

Supporting Information

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

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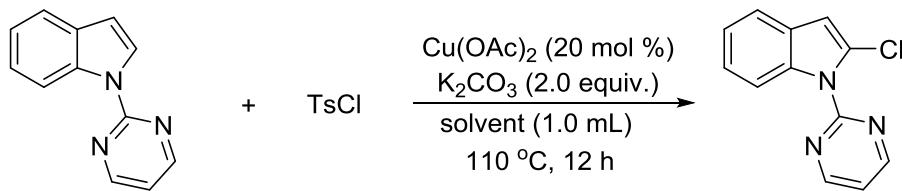
Table of contents

1 Experimental Section	S2
1.1 Optimization of reaction conditions.....	S2
1.2 H/D exchange experiment.....	S5
1.3 Intermolecular competition KIE	S6
1.4 Parallel experiments	S7
1.5 Removal of the directing group	S7
1.6 Pd-catalyzed Suzuki couplings of 3a with phenylboronic acid.....	S9
2 NMR spectra	S10

1 Experimental Section

1.1 Optimization of reaction conditions

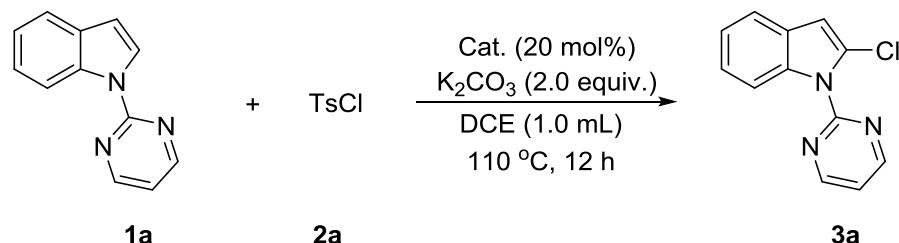
Table S1. Screening of solvent^a



Entry	1a	2a	3a	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 ₂ O		0
6	Acetone	0	15	DCE		25
7	DMF	8	16	DCM		13
8	Et ₂ O	10	17	CHCl ₃		9
9	EtOAc	10	18	1,2,3-Trichloropropane		17

^aReaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), Cu(OAc)₂ (20 mol %), K₂CO₃ (0.4 mmol), solvent (1.0 mL), 110 °C, under air, 12 h. ^bIsolated yields.

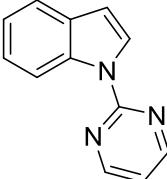
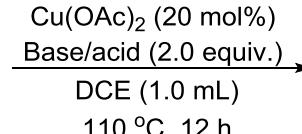
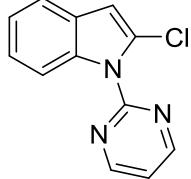
Table S2. Screening of catalyst^a



Entry	Cat.	Yield ^b (%)
1	Cu(OAc)₂	25
2	Cu(OAc) ₂ ·H ₂ O	15
3	CuOAc	10
4	Cu(acac) ₂	0
5	Cu(OTf) ₂	13
6	CuCl ₂	9

^aReaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), cat. (20 mol%), K₂CO₃ (0.4 mmol), DCE (1.0 mL), 110 °C, under air, 12 h. ^bIsolated yields.

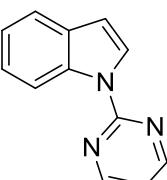
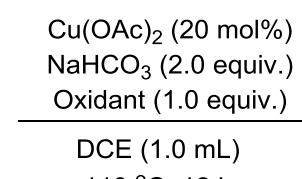
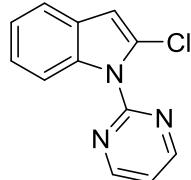
Table S3. Screening of base/acid^a

	1a		2a			3a
Entry	Base/Acid	Yield ^b (%)	Entry	Base/Acid	Yield ^b (%)	
1	/	0	11	PhCOONa	43	
2	K ₂ CO ₃	25	12	PivONa·H ₂ O	24	
3	Na ₂ CO ₃	35	13	NaH ₂ PO ₄ ·2H ₂ O	<5	
4	Li ₂ CO ₃	39	14	CH ₃ ONa	35	
5	NaOAc	34	15	<i>t</i> -BuOK	<5	
6	KOAc	14	16	KOH	15	
7	CsOAc	0	17	K ₃ PO ₄	6	
8	NaHCO₃	43	18 ^c	NaHCO ₃ /PhCOONa	43	
9	KHCO ₃	24	19	TsOH	0	
10	Na ₂ C ₂ O ₄	10	20	AcOH	Trace	

^aReaction 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. ^bIsolated yields.

^cNaHCO₃/PhCOONa = (1/1).

Table S4. Screening of oxidant^a

	1a		2a			3a
Entry	Oxidant	Yield ^b (%)	Entry	Oxidant	Yield ^b (%)	
1	/	43	9	PhI(OAc) ₂	25	
2	K ₂ S ₂ O ₈	43	10	Mn(OAc) ₃ ·H ₂ O	Trace	
3	Ag ₂ CO ₃	0	11	KMnO₄	54	

4	AgOAc	41	12	H ₂ O ₂	35
5	Ag ₂ O	0	13	BQ	40
6	AgTFA	0	14	O ₂	39
8	NMO	17			

^aReaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), Cu(OAc)₂ (20 mol%), NaHCO₃ (0.4 mmol), oxidant (0.2 mmol), DCE (1.0 mL), air, 110 °C, 12 h. ^bIsolated yields.

Table S5. Screening of additive^a

Entry	Additive	Yield ^b (%)
1	/	54
2	Ph ₃ P	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

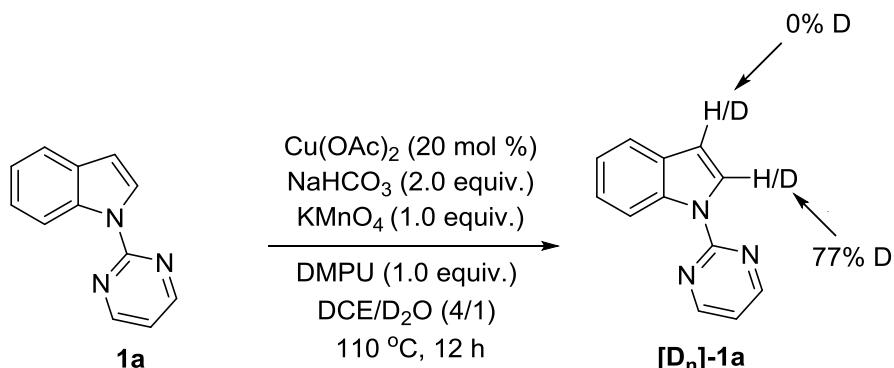
^aReaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), Cu(OAc)₂ (20 mol%), NaHCO₃ (0.4 mmol), KMnO₄ (0.2 mmol), additive (0.2 mmol), DCE (1.0 mL), 110 °C, 12 h. ^bIsolated yields. ^cp-Bromobenzenesulfonyl chloride instead of **2a**. ^dWithout TsCl. ^eWithout Cu(OAc)₂. ^fUnder O₂. ^gUnder Ar. DMPU = 1,3-dimethyltetrahydropyrimidin-2(1*H*)-one.

Table S6 Screening of the loading of **2a, Cu(OAc)₂, KMnO₄, 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

^aReaction conditions : **1a** (0.2 mmol), **2a**, cat., NaHCO₃ (0.4 mmol), KMnO₄, DMPU, DCE (1.0 mL), air, T °C. ^bIsolated yields.

1.2 H/D exchange experiment



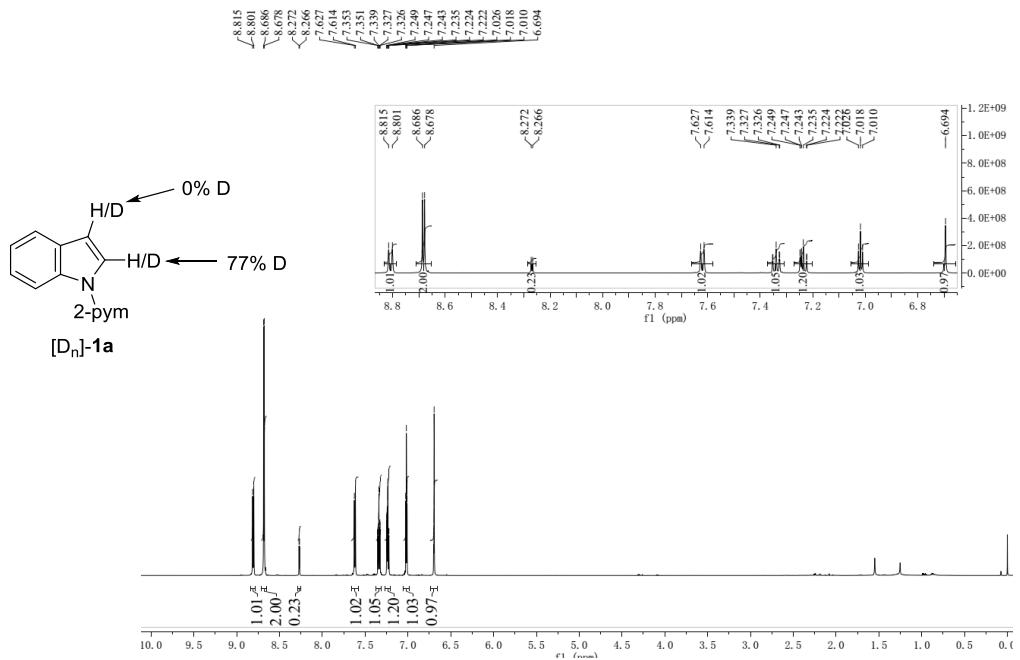


Figure S1 ^1H NMR spectrum of $[\text{D}_n]\text{-1a}$ from H/D exchange experiment

1.3 Intermolecular competition KIE

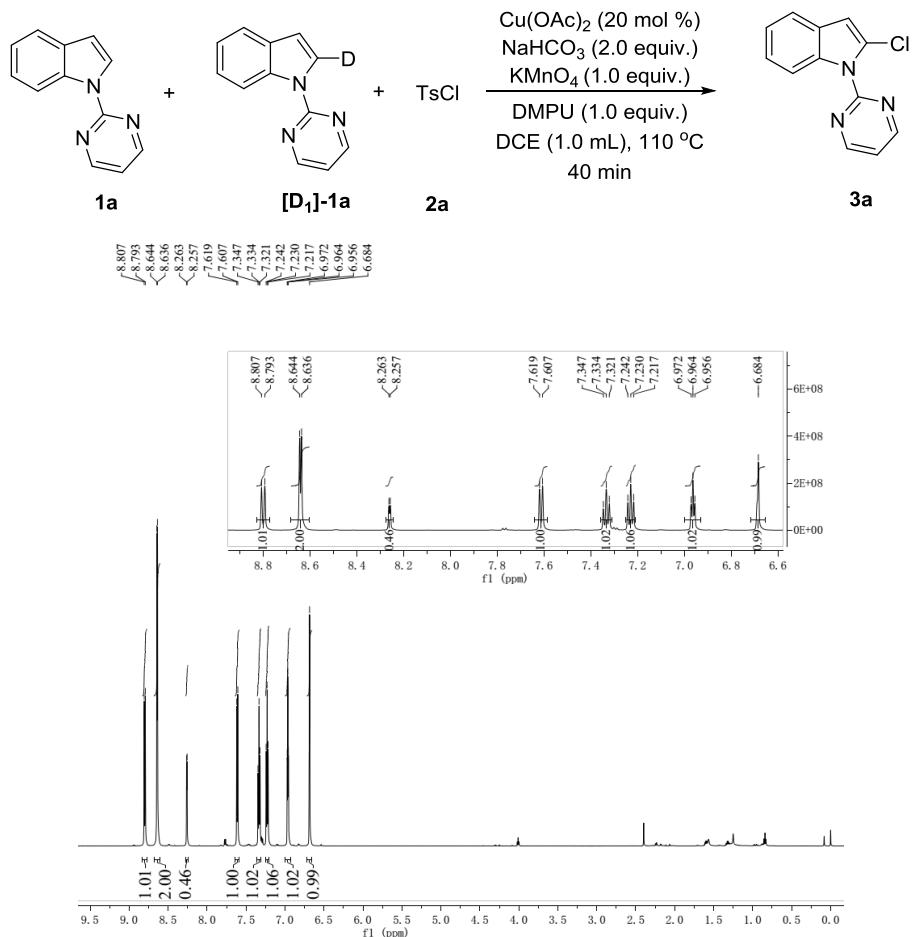
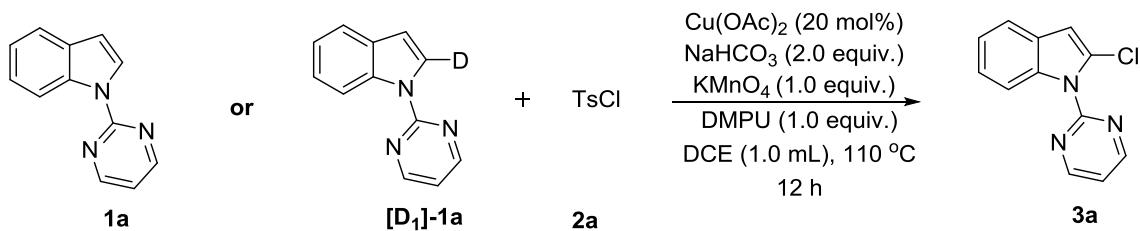


Figure S2 ^1H NMR spectrum of recovered **1a** and $[\text{D}_1]\text{-1a}$ from intermolecular competition

KIE experiment

1.4 Parallel experiments



Entry	Time (min)	Yield of 3a (1a)	Yield of 3a (D₁-1a)
1	30	16.56%	4.58%
2	50	23.31%	8.93%
3	70	31.37%	13.29%
4	90	40.74%	16.12%

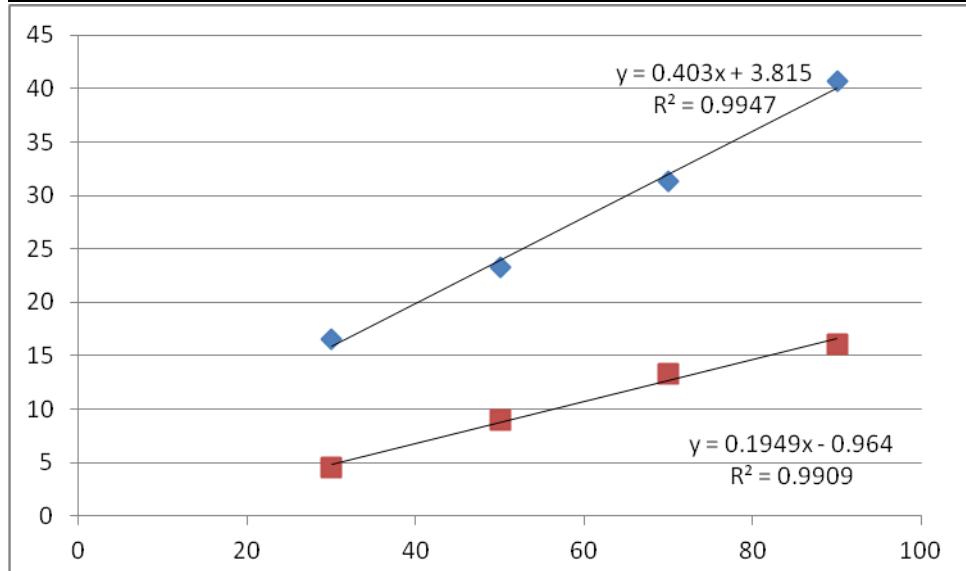
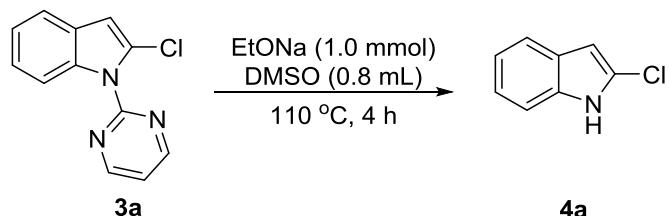
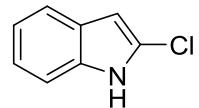


Figure S3 The parallel KIE was calculated as $k_H/k_D = 0.403/0.1949 \approx 2.1$

1.5 Removal of the directing group



YC12138
1H
CDCl₃
218/SMP



4a

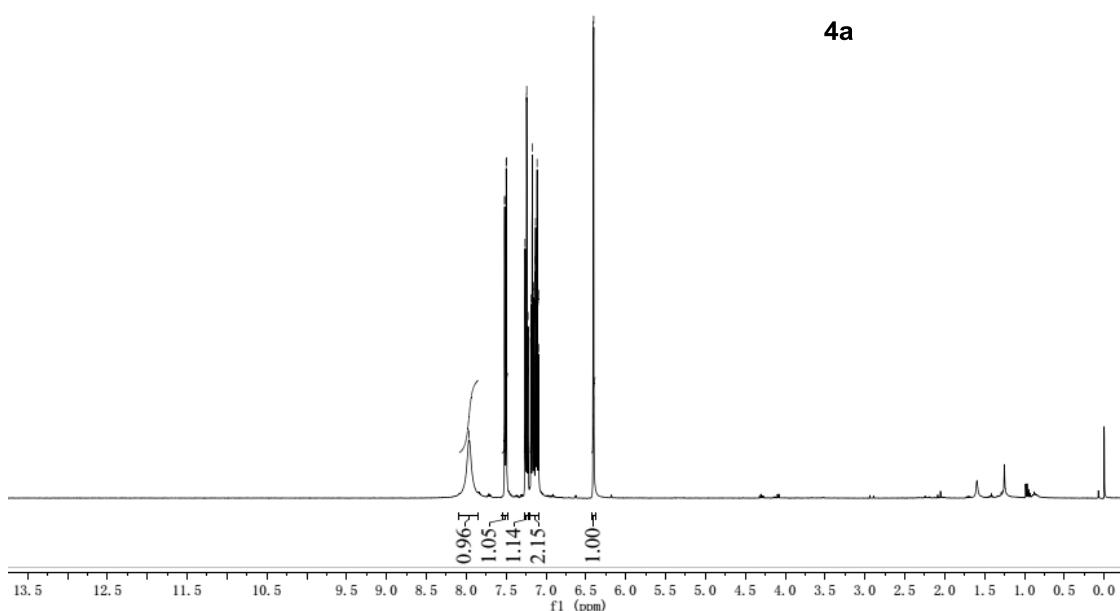
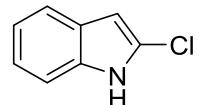


Figure S4 ¹H NMR spectrum of **4a** (400 MHz, CDCl₃)

YC 12138
13C
CDCl₃



4a

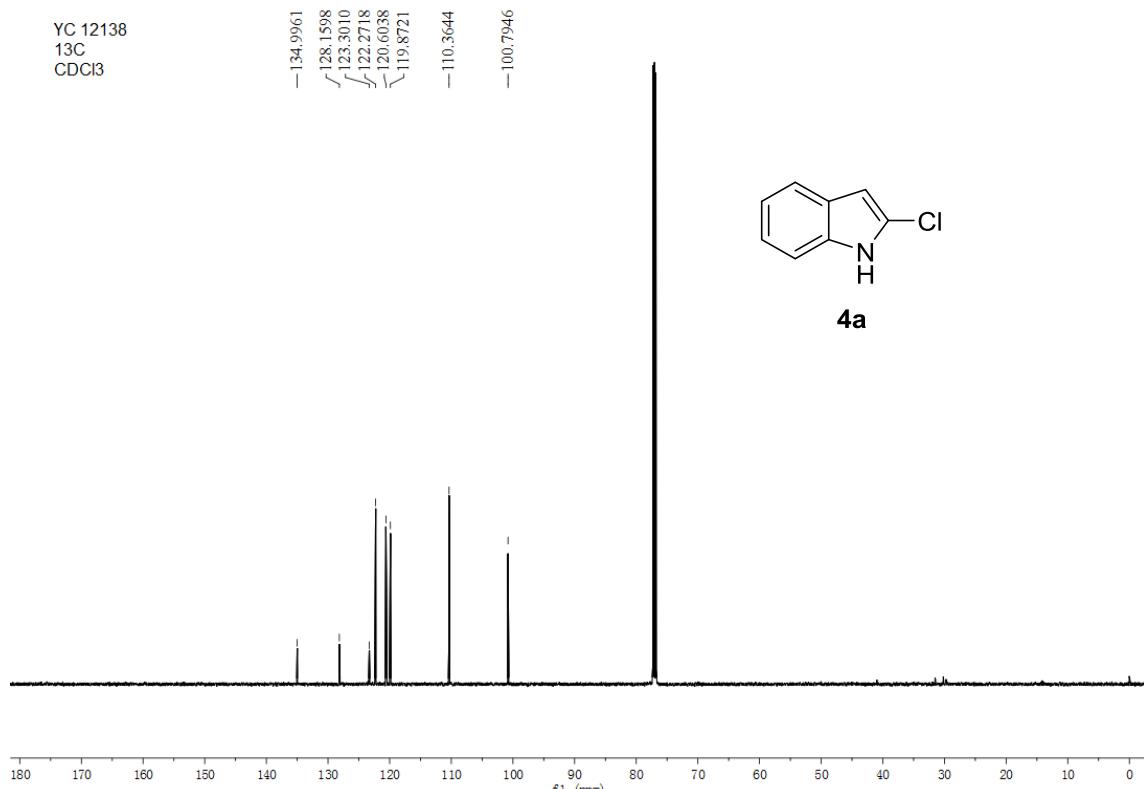
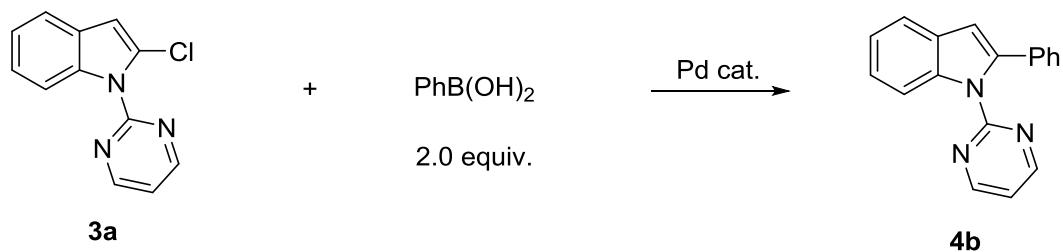


Figure S5 ¹³C{¹H} NMR spectrum of **4a** (150 MHz, CDCl₃)

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

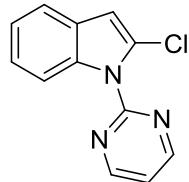


Entry	Reaction conditions	Isolated yield (%)
1	Pd ₂ (dba) ₃ (5 mol%), PCy ₃ ·HBF ₄ (10 mol%), Na ₂ CO ₃ (2 equiv.), dioxane, 110 °C, 12 h	no reaction
2	Pd ₂ (dba) ₃ (1 mol%), X-Phos (4 mol%), K ₃ PO ₄ (2.0 equiv.), <i>n</i> -BuOH, MW, 110 °C, 30 min	no reaction
3	Pd ₂ (dba) ₃ (5 mol%), Na ₂ CO ₃ (aq.), dioxane, MW, 110 °C, 30 min	trace
4	Pd ₂ (dba) ₃ (5 mol%), Na ₂ CO ₃ (aq.), CH ₃ CN, MW, 110 °C, 30 min	trace
5	Pd(OAc) ₂ (5 mol%), Na ₂ CO ₃ (aq.), CH ₃ CN, MW, 110 °C, 30 min	25
6	Pd(PPh ₃) ₂ Cl ₂ (5 mol%), Na ₂ CO ₃ (aq.), CH ₃ CN, MW, 110 °C, 30 min	53
7	Pd(PPh ₃) ₄ (5 mol%), Na ₂ CO ₃ (aq.), CH ₃ CN, MW, 130 °C, 30 min	17
8	Pd(dppf)Cl ₂ (5 mol%), Na ₂ CO ₃ (aq.), CH ₃ CN, MW, 130 °C, 30 min	75

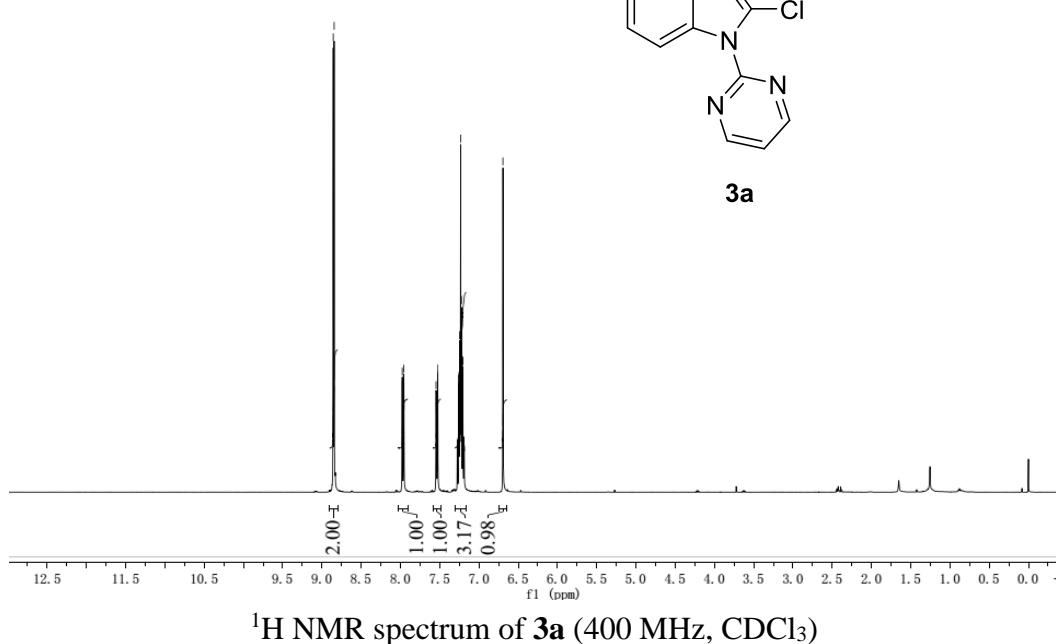
2 NMR spectra

YC11181
1H
CDCl₃
3874/SMP

8.856
8.844
7.976
7.956
7.545
7.541
7.527
7.524
7.257
7.254
7.245
7.243
7.237
7.233
7.226
7.222
7.207
7.204
6.693



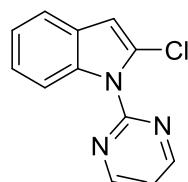
3a



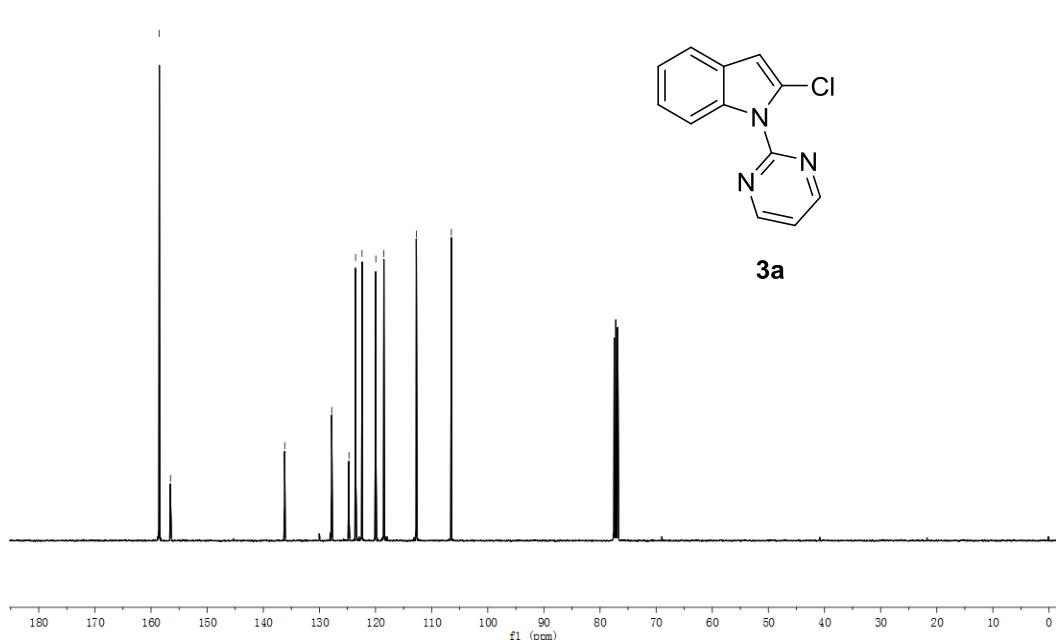
¹H NMR spectrum of **3a** (400 MHz, CDCl₃)

YC 11181
13C
CDCl₃

~158.5300
~156.5351
-127.8015
-124.7379
-123.5419
-122.4048
-119.9436
-118.5206
-112.7233
-106.4970



3a

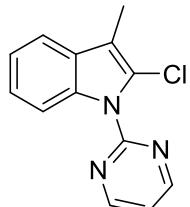


¹³C{¹H} NMR spectrum of **3a** (100 MHz, CDCl₃)

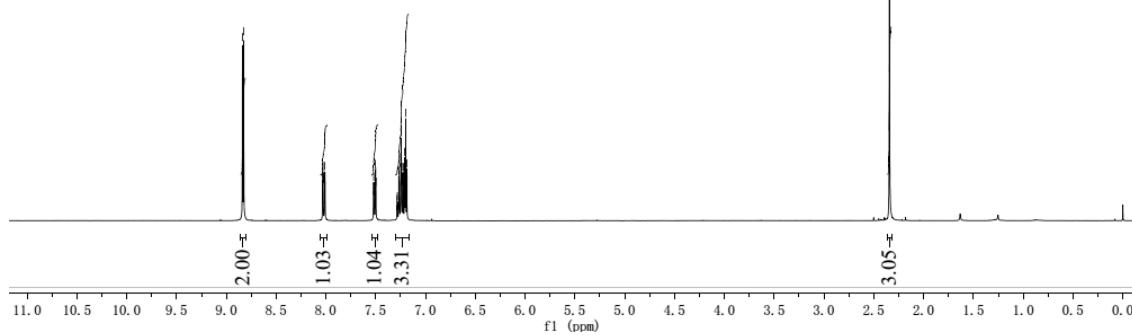
YC12121
1H
CDCl₃
4643/SMP

8.838
8.825
8.032
8.029
8.014
8.011
7.521
7.516
7.503
7.500
7.286
7.283
7.268
7.265
7.249
7.244
7.228
7.225
7.211
7.207
7.199
7.187

-2.343



3b



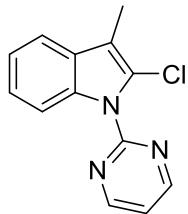
¹H NMR spectrum of **3b** (400 MHz, CDCl₃)

YC12121
13C
CDCl₃
4700/SMP

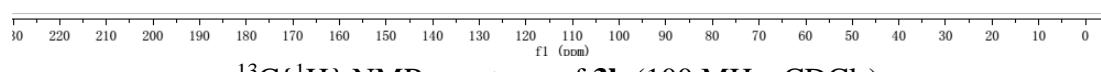
158.390
156.828

135.712
128.682
123.697
122.005
121.809
118.298
117.967
113.915
112.658

8.884
8.856



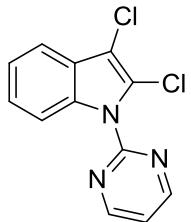
3b



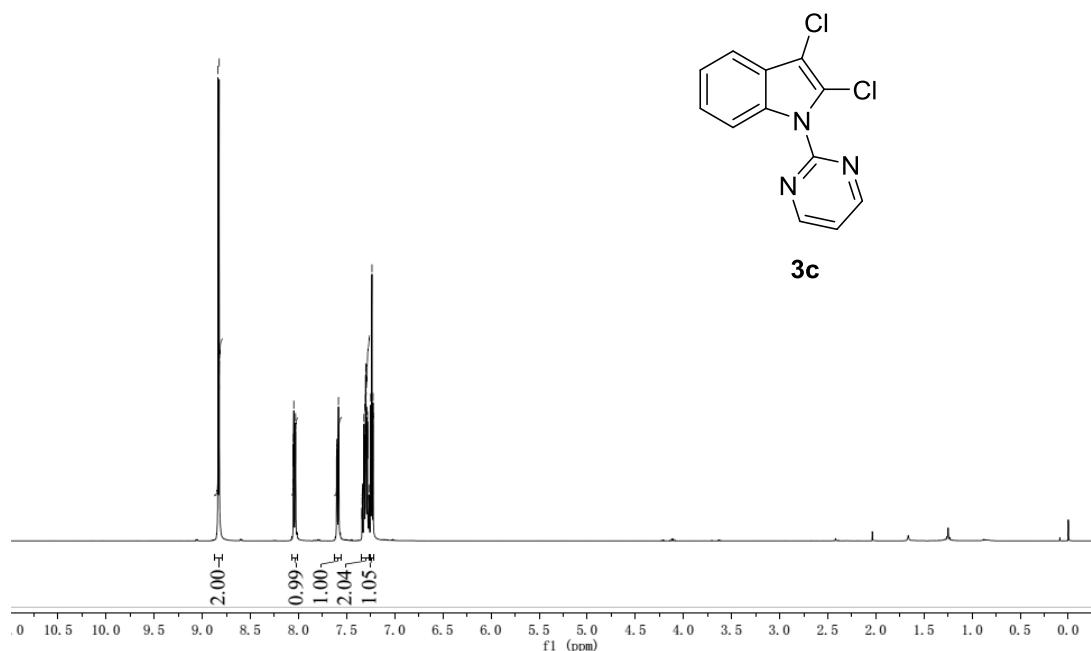
¹³C{¹H} NMR spectrum of **3b** (100 MHz, CDCl₃)

YC1273
1H
CDCl₃
4395/SMP

8.837
8.824
8.053
8.049
8.036
8.031
7.603
7.601
7.597
7.586
7.581
7.339
7.335
7.321
7.317
7.305
7.303
7.300
7.297
7.287
7.283
7.268
7.265
7.249
7.242
7.237
7.225



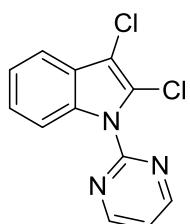
3c



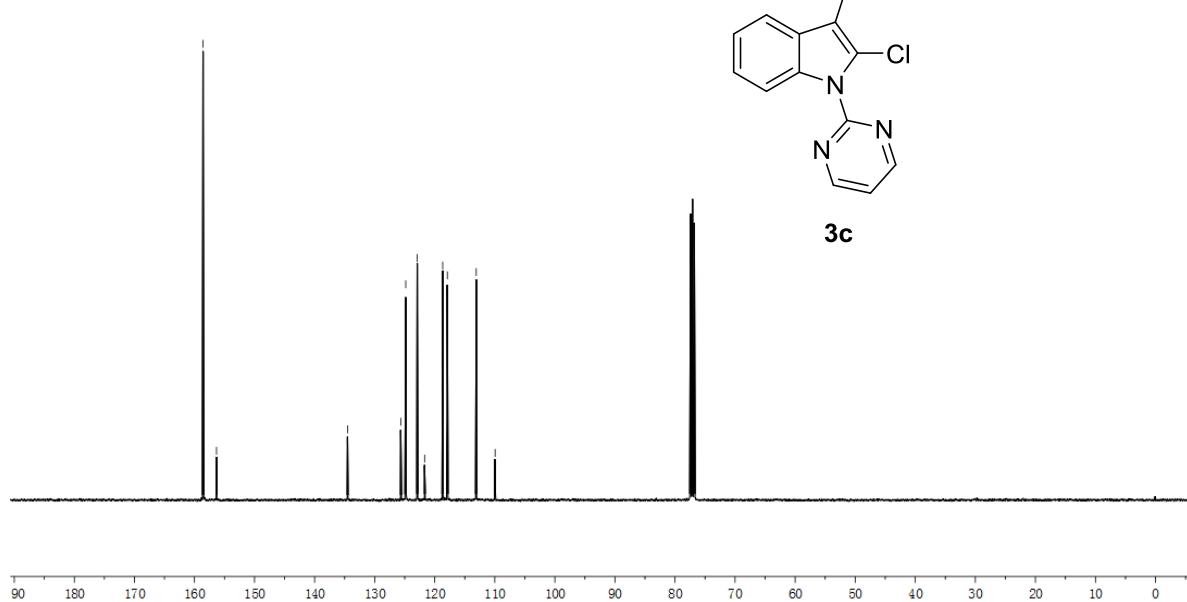
¹H NMR spectrum of **3c** (400 MHz, CDCl₃)

YC 1273
13C
CDCl₃

158.5774
156.3303
134.5147
125.6603
124.8245
122.9165
121.6892
118.6729
117.9058
113.0941
109.9510



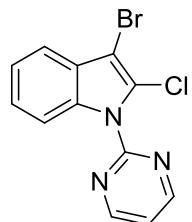
3c



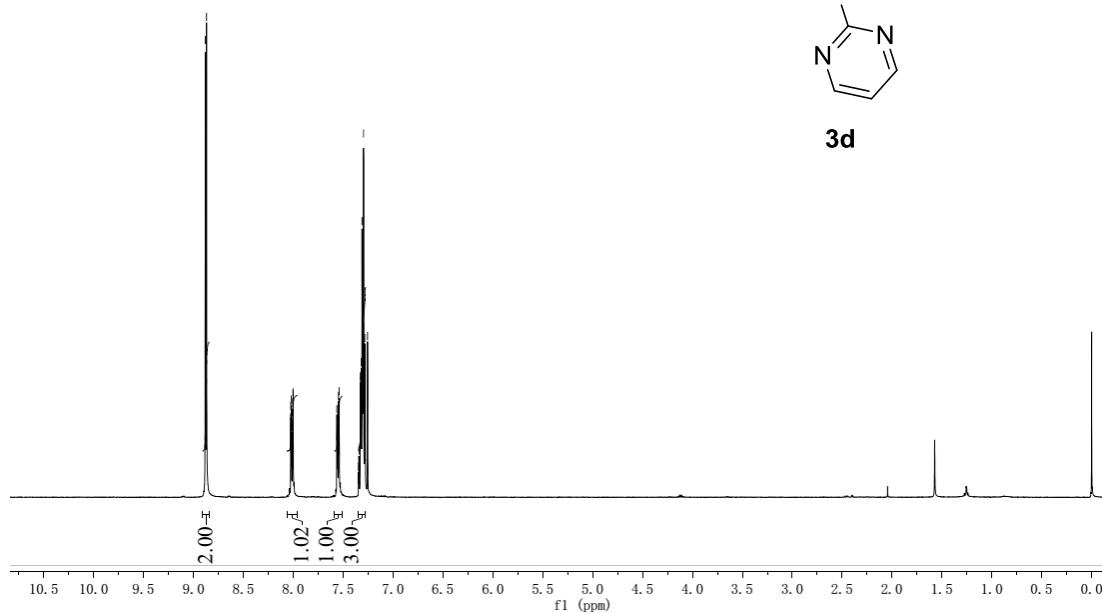
¹³C{¹H} NMR spectrum of **3c** (100 MHz, CDCl₃)

YC12281
1H
CDCl₃
4975/SMP

8.882
8.870
8.021
8.005
8.003
8.002
7.963
7.560
7.555
7.547
7.542
7.347
7.342
7.329
7.324
7.319
7.312
7.308
7.305
7.300
7.296
7.284
7.279
7.256

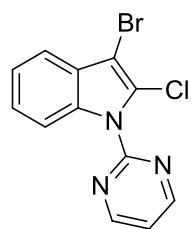


3d

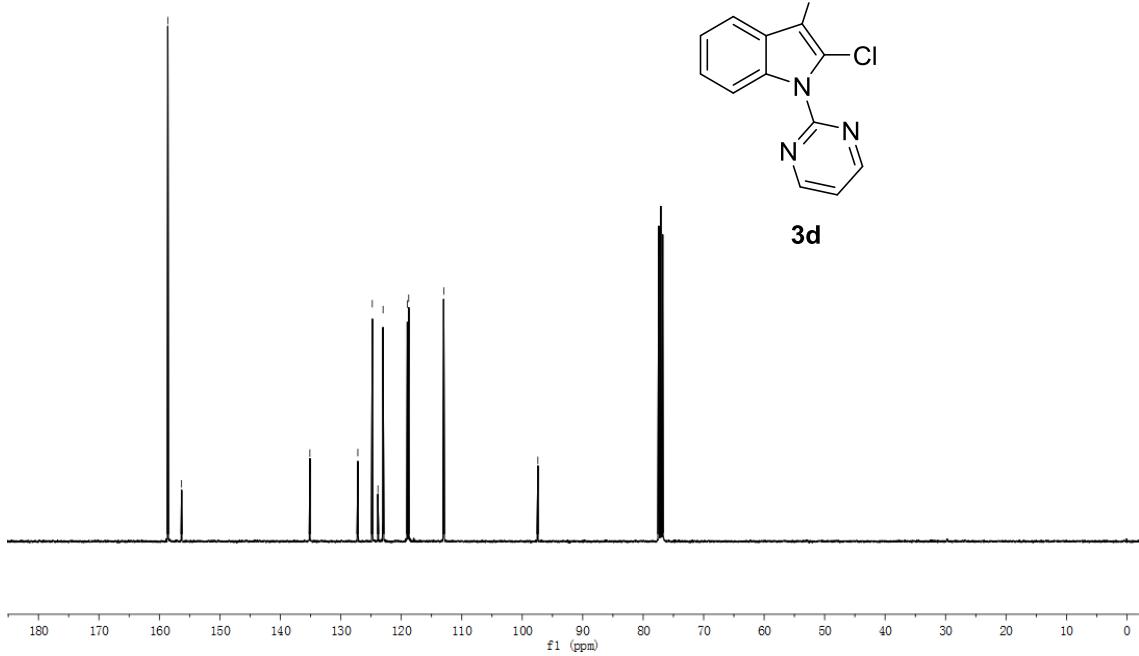


YC 12281
13C
CDCl₃

-158.6003
-156.5304
-127.1142
-127.1795
-124.7951
-123.8575
-123.0082
-118.9068
-118.7693
-112.9797
-97.4124

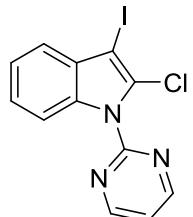


3d

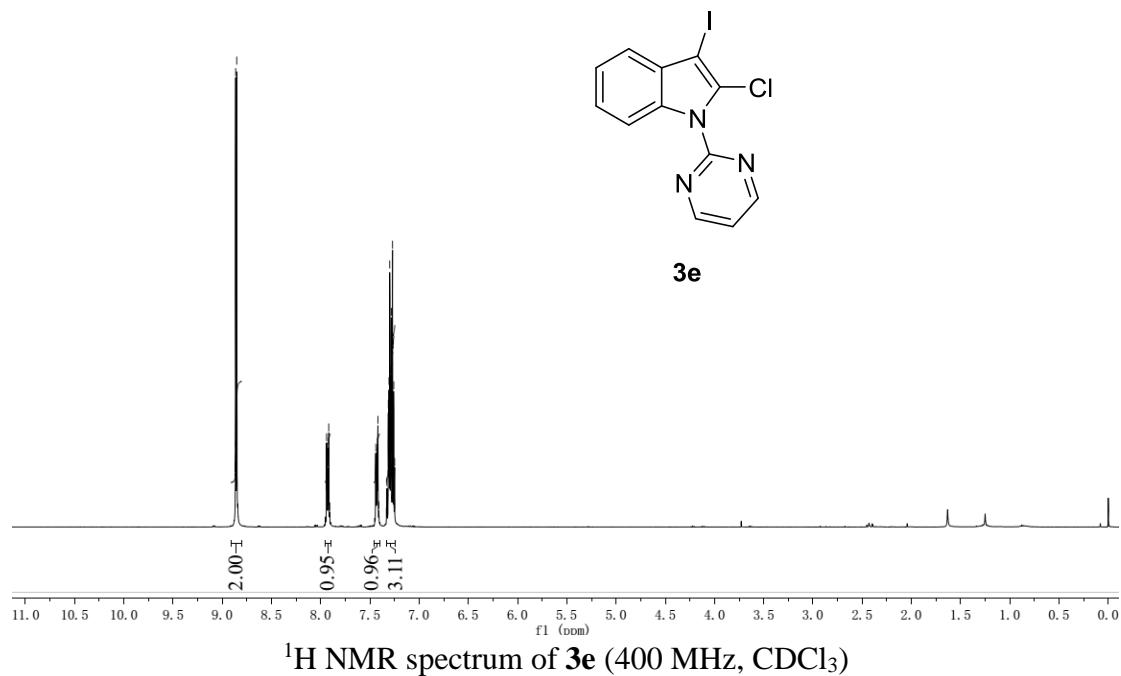


YC12101
1H
CDCl₃
4518/SMP

8.865
8.853
7.941
7.936
7.921
7.919
7.942
7.948
7.438
7.433
7.426
7.425
7.419
7.409
7.332
7.327
7.314
7.309
7.306
7.298
7.289
7.283
7.271
7.259
7.250



3e



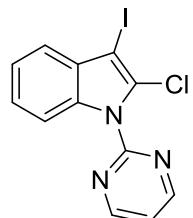
¹H NMR spectrum of **3e** (400 MHz, CDCl₃)

YC 12101
13C
CDCl₃

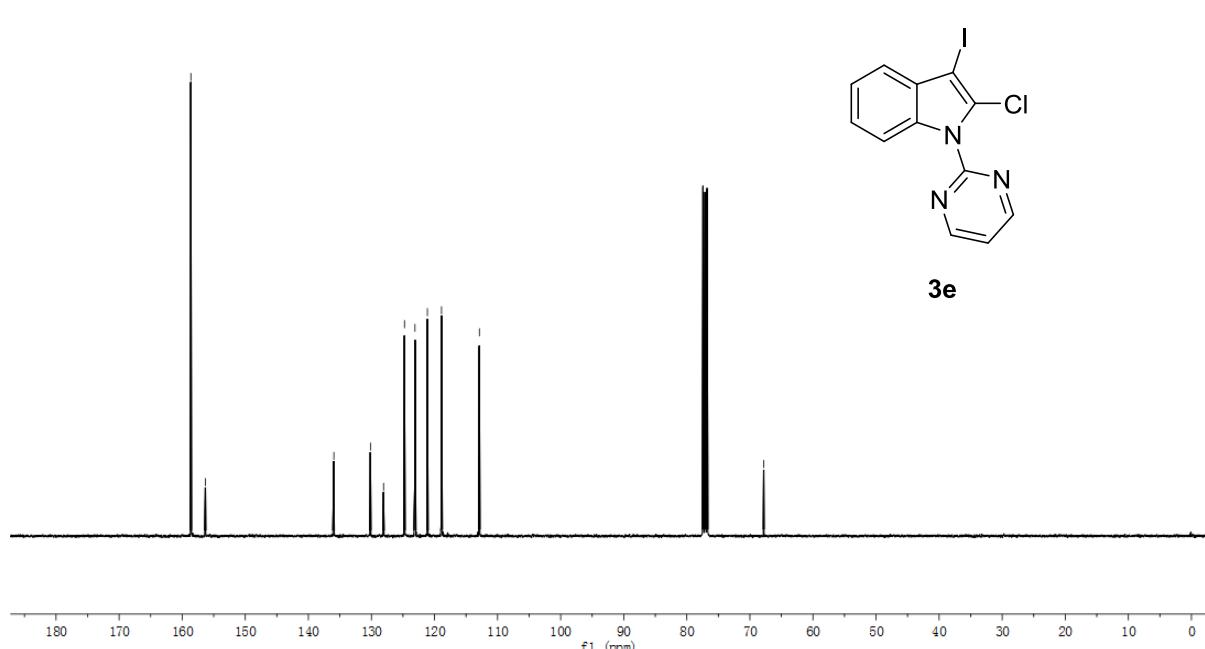
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-156.3169

-135.9529
-130.1561
-128.0784
-124.7592
-123.0937
-121.1292
-118.8843
-112.8884

-67.8100



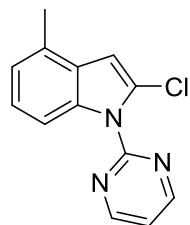
3e



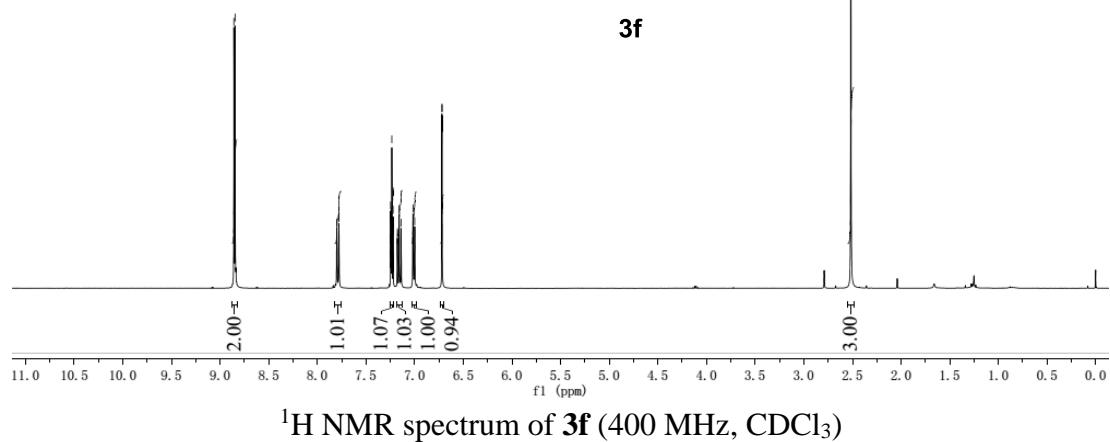
¹³C{¹H} NMR spectrum of **3e** (100 MHz, CDCl₃)

YC1253
1H
CDCl₃
4516/SMP

8.858
8.846
7.800
7.779
7.779
7.246
7.242
7.234
7.222
7.178
7.159
7.139
7.017
6.999
6.720
6.718
-2.516



3f



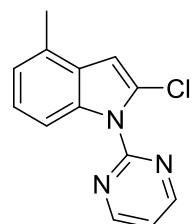
¹H NMR spectrum of **3f** (400 MHz, CDCl₃)

YC 1253
13C
CDCl₃

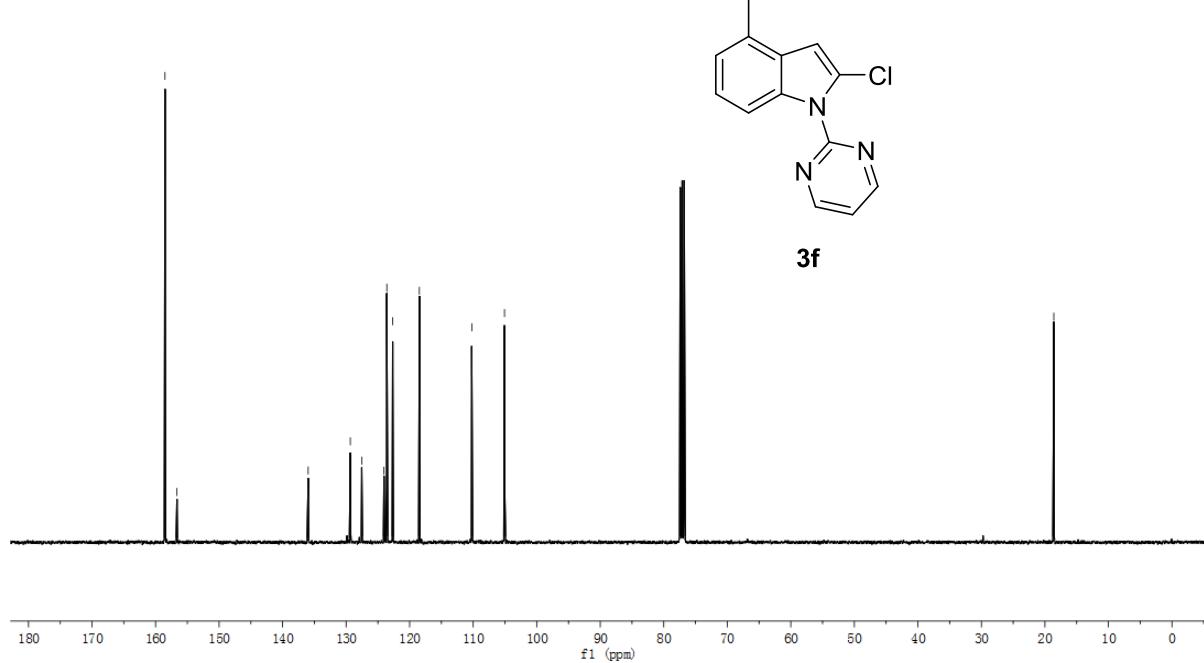
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~156.6356

-135.9727
-129.3442
-127.5375
-124.0468
-123.5949
-122.6794
-118.4687
-110.2188
-105.0726

-18.5929

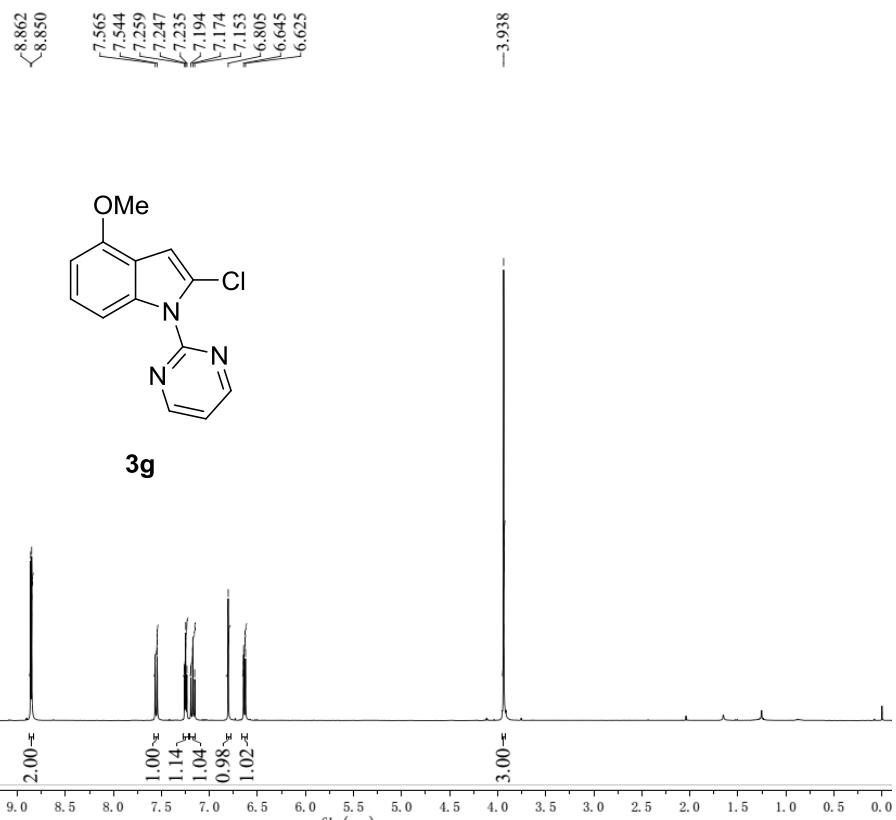


3f

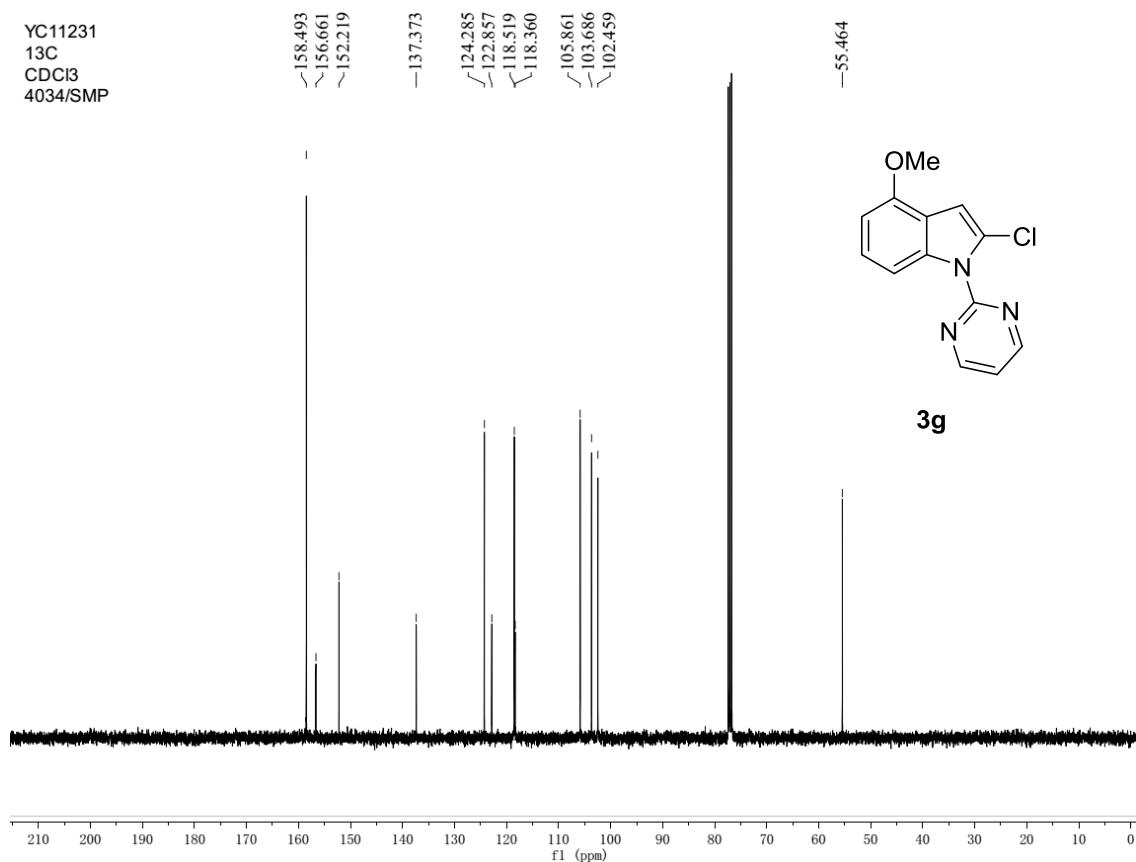


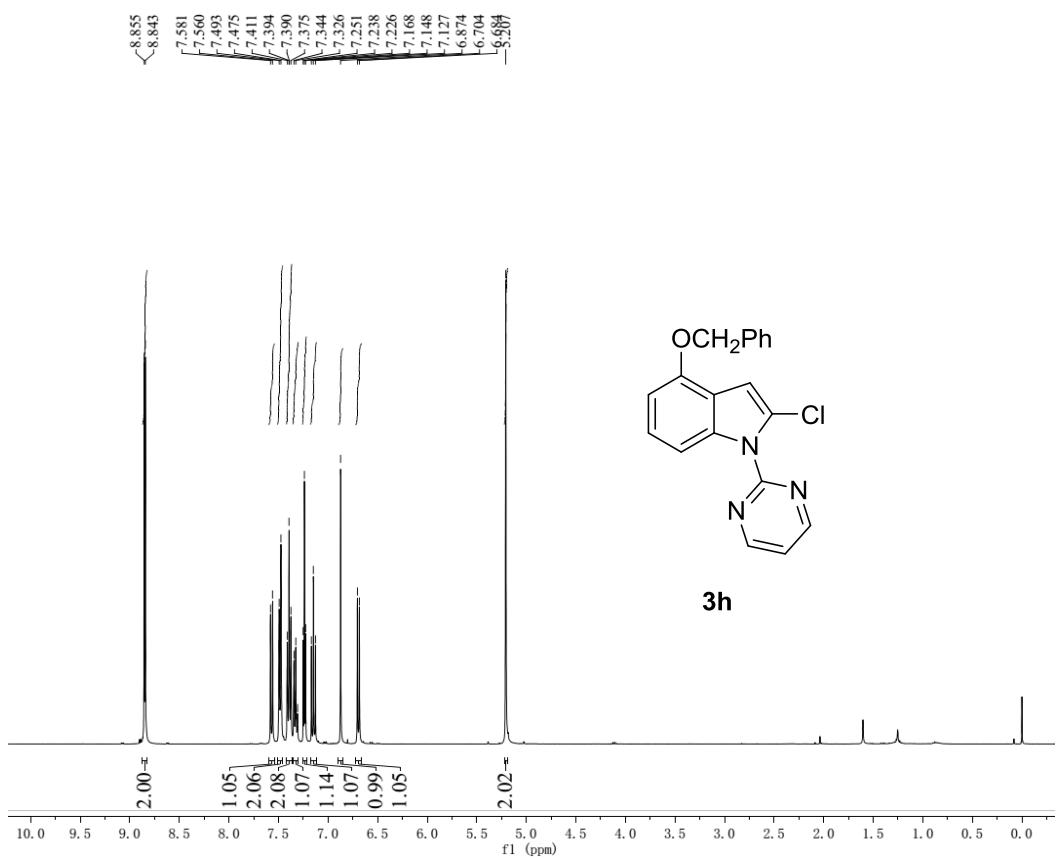
¹³C{¹H} NMR spectrum of **3f** (100 MHz, CDCl₃)

YC11231
1H
CDCl₃
4004/SMP

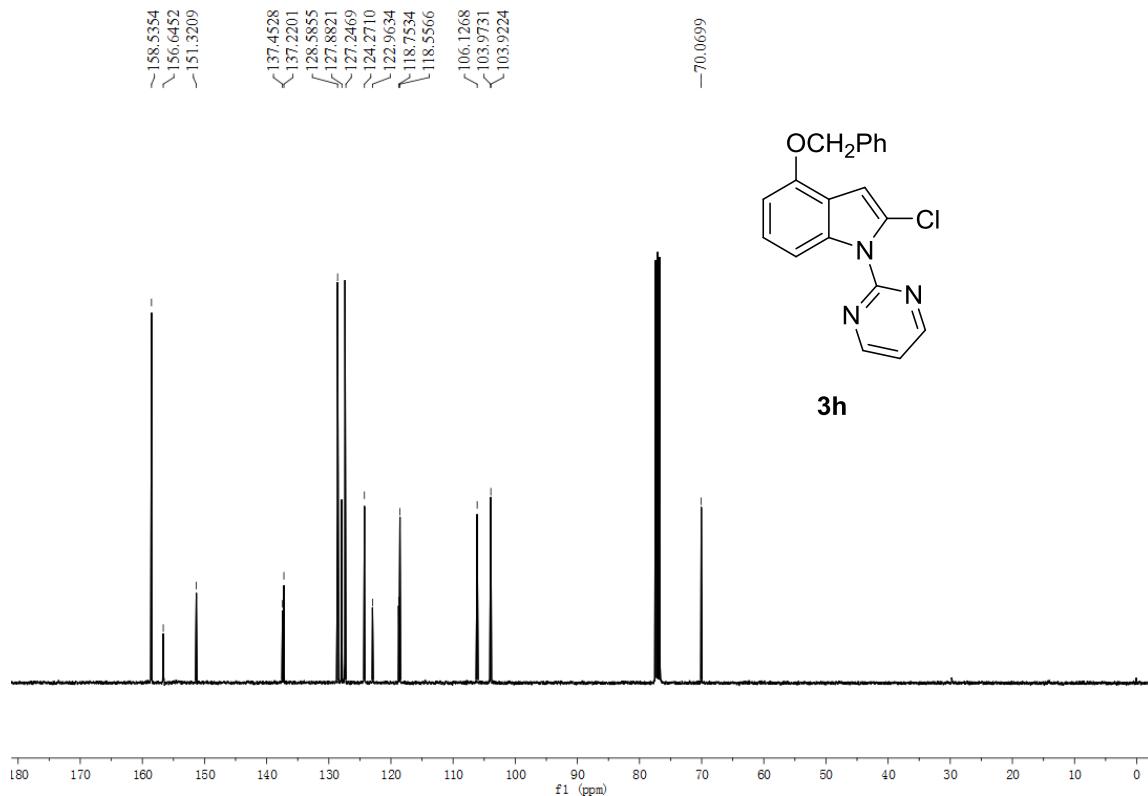


YC11231
13C
CDCl₃
4034/SMP

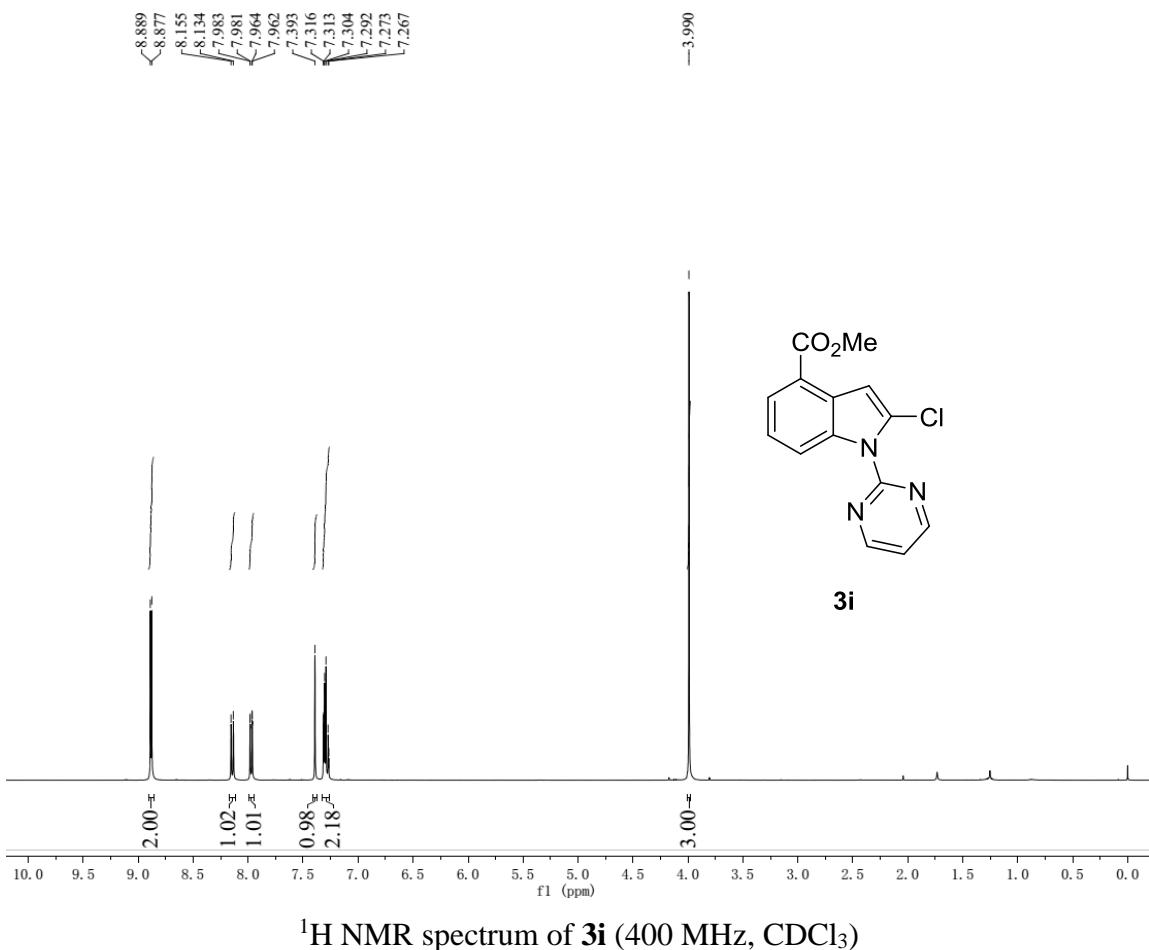




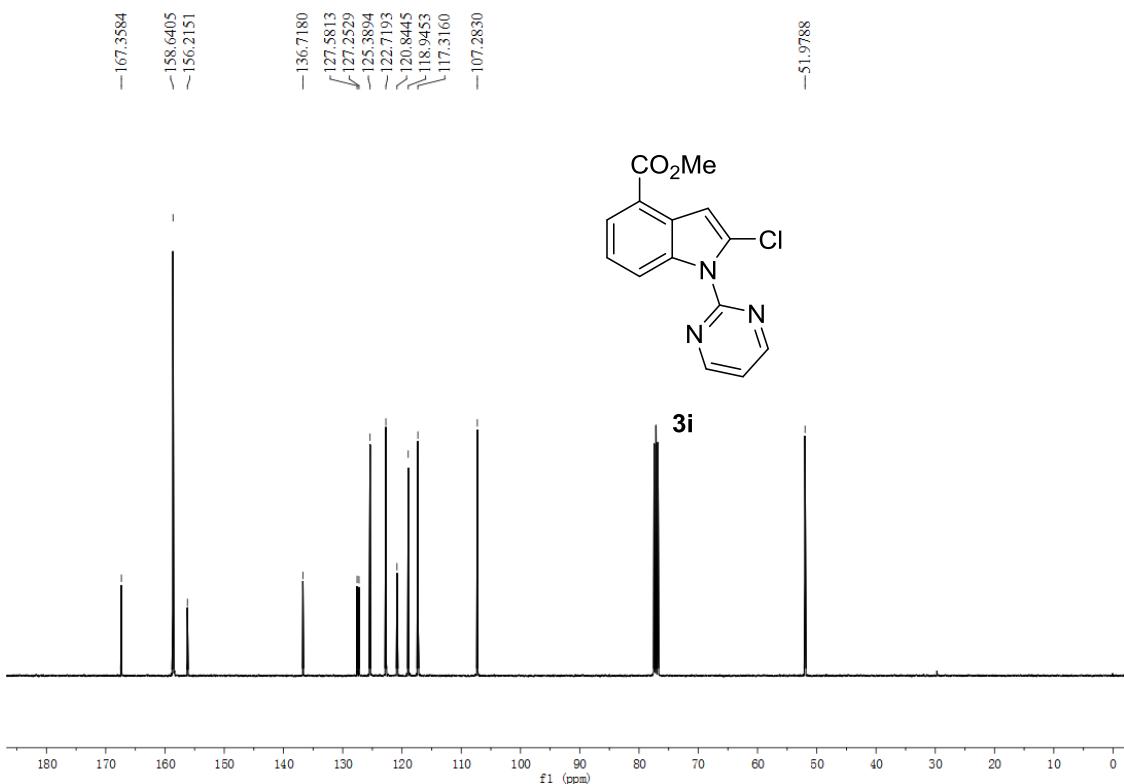
^1H NMR spectrum of **3h** (400 MHz, CDCl_3)



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

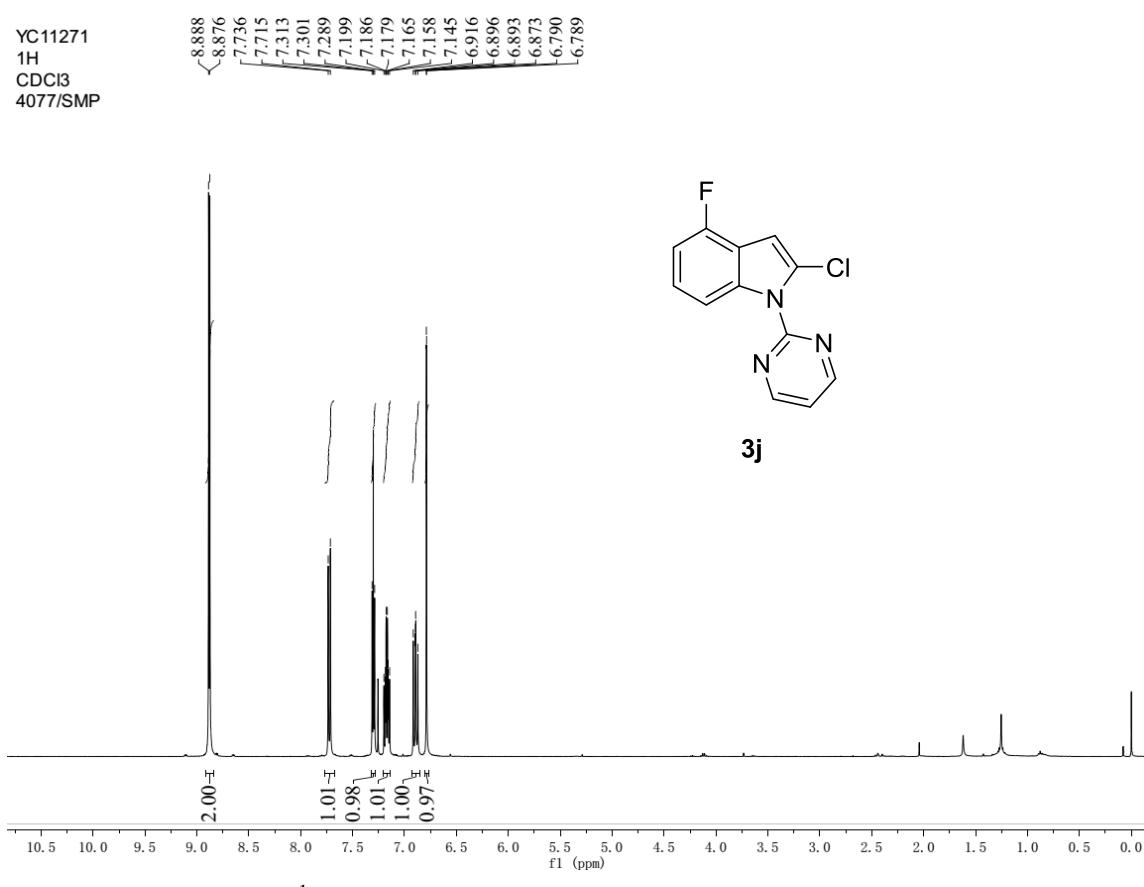


^1H NMR spectrum of **3i** (400 MHz, CDCl_3)



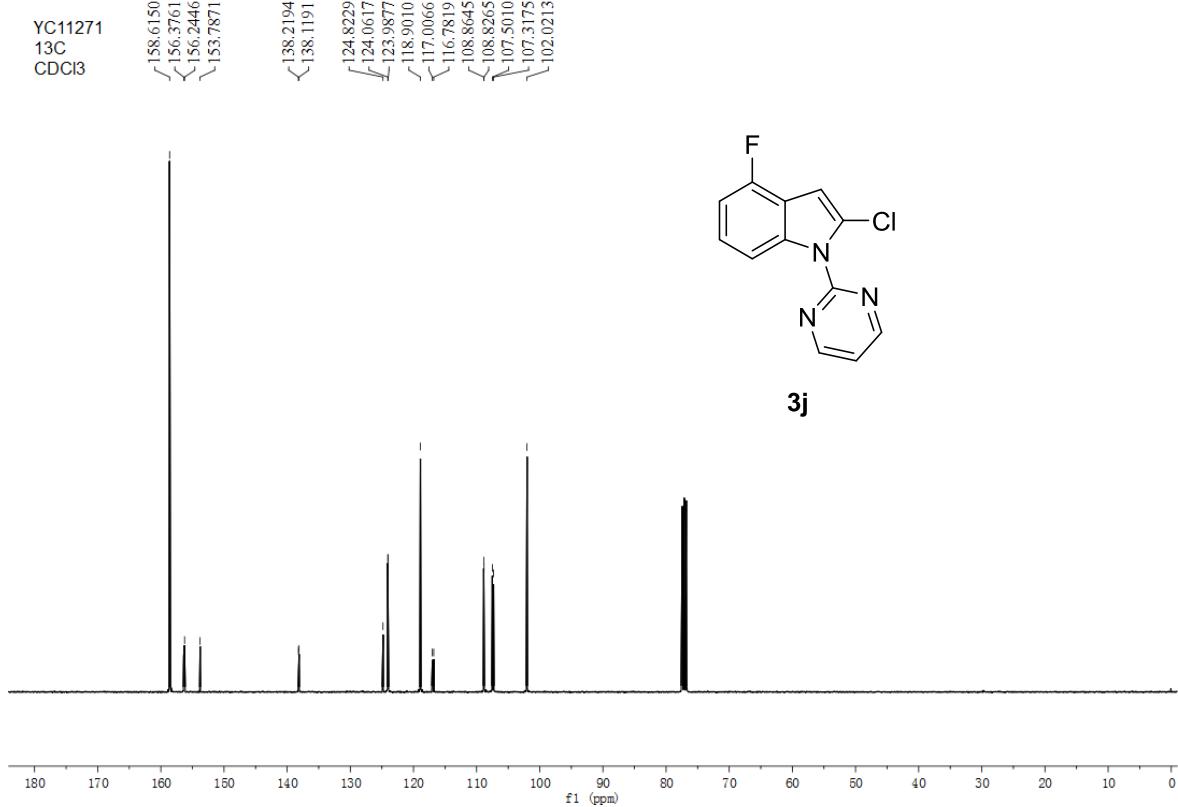
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of **3i** (100 MHz, CDCl_3)

YC11271
1H
CDCl₃
4077/SMP



¹H NMR spectrum of 3j (400 MHz, CDCl₃)

YC11271
13C
CDCl₃

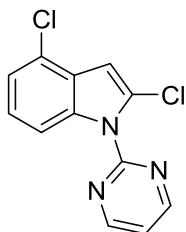


¹³C{¹H} NMR spectrum of 3j (100 MHz, CDCl₃)

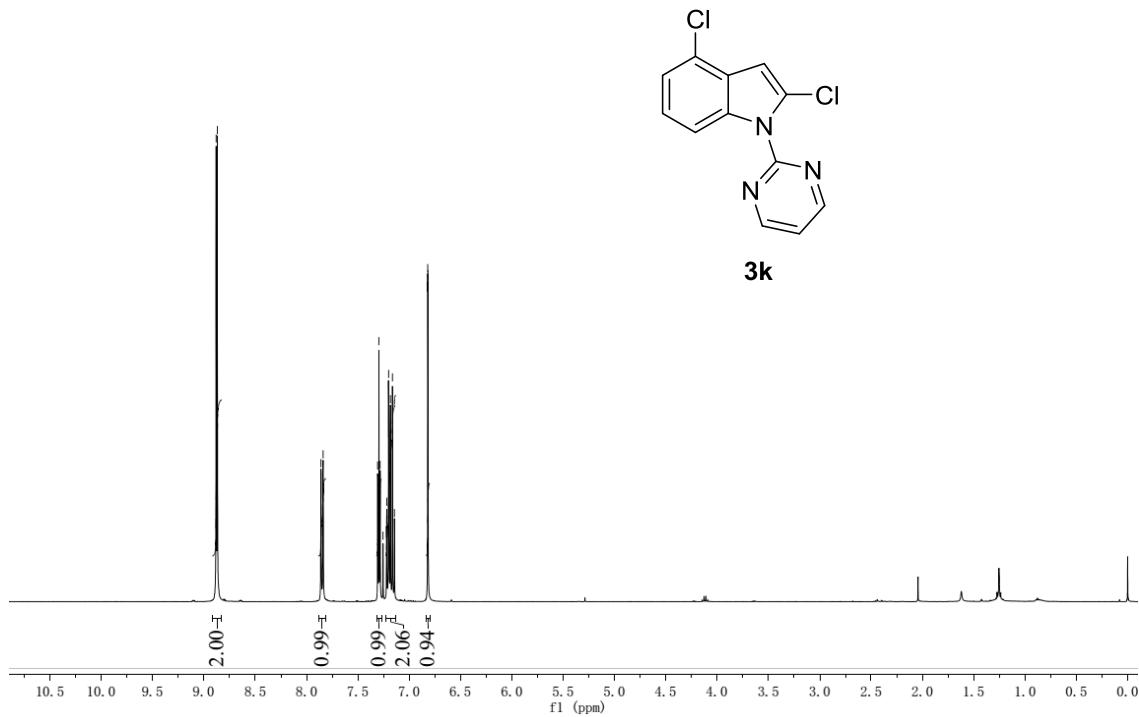
YC11272
1H
CDCl₃
4078/SMP

<8.869
<8.861
<8.881

7.859
7.839
7.307
7.295
7.283
7.255
7.221
7.218
7.201
7.199
7.183
7.163
7.144
6.819
6.818



3k

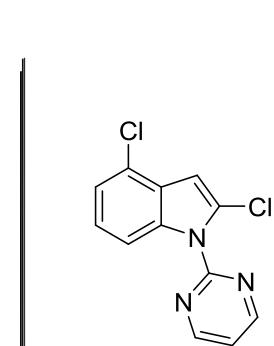


¹H NMR spectrum of **3k** (400 MHz, CDCl₃)

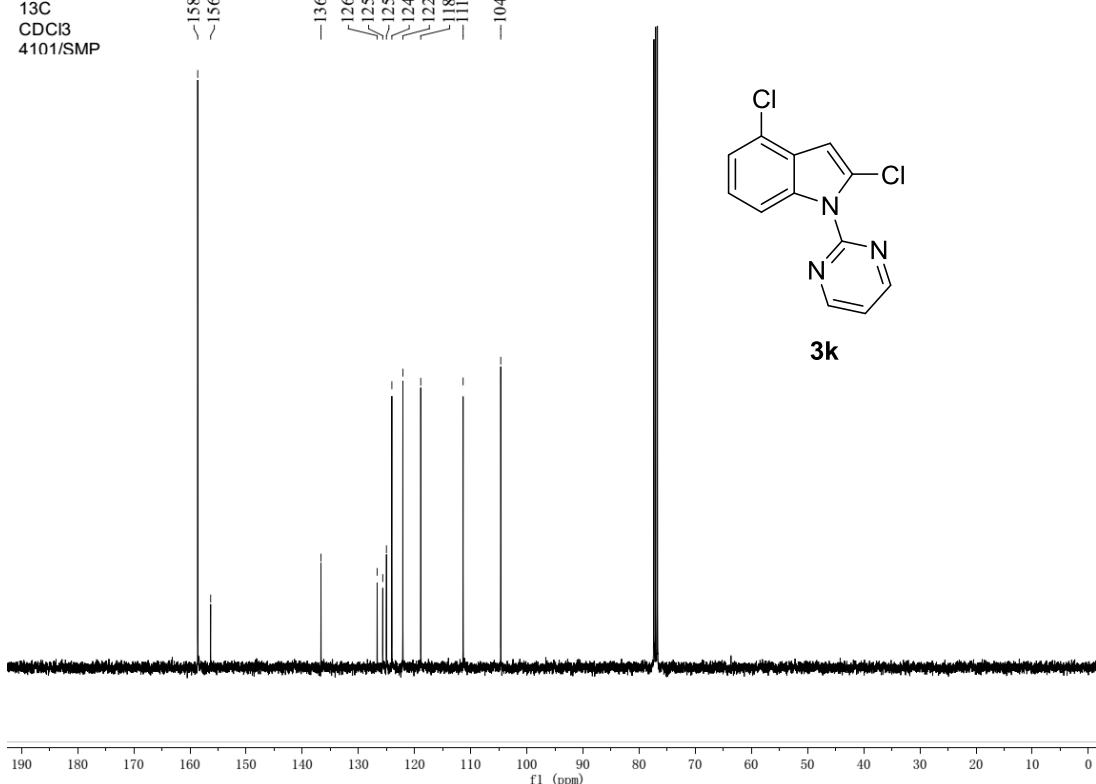
YC11272
13C
CDCl₃
4101/SMP

~158.607
~156.315

-136.659
-126.652
-125.668
-125.023
-124.040
-122.085
-118.891
-111.354
-104.643



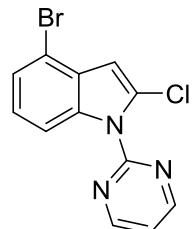
3k



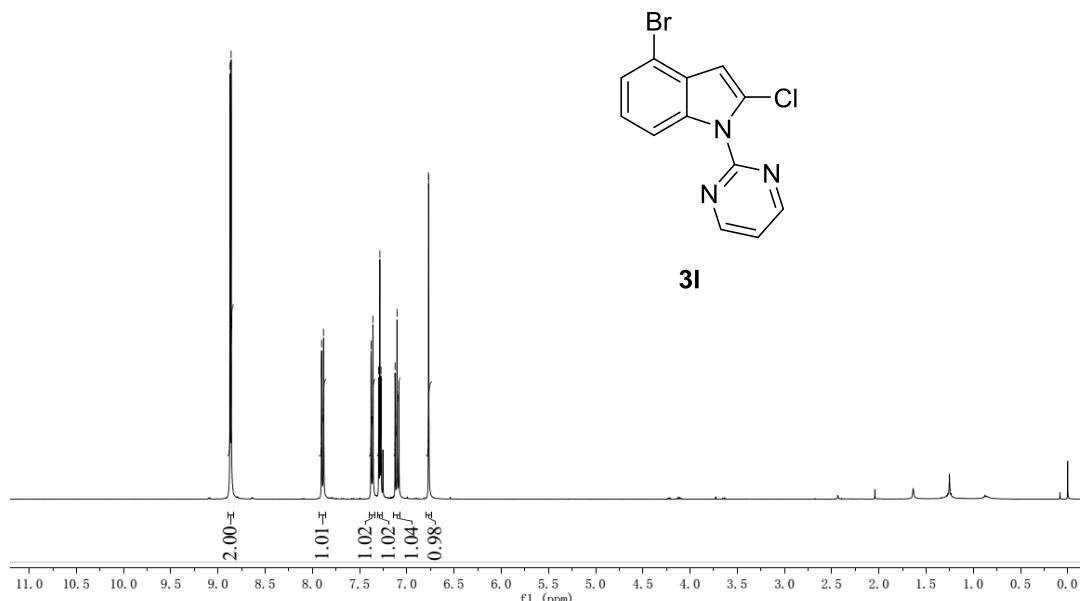
¹³C{¹H} NMR spectrum of **3k** (100 MHz, CDCl₃)

YC11232
1H
CDCl₃
4005/SMP

8.873
<8.861
7.903
<7.882
7.379
7.378
7.360
7.298
7.286
7.274
7.124
7.104
7.084
6.770
6.769



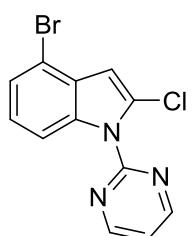
3l



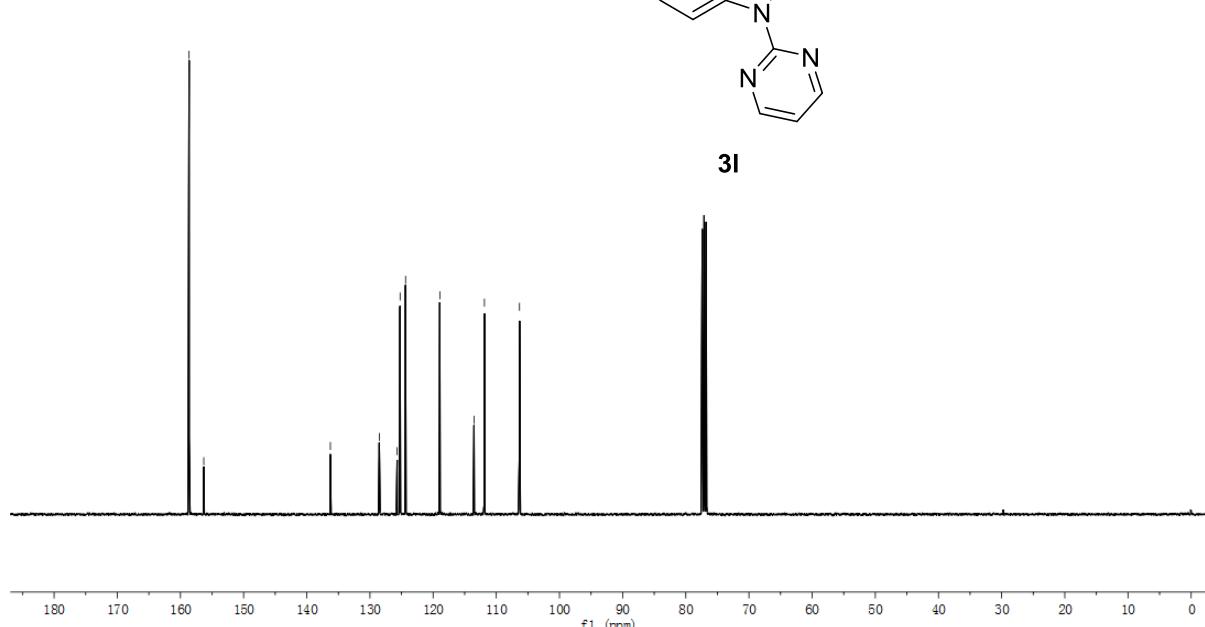
¹H NMR spectrum of **3l** (400 MHz, CDCl₃)

YC 11232
13C
CDCl₃

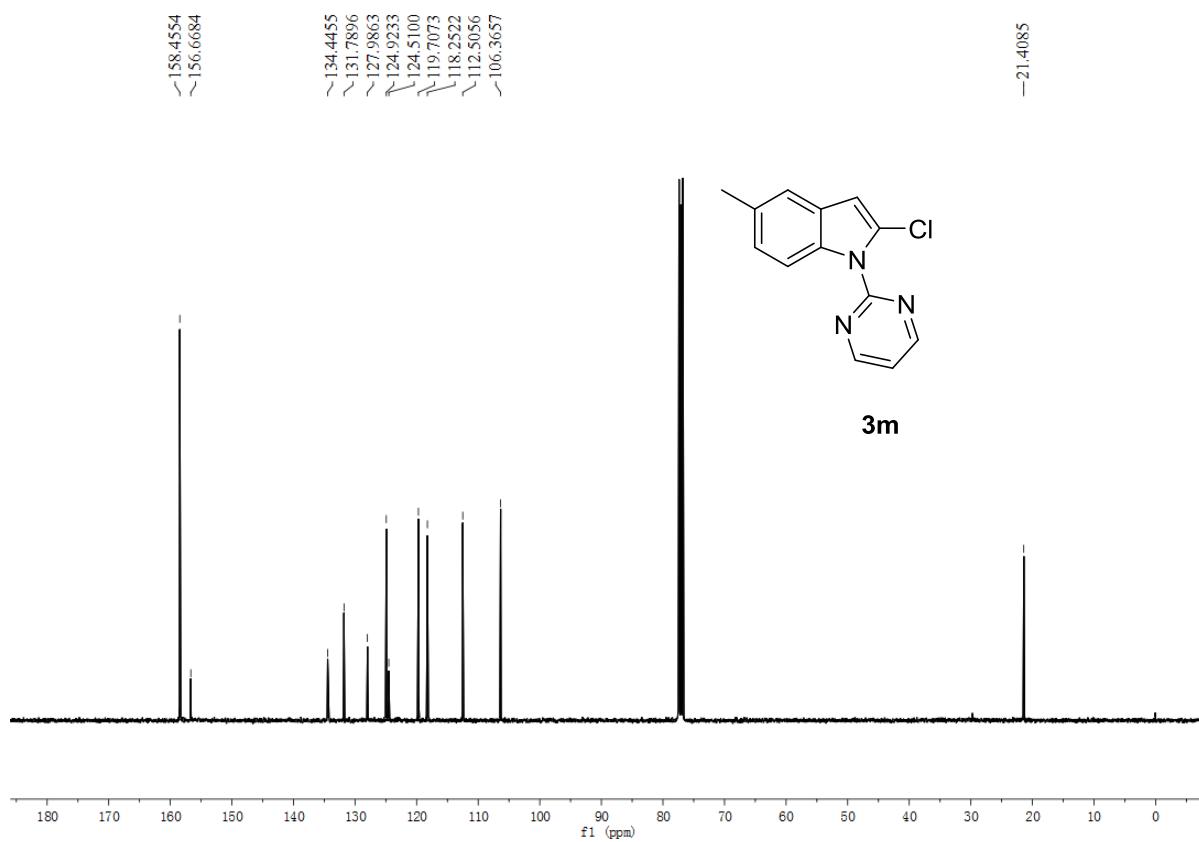
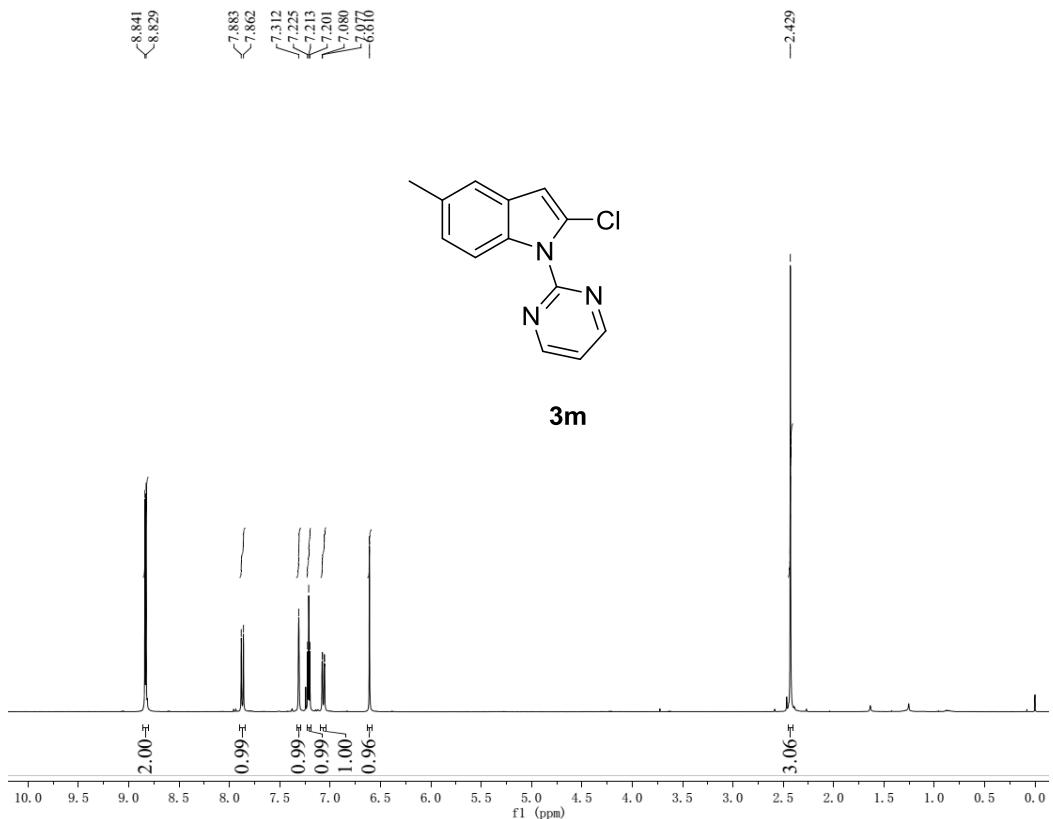
-158.6367
-156.3028
-136.2641
-128.5154
-125.7051
-125.2262
-124.3600
-118.9345
-113.5177
-111.8794
-106.3241

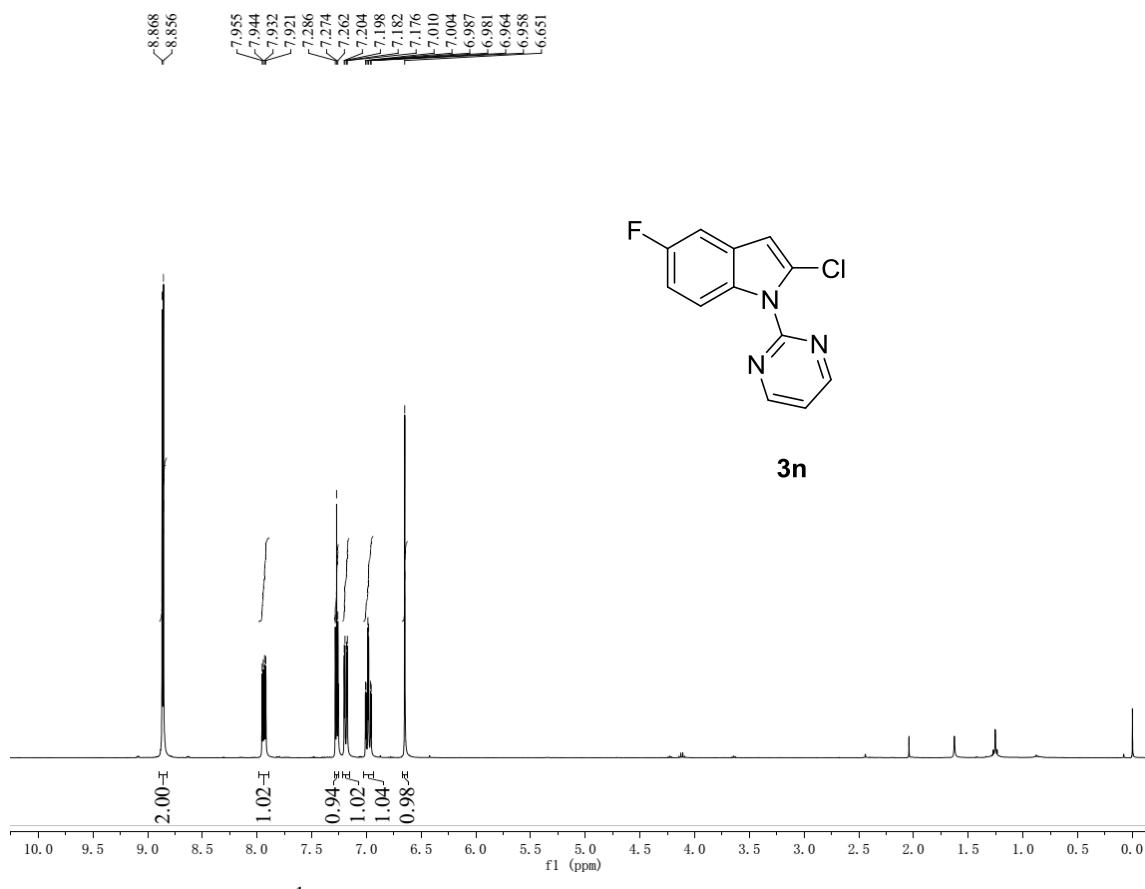


3l

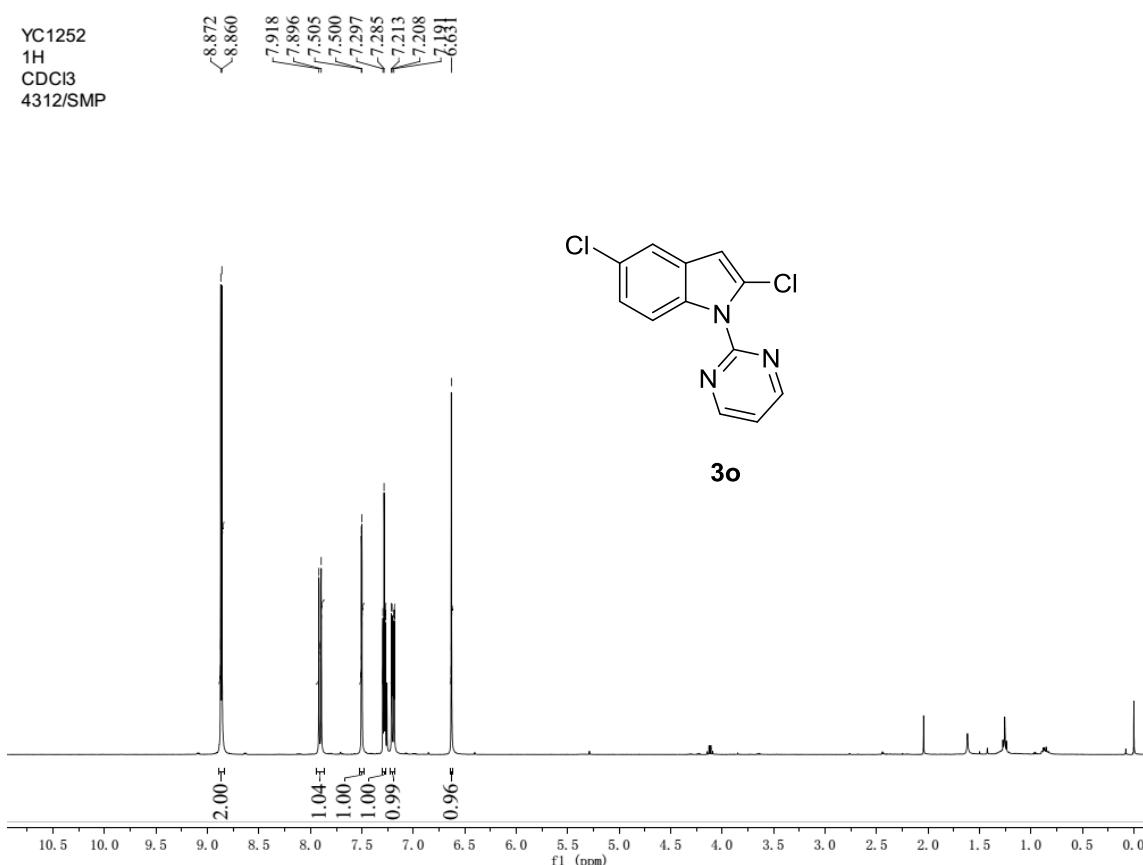


¹³C{¹H} NMR spectrum of **3l** (100 MHz, CDCl₃)



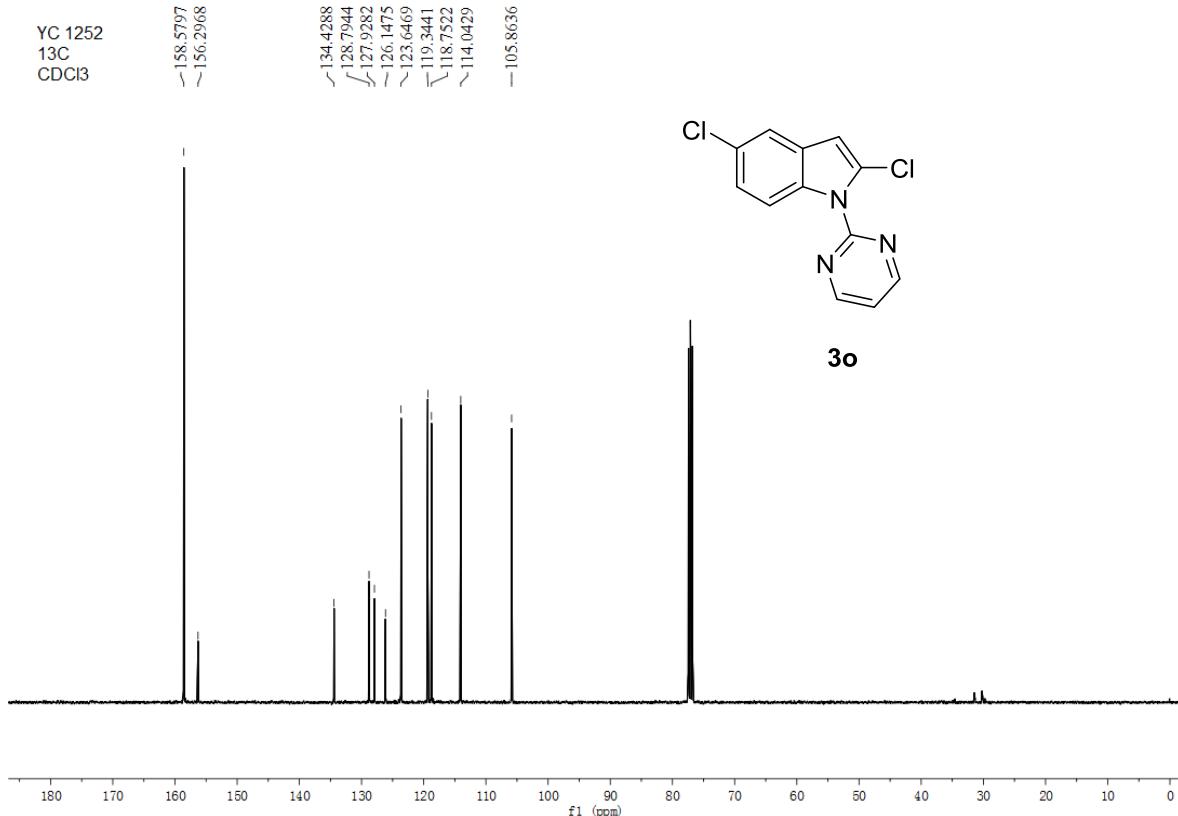


YC1252
1H
CDCl₃
4312/SMP



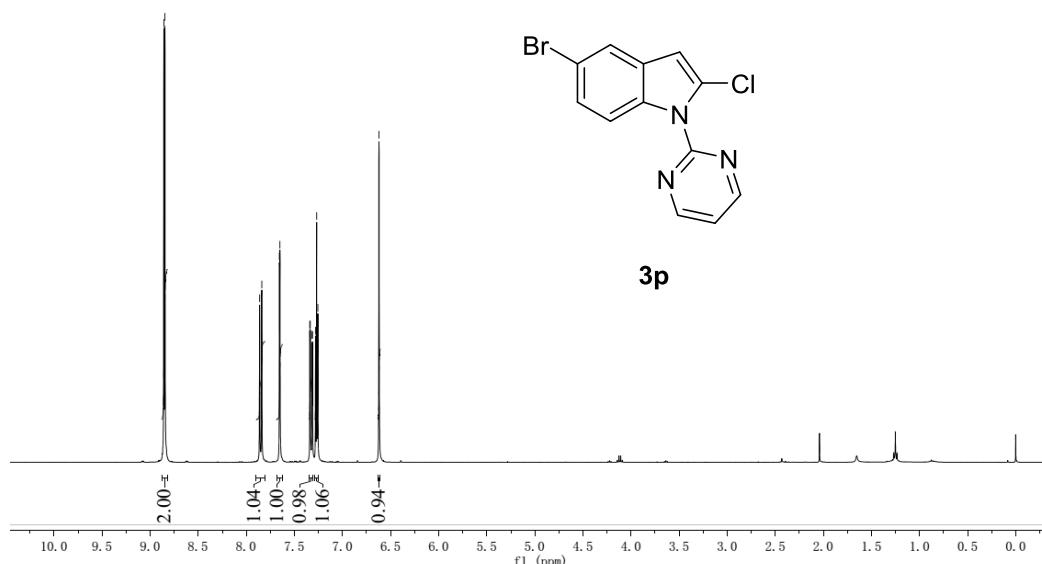
¹H NMR spectrum of **3o** (400 MHz, CDCl₃)

YC 1252
13C
CDCl₃



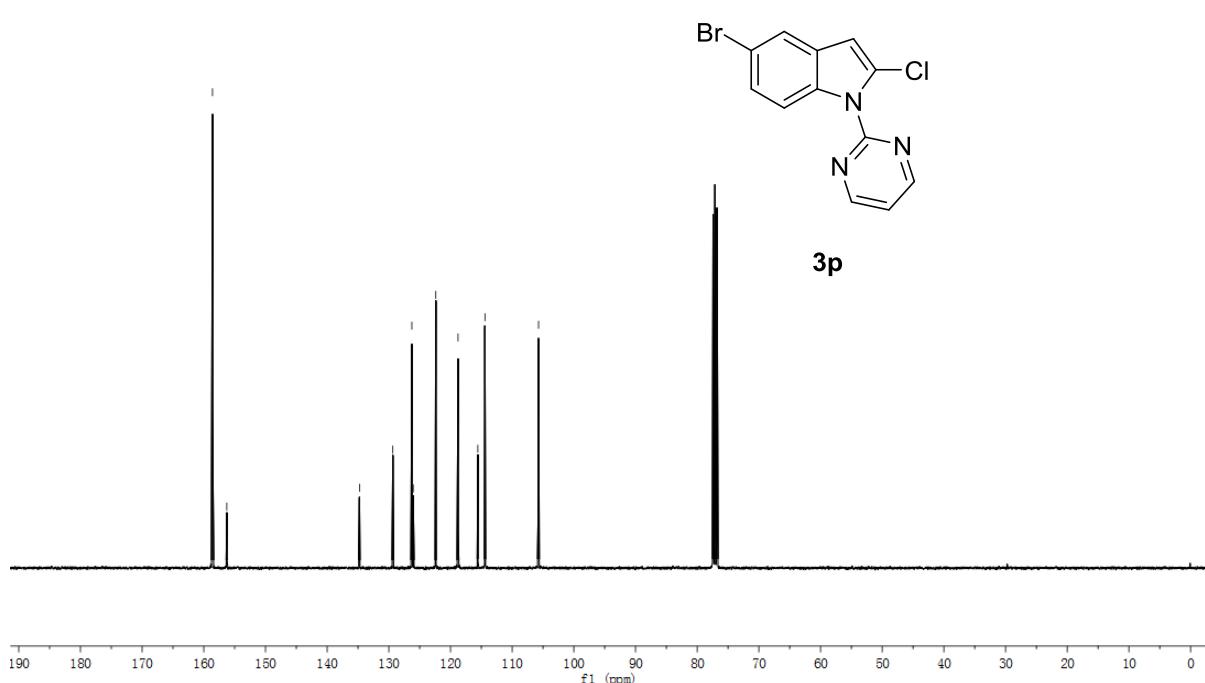
¹³C{¹H} NMR spectrum of **3o** (100 MHz, CDCl₃)

YC11233
1H
CDCl₃
4006/SMP



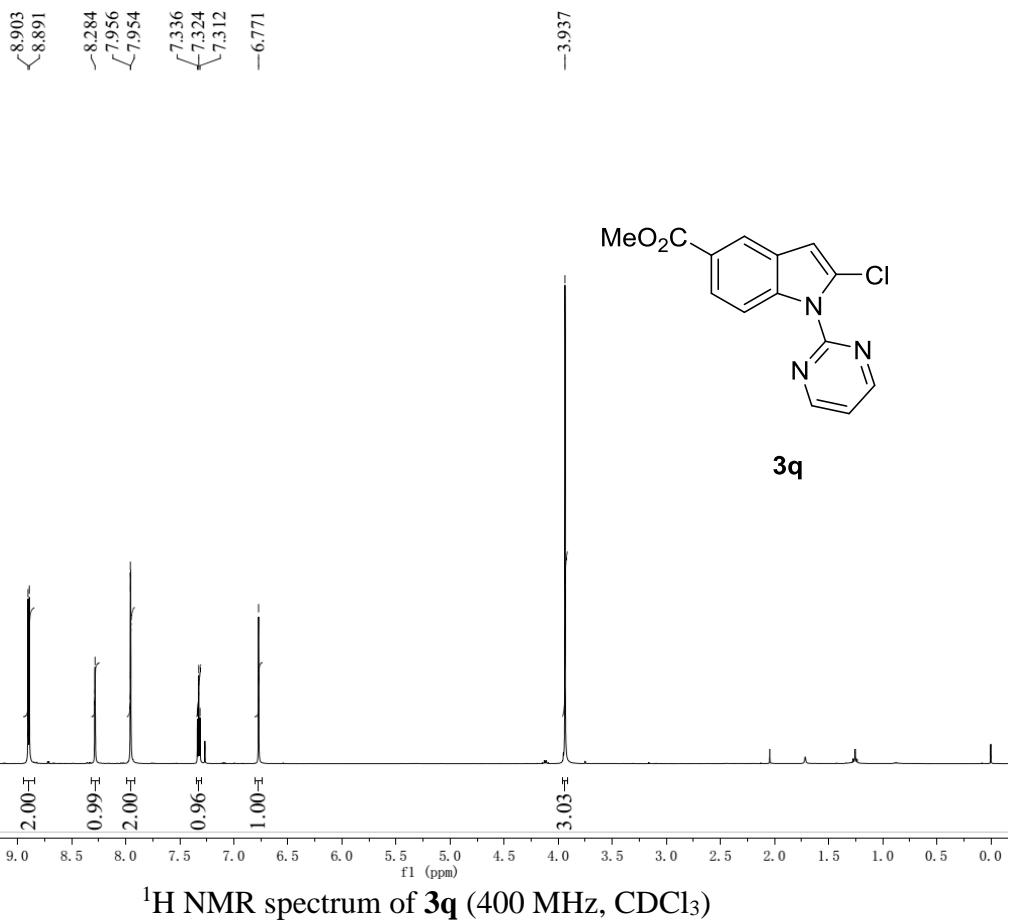
¹H NMR spectrum of **3p** (400 MHz, CDCl₃)

YC 11233
13C
CDCl₃

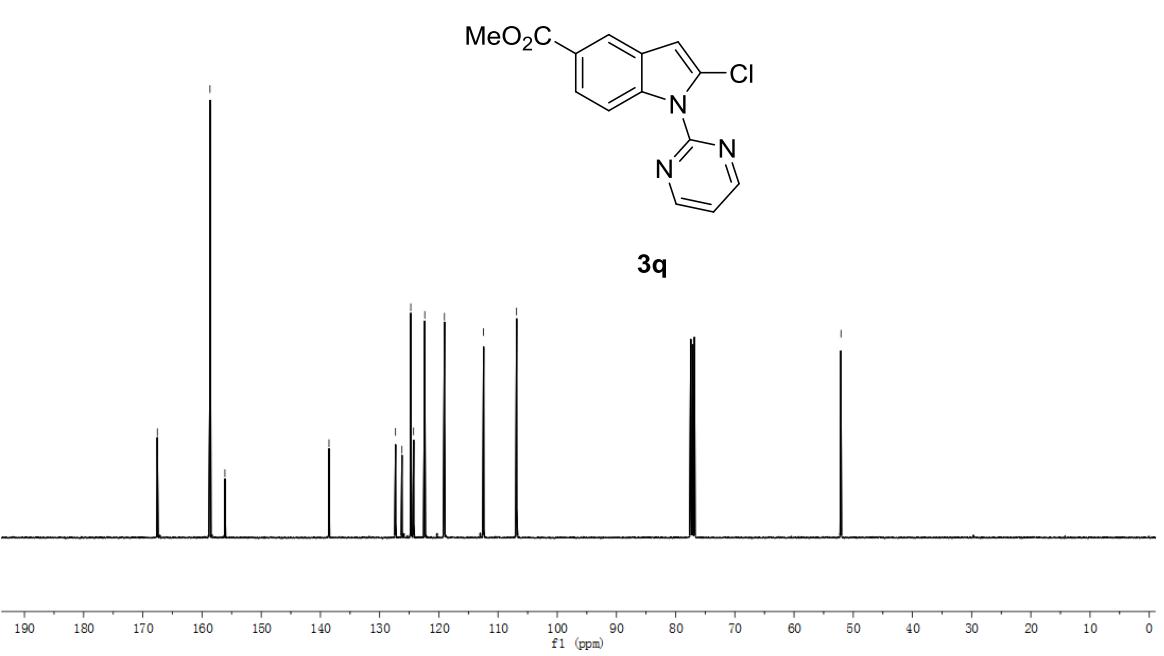


¹³C{¹H} NMR spectrum of **3p** (100 MHz, CDCl₃)

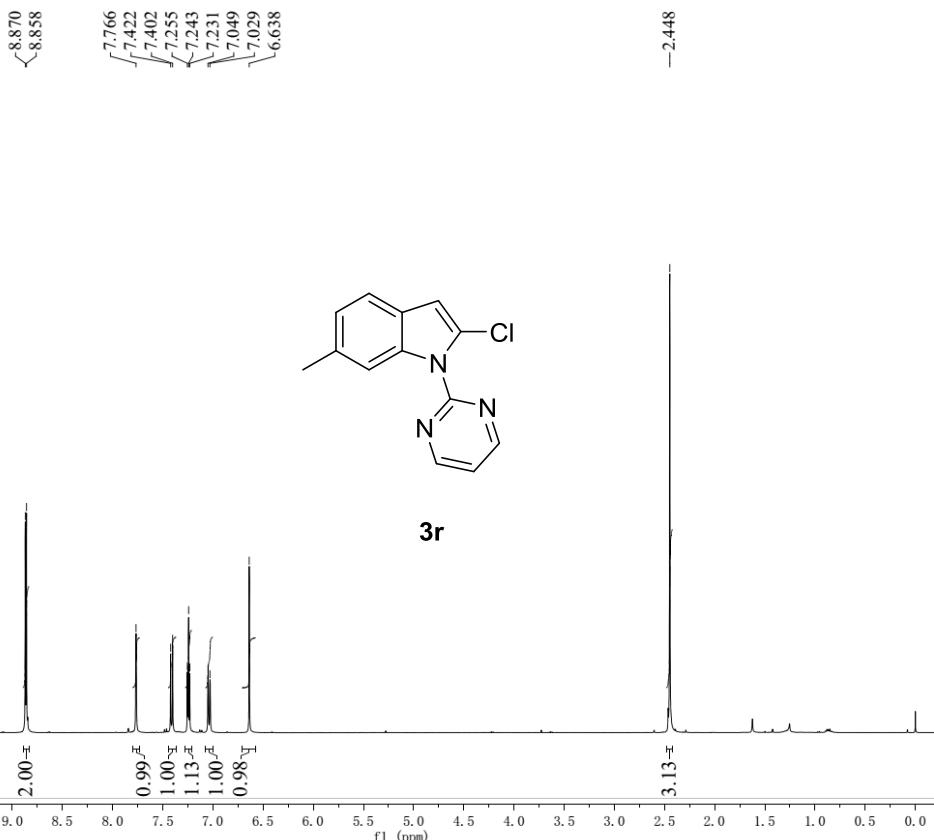
YC11245
1H
CDCl₃
4013/SMP



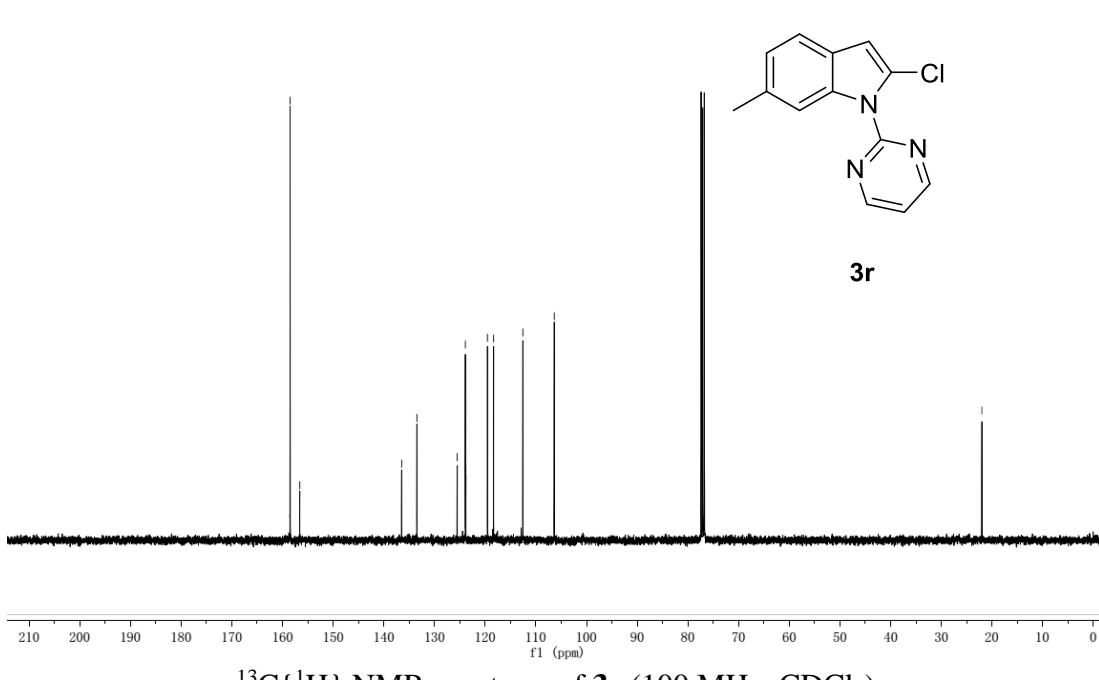
YC 11245
13C
CDCl₃

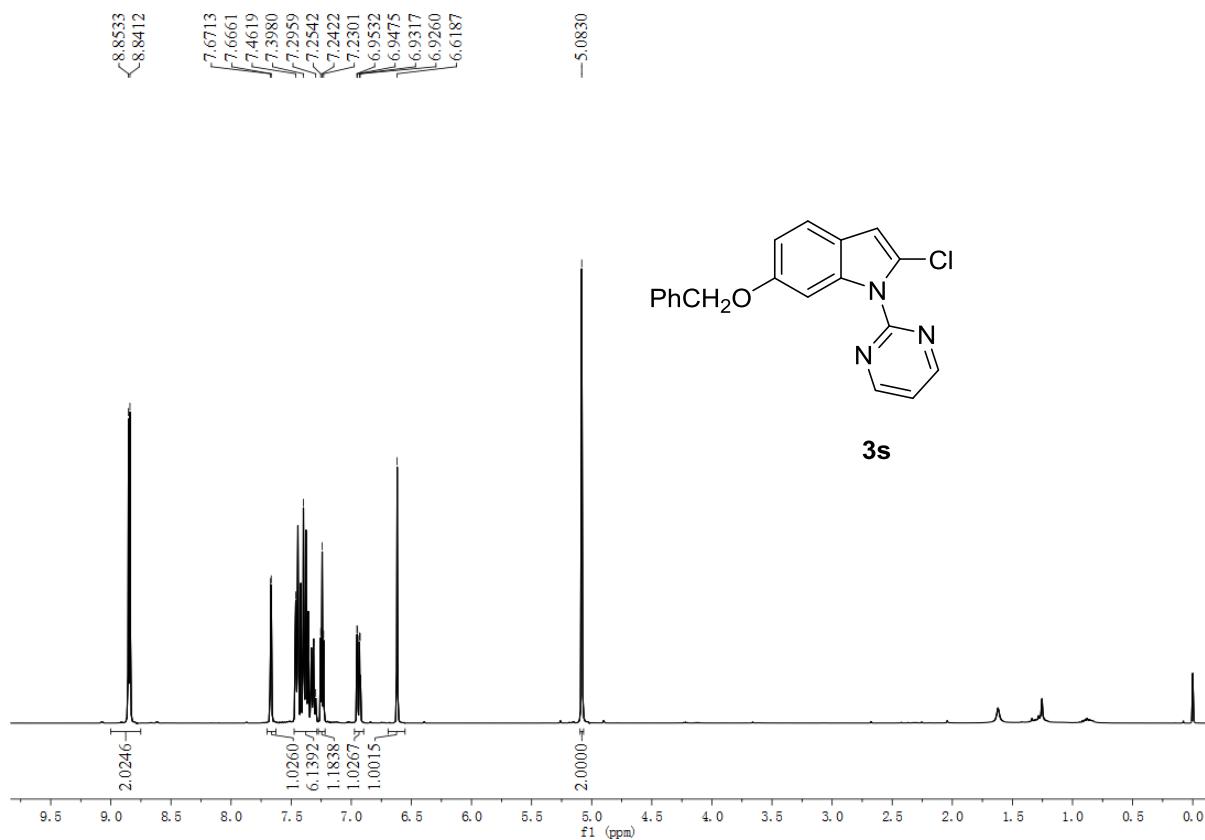


YC1254
1H
CDCl₃
4313/SMP

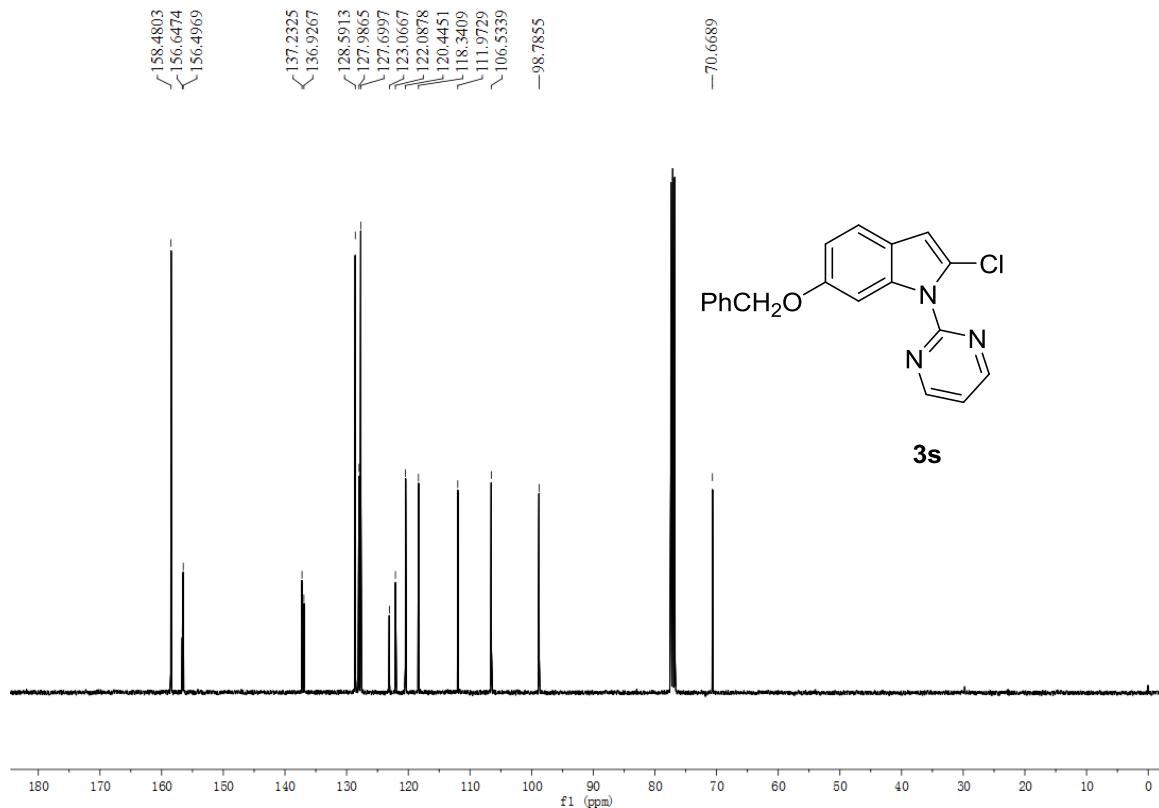


YC1254
13C
CDCl₃
4385/SMP

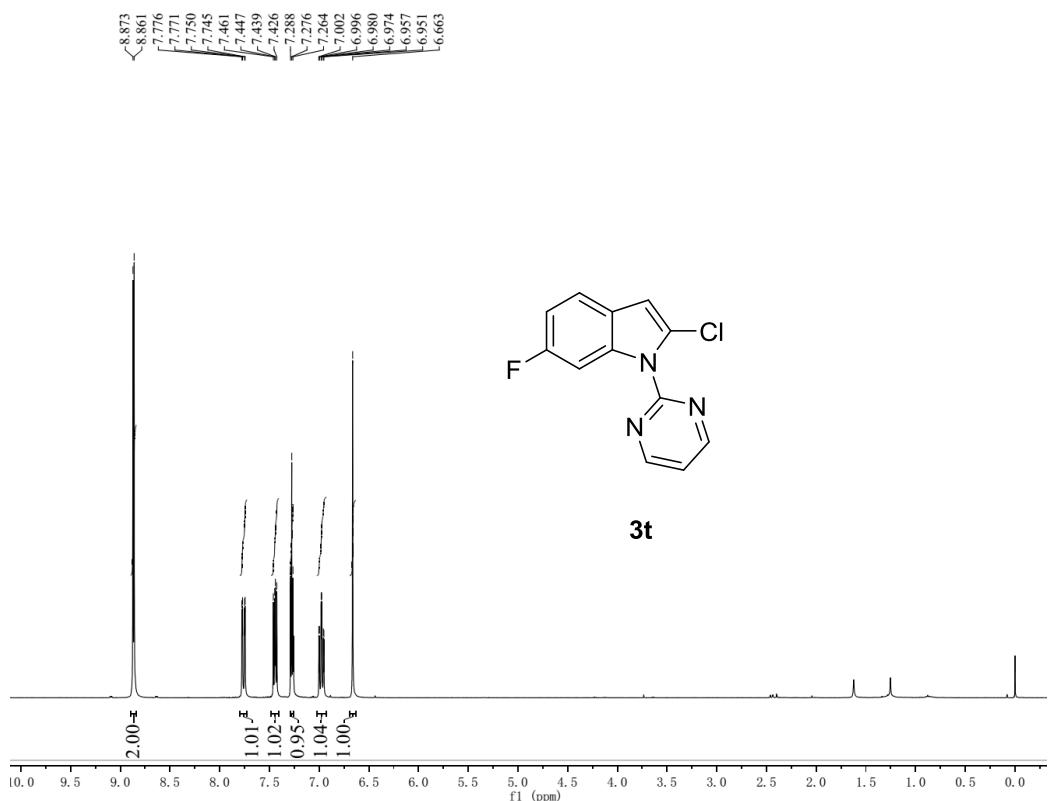




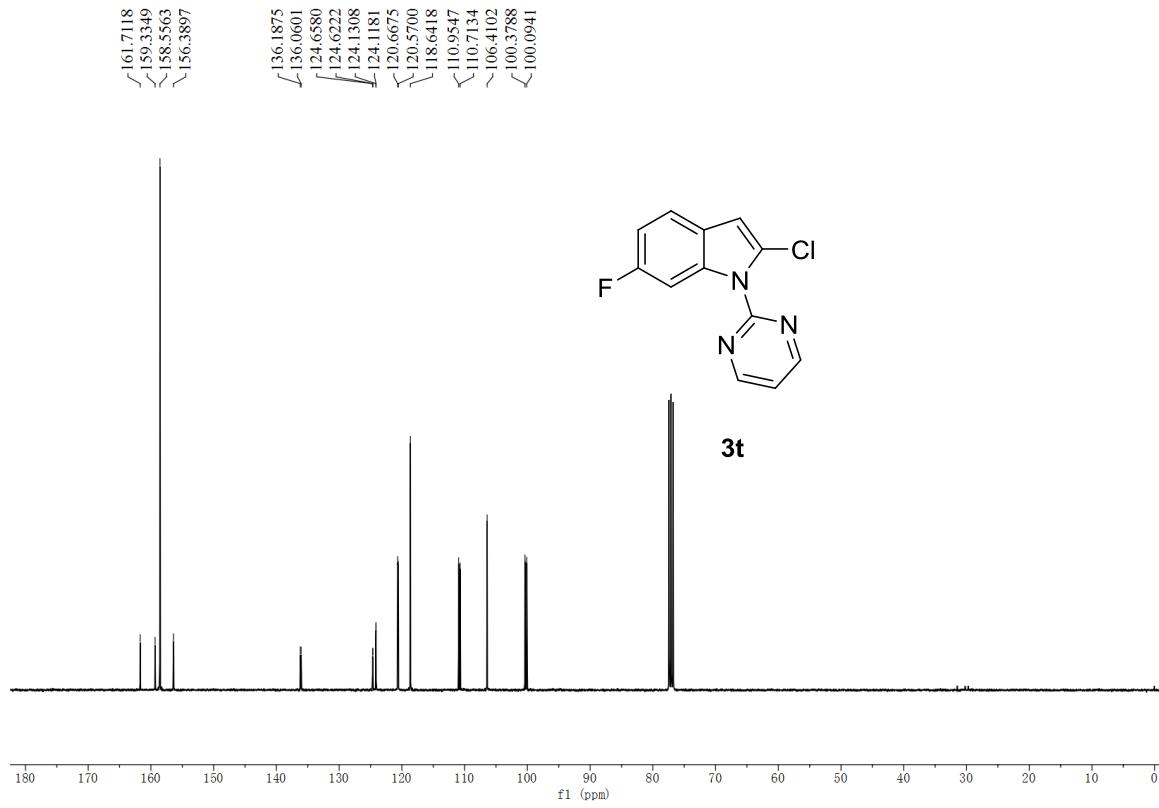
^1H NMR spectrum of **3s** (400 MHz, CDCl_3)



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



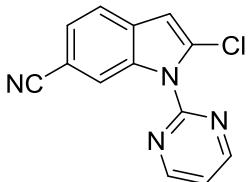
^1H NMR spectrum of **3t** (400 MHz, CDCl_3)



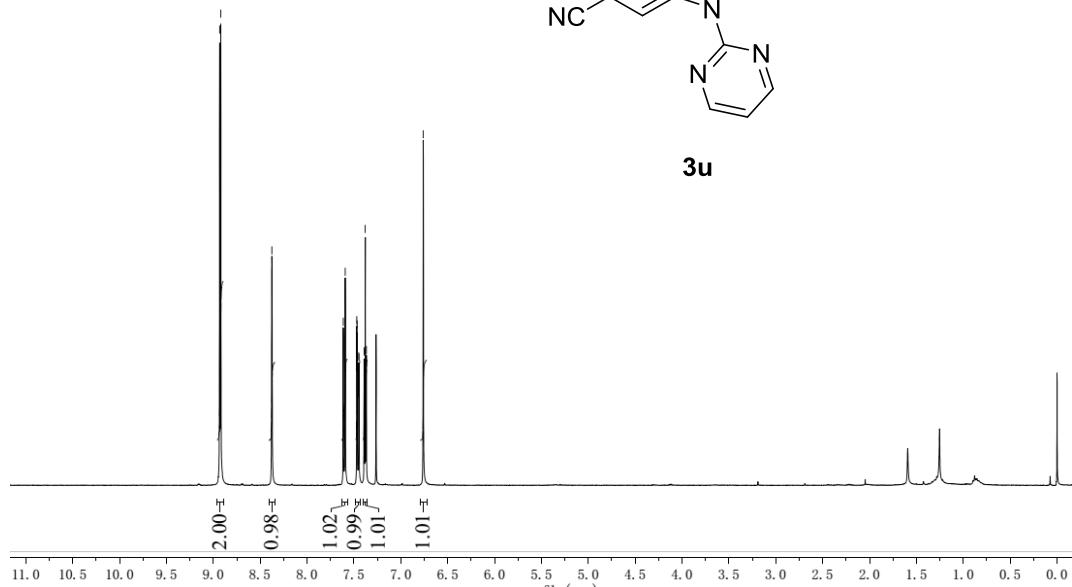
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of **3t** (100 MHz, CDCl_3)

YC11234
1H
CDCl₃
4310/SMP

8.932
8.920
8.375
7.614
7.593
7.410
7.466
7.379
7.366



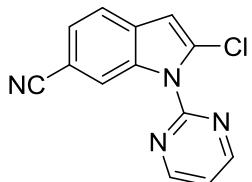
3u



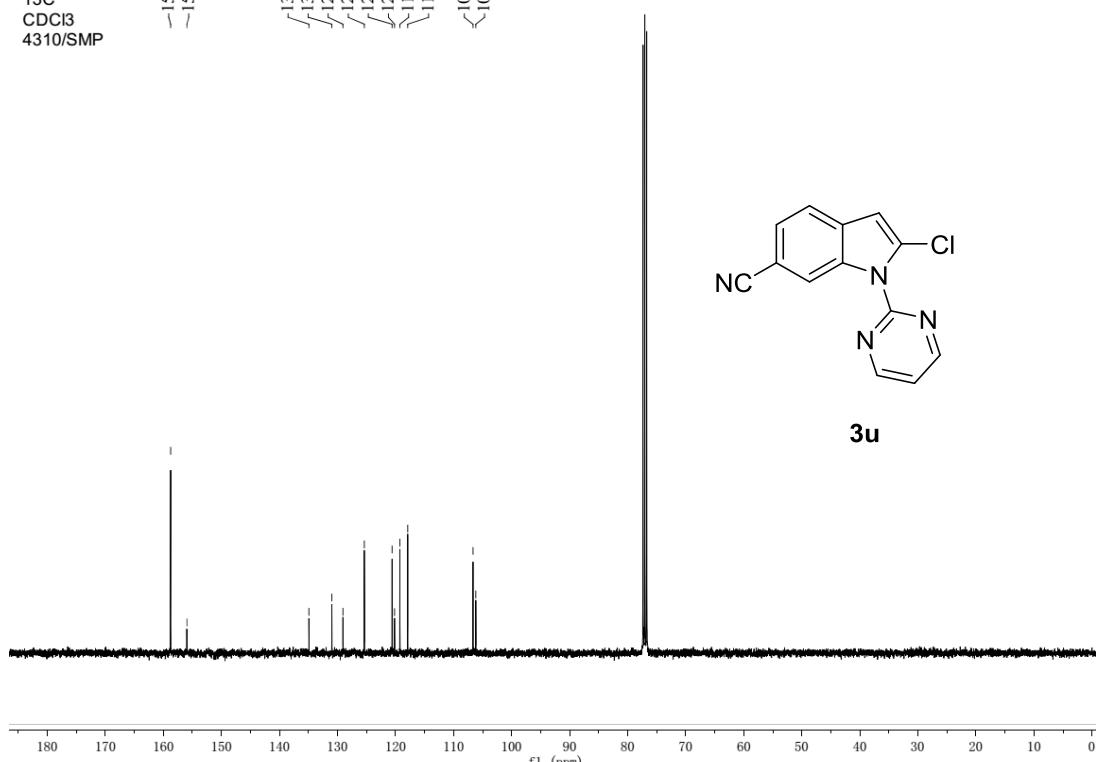
¹H NMR spectrum of **3u** (400 MHz, CDCl₃)

YC11234
13C
CDCl₃
4310/SMP

158.763
153.956
134.926
130.970
129.069
125.381
120.601
120.168
119.254
117.906
106.645
106.174



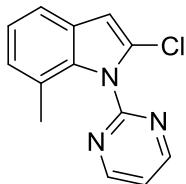
3u



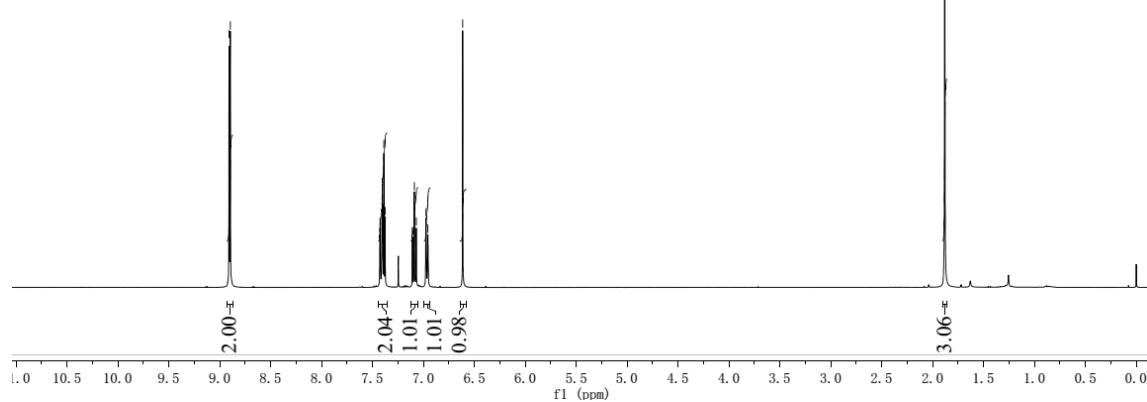
¹³C{¹H} NMR spectrum of **3u** (100 MHz, CDCl₃)

YC1272
1H
CDCl₃
4394/SMP

8.99
<8.96
7.426
7.407
7.401
7.388
7.376
7.370
7.108
7.089
7.070
6.974
6.956
6.615
-1.81



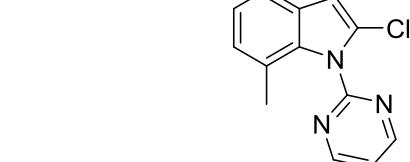
3v



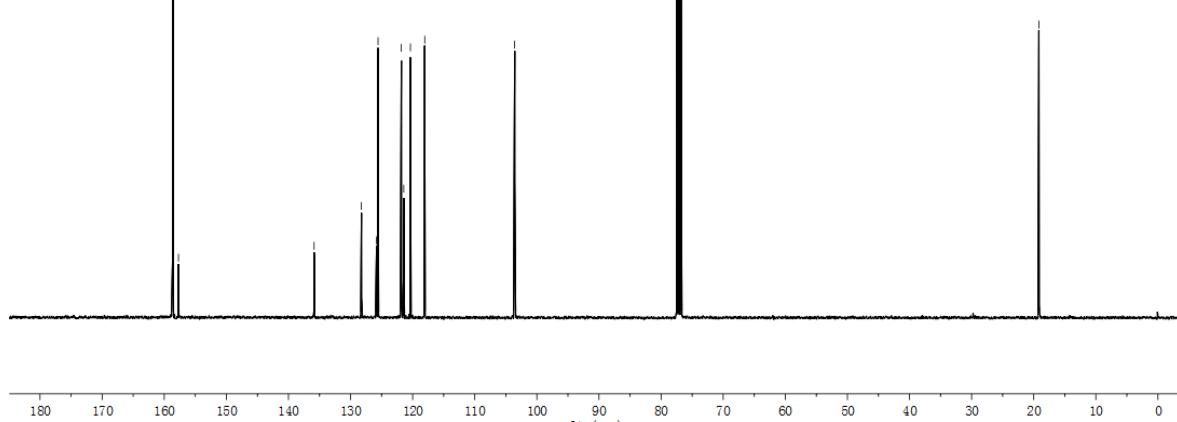
¹H NMR spectrum of **3v** (400 MHz, CDCl₃)

YC 1272
13C
CDCl₃

-158.6318
<-157.7126
-135.8718
-128.2547
-125.8181
-125.5748
-121.8279
-121.4342
-120.3598
-118.0564
-103.5758
-19.1619

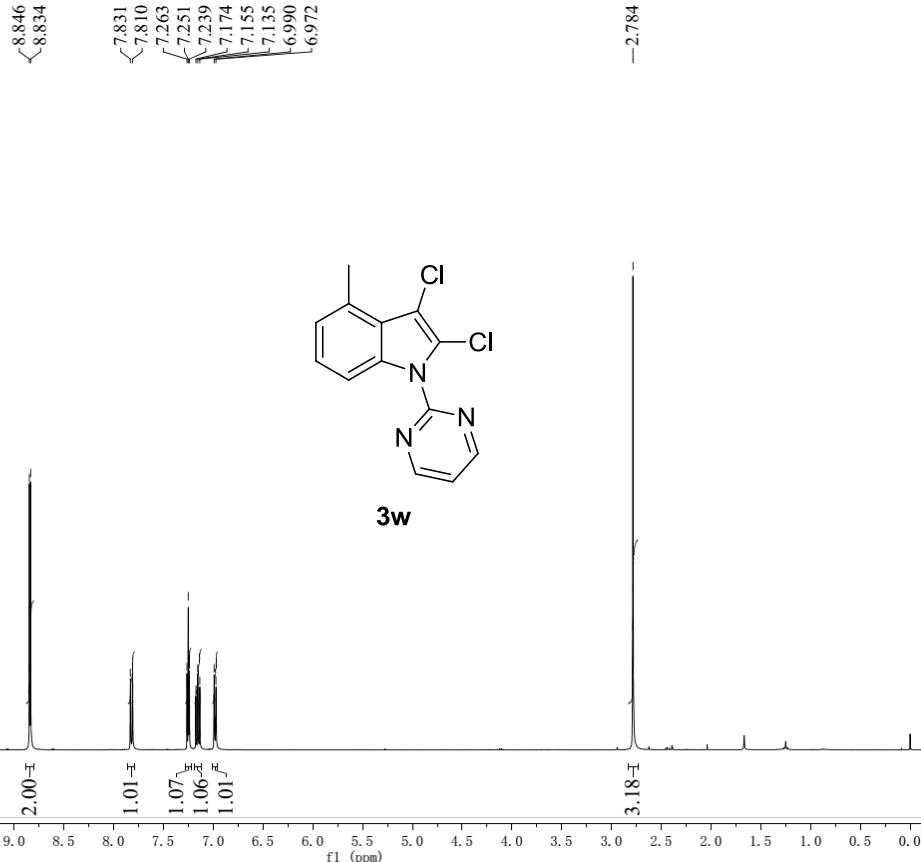


3v



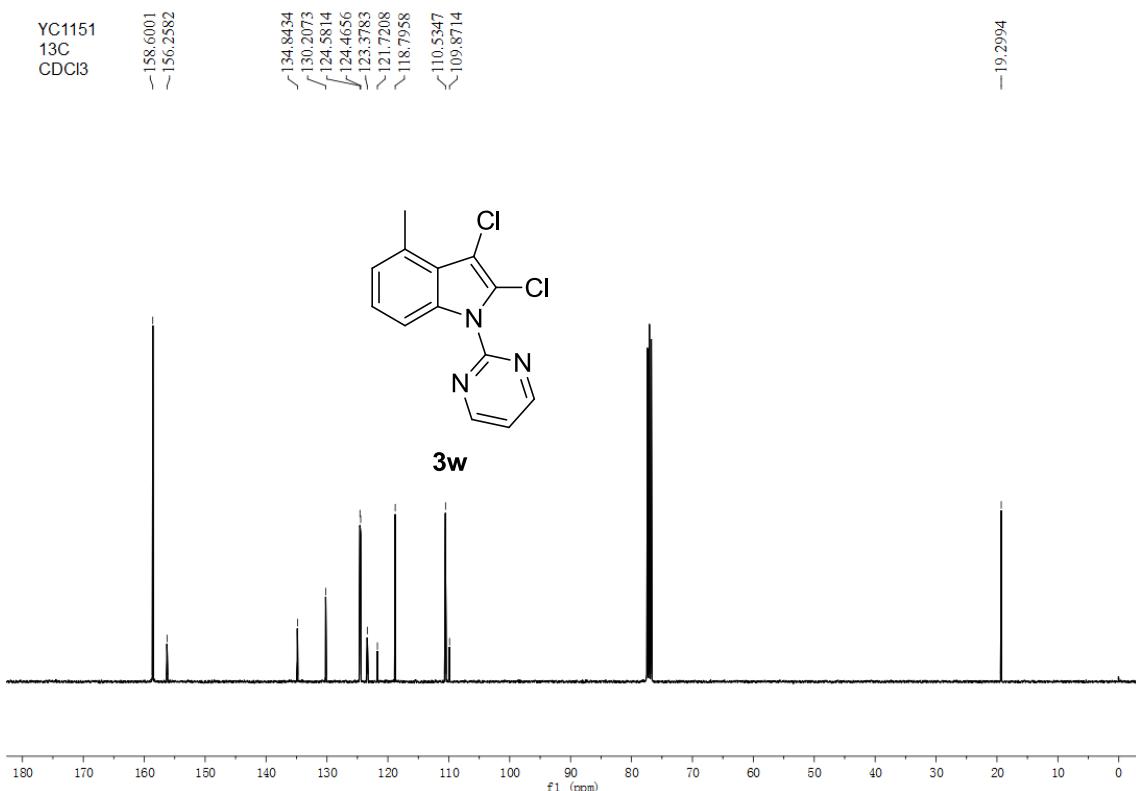
¹³C{¹H} NMR spectrum of **3v** (100 MHz, CDCl₃)

YC1151
1H
CDCl₃
219/SMP



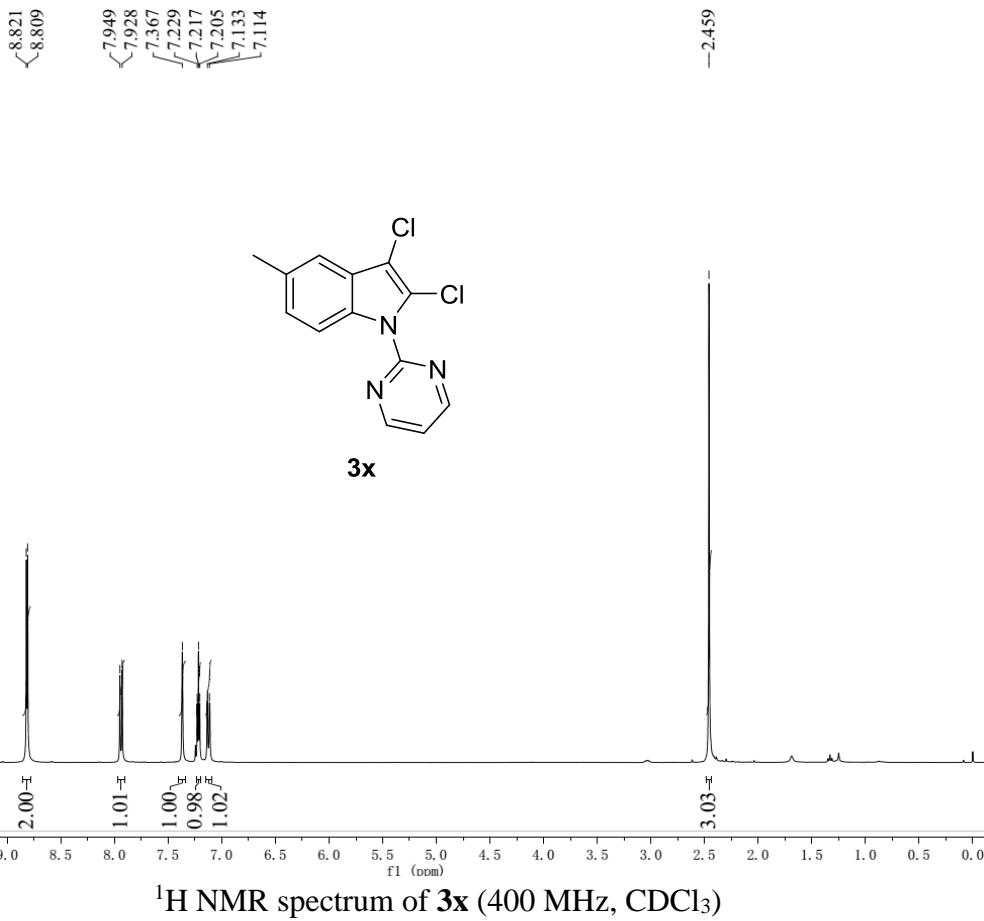
¹H NMR spectrum of **3w** (400 MHz, CDCl₃)

YC1151
13C
CDCl₃

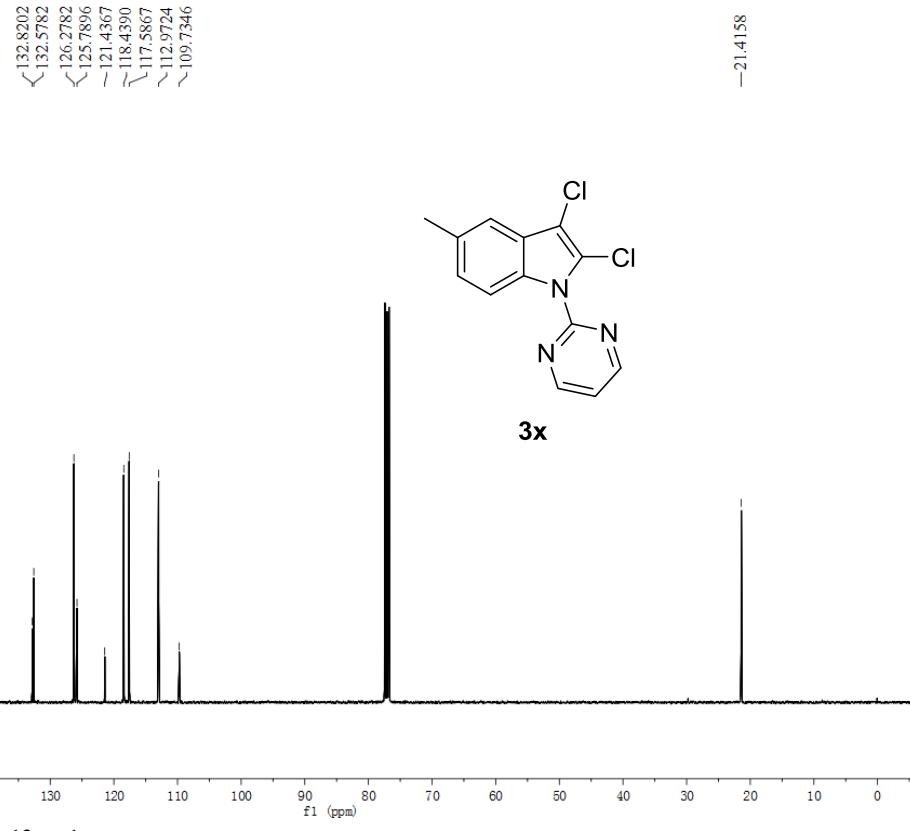


¹³C{¹H} NMR spectrum of **3w** (100 MHz, CDCl₃)

YC1152
1H
CDCl₃
220/SMP

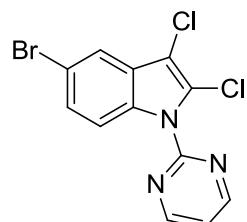


YC 1152
13C
CDCl₃

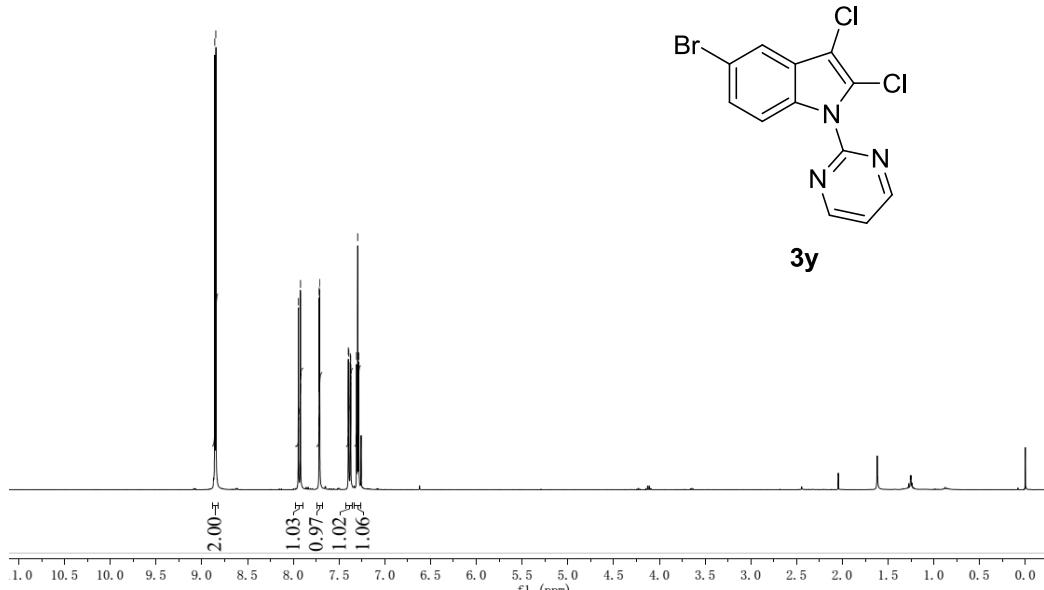


YC1153
1H
CDCl₃
221/SMP

8.858
8.846
7.944
7.922
7.717
7.713
7.399
7.394
7.377
7.372
7.309
7.296
7.284



3y

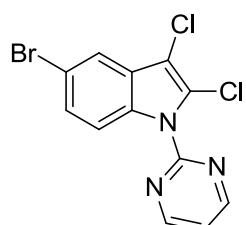


¹H NMR spectrum of **3y** (400 MHz, CDCl₃)

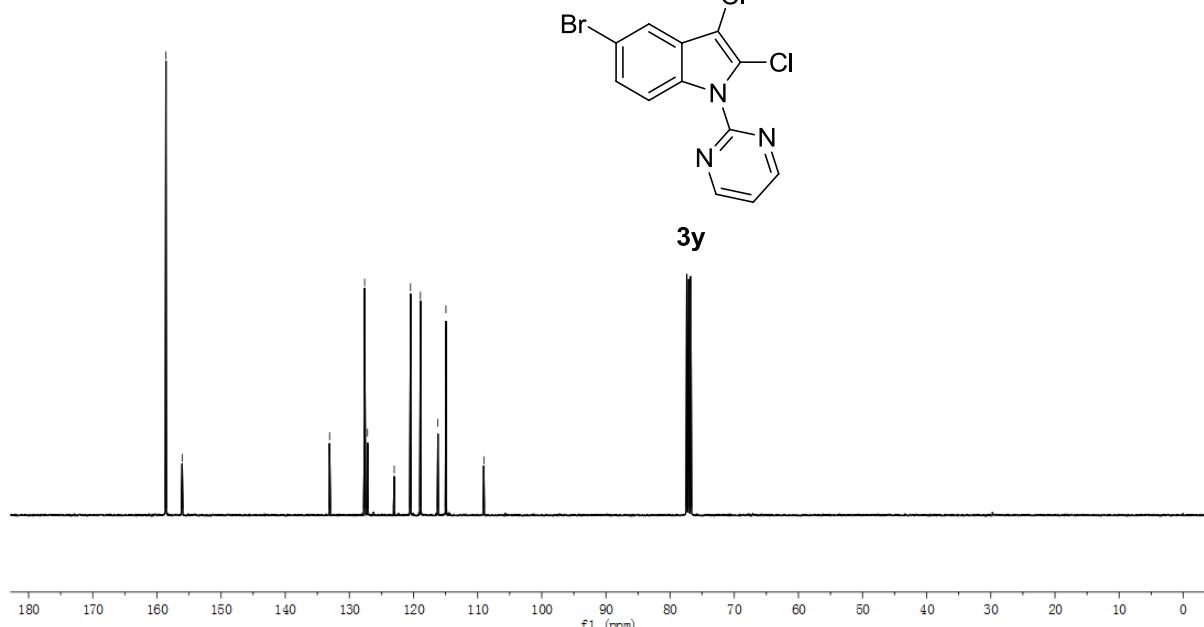
YC1153
13C
CDCl₃

~158.6074
~156.0566

~133.0822
~127.6189
~127.1632
~123.0089
~120.4602
~118.9138
~116.1980
~114.9420
~109.0333

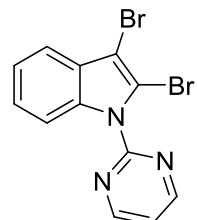


3y

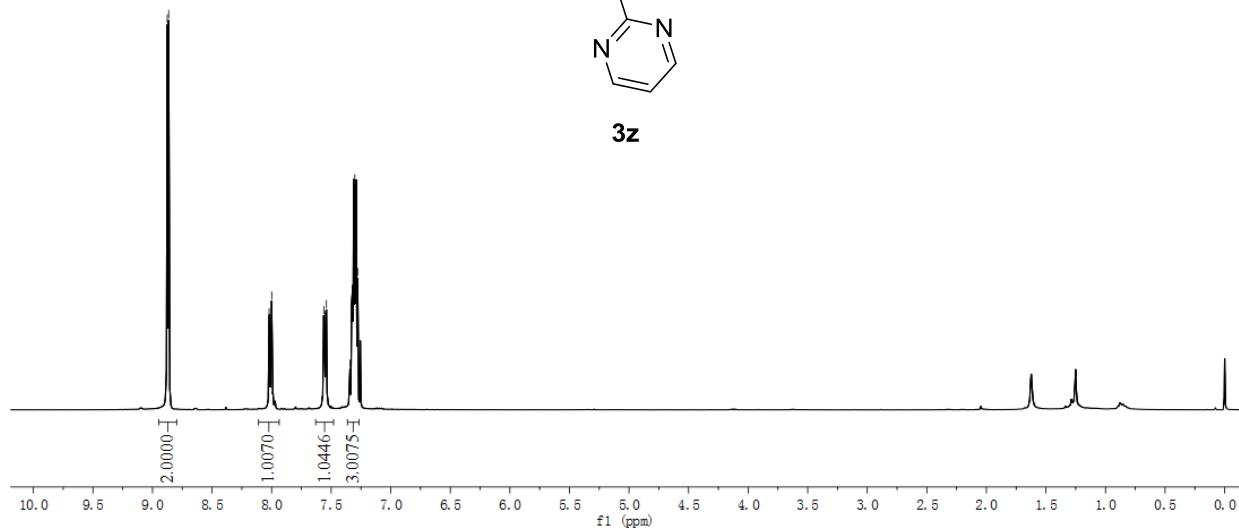


¹³C{¹H} NMR spectrum of **3y** (100 MHz, CDCl₃)

LXH-1
1H
CDCl₃



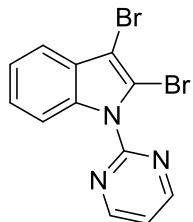
3z



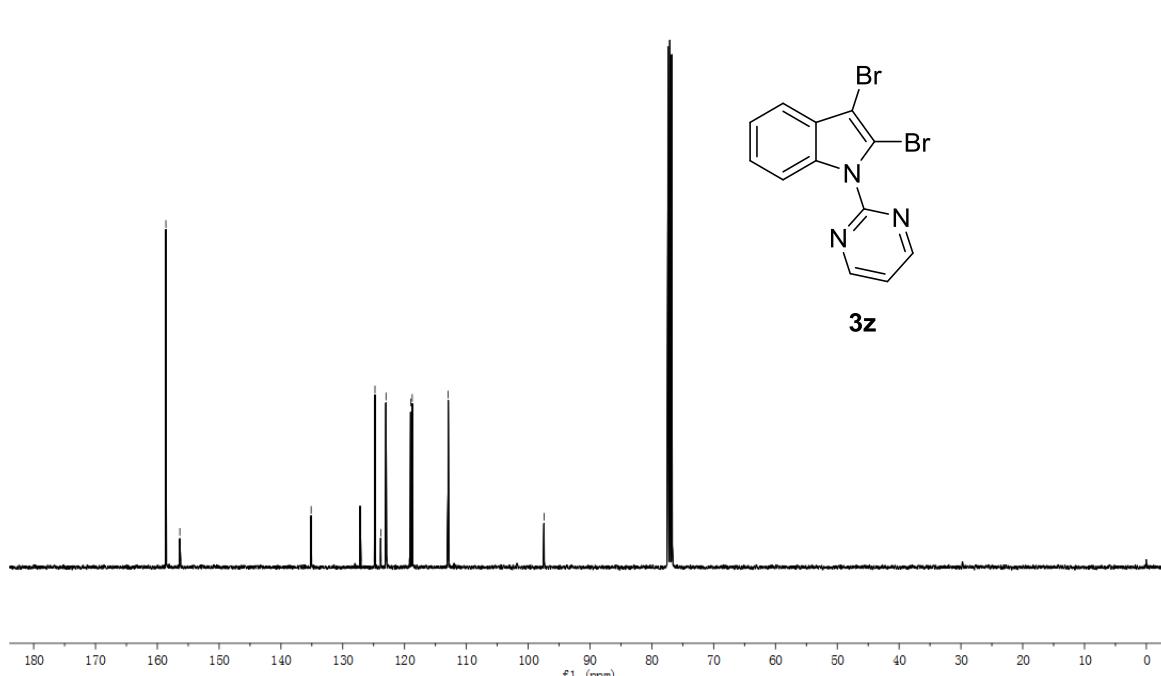
¹H NMR spectrum of **3z** (400 MHz, CDCl₃)

LXH-1
13C
CDCl₃

158.6077
156.3511
135.1136
127.1549
124.7831
123.8505
122.9976
119.0064
118.7611
112.9487
-97.4313

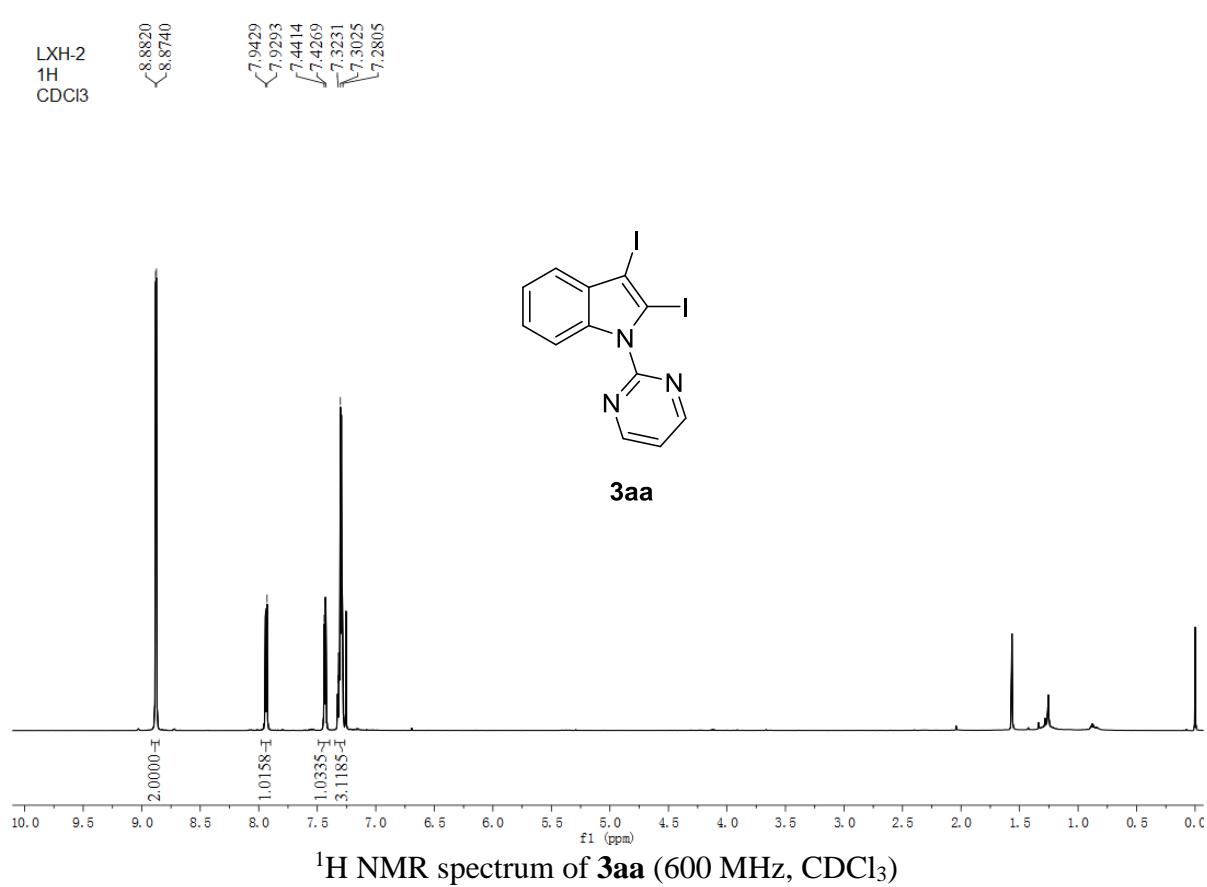


3z



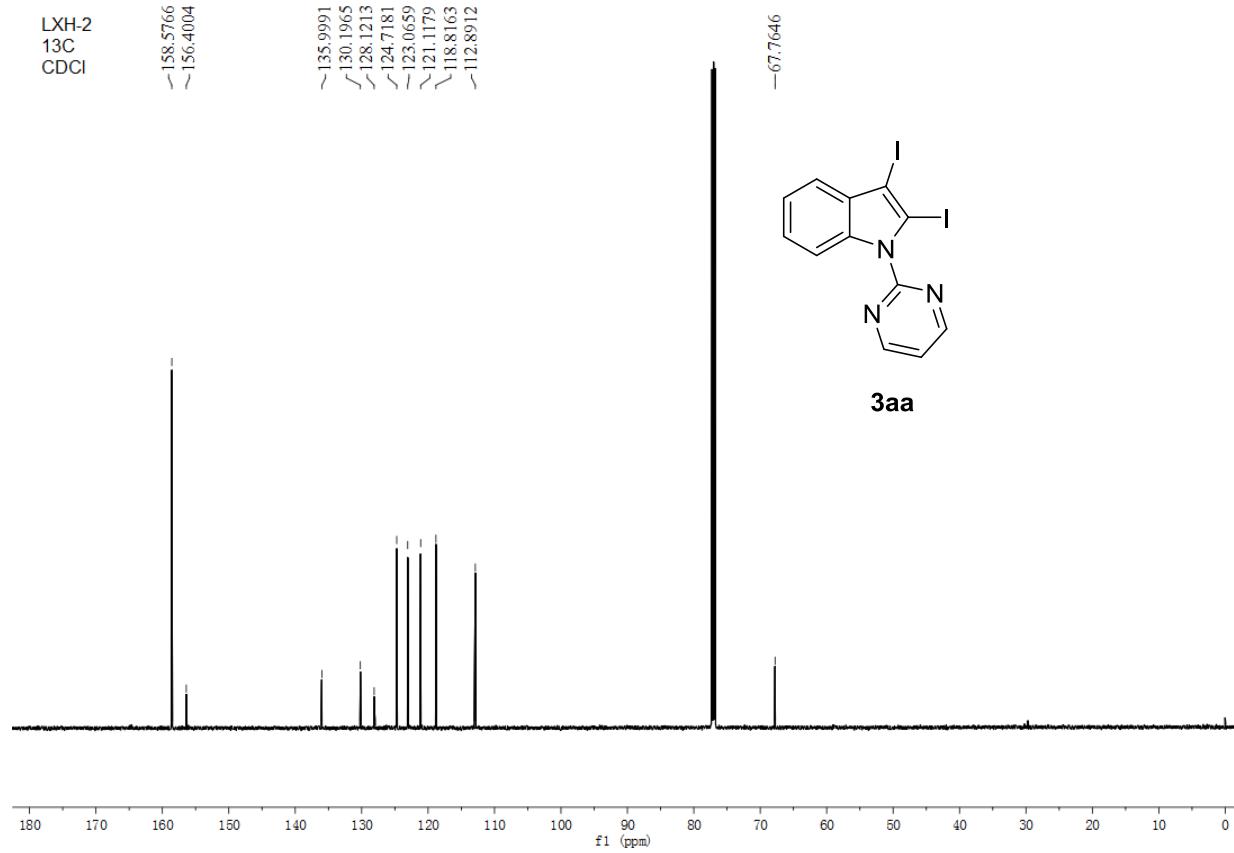
¹³C{¹H} NMR spectrum of **3z** (100 MHz, CDCl₃)

LXH-2
1H
CDCl₃



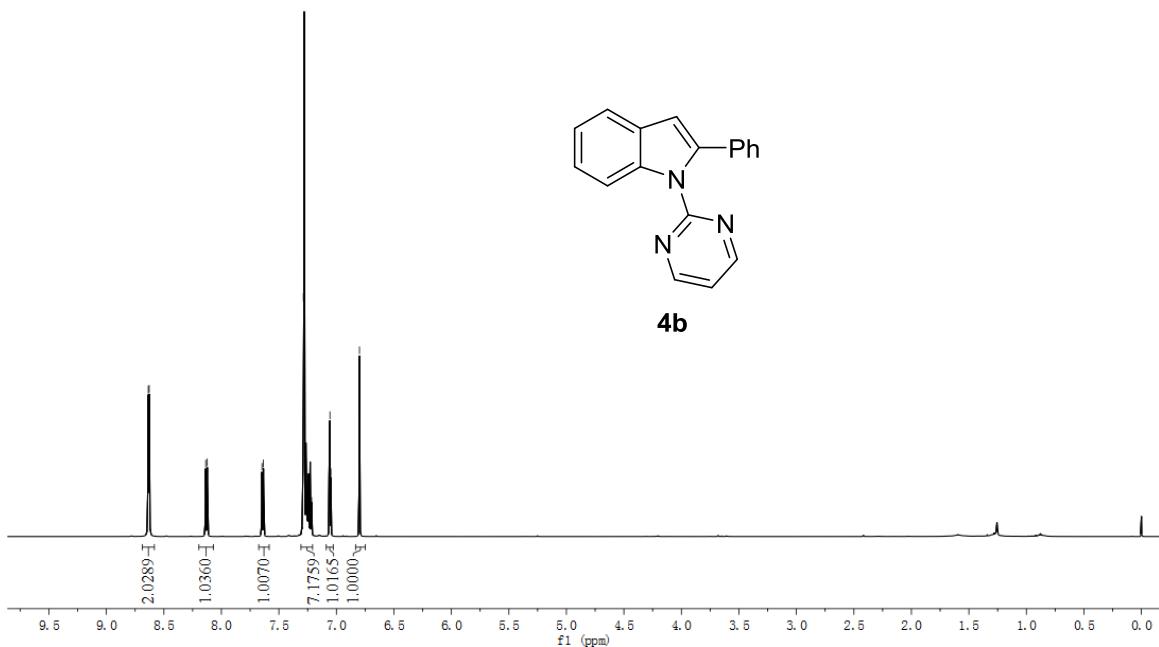
¹H NMR spectrum of 3aa (600 MHz, CDCl₃)

LXH-2
13C
CDCl



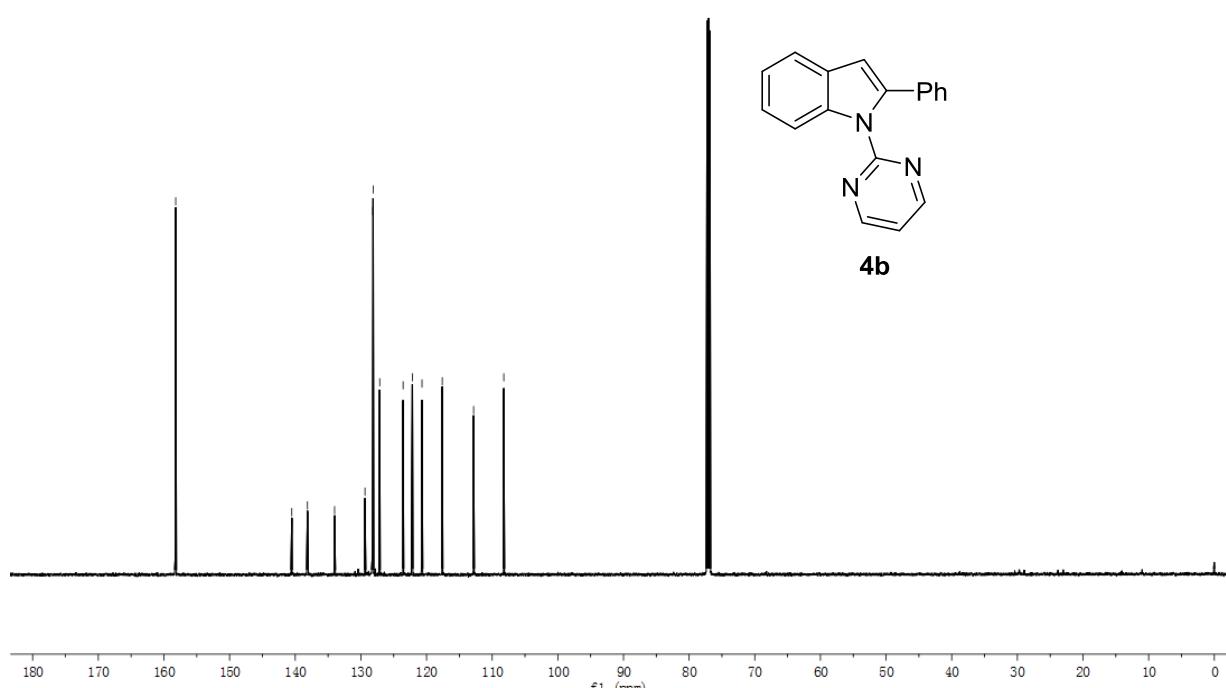
¹³C{¹H} NMR spectrum of 3aa (150 MHz, CDCl₃)

LXH-3
1H
CDCl₃



¹H NMR spectrum of **4b** (600 MHz, CDCl₃)

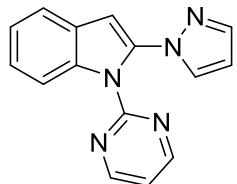
LXH-3
13C
CDCl₃



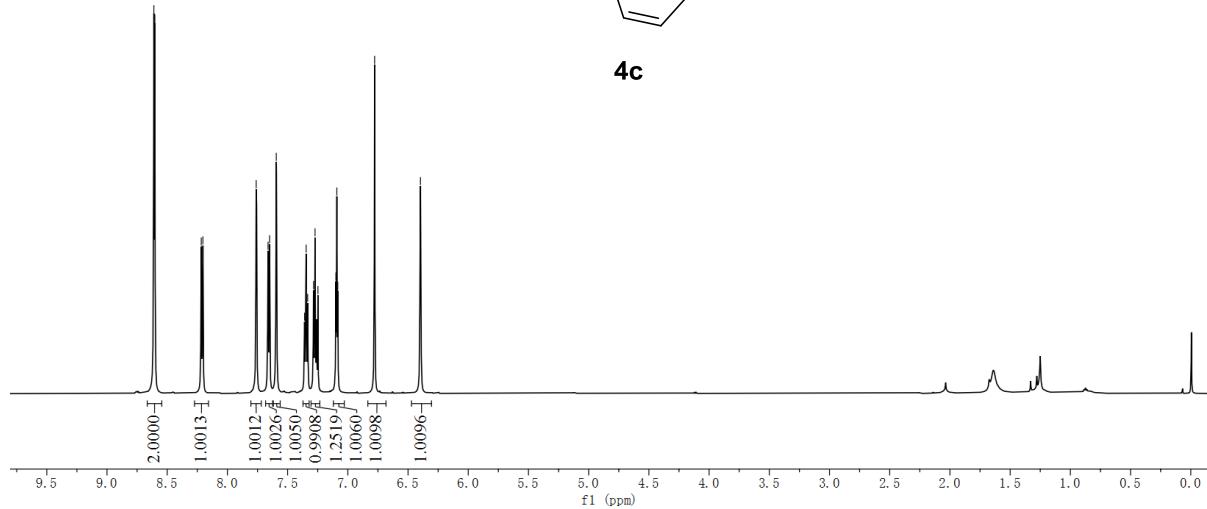
¹³C{¹H} NMR spectrum of **4b** (150 MHz, CDCl₃)

LXH061
1H
CDCl₃

8.6107
8.6028
8.2173
8.2034
7.7611
7.7577
7.6626
7.6497
7.5943
7.3595
7.3463
7.3338
7.2848
7.2722
7.2483
7.0992
7.0833
7.0913
6.7777
6.3966



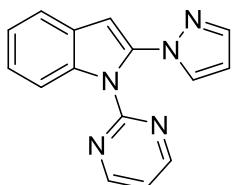
4c



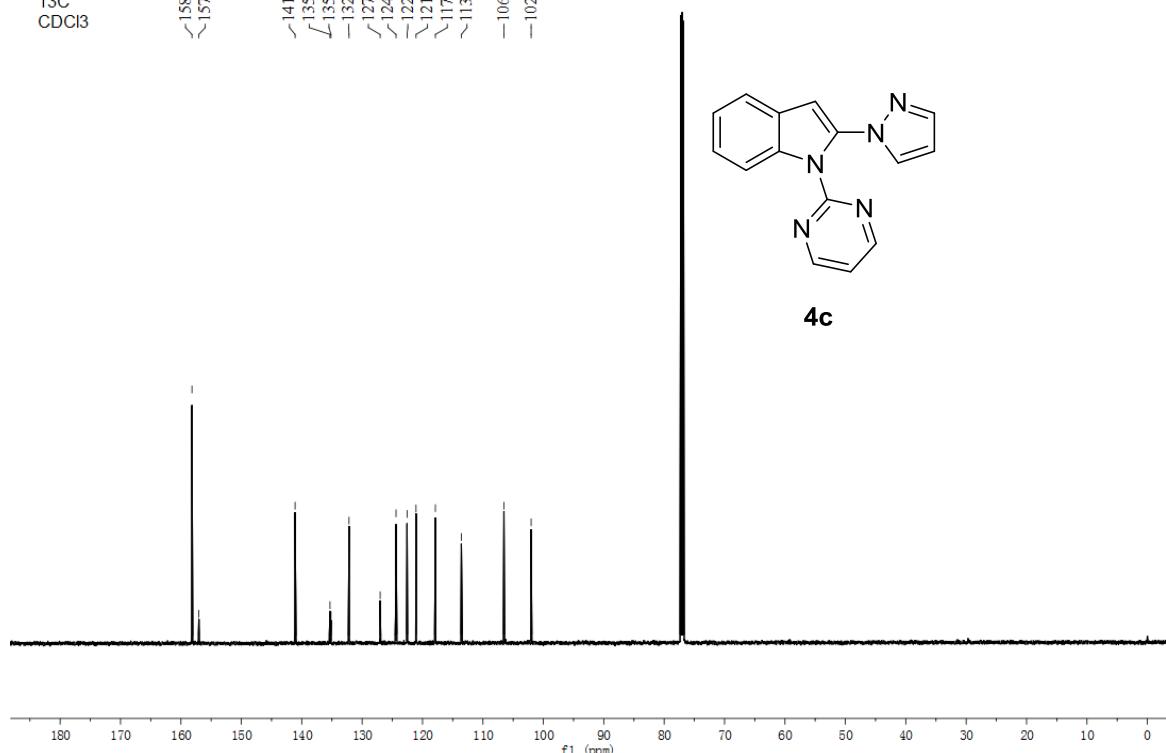
¹H NMR spectrum of **4c** (600 MHz, CDCl₃)

LXH-061
13C
CDCl₃

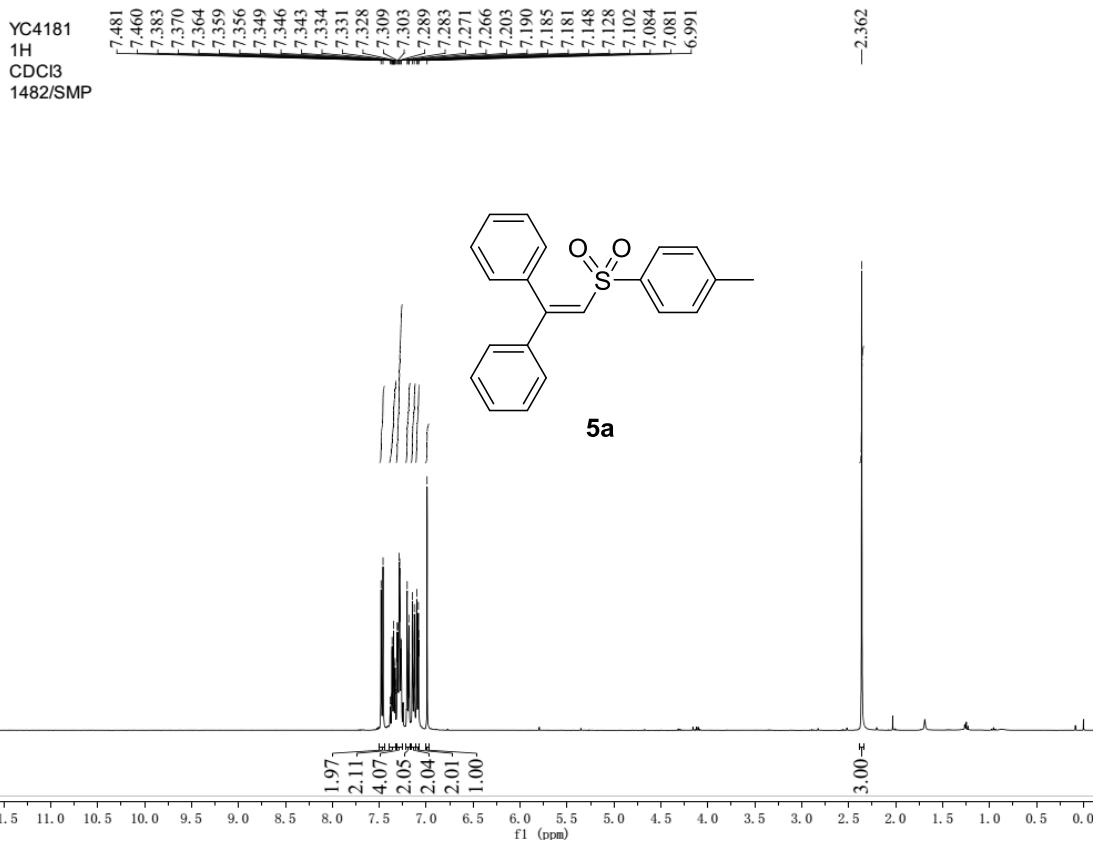
158.1722
157.0386
141.1006
135.3265
135.1596
132.1713
127.0183
124.3882
122.5548
121.0797
117.8770
113.5674
106.5243
102.0228



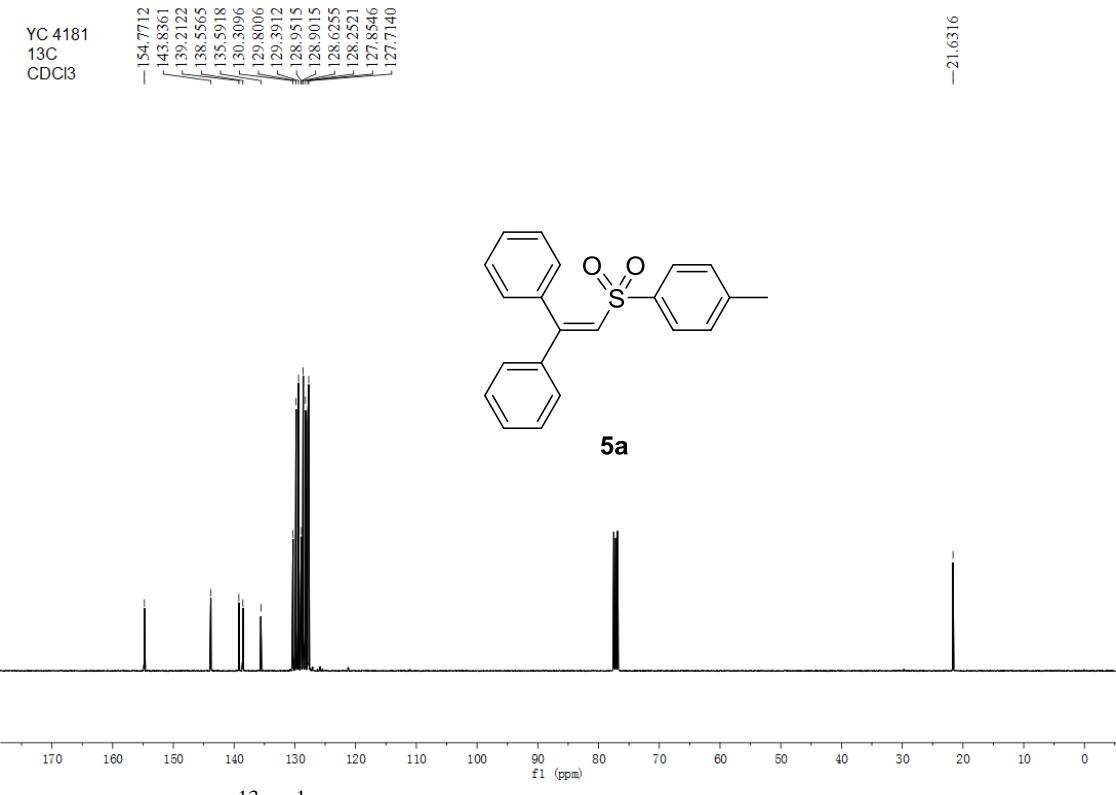
4c



¹³C{¹H} NMR spectrum of **4c** (150 MHz, CDCl₃)



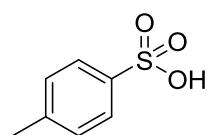
¹H NMR spectrum of **5a** (400 MHz, CDCl₃)



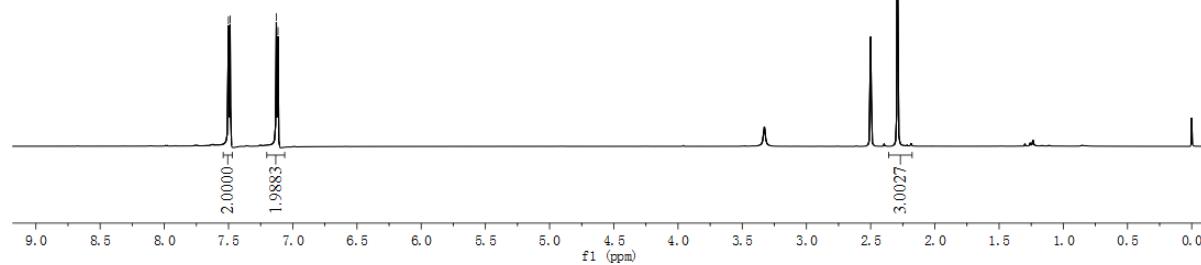
¹³C{¹H} NMR spectrum of **5a** (100 MHz, CDCl₃)

LXH285
1H
DMSO-d₆

7.5008
7.4876
7.1276
7.1147



5f

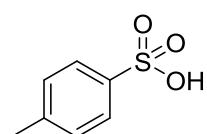


¹H NMR spectrum of **5f** (600 MHz, DMSO-*d*₆)

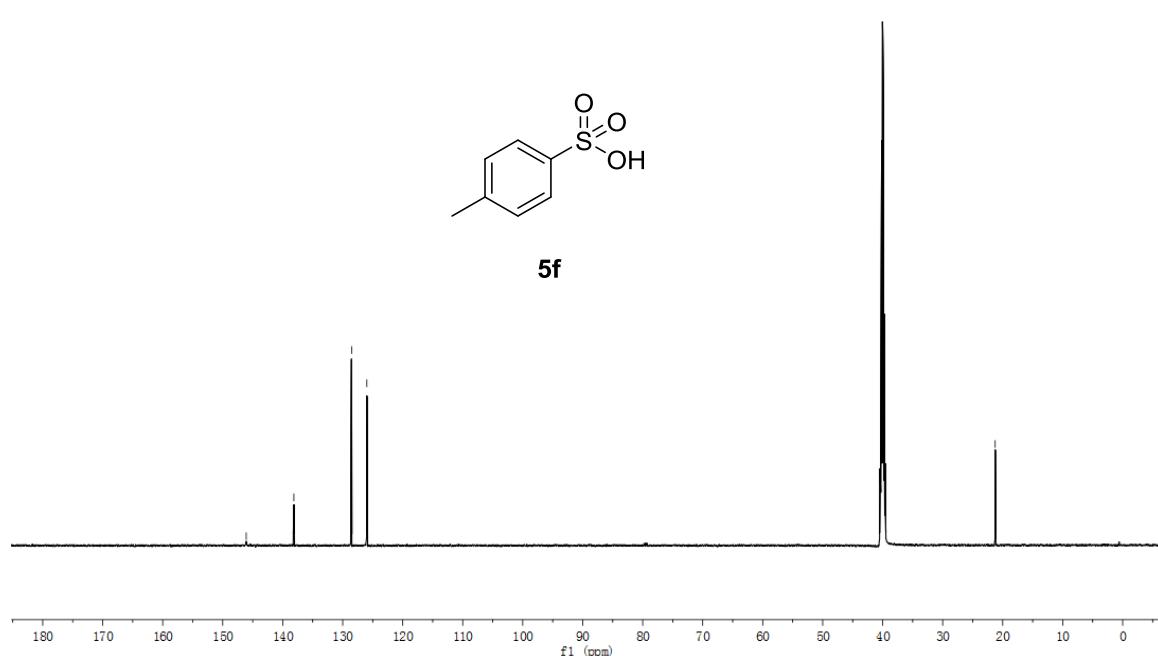
LXH 285
13C
DMSO-d₆

146.0856
138.1428
128.5189
125.9807

21.2529



5f



¹³C{¹H} NMR spectrum of **5f** (150 MHz, DMSO-*d*₆)