

**Amidines for Versatile Cobalt(III)-Catalyzed Synthesis of Isoquinolines through C–H Functionalization with Diazo Compounds**

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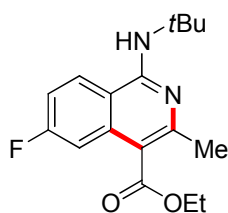
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### General Remarks

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 and cobalt catalyst were synthesized according to previously described methods: Aryl amidines **1a-1n**,<sup>[1]</sup> diazo compounds **2**,<sup>[2]</sup> Cp\*CoI<sub>2</sub>(CO).<sup>[3]</sup> 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 <sup>1</sup>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.

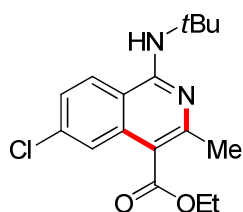
## Representative Procedure

**Representative Procedure A:** A suspension of aryl amidine **1** (0.50 mmol, 1.00 equiv), diazo compound **2** (1.00 mmol, 2.00 equiv), [Cp\*CoI<sub>2</sub>(CO)] (24.0 mg, 10.0 mol %), AgSbF<sub>6</sub> (34.4 mg, 20.0 mol %) and KOPiv (14.0 mg, 20.0 mol %) in anhydrous TFE (2.0 mL) was stirred at 110 °C for 16 h under an atmosphere of N<sub>2</sub>. At ambient temperature, 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**.



### Ethyl 1-(*tert*-butylamino)-6-fluoro-3-methylisoquinoline-4-carboxylate (**3aa**)

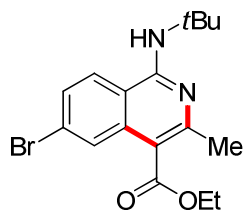
The general procedure **A** was followed using **1a** (97.0 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **3aa** (126 mg, 83%) as a slight yellow solid. M. p. = 87–89 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  = 7.68 (dd,  $J$  = 11.4, 2.5 Hz, 1H), 7.61 (dd,  $J$  = 9.1, 5.5 Hz, 1H), 7.08 (ddd,  $J$  = 9.1, 7.8, 2.6 Hz, 1H), 5.25 (s, 1H), 4.43 (q,  $J$  = 7.1 Hz, 2H), 2.57 (s, 3H), 1.56 (s, 9H), 1.41 (t,  $J$  = 7.1 Hz, 3H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  = 169.1, 163.4 (d,  $J_{C-F}$  = 249.0 Hz), 154.3, 153.1, 137.4 (d,  $J_{C-F}$  = 10.5 Hz), 123.9 (d,  $J_{C-F}$  = 9.8 Hz), 114.3 (d,  $J_{C-F}$  = 24.9 Hz), 112.9, 111.2 (d,  $J_{C-F}$  = 4.1 Hz), 109.3 (d,  $J_{C-F}$  = 23.1 Hz), 60.8, 52.4, 29.0, 24.4, 14.4. <sup>19</sup>F-NMR (CDCl<sub>3</sub>, 376 MHz):  $\delta$  = -108.98 (s). IR (ATR): 3418, 2927, 1699, 1630, 1538, 1262, 769 cm<sup>-1</sup>. HR-MS (ESI)  $m/z$  calcd for C<sub>17</sub>H<sub>22</sub>FN<sub>2</sub>O<sub>2</sub> [M+H<sup>+</sup>] 305.1665, found 305.1669 [M+H<sup>+</sup>].



### Ethyl 1-(*tert*-butylamino)-6-chloro-3-methylisoquinoline-4-carboxylate (**3ba**)

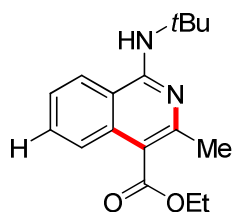
The general procedure **A** was followed using **1b** (105 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **3ba**

(110 mg, 69%) as a slight yellow solid. M. p. = 103–105 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): δ = 7.94 (s, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.22 (d, *J* = 8.8 Hz, 1H), 5.22 (s, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 2.51 (s, 3H), 1.50 (s, 9H), 1.36 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): δ = 168.0, 153.2, 151.7, 135.4, 135.3, 124.5, 123.1, 121.9, 113.1, 109.8, 59.9, 51.4, 28.0, 23.3, 13.4. IR (ATR): 3396, 2962, 1685, 1524, 1258, 1094 cm<sup>-1</sup>. HR-MS (ESI) *m/z* calcd for C<sub>17</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub> [M+H<sup>+</sup>] 321.1370, found 321.1374 [M+H<sup>+</sup>].



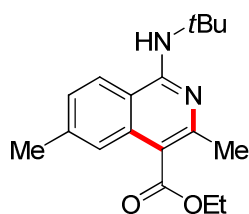
### Ethyl 6-bromo-1-(*tert*-butylamino)-3-methylisoquinoline-4-carboxylate (**3ca**)

The general procedure A was followed using **1c** (127 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **3ca** (133 mg, 73%) as a slight yellow solid. M. p. = 93–96 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): δ = 8.11 (s, 1H), 7.39 (d, *J* = 8.8 Hz, 1H), 7.34 (d, *J* = 8.8 Hz, 1H), 5.20 (s, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.51 (s, 3H), 1.49 (s, 9H), 1.35 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): δ = 169.0, 154.3, 152.7, 136.7, 128.1, 127.3, 125.0, 122.9, 114.4, 110.7, 60.9, 52.4, 29.0, 24.4, 14.4. IR (ATR): 3399, 2965, 1696, 1529, 1355, 1197 cm<sup>-1</sup>. HR-MS (ESI) *m/z* calcd for C<sub>17</sub>H<sub>22</sub>BrN<sub>2</sub>O<sub>2</sub> [M+H<sup>+</sup>] 365.0865, found 365.0871 [M+H<sup>+</sup>].



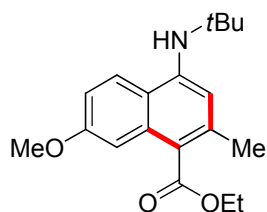
### Ethyl 1-(*tert*-butylamino)-3-methylisoquinoline-4-carboxylate (**3da**)

The general procedure A was followed using **1d** (88.0 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **3da** (112 mg, 78%) as a yellow oil. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): δ = 7.99 (d, *J* = 8.4 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 1H), 7.58 (ddd, *J* = 8.3, 7.0, 1.1 Hz, 1H), 7.39 (ddd, *J* = 8.4, 7.0, 1.1 Hz, 1H), 5.34 (s, 1H), 4.48 (q, *J* = 7.1 Hz, 2H), 2.61 (s, 3H), 1.61 (s, 9H), 1.47 (t, *J* = 7.1 Hz, 2H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): δ = 168.7, 153.4, 149.9, 134.1, 129.0, 124.0, 123.8, 120.1, 115.0, 110.8, 59.8, 51.2, 28.1, 23.1, 13.5. IR (ATR): 3432, 2974, 1700, 1523, 1203, 1062 cm<sup>-1</sup>. HR-MS (ESI) *m/z* calcd for C<sub>17</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub> [M+H<sup>+</sup>] 287.1760, found 287.1766 [M+H<sup>+</sup>].



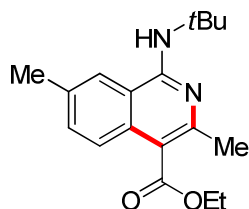
#### Ethyl 1-(*tert*-butylamino)-3,6-dimethylisoquinoline-4-carboxylate (**3ea**)

The general procedure **A** was followed using **1e** (95.0 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **3ea** (98 mg, 65%) as an oil. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz): δ = 7.63 (s, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 5.18 (s, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.48 (s, 3H), 2.37 (s, 3H), 1.49 (s, 9H), 1.35 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): δ = 169.8, 154.4, 150.7, 140.0, 135.3, 126.8, 124.0, 121.0, 114.1, 111.6, 60.7, 52.1, 29.1, 24.1, 22.0, 14.4. IR (ATR): 3415, 2969, 1682, 1626, 1526, 1261 cm<sup>-1</sup>. HR-MS (ESI) *m/z* calcd for C<sub>18</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub> [M+H<sup>+</sup>] 301.1916, found 301.1921 [M+H<sup>+</sup>].



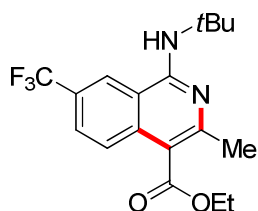
#### Ethyl 4-(*tert*-butylamino)-7-methoxy-2-methyl-1-naphthoate (**3fa**)

The general procedure **A** was followed using **1f** (103 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **3fa** (96 mg, 61%) as a yellow oil. M. p. = 117–119 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): δ = 7.46 (d, *J* = 9.1 Hz, 1H), 7.33 (s, 1H), 6.90 (d, *J* = 9.1 Hz, 1H), 5.12 (s, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 2.50 (s, 3H), 1.49 (s, 9H), 1.36 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): δ = 168.7, 159.7, 153.4, 151.3, 136.3, 121.9, 115.3, 110.1, 109.8, 103.0, 59.5, 54.2, 51.1, 28.2, 23.5, 13.4. IR (ATR): 3426, 2961, 1697, 1520, 1358, 1195 cm<sup>-1</sup>. HR-MS (ESI) *m/z* calcd for C<sub>18</sub>H<sub>25</sub>N<sub>2</sub>O<sub>3</sub> [M+H<sup>+</sup>] 317.1865, found 317.1872 [M+H<sup>+</sup>].



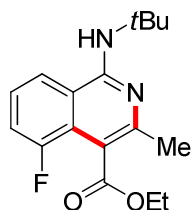
### Ethyl 1-(*tert*-butylamino)-3,7-dimethylisoquinoline-4-carboxylate (**3ga**)

The general procedure **A** was followed using **1g** (95.0 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **3ga** (77 mg, 51%) as an oil. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): δ = 7.80 (d, *J* = 9.2 Hz, 1H), 7.35 – 7.28 (m, 2H), 5.17 (s, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.50 (s, 3H), 2.41 (s, 3H), 1.51 (s, 9H), 1.35 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): δ = 168.7, 152.9, 148.9, 133.6, 132.1, 130.8, 123.7, 119.3, 115.0, 110.6, 59.6, 51.1, 28.1, 23.0, 20.6, 13.4. IR (ATR): 3412, 2969, 1682, 1356, 1260, 1174 cm<sup>-1</sup>. HR-MS (ESI) *m/z* calcd for C<sub>18</sub>H<sub>25</sub>N<sub>2</sub>O<sub>2</sub> [M+H<sup>+</sup>] 301.1916, found 301.1919 [M+H<sup>+</sup>].



### Ethyl 1-(*tert*-butylamino)-3-methyl-7-(trifluoromethyl)isoquinoline-4-carboxylate (**3ha**)

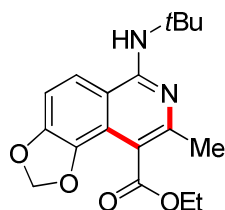
The general procedure **A** was followed using **1h** (122 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1→10:1) yielded **3ha** (74 mg, 42%) as a slight yellow solid. M. p. = 121–123 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): δ = 8.13 (d, *J* = 8.9 Hz, 1H), 7.90 (s, 1H), 7.74 (dd, *J* = 8.9, 1.5 Hz, 1H), 5.39 (s, 1H), 4.49 (q, *J* = 7.1 Hz, 2H), 2.64 (s, 3H), 1.63 (s, 9H), 1.46 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): δ = 169.0, 154.6, 153.7, 137.2, 126.5 (q, *J*<sub>C-F</sub> = 32.7 Hz), 125.9, 125.7 (q, *J*<sub>C-F</sub> = 3.1 Hz), 124.1 (q, *J*<sub>C-F</sub> = 272.1 Hz), 119.0 (q, *J*<sub>C-F</sub> = 4.3 Hz), 114.8, 111.5, 61.0, 52.7, 28.9, 24.4, 14.4. <sup>19</sup>F-NMR (CDCl<sub>3</sub>, 376 MHz): δ = -62.11 (s). IR (ATR): 3398, 2921, 1696, 1531, 1210, 1082 cm<sup>-1</sup>. HR-MS (EI) *m/z* calcd for C<sub>18</sub>H<sub>22</sub>F<sub>3</sub>N<sub>2</sub>O<sub>2</sub> [M+H<sup>+</sup>] 355.1633, found 355.1639 [M+H<sup>+</sup>].



### Ethyl 1-(*tert*-butylamino)-5-fluoro-3-methylisoquinoline-4-carboxylate (**3ia**)

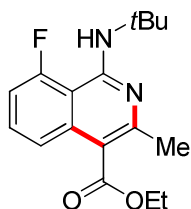
The general procedure **A** was followed using **1i** (97.0 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **3ia**

(116 mg, 76%) as a slight yellow oil.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  = 7.35 (d,  $J$  = 8.2 Hz, 1H), 7.27 – 7.06 (m, 2H), 5.16 (s, 1H), 4.35 (q,  $J$  = 7.1 Hz, 2H), 2.41 (s, 3H), 1.49 (s, 9H), 1.32 (t,  $J$  = 7.1 Hz, 3H).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  = 170.6, 158.6, 154.8 (d,  $J_{\text{C-F}}$  = 270.0 Hz), 148.6, 124.9 (d,  $J_{\text{C-F}}$  = 8.5 Hz), 124.80 (d,  $J_{\text{C-F}}$  = 14.9 Hz), 117.7 (d,  $J_{\text{C-F}}$  = 5.3 Hz), 117.2 (d,  $J_{\text{C-F}}$  = 3.9 Hz), 114.7 (d,  $J_{\text{C-F}}$  = 21.3 Hz), 108.6, 61.3, 52.3, 28.9, 22.4, 14.1.  $^{19}\text{F-NMR}$  ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  = -114.57 (s). IR (ATR): 3410, 2969, 1698, 1528, 1211, 753  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{22}\text{FN}_2\text{O}_2$  [ $\text{M}+\text{H}^+$ ] 305.1665, found 305.1668 [ $\text{M}+\text{H}^+$ ].



#### Ethyl 6-(*tert*-butylamino)-8-methyl-[1,3]dioxolo[4,5-*f*]isoquinoline-9-carboxylate (**3ja**)

The general procedure **A** was followed using **1j** (115 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **3ja** (111 mg, 67%) as a slight yellow solid. M. p. = 112–114 °C.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  = 7.25 (d,  $J$  = 8.7 Hz, 1H), 7.02 (d,  $J$  = 8.7 Hz, 1H), 6.10 (s, 2H), 5.17 (s, 1H), 4.41 (q,  $J$  = 7.2 Hz, 2H), 2.48 (s, 3H), 1.58 (s, 9H), 1.40 (t,  $J$  = 7.2 Hz, 3H).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  = 169.2, 153.0, 147.8, 146.3, 139.3, 119.7, 115.1, 111.7, 107.4, 107.2, 100.8, 60.2, 51.3, 28.2, 21.6, 13.3. IR (ATR): 3398, 2965, 1697, 1531, 1211, 1085  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{23}\text{N}_2\text{O}_4$  [ $\text{M}+\text{H}^+$ ] 331.1658, found 331.1663 [ $\text{M}+\text{H}^+$ ].

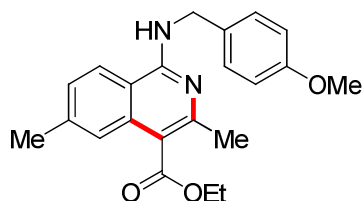


#### Ethyl 1-(*tert*-butylamino)-8-fluoro-3-methylisoquinoline-4-carboxylate (**3ka**)

The general procedure **A** was followed using **1k** (97.0 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **3ka** (87 mg, 57%) as a slight yellow oil.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  = 7.59 (d,  $J$  = 8.5 Hz, 1H), 7.35 (dd,  $J$  = 14.1, 7.9 Hz, 1H), 6.90 (dd,  $J$  = 14.1, 7.9 Hz, 1H), 6.44 (d,  $J$  = 21.4 Hz, 1H), 4.37 (q,  $J$  = 7.1 Hz, 2H), 2.46 (s, 3H), 1.48 (s, 9H), 1.35 (t,  $J$  = 7.1 Hz, 3H).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  = 169.5, 160.1 (d,  $J_{\text{C-F}}$  = 246.4 Hz), 153.1 (d,  $J_{\text{C-F}}$  = 5.8 Hz), 151.9,

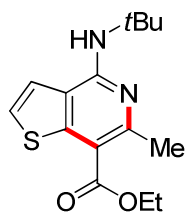


138.2, 130.0 (d,  $J_{C-F} = 10.9$  Hz), 120.4 (d,  $J_{C-F} = 3.8$  Hz), 110.7, 110.0 (d,  $J_{C-F} = 25.4$  Hz), 106.4 (d,  $J_{C-F} = 10.4$  Hz), 60.8, 52.3, 28.9, 23.9, 14.4.  $^{19}\text{F}$ -NMR ( $\text{CDCl}_3$ , 376 MHz):  $\delta = -112.93$  (s). IR (ATR): 3398, 2962, 1697, 1528, 1213, 1094  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{22}\text{FN}_2\text{O}_2$  [ $\text{M}+\text{H}^+$ ] 305.1665, found 305.1671 [ $\text{M}+\text{H}^+$ ].



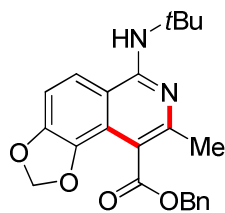
### Ethyl 1-(4-methoxybenzylamino)-3,6-dimethylisoquinoline-4-carboxylate (**3ma**)

The general procedure **A** was followed using **1m** (127.0 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **3ma** (80 mg, 44%) as a slight yellow oil.  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 7.75$  (s, 1H), 7.58 (d,  $J = 8.5$  Hz, 1H), 7.37 (d,  $J = 8.6$  Hz, 2H), 7.22 (dd,  $J = 8.5, 1.4$  Hz, 1H), 6.93 – 6.88 (m, 2H), 5.54 (t,  $J = 4.7$  Hz, 1H), 4.80 (d,  $J = 5.1$  Hz, 2H), 4.50 (q,  $J = 7.1$  Hz, 2H), 3.83 (d,  $J = 4.3$  Hz, 3H), 2.62 (s, 3H), 2.49 (s, 3H), 1.47 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 168.6, 158.0, 153.6, 149.9, 139.6, 134.4, 130.5, 128.5, 126.1, 122.9, 120.1, 113.1, 112.7, 111.7, 59.8, 54.3, 44.1, 23.0, 21.0, 13.4$ . IR (ATR): 3413, 2922, 1698, 1510, 1243, 1160  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{22}\text{H}_{25}\text{N}_2\text{O}_3$  [ $\text{M}+\text{H}^+$ ] 365.1865, found 365.1870 [ $\text{M}+\text{H}^+$ ].



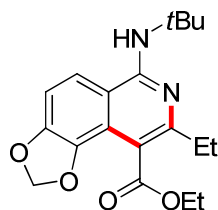
### Ethyl 4-(*tert*-butylamino)-6-methylthieno[3,2-*c*]pyridine-7-carboxylate (**3na**)

The general procedure **A** was followed using **1n** (91.0 mg, 0.50 mmol) and **2a** (156 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 12:1) yielded **3na** (98 mg, 67%; 5.0 mmol scale, 949 mg, 65%) as a slight yellow solid. M. p. = 113–115 °C.  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 7.24$  (d,  $J = 5.6$  Hz, 1H), 7.04 (d,  $J = 5.6$  Hz, 1H), 4.93 (s, 1H), 4.36 (q,  $J = 7.1$  Hz, 2H), 2.75 (s, 3H), 1.50 (s, 9H), 1.37 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 166.2, 156.0, 152.3, 148.0, 125.5, 119.7, 117.2, 107.3, 59.6, 51.4, 28.3, 25.0, 13.5$ . IR (ATR): 3398, 2963, 1696, 1530, 1210, 1086  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{21}\text{N}_2\text{O}_2\text{S}$  [ $\text{M}+\text{H}^+$ ] 293.1324, found 293.1327 [ $\text{M}+\text{H}^+$ ].



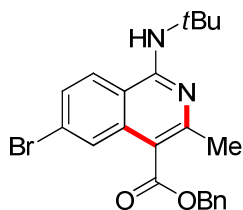
**Benzyl 6-(*tert*-butylamino)-8-methyl-[1,3]dioxolo[4,5-*f*]isoquinoline-9-carboxylate (**3jb**)**

The general procedure **A** was followed using **1j** (115 mg, 0.50 mmol) and **2b** (218 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **3jb** (131 mg, 67%) as a slight yellow solid. M. p. = 122–124 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): δ = 7.37 (m, 2H), 7.31 – 7.21 (m, 3H), 7.13 (d, *J* = 8.7 Hz, 1H), 6.89 (d, *J* = 8.7 Hz, 1H), 5.82 (s, 2H), 5.29 (s, 2H), 5.08 (s, 1H), 2.37 (s, 3H), 1.47 (s, 9H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): δ = 168.9, 152.9, 148.0, 146.1, 139.1, 135.0, 127.6, 127.4, 127.1, 119.5, 115.0, 111.5, 107.2, 106.6, 100.7, 66.0, 51.2, 28.0, 21.5. IR (ATR): 3411, 2964, 1700, 1526, 1203, 103 cm<sup>-1</sup>. HR-MS (ESI) *m/z* calcd for C<sub>23</sub>H<sub>25</sub>N<sub>2</sub>O<sub>4</sub> [M+H<sup>+</sup>] 393.1814, found 393.1819 [M+H<sup>+</sup>].



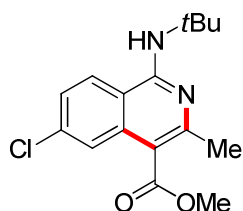
**Ethyl 6-(*tert*-butylamino)-8-ethyl-[1,3]dioxolo[4,5-*f*]isoquinoline-9-carboxylate (**3jc**)**

The general procedure **A** was followed using **1j** (115 mg, 0.50 mmol) and **2c** (170 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **3jc** (138 mg, 80%) as a slight yellow solid. M. p. = 108–109 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): δ = 7.16 (d, *J* = 8.7 Hz, 1H), 6.92 (d, *J* = 8.7 Hz, 1H), 6.00 (s, 2H), 5.08 (s, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.64 (q, *J* = 7.4 Hz, 2H), 1.49 (s, 9H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.25 (t, *J* = 7.4 Hz, 3H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): δ = 170.2, 154.2, 153.3, 147.1, 140.3, 120.5, 116.0, 112.7, 108.3, 107.5, 101.8, 61.1, 52.1, 29.2, 29.0, 14.2, 13.8. IR (ATR): 3397, 2966, 1696, 1530, 1209, 1086 cm<sup>-1</sup>. HR-MS (ESI) *m/z* calcd for C<sub>19</sub>H<sub>25</sub>N<sub>2</sub>O<sub>4</sub> [M+H<sup>+</sup>] 345.1814, found 345.1820 [M+H<sup>+</sup>].



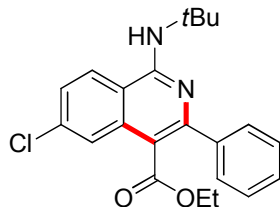
### Benzyl 6-bromo-1-(*tert*-butylamino)-3-methylisoquinoline-4-carboxylate (**3cb**)

The general procedure A was followed using **1c** (127 mg, 0.50 mmol) and **2b** (218 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **3cb** (107 mg, 50%) as a slight yellow solid. M. p. = 125–127 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): δ = 8.21 (d, *J* = 1.4 Hz, 1H), 7.53 – 7.48 (m, 3H), 7.47 – 7.34 (m, 4H), 5.45 (s, 2H), 5.34 (br s, 1H), 2.59 (s, 3H), 1.59 (s, 9H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): δ = 168.7, 154.4, 153.0, 136.7, 135.8, 128.7, 128.7, 128.4, 128.2, 127.3, 125.1, 122.9, 114.4, 110.2, 66.9, 52.5, 29.0, 24.5. IR (ATR): 3398, 2964, 1685, 1520, 1260, 1176 cm<sup>-1</sup>. HR-MS (ESI) *m/z* calcd for C<sub>22</sub>H<sub>24</sub>BrN<sub>2</sub>O<sub>2</sub> [M+H<sup>+</sup>] 427.1021, found 427.1026 [M+H<sup>+</sup>].



### Methyl 1-(*tert*-butylamino)-6-chloro-3-methylisoquinoline-4-carboxylate (**3bd**)

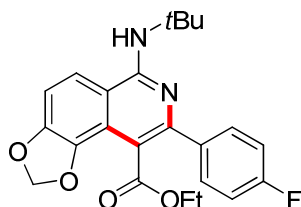
The general procedure A was followed using **1b** (105 mg, 0.50 mmol) and **2d** (142 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **3bd** (109 mg, 71%) as a slight yellow solid. M. p. = 103–105 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): δ = 8.03 (d, *J* = 1.9 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.34 (d, *J* = 8.8, 1.9 Hz, 1H), 5.37 (br s, 1H), 3.99 (s, 3H), 2.60 (s, 3H), 1.60 (s, 9H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): δ = 169.4, 154.3, 152.9, 136.6, 136.4, 125.6, 124.1, 123.0, 114.1, 110.5, 52.5, 51.9, 29.0, 24.4. IR (ATR): 3417, 2924, 1683, 1576, 1210, 868 cm<sup>-1</sup>. HR-MS (ESI) *m/z* calcd for C<sub>16</sub>H<sub>20</sub>ClN<sub>2</sub>O<sub>2</sub> [M+H<sup>+</sup>] 307.1213, found 307.1215 [M+H<sup>+</sup>].



### Ethyl 1-(*tert*-butylamino)-6-chloro-3-phenylisoquinoline-4-carboxylate (**3be**)

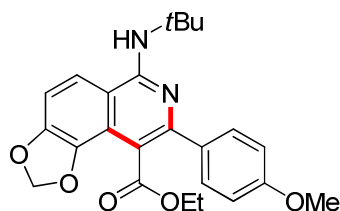
The general procedure A was followed using **1b** (105 mg, 0.50 mmol) and **2e** (218 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **3be** (95 mg, 50%) as a slight yellow solid. M. p. = 123–125 °C. <sup>1</sup>H-NMR (Acetone-*d*<sub>6</sub>, 400 MHz): δ = 8.29 (d, *J* = 9.0 Hz, 1H), 8.11 (t, *J* = 2.1 Hz, 1H), 7.70 – 7.67 (m, 2H), 7.51 – 7.45 (m, 4H),

6.69 (s, 1H), 4.11 (q,  $J = 7.1$  Hz, 2H), 1.64 (s, 9H), 0.93 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$ -NMR (Acetone- $d_6$ , 100 MHz):  $\delta = 168.8, 154.9, 152.9, 141.9, 136.4, 136.2, 128.5, 128.2, 128.0, 125.9, 125.3, 123.3, 114.9, 111.0, 60.6, 52.3, 28.4, 13.0$ . IR (ATR): 3415, 2969, 1682, 1526, 1261, 1174  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{22}\text{H}_{24}\text{ClN}_2\text{O}_2$   $[\text{M}+\text{H}^+]$  383.1526, found 383.1531  $[\text{M}+\text{H}^+]$ .



**Ethyl 6-(tert-butylamino)-8-(4-fluorophenyl)-[1,3]dioxolo[4,5-f]isoquinoline-9-carboxylate (3jf)**

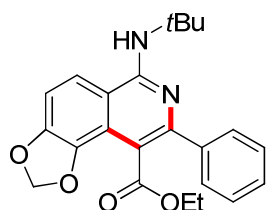
The general procedure **A** was followed using **1j** (110 mg, 0.50 mmol) and **2f** (236 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 12:1) yielded **3jf** (115 mg, 56%) as a yellow oil.  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 7.70 - 7.61$  (m, 2H), 7.22 (d,  $J = 8.8$  Hz, 1H), 7.07 - 6.96 (m, 2H), 7.02 (d,  $J = 8.8$  Hz, 1H), 6.04 (s, 2H), 5.18 (s, 1H), 4.15 (q,  $J = 7.2$  Hz, 2H), 1.49 (s, 9H), 1.11 (t,  $J = 7.2$  Hz, 3H).  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta = 168.9, 161.7$  (d,  $J_{\text{C-F}} = 247.0$  Hz), 152.8, 147.0, 146.5, 139.9, 135.9 (d,  $J_{\text{C-F}} = 3.2$  Hz), 129.4 (d,  $J_{\text{C-F}} = 8.2$  Hz), 119.5, 115.1, 113.8 (d,  $J_{\text{C-F}} = 21.4$  Hz), 111.8, 108.1, 107.7, 100.9, 60.3, 51.2, 28.2, 12.9.  $^{19}\text{F}$ -NMR ( $\text{CDCl}_3$ , 376 MHz):  $\delta = -114.25$  (s). IR (ATR): 3417, 2922, 1715, 1529, 1449, 1160  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{23}\text{H}_{24}\text{FN}_2\text{O}_4$   $[\text{M}+\text{H}^+]$  411.1720, found 411.1728  $[\text{M}+\text{H}^+]$ .



**Ethyl 6-(tert-butylamino)-8-(4-methoxyphenyl)-[1,3]dioxolo[4,5-f]isoquinoline-9-carboxylate (3jg)**

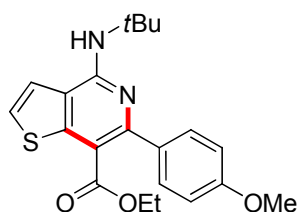
The general procedure **A** was followed using **1j** (110 mg, 0.50 mmol) and **2g** (248 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **3jg** (148 mg, 70%) as a yellow oil.  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 7.74$  (d,  $J = 8.6$  Hz, 2H), 7.28 (d,  $J = 8.4$  Hz, 1H), 7.10 (d,  $J = 8.4$  Hz, 1H), 6.98 ( $J = 8.6$  Hz, 2H), 6.14 (s, 2H), 5.30 (br

s, 1H), 4.28 (q,  $J = 7.1$  Hz, 2H), 3.89 (s, 3H), 1.61 (s, 9H), 1.24 (d,  $J = 7.1$  Hz, 3H).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 170.0, 159.7, 153.7, 149.5, 140.8, 130.0, 129.9, 129.9, 123.0, 120.6, 113.5, 113.4, 112.7, 109.0, 102.0, 61.3, 55.3, 52.4, 29.3, 13.9$ . IR (ATR): 3398, 2935, 1753, 1547, 1356, 1096  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{24}\text{H}_{27}\text{N}_2\text{O}_5$   $[\text{M}+\text{H}^+]$  423.1920, found 423.1926  $[\text{M}+\text{H}^+]$ .



#### Ethyl 6-(*tert*-butylamino)-8-phenyl-[1,3]dioxolo[4,5-*f*]isoquinoline-9-carboxylate (**3je**)

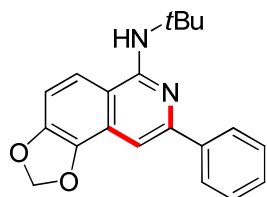
The general procedure **A** was followed using **1j** (110 mg, 0.50 mmol) and **2e** (218 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **3je** (133 mg, 68%) as a solid. M. p. = 119–121 °C.  $^1\text{H-NMR}$  (Acetone- $d_6$ , 400 MHz):  $\delta = 7.85$  (d,  $J = 8.8$  Hz, 1H), 7.79 – 7.75 (m, 2H), 7.48 – 7.35 (m, 3H), 7.18 (d,  $J = 8.8$  Hz, 1H), 6.35 (s, 1H), 6.18 (s, 2H), 4.21 (q,  $J = 7.2$  Hz, 2H), 1.61 (s, 9H), 1.21 (t,  $J = 7.2$  Hz, 3H).  $^{13}\text{C-NMR}$  (Acetone- $d_6$ , 100 MHz):  $\delta = 168.9, 154.4, 148.3, 147.6, 141.1, 140.6, 128.6, 128.0, 127.9, 120.6, 117.7, 112.9, 109.0, 108.9, 102.0, 60.6, 52.0, 29.2, 13.3$ . IR (ATR): 3398, 2924, 1763, 1451, 1340, 1145  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{23}\text{H}_{25}\text{N}_2\text{O}_4$   $[\text{M}+\text{H}^+]$  393.1814, found 393.1817  $[\text{M}+\text{H}^+]$ .



#### Ethyl 4-(*tert*-butylamino)-6-(4-methoxyphenyl)thieno[3,2-*c*]pyridine-7-carboxylate (**3ng**)

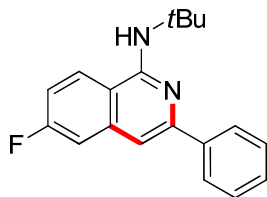
The general procedure **A** was followed using **1n** (91.0 mg, 0.50 mmol) and **2g** (248 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **3ng** (157 mg, 82%) as a colorless solid. M. p. = 131–133 °C.  $^1\text{H-NMR}$  (Acetone- $d_6$ , 400 MHz):  $\delta = 7.68$  (d,  $J = 5.7$  Hz, 1H), 7.56 (d,  $J = 5.7$  Hz, 1H), 7.55 (d,  $J = 8.7$  Hz, 2H), 7.00 (d,  $J = 8.7$  Hz, 2H), 6.37 (s, 1H), 4.12 (q,  $J = 7.1$  Hz, 2H), 3.87 (s, 3H), 1.60 (s, 9H), 1.03 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C-NMR}$  (Acetone- $d_6$ , 100 MHz):  $\delta = 167.6, 159.8, 155.1, 153.3, 148.8, 134.9, 130.6, 126.7, 121.5, 120.2, 112.8, 108.2, 60.0, 54.7, 52.1, 28.7, 13.3$ . IR (ATR): 3496, 2959, 1552,

1311, 1215, 1041  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}_3\text{S}$   $[\text{M}+\text{H}^+]$  385.1586, found 385.1591  $[\text{M}+\text{H}^+]$ .



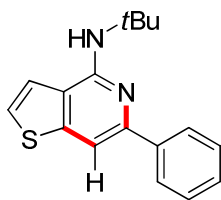
***N*-tert-Butyl-8-phenyl-[1,3]dioxolo[4,5-*f*]isoquinolin-6-amine (4a)**

The general procedure **A** was followed using **1j** (110 mg, 0.50 mmol) and **2h** (250 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **4a** (96 mg, 60%) as a colorless solid. M. p. = 107–109 °C.  $^1\text{H-NMR}$  (Acetone- $d_6$ , 400 MHz):  $\delta$  = 8.24 – 8.20 (m, 2H), 7.76 (d,  $J$  = 8.8 Hz, 1H), 7.51 – 7.47 (m, 2H), 7.41 – 7.38 (m, 1H), 7.37 (s, 1H), 7.09 (d,  $J$  = 8.8 Hz, 1H), 6.24 (s, 2H), 6.15 (s, 1H), 1.69 (s, 9H).  $^{13}\text{C-NMR}$  (Acetone- $d_6$ , 100 MHz):  $\delta$  = 154.2, 148.8, 146.5, 141.3, 140.4, 128.4, 128.1, 126.4, 123.8, 117.2, 114.1, 108.2, 102.2, 97.1, 51.6, 28.5. IR (ATR): 3457, 2962, 1523, 1365, 1211, 693  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{21}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}^+]$  321.1603, found 321.1607  $[\text{M}+\text{H}^+]$ .



***N*-tert-Butyl-6-fluoro-3-phenylisoquinolin-1-amine (4b)**

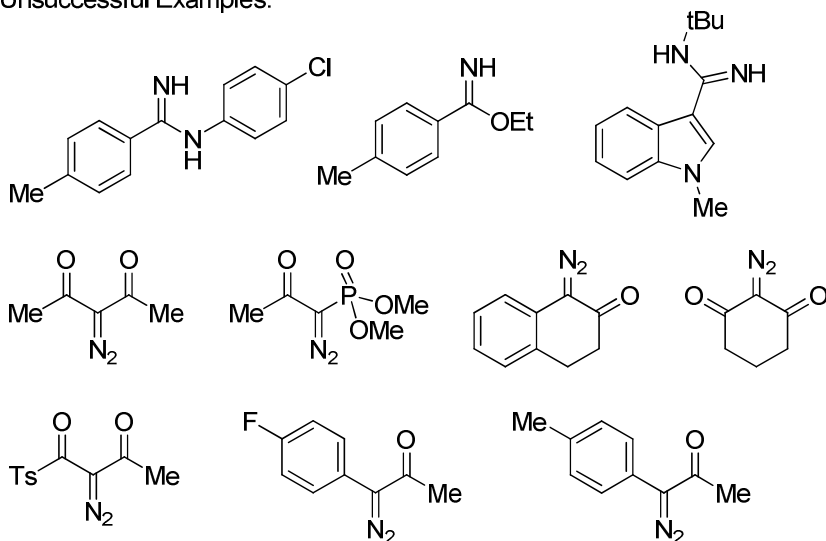
The general procedure **A** was followed using **1a** (97.0 mg, 0.50 mmol) and **2h** (250 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **4b** (79 mg, 54%) as a slight yellow oil.  $^1\text{H-NMR}$  (Acetone- $d_6$ , 400 MHz):  $\delta$  = 8.28 – 8.20 (m, 3H), 7.55 (s, 1H), 7.55 – 7.45 (m, 3H), 7.44 – 7.36 (m, 1H), 7.23 (td,  $J$  = 8.9, 2.7 Hz, 1H), 6.26 (s, 1H), 1.70 (s, 9H).  $^{13}\text{C-NMR}$  (Acetone- $d_6$ , 100 MHz):  $\delta$  = 163.1 (d,  $J_{\text{C-F}}$  = 247.4 Hz), 154.6, 149.8, 140.2, 140.1 (d,  $J_{\text{C-F}}$  = 9.9 Hz), 128.5, 128.2, 126.5, 126.0 (d,  $J_{\text{C-F}}$  = 9.7 Hz), 115.1, 114.3 (d,  $J_{\text{C-F}}$  = 24.6 Hz), 110.6 (d,  $J_{\text{C-F}}$  = 20.6 Hz), 105.1 (d,  $J_{\text{C-F}}$  = 4.2 Hz), 51.7, 28.5.  $^{19}\text{F-NMR}$  (Acetone- $d_6$ , 376 MHz):  $\delta$  = -112.69 (s). IR (ATR): 3401, 2966, 1543, 1251, 1040, 705  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{20}\text{FN}_2$   $[\text{M}^+]$  295.1611, found 295.1614  $[\text{M}+\text{H}^+]$ .



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

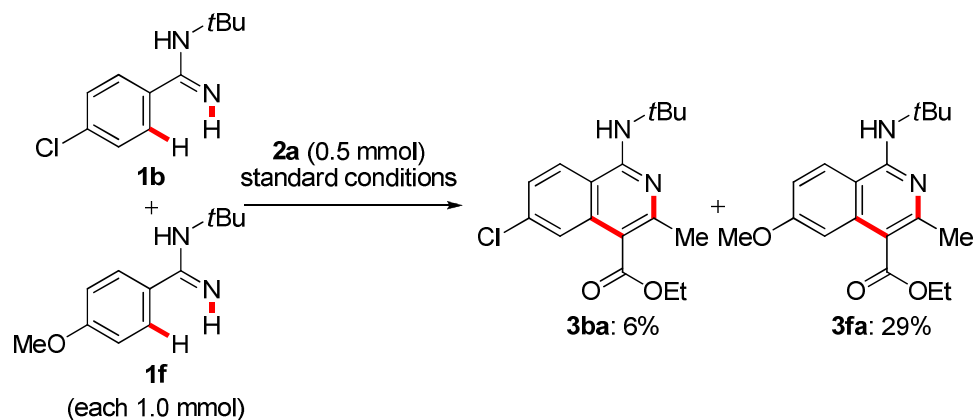
The general procedure A was followed using **1a** (91.0 mg, 0.50 mmol) and **2h** (250 mg, 1.00 mmol) for 16 h. Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **4c** (72 mg, 51%) as a colorless solid. M. p. = 118–121 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): δ = 8.13 (dt, *J* = 8.3, 1.7 Hz, 2H), 7.61 (d, *J* = 0.8 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.42 – 7.35 (m, 1H), 7.31 (d, *J* = 5.5 Hz, 1H), 7.20 (dd, *J* = 5.5, 0.7 Hz, 1H), 4.76 (s, 1H), 1.68 (s, 9H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): δ = 152.6, 149.6, 148.4, 140.3, 128.5, 128.0, 126.7, 123.8, 121.7, 119.2, 102.8, 51.9, 29.6. IR (ATR): 3452, 2959, 1541, 1399, 1211, 689 cm<sup>-1</sup>. HR-MS (ESI) *m/z* calcd for C<sub>17</sub>H<sub>19</sub>N<sub>2</sub>S [M+H<sup>+</sup>] 283.1269, found 283.1273 [M+H<sup>+</sup>].

Unsuccessful Examples:



## Competition Experiment:

### Intermolecular Competition Experiment between Substrates **1b** and **1f**:

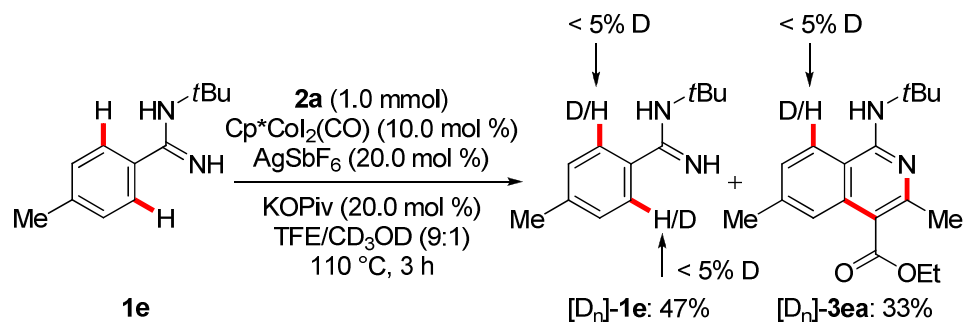


A suspension of ethyl 2-diazo-3-oxobutanoate (**2a**) (78.0 mg, 0.50 mmol), *N*-*tert*-butyl-4-chlorobenzimidamide (**1b**) (210 mg, 1.00 mmol), *N*-*tert*-butyl-4-methoxybenzimidamide (**1f**) (206 mg, 1.00 mmol), Cp\*CoI<sub>2</sub>(CO) (24.0 mg, 10.0 mol %), AgSbF<sub>6</sub> (34.4 mg, 20.0 mol %) and KOPiv (14.0 mg, 20.0 mol %) in TFE (2.0 mL) was stirred at 110 °C for 16 h under an atmosphere of N<sub>2</sub>. At ambient temperature, the reaction mixture was evaporated *in vacuo* and the remaining residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc 25:1) to yield product **3ba** (10 mg, 6%) and **3fa** (46 mg, 29%).

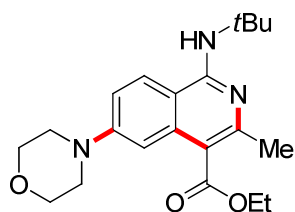


## H/D Exchange Experiment:

### Cobalt(III)-Catalyzed H/D Exchange in Substrate **1e** with CD<sub>3</sub>OD as the Co-solvent with **2a**:

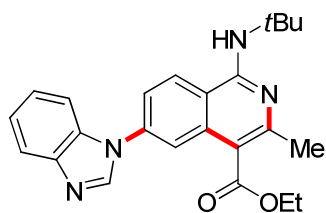


A suspension of *N*-*tert*-butyl-4-methylbenzimidamide (**1e**) (95.0 mg, 0.50 mmol), ethyl 2-diazo-3-oxobutanoate (**2a**) (156 mg, 1.00 mmol), Cp\*CoI<sub>2</sub>(CO) (24.0 mg, 10.0 mol %), AgSbF<sub>6</sub> (34.4 mg, 20.0 mol %) and KO<sub>2</sub>Piv (14.0 mg, 20.0 mol %) in a solvent mixture of TFE and CD<sub>3</sub>OD (1.8/0.2 mL) was stirred at 110 °C for 3 h under an atmosphere of N<sub>2</sub>. At ambient temperature, the reaction mixture was evaporated *in vacuo* and the remaining residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc/Et<sub>3</sub>N 25:1:0→2:1:0.1) to yield **[D<sub>n</sub>]-3ea** (50 mg, 33%) as a slight yellow oil, and reisolated starting material **[D<sub>n</sub>]-1e** (45 mg, 47%) as a colorless solid. The deuterium-incorporation in **[D<sub>n</sub>]-3ea** and **[D<sub>n</sub>]-1e** was estimated by <sup>1</sup>H-NMR spectroscopy.



**Ethyl 1-(*tert*-butylamino)-3-methyl-6-morpholinoisoquinoline-4-carboxylate (11)**

A suspension of ethyl 6-bromo-1-(*tert*-butylamino)-3-methylisoquinoline-4-carboxylate (**3ca**) (72.0 mg, 0.20 mmol) and Pd<sub>2</sub>(dba)<sub>3</sub> (9.2 mg, 5.0 mol %), XantPhos (11.6 mg, 10 mol %), NaO<sup>t</sup>Bu (38.4 mg, 2.0 equiv), morpholine (35.0 mg, 2.0 equiv) in PhMe (2.0 mL) was stirred at 80 °C for 12 h.<sup>5</sup> At ambient temperature, the reaction mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and filtered. The solvent was concentrated *in vacuo* and purification by column chromatography (*n*-Hexane/EtOAc 4:1) yielded **11** (64 mg, 86%) as a colorless solid. M. p. = 139–141 °C. <sup>1</sup>H-NMR (Acetone-*d*<sub>6</sub>, 400 MHz): δ = 7.96 (d, *J* = 9.3 Hz, 1H), 7.29 (s, 1H), 7.14 (d, *J* = 9.3 Hz, 1H), 6.13 (s, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.83 – 3.73 (m, 4H), 3.26 – 3.18 (m, 4H), 2.50 (s 3H), 1.59 (s, 9H), 1.38 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C-NMR (Acetone-*d*<sub>6</sub>, 100 MHz): δ = 169.2, 154.9, 152.2, 150.8, 136.8, 123.7, 115.5, 111.2, 110.0, 105.9, 66.4, 60.0, 51.8, 48.3, 28.6, 23.8, 13.9. IR (ATR): 3423, 2969, 1643, 1551, 1340, 1205 cm<sup>-1</sup>. HR-MS (ESI) *m/z* calcd for C<sub>21</sub>H<sub>30</sub>N<sub>3</sub>O<sub>3</sub> [M+H<sup>+</sup>] 372.2287, found 372.2293 [M+H<sup>+</sup>].



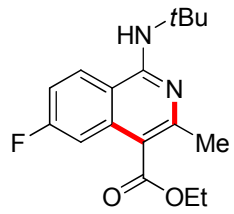
**Ethyl 6-(1*H*-benzo[*d*]imidazol-1-yl)-1-(*tert*-butylamino)-3-methylisoquinoline-4-carboxylate (12)**

A suspension of ethyl 6-bromo-1-(*tert*-butylamino)-3-methylisoquinoline-4-carboxylate (**3ca**) (72.0 mg, 0.20 mmol) and Cu<sub>2</sub>O (2.8 mg, 10.0 mol %), Cs<sub>2</sub>CO<sub>3</sub> (130 mg, 2.0 equiv), 1*H*-benzimidazole (35.4 mg, 1.5 equiv) in DMF (2.0 mL) was stirred at 130 °C for 24 h.<sup>4</sup> At ambient temperature, the reaction mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and filtered. The solvent was concentrated *in vacuo* and purification by column chromatography (*n*-Hexane/EtOAc 2:1→1:1) yielded **12** (33 mg, 41%) as a yellow oil. <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ = 8.73 (s, 1H), 8.62 (d, *J* =

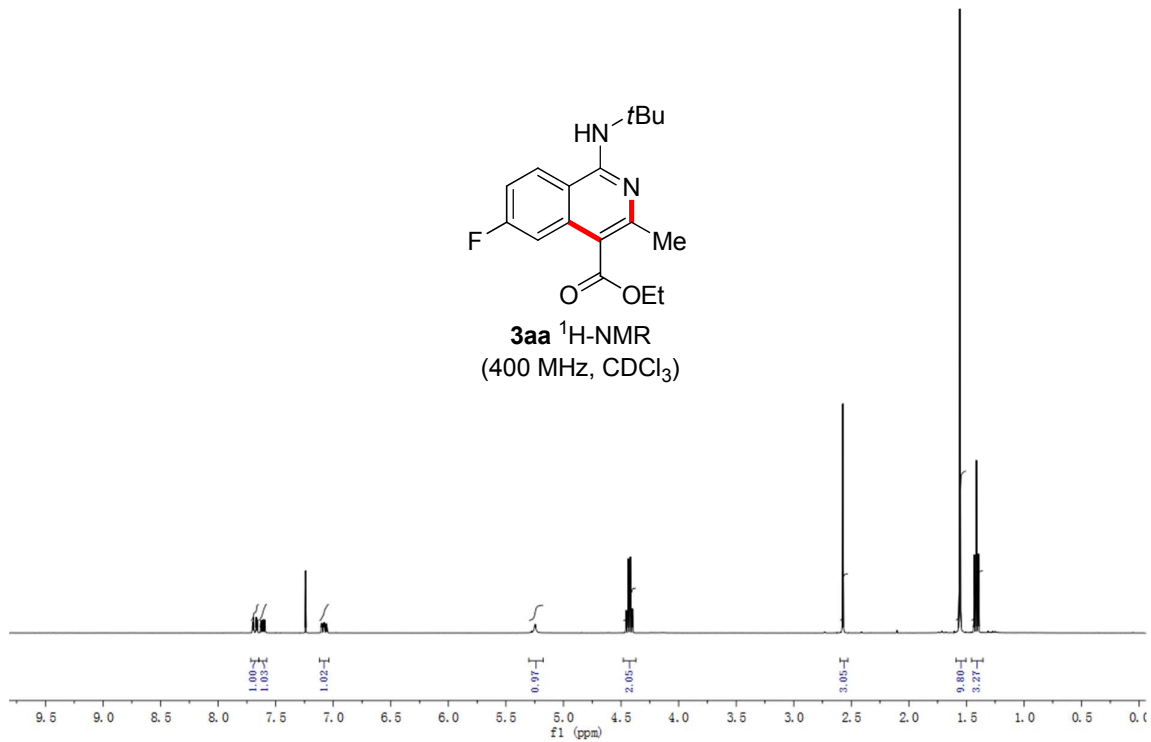
9.0 Hz, 1H), 8.19 (d,  $J = 2.1$  Hz, 1H), 7.82 (d,  $J = 7.6$  Hz, 1H), 7.79 (dd,  $J = 9.0, 2.1$  Hz, 1H), 7.70 (d,  $J = 7.6$  Hz, 1H), 7.34 – 7.32 (m, 2H), 7.15 (s, 1H), 4.37 (q,  $J = 7.1$  Hz, 2H), 2.54 (s, 3H), 1.58 (s, 9H), 1.33 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$ -NMR (DMSO- $d_6$ , 100 MHz):  $\delta = 168.6, 155.4, 152.9, 144.5, 143.8, 137.8, 136.2, 133.3, 126.9, 124.3, 123.3, 120.7, 120.7, 117.5, 115.0, 111.1, 110.4, 61.0, 52.6, 29.2, 24.9, 14.7$ . IR (ATR): 3452, 3301, 2971, 1683, 1551, 1347, 1215  $\text{cm}^{-1}$ . HR-MS (ESI)  $m/z$  calcd for  $\text{C}_{24}\text{H}_{27}\text{N}_4\text{O}_2$   $[\text{M}+\text{H}^+]$  403.2134, found 403.2138  $[\text{M}+\text{H}^+]$ .

#### References:

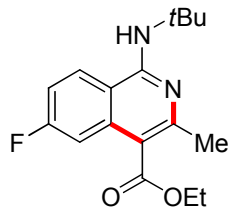
- [1] J. Li, M. John and L. Ackermann, *Chem. – Eur. J.* 2014, **20**, 5403.
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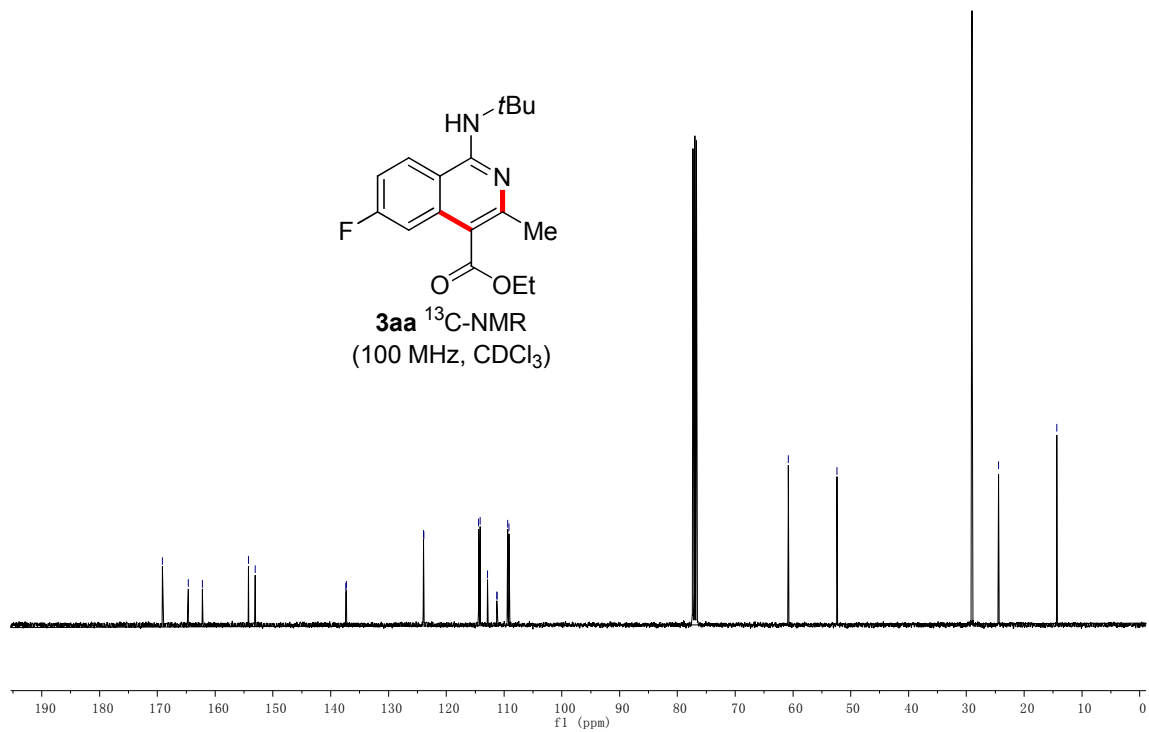
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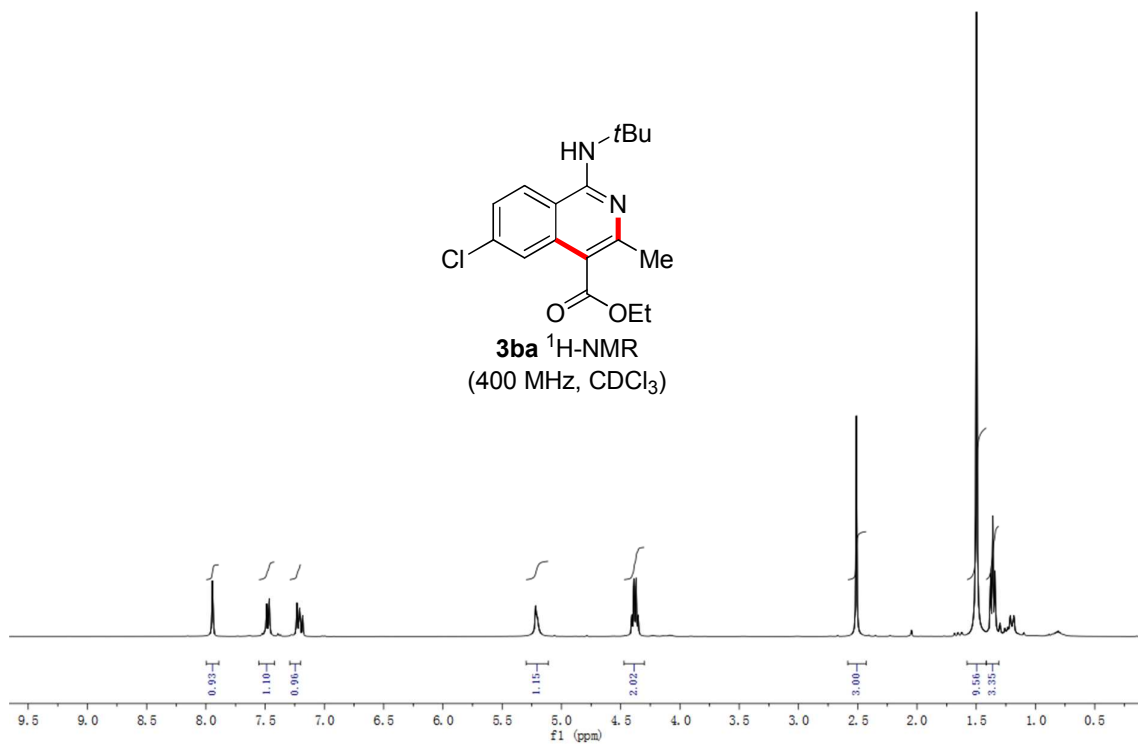
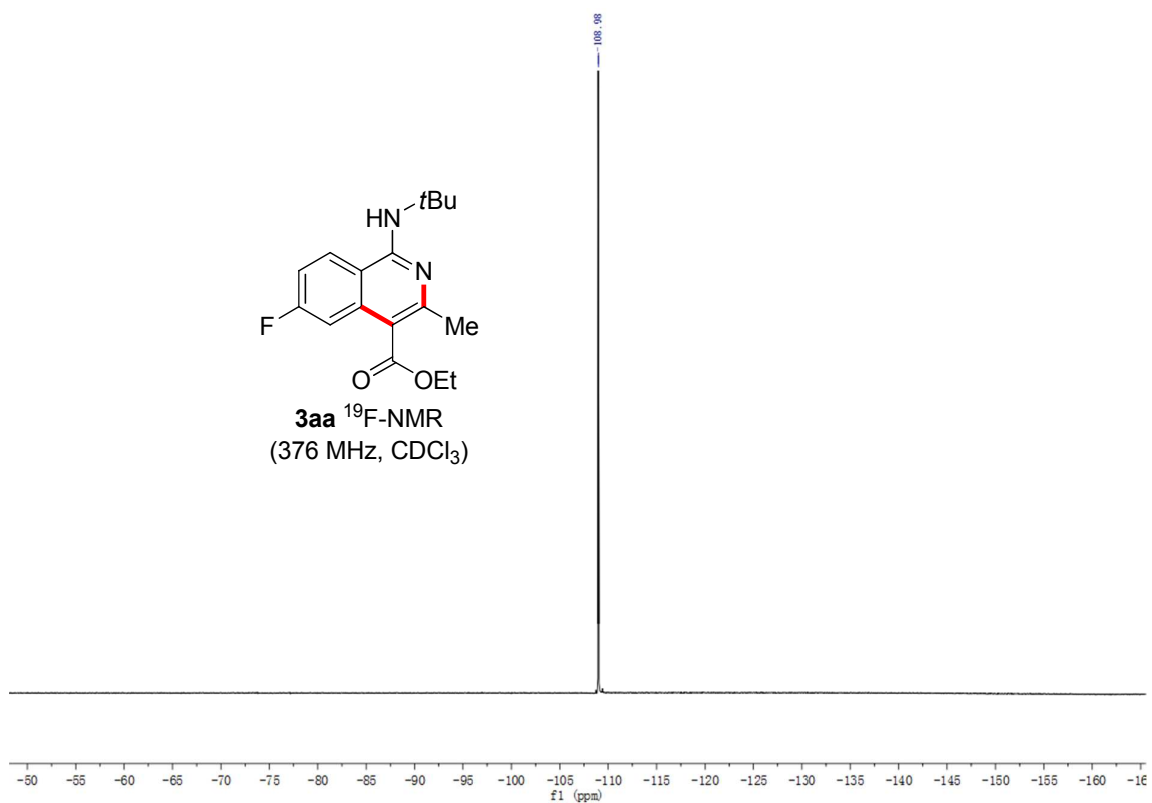


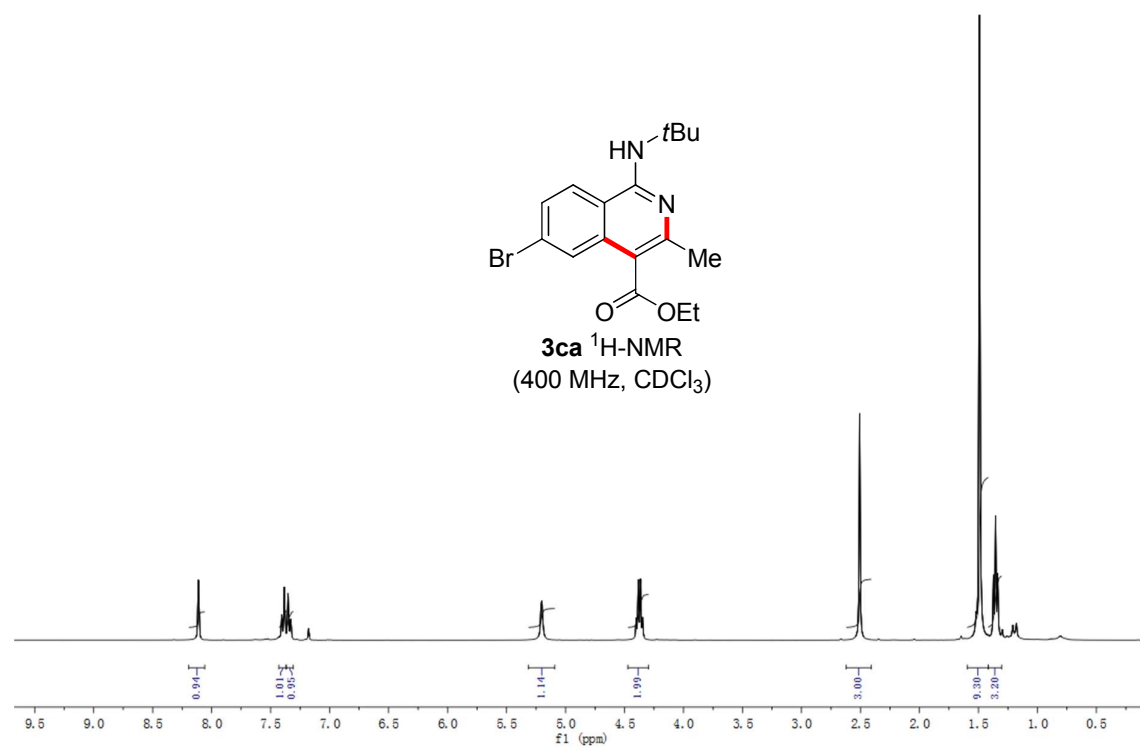
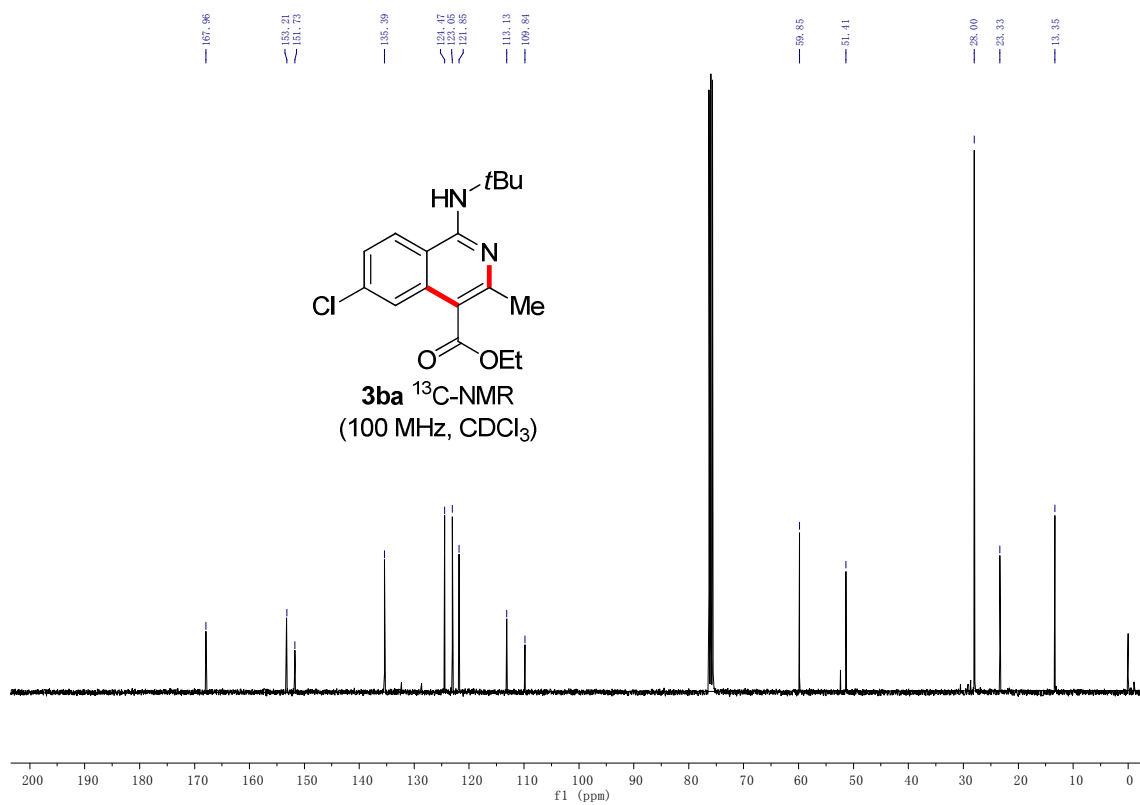
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14.96

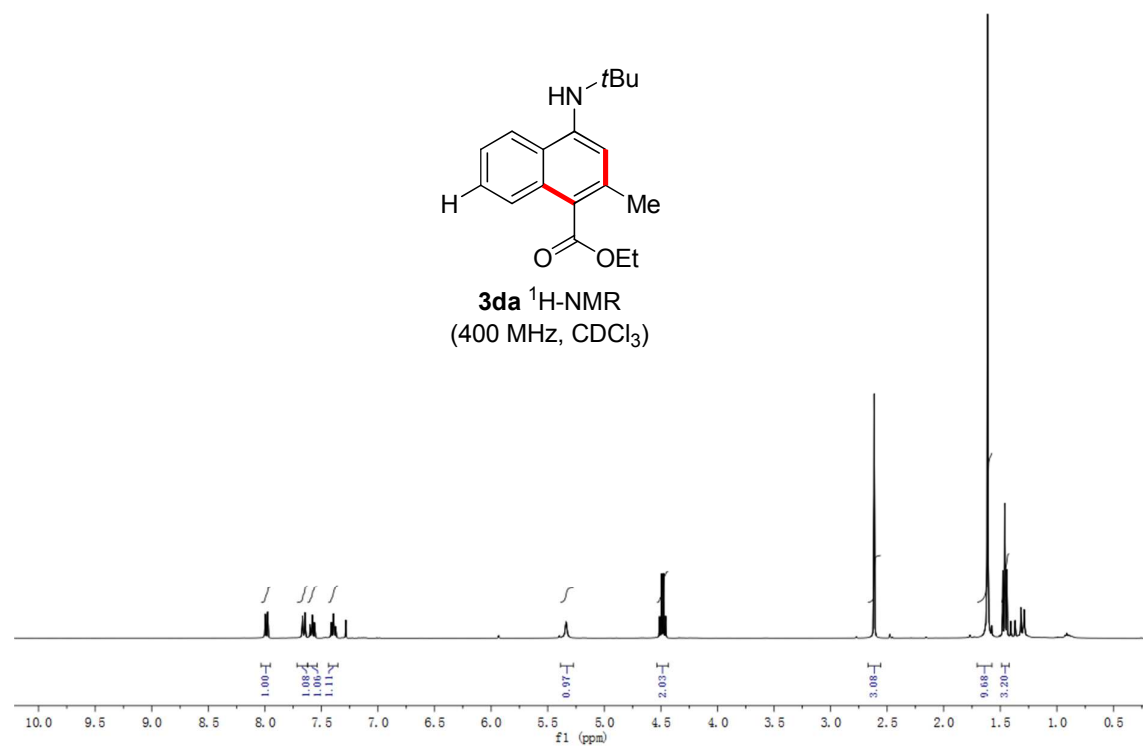
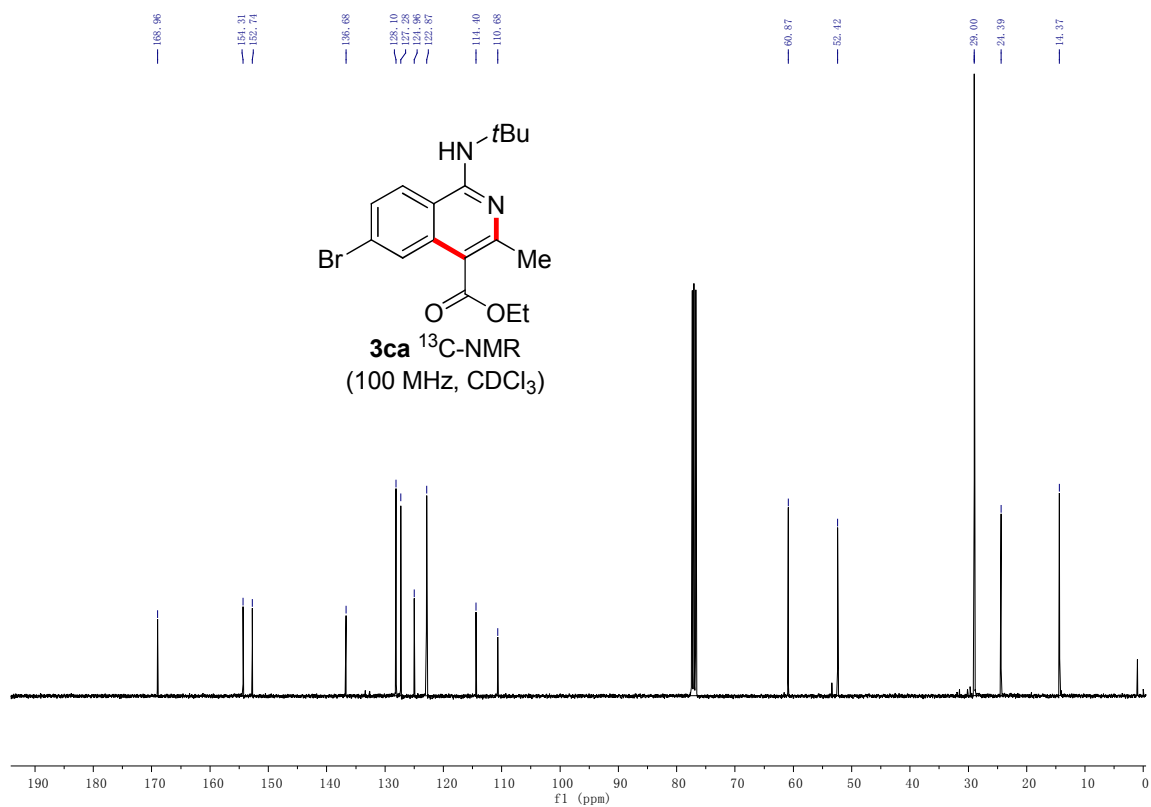


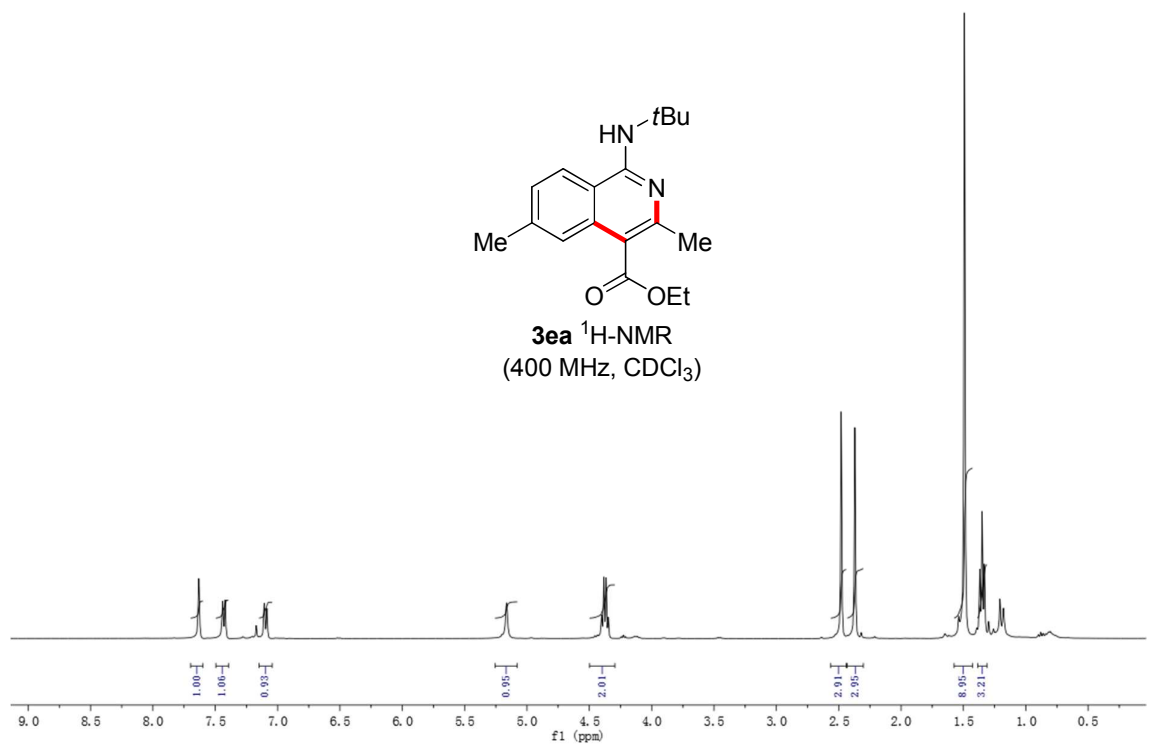
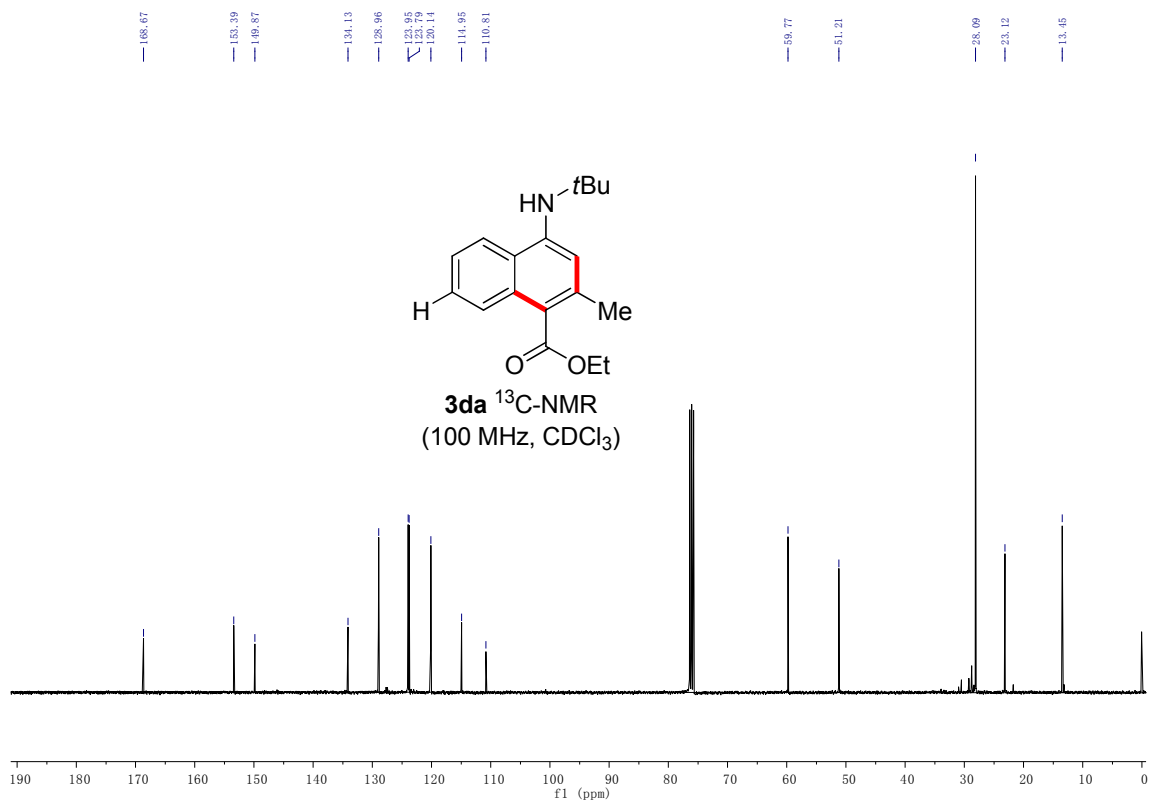
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(100 MHz,  $\text{CDCl}_3$ )



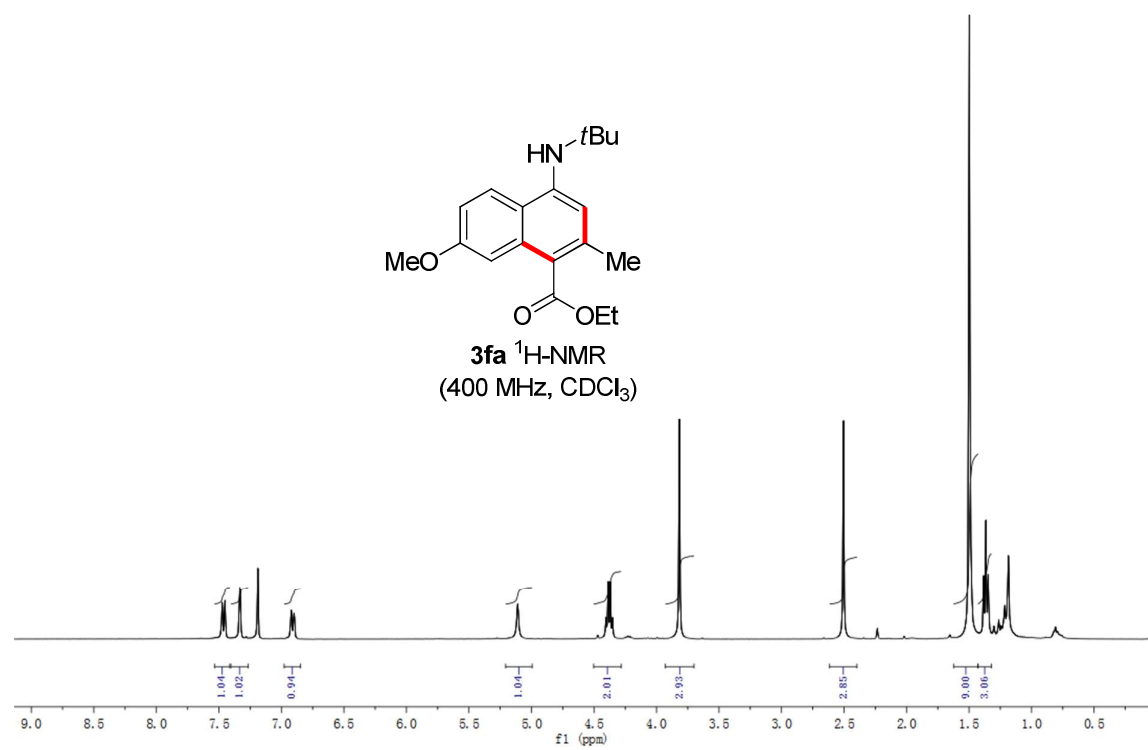
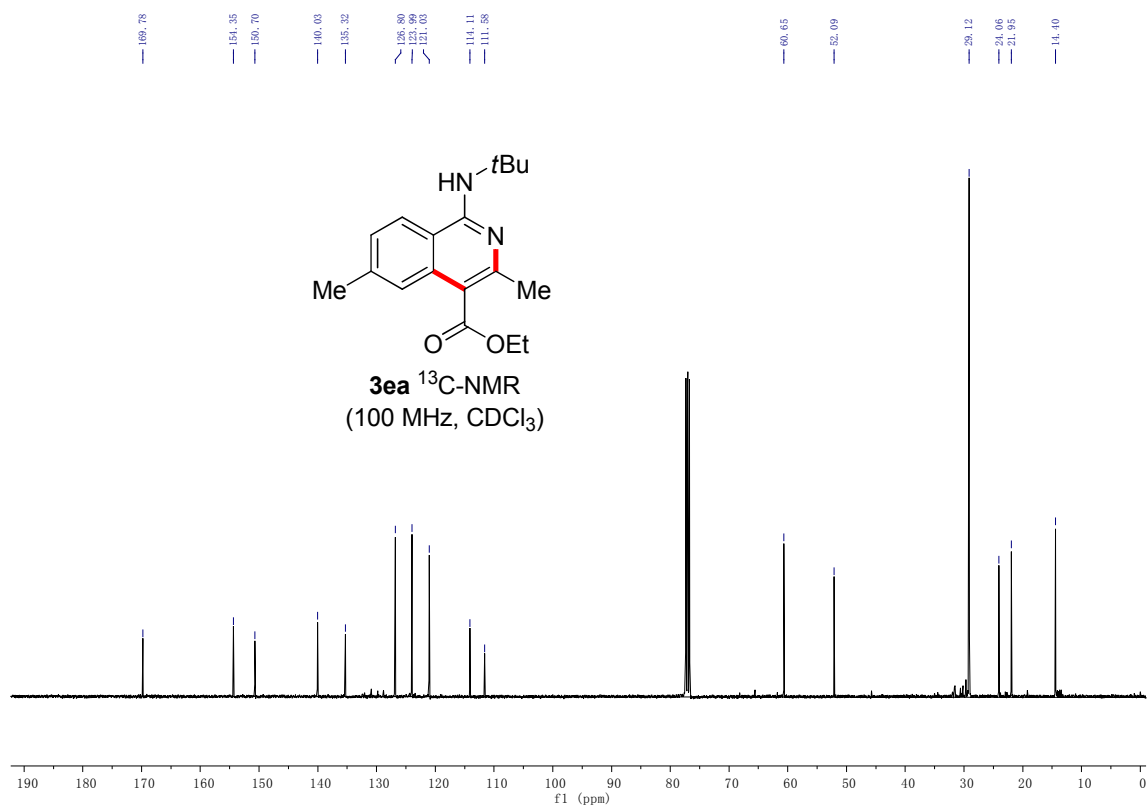


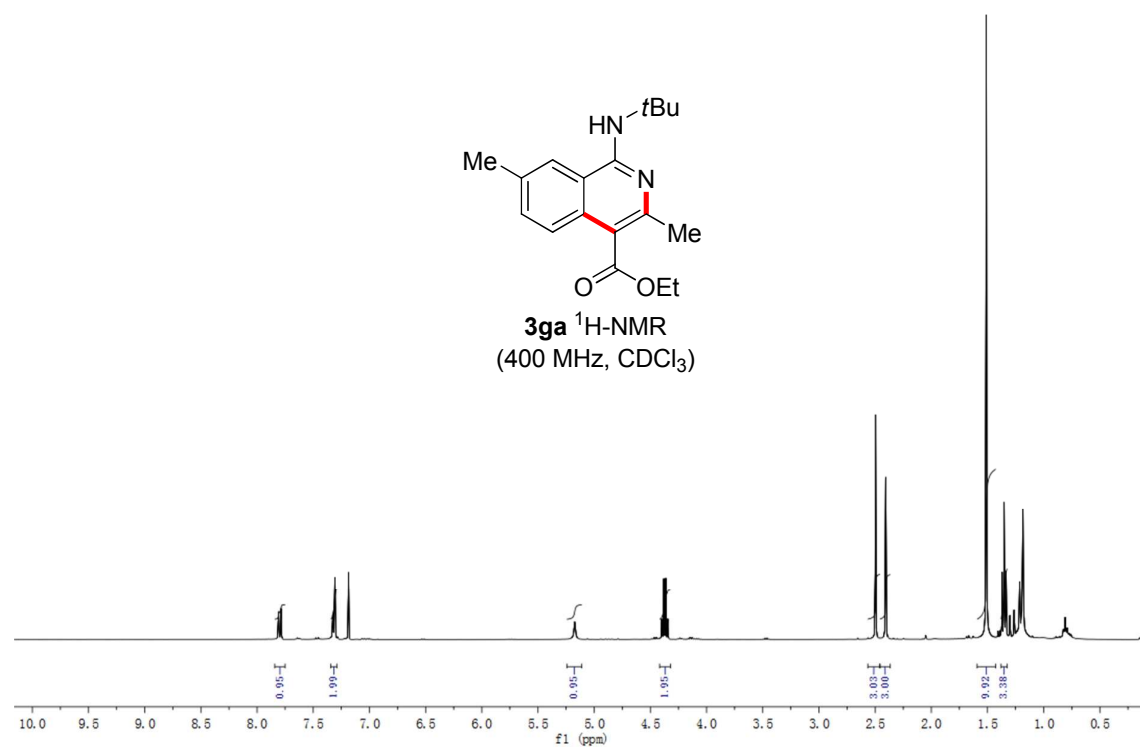
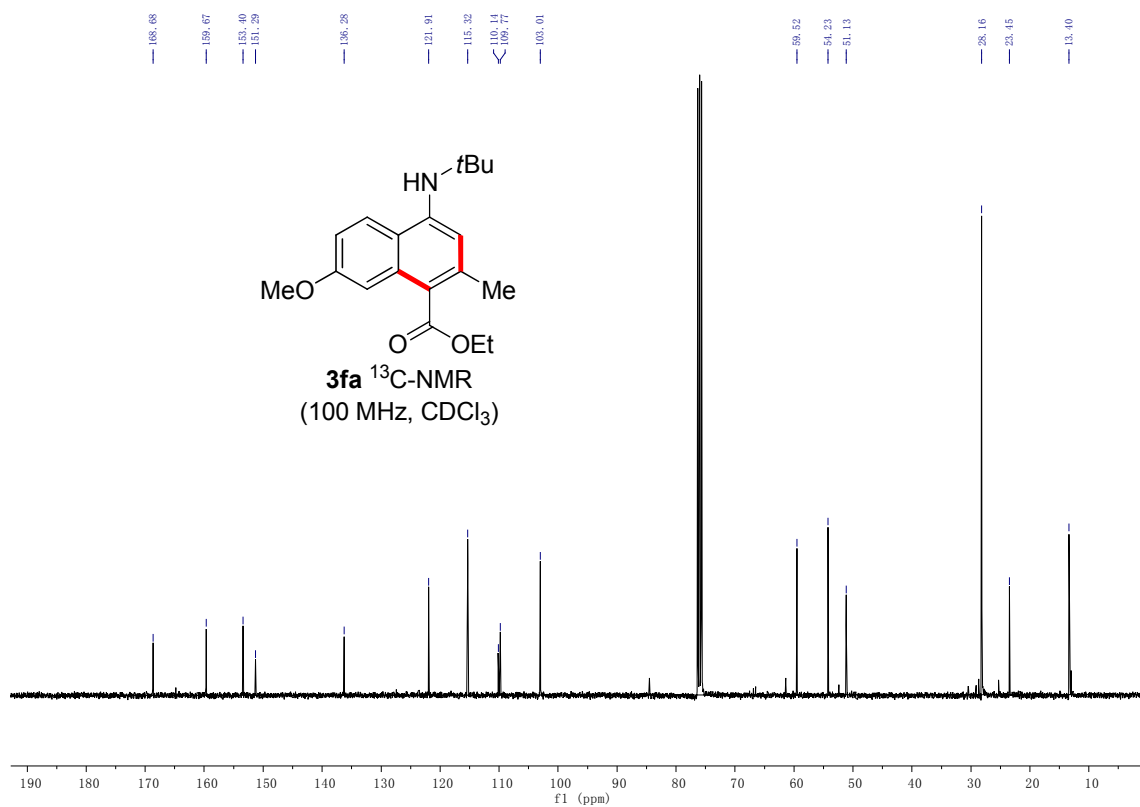


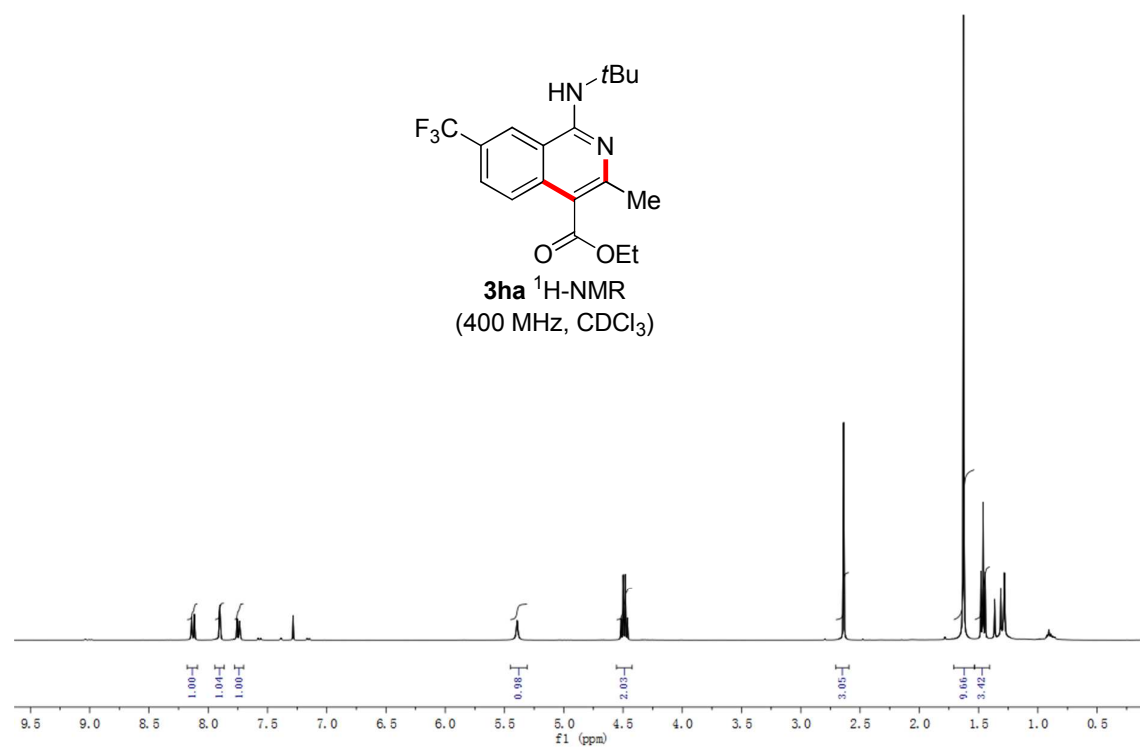
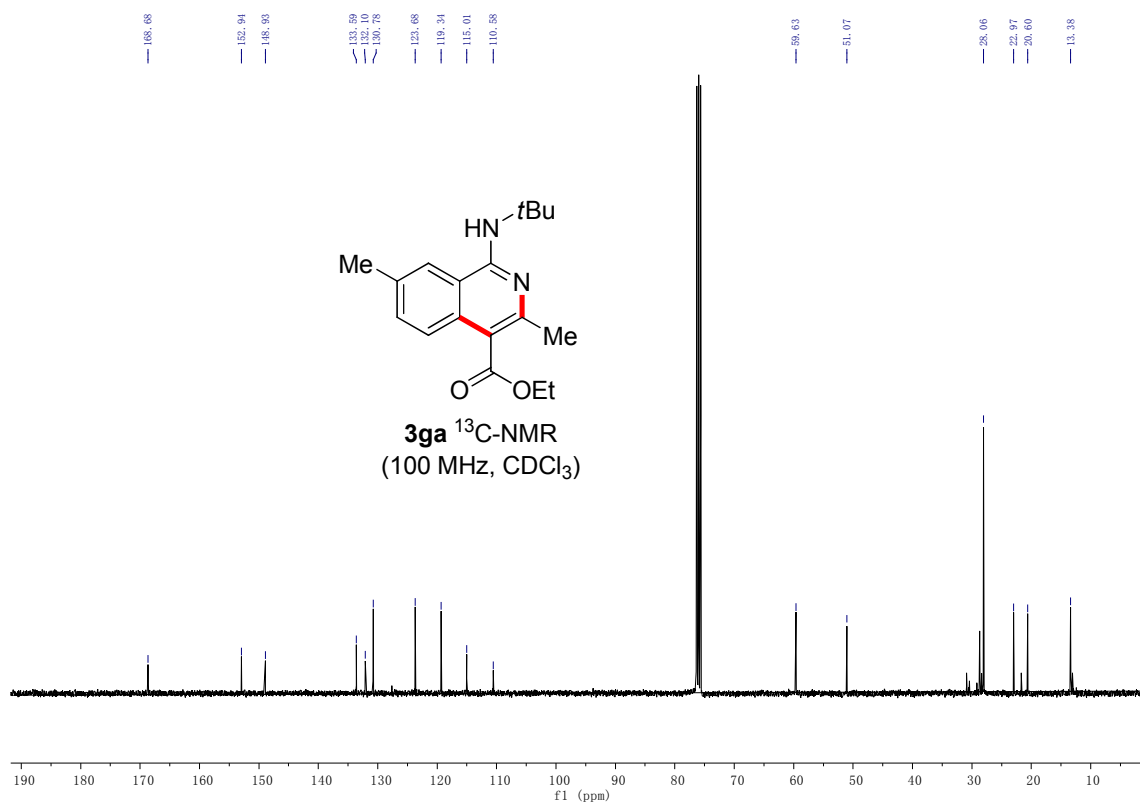


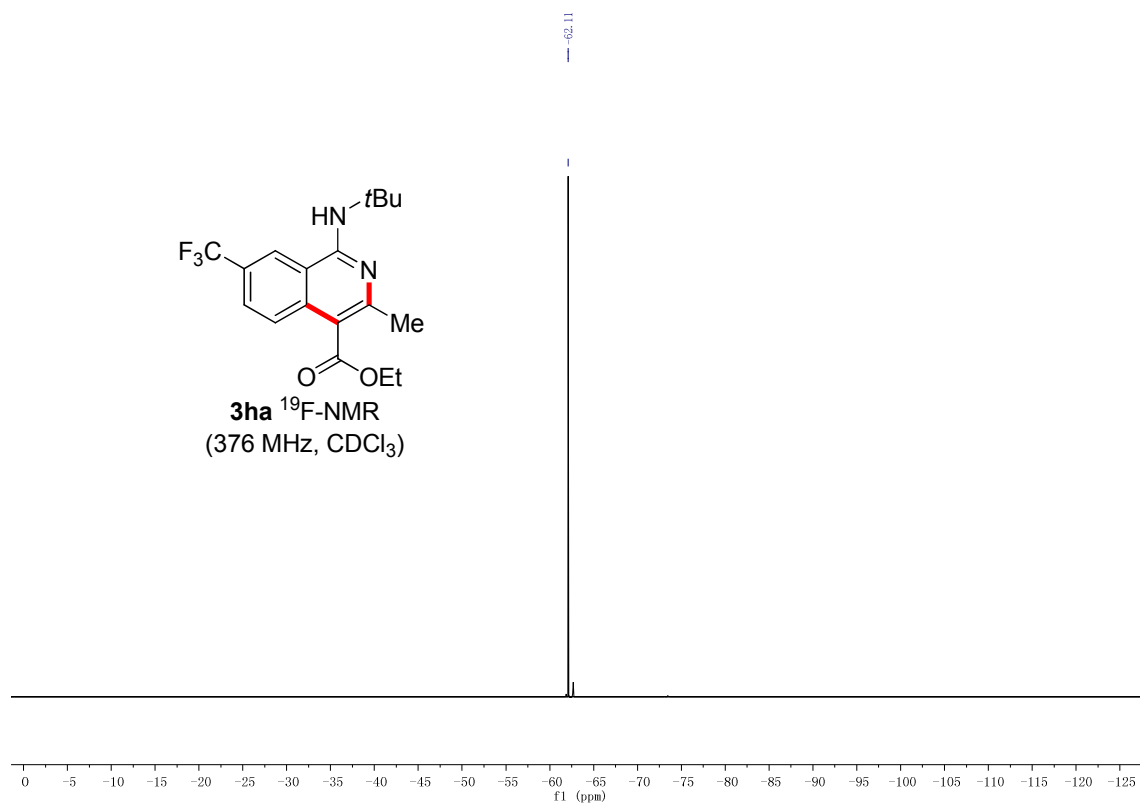
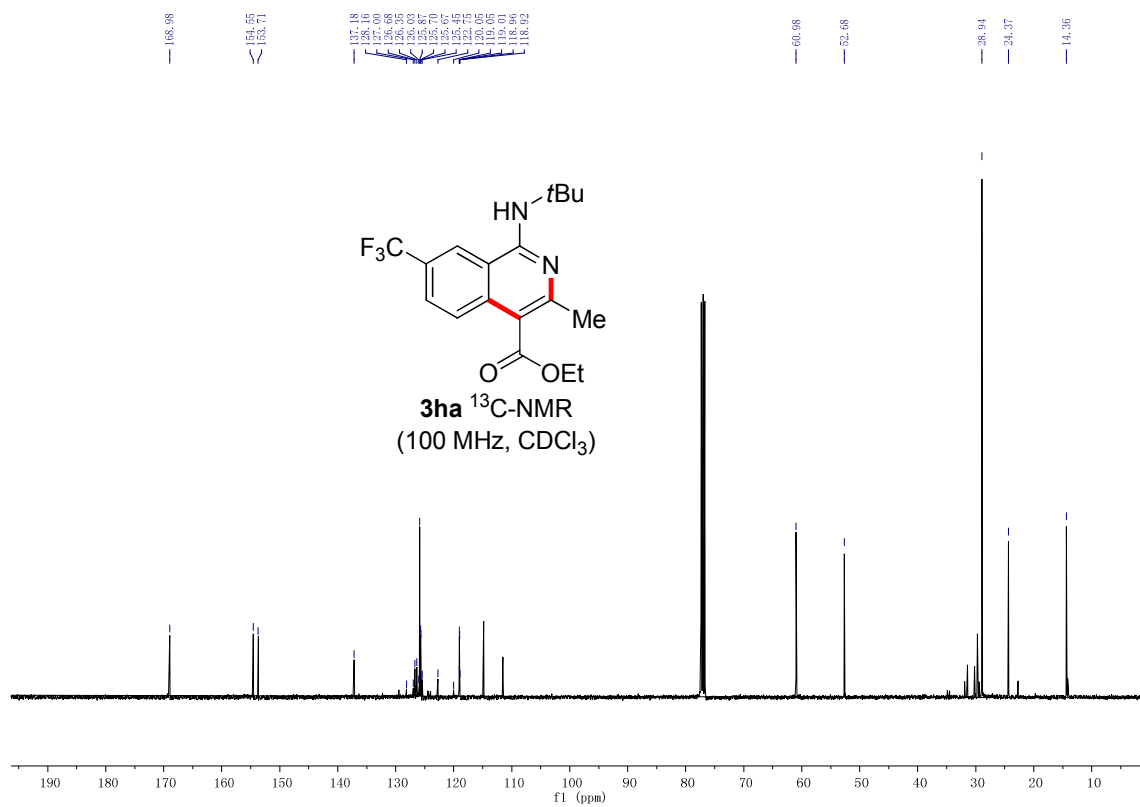


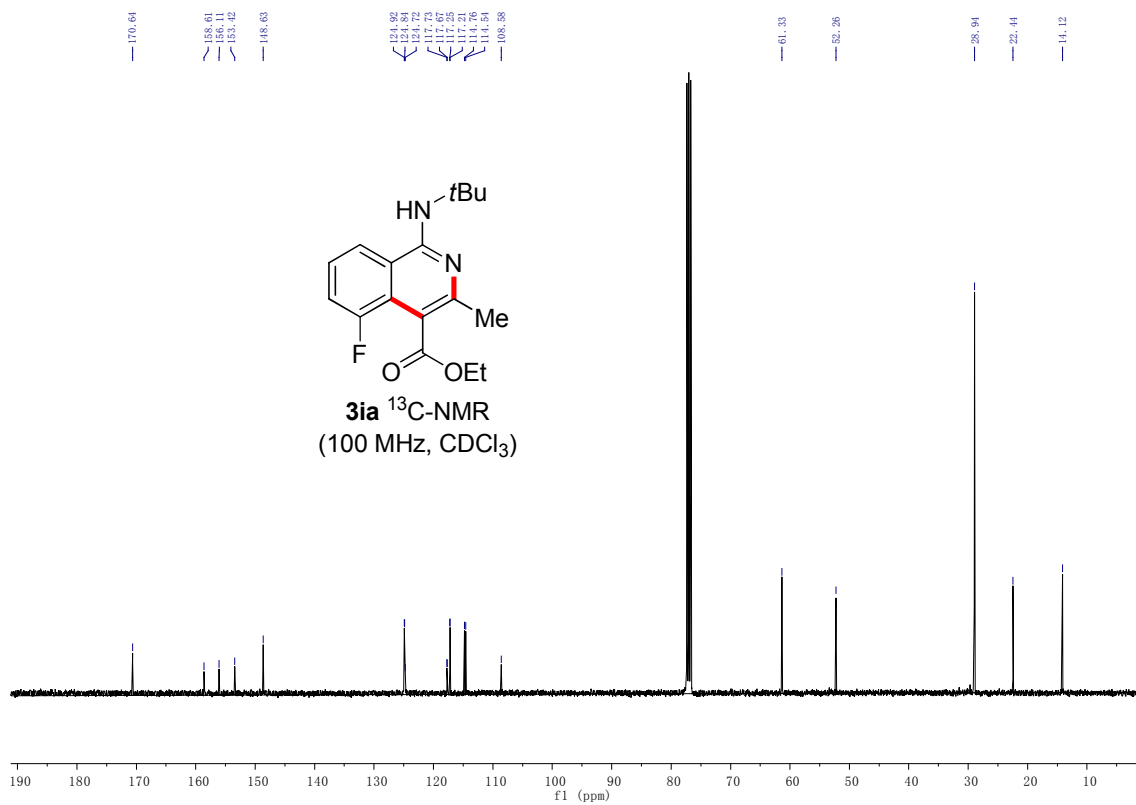
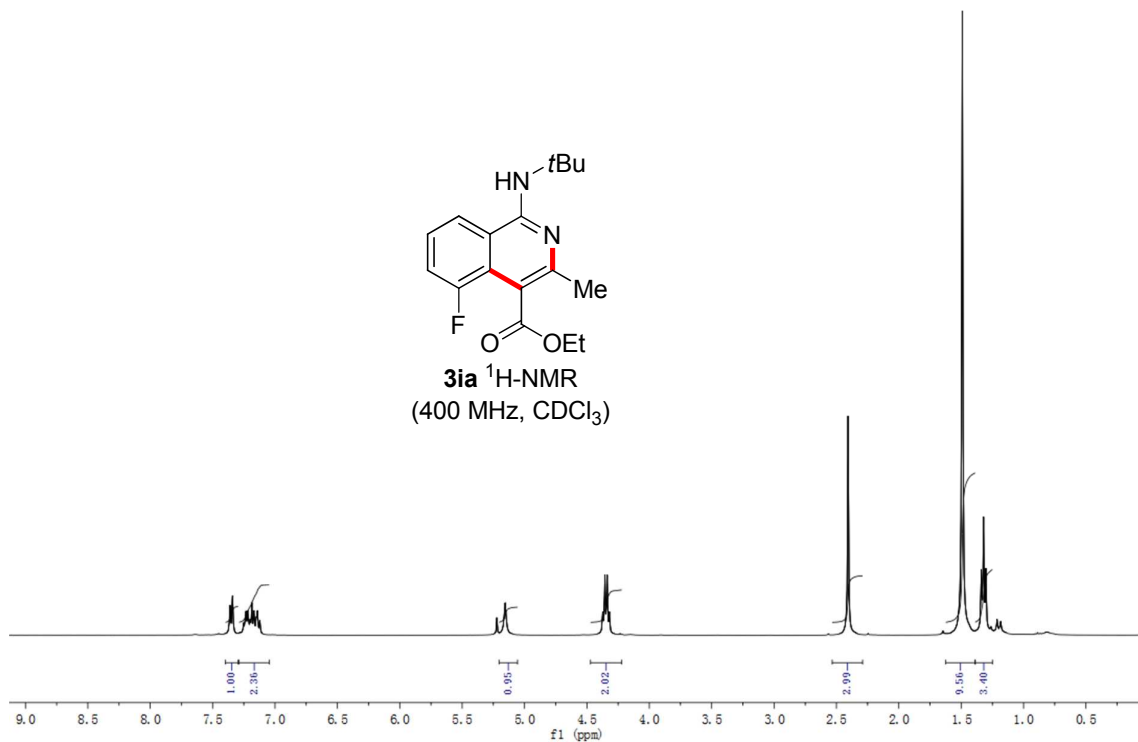


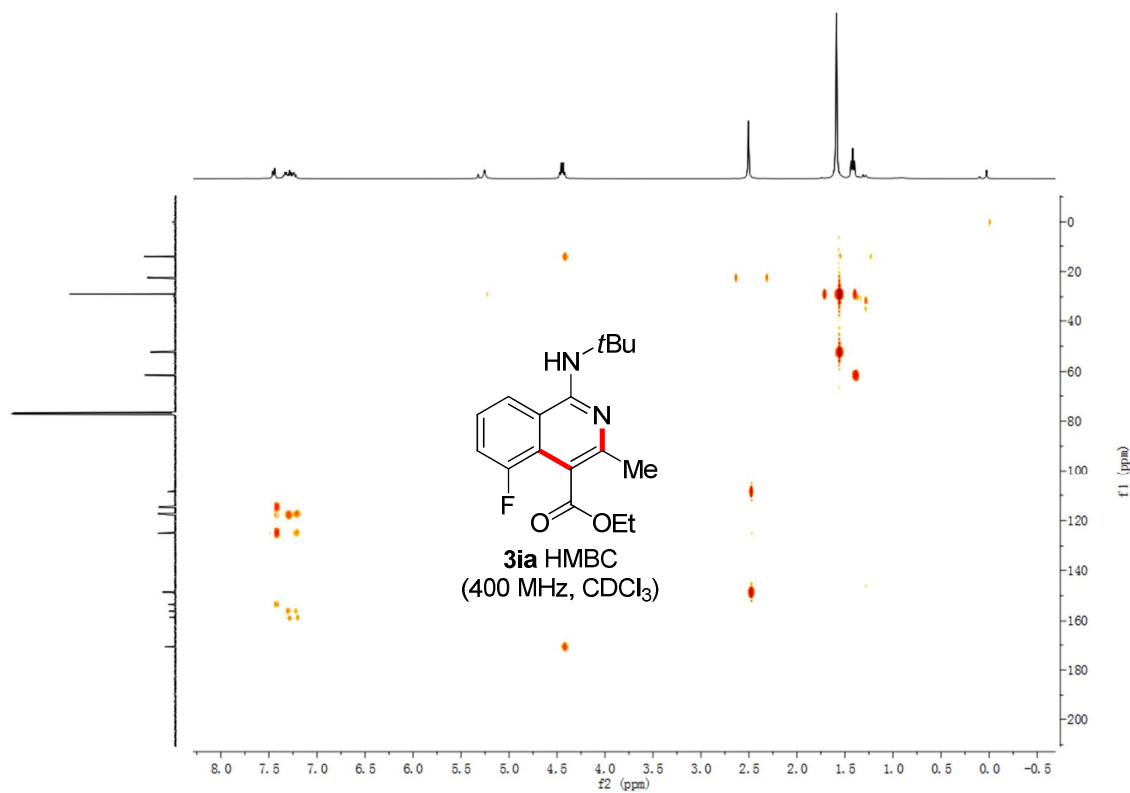
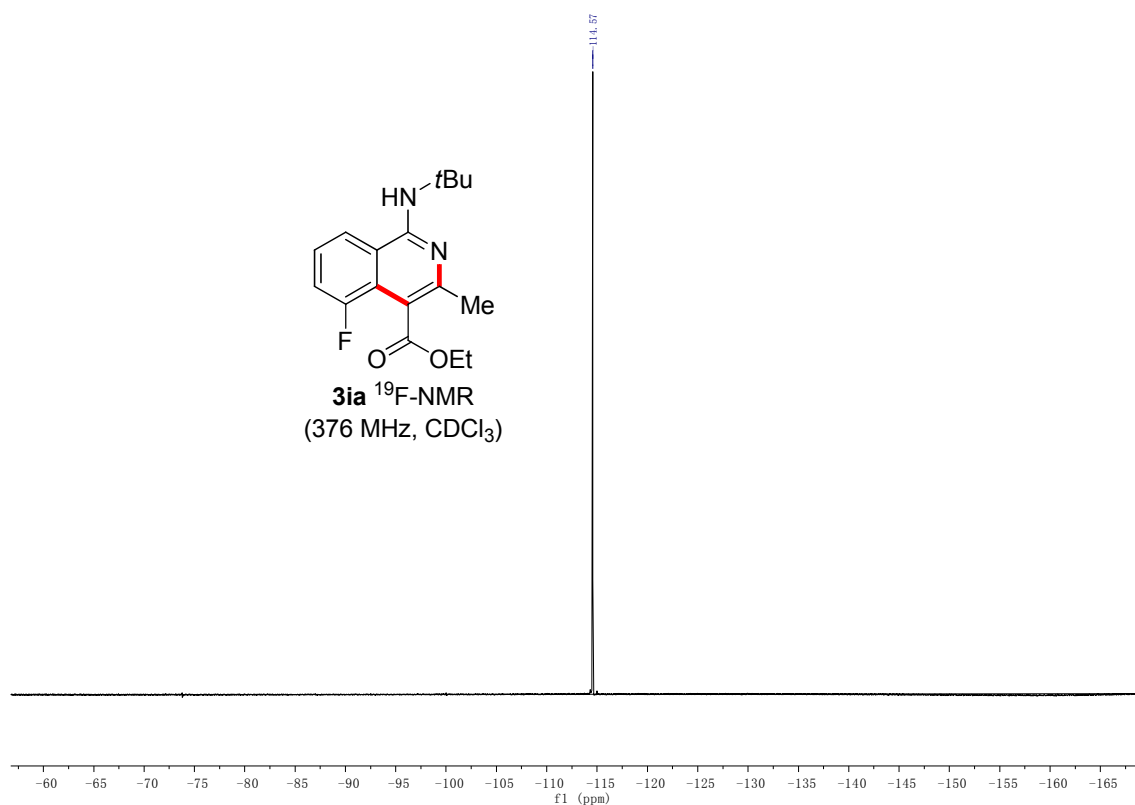


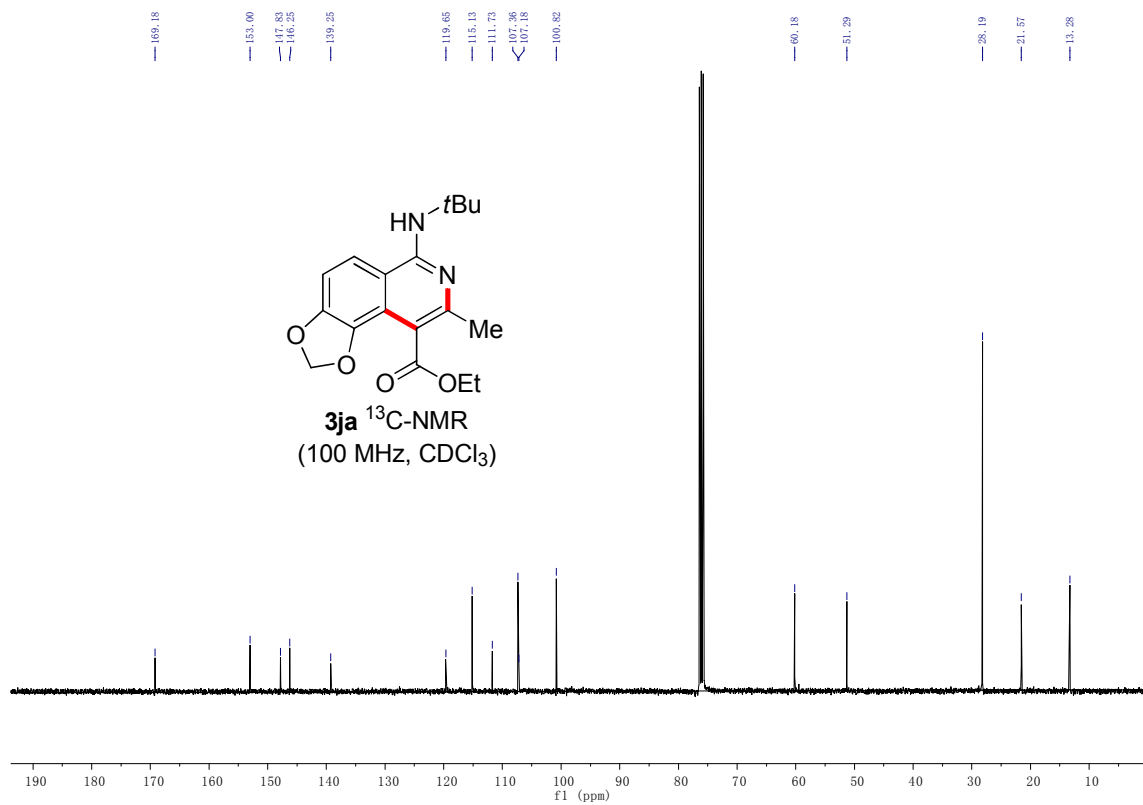
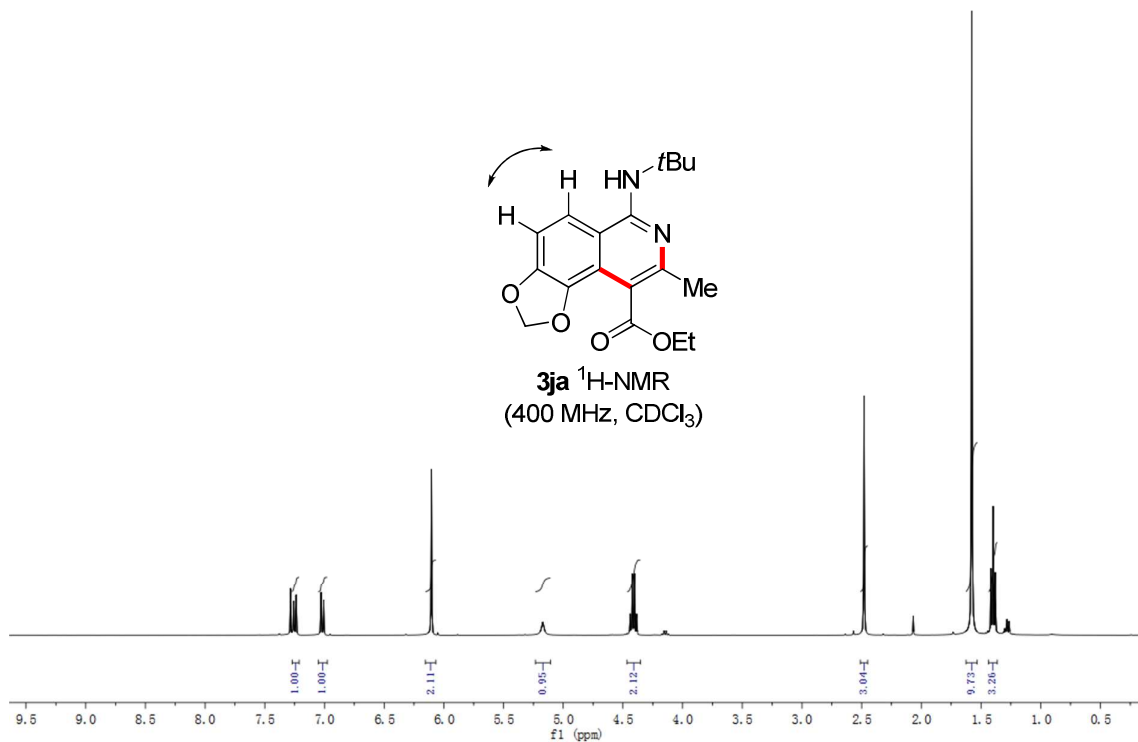


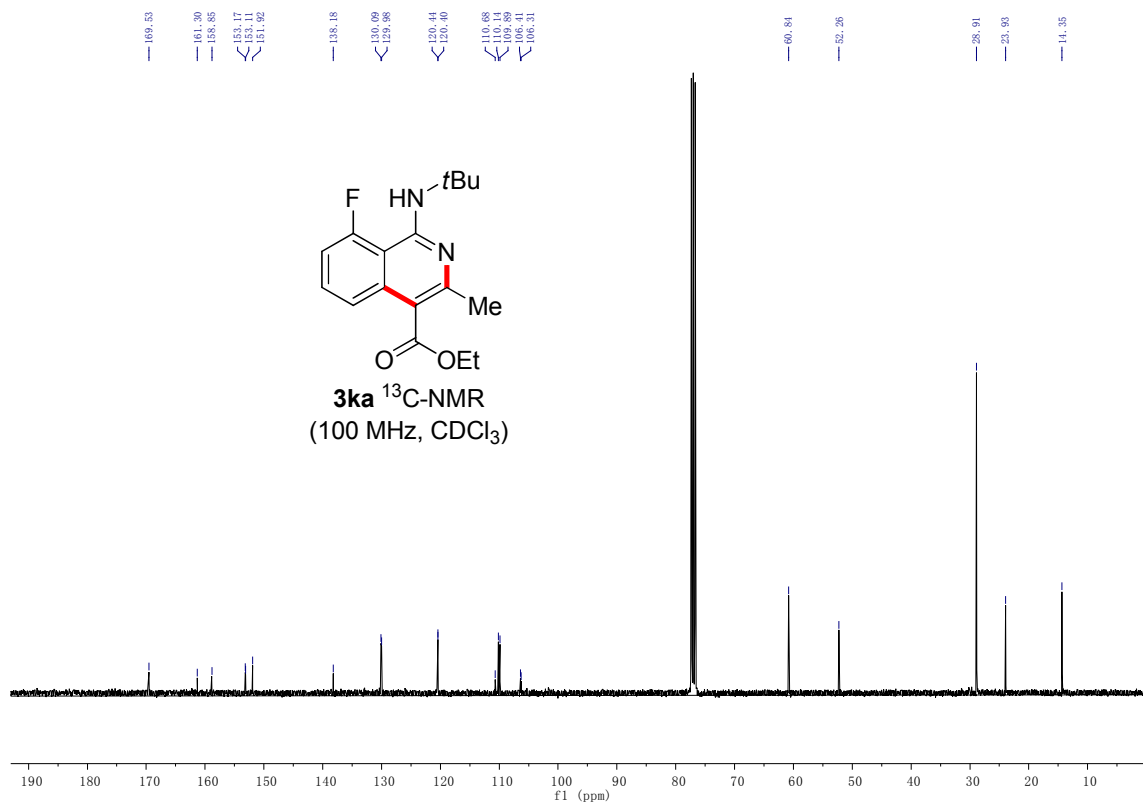
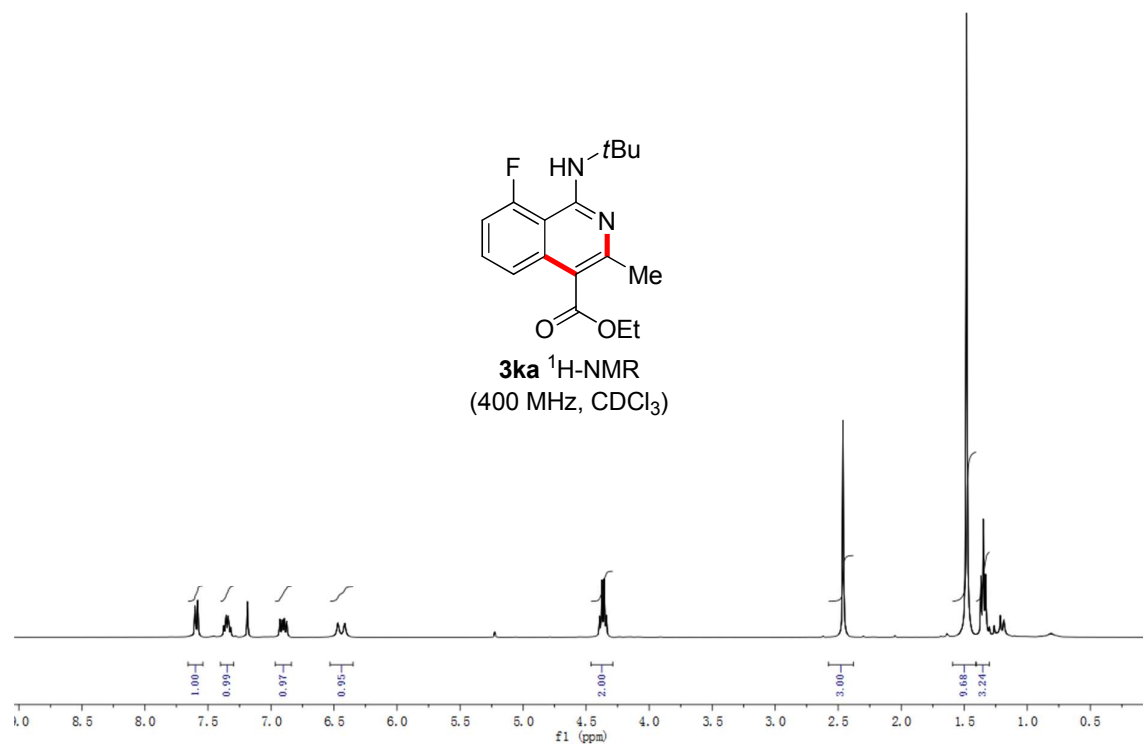




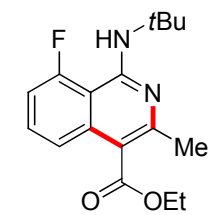




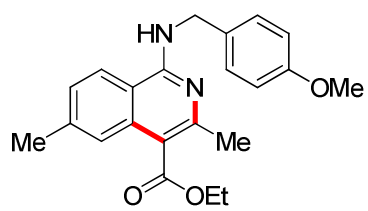
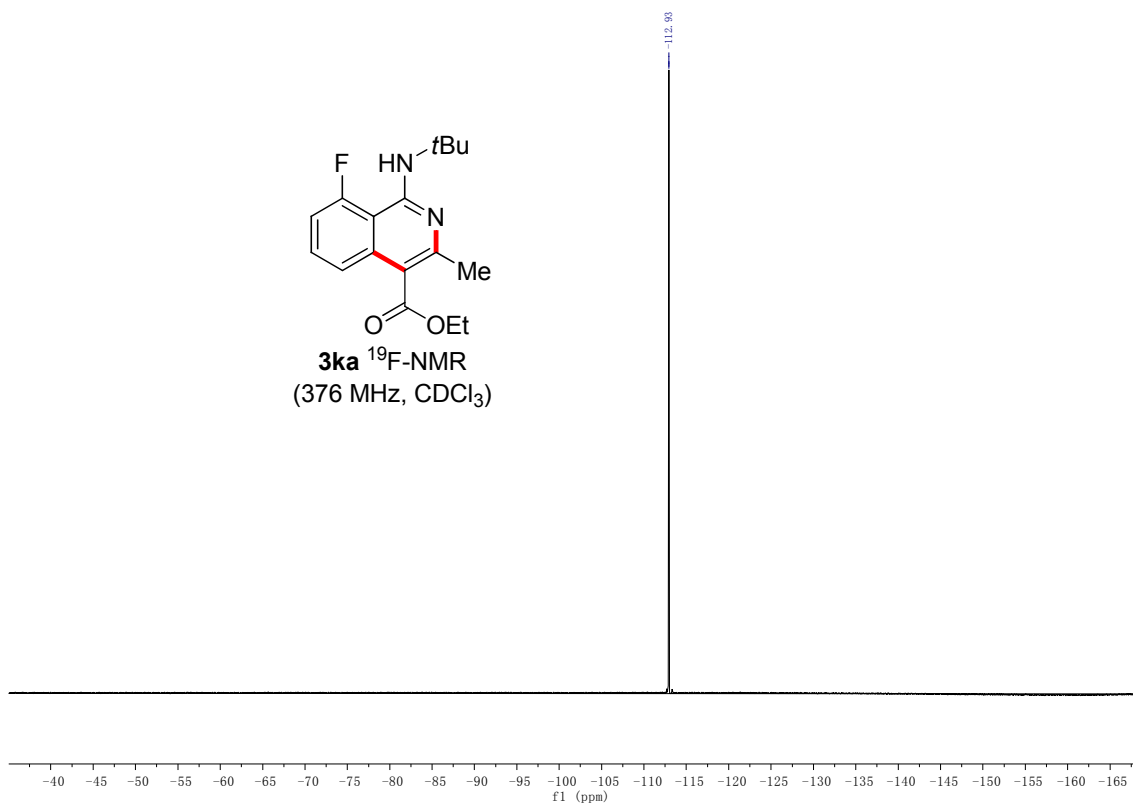




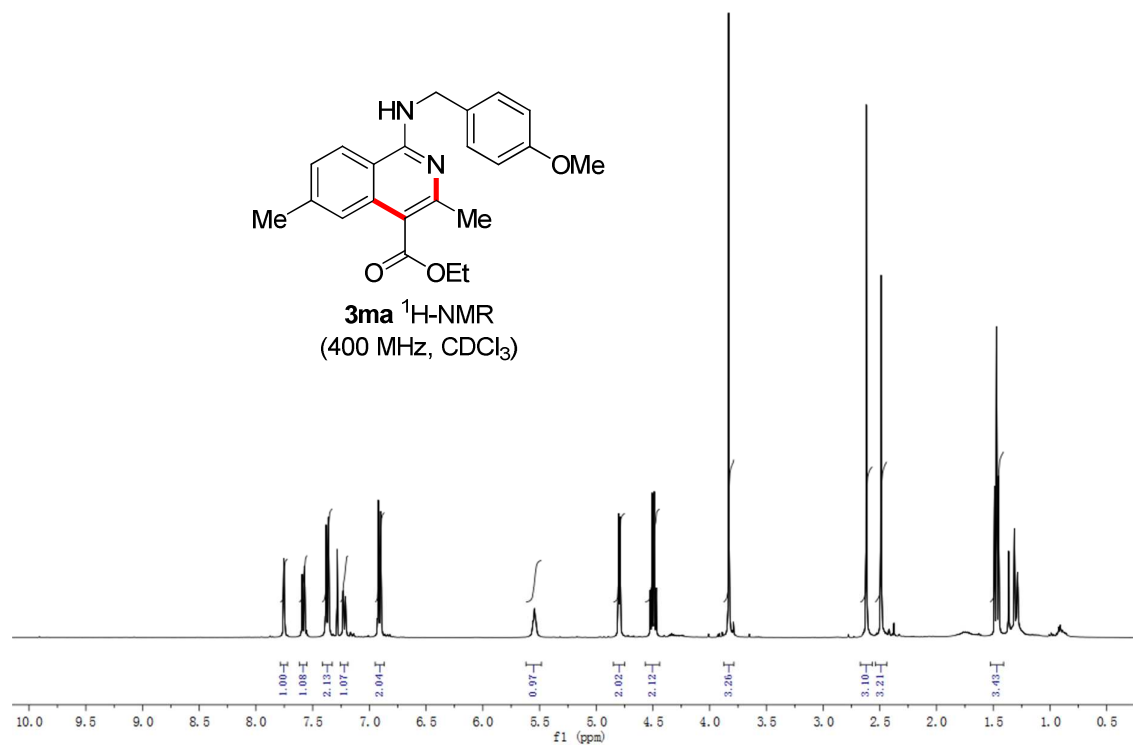


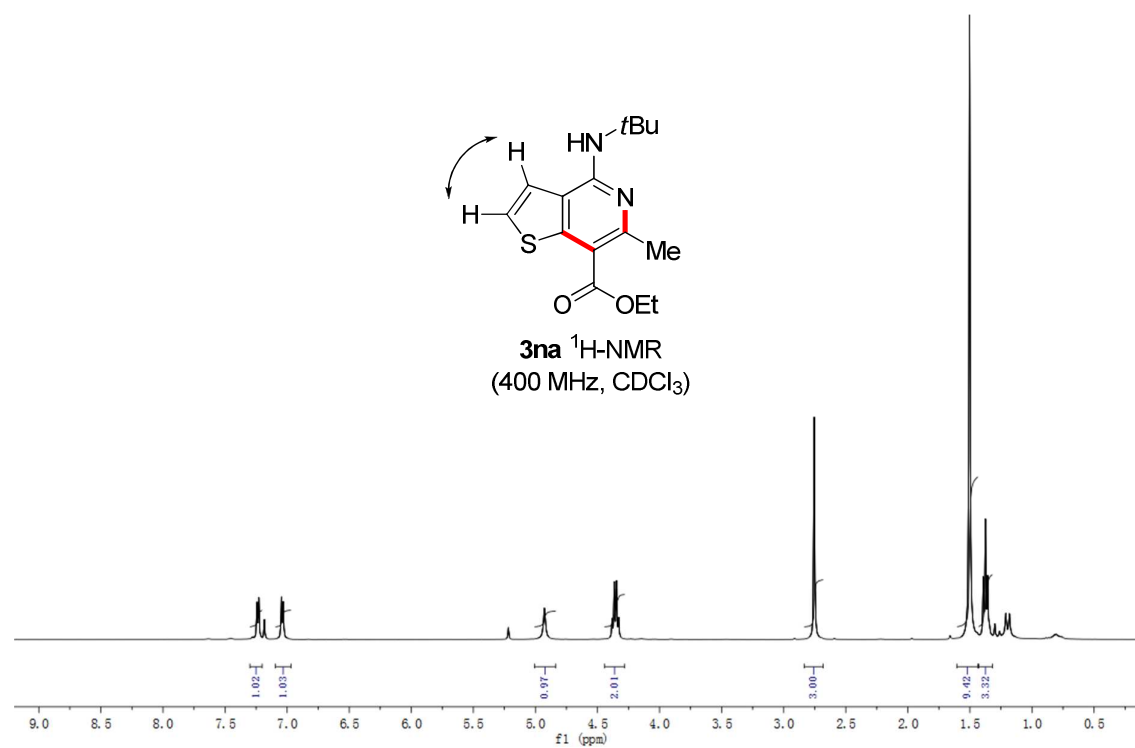
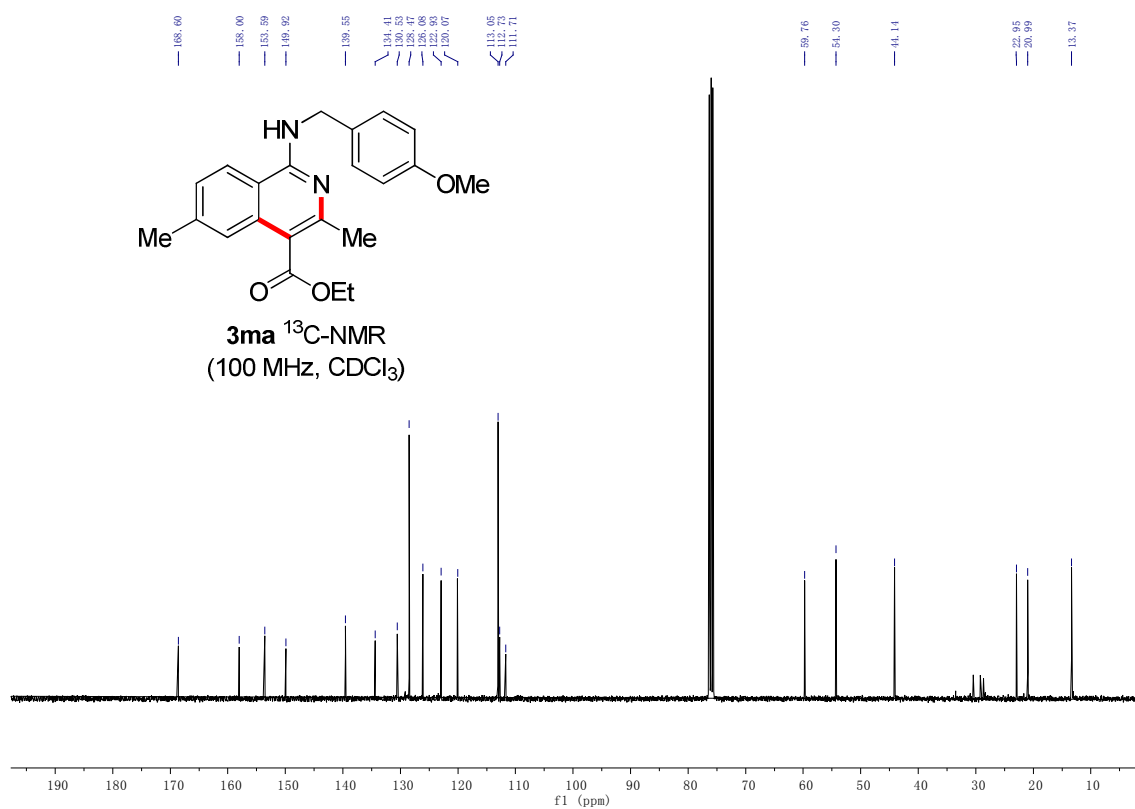


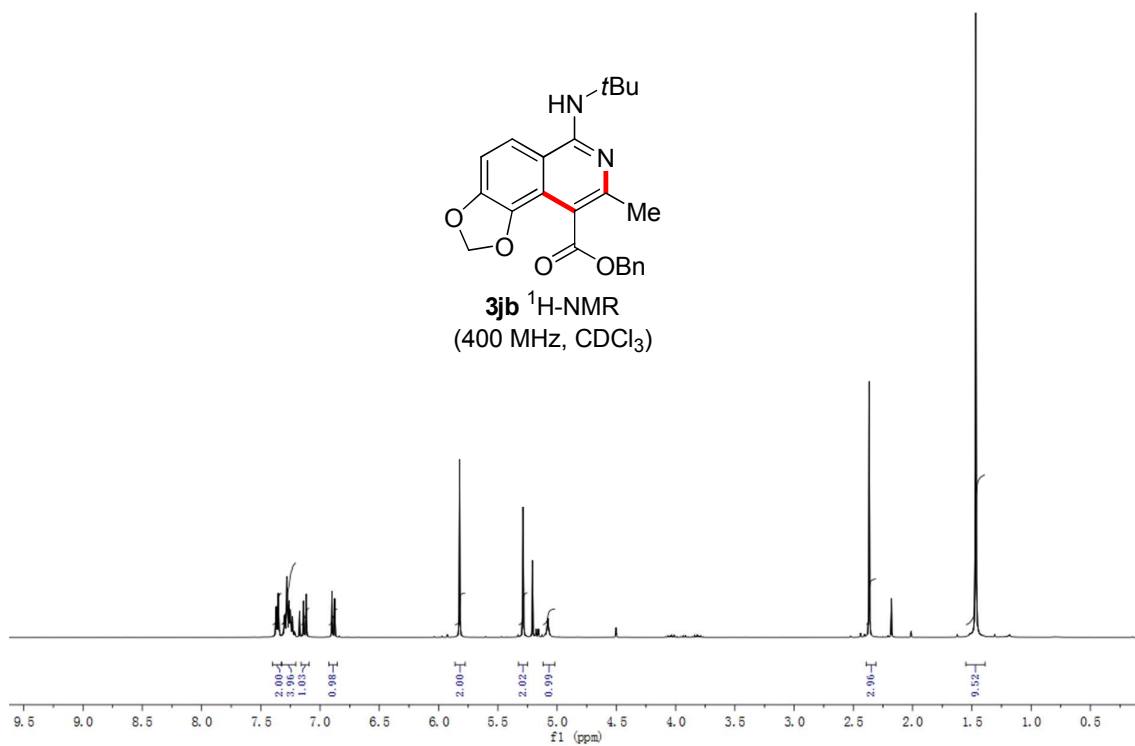
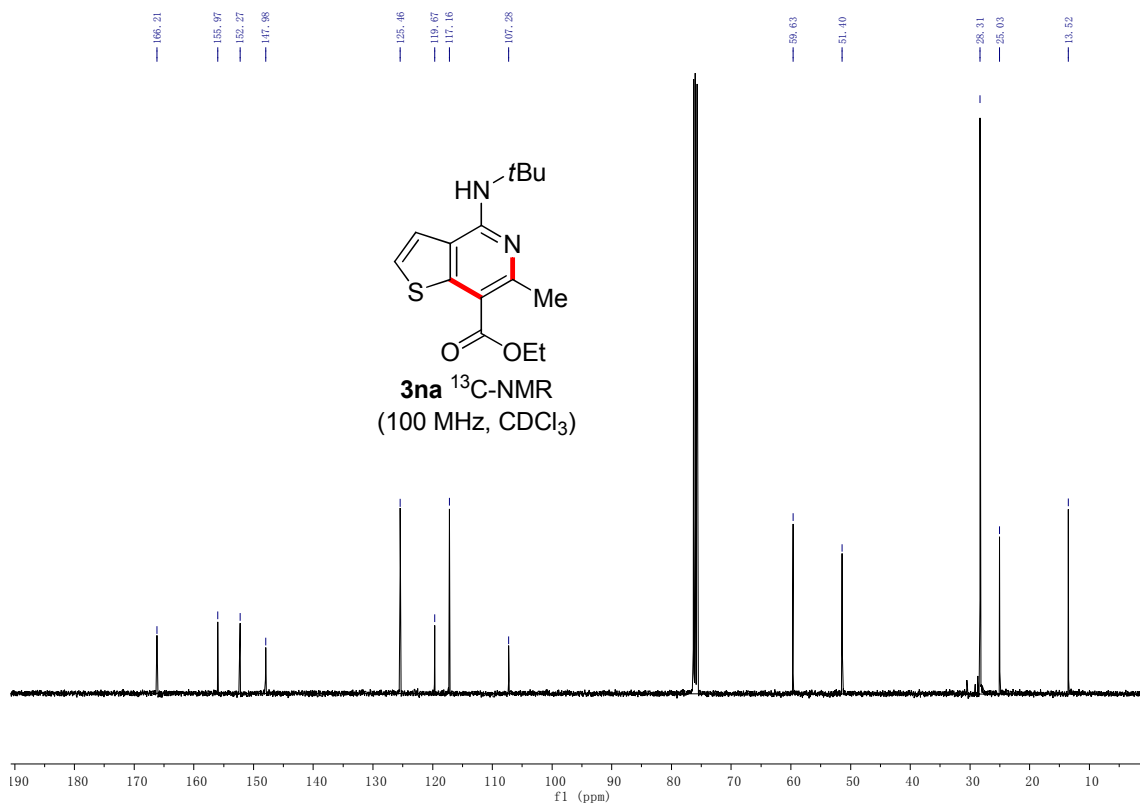
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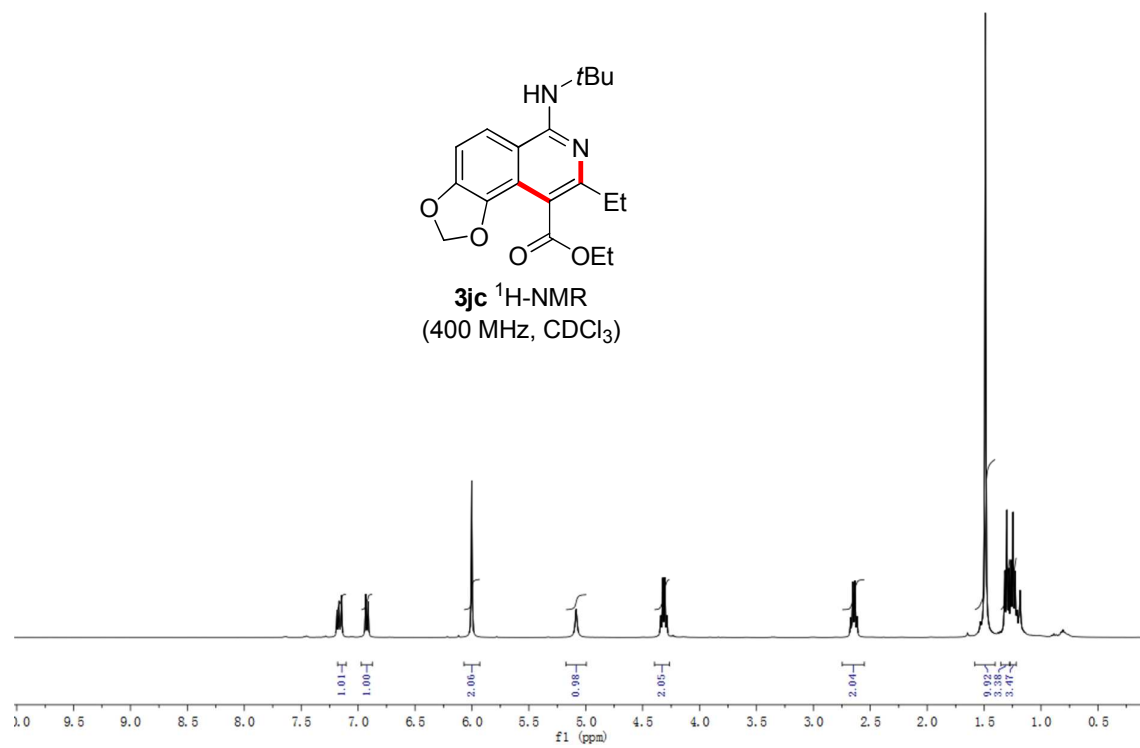
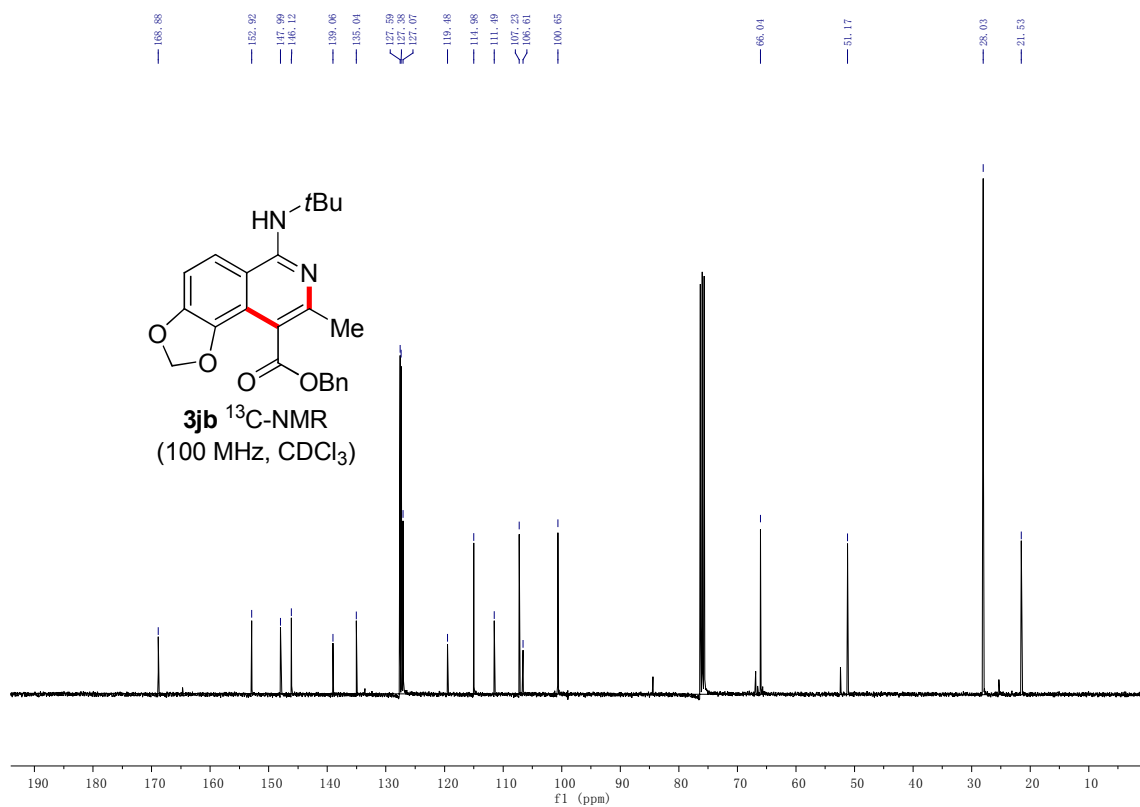


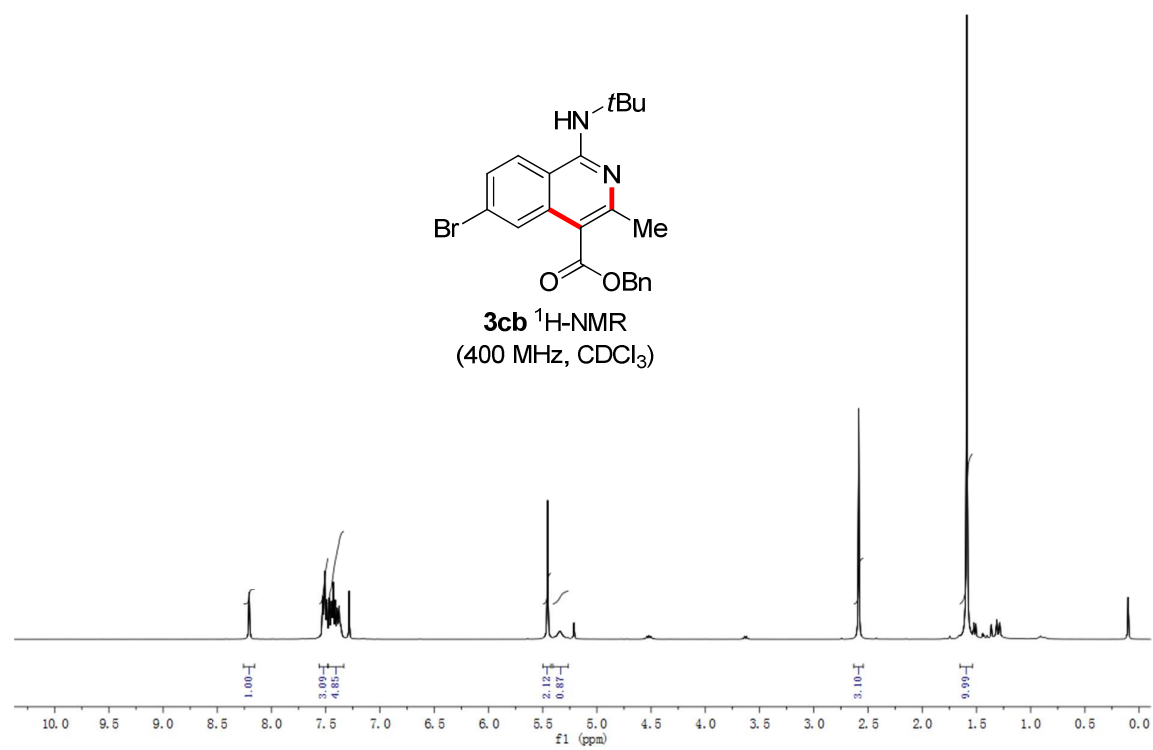
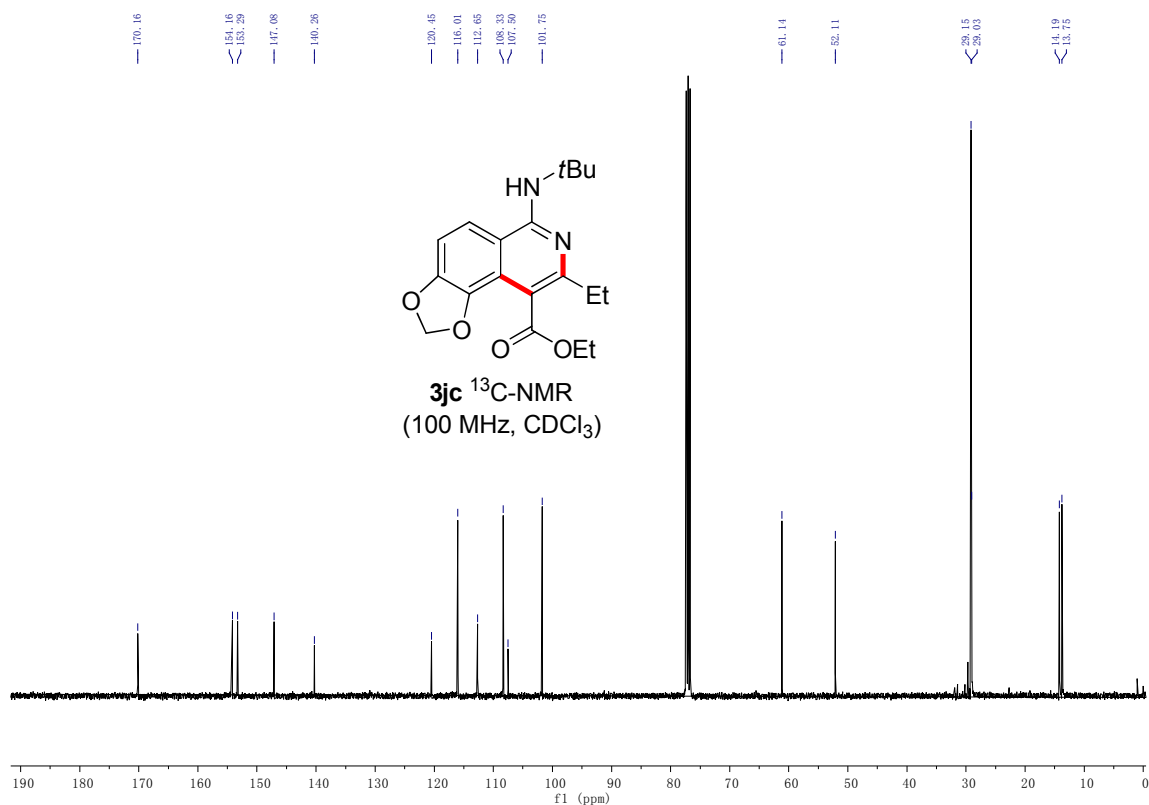
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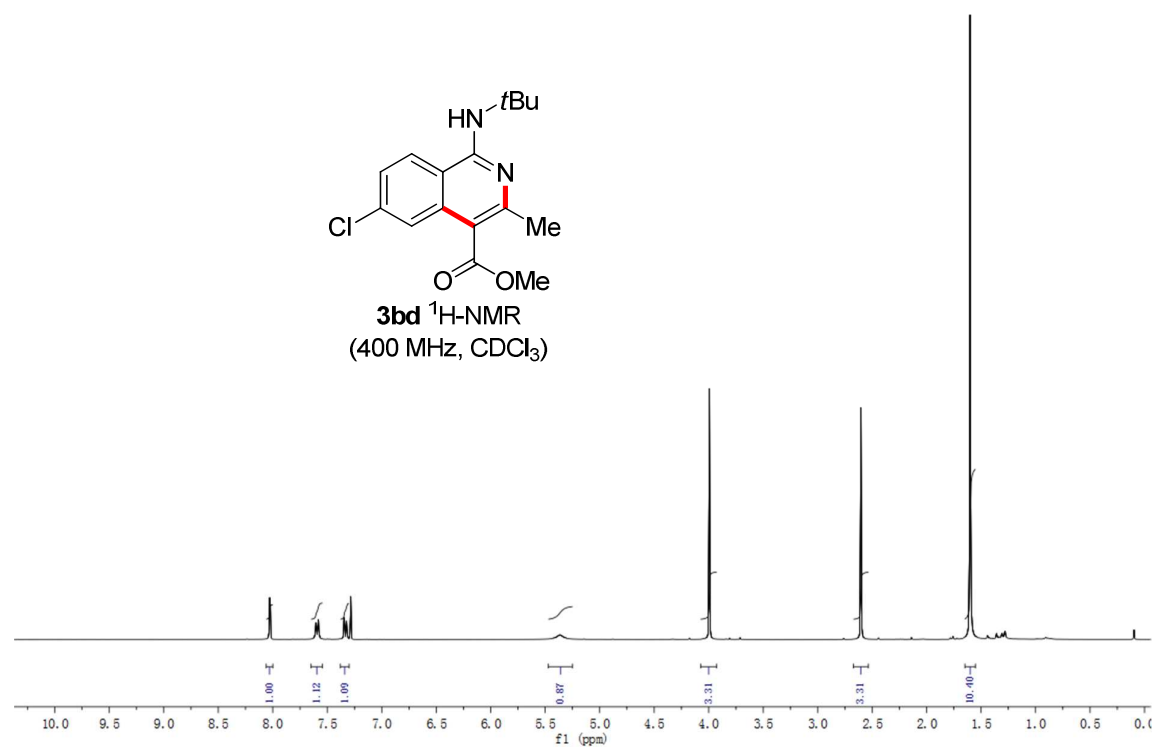
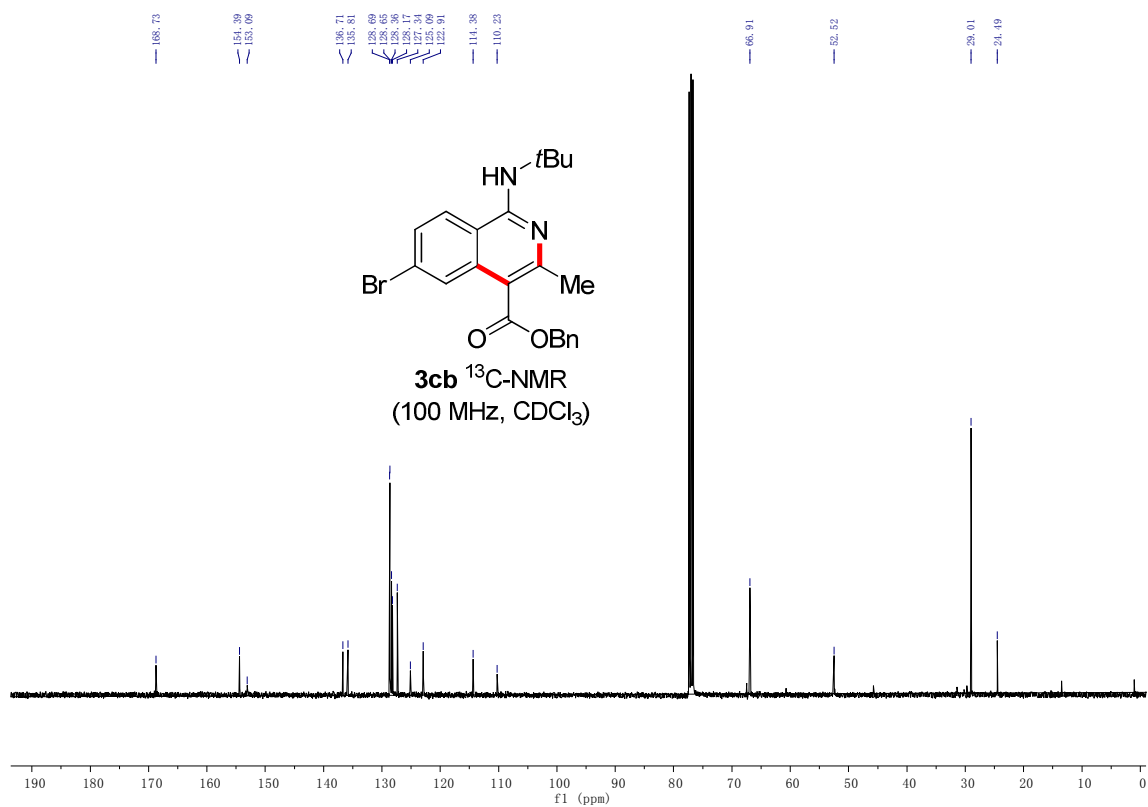


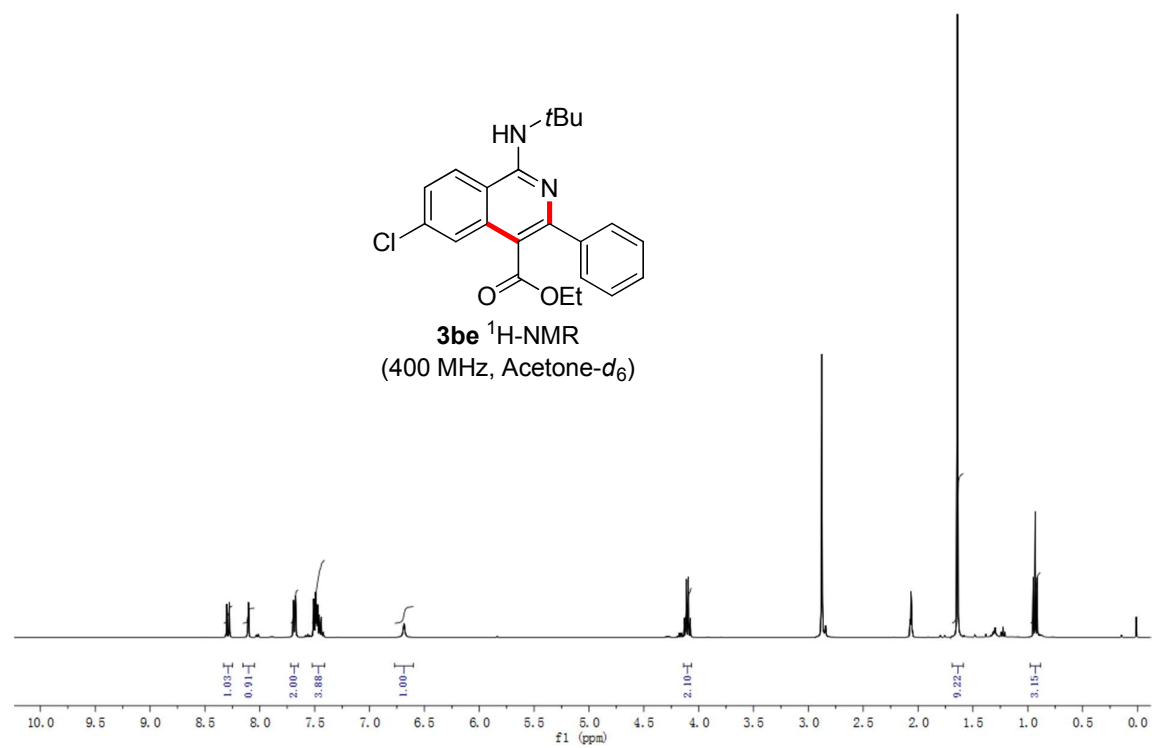
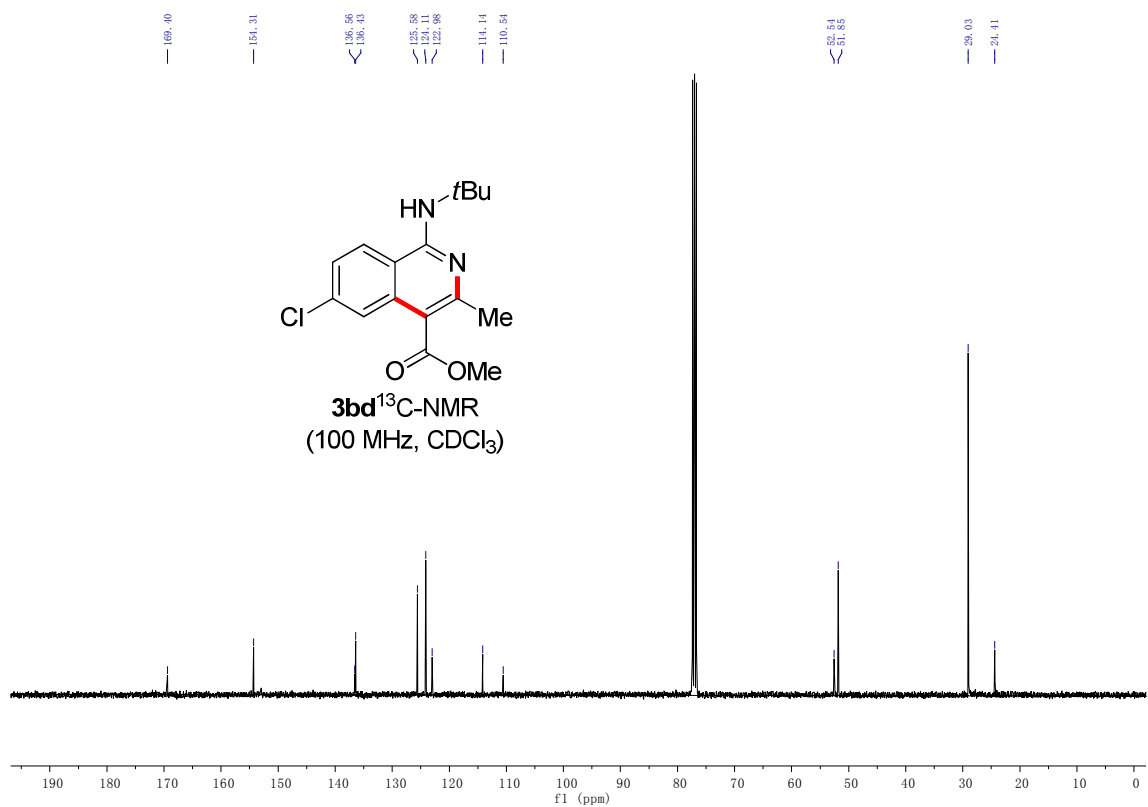


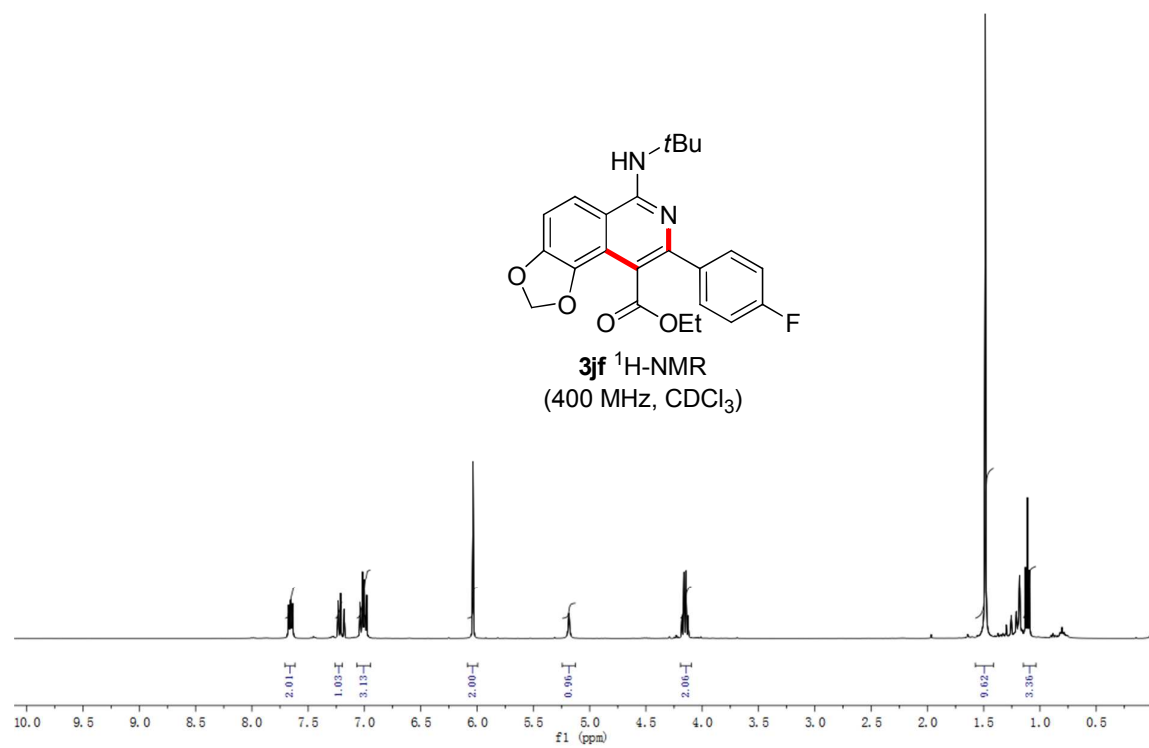
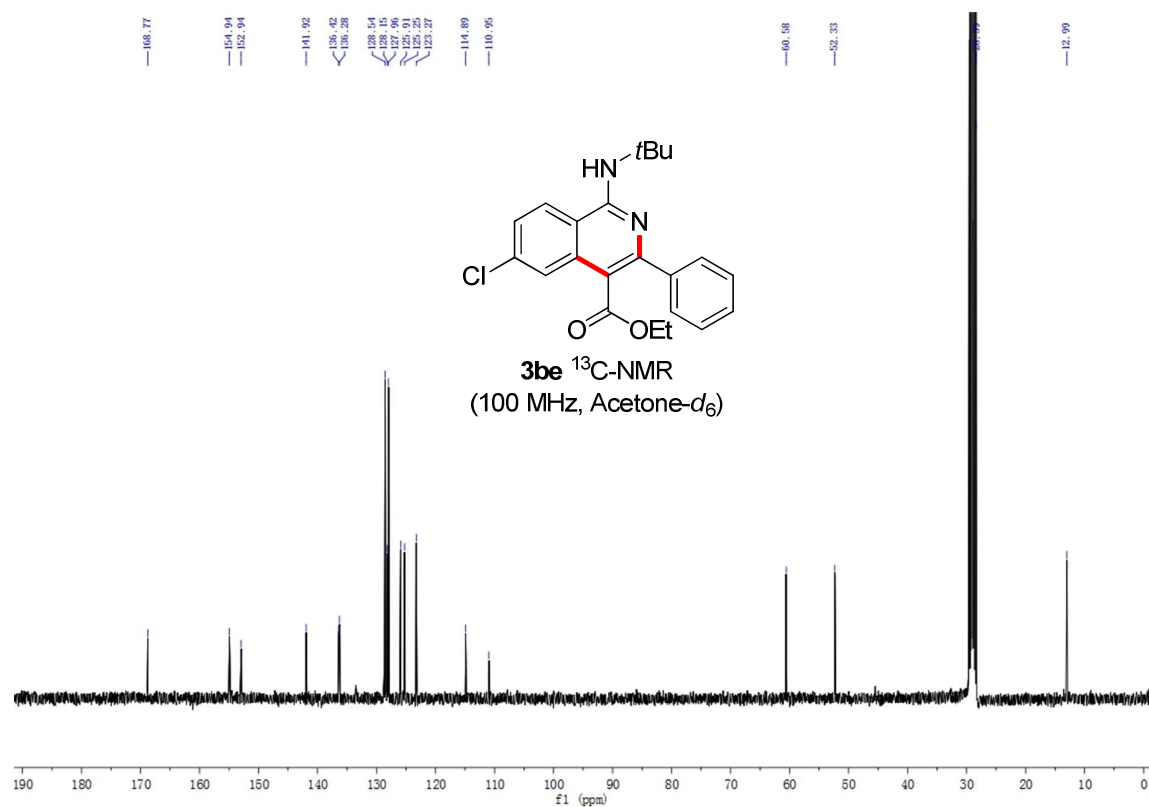




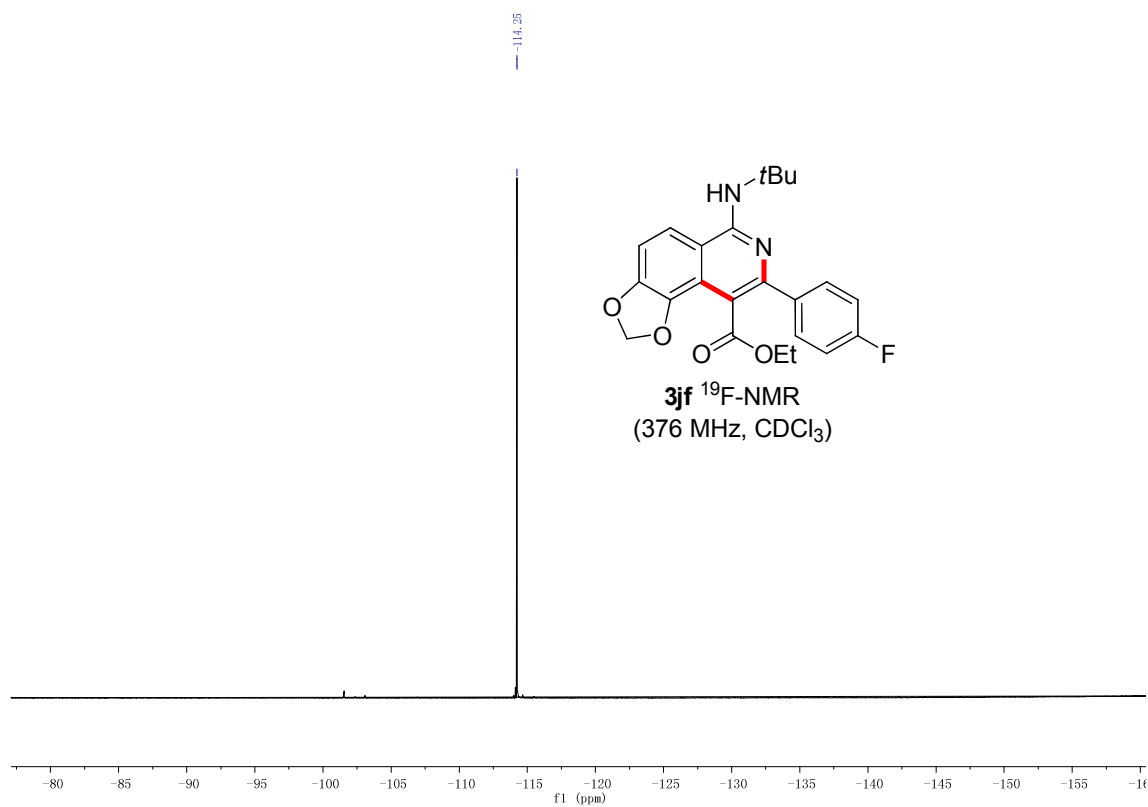
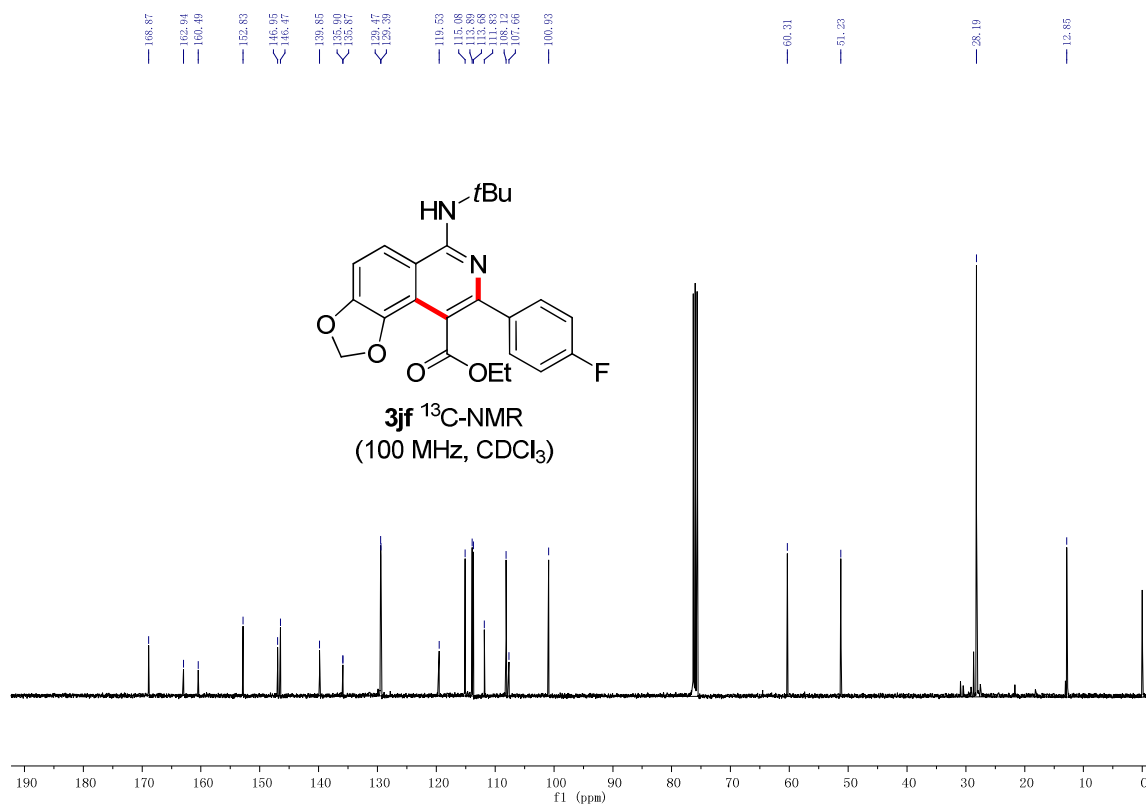


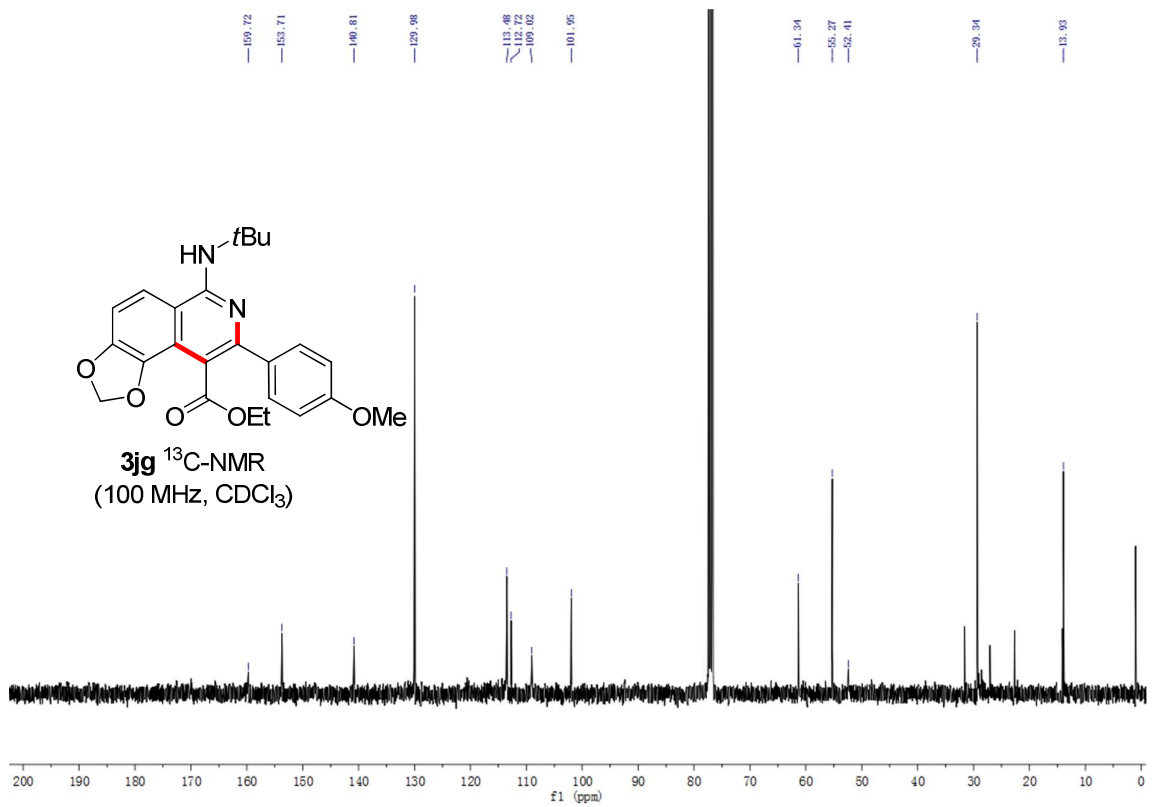
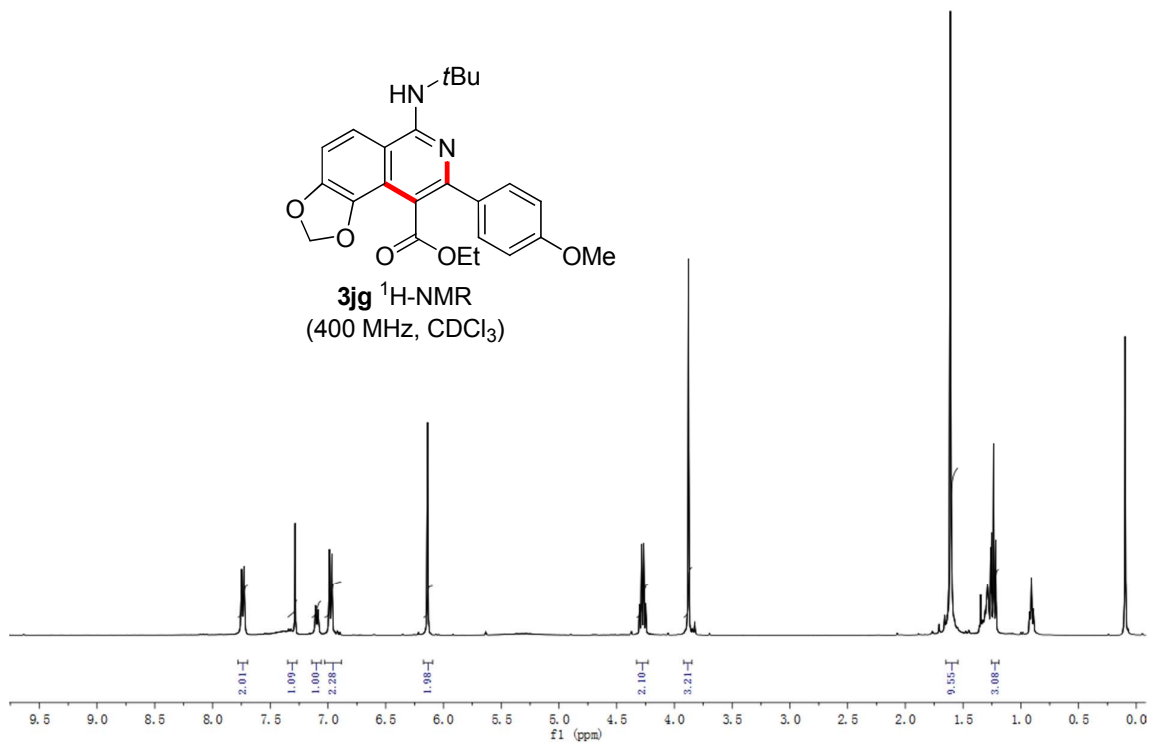


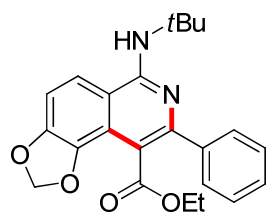




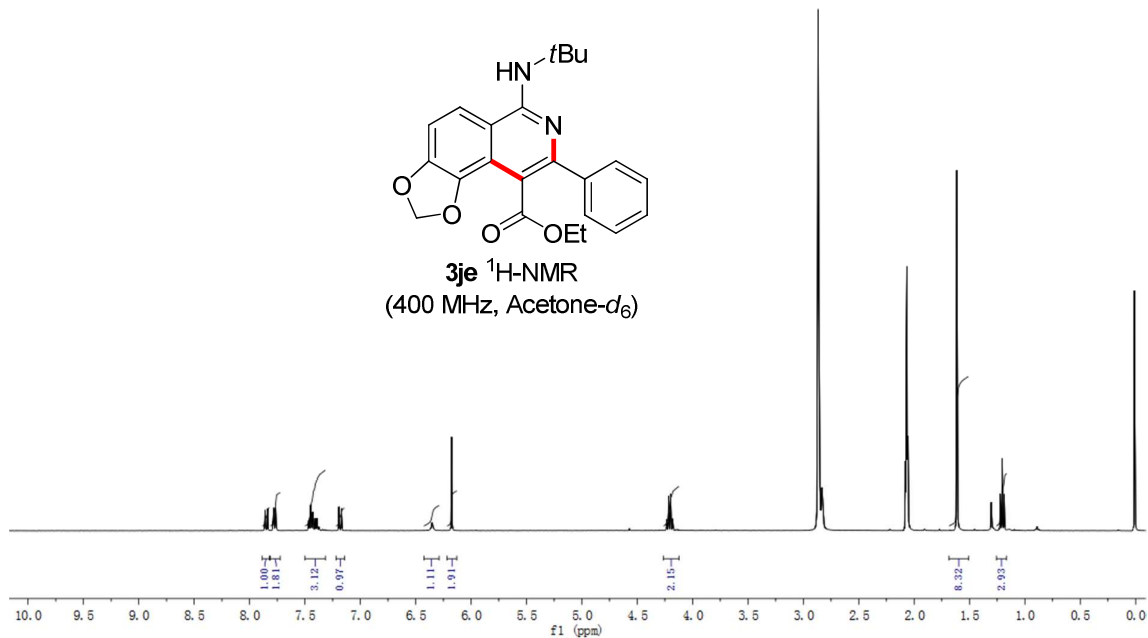




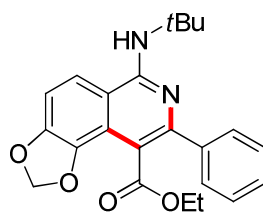




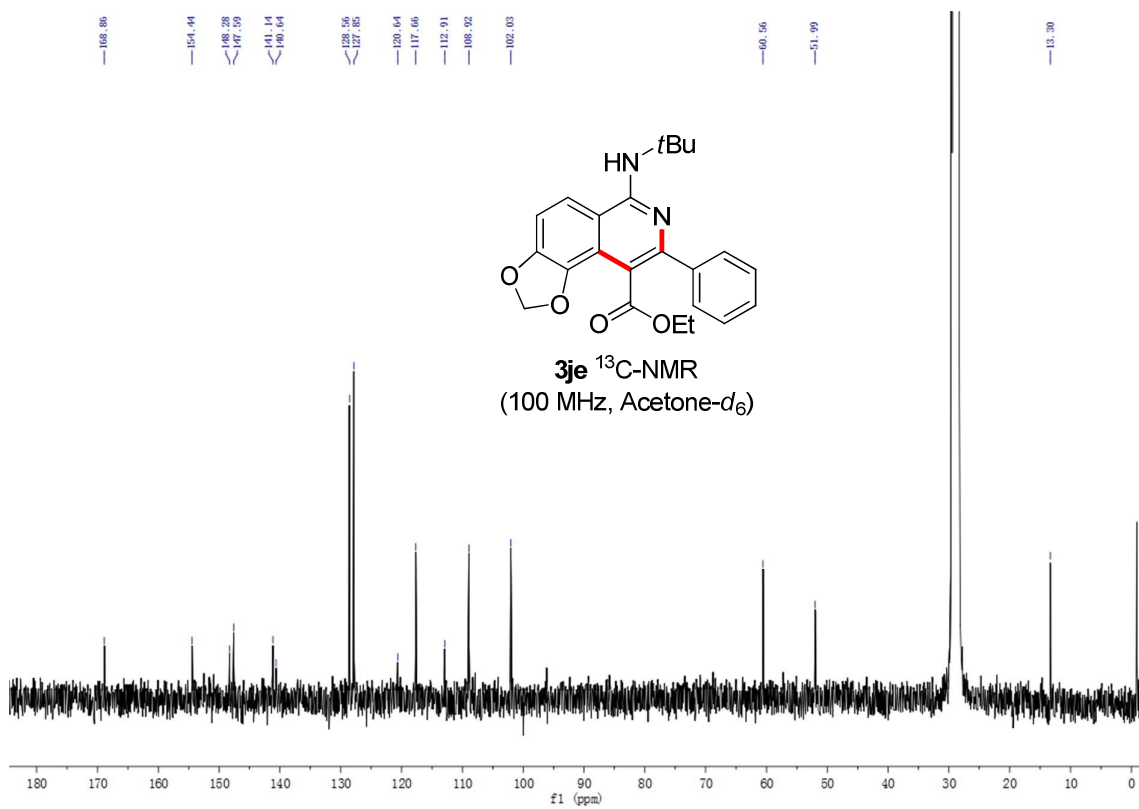
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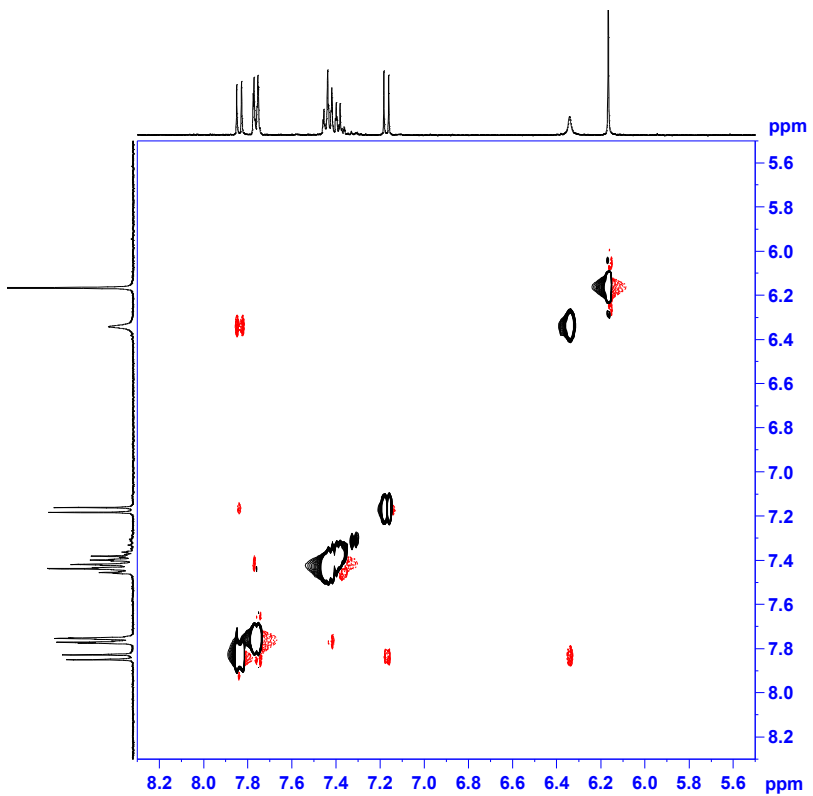
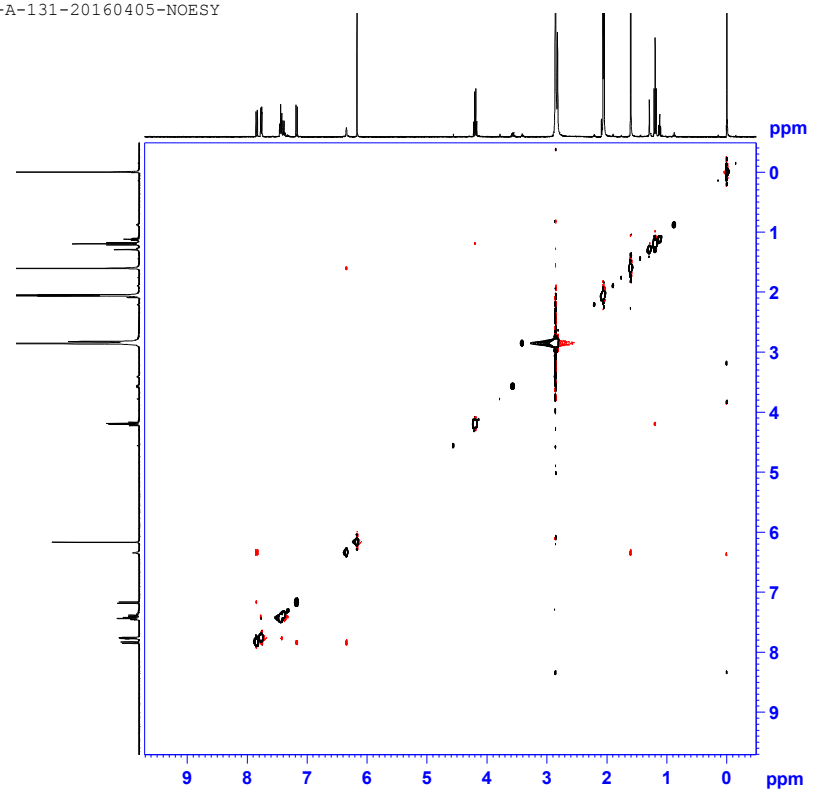
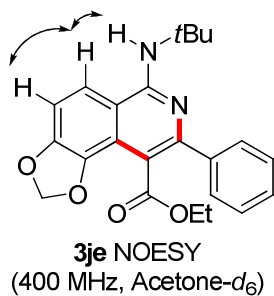


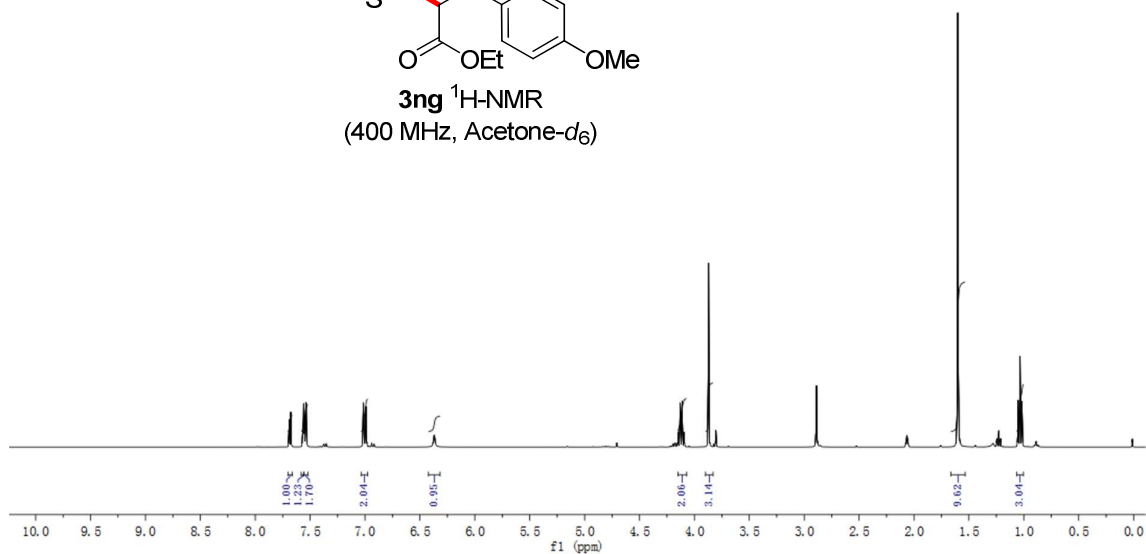
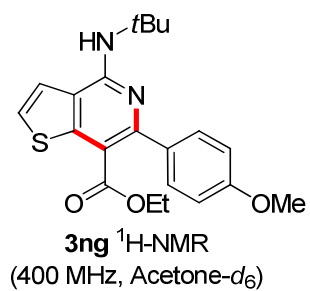
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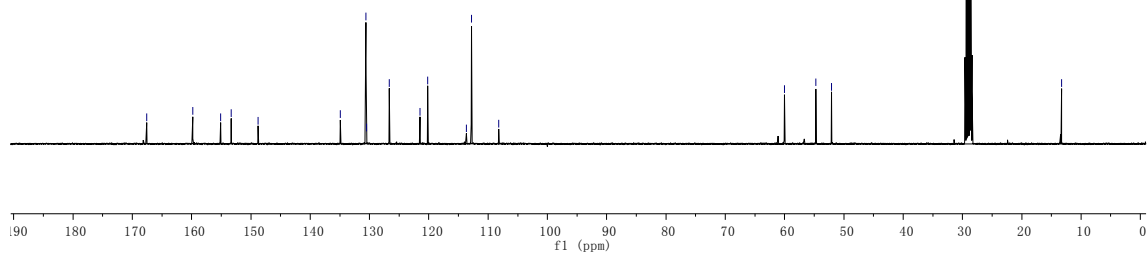
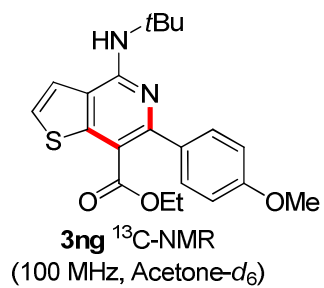
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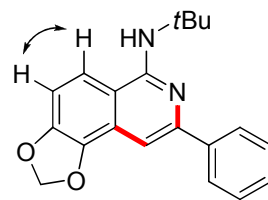




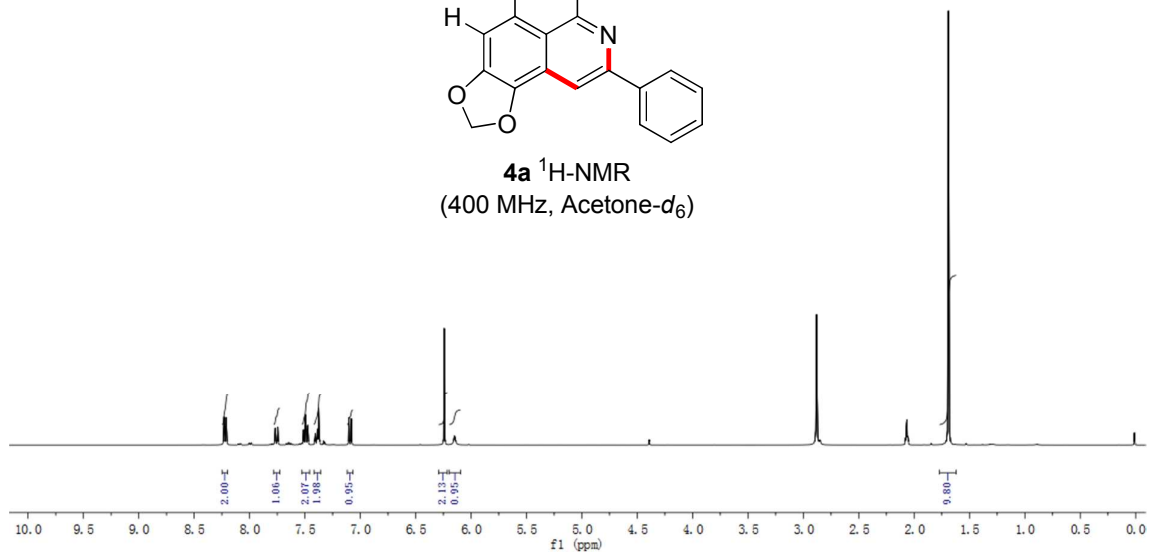


167.60  
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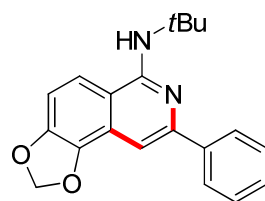




**4a**  $^1\text{H-NMR}$   
(400 MHz, Acetone- $d_6$ )



154.52  
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146.52  
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128.44  
126.91  
123.76  
117.22  
114.14  
108.17  
102.20  
97.09  
51.63



**4a**  $^{13}\text{C-NMR}$   
(100 MHz, Acetone- $d_6$ )

