Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Nickel-catalyzed C-H Bond Trifluoromethylation of 8-Aminoquinoline Derivatives by Acyl-directed Functionalization

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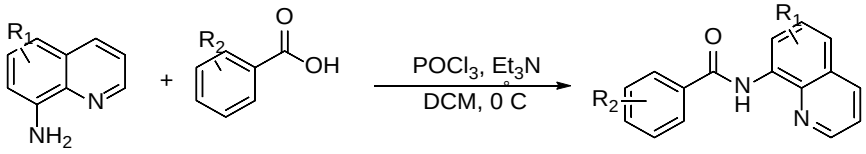
1. Materials and measurements.

All starting materials were purchased from TCI; the reagents were obtained from J&K Chemical Company and used without further purification unless specified. The trifluoromethylation reactions were monitored by thin layer chromatography (TLC), and column chromatography were carried out on silica gel (300 ~ 400 mesh). ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a Bruker Ultrashield™ 400 spectrometer operating at 400 MHz and 100 MHz in $CDCl_3$ or DMSO. ^{1}H NMR and ^{13}C NMR were reported in ppm with tetramethylsilane (TMS) as internal standard. ^{19}F NMR was reported in ppm with trifluoroacetic acid (TFA) as internal standard. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, m = multiple. Coupling constants (*J*) are reported in Hertz (Hz). Melting points were measured by Shang Guang WRR melting point apparatus. Infrared spectroscopy (IR) was measured by SP-100 Fourier transform infrared spectroscopy. TLC was performed using commercially prepared 100-400 mesh silica gel plates (GF254), and visualization was effected at 254 nm.

2. Preparation of the substrates

Preparation of N-(quinolin-8-yl)benzamides (1a-l, 1q-t and **1w)**



The substituted quinolin-8-amine (10 mmol), benzoic acids (12.5 mmol) and Et_3N (20 mmol) were dissolved in DCM (40 mL) followed by dropwise addition of $POCl_3$ (1.88 mL) at 0ºC. The resulting mixture was stirred at 0ºC for 0.5 h and warmed to room temperature for 2 h. Then the reaction mixture was cooled to 0ºC. Ice water was added slowly to quench the reaction. The organic layer was collected, and the aqueous phase was extracted with DCM. The combined organic phase was washed by saturated $NaHCO_3$ and dried over Na_2SO_4. The solvent was evaporated under reduced

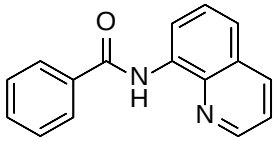
pressure, and the crude product was purified by silica gel column chromatography to give a desired product.

Preparation of N-(quinolin-8-yl)aliphaticamide (1m-1p, 1v).

The quinolin-8-amine (10 mmol), Et_3N (20 mmol) were dissolved in DCM (40 mL) followed by dropwise acyl chloride (11.5 mmol) at 0ºC. The resulting mixture was stirred at 0ºC for 0.5 h and warmed to room temperature for 2 h. Then the reaction mixture was cooled to 0ºC. Ice water was added slowly to quench the reaction. The organic layer was collected, and the aqueous phase was extracted with DCM. The combined organic phase was washed by saturated $NaHCO_3$ and dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and the crude material was purified by silica gel column chromatography to give a desired product.

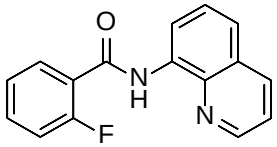
Structures and data of some substrates

N-(quinolin-8-yl)benzamide (**1a**)



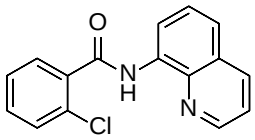
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.59 (s, 1H), 9.04 (dd, *J* = 4.2, 1.4 Hz, 1H), 8.72 (d, *J* = 8.4 Hz, 1H), 8.46 (dd, *J* = 8.5, 1.4 Hz, 1H), 8.05 (d, *J* = 6.9 Hz, 2H), 7.80 – 7.56 (m, 5H), 7.48 (d, *J* = 8.4 Hz, 1H).

2-fluoro-N-(quinolin-8-yl)benzamide (**1c**)



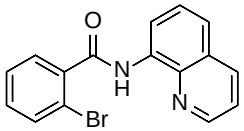
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.02 (d, *J* = 11.2 Hz, 1H), 8.97 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.87 – 8.83 (m, 1H), 8.46 (dd, *J* = 8.3, 1.5 Hz, 1H), 8.11 (td, *J* = 7.9, 1.8 Hz, 1H), 7.78 – 7.74 (m, 1H), 7.74 – 7.70 (m, 1H), 7.69 (dd, *J* = 5.1, 3.1 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.53 – 7.43 (m, 2H).

2-chloro-N-(quinolin-8-yl)benzamide (**1d**)



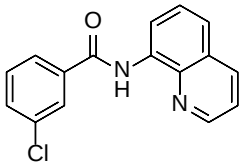
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.45 (s, 1H), 8.91 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.75 (d, *J* = 7.4 Hz, 1H), 8.46 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.83 – 7.76 (m, 2H), 7.66 (dt, *J* = 12.3, 7.8 Hz, 3H), 7.59 (td, *J* = 7.6, 1.7 Hz, 1H), 7.53 (td, *J* = 7.4, 1.2 Hz, 1H).

2-bromo-N-(quinolin-8-yl)benzamide (**1e**)



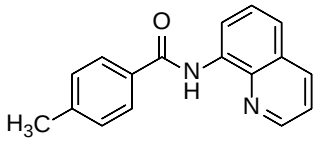
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.32 (s, 1H), 8.94 – 8.88 (m, 1H), 8.74 (d, *J* = 7.2 Hz, 1H), 8.49 – 8.43 (m, 1H), 7.77 (td, *J* = 12.2, 10.0, 5.5 Hz, 3H), 7.71 – 7.63 (m, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.53 – 7.46 (m, 1H).

3-chloro-N-(quinolin-8-yl)benzamide (**1h**)



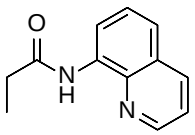
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.66 (s, 1H), 8.99 (d, *J* = 3.8 Hz, 1H), 8.68 (d, *J* = 7.5 Hz, 1H), 8.47 (d, *J* = 8.2 Hz, 1H), 8.09 – 7.97 (m, 2H), 7.90 (dd, *J* = 4.0, 2.3 Hz, 1H), 7.76 (d, *J* = 4.5 Hz, 1H), 7.73 (s, 1H), 7.68 (dt, *J* = 7.9, 3.9 Hz, 3H).

4-methyl-N-(quinolin-8-yl)benzamide (**1j**)



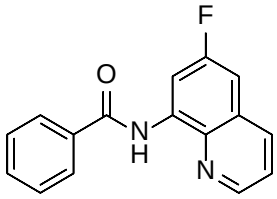
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.63 (s, 1H), 8.99 (d, *J* = 4.0 Hz, 1H), 8.76 (d, *J* = 7.6 Hz, 1H), 8.46 (d, *J* = 8.3 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.71 – 7.63 (m, 2H), 7.43 (d, *J* = 7.8 Hz, 2H), 2.42 (s, 3H).

N-(quinolin-8-yl)propionamide (**1m**)



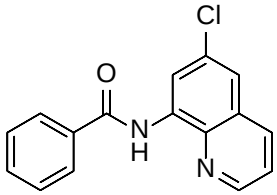
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.81 (s, 1H), 8.81 – 8.74 (m, 2H), 8.11 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.51 (t, *J* = 7.9 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.40 (dd, *J* = 8.3, 4.2 Hz, 1H), 2.58 (q, *J* = 7.6 Hz, 2H), 1.33 (t, *J* = 7.6 Hz, 3H).

N-(6-fluoroquinolin-8-yl)benzamide (**1r**)



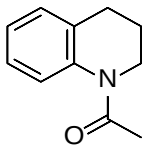
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.73 (s, 1H), 8.95 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.59 (dd, *J* = 11.2, 2.8 Hz, 1H), 8.45 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.05 (d, *J* = 6.9 Hz, 2H), 7.73 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.69 (d, *J* = 7.1 Hz, 1H), 7.66 (s, 1H), 7.65 (s, 1H), 7.56 (dd, *J* = 9.3, 2.8 Hz, 1H).

N-(6-chloroquinolin-8-yl)benzamide (**1s**)



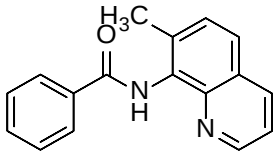
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.67 (s, 1H), 8.99 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.74 (d, *J* = 2.3 Hz, 1H), 8.44 (dd, *J* = 8.3, 1.5 Hz, 1H), 8.05 (s, 1H), 8.03 (d, *J* = 1.5 Hz, 1H), 7.89 (d, *J* = 2.3 Hz, 1H), 7.74 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.69 (d, *J* = 7.1 Hz, 1H), 7.66 (s, 1H), 7.64 (s, 1H).

1-(3,4-dihydroquinolin-1(2H)-yl)ethan-1-one (**1v**)



^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.16 (m, 4H, arom), 3.81 (t, *J* = 6.0 Hz, 2H), 2.73 (t, *J* = 6.0 Hz, 2H), 2.24 (s, 3H), 1.97 (q, *J* = 6.0 Hz, 2H).

N-(7-chloroquinolin-8-yl)benzamide (**1w**)[1]



m.p: 133.3-133.5 °C

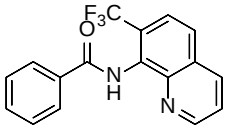
3. Synthesis of target compounds

Synthetic method of N-(7-(trifluoromethyl)quinolin-8-yl)acylamides (2a-u)

A 15 mL screw-cap vial charged with N-(quinolin-8-yl)acylamide (1 mmol), $TMSCF_3$ (3 mmol), KF (3 mmol), PIDA (3 mmol), $Ni(TFA)_2$ (0.1 mmol), DPPBac (0.3 mmol) and 1,2-DCE (5 mL), the mixture was stirred at room temperature for 18 h. After completion of the reaction, the solution was extracted with dichloromethane (3×20 mL). Organic layers were combined and dried over Na_2SO_4, filtered and concentrated under reduced pressure, and the crude material was purified by silica gel column chromatography to give a desired product.

Structures and data of target compounds

N-(7-(trifluoromethyl)quinolin-8-yl)benzamide (**2a**)



white solid (216.6 mg, 85%); m.p: 133.3-133.5 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.88 (s, 1H), 9.12 (d, J = 3.9 Hz, 1H), 8.84 (d, J = 8.2 Hz, 1H), 8.56 (d, J = 8.6 Hz, 1H), 8.15 (d, J = 8.1 Hz, 1H), 8.06 (d, J = 7.6 Hz, 2H), 7.90 (dd, J = 8.7, 4.1 Hz, 1H), 7.74 – 7.68 (m, 1H), 7.65 (t, J = 7.2 Hz, 2H). (Figure S1)

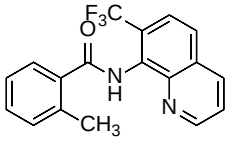
^{13}C NMR (100 MHz, DMSO-d_6) δ 165.4, 150.4, 138.5, 138.4, 134.4, 133.2, 133.1, 133.0, 131.6, 129.6, 127.6, 127.3, 124.6, 124.0, 114.6. (Figure S2)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.58. (Figure S3)

HRMS: (EI) calcd for $C_{17}H_{11}F_3N_2O$ $[M+H]^+$: 317.0902. Found: 317.0909. Anal. calcd for $C_{17}H_{11}F_3N_2O$: C, 64.56; H, 3.51; F, 18.02; N, 8.86; Found: C, 64.59; H, 3.52; F, 18.04; N, 8.87.

FT-IR (KBr disc): 3374, 1680, 1534, 1330, 1092 cm^{-1}.

2-methyl-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide (**2b**)



white solid (281.5 mg, 89%); m.p: 122.7-124.5 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.50 (s, 1H), 9.11 (d, J = 4.1 Hz, 1H), 8.90 (d, J = 8.1 Hz, 1H), 8.61 (d, J = 10.0 Hz, 1H), 8.22 (d, J = 8.2 Hz, 1H), 7.93 (dd, J = 8.7, 4.2 Hz, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.49 – 7.42 (m, 2H), 2.56 (s, 3H). (Figure S4)

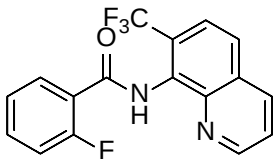
^{13}C NMR (100 MHz, DMSO-d_6) δ 168.0, 150.4, 138.5 (d, J = 40.8 Hz), 136.6, 136.1, 133.1, 133.1, 131.8, 128.8 (q, J = 284.4 Hz), 127.5, 127.4, 127.3, 126.1, 124.0, 118.6, 114.5, 20.2. (Figure S5)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.53. (Figure S6)

HRMS: (EI) calcd for $C_{18}H_{13}F_3N_2O$ $[M+H]^+$: 331.1059. Found: 331.1048. Anal. calcd for $C_{18}H_{13}F_3N_2O$: C, 65.45; H, 3.97; F, 17.26; N, 8.48; Found: C, 65.47; H, 3.98; F, 17.25; N, 8.45.

FT-IR (KBr disc): 3326, 1677, 1537, 1326, 1085 cm^{-1}.

2-fluoro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide (**2c**)



white solid (260.7 mg, 78%); m.p: 134.9-137.2 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.21 (d, J = 11.7 Hz, 1H), 9.07 (d, J = 3.5 Hz, 1H), 8.88 (d, J = 8.2 Hz, 1H), 8.53 (d, J = 8.4 Hz, 1H), 8.11 (dd, J = 11.6, 6.4 Hz, 2H), 7.87 (dd, J = 8.6, 4.1 Hz, 1H), 7.74 (q, J = 6.1 Hz, 1H), 7.53 – 7.42 (m, 2H). (Figure S7)

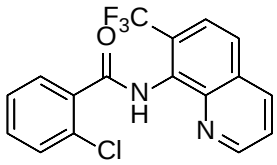
^{13}C NMR (100 MHz, DMSO-d_6) δ 161.7, 159.1, 150.4, 138.3 (d, J = 45.1 Hz), 135.2 (d, J = 9.7 Hz), 133.0, 131.9, 127.3, 127.3, 125.8, 124.6, 122.4 (q, J = 242.1 Hz), 121.5, 117.1 (d, J = 24.0 Hz), 114.8. (Figure S8)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.46, -36.26. (Figure S9)

HRMS: (EI) calcd for $C_{17}H_{10}F_4N_2O$ $[M+H]^+$: 335.0808. Found: 335.0802. Anal. calcd for $C_{17}H_{10}F_4N_2O$: C, 61.08; H, 3.02; F, 22.73; N, 8.38; Found: C, 61.09; H, 3.04; F, 22.71; N, 8.36.

FT-IR (KBr disc): 3355, 1678, 1543, 1330, 1080 cm^{-1}.

2-chloro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide (**2d**)



white solid (280.6 mg, 80%); m.p: 81.3-83.9 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.74 (s, 1H), 9.07 – 9.04 (m, 1H), 8.85 (d, *J* = 8.2 Hz, 1H), 8.55 (d, *J* = 8.7 Hz, 1H), 8.16 (d, *J* = 8.3 Hz, 1H), 7.90 – 7.81 (m, 2H), 7.67 – 7.58 (m, 2H), 7.54 (td, *J* = 7.4, 1.5 Hz, 1H). (Figure S10)

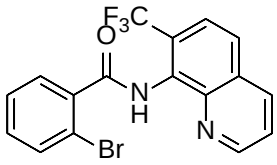
^{13}C NMR (100 MHz, DMSO-d_6) δ 165.3, 150.4, 138.4, 138.3, 135.7, 133.1, 132.7, 130.7, 130.3, 129.4, 128.8 (q, *J* = 282.0 Hz) 127.3, 127.2, 124.0, 119.3, 119.0, 115.0. (Figure S11)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.44. (Figure S12)

HRMS: (EI) calcd for $C_{17}H_{10}ClF_3N_2O$ $[M+H]^+$: 351.0513. Found: 351.0502. Anal. calcd for $C_{17}H_{10}ClF_3N_2O$: C, 58.22; H, 2.87; Cl, 10.11; F, 16.25; N, 7.99; Found: C, 58.25; H, 2.86; Cl, 10.14; F, 16.27; N, 7.96.

FT-IR (KBr disc): 3314, 1680, 1537, 1332, 1093 cm^{-1}.

2-bromo-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide (**2e**)



white solid (304.29 mg, 77%); m.p: 81.3-83.9 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.61 (s, 1H), 9.05 (d, *J* = 3.1 Hz, 1H), 8.84 (d, *J* = 8.1 Hz, 1H), 8.55 (d, *J* = 8.3 Hz, 1H), 8.17 (d, *J* = 8.2 Hz, 1H), 7.87 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.78 (t, *J* = 8.0 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.52 (dd, *J* = 10.8, 4.2 Hz, 1H). (Figure S13)

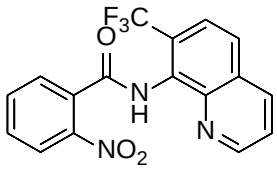
^{13}C NMR (100 MHz, DMSO-d_6) δ 166.4, 150.4, 138.4, 138.3, 138.2, 133.7, 133.0, 132.6, 129.8, 128.5, 127.3, 127.2, 124.6, 124.0, 123.9 (q, *J* = 307.0 Hz), 119.2, 115.0. (Figure S14)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.44. (Figure S15)

HRMS: (EI) calcd for $C_{17}H_{10}BrF_3N_2O$ $[M+H]^+$: 395.0008. Found: 395.0014. Anal. calcd for $C_{17}H_{10}BrF_3N_2O$: C, 51.67; H, 2.55; Br, 20.22; F, 14.42; N, 7.09; Found: C, 51.68; H, 2.57; Br, 20.24; F, 14.41; N, 7.06.

FT-IR (KBr disc): 3325, 1683, 1529, 1331, 1108 cm^{-1}.

2-nitro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide (**2f**)



yellow solid (252.90 mg, 70%); m.p: 163.5-165.2 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.10 (s, 1H), 9.08 (d, J = 4.0 Hz, 1H), 8.86 (d, J = 8.2 Hz, 1H), 8.59 (d, J = 8.3 Hz, 1H), 8.24 (dd, J = 17.7, 8.2 Hz, 2H), 7.99 – 7.81 (m, 4H). (Figure S16)

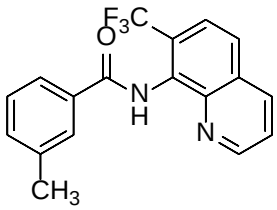
^{13}C NMR (100 MHz, DMSO-d_6) δ 165.7, 150.3, 146.7, 139.0, 138.7, 134.8, 132.9, 132.9, 132.8, 131.6 (q, J = 289.9 Hz), 129.4, 127.2, 124.8, 124.5, 124.1, 123.3, 115.9. (Figure S17)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.47. (Figure S18)

HRMS: (EI) calcd for $C_{17}H_{10}F_3N_3O_3$ $[M+H]^+$: 362.0753. Found: 362.0745. Anal. calcd for $C_{17}H_{10}F_3N_3O_3$: C, 56.52; H, 2.79; F, 15.78; N, 11.63; Found: $C_{17}H_{10}F_3N_3O_3$: C, 56.53; H, 2.76; F, 15.77; N, 11.65.

FT-IR (KBr disc): 3479, 3324, 2963, 1682, 1528, 1262, 1107 cm^{-1}.

3-methyl-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide (**2g**)



white solid (287.37 mg, 87%); m.p: 115.7-118.6 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.84 (s, 1H), 9.13 (s, 1H), 8.84 (d, J = 7.1 Hz, 1H), 8.56 (d, J = 6.6 Hz, 1H), 8.14 (t, J = 6.9 Hz, 1H), 7.88 (d, J = 21.7 Hz, 3H), 7.53 (d, J

= 5.7 Hz, 2H), 2.46 (s, 3H). (Figure S19)

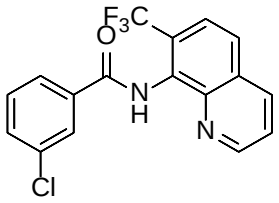
^{13}C NMR (100 MHz, DMSO-d_6) δ 165.5, 150.4, 139.1, 138.6, 138.4, 134.4, 133.6, 133.1, 129.5, 128.2, 127.4, 127.3, 124.7, 124.6, 124.0, 118.9 (q, J = 294.8 Hz), 114.6, 21.4. (Figure S20)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.53. (Figure S21)

HRMS: (EI) calcd for $C_{18}H_{13}F_3N_2O$ $[M+H]^+$: 331.1059. Found: 331.1052. Anal. calcd for $C_{18}H_{13}F_3N_2O$: C, 65.45; H, 3.97; F, 17.26; N, 8.48; Found: C, 65.47; H, 3.95; F, 17.24; N, 8.46.

FT-IR (KBr disc): 3414, 3358, 1675, 1531, 1391, 1315, 1122 cm^{-1}.

3-chloro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide (**2h**)



white solid (291.10 mg, 83%); m.p: 101.6-103.7 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.81 (s, 1H), 9.11 – 9.07 (m, 1H), 8.74 (d, J = 8.2 Hz, 1H), 8.51 (d, J = 8.6 Hz, 1H), 8.08 (d, J = 8.3 Hz, 1H), 8.02 – 7.98 (m, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.86 (dd, J = 8.7, 4.2 Hz, 1H), 7.77 – 7.72 (m, 1H), 7.65 (t, J = 7.9 Hz, 1H). (Figure S22)

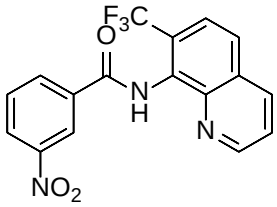
^{13}C NMR (100 MHz, DMSO-d_6) δ 168.8, 155.1, 143.2, 143.0, 141.1, 139.0, 137.7, 137.4, 136.1, 132.4, 131.9, 130.9, 129.2, 128.7, 126.2 (q, J = 373.8 Hz) 123.9, 119.7. (Figure S23)

^{19}F NMR (376 MHz, DMSO-d_6) δ 23.17. (Figure S24)

HRMS: (EI) calcd for $C_{17}H_{10}ClF_3N_2O$ $[M+H]^+$: 351.0513. Found: 351.0502. Anal. calcd for $C_{17}H_{10}ClF_3N_2O$: C, 58.22; H, 2.87; Cl, 10.11; F, 16.25; N, 7.99; Found: C, 58.25; H, 2.84; Cl, 10.14; F, 16.27; N, 7.98.

FT-IR (KBr disc): 3350, 1682, 1534, 1319, 1144, 1086 cm^{-1}.

3-nitro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide (**2i**)



yellow solid (263.73 mg, 73%); m.p: 181.8-182.5 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.11 (s, 1H), 9.20 (d, J = 3.5 Hz, 1H), 8.88 – 8.83 (m, 2H), 8.63 (d, J = 8.6 Hz, 1H), 8.59 – 8.52 (m, 2H), 8.23 (d, J = 8.3 Hz, 1H), 8.01 – 7.93 (m, 2H). (Figure S25)

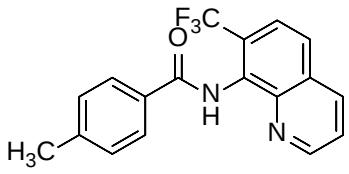
^{13}C NMR (100 MHz, DMSO-d_6) δ 163.8, 150.6, 148.5, 138.8, 138.4, 136.0, 134.0, 133.1, 133.1, 132.2, 131.2, 130.5, 128.1 (q, J = 264.6 Hz), 127.3, 124.6, 122.9, 115.8. (Figure S26)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.46. (Figure S27)

HRMS: (EI) calcd for $C_{17}H_{10}F_3N_3O_3$ $[M+H]^+$: 362.0753. Found: 362.0759. Anal. calcd for $C_{17}H_{10}F_3N_3O_3$: C, 56.52; H, 2.79; F, 15.78; N, 11.63; Found: C, 56.55; H, 2.77; F, 15.79; N, 11.65.

FT-IR (KBr disc): 3331, 2962, 2927, 1684, 1529, 1263, 1112 cm^{-1}.

4-methyl-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide (**2j**)



white solid (284.07 mg, 86%); m.p: 128.1-129.4 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.84 (s, 1H), 9.13 (s, 1H), 8.83 (d, J = 8.2 Hz, 1H), 8.55 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 7.7 Hz, 2H), 7.89 (dd, J = 8.6, 4.2 Hz, 1H), 7.44 (d, J = 7.8 Hz, 2H), 2.43 (s, 3H). (Figure S28)

^{13}C NMR (100 MHz, DMSO-d_6) δ 165.2, 150.4, 143.3, 138.5 (d, J = 22.4 Hz), 133.1, 131.6, 130.1, 128.6 (q, J = 283.3 Hz), 127.7, 127.3, 124.6, 124.0, 118.7, 114.4, 21.5. (Figure S29)

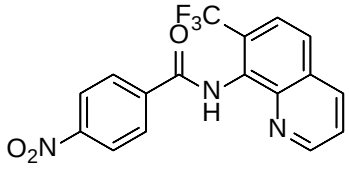
^{19}F NMR (376 MHz, DMSO-d_6) δ 18.54. (Figure S30)

HRMS: (EI) calcd for $C_{18}H_{13}F_3N_2O$ $[M+H]^+$: 331.1059. Found: 331.1065. Anal. calcd

for $C_{18}H_{13}F_3N_2O$: C, 65.45; H, 3.97; F, 17.26; N, 8.48; Found: C, 65.48; H, 3.94; F, 17.29; N, 8.46.

FT-IR (KBr disc): 3363, 1672, 1545, 1391, 1316, 1107 cm^{-1}.

4-nitro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide (**2k**)



yellow solid (274.57 mg, 76%); m.p: 211.6-213.1 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.01 (s, 1H), 9.14 (d, J = 4.0 Hz, 1H), 8.83 (d, J = 8.2 Hz, 1H), 8.58 (d, J = 8.8 Hz, 1H), 8.45 (d, J = 8.6 Hz, 2H), 8.29 (d, J = 8.6 Hz, 2H), 8.19 (d, J = 8.2 Hz, 1H), 7.91 (dd, J = 8.7, 4.1 Hz, 1H). (Figure S31)

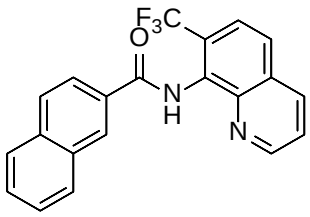
^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 150.5, 150.1, 140.0, 138.7, 138.3, 133.1, 130.6, 129.5, 127.3, 127.2, 124.7, 124.6, 123.3 (q, J = 254.5 Hz), 115.5. (Figure S32)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.46. (Figure S33)

HRMS: (EI) calcd for $C_{17}H_{10}F_3N_3O_3$ $[M+H]^+$: 362.0753. Found: 362.0746. Anal. calcd for $C_{17}H_{10}F_3N_3O_3$: C, 56.52; H, 2.79; F, 15.78; N, 11.63; Found: C, 56.55; H, 2.81; F, 15.75; N, 11.64.

FT-IR (KBr disc): 3301, 1681, 1532, 1311, 1124 cm^{-1}.

N-(7-(trifluoromethyl)quinolin-8-yl)-2-naphthamide (**2l**)



white solid (285.75 mg, 78%); m.p: 253.3-255.4 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.04 (s, 1H), 9.17 (d, J = 3.6 Hz, 1H), 8.90 (d, J = 8.2 Hz, 1H), 8.72 (s, 1H), 8.59 (d, J = 8.3 Hz, 1H), 8.24 – 8.15 (m, 3H), 8.12 – 8.05 (m, 2H), 7.92 (dd, J = 8.6, 4.2 Hz, 1H), 7.74 – 7.65 (m, 2H). (Figure S34)

^{13}C NMR (100 MHz, DMSO-d_6) δ 173.2, 165.6, 150.5, 138.7, 138.5, 135.1, 133.2, 133.2, 132.7, 131.8, 129.7, 129.3, 128.8, 128.5, 128.2, 127.6, 124.6, 124.1, 124.0,

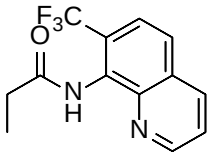
123.0 (q, *J* = 291.2 Hz), 114.8. (Figure S35)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.56. (Figure S36)

HRMS: (EI) calcd for $C_{21}H_{13}F_3N_2O$ $[M+H]^+$: 367.1059. Found: 367.1068. Anal. calcd for $C_{21}H_{13}F_3N_2O$: C, 68.85; H, 3.58; F, 15.56; N, 7.65; Found: C, 68.88; H, 3.55; F, 15.54; N, 7.62.

FT-IR (KBr disc): 3358, 1644, 1502, 1315, 1084 cm^{-1}.

N-(7-(trifluoromethyl)quinolin-8-yl)propionamide (**2m**)



white solid (233.37 mg, 87%); m.p: 109.7-112.5 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.33 (s, 1H), 9.08 (dd, *J* = 4.1, 1.2 Hz, 1H), 8.75 (d, *J* = 8.3 Hz, 1H), 8.54 – 8.49 (m, 1H), 8.08 (d, *J* = 8.3 Hz, 1H), 7.85 (dd, *J* = 8.7, 4.2 Hz, 1H), 2.67 (q, *J* = 7.5 Hz, 2H), 1.16 (t, *J* = 7.5 Hz, 3H). (Figure S37)

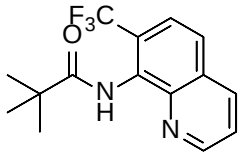
^{13}C NMR (100 MHz, DMSO-d_6) δ 173.6, 150.0, 139.2, 138.2, 132.9, 127.3, 124.3, 124.0, 122.7 (q, *J* = 308.9 Hz), 117.8, 114.5, 30.4, 9.9. (Figure S38)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.68. (Figure S39)

HRMS: (EI) calcd for $C_{13}H_{11}F_3N_2O$ $[M+H]^+$: 269.0902. Found: 269.0891. Anal. calcd for $C_{13}H_{11}F_3N_2O$: C, 58.21; H, 4.13; F, 21.25; N, 10.44; Found: C, 58.24; H, 4.15; F, 21.22; N, 10.47.

FT-IR (KBr disc): 3343, 2994, 1709, 1522, 1393, 1318, 1112 cm^{-1}.

N-(7-(trifluoromethyl)quinolin-8-yl)pivalamide (**2n**)



white solid (260.74 mg, 88%); m.p: 89.7-91.4 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.38 (s, 1H), 9.09 (d, *J* = 4.0 Hz, 1H), 8.72 (d, *J* = 8.2 Hz, 1H), 8.53 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 8.2 Hz, 1H), 7.87 (dd, *J* = 8.6, 4.2 Hz, 1H), 1.36 (s, 9H). (Figure S40)

^{13}C NMR (100 MHz, DMSO-d_6) δ 177.1, 150.3, 138.5, 138.1, 133.1, 127.3, 127.3,

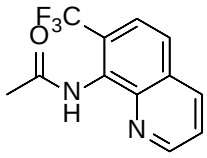
124.5, 123.9, 121.0 (q, *J* = 339.2 Hz), 113.7, 40.5, 27.6. (Figure S41)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.55. (Figure S42)

HRMS: (EI) calcd for $C_{15}H_{15}F_3N_2O$ $[M+H]^+$: 297.1215. Found: 297.1204. Anal. calcd for $C_{15}H_{15}F_3N_2O$: C, 60.81; H, 5.10; F, 19.24; N, 9.45; Found: C, 60.84; H, 5.13; F, 19.27; N, 9.42.

FT-IR (KBr disc): 3370, 3346, 1673, 1525, 1318, 1098 cm^{-1}.

N-(7-(trifluoromethyl)quinolin-8-yl)acetamide (**2o**)



white solid (218.62 mg, 86%); m.p: 73.5-74.3 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.40 (s, 1H), 9.08 (d, *J* = 3.4 Hz, 1H), 8.73 (d, *J* = 8.2 Hz, 1H), 8.51 (d, *J* = 8.0 Hz, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.85 (dd, *J* = 8.6, 4.0 Hz, 1H), 2.35 (s, 3H). (Figure S43)

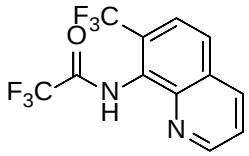
^{13}C NMR (100 MHz, DMSO-d_6) δ 170.1, 150.0, 139.3, 138.2, 132.8, 127.2, 124.3 (q, *J* = 196.7 Hz), 124.3, 124.0, 117.9, 114.6, 25.1. (Figure S44)

^{19}F NMR (376 MHz, DMSO-d_6) δ 18.51. (Figure S45)

HRMS: (EI) calcd for $C_{12}H_9F_3N_2O$ $[M+H]^+$: 255.0746. Found: 255.0752. Anal. calcd for $C_{12}H_9F_3N_2O$: C, 56.70; H, 3.57; F, 22.42; N, 11.02; Found: C, 56.73; H, 3.59; F, 22.41; N, 11.05.

FT-IR (KBr disc): 3358, 3092, 1725, 1523, 1374, 1317, 1102 cm^{-1}.

N-(7-(trifluoromethyl)quinolin-8-yl)trifluoroacetamide (**2p**)



white solid (258.87 mg, 84%); m.p: 91.5-93.3 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ11.16 (s, 1H), 9.15 (d, *J* = 3.4 Hz, 1H), 8.58 (d, *J* = 8.2 Hz, 1H), 8.52 (d, *J* = 8.0 Hz, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.91 (dd, *J* = 8.5, 4.0 Hz, 1H). (Figure S46)

^{13}C NMR (100 MHz, DMSO-d_6) δ155.1 (d, *J* = 37.3 Hz), 151.2, 139.0, 136.1, 133.1,

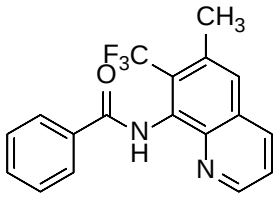
126.9, 126.8, 124.2 (q, *J* = 178.6 Hz), 124.1, 121.3, 121.2 (q, *J* = 279.7 Hz), 114.8. (Figure S47)

^{19}F NMR (376 MHz, DMSO-d_6) δ 14.53, -2.03. (Figure S48)

HRMS: (EI) calcd for $C_{12}H_6F_6N_2O$ $[M+H]^+$: 309.0463. Found: 309.0454. Anal. calcd for $C_{12}H_6F_6N_2O$: C, 46.77; H, 1.96; F, 36.99; N, 9.09; Found: C, 46.75; H, 1.99; F, 36.97; N, 9.06.

FT-IR (KBr disc): 3324, 3085, 1694, 1502, 1374, 1301, 1112 cm^{-1}.

N-(6-methyl-7-(trifluoromethyl)quinolin-8-yl)benzamide (**2q**)



white solid (214.70 mg, 65%); m.p: 131.5-133.3 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.80 (s, 1H), 9.00 (d, *J* = 3.8 Hz, 1H), 8.68 (s, 1H), 8.55 (d, *J* = 8.8 Hz, 1H), 8.04 (d, *J* = 7.2 Hz, 2H), 7.80 (dd, *J* = 8.8, 4.2 Hz, 1H), 7.74 – 7.61 (m, 3H), 2.68 (q, *J* = 3.8 Hz, 3H). (Figure S49)

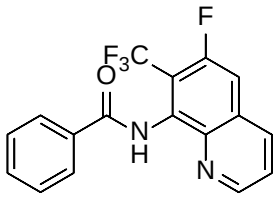
^{13}C NMR (100 MHz, DMSO-d_6) δ 170.0, 154.0, 143.5, 142.1 (d, *J* = 30.6 Hz), 139.1, 138.0, 138.0, 137.7, 134.3, 132.3, 129.9, 129.4, 126.6 (q, *J* = 363.7 Hz), 120.9, 27.4 (d, *J* = 4.4 Hz). (Figure S50)

^{19}F NMR (376 MHz, DMSO-d_6) δ 30.96. (Figure S51)

HRMS: (EI) calcd for $C_{18}H_{13}F_3N_2O$ $[M+H]^+$: 331.1059. Found: 331.1067. Anal. calcd for $C_{18}H_{13}F_3N_2O$: C, 65.45; H, 3.97; F, 17.26; N, 8.48; Found: C, 65.48; H, 3.99; F, 17.23; N, 8.45.

FT-IR (KBr disc): 3338, 1672, 1529, 1283, 1140 cm^{-1}.

N-(6-fluoro-7-(trifluoromethyl)quinolin-8-yl)benzamide (**2r**)



white solid (191.58 mg, 58%); m.p: 136.7-138.9 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.95 (s, 1H), 9.06 (d, *J* = 4.1 Hz, 1H), 8.63 (d, *J* =

14.8 Hz, 1H), 8.59 (d, *J* = 9.2 Hz, 1H), 8.05 (d, *J* = 7.4 Hz, 2H), 7.91 (dd, *J* = 8.8, 4.2 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.65 (t, *J* = 7.4 Hz, 2H). (Figure S52)

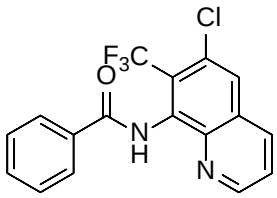
^{13}C NMR (100 MHz, DMSO-d_6) δ165.6, 149.5, 149.5, 148.7, 140.7, 140.5, 135.6, 135.1, 133.8, 133.4, 133.3, 129.6, 128.8 (q, *J* = 256.7 Hz), 127.8, 125.6,105.9 (d, *J* = 33.6 Hz). (Figure S53)

^{19}F NMR (376 MHz, DMSO-d_6) δ 23.83 (d, *J* = 31.2 Hz), -29.88 (q, *J* = 31.2 Hz). (Figure S54)

HRMS: (EI) calcd for $C_{17}H_{10}F_4N_2O$ $[M+H]^+$: 335.0808. Found: 335.0899. Anal. calcd for $C_{17}H_{10}F_4N_2O$: C, 61.08; H, 3.02; F, 22.73; N, 8.38; Found: C, 61.09; H, 3.05; F, 22.74; N, 8.36.

FT-IR (KBr disc): 3326, 1689, 1525, 1293, 1144, 1114, 1024 cm^{-1}.

N-(6-chloro-7-(trifluoromethyl)quinolin-8-yl)benzamide (**2s**)



white solid (175.36 mg, 50%); m.p: 112.7-115.3 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.86 (s, 1H), 9.07 (dd, *J* = 4.1, 1.2 Hz, 1H), 8.83 (s, 1H), 8.63 (dt, *J* = 8.9, 1.6 Hz, 1H), 8.04 (s, 1H), 8.02 (d, *J* = 1.5 Hz, 1H), 7.89 (dd, *J* = 8.9, 4.2 Hz, 1H), 7.73 – 7.69 (m, 1H), 7.67 (s, 1H), 7.65 (s, 1H). (Figure S55)

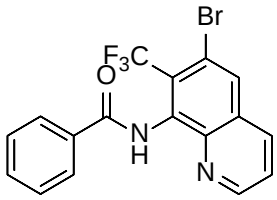
^{13}C NMR (100 MHz, DMSO-d_6) δ 165.5, 150.3, 138.9, 136.9, 133.9, 133.5, 133.5, 133.3, 129.6, 128.7 (q, *J* = 310.0 Hz), 127.7, 125.9, 125.3, 117.7, 115.4. (Figure S56)

^{19}F NMR (376 MHz, DMSO-d_6) δ 25.00. (Figure S57)

HRMS: (EI) calcd for $C_{17}H_{10}ClF_3N_2O$ $[M+H]^+$: 351.0513. Found: 351.0503. Anal. calcd for $C_{17}H_{10}ClF_3N_2O$: C, 58.22; H, 2.87; Cl, 10.11; F, 16.25; N, 7.99; Found: C, 58.24; H, 2.89; Cl, 10.14; F, 16.27; N, 7.96.

FT-IR (KBr disc): 3324, 1685, 1530, 1315, 1035 cm^{-1}.

N-(6-bromo-7-(trifluoromethyl)quinolin-8-yl)benzamide (**2t**)



white solid (169.92 mg, 50%); m.p: 123.7-124.9 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.89 (s, 1H), 9.13 – 9.11 (m, 1H), 9.10 (s, 1H), 8.69 – 8.64 (m, 1H), 8.07 – 8.04 (m, 2H), 7.90 (dd, J = 8.9, 4.2 Hz, 1H), 7.72 (t, J = 7.3 Hz, 1H), 7.66 (d, J = 14.7 Hz, 2H). (Figure S58)

^{13}C NMR (100 MHz, DMSO-d_6) δ 165.6, 150.7, 150.4, 138.7, 137.3, 134.0, 133.6, 136.5 133.3, 129.7, 127.8, 126.4, 125.3, 123.5, 121.8, 121.2, 119.7. (Figure S59)

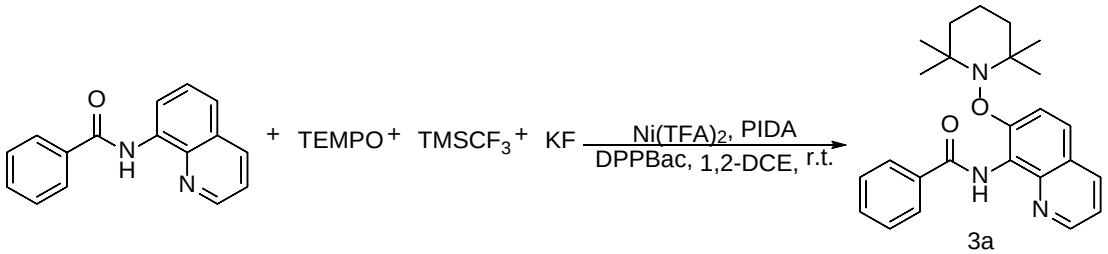
^{19}F NMR (376 MHz, DMSO-d_6) δ 26.23. (Figure S60)

HRMS: (EI) calcd for $C_{17}H_{10}BrF_3N_2O$ $[M+H]^+$: 395.0008. Found: 395.0014. Anal. calcd for $C_{17}H_{10}BrF_3N_2O$: C, 51.67; H, 2.55; Br, 20.22; F, 14.42; N, 7.09; Found: C, 51.65; H, 2.57; Br, 20.19; F, 14.44; N, 7.06.

FT-IR (KBr disc): 3323, 1687, 1535, 1321, 1117 cm^{-1}.

4. Radical scavenging experiment

Synthesis of N-(7-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)quinolin-8-yl)benzamide (3a).

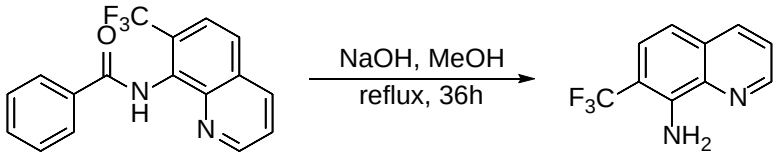


A 15 mL screw-cap vial charged with N-(quinolin-8-yl)benzamide (248.3 mg, 1 mmol), $TMSCF_3$ (426.59mg, 3 mmol), KF (174.29 mg, 3 mmol), PIDA (966.30 mg, 3 mmol), $Ni(TFA)_2$ (25.27 mg, 0.1 mmol), DPPBac (91.85 mg, 0.3 mmol), 2,2,6,6-tetramethylpiperidine-1-oxyl (468.75mg, 3 mmol) and 1,2-DCE (5 mL), the mixture was stirred at room temperature for 18 h. After completion of the reaction, the solution was extracted with dichloromethane (3×20 mL). Organic layers were combined and dried over Na_2SO_4, filtered and concentrated under reduced pressure.

The crude material was purified by silica gel column chromatography to give a white solid (76.6 mg, 19%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.52 (s, 1H), 8.85 (d, J = 3.9 Hz, 1H), 8.67 (d, J = 8.2 Hz, 1H), 8.39 (d, J = 8.6 Hz, 1H), 8.05 (d, J = 8.9 Hz, 2H), 7.80 – 7.56 (m, 5H), 1.58 (p, J = 6.1 Hz, 2H), 1.31 (s, 6H), 1.06 (s, 6H). (Figure S61)

5. Deprotection experiment.

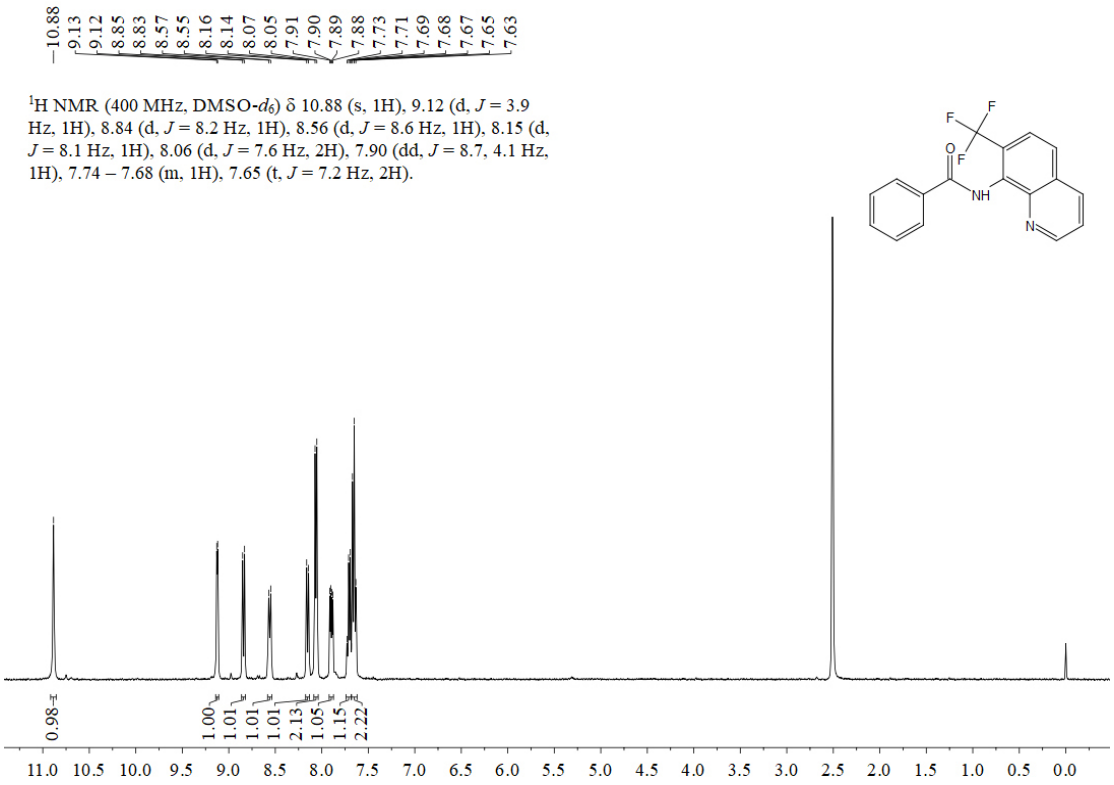


2a

A 15 mL screw-cap vial charged with N-(7-(trifluoromethyl)quinolin-8-yl)benzamide (94.9 mg, 0.3 mmol) and 6 mol/L NaOH in MeOH (9 mL), the mixture was stirred at 120 ºC for 36 h. After completion of the reaction, the solution was cooled to room temperature, and 30 mL MeOH was added. The mixture was concentration in vacuum and extracted with ethyl acetate (3×20 mL). Organic layers were combined and dried over Na_2SO_4, filtered and concentrated under reduced pressure to afforded 7-(trifluoromethyl)quinolin-8-amine (55.1 mg, 85%, m.p. 61-62 ºC[2]).

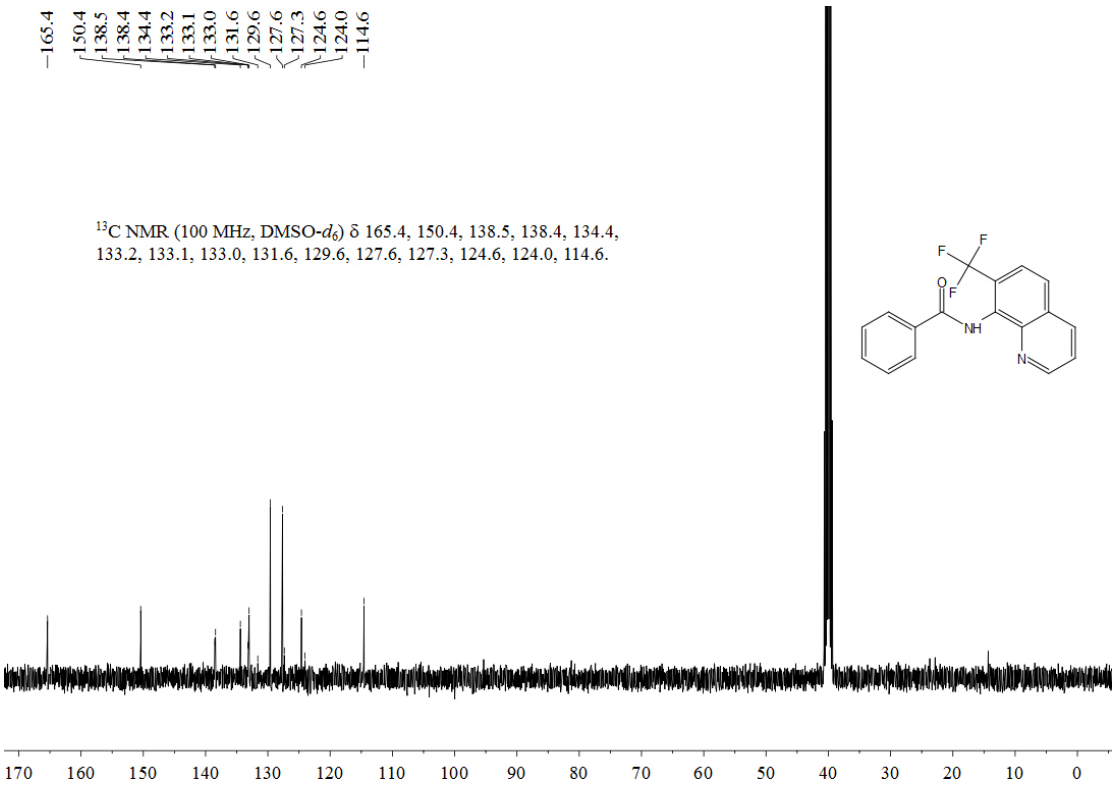
^{1}H NMR (400 MHz, Chloroform-d) δ 8.79 (dd, J = 1.2, 4.3 Hz, 1H), 8.06 (dd, J = 1.4, 8.3 Hz, 1H), 7.52 – 7.42 (m, 2H), 7.09 (d, J = 8.6 Hz, 1H), 5.78 (s, 2H). (Figure S62)

6. NMR spectra for target compounds.



^{1}H NMR (400 MHz, DMSO-d_6) δ 10.88 (s, 1H), 9.12 (d, J = 3.9 Hz, 1H), 8.84 (d, J = 8.2 Hz, 1H), 8.56 (d, J = 8.6 Hz, 1H), 8.15 (d, J = 8.1 Hz, 1H), 8.06 (d, J = 7.6 Hz, 2H), 7.90 (dd, J = 8.7, 4.1 Hz, 1H), 7.74 – 7.68 (m, 1H), 7.65 (t, J = 7.2 Hz, 2H).

Figure S1. ^{1}H NMR of N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2a**.



^{13}C NMR (100 MHz, DMSO-d_6) δ 165.4, 150.4, 138.5, 138.4, 134.4, 133.2, 133.1, 133.0, 131.6, 129.6, 127.6, 127.3, 124.6, 124.0, 114.6.

Figure S2. ^{13}C NMR of N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2a**.

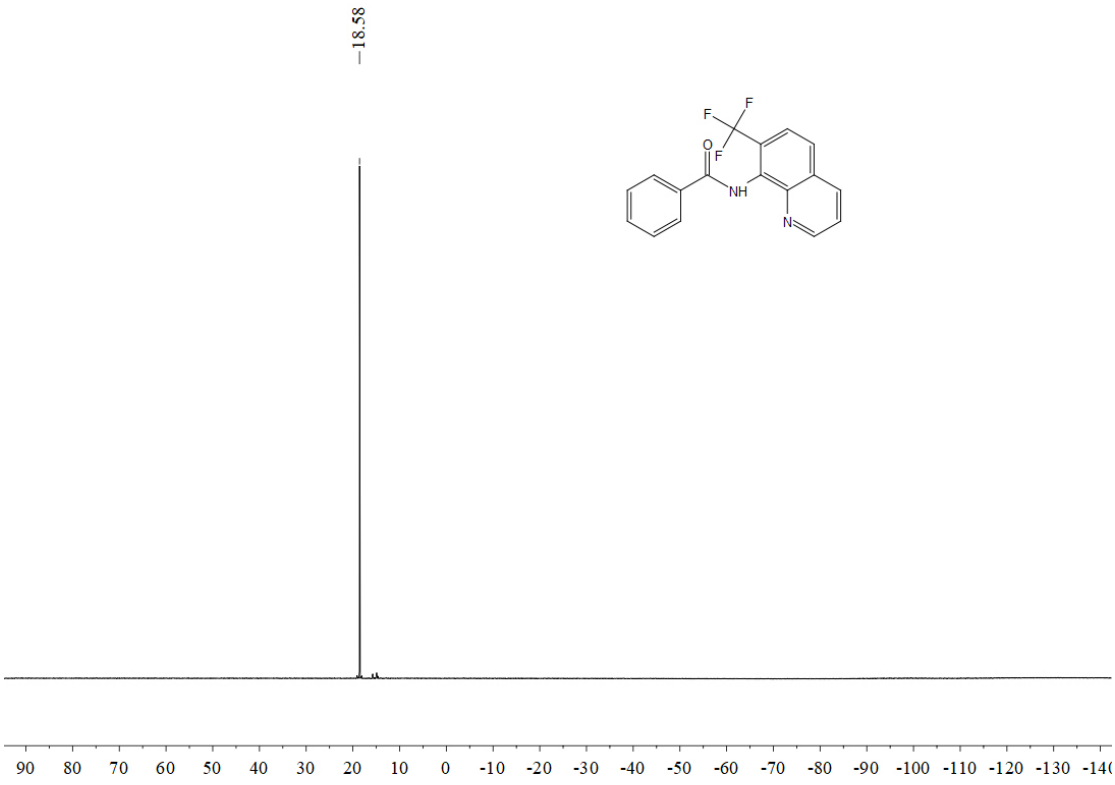
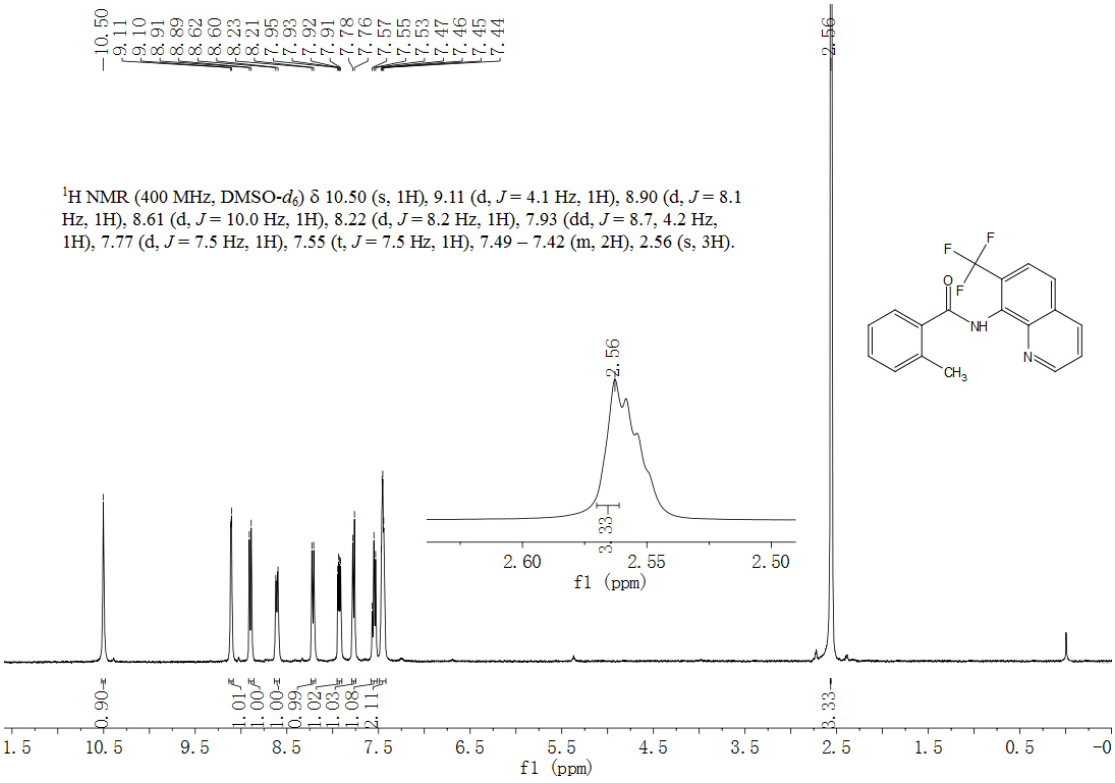
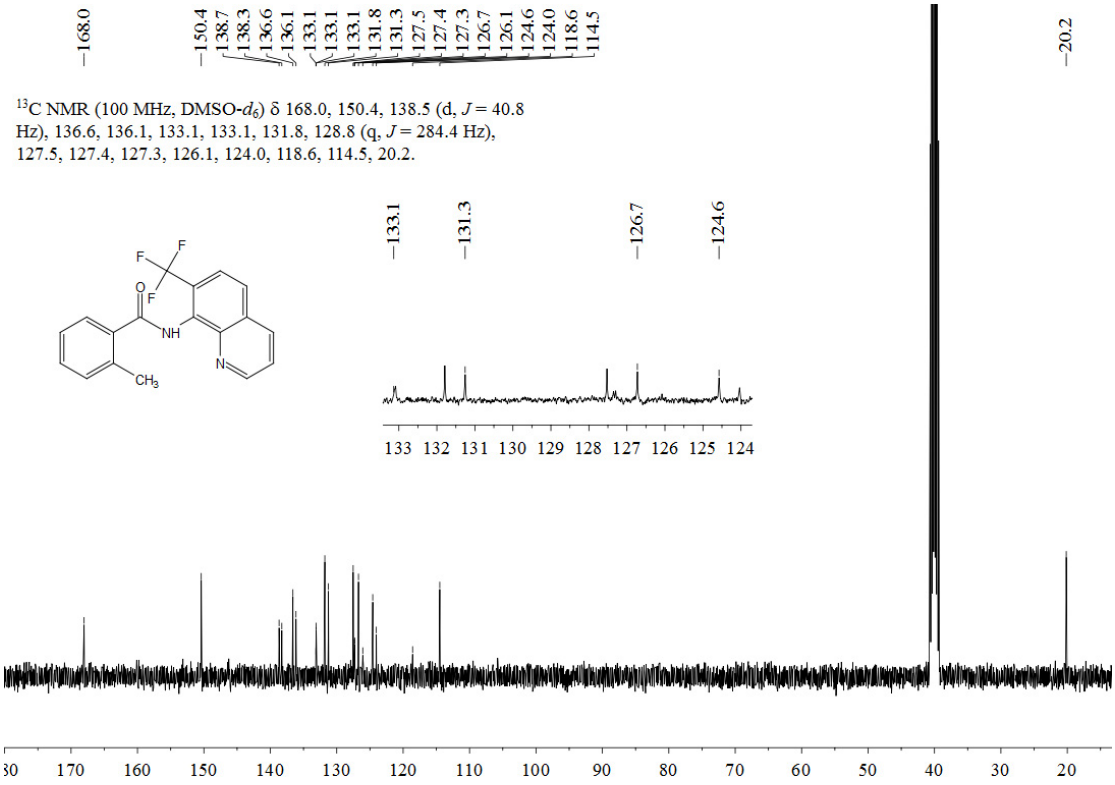


Figure S3. ^{19}F NMR of N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2a**.



^{1}H NMR (400 MHz, DMSO-d_6) δ 10.50 (s, 1H), 9.11 (d, J = 4.1 Hz, 1H), 8.90 (d, J = 8.1 Hz, 1H), 8.61 (d, J = 10.0 Hz, 1H), 8.22 (d, J = 8.2 Hz, 1H), 7.93 (dd, J = 8.7, 4.2 Hz, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.49 – 7.42 (m, 2H), 2.56 (s, 3H).

Figure S4. ^{1}H NMR of 2-methyl-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2b**.



^{13}C NMR (100 MHz, DMSO-d_6) δ 168.0, 150.4, 138.5 (d, J = 40.8 Hz), 136.6, 136.1, 133.1, 133.1, 131.8, 128.8 (q, J = 284.4 Hz), 127.5, 127.4, 127.3, 126.1, 124.0, 118.6, 114.5, 20.2.

Figure S5. ^{13}C NMR of 2-methyl-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2b**.

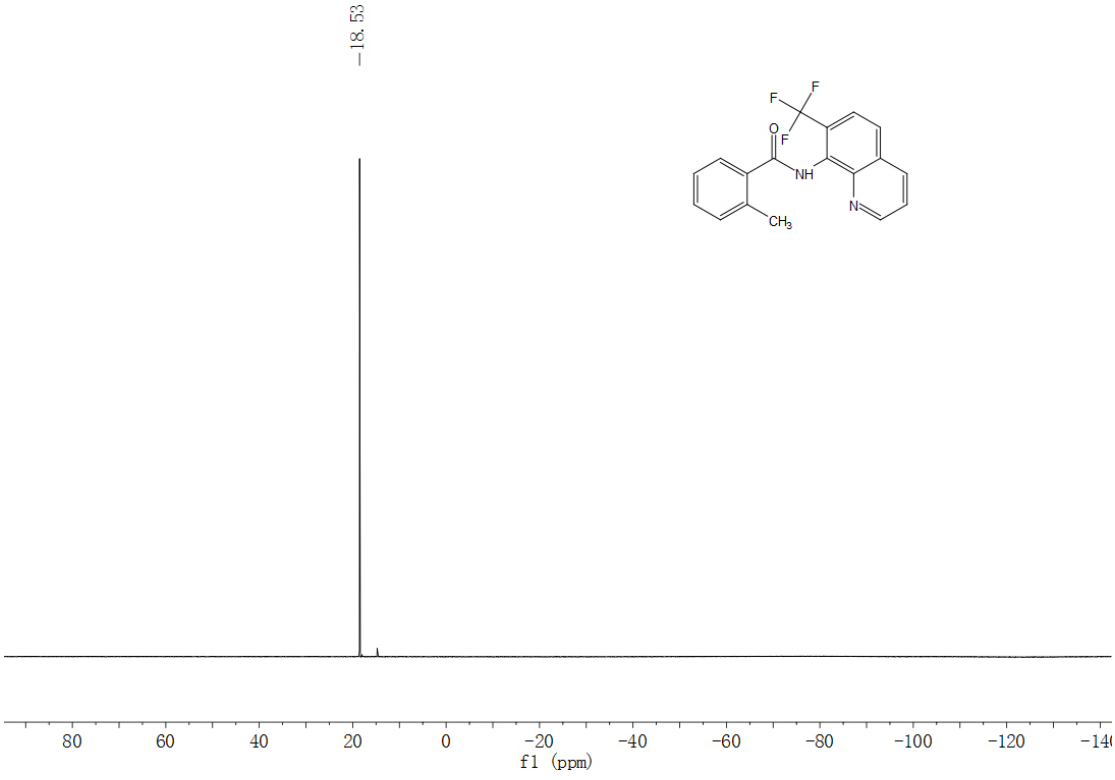


Figure S6. ^{19}F NMR of 2-methyl-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2b**.

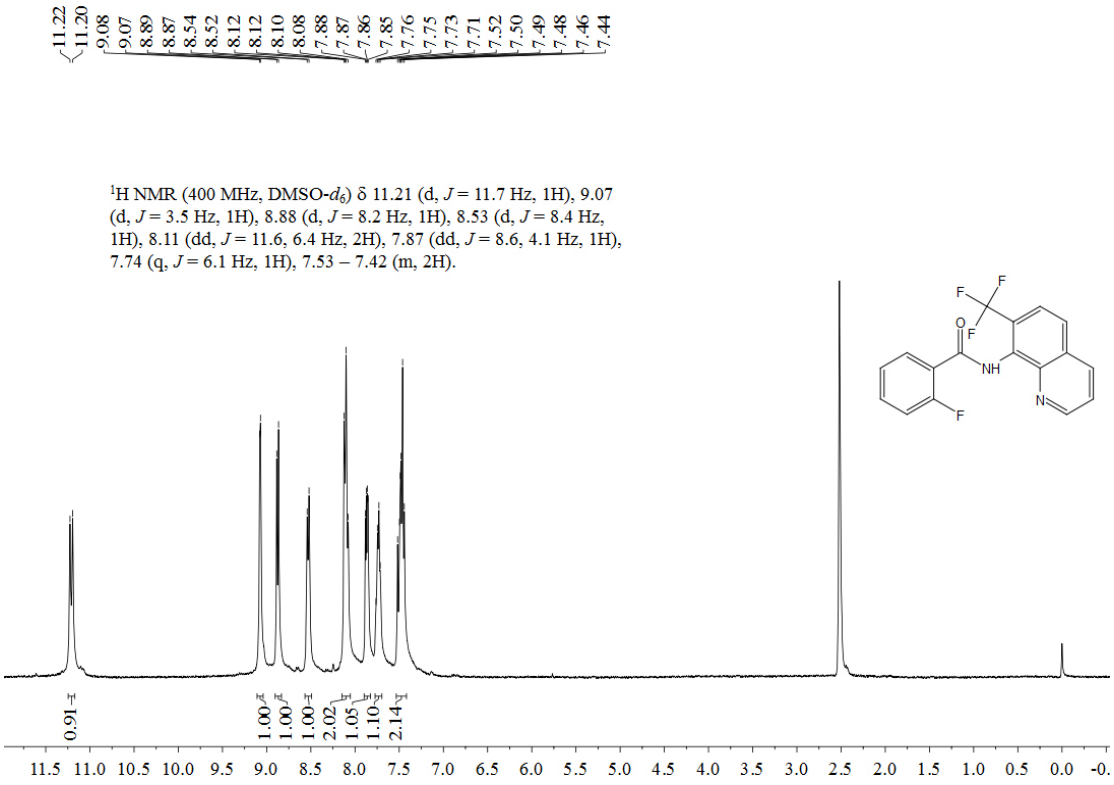


Figure S7. ^{1}H NMR of 2-fluoro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2c**.

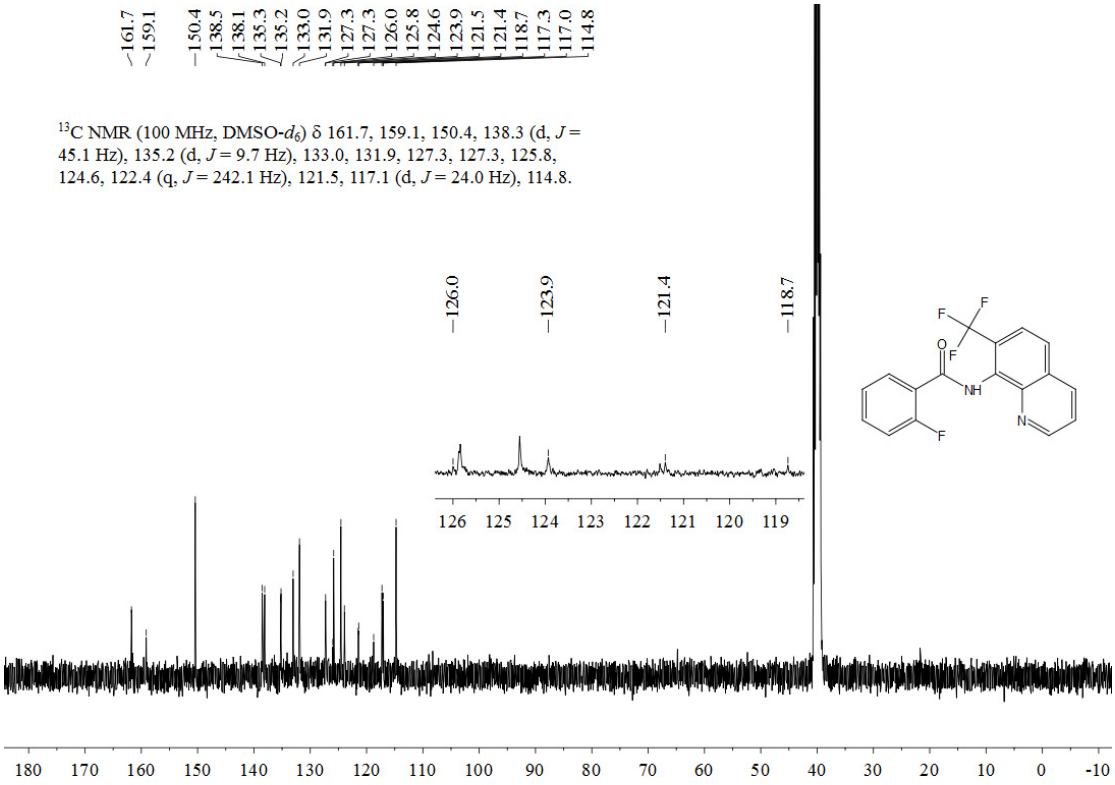
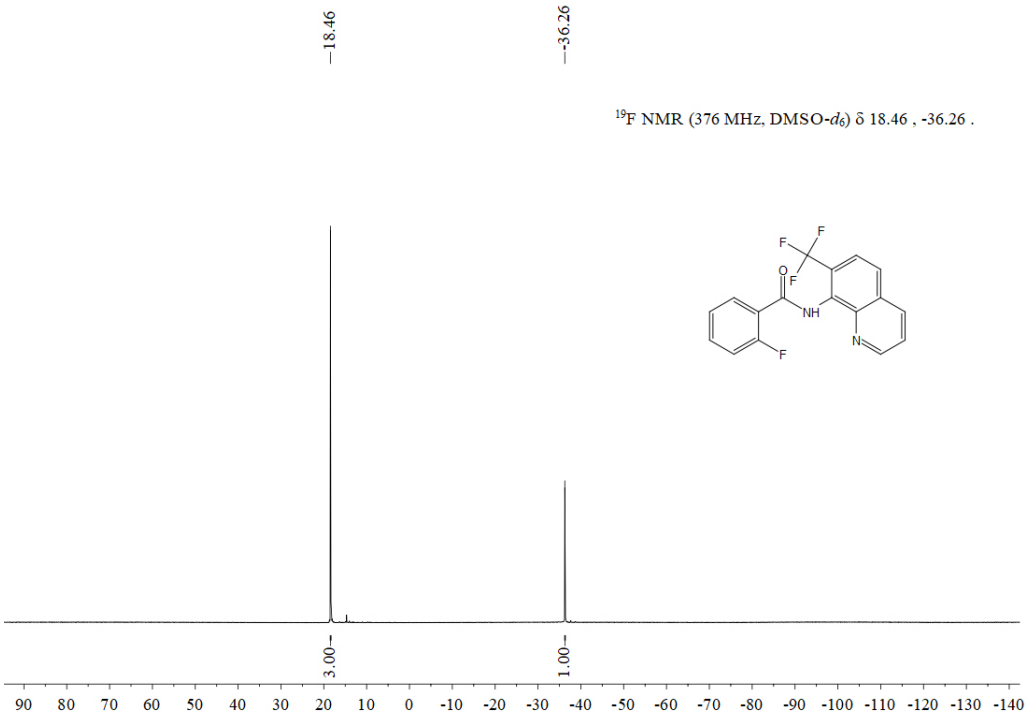
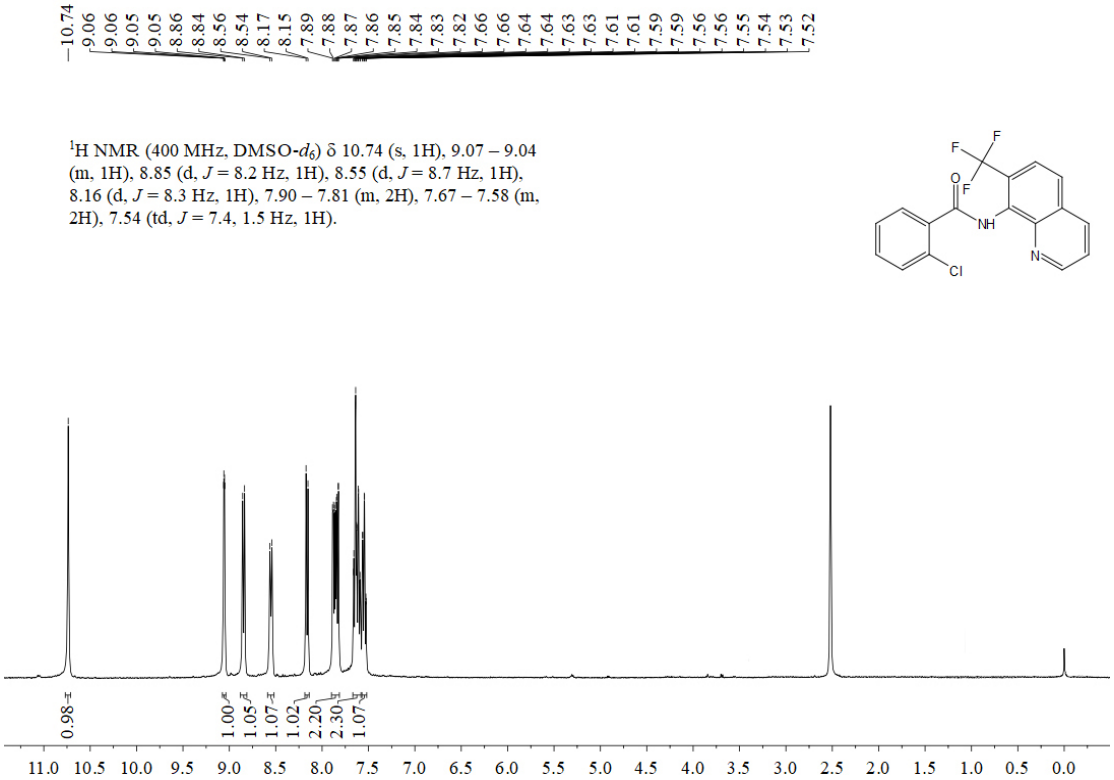


Figure S8. ^{13}C NMR of 2-fluoro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2c**.



^{19}F NMR (376 MHz, DMSO-d_6) δ 18.46 , -36.26 .

Figure S9. ^{19}F NMR of 2-fluoro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2c**.



^{1}H NMR (400 MHz, DMSO-d_6) δ 10.74 (s, 1H), 9.07 – 9.04 (m, 1H), 8.85 (d, J = 8.2 Hz, 1H), 8.55 (d, J = 8.7 Hz, 1H), 8.16 (d, J = 8.3 Hz, 1H), 7.90 – 7.81 (m, 2H), 7.67 – 7.58 (m, 2H), 7.54 (td, J = 7.4, 1.5 Hz, 1H).

Figure S10. ^{1}H NMR of 2-chloro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2d**.

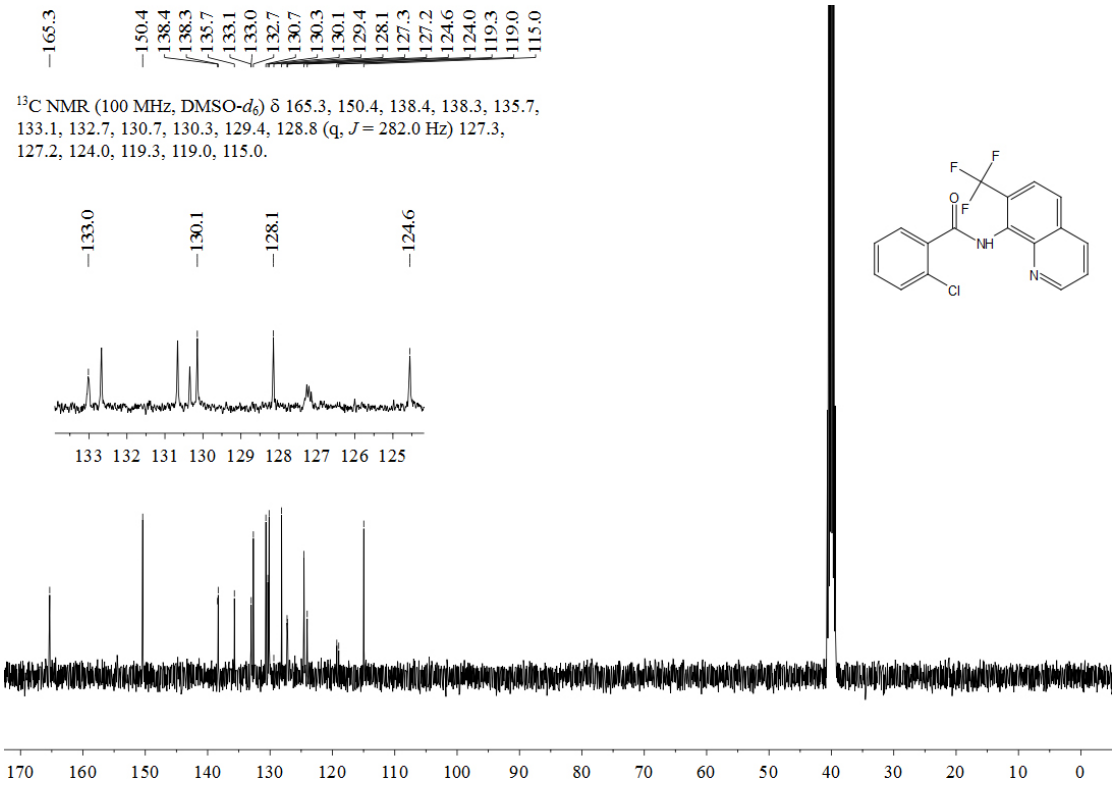


Figure S11. ^{13}C NMR of 2-chloro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2d**.

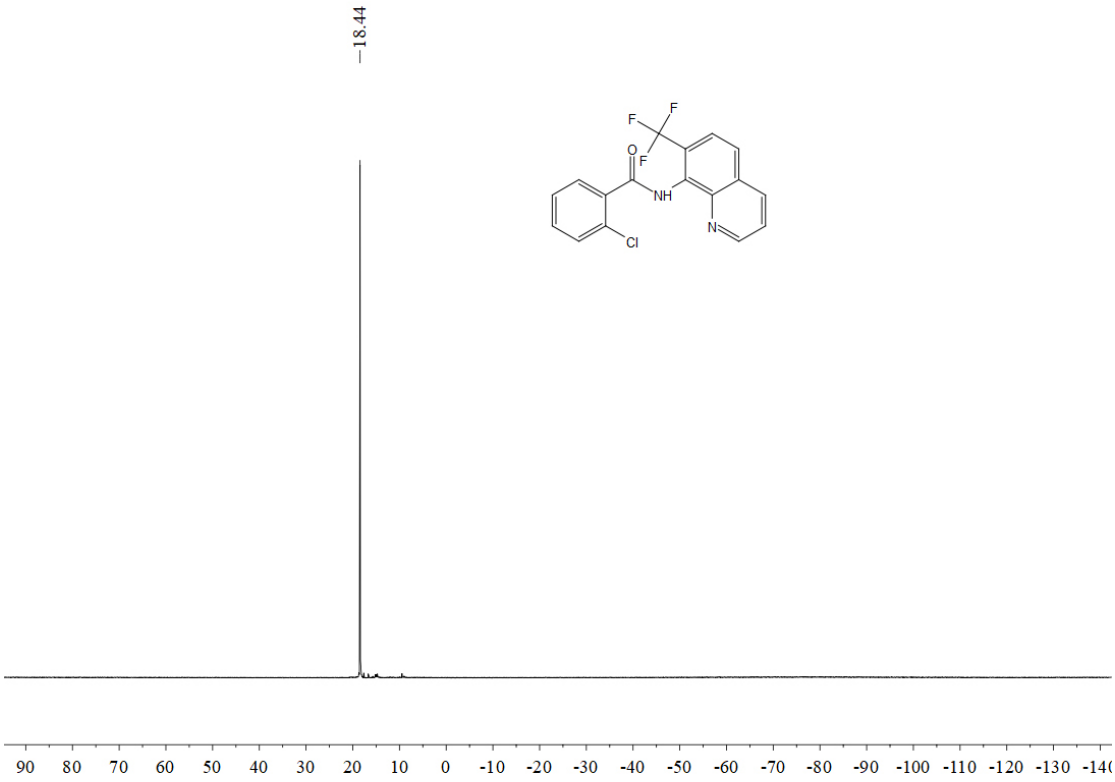


Figure S12. ^{19}F NMR of 2-chloro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2d**.

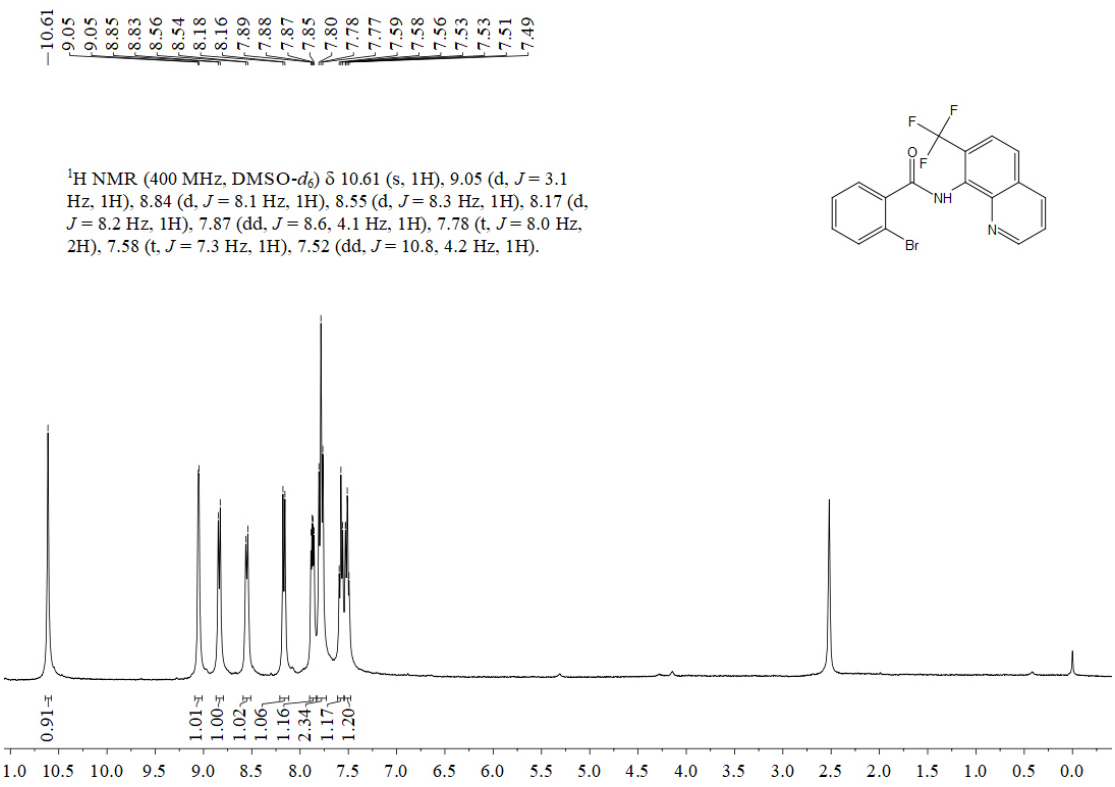


Figure S13. ^{1}H NMR of 2-bromo-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2e**.

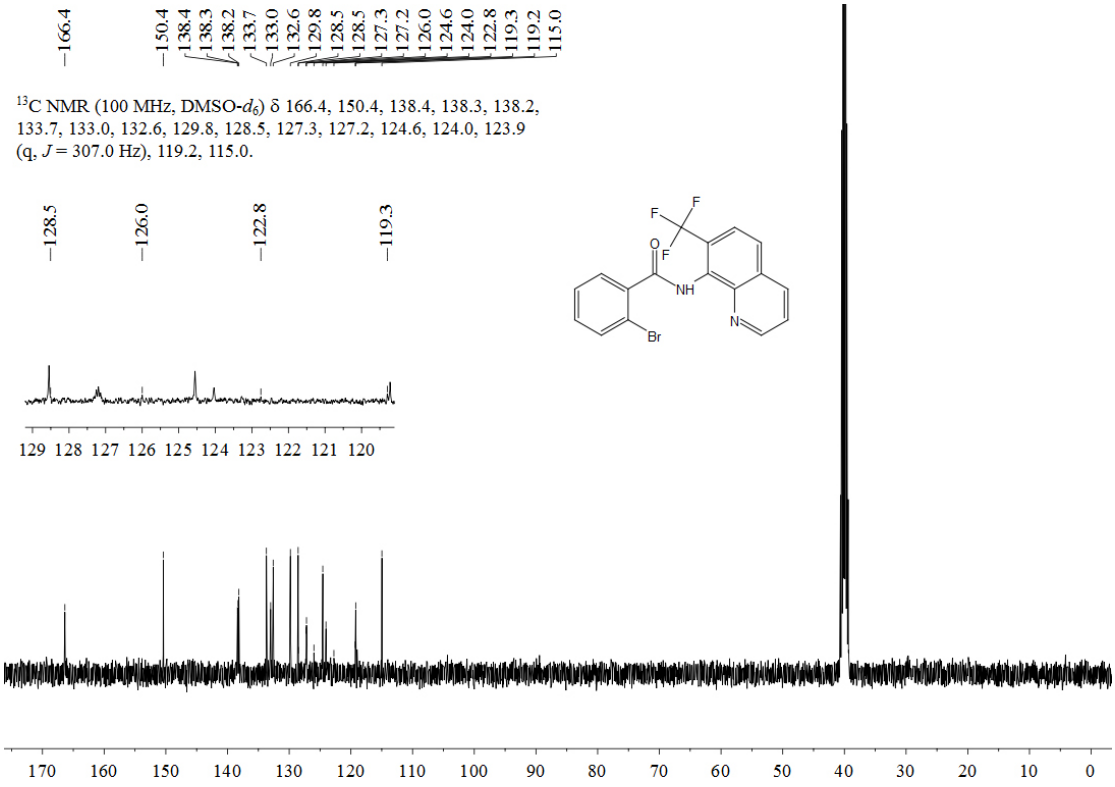


Figure S14. ^{13}C NMR of 2-bromo-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2e**.

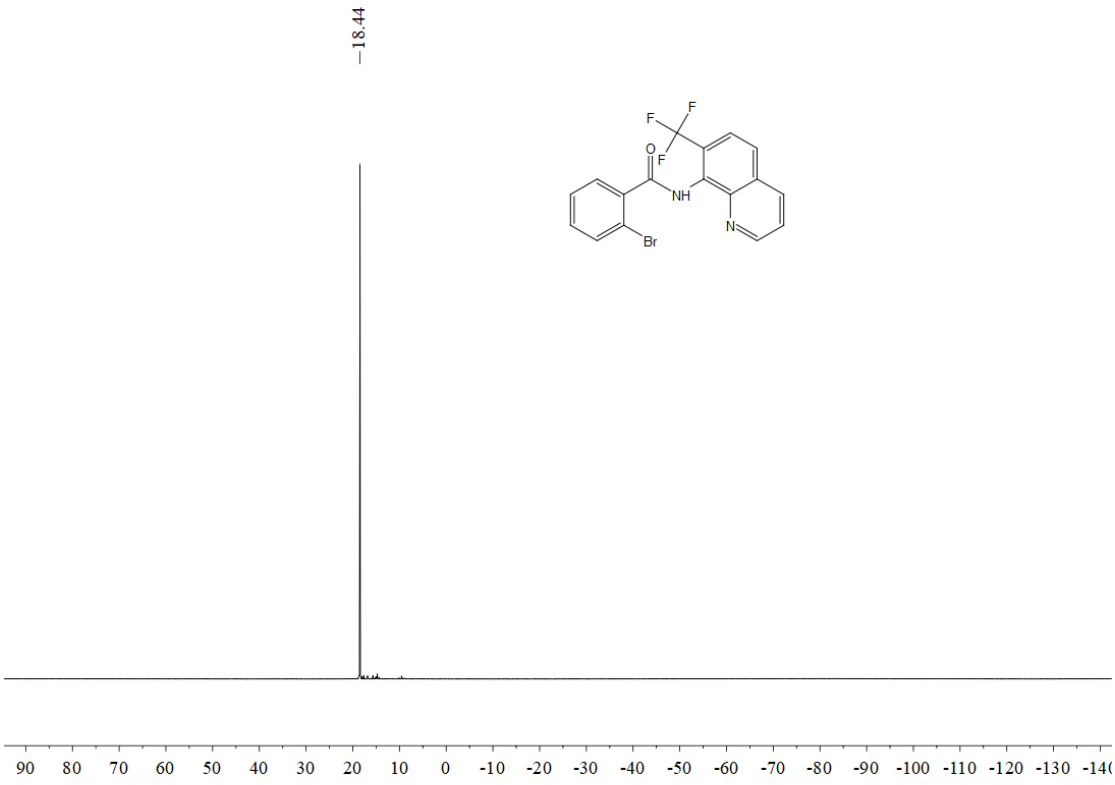


Figure S15. ^{19}F NMR of 2-bromo-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2e**.

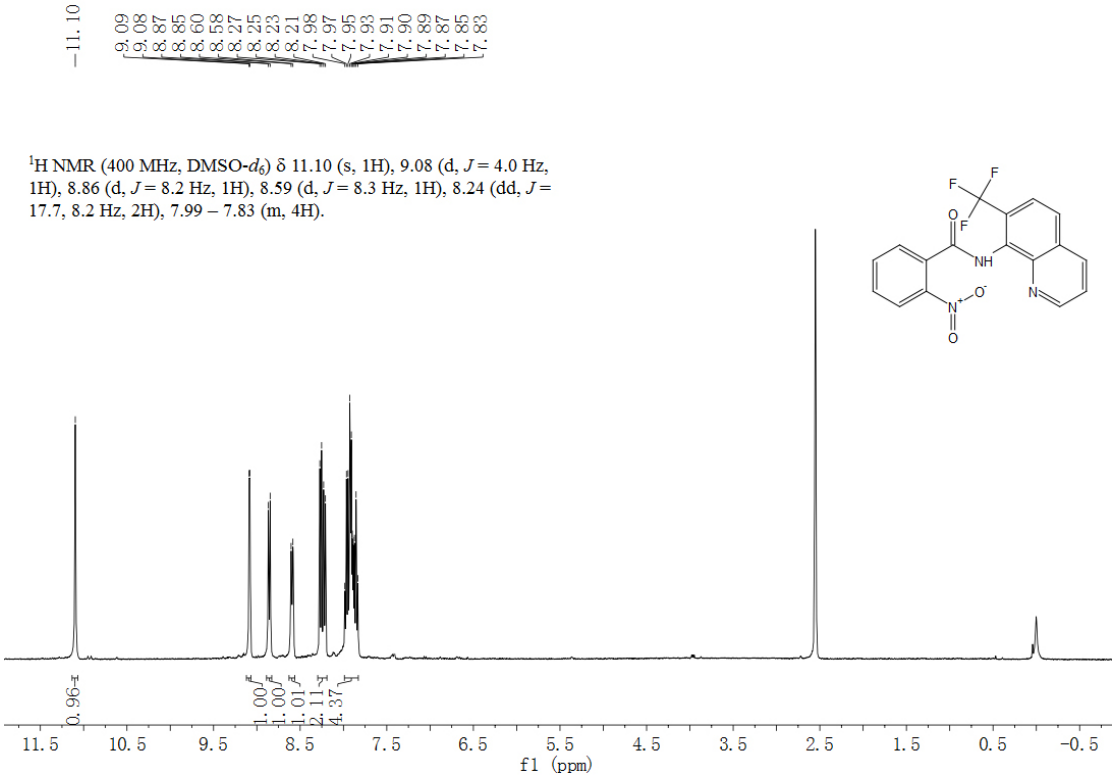
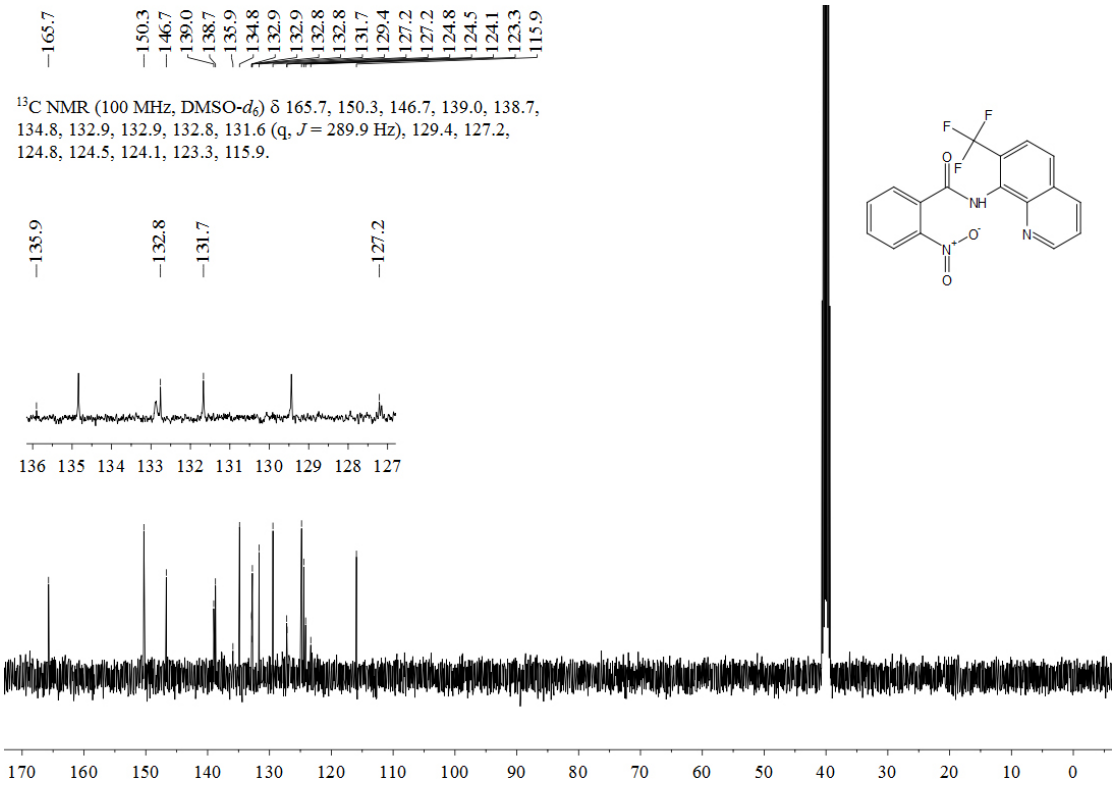


Figure S16. ^{1}H NMR of 2-nitro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2f**.



^{13}C NMR (100 MHz, DMSO-d_6) δ 165.7, 150.3, 146.7, 139.0, 138.7, 134.8, 132.9, 132.9, 132.8, 131.6 (q, J = 289.9 Hz), 129.4, 127.2, 124.8, 124.5, 124.1, 123.3, 115.9.

Figure S17. ^{13}C NMR of 2-nitro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2f**.

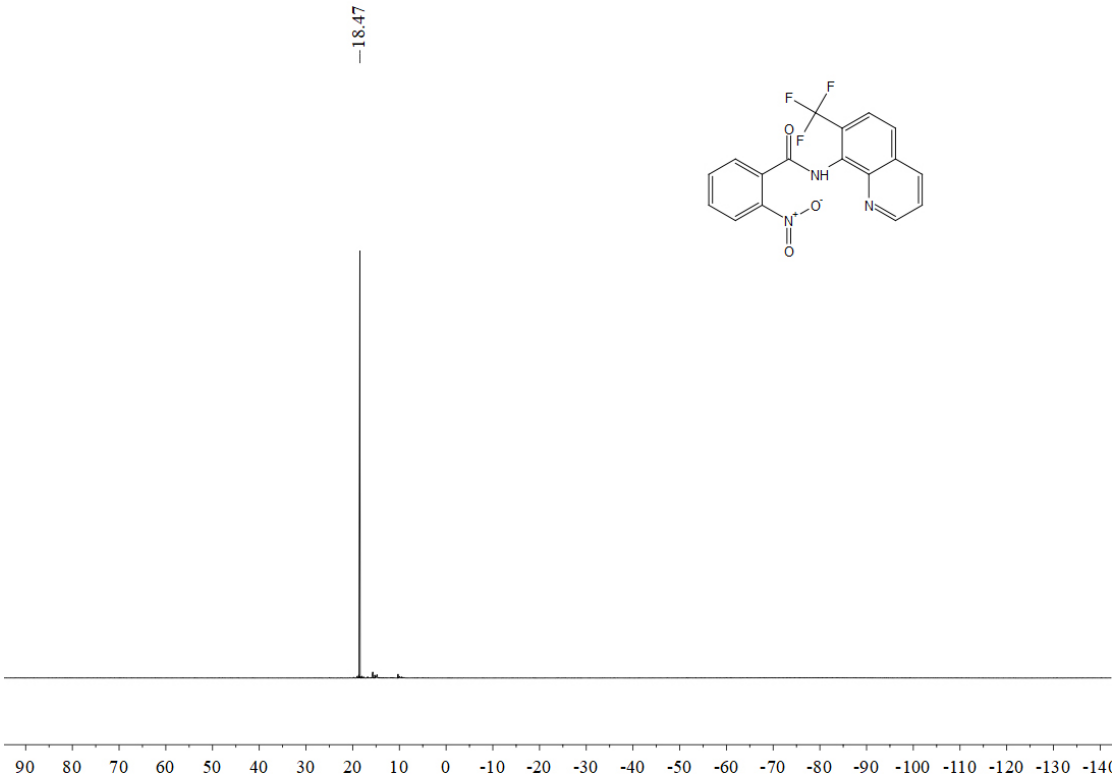


Figure S18. ^{19}F NMR of 2-nitro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2f**.

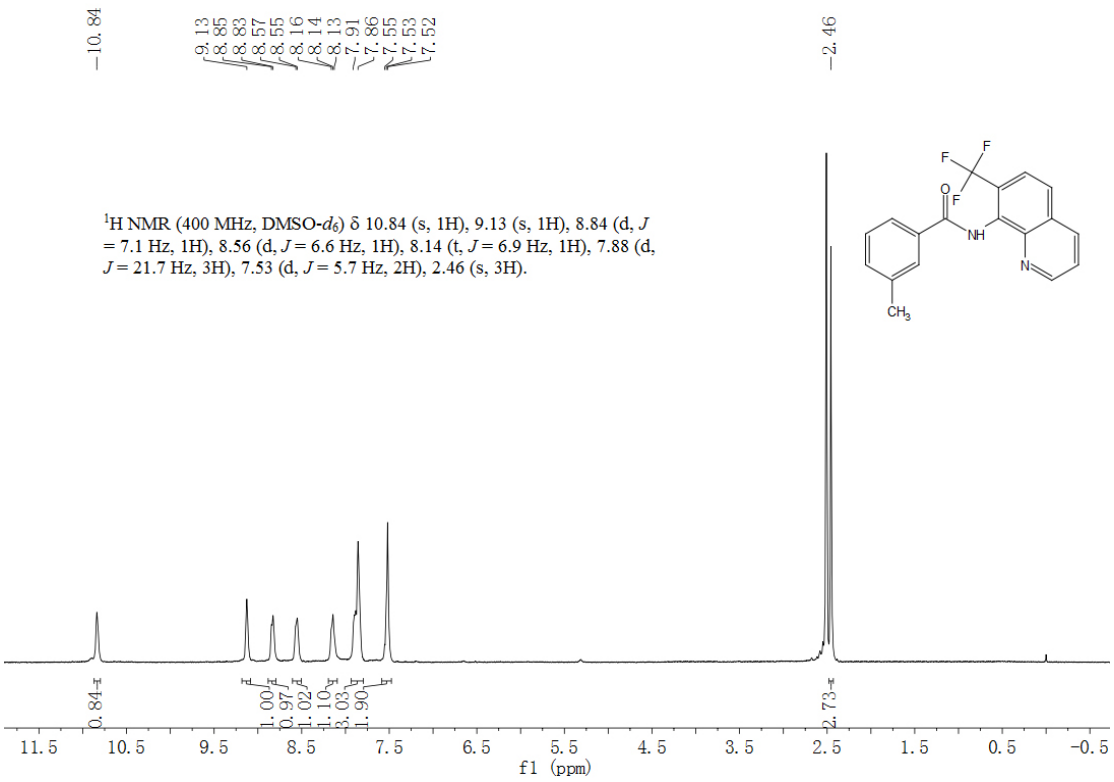


Figure S19. ^{1}H NMR of 3-methyl-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2g**.

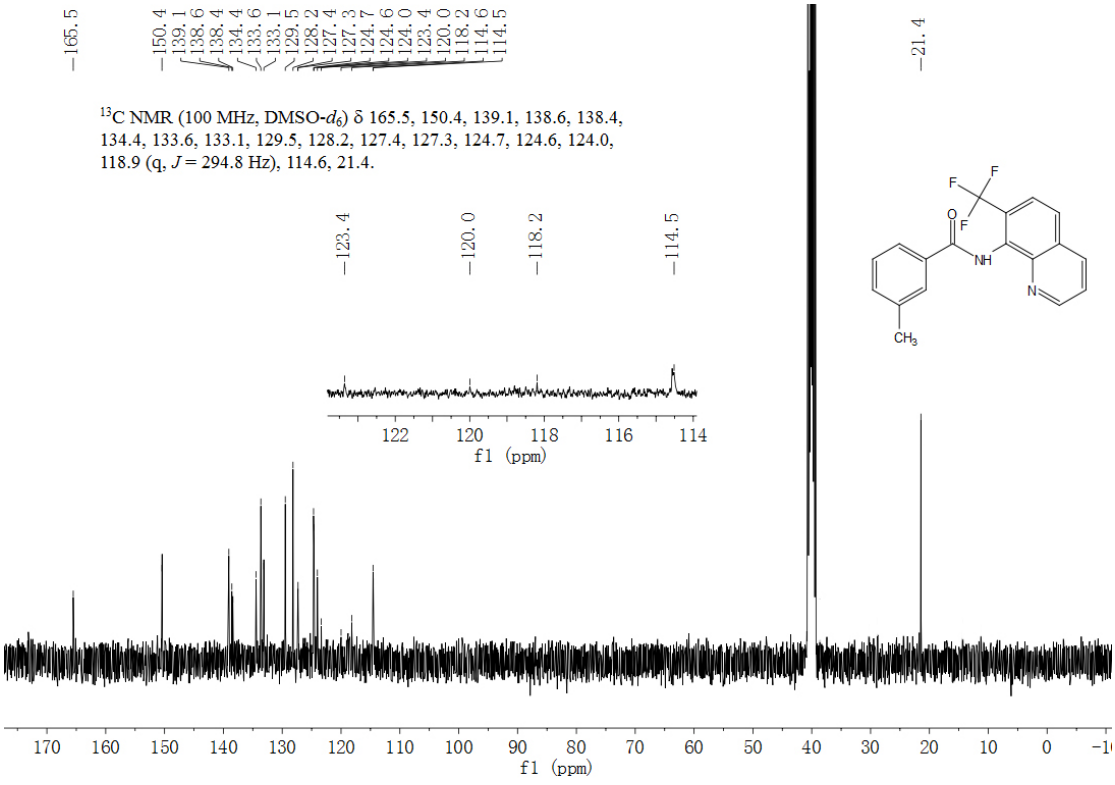


Figure S20. ^{13}C NMR of 3-methyl-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2g**.

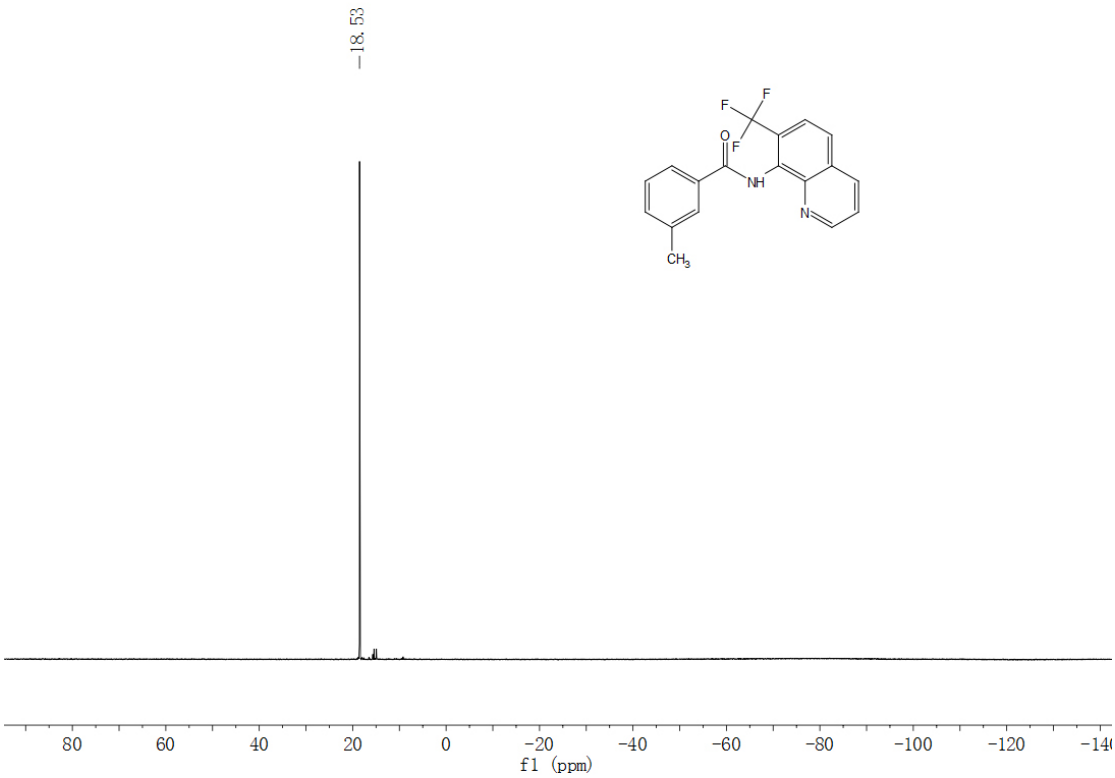


Figure S21. ^{19}F NMR of 3-methyl-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2g**.

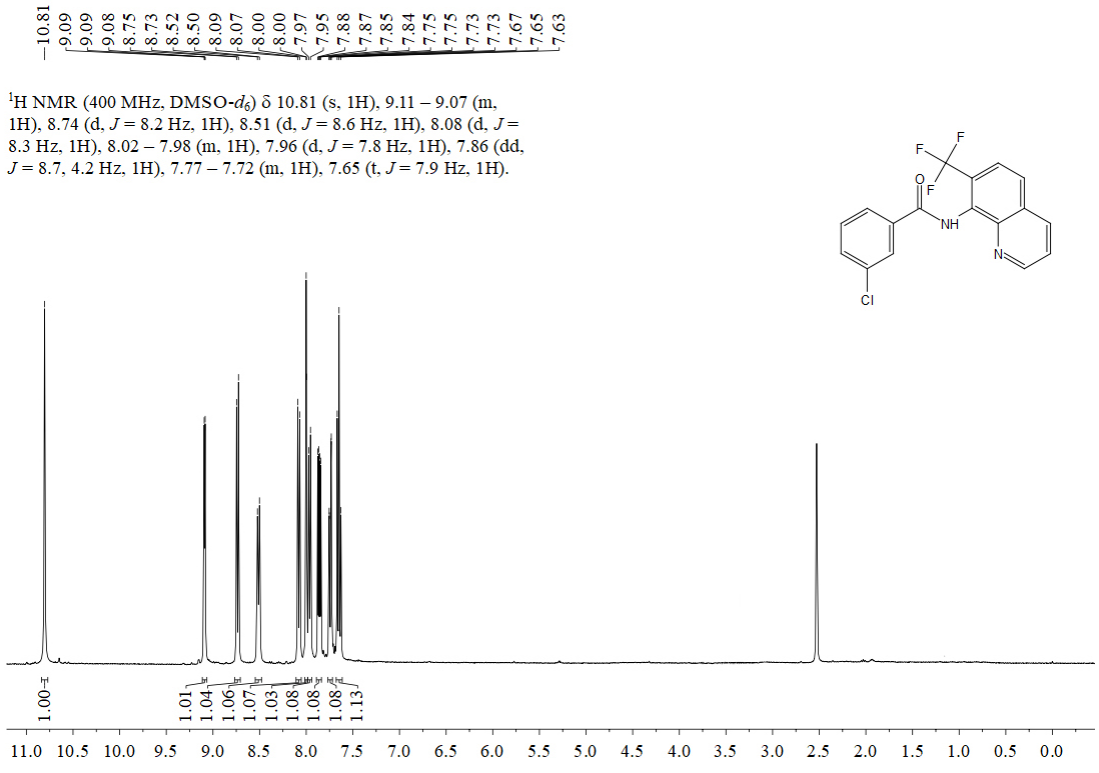


Figure S22. ^{1}H NMR of 3-chloro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2h**.

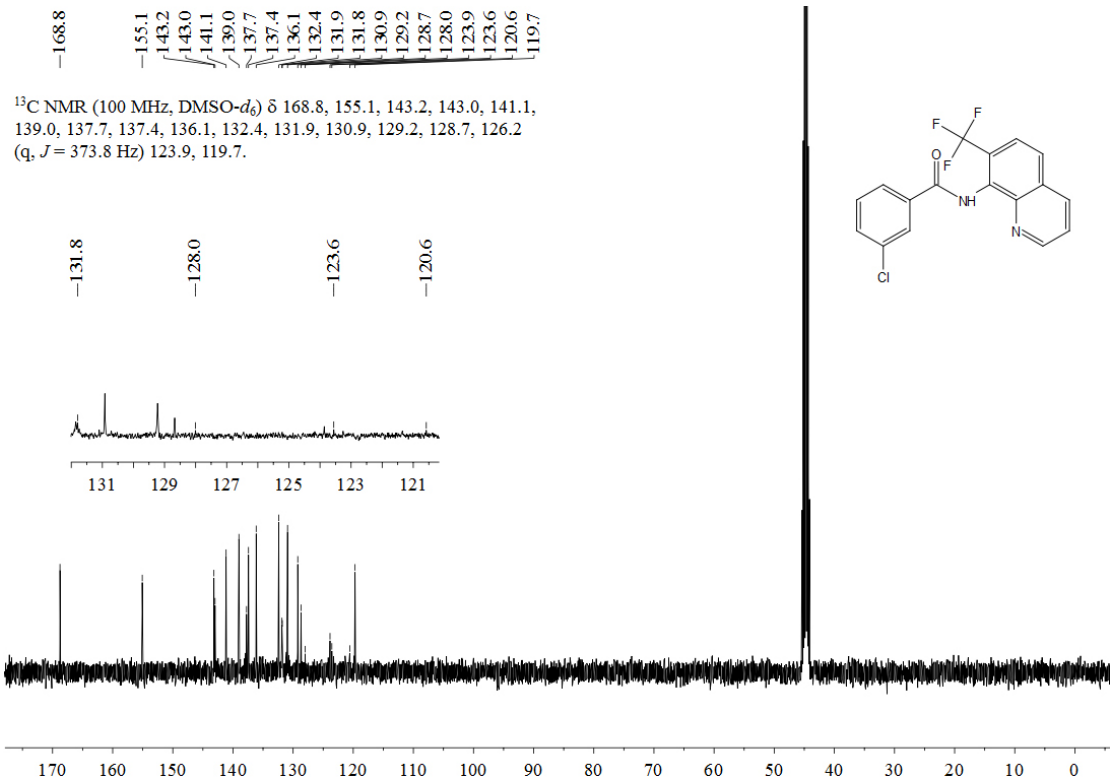


Figure S23. ^{13}C NMR of 3-chloro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2h**.

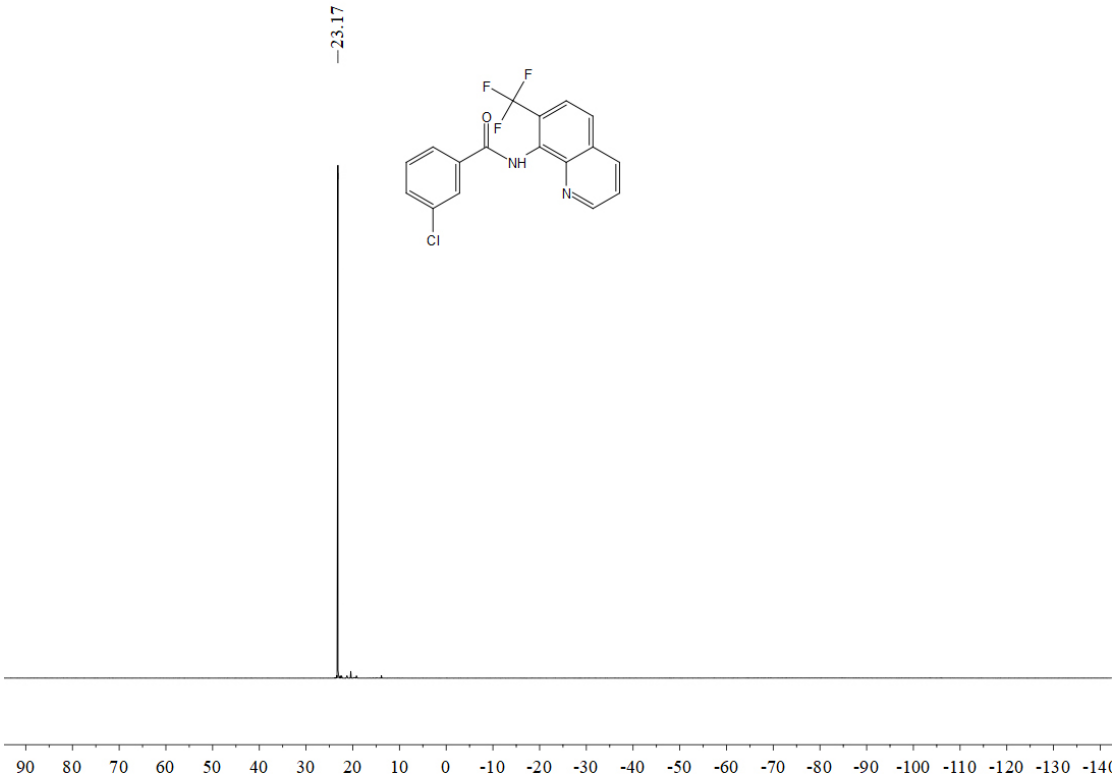


Figure S24. ^{19}F NMR of 3-chloro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2h**.

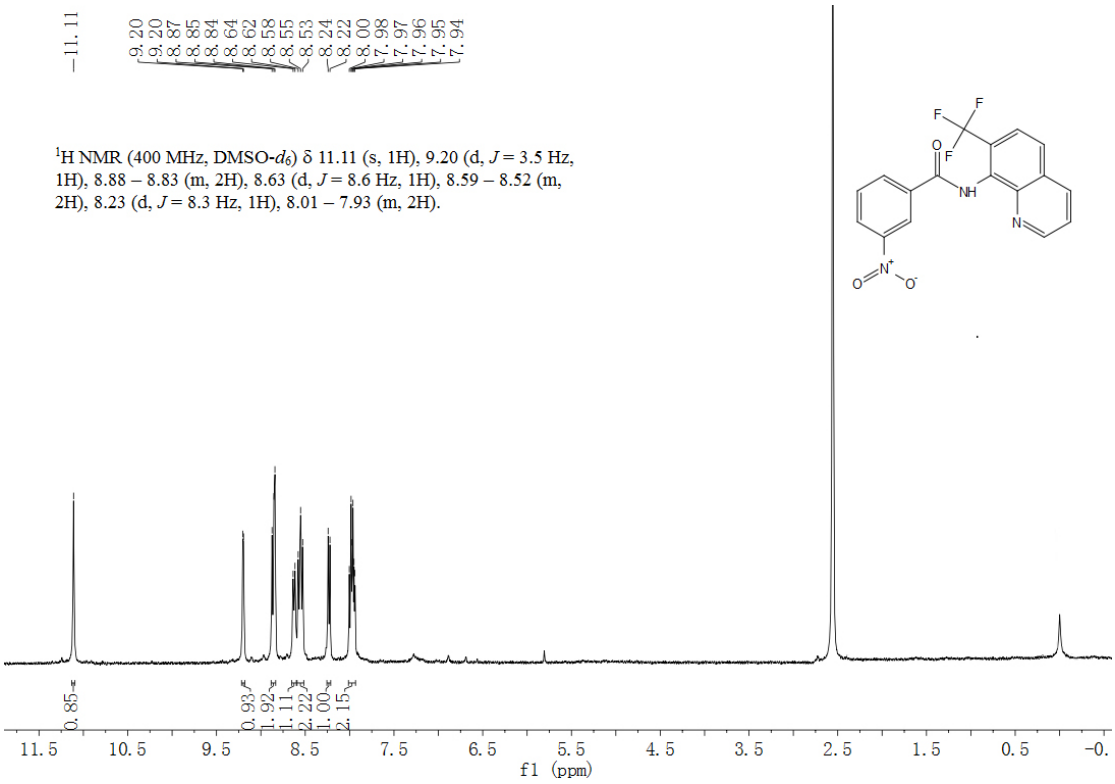


Figure S25. ^{1}H NMR of 3-nitro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2i**.

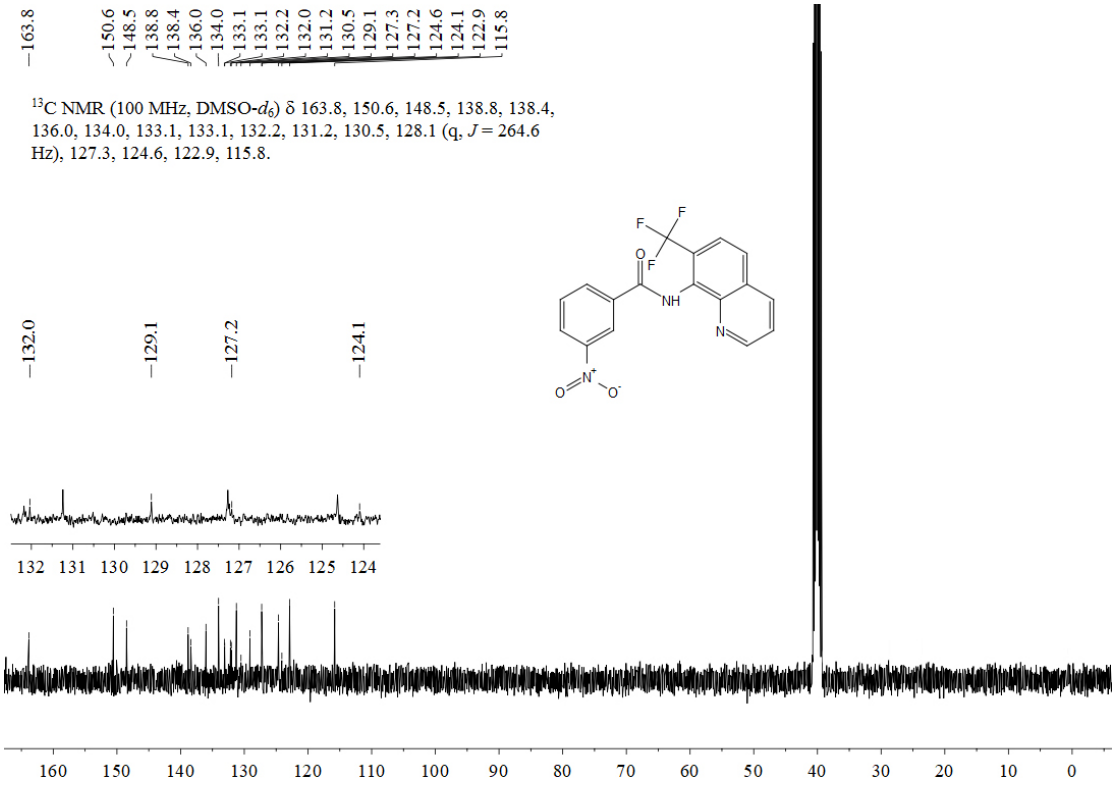


Figure S26. ^{13}C NMR of 3-nitro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2i**.

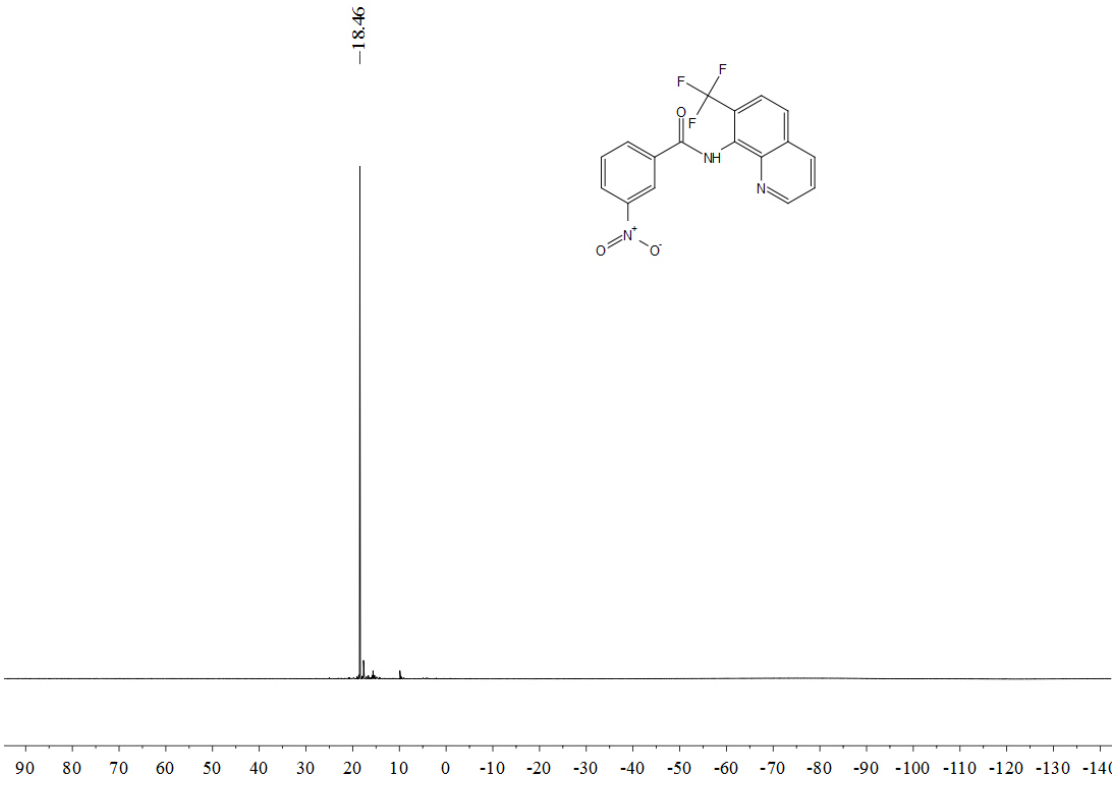
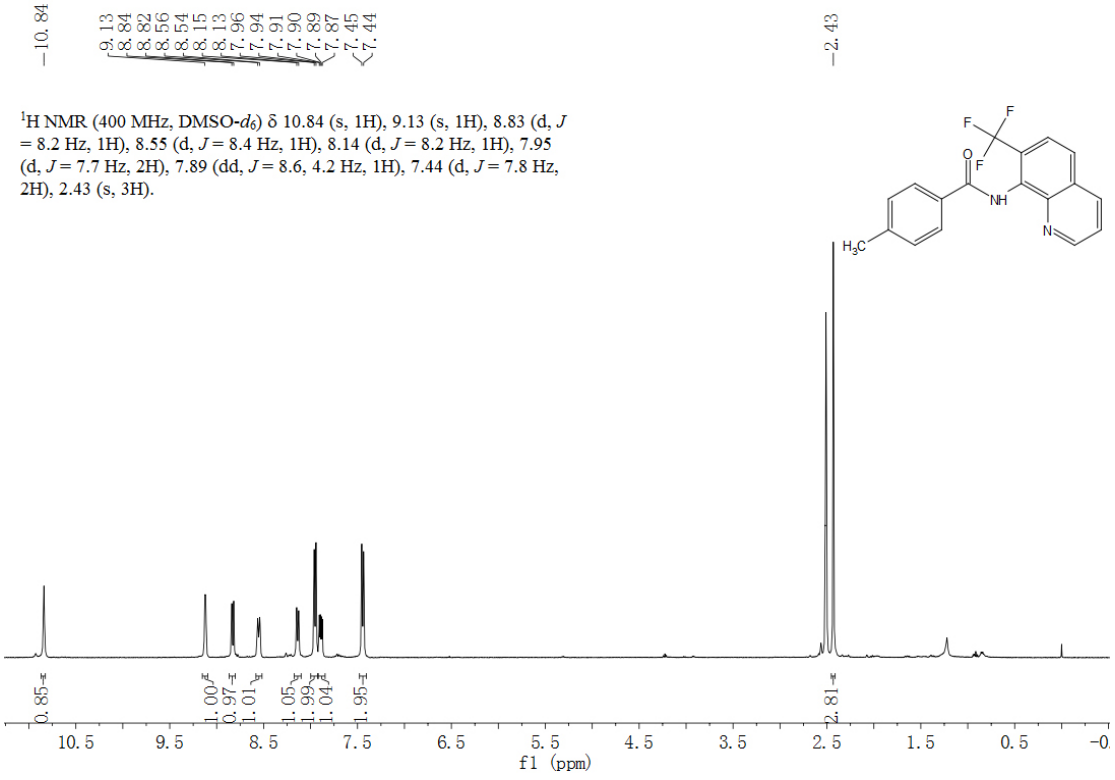


Figure S27. ^{19}F NMR of 3-nitro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2i**.



^{1}H NMR (400 MHz, DMSO-d_6) δ 10.84 (s, 1H), 9.13 (s, 1H), 8.83 (d, J = 8.2 Hz, 1H), 8.55 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 7.7 Hz, 2H), 7.89 (dd, J = 8.6, 4.2 Hz, 1H), 7.44 (d, J = 7.8 Hz, 2H), 2.43 (s, 3H).

Figure S28. ^{1}H NMR of 4-methyl-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2j**.

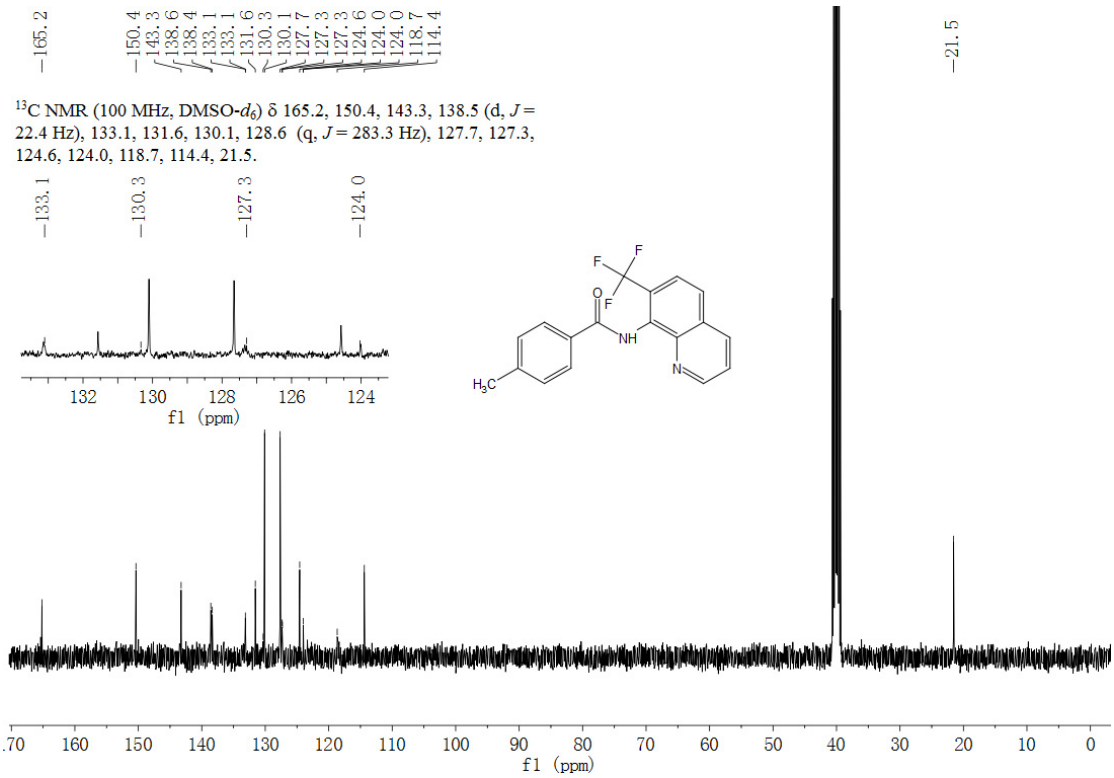


Figure S29. ^{13}C NMR of 4-methyl-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2j**.

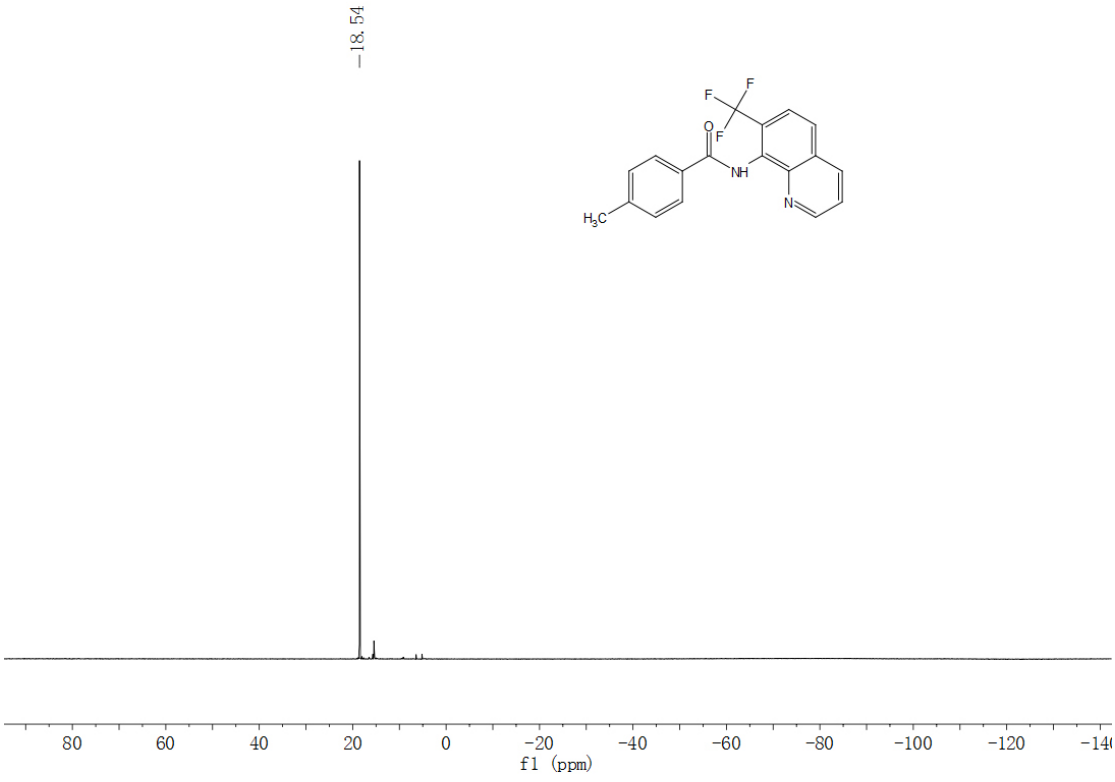


Figure S30. ^{19}F NMR of 4-methyl-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2j**.

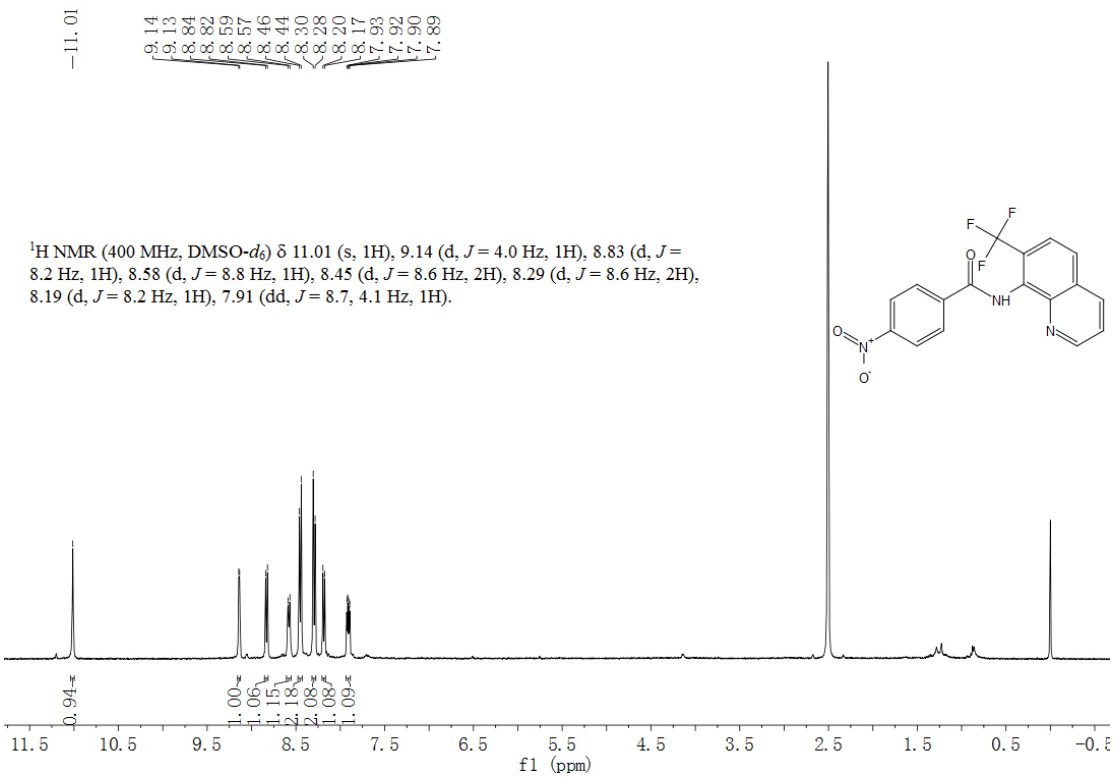


Figure S31 | ^{1}H NMR of 4-nitro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2k**.

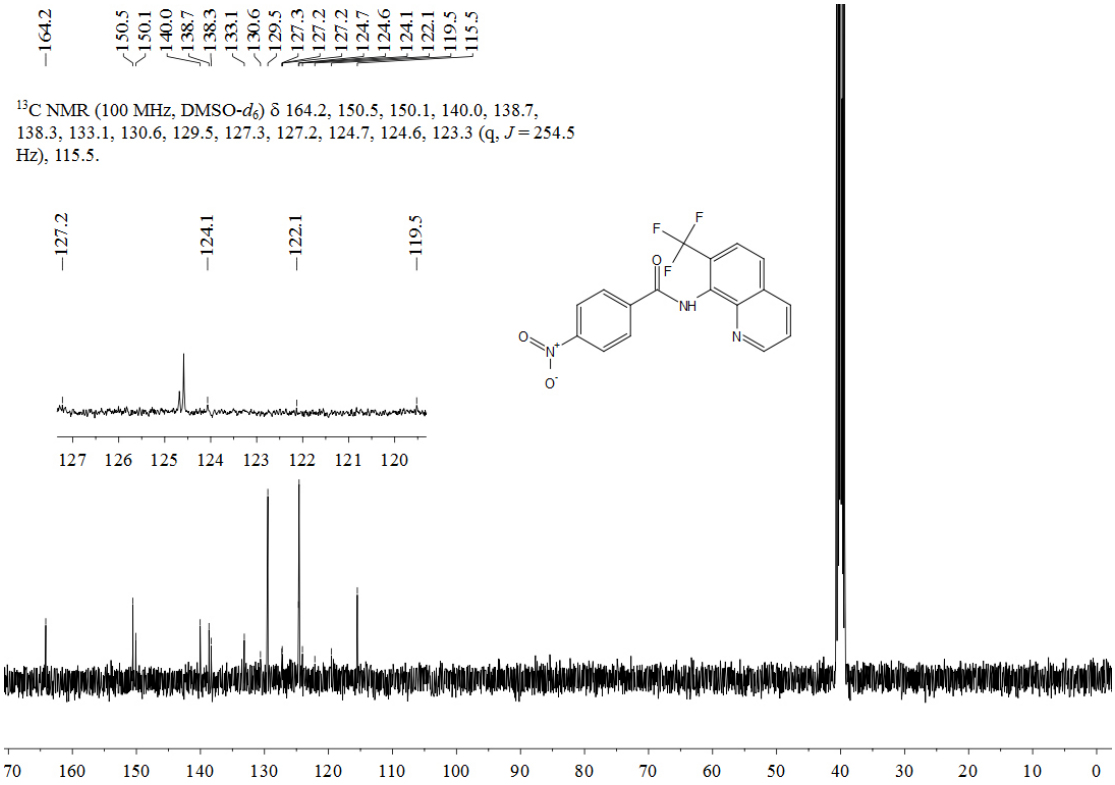


Figure S32. ^{13}C NMR of 4-nitro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2k**.

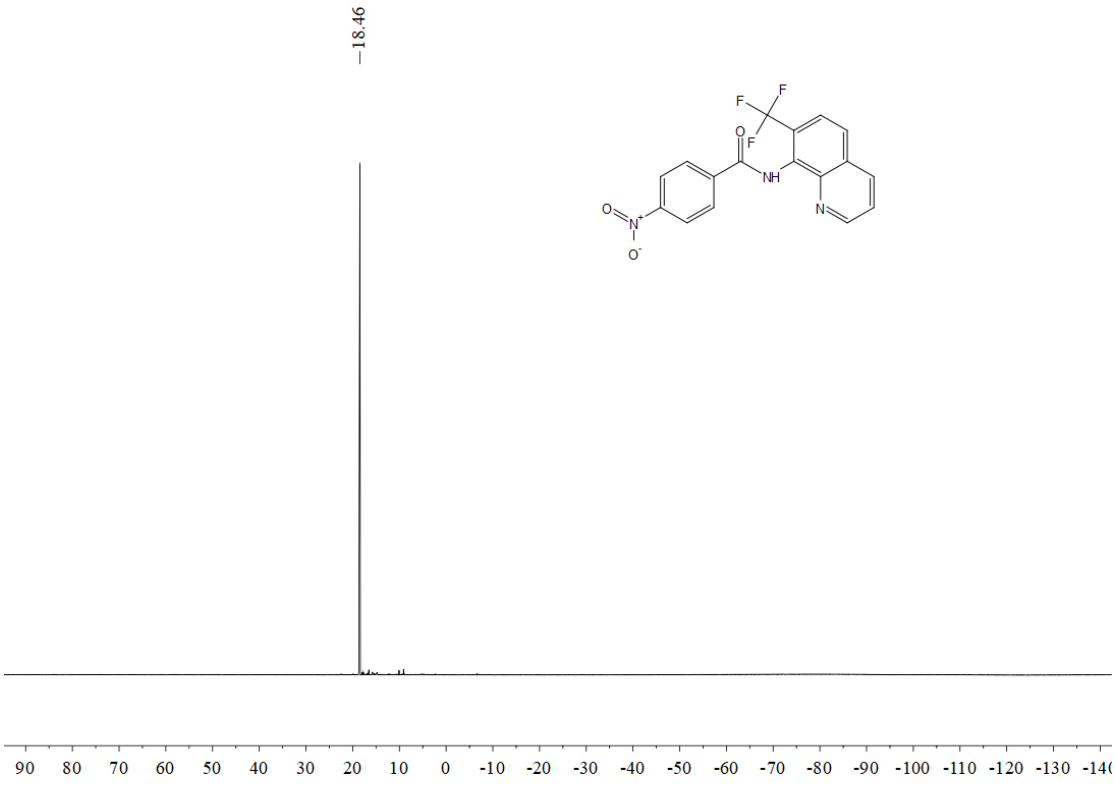


Figure S33. ^{19}F NMR of 4-nitro-N-(7-(trifluoromethyl)quinolin-8-yl)benzamide **2k**.

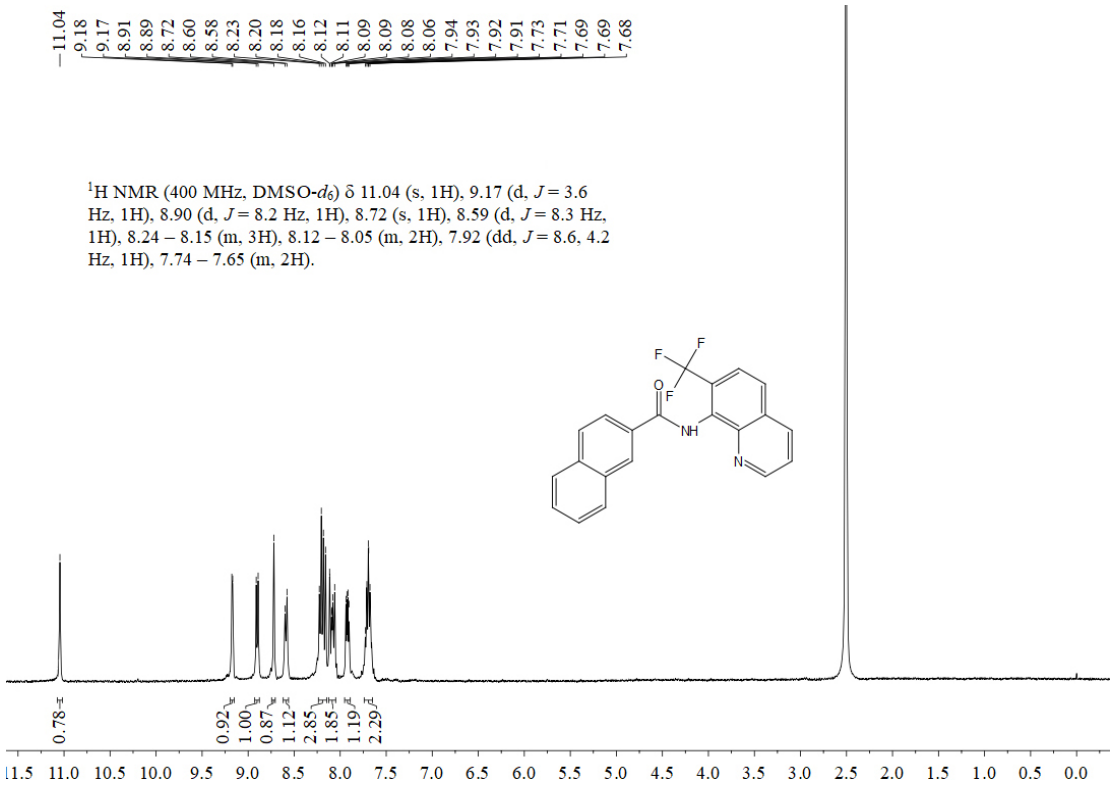
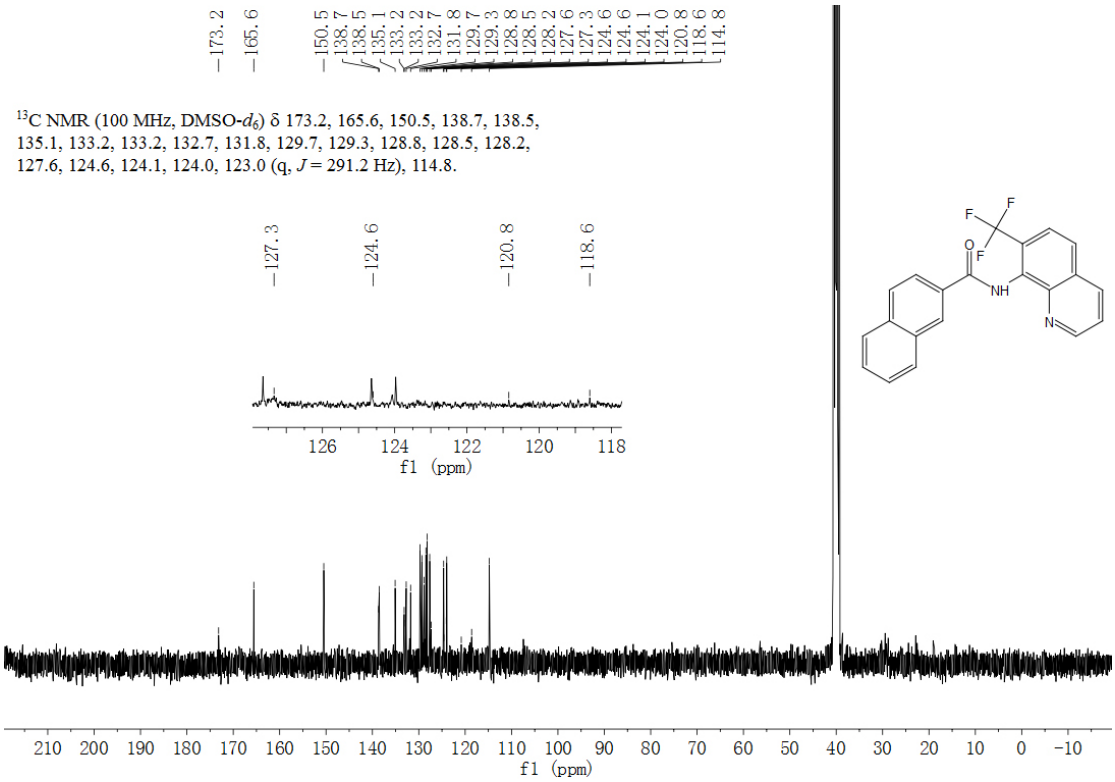


Figure S34. ^{1}H NMR of N-(7-(trifluoromethyl)quinolin-8-yl)-2-naphthamide **2l**.



^{13}C NMR (100 MHz, DMSO-d_6) δ 173.2, 165.6, 150.5, 138.7, 138.5, 135.1, 133.2, 133.2, 132.7, 131.8, 129.7, 129.3, 128.8, 128.5, 128.2, 127.6, 124.6, 124.1, 124.0, 123.0 (q, J = 291.2 Hz), 114.8.

Figure S35. ^{13}C NMR of N-(7-(trifluoromethyl)quinolin-8-yl)-2-naphthamide **2l**.

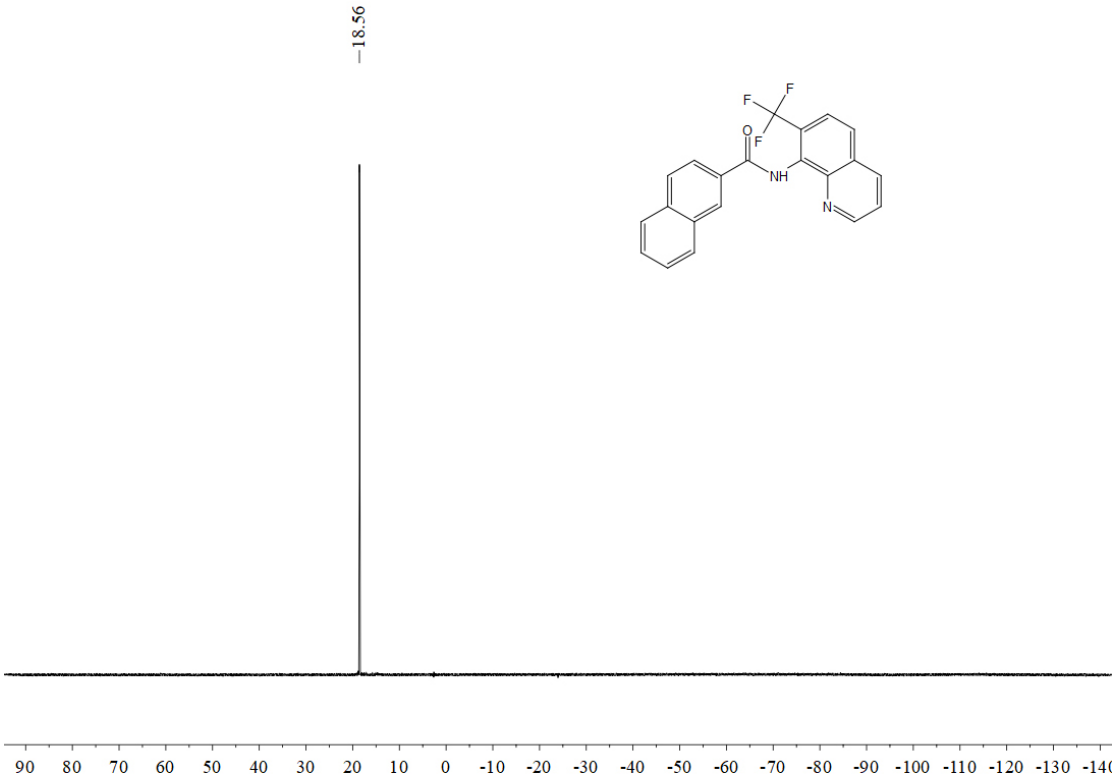


Figure S36. ^{19}F NMR of N-(7-(trifluoromethyl)quinolin-8-yl)-2-naphthamide **2l**.

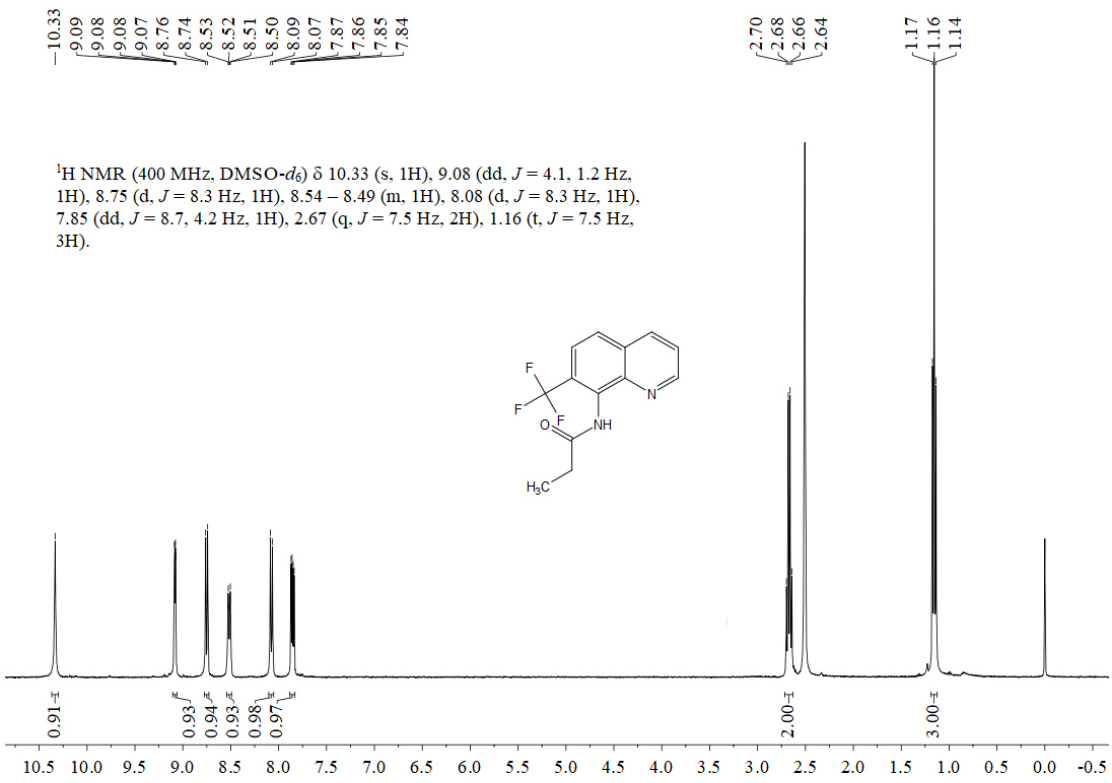


Figure S37. ^{1}H NMR of N-(7-(trifluoromethyl)quinolin-8-yl)propionamide **2m**.

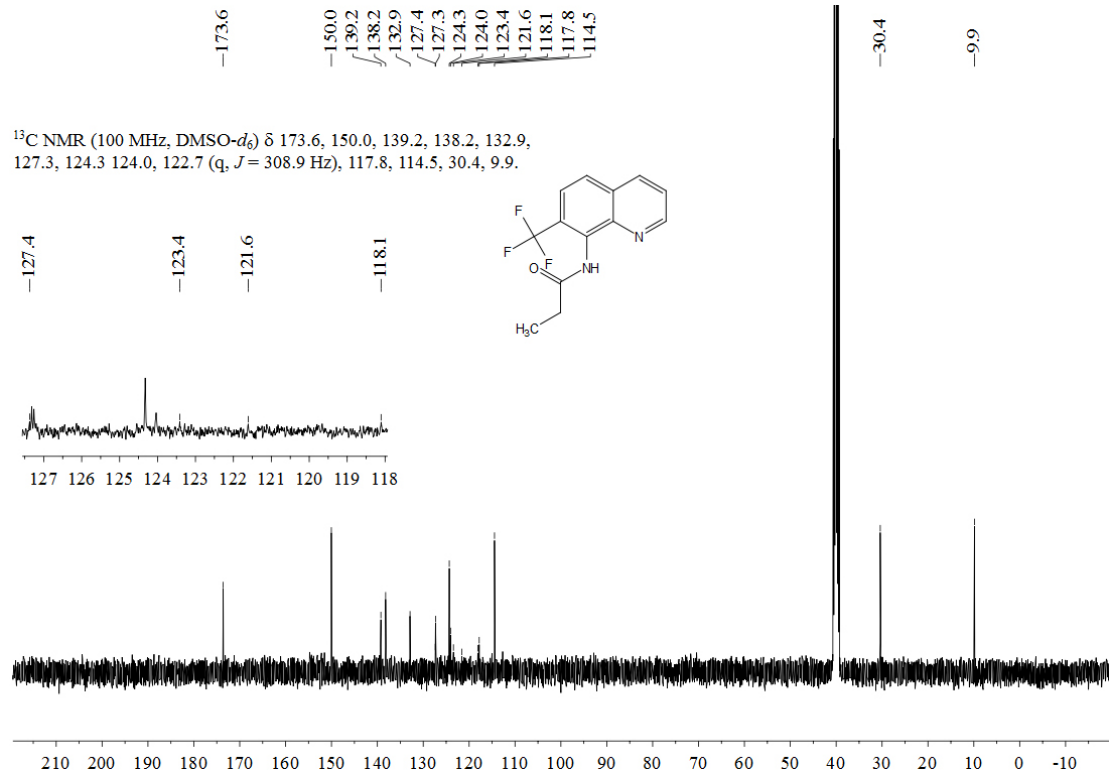


Figure S38. ^{13}C NMR of N-(7-(trifluoromethyl)quinolin-8-yl)propionamide **2m**.

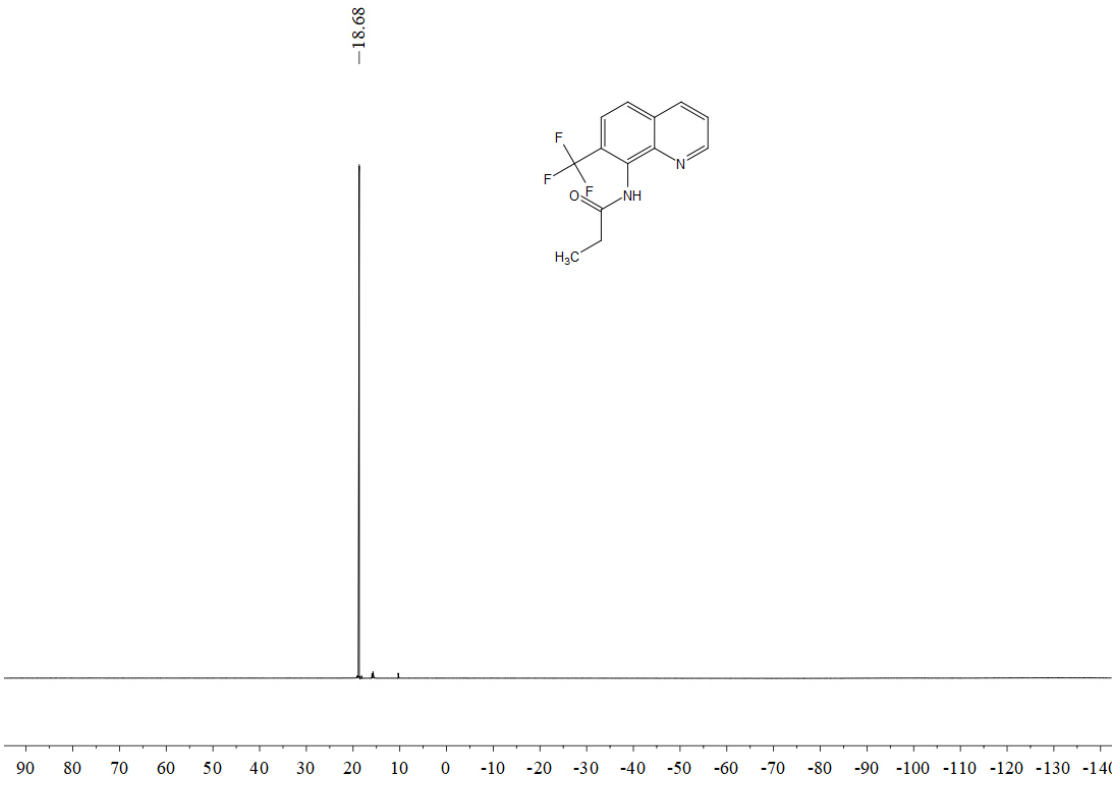


Figure S39. ^{19}F NMR of N-(7-(trifluoromethyl)quinolin-8-yl)propionamide **2m**.

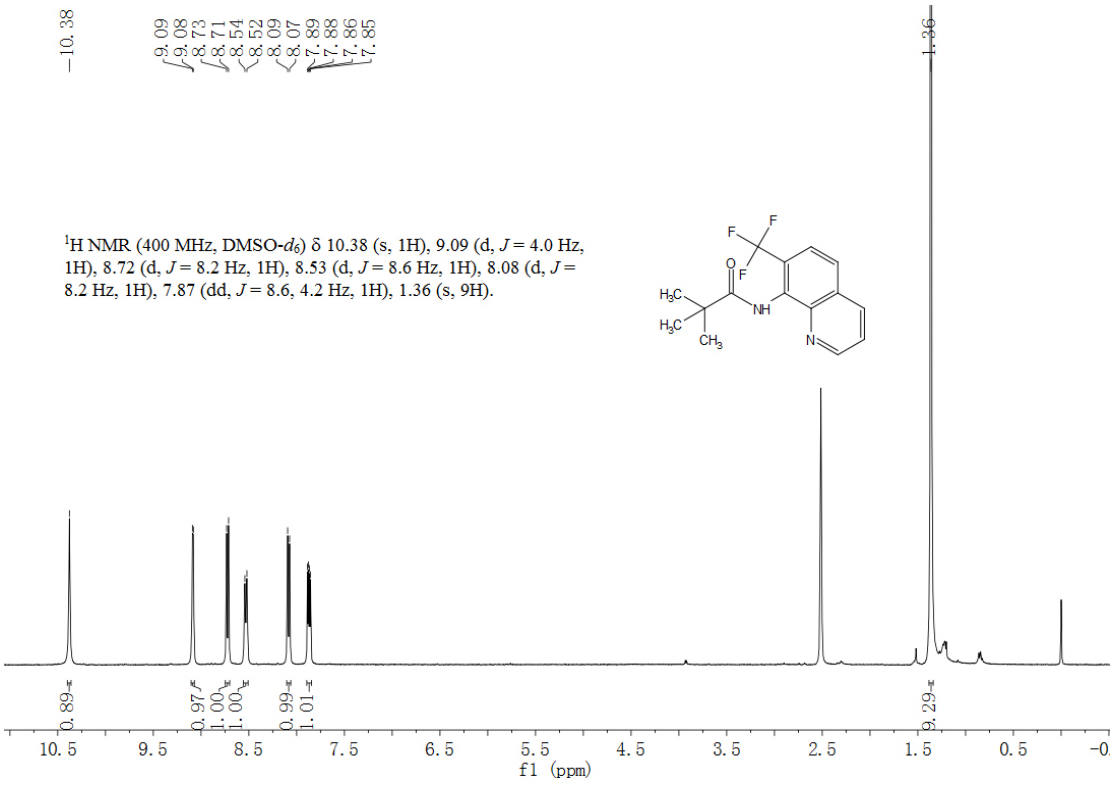


Figure S40. ^{1}H NMR of N-(7-(trifluoromethyl)quinolin-8-yl)pivalamide **2n**.

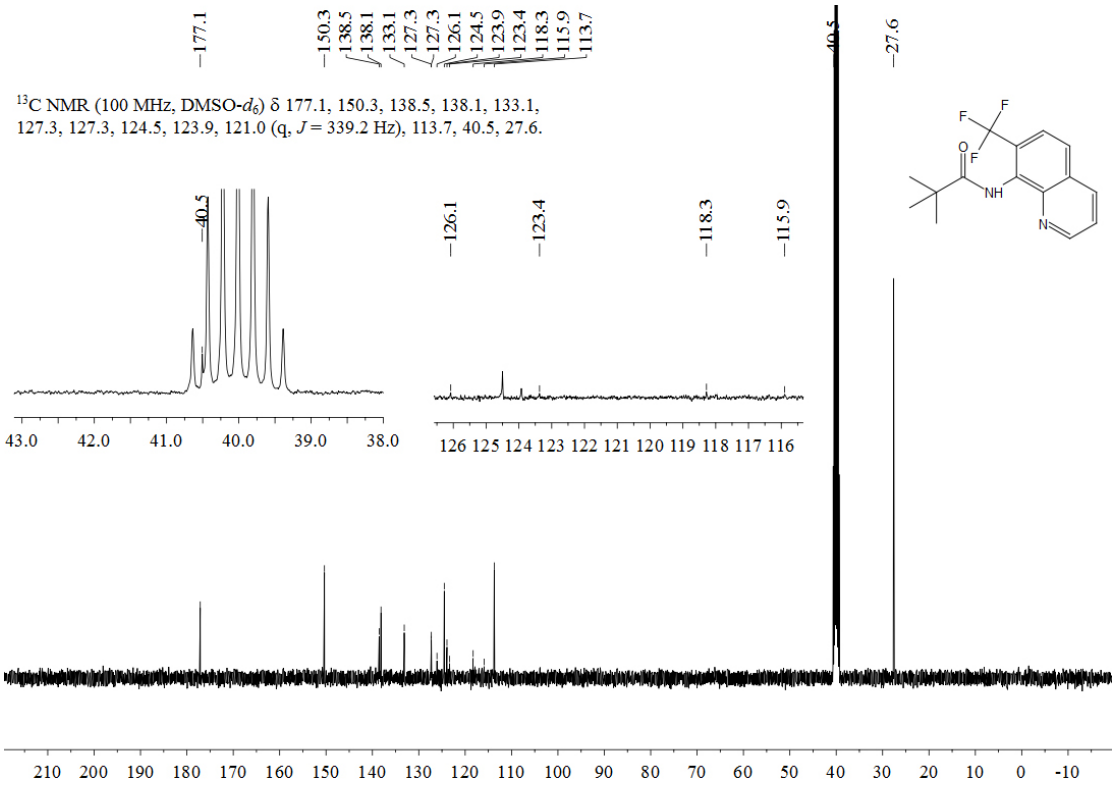


Figure S41. ^{13}C NMR of N-(7-(trifluoromethyl)quinolin-8-yl)pivalamide **2n**.

Figure S42. ^{19}F NMR of N-(7-(trifluoromethyl)quinolin-8-yl)pivalamide **2n**.

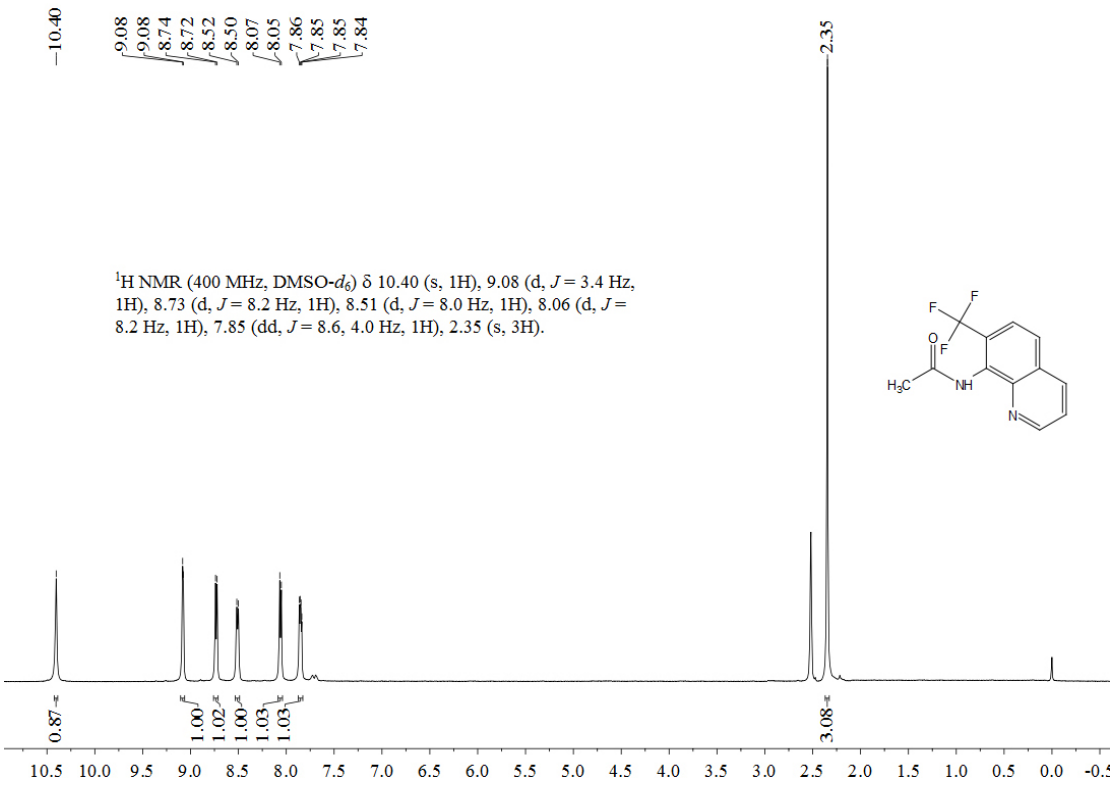


Figure S43. ^{1}H NMR of N-(7-(trifluoromethyl)quinolin-8-yl)acetamide **2o**.

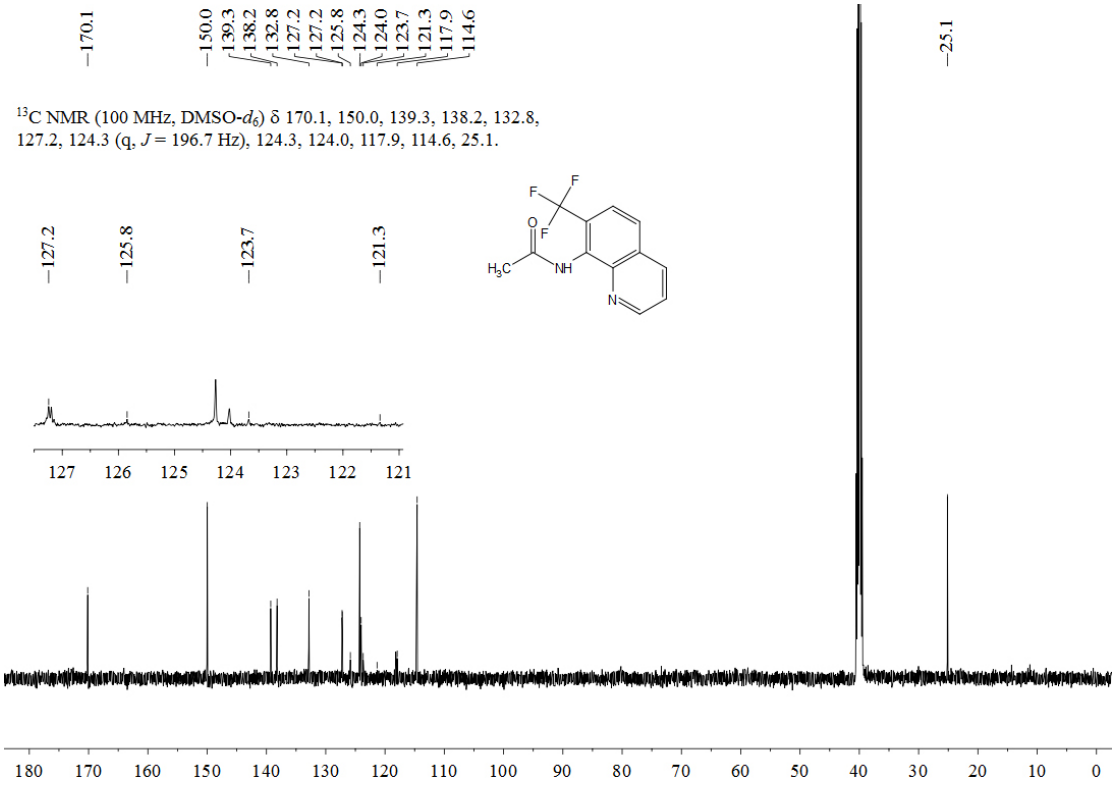


Figure S44. ^{13}C NMR of N-(7-(trifluoromethyl)quinolin-8-yl)acetamide **2o**.

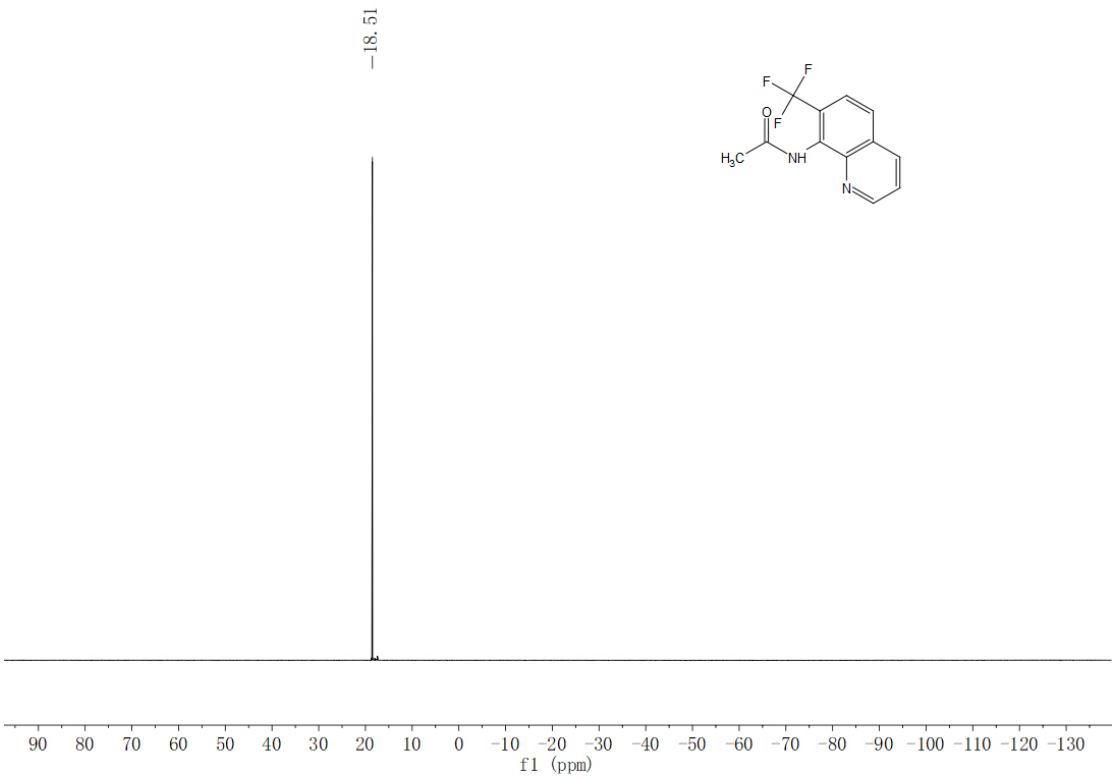


Figure S45. ^{19}F NMR of N-(7-(trifluoromethyl)quinolin-8-yl)acetamide **2o**.

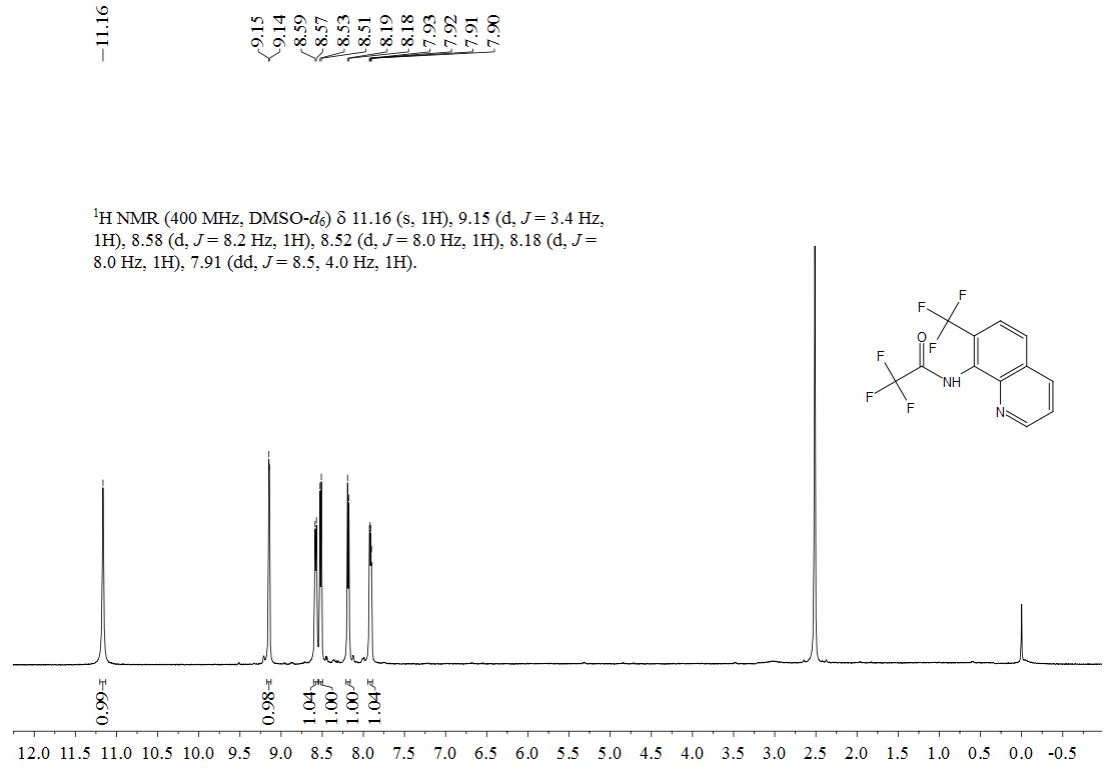


Figure S46. ^{1}H NMR of N-(7-(trifluoromethyl)quinolin-8-yl)trifluoroacetamide **2p**.

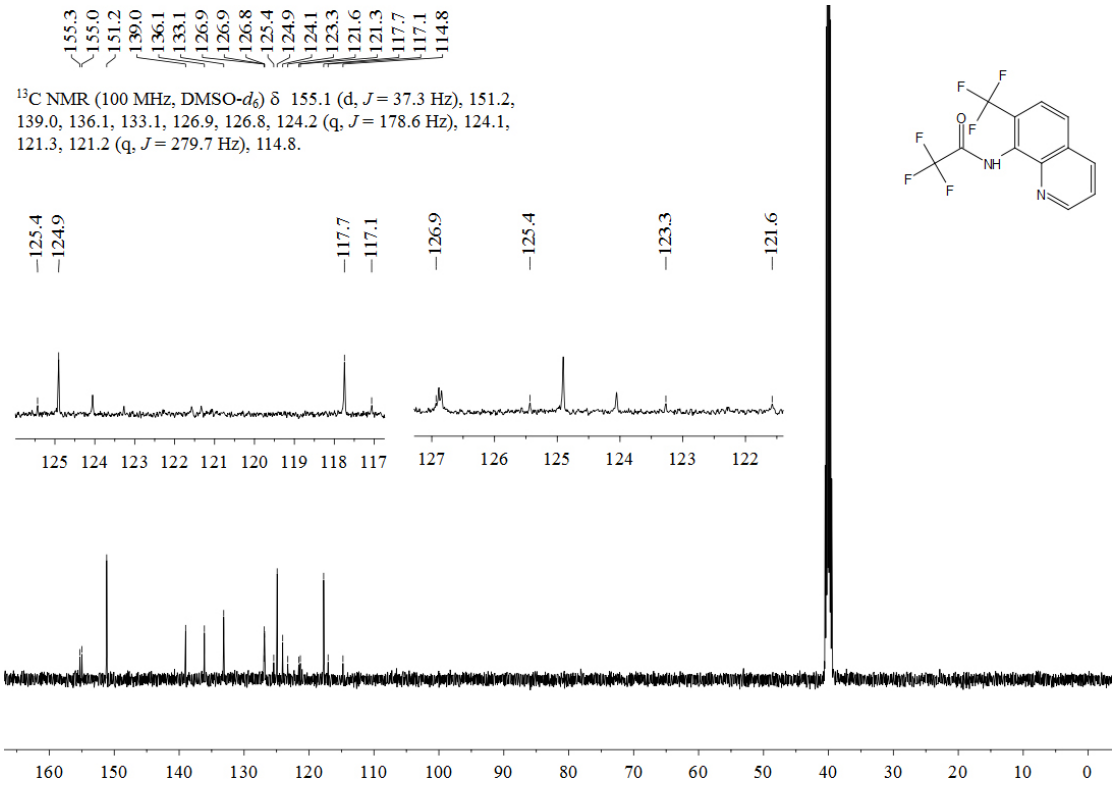


Figure S47. ^{13}C NMR of N-(7-(trifluoromethyl)quinolin-8-yl)trifluoroacetamide **2p**.

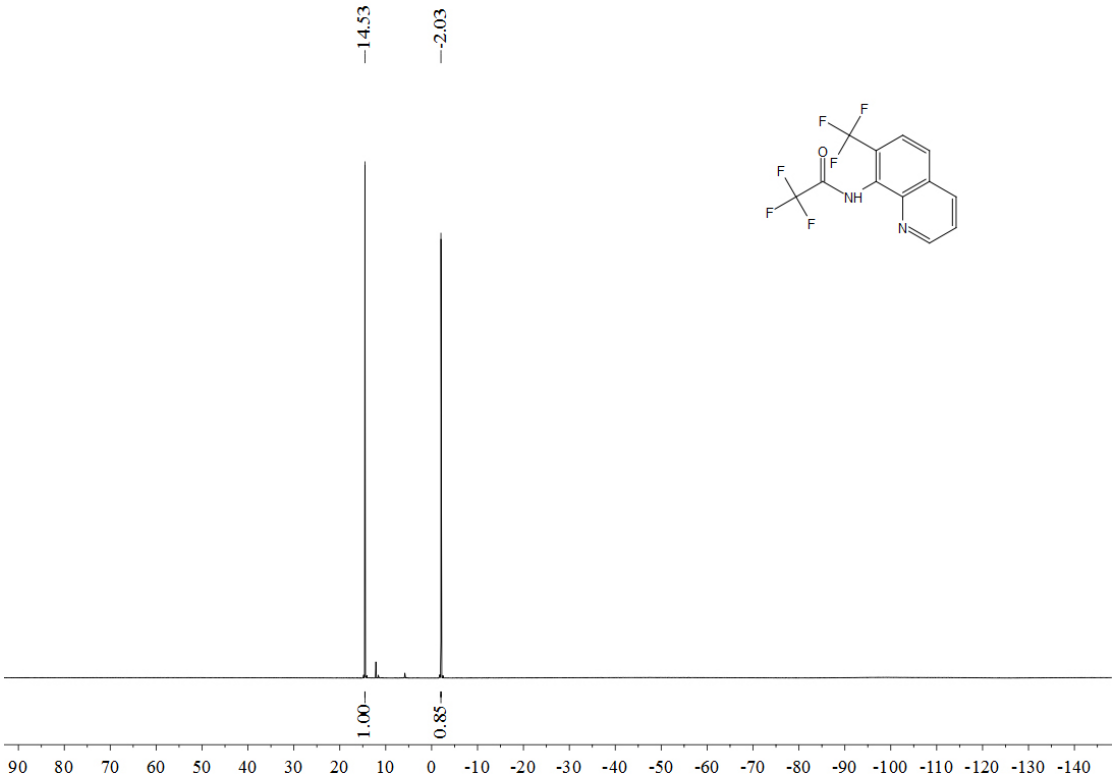


Figure S48. ^{19}F NMR of N-(7-(trifluoromethyl)quinolin-8-yl)trifluoroacetamide **2p**.

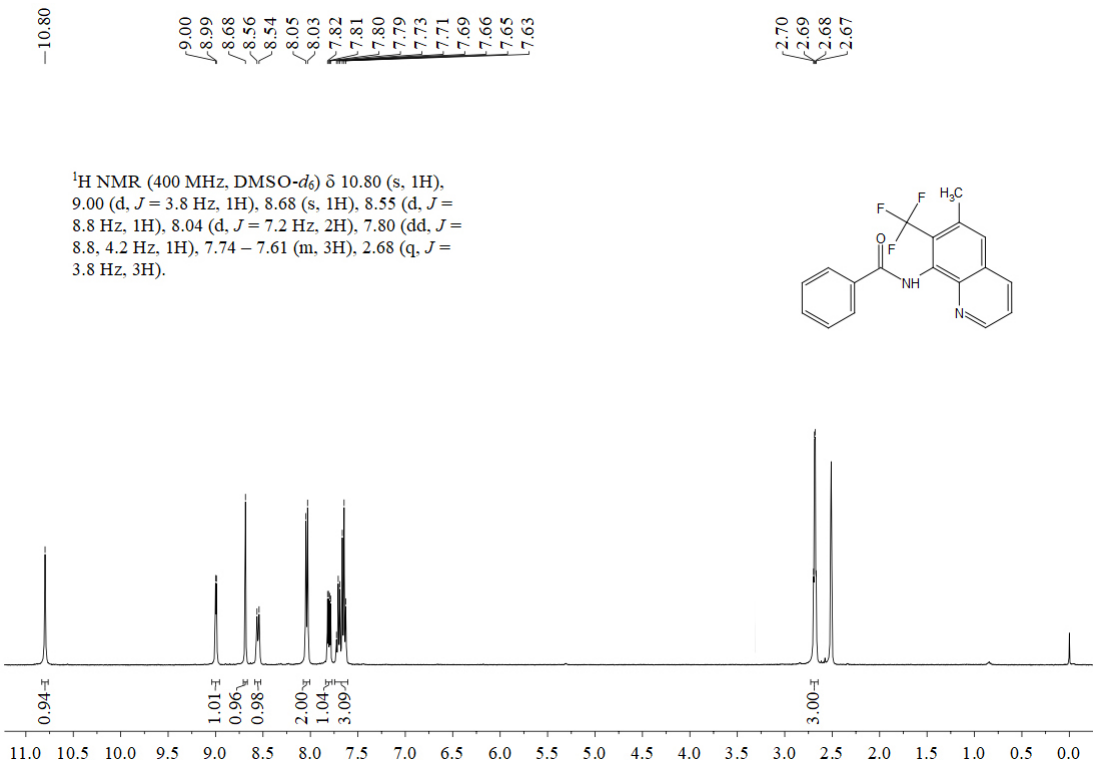


Figure S49. ^{1}H NMR of N-(6-methyl-7-(trifluoromethyl)quinolin-8-yl)benzamide **2q**.

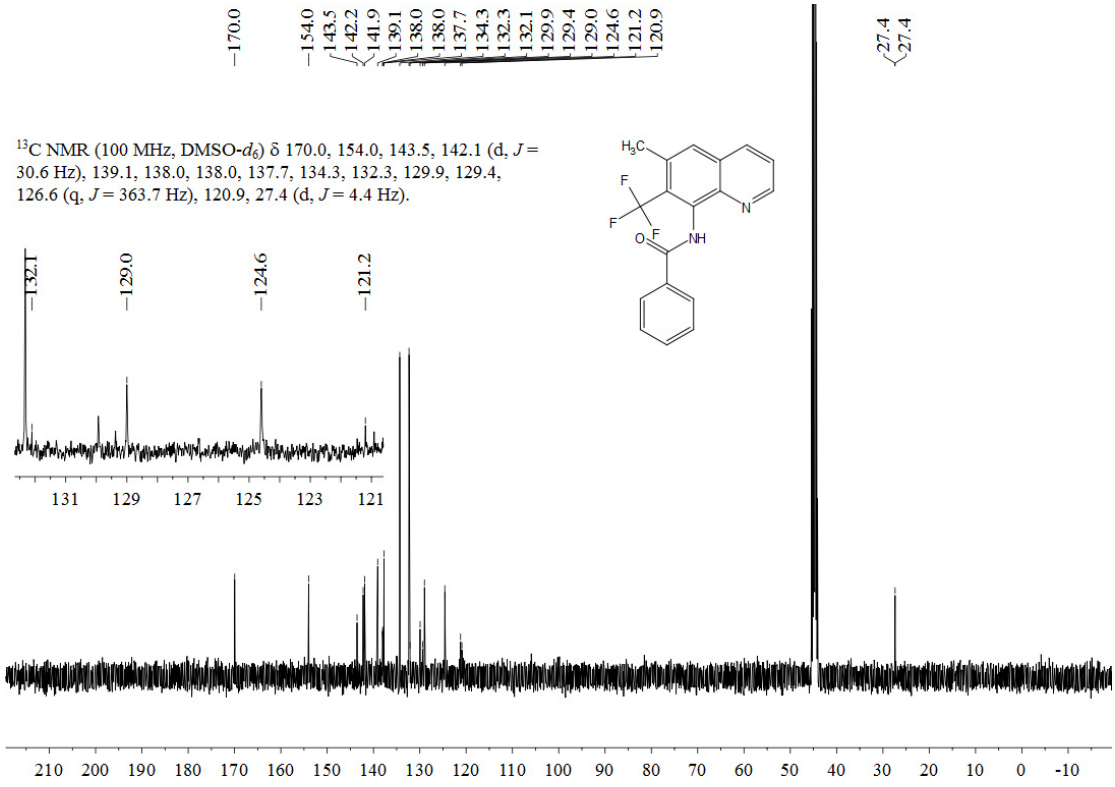


Figure S50. ^{13}C NMR of N-(6-methyl-7-(trifluoromethyl)quinolin-8-yl)benzamide **2q**.

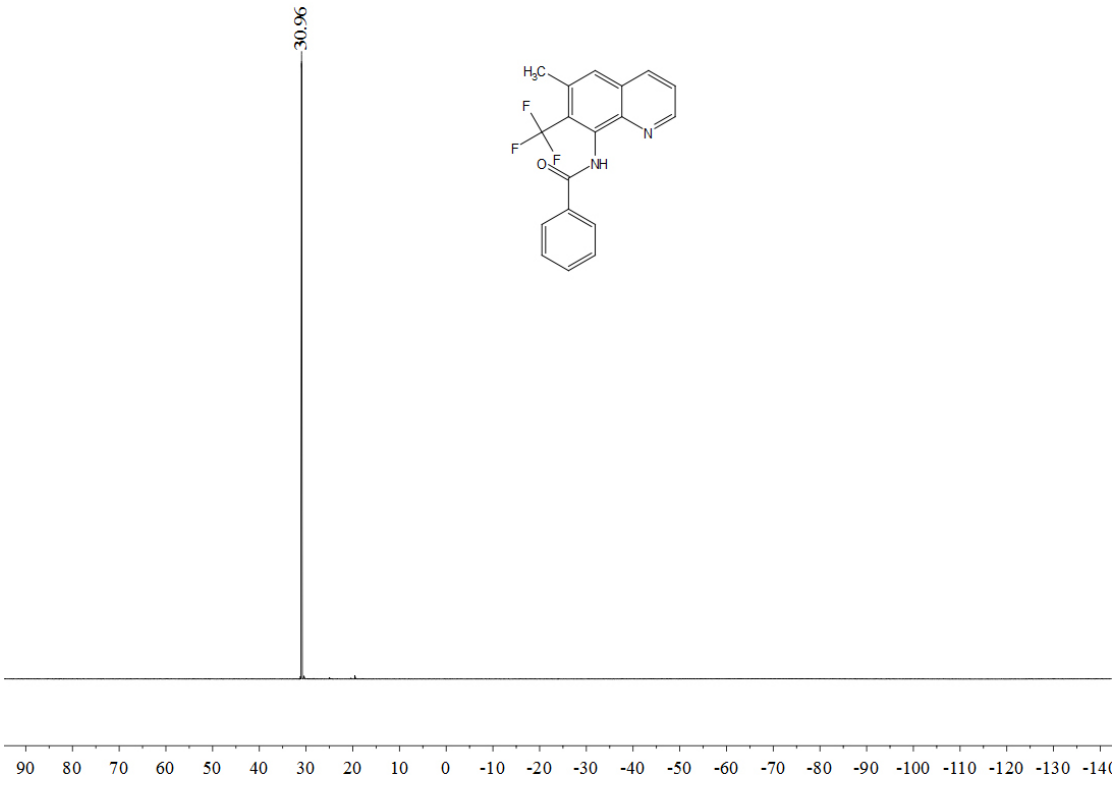
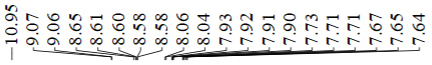


Figure S51. ^{19}F NMR of N-(6-methyl-7-(trifluoromethyl)quinolin-8-yl)benzamide **2q**.



^{1}H NMR (400 MHz, DMSO-d_6) δ 10.95 (s, 1H), 9.06 (d, J = 4.1 Hz, 1H), 8.63 (d, J = 14.8 Hz, 1H), 8.59 (d, J = 9.2 Hz, 1H), 8.05 (d, J = 7.4 Hz, 2H), 7.91 (dd, J = 8.8, 4.2 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.65 (t, J = 7.4 Hz, 2H).

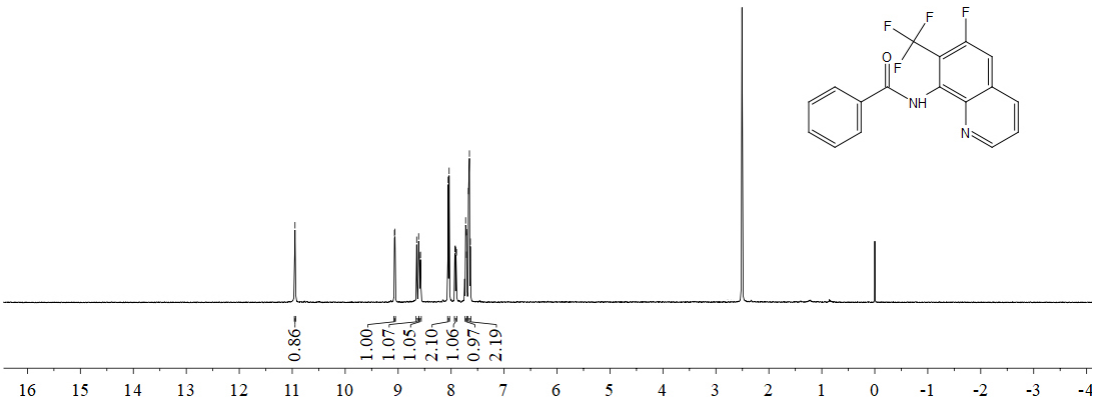


Figure S52. ^{1}H NMR of N-(6-fluoro-7-(trifluoromethyl)quinolin-8-yl)benzamide **2r**.

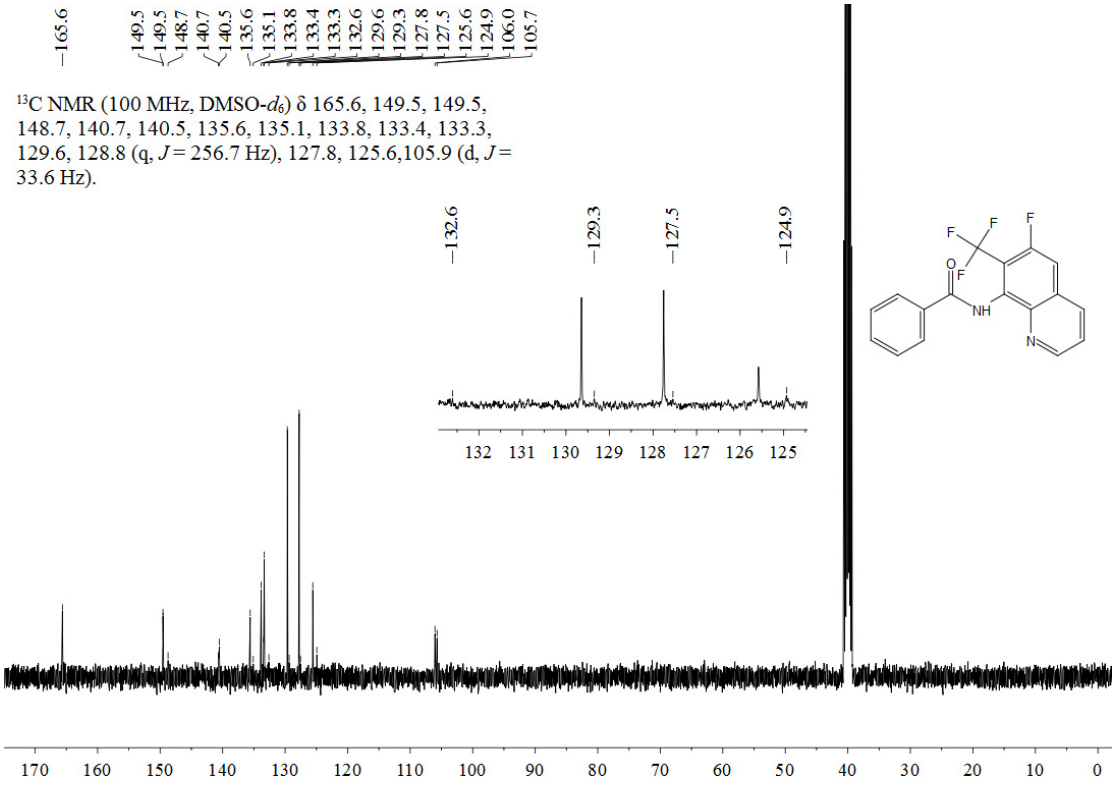


Figure S53. ^{13}C NMR of N-(6-fluoro-7-(trifluoromethyl)quinolin-8-yl)benzamide **2r**.

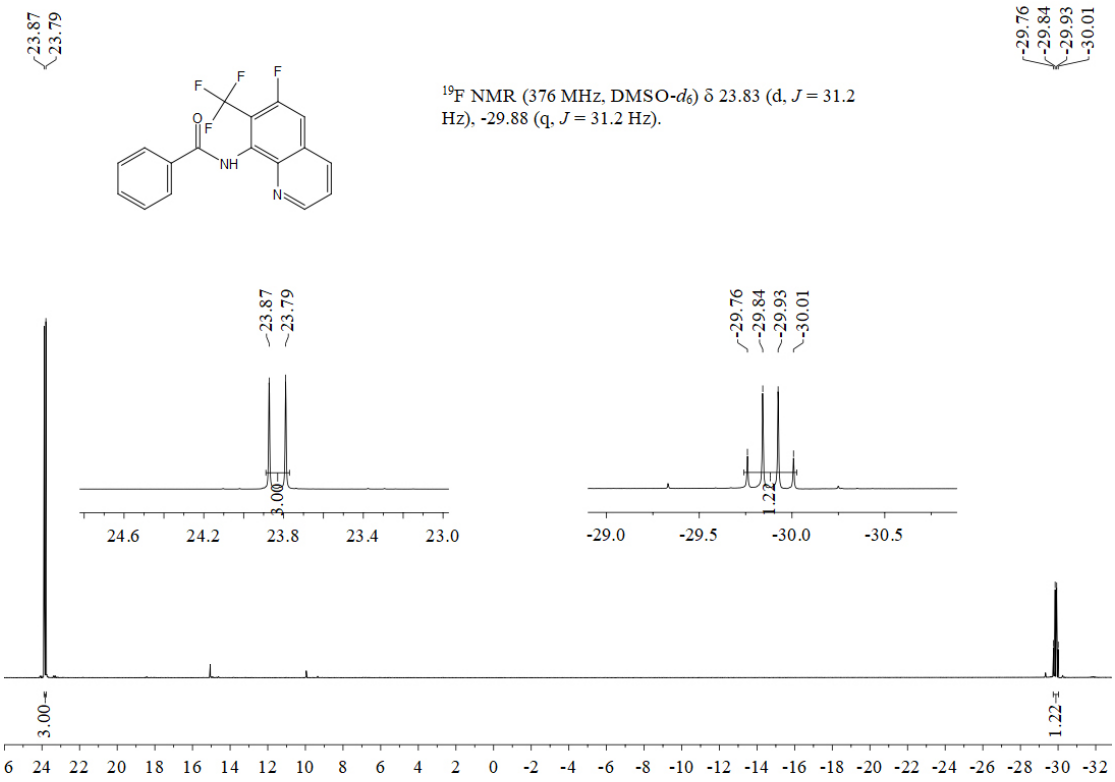


Figure S54. ^{19}F NMR of N-(6-fluoro-7-(trifluoromethyl)quinolin-8-yl)benzamide **2r**.

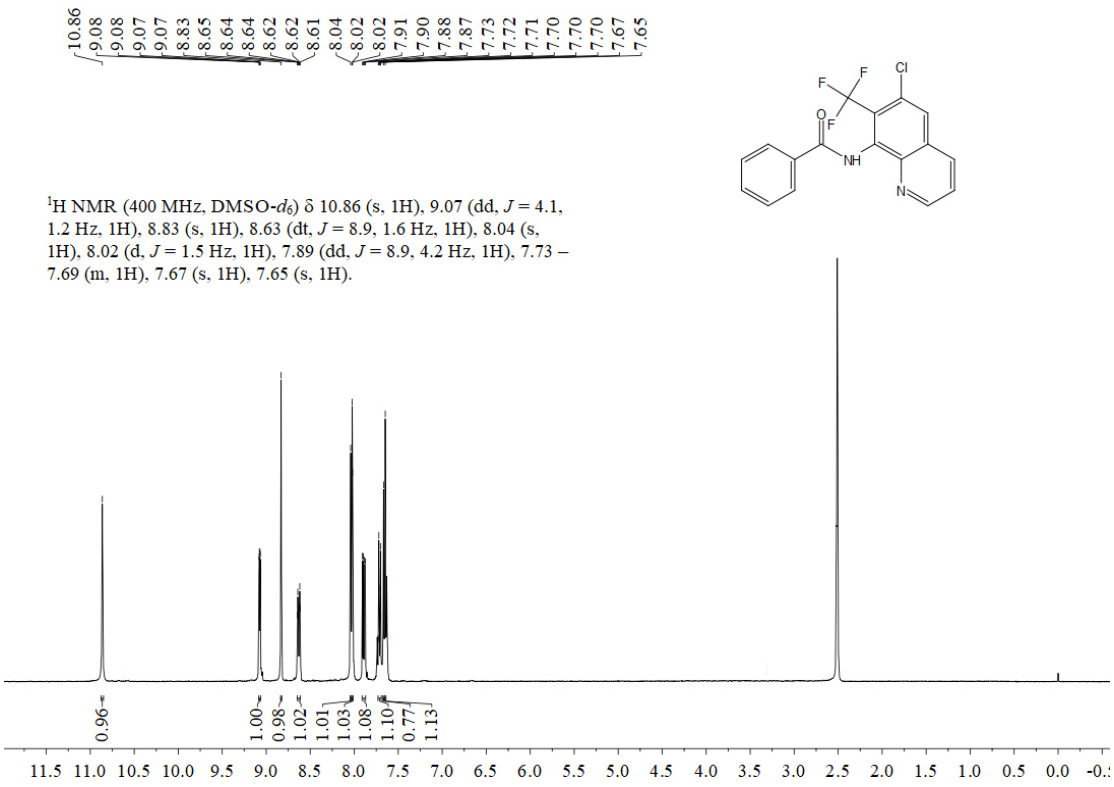


Figure S55. [1]H NMR of N-(6-chloro-7-(trifluoromethyl)quinolin-8-yl)benzamide **2s**.

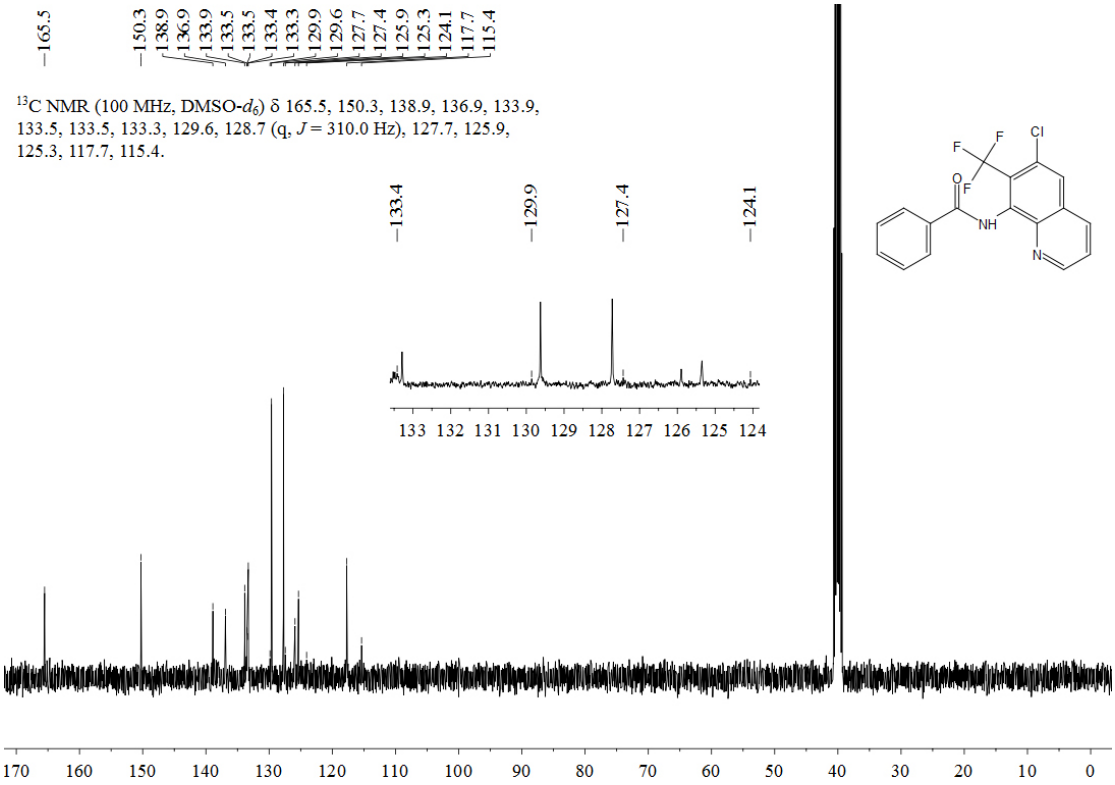


Figure S56. [13]C NMR of N-(6-chloro-7-(trifluoromethyl)quinolin-8-yl)benzamide **2s**.

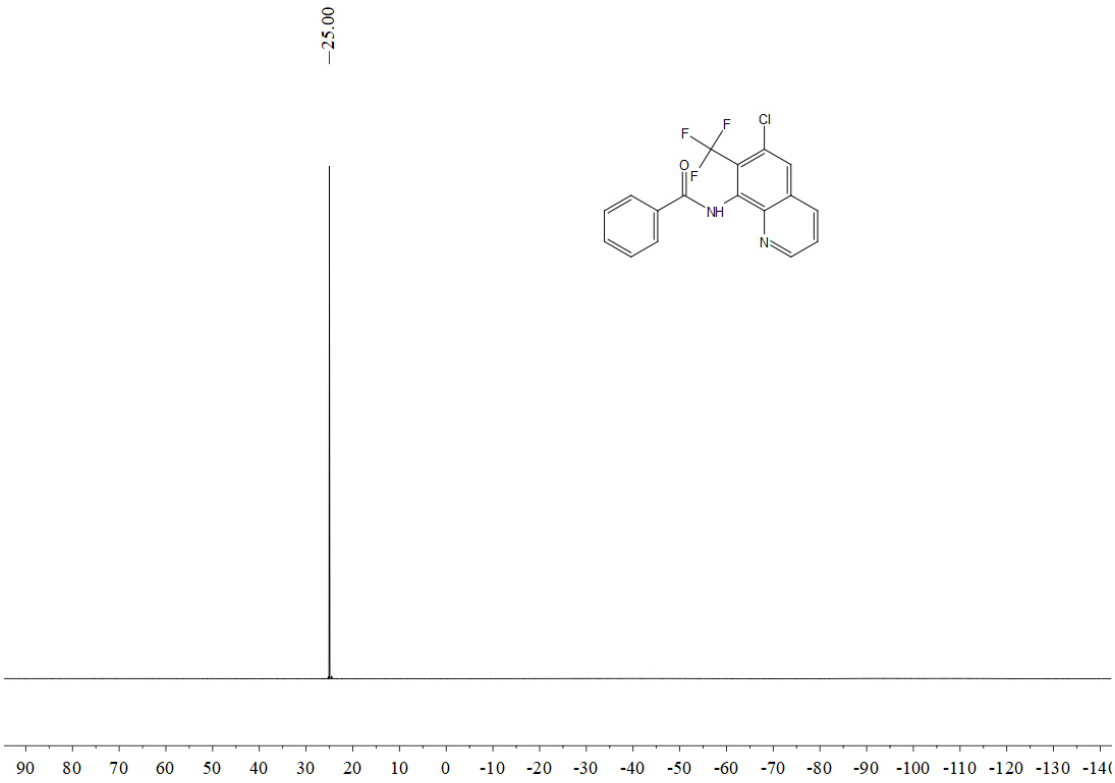
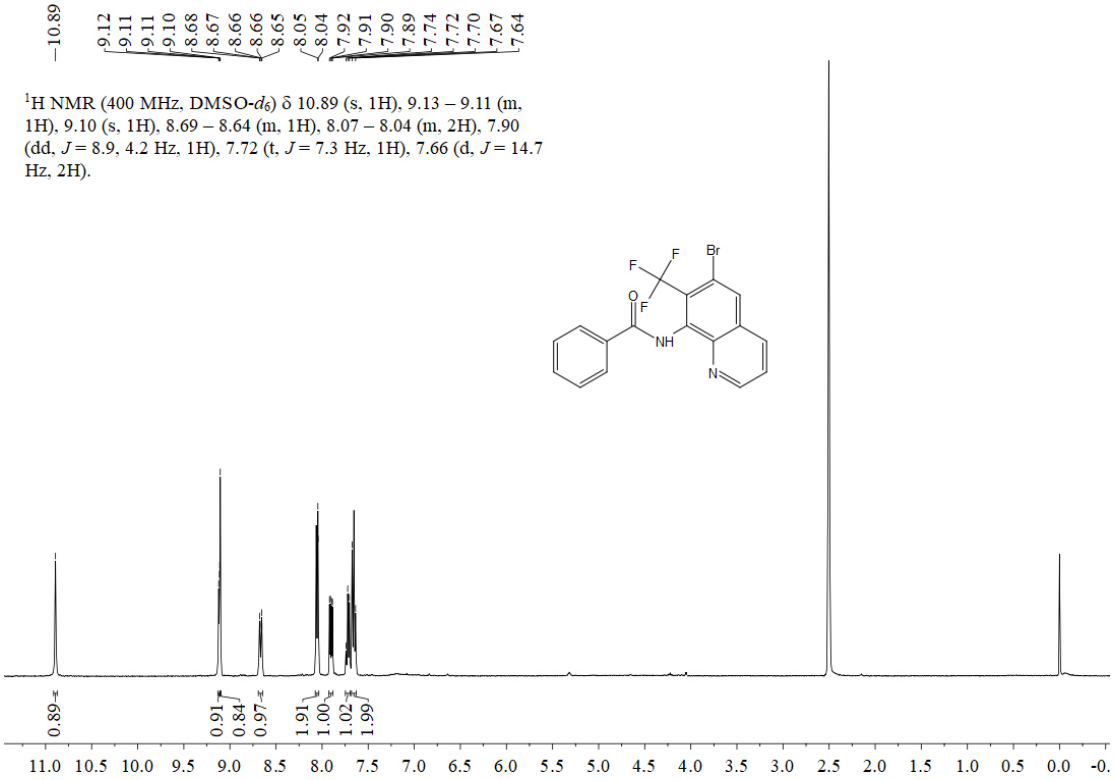
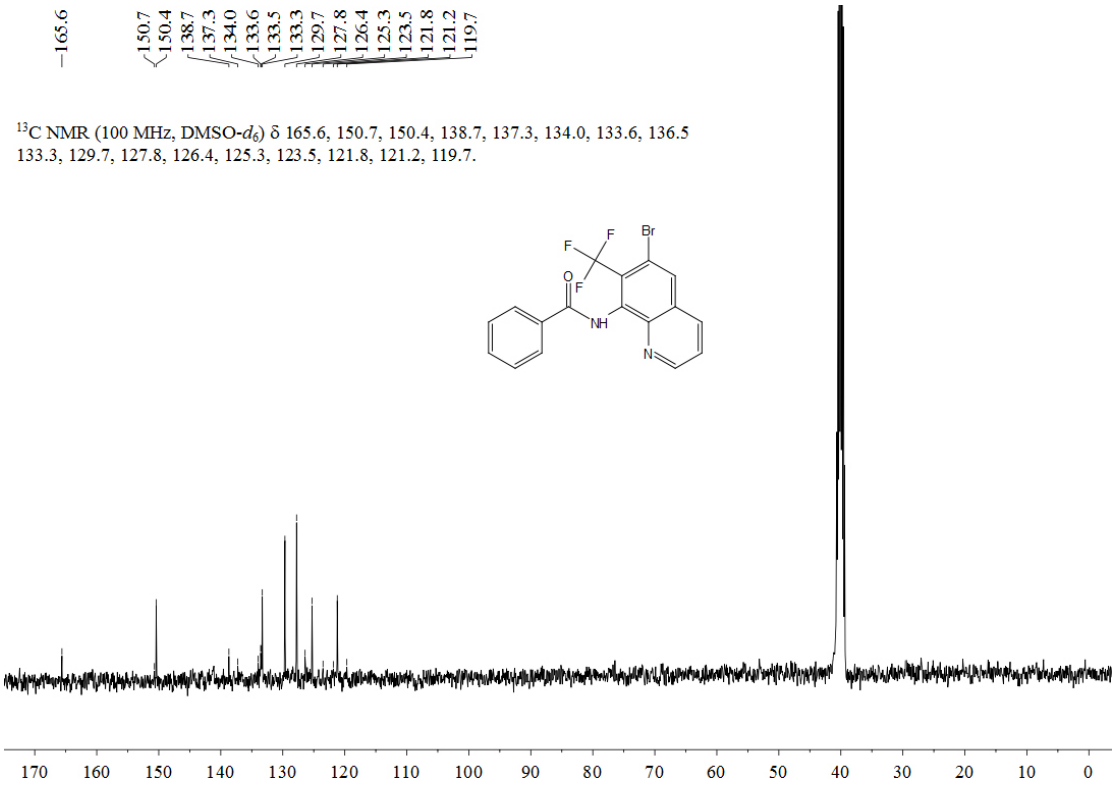


Figure S57. ^{19}F NMR of N-(6-chloro-7-(trifluoromethyl)quinolin-8-yl)benzamide **2s**.



^{1}H NMR (400 MHz, DMSO-d_6) δ 10.89 (s, 1H), 9.13 – 9.11 (m, 1H), 9.10 (s, 1H), 8.69 – 8.64 (m, 1H), 8.07 – 8.04 (m, 2H), 7.90 (dd, J = 8.9, 4.2 Hz, 1H), 7.72 (t, J = 7.3 Hz, 1H), 7.66 (d, J = 14.7 Hz, 2H).

Figure S58. ^{1}H NMR of N-(6-bromo-7-(trifluoromethyl)quinolin-8-yl)benzamide **2t**.



^{13}C NMR (100 MHz, DMSO-d_6) δ 165.6, 150.7, 150.4, 138.7, 137.3, 134.0, 133.6, 136.5 133.3, 129.7, 127.8, 126.4, 125.3, 123.5, 121.8, 121.2, 119.7.

Figure S59. ^{13}C NMR of N-(6-bromo-7-(trifluoromethyl)quinolin-8-yl)benzamide **2t**.

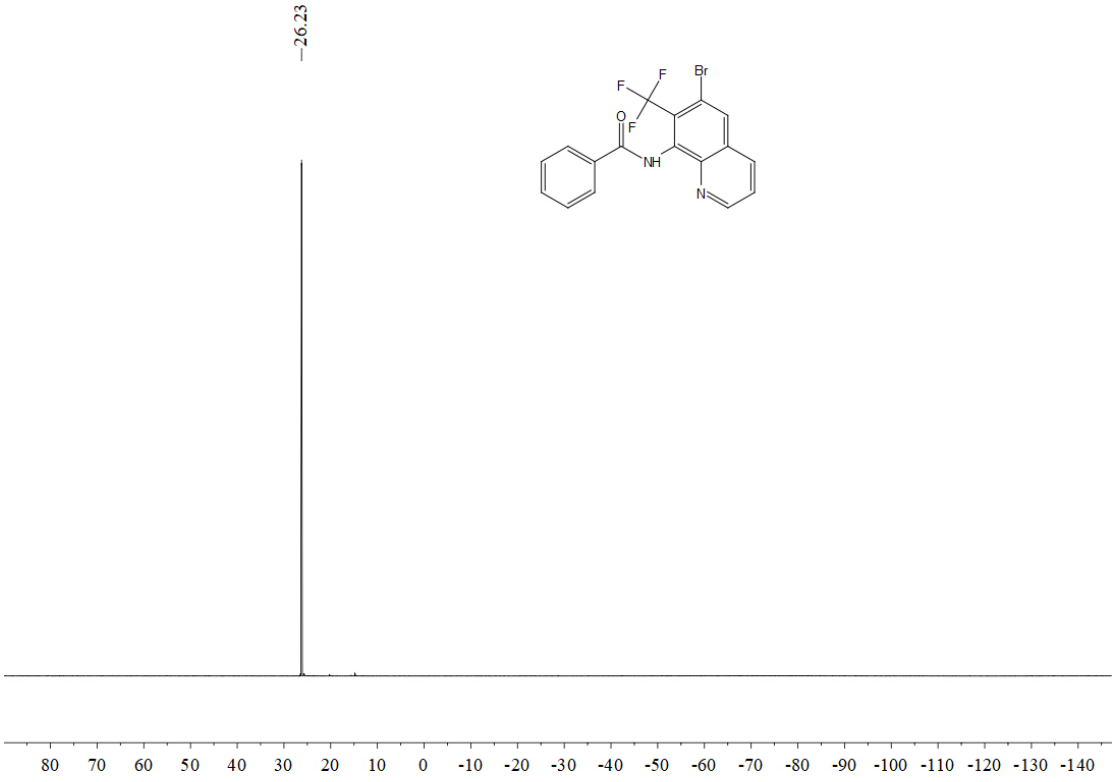


Figure S60. ^{19}F NMR of N-(6-bromo-7-(trifluoromethyl)quinolin-8-yl)benzamide **2t**.

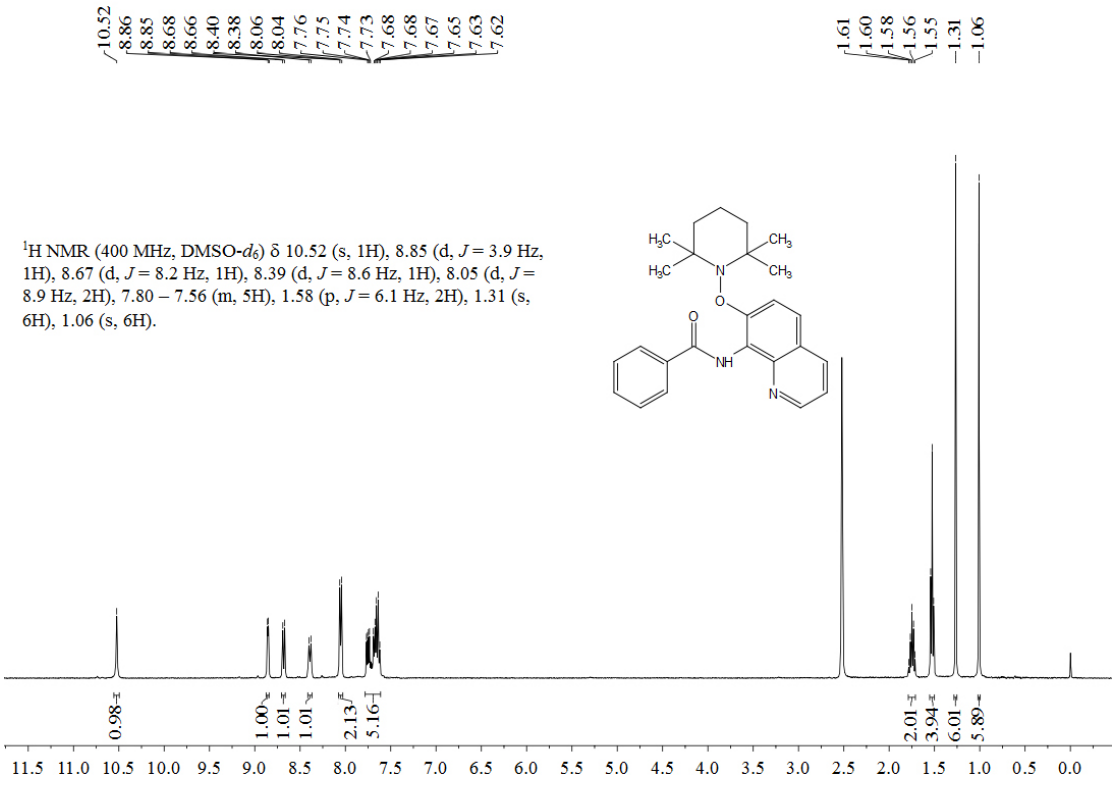


Figure S61. ^{1}H NMR of N-(7-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)quinolin-8-yl)benzamide **3a**.

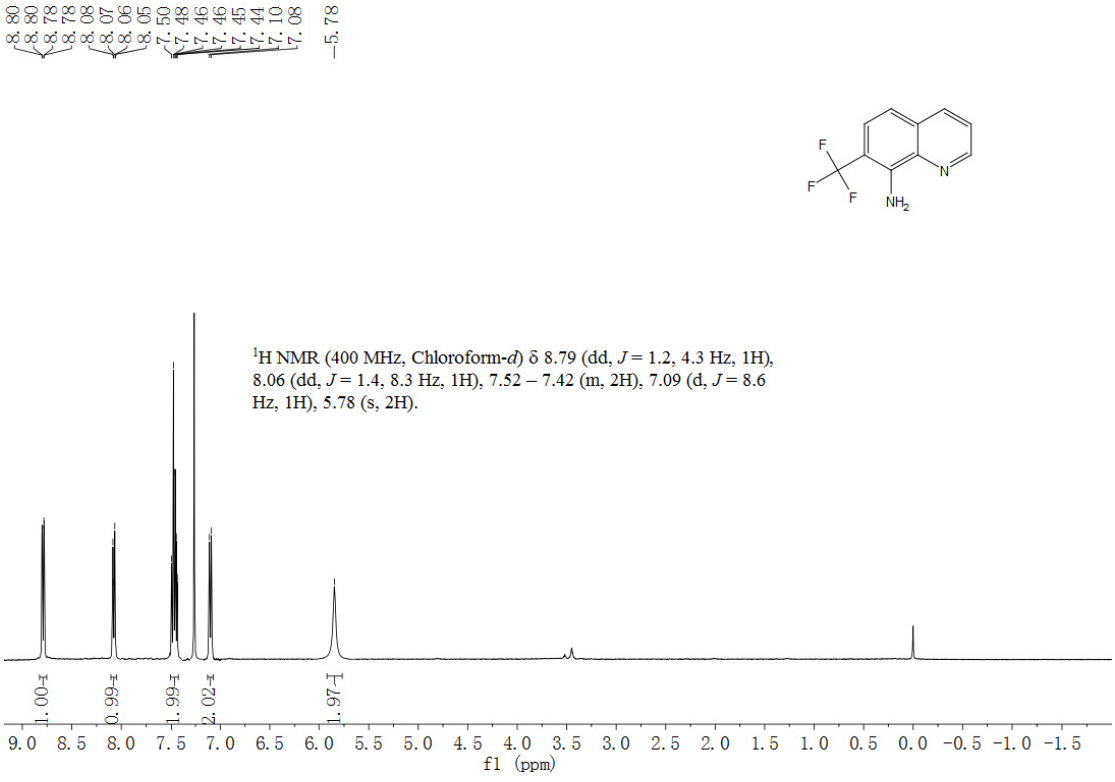


Figure S62. ^{1}H NMR of 7-(trifluoromethyl)quinolin-8-amine.

7. References

1. P. B. Arockiam, G. Lucas and W. D. Joanna, *Adv. Synth. Catal*., 2017, **359**, 2571.

2. H. Egami, Y. Ito, T. Ide, S. Masuda, Y. Hamashima, *Synthesis*, 2018, **50**, 2948.