# Iodine-Catalyzed Sulfuration of Isoquinolin-1(2H)-ones Applying Ethyl Sulfinates

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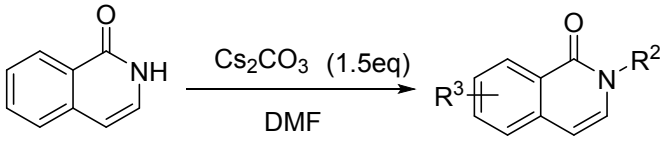
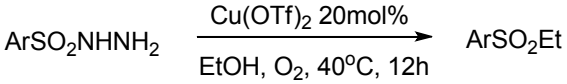
**1. General procedure for preparation of various N-substituted isoquinolones**



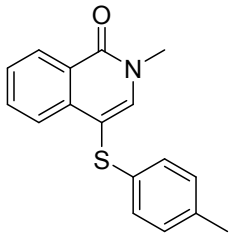

The N-substituted isoquinolones substrates were prepared in the following procedure: isoquinolin-1(2H)-ones (30 mmol, 1.0 equiv), alkyl / aryl halide (45 mmol, 1.5 equiv.), cesium carbonate (45 mmol, 1.5 equiv) and DMF (5 mL) were added into a 10 mL round-bottom flask. The reaction was heated to 50 $^{o}$C in an oil bath for 3 h. Then, the reaction mixture was allowed to warm to ambient temperature, and the reaction mixture was diluted with EtOAc (20 mL). The organic layer was washed with water (2 x 10 mL) and dried over $Na_2SO_4$. The suspension was filtered, and the solvent was removed under reduced pressure. The resulting residue was purified by column chromatography (silica gel, pet. ether/EtOAc=5:1) to give the desired N-substituted isoquinolones as product.

**2. General procedure for preparation of various ethyl C- substituted benzenesulfinate**

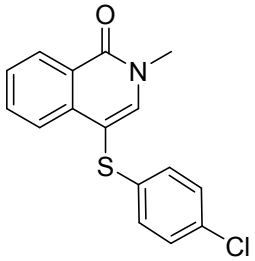



A 100 ml flask was charged with benzenesulfonylhydrazine (5 mmol), $Cu(OTf)_2$ and alcohol (10ml), and the resulting solution was stirred at 40$^{o}$C for 12 h under air. Then, the solvent was evaporated to dryness. The crude residue was purified by column chromatography (EtOAc:Hexanes=1:10) to obtain final product.

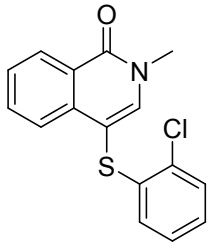
**3.$^{1}$H, $^{13}$C and $^{19}$F NMR spectra data of the products**



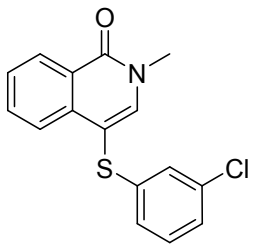
2-methyl-4-(p-tolylthio)isoquinolin-1(2H)-one (**3aa**), 93%, white solid, m.p. 137.5-140.1°C, $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 8.45 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.90 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.66 – 7.41 (m, 3H), 7.08 – 6.92 (m, 4H), 3.63 (s, 3H), 2.25 (s, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 162.56, 140.15, 137.41, 135.62, 133.76, 132.72, 129.83, 128.09, 127.43, 126.64, 126.32, 125.27, 107.27, 37.09, 20.91. HRMS (ESI) calcd for $C_{17}H_{16}NOS$ $(M+H)^+$ 282.0947, found 282.0945.



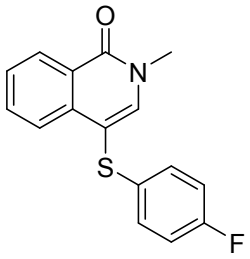
4-((4-chlorophenyl)thio)-2-methylisoquinolin-1(2H)-one (3ab), 87.8%, white solid, m.p. 214.5-215.7°C, $^{1}$H NMR (400 MHz, DMSO-$d_6$) δ 8.40 – 8.33 (m, 1H), 8.21 (s, 1H), 7.84 – 7.76 (m, 2H), 7.62 (ddd, *J* = 8.2, 6.1, 2.2 Hz, 1H), 7.40 – 7.35 (m, 2H), 7.27 – 7.20 (m, 2H), 3.64 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 161.93, 143.10, 137.10, 136.74, 133.45, 130.74, 129.59, 128.19, 128.10, 127.85, 126.23, 124.77, 103.80, 36.94. HRMS (ESI) calcd for $C_{16}H_{13}ClNOS$ $(M+H)^+$ 302.0401, found 302.0398.



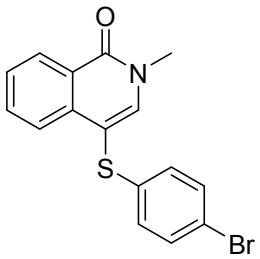
4-((2-chlorophenyl)thio)-2-methylisoquinolin-1(2H)-one (3ac), 89.5%, white solid, m.p. 229.1-231.4°C, $^{1}$H NMR (400 MHz, DMSO-$d_6$) δ 8.35 – 8.30 (m, 1H), 8.18 (s, 1H), 7.74 (ddd, *J* = 8.3, 7.0, 1.4 Hz, 1H), 7.67 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.58 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.19 – 7.07 (m, 2H), 6.78 – 6.73 (m, 1H), 3.59 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 162.00, 143.66, 137.11, 136.83, 133.57, 130.02, 129.74, 128.35, 128.16, 127.96, 127.15, 127.00, 126.27, 124.58, 102.43, 37.00. HRMS (ESI) calcd for $C_{16}H_{13}ClNOS$ $(M+H)^+$ 302.0401, found 302.0398.



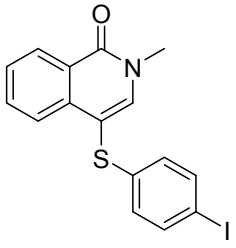
4-((3-chlorophenyl)thio)-2-methylisoquinolin-1(2H)-one (3ad), 82.8%, white solid, m.p. 193.0-96.1°C, $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.47 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.83 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.54 – 7.47 (m, 1H), 7.13 – 7.03 (m, 3H), 6.96 (dt, *J* = 7.6, 1.5 Hz, 1H), 3.65 (s, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 162.52, 140.91, 139.78, 137.03, 134.97, 132.93, 130.06, 128.24, 127.68, 126.35, 125.76, 125.71, 124.97, 124.11, 105.53, 37.18. HRMS (ESI) calcd for $C_{16}H_{13}ClNOS$ $(M+H)^+$ 302.0401, found 302.0398.



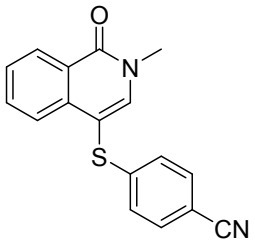

4-((4-fluorophenyl)thio)-2-methylisoquinolin-1(2H)-one (3ae), 94.6%, white solid, m.p. 135.6-138.9°C, $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.45 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.62 (s, 2H), 7.53 – 7.46 (m, 1H), 7.14 – 7.07 (m, 2H), 6.95 – 6.86 (m, 2H), 3.64 (s, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 162.48, 140.35, 137.11, 132.79, 128.37, 128.29, 128.20, 127.55, 126.36, 125.05, 116.29, 116.07, 107.02, 37.12. $^{19}$F NMR (376 MHz, Chloroform-d) δ -116.61. HRMS (ESI) calcd for $C_{16}H_{13}FNOS$ $(M+H)^+$ 286.0696, found 286.0694.



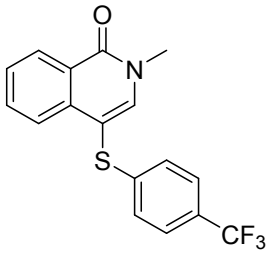

4-((4-bromophenyl)thio)-2-methylisoquinolin-1(2H)-one (3af), 56.3%, yellow solid, m.p. 256.0-258.0°C, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.34 – 8.26 (m, 1H), 8.12 (s, 1H), 7.77 – 7.64 (m, 2H), 7.54 (ddd, *J* = 8.2, 6.8, 1.5 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.14 – 7.06 (m, 2H).$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 170.71, 161.93, 142.98, 137.32, 133.29, 132.34, 128.38, 128.05, 127.72, 126.25, 124.74, 118.93, 103.76, 36.86. HRMS (ESI) calcd for $C_{16}H_{13}BrNOS$ $(M+H)^+$ 345.9896, found 345.9895.



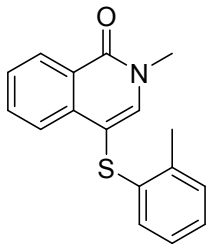

4-((4-iodophenyl)thio)-2-methylisoquinolin-1(2H)-one (3ag), 83.9%, white solid, m.p. 231.3-233.2°C, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.29 (dt, *J* = 7.9, 1.0 Hz, 1H), 8.14 (s, 1H), 7.75 – 7.70 (m, 2H), 7.60 – 7.53 (m, 3H), 6.99 – 6.93 (m, 2H), 3.58 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 161.93, 143.05, 138.20, 137.88, 137.08, 133.43, 128.56, 128.09, 127.84, 126.21, 124.78, 103.60, 91.26, 36.95. HRMS (ESI) calcd for $C_{16}H_{13}INOS$ $(M+H)^+$ 393.9757, found 393.9754.



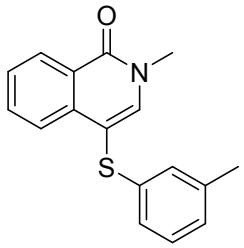
4-((2-methyl-1-oxo-1,2-dihydroisoquinolin-4-yl)thio)benzonitrile(3ah), 17.1%, white solid, m.p. 217.7-219.8°C, $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.50 (ddd, *J* = 8.0, 1.4, 0.6 Hz, 1H), 7.76 (ddd, *J* = 8.1, 1.3, 0.6 Hz, 1H), 7.68 – 7.62 (m, 2H), 7.59 – 7.53 (m, 1H), 7.48 – 7.43 (m, 2H), 7.12 (d, *J* = 8.5 Hz, 2H), 3.67 (s, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 162.47, 145.14, 141.27, 136.69, 133.15, 132.47, 128.48, 127.95, 126.40, 125.69, 124.67, 118.69, 108.68, 104.12, 37.25. HRMS (ESI) calcd for $C_{17}H_{13}N_2OS$ $(M+H)^+$ 293.0743, found 293.0740.



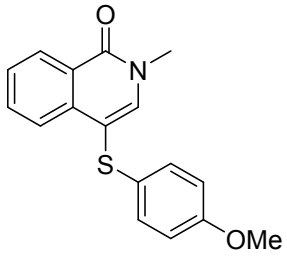
2-methyl-4-((4-(trifluoromethyl)phenyl)thio)isoquinolin-1(2H)-one (3aj), 91.0%, white solid,m.p. 221.2-224.2°C, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.37 (d, *J* = 8.0 Hz, 1H), 8.24 (s, 1H), 7.82-7.75 (m, 2H), 7.64 (dd, *J* = 8.3, 2.3 Hz, 3H), 7.37 (d, *J* = 8.2 Hz, 2H), 3.64 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 162.00, 143.82, 143.47, 137.02, 133.60, 128.17, 127.98, 126.42, 126.38, 126.32, 126.22, 124.61, 102.68, 36.99, 29.46.$^{19}$F NMR (376 MHz, DMSO-$d_6$) δ -60.82. HRMS (ESI) calcd for $C_{17}H_{13}F_3NOS$ $(M+H)^+$ 336.0664, found 336.0661.`



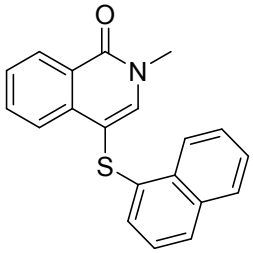
2-methyl-4-(o-tolylthio)isoquinolin-1(2H)-one (3ak), 96%, yellow solid, m.p. 182.6-189.3°C, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.31 (dt, *J* = 8.0, 1.1 Hz, 1H), 8.10 (s, 1H), 7.74 – 7.67 (m, 2H), 7.56 (ddd, *J* = 8.2, 6.3, 2.1 Hz, 1H), 7.22 (dt, *J* = 7.2, 1.2 Hz, 1H), 7.06 – 6.93 (m, 2H), 6.69 (dd, *J* = 7.9, 1.4 Hz, 1H), 3.59 (s, 3H), 2.45 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 161.94, 142.87, 137.39, 136.72, 134.40, 133.36, 130.62, 128.04, 127.80, 127.13, 126.24, 125.60, 125.40, 124.94, 103.68, 19.94. HRMS (ESI) calcd for $C_{17}H_{16}NOS$ $(M+H)^+$ 282.0947, found 282.0945.



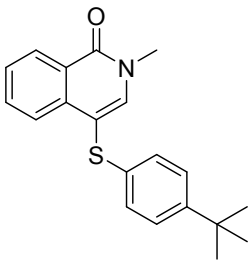
2-methyl-4-(m-tolylthio)isoquinolin-1(2H)-one (3al), 83.5%, yellow solid, $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.45 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.89 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.63 – 7.56 (m, 2H), 7.48 (td, *J* = 7.6, 6.9, 1.3 Hz, 1H), 7.06 (t, *J* = 7.7 Hz, 1H), 6.96 – 6.85 (m, 3H), 3.63 (s, 3H), 2.23 (s, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 162.59, 140.41, 138.91, 137.45, 137.26, 132.76, 128.91, 128.08, 127.47, 126.75, 126.57, 126.31, 125.28, 123.32, 106.73, 37.12, 21.40. HRMS (ESI) calcd for $C_{17}H_{16}NOS$ $(M+H)^+$ 282.0947, found 282.0945.



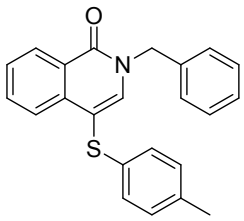
4-((4-methoxyphenyl)thio)-2-methylisoquinolin-1(2H)-one (3am), 82.4%, yellow solid, $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.44 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.96 – 7.91 (m, 1H), 7.61 (ddd, *J* = 8.2, 7.0, 1.4 Hz, 1H), 7.58 (s, 1H), 7.51 – 7.45 (m, 1H), 7.17 – 7.12 (m, 2H), 6.80 – 6.73 (m, 2H), 3.72 (d, *J* = 0.6 Hz, 3H), 3.62 (s, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 162.51, 158.39, 139.58, 137.33, 132.65, 129.12, 128.09, 127.53, 127.39, 126.31, 125.21, 114.81, 108.45, 55.34, 37.09. HRMS (ESI) calcd for $C_{17}H_{16}NO_2S$ $(M+H)^+$ 298.0896, found 298.0893.



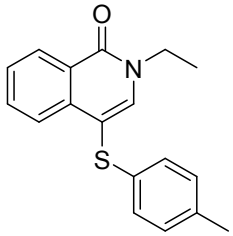
2-methyl-4-(naphthalen-1-ylthio)isoquinolin-1(2H)-one (3an), 95%, yellow solid, m.p. 156.6-157.8°C, $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.47 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.89 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.73 – 7.68 (m, 1H), 7.67 – 7.61 (m, 2H), 7.59 – 7.50 (m, 2H), 7.49 – 7.42 (m, 2H), 7.36 (ddd, *J* = 7.0, 4.8, 1.7 Hz, 2H), 7.27 – 7.21 (m, 1H), 3.62 (s, 3H). $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 162.62, 140.55, 137.34, 135.01, 133.75, 132.84, 131.58, 128.74, 128.16, 127.77, 127.56, 126.99, 126.72, 126.38, 125.61, 125.24, 124.62, 124.16, 106.50, 37.17. HRMS (ESI) calcd for $C_{20}H_{16}NOS$ $(M+H)^+$ 318.0947, found 318.0944.



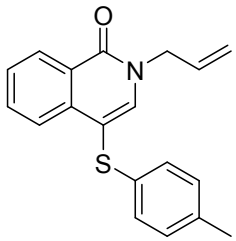
4-((4-(tert-butyl)phenyl)thio)-2-methylisoquinolin-1(2H)-one (3ao), 91%, yellow solid, m.p. 131.2-132.5°C, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.32 – 8.26 (m, 1H), 8.10 (s, 1H), 7.83 (dt, $J$ = 8.1, 1.0 Hz, 1H), 7.70 (ddd, $J$ = 8.3, 7.1, 1.4 Hz, 1H), 7.53 (ddd, $J$ = 8.2, 7.1, 1.2 Hz, 1H), 7.28 – 7.22 (m, 2H), 7.11 – 7.06 (m, 2H), 3.58 (s, 3H), 1.18 (s, 9H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 161.90, 148.82, 142.60, 137.53, 134.08, 133.32, 128.00, 127.72, 126.58, 126.54, 126.13, 125.02, 104.94, 36.89, 34.53, 31.43. HRMS (ESI) calcd for $C_{17}H_{16}NOS$ $(M+H)^+$ 282.0947, found 282.0945.



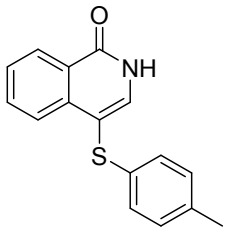
2-benzyl-4-(p-tolylthio)isoquinolin-1(2H)-one (3ba), 99%, white solid, m.p. 79.3-83.0°C, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.30 (dd, $J$ = 8.1, 1.4 Hz, 1H), 8.24 (s, 1H), 7.81 (dd, $J$ = 8.2, 1.2 Hz, 1H), 7.71 (ddd, $J$ = 8.2, 7.0, 1.4 Hz, 1H), 7.55 (ddd, $J$ = 8.2, 7.1, 1.2 Hz, 1H), 7.41 – 7.26 (m, 5H), 7.07 (d, $J$ = 1.3 Hz, 4H), 5.28 (s, 2H), 2.19 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 161.49, 141.49, 137.75, 137.24, 135.80, 133.61, 133.54, 130.35, 129.09, 128.31, 128.15, 128.05, 127.95, 127.05, 126.42, 125.15, 106.03, 51.64, 20.89. HRMS (ESI) calcd for $C_{23}H_{20}NOS$ $(M+H)^+$ 358.1260, found 358.1259.



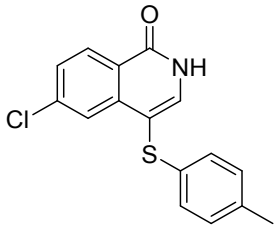
2-ethyl-4-(p-tolylthio)isoquinolin-1(2H)-one (3ca), 68%, yellow oil, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.29 (dd, $J$ = 8.0, 1.4 Hz, 1H), 8.11 (s, 1H), 7.78 (dd, $J$ = 8.2, 1.2 Hz, 1H), 7.68 (ddd, $J$ = 8.3, 7.0, 1.4 Hz, 1H), 7.52 (ddd, $J$ = 8.2, 7.1, 1.3 Hz, 1H), 7.14 – 7.01 (m, 4H), 4.07 (d, $J$ = 7.1 Hz, 2H), 2.18 (s, 3H), 1.30 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 161.22, 141.22, 137.26, 135.68, 133.79, 133.23, 130.30, 128.10, 127.67, 127.01, 126.41, 125.01, 105.57, 44.14, 20.87, 14.89. HRMS (ESI) calcd for $C_{18}H_{18}NOS$ $(M+H)^+$ 296.1104, found 296.1101.



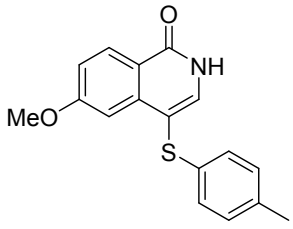
2-allyl-4-(p-tolylthio)isoquinolin-1(2H)-one (3da), 24%.yellow oil, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.30 (dd, $J$ = 8.0, 1.3 Hz, 1H), 8.02 (s, 1H), 7.80 (dd, $J$ = 8.2, 1.3 Hz, 1H), 7.73 (ddd, $J$ = 8.3, 7.1, 1.5 Hz, 1H), 7.63 – 7.53 (m, 2H), 7.08 (s, 4H), 6.03 (dd, $J$ = 17.1, 10.3 Hz, 1H), 5.30 – 5.10 (m, 2H), 4.68 (dt, $J$ = 5.5, 1.6 Hz, 2H), 2.21 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 161.20, 141.22, 137.22, 135.78, 133.81, 133.64, 133.50, 130.37, 128.25, 127.90, 127.01, 126.34, 125.11, 117.97, 105.72, 50.47, 20.89. HRMS (ESI) calcd for $C_{19}H_{18}NOS$ $(M+H)^+$ 308.1104, found 308.1101.



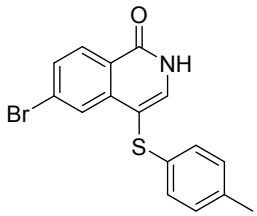
4-(p-tolylthio)isoquinolin-1(2H)-one (3ea), 58%, white solid, m.p. 188.3-203.7°C, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 11.72 (s, 1H), 8.25 (dd, $J$ = 8.0, 1.4 Hz, 1H), 7.80 (dd, $J$ = 8.1, 1.2 Hz, 1H), 7.74 – 7.66 (m, 2H), 7.53 (ddd, $J$ = 8.1, 7.0, 1.2 Hz, 1H), 7.06 (s, 4H), 2.20 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 162.21, 137.97, 137.84, 135.63, 133.86, 133.48, 130.31, 127.86, 127.56, 127.01, 126.99, 125.18, 105.10, 20.89. HRMS (ESI) calcd for $C_{16}H_{14}NOS$ $(M+H)^+$ 268.0791, found 268.0788.



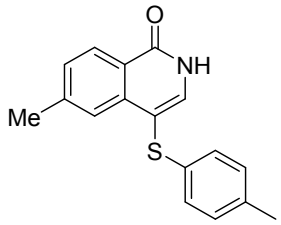
6-chloro-4-(p-tolylthio)isoquinolin-1(2H)-one (3fa), 46%, white solid, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 11.88 (d, $J$ = 5.7 Hz, 1H), 8.24 (d, $J$ = 8.5 Hz, 1H), 7.78 – 7.72 (m, 2H), 7.56 (dd, $J$ = 8.6, 2.1 Hz, 1H), 7.09 (s, 4H), 2.22 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 161.58, 139.75, 139.66, 138.72, 135.91, 133.37, 130.46, 130.40, 127.80, 127.02, 125.65, 124.13, 104.02, 20.91. HRMS (ESI) calcd for $C_{16}H_{13}ClNOS$ $(M+H)^+$ 302.0401, found 302.0398



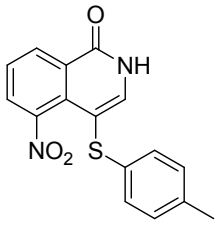
6-methoxy-4-(p-tolylthio)isoquinolin-1(2H)-one (3ga), 32%, yellow solid, m.p. 226.3-229.5°C, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 11.55 (d, $J$ = 5.3 Hz, 1H), 8.17 (d, $J$ = 8.8 Hz, 1H), 7.66 (d, $J$ = 5.5 Hz, 1H), 7.19 (d, $J$ = 2.6 Hz, 1H), 7.14 – 7.06 (m, 5H), 3.74 (s, 3H), 2.21 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 163.13, 161.81, 140.13, 138.34, 135.90, 133.56, 130.33, 130.19, 127.53, 120.52, 115.87, 107.28, 105.08, 55.84, 20.91. HRMS (ESI) calcd for $C_{17}H_{16}NO_2S$ $(M+H)^+$ 298.0896, found 298.0894.



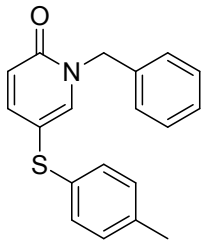

6-bromo-4-(p-tolylthio)isoquinolin-1(2H)-one (3ha), 77%, yellow solid, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 11.89 (d, $J$ = 5.8 Hz, 1H), 8.15 (d, $J$ = 8.5 Hz, 1H), 7.90 (d, $J$ = 2.0 Hz, 1H), 7.75 (d, $J$ = 6.0 Hz, 1H), 7.69 (dd, $J$ = 8.5, 2.0 Hz, 1H), 7.09 (s, 4H), 2.22 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 161.72, 139.85, 139.60, 135.91, 133.39, 130.58, 130.46, 130.35, 127.88, 127.26, 127.01, 125.94, 103.89, 20.91. HRMS (ESI) calcd for $C_{16}H_{13}BrNOS$ $(M+H)^+$ 345.9896, found 345.9895.



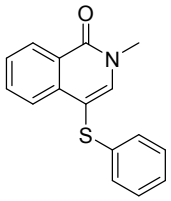

6-methyl-4-(p-tolylthio)isoquinolin-1(2H)-one (3ia),52%, white solid, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 11.63 (d, $J$ = 5.8 Hz, 1H), 8.14 (d, $J$ = 8.1 Hz, 1H), 7.68 – 7.59 (m, 2H), 7.36 (dd, $J$ = 8.2, 1.7 Hz, 1H), 7.07 (s, 4H), 2.37 (s, 3H), 2.21 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 162.11, 143.67, 138.19, 138.08, 135.57, 134.06, 130.32, 128.99, 127.94, 126.92, 124.77, 124.71, 104.86, 22.08, 20.89. HRMS (ESI) calcd for $C_{17}H_{16}NOS$ $(M+H)^+$ 282.0947, found 282.0945.




5-nitro-4-(p-tolylthio)isoquinolin-1(2H)-one (3ja), 29%, yellow solid, m.p. 215.4-219.3°C, $^1$H NMR (400 MHz, DMSO-$d_6$) δ 12.22 (d, $J$ = 5.8 Hz, 1H), 8.50 (dd, $J$ = 8.0, 1.4 Hz, 1H), 8.07 (dd, $J$ = 7.8, 1.4 Hz, 1H), 7.78 – 7.63 (m, 2H), 7.05 (d, $J$ = 8.1 Hz, 2H), 6.99 – 6.94 (m, 2H), 2.20 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 160.45, 147.40, 143.33, 135.96, 135.50, 131.34, 130.20, 130.05, 128.91, 128.65, 127.63, 126.99, 101.08, 20.89. HRMS (ESI) calcd for $C_{16}H_{13}N_2O_3S$ $(M+H)^+$ 313.0641, found 313.0639.

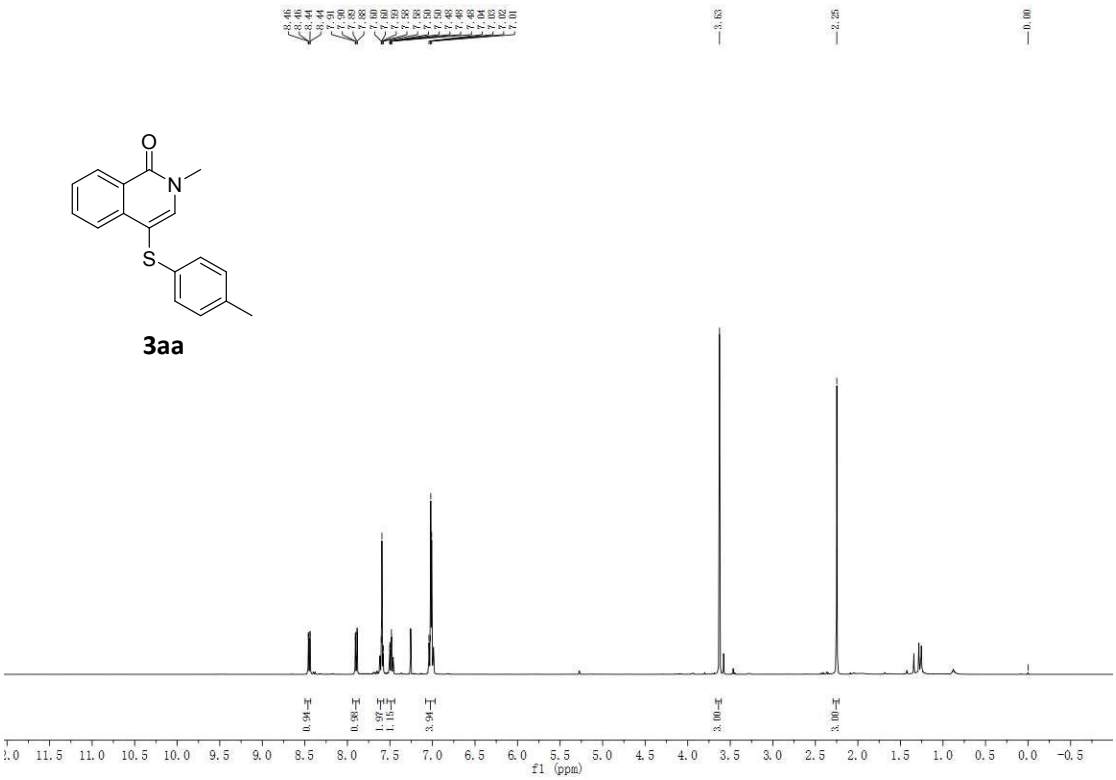


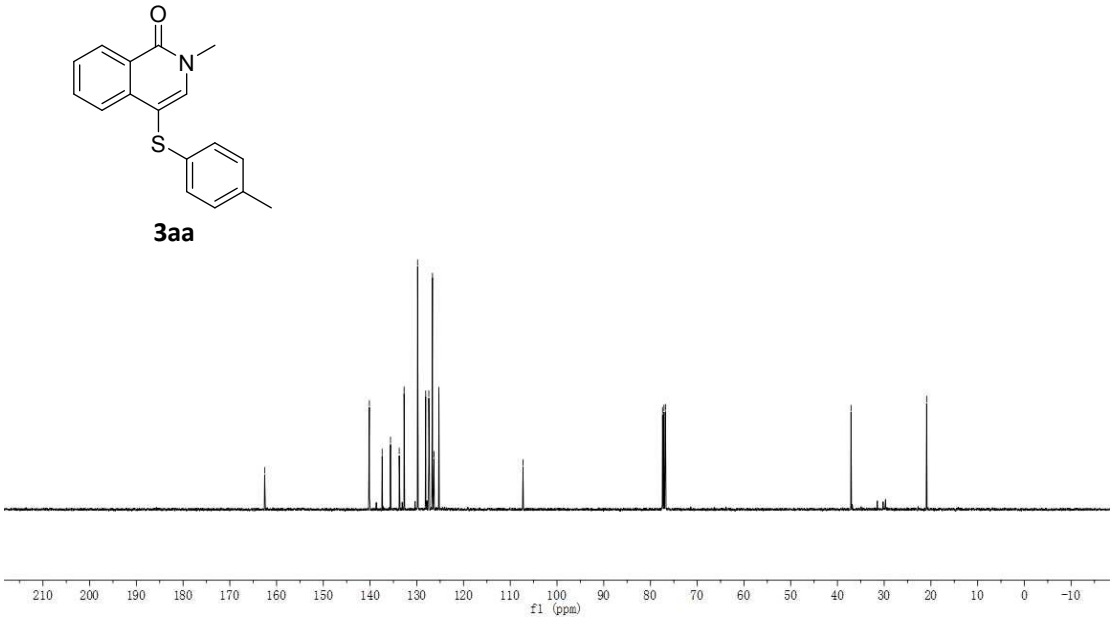
1-benzyl-5-(p-tolylthio)pyridin-2(1H)-one (3ka), 49%, yellow oil, $^{1}$H NMR (400 MHz, DMSO-$d_6$) δ 8.23 (d, $J$ = 2.6 Hz, 1H), 7.48 – 7.25 (m, 7H), 7.12 (q, $J$ = 8.4 Hz, 4H), 6.48 (d, $J$ = 9.4 Hz, 1H), 5.13 (s, 2H), 2.25 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 161.05, 145.81, 145.00, 137.46, 136.29, 133.97, 130.45, 129.07, 128.20, 128.11, 128.04, 121.46, 108.67, 51.84, 20.94. HRMS (ESI) calcd for $C_{19}H_{18}NOS$ $(M+H)^+$ 308.1104, found 308.1101.

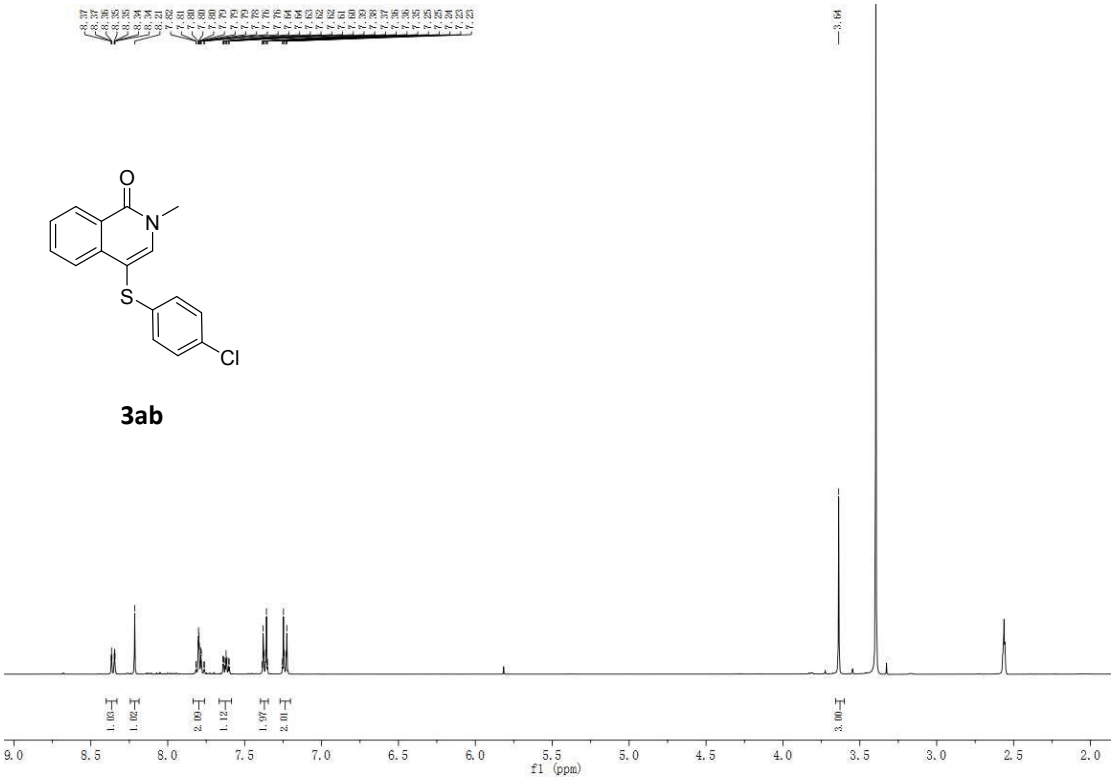


2-methyl-4-(phenylthio)isoquinolin-1(2H)-one (3ap),76%, white solid, m.p. 121.6-123.9°C,$^{1}$H NMR (400 MHz, Chloroform-$d$) δ 8.47 (dd, $J$ = 8.0, 1.4 Hz, 1H), 7.92 – 7.87 (m, 1H), 7.65 – 7.59 (m, 2H), 7.54 – 7.48 (m, 1H), 7.20 (dd, $J$ = 8.1, 7.0 Hz, 2H), 7.14 – 7.07 (m, 3H), 3.65 (s, 3H). $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 162.57, 140.48, 137.54, 137.38, 132.79, 129.05, 128.15, 127.51, 126.34, 126.16, 125.58, 125.24, 106.59, 37.12. HRMS (ESI) calcd for $C_{16}H_{14}NOS$ $(M+H)^+$ 268.0791, found 268.0788.

**4. The copied of $^{1}H$ ,$^{13}C$ and $^{19}F$ NMR spectra.**

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N
S
Cl
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1.02
2.03
1.12
1.97
2.01
3.00
9.0
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8.0
7.5
7.0
6.5
6.0
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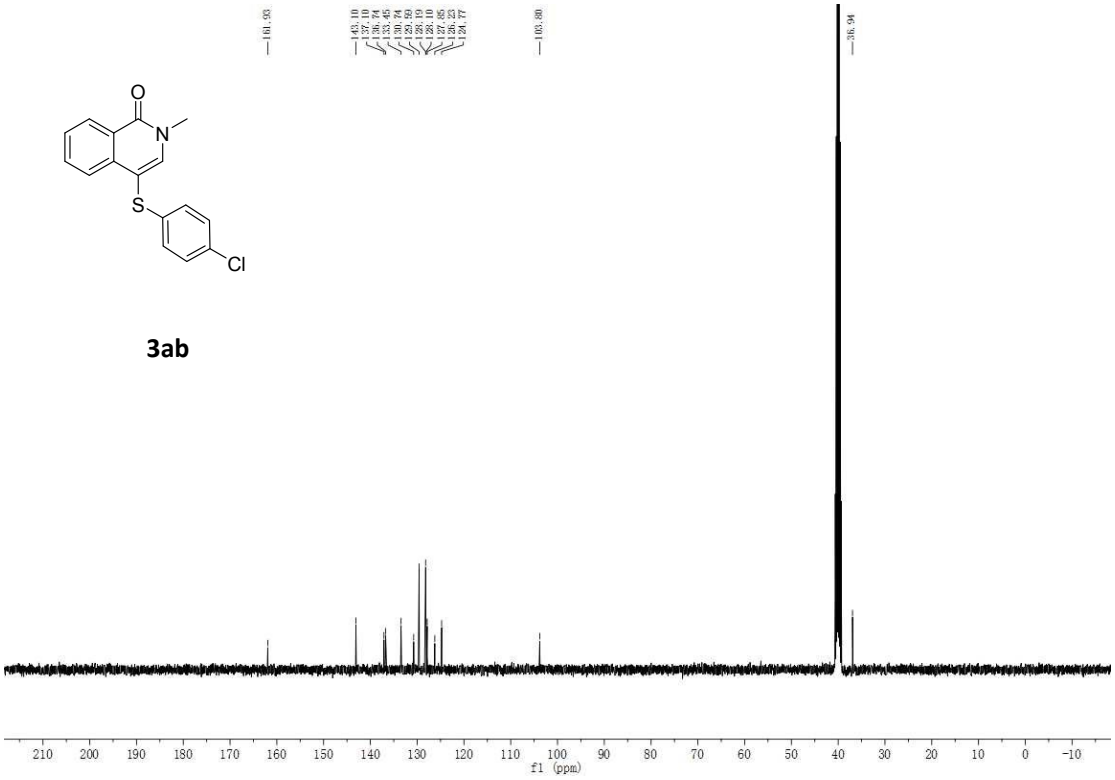
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)

**3ab**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143.10
137.10
136.74
133.45
130.74
129.93
128.19
128.10
127.85
126.23
124.77
103.80
36.94
O
N
S
Cl
210
200
190
180
170
160
150
140
130
120
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100
90
80
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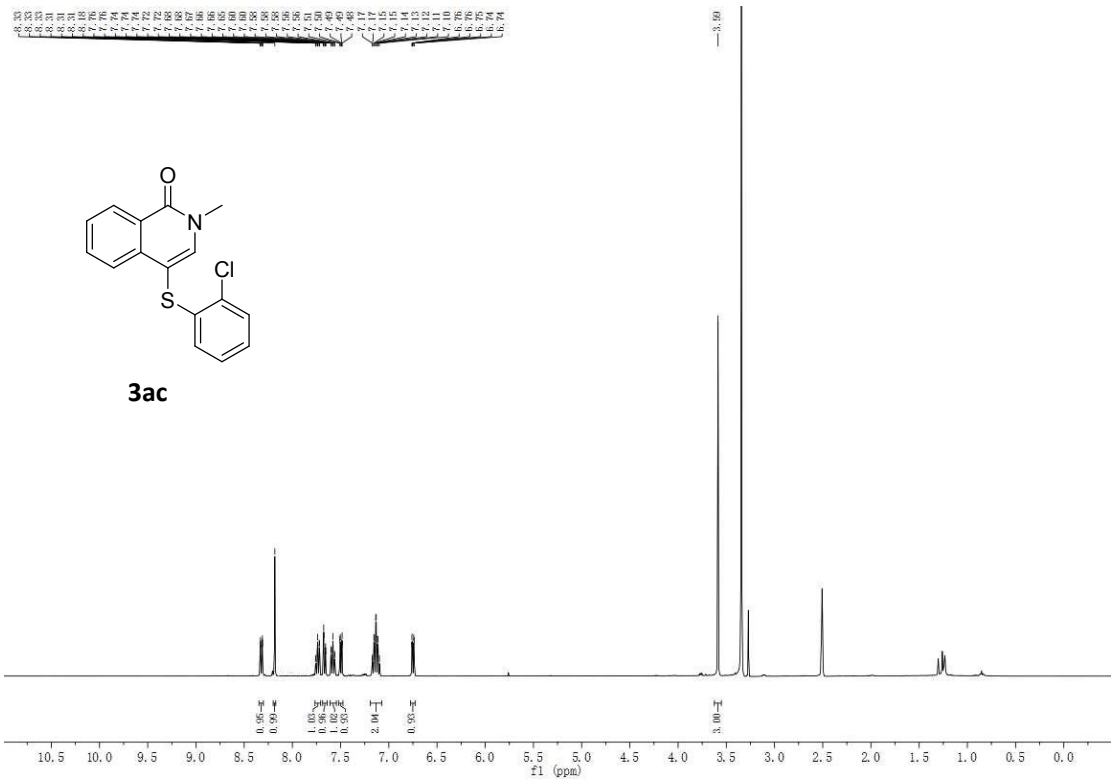
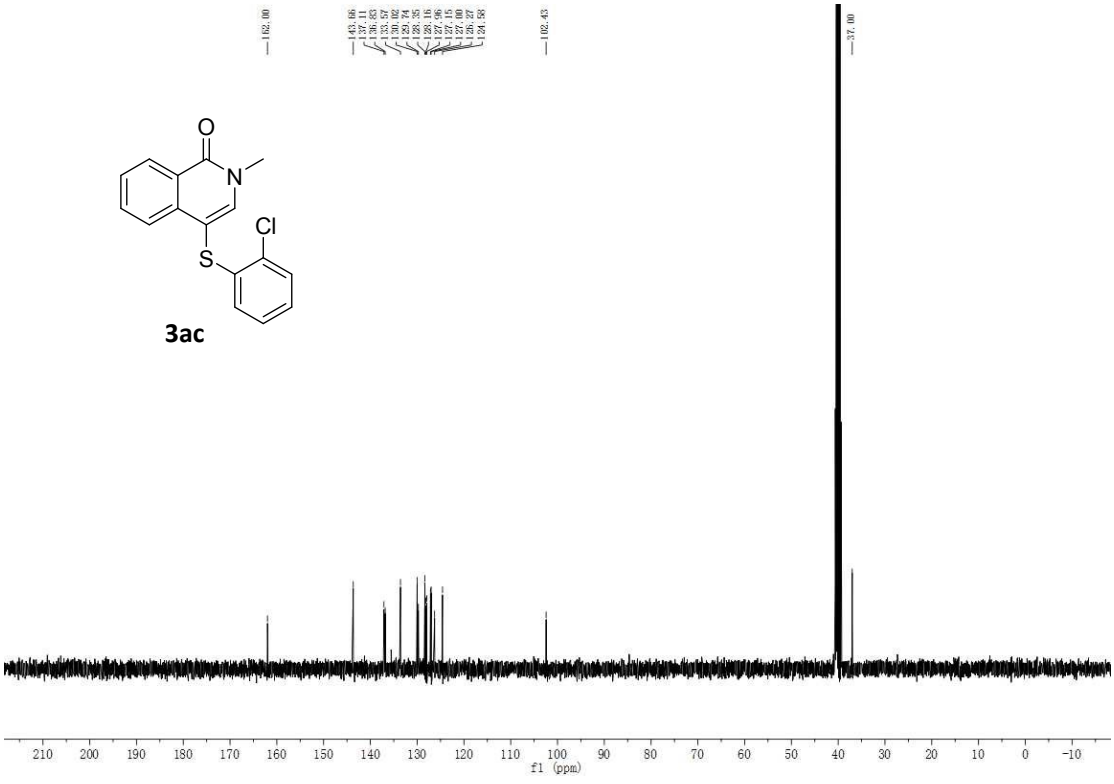
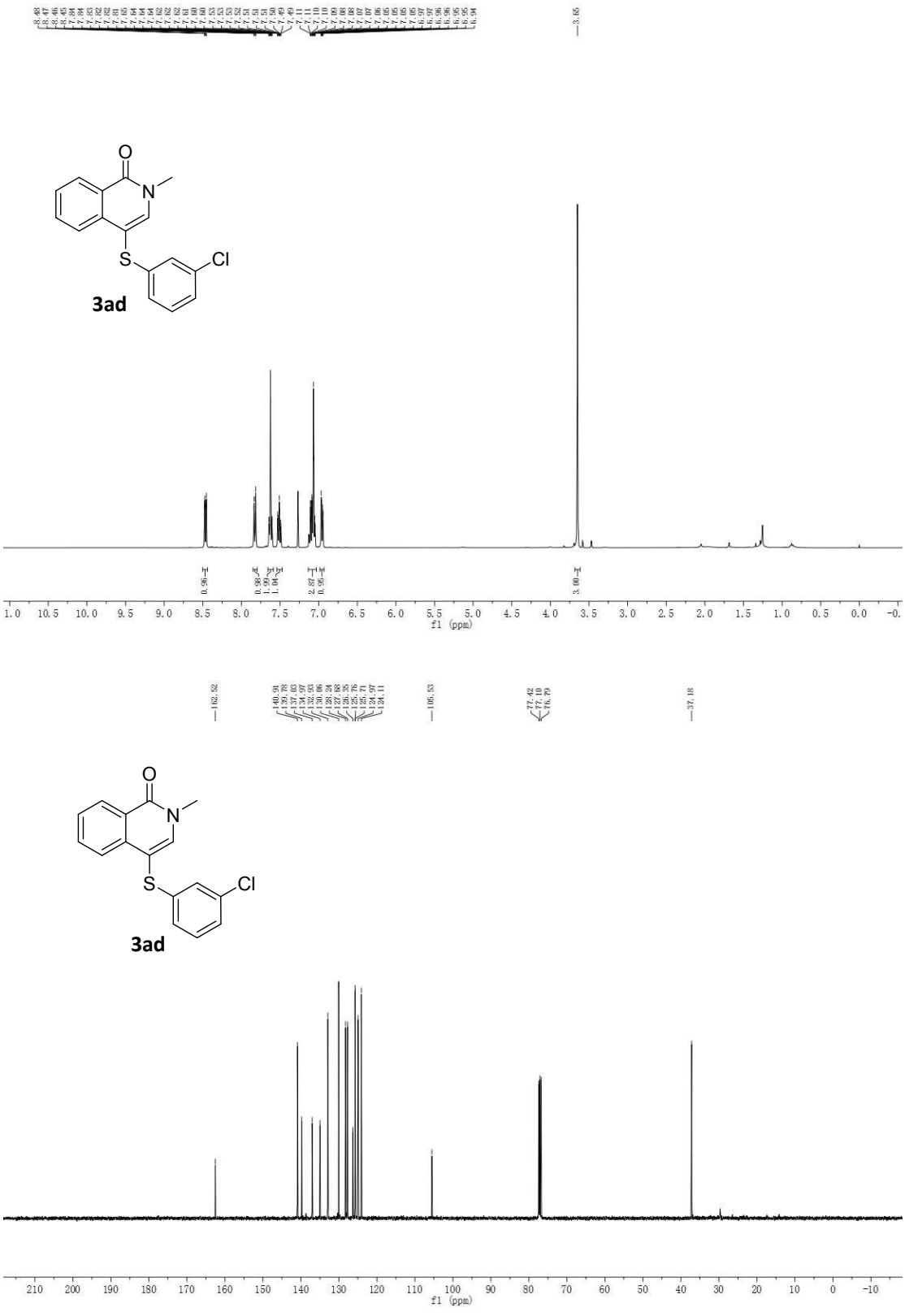
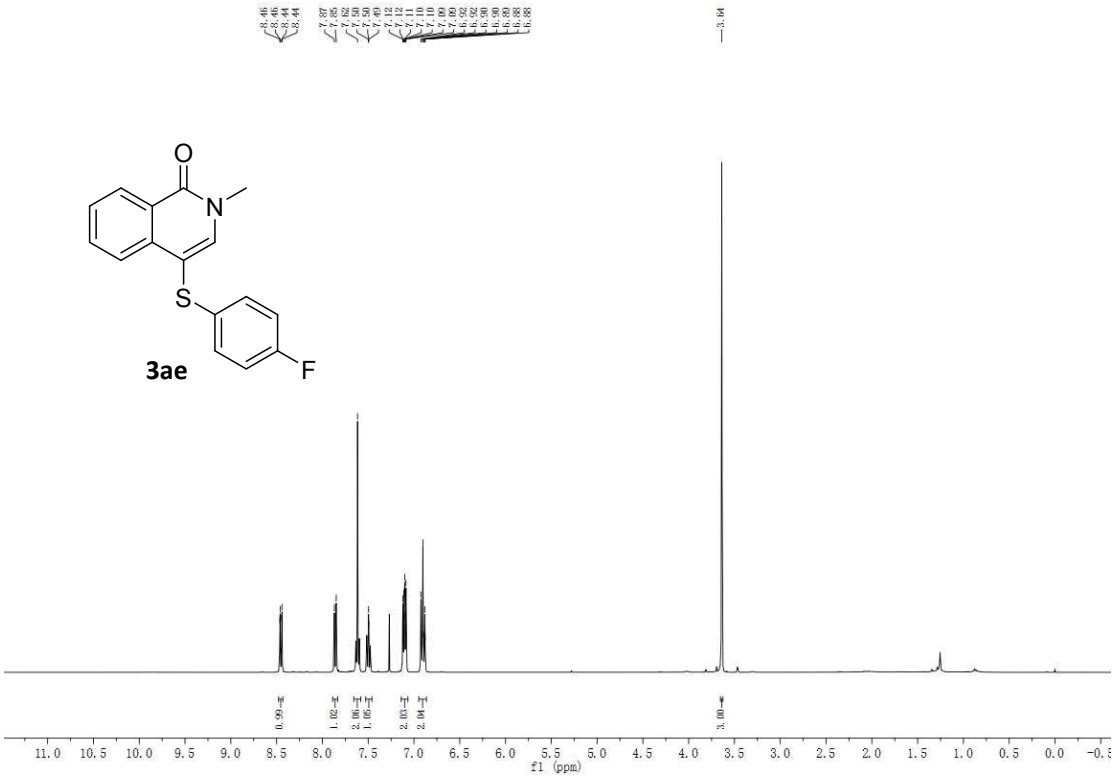
60
50
40
30
20
10
0
-10
f1 (ppm)

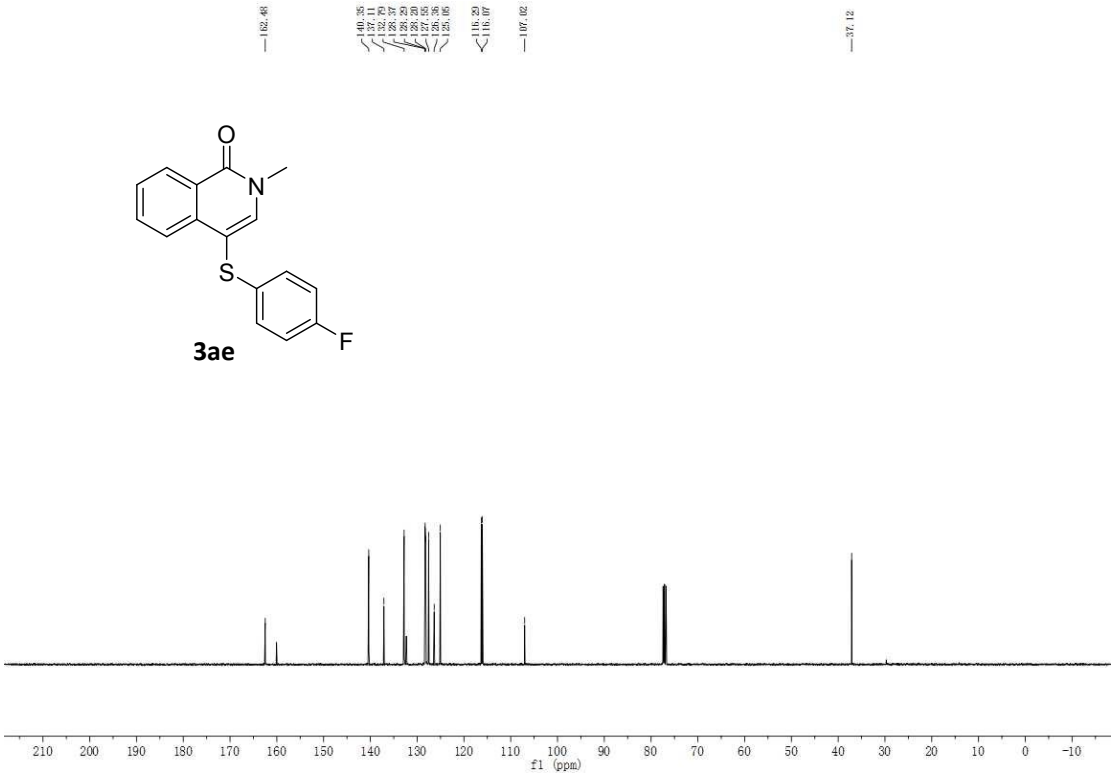
**3ab**


O
N
Cl
S
3ac
f1 (ppm)

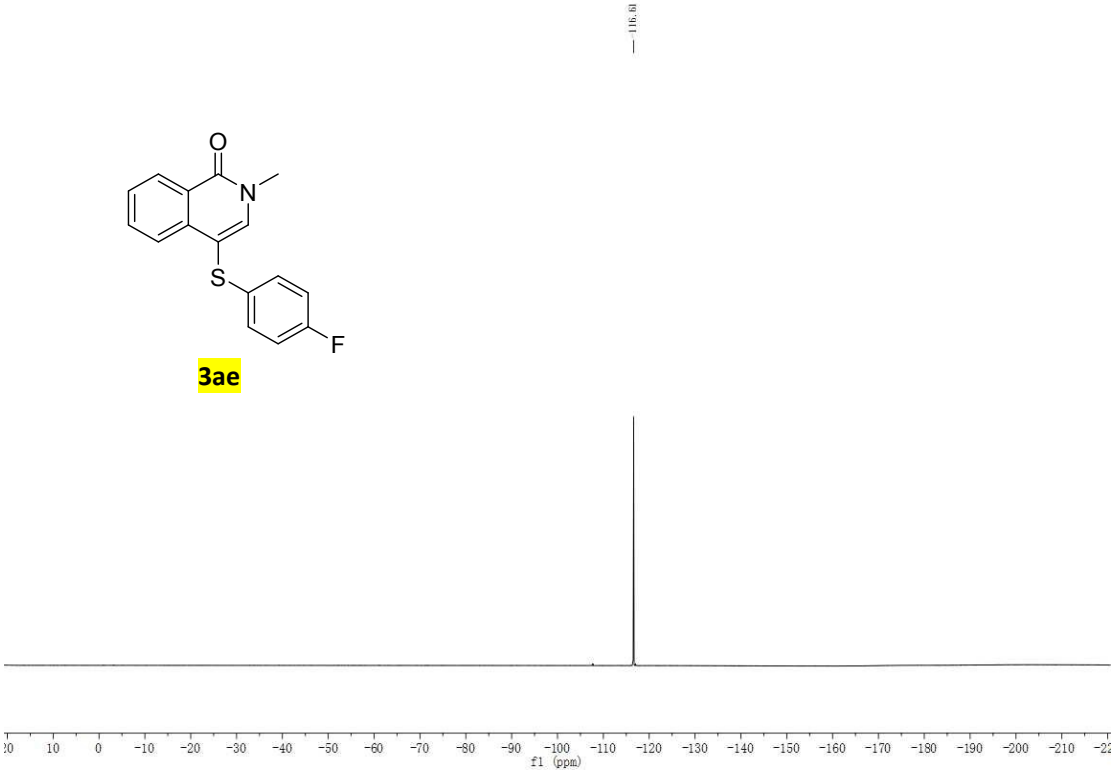

O
N
Cl
S
3ac
f1 (ppm)


3ad
f1 (ppm)
3ad
f1 (ppm)


O
N
S
F
3ae
f1 (ppm)


O
N
S
F
3ae
f1 (ppm)

**3ae**







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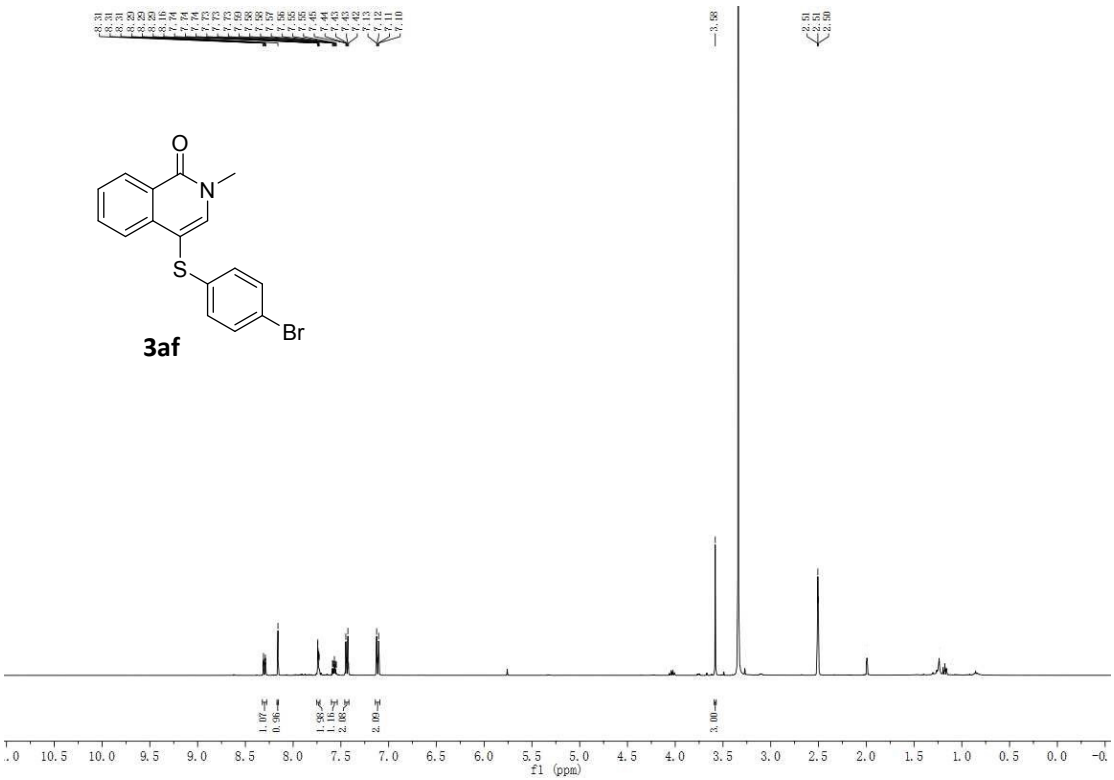

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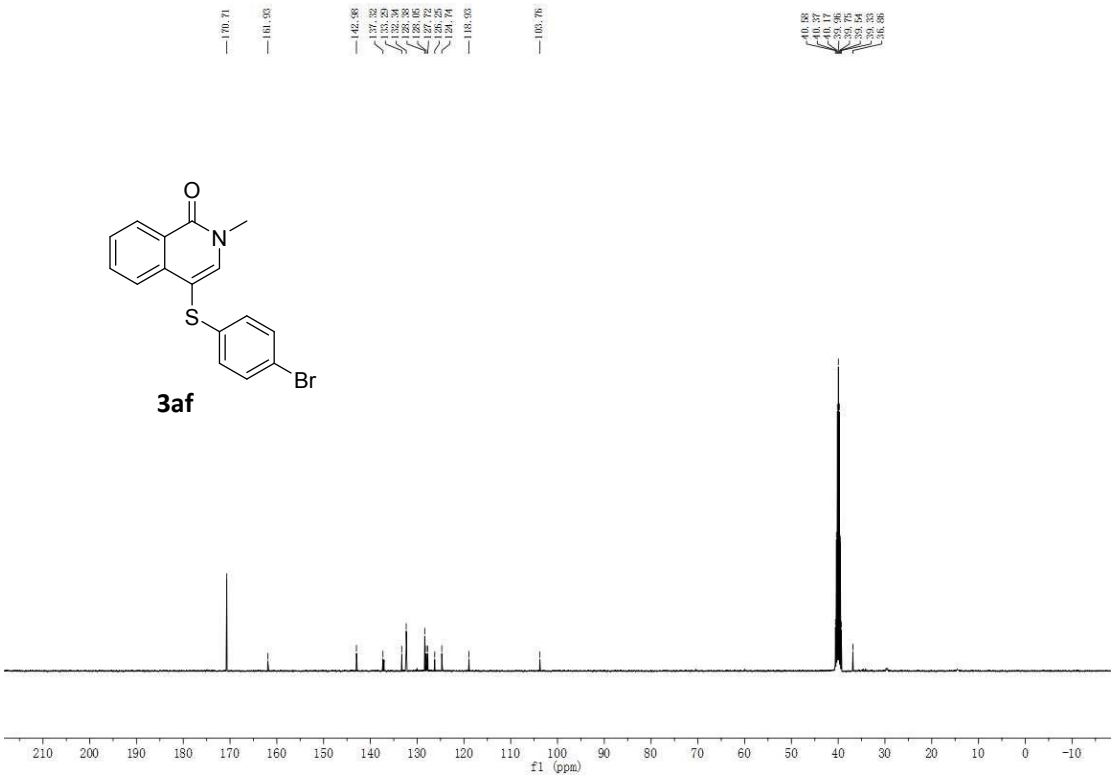


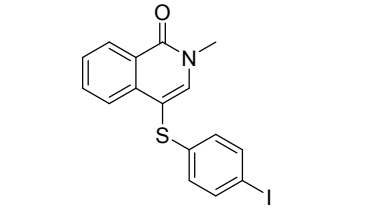


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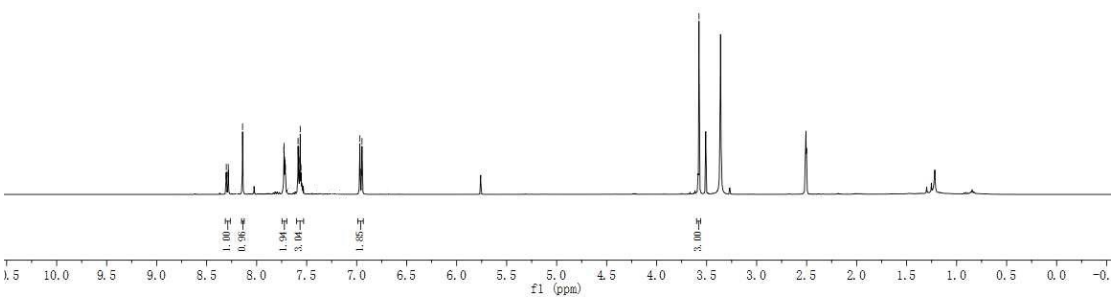
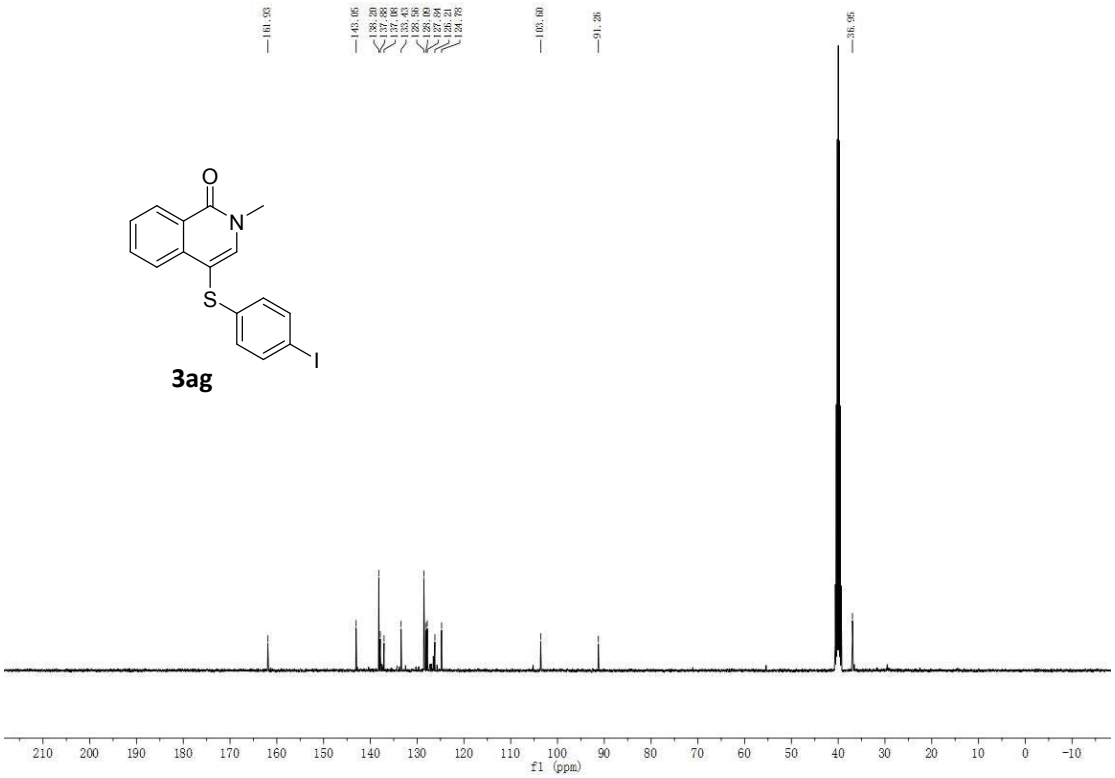
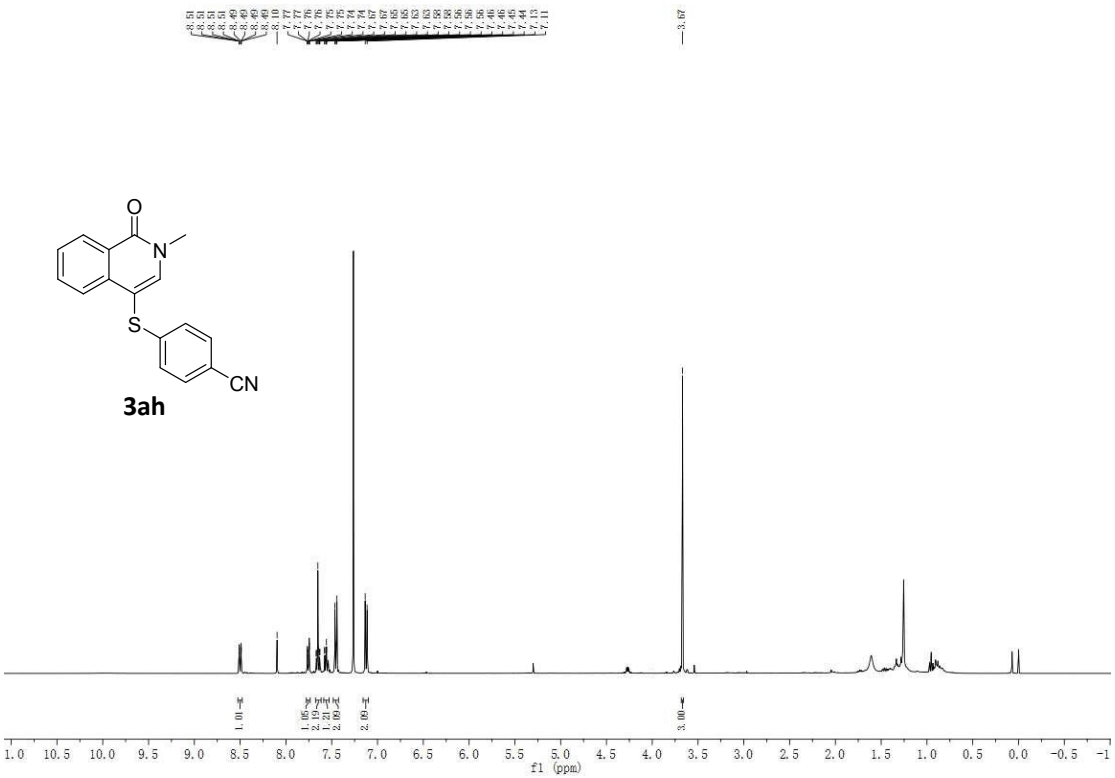





**3ag**

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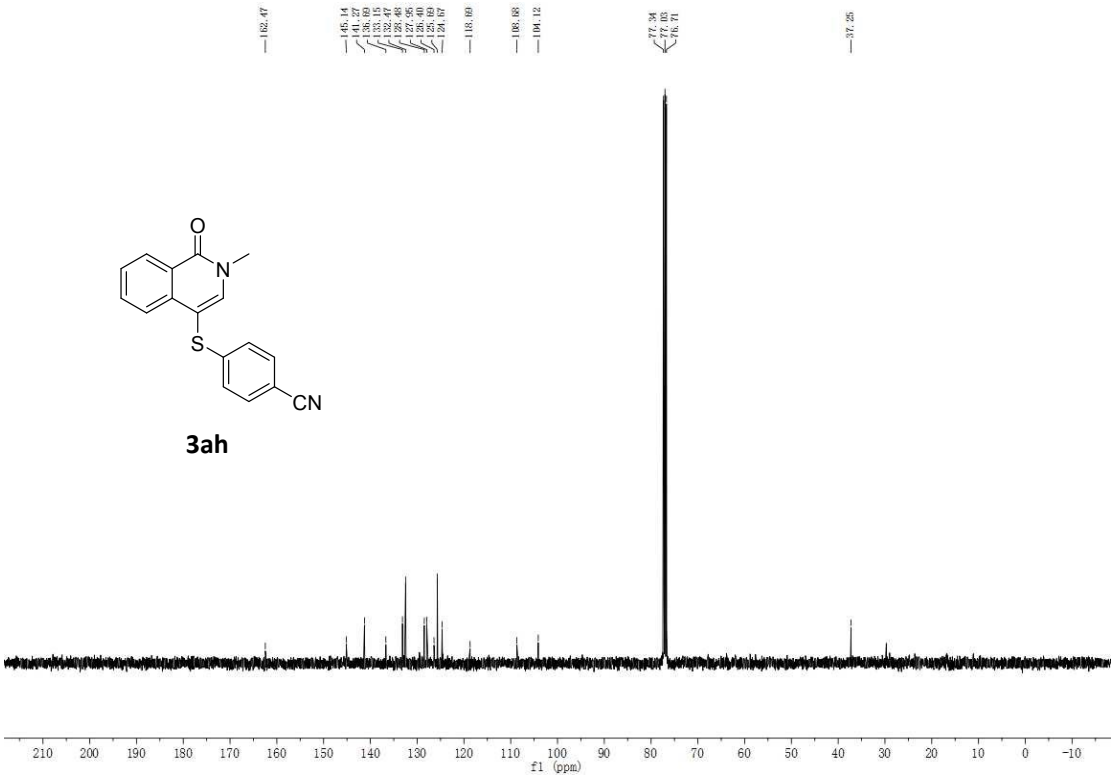


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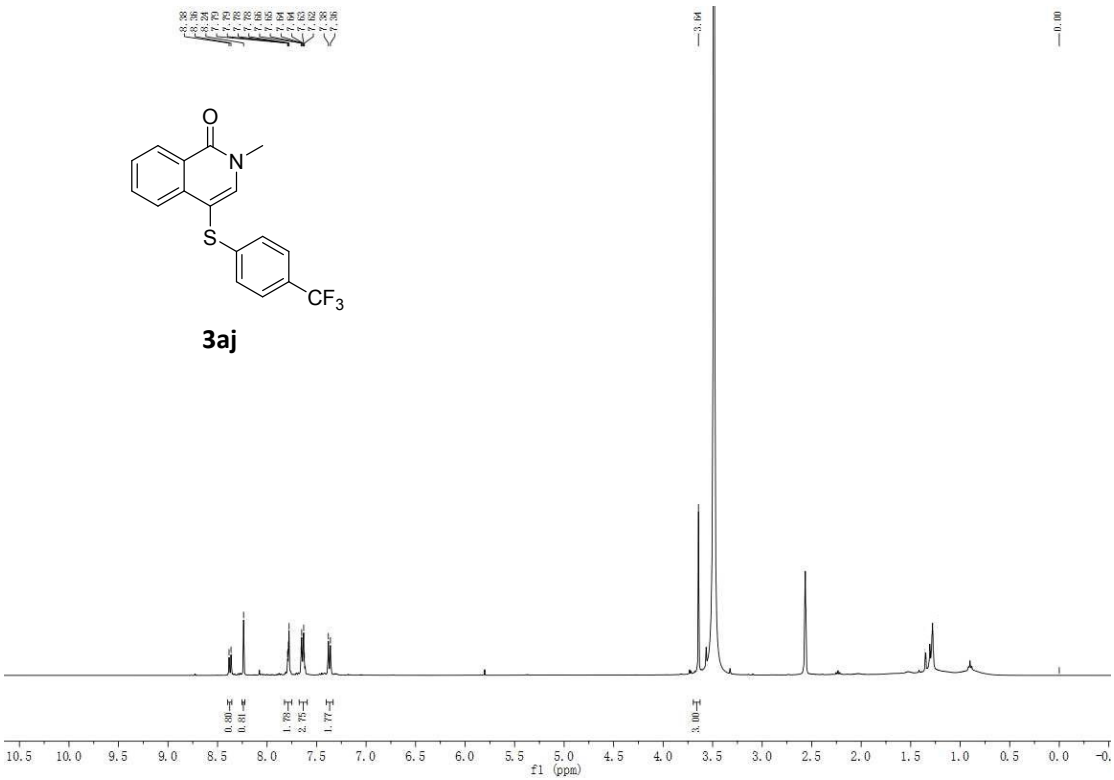


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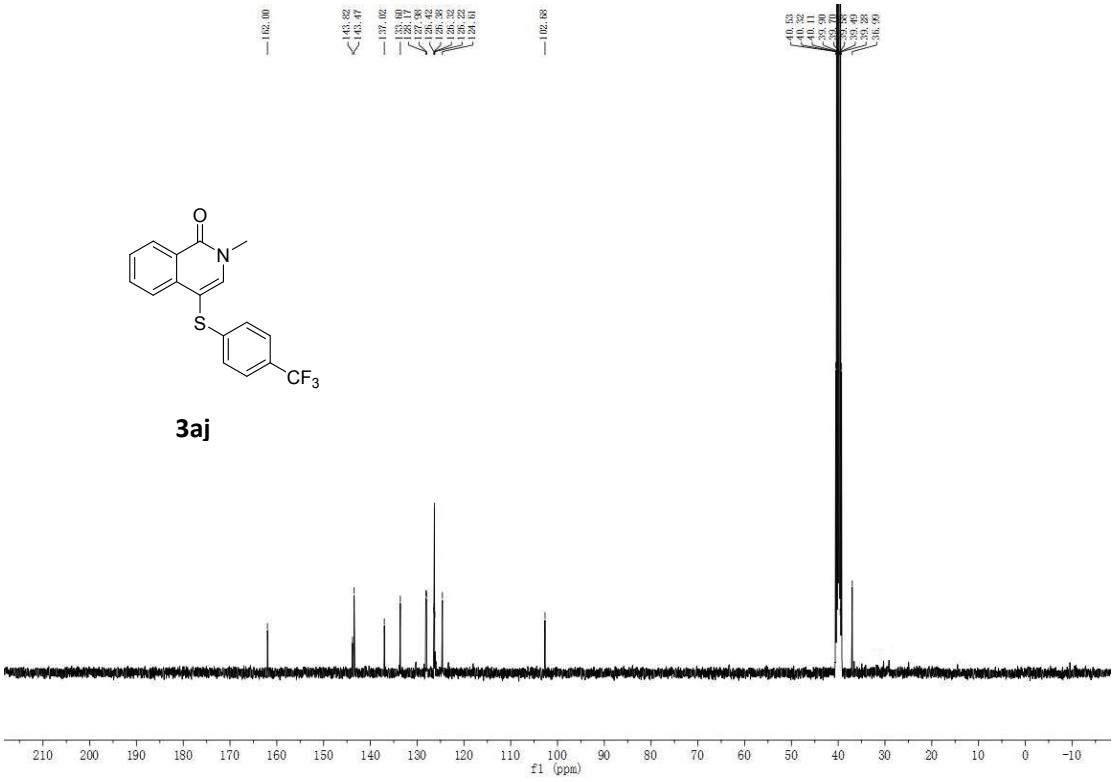
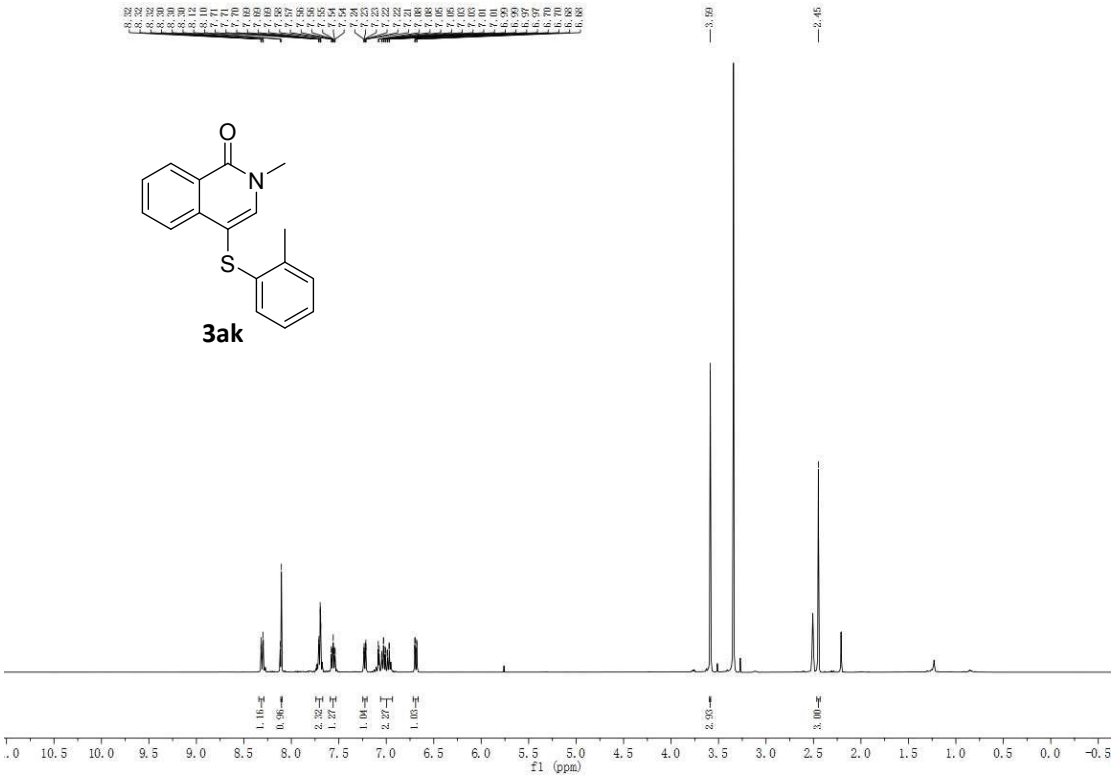

O
N
S
CF3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

**3aj**


O
N
S
CF3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

**3aj**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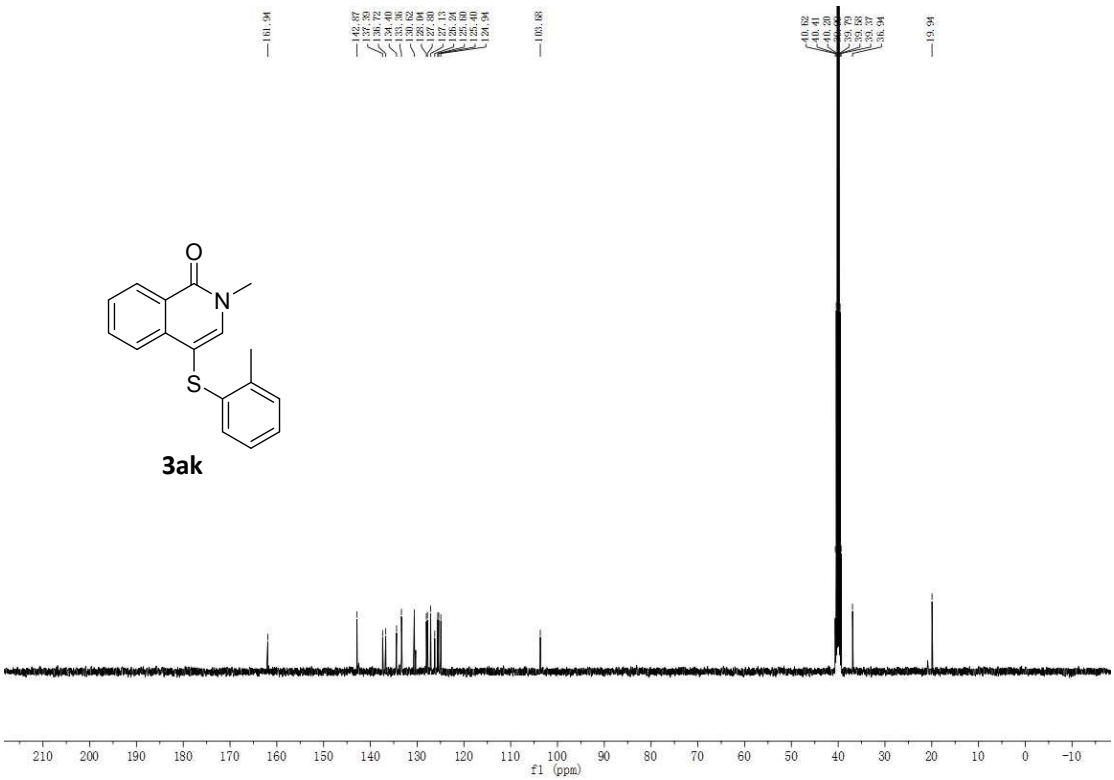
N
S
3ak
f1 (ppm)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S
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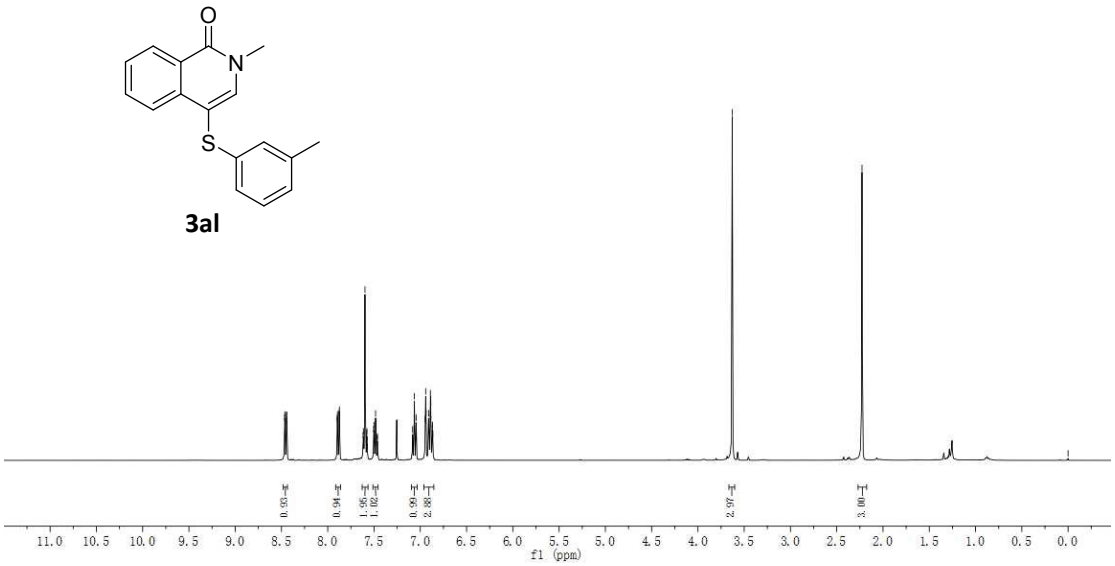
f1 (ppm)



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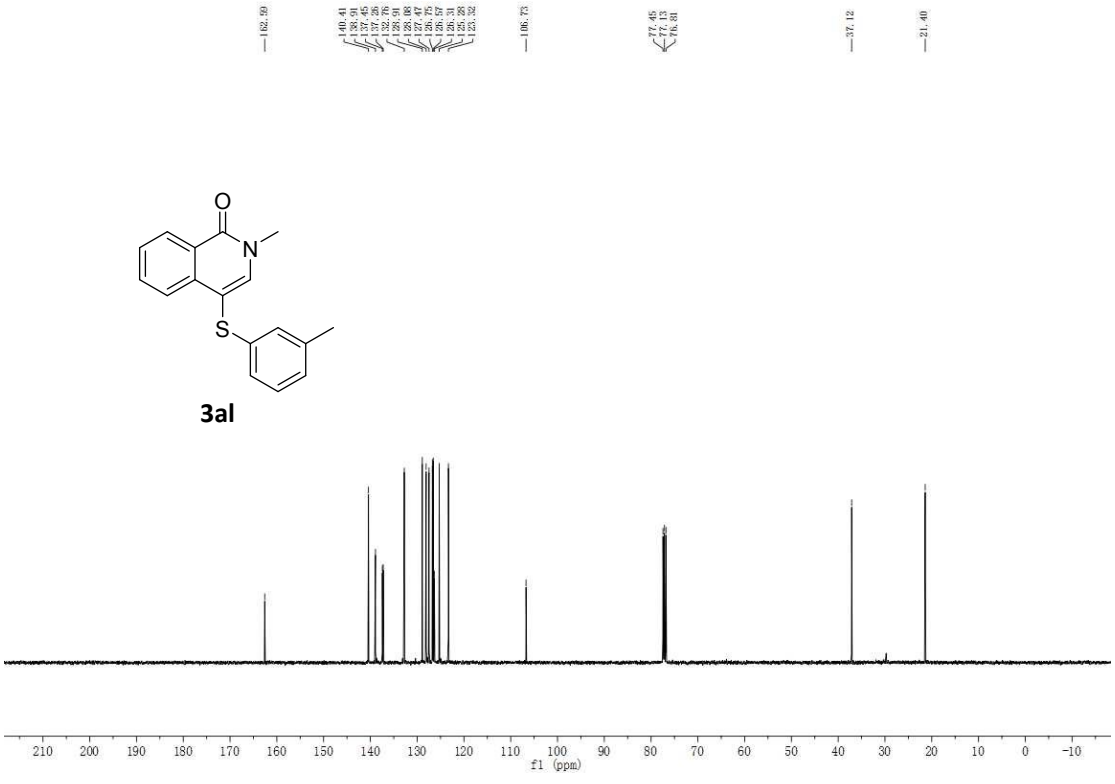

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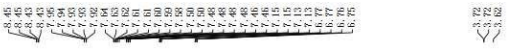

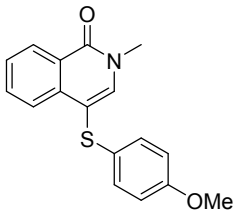

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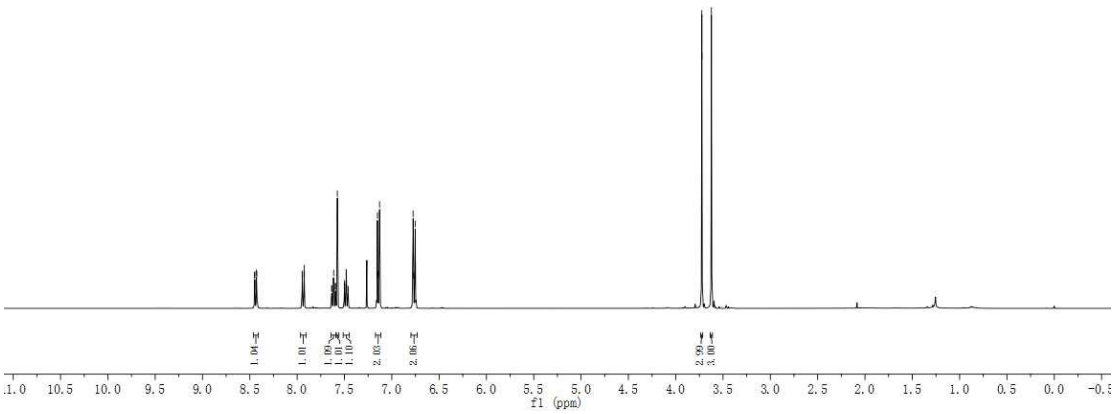

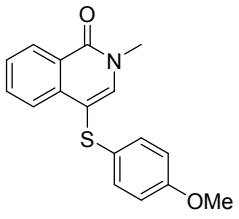

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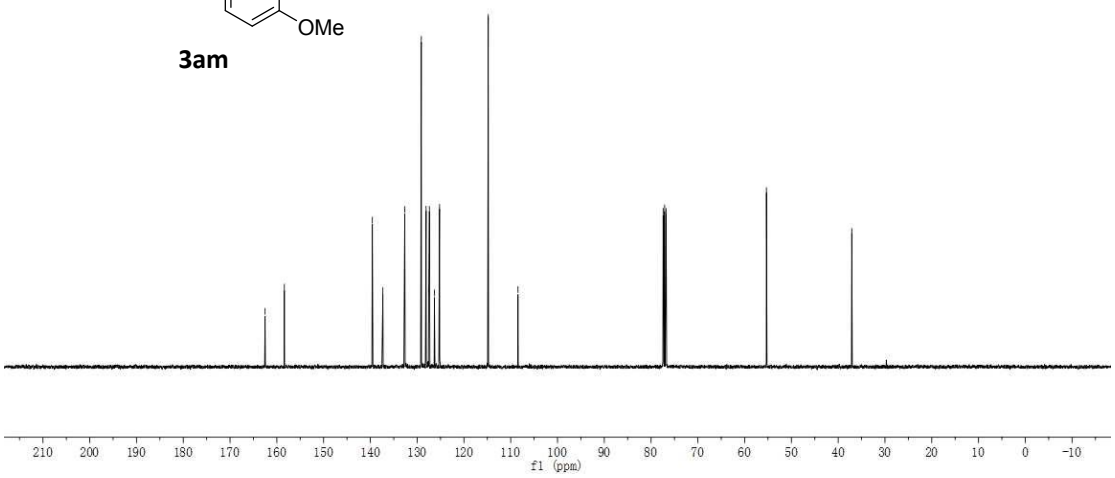

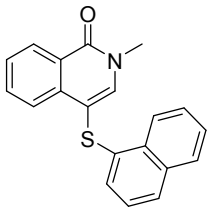

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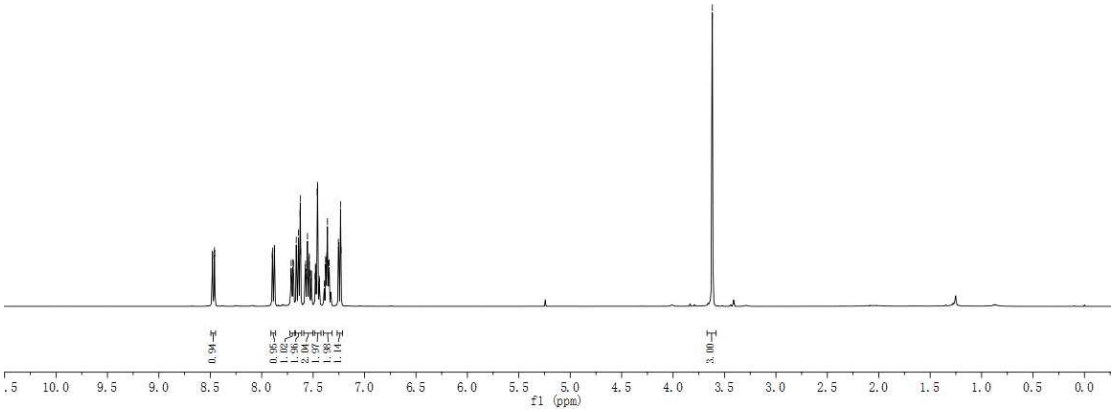

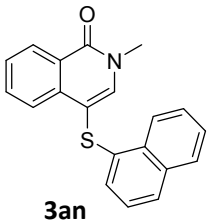

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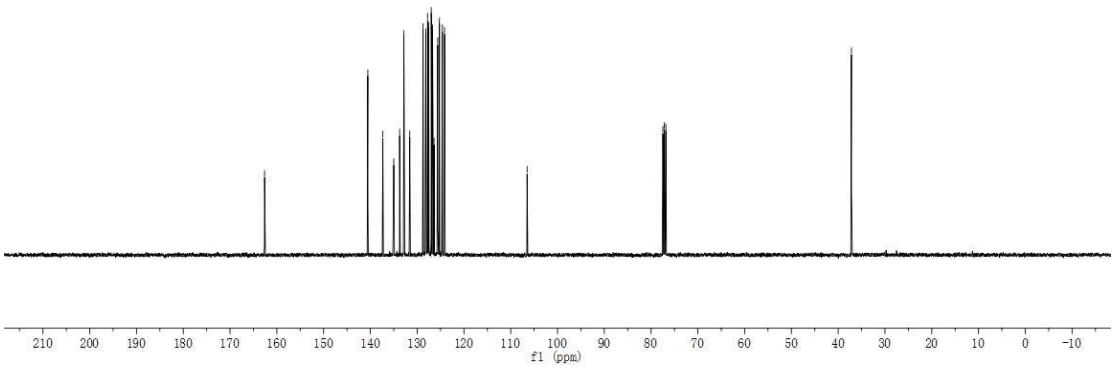
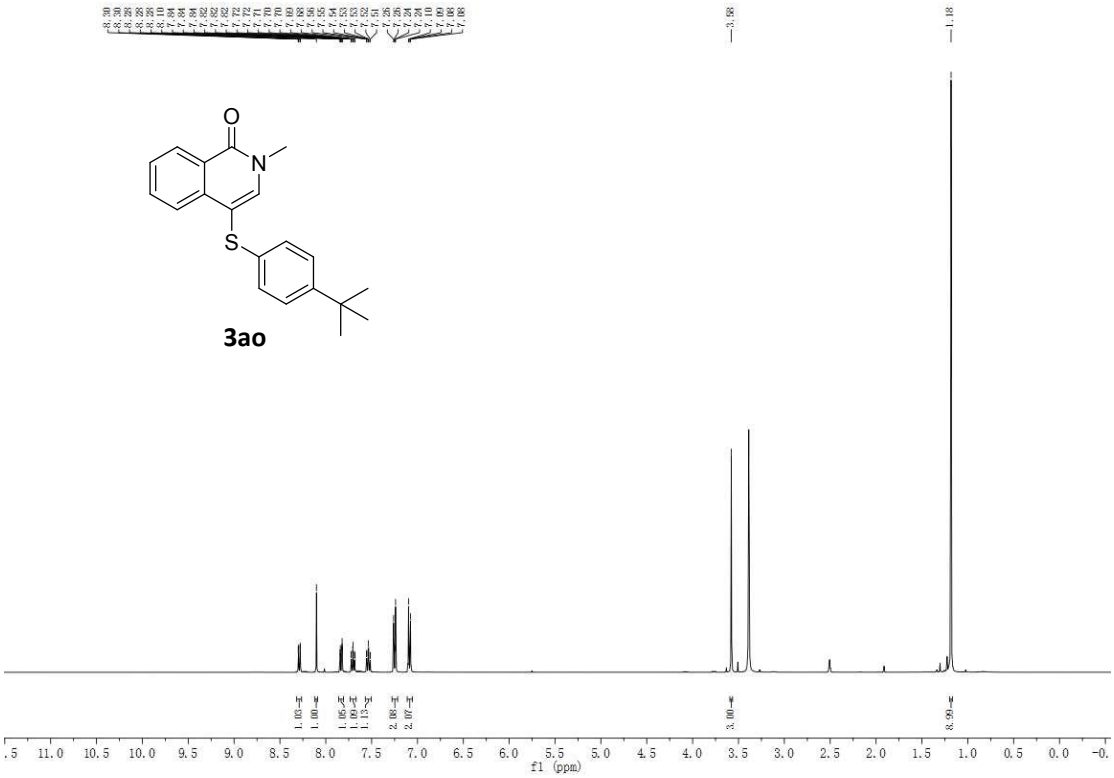
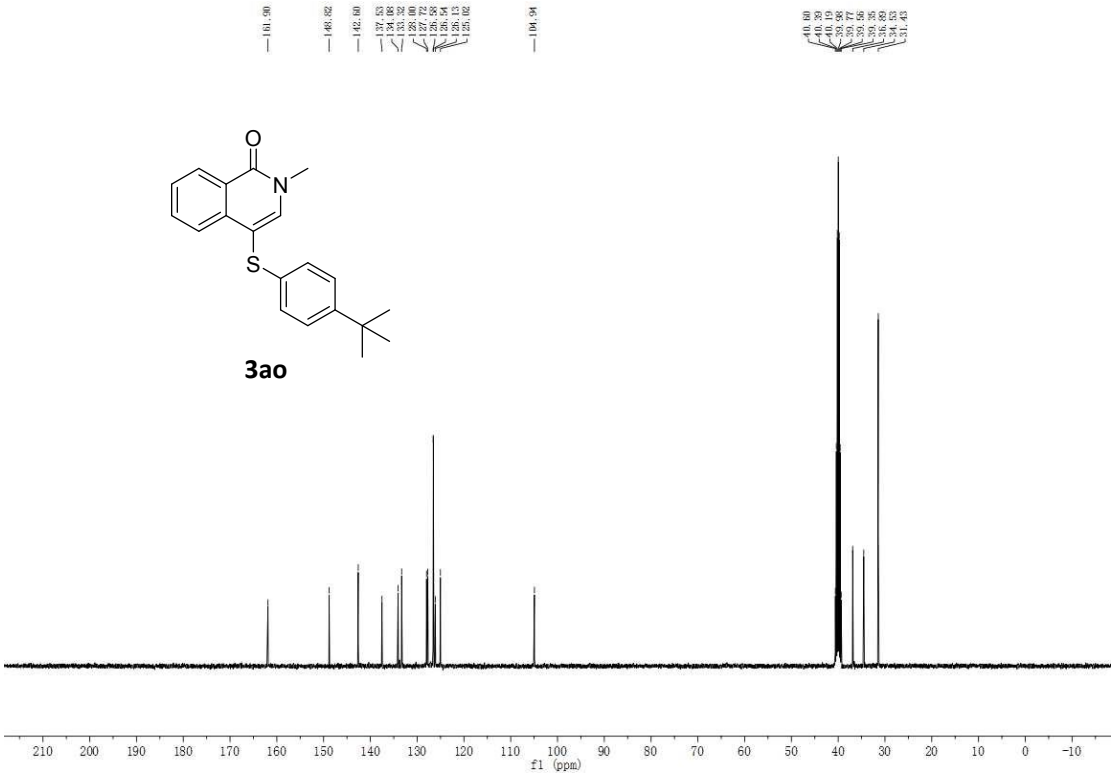
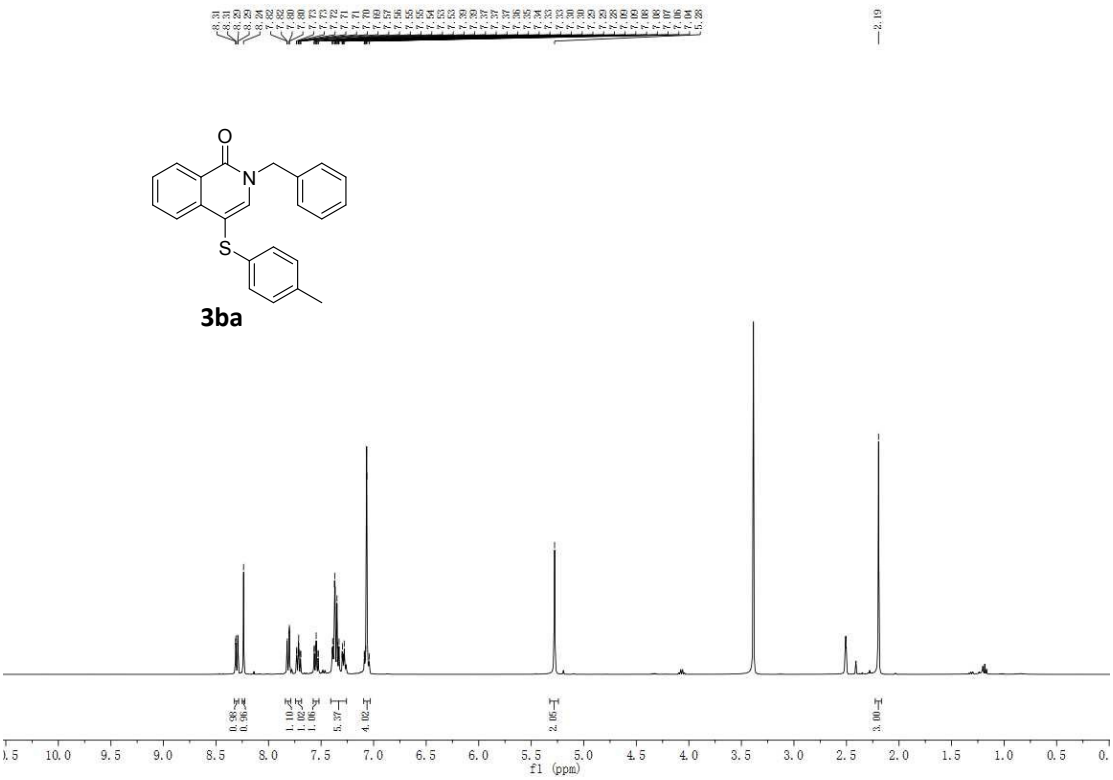



3ao
f1 (ppm)


3ao
f1 (ppm)

**3ba**





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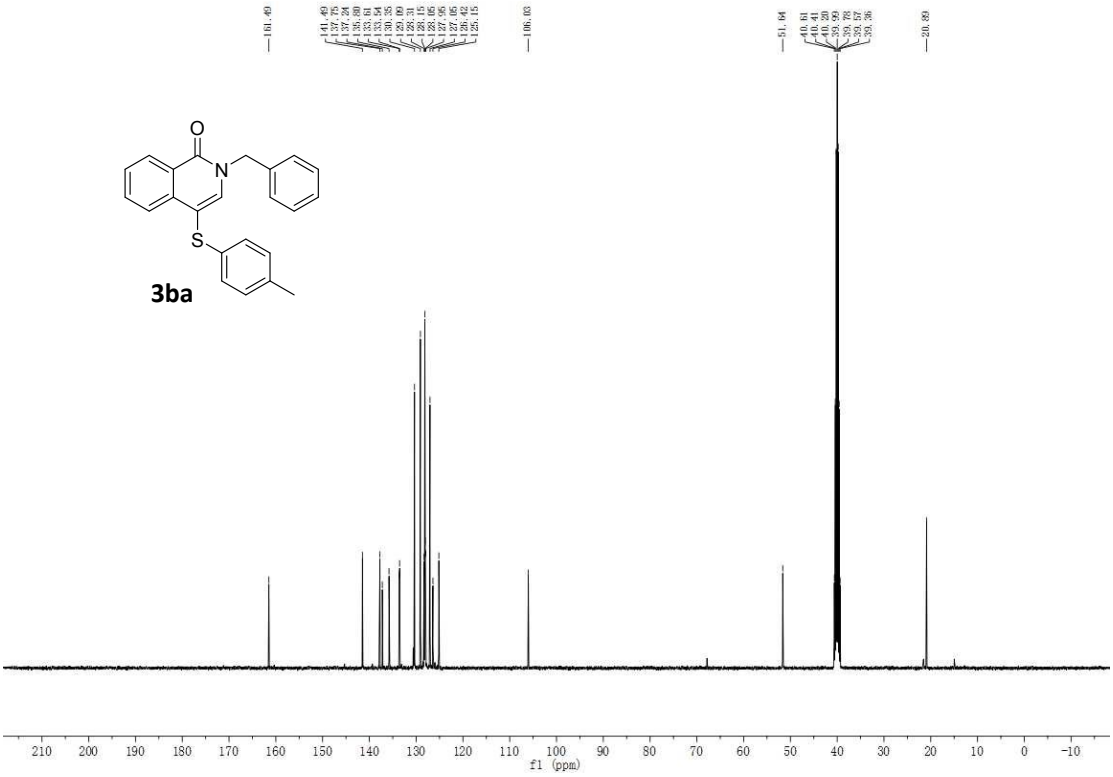

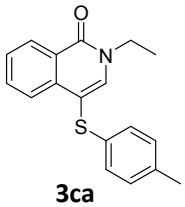

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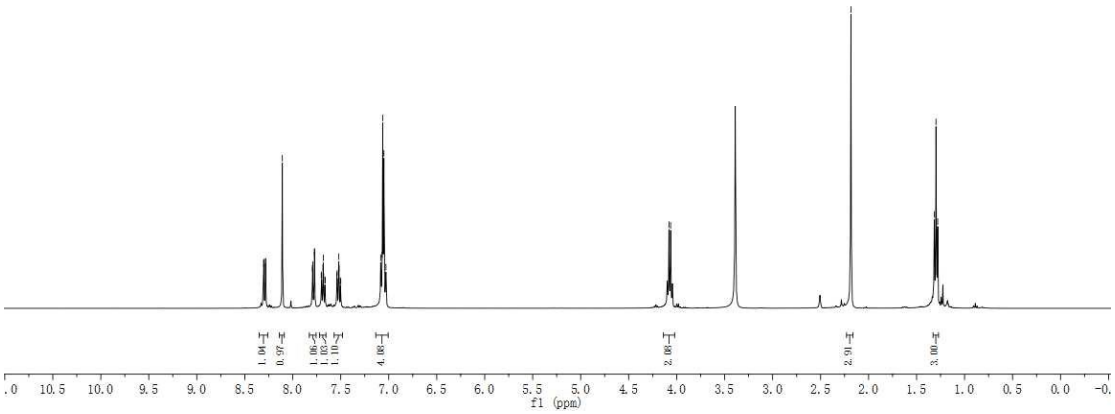
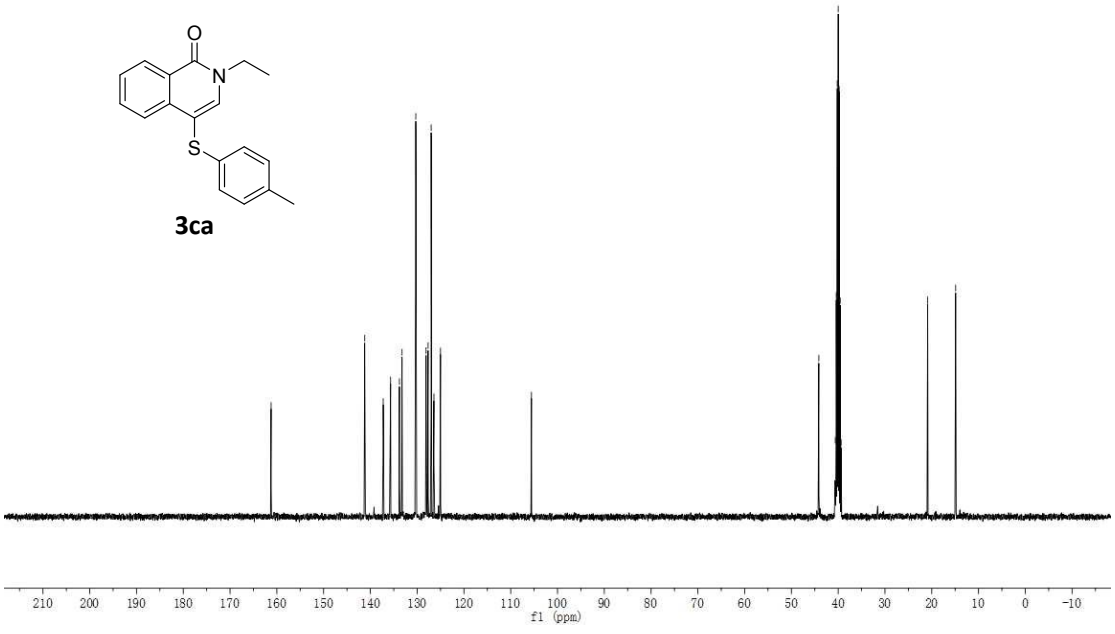
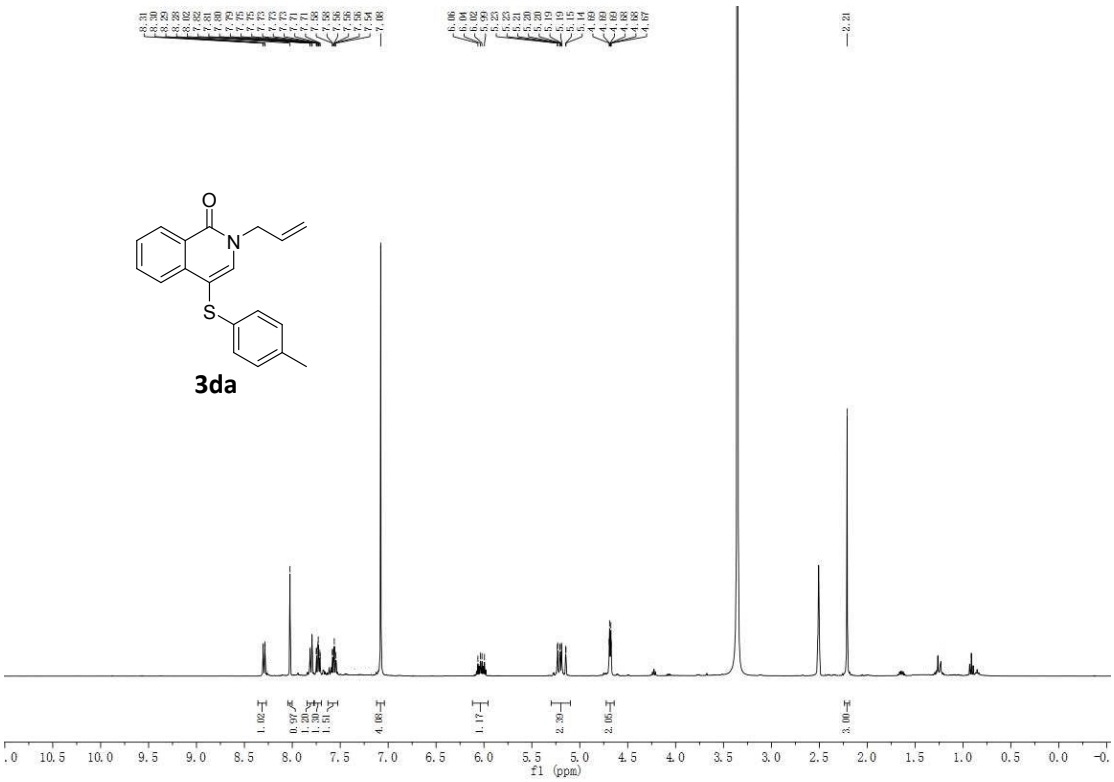
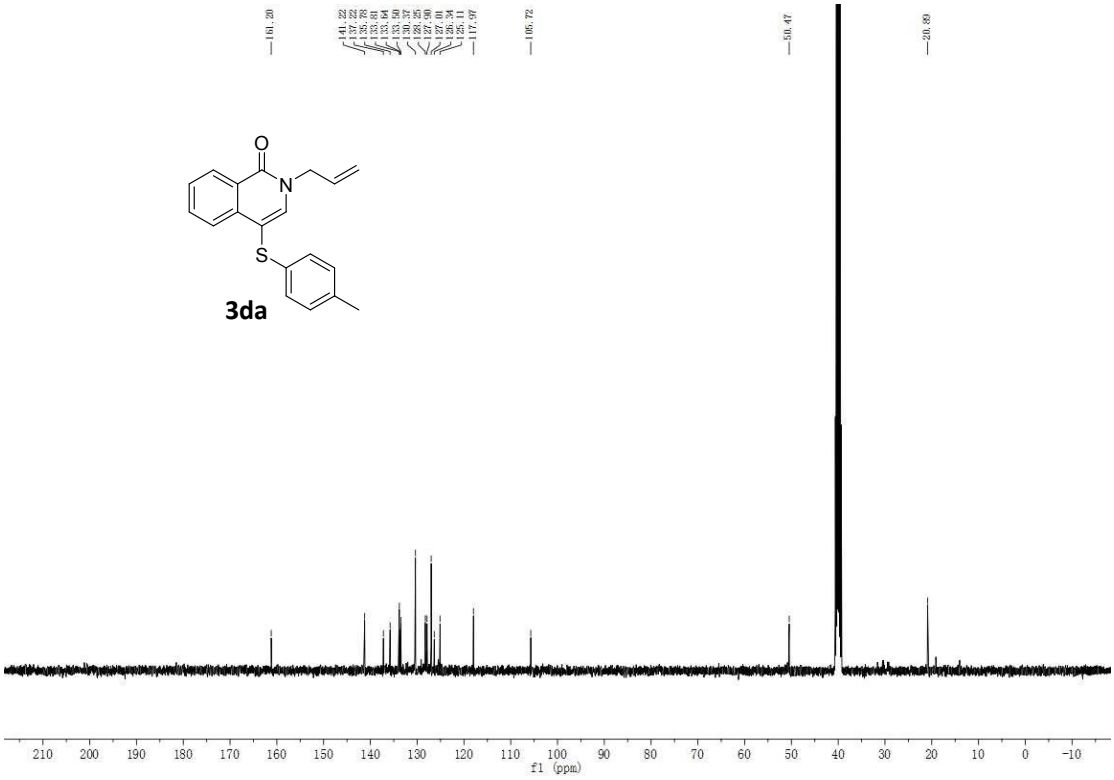




**3ca**




3da
f1 (ppm)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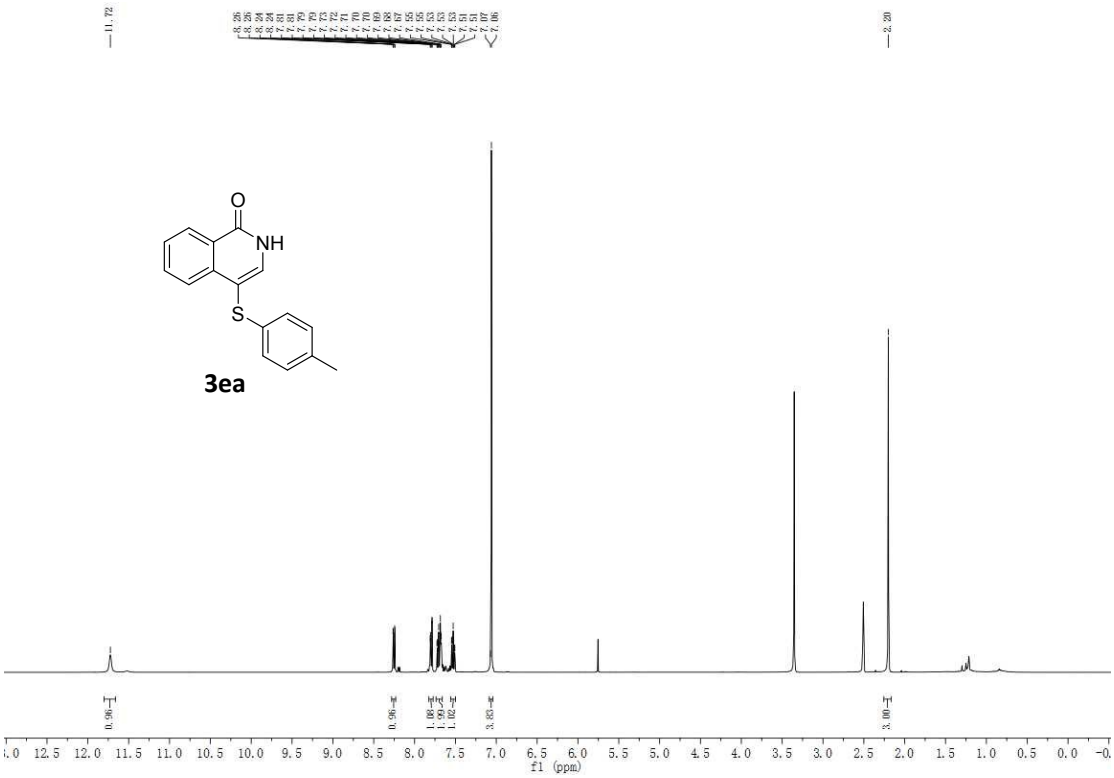
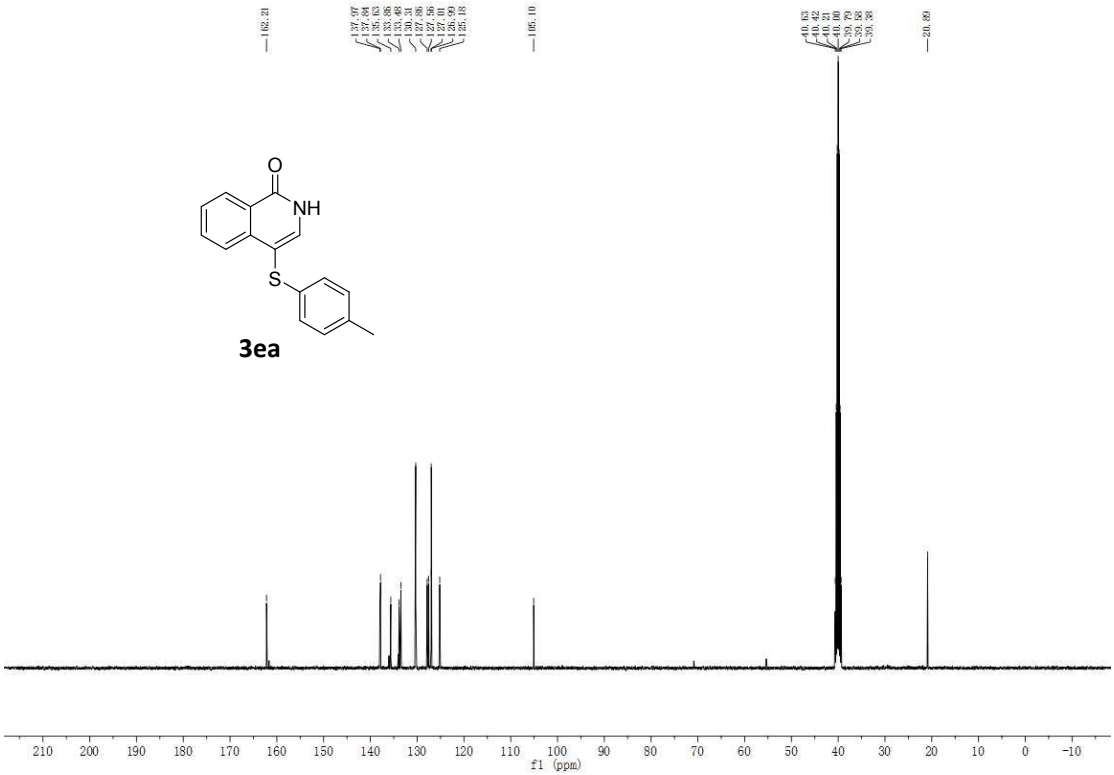
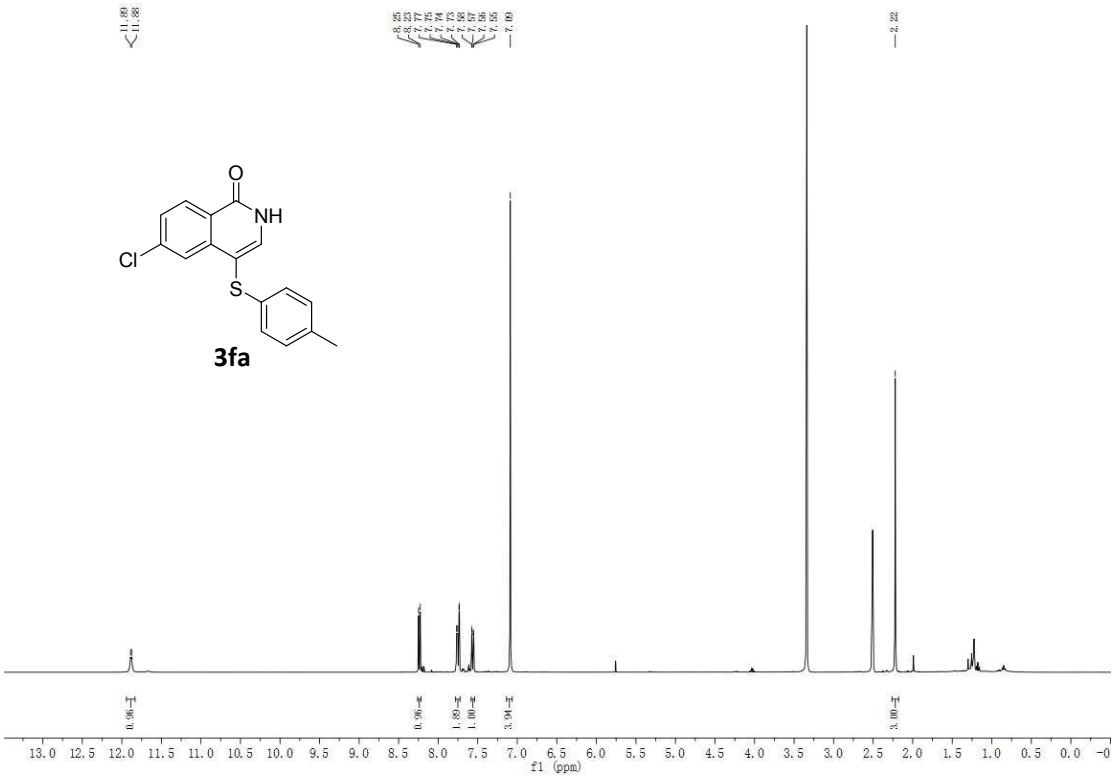
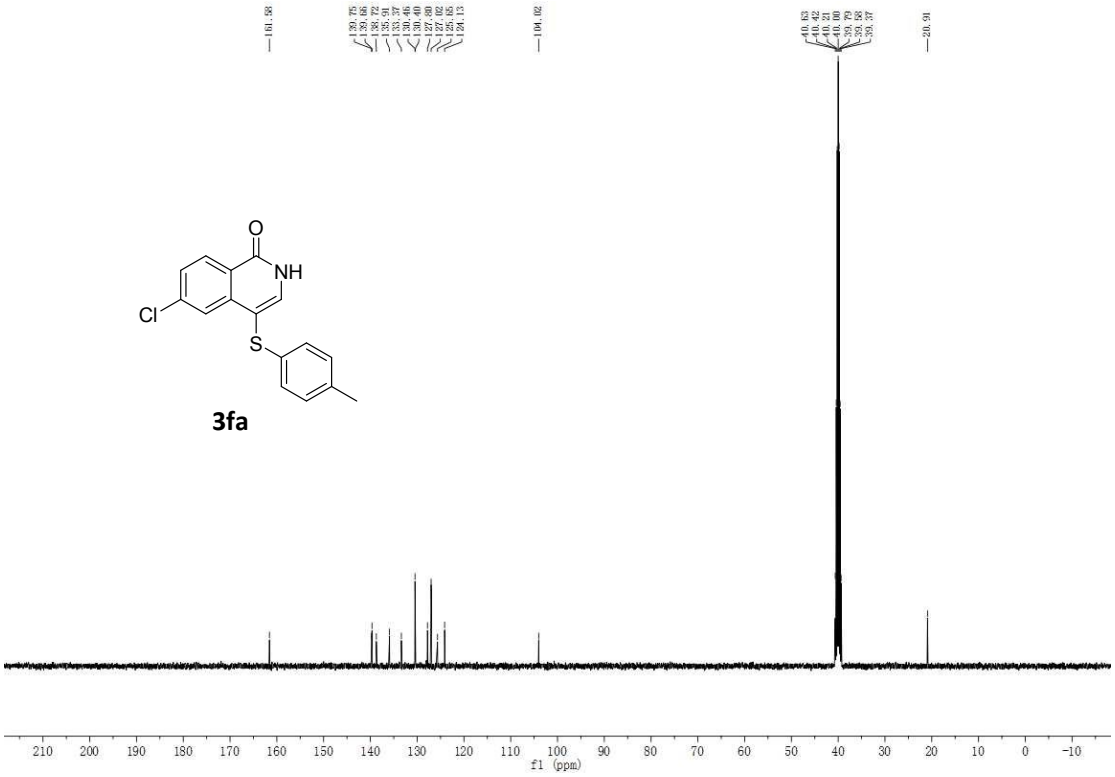
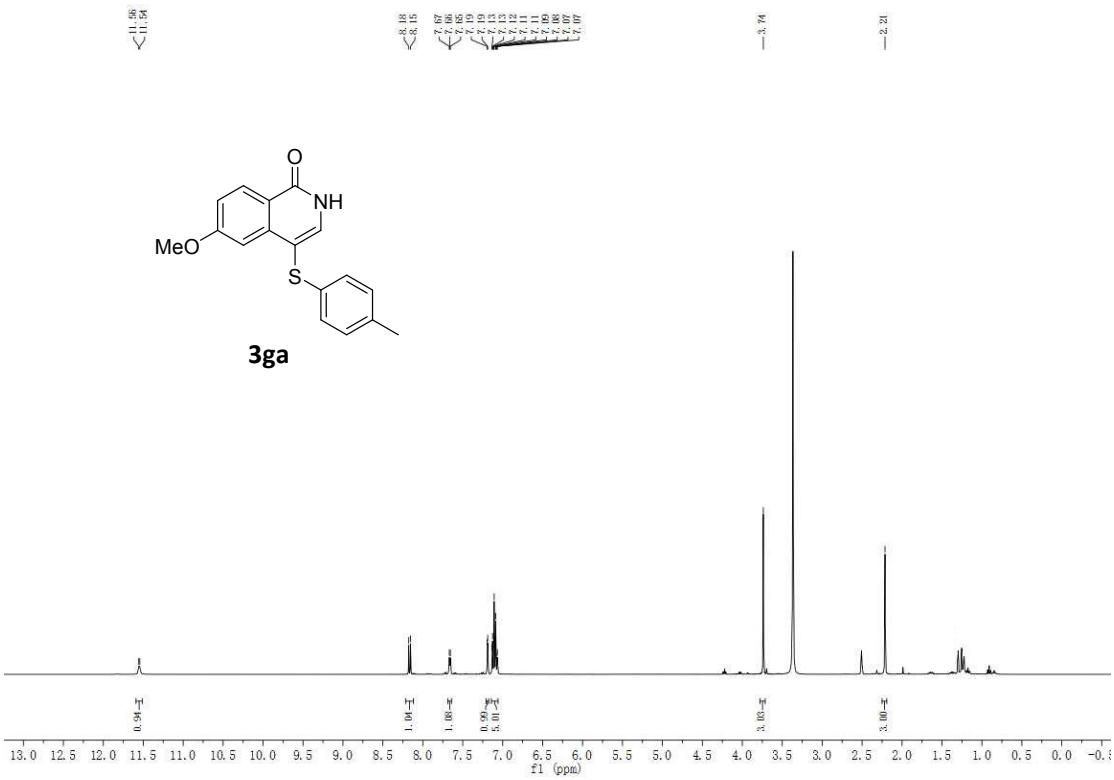
f1 (ppm)


11.72
8.26
8.24
8.23
7.81
7.79
7.73
7.72
7.71
7.70
7.70
7.69
7.68
7.67
7.55
7.55
7.53
7.53
7.51
7.51
7.07
7.06
2.28
O
NH
S
3ea
0.96
0.96
1.86
1.99
1.02
3.83
3.00
f1 (ppm)


162.21
137.97
137.84
135.63
133.86
133.48
131.31
127.38
127.56
127.01
126.99
125.16
105.10
40.63
40.42
40.21
40.00
39.79
39.58
39.36
20.89
O
NH
S
3ea
f1 (ppm)


O
NH
Cl
S
3fa
f1 (ppm)


O
NH
Cl
S
3fa
f1 (ppm)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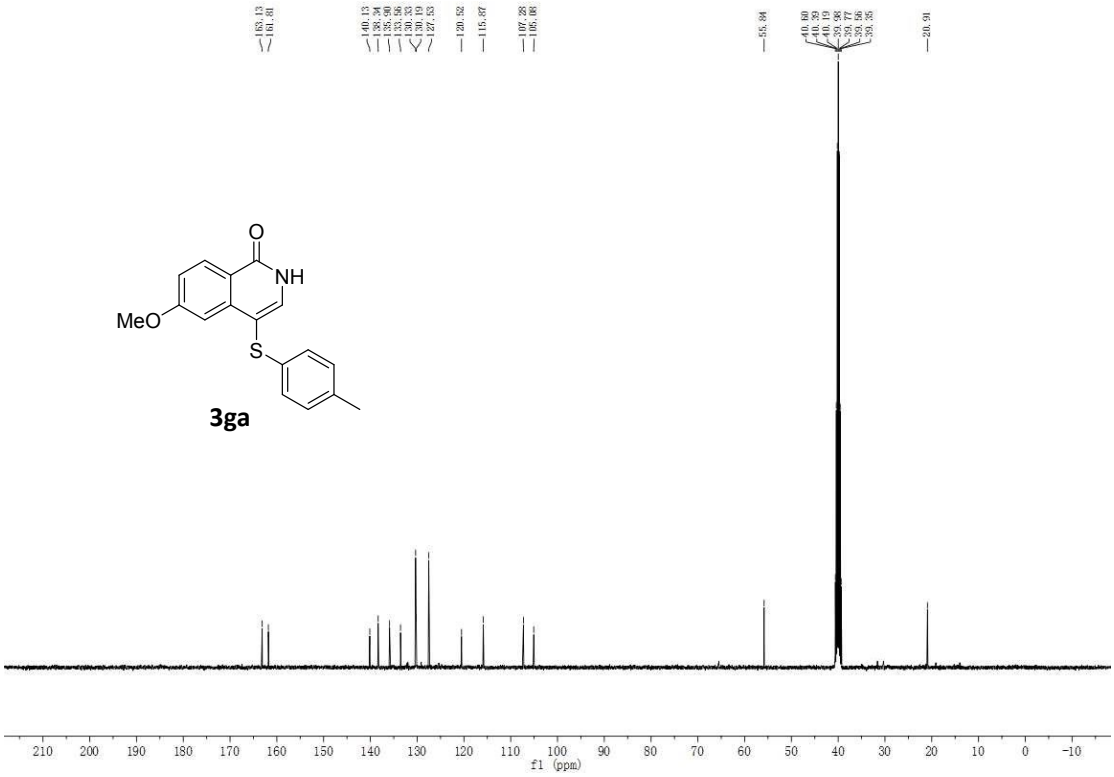
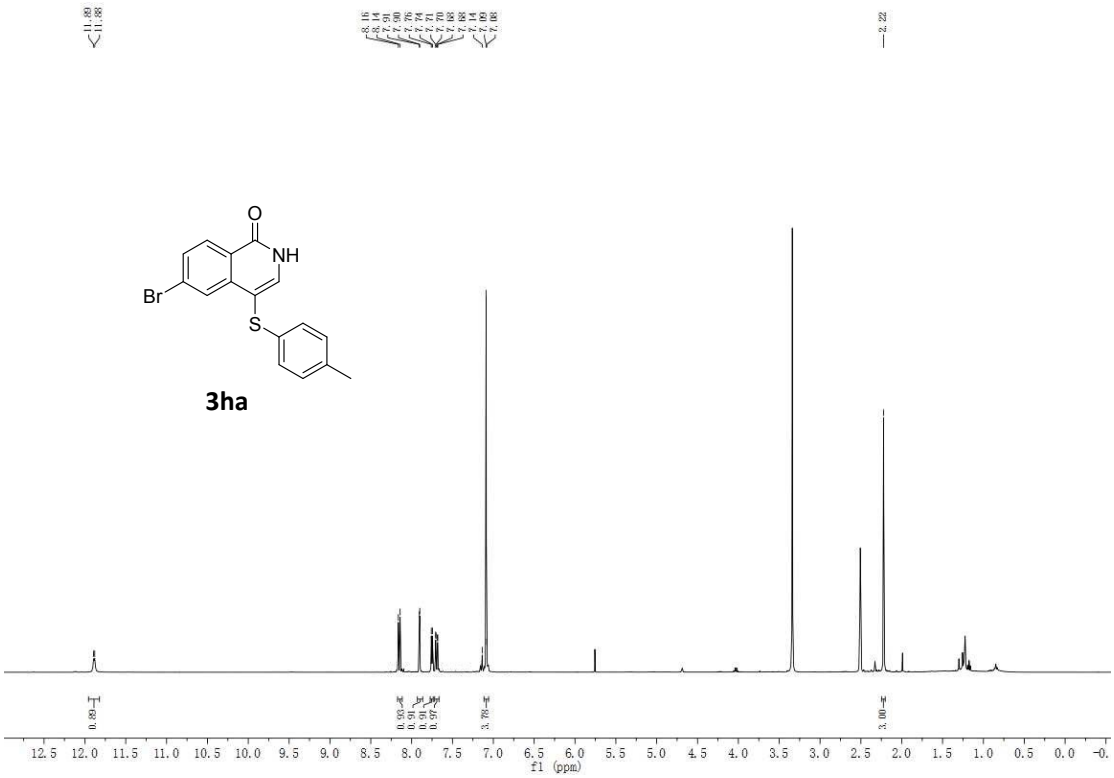
11.54
8.18
8.15
7.87
7.86
7.85
7.19
7.13
7.12
7.11
7.10
7.09
7.08
7.07
3.74
2.21
O
NH
MeO
S
0.94
1.04
1.08
0.99
5.01
3.03
3.00
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

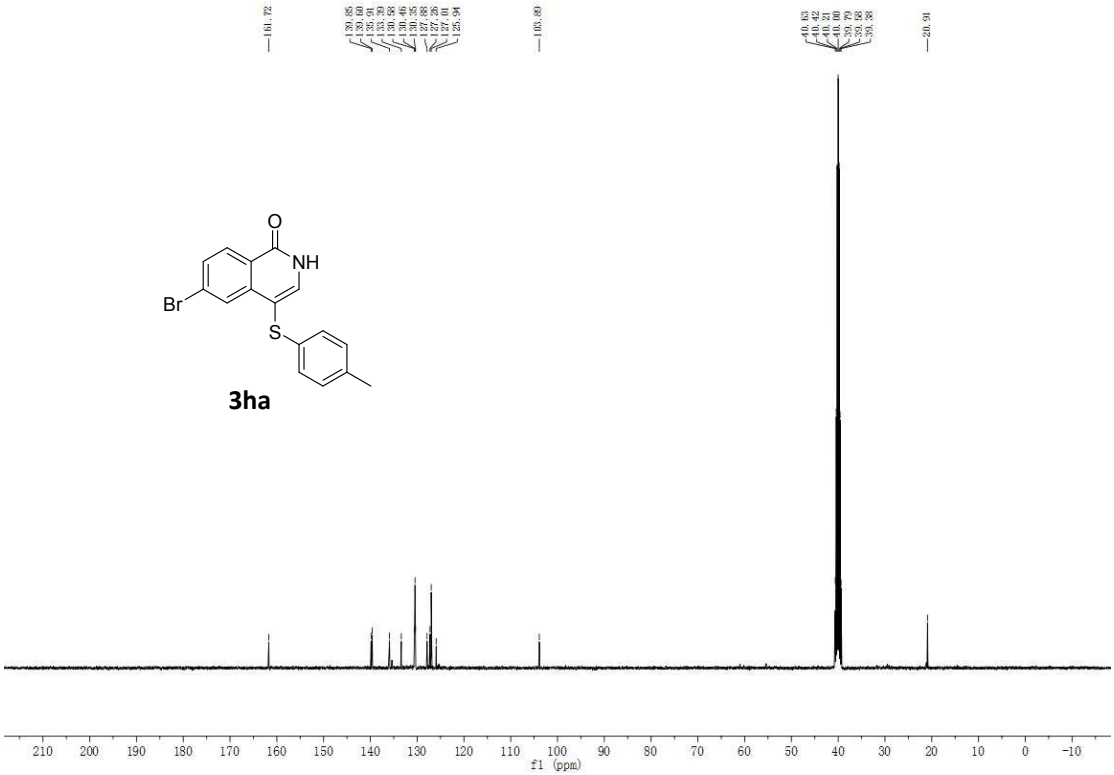
**3ga**


163.13
161.61
140.13
138.34
135.90
133.56
130.33
130.15
127.53
120.52
115.87
107.28
105.86
55.84
40.60
40.39
40.19
39.98
39.77
39.56
39.35
20.91
O
NH
MeO
S
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

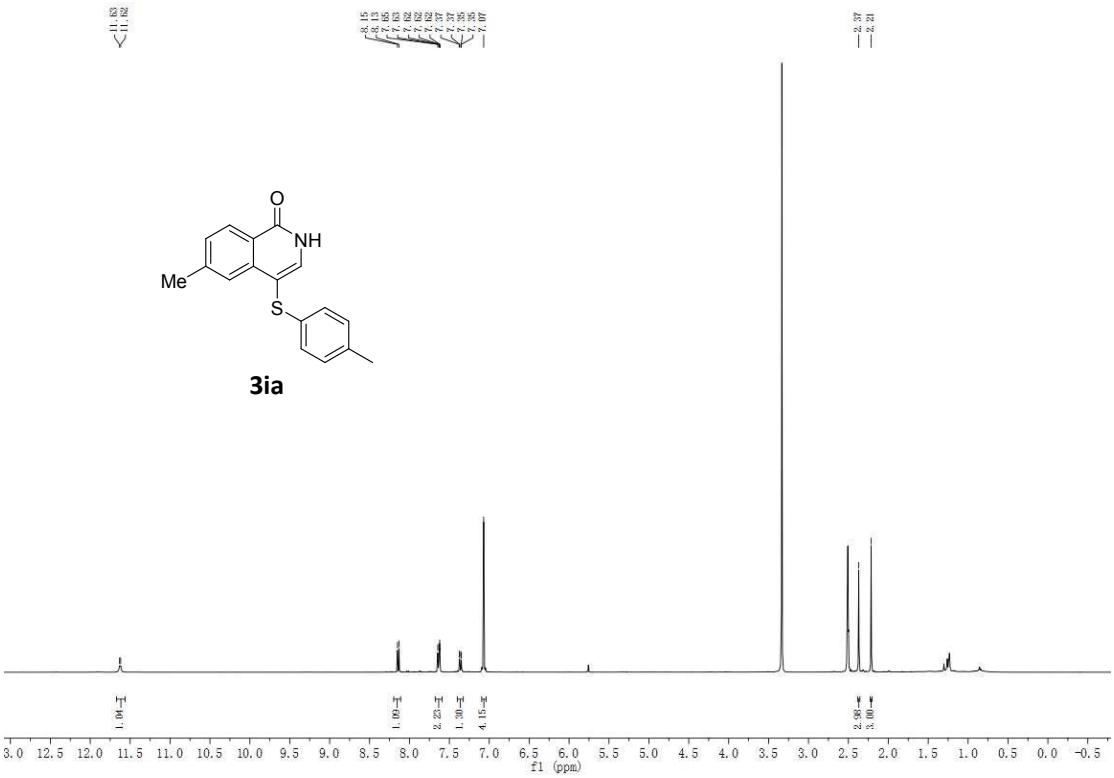
**3ga**


11.89
11.88
8.16
8.14
7.91
7.90
7.75
7.74
7.71
7.70
7.68
7.68
7.14
7.09
7.08
2.22
O
NH
Br
S
0.89
0.93
0.94
0.91
0.97
3.78
3.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)

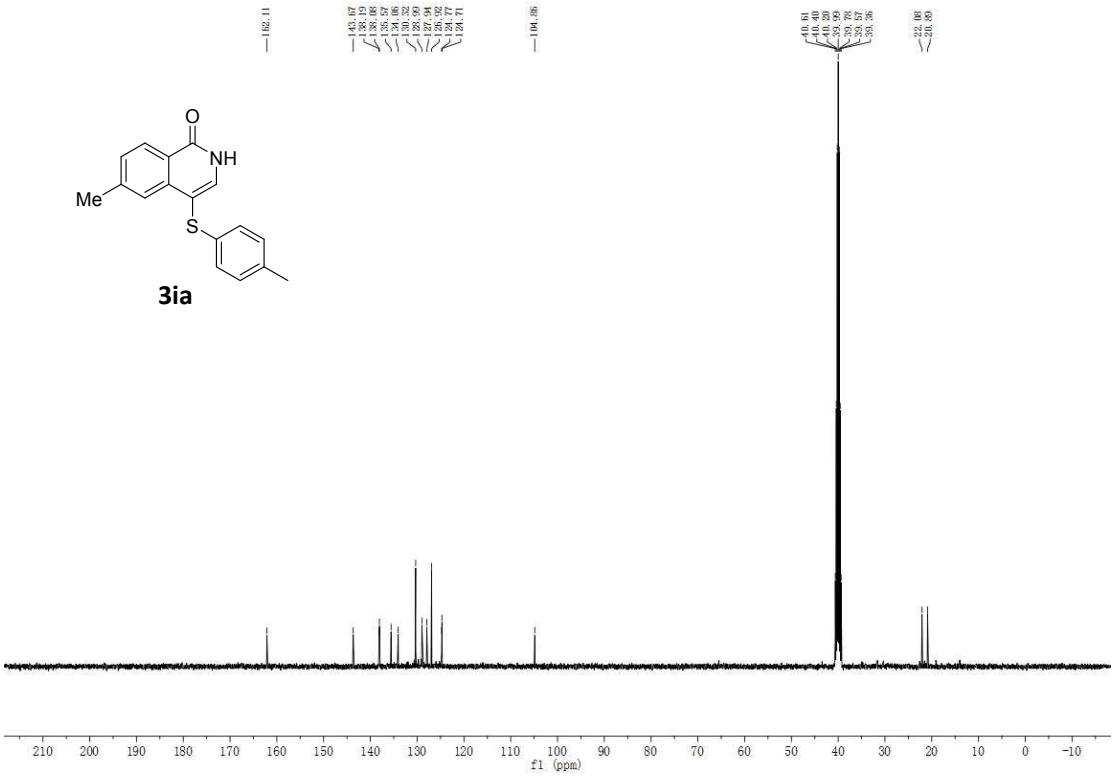
**3ha**


161.72
139.85
139.60
135.91
135.39
133.58
130.46
130.35
127.88
127.26
127.01
125.94
105.89
40.63
40.42
40.21
40.00
39.79
39.58
39.38
20.91
O
NH
Br
S
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

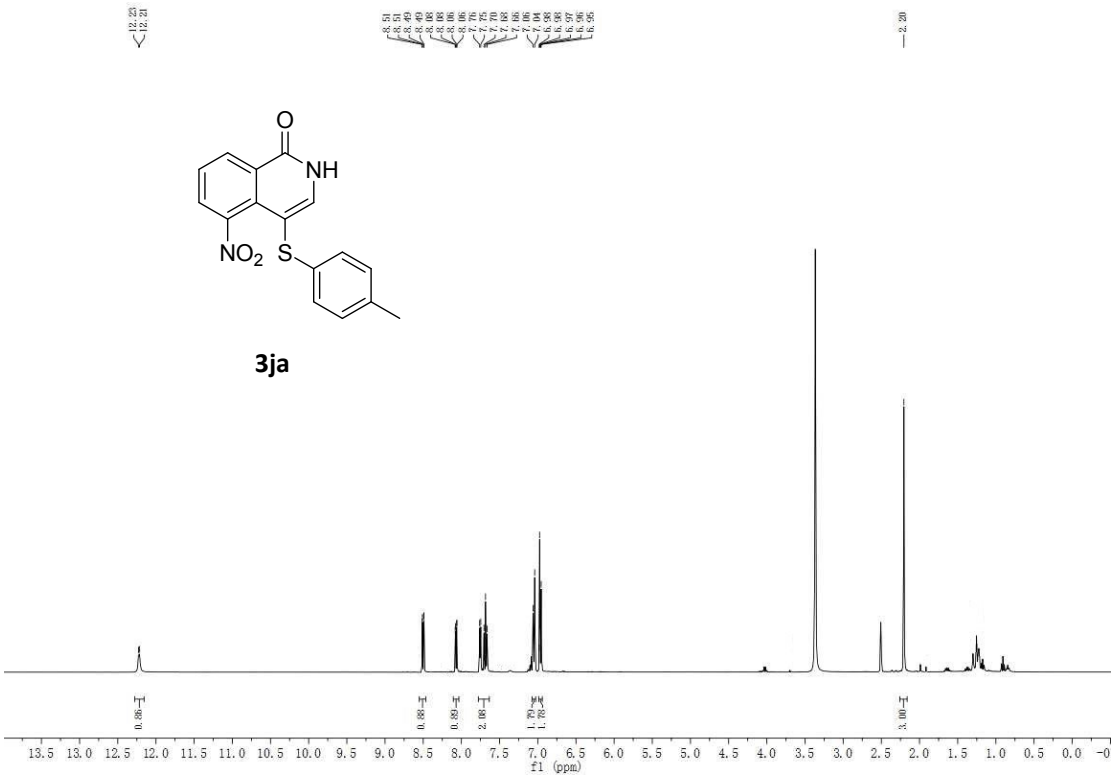
**3ha**


O
NH
Me
S
11.63
11.62
8.15
8.13
7.65
7.63
7.62
7.62
7.62
7.37
7.37
7.35
7.35
7.07
2.37
2.21
1.04
1.09
2.23
1.30
4.15
2.98
3.00
f1 (ppm)

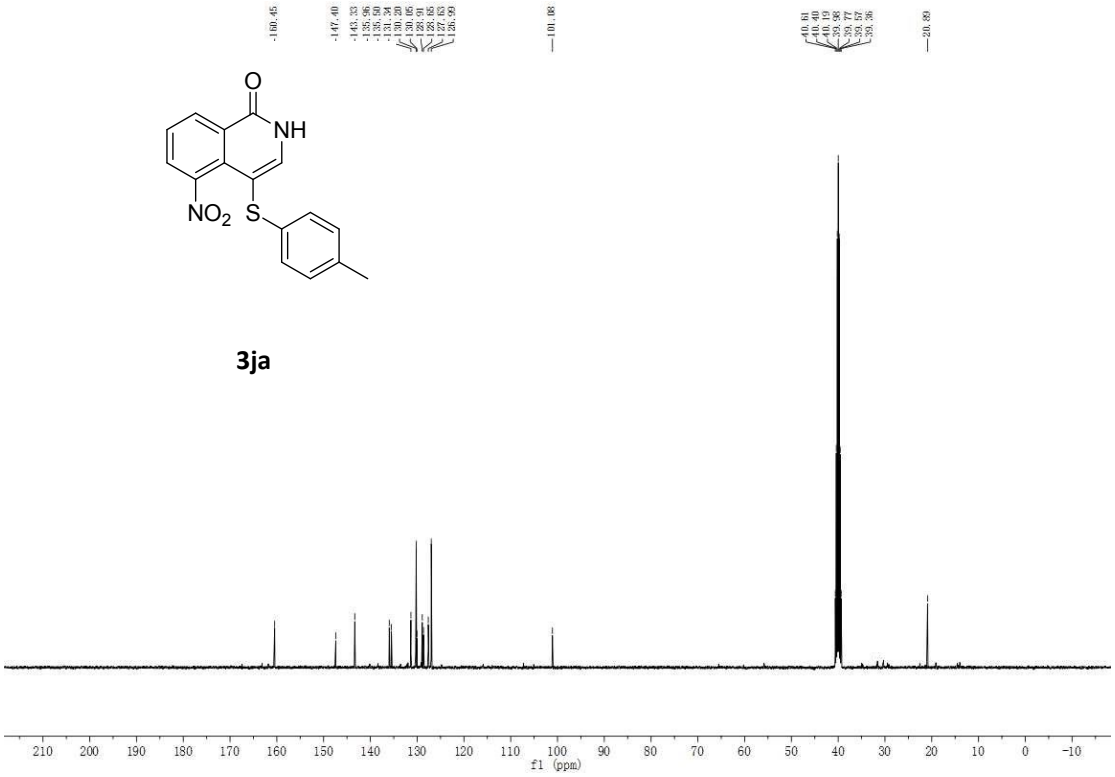
**3ia**


O
NH
Me
S
162.11
143.67
138.19
138.08
135.57
130.05
129.32
128.99
127.94
126.92
124.77
124.71
104.05
40.61
40.40
40.19
39.99
39.78
39.57
39.36
22.88
20.89
f1 (ppm)

**3ia**




**3ja**

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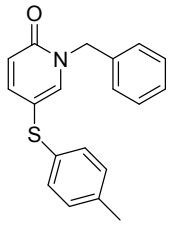

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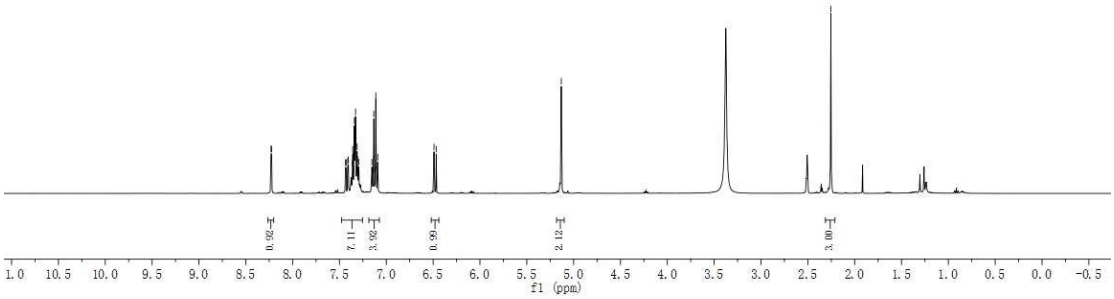
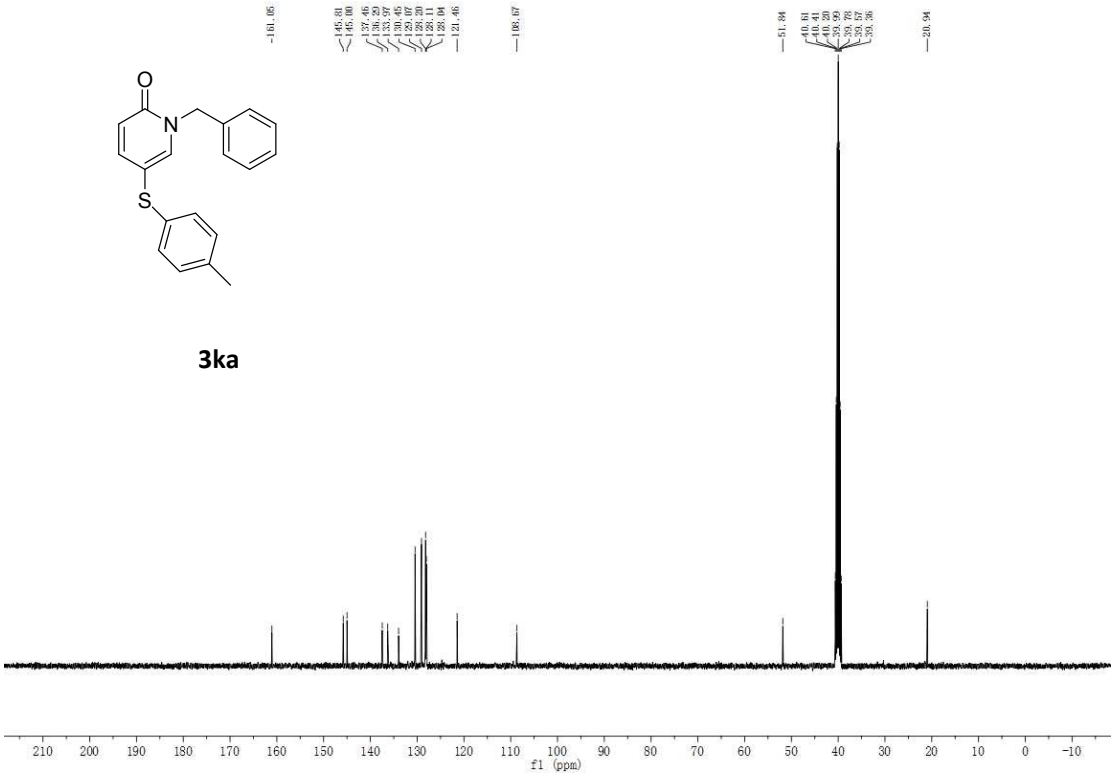
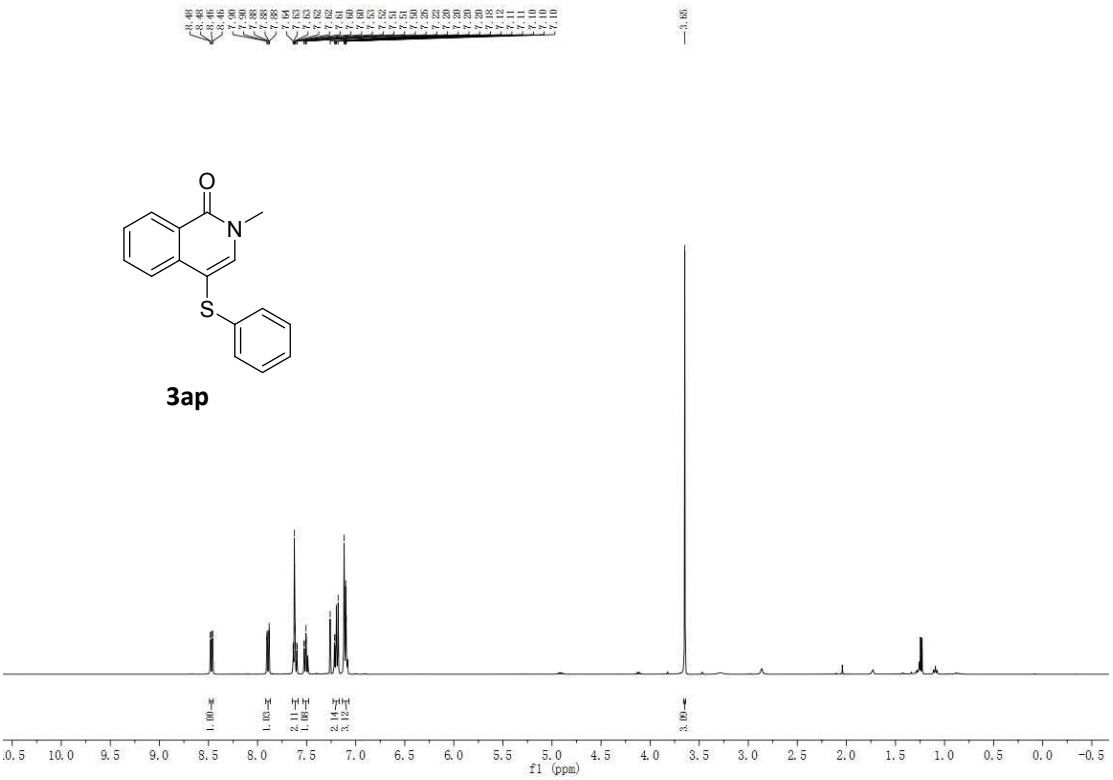




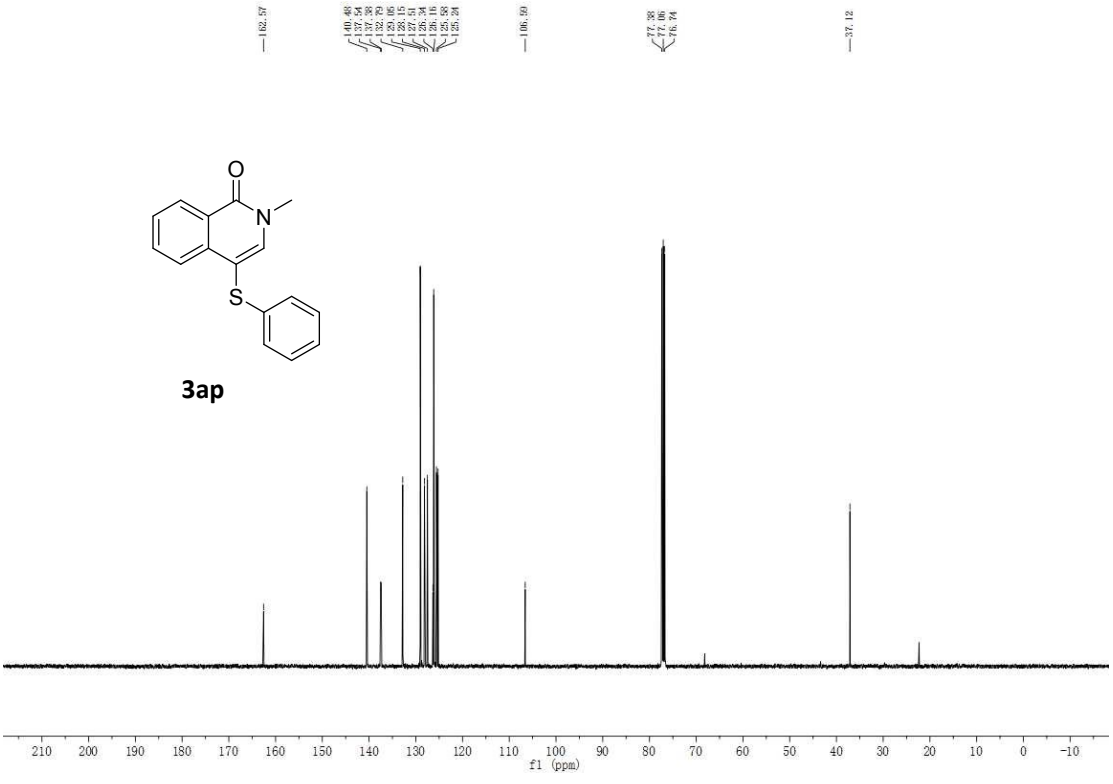


**3ka**






**3ap**




**3ap**