# Ball-Milling Synthesis of Sulfonyl Quinolines via Coupling of Haloquinolines with Sulfonic Acids

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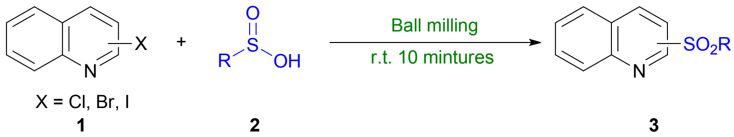
## 1. General information

Unless otherwise specified, all reagents and solvents were obtained from commercial suppliers and used without further purification. All reagents were weighed and handled in air at room temperature. $^1H$ NMR spectra were recorded at 400 MHz and $^{13}C$ NMR spectra were recorded at 101 MHz by using a Bruker Avance 400 spectrometer. Chemical shifts were calibrated using residual undeuterated solvent as an internal reference ($^1H$ NMR: $CDCl_3$ 7.26 ppm, $^{13}C$ NMR: $CDCl_3$ 77.0 ppm). The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet. Mass spectra were performed on a spectrometer operating on ESI-TOF.

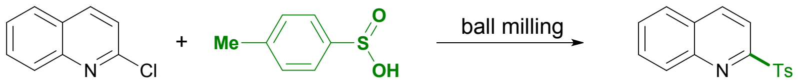
## 2. Experimental Section

## General procedure for the preparation of sulfonyl quinolines




A mixture of halogenated quinolines **1** (0.5 mmol) and sulfonic acids **2** (0.65 mmol) were milled in a stainless steel jar charged with 1 ball (10 mm) of the same material at 20Hz for 10 – 20 min. The resulting powder was direct purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired products sulfonyl quinolines **3.**

### Gram-scale synthesis of 3aa

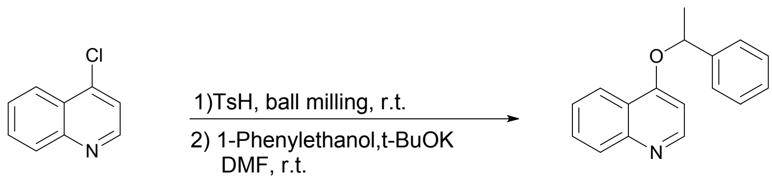



**1a**, 10mmol

**3aa**, 2.55 g, 88%

A mixture of 2-chloroquinoline **1a** (1.63 g, 10 mmol) and 4-methylbenzenesulfinic acid **2a** (2.03 g, 13 mmol) were milled in a stainless steel jar charged with 1 ball (10 mm) of the same material at 20Hz for 10 min. After completion, the resulting powder was direct purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give 2.55 gram of **3aa**, isolated yield 88%**.**

## One pot synthesis of 4-quinolinyl ether

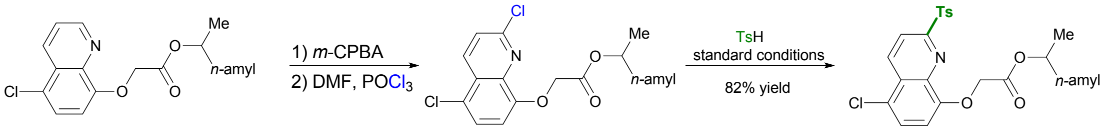



**1j**, 2 mmol

**4a**, 0.37 g, yield 75%

A mixture of halogenated 4-chloroquinoline **1j** (0.33 g, 2 mmol) and 4-methylbenzenesulfinic acid **2a** (0.41 g, 2.6 mmol) was milled in a stainless steel jar charged with 1 ball (10 mm) of the same material at 20Hz for 10 min, the resulting powder was then dissolved in DMF (6mL) and transferred to a round bottom flask, 1-phenylethanol (0.29 g, 2.4mmol) and t-BuOk (1M in THF, 2.4 mmol) were added, the mixture was stirred for about 2 hours. After completion, the resulting mixture was extracted with EtOAc (10 mL× 3) and the organic phase was then removed under vacuum. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give 0.37 gram of **4a**, total yield 75%.

### Synthesis of sulfonated cloquintocet-mexyl (3wa)



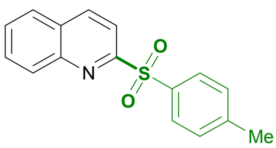

A solution of cloquintocet-mexyl **4b** (0.67 g, 2.0 mmol) in DCM (20 mL) was stirred at 0 °C for 5 min, then 3-chloroperbenzoic acid (m-CPBA, 3.0 mmol) was added to the solution in three portions. The mixture was stirred at 25 °C for 12 h and a saturated aqueous $NaHCO_3$ solution (20 mL) was added. The resulting solution was extracted with DCM (10 mL × 2). Then it was dried by anhydrous $Na_2SO_4$ and concentrated under reduced pressure to obtain the crude product cloquintocet-mexyl N-oxide and used without further purification.

The above-synthesized crude product cloquintocet-mexyl *N*-oxide was added to a solution of $POCl_3$ (0.31 g, 2 mmol), and DMF (0.15 g, 2 mmol) in DCM (10 mL) at 0 - 5 °C. The reaction was allowed to stir at room temperature for 6h, after completion, the reaction was quenched with 2M $Na_2CO_3$ solution (10 mL) and the resulting mixture was extracted with DCM (10 mL× 3). The organic layer was combined and then removed under vacuum. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give 2-chlorocloquintocet-mexyl **1w**. $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.47 (d, *J* = 8.8 Hz, 1H), 7.51 (dd, *J* = 11.8, 8.6 Hz, 2H), 6.93 (d, *J* = 8.5 Hz, 1H), 5.09 – 4.97 (m, 1H), 4.92 (d, *J* = 2.0 Hz, 2H), 1.57 (dd, *J* = 13.1, 5.0 Hz, 1H), 1.49 – 1.42 (m, 1H), 1.26 – 1.20 (m, 9H), 0.85 (t, *J* = 6.7 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 168.1, 152.1, 150.9, 140.1, 136.0, 126.5, 126.0, 124.0, 123.4, 111.2, 72.8, 66.5, 35.7, 31.5, 24.9, 22.5, 19.9, 13.9; HRMS (ESI) m/z calcd. for $C_{18}H_{22}Cl_2NO_3[M+H]^+$ : 370.0971, found 370.0966.

A mixture of 2-chlorocloquintocet-mexyl **1w** (0.19 g, 0.5 mmol) and 4-methylbenzenesulfinic acid **2a** (0.10 g, 0.65 mmol) were milled in a stainless steel jar charged with 1 ball (10 mm) of the same material at 20Hz for 10 min. After completion, the resulting powder was direct purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give 0.20 gram of **3wa**, isolated yield 82%. $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.72 (d, *J* = 8.8 Hz, 1H), 8.29 (d, *J* = 8.8 Hz, 1H), 8.05 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 1H), 5.05 – 4.97 (m, 1H), 4.85 (s, 2H), 2.40 (s, 3H), 1.58 (dq, *J* = 12.3, 6.1, 5.2 Hz, 1H), 1.47 (dt, *J* = 14.0, 7.0 Hz, 1H), 1.28 – 1.20 (m, 9H), 0.85 (t, *J* = 6.7 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 168.1, 158.0, 153.4, 145.0, 140.2, 136.1, 135.6, 129.8, 129.3, 128.8, 127.7, 123.9, 118.6, 114.2, 72.6, 67.6, 35.7, 31.5, 24.9, 22.5, 21.6, 13.9; HRMS (ESI) m/z calcd. for $C_{25}H_{29}ClNO_5S[M+H]^+$ : 490.1449, found 490.1446.

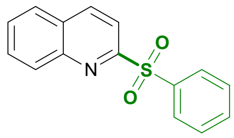
## Characterization data of products

**2-tosylquinoline (3aa)[1]**



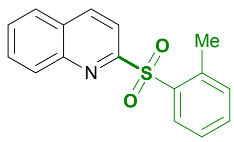

White solid; 93% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 8.6 Hz, 1H), 8.18 (t, *J* = 8.2 Hz, 2H), 8.02 (d, *J* = 8.3 Hz, 2H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.78 (t, *J* = 7.7 Hz, 1H), 7.65 (t, *J* = 7.1 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 2.39 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 158.3, 147.4, 144.8, 138.7, 136.1, 130.9, 130.4, 129.7, 129.1, 129.0, 128.7, 127.6, 117.6, 21.6.

**2-(phenylsulfonyl)quinoline (3ab)[2]**



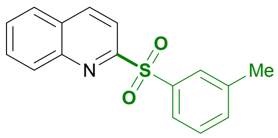
White solid; 82% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.39 (d, *J* = 8.5 Hz, 1H), 8.31 (d, *J* = 7.8 Hz, 1H), 8.17 (d, *J* = 8.5 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.76 (t, *J* = 7.7 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.26 – 7.21 (m, 1H), 2.55 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 158.1, 147.1, 139.0, 138.6, 137.0, 133.9, 132.4, 130.9, 130.5, 130.3, 129.1, 128.8, 127.7, 126.3, 117.7, 20.7.

**2-(o-tolylsulfonyl)quinoline (3ac)[3]**



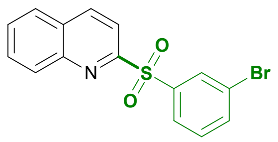
White solid; 83% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.39 (d, *J* = 8.5 Hz, 1H), 8.31 (d, *J* = 7.8 Hz, 1H), 8.17 (d, *J* = 8.5 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.76 (t, *J* = 7.7 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.26 – 7.21 (m, 1H), 2.55 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 158.1, 147.1, 139.0, 138.6, 137.0, 133.9, 132.4, 130.9, 130.5, 130.3, 129.1, 128.8, 127.7, 126.3, 117.7, 20.7.

**2-(m-tolylsulfonyl)quinoline (3ad)[3]**



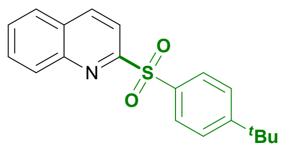
White solid; 84% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 8.6 Hz, 1H), 8.18 (t, *J* = 8.3 Hz, 2H), 7.92 (d, *J* = 6.1 Hz, 2H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.80 – 7.74 (m, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.39 (d, *J* = 7.7 Hz, 2H), 2.39 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 158.0, 147.3, 139.3, 138.8, 138.7, 134.5, 130.9, 130.3, 129.1, 129.1, 128.9, 128.7, 127.6, 126.1, 117.7, 21.2.

**2-((3-bromophenyl)sulfonyl)quinoline (3ae)[2]**



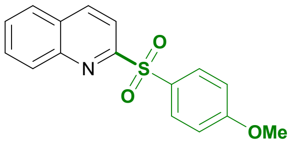
White solid; 87% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 8.5, 2.7 Hz, 1H), 8.31 – 8.25 (m, 1H), 8.24 – 8.13 (m, 2H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.89 (dd, *J* = 8.0, 3.5 Hz, 1H), 7.80 (q, *J* = 6.6 Hz, 1H), 7.70 (dt, *J* = 12.7, 6.4 Hz, 2H), 7.41 (td, *J* = 7.9, 3.6 Hz, 1H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 157.4, 147.4, 140.9, 138.9, 136.8, 131.8, 130.6, 130.4, 129.4, 128.9, 127.7, 127.7, 123.0, 117.6.

**2-((4-(tert-butyl)phenyl)sulfonyl)quinoline (3af)[4]**



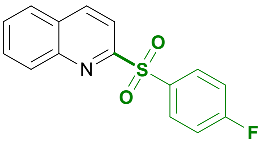
White solid; 92% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 8.5 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 2H), 8.06 (d, $J$ = 8.6 Hz, 2H), 7.87 (d, $J$ = 8.2 Hz, 1H), 7.79 (t, $J$ = 8.4 Hz, 1H), 7.66 (t, $J$ = 7.5 Hz, 1H), 7.53 (d, $J$ = 8.6 Hz, 2H), 1.30 (s, 9H); $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 158.3, 157.6, 147.4, 138.7, 136.1, 130.9, 130.4, 129.1, 128.8, 128.8, 127.7, 126.2, 117.8, 35.2, 31.0.

**2-((4-methoxyphenyl)sulfonyl)quinoline (3ag)[5]**



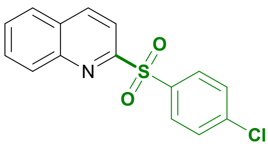

White solid; 82% yield; $^{1}$H NMR (400 MHz, Chloroform-$d$) δ 8.36 (d, $J$ = 8.5 Hz, 1H), 8.17 (dd, $J$ = 8.5, 4.2 Hz, 2H), 8.07 (d, $J$ = 8.8 Hz, 2H), 7.86 (d, $J$ = 8.2 Hz, 1H), 7.77 (t, $J$ = 7.5 Hz, 1H), 7.64 (t, $J$ = 7.5 Hz, 1H), 6.99 (d, $J$ = 8.9 Hz, 2H), 3.83 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 163.8, 147.4, 138.6, 131.2, 130.9, 130.4, 130.3, 129.0, 128.7, 127.6, 117.5, 114.3, 55.6.

**2-((4-fluorophenyl)sulfonyl)quinoline (3ah)[5]**



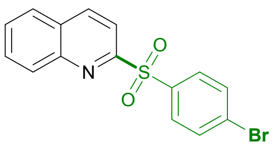

White solid; 86% yield; $^{1}$H NMR (400 MHz, Chloroform-$d$) δ 8.39 (d, $J$ = 8.5 Hz, 1H), 8.23 – 8.10 (m, 4H), 7.88 (d, $J$ = 8.2 Hz, 1H), 7.79 (t, $J$ = 7.7 Hz, 1H), 7.66 (t, $J$ = 7.5 Hz, 1H), 7.21 (t, $J$ = 8.5 Hz, 2H); $^{13}$C NMR (101 MHz, Chloroform-$d$) δ165.9 (d, $J_{C-F}$ = 257.6 Hz), 157.8, 147.3, 138.8, 134.9 (d, $J_{C-F}$ = 4.0 Hz), 131.9 (d, $J_{C-F}$ = 10.1 Hz), 131.1, 130.2, 129.3, 128.8, 127.7, 117.4, 116.4 (d, $J_{C-F}$ = 23.2 Hz); $^{19}$F NMR (376 MHz, Chloroform-$d$) δ -103.3.

**2-((4-chlorophenyl)sulfonyl)quinoline (3ai)[1]**



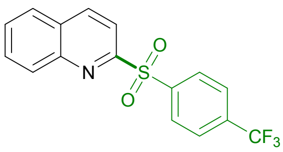

White solid; 88% yield; $^{1}$H NMR (400 MHz, Chloroform-$d$) δ 8.39 (d, $J$ = 8.5 Hz, 1H), 8.20 (d, $J$ = 8.5 Hz, 1H), 8.14 (d, $J$ = 8.6 Hz, 1H), 8.08 (d, $J$ = 8.6 Hz, 2H), 7.88 (d, $J$ = 8.1 Hz, 1H), 7.79 (t, $J$ = 7.7 Hz, 1H), 7.71 – 7.63 (m, 1H), 7.50 (d, $J$ = 8.6 Hz, 2H); $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 157.6, 147.4, 140.5, 138.9, 137.4, 131.1, 130.5, 130.2, 129.4, 129.3, 128.8, 127.7, 117.4.

**2-((4-bromophenyl)sulfonyl)quinoline (3aj)[4]**



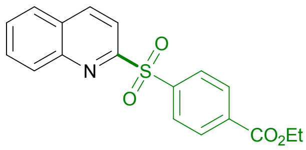

White solid; 87% yield; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, $J$ = 8.5 Hz, 1H), 8.20 (d, $J$ = 8.5 Hz, 1H), 8.15 (d, $J$ = 8.5 Hz, 1H), 8.00 (d, $J$ = 8.5 Hz, 2H), 7.89 (d, $J$ = 8.1 Hz, 1H), 7.80 (t, $J$ = 7.4 Hz, 1H), 7.72 – 7.65 (m, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 157.6, 147.4, 138.9, 138.0, 132.4, 131.1, 130.6, 130.3, 129.4, 129.2, 128.9, 127.7, 117.5.

**2-((4-(trifluoromethyl)phenyl)sulfonyl)quinoline (3ak)[6]**



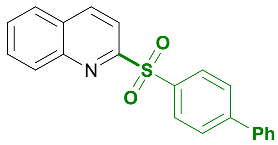
White solid; 81% yield; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, $J$ = 8.5 Hz, 1H), 8.28 (d, $J$ = 8.3 Hz, 2H), 8.24 (s, 1H), 8.13 (d, $J$ = 8.6 Hz, 1H), 7.89 (d, $J$ = 8.2 Hz, 1H), 7.79 (dt, $J$ = 7.0, 2.7 Hz, 3H), 7.67 (t, $J$ = 7.5 Hz, 1H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 157.2, 147.4, 142.6, 139.0, 135.2 (q, $J_{C\text{-}F}$ = 33.3 Hz), 131.2, 130.2, 129.6, 129.5, 128.9, 127.7, 126.1 (q, $J_{C\text{-}F}$ = 3.0 Hz), 123.1 (q, $J_{C\text{-}F}$ = 273.7 Hz), 117.5; $^{19}$F NMR (376 MHz, Chloroform-*d*) δ -63.2.

**ethyl 4-(quinolin-2-ylsulfonyl)benzoate (3al)[1]**



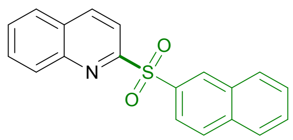

White solid; 83% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.40 (d, $J$ = 8.5 Hz, 1H), 8.26 – 8.16 (m, 5H), 8.14 (d, $J$ = 8.6 Hz, 1H), 7.89 (d, $J$ = 8.2 Hz, 1H), 7.79 (t, $J$ = 7.7 Hz, 1H), 7.67 (t, $J$ = 7.5 Hz, 1H), 4.39 (s, 2H), 1.38 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 165.0, 157.5, 147.4, 142.7, 138.9, 135.0, 131.1, 130.3, 130.1, 129.4, 129.1, 128.9, 127.7, 117.6, 61.7, 14.2.

**2-([1,1'-biphenyl]-4-ylsulfonyl)quinoline (3am)[2]**



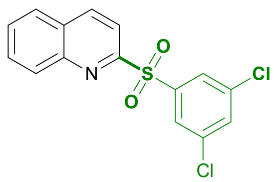

White solid; 80% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.40 (d, $J$ = 8.5 Hz, 1H), 8.24 (d, $J$ = 8.5 Hz, 1H), 8.22 – 8.18 (m, 3H), 7.89 (d, $J$ = 8.2 Hz, 1H), 7.80 (ddd, $J$ = 8.4, 6.9, 1.4 Hz, 1H), 7.76 – 7.71 (m, 2H), 7.67 (t, $J$ = 7.5 Hz, 1H), 7.61 – 7.54 (m, 2H), 7.48 – 7.36 (m, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 158.2, 147.5, 146.7, 139.2, 138.8, 137.6, 131.0, 130.4, 129.6, 129.2, 129.0, 128.9, 128.6, 127.7, 127.7, 127.4, 117.7.

**2-(naphthalen-2-ylsulfonyl)quinoline (3an)[2]**



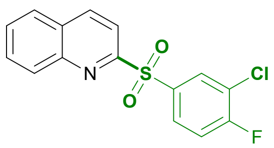

White solid; 84% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.75 (s, 1H), 8.38 (dd, $J$ = 8.3, 3.4 Hz, 1H), 8.27 (d, $J$ = 8.5 Hz, 1H), 8.16 (d, $J$ = 9.9 Hz, 1H), 8.08 (d, $J$ = 8.7 Hz, 1H), 8.03 – 7.91 (m, 2H), 7.92 – 7.82 (m, 2H), 7.81 – 7.71 (m, 1H), 7.70 – 7.55 (m, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 158.1, 147.4, 138.8, 138.7, 136.0, 135.3, 132.1, 131.0, 130.8, 130.3, 129.5, 129.3, 129.2, 128.8, 127.9, 127.7, 127.5, 123.7, 117.8.

**2-((3,5-dichlorophenyl)sulfonyl)quinoline (3ao)[7]**



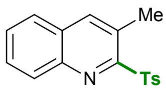

White solid; 81% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.42 (d, $J$ = 8.8 Hz, 1H), 8.20 (d, $J$ = 8.5 Hz, 1H), 8.16 (d, $J$ = 9.3 Hz, 1H), 8.01 (d, $J$ = 1.9 Hz, 2H), 7.90 (dd, $J$ = 8.2, 1.1 Hz, 1H), 7.81 (ddd, $J$ = 8.5, 6.9, 1.5 Hz, 1H), 7.69 (ddd, $J$ = 8.2, 6.9, 1.2 Hz, 1H), 7.54 (t, $J$ = 1.9 Hz, 1H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 156.8, 147.4, 141.8, 139.1, 135.9, 133.7, 131.3, 130.3, 129.6, 129.0, 127.7, 127.3, 117.5.

**2-((3-chloro-4-fluorophenyl)sulfonyl)quinoline (3ap)[7]**



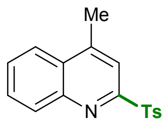
White solid; 87% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.41 (d, *J* = 8.5 Hz, 1H), 8.24 – 8.18 (m, 2H), 8.15 (d, *J* = 8.6 Hz, 1H), 8.06 (ddd, *J* = 8.6, 4.4, 2.3 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.81 (t, *J* = 7.7 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.30 (t, *J* = 8.5 Hz, 1H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 161.3 (d, $J_{C\text{-}F}$ = 259.6 Hz), 157.3, 147.4, 139.0, 135.9 (d, $J_{C\text{-}F}$ = 3.9 Hz), 132.0 (d, $J_{C\text{-}F}$ = 1.6 Hz), 131.2, 130.2, 129.8 (d, $J_{C\text{-}F}$ = 8.9 Hz), 129.4, 128.9, 127.7, 122.5 (d, $J_{C\text{-}F}$ = 19.0 Hz), 117.4 (d, $J_{C\text{-}F}$ = 22.6 Hz), 117.3; $^{19}$F NMR (376 MHz, Chloroform-*d*) δ -105.5.

**3-methyl-2-tosylquinoline (3ba)[8]**



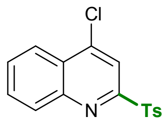
White solid; 82% yield; $^1$H NMR (400 MHz, ) δ 8.05 (s, 1H), 7.96 – 7.89 (m, 3H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 2H), 2.86 (s, 3H), 2.46(s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 157.0, 144.7, 144.5, 139.8, 135.8, 129.9, 129.7, 129.4, 129.1, 128.9, 128.5, 126.6, 21.7, 18.8.

**4-methyl-2-tosylquinoline (3ca)[9]**



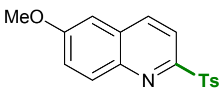
White solid; 83% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.17 (d, *J* = 8.4 Hz, 1H), 8.07 – 7.98 (m, 4H), 7.76 (t, *J* = 7.7 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 2H), 2.78 (s, 3H), 2.39 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 157.9, 147.9, 147.2, 144.7, 136.2, 131.0, 130.5, 129.7, 129.0, 128.8, 128.7, 123.8, 118.1, 21.6, 19.2.

**4-chloro-2-tosylquinoline (3da)[1]**



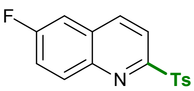
White solid; 86% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.28 (s, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 2H), 7.83 (t, *J* = 7.1 Hz, 1H), 7.75 (t, *J* = 7.3 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 2.41 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 158.1, 148.1, 145.2, 135.5, 131.7, 130.8, 130.1, 129.9, 129.1, 127.0, 124.2, 117.9, 21.7.

**6-methoxy-2-tosylquinoline (3ea)[2]**



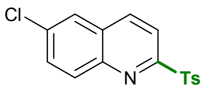
White solid; 81% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.21 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 8.05 (d, *J* = 9.3 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 2H), 7.41 (dd, *J* = 9.3, 2.7 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 2.7 Hz, 1H), 3.94 (s, 3H), 2.40 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 159.7, 155.7, 144.6, 143.6, 136.8, 136.5, 131.8, 130.3, 129.7, 128.9, 124.2, 118.2, 104.5, 55.7, 21.6.

**6-fluoro-2-tosylquinoline(3fa)[10]**



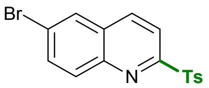
White solid; 84% yield; $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 8.6 Hz, 1H), 8.21 – 8.11 (m, 2H), 7.99 (d, *J* = 8.2 Hz, 2H), 7.55 – 7.43 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 2.37 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 161.7 (d, *J* = 253.5 Hz), 157.7, 144.9, 144.3, 138.0 (d, *J* = 5.9 Hz), 135.8, 132.9 (d, *J* = 9.5 Hz), 129.7, 129.6 (d, *J* = 11.1 Hz), 128.9, 121.5 (d, *J* = 26.3 Hz), 118.4, 110.7 (d, *J* = 22.1 Hz), 21.5; $^{19}$F NMR (376 MHz, Chloroform-*d*) δ -108.3.

**6-chloro-2-tosylquinoline (3ga)[1]**



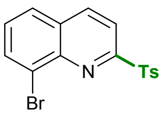

White solid; 84% yield; $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 8.3 (d, *J* = 8.6 Hz, 1H), 8.2 (d, *J* = 8.6 Hz, 1H), 8.1 (d, *J* = 9.1 Hz, 1H), 8.0 (d, *J* = 8.3 Hz, 2H), 7.9 (d, *J* = 2.2 Hz, 1H), 7.7 (dd, *J* = 9.1, 2.2 Hz, 1H), 7.3 (d, *J* = 8.1 Hz, 2H), 2.4 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 158.6, 145.7, 145.0, 137.7, 135.7, 135.2, 132.0, 131.9, 129.8, 129.3, 129.1, 126.3, 118.6, 21.7.

**6-bromo-2-tosylquinoline (3ha)[7]**



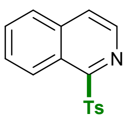

White solid; 82% yield; $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 8.28 (d, *J* = 8.6 Hz, 1H), 8.21 (d, *J* = 8.6 Hz, 1H), 8.05 – 8.01 (m, 3H), 7.99 (s, 1H), 7.84 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 2.41 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 158.7, 145.9, 145.0, 137.6, 135.7, 134.5, 131.9, 129.8, 129.7, 129.1, 123.5, 118.6, 21.7.

**8-bromo-2-tosylquinoline (3ia)[3]**



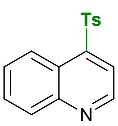

White solid; 81% yield; $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 8.29 (d, *J* = 8.5 Hz, 1H), 8.20 – 8.13 (m, 1H), 8.06 (d, *J* = 8.0 Hz, 2H), 7.99 (t, *J* = 7.4 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 7.8 Hz, 2H), 2.35 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 159.3, 145.0, 144.4, 139.2, 135.2, 134.5, 129.9, 129.8, 129.5, 129.3, 127.4, 125.8, 117.7, 21.7.

**1-tosylisoquinoline (3ja)[3]**



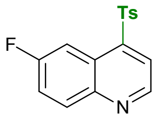

White solid; 85% yield; $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.20 – 9.13 (m, 1H), 8.43 (d, *J* = 5.5 Hz, 1H), 7.97 (d, *J* = 8.2 Hz, 2H), 7.94 – 7.86 (m, 1H), 7.80 – 7.72 (m, 3H), 7.35 (d, *J* = 8.1 Hz, 2H), 2.43 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 157.3, 144.7, 140.5, 137.7, 136.0, 131.1, 129.6, 129.2 (d, *J* = 5.1 Hz), 127.5, 125.3, 124.9, 124.3, 77.3, 77.0, 76.7, 21.7.

**4-tosylquinoline (3ka)[11]**



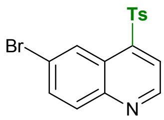

White solid; 90% yield; $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.11 (d, *J* = 4.3 Hz, 1H), 8.65 (d, *J* = 8.4 Hz, 1H), 8.22 – 8.11 (m, 2H), 7.88 (d, *J* = 8.3 Hz, 2H), 7.77 (t, *J* = 8.2 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 8.2 Hz, 2H), 2.38 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 149.6, 149.3, 145.1, 145.1, 137.1, 130.5, 130.3, 130.1, 128.8, 128.0, 124.2, 122.1, 121.0, 21.6.

**6-fluoro-4-tosylquinoline (3la)[3]**



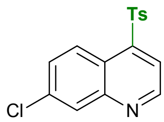

White solid; 88% yield; $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.07 (d, *J* = 4.4 Hz, 1H), 8.31 (dd, *J* = 10.2, 2.7 Hz, 1H), 8.19 (dd, *J* = 10.2, 5.0 Hz, 2H), 7.87 (d, *J* = 8.3 Hz, 2H), 7.54 (ddd, *J* = 9.3, 7.9, 2.8 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 2.39 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 161.3 (d, $J_{C\text{-}F}$ = 253.5 Hz), 148.9 (d, $J_{C\text{-}F}$ = 3.0 Hz), 146.6, 145.4, 144.8 (d, $J_{C\text{-}F}$ = 253.5 Hz), 136.7, 133.1 (d, $J_{C\text{-}F}$ = 10.1 Hz), 130.2, 128.0, 123.1 (d, $J_{C\text{-}F}$ = 11.1 Hz), 121.8, 120.8 (d, $J_{C\text{-}F}$ = 25.3 Hz), 108.5 (d, $J_{C\text{-}F}$ = 25.3 Hz), 21.6; $^{19}$F NMR (376 MHz, Chloroform-*d*) δ -106.9.

**6-bromo-4-tosylquinoline (3ma)[3]**



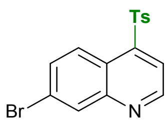

White solid; 85% yield; $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.10 (d, *J* = 4.4 Hz, 1H), 8.86 (d, *J* = 1.8 Hz, 1H), 8.14 (d, *J* = 4.3 Hz, 1H), 8.05 (d, *J* = 9.0 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 2H), 7.84 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 2.40 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 149.9, 147.8, 145.5, 144.5, 136.7, 134.1, 132.0, 130.2, 128.1, 126.7, 123.5, 123.1, 121.7, 21.7.

**7-chloro-4-tosylquinoline (3na)[3]**



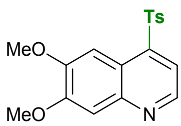

White solid; 81% yield; $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.10 (d, *J* = 4.4 Hz, 1H), 8.62 (d, *J* = 9.2 Hz, 1H), 8.17 (d, *J* = 2.0 Hz, 1H), 8.10 (d, *J* = 4.4 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.59 (dd, *J* = 9.2, 2.1 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 2.38 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 150.8, 149.7, 145.5, 145.4, 136.8, 136.5, 130.1, 129.7, 129.4, 128.0, 125.6, 121.0, 120.5, 21.6.

**7-bromo-4-tosylquinoline (3oa)[11]**



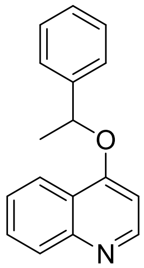

White solid; 88% yield; $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.09 (d, *J* = 4.4 Hz, 1H), 8.54 (d, *J* = 9.1 Hz, 1H), 8.36 (d, *J* = 2.0 Hz, 1H), 8.13 (d, *J* = 4.4 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.73 (dd, *J* = 9.1, 2.0 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 2.39 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 150.7, 149.8, 145.6, 145.4, 136.8, 132.7, 130.2, 128.0, 125.6, 124.8, 121.2, 120.8, 21.6.

**6,7-dimethoxy-4-tosylquinoline (3pa)[3]**




White solid; 94% yield; $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 8.87 (d, *J* = 4.6 Hz, 1H), 7.99 (d, *J* = 4.6 Hz, 1H), 7.93 – 7.80 (m, 3H), 7.45 (s, 1H), 7.29 (d, *J* = 8.1 Hz, 2H), 4.11 – 3.93 (m, 6H), 2.37 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 152.7, 151.1, 147.2, 147.1, 145.0, 142.7, 137.4, 129.9, 127.7, 118.9, 118.2, 108.7, 101.9, 56.2, 56.1, 21.6.

**4-(1-phenylethoxy)quinoline (4a)[12]**



White solid; 75% yield; $^1$H NMR (400 MHz, Chloroform-*d*) δ 8.58 (d, *J* = 5.3 Hz, 1H), 8.38 (d, *J* = 9.3 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.71 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.55 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 7.42 – 7.32 (m, 4H), 7.29 (t, *J* = 7.1 Hz, 1H), 6.57 (d, *J* = 5.3 Hz, 1H), 5.58 (q, *J* = 6.4 Hz, 1H), 1.81 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-*d*) δ 160.4, 151.0, 149.1, 141.7, 128.8, 128.7, 127.9, 125.6, 125.2, 122.0, 121.7, 102.6, 76.7, 24.3.

## 4. References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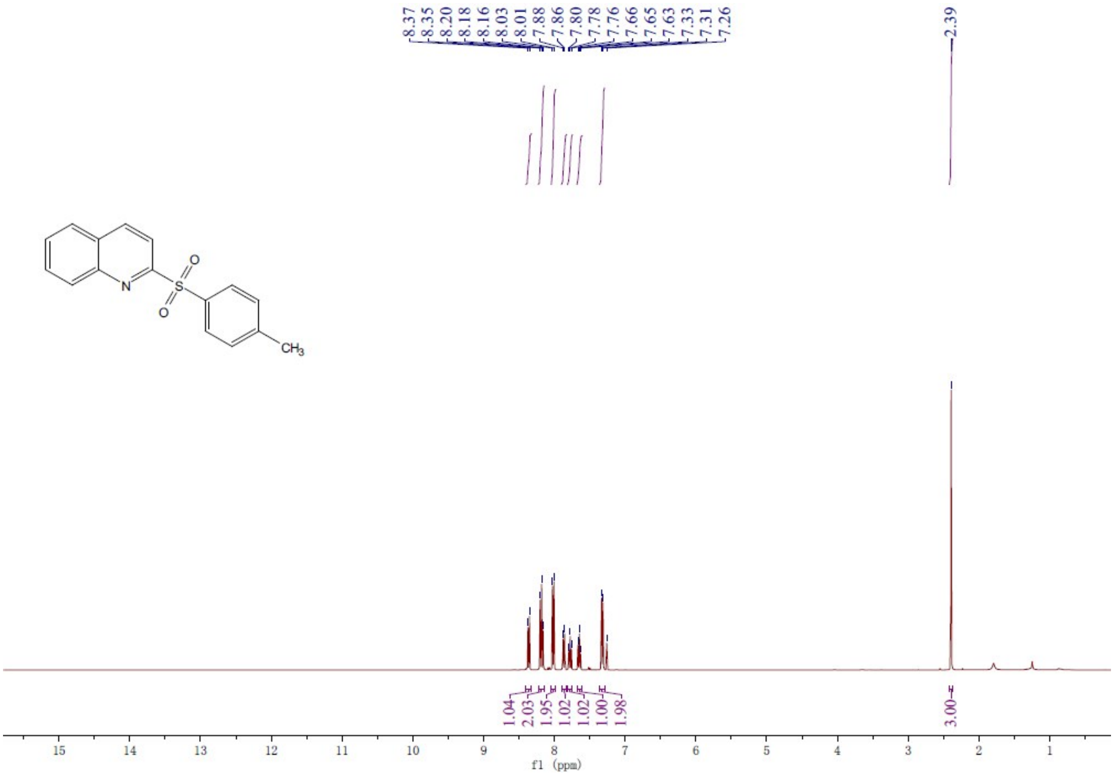
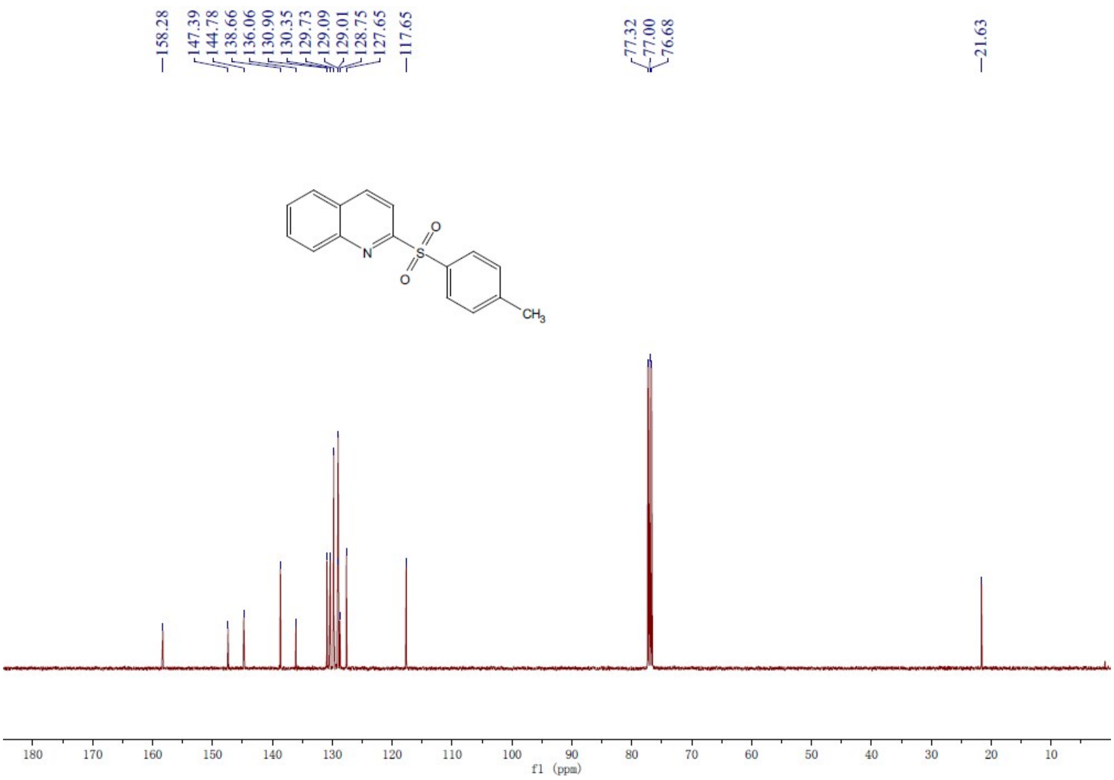
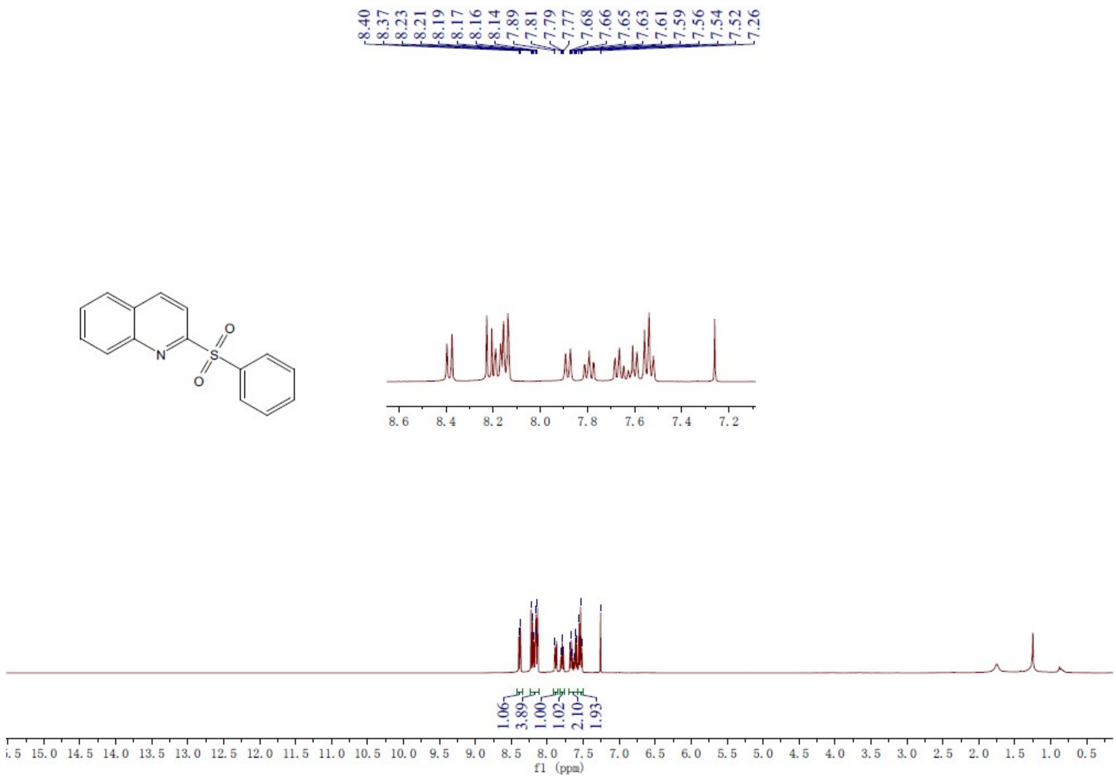
## 5. $^{1}H$ and $^{13}C$ NMR spectra of products



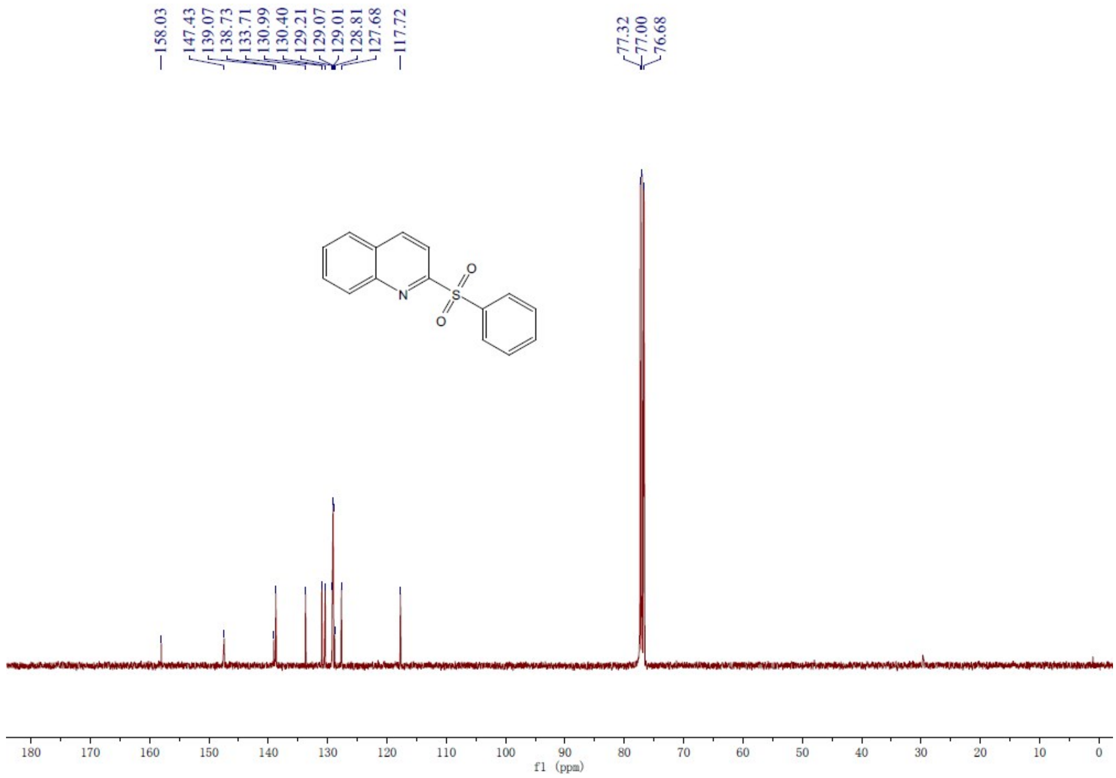

$^{1}H$ spectrum of **3aa**



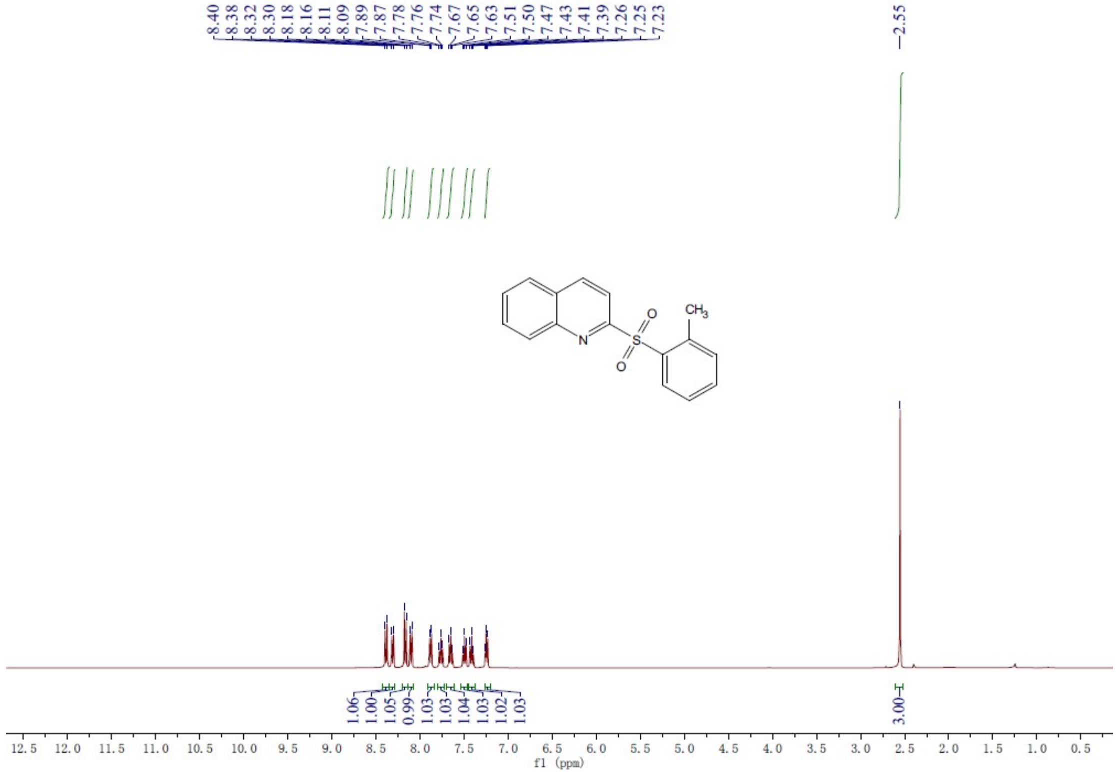

$^{13}C$ spectrum of **3aa**



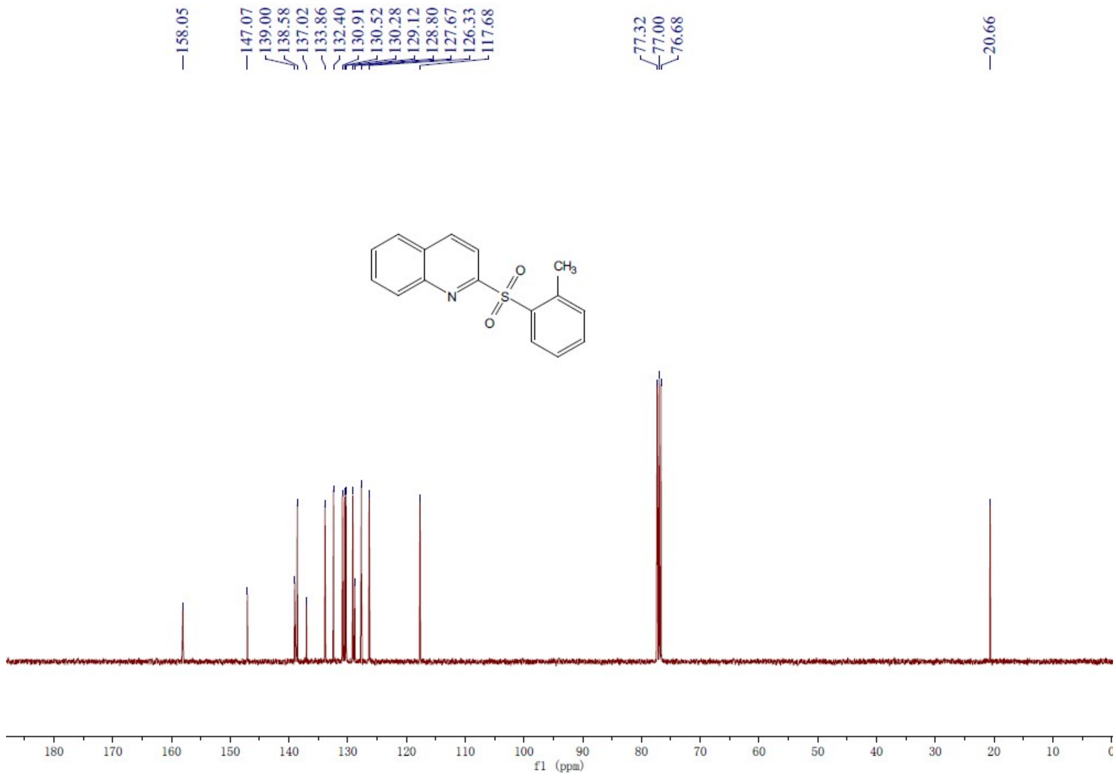

$^{1}$H spectrum of **3ab**



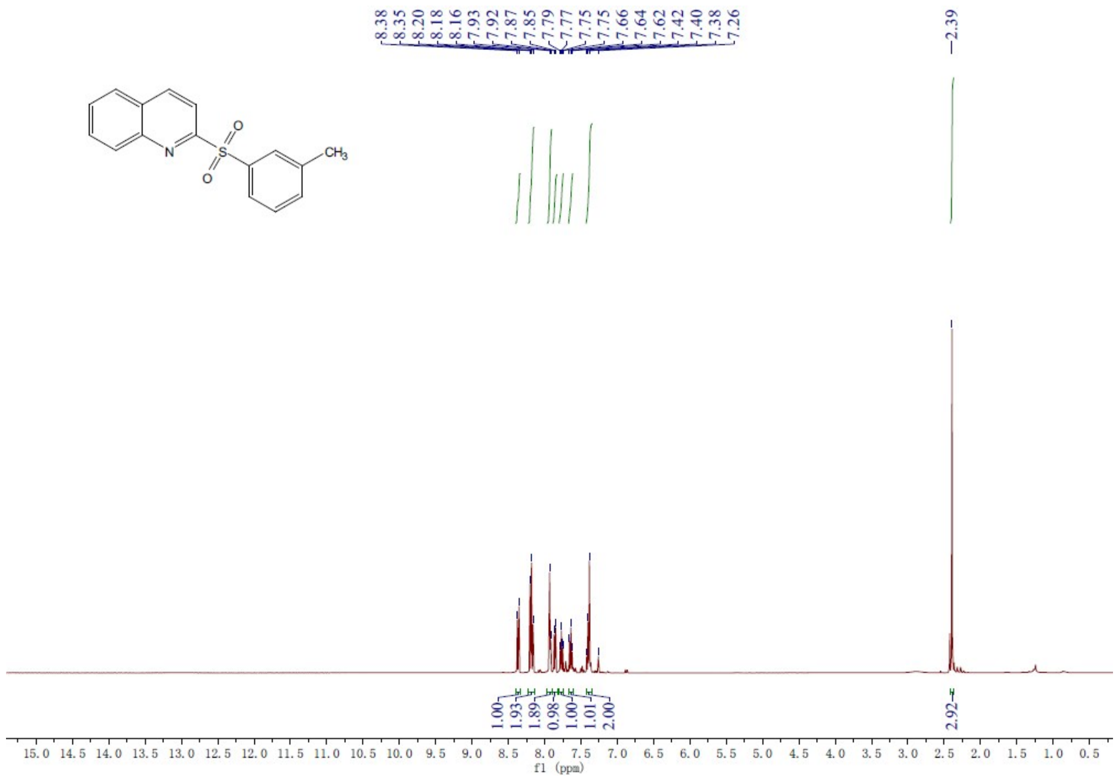

$^{13}$C spectrum of **3ab**



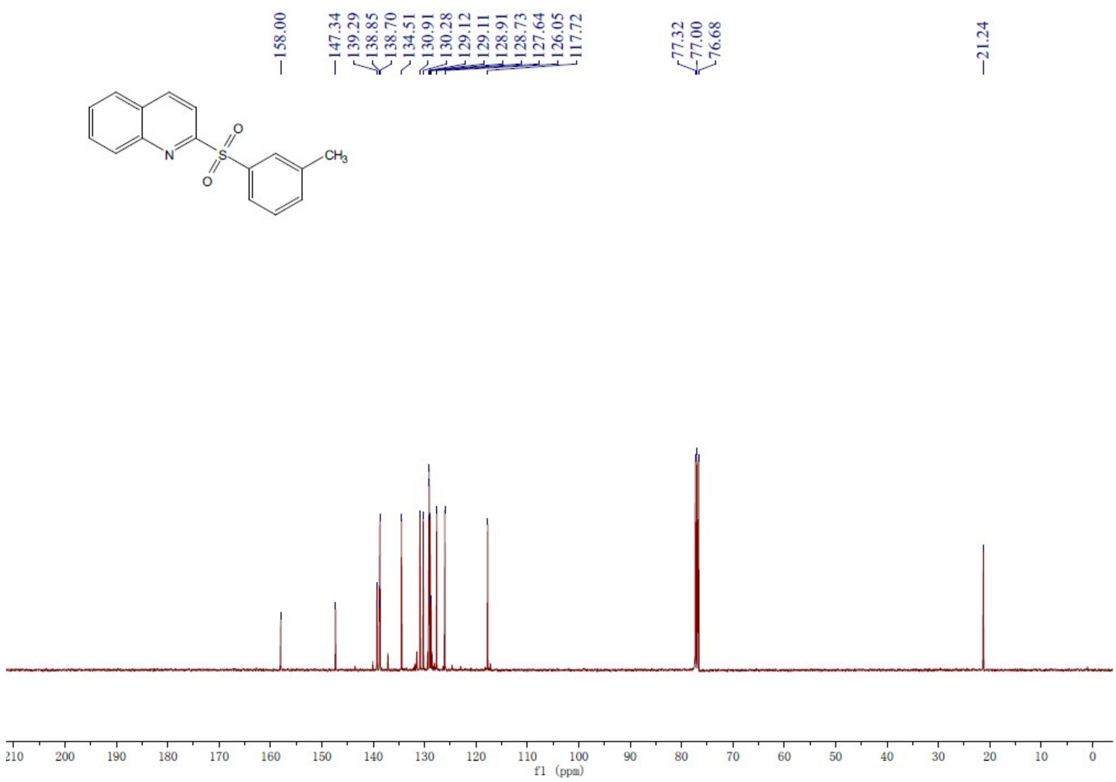

[1]H spectrum of **3ac**



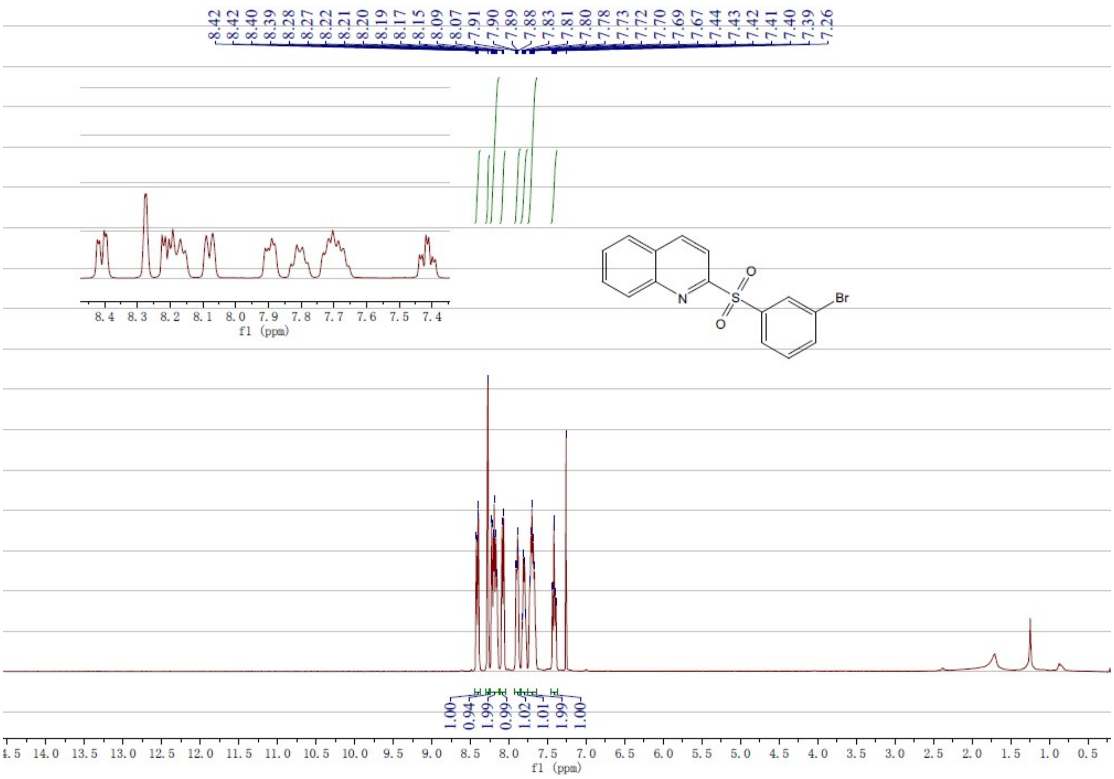

[13]C spectrum of **3ac**



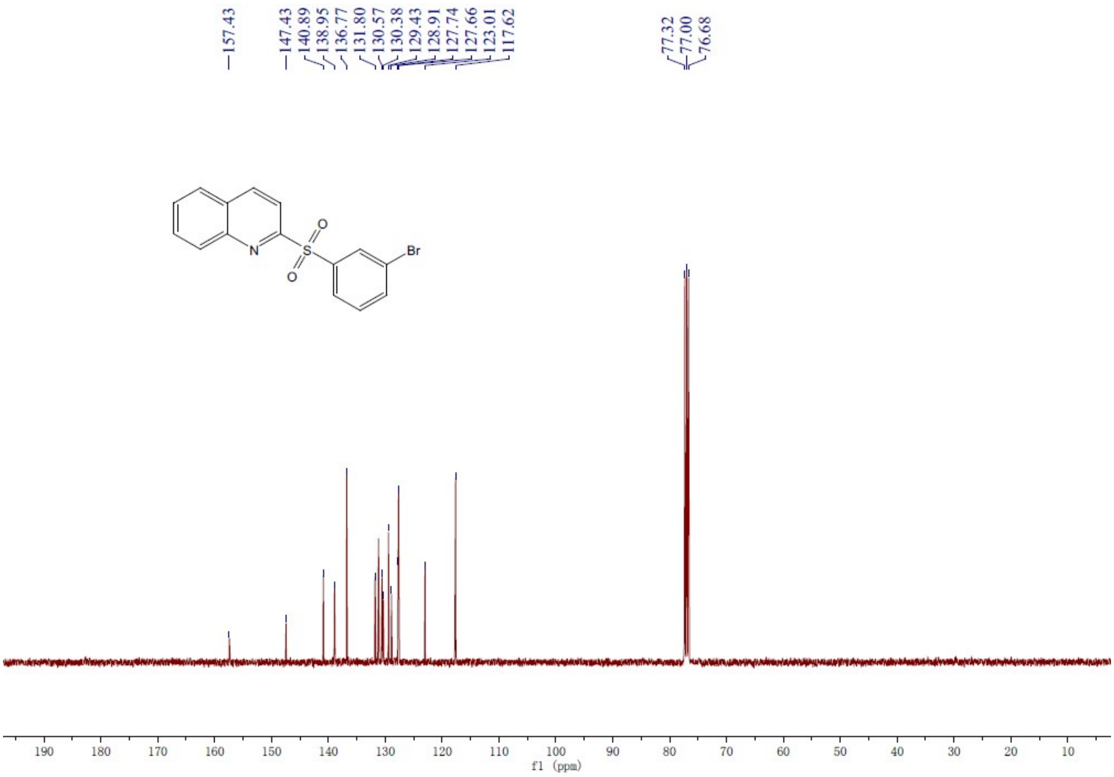
[1]H spectrum of **3ad**



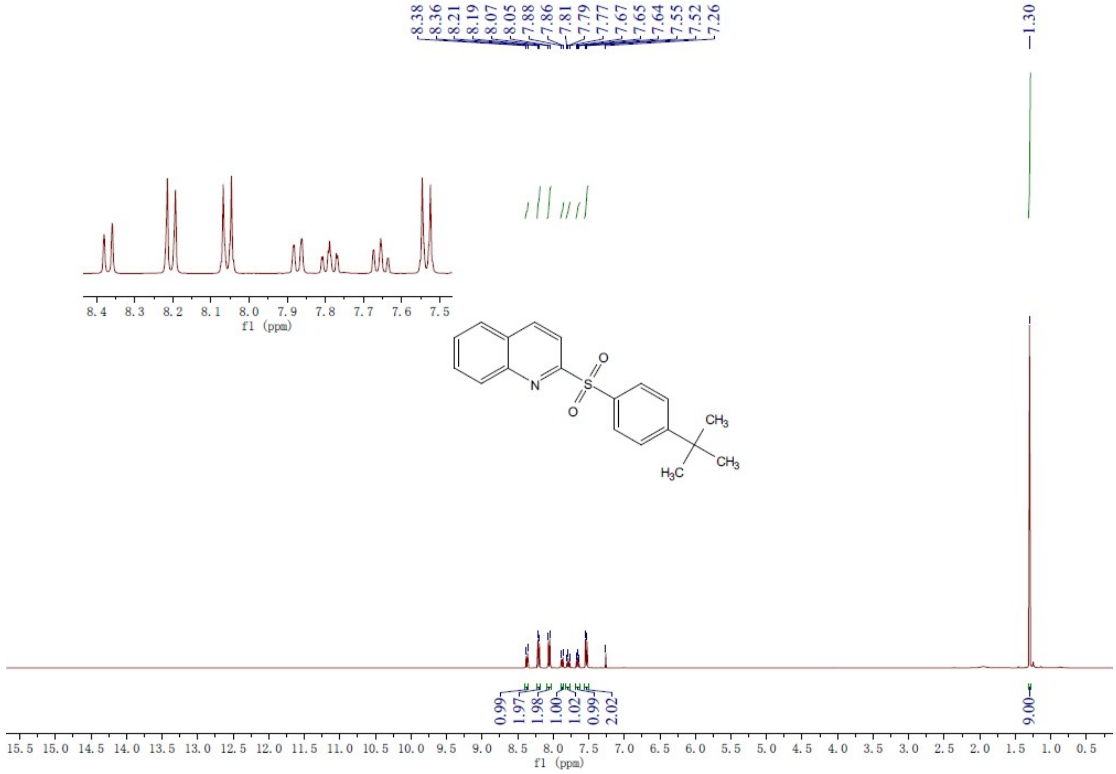
[13]C spectrum of **3ad**



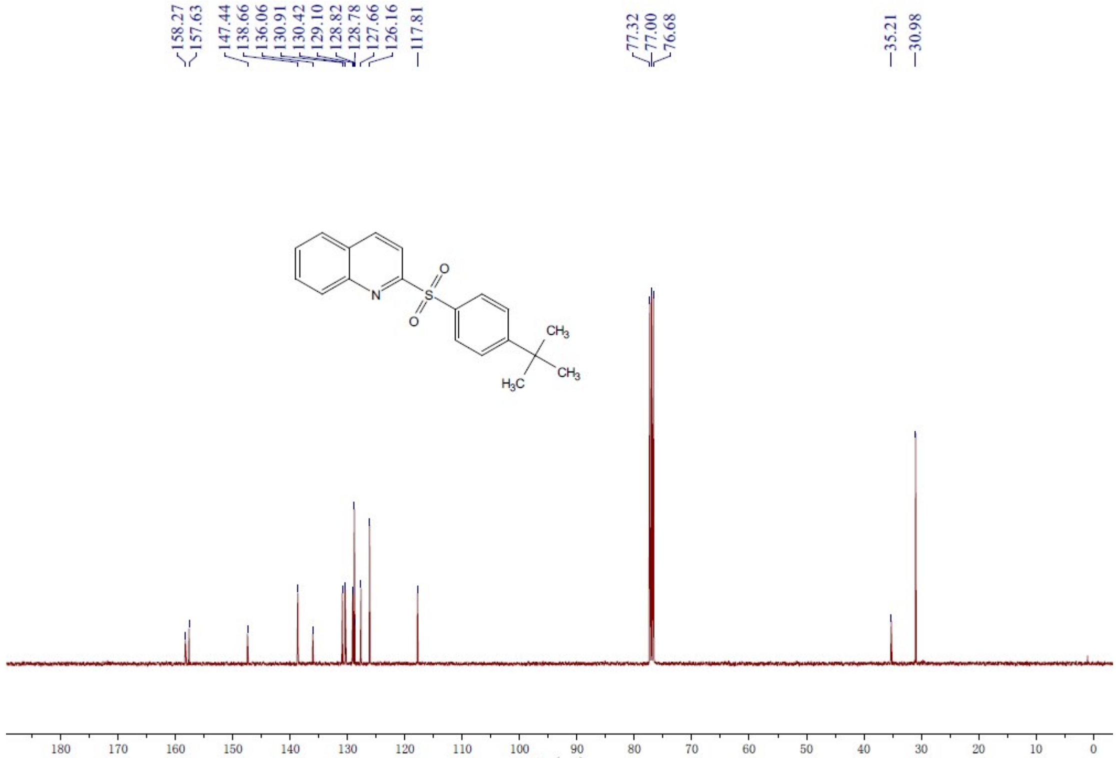

[1]H spectrum of **3ae**



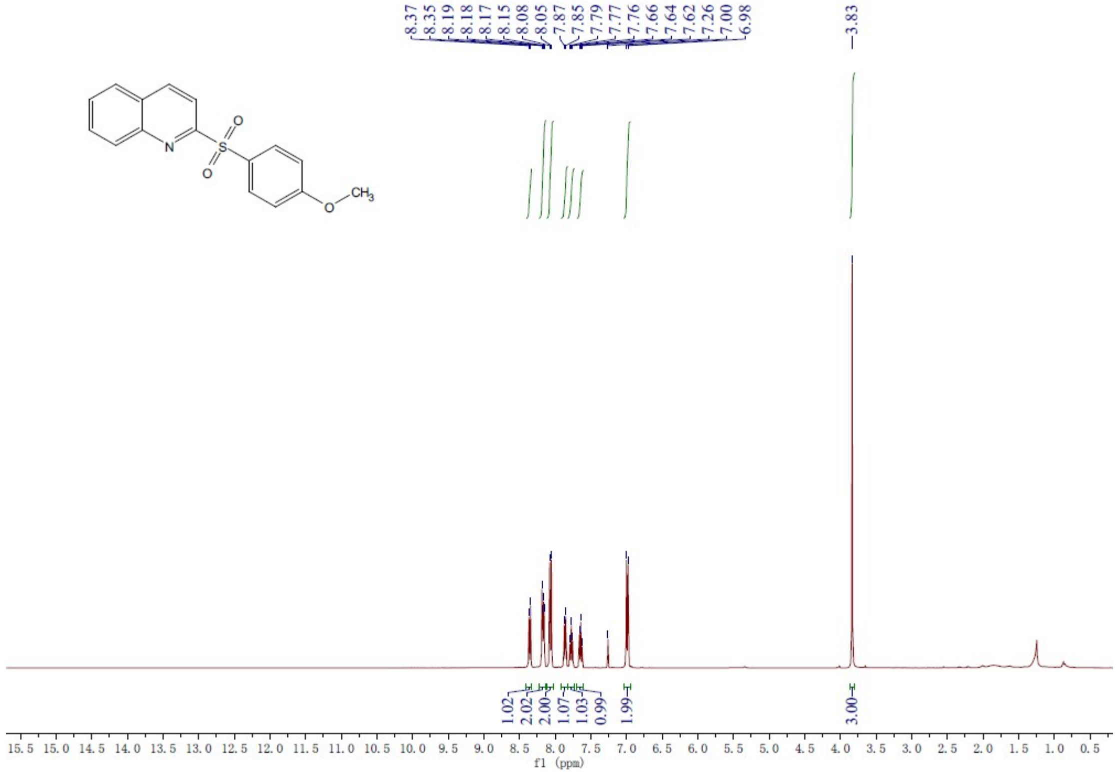

[13]C spectrum of **3ae**



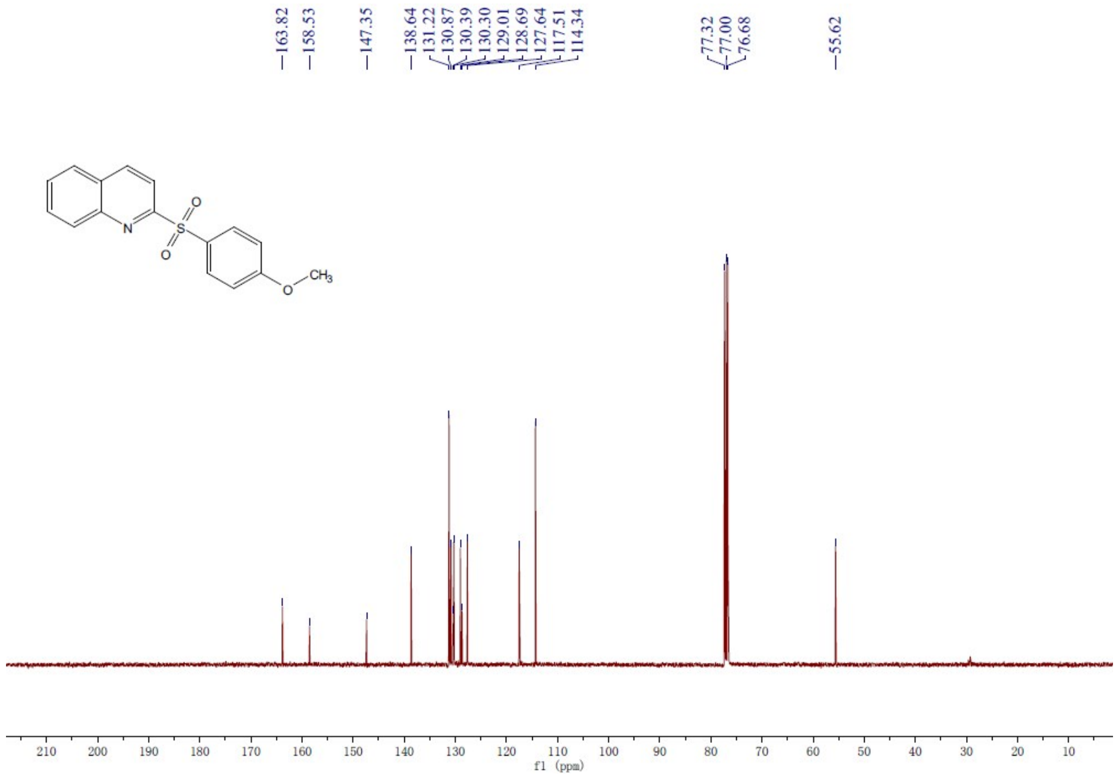
¹H spectrum of **3af**



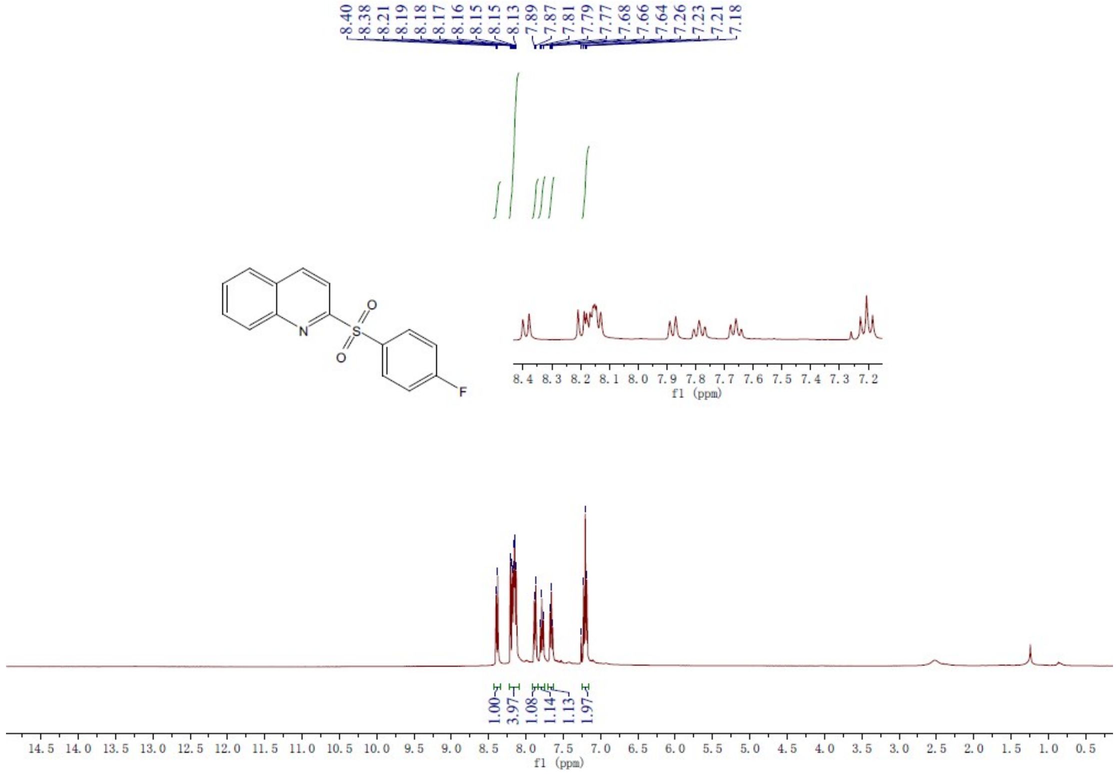
¹³C spectrum of **3af**



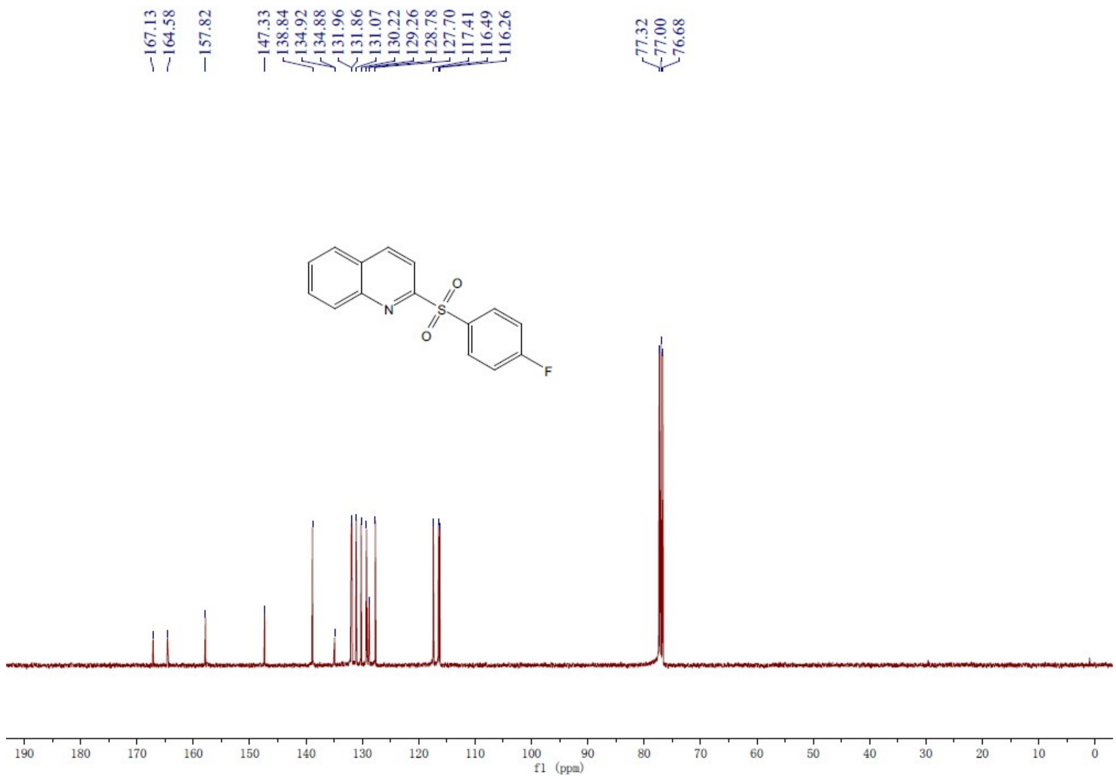

[1]H spectrum of **3ag**



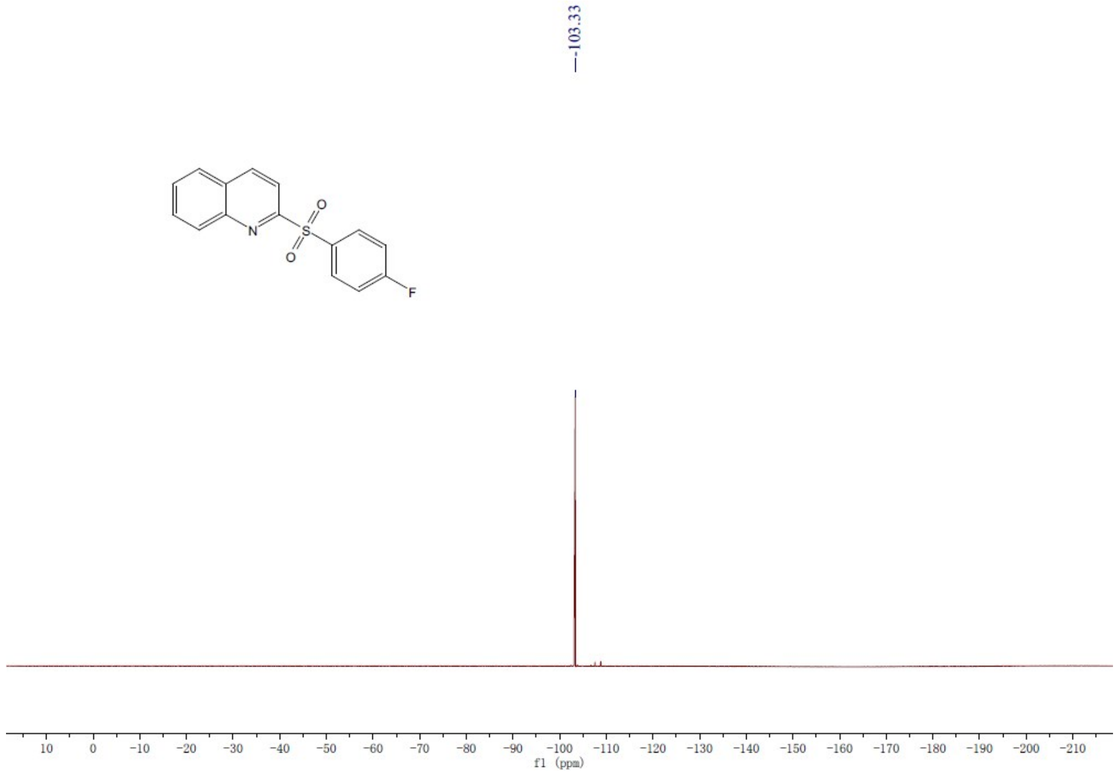

[13]C spectrum of **3ag**



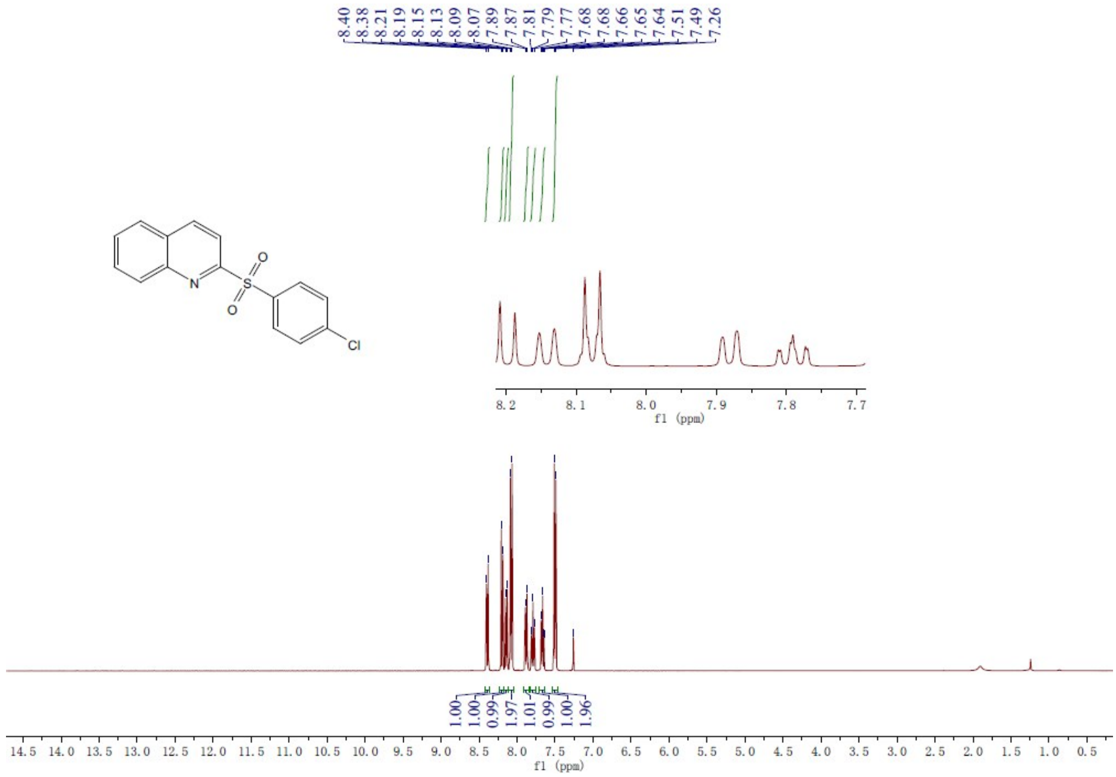
$^{1}H$ spectrum of **3ah**



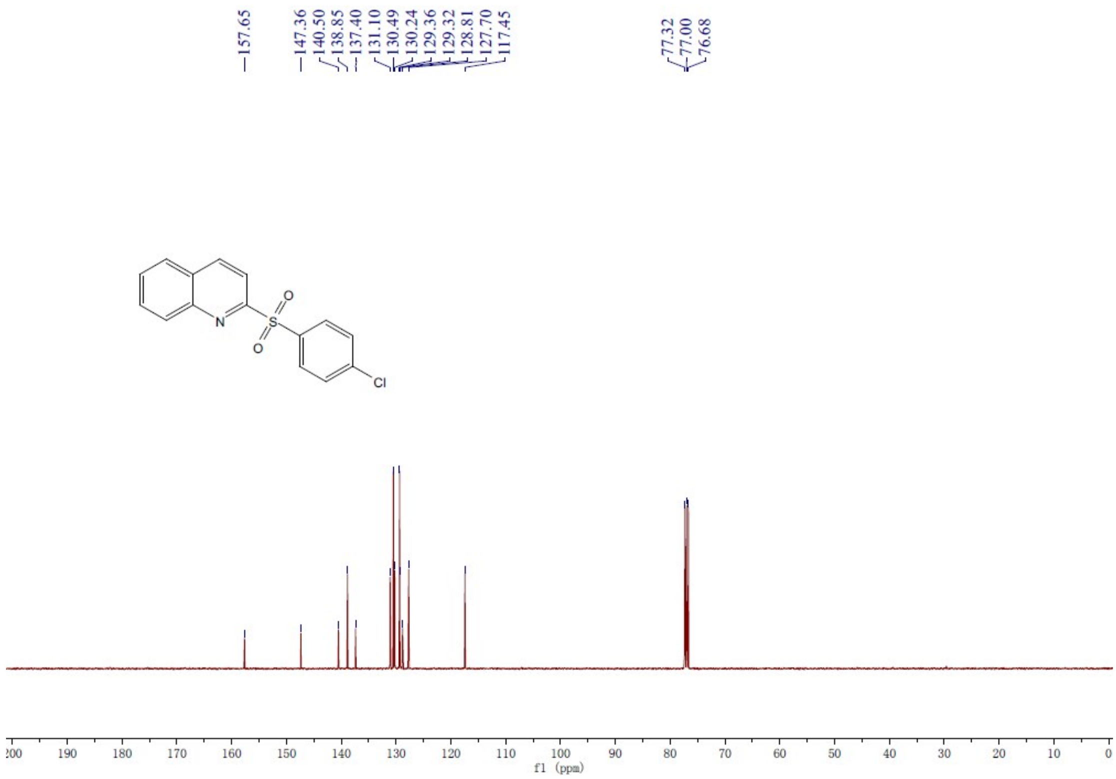
$^{13}C$ spectrum of **3ah**



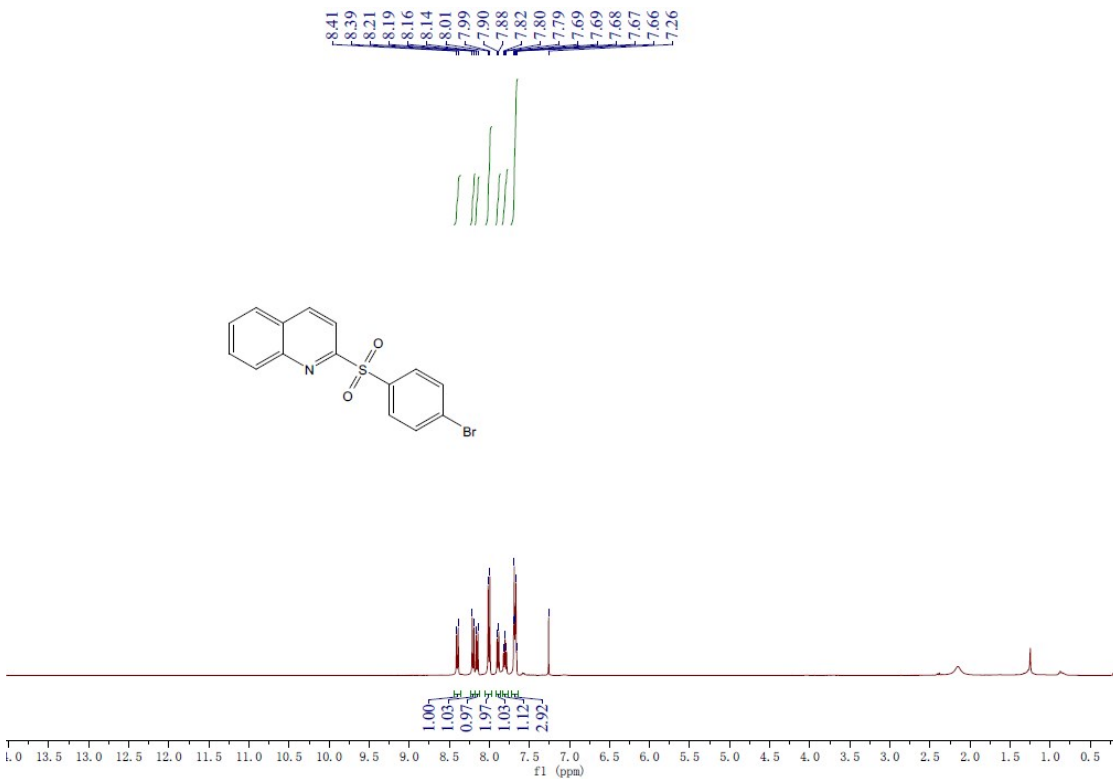

$^{19}$F spectrum of **3ah**



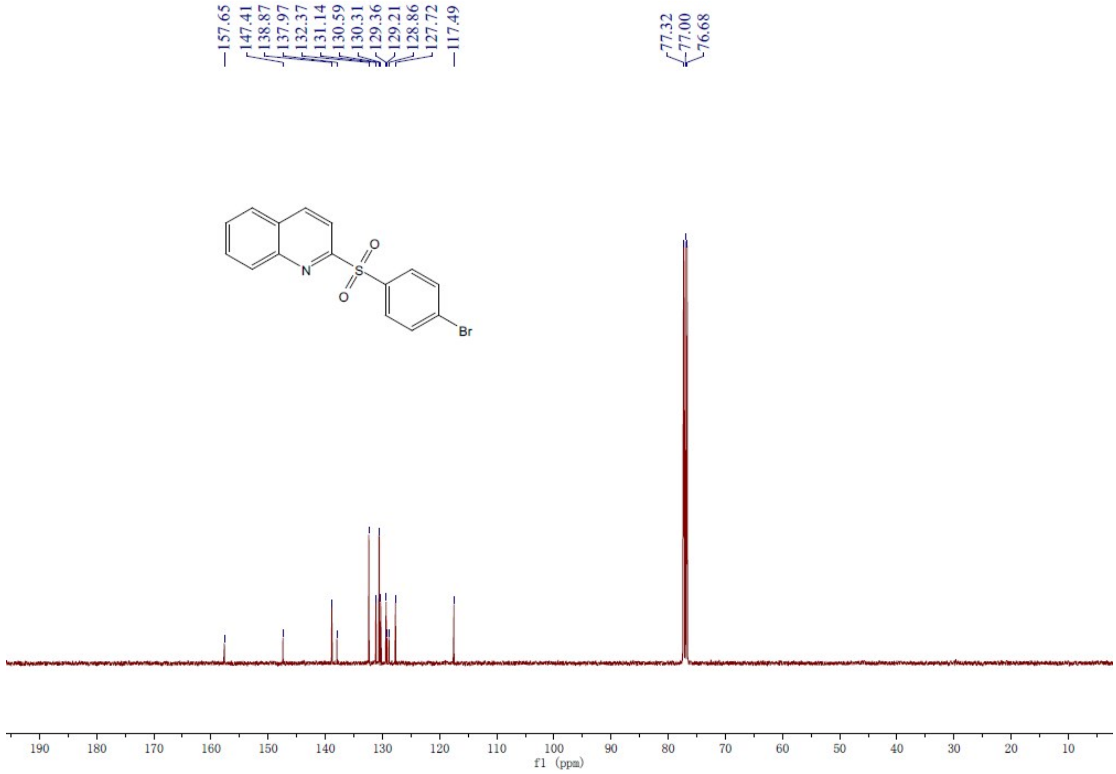

$^{1}$H spectrum of **3ai**



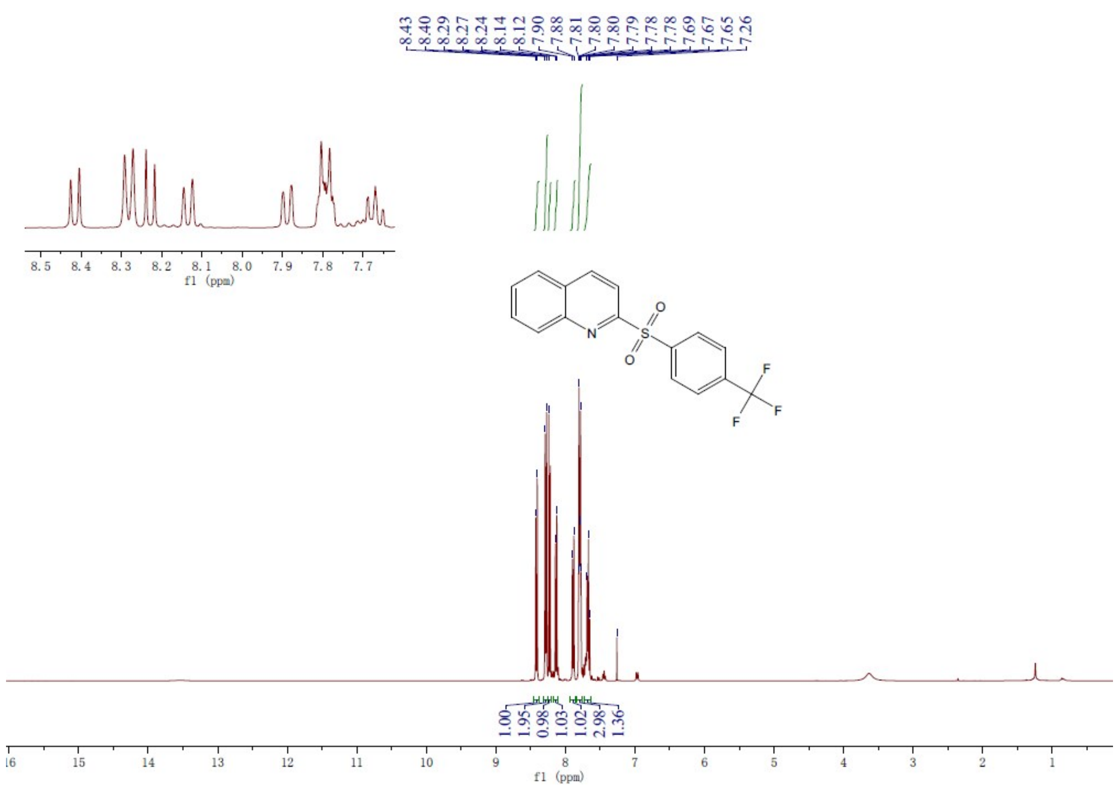

$^{13}$C spectrum of **3ai**



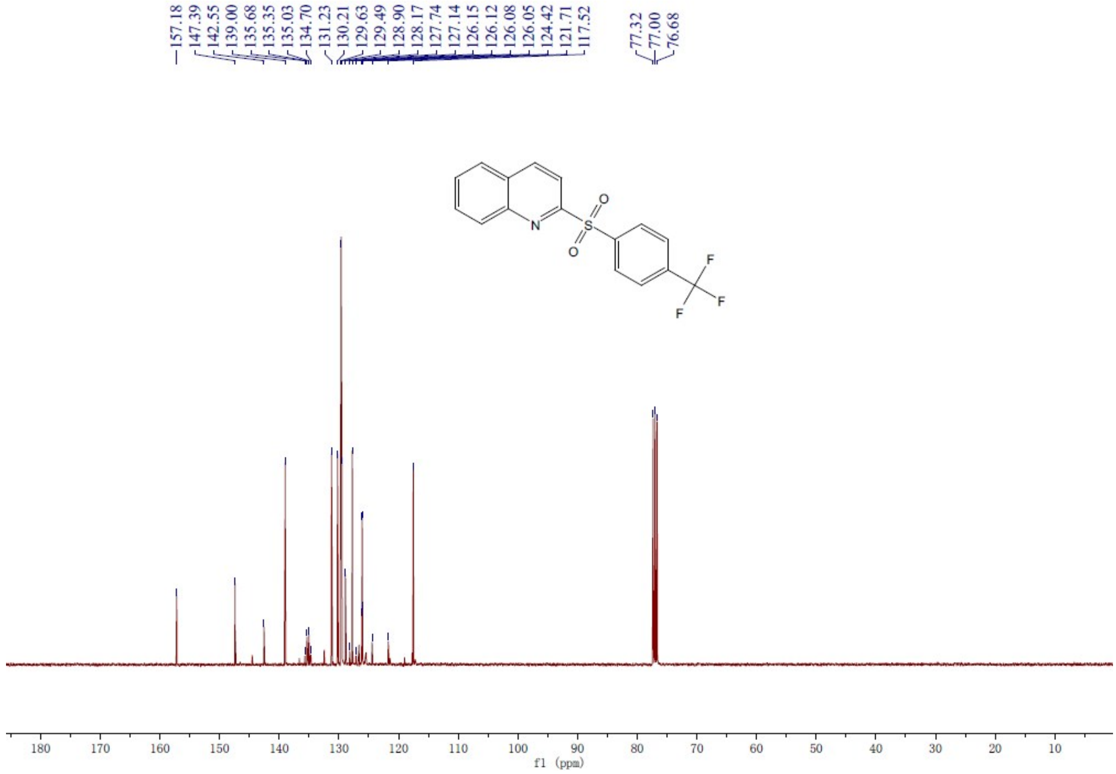

$^{1}$H spectrum of **3aj**



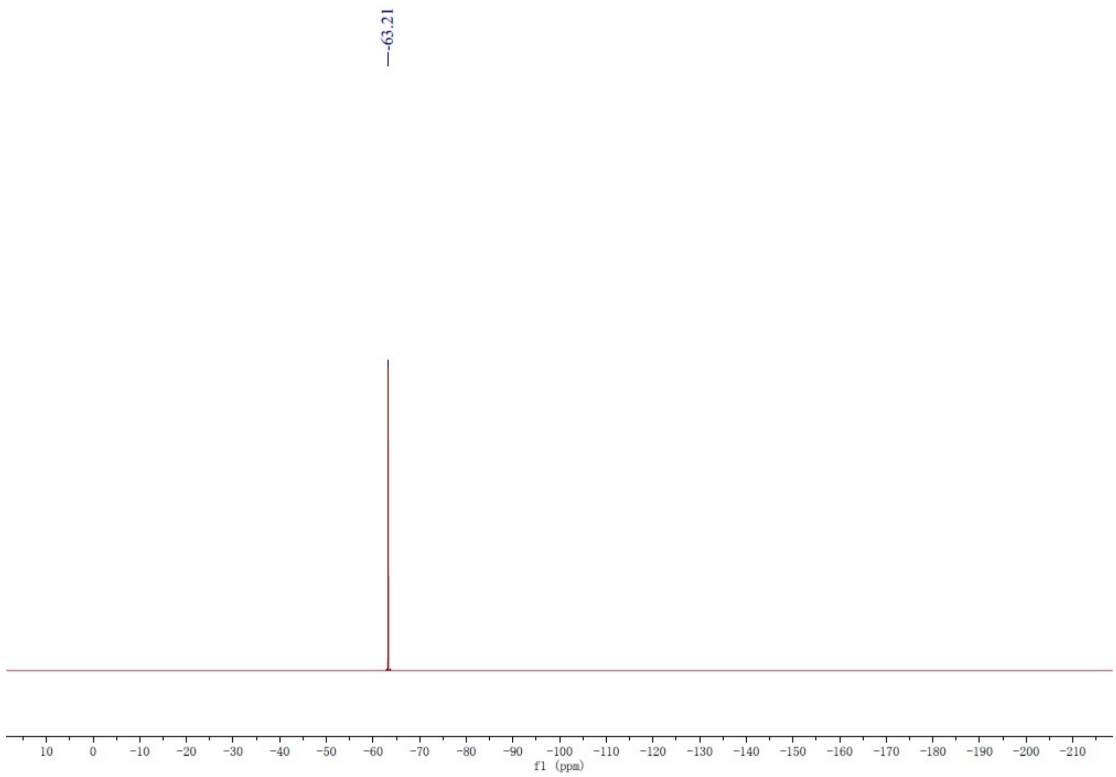
$^{13}C$ spectrum of **3aj**



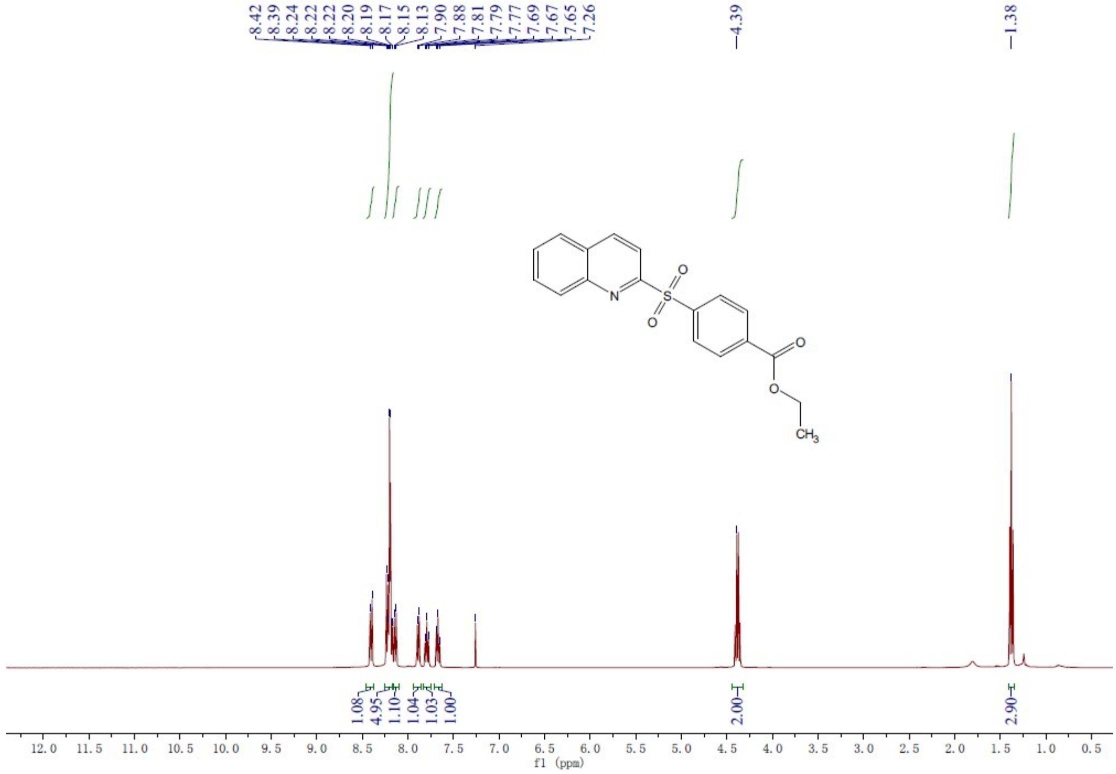
$^{1}H$ spectrum of **3ak**



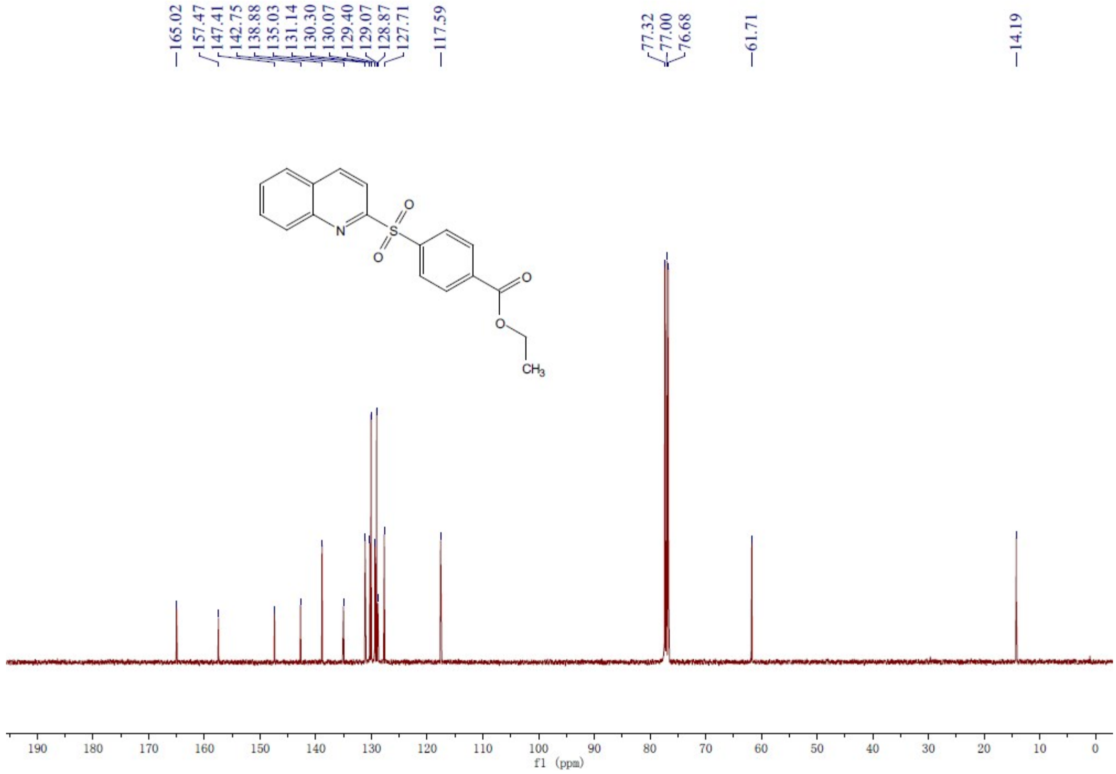

$^{13}$C spectrum of **3ak**



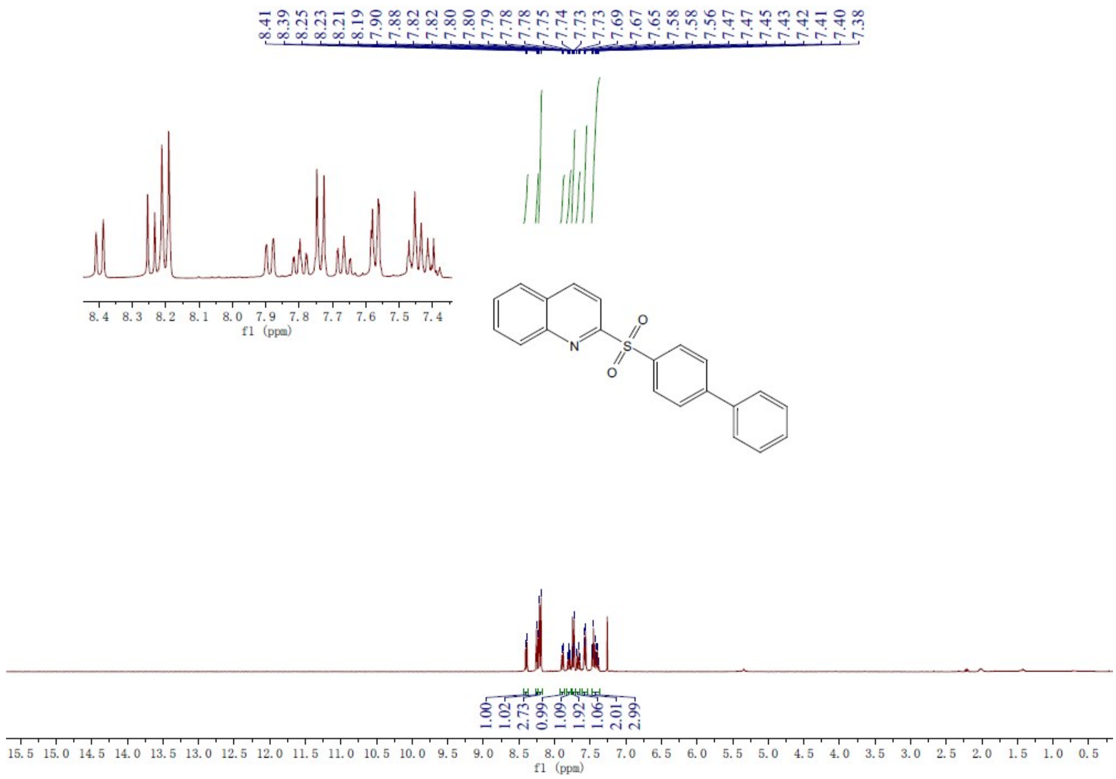

$^{19}$F spectrum of **3ak**



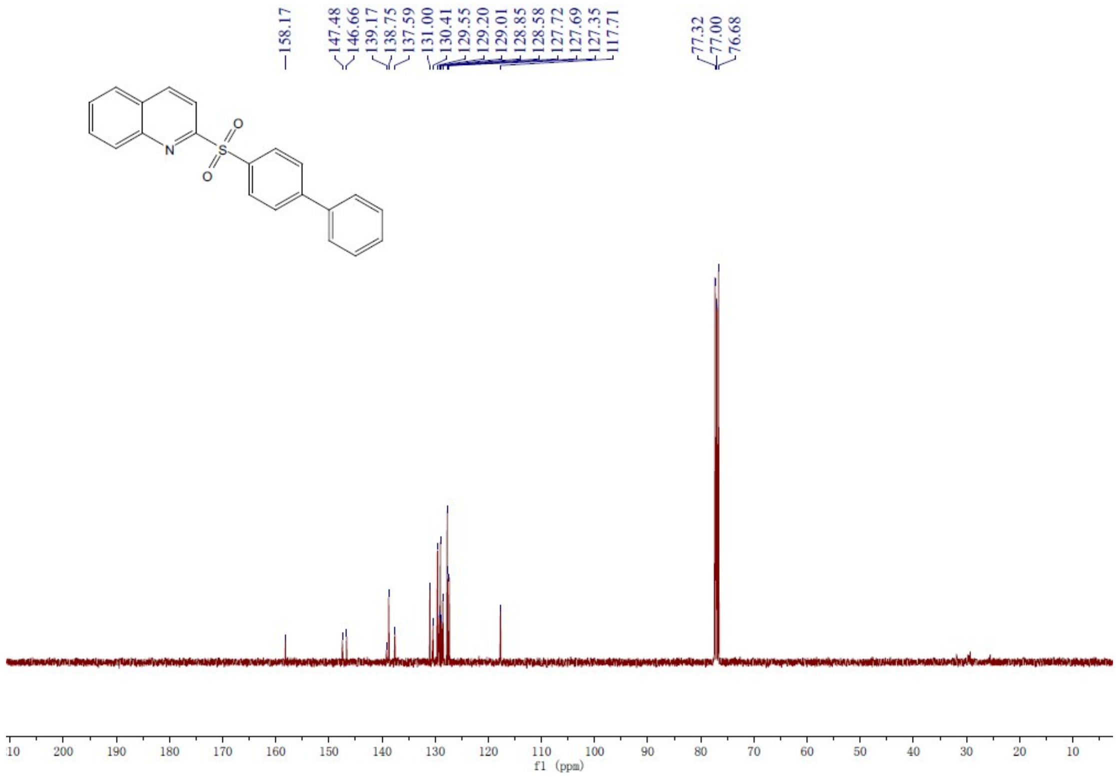

$^{1}H$ spectrum of **3al**



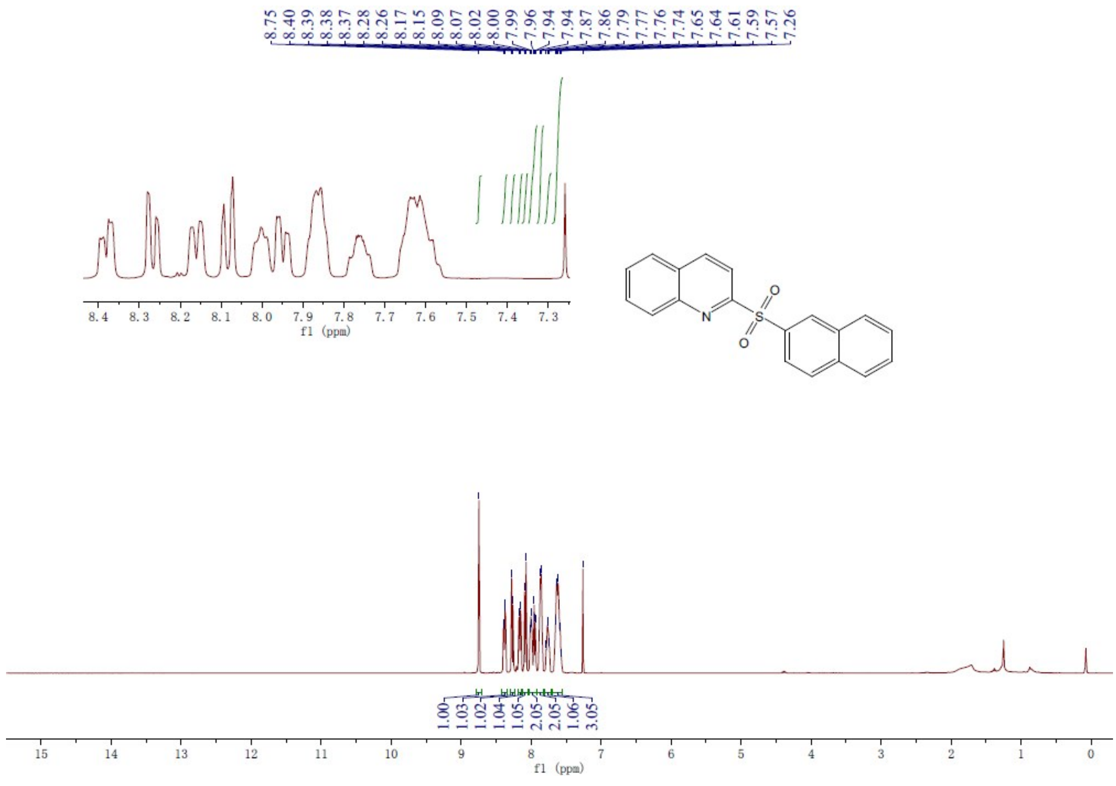

$^{13}C$ spectrum of **3al**



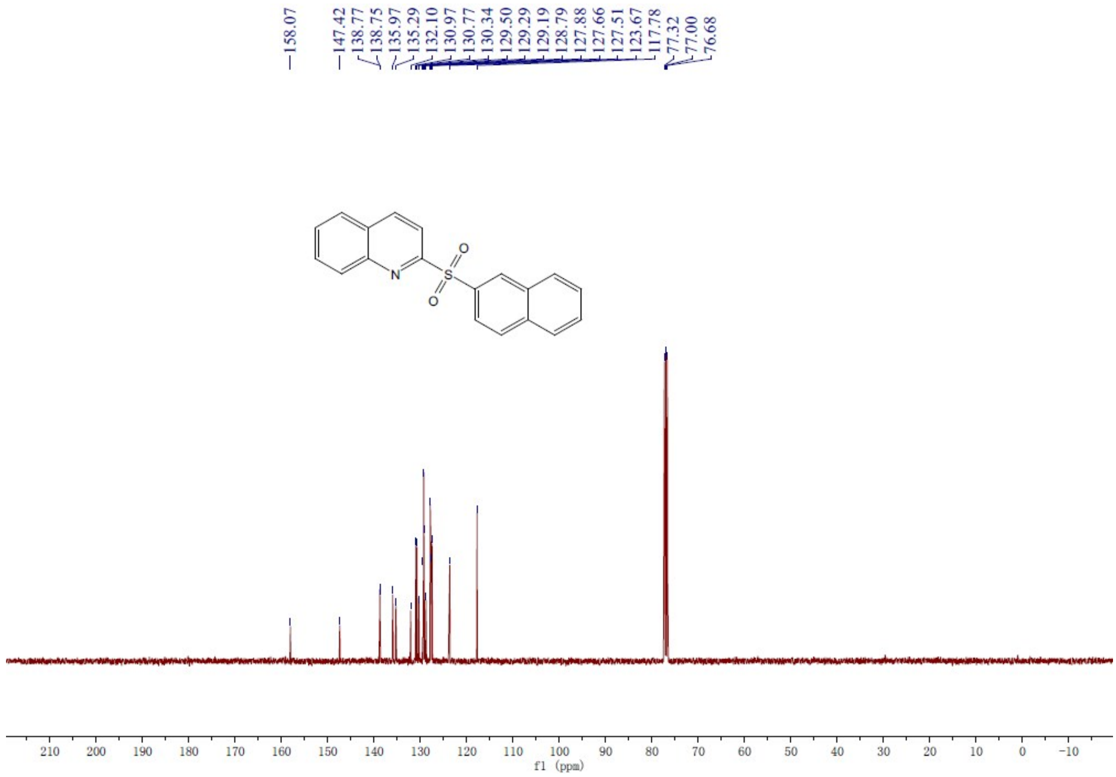
[1]H spectrum of **3am**



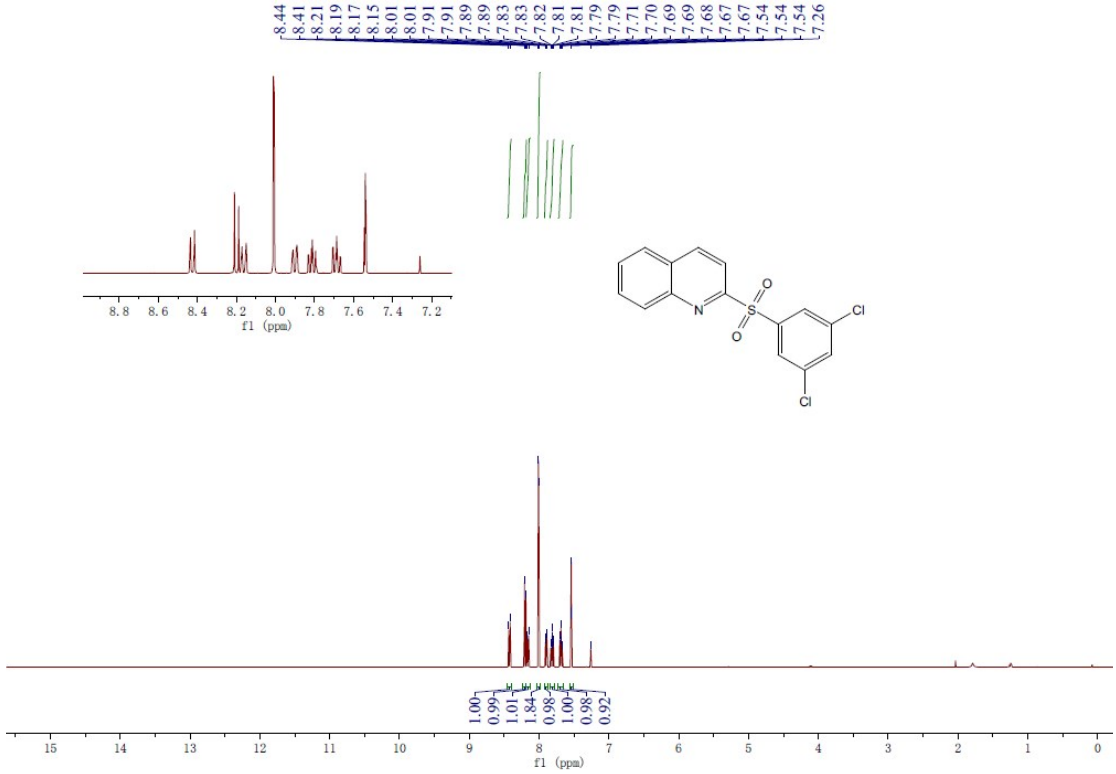
[13]C spectrum of **3am**



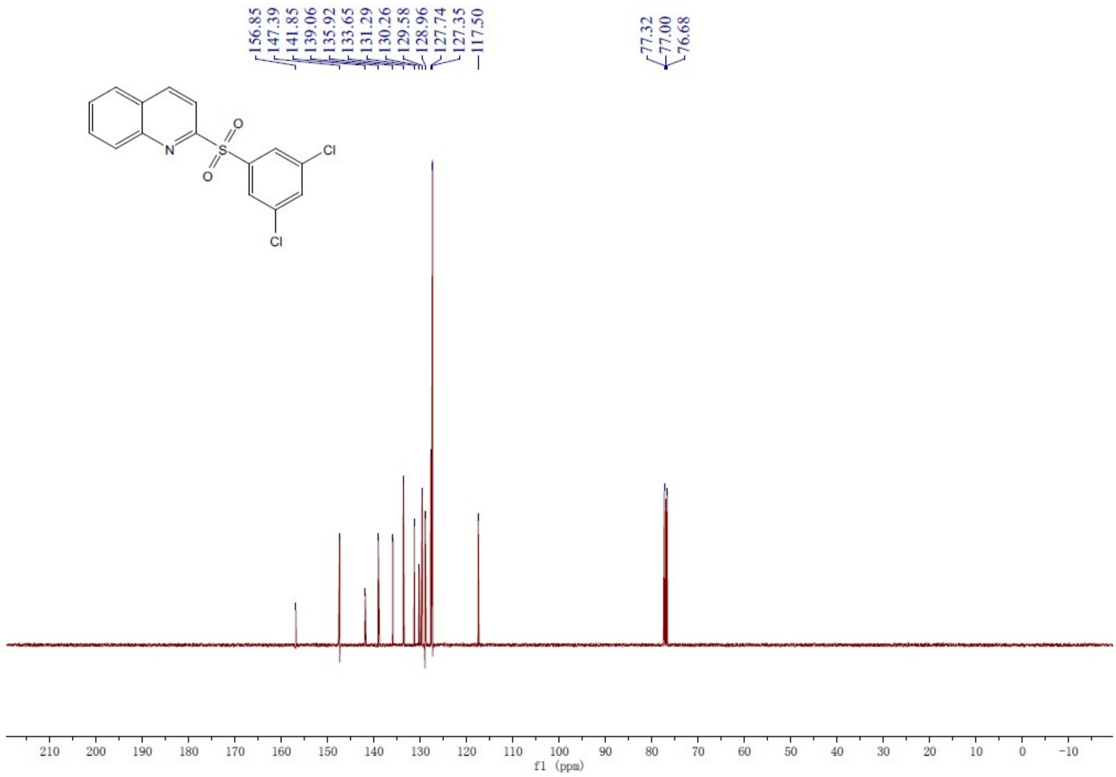

[1]H spectrum of **3an**



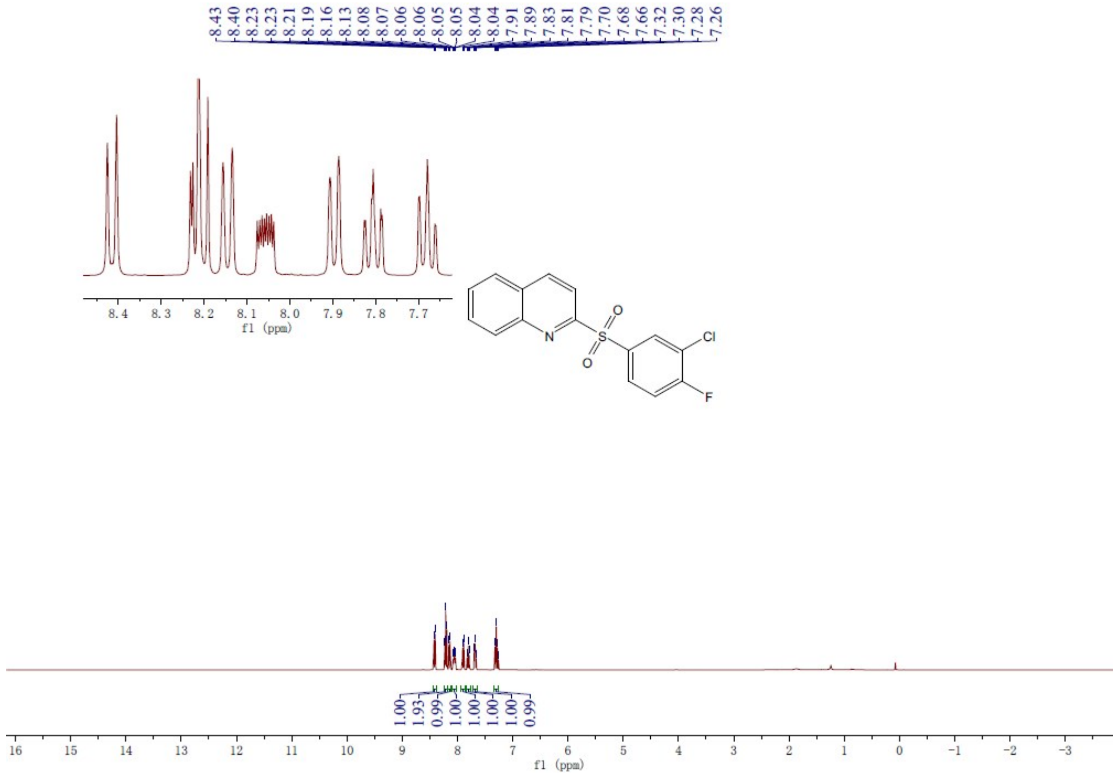

[13]C spectrum of **3an**



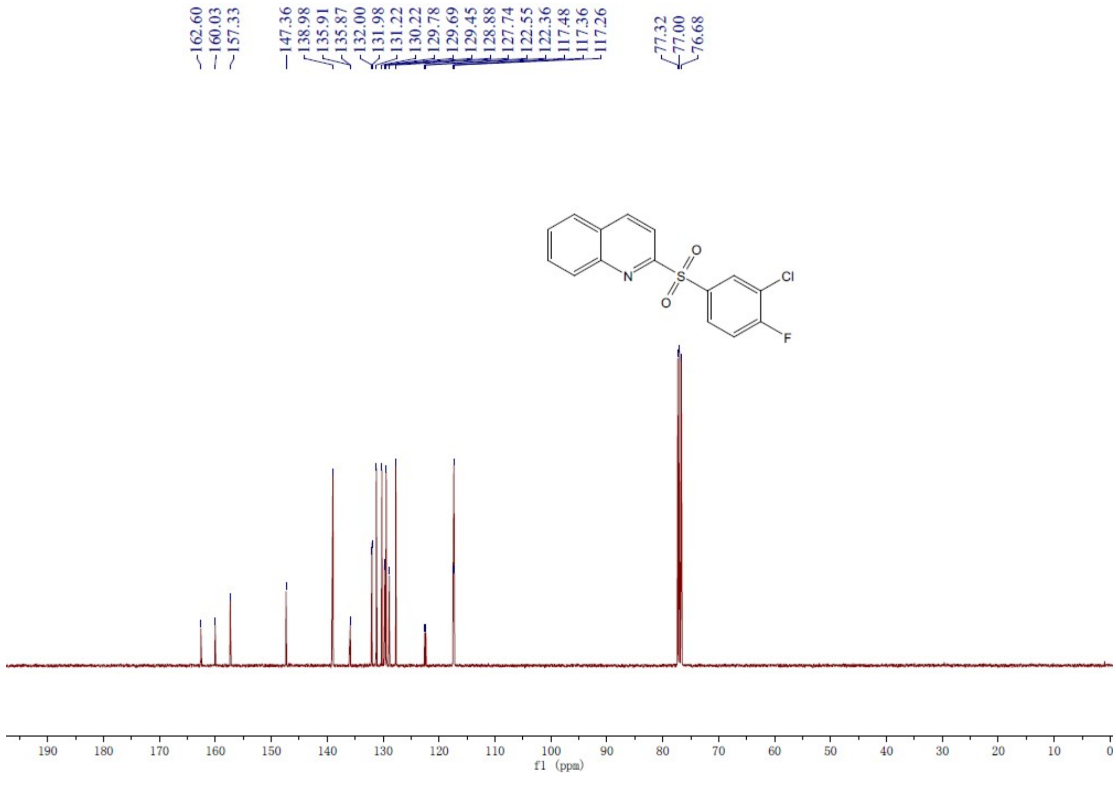

$^{1}$H spectrum of **3ao**



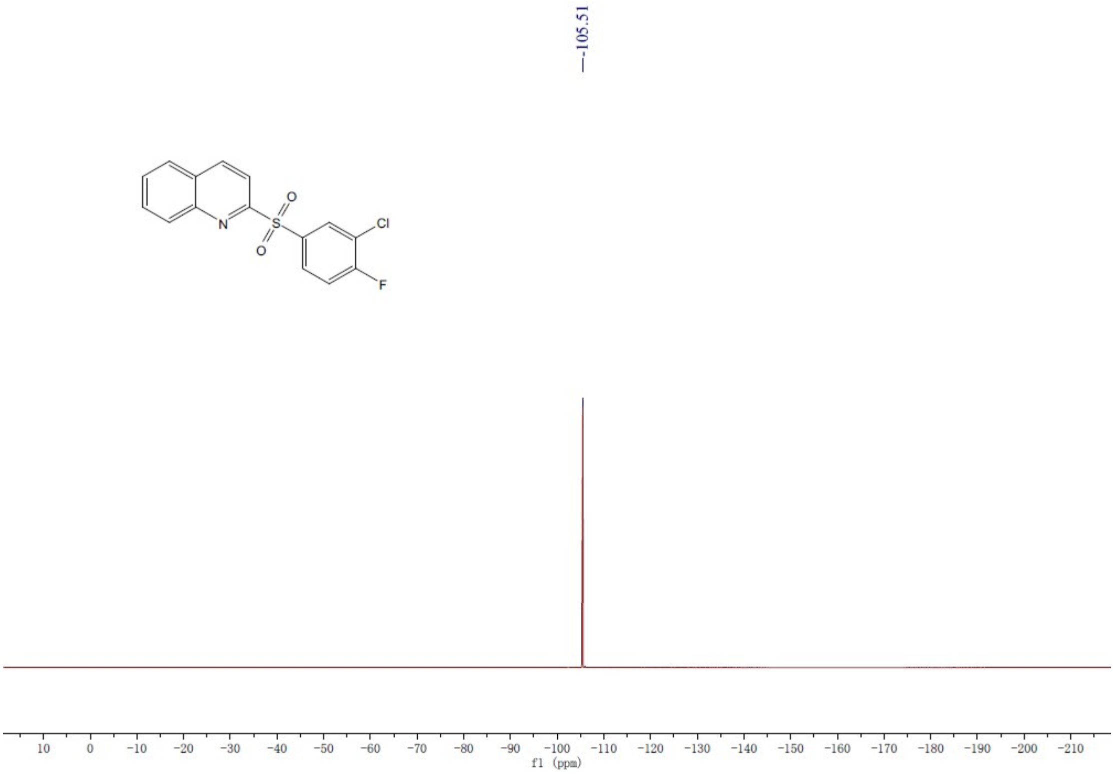

$^{13}$C spectrum of **3ao**



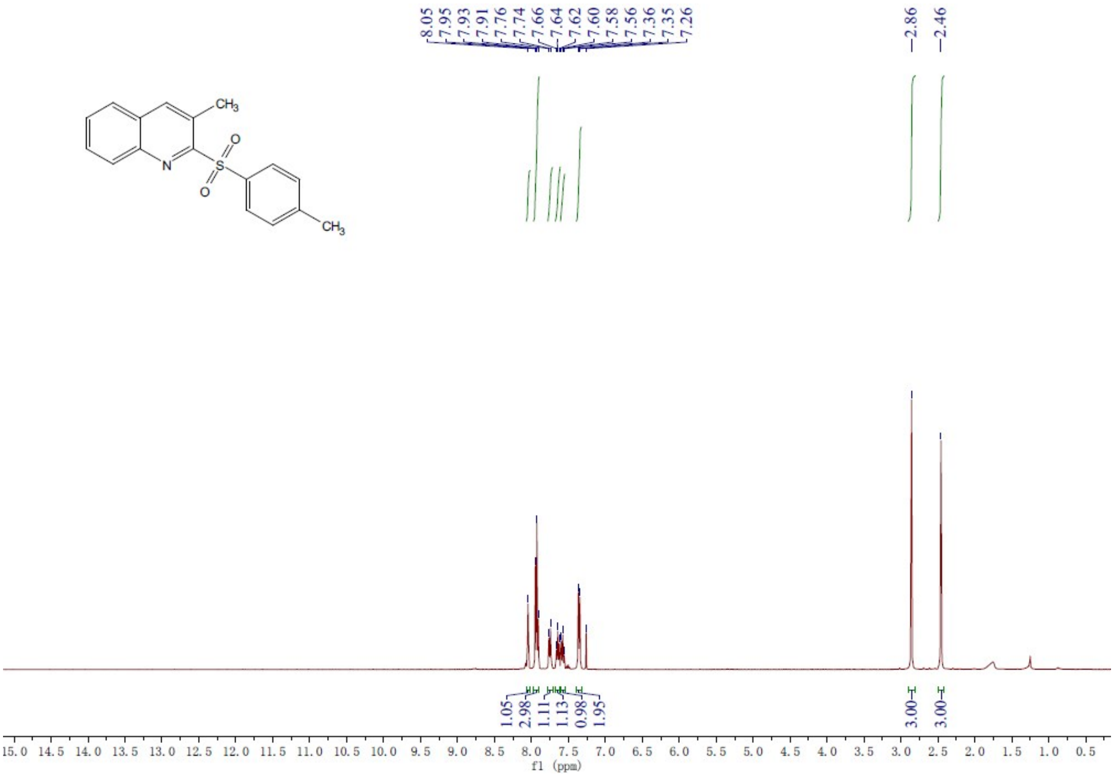
[1]H spectrum of **3ap**



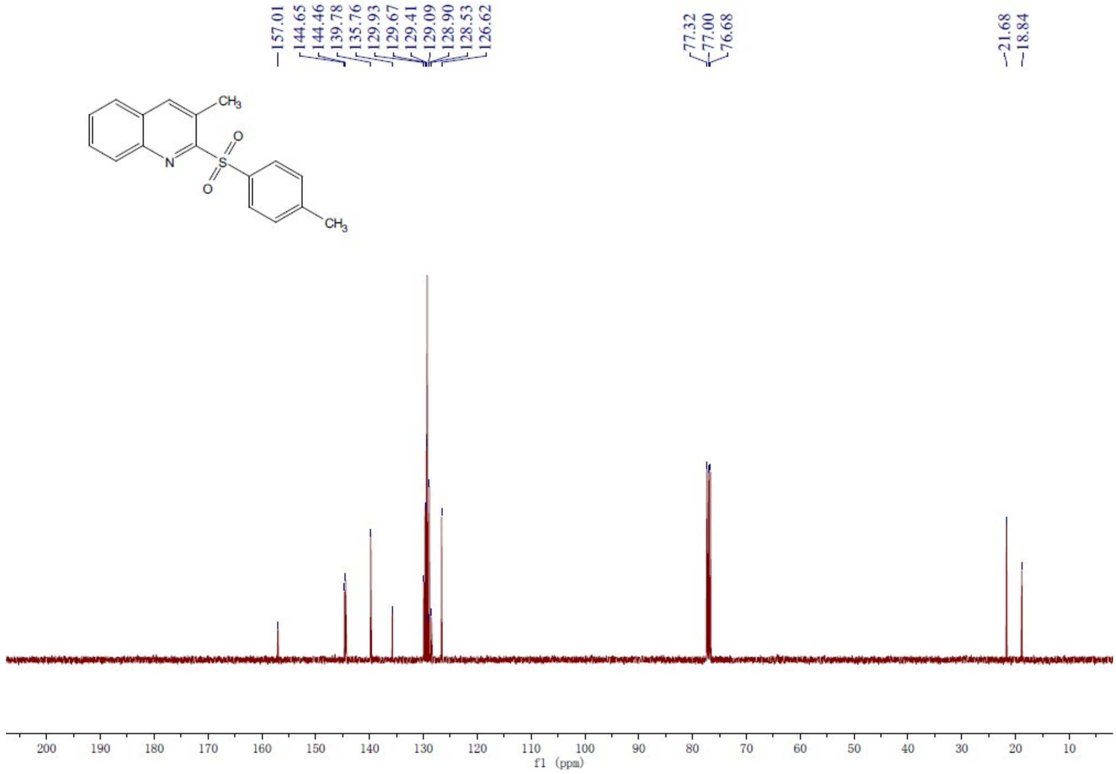
[13]C spectrum of **3ap**



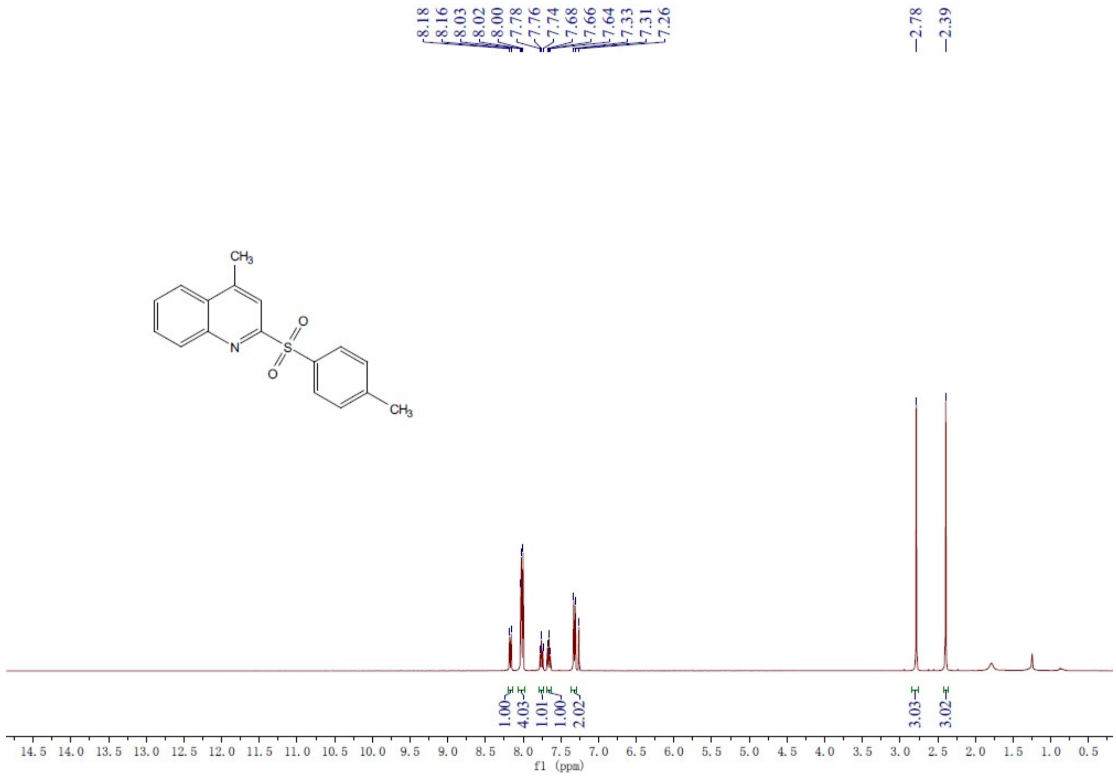

$^{19}$F spectrum of **3ap**



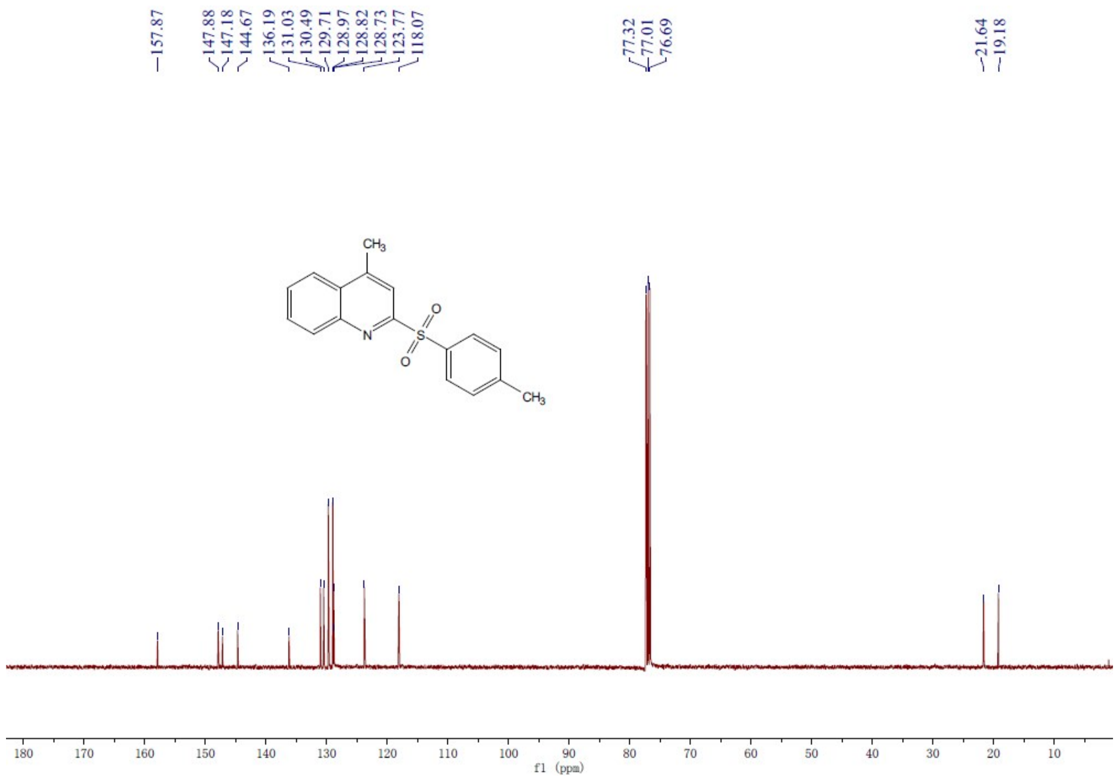

$^{1}$H spectrum of **3ba**



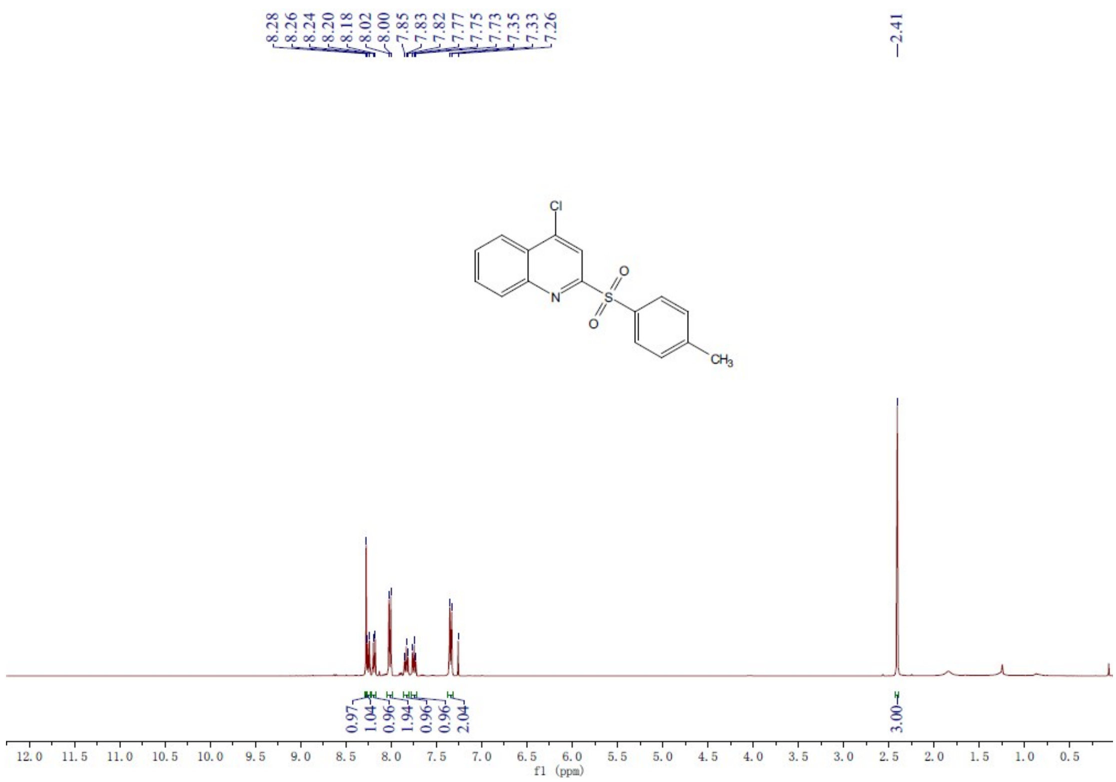

$^{13}C$ spectrum of **3ba**



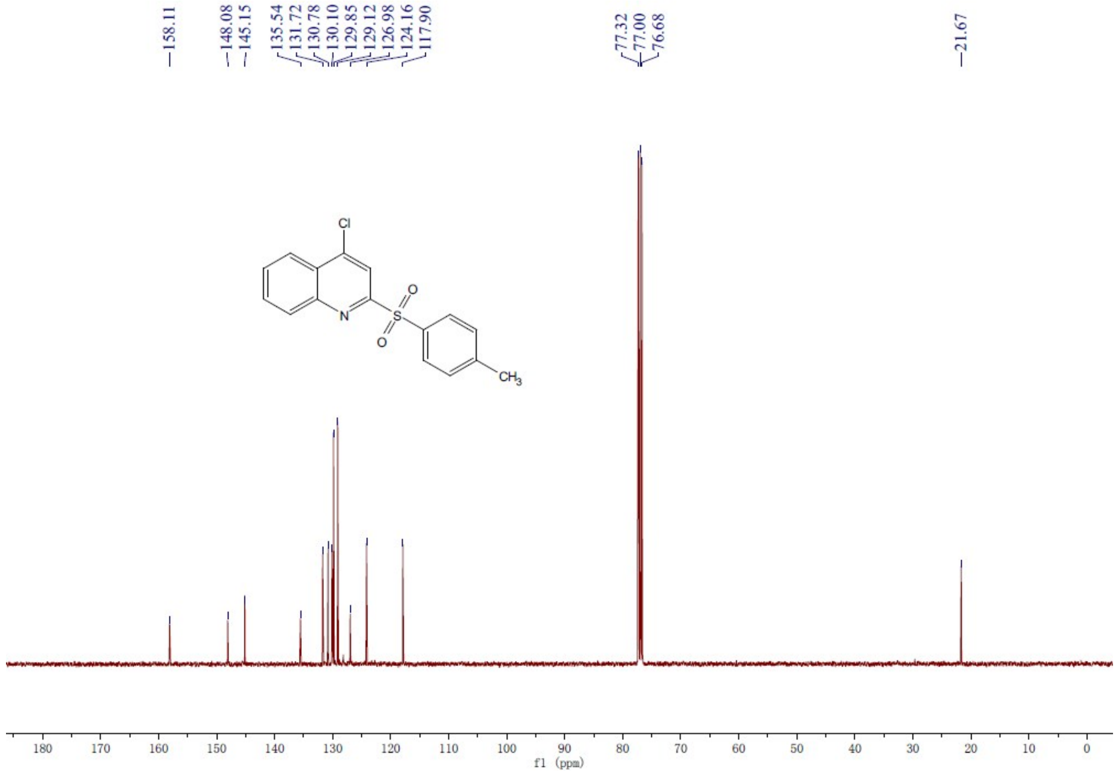

$^{1}H$ spectrum of **3ca**



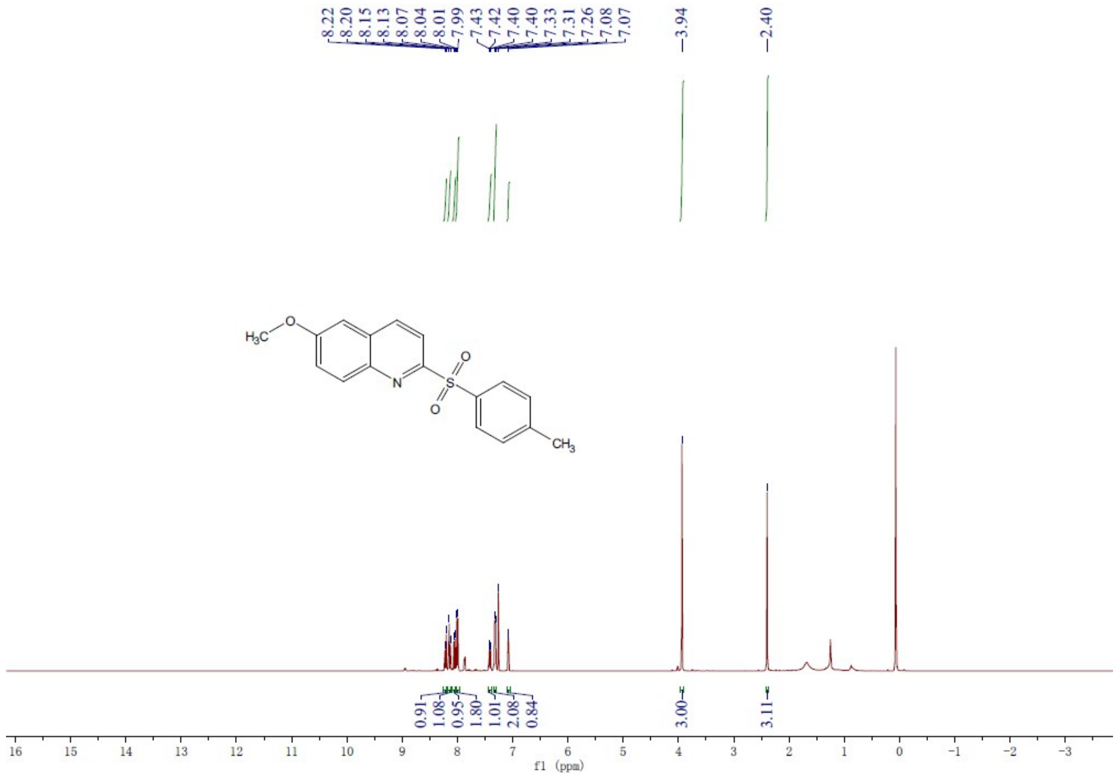

$^{13}C$ spectrum of **3ca**



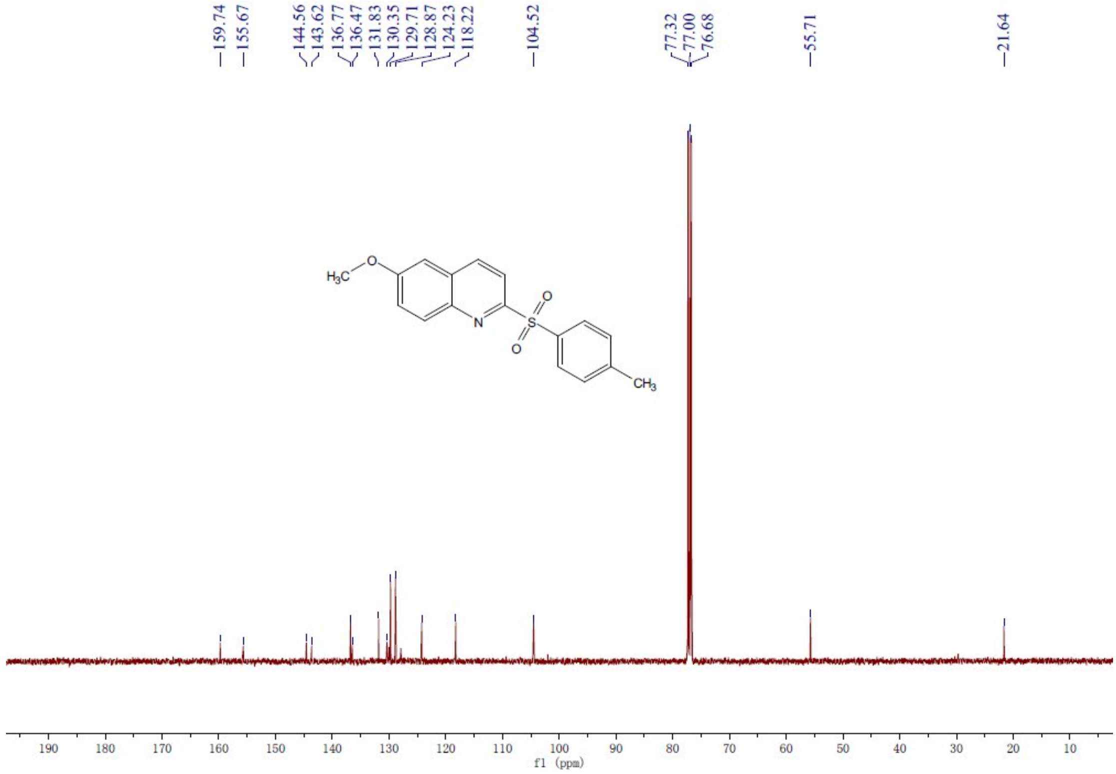

$^{1}H$ spectrum of **3da**



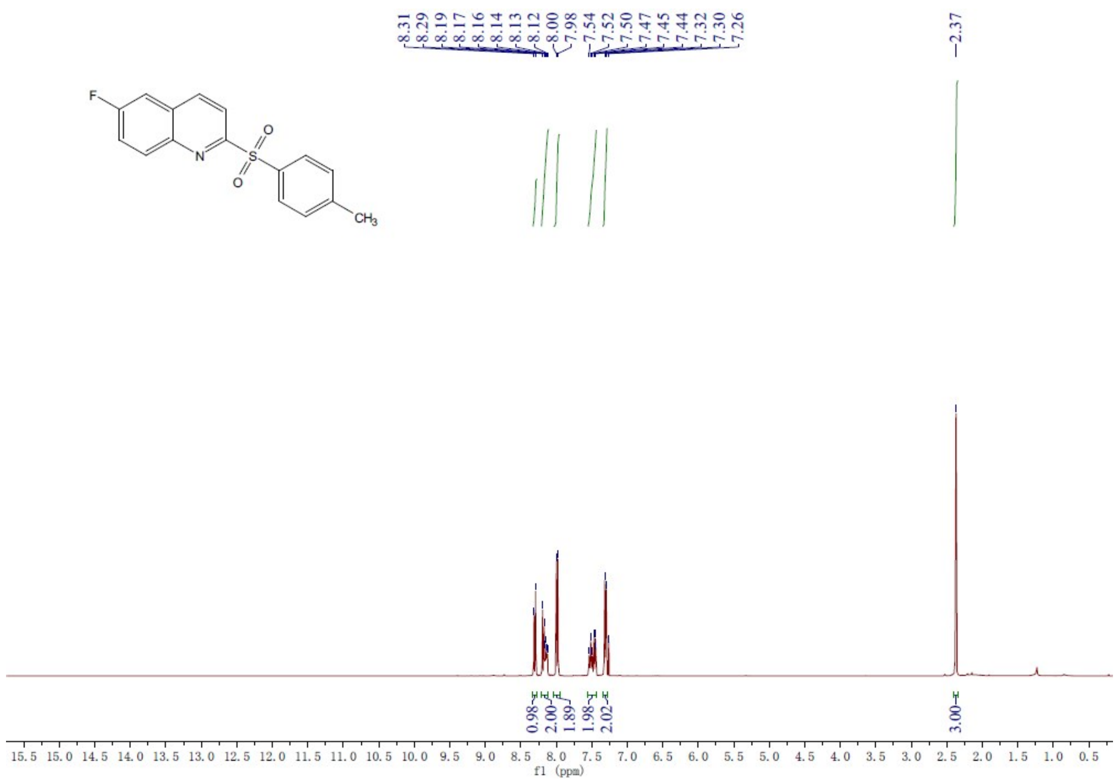
$^{13}$C spectrum of **3da**



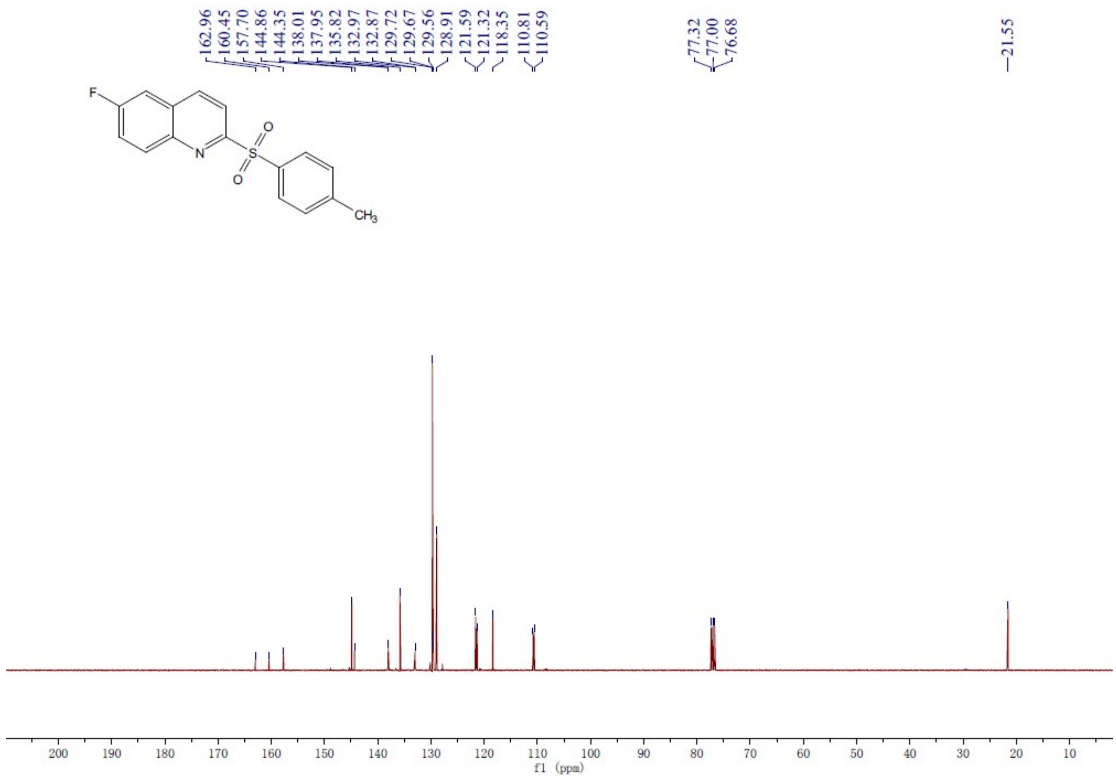
$^{1}$H spectrum of **3ea**



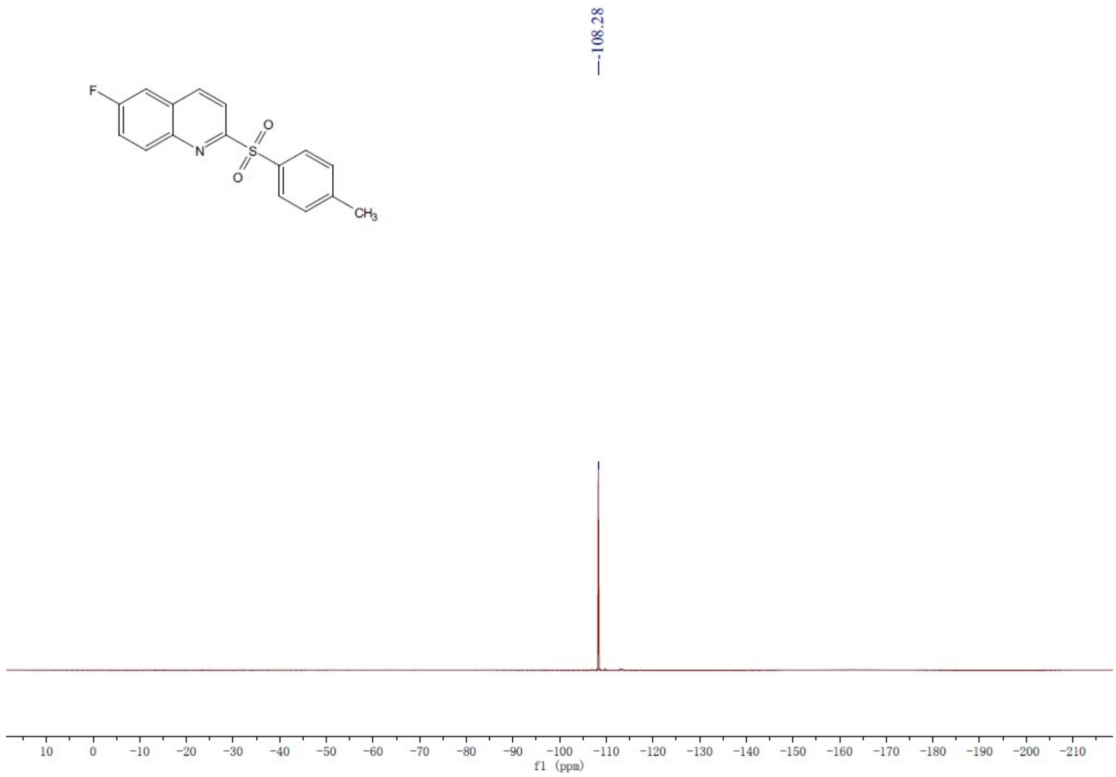

$^{13}C$ spectrum of **3ea**



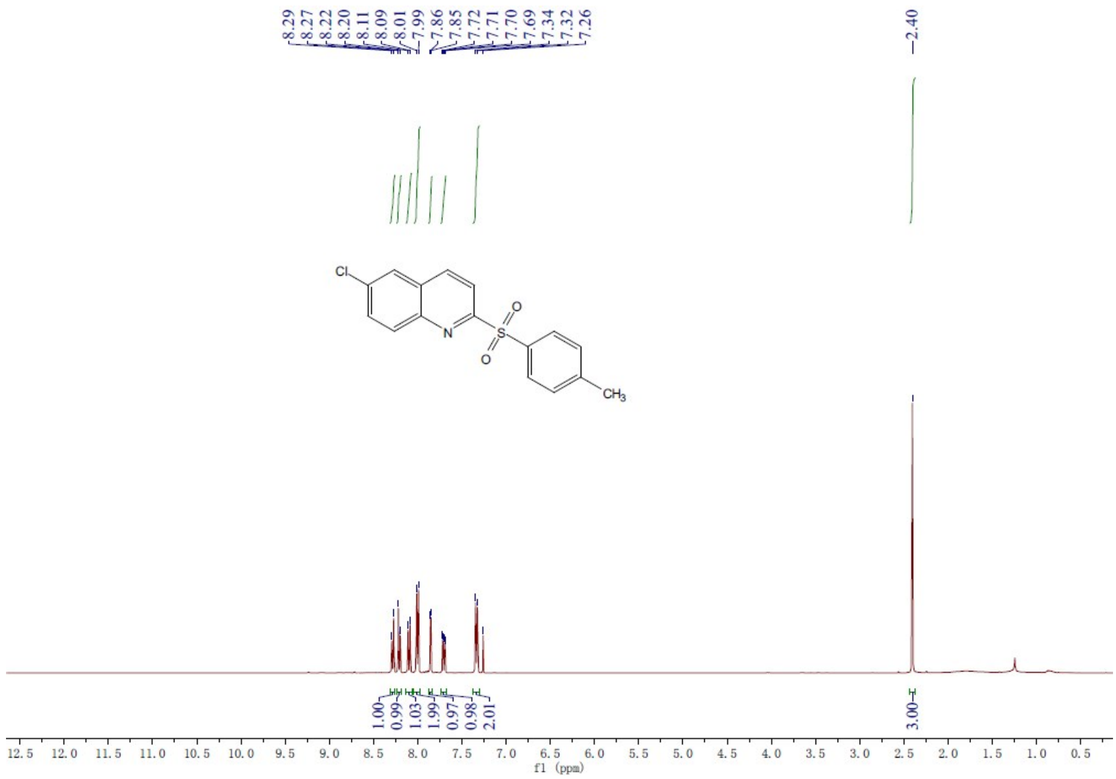

$^{1}H$ spectrum of **3fa**



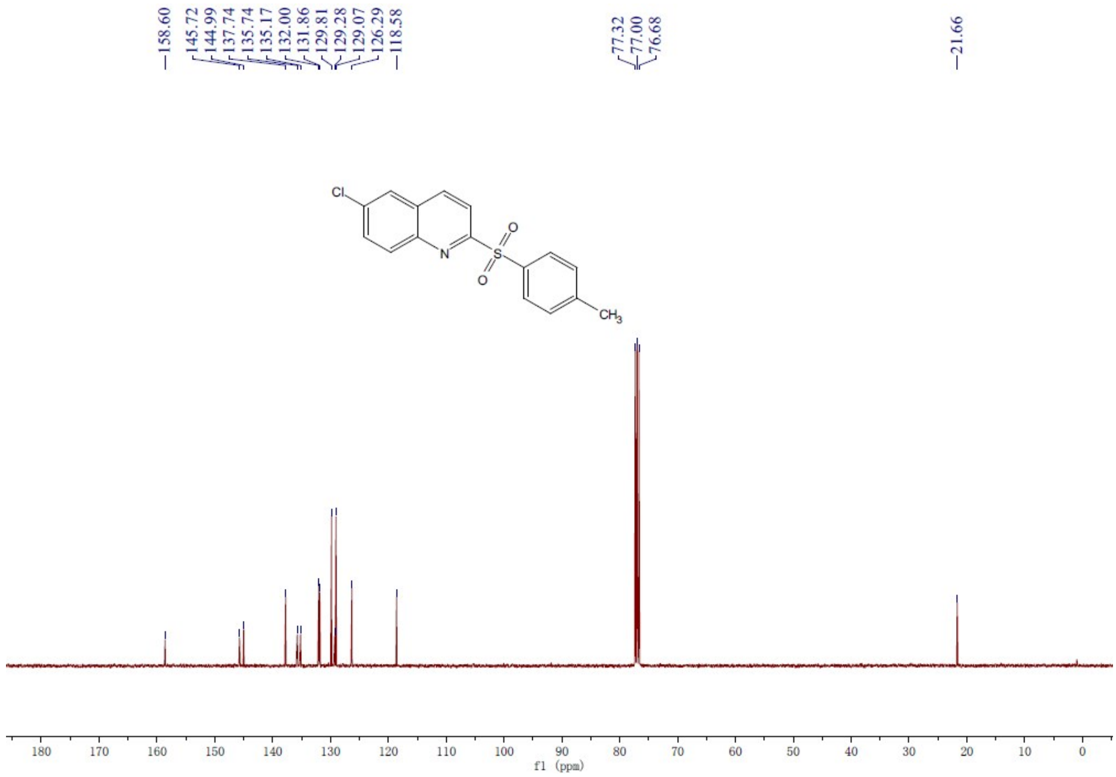
$^{13}C$ spectrum of **3fa**



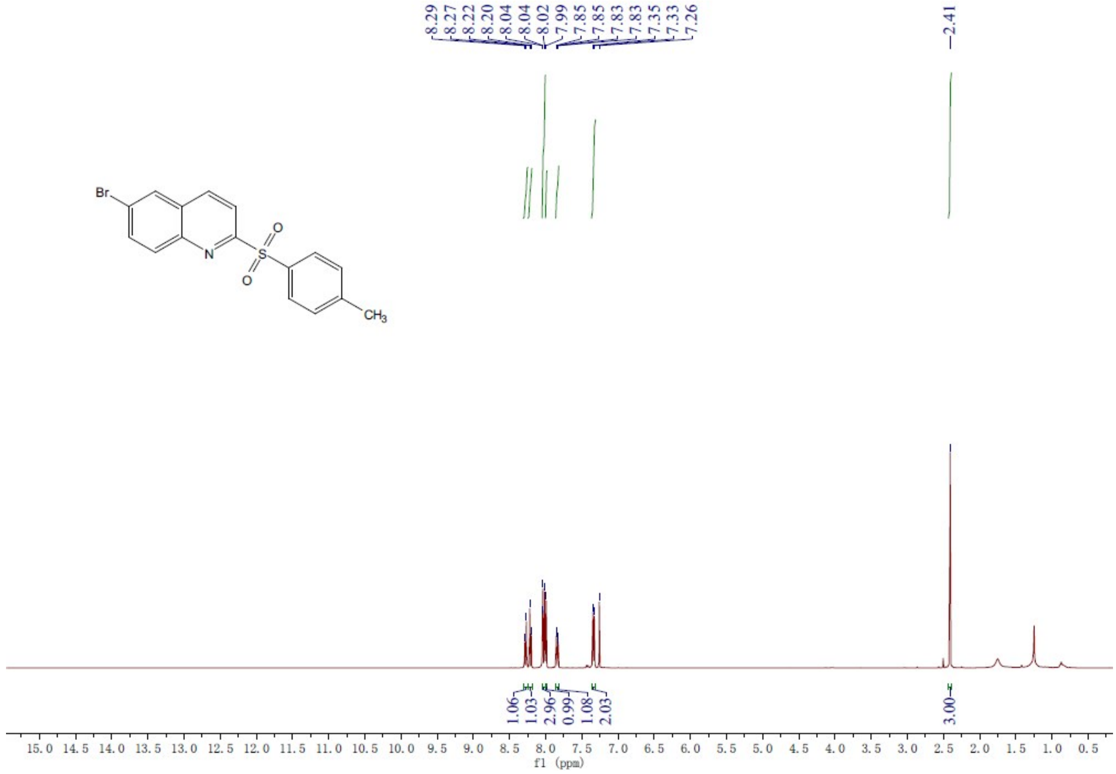
$^{19}F$ spectrum of **3fa**



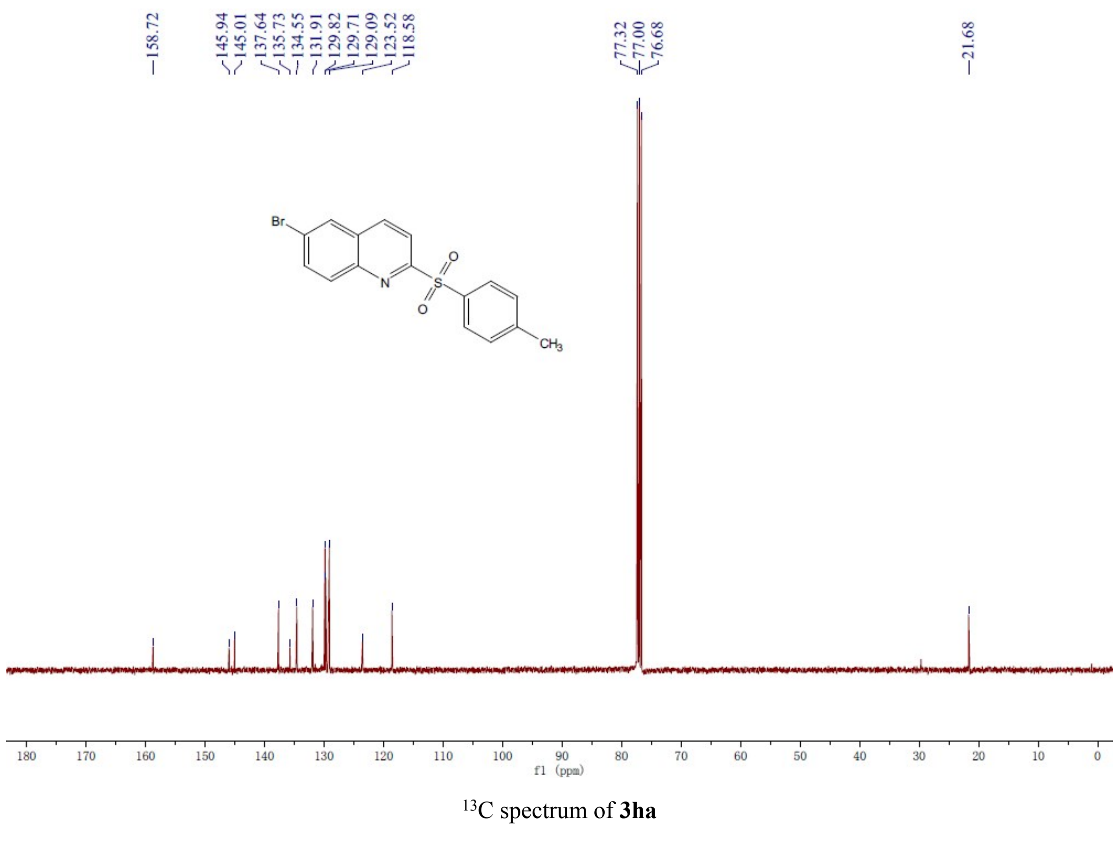

$^{1}$H spectrum of **3ga**



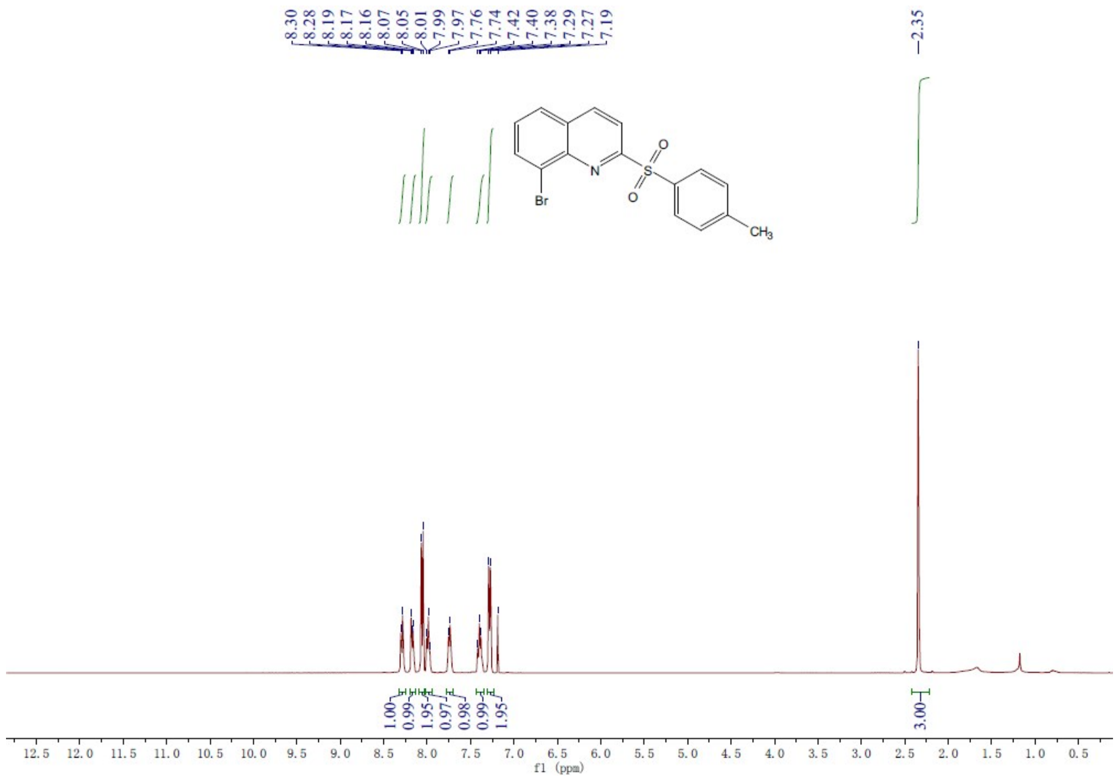

$^{13}$C spectrum of **3ga**



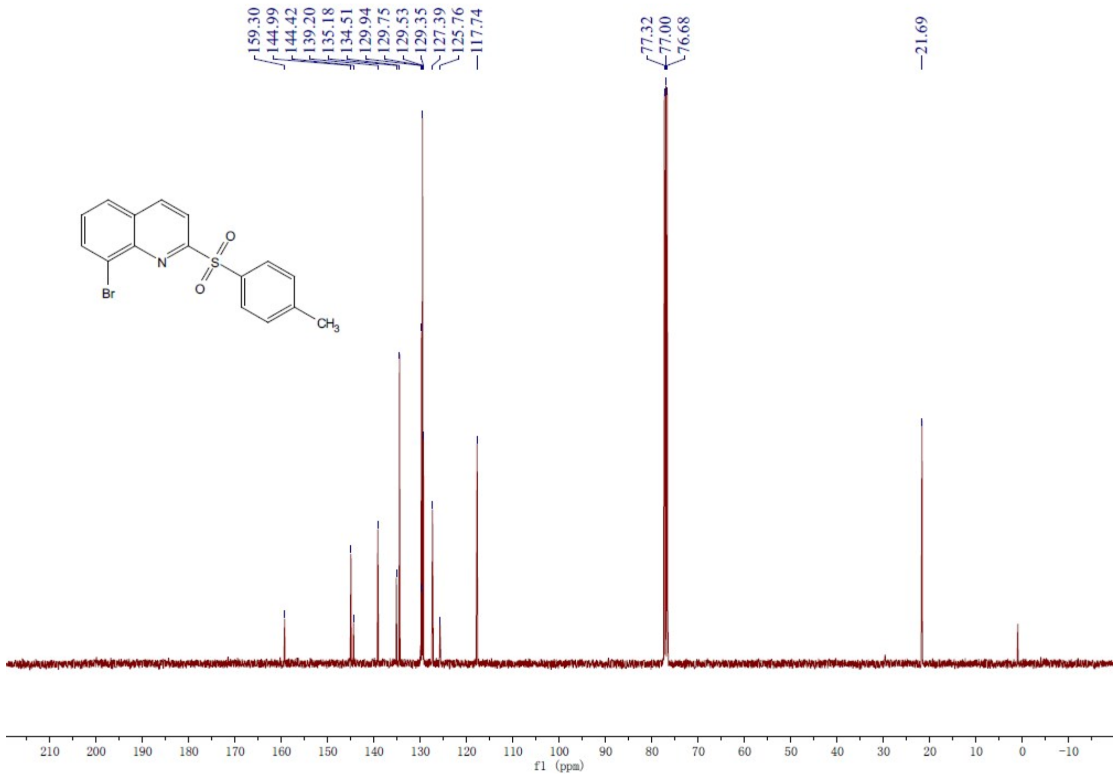

[1]H spectrum of **3ha**



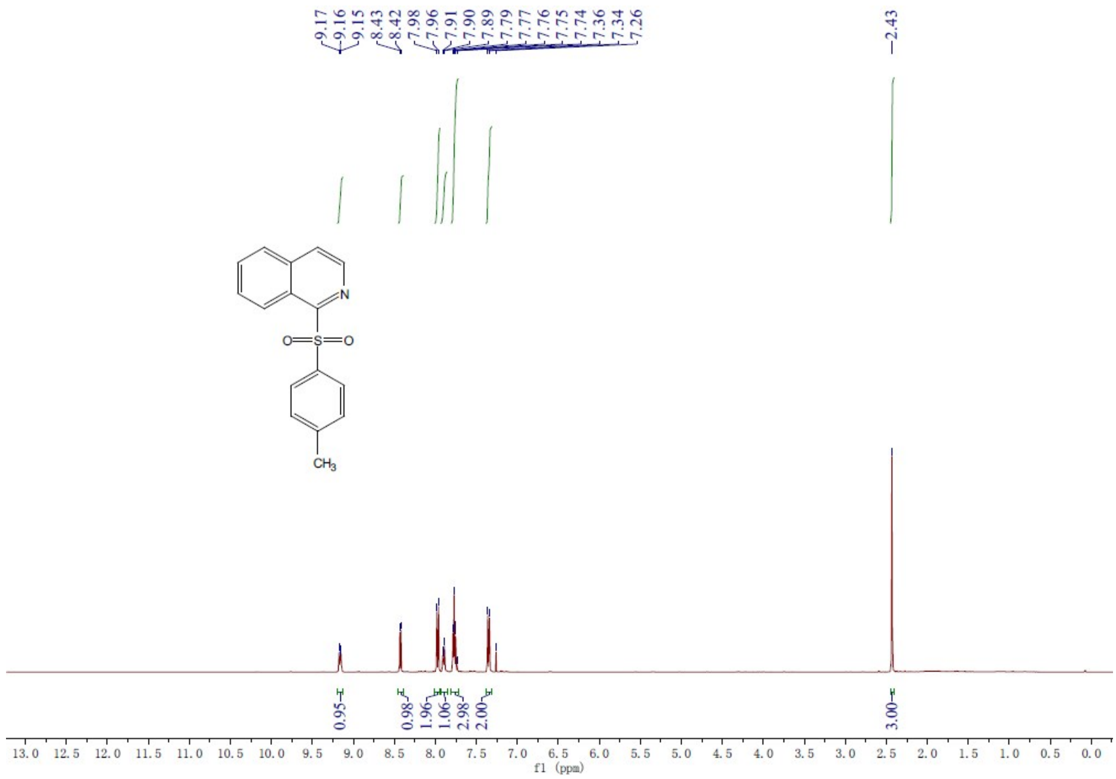

[13]C spectrum of **3ha**



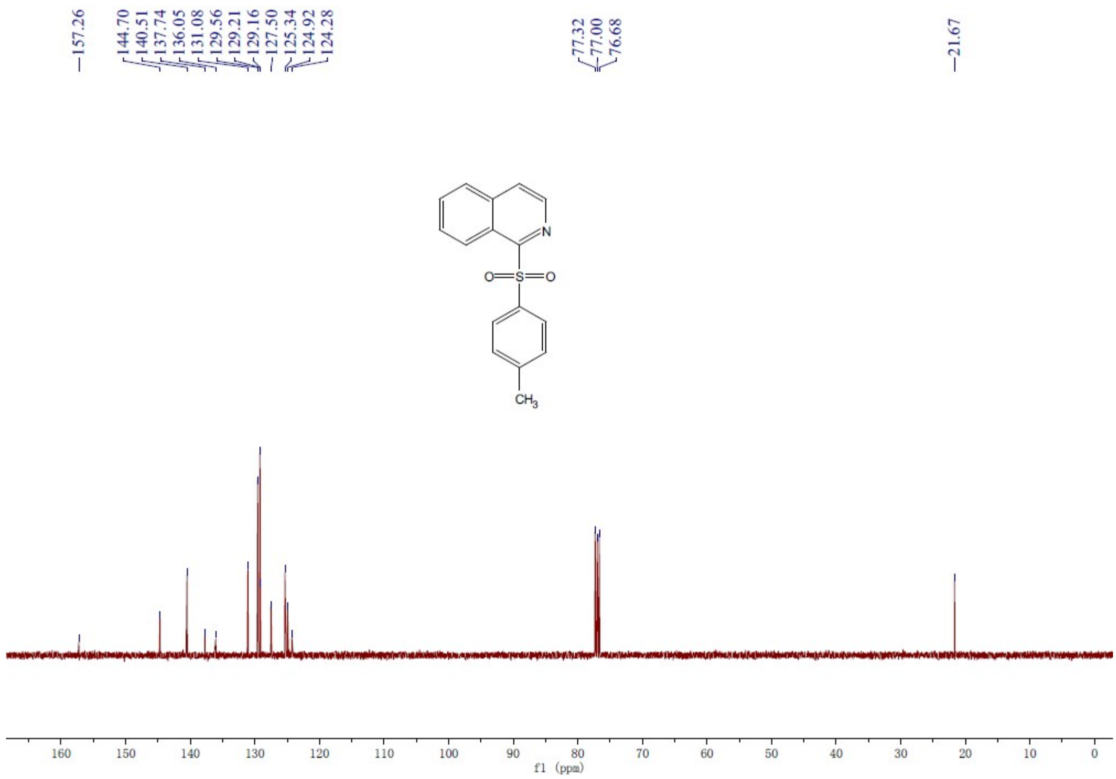

$^{1}H$ spectrum of **3ia**



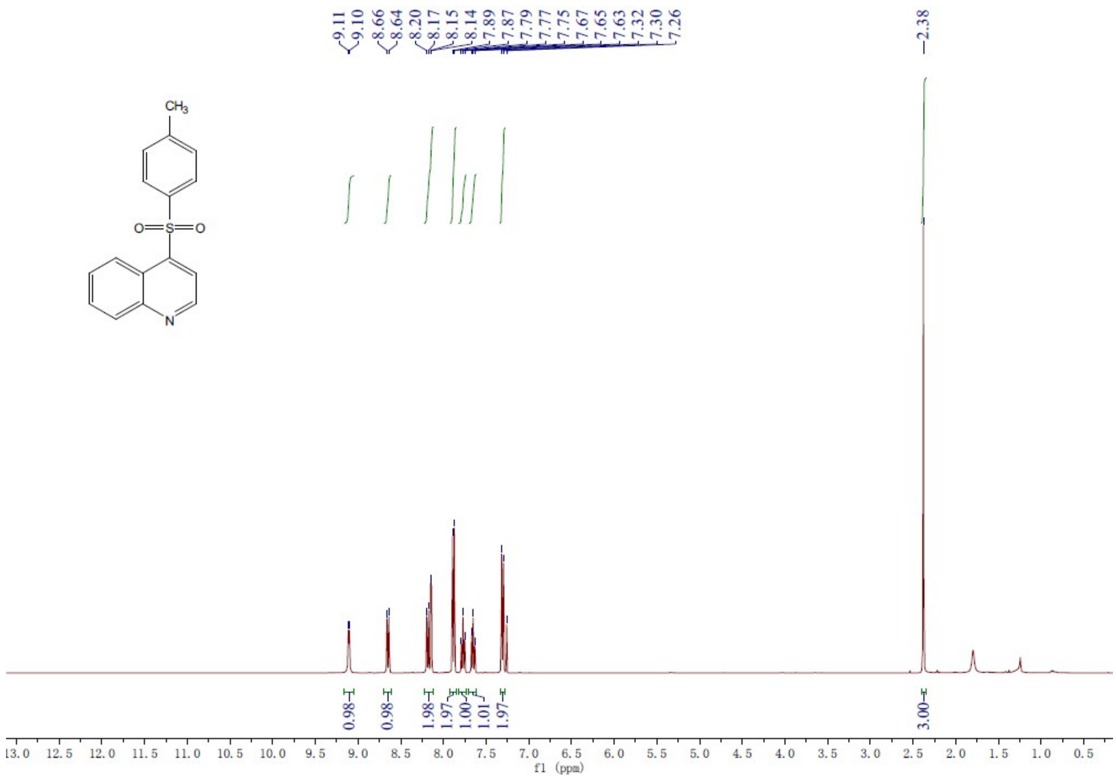

$^{13}C$ spectrum of **3ia**



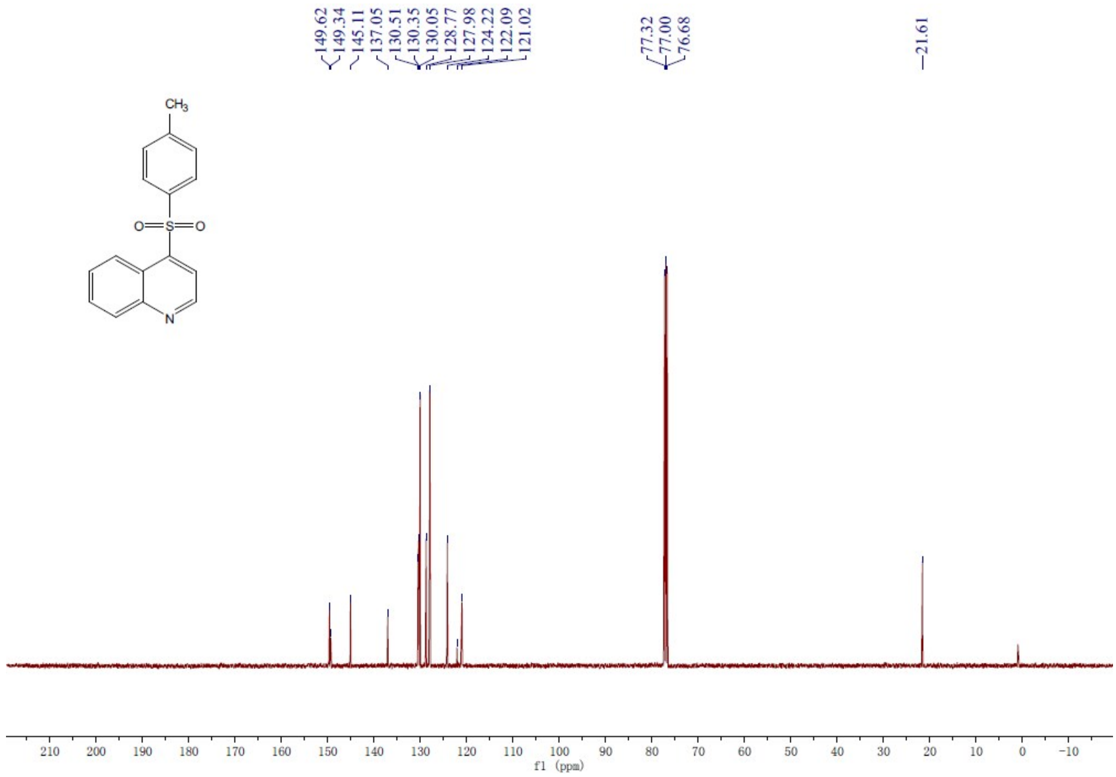

$^{1}H$ spectrum of **3ja**



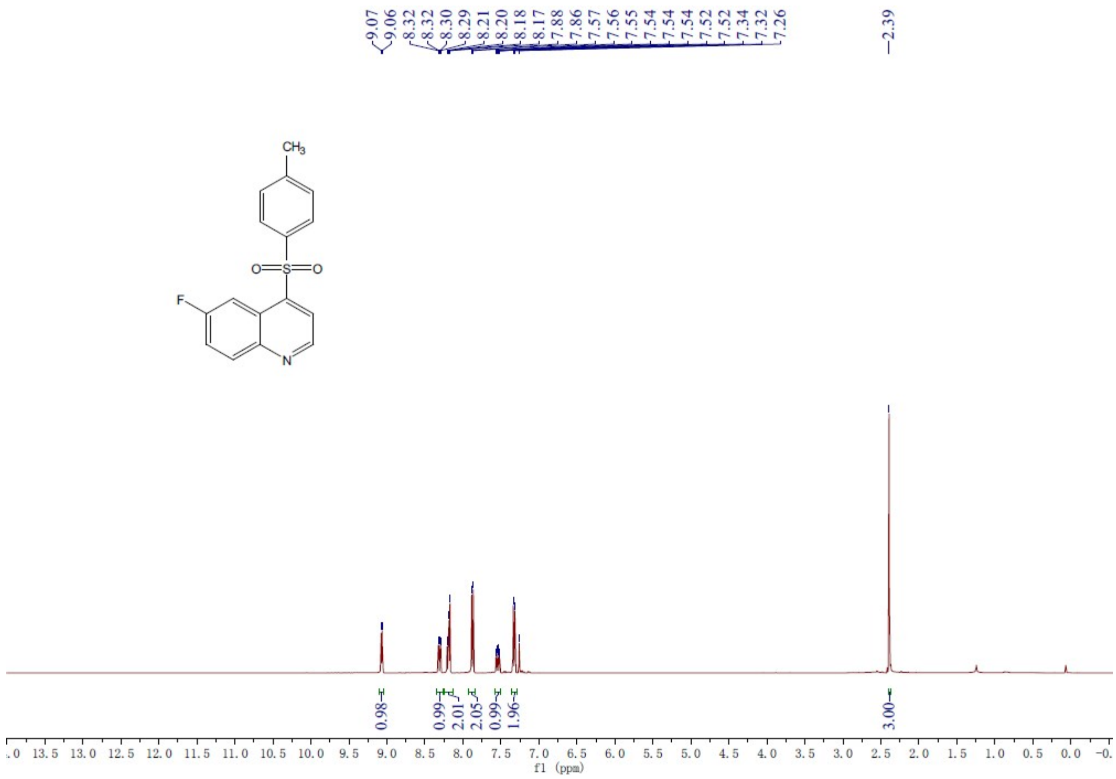

$^{13}C$ spectrum of **3ja**



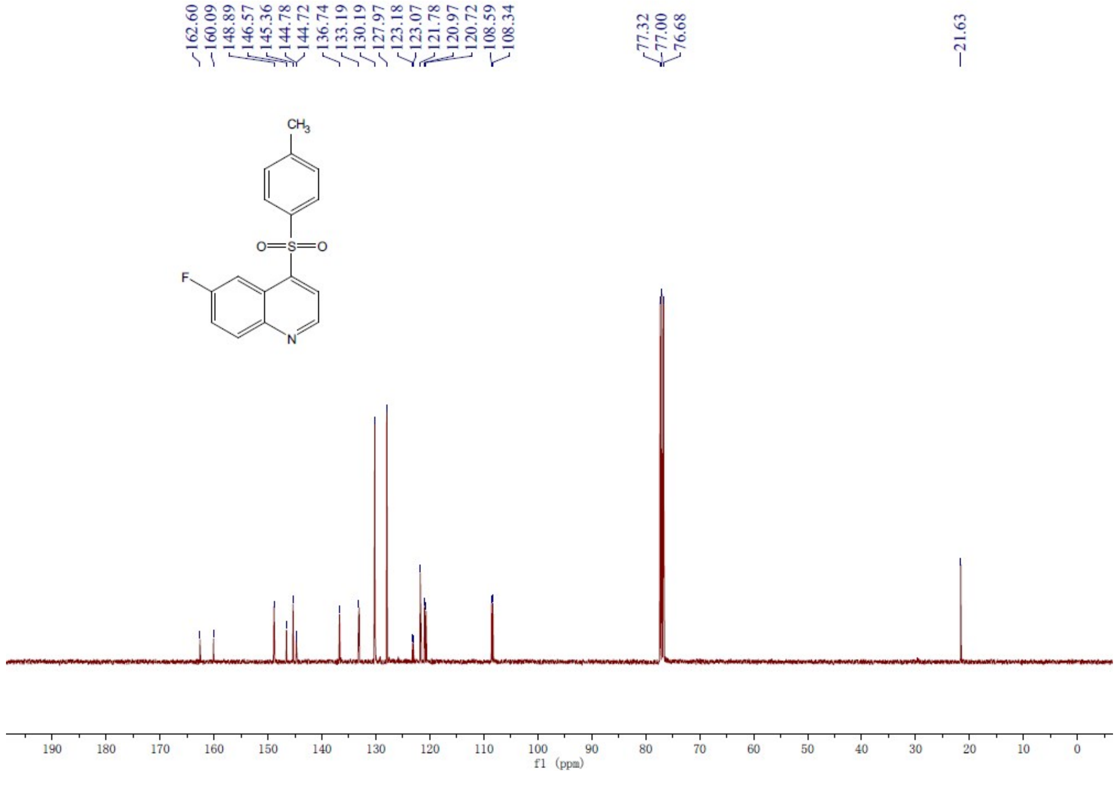
[1]H spectrum of **3ka**



[13]C spectrum of **3ka**

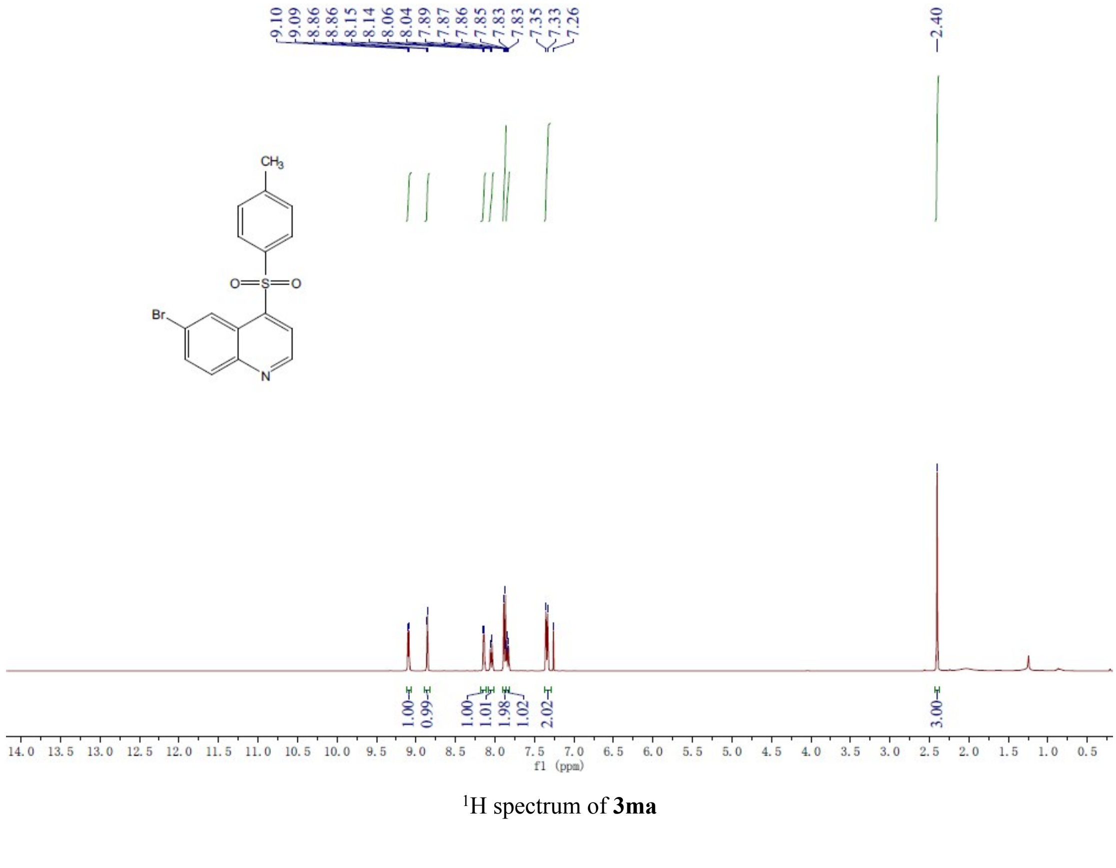


$^1$H spectrum of **3la**

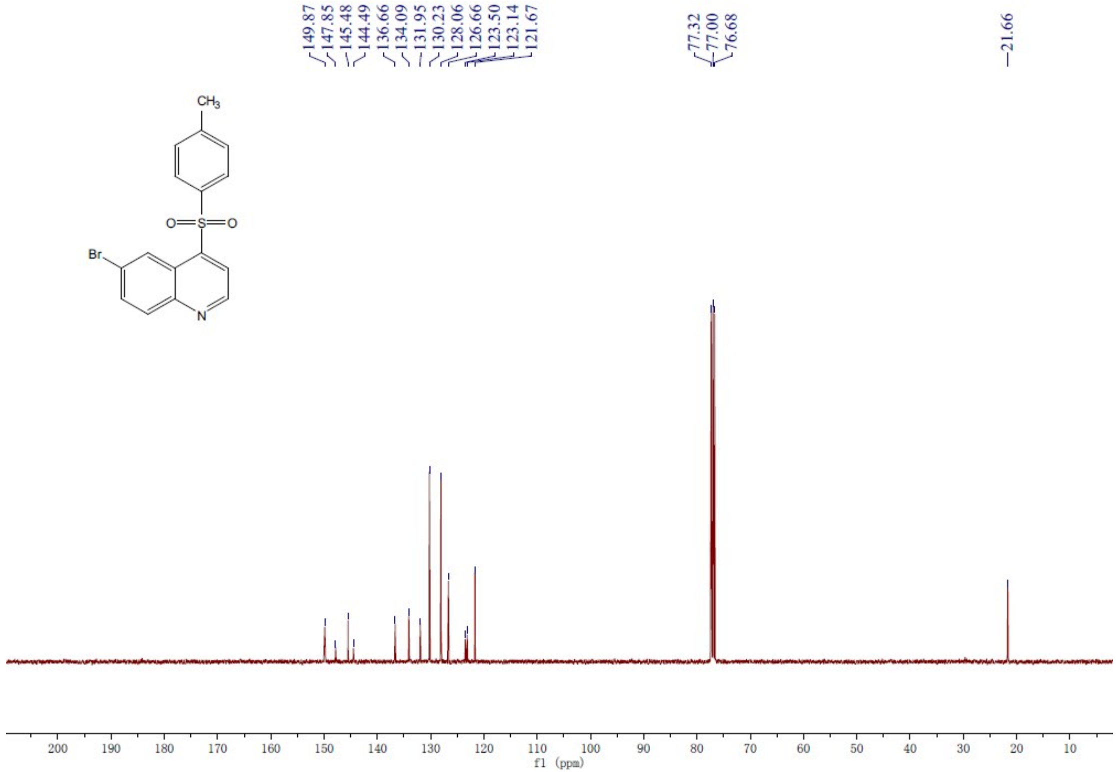


$^{13}$C spectrum of **3la**

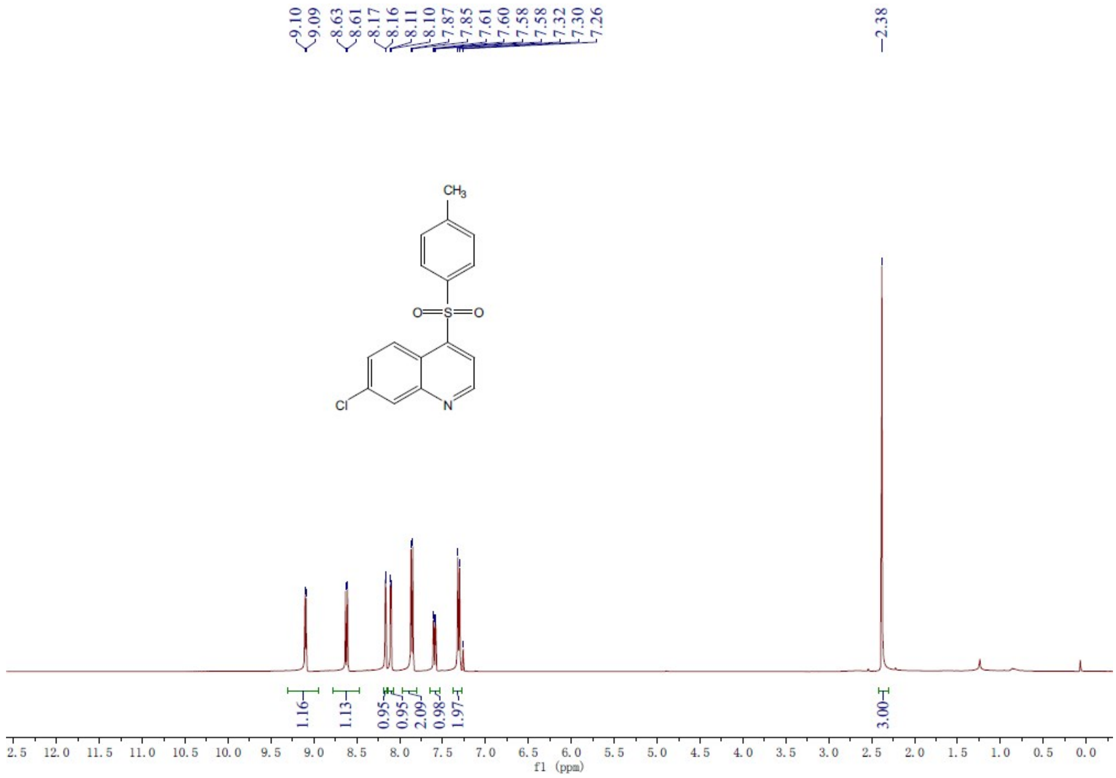

$^{19}$F spectrum of **3la**



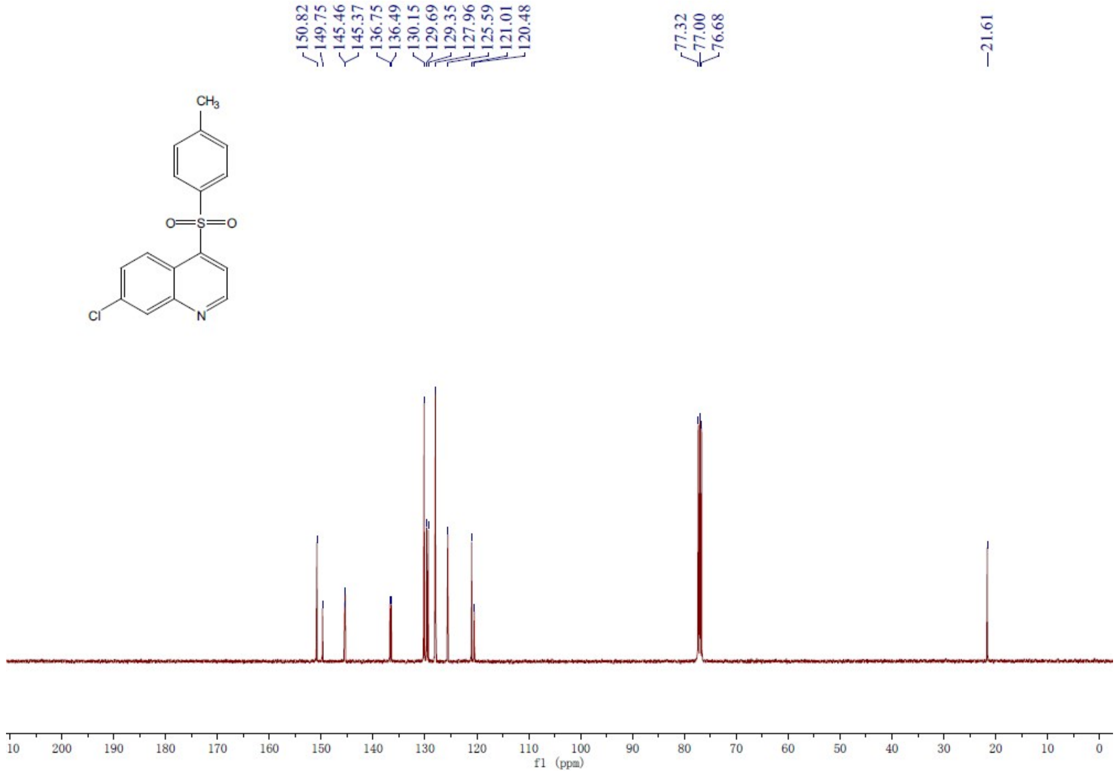

$^{1}$H spectrum of **3ma**



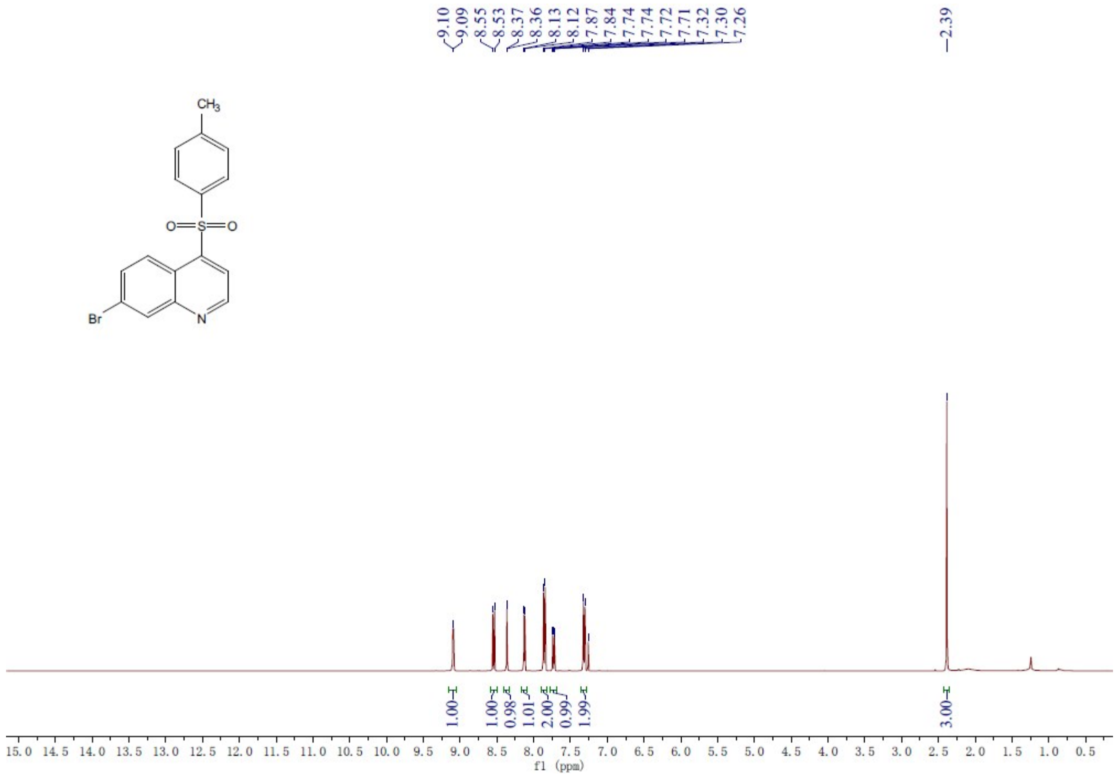

$^{13}C$ spectrum of **3ma**



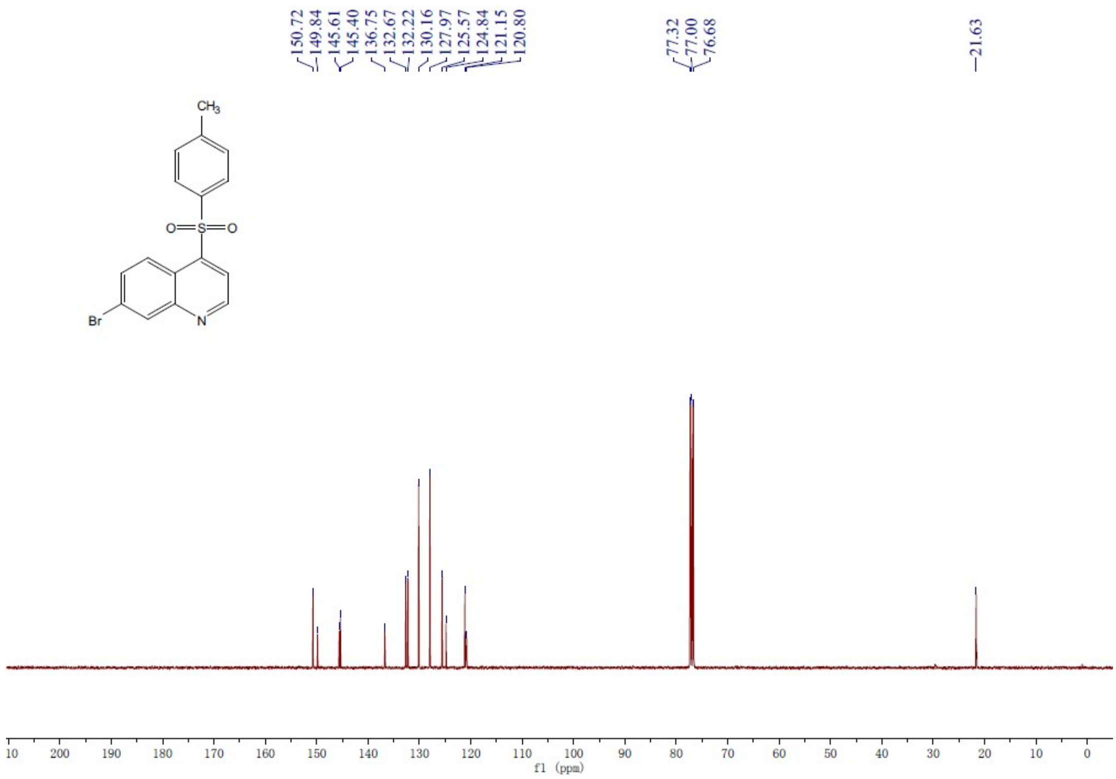

$^{1}H$ spectrum of **3na**



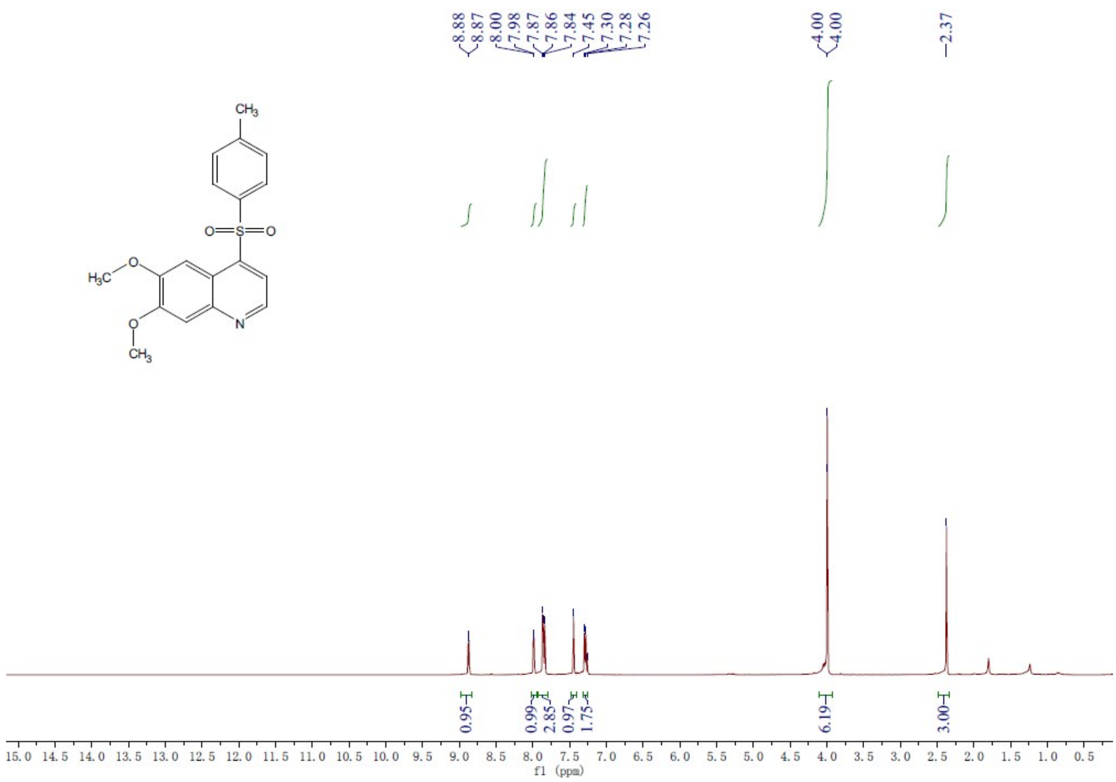

$^{13}$C spectrum of **3na**



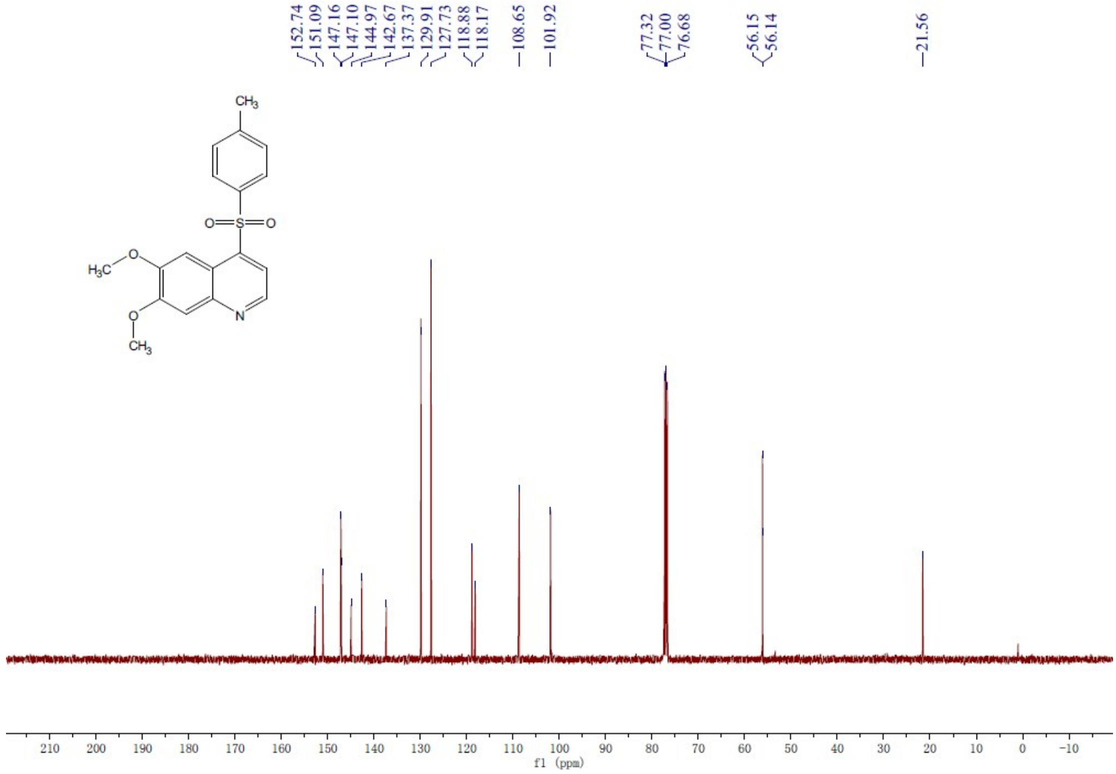

$^{1}$H spectrum of **3oa**



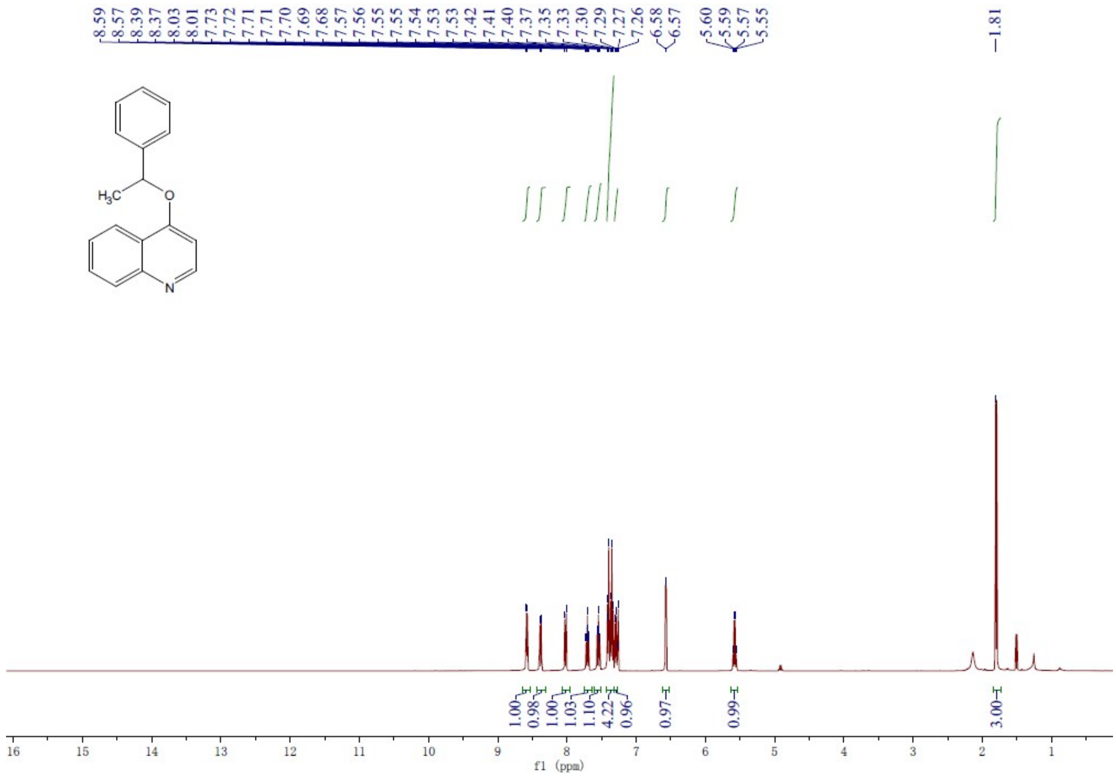

$^{13}$C spectrum of **3oa**



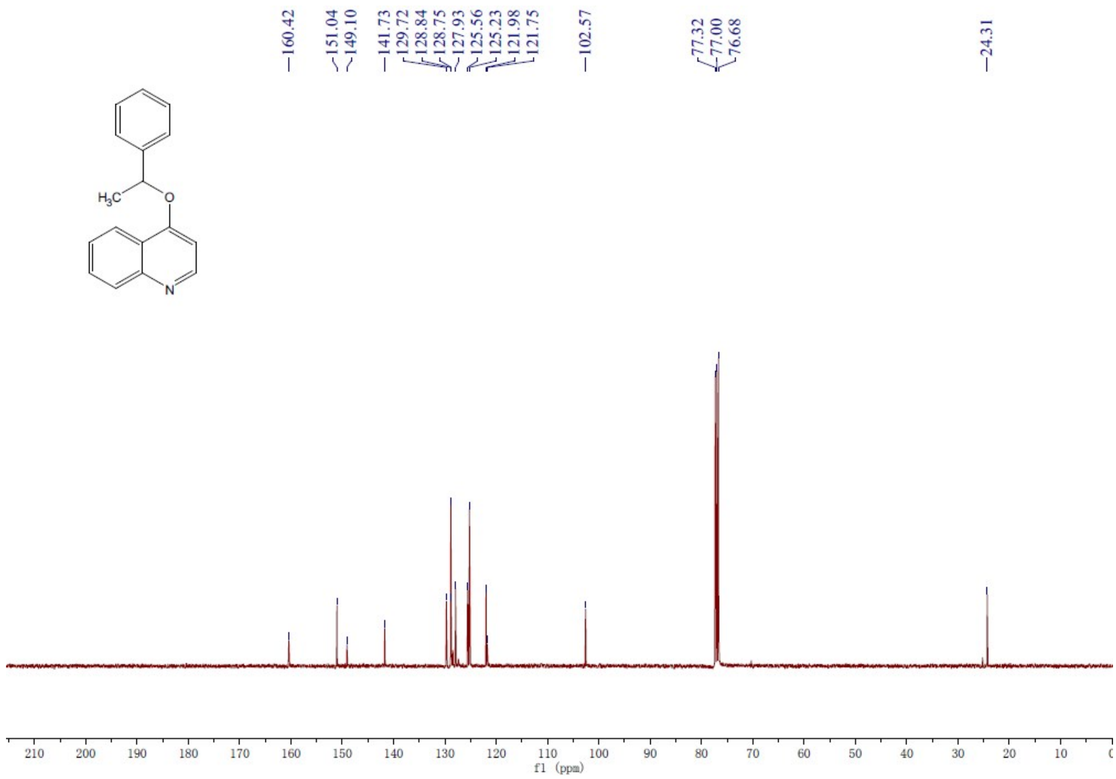

$^{1}$H spectrum of **3pa**



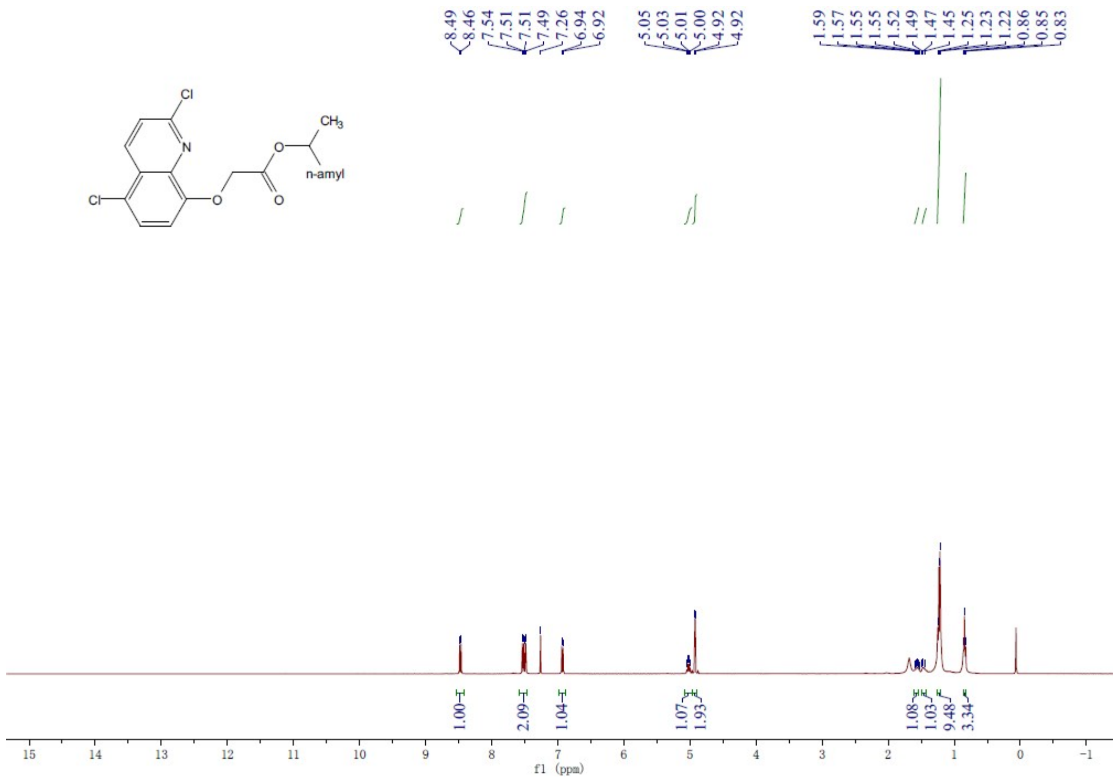
$^{13}$C spectrum of **3pa**



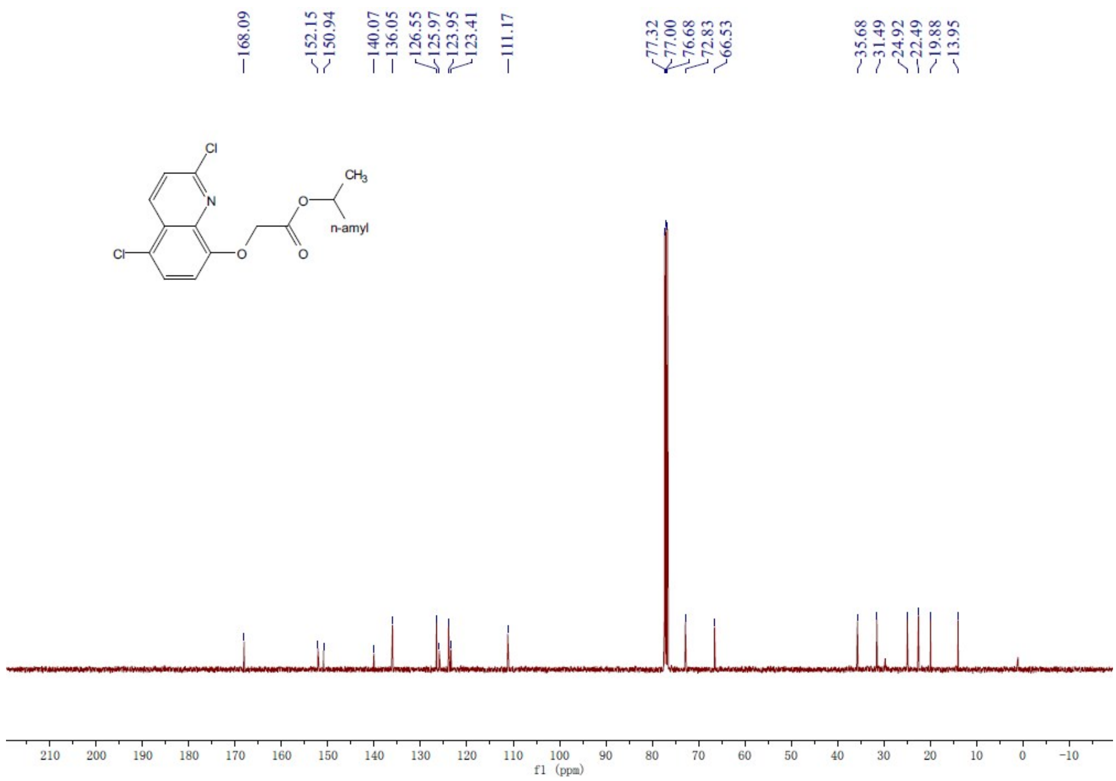
$^{1}$H spectrum of **4a**



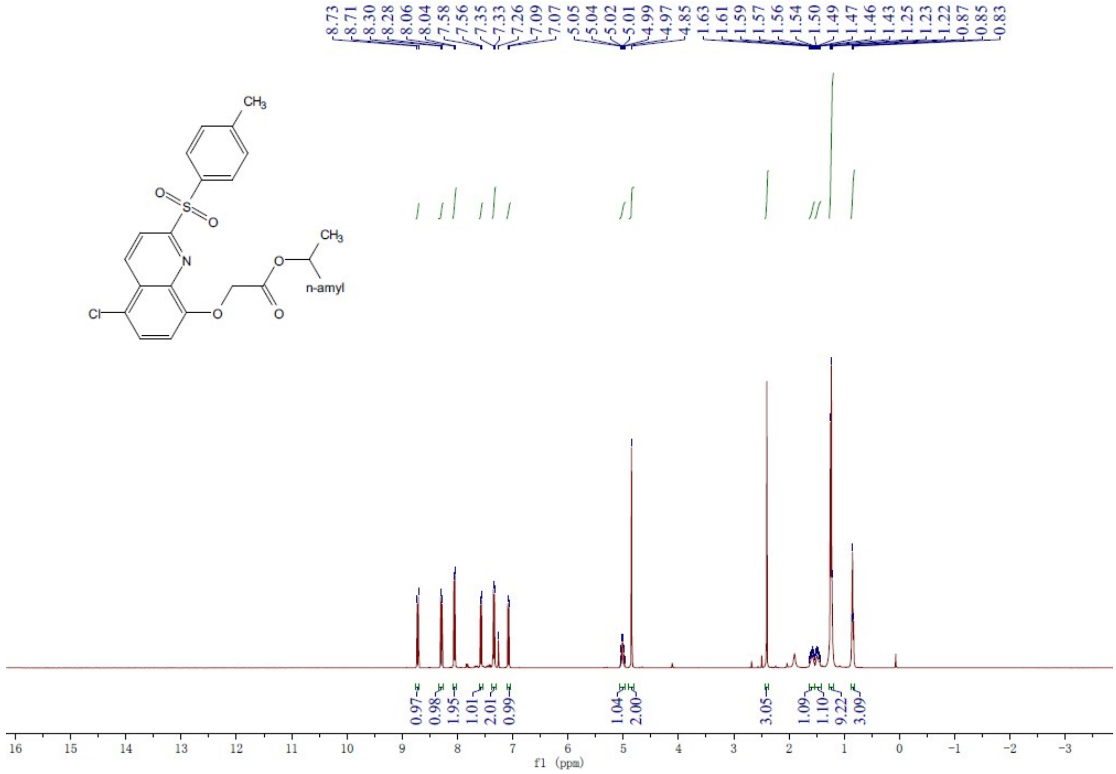
$^{13}C$ spectrum of **4a**



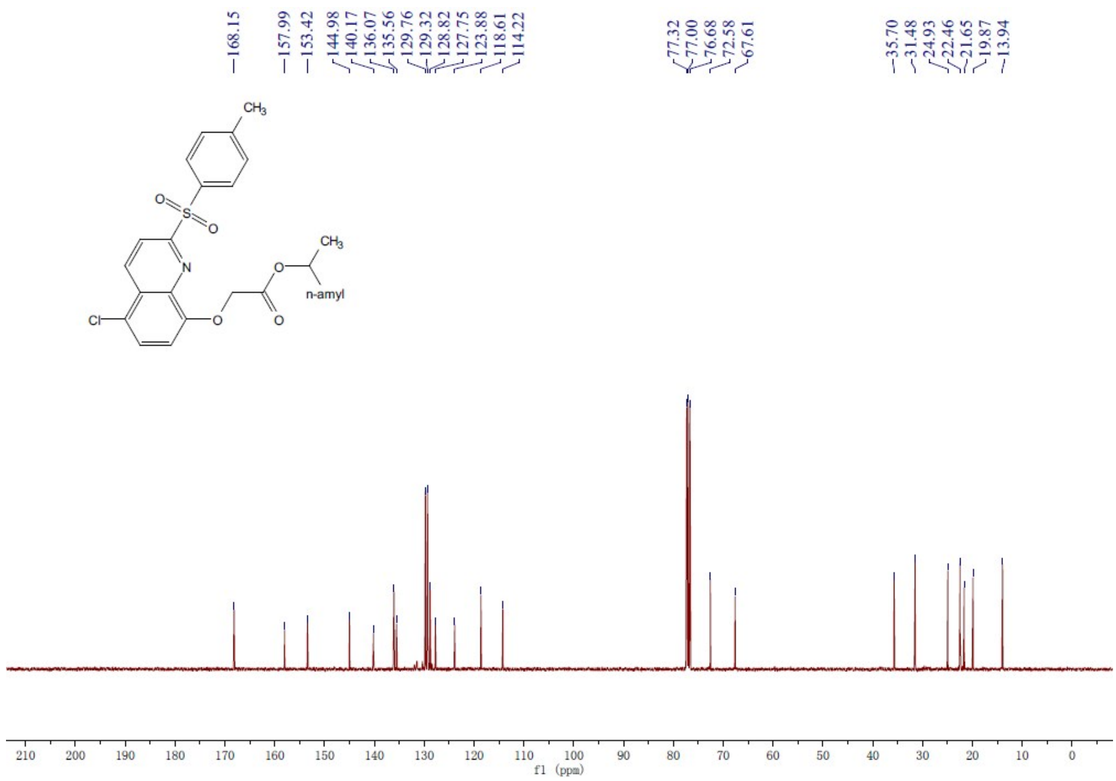
$^{1}H$ spectrum of **1w**




$^{13}C$ spectrum of **1w**




$^{1}H$ spectrum of **3wa**




$^{13}C$ spectrum of **3wa**