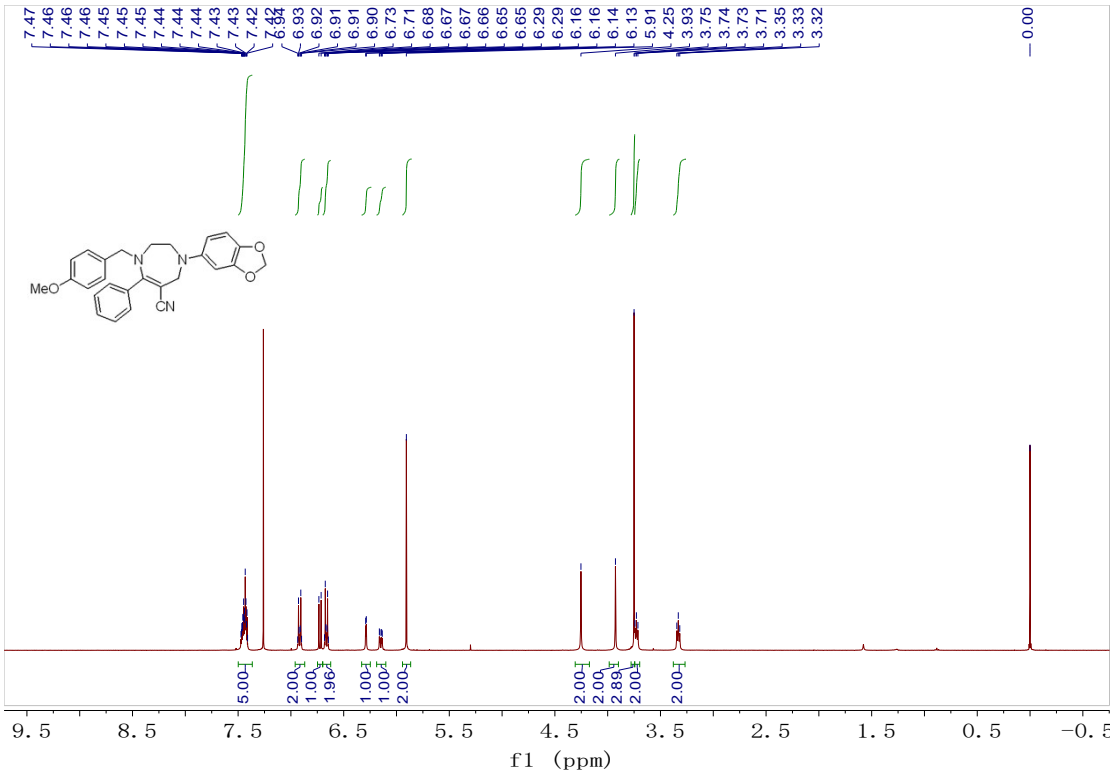
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 14h



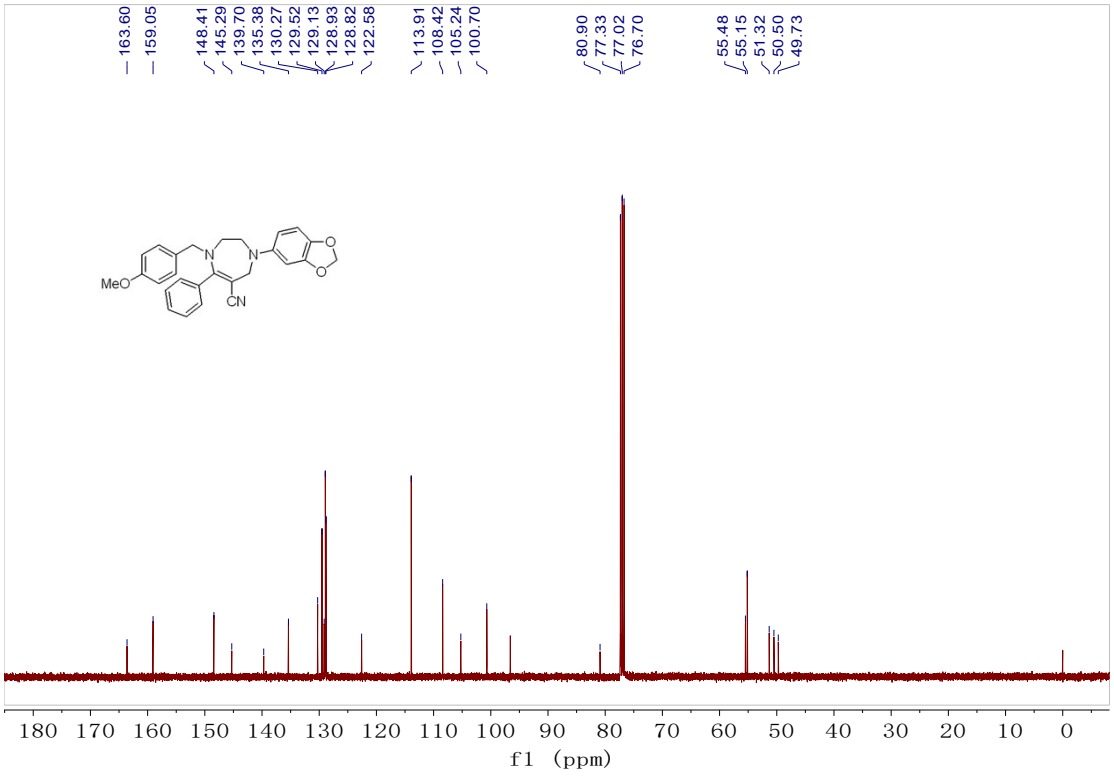
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 14h



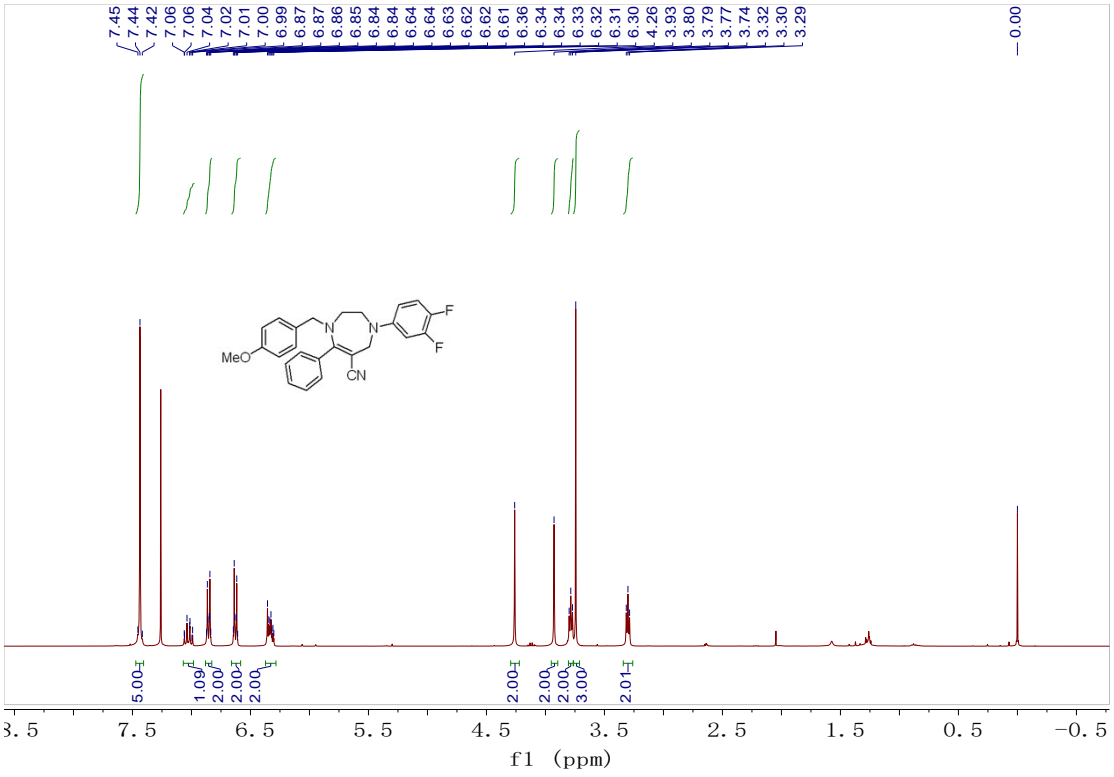
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 14i



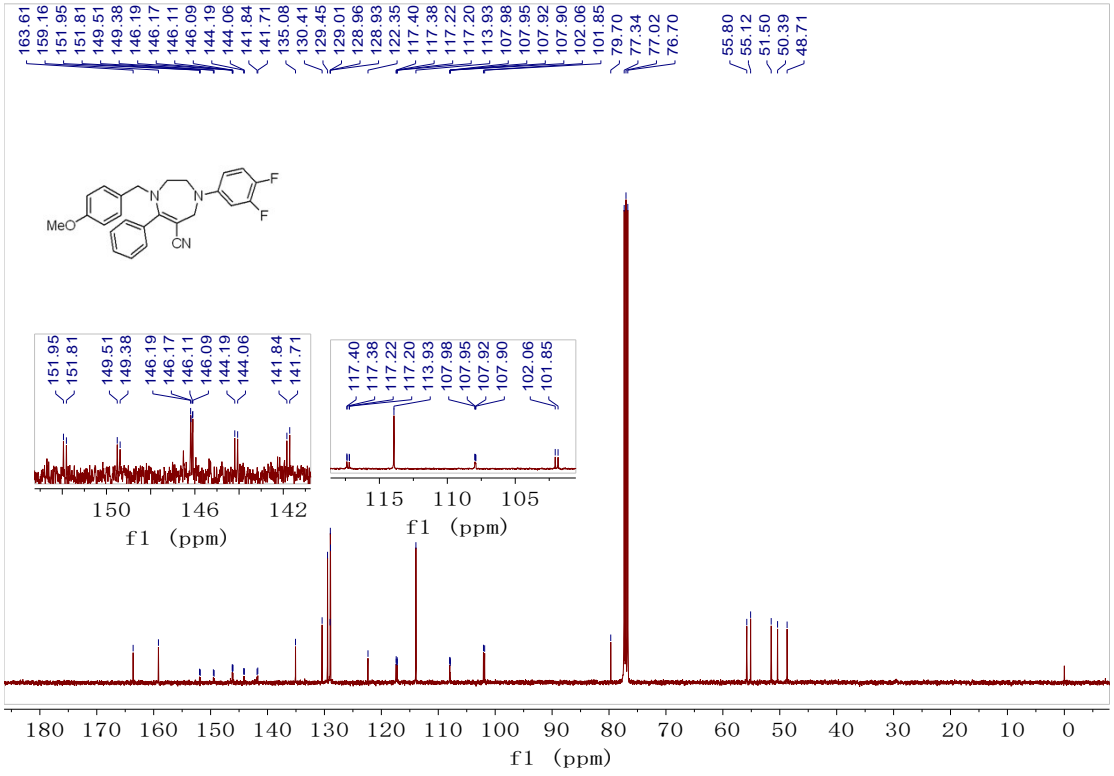
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 14i



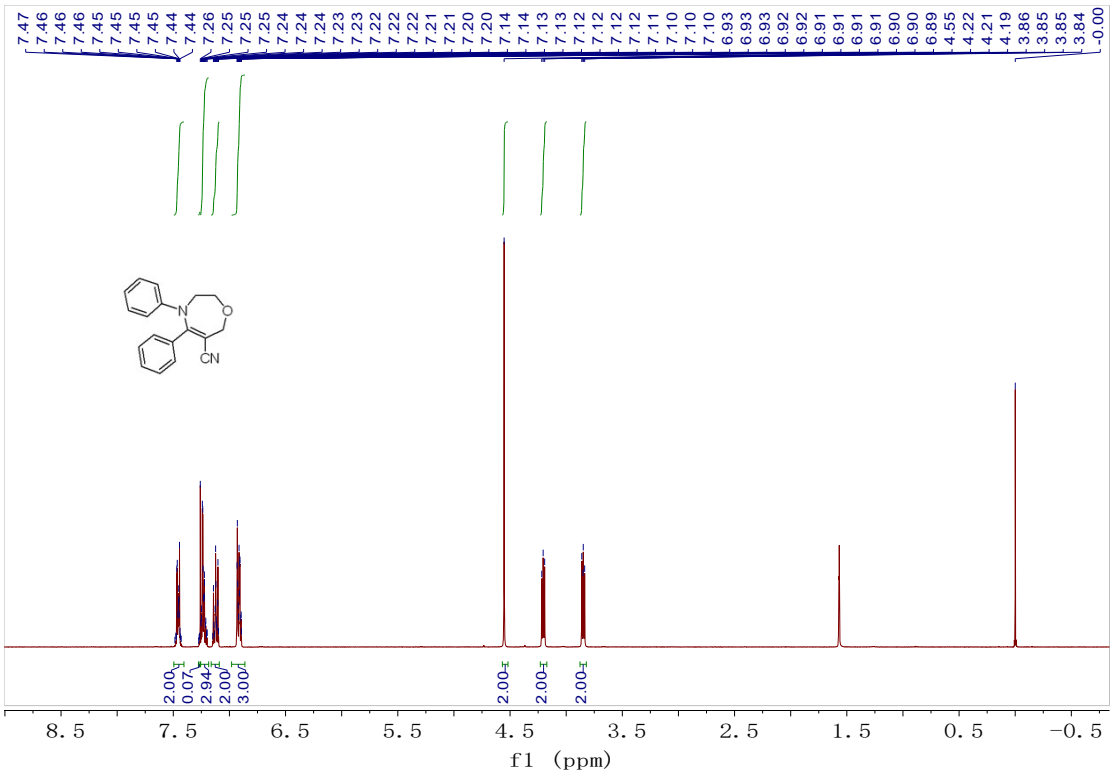
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 14j



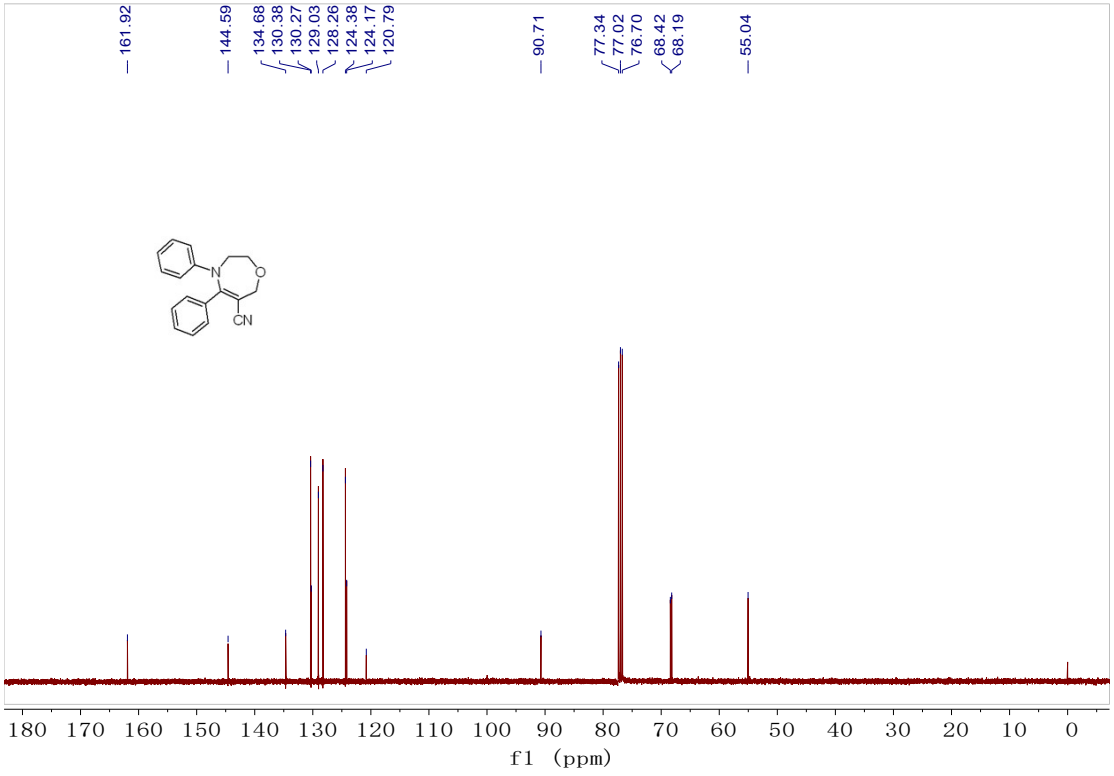
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 14j



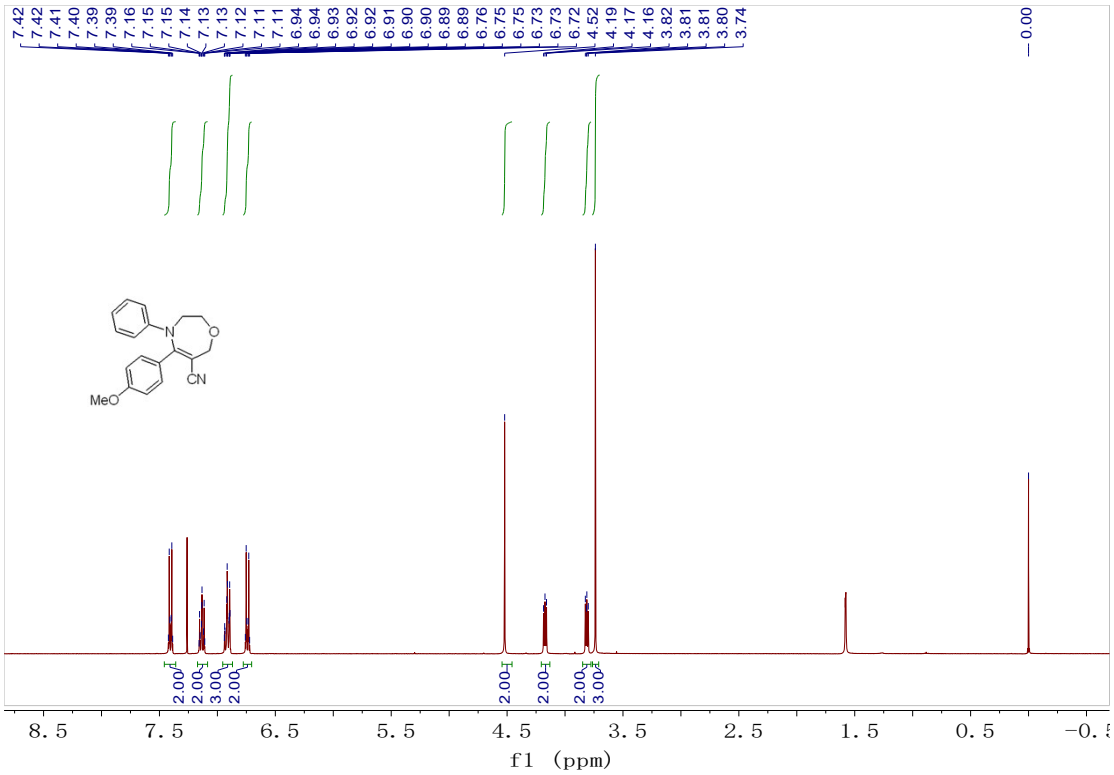
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 19a



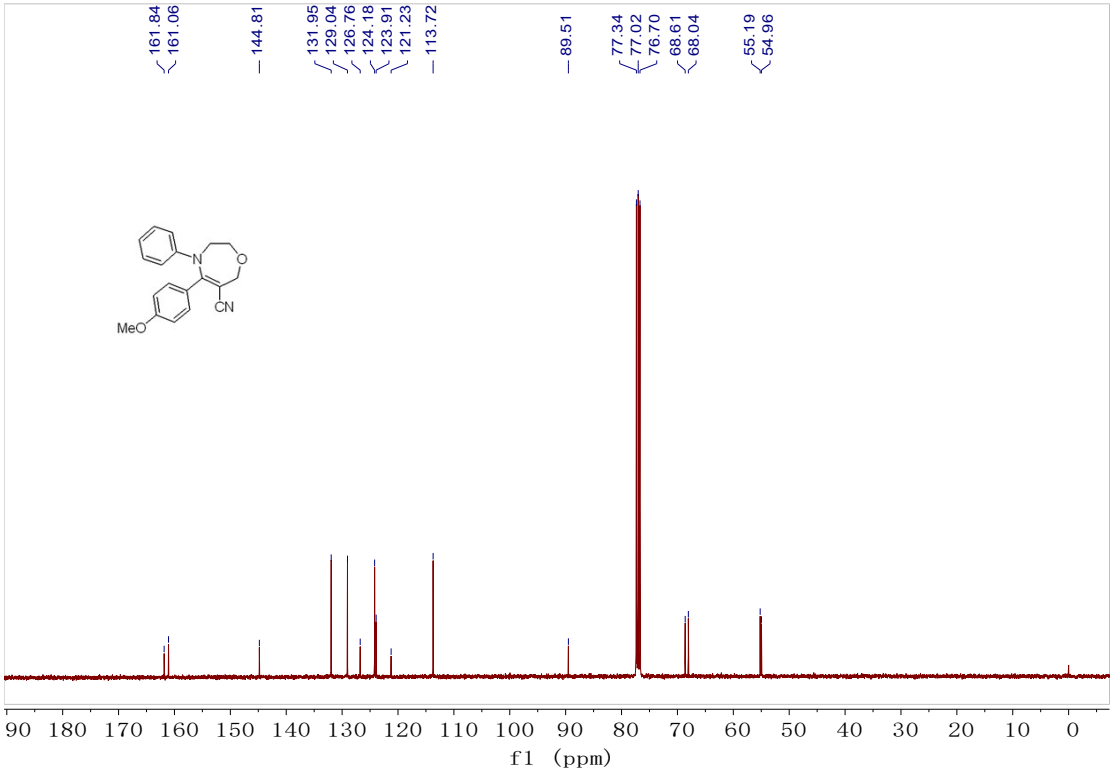
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 19a



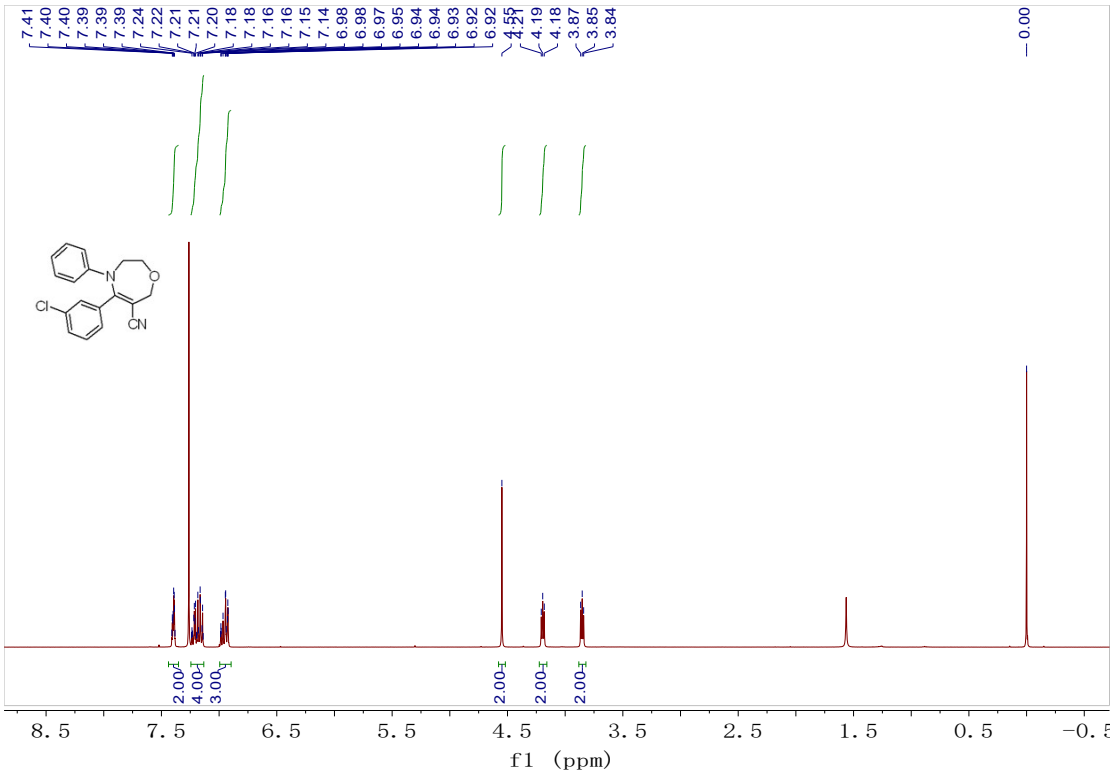
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 19b



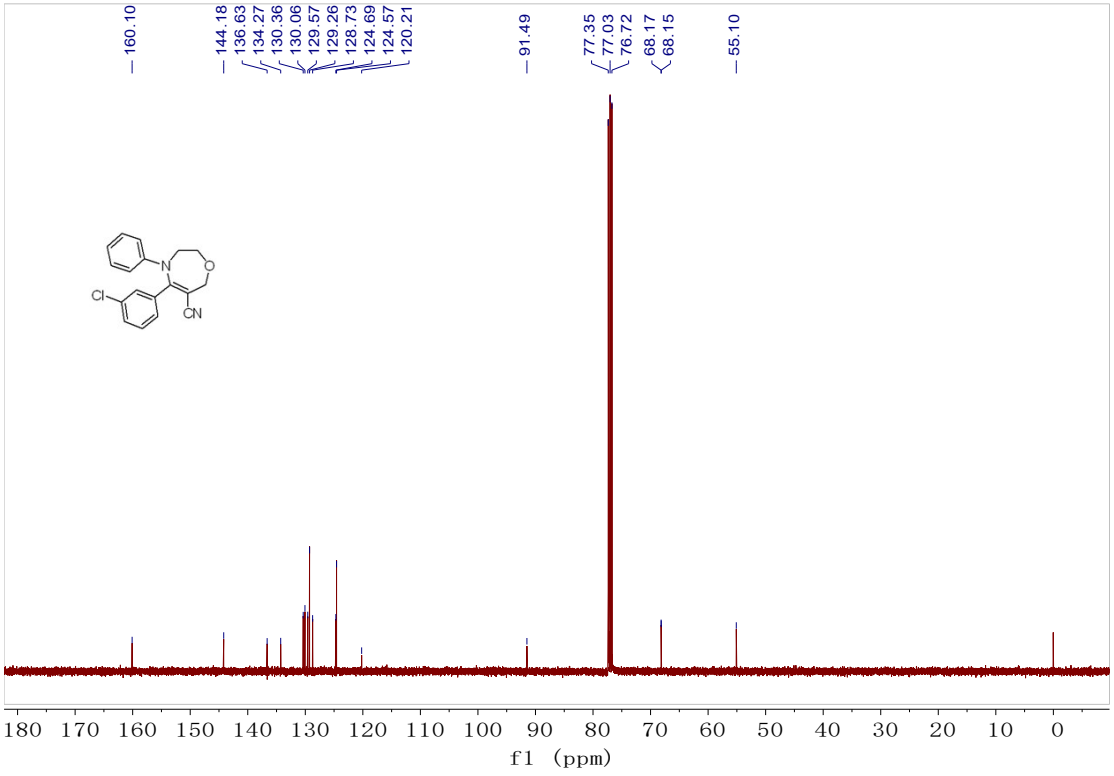
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 19b



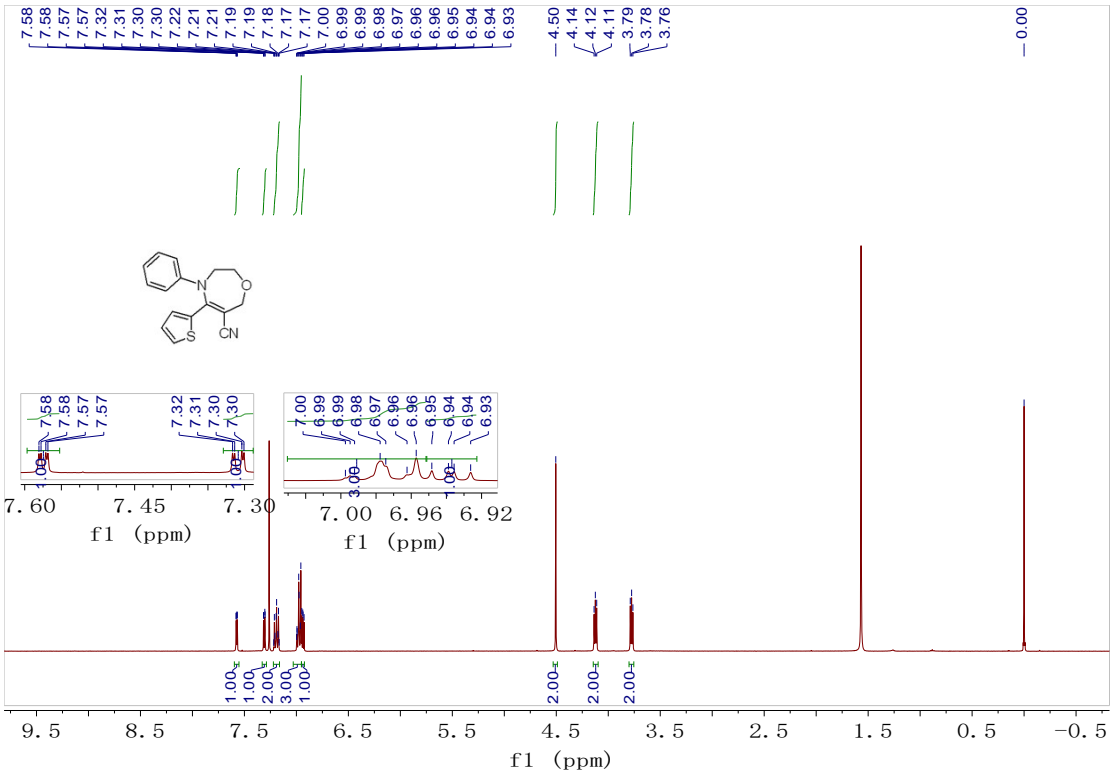
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 19c



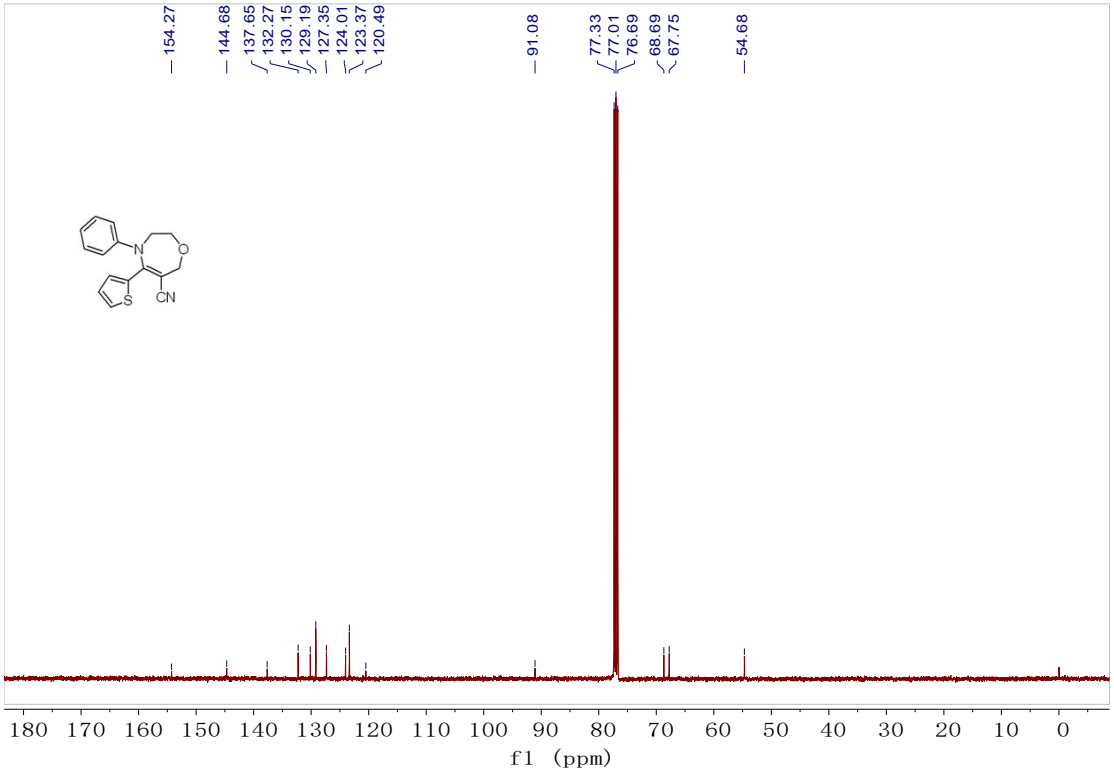
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 19c



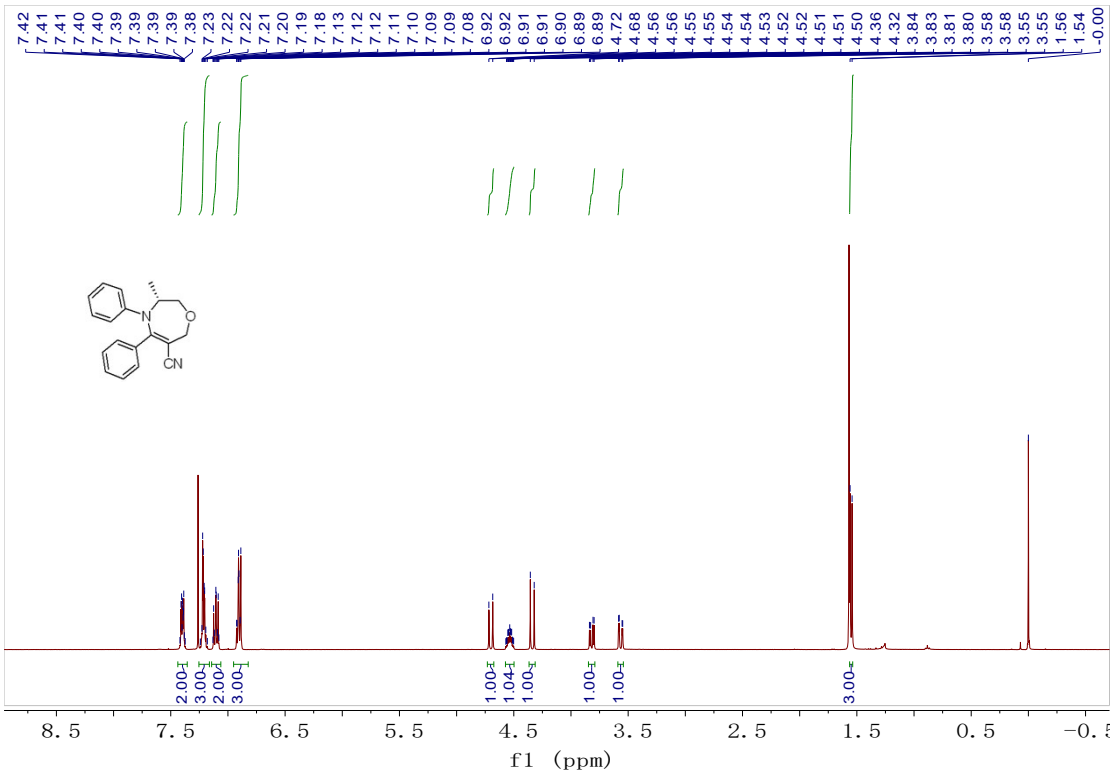
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 19d



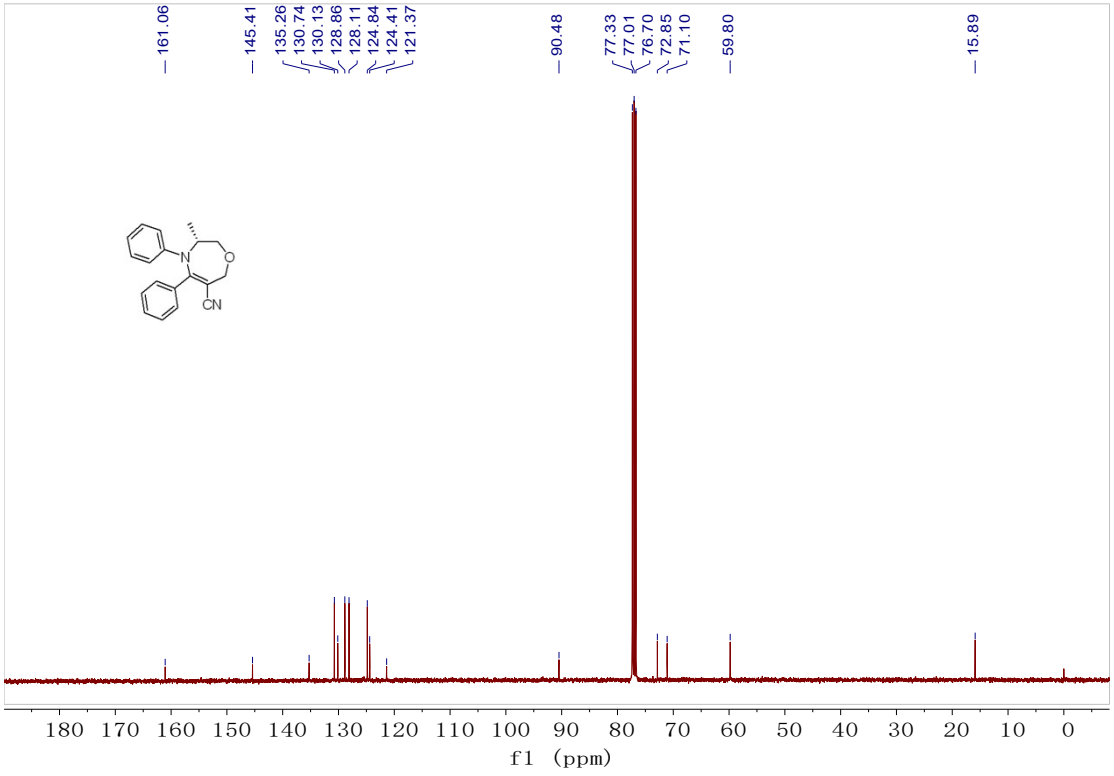
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 19d



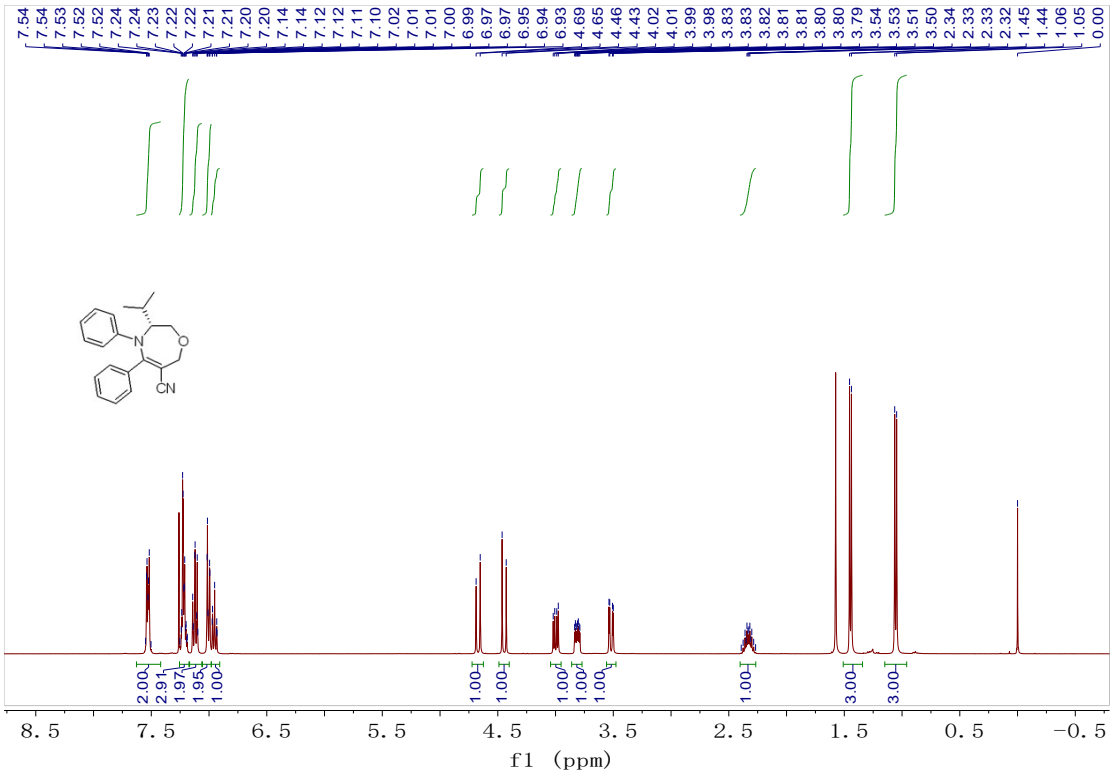
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 19e



^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 19e



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 19f



^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 19f