Selective Synthesis of Isoquinolines by Rhodium(III)-Catalyzed C–H/N–H Functionalization with α-substituted Ketones

Jie Li, Zhao Zhang, Mengyao Tang, Xiaolei Zhang, Jian Jin*

School of Pharmaceutical Sciences, Jiangnan University. Lihu road 1800, 214122 Wuxi, P. R. China

** E-mail: jjackli@jiangnan.edu.cn.*

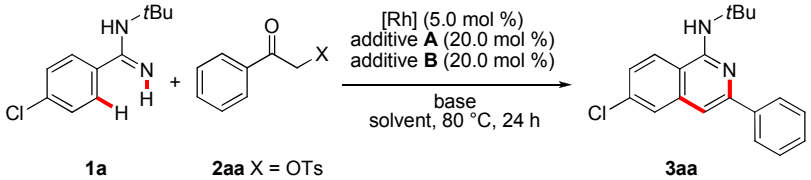
Contents

General Remarks

Catalytic reactions were carried out in Schlenk tubes under an argon atmosphere using pre-dried glassware. 2,2,2-Trifluoroethanol (TFE) was dried and distilled over CaH under nitrogen. The following starting materials were synthesized according to previously described methods: Aryl amidines **1a-1n**,[1] α-MsO/TsO/Cl ketones **2**, **4**,[2] [Cp*Rh(MeCN)$_3$](SbF$_6$)$_2$,[3] [Cp*Rh(MeCN)$_3$](BF$_4$)$_2$.[4] Other chemicals were obtained from commercial sources and were used without further purification. Yields refer to isolated compounds, estimated to be > 95% pure as determined by ^{1}H-NMR. Chromatography: Merck silica gel 60 (40-63 μm). NMR: Spectra were recorded on Bruker Avance III 400 in the solvent indicated; chemical shifts (δ) are given in ppm. All IR spectra were recorded on a Shimadzu IRTracer-100. High resolution mass spectrometry (HRMS) with Anilent 1200HPLC-6120MS. M. p.: Stuart melting point apparatus SMP3, Barlworld Scientific, values are uncorrected.

Optimization

Table 1. Optimization of Rh(III)-catalyzed C–H/N–H functionalization with benzamidine 1a.[a]



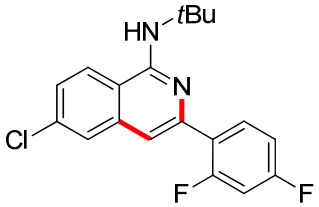
1a **2aa** X = OTs **2ab** X = OMs **3aa**

entry	[Rh]/additive **A**	additive **B**	base	solvent	yield (%)[b]
1	Cp*Rh**L**$_3$(SbF$_6$)$_2$	-	NaOAc	MeOH	<1[c]
2	Cp*Rh**L**$_3$(SbF$_6$)$_2$	-	NaOAc	HFIP	<1[c]
3	Cp*Rh**L**$_3$(SbF$_6$)$_2$	-	NaOAc	DCE	0[c]
4	Cp*Rh**L**$_3$(SbF$_6$)$_2$	-	NaOAc	MeCN	0[c]
5	Cp*Rh**L**$_3$(SbF$_6$)$_2$	-	NaOAc	DMF	0[c]
6	Cp*Rh**L**$_3$(SbF$_6$)$_2$	-	NaOAc	DME	0[c]
7	Cp*Rh**L**$_3$(SbF$_6$)$_2$	-	NaOAc	TFE	24[c]
8	Cp*Rh**L**$_3$(SbF$_6$)$_2$	Cu(OAc)$_2$	NaOAc	TFE	28[c]
9	Cp*Rh**L**$_3$(SbF$_6$)$_2$	Cu(OAc)$_2$	CsOAc	TFE	32[c]
10	Cp*Rh**L**$_3$(SbF$_6$)$_2$	Cu(OAc)$_2$	KOAc	TFE	32[c]
11	Cp*Rh**L**$_3$(SbF$_6$)$_2$	Cu(OAc)$_2$	KOPiv	TFE	30[c]
12	Cp*Rh**L**$_3$(SbF$_6$)$_2$	Cu(OAc)$_2$	KOAc	TFE	40[d]
13	[Cp*RhCl$_2$]$_2$/AgSbF$_6$	Cu(OAc)$_2$	KOAc	TFE	41[d]
14	[Cp*RhCl$_2$]$_2$/AgNTf$_2$	Cu(OAc)$_2$	KOAc	TFE	36[d]
15	[Cp*RhCl$_2$]$_2$/AgPF$_6$	Cu(OAc)$_2$	KOAc	TFE	34[d]
16	[Cp*RhCl$_2$]$_2$/AgBF$_4$	Cu(OAc)$_2$	KOAc	TFE	57[d]
17	Cp*Rh**L**$_3$(SbF$_6$)$_2$	Cu(OAc)$_2$	KOAc	TFE	50[d]
18	[Cp*RhCl$_2$]$_2$/AgBF$_4$	Cu(OAc)$_2$	KOAc	TFE	76
19	**[Cp*RhCl$_2$]$_2$/AgBF$_4$**	**Cu(OAc)$_2$**	**KOAc**	**TFE**	**80[e]**
20	Cp*Rh**L**$_3$(BF$_4$)$_2$	Cu(OAc)$_2$	KOAc	TFE	71[e]
21	AgBF$_4$	Cu(OAc)$_2$	KOAc	TFE	0[e]
22	[Cp*RhCl$_2$]$_2$	Cu(OAc)$_2$	KOAc	TFE	57[e]
23	[Cp*RhCl$_2$]$_2$/AgBF$_4$	-	KOAc	TFE	39[e]
24	[Cp*RhCl$_2$]$_2$/AgBF$_4$	Cu(OAc)$_2$	KOAc	TFE	51[e]
25	[Cp*IrCl$_2$]$_2$/AgBF$_4$	Cu(OAc)$_2$	KOAc	TFE	0[e]
26	[Cp*CoI$_2$(CO)]/AgBF$_4$	Cu(OAc)$_2$	KOAc	TFE	0[e]

[a] General reaction conditions: **1a** (0.25 mmol), **2aa** (0.50 mmol), [Cp*RhCl$_2$]$_2$ (5.0 mol %), AgBF$_4$ (20.0 mol %), Cu(OAc)$_2$ (20.0 mol %), KOAc (2.0 equiv), TFE (2.0 mL), under Ar, 80℃, 24 h. [b] Isolated yield. [c] [Rh] (5.0 mol %), **2aa** (1.2 equiv), KOAc (1.2 equiv), 60℃. [d] [Rh] (5.0 mol %). [e] **2ab** (2.0 equiv). **L** = MeCN, TFE = trifluoroethanol.

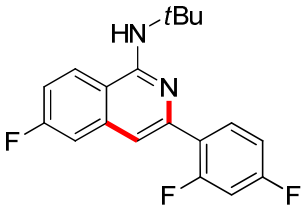
Representative Procedure

Representative Procedure: A suspension of aryl amidine **1** (0.25 mmol, 1.00 equiv), *α*-MsO/TsO/Cl ketone **2** or **4** (0.50 mmol, 2.00 equiv), $[Cp^*RhCl_2]_2$ (7.7 mg, 5.0 mol %), $AgBF_4$ (9.7 mg, 20.0 mol %), $Cu(OAc)_2$ (9.1 mg, 20.0 mol %) and KOAc (49.0 mg, 2.0 equiv) in anhydrous TFE (2.0 mL) was stirred at 80 °C for 24 h under an atmosphere of Ar. At ambient temperature, aq. $NaHCO_3$ (15.0 mL) was added and the reaction mixture was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (15.0 mL), and dried over Na_2SO_4. The solvent was evaporated *in vacuo* and the remaining residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc) to yield products **3** and **5**.



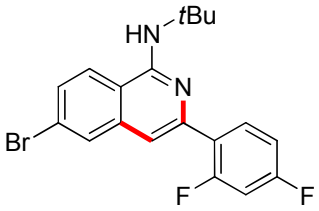
***N-tert*-Butyl-6-chloro-3-(2,4-difluorophenyl)isoquinolin-1-amine (3ab)**

The general procedure was followed using **1b** (53.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3ab** (71 mg, 82%; 5 mmol scale, 75%) as a slight yellow solid. M. p. = 124−126 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.22 (td, J = 8.9, 6.9 Hz, 1H), 7.67 (d, J = 2.1 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.40 (s, 1H), 7.35 (dd, J = 8.8, 2.1 Hz, 1H), 7.00 (td, J = 8.0, 1.9 Hz, 1H), 6.90 (ddd, J = 11.6, 8.9, 2.5 Hz, 1H), 5.14 (s, 1H), 1.62 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 162.6 (dd, $^1J_{C\text{-}F}$ = 250.3, $^3J_{C\text{-}F}$ = 12.0 Hz), 161.0 (dd, $^1J_{C\text{-}F}$ = 252.6, $^3J_{C\text{-}F}$ = 11.6 Hz), 153.8, 144.8 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 138.9, 135.6, 132.0 (dd, $^3J_{C\text{-}F}$ = 9.4, $^4J_{C\text{-}F}$ = 4.7 Hz), 126.8, 126.5, 124.4 (dd, $^3J_{C\text{-}F}$ = 10.8 Hz, $^4J_{C\text{-}F}$ = 3.7 Hz), 123.0, 116.0, 111.4 (dd, $^2J_{C\text{-}F}$ = 20.8 Hz, $^4J_{C\text{-}F}$ = 3.6 Hz), 109.7 (d, $^3J_{C\text{-}F}$ = 12.8 Hz), 104.5 (dd, $^2J_{C\text{-}F}$ = 25.3 Hz, $^2J_{C\text{-}F}$ = 25.3 Hz), 52.0, 29.2. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -110.3 (d, J = 8.5 Hz), -111.0 (d, J = 8.5 Hz). IR (ATR): 2976, 2360, 1606, 1430, 1239, 1082, 974, 840 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{18}ClF_2N_2$ [M+H$^+$] 347.1121, found 347.1119 [M+H$^+$].



***N-tert*-Butyl-3-(2,4-difluorophenyl)-6-fluoroisoquinolin-1-amine (3bb)**

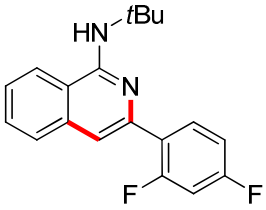
The general procedure was followed using **1b** (49.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **3bb** (59 mg, 72%) as a slight yellow solid. M. p. = 113−116 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.22 (dd, J = 15.9, 8.8 Hz, 1H), 7.68 (dd, J = 8.9, 5.2 Hz, 1H), 7.43 (s, 1H), 7.30 (dd, J = 9.5, 2.2 Hz, 1H), 7.20 – 7.10 (m, 1H), 6.99 (dd, J = 11.8, 4.7 Hz, 1H), 6.94 – 6.85 (m, 1H), 5.13 (s, 1H), 1.62 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 163.0 (d, $^{1}J_{C\text{-}F}$ = 249.6 Hz), 162.5 (dd, $^{1}J_{C\text{-}F}$ = 249.5 Hz, $^{3}J_{C\text{-}F}$ = 12.2 Hz), 161.0 (dd, $^{1}J_{C\text{-}F}$ = 252.9 Hz, $^{3}J_{C\text{-}F}$ = 11.7 Hz), 153.8, 144.7, 139.7 (d, $^{3}J_{C\text{-}F}$ = 9.9 Hz), 132.0 (dd, $^{3}J_{C\text{-}F}$ = 9.4 Hz, $^{4}J_{C\text{-}F}$ = 4.7 Hz), 124.4 (dd, $^{3}J_{C\text{-}F}$ = 11.5 Hz, $^{4}J_{C\text{-}F}$ = 3.2 Hz), 124.1 (d, $^{3}J_{C\text{-}F}$ = 9.4 Hz), 115.3 (d, $^{2}J_{C\text{-}F}$ = 24.8 Hz), 114.7, 111.5 (d, $^{2}J_{C\text{-}F}$ = 20.4 Hz), 111.4 (dd, $^{2}J_{C\text{-}F}$ = 20.8 Hz, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 110.2 (dd, $^{3}J_{C\text{-}F}$ = 12.6 Hz, $^{4}J_{C\text{-}F}$ = 3.8 Hz), 104.3 (dd, $^{2}J_{C\text{-}F}$ = 27.7 Hz, $^{2}J_{C\text{-}F}$ = 25.3 Hz), 51.9, 29.2. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -110.34 (d, J = 8.5 Hz), -110.71 (s), -111.10 (d, J = 8.5 Hz). IR (ATR): 3468, 2920, 2360, 1604, 1431, 1203, 845 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{18}F_3N_2$ [M+H$^+$] 331.1417, found 331.1412 [M+H$^+$].



6-Bromo-*N*-*tert*-butyl-3-(2,4-difluorophenyl)isoquinolin-1-amine (3cb)

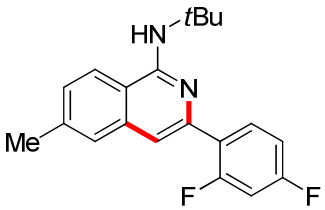
The general procedure was followed using **1c** (64.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3cb** (79 mg, 81%) as a slight yellow solid. M. p. = 130−131 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.21 (td, J = 8.9, 7.0 Hz, 1H), 7.84 (d, J = 1.5 Hz, 1H), 7.53 (d, J = 8.8 Hz, 1H), 7.47 (dd, J = 8.8, 1.5 Hz, 1H), 7.38 (s, 1H), 6.99 (tt, J = 16.4, 8.4 Hz, 1H), 6.90 (ddd, J = 11.5, 8.9, 2.5 Hz, 1H), 5.13 (s, 1H), 1.62 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 162.6 (dd, $^{1}J_{C\text{-}F}$ = 250.3 Hz, $^{3}J_{C\text{-}F}$ = 12.2 Hz), 161.0 (dd, $^{1}J_{C\text{-}F}$ = 252.6, $^{3}J_{C\text{-}F}$ = 11.7 Hz), 153.8, 144.7 (d, $^{4}J_{C\text{-}F}$ = 3.4 Hz), 139.2, 132.0 (dd, $^{3}J_{C\text{-}F}$ = 9.4 Hz, $^{4}J_{C\text{-}F}$ = 4.7 Hz), 130.1, 129.0, 124.3 (dd, $^{3}J_{C\text{-}F}$ = 10.9 Hz, $^{4}J_{C\text{-}F}$

= 3.9 Hz), 124.0, 123.0, 116.2, 111.4 (dd, $^{2}J_{C\text{-}F}$ = 20.8 Hz, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 109.5 (d, $^{3}J_{C\text{-}F}$ = 12.4 Hz), 104.3 (dd, $^{1}J_{C\text{-}F}$ = 27.8 Hz, $^{3}J_{C\text{-}F}$ = 25.4 Hz), 52.0, 29.2. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -110.28 (d, J = 8.6 Hz), -110.98 (d, J = 8.6 Hz). IR (ATR): 3470, 2975, 2360, 1607, 1430, 1237, 840 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{18}BrF_2N_2$ [M+H$^+$] 391.0616, found 391.0623 [M+H$^+$].



***N-tert*-Butyl-3-(2,4-difluorophenyl)isoquinolin-1-amine (3db)**

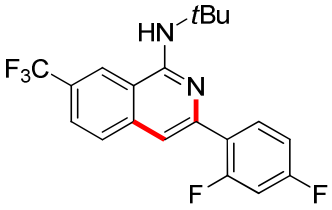
The general procedure was followed using **1d** (44.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3db** (41 mg, 53%) as a slight yellow solid. M. p. = 76−78 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.32 – 8.17 (m, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.54 (dd, J = 8.0, 8.0 Hz, 1H), 7.49 (s, 1H), 7.41 (dd, J = 8.0, 8.0 Hz, 1H), 6.99 (td, J = 8.4, 2.3 Hz, 1H), 6.90 (ddd, J = 11.5, 8.9, 2.5 Hz, 1H), 5.18 (s, 1H), 1.63 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 162.4 (dd, $^{1}J_{C\text{-}F}$ = 249.6 Hz, $^{3}J_{C\text{-}F}$ = 12.1 Hz), 161.0 (dd, $^{1}J_{C\text{-}F}$ = 249.6 Hz, $^{3}J_{C\text{-}F}$ = 12.1 Hz), 153.9, 143.4 (d, $^{4}J_{C\text{-}F}$ = 3.2 Hz), 137.7, 132.0 (dd, $^{3}J_{C\text{-}F}$ = 9.4, $^{4}J_{C\text{-}F}$ = 4.8 Hz), 129.5, 128.1, 126.0, 124.8 (dd, $^{3}J_{C\text{-}F}$ = 10.9, $^{4}J_{C\text{-}F}$ = 3.8 Hz), 121.2, 117.9, 111.3 (dd, $^{2}J_{C\text{-}F}$ = 20.7, $^{4}J_{C\text{-}F}$ = 3.5 Hz), 110.7 (d, $^{3}J_{C\text{-}F}$ = 12.6 Hz), 104.2 (dd, $^{2}J_{C\text{-}F}$ = 27.7, $^{2}J_{C\text{-}F}$ = 25.3 Hz), 51.8, 29.3. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -110.46 (d, J = 8.3 Hz), -111.63 (d, J = 8.2 Hz). IR (ATR): 3446, 2921, 2360, 1598, 1502, 1213, 968, 742 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{19}F_2N_2$ [M+H$^+$] 313.1511, found 313.1501 [M+H$^+$].



***N-tert*-Butyl-3-(2,4-difluorophenyl)-6-methylisoquinolin-1-amine (3eb)**

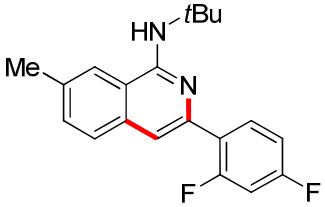
The general procedure was followed using **1e** (48.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3eb** (54 mg, 66%) as a slight yellow solid. M. p. = 112−114 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ =

8.24 (td, J = 8.9, 7.0 Hz, 1H), 7.58 (d, J = 8.5 Hz, 1H), 7.48 (s, 1H), 7.43 (s, 1H), 7.26 (dd, J = 8.5, 1.3 Hz, 1H), 6.99 (td, J = 8.3, 2.3 Hz, 1H), 6.89 (ddd, J = 11.6, 8.9, 2.5 Hz, 1H), 5.13 (s, 1H), 2.48 (s, 3H), 1.63 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 162.4 (dd, $^1J_{C\text{-}F}$ = 249.6 Hz, $^3J_{C\text{-}F}$ = 12.1 Hz), 161.0 (dd, $^1J_{C\text{-}F}$ = 252.6 Hz, $^3J_{C\text{-}F}$ = 12.0 Hz), 153.9, 143.4 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 139.5, 138.0, 132.0 (dd, $^3J_{C\text{-}F}$ = 9.3, $^4J_{C\text{-}F}$ = 4.9 Hz), 127.9, 127.3, 124.9 (dd, $^3J_{C\text{-}F}$ = 11.0 Hz, $^4J_{C\text{-}F}$ = 4.9 Hz), 121.1, 116.1, 111.3 (dd, $^2J_{C\text{-}F}$ = 20.7 Hz, $^4J_{C\text{-}F}$ = 3.6 Hz), 110. 5 (d, $^3J_{C\text{-}F}$ = 12.7 Hz), 104.2 (dd, $^2J_{C\text{-}F}$ = 25.2 Hz, $^2J_{C\text{-}F}$ = 25.3 Hz), 51.7, 29.3, 21.6. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -110.5 (d, J = 8.2 Hz), -111.9 (d, J = 8.2 Hz). IR (ATR): 3469, 2921, 2361, 1598, 1500, 1428, 1238, 967, 842, 671 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{20}H_{21}F_2N_2$ [M+H$^+$] 327.1667, found 327.1665 [M+H$^+$].



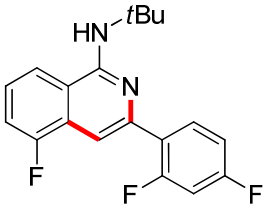
***N-tert*-butyl-3-(2,4-difluorophenyl)-7-(trifluoromethyl)isoquinolin-1-amine (3fb)**

The general procedure was followed using **1f** (61.0 mg, 0.25 mmol) and **2b** (125 mg, 0.25 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3fb** (40 mg, 42%) as a solid. M. p. = 119−121 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.23 (td, J = 8.9, 7.0 Hz, 1H), 7.92 (d, J = 11.5 Hz, 1H), 7.77 (d, J = 8.6 Hz, 1H), 7.71 (d, J = 8.6 Hz, 1H), 7.50 (s, 1H), 7.01 (td, J = 8.2, 2.2 Hz, 1H), 6.91 (ddd, J = 11.5, 8.9, 2.5 Hz, 1H), 5.23 (s, 1H), 1.65 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 162.7 (dd, $^1J_{C\text{-}F}$ = 249.3 Hz, $^3J_{C\text{-}F}$ = 11.8 Hz), 161.1 (dd, $^1J_{C\text{-}F}$ = 254.2 Hz, $^3J_{C\text{-}F}$ = 12.5 Hz), 154.2, 145.8 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 139.7, 132.1 (dd, $^3J_{C\text{-}F}$ = 9.5 Hz, $^4J_{C\text{-}F}$ = 4.6 Hz), 128.9, 127.4 (q, $^2J_{C\text{-}F}$ = 32.5 Hz), 125.2 (q, $^4J_{C\text{-}F}$ = 3.2 Hz), 124.2 (q, $^1J_{C\text{-}F}$ = 272.1 Hz), 124.2 (dd, $^3J_{C\text{-}F}$ = 10.7 Hz, $^4J_{C\text{-}F}$ = 3.8 Hz), 119.1 (q, $^4J_{C\text{-}F}$ = 4.3 Hz), 116.7, 111.5 (dd, $^2J_{C\text{-}F}$ = 20.8 Hz, $^4J_{C\text{-}F}$ = 3.6 Hz), 110.0 (d, $^3J_{C\text{-}F}$ = 12.9 Hz), 104.4 (dd, $^2J_{C\text{-}F}$ = 27.7 Hz, $^2J_{C\text{-}F}$ = 25.3 Hz), 52.2, 29.1. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -62.0 (s), -110.13 (d, J = 8.7 Hz), -110.50 (d, J = 8.7 Hz). IR (ATR): 3468, 2920, 1730, 1434, 1098, 845, 607 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{20}H_{18}F_5N_2$ [M+H$^+$] 381.1385, found 381.1385 [M+H$^+$].



***N-tert*-Butyl-3-(2,4-difluorophenyl)-7-methylisoquinolin-1-amine (3gb)**

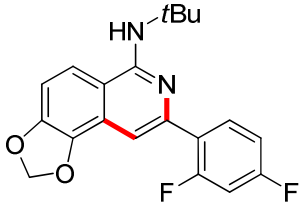
The general procedure was followed using **1g** (48.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3gb** (38 mg, 47%) as a yellow solid. M. p. = 88−90 °C. ^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 8.30 (td, J = 9.0, 7.0 Hz, 1H), 7.95 (s, 1H), 7.66 (d, J = 8.3 Hz, 1H), 7.46 (dd, J = 8.3, 1.1 Hz, 1H), 7.45 (s, 1H), 7.16 – 7.13 (m, 1H), 7.12 – 7.07 (m, 1H), 6.10 (s, 1H), 2.47 (s, 3H), 1.65 (s, 9H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 162.2 (dd, $^{1}J_{C\text{-}F}$ = 239.6 Hz, $^{3}J_{C\text{-}F}$ = 11.7 Hz), 160.8 (dd, $^{1}J_{C\text{-}F}$ = 255.1 Hz, $^{3}J_{C\text{-}F}$ = 11.2 Hz), 154.2, 142.3 (d, $^{4}J_{C\text{-}F}$ = 4.1 Hz), 136.0, 135.7, 132.1 (dd, $^{3}J_{C\text{-}F}$ = 9.8 Hz, $^{4}J_{C\text{-}F}$ = 4.6 Hz), 131.5, 127.5, 125.3 (dd, $^{3}J_{C\text{-}F}$ = 9.7 Hz, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 121.6, 118.3, 111.3 (dd, $^{2}J_{C\text{-}F}$ = 20.9 Hz, $^{4}J_{C\text{-}F}$ = 4.4 Hz), 110.1 (d, $^{3}J_{C\text{-}F}$ = 11.7 Hz), 104.0 (dd, $^{2}J_{C\text{-}F}$ = 28.5 Hz, $^{1}J_{C\text{-}F}$ = 26.3 Hz), 51.5, 28.6, 20.9. ^{19}F-NMR (Acetone-d_6, 376 MHz): δ = -111.73 (d, J = 8.4 Hz), -113.19 (d, J = 8.4 Hz). IR (ATR): 2919, 2361, 1434, 1213, 843, 607 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{20}H_{21}F_2N_2$ [M+H$^+$] 327.1667, found 327.1664 [M+H$^+$].



***N-tert*-Butyl-3-(2,4-difluorophenyl)-5-fluoroisoquinolin-1-amine (3hb)**

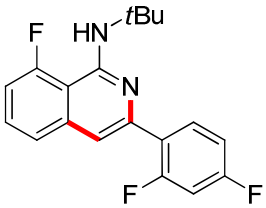
The general procedure was followed using **1h** (48.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3hb** (67 mg, 81%) as a slight yellow solid. M. p. = 99−100 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.21 (td, J = 8.9, 6.9 Hz, 1H), 7.68 (s, 1H), 7.45 (d, J = 8.3 Hz, 1H), 7.32 (td, J = 8.0, 5.6 Hz, 1H), 7.26 – 7.17 (m, 1H), 6.99 (td, J = 8.3, 2.3 Hz, 1H), 6.94 –6.87 (m, 1H), 5.20 (s, 1H), 1.62 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 162.5 (dd, $^{1}J_{C\text{-}F}$ = 249.7 Hz, $^{3}J_{C\text{-}F}$ = 12.1 Hz), 161.0 (dd, $^{1}J_{C\text{-}F}$ = 253.6 Hz, $^{3}J_{C\text{-}F}$ = 11.7 Hz), 158.8 (d, $^{1}J_{C\text{-}F}$ = 252.7 Hz), 153.4 (d, $^{4}J_{C\text{-}F}$ = 3.4 Hz), 144.1, 132.0 (dd, $^{3}J_{C\text{-}F}$ = 9.4 Hz, $^{4}J_{C\text{-}F}$ = 4.7 Hz), 128.2 (d, $^{2}J_{C\text{-}F}$ = 17.2 Hz), 125.4 (d, $^{3}J_{C\text{-}F}$ = 8.2 Hz), 124.6 (dd, $^{3}J_{C\text{-}F}$ = 10.8 Hz, $^{4}J_{C\text{-}F}$ = 3.8 Hz), 119.1 (d, $^{4}J_{C\text{-}F}$ = 5.7 Hz), 117.0 (d, $^{4}J_{C\text{-}F}$ = 4.1 Hz), 113.4 (d, $^{2}J_{C\text{-}F}$ = 19.8 Hz), 111.4 (dd, $^{2}J_{C\text{-}F}$ = 20.8 Hz, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 104.3 (dd, $^{2}J_{C\text{-}F}$

= 27.6 Hz, $^{2}J_{C\text{-}F}$ = 25.3 Hz), 102.6 (dd, $^{3}J_{C\text{-}F}$ = 12.6 Hz, $^{4}J_{C\text{-}F}$ =5.3 Hz), 52.0, 29.2. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -110.27 (d, J = 8.6 Hz), -111.10 (d, J = 8.6 Hz), -121.36 (s). IR (ATR): 3477, 2920, 2360, 1568, 1211, 967, 735 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{18}F_3N_2$ [M+H$^+$] 331.1417, found 331.1405 [M+H$^+$].



***N-tert*-Butyl-8-(2,4-difluorophenyl)-[1,3]dioxolo[4,5-*f*]isoquinolin-6-amine (3ib)**

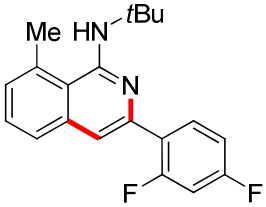
The general procedure was followed using **1i** (55.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 40:1) yielded **3ib** (83 mg, 93%) as a slight yellow solid. M. p. = 128−130 °C. ^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 8.33 (dd, J = 15.9, 8.5 Hz, 1H), 7.75 (d, J = 8.7 Hz, 1H), 7.39 (s, 1H), 7.23 – 7.12 (m, 2H), 7.11 (d, J = 8.7 Hz, 1H), 6.22 (s, 2H), 6.15 (s, 1H), 1.64 (s, 9H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 162.4 (dd, $^{1}J_{C\text{-}F}$ = 247.7 Hz, $^{3}J_{C\text{-}F}$ = 12.3 Hz), 160.9 (dd, $^{1}J_{C\text{-}F}$ = 252.2, $^{3}J_{C\text{-}F}$ = 11.7 Hz), 154.5, 146.7, 143.3 (d, $^{1}J_{C\text{-}F}$ = 3.0 Hz), 141.5, 132.1 (dd, $^{3}J_{C\text{-}F}$ = 9.6 Hz, $^{4}J_{C\text{-}F}$ = 4.7 Hz), 124.9 (d, $^{3}J_{C\text{-}F}$ = 10.9 Hz), 123.3, 117.1, 114.1, 111.4 (dd, $^{2}J_{C\text{-}F}$ = 21.0 Hz, $^{4}J_{C\text{-}F}$ = 3.7 Hz), 108.7, 104.1 (dd, $^{2}J_{C\text{-}F}$ = 28.1 Hz, $^{2}J_{C\text{-}F}$ = 25.7 Hz), 102.3, 101.9 (d, $^{3}J_{C\text{-}F}$ = 12.9 Hz), 51.6, 28.5. ^{19}F-NMR (Acetone-d_6, 376 MHz): δ = -111.61 (dd, J = 9.2, 4.8 Hz), -112.60 (d, J = 8.3 Hz). IR (ATR): 2969, 2360, 1611, 1414, 1237, 961, 695 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{20}H_{19}F_2N_2O_2$ [M+H$^+$] 357.1409, found 357.1398 [M+H$^+$].



***N-tert*-Butyl-3-(2,4-difluorophenyl)-8-fluoroisoquinolin-1-amine (3jb)**

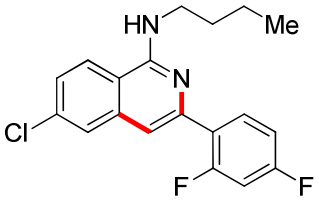
The general procedure was followed using **1j** (49.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3jb** (60 mg, 73%) as a colorless solid. M. p. = 88−90 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.22 (td, J = 8.9, 7.0 Hz, 1H), 7.46 – 7.32 (m, 3H), 7.07 – 6.93 (m, 2H), 6.89 (ddd, J = 11.6, 8.9, 2.5 Hz, 1H), 6.37 (d, J = 20.1 Hz, 1H), 1.60 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 162.5 (dd, $^{1}J_{C\text{-}F}$ = 249.3 Hz, $^{3}J_{C\text{-}F}$ = 12.2 Hz), 161.0 (dd, $^{1}J_{C\text{-}F}$ = 252.6 Hz, $^{3}J_{C\text{-}F}$ = 11.6 Hz), 159.7 (d,

$^{1}J_{C\text{-}F}$ = 247.5 Hz), 152.8 (d, $^{3}J_{C\text{-}F}$ = 5.8 Hz), 144.5, 141.0 (d, $^{4}J_{C\text{-}F}$ = 2.8 Hz), 132.0 (dd, $^{3}J_{C\text{-}F}$ = 9.4 Hz, $^{4}J_{C\text{-}F}$ = 4.7 Hz), 129.6 (d, $^{3}J_{C\text{-}F}$ = 10.6 Hz), 124.3 (dd, $^{3}J_{C\text{-}F}$ = 10.8 Hz, $^{4}J_{C\text{-}F}$ = 3.8 Hz), 123.8 (d, $^{4}J_{C\text{-}F}$ = 3.7 Hz), 111.4 (dd, $^{2}J_{C\text{-}F}$ = 20.8 Hz, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 110.9 (d, $^{2}J_{C\text{-}F}$ = 25.6 Hz), 109.1 (dd, $^{3}J_{C\text{-}F}$ = 12.9 Hz, $^{4}J_{C\text{-}F}$ = 2.6 Hz), 108.0 (d, $^{3}J_{C\text{-}F}$ = 10.1 Hz), 104.3 (dd, $^{2}J_{C\text{-}F}$ = 27.7 Hz, $^{2}J_{C\text{-}F}$ = 25.3 Hz), 51.8, 29.1. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -110.21 (d, J = 8.5 Hz), -111.09 (d, J = 8.4 Hz), -113.26 (s). IR (ATR): 3477, 2919, 2360, 1580, 1416, 1222, 812, 668 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{18}F_3N_2$ [M+H$^+$] 331.1417, found 331.1405 [M+H$^+$].



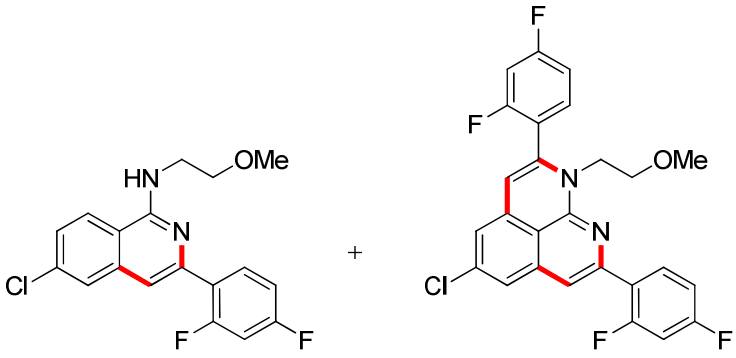
***N*-*tert*-Butyl-3-(2,4-difluorophenyl)-8-methylisoquinolin-1-amine (3kb)**

The general procedure was followed using **1k** (48.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3kb** (39 mg, 49%) as a colorless solid. M. p. = 124−126 °C. ^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 8.30 (td, J = 9.0, 7.0 Hz, 1H), 7.96 (s, 1H), 7.67 (d, J = 8.3 Hz, 1H), 7.46 (dd, J = 8.3, 1.0 Hz, 1H), 7.45 (d, J = 1.0 Hz, 1H), 7.22 – 7.04 (m, 2H), 6.10 (s, 1H), 2.47 (s, 3H), 1.65 (s, 9H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 162.2 (dd, $^{1}J_{C\text{-}F}$ = 247.1 Hz, $^{3}J_{C\text{-}F}$ = 12.3 Hz), 160.7 (dd, $^{1}J_{C\text{-}F}$ = 251.4 Hz, $^{3}J_{C\text{-}F}$ = 11.8 Hz), 154.2, 142.3 (d, $^{4}J_{C\text{-}F}$ = 3.2 Hz), 135.9, 135.7, 132.0 (dd, $^{3}J_{C\text{-}F}$ = 9.5 Hz, $^{4}J_{C\text{-}F}$ = 4.9 Hz), 131.5, 127.5, 125.2 (dd, $^{3}J_{C\text{-}F}$ = 11.2 Hz, $^{4}J_{C\text{-}F}$ = 3.9 Hz), 121.6, 118.3, 111.3 (dd, $^{2}J_{C\text{-}F}$ = 21.0 Hz, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 110.1 (d, $^{3}J_{C\text{-}F}$ = 12.0 Hz), 104.0 (dd, $^{2}J_{C\text{-}F}$ = 28.0 Hz, $^{2}J_{C\text{-}F}$ = 25.6 Hz), 51.5, 28.6, 20.8. ^{19}F-NMR (Acetone-d_6, 376 MHz): δ = -111.76 (d, J = 7.9 Hz), -113.21 (d, J = 7.9 Hz). IR (ATR): 3432, 2919, 2360, 1600, 1434, 1237, 1096, 843, 597 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{20}H_{21}F_2N_2$ [M+H$^+$] 327.1667, found 327.1662 [M+H$^+$].



***N*-Butyl-6-chloro-3-(2,4-difluorophenyl)isoquinolin-1-amine (3lb)**

The general procedure was followed using **1l** (53.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 40:1) yielded **3lb** (56 mg, 64%) as a yellow solid. M. p. = 124−126 °C. ^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 8.41 – 8.31 (m, 1H), 8.17 (d, J = 8.9 Hz, 1H), 7.79 (d, J = 2.1 Hz, 1H), 7.42 (dd, J = 8.9, 2.1 Hz, 1H), 7.41 (s, 1H), 7.16 – 7.04 (m, 2H), 6.93 (t, J = 5.6 Hz, 1H), 3.68 (td, J = 7.1, 5.6 Hz, 2H), 1.86 – 1.65 (m, 2H), 1.53 – 1.43 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 162.5 (dd, $^{1}J_{C\text{-}F}$ = 248.1 Hz, $^{3}J_{C\text{-}F}$ = 12.3 Hz), 160.9 (dd, $^{1}J_{C\text{-}F}$ = 251.5 Hz, $^{3}J_{C\text{-}F}$ = 11.9 Hz), 155.1, 144.9 (d, $^{4}J_{C\text{-}F}$ = 3.2 Hz), 139.1, 135.4, 132.4 (dd, $^{3}J_{C\text{-}F}$ = 9.5 Hz, $^{4}J_{C\text{-}F}$ = 4.7 Hz), 126.1, 126.1, 124.6, 124.5 (dd, $^{2}J_{C\text{-}F}$ = 11.0 Hz, $^{4}J_{C\text{-}F}$ = 3.8 Hz), 115.9, 111.3 (dd, $^{2}J_{C\text{-}F}$ = 21.0 Hz, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 108.9 (d, $^{3}J_{C\text{-}F}$ = 12.7 Hz), 104.0 (dd, $^{2}J_{C\text{-}F}$ = 27.9 Hz, $^{2}J_{C\text{-}F}$ = 25.7 Hz), 41.1, 31.3, 20.2, 13.4. ^{19}F-NMR (Acetone-d_6, 376 MHz): δ = -111.37 (d, J = 8.6 Hz), -112.27 (d, J = 8.6 Hz). IR (ATR): 3435, 2929, 2450, 1611, 1453, 1197, 1096, 845, 617 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{18}ClF_2N_2$ [M+H$^+$] 347.1131, found 347.1125 [M+H$^+$].



The general procedure was followed using **1m** (53.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) yielded **3mb** (14 mg, 23%) as a yellow oil, and **3mb'** (48 mg, 40%) as a yellow solid.

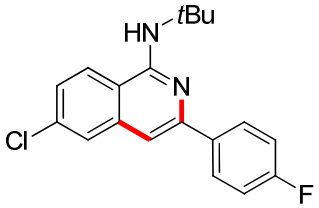
6-Chloro-3-(2,4-difluorophenyl)-*N*-(2-methoxyethyl)isoquinolin-1-amine (3mb)

^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.27 – 8.18 (m, 1H), 7.72 (d, J = 8.9 Hz, 1H), 7.69 (d, J = 1.9 Hz, 1H), 7.41 (s, 1H), 7.37 (dd, J = 8.9, 1.9 Hz, 1H), 7.02 – 6.95 (m, 1H), 6.90 (ddd, J = 11.5, 9.0, 2.5 Hz, 1H), 5.69 (s, 1H), 3.89 (dd, J = 9.9, 5.0 Hz, 2H), 3.72 (t, J = 5.1 Hz, 2H), 3.44 (s, 3H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 162.7 (dd, $^{1}J_{C\text{-}F}$ = 250.6 Hz, $^{3}J_{C\text{-}F}$ = 12.8 Hz), 160.9 (dd, $^{1}J_{C\text{-}F}$ = 253.0 Hz, $^{3}J_{C\text{-}F}$ = 12.6 Hz), 154.4, 144.6 (d, $^{4}J_{C\text{-}F}$ = 2.8 Hz), 138.9, 136.0, 132.0 (dd, $^{3}J_{C\text{-}F}$ = 9.4, $^{4}J_{C\text{-}F}$ = 4.7 Hz), 126.7, 126.6, 124.0 (dd, $^{3}J_{C\text{-}F}$ = 10.5 Hz, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 123.3, 115.7, 111.4 (dd, $^{1}J_{C\text{-}F}$ = 20.7 Hz, $^{1}J_{C\text{-}F}$ = 3.4 Hz), 110.3 (d, $^{3}J_{C\text{-}F}$ = 12.7 Hz), 104.3 (dd, $^{1}J_{C\text{-}F}$ = 27.4, $^{1}J_{C\text{-}F}$ = 25.5), 71.3, 58.8, 41.3. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -110.57 (d, J = 8.5 Hz), -110.70 (s). IR (ATR): 3398, 2919, 2360, 1603, 1354, 1095, 836, 667 cm^{-1}. HR-MS

(ESI) m/z calcd for $C_{18}H_{16}ClF_2N_2O$ [M+H$^+$] 349.0914, found 349.0908 [M+H$^+$].

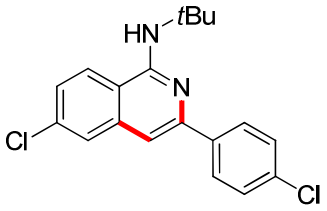
5-Chloro-2, 8-bis(2,4-difluorophenyl)-1-(2-methoxyethyl)-1*H*-benzo[*de*][1,8]naphthyridine (3mb')

M. p. = 175−177 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.09 – 8.03 (m, 1H), 7.44 – 7.38 (m, 1H), 7.28 (d, J = 1.0 Hz, 1H), 7.15 (d, J = 1.6 Hz, 1H), 7.04 – 6.85 (m, 4H), 6.77 (d, J = 1.6 Hz, 1H), 5.97 (s, 1H), 4.43 – 4.35 (m, 1H), 3.91 – 3.83 (m, 1H), 3.69 – 3.64 (m, 1H), 3.55 – 3.47 (m, 1H), 3.17 (s, 3H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 163.6 (dd, $^1J_{C\text{-}F}$ = 251.8 Hz, $^3J_{C\text{-}F}$ = 11.5 Hz), 162.7 ($^1J_{C\text{-}F}$ = 251.0 Hz, $^3J_{C\text{-}F}$ = 12.5 Hz), 160.9 ($^1J_{C\text{-}F}$ = 253.3 Hz, $^3J_{C\text{-}F}$ = 12.3 Hz), 160.0 ($^1J_{C\text{-}F}$ = 250.3 Hz, $^3J_{C\text{-}F}$ = 11.8 Hz), 152.3, 146.5 (d, $^4J_{C\text{-}F}$ = 2.8 Hz,), 140.7, 140.4, 138.1, 136.8, 132.8 (dd, $^3J_{C\text{-}F}$ = 9.6 Hz, $^4J_{C\text{-}F}$ = 3.9 Hz), 131. 7 (dd, $^3J_{C\text{-}F}$ = 9.3 Hz, $^4J_{C\text{-}F}$ = 4.7 Hz), 124.0 (dd, $^3J_{C\text{-}F}$ = 10.6 Hz, $^4J_{C\text{-}F}$ = 3.7 Hz), 120.2 (dd, $^3J_{C\text{-}F}$ = 16.2 Hz, $^4J_{C\text{-}F}$ = 3.9 Hz), 119.7, 118.1, 115.7, 111.8 (dd, $^2J_{C\text{-}F}$ = 21.5 Hz, $^4J_{C\text{-}F}$ = 3.8 Hz), 111.4 (dd, $^2J_{C\text{-}F}$ = 20.0 Hz, $^4J_{C\text{-}F}$ = 4.5 Hz), 111.2 (d, $^3J_{C\text{-}F}$ = 11.8 Hz), 108.3, 104.4 (dd, $^2J_{C\text{-}F}$ = 27.4 Hz, $^2J_{C\text{-}F}$ = 25.4 Hz), 104.3 (t, $^2J_{C\text{-}F}$ = 25.6 Hz), 68.8, 58.8, 45.4. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -107.1 (d, J = 8.7 Hz), -108.7 (d, J = 8.7 Hz), -110.4 (d, J = 8.7 Hz), -110.5 (d, J = 8.7 Hz). IR (ATR): 3478, 2956, 2430, 1672, 1344, 1125, 855 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{26}H_{18}ClF_4N_2O$ [M+H$^+$] 485.1033, found 485.1038 [M+H$^+$].



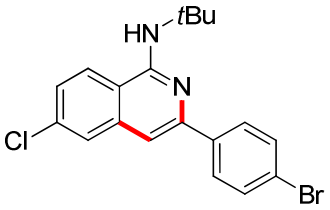
***N*-*tert*-Butyl-6-chloro-3-(4-fluorophenyl)isoquinolin-1-amine (3ac)**

The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **2c** (154 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3ac** (55 mg, 67%) as a slight yellow solid. M. p. = 107−108 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.10 (dd, J = 8.8, 5.6 Hz, 2H), 7.65 (d, J = 2.0 Hz, 1H), 7.59 (d, J = 8.9 Hz, 1H), 7.31 (dd, J = 8.9, 2.0 Hz, 1H), 7.22 (s, 1H), 7.14 (t, J = 8.7 Hz, 2H), 5.14 (s, 1H), 1.65 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 163.1 (d, $^1J_{C\text{-}F}$ = 247.3 Hz), 154.0, 149.2, 139.2, 136.2 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 135.6, 128.4 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 126.4, 126.0, 123.2, 115.9, 115.3 (d, $^2J_{C\text{-}F}$ = 21.4 Hz), 104.7, 52.0, 29.2. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -114.23 (s). IR (ATR): 3461, 2977, 2360, 1602, 1503, 1423, 1229, 833, 665 cm^{-1}. HR-MS (EI) m/z calcd for $C_{19}H_{19}ClFN_2$ [M+H$^+$] 329.1215, found 329.1206 [M+H$^+$].



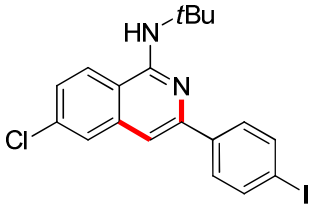
***N-tert*-Butyl-6-chloro-3-(4-chlorophenyl)isoquinolin-1-amine (3ad)**

The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **2d** (124 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3ad** (60 mg, 70%) as a colorless solid. M. p. = 99−101 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.05 (d, J = 8.6 Hz, 2H), 7.64 (d, J = 2.0 Hz, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.42 (d, J = 8.6 Hz, 2H), 7.32 (dd, J = 8.8, 2.0 Hz, 1H), 7.24 (s, 1H), 5.14 (s, 1H), 1.64 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 154.0, 149.0, 139.1, 138.5, 135.6, 134.2, 128.6, 128.0, 126.5, 126.1, 123.12, 116.1, 105.0, 52.0, 29.2. IR (ATR): 3467, 2921, 2360, 1612, 1237, 1082, 833, 666 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{19}Cl_2N_2$ [M+H$^+$] 345.0920, found 345.0910 [M+H$^+$].



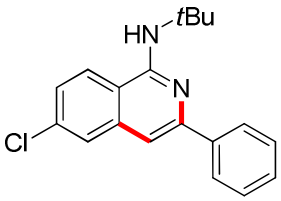
3-(4-Bromophenyl)-*N-tert*-butyl-6-chloroisoquinolin-1-amine (3ae)

The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **2e** (186 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3ae** (66 mg, 68%) as a colorless solid. M. p. = 114−117 °C. ^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 8.16 (d, J = 8.9 Hz, 1H), 8.12 (d, J = 9.0, 2.2 Hz, 2H), 7.77 (d, J = 2.0 Hz, 1H), 7.64 (dd, J = 9.0, 2.2 Hz, 2H), 7.48 (s, 1H), 7.38 (dd, J = 8.9, 2.0 Hz, 1H), 6.28 (s, 1H), 1.67 (s, 9H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 154.7, 148.7, 139.4, 139.3, 135.2, 131.5, 128.4, 126.1, 125.8, 125.0, 122.0, 116.5, 104.7, 51.7, 28.5. IR (ATR): 2919, 2360, 1609, 1235, 808, 658 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{19}ClBrN_2$ [M+H$^+$] 389.0415, found 389.0407 [M+H$^+$].



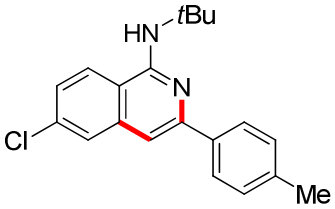
***N-tert*-Butyl-6-chloro-3-(4-iodophenyl)isoquinolin-1-amine (3af)**

The general procedure was followed using **1a** (53 mg, 0.25 mmol) and **2f** (207 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3af** (52 mg, 48%) as a colorless solid. M. p. = 149−152 °C. ^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 8.17 (d, J = 8.9 Hz, 1H), 7.99 (d, J = 8.7 Hz, 2H), 7.86 (d, J = 8.7 Hz, 2H), 7.80 (d, J = 2.1 Hz, 1H), 7.52 (s, 1H), 7.40 (dd, J = 8.9, 2.1 Hz, 1H), 6.31 (s, 1H), 1.67 (s, 9H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 154.7, 148.8, 139.9, 139.3, 137.6, 135.2, 128.5, 126.1, 125.8, 125.0, 116.6, 104.7, 93.7, 51.8, 28.4. IR (ATR): 2921, 2360, 1611, 1239, 799, 666 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{19}ClIN_2$ [M+H$^+$] 437.0276, found 437.0279 [M+H$^+$].



***N-tert*-Butyl-6-chloro-3-phenylisoquinolin-1-amine (3aa)**

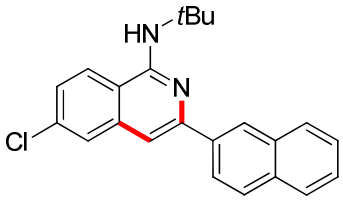
The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **2a** (107 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3aa** (62 mg, 80%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.14 (dd, J = 8.5, 1.4 Hz, 2H), 7.66 (d, J = 2.1 Hz, 1H), 7.60 (d, J = 8.7 Hz, 1H), 7.49 – 7.44 (m, 2H), 7.40 – 7.35 (m, 1H), 7.31 (dd, J = 8.7, 2.1 Hz, 1H), 7.30 (s, 1H), 5.13 (s, 1H), 1.66 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 153.9, 150.1, 140.0, 139.2, 135.4, 128.5, 128.3, 126.7, 126.5, 125.9, 123.2, 116.0, 105.1, 52.0, 29.2. IR (ATR): 3466, 2922, 2360, 1611, 1514, 1429, 1359, 1233, 1085, 760, 690 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{20}ClN_2$ [M+H$^+$] 311.1301, found 311.1310 [M+H$^+$].



***N-tert*-Butyl-6-chloro-3-*p*-tolylisoquinolin-1-amine (3ag)**

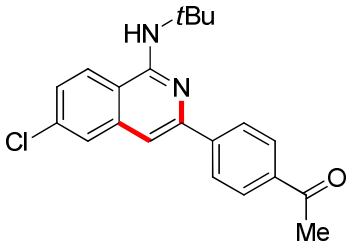
The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **2g** (114 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3ag** (50 mg, 61%) as a yellow oil. ^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 8.14 (d, J = 8.9 Hz, 1H), 8.09 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 2.1 Hz, 1H), 7.45 (s, 1H), 7.34 (dd, J = 8.9, 2.1 Hz, 1H), 7.28 (d, J = 8.0 Hz, 2H), 6.23 (s, 1H), 2.37 (s, 3H), 1.68 (s, 9H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 154.6, 150.1, 139.5, 138.0, 137.4, 135.0, 129.1, 126.5, 125.9, 125.3, 124.9, 116.2,

104.1, 51.6, 28.5, 20.4. IR (ATR): 3457, 2962, 1528, 1355, 1211, 753 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{20}H_{22}ClN_2$ $[M+H^+]$ 325.1472, found 325.1477 $[M+H^+]$.



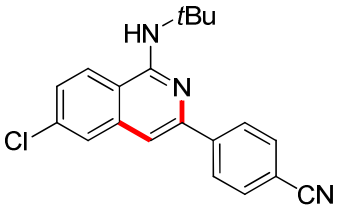
***N-tert*-Butyl-6-chloro-3-(naphthalen-2-yl)isoquinolin-1-amine (3ah)**

The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **2h** (132 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3ah** (50 mg, 56%) as a slight yellow solid. M. p. = 98−100 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.28 (d, J = 8.3 Hz, 1H), 7.87 (dd, J = 8.3, 8.3 Hz, 2H), 7.69 (d, J = 7.3 Hz, 1H), 7.64 – 7.61 (m, 2H), 7.52 (dd, J = 7.3, 8.0 Hz, 1H), 7.49 – 7.39 (m, 2H), 7.33 (dd, J = 8.9, 2.0 Hz, 1H), 7.05 (s, 1H), 5.16 (s, 1H), 1.53 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 153.9, 152.4, 140.0, 138.9, 135.5, 134.0, 131.5, 128.2, 128.2, 127.2, 126.7, 126.4, 126.1, 125.8, 125.6, 125.4, 123.2, 115.6, 110.3, 52.1, 29.4. IR (ATR): 3473, 2921, 2360, 1612, 1513, 1388, 1212, 774 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{23}H_{22}ClN_2$ $[M+H^+]$ 361.1466, found 361.1460 $[M+H^+]$.



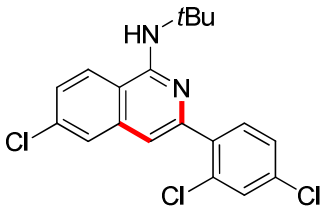
1-{4-[1-(*tert*-Butylamino)-6-chloroisoquinolin-3-yl]phenyl}ethanone (3ai)

The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **2i** (128 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 7:1) yielded **3ai** (76 mg, 86%) as a slight yellow solid. M. p. = 139−141°C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.19 (d, J = 8.4 Hz, 2H), 8.04 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 2.0 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.33 (dd, J = 8.8, 2.0 Hz, 1H), 7.32 (s, 1H), 5.19 (s, 1H), 2.63 (s, 3H), 1.66 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 197.8, 154.0, 148.8, 144.5, 138.9, 136.6, 135.7, 128.7, 126.7, 126.7, 126.6, 123.2, 116.4, 106.3, 52.1, 29.2, 26.7. IR (ATR): 3628, 2917, 1770, 1241, 669 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{21}H_{22}ClN_2O$ $[M+H^+]$ 353.1412, found 353.1415 $[M+H^+]$.



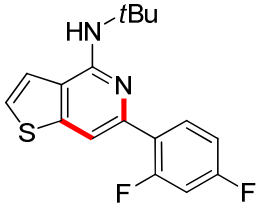
4-(1-(*tert*-Butylamino)-6-chloroisoquinolin-3-yl)benzonitrile (3aj)

The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **2ja** (158 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1→10:1) yielded **3aj** [(42 mg, 50%); (0.50 mmol **2jb**, 40 mg, 48%); (0.50 mmol **2jc**, 48 mg, 57%)] as a slight yellow solid. M. p. = 213−215 °C. ^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 8.38 (d, J = 8.4 Hz, 2H), 8.21 (d, J = 8.9 Hz, 1H), 7.89 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 1.8 Hz, 1H), 7.65 (s, 1H), 7.45 (dd, J = 8.9, 1.8 Hz, 1H), 6.38 (br s, 1H), 1.68 (s, 9H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 154.8, 147.8, 144.4, 139.1, 135.4, 132.4, 127.1, 126.4, 126.3, 125.1, 118.6, 117.0, 111.5, 106.2, 51.8, 28.4. IR (ATR): 3408, 2921, 2360, 1602, 1237, 808, 667 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{20}H_{19}ClN_3$ [M+H$^+$] 336.1262, found 336.1258 [M+H$^+$].



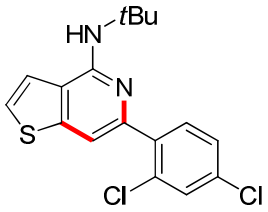
***N*-*tert*-Butyl-6-chloro-3-(2,4-dichlorophenyl)isoquinolin-1-amine (3ak)**

The general procedure was followed using **1a** (53.0 mg, 0.50 mmol) and **2k** (111 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3ak** (60 mg, 63%) as a slight yellow solid. M. p. = 128−130 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.66 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 2.1 Hz, 1H), 7.61 (d, J = 8.9 Hz, 1H), 7.47 (d, J = 2.1 Hz, 1H), 7.35 (dd, J = 8.9, 2.1 Hz, 1H), 7.31 (dd, J = 8.4, 2.1 Hz, 1H), 7.16 (s, 1H), 5.14 (s, 1H), 1.56 (d, J = 5.8 Hz, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 153.9, 148.5, 138.7, 138.3, 135.6, 133.8, 133.0, 132.7, 129.9, 127.0, 126.6, 126.6, 123.1, 115.8, 110.1, 52.1, 29.3. IR (ATR): 3465, 2920, 2360, 1518, 1356, 1214, 821 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{18}Cl_3N_2$ [M$^+$] 379.0530, found 379.0529 [M+H$^+$].



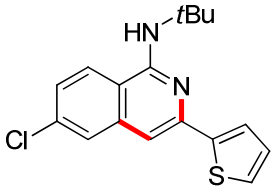
***N-tert*-Butyl-6-(2,4-difluorophenyl)thieno[3,2-*c*]pyridin-4-amine (3nb)**

The general procedure was followed using **1n** (46.0 mg, 0.25 mmol) and **2b** (125 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3nb** (61 mg, 77%) as a slight yellow solid. M. p. = 67−69 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.19 (td, J = 8.9, 7.0 Hz, 1H), 7.64 (s, 1H), 7.28 (d, J = 5.5 Hz, 1H), 7.15 (d, J = 5.5 Hz, 1H), 6.98 (td, J = 8.3, 2.5 Hz, 1H), 6.88 (ddd, J = 11.5, 8.9, 2.5 Hz, 1H), 4.71 (s, 1H), 1.60 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 162.4 (dd, $^{1}J_{C\text{-}F}$ = 249.1 Hz, $^{3}J_{C\text{-}F}$ = 12.0 Hz), 160.8 (dd, $^{1}J_{C\text{-}F}$ = 252.0 Hz, $^{3}J_{C\text{-}F}$ = 11.2 Hz), 152.5, 148.1, 144.0, 132.2 (dd, $^{3}J_{C\text{-}F}$ = 9.4 Hz, $^{4}J_{C\text{-}F}$ = 4.8 Hz), 124.6 (dd, $^{1}J_{C\text{-}F}$ = 11.4 Hz, $^{3}J_{C\text{-}F}$ = 3.6 Hz), 124.5, 121.9, 119.1, 111.4 (dd, $^{2}J_{C\text{-}F}$ = 20.8 Hz, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 107.0 (d, $^{3}J_{C\text{-}F}$ = 12.9 Hz), 104.2 (dd, $^{2}J_{C\text{-}F}$ = 27.8 Hz, $^{2}J_{C\text{-}F}$ = 25.3 Hz), 51.9, 29.5. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -110.97 (d, J = 8.1 Hz), -111.46 (d, J = 7.9 Hz). IR (ATR): 3465, 2920, 2360, 1536, 1401, 1238, 964, 682 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{17}H_{17}F_2N_2S$ [M+H$^+$] 319.1075, found 319.1070 [M+H$^+$].



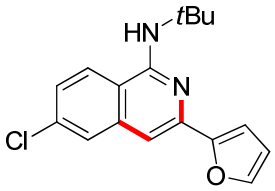
***N-tert*-Butyl-6-(2,4-dichlorophenyl)thieno[3,2-*c*]pyridin-4-amine (3nk)**

The general procedure was followed using **1n** (46.0 mg, 0.25 mmol) and **2k** (111 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3nk** (53 mg, 61%) as a yellow oil. ^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 7.73 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 5.5Hz, 1H), 7.58 (d, J = 2.1 Hz, 1H), 7.54 (d, J = 5.5 Hz, 1H), 7.48 (dd, J = 8.4, 2.1 Hz, 1H), 7.44 (d, J = 0.6 Hz, 1H), 5.96 (s, 1H), 1.56 (s, 9H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 153.2, 147.5, 147.3, 139.5, 133.3, 133.0, 132.7, 129.5, 127.1, 124.5, 122.3, 120.7, 106.8, 51.5, 28.8. IR (ATR): 3457, 2962, 1523, 1365, 1211, 693 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{17}H_{17}Cl_2N_2S$ [M+H$^+$] 351.0489, found 351.0493 [M+H$^+$].



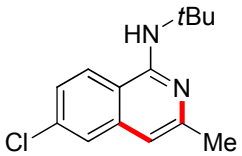
***N-tert*-Butyl-6-chloro-3-(thiophen-2-yl)isoquinolin-1-amine (3al)**

The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **2l** (148 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3al** (40 mg, 51%) as a yellow solid. M. p. = 105−108 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.59 – 7.57 (m, 2H), 7.54 (d, J = 8.8 Hz, 1H), 7.33 (d, J = 5.0 Hz, 1H), 7.25 (dd, J = 8.8, 1.9 Hz, 1H), 7.16 (s, 1H), 7.10 (dd, J = 5.0, 3.8 Hz, 1H), 5.11 (s, 1H), 1.64 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 153.7, 146.8, 145.5, 139.1, 135.7, 127.9, 126.5, 126.2, 125.6, 123.2, 123.2, 116.0, 102.9, 52.1, 29.0. IR (ATR): 3474, 2920, 2360, 1608, 1442, 1230, 1084, 706 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{17}H_{18}ClN_2S$ [M+H$^+$] 317.0874, found 317.0868 [M+H$^+$].



***N-tert*-Butyl-6-chloro-3-(furan-2-yl)isoquinolin-1-amine (3am)**

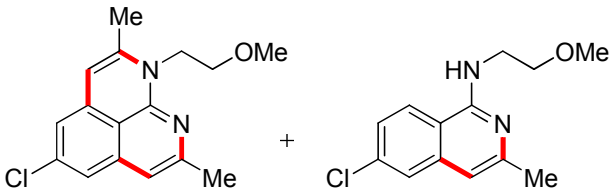
The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **2m** (102 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **3am** (37 mg, 49%) as a yellow oil. ^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 8.14 (d, J = 8.9 Hz, 1H), 7.79 (d, J = 2.1 Hz, 1H), 7.67 (d, J = 1.8 Hz, 1H), 7.35 (dd, J = 8.9, 2.1 Hz, 1H), 7.27 (s, 1H), 7.03 (d, J = 3.2 Hz, 1H), 6.60 (dd, J = 3.2, 1.8 Hz, 1H), 6.26 (s, 1H), 1.65 (s, 9H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 155.3, 154.6, 143.0, 142.5, 139.1, 135.3, 125.9, 125.3, 125.0, 116.6, 111.8, 108.2, 102.3, 51.8, 28.3. IR (ATR): 3466, 2959, 2360, 1612, 1513, 1211, 732 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{17}H_{18}ClN_2O$ [M+H$^+$] 301.1102, found 301.1099 [M+H$^+$].



***N-tert*-butyl-6-chloro-3-methylisoquinolin-1-amine (5aa)**

The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **4a** (114 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **5aa**

(42 mg, 68%) as a colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.52 (d, J = 8.9 Hz, 1H), 7.48 (d, J = 1.9 Hz, 1H), 7.22 (dd, J = 8.9, 1.9 Hz, 1H), 6.60 (s, 1H), 4.96 (s, 1H), 2.44 (s, 3H), 1.57 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 153.8, 151.6, 139.1, 135.1, 125.4, 125.0, 123.1, 114.8, 106.9, 52.0, 29.1, 24.6. IR (ATR): 3468, 2958, 2360, 1514, 1377, 1234, 875, 665 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{14}H_{18}ClN_2$ [M+H$^+$] 249.1153, found 249.1152 [M+H$^+$].



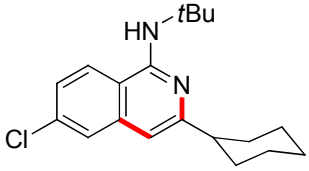
The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **4a** (114 mg, 0.25 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **5ma'** (18 mg, 25%) as a yellow solid, and **5ma** (25 mg, 40%) as a yellow oil.

5-Chloro-1-(2-methoxyethyl)-2,8-dimethyl-1*H*-benzo[*de*][1,8]naphthyridine (5ma')

M. p. = 114−116 °C. ^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 6.89 (d, J = 1.8 Hz, 1H), 6.63 (d, J = 1.8 Hz, 1H), 6.57 (s, 1H), 6.01 (s, 1H), 4.29 (t, J = 5.5 Hz, 2H), 3.67 (t, J = 5.5 Hz, 2H), 3.29 (s, 3H), 2.36 (s, 4H), 2.31 (s, 3H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 153.1, 152.2, 143.9, 141.2, 138.4, 137.3, 118.1, 114.6, 112.5, 107.9, 104.5, 69.3, 58.2, 44.1, 23.8, 20.2. IR (ATR): 3398, 2962, 1697, 1528, 1213, 1094 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{16}H_{18}ClN_2O$ [M+H$^+$] 289.1102, found 289.1096 [M+H$^+$].

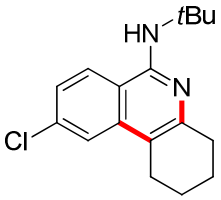
6-Chloro-*N*-(2-methoxyethyl)-3-methylisoquinolin-1-amine (5ma)

^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 8.09 (d, J = 8.9 Hz, 1H), 7.62 (d, J = 1.9 Hz, 1H), 7.33 (dd, J = 8.9, 2.0 Hz, 1H), 6.72 (s, 1H), 6.72 (br s, 1H), 3.77 (q, J = 5.7 Hz, 2H), 3.62 (t, J = 5.7 Hz, 2H), 3.33 (s, 3H), 2.39 (s, 3H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 154.8, 151.8, 139.4, 135.0, 124.8, 124.7, 124.6, 114.7, 106.7, 70.9, 57.8, 40.8, 23.8. IR (ATR): 3376, 2942, 1685, 1558, 1353, 1114 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{13}H_{16}ClN_2O$ [M+H$^+$] 251.0946, found 251.0938 [M+H$^+$].



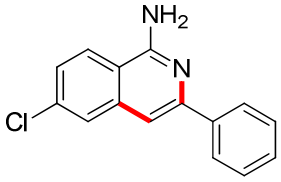
***N-tert*-Butyl-6-chloro-3-cyclohexylisoquinolin-1-amine (5ab)**

The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **4b** (148 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **5ab** (66 mg, 84%) as a colorless solid. M. p. = 116−118 °C. ^{1}H-NMR (Acetone-d_6, 400 MHz): δ = 8.07 (d, J = 8.9 Hz, 1H), 7.64 (d, J = 2.1 Hz, 1H), 7.29 (dd, J = 8.9, 2.1 Hz, 1H), 6.71 (s, 1H), 6.07 (s, 1H), 2.59 (tt, J = 11.7, 3.4 Hz, 1H), 1.94 (dd, J = 13.4, 1.8 Hz, 2H), 1.90 – 1.80 (m, 2H), 1.80 – 1.63 (m, 2H), 1.61 (s, 9H), 1.50 – 1.37 (m, 2H), 1.35 – 1.24 (m, 2H). ^{13}C-NMR (Acetone-d_6, 100 MHz): δ = 159.6, 154.5, 139.4, 134.6, 125.2, 124.8, 124.5, 115.7, 104.5, 51.6, 46.4, 32.7, 28.6, 26.5, 26.2. IR (ATR): 3452, 2923, 2360, 1614, 1431, 1236, 809, 669 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{19}H_{26}ClN_2$ [M+H$^+$] 317.1777, found317.1779 [M+H$^+$].



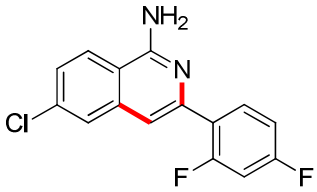
***N*-*tert*-Butyl-9-chloro-1,2,3,4-tetrahydrophenanthridin-6-amine (5ac)**

The general procedure was followed using **1a** (53.0 mg, 0.25 mmol) and **4c** (66.0 mg, 0.50 mmol) for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 50:1) yielded **5ac** (15 mg, 21%) as a colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.69 (d, J = 1.9 Hz, 1H), 7.58 (d, J = 8.8 Hz, 1H), 7.28 (dd, J = 8.8, 1.9 Hz, 1H), 4.89 (s, 1H), 2.83 (t, J = 5.2 Hz, 2H), 2.78 (t, J = 5.2 Hz, 2H), 1.92 – 1.82 (m, 4H), 1.56 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 152.2, 149.5, 138.1, 135.2, 124.5, 123.4, 121.8, 115.6, 112.3, 51.8, 29.7, 29.2, 24.3, 23.2, 23.1. IR (ATR): 2922, 1607, 1515, 1233, 759 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{17}H_{22}ClN_2$ [M+H$^+$] 289.1466, found 289.1463 [M+H$^+$].



6-Chloro-3-phenylisoquinolin-1-amine (6a)

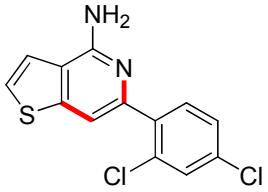
A suspension of *N*-*tert*-butyl-6-chloro-3-phenylisoquinolin-1-amine (**3aa**) (93.0 mg, 0.30 mmol) and *tert*-butyl-dimethylsilyl trifluormethansulfonate (TBDMSOTf, 79.0 mg, 0.30 mmol, 1.0 mol %) in CH_2Cl_2 (5.0 mL) was stirred at 25 °C for 8 h. The reaction mixture was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over Na_2SO_4 and filtered. The solvent was concentrated *in vacuo* and purification by column chromatography (*n*-Hexane/EtOAc/Et_3N 1:1/0.05) yielded **6a** (59 mg, 77%) as a slight yellow solid. M. p. = 154−157 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.04 – 7.99 (m, 2H), 7.69 (d, J = 2.0 Hz, 1H), 7.65 (d, J = 8.8 Hz, 1H), 7.48 – 7.43 (m, 2H), 7.41 – 7.35 (m, 1H), 7.34 (s, 1H), 7.32 (dd, J = 8.8, 2.0 Hz, 1H), 5.32 (br s, 2H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 155.9, 150.9, 139.5, 139.3, 136.4, 128.7, 128.6, 126.9, 126.5, 126.3, 124.4, 115.1, 108.0. IR (ATR): 2360, 1613, 1246, 870, 693 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{15}H_{12}ClN_2$ [M+H$^+$] 255.0689, found 255.0692 [M+H$^+$].



6-Chloro-3-(2,4-difluorophenyl)isoquinolin-1-amine (6b)

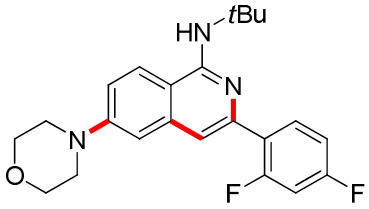
A suspension of *N*-*tert*-butyl-6-chloro-3-(2,4-difluorophenyl)isoquinolin-1-amine (**3ab**) (69.0 mg, 0.20 mmol) and *tert*-butyl-dimethylsilyl trifluormethansulfonate (TBDMSOTf, 53.0 mg, 0.20 mmol, 1.0 mol %) in CH_2Cl_2 (5.0 mL) was stirred at 25 °C for 8 h. The reaction mixture was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over Na_2SO_4 and filtered. The solvent was concentrated *in vacuo* and purification by column chromatography (*n*-Hexane/EtOAc/Et_3N 1:1/0.05) yielded **6b** (50 mg, 86%) as a slight yellow solid. M. p. = 176−178 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.06 (dd, J = 15.6, 8.2 Hz, 1H), 7.78 – 7.68 (m, 2H), 7.50 – 7.39 (m, 2H), 7.04 – 6.85 (m, 2H), 5.23 (br s, 2H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 162.8 (dd, $^1J_{C\text{-}F}$ = 251.5 Hz, $^3J_{C\text{-}F}$ = 13.7 Hz), 160.7 (dd, $^1J_{C\text{-}F}$ = 253.4 Hz, $^3J_{C\text{-}F}$ = 11.9 Hz), 155.7, 145.2, 139.0, 136.6, 132.0 (dd, $^3J_{C\text{-}F}$ = 9.4 Hz, $^4J_{C\text{-}F}$ = 4.2 Hz), 127.1, 126.6, 124.2, 123.7 (dd, $^3J_{C\text{-}F}$ = 11.6 Hz, $^4J_{C\text{-}F}$ = 3.8 Hz), 115.1, 112.1 (d, $^3J_{C\text{-}F}$ = 10.4

Hz), 111.6 (dd, $^{2}J_{C\text{-}F}$ = 20.5 Hz, $^{4}J_{C\text{-}F}$ = 3.1 Hz), 104.4 (dd, $^{1}J_{C\text{-}F}$ = 27.8 Hz, $^{3}J_{C\text{-}F}$ = 24.5 Hz). ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -110.15 (d, J = 8.5 Hz), -111.28 (d, J = 8.5 Hz). IR (ATR): 2360, 1613, 1246, 870, 693 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{15}H_{12}ClN_2$ [M+H$^+$] 291.0496, found 291.0503 [M+H$^+$].



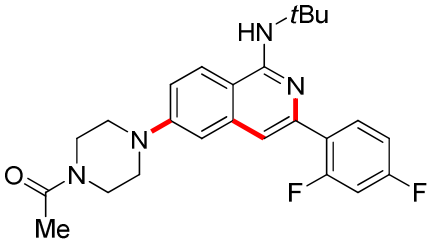
6-(2,4-Dichlorophenyl)thieno[3,2-*c*]pyridin-4-amine (**6c**)

A suspension of *N*-*tert*-butyl-6-(2,4-dichlorophenyl)thieno[3,2-*c*]pyridin-4-amine (**3nk**) (70.0 mg, 0.20 mmol) and *tert*-butyl-dimethylsilyl trifluormethansulfonate (TBDMSOTf, 53.0 mg, 0.20 mmol, 1.0 mol %) in CH_2Cl_2 (5.0 mL) was stirred at 25 °C for 8 h. The reaction mixture was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over Na_2SO_4 and filtered. The solvent was concentrated *in vacuo* and purification by column chromatography (*n*-Hexane/EtOAc/Et_3N 1:1/0.05) yielded **6c** (50 mg, 85%) as a slight yellow solid. M. p. = 160−162 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.55 (d, J = 8.3 Hz, 1H), 7.49 (d, J = 2.0 Hz, 1H), 7.48 (s, 1H), 7.41 (d, J = 5.5 Hz, 1H), 7.32 (dd, J = 8.3, 2.0 Hz, 1H), 7.28 (d, J = 5.5 Hz, 1H), 5.03 (br s, 2H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 153.1, 148.5, 148.0, 138.1, 134.2, 133.1, 132.5, 129.9, 127.2, 125.6, 121.3, 119.7, 109.7. IR (ATR): 3306, 2360, 1628, 1416, 1247, 1105, 820, 697 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{13}H_9Cl_2N_2S$ [M+H$^+$] 294.9858, found 294.9855 [M+H$^+$].



***N-tert*-Butyl-3-(2,4-difluorophenyl)-6-morpholinoisoquinolin-1-amine (8a)**

A suspension of 6-bromo-*N*-*tert*-butyl-3-(2,4-difluorophenyl)isoquinolin-1-amine (**3cb**) (39.0 mg, 0.10 mmol) and $Pd_2(dba)_3$ (4.6 mg, 5.0 mol %), XantPhos (6.0 mg, 10 mol %), NaO^{t}Bu (19.2 mg, 2.0 equiv), morpholine (**7a**, 17.0 mg, 2.0 equiv) in PhMe (1.0 mL) was stirred at 80 °C for 12 h.[5] At ambient temperature, the reaction mixture was extracted with EtOAc (3×10 mL). The combined organic layers were dried over Na_2SO_4 and filtered. The solvent was concentrated *in vacuo* and purification by column chromatography (*n*-Hexane/EtOAc 5:1) yielded **8a** (28 mg, 71%, calculated from **1c**) as a colorless solid. M. p. = 139−141 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.24 (td, J = 8.9, 7.0 Hz, 1H), 7.58 (d, J = 9.1 Hz, 1H), 7.38 (d, J = 2.5 Hz, 1H), 7.11 (dd, J = 9.1, 2.5 Hz, 1H), 7.03 – 6.95 (m, 2H), 6.92 – 6.86 (m, 1H), 5.03 (s, 1H), 3.93 – 3.86 (m, 4H), 3.33 – 3.25 (m, 4H), 1.62 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 162.3 (dd, $^1J_{C\text{-}F}$ = 248.9 Hz, $^3J_{C\text{-}F}$ =12.4 Hz), 160.9 (dd, $^1J_{C\text{-}F}$ = 252.7 Hz, $^3J_{C\text{-}F}$ =11.8 Hz), 153.9, 151.7, 143. 9 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 139.3, 132.0 (dd, $^3J_{C\text{-}F}$ = 9.4 Hz, $^4J_{C\text{-}F}$ = 4.9 Hz), 124.9 (dd, $^3J_{C\text{-}F}$ = 10.8 Hz, $^4J_{C\text{-}F}$ = 3.7 Hz), 122.5, 116.9, 112.1, 111.3 (dd, $^2J_{C\text{-}F}$ = 20.9 Hz, $^4J_{C\text{-}F}$ = 3.6 Hz), 110.5 (d, $^3J_{C\text{-}F}$ = 12.7 Hz), 109.8, 104.17 (dd, $^2J_{C\text{-}F}$ = 27.8 Hz, $^2J_{C\text{-}F}$ = 25.2 Hz), 66.8, 51.7, 48.8, 29.4. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -110.5 (d, J = 8.2 Hz), -111.9 (d, J = 8.2 Hz). IR (ATR): 3442, 2978, 1673, 1651, 1540, 1295 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{23}H_{26}F_2N_3O$ [M+H$^+$] 398.2049, found 398.2044 [M+H$^+$].



1-{4-[1-(*tert*-Butylamino)-3-(2,4-difluorophenyl)isoquinolin-6-yl]piperazin-1-yl}ethanone (8b)

A suspension of 6-bromo-*N*-*tert*-butyl-3-(2,4-difluorophenyl)isoquinolin-1-amine (**3cb**) (39.0 mg, 0.10 mmol) and $Pd_2(dba)_3$ (4.6 mg, 5.0 mol %), XantPhos (6.0 mg, 10 mol %), NaO^{t}Bu (19.2 mg, 2.0 equiv), *N*-acetylpiperazine (**7b**, 26.0 mg, 2.0 equiv) in PhMe (1.0 mL) was stirred at 80 °C for 12 h.[5] At ambient temperature, the reaction mixture was extracted with

EtOAc (3×10 mL). The combined organic layers were dried over Na_2SO_4 and filtered. The solvent was concentrated *in vacuo* and purification by column chromatography (*n*-Hexane/EtOAc/Et_3N 3:1:0.05) yielded **8b** (30 mg, 68%, calculated from **1c**) as a colorless solid. M. p. = 176−177 °C. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 8.24 (dd, J = 16.0, 8.7 Hz, 1H), 7.59 (d, J = 9.0 Hz, 1H), 7.38 (s, 1H), 7.11 (d, J = 9.0 Hz, 1H), 7.02 – 6.83 (m, 3H), 5.05 (s, 1H), 3.80 (t, J = 4.7 Hz, 2H), 3.64 (t, J = 4.7 Hz, 2H), 3.36 – 3.18 (m, 4H), 2.15 (s, 3H), 1.62 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 169.1, 162.3 (dd, $^1J_{C\text{-}F}$ = 249.0 Hz, $^3J_{C\text{-}F}$ =12.5 Hz), 160.9 (dd, $^1J_{C\text{-}F}$ = 252.2 Hz, $^3J_{C\text{-}F}$ = 11.5 Hz), 153.9, 151.2, 144.0, 139.3, 132.0 (dd, $^3J_{C\text{-}F}$ = 9.6 Hz, $^4J_{C\text{-}F}$ = 4.5 Hz), 124.8 (dd, $^3J_{C\text{-}F}$ = 10.7 Hz, $^4J_{C\text{-}F}$ = 2.6 Hz), 122.6, 117.5, 112.2, 111.3 (dd, $^2J_{C\text{-}F}$ = 20.4 Hz, $^4J_{C\text{-}F}$ = 2.3 Hz), 110.5, 110.4 (d, $^3J_{C\text{-}F}$ = 12.6 Hz), 104.2 (dd, $^2J_{C\text{-}F}$ = 27.7 Hz, $^2J_{C\text{-}F}$ = 25.9 Hz), 51.7, 48.9, 48.7, 46.0, 41.2, 29.4, 21.3. ^{19}F-NMR ($CDCl_3$, 376 MHz): δ = -110.51 (d, J = 8.3 Hz), -111.74 (d, J = 8.2 Hz). IR (ATR): 3423, 2969, 1643, 1551, 1340, 1205 cm^{-1}. HR-MS (ESI) m/z calcd for $C_{25}H_{29}F_2N_4O$ [M+H$^+$] 439.2304, found 439.2302 [M+H$^+$].

References:

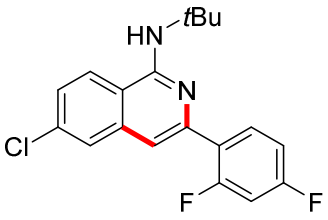
[1] J. Li, M. John and L. Ackermann, *Chem. – Eur. J*. 2014, **20**, 5403.

[2] (a) H. Kikuri, K. Moriyama, H. Togo, *Synthesis* **2013**, *45*, 791. (b) S. Giboulot, F. Liron, G. Prestat, B. Wahl, M. Sauthier, Y. Castanet, A. Mortreux, G. Poli. *Chem. Commun*. **2012**, *48*, 5889. (c) M. Remeš, J. Roithová, D. Schröder, E. D. Cope, C. Perera, S. N. Senadheera, K. Stensrud, C.-C. Ma, R. S. Givens, *J. Org. Chem*. **2011**, *76*, 2180. (d) M. Calter, A. Korotkv, *Org. lett*. **2011**, *13*, 6328. (e) N. Sakurai, T. Mukaiyama, *Chem. Lett*. **2008**, *37*, 388.

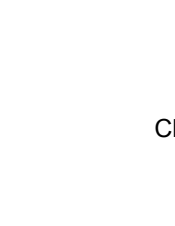
[3] K. Shin, J. Ryu, S. Chang, *Org. Lett*. **2014**, *16*, 2022.

[4] (a) C. White, A. Yates, P. M. Maitlis, *Inorg. Synth*. **1992**, *29*, 228. (b) C. White, S. J. Thompson, P. M. Maitlis, *J. C. S. Dalton* **1977**, 1654.

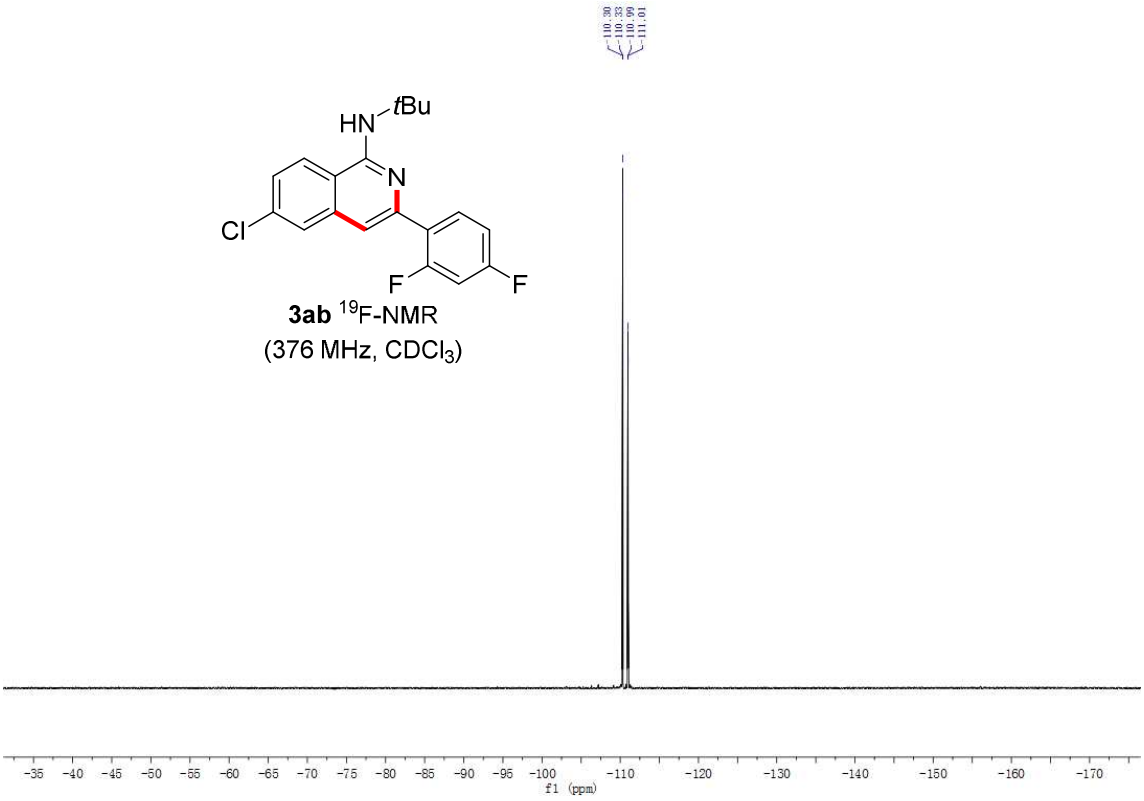
[5] P. Sun, Y. Wu, Y. Huang, X. Wu, J. Xu, H. Yao, A. Lin, *Org. Chem. Front*. 2016, **3**, 91.



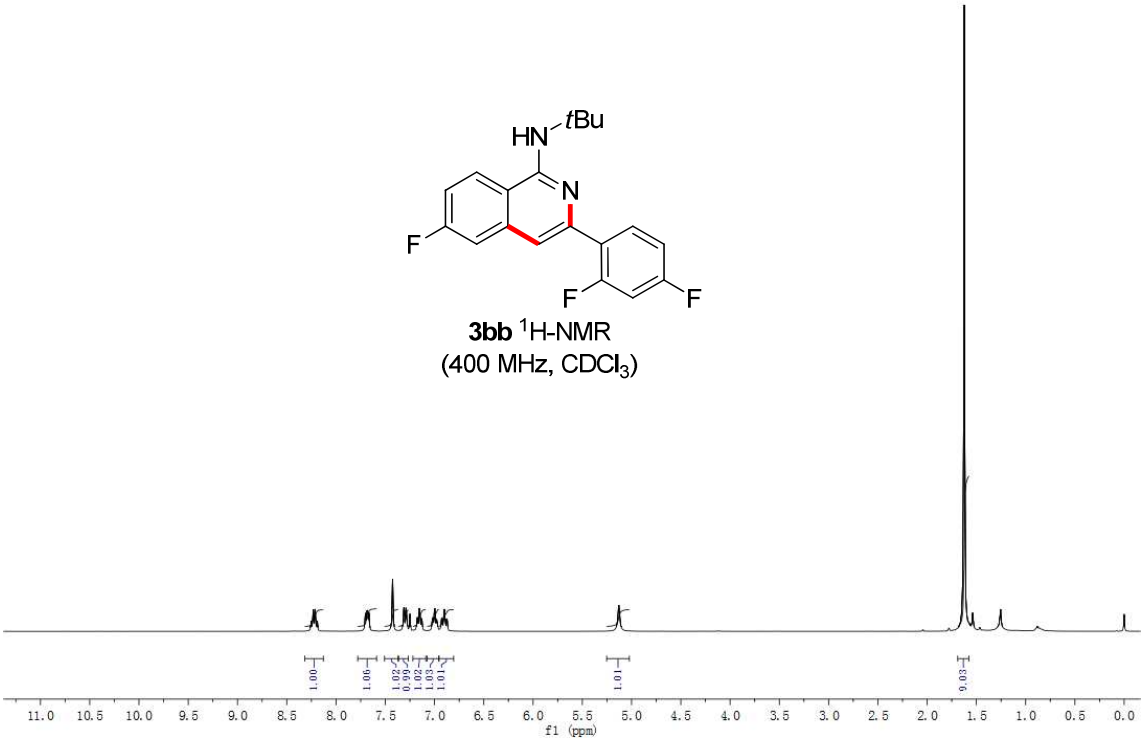
3ab ^{1}H-NMR
(400 MHz, $CDCl_3$)



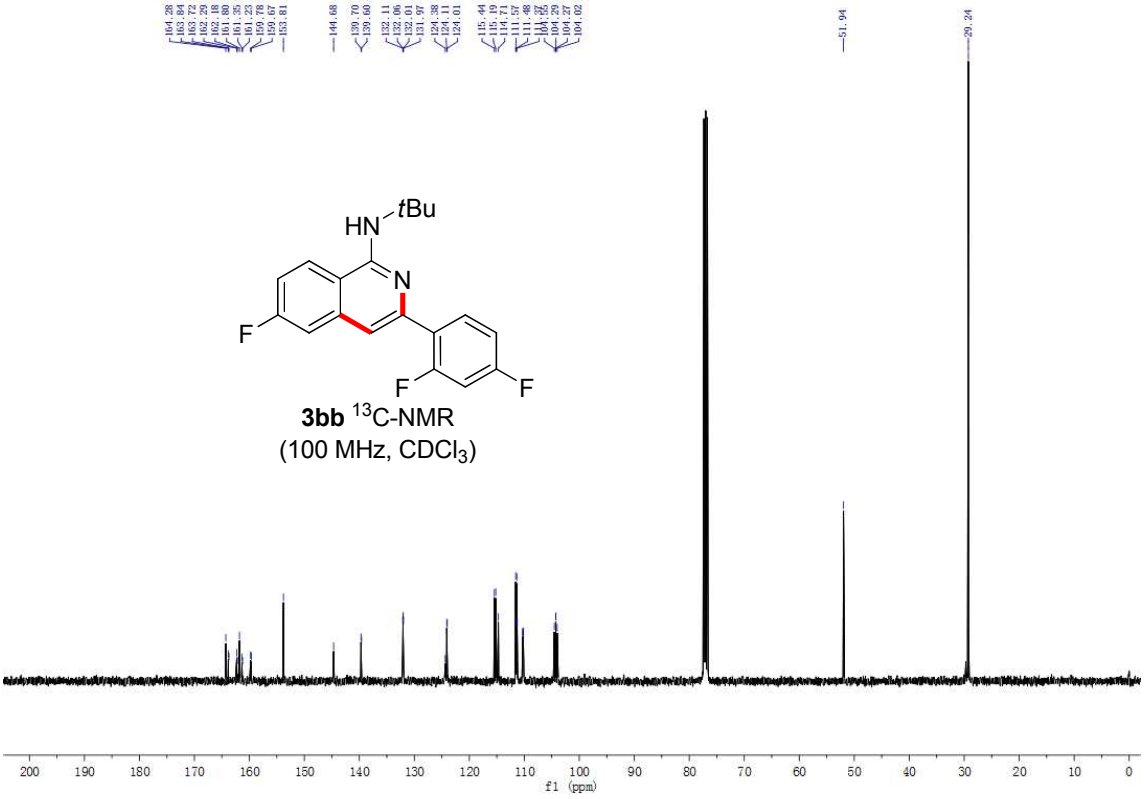
3ab ^{13}C-NMR
(100 MHz, $CDCl_3$)



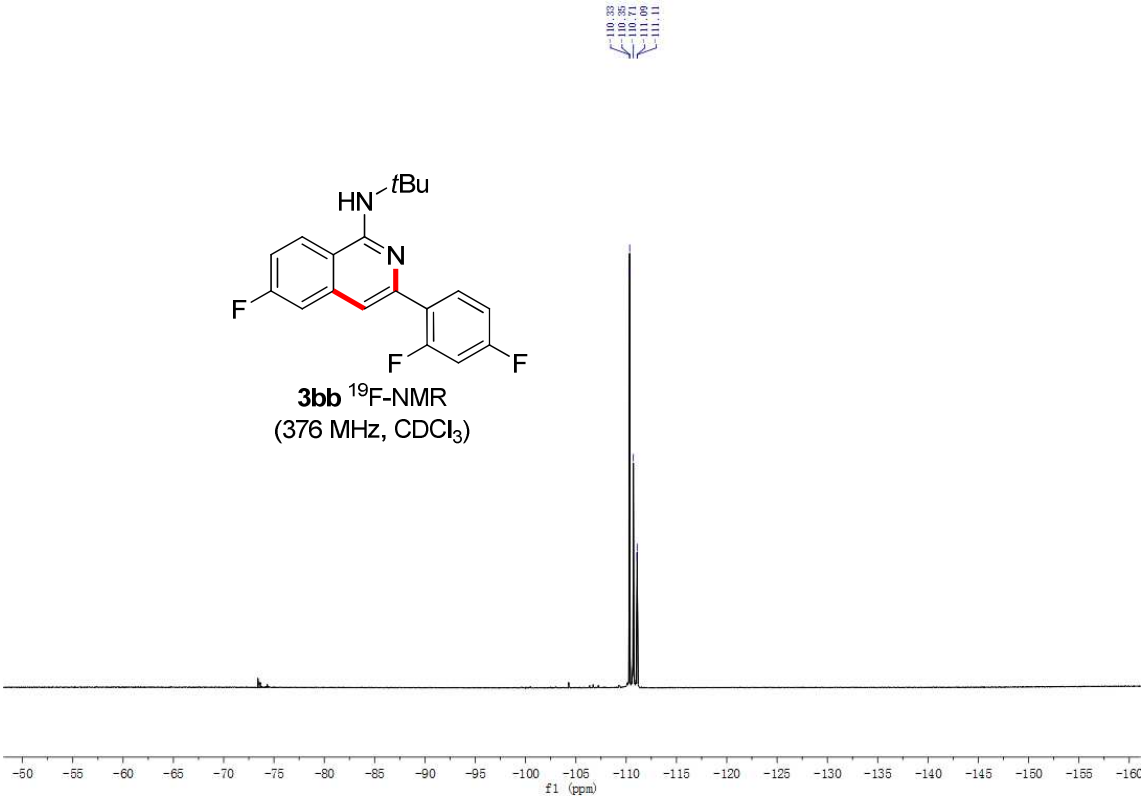
3ab ^{19}F-NMR
(376 MHz, $CDCl_3$)



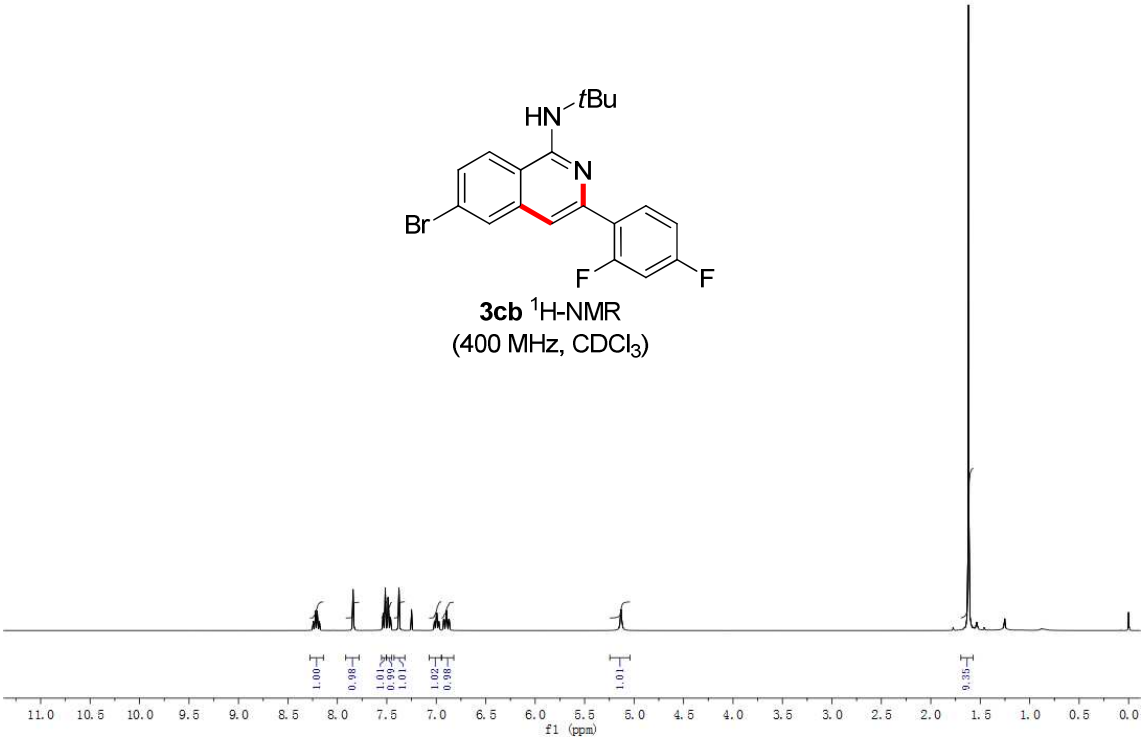
3bb ^{1}H-NMR
(400 MHz, $CDCl_3$)



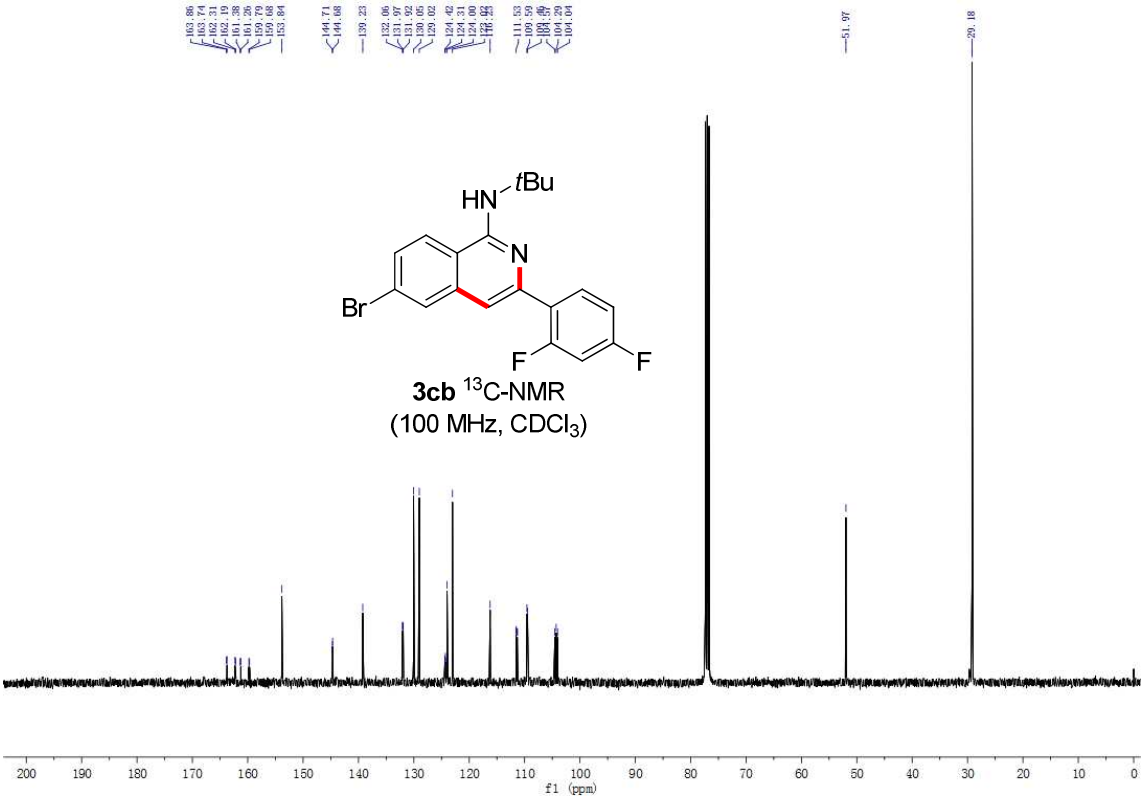
3bb ^{13}C-NMR
(100 MHz, $CDCl_3$)



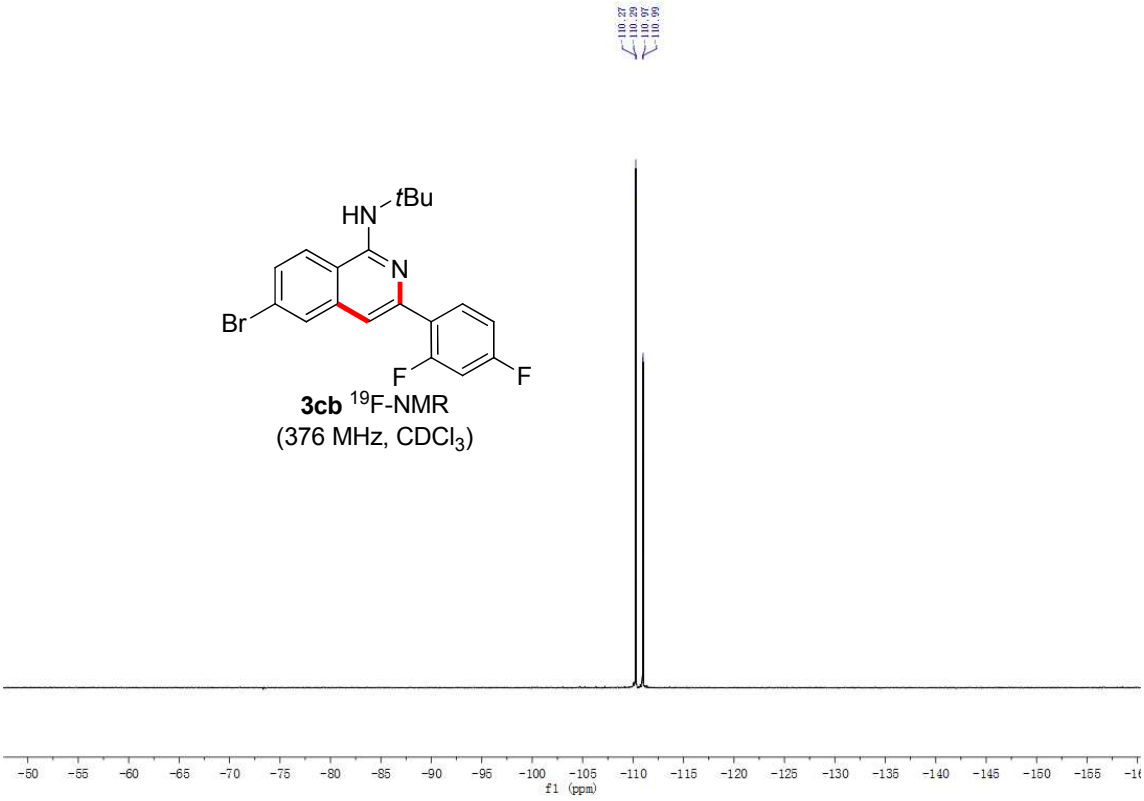
3bb ^{19}F-NMR
(376 MHz, $CDCl_3$)



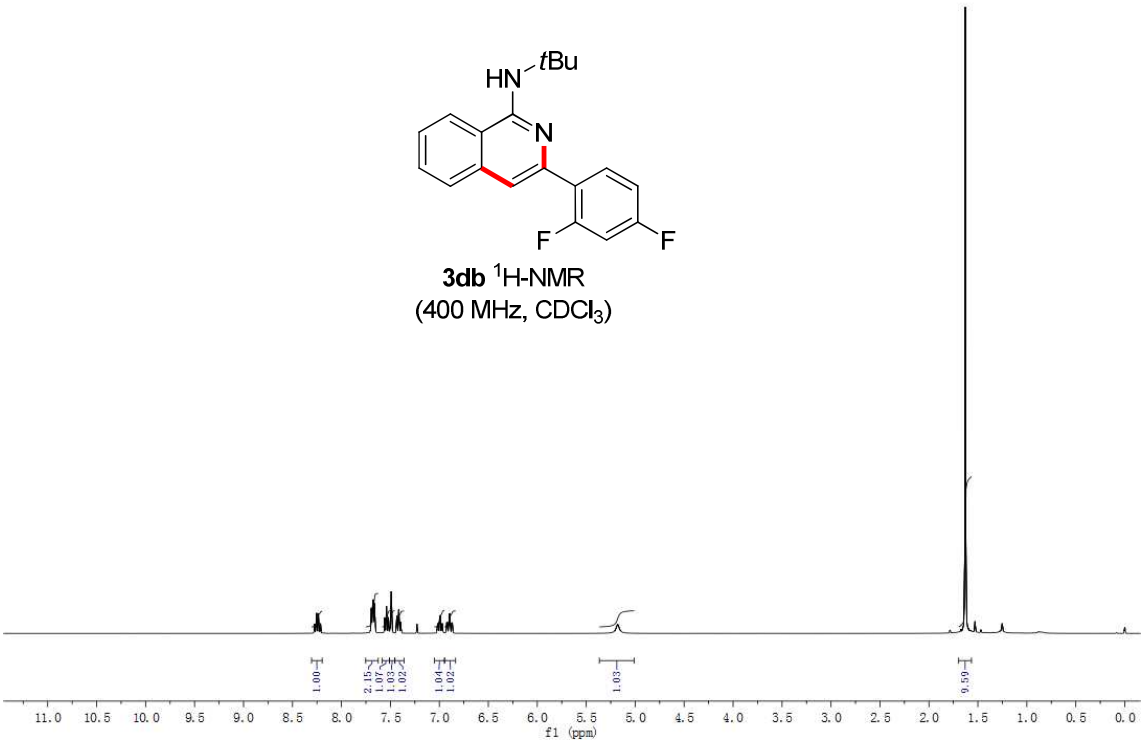
3cb ^{1}H-NMR
(400 MHz, $CDCl_3$)



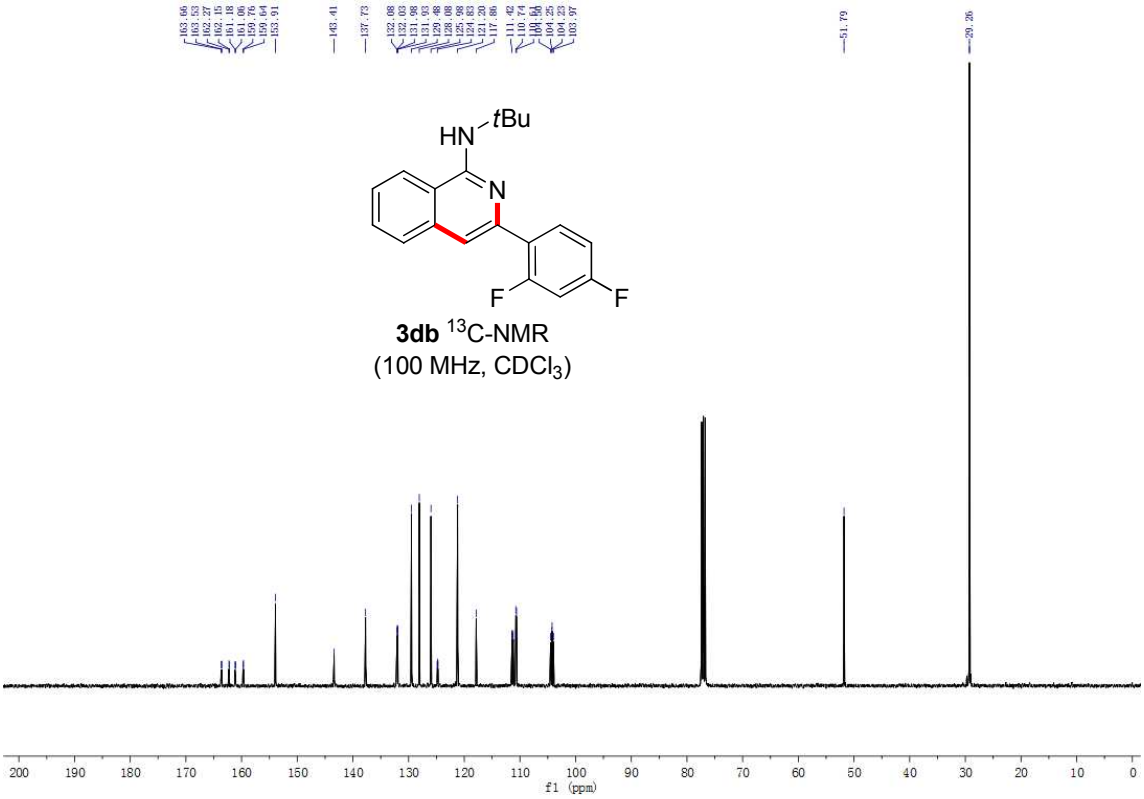
3cb ^{13}C-NMR
(100 MHz, $CDCl_3$)



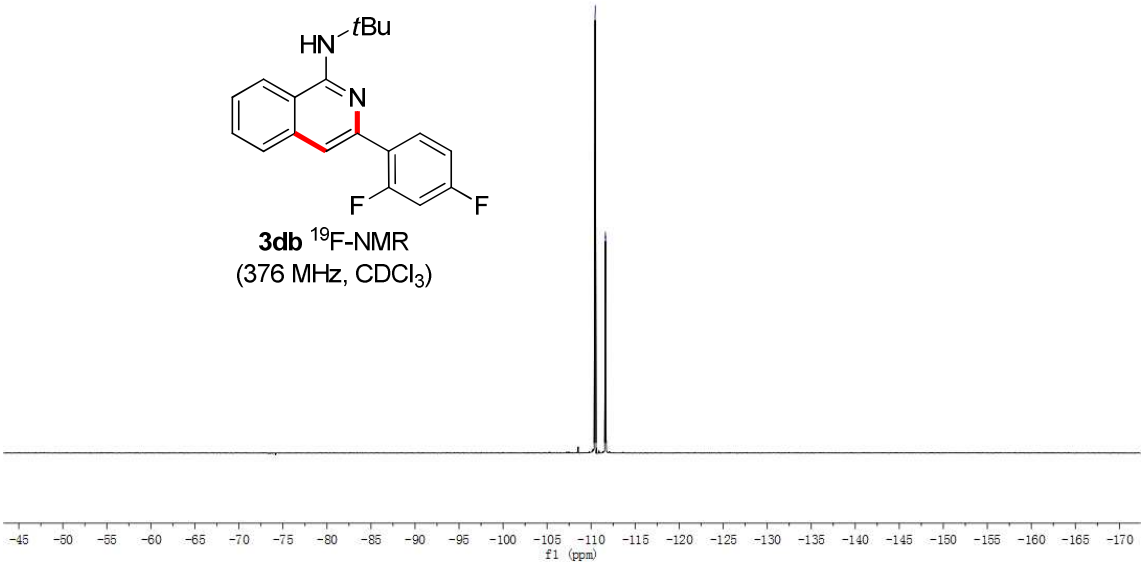
3cb ^{19}F-NMR
(376 MHz, $CDCl_3$)



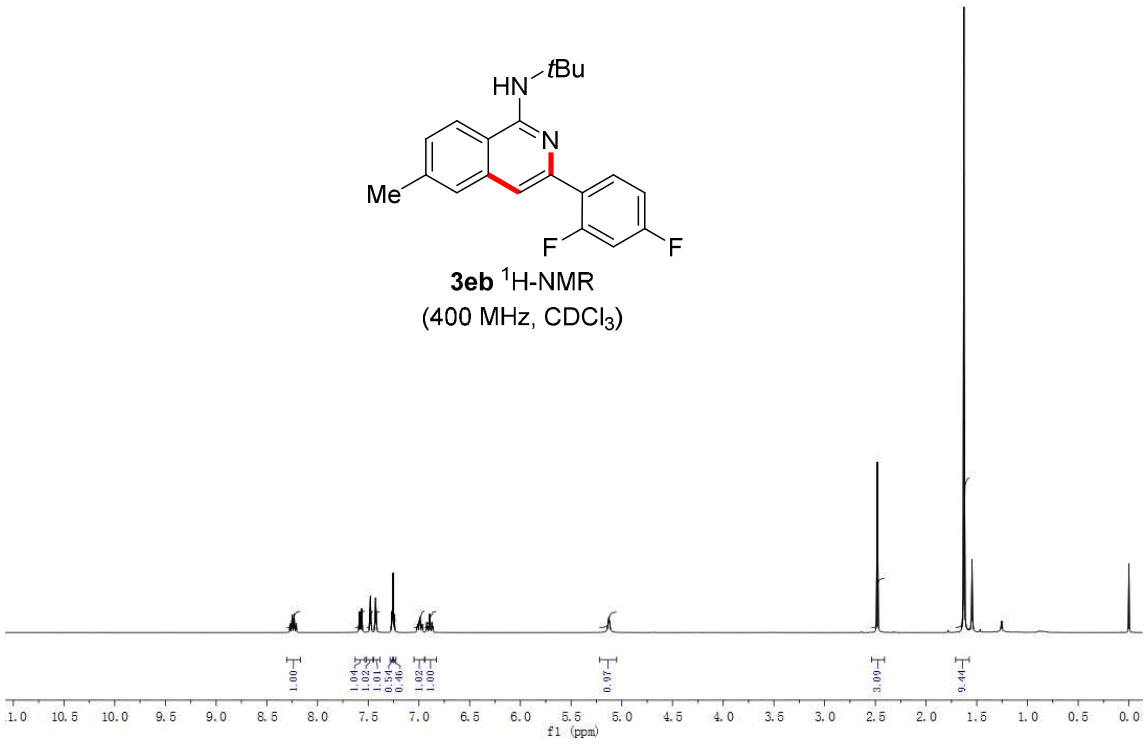
3db ^{1}H-NMR
(400 MHz, $CDCl_3$)



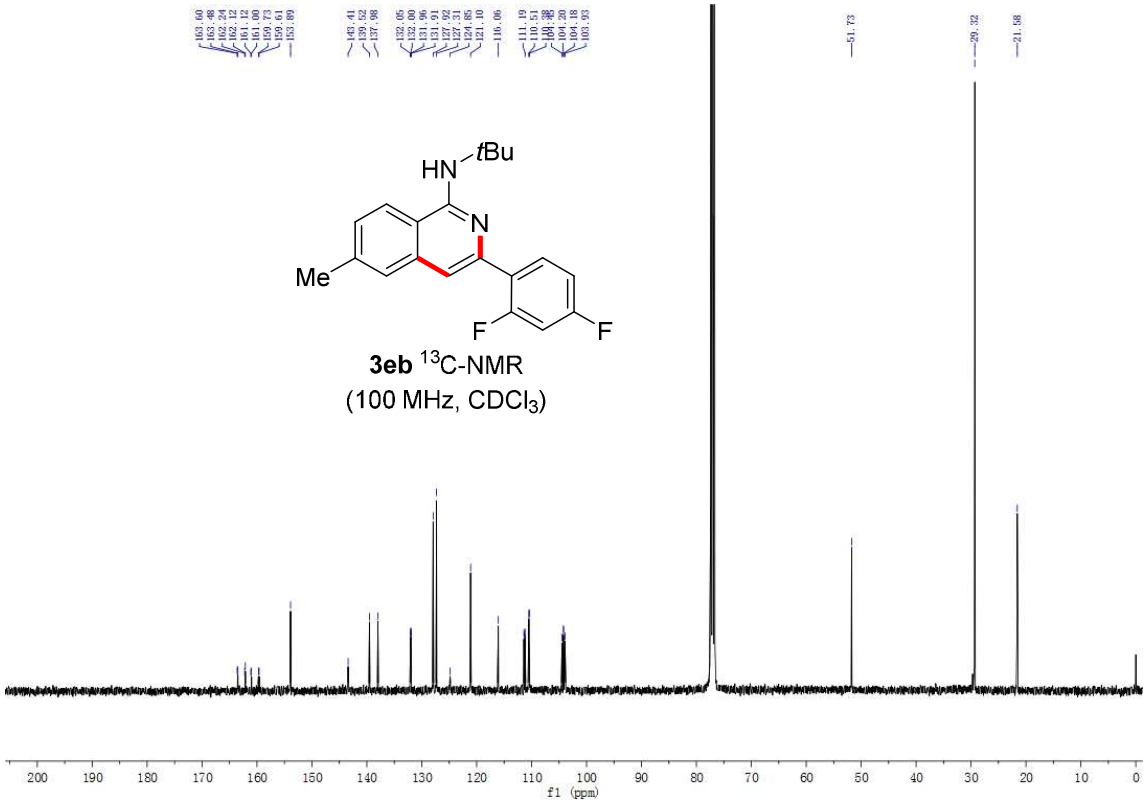
3db ^{13}C-NMR
(100 MHz, $CDCl_3$)



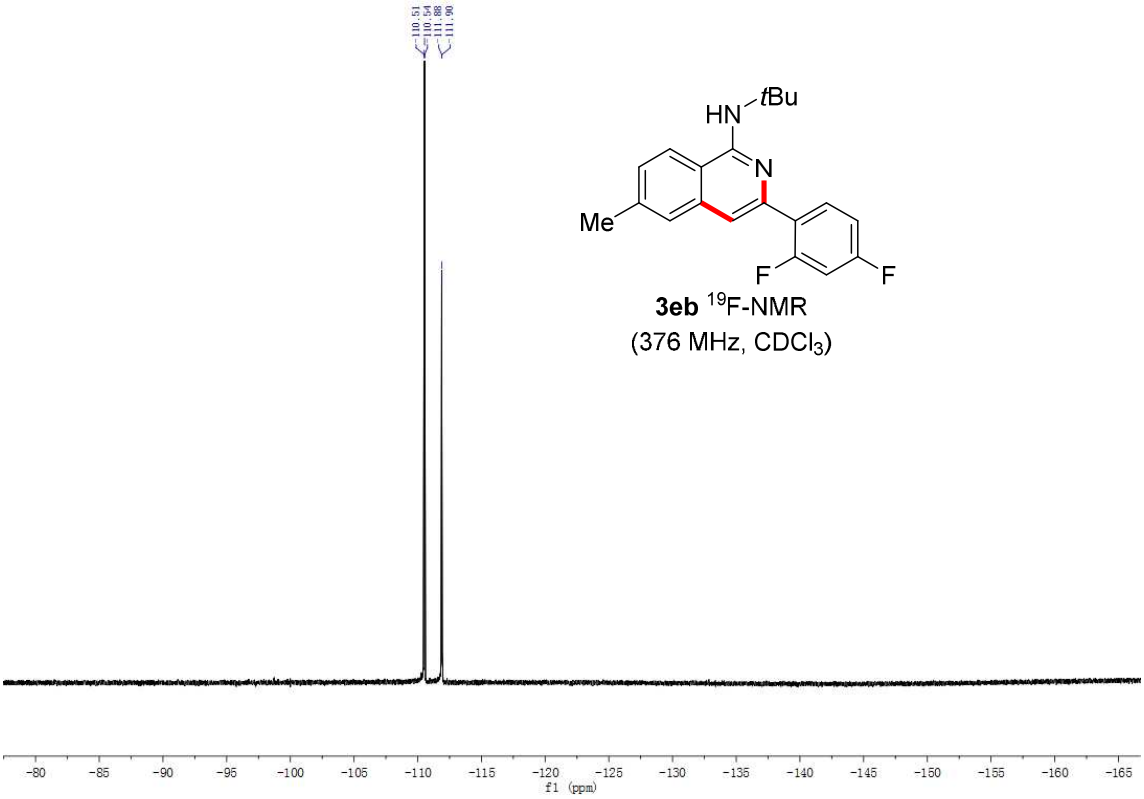
3db ^{19}F-NMR
(376 MHz, $CDCl_3$)



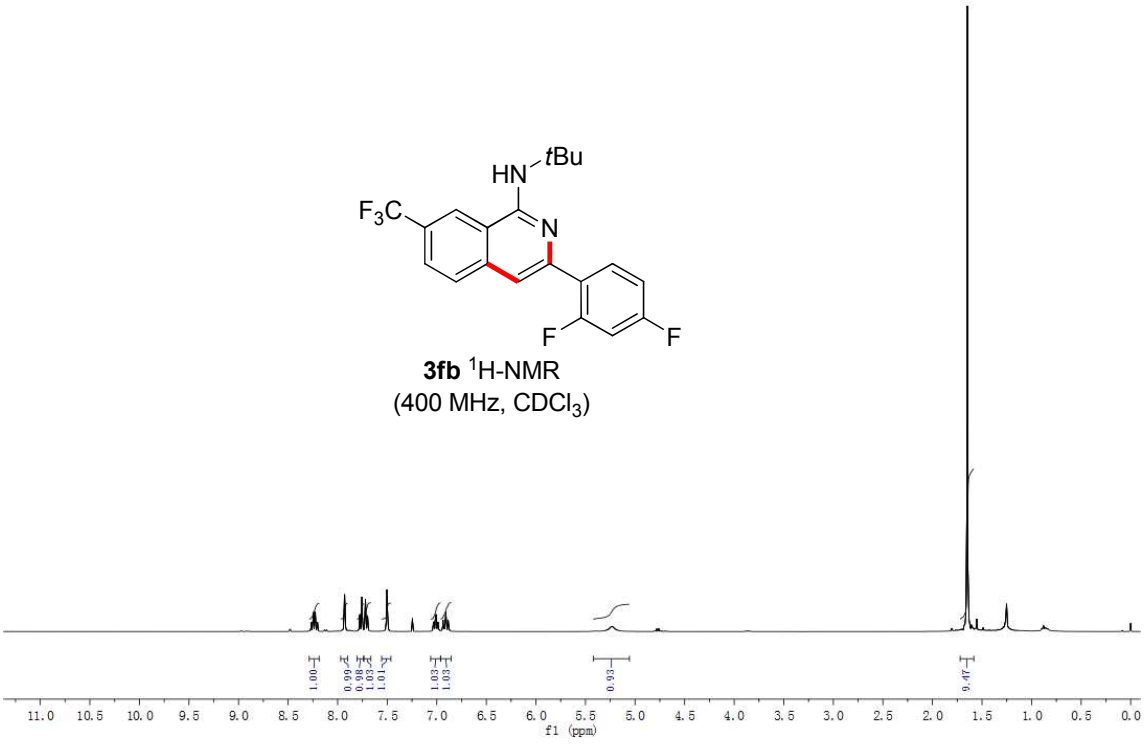
3eb ^{1}H-NMR
(400 MHz, $CDCl_3$)



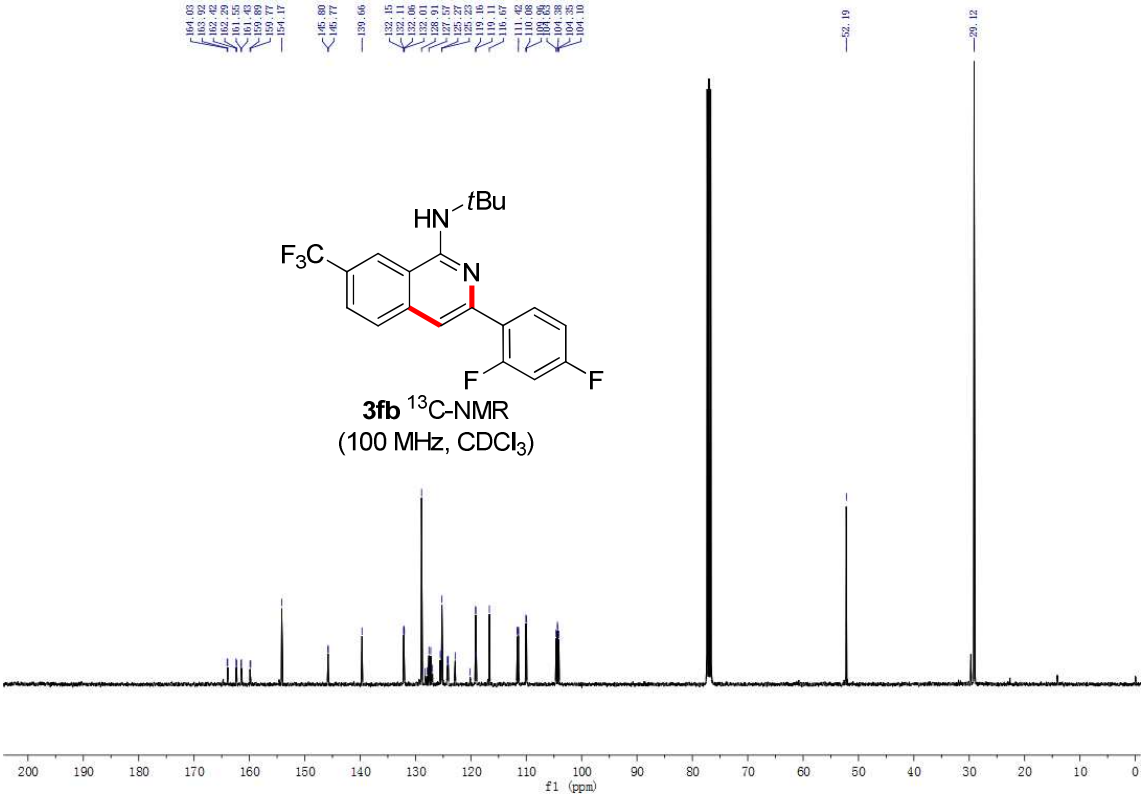
3eb ^{13}C-NMR
(100 MHz, $CDCl_3$)

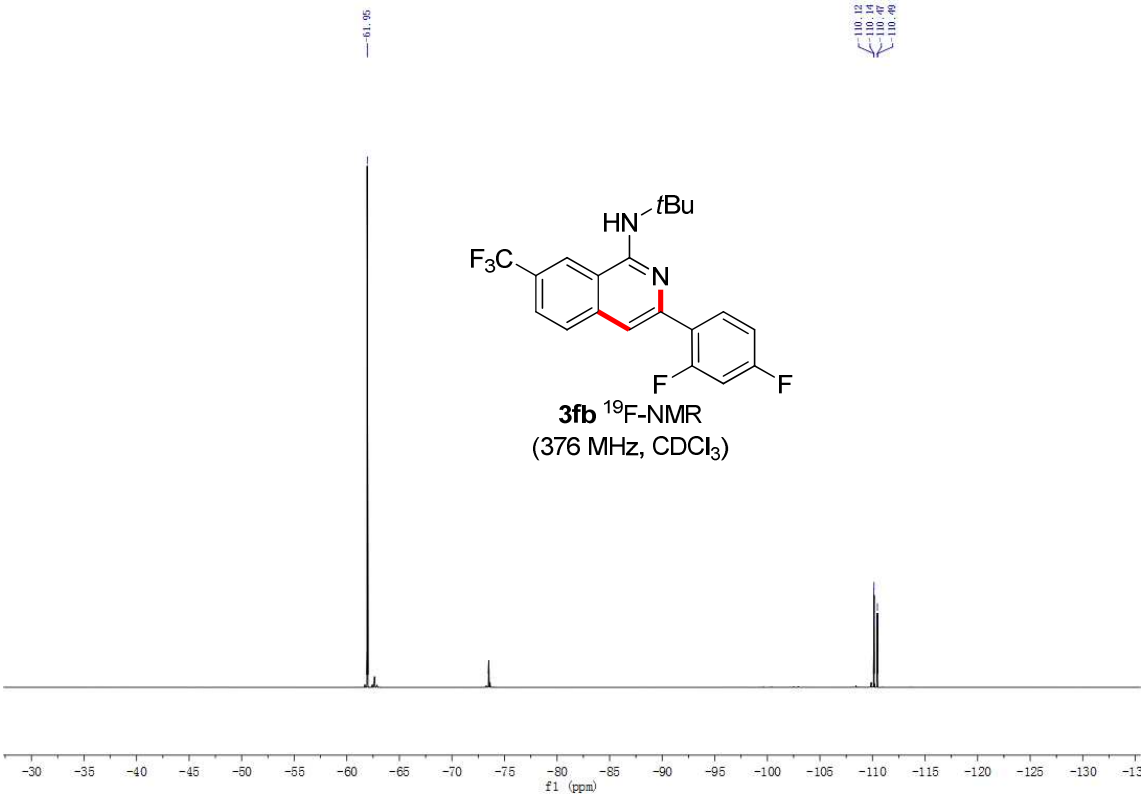


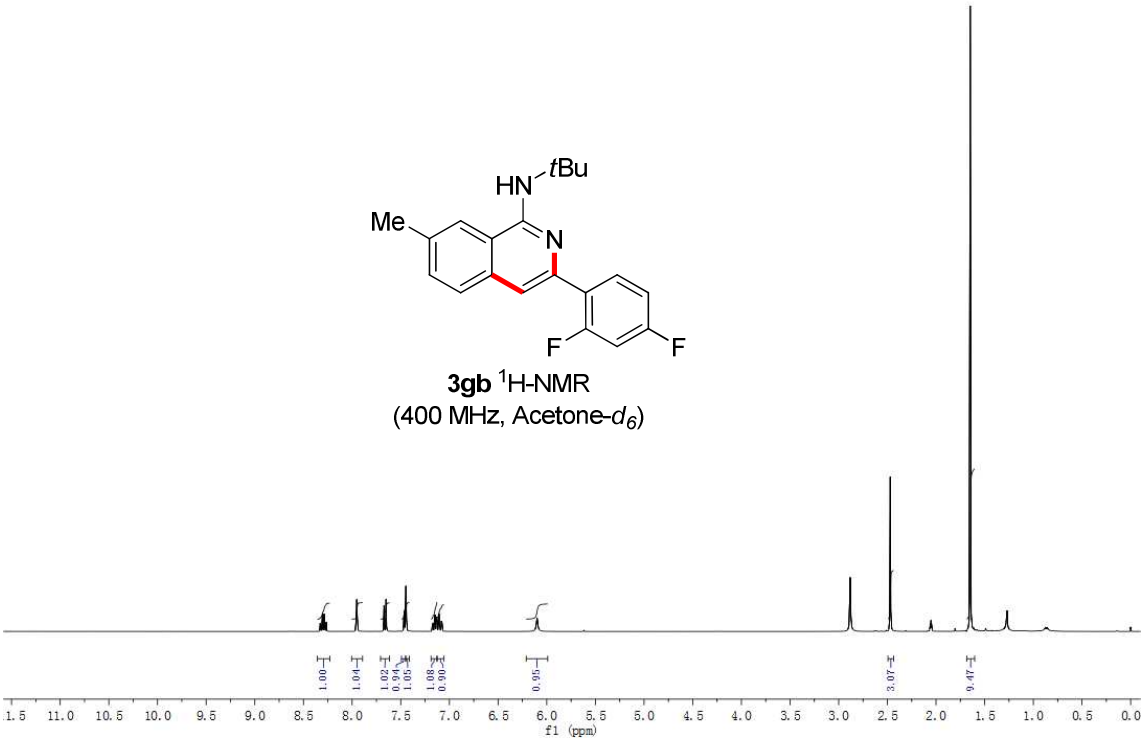
3eb ^{19}F-NMR
(376 MHz, $CDCl_3$)



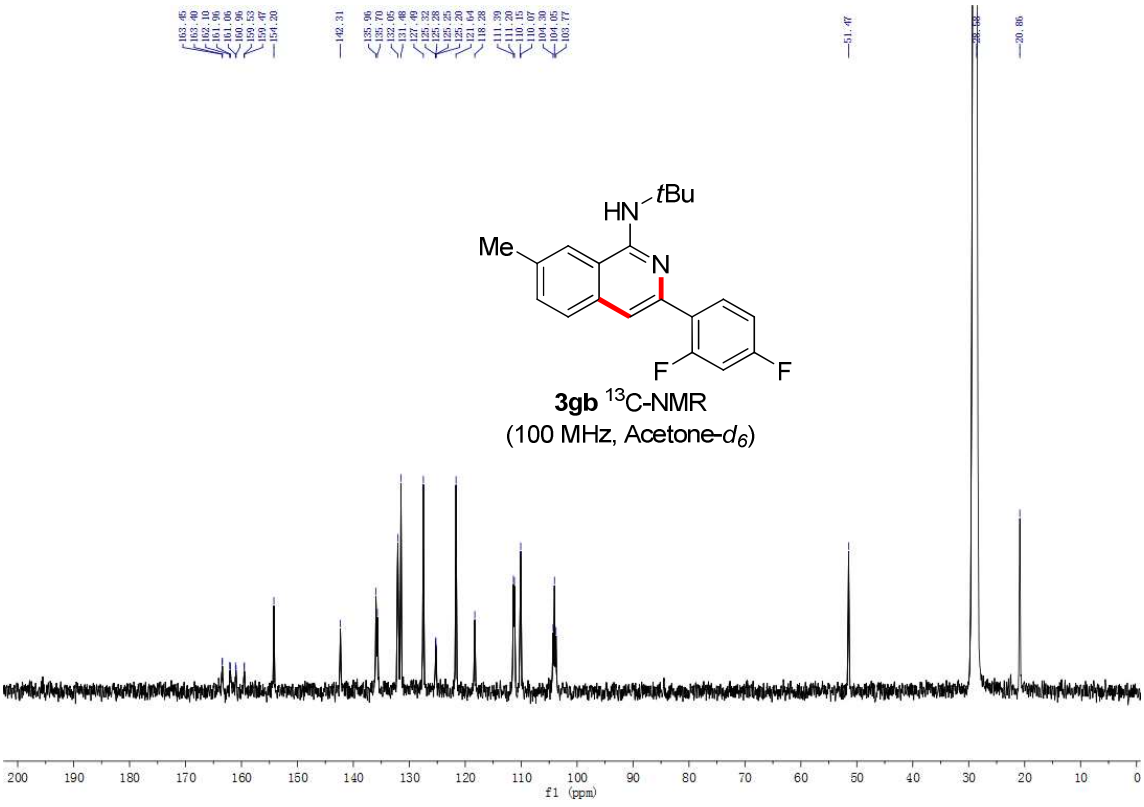
3fb ^{1}H-NMR
(400 MHz, $CDCl_3$)


HN
tBu
F3C
N
F
F
3fb 13C-NMR
(100 MHz, CDCl3)
f1 (ppm)

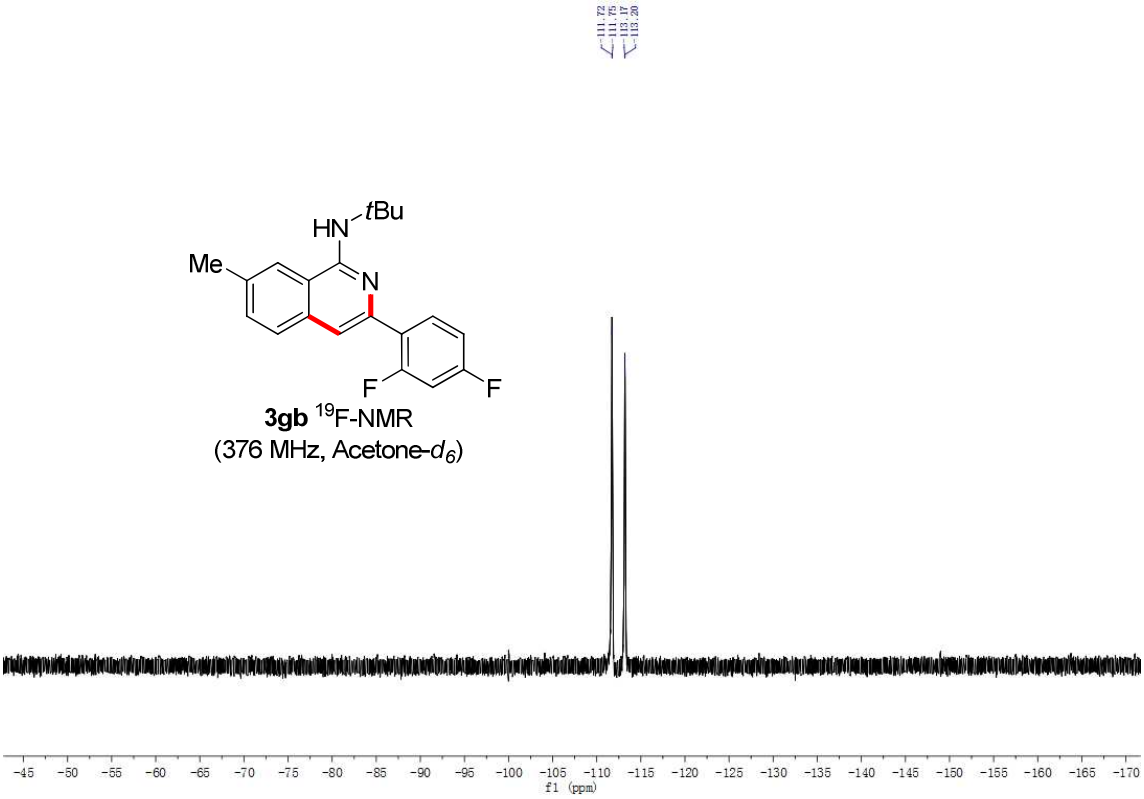

HN
tBu
F3C
N
F
F
3fb 19F-NMR
(376 MHz, CDCl3)
f1 (ppm)



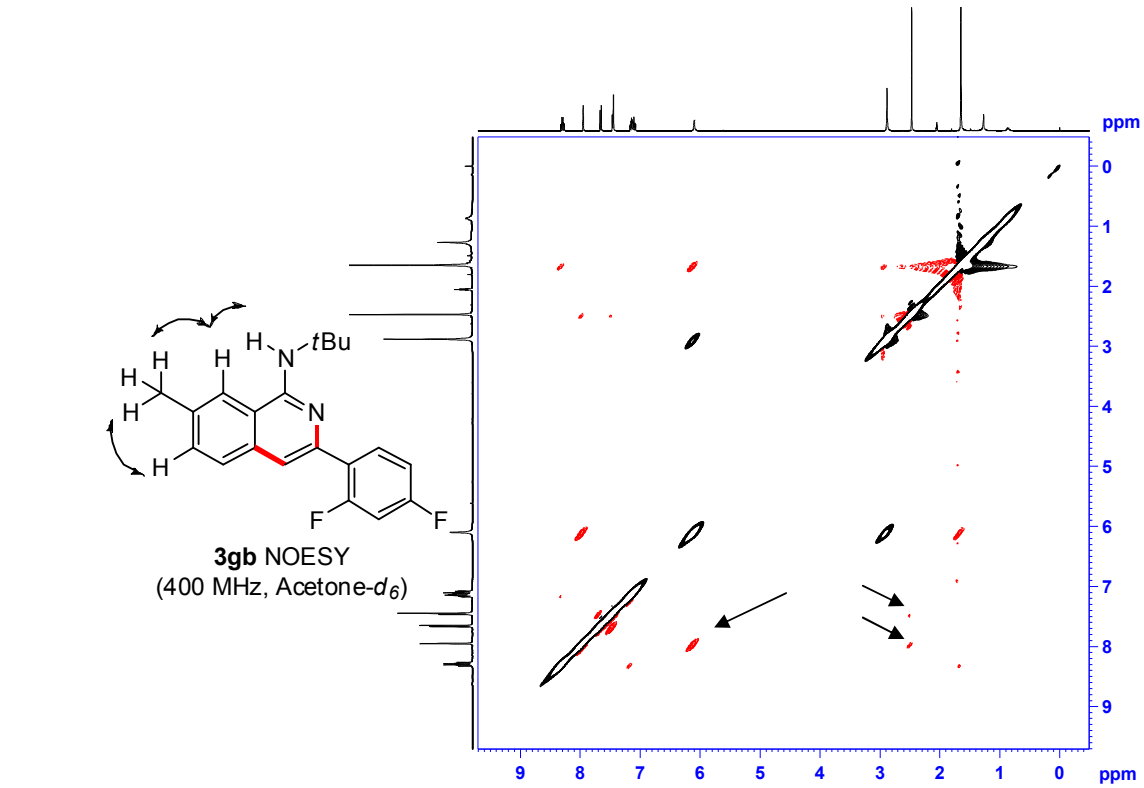
3gb ^{1}H-NMR
(400 MHz, Acetone-d_6)



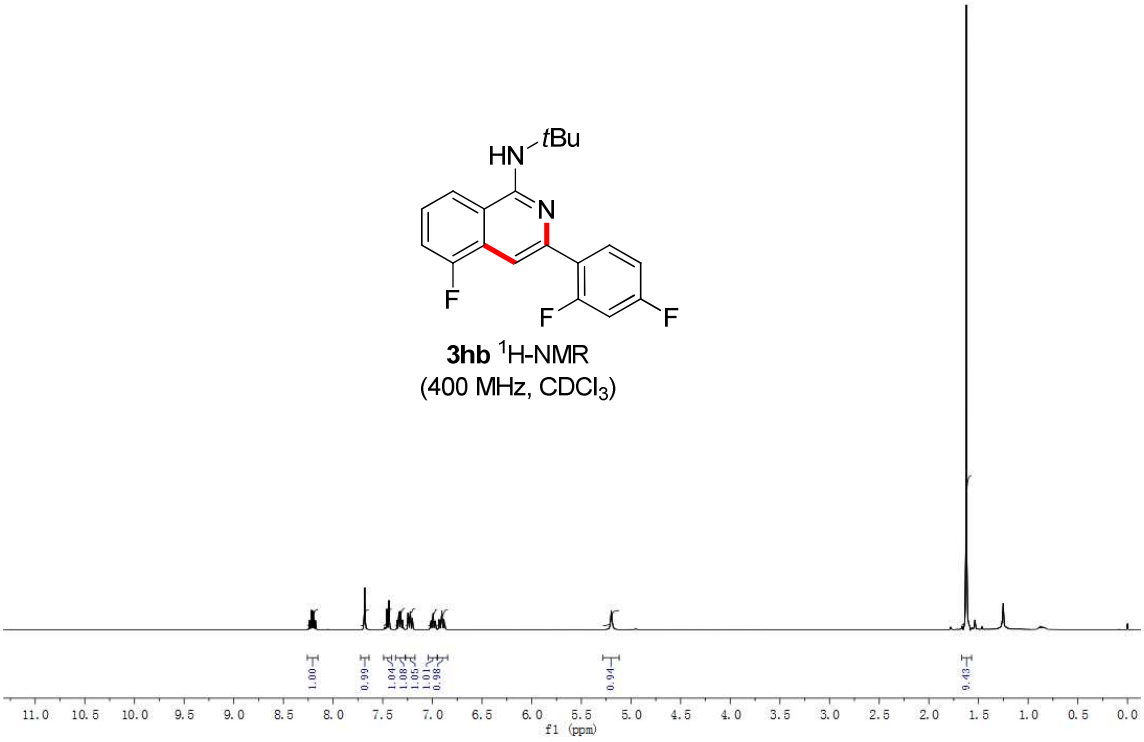
3gb ^{13}C-NMR
(100 MHz, Acetone-d_6)



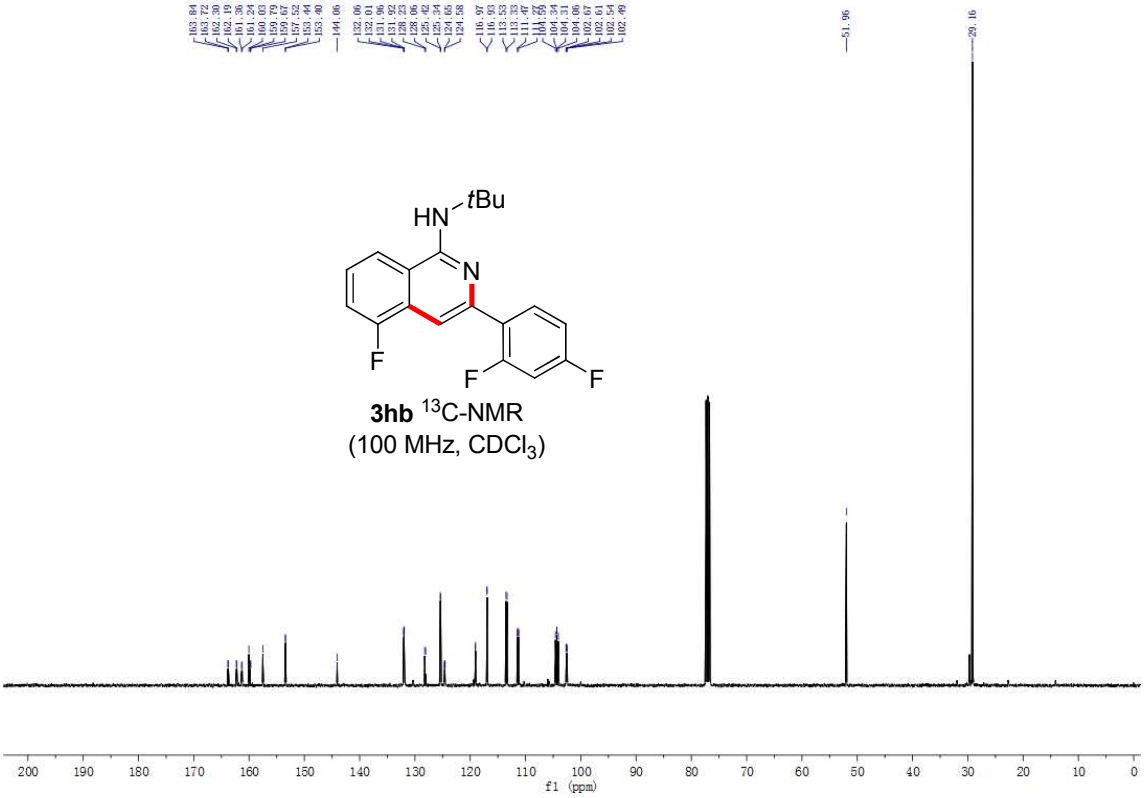
3gb ^{19}F-NMR
(376 MHz, Acetone-d_6)



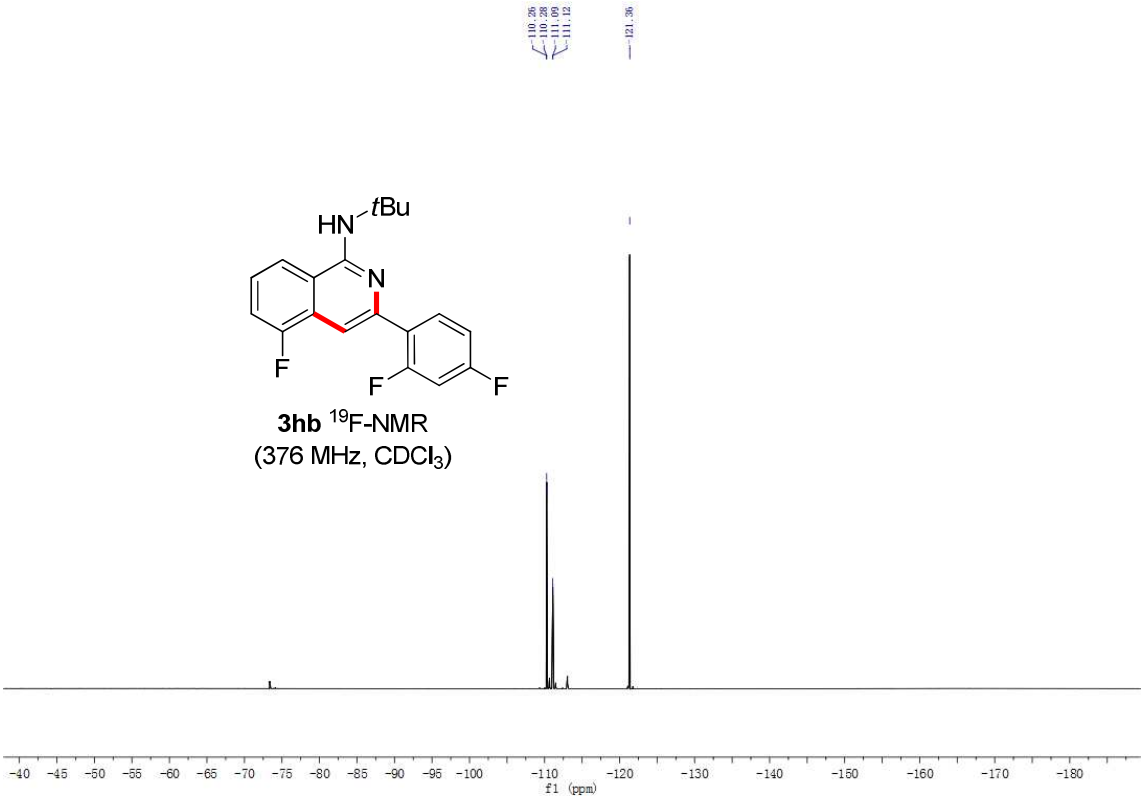
3gb NOESY
(400 MHz, Acetone-d_6)



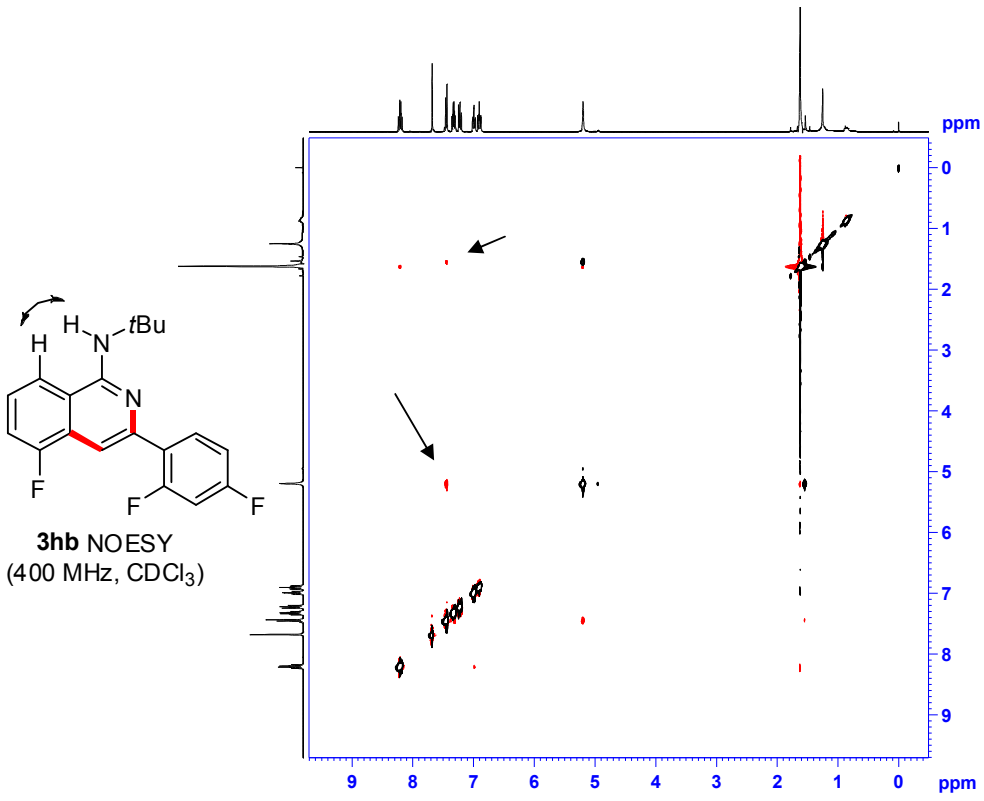
3hb ^{1}H-NMR
(400 MHz, $CDCl_3$)



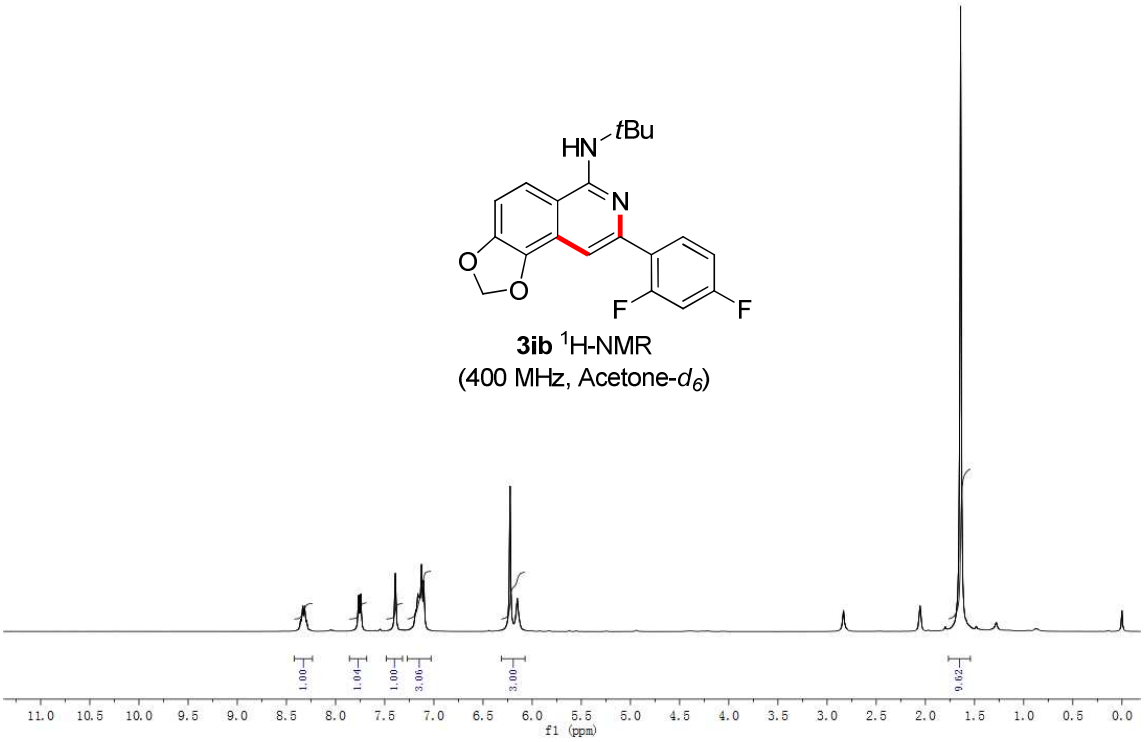
3hb ^{13}C-NMR
(100 MHz, $CDCl_3$)



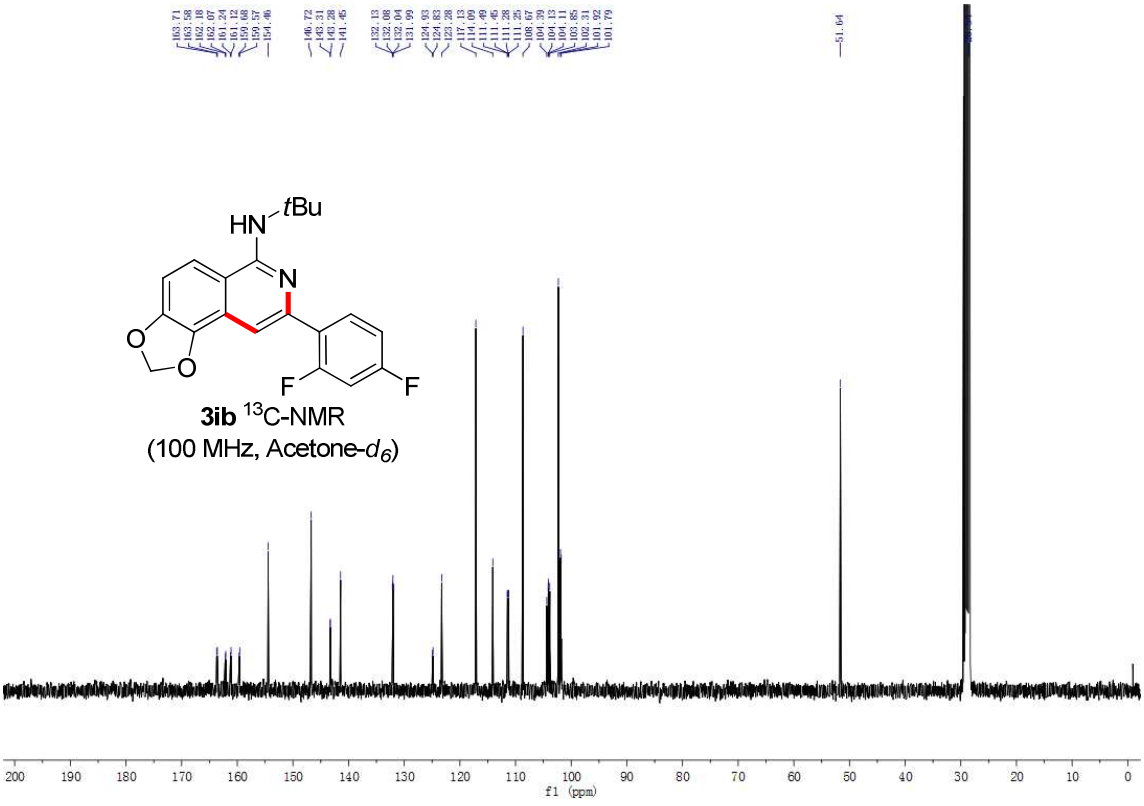
3hb ^{19}F-NMR
(376 MHz, $CDCl_3$)



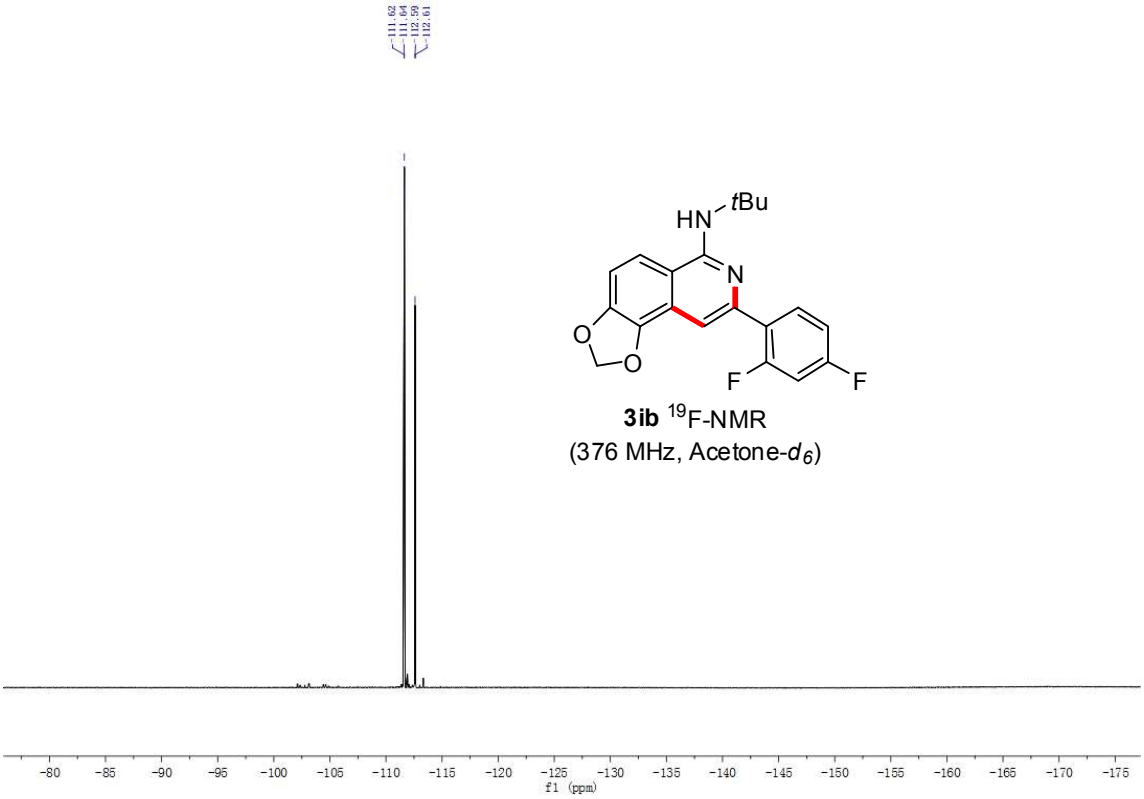
3hb NOESY
(400 MHz, $CDCl_3$)



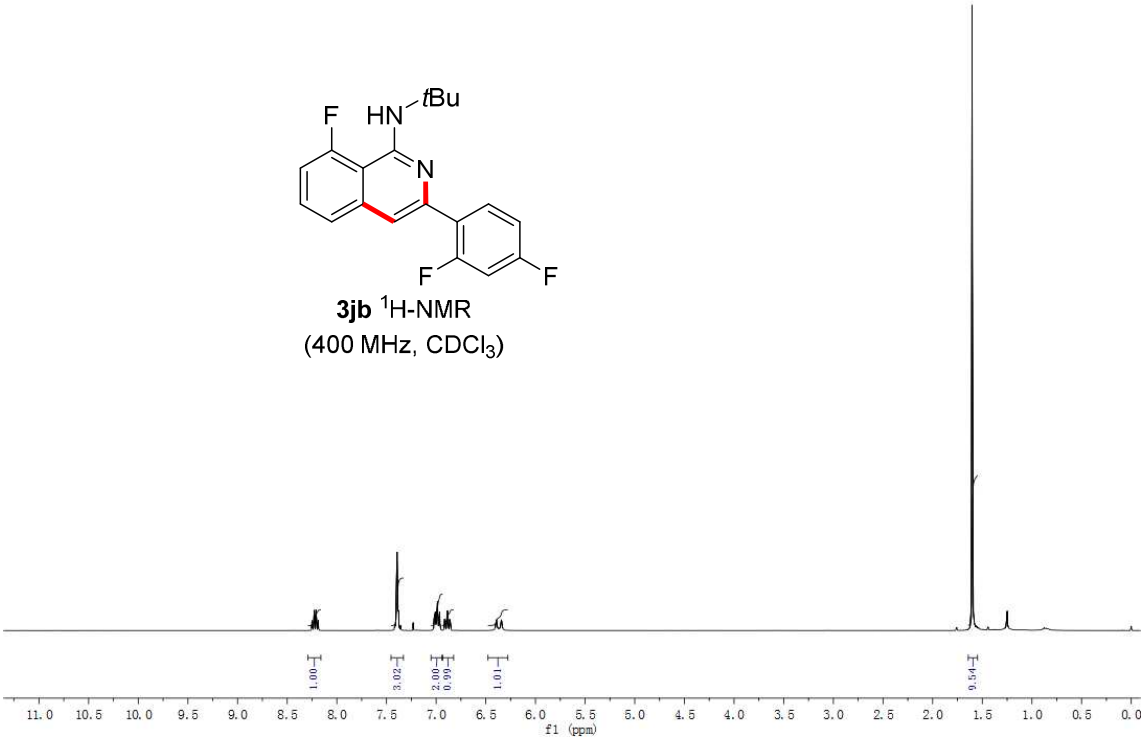
3ib ^{1}H-NMR
(400 MHz, Acetone-d_6)



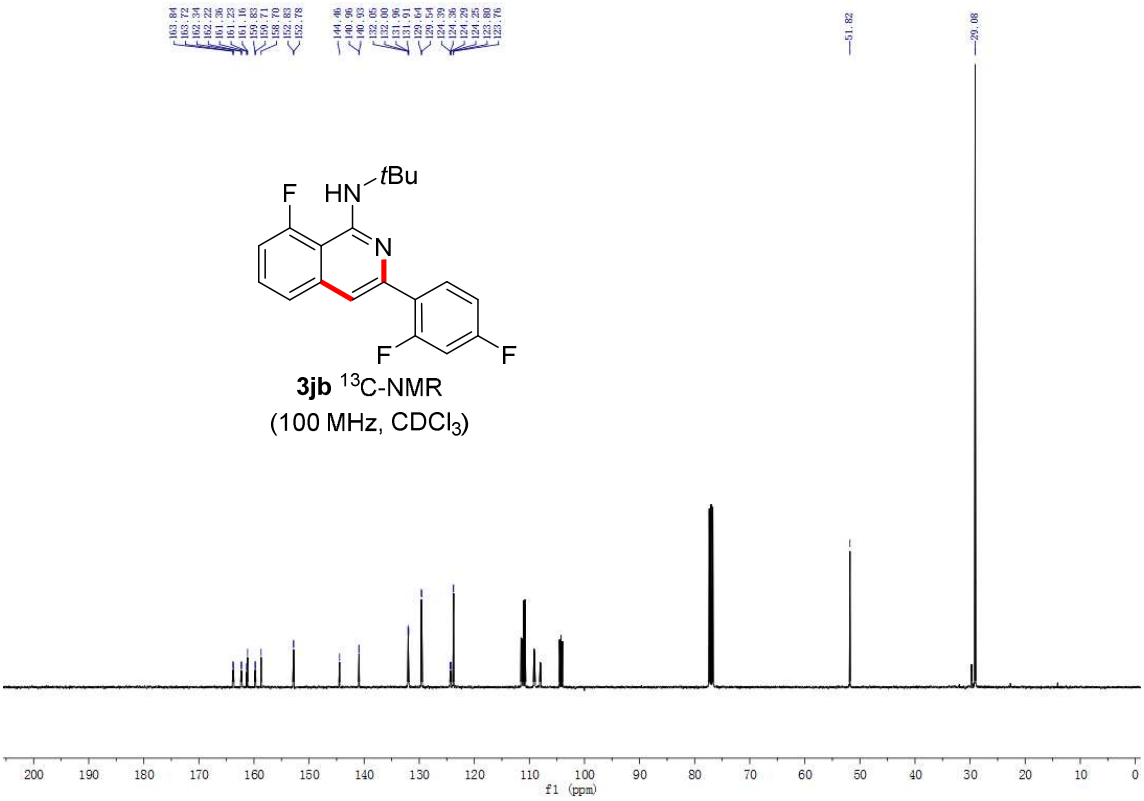
3ib ^{13}C-NMR
(100 MHz, Acetone-d_6)

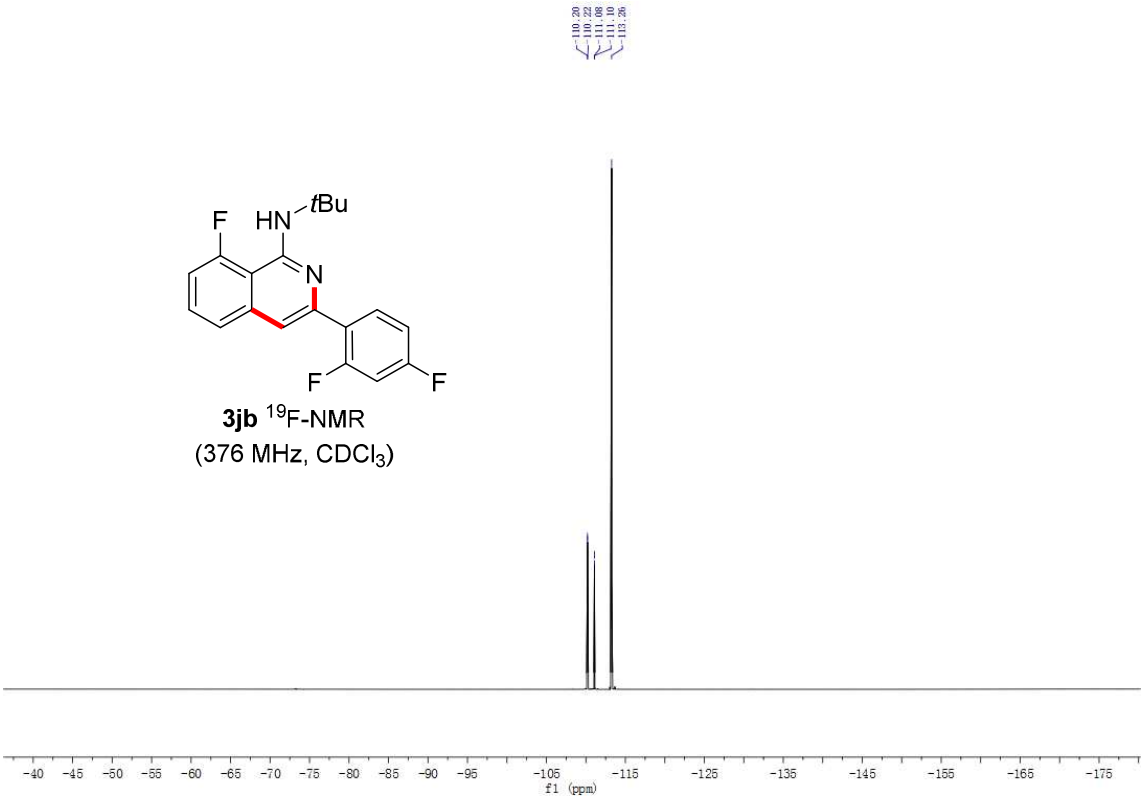


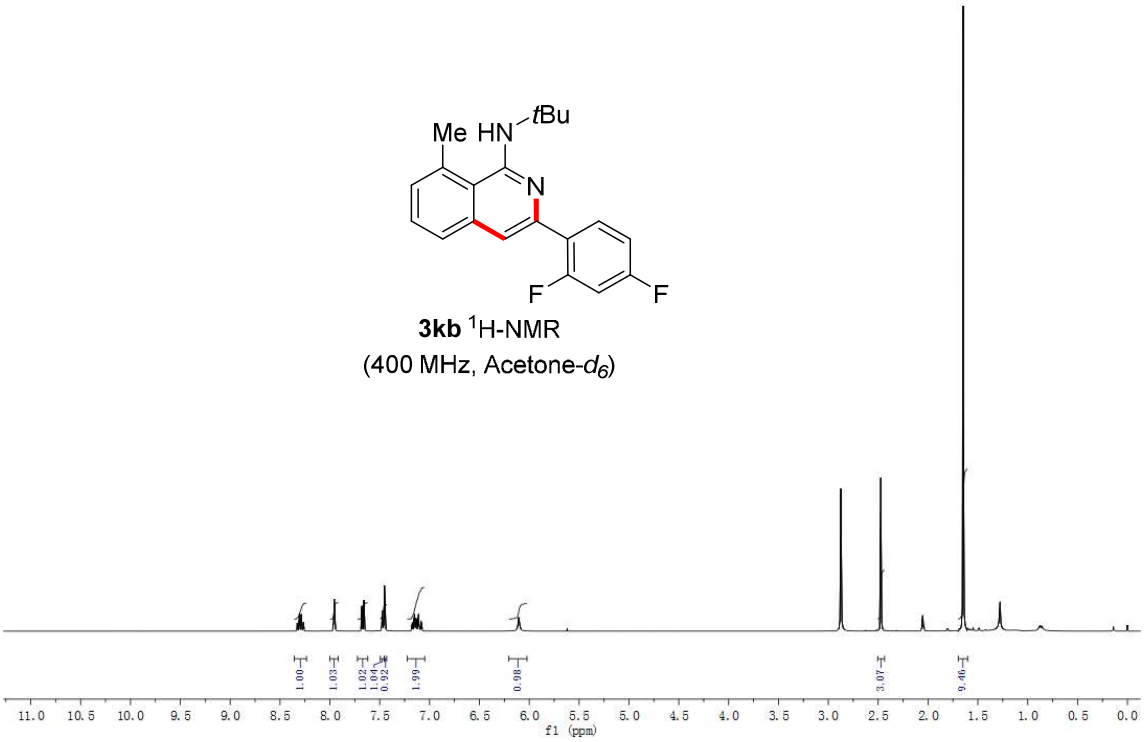
3ib ^{19}F-NMR
(376 MHz, Acetone-d_6)



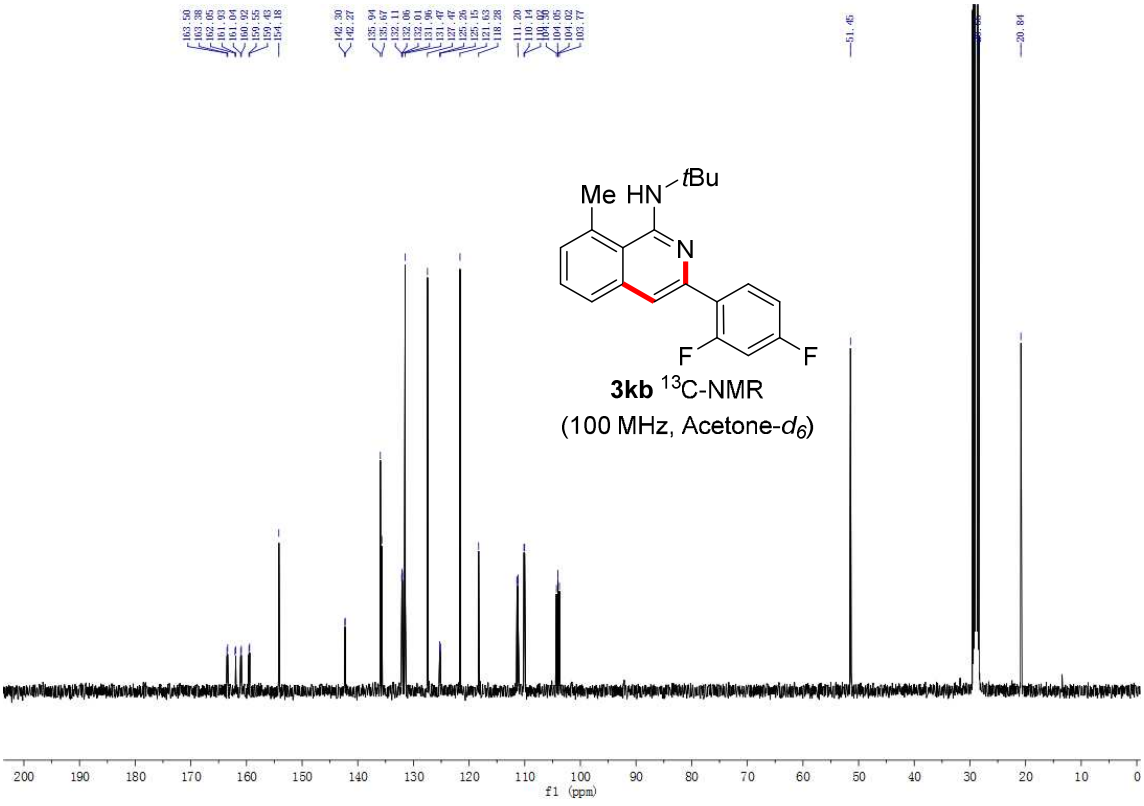
3jb ^{1}H-NMR
(400 MHz, $CDCl_3$)


F
HN
tBu
N
F
F
3jb 13C-NMR
(100 MHz, CDCl3)
f1 (ppm)

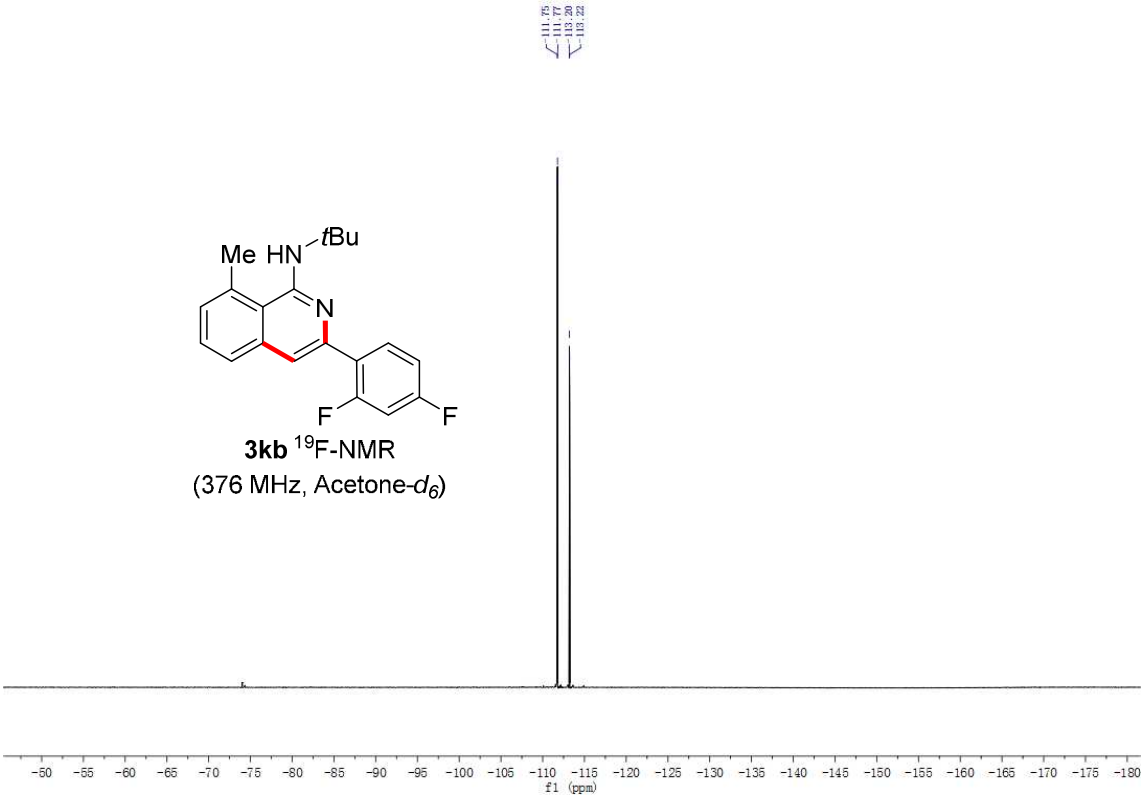

F
HN
tBu
N
F
F
3jb 19F-NMR
(376 MHz, CDCl3)
f1 (ppm)



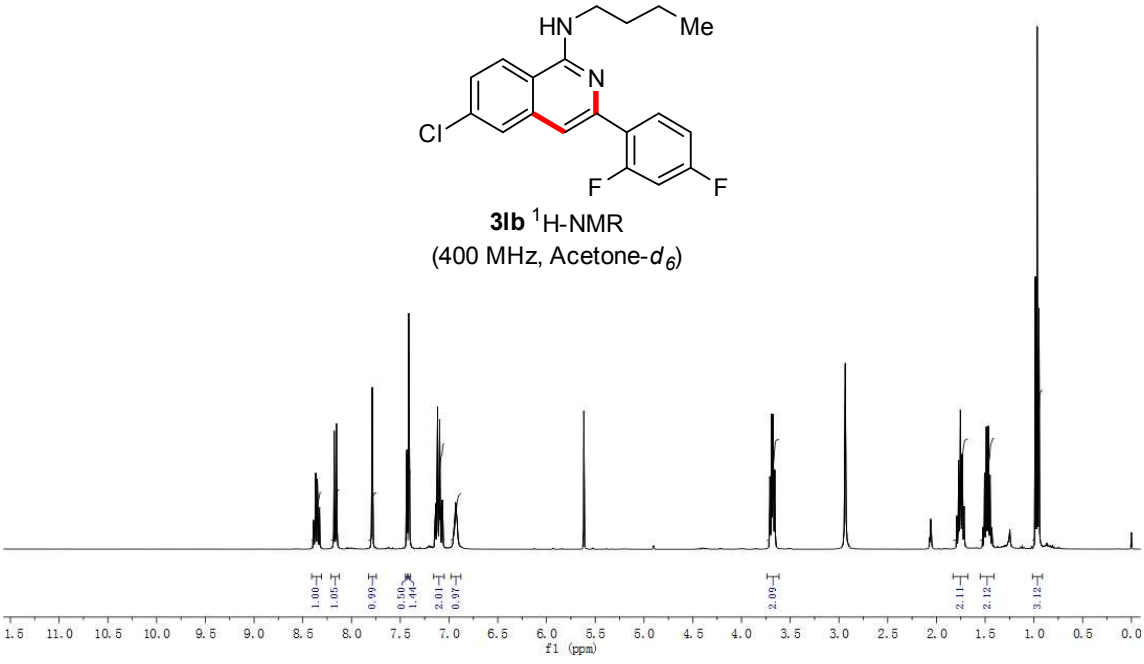
3kb ^{1}H-NMR
(400 MHz, Acetone-d_6)



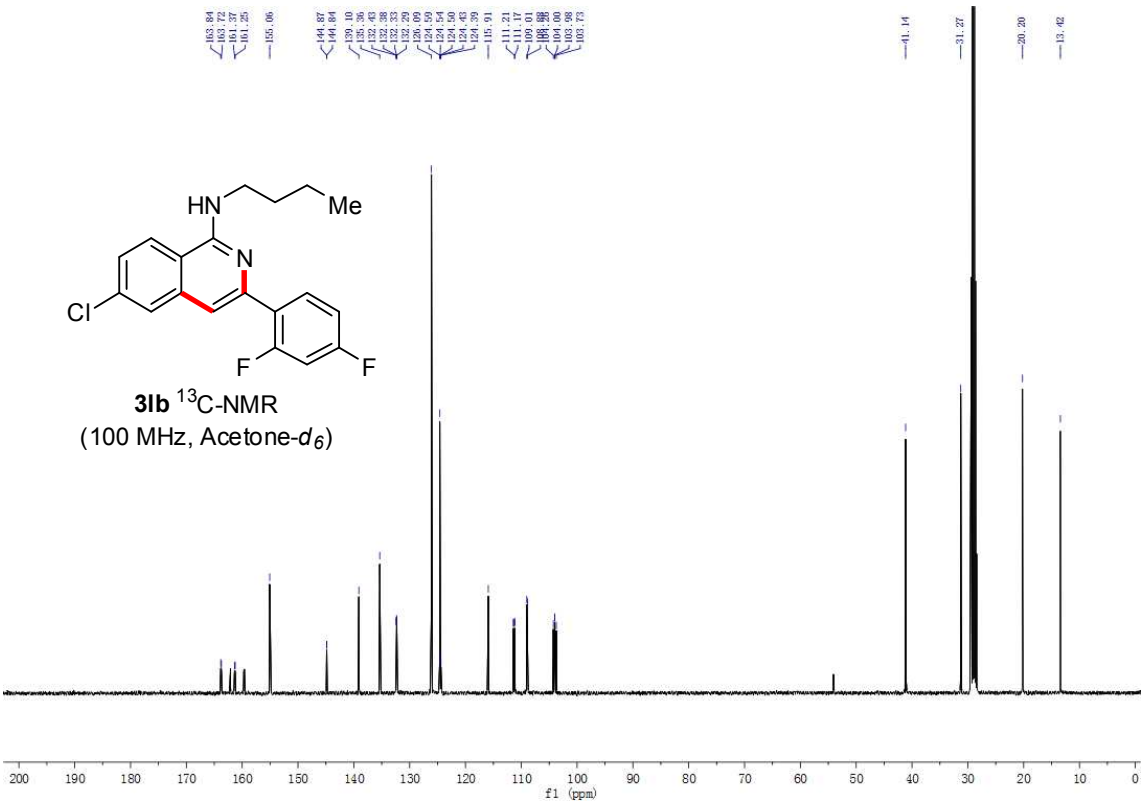
3kb ^{13}C-NMR
(100 MHz, Acetone-d_6)



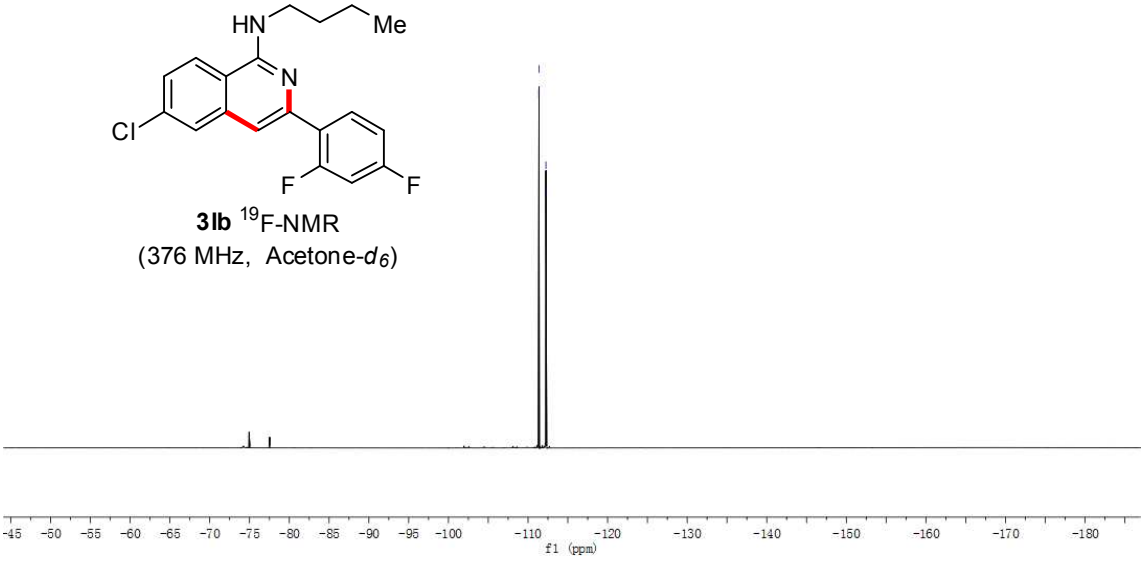
3kb ^{19}F-NMR
(376 MHz, Acetone-d_6)



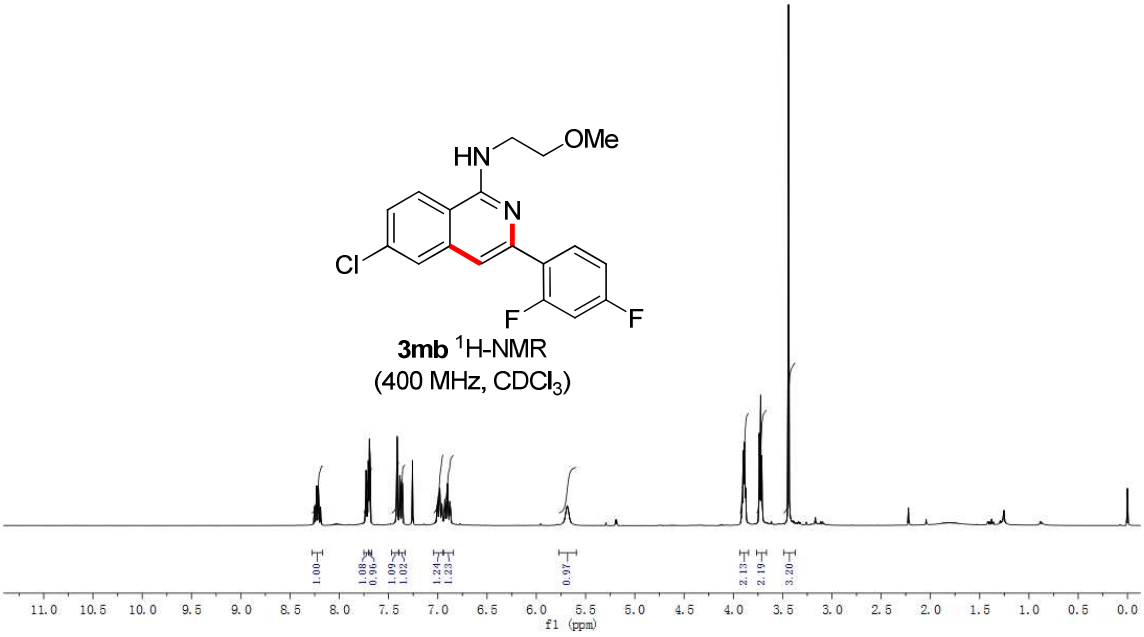
3lb ^{1}H-NMR
(400 MHz, Acetone-d_6)



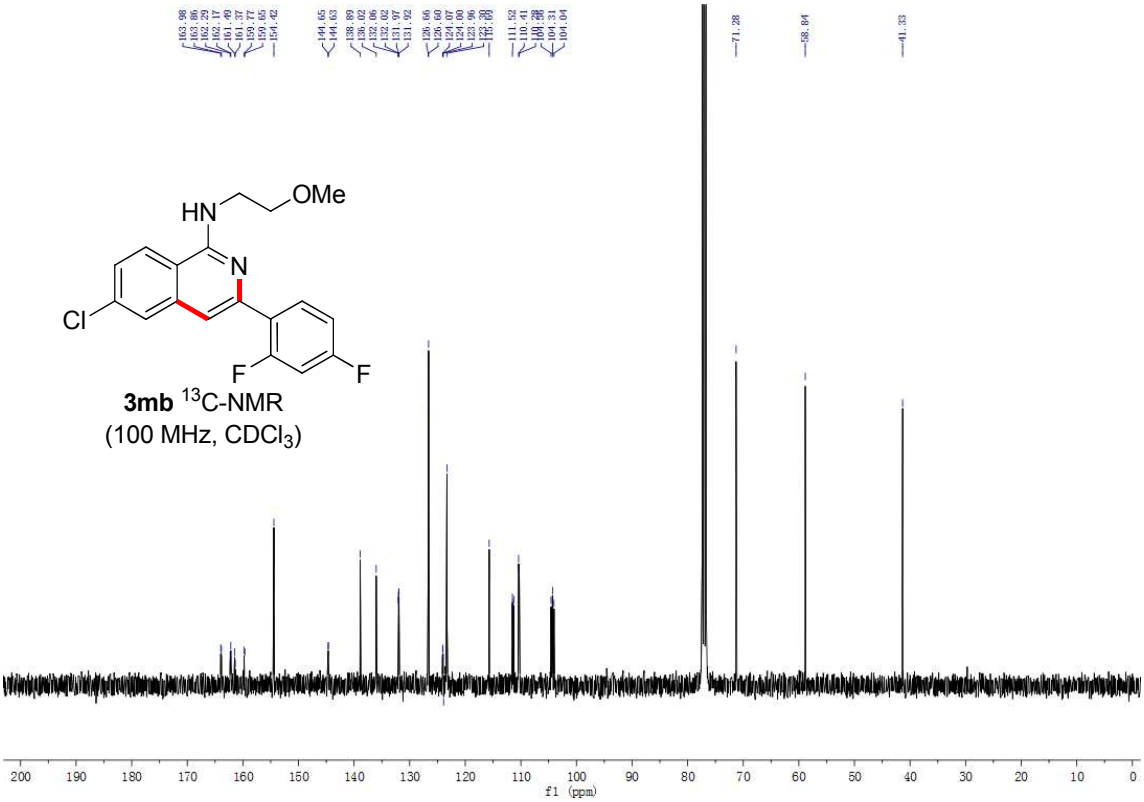
3lb ^{13}C-NMR
(100 MHz, Acetone-d_6)



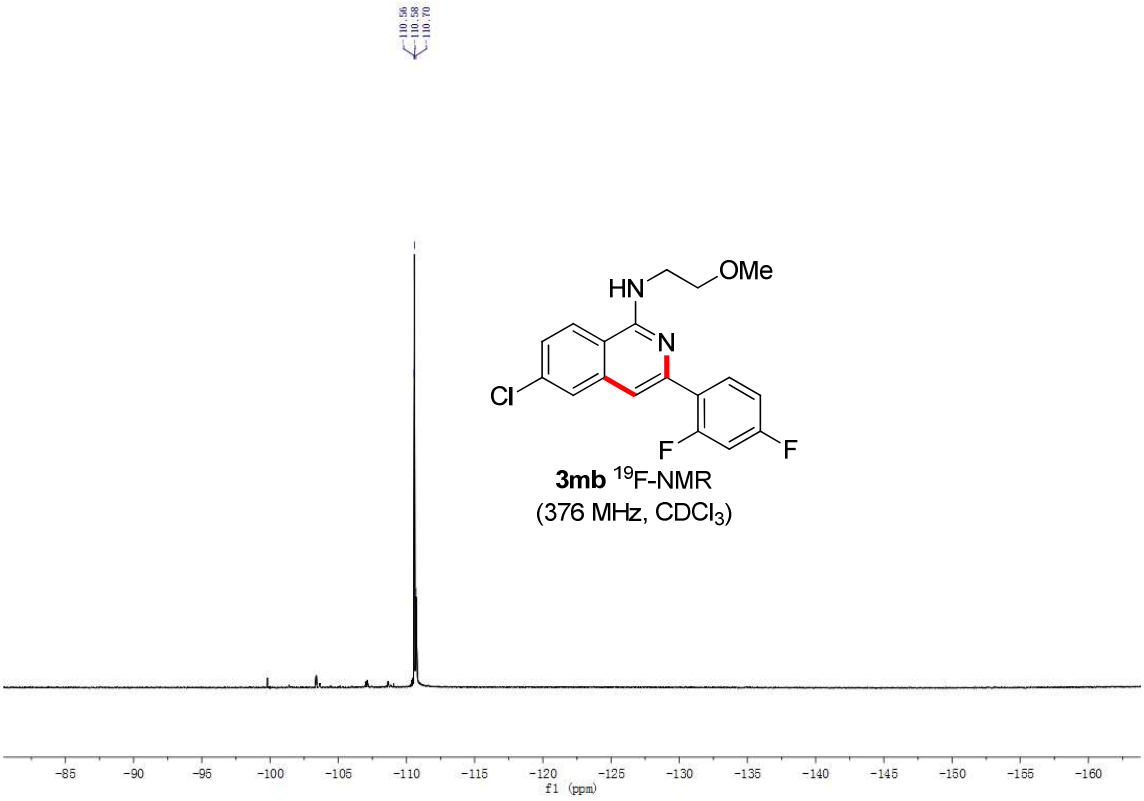
3lb ^{19}F-NMR
(376 MHz, Acetone-d_6)



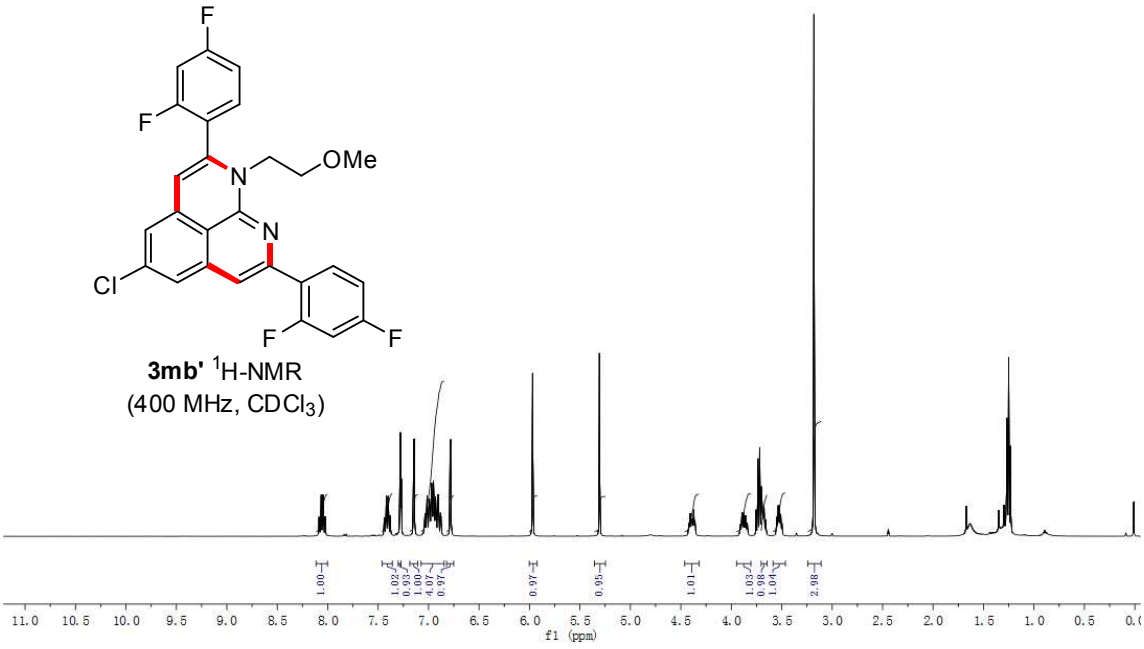
3mb ^{1}H-NMR
(400 MHz, $CDCl_3$)



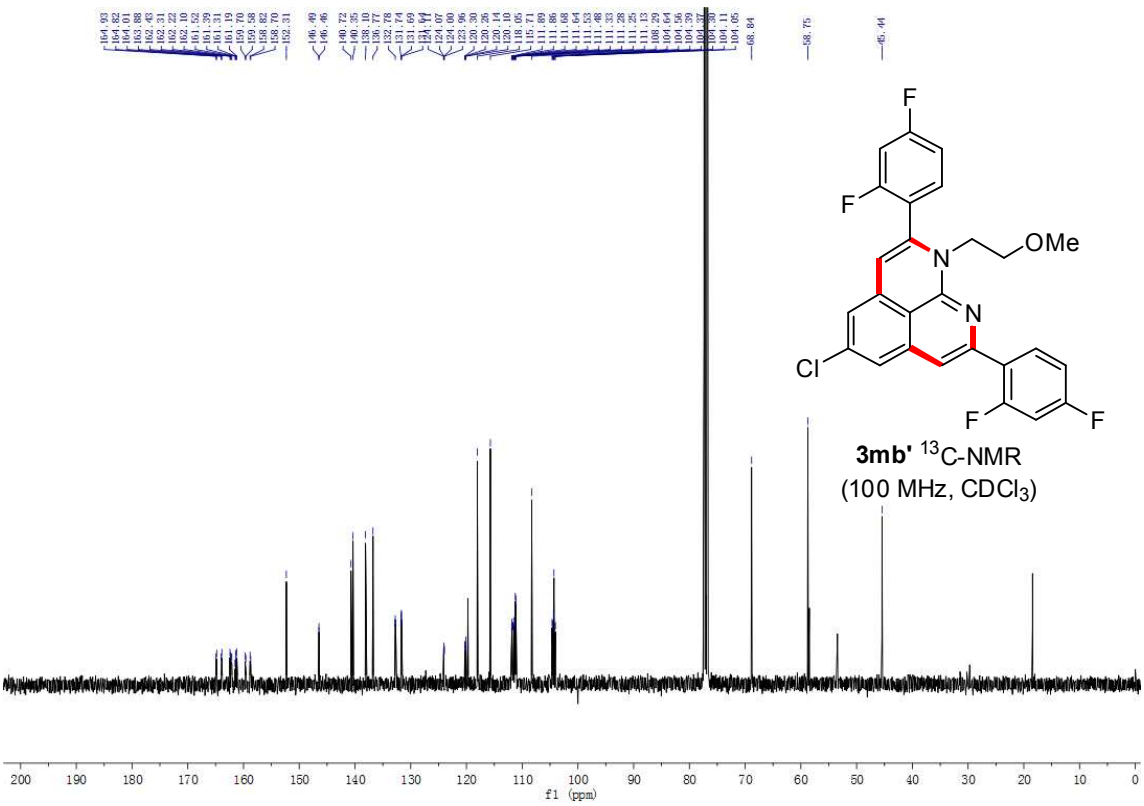
3mb ^{13}C-NMR
(100 MHz, $CDCl_3$)



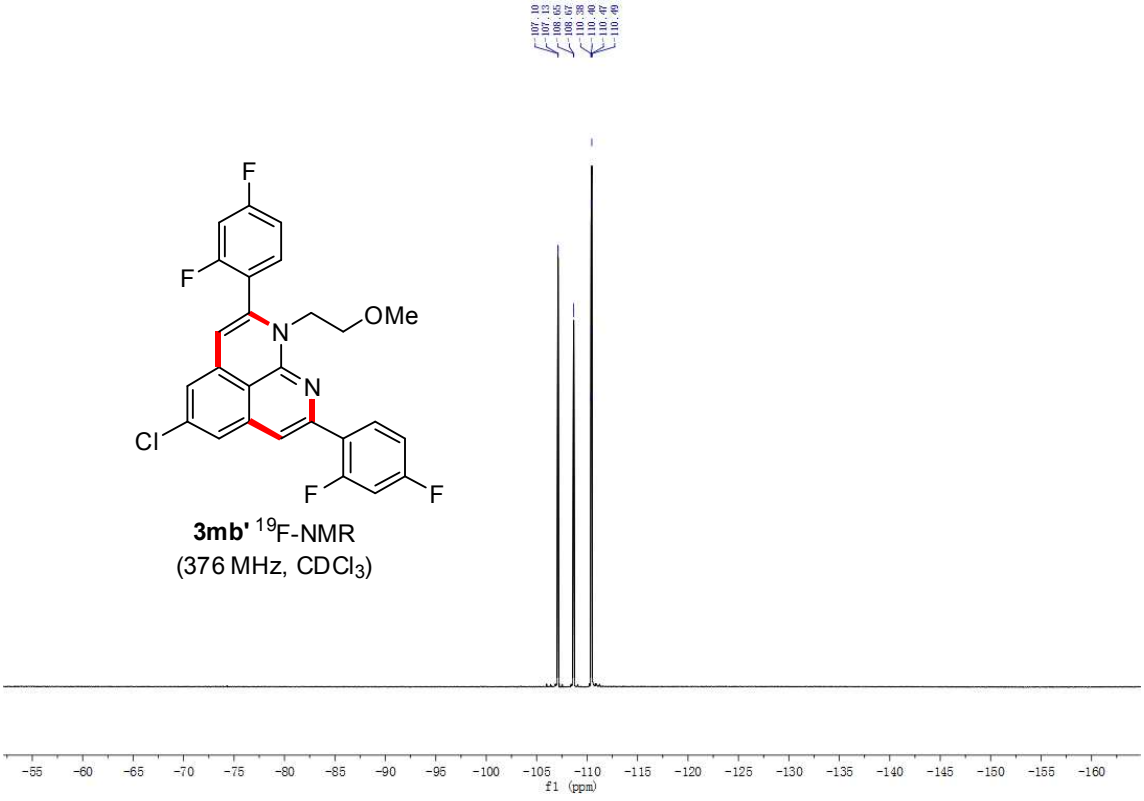
3mb ^{19}F-NMR
(376 MHz, $CDCl_3$)



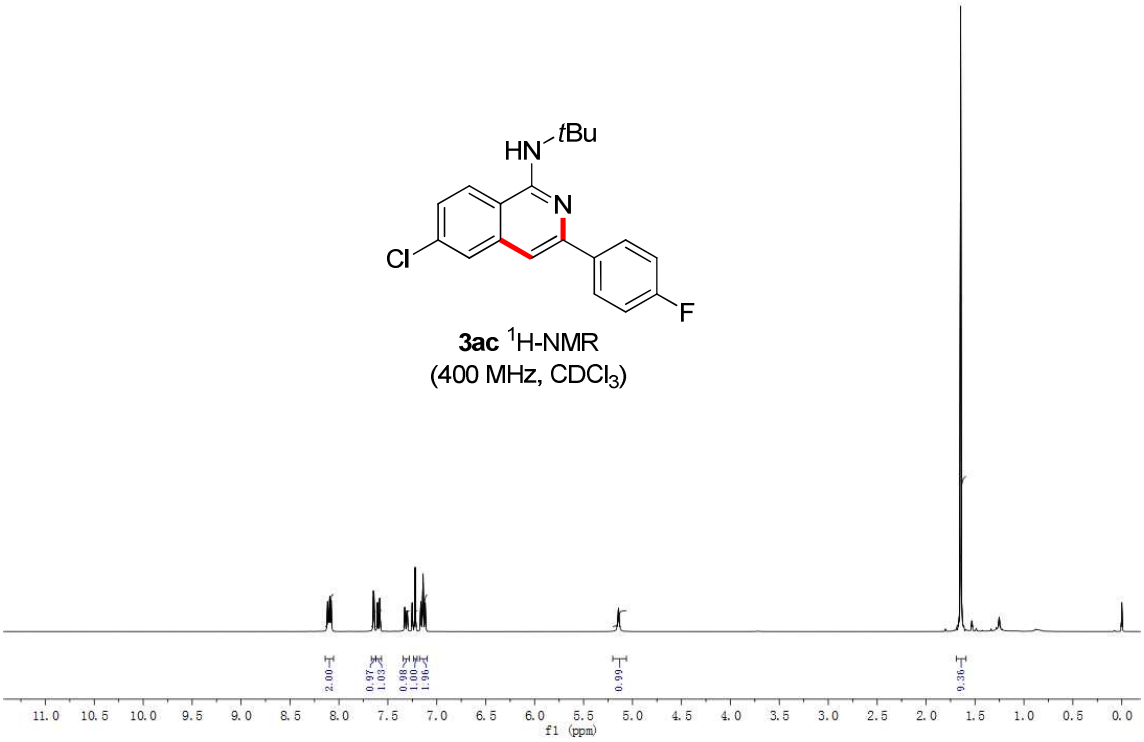
3mb' ^{1}H-NMR
(400 MHz, $CDCl_3$)



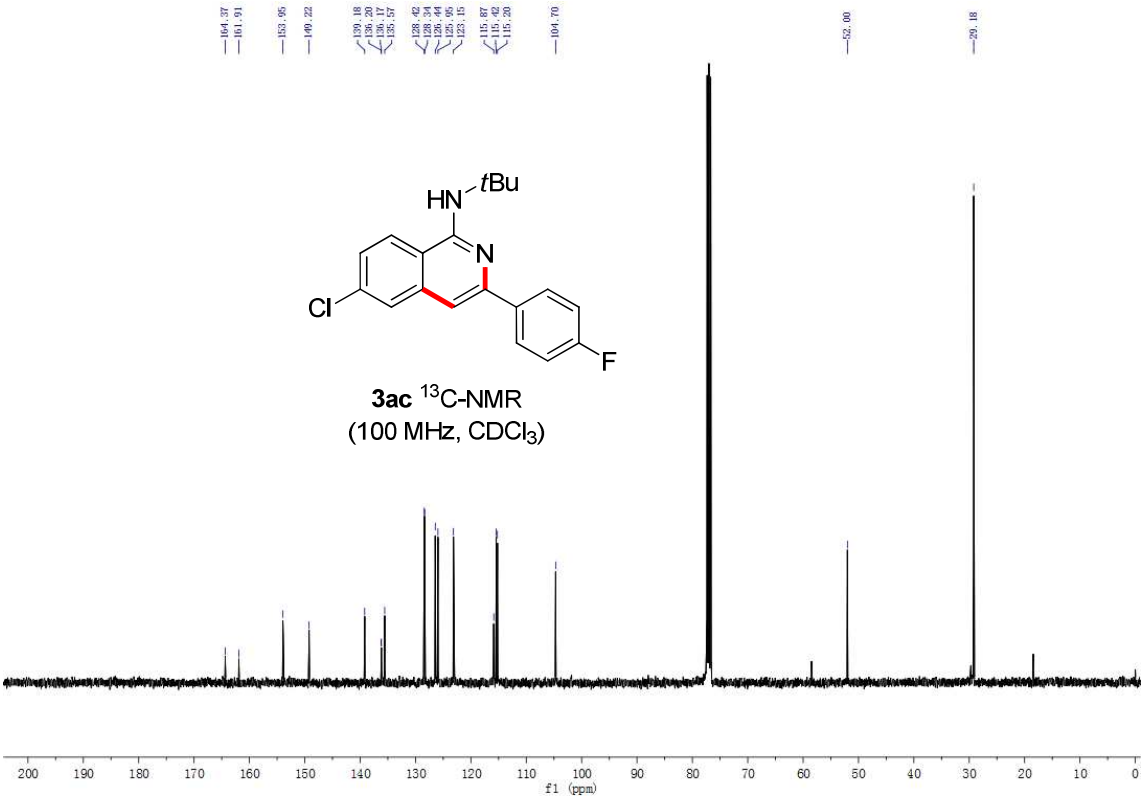
3mb' ^{13}C-NMR
(100 MHz, $CDCl_3$)



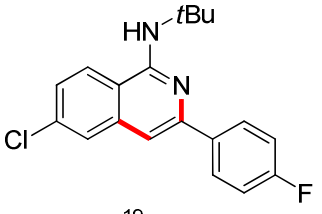
3mb' ^{19}F-NMR
(376 MHz, $CDCl_3$)



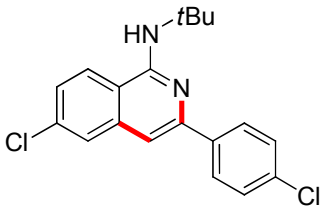
3ac ^{1}H-NMR
(400 MHz, $CDCl_3$)



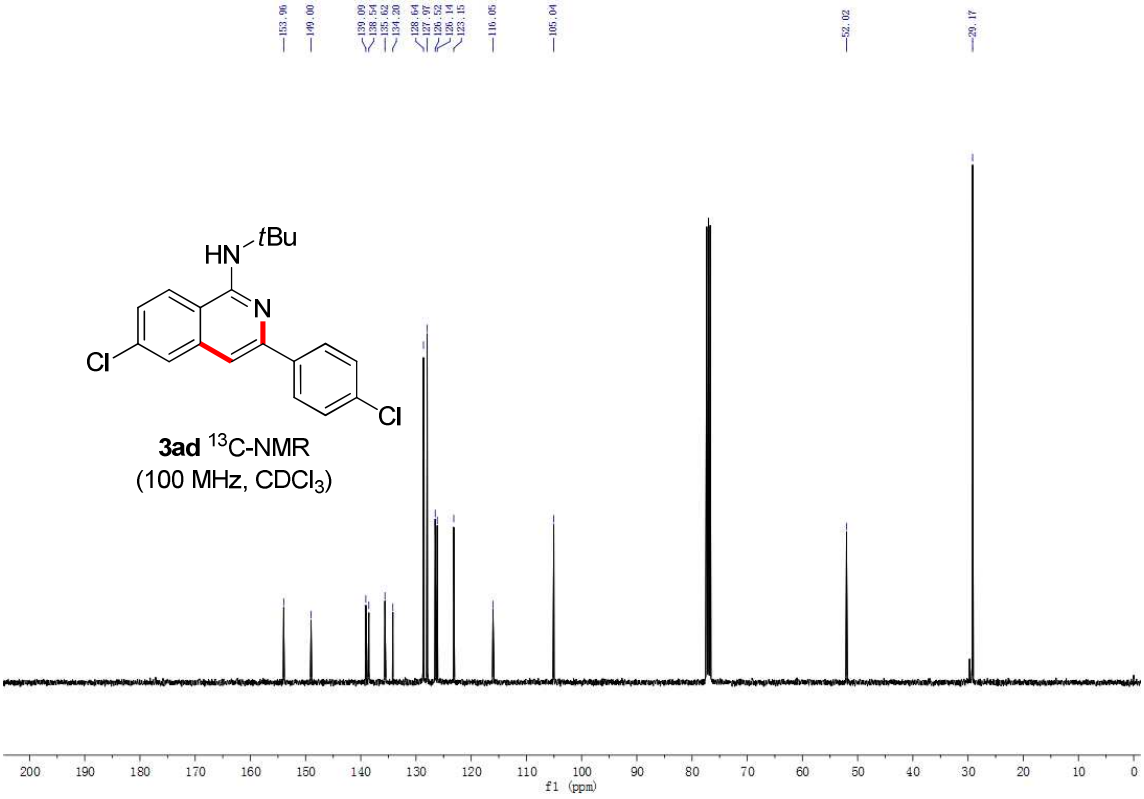
3ac ^{13}C-NMR
(100 MHz, $CDCl_3$)



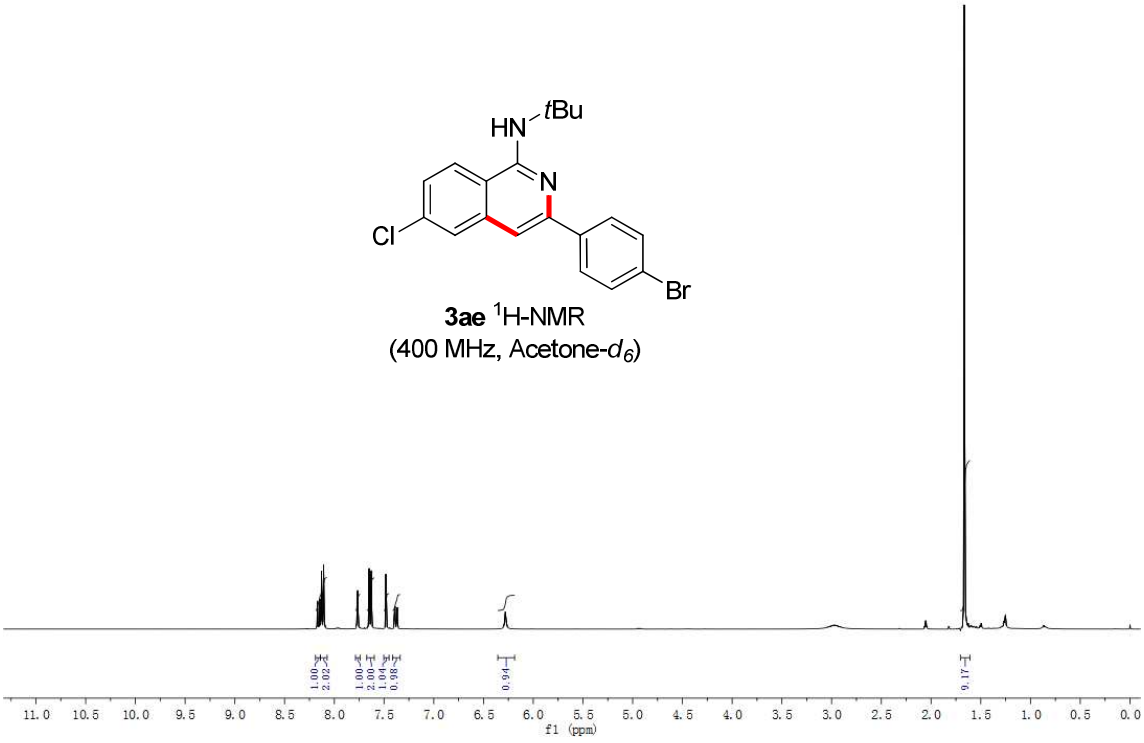
3ac ^{19}F-NMR
(376 MHz, $CDCl_3$)



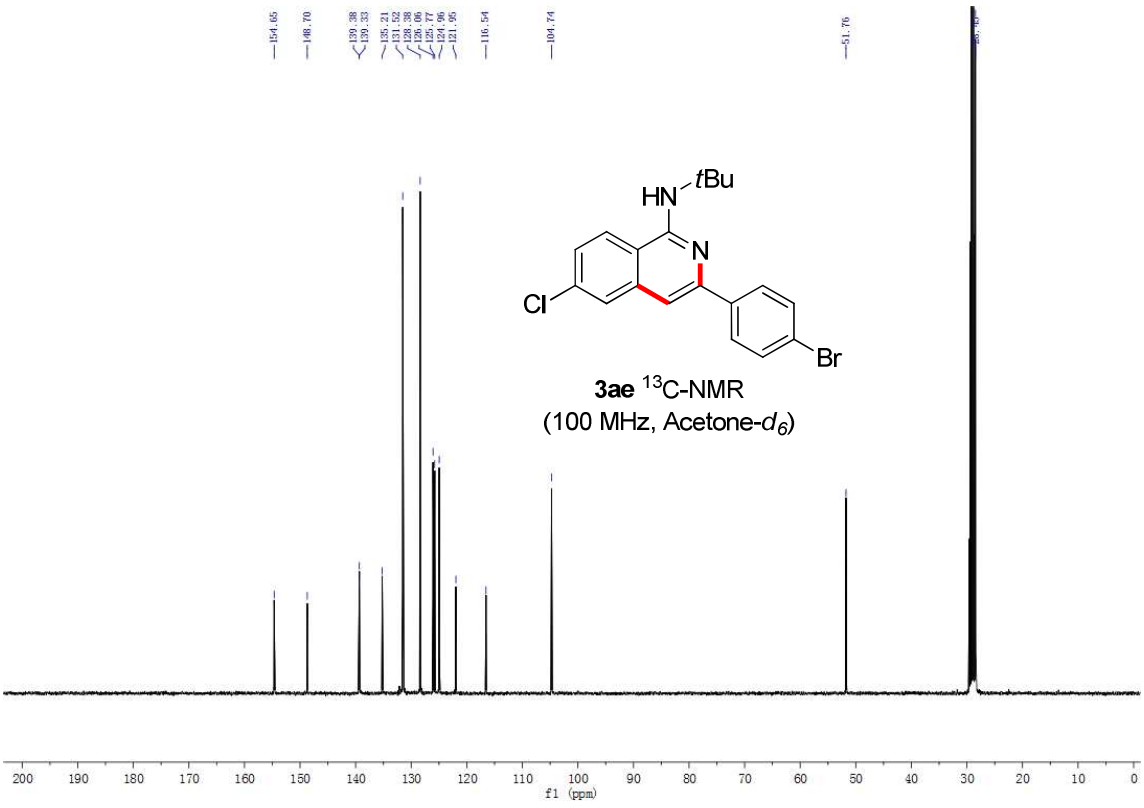
3ad ^{1}H-NMR
(400 MHz, $CDCl_3$)



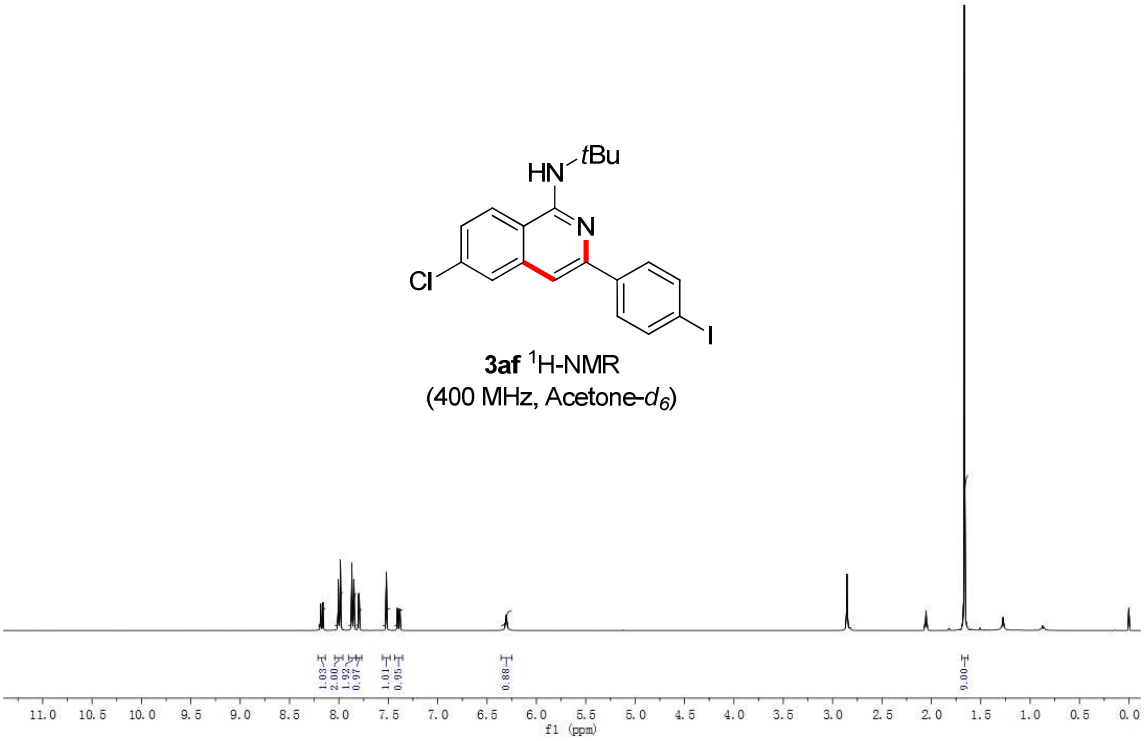
3ad ^{13}C-NMR
(100 MHz, $CDCl_3$)



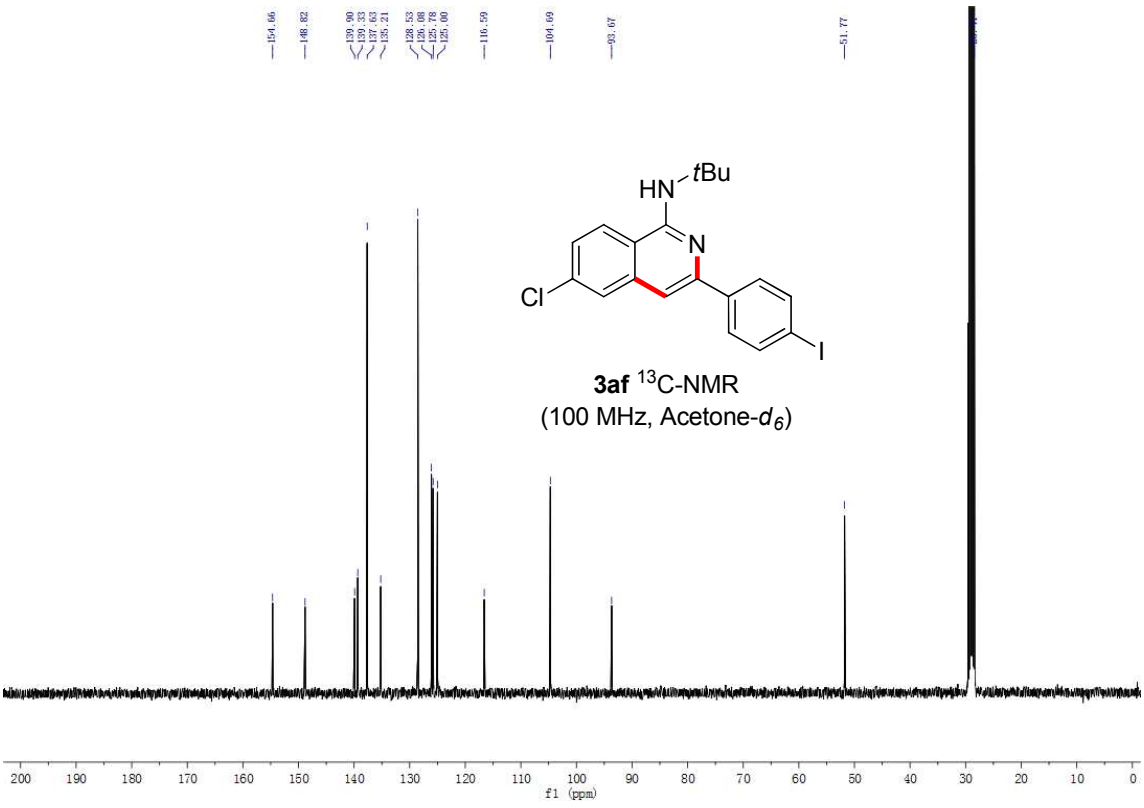
3ae ^{1}H-NMR
(400 MHz, Acetone-d_6)



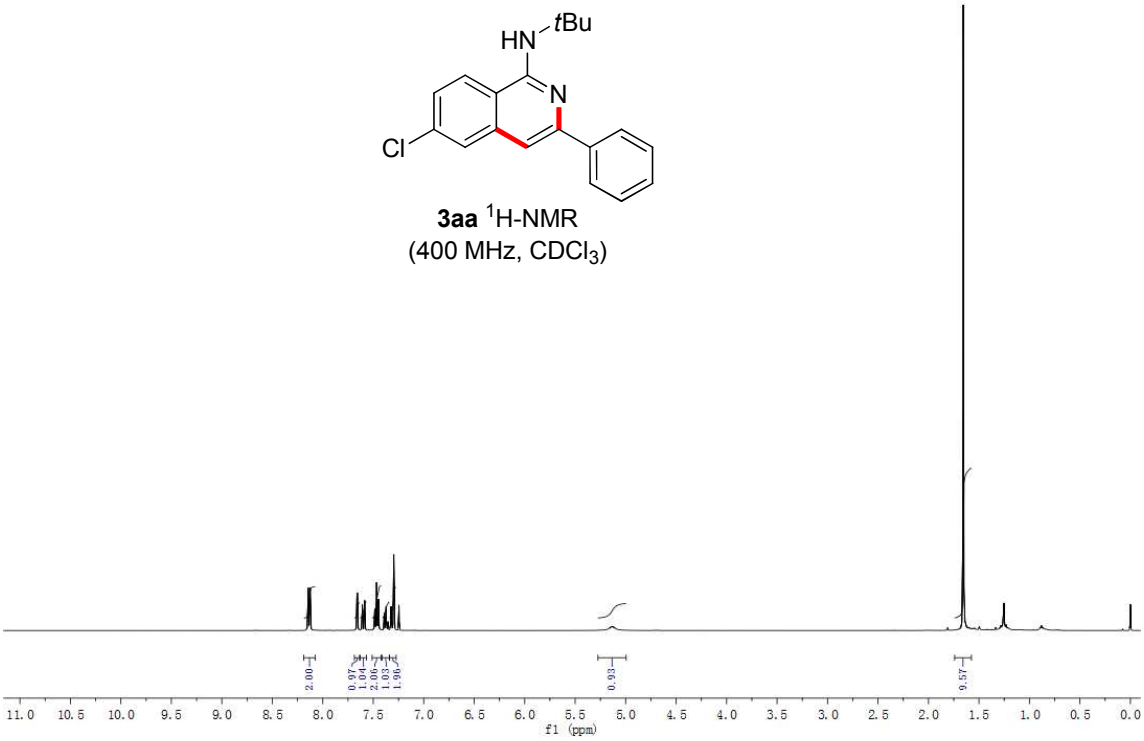
3ae ^{13}C-NMR
(100 MHz, Acetone-d_6)



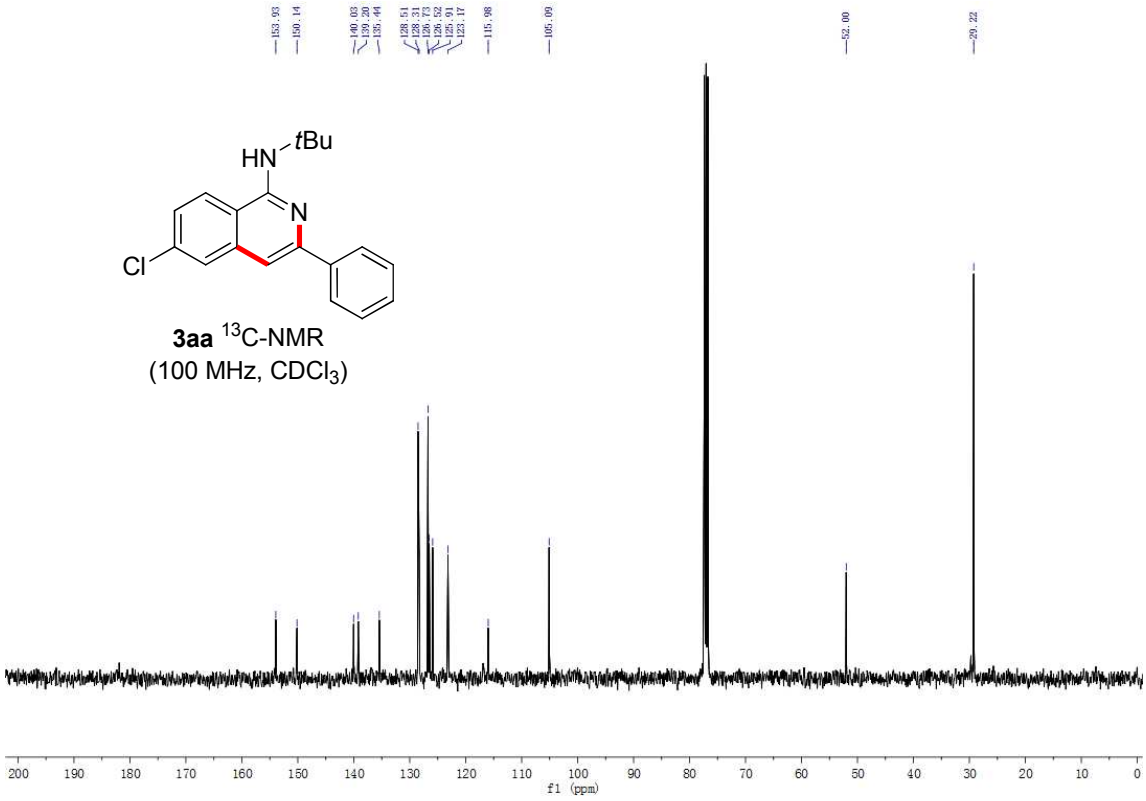
3af ^{1}H-NMR
(400 MHz, Acetone-d_6)



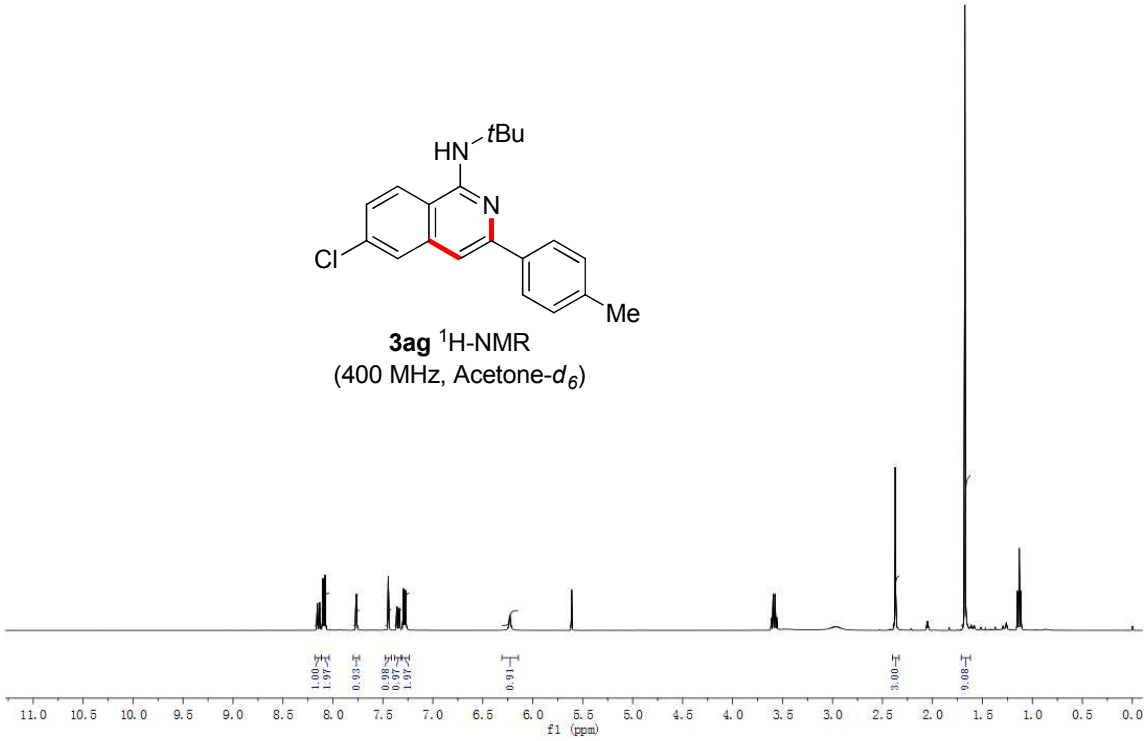
3af ^{13}C-NMR
(100 MHz, Acetone-d_6)



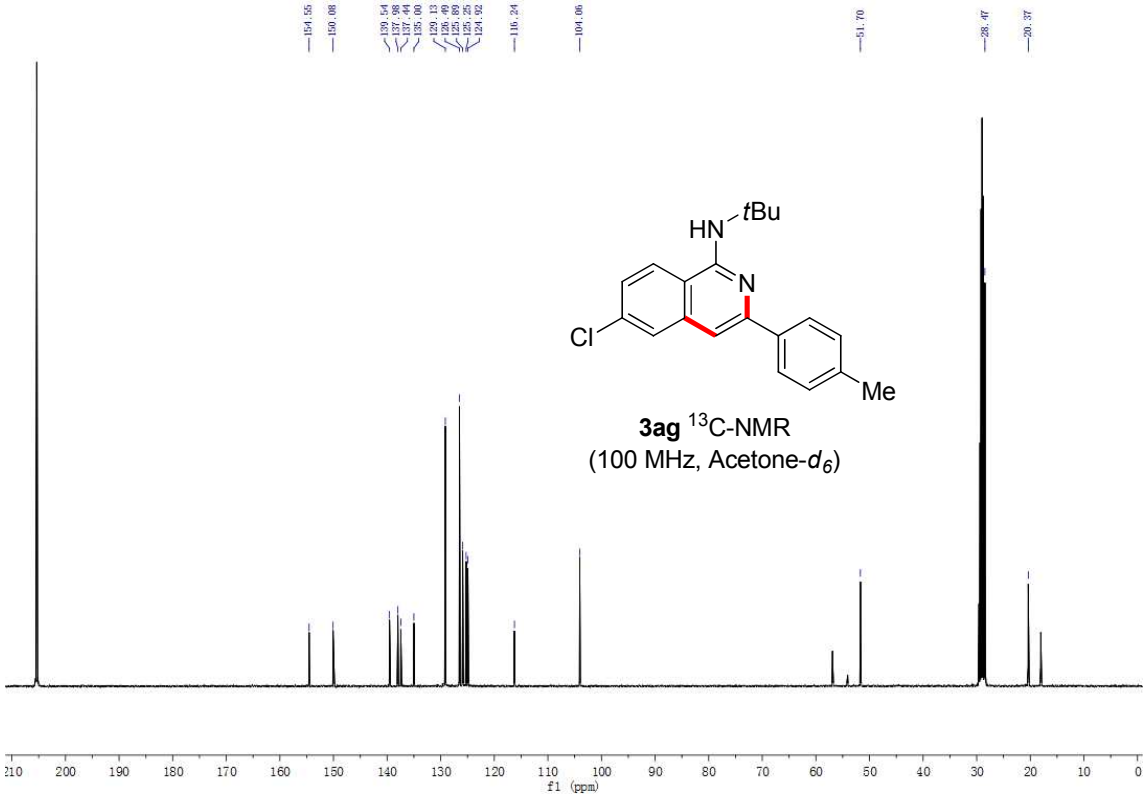
3aa ^{1}H-NMR
(400 MHz, $CDCl_3$)



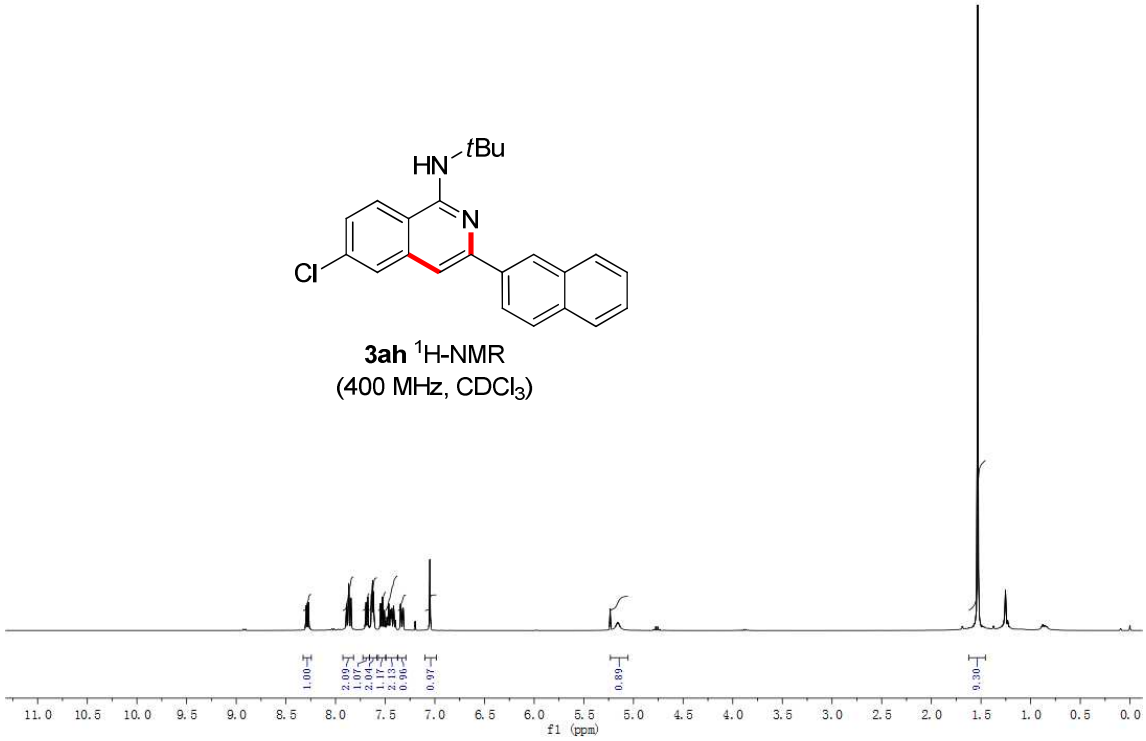
3aa ^{13}C-NMR
(100 MHz, $CDCl_3$)



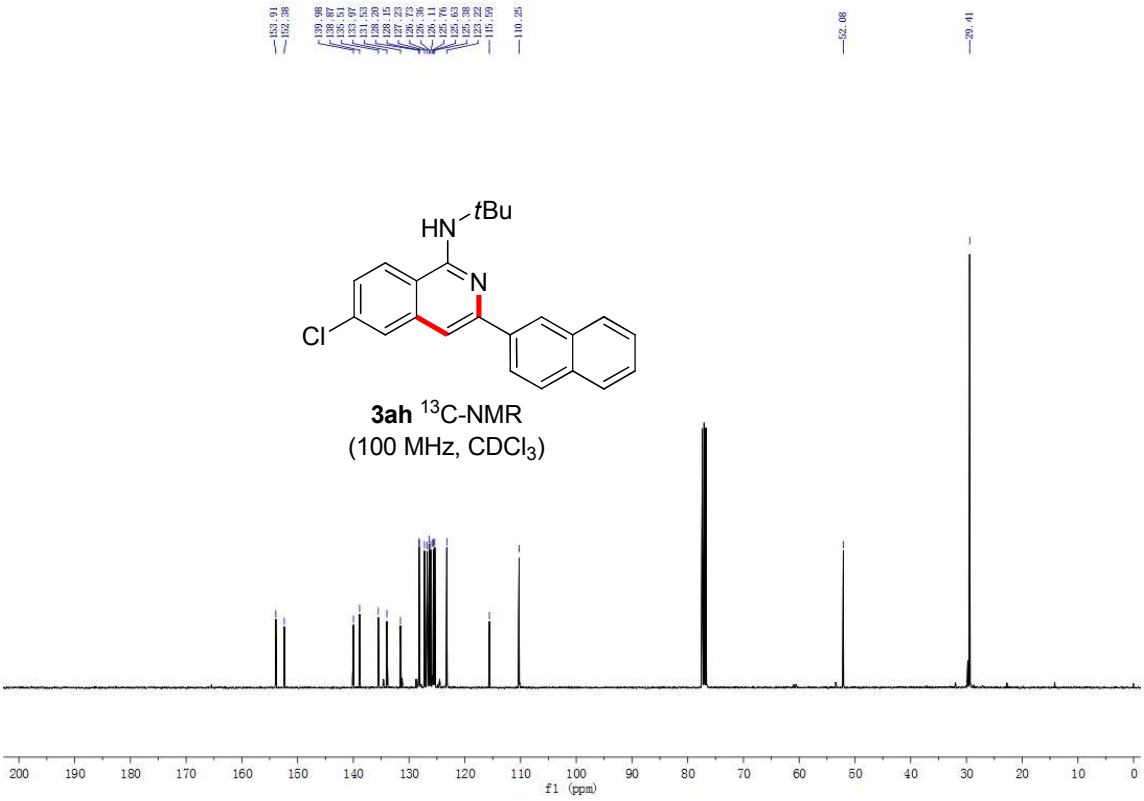
3ag ^{1}H-NMR
(400 MHz, Acetone-d_6)



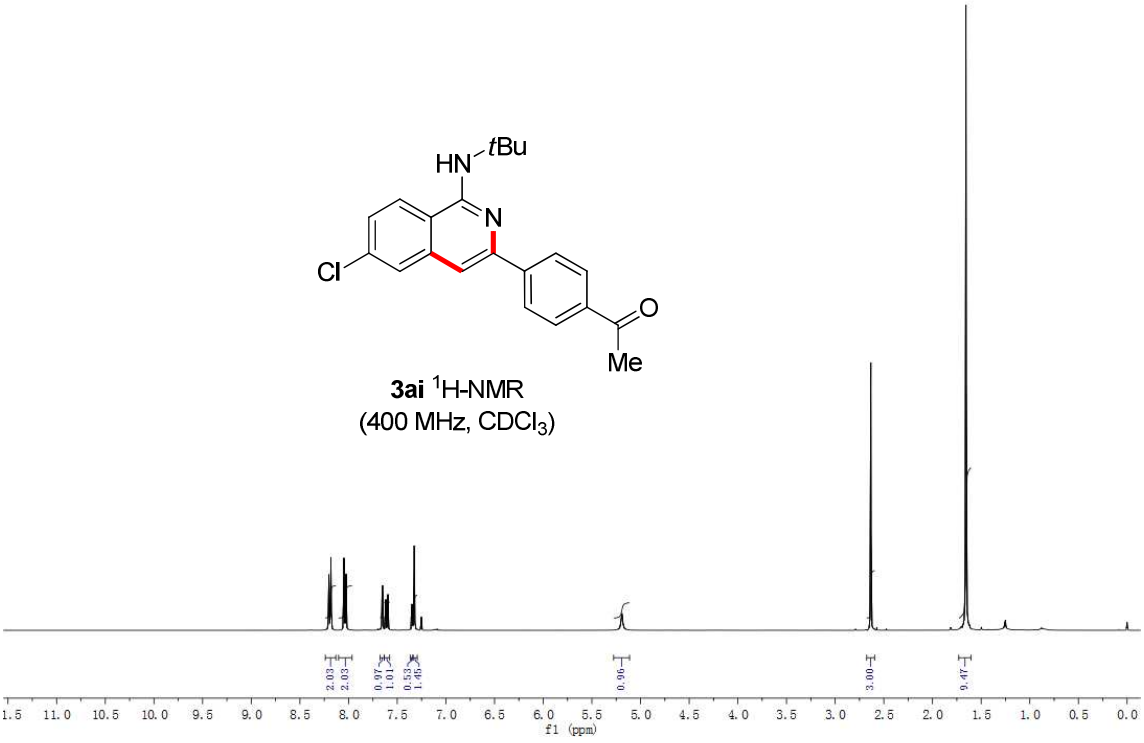
3ag ^{13}C-NMR
(100 MHz, Acetone-d_6)



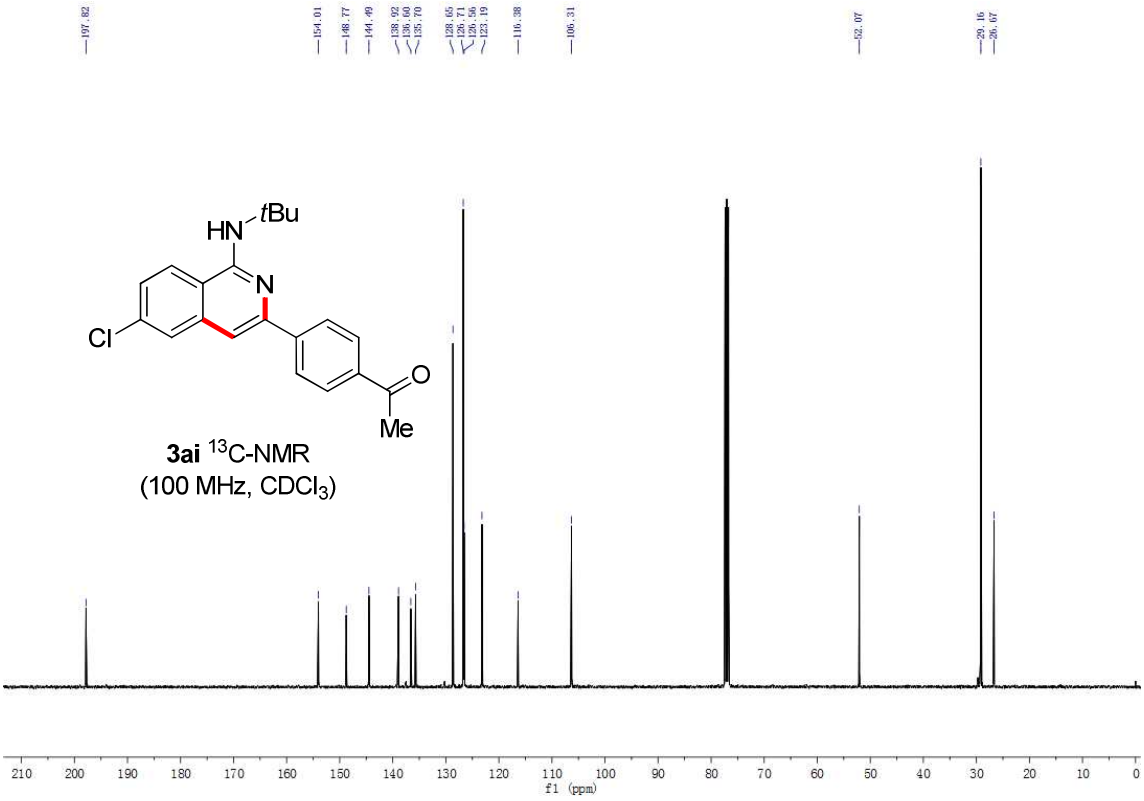
3ah ^{1}H-NMR
(400 MHz, $CDCl_3$)



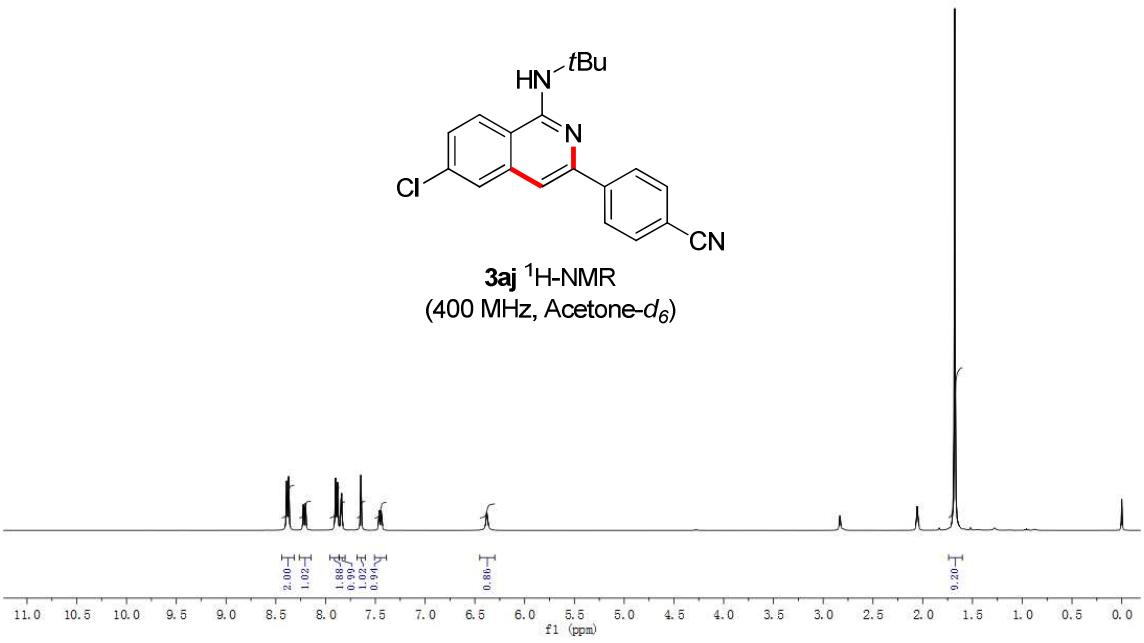
3ah ^{13}C-NMR
(100 MHz, $CDCl_3$)



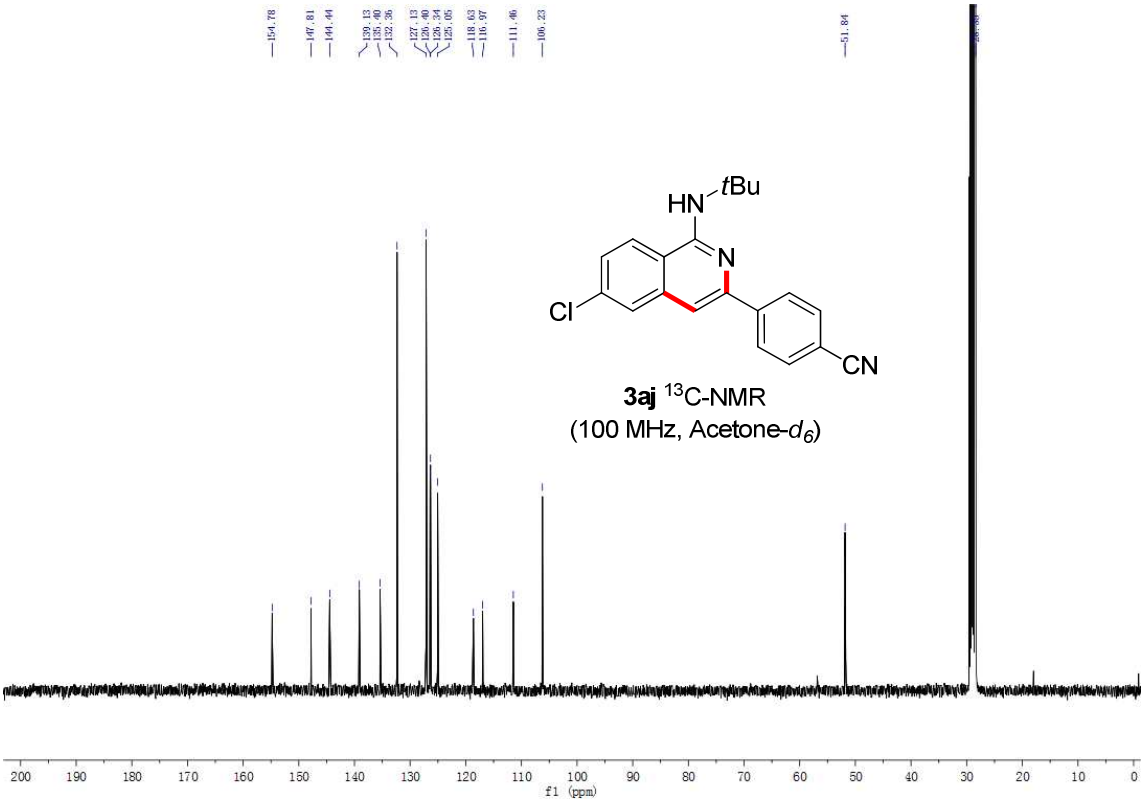
3ai ^{1}H-NMR
(400 MHz, $CDCl_3$)



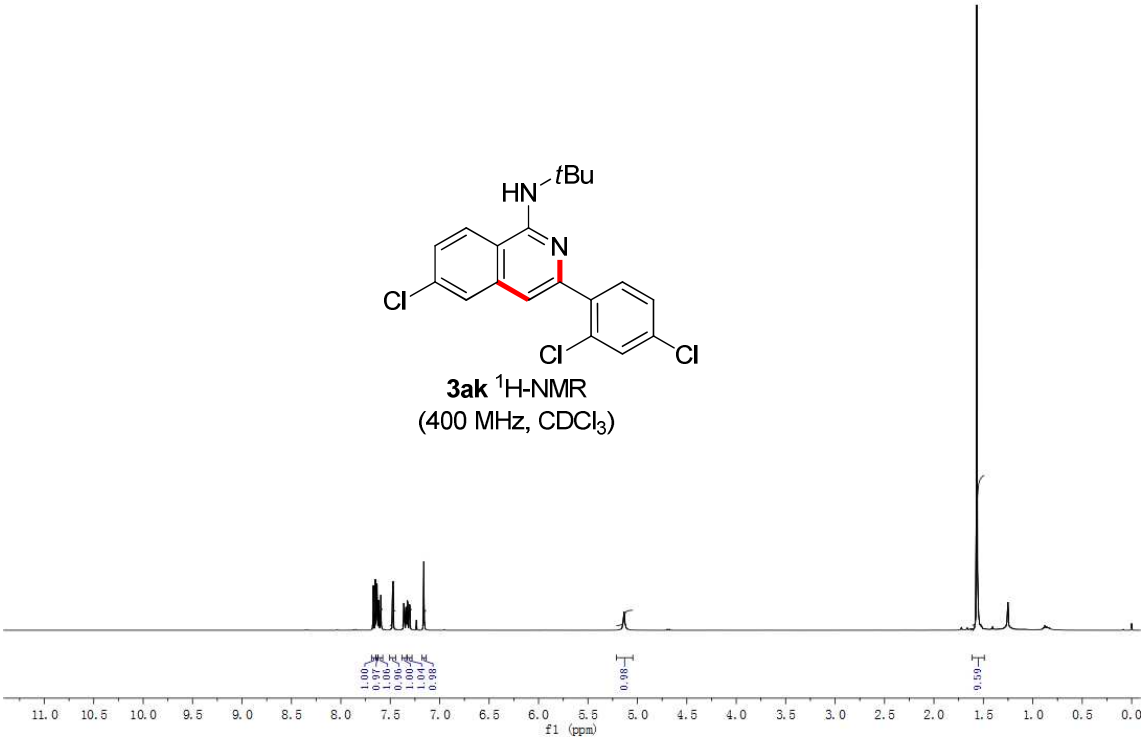
3ai ^{13}C-NMR
(100 MHz, $CDCl_3$)



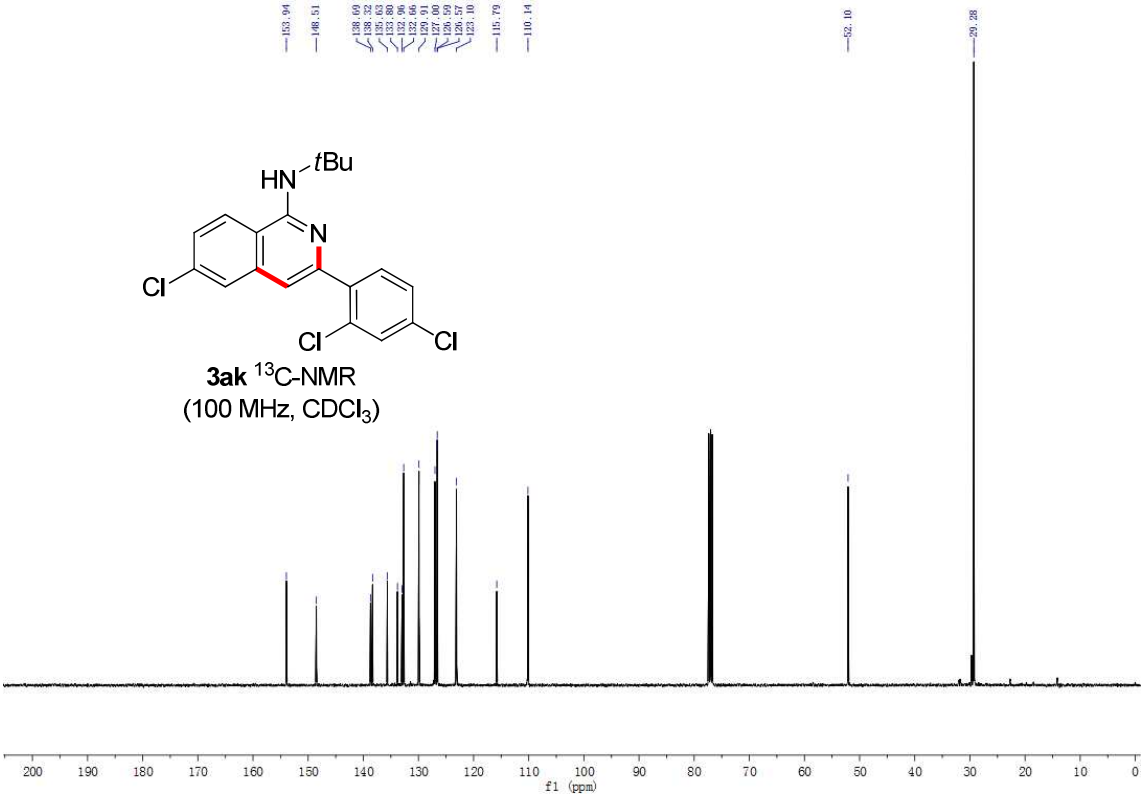
3aj ^{1}H-NMR
(400 MHz, Acetone-d_6)



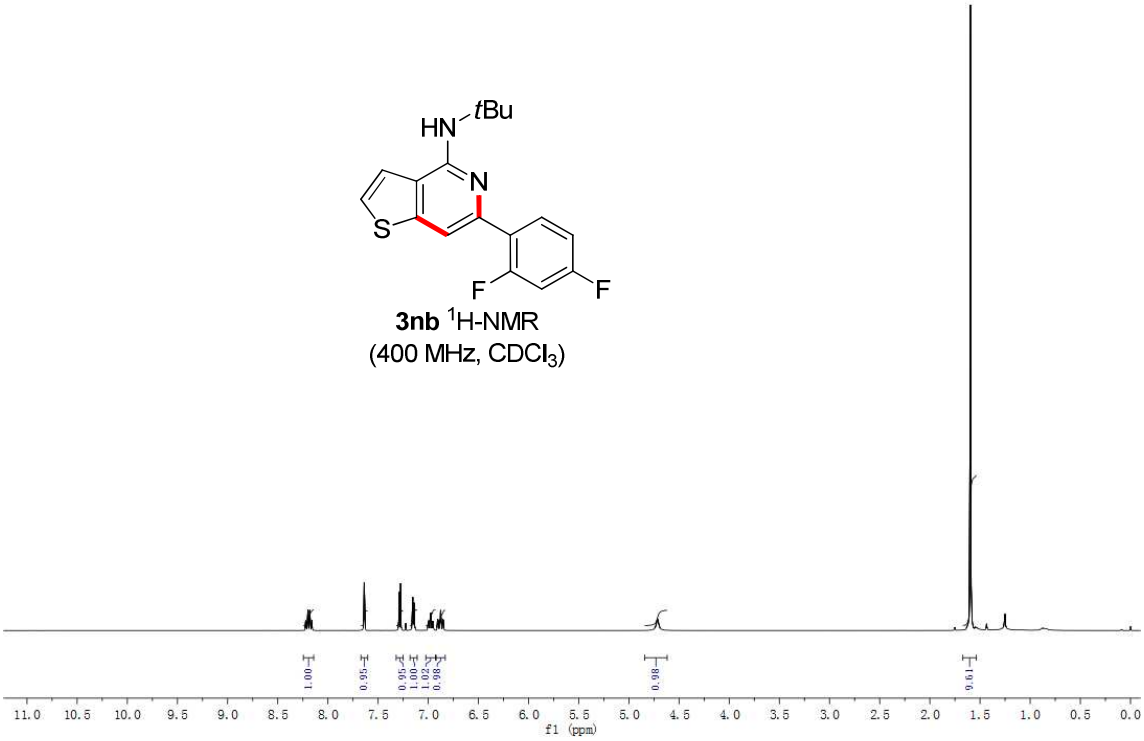
3aj ^{13}C-NMR
(100 MHz, Acetone-d_6)



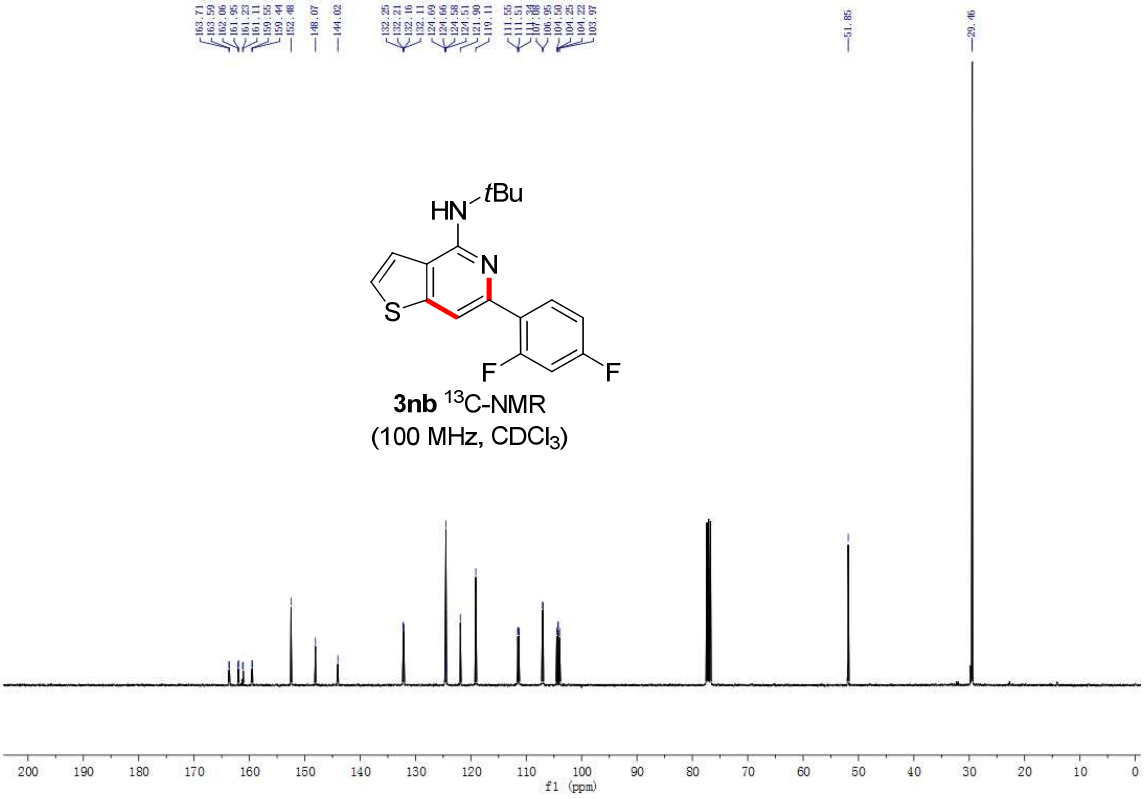
3ak ^{1}H-NMR
(400 MHz, $CDCl_3$)



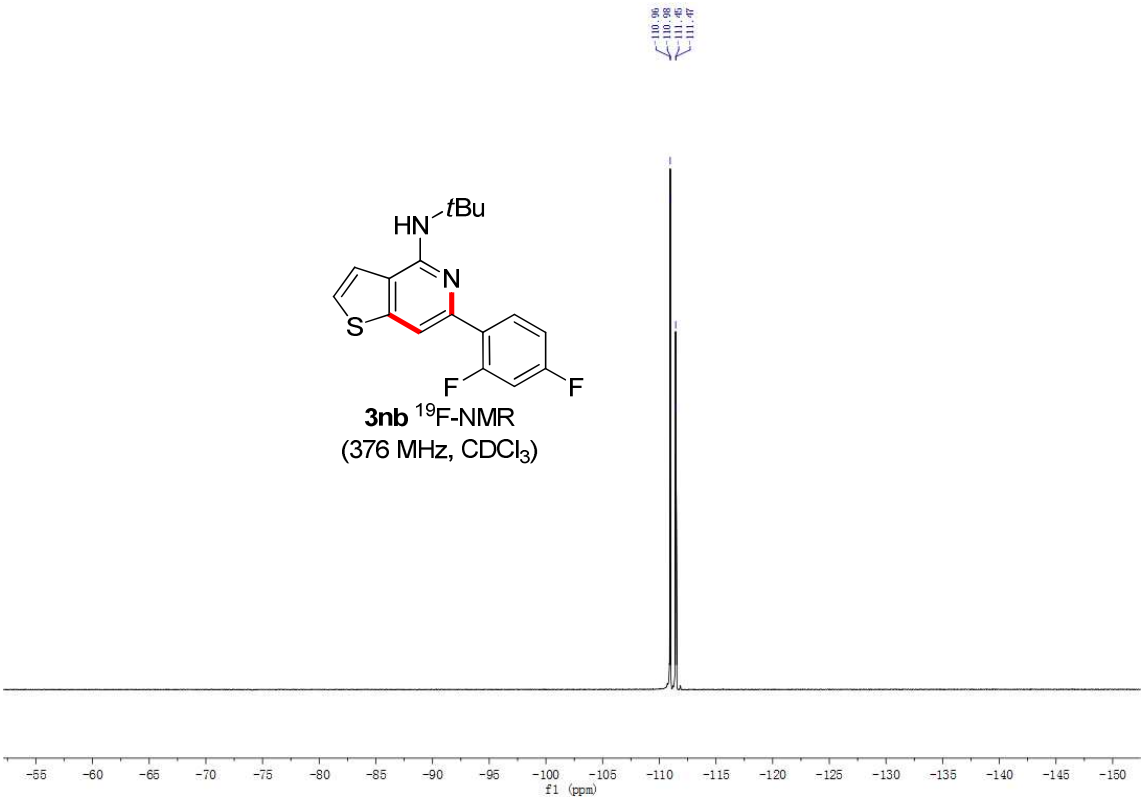
3ak ^{13}C-NMR
(100 MHz, $CDCl_3$)



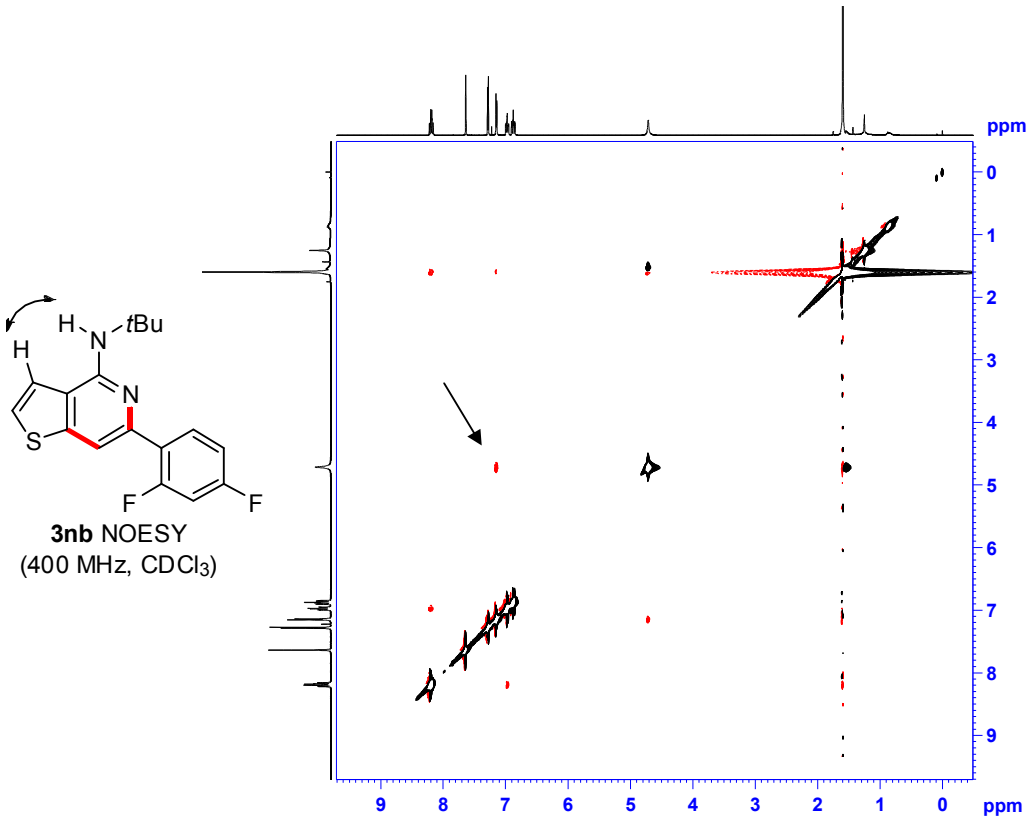
3nb ^{1}H-NMR
(400 MHz, $CDCl_3$)



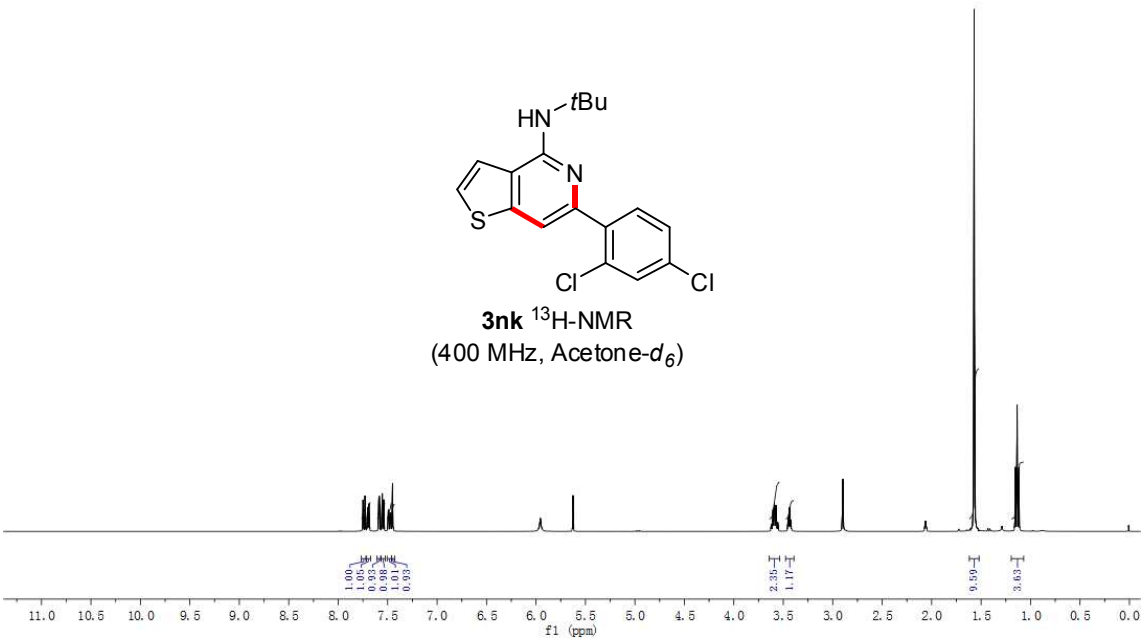
3nb ^{13}C-NMR
(100 MHz, $CDCl_3$)



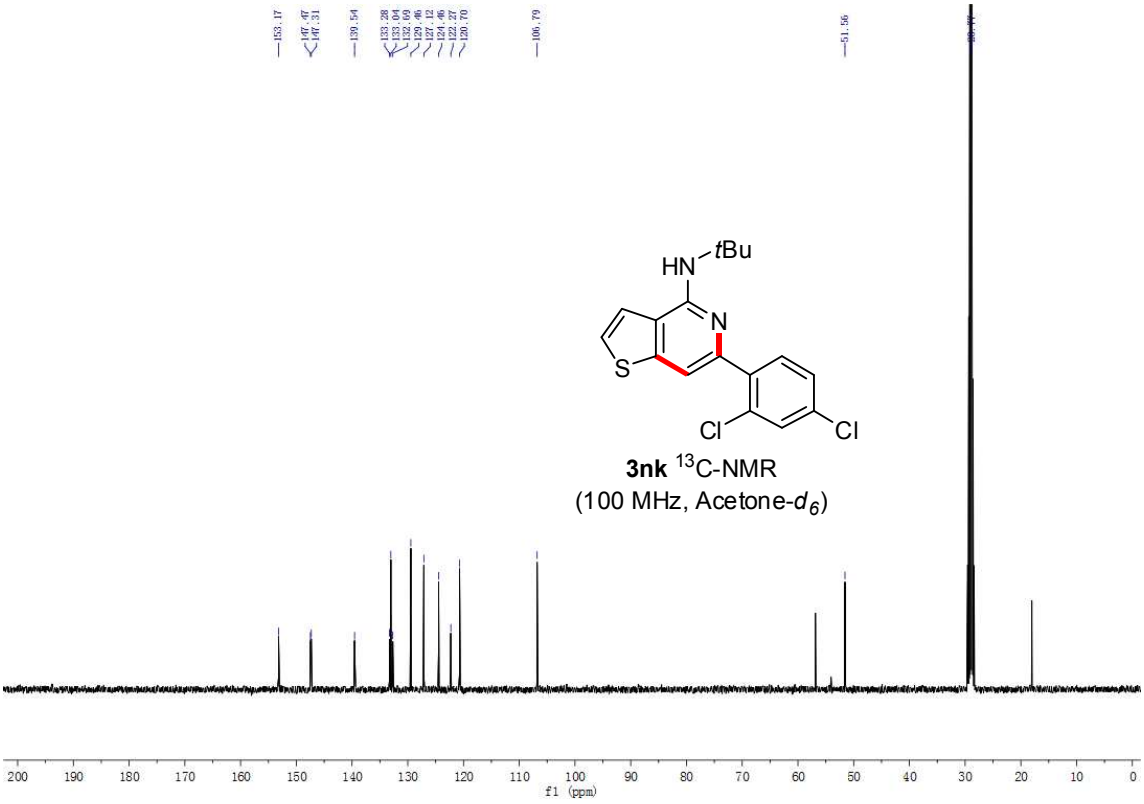
3nb ^{19}F-NMR
(376 MHz, $CDCl_3$)



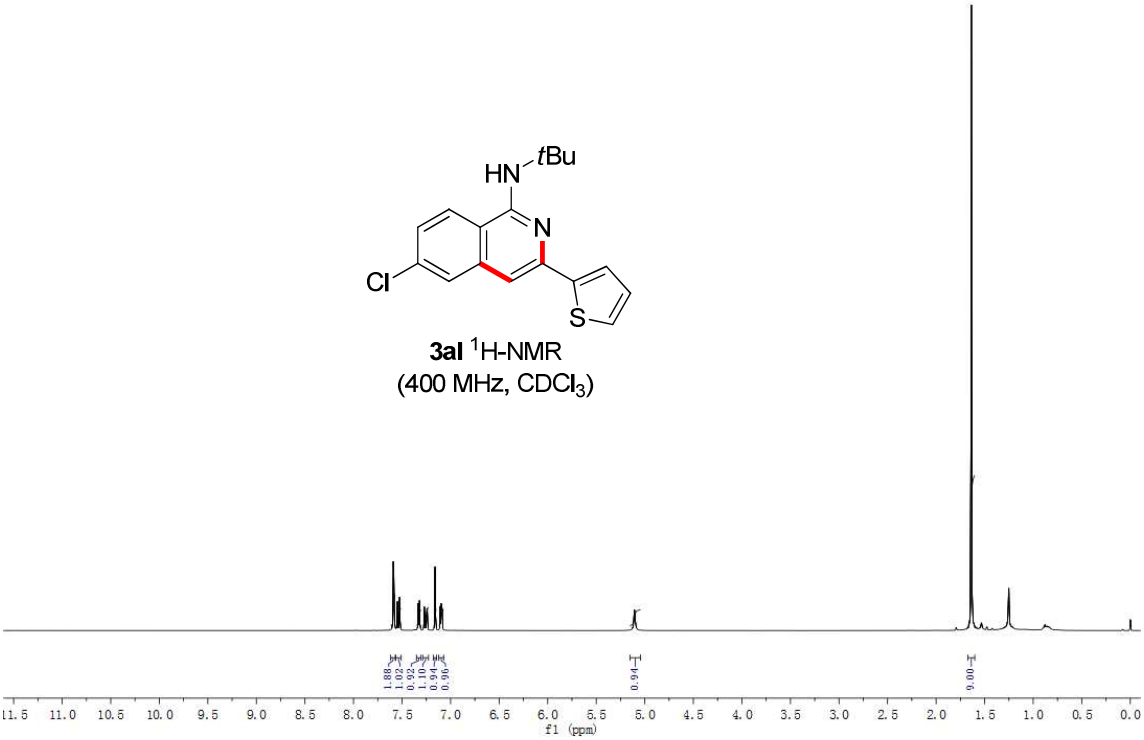
3nb NOESY
(400 MHz, $CDCl_3$)



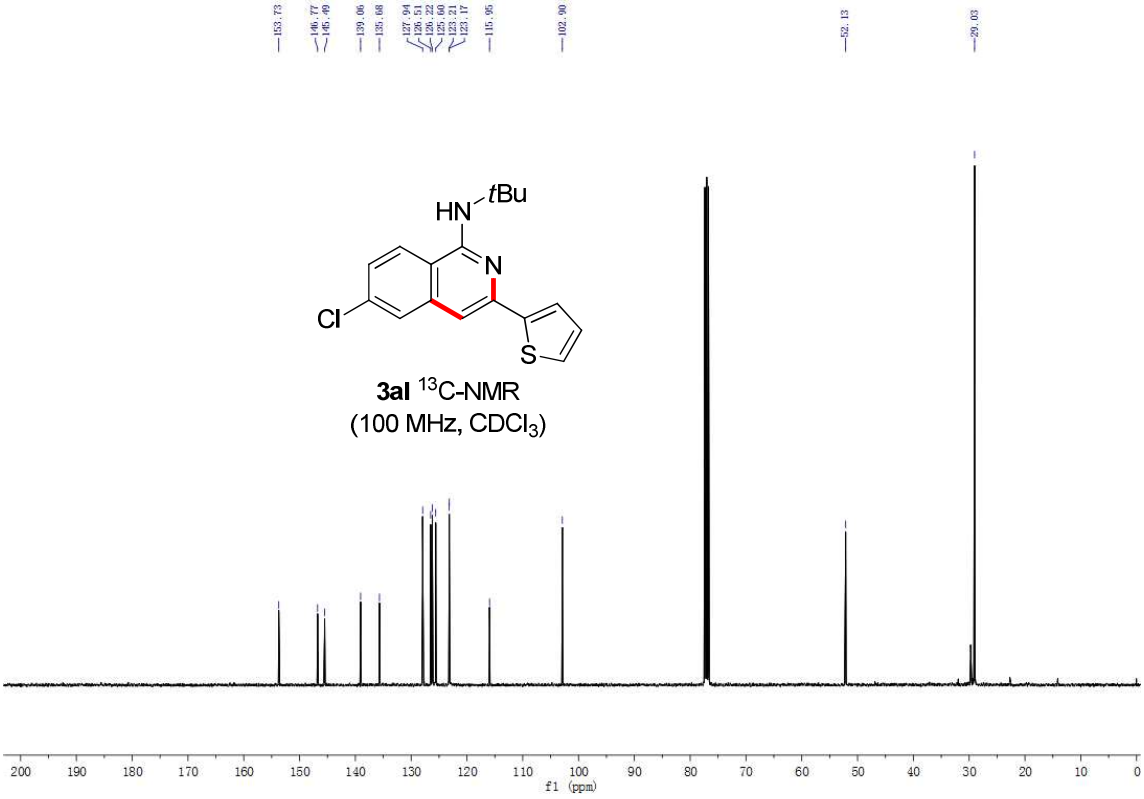
3nk ^{13}H-NMR
(400 MHz, Acetone-d_6)



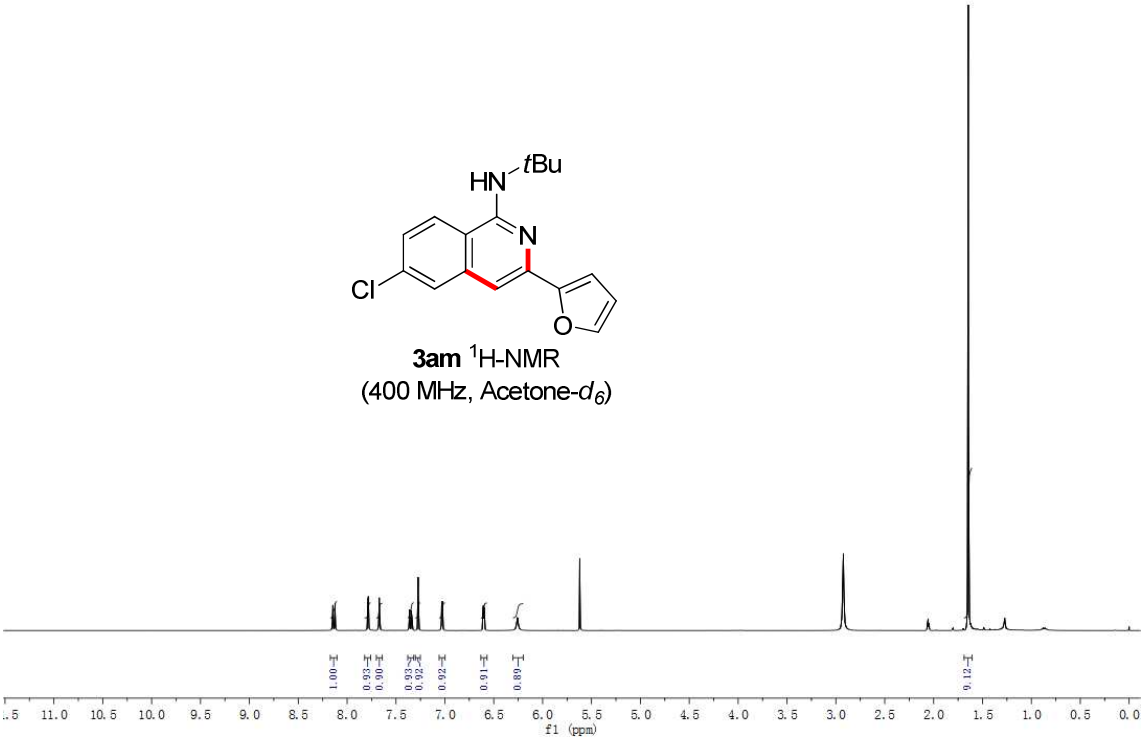
3nk ^{13}C-NMR
(100 MHz, Acetone-d_6)



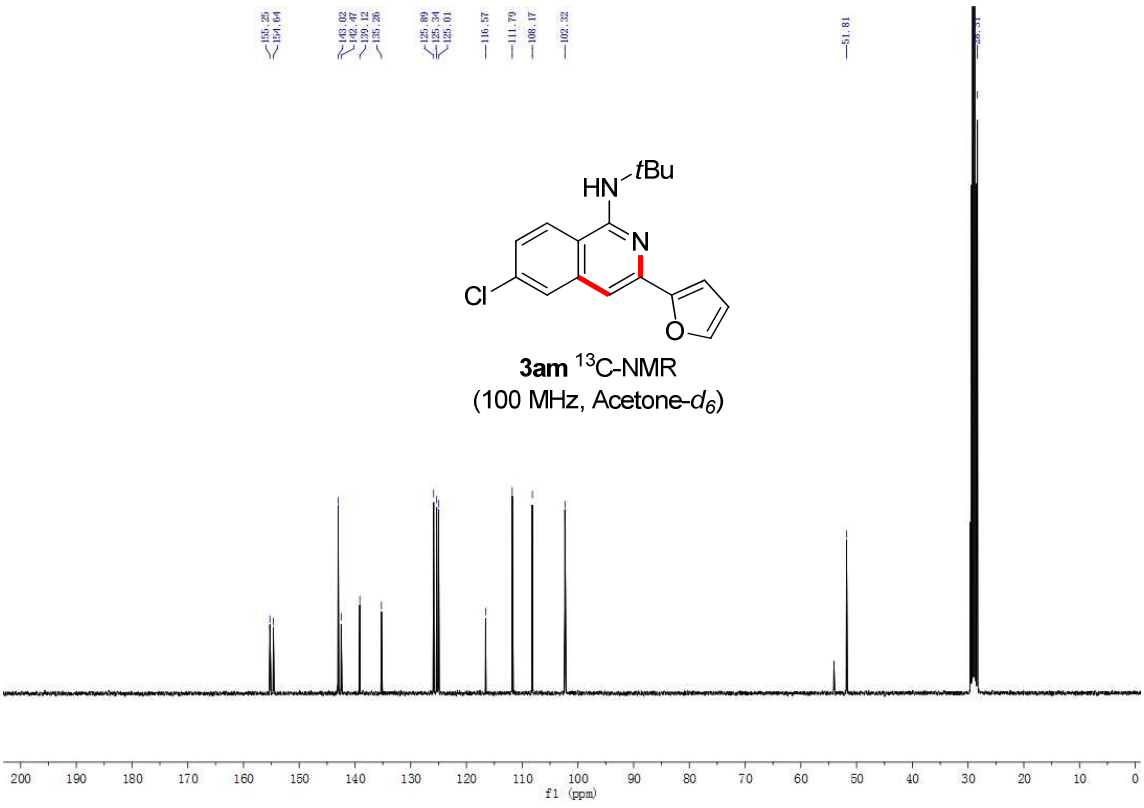
3al ^{1}H-NMR
(400 MHz, $CDCl_3$)



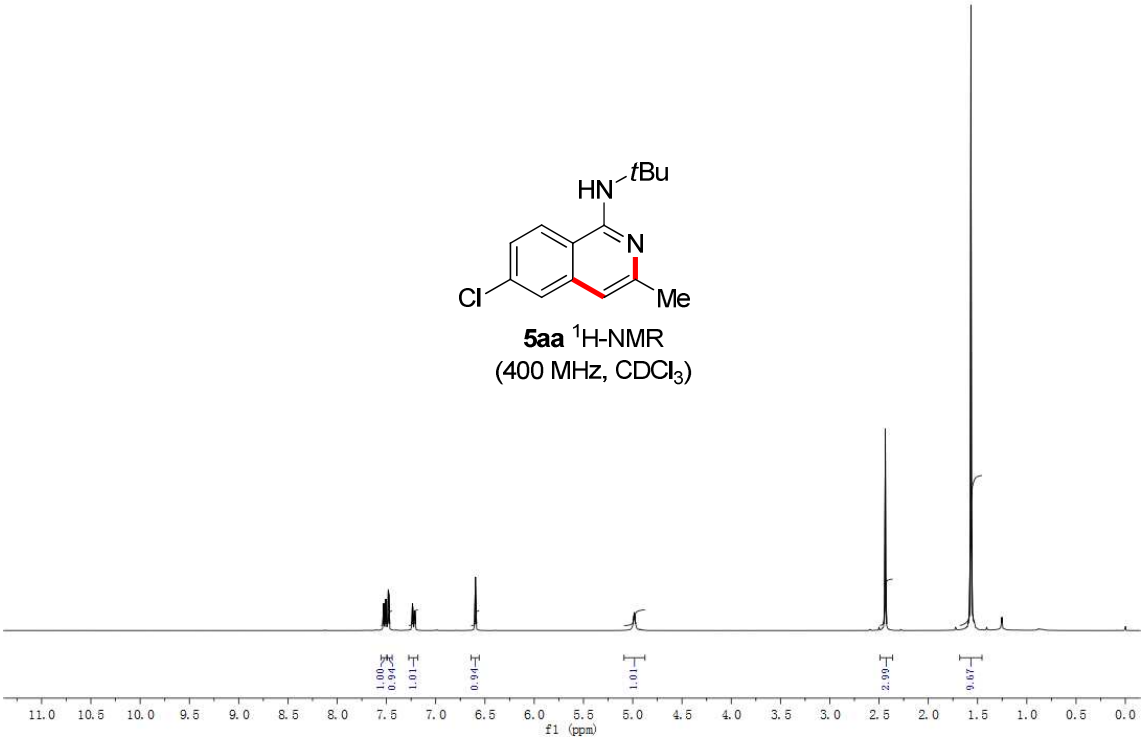
3al ^{13}C-NMR
(100 MHz, $CDCl_3$)



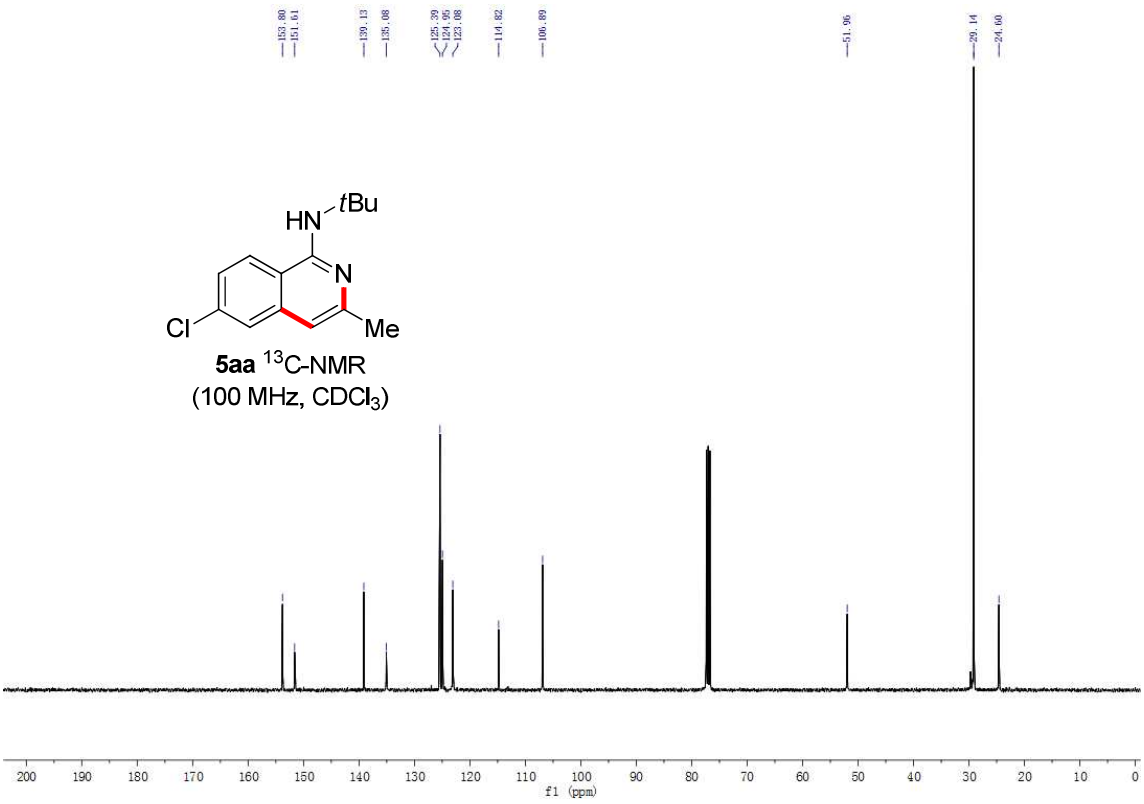
3am ^{1}H-NMR
(400 MHz, Acetone-d_6)



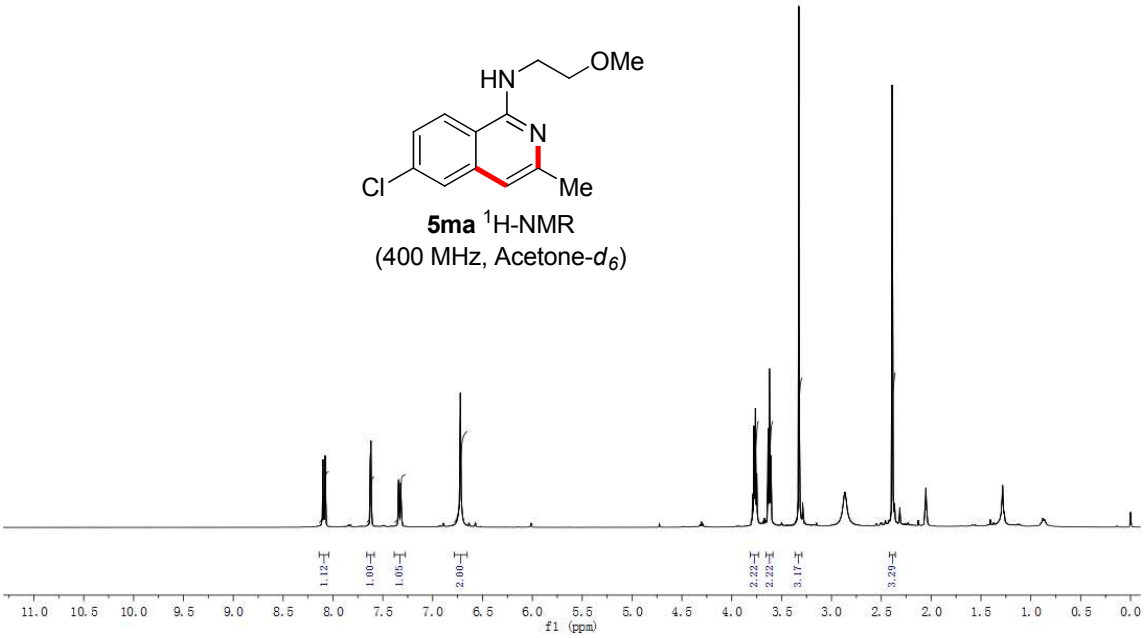
3am ^{13}C-NMR
(100 MHz, Acetone-d_6)



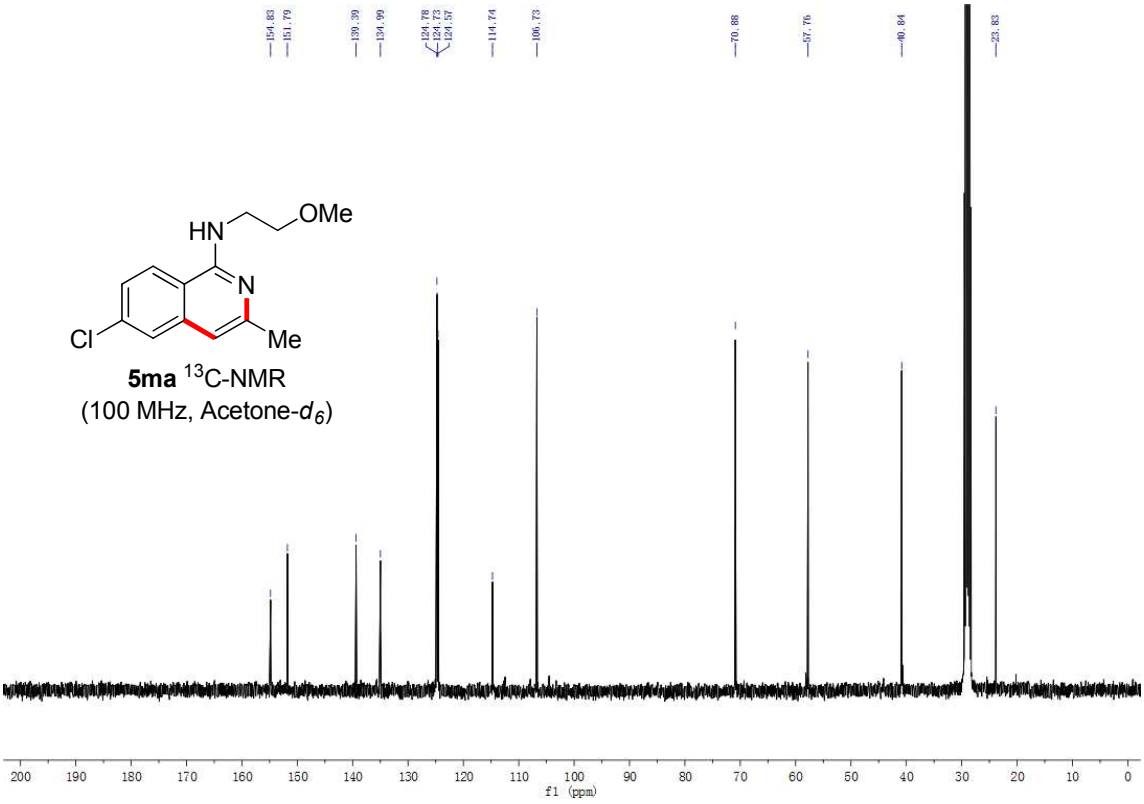
5aa ^{1}H-NMR
(400 MHz, $CDCl_3$)



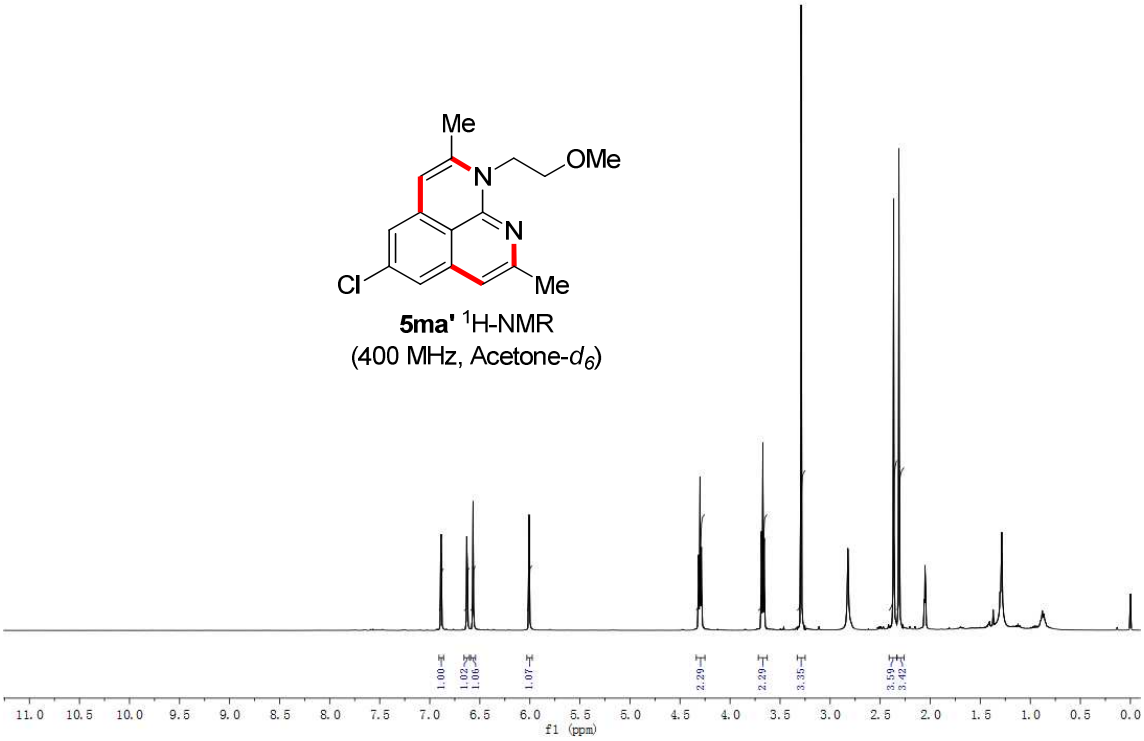
5aa ^{13}C-NMR
(100 MHz, $CDCl_3$)



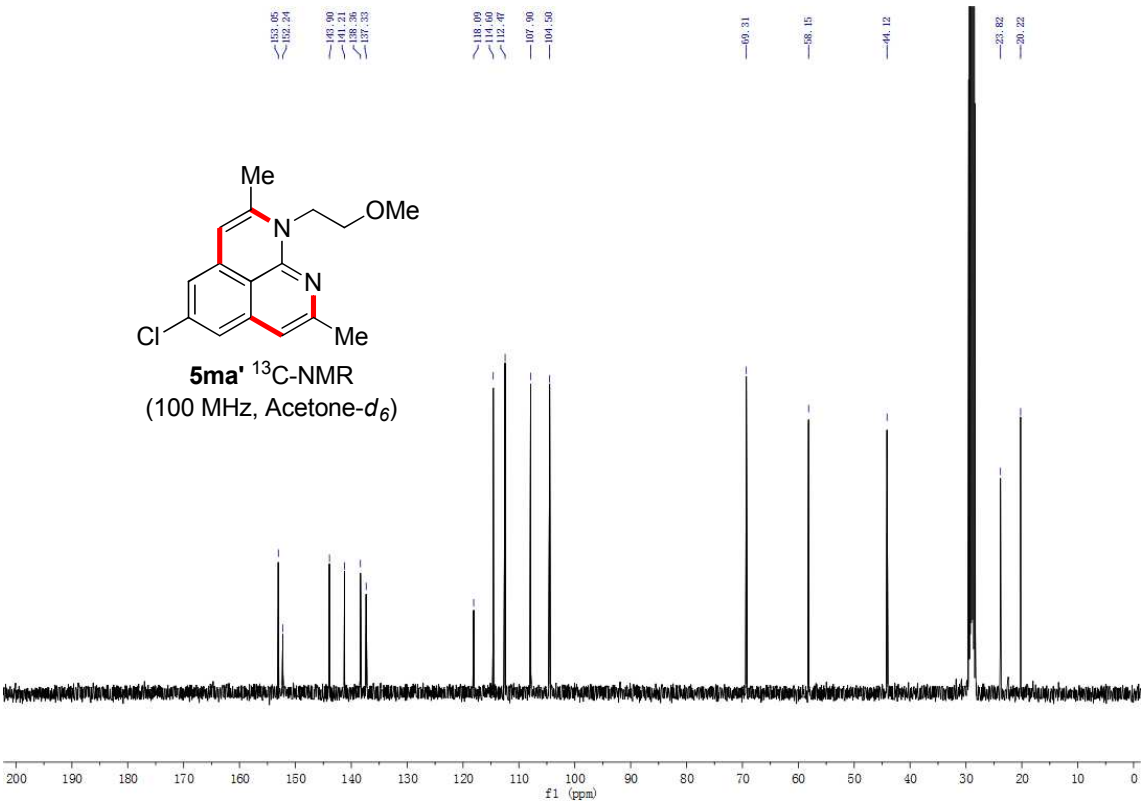
5ma ^{1}H-NMR
(400 MHz, Acetone-d_6)



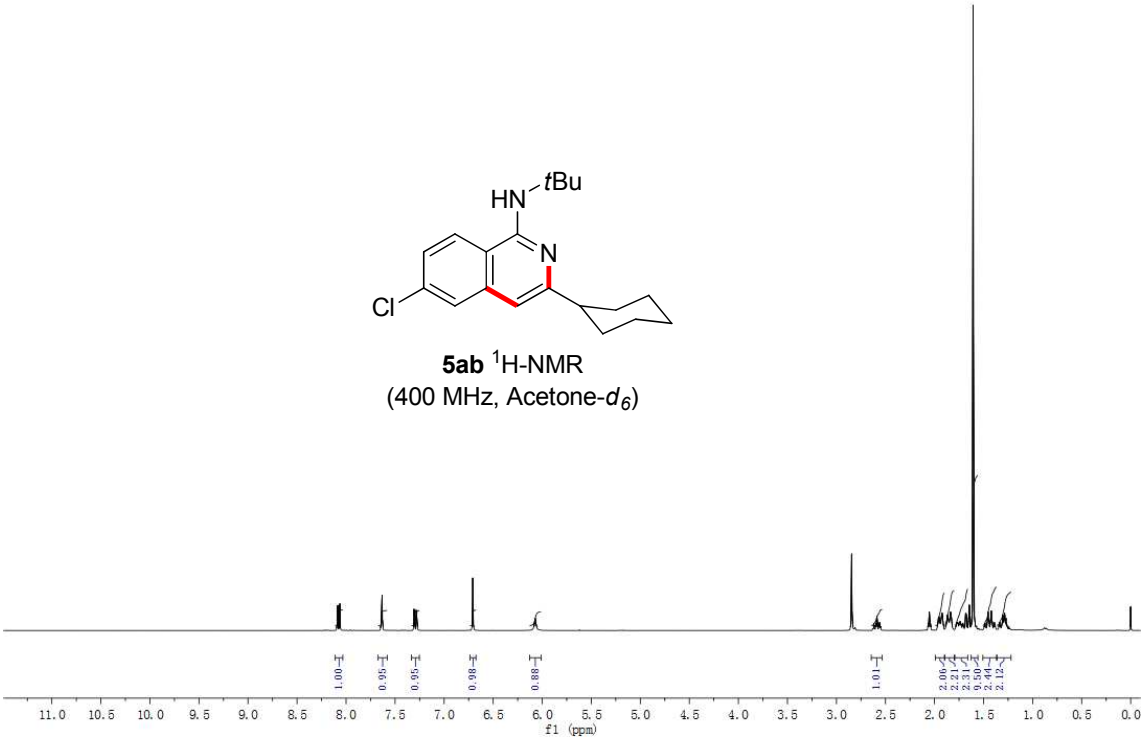
5ma ^{13}C-NMR
(100 MHz, Acetone-d_6)



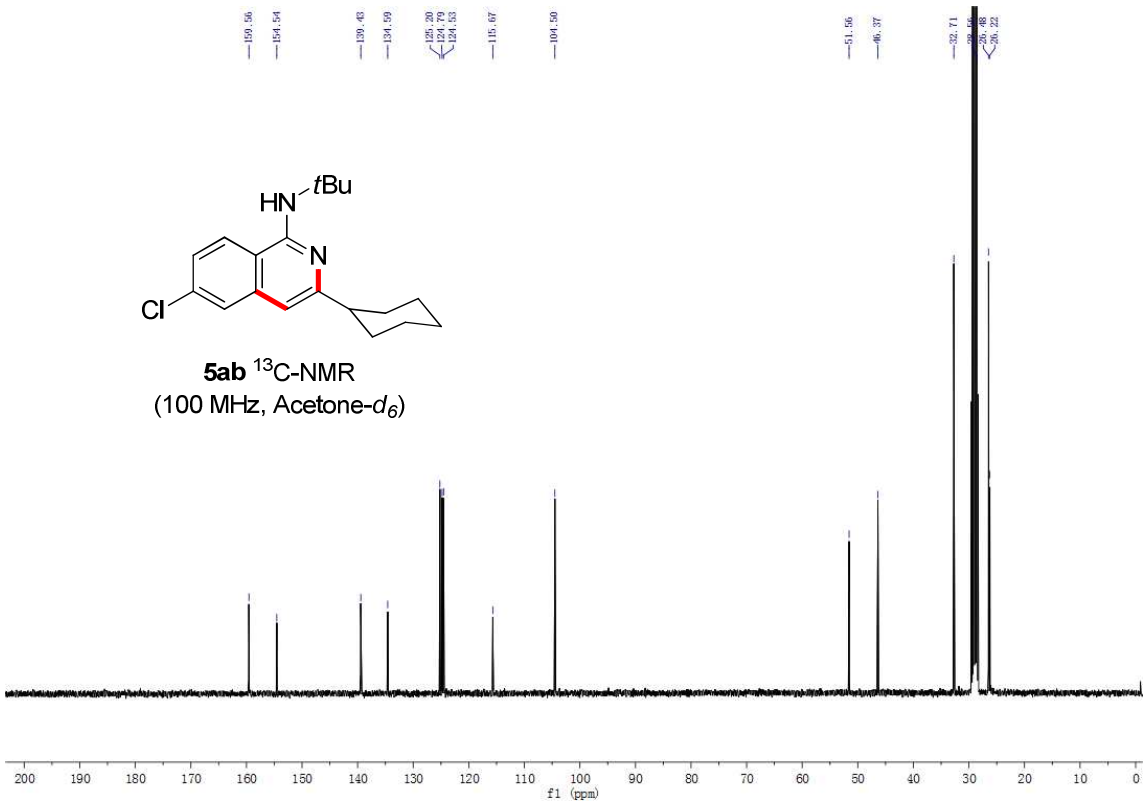
5ma' ^{1}H-NMR
(400 MHz, Acetone-d_6)



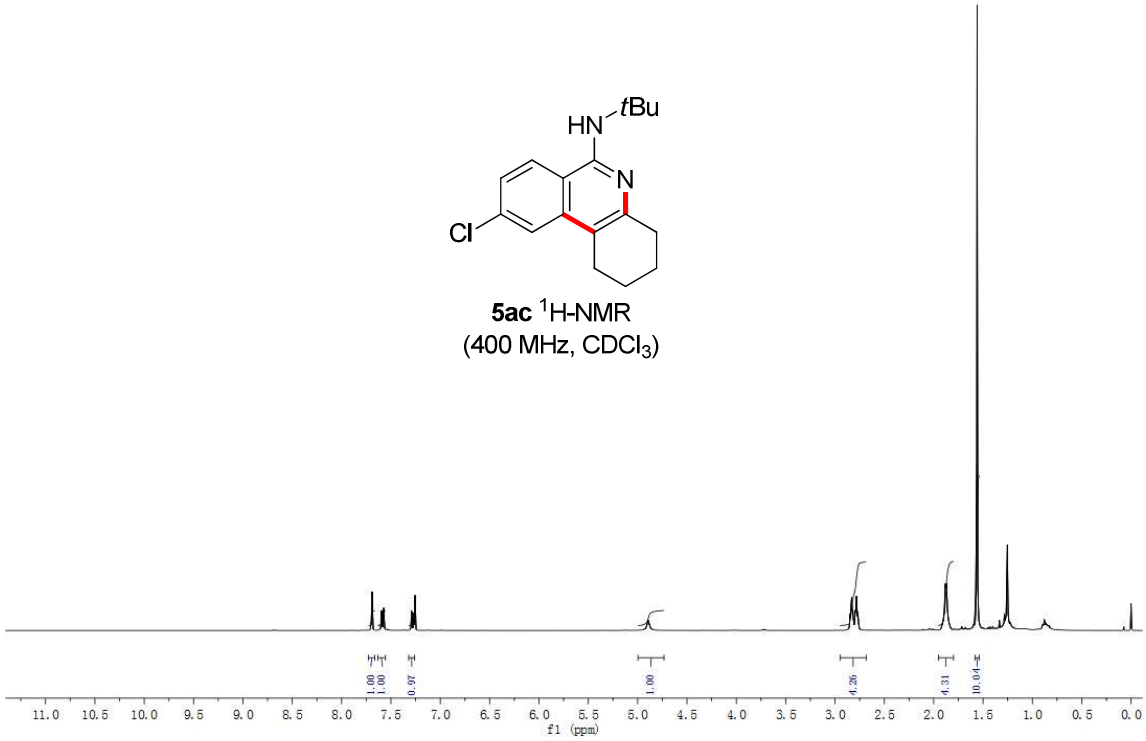
5ma' ^{13}C-NMR
(100 MHz, Acetone-d_6)



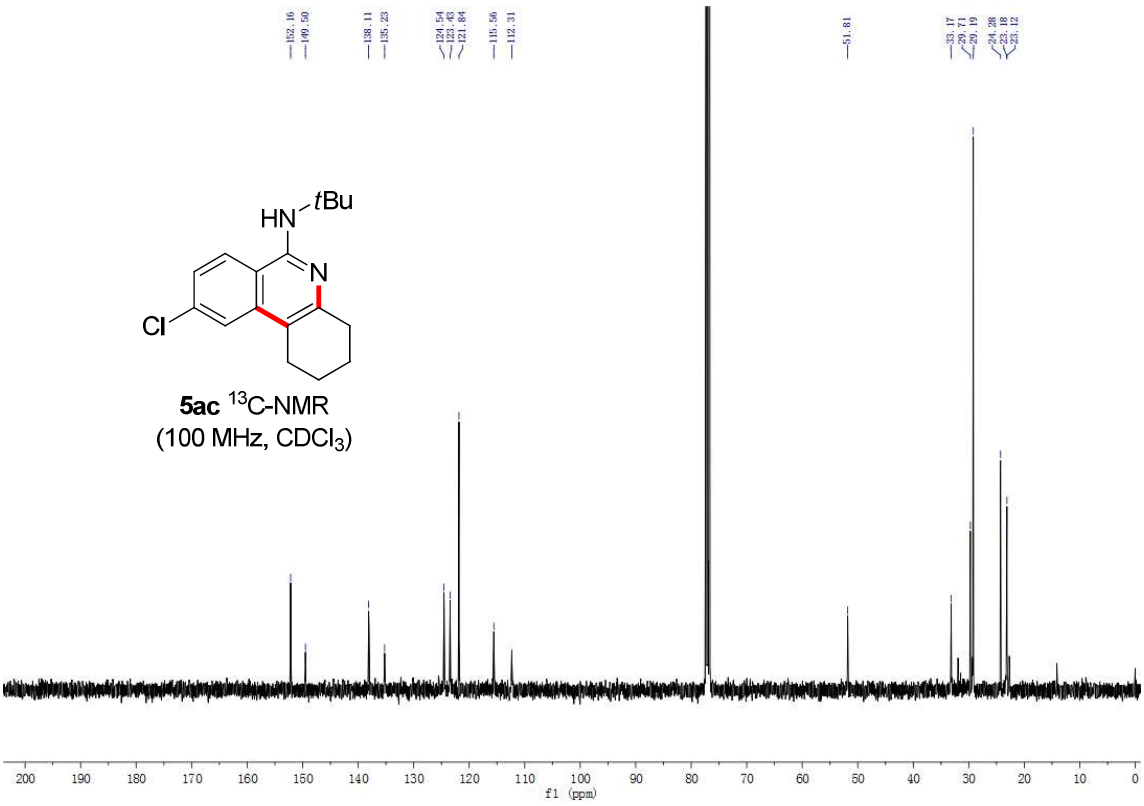
5ab ^{1}H-NMR
(400 MHz, Acetone-d_6)



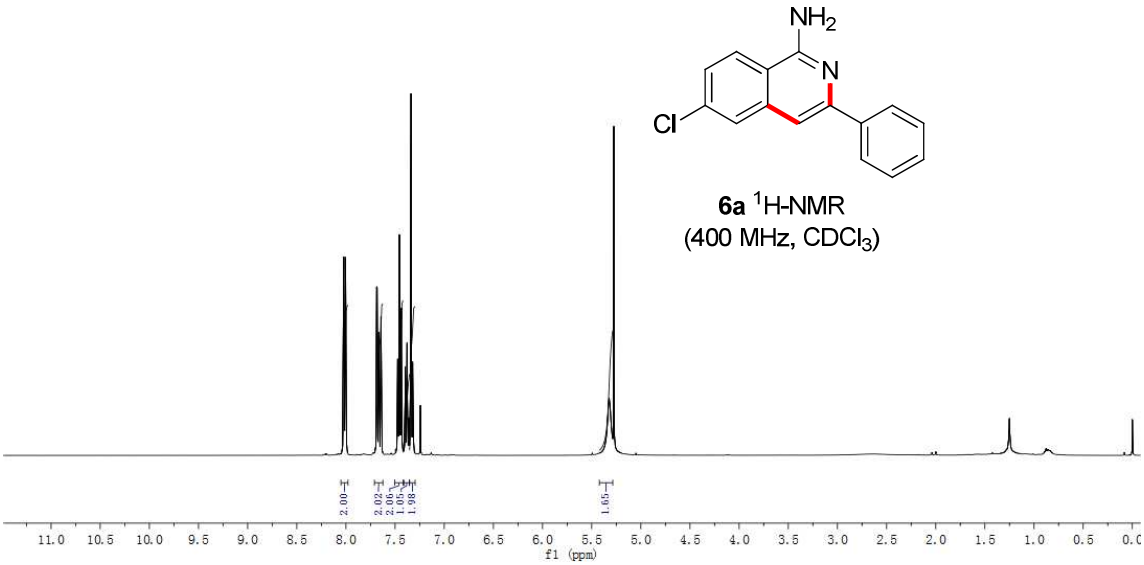
5ab ^{13}C-NMR
(100 MHz, Acetone-d_6)



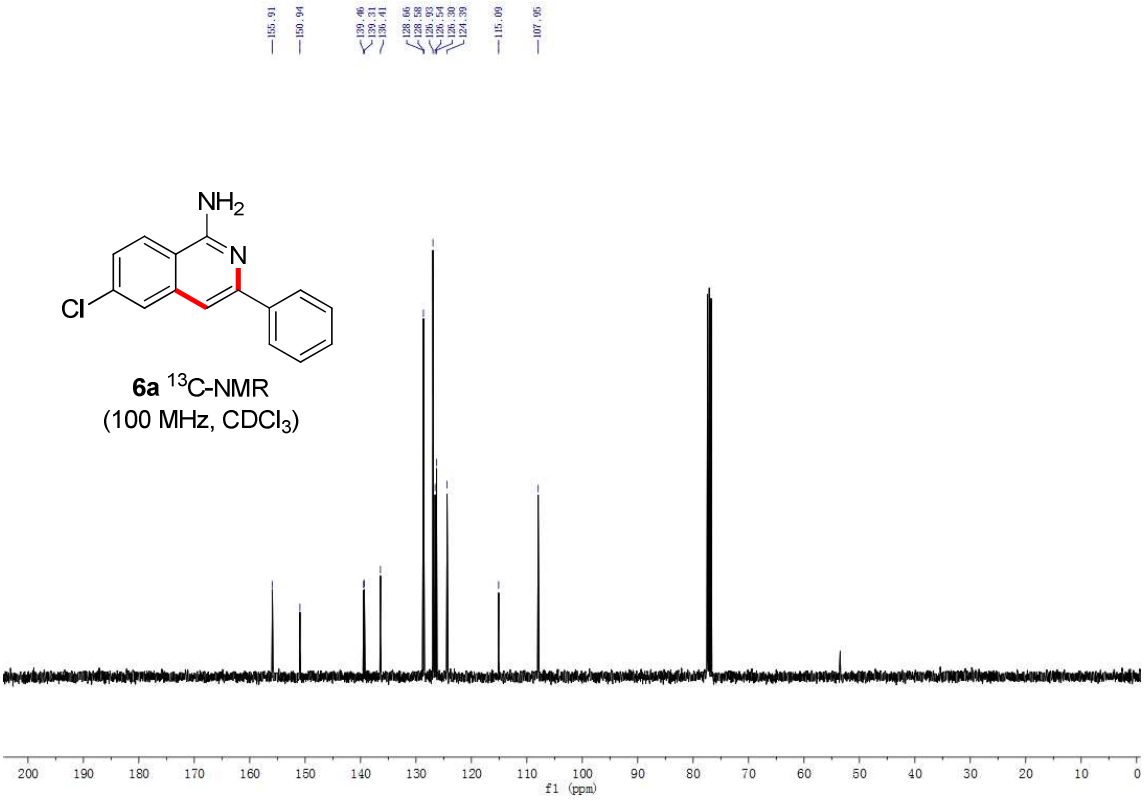
5ac ^{1}H-NMR
(400 MHz, $CDCl_3$)



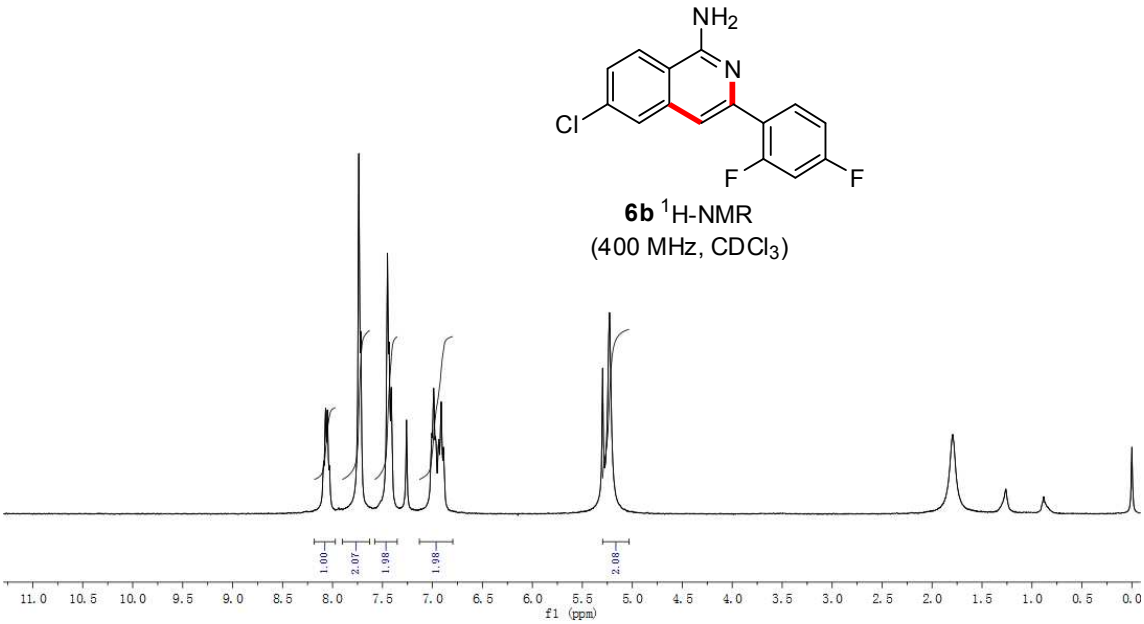
5ac ^{13}C-NMR
(100 MHz, $CDCl_3$)



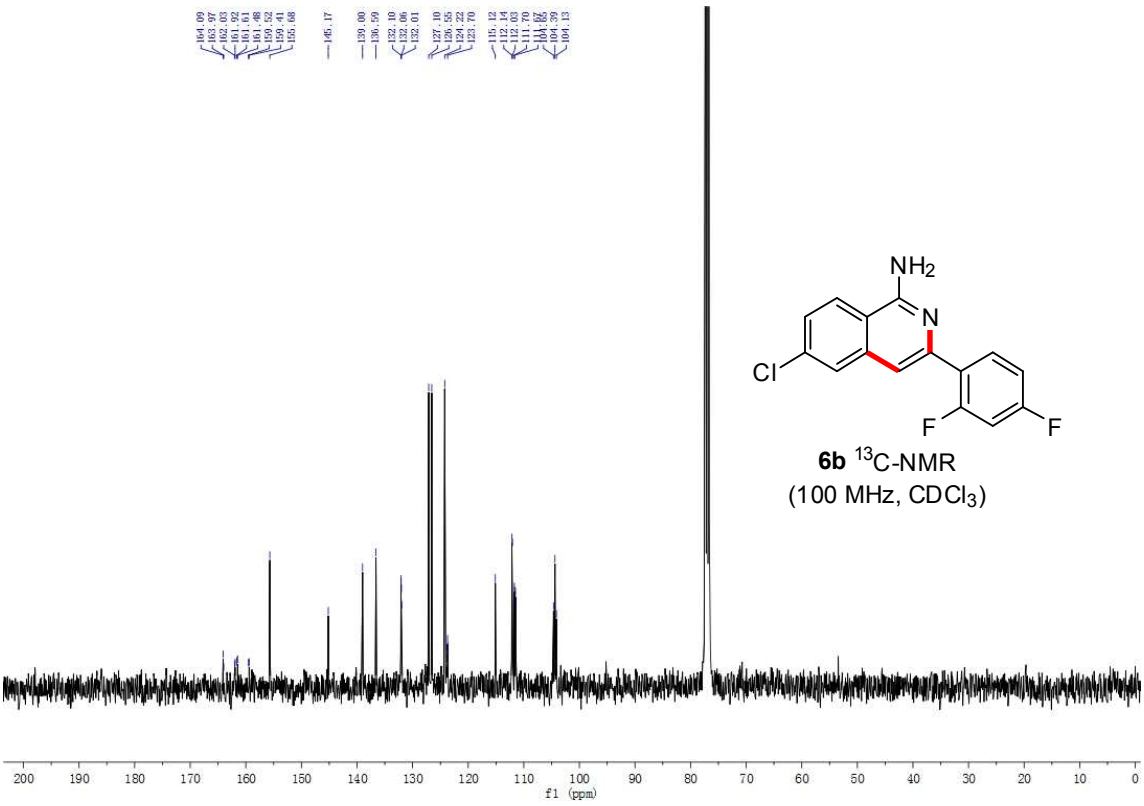
6a ^{1}H-NMR
(400 MHz, $CDCl_3$)



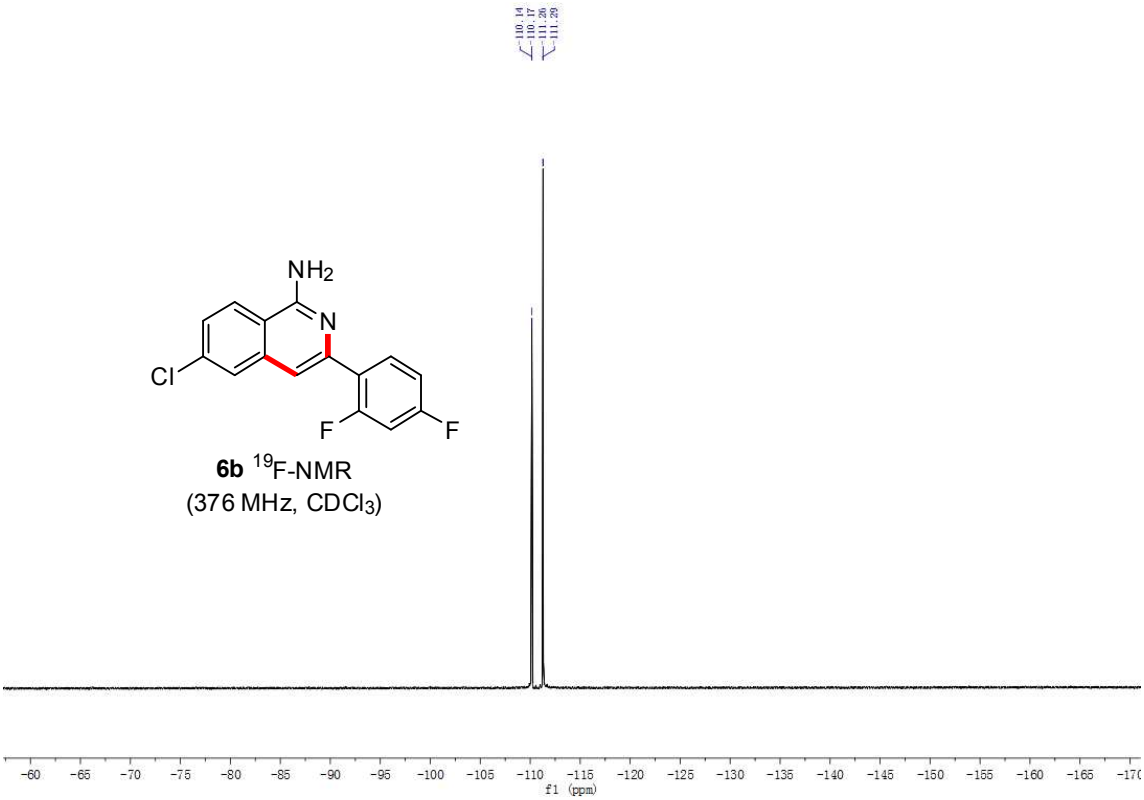
6a ^{13}C-NMR
(100 MHz, $CDCl_3$)



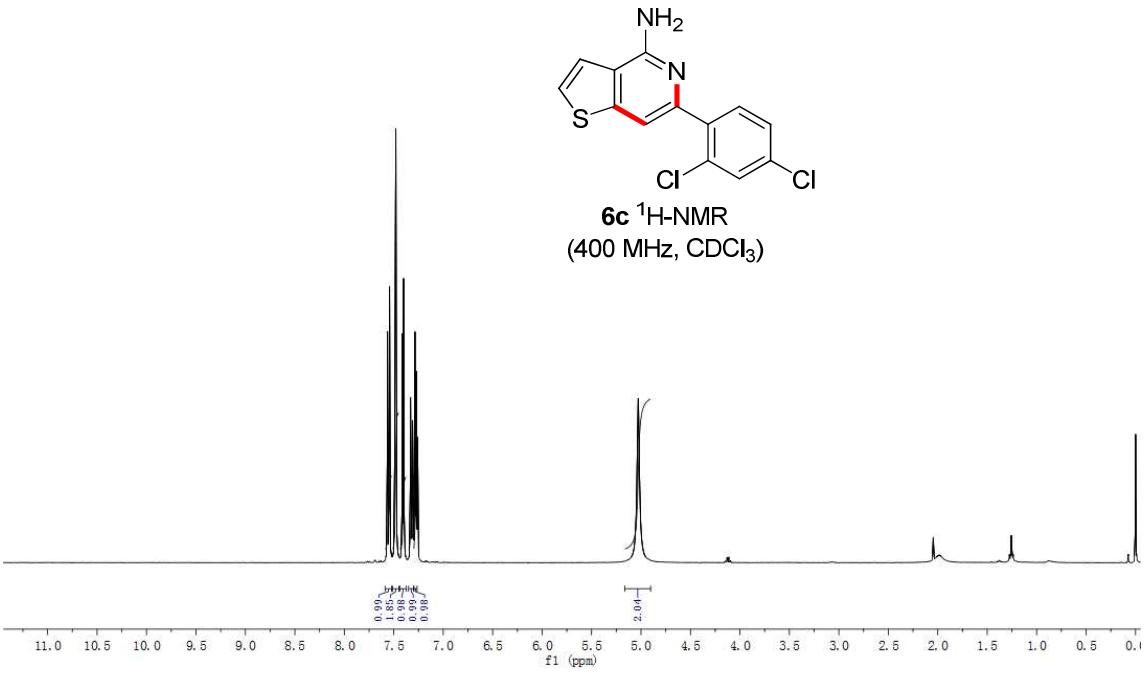
6b ^{1}H-NMR
(400 MHz, $CDCl_3$)



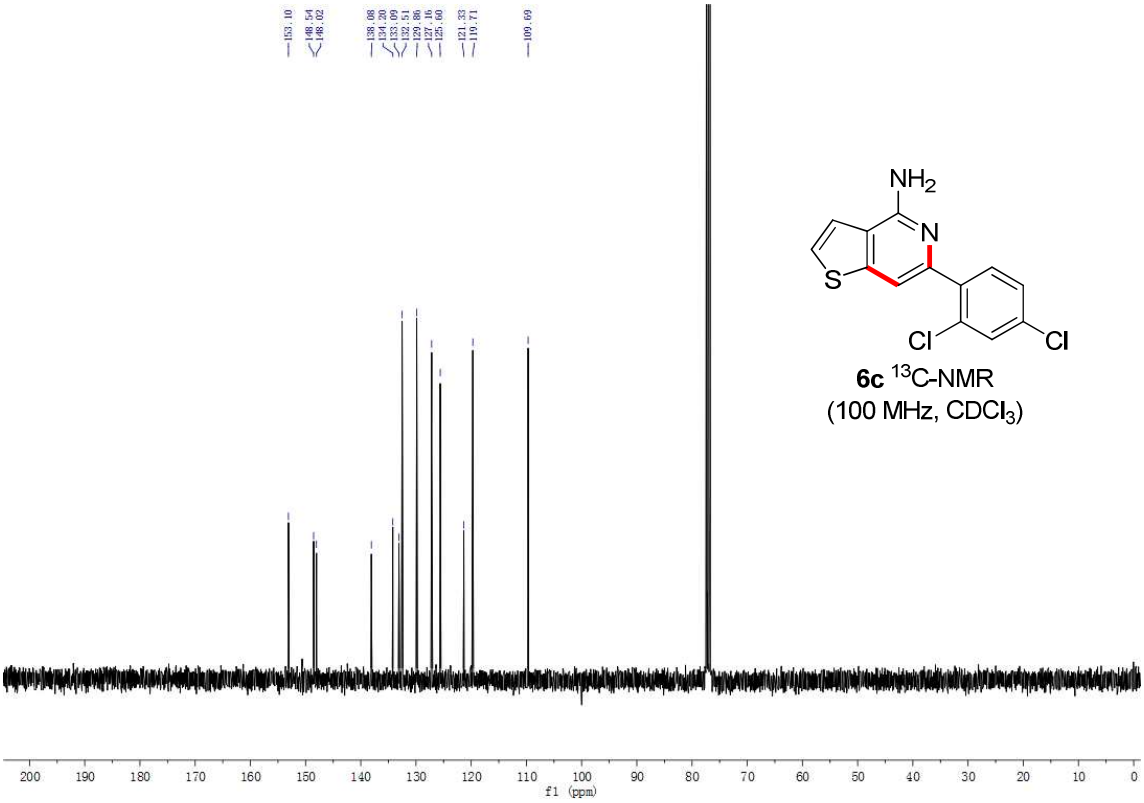
6b ^{13}C-NMR
(100 MHz, $CDCl_3$)



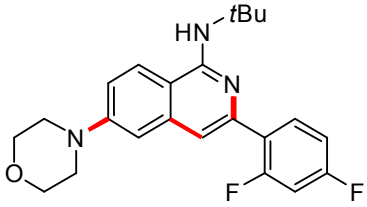
6b ^{19}F-NMR
(376 MHz, $CDCl_3$)



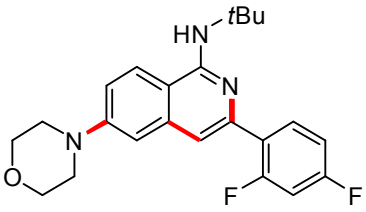
6c ^{1}H-NMR
(400 MHz, $CDCl_3$)



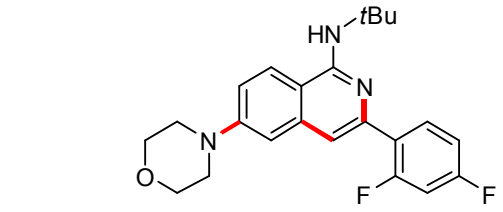
6c ^{13}C-NMR
(100 MHz, $CDCl_3$)



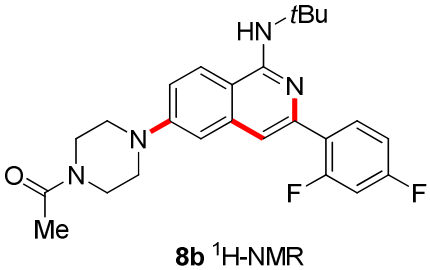
8a ^{1}H-NMR
(400 MHz, $CDCl_3$)



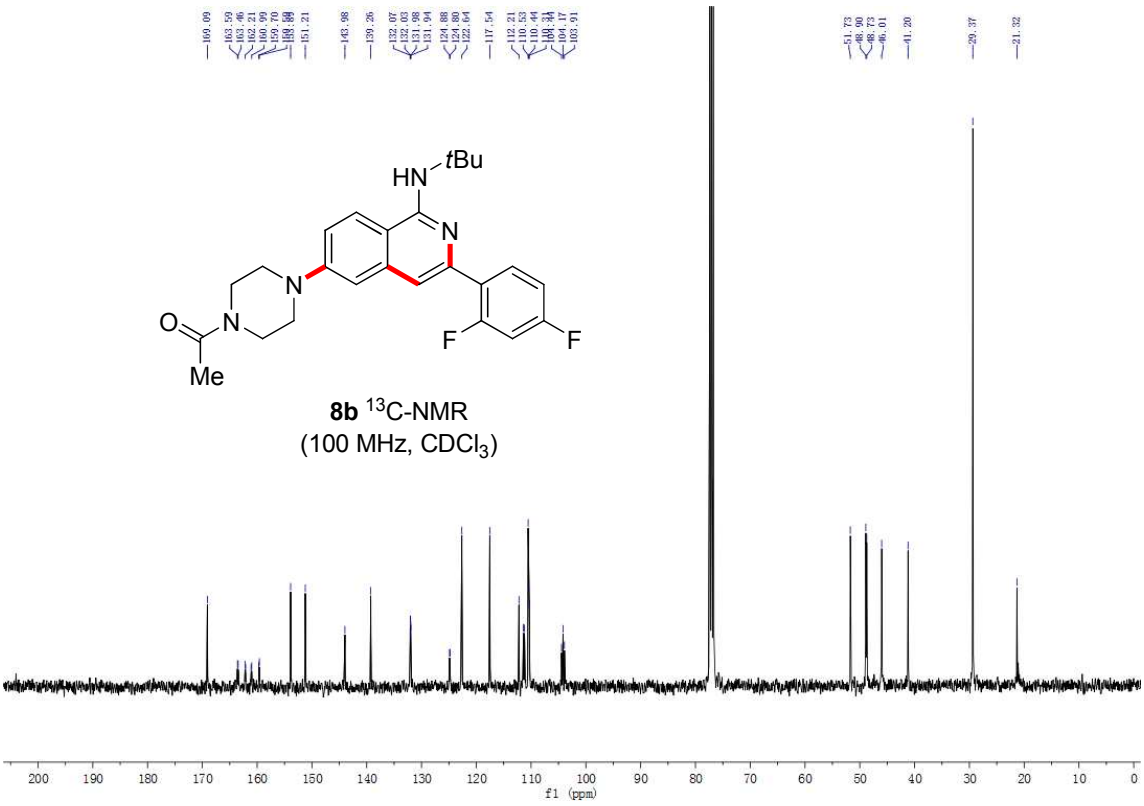
8a ^{13}C-NMR
(100 MHz, $CDCl_3$)



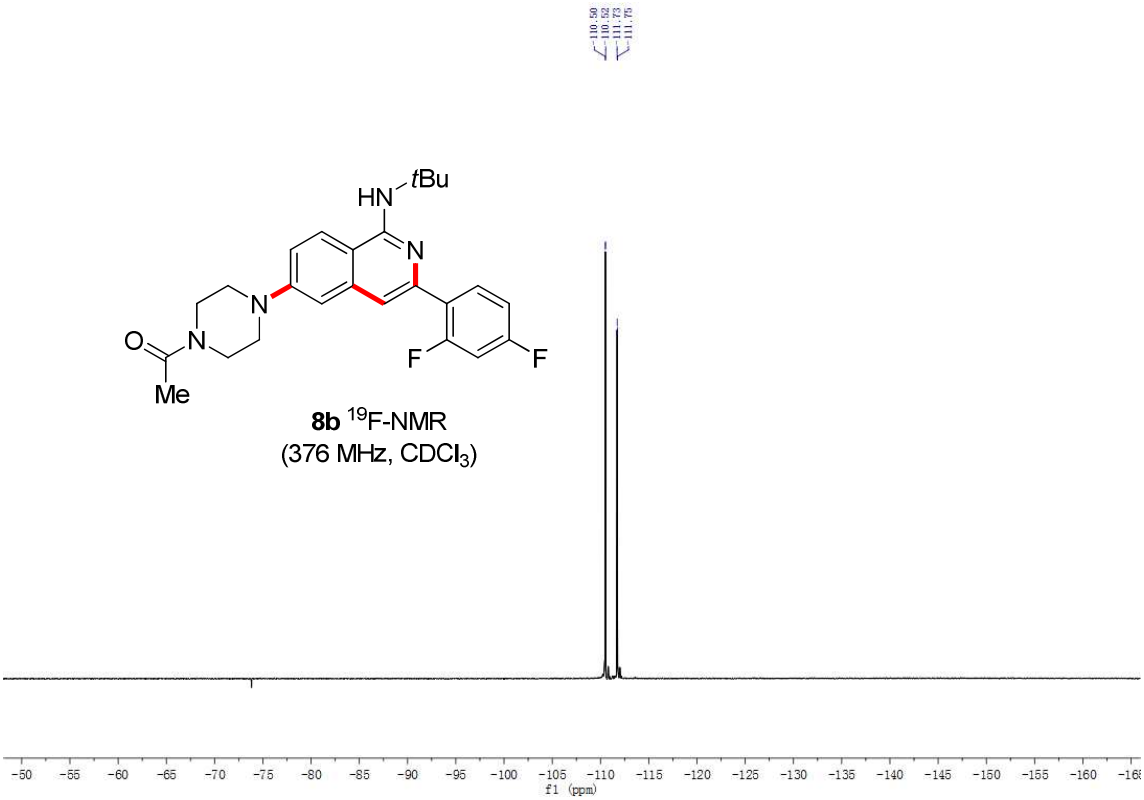
8a ^{19}F-NMR
(376 MHz, $CDCl_3$)



8b ^{1}H-NMR
(400 MHz, $CDCl_3$)



8b ^{13}C-NMR
(100 MHz, $CDCl_3$)



8b ^{19}F-NMR
(376 MHz, $CDCl_3$)