Cobalt Catalyzed Remote C-4 Functionalization of 8-Aminoquinoline Amides with Ethers *via* C-H Activation under Visible Light Irradiation. Access to α-Heteroarylated Ether Derivatives

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Experimental Section

General Information

Unless otherwise stated, all reagents and solvents were purchased from commercial suppliers and used without further purification. All reactions were performed in oven-dried screw cap tube (10 mL) with a Teflon coated magnetic stirring bar at room temperature, under the irradiation of a 32 W household CFL bulb unless otherwise noted. Reactions were monitored by thin layer chromatography (TLC) on silica gel 60 GF254 and visualization was accomplished by irradiation with UV light at 254 nm vaniline staining solution followed by heating. The crude product was purified by column chromatography on Merck silica gel (100-200 mesh). All ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Bruker Avance III 500, 400 and 300 MHz spectrometers in deuterated solvents ($CDCl_3$). Proton chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$ δ 7.26 ppm). NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, dd = double doublet, ddd = doublet of doublet of doublets), coupling constants (Hz) and integration. ^{13}C chemical shifts are reported in ppm (δ) from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ δ 77.16 ppm). High resolution mass spectra were taken using Q-Tof micro MS system by electron spray ionization (ESI) technique. Elemental analyses were done in our Institute with a Perkin Elmer series II CHNS/O autoanalyser. IR spectra were recorded on Perkin Elmer Spectrum 100 FT-IR Infrared Spectrophotometer as neat for liquid compounds and represented as IR (neat). For solid compounds, IR spectra were recorded by pelletizing them with KBr powder and represented as IR (KBr). The wave numbers (n) are reported in cm^{-1}.

Experimental Procedures

Amides were synthesized according to literature procedures from 8-aminoquinoline and corresponding acids.[1]

General Procedure

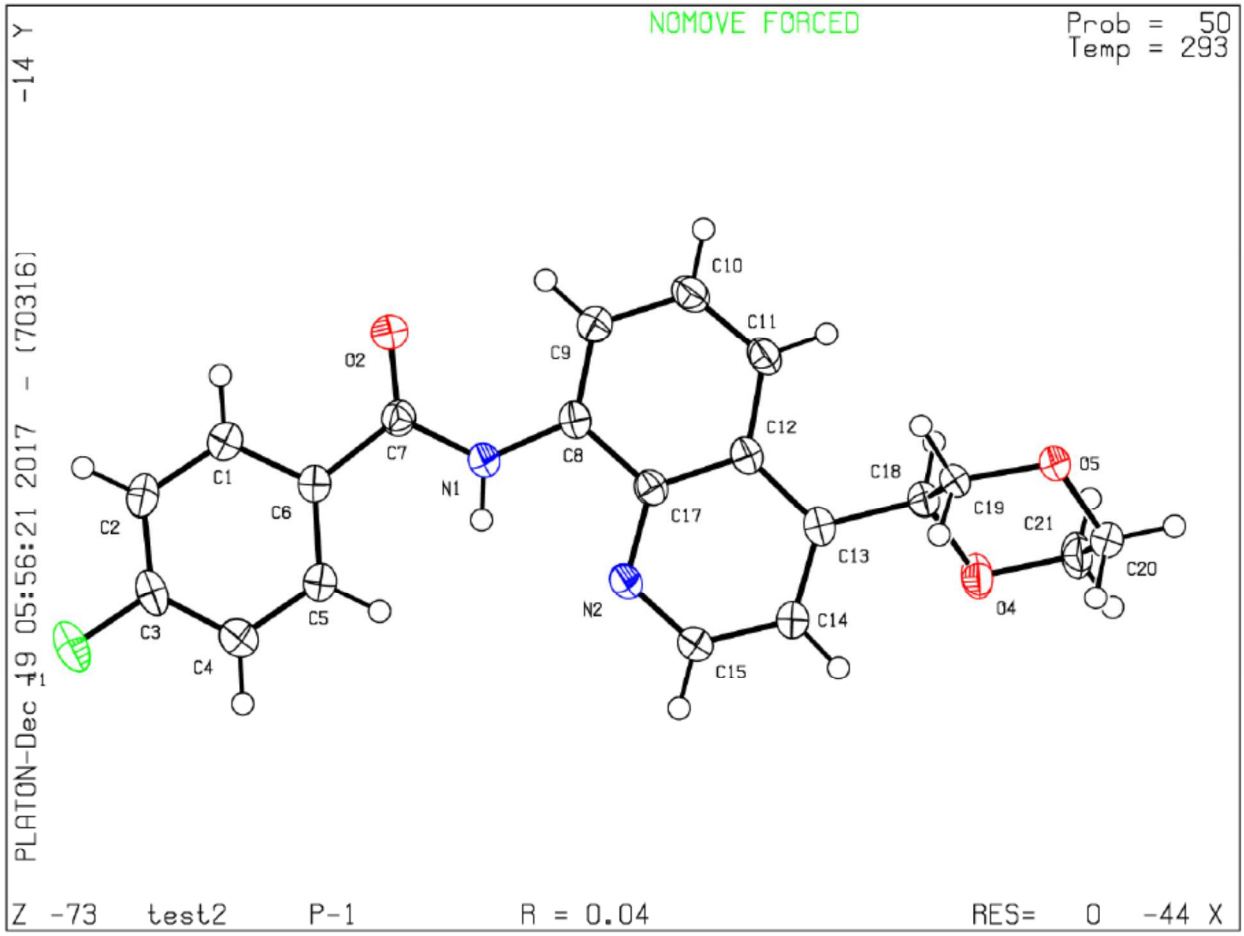
Representative experimental procedure for the reaction of 4-methyl-N-(quinolin-8-yl)benzamide and tetrahydrofuran to 4-methyl-N-(4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (Scheme 2, 1)

A dry screw cap tube (20 mL) equipped with a magnetic stir bar was charged with 4-methyl-N-(quinolin-8-yl)benzamide (260 mg, 1.0 mmol), $Co(acac)_2$ (25 mg, 0.1 mmol, 10 mol %), Eosin Y (13 mg, 0.02 mmol, 2 mol %), Cs_2CO_3 (650 mg, 2.0 mmol, 2 equiv.), DMSO (5 mL) and THF (5 mL) followed by the addition of *t*-BuOOH (5.5 M in decane) (4.0 mmol, 4.0 equiv). Then the reaction vessel was irradiated with a 32 W household CFL bulb under nitrogen atmosphere at

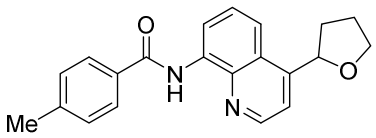
room temperature for 4 h (TLC). After completion of the reaction the mixture was extracted with EtOAc (3x20 mL). The organic phase was dried (Na_2SO_4) and evaporated to leave the crude product, which was purified by silica gel column chromatography (hexane –EtOAc, 94:6) to provide the pure 4-methyl-N-(4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide as a yellowish liquid. (245 mg, 74%): **^{1}H NMR** (300 MHz, Chloroform-*d*) δ 10.86 (s, 1H), 8.93 (t, *J* = 4.5 Hz, 1H), 8.81 (d, *J* = 4.5 Hz, 1H), 8.01 – 7.95 (m, 2H), 7.63 (dd, *J* = 4.5, 1.0 Hz, 1H), 7.60 – 7.56 (m, 2H), 7.36 – 7.29 (m, 2H), 5.66 – 5.57 (m, 1H), 4.24 (ddd, *J* = 8.3, 7.2, 5.6 Hz, 1H), 4.06 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.64 (dtd, *J* = 12.2, 7.7, 6.4 Hz, 1H), 2.45 (s, 4H), 2.13 – 1.97 (m, 2H), 1.93 – 1.81 (m, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.62, 150.29, 148.34, 142.45, 138.75, 135.44, 132.53, 129.58, 127.46, 127.39, 125.37, 117.20, 117.12, 116.19, 76.97, 69.21, 34.17, 26.13, 21.68.

This above procedure was followed for all the reactions listed in Scheme 2 and Scheme 3. These compounds are not reported earlier and were characterized properly by their spectroscopic and spectrometric data (IR, ^{1}H NMR, ^{13}C NMR, HRMS and elemental analysis).

ORTEP Diagram of Compound 29



Characterization data of all synthesized compounds



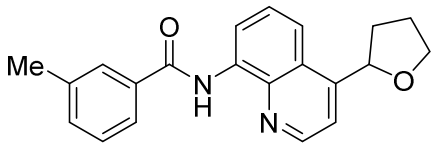
4-Methyl-N-(4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (1): Pale yellow liquid (245 mg, 74%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.86 (s, 1H), 8.93 (t, *J* = 4.5 Hz, 1H), 8.81 (d, *J* = 4.5 Hz, 1H), 8.01 – 7.95 (m, 2H), 7.63 (dd, *J* = 4.5, 1.0 Hz, 1H), 7.60 – 7.56 (m, 2H), 7.36 – 7.29 (m, 2H), 5.66 – 5.57 (m, 1H), 4.24 (ddd, *J* = 8.3, 7.2, 5.6 Hz, 1H), 4.06 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.64 (dtd, *J* = 12.2, 7.7, 6.4 Hz, 1H), 2.45 (s, 4H), 2.13 – 1.97 (m, 2H), 1.93 – 1.81 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.62, 150.29, 148.34, 142.45, 138.75, 135.44, 132.53, 129.58, 127.46, 127.39, 125.37, 117.20, 117.12, 116.19, 76.97, 69.21, 34.17, 26.13, 21.68.

IR (neat): 3349, 2869, 1670, 1531, 1486, 1612 cm^{-1}

Anal. calcd. for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43; found: C 75.69, H 6.31, N 8.78%



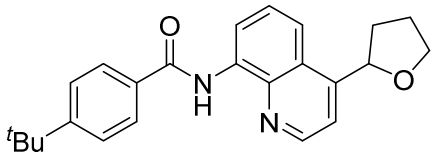
3-Methyl-N-(4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (2): Pale yellow liquid (235 mg, 70%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.85 (s, 1H), 8.93 (t, *J* = 4.5 Hz, 1H), 8.82 (d, *J* = 4.5 Hz, 1H), 7.92 – 7.78 (m, 1H), 7.70 – 7.59 (m, 1H), 7.63 – 7.45 (m, 2H), 7.51 – 7.31 (m, 2H), 5.67 – 5.53 (m, 1H), 4.24 (ddd, *J* = 8.3, 7.2, 5.6 Hz, 1H), 4.06 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.64 (dtd, *J* = 12.1, 7.6, 6.3 Hz, 1H), 2.48 (s, 3H), 2.16 – 1.95 (m, 2H), 1.94 – 1.78 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.84, 150.31, 148.36, 138.78, 138.74, 135.39, 135.34, 132.70, 128.76, 128.20, 127.37, 125.38, 124.38, 117.29, 117.13, 116.28, 76.95, 69.19, 34.17, 26.12, 21.62.

IR (neat): 3348, 2968, 1672, 1530,1483 cm^{-1}

Anal. calcd. for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43; found: C 75.39, H 6.19, N 8.81%



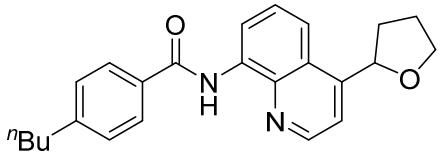
4-(Tert-butyl)-N-(4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (3): Orange liquid (260 mg, 69%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.87 (s, 1H), 8.93 (t, *J* = 4.5 Hz, 1H), 8.81 (d, *J* = 4.5 Hz, 1H), 8.03 (d, *J* = 8.6 Hz, 1H), 7.63 (dd, *J* = 4.5, 1.0 Hz, 1H), 7.63 – 7.42 (m, 4H), 5.62 (t, *J* = 6.9 Hz, 1H), 4.24 (ddd, *J* = 8.3, 7.2, 5.5 Hz, 1H), 4.06 (dt, *J* = 8.4, 7.0 Hz, 1H), 2.64 (dtd, *J* = 12.2, 7.7, 6.3 Hz, 1H), 2.16 – 1.93 (m, 2H), 1.95 – 1.76 (m, 1H), 1.38 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.66, 155.50, 150.36, 148.31, 138.73, 135.46, 132.53, 127.42, 127.32, 125.87, 125.40, 117.20, 117.13, 116.27, 76.98, 69.21, 35.16, 34.19, 31.34, 26.13.

IR (neat): 3356, 2921, 2850, 1675, 1532, 1489 cm^{-1}

HRMS: m/z calcd for $C_{24}H_{26}N_2O_2$: 374.1994 $[M + H]^+$; found: 375.2006.



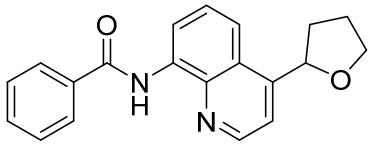
4-Butyl-N-(4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (4): Pale yellow liquid (255 mg, 69%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.86 (s, 1H), 8.98 – 8.88 (m, 1H), 8.81 (d, *J* = 4.5 Hz, 1H), 8.05 – 7.95 (m, 2H), 7.63 (dd, *J* = 4.5, 0.9 Hz, 1H), 7.62 – 7.54 (m, 2H), 7.39 – 7.30 (m, 2H), 5.65 – 5.56 (m, 1H), 4.23 (ddd, *J* = 8.3, 7.2, 5.5 Hz, 1H), 4.05 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.74 – 2.66 (m, 2H), 2.66 – 2.53 (m, 1H), 2.14 – 1.94 (m, 2H), 1.91 – 1.82 (m, 1H), 1.72 – 1.57 (m, 2H), 1.47 – 1.30 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.63, 150.27, 148.31, 147.37, 138.72, 135.45, 132.73, 128.93, 127.45, 127.37, 125.35, 117.16, 117.10, 116.16, 77.58, 77.16, 76.94, 76.74, 69.17, 35.72, 34.15, 33.47, 26.11, 22.44, 14.05.

IR (neat): 333, 2934, 1679, 1533, 1413 cm^{-1}

Anal. calcd. for $C_{24}H_{26}N_2O_2$: C, 76.98; H, 7.00; N, 7.48; found: C 74.68, H 6.77, N 7.27%.



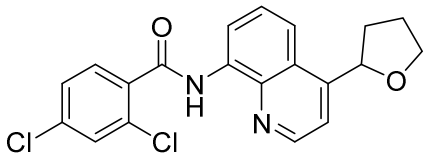
N-(4-(Tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (5): Yellowish gummy liquid (235 mg, 75%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.89 (s, 1H), 8.93 (dd, *J* = 4.9, 4.0 Hz, 1H), 8.81 (d, *J* = 4.5 Hz, 1H), 8.09 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.63 (dd, *J* = 4.5, 0.9 Hz, 1H), 7.61 – 7.51 (m, 5H), 5.61 (t, *J* = 7.1 Hz, 1H), 4.23 (ddd, *J* = 8.3, 7.3, 5.6 Hz, 1H), 4.05 (dt, *J* = 8.2, 7.0 Hz, 1H), 2.63 (dtd, *J* = 12.1, 7.7, 6.3 Hz, 1H), 2.04 (ddt, *J* = 14.0, 12.3, 6.3 Hz, 2H), 1.85 (ddt, *J* = 12.7, 8.0, 6.5 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.57, 150.29, 148.37, 138.74, 135.33, 131.92, 128.90, 127.42, 127.34, 125.37, 117.34, 117.15, 116.23, 76.94, 69.17, 34.15, 26.11.

IR (neat): 3345, 2976, 2868, 1670, 1526, 1483 cm^{-1}

Anal. calcd. For $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80; found: C 75.02, H, 5.76, N, 8.78 %



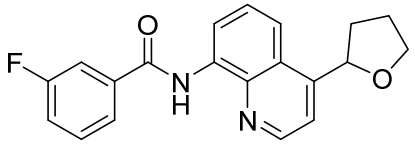
2,4-Dichloro-N-(4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (6): Pale yellow liquid (215 mg, 56%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.85 (s, 1H), 8.89 (dd, *J* = 6.2, 2.7 Hz, 1H), 8.81 (d, *J* = 4.5 Hz, 1H), 8.05 – 7.95 (m, 2H), 7.64 (dd, *J* = 4.5, 1.0 Hz, 1H), 7.62 – 7.56 (m, 2H), 7.55 – 7.48 (m, 2H), 5.61 (ddd, *J* = 7.5, 6.4, 0.9 Hz, 1H), 4.24 (ddd, *J* = 8.3, 7.2, 5.6 Hz, 1H), 4.06 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.71 – 2.58 (m, 1H), 2.14 – 1.97 (m, 2H), 1.92 – 1.81 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.48, 150.41, 148.46, 138.72, 138.26, 135.11, 133.75, 129.20, 128.89, 127.35, 125.41, 117.59, 117.26, 116.33, 76.96, 69.21, 34.19, 26.15.

IR (neat): 3344, 2870, 1676, 1595, 1532, 1481 cm^{-1}

Anal. calcd. for $C_{20}H_{16}Cl_2N_2O_2$: C, 62.03; H, 4.16; N, 7.23; found: C 62.35, H 4.11, N 7.81%



3-Fluoro-N-(4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (7): Yellow liquid (235 mg, 70%)

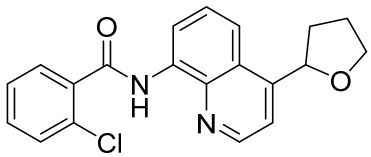
^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.87 (s, 1H), 8.90 (dd, *J* = 6.4, 2.5 Hz, 1H), 8.81 (d, *J* = 4.5 Hz, 1H), 7.86 (ddd, *J* = 7.7, 1.7, 1.0 Hz, 1H), 7.79 (ddd, *J* = 9.4, 2.6, 1.6 Hz, 1H), 7.64 (dd, *J* = 4.5, 1.0 Hz, 1H), 7.64 – 7.55 (m, 2H), 7.52 (td, *J* = 8.0, 5.5 Hz, 1H), 7.34 – 7.21 (m, 1H), 5.61 (ddd, *J* = 7.5, 6.4, 0.9 Hz, 1H), 4.24 (ddd, *J* = 8.4, 7.2, 5.6 Hz, 1H), 4.06 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.64 (dtd, *J* = 12.2, 7.7, 6.3 Hz, 1H), 2.16 – 1.95 (m, 2H), 1.94 – 1.79 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.08 (d, $J_{C\text{-}F}$ = 246.7 Hz), 164.18 (d, $J_{C\text{-}F}$ = 2.2 Hz), 150.41, 148.48, 138.67, 137.61 (d, $J_{C\text{-}F}$ = 7.5 Hz), 135.00, 130.57 (d, $J_{C\text{-}F}$ = 8.2 Hz), 127.32, 125.38, 122.86 (d, $J_{C\text{-}F}$ = 2.2 Hz), 119.11, 118.82, 117.67, 117.26, 116.38, 115.00, 114.69, 76.93, 69.21, 34.17, 26.13.

^{19}F NMR (471 MHz, $CDCl_3$) δ -114.83.

IR (neat): 3342, 2978, 1676, 1587,1531, 1481 cm^{-1}

Anal. calcd. for $C_{20}H_{17}FN_2O_2$: C, 71.42; H, 5.09; N, 8.33; found: C 71.35, H 5.11, N 8.81%.



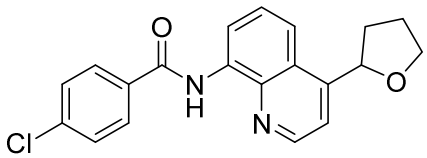
2-Chloro-N-(4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (8): Colorless liquid (200 mg, 57%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.60 (s, 1H), 8.95 (dd, *J* = 6.5, 2.4 Hz, 1H), 8.75 (d, *J* = 4.5 Hz, 1H), 7.85 – 7.73 (m, 1H), 7.61 (dt, *J* = 4.7, 2.5 Hz, 3H), 7.53 – 7.48 (m, 1H), 7.44 – 7.35 (m, 2H), 5.61 (t, *J* = 7.1 Hz, 1H), 4.23 (ddd, *J* = 8.3, 7.2, 5.5 Hz, 1H), 4.05 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.64 (dtd, *J* = 12.2, 7.7, 6.4 Hz, 1H), 2.14 – 1.95 (m, 2H), 1.85 (ddd, *J* = 12.3, 8.0, 6.2 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.05, 150.28, 148.47, 138.59, 136.06, 135.17, 131.60, 131.35, 130.65, 130.16, 127.30, 127.27, 125.39, 117.82, 117.19, 116.64, 76.94, 69.20, 34.18, 26.44, 26.12.

IR (neat): 3332, 2870, 1676, 1527, 1489 cm^{-1}

HRMS: m/z calcd for $C_{20}H_{17}ClN_2O_2$: 352.0979 $[M + Na]^+$; found: 375.0633.



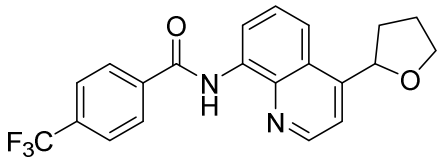
4-Chloro-N-(4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (9): Yellowish gummy liquid (255 mg, 74%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.85 (s, 1H), 8.89 (dd, *J* = 6.2, 2.7 Hz, 1H), 8.80 (d, *J* = 4.3 Hz, 1H), 8.05 – 7.92 (m, 2H), 7.64 (dd, *J* = 4.5, 1.0 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.55 – 7.40 (m, 2H), 5.61 (ddd, *J* = 7.5, 6.5, 0.9 Hz, 1H), 4.23 (ddd, *J* = 8.3, 7.2, 5.6 Hz, 1H), 4.06 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.64 (dtd, *J* = 12.2, 7.7, 6.4 Hz, 1H), 2.13 – 1.98 (m, 2H), 1.92 – 1.81 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.44, 150.40, 148.44, 138.67, 138.23, 135.07, 133.70, 129.17, 128.86, 127.33, 117.58, 117.24, 116.30, 76.93, 69.20, 34.17, 26.13.

IR (neat): 3349, 3010, 2878, 1682, 1447, 1413 cm^{-1}

Anal. calcd. for $C_{20}H_{17}ClN_2O_2$: C, 68.09; H, 4.86; N, 7.94; found: C 68.39, H 4.59, N 7.81%



N-(4-(Tetrahydrofuran-2-yl)quinolin-8-yl)-4-(trifluoromethyl)benzamide (10): Pale yellow liquid (290 mg, 76%)

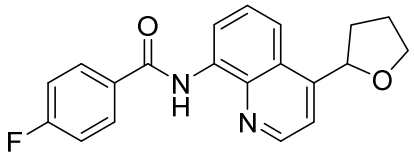
^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.92 (s, 1H), 8.91 (dd, *J* = 6.8, 2.1 Hz, 1H), 8.81 (d, *J* = 4.5 Hz, 1H), 8.19 (dt, *J* = 8.0, 0.8 Hz, 2H), 7.81 (dt, *J* = 8.0, 0.8 Hz, 2H), 7.65 (t, *J* = 2.2 Hz, 1H), 7.66 – 7.52 (m, 2H), 5.61 (ddd, *J* = 7.6, 6.5, 0.9 Hz, 1H), 4.24 (ddd, *J* = 8.3, 7.2, 5.6 Hz, 1H), 4.06 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.65 (dtd, *J* = 12.2, 7.7, 6.3 Hz, 1H), 2.16 – 1.96 (m, 2H), 1.86 (ddt, *J* = 12.2, 8.0, 6.6 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.17, 150.47, 148.54, 138.68, 138.60, 134.89, 133.59 (q, J_{C-F} = 32.6 Hz), 127.90, 127.31, 126.0 (q, J_{C-F} = 3.7 Hz), 125.40, 117.87, 117.33, 116.44, 76.93, 69.21, 34.19, 26.14.

^{19}F NMR (471 MHz, $CDCl_3$) δ -66.18.

IR (neat): 3341, 2872, 1678, 1534, 1489, 1068 cm^{-1}

Anal. calcd. for $C_{21}H_{17}F_3N_2O_2$: C, 65.28; H, 4.44; N, 7.25, 8.09; found: 65.06, 4.69, 7.18%.



4-Fluoro-N-(4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (11): Pale yellow liquid (245 mg, 73%)

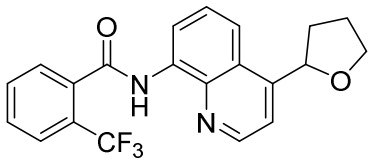
^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.83 (s, 1H), 8.89 (dd, *J* = 5.8, 3.1 Hz, 1H), 8.81 (d, *J* = 4.5 Hz, 1H), 8.14 – 8.02 (m, 2H), 7.64 (dd, *J* = 4.5, 1.0 Hz, 1H), 7.61 – 7.51 (m, 2H), 7.22 (t, *J* = 8.6 Hz, 2H), 5.61 (dd, *J* = 7.6, 6.6 Hz, 1H), 4.24 (ddd, *J* = 8.4, 7.2, 5.6 Hz, 1H), 4.06 (dt, *J* = 8.4, 7.0 Hz, 1H), 2.64 (dtd, *J* = 12.0, 7.6, 6.2 Hz, 1H), 2.15 – 1.93 (m, 2H), 1.93 – 1.76 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.12 (d, J_{C-F} = 250.5 Hz), 164.46, 150.42, 148.41, 138.68, 135.18, 131.53 (d, J_{C-F} = 3.75 Hz), 129.87, 129.75, 127.35, 125.39, 117.47, 117.22, 116.27, 115.96 (d, J_{C-F} = 21.75 Hz), 76.94, 69.20, 34.17, 26.14.

^{19}F NMR (471 MHz, $CDCl_3$) δ -111.03.

IR (neat): 3346, 2870, 1672, 1601, 1534, 1487 cm^{-1}

HRMS: m/z calcd for $C_{20}H_{17}FN_2O_2$: 336.1274 [M + H]+ ; found: 337.1345



N-(4-(Tetrahydrofuran-2-yl)quinolin-8-yl)-2-(trifluoromethyl)benzamide (12): Brownish gummy liquid (44 mg, 57%)

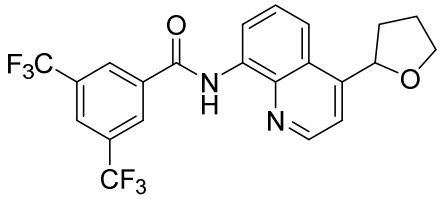
^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.29 (s, 1H), 8.92 (dd, *J* = 6.9, 2.0 Hz, 1H), 8.71 (d, *J* = 4.5 Hz, 1H), 7.78 (ddd, *J* = 10.1, 7.7, 1.5 Hz, 2H), 7.74 – 7.54 (m, 6H), 5.67 – 5.56 (m, 1H), 4.22 (ddd, *J* = 8.3, 7.2, 5.5 Hz, 1H), 4.05 (dt, *J* = 8.5, 7.1 Hz, 1H), 2.63 (dtd, *J* = 12.3, 7.8, 6.4 Hz, 1H), 2.13 – 1.95 (m, 2H), 1.90 – 1.80 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.47, 150.59, 148.78, 138.60, 137.49, 134.44, 132.82 (q, $J_{C\text{-}F}$ = 33.7 Hz), 127.73, 127.69, 127.25, 125.40 (q, $J_{C\text{-}F}$ = 6.0 Hz), 124.93, 121.31, 118.35, 117.48, 116.70, 77.58, 77.16, 76.92, 76.74, 69.24, 34.20, 26.15.

^{19}F NMR (471 MHz, $CDCl_3$) δ -66.18.

IR (neat): 3335, 2978, 2872, 1683, 152, 1483 cm^{-1}

HRMS: m/z calcd for $C_{21}H_{17}F_3N_2O_2$: 386.1242 $[M + H]^+$; found: 387.1143.



N-(4-(Tetrahydrofuran-2-yl)quinolin-8-yl)-3,5-bis(trifluoromethyl)benzamide (13): Orange liquid (310 mg, 69%)

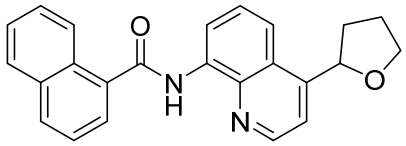
^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.96 (s, 1H), 8.94 – 8.76 (m, 2H), 8.50 (s, 2H), 8.09 (s, 1H), 7.71 – 7.65 (m, 2H), 7.61 (dd, *J* = 8.6, 7.3 Hz, 1H), 5.62 (t, *J* = 7.1 Hz, 1H), 4.25 (td, *J* = 7.8, 5.7 Hz, 1H), 4.07 (dt, *J* = 8.4, 7.1 Hz, 1H), 2.74 – 2.59 (m, 1H), 2.15 – 1.99 (m, 2H), 1.88 (ddd, *J* = 12.4, 7.9, 6.2 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.06, 150.35, 148.44, 138.40, 137.19, 136.35, 135.06, 132.29, 130.24, 128.64, 127.28, 126.80 (q, $J_{C\text{-}F}$ = 4.5 Hz), 125.35, 117.97, 117.21, 116.62, 77.58, 77.16, 76.91, 76.74, 69.19, 34.17, 26.09.

^{19}F NMR (471 MHz, $CDCl_3$) δ -62.20.

IR (neat): 3343, 2920, 1674, 1447, 1533, 1403 cm^{-1}

Anal. calcd. for $C_{22}H_{16}F_6N_2O_2$: C, 58.16; H, 3.55; N, 6.17; found: C 57.91, H 3.52, N 6.01%.



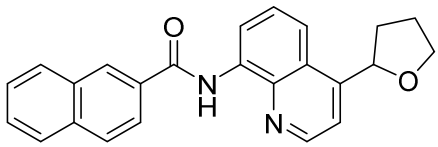
N-(4-(Tetrahydrofuran-2-yl)quinolin-8-yl)-1-naphthamide (14): Pale yellow liquid (240 mg, 66%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.56 (s, 1H), 9.05 (dd, *J* = 5.0, 3.9 Hz, 1H), 8.71 (d, *J* = 4.5 Hz, 1H), 8.53 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.93 (dd, *J* = 7.2, 1.4 Hz, 2H), 7.65 (d, *J* = 1.3 Hz, 1H), 7.63 (s, 1H), 7.65 – 7.57 (m, 2H), 7.61 – 7.51 (m, 3H), 5.62 (t, *J* = 7.1 Hz, 1H), 4.30 – 4.16 (m, 1H), 4.05 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.65 (dtd, *J* = 12.1, 7.7, 6.3 Hz, 1H), 2.15 – 1.94 (m, 2H), 1.94 – 1.74 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.87, 150.27, 148.39, 138.59, 135.56, 134.85, 134.02, 131.23, 130.49, 128.51, 127.41, 127.33, 126.62, 125.71, 125.65, 125.40, 125.01, 117.60, 117.17, 116.44, 76.95, 69.18, 34.18, 26.11.

IR (neat): 3339, 2983, 1670, 1525, 1485 cm^{-1}

Anal. calcd. for $C_{24}H_{20}N_2O_2$: C, 78.24; H, 5.47; N, 7.60; found: C 78.01, H 5.52, N 7.41%



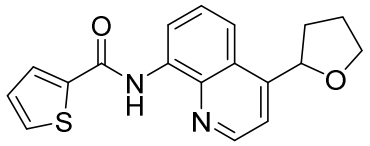
N-(4-(Tetrahydrofuran-2-yl)quinolin-8-yl)-2-naphthamide (15): Pale yellow liquid (250 mg, 69%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 11.04 (s, 1H), 9.08 – 8.94 (m, 1H), 8.86 (dd, *J* = 4.4, 1.7 Hz, 1H), 8.61 (s, 1H), 8.15 (dd, *J* = 8.6, 2.0 Hz, 1H), 8.03 (dd, *J* = 15.2, 8.0 Hz, 2H), 7.98 – 7.85 (m, 1H), 7.62 (qd, *J* = 10.1, 9.5, 4.2 Hz, 5H), 5.64 (t, *J* = 7.2 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 1H), 4.07 (q, *J* = 7.5 Hz, 1H), 2.66 (dq, *J* = 14.4, 7.3 Hz, 1H), 2.08 (tt, *J* = 14.7, 5.9 Hz, 2H), 1.89 (dt, *J* = 13.1, 6.9 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.69, 150.37, 148.46, 138.83, 135.44, 135.11, 132.94, 132.61, 129.38, 128.84, 128.14, 128.00, 127.95, 127.44, 126.95, 125.44, 123.93, 117.41, 117.21, 116.36, 77.00, 69.23, 34.22, 26.17.

IR (neat): 3353, 2924, 1671, 1490, 1531, 1413 cm^{-1}

Anal. calcd. for $C_{24}H_{20}N_2O_2$: C, 78.24; H, 5.47; N, 7.60; found: C 78.01, H 5.52, N 7.31%



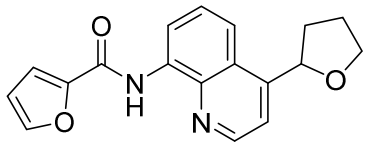
N-(4-(Tetrahydrofuran-2-yl)quinolin-8-yl)thiophene-2-carboxamide (16): Colorless liquid (210 mg, 65%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.74 (s, 1H), 8.91 – 8.63 (m, 2H), 7.84 (dd, *J* = 3.8, 1.2 Hz, 1H), 7.64 (dd, *J* = 4.5, 1.0 Hz, 1H), 7.61 – 7.47 (m, 3H), 7.18 (dd, *J* = 5.0, 3.7 Hz, 1H), 5.64 – 5.55 (m, 1H), 4.24 (ddd, *J* = 8.3, 7.2, 5.6 Hz, 1H), 4.06 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.64 (dtd, *J* = 12.2, 7.7, 6.4 Hz, 1H), 2.13 – 1.94 (m, 2H), 1.85 (ddt, *J* = 12.2, 8.0, 6.5 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.15, 150.32, 148.42, 140.30, 138.48, 135.07, 131.02, 128.56, 127.98, 127.36, 125.36, 117.35, 117.20, 116.21, 76.95, 69.20, 34.17, 26.13.

IR (neat): 3334, 3083, 2869, 1657,1595, 1525 cm^{-1}

HRMS: m/z calcd for $C_{18}H_{16}N_2O_2S$: 324.0932 found $[M + H]^+$; found: 325.0933.



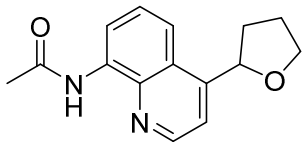
N-(4-(Tetrahydrofuran-2-yl)quinolin-8-yl)furan-2-carboxamide (17): Brownish liquid (215 mg, 71%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.90 (s, 1H), 8.92 – 8.77 (m, 2H), 7.68 – 7.49 (m, 5H), 7.30 (dd, *J* = 3.5, 0.9 Hz, 1H), 6.58 (dd, *J* = 3.5, 1.7 Hz, 1H), 5.61 (t, *J* = 7.1 Hz, 1H), 4.24 (ddd, *J* = 8.4, 7.2, 5.5 Hz, 1H), 4.06 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.64 (dtd, *J* = 12.1, 7.7, 6.3 Hz, 1H), 2.13 – 2.06 (m, 1H), 2.06 – 2.00 (m, 1H), 1.92 – 1.82 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.55, 150.27, 148.52, 144.66, 138.61, 137.16, 134.95, 127.30, 125.41, 117.50, 117.20, 116.43, 115.23, 112.55, 76.96, 69.21, 34.16, 26.14.

IR (neat): 3333, 2870, 1674, 1530, 1586, 1494 cm^{-1}

HRMS: m/z calcd for $C_{18}H_{16}N_2O_3$: 308.1161 [M + H]+ ; found: 309.1168



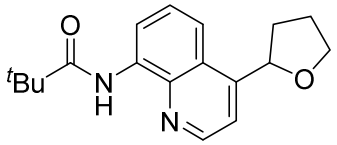
N-(4-(Tetrahydrofuran-2-yl)quinolin-8-yl)acetamide (18): Pale yellow liquid (130 mg, 51%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.90 (s, 1H), 8.79 – 8.69 (m, 2H), 7.60 (dd, *J* = 4.6, 1.0 Hz, 1H), 7.57 – 7.47 (m, 2H), 5.58 (t, *J* = 7.1 Hz, 1H), 4.21 (td, *J* = 7.7, 5.7 Hz, 1H), 4.04 (dt, *J* = 8.3, 7.1 Hz, 1H), 2.61 (dq, *J* = 12.4, 7.6 Hz, 1H), 2.34 (s, 3H), 2.03 (ddt, *J* = 15.2, 12.5, 6.2 Hz, 2H), 1.91 – 1.75 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 168.89, 150.23, 148.16, 138.15, 135.22, 127.26, 125.25, 117.07, 117.03, 116.06, 76.90, 69.15, 34.11, 26.09, 25.28.

IR (neat): 3249, 2861, 1671, 1529, 1477 cm^{-1}

Anal. calcd. for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93; found: C 70.39, H 6.00, N 10.69%



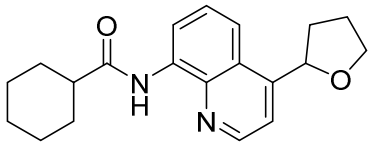
N-(4-(Tetrahydrofuran-2-yl)quinolin-8-yl)pivalamide (19): Pale yellow liquid (160 mg, 55%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.40 (s, 1H), 8.83 – 8.67 (m, 2H), 7.60 (dd, *J* = 4.5, 1.0 Hz, 1H), 7.57 – 7.49 (m, 2H), 5.65 – 5.54 (m, 1H), 4.23 (ddd, *J* = 8.3, 7.2, 5.5 Hz, 1H), 4.05 (dt, *J* = 8.3, 7.0 Hz, 1H), 2.69 – 2.53 (m, 1H), 2.04 (ddtd, *J* = 17.4, 13.7, 7.0, 6.2, 1.5 Hz, 2H), 1.82 (ddt, *J* = 12.2, 8.1, 6.5 Hz, 1H), 1.42 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 177.42, 150.17, 148.32, 138.77, 135.47, 127.35, 125.29, 116.98, 116.87, 115.91, 76.96, 69.18, 40.52, 34.19, 27.88, 26.11.

IR (neat): 3359, 2961, 1681, 1529, 1489 cm^{-1}

Anal. calcd. for $C_{18}H_{22}N_2O_2$: C, 72.46; H, 7.43; N, 9.39; found: C 72.39, H 7.38, N 9.09 %



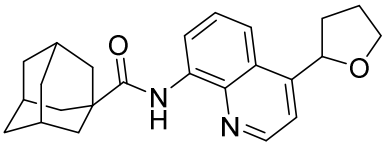
N-(4-(Tetrahydrofuran-2-yl)quinolin-8-yl)cyclohexanecarboxamide (20): Pale Orange liquid (210 mg, 66%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.01 (s, 1H), 8.83 – 8.69 (m, 2H), 7.60 (dd, *J* = 4.5, 0.9 Hz, 1H), 7.56 – 7.47 (m, 2H), 5.58 (t, *J* = 7.1 Hz, 1H), 4.21 (ddd, *J* = 8.3, 7.2, 5.5 Hz, 1H), 4.03 (dt, *J* = 8.4, 7.1 Hz, 1H), 2.61 (dtd, *J* = 12.2, 7.7, 6.4 Hz, 1H), 2.47 (tt, *J* = 11.6, 3.5 Hz, 1H), 2.15 – 1.99 (m, 4H), 2.04 – 1.90 (m, 1H), 1.94 – 1.79 (m, 2H), 1.84 – 1.65 (m, 1H), 1.61 (td, *J* = 12.2, 3.3 Hz, 2H), 1.42 (dt, *J* = 13.7, 3.2 Hz, 1H), 1.40 – 1.26 (m, 2H), 1.31 – 1.19 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 174.98, 150.19, 148.16, 138.42, 135.38, 127.31, 125.27, 116.97, 116.85, 116.08, 76.91, 69.14, 47.04, 34.12, 29.88, 26.08, 25.91, 25.88.

IR (neat): 3352, 2928, 2854, 1686, 1526, 1486 cm^{-1}

HRMS: m/z calcd for $C_{20}H_{24}N_2O_2$: 324.1838 $[M + H]^+$; found: 325.1837.



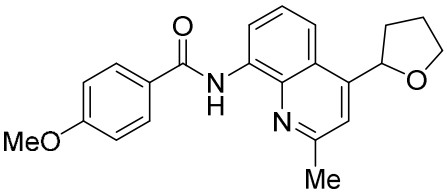
(3r,5r,7r)-N-(4-(Tetrahydrofuran-2-yl)quinolin-8-yl)adamantane-1-carboxamide (21): Gummy Yellow liquid (230 mg, 61%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.35 (s, 1H), 8.80 (dd, *J* = 8.0, 4.7 Hz, 2H), 7.60 (dd, *J* = 4.5, 0.9 Hz, 1H), 7.52 (s, 1H), 7.51 (d, *J* = 1.4 Hz, 1H), 5.58 (t, *J* = 7.1 Hz, 1H), 4.22 (td, *J* = 7.7, 5.6 Hz, 1H), 4.04 (dt, *J* = 8.3, 7.1 Hz, 1H), 2.68 – 2.52 (m, 1H), 2.19 – 2.04 (m, 10H), 2.09 – 1.83 (m, 2H), 1.79 (t, *J* = 3.1 Hz, 7H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 176.89, 150.12, 148.26, 138.77, 135.38, 127.32, 125.24, 116.91, 116.79, 115.99, 76.90, 69.15, 42.37, 39.44, 36.64, 34.13, 28.35, 26.07.

IR (neat): 3356, 2904, 2850, 1677, 1528, 1488 cm^{-1}

HRMS: m/z calcd for $C_{24}H_{28}N_2O_2$: 376.2151 $[M + H]^+$; found: 377.2158.



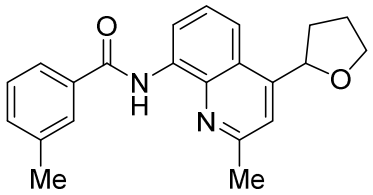
4-Methoxy-N-(2-methyl-4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (22): Pale orange liquid (265 mg, 73%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.89 (s, 1H), 8.87 (dd, *J* = 5.5, 3.4 Hz, 1H), 8.05 (d, *J* = 8.9 Hz, 1H), 7.58 – 7.38 (m, 3H), 7.05 (d, *J* = 8.9 Hz, 2H), 5.57 (ddd, *J* = 7.6, 6.6, 1.0 Hz, 1H), 4.24 (ddd, *J* = 8.3, 7.2, 5.6 Hz, 1H), 4.05 (dt, *J* = 8.3, 7.1 Hz, 1H), 3.90 (s, 3H), 2.77 (s, 3H), 2.72 – 2.54 (m, 1H), 2.15 – 1.95 (m, 2H), 1.84 (ddt, *J* = 12.2, 8.1, 6.7 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.04, 162.60, 157.19, 150.10, 138.34, 134.88, 129.26, 127.87, 126.36, 123.63, 117.66, 116.92, 116.08, 114.15, 77.01, 69.15, 55.62, 34.15, 26.16, 25.76.

IR (neat): 3344, 2953, 1667, 1606, 1535, 1488, 1248 cm^{-1}

Anal. calcd. for $C_{22}H_{22}N_2O_3$: C, 72.91; H, 6.12; N, 7.73; found: C 72.71, H 6.22, N 7.71%



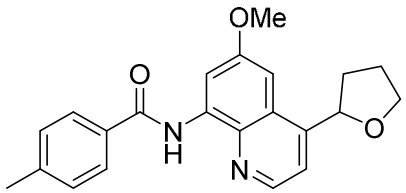
3-Methyl-N-(2-methyl-4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide (23): Pale yellow liquid (225 mg, 65%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.94 (s, 1H), 8.88 (dd, *J* = 6.1, 2.8 Hz, 1H), 7.91 (tt, *J* = 1.7, 0.8 Hz, 1H), 7.91 – 7.63 (m, 1H), 7.57 – 7.48 (m, 3H), 7.48 – 7.35 (m, 2H), 5.57 (ddd, *J* = 7.6, 6.6, 1.0 Hz, 1H), 4.24 (ddd, *J* = 8.3, 7.2, 5.6 Hz, 1H), 4.05 (dt, *J* = 8.3, 7.1 Hz, 1H), 2.76 (s, 3H), 2.63 (dtd, *J* = 12.2, 7.7, 6.2 Hz, 1H), 2.49 (s, 3H), 2.16 – 1.96 (m, 2H), 1.84 (ddt, *J* = 12.2, 8.1, 6.7 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.69, 157.28, 150.10, 138.79, 138.37, 135.55, 134.77, 132.61, 128.79, 128.30, 126.34, 124.29, 123.64, 117.70, 117.15, 116.24, 77.01, 69.16, 34.16, 26.17, 25.75, 21.64.

IR (neat): 335, 2986,1672, 1533, 1485, 1604 cm^{-1}

Anal. calcd. for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09; found: C 76.09, H 6.46, N 7.95 %.



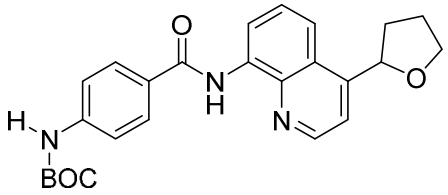
N-(6-Methoxy-4-(tetrahydrofuran-2-yl)quinolin-8-yl)-4-methylbenzamide (24): Pale Orange liquid (250 mg, 70%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.83 (s, 1H), 8.71 (d, *J* = 2.6 Hz, 1H), 8.64 (d, *J* = 4.5 Hz, 1H), 8.00 – 7.93 (m, 2H), 7.57 (dd, *J* = 4.5, 0.9 Hz, 1H), 7.37 – 7.30 (m, 2H), 6.84 (d, *J* = 2.6 Hz, 1H), 5.51 (dd, *J* = 7.6, 6.4 Hz, 1H), 4.23 (ddd, *J* = 8.3, 7.2, 5.5 Hz, 1H), 4.03 (dd, *J* = 8.3, 7.1 Hz, 1H), 3.97 (s, 3H), 2.61 (dtd, *J* = 12.1, 7.7, 6.3 Hz, 1H), 2.44 (s, 4H), 2.06 (dddd, *J* = 14.7, 9.5, 7.2, 6.1 Hz, 2H), 1.92 – 1.82 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.61, 158.33, 148.54, 145.74, 142.54, 136.38, 132.33, 129.58, 127.43, 126.21, 117.60, 107.60, 97.12, 77.59, 77.16, 77.02, 76.74, 69.13, 55.78, 33.60, 26.08, 21.67.

IR (neat): 3359, 2921, 2907, 1673, 1612, 1546 cm^{-1}

Anal. calcd. for $C_{22}H_{22}N_2O_3$: C, 72.91; H, 6.12; N, 7.73; found: C 72.75, H 6.38, N 7.51%



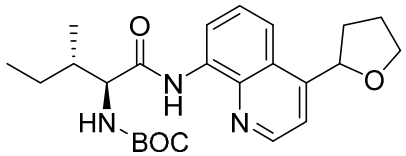
***Tert*-butyl (4-((4-(tetrahydrofuran-2-yl)quinolin-8-yl)carbamoyl)phenyl)carbamate (25):** Colorless liquid (270 mg, 62%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.83 (s, 1H), 8.91 (t, *J* = 4.5 Hz, 1H), 8.81 (d, *J* = 4.5 Hz, 1H), 8.06 – 8.01 (m, 2H), 7.63 (dd, *J* = 4.5, 0.9 Hz, 1H), 7.58 (d, *J* = 4.5 Hz, 2H), 7.56 – 7.51 (m, 2H), 6.76 (s, 1H), 5.62 (t, *J* = 7.1 Hz, 1H), 4.28 – 4.19 (m, 1H), 4.15 – 3.98 (m, 1H), 2.71 – 2.56 (m, 1H), 2.14 – 1.97 (m, 2H), 1.93 – 1.82 (m, 1H), 1.54 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.04, 152.43, 150.33, 148.34, 141.94, 138.72, 135.43, 129.50, 128.66, 127.40, 125.38, 118.05, 117.16, 117.13, 116.20, 81.30, 77.58, 77.37, 77.16, 76.98, 76.74, 69.21, 34.18, 28.45, 26.14.

IR (neat): 3336, 297, 1658, 1729, 1487, 1523 cm^{-1}

Anal. calcd. for $C_{25}H_{27}N_3O_4$: C, 69.27; H, 6.28; N, 9.69; found: C 69.28, H 6.20, N 9.66 %.



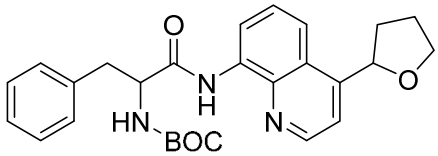
***Tert*-butyl ((2S,3S)-3-methyl-1-oxo-1-((4-(tetrahydrofuran-2-yl)quinolin-8-yl)amino)pentan-2-yl)carbamate (26):** Colorless liquid (250 mg, 59%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.35 (d, *J* = 7.7 Hz, 1H), 8.82 – 8.66 (m, 2H), 7.65 – 7.44 (m, 3H), 5.58 (t, *J* = 7.1 Hz, 1H), 5.31 (d, *J* = 8.7 Hz, 1H), 4.41 – 4.27 (m, 1H), 4.21 (td, *J* = 7.7, 5.6 Hz, 1H), 4.11 – 3.96 (m, 1H), 2.61 (dq, *J* = 12.2, 7.4, 6.9 Hz, 1H), 2.54 – 2.42 (m, 1H), 2.33 – 2.18 (m, 1H), 2.13 – 1.94 (m, 3H), 1.89 – 1.75 (m, 1H), 1.46 (s, 9H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.35, 155.84, 150.11, 148.40, 138.49, 134.69, 127.13, 125.26, 117.47, 117.10, 116.17, 77.58, 77.16, 76.89, 76.74, 69.15, 68.58, 34.13, 28.48, 27.89, 26.07, 25.00, 22.29, 15.87, 11.79.

IR (neat): 3332, 2968, 2876, 1682, 1530, 1488, 1414 cm^{-1}

Anal. calcd. for $C_{24}H_{33}N_3O_4$: 67.42; H, 7.78; N, 9.83; found: C 67.31, H 7.62, N 9.77 %.



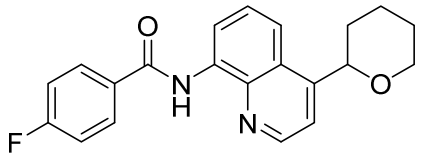
***Tert*-butyl (1-oxo-3-phenyl-1-((4-(tetrahydrofuran-2-yl)quinolin-8-yl)amino)propan-2-yl)carbamate (27):** colorless liquid (285 mg, 62%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.29 (d, *J* = 19.9 Hz, 1H), 8.73 (dt, *J* = 7.0, 2.3 Hz, 1H), 8.66 (dd, *J* = 4.5, 2.2 Hz, 1H), 7.62 – 7.45 (m, 3H), 7.30 – 7.15 (m, 5H), 5.57 (t, *J* = 7.1 Hz, 1H), 5.23 (s, 1H), 4.70 (s, 1H), 4.21 (td, *J* = 7.7, 5.6 Hz, 1H), 4.13 – 3.97 (m, 1H), 3.24 (t, *J* = 5.7 Hz, 2H), 2.68 – 2.52 (m, 1H), 2.12 – 1.96 (m, 2H), 1.82 (dtd, *J* = 12.3, 8.0, 7.3, 2.0 Hz, 1H), 1.42 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.01, 150.07, 148.27, 138.44, 136.66, 136.63, 134.62, 129.48, 128.83, 127.15, 127.05, 125.25, 117.58, 117.08, 116.30, 77.58, 77.16, 76.92, 76.74, 69.18, 38.96, 34.13, 28.45, 26.11.

IR (neat): 3326, 2976, 2928, 2857, 1681, 1530cm^{-1}

Anal. calcd. for $C_{27}H_{31}N_3O_4$: C, 70.26; H, 6.77; N, 9.10; found: C .70.47 H 6.91, N 9.19 %.



4-Fluoro-N-(4-(tetrahydro-2H-pyran-2-yl)quinolin-8-yl)benzamide (28): Yellow liquid (215 mg, 61%)

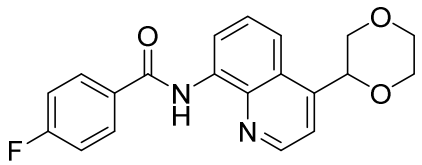
^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.87 (s, 1H), 8.89 (d, *J* = 7.7 Hz, 1H), 8.83 (d, *J* = 4.5 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 9.6 Hz, 1H), 7.69 (d, *J* = 9.1 Hz, 2H), 7.62 – 7.45 (m, 3H), 7.38 – 7.22 (m, 1H), 5.04 (d, *J* = 11.0 Hz, 1H), 4.39 – 4.09 (m, 1H), 3.98 – 3.55 (m, 1H), 2.04 (dd, *J* = 22.1, 10.5 Hz, 2H), 1.90 – 1.46 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.15 (d, $J_{C\text{-}F}$ = 3Hz), 163.08 (d, $J_{C\text{-}F}$ = 269.2 Hz), 149.53, 148.55, 138.77, 137.65 (d, $J_{C\text{-}F}$ = 7.5 Hz), 134.99, 130.55 (d, $J_{C\text{-}F}$ = 8.25 Hz), 127.26, 125.16, 122.85 (d, $J_{C\text{-}F}$ = 3.0 Hz), 119.07, 118.79, 118.21, 117.47, 116.28, 114.99, 114.69, 77.58, 77.16, 76.74, 76.18, 69.36, 33.89, 26.02, 24.15.

^{19}F NMR (471 MHz, $CDCl_3$) δ -114.92, -165.05.

IR (neat): 3344, 2981, 2907, 1663, 1592, 1536 cm^{-1}.

Anal. calcd. for $C_{21}H_{19}FN_2O_2$: C, 71.99; H, 5.47; N, 8.00; found: C 71.78, H 5.51, N 7.75%.



N-(4-(1,4-Dioxan-2-yl)quinolin-8-yl)-4-fluorobenzamide (29): Crystalline solid (230 mg, 66%)

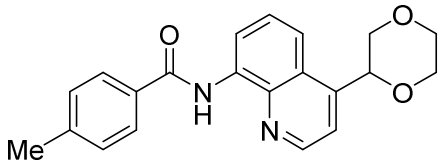
^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.81 (s, 1H), 8.91 (dd, *J* = 7.6, 1.3 Hz, 1H), 8.85 (d, *J* = 4.5 Hz, 1H), 8.13 – 8.05 (m, 2H), 7.73 – 7.67 (m, 2H), 7.62 (dd, *J* = 8.6, 7.6 Hz, 1H), 7.24 – 7.14 (m, 2H), 5.38 (dd, *J* = 9.9, 2.6 Hz, 1H), 4.15 (dd, *J* = 11.8, 2.6 Hz, 1H), 4.10 – 4.04 (m, 2H), 3.90 (dt, *J* = 11.9, 2.0 Hz, 1H), 3.80 (ddd, *J* = 11.8, 8.1, 5.9 Hz, 1H), 3.46 (dd, *J* = 11.8, 9.9 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.66 (d, J_{C-F} = 250.50 Hz), 164.49, 148.35, 144.46, 138.63, 135.30, 131.46 (d, J_{C-F} = 3.0 Hz), 129.88, 129.77, 127.92, 125.20, 119.03, 116.73, 116.30 (d, J_{C-F} = 22.50 Hz), 115.86, 74.32, 72.08, 67.46, 66.75.

^{19}F NMR (471 MHz, $CDCl_3$) δ -110.94.

IR (neat): 3359, 2961, 2917, 1673, 1602, 1536 cm-1

Anal. calcd. for $C_{20}H_{17}FN_2O_3$: C, 68.17; H, 4.86; N, 7.95; found: C 68.01, H 4.52, N 7.71%



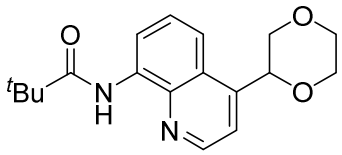
N-(4-(1,4-Dioxan-2-yl)quinolin-8-yl)-4-methylbenzamide (30): Gummy liquid (210 mg, 60%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.82 (s, 1H), 8.94 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.85 (d, *J* = 4.5 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 2H), 7.72 – 7.66 (m, 2H), 7.61 (dd, *J* = 8.6, 7.5 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 5.37 (dd, *J* = 9.9, 2.6 Hz, 1H), 4.15 (dd, *J* = 11.8, 2.6 Hz, 1H), 4.09 – 3.96 (m, 2H), 3.94 – 3.70 (m, 2H), 3.45 (dd, *J* = 11.8, 9.9 Hz, 1H), 2.45 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.59, 148.25, 144.32, 142.50, 138.67, 135.54, 132.44, 129.58, 127.93, 127.44, 125.16, 118.91, 116.43, 116.37, 74.31, 72.07, 67.44, 66.73, 21.67.

IR (neat): 3353, 2962, 2854, 1670, 1531, 1488, 1575 cm^{-1}

Anal. calcd. for $C_{21}H_{20}N_2O_3$: C, 72.40; H, 5.79; N, 8.04; found: C 72.55, H 5.73, N 7.92%.



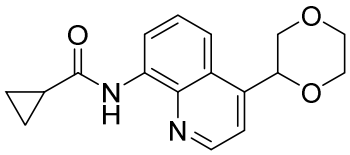
N-(4-(1,4-dioxan-2-yl)quinolin-8-yl)pivalamide (31): Gummy liquid (215 mg, 69%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.37 (s, 1H), 8.84 – 8.75 (m, 2H), 7.68 – 7.60 (m, 2H), 7.55 (dd, *J* = 8.6, 7.6 Hz, 1H), 5.36 (ddd, *J* = 9.9, 2.7, 0.8 Hz, 1H), 4.12 (dd, *J* = 11.8, 2.6 Hz, 1H), 4.08 – 4.02 (m, 2H), 3.87 (t, *J* = 1.8 Hz, 1H), 3.84 – 3.76 (m, 1H), 3.42 (dd, *J* = 11.8, 9.9 Hz, 1H), 1.42 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 177.41, 148.23, 144.24, 138.71, 135.59, 127.90, 125.09, 118.78, 116.11, 74.33, 72.08, 67.44, 66.74, 40.52, 27.87.

IR (neat): 3362, 2962, 1680, 153, 1492, 1116 cm^{-1}

Anal. calcd. for $C_{18}H_{22}N_2O_3$: C, 68.77; H, 7.05; N, 8.91; found: C 68.56, H 7.02, N 9.01 %



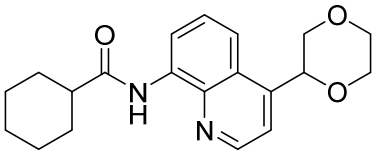
N-(4-(1,4-Dioxan-2-yl)quinolin-8-yl)cyclopropanecarboxamide (32): Gummy liquid (165 mg, 56%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.11 (s, 1H), 8.79 (dd, *J* = 4.5, 1.8 Hz, 1H), 8.73 (d, *J* = 7.6 Hz, 1H), 7.67 – 7.58 (m, 2H), 7.56 – 7.47 (m, 1H), 5.33 (d, *J* = 9.8 Hz, 1H), 4.12 (d, *J* = 11.8 Hz, 1H), 4.03 (dd, *J* = 6.6, 4.2 Hz, 3H), 3.93 – 3.72 (m, 3H), 3.47 – 3.33 (m, 1H), 1.83 – 1.73 (m, 1H), 1.47 (d, *J* = 2.0 Hz, 1H), 1.17 – 1.10 (m, 3H), 0.96 – 0.85 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 172.37, 148.03, 144.23, 138.08, 135.52, 127.84, 125.07, 118.79, 116.22, 116.03, 74.26, 72.01, 67.39, 66.68, 28.18, 16.39, 8.27.

IR (neat): 3349, 2855, 1681, 1526, 1492,1417 cm^{-1}

Anal. calcd. for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39; found: C 68.77, H 6.18, N 9.12 %



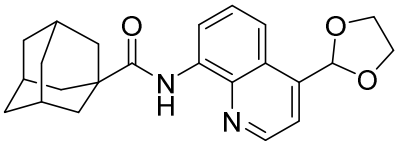
N-(4-(1,4-Dioxan-2-yl)quinolin-8-yl)cyclohexanecarboxamide (33): Gummy liquid (210 mg, 62%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.98 (s, 1H), 8.84 – 8.72 (m, 2H), 7.68 – 7.44 (m, 3H), 5.34 (d, *J* = 9.8 Hz, 1H), 4.08 (dd, *J* = 21.2, 9.3 Hz, 3H), 3.93 – 3.72 (m, 2H), 3.41 (t, *J* = 10.8 Hz, 1H), 2.46 (t, *J* = 12.0 Hz, 1H), 2.12 – 2.00 (m, 3H), 1.86 (d, *J* = 11.7 Hz, 2H), 1.67 (dd, *J* = 27.6, 13.7 Hz, 3H), 1.47 – 1.21 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 174.96, 148.07, 144.23, 138.35, 135.48, 127.85, 125.05, 118.76, 116.26, 116.08, 74.26, 72.02, 67.39, 66.69, 47.02, 29.86, 29.84, 25.89, 25.86.

IR (neat): 3335, 2978, 2872, 1683, 1526, 1483 cm^{-1}

Anal. calcd. for $C_{18}H_{22}N_2O_3$: C, 68.77; H, 7.05; N, 8.91; found: C 68.98, H 7.12, N 9.16 %.



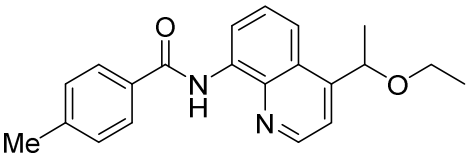
(3*r*,5*r*,7*r*)-N-(4-(1,3-Dioxolan-2-yl)quinolin-8-yl)adamantane-1-carboxamide (34): Pale yellow liquid (305 mg, 81%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.30 (s, 1H), 8.97 – 8.76 (m, 2H), 7.81 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.67 (d, *J* = 4.4 Hz, 1H), 7.56 (t, *J* = 8.1 Hz, 1H), 6.43 (s, 1H), 4.15 (s, 4H), 2.16 – 2.07 (m, 11H), 1.83 – 1.77 (m, 8H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 176.85, 147.99, 143.01, 139.14, 135.17, 127.90, 125.72, 117.87, 117.67, 116.32, 100.65, 77.58, 77.16, 76.74, 65.60, 42.38, 39.44, 38.75, 36.65, 36.53, 28.35, 27.95.

IR (neat): 3361, 2977, 2877, 1678, 1565, 1535, 1484 cm^{-1}

Anal. calcd. for $C_{23}H_{26}N_2O_3$: C, 72.99; H, 6.92; N, 7.40; found: C 73.01, H 6.82, N 7.21%



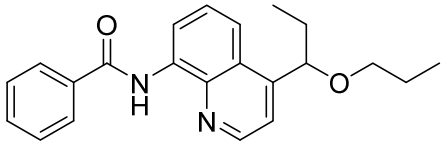
N-(4-(1-Ethoxyethyl)quinolin-8-yl)-4-methylbenzamide (35): Colorless liquid (235 mg, 70%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.87 (s, 1H), 8.94 (d, *J* = 7.7 Hz, 1H), 8.83 (dd, *J* = 4.3, 1.9 Hz, 1H), 8.04 – 7.92 (m, 2H), 7.75 (d, *J* = 8.8 Hz, 1H), 7.59 (q, *J* = 7.9, 5.8 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 3H), 5.16 (q, *J* = 6.7 Hz, 1H), 3.55 – 3.38 (m, 2H), 2.45 (s, 4H), 1.63 – 1.49 (m, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.55, 150.66, 148.34, 142.42, 139.03, 136.48, 135.49, 132.53, 129.57, 127.43, 125.89, 118.08, 116.94, 116.21, 74.19, 64.85, 23.54, 21.66, 15.58.

IR (neat): 3352, 2975, 1672, 1486, 1531, 1413 cm^{-1}

Anal. calcd. for $C_{21}H_{22}N_2O_2$: C, 75.42; H, 6.63; N, 8.38; found: C 75.01, H 6.52, N 8.48%



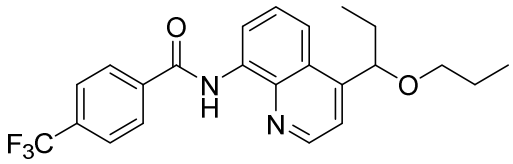
N-(4-(1-Propoxypropyl)quinolin-8-yl)benzamide (36): Colorless liquid (235 mg, 68%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.88 (s, 1H), 8.94 (dd, *J* = 7.7, 1.2 Hz, 1H), 8.83 (d, *J* = 4.5 Hz, 1H), 8.00 (dd, *J* = 8.3, 1.8 Hz, 2H), 7.77 (dd, *J* = 8.7, 1.2 Hz, 1H), 7.65 – 7.52 (m, 2H), 7.35 (d, *J* = 7.9 Hz, 3H), 4.90 (dd, *J* = 7.4, 4.9 Hz, 1H), 3.41 – 3.27 (m, 2H), 2.71 (t, *J* = 7.7 Hz, 3H), 1.95 – 1.82 (m, 2H), 1.65 (q, *J* = 7.1 Hz, 5H), 1.46 – 1.32 (m, 3H), 1.07 – 0.89 (m, 11H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.65, 149.61, 148.09, 147.37, 139.05, 135.46, 132.77, 129.02, 128.95, 127.46, 127.37, 127.32, 126.28, 118.92, 117.17, 116.21, 79.88, 77.58, 77.16, 76.74, 71.57, 35.73, 33.48, 30.62, 23.31, 22.45, 14.05, 10.86, 10.61.

IR (neat): 3363, 2961, 2876, 1674, 1531, 1487, 1386 cm^{-1}

Anal. calcd. for $C_{22}H_{24}N_2O_2$: C, 75.83; H, 6.94; N, 8.04; found: C 75.66, H 6.72, N 8.01%



N-(4-(1-Propoxypropyl)quinolin-8-yl)-4-(trifluoromethyl)benzamide (37): Colorless liquid (290 mg, 70%)

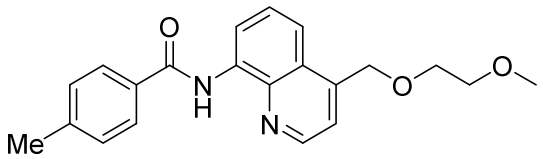
^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.95 (s, 1H), 8.92 (dd, *J* = 7.6, 1.2 Hz, 1H), 8.83 (d, *J* = 4.5 Hz, 1H), 8.24 – 8.15 (m, 3H), 7.82 (dd, *J* = 8.5, 1.4 Hz, 3H), 7.66 – 7.54 (m, 2H), 4.90 (dd, *J* = 7.4, 5.0 Hz, 1H), 3.35 (td, *J* = 6.6, 4.1 Hz, 2H), 1.89 (td, *J* = 7.3, 4.9 Hz, 2H), 1.65 (q, *J* = 6.9 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.18, 149.85, 148.31, 139.00, 138.64, 134.91, 133.56 (q, $J_{C\text{-}H}$ = 13.5 Hz), 127.90, 127.79, 127.25, 126.30, 126.0 (q, $J_{C\text{-}H}$ = 3.7 Hz), 119.15, 117.92, 116.49, 79.94, 77.58, 77.16, 76.74, 71.63, 30.64, 23.32, 10.87, 10.60.

^{19}F NMR (471 MHz, $CDCl_3$) δ -66.19.

IR (neat): 3344, 2935, 2966, 1680, 1532, 1489, 1325 cm^{-1}

Anal. calcd. for $C_{23}H_{23}F_3N_2O_2$: C, 66.34; H, 5.57; N, 6.73;; found: C 66.31, H 5.42, N 6.91 %



N-(4-((Methoxyethoxy)methyl)quinolin-8-yl)-4-methylbenzamide (38): Pale orange liquid (240 mg, 72%)

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.82 (s, 1H), 8.93 (dd, *J* = 7.2, 1.8 Hz, 1H), 8.82 (d, *J* = 4.4 Hz, 1H), 8.09 – 7.83 (m, 3H), 7.65 – 7.60 (m, 2H), 7.60 (d, *J* = 2.6 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 3H), 5.07 (d, *J* = 1.0 Hz, 2H), 3.97 – 3.71 (m, 2H), 3.71 – 3.60 (m, 2H), 3.43 (s, 3H), 2.45 (s, 3H).

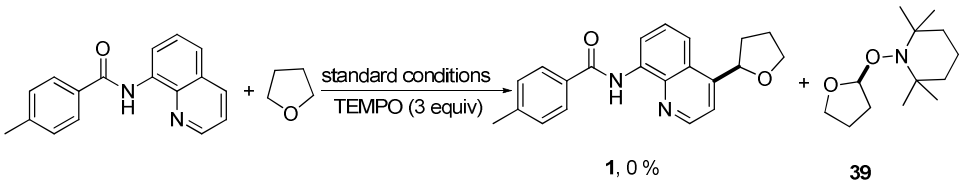
^{13}C NMR (75 MHz, $CDCl_3$) δ 165.57, 148.18, 144.33, 142.44, 138.66, 135.36, 132.52, 129.58, 127.68, 127.45, 125.95, 119.81, 116.98, 116.40, 77.58, 77.16, 76.74, 72.13, 70.57, 69.93, 59.32, 21.68.

IR (neat): 3353, 2926, 1671, 1529, 1487 cm^{-1}

HRMS: m/z calcd for $C_{21}H_{22}N_2O_3$: 351.1703 $[M + H]^+$; found: 351.1705.

Mechanism study

Scheme S1a: Radical Trapping Experiment:

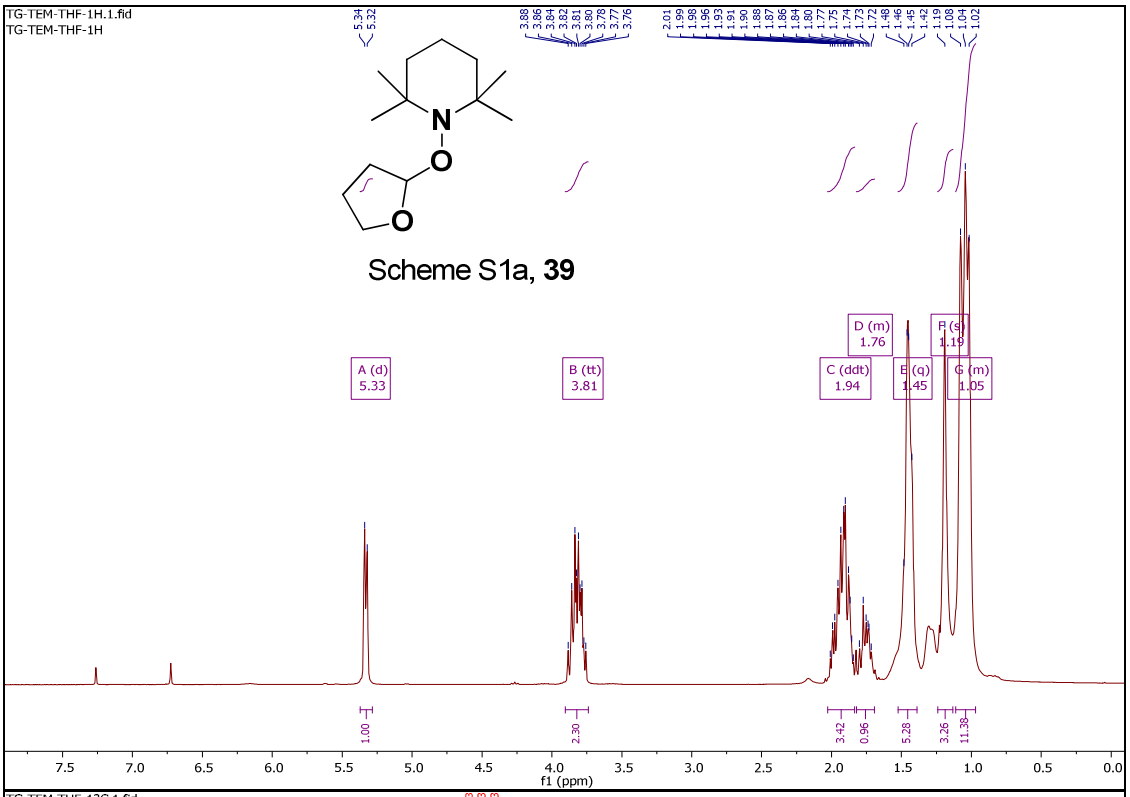


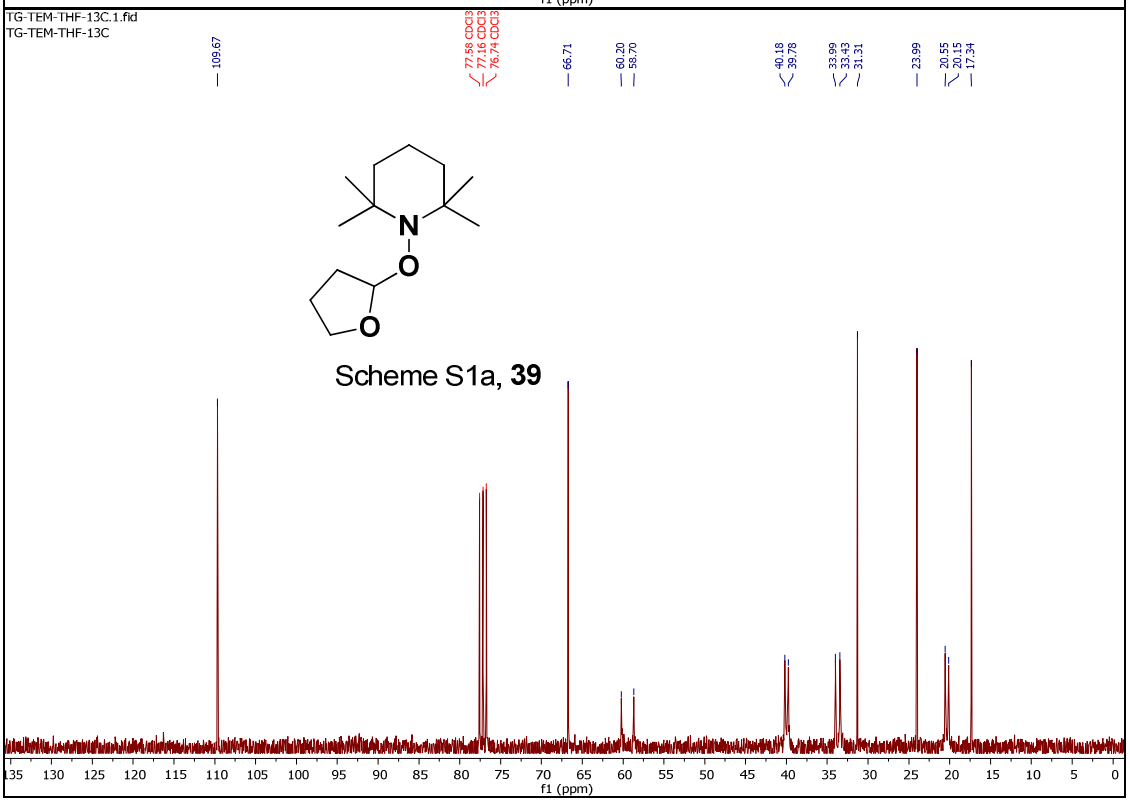
Characterization data of THF-TEMPO adduct:

2,2,6,6-tetramethyl-1-((tetrahydrofuran-2-yl)oxy)piperidine (39)[2]: Colorless liquid

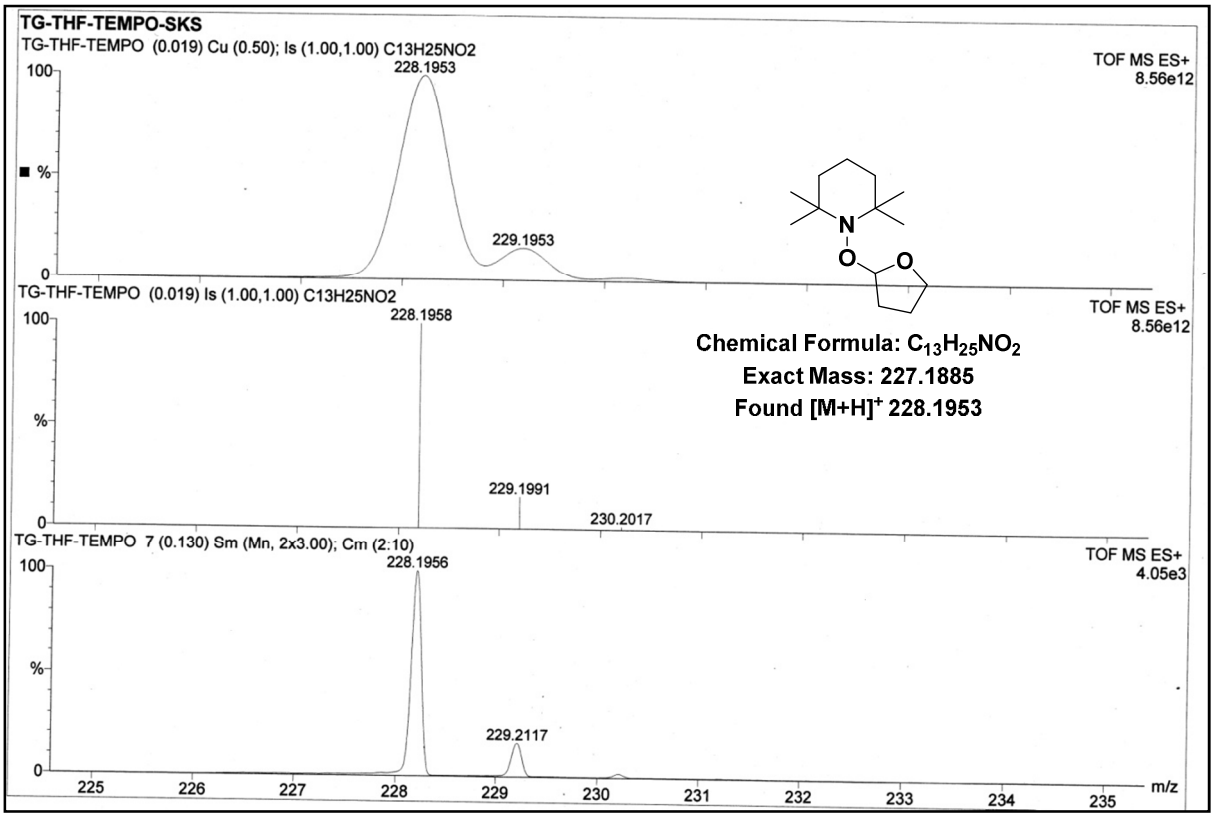
^{1}H NMR (300 MHz, Chloroform-*d*) δ 5.33 (d, *J* = 5.3 Hz, 1H), 3.81 (tt, *J* = 8.2, 6.2 Hz, 2H), 1.94 (ddt, *J* = 20.2, 10.2, 4.2 Hz, 3H), 1.82 – 1.69 (m, 1H), 1.45 (q, *J* = 6.9 Hz, 5H), 1.19 (s, 3H), 1.11 – 0.97 (m, 11H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 109.67, 77.58, 77.16, 76.74, 66.71, 60.20, 58.70, 40.18, 39.78, 33.99, 33.43, 31.31, 23.99, 20.55, 20.15, 17.34.

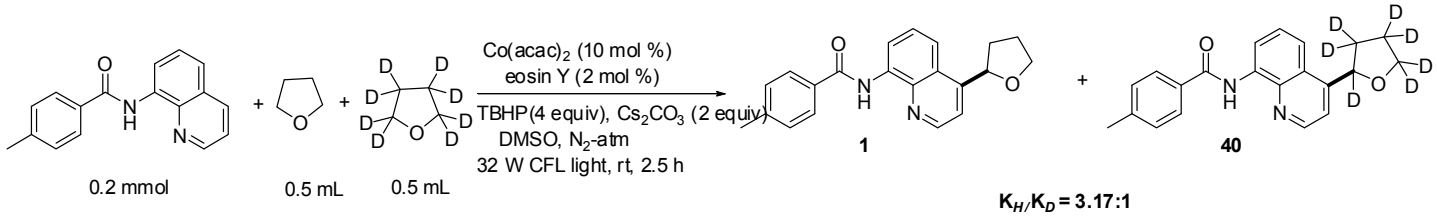




High resolution mass spectrum of 39



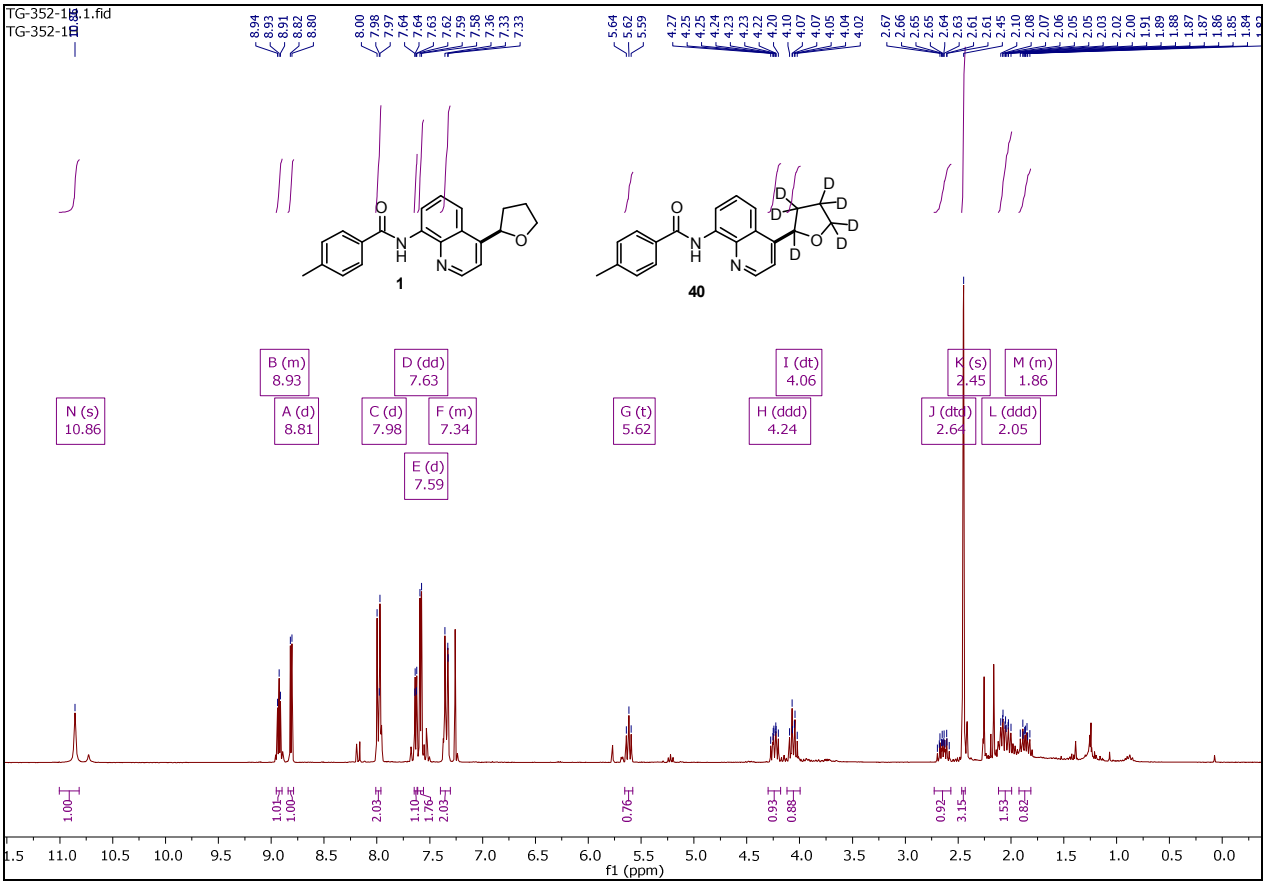
Scheme S1b: Kinetic isotope effect experiment



Experimental procedure for kinetic isotope experiment:

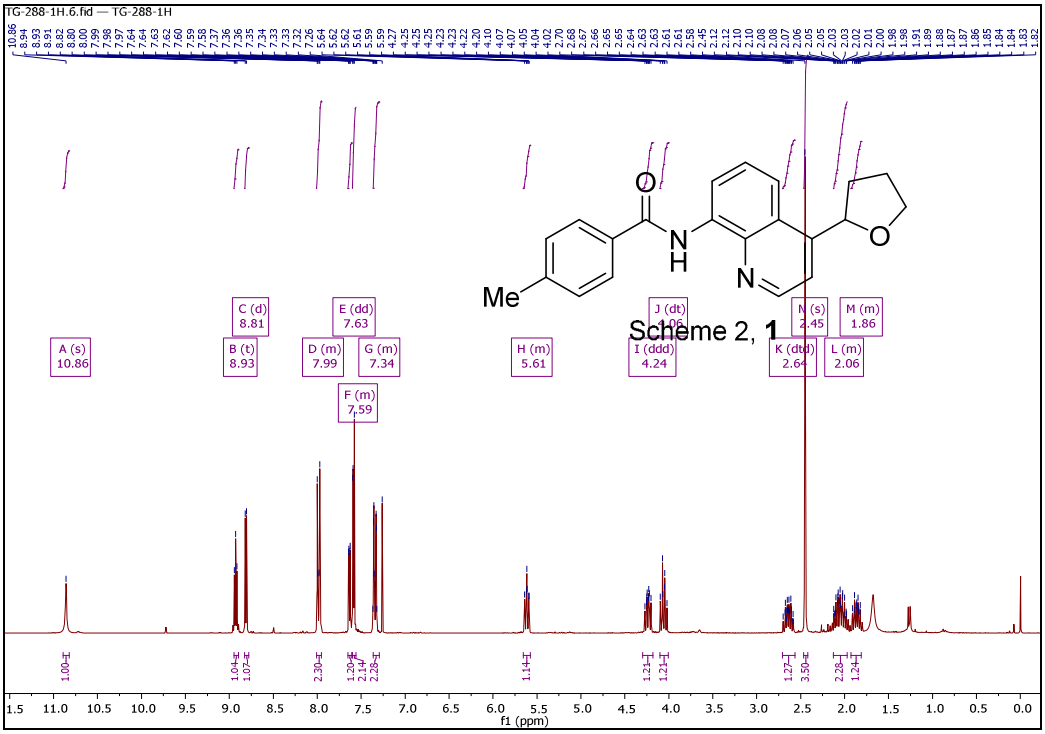
A dry screw cap tube (10 mL) equipped with a magnetic stir bar was charged with 4-methyl-N-(quinolin-8-yl)benzamide (52 mg, 0.2 mmol), $Co(acac)_2$ (5 mg, 0.02 mmol, 10 mol %), Eosin Y (2.6 mg, 0.004 mmol, 2 mol %), Cs_2CO_3 (130 mg, 0.4 mmol, 2 equiv.) followed by the addition of DMSO (2 mL) and THF (0.5 mL) and d^8-THF(0.5 mL). Finally *t*-BuOOH (5.5 M in decane) (0.8 mmol, 4.0 equiv) was added to the mixture. Then the reaction vessel was irradiated with a

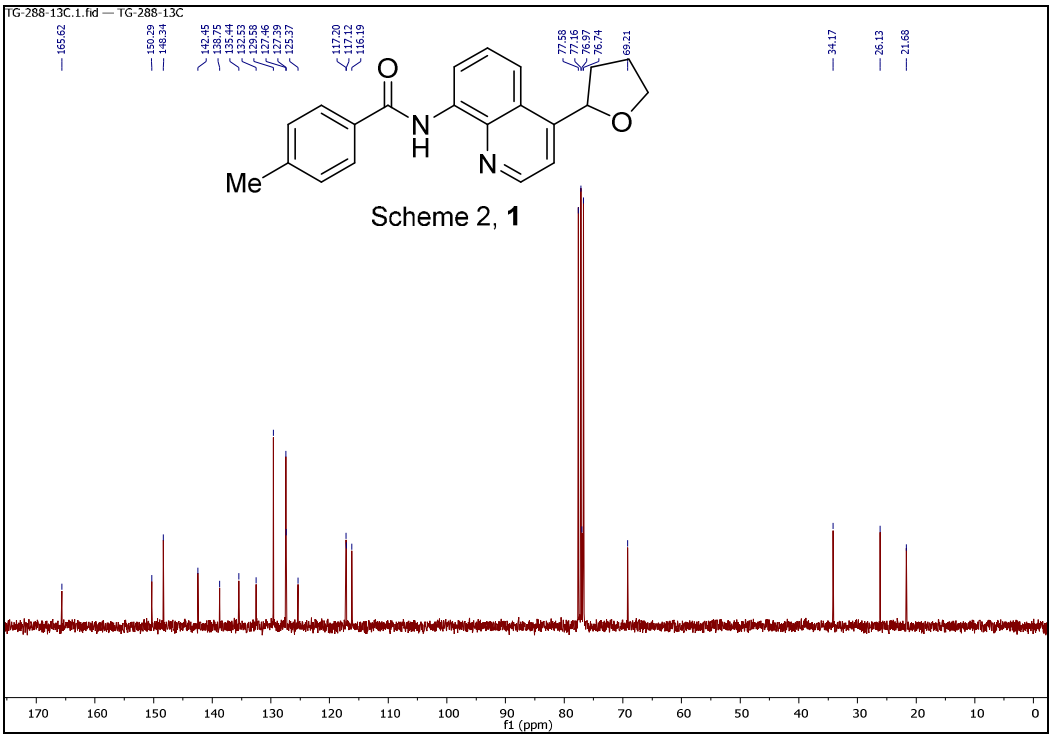
32 W household CFL bulb under nitrogen atmosphere at room temperature for 2.5 h. Then the resultant mixture was extracted with EtOAc (3x20 mL). The organic phase was dried (Na_2SO_4) and evaporated to leave the crude product, which was further purified by silica gel column chromatography to provide the pure 4-methyl-N-(4-(tetrahydrofuran-2-yl)quinolin-8-yl)benzamide as a yellowish liquid.

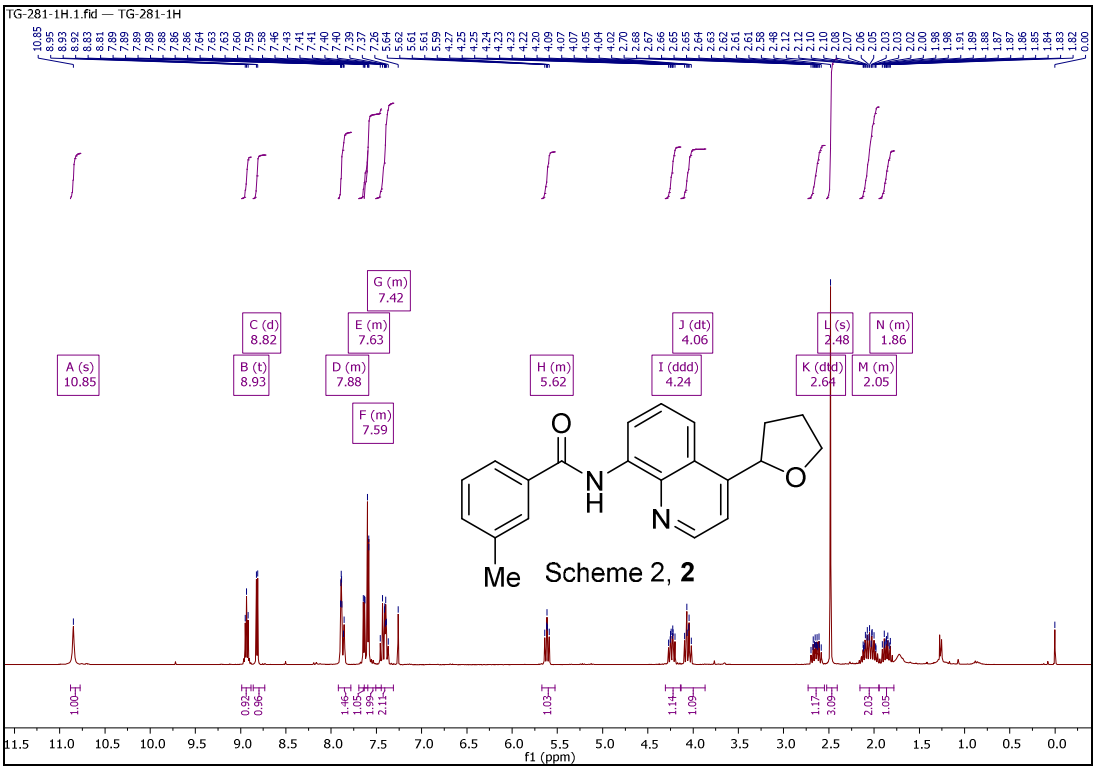


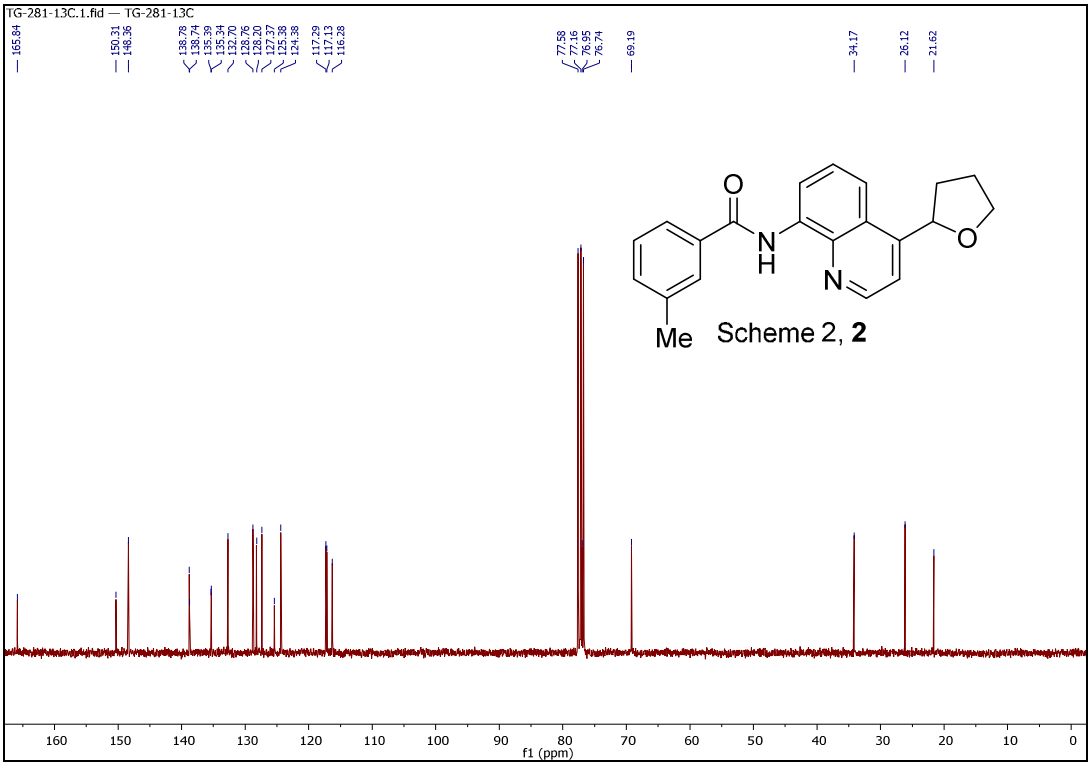
References:

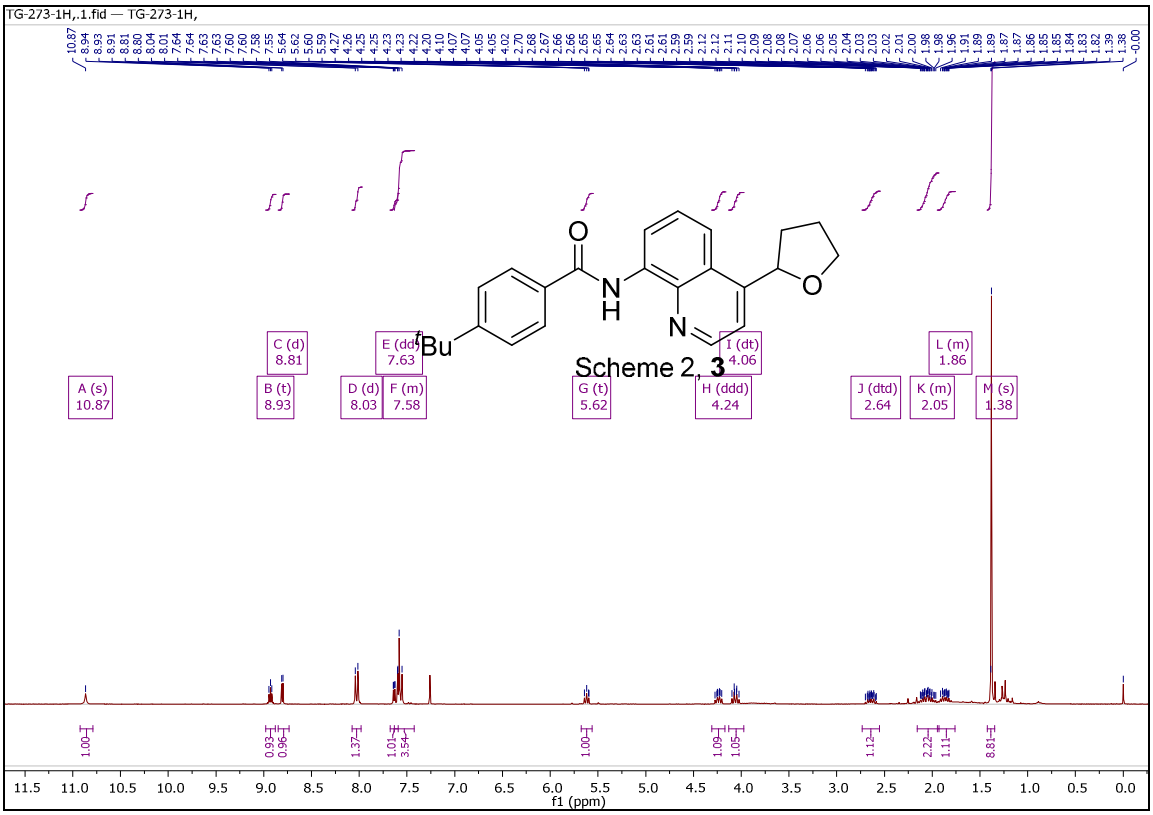
(1) Ano, Y.; Tobisu, M.; Chatani, N. *Org. Lett.*, **2012**, *14*, 354.
(2) Li, L.; Yu, Z.; Shen, Z. *Adv. Synth. Catal.* **2015**, *357*, 3495.

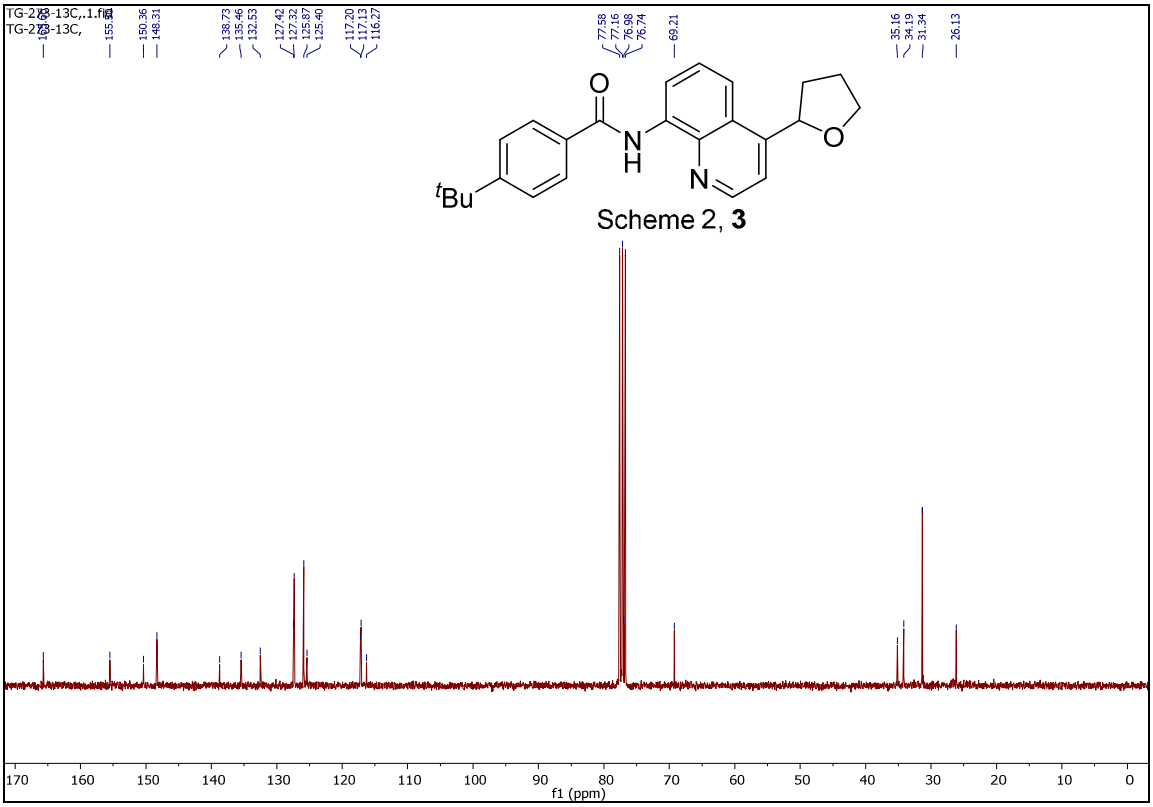

TG-288-1H.6.fid — TG-288-1H
Scheme 2, 1
A (s) 10.86
B (t) 8.93
C (d) 8.81
D (m) 7.99
E (dd) 7.63
F (m) 7.59
G (m) 7.34
H (m) 5.61
I (ddd) 4.24
J (dt) 4.06
K (dtd) 2.64
L (m) 2.06
M (m) 1.86
N (s) 2.45
f1 (ppm)

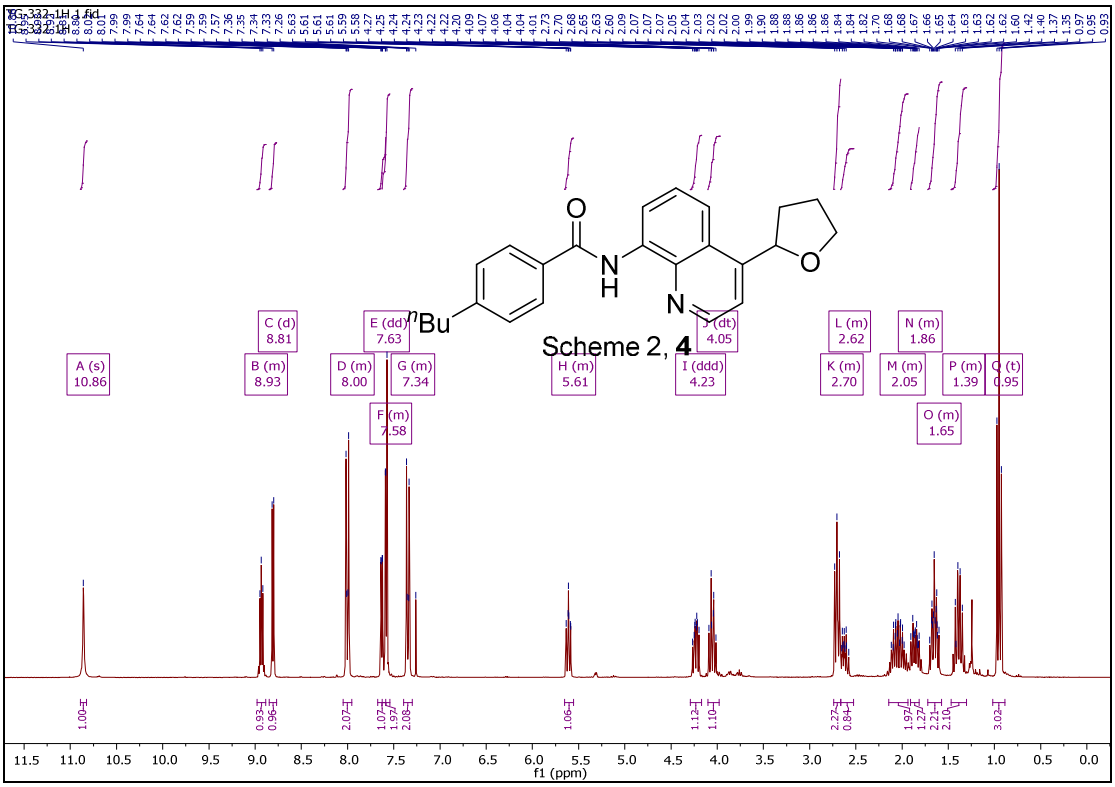

TG-288-13C.1.fid — TG-288-13C
Scheme 2, 1
f1 (ppm)

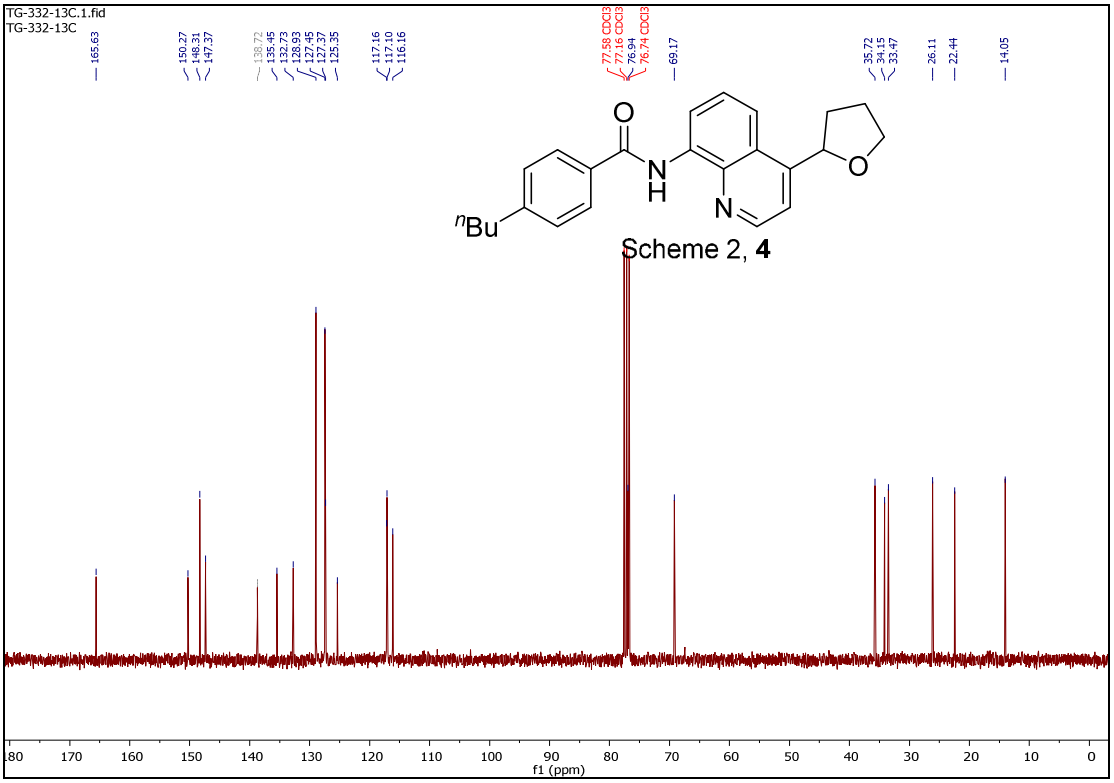

TG-281-1H.1.fid — TG-281-1H
A (s) 10.85
B (t) 8.93
C (d) 8.82
D (m) 7.88
E (m) 7.63
F (m) 7.59
G (m) 7.42
H (m) 5.62
I (ddd) 4.24
J (dt) 4.06
K (dtd) 2.64
L (s) 2.48
M (m) 2.05
N (m) 1.86
Me
Scheme 2, 2
f1 (ppm)

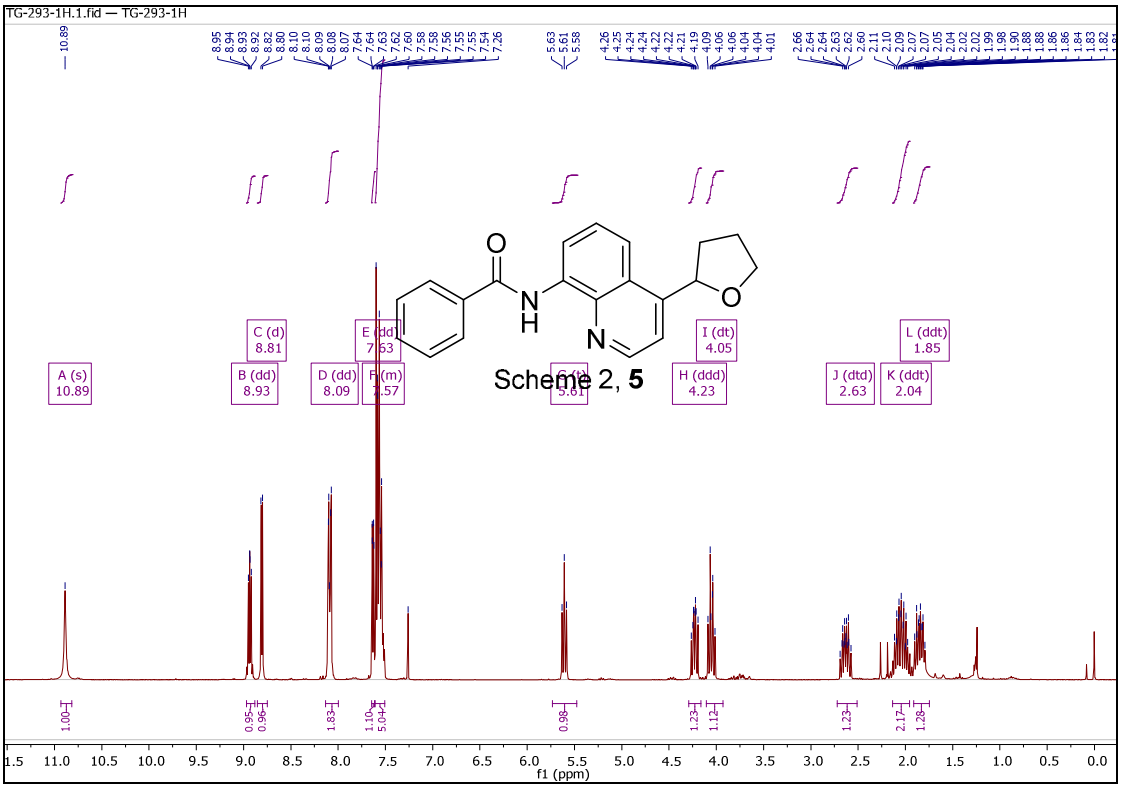

TG-281-13C.1.fid — TG-281-13C
165.84
150.31
148.36
138.78
138.74
135.39
135.34
132.70
128.76
128.20
127.37
125.38
124.38
117.39
117.13
116.28
77.58
77.16
76.95
76.74
69.19
34.17
26.12
21.62
Me
Scheme 2, 2
f1 (ppm)

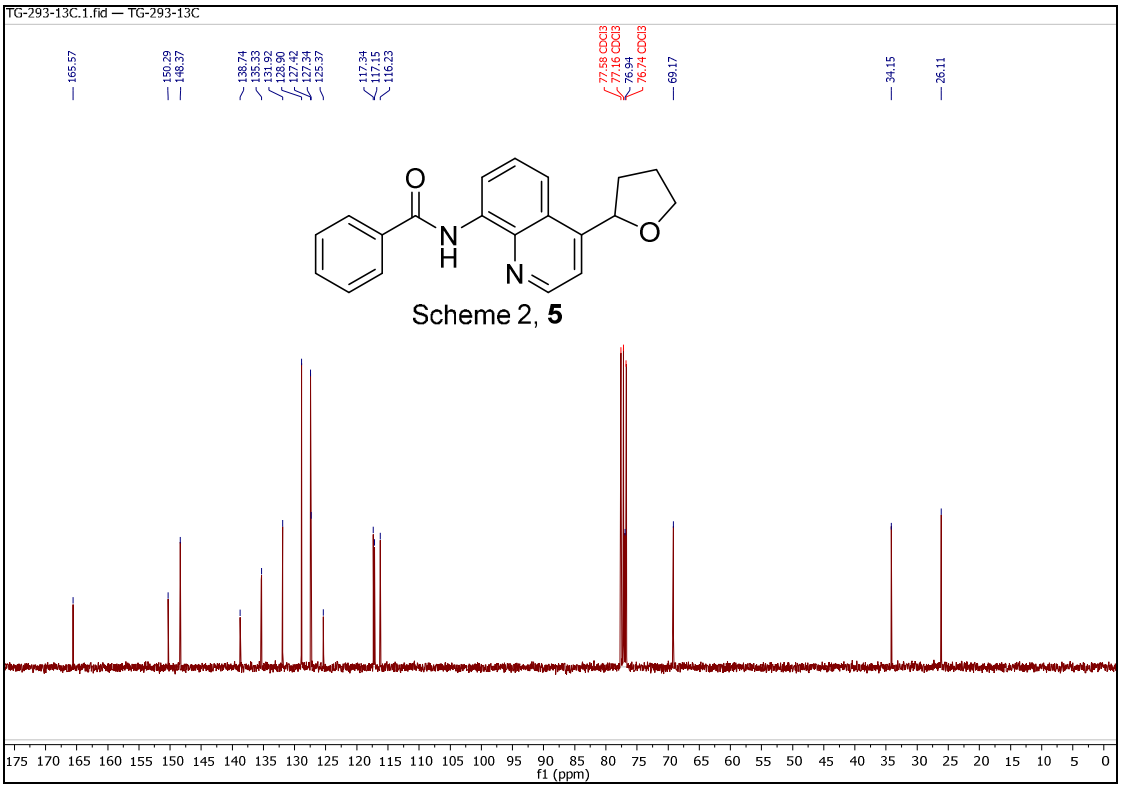

TG-273-1H,.1.fid — TG-273-1H,
A (s) 10.87
B (t) 8.93
C (d) 8.81
D (d) 8.03
E (dd) 7.63
F (m) 7.58
G (t) 5.62
H (ddd) 4.24
I (dt) 4.06
J (dtd) 2.64
K (m) 2.05
L (m) 1.86
M (s) 1.38
Scheme 2, 3
f1 (ppm)

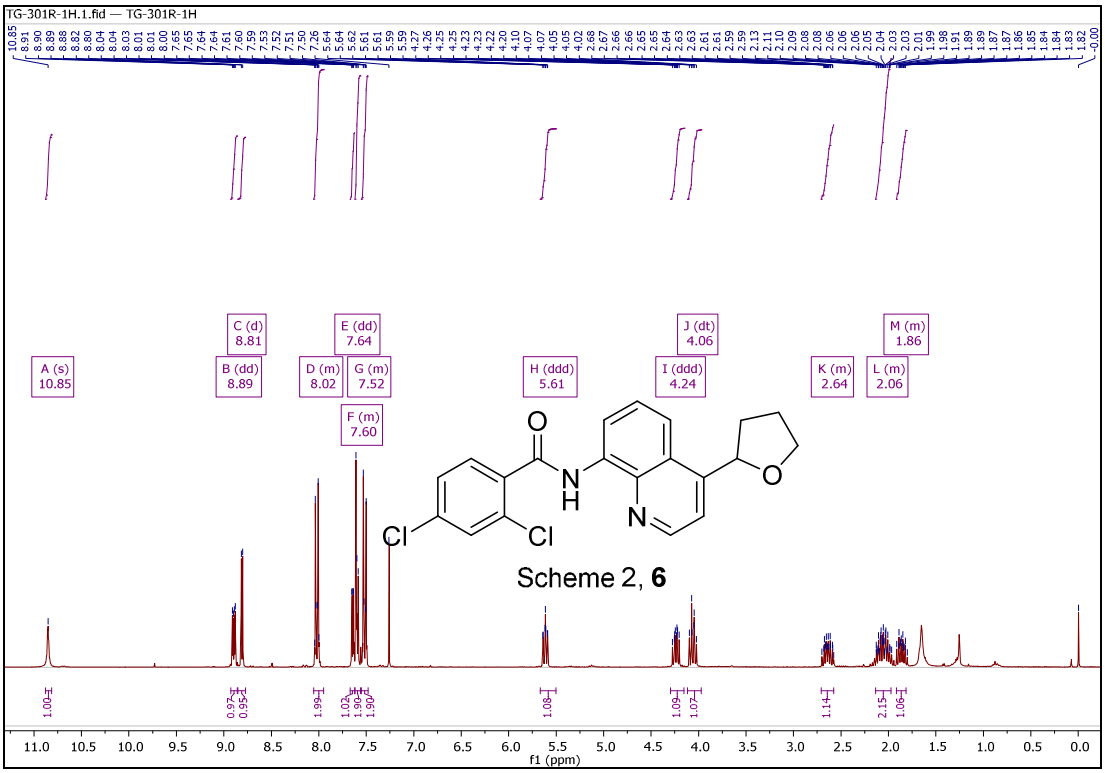

TG-273-13C,.1.fid
TG-273-13C,
Scheme 2, 3
f1 (ppm)

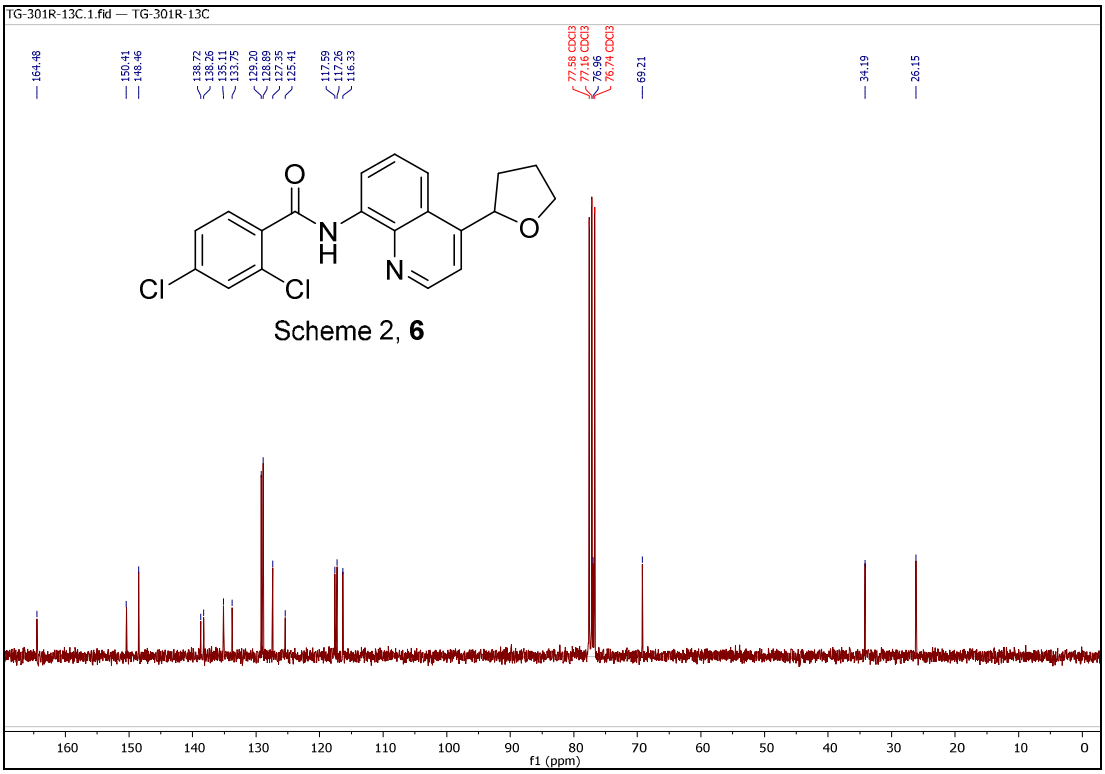

TG-332-1H.1.fid
Scheme 2, 4
A (s) 10.86
B (m) 8.93
C (d) 8.81
D (m) 8.00
E (dd) 7.63
F (m) 7.58
G (m) 7.34
H (m) 5.61
I (ddd) 4.23
J (dt) 4.05
K (m) 2.70
L (m) 2.62
M (m) 2.05
N (m) 1.86
O (m) 1.65
P (m) 1.39
Q (t) 0.95
f1 (ppm)

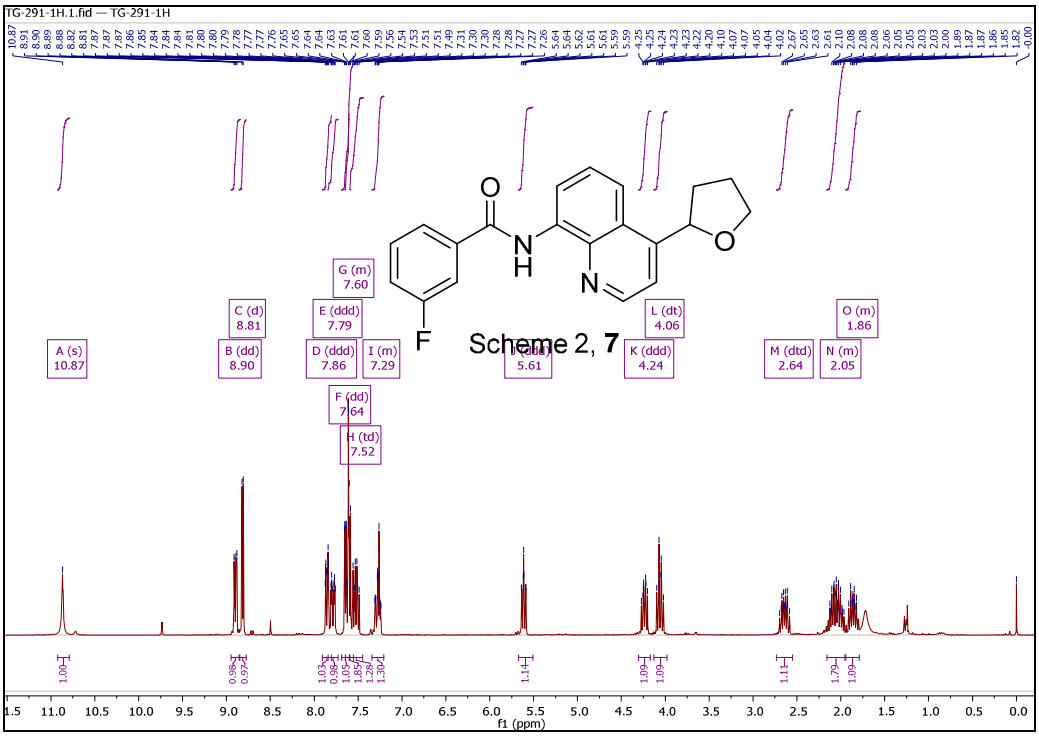

TG-332-13C.1.fid
TG-332-13C
Scheme 2, 4
165.63
150.27
148.31
147.37
138.72
135.45
132.73
128.93
127.45
127.37
125.35
117.16
117.10
116.16
77.58 CDCl3
77.16 CDCl3
76.94
76.74 CDCl3
69.17
35.72
34.15
33.47
26.11
22.44
14.05
f1 (ppm)

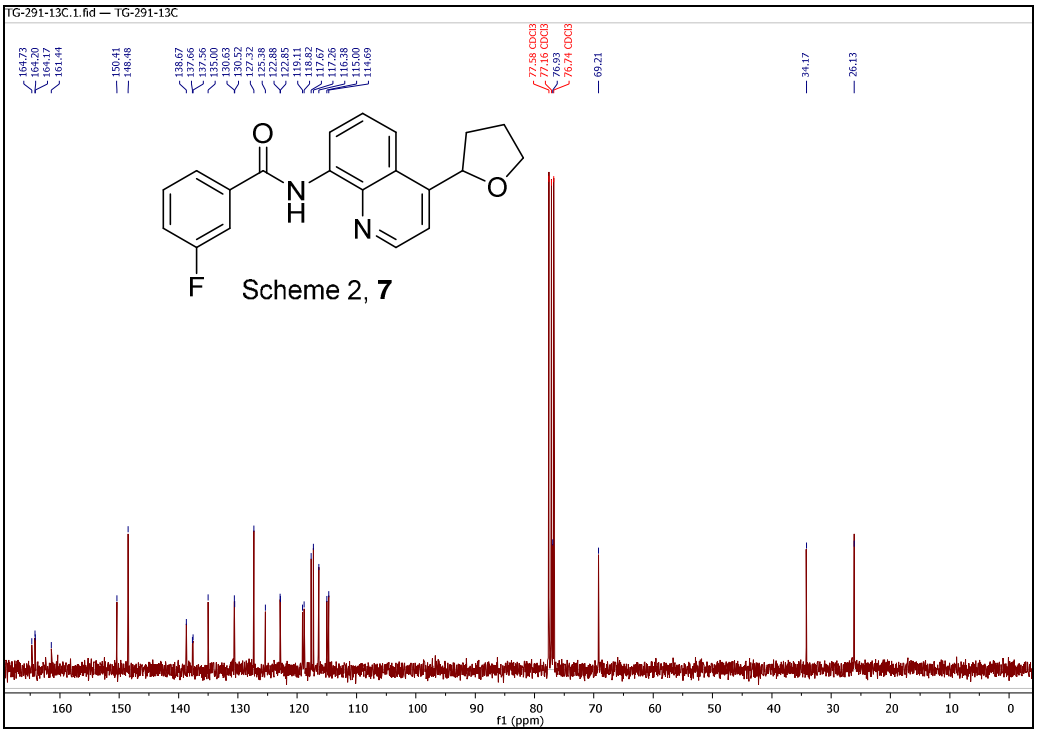

TG-293-1H.1.fid — TG-293-1H
A (s) 10.89
B (dd) 8.93
C (d) 8.81
D (dd) 8.09
E (dd) 7.63
F (m) 7.57
G (t) 5.61
H (ddd) 4.23
I (dt) 4.05
J (dtd) 2.63
K (ddt) 2.04
L (ddt) 1.85
Scheme 2, 5
f1 (ppm)

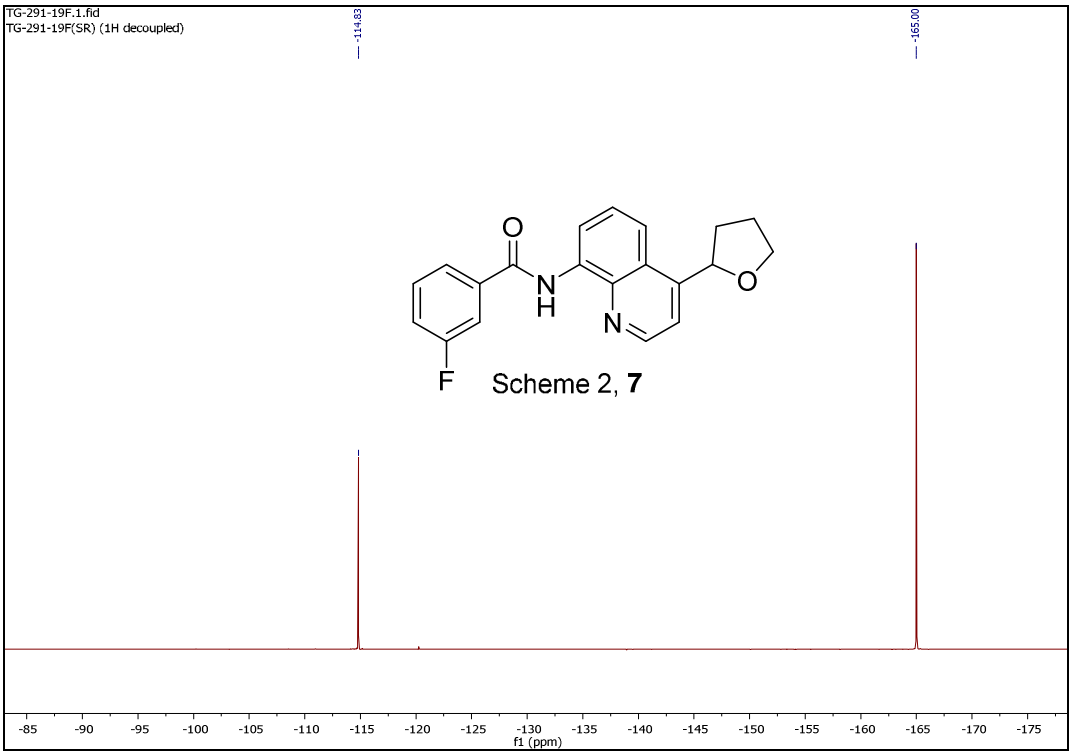

TG-293-13C.1.fid — TG-293-13C
165.57
150.29
148.37
138.74
135.33
131.92
128.90
127.42
127.34
125.37
117.34
117.15
116.23
77.58 CDCl3
77.16 CDCl3
76.94
76.74 CDCl3
69.17
34.15
26.11
Scheme 2, 5
f1 (ppm)

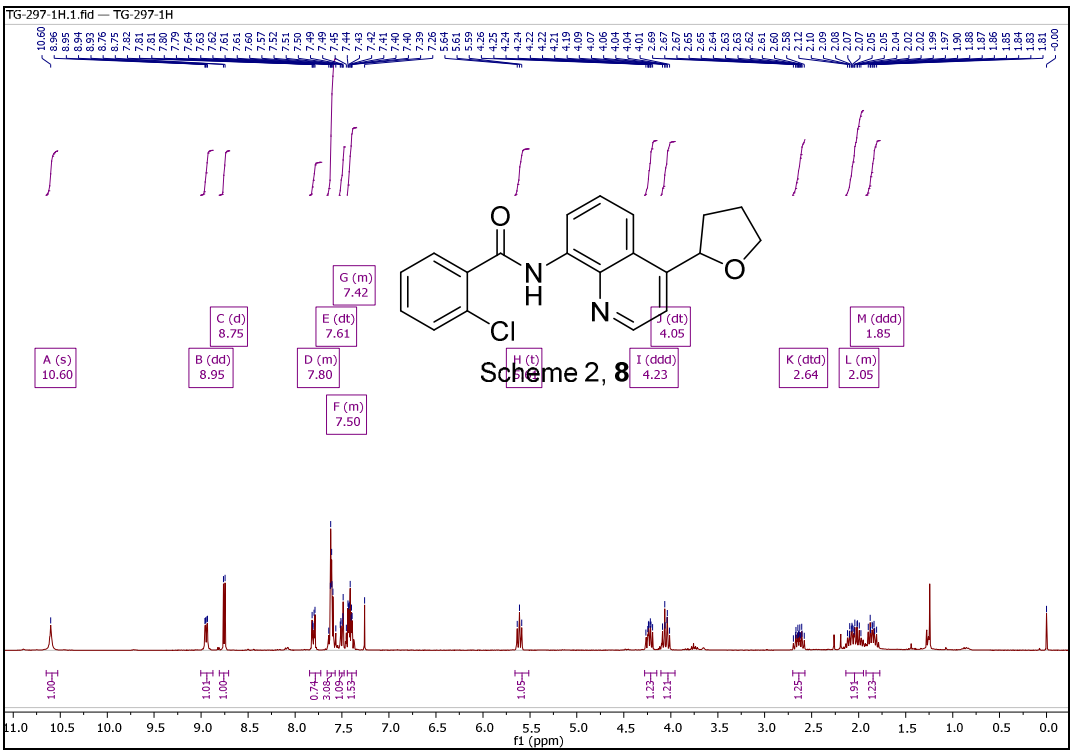

TG-301R-1H.1.fid — TG-301R-1H
A (s) 10.85
B (dd) 8.89
C (d) 8.81
D (m) 8.02
E (dd) 7.64
F (m) 7.60
G (m) 7.52
H (ddd) 5.61
I (ddd) 4.24
J (dt) 4.06
K (m) 2.64
L (m) 2.06
M (m) 1.86
Scheme 2, 6
f1 (ppm)

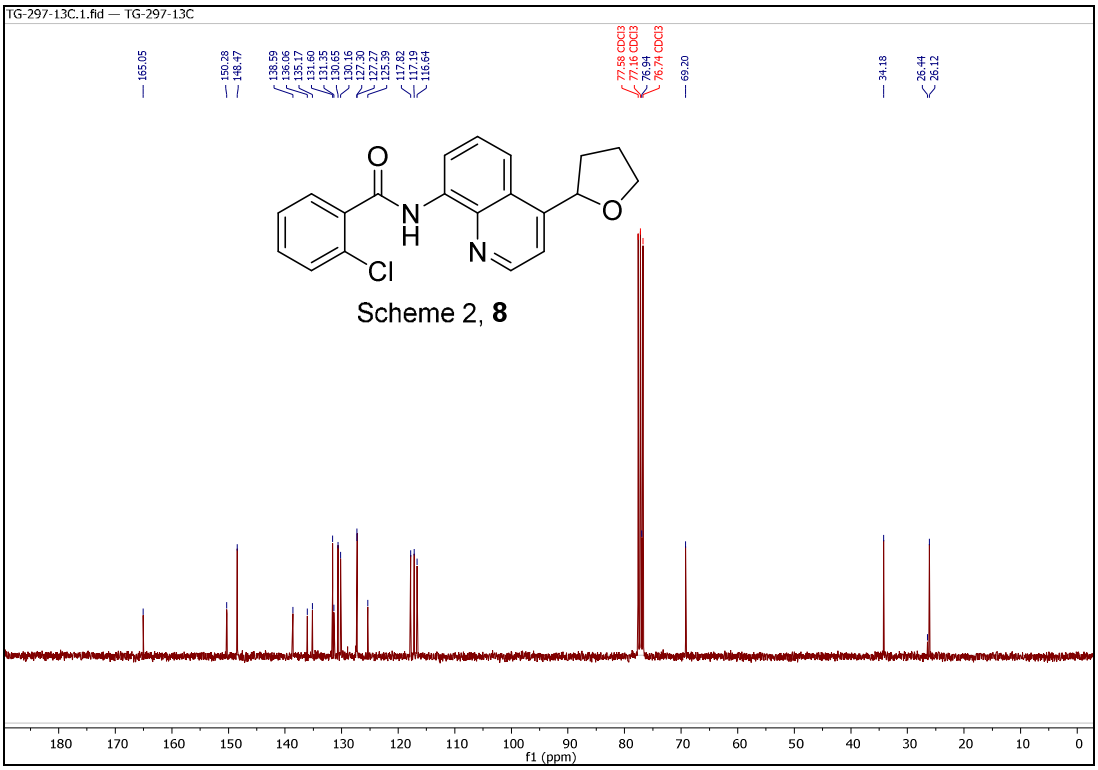

TG-301R-13C.1.fid — TG-301R-13C
164.48
150.41
148.46
138.72
138.26
135.11
133.75
129.20
128.89
127.35
125.41
117.59
117.26
116.33
77.58 CDCl3
77.16 CDCl3
76.95
76.74 CDCl3
69.21
34.19
26.15
Scheme 2, 6
f1 (ppm)

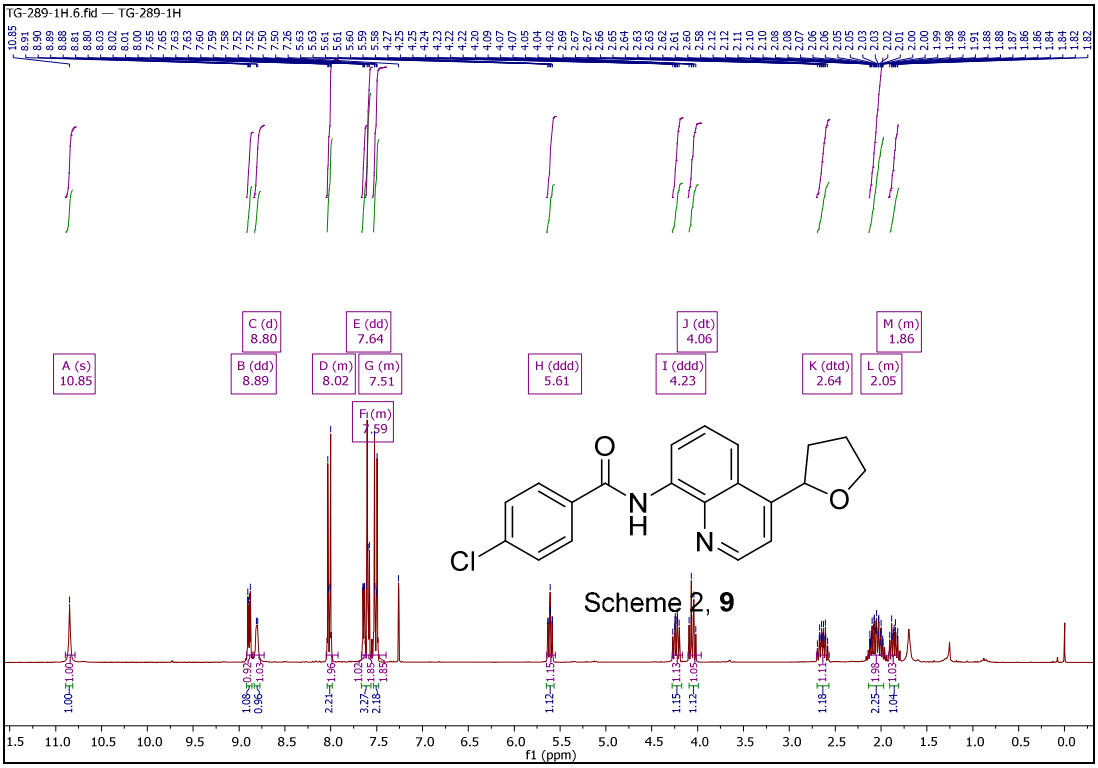

TG-291-1H.1.fid — TG-291-1H
A (s) 10.87
B (dd) 8.90
C (d) 8.81
D (ddd) 7.86
E (ddd) 7.79
F (dd) 7.64
G (m) 7.60
H (td) 7.52
I (m) 7.29
K (ddd) 4.24
L (dt) 4.06
M (dtd) 2.64
N (m) 2.05
O (m) 1.86
Scheme 2, 7
f1 (ppm)

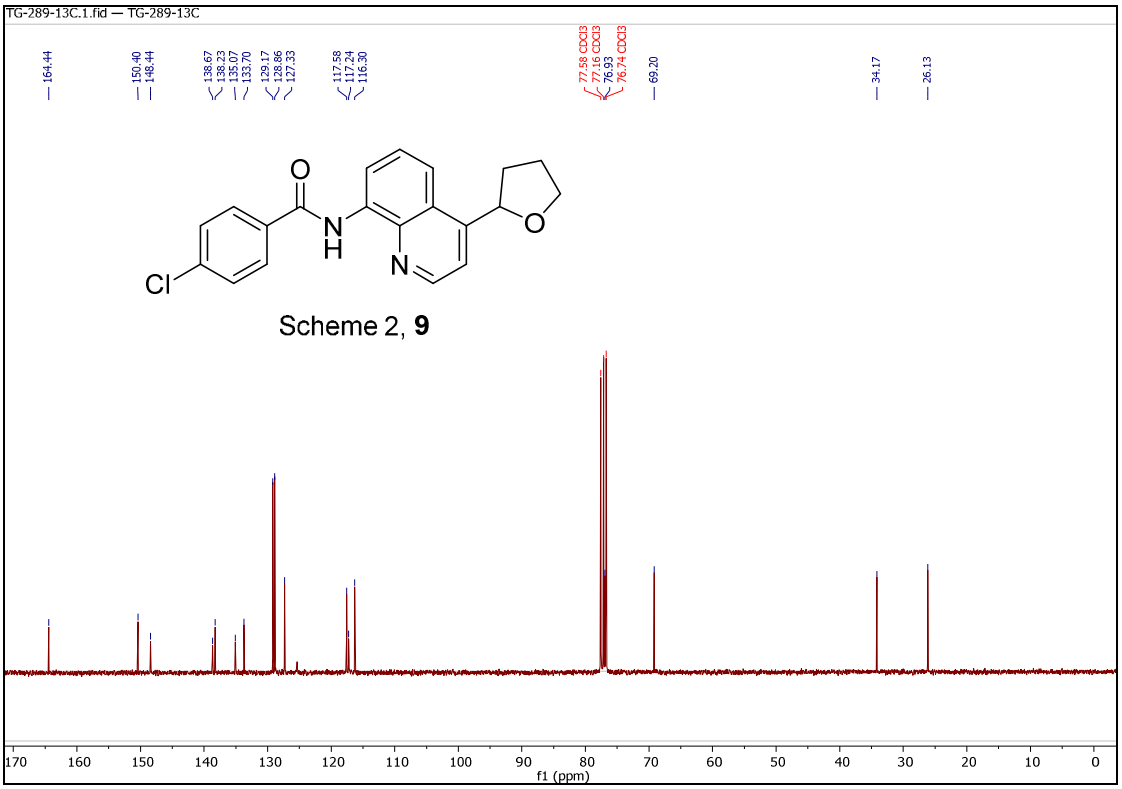

TG-291-13C.1.fid — TG-291-13C
77.58 CDCl3
77.16 CDCl3
76.93
76.74 CDCl3
69.21
34.17
26.13
Scheme 2, 7
f1 (ppm)

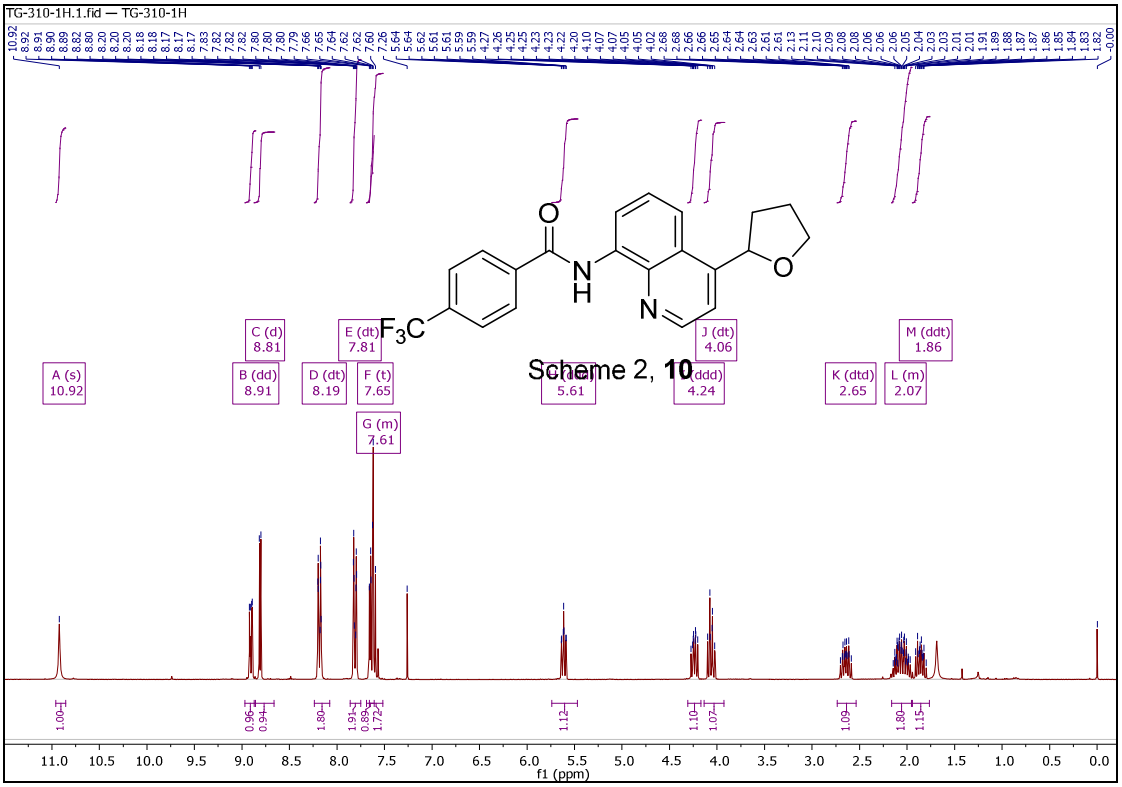

TG-291-19F.1.fid
TG-291-19F(SR) (1H decoupled)
-114.83
-165.00
O
N
H
N
O
F
Scheme 2, 7
f1 (ppm)

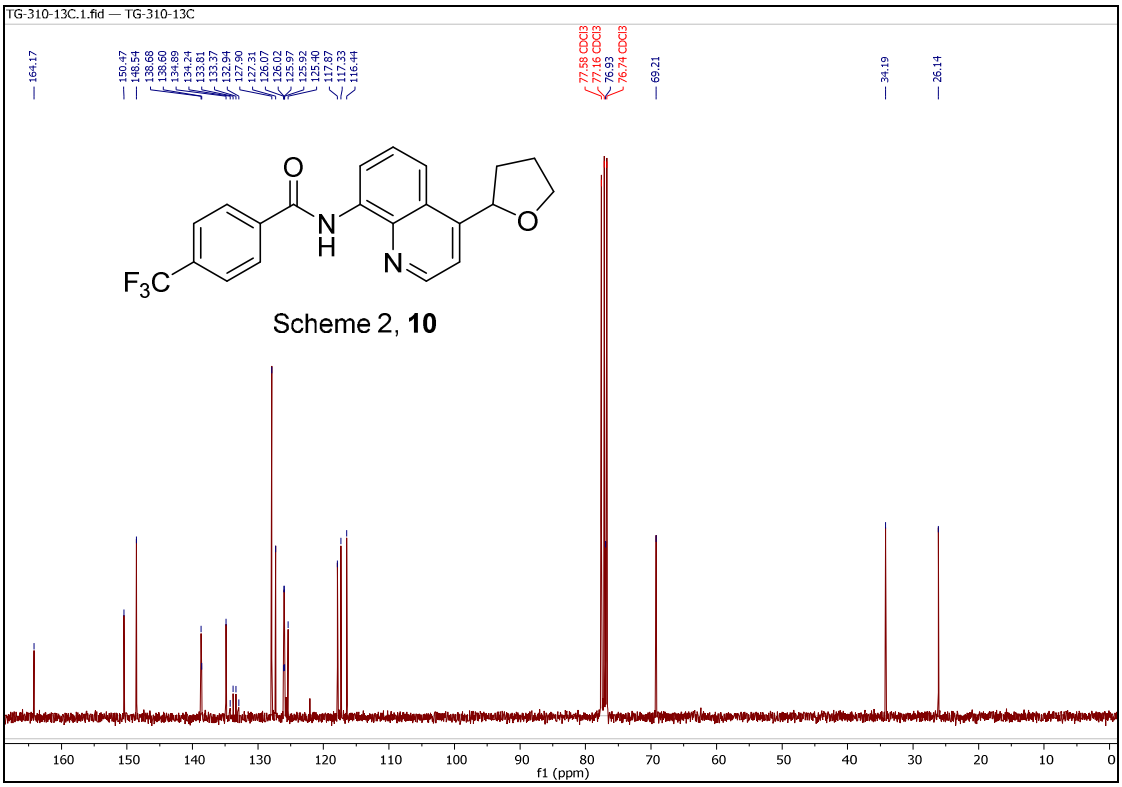

TG-297-1H.1.fid — TG-297-1H
A (s) 10.60
B (dd) 8.95
C (d) 8.75
D (m) 7.80
E (dt) 7.61
F (m) 7.50
G (m) 7.42
H (t)
I (ddd) 4.23
J (dt) 4.05
K (dtd) 2.64
L (m) 2.05
M (ddd) 1.85
O
N
H
N
O
Cl
Scheme 2, 8
f1 (ppm)

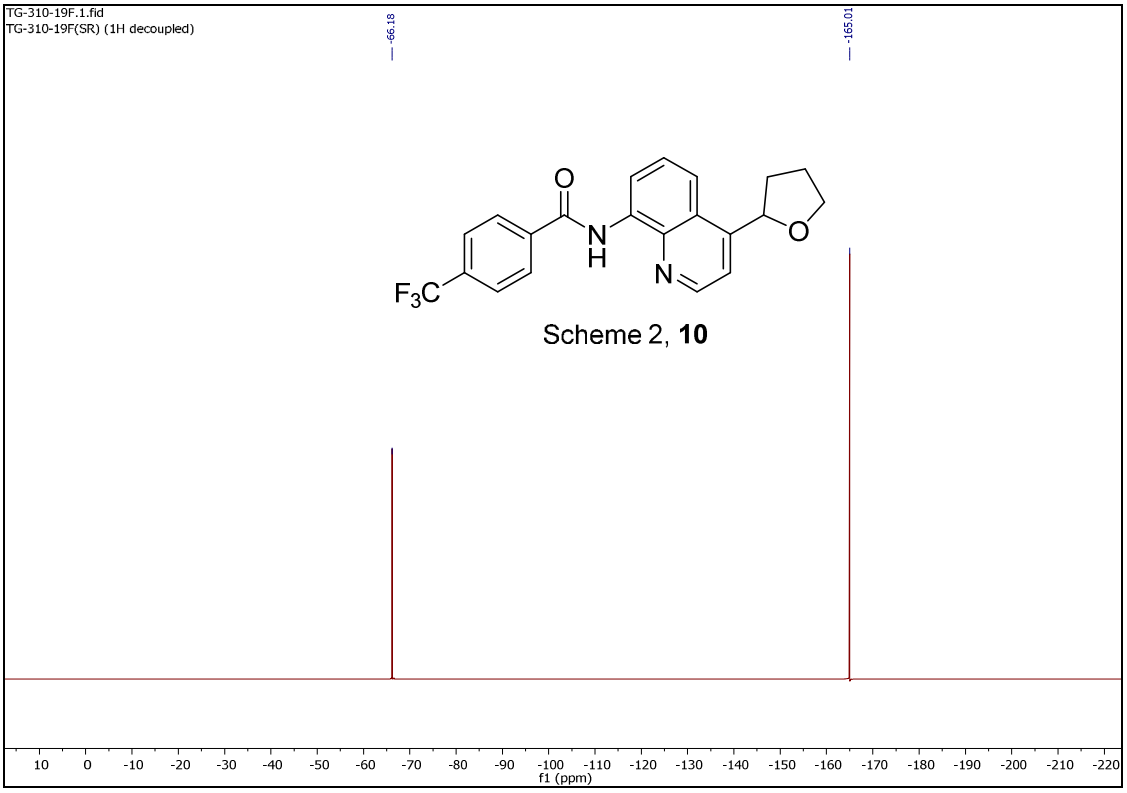

TG-297-13C.1.fid — TG-297-13C
165.05
150.28
148.47
138.59
136.06
135.17
131.60
131.35
130.65
130.16
127.30
127.77
125.39
117.82
117.19
116.64
77.58 CDCl3
77.16 CDCl3
76.94
76.74 CDCl3
69.20
34.18
26.44
26.12
Scheme 2, 8
f1 (ppm)

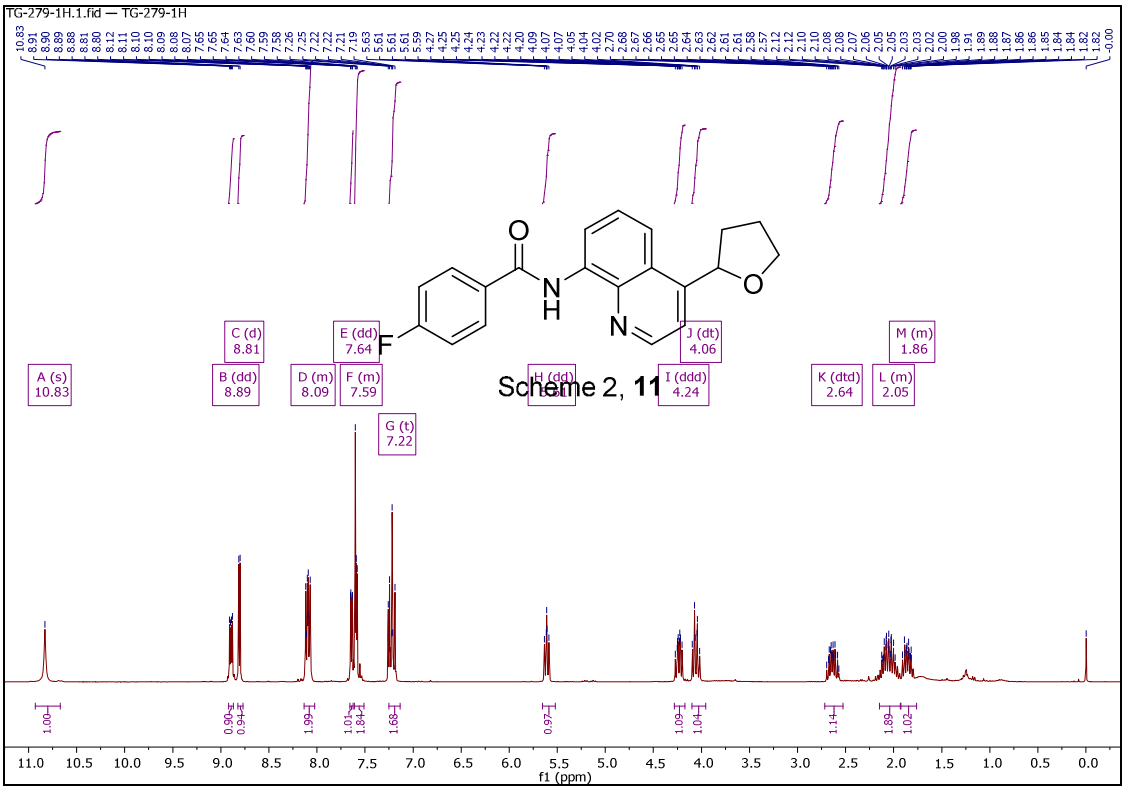

TG-289-1H.6.fid — TG-289-1H
A (s) 10.85
B (dd) 8.89
C (d) 8.80
D (m) 8.02
E (dd) 7.64
F (m) 7.59
G (m) 7.51
H (ddd) 5.61
I (ddd) 4.23
J (dt) 4.06
K (dtd) 2.64
L (m) 2.05
M (m) 1.86
Scheme 2, 9
f1 (ppm)

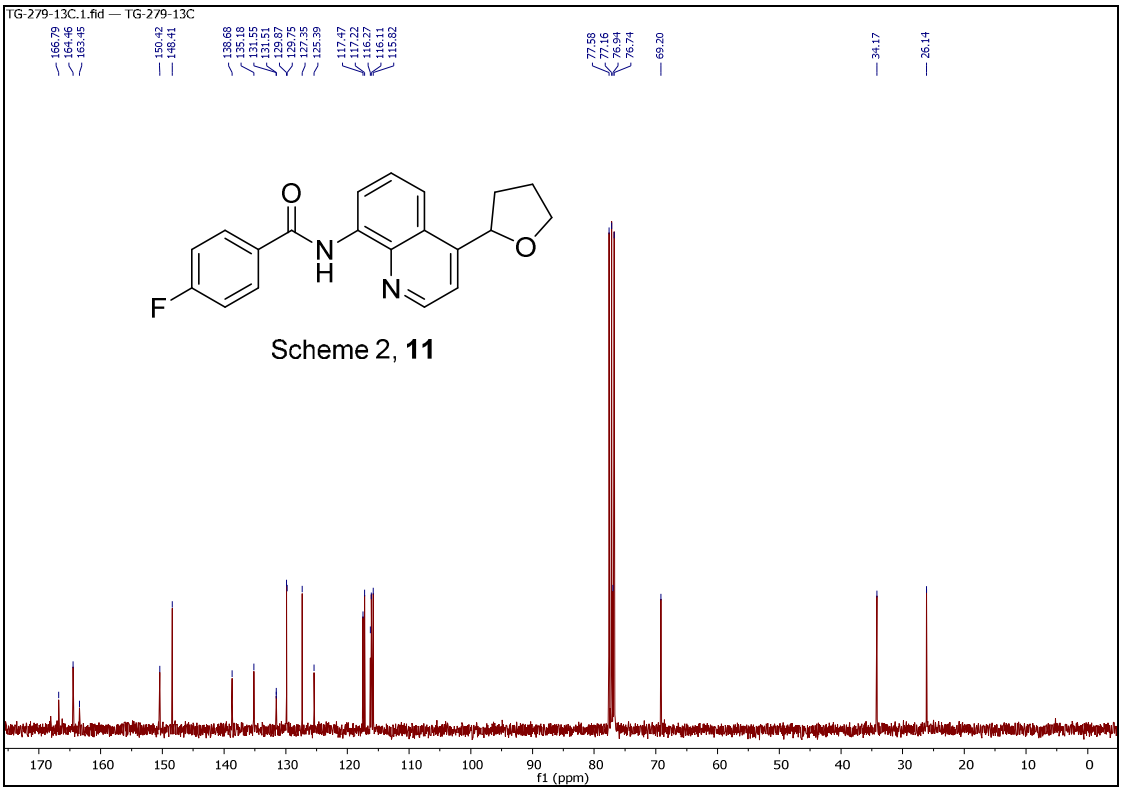

TG-289-13C.1.fid — TG-289-13C
164.44
150.40
148.44
138.67
138.23
135.07
133.70
129.17
128.86
127.33
117.58
117.24
116.30
77.58 CDCl3
77.16 CDCl3
76.93
76.74 CDCl3
69.20
34.17
26.13
Scheme 2, 9
f1 (ppm)

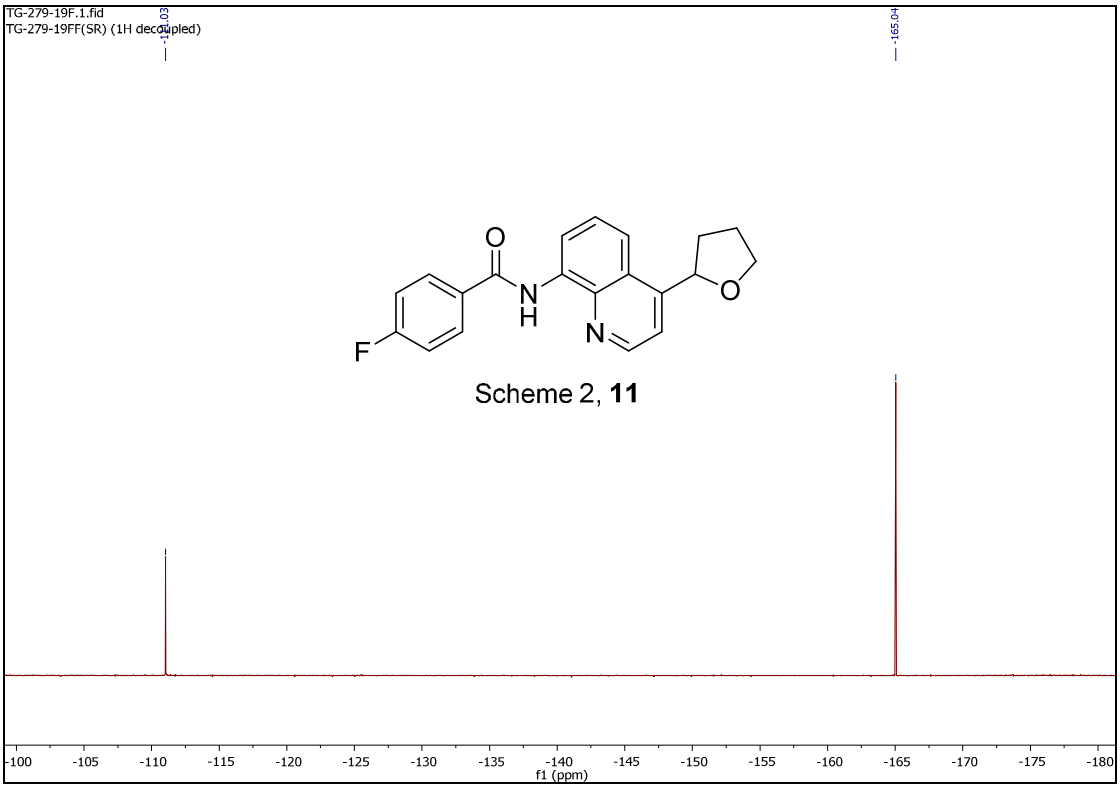

TG-310-1H.1.fid — TG-310-1H
A (s) 10.92
B (dd) 8.91
C (d) 8.81
D (dt) 8.19
E (dt) 7.81
F (t) 7.65
G (m) 7.61
5.61
J (dt) 4.06
(ddd) 4.24
K (dtd) 2.65
L (m) 2.07
M (ddt) 1.86
Scheme 2, 10
f1 (ppm)

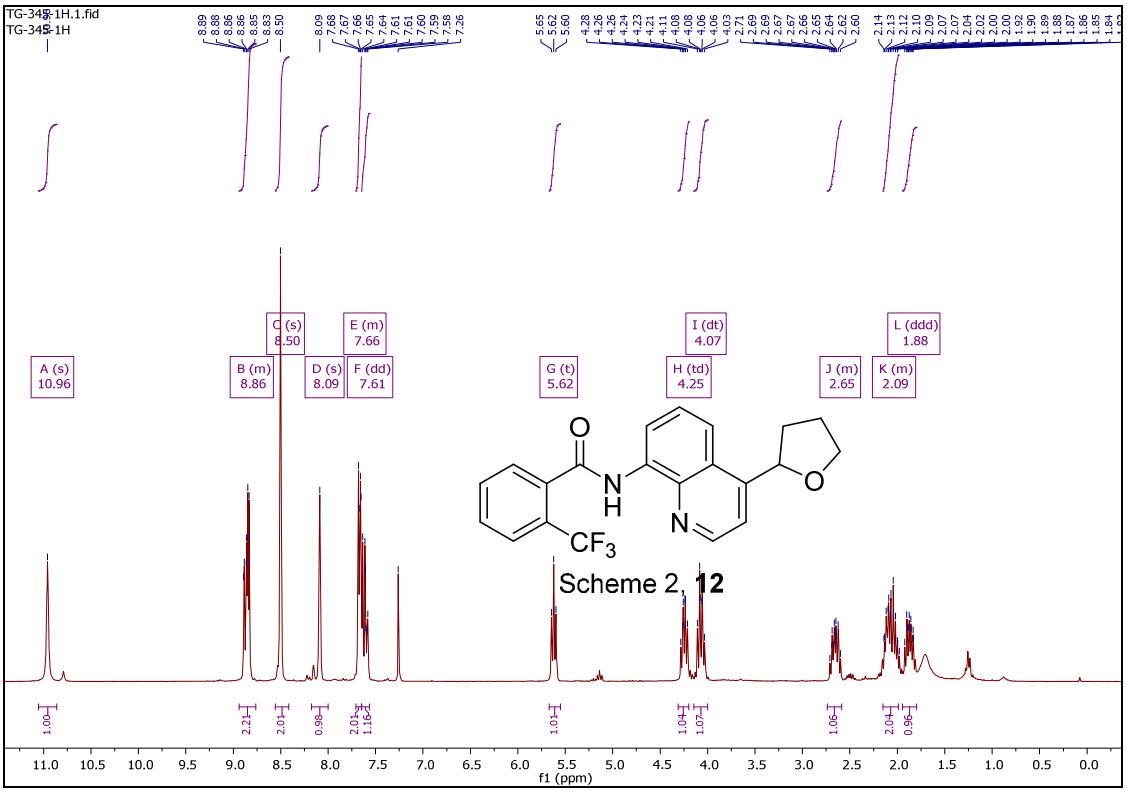

TG-310-13C.1.fid — TG-310-13C
164.17
150.47
148.54
138.68
138.60
134.89
134.24
133.81
133.37
132.94
127.90
127.31
126.07
126.02
125.97
125.92
125.40
117.87
117.33
116.44
77.58 CDCl3
77.16 CDCl3
76.93
76.74 CDCl3
69.21
34.19
26.14
O
N
H
N
O
F3C
Scheme 2, 10
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

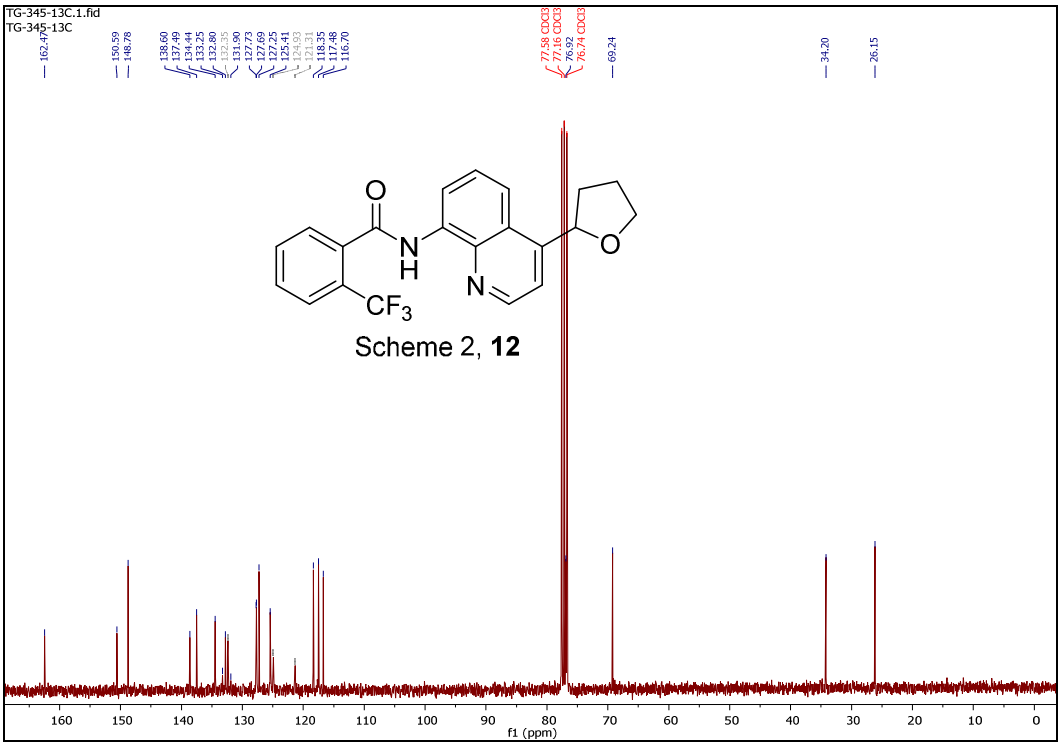

TG-310-19F.1.fid
TG-310-19F(SR) (1H decoupled)
-66.18
-165.01
O
N
H
N
O
F3C
Scheme 2, 10
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
f1 (ppm)

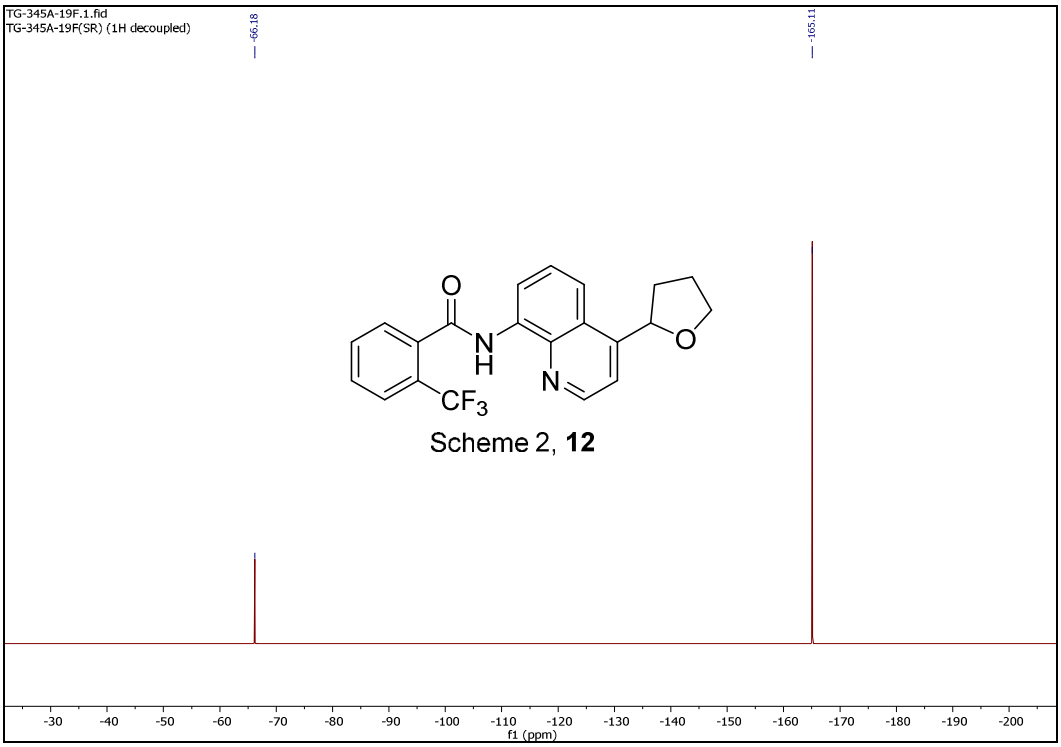

TG-279-1H.1.fid — TG-279-1H
A (s) 10.83
B (dd) 8.89
C (d) 8.81
D (m) 8.09
E (dd) 7.64
F (m) 7.59
G (t) 7.22
H (dd)
I (ddd) 4.24
J (dt) 4.06
K (dtd) 2.64
L (m) 2.05
M (m) 1.86
Scheme 2, 11
f1 (ppm)

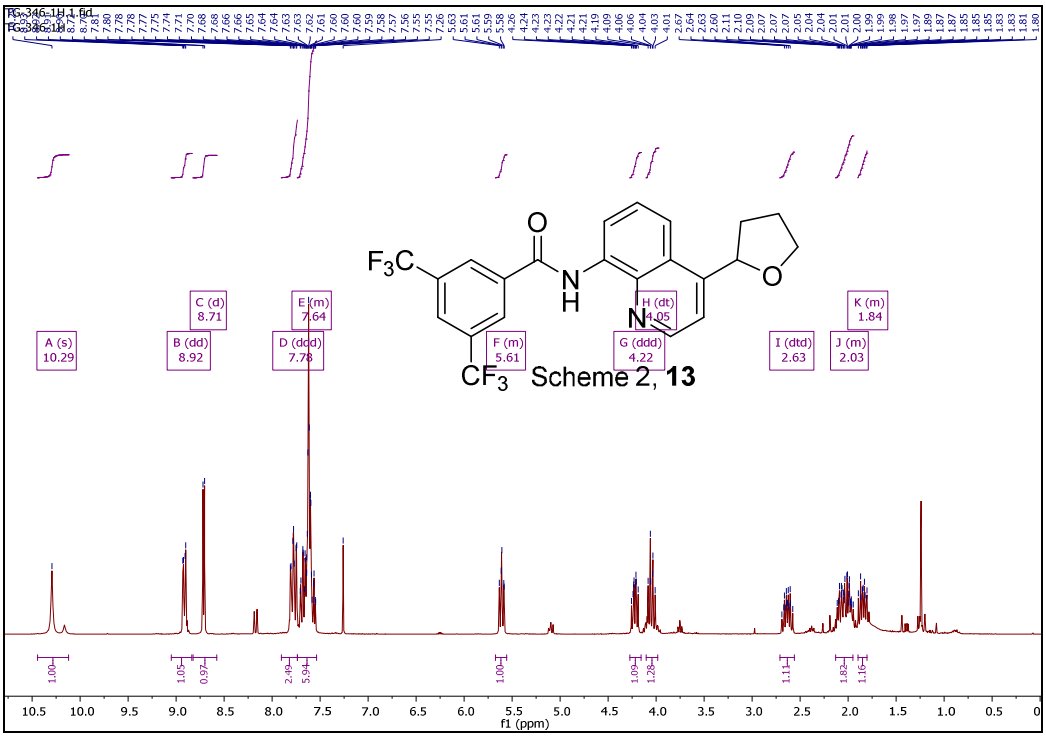

TG-279-13C.1.fid — TG-279-13C
166.79
164.46
163.45
150.42
148.41
138.68
135.18
131.55
131.51
129.87
129.75
127.35
125.39
117.47
117.22
116.27
116.11
115.82
77.58
77.16
76.94
76.74
69.20
34.17
26.14
Scheme 2, 11
f1 (ppm)

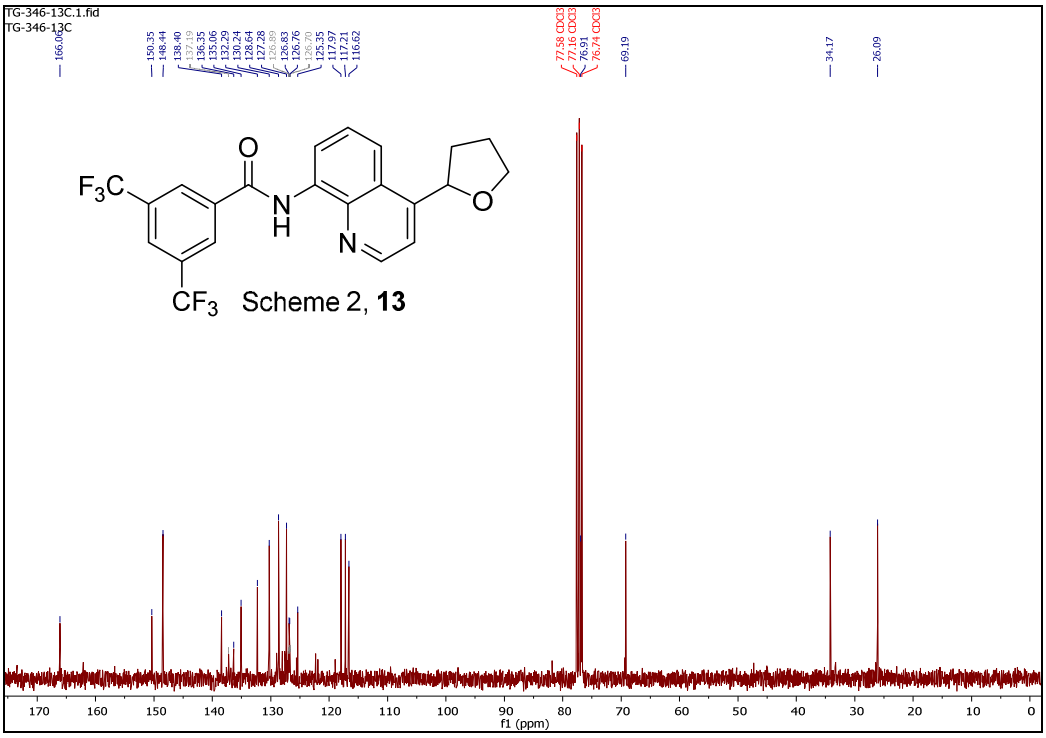

TG-279-19F.1.fid
TG-279-19FF(SR) (1H decoupled)
-110.03
-165.04
O
N
H
N
O
F
Scheme 2, 11
-100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180
f1 (ppm)

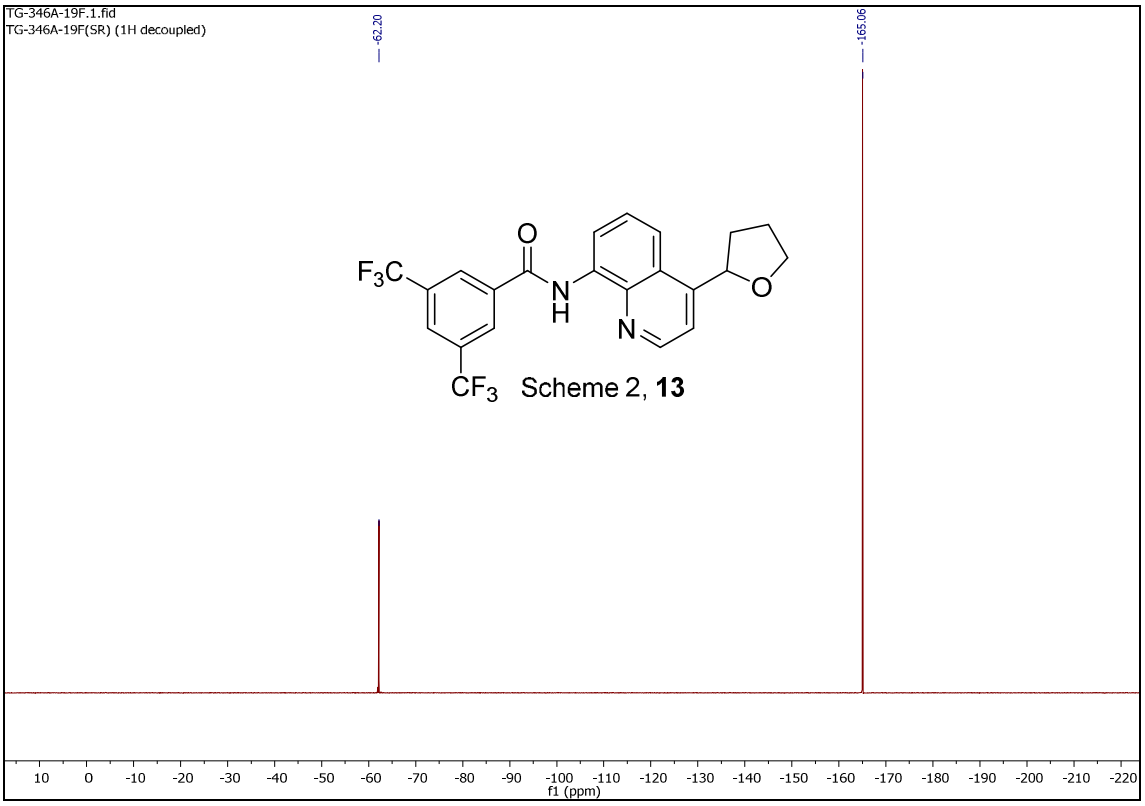

TG-345-1H.1.fid
TG-345-1H
A (s) 10.96
B (m) 8.86
C (s) 8.50
D (s) 8.09
E (m) 7.66
F (dd) 7.61
G (t) 5.62
H (td) 4.25
I (dt) 4.07
J (m) 2.65
K (m) 2.09
L (ddd) 1.88
O
N
H
N
O
CF3
Scheme 2, 12
1.00 2.21 2.01 0.98 2.01 1.16 1.01 1.04 1.07 1.06 2.04 0.96
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

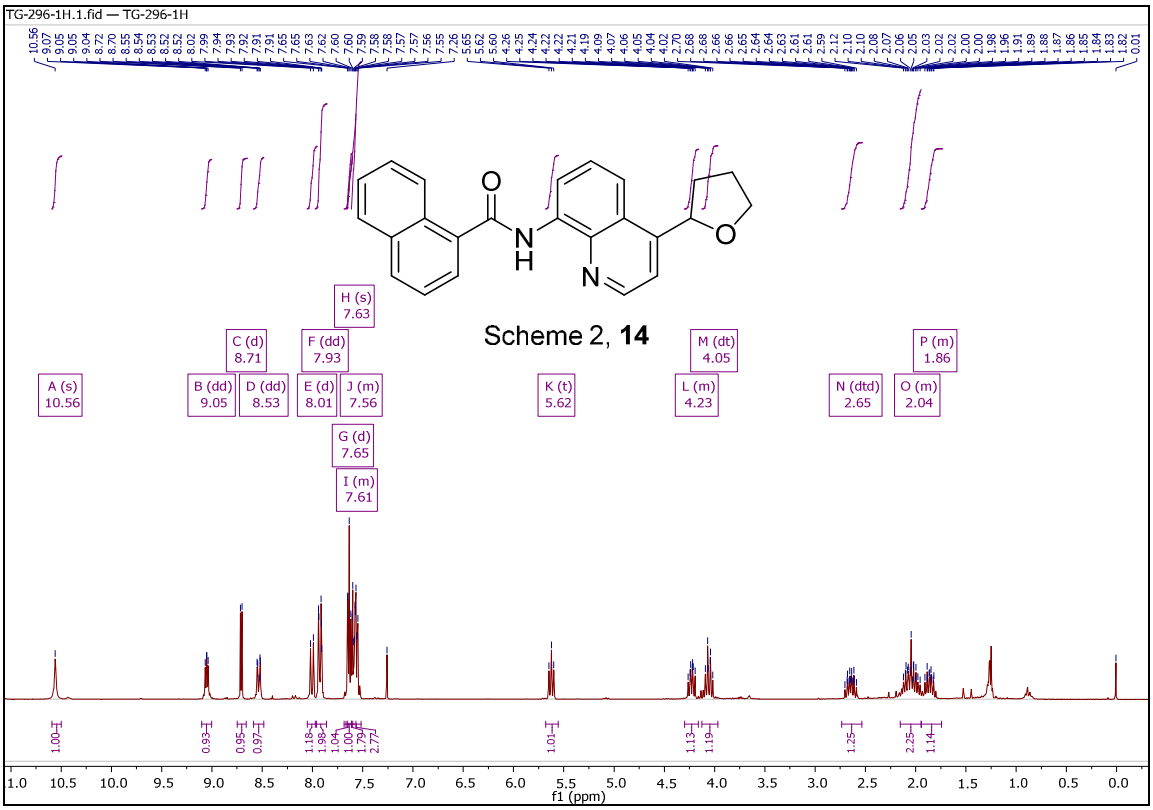

TG-345-13C.1.fid
TG-345-13C
162.47
150.59
148.78
138.60
137.49
134.44
133.25
132.80
132.35
131.90
127.73
127.69
127.25
125.41
124.93
121.31
118.35
117.48
116.70
77.58 CDCl3
77.16 CDCl3
76.92
76.74 CDCl3
69.24
34.20
26.15
O
N
H
N
O
CF3
Scheme 2, 12
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

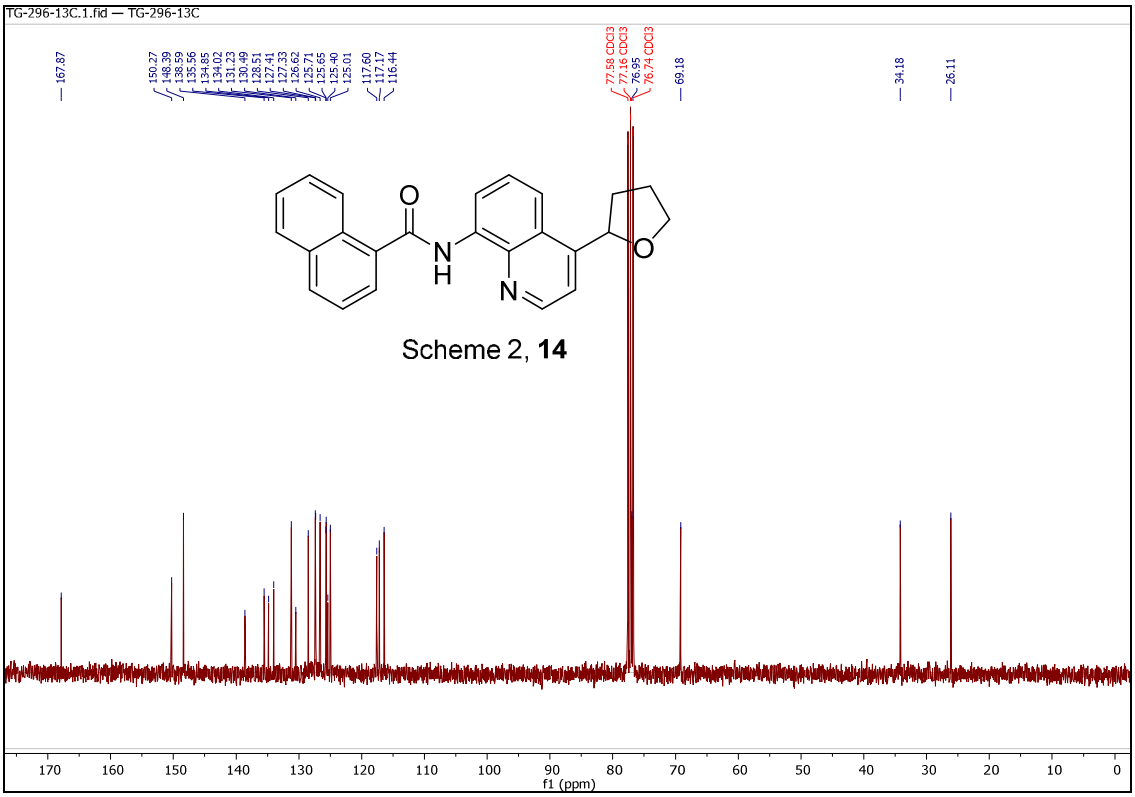

TG-345A-19F.1.fid
TG-345A-19F(SR) (1H decoupled)
-66.18
-165.11
O
N
H
N
O
CF3
Scheme 2, 12
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

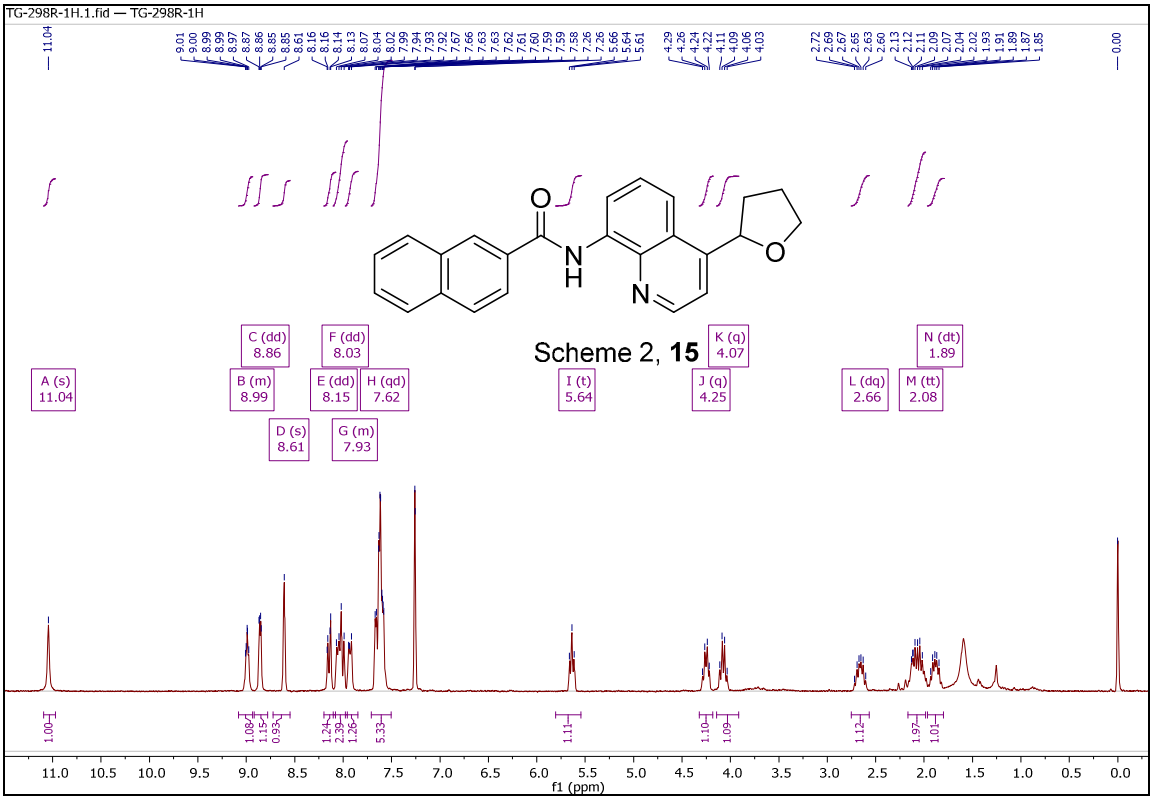

TG-346-1H.1.fid
TG-346-1H
A (s) 10.29
B (dd) 8.92
C (d) 8.71
D (ddd) 7.78
E (m) 7.64
F (m) 5.61
G (ddd) 4.22
H (dt) 4.05
I (dtd) 2.63
J (m) 2.03
K (m) 1.84
Scheme 2, 13
f1 (ppm)

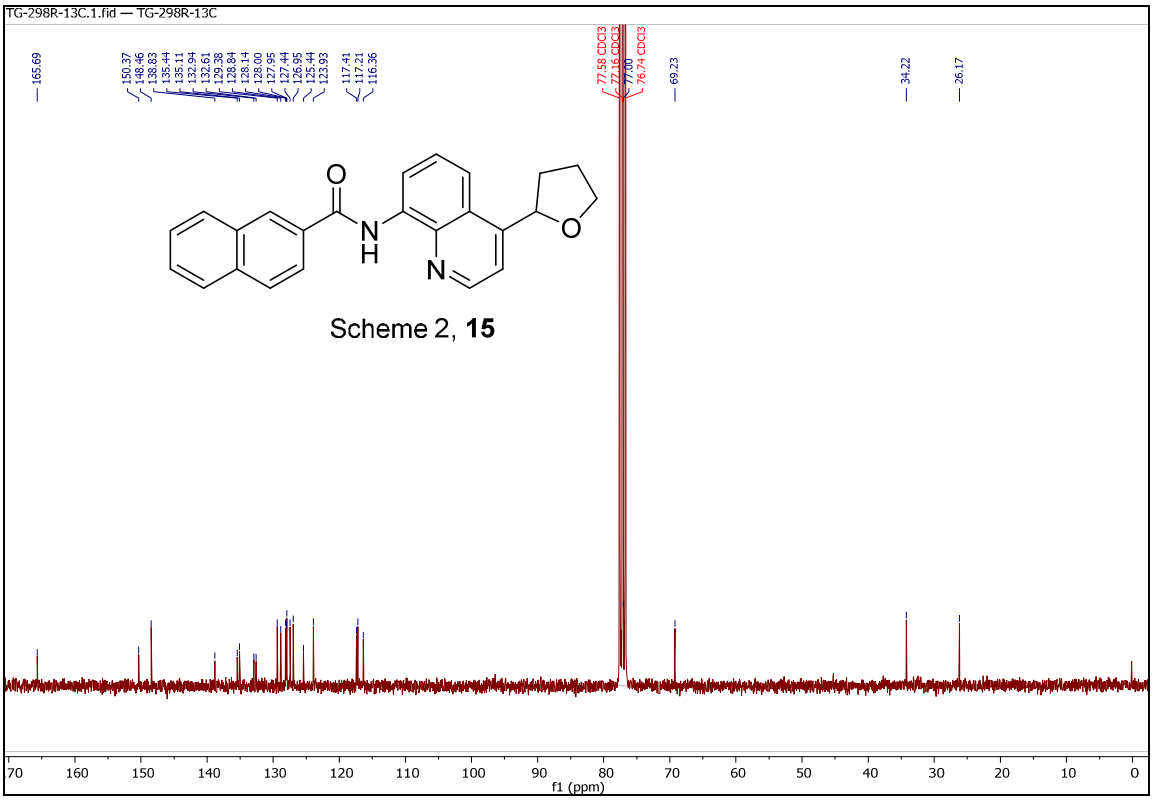

TG-346-13C.1.fid
TG-346-13C
Scheme 2, 13
f1 (ppm)

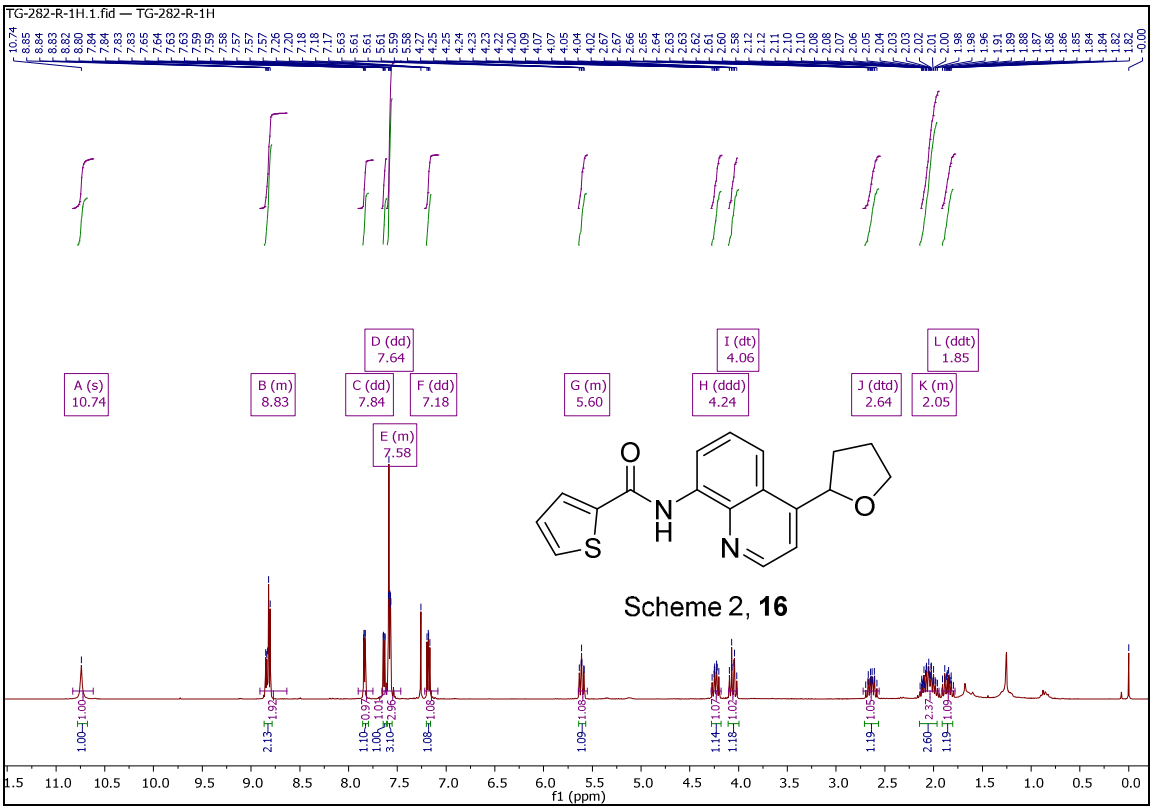

TG-346A-19F.1.fid
TG-346A-19F(SR) (1H decoupled)
-62.20
-165.06
Scheme 2, 13
f1 (ppm)

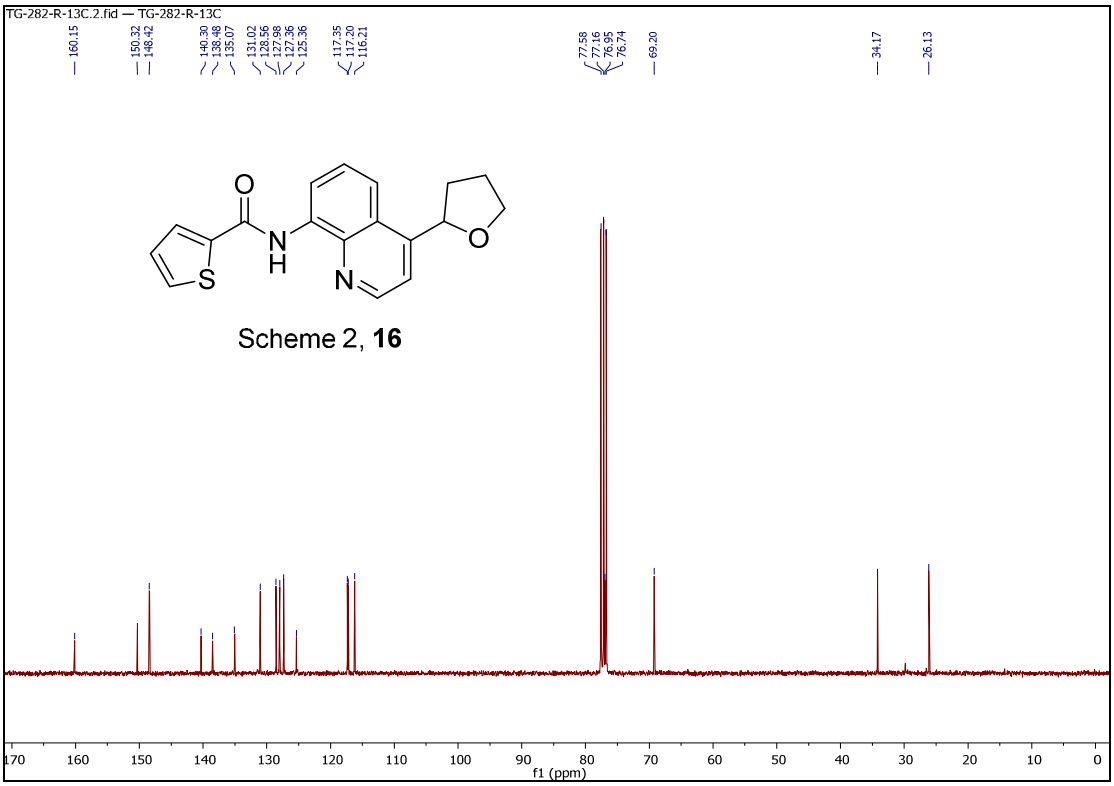

TG-296-1H.1.fid — TG-296-1H
Scheme 2, 14
A (s) 10.56
B (dd) 9.05
C (d) 8.71
D (dd) 8.53
E (d) 8.01
F (dd) 7.93
G (d) 7.65
H (s) 7.63
I (m) 7.61
J (m) 7.56
K (t) 5.62
L (m) 4.23
M (dt) 4.05
N (dtd) 2.65
O (m) 2.04
P (m) 1.86
f1 (ppm)

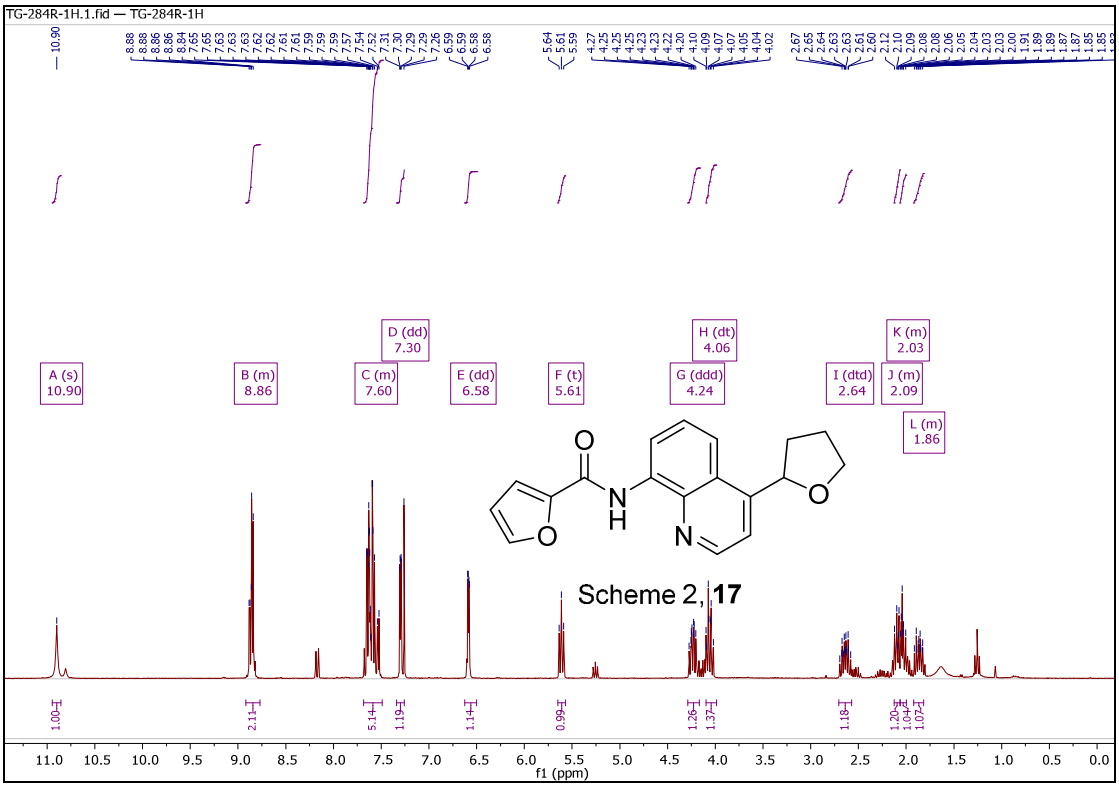

TG-296-13C.1.fid — TG-296-13C
167.87
150.27
148.39
138.59
135.56
134.65
134.02
131.23
130.49
128.51
127.41
127.33
126.62
125.71
125.65
125.40
125.01
117.60
117.17
116.44
77.58 CDCl3
77.16 CDCl3
76.95
76.74 CDCl3
69.18
34.18
26.11
Scheme 2, 14
f1 (ppm)

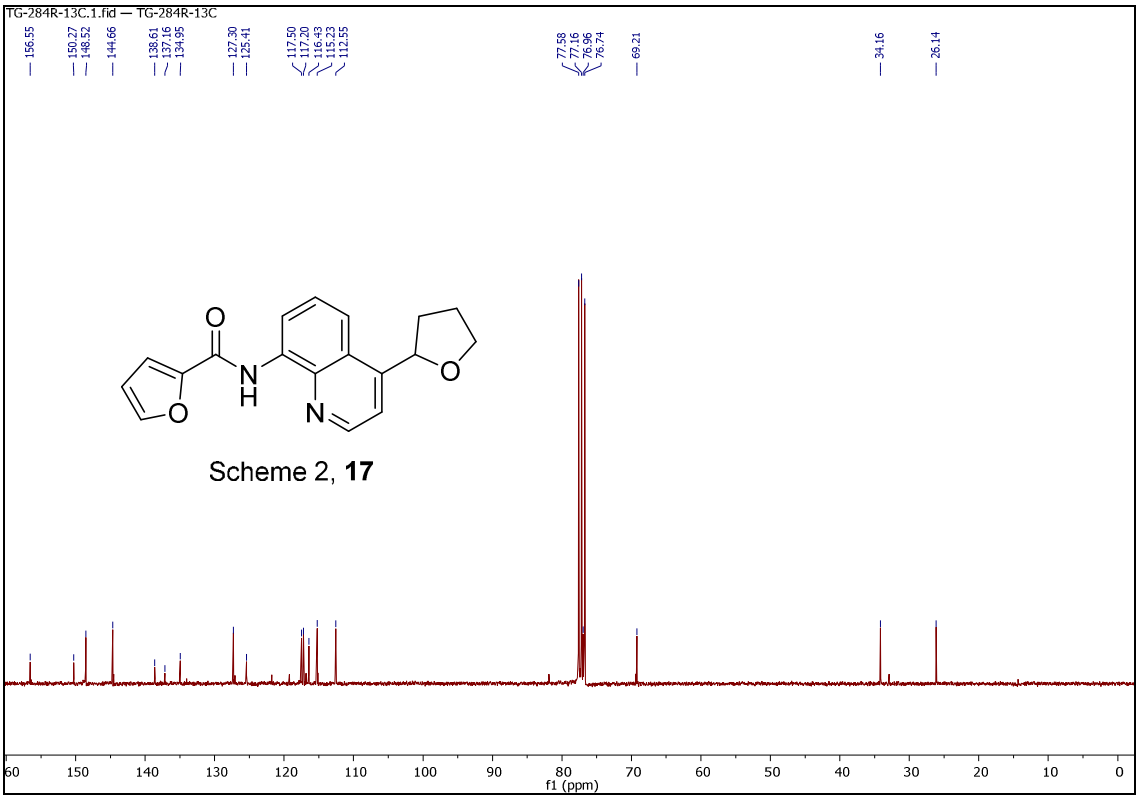

TG-298R-1H.1.fid — TG-298R-1H
11.04
0.00
Scheme 2, 15
A (s) 11.04
B (m) 8.99
C (dd) 8.86
D (s) 8.61
E (dd) 8.15
F (dd) 8.03
G (m) 7.93
H (qd) 7.62
I (t) 5.64
J (q) 4.25
K (q) 4.07
L (dq) 2.66
M (tt) 2.08
N (dt) 1.89
f1 (ppm)


TG-298R-13C.1.fid — TG-298R-13C
165.69
150.37
148.46
138.83
135.44
135.11
132.94
132.61
129.38
128.84
128.14
128.00
127.95
127.44
126.95
125.44
123.93
117.41
117.21
116.36
77.58 CDCl3
77.16 CDCl3
77.00
76.74 CDCl3
69.23
34.22
26.17
Scheme 2, 15
f1 (ppm)

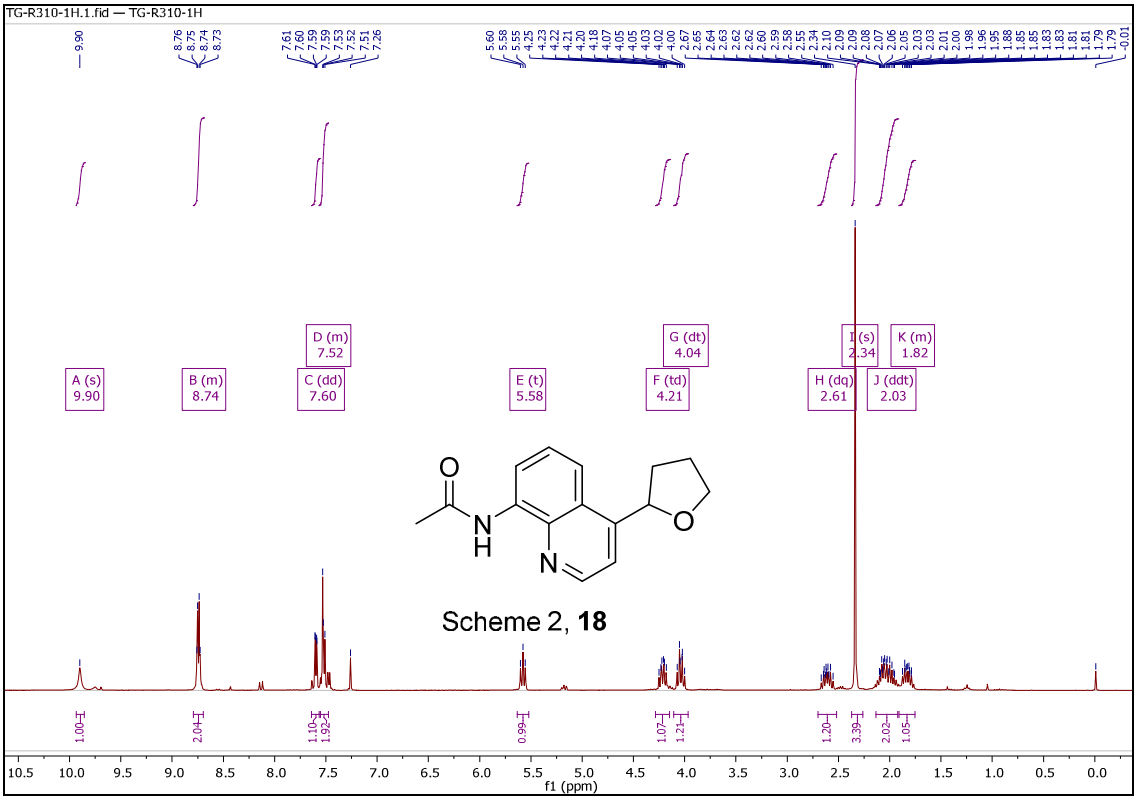

TG-282-R-1H.1.fid — TG-282-R-1H
A (s) 10.74
B (m) 8.83
C (dd) 7.84
D (dd) 7.64
E (m) 7.58
F (dd) 7.18
G (m) 5.60
H (ddd) 4.24
I (dt) 4.06
J (dtd) 2.64
K (m) 2.05
L (ddt) 1.85
Scheme 2, 16
f1 (ppm)


TG-282-R-13C.2.fid — TG-282-R-13C
160.15
150.32
148.42
140.30
138.48
135.07
131.02
128.56
127.98
127.36
125.36
117.35
117.20
116.21
77.58
77.16
76.95
76.74
69.20
34.17
26.13
Scheme 2, 16
f1 (ppm)

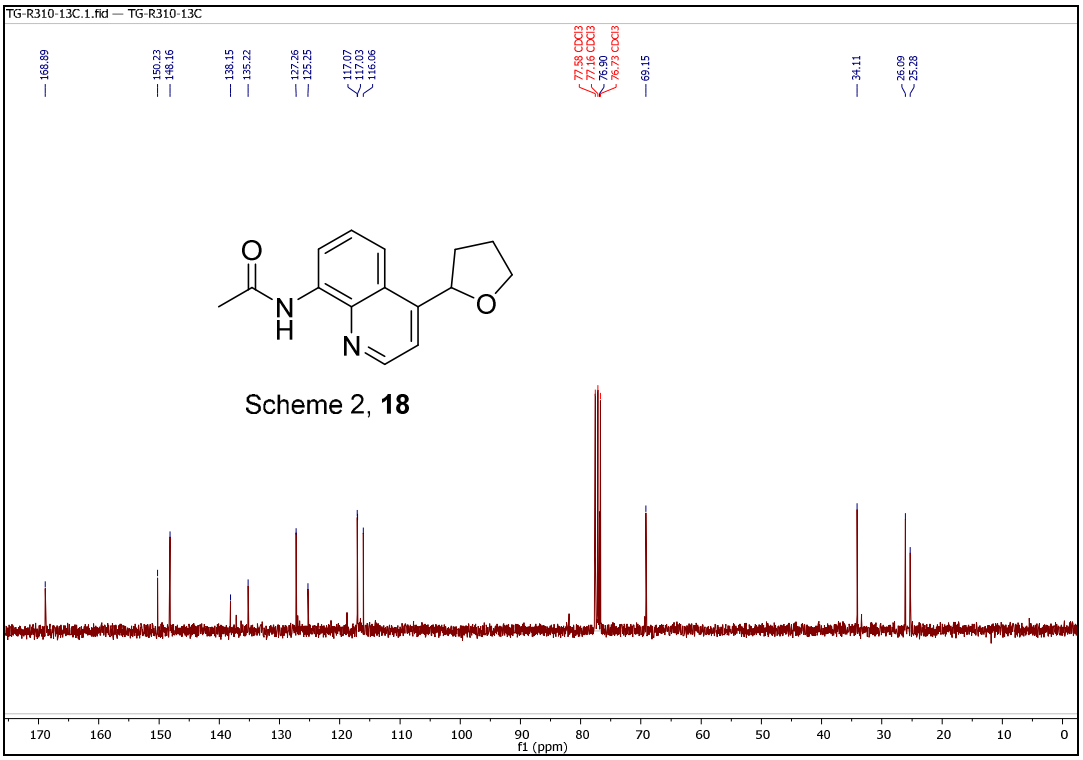

TG-284R-1H.1.fid — TG-284R-1H
A (s) 10.90
B (m) 8.86
C (m) 7.60
D (dd) 7.30
E (dd) 6.58
F (t) 5.61
G (ddd) 4.24
H (dt) 4.06
I (dtd) 2.64
J (m) 2.09
K (m) 2.03
L (m) 1.86
Scheme 2, 17
f1 (ppm)

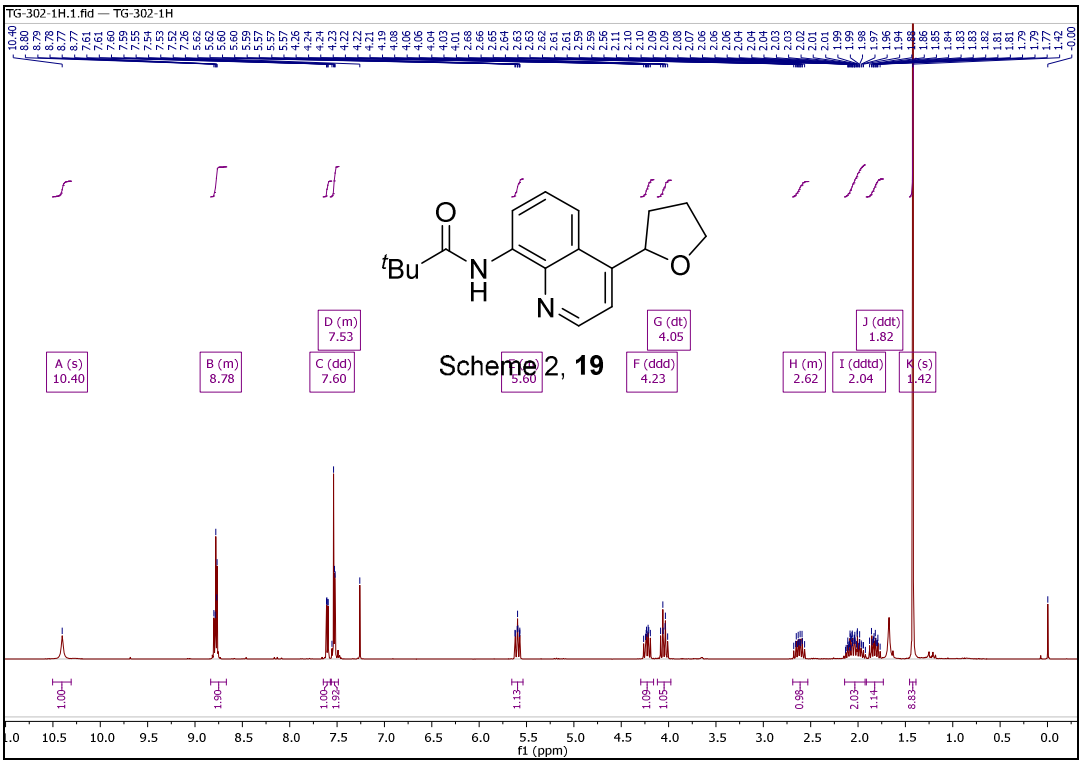


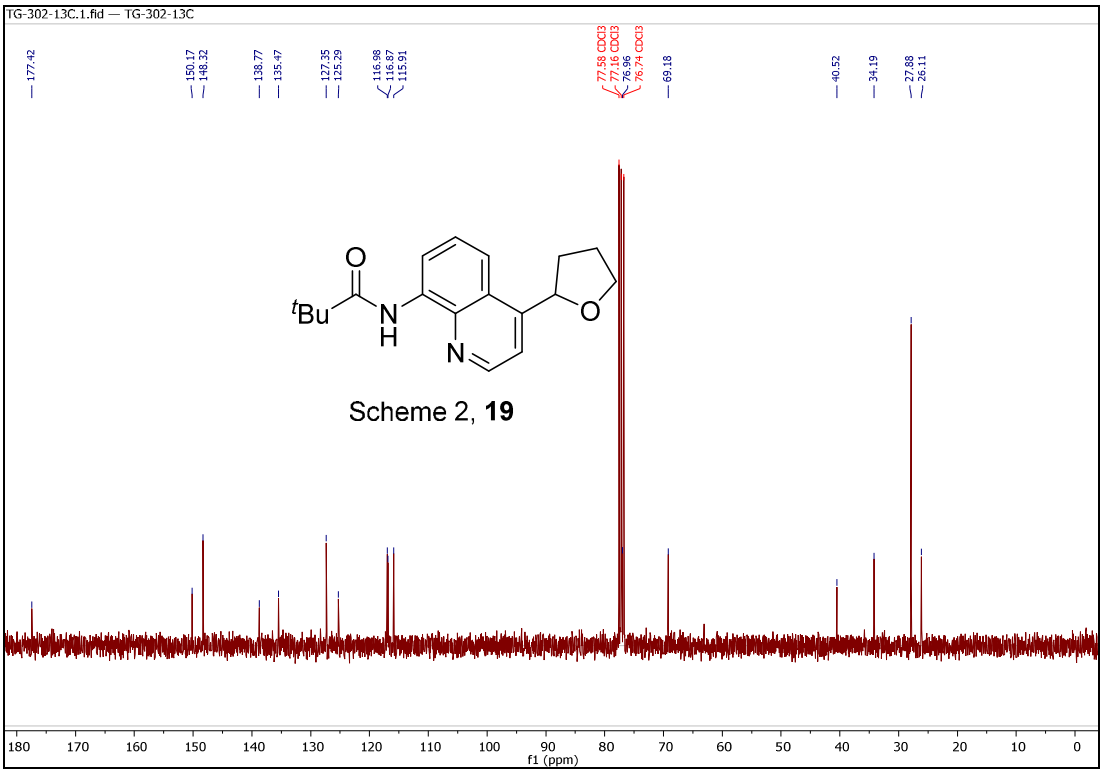
Scheme 2, **17**

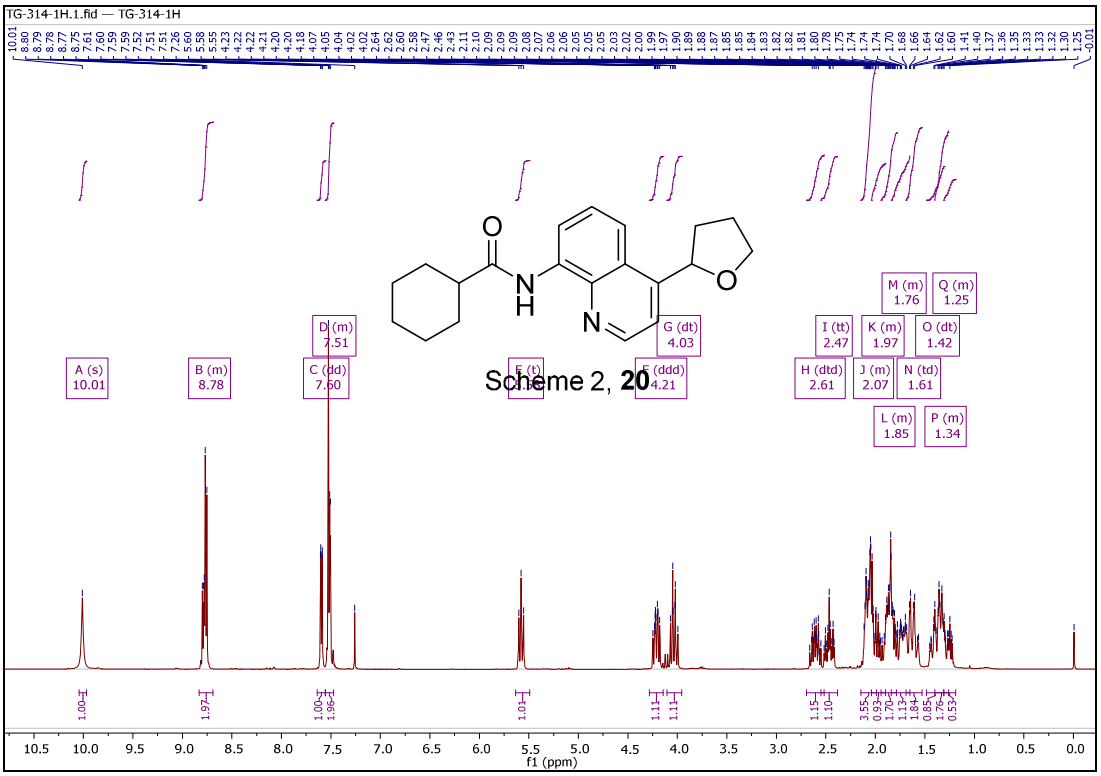


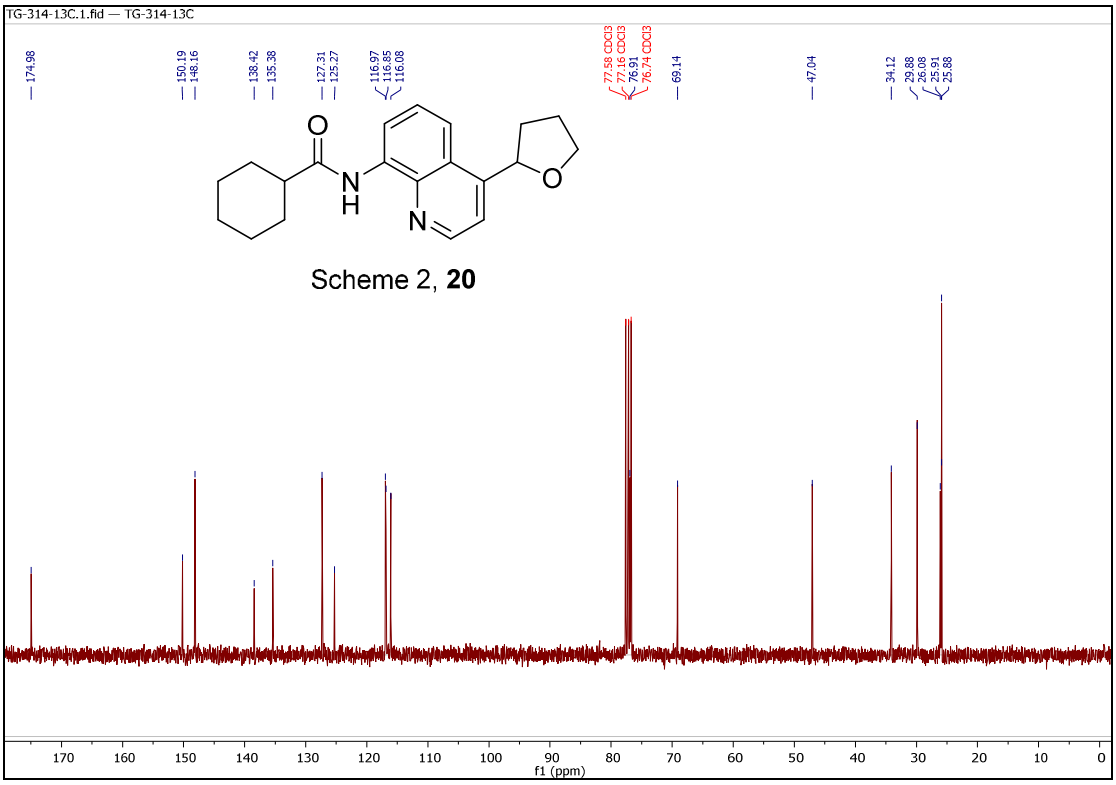
Scheme 2, **18**

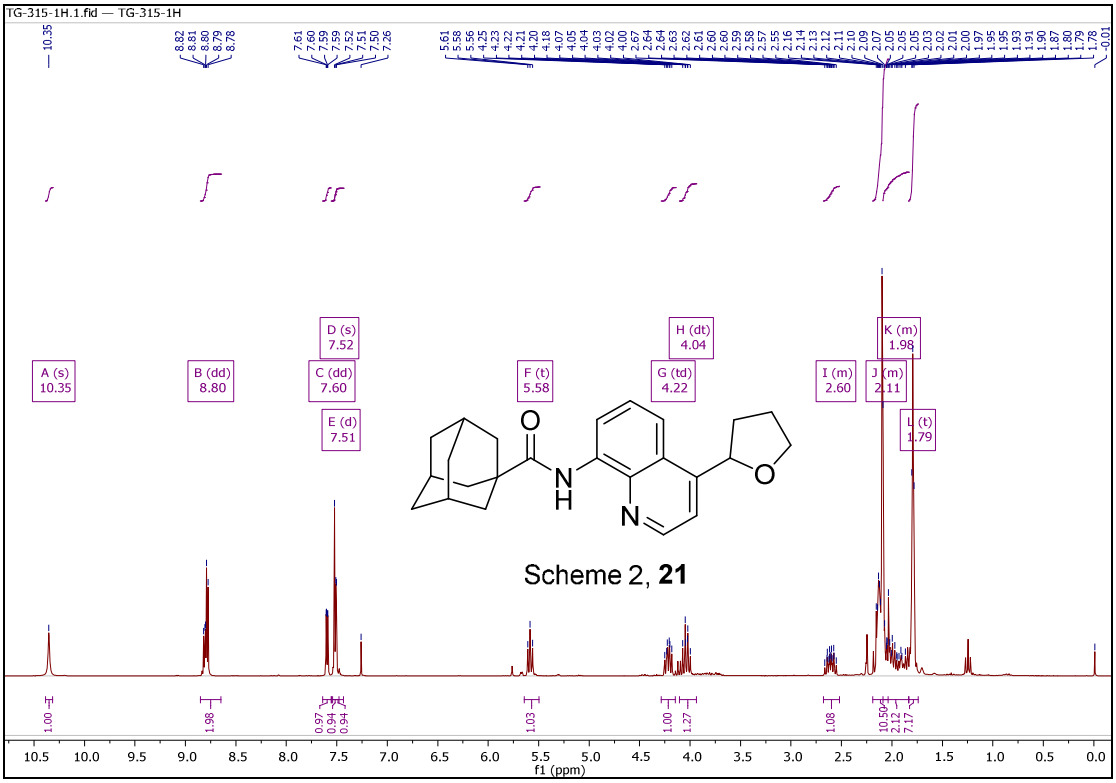

TG-R310-13C.1.fid — TG-R310-13C
168.89
150.23
148.16
138.15
135.22
127.26
125.25
117.07
117.03
116.06
77.58 CDCl3
77.16 CDCl3
76.90
76.73 CDCl3
69.15
34.11
26.09
25.28
Scheme 2, 18
f1 (ppm)

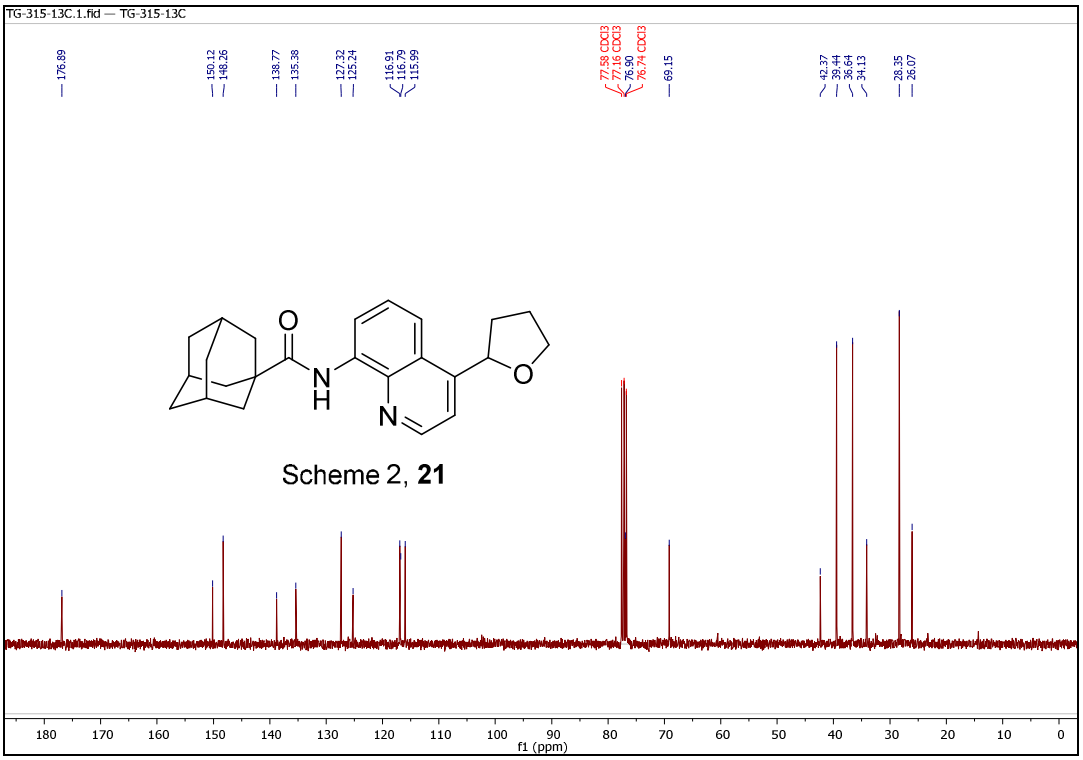

TG-302-1H.1.fid — TG-302-1H
Scheme 2, 19
A (s) 10.40
B (m) 8.78
C (dd) 7.60
D (m) 7.53
F (ddd) 4.23
G (dt) 4.05
H (m) 2.62
I (ddtd) 2.04
J (ddt) 1.82
K (s) 1.42
f1 (ppm)

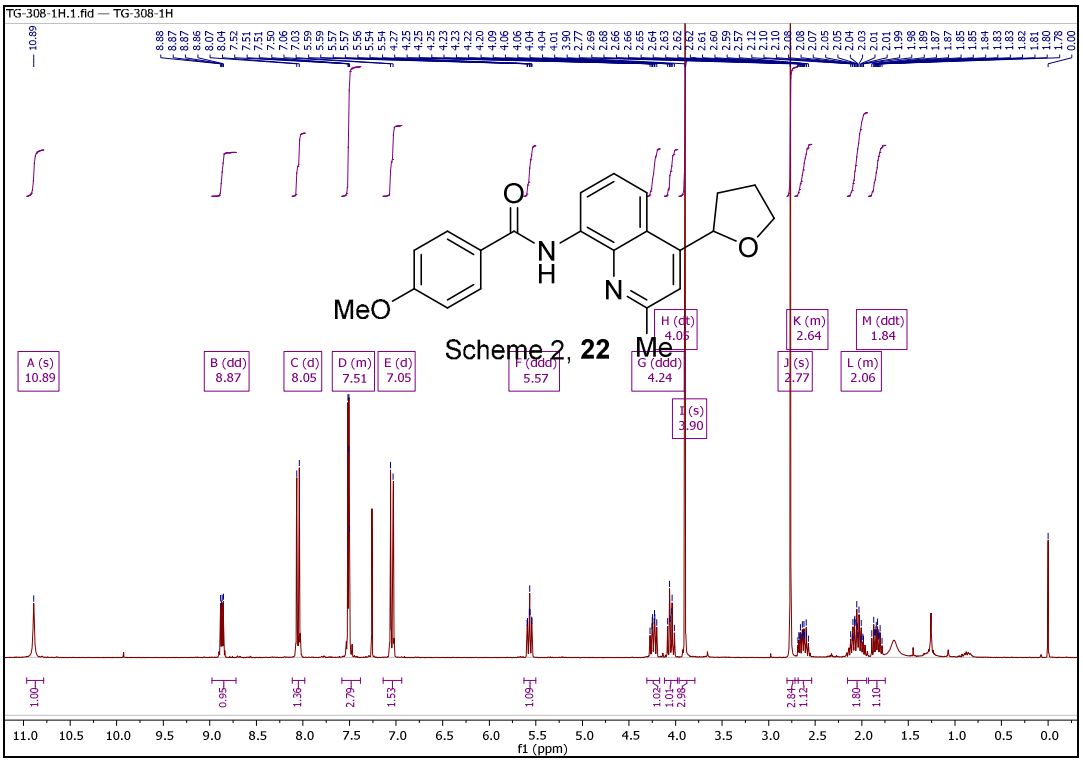

TG-302-13C.1.fid — TG-302-13C
177.42
150.17
148.32
138.77
135.47
127.35
125.29
116.98
116.87
115.91
77.58 CDCl3
77.16 CDCl3
76.96
76.74 CDCl3
69.18
40.52
34.19
27.88
26.11
O
tBu
N
H
N
O
Scheme 2, 19
f1 (ppm)

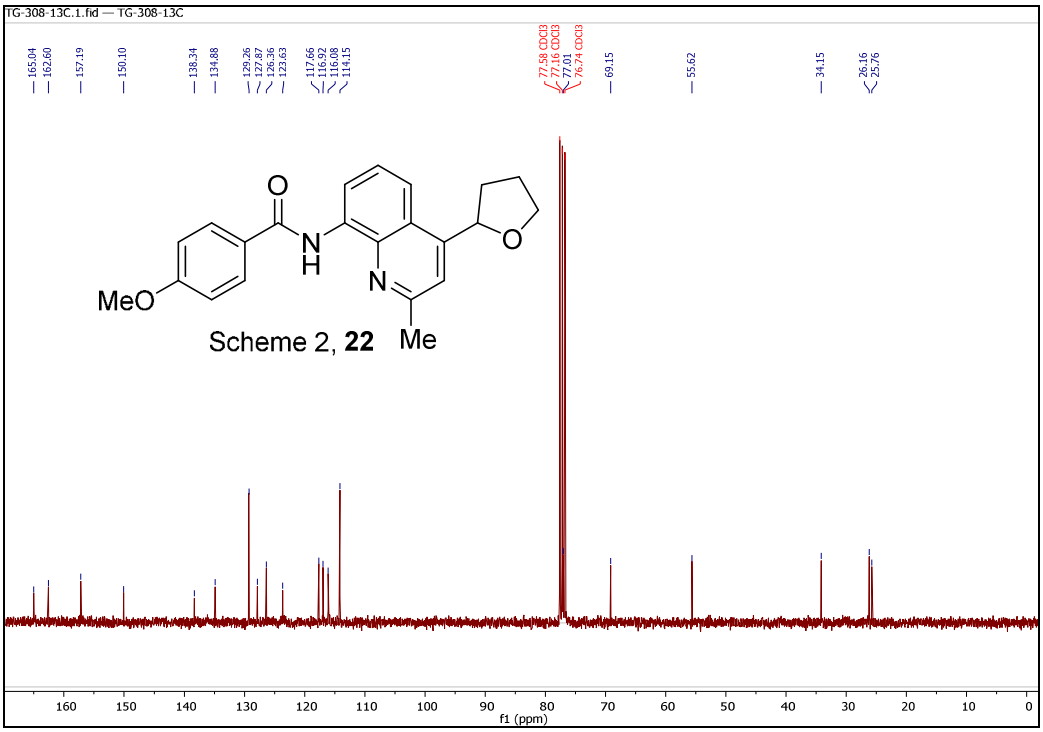

TG-314-1H.1.fid — TG-314-1H
A (s) 10.01
B (m) 8.78
C (dd) 7.60
D (m) 7.51
E (t)
F (ddd) 4.21
G (dt) 4.03
H (dtd) 2.61
I (tt) 2.47
J (m) 2.07
K (m) 1.97
L (m) 1.85
M (m) 1.76
N (td) 1.61
O (dt) 1.42
P (m) 1.34
Q (m) 1.25
Scheme 2, 20
f1 (ppm)

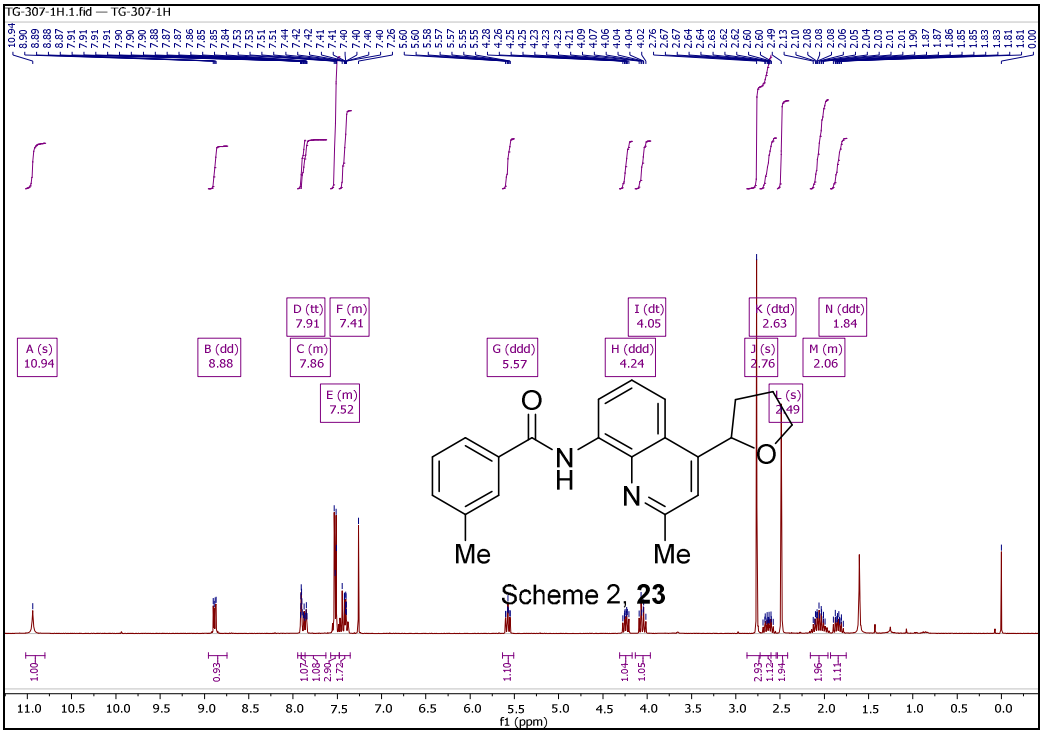

TG-314-13C.1.fid — TG-314-13C
174.98
150.19
148.16
138.42
135.38
127.31
125.27
116.97
116.85
116.08
77.58 CDCl3
77.16 CDCl3
76.91
76.74 CDCl3
69.14
47.04
34.12
29.88
26.08
25.91
25.88
Scheme 2, 20
f1 (ppm)

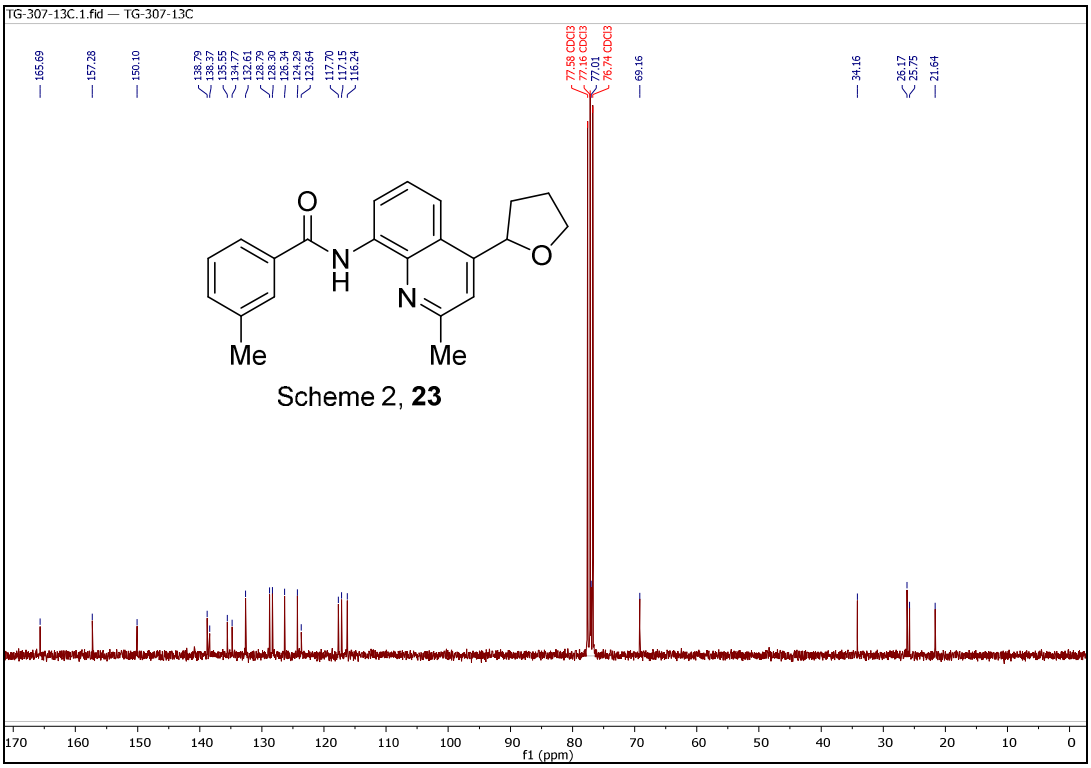

TG-315-1H.1.fid — TG-315-1H
10.35
8.82
8.81
8.80
8.79
8.78
7.61
7.60
7.59
7.52
7.51
7.50
7.26
5.61
5.58
5.56
4.25
4.23
4.22
4.21
4.20
4.18
4.07
4.05
4.04
4.03
4.02
4.00
2.67
2.64
2.64
2.63
2.62
2.61
2.60
2.60
2.59
2.59
2.57
2.55
2.16
2.14
2.13
2.12
2.11
2.10
2.09
2.07
2.05
2.05
2.05
2.03
2.02
2.01
2.00
1.97
1.95
1.95
1.93
1.91
1.90
1.87
1.80
1.79
1.78
-0.01
A (s) 10.35
B (dd) 8.80
C (dd) 7.60
D (s) 7.52
E (d) 7.51
F (t) 5.58
G (td) 4.22
H (dt) 4.04
I (m) 2.60
J (m) 2.11
K (m) 1.98
L (t) 1.79
Scheme 2, 21
f1 (ppm)

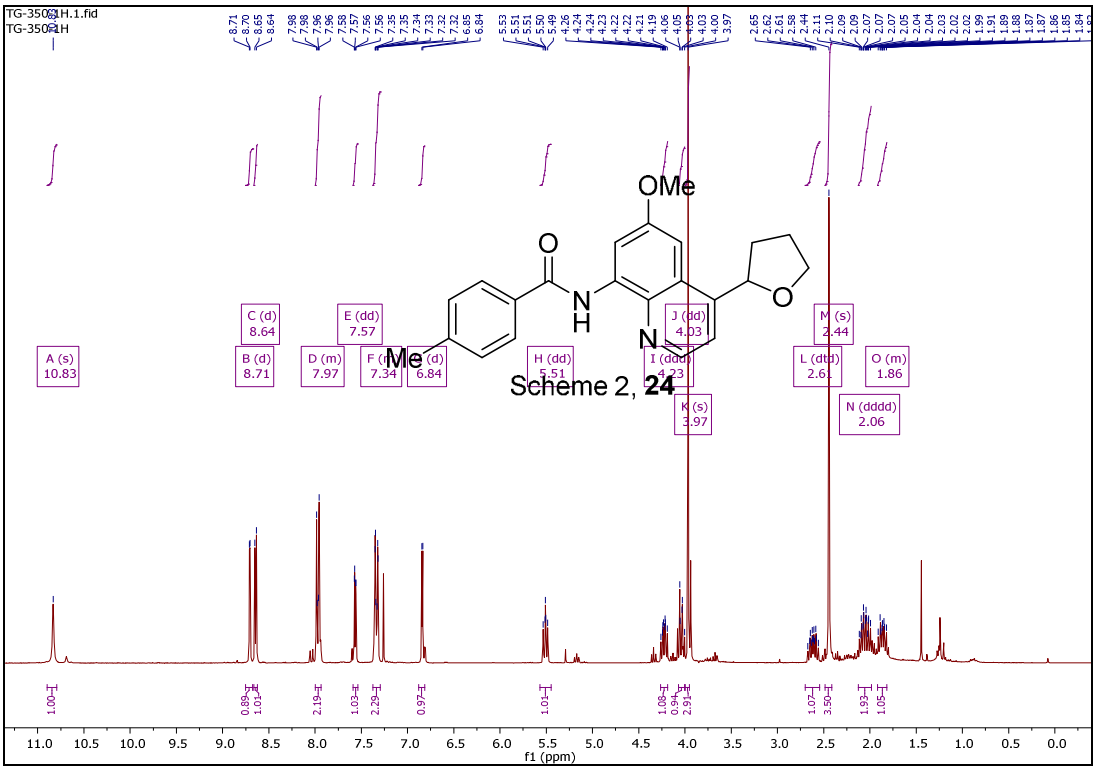

TG-315-13C.1.fid — TG-315-13C
176.89
150.12
148.26
138.77
135.38
127.32
125.24
116.91
116.79
115.99
77.58 CDCl3
77.16 CDCl3
76.90
76.74 CDCl3
69.15
42.37
39.44
36.64
34.13
28.35
26.07
Scheme 2, 21
f1 (ppm)

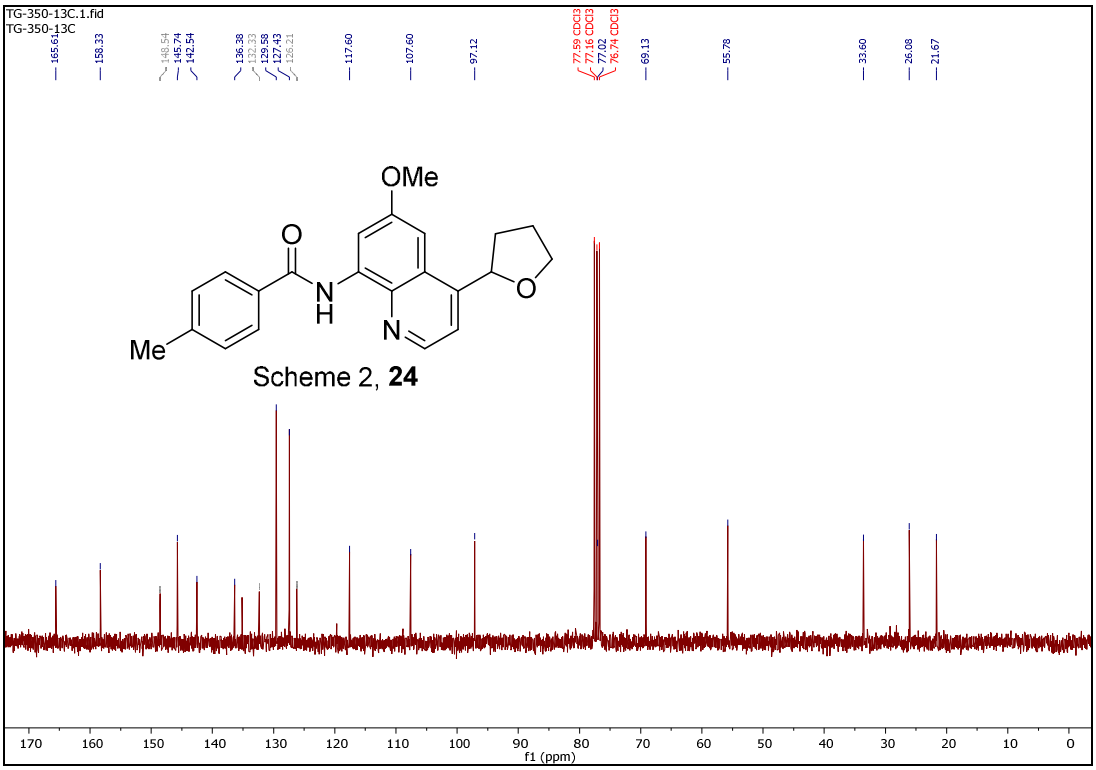

TG-308-1H.1.fid — TG-308-1H
MeO
Me
Scheme 2, 22
A (s) 10.89
B (dd) 8.87
C (d) 8.05
D (m) 7.51
E (d) 7.05
F (ddd) 5.57
G (ddd) 4.24
H (dt) 4.05
I (s) 3.90
J (s) 2.77
K (m) 2.64
L (m) 2.06
M (ddt) 1.84
f1 (ppm)

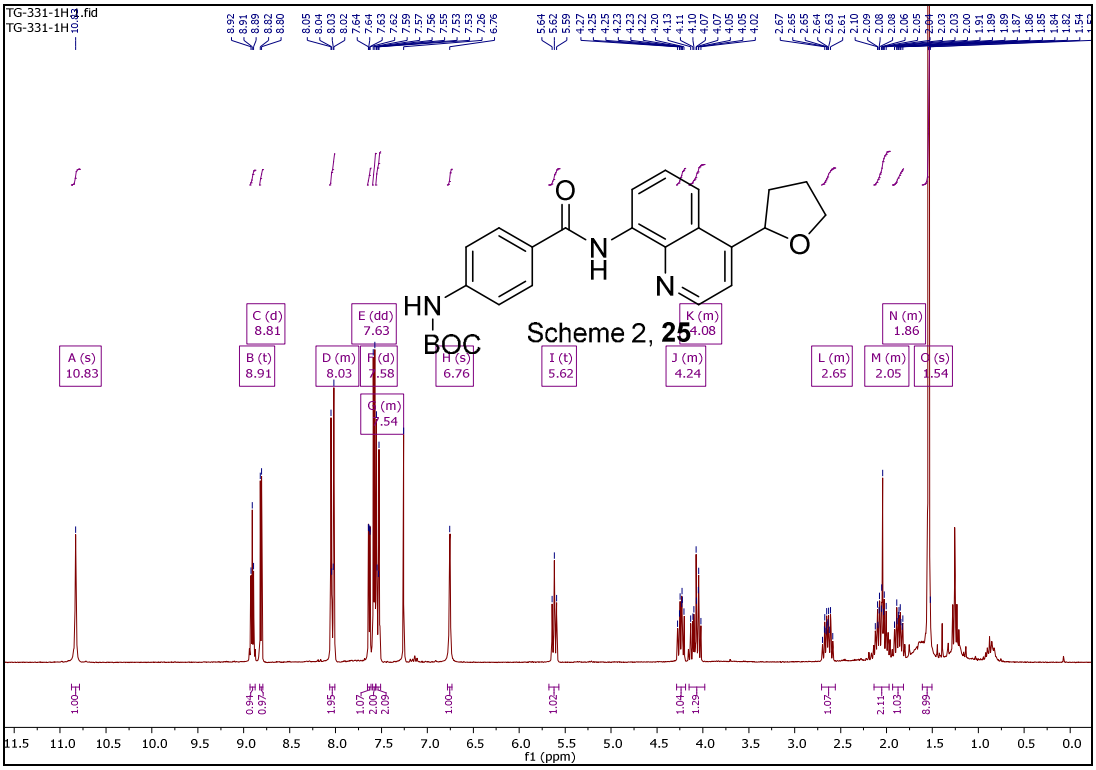

TG-308-13C.1.fid — TG-308-13C
165.04
162.60
157.19
150.10
138.34
134.88
129.26
127.87
126.36
123.63
117.66
116.92
116.08
114.15
77.58 CDCl3
77.16 CDCl3
77.01
76.74 CDCl3
69.15
55.62
34.15
26.16
25.76
O
N
H
N
O
MeO
Me
Scheme 2, 22
f1 (ppm)

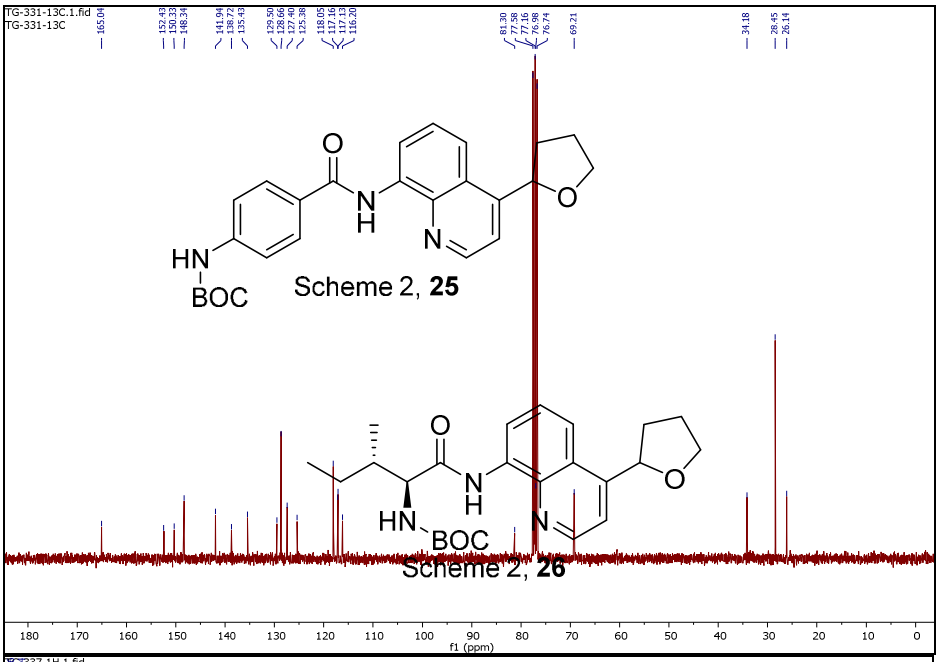

TG-307-1H.1.fid — TG-307-1H
A (s) 10.94
B (dd) 8.88
C (m) 7.86
D (tt) 7.91
E (m) 7.52
F (m) 7.41
G (ddd) 5.57
H (ddd) 4.24
I (dt) 4.05
J (s) 2.76
K (dtd) 2.63
L (s) 2.49
M (m) 2.06
N (ddt) 1.84
O
N
H
N
O
Me
Me
Scheme 2, 23
f1 (ppm)

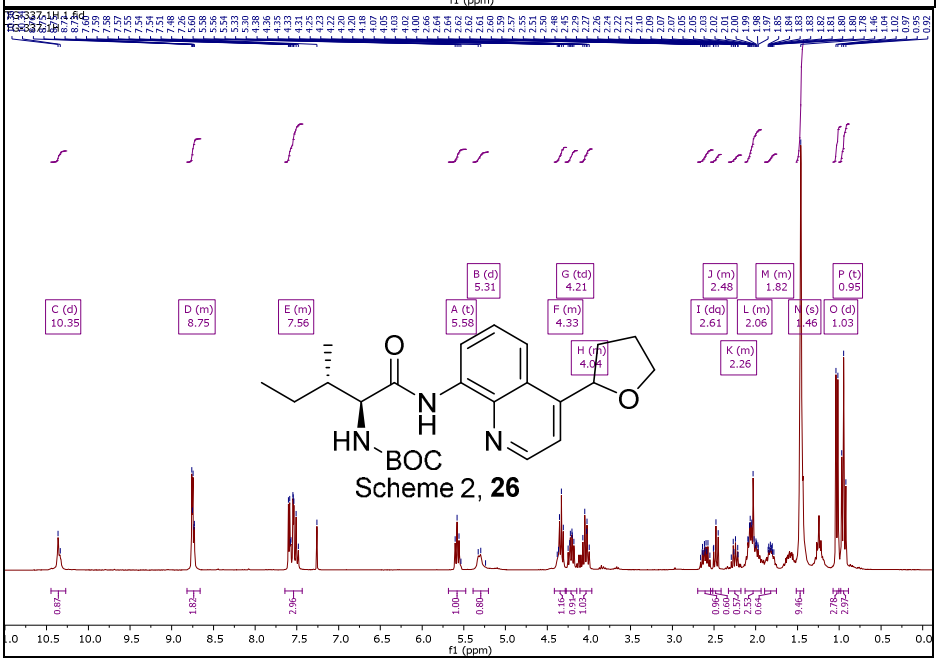

TG-307-13C.1.fid — TG-307-13C
Scheme 2, 23
f1 (ppm)

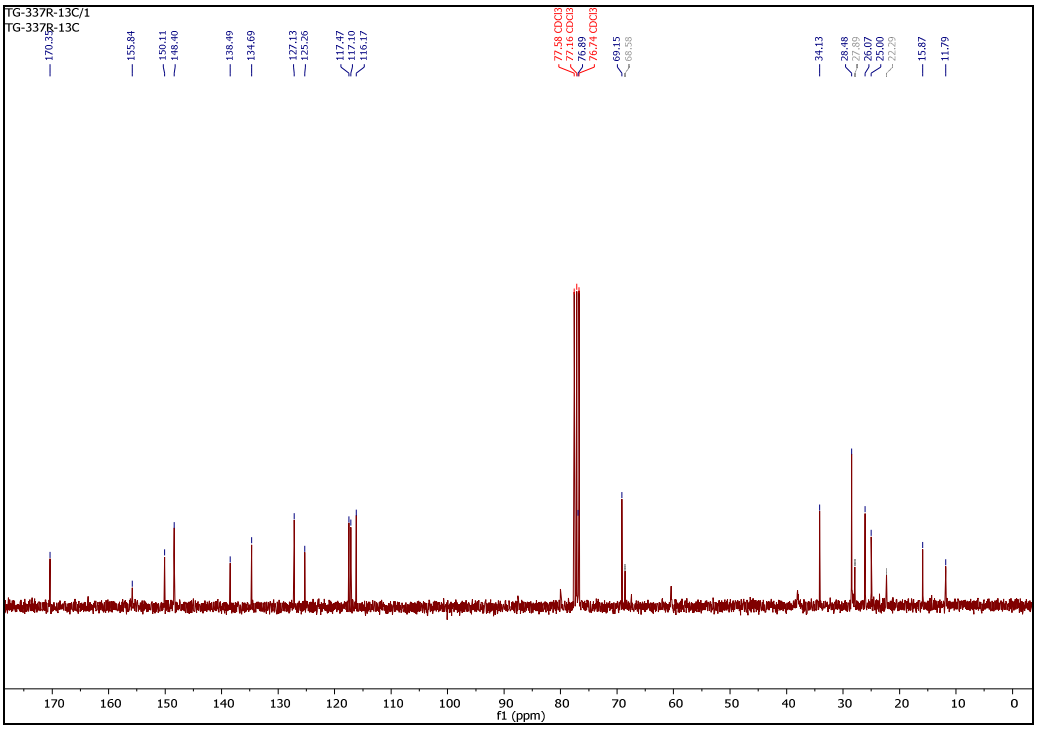

TG-350-1H.1.fid
Scheme 2, 24
f1 (ppm)

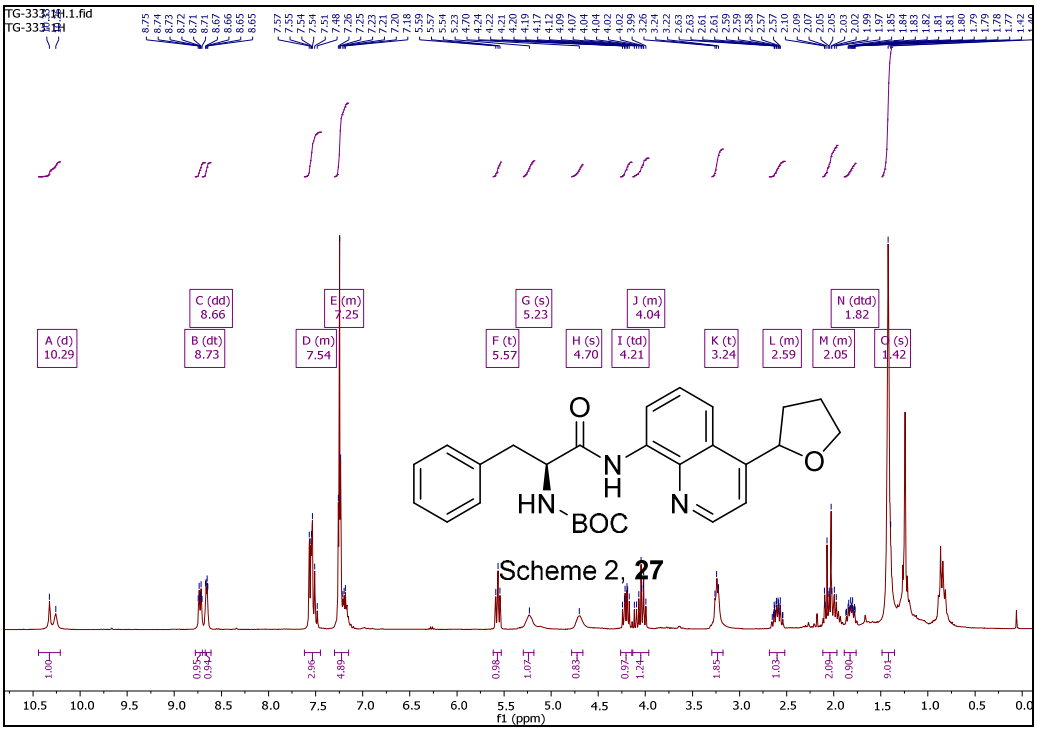

TG-350-13C.1.fid
TG-350-13C
OMe
O
N
H
N
O
Me
Scheme 2, 24
f1 (ppm)

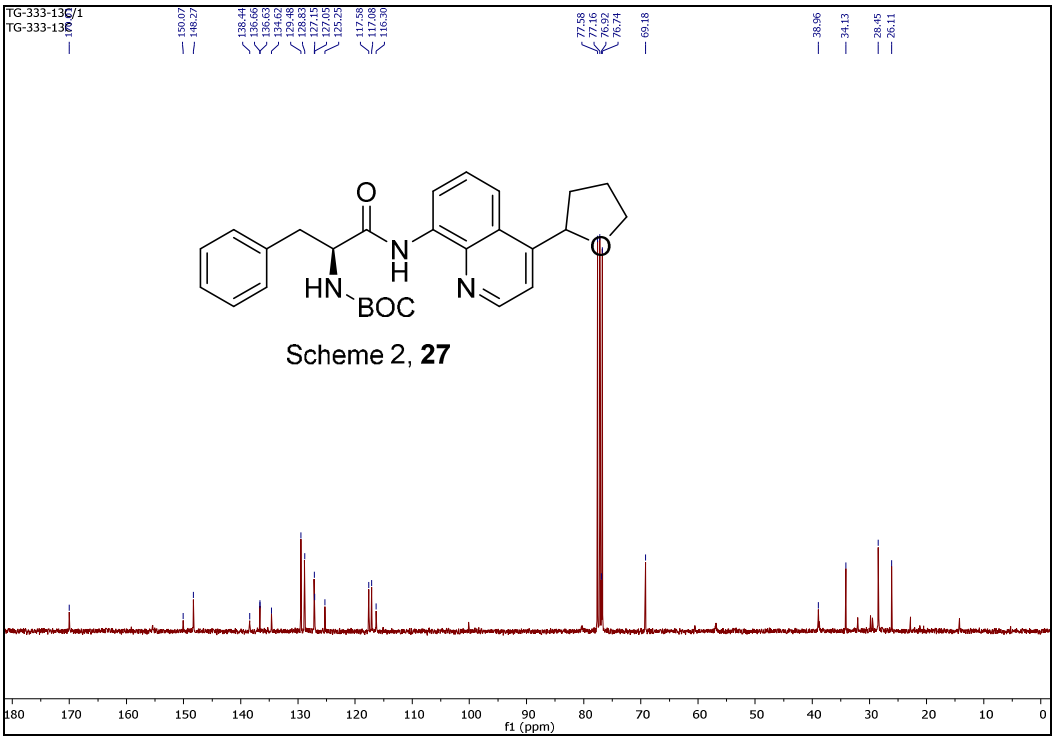

TG-331-1H.1.fid
TG-331-1H
O
N
H
N
O
HN
BOC
Scheme 2, 25
A (s) 10.83
B (t) 8.91
C (d) 8.81
D (m) 8.03
E (dd) 7.63
F (d) 7.58
G (m) 7.54
H (s) 6.76
I (t) 5.62
J (m) 4.24
K (m) 4.08
L (m) 2.65
M (m) 2.05
N (m) 1.86
O (s) 1.54
f1 (ppm)

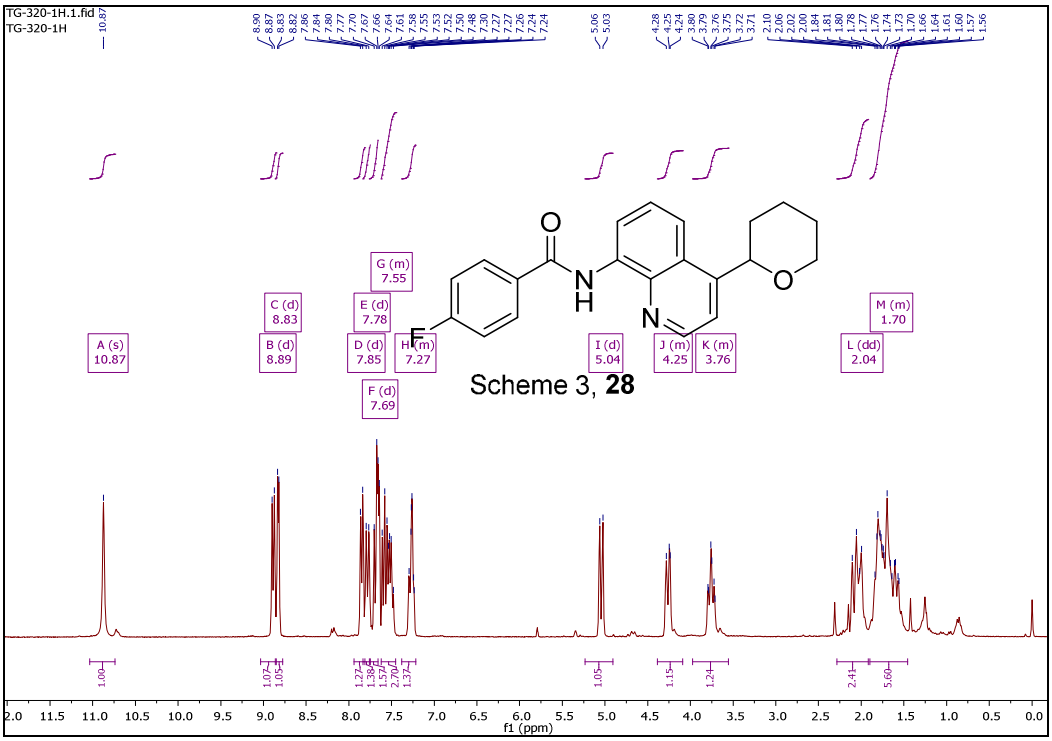

TG-331-13C.1.fid
TG-331-13C
Scheme 2, 25
Scheme 2, 26
f1 (ppm)

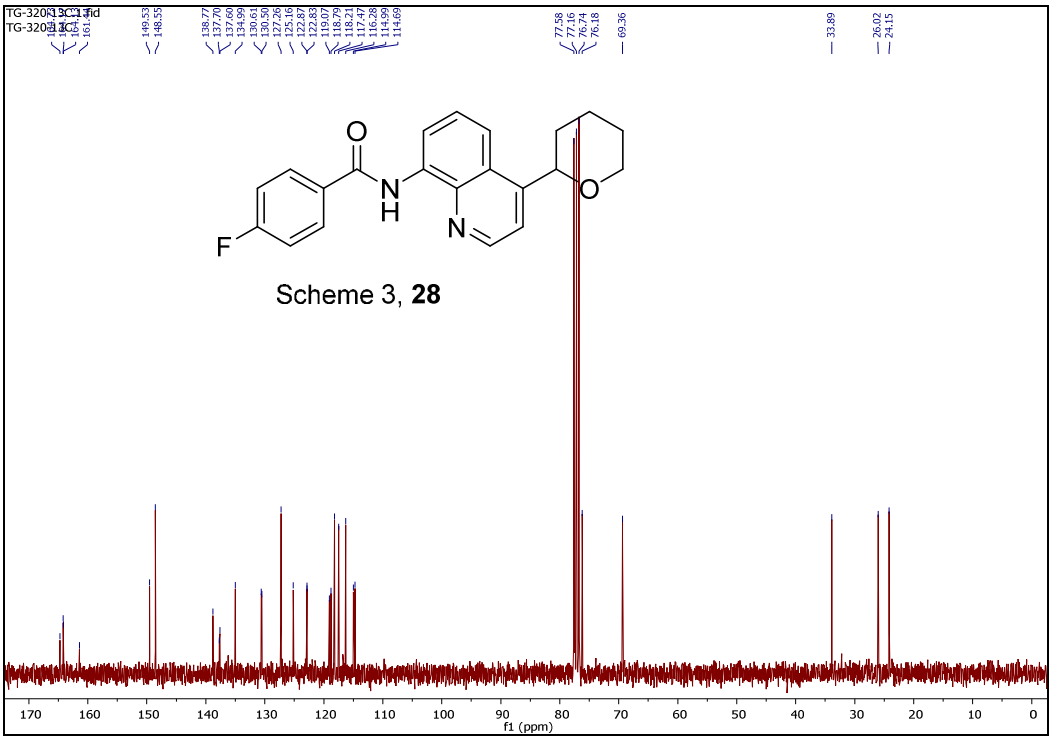

C (d) 10.35
D (m) 8.75
E (m) 7.56
B (d) 5.31
A (t) 5.58
G (td) 4.21
F (m) 4.33
H (m) 4.04
J (m) 2.48
I (dq) 2.61
L (m) 2.06
K (m) 2.26
M (m) 1.82
N (s) 1.46
P (t) 0.95
O (d) 1.03
Scheme 2, 26
f1 (ppm)

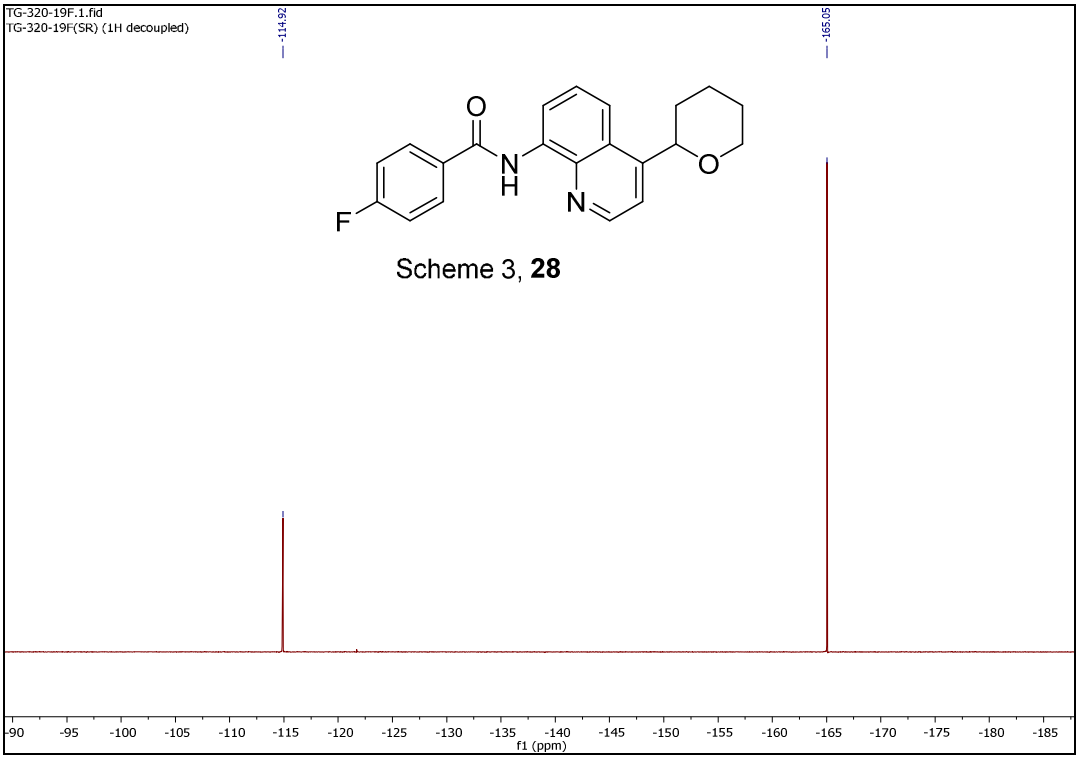

TG-337R-13C/1
TG-337R-13C
170.38
155.84
150.11
148.40
138.49
134.69
127.13
125.26
117.47
117.10
116.17
77.58 CDCl3
77.16 CDCl3
76.89
76.74 CDCl3
69.15
68.58
34.13
28.48
27.89
26.07
25.00
22.29
15.87
11.79
f1 (ppm)

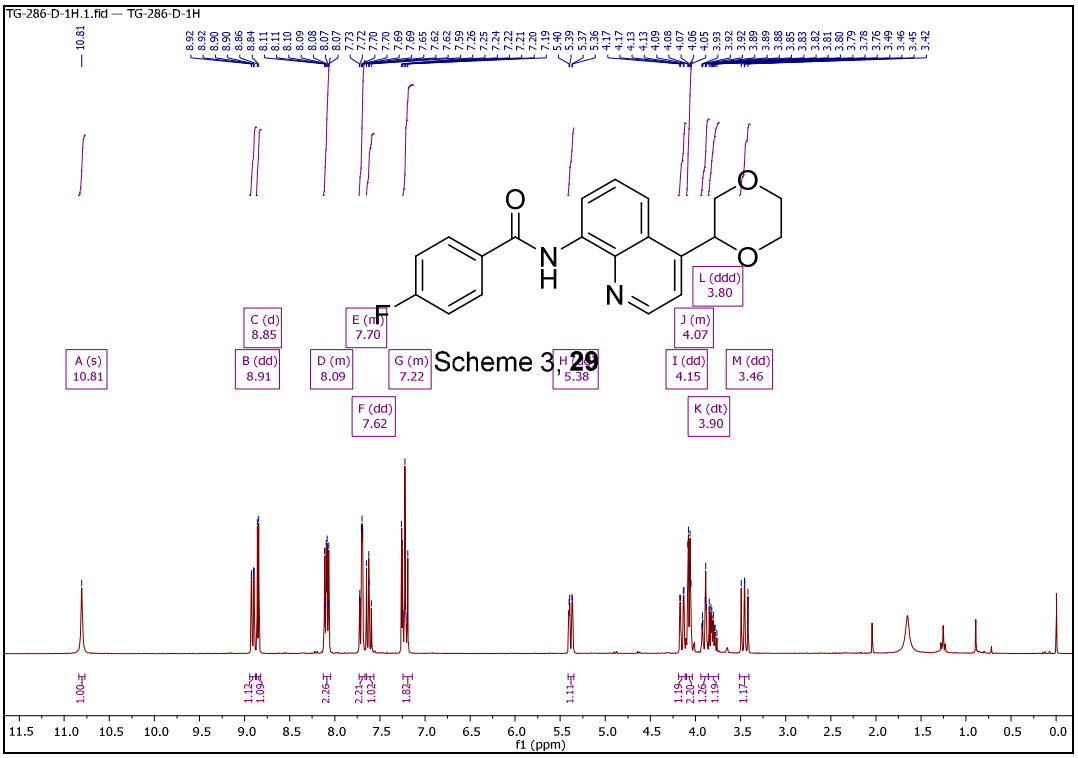

TG-337R-1H.1.fid
TG-337R-1H
A (d) 10.29
B (dt) 8.73
C (dd) 8.66
D (m) 7.54
E (m) 7.25
F (t) 5.57
G (s) 5.23
H (s) 4.70
I (td) 4.21
J (m) 4.04
K (t) 3.24
L (m) 2.59
M (m) 2.05
N (dtd) 1.82
O (s) 1.42
O
N
H
HN
BOC
N
O
Scheme 2, 27
f1 (ppm)

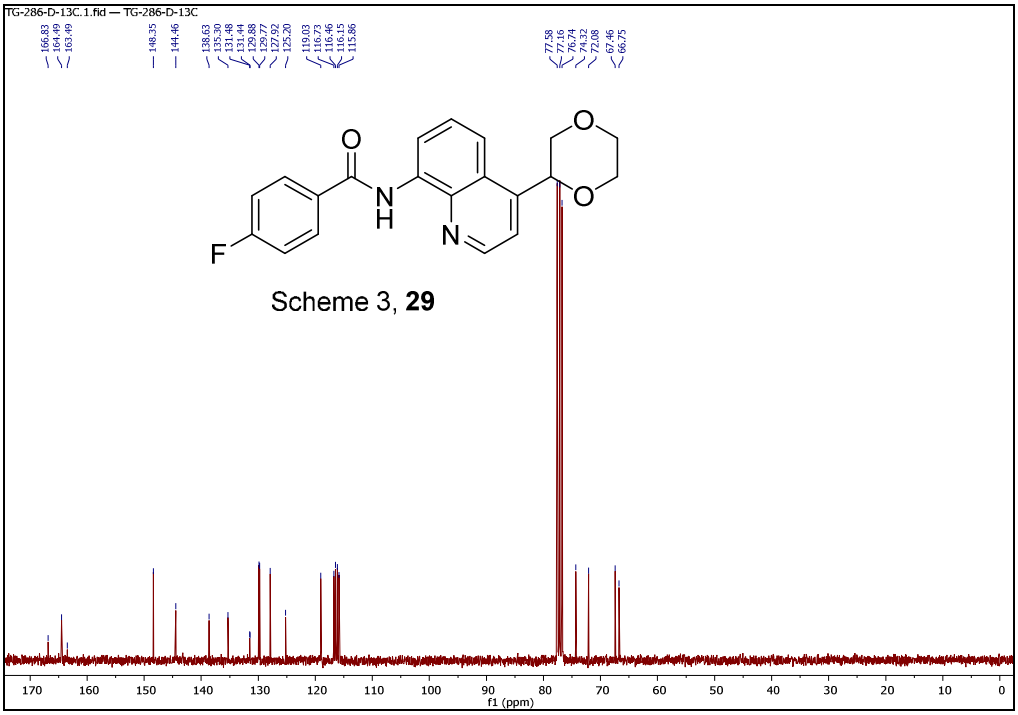

TG-333-13C/1
TG-333-13C
Scheme 2, 27
f1 (ppm)

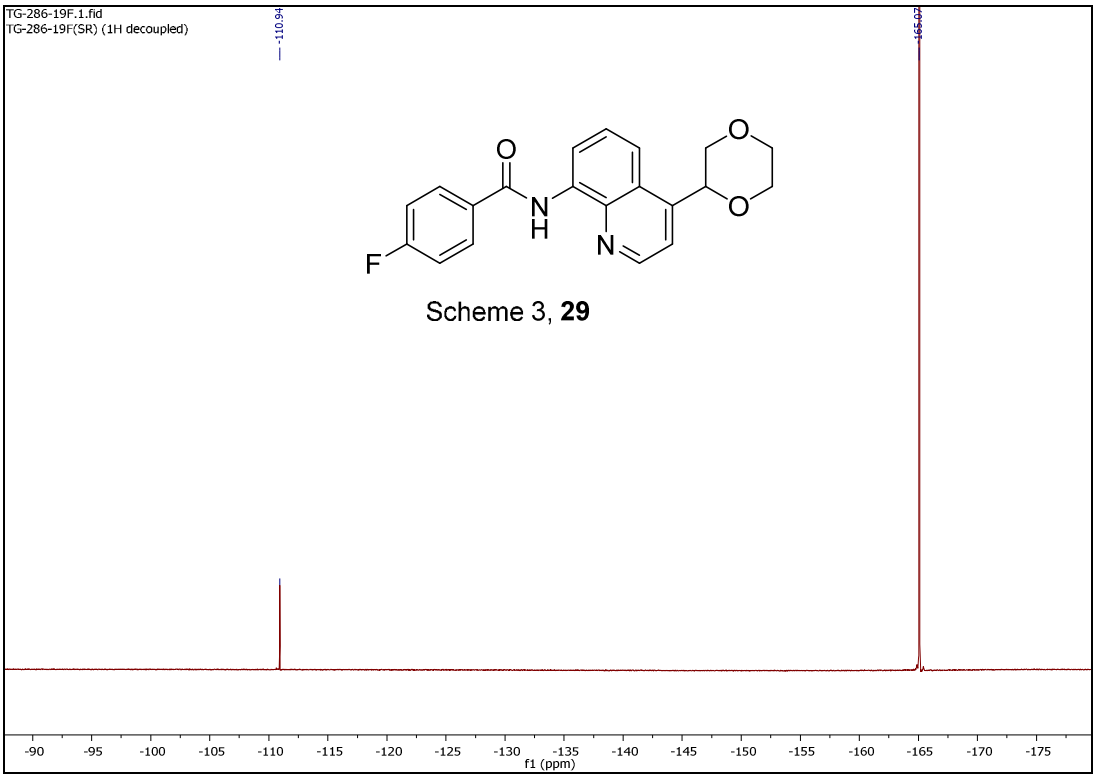

TG-320-1H.1.fid
TG-320-1H
A (s) 10.87
B (d) 8.89
C (d) 8.83
D (d) 7.85
E (d) 7.78
F (d) 7.69
G (m) 7.55
H (m) 7.27
I (d) 5.04
J (m) 4.25
K (m) 3.76
L (dd) 2.04
M (m) 1.70
Scheme 3, 28
f1 (ppm)

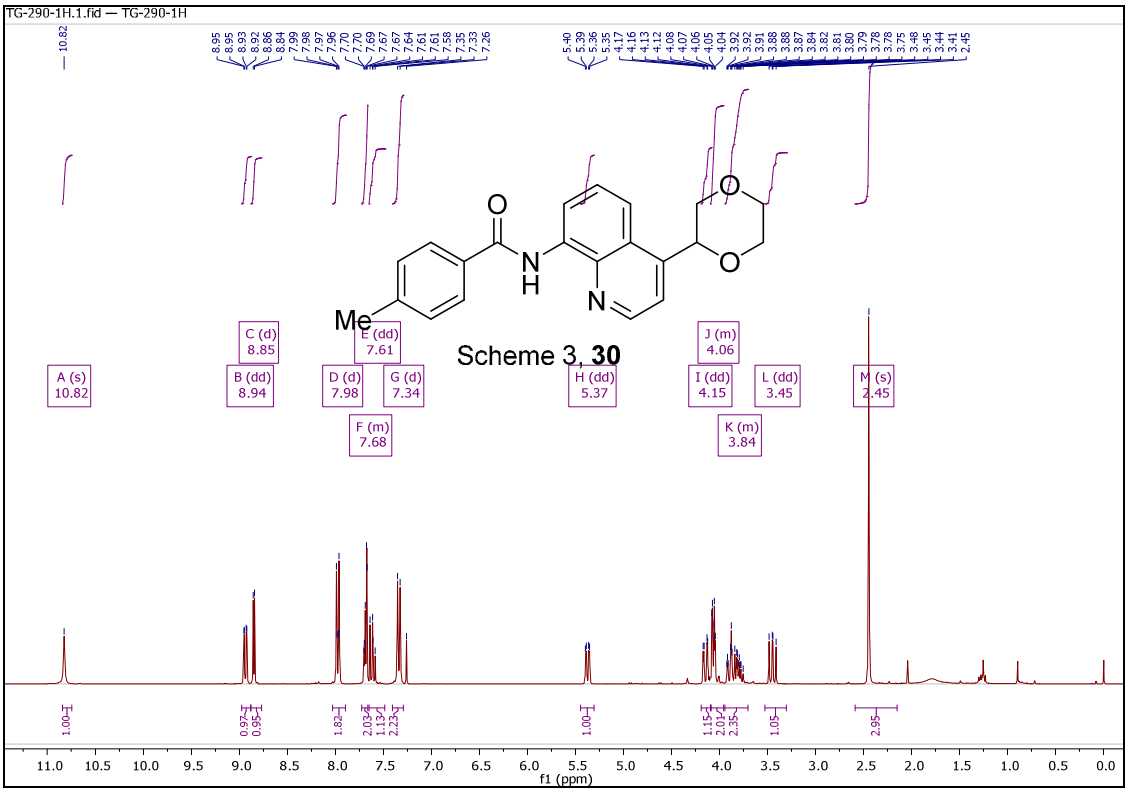

TG-320-13C.1.fid
149.53
148.55
138.77
137.70
137.60
134.99
130.61
130.50
127.26
125.16
122.87
122.83
119.07
118.79
118.21
117.47
115.28
114.99
114.69
77.58
77.16
76.74
76.18
69.36
33.89
26.02
24.15
O
N
H
N
O
F
Scheme 3, **28**
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

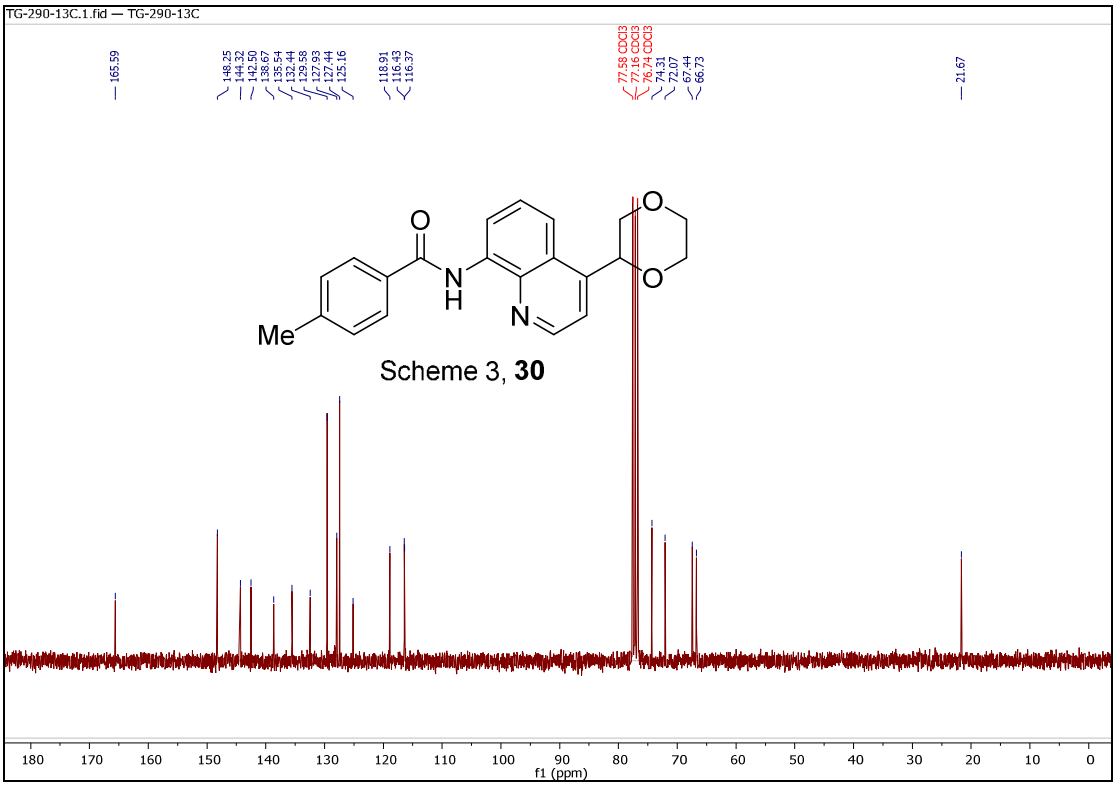

TG-320-19F.1.fid
TG-320-19F(SR) (1H decoupled)
-114.92
-165.05
O
N
H
N
O
F
Scheme 3, **28**
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
-165
-170
-175
-180
-185
f1 (ppm)

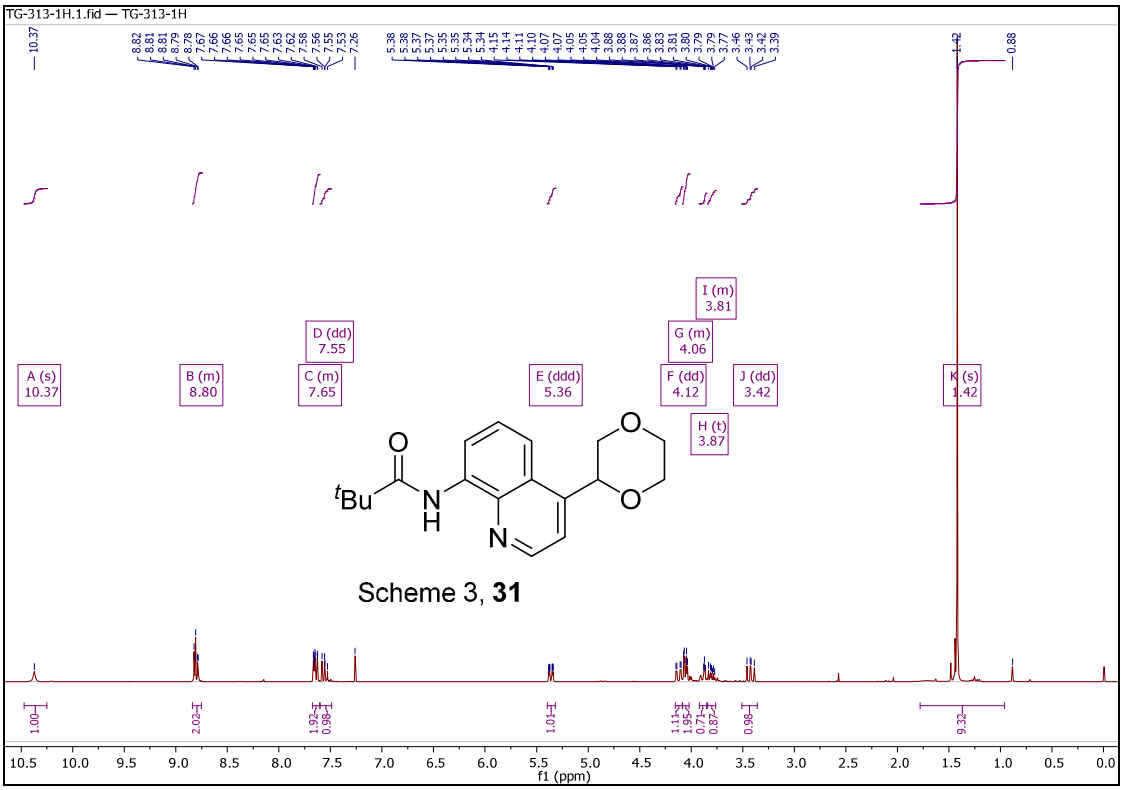

TG-286-D-1H.1.fid — TG-286-D-1H
A (s) 10.81
B (dd) 8.91
C (d) 8.85
D (m) 8.09
E (m) 7.70
F (dd) 7.62
G (m) 7.22
H 5.38
I (dd) 4.15
J (m) 4.07
K (dt) 3.90
L (ddd) 3.80
M (dd) 3.46
Scheme 3, 29
f1 (ppm)

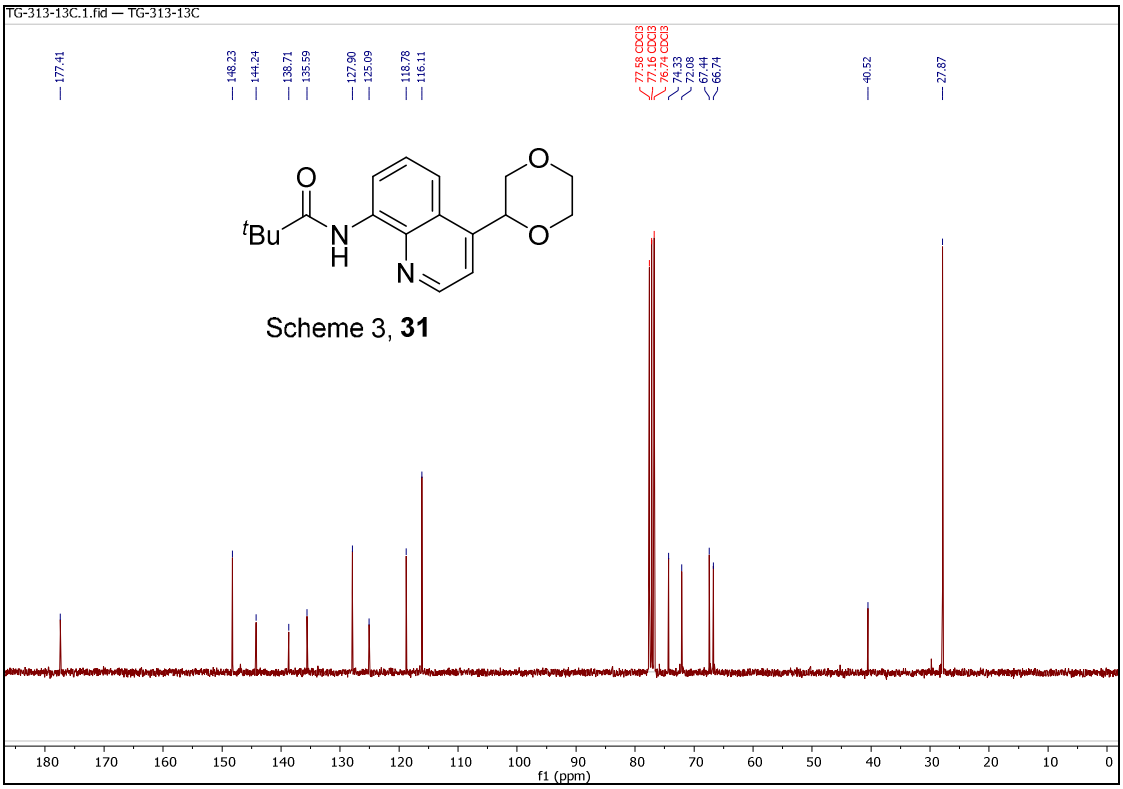

TG-286-D-13C.1.fid — TG-286-D-13C
Scheme 3, 29
f1 (ppm)

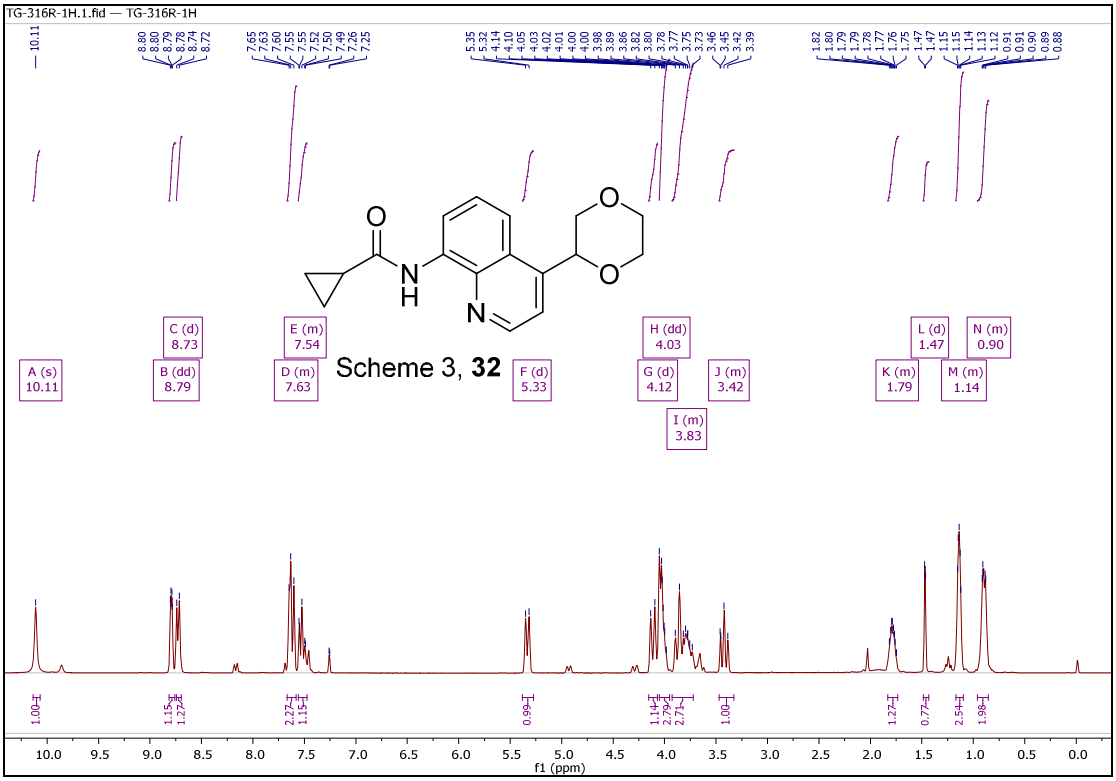

TG-286-19F.1.fid
TG-286-19F(SR) (1H decoupled)
-110.94
-165.02
Scheme 3, 29
f1 (ppm)

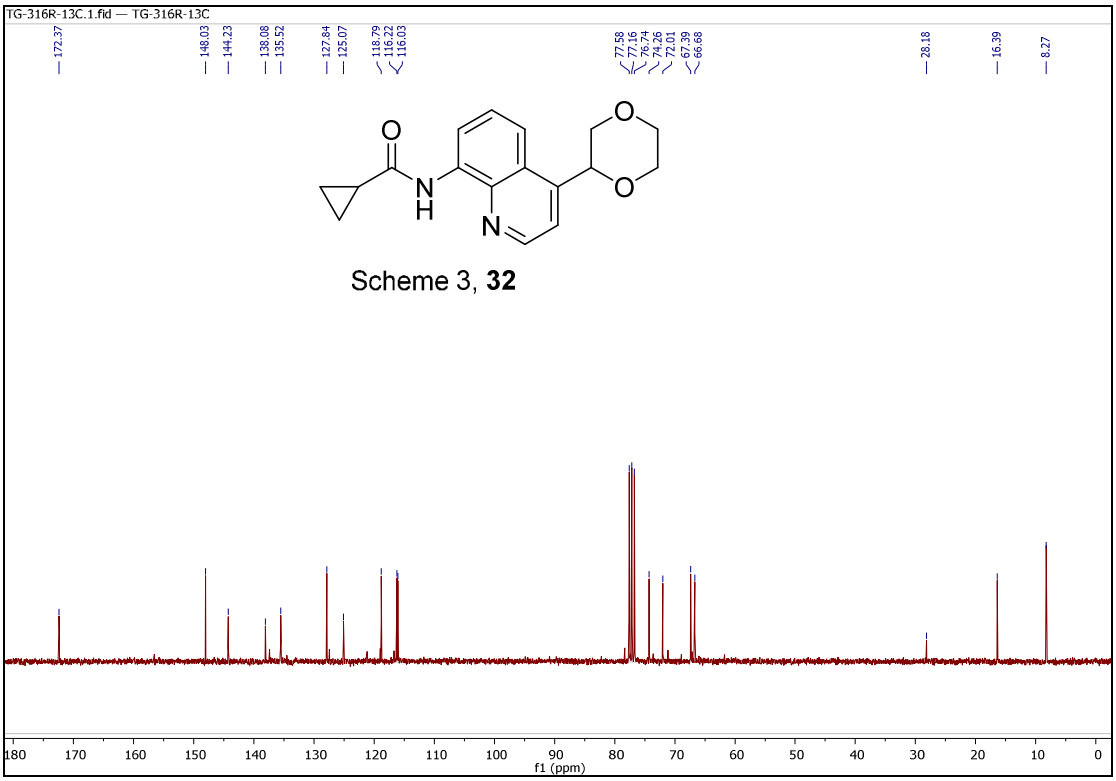

TG-290-1H.1.fid — TG-290-1H
Scheme 3, 30
A (s) 10.82
B (dd) 8.94
C (d) 8.85
D (d) 7.98
E (dd) 7.61
F (m) 7.68
G (d) 7.34
H (dd) 5.37
I (dd) 4.15
J (m) 4.06
K (m) 3.84
L (dd) 3.45
M (s) 2.45
f1 (ppm)

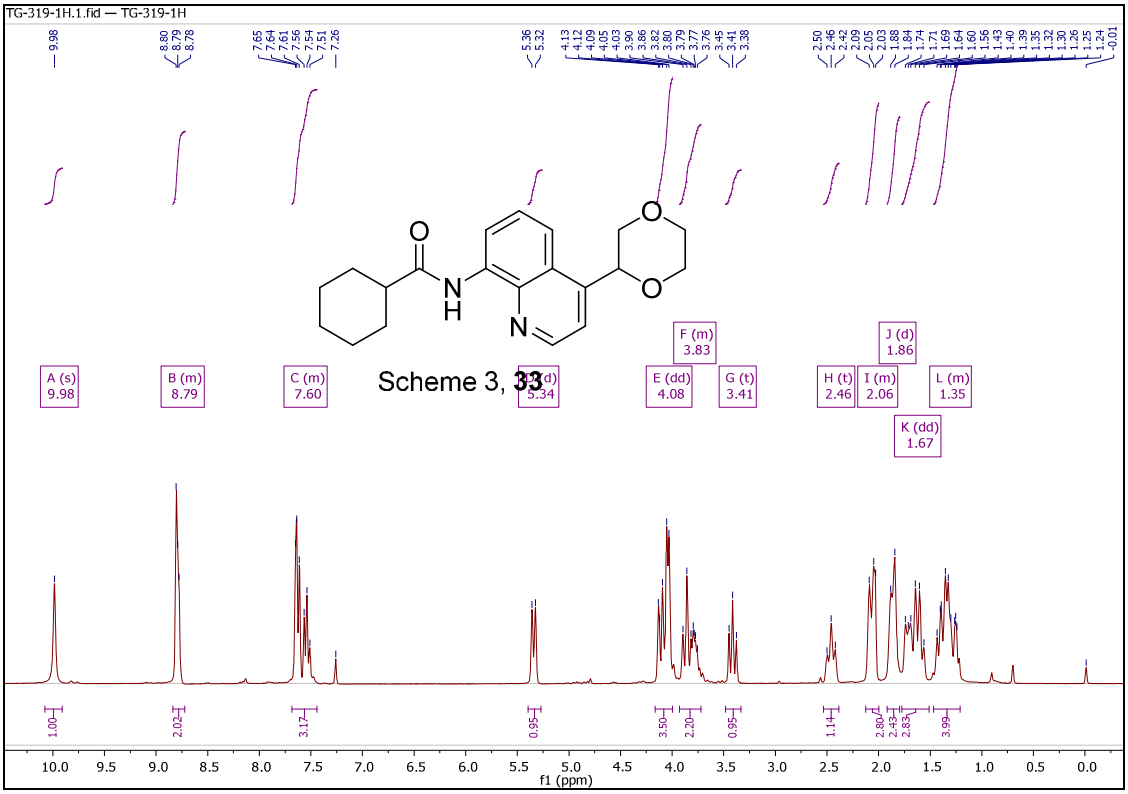

TG-290-13C.1.fid — TG-290-13C
165.59
148.25
144.32
142.50
138.67
135.54
132.44
129.58
129.93
127.44
125.16
118.91
116.43
116.37
77.58 CDCl3
77.16 CDCl3
76.74 CDCl3
74.31
72.07
67.44
66.73
21.67
Me
Scheme 3, 30
f1 (ppm)

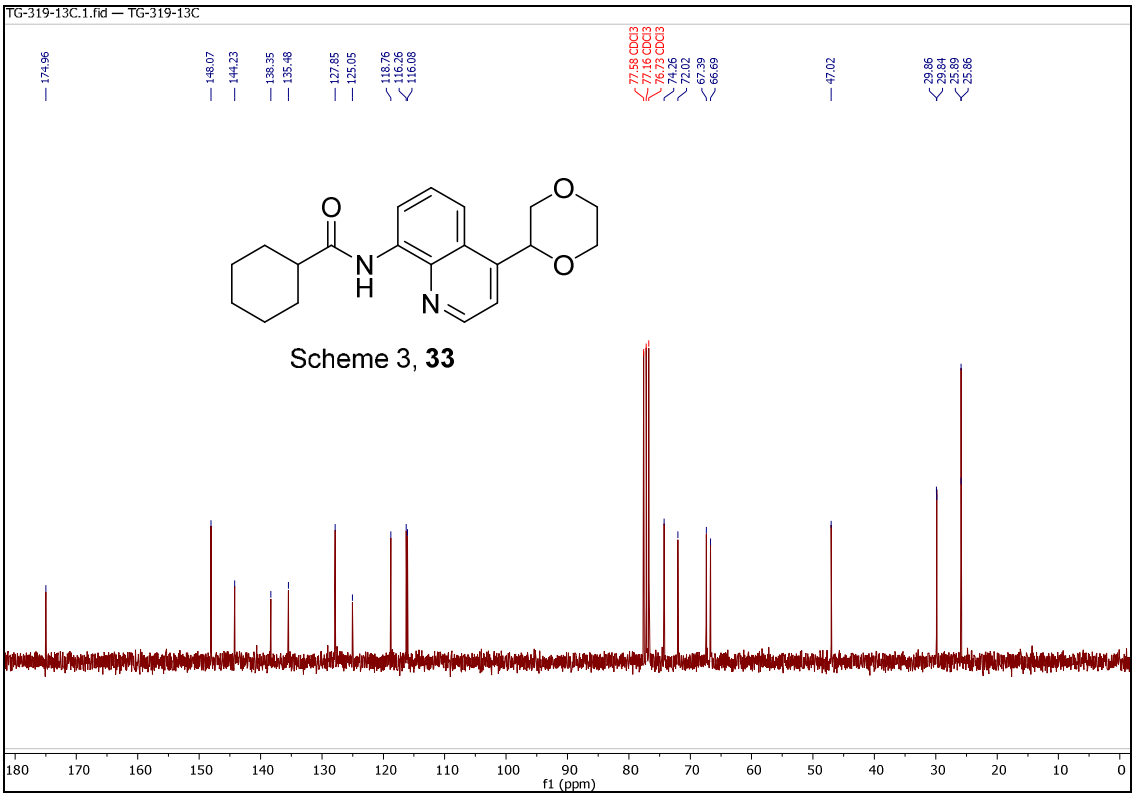

TG-313-1H.1.fid — TG-313-1H
10.37
8.82
8.81
8.81
8.79
8.78
7.67
7.66
7.66
7.65
7.65
7.65
7.63
7.62
7.58
7.56
7.55
7.53
7.26
5.38
5.38
5.37
5.37
5.35
5.35
5.34
5.34
4.15
4.14
4.11
4.10
4.07
4.07
4.05
4.05
4.04
4.04
3.88
3.88
3.87
3.86
3.83
3.81
3.80
3.79
3.79
3.77
3.46
3.43
3.42
3.39
1.42
0.88
A (s) 10.37
B (m) 8.80
C (m) 7.65
D (dd) 7.55
E (ddd) 5.36
F (dd) 4.12
G (m) 4.06
H (t) 3.87
I (m) 3.81
J (dd) 3.42
K (s) 1.42
tBu
Scheme 3, 31
1.00
2.03
1.92
0.98
1.01
1.11
1.95
0.71
0.87
0.98
9.32
f1 (ppm)

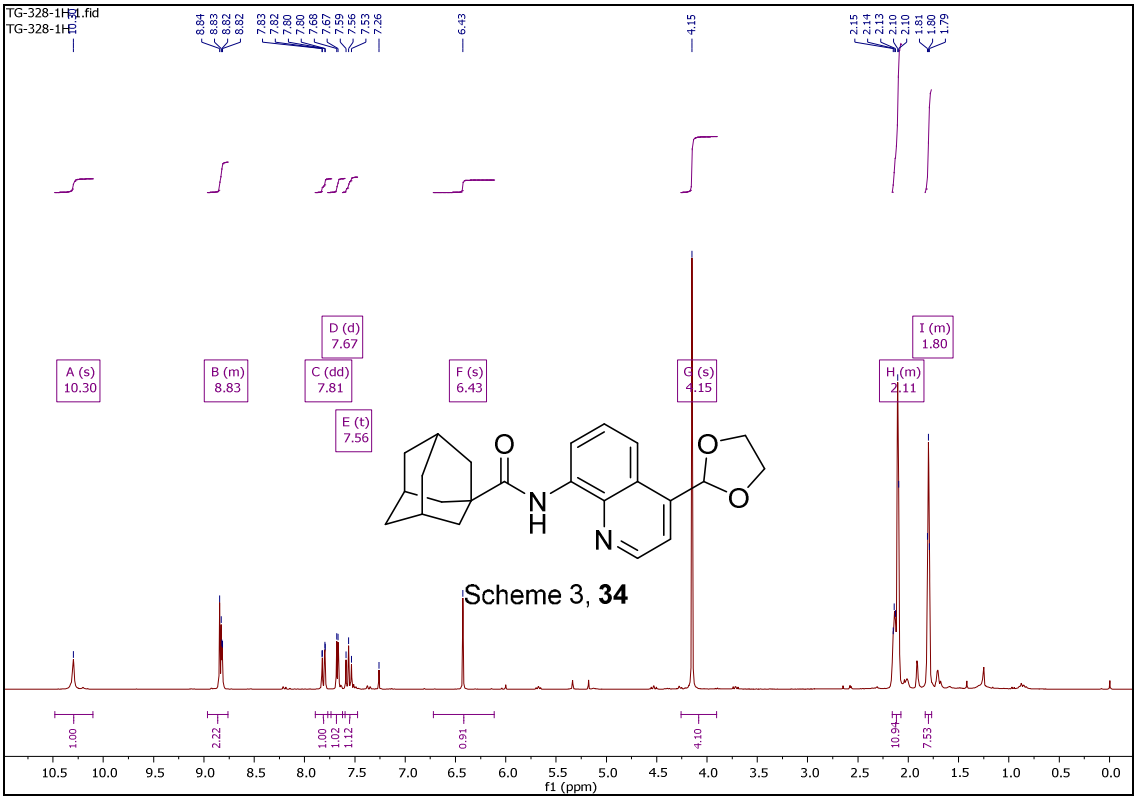

TG-313-13C.1.fid — TG-313-13C
177.41
148.23
144.24
138.71
135.59
127.90
125.09
118.78
116.11
77.58 CDCl3
77.16 CDCl3
76.74 CDCl3
74.33
72.08
67.44
66.74
40.52
27.87
Scheme 3, 31
f1 (ppm)

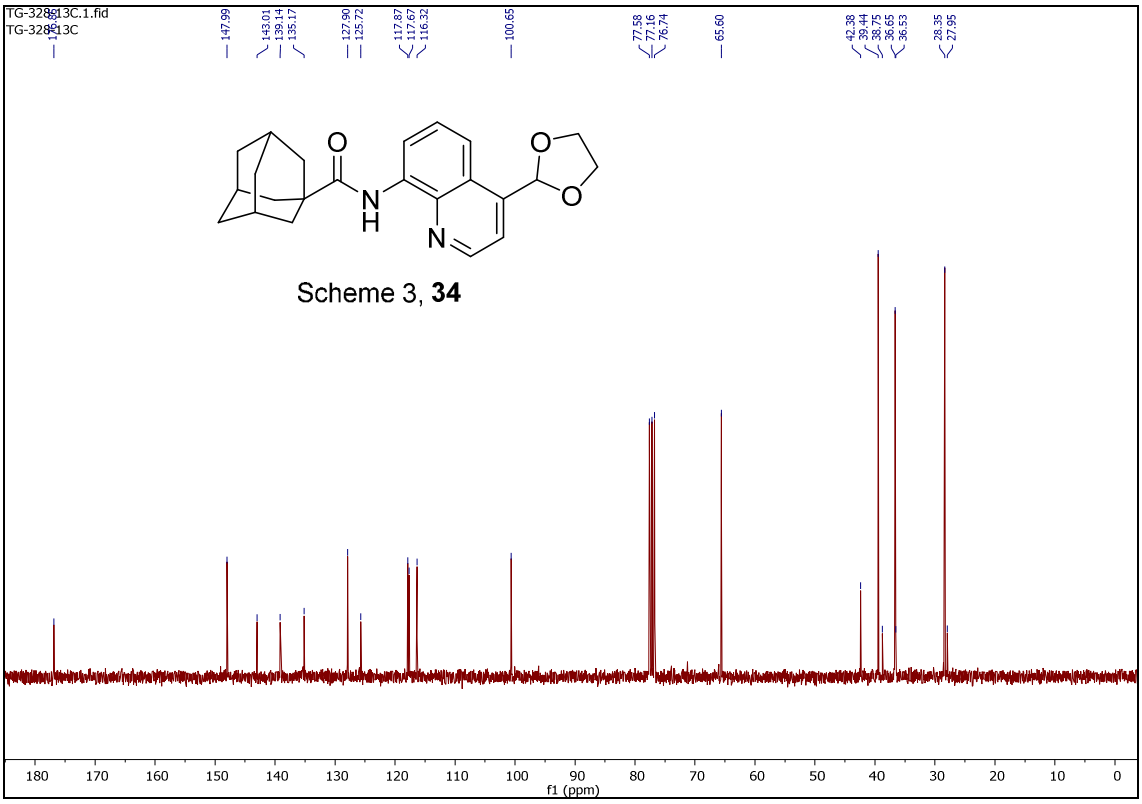

TG-316R-1H.1.fid — TG-316R-1H
A (s) 10.11
B (dd) 8.79
C (d) 8.73
D (m) 7.63
E (m) 7.54
F (d) 5.33
G (d) 4.12
H (dd) 4.03
I (m) 3.83
J (m) 3.42
K (m) 1.79
L (d) 1.47
M (m) 1.14
N (m) 0.90
Scheme 3, 32
f1 (ppm)

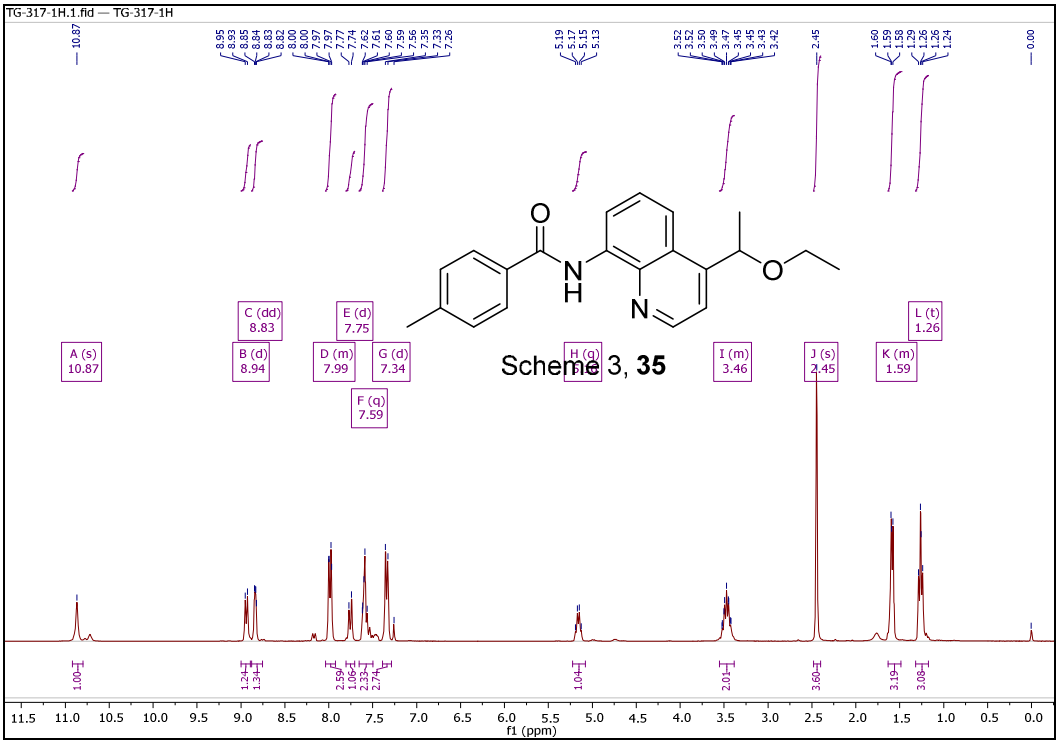

TG-316R-13C.1.fid — TG-316R-13C
172.37
148.03
144.23
138.08
135.52
127.84
125.07
118.79
116.22
116.03
77.58
77.16
76.74
74.26
72.01
67.39
66.68
28.18
16.39
8.27
Scheme 3, 32
f1 (ppm)

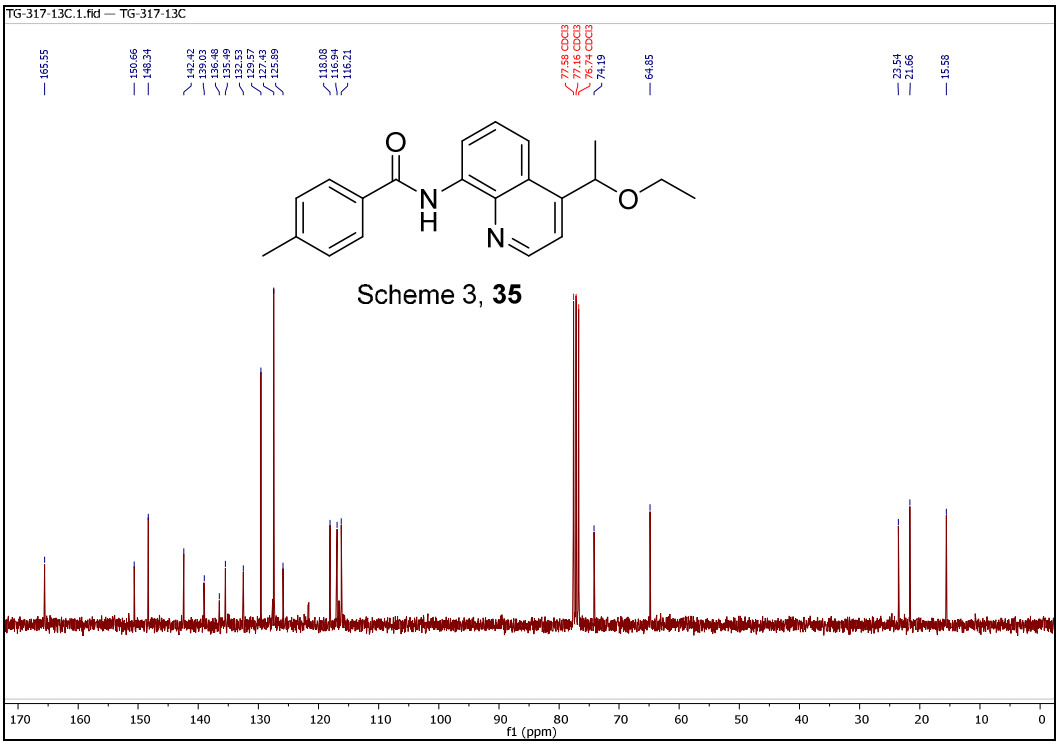

TG-319-1H.1.fid — TG-319-1H
Scheme 3, 33
A (s) 9.98
B (m) 8.79
C (m) 7.60
E (dd) 4.08
F (m) 3.83
G (t) 3.41
H (t) 2.46
I (m) 2.06
J (d) 1.86
K (dd) 1.67
L (m) 1.35
f1 (ppm)

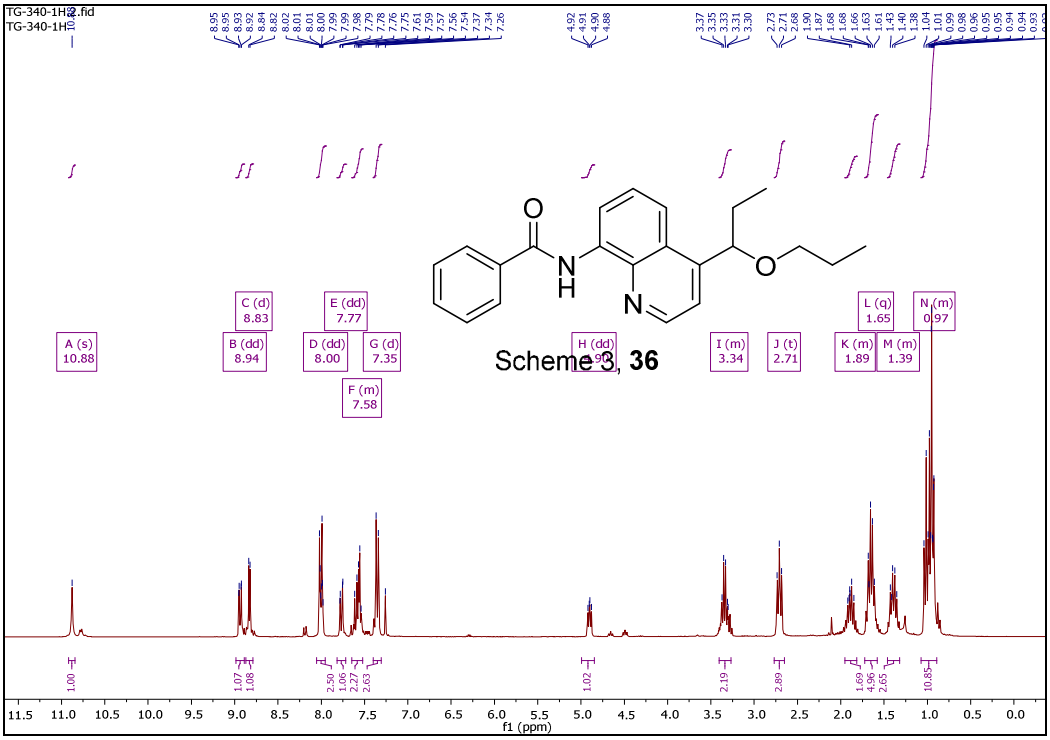

TG-319-13C.1.fid — TG-319-13C
174.96
148.07
144.23
138.35
135.48
127.85
125.05
118.76
116.26
116.08
77.58 CDCl3
77.16 CDCl3
76.73 CDCl3
74.26
72.02
67.39
66.69
47.02
29.86
29.84
25.89
25.86
Scheme 3, 33
f1 (ppm)

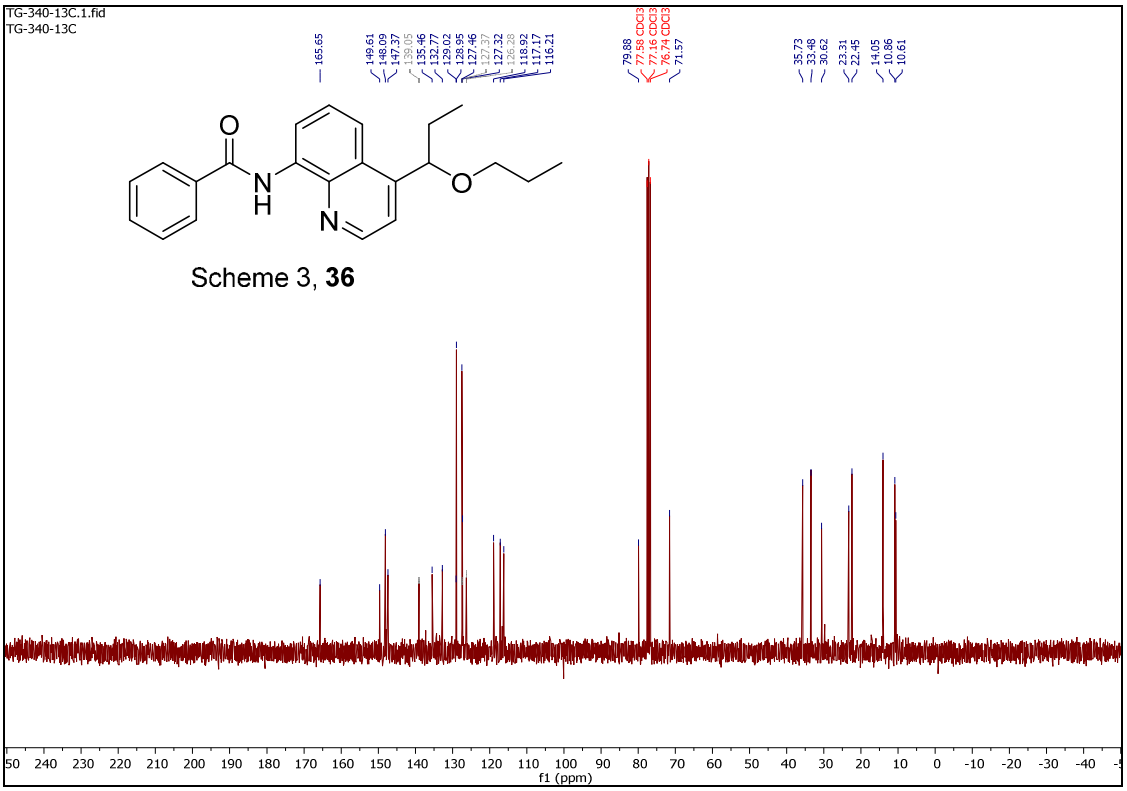

TG-328-1H-1.fid
8.84
8.83
8.82
8.82
7.83
7.82
7.82
7.80
7.80
7.68
7.67
7.59
7.56
7.53
7.26
6.43
4.15
2.15
2.14
2.13
2.10
2.10
1.81
1.80
1.79
A (s) 10.30
B (m) 8.83
C (dd) 7.81
D (d) 7.67
E (t) 7.56
F (s) 6.43
G (s) 4.15
H (m) 2.11
I (m) 1.80
Scheme 3, 34
f1 (ppm)

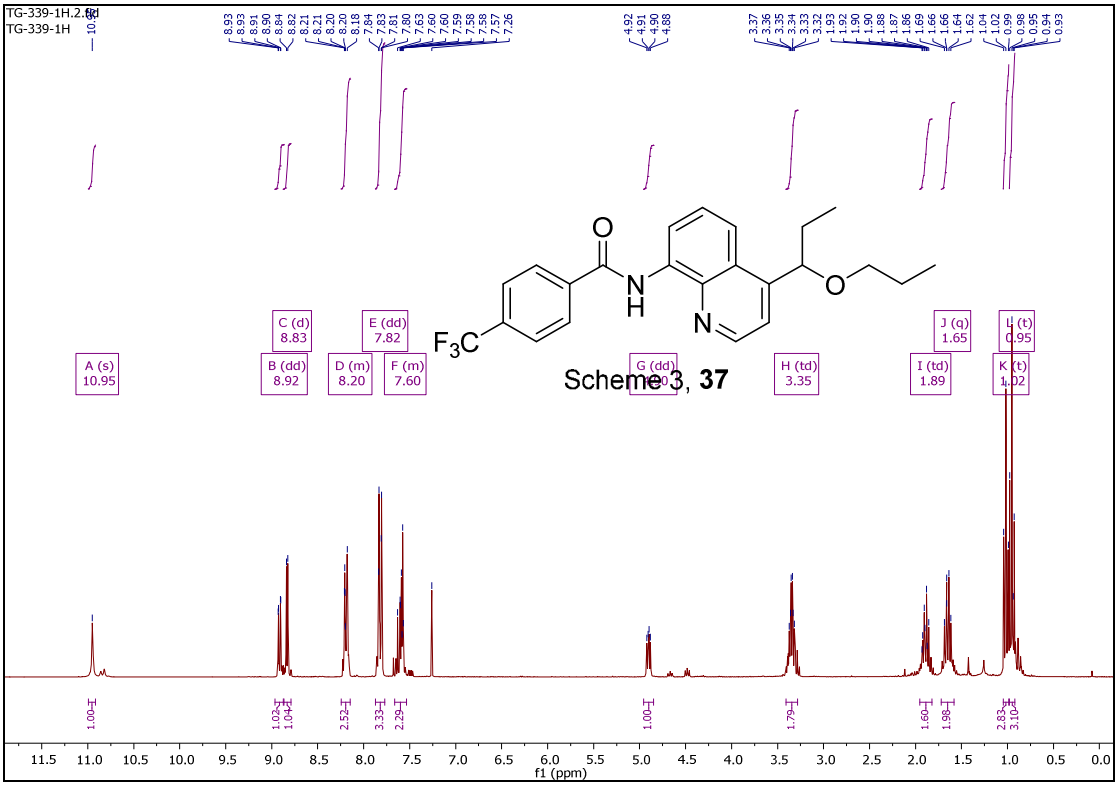

TG-328-13C.1.fid
TG-328-13C
Scheme 3, **34**
f1 (ppm)

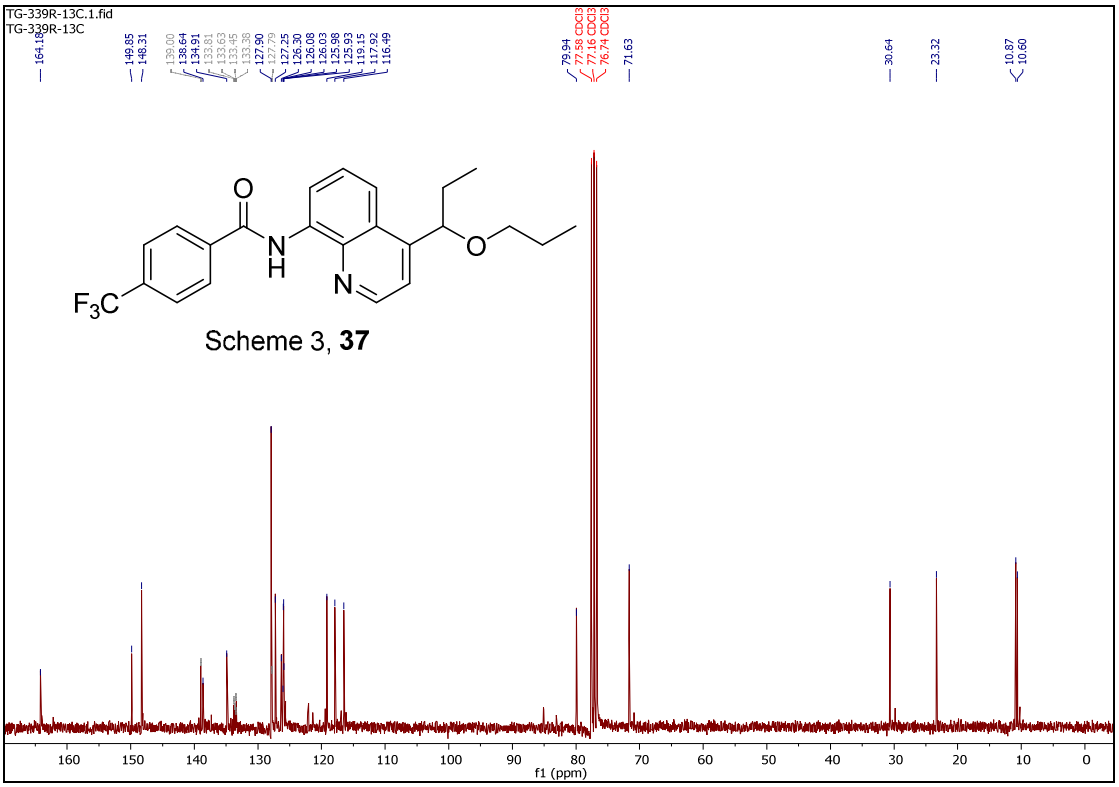

TG-317-1H.1.fid — TG-317-1H
A (s) 10.87
B (d) 8.94
C (dd) 8.83
D (m) 7.99
E (d) 7.75
F (q) 7.59
G (d) 7.34
H (q)
I (m) 3.46
J (s) 2.45
K (m) 1.59
L (t) 1.26
Scheme 3, **35**
f1 (ppm)

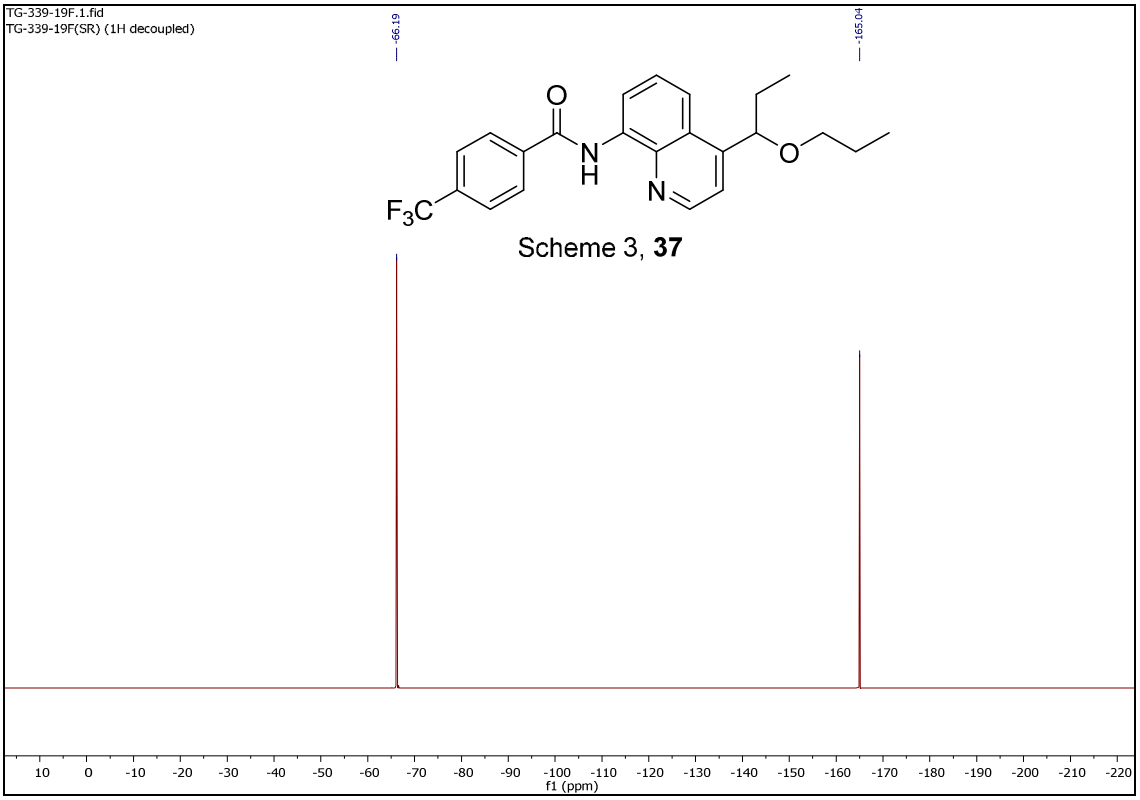

TG-317-13C.1.fid — TG-317-13C
165.55
150.66
148.34
142.42
139.03
136.48
135.49
132.53
129.57
127.43
125.89
118.08
116.94
116.21
77.58 CDCl3
77.16 CDCl3
76.74 CDCl3
74.19
64.85
23.54
21.66
15.58
O
N
H
N
O
Scheme 3, 35
f1 (ppm)

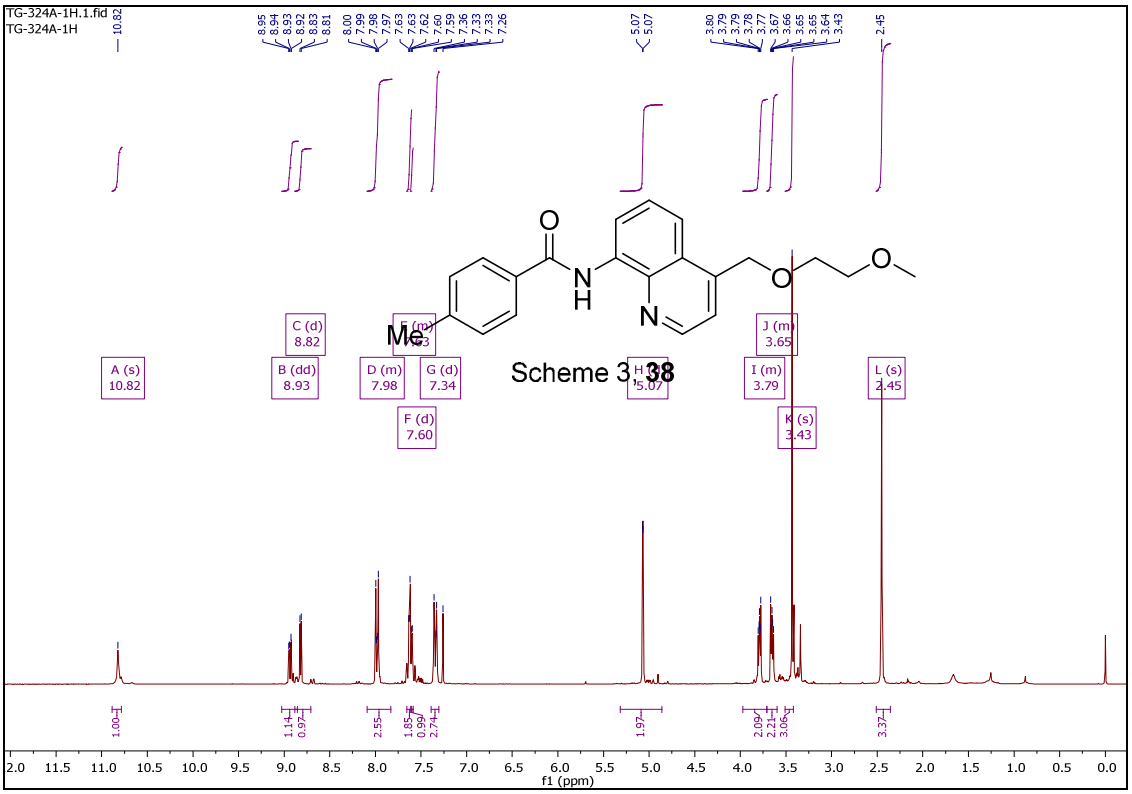

TG-340-1H.2.fid
TG-340-1H
A (s) 10.88
B (dd) 8.94
C (d) 8.83
D (dd) 8.00
E (dd) 7.77
F (m) 7.58
G (d) 7.35
H (dd)
I (m) 3.34
J (t) 2.71
K (m) 1.89
L (q) 1.65
M (m) 1.39
N (m) 0.97
O
N
H
N
O
Scheme 3, 36
f1 (ppm)

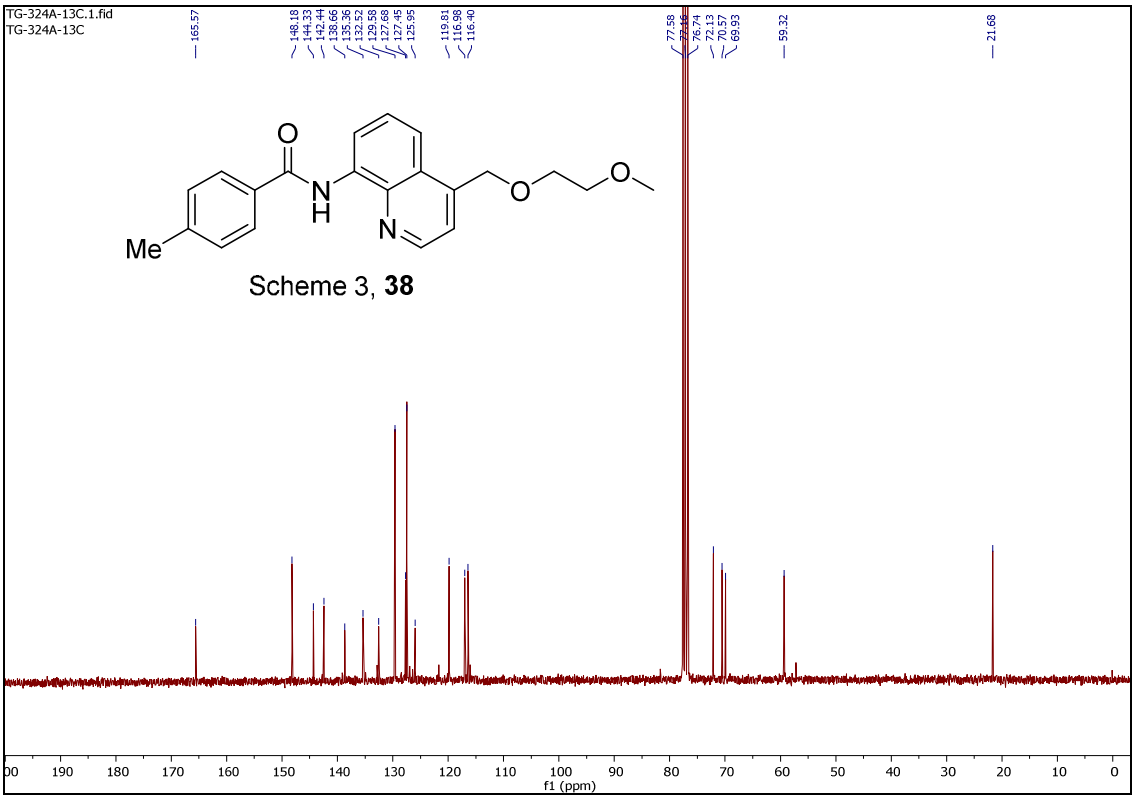

TG-340-13C.1.fid
TG-340-13C
Scheme 3, **36**
f1 (ppm)


TG-339-1H.2.fid
TG-339-1H
A (s) 10.95
B (dd) 8.92
C (d) 8.83
D (m) 8.20
E (dd) 7.82
F (m) 7.60
G (dd)
H (td) 3.35
I (td) 1.89
J (q) 1.65
L (t) 0.95
K (t) 1.02
Scheme 3, **37**
f1 (ppm)


TG-339R-13C.1.fid
TG-339R-13C
164.18
149.85
148.31
139.00
138.64
134.91
133.81
133.63
133.45
133.36
127.90
127.79
127.25
126.30
126.08
126.03
125.98
125.93
119.15
117.92
116.49
79.94
77.58 CDCl3
77.16 CDCl3
76.74 CDCl3
71.63
30.64
23.32
10.87
10.60
O
N
H
N
O
F3C
Scheme 3, 37
f1 (ppm)


TG-339-19F.1.fid
TG-339-19F(SR) (1H decoupled)
-66.19
-165.04
O
N
H
N
O
F3C
Scheme 3, 37
f1 (ppm)


TG-324A-1H.1.fid
TG-324A-1H
Scheme 3, 38
A (s) 10.82
B (dd) 8.93
C (d) 8.82
D (m) 7.98
F (d) 7.60
G (d) 7.34
I (m) 3.79
J (m) 3.65
K (s) 3.43
L (s) 2.45
f1 (ppm)


TG-324A-13C.1.fid
TG-324A-13C
Scheme 3, 38
f1 (ppm)