Supplementary Information

Regiodivergent Metalations of Pyridines Using Mixed TMP-Titanate and TMP-Fe-Titanate Bases

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1. General Information

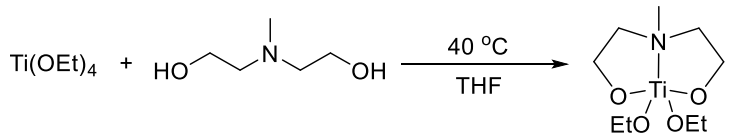
^{1}H NMR (400, 600 MHz) and ^{13}C NMR (101, 151 MHz) spectra were recorded on JNM-ECE 400R or 600R spectrometers unless otherwise noted. The chemical shifts (δ) were quoted in parts per million from tetramethylsilane for ^{1}H and ^{13}C spectroscopy. High resolution mass spectra (HRMS) were obtained with a Bruker microTOF (ESI).

Single crystal data were collected on a Rigaku Oxford diffractometer (device type 'XtaLAB Synergy R, DW system, HyPix′) with Mo-Kα radiation (λ = 0.71073 Å) and Cu-Kα radiation (λ = 1.54184 Å) at 100 K. The crystal structures were solved by the direct method and refined using the Olex2 program.

General remarks for the preparation of Grignard reagents

All reagents and solvents used for aryl magnesium reagents or lithium reagents and reactions were freshly dehydrated before use. The corresponding glassware was oven dried (120 °C) and cooled under a stream of argon gas. Common aryl Grignard reagents such as C_6H_5MgBr, RC_6H_4MgBr (R = 4- or 2-CH_3, 4- or 3-Cl, etc.) were prepared according to standard procedure. Functionalized aryl Grignard reagents such as 4-cyanophenyl magnesium chloride was prepared *via* iodine-magnesium exchange using *i*-PrMgCl·LiCl according to Knochel's method.[1] All the Grignard reagents were titrated before use.[2]

Preparation of Ti-1



Under Ar atmosphere, $Ti(OEt)_4$ (34.2 g, 150 mmol) was dissolved in 100 mL THF. Under stirring, *N*-methyldiethanolamine (17.9 g, 150 mmol) was added dropwise. The mixture was stirred at 40 °C for 4 − 5 h and the solvent was removed by vacuum distillation. The residue was dissolved in hexane (20 mL) and frozen in the refrigerator to form a solid. After filtration and vacuum drying, the desired **Ti-1** was obtained as a pale yellow solid (38.3g, 98%).[3]

2. Condition optimizations

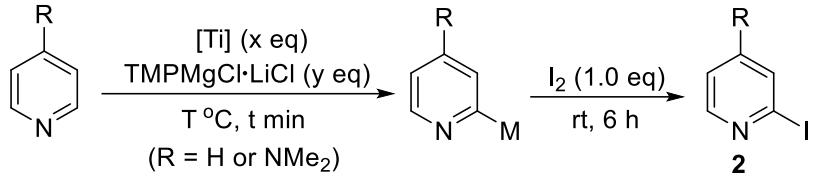
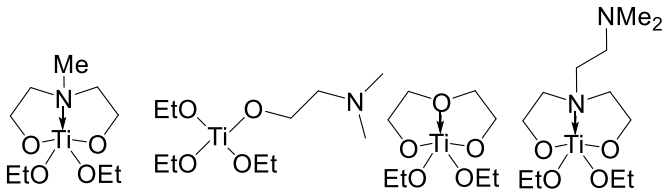


Table S1 Condition optimizations for reagent A

Entry	[Ti]	x	y	T (°C)	t (min)	Yield (%)[b]
1	**Ti-1**	**0.75**	**1.5**	**25**	**40**	**92**
2	$Ti(OEt)_4$	0.25	1	25	60	15
3	$Ti(OEt)_4$	0.5	1	25	60	26
4	$Ti(OEt)_4$	0.75	1.5	25	60	34
5	**Ti-2**	0.75	1.5	25	60	37
6	**Ti-3**	0.75	1.5	25	60	49
7	**Ti-4**	0.75	1.5	25	60	83
8	**Ti-1**	--	1.5	25	60	10
9	**Ti-1**	--	1.5	65	60	13
10	**Ti-1**	0.5	1.5	25	60	45
11	**Ti-1**	1	1.5	25	60	86
12	**Ti-1**	0.5	1	25	60	64
13	**Ti-1**	0.75	1.5	25	40	48[d]
14	**Ti-1**	0.75	1	25	60	63
15	**Ti-1**	0.75	1.2	25	60	79
16	**Ti-1**	0.75	2	25	60	90
17	**Ti-1**	0.75	1.5	45	60	89
18	**Ti-1**	0.75	1.5	65	60	91
19	**Ti-1**	0.75	1.5	25	20	63
20	**Ti-1**	0.75	1.5	25	30	78
21	**Ti-1**	0.75	1.5	25	60	88
22	**Ti-1**	0.75	1.5	25	40	75[e]

[a] The reactions were carried out on a 1 mmol scale; [b] Isolated yields; [c] R = H; [d] Without LiCl; [e] R = NME_2.



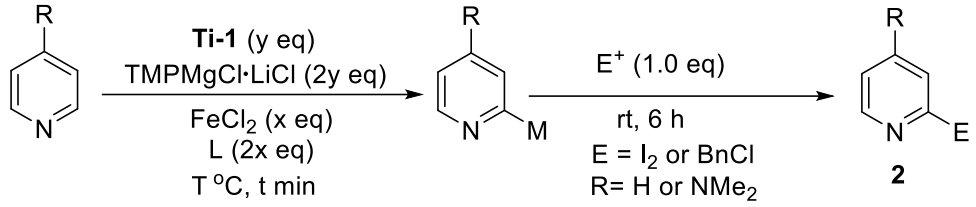
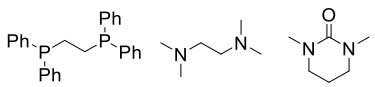


Table S2 Condition optimizations for reagent B

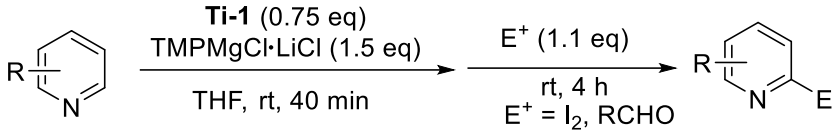
Entry	L	x	y	T (°C)	t (min)	Yield (%)[b]
1	**--**	**0.75**	**0.75**	**25**	**60**	**80**[c, d]
2	TMEDA	0.75	0.75	25	60	81 [c, d]
3	DMPU	0.75	0.75	25	60	46[c, d]
4	PPh_3	0.75	0.75	25	60	38[c, d]
5	PBu_3	0.75	0.75	25	60	29[c, d]
6	DPPE	0.75	0.75	25	60	47[c, d]
7	--	--	0.75	25	60	11[c,d] (79[c,d,e,f])
8	TMEDA	0.75	0.75	45	60	76[c, d]
9	TMEDA	0.75	0.75	65	60	77[c, d]
10	TMEDA	0.2	0.75	25	60	17[c, d]
11	TMEDA	0.5	0.75	25	60	43[c, d]
12	TMEDA	1	0.75	25	60	72[c, d]
13	TMEDA	1.2	0.75	25	60	78[c, d]
14	TMEDA	0.75	0.75	25	20	35[c, d]
15	TMEDA	0.75	0.75	25	40	68[c, d]
16	TMEDA	0.75	0.75	25	120	81[c, d]
17	TMEDA	0.75	1.0	25	60	79[c, d]
18	TMEDA	0.75	0	25	60	7[c, d]
19	TMEDA	0.75	0	65	60	9[c, d]
20	TMEDA	0.75	0.75	25	60	50[c, d, g]
21	--	0.75	0.75	25	60	48 [c, d, g]
22	--	0.75	0.75	25	60	65[h, d]
23	--	0.75	0.75	25	60	86[c, i]
24	--	0.75	0.75	25	60	71[h, i]

[a] The reactions were carried out on a 1 mmol scale. [b] Isolated yields. [c] R = H. [d] E = BnCl. [e] 0.1 eq CuCN·2LiCl was used. [f] The reaction temperature with the electrophilic reagent was -20 °C. [g] Without LiCl. [h] R = NMe_2. [i] E = I_2.



3. General procedures for functionalization and cross coupling of pyridines via direct metalation using reagents A and B

GPA–1 (for reactions using A in Table 2 and E = I_2, RCHO):



Under argon atmosphere, to a solution of **Ti-1** (956 mg, 3.75 mmol, 0.75 eq) in dry THF (4 mL) was added dropwise a solution of TMPMgCl·LiCl (7.5 mmol, 1.5 eq) in THF though a syringe in 10 − 15 minutes at 25 ºC. The mixture was stirred at 25 ºC for 40 min.

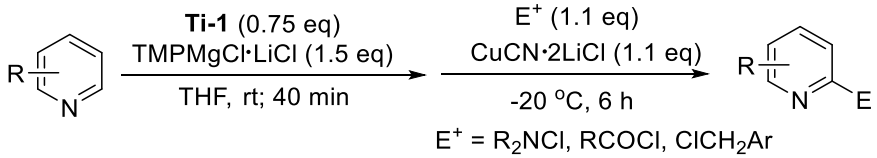
In another three-necked flask (50 mL), a pyridine or quinoline compound (5 mmol, 1.0 eq) was dissolved in 5 mL THF under argon atmosphere. To this solution, the reagent A prepared above was slowly added dropwise. After stirred for 40 min at room temperature, the electrophilic reagent (1.1 eq; E = I_2, RCHO) was added and the resulting mixture was stirred for 4h until the reaction was completed (monitored by TLC).

The reaction was quenched by adding 50 mL distilled water under stirring. The resulting solid was filtered and washed by CH_2Cl_2 (50 mL). The filtrate was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration and removing the solvent *in vacuum*, the residue was purified by flash column chromatography on silica gel to afford the desired compound.

Note:

1. This general procedure is well applicable to **2Aa, 2Ab**, **2Ae - 2Ag, 2Aj - 2Am, 2Ao - 2At**, **3u – 3x (by A)**.
2. The resulting solution of **Ti-1** and TMPMgCl·LiCl in THF was evaporated under an argon atmosphere below 40°C to obtain solid **A**. It was stored in a sealed container under argon atmosphere at room temperature. When used for the preparation of **2Am** one week later, only a slight decrease in product yield was observed.

GPA-2 (for reactions using A in Table 2 and E = R_2NCl, RCOCl, $ClCH_2Ar$):



Under argon atmosphere, to a solution of **Ti-1** (956 mg, 3.75 mmol, 0.75 eq) in dry THF (4 mL) was added dropwise a solution of TMPMgCl·LiCl (7.5 mmol, 1.5 eq)

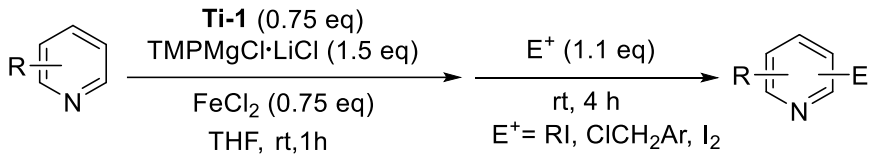
in THF though a syringe in 10 − 15 minutes at 25 °C. The mixture was stirred at 25 °C for 40 min.

In another three-necked flask (50 mL), a pyridine or quinoline compound (5 mmol, 1.0 eq) was dissolved in 5 mL THF under argon atmosphere. To this solution, the reagent A prepared above was slowly added dropwise. After stirred for 40 min at room temperature, the mixture was cooled to -20 °C, and the electrophilic reagent (1.1 eq; E= R_2NCl, RCOCl or $ClCH_2Ar$) and CuCN·2LiCl (960 mg, 5.5 mmol, 1.1 eq) were added. The mixture was stirred at that temperature for 6 hours until the reaction was completed (monitored by TLC).

The reaction was quenched by adding 50 mL distilled water under stirring. The resulting solid was filtered and washed by CH_2Cl_2 (50 mL); and the filtrate was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration and removing the solvent *in vacuum*, the residue was purified by flash column chromatography on silica gel to afford the desired compound.

Note: This general procedure is well applicable to **2Ac, 2Ad, 2Ah**, **2Ai, 2An**.

GPB-3 (for reactions using B in Table 2 and E = RI, $ClCH_2Ar$, I_2):



Under argon atmosphere, to a solution of **Ti-1** (956 mg, 3.75 mmol, 0.75 eq) and $FeCl_2$ (475 mg, 3.75 mmol, 0.75 eq) in dry THF (8 mL) was added dropwise a solution of TMPMgCl·LiCl (7.5 mmol, 1.5 eq) in THF though a syringe in 10 − 15 minutes at 25 °C. The mixture was stirred at 25 °C for 1h.

In another three-necked flask (50 mL), a pyridine or quinoline compound (5 mmol, 1.0 eq) was dissolved in 5 mL THF under argon atmosphere. To this solution, the reagent B prepared above was slowly added dropwise. After stirred for 1 h at room temperature, the electrophilic reagent (1.1 eq; E = RI, $ClCH_2Ar$, I_2,) was added. The resulting mixture was stirred for 4 h until the reaction was completed (monitored by TLC).

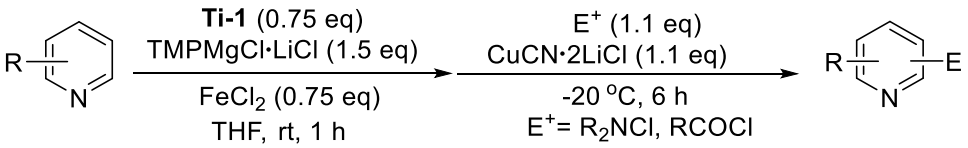
The reaction was quenched by adding 50 mL distilled water under stirring. The resulting solid was filtered and washed by CH_2Cl_2 (50 mL); and the filtrate was

extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration and removing the solvent *in vacuum*, the residue was purified by flash column chromatography on silica gel to afford the desired compound.

Note:

1. By adjusting the addition manner of $FeCl_2$, this process can also start with the preparation of reagent **A**. $FeCl_2$ (475 mg, 3.75 mmol, 0.75 eq) was added into the second flask along with a pyridine or quinoline compound, and dissolved in dry THF. To this solution, the reagent **A** was slowly added dropwise; and the following operations can be performed as described above (see the procedure in "**Preparation of 7**").
2. This general procedure is well applicable to **2Ba, 2Bb, 2Bf, 2Bg, 2Bl – 2Bo, 2Bq, 2Bs, 2Bt, 3u – 3x (by B)**.
3. The resulting solution of **Ti-1,** $FeCl_2$ and TMPMgCl·LiCl in THF was evaporated under an argon atmosphere below 40°C to obtain solid **B**. It was stored in a sealed container under argon atmosphere at room temperature. When used for the preparation of **2Bm** one week later, only a slight decrease in product yield was observed.

GPB-4 (for reactions using B in Table 2 and E = R_2NCl, RCOCl):



Under argon atmosphere, to a solution of **Ti-1** (956 mg, 3.75 mmol, 0.75 eq) and $FeCl_2$ (475 mg, 3.75 mmol, 0.75 eq) in dry THF (8 mL) was added dropwise a solution of TMPMgCl·LiCl (7.5 mmol, 1.5 eq) in THF though a syringe in 10 − 15 minutes at 25 °C. The mixture was stirred at 25 °C for 1h.

In another three-necked flask (50 mL), corresponding pyridine or quinoline (5 mmol, 1.0 eq) was dissolved in 5 mL dry THF under argon atmosphere. To this solution, the reagent B prepared above was slowly added dropwise. After stirred for 1 h at room temperature, the mixture was cooled to -20 °C, and the electrophilic reagent (E = R_2NCl/RCOCl, 1.1 eq) and CuCN·2LiCl (960 mg, 5.5 mmol, 1.1 eq) were added. The mixture was stirred at that temperature for 6 hours until the reaction was completed

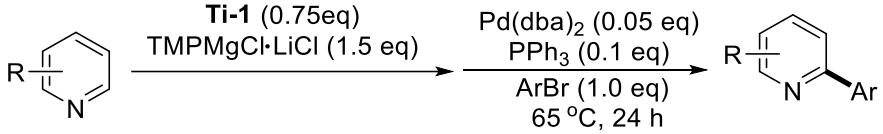
(monitored by TLC).

After the reaction finished, the reaction was quenched by adding 50 mL distilled water. After filtered, the solid was washed by CH_2Cl_2. Then the filtrate was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration and removing the solvent *in vacuum*, the residue was purified by flash column chromatography on silica gel affording the desired compound.

Note:

1. By adjusting the addition manner of $FeCl_2$, this process can also start with the preparation of reagent **A**. $FeCl_2$ (475 mg, 3.75 mmol, 0.75 eq) was added into the second flask along with a pyridine or quinoline compound, and dissolved in dry THF. To this solution, the reagent A was slowly added dropwise; and the following operations can be performed as described above (see the procedure in "**Preparation of 7**").
2. The amount of CuCN·2LiCl can be reduced to 0.5 equivalent.
3. This general procedure is well applicable to **2Bc – 2Be, 2Bh – 2Bk, 2Bp, 2Br**.

GPC-5 (for Pd-catalyzed cross couplings in table 3):



Under argon atmosphere, to a solution of **Ti-1** (956 mg, 3.75 mmol, 0.75 eq) in dry THF (4 mL) was added dropwise a solution of TMPMgCl·LiCl (7.5 mmol, 1.5 eq) in THF though a syringe in 10-15 minutes at 25 °C. The mixture was stirred at 25 °C for 30 min.

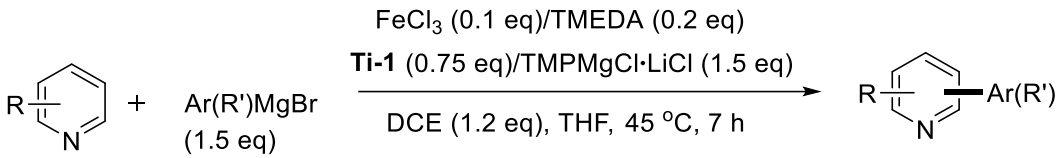
In another three-necked flask (50 mL), a pyridine or quinoline compound (5 mmol, 1.0 eq) was dissolved in 5 mL THF under argon atmosphere. To this solution, the reagent A prepared above was slowly added dropwise. After stirred for 40 min at room temperature, $Pd(dba)_2$ (144 mg, 0.25 mmol, 0.05 eq), PPh_3 (131 mg, 0.5 mmol, 0.1 eq) and ArBr (5.0 mmol, 1.0 eq) were added. The resulting mixture was stirred at reflux in a heating mantle for 24 h until the reaction was completed (monitored by TLC).

The reaction was quenched by adding 50 mL distilled water under stirring. The resulting solid was filtered and washed by CH_2Cl_2 (50 mL); and the filtrate was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over

anhydrous Na_2SO_4. After filtration and removing the solvent *in vacuum*, the residue was purified by flash column chromatography on silica gel to afford the desired compound.

Note: This general procedure is well applicable to **4Ac – 4Ao, 5u**.

GPC-6 (for Fe-catalyzed cross couplings in table 3):



Under argon atmosphere, to a solution of **Ti-1** (956 mg, 3.75 mmol, 0.75 eq) in dry THF (4 mL), a solution of TMPMgCl·LiCl (7.5 mmol, 1.0 M in THF, 1.5 eq) was added dropwise in 10 − 15 min through a syringe, and stirred at room temperature for 30 min. To the resulting mixture, a solution of Grignard reagent (7.5 mmol, 1.0 M in THF, 1.5 eq) through a syringe was added dropwise in 10 − 15 min through a syringe (Notes 1 and 2). The mixture was then stirred for 30 min at room temperature.

Under argon atmosphere and magnetic stirring, a pyridine or quinoline compound (5 mmol, 1.0 eq) and 5 mL THF were added to another three-necked round-bottom flask. To the resulting solution, $FeCl_3$ (81 mg, 0.5 mmol, 0.1 eq) and TMEDA (116 mg, 1 mmol, 0.2 eq) were added and stirred for 10 min at room temperature. The above-prepared mixed titanate was added in and the mixture was heated to 45 °C. After stirring at that temperature for 1h, 1,2-dichloroethane (588 mg, 6 mmol, 1.2 eq) was added dropwise and stirred for 7 h until the reaction was completed (monitored by TLC).

The reaction was quenched by adding 50 mL distilled water under stirring. The resulting solid was filtered and washed by CH_2Cl_2 (50 mL); and the filtrate was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration and removing the solvent *in vacuum*, the residue was purified by flash column chromatography on silica gel to afford the desired compound.

Note:

1. When common Grignard reagents were employed, their addition was performed at room temperature. For the addition of functionalized aryl Grignard reagents (such as 3-$EtOOCC_6H_4MgCl$·LiCl), the system was pre-cooled to -50 °C, and stirred at this temperature for 1h after addition, and then allowed to return to room temperature.

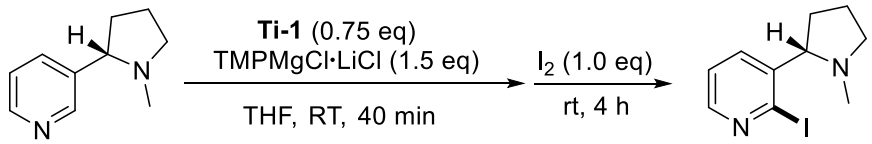
2. Mixing **Ti-1**, TMPMgCl·LiCl and Grignard reagent can also be performed by

adding Grignard reagent first and then TMPMgCl·LiCl.

3. This general procedure is well applicable to **4Bc – 4Bf, 4Bh, 4Bj – 4Bl, 4Bm-2, 4Bn, 4Bo, 5w, 4Bg, 4Bi, 4Bm-1, 5v.**

4. Preparations of compounds 6 − 12 in scheme 3

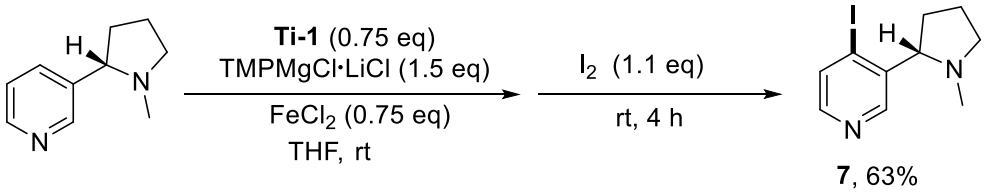
Preparation of 6



6, 77%

According to **GPA-1**, nicotine (810 mg, 5 mmol, 1.0 eq) reacted with reagent A [prepared from **Ti-1** (956 mg, 3.75 mmol) and TMPMgCl·LiCl (7.5 mmol)] at room temperature for 40 min. After reacting with I_2 (1.4g, 1.1 eq) for 4h at room temperature, the mixture was quenched with water. The product was taken up according to the general procedure and purified by flash column chromatography on silica gel to afford compound **6** (1.1 g, 77%).

Preparation of 7



7, 63%

According to **GPB-3** and the addition manner of $FeCl_2$ was adjusted.

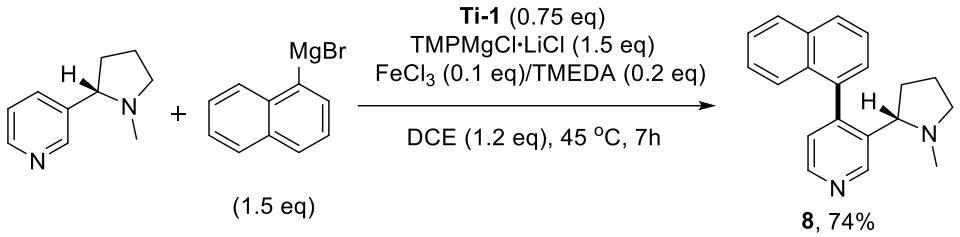
Under argon atmosphere, to a solution of **Ti-1** (956 mg, 3.75 mmol, 0.75 eq) in dry THF (4 mL) was added dropwise a solution of TMPMgCl·LiCl (7.5 mmol, 1.5 eq) in THF though a syringe in 10-15 minutes at 25 ºC. The mixture was stirred at 25 ºC for 40 min.

In another three-necked flask (50 mL), nicotine (810 mg, 5 mmol, 1.0 eq) was dissolved in 5 mL THF under argon atmosphere. Then $FeCl_2$ (475 mg, 3.75 mmol, 0.75 eq) was added. To this solution, reagent A prepared above was slowly added dropwise. After stirred for 1 h at room temperature, I_2 (1.4 g, 1.1 eq) was added in and stirred for 4 h until the reaction was completed (monitored by TLC).

The reaction was quenched and the product was taken up according to the

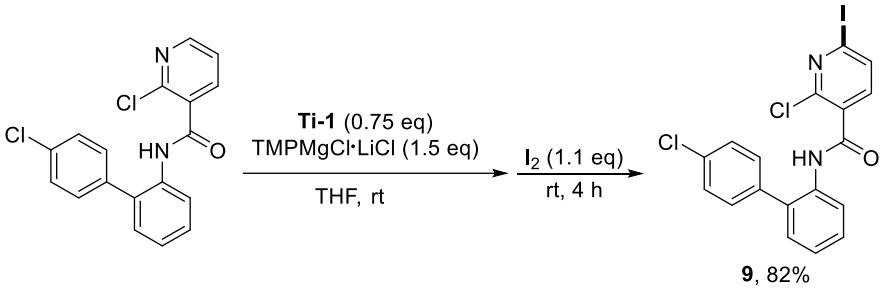
procedures in **GPB-3**. Flash column chromatography on silica gel furnished compound **7** (908 mg, 63%).

Preparation of 8



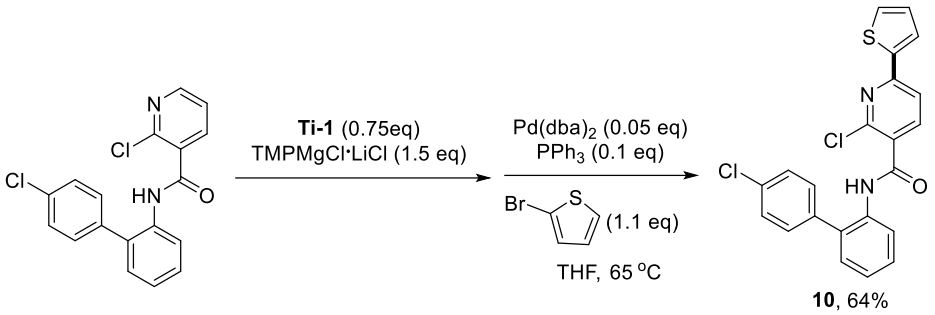
According to **GPC-6**, nicotine (810 mg, 5 mmol, 1.0 eq) reacted with the mixed titanium reagent [prepared from **Ti-1** (956 mg, 3.75 mmol), TMPMgCl·LiCl (7.5 mmol) and naphthalen-1-ylmagnesium bromide (7.5 mmol, 1.0 M in THF, 1.5 eq)] in the presence of $FeCl_3$ (81 mg, 0.5 mmol, 0.1 eq), TMEDA (116 mg, 1 mmol, 0.2 eq) and 1,2-dichloroethane (588 mg, 6 mmol, 1.2 eq) at 45 °C for 7 h. The mixture was quenched with water and the product was taken up according to the general procedure. Flash column chromatography on silica gel afforded compound **8** (1.1 g, 74%).

Preparation of 9



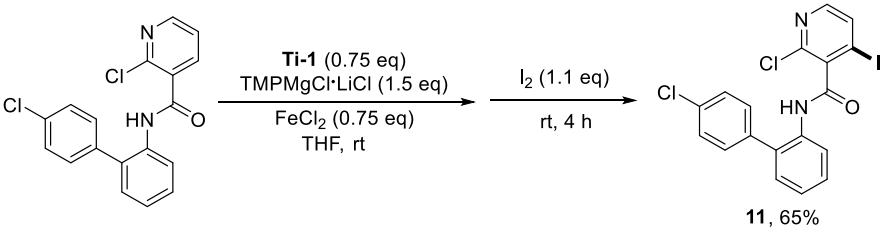
According to **GPA-1**, boscalid (2-chloro-*N*-(4'-chloro-[1,1'-biphenyl]-2-yl)-nicotinamide, 1.7 g, 5 mmol, 1.0 eq) was first treated with *i*-PrMgCl in THF (5.0 mL, 1 M in THF, 5.0 mmol, 1.0 eq) at room temperature for 1h to neutralize active hydrogen of the amide group, and then reacted with reagent A [prepared from **Ti-1** (956 mg, 3.75 mmol) and TMPMgCl·LiCl (7.5 mmol)] at room temperature for 40 min. After reacting with I_2 (1.4g, 1.1 eq) for 4h at room temperature, the mixture was quenched with water. The product was taken up according to the general procedure and purified by flash column chromatography on silica gel to afford compound **9** (1.9 g, 82%).

Preparation of 10



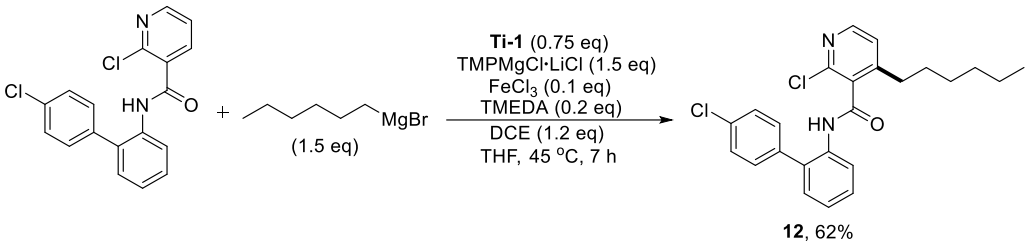
According to **GPC-5**, boscalid (1.7 g, 5 mmol, 1.0 eq) was first treated with *i*-PrMgCl in THF (5.0 mL, 1 M in THF, 5.0 mmol, 1.0 eq) at room temperature for 1h to neutralize active hydrogen of the amide group, and then reacted with reagent A [prepared from **Ti-1** (956 mg, 3.75 mmol) and TMPMgCl·LiCl (7.5 mmol)] and 2-bromothiophene (897 mg, 5.5 mmol, 1.1 eq) in the presence of $Pd(dba)_2$ (144 mg, 0.25 mmol, 0.05 eq) and PPh_3 (131 mg, 0.5 mmol, 0.1 eq) at reflux for 24 h. The mixture was quenched with water and the product was taken up according to the general procedure. Flash column chromatography on silica gel afforded compound**10** (1.4 g, 64%).

Preparation of 11



According to **GPB-3**, boscalid (1.7 g, 5 mmol, 1.0 eq) was first treated with *i*-PrMgCl in THF (5.0 mL, 1 M in THF, 5.0 mmol, 1.0 eq) at room temperature for 1h to neutralize active hydrogen of the amide group, and then reacted with reagent B [prepared from **Ti-1** (956 mg, 3.75 mmol), TMPMgCl·LiCl (7.5 mmol) and $FeCl_2$ (475 mg, 3.75 mmol, 0.75 eq)] for 1h at room temperature. After reacting with I_2 (1.4g, 1.1 eq) for 4h at room temperature, the mixture was quenched with water. The product was taken up according to the general procedure and purified by flash column chromatography on silica gel to afford compound **11** (1.5 g, 65%).

Preparation of 12



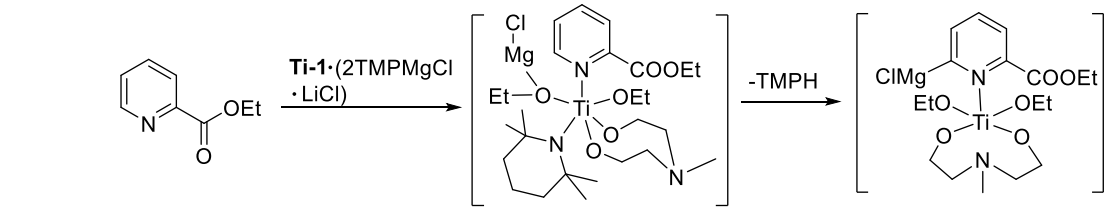
According to **GPC-6**, boscalid (1.7 g, 5 mmol, 1.0 eq) was first treated with *i*-PrMgCl in THF (5.0 mL, 1 M in THF, 5.0 mmol, 1.0 eq) at room temperature for 1h to neutralize active hydrogen of the amide group, and then reacted with the mixed titanium reagent [prepared from **Ti-1** (956 mg, 3.75 mmol), TMPMgCl·LiCl (7.5 mmol) and hexylmagnesium bromide (7.5 mmol, 1.0 M in THF, 1.5 eq)] in the presence of $FeCl_3$ (81 mg, 0.5 mmol, 0.1 eq), TMEDA (116 mg, 1 mmol, 0.2 eq) and 1,2-dichloroethane (588 mg, 6 mmol, 1.2 eq) at 45 °C for 7 h. The mixture was quenched with water and the product was taken up according to the general procedure. Flash column chromatography on silica gel afforded compound **12** (1.3 g, 62%).

5. DFT calculations

Computational details

Based on the density functional theory (DFT),[4, 5] a computational method of quantum mechanics, the thermodynamic parameters (enthalpy, entropy, and Gibbs free energy) were calculated using the Materials Studio (2020) software and the DMol3 module. The temperature was set at 298.15K and the pressure at 101.325kPa. For the specific calculation process, the Task was selected as Geometry Optimization, with the Basis set and Basis file set to DND and 3.5 respectively, and symmetry was utilized. The self-consistent convergence threshold was set at 1.0 e -5, the maximum number of iterations at 50, and the convergence range was set at energy < 2.0 e -5 Ha, maximum force < 0.004, and maximum displacement < 0.005. The functional was selected as GGA and the basis set as PW92. All molecular structure optimizations were completed at the GGA/PW92 level, followed by the calculation of thermodynamic parameters and others.

DFT calculation on the pathway for direct metalation of ethyl picolinate using reagent A



GGA/PW92

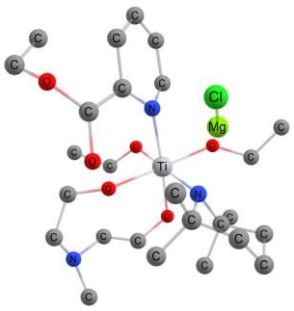
ΔG (kal/mol) 0

INT1

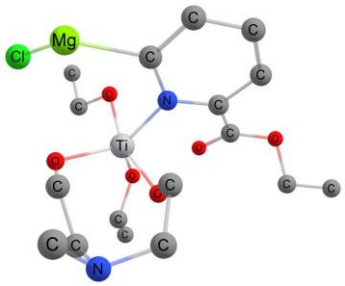
-13.989

INT2

-51.493



INT1



INT2

The reduction of Gibbs free energies from ethyl picolinate to **INT1** and from **INT1** to **INT2** in the reaction indicates that **INT1** and **INT2** are thermodynamically favorable.

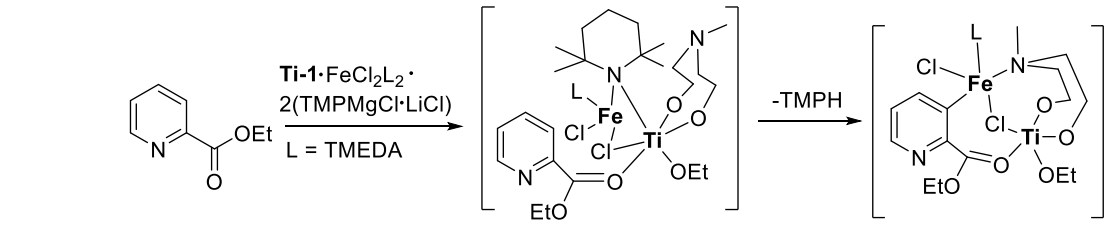
Table S3. Geometric coordinates of INT1 and INT2 after DFT optimization

INT1	INT2
C 1.08390000 -4.53071000 0.69790300	Ti -0.28189000 -0.96129500 0.56155400
C 0.88360400 -2.99446000 0.69997700	O 0.71640300 -2.50190000 -0.23854100
N 0.16081500 -2.32182000 -0.49036600	O 1.18705000 0.38042800 0.32618400
C 0.09534900 -3.16128000 -1.78858000	C 2.17008000 -2.14396000 -0.06856530
C 0.38631600 -4.66655000 -1.82760000	C 2.69238000 -1.14216000 -1.11651000
C 0.84035800 -5.36941000 -0.55965300	N 3.96337000 -0.59366400 -0.51608200
Ti -0.14625000 -0.20107600 -1.02390000	C 2.35580000 0.28010800 1.28350000
O 1.44413000 0.42835500 0.31293500	C 3.64309000 0.51863800 0.46463500
O -0.26984500 1.85389000 -1.69395000	C 4.63851000 -1.74217000 0.19639900
C 2.92450000 0.74264000 0.31048100	O -1.44992000 -0.10269600 -0.81298500
C 3.13990000 2.10597000 1.01142000	C -1.58315000 0.66557400 -3.17280000
N 2.84159000 3.23877000 0.05207540	C -0.67515700 0.03503910 -2.10025000
C 0.63156300 2.59644000 -0.72779100	O -1.85605000 -1.91433000 1.33635000
C 2.09582000 2.70408000 -1.14024000	C -3.79041000 -3.39417000 0.81304000
C 2.01053000 4.31736000 0.70835500	C -2.56544000 -2.66231000 0.23350400
N -1.67570000 0.33608500 0.47365500	Mg 0.97532200 -3.42569000 3.03877000
C -2.43282000 1.52235000 -0.23474800	Cl -0.51120200 -4.60098000 1.64739000
C -3.91015000 1.61648000 0.16303200	C -1.21801000 2.01336000 2.07296000
C -3.92848000 2.12264000 1.60473000	O -2.02090000 1.56577000 0.87994100
C -3.13434000 1.08439000 2.40782000	O -1.32558000 3.45292000 2.51987000
C -1.68289000 0.78889000 1.94379000	C -0.76297800 5.80995000 1.98380000
C -2.66755000 1.70778000 -1.75645000	C -0.64942600 4.34920000 1.51085000

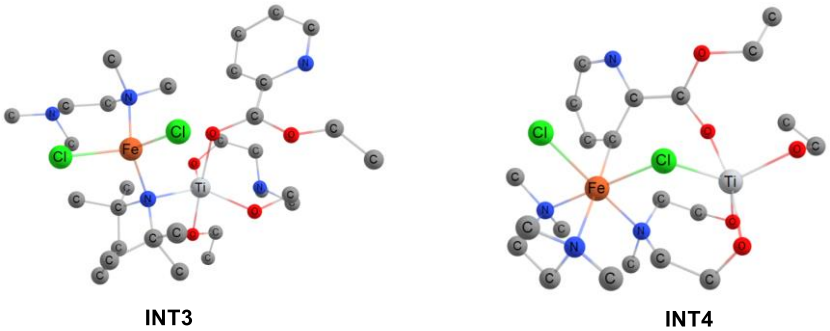
C -1.97300000 2.94501000 0.14355200	H 2.82372000 -3.07617000 -0.10266400
C -0.68752300 1.93424000 2.23456000	H 2.26506000 -1.68297000 0.96363900
C -1.33776000 -0.26998400 3.00321000	H 1.97848000 -0.27605800 -1.31294000
Cl -2.21008000 -2.88544000 1.76285000	H 2.88103000 -1.70704000 -2.08894000
Mg -2.13440000 -1.82162000 -0.33127800	H 2.23743000 1.10295000 2.06275000
C 1.57120000 -2.29626000 1.88257000	H 2.40235000 -0.72677900 1.81268000
O 1.32202000 -0.86104400 2.24334000	H 4.53792000 0.64754100 1.15790000
O 2.47162000 -3.14834000 2.75708000	H 3.48199000 1.48445000 -0.11793200
C 3.62534000 -4.45216000 0.85198800	H 5.61325000 -1.37863000 0.65951200
C 3.78093000 -3.58674000 2.12181000	H 4.85560000 -2.57692000 -0.54703100
O 1.26471000 -0.61807300 -2.62403000	H 3.95459000 -2.13390000 1.01843000
C 3.72088000 -0.28489900 -2.31589000	H -1.00550000 0.76392000 -4.14902000
C 2.42894000 0.29007800 -2.93115000	H -2.49240000 0.00004916 -3.33627000
O -1.82205000 -0.91191300 -2.21364000	H -1.92375000 1.69409000 -2.82267000
C -4.32712000 -1.71069000 -2.45754000	H 0.23797800 0.69469600 -1.92827000
C -3.29373000 -0.53961200 -2.33770000	H -0.33377200 -0.99540500 -2.44738000
H 1.49906000 -5.03860000 1.63194000	H -4.32565000 -3.95895000 -0.01945720
H -0.20909200 -2.65067000 -2.73934000	H -3.44845000 -4.13284000 1.61046000
H 0.26152400 -5.24941000 -2.80254000	H -4.50173000 -2.63495000 1.27798000
H 1.03134000 -6.49610000 -0.55555900	H -2.90727000 -1.92359000 -0.56421500
H 3.36406000 0.80242600 -0.72498900	H -1.85274000 -3.41947000 -0.23290200
H 3.43471000 -0.07036700 0.91246800	H -0.26409000 6.49901000 1.22377000
H 4.23579000 2.21173000 1.30757000	H -1.86374000 6.09323000 2.08230000
H 2.49526000 2.15518000 1.93438000	H -0.25127800 5.92128000 2.99746000
H 0.53338800 2.10659000 0.28269500	H 0.44892200 4.06164000 1.42144000
H 0.26863100 3.68620000 -0.63013200	H -1.15918000 4.23438000 0.49863800
H 2.17353000 3.40111000 -2.02655000	C 0.74031400 0.57555000 5.29644000
H 2.54487000 1.68546000 -1.39913000	C 0.93914800 -0.89277300 4.90471000
H 1.01184000 3.86325000 1.04509000	C 0.53312200 -1.38575000 3.50312000
H 1.80881000 5.14935000 -0.03721930	N -0.06320570 -0.40876300 2.48645000
H 2.55758000 4.73314000 1.60980000	C -0.39843800 1.02132000 2.93281000
H -4.42528000 0.60434600 0.03640370	C 0.06272260 1.52914000 4.31093000
H -4.42456000 2.39144000 -0.48602300	H 1.40650000 -1.61946000 5.64894000
H -5.00633000 2.19746000 1.98316000	H -0.12859000 2.61287000 4.60806000
H -3.43285000 3.14124000 1.67199000	H 1.07930000 0.94965300 6.31826000
H -3.71673000 0.09665650 2.32344000	
H -3.11793000 1.40194000 3.48928000	
H -2.84974000 2.82036000 -1.92877000	
H -3.64619000 1.20051000 -2.05593000	
H -1.84105000 1.36819000 -2.44376000	
H -2.76493000 3.73784000 -0.40536700	
H -1.19716000 3.19438000 -0.05512820	
H -2.13165000 3.09264000 1.36323000	
H -0.87525600 2.88536000 1.62382000	

H 0.36616200 1.56691000 2.00570000 H -0.75848500 2.19770000 3.33025000 H -0.36041200 -0.74978200 2.81142000 H -2.15989000 -1.06140000 3.01762000 H -1.32504000 0.23537300 4.02141000 H 3.07495000 -3.86088000 0.05405210 H 3.03177000 -5.39904000 1.09983000 H 4.65135000 -4.74494000 0.46513700 H 4.38373000 -2.67127000 1.86083000 H 4.35830000 -4.20192000 2.89314000 H 4.59888000 0.41778200 -2.54811000 H 3.93193000 -1.31743000 -2.78714000 H 3.61323000 -0.41177200 -1.21666000 H 2.57586000 0.31532200 -4.06511000 H 2.19682000 1.33759000 -2.58474000 H -4.08169000 -2.33440000 -3.33300000 H -5.36151000 -1.21473000 -2.63477000 H -4.43425000 -2.33122000 -1.58544000 H -3.57464000 -0.01065080 -1.44233000 H -3.39910000 0.11374100 -3.21952000	

DFT calculation on the pathway for direct metalation of ethyl picolinate using reagent B



GGA/PW92		**INT3**	**INT4**
ΔG (kal/mol)	0	-1.41	-2.12



INT3 **INT4**

The reduction of Gibbs free energies from ethyl picolinate to **INT3** and from **INT3** to **INT4** in the reaction indicates that **INT3** and **INT4** are thermodynamically favorable.

Table S4. Geometric coordinates of INT3 and INT4 after DFT optimization

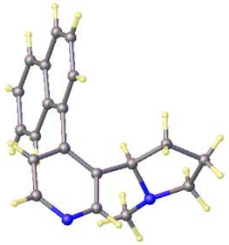
INT3	INT4
N 0.91436700 0.71336900 1.64382000	C -3.55088000 -0.44449200 2.82907000
C 1.87504000 0.07375410 2.66176000	C -3.98831000 -1.79390000 2.22228000
C 2.18619000 1.08423000 3.77194000	N -3.08912000 -2.49912000 1.23421000
C 0.93834600 1.20334000 4.66502000	C -1.77228000 -1.86701000 0.85623700
C -0.32709800 0.98519600 3.81340000	C -1.58388000 -0.34208100 1.06749000
C -0.10768700 1.57220000 2.41178000	C -2.32992000 0.29170800 2.24527000
C 0.31248900 3.03082000 2.68768000	C -0.59425800 -2.77104000 0.45601400
C -1.48201000 1.62938000 1.71827000	O 0.79456900 -2.36208000 0.84953100
C 3.20816000 -0.41529600 2.06596000	Ti 2.07766000 -1.50302000 -0.59843900
C 1.35624000 -1.17164000 3.41002000	O 3.20841000 -0.41572800 0.84344200
H 2.42116000 2.07895000 3.27001000	O 3.08606000 -0.28684400 -2.01011000
H 3.06646000 0.76189600 4.42044000	C 2.30473000 0.10758000 1.92999000
H 0.96413800 2.23865000 5.14182000	C 3.08538000 1.09923000 -1.39684000
H 0.92626400 0.40787700 5.48178000	C 0.90416700 0.40067800 1.36220000
H -1.21282000 1.45796000 4.35299000	C 1.63940000 1.49777000 -1.04003000
H -0.53596900 -0.12207000 3.67112000	N 0.87050700 1.43993000 0.26767000
H -0.46416100 3.51201000 3.37046000	Fe -1.04186000 0.94681400 -0.62773400
H 0.35207500 3.62430000 1.71609000	Cl -3.13404000 0.36543400 -1.65590000
H 1.32647000 3.05353000 3.20725000	N -0.60793600 2.23418000 -2.31058000
H -1.96524000 0.59822000 1.68738000	N -1.99046000 2.64851000 0.31119900
H -1.37380000 2.04013000 0.66396000	C -0.64969900 3.58913000 -1.63342000
H -2.16264000 2.31830000 2.32037000	C -1.97150000 3.65962000 -0.82038300
H 3.83704000 0.46072000 1.70223000	C 0.54912900 2.06099000 -3.27521000
H 3.01424000 -1.15396000 1.21944000	C -1.82362000 2.19580000 -3.20761000
H 3.79352000 -0.93957300 2.89177000	C -3.42352000 2.42616000 0.73809400
H 1.18374000 -2.04012000 2.69377000	C -1.25401000 3.22365000 1.49384000
H 0.39948000 -0.94971400 3.98275000	C 1.30528000 2.71282000 0.94704000
H 2.15645000 -1.48314000 4.15970000	Cl 0.02515920 -0.93664700 -1.69457000
Ti -0.05860040 -0.88652500 0.59022600	O -0.82734000 -4.12724000 -0.16507200
Fe 1.96308000 1.83087000 0.32365200	C 0.28082900 -6.33960000 0.22132900
O -1.11124000 -1.41848000 2.37333000	C 0.35769000 -4.99413000 -0.52344200
C -3.10771000 -2.69166000 3.26271000	O 2.98586000 -3.36338000 -1.09225000
C -2.20693000 -2.40362000 2.04575000	C 2.81532000 -4.14186000 1.32782000
H -3.89284000 -3.46883000 2.97024000	C 3.73046000 -3.91559000 0.10624200
H -3.63110000 -1.73344000 3.59242000	H -4.16481000 0.03497610 3.66137000
H -2.47830000 -3.09568000 4.11887000	H -4.96923000 -2.27583000 2.54650000
H -2.84870000 -1.97736000 1.20643000	H -2.07691000 1.34913000 2.58658000
H -1.72877000 -3.37761000 1.69472000	H 2.75941000 1.05131000 2.37996000

C -0.45472000 -1.01239000 -6.56584000	H 2.19793000 -0.68659000 2.74069000
C 0.33143400 -2.28179000 -6.19609000	H 3.43741000 1.78632000 -2.23567000
N 0.78221000 -2.48870000 -4.76699000	H 3.77920000 1.21576000 -0.50003400
C 0.43924500 -1.47017000 -3.69702000	H 0.25293300 0.79342100 2.21153000
C -0.66950100 -0.43420900 -3.97313000	H 0.39612200 -0.54609600 1.00233000
C -0.90717600 -0.05351280 -5.44942000	H 1.02302000 0.96421300 -1.82434000
C 1.16370000 -1.51114000 -2.32372000	H 1.56461000 2.60428000 -1.30442000
O 0.92474500 -0.45495600 -1.26226000	H -0.64370700 4.40104000 -2.43341000
O 2.12954000 -2.62895000 -2.01274000	H 0.24385800 3.72300000 -0.93787600
C 2.64343000 -5.05787000 -2.18467000	H -2.15879000 4.70079000 -0.39551200
C 1.84700000 -3.88911000 -2.79699000	H -2.80619000 3.40113000 -1.55216000
H -0.70011900 -0.78409300 -7.65685000	H 0.45070100 2.84436000 -4.09760000
H 0.60768300 -3.04020000 -7.00061000	H 0.50036200 1.02178000 -3.74128000
H -0.83481900 0.37149700 -3.18560000	H 1.55762000 2.20691000 -2.76969000
H -1.42032000 0.93029700 -5.71216000	H -1.92794000 1.16120000 -3.67495000
H 3.75933000 -4.85492000 -2.27635000	H -1.69716000 2.97052000 -4.03417000
H 2.38645000 -6.02599000 -2.73223000	H -2.75629000 2.45326000 -2.60575000
H 2.36853000 -5.16455000 -1.08314000	H -3.85145000 3.41419000 1.11246000
H 0.73407700 -4.12437000 -2.72579000	H -3.48807000 1.66068000 1.57645000
H 2.13959000 -3.74512000 -3.88930000	H -4.03984000 2.06782000 -0.15043700
N 1.07402000 2.63431000 -1.28926000	H -0.26063300 3.65171000 1.14997000
N -1.02998000 5.38429000 0.16450600	H -1.10312000 2.42412000 2.29254000
C -0.16352600 3.40876000 -0.94482300	H -1.86828000 4.08197000 1.92419000
C 0.24971500 4.70096000 -0.23225400	H 1.14982000 3.59211000 0.23819900
C 0.59513600 1.59038000 -2.24788000	H 2.40957000 2.63076000 1.21839000
C 2.05070000 3.47742000 -2.07790000	H 0.69869800 2.87015000 1.89844000
C -1.86582000 4.41563000 0.97183200	H 1.18415000 -6.97776000 -0.05529470
C -0.78312100 6.71435000 0.84242700	H -0.67504500 -6.88487000 -0.07622890
H -0.83298300 2.76566000 -0.28845300	H 0.27874400 -6.15200000 1.34573000
H -0.72301200 3.67968000 -1.90133000	H 0.36347900 -5.18258000 -1.64763000
H 0.85900400 4.46883000 0.70046100	H 1.31810000 -4.45689000 -0.22672700
H 0.85543000 5.34964000 -0.94627500	H 3.42561000 -4.60654000 2.17111000
H 0.15558400 2.08849000 -3.17237000	H 1.96407000 -4.84582000 1.04547000
H -0.21703100 0.97492700 -1.73748000	H 2.38898000 -3.15118000 1.69350000
H 1.47627000 0.93171800 -2.54871000	H 4.19339000 -4.91463000 -0.18852800
H 1.53004000 3.87299000 -3.01208000	H 4.56173000 -3.19236000 0.39892900
H 2.93890000 2.83308000 -2.38803000	
H 2.41568000 4.35322000 -1.44627000	
H -1.95561000 3.43858000 0.39553400	
H -2.90645000 4.85614000 1.12473000	

H -1.38286000 4.20766000 1.98577000 H -0.20661800 7.39577000 0.13693400 H -0.18225500 6.56919000 1.80311000 H -1.78631000 7.19596000 1.09120000 Cl 2.92207000 3.57937000 1.36663000 Cl 3.67381000 0.68252800 -0.58726800 O -1.99752000 -0.48469900 -0.22127700 O 0.93652000 -2.78067000 0.63258500 C -2.29462000 -1.15908000 -1.54025000 C 0.49990600 -3.81436000 -0.38848200 C -1.57210000 -2.51491000 -1.60761000 C -0.90297900 -4.42693000 -0.22491400 N -1.87828000 -3.29038000 -0.35227900 C -3.30929000 -3.75744000 -0.32029100 H -1.93225000 -0.50388000 -2.39853000 H -3.42084000 -1.31053000 -1.62749000 H 1.25895000 -4.66390000 -0.37941400 H 0.49918700 -3.32394000 -1.41370000 H -0.45328900 -2.32604000 -1.64432000 H -1.86829000 -3.09878000 -2.54072000 H -1.01619000 -4.95139000 0.78089000 H -1.08042000 -5.16880000 -1.07223000 H -3.49319000 -4.46778000 -1.19232000 H -4.00015000 -2.85499000 -0.40711800 H -3.50560000 -4.29777000 0.66430700	

6. X-ray single crystal structure and data

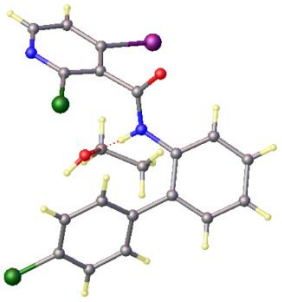
X-ray single crystal structure and data of 8



Crystal data	
Name	**8**

CCDC NO.	2349880
Chemical formula	$C_{20}H_{20}N_2$
M_r	288.38
Crystal system	Monoclinic
space group	$P2_1\,2_1\,2_1$
Temperature (K)	100
a(Å)	7.529 (3)
b(Å)	9.995 (3)
c(Å)	20.877 (7)
β (°)	90
V (Å^3)	1571.1 (9)
Z	4
Radiation	MoKα (λ = 0.71073)
μ (mm^{-1})	0..072
Crystal size (mm^3)	0.5 × 0.25 × 0.25
F(000)	616.0

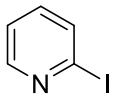
X-ray single crystal structure and data of 11·EtOH



Crystal data	
Name	**11**
CCDC NO.	2349987
Chemical formula	$C_{20}H_{15}Cl_2IN_2O_2$
M_r	513.14
Crystal system	Monoclinic
space group	*P 21/c*
Temperature (K)	100
a(Å)	7.43380(10)
b(Å)	34.7544(4)
c(Å)	8.01080(10)
β (°)	106.207(2)
V (Å^3)	1987.40(5)
Z	4

Radiation	CuK\a (λ = 1.54184)
μ (mm^{-1})	1.715
Crystal size (mm^3)	0.2 × 0.12 × 0.08
F(000)	1008

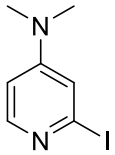
7. Characterization data



2-iodopyridine (2Aa)[6]

Yellow oil; 92% yield (943 mg); R_f = 0.35 (petroleum ether/ethyl acetate = 3:1, v/v).

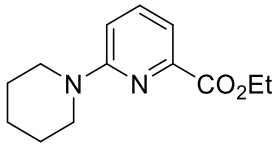
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.33 (ddd, *J* = 15.1, 7.0, 6.3 Hz, 1H), 7.80 – 7.63 (m, 1H), 7.32 – 7.26 (m, 1H), 7.25 – 7.22 (m, 1H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 150.9, 137.7, 135.1, 123.0, 118.2.



2-iodo-*N*,*N*-dimethylpyridin-4-amine (2Ab)[7]

Yellow oil; 75% yield (930 mg); R_f = 0.29 (petroleum ether/ethyl acetate = 10:1, v/v).

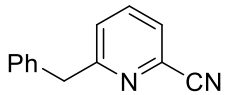
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.81 (d, *J* = 6.0 Hz, 1H), 6.80 (d, *J* = 2.5 Hz, 1H), 6.37 (dd, *J* = 6.0, 2.5 Hz, 1H), 2.89 (s, 6H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 154.9, 149.6, 119.3, 116.43, 106.6, 39.3.



Ethyl 6-(piperidin-1-yl)picolinate (2Ac)

Yellow oil; 77% yield (902 mg); R_f = 0.30 (petroleum ether/ethyl acetate = 3:1, v/v).

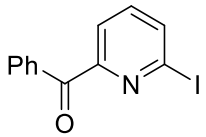
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.47 – 7.45 (m, 1H), 7.29 (dd, *J* = 7.2, 4.5 Hz, 1H), 6.74 (dd, *J* = 8.5, 5.3 Hz, 1H), 4.37 – 4.29 (m, 2H), 3.54 (d, *J* = 4.3 Hz, 4H), 1.59 (s, 6H), 1.34 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 166.0, 159.2, 146.5, 137.8, 113.7, 110.4, 61.3, 46.1, 25.6, 24.7, 14.3; **HRMS** (ESI+) m/z calcd for $C_{13}H_{19}N_2O_2^+$ $[M+H]^+$ 235.1441 , Found 235.1446.



6-benzylpicolinonitrile (2Ad)

Yellow oil; 71% yield (690 mg); R_f = 0.31 (petroleum ether/ethyl acetate = 5:1, v/v).

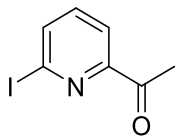
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.41 (t, *J* = 5.1 Hz, 1H), 7.32 – 7.30 (m, 2H), 7.26 (d, *J* = 5.8 Hz, 2H), 7.19 (d, *J* = 5.4 Hz, 2H), 7.00 (d, *J* = 5.0 Hz, 1H), 4.14 (s, 2H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 141.6, 138.9, 129.3, 128.8, 128.5, 128.4, 126.8, 126.0, 125.7, 121.9, 44.3; **HRMS** (ESI+) m/z calcd for $C_{13}H_{11}N_2^+$ $[M+H]^+$ 195.0917, Found 195.0921.



(6-iodopyridin-2-yl)(phenyl)methanone (2Ae)

Colorless oil; 76% yield (1.2 g); R_f = 0.40 (petroleum ether/ethyl acetate = 3:1, v/v).

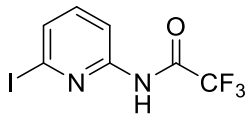
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.87 (dd, *J* = 3.6, 2.0 Hz, 2H), 8.24 (dd, *J* = 2.9, 1.2 Hz, 1H), 7.79 (dd, *J* = 7.9, 1.2 Hz, 2H), 7.67 – 7.63 (m, 1H), 7.52 (t, *J* = 7.7 Hz, 2H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 190.9, 155.4, 139.3, 138.3, 133.4, 132.5, 131.9, 130.3, 129.6, 126.2; **HRMS** (ESI+) m/z calcd for $C_{12}H_9INO^+$ $[M+H]^+$ 309.9724, Found 309.9725.



1-(6-iodopyridin-2-yl)ethan-1-one (2Af)

Yellow oil; 81% yield (1.0 g); R_f = 0.24 (petroleum ether/ethyl acetate = 5:1, v/v).

^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.75 – 7.72 (m, 2H), 7.30 (d, *J* = 5.3 Hz, 1H), 2.34 (s, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 159.5, 149.6, 136.8, 124.4, 122.6, 97.1, 23.0; **HRMS** (ESI+) m/z calcd for $C_7H_7INO^+$ $[M+H]^+$ 247.9567, Found 247.9571.

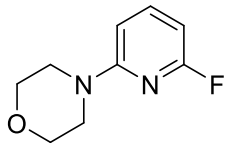


2,2,2-trifluoro-*N*-(6-iodopyridin-2-yl)acetamide (2Ag)

Yellow oil; 60% yield (948 mg); R_f = 0.41 (petroleum ether/ethyl acetate = 2:1,

v/v).

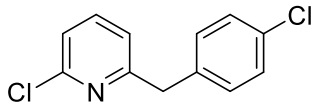
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.85 (s, 1H), 8.10 (d, *J* = 8.1 Hz, 1H), 7.61 (dd, *J* = 11.3, 4.6 Hz, 1H), 7.31 (d, *J* = 7.7 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 158.1, 155.1 (q, *J* = 102.6 Hz), 149.0, 141.1, 139.9, 125.8, 113.1; **^{19}F NMR** ($CDCl_3$, 376 MHz) δ (ppm) -76.0; **HRMS** (ESI+) m/z calcd for $C_7H_4F_3IN_2O^+$ $[M+H]^+$ 316.9393, Found 316.9399.



4-(6-fluoropyridin-2-yl)morpholine (2Ah)

Yellow oil; 73% yield (665 mg); R_f = 0.32 (petroleum ether/ethyl acetate = 6:1, v/v).

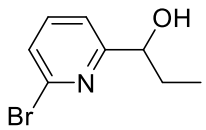
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.25 (td, *J* = 8.2, 7.6, 1.4 Hz, 1H), 6.88 – 6.60 (m, 1H), 6.53 – 6.38 (m, 1H), 3.73 (dd, *J* = 6.8, 2.9 Hz, 4H), 3.43 (dt, *J* = 4.9, 2.5 Hz, 4H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 159.4, 140.3, 139.7, 116.6, 104.8, 66.6, 45.3; **^{19}F NMR** ($CDCl_3$, 376 MHz) δ (ppm) -68.3; **HRMS** (ESI+) m/z calcd for $C_9H_{12}FN_2O^+$ $[M+H]^+$ 183.0928, Found 183.0931.



2-chloro-6-(4-chlorobenzyl)pyridine (2Ai)

Yellow oil; 66% yield (786 mg); R_f = 0.31 (petroleum ether/ethyl acetate = 15:1, v/v).

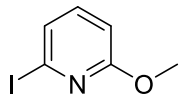
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.50 (t, *J* = 7.7 Hz, 1H), 7.26 – 7.22 (m, 2H), 7.14 (dd, *J* = 20.2, 8.1 Hz, 3H), 6.95 (d, *J* = 7.6 Hz, 1H), 4.05 (s, 2H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 161.5, 150.9, 139.3, 137.2, 132.6, 130.6, 128.9, 122.1, 121.5, 43.5; **HRMS** (ESI+) m/z calcd for $C_{12}H_{10}Cl_2N^+$ $[M+H]^+$ 238.0185, Found 238.0195.



1-(6-bromopyridin-2-yl)propan-1-ol[8] (2Aj)

Yellow oil; 88% yield (951 mg); R_f = 0.22 (petroleum ether/ethyl acetate = 10:1, v/v).

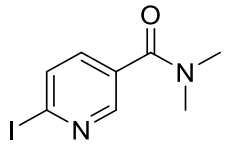
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.52 (t, *J* = 7.7 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 4.64 (dd, *J* = 7.3, 4.8 Hz, 1H), 3.30 (s, 1H), 1.85 (dtt, *J* = 14.8, 7.4, 3.7 Hz, 1H), 1.71 (dp, *J* = 14.6, 7.4 Hz, 1H), 0.94 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 164.4, 141.2, 139.0, 126.6, 119.2, 74.2, 31.2, 9.5.



2-iodo-6-methoxypyridine[9] (2Ak)

Yellow oil; 80% yield (940 mg); R_f = 0.3 (petroleum ether/ethyl acetate = 8:1, v/v).

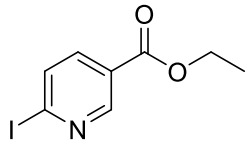
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.46 – 7.31 (m, 1H), 7.10 – 6.96 (m, 1H), 6.75 – 6.51 (m, 1H), 3.91 (s, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 163.8, 140.42, 138.7, 120.3, 109.5, 54.1.



6-iodo-N,N-dimethylnicotinamide (2Al)

Yellow oil; 69% yield (952 mg); R_f = 0.20 (petroleum ether/ethyl acetate = 2:1, v/v).

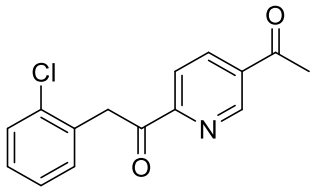
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.40 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.63 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.28 (dd, *J* = 7.5, 4.8 Hz, 1H), 3.11 (s, 3H), 2.87 (s, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) 166.7, 150.1, 147.2, 137.0, 132.8, 122.8, 38.2, 34.9; **HRMS** (ESI+) m/z calcd for $C_8H_{10}IN_2O^+$ $[M+H]^+$ 276.9833, Found 276.9836.



ethyl 6-iodonicotinate[10] (2Am)

Black solid; 74% yield (1.0 g) [when using solid **A**, 68% (0.92 g)]; R_f = 0.35 (petroleum ether/ethyl acetate = 4:1, v/v).

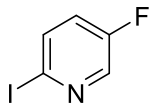
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) δ 8.89 (d, *J* = 2.3 Hz, 1H), 7.96 – 7.77 (m, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 164.9, 151.6, 138.1, 134.9, 125.9, 123.3, 61.8, 14.3.



1-(5-acetylpyridin-2-yl)-2-(2-chlorophenyl)ethan-1-one (2An)

Green oil; 69% yield (944 mg); R_f = 0.21 (petroleum ether/ethyl acetate = 10:1, v/v).

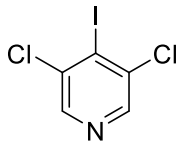
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 9.06 (d, *J* = 2.2 Hz, 1H), 8.09 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.38 – 7.34 (m, 1H), 7.27 (dd, *J* = 7.0, 2.4 Hz, 1H), 7.22 – 7.19 (m, 1H), 7.18 (t, *J* = 1.7 Hz, 1H), 7.17 – 7.11 (m, 1H), 4.32 (s, 2H), 2.56 (s, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 196.6, 164.2, 149.8, 136.3, 134.4, 131.7, 129.8, 129.6, 128.5, 128.0, 127.2, 126.9, 123.1, 42.2, 26.8; **HRMS** (ESI+) m/z calcd for $C_{15}H_{13}ClNO_2^+$ $[M+H]^+$ 274.0630, Found 274.0633.



5-fluoro-2-iodopyridine[11] (2Ao)

Yellow oil; 77% yield (859 mg); R_f = 0.26 (petroleum ether/ethyl acetate = 10:1, v/v).

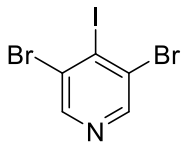
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.55(s, 1H), 7.97 (d, *J* = 5.1 Hz, 1H), 7.87 (d, *J* = 5.1 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm)151.2, 149.1, 146.3 (d, *J* = 31.6 Hz), 141.00 (d, *J* = 6.4 Hz), 135.2; **^{19}F NMR** ($CDCl_3$, 376 MHz) δ (ppm) -100.33.



3,5-dichloro-4-iodopyridine[12] (2Ap)

Yellow oil; 69% yield (945 mg); R_f = 0.31 (petroleum ether/ethyl acetate = 20:1, v/v).

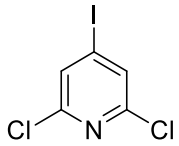
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.61 (s, 2H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 138.7, 135.2, 116.7.



3,5-dibromo-4-iodopyridine[13] (2Aq)

Yellow oil; 77% yield (1.4 g); R_f = 0.36 (petroleum ether/ethyl acetate = 20:1, v/v).

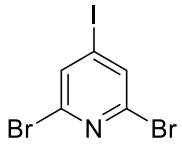
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.85 (s, 2H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 141.7, 130.0, 120.0.



2,6-dichloro-4-iodopyridine (2Ar)[14]

Yellow oil; 78% yield (1.1 g); R_f = 0.38 (petroleum ether/ethyl acetate = 20:1, v/v).

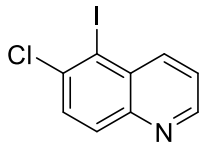
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.64 (s, 2H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 150.7, 131.6, 107.6.



2,6-Dibromo-4-iodopyridine (2As) [15]

Yellow oil; 81% yield (1.5 g); R_f = 0.42 (petroleum ether/ethyl acetate = 20:1, v/v).

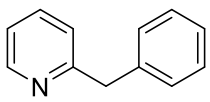
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.84 (s, 2H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 141.0, 135.5, 107.5.



6-chloro-5-iodoquinoline (2At)

Yellow oil; 82% yield (1.2 g); R_f = 0.30 (petroleum ether/ethyl acetate = 10:1, v/v).

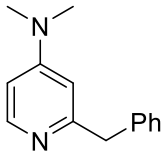
^{1}H NMR ($CDCl_3$, 400 MHz) 8.98 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.30 (d, *J* = 2.2 Hz, 1H), 8.02 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.81 (d, *J* = 2.2 Hz, 1H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 151.7, 145.8, 140.2, 136.0, 132.7, 128.6, 127.4, 122.7, 104.4; **HRMS** (ESI+) m/z calcd for $C_9H_6ClIN^+$ $[M+H]^+$ 289.9228, Found 289.9233.



2-benzylpyridine (2Ba) [16]

Yellow solid; 81% yield (685 mg); R_f = 0.32 (petroleum ether/ethyl acetate = 5:1, v/v).

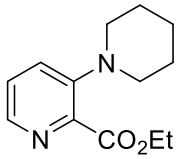
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.57 – 8.50 (m, 1H), 7.52 (ddd, *J* = 8.9, 2.7, 1.4 Hz, 1H), 7.31 – 7.24 (m, 4H), 7.23 – 7.17 (m, 1H), 7.07 (dd, *J* = 10.2, 6.0 Hz, 2H), 4.15 (s, 2H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 161.1, 149.4, 139.6, 136.6, 129.2, 128.7, 126.5, 123.2, 121.4, 44.8.



2-benzyl-*N*,*N*-dimethylpyridin-4-amine (2Bb)

Yellow oil; 80% yield (933 mg); R_f = 0.21 (petroleum ether/ethyl acetate = 10:1, v/v).

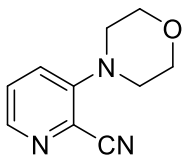
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.15 (d, *J* = 5.9 Hz, 1H), 7.27 (d, *J* = 4.4 Hz, 4H), 7.19 – 7.17 (m, 1H), 6.36 – 6.28 (m, 2H), 4.03 (s, 2H), 2.91 (s, 6H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 160.7, 155.1, 149.2, 140.1, 129.1, 128.5, 126.3, 105.8, 104.7, 44.9, 39.2; **HRMS** (ESI+) m/z calcd for $C_{14}H_{17}N_2^+$ $[M+H]^+$ 213.1386, Found 213.1394.



Ethyl 3-(piperidin-1-yl)picolinate (2Bc)

Yellow oil; 72% yield (843 mg); R_f = 0.26 (petroleum ether/ethyl acetate = 3:1, v/v).

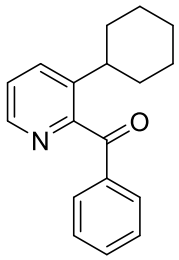
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.33 – 8.18 (m, 1H), 7.43 (ddd, *J* = 4.1, 3.1, 2.0 Hz, 1H), 7.35 – 7.30 (m, 1H), 4.52 – 4.38 (m, 2H), 3.29 – 2.89 (m, 4H), 1.73 – 1.69 (m, 4H), 1.60 – 1.57 (m, 2H), 1.43 (d, *J* = 4.8 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 172.1, 149.9, 139.0, 132.5, 121.0, 110.4, 53.4, 31.6, 30.2, 26.0, 14.3; **HRMS** (ESI+) m/z calcd for $C_{13}H_{19}N_2O_2^+$ $[M+H]^+$ 235.1441, Found 235.1449.



3-morpholinopicolinonitrile (2Bd)

Yellow oil; 69% yield (653 mg); R_f = 0.33 (petroleum ether/ethyl acetate = 3:1, v/v).

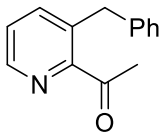
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.19 (d, *J* = 4.8 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 6.86 (ddd, *J* = 7.7, 3.5, 1.3 Hz, 1H), 3.89 – 3.82 (m, 4H), 3.42 – 3.35 (m, 4H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 148.4, 145.0, 126.9, 118.2, 100.0, 93.9, 67.0, 49.7; **HRMS** (ESI+) m/z calcd for $C_{10}H_{12}N_3O^+$ $[M+H]^+$ 190.0975, Found 190.0985.



(3-cyclohexylpyridin-2-yl)(phenyl)methanone (2Be)

Yellow oil; 59% yield (783 mg); R_f = 0.32 (petroleum ether/ethyl acetate = 3:1, v/v).

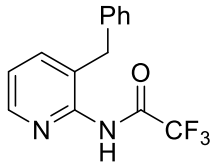
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.44 (dd, *J* = 4.7, 1.2 Hz, 1H), 7.59 – 7.51 (m, 3H), 7.28 – 7.25 (m, 2H), 7.19 – 7.13 (m, 2H), 3.18 (tt, *J* = 11.4, 2.8 Hz, 1H), 1.90 (d, *J* = 13.0 Hz, 1H), 1.82 – 1.77 (m, 1H), 1.73 – 1.66 (m, 2H), 1.47 (qd, *J* = 13.3, 3.1 Hz, 1H), 1.40 – 1.29 (m, 2H), 1.26 – 1.17 (m, 2H), 0.96 (d, *J* = 11.8 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 159.2, 144.6, 143.0, 140.0, 130.2, 128.1, 127.57, 127.55, 126.8, 123.6, 40.9, 27.5, 27.4, 26.9, 26.8, 26.6; **HRMS** (ESI+) m/z calcd for $C_{18}H_{20}NO^+$ $[M+H]^+$ 266.1549, Found 266.1544.



1-(3-benzylpyridin-2-yl)ethan-1-one (2Bf)

Colorless oil; 71% yield (750 mg); R_f = 0.26 (petroleum ether/ethyl acetate = 4:1, v/v).

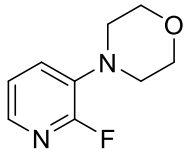
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.25 (dd, *J* = 4.6, 1.4 Hz, 1H), 7.91 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.17 – 7.05 (m, 5H), 7.00 (ddd, *J* = 7.9, 4.6, 1.9 Hz, 1H), 3.66 (d, *J* = 13.6 Hz, 1H), 3.21 (d, *J* = 13.6 Hz, 1H), 1.84 (s, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 160.2, 145.3, 143.2, 137.4, 130.3, 127.7, 126.17, 126.16, 123.7, 118.2, 75.1, 45.3, 26.7; **HRMS** (ESI+) m/z calcd for $C_{14}H_{14}NO^+$ $[M+H]^+$ 212.1070, Found 212.1077.



***N*-(3-benzylpyridin-2-yl)-2,2,2-trifluoroacetamide (2Bg)**

Yellow oil; 62% yield (868 mg); R_f = 0.23 (petroleum ether/ethyl acetate = 3:1, v/v).

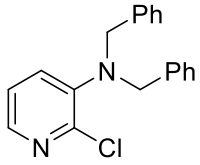
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.13 – 8.06 (m, 1H), 7.48 (t, *J* = 4.9 Hz, 1H), 7.34 (d, *J* = 5.0 Hz, 2H), 7.31 – 7.28 (m, 2H), 7.11 (dt, *J* = 5.7, 2.9 Hz, 1H), 6.80 (d, *J* = 3.3 Hz, 1H), 4.76 (s, 1H), 4.23 (d, *J* = 1.7 Hz, 2H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 166.7, 158.4, 155.0, 140.0, 138.6, 131.2, 130.9, 129.7, 128.7, 128.0, 117.9 (q, *J* = 237.7 Hz), 61.2; **^{19}F NMR** ($CDCl_3$, 376 MHz) δ (ppm) -76.3; **HRMS** (ESI+) m/z calcd for $C_{14}H_{12}F_3N_2O^+$ $[M+H]^+$ 281.0896, Found 281.0902.



4-(2-fluoropyridin-3-yl)morpholine (2Bh)

White solid; 67% yield (610 mg); R_f = 0.29 (petroleum ether/ethyl acetate = 6:1, v/v).

^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.25 – 8.19 (m, 1H), 7.81 – 7.69 (m, 1H), 6.78 (dd, *J* = 7.7, 4.7 Hz, 1H), 3.86 – 3.84 (m, 4H), 3.34 – 3.31 (m, 4H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 159.3, 146.5, 142.5, 118.9, 112.9, 67.0, 50.1; **^{19}F NMR** ($CDCl_3$, 376 MHz) δ (ppm) -66.24; **HRMS** (ESI+) m/z calcd for $C_9H_{12}FN_2O^+$ $[M+H]^+$ 183.0928 , Found 183.0937.

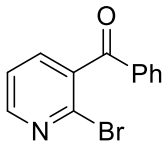


***N,N*-dibenzyl-2-chloropyridin-3-amine (2Bi)**

Yellow solid; 61% yield (942 mg); R_f = 0.33 (petroleum ether/ethyl acetate = 15:1, v/v).

^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.06 – 7.96 (m, 1H), 7.34 – 7.22 (m, 10H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.07 – 6.98 (m, 1H), 4.26 (s, 4H); **^{13}C NMR** ($CDCl_3$, 151

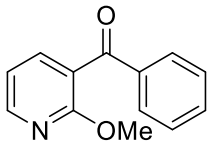
MHz) δ (ppm) 147.6, 143.2, 137.3, 131.7, 128.52, 128.51, 128.49, 127.4, 122.5, 55.9; **HRMS** (ESI+) m/z calcd for $C_{19}H_{18}ClN_2^+$ $[M+H]^+$ 309.1153, Found 309.1156.



(2-bromopyridin-3-yl)(phenyl)methanone[17] (2Bj)

Brown oil; 71% yield (930 mg); R_f = 0.34 (petroleum ether/ethyl acetate = 15:1, v/v).

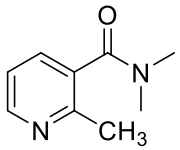
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.48 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.80 – 7.74 (m, 2H), 7.65 – 7.59 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.39 (dd, *J* = 7.4, 4.8 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 193.9, 151.1, 138.5, 137.8, 137.4, 135.6, 134.4, 130.2, 129.0, 122.6.



(2-methoxypyridin-3-yl)(phenyl)methanone[18] (2Bk)

White solid; 66% yield (704 mg); R_f = 0.26 (petroleum ether/ethyl acetate = 9:1, v/v).

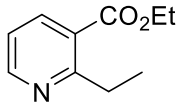
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.27 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.72 – 7.64 (m, 1H), 7.59 – 7.49 (m, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.01 – 6.91 (m, 1H), 3.83 (s, 3H). **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 194.8, 161.2, 149.3, 139.0, 137.2, 133.4, 129.8, 128.5, 122.7, 116.6, 53.7.



***N,N*,2-trimethylnicotinamide (2Bl)**

Yellow oil; 73% yield (by **GPB** in table2, 599 mg); (57% yield by **GPD** in table3, 468 mg); R_f = 0.24 (petroleum ether/ethyl acetate = 2:1, v/v).

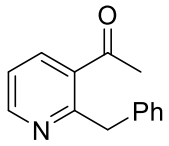
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.45 (d, *J* = 2.3 Hz, 1H), 7.73 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.37 (dd, *J* = 8.2, 0.5 Hz, 1H), 3.10 (s, 3H), 3.00 (s, 3H), 2.14 (s, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 167.9, 152.5, 148.2, 138.0, 131.0, 124.3, 39.6, 35.6, 29.8; **HRMS** (ESI+) m/z calcd for $C_9H_{13}N_2O^+$ $[M+H]^+$ 165.1023, Found 165.1026.



ethyl 2-ethylnicotinate[19] (2Bm)

Yellow oil; 72% yield (645 mg) [when using solid B; 67% (600 mg)]; R_f = 0.26 (petroleum ether/ethyl acetate = 4:1, v/v).

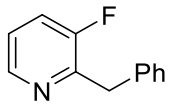
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.70 – 8.51 (m, 1H), 8.18 – 8.02 (m, 1H), 7.13 (dt, *J* = 7.9, 4.0 Hz, 1H), 4.38 – 4.28 (m, 2H), 3.16 – 3.08 (m, 2H), 1.39 – 1.31 (m, 3H), 1.29 – 1.22 (m, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 166.7, 164.4, 151.8, 138.4, 125.5, 120.8, 61.3, 30.3, 14.2, 14.0.



1-(2-benzylpyridin-3-yl)ethan-1-one[20] (2Bn)

Yellow oil; 64% yield (676 mg); R_f = 0.25 (petroleum ether/ethyl acetate = 10:1, v/v).

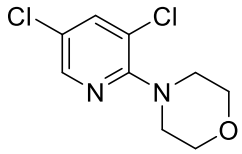
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.24 (dd, *J* = 3.1, 1.2 Hz, , 1H), 7.84 (dd, *J* = 5.2, 1.3 Hz, 1H), 7.19 – 7.15 (m, 3H), 7.12 (dd, *J* = 5.2, 3.1 Hz, 1H), 7.04 – 6.98 (m, 2H), 3.61 (d, *J* = 9.1 Hz, 1H), 3.24 (d, *J* = 9.1 Hz, 1H), 1.75(s, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 151.6, 148.0, 157.9, 140.8, 137.5, 136.2, 130.5, 128.4, 127.0, 122.6, 74.2, 27.2.



2-benzyl-3-fluoropyridine (2Bo)

Yellow oil; 71% yield (665 mg); R_f = 0.23 (petroleum ether/ethyl acetate = 10:1, v/v).

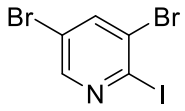
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.40 – 8.29 (m, 1H), 7.34 (d, *J* = 7.5 Hz, 2H), 7.30 (ddd, *J* = 12.9, 5.6, 2.1 Hz, 3H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.11 (dt, *J* = 8.5, 4.4 Hz, 1H), 4.23 (d, *J* = 2.6 Hz, 2H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 158.6, 156.9, 149.2 (d, *J* = 15.2 Hz), 145.2 (d, *J* = 5.4 Hz), 138.5, 129.0, 128.6, 126.6, 123.0 (dd, *J* = 11.4, 7.8 Hz), 38.3 (d, *J* = 2.1 Hz); ^{19}F NMR ($CDCl_3$, 565 MHz) δ -124.2; **HRMS** (ESI+) m/z calcd for $C_{12}H_{11}FN^+$ $[M+H]^+$ 188.0870, Found 188.0874.



4-(3,5-dichloropyridin-2-yl)morpholine[21] (2Bp)

Yellow solid; 72% yield (839 mg); R_f = 0.31 (petroleum ether/ethyl acetate = 20:1, v/v).

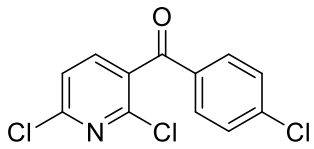
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.05 (d, *J* = 2.3 Hz, 1H), 7.52 (d, *J* = 2.3 Hz, 1H), 3.79 – 3.73 (m, 4H), 3.29 – 3.23 (m, 4H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 156.6, 144.4, 138.3, 124.5, 122.5, 66.8, 49.5.



3,5-dibromo-2-iodopyridine[22] (2Bq)

Yellow oil; 63% yield (1.1 g); R_f = 0.20 (petroleum ether/ethyl acetate = 20:1, v/v).

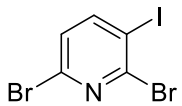
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.75 (s, 1H), 8.22 (s, 1H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 154.5, 149.3, 142.8, 120.9, 120.6.



(4-chlorophenyl)(2,6-dichloropyridin-3-yl)methanone[23] (2Br)

Yellow oil; 72% yield (1.0 g); R_f = 0.20 (petroleum ether/ethyl acetate = 20:1, v/v).

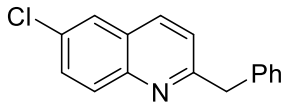
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.72 (d, *J* = 8.6 Hz, 2H), 7.70 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.42 (dd, *J* = 7.9, 0.7 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 191.5, 152.1, 147.3, 141.2, 140.3, 134.0, 133.1, 131.3, 129.5, 123.2.



2,6-Dibromo-3-iodopyridine (2Bs)[15]

Yellow oil; 59% yield (1.1 g); R_f = 0.37 (petroleum ether/ethyl acetate = 20:1, v/v).

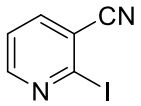
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.93 (d, *J* = 6.3 Hz, 1H), 7.19 (d, *J* = 6.3 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) δ 150.0, 147.4, 140.0, 128.1, 98.3.



2-benzyl-6-chloroquinoline[24] (2Bt)

Yellow solid; 74% yield (739 mg); R_f = 0.31 (petroleum ether/ethyl acetate = 5:1, v/v).

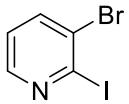
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.09 (dd, *J* = 8.6, 3.2 Hz, 1H), 8.00 (dd, *J* = 8.6, 3.2 Hz, 1H), 7.79 (s, 1H), 7.70 – 7.64 (m, 1H), 7.42 – 7.34 (m, 4H), 7.32 – 7.27 (m, 2H), 4.33 (s, 2H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 161.7, 146.3, 139.0, 135.7, 131.7, 130.8, 130.5, 129.3, 128.8, 127.5, 126.7, 126.3, 122.5, 45.6.



2-iodonicotinonitrile (3u)[25]

Yellow oil; 73% yield (by **GPA** in table2, 839 mg); 80% yield (by **GPB** in table2, 920 mg); R_f = 0.22 (petroleum ether/ethyl acetate = 4:1, v/v).

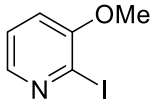
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.72 – 8.36 (m, 1H), 7.80 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.41 (dd, *J* = 7.7, 4.9 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 153.0, 141.3, 122.6, 121.1, 120.1, 117.8.



3-bromo-2-iodopyridine (3v)[26]

Yellow oil; 72% yield (by **GPA** in table2, 1.0 g); 79% yield (by **GPB** in table2, 1.1 g); R_f = 0.28 (petroleum ether/ethyl acetate = 5:1, v/v).

^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) δ 8.29 – 8.24 (m, 1H), 7.78 (d, *J* = 5.1 Hz, 1H), 7.12 (dd, *J* = 4.9, 2.4 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 148.4, 139.8, 130.0, 124.2, 123.8.

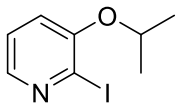


2-iodo-3-methoxypyridine (3w)[27]

Yellow oil; 77% yield (by **GPA** in table2, 904 mg); 86 % yield (by **GPB** in table2, 1.0 g); R_f = 0.26 (petroleum ether/ethyl acetate = 5:1, v/v).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.96 (ddd, *J* = 3.0, 2.1, 1.0 Hz, 1H), 7.16

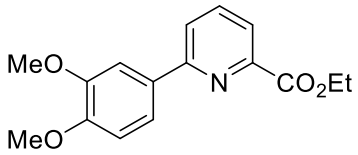
(ddd, J = 5.3, 3.1, 1.8 Hz, 1H), 6.97 (dt, J = 5.4, 1.2 Hz, 1H), 3.87 (s, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 155.3, 142.6, 123.6, 116.9, 111.8, 56.3.



2-iodo-3-isopropoxypyridine (3x)[28]

Yellow oil; 75% yield (by **GPA** in table2, 986 g); 81% yield (by **GPB** in table2, 1.0 g); R_f = 0.24 (petroleum ether/ethyl acetate = 5:1, v/v).

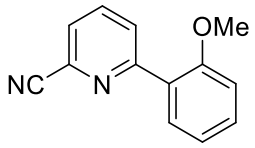
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.89 (dd, J = 4.6, 1.1 Hz, 1H), 7.09 (dd, J = 8.1, 4.6 Hz, 1H), 6.97 – 6.86 (m, 1H), 4.49 (dt, J = 12.1, 6.1 Hz, 1H), 1.33 (d, J = 6.1 Hz, 6H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 153.9, 142.5, 123.5, 119.8, 114, 72.6, 22.0.



Ethyl 6-(3,4-dimethoxyphenyl)picolinate (4Ac)

Colorless oil; 71% yield (1.0 g); R_f = 0.28 (petroleum ether/ethyl acetate = 3:1, v/v).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.62 – 8.52 (m, 1H), 7.77 – 7.66 (m, 1H), 7.38 (dd, J = 7.4, 4.8 Hz, 1H), 6.85 (d, J = 12.9 Hz, 3H), 4.19 (d, J = 7.1 Hz, 2H), 3.86 (s, 3H), 3.83 (s, 3H), 1.11 (t, J = 7.1 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 167.3, 149.4, 149.2, 149.0, 147.8, 138.3, 136.8, 130.8, 125.0, 120.9, 111.7, 111.2, 61.8, 56.02, 56.00, 14.0; **HRMS** (ESI+) m/z calcd for $C_{16}H_{18}NO_4^+$ $[M+H]^+$ 288.1231, Found 288.1234.

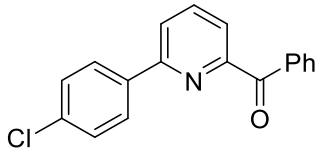


6-(2-methoxyphenyl)picolinonitrile[29] (4Ad)

Yellow oil; 63% yield (662 mg); R_f = 0.35 (petroleum ether/ethyl acetate = 3:1, v/v).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.11 (d, J = 8.2 Hz, 1H), 7.87 – 7.78 (m, 2H), 7.58 (d, J = 7.6 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.10 (t, J = 7.5 Hz, 1H), 7.01 (d, J

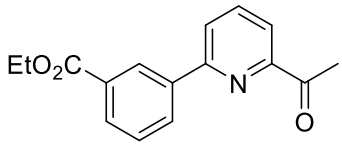
= 8.3 Hz, 1H), 3.87 (s, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 157.9, 157.2, 136.5, 133.6, 131.4, 131.2, 128.6, 127.0, 126.4, 126.3, 121.4, 111.5, 55.7.



(6-(4-chlorophenyl)pyridin-2-yl)(phenyl)methanone[30] (4Ae)

Yellow oil; 66% yield (969 mg); R_f = 0.22 (petroleum ether/ethyl acetate = 5:1, v/v).

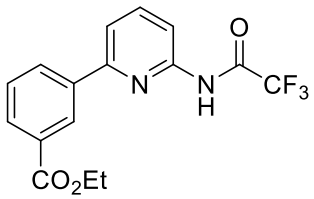
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.91 (d, *J* = 8.8 Hz, 3H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.81 – 7.77 (m, 1H), 7.63 (d, *J* = 8.2 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 5H), 7.29 (q, *J* = 8.7, 7.9 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 163.0, 153.3, 139.1, 137.8, 135.4, 129.0, 128.3, 128.1, 127.9, 127.5, 126.9, 122.4, 122.1, 118.9.



Ethyl 3-(6-acetylpyridin-2-yl)benzoate (4Af)

Yellow oil; 63% yield (848 mg); R_f = 0.25 (petroleum ether/ethyl acetate = 4:1, v/v).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.64 (s, 1H), 8.26 (d, *J* = 7.8 Hz, 1H), 8.05 (d, *J* = 7.7 Hz, 1H), 7.90 (dd, *J* = 9.1, 8.4 Hz, 2H), 7.82 (t, *J* = 7.7 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.75 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 200.2, 166.3, 155.3, 153.4, 138.6, 137.8, 131.18, 131.15, 130.4, 129.0, 127.9, 123.5, 120.2, 61.2, 25.7, 14.4; **HRMS** (ESI+) m/z calcd for $C_{16}H_{16}NO_3^+$ $[M+H]^+$ 270.1125, Found 270.1135.

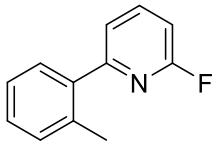


Ethyl 3-(6-(2,2,2-trifluoroacetamido)pyridin-2-yl)benzoate (4Ag)

Yellow oil; 58% yield (978 mg); R_f = 0.22 (petroleum ether/ethyl acetate = 3:1, v/v).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.58 (s, 1H), 8.13 (d, *J* = 5.1 Hz, 1H), 8.04

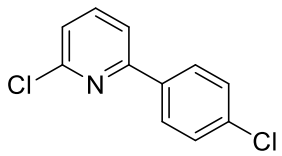
(d, J = 4.9 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.13 (d, J = 4.9 Hz, 1H), 6.47 (d, J = 5.4 Hz, 1H), 4.62 (s, 1H), 4.40 (q, J = 4.7 Hz, 2H), 1.40 (t, J = 4.7 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 166.7, 158.4, 155.0, 141.1, 140.0, 138.6, 131.2, 130.9, 129.7, 128.7, 128.0, 126.2, 111.4 (q, J = 249.8 Hz), 107.7, 61.2, 14.5; **^{19}F NMR** ($CDCl_3$, 376 MHz) δ (ppm) -76.4; **HRMS** (ESI+) m/z calcd for $C_{16}H_{14}F_3N_2O_3^+$ $[M+H]^+$ 339.0951, Found 339.0957.



2-fluoro-6-(o-tolyl)pyridine[31] (4Ah)

Yellow oil; 69% yield (646 mg); R_f = 0.35 (petroleum ether/ethyl acetate = 8:1, v/v).

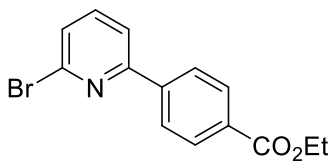
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.82 (dd, J = 15.7, 8.2 Hz, 1H), 7.41 (dd, J = 6.9, 2.4 Hz, 1H), 7.34 – 7.23 (m, 4H), 6.87 (dd, J = 8.2, 2.9 Hz, 1H), 2.40 (s, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 164.1, 161.7, 158.9 (d, J = 13.6 Hz), 141.2 (d, J = 7.7 Hz), 136.0 (d, J = 0.9 Hz), 131.0, 129.8, 128.8, 126.1, 121.4 (d, J = 4.3 Hz), 107.40 (d, J = 37.2 Hz), 20.5; **^{19}F NMR** ($CDCl_3$, 376 MHz) δ (ppm) -66.9.



2-chloro-6-(4-chlorophenyl)pyridine[32] (4Ai)

Yellow oil; 71% yield (795 mg); R_f = 0.22 (petroleum ether/ethyl acetate = 10:1, v/v).

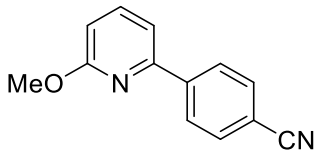
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.95 – 7.89 (m, 2H), 7.68 (td, J = 7.8, 1.2 Hz, 1H), 7.59 (ddd, J = 7.8, 1.2, 0.7 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.26 – 7.24 (m, 1H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 156.9, 151.6, 139.5, 136.2, 135.9, 129.1, 128.3, 122.9, 118.5.



Ethyl 4-(6-bromopyridin-2-yl)benzoate[33] (4Aj)

Yellow oil; 59% yield (903 mg); R_f = 0.26 (petroleum ether/ethyl acetate = 10:1, v/v).

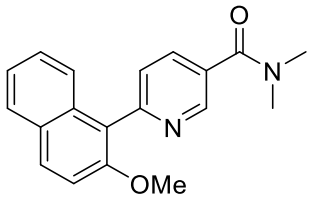
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.13 – 8.11 (m, 2H), 8.06 – 8.04 (m, 2H), 7.72 (dd, *J* = 7.6, 0.6 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.45 (dd, *J* = 7.9, 0.6 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 166.3, 157.4, 142.4, 141.6, 139.2, 131.4, 130.1, 127.3, 127.0, 119.6, 61.3, 14.4.



4-(6-methoxypyridin-2-yl)benzonitrile[34] (4Ak)

Yellow oil; 61% yield (641 mg); R_f = 0.21 (petroleum ether/ethyl acetate = 8:1, v/v).

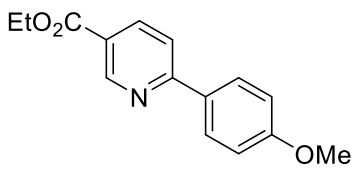
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.16 – 8.13 (m, 2H), 7.74 – 7.72 (m, 2H), 7.68 (dd, *J* = 8.2, 7.5 Hz, 1H), 7.37 (dd, *J* = 7.3, 0.4 Hz, 1H), 6.77 (dd, *J* = 8.3, 0.5 Hz, 1H), 4.03 (s, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 164.0, 152.4, 139.6, 132.5, 127.3, 119.0, 113.7, 112.3, 111.0, 105.8, 53.5.



6-(2-methoxynaphthalen-1-yl)-N,N-dimethylnicotinamide (4Al)

Yellow solid; 59% yield (904 mg); R_f = 0.22 (petroleum ether/ethyl acetate = 1:1, v/v).

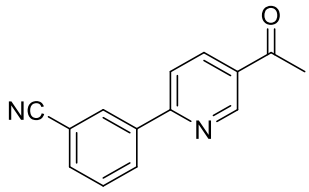
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.85 (s, 1H), 7.85 (dd, *J* = 13.3, 5.3 Hz, 2H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.9 Hz,1H), 7.41 (d, *J* = 8.1 Hz, 1H), 7.37 – 7.23 (m, 3H), 3.78 (s, 3H), 3.09 (d, *J* = 17.3 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 169.3, 157.5, 154.3, 147.9, 135.2, 133.1, 130.7, 130.2, 129.1, 128.1, 127.0, 126.6, 124.6, 123.8, 123.2, 113.4, 56.6, 39.8, 35.6; **HRMS** (ESI+) m/z calcd for $C_{19}H_{19}N_2O_2^+$ $[M+H]^+$ 307.1441, Found 307.1449.



Ethyl 6-(4-methoxyphenyl)nicotinate[35] (4Am)

Yellow oil; 73% yield (939 mg); R_f = 0.31 (petroleum ether/ethyl acetate = 3:1, v/v).

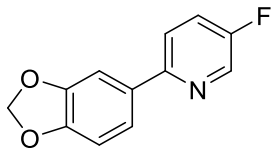
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 9.23 (d, *J* = 1.9 Hz, 1H), 8.30 (dd, *J* = 8.3, 1.8 Hz, 1H), 8.03 (d, *J* = 8.7 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.05 – 6.96 (m, 2H), 4.41 (q, *J* = 7.2 Hz, 2H), 3.87 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 174.0, 147.9, 147.5, 142.6, 132.1, 129.4, 129.1, 128.2, 114.5, 100.0, 61.5, 55.5, 14.4.



3-(5-acetylpyridin-2-yl)benzonitrile (4An)

Yellow oil; 62% yield (689 mg); R_f = 0.31 (petroleum ether/ethyl acetate = 8:1, v/v).

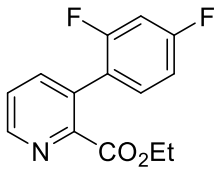
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 9.23 – 9.20 (m, 1H), 8.37 (t, *J* = 1.7 Hz, 1H), 8.34 – 8.26 (m, 2H), 7.86 – 7.82 (m, 1H), 7.72 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.60 (t, *J* = 7.8 Hz, 1H), 2.66 (s, 3H).; **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 196.2, 158.3, 150.2, 139.2, 137.0, 133.3, 131.5, 131.1, 129.9, 120.3, 118.5, 113.4, 26.9; **HRMS** (ESI+) m/z calcd for $C_{14}H_{11}N_2O^+$ $[M+H]^+$ 223.0866, Found 223.0879.



2-(benzo[d][1,3]dioxol-5-yl)-5-fluoropyridine (4Ao)

White solid; 72% yield (782 mg); R_f = 0.21 (petroleum ether/ethyl acetate = 8:1, v/v).

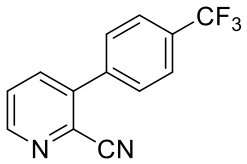
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.48 (dd, *J* = 4.5, 3.0 Hz, 1H), 7.61 (dt, *J* = 8.8, 4.4 Hz, 1H), 7.53 – 7.37 (m, 3H), 6.88 (dd, *J* = 8.1, 4.8 Hz, 1H), 6.00 (s, 2H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 159.9, 157.4, 153.3 (d, *J* = 3.9 Hz), 148.5 (d, *J* = 11.6 Hz), 137.4 (d, *J* = 23.7 Hz), 132.7, 123.9 (d, *J* = 18.6 Hz), 120.9 (d, *J* = 2.4 Hz), 108.6, 107.4, 101.5 (d, *J* = 1.4 Hz), 31.0; **^{19}F NMR** ($CDCl_3$, 376 MHz) δ (ppm) -130.2; **HRMS** (ESI+) m/z calcd for $C_{12}H_9FNO_2^+$ $[M+H]^+$ 218.0612, Found 218.0622.



Ethyl 3-(2,4-difluorophenyl)picolinate (4Bc)

Yellow oil; 69% yield (908 mg); R_f = 0.35 (petroleum ether/ethyl acetate = 3:1, v/v).

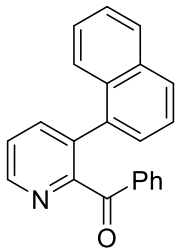
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.74 (dd, *J* = 4.7, 1.6 Hz, 1H), 7.71 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.51 (dd, *J* = 7.8, 4.7 Hz, 1H), 7.28 – 7.24 (m, 1H), 6.96 (td, *J* = 8.2, 2.3 Hz, 1H), 6.93 – 6.86 (m, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.23 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 165.7, 158.4(d, *J* = 11.9 Hz), 149.0, 139.8, 131.5, 131.3 – 131.2 (m), 125.8, 122.7 (dd, *J* = 16.1, 3.9 Hz), 111.7 (dd, *J* = 21.4, 3.8 Hz), 104.4, 104.1, 103.9, 62.0, 14.1; **^{19}F NMR** ($CDCl_3$, 376 MHz) δ (ppm) -115.3, -117.2; **HRMS** (ESI+) m/z calcd for $C_{14}H_{12}F_2NO_2^+$ $[M+H]^+$ 264.0831, Found 264.0839.



3-(4-(trifluoromethyl)phenyl)picolinonitrile (4Bd)

Yellow oil; 69% yield (856 mg); R_f = 0.30 (petroleum ether/ethyl acetate = 3:1, v/v).

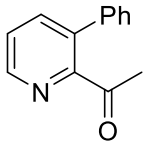
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.76 (dd, *J* = 4.7, 1.6 Hz, 1H), 7.87 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 8.1 Hz, 2H), 7.63 (dd, *J* = 8.0, 4.8 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 150.3, 140.8, 138.9, 137.6, 132.4, 129.3, 126.8, 126.2, 123.0, 116.6, 100.0; **^{19}F NMR** ($CDCl_3$, 565 MHz) (ppm) -62.7; **HRMS** (ESI+) m/z calcd for $C_{13}H_8F_3N_2^+$ $[M+H]^+$ 249.0634, Found 249.0643.



(3-(naphthalen-1-yl)pyridin-2-yl)(phenyl)methanone (4Be)

Yellow oil; 74% yield (1.1 g); R_f = 0.36 (petroleum ether/ethyl acetate = 3:1, v/v).

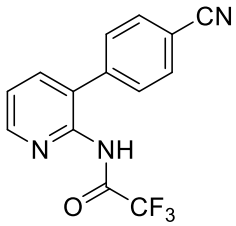
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.73 – 8.66 (m, 1H), 8.23 (d, *J* = 8.7 Hz, 1H), 7.87 (dd, *J* = 13.0, 8.2 Hz, 2H), 7.58 (td, *J* = 7.7, 1.7 Hz, 1H), 7.53 – 7.48 (m, 2H), 7.46 – 7.41 (m, 1H), 7.40 – 7.28 (m, 3H), 7.24 (ddd, *J* = 7.4, 4.8, 0.8 Hz, 1H), 7.09 (d, *J* = 7.9 Hz, 1H), 6.79 (dd, *J* = 9.0, 1.6 Hz, 2H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 163.4, 148.1, 146.7, 141.8, 136.7, 135.3, 132.1, 129.4, 128.8, 128.7, 128.4, 128.2, 127.9, 127.43, 127.36, 125.5, 124.3, 123.8, 122.6, 121.8; **HRMS** (ESI+) m/z calcd for $C_{22}H_{16}NO^+$ $[M+H]^+$ 310.1227, Found 310.1238.



1-(3-phenylpyridin-2-yl)ethan-1-one (4Bf)

Yellow oil; 66% yield (651 mg); R_f = 0.22 (petroleum ether/ethyl acetate = 3:1, v/v).

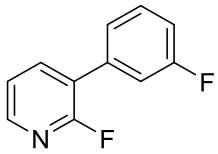
^{1}H NMR ($CDCl_3$,600 MHz) δ 8.62 (d, *J* = 4.2 Hz, 1H), 7.70 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.47 – 7.37 (m, 4H), 7.31 – 7.25 (m, 2H), 2.55 (s, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 201.9, 154.2, 147.7, 139.0, 138.7, 136.6, 128.6, 128.0, 126.7, 125.4, 28.8; **HRMS** (ESI+) m/z calcd for $C_{13}H_{12}NO^+$ $[M+H]^+$ 198.0914, Found 198.0926.



***N*-(3-(4-cyanophenyl)pyridin-2-yl)-2,2,2-trifluoroacetamide (4Bg)**

Yellow oil; 61% yield (888 mg); R_f = 0.20 (petroleum ether/ethyl acetate = 3:1, v/v).

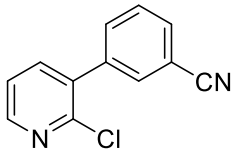
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.16 – 8.05 (m, 1H), 7.73 (d, *J* = 5.4 Hz, 2H), 7.58 (d, *J* = 5.4 Hz, 2H), 7.34 (dd, *J* = 4.9, 0.9 Hz, 1H), 6.76 (dd, *J* = 4.8, 3.4 Hz, 1H), 4.68 (s, 1H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 155.5, 148.4, 143.1, 138.1, 133.0, 129.6, 124.5, 124.1, 119.9, 118.6, 115.1 (q, *J* = 281.6 Hz), 111.7; **^{19}F NMR** ($CDCl_3$, 376 MHz) δ (ppm) -75.9. **HRMS** (ESI+) m/z calcd for $C_{14}H_9F_3N_3O^+$ $[M+H]^+$ 292.0692, Found 292.0699.



2-fluoro-3-(3-fluorophenyl)pyridine (4Bh)

White solid; 77% yield (736 mg); R_f = 0.33 (petroleum ether/ethyl acetate = 8:1, v/v).

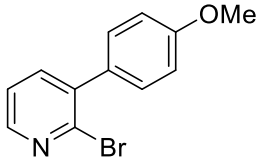
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.21 (dq, *J* = 4.8, 1.5 Hz, 1H), 7.86 (ddd, *J* = 9.7, 7.4, 1.9 Hz, 1H), 7.45 – 7.39 (m, 1H), 7.36 – 7.32 (m, 1H), 7.30 – 7.26 (m, 2H), 7.10 (tdd, *J* = 8.4, 2.6, 1.0 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 163.7, 162.1, 161.1, 159.5, 147.0 (d, *J* = 14.9 Hz), 140.7 (d, *J* = 4.1 Hz), 130.4 (d, *J* = 8.4 Hz), 124.6 (t, *J* = 3.2 Hz), 122.0 (d, *J* = 4.6 Hz), 116.0 (dd, *J* = 22.7, 3.3 Hz), 115.5 (21.0 Hz); **^{19}F NMR** ($CDCl_3$, 565 MHz) δ (ppm) -70.6, -112.4; **HRMS** (ESI+) m/z calcd for $C_{11}H_8F_2N^+$ $[M+H]^+$ 192.0620, Found 190.0625.



3-(2-chloropyridin-3-yl)benzonitrile (4Bi)

White solid; 72% yield (773 mg); R_f = 0.26 (petroleum ether/ethyl acetate = 10:1, v/v).

^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.45 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.73 (s, 1H), 7.72 – 7.68 (m, 2H), 7.66 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.58 (t, *J* = 7.8 Hz, 1H), 7.36 (dd, *J* = 7.5, 4.8 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 149.55, 149.5, 139.6, 138.7, 134.9, 133.8, 132.9, 132.0, 129.4, 122.9, 118.4, 113.0; **HRMS** (ESI+) m/z calcd for $C_{12}H_8ClN_2^+$ $[M+H]^+$ 215.0371, Found 215.0374.

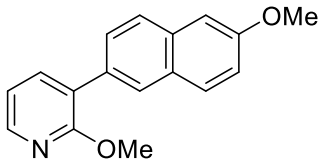


2-bromo-3-(4-methoxyphenyl)pyridine (4Bj)

Yellow oil; 76% yield (1.0 g); R_f = 0.3 (petroleum ether/ethyl acetate = 10:1, v/v).

^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.33 (dd, *J* = 4.7, 1.9 Hz, 1H), 7.59 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.37 – 7.33 (m, 2H), 7.30 (dd, *J* = 7.5, 4.7 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 159.8, 148.3, 142.6, 139.6,

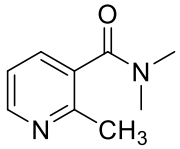
139.3, 131.2, 130.6, 122.8, 113.8, 55.4; **HRMS** (ESI+) m/z calcd for $C_{12}H_{11}BrNO^+$ $[M+H]^+$ 264.0019, Found 264.0028.



2-methoxy-3-(6-methoxynaphthalen-2-yl)pyridine (4Bk)

White solid; 73% yield (968 mg); R_f = 0.27 (petroleum ether/ethyl acetate = 10:1, v/v).

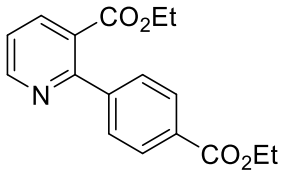
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.18 (dd, *J* = 5.0, 1.9 Hz, 1H), 7.92 (d, *J* = 1.1 Hz, 1H), 7.77 (dd, *J* = 9.1, 3.8 Hz, 2H), 7.71 (dd, *J* = 7.3, 1.9 Hz, 1H), 7.65 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.19 – 7.14 (m, 2H), 7.01 (dd, *J* = 7.3, 5.0 Hz, 1H), 4.01 (s, 3H), 3.93 (s, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 161.1, 158.1, 145.4, 139.0, 134.0, 132.0, 129.8, 128.9, 128.0, 127.8, 126.6, 125.0, 119.1, 117.3, 105.7, 55.4, 53.9; **HRMS** (ESI+) m/z calcd for $C_{17}H_{16}NO_2^+$ $[M+H]^+$ 266.1176, Found 266.1183.



***N,N*,2-trimethylnicotinamide (4Bl)**

Yellow oil; 57% yield (by **GPD** in table3, 468 mg); (73% yield by **GPB** in table2, 599 mg); R_f = 0.24 (petroleum ether/ethyl acetate = 2:1, v/v).

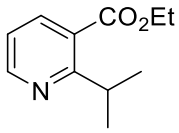
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.45 (d, *J* = 2.3 Hz, 1H), 7.73 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.37 (dd, *J* = 8.2, 0.5 Hz, 1H), 3.10 (s, 3H), 3.00 (s, 3H), 2.14 (s, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 167.9, 152.5, 148.2, 138.0, 131.0, 124.3, 39.6, 35.6, 29.8; **HRMS** (ESI+) m/z calcd for $C_9H_{13}N_2O^+$ $[M+H]^+$ 165.1023, Found 165.1026.



ethyl 2-(4-(ethoxycarbonyl)phenyl)nicotinate[36] (4Bm-1)

Yellow oil; 58% yield (868 mg); R_f = 0.21 (petroleum ether/ethyl acetate = 3:1, v/v).

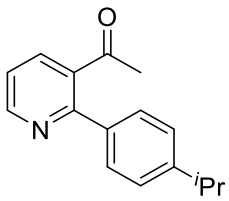
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.78 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.15 (dd, *J* = 7.9, 1.7 Hz, 1H), 8.13 – 8.09 (m, 2H), 7.61 – 7.58 (m, 2H), 7.38 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.40 (q, *J* = 7.2 Hz, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 167.6, 166.4, 158.0, 151.3, 144.5, 138.3, 130.6, 129.4, 128.7, 127.6, 122.3, 61.8, 61.2, 14.4, 13.8.



ethyl 2-isopropylnicotinate[37] (4Bm-2)

Yellow oil; 46% yield (444 mg); R_f = 0.22 (petroleum ether/ethyl acetate = 3:1, v/v).

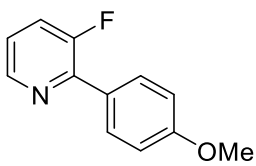
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.55 (ddt, *J* = 4.7, 3.2, 1.7 Hz, 1H), 7.92 (ddt, *J* = 7.9, 3.0, 1.7 Hz, 1H), 7.06 – 7.01 (m, 1H), 4.30 – 4.23 (m, 2H), 3.73 (pd, *J* = 6.8, 2.1 Hz, 1H), 1.27 (tdd, *J* = 7.1, 2.9, 1.3 Hz, 3H), 1.22 – 1.17 (m, 6H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 167.1, 167.05, 151.5, 137.7, 125.6, 120.4, 61.2, 32.3, 22.2, 14.1.



1-(2-(4-isopropylphenyl)pyridin-3-yl)ethan-1-one (4Bn)

White solid; 57% yield (682 mg); R_f = 0.26 (petroleum ether/ethyl acetate = 10:1, v/v).

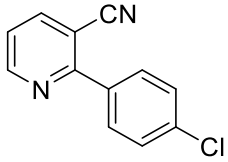
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.69 (dd, *J* = 4.8, 1.7 Hz, 1H), 7.79 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.27 – 7.24 (m, 1H), 2.92 (dt, *J* = 13.8, 6.9 Hz, 1H), 2.03 (s, 3H), 1.23 (s, 6H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 203.8, 157.3, 150.9, 150.5, 137.2, 136.23, 136.21, 129.2, 126.9, 121.7, 34.0, 30.3, 24.0; **HRMS** (ESI+) m/z calcd for $C_{16}H_{18}NO^+$ $[M+H]^+$ 240.1383, Found 240.1395.



3-fluoro-2-(4-methoxyphenyl)pyridine[38] (4Bo)

Yellow oil; 78% yield (793 mg); R_f = 0.36 (petroleum ether/ethyl acetate = 15:1, v/v).

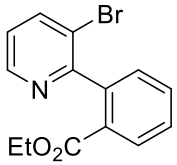
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.51 – 8.35 (m, 1H), 7.98 – 7.92 (m, 2H), 7.42 – 7.34 (m, 1H), 7.12 (dddd, *J* = 8.2, 4.5, 3.7, 0.8 Hz, 1H), 7.00 – 6.95 (m, 2H), 3.80 (s, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 160.5 (d, *J* = 3.2 Hz), 158.7, 156.1, 145.6 (d, *J* = 31.0 Hz), 130.3 (d, *J* = 24.8 Hz), 128.0 (d, *J* = 22.2 Hz), 124.0 (d, *J* = 82.7 Hz), 122.8 (d, *J* = 15.5 Hz), 113.9, 55.3; **^{19}F NMR** ($CDCl_3$, 376 MHz) δ (ppm) -123.0.



2-(4-chlorophenyl)nicotinonitrile(5u)[39]

Yellow oil; 69% yield (738 mg); R_f = 0.27 (petroleum ether/ethyl acetate = 2:1, v/v).

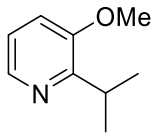
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.87 (dd, *J* = 3.1, 1.3 Hz, 1H), 8.09 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.94 – 7.88 (m, 2H), 7.54 – 7.49 (m, 2H), 7.41 (dd, *J* = 5.0, 3.1 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 159.6, 152.7, 141.8, 136.5, 135.4, 130.2, 129.1, 121.8, 117.5, 107.4.



Ethyl 2-(3-bromopyridin-2-yl)benzoate (5v)

Yellow oil; 64 yield (980 mg); R_f = 0.24 (petroleum ether/ethyl acetate = 2:1, v/v).

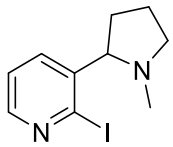
^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.57 (d, *J* = 4.7 Hz, 1H), 8.08 (d, *J* = 7.9 Hz, 1H), 7.93 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.61 (dd, *J* = 8.1, 7.0 Hz, 1H), 7.50 (dd, *J* = 10.9, 4.5 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.17 (ddd, *J* = 8.0, 4.7, 0.9 Hz, 1H), 4.11 (qd, *J* = 7.2, 1.2 Hz, 2H), 1.04 (td, *J* = 7.2, 1.2 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ (ppm) 166.4, 159.3, 146.7, 140.7, 132.3, 130.5, 130.2, 129.9, 129.1, 123.6, 121.2, 61.1, 13.9. **HRMS** (ESI+) m/z calcd for $C_{14}H_{13}BrNO_2^+$ $[M+H]^+$306.0781, Found 306.0787.



2-isopropyl-3-methoxypyridine (5w)

Yellow oil; 66% yield (499 mg); R_f = 0.22 (petroleum ether/ethyl acetate = 4:1, v/v).

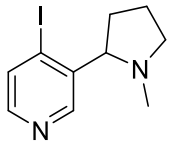
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.86 (t, *J* = 5.1 Hz, 1H), 7.11 (d, *J* = 4.8 Hz, 1H), 6.94 (d, *J* = 5.5 Hz, 1H), 3.92 (s, 3H), 2.94 (dt, *J* = 9.2, 4.6 Hz, 1H), 1.30 – 1.27 (m, 6H); **^{13}C** NMR ($CDCl_3$, 151 MHz) δ (ppm) 154.9, 153.3, 138.7, 124.8, 112.9, 52.9, 36.0, 22.4; **HRMS** (ESI+) m/z calcd for $C_9H_{14}NO^+$ $[M+H]^+$152.107, Found 152.112.



2-iodo-3-(1-methylpyrrolidin-2-yl)pyridine[40] (6)

Yellow oil; 78% yield (1.1 g); R_f = 0.24 (petroleum ether/ethyl acetate = 3:1, v/v).

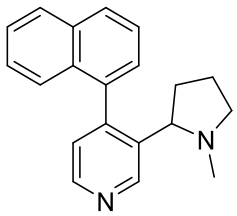
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.19 (dd, *J* = 4.6, 2.1 Hz, 1H), 7.76 – 7.70 (m, 1H), 7.21 (dd, *J* = 7.7, 4.6 Hz, 1H), 3.33 (t, *J* = 8.2 Hz, 1H), 3.27 – 3.18 (m, 1H), 2.45 – 2.34 (m, 2H), 2.18 (s, 3H), 1.89 – 1.79 (m, 2H), 1.44 (ddt, *J* = 12.7, 5.0, 2.2 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 149.3, 143.7, 137.0, 135.8, 123.6, 72.3, 56.9, 40.5, 33.8, 22.9.



4-iodo-3-(1-methylpyrrolidin-2-yl)pyridine[41] (7)

Yellow oil; 63% yield (908 mg); R_f = 0.24 (petroleum ether/ethyl acetate = 3:1, v/v).

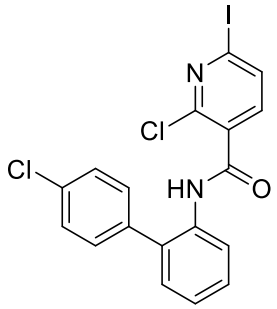
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.65 (s, 1H), 8.02 (d, *J* = 6.1 Hz, 1H), 7.73 (d, *J* = 6.1 Hz, 1H), 3.28 (ddd, *J* = 16.3, 12.7, 5.0 Hz, 2H), 2.48 – 2.34 (m, 2H), 2.20 (s, 3H), 1.97 – 1.73 (m, 2H), 1.49 – 1.40 (m, 1H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 149.8, 148.4, 141.9, 134.3, 111.4, 72.8, 57.1, 40.8, 33.9, 23.0.



3-(1-methylpyrrolidin-2-yl)-4-(naphthalen-1-yl)pyridine (8)

Yellow oil; 74% yield (1.1 g); R_f = 0.18 (petroleum ether/ethyl acetate = 3:1, v/v).

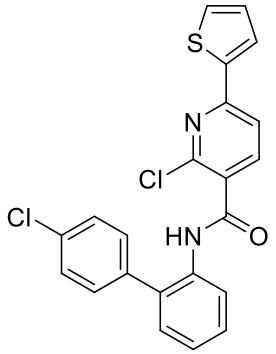
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.53 (s, 1H), 7.97 (d, *J* = 7.5 Hz, 2H), 7.75 (d, *J* = 8.9 Hz, 1H), 7.65 (d, *J* = 8.9 Hz, 1H), 7.27 (t, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 7.5 Hz, 2H), 6.80 (dd, *J* = 4.3, 2.2 Hz, 2H), 3.25 (t, *J* = 8.3 Hz, 1H), 3.16 – 3.11 (m, 1H), 2.39 (d, *J* = 8.5 Hz, 1H), 2.23 – 2.12 (m, 4H), 1.92 – 1.81 (m, 1H), 1.57 – 1.52 (m, 2H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ (ppm) 157.8, 149.2, 134.3, 134.0, 132.7, 131.4, 130.7, 129.9, 128.5, 128.3, 127.3, 127.0, 126.5, 125.6, 122.3, 68.3, 57.0, 40.4, 35.1, 22.6; **HRMS** (ESI+) m/z calcd for $C_{18}H_{12}Cl_2IN_2O^+$ $[M+H]^+$ 289.1699, Found 289.1697.



2-chloro-N-(4'-chloro-[1,1'-biphenyl]-2-yl)-6-iodonicotinamide (9)

Yellow oil; 82% yield (1.9 g); R_f = 0.21 (petroleum ether/ethyl acetate = 3:1, v/v) .

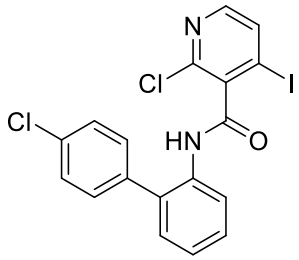
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.42 (d, *J* = 3.1 Hz, 1H), 7.49 – 7.44 (m, 3H), 7.41 (ddd, *J* = 6.3, 4.2, 2.7 Hz, 3H), 7.39 – 7.31 (m, 3H); **^{13}C NMR** ($CDCl_3$, 101MHz) δ (ppm) 163.7, 149.9, 147.0, 139.1, 136.6, 135.1, 134.2, 134.0, 133.1, 131.2, 130.5, 129.0, 127.1, 124.6, 118.1, 110.1; **HRMS** (ESI+) m/z calcd for $C_{18}H_{12}Cl_2IN_2O^+$ $[M+H]^+$ 468.9372, Found 468.9371.



2-chloro-N-(4'-chloro-[1,1'-biphenyl]-2-yl)-4-(thiophen-2-yl)nicotinamide (10)

White oil; 64% yield (1.4 g); R_f = 0.31 (petroleum ether/ethyl acetate = 2:1, v/v).

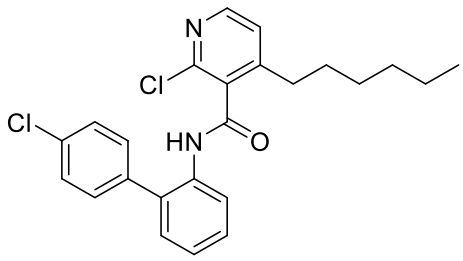
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.46 – 8.23 (m, 2H), 7.53 (d, *J* = 4.4 Hz, 2H), 7.47 – 7.42 (m, 1H), 7.35 (dd, *J* = 5.3, 2.0 Hz, 1H), 7.27 – 7.17 (m, 5H), 7.14 (dd, *J* = 5.1, 3.6 Hz, 1H), 7.00 – 6.89 (m, 2H); **^{13}C NMR** ($CDCl_3$, 101MHz) δ (ppm) 163.7, 150.0, 149.1, 142.0, 137.4, 135.8, 134.2, 133.9, 131.8, 130.7, 130.4, 129.9, 129.4, 129.3, 129.25, 129.0, 128.9, 125.6, 122.6, 122.5; **HRMS** (ESI+) m/z calcd for $C_{22}H_{15}Cl_2N_2OS^+$ $[M+H]^+$ 468.9372, Found 468.9375.



2-chloro-N-(4'-chloro-[1,1'-biphenyl]-2-yl)-4-iodonicotinamide (11)

White solid; 65% yield (1.5 g); R_f = 0.34 (petroleum ether/ethyl acetate = 2:1, v/v).

^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.36 (d, *J* = 8.2 Hz, 1H), 8.00 (d, *J* = 5.2 Hz, 1H), 7.70 (d, *J* = 5.2 Hz, 1H), 7.47 (ddd, *J* = 8.5, 5.1, 4.0 Hz, 1H), 7.42 (s, 4H), 7.30 – 7.28 (m, 2H), 7.18 – 7.11 (m, 1H); **^{13}C NMR** ($CDCl_3$, 101MHz) δ (ppm) 163.7, 149.9, 147.0, 138.2, 136.0, 134.4, 133.6, 133.3, 132.4, 131.2, 130.5, 129.3, 129.0, 126.0, 122.9, 106.2; **HRMS** (ESI+) m/z calcd for $C_{18}H_{12}Cl_2IN_2O^+$ $[M+H]^+$ 468.9372, Found 468.9375.

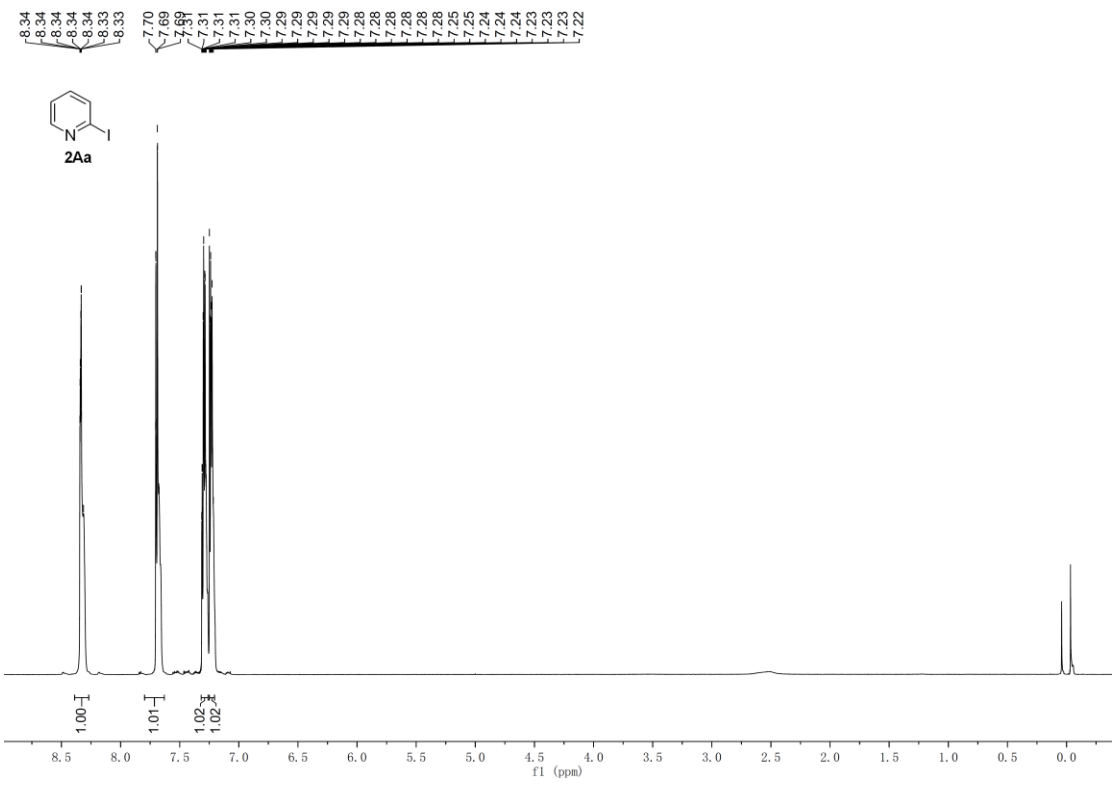


2-chloro-N-(4'-chloro-[1,1'-biphenyl]-2-yl)-4-hexylnicotinamide (12)

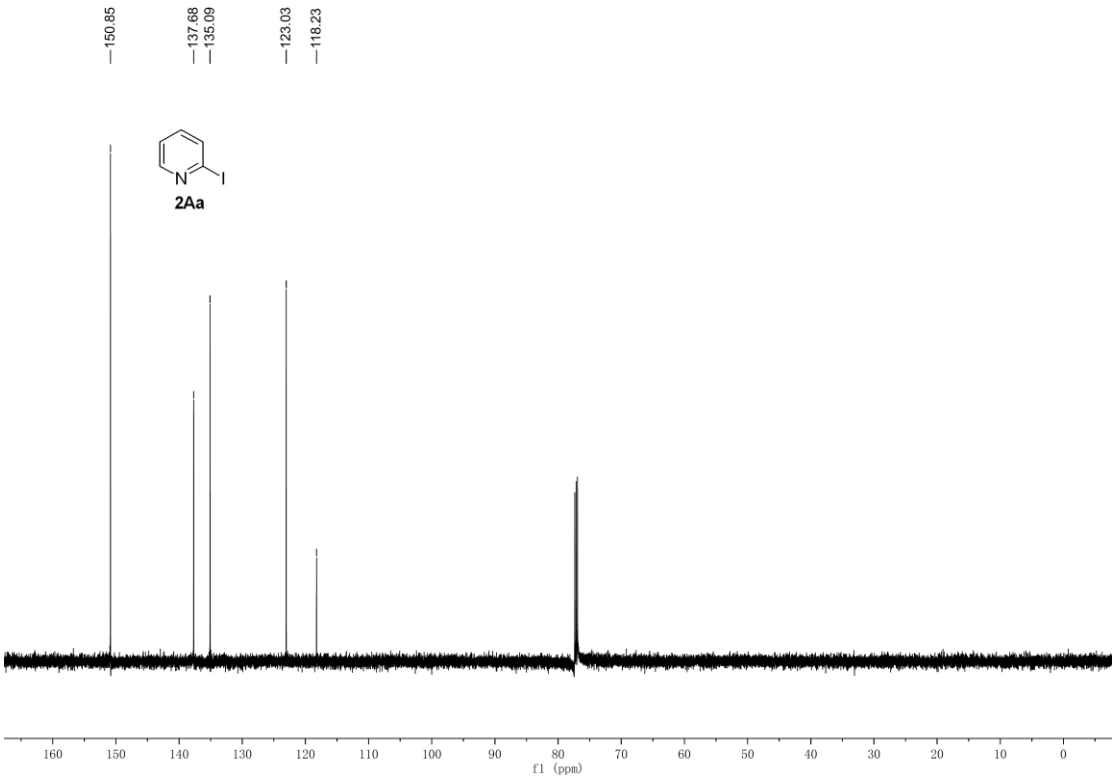
Yellow oil; 62% yield (1.3 g); R_f = 0.24 (petroleum ether/ethyl acetate = 2:1, v/v).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.61 – 8.48 (m, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 7.59 – 7.44 (m, 3H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 7.10 (dd, *J* = 7.4, 4.9 Hz, 1H), 3.88 (s, 1H), 2.87 – 2.81 (m, 2H), 1.68 (dd, *J* = 15.3, 7.6 Hz, 3H), 1.25 (d, *J* = 10.8 Hz, 4H), 0.91 (dd, *J* = 14.0, 6.7 Hz, 4H); **^{13}C NMR** ($CDCl_3$, 101MHz) δ (ppm) 166.8, 160.1, 150.6, 136.5, 134.6, 134.4, 134.3, 131.2, 131.0, 130.6, 130.4, 129.4, 129.0, 125.6, 122.7, 120.9, 52.7, 37.8, 23.3, 19.3, 14.2, 13.8; **HRMS** (ESI+) m/z calcd for $C_{24}H_{25}Cl_2N_2O^+$ $[M+H]^+$ 427.1345, Found 427.1342.

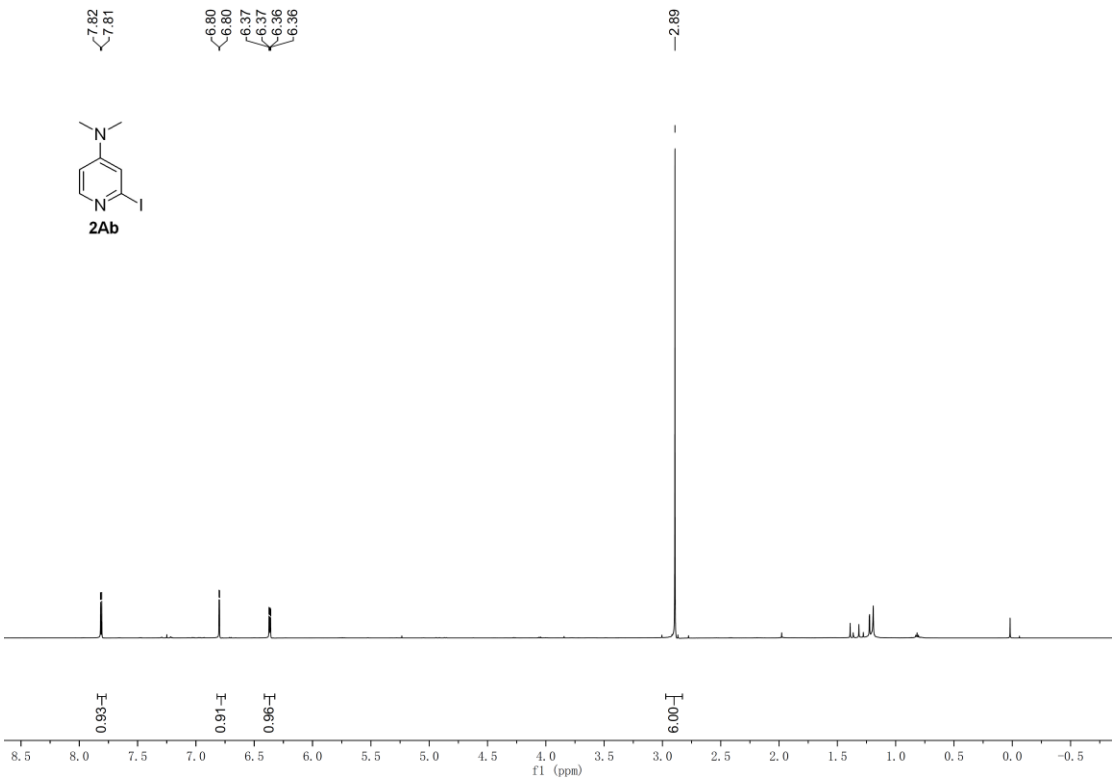
8. NMR spectra for products



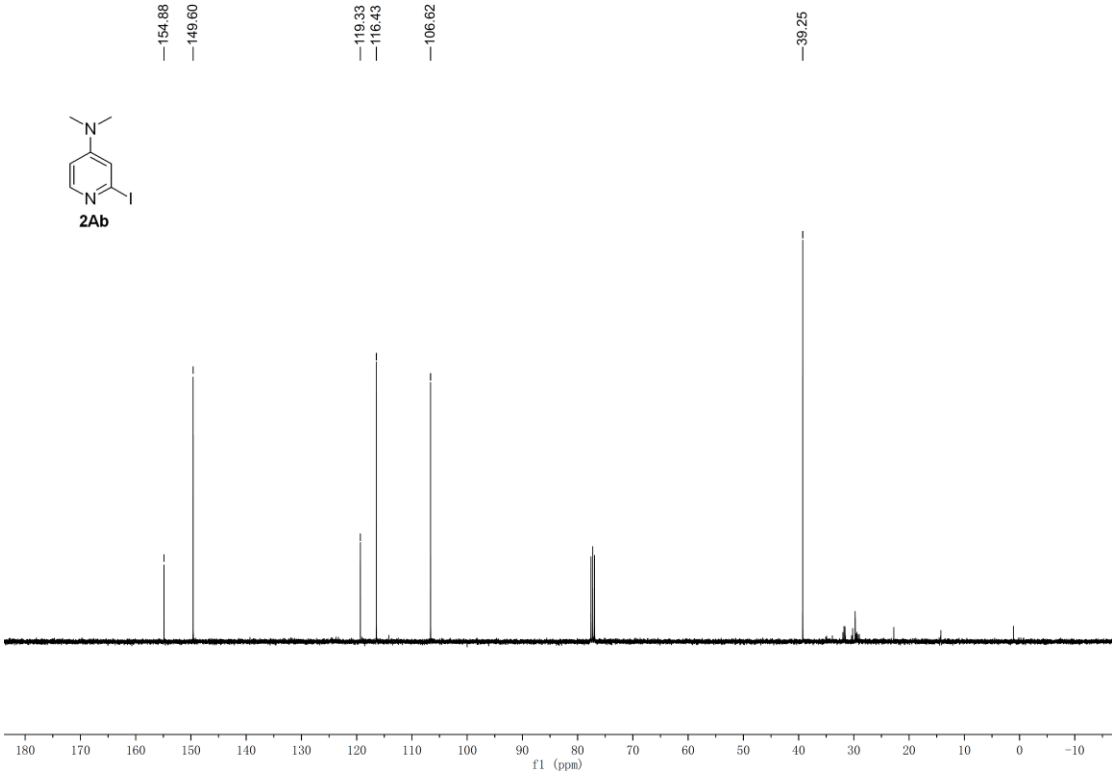
^{1}H NMR (600 MHz) spectrum of **2Aa** in $CDCl_3$



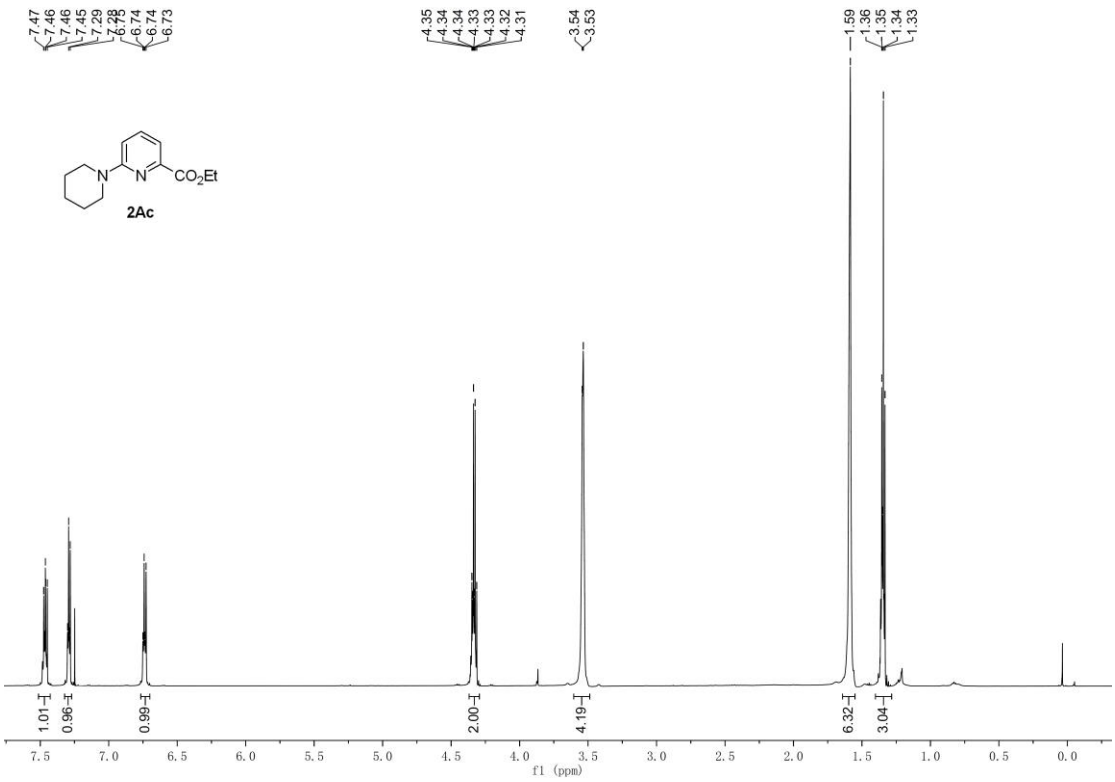
^{13}C NMR (151 MHz) spectrum of **2Aa** in $CDCl_3$



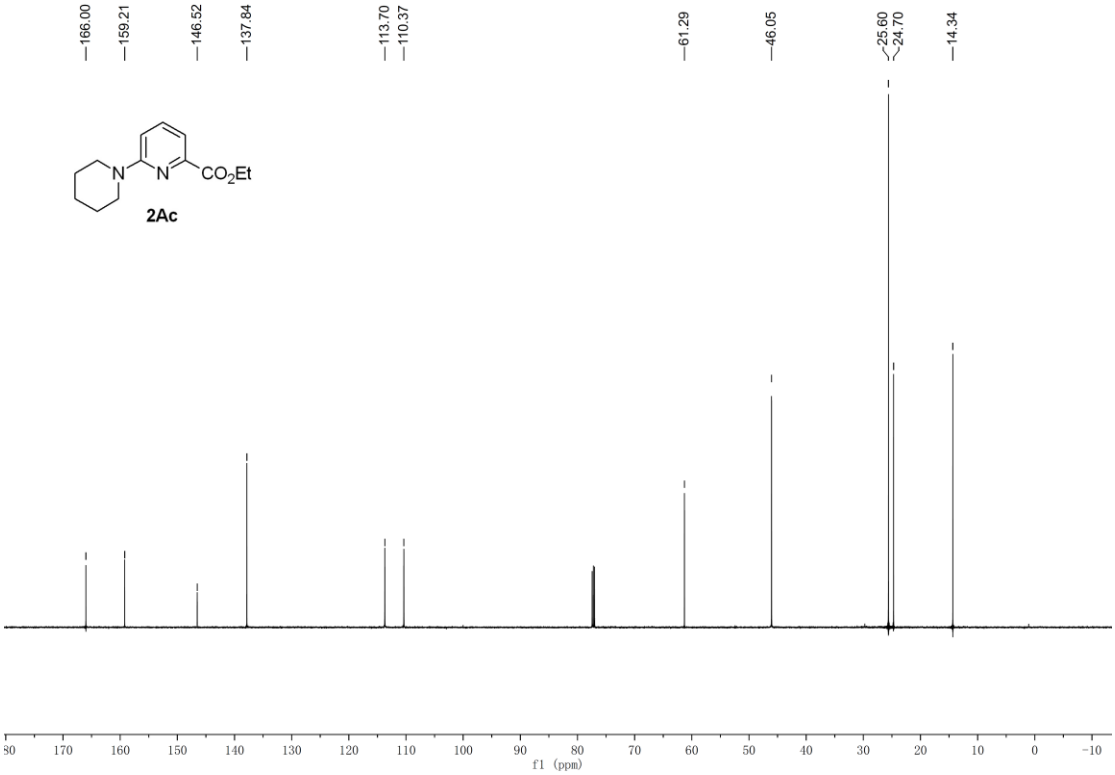
^{1}H NMR (600 MHz) spectrum of **2Ab** in $CDCl_3$



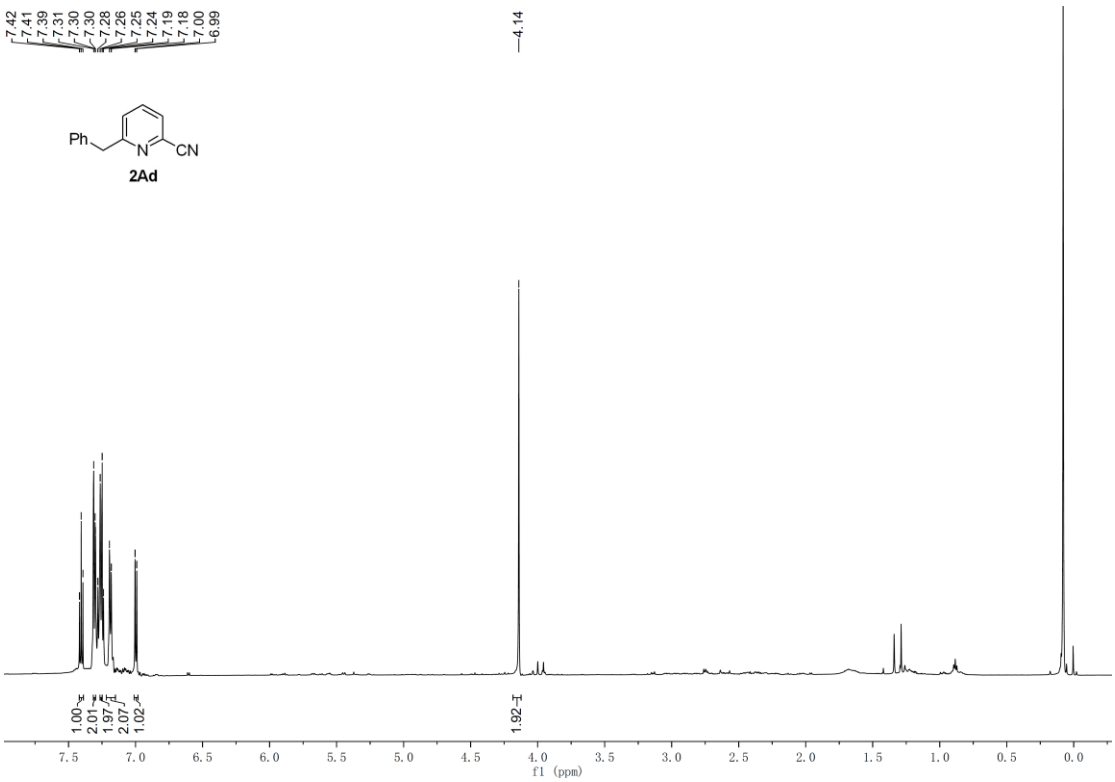
^{13}C NMR (101 MHz) spectrum of **2Ab** in $CDCl_3$



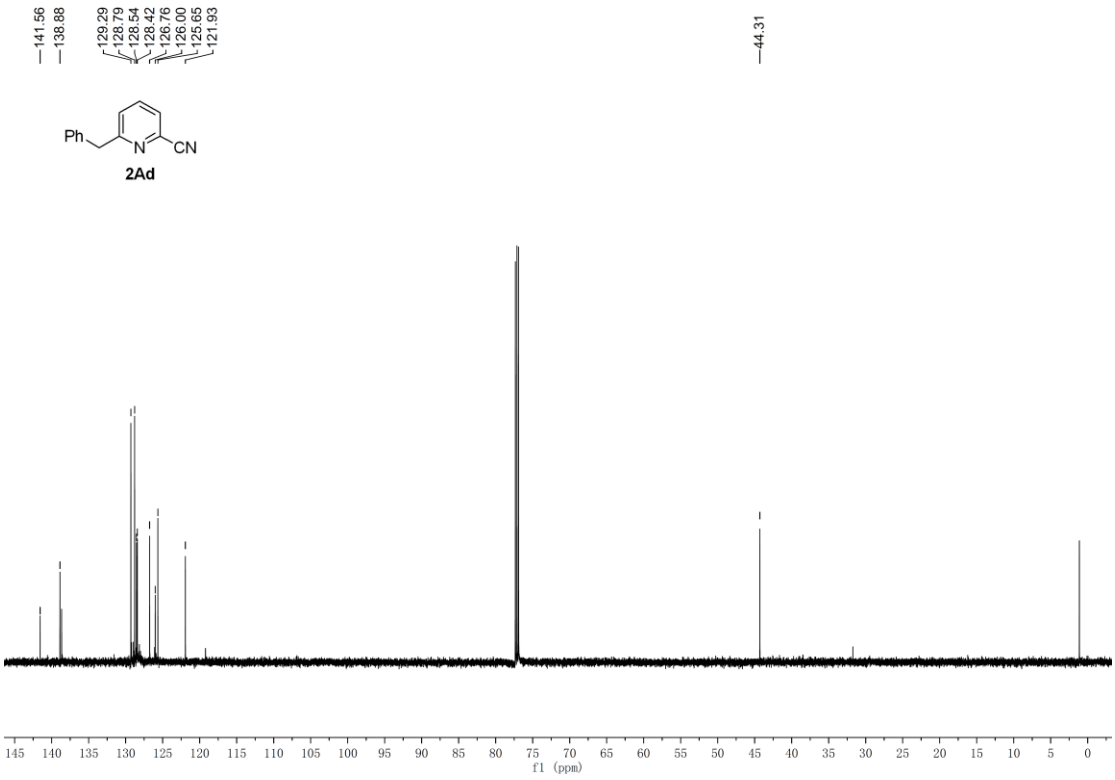
^{1}H NMR (600 MHz) spectrum of **2Ac** in $CDCl_3$



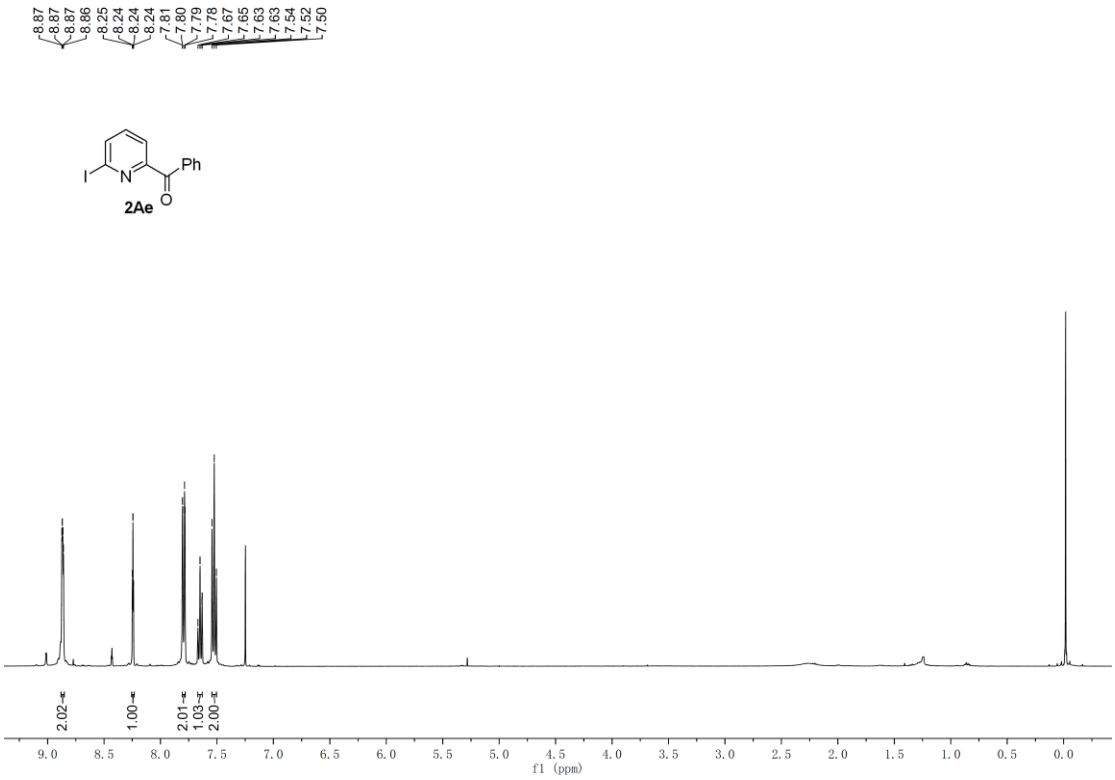
^{13}C NMR (151 MHz) spectrum of **2Ac** in $CDCl_3$



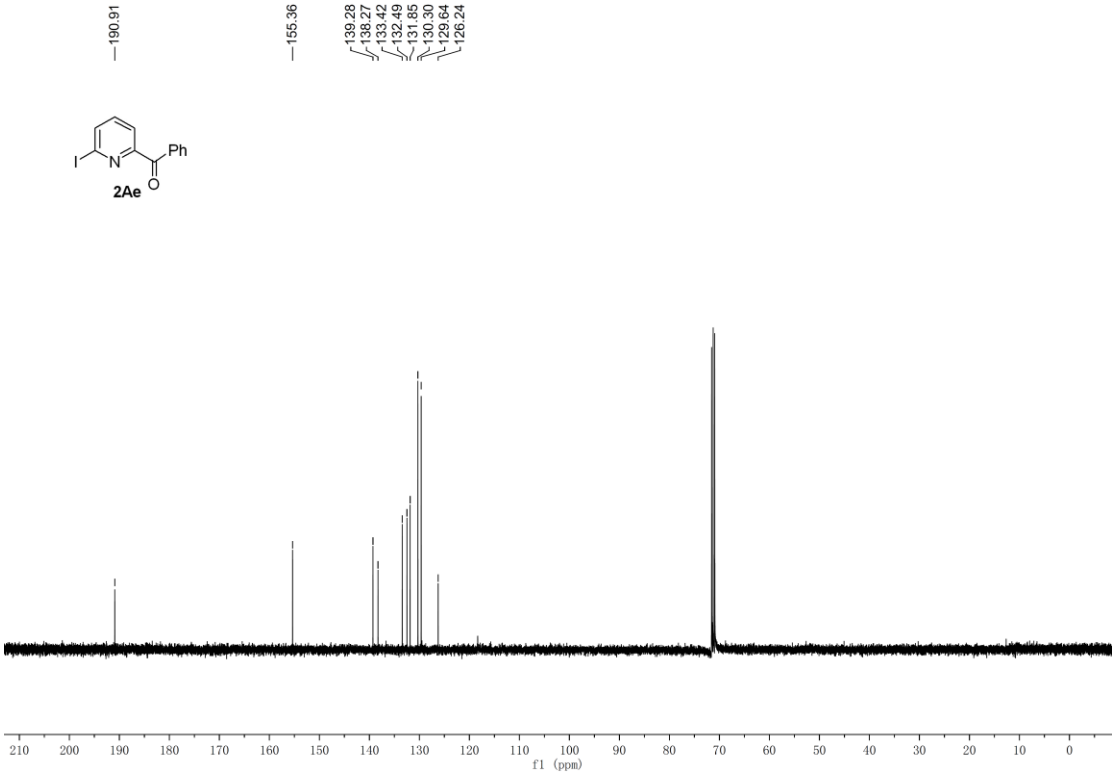
^{1}H NMR (400 MHz) spectrum of **2Ad** in $CDCl_3$



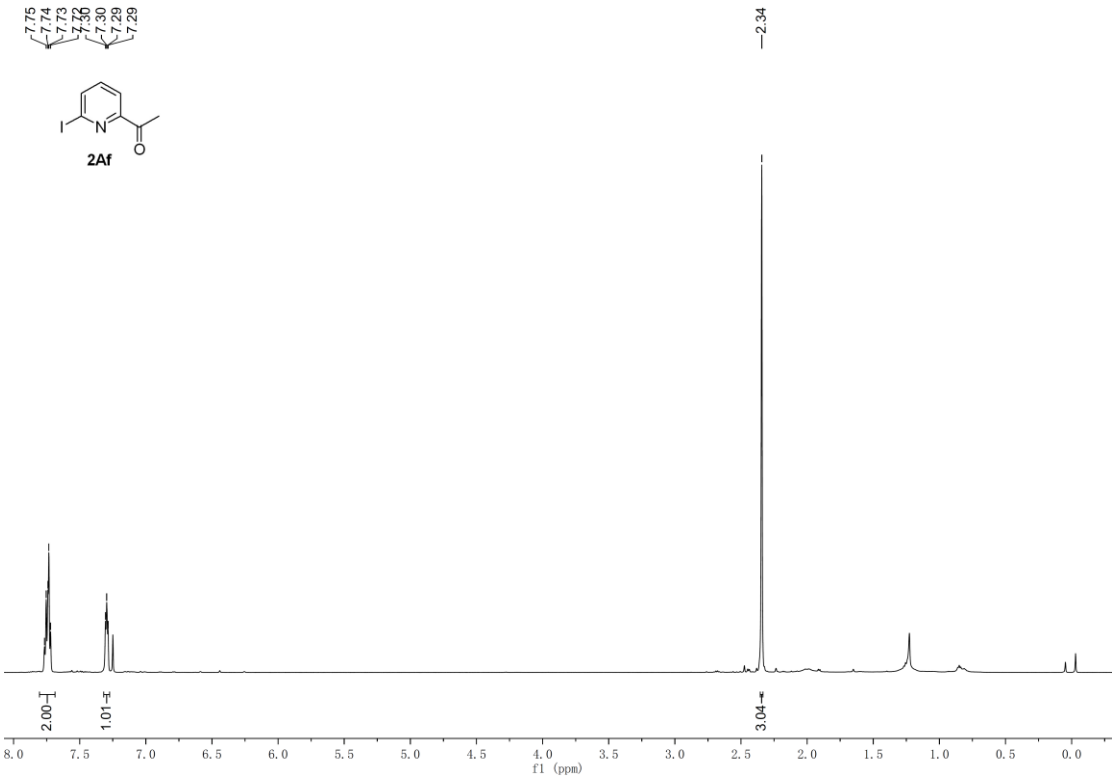
^{13}C NMR (151 MHz) spectrum of **2Ad** in $CDCl_3$



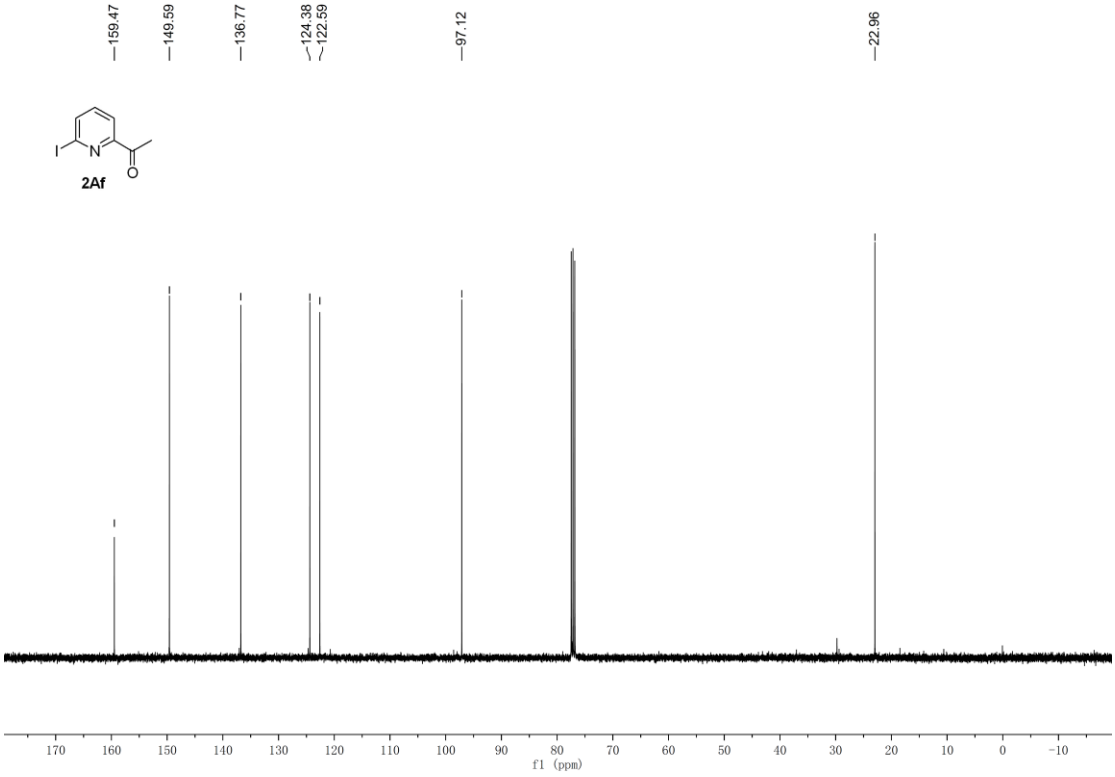
^{1}H NMR (400 MHz) spectrum of **2Ae** in $CDCl_3$



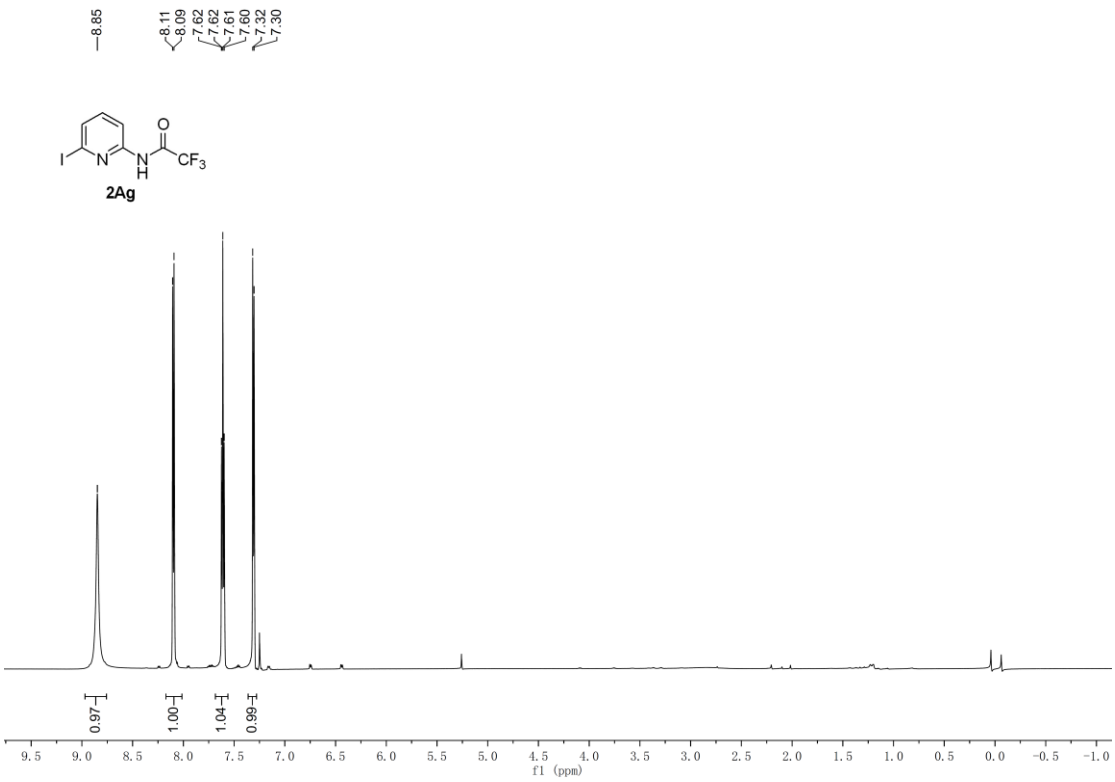
^{13}C NMR (101 MHz) spectrum of **2Ae** in $CDCl_3$



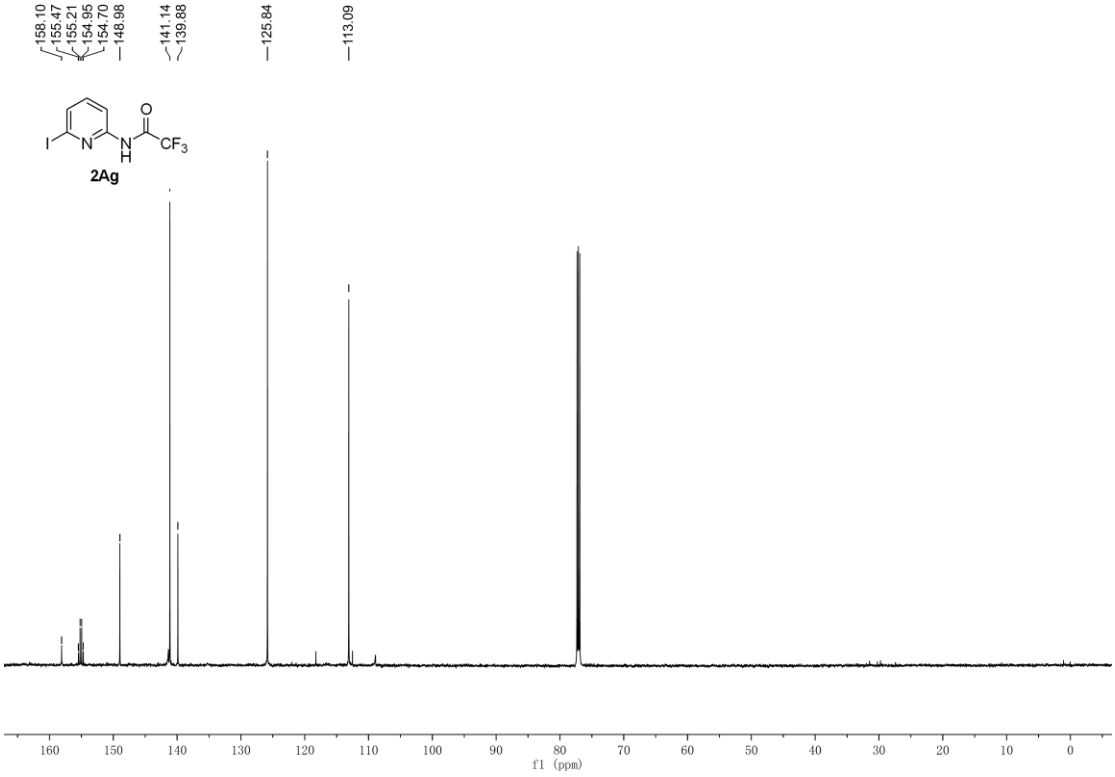
^{1}H NMR (600 MHz) spectrum of **2Af** in $CDCl_3$



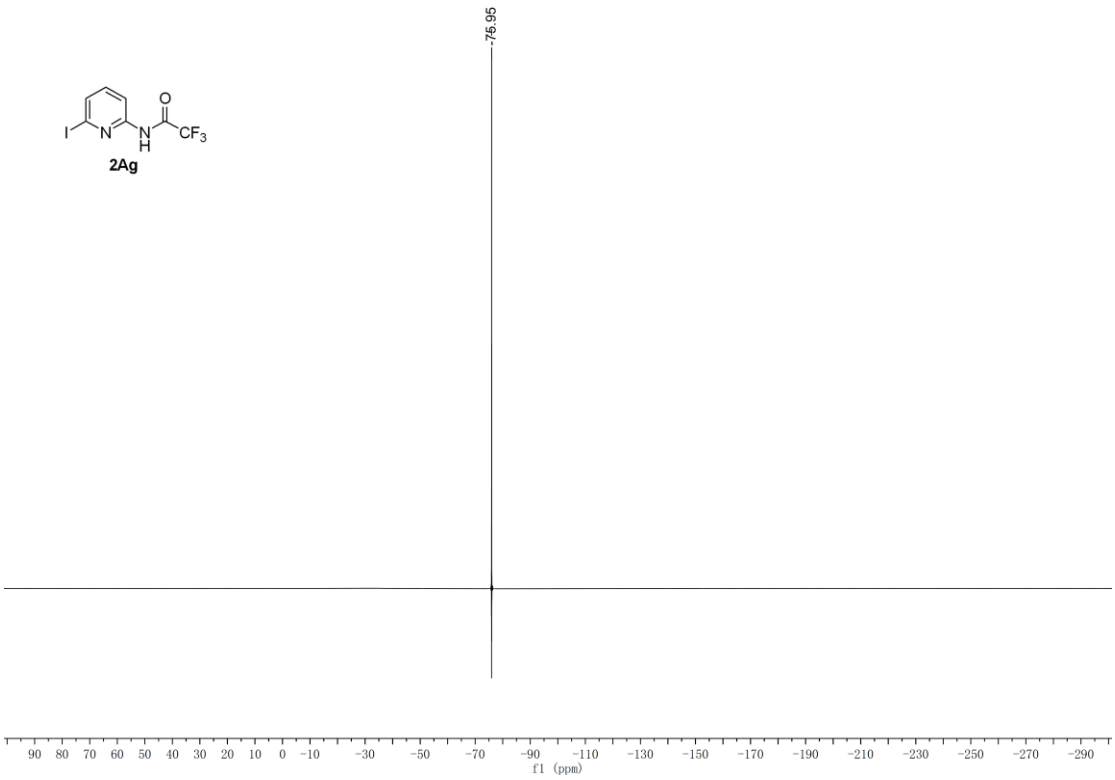
^{13}C NMR (101 MHz) spectrum of **2Af** in $CDCl_3$



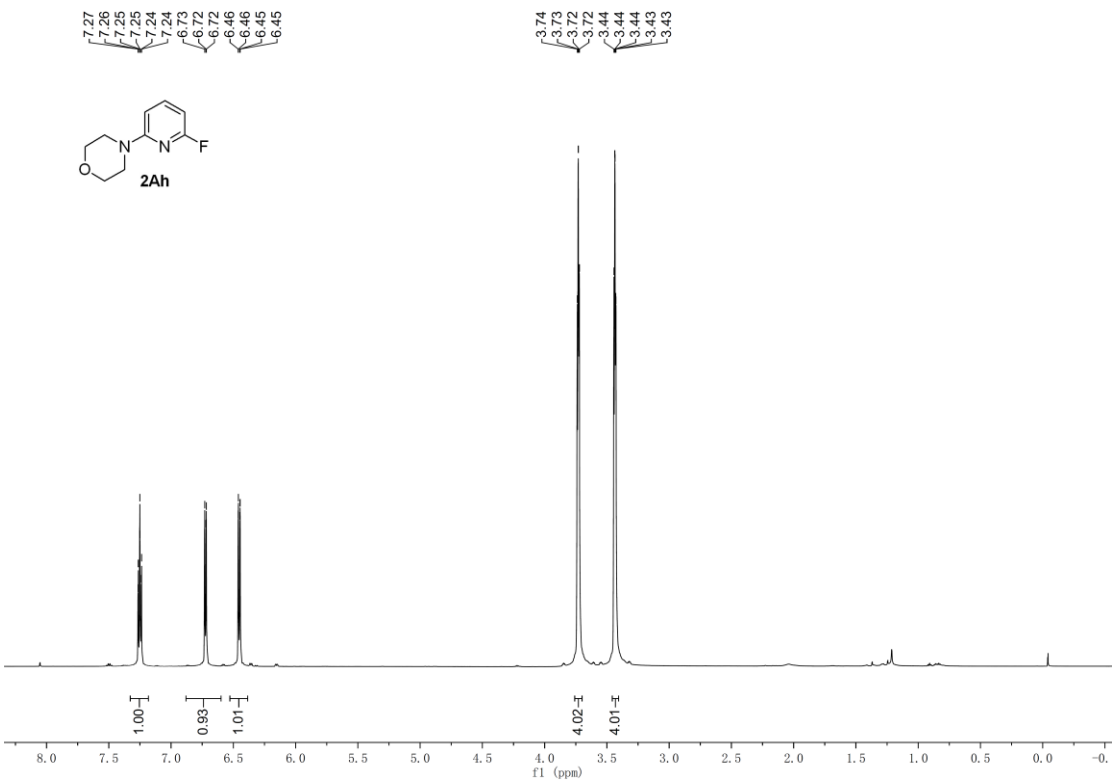
^{1}H NMR (600 MHz) spectrum of **2Ag** in $CDCl_3$



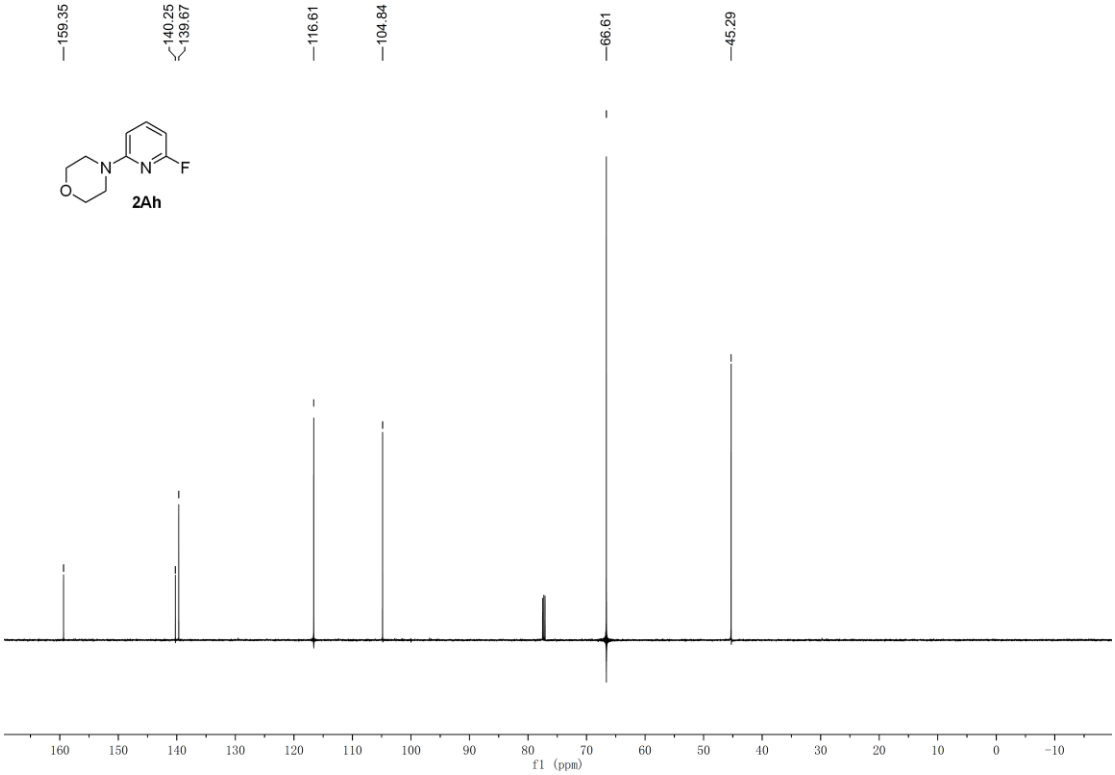
^{13}C NMR (101 MHz) spectrum of **2Ag** in $CDCl_3$



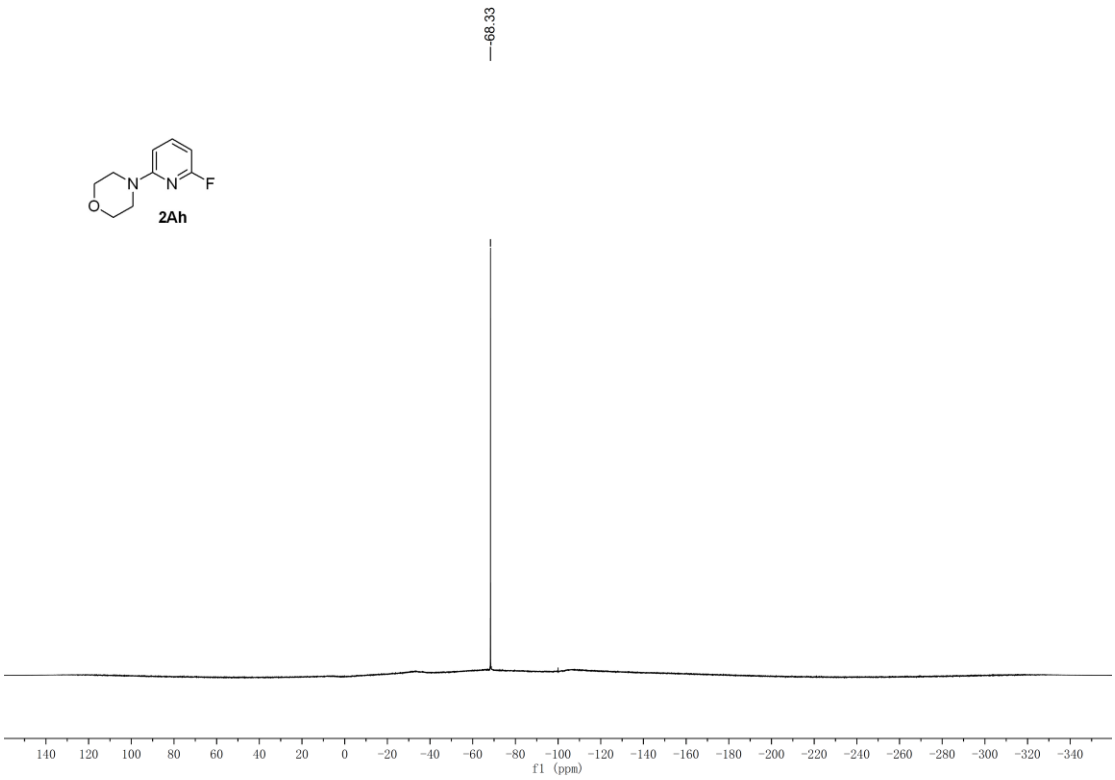
^{13}F NMR (376 MHz) spectrum of **2Ag** in $CDCl_3$



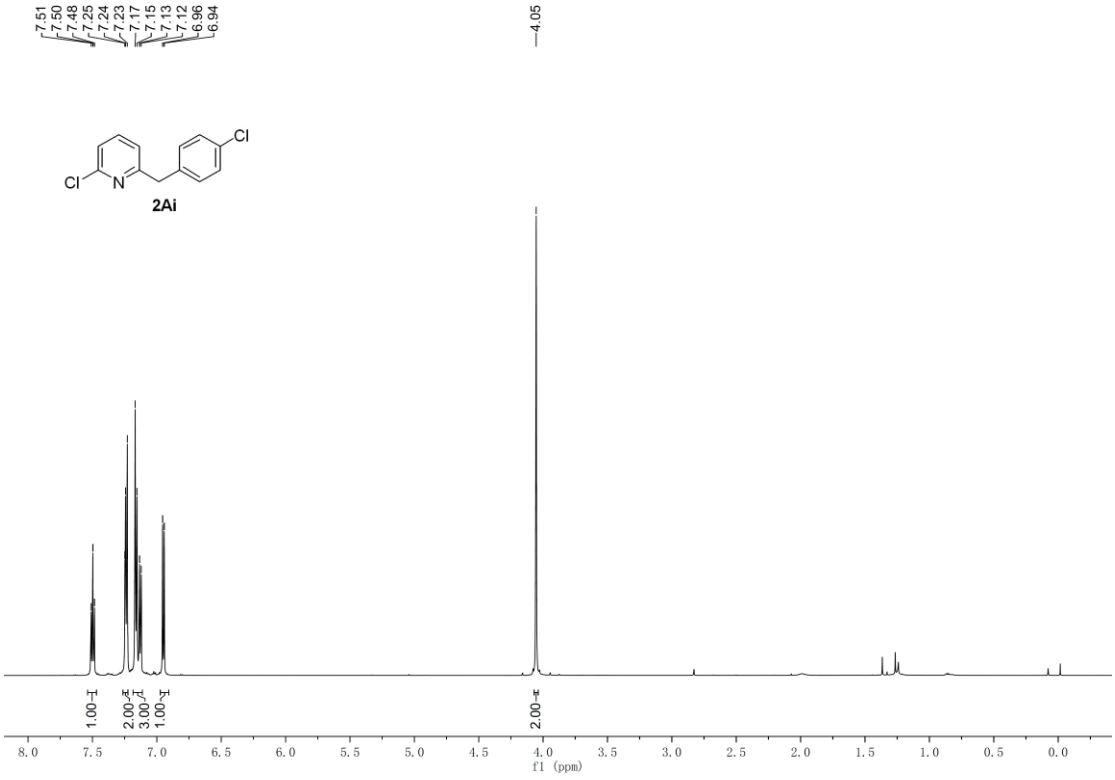
^{1}H NMR (600 MHz) spectrum of **2Ah** in $CDCl_3$



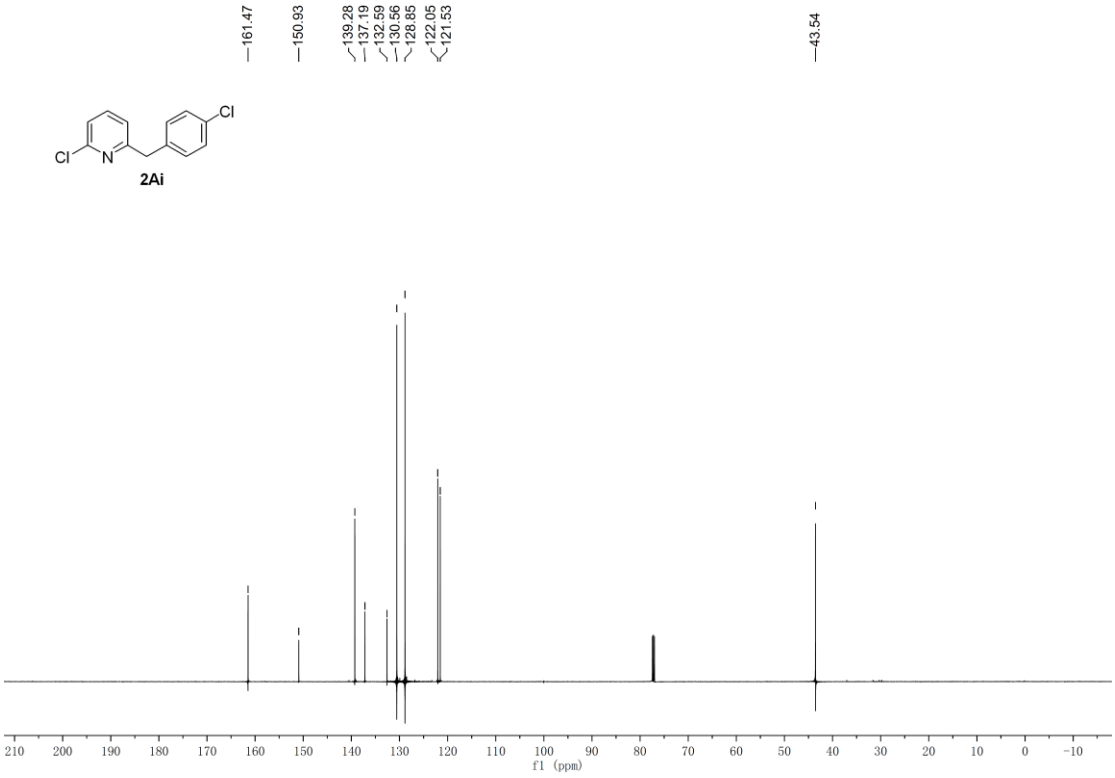
^{13}C NMR (151 MHz) spectrum of **2Ah** in $CDCl_3$



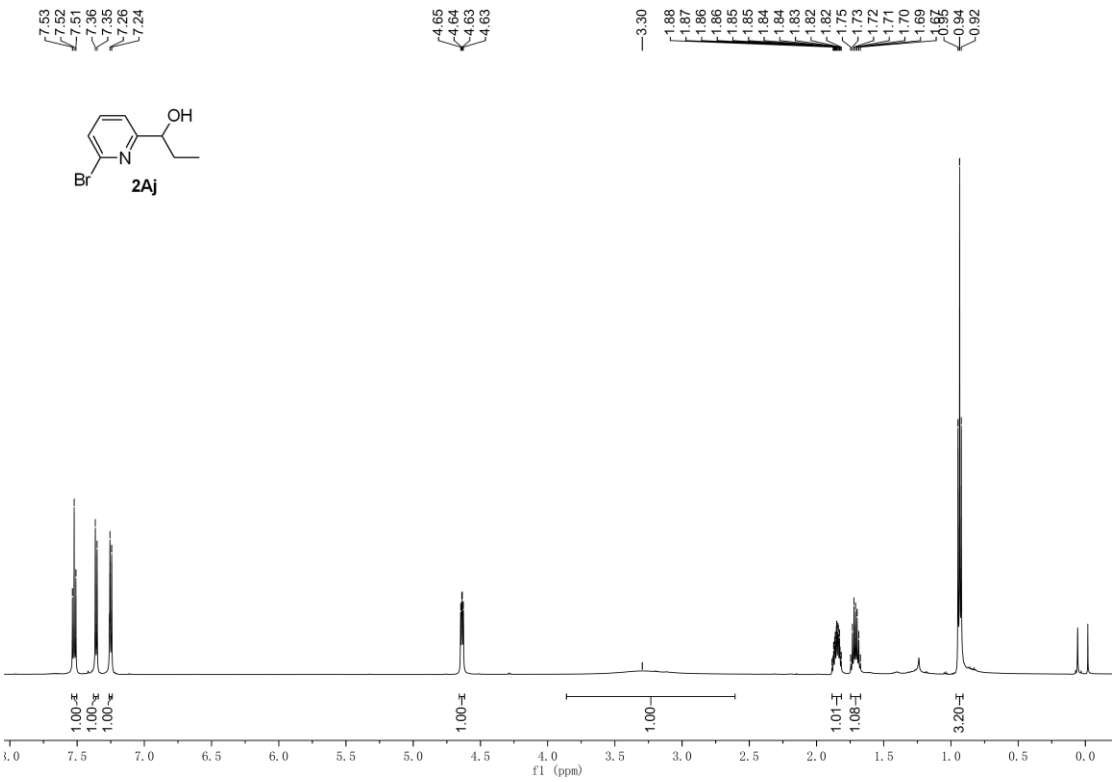
^{19}F NMR (376 MHz) spectrum of **2Ah** in $CDCl_3$



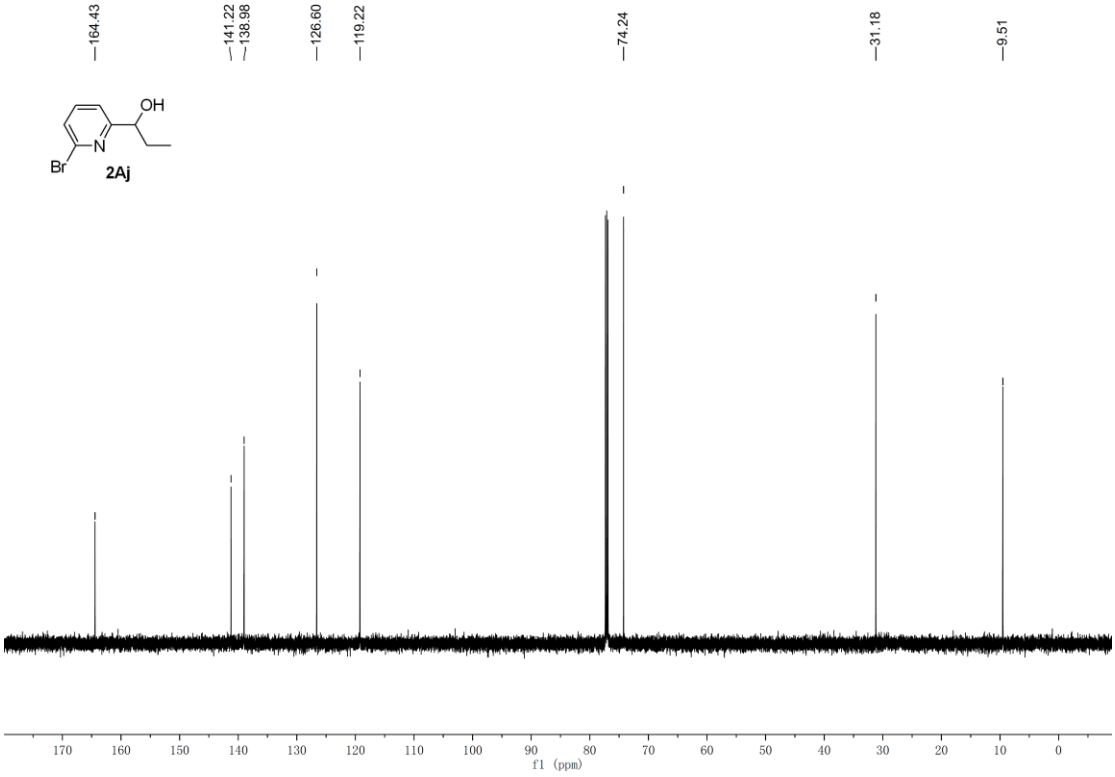
^{1}H NMR (600 MHz) spectrum of **2Ai** in $CDCl_3$



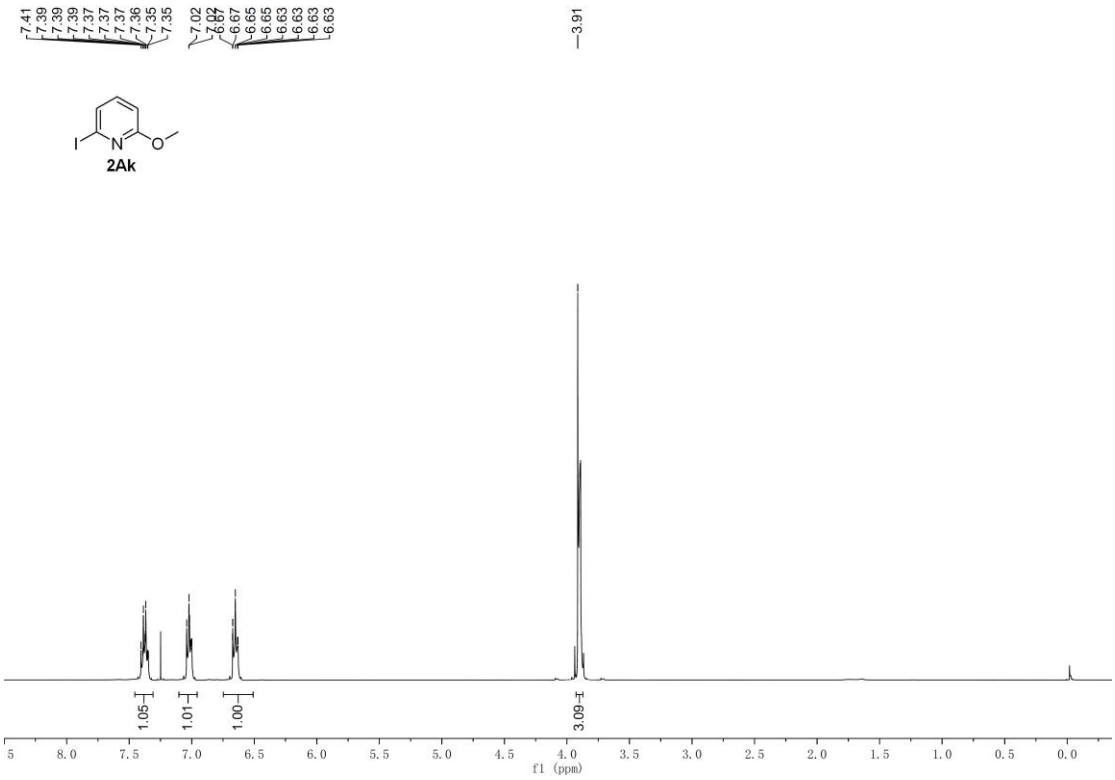
^{13}C NMR (151 MHz) spectrum of **2Ai** in $CDCl_3$



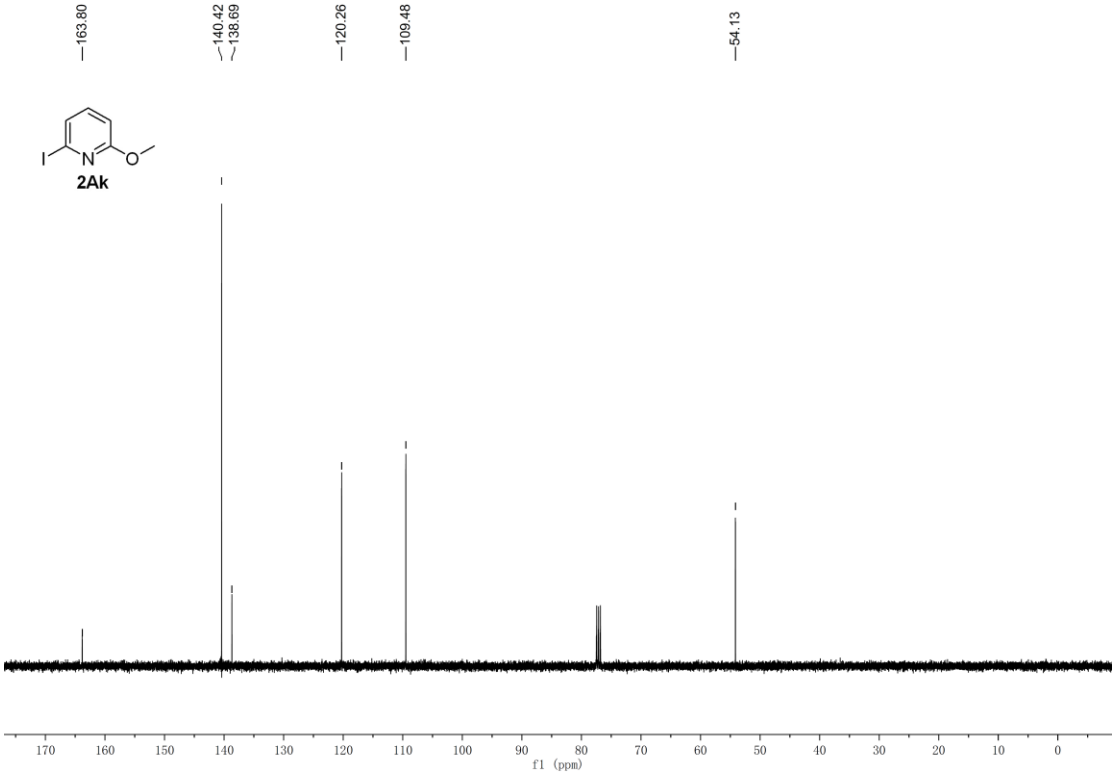
^{1}H NMR (600 MHz) spectrum of **2Aj** in $CDCl_3$



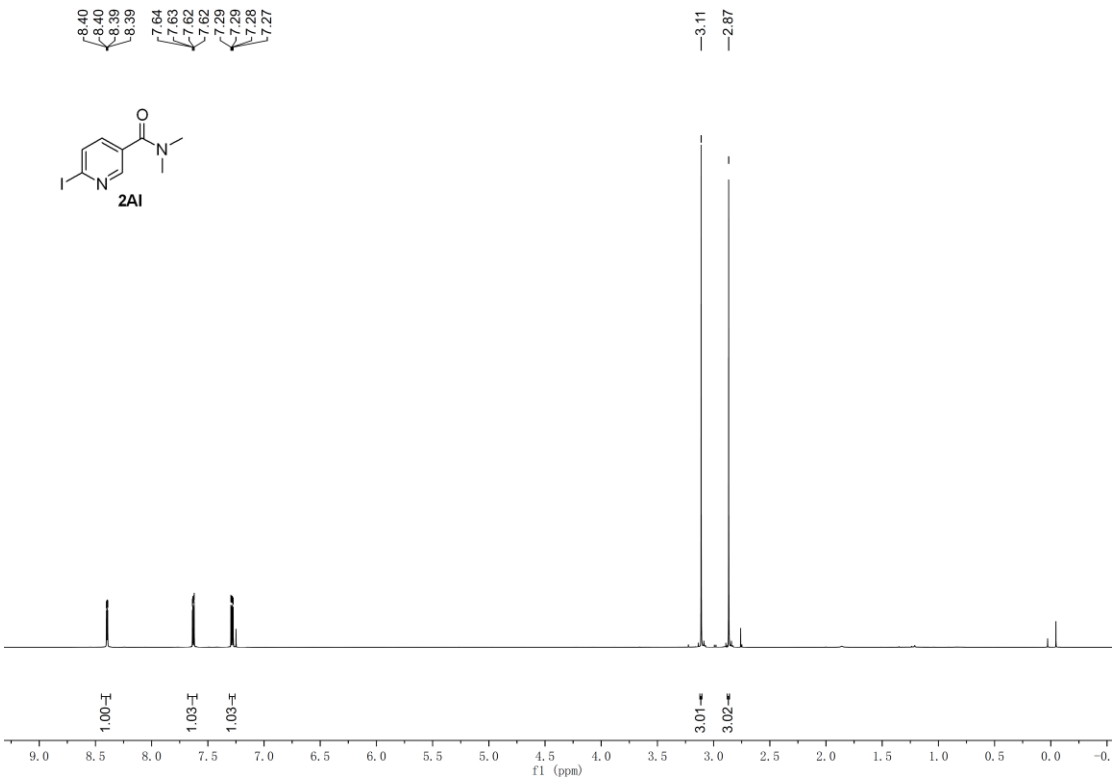
^{13}C NMR (151 MHz) spectrum of **2Aj** in $CDCl_3$



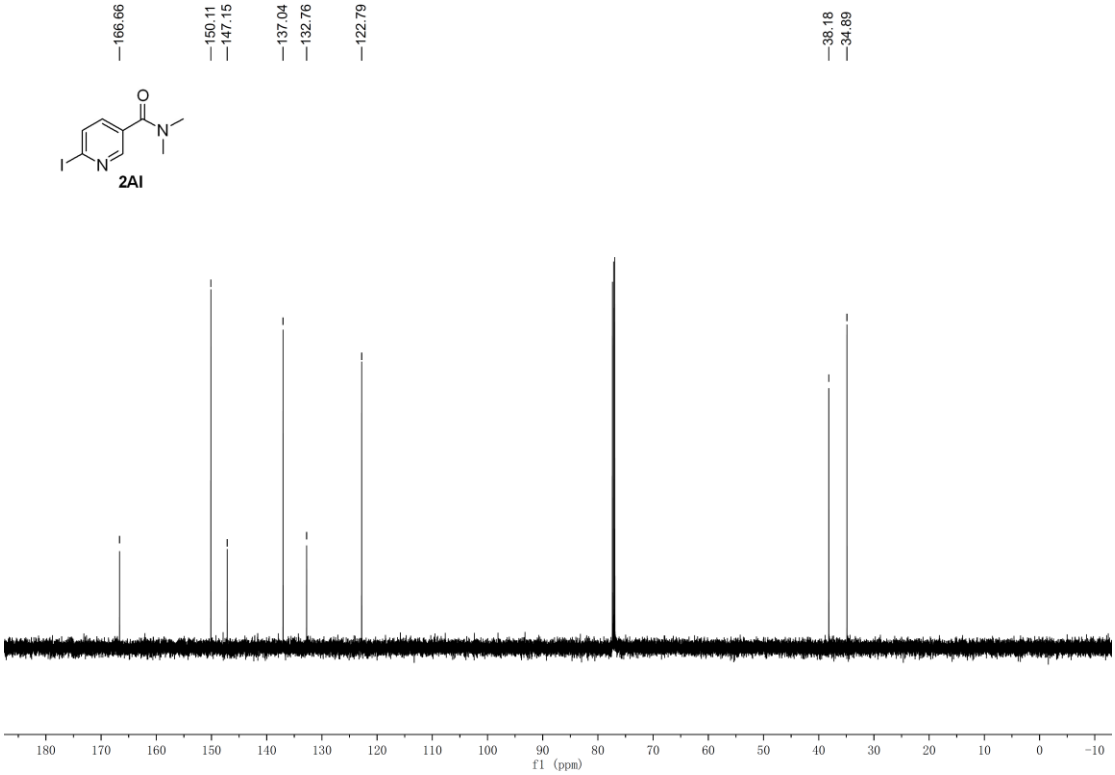
^{1}H NMR (400 MHz) spectrum of **2Ak** in $CDCl_3$



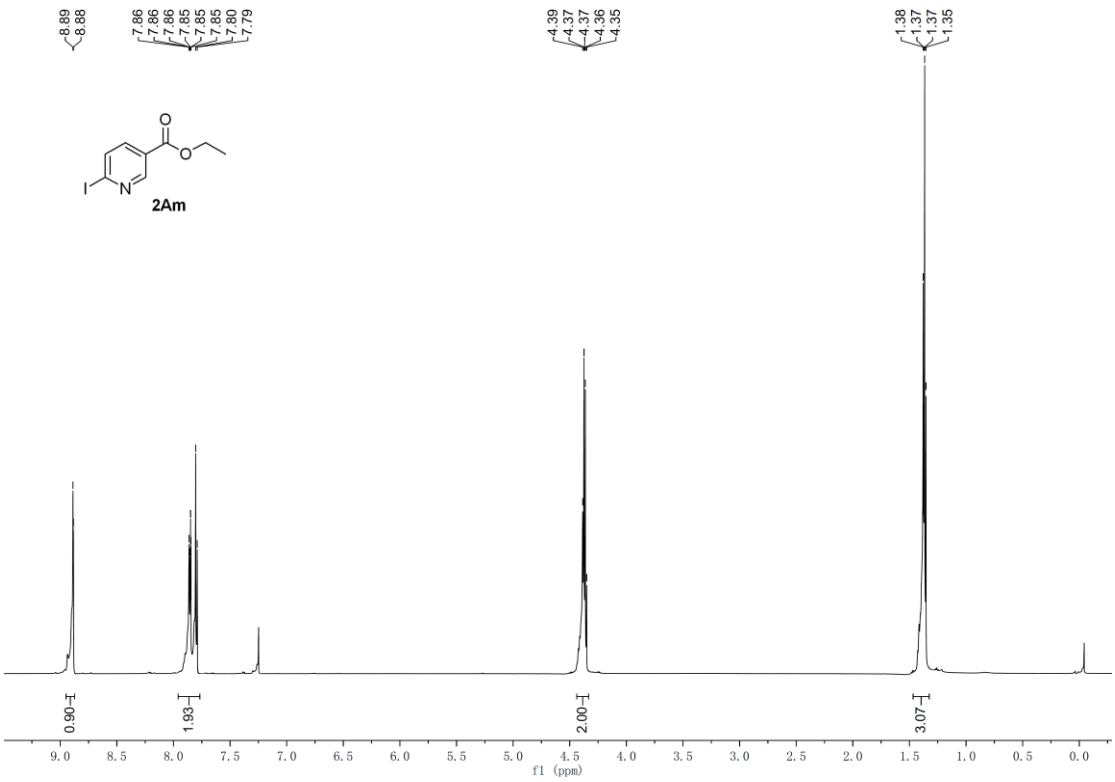
^{13}C NMR (101 MHz) spectrum of **2Ak** in $CDCl_3$



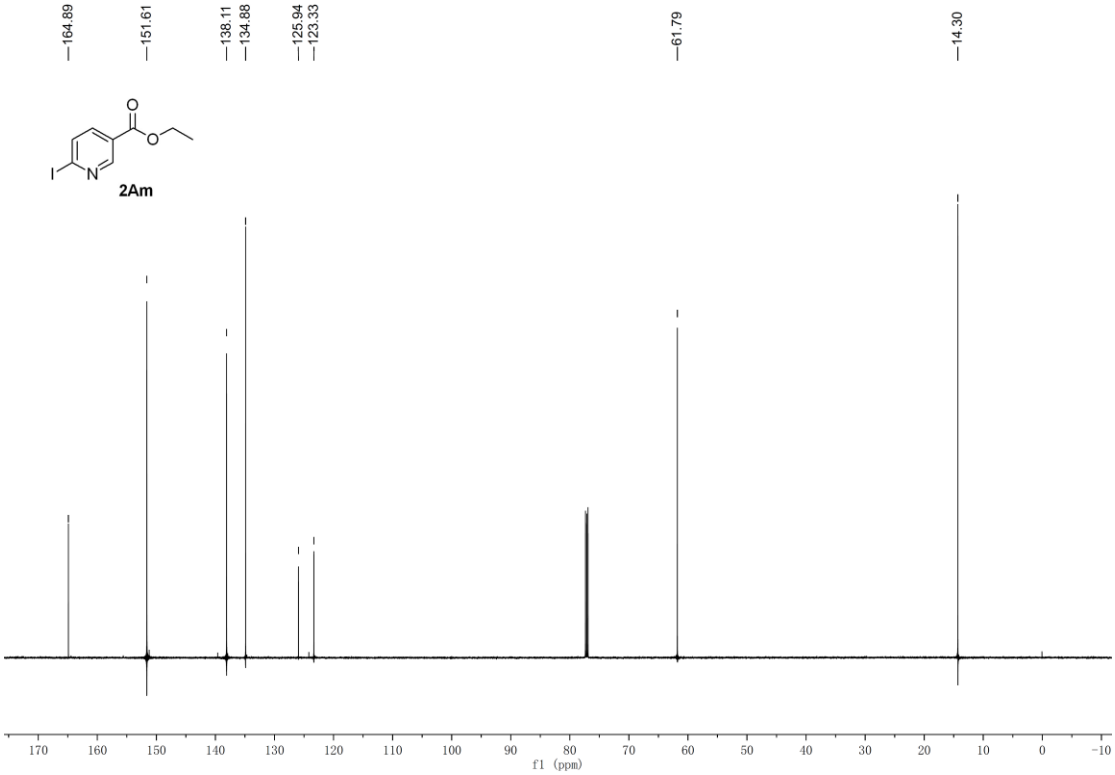
^{1}H NMR (600 MHz) spectrum of **2AI** in $CDCl_3$



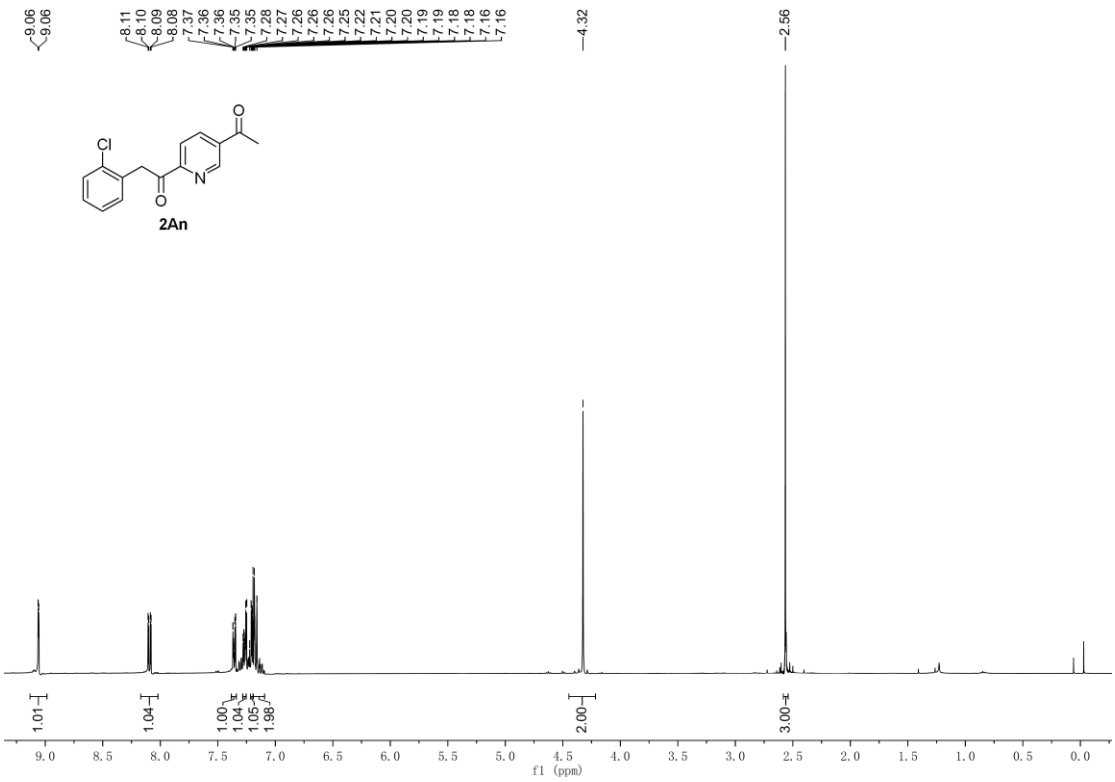
^{13}C NMR (151 MHz) spectrum of **2AI** in $CDCl_3$



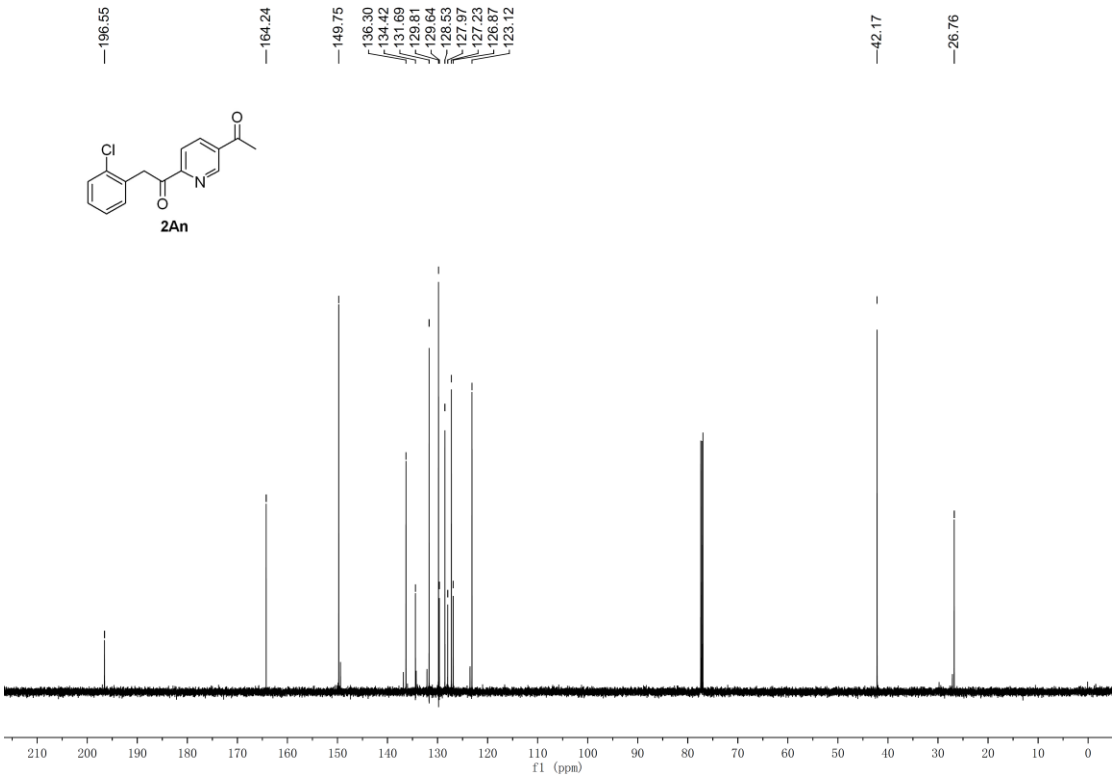
^{1}H NMR (600 MHz) spectrum of **2Am** in $CDCl_3$



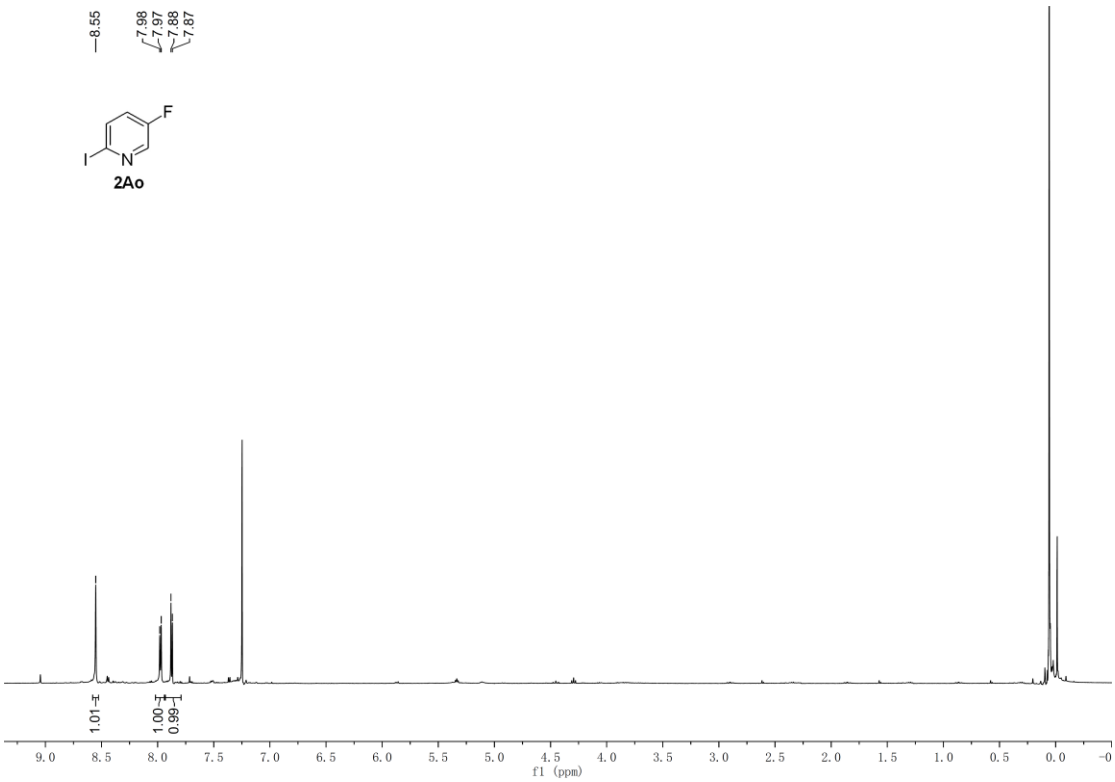
^{13}C NMR (151 MHz) spectrum of **2Am** in $CDCl_3$



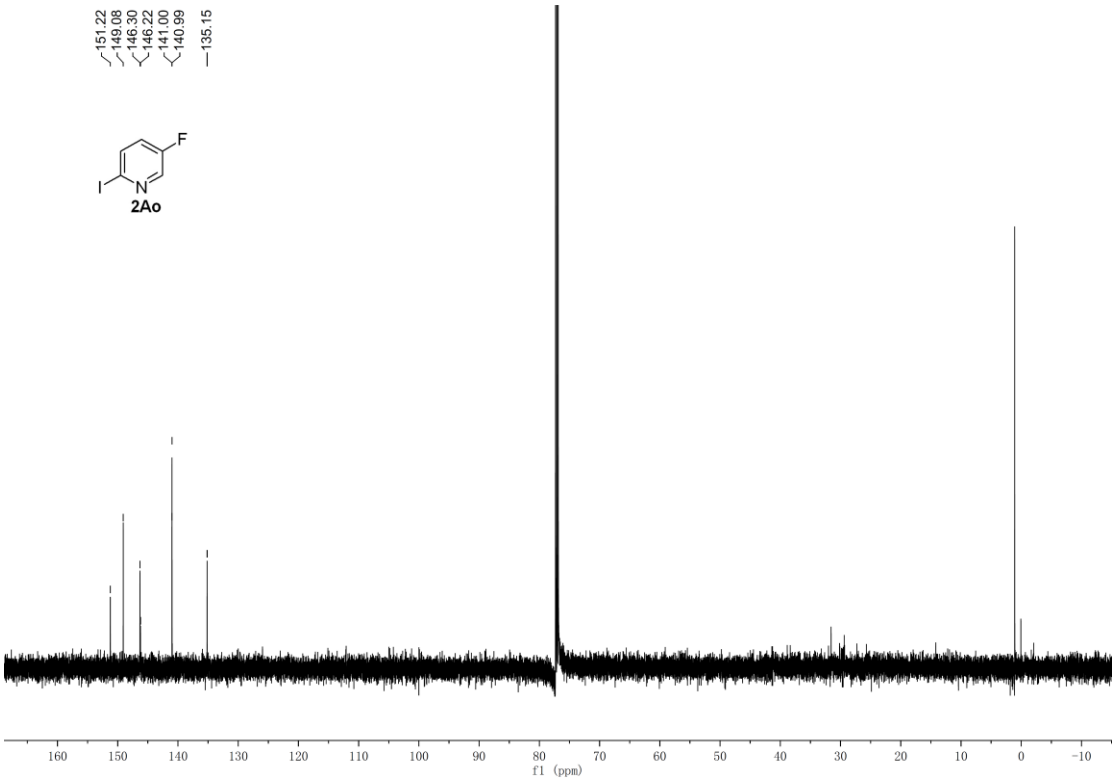
^{1}H NMR (400 MHz) spectrum of **2An** in $CDCl_3$



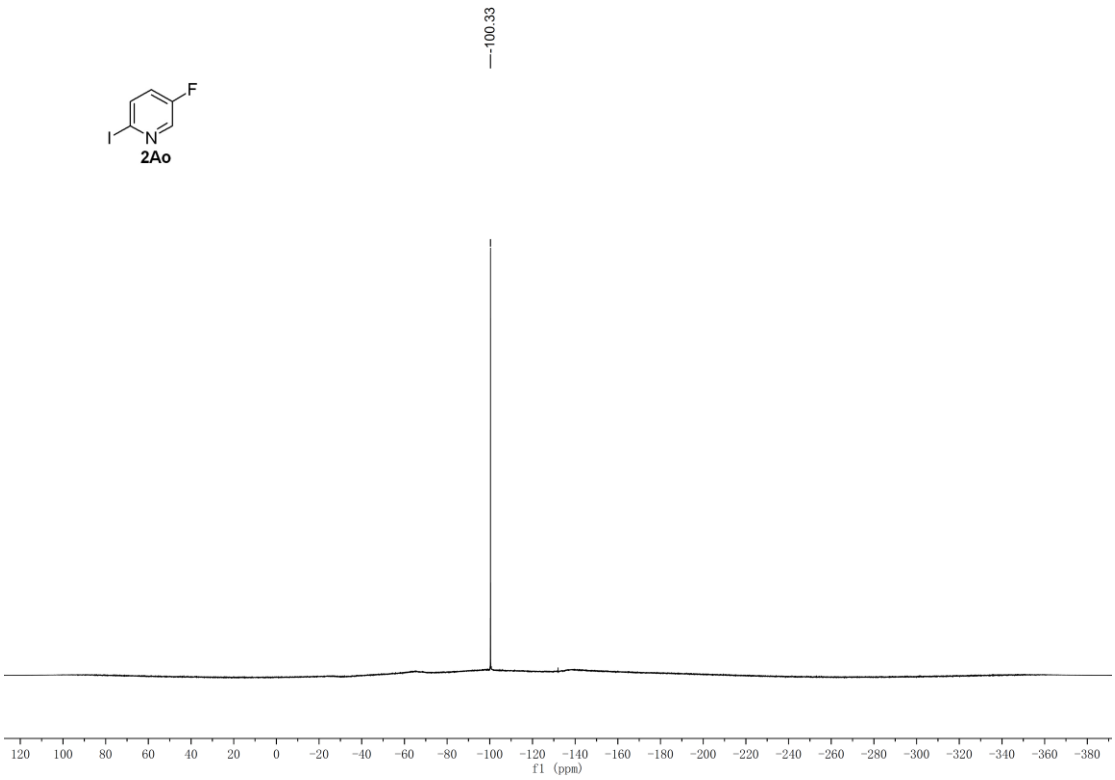
^{13}C NMR (151 MHz) spectrum of **2An** in $CDCl_3$



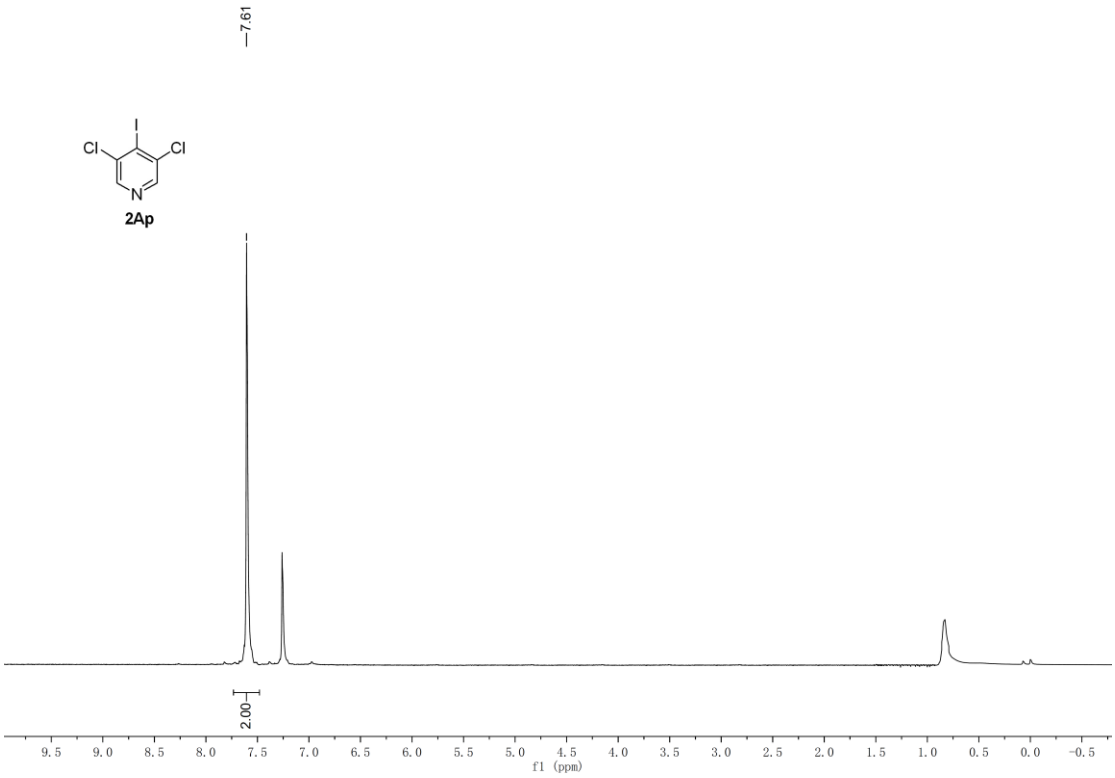
^{1}H NMR (400 MHz) spectrum of **2Ao** in $CDCl_3$



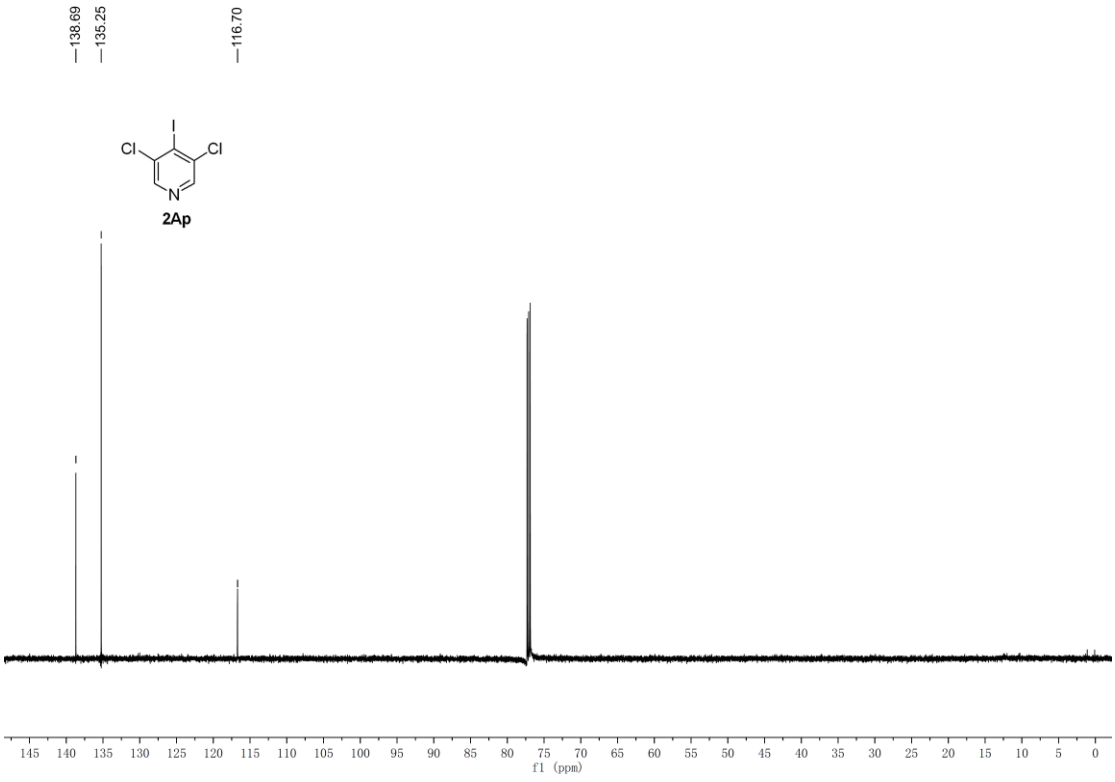
^{13}C NMR (101 MHz) spectrum of **2Ao** in $CDCl_3$



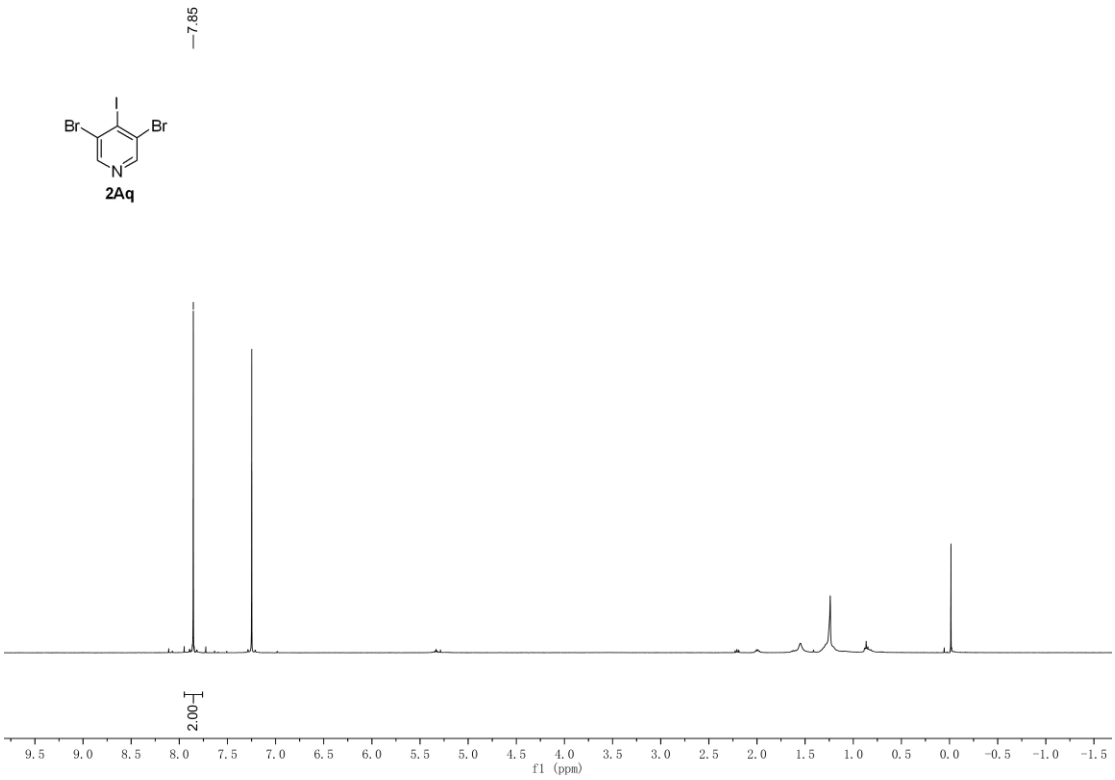
^{19}F NMR (376 MHz) spectrum of **2Ao** in $CDCl_3$



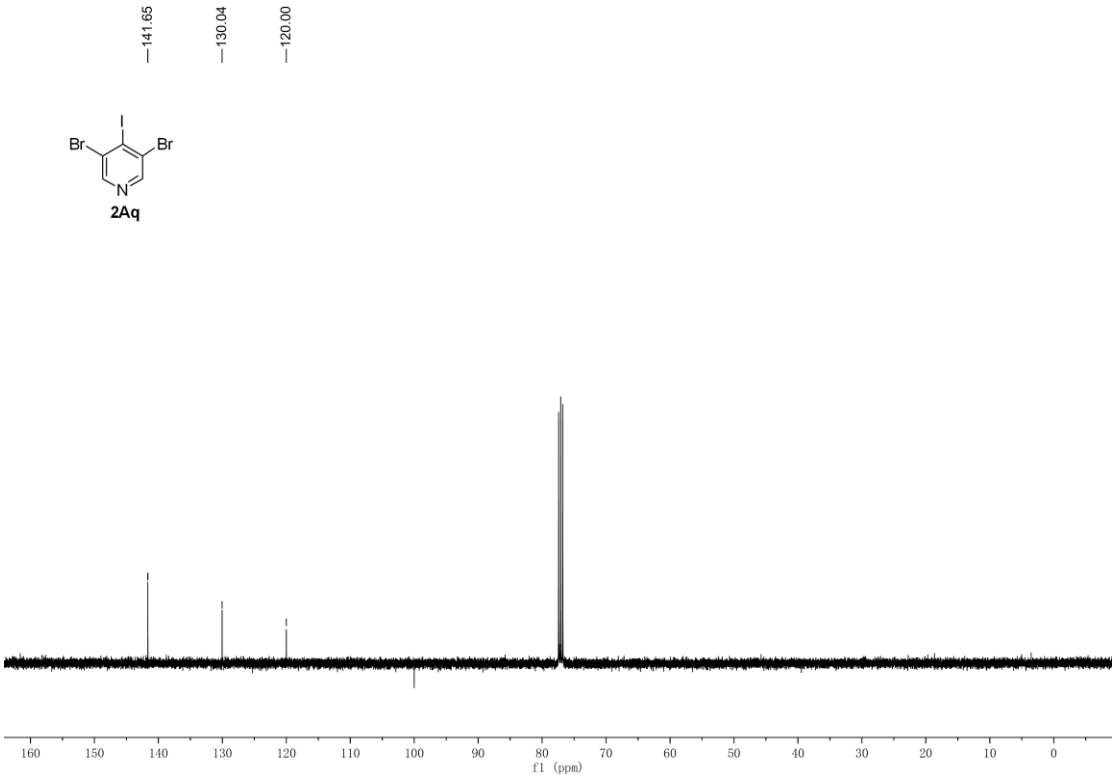
^{1}H NMR (400 MHz) spectrum of **2Ap** in $CDCl_3$



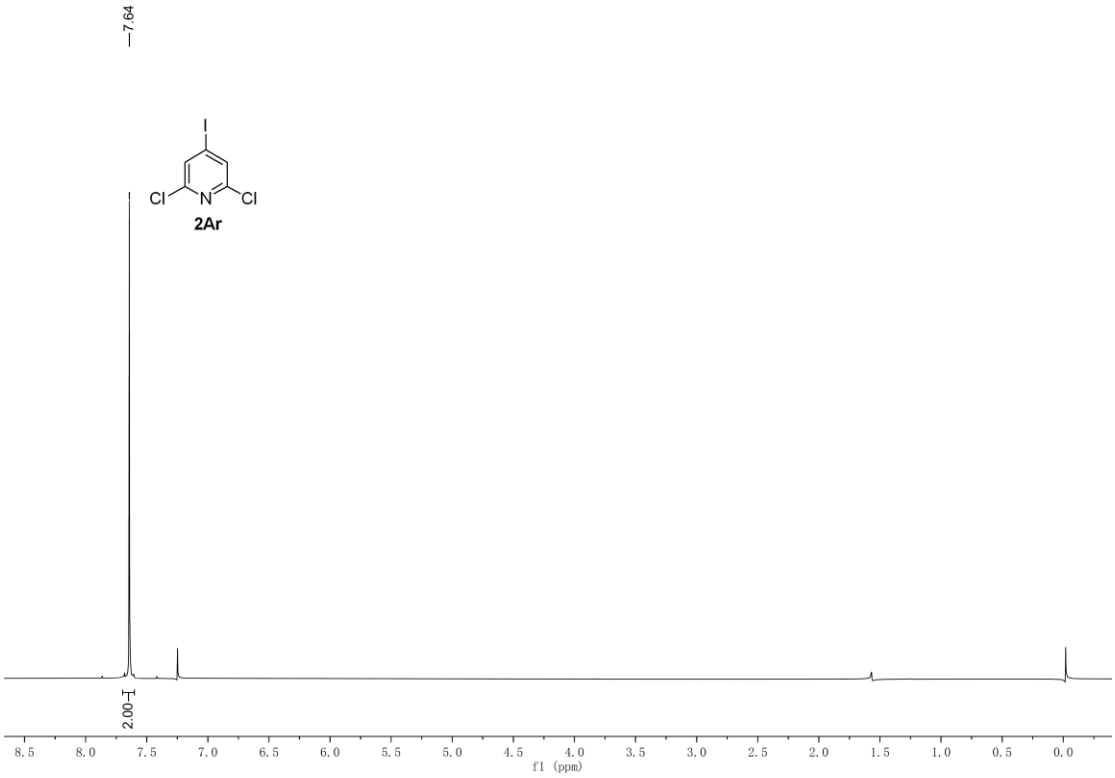
^{13}C NMR (101 MHz) spectrum of **2Ap** in $CDCl_3$



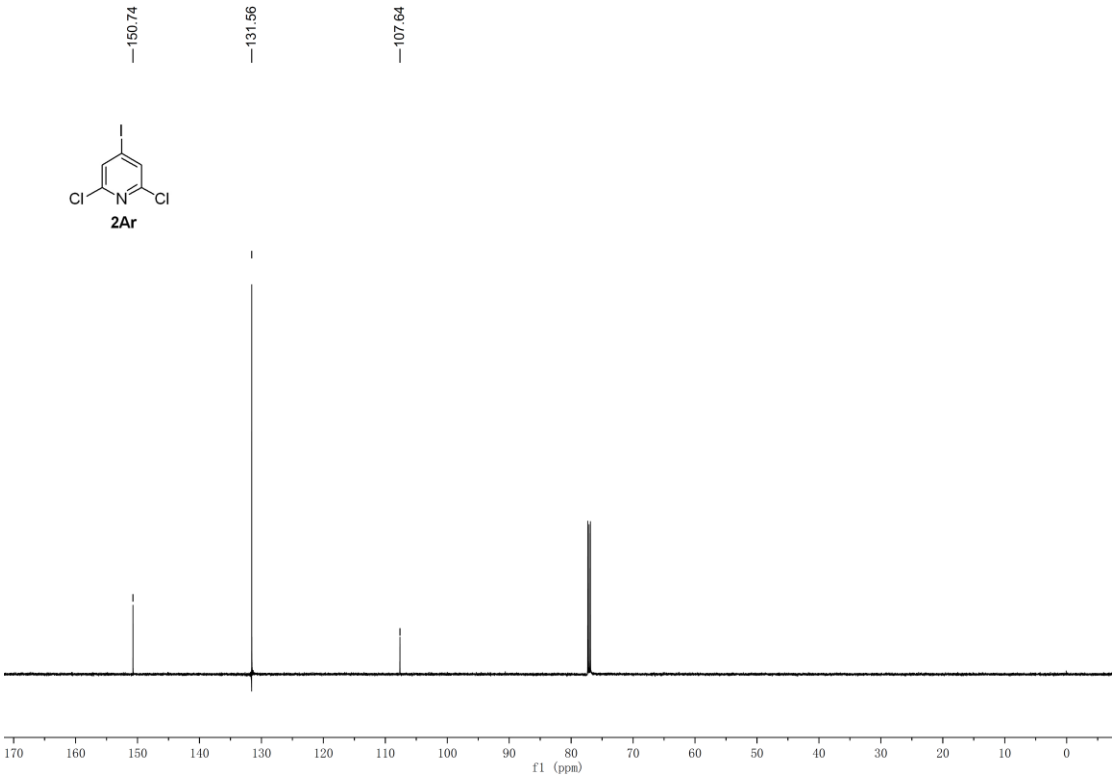
^{1}H NMR (400 MHz) spectrum of **2Aq** in $CDCl_3$



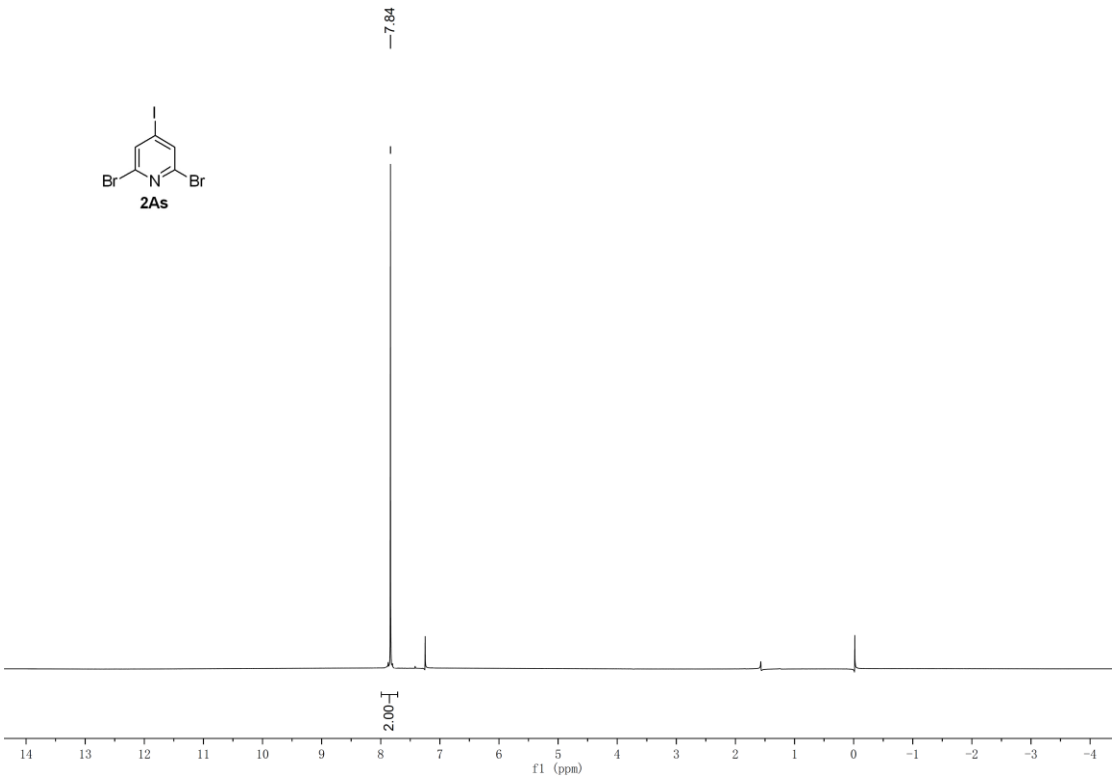
^{13}C NMR (101 MHz) spectrum of **2Aq** in $CDCl_3$



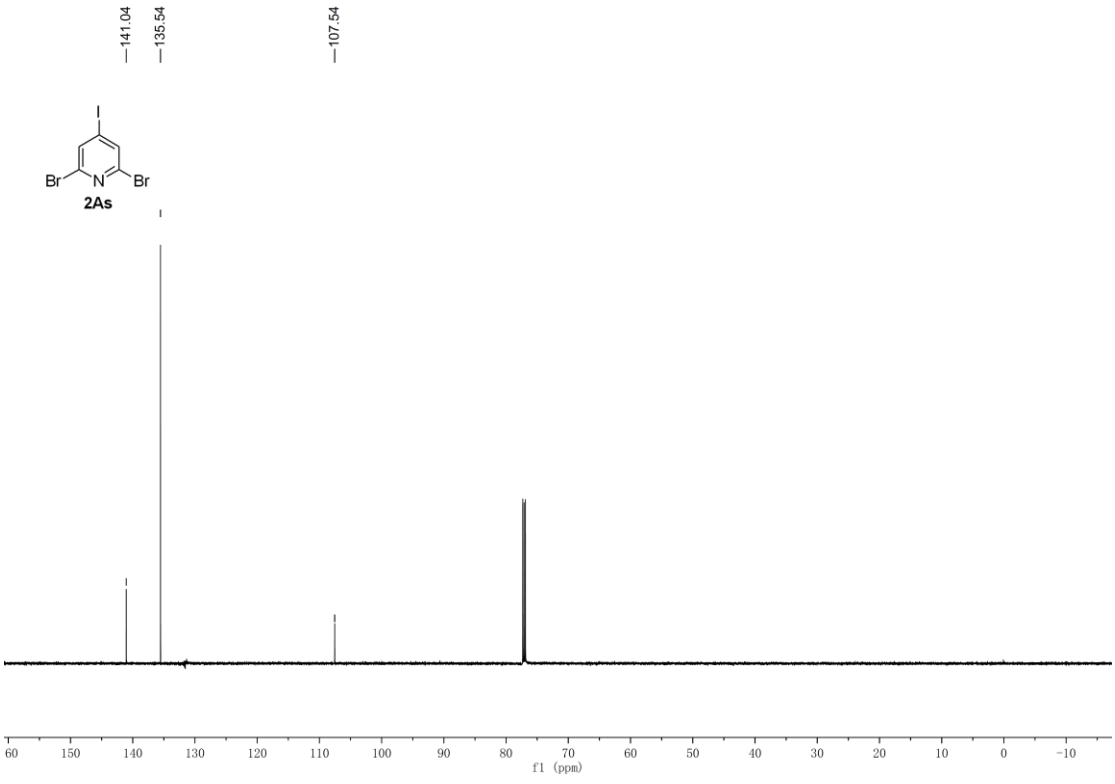
^{1}H NMR (400 MHz) spectrum of **2Ar** in $CDCl_3$



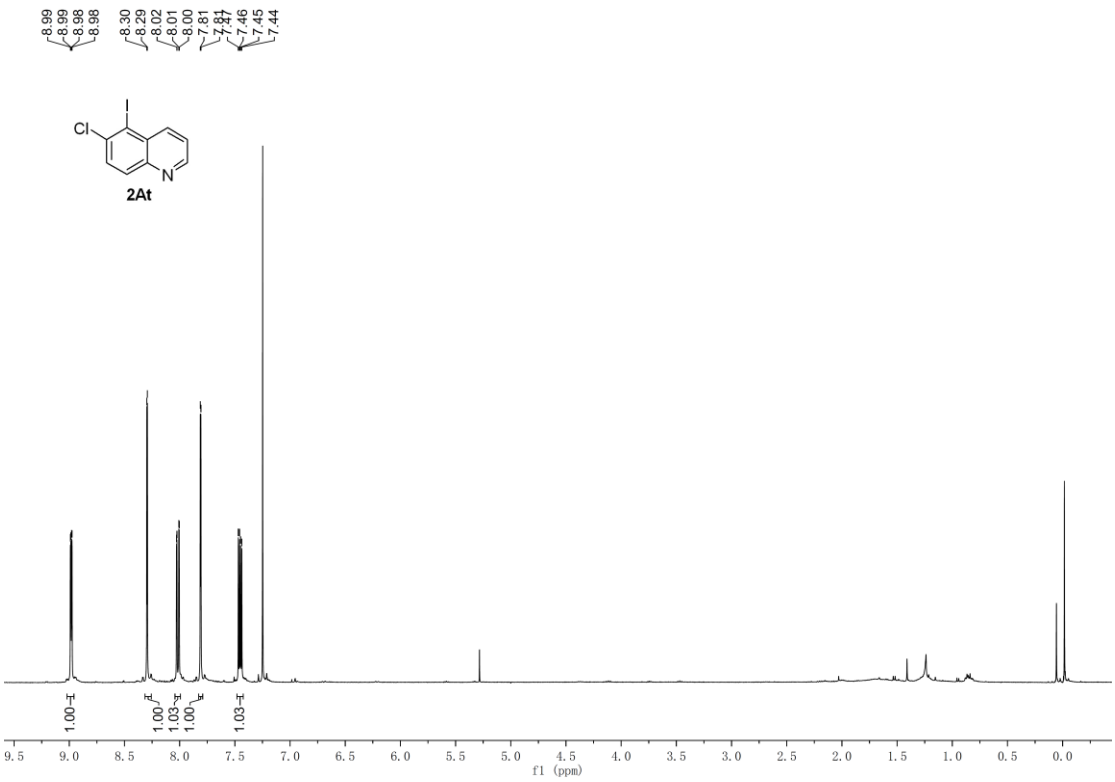
^{13}C NMR (151 MHz) spectrum of **2Ar** in $CDCl_3$



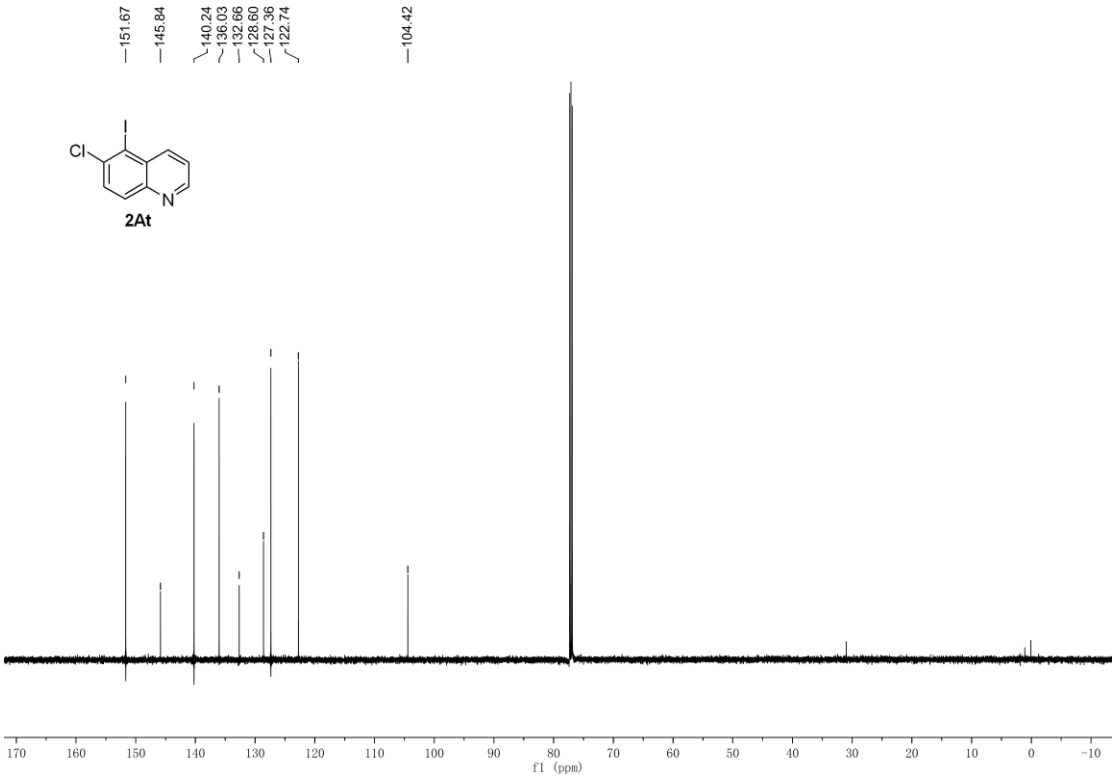
^{1}H NMR (600 MHz) spectrum of **2As** in $CDCl_3$



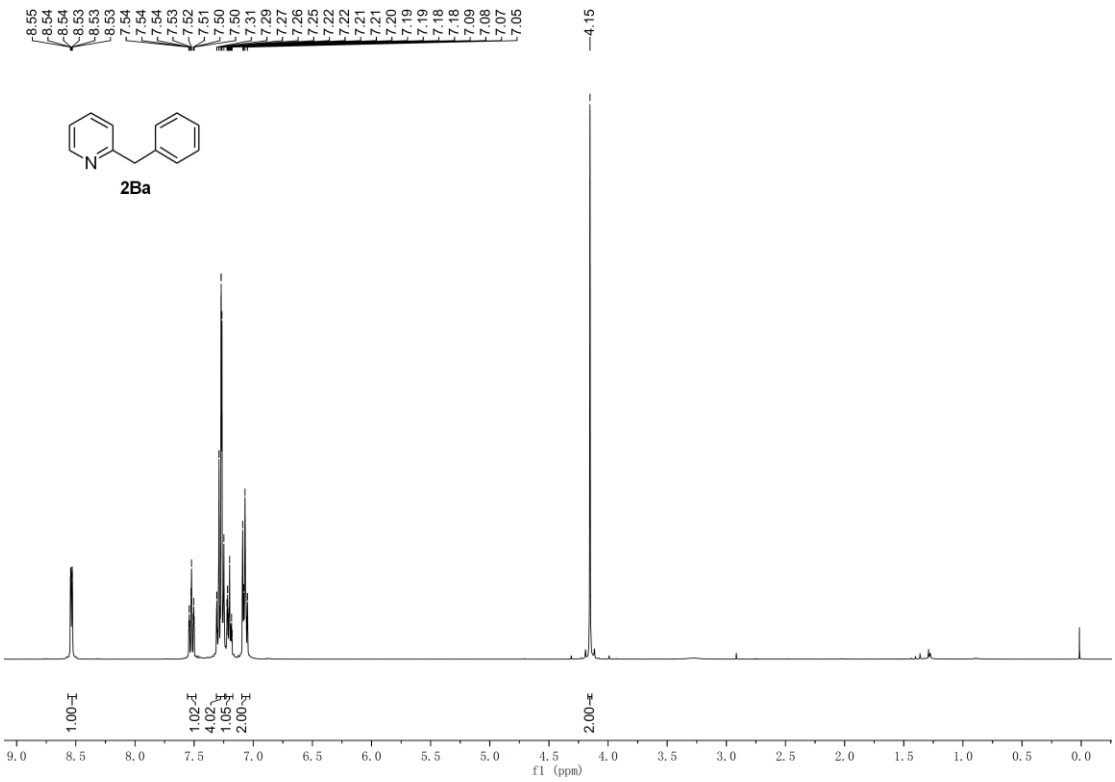
^{13}C NMR (101 MHz) spectrum of **2As** in $CDCl_3$



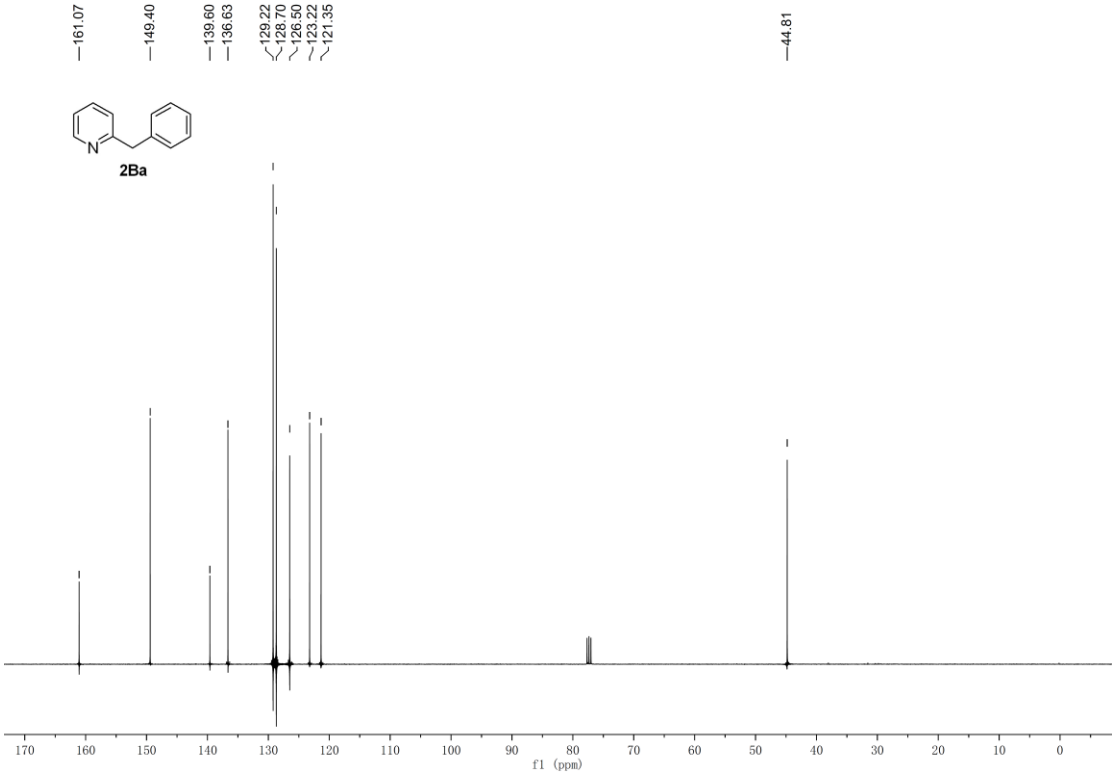
^{1}H NMR (400 MHz) spectrum of **2At** in $CDCl_3$



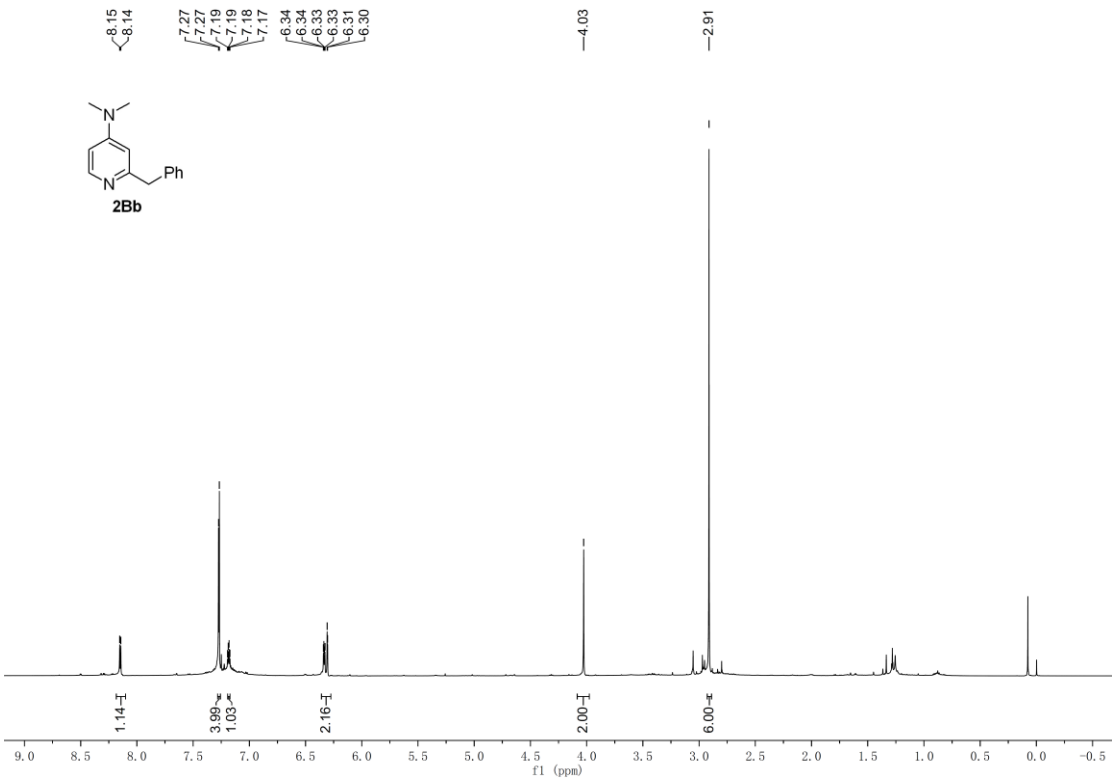
^{13}C NMR (101 MHz) spectrum of **2At** in $CDCl_3$



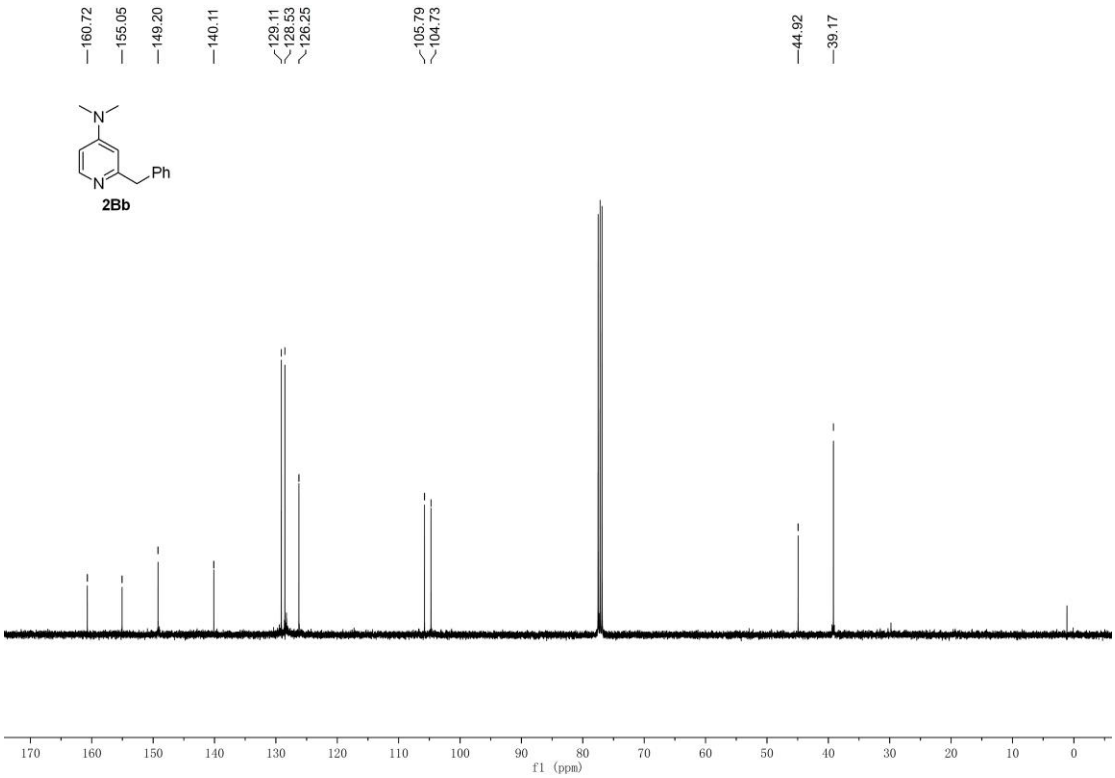
^{1}H NMR (600 MHz) spectrum of **2Ba** in $CDCl_3$



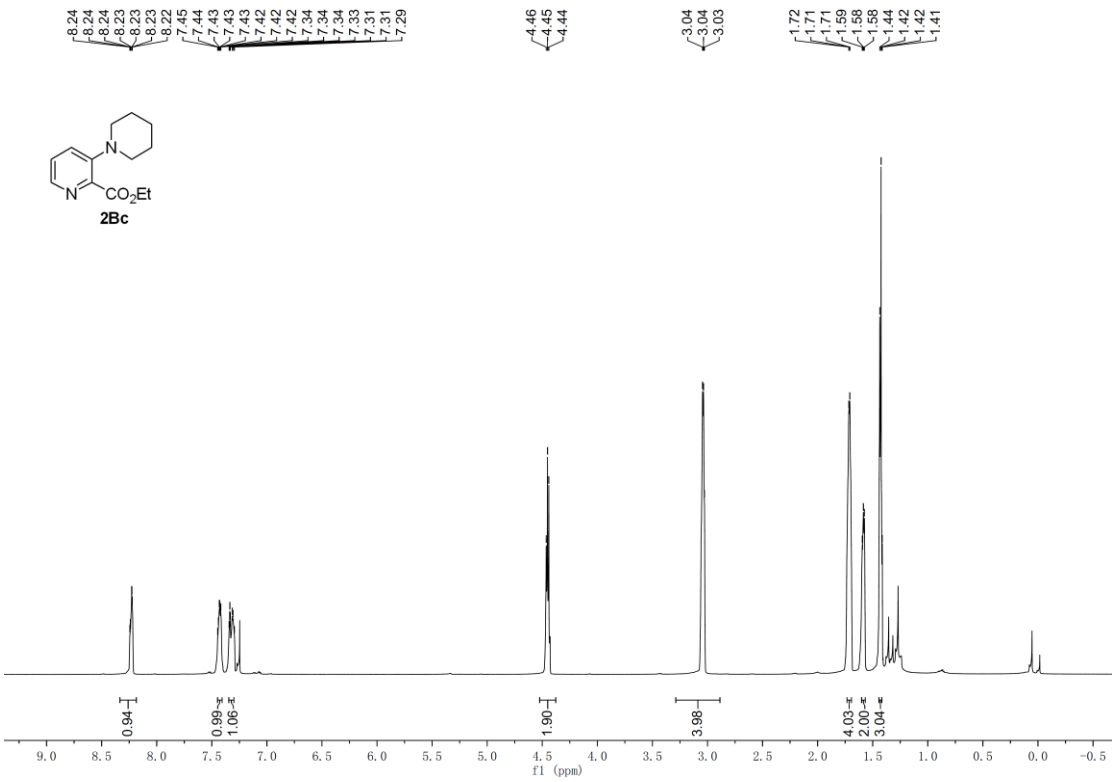
^{13}C NMR (151 MHz) spectrum of **2Ba** in $CDCl_3$



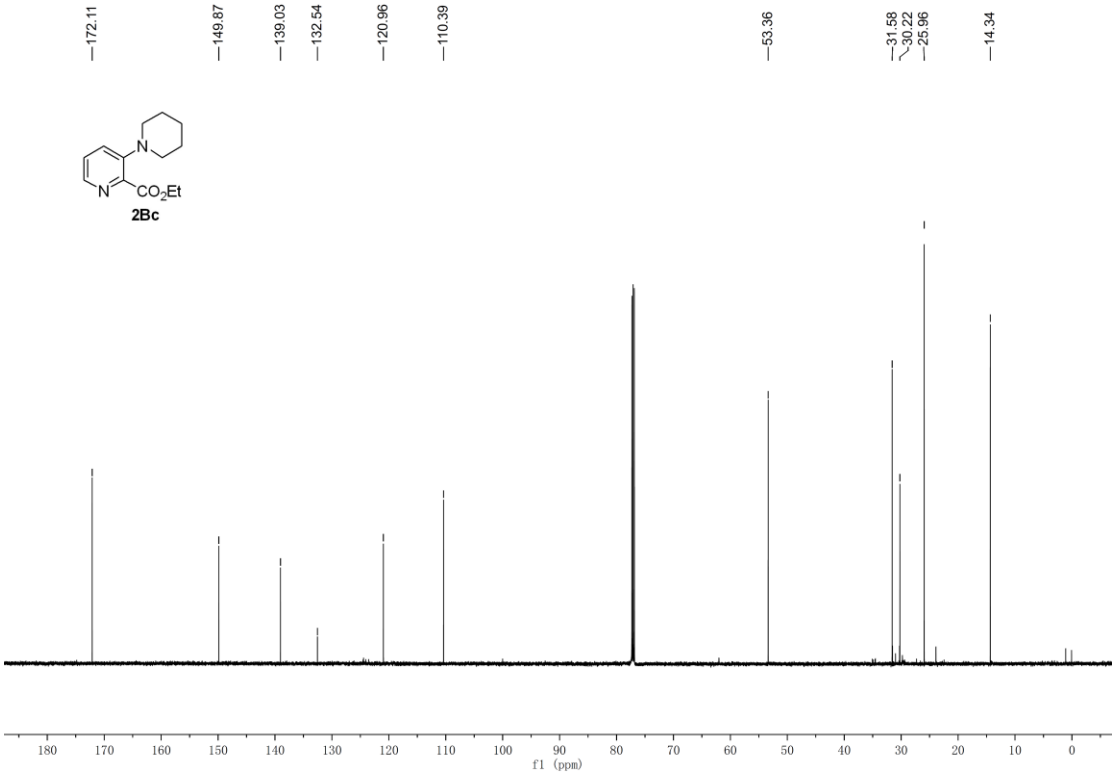
^{1}H NMR (600 MHz) spectrum of **2Bb** in $CDCl_3$



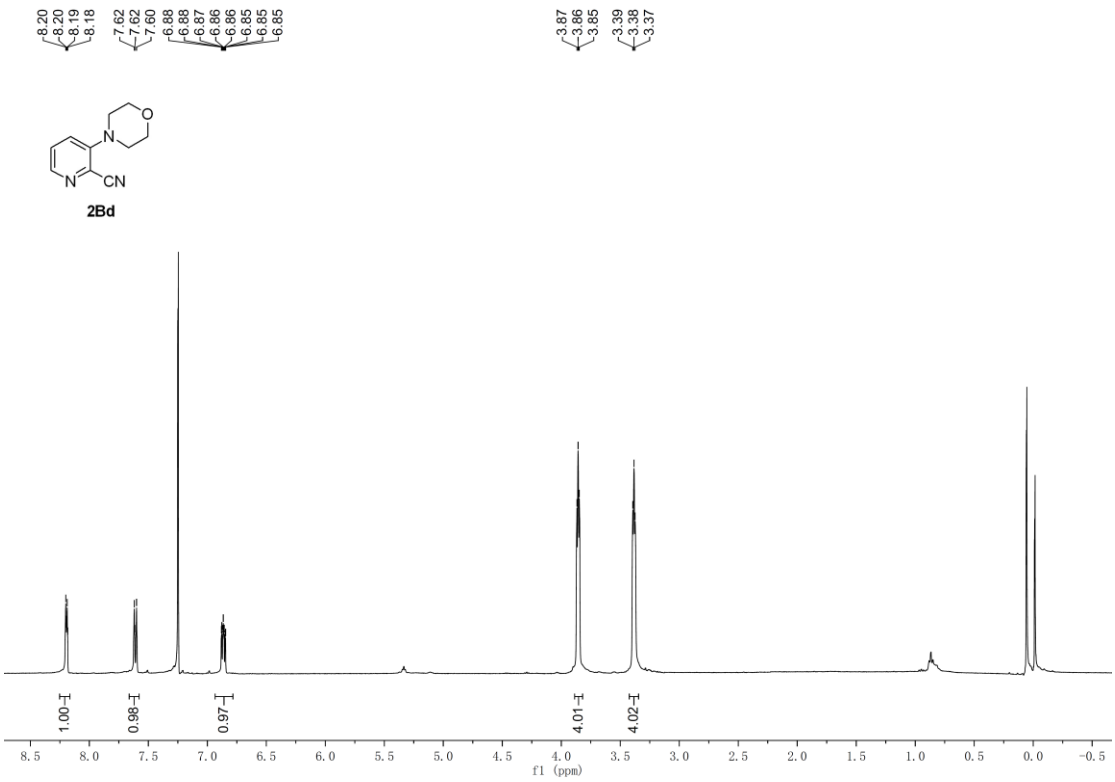
^{13}C NMR (101 MHz) spectrum of **2Bb** in $CDCl_3$



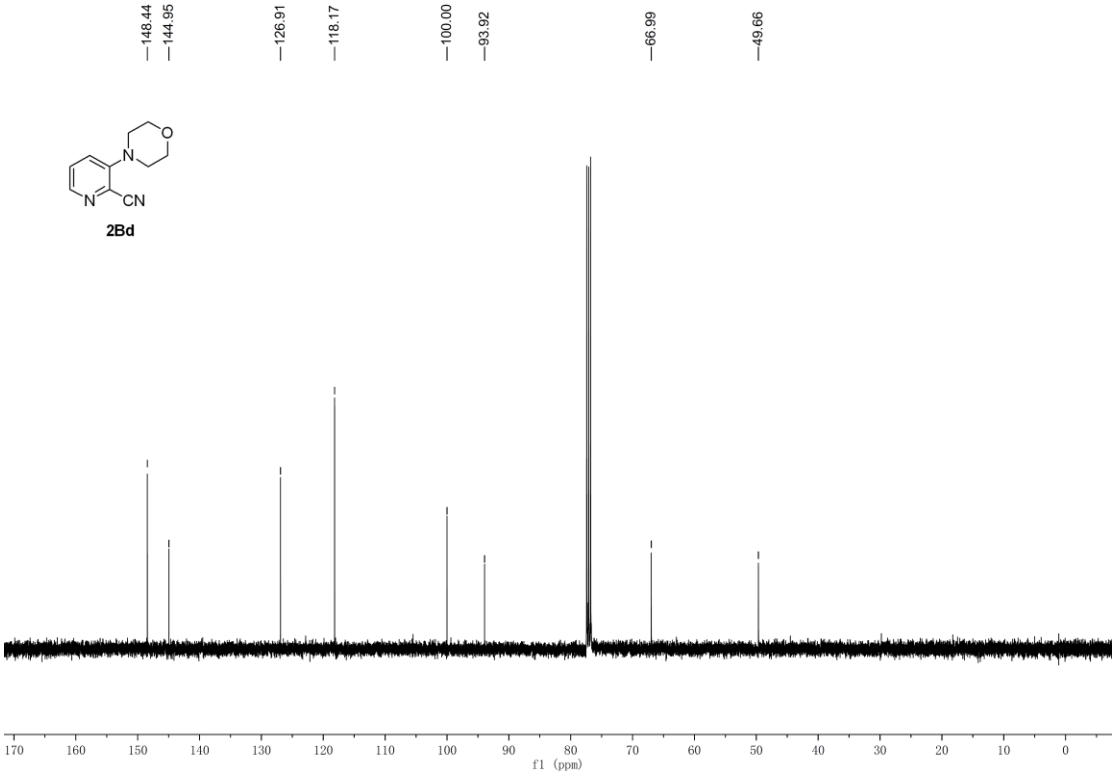
^{1}H NMR (400 MHz) spectrum of **2Bc** in $CDCl_3$



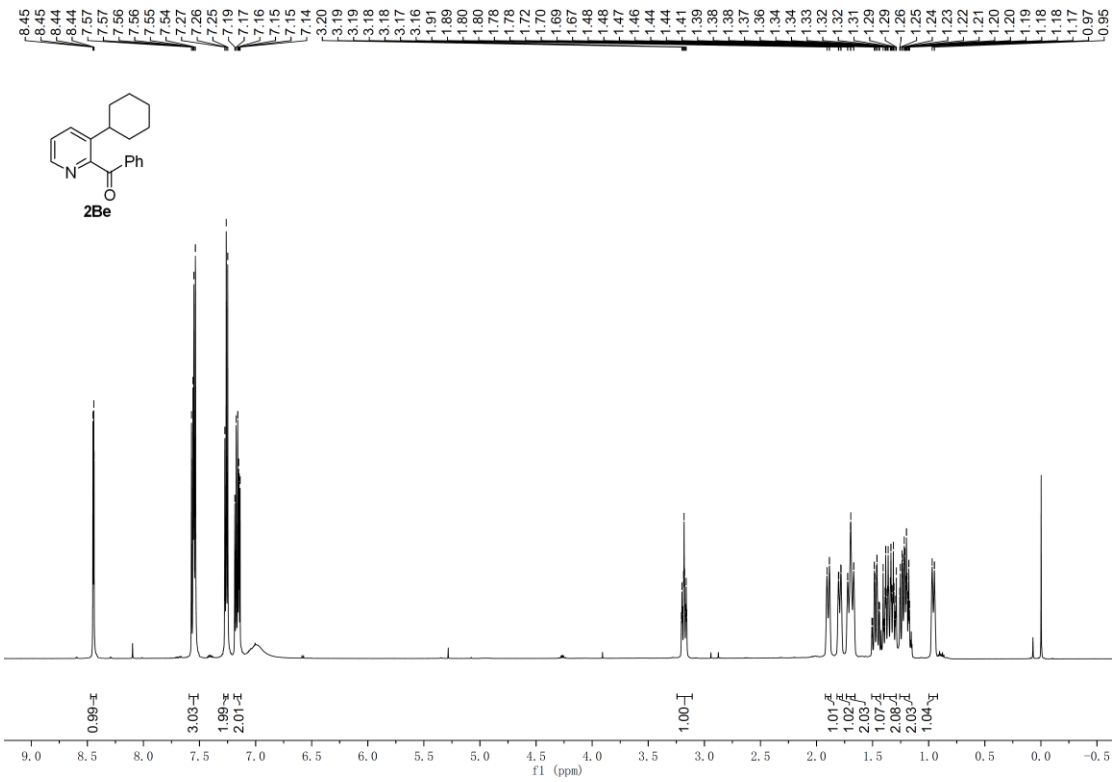
^{13}C NMR (101 MHz) spectrum of **2Bc** in $CDCl_3$



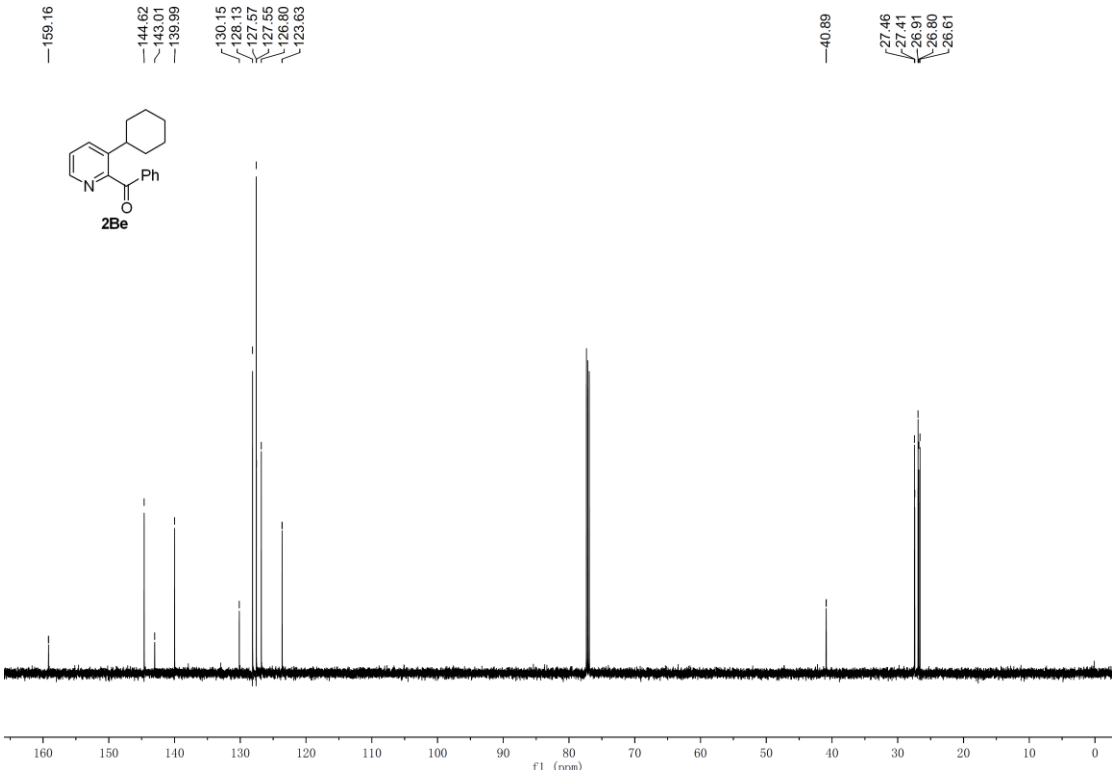
^{1}H NMR (400 MHz) spectrum of **2Bd** in $CDCl_3$



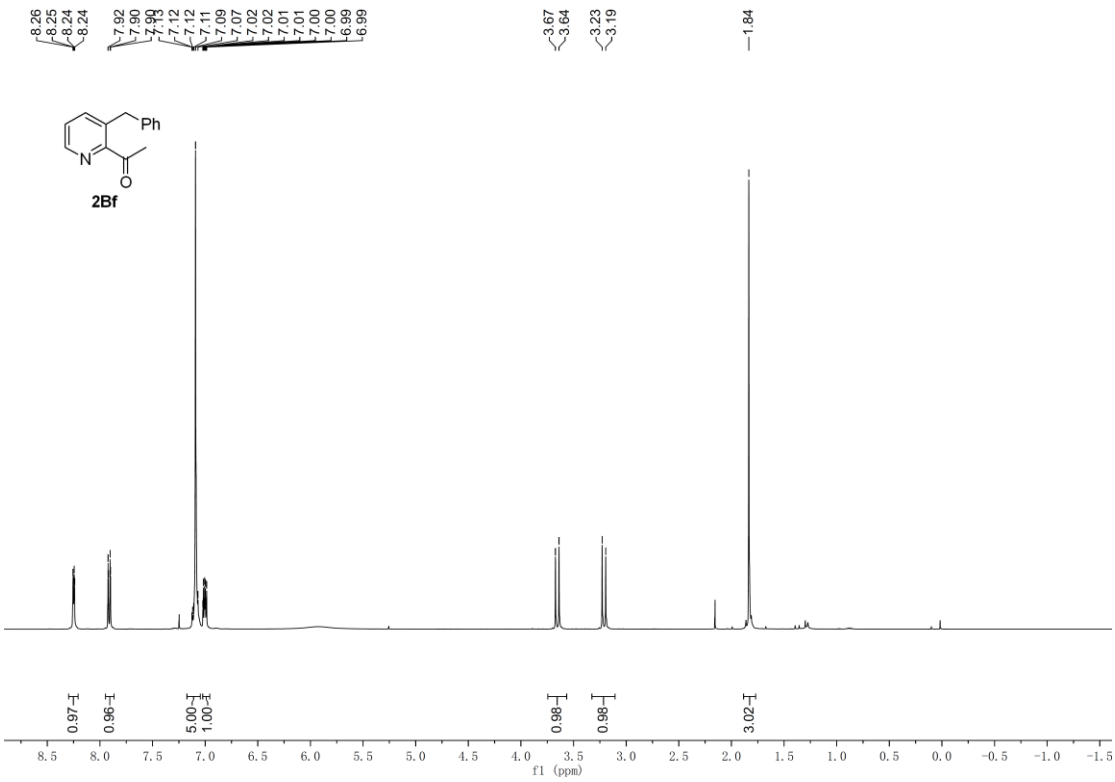
^{13}C NMR (101 MHz) spectrum of **2Bd** in $CDCl_3$



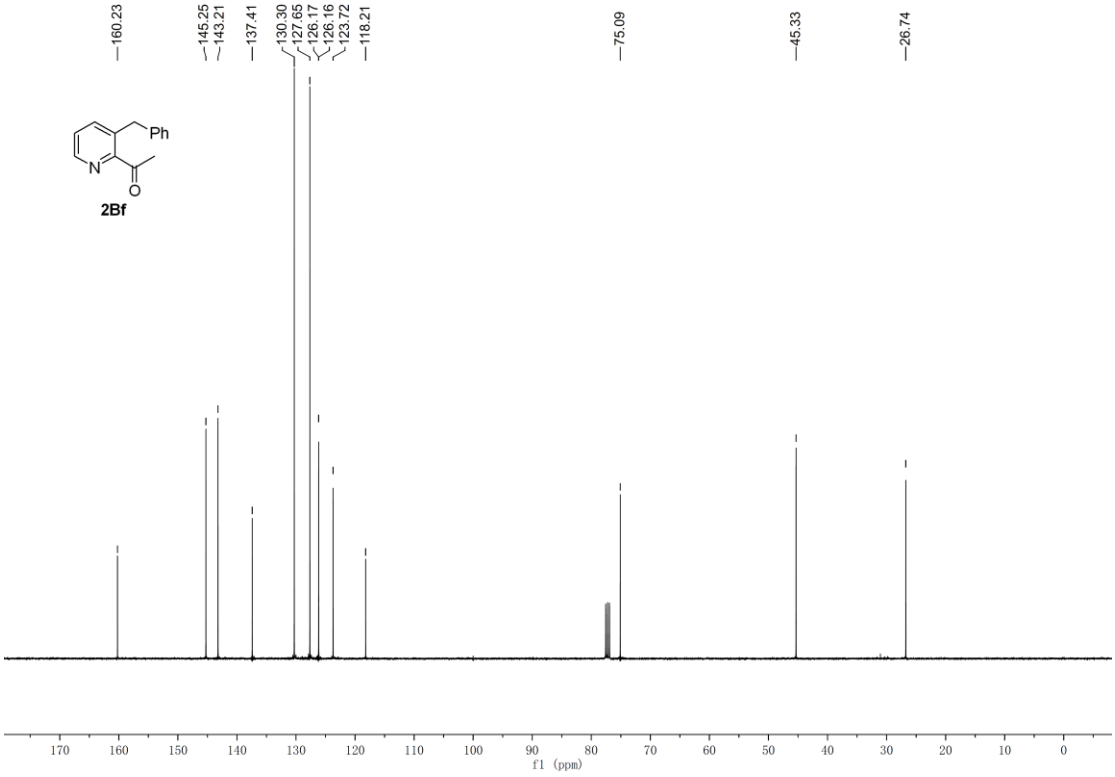
^{1}H NMR (400 MHz) spectrum of **2Be** in $CDCl_3$



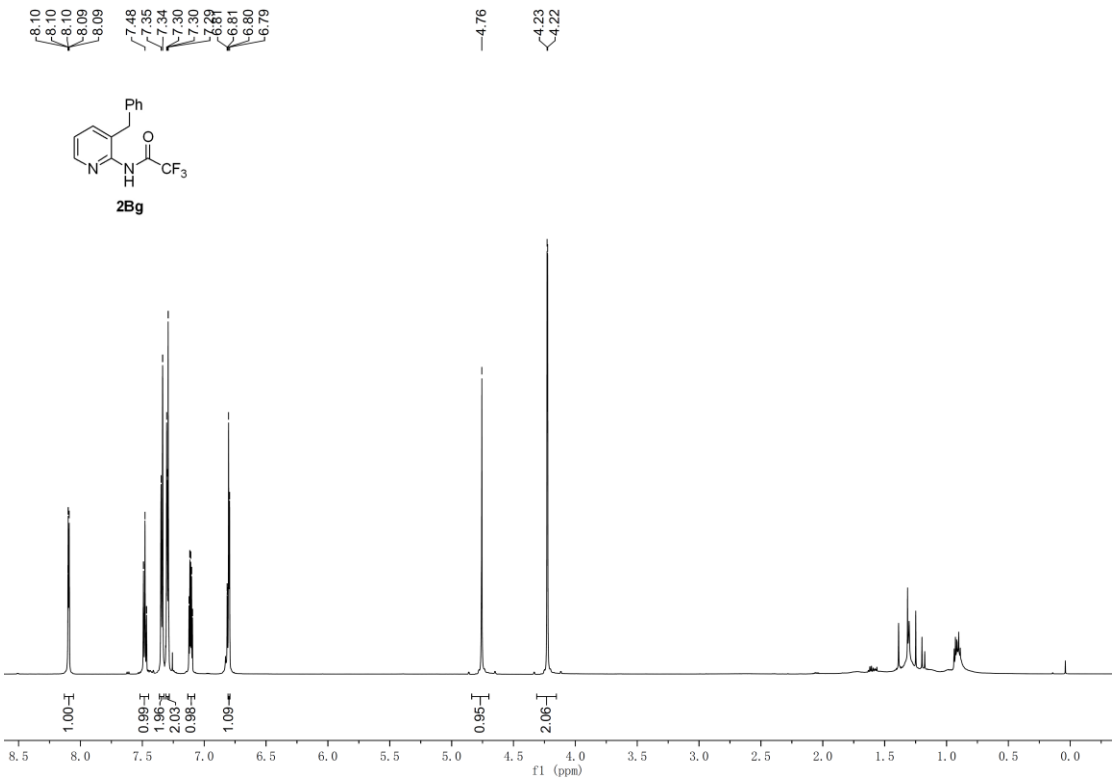
^{13}C NMR (151 MHz) spectrum of **2Be** in $CDCl_3$



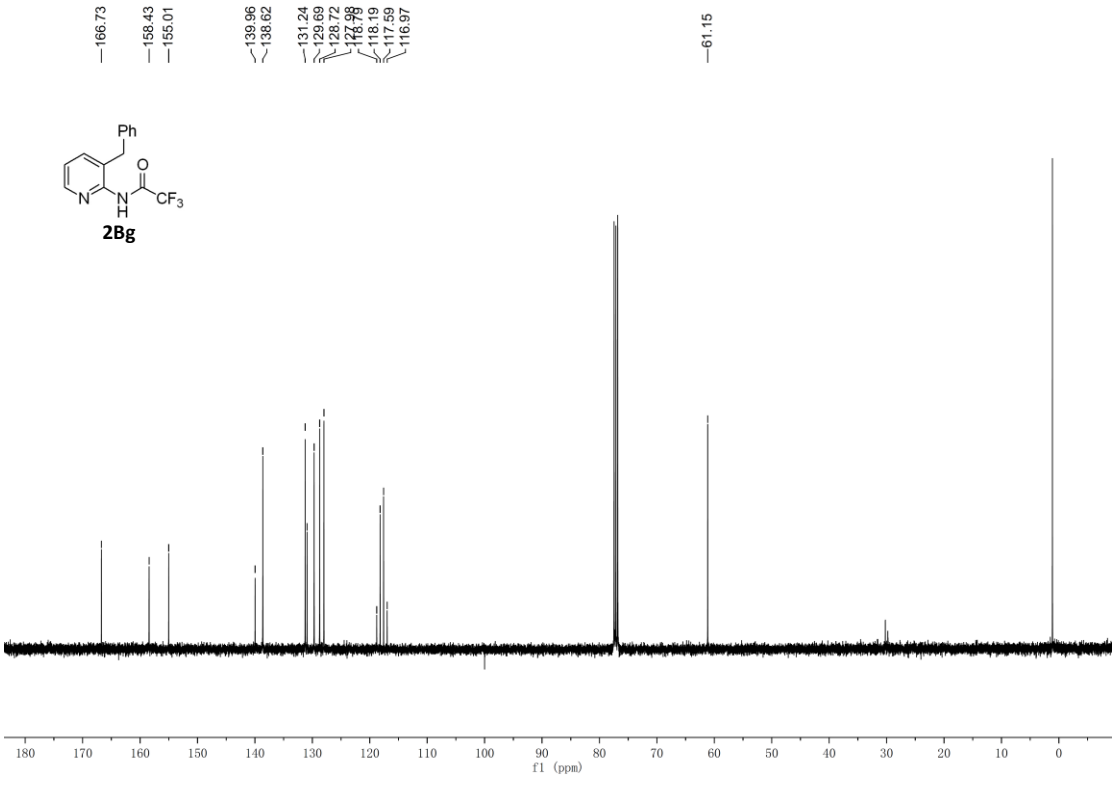
^{1}H NMR (400 MHz) spectrum of **2Bf** in $CDCl_3$



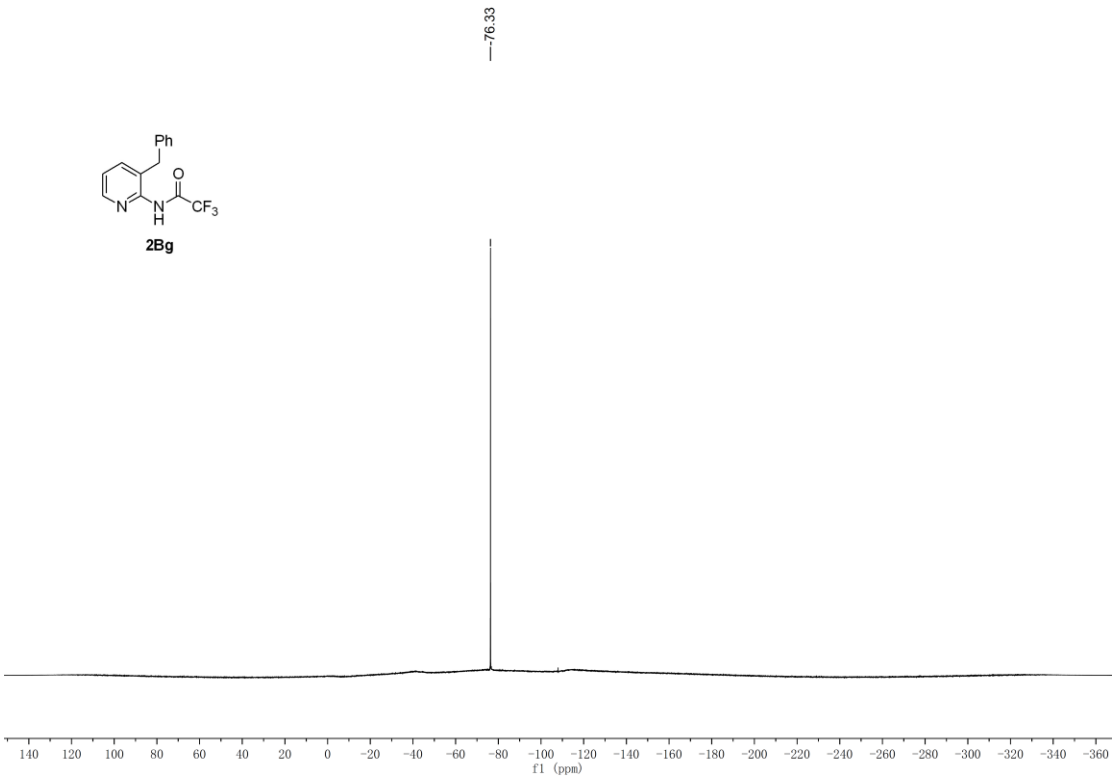
^{13}C NMR (101 MHz) spectrum of **2Bf** in $CDCl_3$



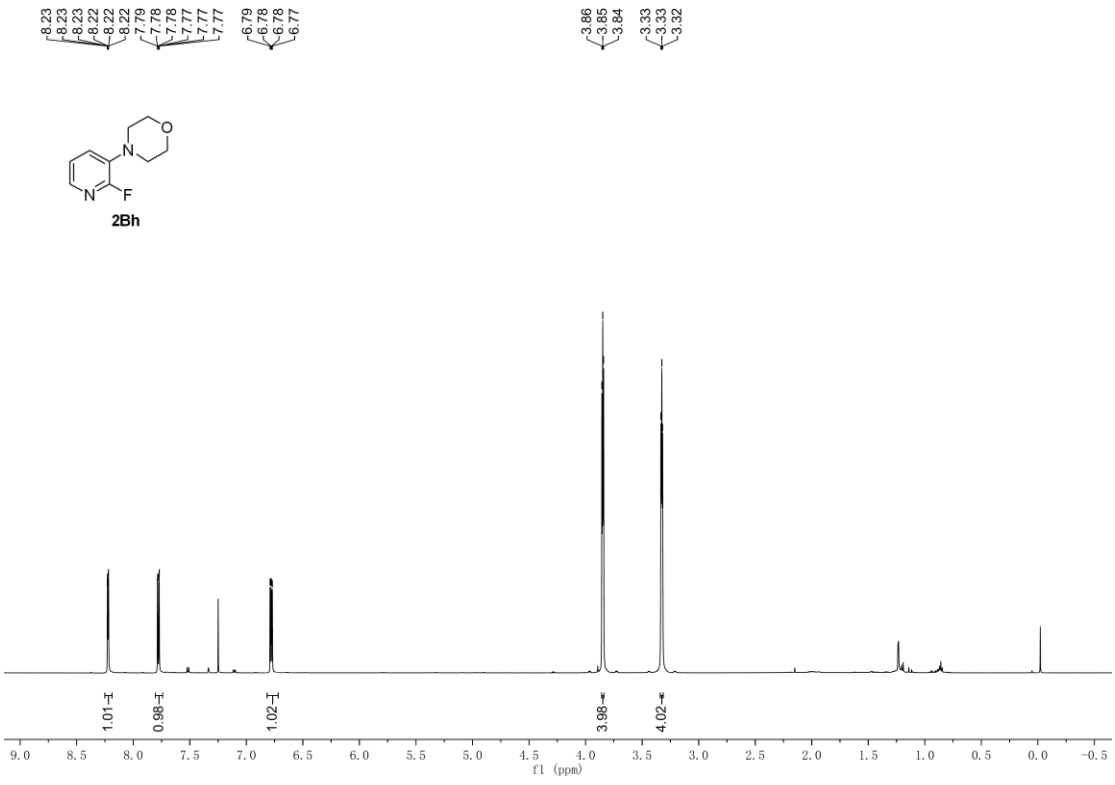
^{1}H NMR (400 MHz) spectrum of **2Bg** in $CDCl_3$



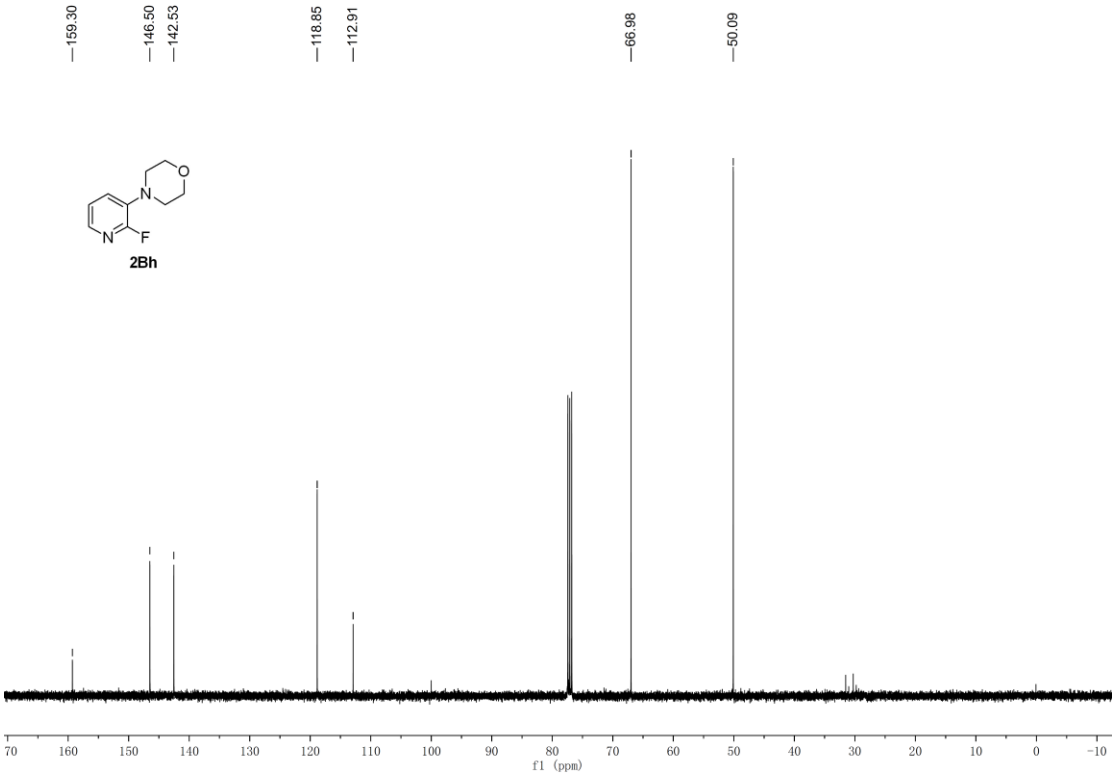
^{13}C NMR (101 MHz) spectrum of **2Bg** in $CDCl_3$



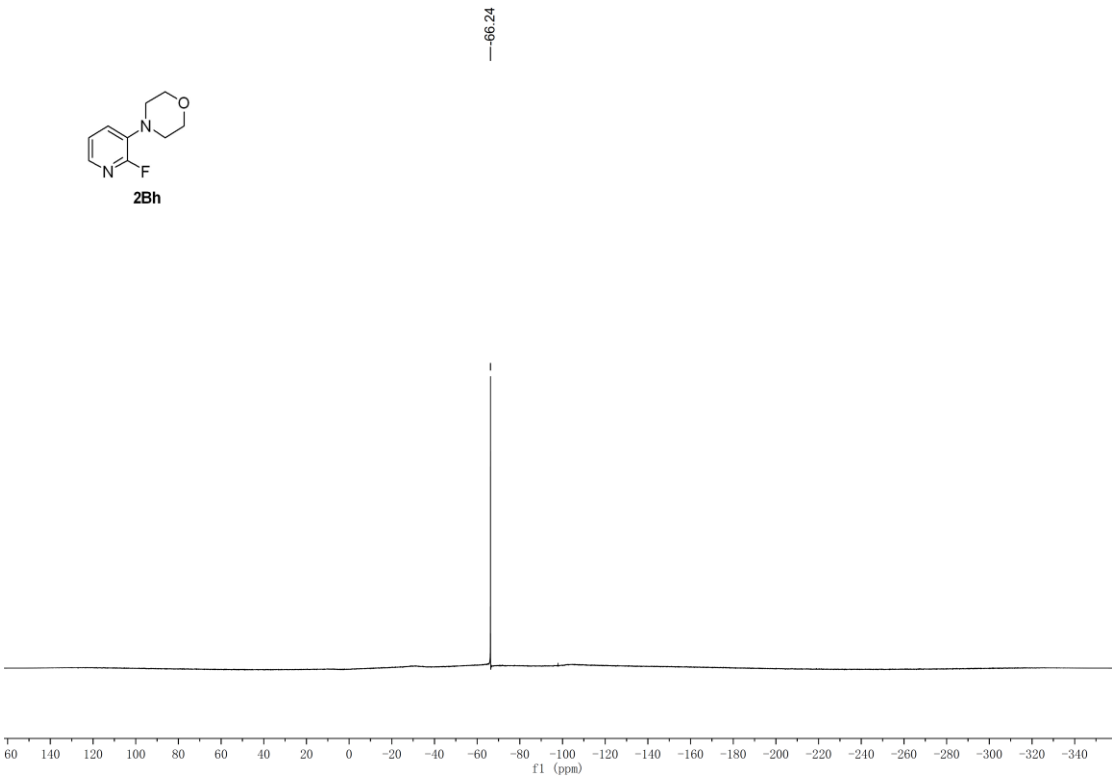
^{19}F NMR (376 MHz) spectrum of **2Bg** in $CDCl_3$



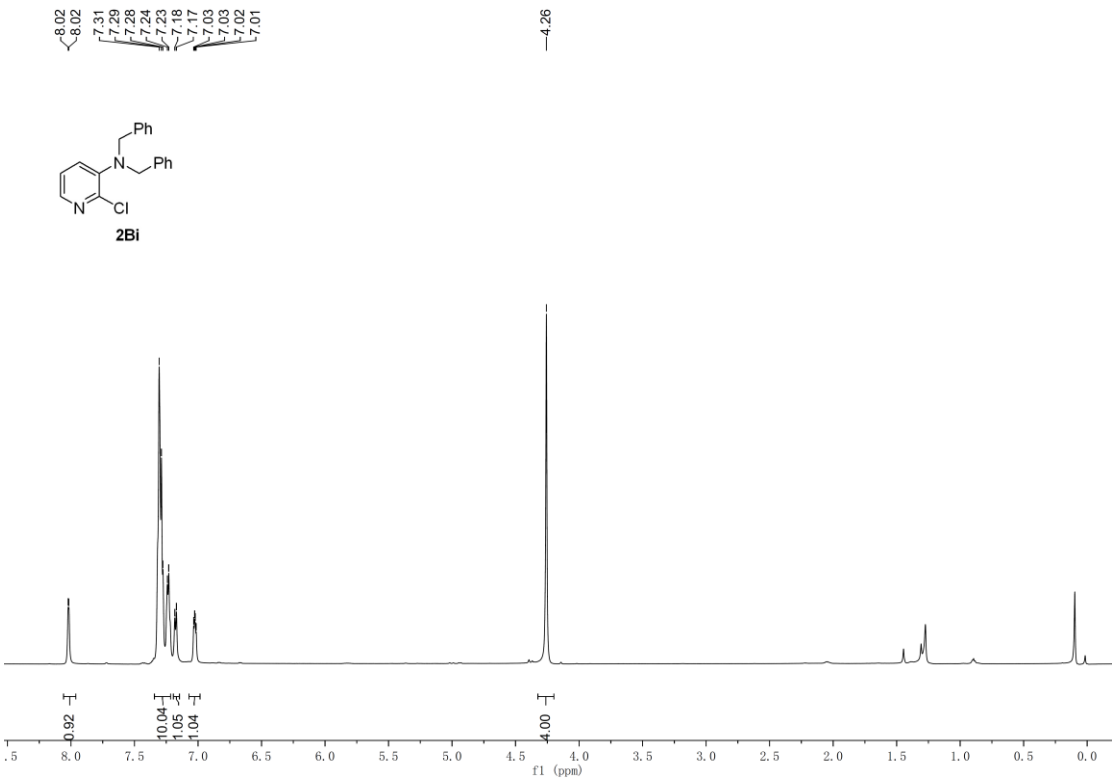
^{1}H NMR (600 MHz) spectrum of **2Bh** in $CDCl_3$



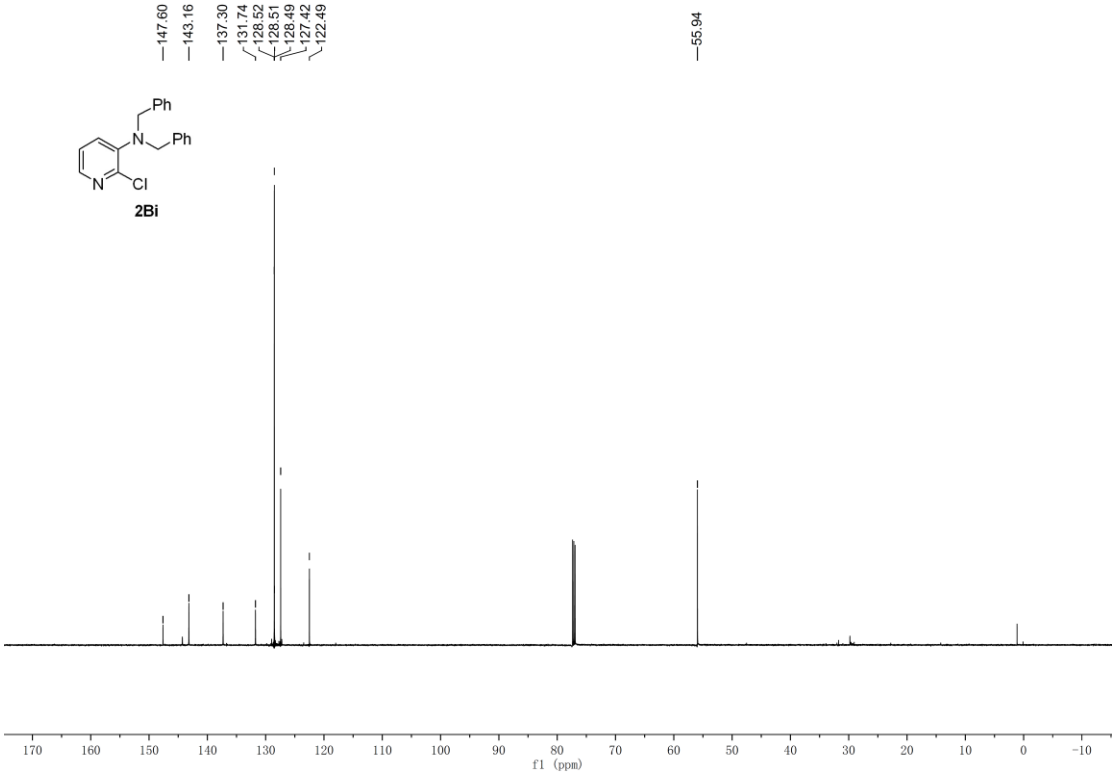
^{13}C NMR (101 MHz) spectrum of **2Bh** in $CDCl_3$



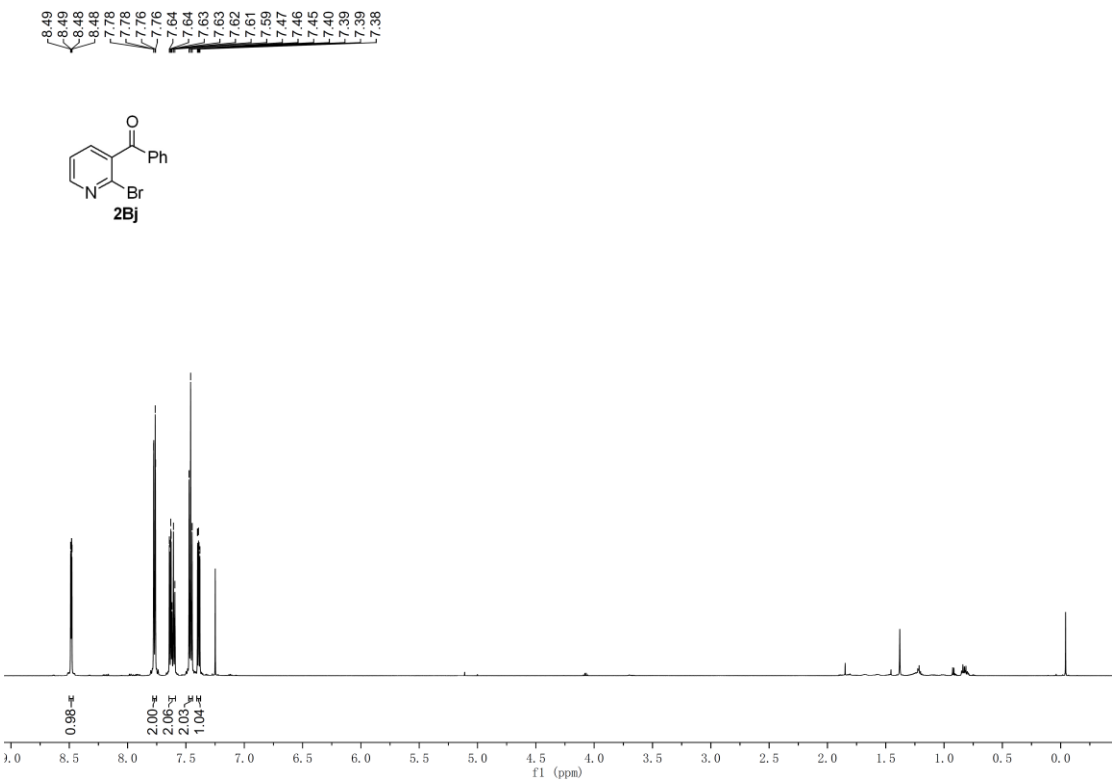
^{19}F NMR (376 MHz) spectrum of **2Bh** in $CDCl_3$



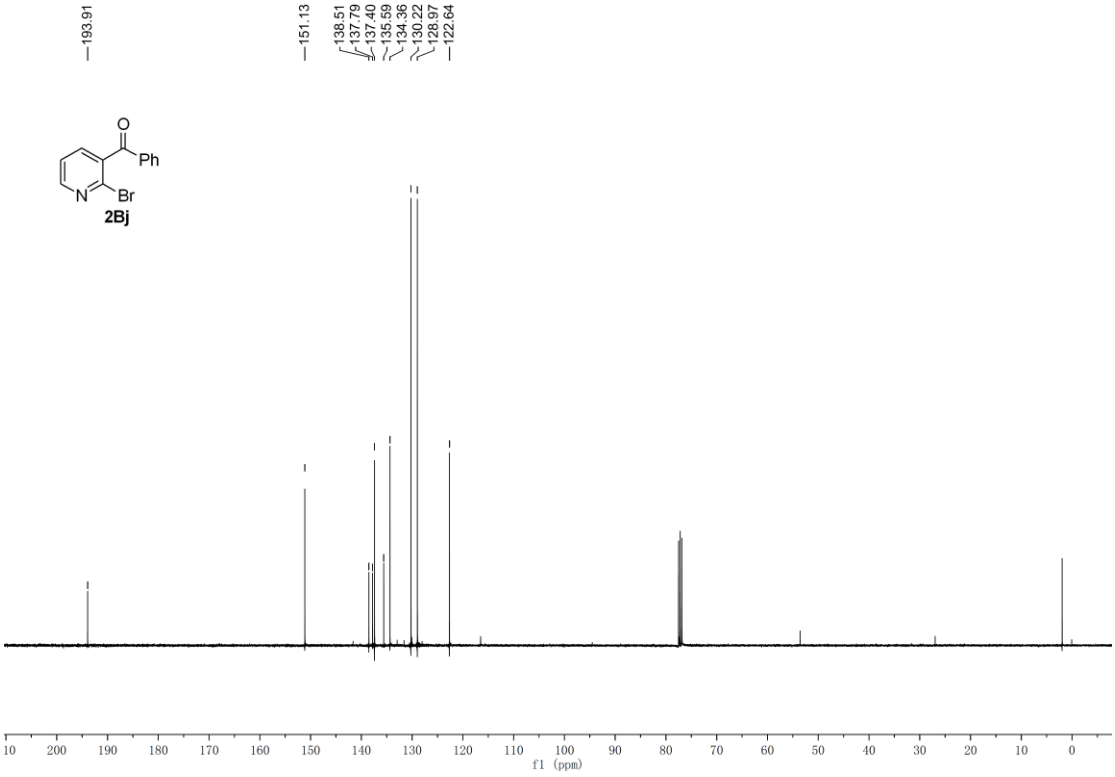
^{1}H NMR (600 MHz) spectrum of **2Bi** in $CDCl_3$



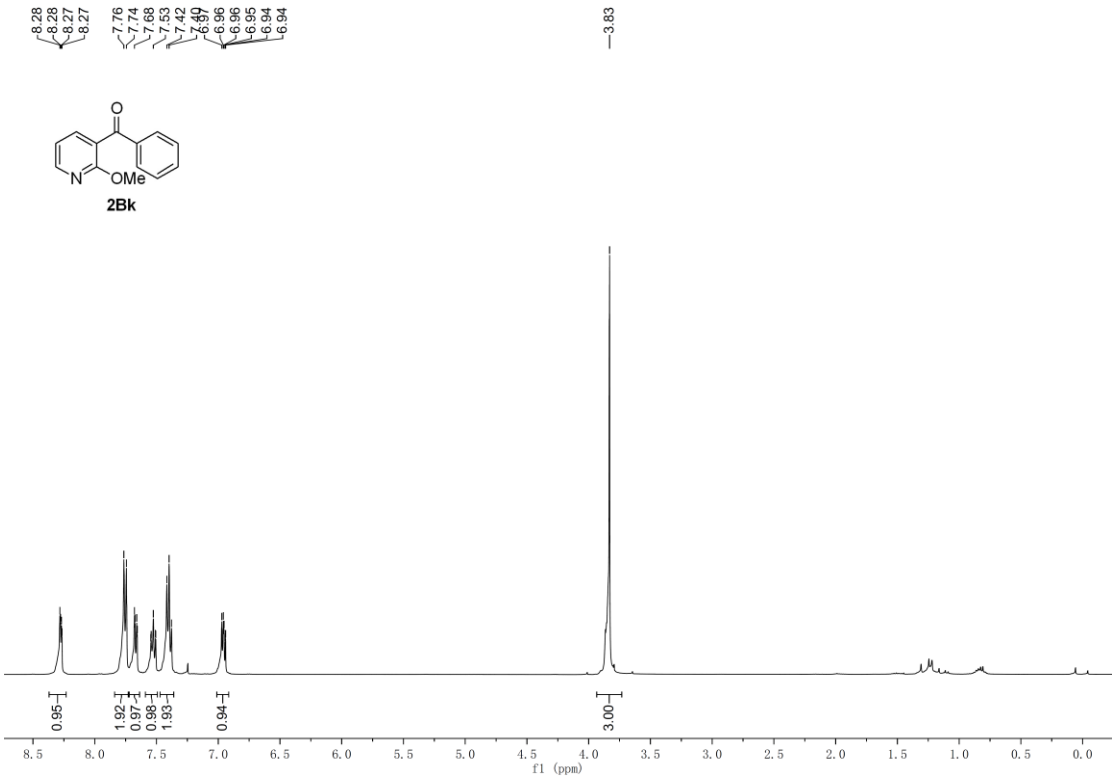
^{13}C NMR (151 MHz) spectrum of **2Bi** in $CDCl_3$



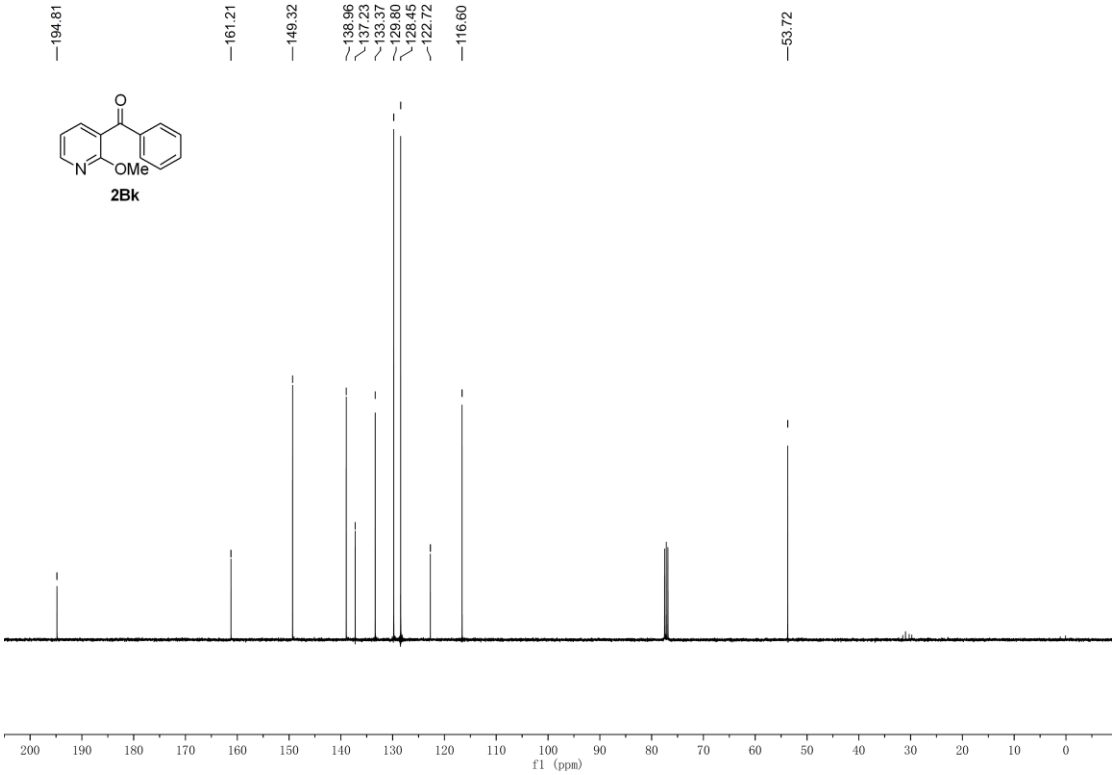
^{1}H NMR (600 MHz) spectrum of **2Bj** in $CDCl_3$



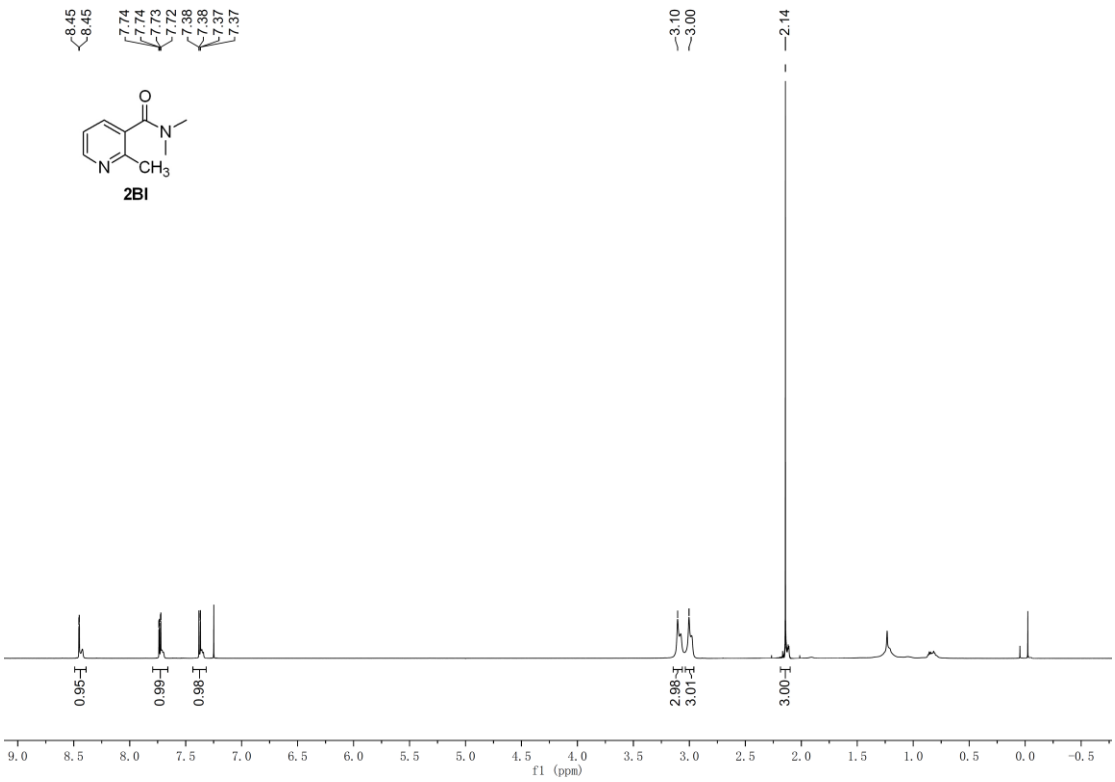
^{13}C NMR (101 MHz) spectrum of **2Bj** in $CDCl_3$



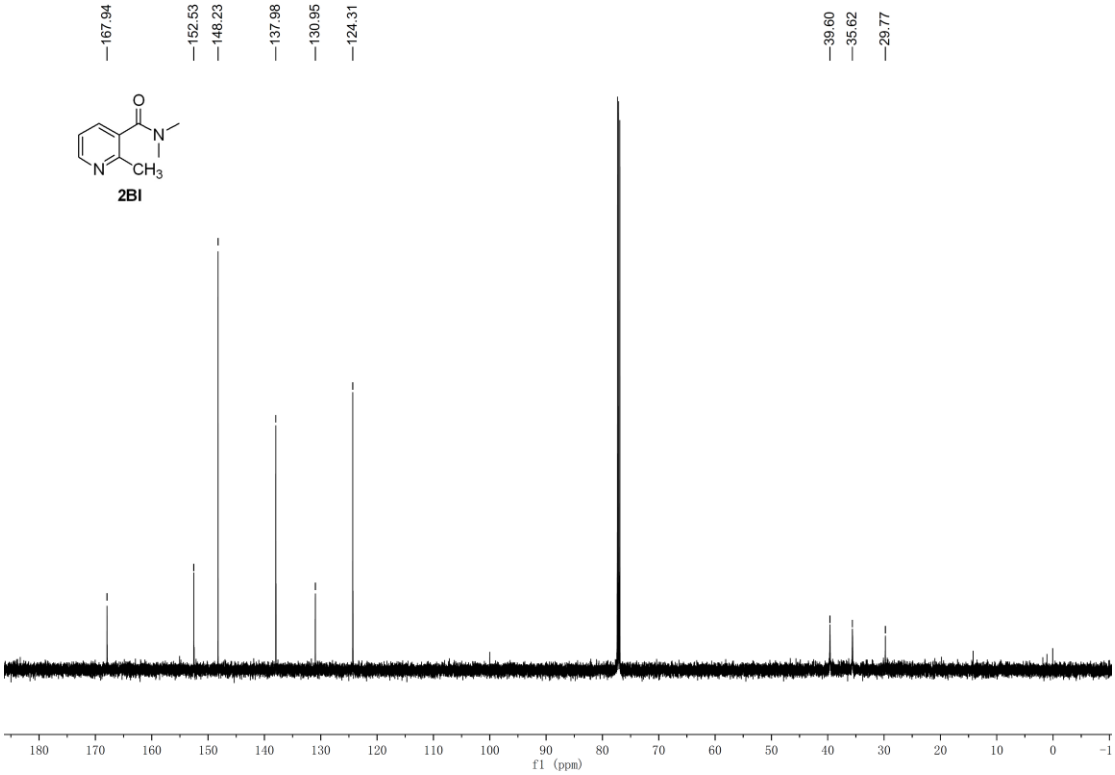
^{1}H NMR (400 MHz) spectrum of **2Bk** in $CDCl_3$



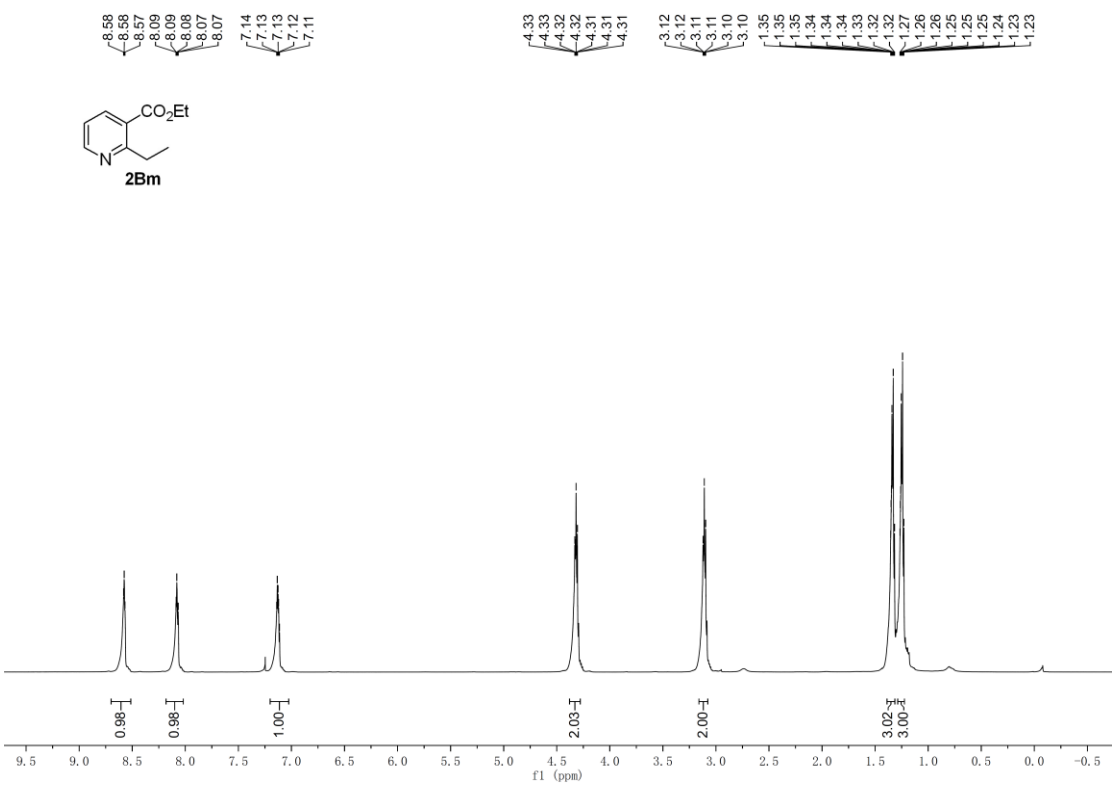
^{13}C NMR (101 MHz) spectrum of **2Bk** in $CDCl_3$



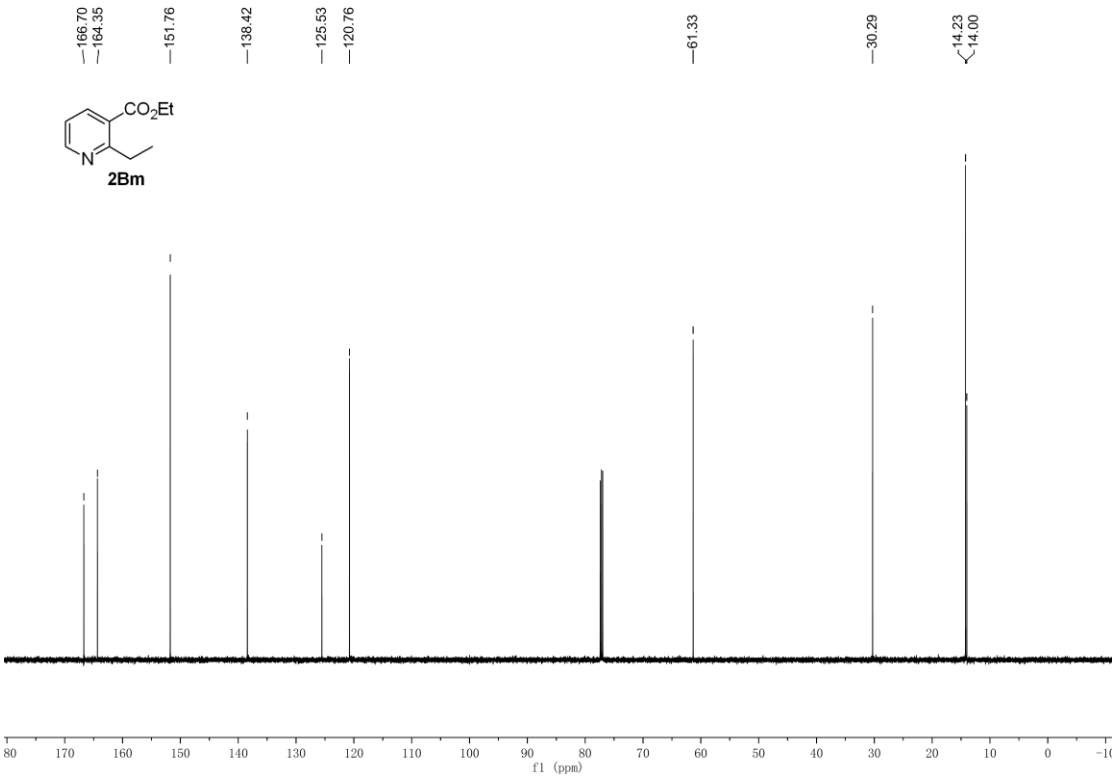
^{1}H NMR (600 MHz) spectrum of **2Bl** in $CDCl_3$



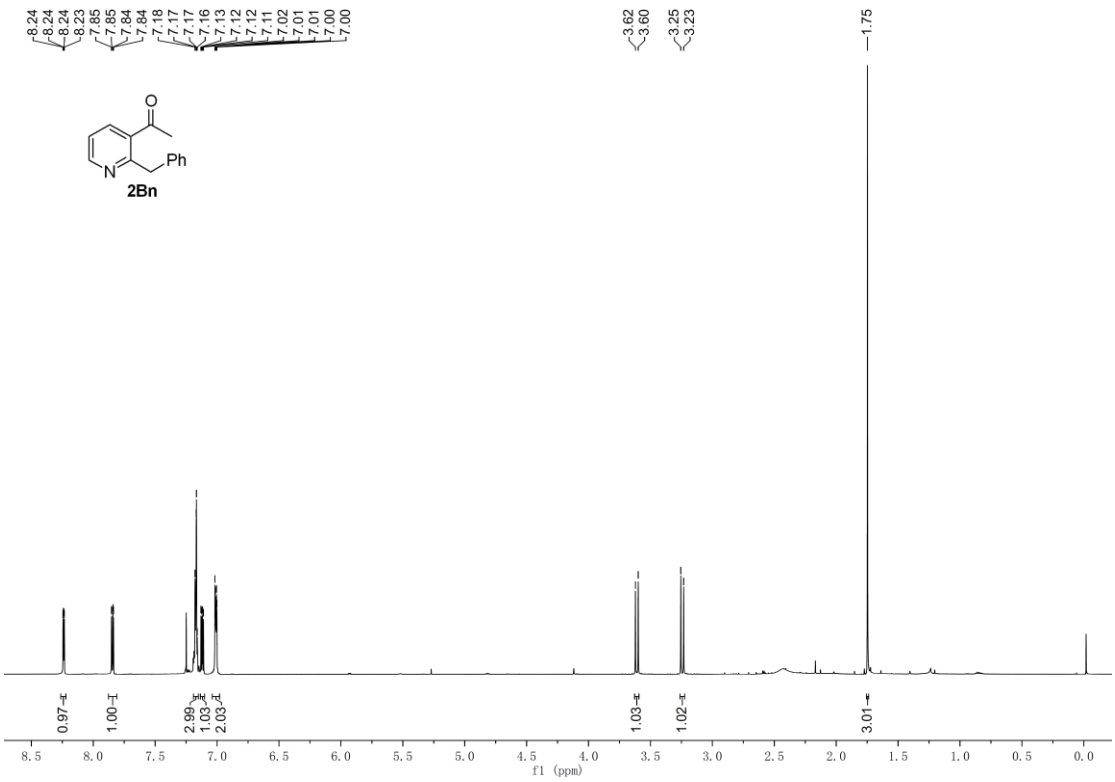
^{13}C NMR (151 MHz) spectrum of **2Bl** in $CDCl_3$



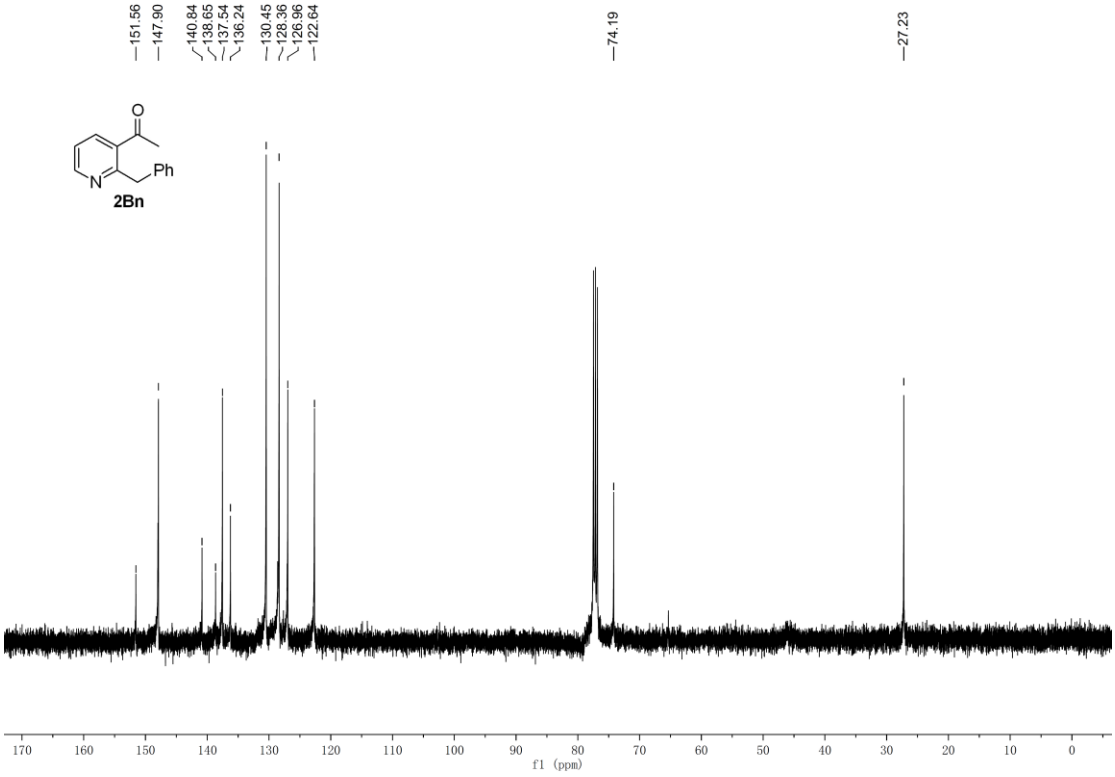
^{1}H NMR (600 MHz) spectrum of **2Bm** in $CDCl_3$



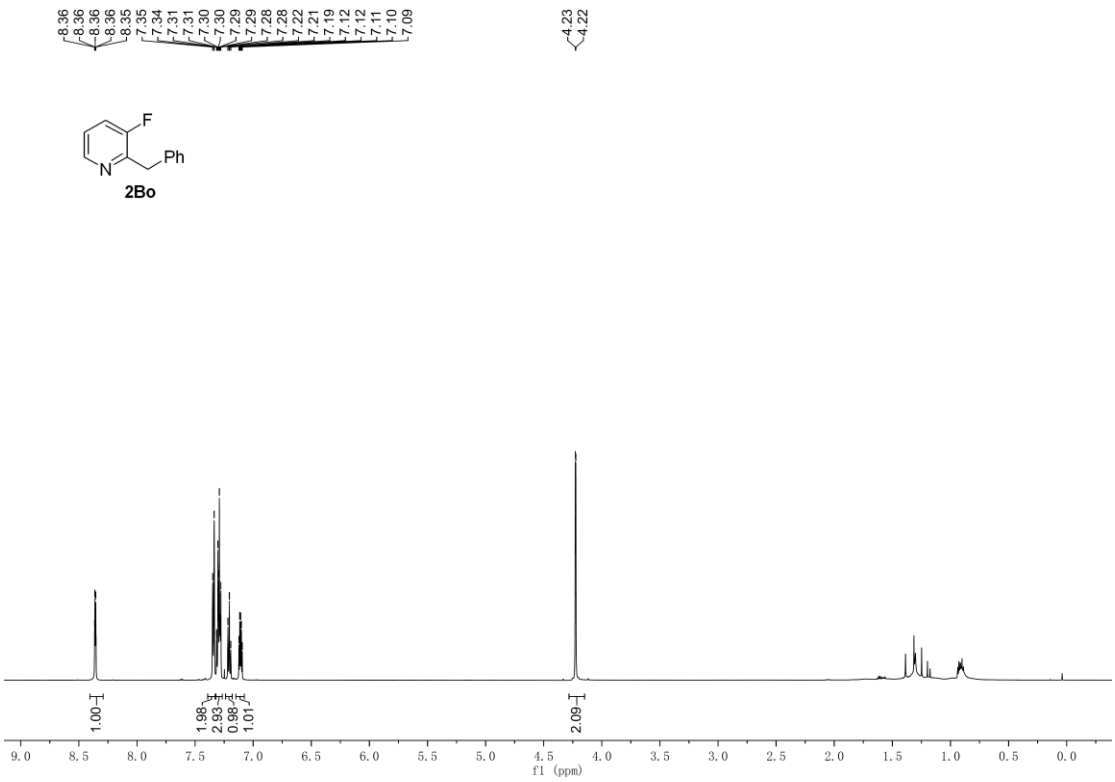
^{13}C NMR (151 MHz) spectrum of **2Bm** in $CDCl_3$



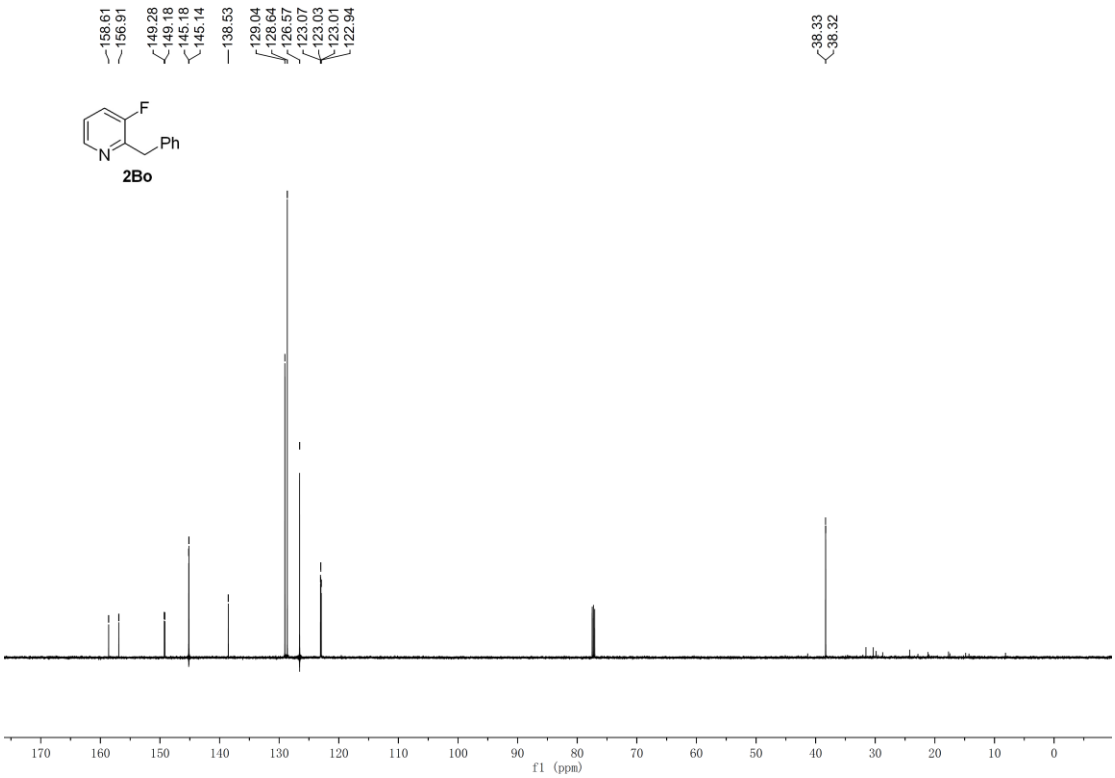
^{1}H NMR (400 MHz) spectrum of **2Bn** in $CDCl_3$



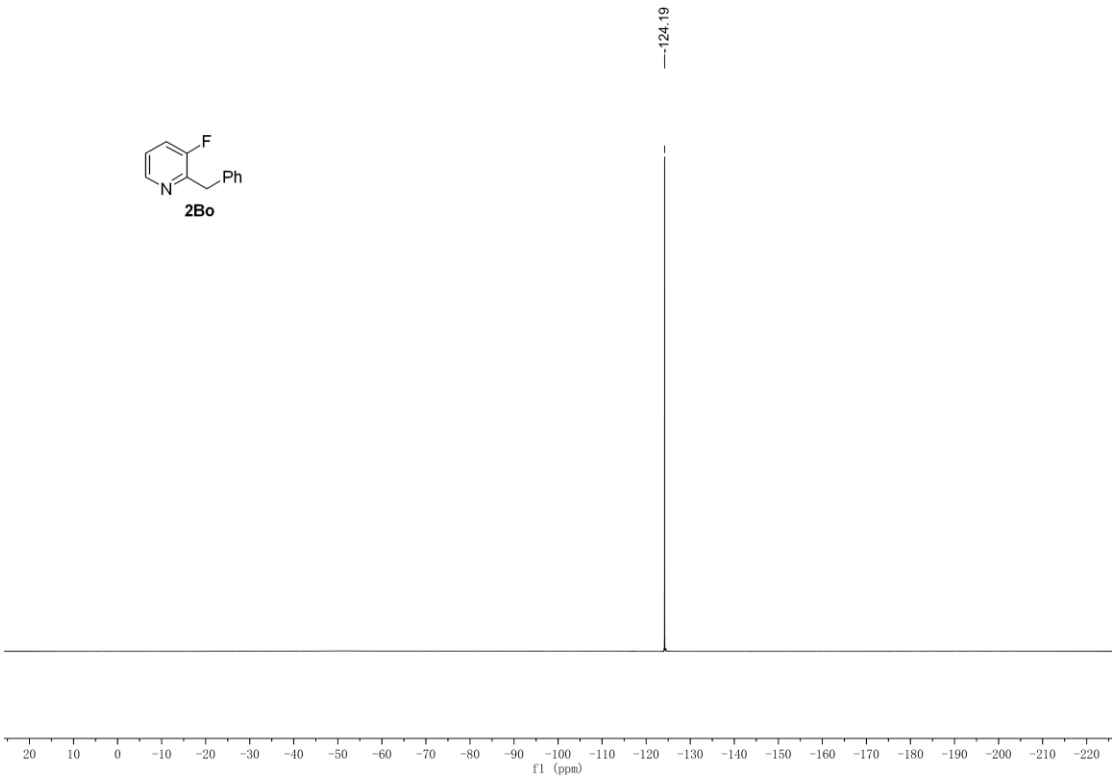
^{13}C NMR (101 MHz) spectrum of **2Bn** in $CDCl_3$



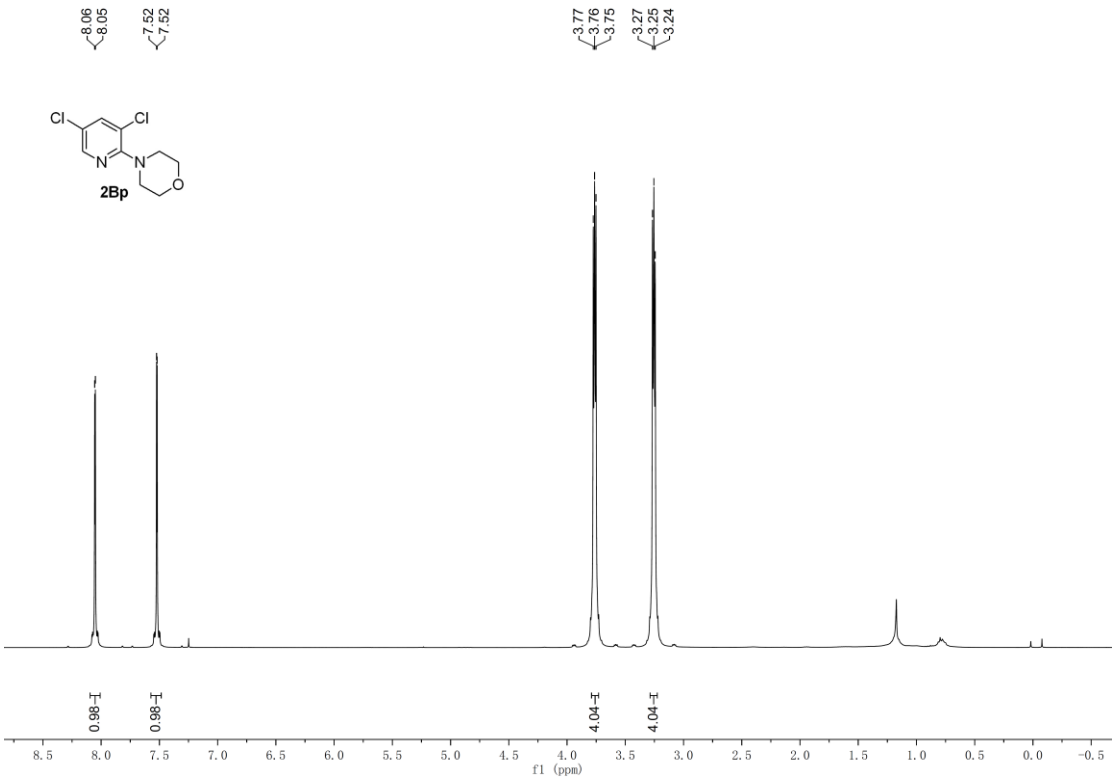
^{1}H NMR (600 MHz) spectrum of **2Bo** in $CDCl_3$



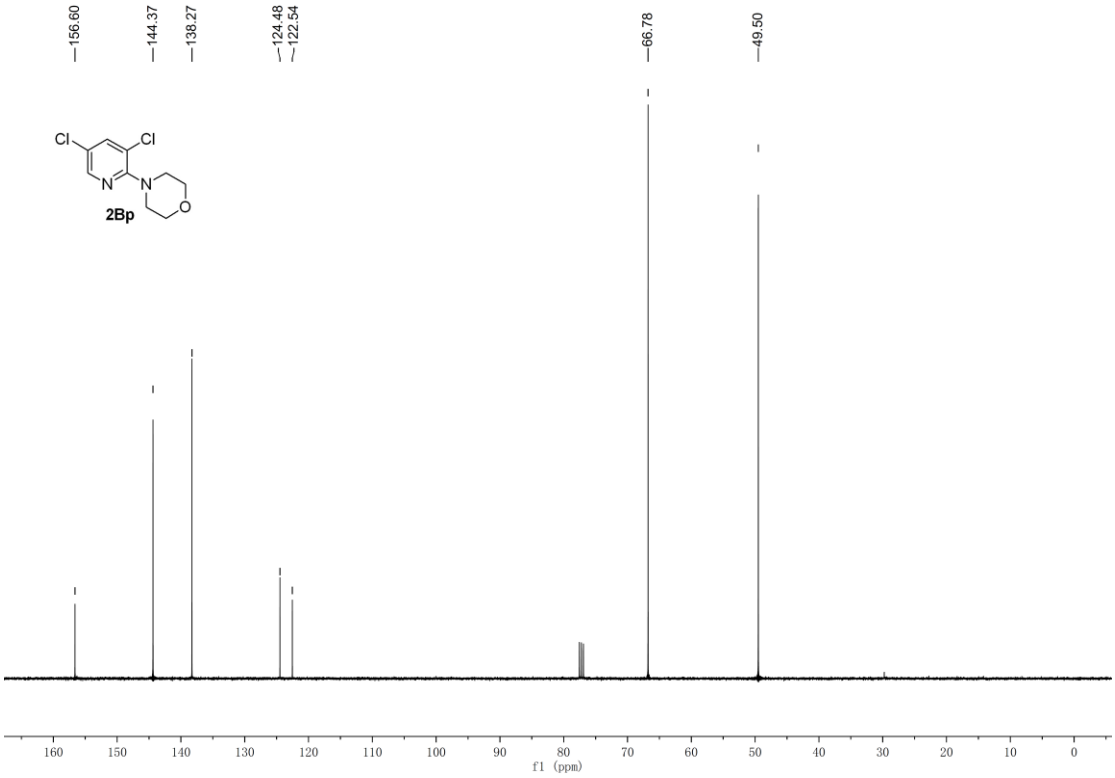
^{13}C NMR (151 MHz) spectrum of **2Bo** in $CDCl_3$



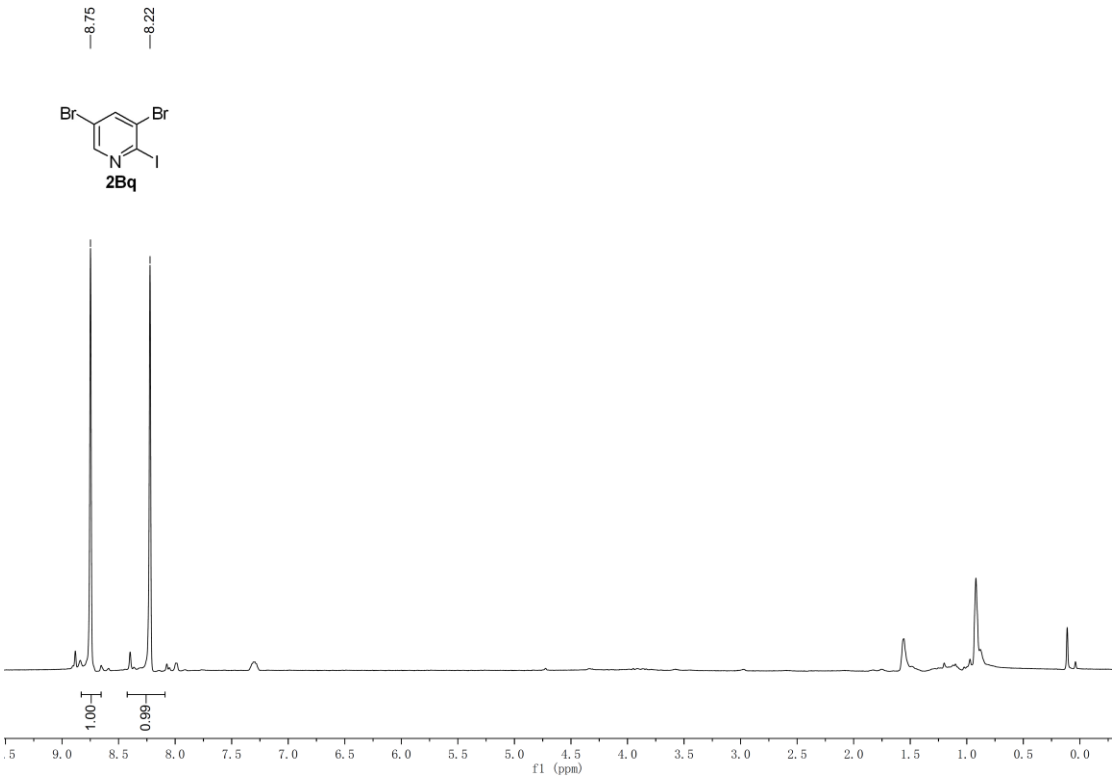
^{19}F NMR (565 MHz) spectrum of **2Bo** in $CDCl_3$



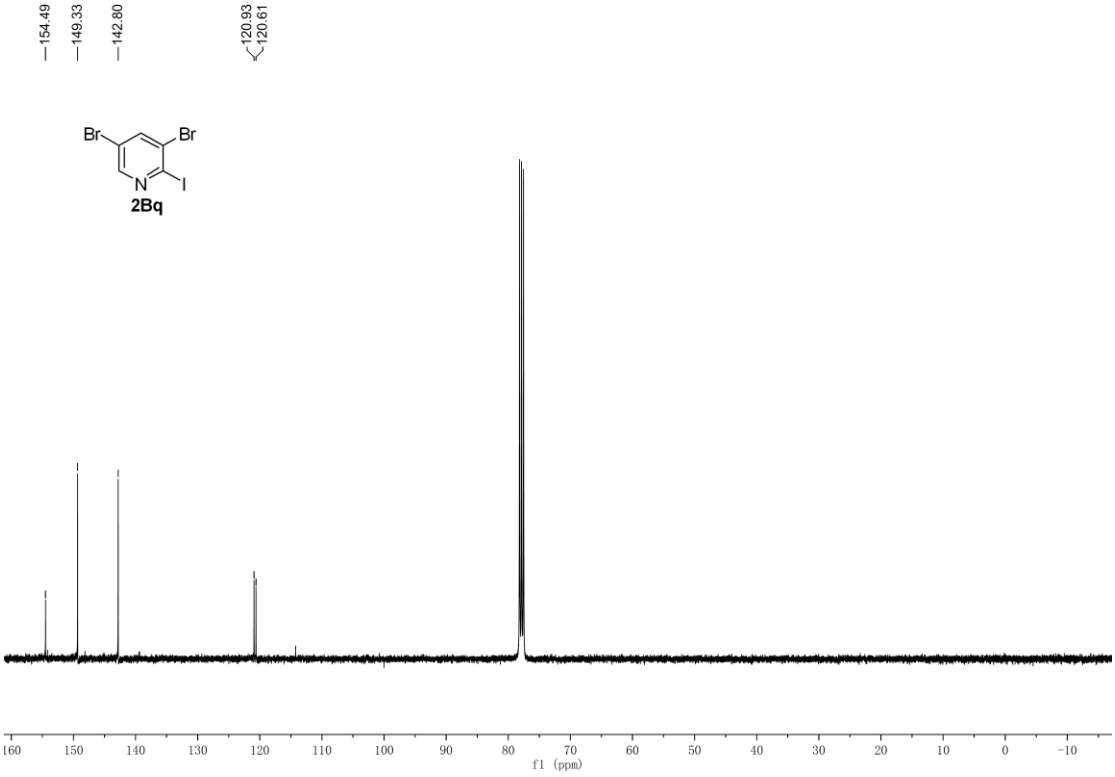
^{1}H NMR (400 MHz) spectrum of **2Bp** in $CDCl_3$



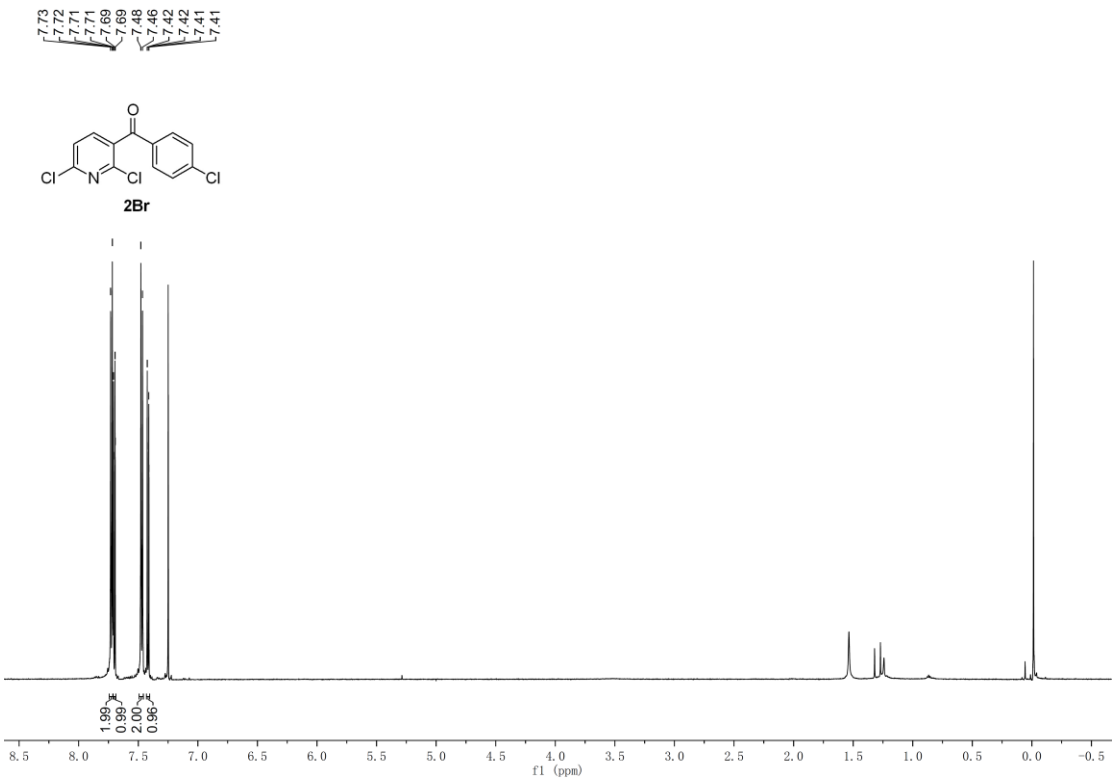
^{13}C NMR (101 MHz) spectrum of **2Bp** in $CDCl_3$



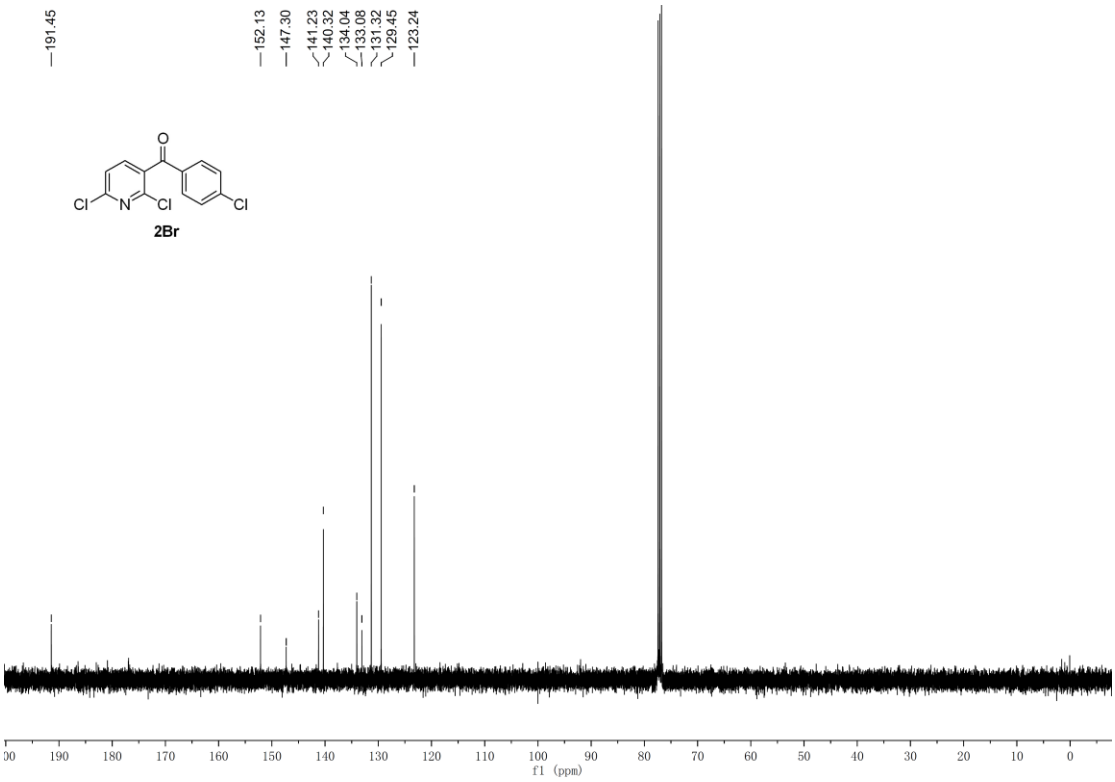
^{1}H NMR (600 MHz) spectrum of **2Bq** in $CDCl_3$



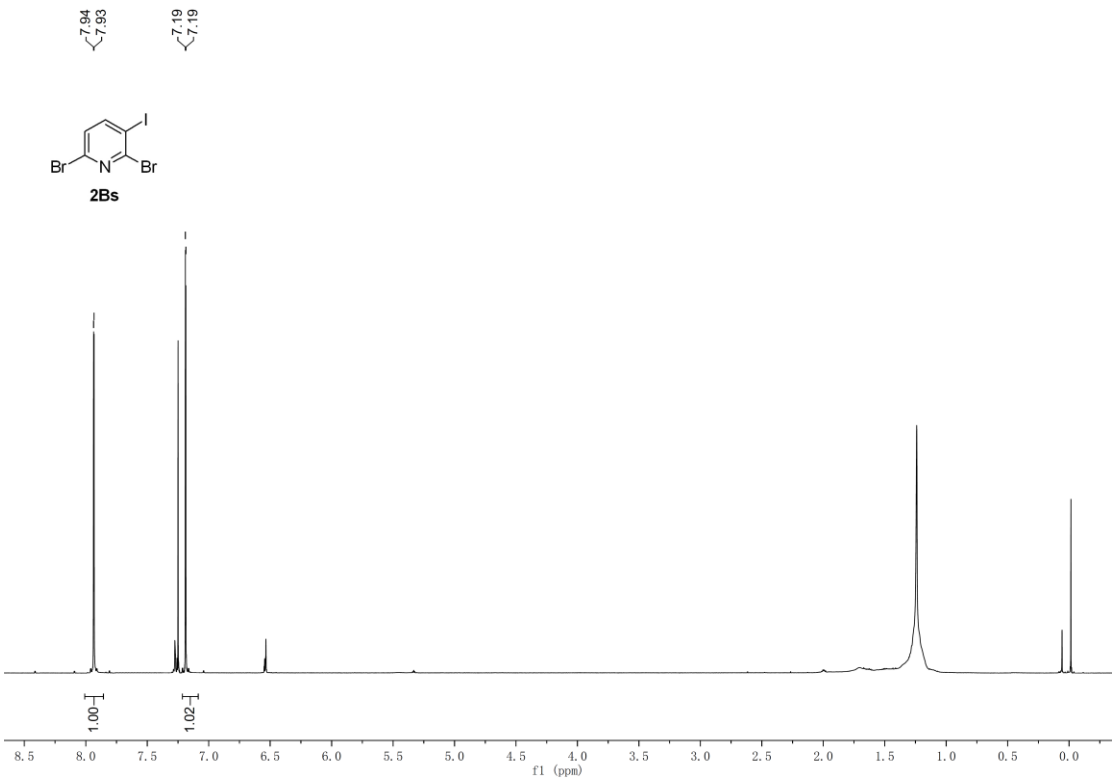
^{13}C NMR (101 MHz) spectrum of **2Bq** in $CDCl_3$



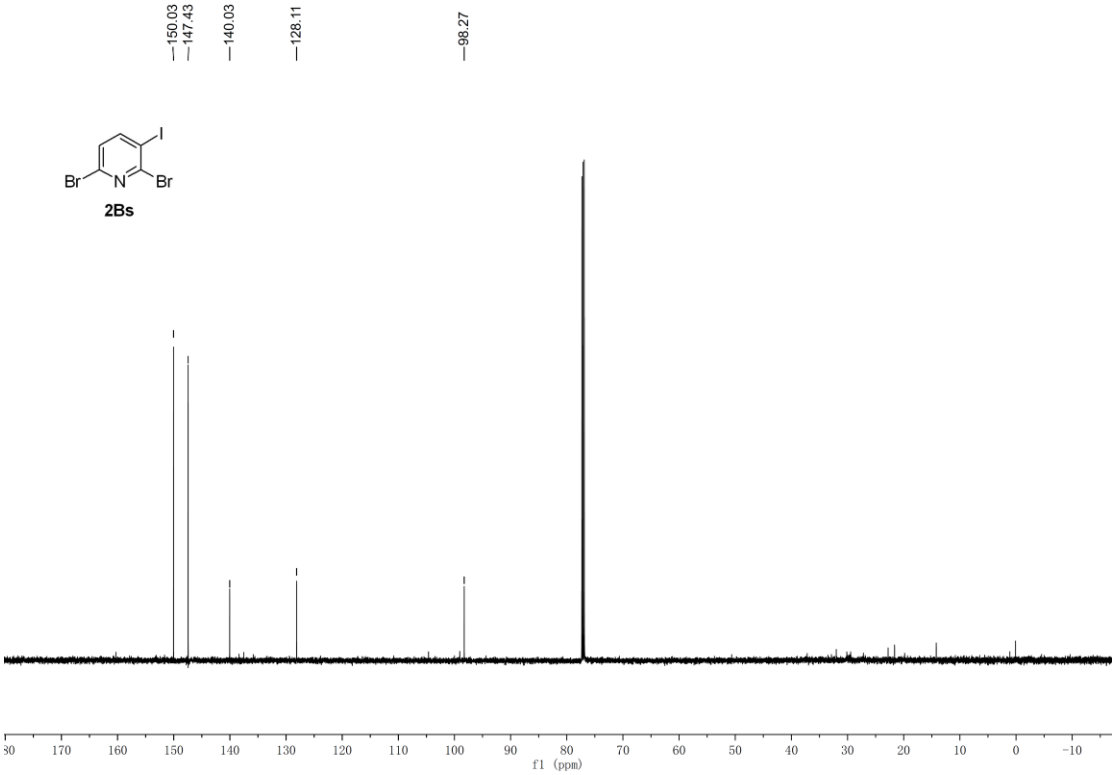
^{1}H NMR (400 MHz) spectrum of **2Br** in $CDCl_3$



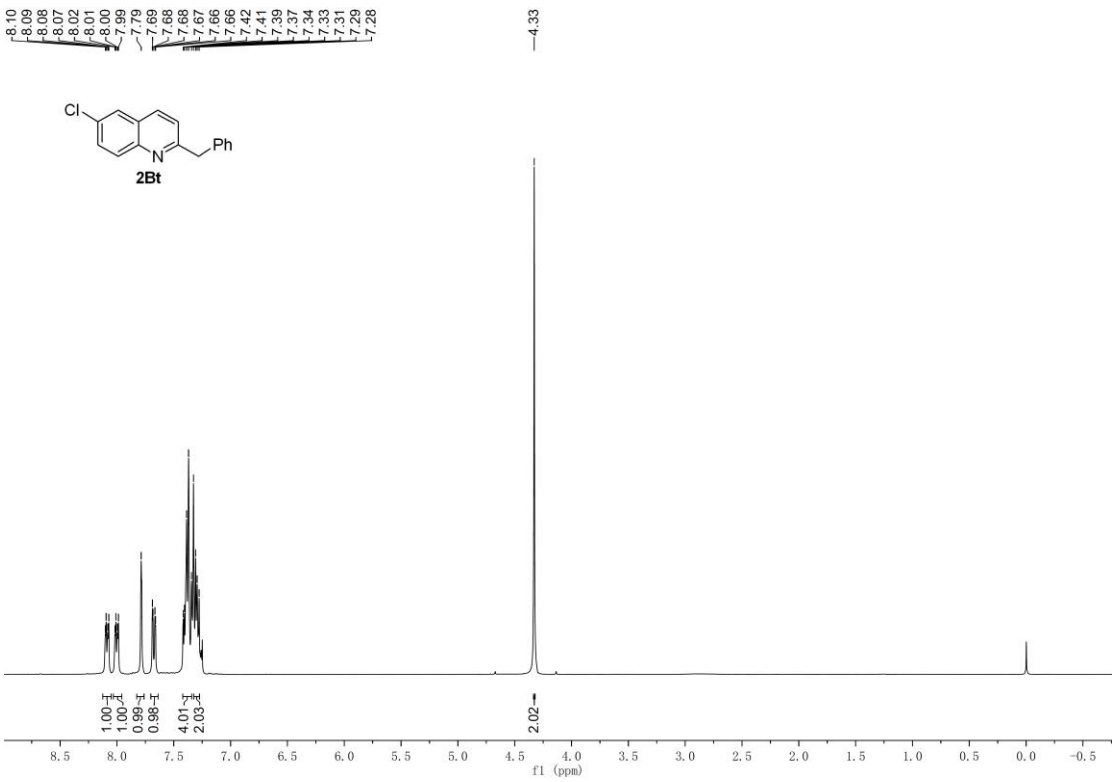
^{13}C NMR (151 MHz) spectrum of **2Br** in $CDCl_3$



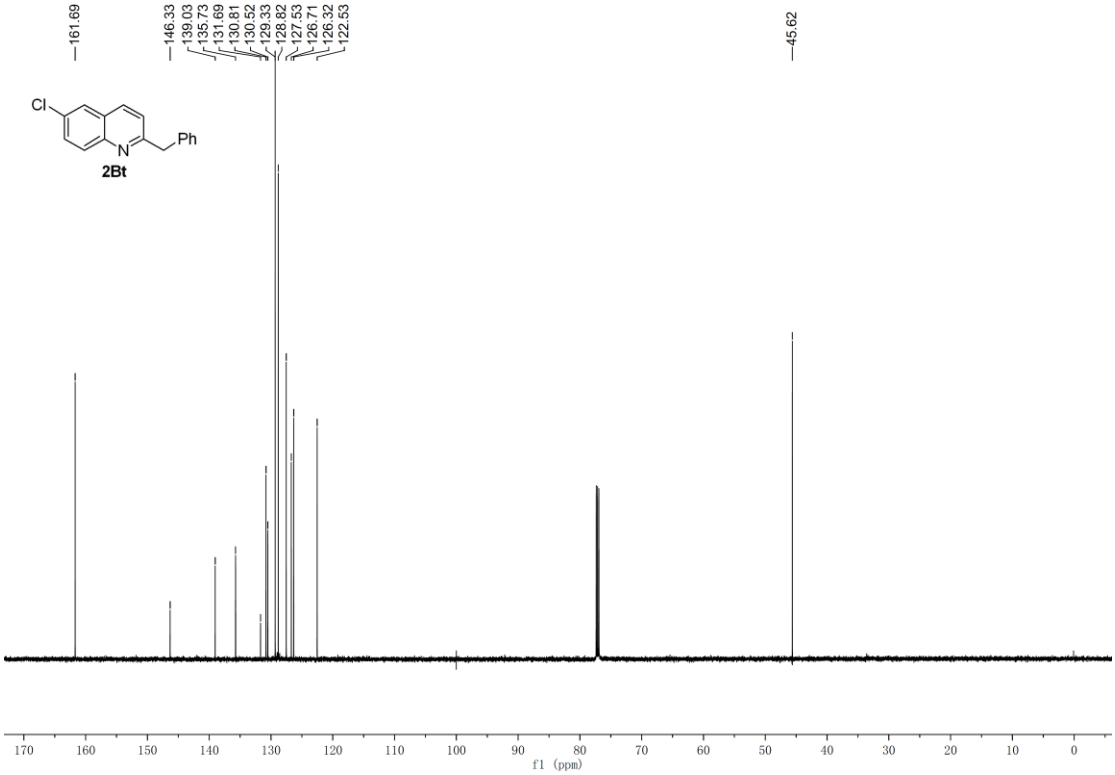
^{1}H NMR (400 MHz) spectrum of **2Bs** in $CDCl_3$



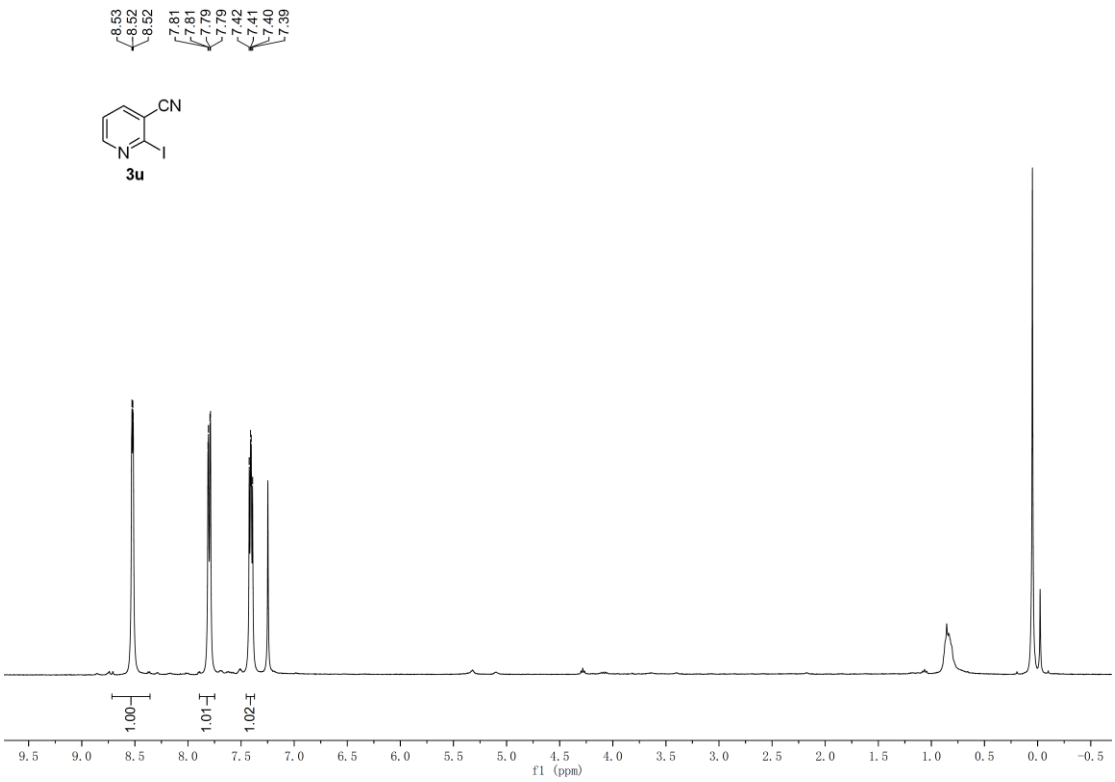
^{13}C NMR (101 MHz) spectrum of **2Bs** in $CDCl_3$



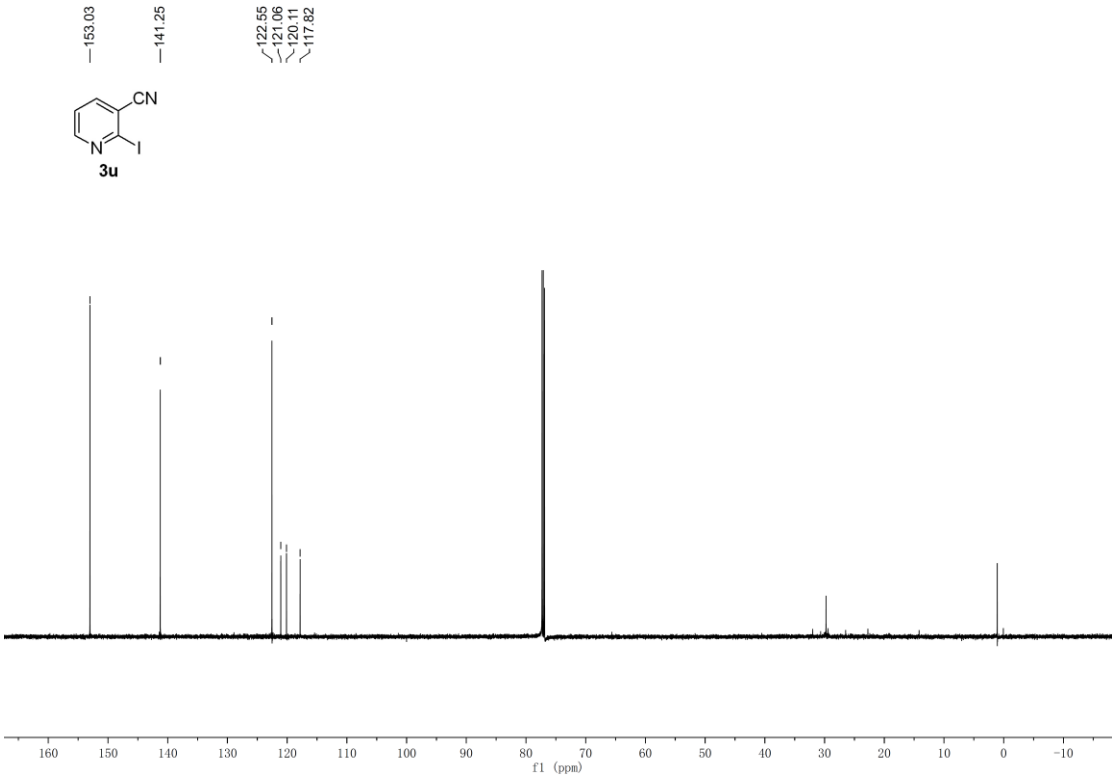
^{1}H NMR (400 MHz) spectrum of **2Bt** in $CDCl_3$



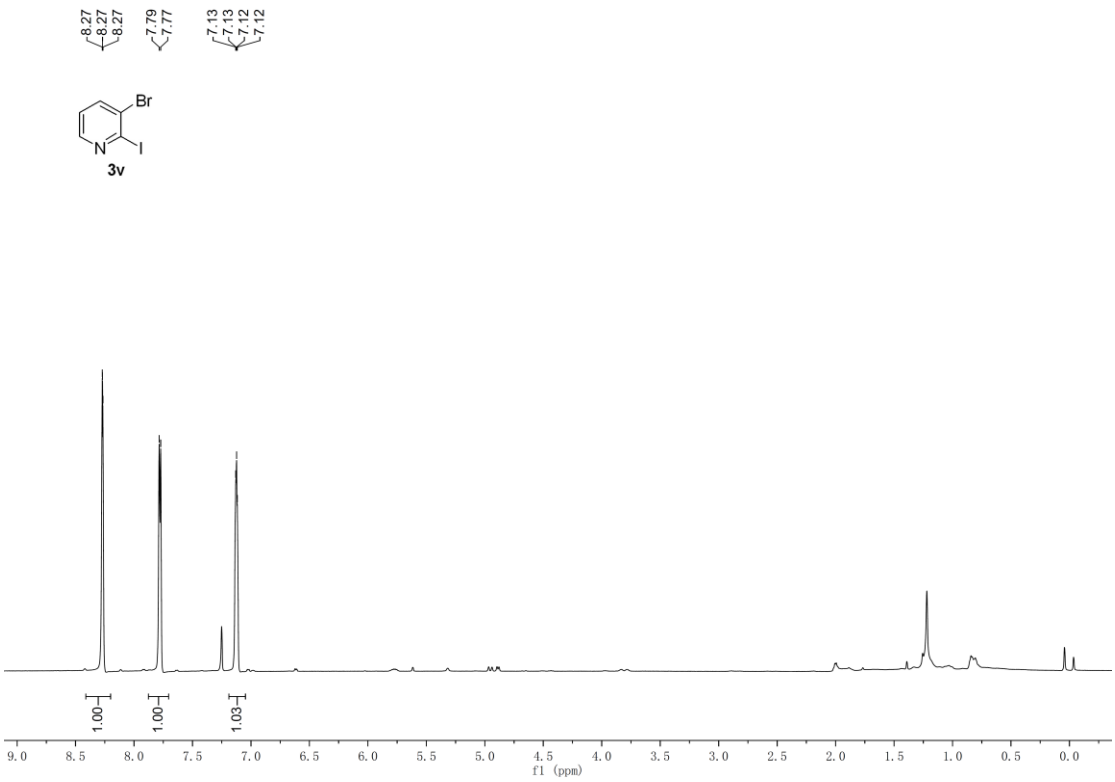
^{13}C NMR (101 MHz) spectrum of **2Bt** in $CDCl_3$



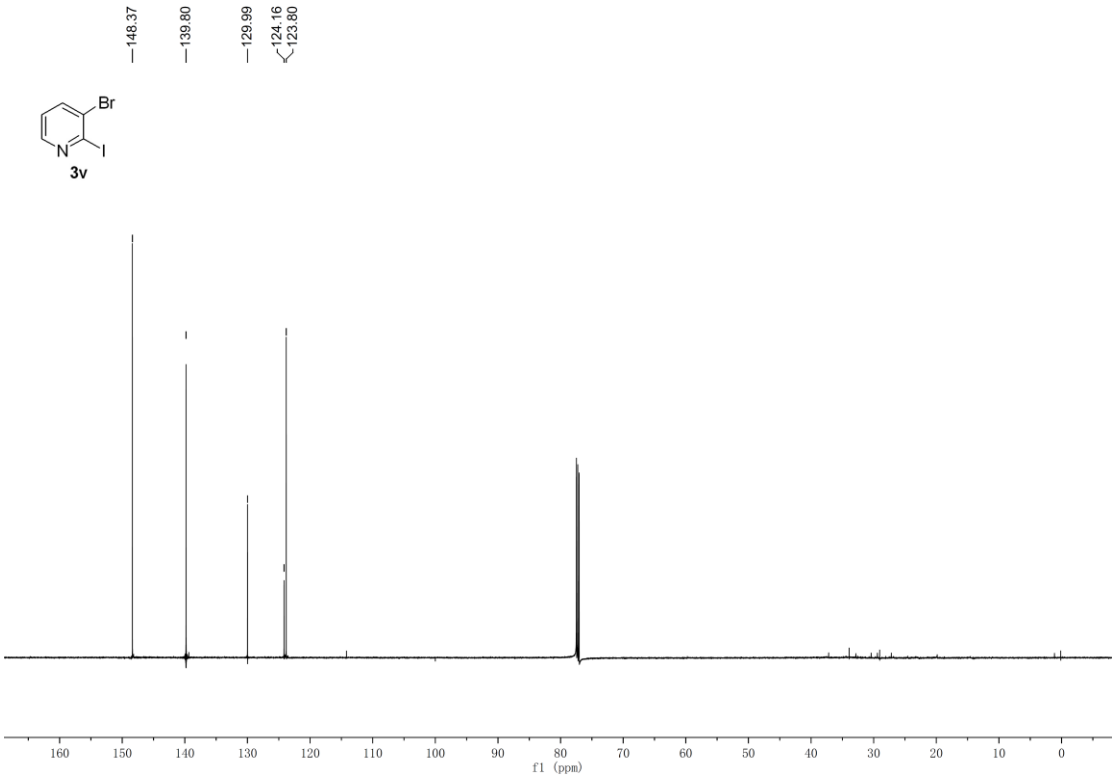
^{1}H NMR (400 MHz) spectrum of **3u** in $CDCl_3$



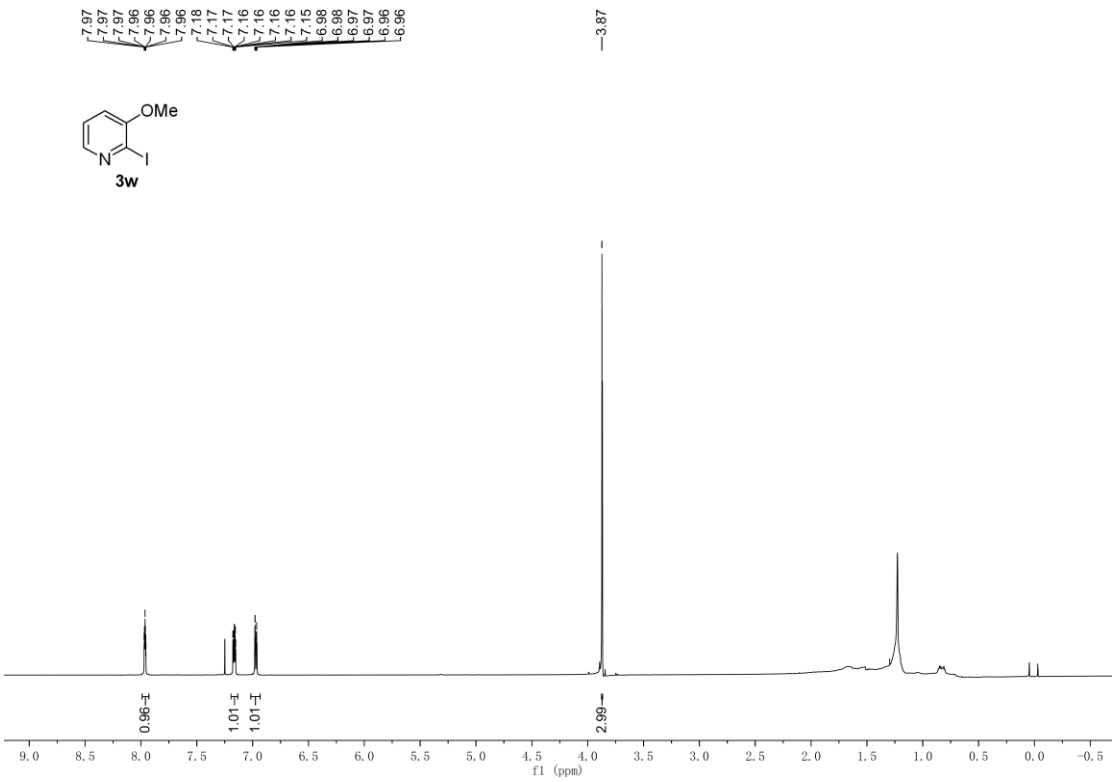
^{13}C NMR (151 MHz) spectrum of **3u** in $CDCl_3$



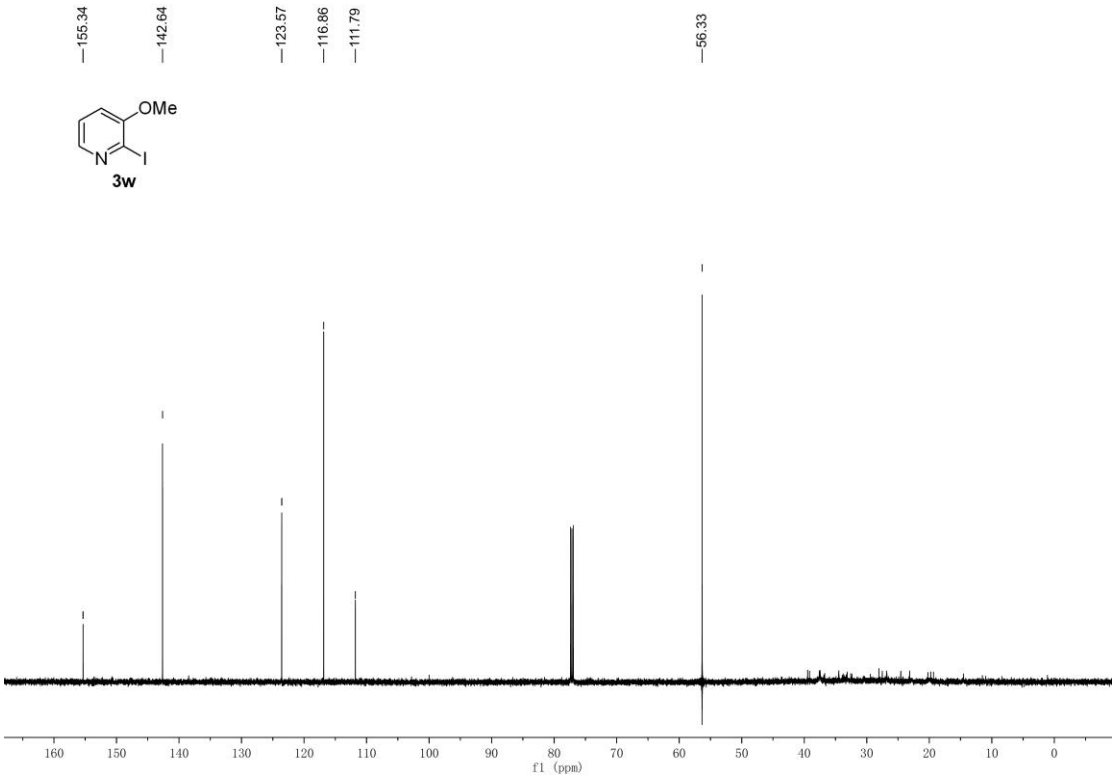
^{1}H NMR (600 MHz) spectrum of **3v** in $CDCl_3$



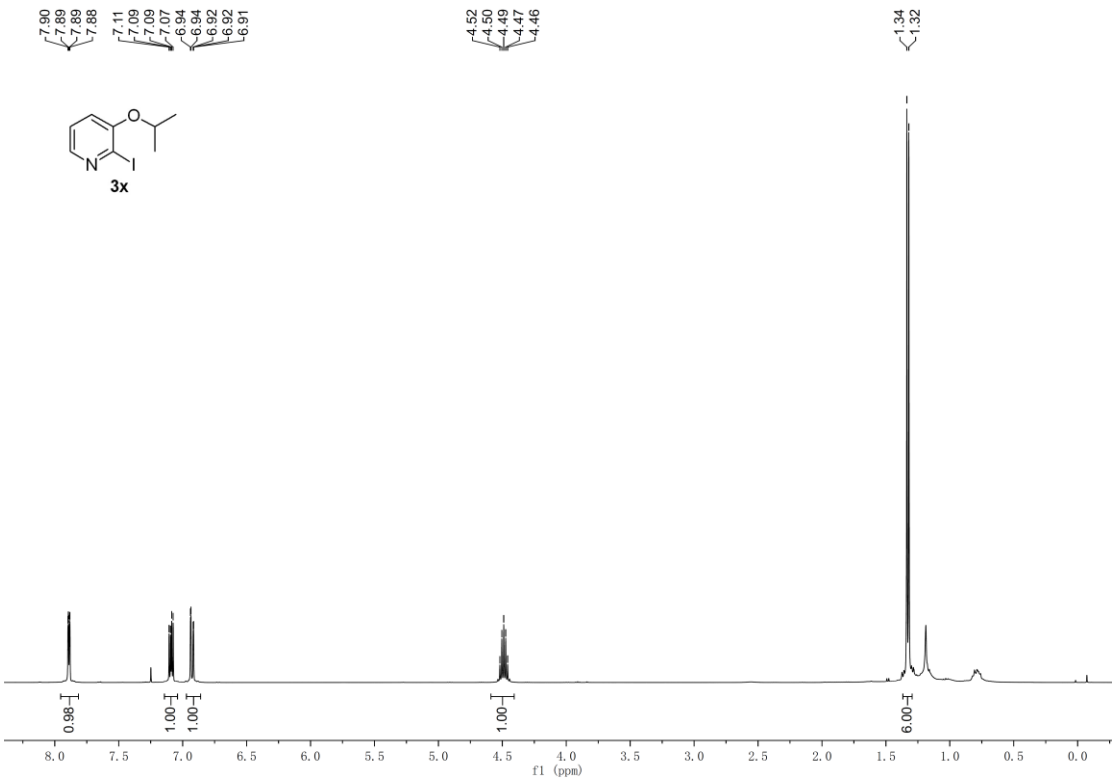
^{13}C NMR (151 MHz) spectrum of **3v** in $CDCl_3$



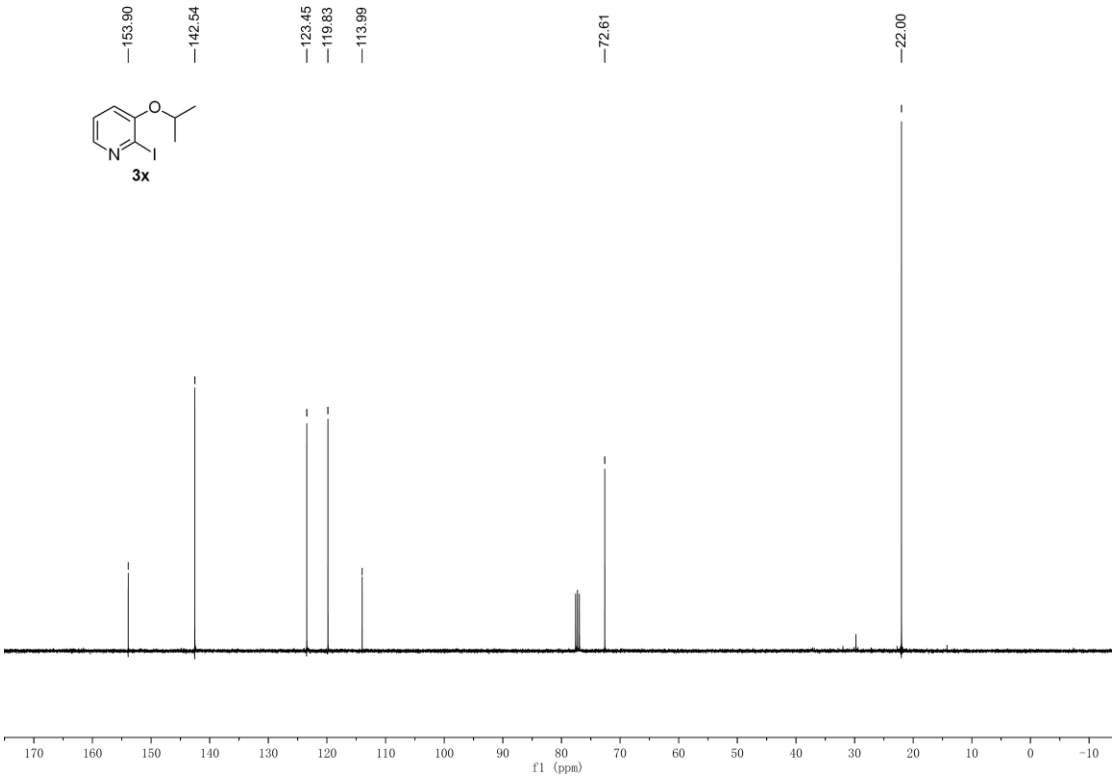
^{1}H NMR (400 MHz) spectrum of **3w** in $CDCl_3$



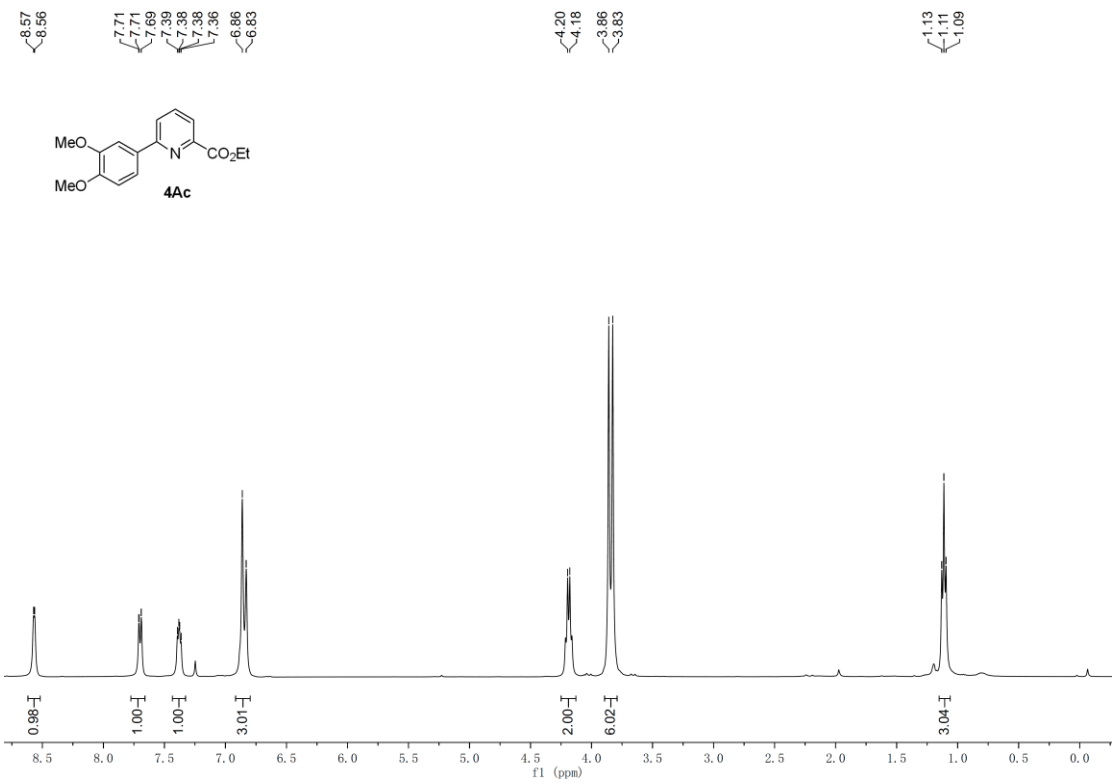
^{13}C NMR (151 MHz) spectrum of **3w** in $CDCl_3$



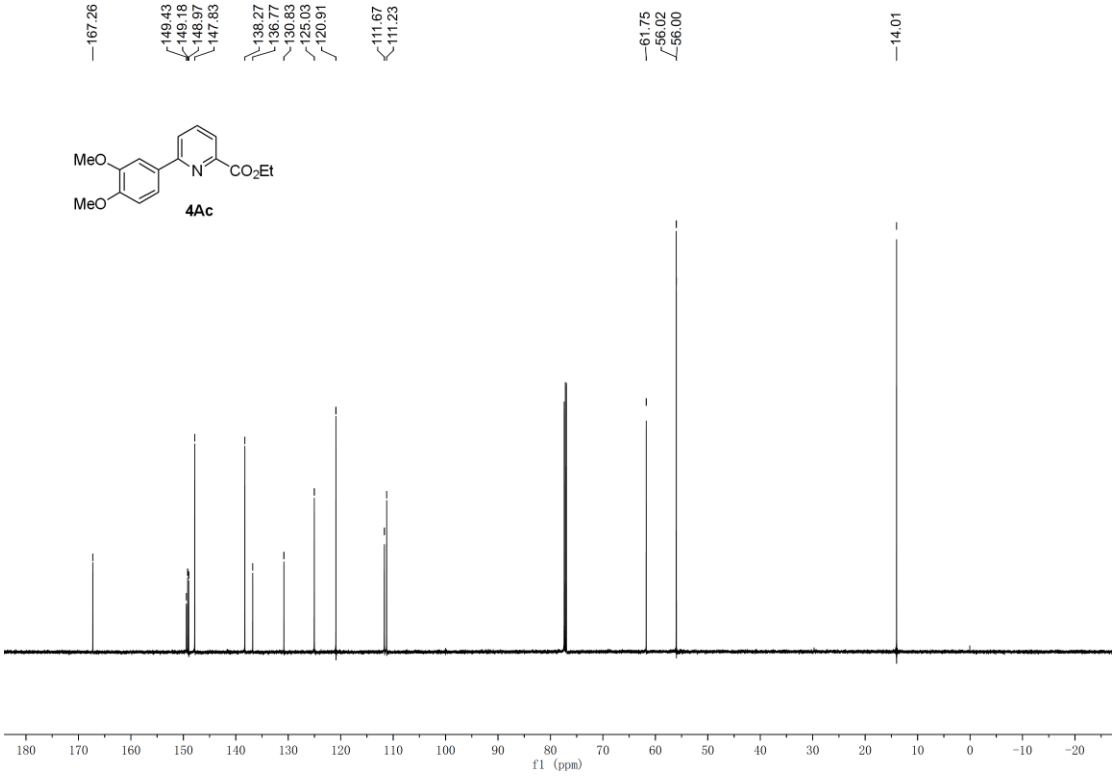
^{1}H NMR (400 MHz) spectrum of **3x** in $CDCl_3$



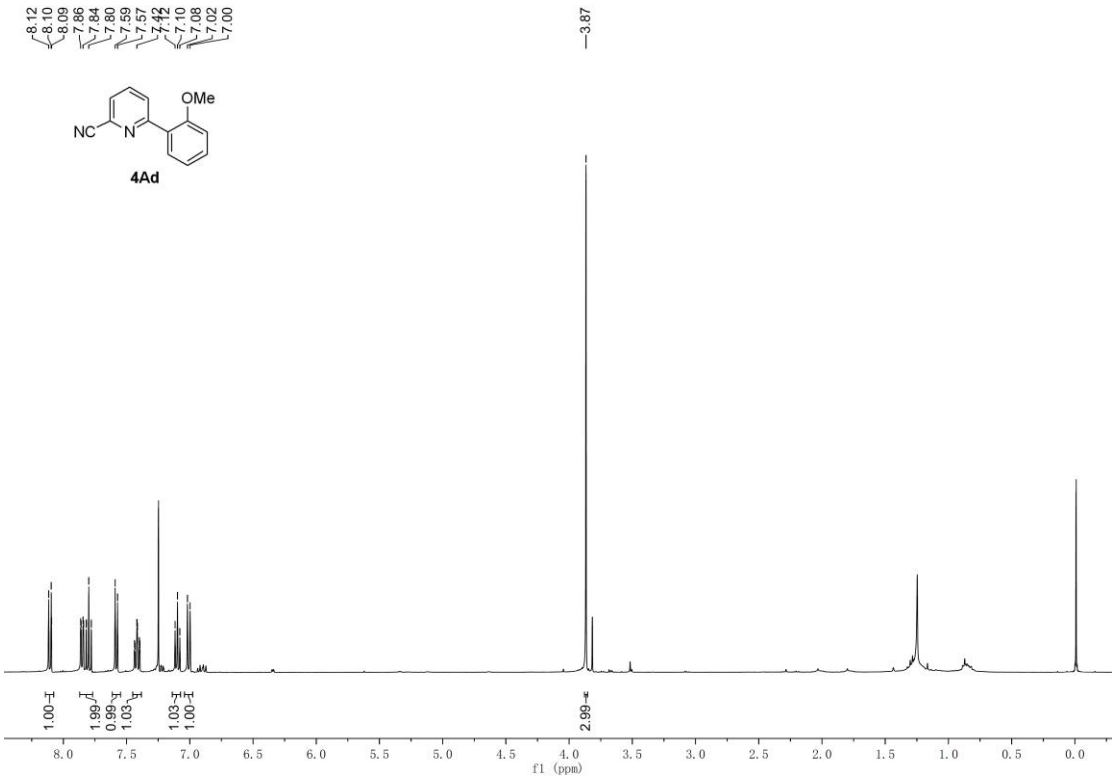
^{13}C NMR (151 MHz) spectrum of **3x** in CDCl



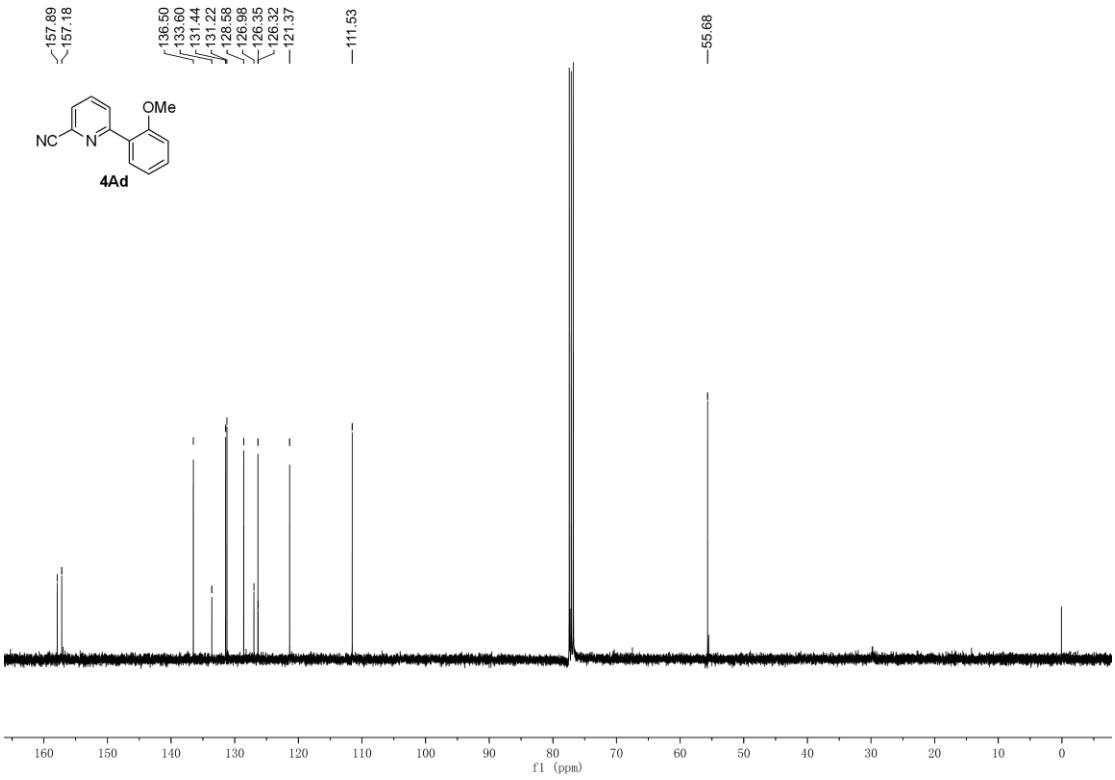
^{1}H NMR (400 MHz) spectrum of **4Ac** in $CDCl_3$



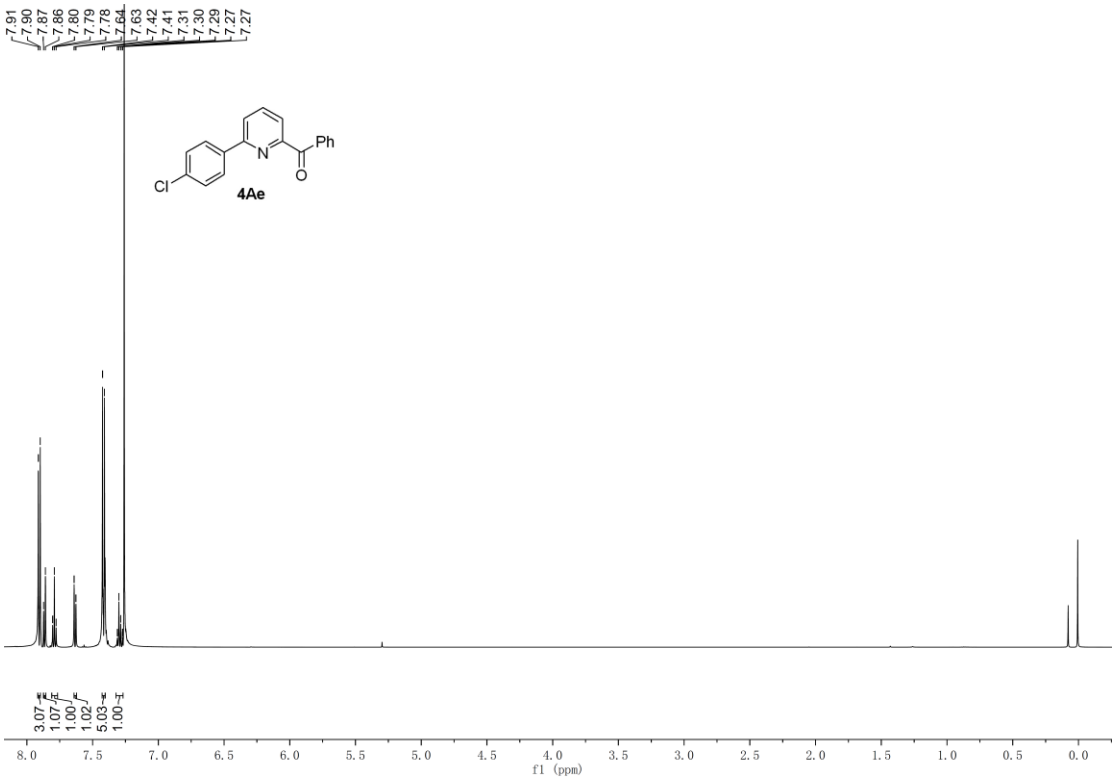
^{13}C NMR (151 MHz) spectrum of **4Ac** in $CDCl_3$



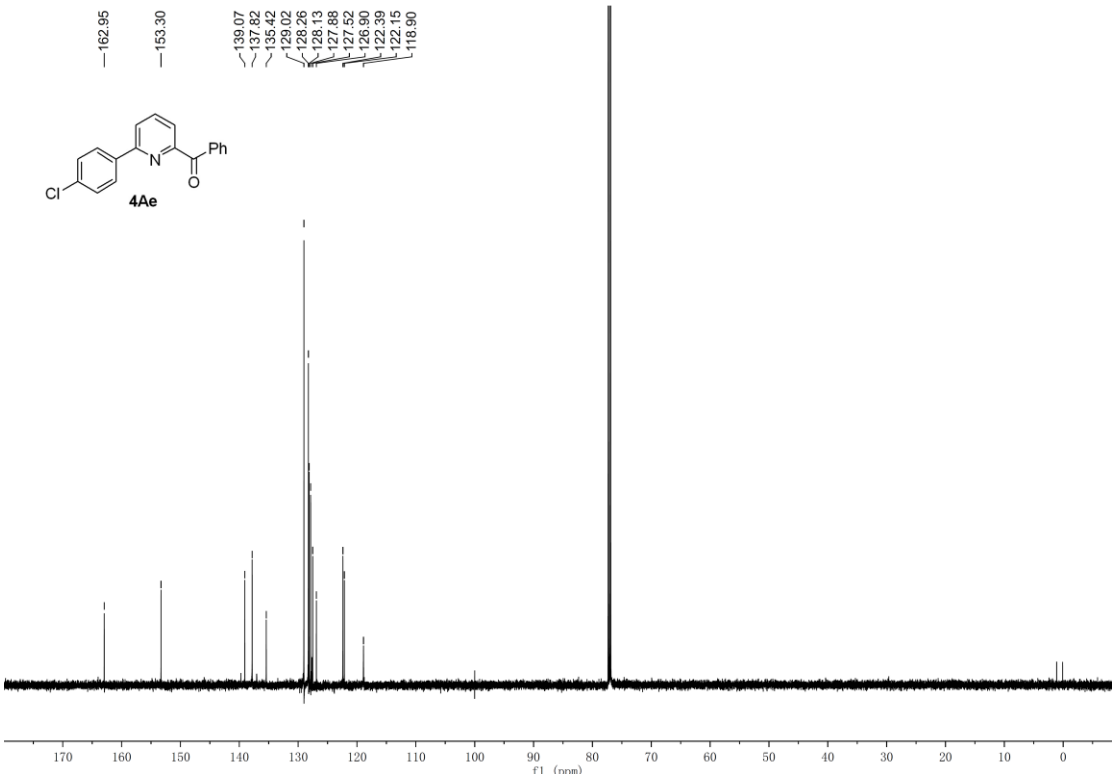
^{1}H NMR (400 MHz) spectrum of **4Ad** in $CDCl_3$



^{13}C NMR (101 MHz) spectrum of **4Ad** in $CDCl_3$

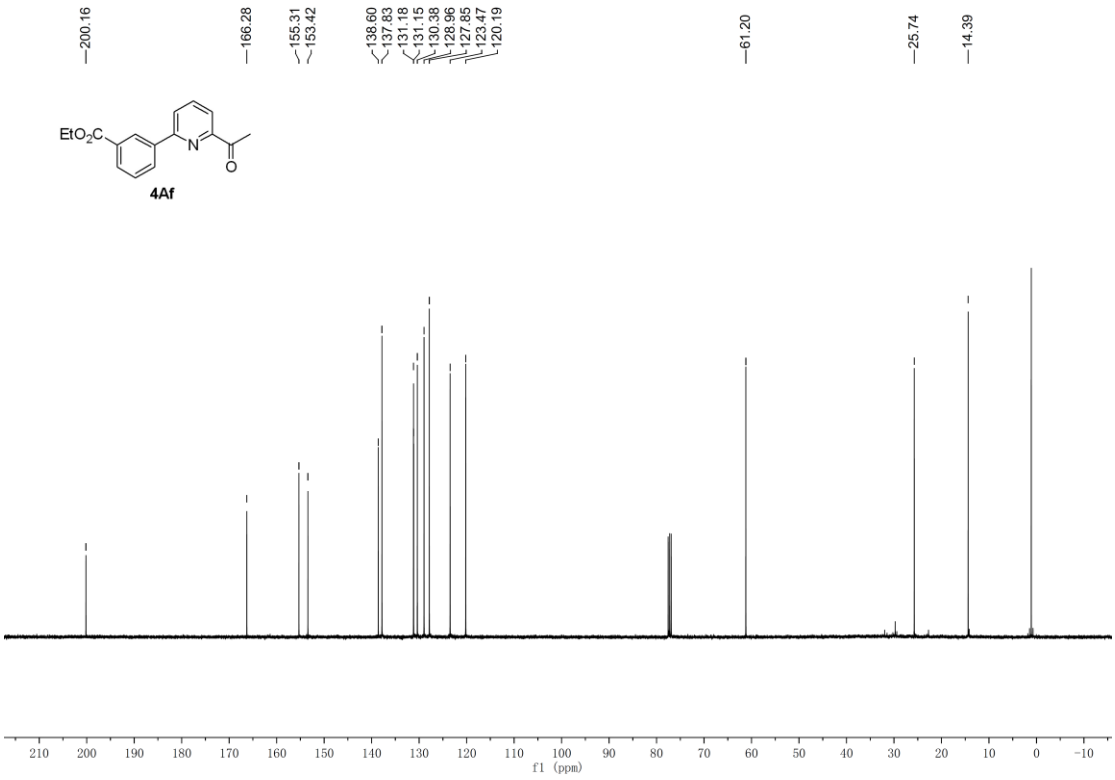


^{1}H NMR (600 MHz) spectrum of **4Ae** in $CDCl_3$

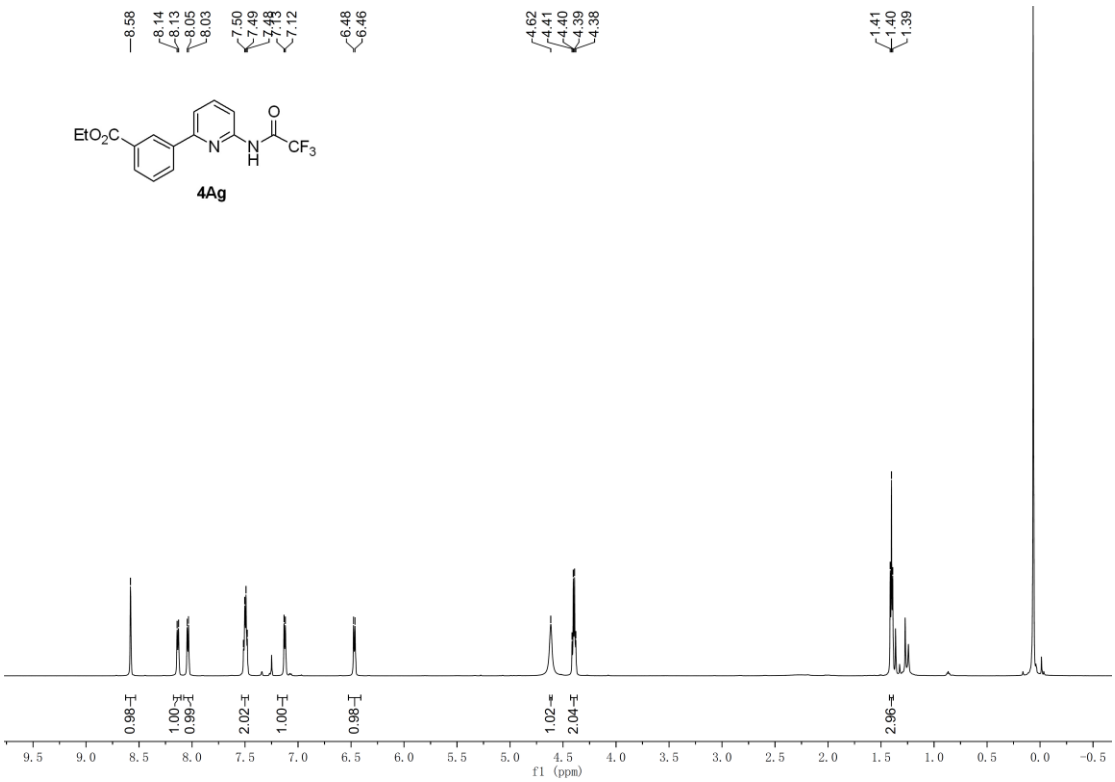


^{13}C NMR (151 MHz) spectrum of **4Ae** in $CDCl_3$

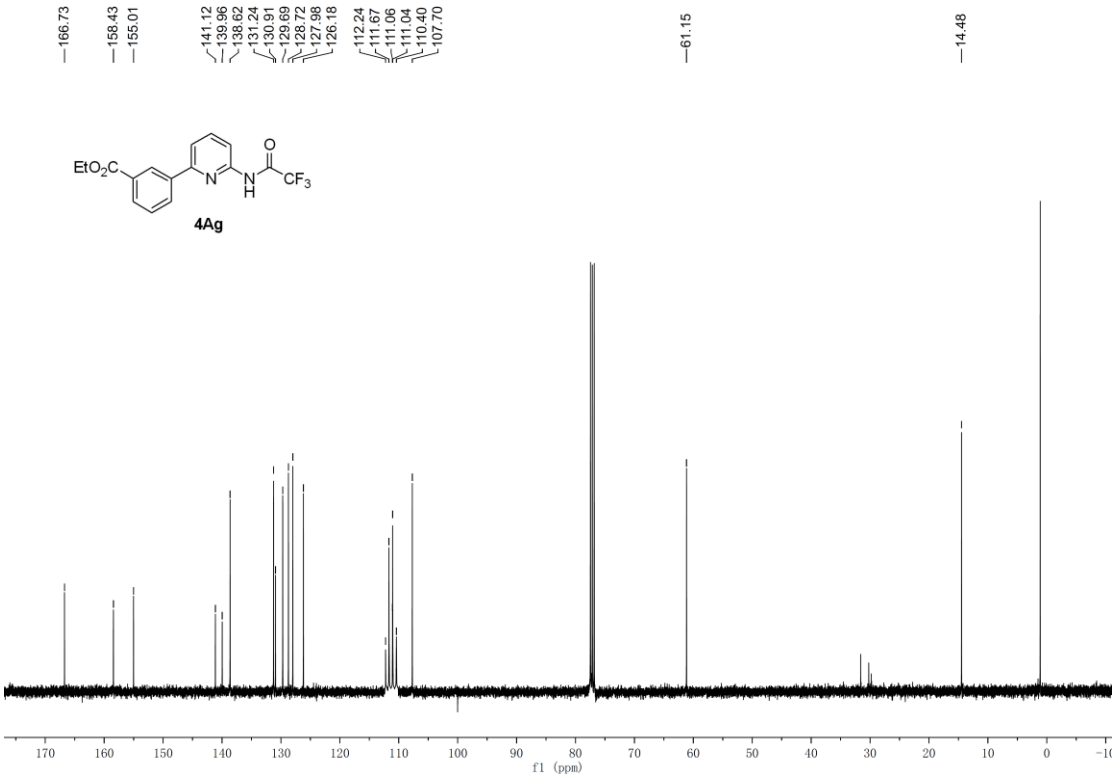
^{1}H NMR (400 MHz) spectrum of **4Af** in $CDCl_3$



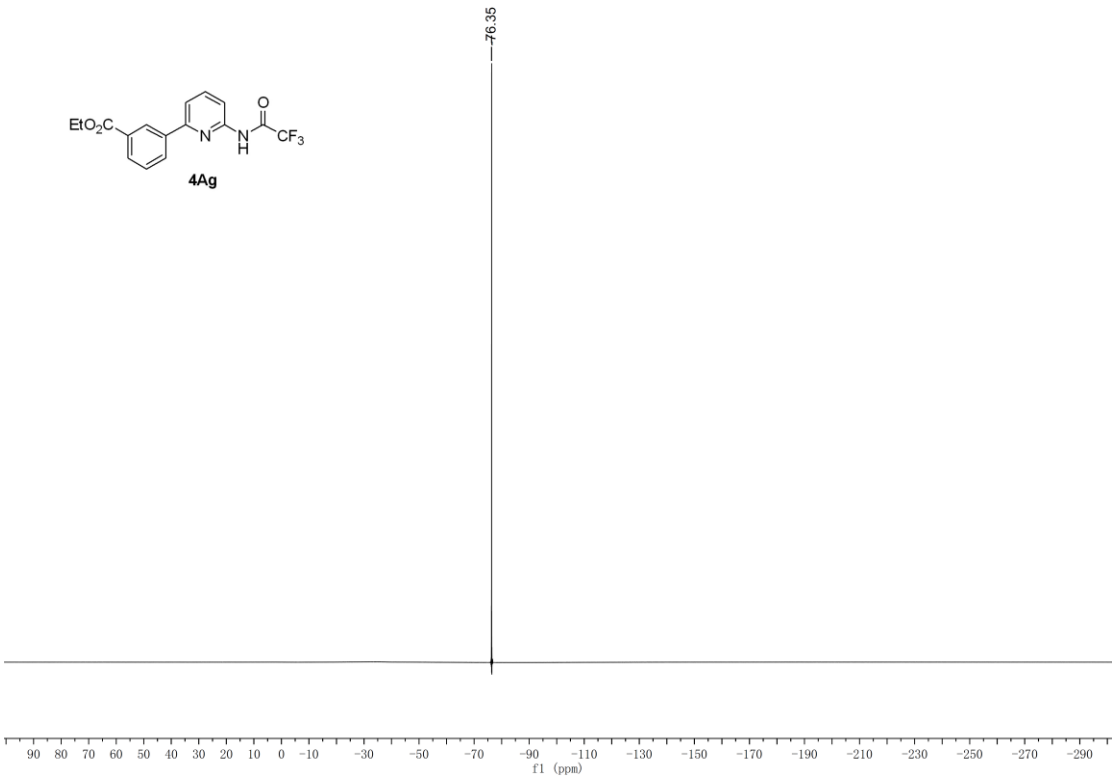
^{13}C NMR (101 MHz) spectrum of **4Af** in $CDCl_3$



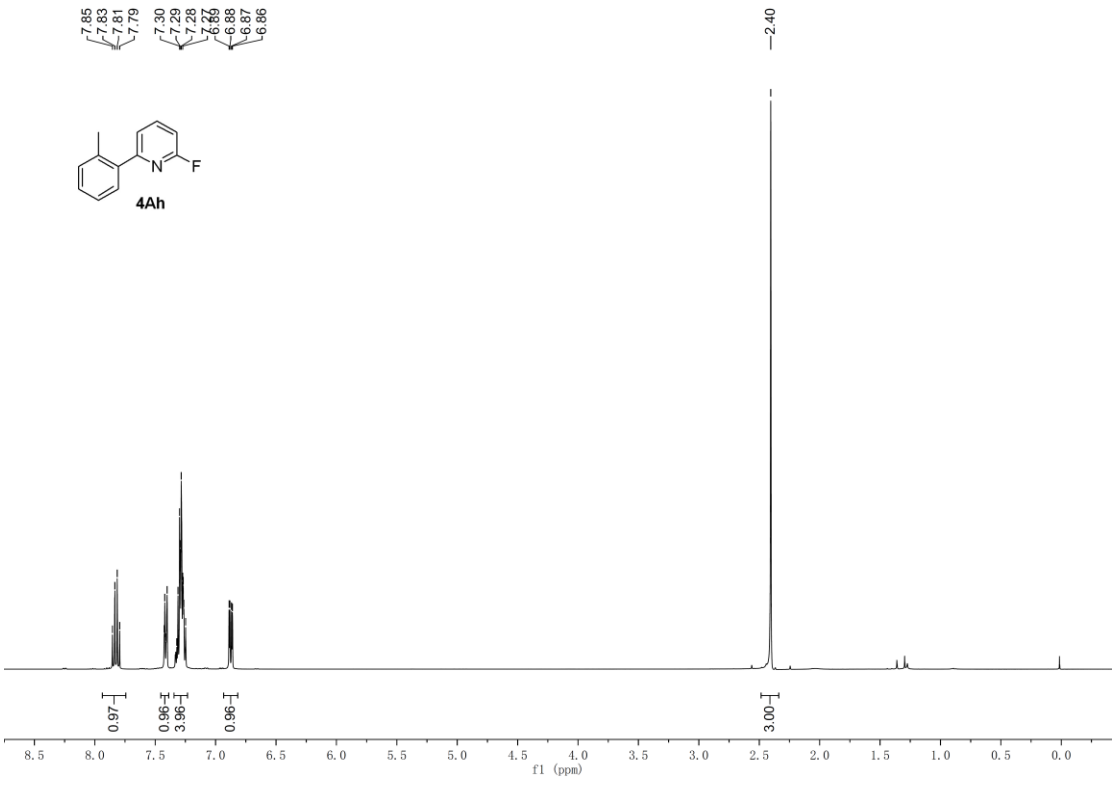
^{1}H NMR (400 MHz) spectrum of **4Ag** in $CDCl_3$



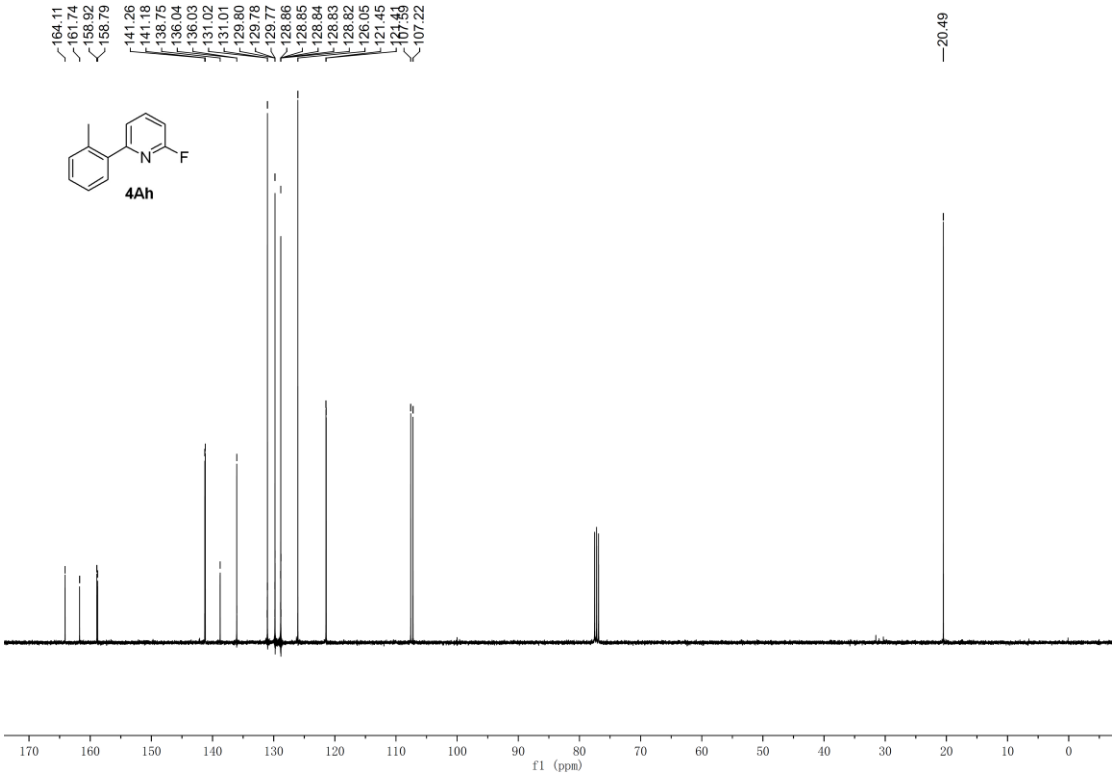
^{13}C NMR (101 MHz) spectrum of **4Ag** in $CDCl_3$



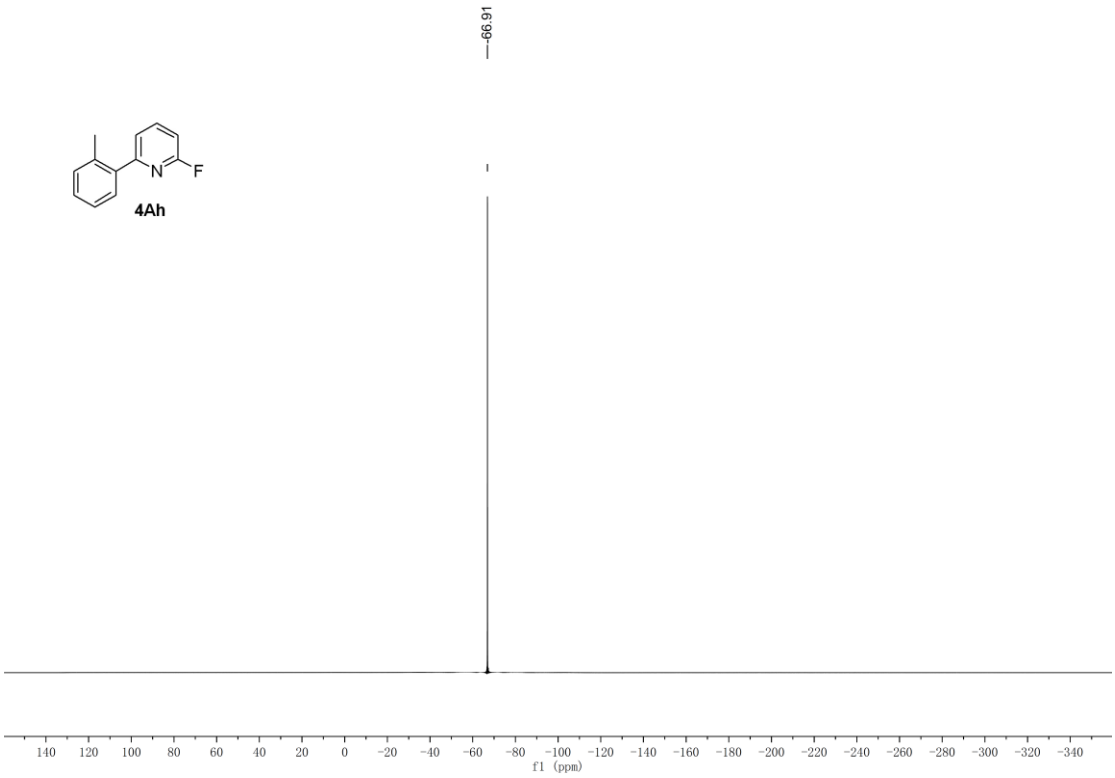
^{19}F NMR (376 MHz) spectrum of **4Ag** in $CDCl_3$



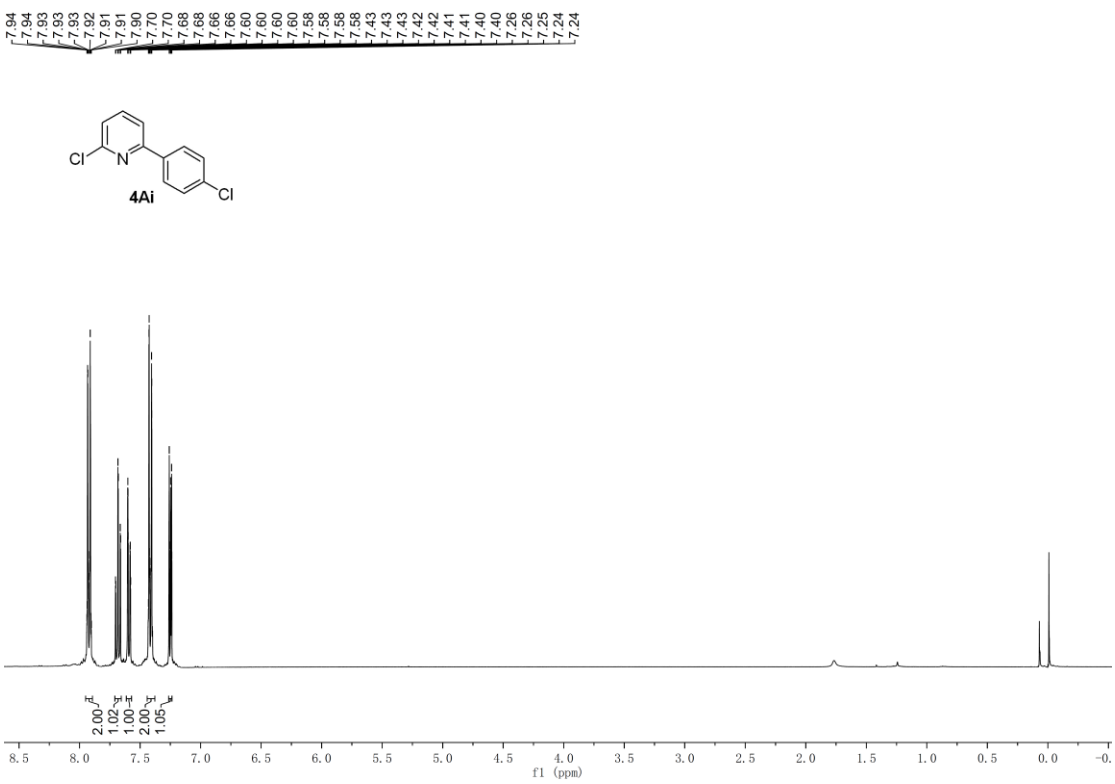
^{1}H NMR (400 MHz) spectrum of **4Ah** in $CDCl_3$



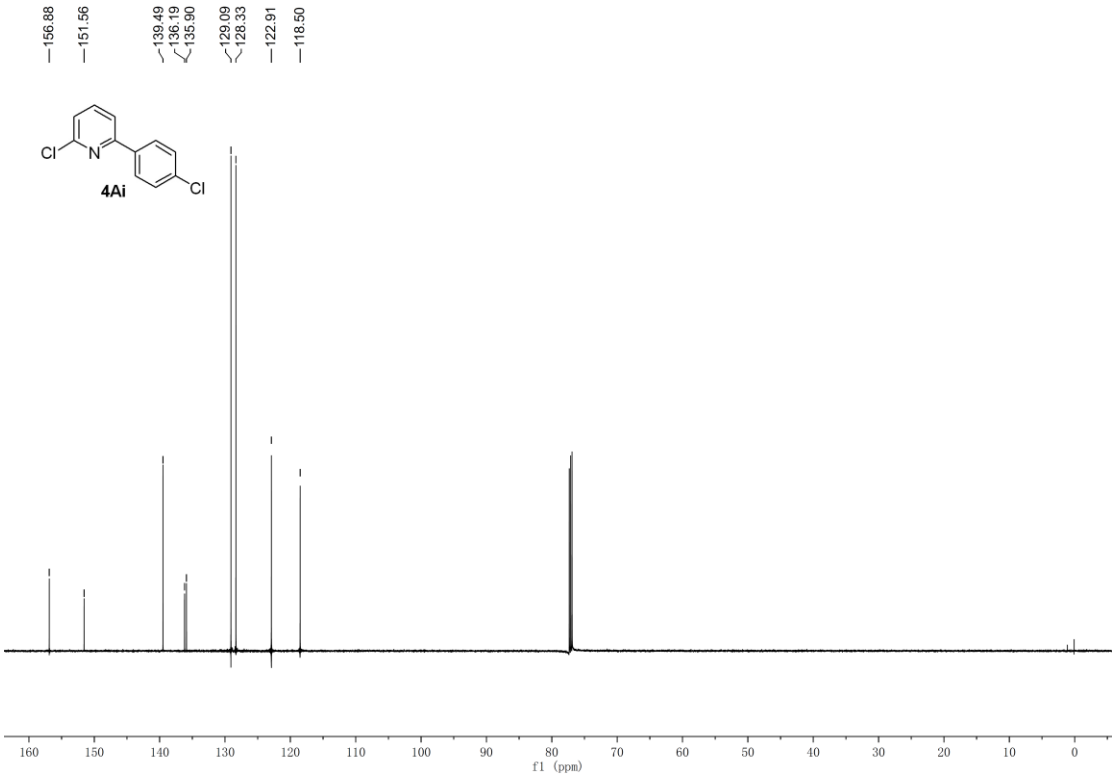
^{13}C NMR (101 MHz) spectrum of **4Ah** in $CDCl_3$



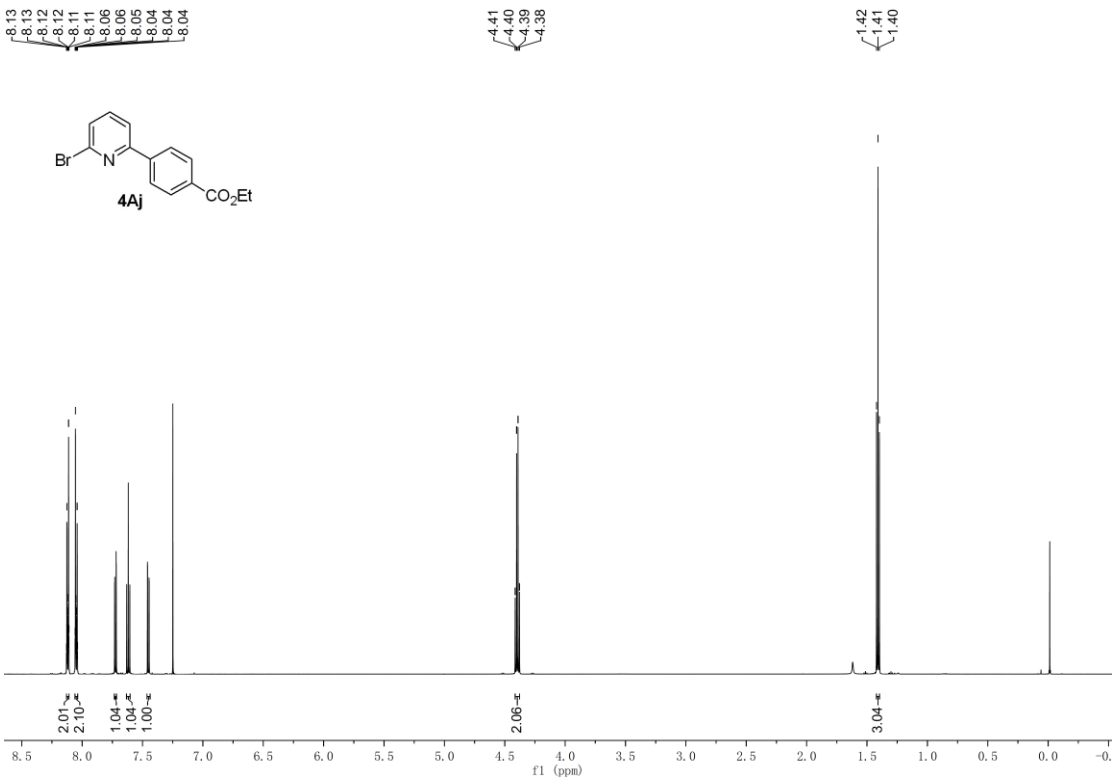
^{19}F NMR (376 MHz) spectrum of **4Ah** in $CDCl_3$



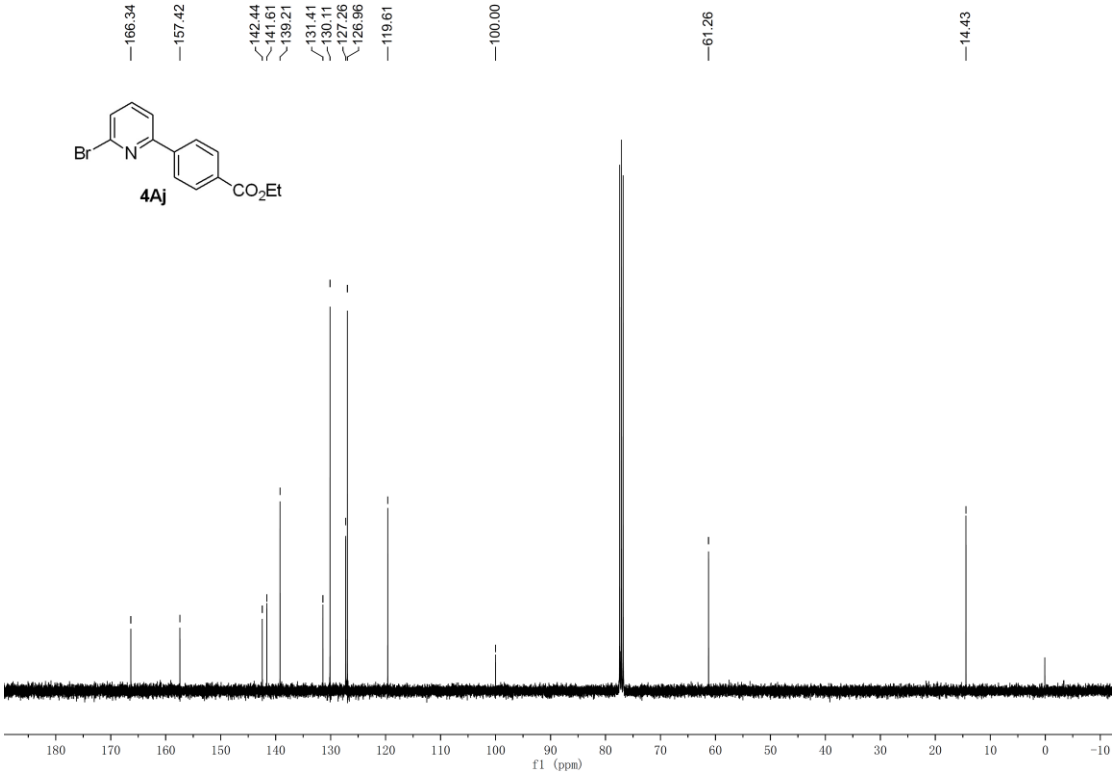
^{1}H NMR (400 MHz) spectrum of **4Ai** in $CDCl_3$



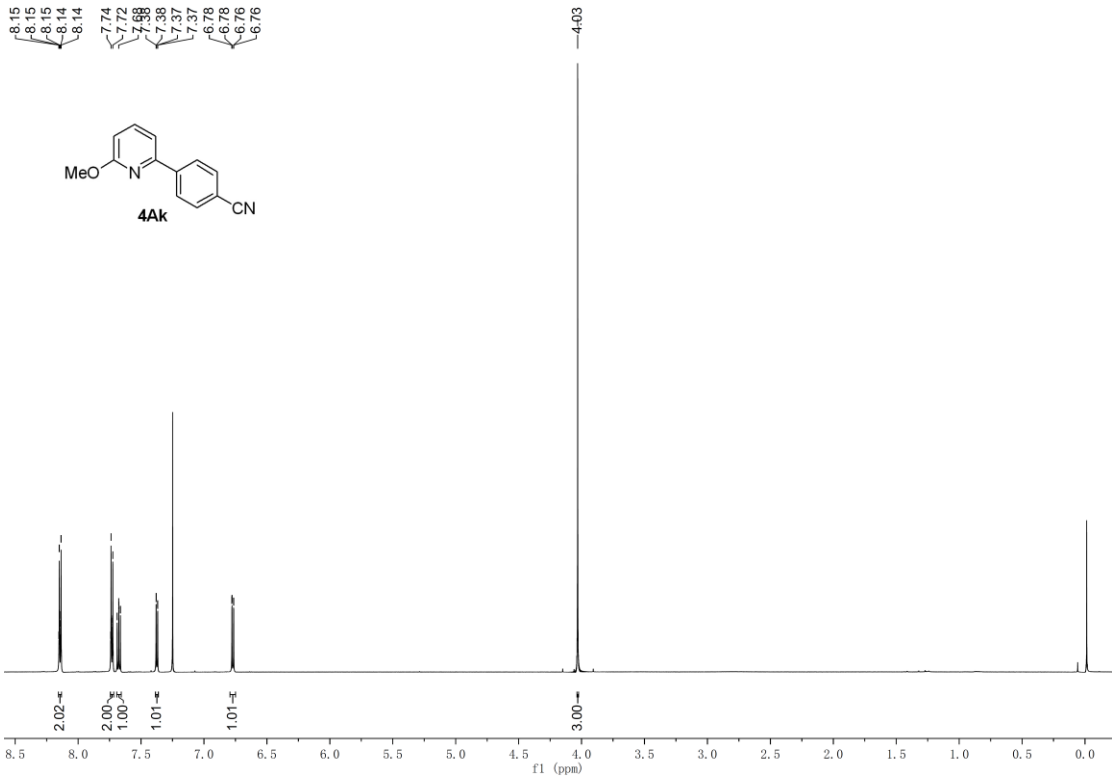
^{13}C NMR (151 MHz) spectrum of **4Ai** in $CDCl_3$



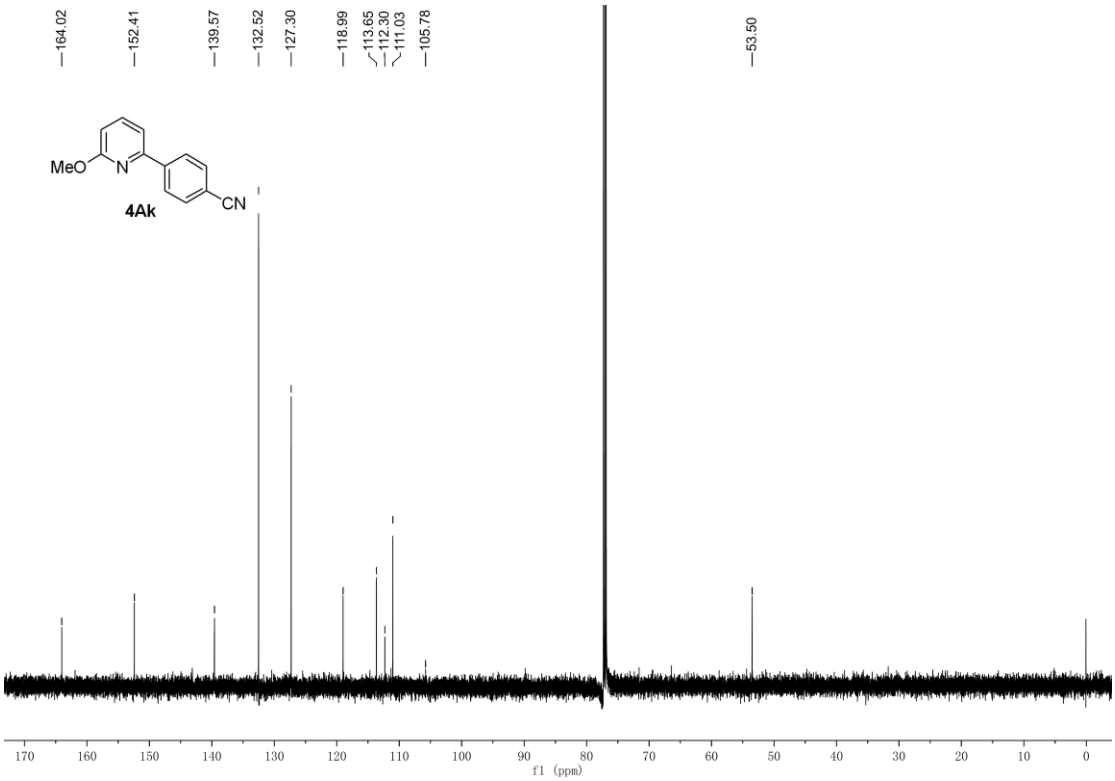
^{1}H NMR (600 MHz) spectrum of **4Aj** in $CDCl_3$



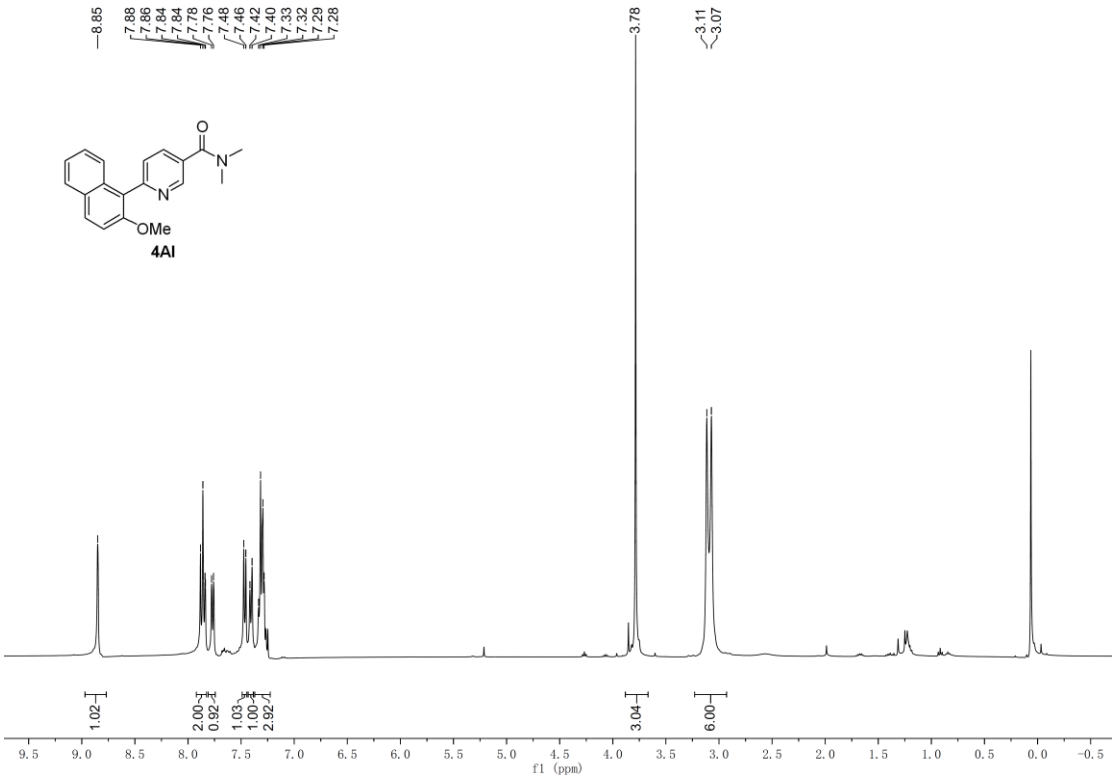
^{13}C NMR (101 MHz) spectrum of **4Aj** in $CDCl_3$



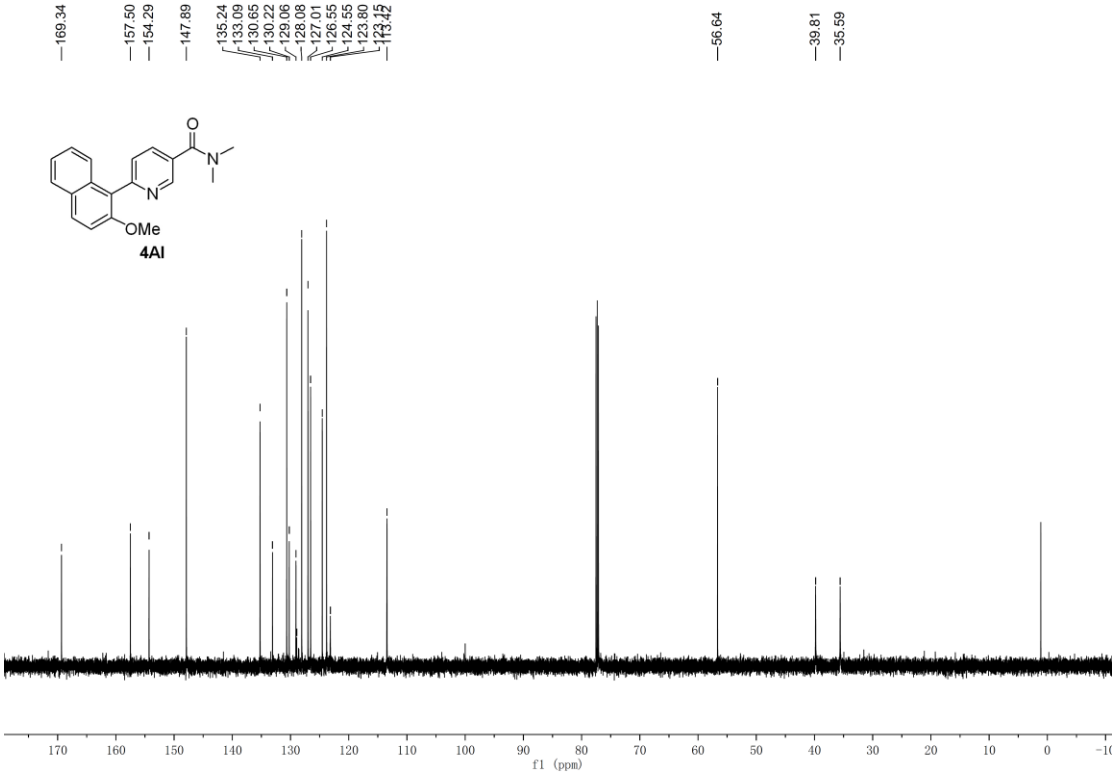
^{1}H NMR (600 MHz) spectrum of **4Ak** in $CDCl_3$



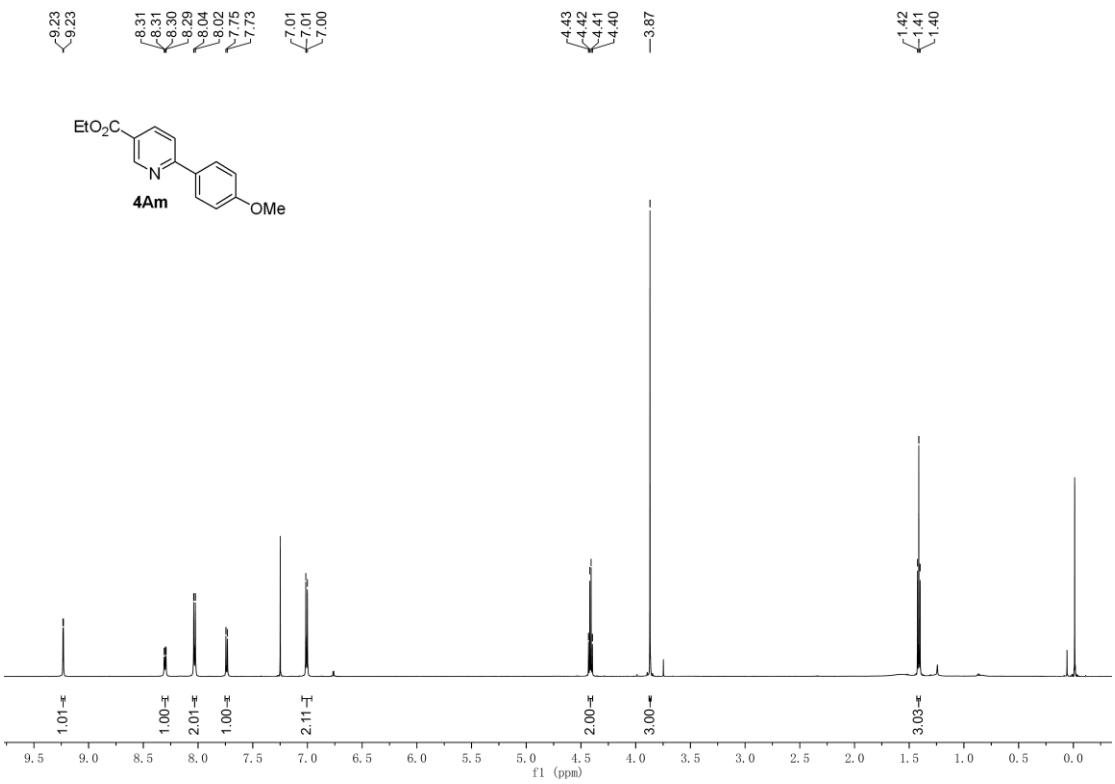
^{13}C NMR (151 MHz) spectrum of **4Ak** in $CDCl_3$



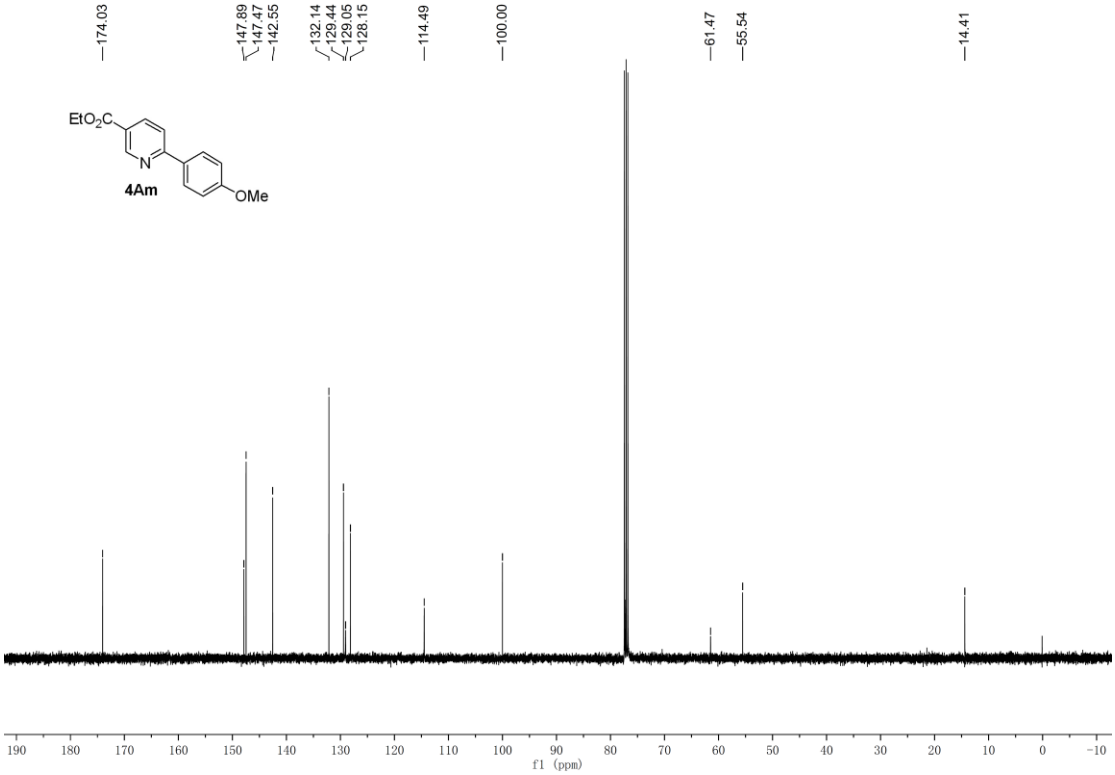
^{1}H NMR (400 MHz) spectrum of **4Al** in $CDCl_3$



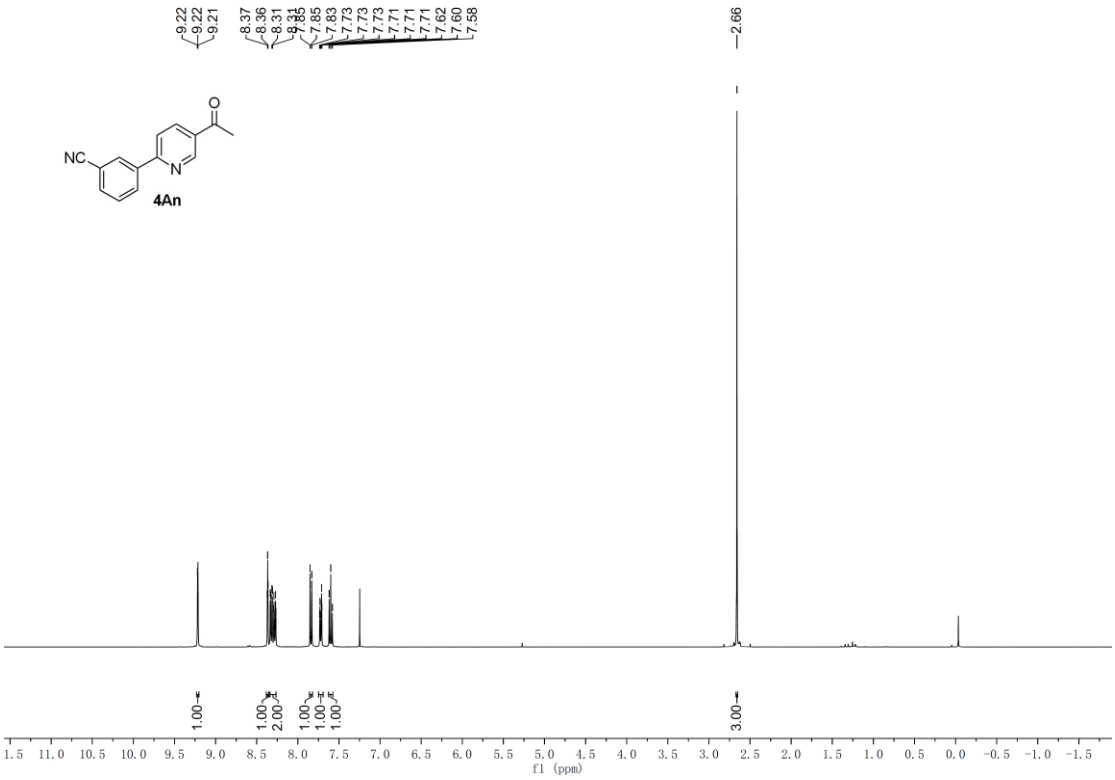
^{13}C NMR (151 MHz) spectrum of **4Al** in $CDCl_3$



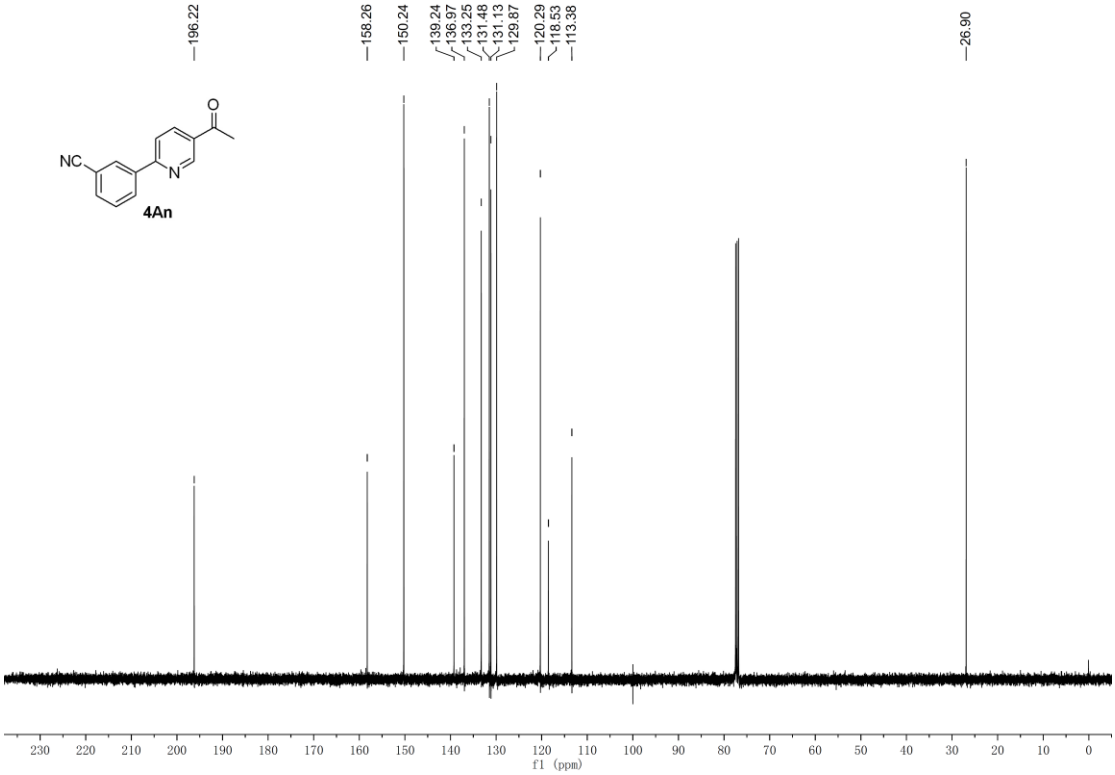
^{1}H NMR (600 MHz) spectrum of **4Am** in $CDCl_3$



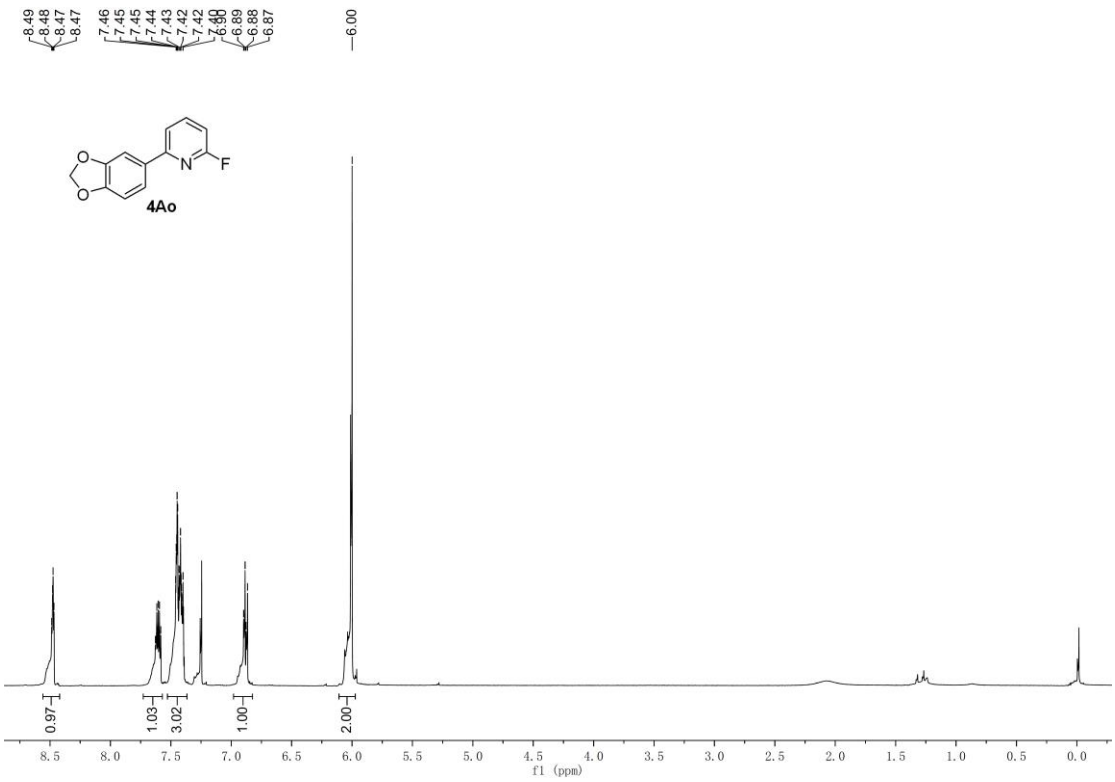
^{13}C NMR (101 MHz) spectrum of **4Am** in $CDCl_3$



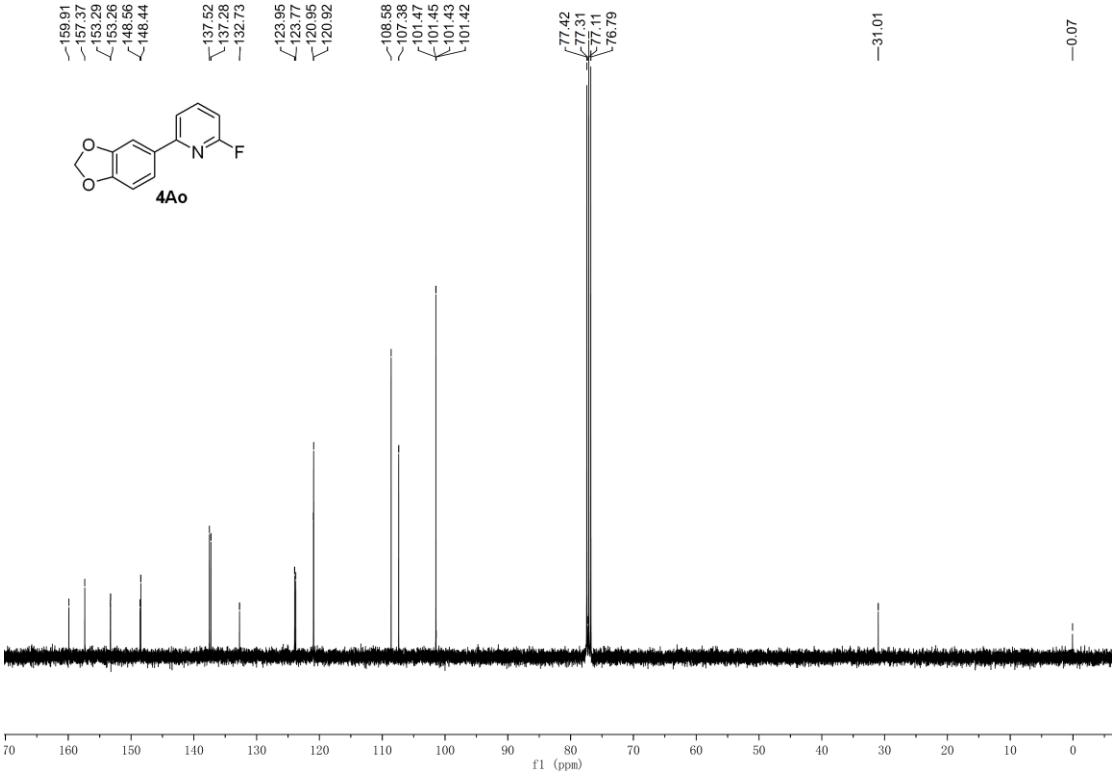
^{1}H NMR (400 MHz) spectrum of **4An** in $CDCl_3$



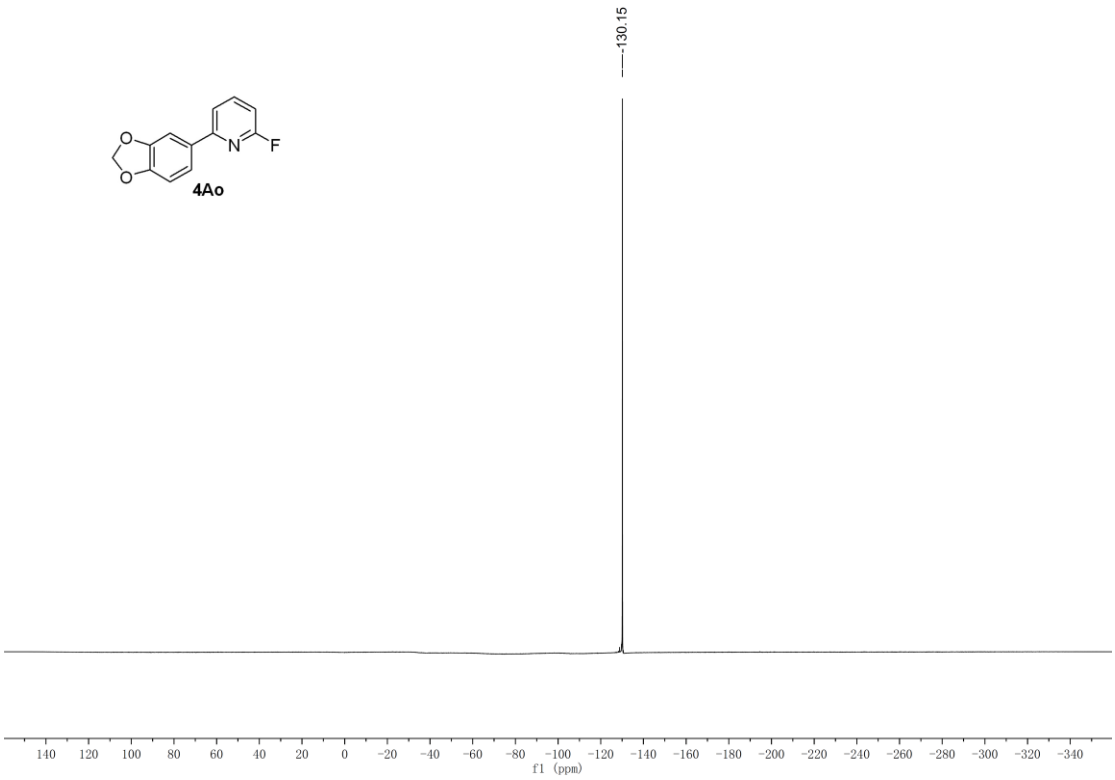
^{13}C NMR (101 MHz) spectrum of **4An** in $CDCl_3$



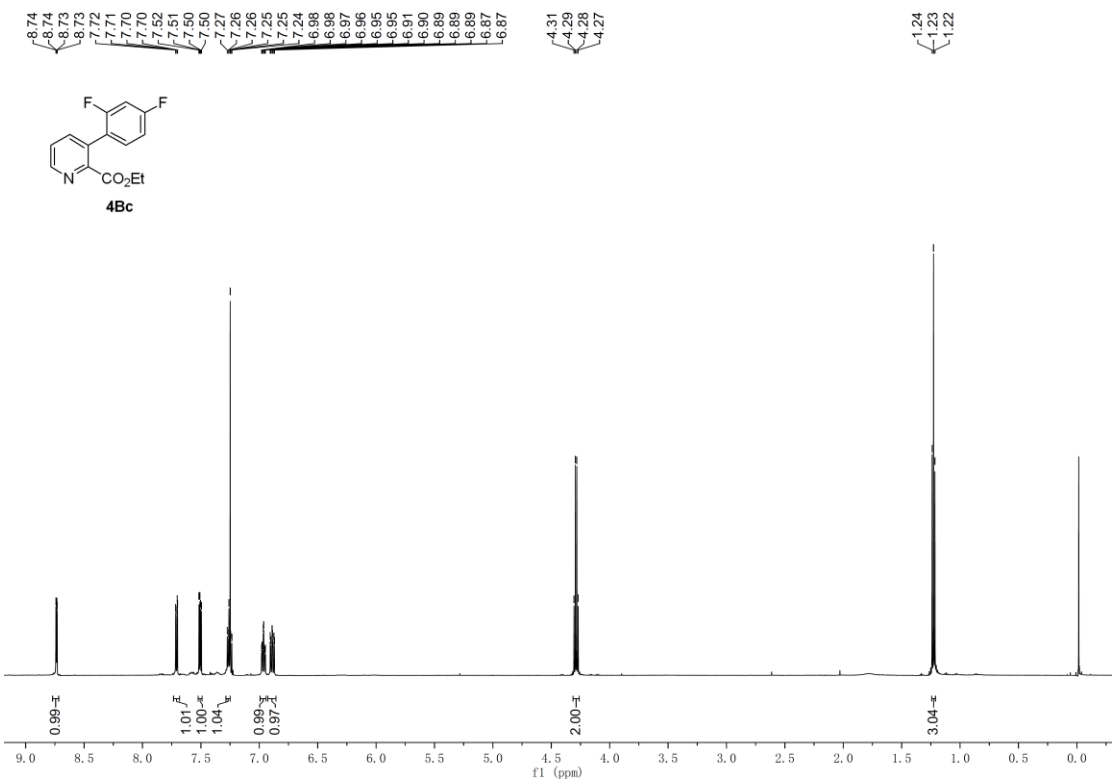
^{1}H NMR (400 MHz) spectrum of **4Ao** in $CDCl_3$



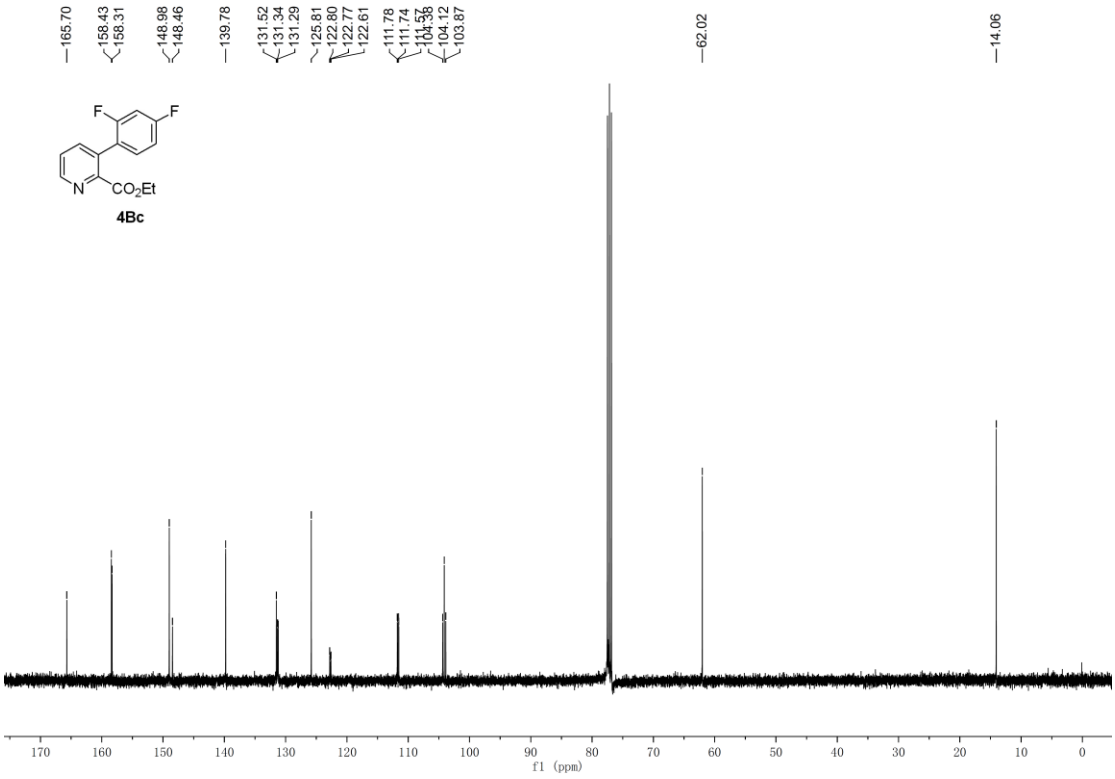
^{13}C NMR (101 MHz) spectrum of **4Ao** in $CDCl_3$



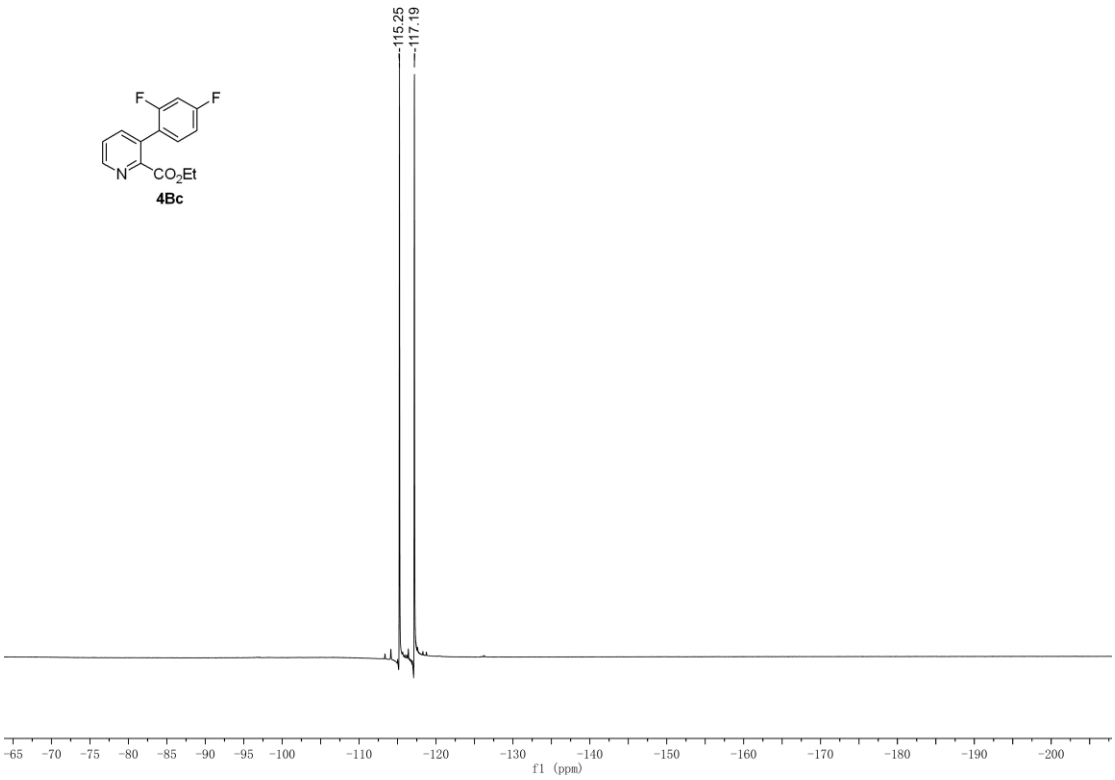
^{19}F NMR (376 MHz) spectrum of **4Ao** in $CDCl_3$



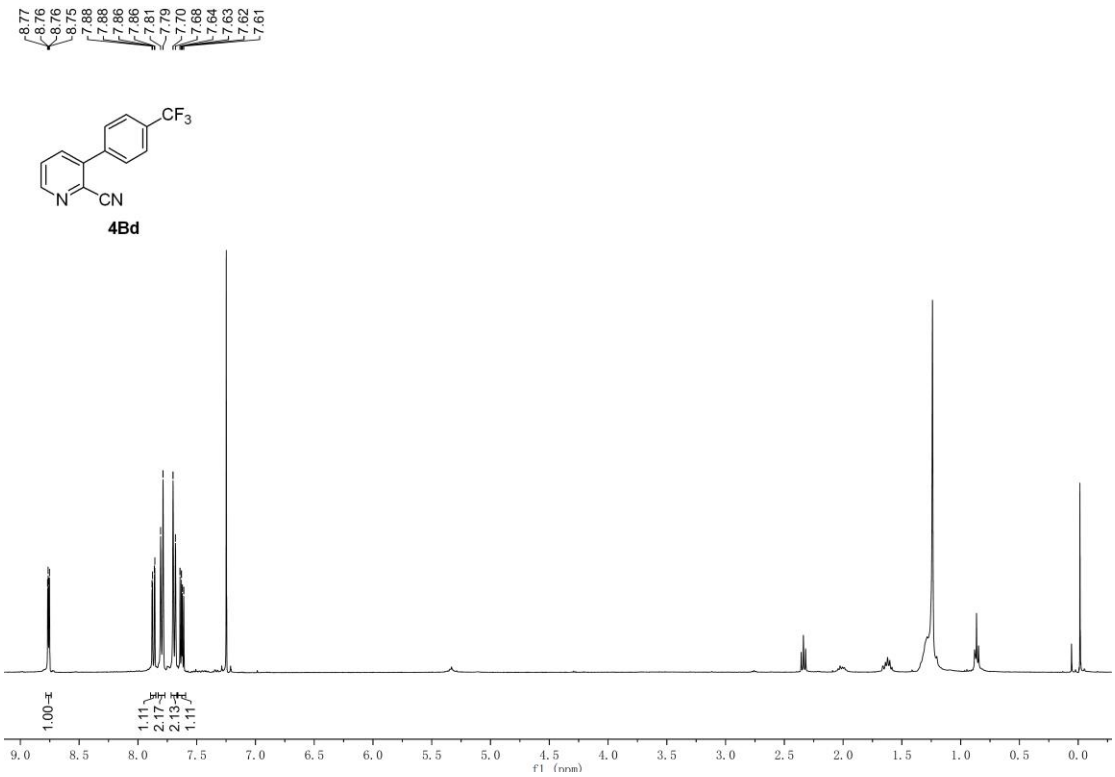
^{1}H NMR (600 MHz) spectrum of **4Bc** in $CDCl_3$



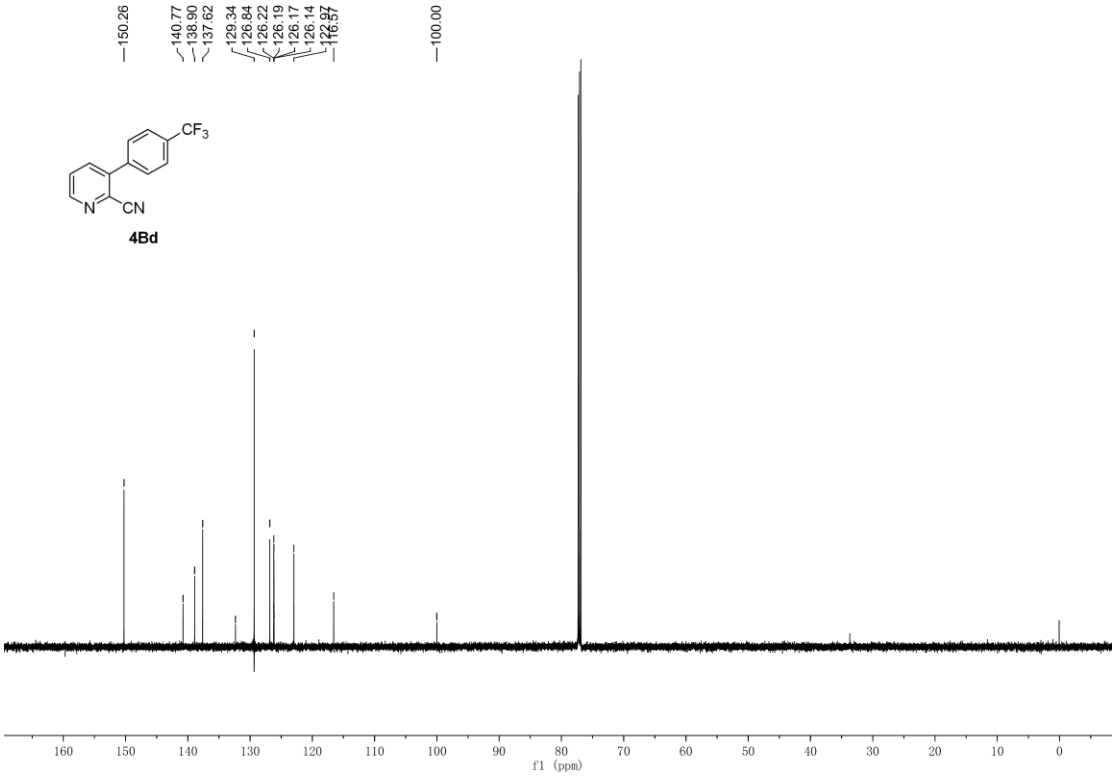
^{13}C NMR (151 MHz) spectrum of **4Bc** in $CDCl_3$



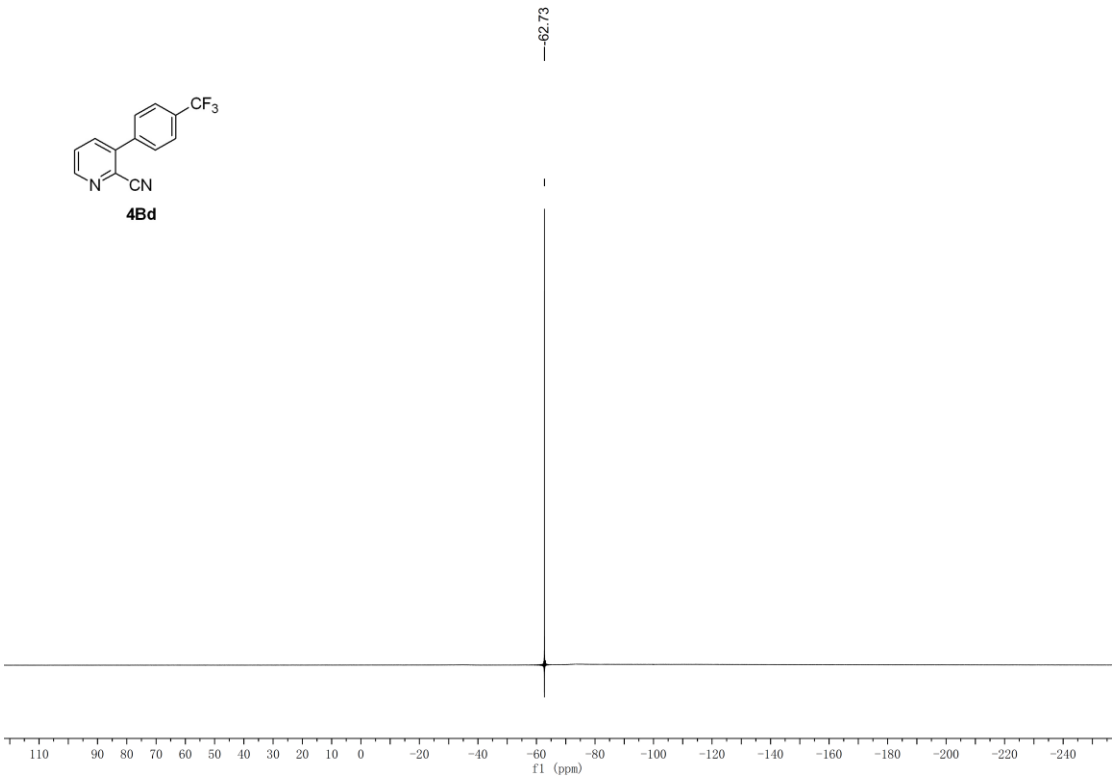
^{19}F NMR (376 MHz) spectrum of **4Bc** in $CDCl_3$



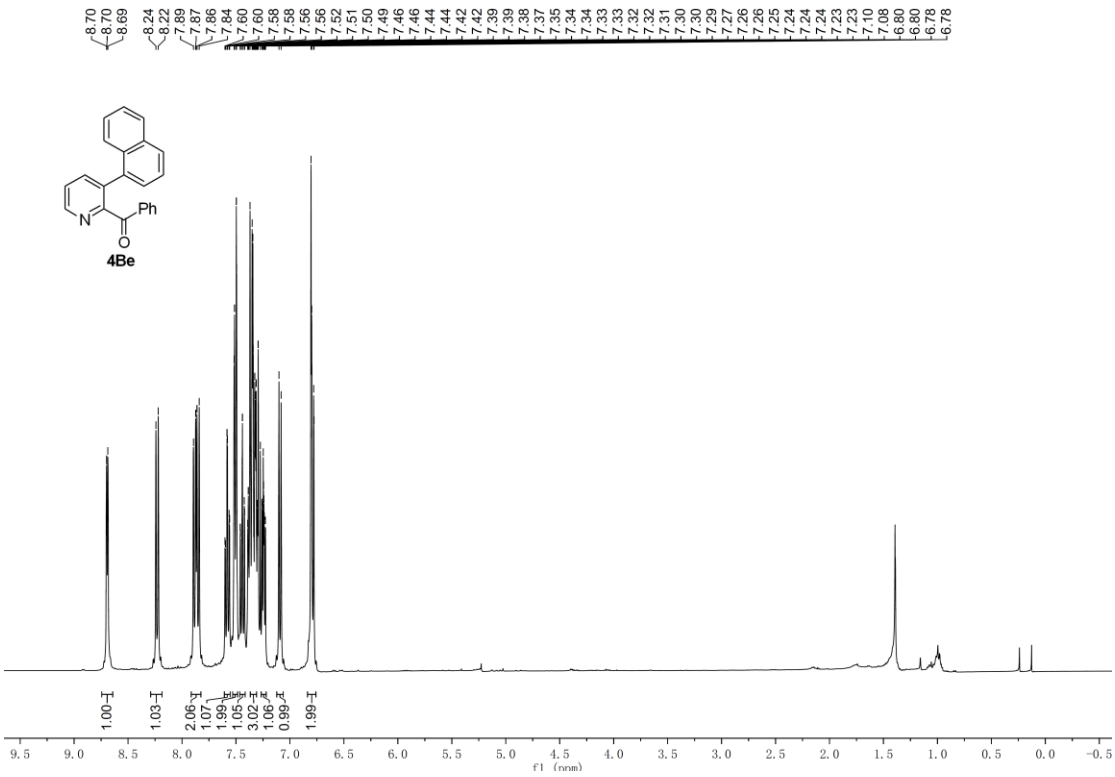
^{1}H NMR (400 MHz) spectrum of **4Bd** in $CDCl_3$



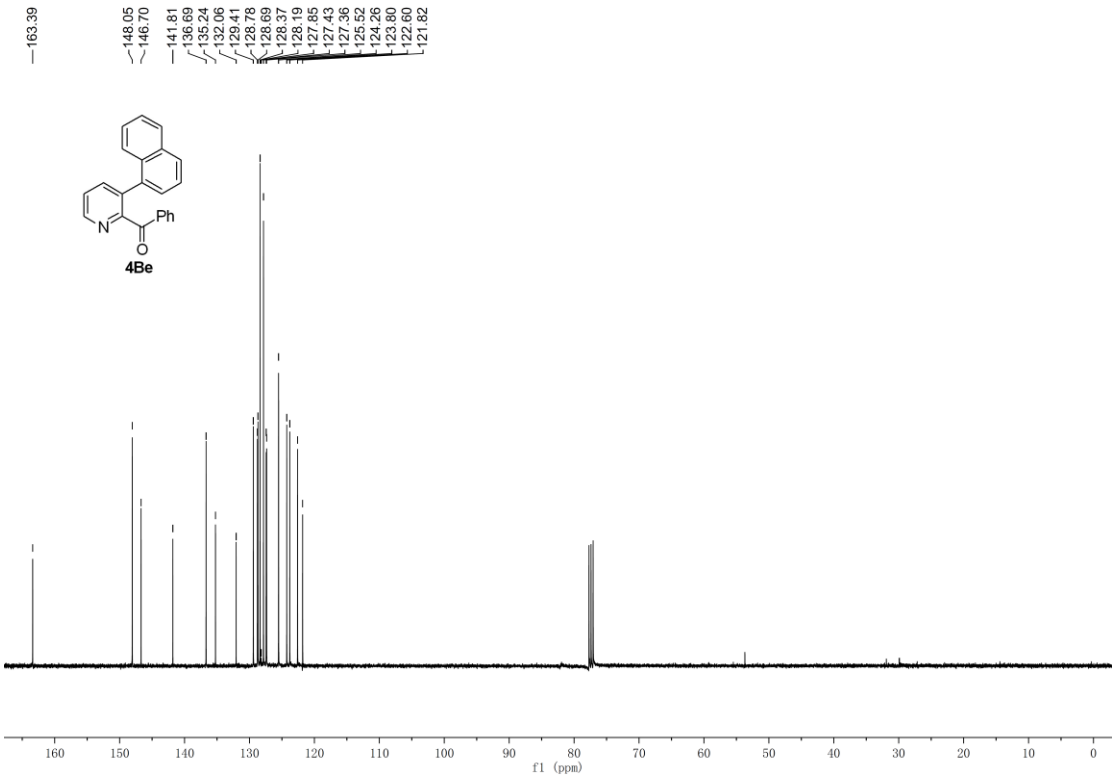
^{13}C NMR (151 MHz) spectrum of **4Bd** in $CDCl_3$



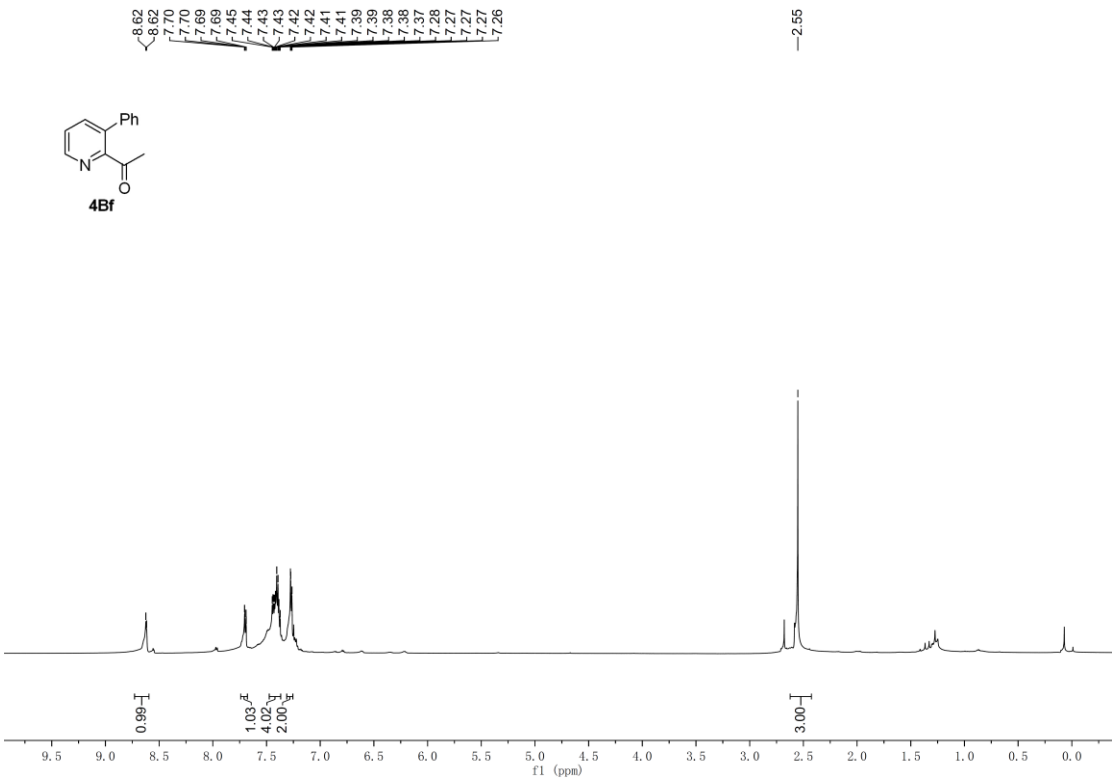
^{19}F NMR (565 MHz) spectrum of **4Bd** in $CDCl_3$



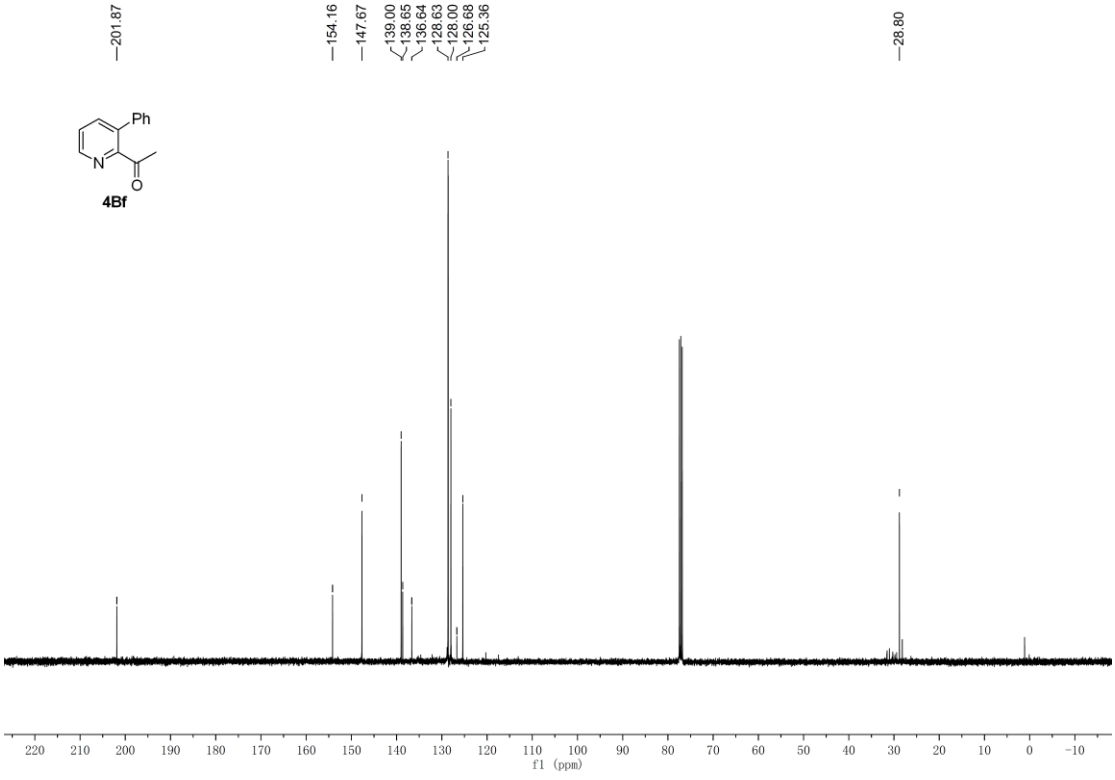
^{1}H NMR (400 MHz) spectrum of **4Be** in $CDCl_3$



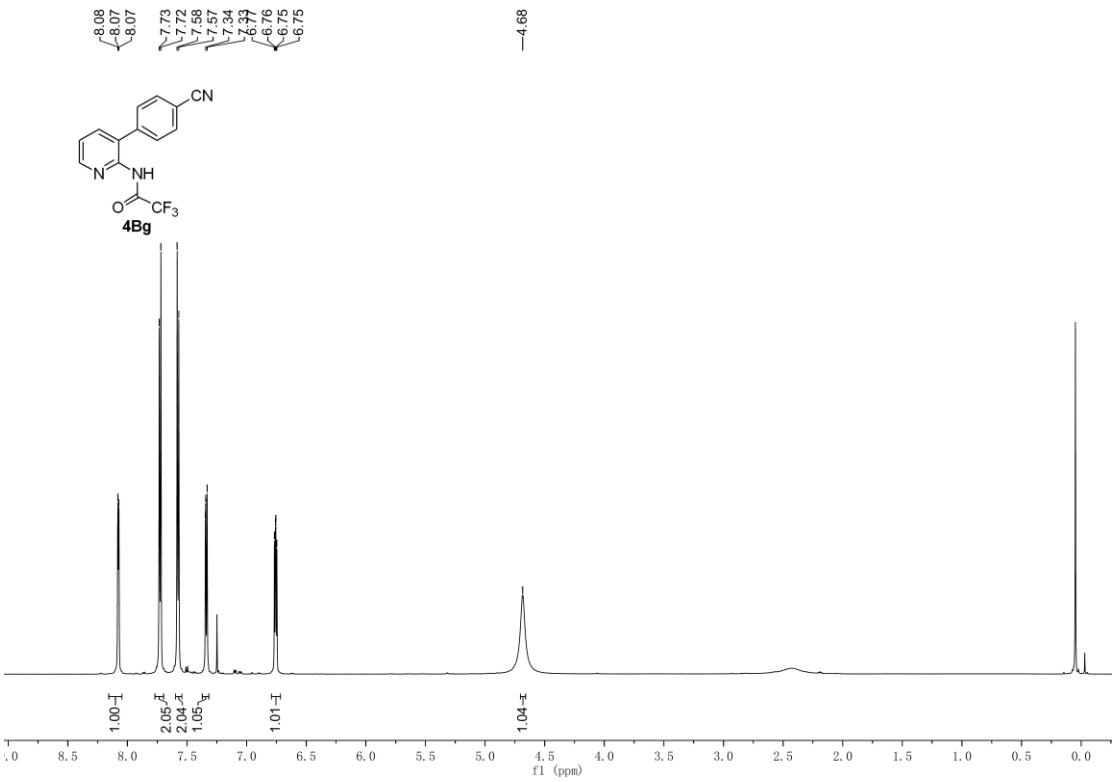
^{13}C NMR (101 MHz) spectrum of **4Be** in $CDCl_3$



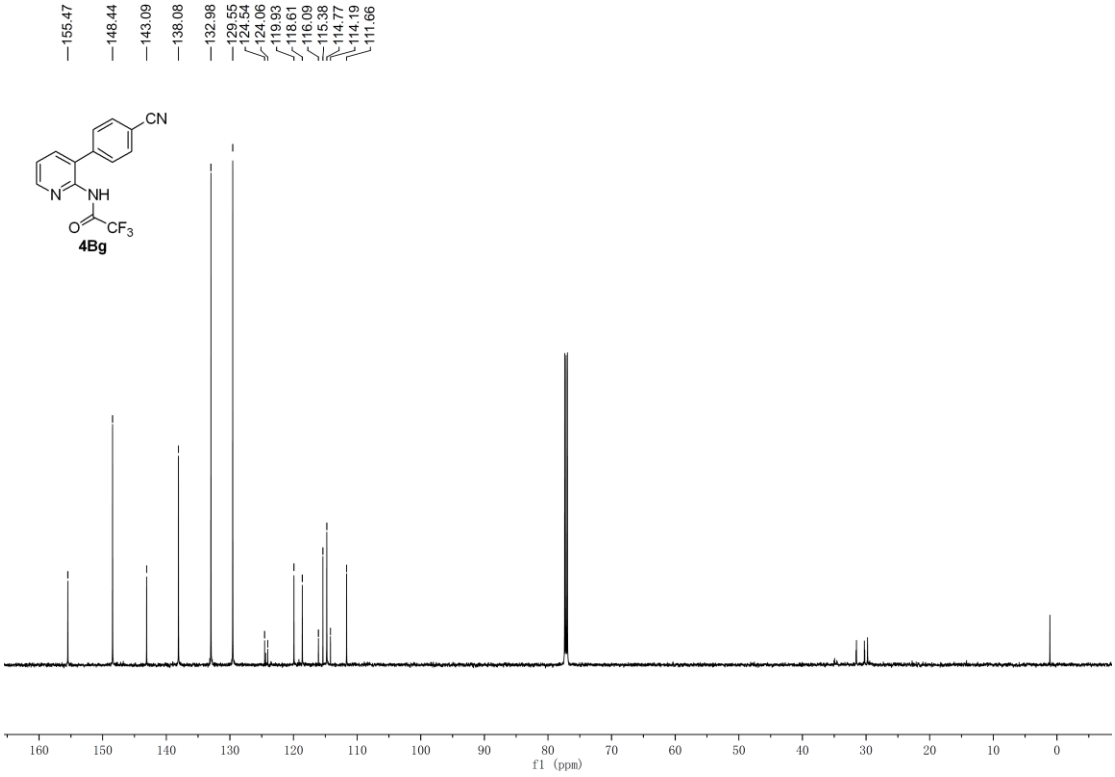
^{1}H NMR (600 MHz) spectrum of **4Bf** in $CDCl_3$



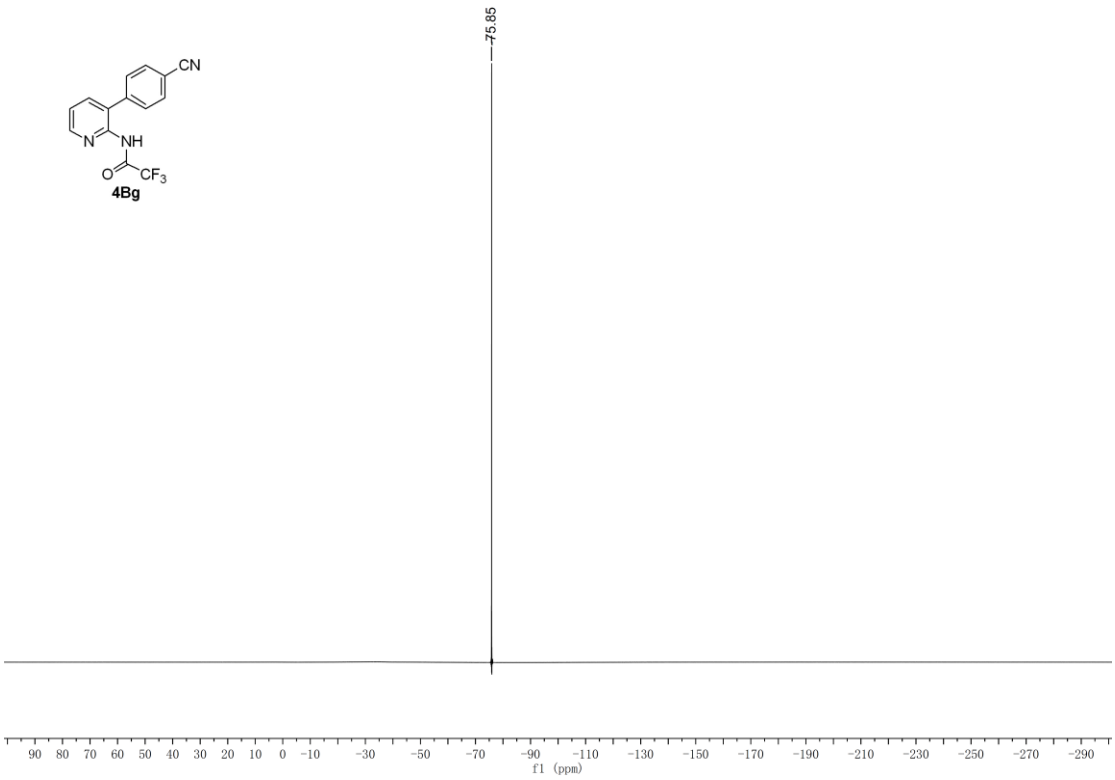
^{13}C NMR (101 MHz) spectrum of **4Bf** in $CDCl_3$



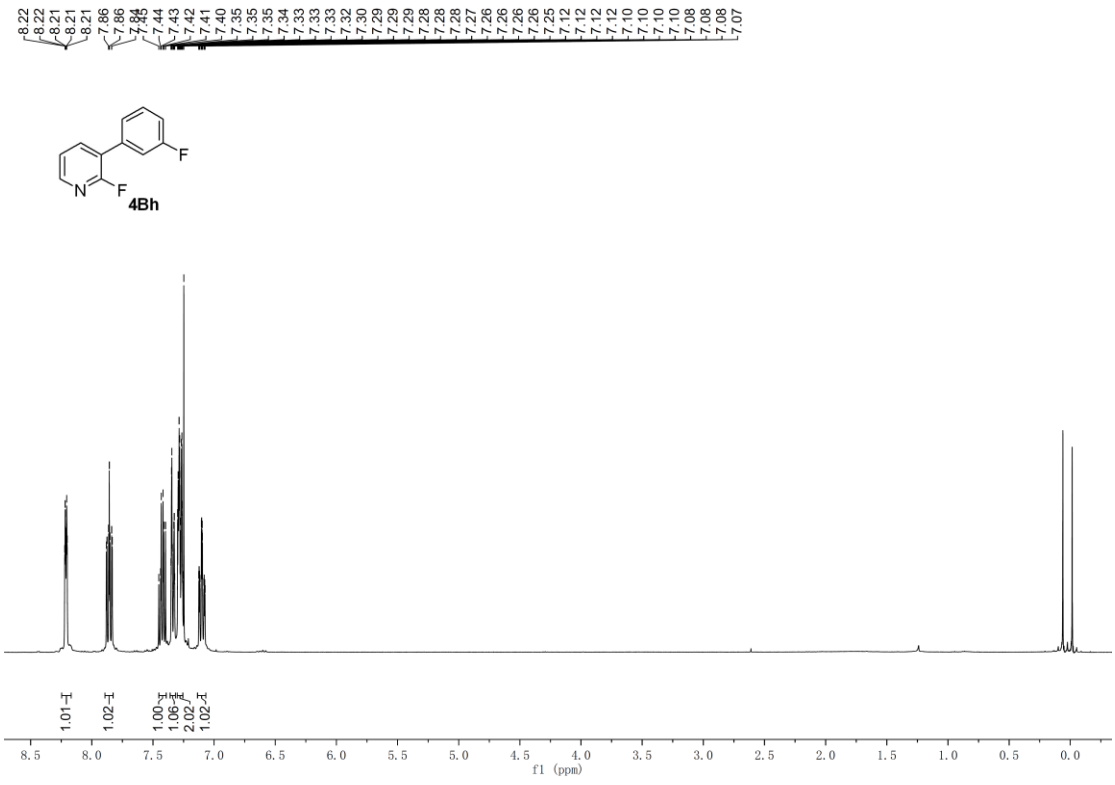
^{1}H NMR (400 MHz) spectrum of **4Bg** in $CDCl_3$



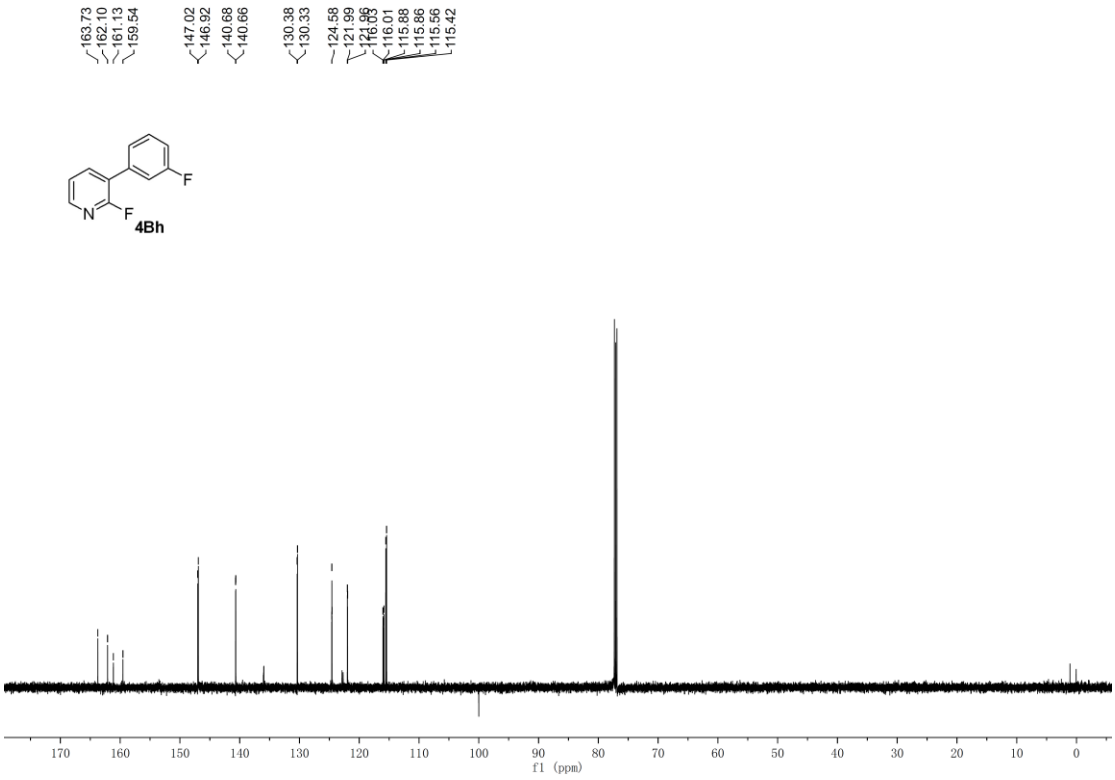
^{13}C NMR (101 MHz) spectrum of **4Bg** in $CDCl_3$



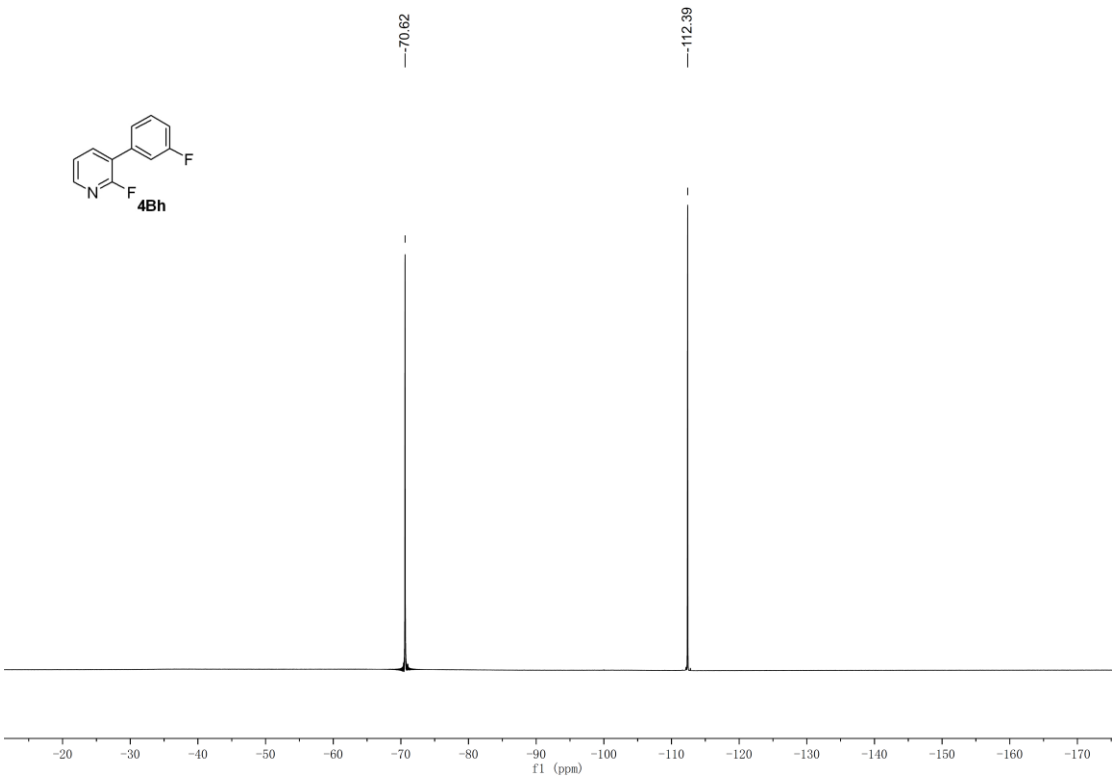
^{19}F NMR (376 MHz) spectrum of **4Bg** in $CDCl_3$



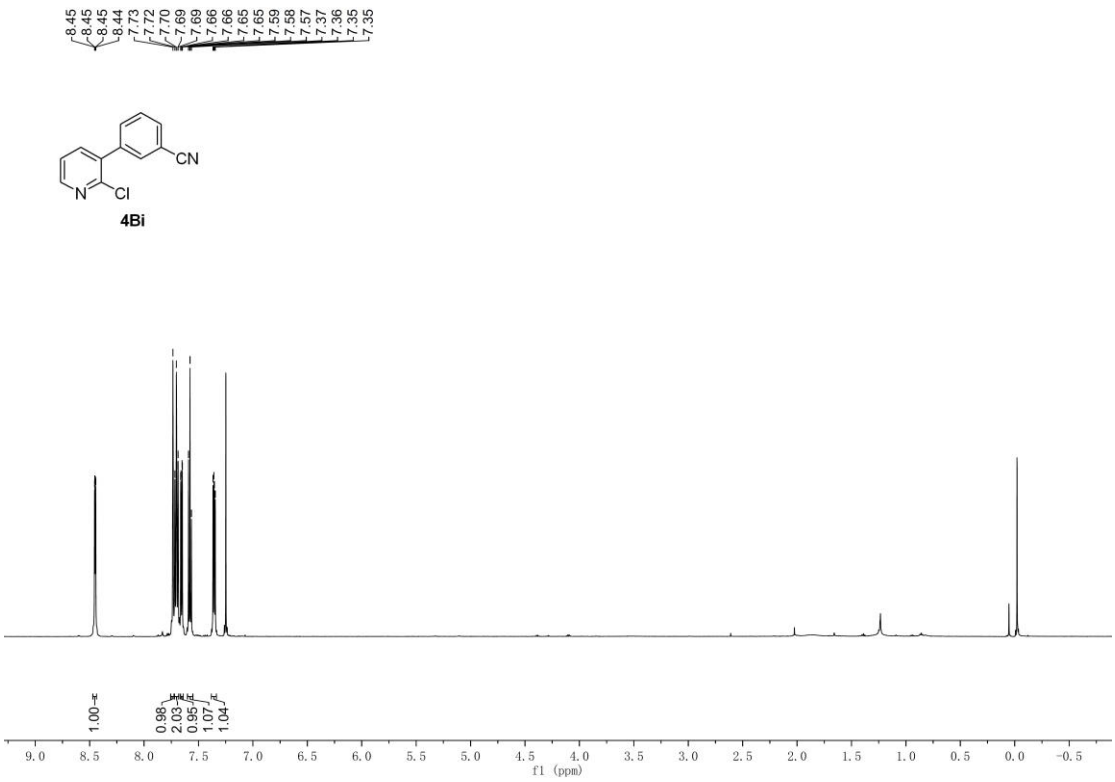
^{1}H NMR (400 MHz) spectrum of **4Bh** in $CDCl_3$



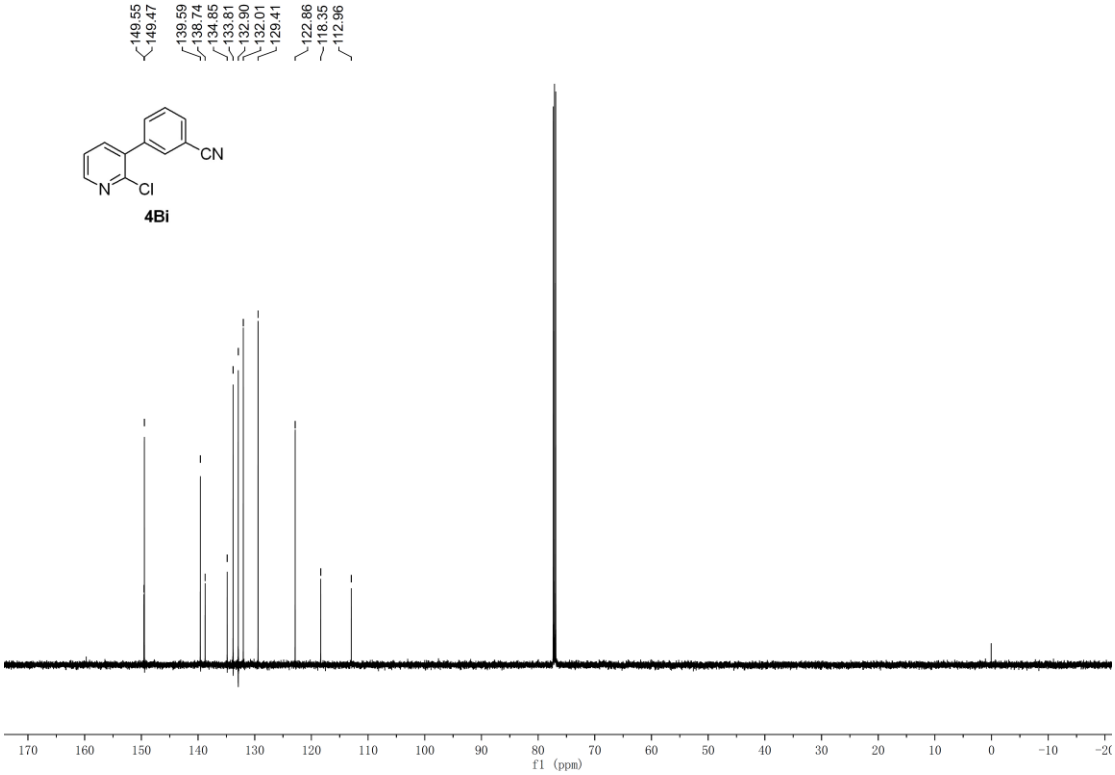
^{13}C NMR (151 MHz) spectrum of **4Bh** in $CDCl_3$



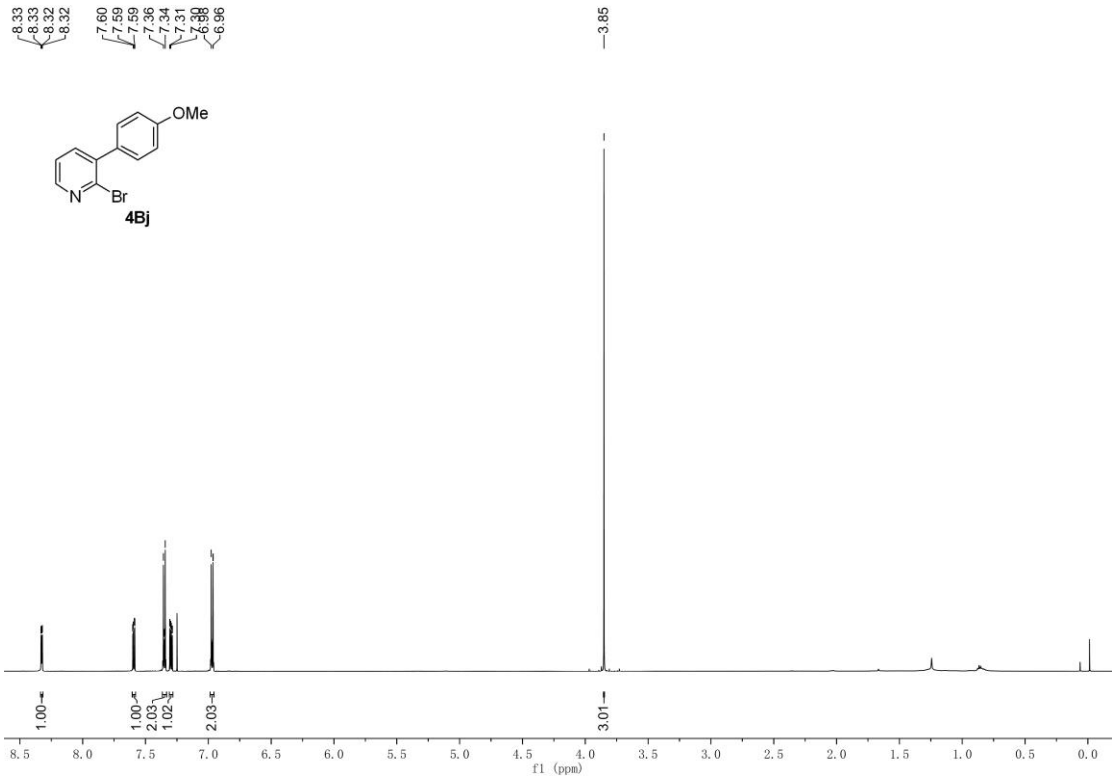
^{19}F NMR (376 MHz) spectrum of **4Bh** in $CDCl_3$



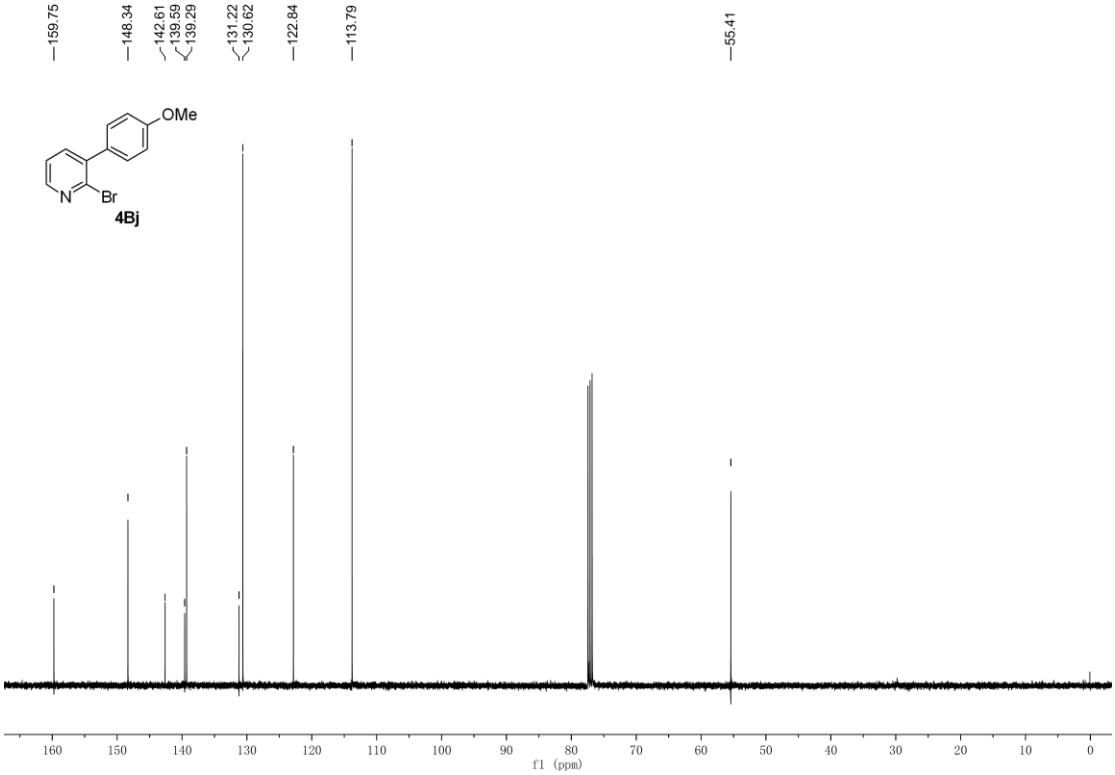
^{1}H NMR (600 MHz) spectrum of **4Bi** in $CDCl_3$



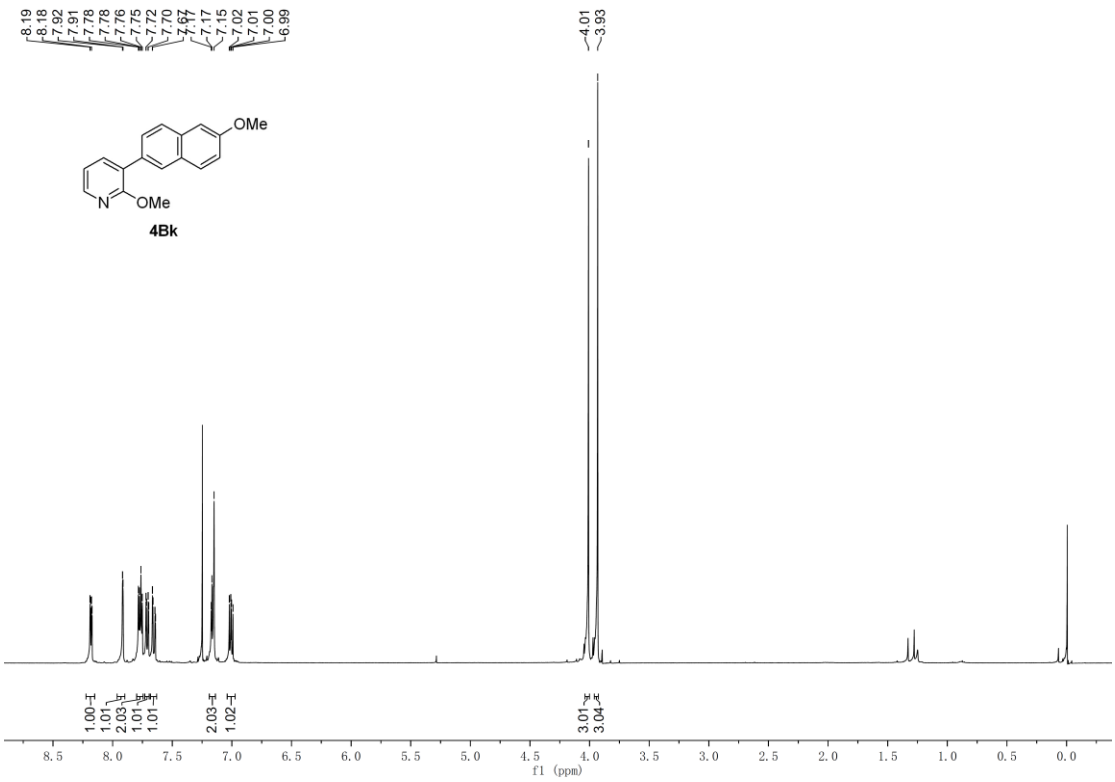
^{13}C NMR (151 MHz) spectrum of **4Bi** in $CDCl_3$



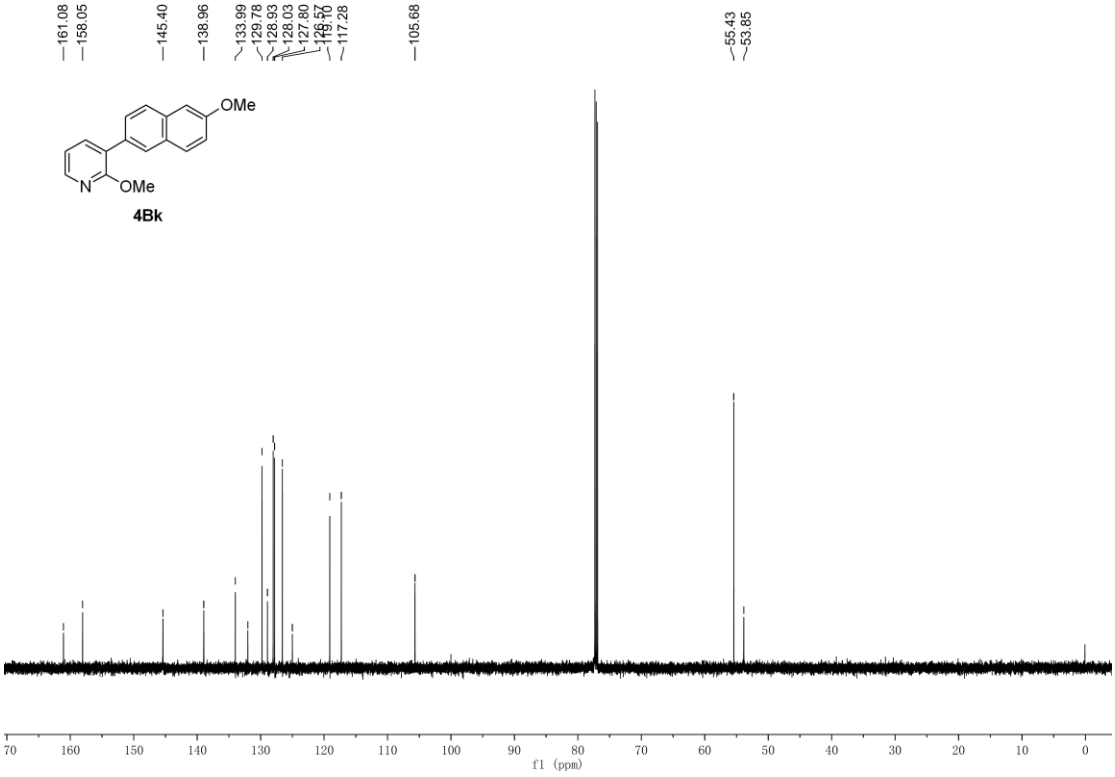
^{1}H NMR (600 MHz) spectrum of **4Bj** in $CDCl_3$



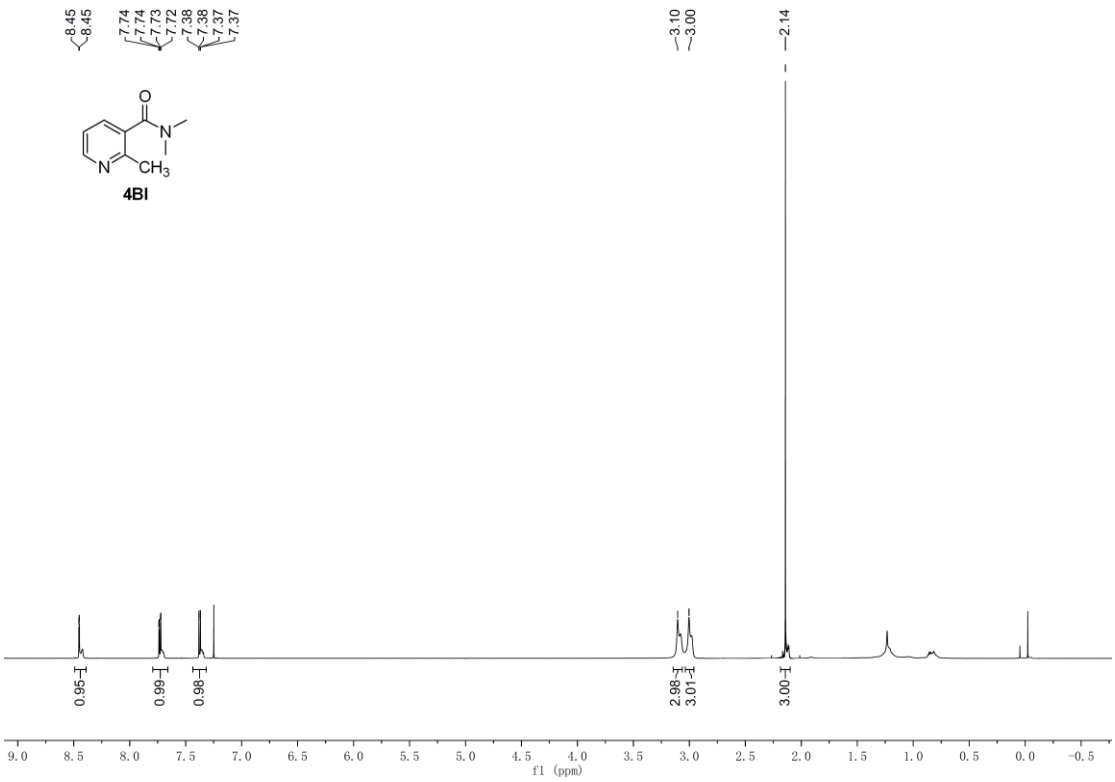
^{13}C NMR (101 MHz) spectrum of **4Bj** in $CDCl_3$



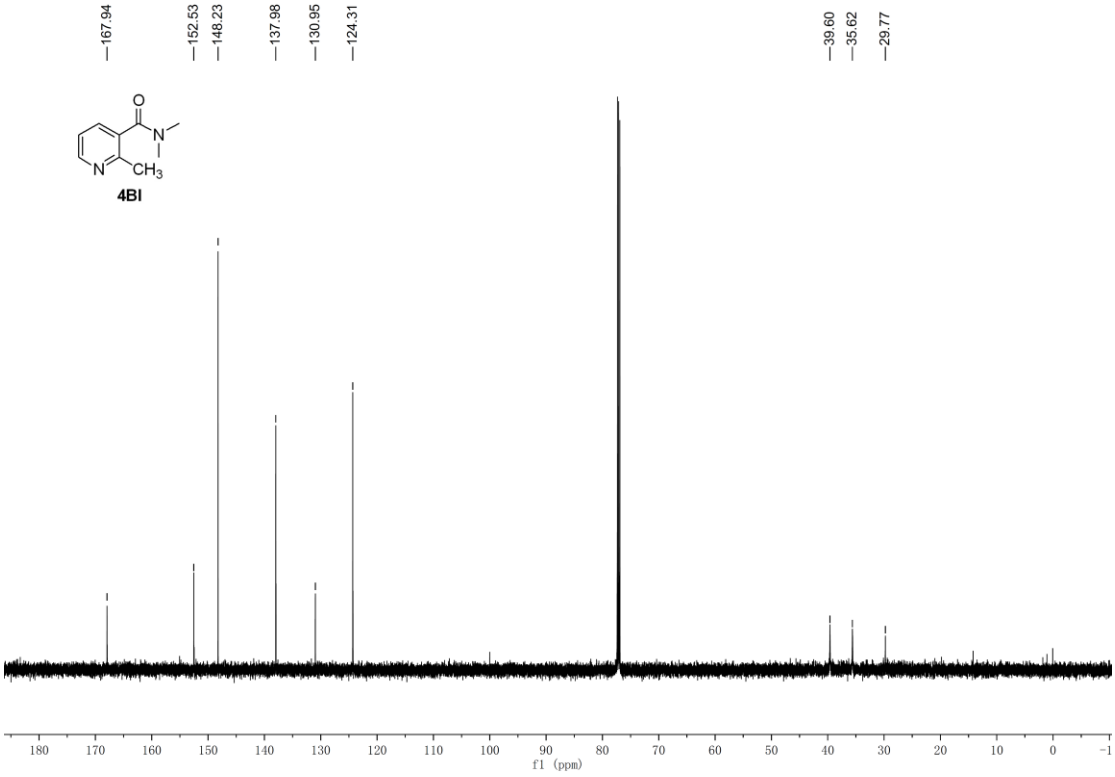
^{1}H NMR (400 MHz) spectrum of **4Bk** in $CDCl_3$



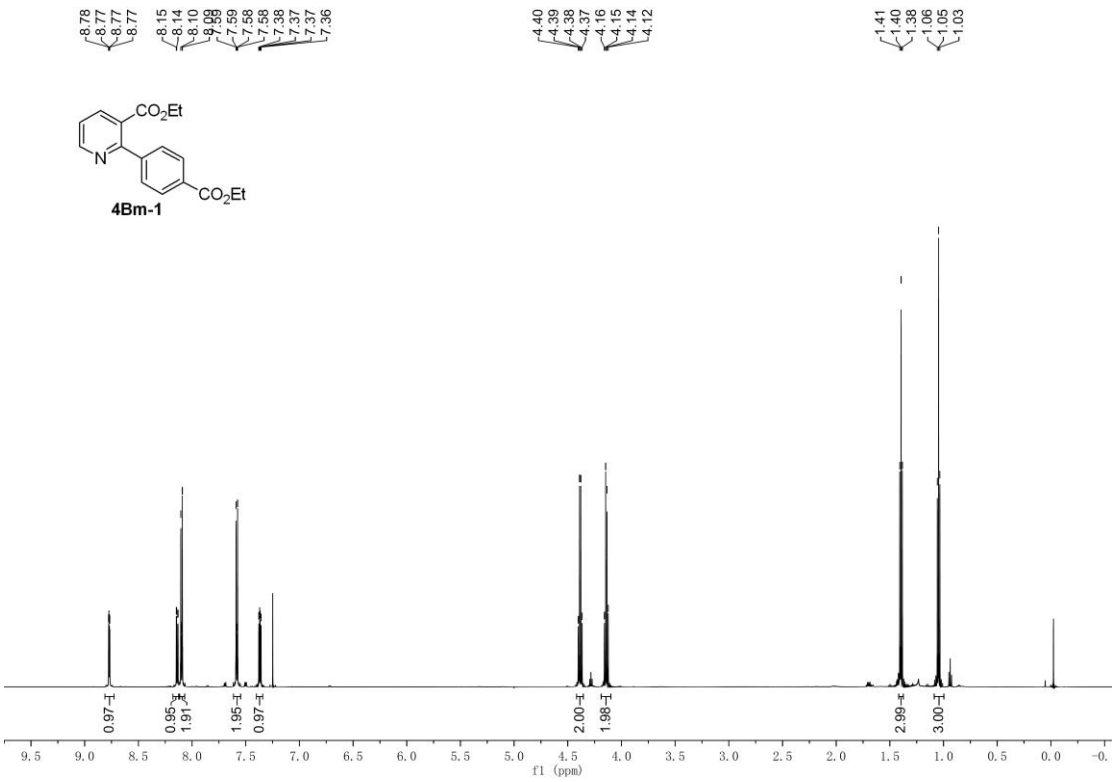
^{13}C NMR (151 MHz) spectrum of **4Bk** in $CDCl_3$



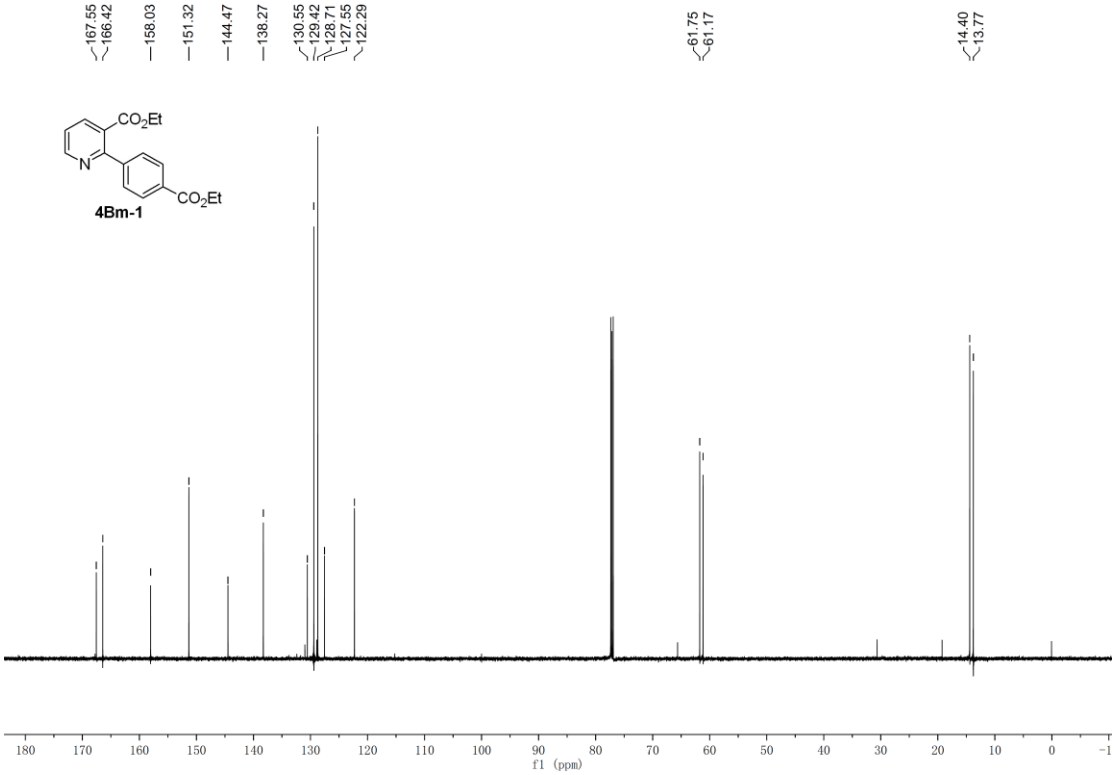
^{1}H NMR (600 MHz) spectrum of **4Bl** in $CDCl_3$



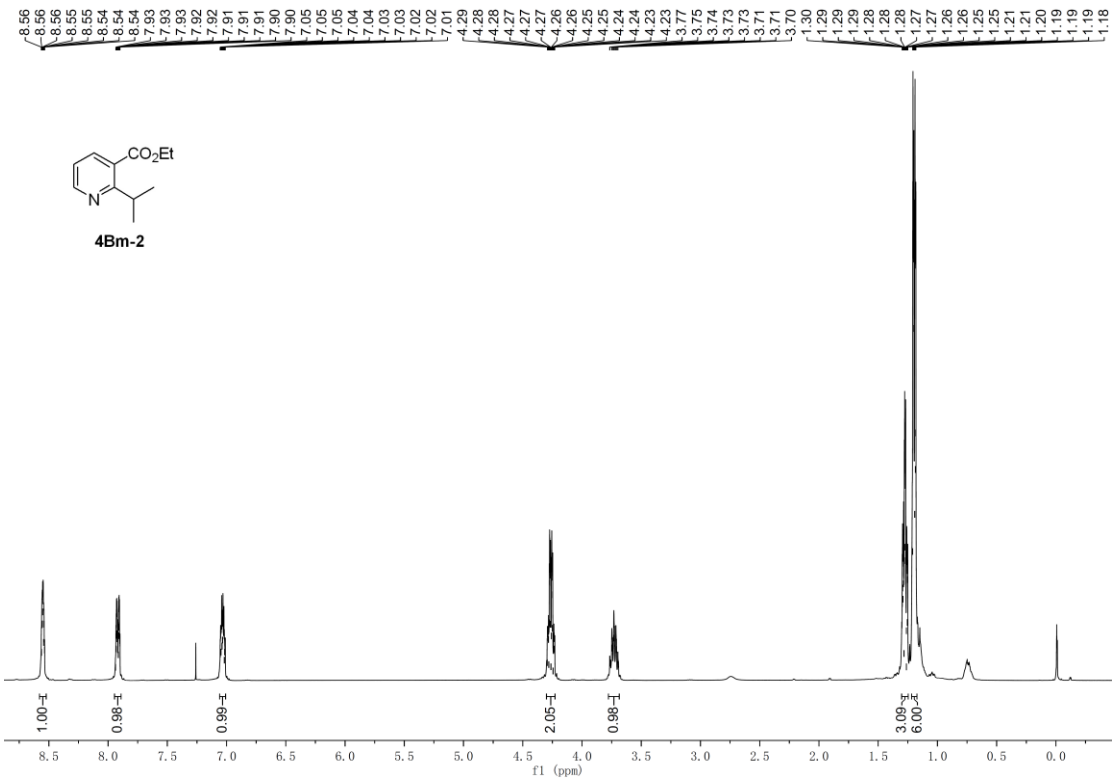
^{13}C NMR (151 MHz) spectrum of **4Bl** in $CDCl_3$



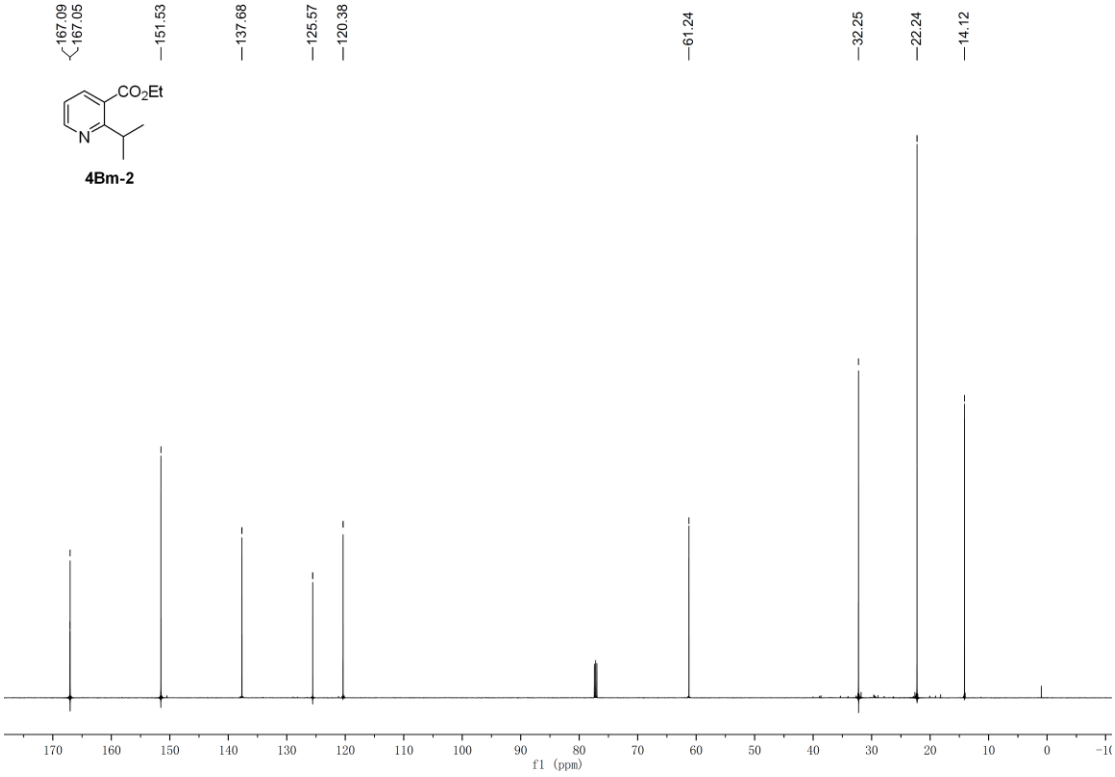
^{1}H NMR (600 MHz) spectrum of **4Bm-1** in $CDCl_3$



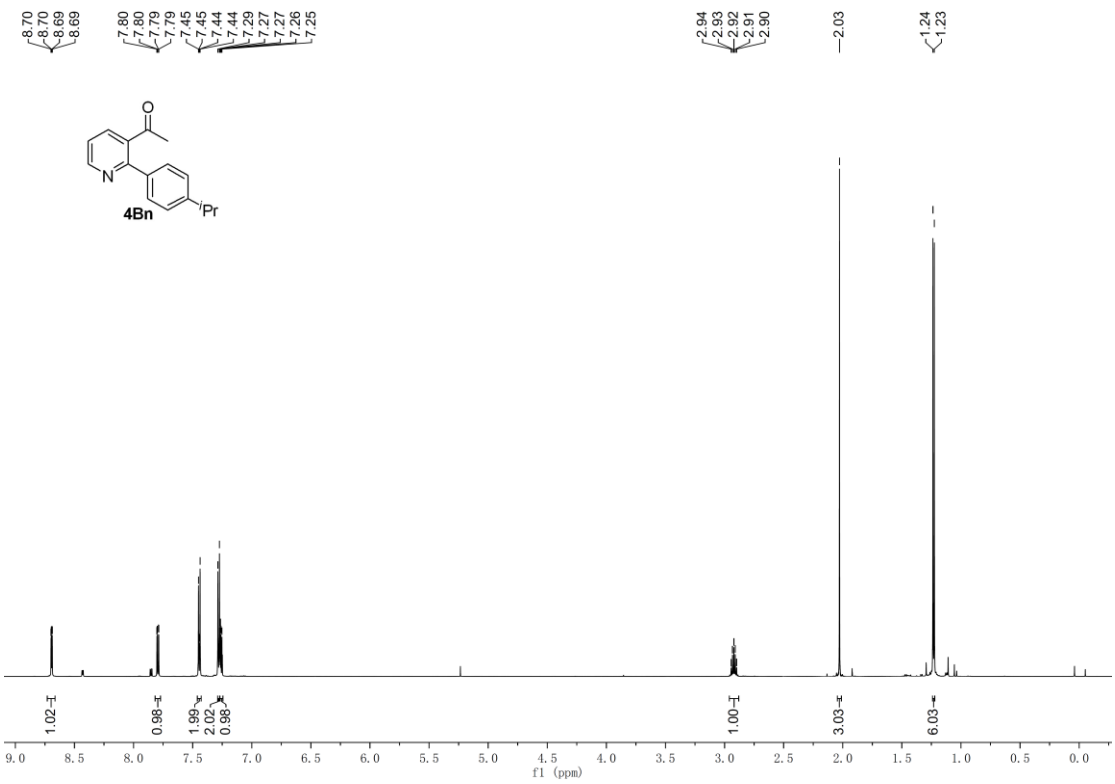
^{13}C NMR (151 MHz) spectrum of **4Bm-1** in $CDCl_3$



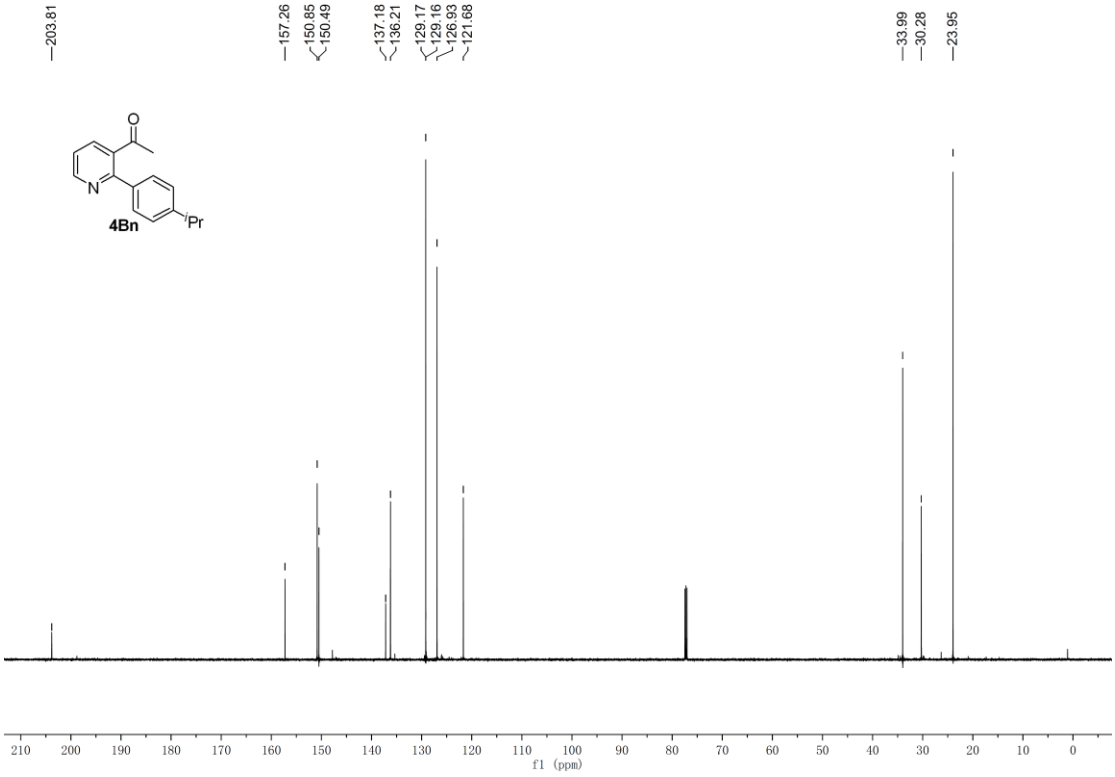
^{1}H NMR (400 MHz) spectrum of **4Bm-2** in $CDCl_3$



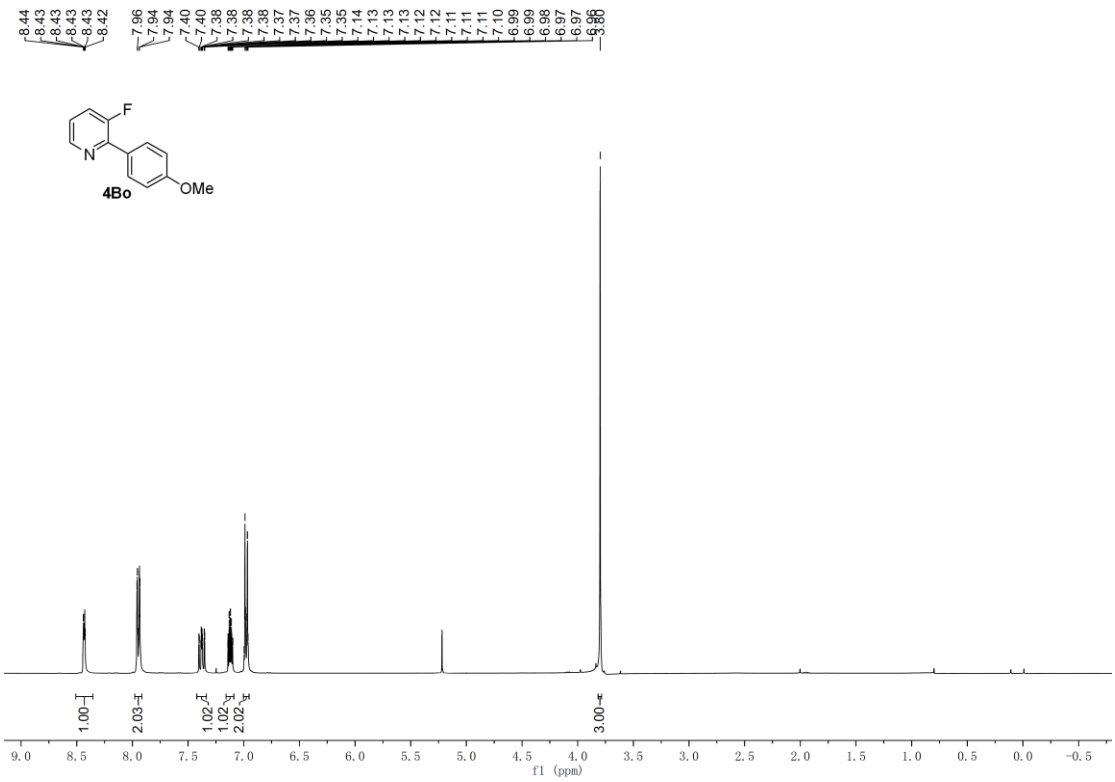
^{13}C NMR (151 MHz) spectrum of **4Bm-2** in $CDCl_3$



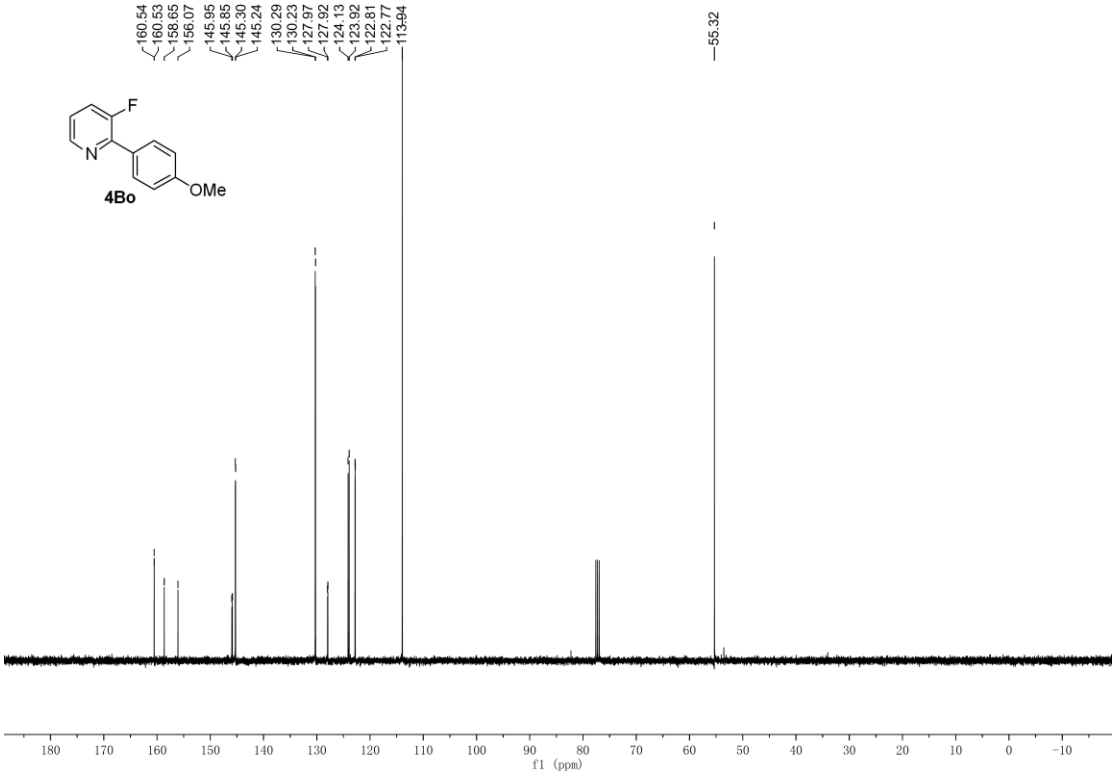
^{1}H NMR (600 MHz) spectrum of **4Bn** in $CDCl_3$



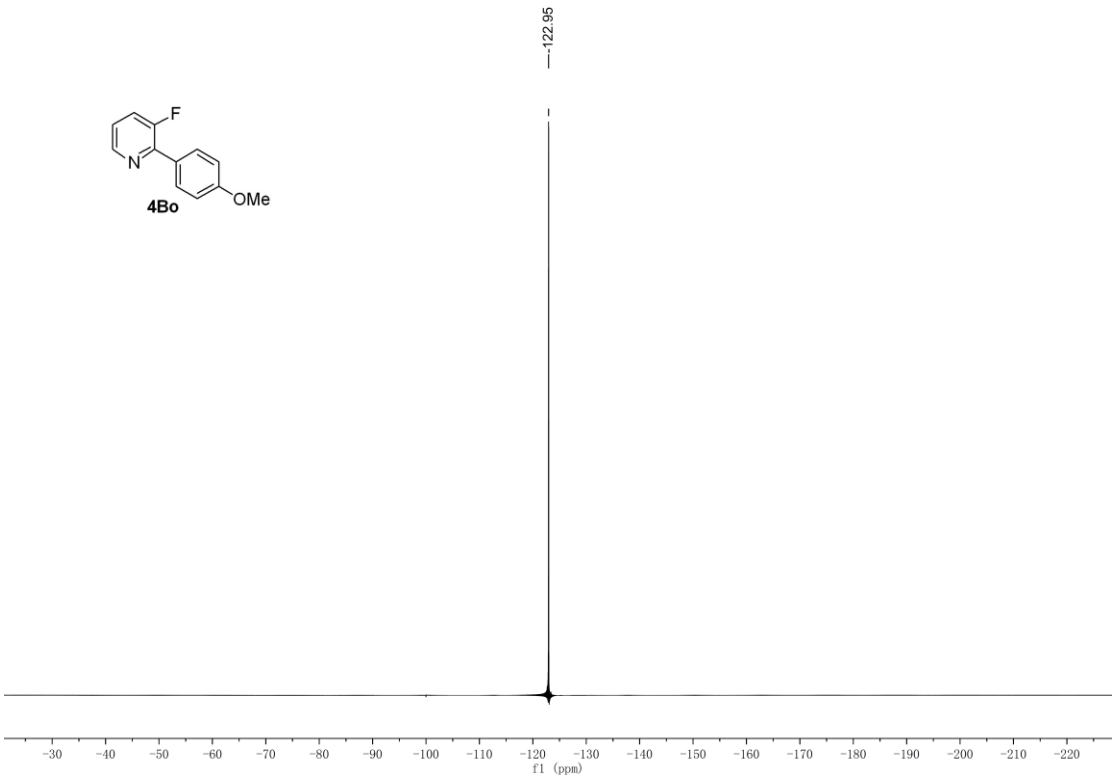
^{13}C NMR (101 MHz) spectrum of **4Bn** in $CDCl_3$



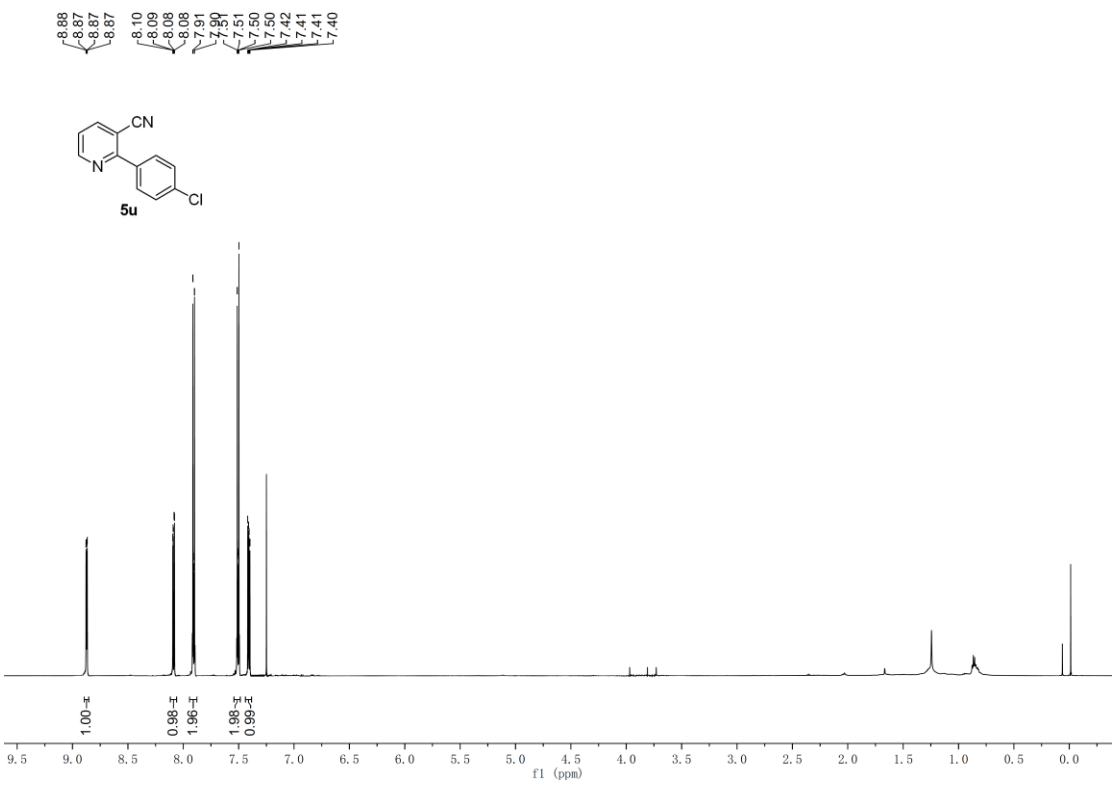
^{1}H NMR (400 MHz) spectrum of **4Bo** in $CDCl_3$



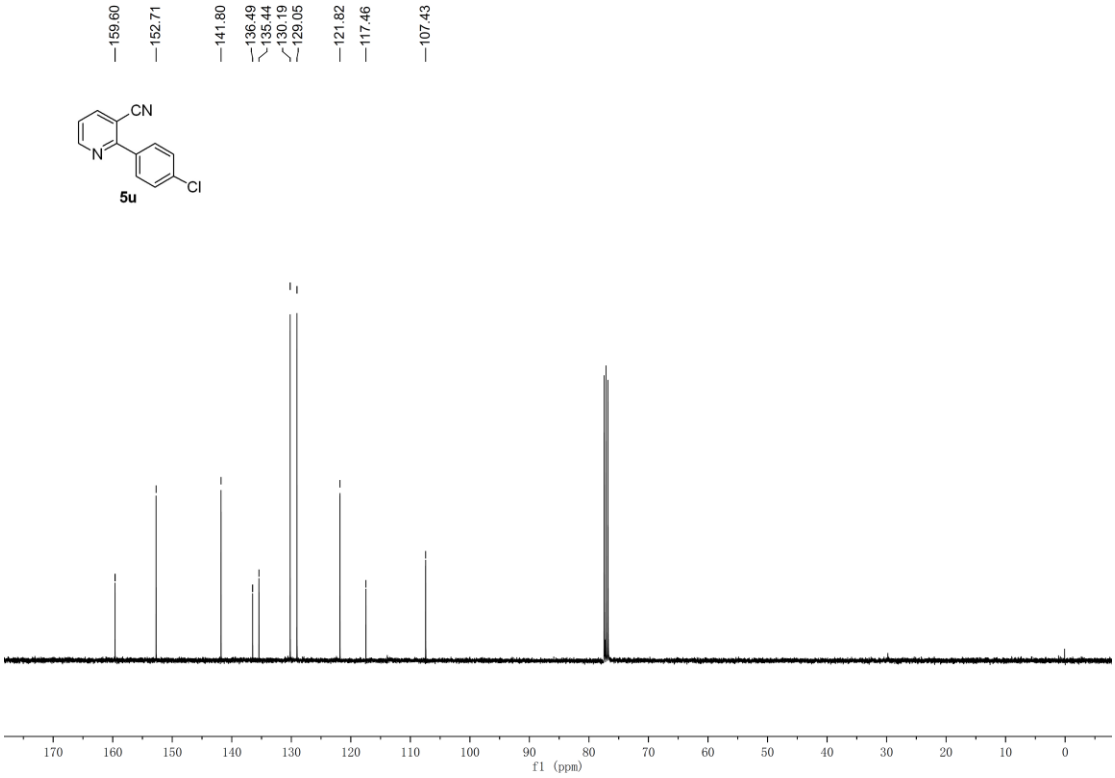
^{13}C NMR (101 MHz) spectrum of **4Bo** in $CDCl_3$



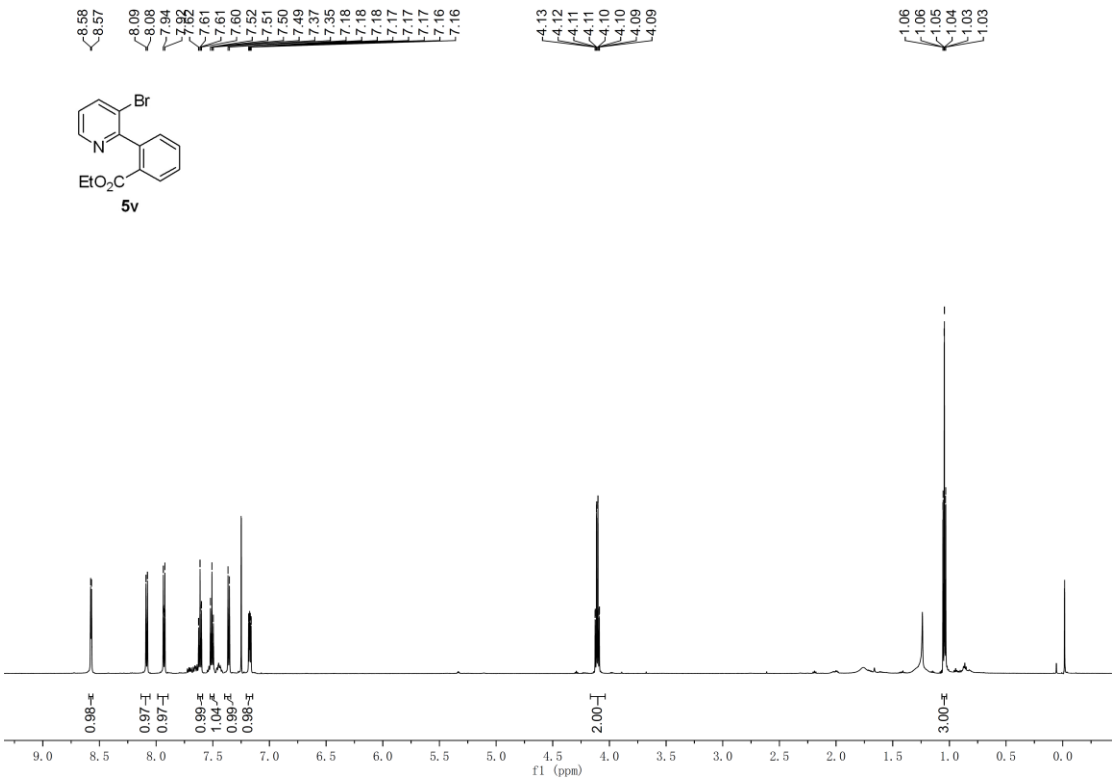
^{19}F NMR (376 MHz) spectrum of **4Bo** in $CDCl_3$



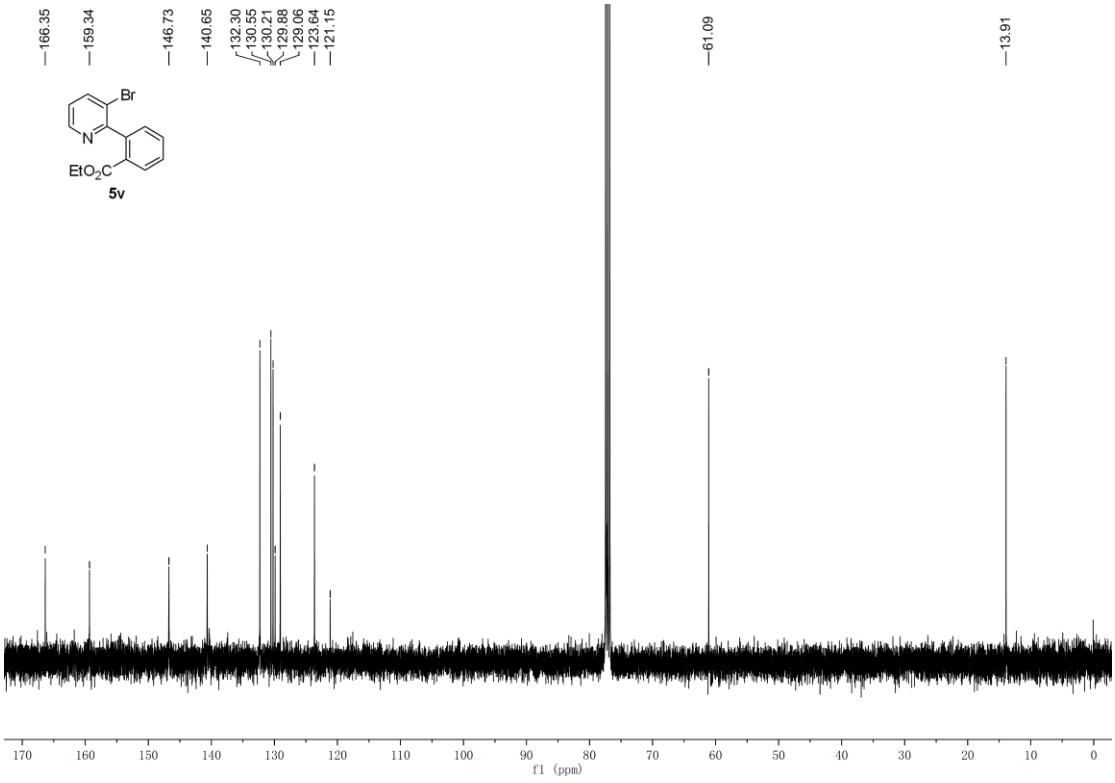
^{1}H NMR (400 MHz) spectrum of **5u** in $CDCl_3$



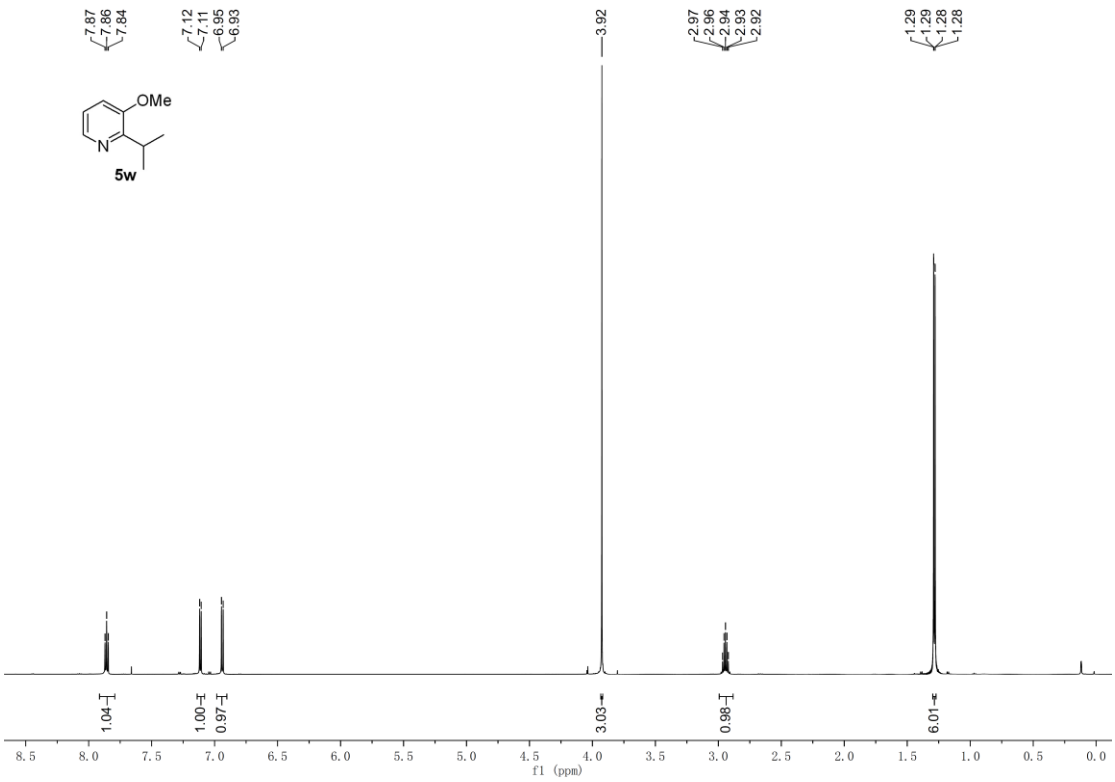
^{13}C NMR (101 MHz) spectrum of **5u** in $CDCl_3$



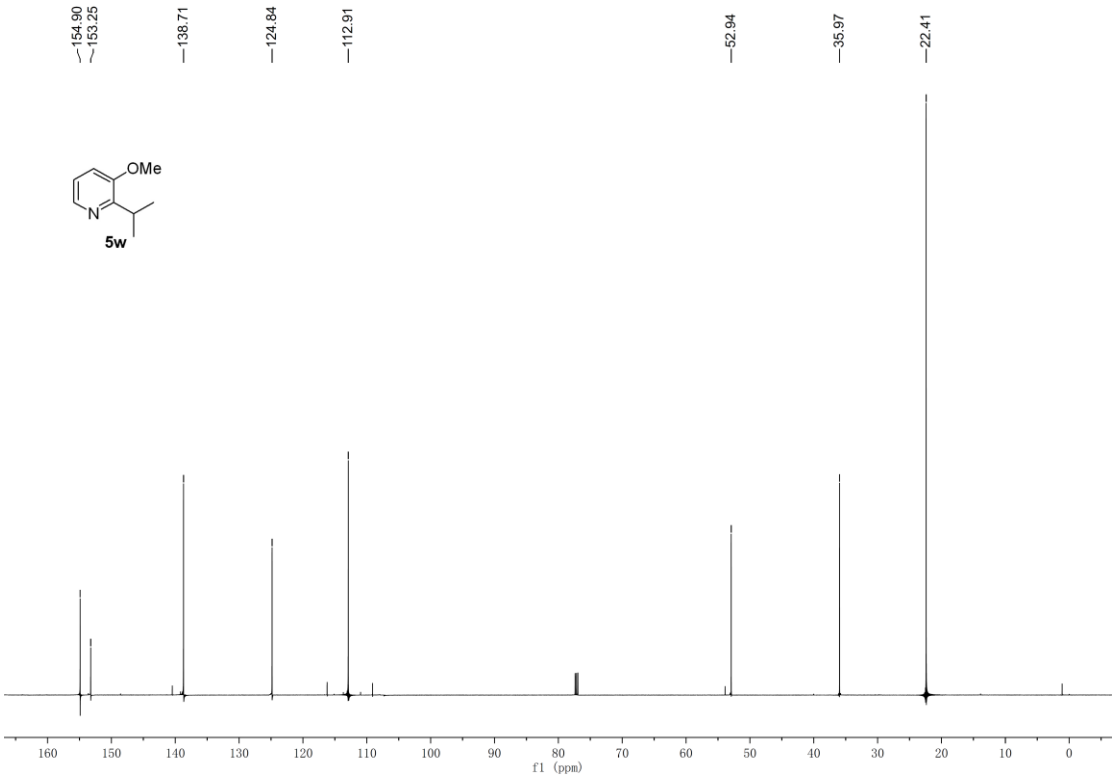
^{1}H NMR (400 MHz) spectrum of **5v** in $CDCl_3$



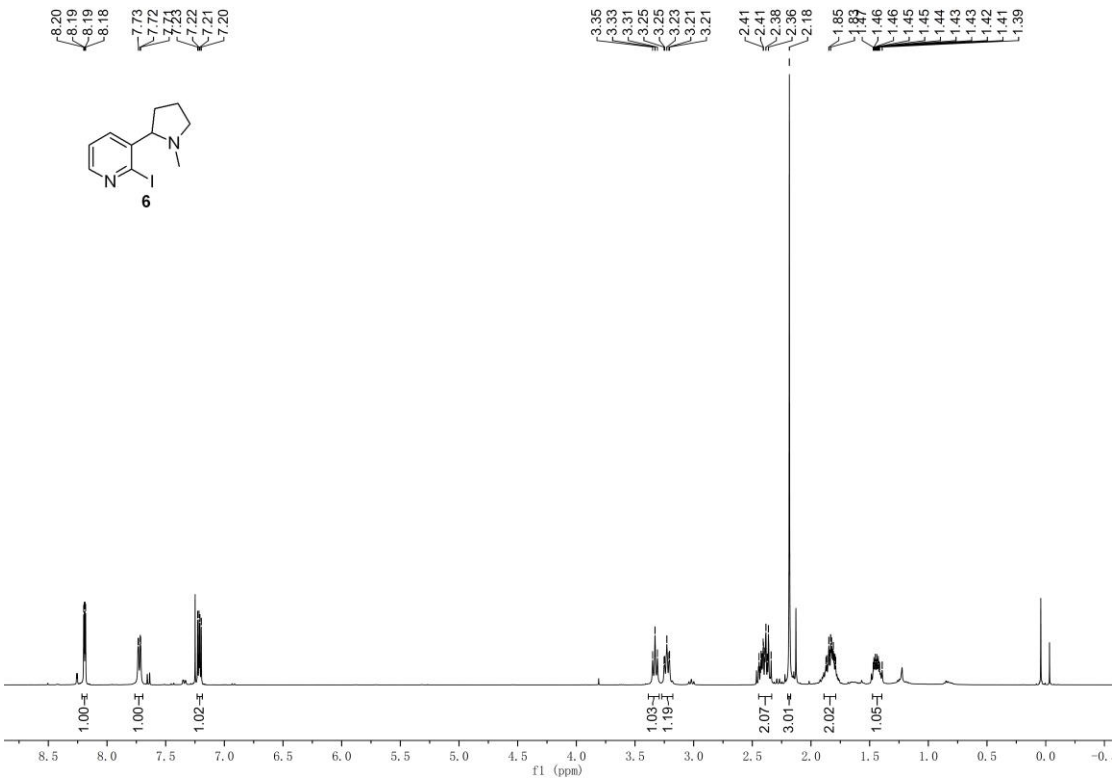
^{13}C NMR (101 MHz) spectrum of **5v** in $CDCl_3$



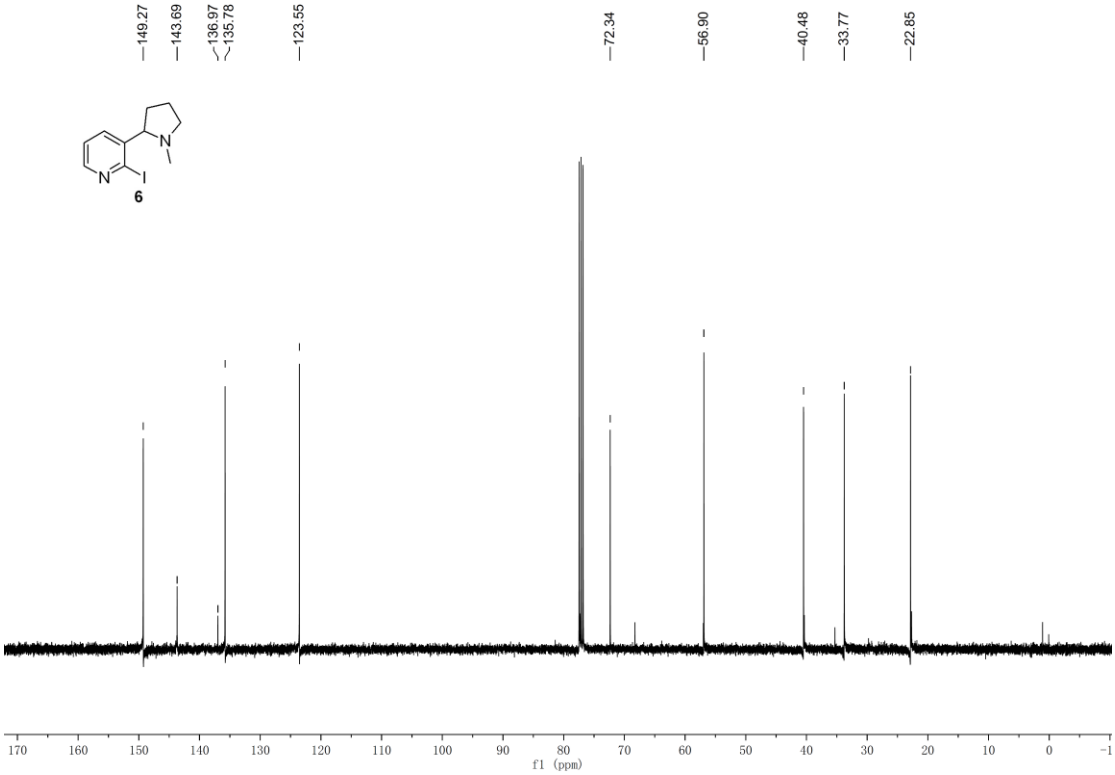
^{1}H NMR (400 MHz) spectrum of **5w** in $CDCl_3$



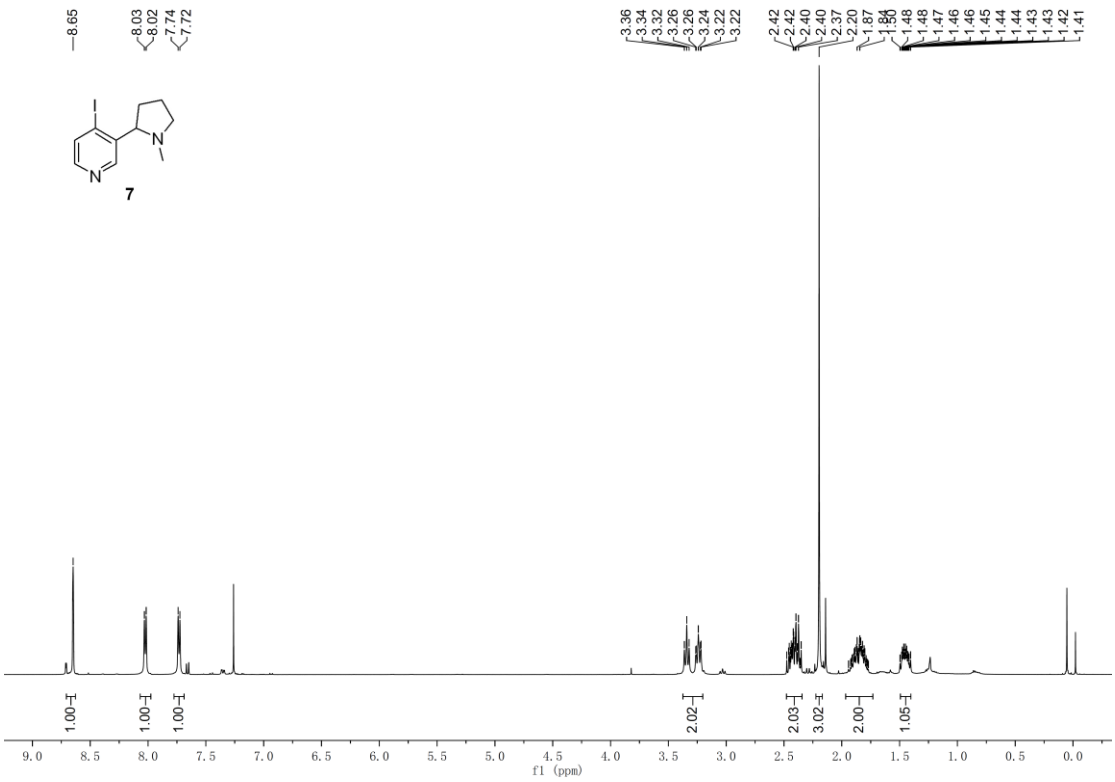
^{13}C NMR (151 MHz) spectrum of **5w** in $CDCl_3$



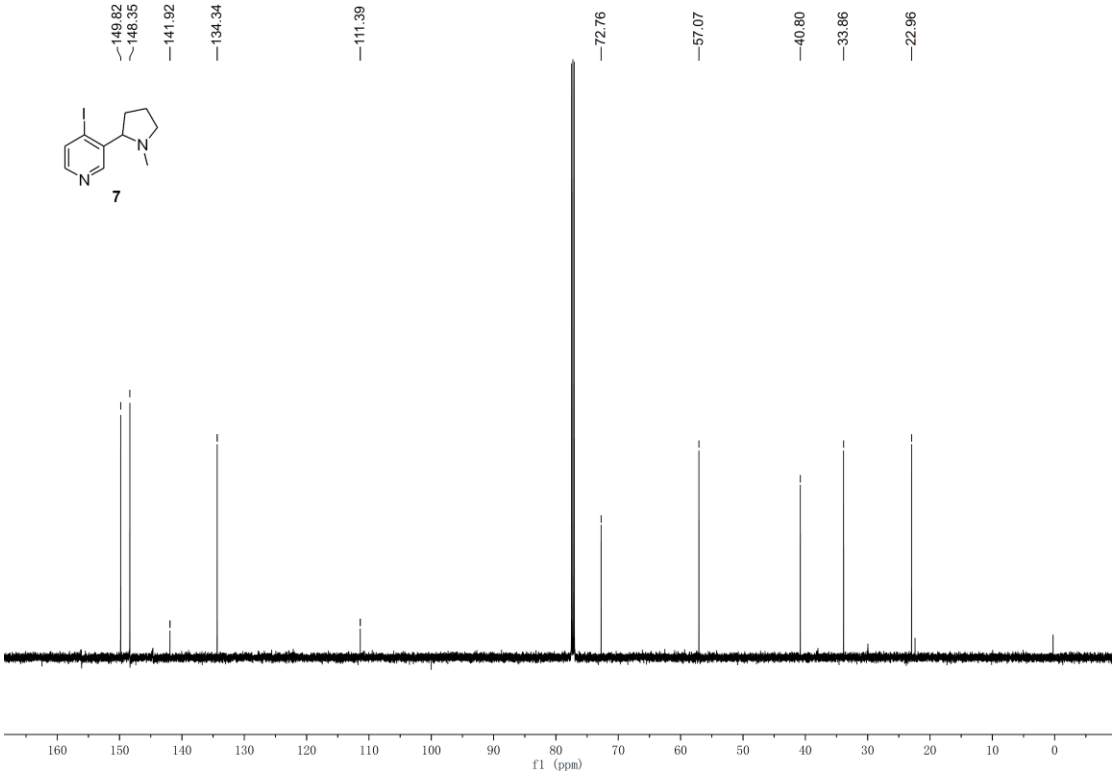
^{1}H NMR (400 MHz) spectrum of **6** in $CDCl_3$



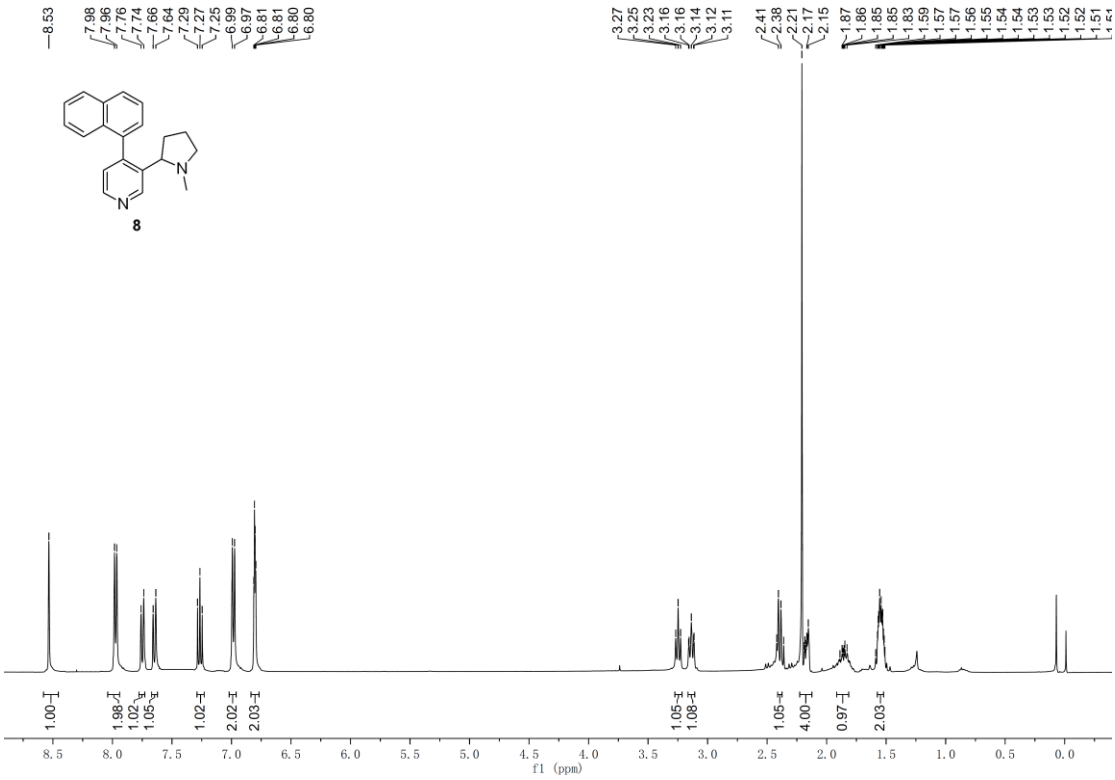
^{13}C NMR (101 MHz) spectrum of **6** in $CDCl_3$



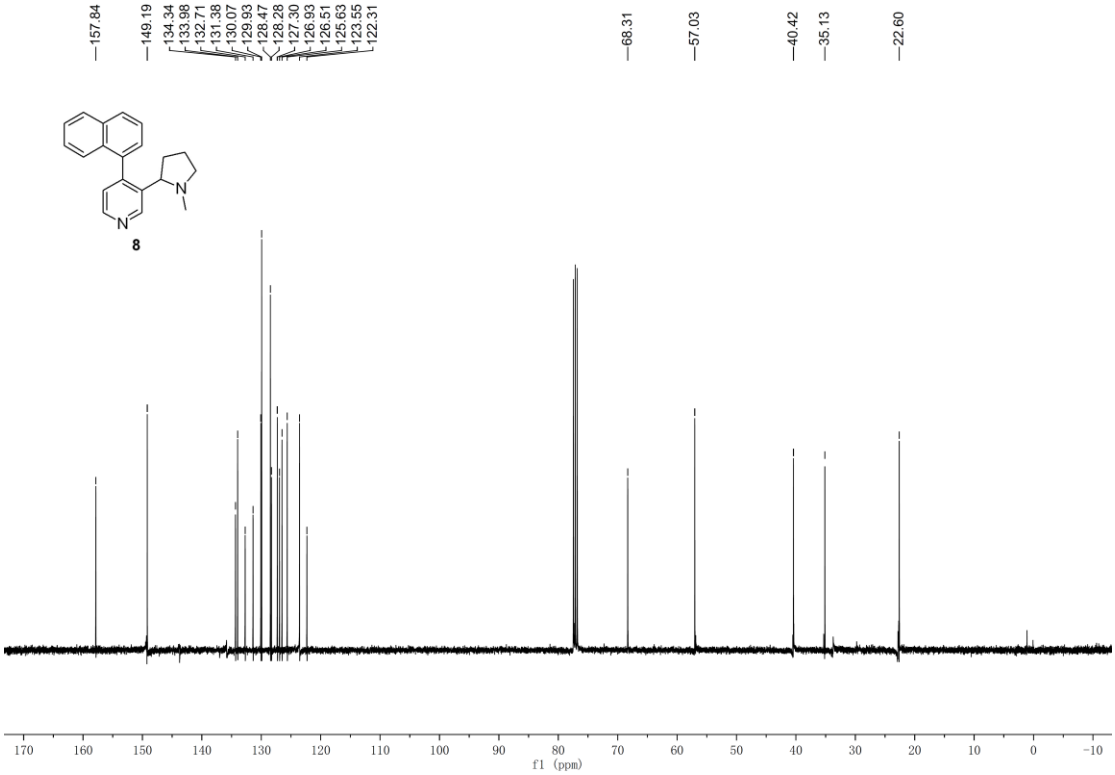
^{1}H NMR (400 MHz) spectrum of **7** in $CDCl_3$



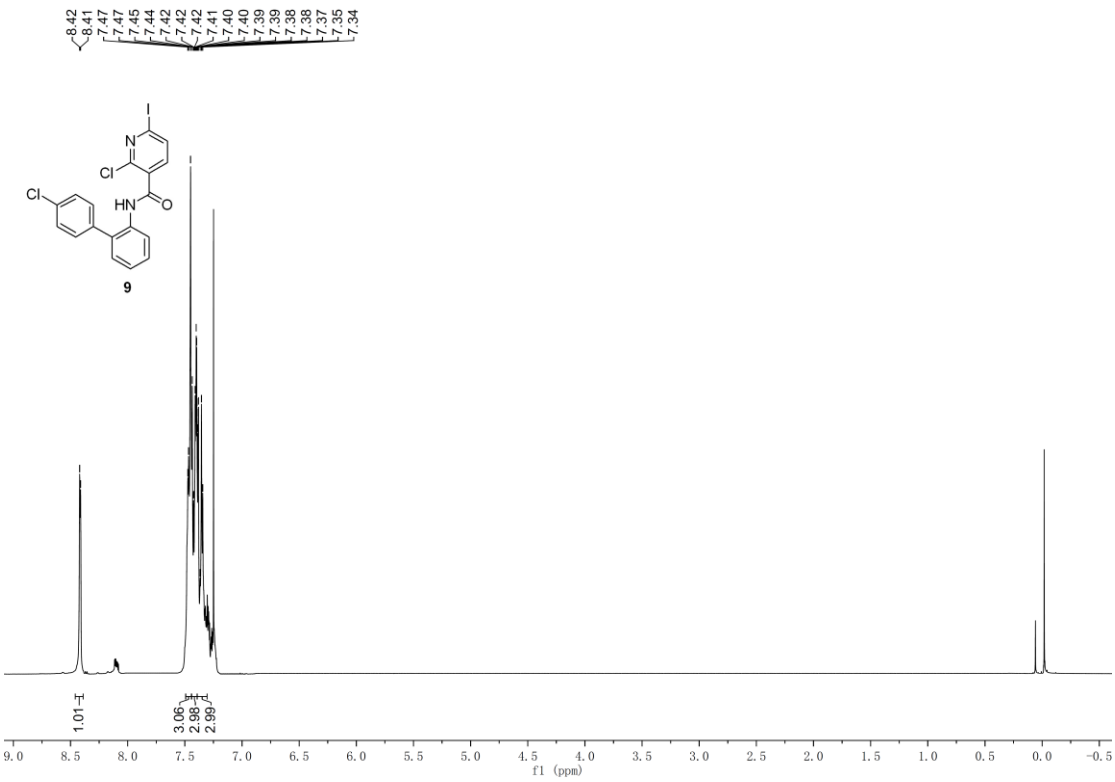
^{13}C NMR (101 MHz) spectrum of **7** in $CDCl_3$



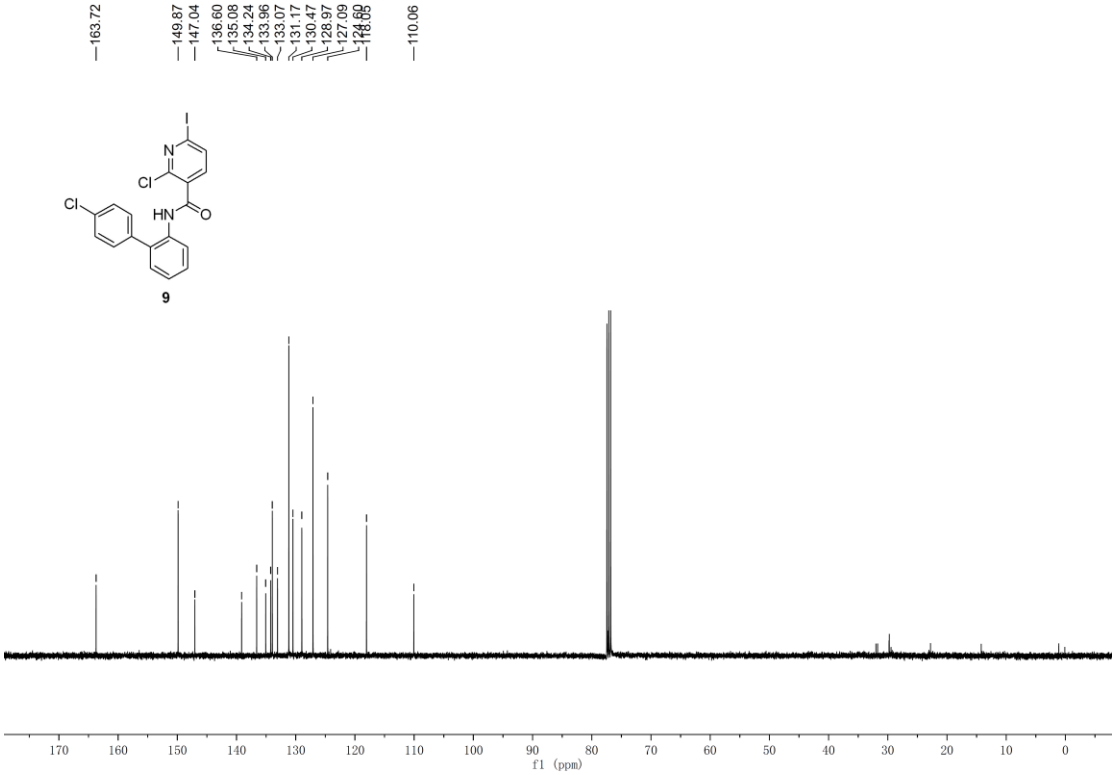
^{1}H NMR (400 MHz) spectrum of **8** in $CDCl_3$



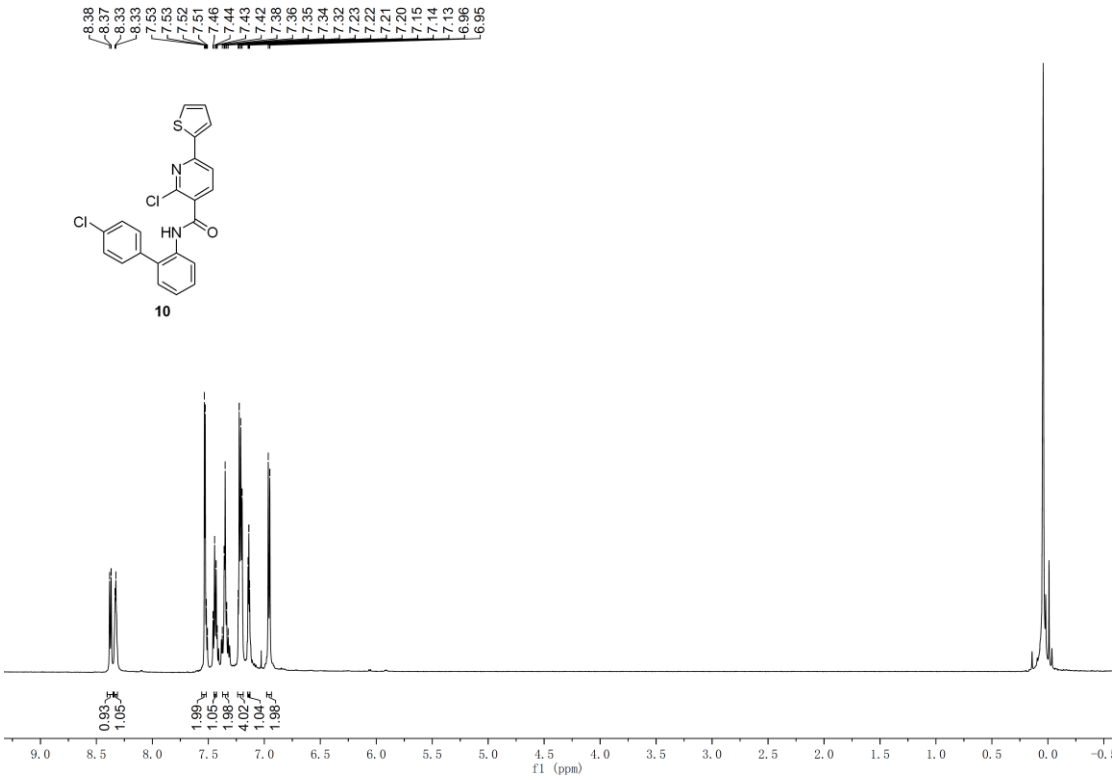
^{13}C NMR (101 MHz) spectrum of **8** in $CDCl_3$



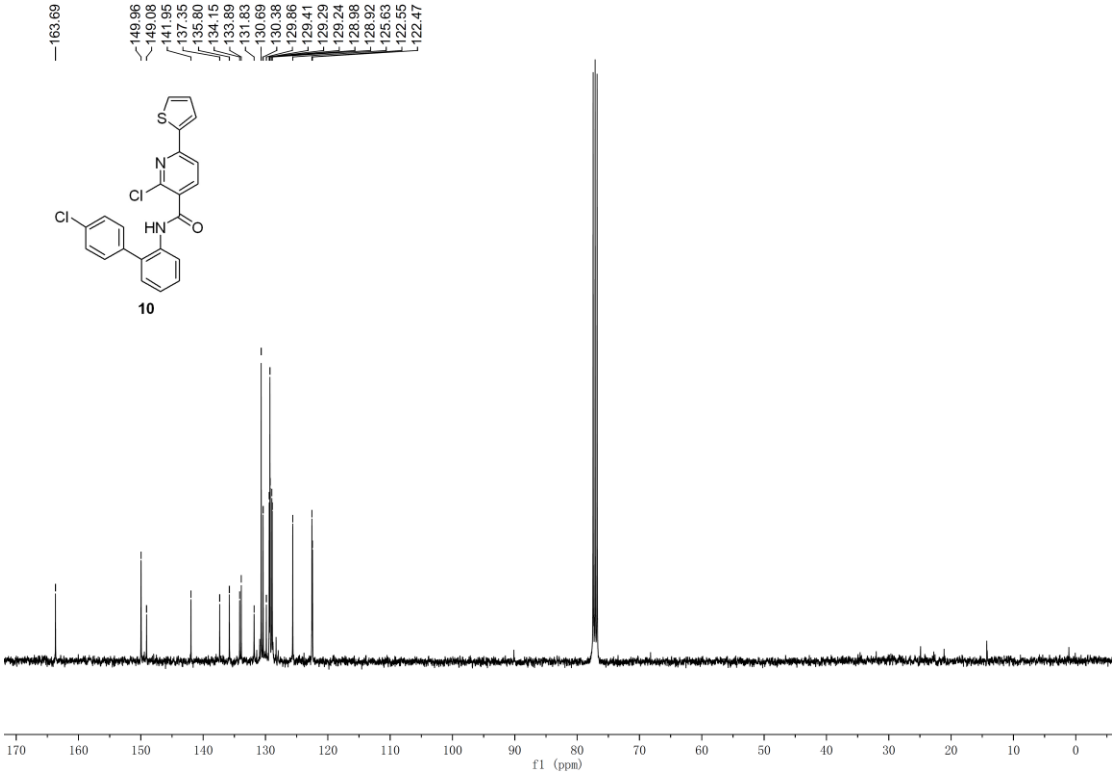
^{1}H NMR (400 MHz) spectrum of **9** in $CDCl_3$



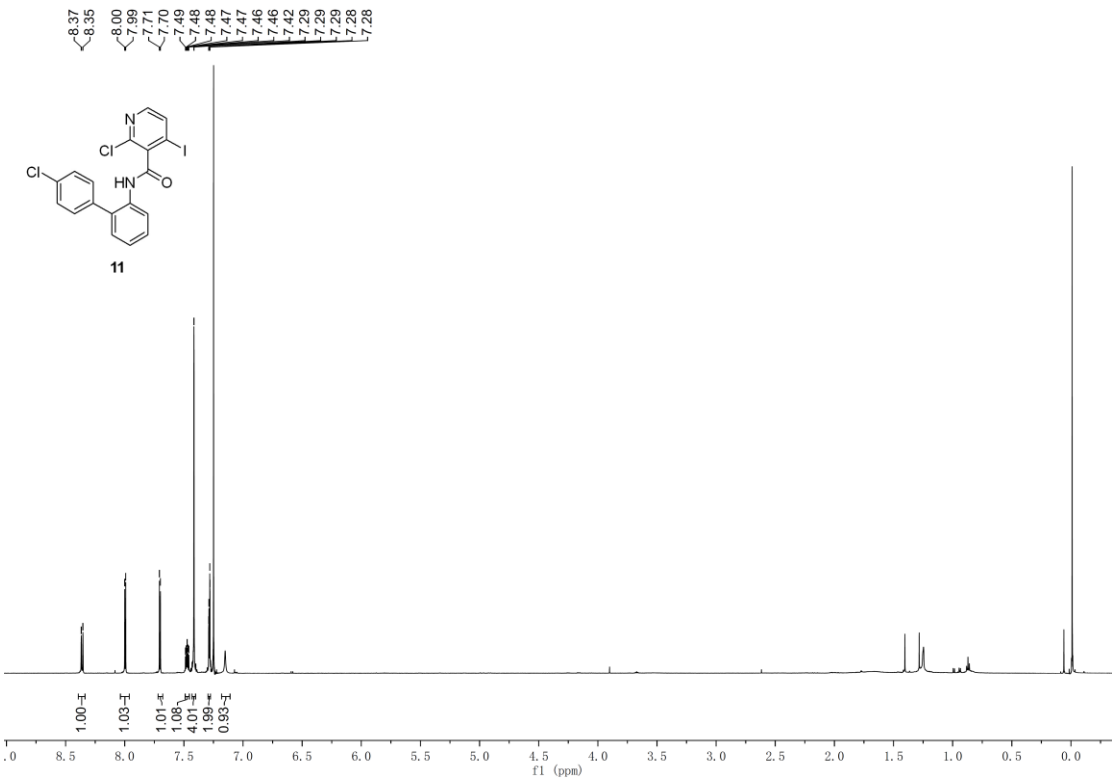
^{13}C NMR (101 MHz) spectrum of **9** in $CDCl_3$



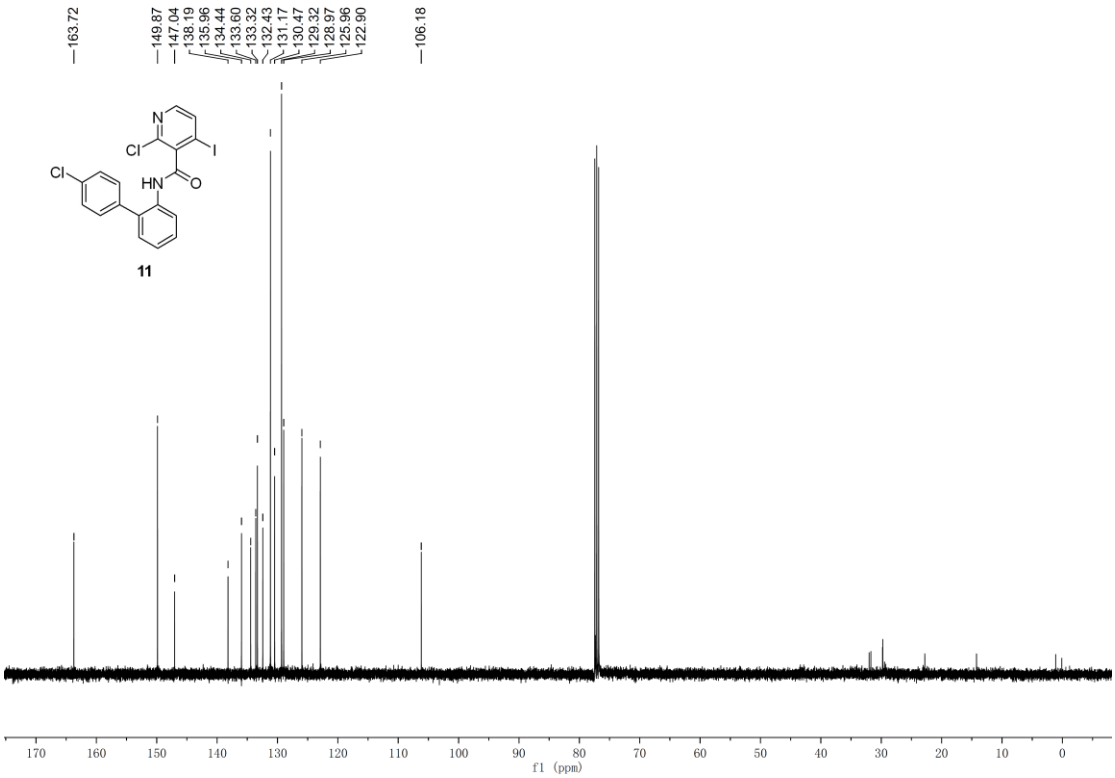
^{1}H NMR (400 MHz) spectrum of **10** in $CDCl_3$



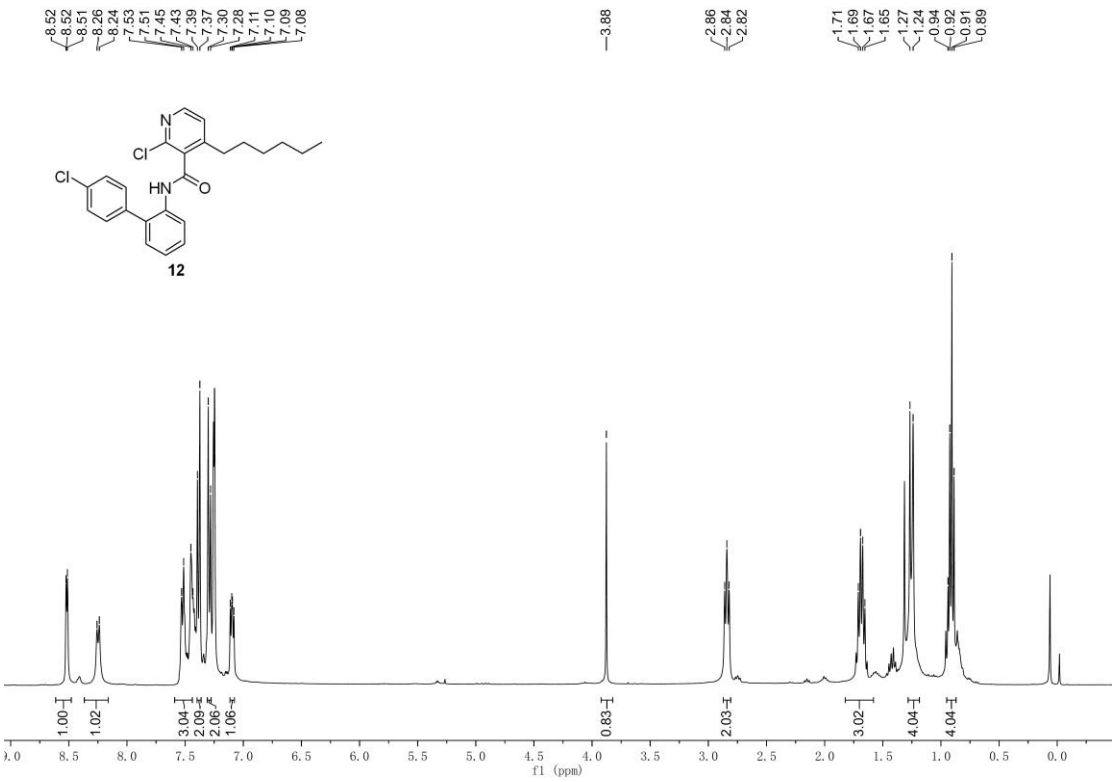
^{13}C NMR (101 MHz) spectrum of **10** in $CDCl_3$



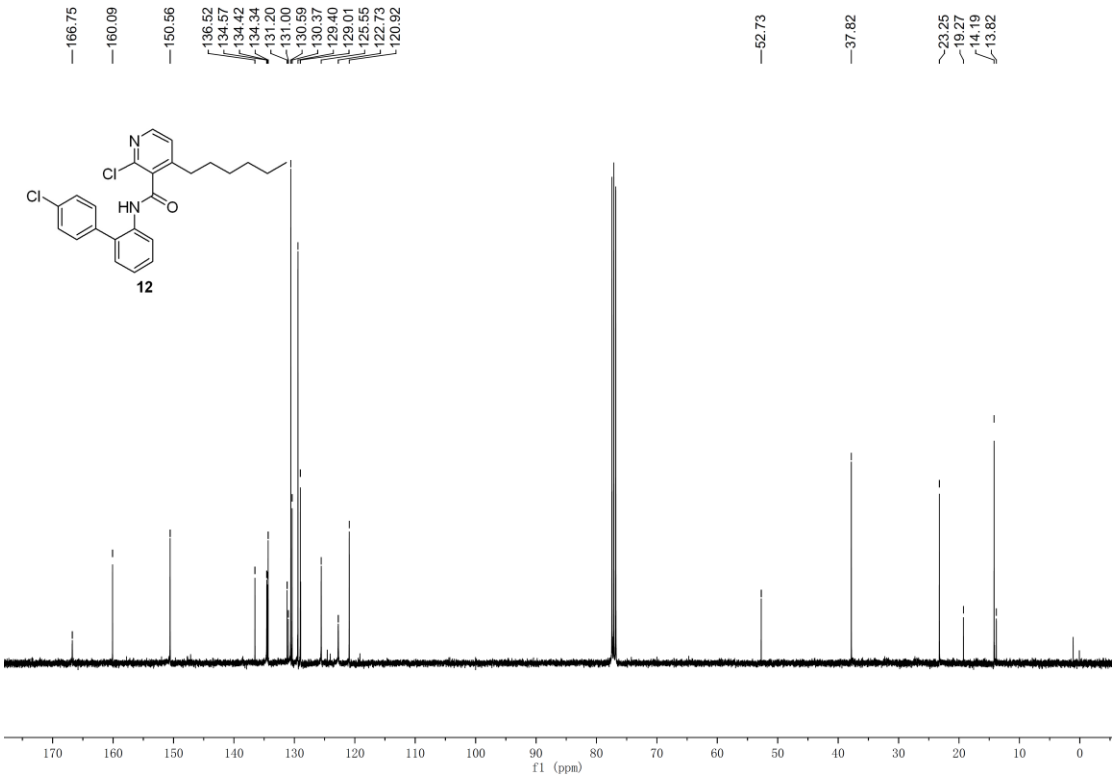
^{1}H NMR (600 MHz) spectrum of **11** in $CDCl_3$



^{13}C NMR (151 MHz) spectrum of **11** in $CDCl_3$



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



^{13}C NMR (101 MHz) spectrum of **12** in $CDCl_3$

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