Electronic Supplementary Information for

Copper-Mediated 8-Amido Chelation-Induced Regioselective C-H Perfluoroalkylation of Quinolines

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1. General Information
2. General Procedure
3. Characterization of Products
4. Kinetic Isotope Experiments for Quinolinyl Moiety Fluoroalkylation
5. Crystallographic Experimental Section
6. NMR Spectra

1. General Information

All chemical reagents are obtained from commercial suppliers and used without further purification. All unknown compounds are characterized by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS. Analytical thin-layer chromatography are performed on glass plates precoated with silica gel impregnated with a fluorescent indicator (254 nm), and the plates are visualized by exposure to ultraviolet light. Mass spectra are taken on a Thermo Scientific ISQ LT GC-MS instrument in the electron ionization (EI) mode. ^{1}H NMR and ^{13}C NMR spectra are recorded on an AVANCE 500 Bruker spectrometer operating at 500 MHz and 125 MHz in $CDCl_3$, respectively, and chemical shifts are reported in ppm. GC analyses are performed on an Agilent 7890A instrument (Column: Agilent 19091J-413: 30 m × 320 μm × 0.25 μm, carrier gas: H_2, FID detection. High-resolution mass spectra (HRMS) were obtained on an Agilent mass spectrometer using ESI-TOF (electrospray ionization-time of flight).

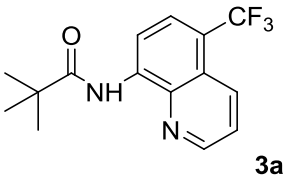
The 8-aminoquinolines **1** were synthesized following previously published procedures and determined by comparison with the reported data (*J. Am. Chem. Soc.* **2013**, *135*, 9797; *Org. Lett.* **2012**, *14*, 354; *J. Am. Chem. Soc.* **2014**, *136*, 11590). The sodium perfluoroalkanesulfinates (R_fSO_2Na, 2b-f) were synthesized according to the procedure reported by Hu and DesMarteau. (*Inorg. Chem.* **1993**, *32*, 5007; *Org. Lett.* **2015**, *17*, 1838)

2. General Procedure

General procedure for copper-catalyzed C5-selective fluoroalkylation of quinolines:

The 8-aminoquinoline **1** (0.20 mmol), R_fSO_2Na **2** (0.40 mmol), $CuBr_2$ (0.02 mmol), AIBN (0.24 mmol) and MeCN (1.0 mL) were sequentially added to a 25 mL Schlenk tube with a magnetic stir bar. The resulting mixture was stirred at 120 ^oC for 12 h. The reaction solution was allowed to cool to ambient temperature, and then diluted with ethyl acetate, washed with water, dried over anhydrous Na_2SO_4. After the solvent had been removed under reduced pressure, the residue was purified by flash chromatography using PE-AcOEt (10:1-5:1, v/v) as the eluent to give the desired fluoroalkylated product **3**.

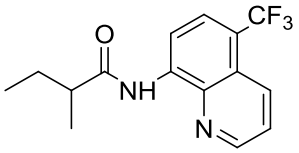
3. Characterization Data



3a

N-(5-(trifluoromethyl)quinolin-8-yl)pivalamide
Chemical Formula: $C_{15}H_{15}F_3N_2O$
Exact Mass: 296.1136
Molecular Weight: 296.2876
m/z: 296.1136 (100.0%), 297.1170 (16.2%), 298.1204 (1.2%)

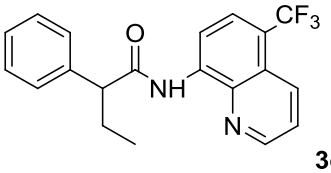
N-(5-(trifluoromethyl)quinolin-8-yl)pivalamide **3a,** colorless solid. Yield: 43 mg (73%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.46 (s, 1H), 8.91 (dd, *J* = 4.1, 1.3 Hz, 1H), 8.82 (d, *J* = 8.2 Hz, 1H), 8.52 (dd, *J* = 7.1, 1.5 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.61 (dd, *J* = 8.7, 4.2 Hz, 1H), 1.44 (s, 9H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.65. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.76, 148.77, 138.73, 138.37, 133.28, 126.72, 124,43 (q, *J* = 271 Hz), 122.84, 119.40 (q, *J* = 31 Hz), 114.00, 40.64, 27.76. HRMS (ESI-TOF) *m/z* calcd for $C_{15}H_{16}F_3N_2O$ $[M + H]^+$ 297.1215, found 297.1219



3b

2-methyl-*N*-(5-(trifluoromethyl)quinolin-8-yl)butanamide
Chemical Formula: $C_{15}H_{15}F_3N_2O$
Exact Mass: 296.1136
Molecular Weight: 296.2876
m/z: 296.1136 (100.0%), 297.1170 (16.2%), 298.1204 (1.2%)

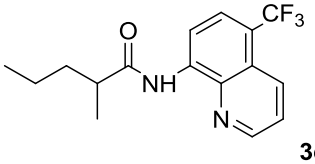
2-methyl-N-(5-(trifluoromethyl)quinolin-8-yl)butanamide **3b,** colorless oil. Yield: 45 mg (76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.04 (s, 1H), 8.87 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.82 (d, *J* = 8.1 Hz, 1H), 8.50 – 8.46 (m, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.57 (dd, *J* = 8.7, 4.2 Hz, 1H), 2.59 – 2.50 (m, 1H), 1.91 – 1.81 (m, 1H), 1.67 – 1.57 (m, 1H), 1.32 (d, *J* = 6.9 Hz, 3H), 1.01 (t, *J* = 7.4 Hz, 3H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.68. ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.83, 148.69, 138.38, 138.23, 133.30, 126.75, 124.42 (q, *J* = 271 Hz), 124.38, 122.87, 119.48 (q, *J* = 31 Hz), 114.20, 44.73, 27.55, 17.53, 11.99. HRMS (ESI-TOF) *m/z* calcd for $C_{15}H_{16}F_3N_2O$ $[M + H]^+$ 297.1215, found 297.1219



3c

2-phenyl-*N*-(5-(trifluoromethyl)quinolin-8-yl)butanamide
Chemical Formula: $C_{20}H_{17}F_3N_2O$
Exact Mass: 358.1293
Molecular Weight: 358.3570
m/z: 358.1293 (100.0%), 359.1327 (21.6%), 360.1360 (2.2%)

2-phenyl-N-(5-(trifluoromethyl)quinolin-8-yl)butanamide **3c,** yellow solid. Yield: 56 mg (78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.79 (dd, *J* = 4.8, 3.4 Hz, 2H), 8.44 (dd, *J* = 8.6, 1.5 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 1H), 7.53 (dd, *J* = 8.7, 4.2 Hz, 1H), 7.46 (d, *J* = 7.3 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 3.64 (t, *J* = 7.6 Hz, 1H), 2.34 (dt, *J* = 13.9, 7.3 Hz, 1H), 2.02 – 1.93 (m, 1H), 0.99 (t, *J* = 7.4 Hz, 3H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.71. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.70, 148.67, 139.48, 138.36, 138.15, 133.21, 129.08, 128.18, 127.59, 126.64, 124.37 (q, *J* = 271 Hz), 124.31, 122.83, 119.35 (q, *J* = 30 Hz), 114.09, 56.91, 26.55, 12.48. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{18}F_3N_2O$ $[M + H]^+$ 359.1371, found 359.1377

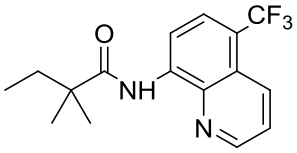


3d

2-methyl-*N*-(5-(trifluoromethyl)quinolin-8-yl)pentanamide
Chemical Formula: $C_{16}H_{17}F_3N_2O$
Exact Mass: 310.1293
Molecular Weight: 310.3142
m/z: 310.1293 (100.0%), 311.1327 (17.3%), 312.1360 (1.4%)

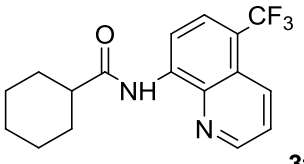
2-methyl-N-(5-(trifluoromethyl)quinolin-8-yl)pentanamide **3d,** white solid. Yield: 41 mg (66%).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.04 (s, 1H), 8.88 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.82 (d, *J* = 8.1 Hz, 1H), 8.51 – 8.47 (m, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.58 (dd, *J* = 8.7, 4.2 Hz, 1H), 2.63 (dt, *J* = 13.9, 6.9 Hz, 1H), 1.86 – 1.78 (m, 1H), 1.58 – 1.50 (m, 1H), 1.44 (dd, *J* = 4.6, 2.8 Hz, 3H), 1.32 (d, *J* = 6.9 Hz, 3H), 0.95 (dd, *J* = 8.7, 5.9 Hz, 4H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.67. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.98, 148.70, 138.40, 138.23, 133.31, 126.76, 124.42 (q, *J* = 271 Hz), 124.39, 122.88, 119.49 (q, *J* = 30 Hz), 114.21, 43.00, 36.72, 20.75, 17.97, 14.20. HRMS (ESI-TOF) *m/z* calcd for $C_{16}H_{18}F_3N_2O$ $[M + H]^+$ 311.1371, found 311.1376



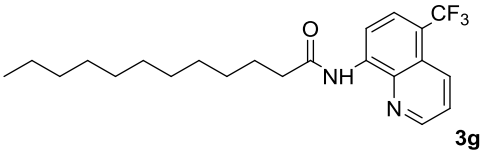
2,2-dimethyl-*N*-(5-(trifluoromethyl)quinolin-8-yl)butanamide
Chemical Formula: $C_{16}H_{17}F_3N_2O$
Exact Mass: 310.1293
Molecular Weight: 310.3142
3e m/z: 310.1293 (100.0%), 311.1327 (17.3%), 312.1360 (1.4%)

2,2-dimethyl-N-(5-(trifluoromethyl)quinolin-8-yl)butanamide **3e,** white solid. Yield: 38 mg (61%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.40 (s, 1H), 8.89 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.82 (d, *J* = 8.2 Hz, 1H), 8.52 – 8.45 (m, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.59 (dd, *J* = 8.7, 4.2 Hz, 1H), 1.76 (q, *J* = 7.5 Hz, 2H), 1.38 (s, 7H), 0.94 (t, *J* = 7.5 Hz, 3H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.66.^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.20, 148.78, 138.73, 138.33, 133.30, 126.76, 124.45 (q, *J* = 271 Hz), 124.40, 122.84, 119.37 (q, *J* = 30 Hz), 113.98, 44.40, 34.22, 25.14, 9.40, 1.15. HRMS (ESI-TOF) *m/z* calcd for $C_{16}H_{18}F_3N_2O$ $[M + H]^+$ 311.1371, found 311.1374.



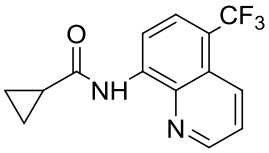
N-(5-(trifluoromethyl)quinolin-8-yl)cyclohexanecarboxamide
Chemical Formula: $C_{17}H_{17}F_3N_2O$
Exact Mass: 322.1293
Molecular Weight: 322.3249
3f m/z: 322.1293 (100.0%), 323.1327 (18.4%), 324.1360 (1.6%)

N-(5-(trifluoromethyl)quinolin-8-yl)cyclohexanecarboxamide **3f,** white solid. Yield: 37 mg (57%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.84 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.76 (d, *J* = 8.2 Hz, 1H), 8.48 – 8.42 (m, 1H), 7.85 (d, *J* = 8.3 Hz, 1H), 7.54 (dd, *J* = 8.7, 4.2 Hz, 1H), 2.44 (tt, *J* = 11.7, 3.5 Hz, 1H), 2.03 (dd, *J* = 13.6, 1.9 Hz, 2H), 1.87 – 1.79 (m, 2H), 1.70 (ddd, *J* = 12.6, 4.8, 2.5 Hz, 1H), 1.62 – 1.54 (m, 3H), 1.42 – 1.16 (m, 3H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.65. ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.35, 148.66, 138.44, 138.31, 133.33, 126.77, 124.43 (q, *J* = 271 Hz), 124.40, 122.87, 119.42 (q, *J* = 30 Hz), 114.19, 47.03, 29.80, 25.83. HRMS (ESI-TOF) *m/z* calcd for $C_{17}H_{18}F_3N_2O$ $[M + H]^+$ 323.1371, found 323.1376



N-(5-(trifluoromethyl)quinolin-8-yl)dodecanamide
Chemical Formula: $C_{22}H_{29}F_3N_2O$
Exact Mass: 394.2232
Molecular Weight: 394.4737
3g m/z: 394.2232 (100.0%), 395.2266 (23.8%), 396.2299 (2.7%)

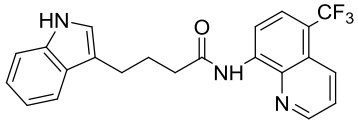
N-(5-(trifluoromethyl)quinolin-8-yl)dodecanamide **3g,** white solid. Yield: 52 mg (68%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.93 (s, 1H), 8.82 (d, *J* = 4.1 Hz, 1H), 8.75 (d, *J* = 8.2 Hz, 1H), 8.44 (d, *J* = 8.6 Hz, 1H), 7.84 (d, *J* = 8.3 Hz, 1H), 7.53 (dd, *J* = 8.7, 4.2 Hz, 1H), 2.56 – 2.50 (m, 2H), 1.81 – 1.73 (m, 2H), 1.36 (ddd, *J* = 28.7, 14.6, 4.9 Hz, 4H), 1.22 (dd, *J* = 9.5, 8.2 Hz, 12H), 0.82 (t, *J* = 6.9 Hz, 3H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.68.^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.41, 148.64, 138.26, 138.20, 133.31, 126.73, 124.41(q, *J* = 271 Hz), 124.38, 122.87, 119.48(q, *J* = 30 Hz), 114.15, 38.41, 32.03, 29.73, 29.62, 29.51, 29.46, 29.40, 25.64, 22.81, 14.23. HRMS (ESI-TOF) *m/z* calcd for $C_{22}H_{30}F_3N_2O$ $[M + H]^+$ 395.2310, found 395.2319



3h

N-(5-(trifluoromethyl)quinolin-8-yl)cyclopropanecarboxamide
Chemical Formula: $C_{14}H_{11}F_3N_2O$
Exact Mass: 280.0823
Molecular Weight: 280.2451
m/z: 280.0823 (100.0%), 281.0857 (15.1%), 282.0891 (1.1%)

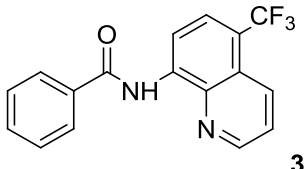
N-(5-(trifluoromethyl)quinolin-8-yl)cyclopropanecarboxamide **3h,** pale yellow solid. Yield: 30 mg (53%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.90 (d, *J* = 3.9 Hz, 1H), 8.77 (d, *J* = 8.2 Hz, 1H), 8.52 (d, *J* = 8.6 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.61 (dd, *J* = 8.7, 4.2 Hz, 1H), 1.88 – 1.78 (m, 1H), 1.21 – 1.16 (m, 2H), 1.00 – 0.94 (m, 2H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.64. ^{13}C NMR ($CDCl_3$ 125 MHz) δ 172.85, 148.64, 138.28, 138.17, 133.33, 126.77, 124.41 (q, *J* = 271 Hz), 124.42, 122.90, 119.35 (q, *J* = 31 Hz), 114.13, 16.53, 8.71. HRMS (ESI-TOF) *m/z* calcd for $C_{14}H_{12}F_3N_2O$ [M + H]$^+$ 281.0902, found 281.0906



3i

4-(1*H*-indol-3-yl)-*N*-(5-(trifluoromethyl)quinolin-8-yl)butanamide
Chemical Formula: $C_{22}H_{18}F_3N_3O$
Exact Mass: 397.1402
Molecular Weight: 397.3930
m/z: 397.1402 (100.0%), 398.1436 (23.8%), 399.1469 (2.7%), 398.1372 (1.1%)

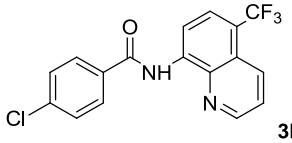
4-(1H-indol-3-yl)-N-(5-(trifluoromethyl)quinolin-8-yl)butanamide **3i,** yellow oil. Yield: 64 mg (81%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.79 (s, 1H), 8.84 – 8.74 (m, 2H), 8.43 (s, 1H), 8.16 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.45 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.40 (d, *J* = 8.3 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 1H), 3.07 (t, *J* = 7.5 Hz, 2H), 2.64 (t, *J* = 7.5 Hz, 2H), 2.29 – 2.20 (m, 2H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.02. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.44, 148.23, 138.48, 136.49, 135.45, 134.62, 128.07, 127.57, 124.92, 121.70, 121.54, 120.72, 120.60, 118.02, 116.64, 111.81, 37.56, 26.49, 23.40. HRMS (ESI-TOF) *m/z* calcd for $C_{22}H_{19}F_3N_3O$ [M + H]$^+$ 398.1480, found 398.1483



3j

N-(5-(trifluoromethyl)quinolin-8-yl)benzamide
Chemical Formula: $C_{17}H_{11}F_3N_2O$
Exact Mass: 316.0823
Molecular Weight: 316.2772
m/z: 316.0823 (100.0%), 317.0857 (18.4%), 318.0891 (1.6%)

N-(5-(trifluoromethyl)quinolin-8-yl)benzamide **3j,** colorless solid. Yield: 51 mg (81%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.94 (s, 1H), 8.96 (dd, *J* = 15.1, 6.1 Hz, 2H), 8.55 (d, *J* = 8.6 Hz, 1H), 8.10 (d, *J* = 7.2 Hz, 2H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.62 (ddd, *J* = 23.2, 11.6, 5.5 Hz, 4H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.66. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.83, 148.87, 138.72, 138.25, 134.74, 133.42, 132.41, 129.06, 127.52, 126.77, 124.47, 124.40 (q, *J* = 271 Hz), 123.04, 119.97 (q, *J* = 30 Hz), 114.36. HRMS (ESI-TOF) *m/z* calcd for $C_{17}H_{12}F_3N_2O$ [M + H]$^+$ 317.0902, found 317.0908

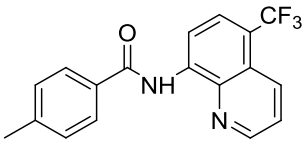


3k

4-chloro-*N*-(5-(trifluoromethyl)quinolin-8-yl)benzamide
Chemical Formula: $C_{17}H_{10}ClF_3N_2O$
Exact Mass: 350.0434
Molecular Weight: 350.7223
m/z: 350.0434 (100.0%), 352.0404 (32.0%), 351.0467 (18.4%), 353.0438 (5.9%), 352.0501 (1.6%)

4-chloro-N-(5-(trifluoromethyl)quinolin-8-yl)benzamide **3k,** colorless solid. Yield: 59 mg (84%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.90 (s, 1H), 8.94 (d, *J* = 8.6 Hz, 2H), 8.55 (d, *J* = 8.6 Hz, 1H), 8.03 (t, *J* = 7.2 Hz, 2H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.65 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 2H).

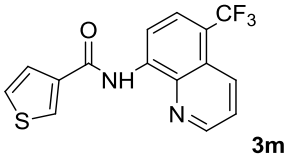
^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.70. ^{13}C NMR ($CDCl_3$, 125 MHz). δ 164.71, 138.77, 138.66, 137.98, 133.49, 133.10, 129.35, 128.94, 126.51 (q, *J* = 270 Hz), 126.76, 124.46, 123.11, 120.10 (q, *J* = 32 Hz), 114.44. HRMS (ESI-TOF) *m/z* calcd for $C_{17}H_{11}ClF_3N_2O$ [M + H]$^+$ 351.0512, found 351.0518



3l

4-methyl-*N*-(5-(trifluoromethyl)quinolin-8-yl)benzamide
Chemical Formula: $C_{18}H_{13}F_3N_2O$
Exact Mass: 330.0980
Molecular Weight: 330.3038
m/z: 330.0980 (100.0%), 331.1014 (19.5%), 332.1047 (1.8%)

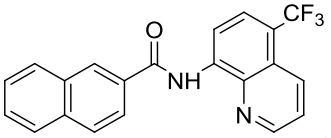
4-methyl-N-(5-(trifluoromethyl)quinolin-8-yl)benzamide **3l,** white solid. Yield: 54 mg (82%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.89 (s, 1H), 8.94 (dd, *J* = 12.7, 6.0 Hz, 2H), 8.52 (d, *J* = 8.6 Hz, 1H), 7.97 (dd, *J* = 12.1, 8.2 Hz, 3H), 7.61 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.36 (d, *J* = 7.9 Hz, 2H), 2.46 (s, 3H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.64. ^{13}C NMR ($CDCl_3$, 125 MHz). δ 165.76, 148.81, 143.01, 138.69, 138.34, 133.35, 131.89, 129.70, 127.52, 126.76, 124.43 (q, *J* = 270 Hz), 124.43, 122.98, 119.88 (q, *J* = 32 Hz), 114.23, 21.71. HRMS (ESI-TOF) *m/z* calcd for $C_{18}H_{14}F_3N_2O$ [M + H]$^+$ 331.1058, found 331.1064.



3m

N-(5-(trifluoromethyl)quinolin-8-yl)thiophene-3-carboxamide
Chemical Formula: $C_{15}H_9F_3N_2OS$
Exact Mass: 322.0388
Molecular Weight: 322.3050
m/z: 322.0388 (100.0%), 323.0421 (16.2%), 324.0346 (4.5%), 324.0455 (1.2%)

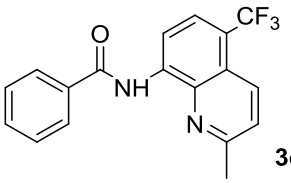
N-(5-(trifluoromethyl)quinolin-8-yl)thiophene-3-carboxamide **3m,** white solid. Yield: 44 mg (69%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.70 (s, 1H), 8.96 – 8.83 (m, 2H), 8.52 (d, *J* = 8.6 Hz, 1H), 8.21 – 8.13 (m, 1H), 7.95 (d, *J* = 8.2 Hz, 1H), 7.69 – 7.66 (m, 1H), 7.61 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.45 (dd, *J* = 5.0, 3.0 Hz, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.66. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 161.28, 148.84, 138.51, 138.15, 137.96, 133.40, 129.65, 127.12, 126.74, 126.45, 124.44, 124.40 (q, *J* = 271 Hz), 123.01, 119.74 (q, *J* = 30 Hz), 114.27. HRMS (ESI-TOF) *m/z* calcd for $C_{15}H_{10}F_3N_2OS$ [M + H]$^+$ 323.3129, found 323.3134.



3n

N-(5-(trifluoromethyl)quinolin-8-yl)-2-naphthamide
Chemical Formula: $C_{21}H_{13}F_3N_2O$
Exact Mass: 366.0980
Molecular Weight: 366.3359
m/z: 366.0980 (100.0%), 367.1014 (22.7%), 368.1047 (2.5%)

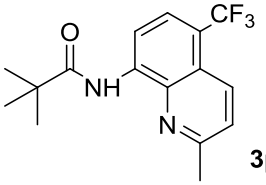
N-(5-(trifluoromethyl)quinolin-8-yl)-2-naphthamide **3n**, yellow oil. Yield: 42 mg (57%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 11.08 (s, 1H), 9.07 – 8.94 (m, 2H), 8.66 – 8.52 (m, 2H), 8.14 (dd, *J* = 8.5, 1.6 Hz, 1H), 8.07 (d, *J* = 7.4 Hz, 1H), 8.04 – 7.99 (m, 2H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.67 – 7.59 (m, 3H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.64. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.89, 148.91, 138.77, 138.31, 135.25, 133.44, 132.86, 131.94, 129.39, 129.00, 128.35, 128.26, 127.97, 127.10, 126.80, 124.49, 124.43 (q, *J* = 271 Hz), 123.73, 123.04, 114.43. HRMS (ESI-TOF) *m/z* calcd for $C_{21}H_{14}F_3N_2O$ [M + H]$^+$ 367.1058, found 367.1065.



3o

N-(2-methyl-5-(trifluoromethyl)quinolin-8-yl)benzamide
Chemical Formula: $C_{18}H_{13}F_3N_2O$
Exact Mass: 330.0980
Molecular Weight: 330.3038
m/z: 330.0980 (100.0%), 331.1014 (19.5%), 332.1047 (1.8%)

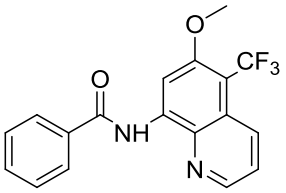
N-(2-methyl-5-(trifluoromethyl)quinolin-8-yl)benzamide **3o**, white solid. Yield: 55 mg (83%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.98 (s, 1H), 8.91 (d, *J* = 8.2 Hz, 1H), 8.40 (d, *J* = 8.7 Hz, 1H), 8.14 – 8.02 (m, 2H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.64 – 7.54 (m, 3H), 7.48 (d, *J* = 8.7 Hz, 1H), 2.81 (s, 3H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.66. ^{13}C NMR ($CDCl_3$, 125MHz) δ 165.68, 158.07, 138.20, 137.58, 134.92, 133.39, 132.30, 129.06, 127.45, 125.61, 124.79 (q, *J* = 271 Hz), 123.42, 122.55, 119.75 (q, *J* = 30 Hz), 114.34, 25.42. HRMS (ESI-TOF) *m/z* calcd for $C_{18}H_{14}F_3N_2O$ $[M + H]^+$ 331.1058, found 331.1064.



3p

N-(2-methyl-5-(trifluoromethyl)quinolin-8-yl)pivalamide
Chemical Formula: $C_{16}H_{17}F_3N_2O$
Exact Mass: 310.1293
Molecular Weight: 310.3142
m/z: 310.1293 (100.0%), 311.1327 (17.3%), 312.1360 (1.4%)

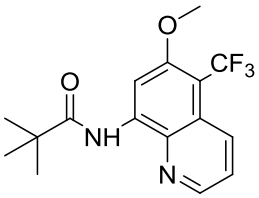
N-(2-methyl-5-(trifluoromethyl)quinolin-8-yl)pivalamide **3p** white solid. Yield: 49 mg (79%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.53 (s, 1H), 8.76 (d, *J* = 8.2 Hz, 1H), 8.38 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.46 (d, *J* = 8.8 Hz, 1H), 2.78 (s, 3H), 1.44 (s, 9H). ^{19}F NMR ($CDCl_3$, 470 MHz) δ -58.65. ^{13}C NMR ($CDCl_3$, 125 MHz). δ 177.65, 157.82, 138.19, 137.68, 133.32, 125.62, 124.54 (q, *J* = 272 Hz), 123.64, 122.46, 119.32 (q, *J* = 31 Hz), 113.98, 40.66, 27.75, 25.39. HRMS (ESI-TOF) *m/z* calcd for $C_{16}H_{18}F_3N_2O$ $[M + H]^+$ 311.1371, found 311.1376.



3q

N-(6-methoxy-5-(trifluoromethyl)quinolin-8-yl)benzamide
Chemical Formula: $C_{18}H_{13}F_3N_2O_2$
Exact Mass: 346.0929
Molecular Weight: 346.3032
m/z: 346.0929 (100.0%), 347.0963 (19.5%), 348.0996 (1.8%)

N-(6-methoxy-5-(trifluoromethyl)quinolin-8-yl)benzamide **3q,** white solid. Yield: 62 mg (89%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 11.01 (s, 1H), 8.96 (s, 1H), 8.73 (d, *J* = 3.2 Hz, 1H), 8.57 (d, *J* = 8.9 Hz, 1H), 8.11 – 8.06 (m, 2H), 7.63 – 7.56 (m, 3H), 7.53 (dd, *J* = 8.9, 4.1 Hz, 1H), 4.11 (s, 3H). ^{19}F NMR (470 MHz, $CDCl_3$) δ -52.02. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 166.00, 158.40, 146.13, 139.43, 134.94, 134.54, 134.11, 132.89, 132.53, 129.11, 127.47, 126.45, 125.23 (q, *J* = 272 Hz), 123.46, 104.04, 57.15. HRMS (ESI-TOF) *m/z* calcd for $C_{18}H_{14}F_3N_2O_2$ $[M + H]^+$ 347.1007, found 347.1012.

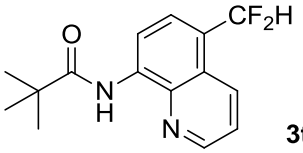


3r

N-(6-methoxy-5-(trifluoromethyl)quinolin-8-yl)pivalamide
Chemical Formula: $C_{16}H_{17}F_3N_2O_2$
Exact Mass: 326.1242
Molecular Weight: 326.3136
m/z: 326.1242 (100.0%), 327.1276 (17.3%), 328.1309 (1.4%)

N-(6-methoxy-5-(trifluoromethyl)quinolin-8-yl)pivalamide **3r,** colorless oil. Yield: 59 mg (91%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.53 (s, 1H), 8.82 (s, 1H), 8.69 (dd, *J* = 4.1, 1.2 Hz, 1H), 8.56 – 8.51 (m, 1H), 7.50 (dd, *J* = 8.9, 4.1 Hz, 1H), 4.06 (s, 3H), 1.43 (s, 9H). ^{19}F NMR (470 MHz, $CDCl_3$) δ

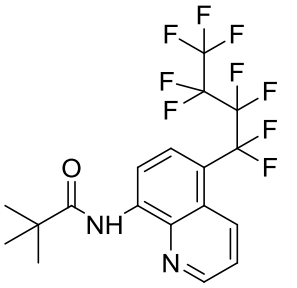
-52.00. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 178.20, 158.39, 146.06, 139.53, 134.86, 134.13, 132.80, 126.38, 124.16, 123.30, 103.76, 57.03, 40.72, 27.72. HRMS (ESI-TOF) *m/z* calcd for $C_{16}H_{18}F_3N_2O_2$ $[M + H]^+$ 327.1320, found 327.1326.



3t

N-(5-(difluoromethyl)quinolin-8-yl)pivalamide
Chemical Formula: $C_{15}H_{16}F_2N_2O$
Exact Mass: 278.1231
Molecular Weight: 278.2971
m/z: 278.1231 (100.0%), 279.1264 (16.2%), 280.1298 (1.2%)

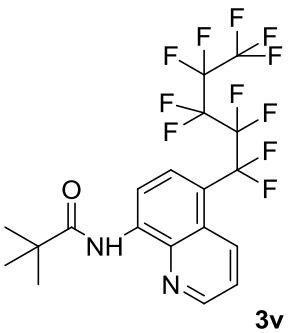
N-(5-(difluoromethyl)quinolin-8-yl)pivalamide **3t,** colorless solid. Yield: 9 mg (17%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.41 (s, 1H), 8.88 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.79 (d, *J* = 8.0 Hz, 1H), 8.60 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.56 (dd, *J* = 8.6, 4.2 Hz, 1H), 6.95 (t, *J* = 54.9 Hz, 1H), 1.43 (s, 8H). ^{19}F NMR (470 MHz, $CDCl_3$) δ -106.75. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.71, 148.69, 139.01, 137.52, 133.31, 130.04, 127.58, 124.88, 122.46, 116.31, 114.45, 40.61, 27.79. HRMS (ESI-TOF) *m/z* calcd for $C_{15}H_{17}F_2N_2O$ $[M + H]^+$ 279.1309, found 279.1315.



3u

N-(5-(perfluorobutyl)quinolin-8-yl)pivalamide
Chemical Formula: $C_{18}H_{15}F_9N_2O$
Exact Mass: 446.1041
Molecular Weight: 446.3101
m/z: 446.1041 (100.0%), 447.1074 (19.5%), 448.1108 (1.8%)

N-(5-(perfluorobutyl)quinolin-8-yl)pivalamide **3u,** white solid. Yield: 42 mg (47%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.52 (s, 1H), 8.91 – 8.84 (m, 2H), 8.53 (d, *J* = 8.7 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.57 (dd, *J* = 8.8, 4.1 Hz, 1H), 1.43 (s, 10H). ^{19}F NMR (470 MHz, $CDCl_3$) δ -80.91 (t, *J* = 9.7 Hz), -104.47 (dd, *J* = 20.5, 7.6 Hz), -121.17 – -121.70 (m), -125.56 (dd, *J* = 15.5, 13.1 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.80, 148.55, 138.84, 138.58, 133.87, 130.00, 125.73, 122.79, 117.60, 117.43, 117.24, 114.33, 40.67, 27.75. HRMS (ESI-TOF) *m/z* calcd for $C_{18}H_{16}F_9N_2O$ $[M + H]^+$ 447.1119, found 447.1128.

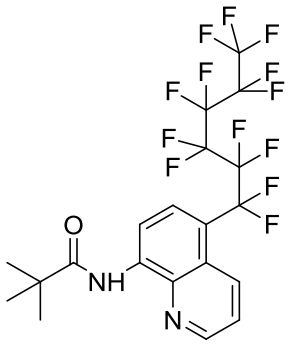


3v

N-(5-(perfluoropentyl)quinolin-8-yl)pivalamide
Chemical Formula: $C_{19}H_{15}F_{11}N_2O$
Exact Mass: 496.1009
Molecular Weight: 496.3176
m/z: 496.1009 (100.0%), 497.1042 (20.5%), 498.1076 (2.0%)

N-(5-(perfluoropentyl)quinolin-8-yl)pivalamide **3v,** white solid. Yield: 43 mg (43%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.53 (s, 1H), 8.87 (dd, *J* = 4.8, 3.5 Hz, 2H), 8.53 (d, *J* = 8.7 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.57 (dd, *J* = 8.8, 4.1 Hz, 1H), 1.43 (s, 9H). ^{19}F NMR (470 MHz, $CDCl_3$) δ -80.75 (dd, *J* = 13.9, 5.6 Hz), -104.32 (t, *J* = 14.8 Hz), -120.75 (s), -122.22 (s), -126.10 (s). ^{13}C NMR (DMSO, 125 MHz) δ 177.82, 148.55, 138.84, 138.58, 133.88, 130.02, 125.74, 122.80, 117.68, 117.49, 117.30, 114.33, 40.68, 27.75. HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{16}F_{11}N_2O$ $[M + H]^+$ 497.1087, found

497.1090.



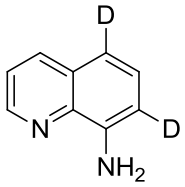
3w

N-(5-(perfluorohexyl)quinolin-8-yl)pivalamide
Chemical Formula: $C_{20}H_{15}F_{13}N_2O$
Exact Mass: 546.0977
Molecular Weight: 546.3251
m/z: 546.0977 (100.0%), 547.1010 (21.6%), 548.1044 (2.2%)

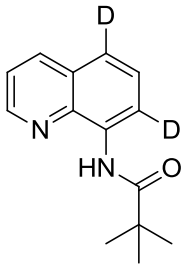
N-(5-(perfluorohexyl)quinolin-8-yl)pivalamide **3w,** white solid. Yield: 42 mg (38%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.53 (s, 1H), 8.88 (dd, *J* = 4.8, 3.6 Hz, 2H), 8.54 (d, *J* = 8.6 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.57 (dd, *J* = 8.8, 4.1 Hz, 1H), 1.43 (s, 9H). ^{19}F NMR (470 MHz, $CDCl_3$) δ -80.74 (t, *J* = 9.9 Hz), -104.27 (t, *J* = 15.3 Hz), -120.51 (d, *J* = 13.6 Hz), -121.41 (d, *J* = 12.9 Hz), -122.67 (s), -125.87 – -127.05 (m). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.82, 148.55, 138.83, 138.58, 133.89, 130.03, 125.75, 122.80, 117.52, 114.33, 40.67, 27.76. HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{16}F_{13}N_2O$ $[M + H]^+$ 547.1055, found 547.1061.

4. Kinetic Isotope Experiments for Quinolinyl Moiety Fluoroalkylation

I. Synthesis and Characterization of Deuterated Substrates



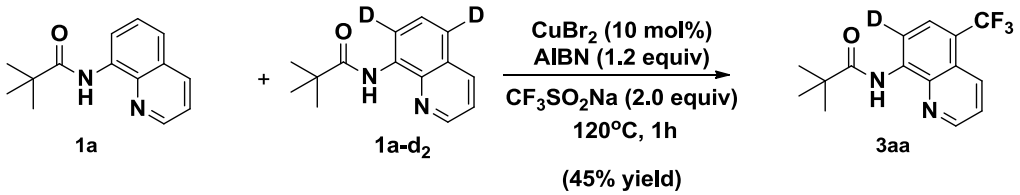
S1 (5,7-dideuterio-8-aminoquinoline). The deuterated aminoquinoline was synthesized from 8-aminoquinoline and DCl/D_2O in a microwave according to literature method (*Org.Lett.* **2008**, *10*, 4351); Spectral properties are consistent with literature values. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.46 (s, 1H), 7.20 (d, *J* = 8.2 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.1 Hz, 1H), 6.39 (d, *J* = 0.8 Hz, 1H), 4.88 (dd, *J* = 9.4, 2.8 Hz, 1H), 4.06 (dd, *J* = 11.7, 2.9 Hz,



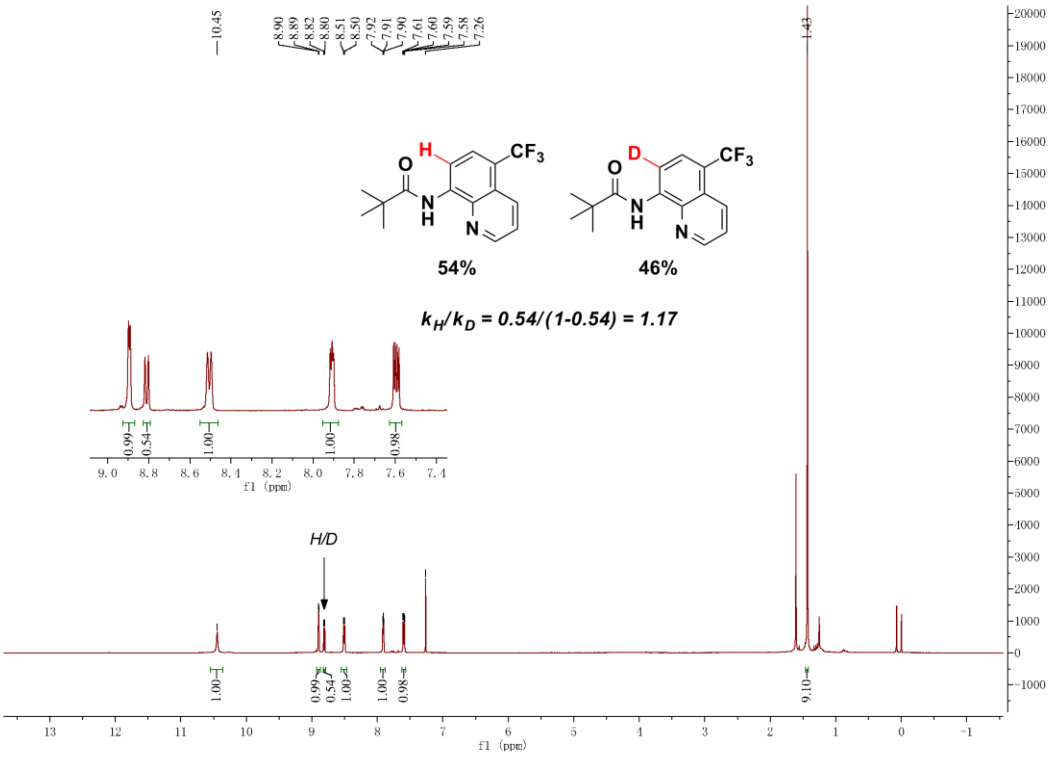
1a-d_2 (*N*-(5,7-dideuterio-8-quinolinyl)pivalamide). The amide was synthesized from pivaloyl chloride and 8-aminoquinoline **S1** according to the general amide synthesis procedure. Colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.46 (s, 1H), 7.20 (d, *J* = 8.2 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.1 Hz, 1H), 6.39 (d, *J* = 0.8 Hz, 1H), 4.88 (dd, *J* = 9.4, 2.8 Hz, 1H), 4.06 (dd, *J* = 11.7, 2.9 Hz,

II. Intermolecular Competition KIE.

To determine the intermolecular competition KIE, an equal mixture of substrates **1a** and **1a-d_2** were subjected to the typical reaction conditions. After 1 h, the starting material and product were separated by column chromatography (silica gel, 10 % EtOAc: hexanes). ^{1}H NMR result of the isolated product demonstrated an intermolecular competition KIE of k_H/k_D =1.17 was determined for the trifluoromethylation reaction. Unless there is an initial irreversible binding of the substrate to the catalyst, this result indicates the turnover-limiting step does not involve C-H activation.

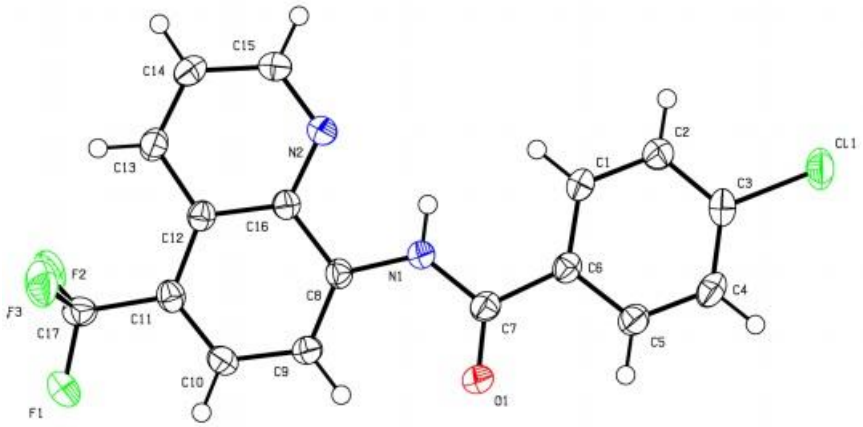


Intermolecular KIE
k_H/k_D =1.17


10.45
8.90
8.89
8.82
8.80
8.51
8.50
7.92
7.91
7.90
7.61
7.60
7.59
7.58
7.26
1.43
H
D
CF3
O
N
H
54%
46%
kH/kD = 0.54/(1-0.54) = 1.17
H/D
f1 (ppm)

5. Crystallographic Experimental Section

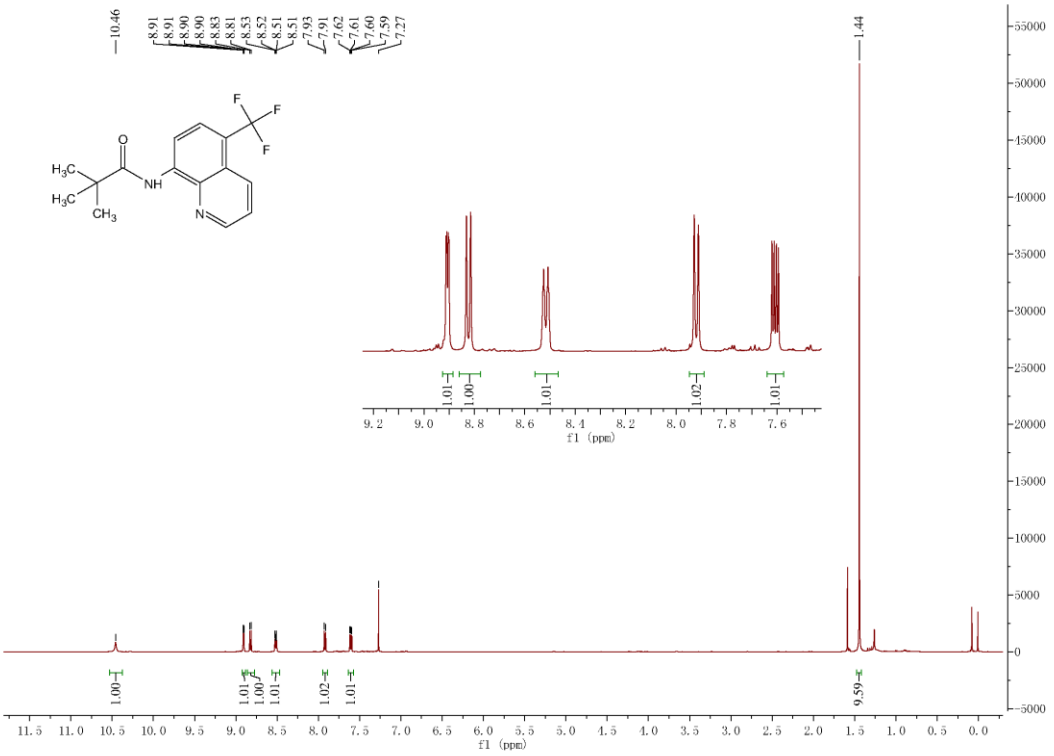
Crystal Structure of Compound 3k: CCDC NO. 1478785



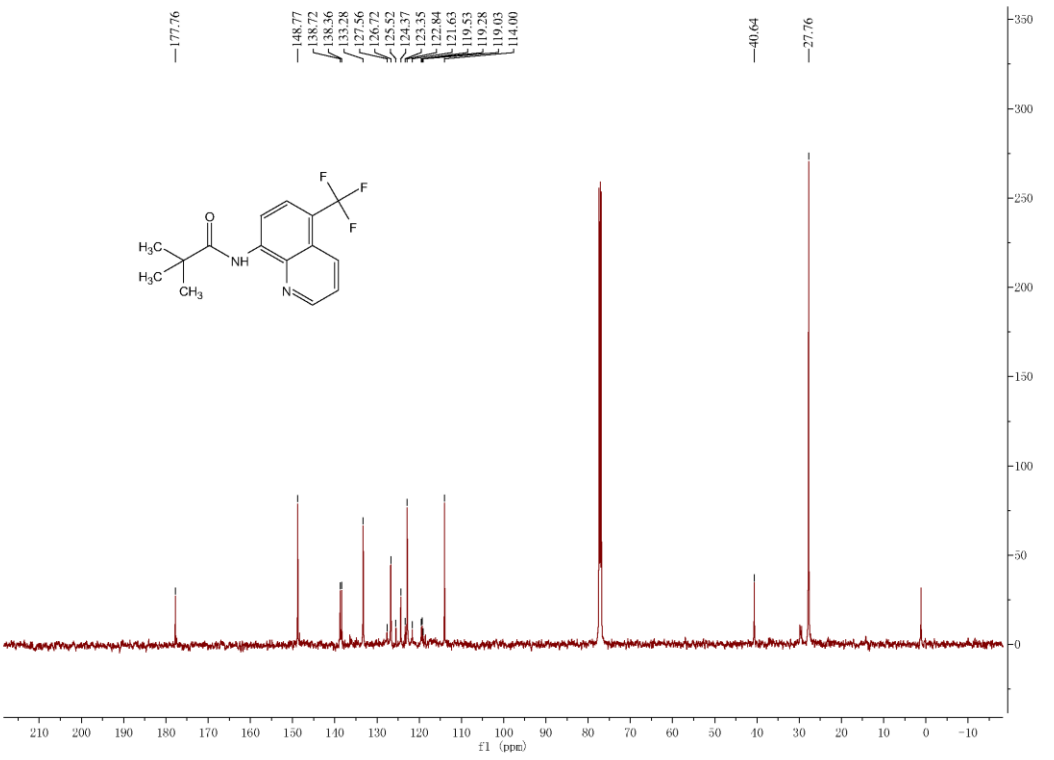
Formula	C17H10ClF3N2O
Formula weight	350.72
Crystal system	Triclinic
space group	*P*-1
a (Å)	8.165(2)
b (Å)	9.432(2)
c (Å)	10.126(3)
α (°)	85.485(7)
β (°)	83.241(8)
γ (°)	73.145(7)
Volume(Å^3)	740.3(3)
Z	2
T (K)	296(2)
D_{calcd} (g/m^3)	1.573
F(000)	356
Reflections collected	3470
Unique reflections	2752
Goof	1.057
R_1[I> 2σ(I)]	0.0630

[a] $w = 1/[\sigma^2(F_0)^2+(0.0797P)^2 +0.4099P]$, where P = $(F_0^2 + 2F_c^2)/3$;

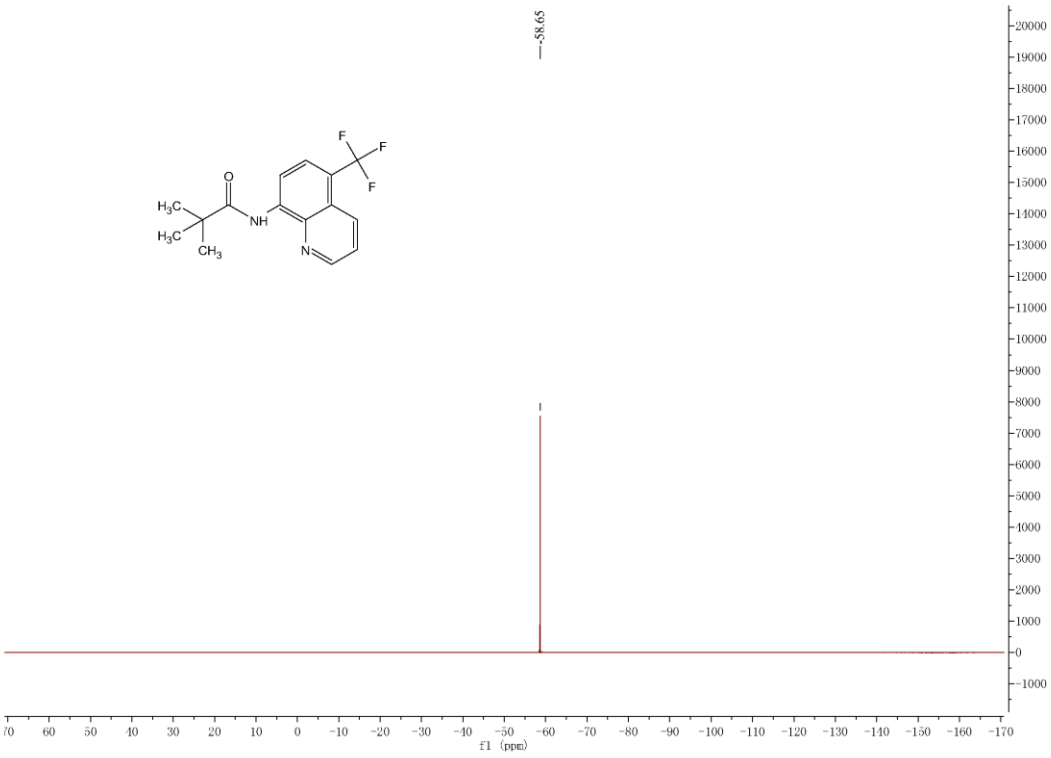
6. NMR Spectra of All Products



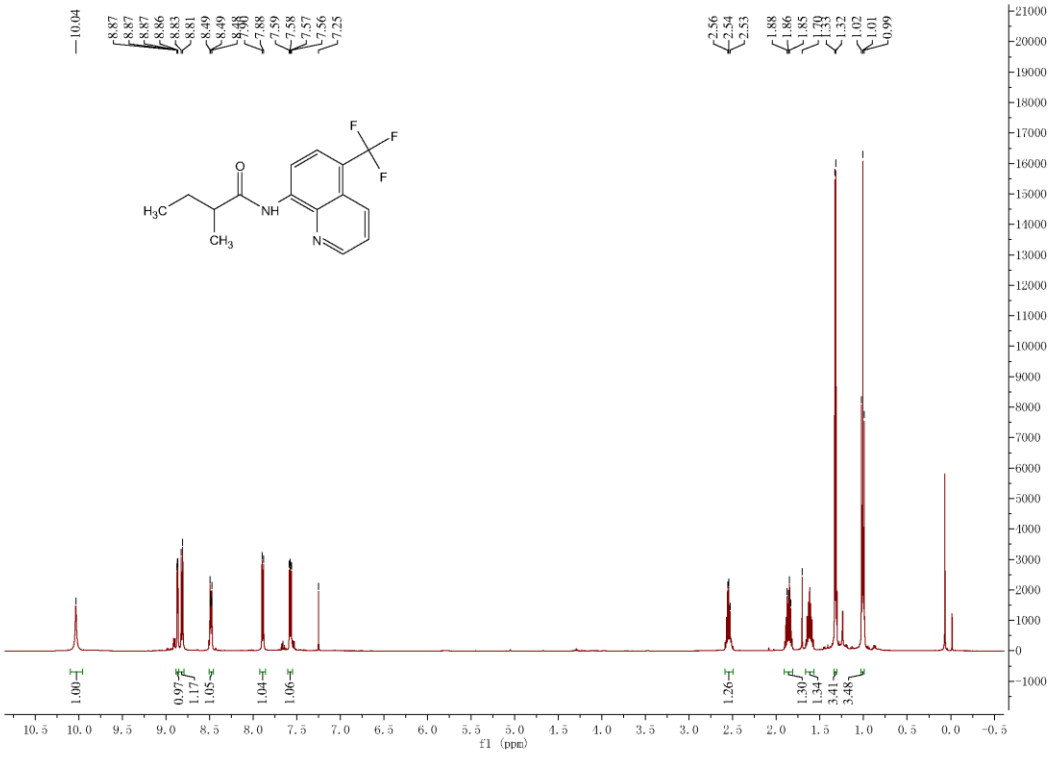
^{1}H NMR **3a**



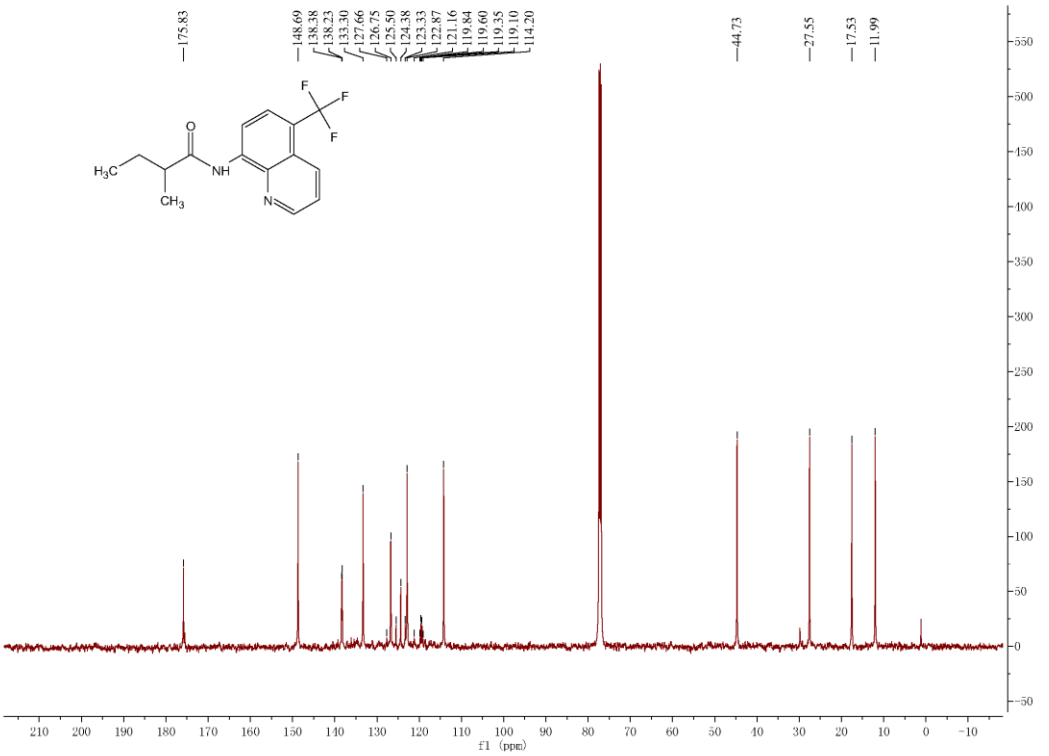
^{13}C NMR **3a**



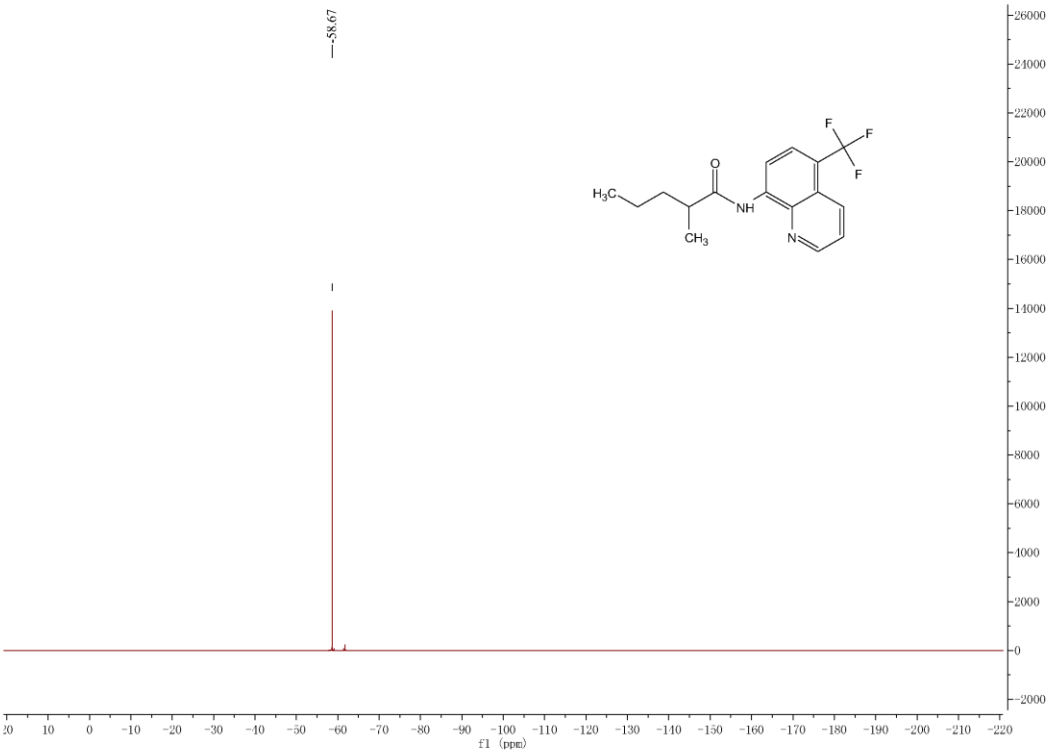
^{19}F NMR **3a**



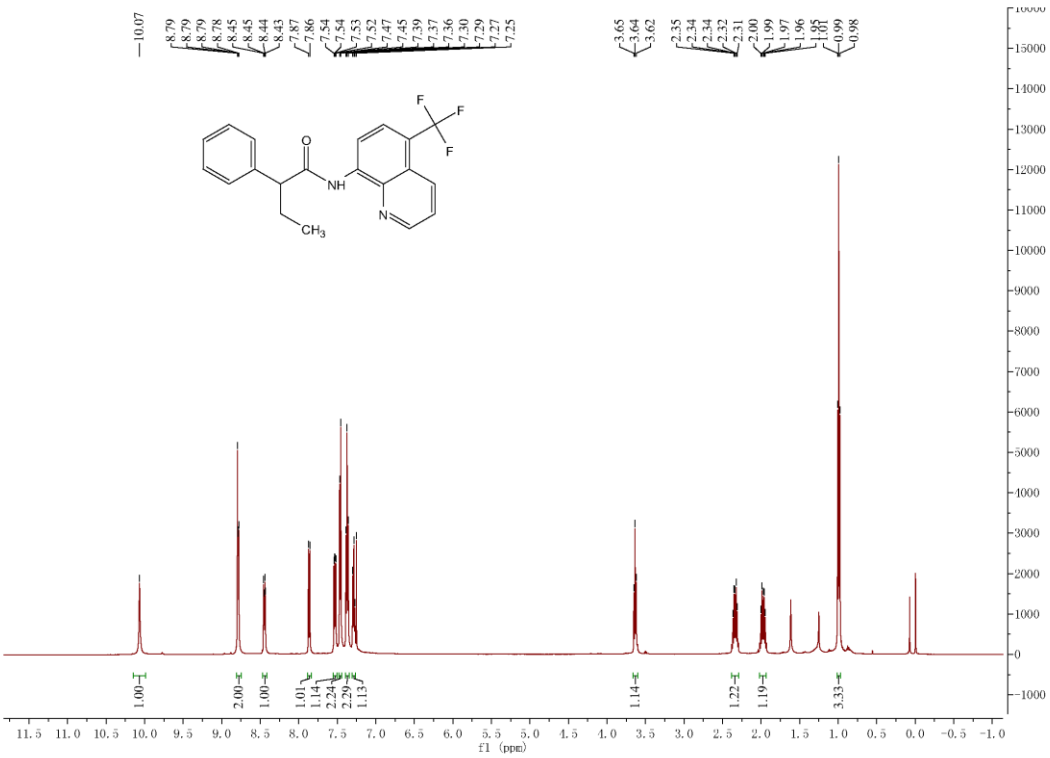
^{1}H NMR **3b**



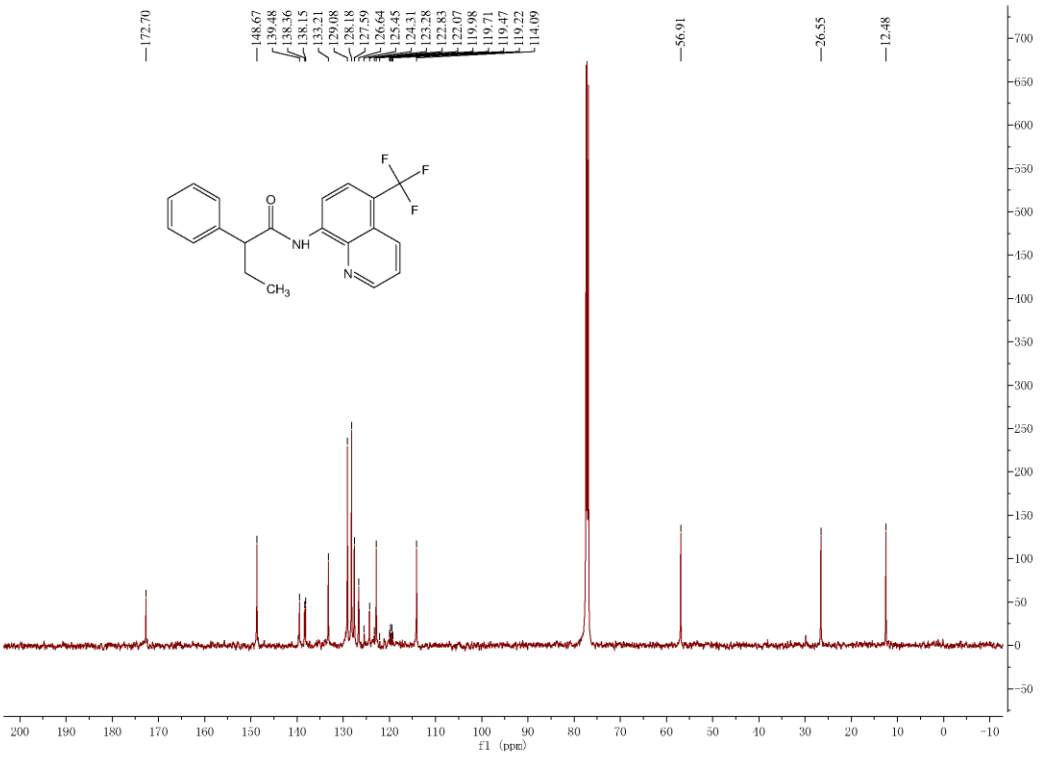
^{13}C NMR **3b**



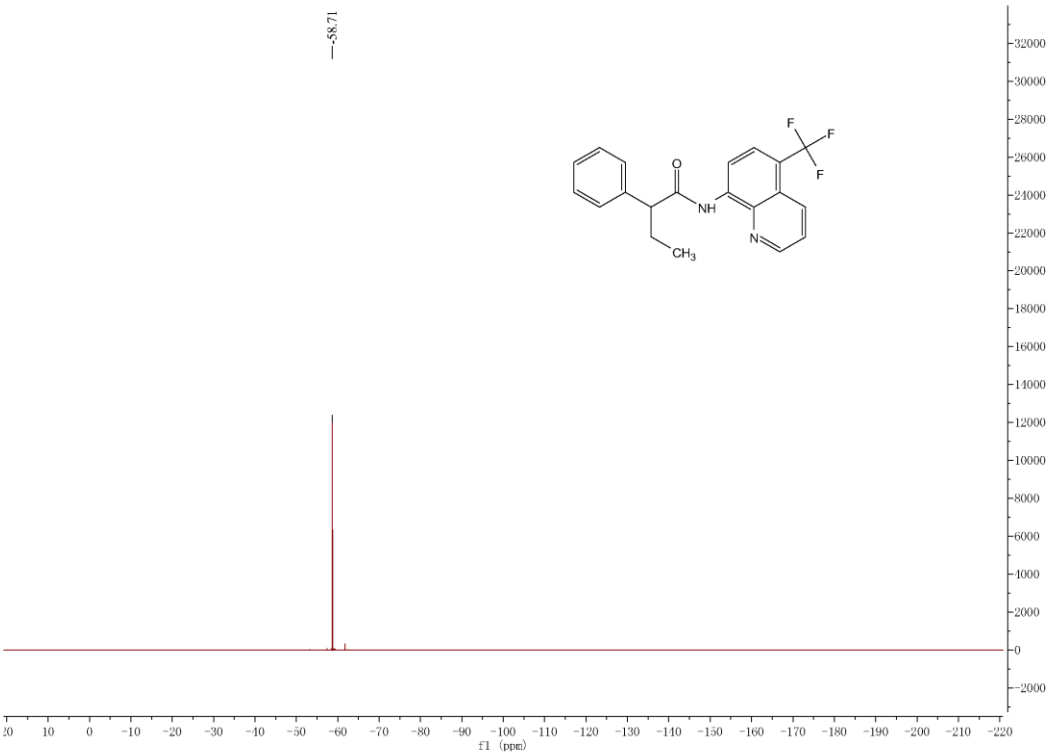
^{19}F NMR **3b**



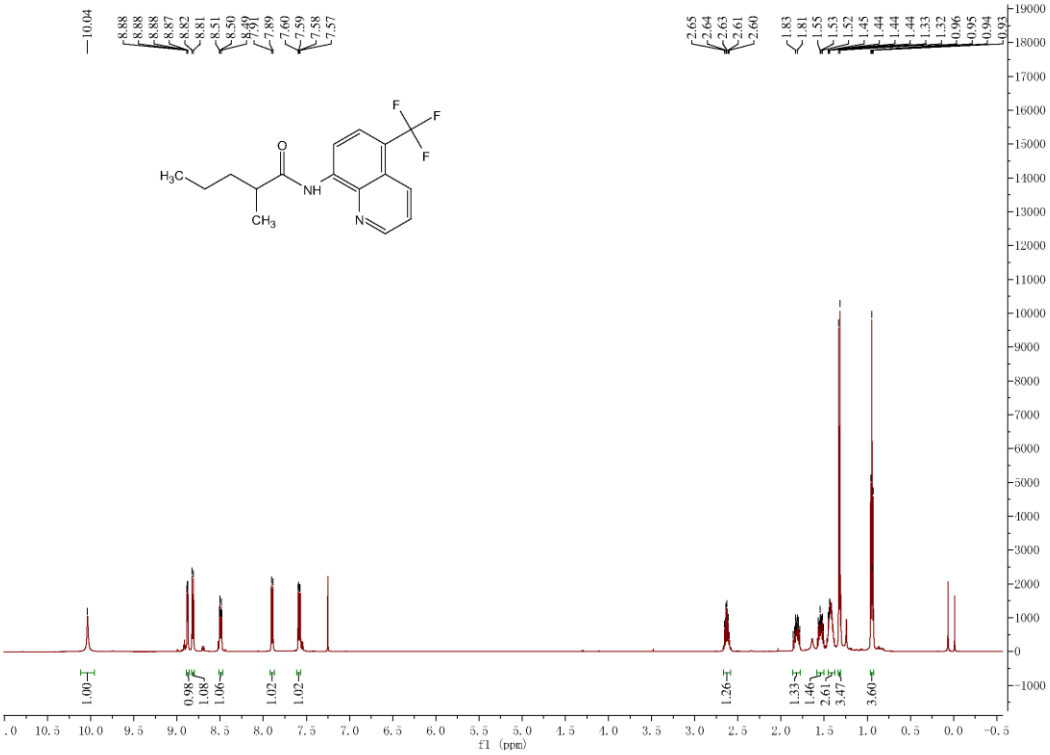
^{1}H NMR **3c**



^{13}C NMR **3c**



^{19}F NMR **3c**



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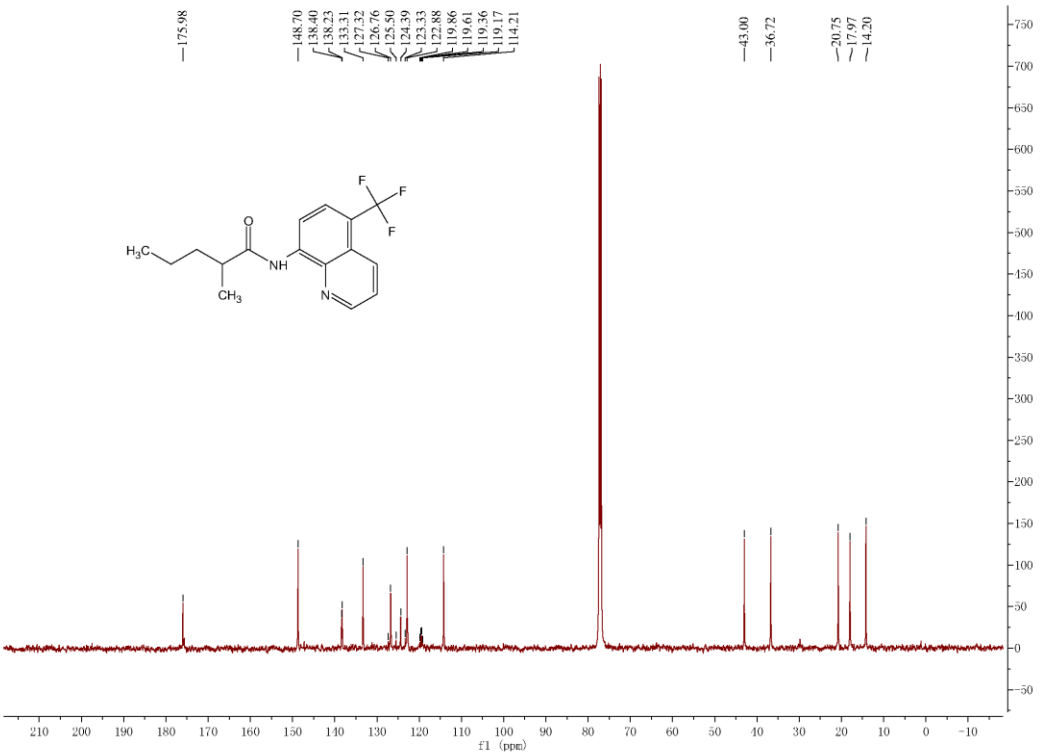
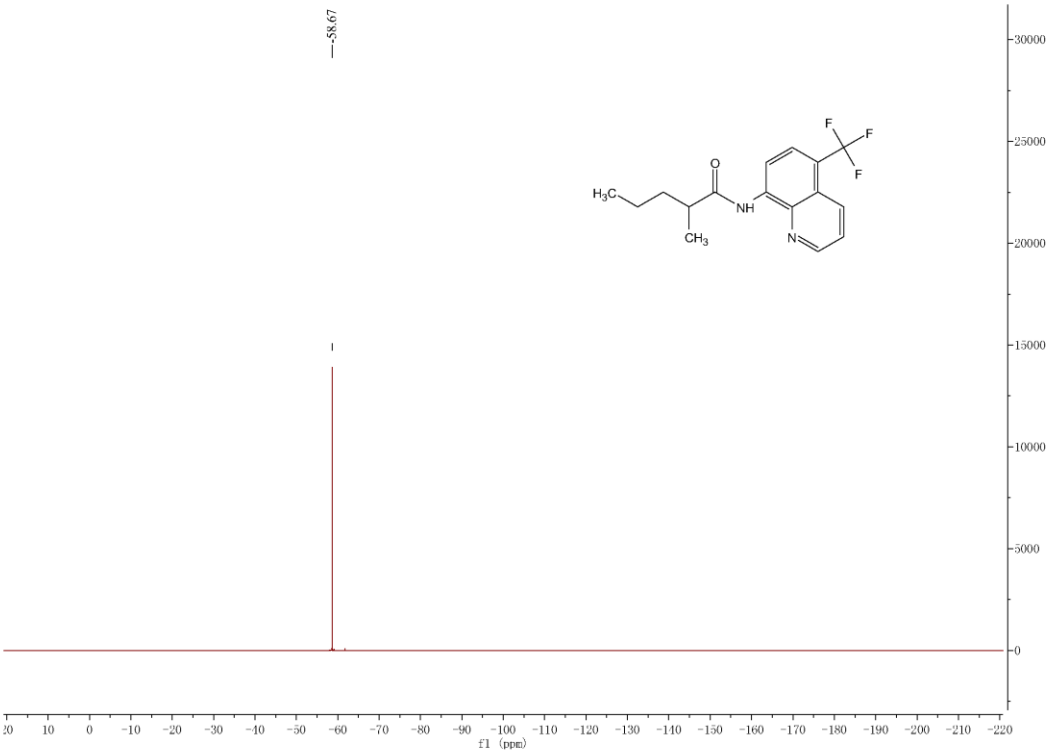


^{13}C NMR **3d**



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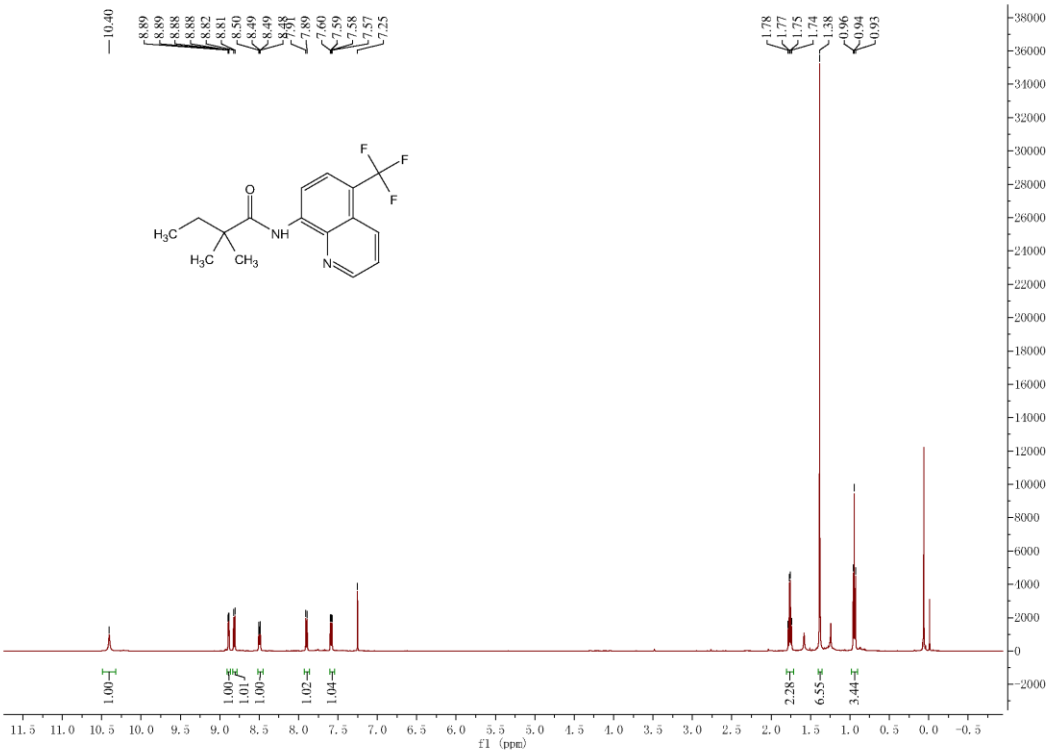

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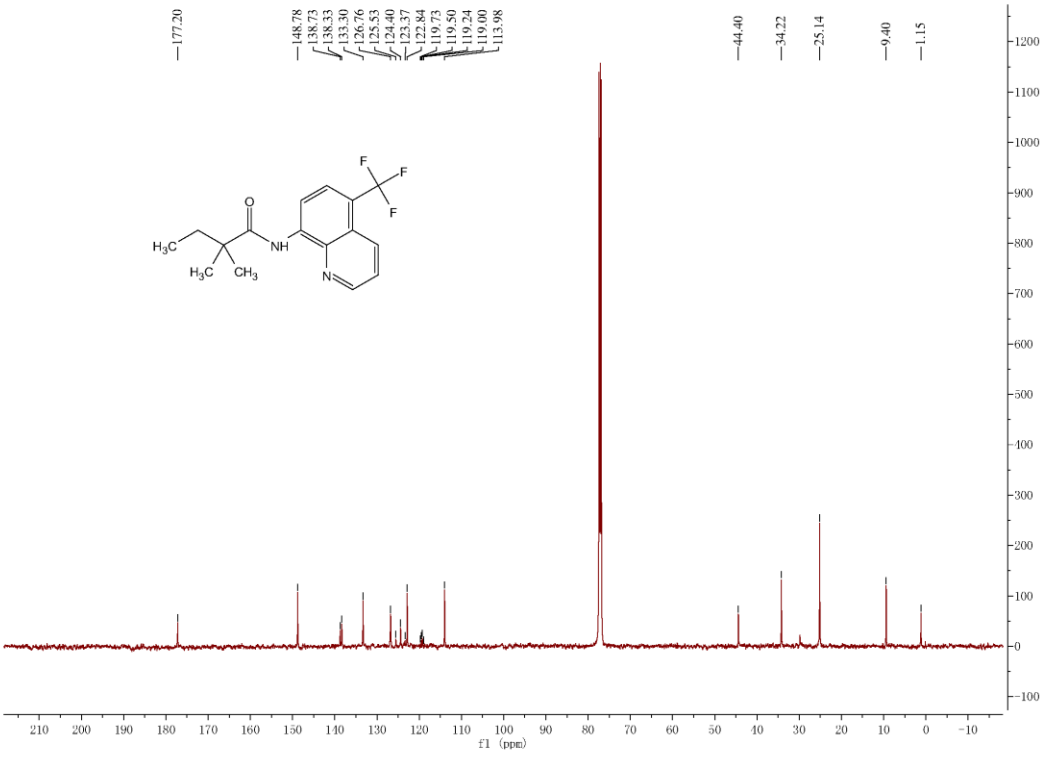

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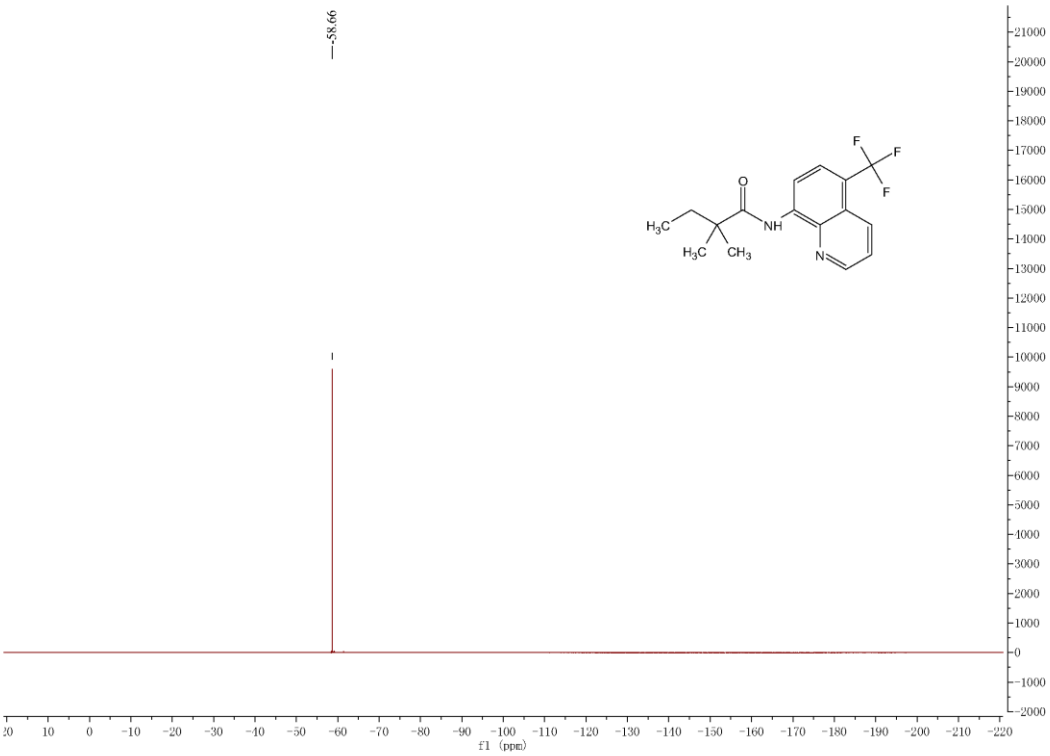

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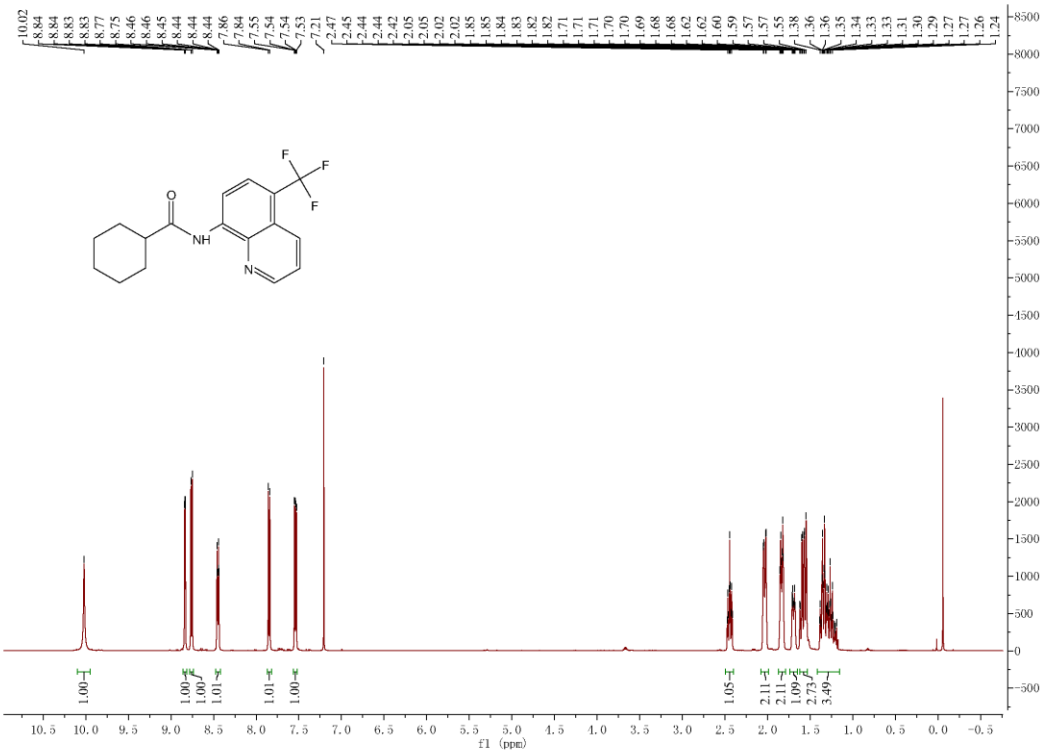

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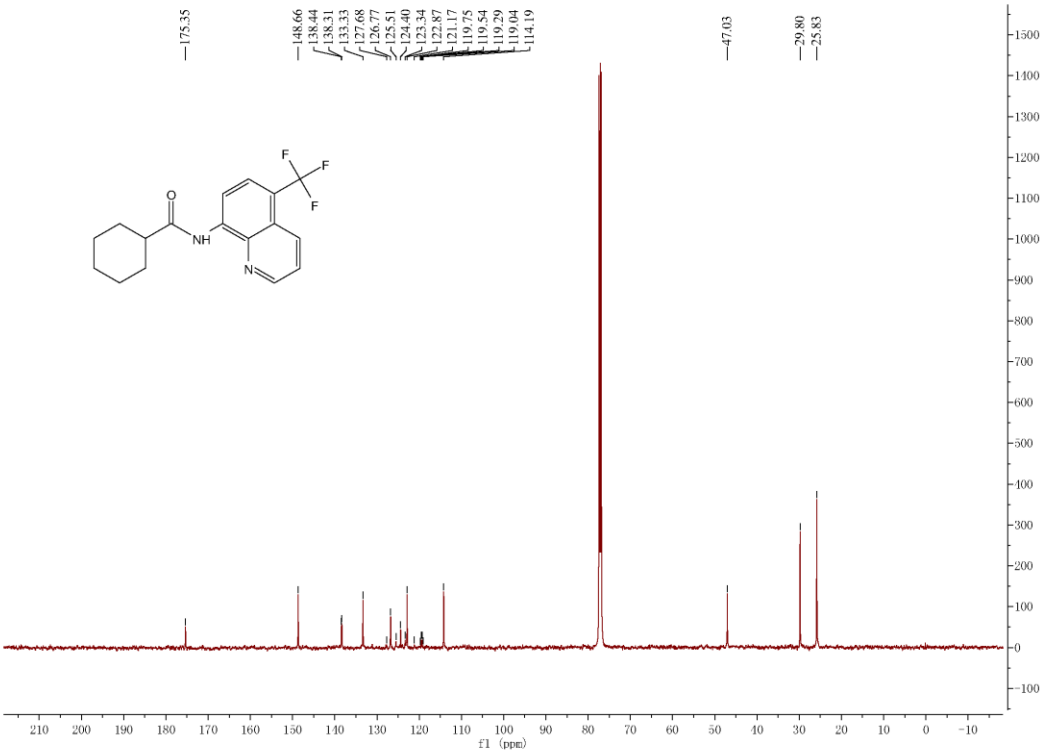
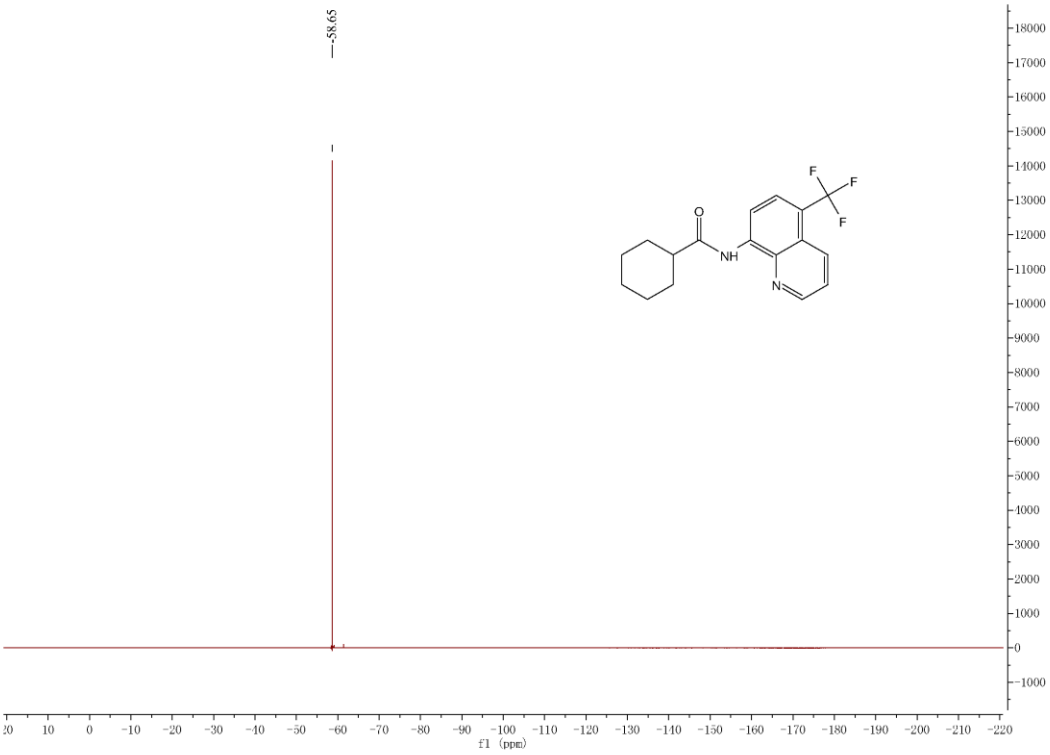
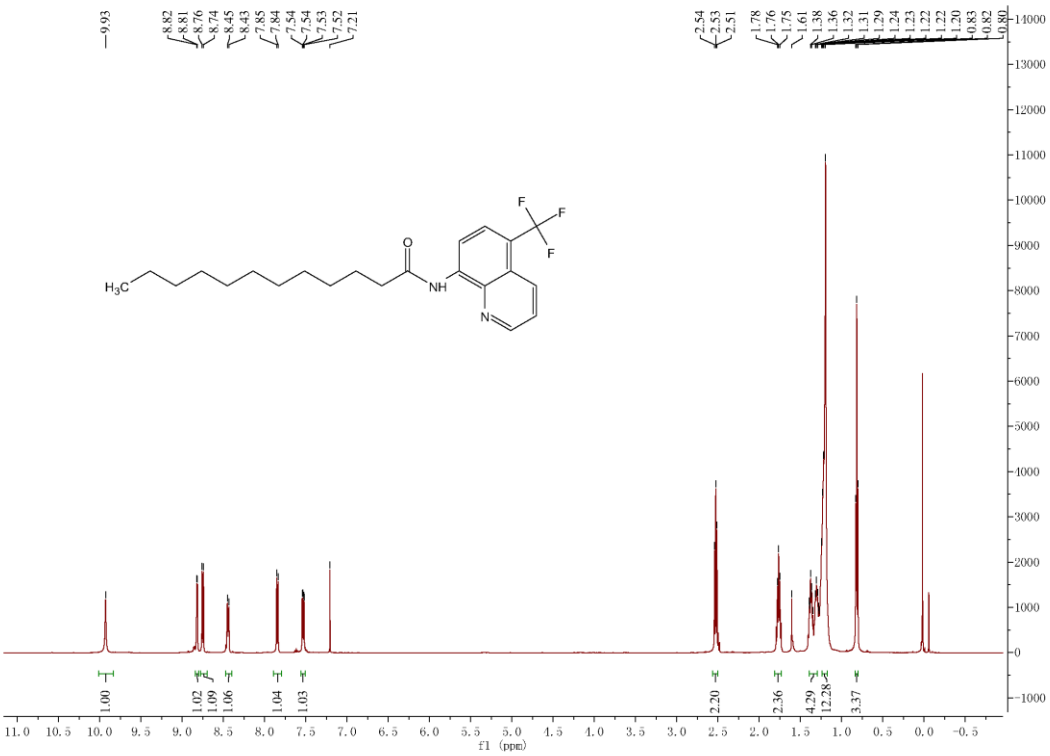


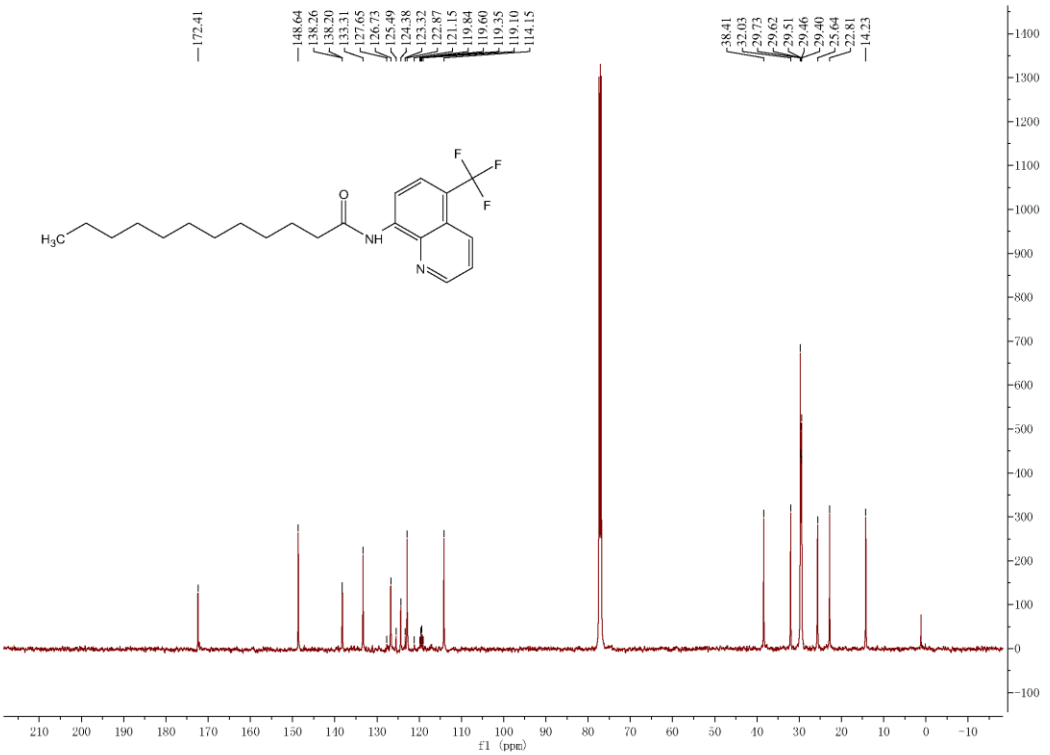
^{13}C NMR **3f**



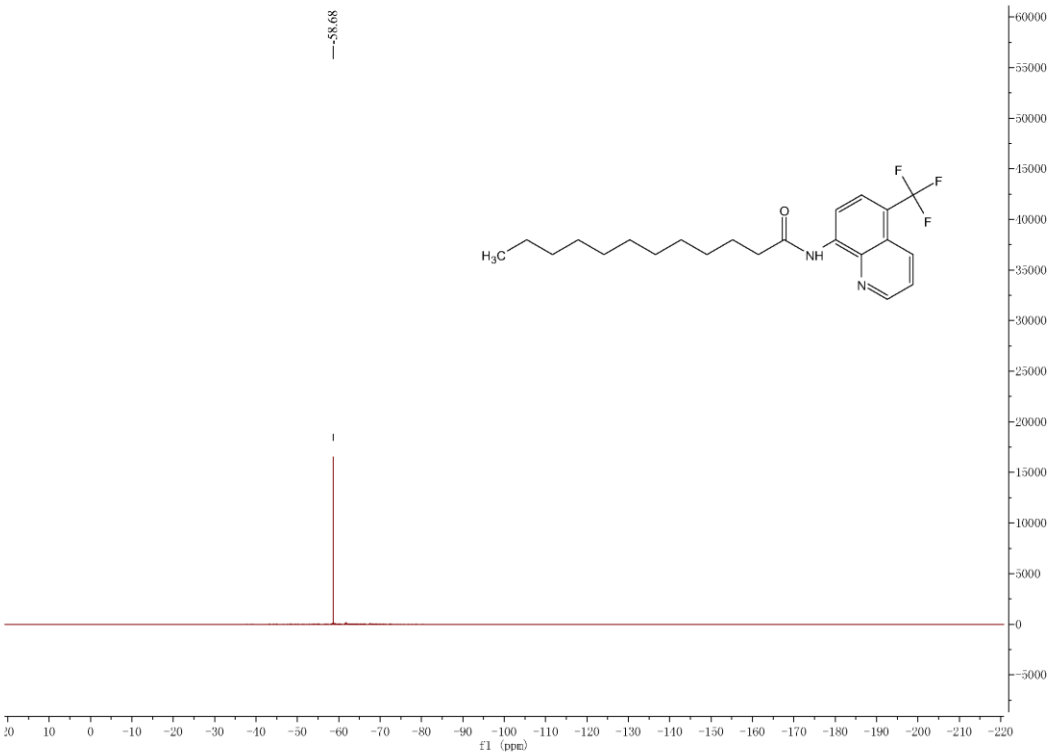
^{19}F NMR **3f**



^{1}H NMR **3g**

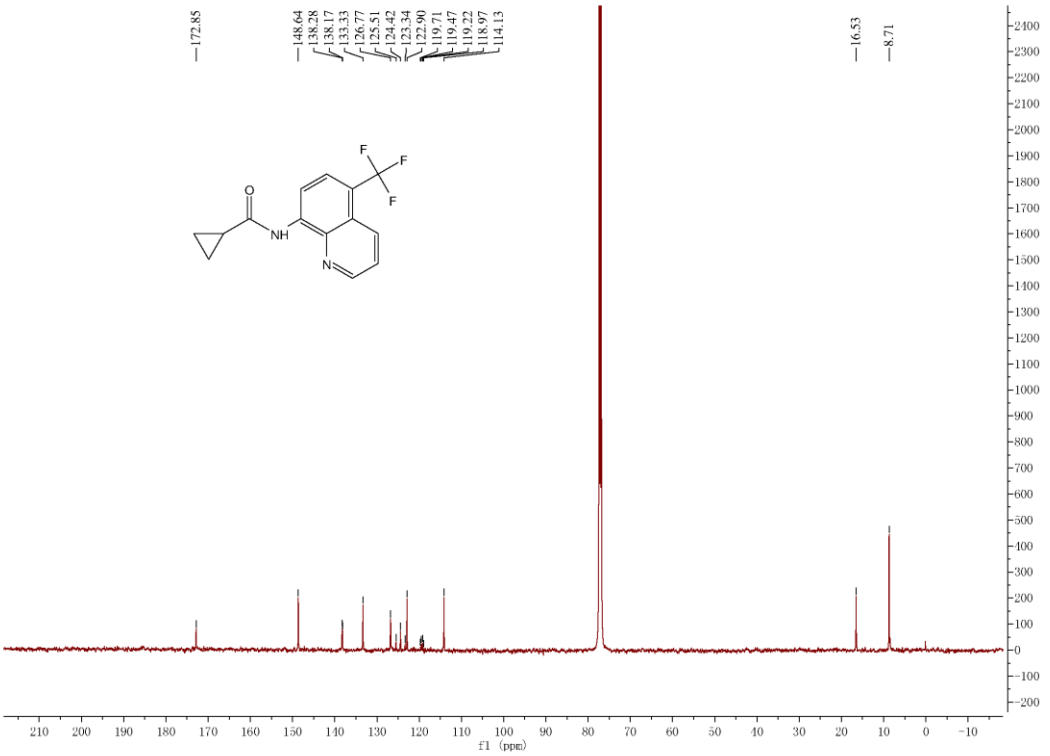


^{13}C NMR **3g**

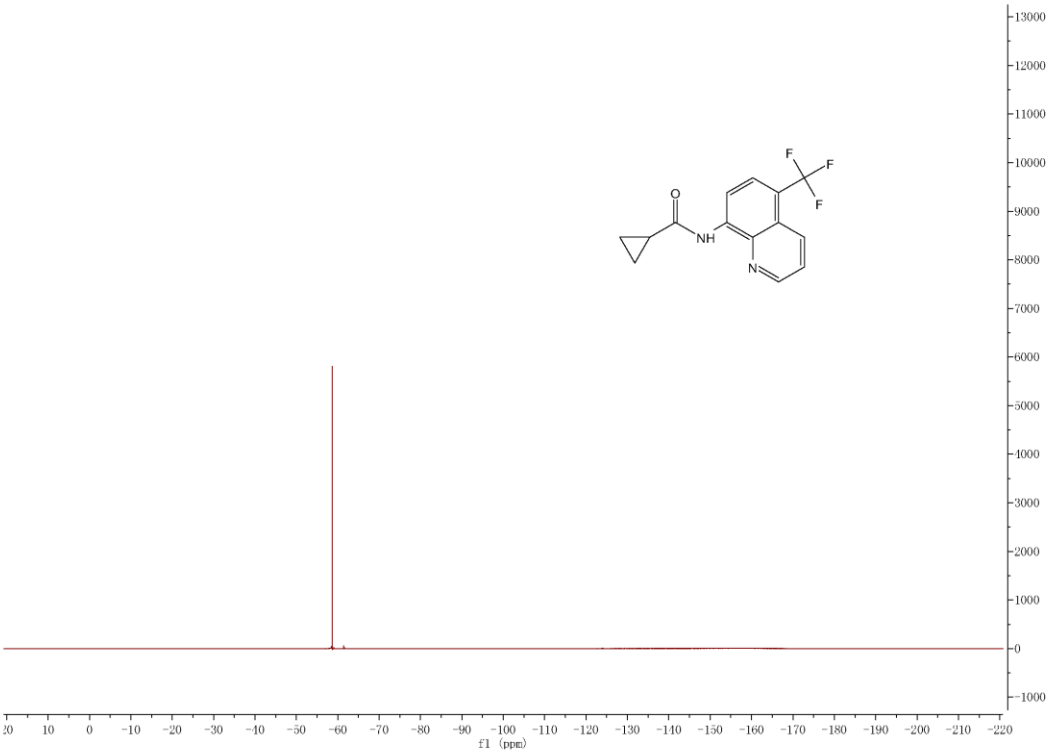


^{19}F NMR **3g**

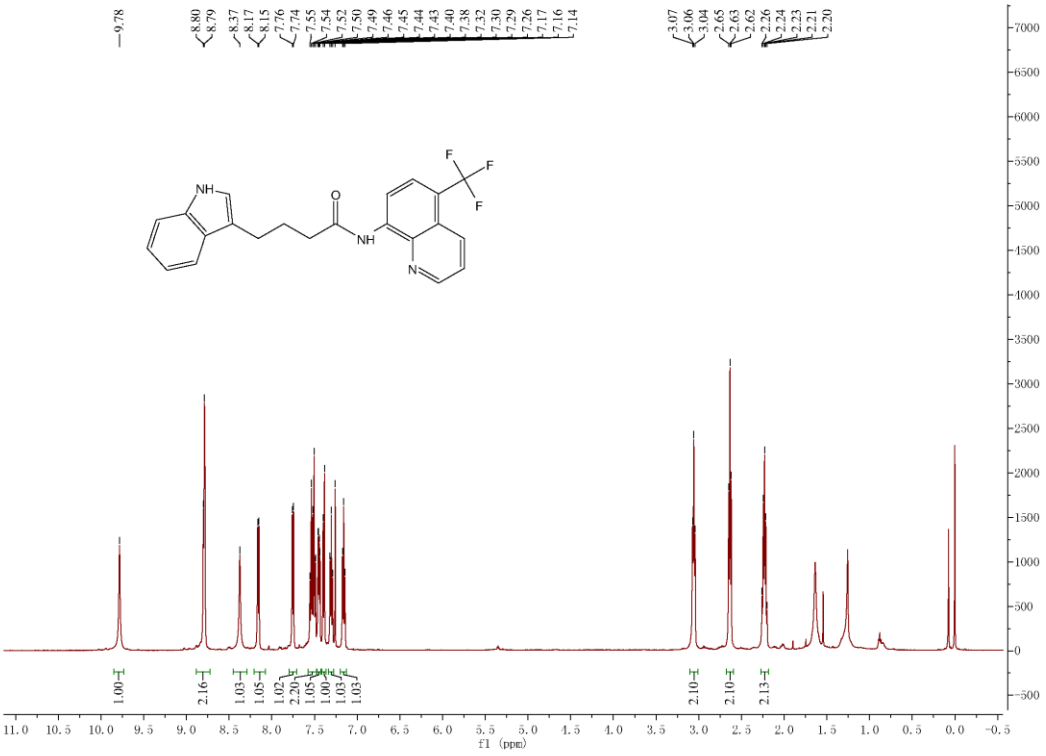
^{1}H NMR **3h**



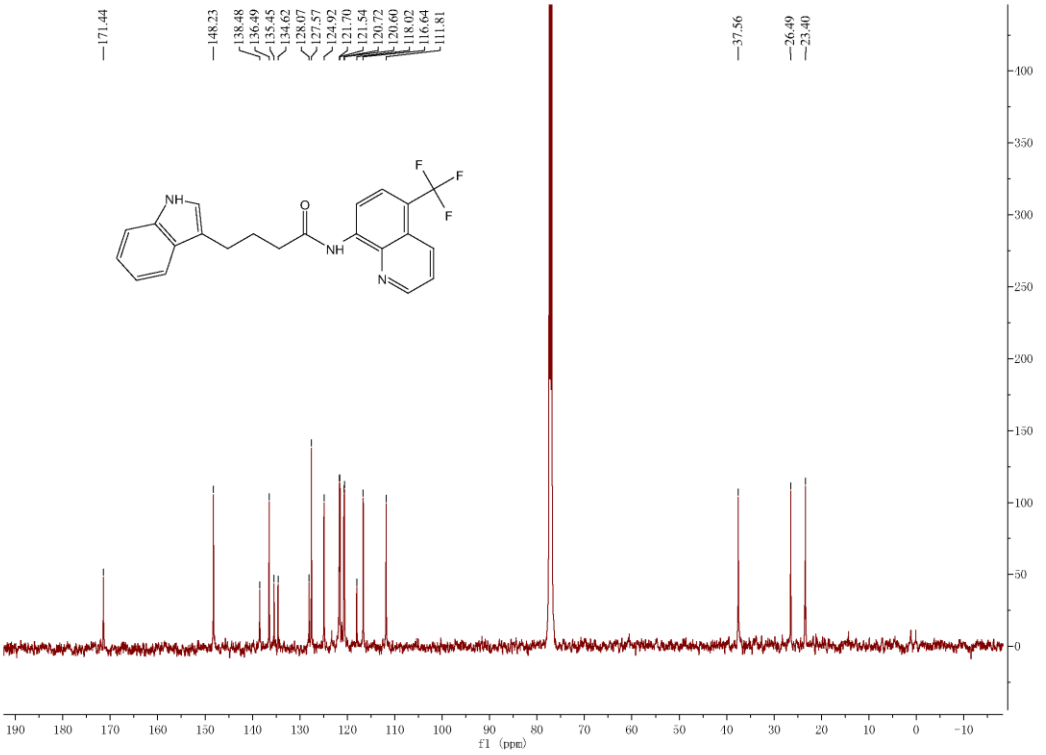
^{13}C NMR **3h**



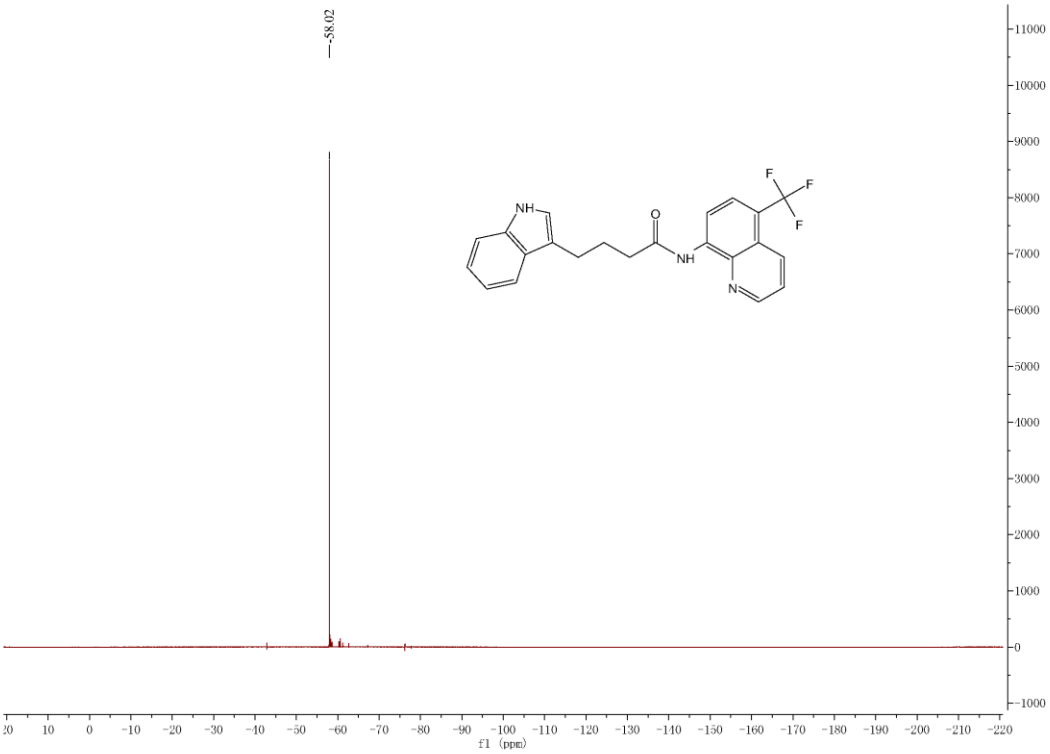
^{19}F NMR **3h**



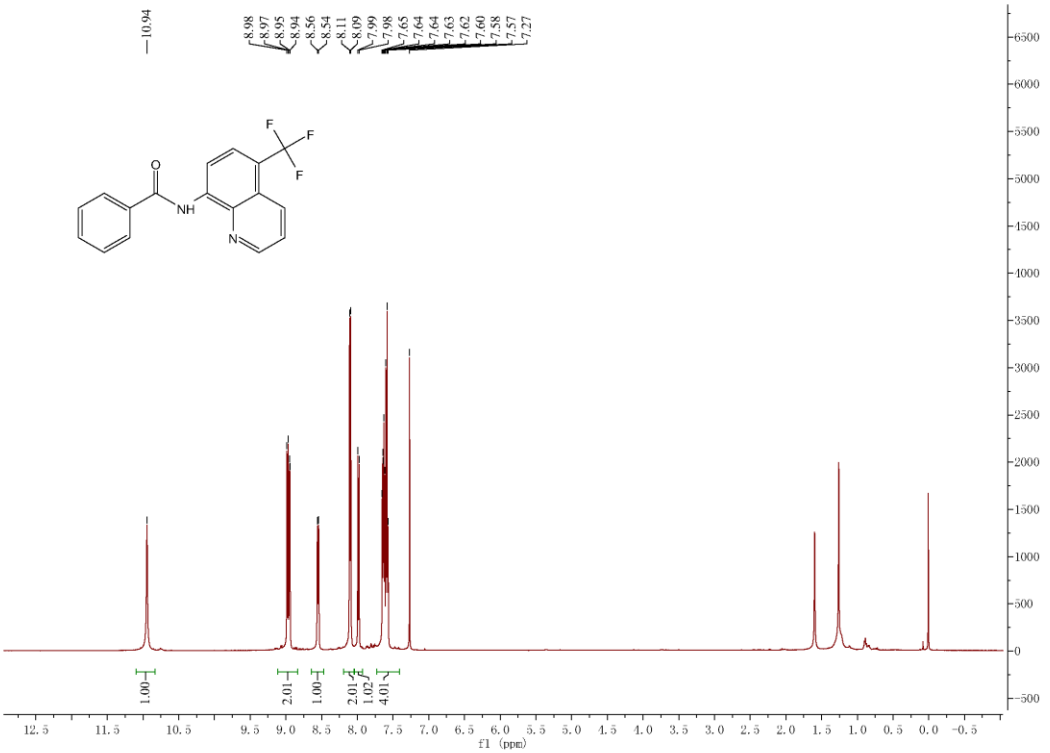
^{1}H NMR **3i**



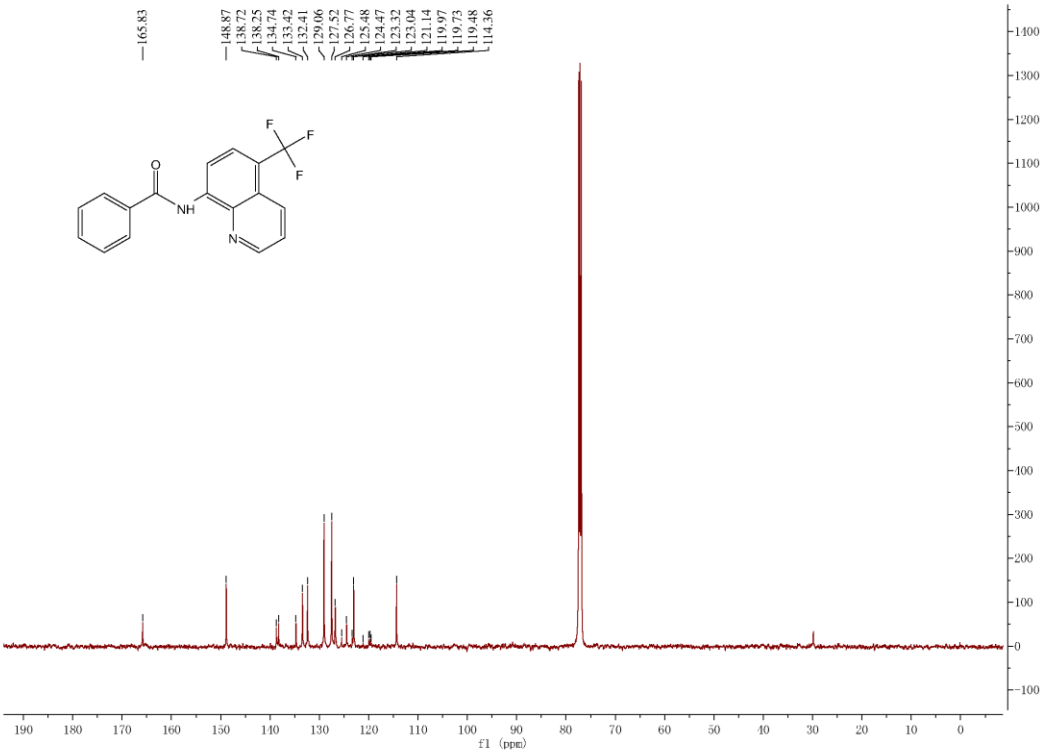
^{13}C NMR **3i**



^{19}F NMR **3i**



^{1}H NMR **3j**



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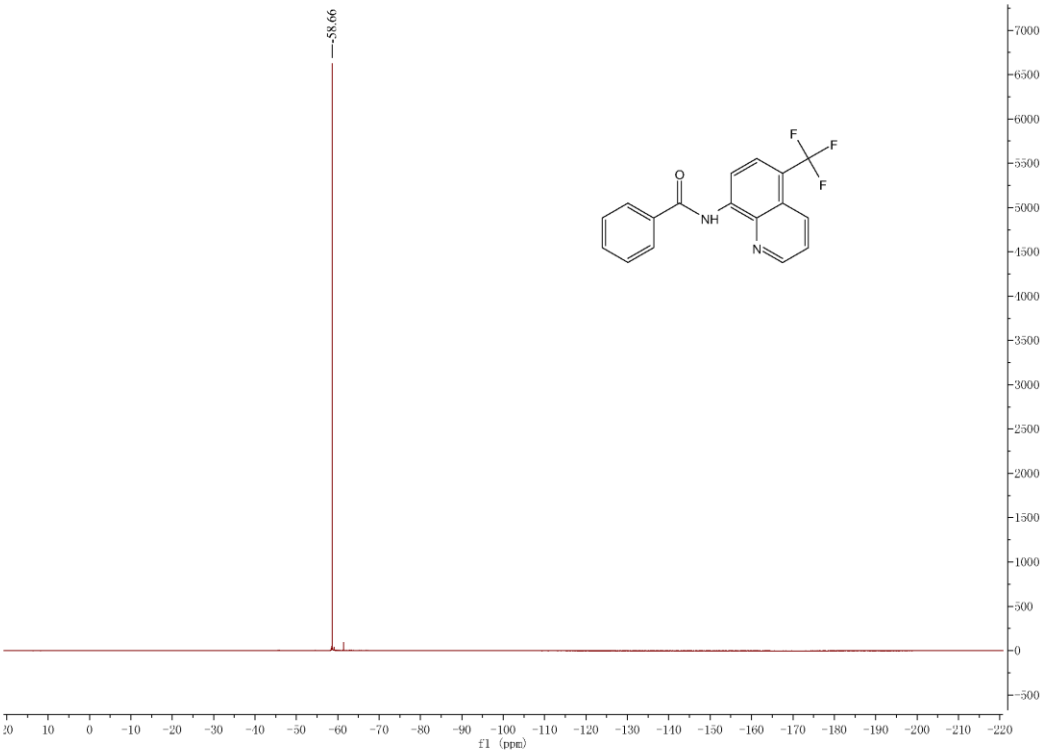

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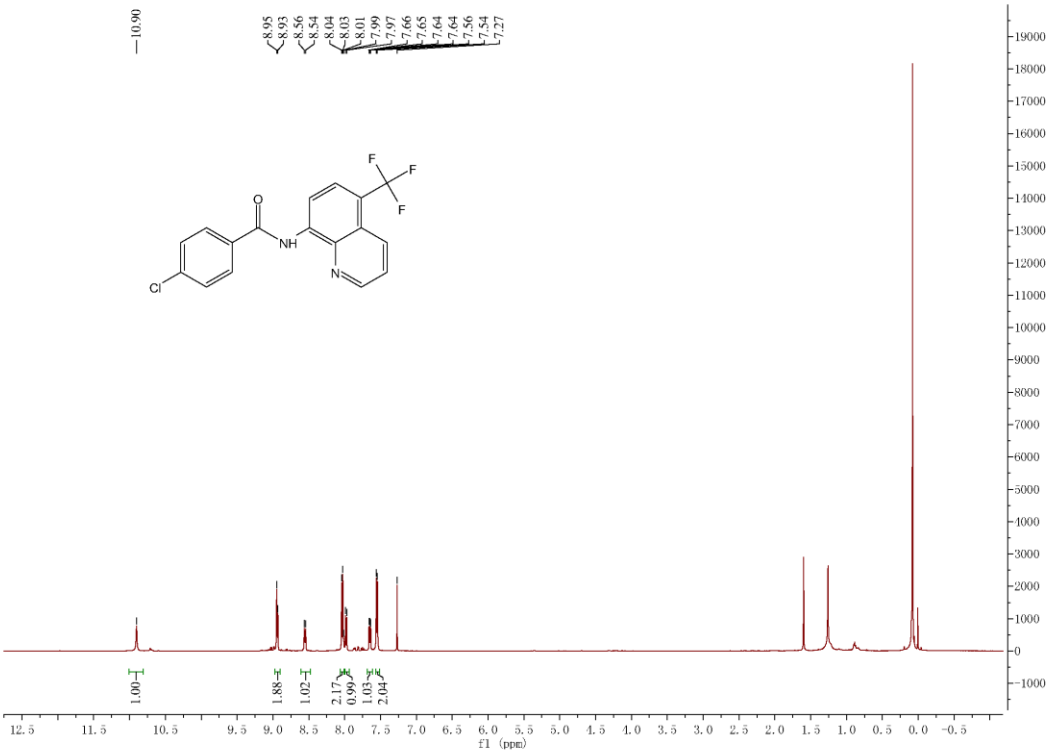

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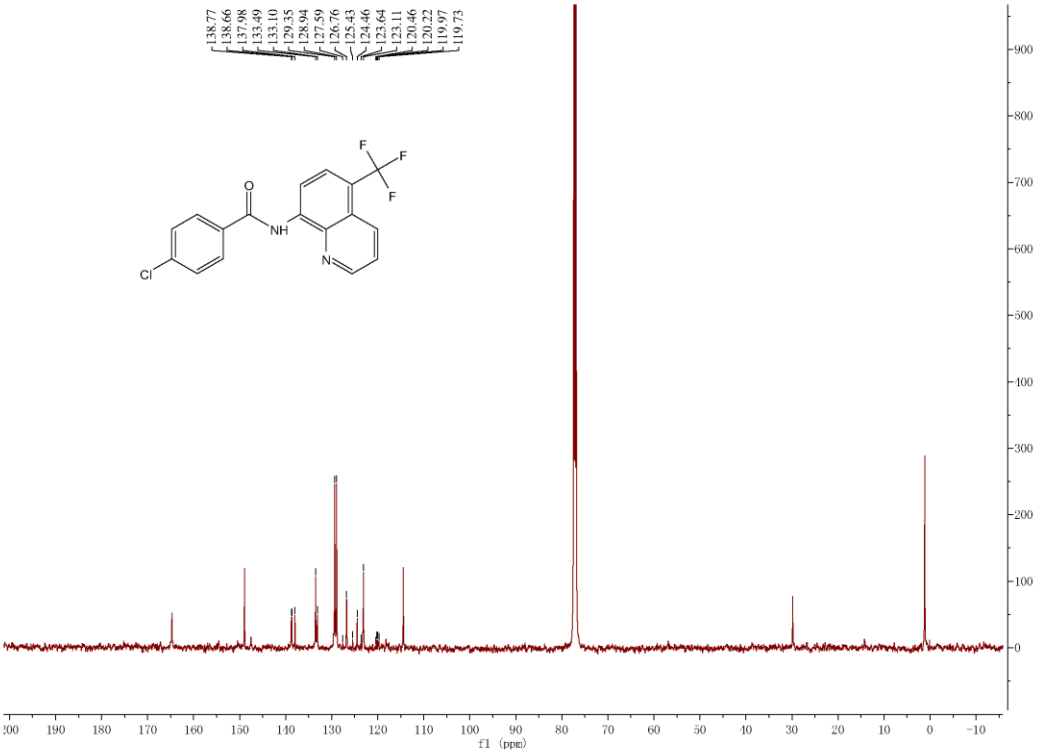
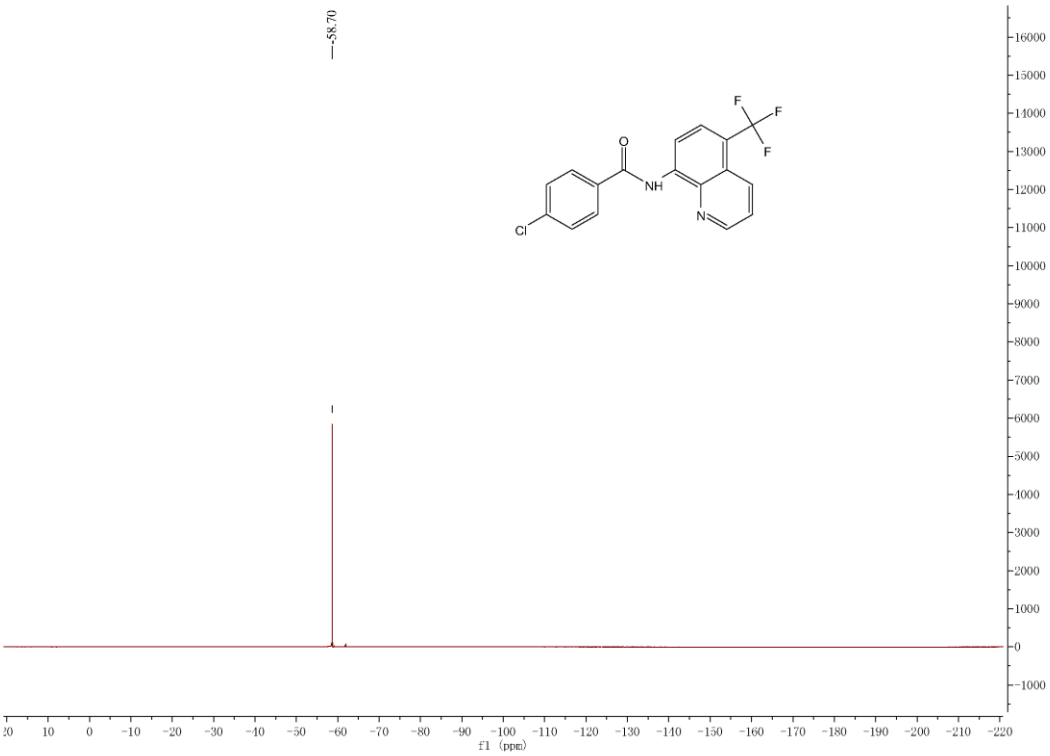


^{13}C NMR **3k**



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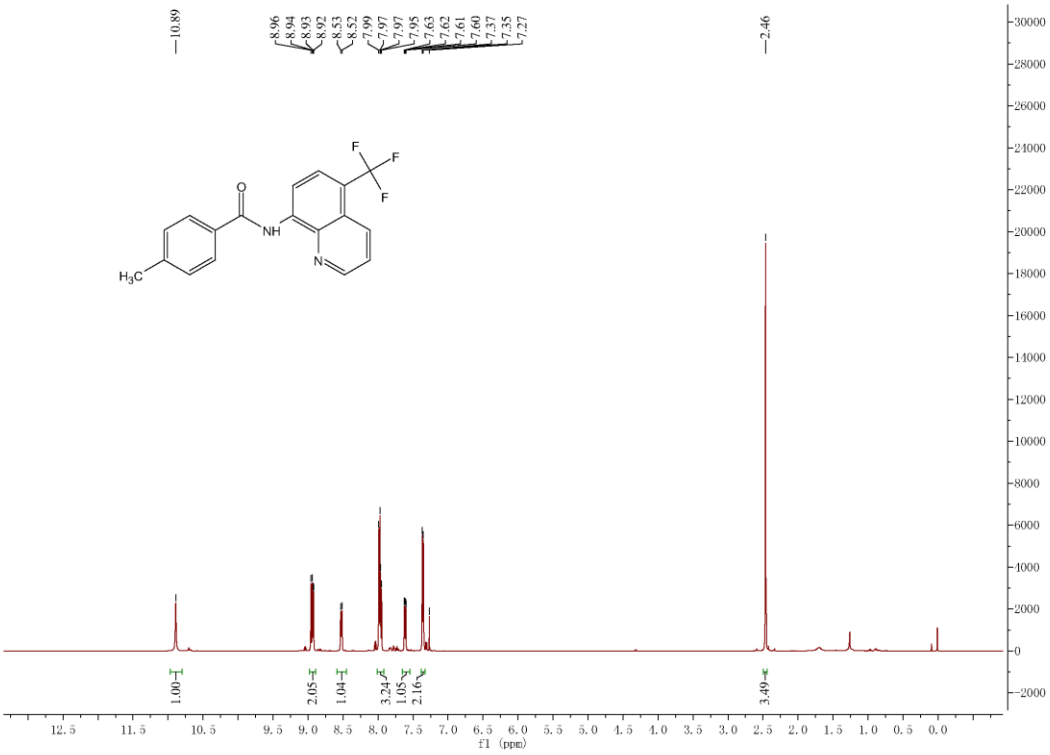
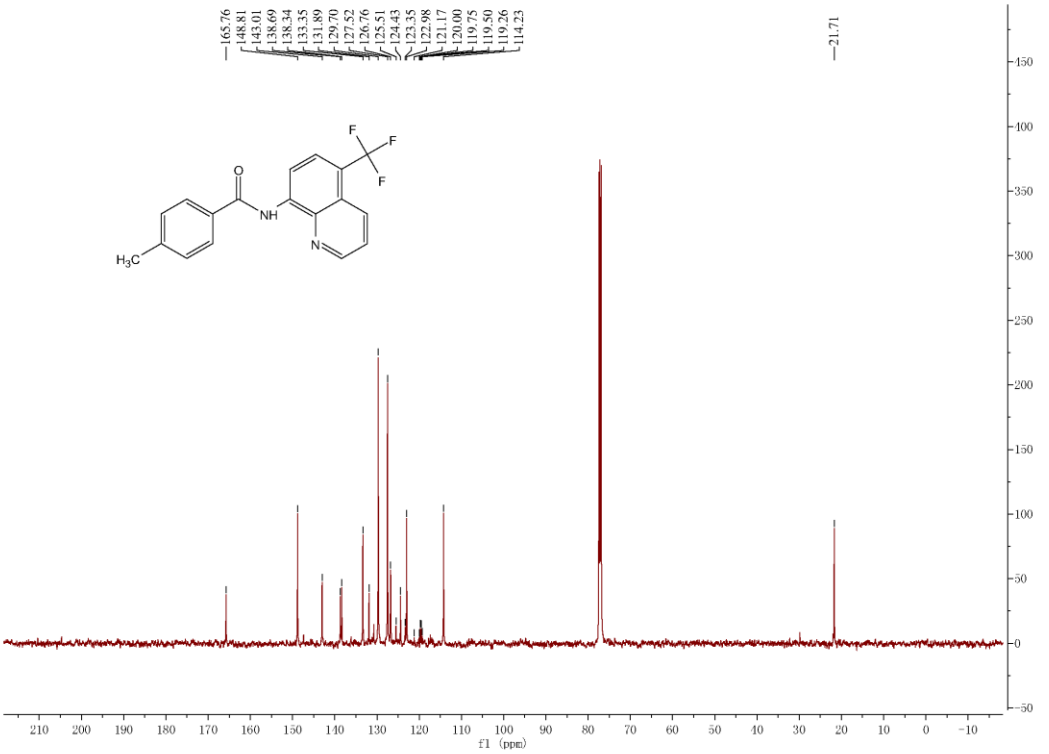
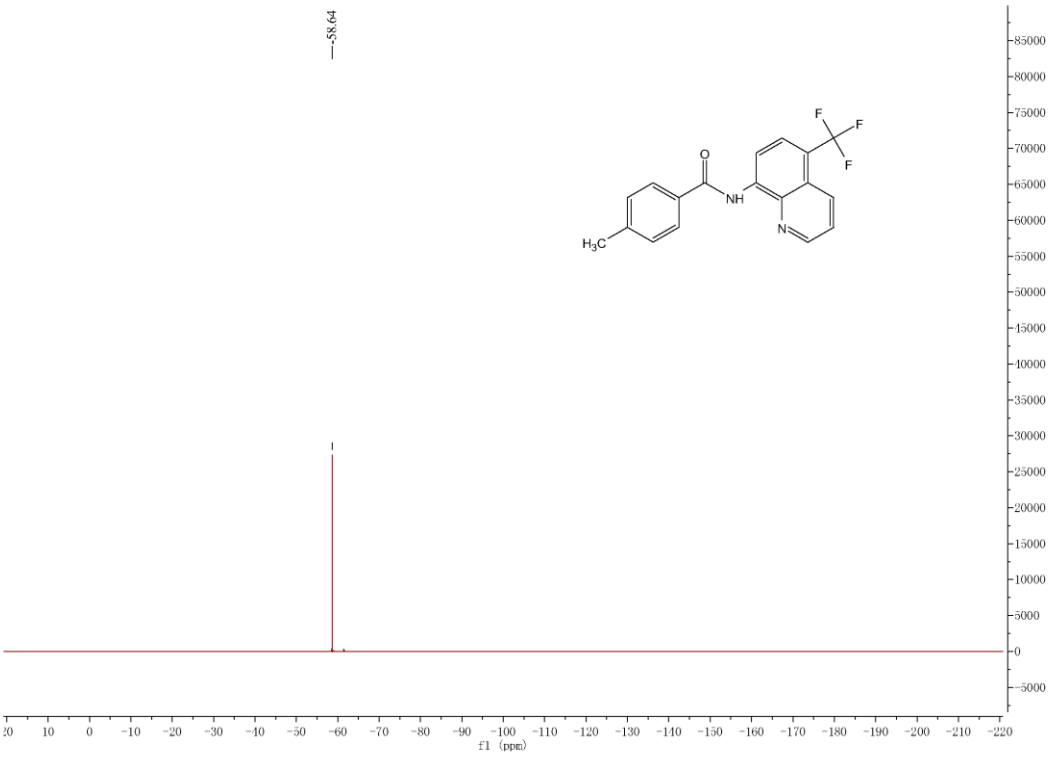


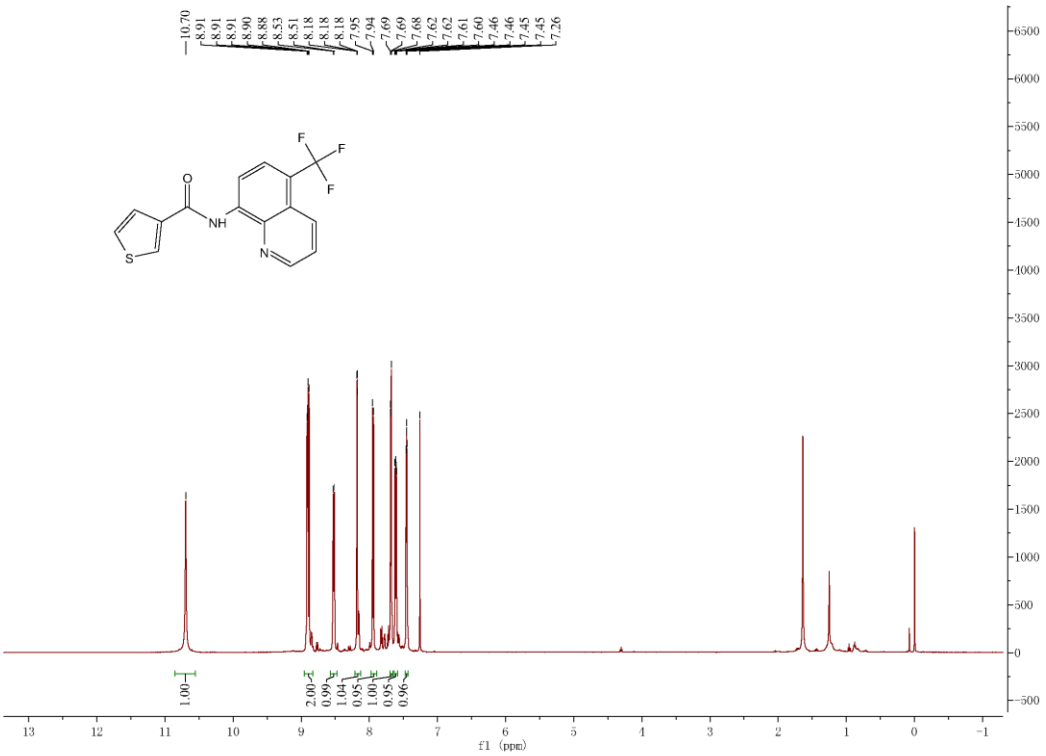
^{1}H NMR **3l**



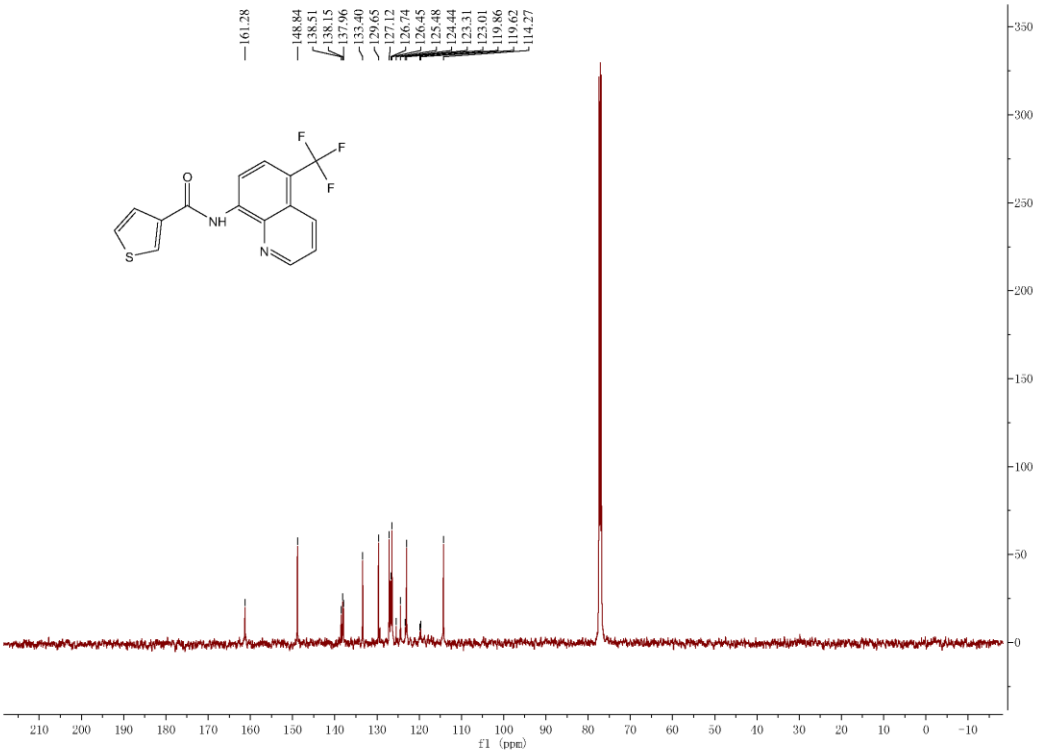
^{13}C NMR **3l**



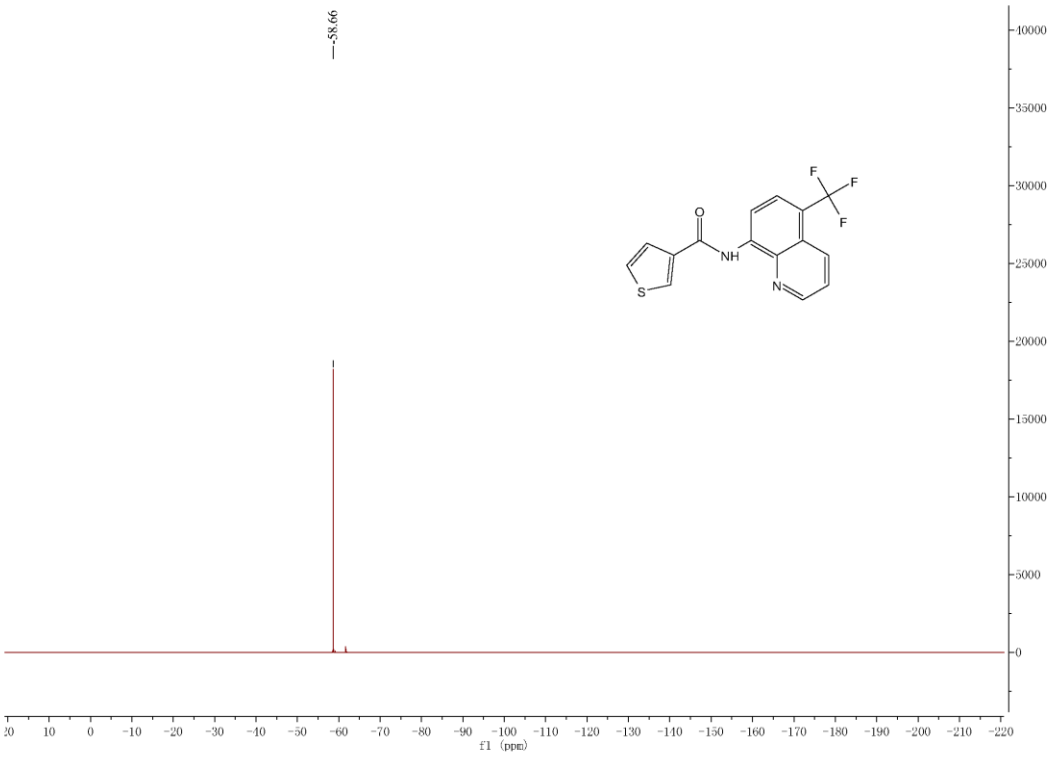
^{19}F NMR **3l**



^{1}H NMR **3m**



^{13}C NMR **3m**



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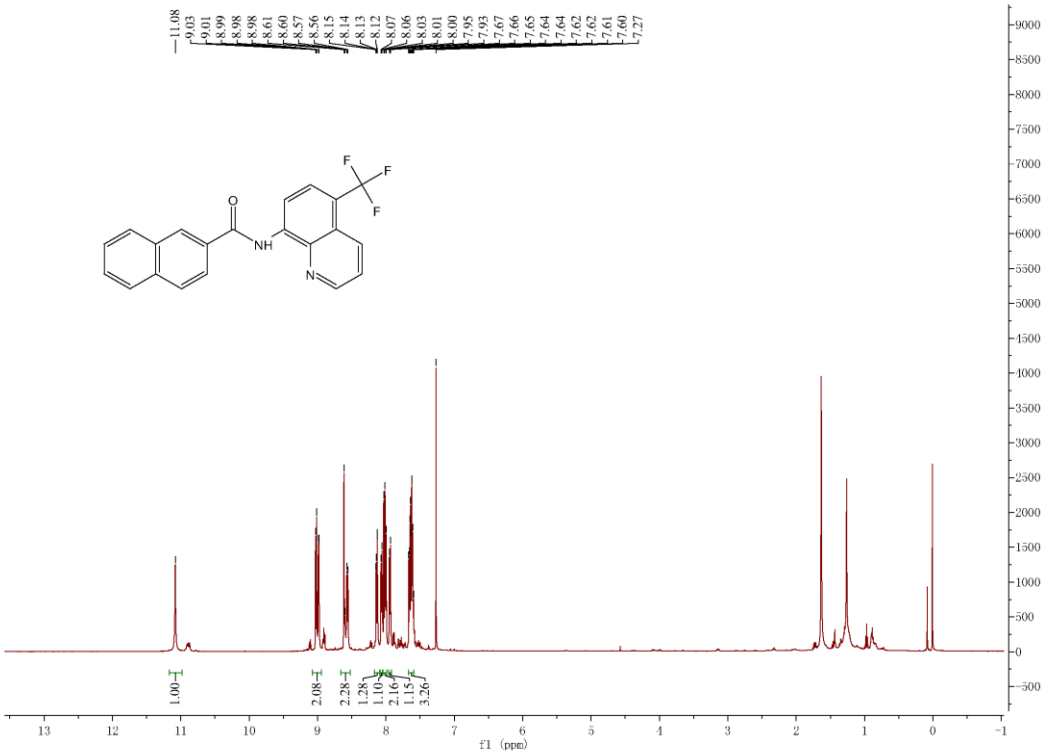

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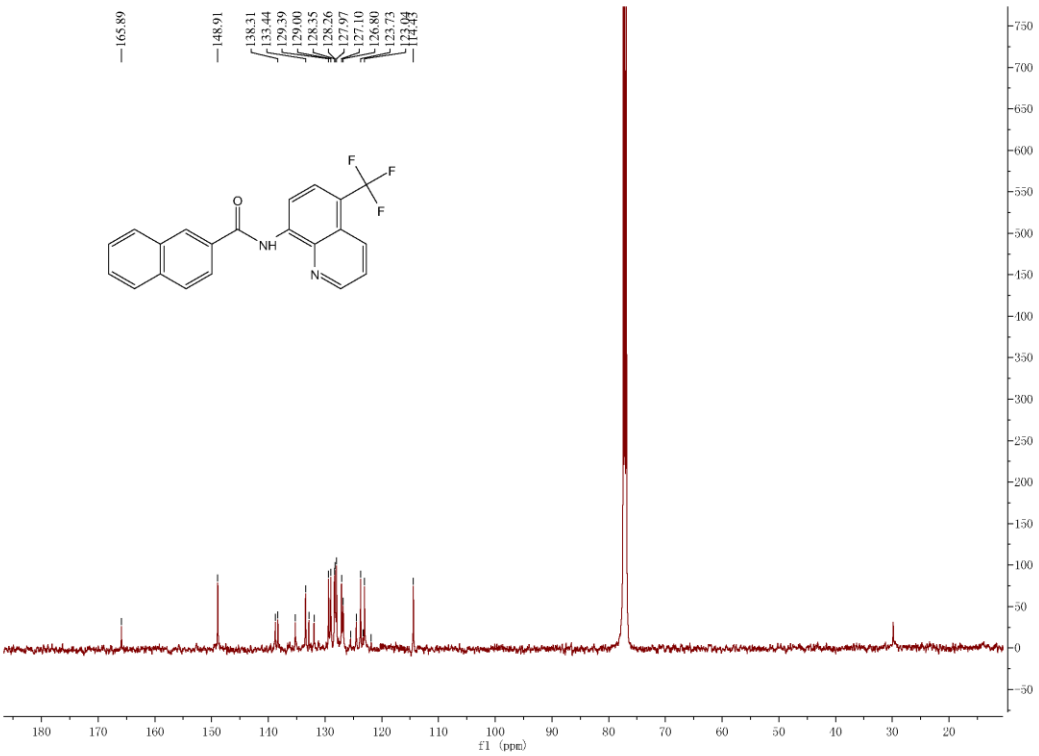
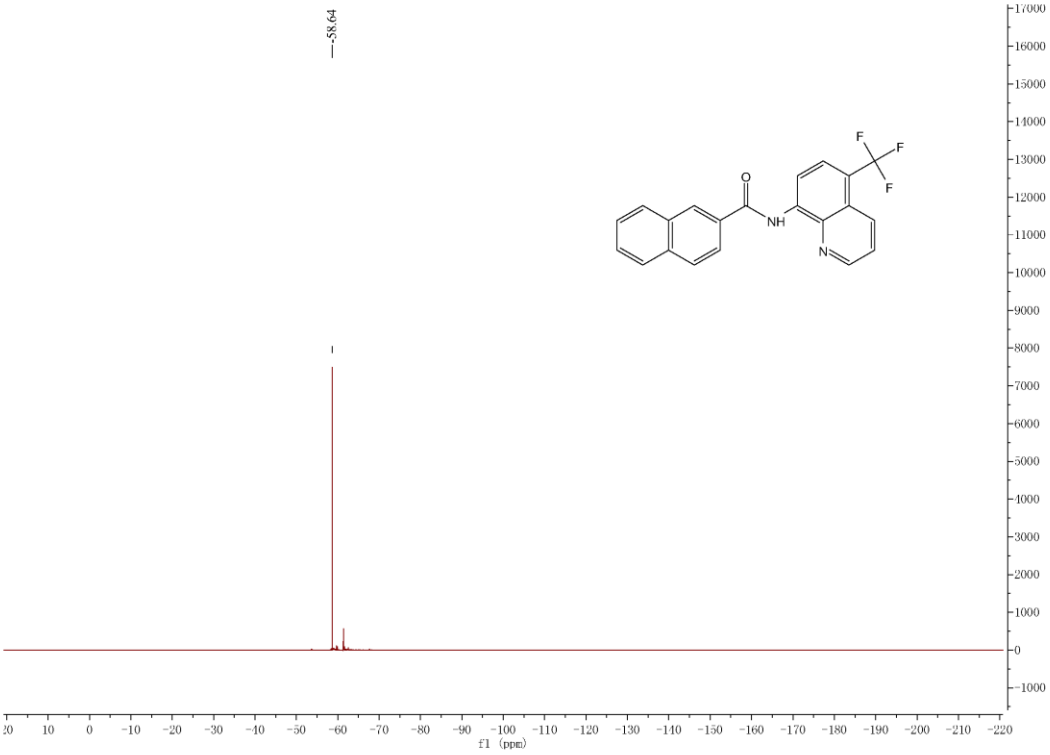
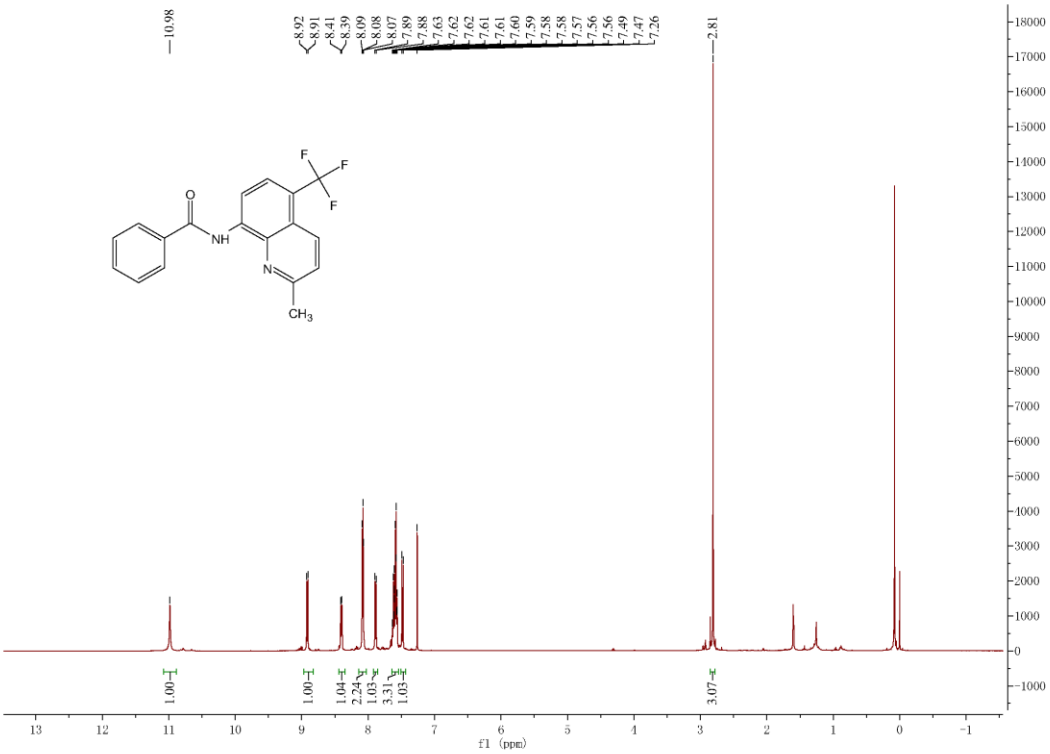


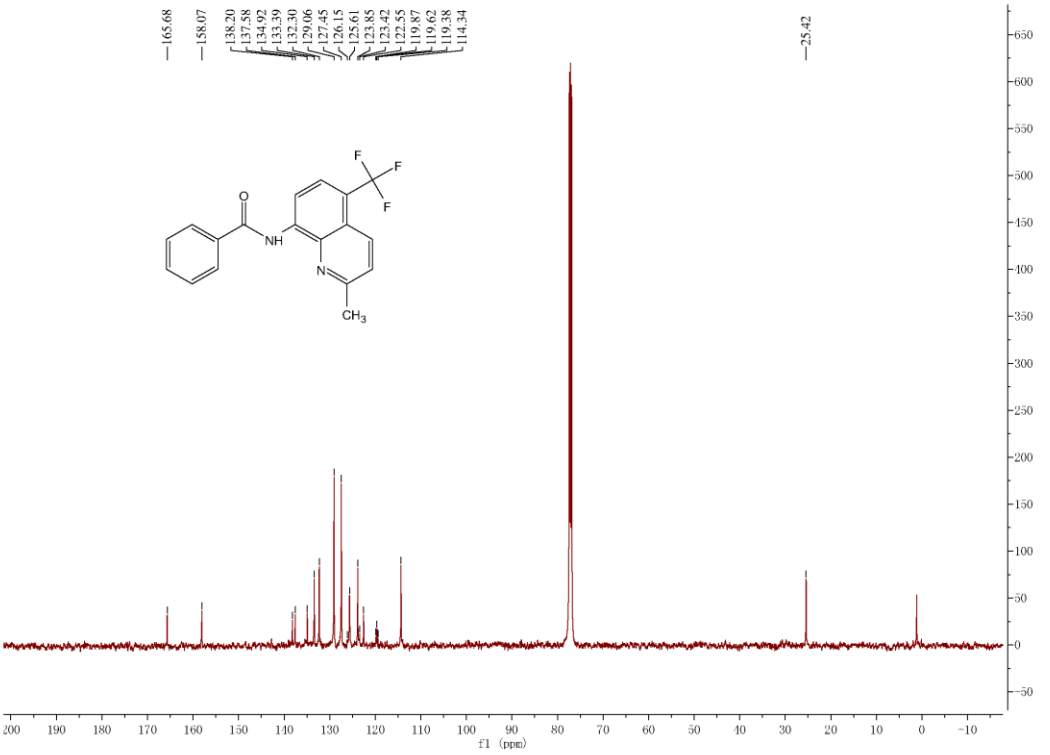
^{13}C NMR **3n**



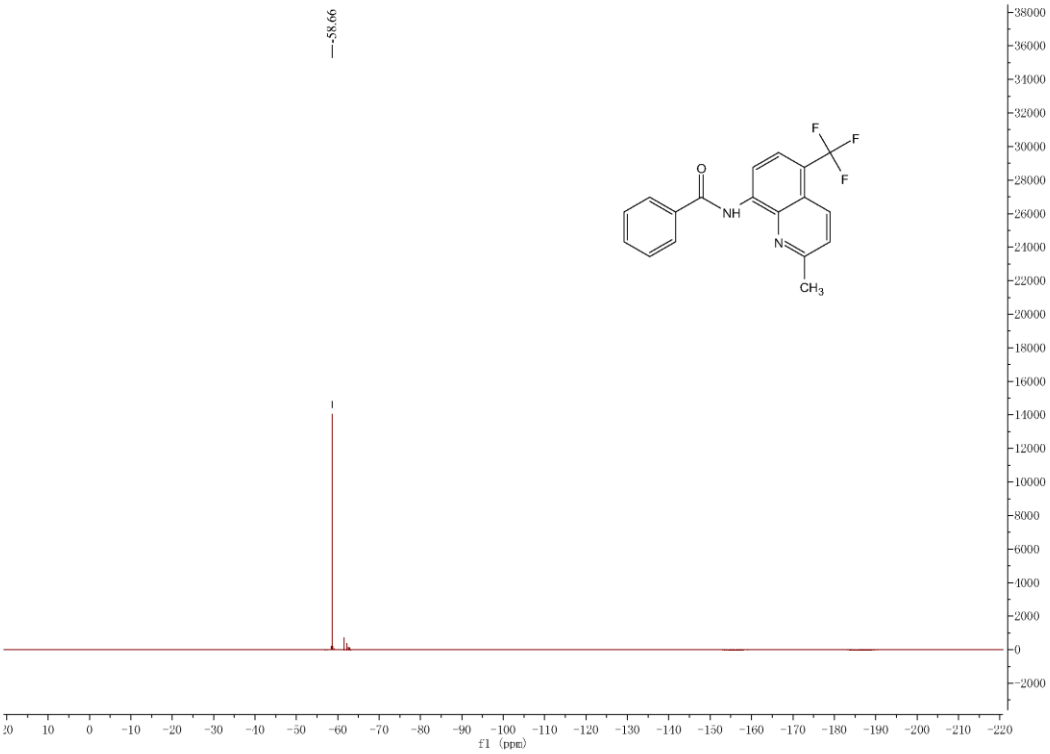
^{19}F NMR **3n**



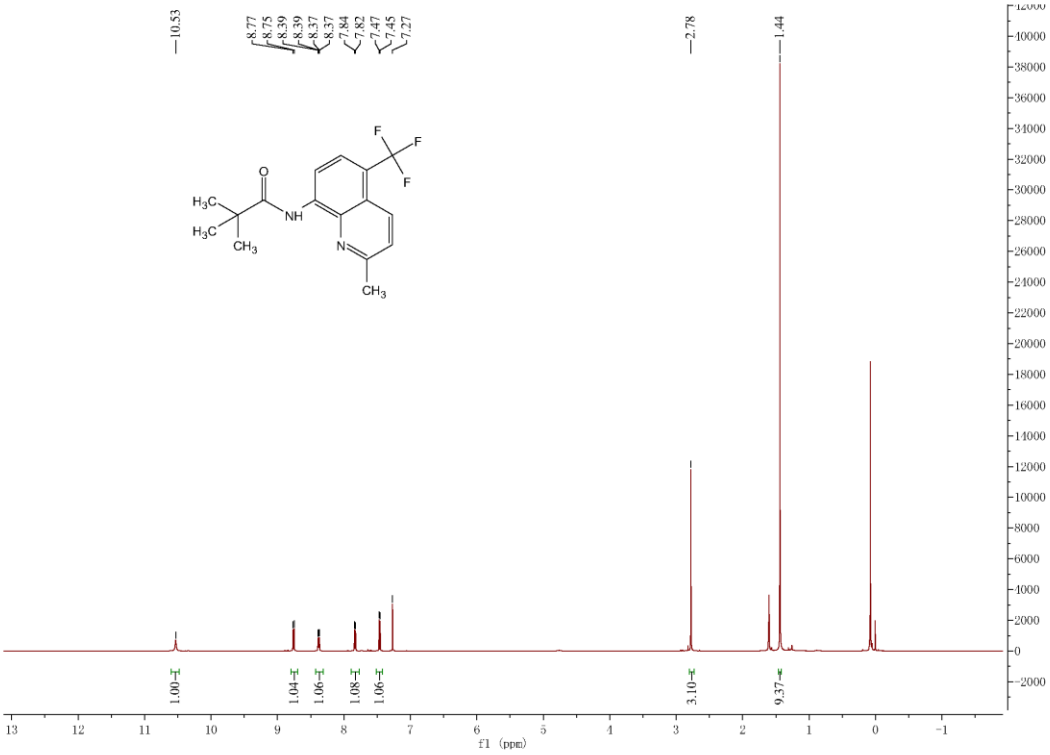
^{1}H NMR **3o**



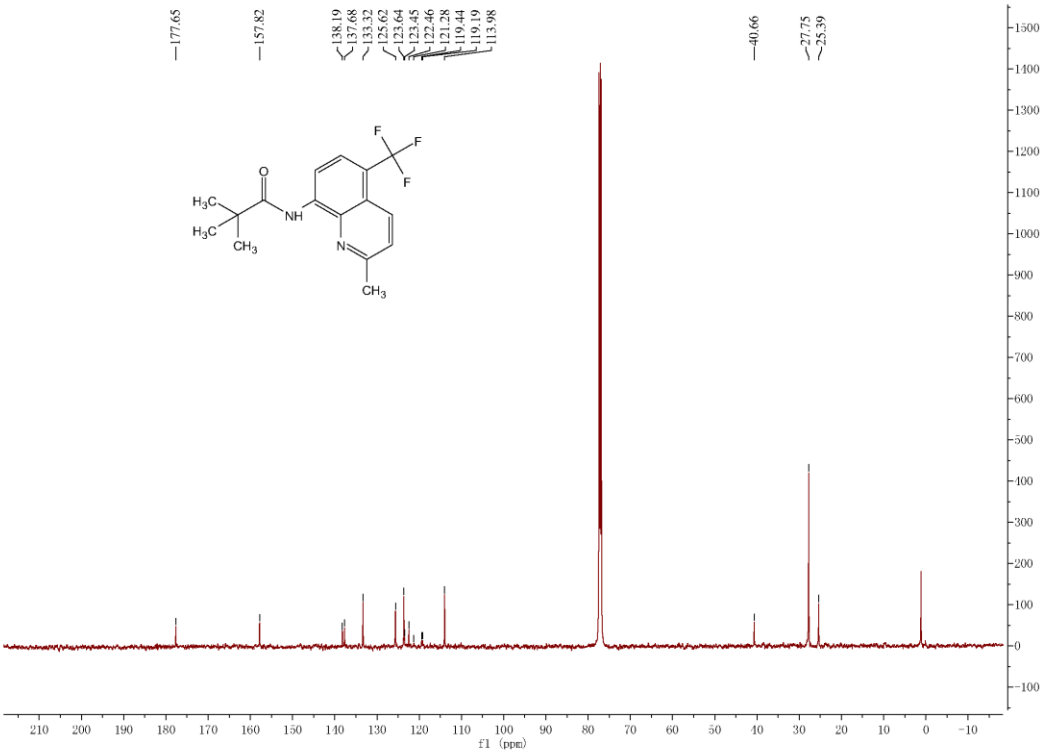
^{13}C NMR **3o**



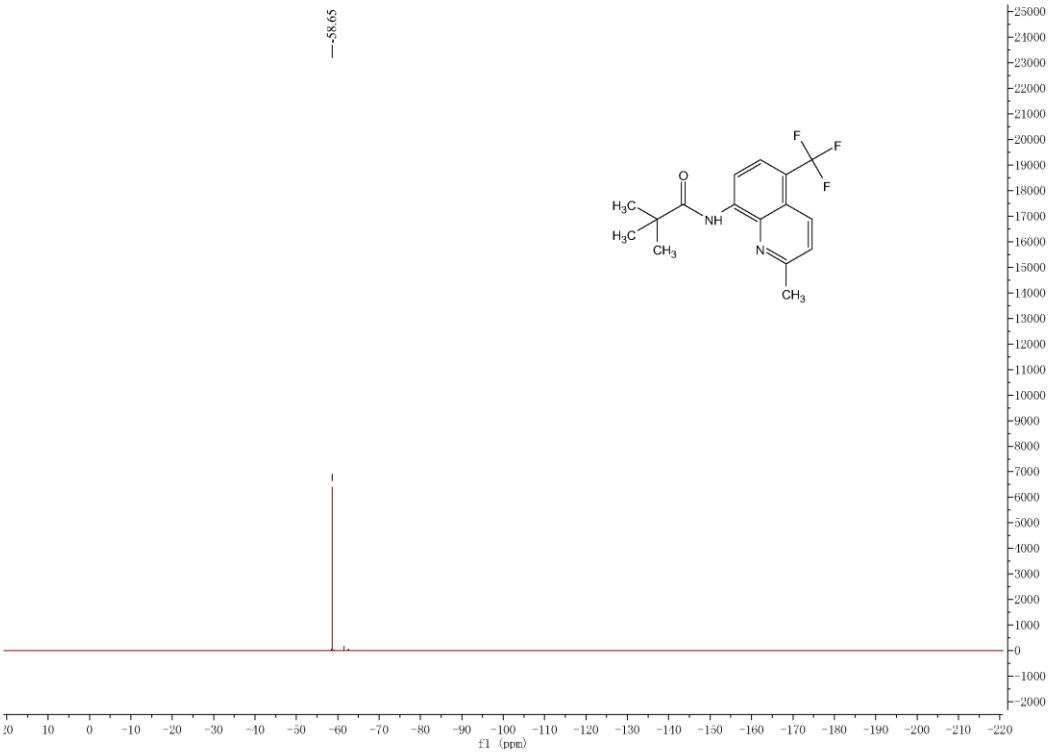
^{19}F NMR **3o**



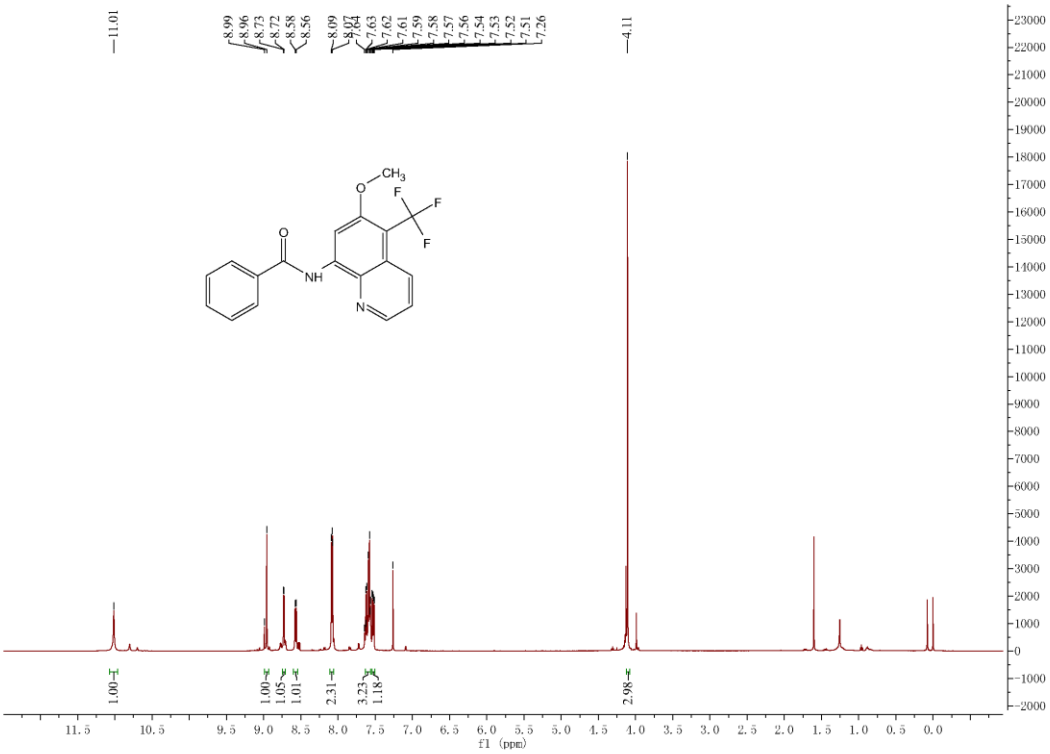
^{1}H NMR **3p**



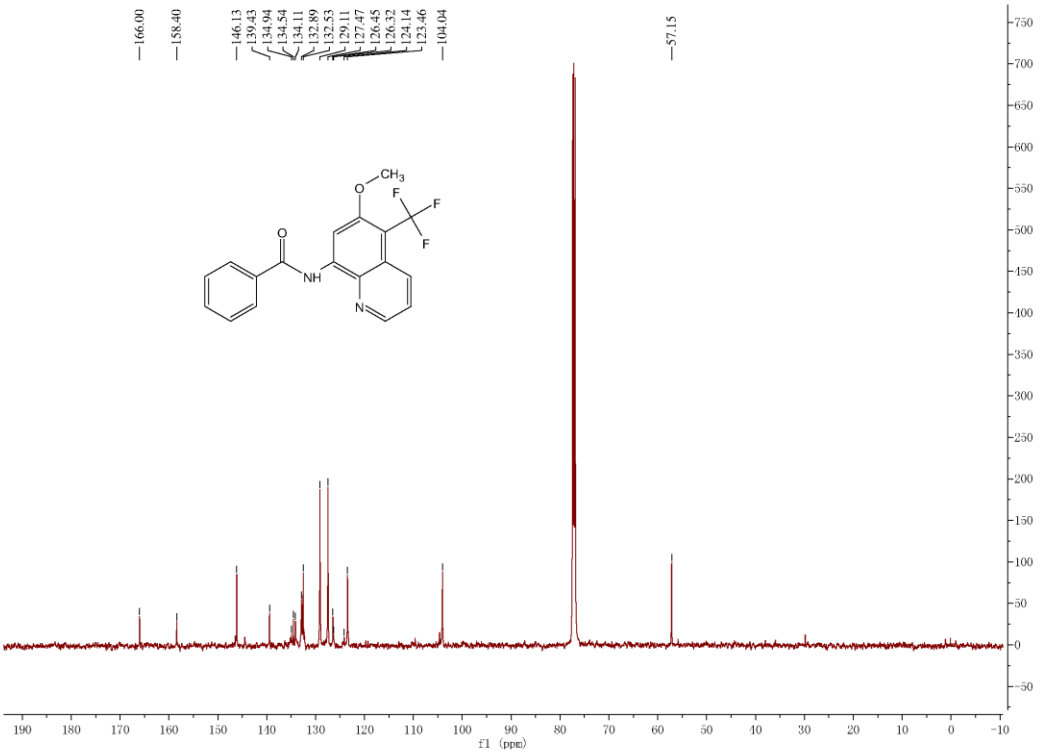
^{13}C NMR **3p**



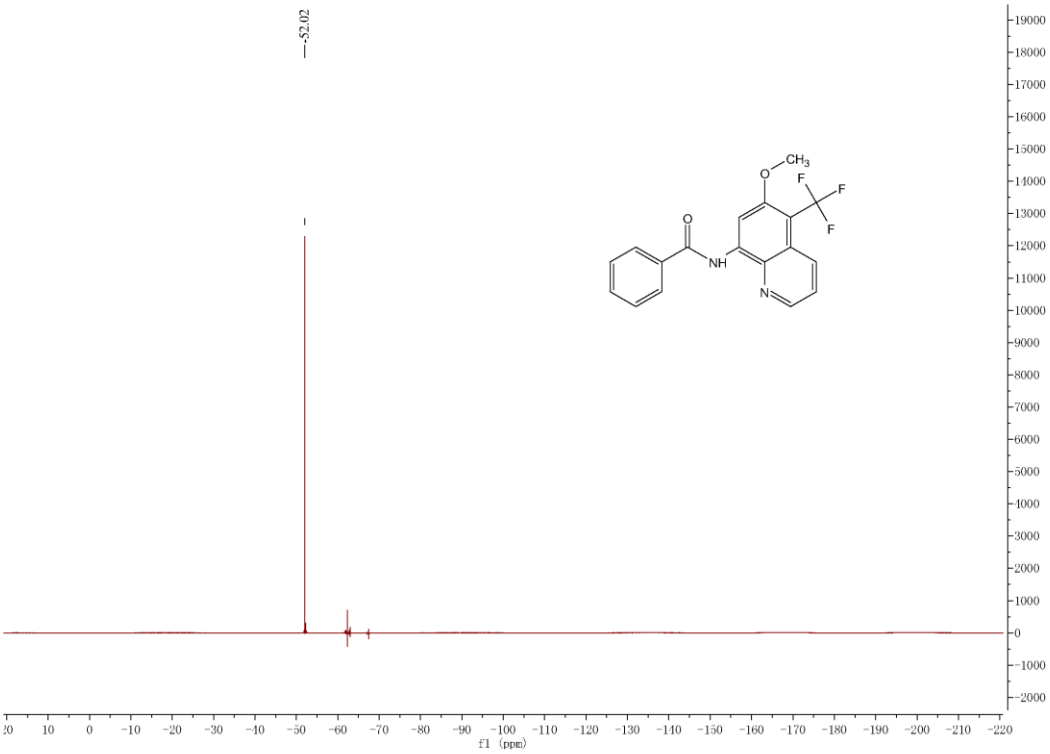
^{19}F NMR **3p**



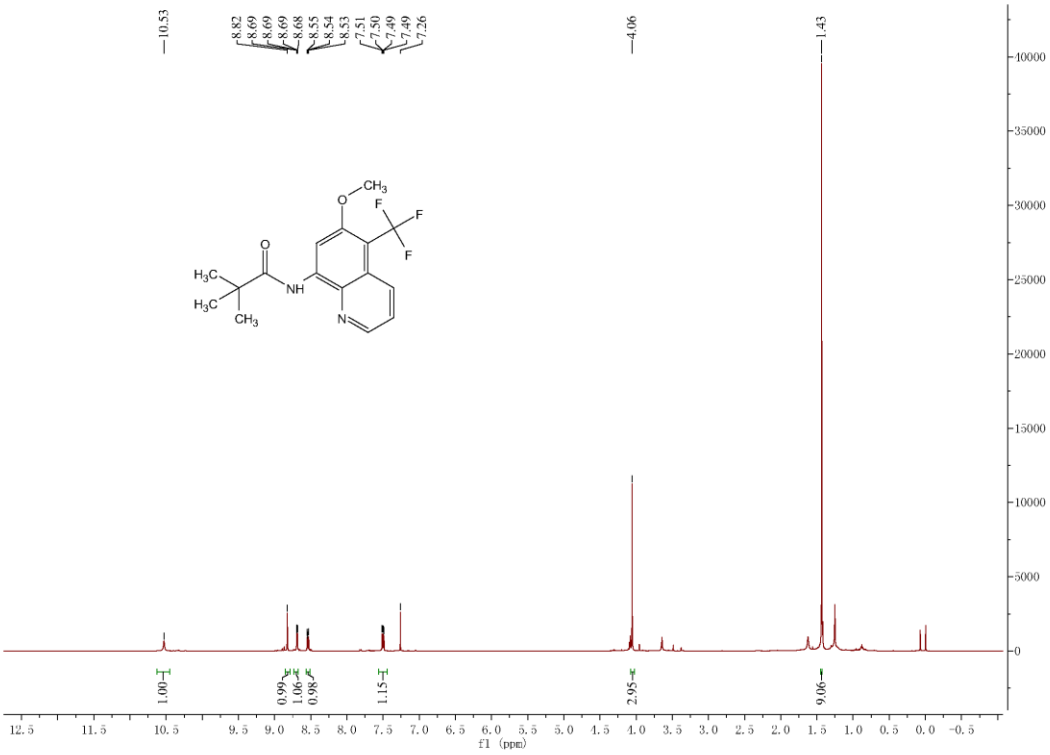
^{1}H NMR **3q**



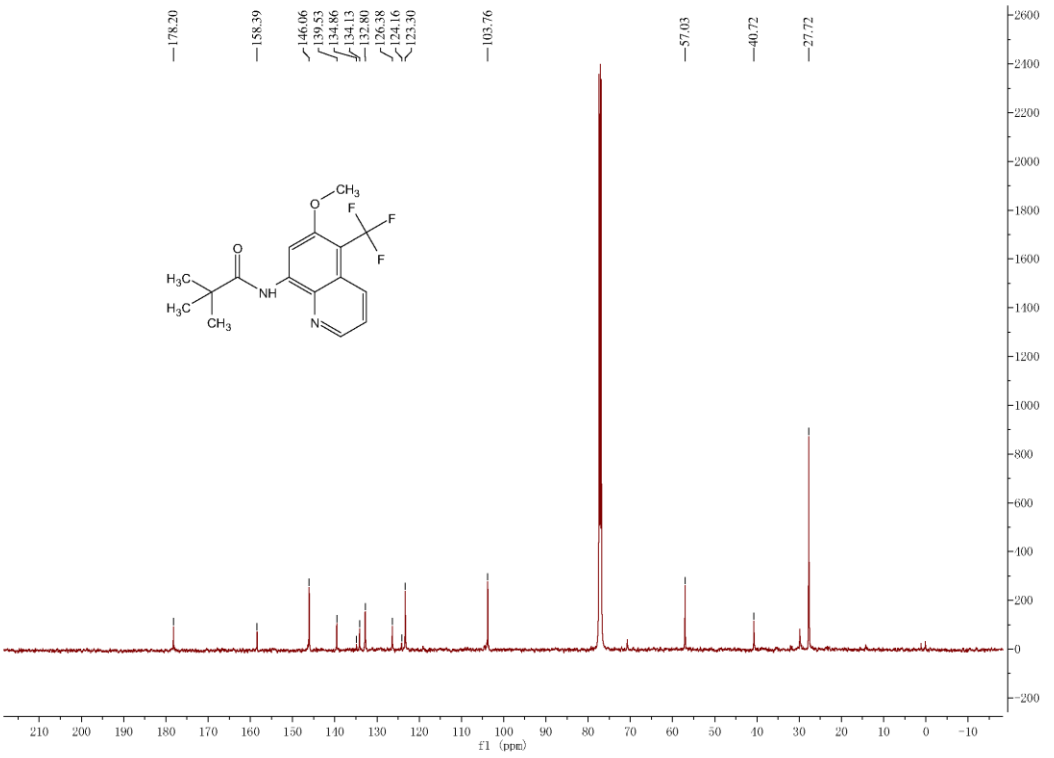
^{13}C NMR **3q**



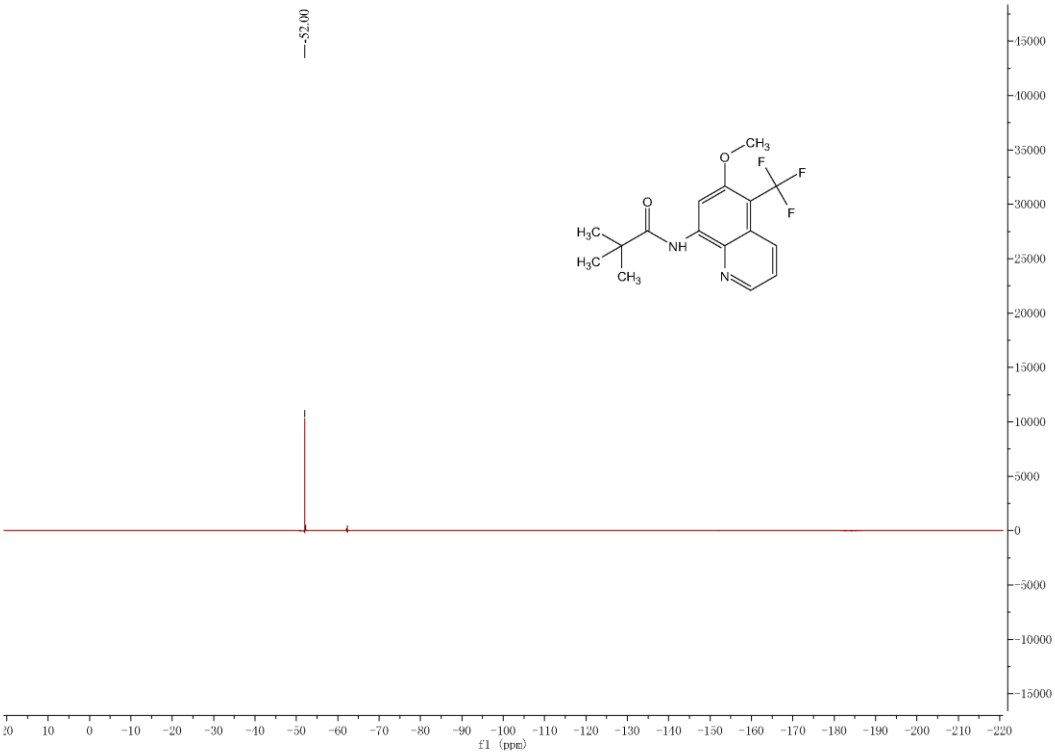
^{19}F NMR **3q**



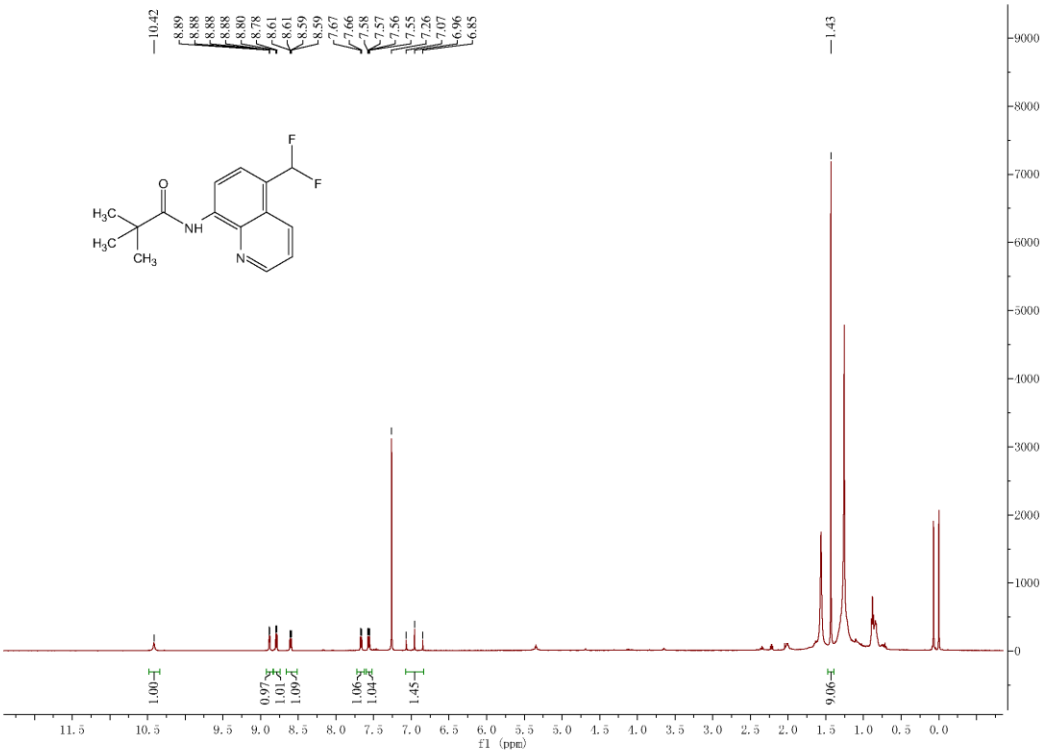
^{1}H NMR **3r**



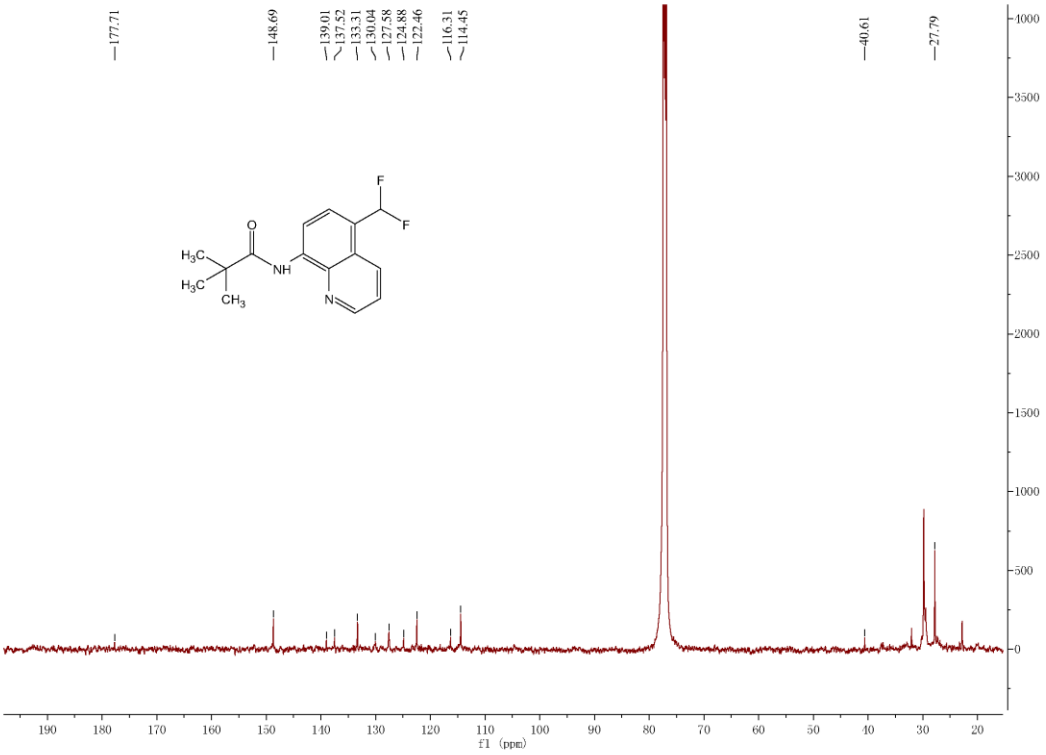
^{13}C NMR **3r**



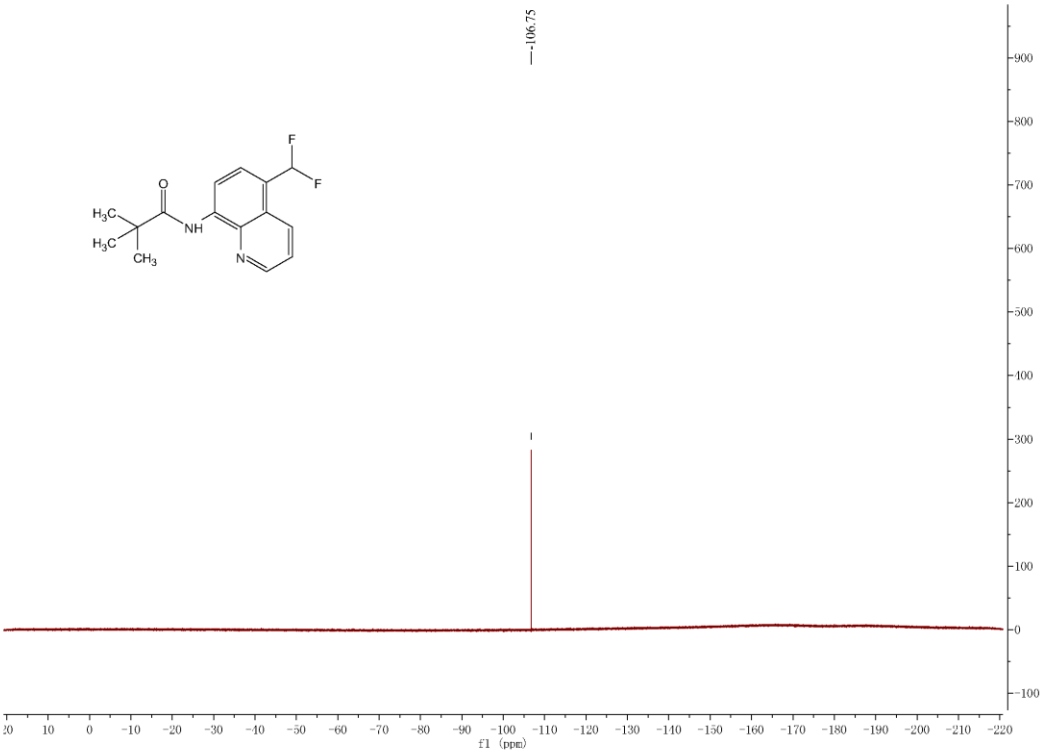
^{19}F NMR **3r**



^{1}H NMR **3t**



^{13}C NMR **3t**



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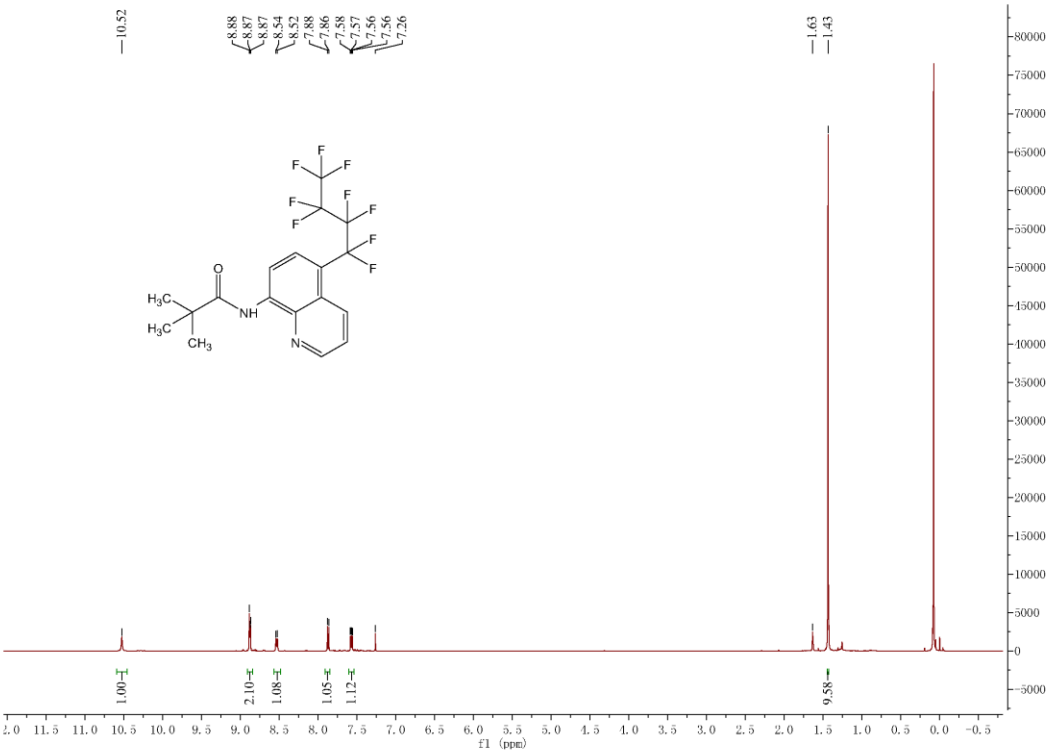
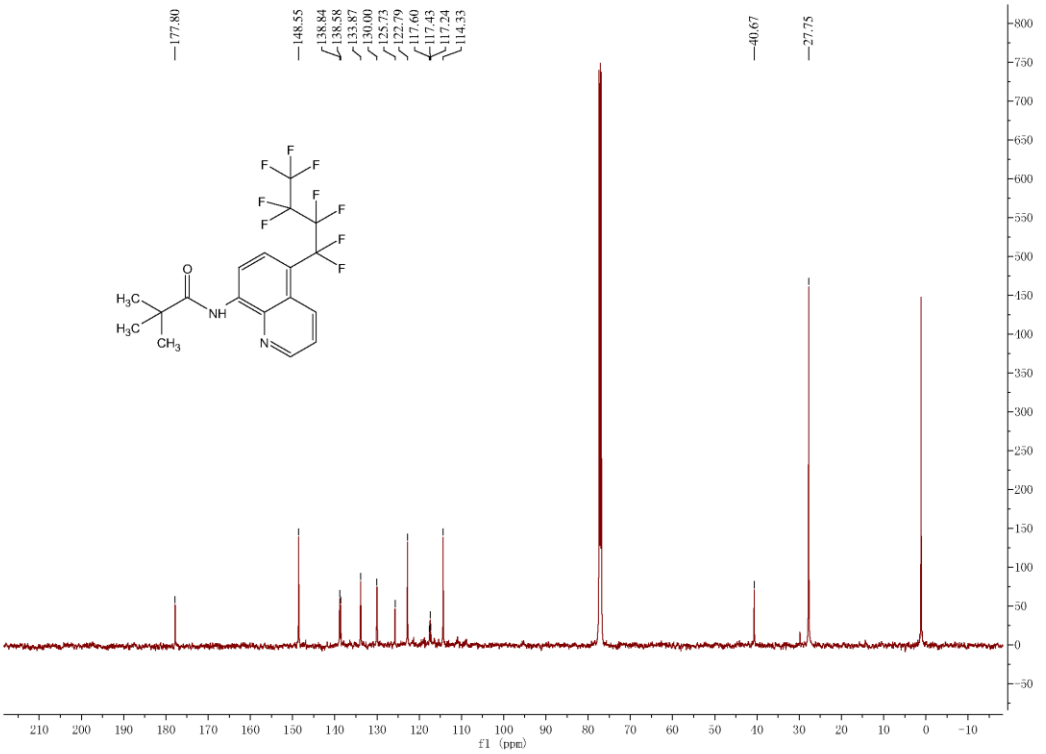
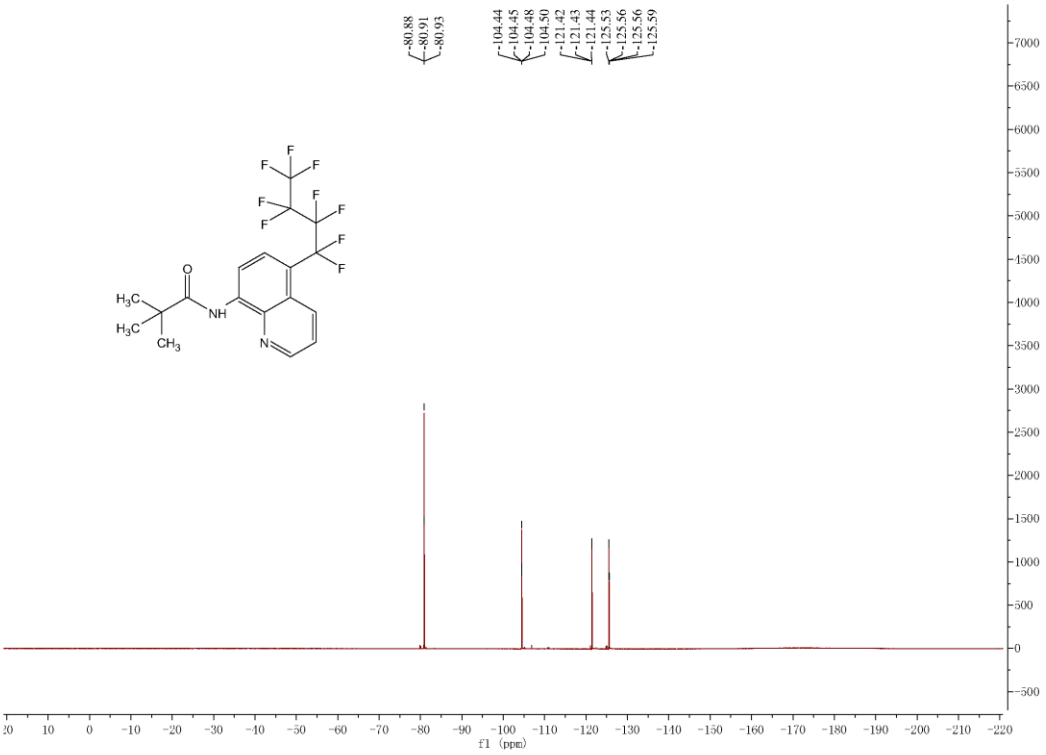


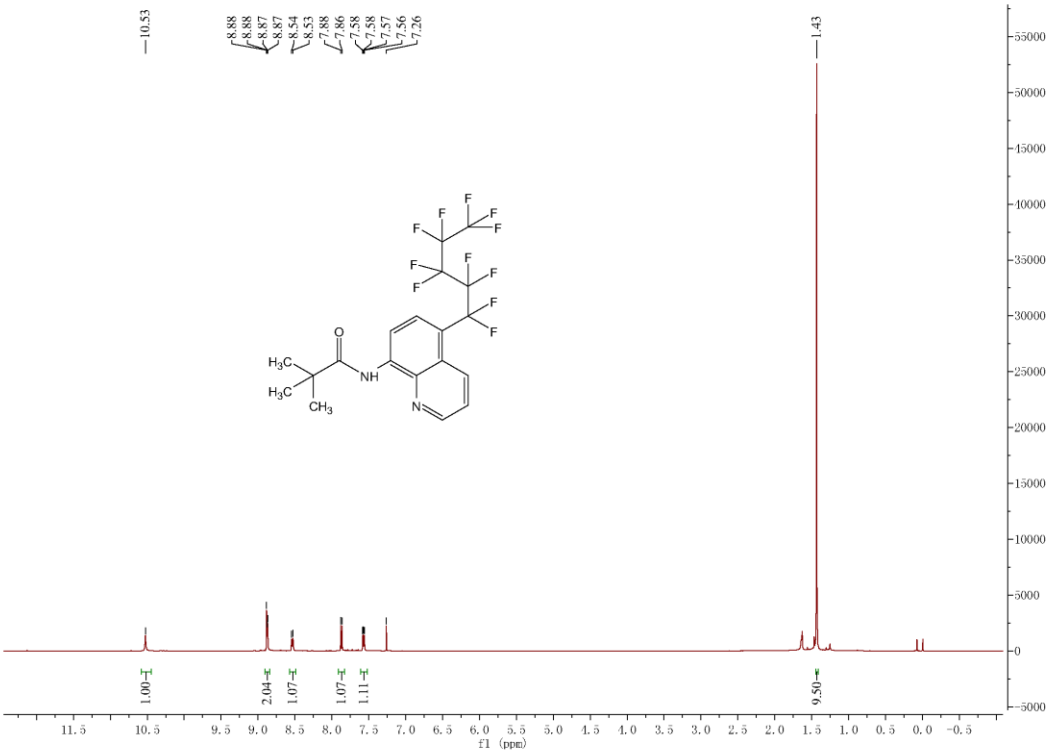
^{1}H NMR **3u**



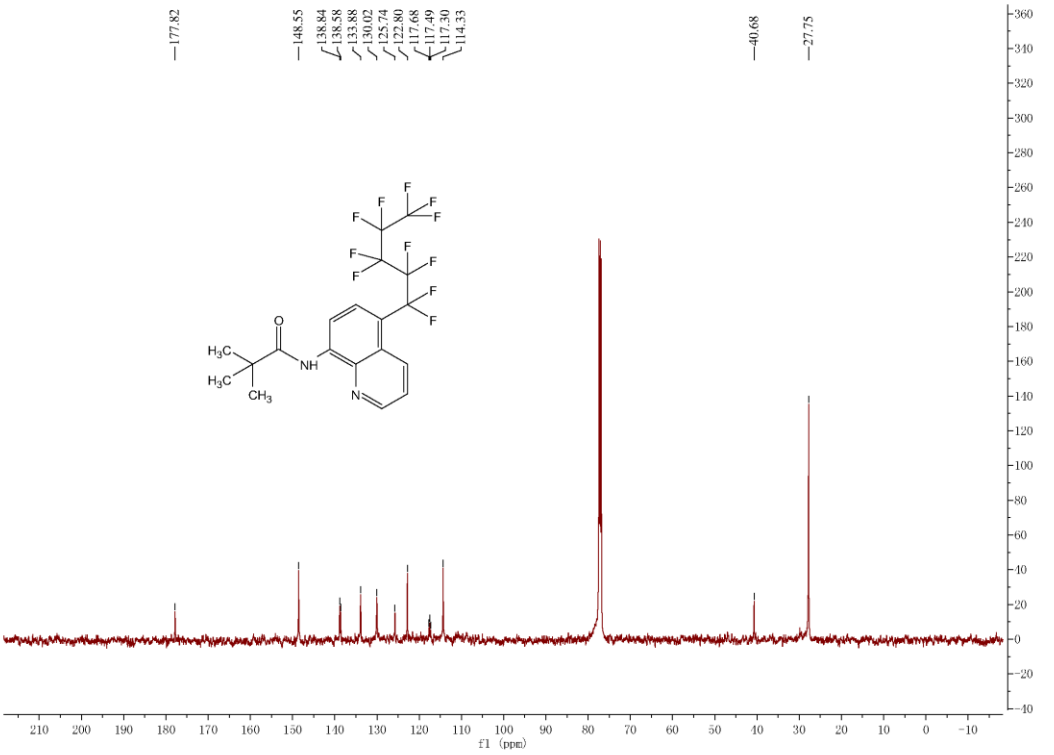
^{13}C NMR **3u**



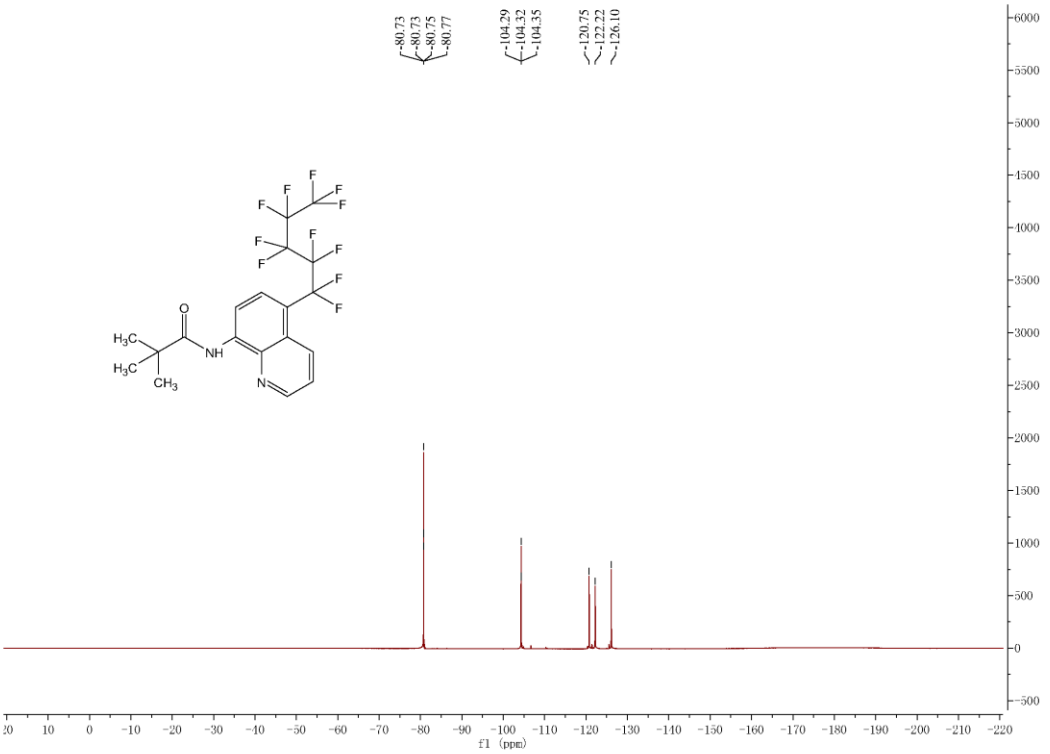
^{19}F NMR **3u**



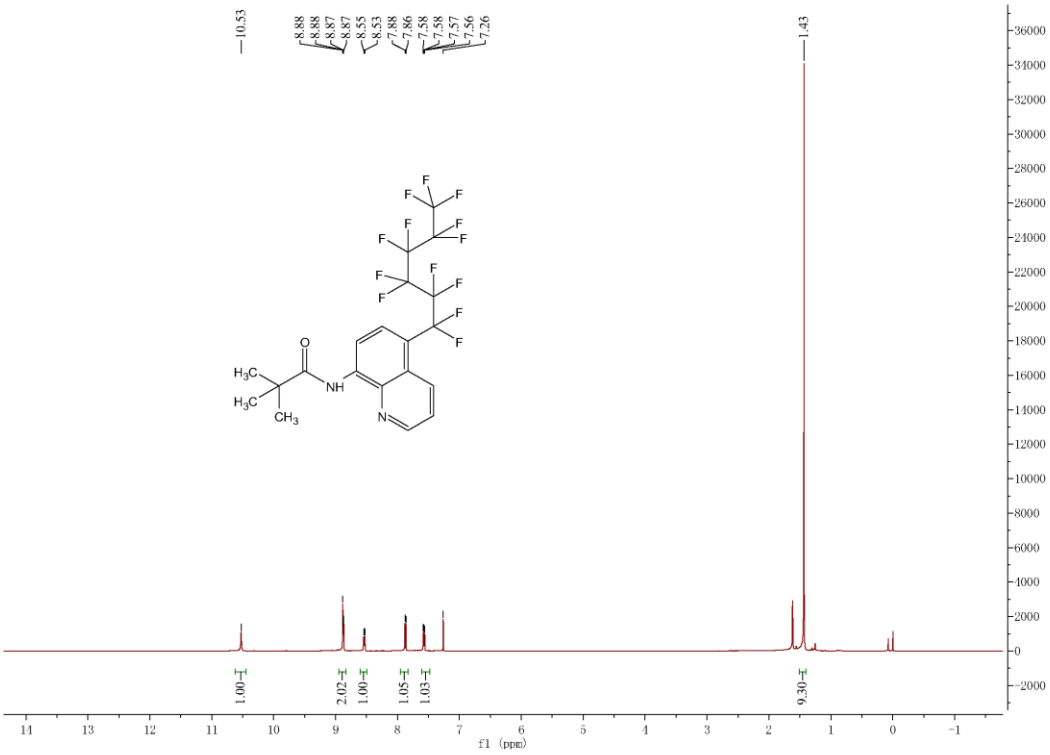
^{1}H NMR **3v**



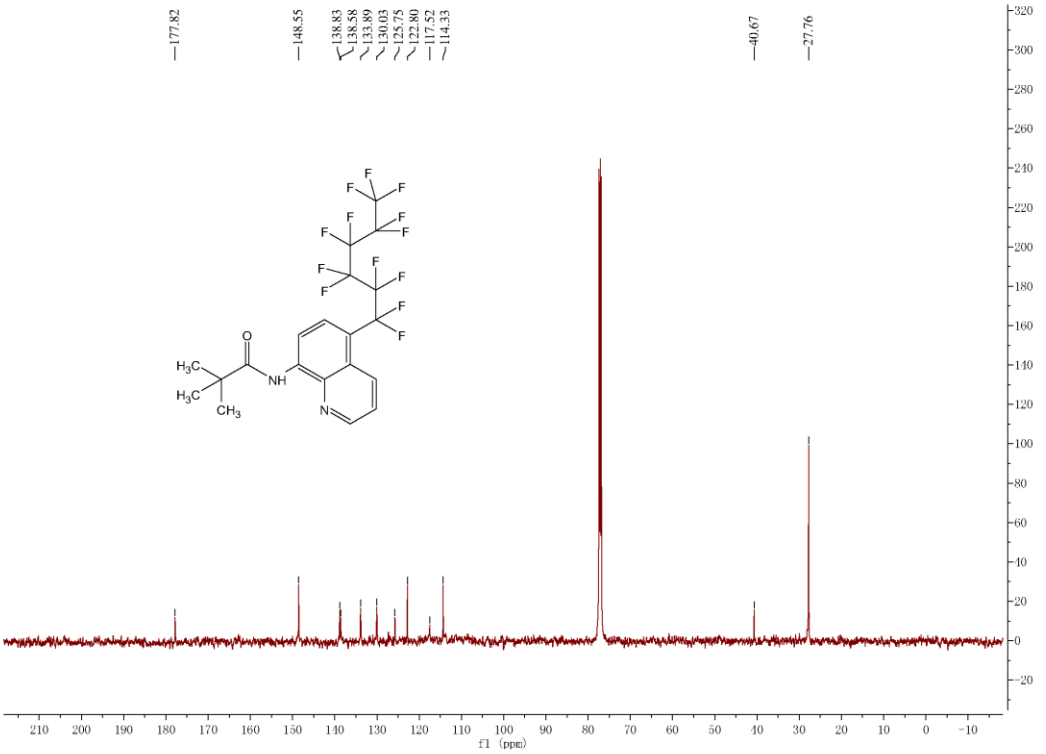
^{13}C NMR **3v**



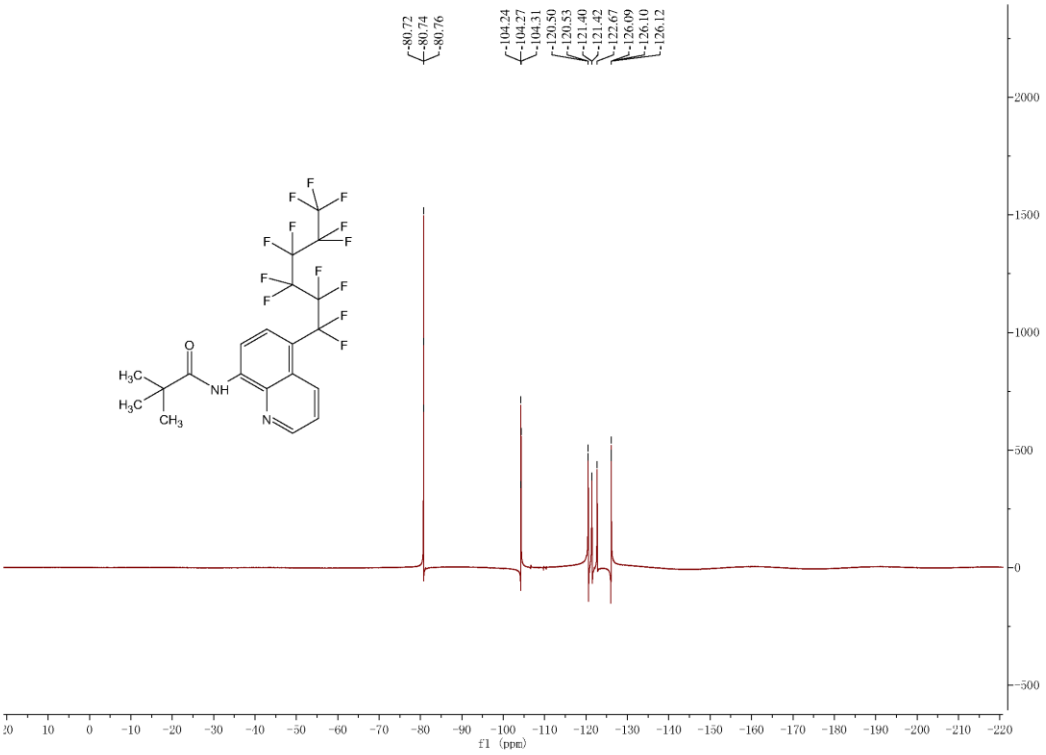
^{19}F NMR **3v**



^{1}H NMR **3w**



^{13}C NMR **3w**



^{19}F NMR **3w**