Supporting Information

Copper-catalyzed regioselective C2-H chlorination of indoles with *para*-toluenesulfonyl chloride

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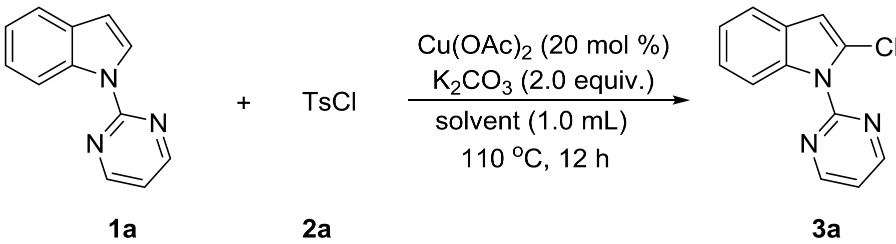
1 Experimental Section

1.1 Optimization of reaction conditions

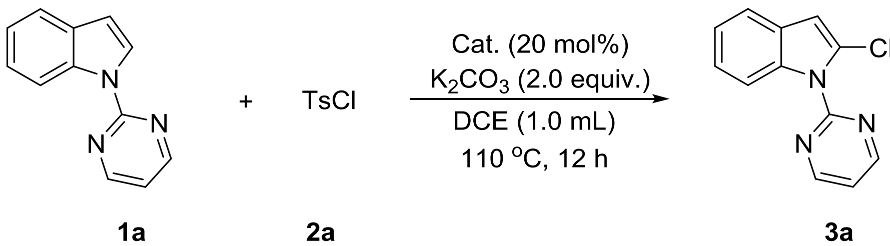
Table S1. Screening of solvent[a]



Entry	Solvent	Yield[b] (%)	Entry	Solvent	Yield[b] (%)
1	1,4-Dioxane	10	10	Hexane	6
2	Toluene	15	11	DMSO	10
3	PhBr	11	12	MeOH	0
4	THF	trace	13	TFE	0
5	MeCN	11	14	H_2O	0
6	Acetone	0	**15**	**DCE**	**25**
7	DMF	8	16	DCM	13
8	Et_2O	10	17	$CHCl_3$	9
9	EtOAc	10	18	1,2,3-Trichloropropane	17

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $Cu(OAc)_2$ (20 mol %), K_2CO_3 (0.4 mmol), solvent (1.0 mL), 110 ^{o}C, under air, 12 h. [b]Isolated yields.

Table S2. Screening of catalyst[a]

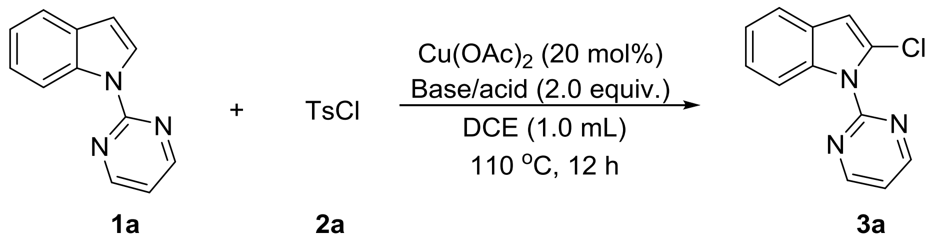


Entry	Cat.	Yield[b] (%)
1	**$Cu(OAc)_2$**	**25**
2	$Cu(OAc)_2 \cdot H_2O$	15
3	CuOAc	10
4	$Cu(acac)_2$	0
5	$Cu(OTf)_2$	13
6	$CuCl_2$	9

7	CuCl	Trace

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), cat. (20 mol%), K_2CO_3 (0.4 mmol), DCE (1.0 mL), 110 °C, under air, 12 h. [b]Isolated yields.

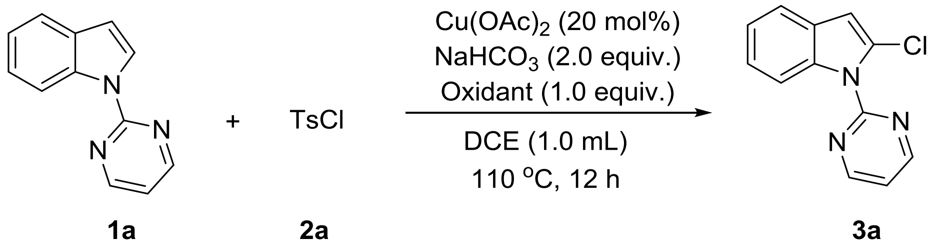
Table S3. Screening of base/acid[a]



Entry	Base/Acid	Yield[b] (%)	Entry	Base/Acid	Yield[b] (%)
1	/	0	11	PhCOONa	43
2	K_2CO_3	25	12	$PivONa{\cdot}H_2O$	24
3	Na_2CO_3	35	13	$NaH_2PO_4{\cdot}2H_2O$	<5
4	Li_2CO_3	39	14	CH_3ONa	35
5	NaOAc	34	15	*t*-BuOK	<5
6	KOAc	14	16	KOH	15
7	CsOAc	0	17	K_3PO_4	6
8	**$NaHCO_3$**	**43**	18[c]	$NaHCO_3$/PhCOONa	43
9	$KHCO_3$	24	19	TsOH	0
10	$Na_2C_2O_4$	10	20	AcOH	Trace

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $Cu(OAc)_2$ (20 mol %), base/acid (0.4 mmol), DCE (1.0 mL), 110 °C, under air, 12 h. [b]Isolated yields. [c]$NaHCO_3$/PhCOONa = (1/1).

Table S4. Screening of oxidant[a]

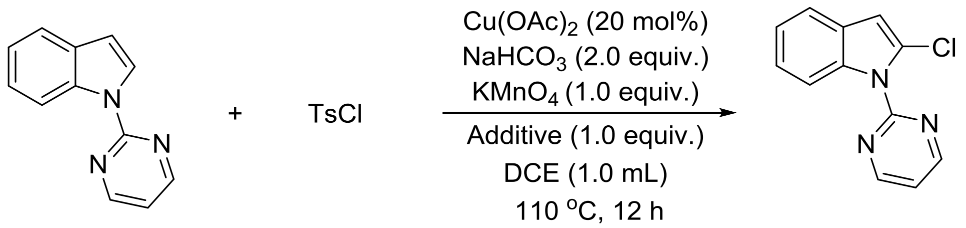


Entry	Oxidant	Yield[b] (%)	Entry	Oxidant	Yield[b] (%)
1	/	43	9	$PhI(OAc)_2$	25
2	$K_2S_2O_8$	43	10	$Mn(OAc)_3{\cdot}H_2O$	Trace
3	Ag_2CO_3	0	**11**	**$KMnO_4$**	**54**

4	AgOAc	41	12	H_2O_2	35
5	Ag_2O	0	13	BQ	40
6	AgTFA	0	14	O_2	39
8	NMO	17			

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $Cu(OAc)_2$ (20 mol%), $NaHCO_3$ (0.4 mmol), oxidant (0.2 mmol), DCE (1.0 mL), air, 110 °C, 12 h. [b]Isolated yields.

Table S5. Screening of additive[a]

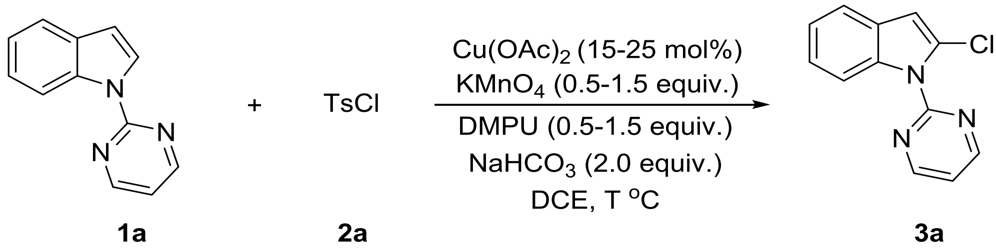


1a **2a** **3a**

Entry	Additive	Yield[b] (%)
1	/	54
2	Ph_3P	17
3	$Zn(OAc)_2$	18
4	**DMPU**	**81**
5[c]	DMPU	58
6[d]	DMPU	0
7[e]	DMPU	0
8[f]	DMPU	72
9[g]	DMPU	81

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $Cu(OAc)_2$ (20 mol%), $NaHCO_3$ (0.4 mmol), $KMnO_4$ (0.2 mmol), additive (0.2 mmol), DCE (1.0 mL), 110 °C, 12 h. [b]Isolated yields. [c]*p*-Bromobenzenesulfonyl chloride instead of **2a**. [d]Without TsCl. [e]Without $Cu(OAc)_2$. [f]Under O_2. [g]Under Ar. DMPU = 1,3-dimethyltetrahydropyrimidin-2(1*H*)-one.

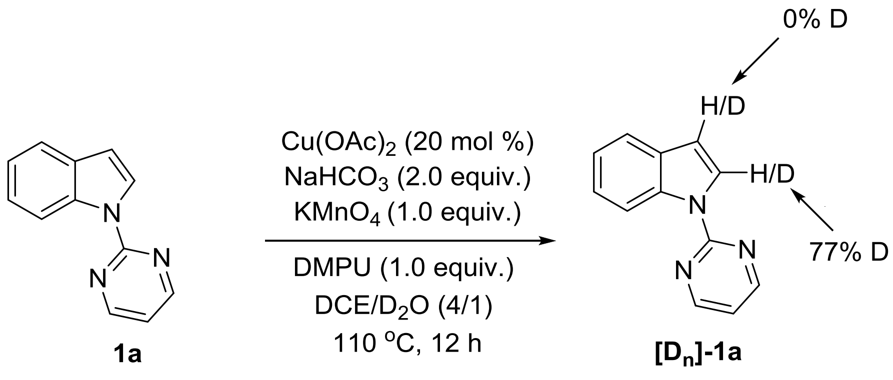
Table S6 Screening of the loading of 2a, $Cu(OAc)_2$, $KMnO_4$, DMPU, reaction time and temperature[a]



Entry	**2a** (mmol)	$Cu(OAc)_2$ (mol%)	$KMnO_4$ (equiv.)	DMPU (equiv.)	Time (h)	Temp (°C)	Yield[b] (%)
1	0.3	20	1	1	12	110	76
2	**0.4**	**20**	**1**	**1**	**12**	**110**	**81**
3	0.5	20	1	1	12	110	78
4	0.4	15	1	1	12	110	67
5	0.4	25	1	1	12	110	79
6	0.4	20	0.5	1	12	110	75
7	0.4	20	1.5	1	12	110	75
8	0.4	20	1	0.5	12	110	64
9	0.4	20	1	1.5	12	110	80
10	0.4	20	1	1	8	110	54
11	0.4	20	1	1	16	110	79
12	0.4	20	1	1	12	100	76
13	0.4	20	1	1	12	120	67

[a]Reaction conditions : **1a** (0.2 mmol), **2a**, cat., $NaHCO_3$ (0.4 mmol), $KMnO_4$, DMPU, DCE (1.0 mL), air, T °C. [b]Isolated yields.

1.2 H/D exchange experiment



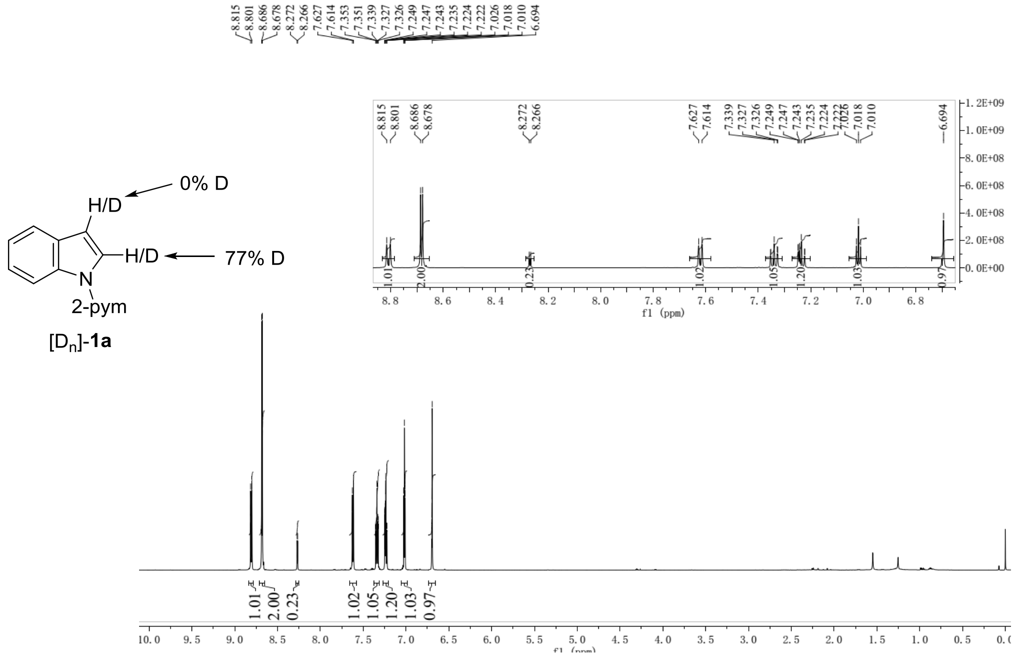
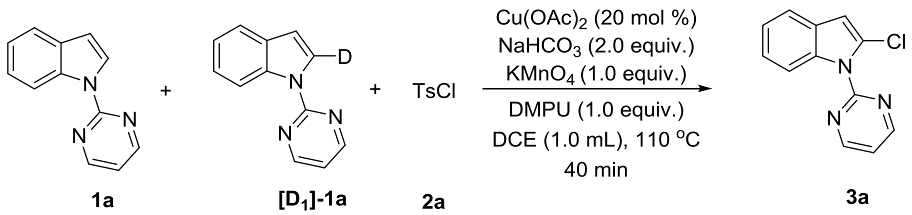


Figure S1 ^{1}H NMR spectrum of **[D$_n$]-1a** from H/D exchange experiment

1.3 Intermolecular competition KIE



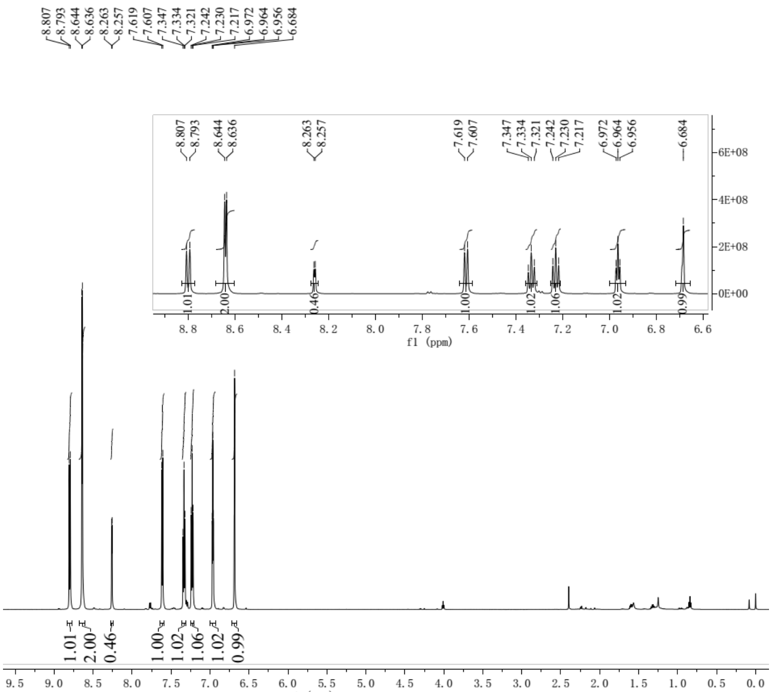
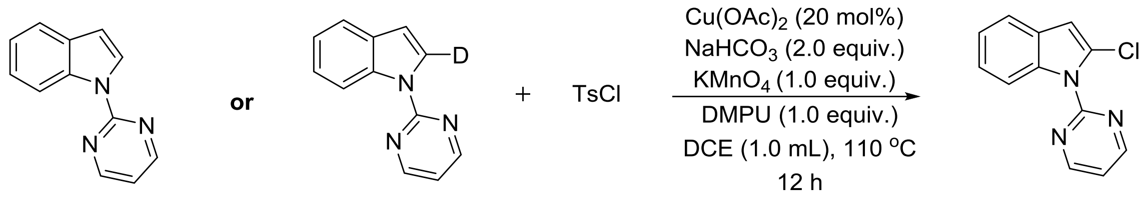


Figure S2 ^{1}H NMR spectrum of recovered **1a** and **[D$_1$]-1a** from intermolecular competition

KIE experiment

1.4 Parallel experiments



1a **[D$_1$]-1a** **2a** **3a**

Entry	Time (min)	Yield of **3a** (**1a**)	Yield of **3a** (**D$_1$-1a**)
1	30	16.56%	4.58%
2	50	23.31%	8.93%
3	70	31.37%	13.29%
4	90	40.74%	16.12%

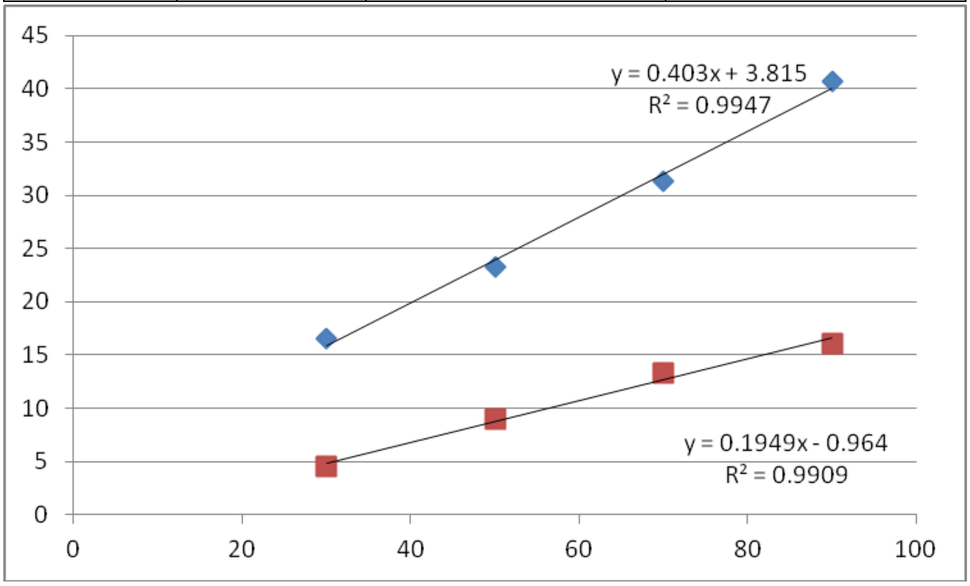
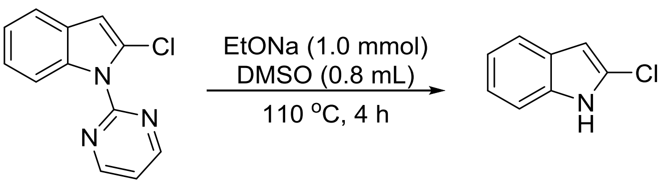


Figure S3 The parallel KIE was calculated as $k_H/k_D = 0.403/0.1949 \approx 2.1$

1.5 Removal of the directing group



3a **4a**

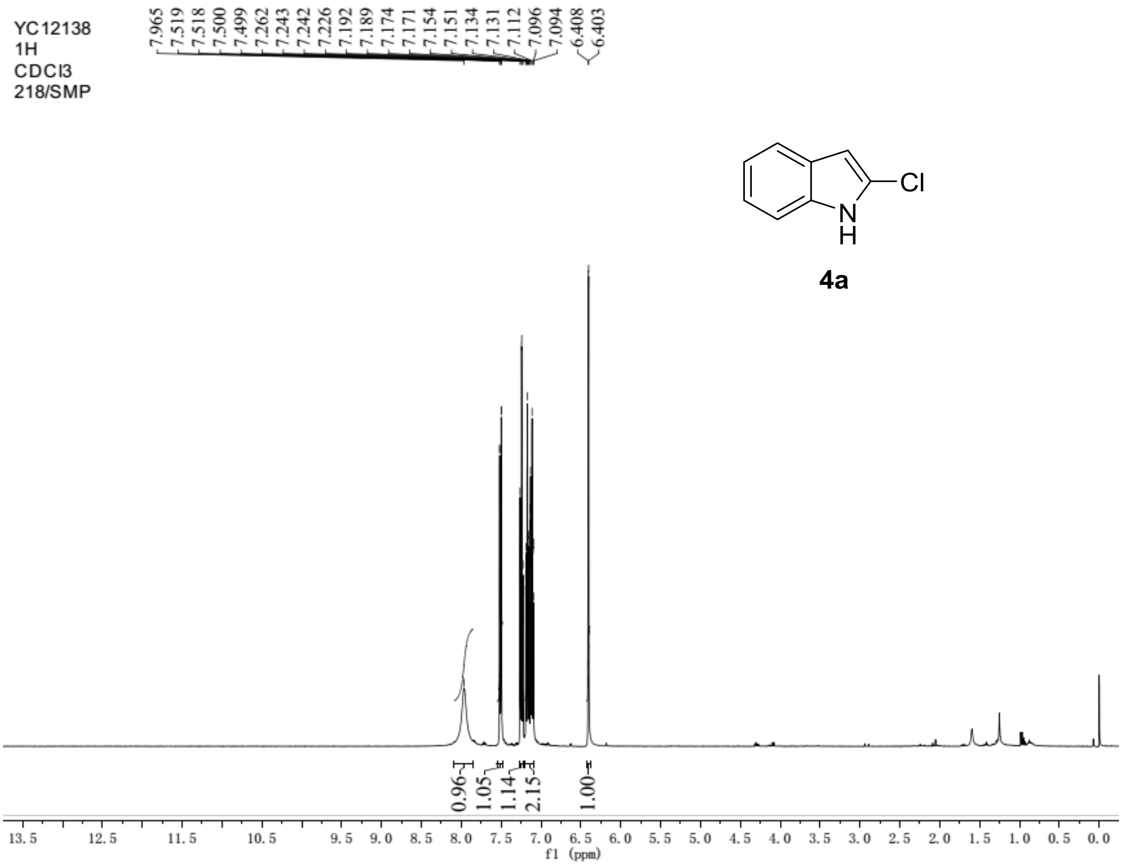


Figure S4 ^{1}H NMR spectrum of **4a** (400 MHz, $CDCl_3$)

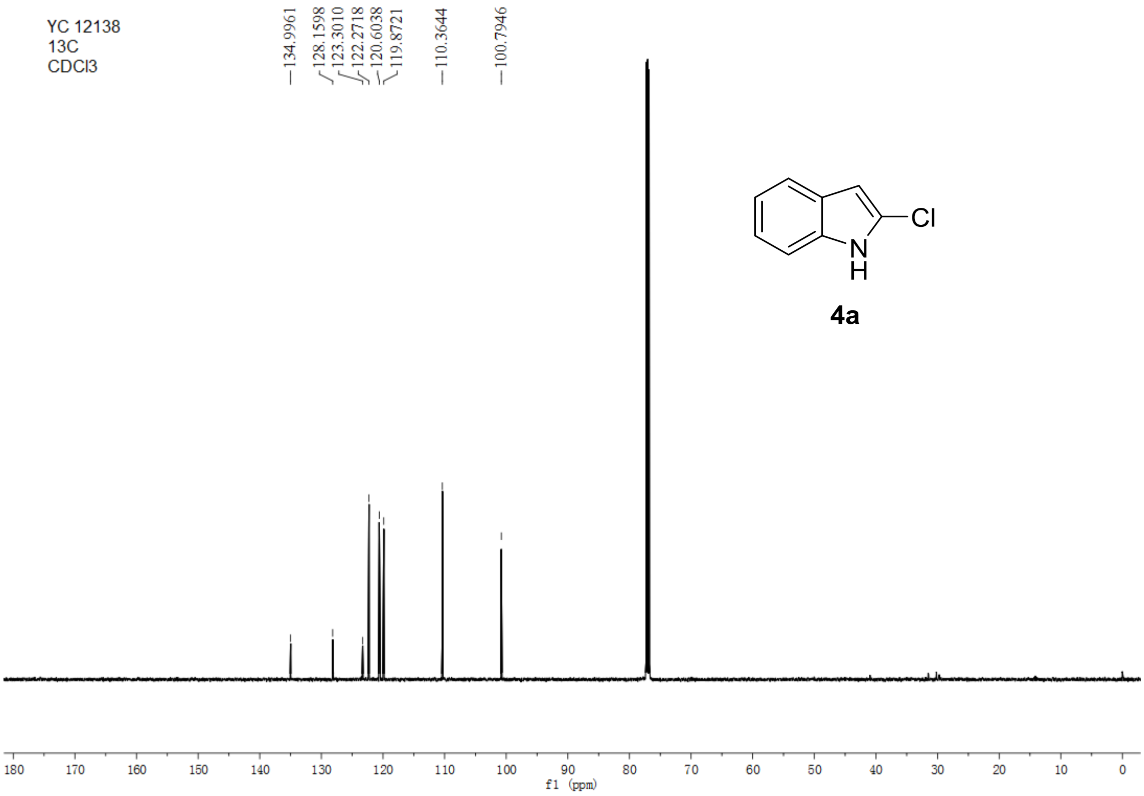
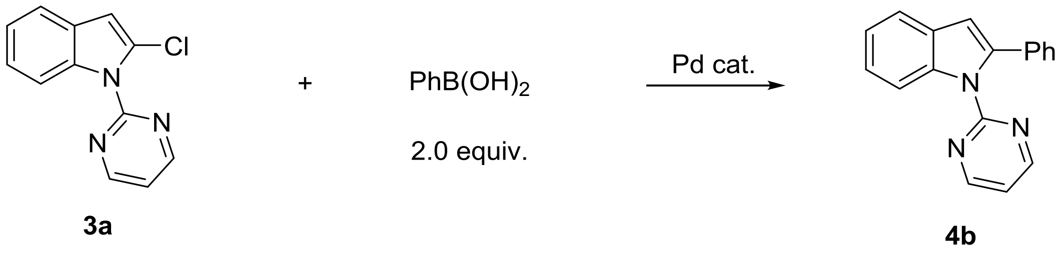


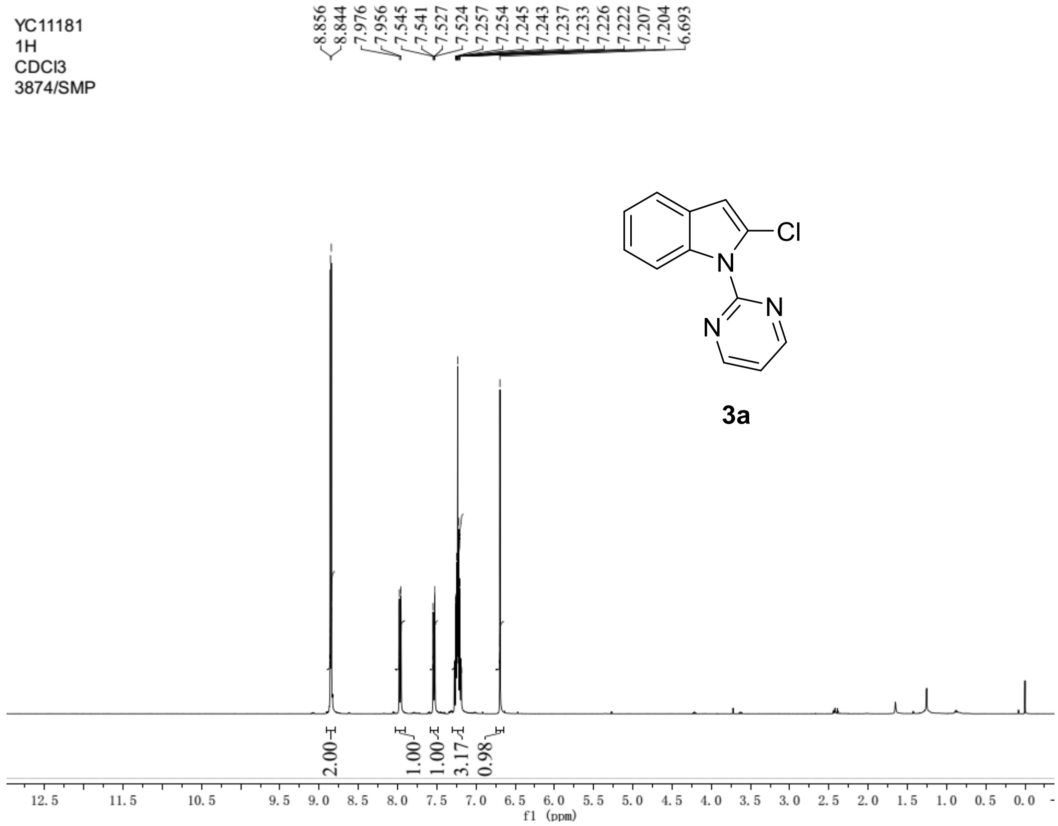
Figure S5 $^{13}C\{^{1}H\}$ NMR spectrum of **4a** (150 MHz, $CDCl_3$)

1.6 Pd-catalyzed Suzuki couplings of 3a with phenylboronic acid

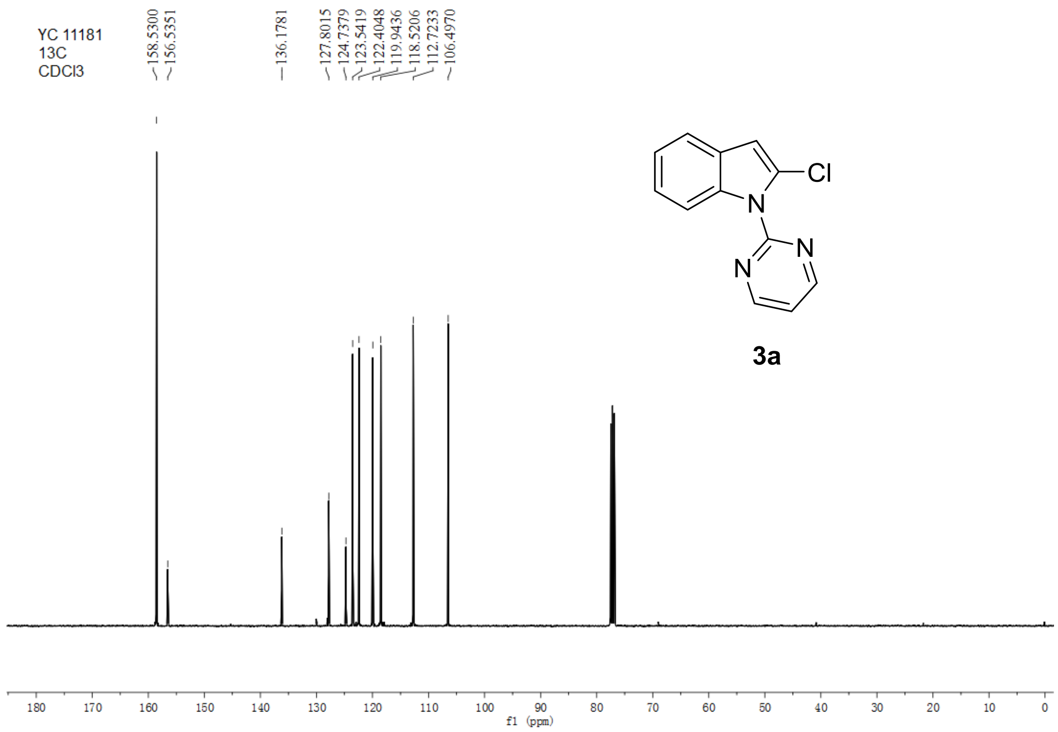


Entry	Reaction conditions	Isolated yield (%)
1	$Pd_2(dba)_3$ (5 mol%), $PCy_3{\cdot}HBF_4$ (10 mol%), Na_2CO_3 (2 equiv.), dioxane, 110 °C, 12 h	no reaction
2	$Pd_2(dba)_3$ (1 mol%), X-Phos (4 mol%), K_3PO_4 (2.0 equiv.), *n*-BuOH, MW, 110 °C, 30 min	no reaction
3	$Pd_2(dba)_3$ (5 mol%), Na_2CO_3 (aq.), dioxane, MW, 110 °C, 30 min	trace
4	$Pd_2(dba)_3$ (5 mol%), Na_2CO_3 (aq.), CH_3CN, MW, 110 °C, 30 min	trace
5	$Pd(OAc)_2$ (5 mol%), Na_2CO_3 (aq.), CH_3CN, MW, 110 °C, 30 min	25
6	$Pd(PPh_3)_2Cl_2$ (5 mol%), Na_2CO_3 (aq.), CH_3CN, MW, 110 °C, 30 min	53
7	$Pd(PPh_3)_4$ (5 mol%), Na_2CO_3 (aq.), CH_3CN, MW, 130 °C, 30 min	17
8	$Pd(dppf)Cl_2$ (5 mol%), Na_2CO_3 (aq.), CH_3CN, MW, 130 °C, 30 min	75

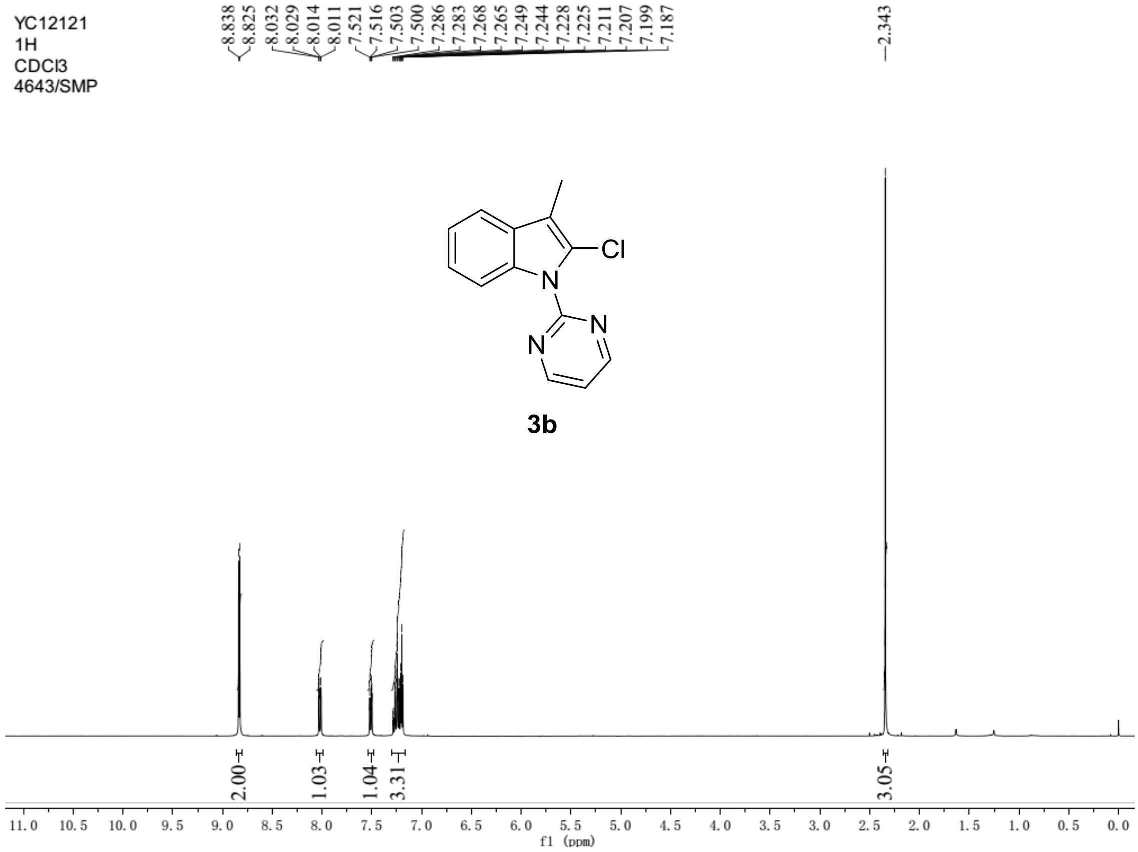
2 NMR spectra



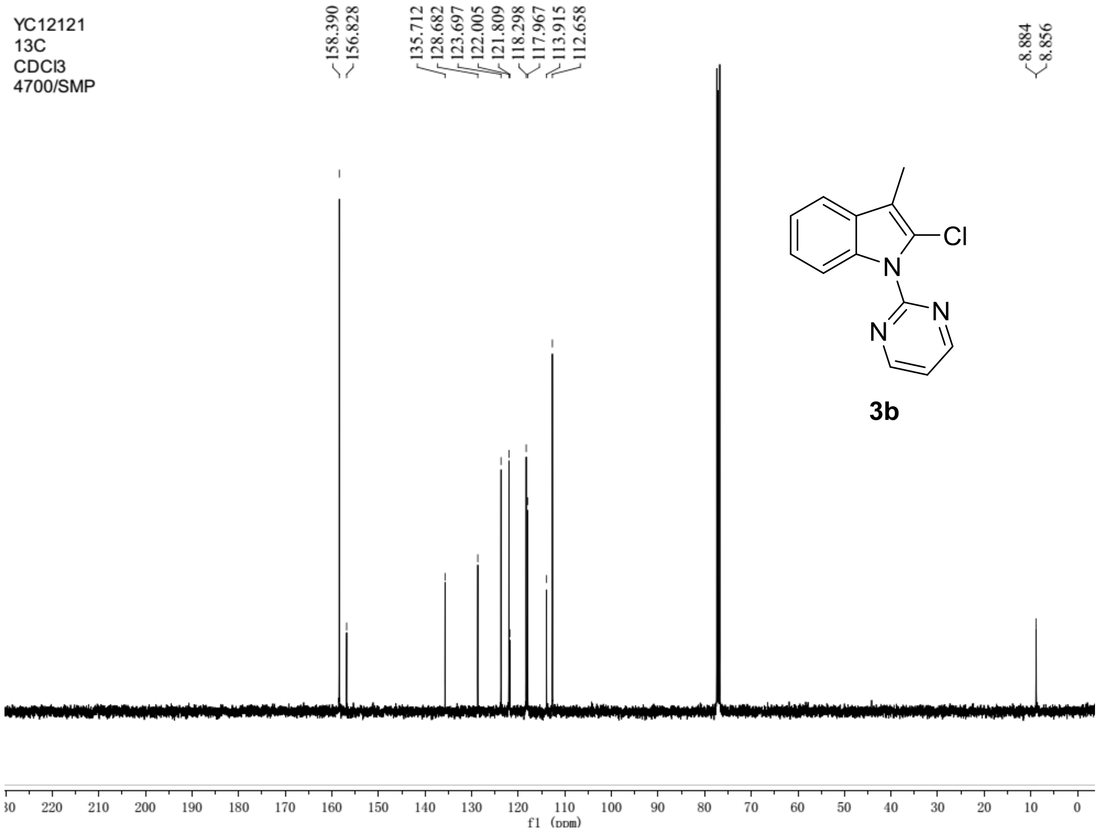
^{1}H NMR spectrum of **3a** (400 MHz, $CDCl_3$)



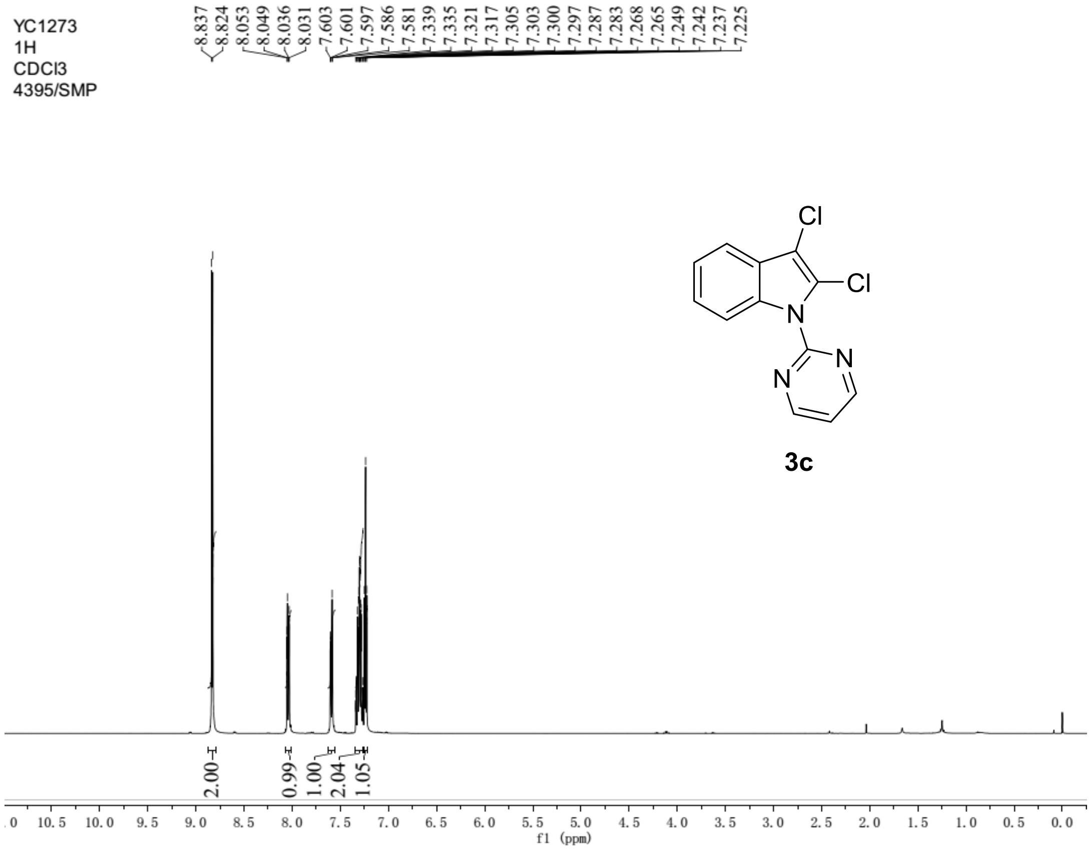
$^{13}C\{^{1}H\}$ NMR spectrum of **3a** (100 MHz, $CDCl_3$)



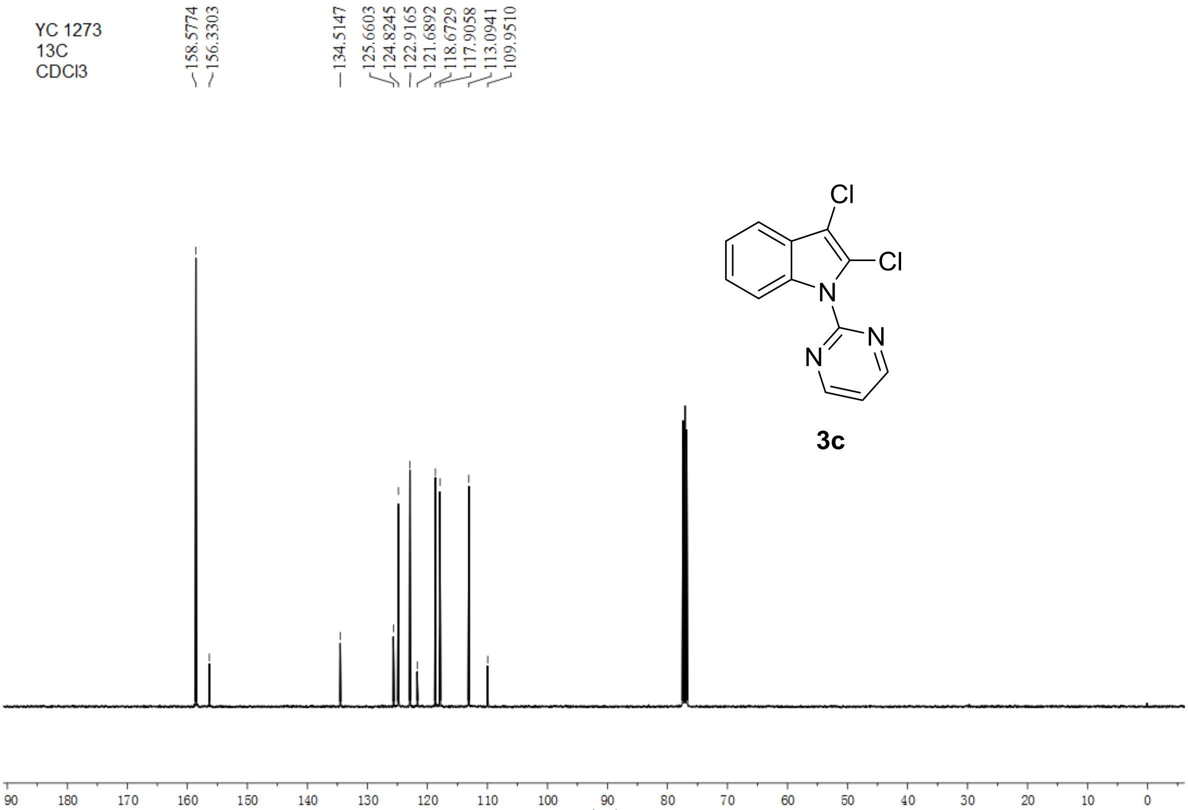
^{1}H NMR spectrum of **3b** (400 MHz, $CDCl_3$)



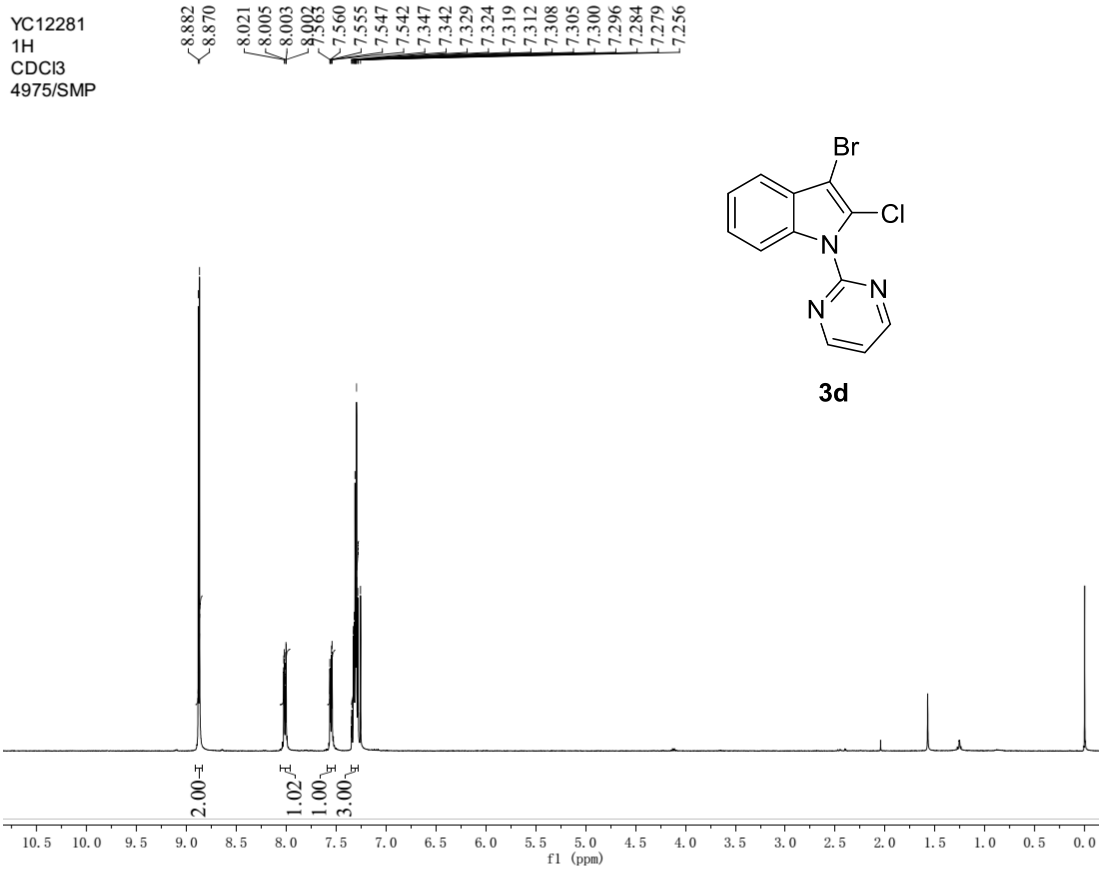
$^{13}C\{^{1}H\}$ NMR spectrum of **3b** (100 MHz, $CDCl_3$)



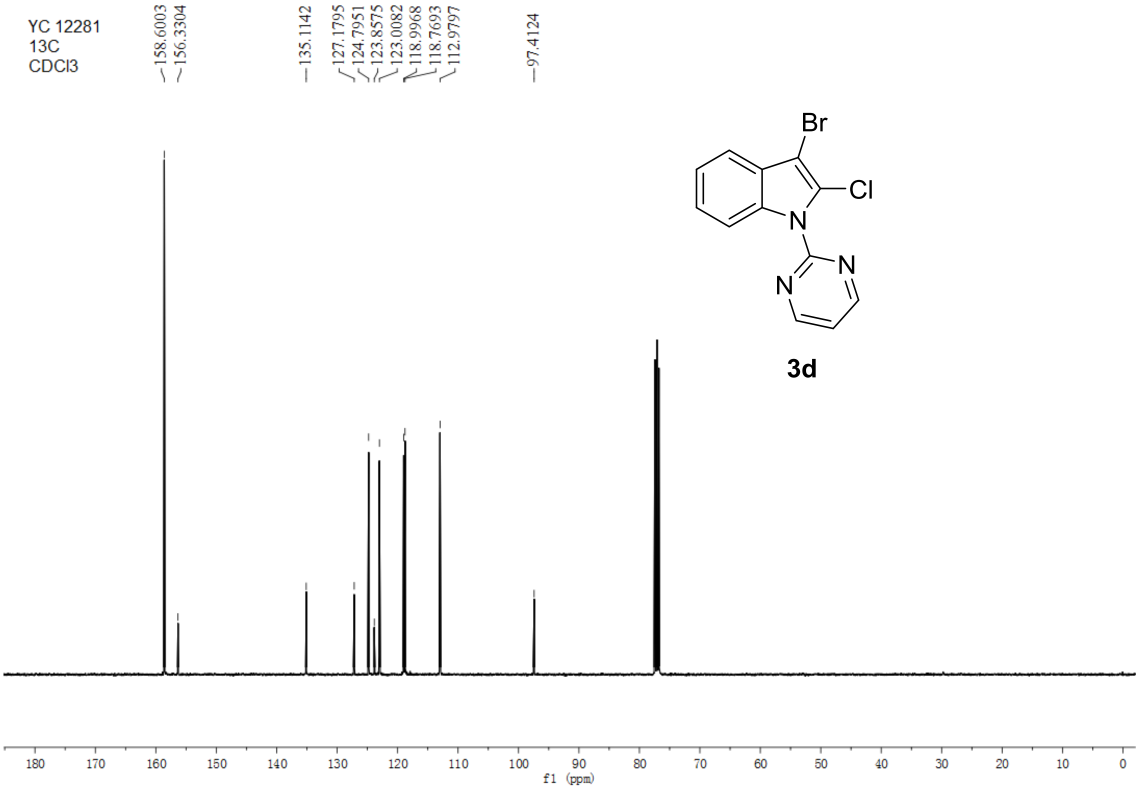
^{1}H NMR spectrum of **3c** (400 MHz, $CDCl_3$)



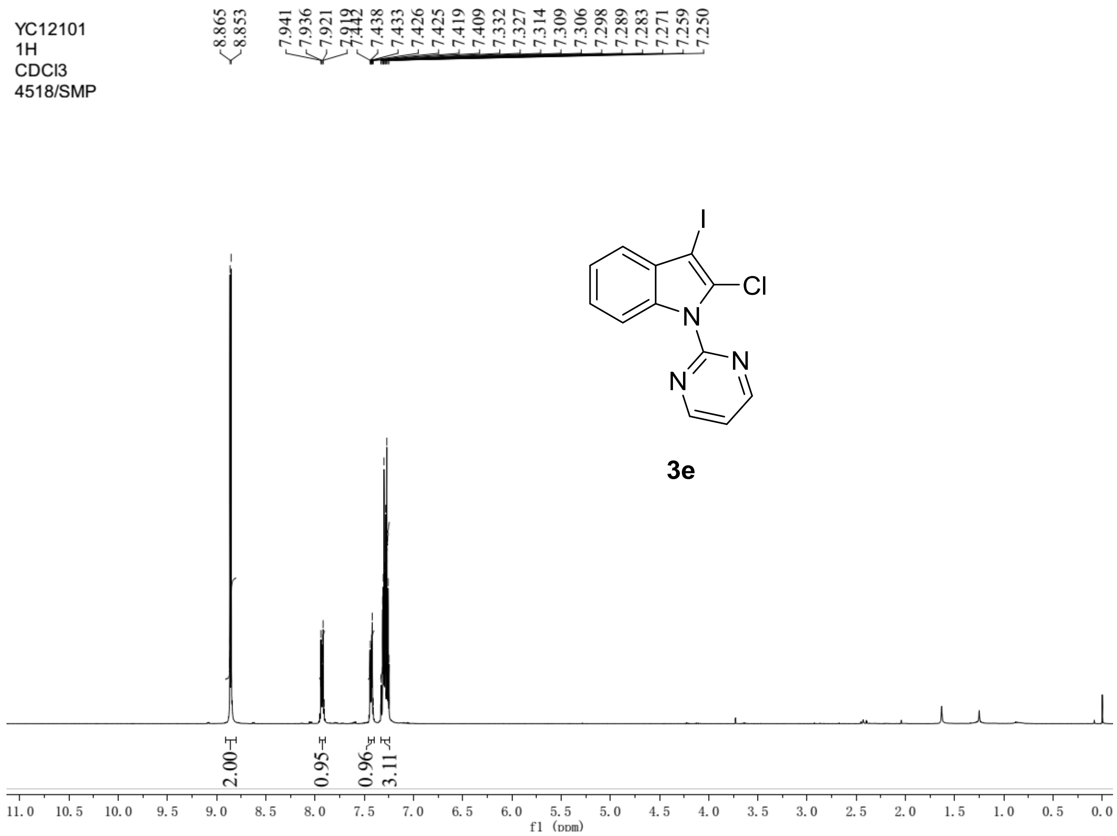
^{13}C{^{1}H} NMR spectrum of **3c** (100 MHz, $CDCl_3$)



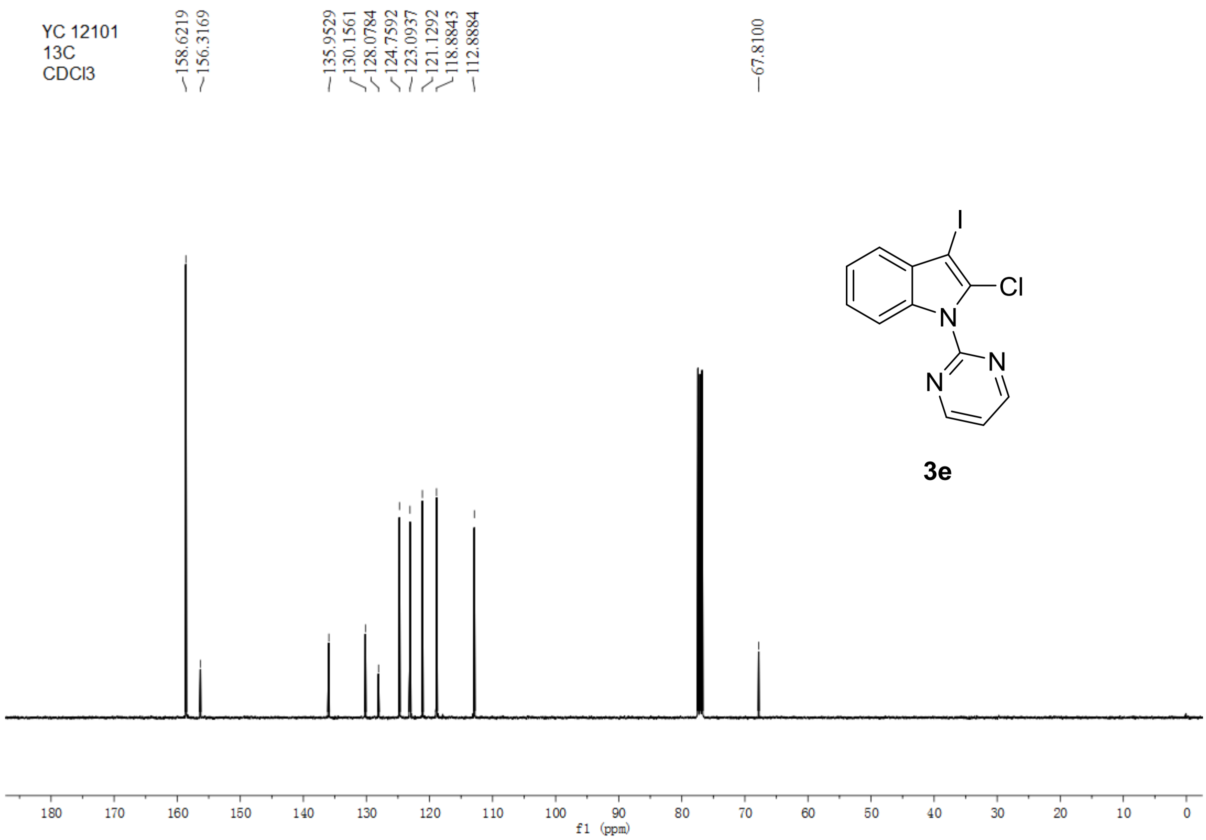
^{1}H NMR spectrum of **3d** (400 MHz, $CDCl_3$)



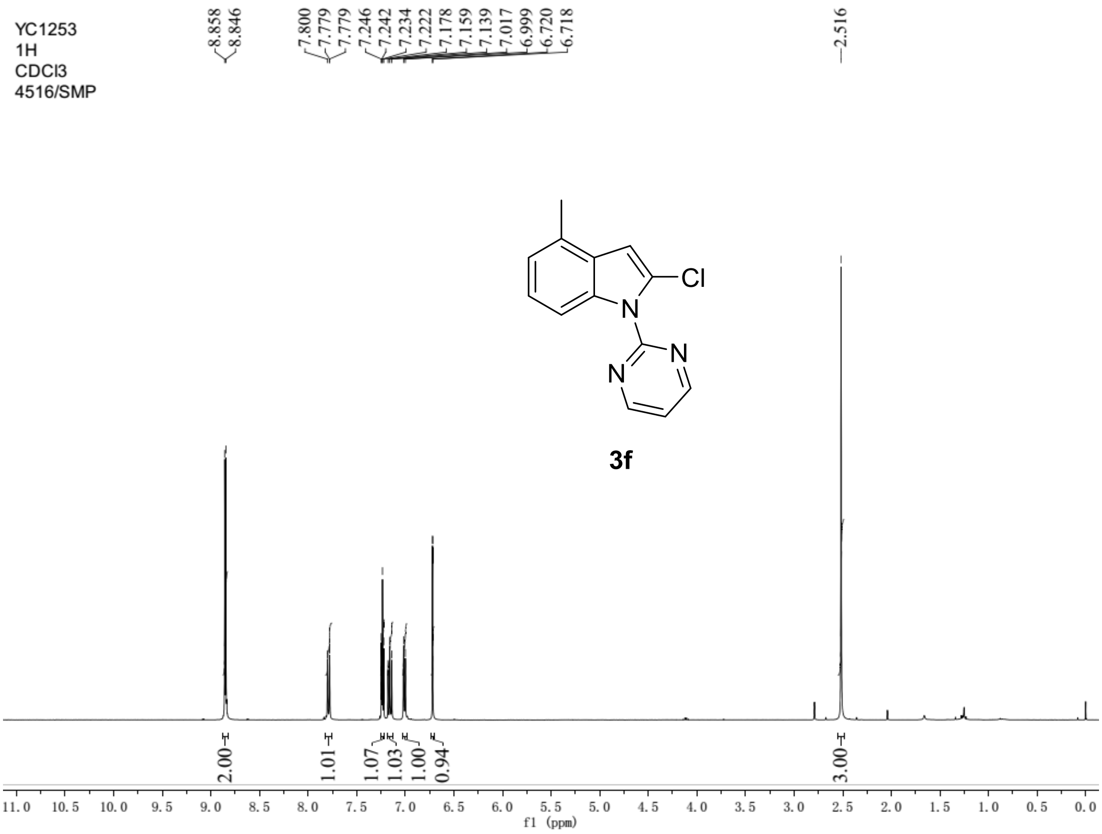
^{13}C{^{1}H} NMR spectrum of **3d** (100 MHz, $CDCl_3$)



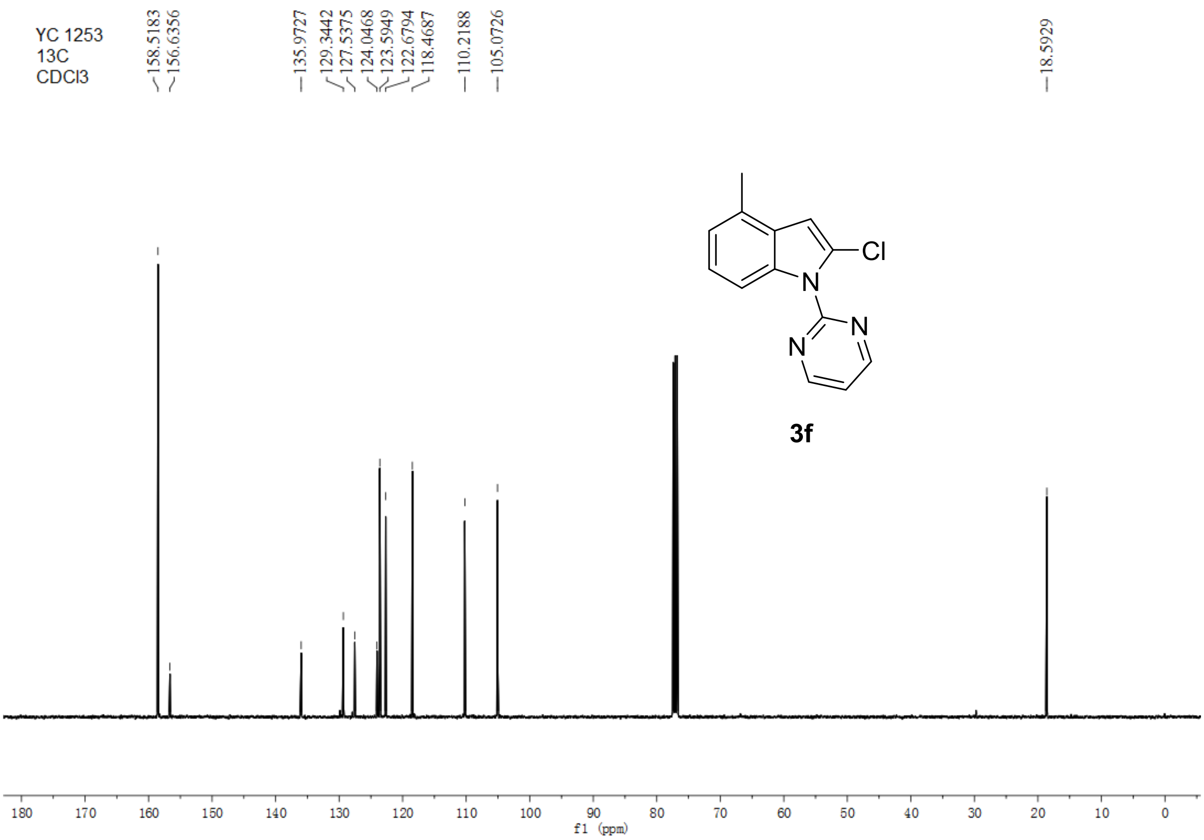
^{1}H NMR spectrum of **3e** (400 MHz, $CDCl_3$)



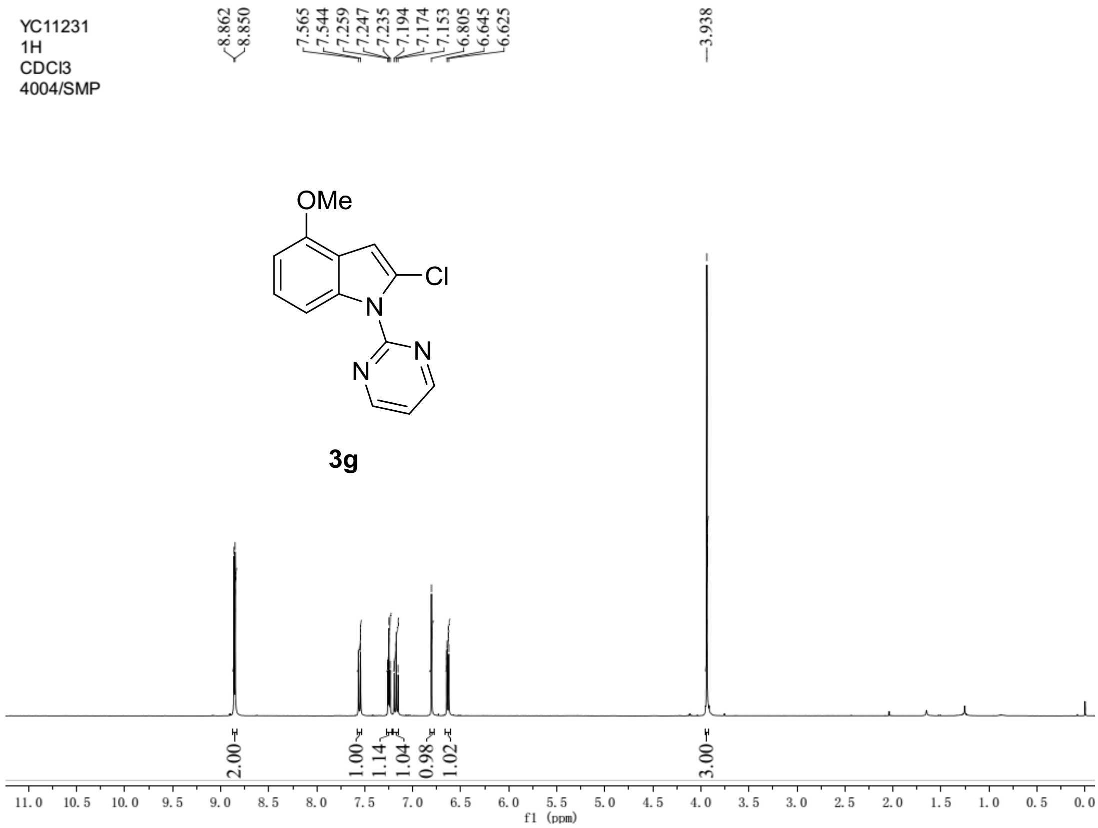
^{13}C{^{1}H} NMR spectrum of **3e** (100 MHz, $CDCl_3$)



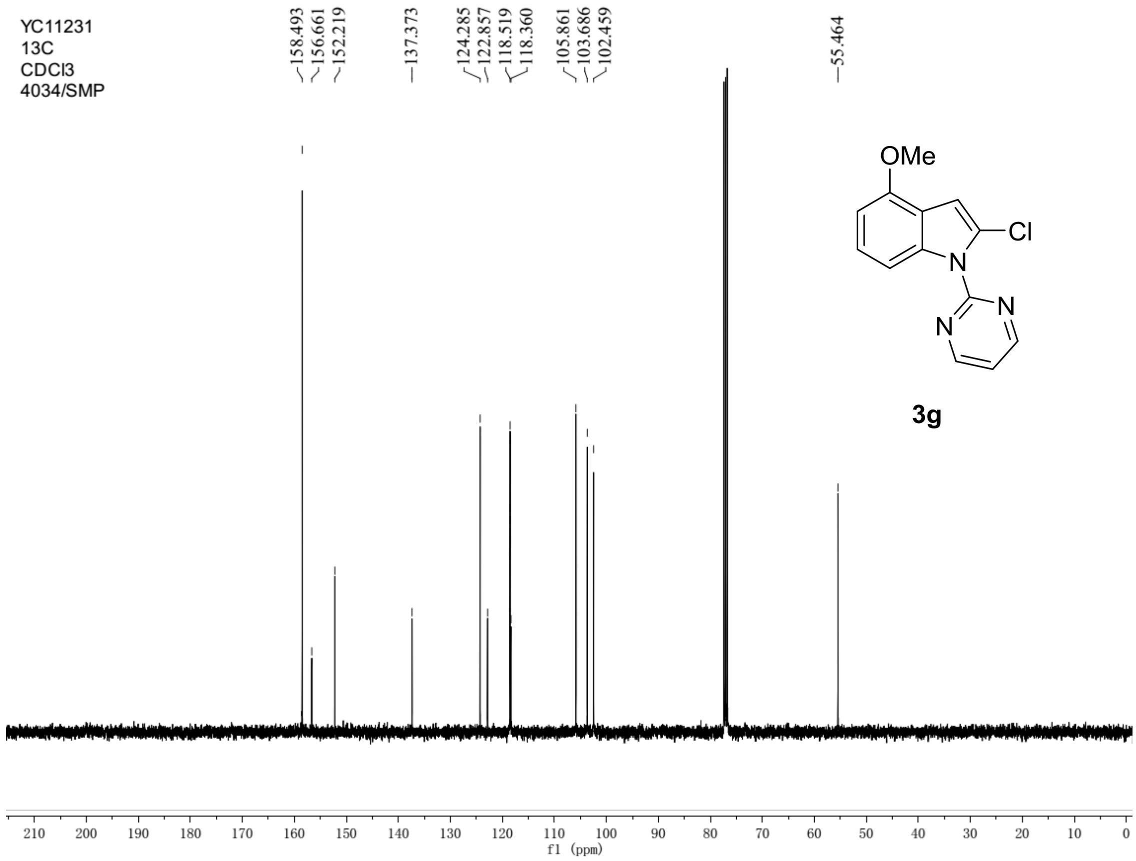
^{1}H NMR spectrum of **3f** (400 MHz, $CDCl_3$)



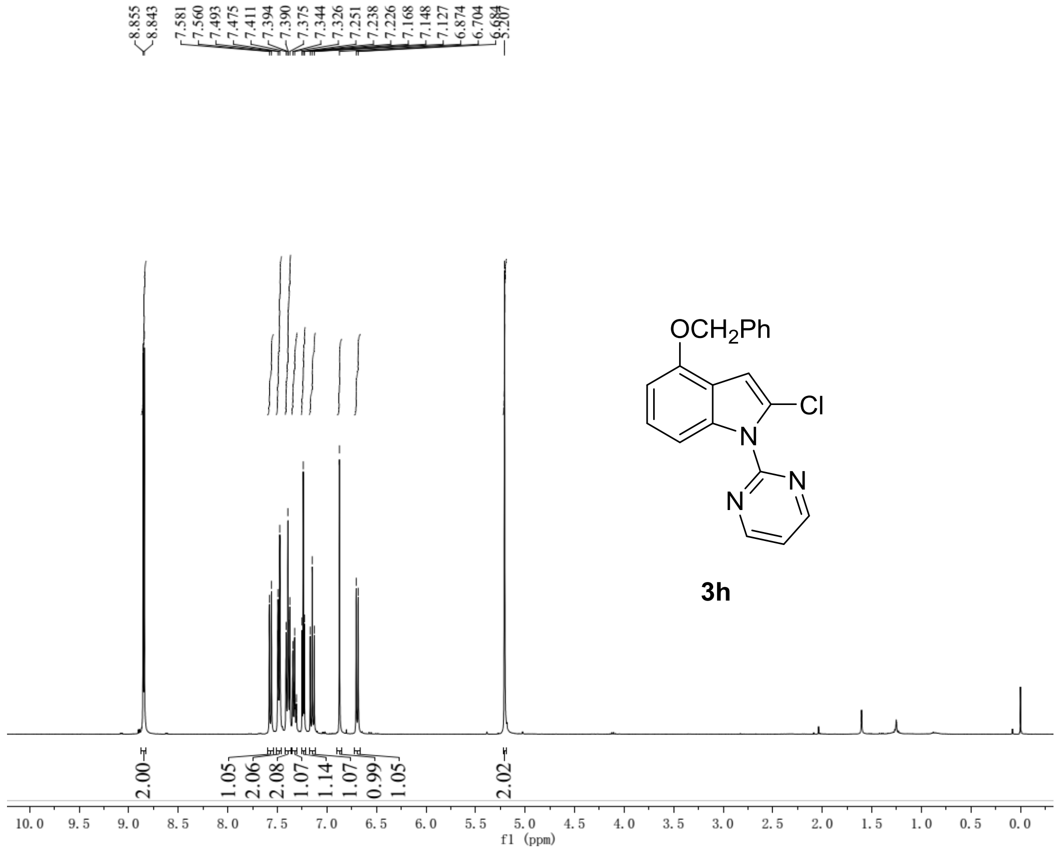
$^{13}C\{^1H\}$ NMR spectrum of **3f** (100 MHz, $CDCl_3$)



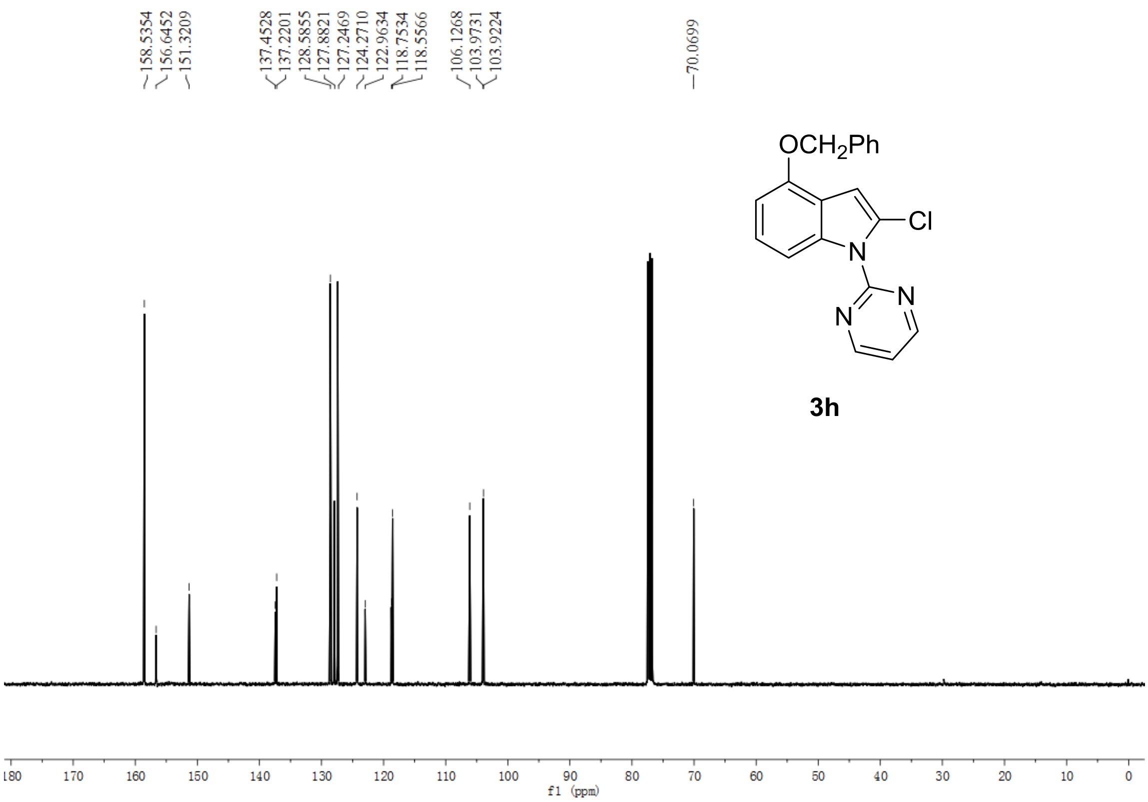
^{1}H NMR spectrum of **3g** (400 MHz, $CDCl_3$)



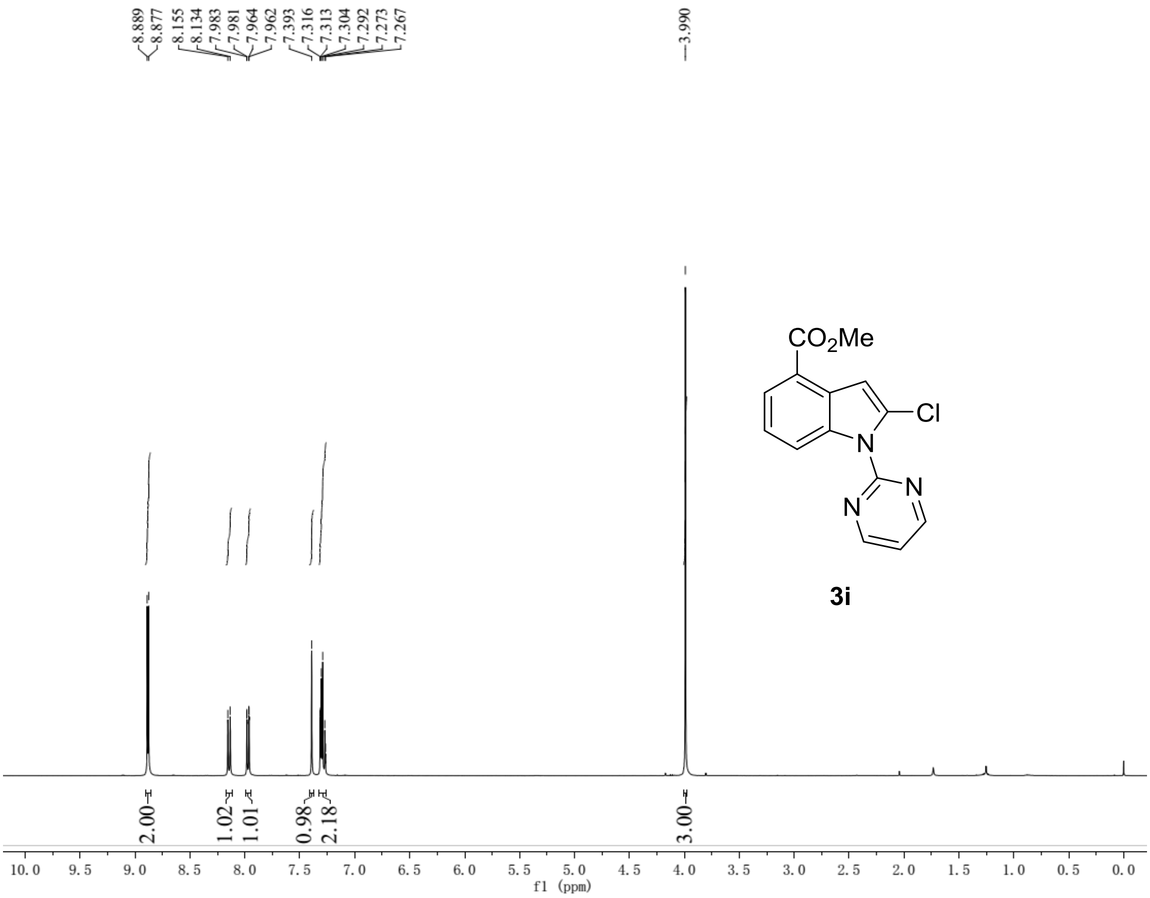
^{13}C{^{1}H} NMR spectrum of **3g** (100 MHz, $CDCl_3$)



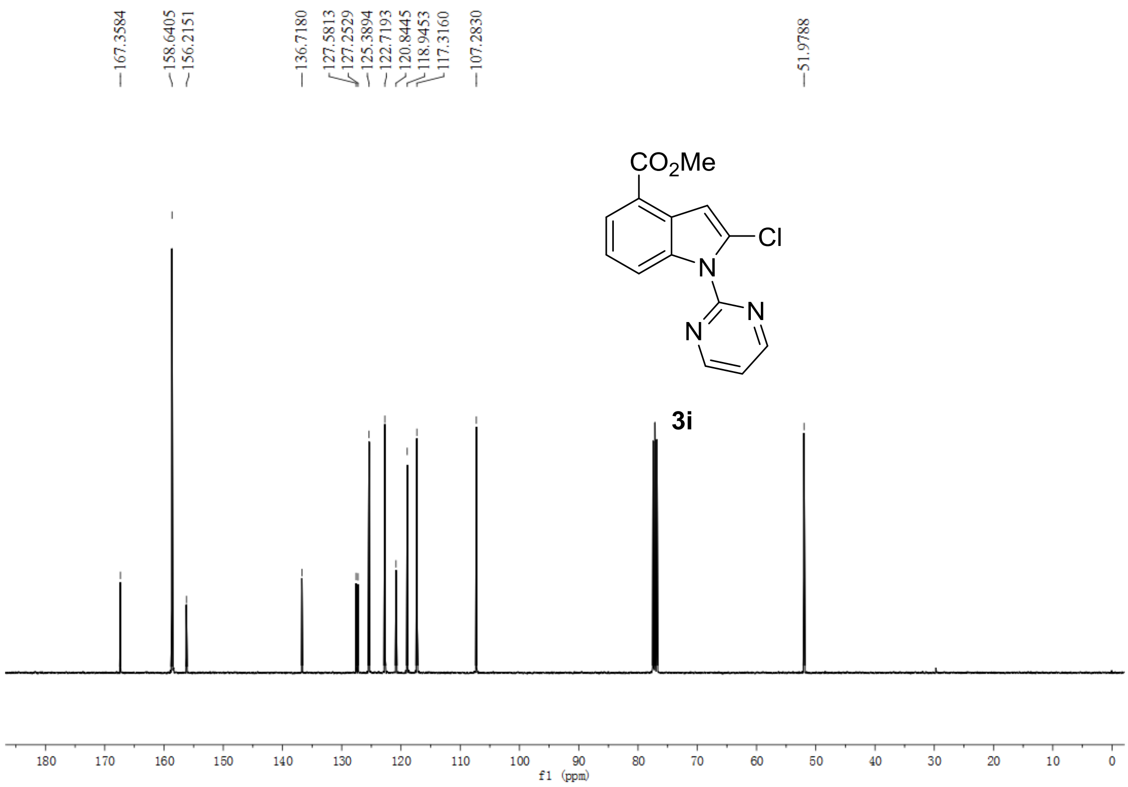
^{1}H NMR spectrum of **3h** (400 MHz, $CDCl_3$)



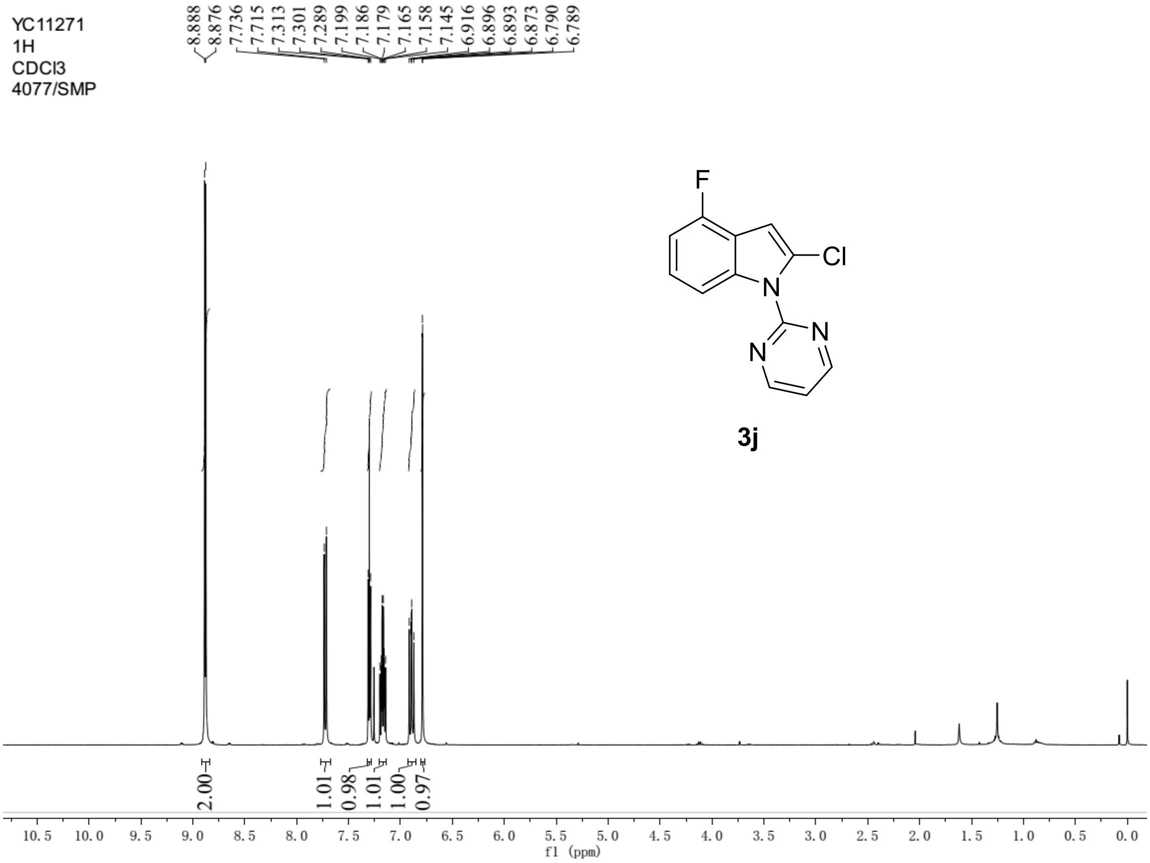
^{13}C{^{1}H} NMR spectrum of **3h** (100 MHz, $CDCl_3$)



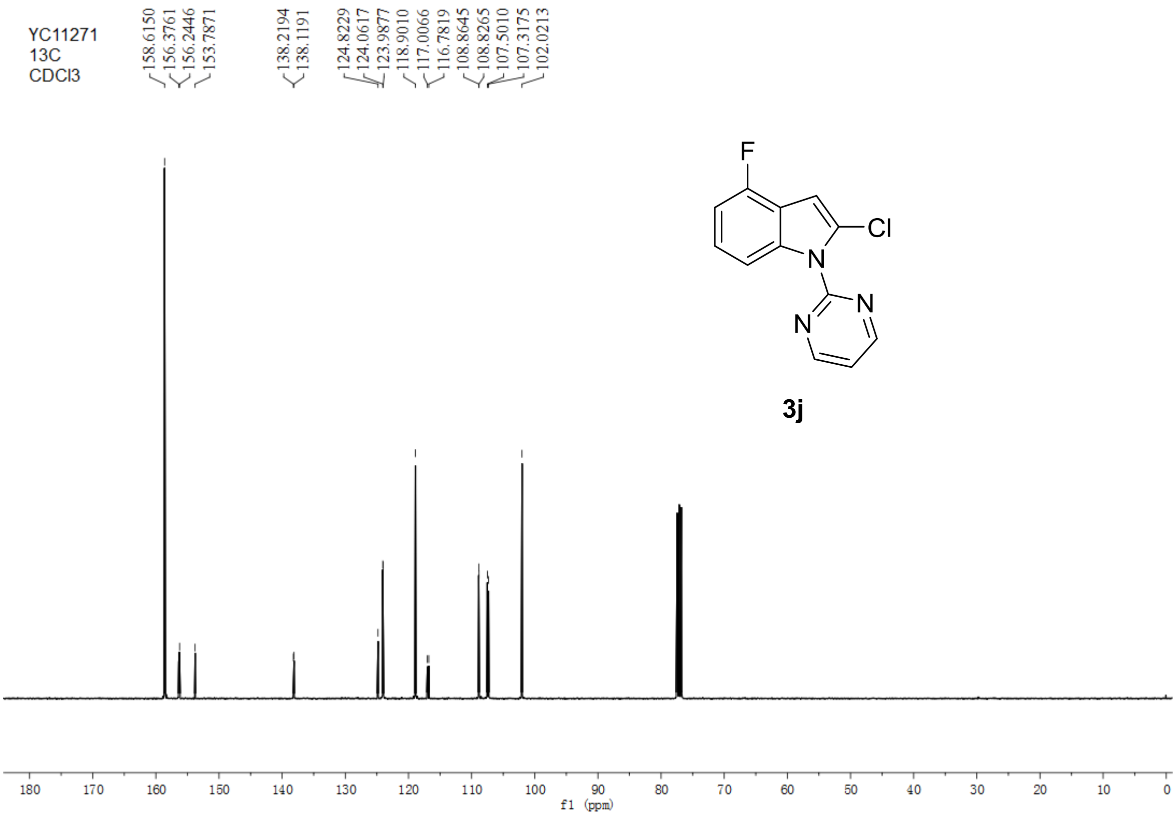
^{1}H NMR spectrum of **3i** (400 MHz, $CDCl_3$)



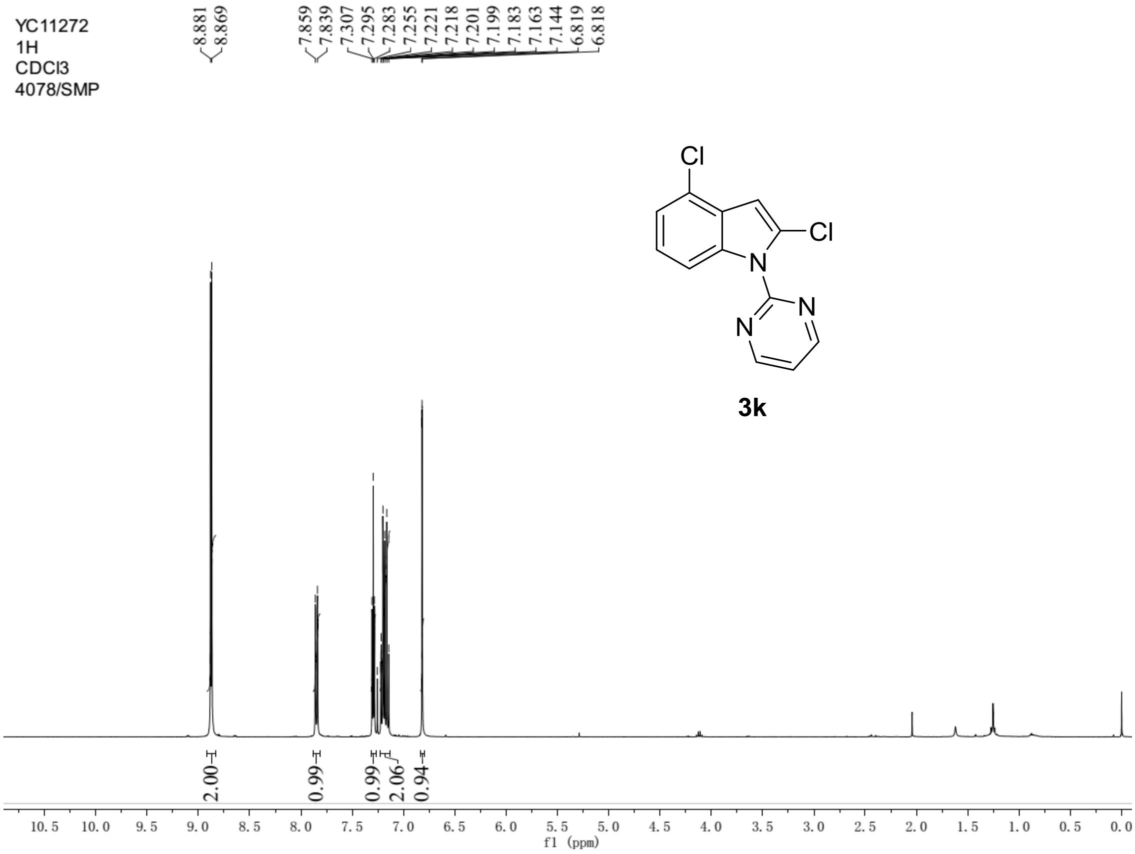
$^{13}C\{^{1}H\}$ NMR spectrum of **3i** (100 MHz, $CDCl_3$)



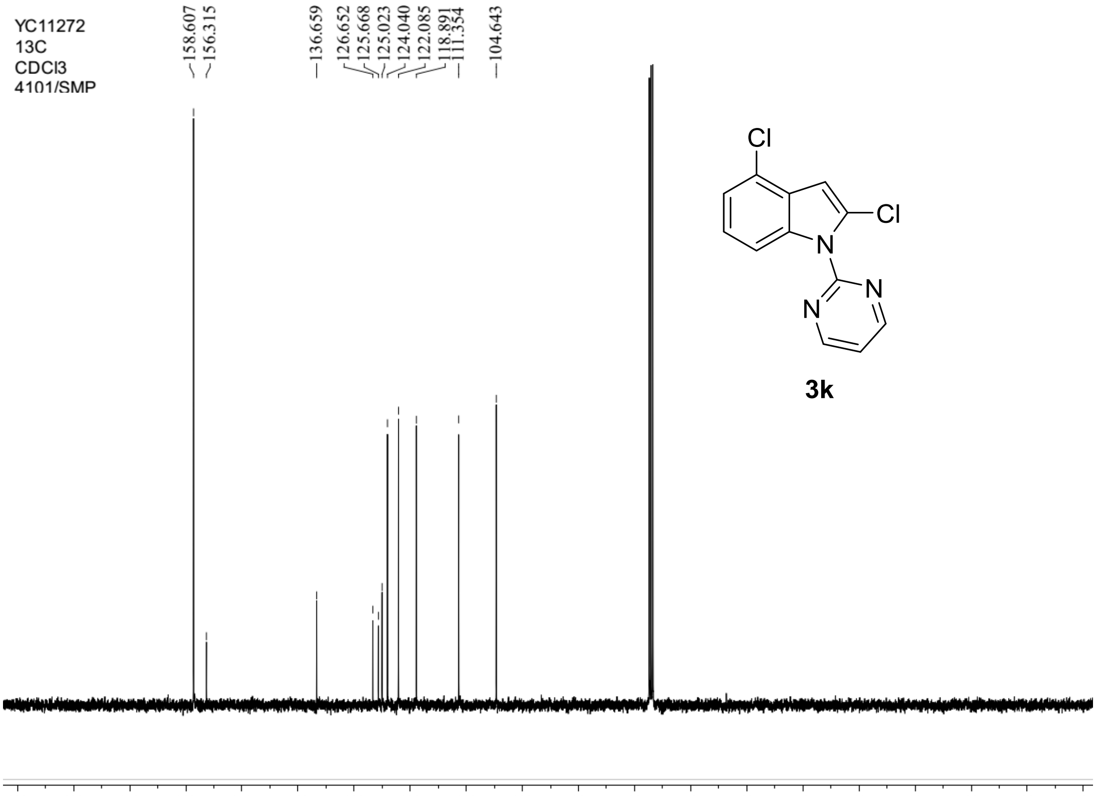
[1]H NMR spectrum of **3j** (400 MHz, $CDCl_3$)



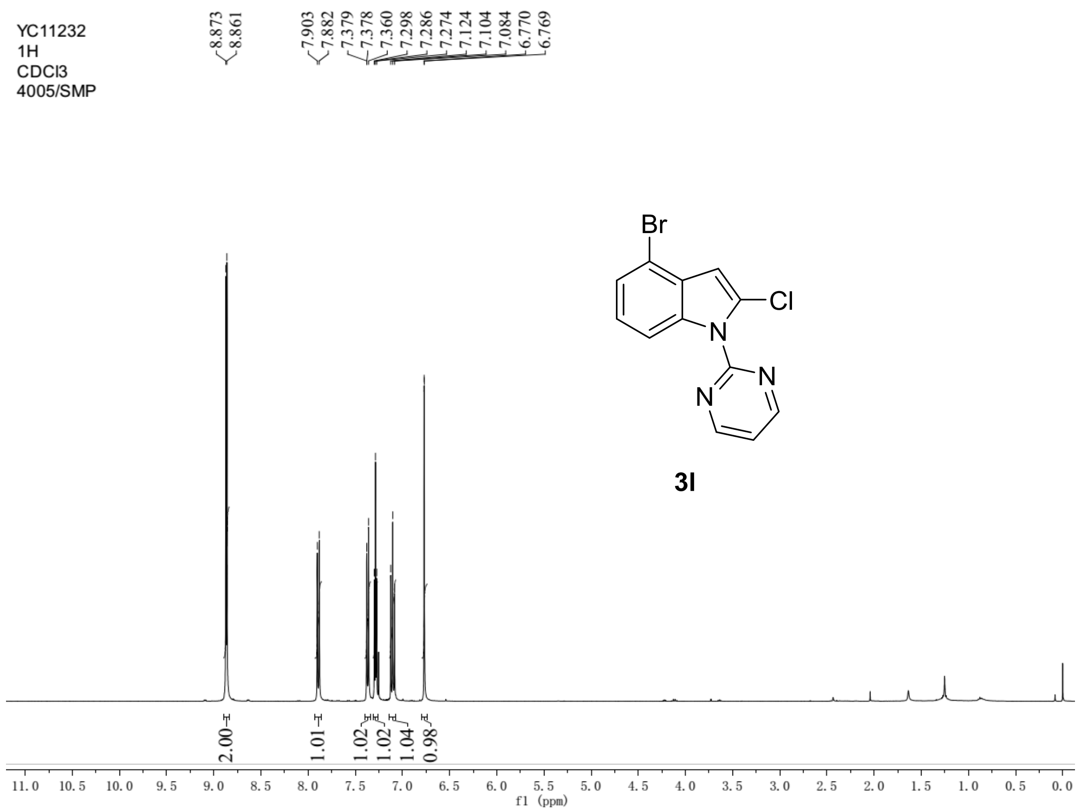
[13]C{[1]H} NMR spectrum of **3j** (100 MHz, $CDCl_3$)



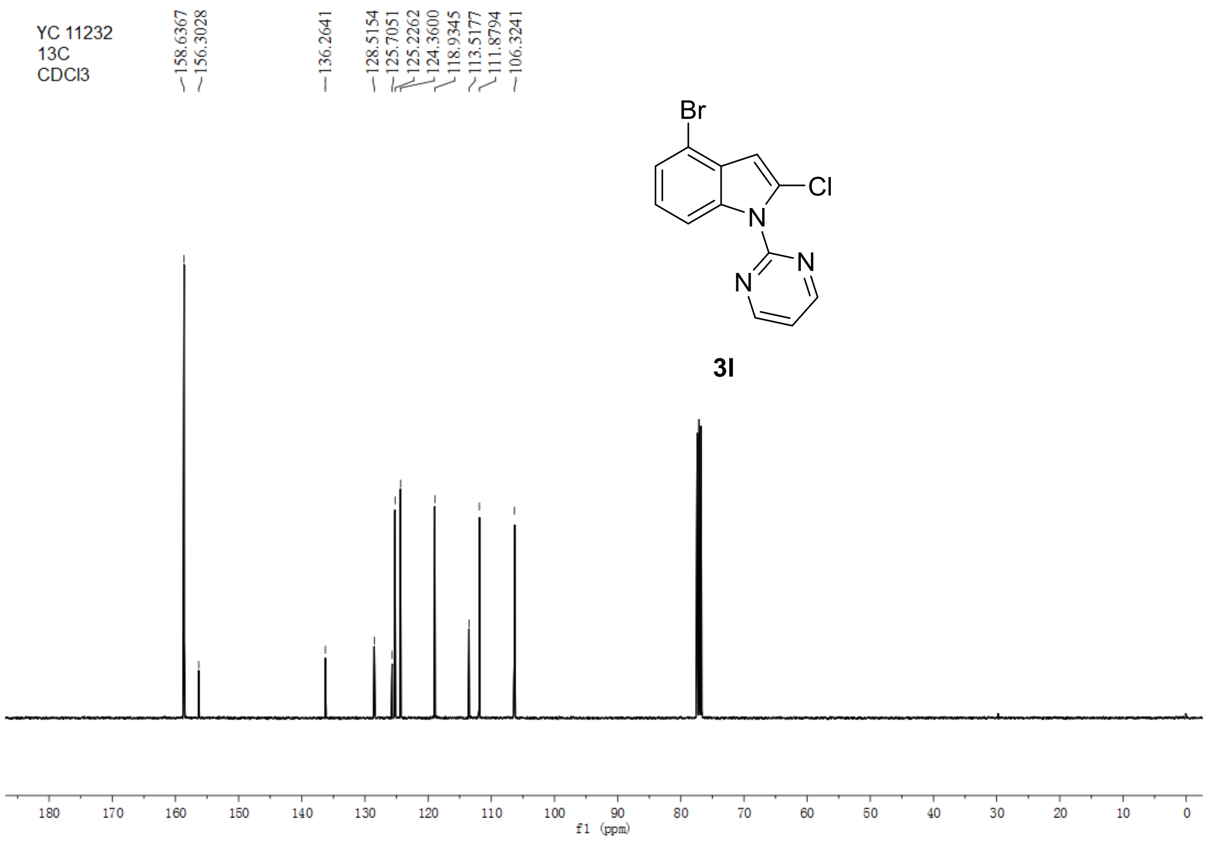
^{1}H NMR spectrum of **3k** (400 MHz, $CDCl_3$)



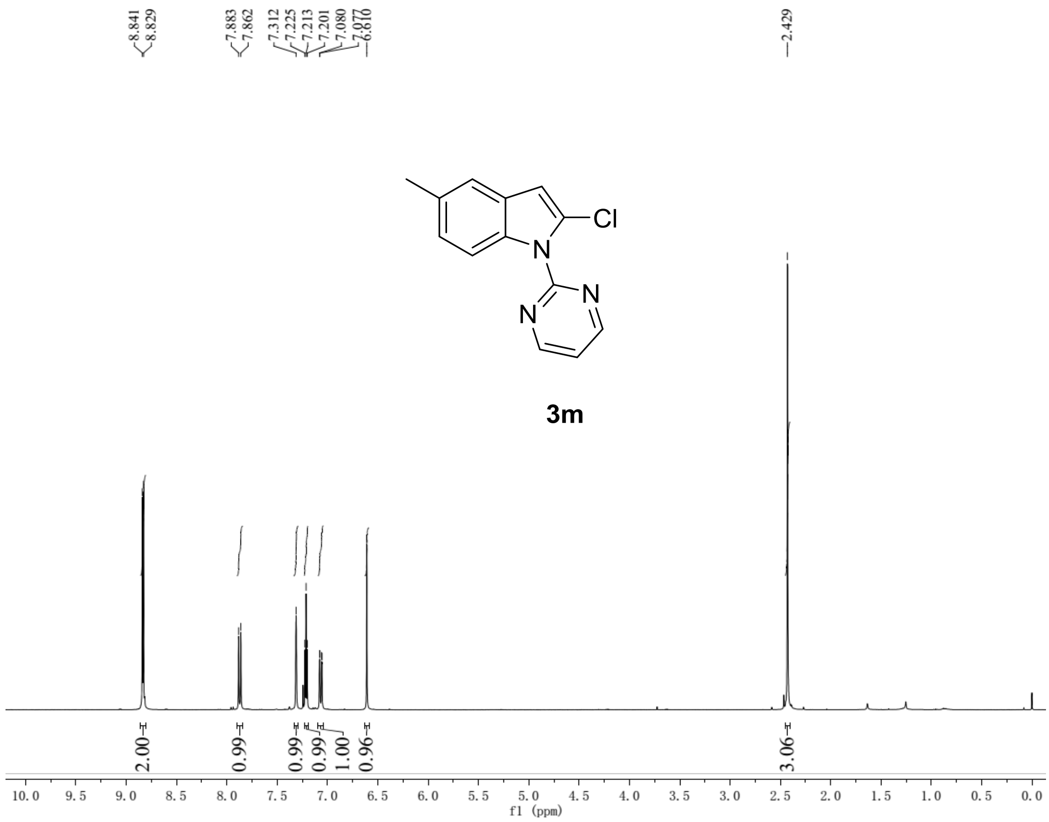
^{13}C{^{1}H} NMR spectrum of **3k** (100 MHz, $CDCl_3$)



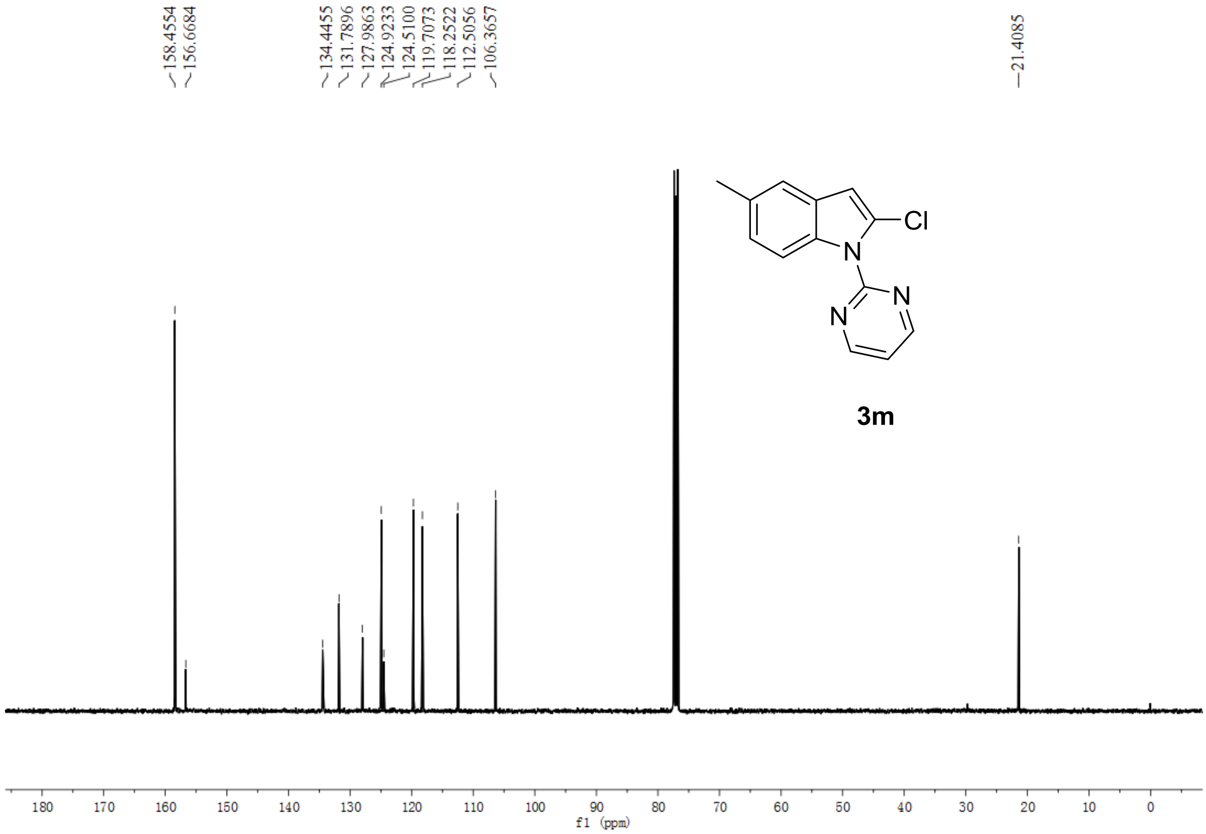
^{1}H NMR spectrum of **3l** (400 MHz, $CDCl_3$)



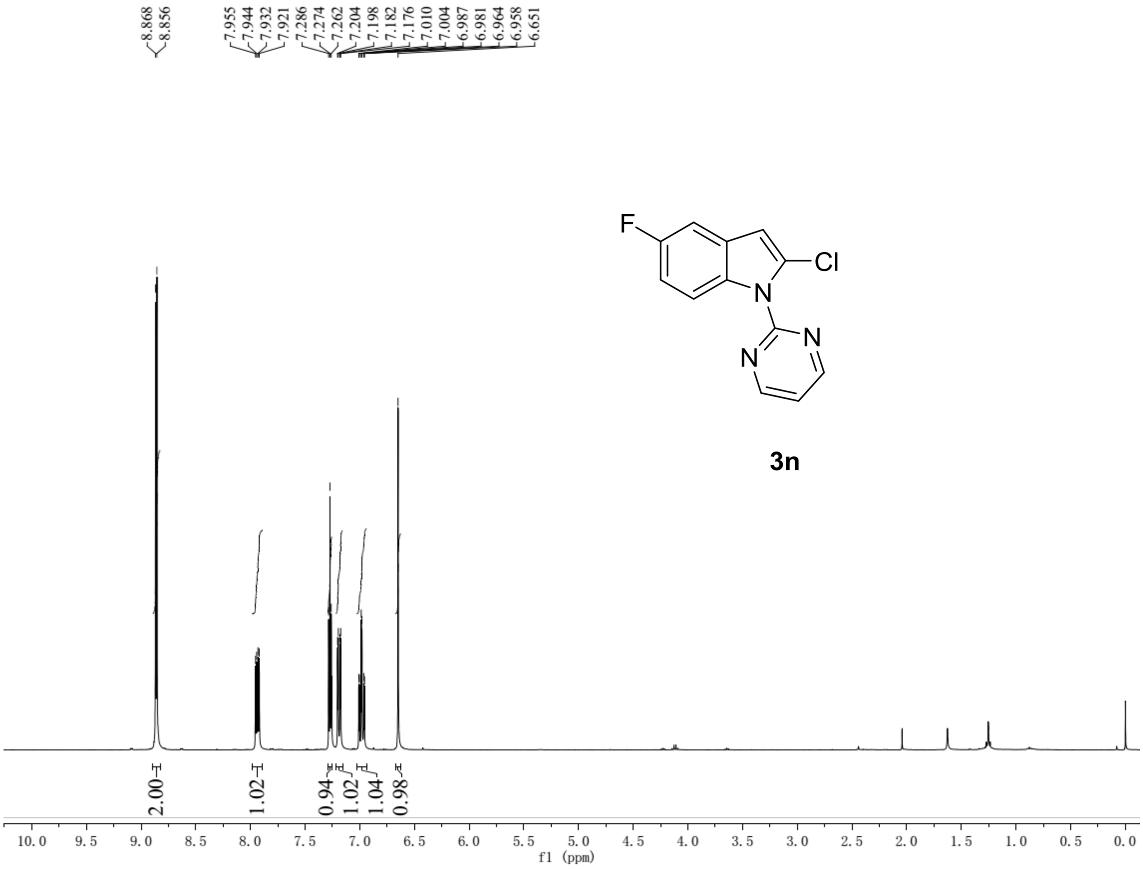
$^{13}C\{^{1}H\}$ NMR spectrum of **3l** (100 MHz, $CDCl_3$)



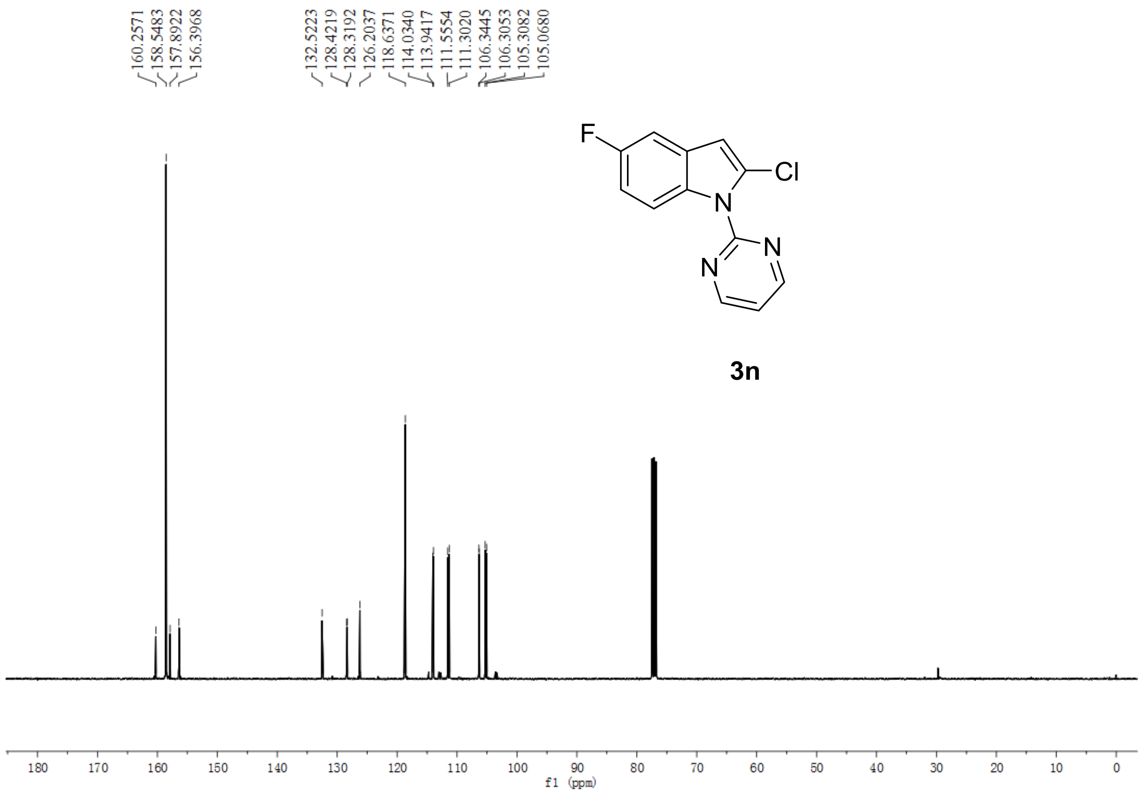
^{1}H NMR spectrum of **3m** (400 MHz, $CDCl_3$)



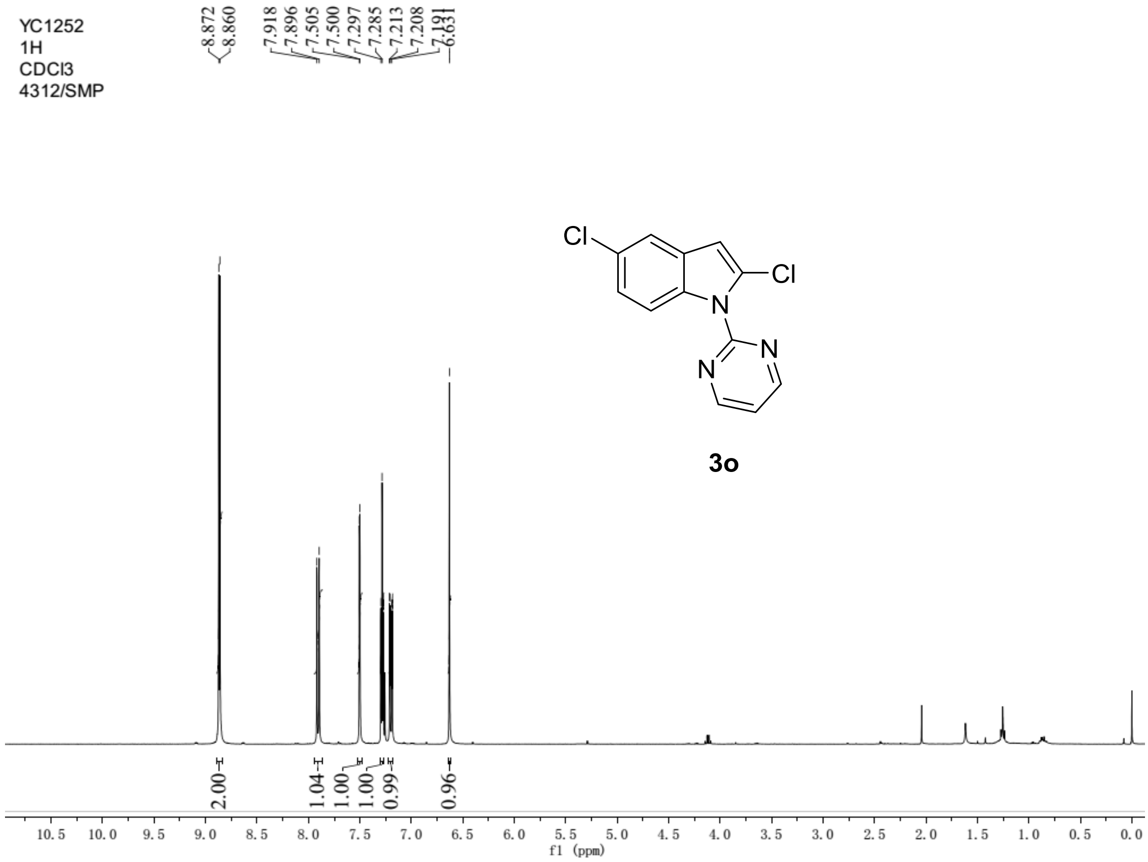
$^{13}C\{^{1}H\}$ NMR spectrum of **3m** (100 MHz, $CDCl_3$)



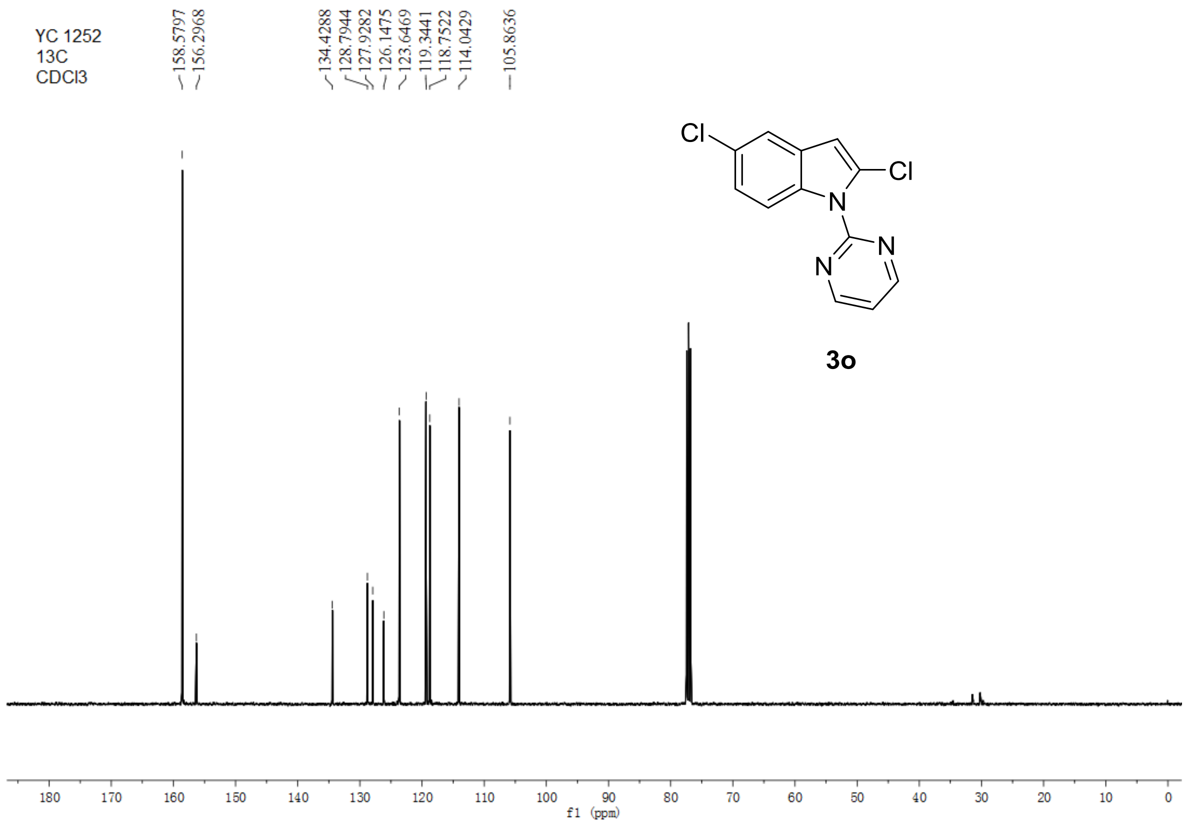
[1]H NMR spectrum of **3n** (400 MHz, $CDCl_3$)



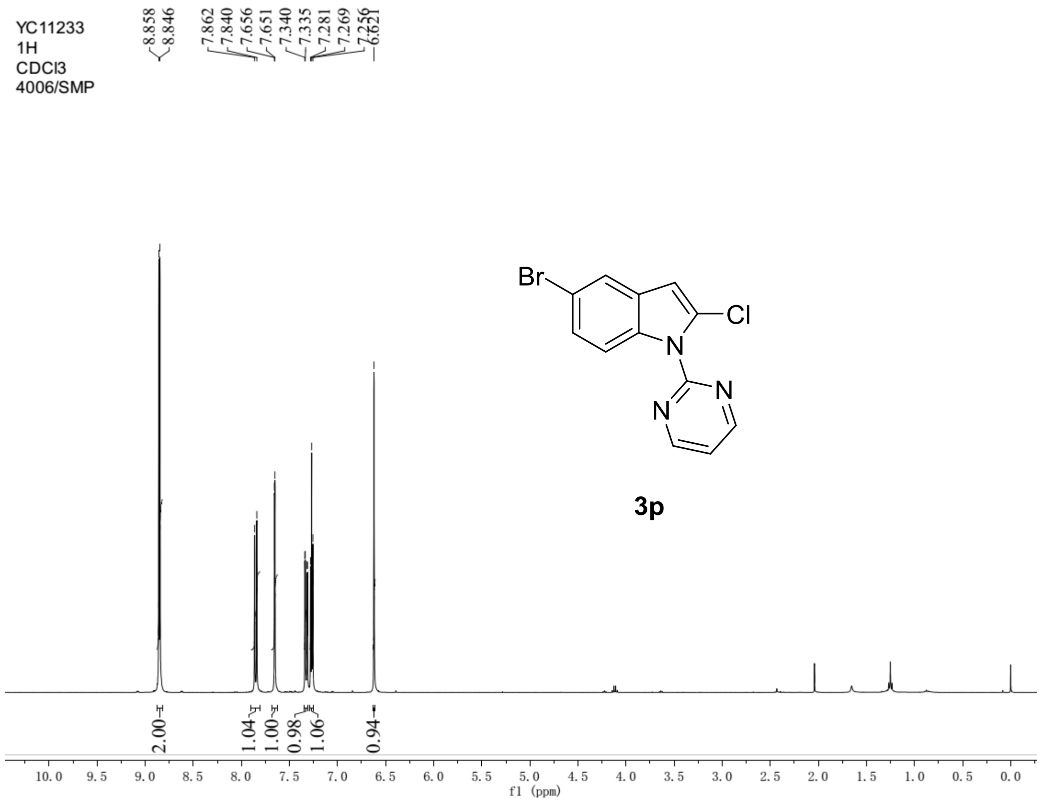
[13]C{[1]H} NMR spectrum of **3n** (100 MHz, $CDCl_3$)



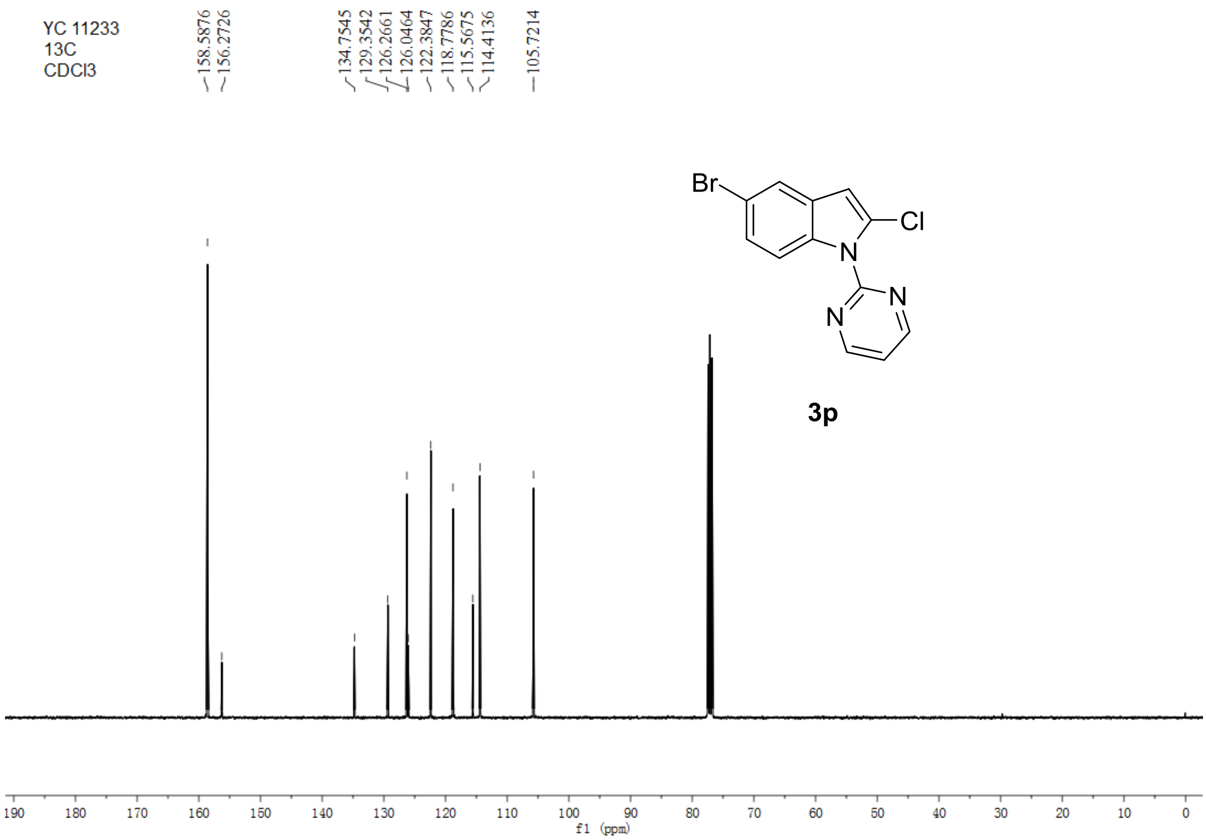
^{1}H NMR spectrum of **3o** (400 MHz, $CDCl_3$)



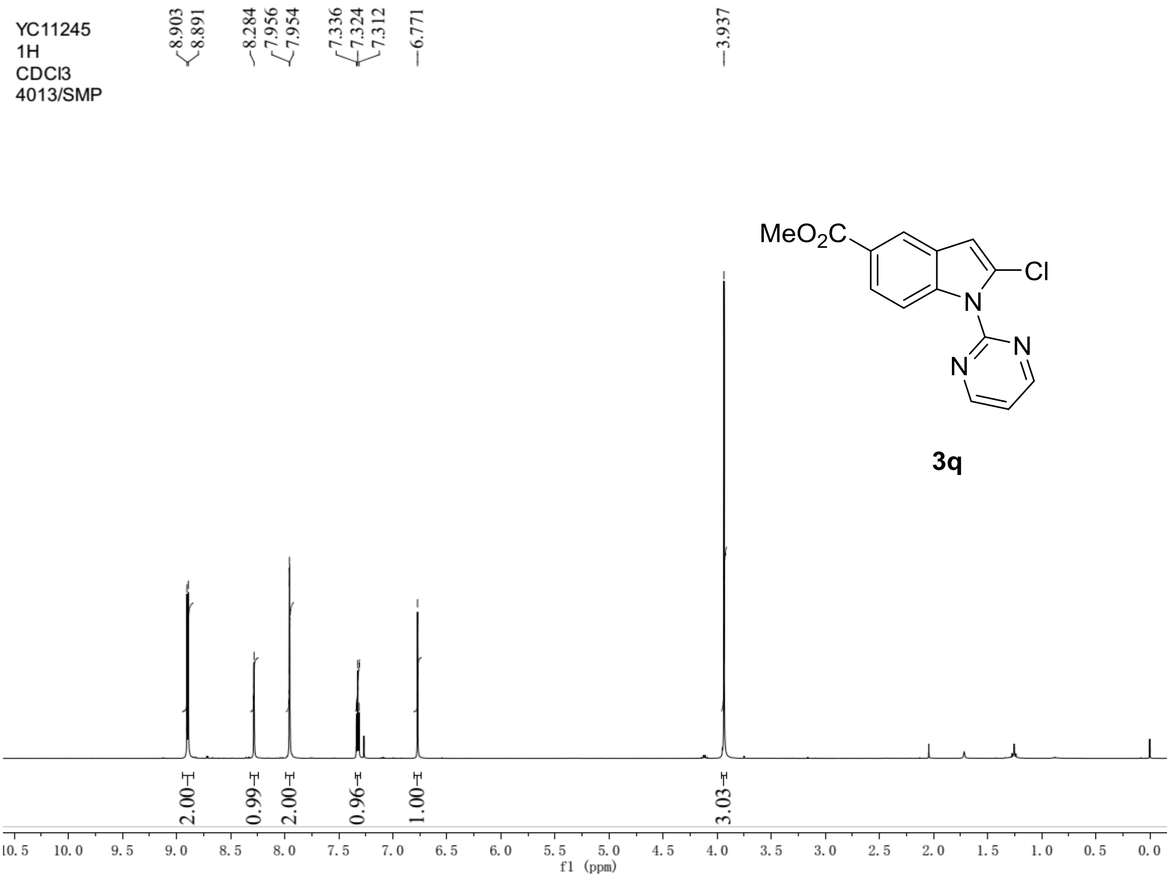
^{13}C{^{1}H} NMR spectrum of **3o** (100 MHz, $CDCl_3$)



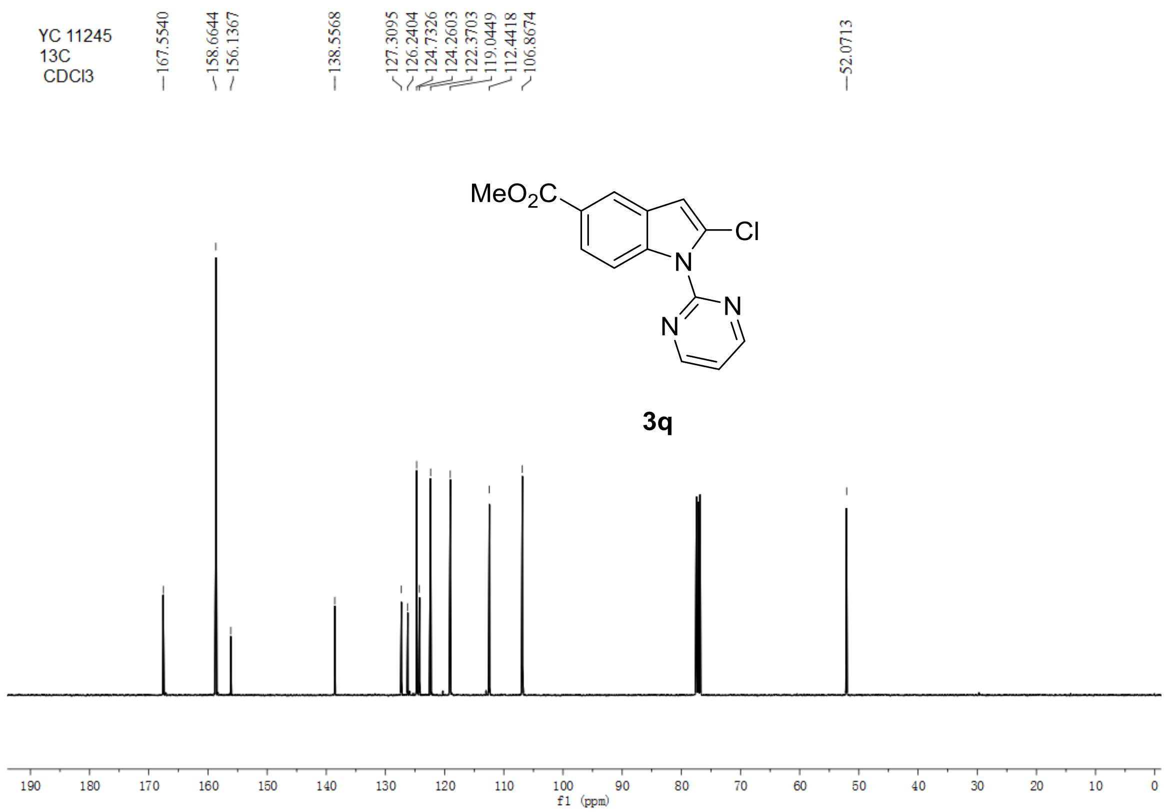
^{1}H NMR spectrum of **3p** (400 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR spectrum of **3p** (100 MHz, $CDCl_3$)

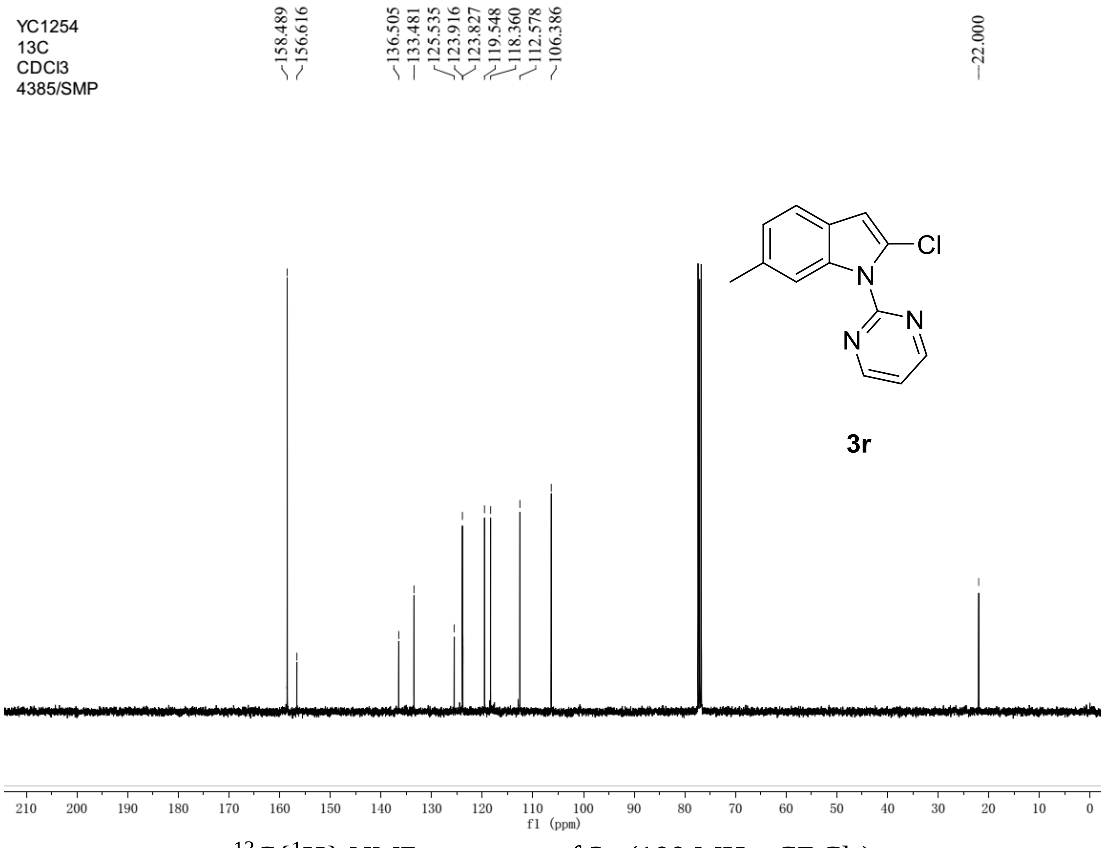


^{1}H NMR spectrum of **3q** (400 MHz, $CDCl_3$)

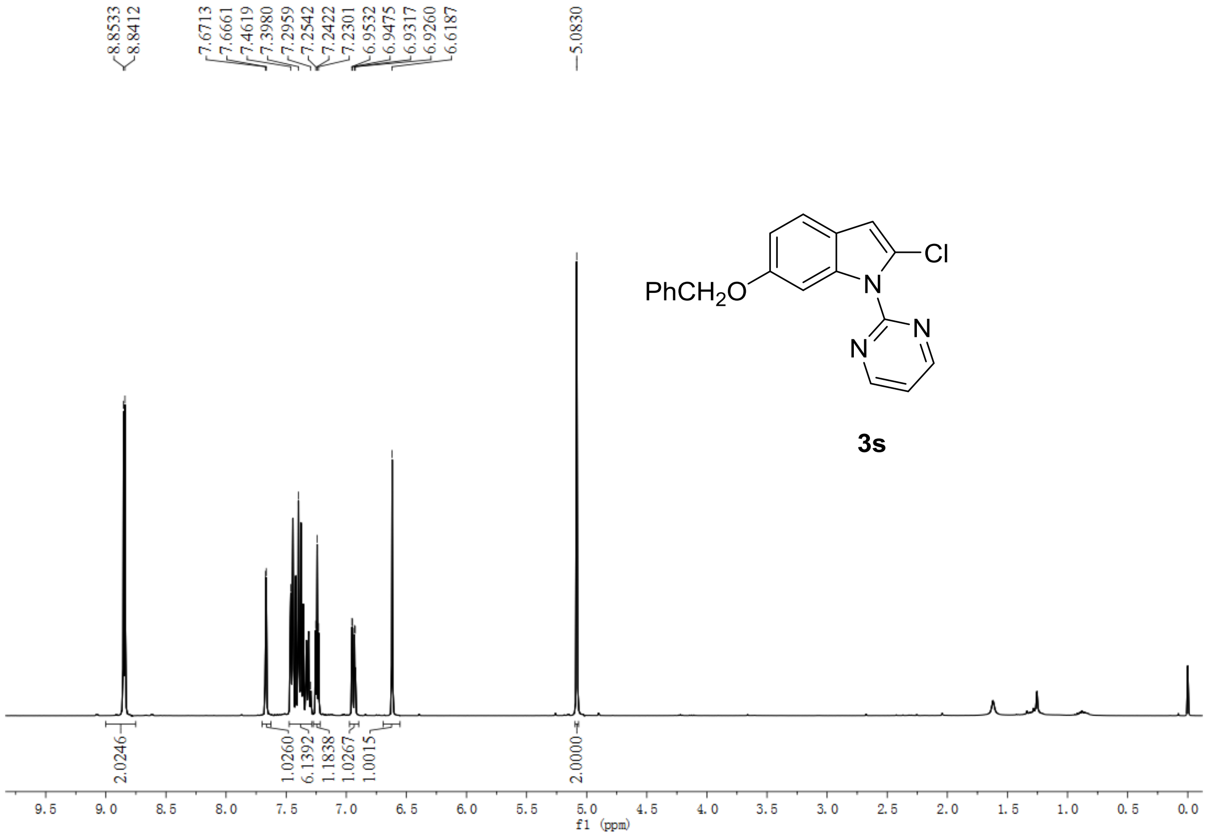


^{13}C{^{1}H} NMR spectrum of **3q** (100 MHz, $CDCl_3$)

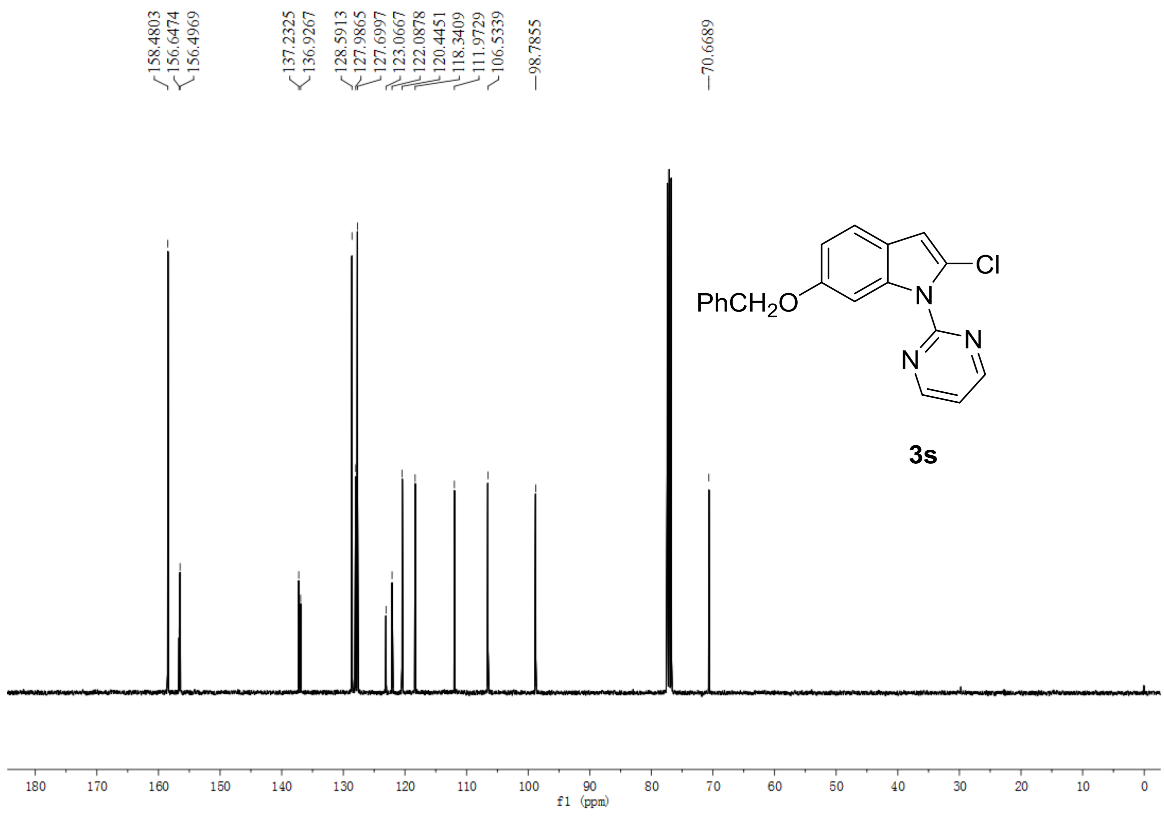
^{1}H NMR spectrum of **3r** (400 MHz, $CDCl_3$)



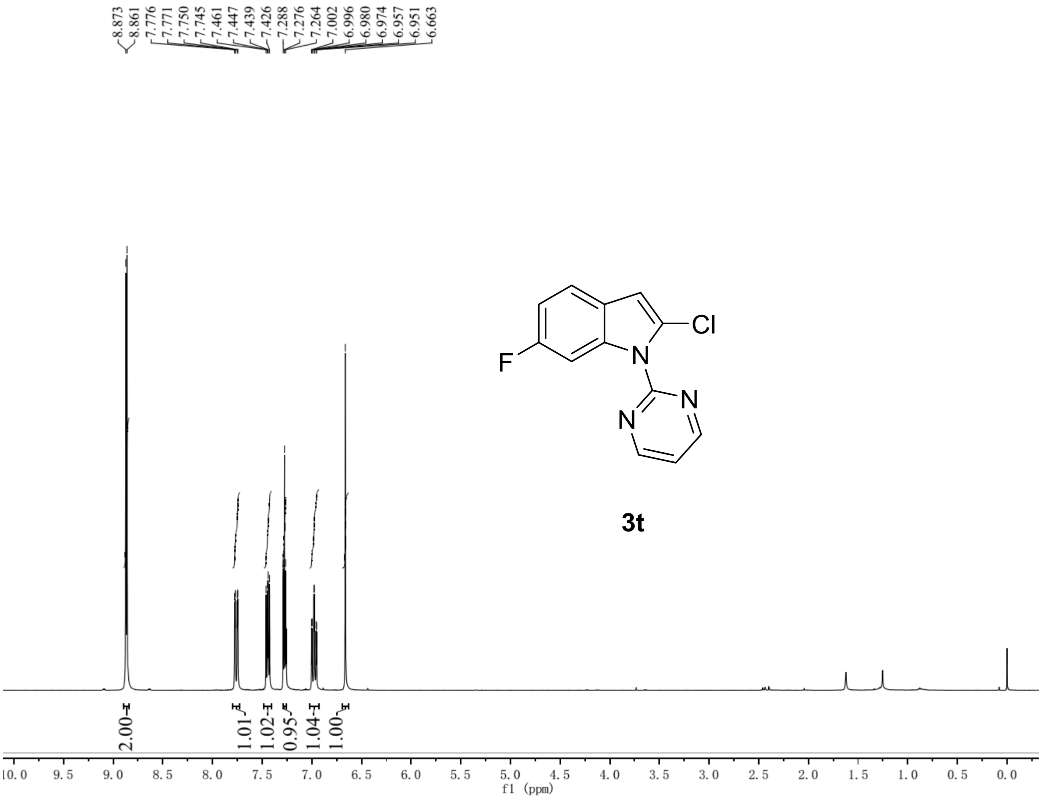
$^{13}C\{^{1}H\}$ NMR spectrum of **3r** (100 MHz, $CDCl_3$)



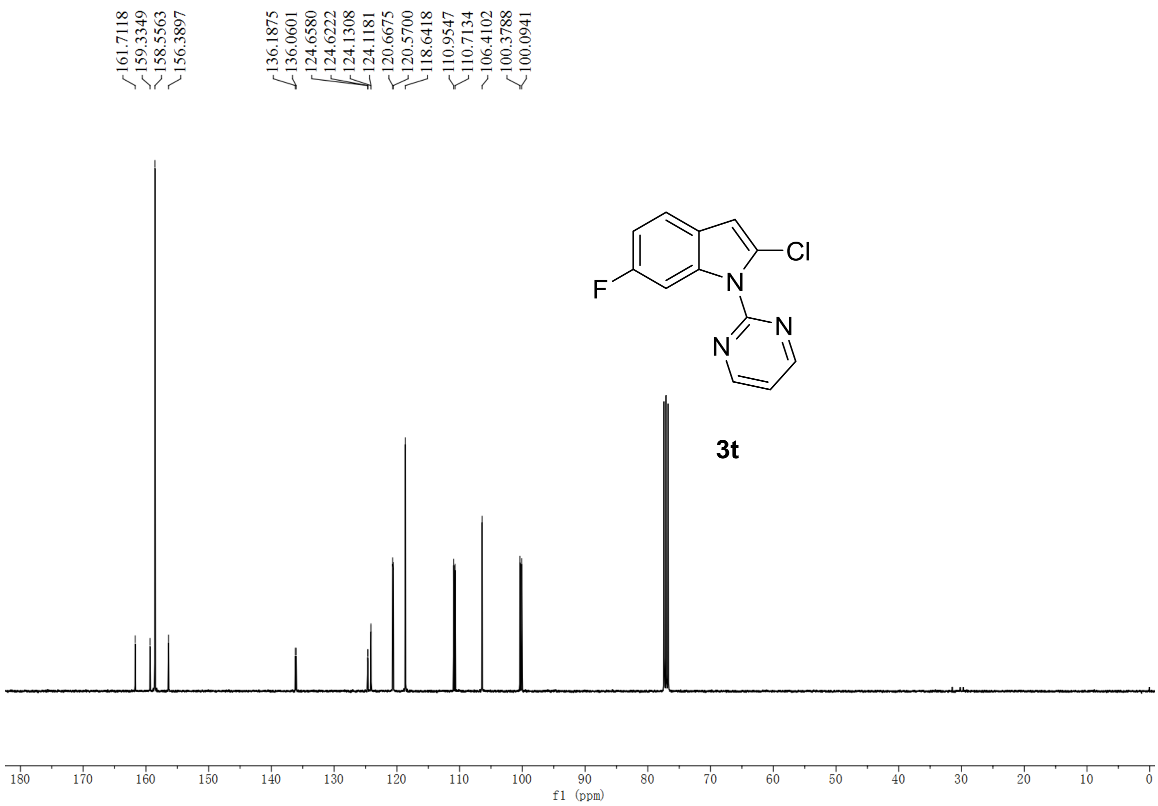
^{1}H NMR spectrum of **3s** (400 MHz, $CDCl_3$)



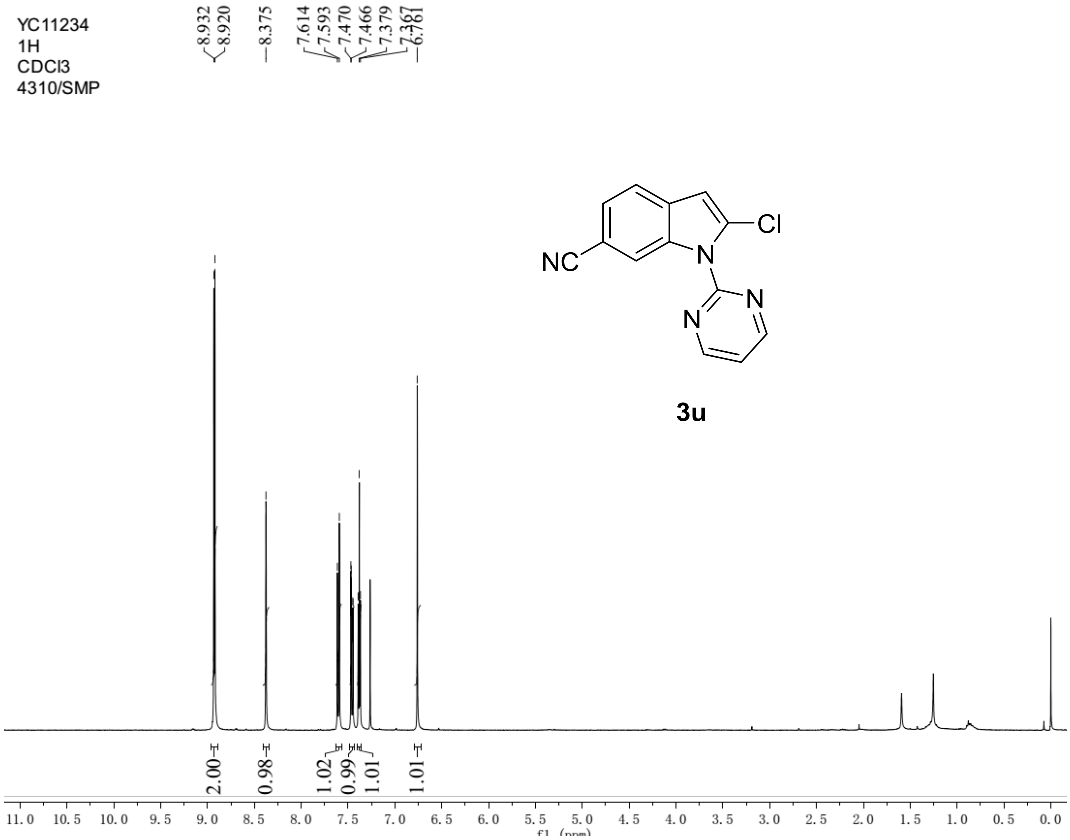
$^{13}C\{^{1}H\}$ NMR spectrum of **3s** (100 MHz, $CDCl_3$)



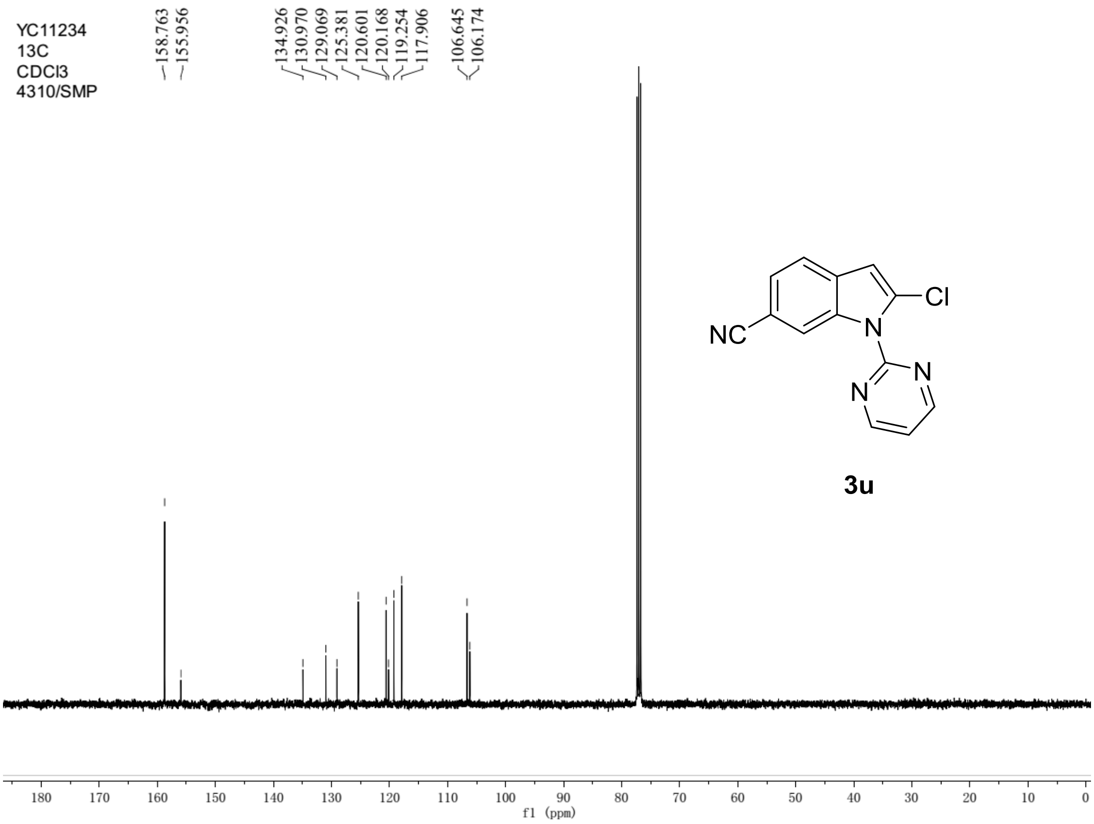
^{1}H NMR spectrum of **3t** (400 MHz, $CDCl_3$)



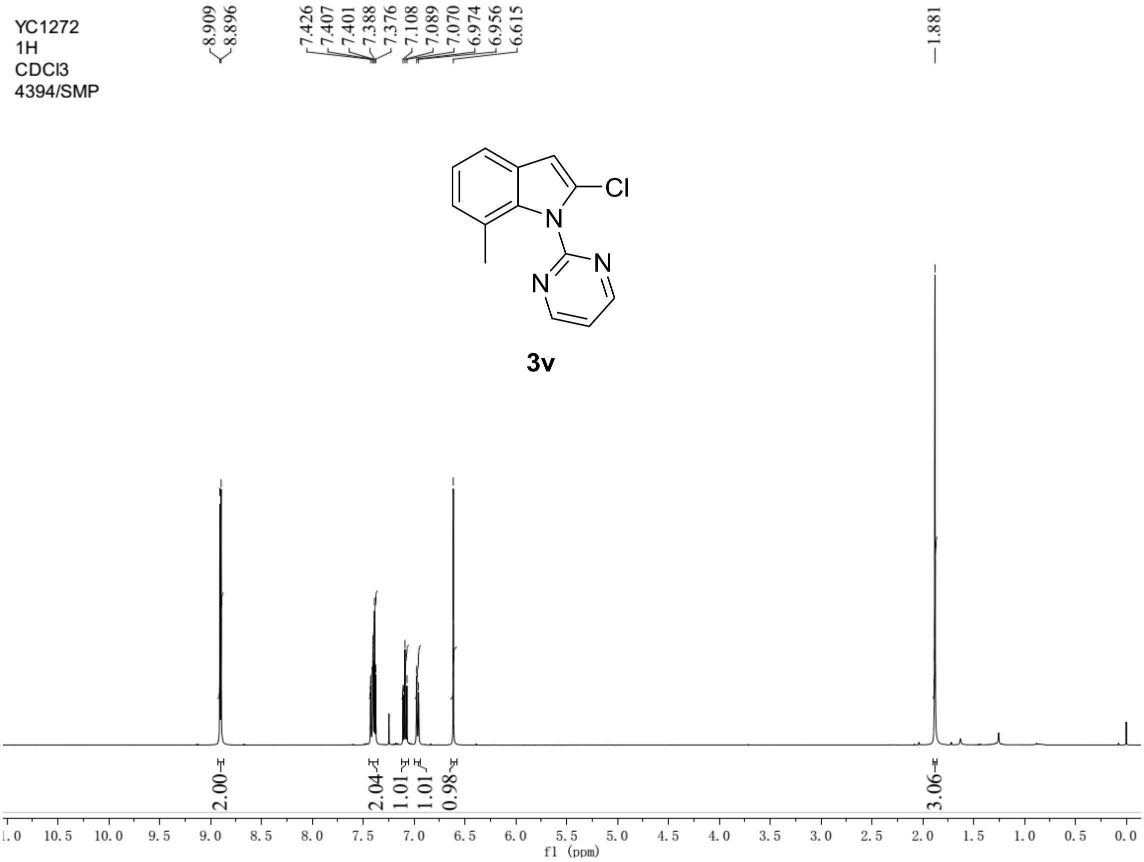
^{13}C{^{1}H} NMR spectrum of **3t** (100 MHz, $CDCl_3$)



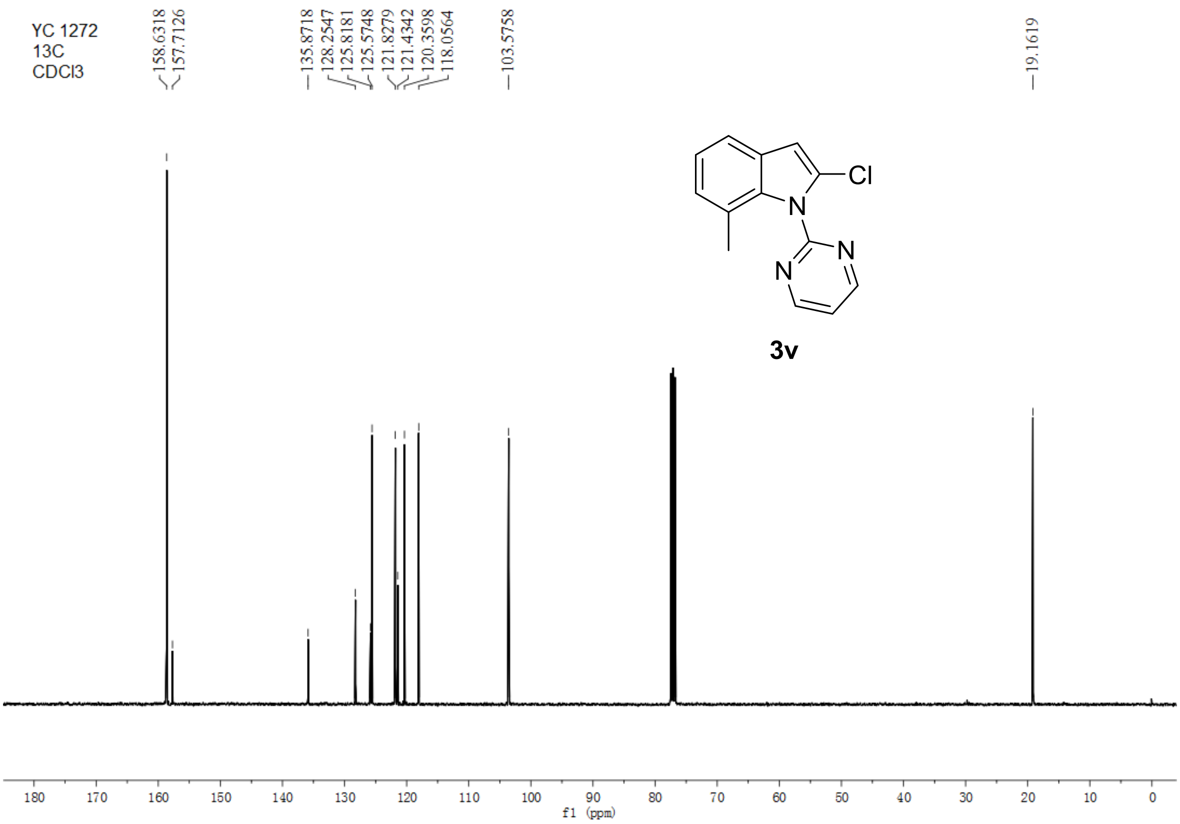
^{1}H NMR spectrum of **3u** (400 MHz, $CDCl_3$)



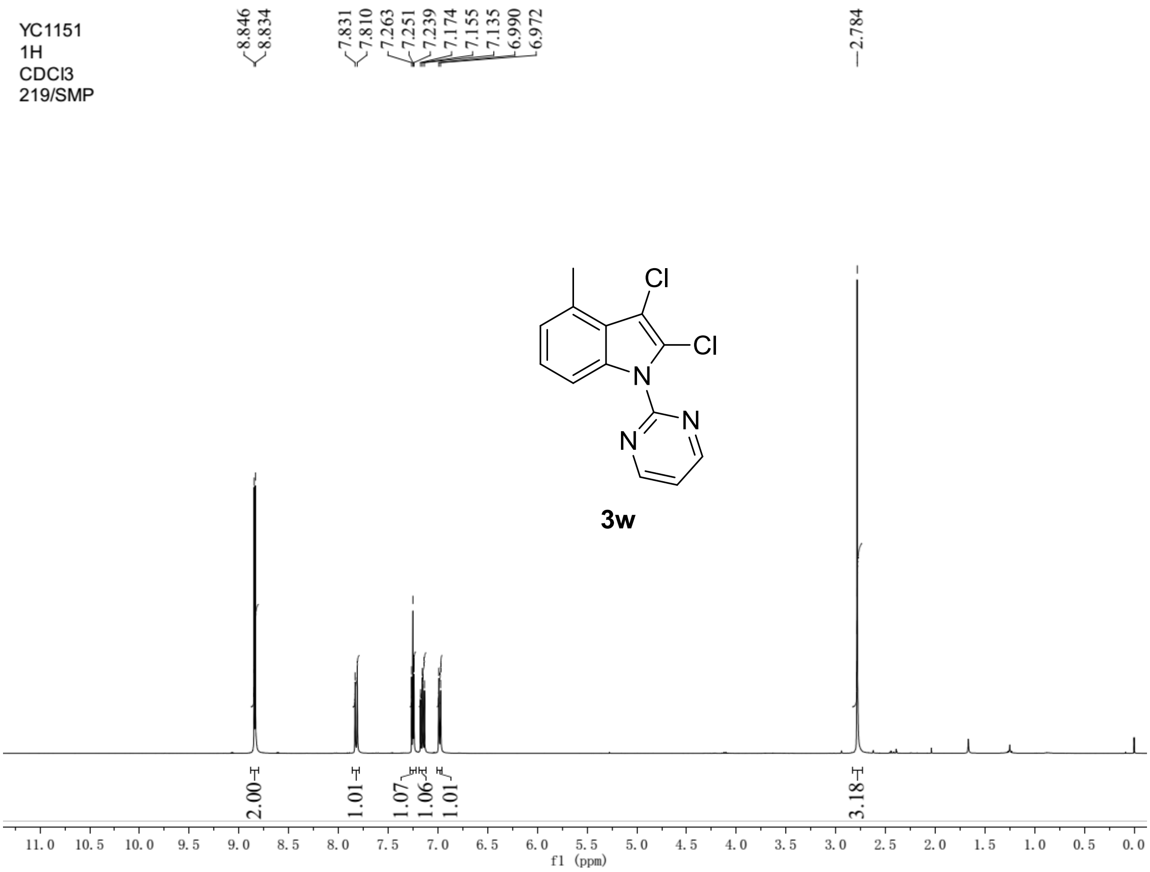
$^{13}C\{^{1}H\}$ NMR spectrum of **3u** (100 MHz, $CDCl_3$)



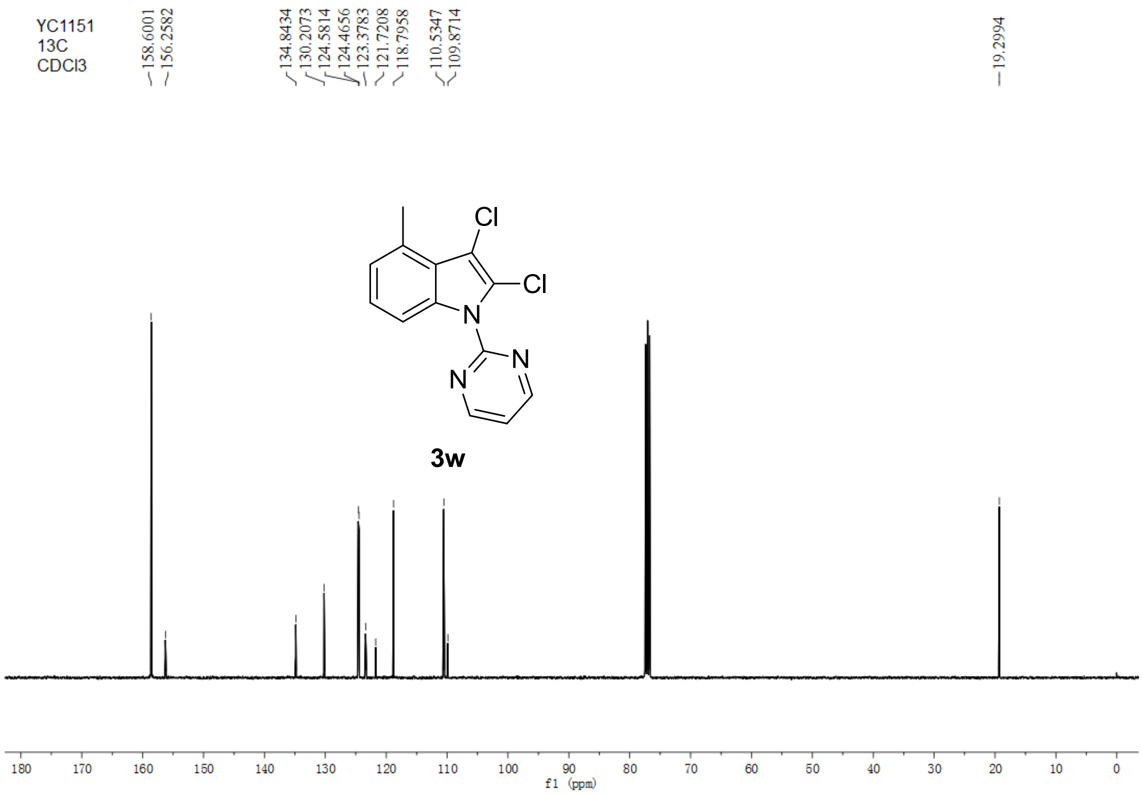
^{1}H NMR spectrum of **3v** (400 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR spectrum of **3v** (100 MHz, $CDCl_3$)

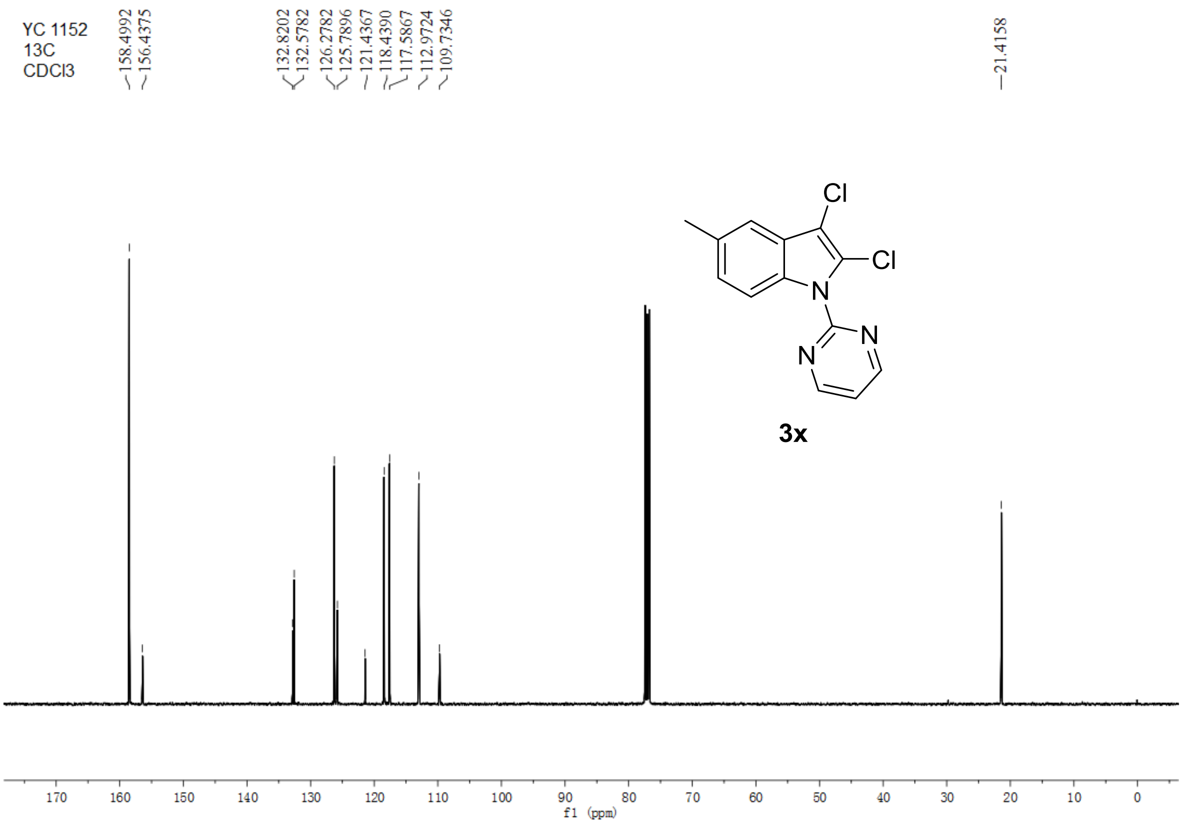


^{1}H NMR spectrum of **3w** (400 MHz, $CDCl_3$)

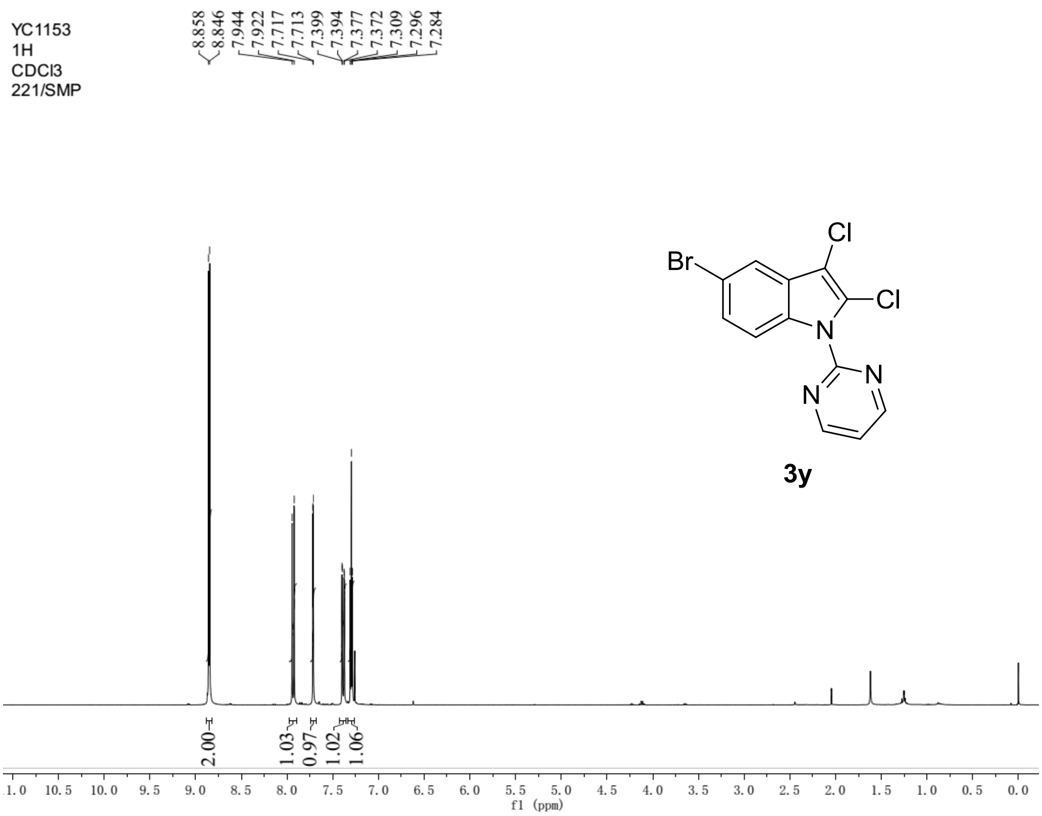


$^{13}C\{^{1}H\}$ NMR spectrum of **3w** (100 MHz, $CDCl_3$)

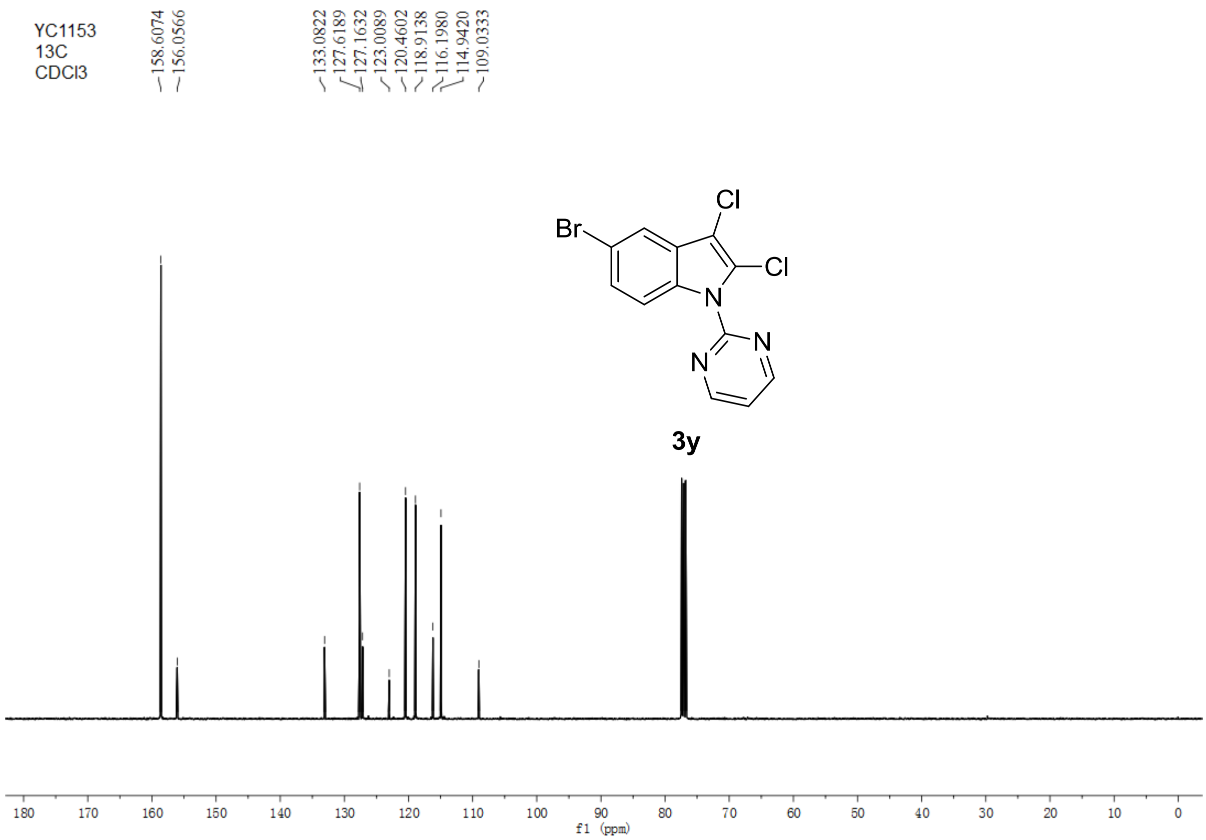
[1]H NMR spectrum of **3x** (400 MHz, $CDCl_3$)



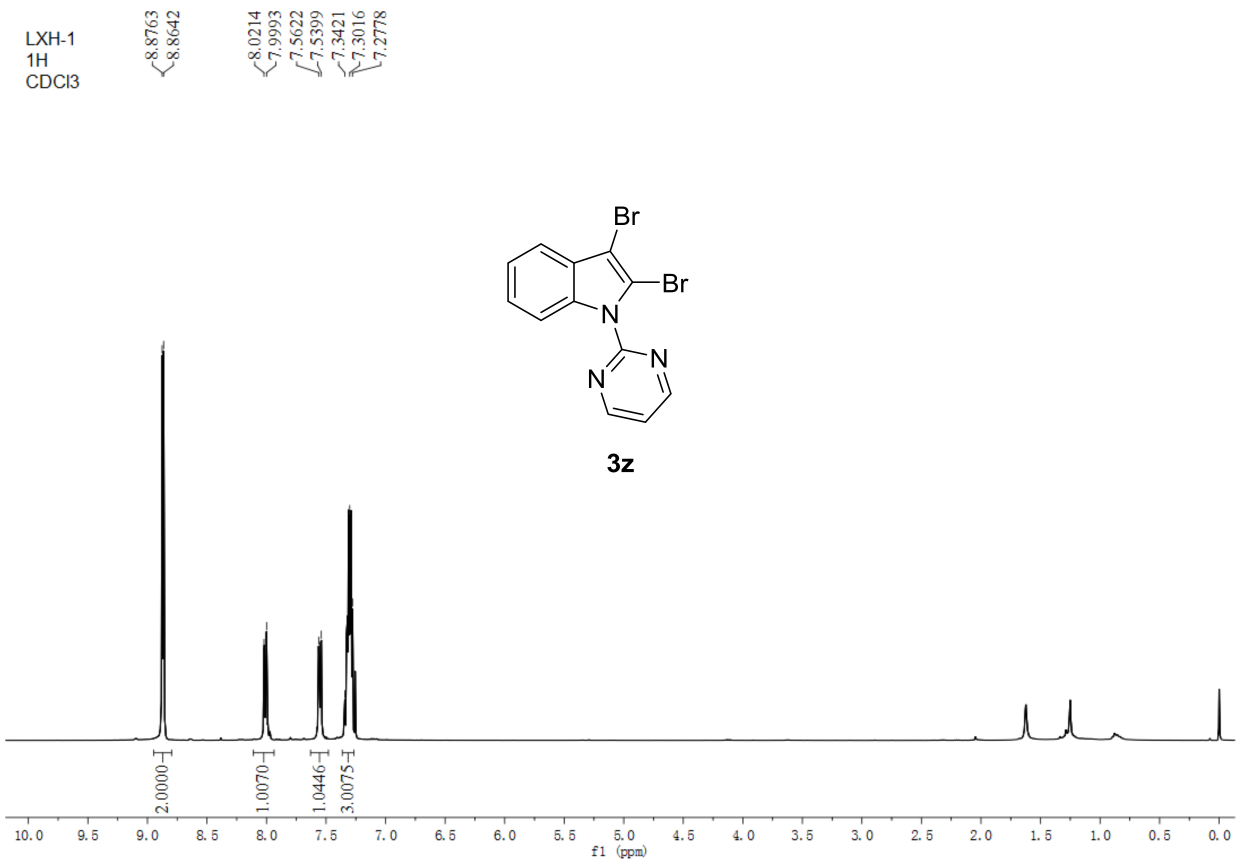
[13]C{[1]H} NMR spectrum of **3x** (100 MHz, $CDCl_3$)



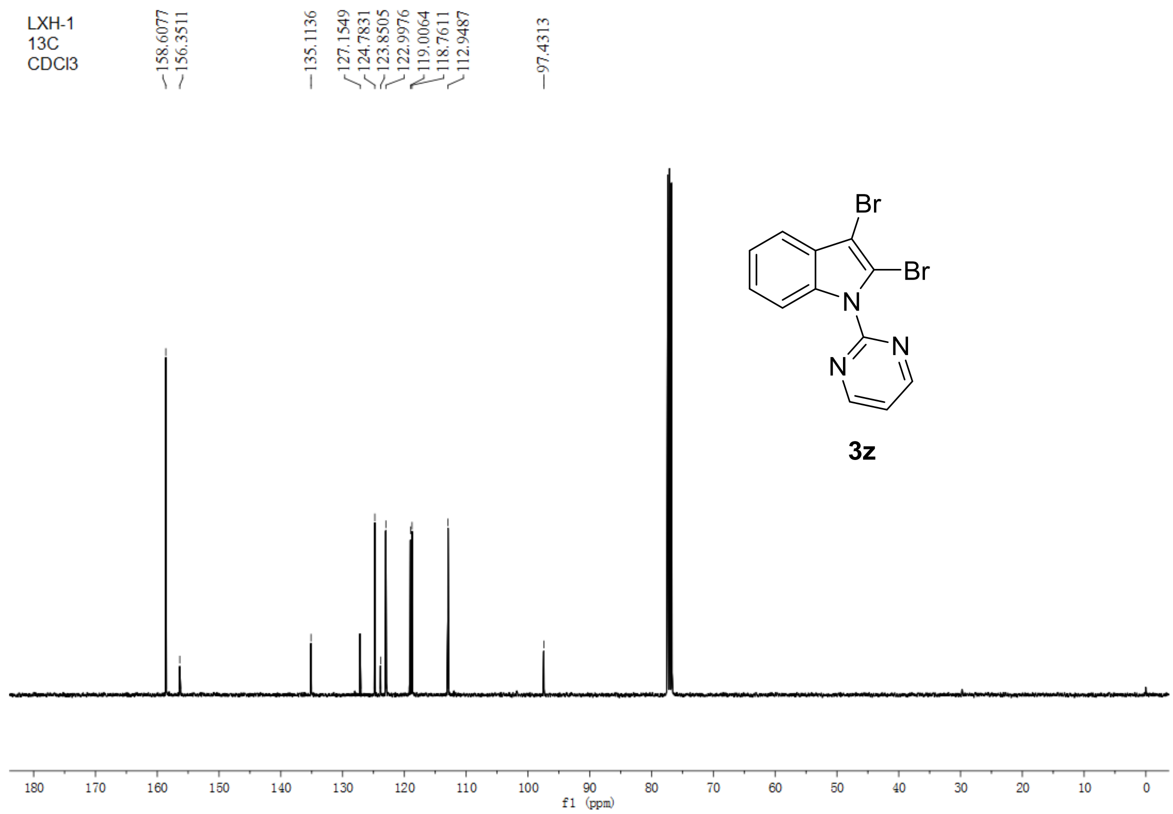
^{1}H NMR spectrum of **3y** (400 MHz, $CDCl_3$)



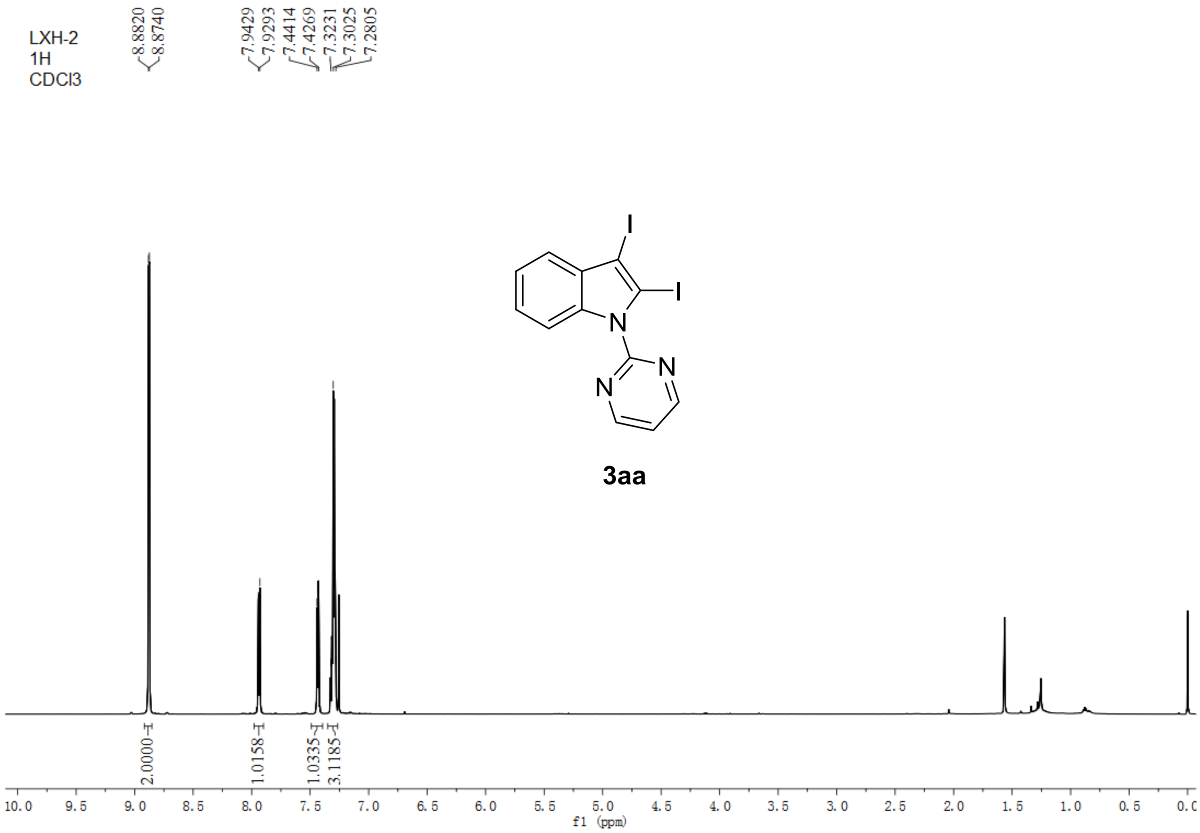
$^{13}C\{^{1}H\}$ NMR spectrum of **3y** (100 MHz, $CDCl_3$)



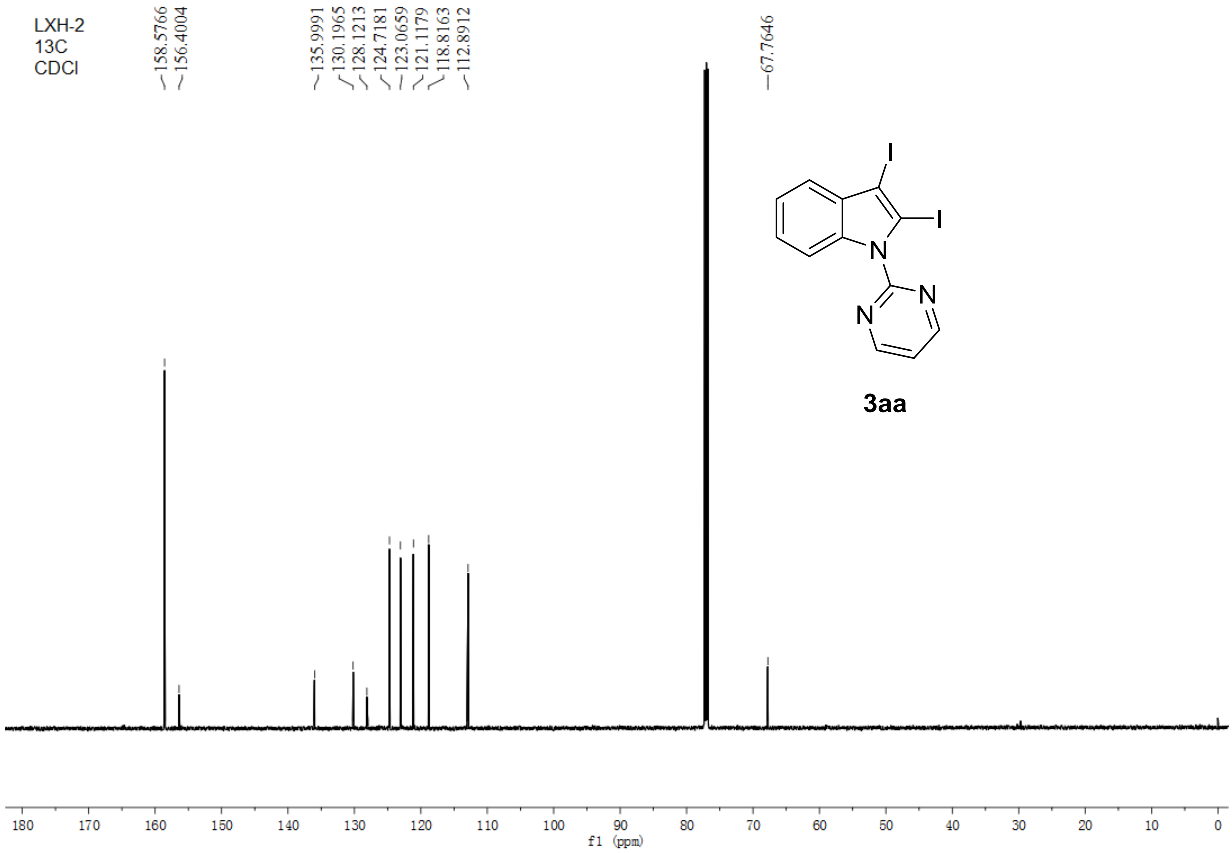
^{1}H NMR spectrum of **3z** (400 MHz, $CDCl_3$)



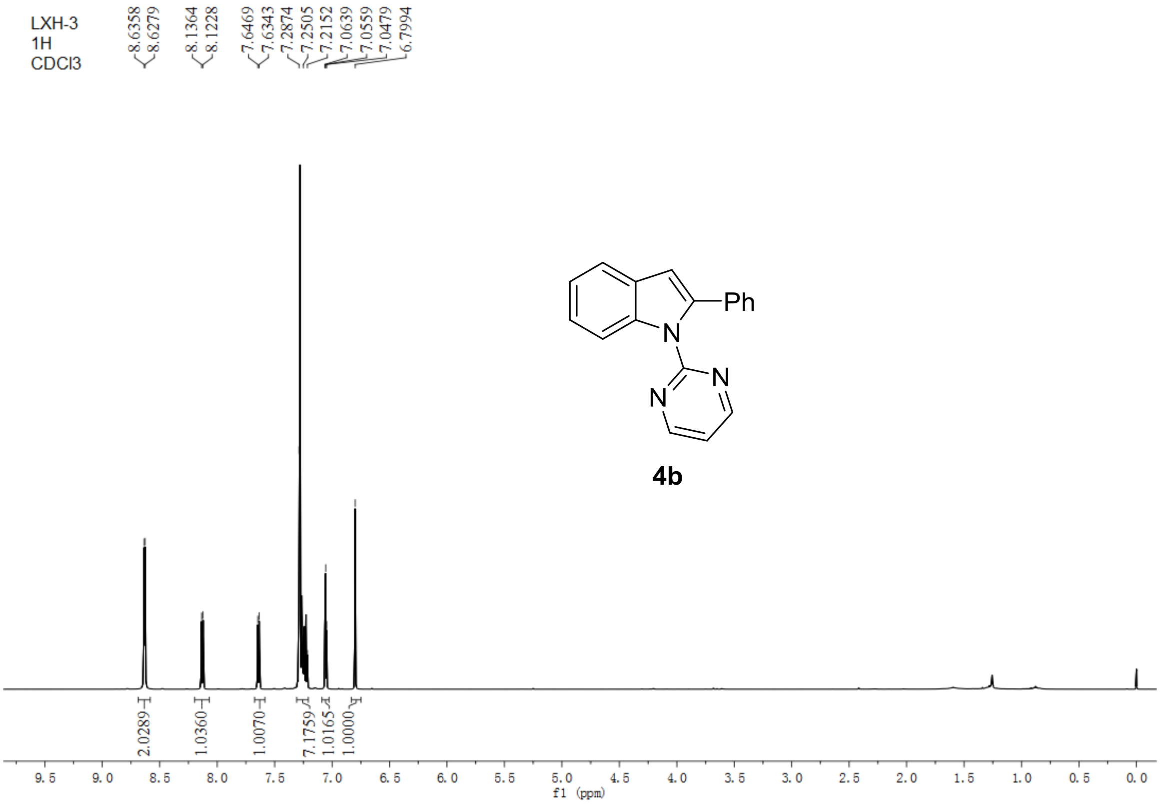
$^{13}C\{^{1}H\}$ NMR spectrum of **3z** (100 MHz, $CDCl_3$)



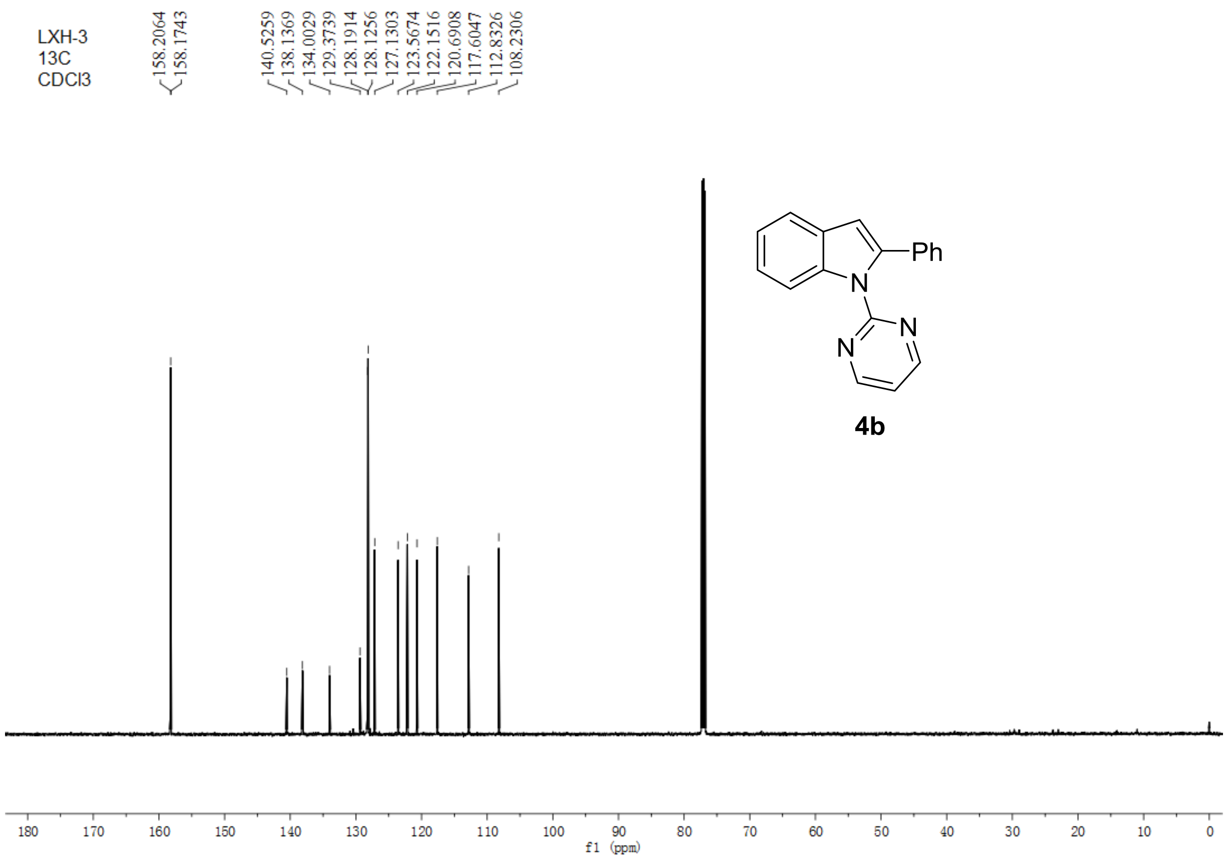
^{1}H NMR spectrum of **3aa** (600 MHz, $CDCl_3$)



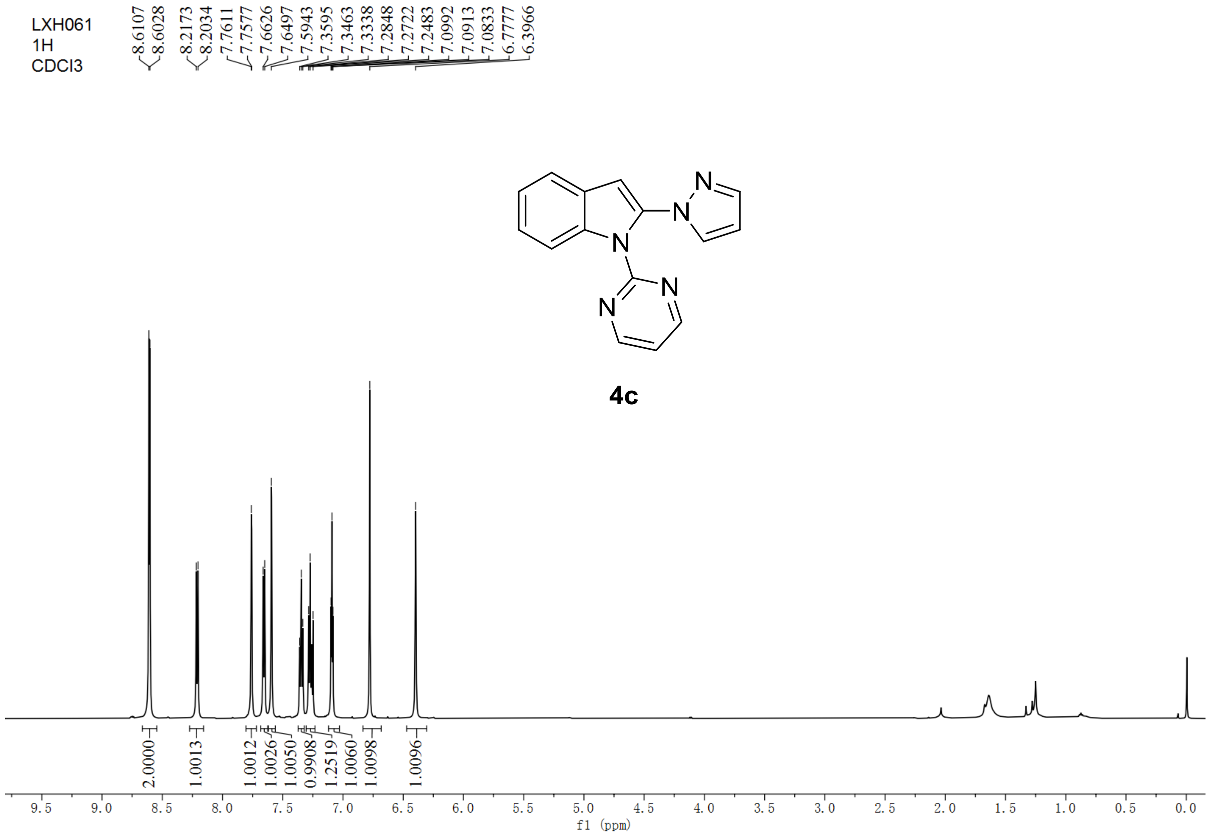
$^{13}C\{^{1}H\}$ NMR spectrum of **3aa** (150 MHz, $CDCl_3$)



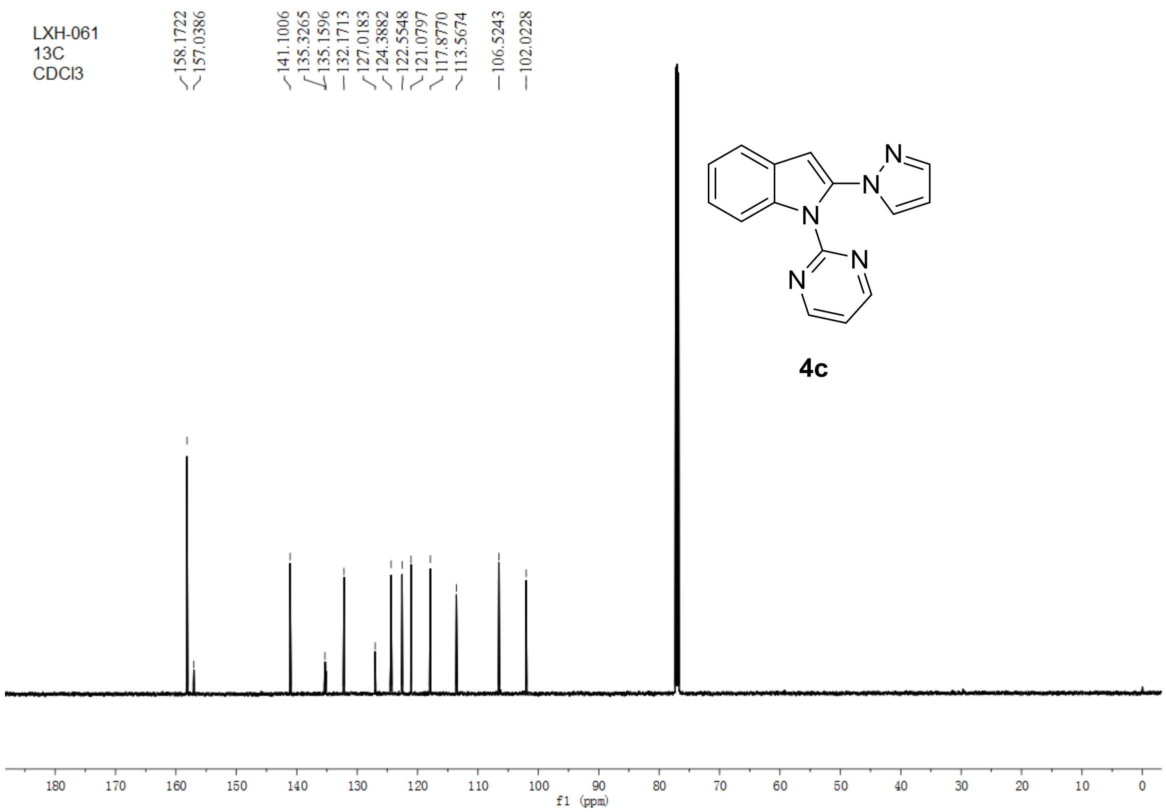
^{1}H NMR spectrum of **4b** (600 MHz, $CDCl_3$)



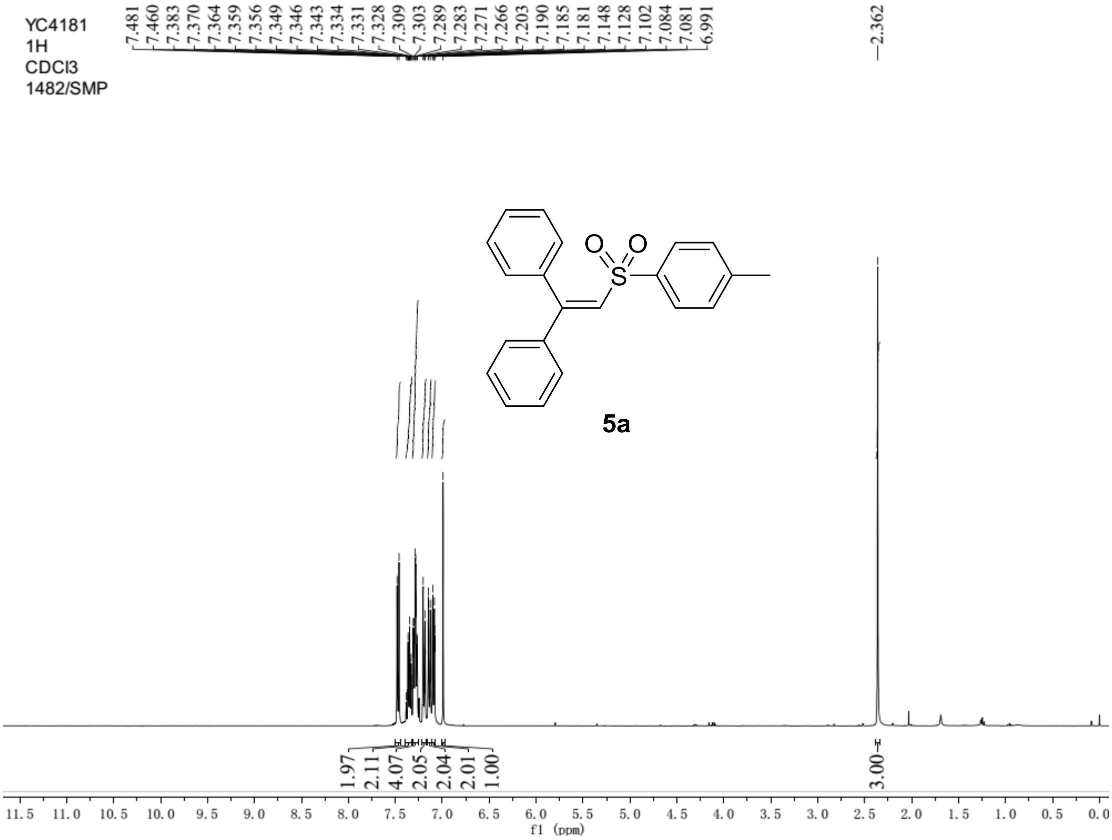
^{13}C{^{1}H} NMR spectrum of **4b** (150 MHz, $CDCl_3$)



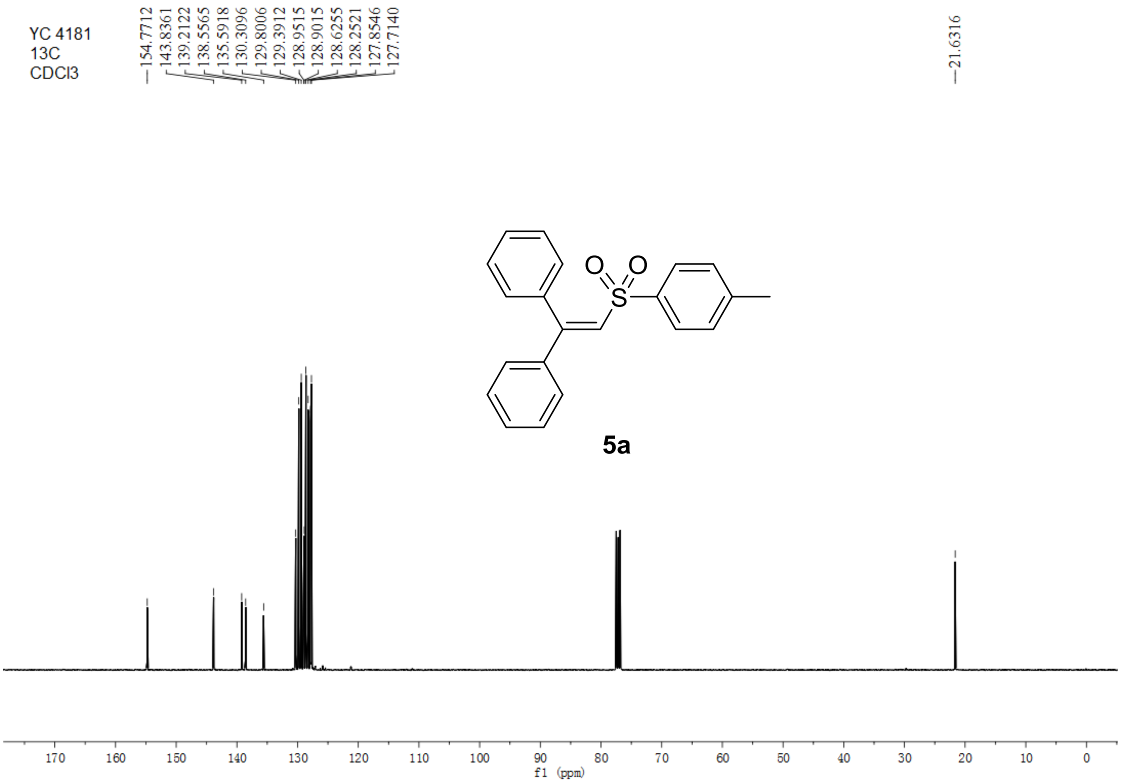
^{1}H NMR spectrum of **4c** (600 MHz, $CDCl_3$)



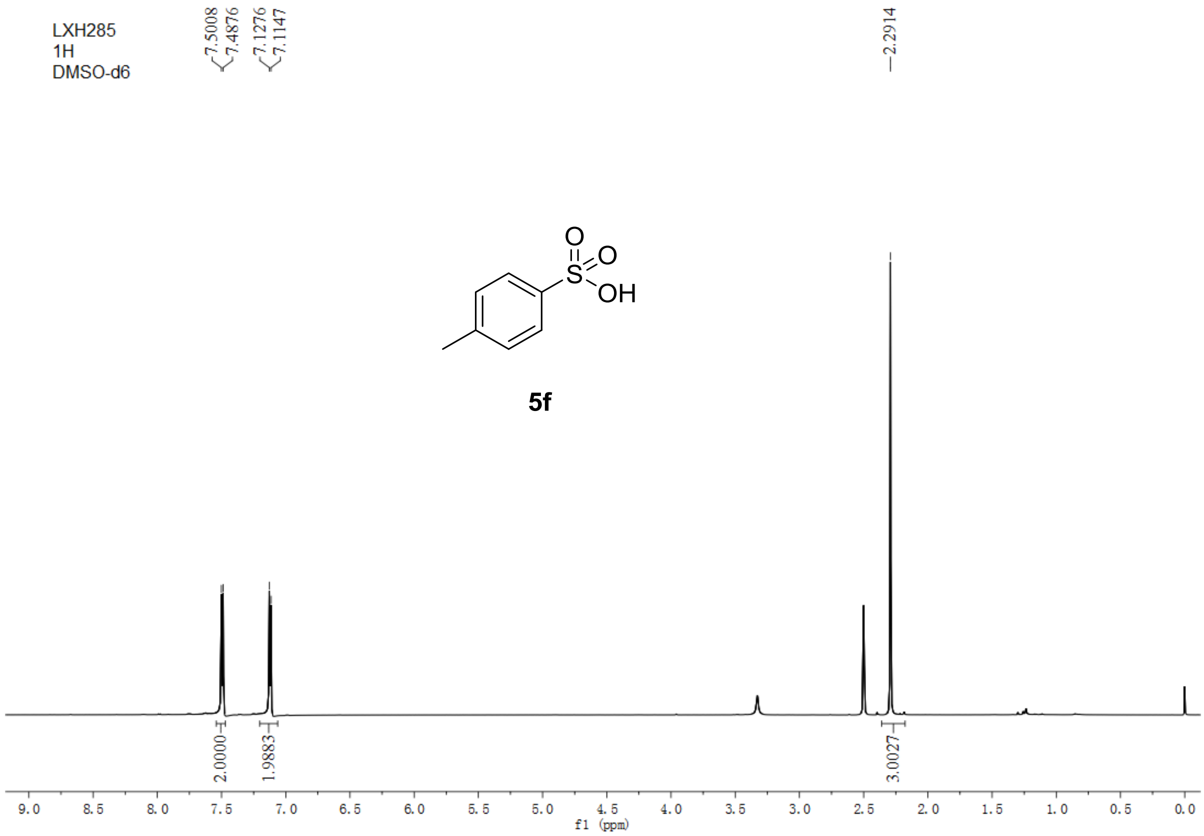
$^{13}C\{^{1}H\}$ NMR spectrum of **4c** (150 MHz, $CDCl_3$)



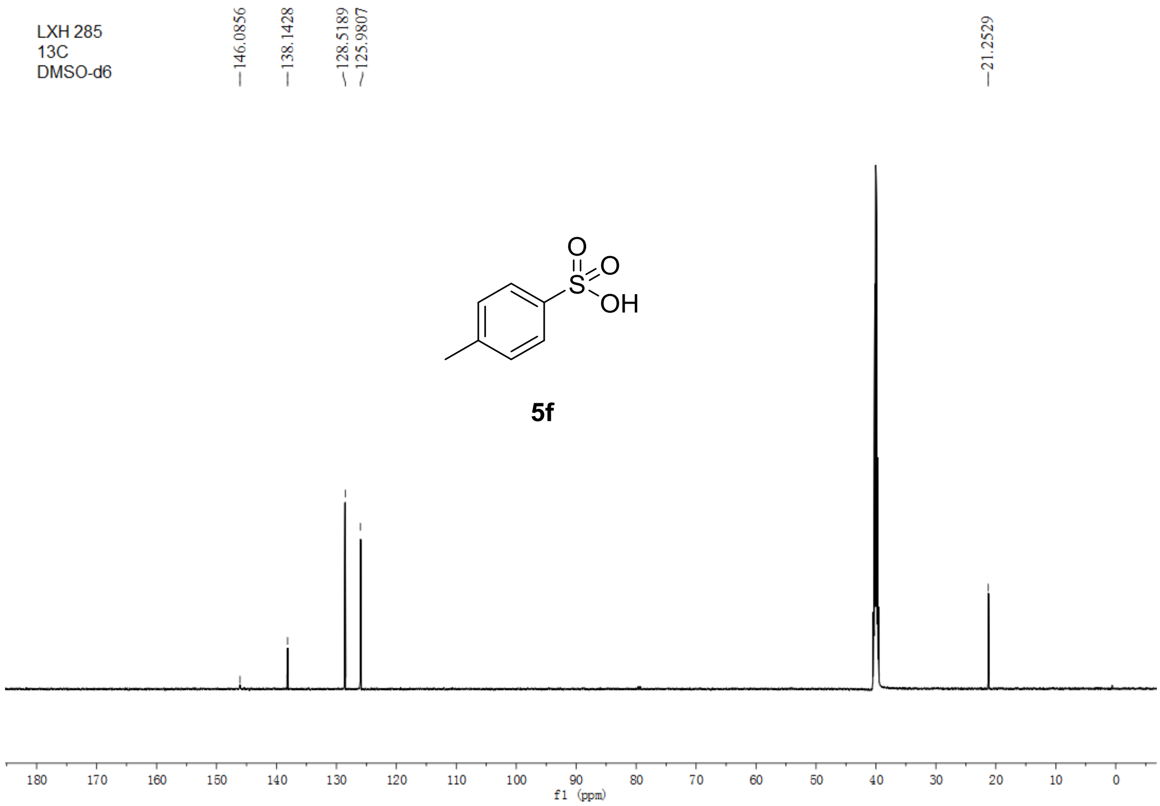
^{1}H NMR spectrum of **5a** (400 MHz, $CDCl_3$)



^{13}C{^{1}H} NMR spectrum of **5a** (100 MHz, $CDCl_3$)



^{1}H NMR spectrum of **5f** (600 MHz, DMSO-d_6)



$^{13}C\{^{1}H\}$ NMR spectrum of **5f** (150 MHz, DMSO-d_6)