Supporting Information

A General Method for Aminoquinoline-Directed, Copper-Catalyzed sp^2 C–H Bond Amination

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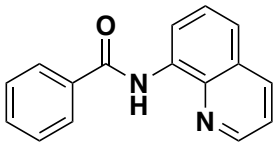
Contents:

General Considerations:

Reactions were run using standard glassware and techniques. Optimization was performed in 1 or 2-dram screw cap pressure vials with PTFE liners. Isolation-scale reactions were performed in 60 mL screw cap vials fitted with polyseal screw caps or in 100 mL pressure tubes fitted with PTFE threaded female bushings. Column chromatography was performed using 60Å silica gel (Dynamic Adsorbents Inc.). ^{1}H, ^{13}C and ^{19}F NMR experiments were conducted on JEOL EC-500 or JEOL EC-600 spectrometers. High-resolution mass spectrometry was collected using chemical ionization on a Micromass Autospec Ultima spectrometer at the Mass Spectrometry Facility of the Department of Chemistry and Biochemistry of University of Texas-Austin. Gas Chromatography was performed on a Shimadzu GC-2010 Gas Chromatograph. FT-IR experiments were run on a ThermoScientific Nicolet iS10 spectrometer. All reactions and manipulations were performed under an atmosphere of ambient air unless otherwise noted. Reagents and starting materials were purchased form commercial vendors and used without further purification.

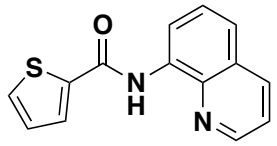
Synthesis of 8-Aminoquinoline Amides

N-(Quinolin-8-yl)benzamide (1)



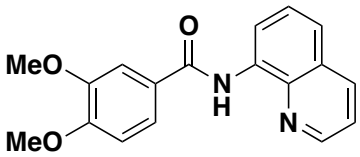
8-Aminoquinoline (2.88 g, 20.0 mmol) was dissolved in dichloromethane (100 mL) in a 500 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (3.48 mL, 25 mmol) was added followed by drop-wise addition of benzoyl chloride (2.32 mL, 20 mmol). The mixture was allowed to stir overnight (16 h). The reaction was quenched with deionized water (50 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (100 mL), washed with brine and dried over Na_2SO_4. Column chromatography (8-1 hexanes / ethyl acetate) gave 4.55 g (92 %) of the product as a white solid. This compound is known.[1] ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.76 (s, 1H), 8.95 (dd, J = 7.6, 1.2 Hz, 1H), 8.85 (dd, J = 4.2, 1.6 Hz, 1H), 8.19 (dd, J = 8.2, 1.6 Hz, 1H), 8.13 – 8.07 (m, 3H), 7.64 – 7.53 (m, 7H), 7.48 (dd, J = 8.2, 4.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.6, 148.4, 138.9, 136.5, 135.3, 134.71, 132.0, 128.9, 128.1, 127.6, 127.4, 122.5, 121.8, 116.7.

_N_-(Quinolin-8-yl)thiophenecarboxamide (3)



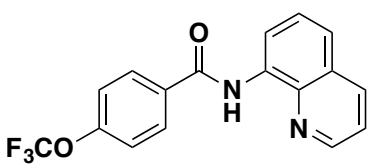
8-Aminoquinoline (2.88 g, 20.0 mmol) was dissolved in dichloromethane (50 mL) in a 500 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (3.48 mL, 25 mmol) was added followed by drop-wise addition of 2-thiophenecarbonyl chloride (2.14 g, 20 mmol). The mixture was allowed to stir overnight (16 h). The reaction was quenched with deionized water (50 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (100 mL), washed with brine (50 mL) and dried over Na_2SO_4. Column chromatography (8 - 1 hexanes / ethyl acetate) gave 4.86 g (96 %) of the product as a white solid. This compound is known.[2] ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.61 (s, 1H), 8.88 – 8.83 (m, 2H), 8.19 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.85 (dd, *J* = 3.7, 1.1 Hz, 1H), 7.62 – 7.56 (m, 2H), 7.54 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.49 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.19 (dd, *J* = 4.9, 3.7 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.2, 148.5, 140.2, 138.6, 136.6, 134.5, 131.1, 128.6, 128.1, 128.0, 127.6, 121.9, 121.8, 116.7.

3,4-Dimethoxy-_N_-(quinolin-8-yl)benzamide (8)



8-Aminoquinoline (2.88 g, 20.0 mmol) was dissolved in dichloromethane (50 mL) in a 500 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (3.48 mL, 25 mmol) was added followed by drop-wise addition of 3,4-dimethoxybenzoyl chloride (4.01 g, 20 mmol). The mixture was allowed to stir overnight (18 h). The reaction was quenched with deionized water (50 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (100 mL), washed with brine (50 mL) and dried over Na_2SO_4. Column chromatography (4 - 1 hexanes / ethyl acetate) gave 5.81 g (94 %) of the product as a light beige solid. This compound is known.[3] ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.70 (s, 1H), 8.91 (d, *J* = 7.6 Hz, 1H), 8.83 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.17 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.66 (m, *J* = 6.3 Hz, 2H), 7.58 (t, *J* = 7.9 Hz, 1H), 7.52 (d, *J* = 8.2 Hz, 1H), 7.46 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 1H), 4.00 (s, 3H), 3.96 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.1, 152.2, 149.2, 148.3, 138.8, 136.5, 134.8, 128.1, 127.9, 127.6, 121.8, 121.5, 119.9, 116.4, 110.9, 110.5, 56.2, 56.2.

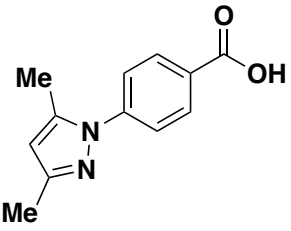
4-(Trifluoromethoxy)-_N_-(quinolin-8-yl)benzamide (10)



8-Aminoquinoline (2.88 g, 20.0 mmol) was dissolved in dichloromethane (100 mL) in a 500 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath.

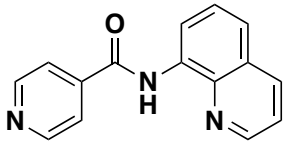
Triethylamine (3.48 mL, 25 mmol) was added followed by drop-wise addition of 4-(trifluoromethoxy)benzoyl chloride (3.15 mL, 20 mmol). The mixture was allowed to stir overnight (12 h). The reaction was quenched with deionized water (50 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (100 mL), washed with brine (50 mL) and dried over Na_2SO_4. Column chromatography (10 - 1 hexanes / ethyl acetate) gave 6.43 g (97 %) of the product as a light solid. This compound is known.[1] ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.73 (s, 1H), 8.91 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.85 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.2, 1.6 Hz, 1H), 8.15 – 8.10 (m, 2H), 7.63 – 7.58 (m, 1H), 7.56 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.49 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.42 – 7.35 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.2, 151.9, 148.5, 138.8, 136.6, 134.4, 133.7, 129.3, 128.1, 127.6, 122.1, 121.9, 120.9, 120.5 (q, J_{C-F} = 258.6 Hz), 116.7. ^{19}F NMR (565 MHz, $CDCl_3$) δ -57.52.

Synthesis of 4-(3,5-dimethyl-1H-pyrazo-1-yl)benzoic acid (A-1)



4-Hydrazinobonzoic acid (3.80 g, 25 mmol), pentane-2,4-dione (2.57 mL, 25 mmol), and isopropanol (80 mL) were added to a 250 mL round bottom flask containing a magnetic stir-bar. The mixture was heated at reflux for 15 hours. Evaporation gave the product in quantitative yield (5.15 g) as a light brown solid. This compound is known.[4] ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.52 (bs, 1H), 8.23 – 8.14 (m, 2H), 7.63 – 7.54 (m, 2H), 6.05 (s, 1H), 2.38 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.7, 150.2, 144.0, 139.9, 131.3, 128.0, 123.9, 108.5, 76.9, 13.5, 12.9.

***N*-(Quinolin-8-yl)isonicotinamide (SM-1)**

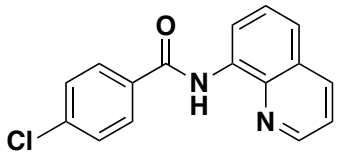


Isonicotinic acid (3.08 g, 25 mmol) was added to a 250 mL round bottom flask containing a magnetic stir-bar. Thionyl chloride (130 mL, 60 equiv) was added and the flask was affixed with a reflux condenser. The mixture was heated at 60 °C under nitrogen for 6 hours followed by removal of the solvent via short-path distillation. The crude product was dissolved in toluene (100 mL) and the remaining thionyl chloride was removed via co-distilation. The resulting solid was dissolved in tetrahydrofuran (30 mL) and used immediately in the next reaction.

8-Aminoquinoline (2.88 g, 20.0 mmol) was dissolved in dichloromethane (100 mL) in a 500 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (6.27 mL, 45 mmol) was added followed by drop-wise addition of isonicotinoyl chloride as prepared above. The mixture was allowed to stir overnight (17 h). The reaction was quenched with deionized water (50 mL) and allowed to stir for 30 min. The

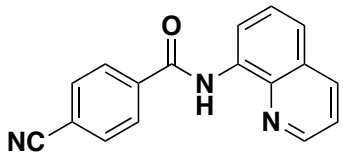
organic layer was extracted with dichloromethane (100 mL), washed with brine and dried over Na_2SO_4. Column chromatography (12 : 6 : 1 hexanes / ethyl acetate / triethylamine) gave 4.67 g (93 %) of the product as a white solid. This compound is known.[3] ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.82 (s, 1H), 8.91 (dd, *J* = 6.6, 2.2 Hz, 1H), 8.86 (td, *J* = 3.9, 1.5 Hz, 3H), 8.21 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.94 – 7.87 (m, 2H), 7.64 – 7.56 (m, 2H), 7.51 (dd, *J* = 8.2, 4.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.4, 151.0, 148.6, 142.2, 138.8, 136.6, 134.0, 128.1, 127.5, 122.6, 122.5, 122.0, 121.1, 117.0.

4-Chloro-*N*-(quinolin-8-yl)benzamide (SM-2)



8-Aminoquinoline (2.88 g, 20.0 mmol) was dissolved in dichloromethane (100 mL) in a 500 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (3.48 mL, 25 mmol) was added followed by drop-wise addition of 4-chlorobenzoyl chloride (2.56 mL, 20 mmol). The mixture was allowed to stir overnight (16 h). The reaction was quenched with deionized water (50 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (100 mL), washed with brine and dried over Na_2SO_4. Column chromatography (10-1 hexanes / ethyl acetate) gave 5.34 g (94 %) of the product as a white solid. This compound is known.[5] ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.72 (s, 1H), 8.91 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.86 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.20 (dd, *J* = 8.2, 1.6 Hz, 1H), 8.06 – 7.98 (m, 2H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.56 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.55 – 7.51 (m, 2H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.5, 148.5, 138.8, 138.3, 136.6, 134.5, 133.7, 129.2, 128.9, 128.1, 127.6, 122.0, 121.9, 116.7.

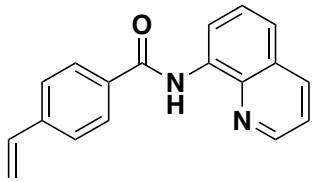
4-Cyano-*N*-(quinolin-8-yl)benzamide (SM-3)



8-Aminoquinoline (2.88 g, 20.0 mmol) was dissolved in dichloromethane (100 mL) in a 500 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (3.48 mL, 25 mmol) was added followed by drop-wise addition of 4-cyanobenzoyl chloride (3.31 g, 20 mmol) in 30 mL dichloromethane. The mixture was allowed to stir overnight (16 h). The reaction was quenched with deionized water (50 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (100 mL), washed with brine and dried over Na_2SO_4. Column chromatography (4 - 1 hexanes / ethyl acetate) gave 5.25 g (96 %) of the product as a light yellow solid. This compound is known.[3] ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.80 (s, 1H), 8.90 (dd, *J* = 6.8, 2.1 Hz, 1H), 8.86 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.22 (dd, *J* = 8.2, 1.6 Hz, 1H), 8.20 – 8.15 (m, 2H), 7.89 – 7.83 (m, 2H), 7.65 – 7.58 (m, 2H), 7.51 (dd, *J* = 8.2, 4.2 Hz, 1H). ^{13}C

NMR (151 MHz, $CDCl_3$) δ 163.6, 148.6, 139.1, 138.8, 136.7, 134.1, 132.8, 128.1, 128.1, 127.6, 122.5, 122.0, 118.2, 116.9, 115.5.

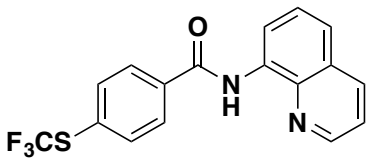
4-Vinyl-*N*-(quinolin-8-yl)benzamide (SM-4)



4-Vinylbenzoic acid (1.78 g, 12 mmol) was added to a 100 mL round bottom flask containing a magnetic stir-bar. Thionyl chloride (52 mL, 60 equiv) was added and the flask was affixed with a reflux condenser. The mixture was heated at 60 °C under nitrogen for 5 hours followed by removal of the solvent via short-path distillation. The crude product was dissolved in toluene (30 mL) and the remaining thionyl chloride was removed via co-distilation. The resulting oil was dissolved in dichloromethane (10 mL) and used immediately in the next reaction.

8-Aminoquinoline (1.44 g, 10.0 mmol) was dissolved in dichloromethane (50 mL) in a 250 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (2.09 mL, 15 mmol) was added followed by drop-wise addition of 4-vinylbenzoyl chloride as prepared above. The mixture was allowed to stir overnight (17 h). The reaction was quenched with deionized water (25 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (50 mL), washed with brine (25 mL) and dried over Na_2SO_4. Column chromatography (8 - 1 hexanes / ethyl acetate) gave 2.43 g (90 %) of the product as a white solid. R_f = 0.45 (30:1 toluene / ethyl acetate). MP = 112.3 – 112.5 °C, 6:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.76 (s, 1H), 8.94 (dd, *J* = 7.6, 1.3 Hz, 1H), 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.2, 1.6 Hz, 1H), 8.09 – 8.02 (m, 2H), 7.63 – 7.57 (m, 3H), 7.55 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.49 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.80 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.90 (dd, *J* = 17.6, 0.6 Hz, 1H), 5.44 – 5.36 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.2, 148.4, 141.1, 138.9, 136.5, 136.1, 134.7, 134.3, 128.1, 127.8, 127.6, 126.7, 121.8, 121.8, 116.6, 116.3. HRMS (ESI+) Calculated for ($C_{18}H_{14}N_2ONa$) $[M+Na]^+$ 297.09980, Found 297.10050. FT-IR (neat, cm^{-1}) v 3354, 1660, 1532, 1328.

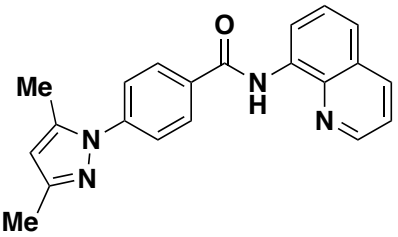
4-(Trifluoromethylthio)-*N*-(quinolin-8-yl)benzamide (SM-5)



8-Aminoquinoline (1.44 g, 10.0 mmol) was dissolved in dichloromethane (50 mL) in a 250 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (1.74 mL, 12.5 mmol) was added followed by drop-wise addition of 4-(trifluoromethylthio)benzoyl chloride (1.67 mL, 10 mmol). The mixture was allowed to stir overnight (12 h). The reaction was quenched with deionized water (25 mL) and allowed to stir for 30 min. The

organic layer was extracted with dichloromethane (50 mL), washed with brine (25 mL) and dried over Na_2SO_4. Column chromatography (10 - 1 hexanes / ethyl acetate) gave 6.43 g (97 %) of the product as a light solid. R_f = 0.21 (10:1 hexanes / ethyl acetate). MP = 111 – 112 °C, 6:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.77 (s, 1H), 8.92 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.86 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.20 (dd, *J* = 8.2, 1.6 Hz, 1H), 8.15 – 8.09 (m, 2H), 7.83 (d, *J* = 8.2 Hz, 2H), 7.64 – 7.59 (m, 1H), 7.58 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.3, 148.6, 138.8, 137.4, 136.6, 136.3, 134.3, 128.4, 129.5 (q, J_{C-F} = 307.8 Hz), 128.1, 127.6, 122.5, 122.3, 116.8. ^{19}F NMR (565 MHz, $CDCl_3$) δ -41.83. HRMS (ESI+) Calculated for ($C_{17}H_{11}F_3N_2OSNa$) $[M+Na]^+$ 371.04360, Found 371.04480. FT-IR (neat, cm^{-1}) ν 3346, 1674, 1538, 1481.

4-(3,5-Dimethyl-1H-pyrazo-1-yl)-*N*-(quinolin-8-yl)benzamide (SM-6)

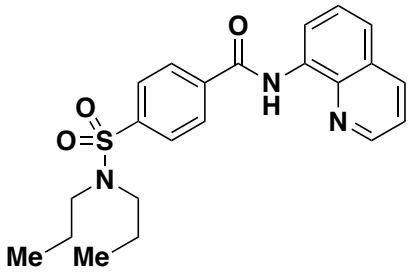


4-(3,5-Dimethyl-1H-pyrazo-1-yl)benzoic acid (2.59 g, 12 mmol) was added to a 100 mL round bottom flask containing a magnetic stir-bar. Thionyl chloride (52 mL, 60 equiv) was added and the flask was affixed with a reflux condenser. The mixture was heated at 60 °C under nitrogen for 5 hours followed by removal of the solvent via short-path distillation. The crude product was dissolved in toluene (30 mL) and the remaining thionyl chloride was removed via co-distilation. The resulting oil was dissolved in dichloromethane (10 mL) and used immediately in the following reaction.

8-Aminoquinoline (1.44 g, 10.0 mmol) was dissolved in dichloromethane (50 mL) in a 250 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (2.09 mL, 15 mmol) was added followed by drop-wise addition of 4-(3,5-Dimethyl-1H-pyrazo-1-yl)benzoyl chloride as prepared above. The mixture was allowed to stir overnight (15 h). The reaction was quenched with deionized water (25 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (50 mL), washed with brine (25 mL) and dried over Na_2SO_4. Column chromatography (4 - 1 hexanes / ethyl acetate) gave 2.89 g (84 %) of the product as a light yellow solid. R_f = 0.15 (10:1 toluene / ethyl acetate). MP = 150 – 151 °C, 2:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.79 (s, 1H), 8.94 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.87 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.21 (dd, *J* = 8.2, 1.6 Hz, 1H), 8.19 – 8.16 (m, 2H), 7.69 – 7.63 (m, 2H), 7.64 – 7.59 (m, 1H), 7.57 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.06 (s, 1H), 2.41 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.6, 149.9, 148.4, 142.9, 139.7, 138.9, 136.5, 134.6, 133.4, 128.3, 128.1, 127.6, 124.2, 121.9, 121.8, 116.7, 108.2, 76.9, 13.7, 12.9. HRMS (ESI+)

Calculated for ($C_{21}H_{18}N_4ONa$) $[M+Na]^+$ 365.13730, Found 365.13760. FT-IR (neat, cm^{-1}) v 3365, 1678, 1542, 1515, 1485, 1330.

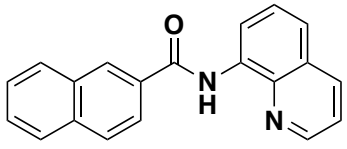
4-(*N,N*-Dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (SM-7)



4-(N,N-Dipropylsulfamoyl)benzoic acid (7.13 g, 25 mmol) was added to a 250 mL round bottom flask containing a magnetic stir-bar. Thionyl chloride (130 mL, 60 equiv) was added and the flask was affixed with a reflux condenser. The mixture was heated at 60 °C under nitrogen for 6 hours followed by removal of the solvent via short-path distillation. The crude product was dissolved in toluene (100 mL) and the remaining thionyl chloride was removed via co-distilation. The resulting solid was dissolved in dichloromethane (25 mL) and used immediately in the next reaction.

8-Aminoquinoline (2.88 g, 20.0 mmol) was dissolved in 1dichloromethane (50 mL) in a 500 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (4.18 mL, 30 mmol) was added followed by drop-wise addition of 4-(-(*N*,*N*-dipropylsulfamoyl)benzoyl chloride as prepared above. The mixture was allowed to stir overnight (15 h). The reaction was quenched with deionized water (25 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (150 mL), washed with brine (50 mL) and dried over Na_2SO_4. Column chromatography (4 - 1 hexanes / ethyl acetate) gave 7.93 g (96 %) of the product as a light yellow solid. R_f = 0.23 (30:1 toluene / ethyl acetate). MP = 138 – 139 °C, 4:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.80 (s, 1H), 8.92 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.87 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.22 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.21 – 8.17 (m, 2H), 8.01 – 7.97 (m, 2H), 7.65 – 7.56 (m, 2H), 7.51 (dd, *J* = 8.2, 4.2 Hz, 1H), 3.17 – 3.10 (m, 4H), 1.58 (h, *J* = 7.4 Hz, 4H), 0.89 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.0, 148.6, 143.3, 138.8, 138.6, 136.7, 134.2, 128.1, 127.6, 127.6, 122.4, 122.0, 116.9, 50.2, 22.2, 11.3. HRMS (ESI+) Calculated for ($C_{22}H_{25}N_3O_2SNa$) $[M+Na]^+$ 434.15090, Found 434.15140. FT-IR (neat, cm^{-1}) v 3350, 2963, 2875, 1663, 1530, 1190.

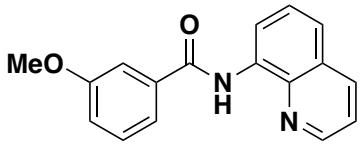
2-(*N*-(Quinolin-8-yl)naphthalenecarboxamide (SM-8)



8-Aminoquinoline (1.44 g, 10.0 mmol) was dissolved in dichloromethane (50 mL) in a 250 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (1.74 mL, 12.5 mmol) was added followed by drop-wise addition of 2-napthaloyl chloride (1.91 g, 10 mmol) in 15 mL

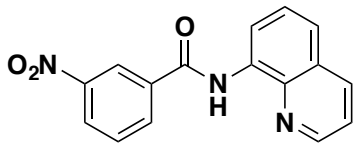
dichloromethane. The mixture was allowed to stir overnight (14 h). The reaction was quenched with deionized water (25 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (50 mL), washed with brine (25 mL) and dried over Na_2SO_4. Column chromatography (10 - 1 hexanes / ethyl acetate) gave 2.78 g (93 %) of the product as a white solid. This compound is known.[6] ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.91 (s, 1H), 9.00 (d, *J* = 7.6 Hz, 1H), 8.90 (d, *J* = 4.1 Hz, 1H), 8.21 (d, *J* = 8.2 Hz, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 7.7 Hz, 1H), 7.67 – 7.55 (m, 4H), 7.51 (dd, *J* = 8.2, 4.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.7, 148.5, 139.0, 136.6, 135.1, 134.8, 132.9, 132.5, 129.3, 128.8, 128.2, 128.1, 128.0, 127.9, 127.7, 126.9, 123.9, 122.5, 121.9, 116.7.

3-Methoxy-*N*-(quinolin-8-yl)benzamide (SM-9)



8-Aminoquinoline (1.44 g, 10.0 mmol) was dissolved in dichloromethane (50 mL) in a 250 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (1.74 mL, 12.5 mmol) was added followed by drop-wise addition of 3-methoxybenzoyl chloride (1.41 mL, 10 mmol). The mixture was allowed to stir overnight (14 h). The reaction was quenched with deionized water (25 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (50 mL), washed with brine (25 mL) and dried over Na_2SO_4. Column chromatography (10 - 1 hexanes / ethyl acetate) gave 2.51 g (90 %) of the product as a light yellow solid. This compound is known.[6] ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.74 (s, 1H), 8.93 (d, *J* = 7.6 Hz, 1H), 8.85 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.18 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.68 – 7.62 (m, 2H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.16 – 7.09 (m, 1H), 3.92 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.4, 160.1, 148.4, 138.9, 136.8, 136.5, 134.7, 129.9, 128.1, 127.6, 122.5, 121.8, 119.2, 118.1, 116.6, 112.8, 55.6.

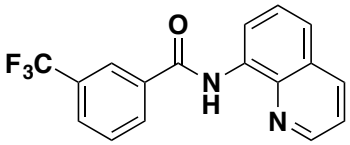
3-Nitro-*N*-(quinolin-8-yl)benzamide (SM-10)



8-Aminoquinoline (1.44 g, 10.0 mmol) was dissolved in dichloromethane (50 mL) in a 250 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (1.74 mL, 12.5 mmol) was added followed by drop-wise addition of 2-napthaloyl chloride (1.86 g, 10 mmol) dissolved in 30 mL dichloromethane. The mixture was allowed to stir overnight (12 h). The reaction was quenched with deionized water (25 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (100 mL), washed with brine (25 mL) and dried over Na_2SO_4. Column chromatography (6 - 1 hexanes / ethyl acetate) gave 2.62 g (89 %) of the product as a light yellow solid. This compound is known.[5] R_f =

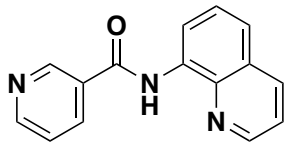
0.36 (30:1 toluene / ethyl acetate). MP = 228.8 – 229.1 °C, 1:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.83 (s, 1H), 8.94 – 8.89 (m, 2H), 8.88 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.44 (ddd, *J* = 8.2, 2.2, 1.0 Hz, 1H), 8.41 (dt, *J* = 7.7, 1.3 Hz, 1H), 8.22 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.76 (t, *J* = 7.9 Hz, 1H), 7.66 – 7.56 (m, 2H), 7.52 (dd, *J* = 8.2, 4.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.0, 148.7, 148.6, 138.8, 137.0, 136.7, 134.0, 133.2, 130.2, 128.1, 127.5, 126.5, 122.6, 122.5, 122.1, 117.0.

3-(Trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (SM-11)



8-Aminoquinoline (2.88 g, 20.0 mmol) was dissolved in dichloromethane (50 mL) in a 500 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (3.48 mL, 25 mmol) was added followed by drop-wise addition of 3-(trifluoromethyl)benzoyl chloride (3.02 mL, 20 mmol). The mixture was allowed to stir overnight (14 h). The reaction was quenched with deionized water (50 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (100 mL), washed with brine (50 mL) and dried over Na_2SO_4. Column chromatography (10 - 1 hexanes / ethyl acetate) gave 6.02 g (95 %) of the product as a white solid. This compound is known.[3] ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.78 (s, 1H), 8.92 (dd, *J* = 7.4, 1.1 Hz, 1H), 8.86 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.35 (s, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 8.20 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.69 (t, *J* = 7.8 Hz, 1H), 7.64 – 7.56 (m, 2H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.0, 148.6, 138.8, 136.6, 136.1, 134.3, 131.6 (q, $J_{C–F}$ = 33.0, 32.5 Hz), 130.4, 129.5, 128.5, (q, $J_{C–F}$ = 4.0 Hz), 128.1, 127.6, 124.7 (q, $J_{C–F}$ = 4.2 Hz), 123.9 (q, $J_{C–F}$ = 271.9 Hz), 122.3, 122.0, 116.9. ^{19}F NMR (565 MHz, $CDCl_3$) δ -62.56.

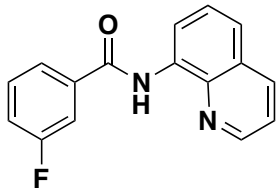
***N*-(Quinolin-8-yl)nicotinamide (SM-12)**



8-Aminoquinoline (2.88 g, 20.0 mmol) was dissolved in 25 mL of anhydrous dichloromethane in a 50 mL round bottom flask. Nicotinoyl chloride hydrogen chloride (3.56 g, 20.0 mmol) and dichloromethane (100 mL) were added to a seperate 500 mL round bottom flask with a magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (6.27 mL, 45 mmol) was added followed by drop-wise addition of a dichloromethane solution of 8-aminoquinoline as prepared above. The mixture was allowed to stir overnight (17 h). The reaction was quenched with deionized water (50 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (100 mL), washed with brine and dried over Na_2SO_4. Column chromatography (12 : 6 : 1 hexanes / ethyl acetate / triethylamine) gave 4.61 g (91 %) of the product as a tan solid. This compound is known.[7] ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.76 (s, 1H),

9.32 (d, *J* = 2.2 Hz, 1H), 8.88 (dd, *J* = 7.3, 1.4 Hz, 1H), 8.83 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.80 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.35 (dt, *J* = 7.9, 1.9 Hz, 1H), 8.17 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.63 – 7.53 (m, 2H), 7.47 (dt, *J* = 8.3, 4.1 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.6, 152.6, 148.6, 148.5, 138.7, 136.5, 135.3, 134.2, 130.8, 128.0, 127.5, 123.7, 122.3, 121.9, 116.8.

3-Fluoro-N-(Quinolin-8-yl)benzamide (SM-13)



3-Fluorobenzoic acid (3.50 g, 25 mmol) was added to a 250 mL round bottom flask containing a magnetic stir-bar. Thionyl chloride (130 mL, 60 equiv) was added and the flask was affixed with a reflux condenser. The mixture was heated at 60 °C under nitrogen for 6 hours followed by removal of the solvent via short-path distillation. The crude product was dissolved in toluene (100 mL) and the remaining thionyl chloride was removed via co-distilation. The resulting solid was dissolved in tetrahydrofuran (30 mL) and used immediately in the next reaction.

8-Aminoquinoline (2.88 g, 20.0 mmol) was dissolved in dichloromethane (100 mL) in a 500 mL round bottom flask with magnetic stir-bar. The flask was purged with nitrogen and placed in an ice water bath. Triethylamine (6.27 mL, 45 mmol) was added followed by drop-wise addition of 3-fluorobenzoyl chloride as prepared above. The mixture was allowed to stir overnight (17 h). The reaction was quenched with deionized water (50 mL) and allowed to stir for 30 min. The organic layer was extracted with dichloromethane (100 mL), washed with brine and dried over Na_2SO_4. Column chromatography (10 : 1 hexanes / ethyl acetate) gave 4.42 g (83 %) of the product as a white solid. This compound is known.[2] ^{1}H NMR (500 MHz, Chloroform-*d*) δ 10.74 (s, 1H), 8.91 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.86 (ddd, *J* = 7.7, 1.6, 0.9 Hz, 1H), 7.79 (ddd, *J* = 9.4, 2.5, 1.7 Hz, 1H), 7.64 – 7.58 (m, 1H), 7.58 – 7.55 (m, 1H), 7.55 – 7.52 (m, 1H), 7.49 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.28 (tdd, *J* = 8.3, 2.6, 0.9 Hz, 1H).

Aerobic C–H Amination: Investigation of Reaction Conditions

A 2-dram screw cap vial containing a stirbar was charged with *N*-(quinolin-8-yl)benzamide (0.0248 g, 0.1 mmol), copper (II) acetate (20-30 mol %), base (2 equiv., entries 1-2) oxidant, morpholine (2-3 equiv.) and solvent (0.2-1.0 mL). The vial was placed in a parallel synthesis well pre-heated to 80 °C for the indicated time and quenched with 0.2 mL of a saturated aqueous solution of EDTA disodium salt and 0.5 mL of a saturated sodium bicarbonate solution. Yields were

calculated after gas chromatography using 2,6-diisopropyl naphthalene as an internal standard. See Table S1.

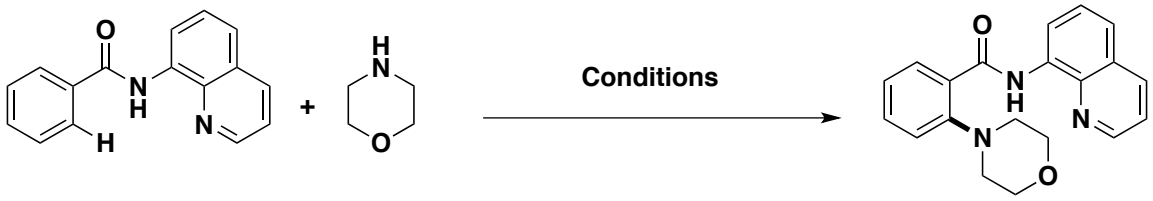


Table S1: Screening Conditions

Entry	Cu Cat.	Equiv. Amine	Oxidant	Base	Solvent	Time (h)	Yield (GC Calculated)
1	$Cu(OAc)_2$ (20 mol %)	2.0	NMO (2 equiv)	K_2CO_3 (2 equiv)	DMF (1 mL)	20	33 %
2	$Cu(OAc)_2$ (20 mol %)	2.0	NMO (2 equiv)	K_2CO_3 (2 equiv)	Pyridine (1 mL)	20	38 %
3	$Cu(OAc)_2$ (20 mol %)	2.0	NMO (2 equiv)	---------- ----------	Pyridine (1 mL)	16	68 %
4	$Cu(OAc)_2$ (20 mol %)	2.0	Air (~3.5 mL)	---------- ----------	Pyridine (1 mL)	6 18	56 % 53 %
5	$Cu(OAc)_2$ (20 mol %)	2.0	Air (~3.5 mL)	---------- ----------	Pyridine (0.2 mL)	6	87 %
6	$Cu(OAc)_2$ (20 mol %)	2.0	Air (~3.5 mL)	---------- ----------	Pyridine (0.2 mL)	6	92 %
7	$Cu(OAc)_2$ (20 mol %)	3.0	Air (~3.5 mL)	---------- ----------	Pyridine (0.2 mL)	6	Quant
8	---------- ----------	3.0	Air (~3.5 mL)	---------- ----------	Pyridine (0.2 mL)	6	No Product Observed

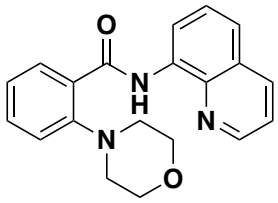
Copper-Catalyzed Aerobic C–H Amination with Morpholine

General Procedure for Amination with Secondary Amines (General Procedure 1)

Reactions were run in a 100 mL heavy wall glass pressure vessel with a magnetic stir-bar and a PTFE bushing or in 60 mL screw cap vials. Stirbars should be large enough to break the surface of the solvent and set to between 350 and 550 rpm. Benzamide (1.0 mmol), copper acetate (0.3 mmol), pyridine (2.0 mL), and amine (3.0 mmol) were added sequentially to the vessel. Reactions were heated to the indicated temperature in a pre-heated oil bath (in case of pressure vessel) or in a parallel synthesis plate of appropriate size (in case of vial). Reactions were monitored at regular intervals by TLC analysis and stopped

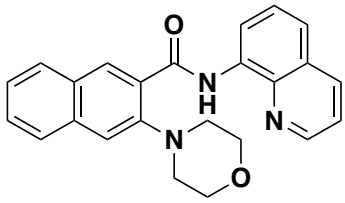
when complete consumption of the starting material was observed, or when the reaction failed to proceed to completion after 36 hours. Reactions were quenched up by addition of solid EDTA (0.3 mmol) to the room temperature reaction mixture and stirring for one hour. The reaction was then diluted with dichloromethane, treated with SiO_2 (15 mL per mmol of starting amide), and evaporated to dryness on a rotary evaporator. Subsequent column chromatography in the appropriate solvent resulted in the pure compound.

2-(Morpholino)-*N*-(quinolin-8-yl)benzamide (T2-1)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar *N*-(quinolin-8-yl)benzamide (0.248 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 80 °C. After 15.5 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (3:1 hexanes / ethyl acetate) provided 0.318 g (95 % yield) of analytically pure compound T2-1. This compound is known.[2] ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.68 (s, 1H), 9.13 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.88 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (ddd, *J* = 7.9, 4.4, 1.7 Hz, 2H), 7.61 (t, *J* = 7.9 Hz, 1H), 7.55 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.53 – 7.46 (m, 2H), 7.29 – 7.23 (m, 2H), 4.07 – 3.91 (m, 4H), 3.28 – 3.09 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 151.2, 148.2, 138.9, 136.5, 135.7, 132.4, 132.2, 129.0, 128.4, 127.7, 124.4, 121.8, 121.7, 119.3, 117.8, 66.3, 54.0.

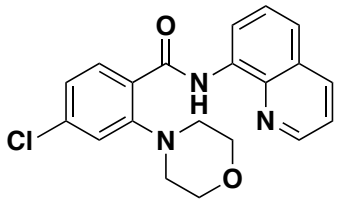
3-(Morpholino)-2-(*N*-(quinolin-8-yl))naphthalenecarboxamide (T2-2)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 2-(*N*-(quinolin-8-yl))napthalenecarboxamide (0.298 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 110 °C. After 35 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (5:1 → 4:1 hexanes / ethyl acetate) provided 0.242 g (62 % yield) of analytically pure compound T2-2. This compound is known[6]. ^{1}H NMR

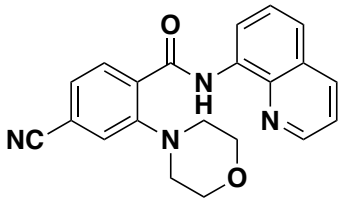
(500 MHz, $CDCl_3$) δ 12.68 (s, 1H), 9.19 (dd, *J* = 7.7, 1.3 Hz, 1H), 8.89 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.72 (s, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.99 – 7.89 (m, 2H), 7.86 – 7.78 (m, 1H), 7.63 (t, *J* = 7.9 Hz, 1H), 7.59 – 7.52 (m, 3H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.46 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 4.00 (dd, *J* = 5.5, 3.5 Hz, 4H), 3.35 – 3.18 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 148.3, 147.9, 138.9, 136.5, 135.6, 135.3, 133.7, 130.0, 129.0, 128.5, 128.4, 128.2, 127.7, 126.9, 125.6, 121.9, 121.8, 117.9, 116.0, 66.2, 54.1.

2-(Morpholino)-4-chloro-*N*-(quinolin-8-yl)benzamide (T2-3)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-chloro-*N*-(quinolin-8-yl)benzamide (0.283 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 110 °C. After 15 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (5:1 → 4:1 hexanes / ethyl acetate) provided 0.260 g (71 % yield) of analytically pure compound T2-3. This compound is known.[2] ^1H NMR (500 MHz, $CDCl_3$) δ 12.48 (s, 1H), 9.09 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.87 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.11 (d, *J* = 8.2 Hz, 1H), 7.64 – 7.58 (m, 1H), 7.56 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.25 – 7.19 (m, 2H), 4.07 – 3.91 (m, 4H), 3.24 – 3.06 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.8, 152.2, 148.3, 138.8, 138.2, 136.6, 135.4, 133.6, 128.4, 127.7, 127.4, 124.4, 122.1, 121.8, 119.8, 117.8, 66.1, 53.9.

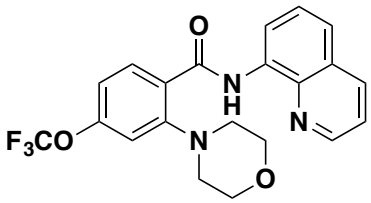
2-(Morpholino)-4-cyano-*N*-(quinolin-8-yl)benzamide (T2-4)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-cyano-*N*-(quinolin-8-yl)benzamide (0.273 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 80 °C. After 16 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (6:1 → 4:1 hexanes / ethyl acetate) provided 0.281 g (78 %

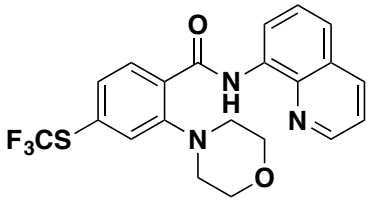
yield) of analytically pure compound T2-4. R_f = 0.25 (10:1 toluene / ethyl acetate). MP = 145 – 146 °C, 2:1 hexanes / ethyl acetate. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.38 (s, 1H), 9.07 (dd, *J* = 6.9, 2.2 Hz, 1H), 8.87 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.25 – 8.18 (m, 2H), 7.65 – 7.57 (m, 2H), 7.55 – 7.52 (m, 1H), 7.52 – 7.50 (m, 1H), 7.48 (d, *J* = 1.4 Hz, 1H), 4.03 – 3.83 (m, 4H), 3.26 – 3.09 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.0, 151.3, 148.5, 138.7, 136.7, 134.9, 133.1, 133.0, 128.4, 127.7, 127.4, 122.8, 122.5, 122.0, 118.2, 117.9, 115.6, 66.0, 53.6. HRMS (ESI+) Calculated for ($C_{21}H_{18}N_4O_2Na$) $[M+Na]^+$ 381.13220, Found 381.13270. FT-IR (neat, cm^{-1}) v 2980, 2231, 1666, 1521, 1487, 1323, 1110.

2-(Morpholino)-4-(trifluoromethoxy)-*N*-(quinolin-8-yl)benzamide (T2-5)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-(trifluoromethoxy)-*N*-(quinolin-8-yl)benzamide (0.332 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 110 °C. After 12 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (6:1 → 5:1 hexanes / ethyl acetate) provided 0.362 g (87 % yield) of analytically pure compound T2-5. R_f = 0.48 (10:1 toluene / ethyl acetate). MP = 115 – 116 °C, 6:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.44 (s, 1H), 9.09 (dd, *J* = 7.6, 1.2 Hz, 1H), 8.87 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.26 – 8.15 (m, 2H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.56 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.12 – 7.07 (m, 1H), 7.04 (s, 1H), 4.02 – 3.89 (m, 4H), 3.22 – 3.09 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.6, 152.8, 152.1, 148.4, 138.8, 136.6, 135.3, 134.0, 128.4, 127.7, 127.4, 122.5, 122.1, 121.9, 120.4 (d, *J* = 258.5 Hz), 117.8, 115.6, 111.7, 66.1, 53.8. ^{19}F NMR (565 MHz, $CDCl_3$) δ -57.37. HRMS (ESI+) Calculated for ($C_{21}H_{18}F_3N_3O_3Na$) $[M+Na]^+$ 440.11920, Found 440.11950. FT-IR (neat, cm^{-1}) v 2980, 1667, 1522, 1250, 1147, 1146, 1114.

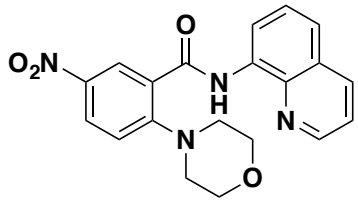
2-(Morpholino)-4-(trifluoromethylthio)-*N*-(quinolin-8-yl)benzamide (T2-6)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-(trifluoromethylthio)-*N*-(quinolin-8-yl)benzamide (0.348 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g,

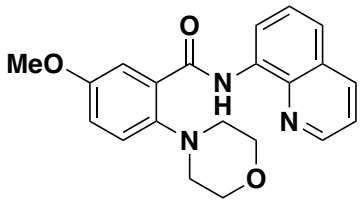
3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 80 °C. After 12 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (6:1 → 5:1 hexanes / ethyl acetate) provided 0.374 g (86 % yield) of analytically pure compound T2-6. R_f = 0.27 (30:1 toluene / ethyl acetate). MP = 131.8 – 131.0 °C, 6:1 hexanes / ethyl acetate. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.48 (s, 1H), 9.09 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.87 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.11 (d, *J* = 8.2 Hz, 1H), 7.63 – 7.58 (m, 1H), 7.56 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.24 – 7.20 (m, 2H), 4.00 – 3.92 (m, 4H), 3.19 – 3.12 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.7, 151.5, 148.4, 138.8, 136.6, 135.2, 133.11, 131.2, 131.0, 129.5 (q, *J* = 308.4 Hz), 128.7, 128.4, 127.7, 126.4, 122.3, 121.9, 117.9, 66.1, 53.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ -41.68. HRMS (ESI+) Calculated for ($C_{21}H_{18}F_3N_3O_2SH$) $[M+H]^+$ 434.11450, Found 434.11470. FT-IR (neat, cm^{-1}) ν 1648, 1519, 1489.

2-(Morpholino)-5-nitro-*N*-(quinolin-8-yl)benzamide (T2-7)



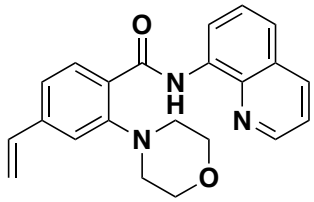
According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 3-nitro-*N*-(quinolin-8-yl)benzamide (0.293 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine. To the mixture morpholine (0.262 g, 3.0 mmol) of was added. The vessel was placed in a pre-heated oil bath set to 110 °C. After 15 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (4:1 → 2:1 hexanes / ethyl acetate) provided 0.275 g (73 % yield) of analytically pure compound T2-7. R_f = 0.20 (10:1 toluene / ethyl acetate). MP = 205 – 206 °C, ethanol. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.93 (s, 1H), 9.04 (dd, *J* = 7.2, 1.4 Hz, 1H), 8.90 (d, *J* = 2.7 Hz, 1H), 8.88 – 8.82 (m, 1H), 8.31 (dd, *J* = 8.9, 2.7 Hz, 1H), 8.25 – 8.15 (m, 1H), 7.67 – 7.55 (m, 2H), 7.51 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.29 – 7.19 (m, 1H), 3.97 – 3.83 (m, 4H), 3.35 – 3.18 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.8, 155.8, 148.5, 143.2, 138.5, 136.7, 134.6, 129.1, 128.4, 128.0, 127.7, 127.3, 122.5, 122.0, 118.9, 117.7, 65.9, 53.3. HRMS (ESI+) Calculated for ($C_{20}H_{18}N_4O_4Na$) $[M+Na]^+$ 401.12200, Found 401.12250. FT-IR (neat, cm^{-1}) ν 1665, 1515, 1484, 1325, 1112.

2-(Morpholino)-5-methoxy-*N*-(quinolin-8-yl)benzamide (T2-8)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 3-methoxy-*N*-(quinolin-8-yl)benzamide (0.278 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 110 °C. After 15 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (4:1 → 3:1 hexanes / ethyl acetate) provided 0.262 g (72 % yield) of analytically pure compound T2-8. This compound is known.[6] ^{1}H NMR (600 MHz, $CDCl_3$) δ 13.11 (s, 1H), 9.13 (d, *J* = 7.6 Hz, 1H), 8.88 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.18 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.82 (d, *J* = 3.2 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.55 (d, *J* = 7.3 Hz, 1H), 7.48 (dd, *J* = 8.2, 4.1 Hz, 1H), 7.25 (d, *J* = 4.3 Hz, 1H), 7.05 (dd, *J* = 8.8, 3.1 Hz, 1H), 4.08 – 3.96 (m, 4H), 3.86 (s, 3H), 3.12 – 3.06 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.3, 156.6, 148.2, 144.7, 139.1, 136.5, 135.9, 129.9, 128.4, 127.7, 122.0, 121.7, 121.4, 119.1, 118.2, 115.7, 66.3, 55.8, 54.4.

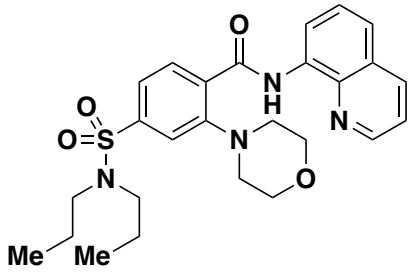
2-(Morpholino)-4-vinyl-*N*-(quinolin-8-yl)benzamide (T2-9)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-vinyl-*N*-(quinolin-8-yl)benzamide (0.274 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 80 °C. After 36 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (6:1 → 4:1 hexanes / ethyl acetate) provided 0.281 g (78 % yield) of analytically pure compound T2-9. R_f = 0.18 (30:1 toluene / ethyl acetate). MP = 156 – 157 °C, 6:1 hexanes / ethyl acetate. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.68 (s, 1H), 9.13 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.88 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.16 (d, *J* = 8.1 Hz, 1H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.55 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.49 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.31 (dd, *J* = 8.1, 1.5 Hz, 1H), 6.76 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.88 (dd, *J* = 17.6, 0.6 Hz, 1H), 5.39 (dd, *J* = 10.9, 0.5 Hz, 1H), 4.05 – 3.93 (m, 4H), 3.23 – 3.12 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5,

151.5, 148.2, 141.6, 138.9, 136.5, 136.2, 135.7, 132.6, 128.4, 128.1, 127.7, 122.0, 121.8, 121.7, 117.9, 117.2, 116.2, 77.4, 66.2, 54.0. HRMS (ESI+) Calculated for ($C_{22}H_{21}N_3O_2Na$) $[M+Na]^+$ 382.15260, Found 382.15320. FT-IR (neat, cm^{-1}) v 3240, 2971, 2829, 1655, 1520, 1484, 1110.

2-(Morpholino)-4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (T2-10)



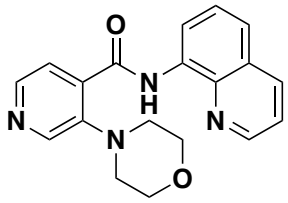
According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (0.412 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 110 °C. After 5 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (4:1 hexanes / ethyl acetate) provided 0.375 g (76 % yield) of analytically pure compound T2-10. R_f = 0.25 (10:1 toluene / ethyl acetate). MP = 146 – 147 °C, 4:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.45 (s, 1H), 9.08 (dd, *J* = 7.3, 1.5 Hz, 1H), 8.88 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.25 (d, *J* = 8.1 Hz, 1H), 8.21 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.67 – 7.57 (m, 4H), 7.51 (dd, *J* = 8.2, 4.2 Hz, 1H), 4.01 – 3.89 (m, 4H), 3.24 – 3.16 (m, 4H), 3.16 – 3.09 (m, 4H), 1.59 (h, *J* = 7.4 Hz, 4H), 0.90 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 151.5, 148.4, 143.6, 138.7, 136.7, 135.0, 133.1, 132.2, 128.4, 127.7, 122.4, 122.1, 121.9, 117.9, 117.8, 66.0, 53.8, 50.1, 22.1, 11.3. HRMS (ESI+) Calculated for ($C_{26}H_{32}N_4O_4SNa$) $[M+Na]^+$ 519.20360, Found 519.20420. FT-IR (neat, cm^{-1}) v 2980, 1655, 1518, 1344, 1156, 1113.

Gram-Scale Synthesis of T2-10

According to General Procedure 1. In a 250 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (2.058 g, 5.0 mmol) and copper acetate (0.270 g, 1.5 mmol) were dissolved in pyridine (10 mL). To the mixture morpholine (1.310 g, 15.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 110 °C. The reaction was monitored by TLC at 3 and 5 hours. After 5 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.440 g, 1.5 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (250 mL), combined with SiO_2 (70 mL), and evaporated to give a free-flowing solid. Column

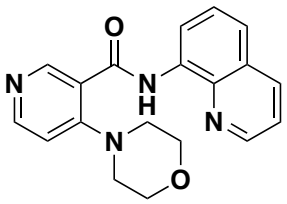
chromatography (4:1 hexanes / ethyl acetate) provided 1.830 g (74 % yield) of analytically pure compound T2-10.

3-(Morpholino)-*N*-(quinolin-8-yl)isonicotinamide (T2-11)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar *N*-(quinolin-8-yl)isonicotinamide (0.249 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 80 °C. After 12 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (2:1 → 1:1 hexanes / ethyl acetate) provided 0.252 g (75 % yield) of analytically pure compound F1-12. R_f = 0.13 (1:2 hexanes / ethyl acetate). MP = 227 – 228 °C, 1:1 hexanes / ethyl acetate. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.54 (s, 1H), 9.08 (dd, *J* = 6.6, 2.5 Hz, 1H), 8.89 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.63 (s, 1H), 8.56 (d, *J* = 4.9 Hz, 1H), 8.22 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.98 (d, *J* = 4.8 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.52 (dd, *J* = 8.3, 4.2 Hz, 1H), 4.04 – 3.92 (m, 6H), 3.30 – 3.20 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.7, 148.5, 146.4, 145.2, 142.5, 138.8, 136.6, 135.4, 134.9, 128.4, 127.6, 124.6, 122.6, 122.0, 118.1, 66.1, 53.6. HRMS (ESI+) Calculated for ($C_{19}H_{18}N_4O_2H$) $[M+H]^+$ 335.15030, Found 335.15050. FT-IR (neat, cm^{-1}) ν 1652, 1516, 1489, 1322, 1106.

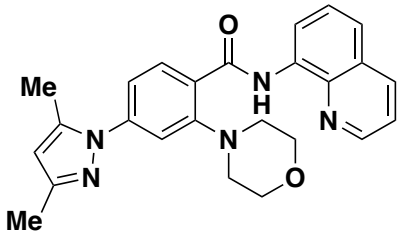
3-(Morpholino)-*N*-(quinolin-8-yl)nicotinamide (T2-12)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar *N*-(quinolin-8-yl)nicotinamide (0.249 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 110 °C. After 5 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (ethyl acetate) provided 0.257 g (77 % yield) of analytically pure compound F1-13. R_f = 0.13 (ethyl acetate). MP = 178 – 179 °C, 1:2 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.72 (s, 1H), 9.07 (s, 1H), 9.05 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.85 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.59 (d, *J* = 5.6 Hz, 1H), 8.21 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.61 (t, *J* = 7.9 Hz, 1H),

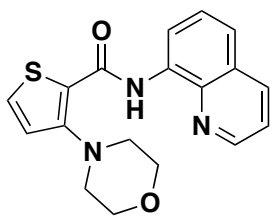
7.57 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.00 (d, *J* = 5.6 Hz, 1H), 3.93 – 3.83 (m, 4H), 3.29 – 3.19 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.6, 156.8, 153.1, 153.0, 148.4, 138.6, 136.7, 134.9, 128.4, 127.7, 123.5, 122.2, 122.0, 117.5, 112.6, 66.0, 52.4. FT-IR (neat, cm^{-1}) ν 1663, 1582, 1526, 1486, 1112.

2-(Morpholino)-4-(3,5-dimethyl-1H-pyrazo-1-yl)-*N*-(quinolin-8-yl)benzamide (T2-13)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-(3,5-dimethyl-1H-pyrazo-yl)-*N*-(quinolin-8-yl)benzamide (0.342 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine. To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 110 °C. After 15 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (5:1 → 3:1 hexanes / ethyl acetate) provided (0.386 g, 90 % yield) of analytically pure compound T2-14 as a pale yellow solid. R_f = 0.34 (1:1 hexanes / ethyl acetate). MP = 178.8 – 180.0 °C, 6:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.61 (s, 1H), 9.12 (d, *J* = 7.6 Hz, 1H), 8.91 – 8.86 (m, 1H), 8.24 (d, *J* = 8.3 Hz, 1H), 8.20 (d, *J* = 8.2 Hz, 1H), 7.61 (t, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.50 (dd, *J* = 8.1, 4.1 Hz, 1H), 7.41 (s, 1H), 7.30 – 7.24 (m, 1H), 6.05 (s, 1H), 3.97 (s, 4H), 3.21 (d, *J* = 3.6 Hz, 4H), 2.39 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.1, 149.9, 148.3, 143.2, 139.7, 138.9, 136.6, 135.6, 133.0, 128.5, 127.7, 127.2, 122.5, 122.0, 121.8, 119.2, 117.9, 115.5, 108.2, 66.2, 53.9, 13.7, 13.0. HRMS (ESI+) Calculated for ($C_{25}H_{25}N_5O_2Na$) $[M+Na]^+$ 450.19000, Found 450.19100. FT-IR (neat, cm^{-1}) ν 2980, 1657, 1515, 1482, 1109.

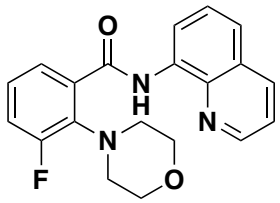
3-(Morpholino)-*N*-(quinolin-8-yl)thiophenecarboxamide (T2-14)



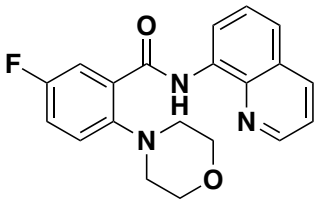
According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar *N*-(quinolin-8-yl)thoiphenecarboxamide (0.254 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 110 °C. After 20 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was

diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (5:1 → 4:1 hexanes / ethyl acetate) provided 0.221 g (65 % yield) of analytically pure compound T2-15. This compound is known.[2] ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.60 (s, 1H), 9.05 (dd, *J* = 7.6, 1.5 Hz, 1H), 8.94 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.61 – 7.56 (m, 1H), 7.54 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.53 – 7.49 (m, 2H), 7.21 (d, *J* = 5.3 Hz, 1H), 4.23 – 4.09 (m, 4H), 3.16 – 3.07 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.7, 152.3, 148.1, 139.0, 136.5, 135.8, 130.3, 130.2, 128.3, 127.7, 122.2, 121.8, 121.7, 118.1, 66.6, 54.4.

2-(Morpholino)-3-fluoro-*N*-(quinolin-8-yl)benzamide (T2-15a) and 2-(Morpholino)-5-fluoro-*N*-(quinolin-8-yl)benzamide (T2-15-b)



T2-15a



T2-15b

According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 3-fluoro-*N*-(quinolin-8-yl)benzamide (0.266 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture morpholine (0.262 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 80 °C. After 24 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (10:1 → 4:1 hexanes / ethyl acetate) provided T2-15a 0.126 g (36 % yield) followed by 0.138 g of T2-15b (39 % yield). T2-15b is known.[2] Regioisomeric assignment based on the report by Zhang et. al.[2]

T2-15a

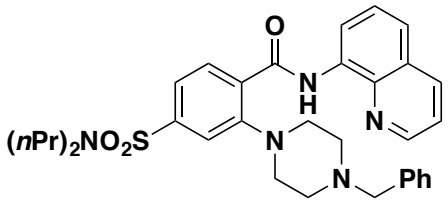
R_f = 0.15 (8:1 hexanes / ethyl acetate). MP = 166 – 167 °C, 6:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 12.72 (s, 1H), 9.07 (d, *J* = 7.4 Hz, 1H), 8.91 – 8.85 (m, 1H), 8.20 (d, *J* = 8.2 Hz, 1H), 8.09 (d, *J* = 7.5 Hz, 1H), 7.60 (t, *J* = 7.8 Hz, 1H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.49 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.29 (q, *J* = 7.2 Hz, 1H), 7.26 – 7.21 (m, 1H), 4.07 (s, 4H), 3.36 (s, 4H). ^{13}C NMR (151 MHz, CHLOROFORM-*D*) δ 164.5 (d, J_{C-F} = 4.0 Hz), 161.0 (d, J_{C-F} = 252.0 Hz), 148.2, 139.2, 137.1 (d, J_{C-F} = 10.1 Hz), 136.6, 135.5, 133.3 (d, J_{C-F} = 4.3 Hz), 128.4, 127.6, 127.5 126.8 (d, J_{C-F} = 9.5 Hz), 122.3, 121.7, 120.2 (d, J_{C-F} = 21.8 Hz), 118.8, 66.5, 52.0. ^{19}F NMR (565 MHz, Chloroform-*d*) δ -117.47 – -117.75 (m). FT-IR (neat, cm^{-1}) v 2857, 2830, 1658, 1520, 1264, 1110.

T2-15b

R_f = 0.11 (6:1 hexanes / ethyl acetate). MP = 142 – 143 °C, 6:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 12.90 (s, 1H), 9.10 (d, *J* = 7.5 Hz, 1H), 8.92 – 8.85 (m, 1H), 8.19 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 9.5 Hz, 1H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.49 (dd, *J* = 5.1, 3.1 Hz, 1H), 7.26 (d, *J* = 12.1 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 4.00 (s, 4H), 3.10 (s, 4H). ^{13}C NMR (151 MHz, CHLOROFORM-*D*) δ 159.7 (d, *J* = 244.3 Hz), 148.3, 147.4 (d, *J* = 2.7 Hz), 139.0, 136.5, 135.52, 131.0 (d, *J* = 7.3 Hz), 128.4, 127.7, 122.5, 122.2, 121.8, 121.5 (d, *J* = 7.7 Hz), 119.0 (d, *J* = 22.3 Hz), 118.8 (d, *J* = 24.4 Hz), 118.2, 66.2, 54.3. ^{19}F NMR (565 MHz, Chloroform-*d*) δ -117.07 – -118.25 (m). FT-IR (neat, cm^{-1}) v 2954, 2848, 1661, 1522, 1471, 1257, 1110.

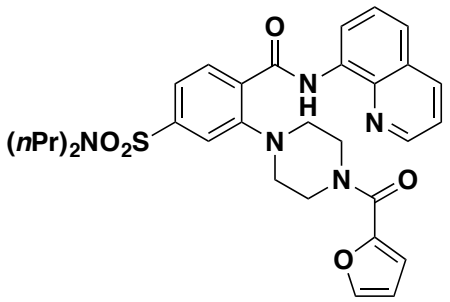
Copper-Catalyzed Aerobic C–H Amination with Secondary Amines

2-(4-Benzylpiperazin-1-yl)-4-(-(*N*,*N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (T3-1)



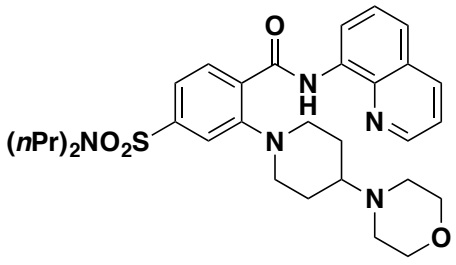
According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-(-(*N*,*N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (0.412 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine. 1-Benzylpiperazine (0.529 g, 3.0 mmol) was added and the vessel was placed in a pre-heated oil bath set to 110 °C. After 23 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (4:1 → 2:1 hexanes / ethyl acetate) provided 0.366 g (63 % yield) of analytically pure compound T3-1. R_f = 0.29 (2:1 hexanes / ethyl acetate). MP = 181 – 182 °C, 2:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.45 (s, 1H), 9.09 (dd, *J* = 7.2, 1.5 Hz, 1H), 8.86 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.28 – 8.18 (m, 2H), 7.65 (d, *J* = 1.3 Hz, 1H), 7.64 – 7.57 (m, 3H), 7.53 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.31 – 7.24 (m, 2H), 7.22 (t, *J* = 8.1 Hz, 3H), 3.40 (s, 2H), 3.22 (s, 4H), 3.15 – 3.08 (m, 4H), 2.72 (s, 4H), 1.58 (h, *J* = 7.4 Hz, 4H), 0.90 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.7, 151.9, 148.4, 143.4, 138.9, 137.8, 136.5, 135.2, 132.9, 132.2, 129.1, 128.4, 128.4, 127.7, 127.3, 122.3, 121.8, 121.8, 117.9, 117.8, 62.8, 53.7, 51.9, 50.2, 22.2, 11.3. HRMS (ESI+) Calculated for ($C_{33}H_{39}N_5O_3SH$) $[M+H]^+$ 586.28460, Found 586.28500. FT-IR (neat, cm^{-1}) v 1661, 1520, 1340, 1157.

2-(4-(2-Furoyl)piperazin-1-yl)-4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (T3-2)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (0.412 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine. 1-(2-Fuoryl)piperazine (0.541 g, 3.0 mmol) was added and the vessel was placed in a pre-heated oil bath set to 110 °C. After 6 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (4:1 → 2:1 hexanes / ethyl acetate) provided 0.375 g (64 % yield) of analytically pure compound T2-2. R_f = 0.40 (1:1 hexanes / ethyl acetate). MP = 152 – 153 °C, 3:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.55 (s, 1H), 9.11 (dd, *J* = 7.4, 1.3 Hz, 1H), 8.83 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.29 (d, *J* = 8.1 Hz, 1H), 8.21 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.70 – 7.56 (m, 4H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.01 (d, *J* = 3.4 Hz, 1H), 6.46 (dd, *J* = 3.4, 1.7 Hz, 1H), 4.13 (s, 4H), 3.32 – 3.19 (m, 4H), 3.17 – 3.08 (m, 4H), 1.58 (h, *J* = 7.4 Hz, 4H), 0.89 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.18, 159.19, 151.11, 148.29, 147.82, 143.90, 143.81, 138.72, 136.81, 134.99, 133.18, 132.35, 128.48, 127.72, 122.64, 122.51, 122.02, 118.23, 118.11, 117.10, 111.54, 53.72, 50.09, 22.11, 11.31. ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.2, 159.2, 151.1, 148.3, 147.8, 143.9, 143.8, 138.7, 136.8, 135.0, 133.2, 132.4, 128.5, 127.7, 122.6, 122.5, 122.0, 118.2, 118.1, 117.1, 111.6, 53.7, one piperazine carbon was not found, 50.1, 22.1, 11.3. HRMS (ESI+) Calculated for ($C_{31}H_{35}N_5O_5SH$) $[M+H]^+$ 590.24320, Found 590.24270. FT-IR (neat, cm^{-1}) ν 2980, 1622, 1519, 1484, 1265, 1160.

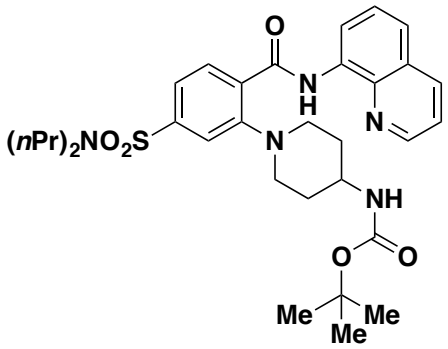
2-(4-(4-Morpholinopiperidin-1-yl)-4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (T3-3)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (0.412 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine. 4-(Morpholino)piperidine (0.511 g, 3.0 mmol) was added the vessel was placed in a pre-heated oil bath set to 110 °C. After 5 hours the reaction reached completion.

After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (12:6:1 → 9:9:1 hexanes / ethyl acetate / triethylamine) provided 0.420 g (73 % yield) of analytically pure compound T3-3. R_f = 0.16 (9:9:1 hexanes / ethyl acetate / triethylamine). MP = 186 – 187 °C, 1:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.40 (s, 1H), 9.09 (d, *J* = 7.5 Hz, 1H), 8.89 (dd, *J* = 4.0, 1.3 Hz, 1H), 8.20 (d, *J* = 8.1 Hz, 2H), 7.65 – 7.59 (m, 2H), 7.59 – 7.54 (m, 2H), 7.46 (dd, *J* = 8.2, 4.2 Hz, 1H), 3.62 – 3.52 (m, 4H), 3.49 (d, *J* = 11.7 Hz, 2H), 3.18 – 3.06 (m, 4H), 2.87 (t, *J* = 10.9 Hz, 2H), 2.36 (t, *J* = 10.9 Hz, 1H), 2.31 – 2.23 (m, 4H), 1.90 (qd, *J* = 12.0, 3.2 Hz, 2H), 1.83 (d, *J* = 10.7 Hz, 2H), 1.58 (h, *J* = 7.4 Hz, 4H), 0.90 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.7, 151.2, 147.5, 142.3, 137.9, 135.7, 134.2, 131.7, 131.2, 127.4, 126.8, 121.5, 121.3, 120.6, 120.5, 116.9, 116.9, 66.4, 60.2, 52.6, 49.2, 48.4, 26.3, 21.2, 10.3. HRMS (ESI+) Calculated for ($C_{31}H_{41}N_5O_4SNa$) $[M+Na]^+$ 602.27710, Found 602.27810. FT-IR (neat, cm^{-1}) ν 2980, 1660, 1524, 1156, 1113.

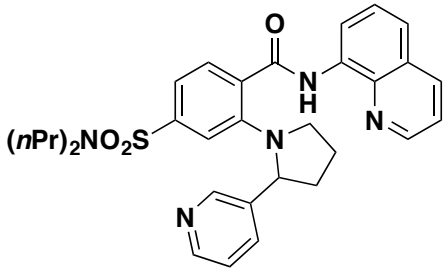
2-(4-[(*tert*-Butoxycarbonyl)amino]piperidin-1-yl)-4-(-(*N*,*N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (T3-4)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-(-(*N*,*N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (0.412 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine. 4-[(*tert*-Butoxycarbonyl)amino]piperidine (0.601 g, 3.0 mmol) was added the vessel was placed in a pre-heated oil bath set to 110 °C. After 5 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (2:1 → 1:1 hexanes / ethyl acetate) provided 0.410 g (67 % yield) of analytically pure compound T3-4. R_f = 0.44 (2:1 hexanes / ethyl acetate). MP = 215 – 216 °C, ethanol. ^{1}H NMR (600 MHz, $CDCl_3$, 10% DMSO-d_6) δ 12.55 (d, *J* = 6.9 Hz, 1H), 9.13 – 9.01 (m, 1H), 8.90 (s, 1H), 8.24 (dt, *J* = 15.9, 7.6 Hz, 2H), 7.71 – 7.45 (m, 5H), 5.09 (s, 1H), 3.60 (s, 1H), 3.40 (s, 2H), 3.12 (q, *J* = 7.8 Hz, 4H), 3.00 (s, 2H), 2.07 (s, 2H), 1.93 – 1.80 (m, 2H), 1.58 (m, *J* = 14.7, 7.4 Hz, 4H), 1.42 (s, 9H), 0.90 (q, *J* = 7.5 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.2, 153.2, 150.1, 146.2, 141.1, 136.6, 134.5, 133.0, 130.6, 130.0, 126.2, 125.4, 120.2, 119.8, 119.6, 115.9, 115.7, 50.5, 48.0, 44.7, 29.2, 26.4, 19.9, 9.2. Missing one carbon signal. HRMS (ESI+)

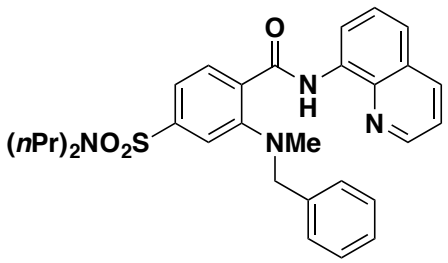
Calculated for ($C_{32}H_{43}N_5O_5SNa$) $[M+Na]^+$ 632.28770, Found 632.28890. FT-IR (neat, cm^{-1}) v 3342, 1694, 1659, 1521, 1156.

2-(2-Pyridin-3-ylpyrrolidin-1yl)-4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (T3-5)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar. 4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (0.412 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). (-)-Nornicotine was added (0.445 g, 3.0 mmol) and the vessel was placed in a pre-heated oil bath set to 110 °C. After 36 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (12:6:1 → 9:9:1 hexanes / ethyl acetate / triethylamine) provided 0.263 g (47 % yield) of analytically pure compound T3-5. R_f = 0.47 (1:2 hexanes / ethyl acetate). MP = 168 – 169 °C, 1:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.37 (s, 1H), 9.08 – 9.05 (m, 1H), 9.03 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.87 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.51 – 8.47 (m, 1H), 8.23 (dd, *J* = 8.2, 1.6 Hz, 1H), 8.11 (dt, *J* = 7.9, 1.8 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.66 – 7.62 (m, 1H), 7.60 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.34 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.28 (d, *J* = 1.5 Hz, 1H), 7.23 (dd, *J* = 7.8, 4.7 Hz, 1H), 4.81 (dd, *J* = 9.9, 6.2 Hz, 1H), 4.01 (q, J = 9.5 Hz, 1H), 3.25 (td, *J* = 8.8, 3.8 Hz, 1H), 2.83 – 2.65 (m, 4H), 2.50 (dtd, *J* = 12.1, 6.2, 2.0 Hz, 2H), 2.11 – 2.00 (m, 1H), 1.95 (m, 2H), 1.39 (m, 4H), 0.78 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.9, 149.3, 149.1, 148.3, 146.7, 142.2, 138.9, 137.7, 136.7, 134.9, 134.7, 132.1, 129.9, 128.3, 127.7, 123.8, 122.2, 122.0, 118.5, 117.3, 115.9, 63.2, 55.7, 50.2, 37.2, 24.8, 22.2, 11.3. HRMS (ESI+) Calculated for ($C_{31}H_{35}N_5O_3SNa$) $[M+Na]^+$ 580.23530, Found 580.23590. FT-IR (neat, cm^{-1}) v 1669, 1519, 1481, 1328, 1157.

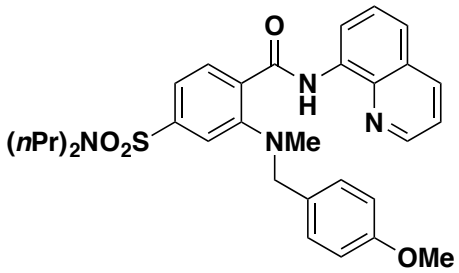
2-*(N*-Methylbenzylamino)-4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (T3-6)



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (0.412 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine. *N*-Methylbenzylamine

(0.364 g, 3.0 mmol) was added and the vessel was placed in a pre-heated oil bath set to 110 °C. After 8 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (30:1 toluene / ethyl acetate) provided 0.389 g (73 % yield) of analytically pure compound T3-6. R_f = 0.21 (30:1 toluene / ethyl acetate). MP = 114 – 115 °C, 4:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 13.50 (s, 1H), 9.03 (d, *J* = 7.4 Hz, 1H), 8.85 – 8.78 (m, 1H), 8.33 (d, *J* = 8.1 Hz, 1H), 8.21 (d, *J* = 8.1 Hz, 1H), 7.62 (t, *J* = 7.9 Hz, 1H), 7.57 (dd, *J* = 15.8, 8.1 Hz, 2H), 7.53 (s, 1H), 7.48 (dd, *J* = 8.2, 4.1 Hz, 1H), 7.30 (d, *J* = 6.5 Hz, 2H), 7.12 (q, *J* = 6.3 Hz, 3H), 4.42 (s, 2H), 2.98 (s, 3H), 2.96 – 2.88 (m, 4H), 1.48 (h, *J* = 7.4 Hz, 4H), 0.84 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (151 MHz, NONE) δ 164.0, 150.8, 148.6, 142.9, 139.6, 136.6, 136.2, 135.6, 132.9, 132.3, 129.4, 128.6, 128.5, 127.8, 127.7, 122.2, 122.0, 121.8, 120.6, 117.9, 60.7, 50.2, 44.2, 22.2, 11.4. HRMS (ESI+) Calculated for ($C_{30}H_{34}N_4O_3SH$) $[M+H]^+$ 531.24240, Found 531.24220. FT-IR (neat, cm^{-1}) ν 1652, 1525, 1339, 1153.

2-(*N*-Methyl-4-methoxybenzylamino)-4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide T3-7



According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar 4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (0.412 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine. *N*-Methyl-4-methoxybenzylamine (0.454 g, 3.0 mmol) was added and the vessel was placed in a pre-heated oil bath set to 110 °C. After 6.5 hours the reaction reached completion. After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (30:1 toluene / ethyl acetate) provided 0.434 g (77 % yield) of analytically pure compound T3-7 as a pale yellow oil. R_f = 0.43 (10:1 toluene / ethyl acetate). ^{1}H NMR (600 MHz, $CDCl_3$) δ 13.60 (s, 1H), 9.03 (d, *J* = 7.5 Hz, 1H), 8.82 (dd, *J* = 4.0, 1.4 Hz, 1H), 8.34 (d, *J* = 8.1 Hz, 1H), 8.23 – 8.18 (m, 2H), 7.61 (t, *J* = 7.9 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 6.8 Hz, 1H), 7.47 (dd, *J* = 8.2, 4.1 Hz, 1H), 7.19 (d, *J* = 8.5 Hz, 2H), 6.63 (d, *J* = 8.6 Hz, 2H), 4.35 (s, 2H), 3.67 (s, 3H), 2.98 (t, J = 7.5 Hz, 4H), 2.96 (s, 3H), 1.50 (h, *J* = 7.4 Hz, 4H), 0.85 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.8, 159.0, 150.8, 148.5, 142.7, 139.5, 136.4, 135.6, 132.7, 132.3, 130.5, 128.3, 128.1, 127.6, 122.1, 121.9, 121.7, 120.8, 117.8, 113.7, 60.1, 55.2, 50.0, 43.8, 22.1. HRMS

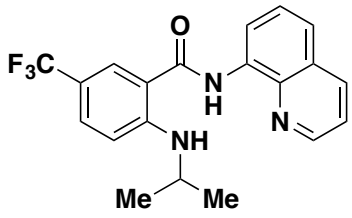
(ESI+) Calculated for ($C_{31}H_{36}N_4O_4SNa$) $[M+Na]^+$ 583.23490, Found 583.23260. FT-IR (neat, cm^{-1}) ν 1661, 1526, 1325, 1247, 1152.

Copper-Mediated C–H Amination with Primary Amines

General Procedure for Amination with Primary Amines (General Procedure 2)

Reactions were run in a 100 mL heavy wall glass pressure vessel with a magnetic stir-bar and a PTFE bushing or in 60 mL screw cap vials. Stirbars were large enough to break the surface of the solvent and set to between 350 and 550 rpm. Benzamide (1.0 equiv), copper acetate (1.0 equiv), tetrabutylammonium iodide (1.0 equiv), pyridine / dimethyl sulfoxide (0.5 M, 1:1 v/v), and amine (3.0 equiv) were added sequentially to the vessel. Reactions were heated to the indicated temperature in a pre-heated oil bath (in case of pressure vessel) or in a parallel synthesis plate of appropriate size (in case of vial). Reactions were monitored at regular intervals by TLC analysis and stopped when complete consumption of the starting material was observed, or when the reaction failed to proceed to completion after 36 hours. Reactions were quenched up by addition of solid EDTA (1.0 equiv) to the room temperature reaction mixture and stirring for one hour. The reaction was then diluted with dichloromethane, treated with SiO_2 (15 mL per mmol of starting amide), and evaporated to dryness on a rotary evaporator. Subsequent column chromatography in the appropriate solvent resulted in the pure compound.

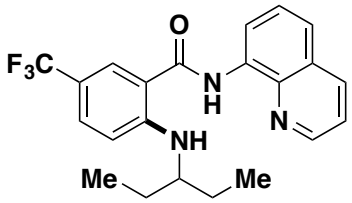
2-(Isopropylamino)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T4-1)



According to general procedure 2. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), copper acetate (0.182 g, 1.0 mmol) and tetrabutylammonium iodide (0.369 g, 1.0 mmol) were dissolved in pyridine / dimethyl sulfoxide (2.0 mL, 1:1 v/v). Isopropyl amine (0.177 g, 3.0 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 80 °C. After 8.5 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (8:1 hexanes / ethyl acetate) provided 0.216 g (58 % yield) of analytically pure compound T4-1 as a pale yellow solid. R_f = 0.35 (10:1 hexanes / ethyl acetate). MP = 152 – 153 °C, 6:1 hexanes / ethyl acetate. ^1H NMR (600 MHz, $CDCl_3$) δ 10.59 (s, 1H), 8.86 (dd, *J* =

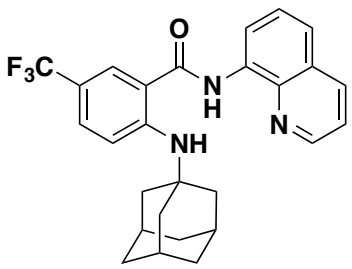
4.1, 1.5 Hz, 1H), 8.77 (dd, *J* = 7.4, 1.1 Hz, 1H), 8.19 (dd, *J* = 8.2, 1.4 Hz, 1H), 8.07 (d, *J* = 6.9 Hz, 1H), 7.99 (s, 1H), 7.63 – 7.52 (m, 3H), 7.49 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.79 (d, *J* = 8.9 Hz, 1H), 3.77 (h, *J* = 12.9, 6.4 Hz, 1H), 1.31 (d, *J* = 6.3 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.5, 151.4, 148.6, 139.0, 136.5, 134.5, 129.9 (q, J_{C-F} = 3.7 Hz), 128.1, 127.4, 125.8 (q, J_{C-F} = 4.3 Hz), 123.0 (q, J_{C-F} = 294.5 Hz), 121.9, 116.6, 115.9 (q, J_{C-F} = 33.3 Hz), 112.0, 43.7, 22.7. ^{19}F NMR (565 MHz, $CDCl_3$) δ -60.85. HRMS (ESI+) Calculated for ($C_{20}H_{18}F_3N_3ONa$) $[M+Na]^+$ 396.12940, Found 396.13090. FT-IR (neat, cm^{-1}) v 1655, 1533, 1326, 1086.

2-(3-Pentylamino)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T4-2)



According to general procedure 2. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), copper acetate (0.182 g, 1.0 mmol) and tetrabutylammonium iodide (0.369 g, 1.0 mmol) were dissolved in pyridine / dimethyl sulfoxide (2.0 mL, 1:1 v/v). 3-Aminopentane (0.262 g, 3.0 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 60 °C. After 14 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (10:1 hexanes / ethyl acetate) provided 0.227 g (57 % yield) of analytically pure compound T4-2 as a pale yellow solid. R_f = 0.41 (10:1 hexanes / ethyl acetate). MP = 104 – 105 °C, 8:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.60 (s, 1H), 8.91 – 8.82 (m, 1H), 8.77 (d, *J* = 7.2 Hz, 1H), 8.23 – 8.16 (m, 1H), 8.13 (d, *J* = 7.9 Hz, 1H), 8.00 (s, 1H), 7.56 (dq, *J* = 18.4, 9.6, 8.8 Hz, 2H), 7.49 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.79 (d, *J* = 8.9 Hz, 1H), 3.40 (h, *J* = 6.3 Hz, 1H), 1.81 – 1.48 (m, 4H), 0.98 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.6, 152.5, 148.6, 139.0, 136.5, 134.6, 129.9 (q, J_{C-F} = 2.7 Hz), 128.2, 127.4, 125.8 (q, J_{C-F} = 3.7 Hz), Missing CF_3 quartet, one peak found: 124.0, 121.9, 121.9, 116.6, 115.6 (q, J_{C-F} = 32.6 Hz), 114.2, 55.2, 27.0, 10.4. ^{19}F NMR (565 MHz, $CDCl_3$) δ -60.85. HRMS (ESI+) Calculated for ($C_{22}H_{22}F_3N_3ONa$) $[M+Na]^+$ 424.16070, Found 424.16210. 1652, 1530, 1322, 1099, 1086.

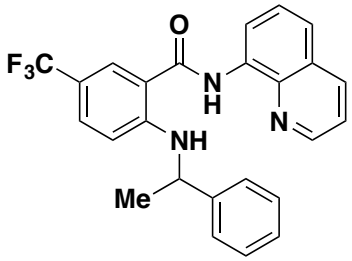
2-(1-Adamantylamino)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T4-3)



According to general procedure 2. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), copper acetate (0.182 g, 1.0 mmol) and tetrabutylammonium iodide (0.369 g, 1.0 mmol) were

dissolved in pyridine / dimethyl sulfoxide (2.0 mL, 1:1 v/v). 1-Adamantylamine (0.454 g, 3.0 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 80 °C. After 14 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (8:1 hexanes / ethyl acetate) provided 0.188 g (40 % yield) of analytically pure compound T4-3 as a pale yellow solid. R_f = 0.39 (10:1 hexanes / ethyl acetate). MP = 159 – 160 °C, 6:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.56 (s, 1H), 8.85 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.77 (dd, *J* = 7.4, 1.3 Hz, 1H), 8.19 (dd, *J* = 8.4, 1.5 Hz, 2H), 7.97 (s, 1H), 7.62 – 7.52 (m, 2H), 7.48 (dd, *J* = 8.2, 4.4 Hz, 1H), 7.12 (d, *J* = 9.0 Hz, 1H), 2.16 (s, 3H), 2.10 (s, 6H), 1.73 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.76, 151.14, 148.57, 138.91, 136.44, 134.57, 128.09, 127.39, 121.86, 121.84, 116.62, 115.72, 114.81, 52.05, 42.33, 36.52, 29.67. ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.8, 151.2, 148.6, 139.0, 136.5, 134.6, 128.9 (q, J_{C-F} = 3.3 Hz), 128.1, 127.4, 126.0 (q, J_{C-F} = 3.9 Hz), 124.9 (q, J_{C-F} = 270.1 Hz), 121.9, 121.9, 116.6, 115.8 (q, J_{C-F} = 9.6 Hz), 115.8, 114.8, 52.1, 42.4, 36.6, 29.7. ^{19}F NMR (565 MHz, $CDCl_3$) δ -60.95. HRMS (ESI+) Calculated for ($C_{27}H_{26}F_3N_3ONa$) $[M+Na]^+$ 488.19200, Found 488.19270. FT-IR (neat, cm^{-1}) ν 2899, 1652, 1526, 1323, 1104, 1084.

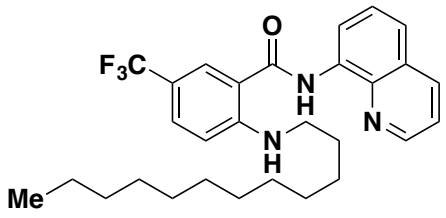
2-(1-Phenethylamino)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T4-4)



According to general procedure 2. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), copper acetate (0.182 g, 1.0 mmol) and tetrabutylammonium iodide (0.369 g, 1.0 mmol) were dissolved in pyridine / dimethyl sulfoxide (2.0 mL, 1:1 v/v). 1-Methylbenzylamine (0.364 g, 3.0 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 80 °C. After 7 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (8:1 hexanes / ethyl acetate) provided 0.236 g (54 % yield) of analytically pure compound T4-4. R_f = 0.33 (10:1 hexanes / ethyl acetate). MP = 179 – 180 °C, 6:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.69 (s, 1H), 8.90 (d, *J* = 3.4 Hz, 1H), 8.85 (d, *J* = 7.4 Hz, 1H), 8.64 (d, *J* = 4.5 Hz, 1H), 8.23 (d, *J* = 8.2 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.52 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.45 – 7.38 (m, 3H), 7.36 (t, *J* = 7.3 Hz, 2H), 7.31 – 7.24 (m, 1H), 6.57 (d, *J* = 8.8 Hz, 1H), 4.70 – 4.58 (m, 1H), 1.66 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.5, 151.3, 148.7, 144.3, 139.0, 136.5, 134.5, 129.0, 129.8 (q, J_{C-F} = 3.6 Hz), 128.2, 127.4, 127.3, 125.8, 125.4 (q, J_{C-F} = 4.4 Hz), 124.7 (q, J_{C-F} =

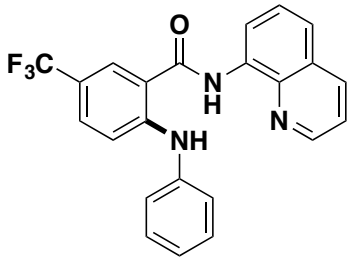
270.3 Hz), 122.0, 122.0-,116.8 (q, J_{C-F} = 34.4 Hz), 116.7, 114.9, 113.2, 53.1, 25.2. ^{19}F NMR (565 MHz, $CDCl_3$) δ -60.98. HRMS (ESI+) Calculated for ($C_{25}H_{20}F_3N_3ONa$) $[M+Na]^+$ 458.14510, Found 458.14660. FT-IR (neat, cm^{-1}) ν 1655, 1527, 1323, 1111.

2-(1-Dodecylamino)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T4-5)



According to general procedure 2. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), copper acetate (0.182 g, 1.0 mmol) and tetrabutylammonium iodide (0.369 g, 1.0 mmol) were dissolved in pyridine / dimethyl sulfoxide (2.0 mL, 1:1 v/v). Dodecylamine (0.556 g, 3.0 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 80 °C. After 8 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (8:1 hexanes / ethyl acetate) provided 0.219 g (44 % yield) of analytically pure compound T4-5. This compound is known.[6] R_f = 0.49 (10:1 hexanes / ethyl acetate). ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.61 (s, 1H), 8.85 (d, *J* = 3.9 Hz, 1H), 8.78 (d, *J* = 7.4 Hz, 1H), 8.21 – 8.11 (m, 2H), 7.99 (s, 1H), 7.61 – 7.51 (m, 3H), 7.47 (dd, *J* = 8.1, 4.1 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 1H), 3.22 (q, *J* = 6.5 Hz, 2H), 1.72 (p, *J* = 7.2 Hz, 2H), 1.45 (p, *J* = 7.1 Hz, 2H), 1.27 (m, 20H), 0.88 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.4, 152.4, 148.6, 148.6, 138.9, 136.5, 136.4, 134.5, 130.0 (q, J_{C-F} = 3.2 Hz), 128.1, 127.4 (q, J_{C-F} = 3.8 Hz), 124.9 (q, J_{C-F} = 270.3 Hz), 121.9, 116.6, 116.1 (q, J_{C-F} = 33.1 Hz), 114.4, 111.6, 43.2, 32.0, 29.8, 29.8, 29.7, 29.7, 29.5, 29.5, 29.1, 27.3, 22.8, 14.2. ^{19}F NMR (565 MHz, $CDCl_3$) δ -60.81.

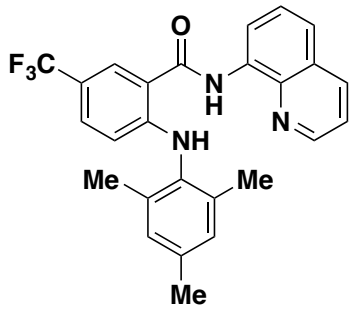
2-(Phenylamino)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T4-6)



According to general procedure 2. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), copper acetate (0.182 g, 1.0 mmol) and tetrabutylammonium iodide (0.369 g, 1.0 mmol) were dissolved in pyridine / dimethyl sulfoxide (2.0 mL, 1:1 v/v). Aniline (0.279 g, 3.0 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 80 °C. After 14 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL),

and evaporated to give a free-flowing solid. Column chromatography (8:1 hexanes / ethyl acetate) provided 0.187 g (46 % yield) of analytically pure compound T4-6 as a yellow solid. R_f = 0.32 (10:1 hexanes / ethyl acetate). MP = 172 – 173 °C, 4:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.71 (s, 1H), 9.90 (s, 1H), 8.87 (d, *J* = 4.0 Hz, 1H), 8.82 (d, *J* = 7.3 Hz, 1H), 8.18 (d, *J* = 8.2 Hz, 1H), 8.07 (s, 1H), 7.64 – 7.55 (m, 2H), 7.53 (d, *J* = 8.8 Hz, 1H), 7.49 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.38 (q, *J* = 9.2, 8.5 Hz, 3H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.0, 149.4, 148.7, 140.0, 138.9, 136.5, 134.3, 129.6, 129.5 (q, $J_{C–F}$ = 3.2 Hz), 128.1, 127.4, 125.5 (q, $J_{C–F}$ = 3.9 Hz), 124.5 (q, $J_{C–F}$ = 270.9 Hz), 124.4, 122.8, 122.2, 122.0, 119.1 (q, $J_{C–F}$ = 33.2 Hz), 117.0, 116.7, 114.7. ^{19}F NMR (565 MHz, $CDCl_3$) δ -61.22. HRMS (ESI+) Calculated for ($C_{23}H_{16}F_3N_3ONa$) $[M+Na]^+$ 430.11380, Found 430.11510. FT-IR (neat, cm^{-1}) ν 1652, 1537, 1317, 1101, 1089.

2-(Mesitylamino)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T4-7)



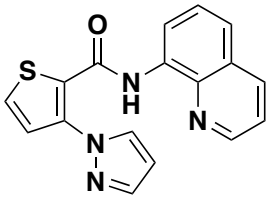
According to general procedure 2. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), copper acetate (0.182 g, 1.0 mmol) and tetrabutylammonium iodide (0.369 g, 1.0 mmol) were dissolved in pyridine / dimethyl sulfoxide (2.0 mL, 1:1 v/v). 2,4,6-Trimethylanaline (0.406 g, 3.0 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 80 °C. After 14 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (8:1 hexanes / ethyl acetate) provided (0.215 g, 48 % yield) of analytically pure compound T4-7 as a pale yellow solid. R_f = 0.39 (10:1 hexanes / ethyl acetate). MP = 182.6 – 182.7 °C, 4:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.76 (s, 1H), 9.44 (s, 1H), 8.90 (dd, *J* = 4.1, 1.3 Hz, 1H), 8.85 (dd, *J* = 7.3, 1.3 Hz, 1H), 8.22 (dd, *J* = 8.2, 1.2 Hz, 1H), 8.08 (s, 1H), 7.63 – 7.56 (m, 2H), 7.52 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.41 (d, *J* = 8.9 Hz, 1H), 6.98 (s, 2H), 6.34 (d, *J* = 8.8 Hz, 1H), 2.33 (s, 3H), 2.20 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.4, 151.6, 148.7, 139.0, 136.7, 136.6, 136.4, 134.5, 133.9, 129.8 (q, $J_{C–F}$ = 3.7 Hz), 129.4, 128.2, 127.4, 125.6 (q, $J_{C–F}$ = 4.0 Hz), 124.8 (q, $J_{C–F}$ = 270.6 Hz), 122.1, 122.0, 117.4 (q, $J_{C–F}$ = 33.0 Hz), 116.7, 114.6, 113.3, 21.1, 18.3. ^{19}F NMR (565 MHz, $CDCl_3$) δ -60.97. HRMS (ESI+) Calculated for ($C_{26}H_{22}F_3N_3ONa$) $[M+Na]^+$ 472.16070, Found 472.16210. FT-IR (neat, cm^{-1}) ν 1652, 1525, 1314, 1097.

Copper-Catalyzed Aerobic *N*-Arylation of Heterocycles

General Procedure for Amination with N–H(Heterocycles) and Acidic N–H Bonds (General Procedure 3)

Reactions were run in a 100 mL heavy wall glass pressure vessel with a magnetic stir-bar and a PTFE bushing or in 60 mL screw cap vials. Stirbars were large enough to break the surface of the solvent and set to between 350 and 550 rpm. Benzamide (1.0 equiv), $(CuOH)_2CO_3$ (0.3 equiv), appropriate coupling partner (1.5 equiv), pyridine (0.5 M) and 1,1,3,3-tetramethylguanidine (1.2 equiv) were added sequentially to the vessel. Reactions were heated to the indicated temperature in a pre-heated oil bath (in case of pressure vessel) or in a parallel synthesis plate of appropriate size (in case of vial). Reactions were monitored at regular intervals by TLC analysis and stopped when complete consumption of the starting material was observed, or when the reaction failed to proceed to completion after 36 hours. Reactions were quenched up by addition of solid EDTA (0.3 equiv) to the room temperature reaction mixture and stirring for one hour. The reaction was then diluted with dichloromethane, treated with SiO_2 (15 mL per mmol of starting amide), and evaporated to dryness on a rotary evaporator. Subsequent column chromatography in the appropriate solvent resulted in the pure compound.

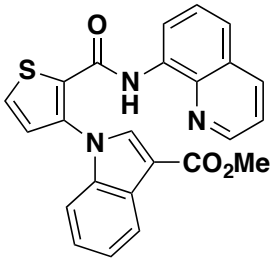
3-(Pyrazol-1-yl)-*N*-(quinolin-8-yl)thiophenecarboxamide (4)



According to general procedure 3. In a 42 mL screw-cap vial equipped with a magnetic stir-bar *N*-(quinolin-8-yl)thiophenecarboxamide (0.254 g, 1.0 mmol), basic copper carbonate (0.033 g, 0.15 mmol) and pyrazole (0.102 g, 1.5 mmol) were dissolved in pyridine (2.0 mL). 1,1,3,3-Tetramethylguanidine (0.138 g, 1.2 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 16 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.088g, 0.3 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (16:4:1 hexanes / ethyl acetate / triethylamine) provided 0.210 g (66 % yield) of analytically pure compound 4 as a pale yellow solid. R_f = 0.31 (10:1 toluene / ethyl acetate). MP = 177 – 178 °C, 2:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.38 (s, 1H), 8.88 (d, *J* = 7.1 Hz, 1H), 8.81 (d, *J* = 4.1 Hz, 1H), 8.13 (d, *J* = 8.2 Hz, 1H), 7.97 – 7.87 (m, 2H), 7.59 – 7.48 (m, 3H), 7.43 (dd, *J* = 8.2, 4.1 Hz, 1H), 7.21 (d, *J* = 5.3 Hz, 1H), 6.55 – 6.48 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.4, 148.2, 141.6, 139.6, 136.2, 136.1, 135.5, 131.2, 130.9, 129.9, 128.2, 127.4, 125.0, 122.4, 121.6, 118.3, 107.8. HRMS (ESI+) Calculated for ($C_{17}H_{12}N_4OSNa$)

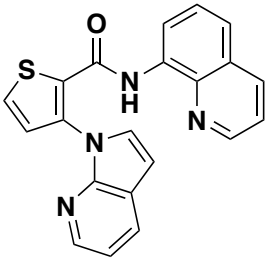
[M+Na]$^+$ 343.06240, Found 343.06370. FT-IR (neat, cm^{-1}) ν 1615, 1533, 1491, 1323,

3-(3-(Methoxycarbonyl)-1H-indol-1-yl)-*N*-(quinolin-8-yl) thiophenecarboxamide (5)



According to general procedure 3. In a 42 mL screw-cap vial equipped with a magnetic stir-bar *N*-(quinolin-8-yl)thiophenecarboxamide (0.254 g, 1.0 mmol), basic copper carbonate (0.033 g, 0.15 mmol) and 3-methoxycarbonylindole (0.263 g, 1.5 mmol) were dissolved in pyridine (2.0 mL). 1,1,3,3-Tetramethylguanidine (0.138 g, 1.2 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 9 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.088g, 0.3 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (30:1 → 20:1 toluene / ethyl acetate) provided (0.281 g, 66 % yield) of analytically pure compound 5 as a white solid. R_f = 0.44 (10:1 toluene / ethyl acetate). MP = 204.6 – 204.8 °C, 2:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.14 (s, 1H), 8.71 (d, *J* = 7.6 Hz, 1H), 8.36 (d, *J* = 8.0 Hz, 1H), 8.05 (s, 1H), 8.01 (dd, *J* = 4.1, 1.3 Hz, 1H), 7.97 – 7.92 (m, 1H), 7.69 (d, *J* = 5.2 Hz, 1H), 7.44 (t, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 8.1 Hz, 2H), 7.28 – 7.19 (m, 2H), 7.14 (d, *J* = 5.2 Hz, 1H), 3.90 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.2, 158.0, 147.7, 138.2, 138.1, 135.8, 135.2, 134.6, 134.5, 133.8, 130.3, 128.3, 127.6, 127.4, 127.1, 124.2, 123.0, 122.0, 121.8, 121.6, 116.6, 111.1, 111.1, 51.3. HRMS (ESI+) Calculated for ($C_{24}H_{17}N_3O_3SNa$) [M+Na]$^+$ 450.08830, Found 450.08940. FT-IR (neat, cm^{-1}) ν 2981, 1691, 1654, 1525, 1484, 1376, 1207, 1068.

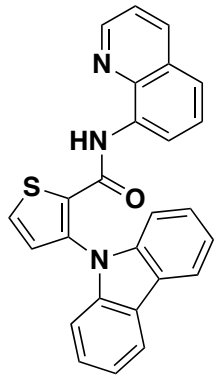
3-(7-Azaindol-1-yl)-*N*-(quinolin-8-yl)thiophenecarboxamide (6)



According to general procedure 3. In a 42 mL screw-cap vial equipped with a magnetic stir-bar *N*-(quinolin-8-yl)thiophenecarboxamide (0.254 g, 1.0 mmol), basic copper carbonate (0.033 g, 0.15 mmol) and 7-azaindole (0.177 g, 1.5 mmol) were dissolved in pyridine (2.0 mL). 1,1,3,3-Tetramethylguanidine (0.138 g, 1.2 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 9 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.088g, 0.3 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (12 : 6 : 1 hexanes / ethyl acetate / triethylamine)

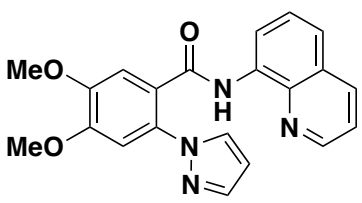
provided 0.319 g (86 % yield) of analytically pure compound 6 as a yellow solid. R_f = 0.30 (2:1 hexanes / ethyl acetate). MP = 163 – 164 °C, 1:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.20 (s, 1H), 8.75 (dd, *J* = 7.7, 1.0 Hz, 1H), 8.34 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.05 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.98 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.93 (dd, *J* = 4.2, 1.6 Hz, 1H), 7.65 (d, *J* = 5.2 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.27 – 7.23 (m, 1H), 7.21 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.15 (dd, *J* = 7.8, 4.7 Hz, 1H), 6.69 (d, *J* = 3.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.0, 149.1, 147.4, 144.3, 138.3, 135.9, 135.2, 134.2, 133.5, 129.4, 129.3, 129.0, 128.4, 127.7, 127.3, 121.7, 121.7, 121.4, 117.1, 116.6, 103.4. HRMS (ESI+) Calculated for ($C_{21}H_{14}N_4OSNa$) $[M+Na]^+$ 393.07810, Found 393.07890. FT-IR (neat, cm^{-1}) ν 3292, 2981, 1648, 1533, 1486, 1417, 1392, 1270.

3-(Carbazol-1-yl)-*N*-(quinolin-8-yl)thiophenecarboxamide (7)



According to general procedure 3. In a 42 mL screw-cap vial equipped with a magnetic stir-bar *N*-(quinolin-8-yl)thiophenecarboxamide (0.254 g, 1.0 mmol), basic copper carbonate (0.033 g, 0.15 mmol) and carbazole (0.251 g, 1.5 mmol) were dissolved in pyridine (2.0 mL). 1,1,3,3-Tetramethylguanidine (0.138 g, 1.2 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 16 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.088g, 0.3 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (6:1 hexanes / ethyl acetate) provided 0.268 g (64 % yield) of analytically pure compound 9 as a white solid. R_f = 0.27 (6:1 hexanes / ethyl acetate). MP = 201 – 202 °C, 2:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.68 (s, 1H), 8.71 (d, *J* = 7.7 Hz, 1H), 8.22 (d, *J* = 7.7 Hz, 2H), 7.83 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.75 (d, *J* = 5.2 Hz, 1H), 7.63 (dd, *J* = 4.2, 1.4 Hz, 1H), 7.43 – 7.34 (m, 3H), 7.34 – 7.27 (m, 5H), 7.10 (d, *J* = 5.2 Hz, 1H), 7.07 (dd, *J* = 8.2, 4.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.7, 147.3, 141.7, 138.2, 136.5, 135.5, 134.6, 134.1, 130.6, 128.3, 127.5, 127.0, 126.6, 125.0, 121.6, 121.3, 121.0, 120.2, 116.5, 110.6, 77.4. HRMS (ESI+) Calculated for ($C_{26}H_{17}N_3OSNa$) $[M+Na]^+$ 442.09850, Found 442.09960. FT-IR (neat, cm^{-1}) ν 1654, 1645, 1526, 1478, 1452, 1423, 1228.

2-(Pyrazol-1-yl)-4,5-dimethoxy-*N*-(quinolin-8-yl)benzamide (9)



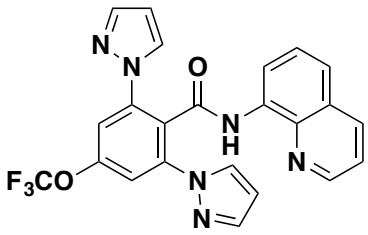
According to general procedure 3. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3,4-dimethoxy(quinolin-8-yl)benzamide (0.308 g, 1.0 mmol), basic copper carbonate (0.033 g, 0.15 mmol)

and pyrazole (0.102 g, 1.5 mmol) were dissolved in pyridine (2.0 mL). 1,1,3,3-Tetramethylguanidine (0.138 g, 1.2 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 16 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.088g, 0.3 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (16:4:1 hexanes / ethyl acetate / triethylamine) provided 0.250 g (67 % yield) of analytically pure compound 9 as an off-white solid. R_f = 0.51 (1:2 hexanes / ethyl acetate). MP = 201 – 202 °C, 2:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.81 – 8.76 (m, 1H), 8.65 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.08 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.68 (d, *J* = 2.3 Hz, 1H), 7.64 (d, *J* = 1.6 Hz, 1H), 7.51 (t, *J* = 7.9 Hz, 1H), 7.47 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.39 (s, 1H), 7.37 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.07 (s, 1H), 6.20 (t, *J* = 2.1 Hz, 1H), 3.98 (s, 3H), 3.96 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.0, 151.2, 148.9, 148.0, 141.3, 138.4, 136.1, 134.6, 131.9, 131.4, 127.8, 127.3, 124.4, 121.9, 121.7, 116.6, 111.8, 109.4, 107.5, 56.5, 56.4. HRMS (ESI+) Calculated for ($C_{21}H_{18}N_4O_3Na$) $[M+Na]^+$ 397.12710, Found 397.12780. FT-IR (neat, cm^{-1}) v 3320, 2980, 1651, 1534, 1267, 1216,1029.

Gram-Scale Synthesis of (9)

According to general procedure 3. In a 250 mL round-bottom flask equipped with a magnetic stir-bar 3,4-dimethoxy(quinolin-8-yl)benzamide (4.620 g, 15.0 mmol), basic copper carbonate (0.498 g, 2.25 mmol) and pyrazole (1.530. g, 22.5 mmol) were dissolved in pyridine (30 mL). 1,1,3,3-Tetramethylguanidine (2.07 g, 18 mmol) was added and the flask was affixed with an 18” vigreux condenser and the placed in an oil-bath pre-heated to 130 °C. After 30 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (1.32 g, 4.5 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with chloroform (200 mL), combined with SiO_2 (70 mL), and evaporated to give a free-flowing solid. Column chromatography (20:10:1 toluene / chloroform / acetonitrile) provided 3.940 g (70 % yield) of analytically pure compound 9 as a light yellow solid.

2,6-Di(pyrazol-1-yl)-4-(trifluoromethoxy)-*N*-(quinolin-8-yl)benzamide (11)



In a 42 mL screw-cap vial equipped with a magnetic stir-bar 4-(trifluoromethoxy)-*N*-(quinolin-8-yl)benzamide (0.308 g, 1.0 mmol), basic copper carbonate (0.066 g, 0.30 mmol) and pyrazole (0.204 g, 3.0 mmol) were dissolved in pyridine (2.0 mL). 1,1,3,3-Tetramethylguanidine (0.323 g, 2.8 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 11 hours the reaction was allowed to cool to room temperature, quenched

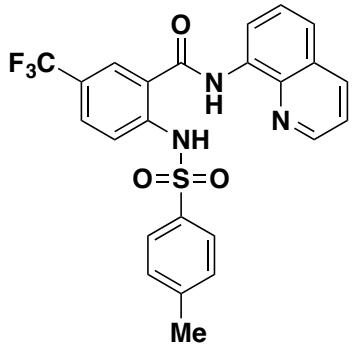
with solid EDTA (0.088g, 0.3 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (4:1 → 3:1 hexanes / ethyl acetate) provided (0.304 g, 65 % yield) of analytically pure compound 11 as a pale yellow solid. R_f = 0.46 (2:1 hexanes / ethyl acetate). MP = 198 – 199 °C, 3:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.95 (s, 1H), 8.71 – 8.60 (m, 2H), 8.09 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.97 (d, *J* = 2.4 Hz, 2H), 7.66 – 7.57 (m, 4H), 7.50 (d, *J* = 6.9 Hz, 2H), 7.38 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.37 – 6.23 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.55, 149.97, 148.43, 142.11, 140.32, 138.30, 136.12, 133.95, 130.82, 127.82, 127.16, 124.95, 122.59, 121.83, 120.39 (q, *J* = 259.9 Hz), 116.83, 116.59, 108.28. ^{19}F NMR (565 MHz, $CDCl_3$) δ -57.47. ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.6, 150.0, 148.5, 142.1, 140.3, 138.3, 136.2, 134.0, 130.8, 127.8, 127.2, 125.0, 122.6, 121.9, 120.4 (q, *J* = 259.9 Hz), 116.9, 116.6, 108.3. HRMS (ESI+) Calculated for ($C_{23}H_{15}F_3N_6O_2Na$) $[M+Na]^+$ 487.11010, Found 487.11110. FT-IR (neat, cm^{-1}) v 1660, 1519, 1468, 1403, 1322, 1259, 1188, 1169, 1048.

Amination with Acidic Primary N–H Bonds

General Procedure for Coupling of Acidic Primary N-H Bonds

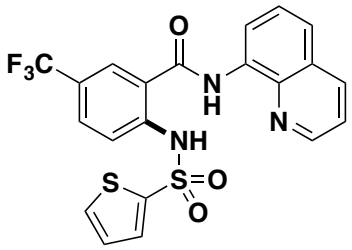
Reactions were run in a 100 mL heavy wall glass pressure vessel with a magnetic stir-bar and a PTFE bushing or in 60 mL screw cap vials. Stirbars were large enough to break the surface of the solvent and set to between 350 and 550 rpm. Benzamide (1.0 equiv), $(CuOH)_2CO_3$ (0.5 equiv), appropriate coupling partner (1.5 equiv), pyridine (2 mL, 0.5 M) and 1,1,3,3-tetramethylguanidine (1.2 equiv) were added sequentially to the vessel. Reactions were heated to the indicated temperature in a pre-heated oil bath (in case of pressure vessel) or in a parallel synthesis plate of appropriate size (in case of vial). Reactions were monitored at regular intervals by TLC analysis and stopped when complete consumption of the starting material was observed, or when the reaction failed to proceed to completion after 36 hours. Reactions were quenched by addition of solid EDTA (1.0 mmol) to the room temperature reaction mixture and stirring for 15 min at 80 °C. The reaction was then diluted with dichloromethane, treated with SiO_2 (15 mL per mmol of starting amide), and evaporated to dryness on a rotary evaporator. Subsequent column chromatography in the appropriate solvent resulted in the pure compound.

2-(*p*-Toluenesulfonamido)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T5-1)



According to general procedure 4. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), basic copper carbonate (0.111 g, 1.0 mmol) and *p*-toluenesulfonamide (0.257 g, 1.5 mmol) were dissolved in pyridine (2.0 mL, 0.5 M). 1,1,3,3-Tetramethylguanidine (0.138 g, 1.2 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 5 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (10:1 hexanes / ethyl acetate) provided 0.399 g (82 % yield) of analytically pure compound T5-1 as a white solid. R_f = 0.19 (6:1 hexanes / ethyl acetate). MP = 184 – 185 °C, 1:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.93 (s, 1H), 10.57 (s, 1H), 8.85 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.77 (dd, *J* = 6.6, 2.3 Hz, 1H), 8.23 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.99 (s, 1H), 7.87 (d, *J* = 8.7 Hz, 1H), 7.77 – 7.68 (m, 2H), 7.67 – 7.59 (m, 2H), 7.52 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.09 (d, *J* = 8.2 Hz, 2H), 2.09 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.5, 148.8, 144.2, 142.3, 138.6, 136.7, 136.2, 133.5, 129.9, 129.7 (q, J_{C-F} = 3.8 Hz), 128.0, 127.4, 127.3, 125.6 (q, J_{C-F} = 33.3 Hz), 124.4 (q, J_{C-F} = 4.2 Hz), 123.6 (q, J_{C-F} = 272.2 Hz), 123.0, 122.2, 122.2, 121.4, 117.2, 21.4. ^{19}F NMR (565 MHz, $CDCl_3$) δ -62.10. HRMS (ESI+) Calculated for ($C_{24}H_{18}F_3N_3O_3SNa$) $[M+Na]^+$ 508.09130, Found 508.09270. FT-IR (neat, cm^{-1}) ν 2980, 1647, 1544, 1320, 1292, 1156, 1114, 1089.

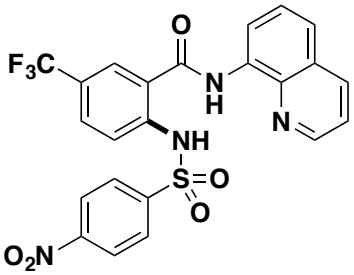
2-(2-Thiophenesulfonamido)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T5-2)



According to general procedure 4. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), basic copper carbonate (0.111 g, 1.0 mmol) and 2-thiophenesulfonamide (0.245 g, 1.5 mmol) were dissolved in pyridine (2.0 mL, 0.5 M). 1,1,3,3-Tetramethylguanidine (0.138 g, 1.2 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 6 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined

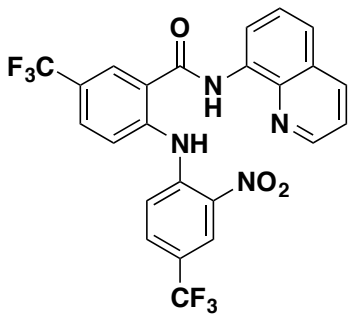
with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (10:1 hexanes / ethyl acetate) provided 0.370 g (77 % yield) of analytically pure compound T5-2 as a white solid. R_f = 0.14 (6:1 hexanes / ethyl acetate). MP = 177 – 178 °C, 1:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.28 (s, 1H), 10.70 (s, 1H), 8.86 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.77 (dd, *J* = 7.0, 1.6 Hz, 1H), 8.22 (dd, *J* = 8.2, 1.4 Hz, 1H), 8.05 (s, 1H), 7.97 (d, *J* = 8.7 Hz, 1H), 7.77 (d, *J* = 8.7 Hz, 1H), 7.68 – 7.57 (m, 3H), 7.52 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.43 (dd, *J* = 4.9, 1.1 Hz, 1H), 6.97 – 6.88 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.4, 148.9, 142.2, 139.9, 138.7, 136.7, 133.4, 133.2, 132.9, 129.8 (q, $J_{C–F}$ = 3.8 Hz), 128.2, 127.6, 127.4, 125.8 (q, $J_{C–F}$ = 34.2 Hz), 124.5 (q, $J_{C–F}$ = 4.1 Hz), 123.6 (q, $J_{C–F}$ = 279.6 Hz), 123.1, 122.2, 121.7, 121.0, 117.3. ^{19}F NMR (565 MHz, $CDCl_3$) δ -62.10. HRMS (ESI+) Calculated for ($C_{21}H_{14}F_3N_3O_3S_2Na$) $[M+Na]^+$ 500.03210, Found 500.03350. FT-IR (neat, cm^{-1}) ν 1656, 1542, 1327, 1293, 1154, 1114, 1091, 1015.

2-(4-Nitrobenzenesulfonamido)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T5-3)



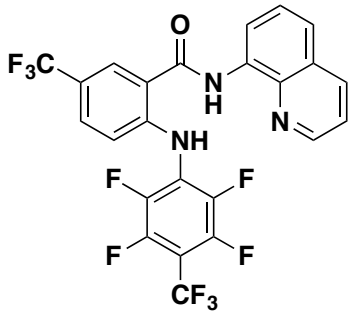
According to general procedure 4. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), basic copper carbonate (0.111 g, 1.0 mmol) and 4-nitrobenzenesulfonamide (0.303 g, 1.5 mmol) were dissolved in pyridine (2.0 mL, 0.5 M). 1,1,3,3-Tetramethylguanidine (0.138 g, 1.2 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 7 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (4:1 hexanes / ethyl acetate) provided 0.418 g (81 % yield) of analytically pure compound T5-3 as a pale yellow solid. R_f = 0.17 (6:1 hexanes / ethyl acetate). MP = 235 – 236 °C, ethanol. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.92 (s, 1H), 10.41 (s, 1H), 8.70 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.58 (d, *J* = 7.5 Hz, 1H), 8.18 – 8.12 (m, 1H), 7.97 (d, *J* = 8.9 Hz, 2H), 7.90 (s, 1H), 7.87 (d, *J* = 8.9 Hz, 2H), 7.79 (d, *J* = 8.6 Hz, 1H), 7.68 (d, *J* = 8.6 Hz, 1H), 7.57 (d, *J* = 8.3 Hz, 1H), 7.51 (t, *J* = 7.9 Hz, 1H), 7.44 (dd, *J* = 8.2, 4.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.1, 150.0, 149.0, 144.6, 140.8, 138.4, 136.7, 133.0, 129.8 (q, $J_{C–F}$ = 3.3 Hz), 128.5, 128.0, 127.1, 127.0 (q, $J_{C–F}$ = 33.3 Hz), 124.5 (q, $J_{C–F}$ = 3.6 Hz), missing CF_3 quartet, 124.3, 123.8, 123.5, 122.8, 122.3, 117.3. ^{19}F NMR (565 MHz, $CDCl_3$) δ -62.25. HRMS (ESI+) Calculated for ($C_{23}H_{15}F_3N_4O_5SNa$) $[M+Na]^+$ 539.06070, Found 539.06120. FT-IR (neat, cm^{-1}) ν 1651, 1547, 1352, 1350, 1326, 1294, 1162, 1118, 1087.

2-(2-Nitro-4-(trifluoromethyl)phenylamino)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T5-4)



According to general procedure 4. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), basic copper carbonate (0.111 g, 1.0 mmol) and 2-nitro-4-(trifluoromethyl)aniline (0.309 g, 1.5 mmol) were dissolved in pyridine (2.0 mL, 0.5 M). 1,1,3,3-Tetramethylguanidine (0.138 g, 1.2 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 6 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (10:1 hexanes / ethyl acetate) provided 0.325 g (62 % yield) of analytically pure compound T5-4 as a bright yellow solid. R_f = 0.34 (6:1 hexanes / ethyl acetate). MP = 184 – 185 °C, 3:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.47 (s, 1H), 10.75 (s, 1H), 8.96 – 8.85 (m, 1H), 8.79 (dd, J = 4.2, 1.5 Hz, 1H), 8.48 (s, 1H), 8.27 – 8.16 (m, 2H), 7.78 (dd, J = 8.6, 1.5 Hz, 1H), 7.70 (d, J = 8.6 Hz, 1H), 7.66 (dd, J = 9.0, 1.8 Hz, 1H), 7.64 – 7.57 (m, 3H), 7.50 (dd, J = 8.2, 4.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.7, 148.7, 142.4, 141.7, 138.7, 136.6, 135.9, 133.8, 131.5 (q, $J_{C–F}$ = 2.3 Hz), 129.1 (q, $J_{C–F}$ = 2.8 Hz), 128.1, 127.5, 126.9, 126.3 (q, $J_{C–F}$ = 2.9 Hz), 126.2 (q, $J_{C–F}$ = 33.5 Hz), 124.8 (q, $J_{C–F}$ = 3.9 Hz), 124.6 (missing q, one peak found) 123.2 (q, $J_{C–F}$ = 272.2 Hz) 122.8, 122.3 (q, $J_{C–F}$ = 34.6 Hz), 122.1, 121.7, 118.4, 117.3. ^{19}F NMR (565 MHz, $CDCl_3$) δ -62.09, -62.21. HRMS (ESI+) Calculated for ($C_{24}H_{14}F_6N_4O_3Na$) $[M+Na]^+$ 543.08620, Found 543.08760. FT-IR (neat, cm^{-1}) v 1526, 1424, 1327, 1282, 1150, 1116, 1089.

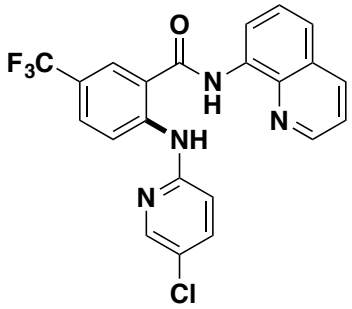
2-(2,3,5,6-Tetrafluoro-4-(trifluoromethyl)phenylamino)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T5-5)



According to general procedure 4. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), basic copper carbonate (0.111 g, 1.0 mmol) and 2,3,5,6-tetrafluoro-4-(trifluoromethyl)aniline (0.350 g, 1.5 mmol) were dissolved in pyridine (2.0 mL, 0.5 M). 1,1,3,3-Tetramethylguanidine (0.138 g, 1.2 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 8 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the

reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (10:1 hexanes / ethyl acetate) provided 0.340 g (62 % yield) of analytically pure compound T5-5 as a pale yellow solid. R_f = 0.48 (6:1 hexanes / ethyl acetate). MP = 185 – 186 °C, 6:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.83 (s, 1H), 10.21 (s, 1H), 8.89 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.82 (dd, *J* = 5.8, 3.0 Hz, 1H), 8.23 (dd, *J* = 8.2, 1.4 Hz, 1H), 8.13 (s, 1H), 7.69 (d, *J* = 8.6 Hz, 1H), 7.65 – 7.58 (m, 2H), 7.53 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.97 – 6.88 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.4, 148.9, 145.0 (m, A-B, J_{C-F} = 258.3 Hz), 145.4, 141.0 (m, A-B, J_{C-F} = 235.4 Hz), 138.8, 136.6, 133.8, 129.5 (q, J_{C-F} = 3.8 Hz), 128.2, 127.4, 125.1 (q, J_{C-F} = 2.9 Hz), 124.2 – 123.8 (m), 124.0 (q, J_{C-F} = 271.0 Hz), 122.9 (q, J_{C-F} = 33.4, 32.0 Hz), 122.9, 122.2, Missing CF_3 quartet, peak found at 120.3, 119.8, 117.1, 116.6. One ^{13}C peak not found. ^{19}F NMR (565 MHz, $CDCl_3$) δ -55.46 (t, J_{F-F} = 21.3 Hz, 3F), -61.70 (s, 3F), -140.65 (qt, J_{F-F} = 21.3, 10.7 Hz, 2F), -144.90 (dt, J_{F-F} = 19.3, 7.2 Hz, 2F). HRMS (ESI+) Calculated for ($C_{24}H_{11}F_{10}N_3ONa$) $[M+Na]^+$ 570.06350, Found 570.06450. FT-IR (neat, cm^{-1}) ν 1652, 1530, 1486, 1342, 1307, 1187, 1139, 1104, 1084, 985.

2-(2-(5-Chloropyridyl)amino)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (T5-6)

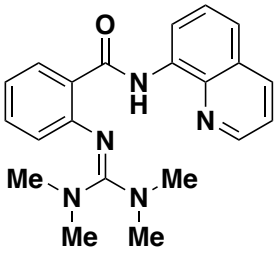


According to general procedure 4. In a 42 mL screw-cap vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.316 g, 1.0 mmol), basic copper carbonate (0.111 g, 1.0 mmol) and 2-amino-5-chloropyridine (0.193 g, 1.5 mmol) were dissolved in pyridine (2.0 mL, 0.5 M). 1,1,3,3-Tetramethylguanidine (0.138 g, 1.2 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 6 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.292 g, 1.0 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (10:1 hexanes / ethyl acetate) provided 0.215 g (48 % yield) of analytically pure compound T5-6 as a light yellow solid. R_f = 0.40 (6:1 hexanes / ethyl acetate). MP = 186 – 187 °C, 2:1 hexanes / ethyl acetate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.90 (s, 1H), 10.76 (s, 1H), 8.87 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.84 (d, *J* = 8.9 Hz, 1H), 8.80 (dd, *J* = 6.3, 2.5 Hz, 1H), 8.24 (d, *J* = 2.5 Hz, 1H), 8.20 (dd, *J* = 8.2, 1.4 Hz, 1H), 8.09 (s, 1H), 7.72 (d, *J* = 8.9 Hz, 1H), 7.64 – 7.57 (m, 2H), 7.53 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.0, 152.7, 148.8, 146.0, 145.7, 138.9, 137.6, 136.5, 134.0, 129.6 (q, J_{C-F} = 3.8 Hz), 127.3, 124.7 (q, J_{C-F} = 4.1 Hz), 124.2 (q, J_{C-F} = 271.1 Hz), 123.8, 122.6, 122.1, 121.6 (q, J_{C-F} = 33.3 Hz), 119.2, 118.7, 116.9, 114.2. ^{19}F NMR (565 MHz, $CDCl_3$)

δ -61.61. HRMS (ESI+) Calculated for ($C_{22}H_{14}ClF_3N_4O_2Na$) $[M+Na]^+$ 465.07000, Found 465.07120. FT-IR (neat, cm^{-1}) v 1657, 1530, 1308, 1088.

N-Arylation of 1,1,3,3-Tetramethylguanidine

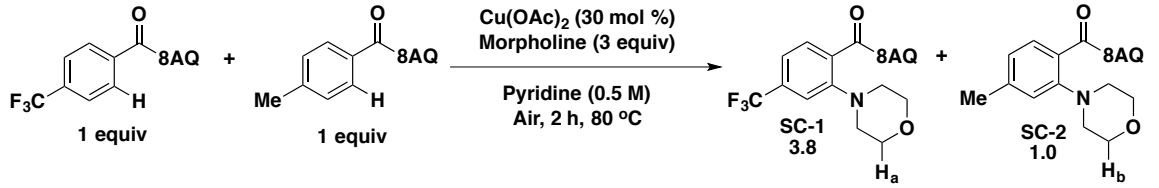
2-(Tetramethylguanido)-*N*-(quinolin-8-yl)benzamide (12)



In a 42 mL screw-cap vial equipped with a magnetic stir-bar *N*-(quinolin-8-yl)benzamide (0.248 g, 1.0 mmol), copper iodide (0.057 g, 0.3 mmol) and 1,1,3,3-tetramethylguanidine (0.346 g, 3.0 mmol) were dissolved in *N*-methylmorpholine (5.0 mL, 1.25 M). The vial was purged with O_2 and placed in a parallel synthesis well pre-heated to 110 °C. After 6 hours the reaction was allowed to cool to room temperature, quenched with solid EDTA (0.088 g, 0.3 mmol) and stirred at 80 °C for 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (6:1 → 4:1 hexanes / ethyl acetate) provided 0.225 g (62 % yield) of analytically pure compound 12 as a light brown oil. R_f = 0.34 (12:6:1 hexanes / ethyl acetate / triethylamine). ^{1}H NMR (600 MHz, $CDCl_3$) δ 13.49 (s, 1H), 9.18 (d, *J* = 7.7 Hz, 1H), 8.81 (d, *J* = 3.9 Hz, 1H), 8.38 (d, *J* = 7.8 Hz, 1H), 8.10 (d, *J* = 8.1 Hz, 1H), 7.55 (t, *J* = 7.9 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.38 (dd, *J* = 8.2, 4.1 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.47 (d, *J* = 7.1 Hz, 1H), 2.82 (s, 12H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.3, 160.8, 151.4, 147.7, 140.0, 137.2, 136.1, 131.8, 131.4, 128.4, 127.5, 124.2, 121.9, 121.2, 121.1, 119.9, 118.4, 39.8. HRMS (ESI+) Calculated for ($C_{21}H_{23}N_5ONa$) $[M+Na]^+$ 384.18070, Found 184.17950. FT-IR (neat, cm^{-1}) v 1651, 1556, 1507, 1469, 1420, 1386, 1320, 1128, 1023.

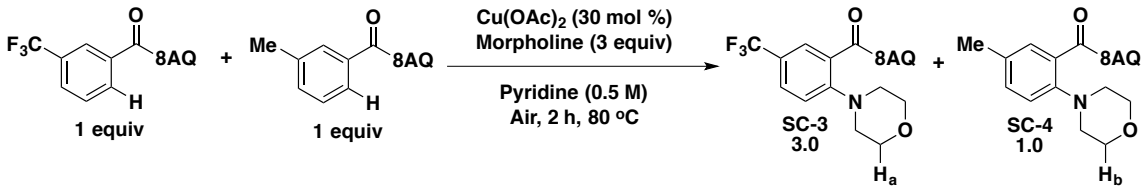
Aerobic C–H Amination: Probing Reactivity

Scheme S1: Reactivity of 4-(Trifluoromethyl)-*N*-(quinolin-8-yl)benzamide Vs. 4-Methyl-*N*-(quinolin-8-yl)benzamide Toward Morpholine



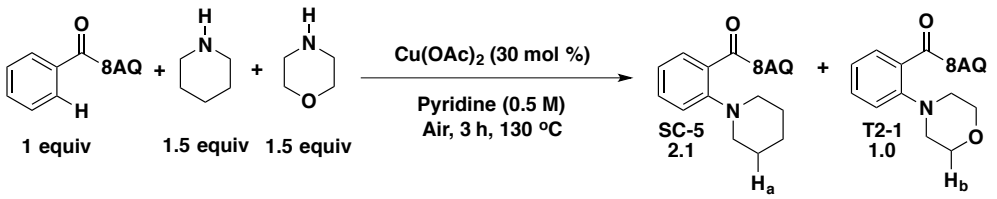
In a 3.5 mL screw cap pressure vial equipped with a magnetic stir-bar 4-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.0316 g, 0.1 mmol), 4-methyl-*N*-(quinolin-8-yl)benzamide (0.0262 g, 0.1 mmol) and copper acetate (0.0054 g, 0.03 mmol) were dissolved in pyridine (0.2 mL). To the mixture morpholine (0.0262 g, 0.3 mmol) was added. The vial was placed in a parallel synthesis well pre-heated to 80 °C. After 2.0 hours the reaction was quenched with solid EDTA (0.009 g, 0.03 mmol) and stirred for an additional 30 minutes at room temperature. Subsequently the reaction was diluted with dichloromethane (3 mL) and filtered through SiO_2 (3 mL). 1,3,5-Trimethoxybenzene (0.033 mL of a 0.01 M solution, 0.0033 mmol) was added and the solution was concentrated under vacuum. Yields were calculated by ^{1}H NMR analysis at 47 % conversion. Compounds SC-1 and SC-2 are known.[2]

Scheme S-2: Reactivity of 3-(Trifluoromethyl)-*N*-(quinolin-8-yl)benzamide Vs. 3-Methyl-*N*-(quinolin-8-yl)benzamide Toward Morpholine



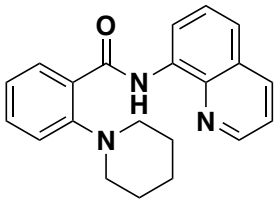
In a 3.5 mL screw cap pressure vial equipped with a magnetic stir-bar 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.0316 g, 0.1 mmol), 3-methyl-*N*-(quinolin-8-yl)benzamide (0.0262 g, 0.1 mmol) and copper acetate (0.0054 g, 0.03 mmol) were dissolved in pyridine (0.2 mL). To the mixture morpholine (0.0262 g, 0.3 mmol) was added. The vial was placed in a parallel synthesis well pre-heated to 80 °C. After 2.0 hours the reaction was quenched with solid EDTA (0.009 g, 0.03 mmol) and stirred for an additional 30 minutes at room temperature. Subsequently the reaction was diluted with dichloromethane (3 mL) and filtered through SiO_2 (3 mL). 1,3,5-Trimethoxybenzene (0.033 mL of a 0.01 M solution, 0.0033 mmol) was added and the solution was concentrated under vacuum. Yields were calculated by ^{1}H NMR analysis at 31 % conversion. SC-3 / SC-4 = 3.0. Compounds SC-3[6] and SC-4[2] are known.

Scheme S3: Reactivity of Piperidine Vs. Morpholine Toward *N*-(Quinolin-8-yl)benzamide



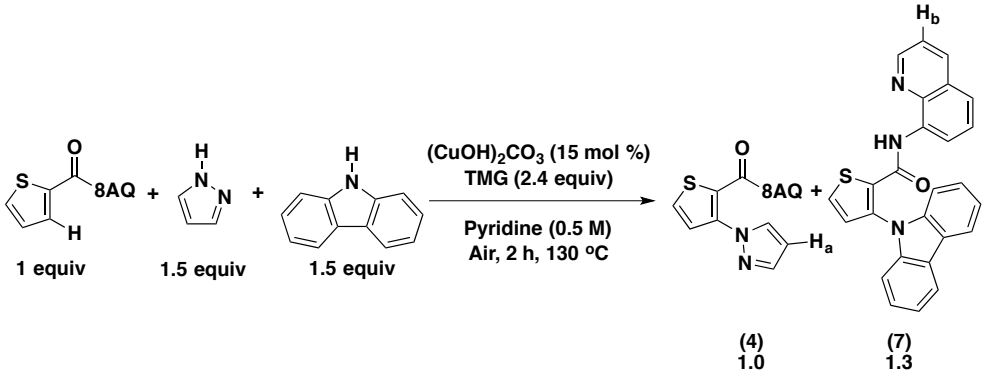
In a 3.5 mL screw cap pressure vial equipped with a magnetic stir-bar *N*-(quinolin-8-yl)benzamide (0.0248 g, 0.1 mmol) and copper acetate (0.0054 g, 0.03 mmol) were dissolved in pyridine (0.2 mL). To the mixture piperidine (0.0255 g, 0.3 mmol) and morpholine (0.0262 g, 0.3 mmol) were added. The vial was placed in a parallel synthesis well pre-heated to 80 °C. After 2.0 hours the reaction was quenched with solid EDTA (0.009 g, 0.03 mmol) and stirred for an additional 30 minutes at room temperature. Subsequently the reaction was diluted with dichloromethane (3 mL) and filtered through SiO_2 (3 mL). 1,3,5-Trimethoxybenzene (0.033 mL of a 0.01 M solution, 0.0033 mmol) was added and the solution was concentrated under vacuum. Ratios were calculated by ^{1}H NMR analysis at 62 % conversion.

2-(Piperidino)-*N*-(quinolin-8-yl)benzamide (SC-5)



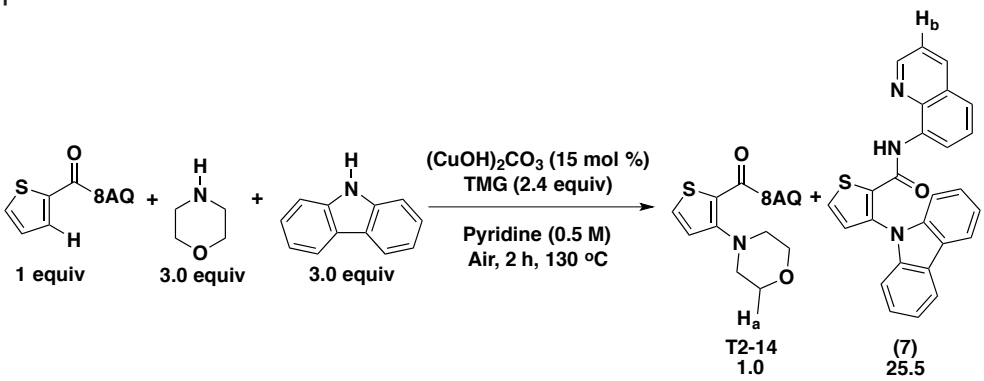
According to General Procedure 1. In a 100 mL heavy wall pressure vessel equipped with a magnetic stir-bar *N*-(quinolin-8-yl)benzamide (0.248 g, 1.0 mmol) and copper acetate (0.054 g, 0.3 mmol) were dissolved in pyridine (2 mL). To the mixture piperidine (0.255 g, 3.0 mmol) was added. The vessel was placed in a pre-heated oil bath set to 110 °C. After 4.5 hours the reaction reached completion**.** After cooling to room temperature, solid EDTA (0.088 g, 0.3 mmol) was added and the mixture was stirred for an additional 30 minutes. Subsequently the reaction was diluted with dichloromethane (50 mL), combined with SiO_2 (15 mL), and evaporated to give a free-flowing solid. Column chromatography (30:1 toluene / ethyl acetate) provided 0.288 g (87 % yield) of analytically pure compound SC-5. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 12.85 (s, 1H), 9.14 (d, *J* = 7.7 Hz, 1H), 8.89 – 8.80 (m, 1H), 8.26 – 8.11 (m, 2H), 7.58 (t, *J* = 7.9 Hz, 1H), 7.52 (d, *J* = 8.1 Hz, 1H), 7.45 (q, *J* = 5.8, 4.0 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 3.07 (s, 4H), 1.89 – 1.76 (m, 4H), 1.53 – 1.43 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 151.2, 148.2, 138.9, 136.5, 135.7, 132.4, 132.2, 129.0, 128.4, 127.7, 124.4, 121.8, 121.7, 119.3, 117.8, 66.3, 54.0.

Scheme S4: Reactivity of Pyrrole Vs. Pyrazole Toward *N*-(Quinolin-8-yl)thiophenecarboxamide



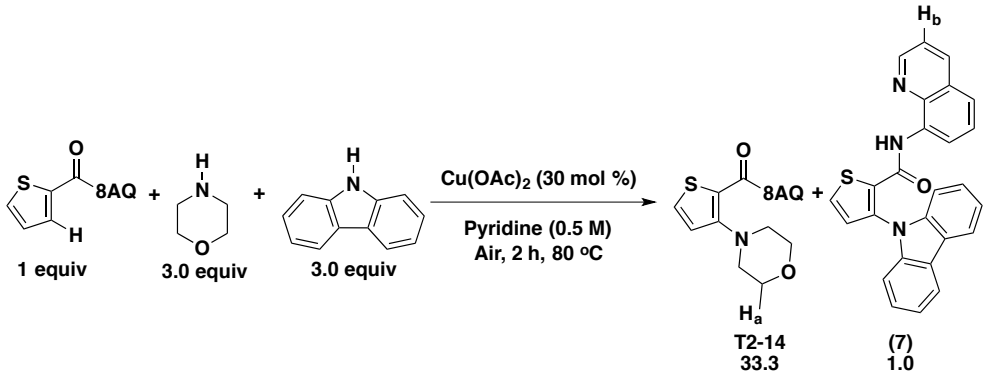
In a 3.5 mL screw cap pressure vial equipped with a magnetic stir-bar *N*-(quinolin-8-yl)thiophenecarboxamide (0.0254 g, 0.1 mmol), pyrazole (0.0102 g, 0.15 mmol), carbazole (0.0251 g, 0.15 mmol) and basic copper carbonate (0.0033 g, 0.03 mmol) were combined with pyridine (0.2 mL, 0.5 M). 1,1,3,3-Tetramethylguanidine (0.0276 g, 0.24 mmol) was added and the vial placed in a parallel synthesis well pre-heated to 130 °C. After 2.0 hours the reaction was quenched with solid EDTA (0.009 g, 0.03 mmol) and stirred for an additional 30 minutes at room temperature. Subsequently the reaction was diluted with dichloromethane (3 mL) and filtered through SiO_2 (3 mL). 1,3,5-Trimethoxybenzene (0.033 mL of a 0.01 M solution, 0.0033 mmol) was added and the solution was concentrated under vacuum. Yields were calculated by ^1H NMR analysis at 56 % conversion.

Scheme S5: Reactivity of Morpholine Vs. Pyrazole Toward *N*-(Quinolin-8-yl)thiophenecarboxamide under General Procedure 1.



In a 3.5 mL screw cap pressure vial equipped with a magnetic stir-bar *N*-(quinolin-8-yl)thiophenecarboxamide (0.0254 g, 0.1 mmol), carbazole (0.0501 g, 0.15 mmol) and basic copper carbonate (0.0033 g, 0.03 mmol) were combined with pyridine (0.2 mL, 0.5 M). 1,1,3,3-Tetramethylguanidine (0.0276 g, 0.24 mmol) and morpholine (0.0261 g, 0.3 mmol) were added and the vial was placed in a parallel synthesis well pre-heated to 130 °C. After 2.0 hours the reaction was quenched with solid EDTA (0.009 g, 0.03 mmol) and stirred for an additional 30 minutes at room temperature. Subsequently the reaction was diluted with dichloromethane (3 mL) and filtered through SiO_2 (3 mL). 1,3,5-Trimethoxybenzene (0.033 mL of a 0.01 M solution, 0.0033 mmol) was added and the solution was concentrated under vacuum. Yields were calculated by ^1H NMR analysis at 83 % conversion.

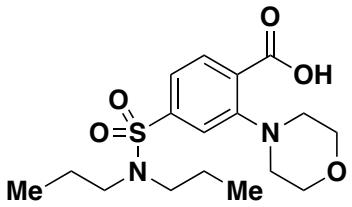
Scheme S6: Reactivity of Morpholine Vs. Pyrazole Toward *N*-(Quinolin-8-yl)thiophenecarboxamide Under General Procedure 3



In a 3.5 mL screw cap pressure vial equipped with a magnetic stir-bar *N*-(quinolin-8-yl)thiophenecarboxamide (0.0254 g, 0.1 mmol), carbazole (0.0501 g, 0.3 mmol) and copper acetate (0.0054 g, 0.03 mmol) were dissolved in pyridine (0.2 mL). To the mixture morpholine (0.0262 g, 0.3 mmol) was added. The vial was placed in a parallel synthesis well pre-heated to 80 °C. After 2.0 hours the reaction was quenched with solid EDTA (0.009 g, 0.03 mmol) and stirred for an additional 30 minutes at room temperature. Subsequently the reaction was diluted with dichloromethane (3 mL) and filtered through SiO_2 (3 mL). 1,3,5-Trimethoxybenzene (0.033 mL of a 0.01 M solution, 0.0033 mmol) was added and the solution was concentrated under vacuum. Yields were calculated by ^{1}H NMR analysis at 51 % conversion.

Cleavage of the Auxiliary

2-(Morpholino)-4-(-(*N,N*-dipropylsulfamoyl)benzoic acid (14)

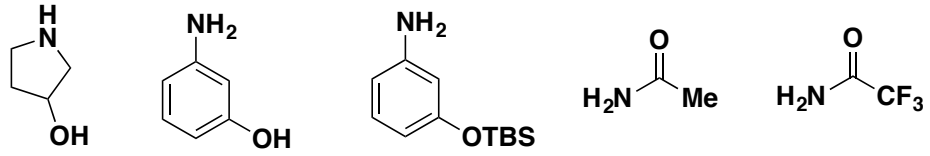


2-(Morpholino)-4-(-(*N,N*-dipropylsulfamoyl)-*N*-(quinolin-8-yl)benzamide (0.124 g, 0.25 mmol) and NaOH (0.150 g, 3.75 mmol) were combined with EtOH (1 mL, 0.25 M) in a 50 mL pressure tube. The tube was then heated at 130 °C for 8 hours and subsequently allowed to cool to room temperature. The reaction was diluted in 50 mL EtOAc and washed with HCl (4 × 20 mL of 0.5 N aqueous solution). The aqueous layers were combined and extracted with ethyl acetate (3 × 15 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated to give analytically pure 14 (0.089 g, 96 % yield) as a light brown oil. R_f = 0.21 (49:49:2 hexanes / ethyl acetate / acetic acid). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.1 Hz, 1H), 7.87 (s, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 3.95 (s, 4H), 3.25 – 2.83 (m, 8H), 1.52 (h, *J* = 7.3 Hz, 4H), 0.84 (t, *J* = 7.3 Hz,

6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.2, 150.9, 145.9, 133.6, 128.3, 125.7, 121.6, 66.8, 53.7, 49.9, 21.9, 11.2. HRMS (ESI+) Calculated for ($C_{17}H_{26}N_2O_5SNa$) $[M+Na]^+$ 393.14550, Found 393.14690. FT-IR (neat, cm^{-1}) ν 2958, 1694, 1346, 1156, 1128, 1000.

Substrates that Provided Low Conversions:

Figure S-1: List of Substrates that Resulted in Low Conversions.



References:

1: Grigorjeva, L.; Daugulis, O. *Org. Lett.* **2014**, *16*, 4688.

2: Yan, Q.; Chen, Z.; Yu, W.; Yin, H.; Liu, Z.; Zhang, Y. *Org. Lett.* **2015**, *17*, 2482.

3: Roane, J.; Daugulis, O. *Org. Lett.* **2013**, *15*, 5842.

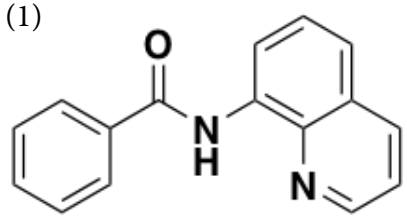
4: Moradei, O.; Paquin, I.; Leit, S.; Frechette, S.; Vaisburg, A.; Besterman, J. M.; Tessier, P.; Mallais, T. C. Inhibitors of Histone Deacetylace, International Patent Application, WO 2005/030704 A1, 2005.

5: Yang, Y.; Shi, L.; Zhou, Y.; Li, H-Q.; Zhu, Z-W.; Zhu, H-L. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 6653.

6: Tran, L. D.; Roane, J.; Daugulis, O. *Angew. Chem. Int. Ed.* **2013**, *52*, 6043.

7: Tran, L. D.; Popov, I.; Daugulis, O. *J. Am. Chem. Soc.* **2012**, *134*, 18237.

(1)


O
N
H
N

10.76
8.96 8.96 8.95 8.94 8.86 8.86 8.85 8.85 8.20 8.18 8.18 8.10 8.10 8.10 8.09 8.09 7.62 7.60 7.60 7.59 7.58 7.58 7.58 7.57 7.57 7.56 7.55 7.54 7.54 7.49 7.49 7.48 7.47 7.26
7.62 7.60 7.60 7.59 7.58 7.58 7.58 7.57 7.57 7.56 7.55 7.54 7.54 7.49 7.49 7.48 7.47
5.29
1.09
7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35
f1 (ppm)
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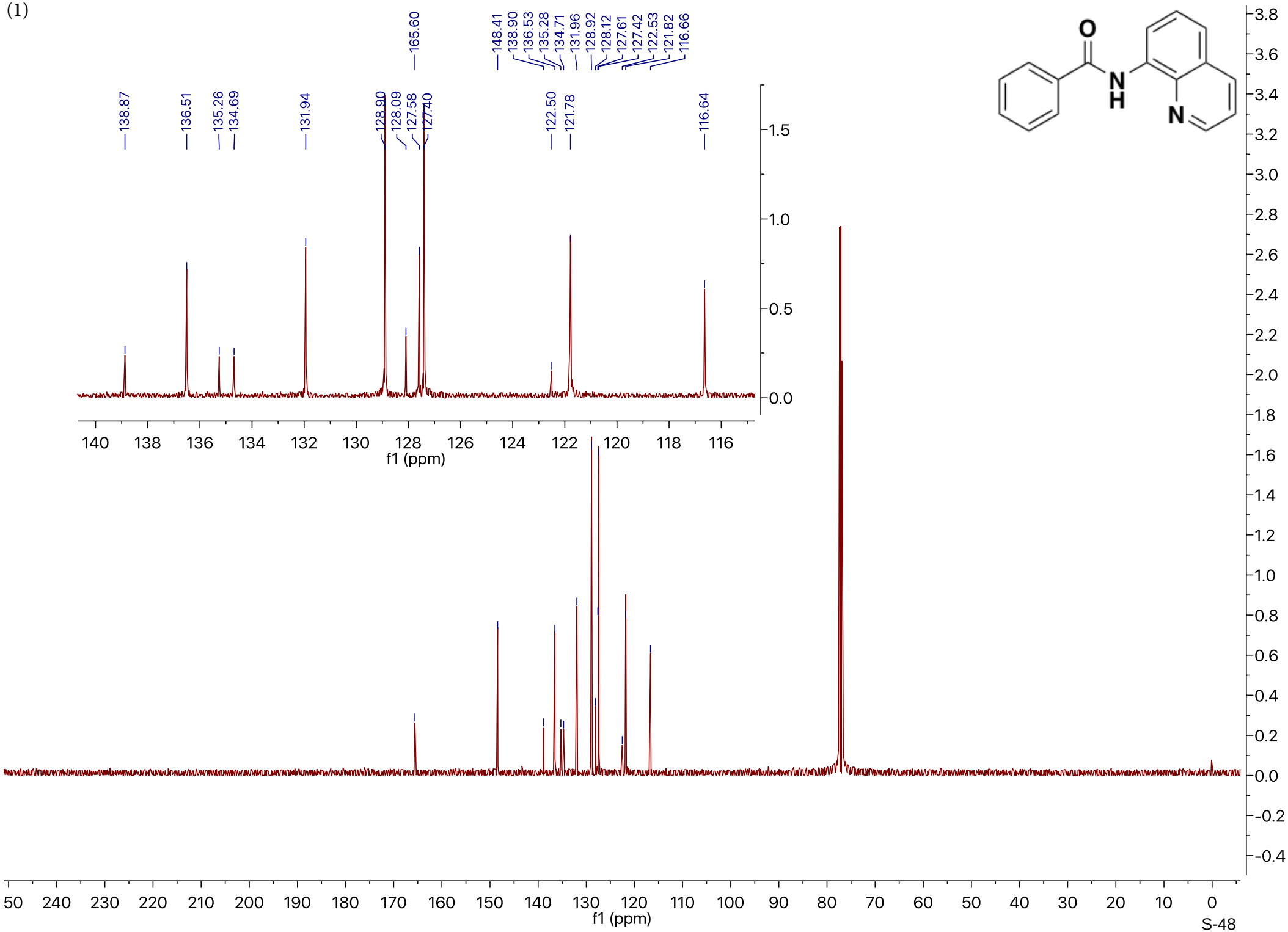
1.00 1.03
1.07 2.12
5.29 1.09
4 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

(1)


165.60
148.41
138.90
136.53
135.28
134.71
131.96
128.92
128.12
127.61
127.42
122.53
121.82
116.66
138.87
136.51
135.26
134.69
131.94
128.90
128.09
127.58
127.40
122.50
121.78
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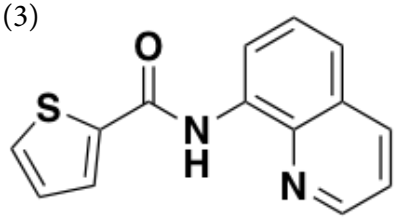
N
H
N
f1 (ppm)
f1 (ppm)

(3)


O
S
N
H
N

10.61
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7.60 7.60 7.60 7.59 7.59 7.57 7.55 7.55 7.54 7.54 7.50 7.49 7.49 7.48
1.96 1.03 1.05
7.62 7.60 7.58 7.56 7.54 7.52 7.50 7.48 7.46
f1 (ppm)
8.86 8.86 8.86 8.86 8.86 8.85 8.84
1.98
8.90 8.88 8.86 8.84 8.82 8.80
f1 (ppm)
1.02 1.98 1.00 1.01 1.96 1.03 1.05 0.99
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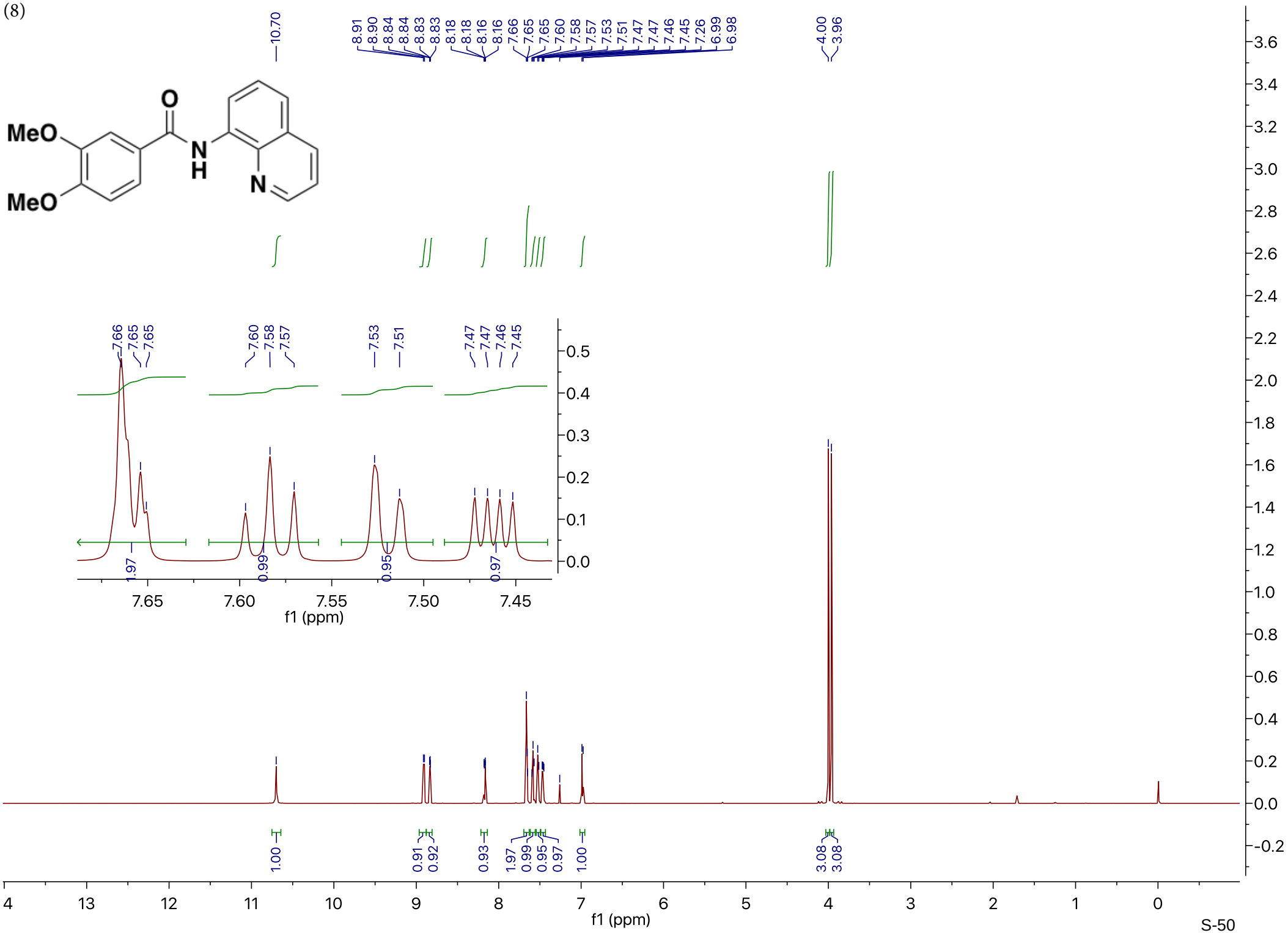
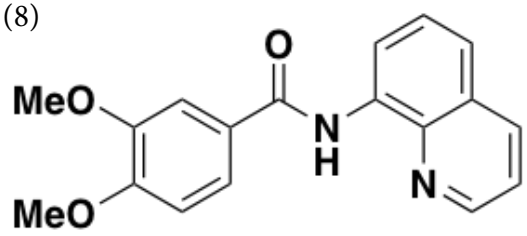
f1 (ppm)

(8)

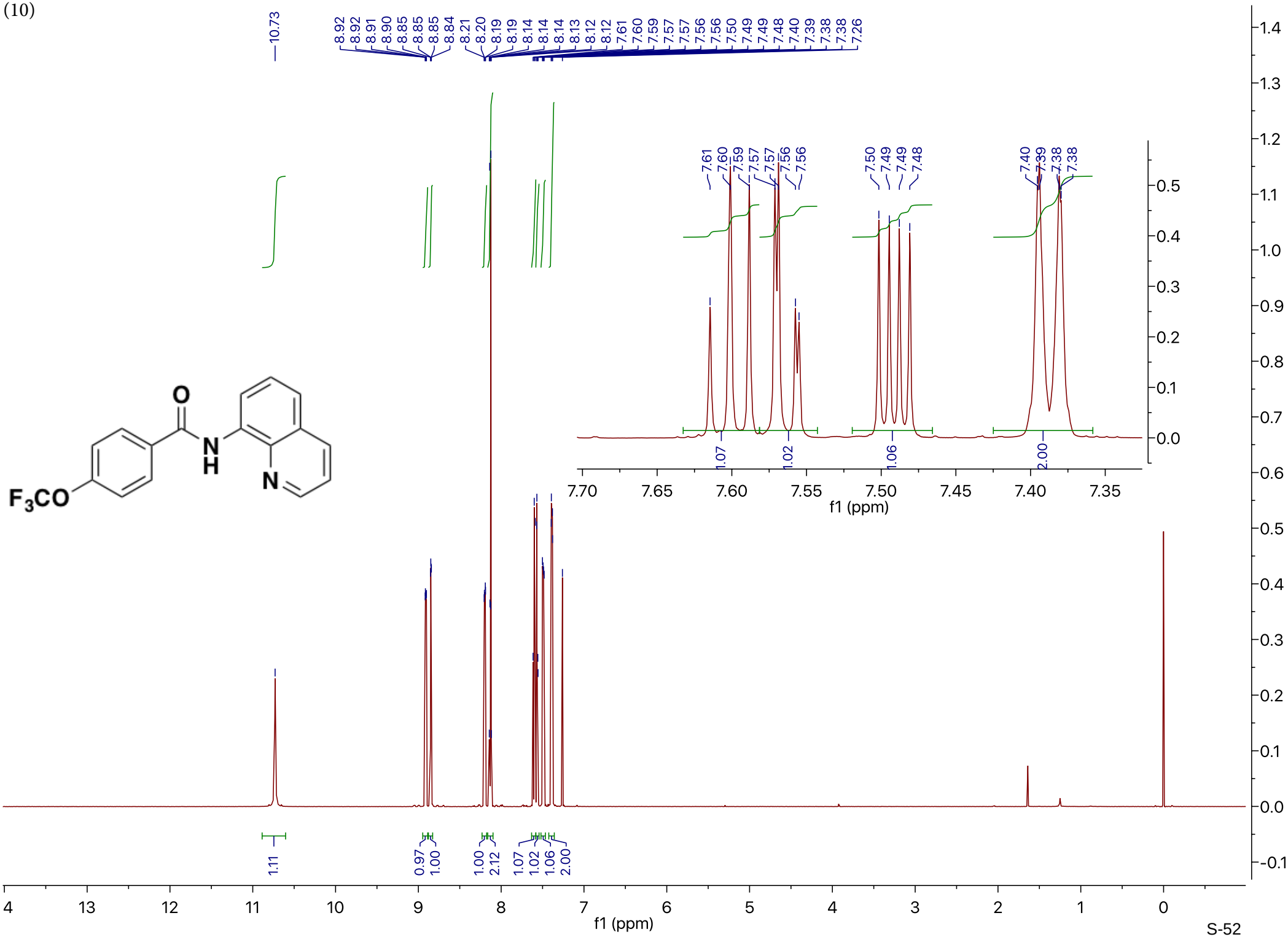

MeO
MeO
O
N
H
N
10.70
8.91
8.90
8.84
8.84
8.83
8.83
8.18
8.18
8.16
8.16
7.66
7.65
7.65
7.60
7.58
7.57
7.53
7.51
7.47
7.47
7.46
7.45
7.26
6.99
6.98
4.00
3.96
1.97
0.99
0.95
0.97
1.00
0.91
0.92
0.93
1.97
0.99
0.95
0.97
1.00
3.08
3.08
f1 (ppm)
f1 (ppm)

(8)

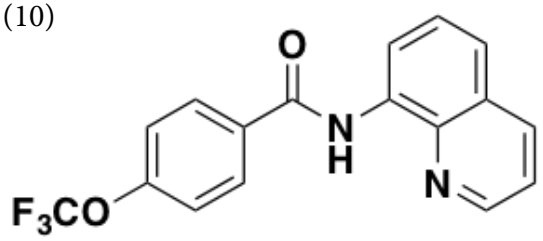

MeO
MeO
O
N
H
N

165.13
152.15
149.24
148.33
138.84
136.49
134.80
128.09
127.91
127.60
121.75
121.54
119.91
116.41
110.92
110.49
77.36
56.18
56.16
f1 (ppm)
f1 (ppm)

(10)

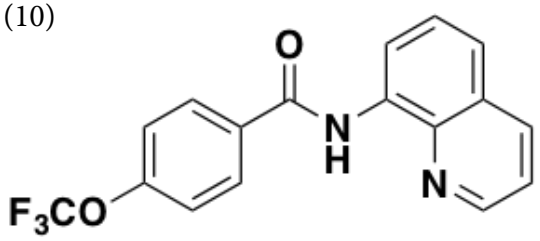

10.73
8.92 8.92 8.91 8.90 8.85 8.85 8.85 8.84 8.21 8.20 8.19 8.19 8.14 8.14 8.14 8.13 8.12 8.12 7.61 7.60 7.59 7.57 7.57 7.56 7.56 7.50 7.49 7.49 7.48 7.40 7.39 7.38 7.38 7.26
7.61 7.60 7.59 7.57 7.57 7.56 7.56 7.50 7.49 7.49 7.48 7.40 7.39 7.38 7.38
1.07 1.02 1.06 2.00
7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35
f1 (ppm)
O
N
H
N
F3CO
1.11 0.97 1.00 1.00 2.12 1.07 1.02 1.06 2.00
4 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

(10)


O
N
H
N
F3CO

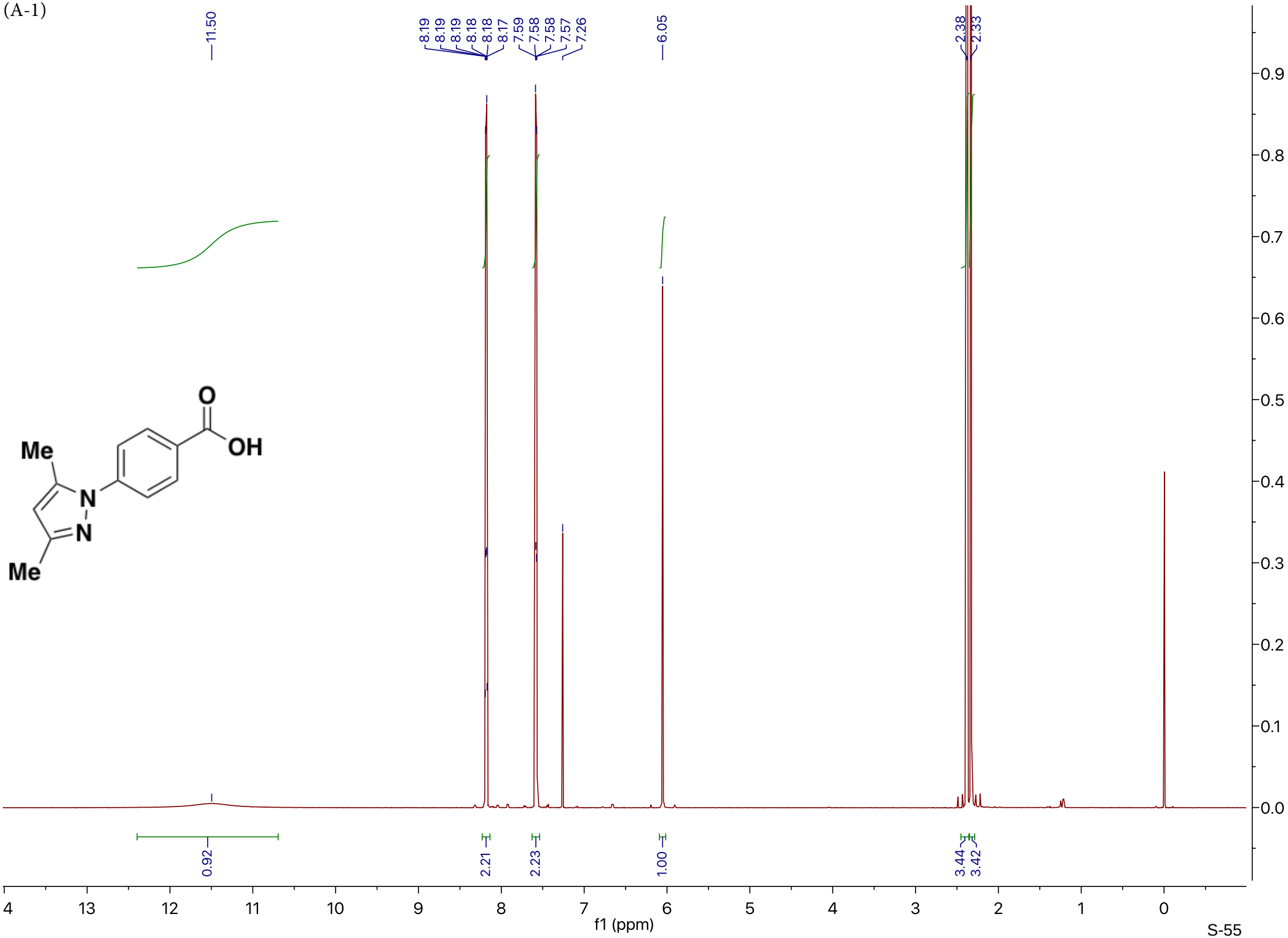
164.19
151.86
148.49
138.83
136.59
134.43
133.72
129.33
128.12
127.57
122.09
121.91
121.35
120.94
119.64
117.92
116.73
f1 (ppm)
f1 (ppm)

(10)

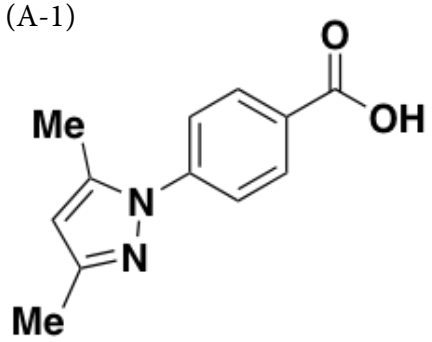

O
N
H
N
F3CO

-57.52
40
35
30
25
20
15
10
5
0
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(A-1)

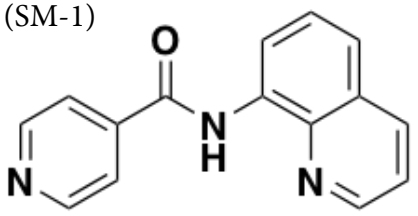

11.50
8.19
8.19
8.19
8.18
8.18
8.17
7.59
7.58
7.58
7.57
7.26
6.05
2.38
2.33
Me
N
N
Me
O
OH
0.92
2.21
2.23
1.00
3.44
3.42
f1 (ppm)

(A-1)


Me
N
N
Me
O
OH

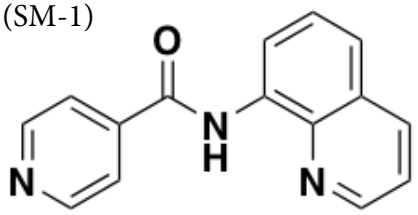
170.69
150.22
143.98
139.93
131.31
128.04
123.86
108.46
76.94
13.53
12.94
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
50 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

(SM-1)


O
N
H
N
N

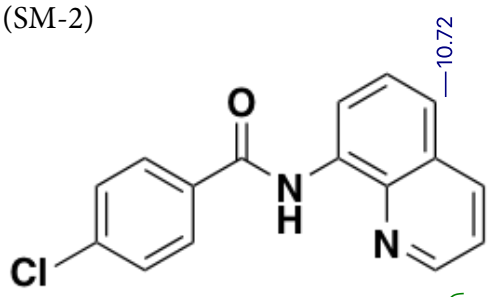
10.82
8.91 8.91 8.90 8.90 8.87 8.87 8.86 8.86 8.86 8.86 8.22 8.21 8.20 8.20 7.92 7.91 7.91 7.91 7.62 7.61 7.60 7.59 7.58 7.52 7.51 7.50 7.50 7.26
1.06
0.99
3.11
1.00
2.06
2.07
1.04
f1 (ppm)

(SM-1)


O
N
H
N
N

163.41
150.98
148.64
142.18
138.76
136.63
133.96
128.09
127.51
122.57
122.52
122.03
121.13
117.01
f1 (ppm)
f1 (ppm)

(SM-2)


O
N
H
N
Cl

10.72
8.92 8.92 8.91 8.90 8.86 8.86 8.85 8.85 8.21 8.21 8.20 8.19 8.04 8.04 8.03 8.03 8.02 8.02 7.62 7.60 7.59 7.57 7.57 7.56 7.56 7.54 7.53 7.53 7.52 7.52 7.52 7.51 7.50 7.49 7.49 7.26
7.62 7.60 7.59 7.57 7.57 7.56 7.56 7.54 7.53 7.53 7.52 7.52 7.52 7.51 7.50 7.49 7.49
7.63 7.61 7.59 7.57 7.55 7.53 7.51 7.49 7.47
f1 (ppm)
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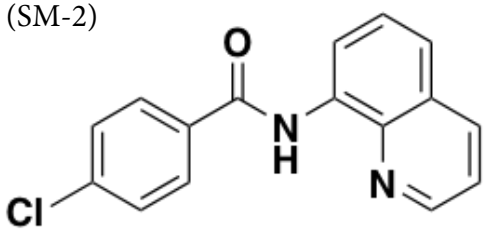
f1 (ppm)

(SM-2)


O
N
H
N
Cl

164.48
148.49
138.84
138.26
136.60
134.47
133.65
129.20
128.87
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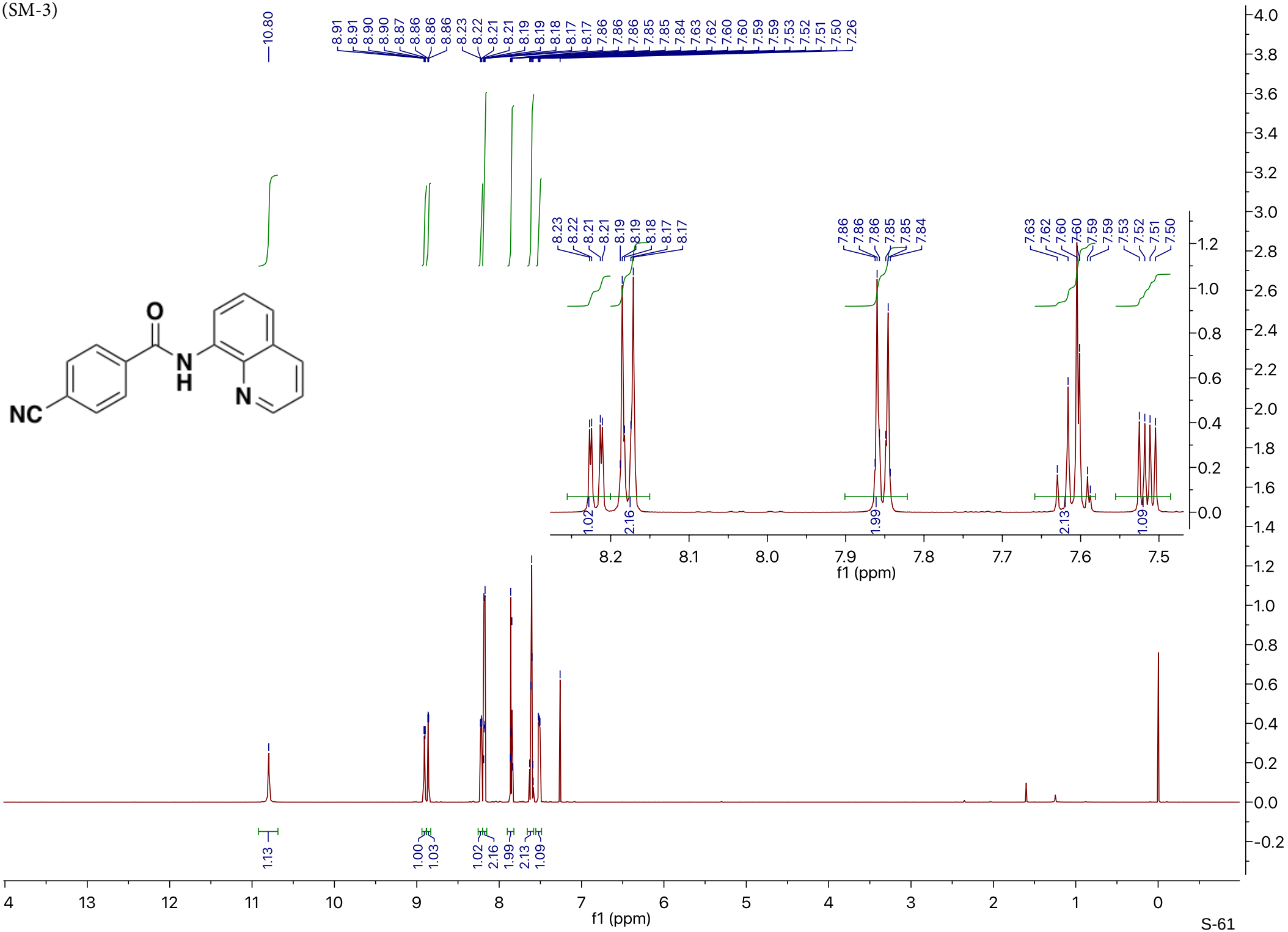
116.74
f1 (ppm)
f1 (ppm)

(SM-3)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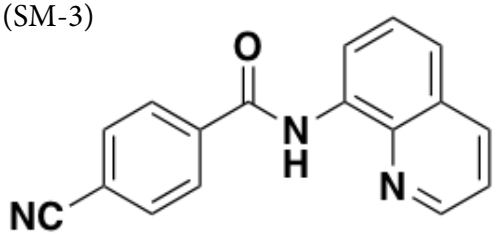
O
N
H
N
NC
1.13
1.00
1.03
1.02
2.16
1.99
2.13
1.09
f1 (ppm)
S-61

(SM-3)


O
N
H
N
NC

163.55
148.62
139.10
138.78
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134.07
132.80
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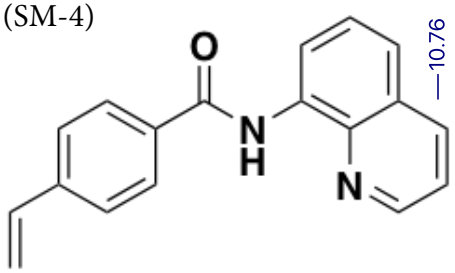
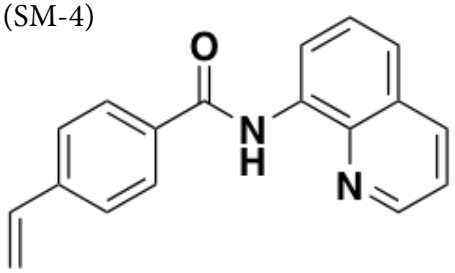
122.53
122.04
118.21
116.94
115.47
f1 (ppm)
f1 (ppm)

(SM-4)


O
N
H
N
10.76

8.95 8.95 8.94 8.94 8.86 8.86 8.86 8.85 8.20 8.20 8.19 8.19 8.07 8.06 8.06 8.05 8.05 7.62 7.60 7.59 7.59 7.58 7.58 7.58 7.57 7.56 7.56 7.54 7.54 7.50 7.49 7.48 7.48 7.26 7.26 7.26 6.83 6.81 6.80 6.78 5.91 5.91 5.88 5.88 5.88 5.41 5.41 5.39 5.39
8.20 8.20 8.19 8.19 8.07 8.06 8.06 8.05 8.05 7.62 7.60 7.59 7.59 7.58 7.58 7.58 7.57 7.56 7.56 7.54 7.54 7.50 7.49 7.48 7.48
1.05 2.21 3.33 1.10 1.15
8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4
f1 (ppm)
1.16 1.00 1.05 1.05 2.21 3.33 1.10 1.15 1.05 1.21 1.17
4 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)
S-63

(SM-4)

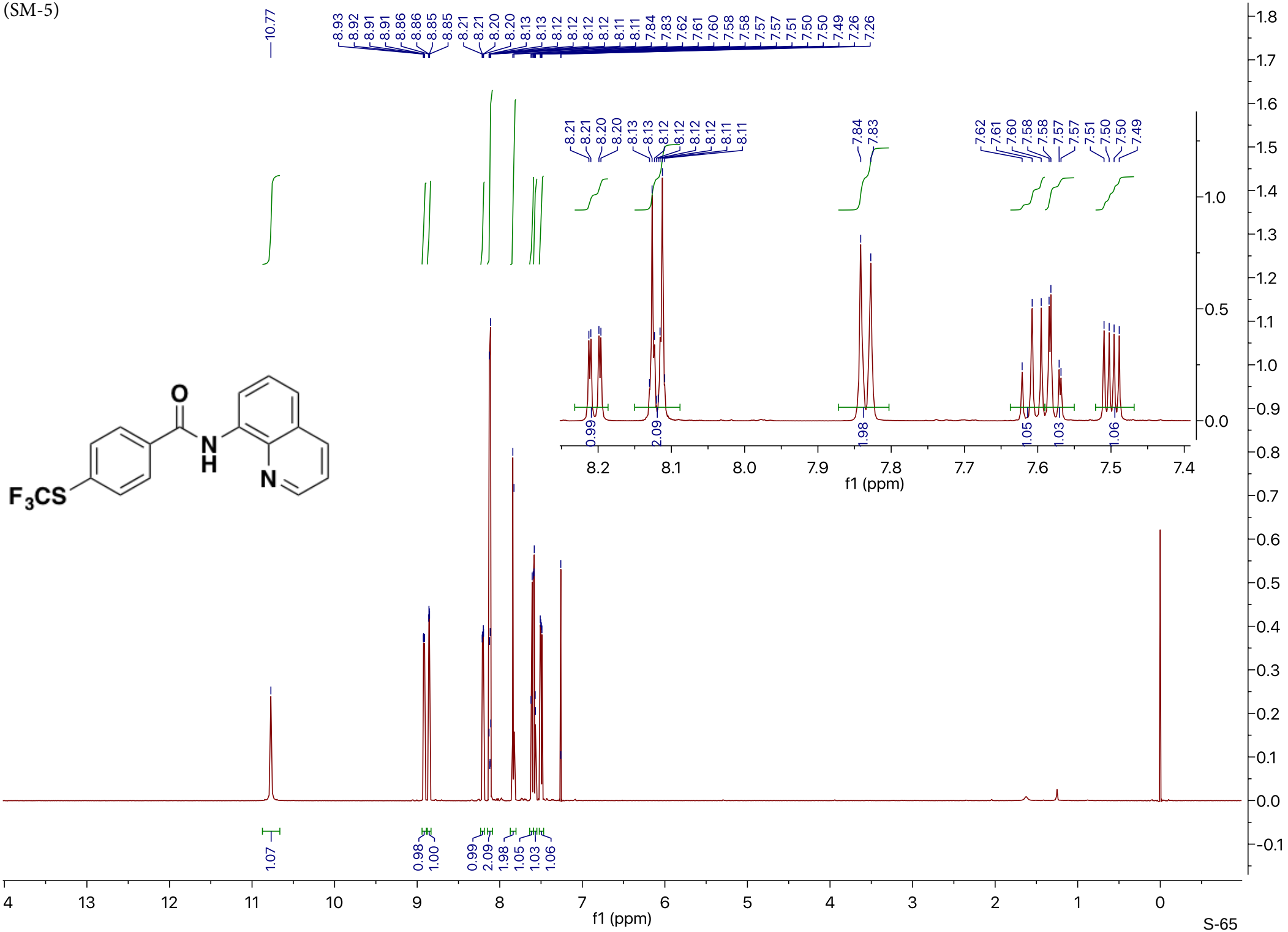


165.19
148.42
141.09
138.91
136.54
136.12
134.73
134.34
128.13
127.76
127.63
126.67
121.83
121.78
116.65
116.28

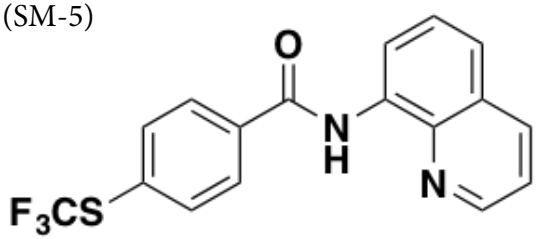
f1 (ppm)

f1 (ppm)

(SM-5)

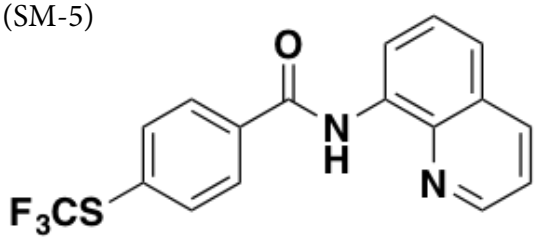

10.77
8.93 8.92 8.91 8.91 8.86 8.86 8.85 8.85 8.21 8.21 8.20 8.20 8.13 8.13 8.12 8.12 8.12 8.12 8.11 8.11 7.84 7.83 7.62 7.61 7.60 7.58 7.58 7.57 7.57 7.51 7.50 7.50 7.49 7.26 7.26
O
N
H
N
F3CS
0.99 2.09 1.98 1.05 1.03 1.06
f1 (ppm)
1.07 0.98 1.00 0.99 2.09 1.98 1.05 1.03 1.06
f1 (ppm)

(SM-5)


O
N
H
N
F3CS

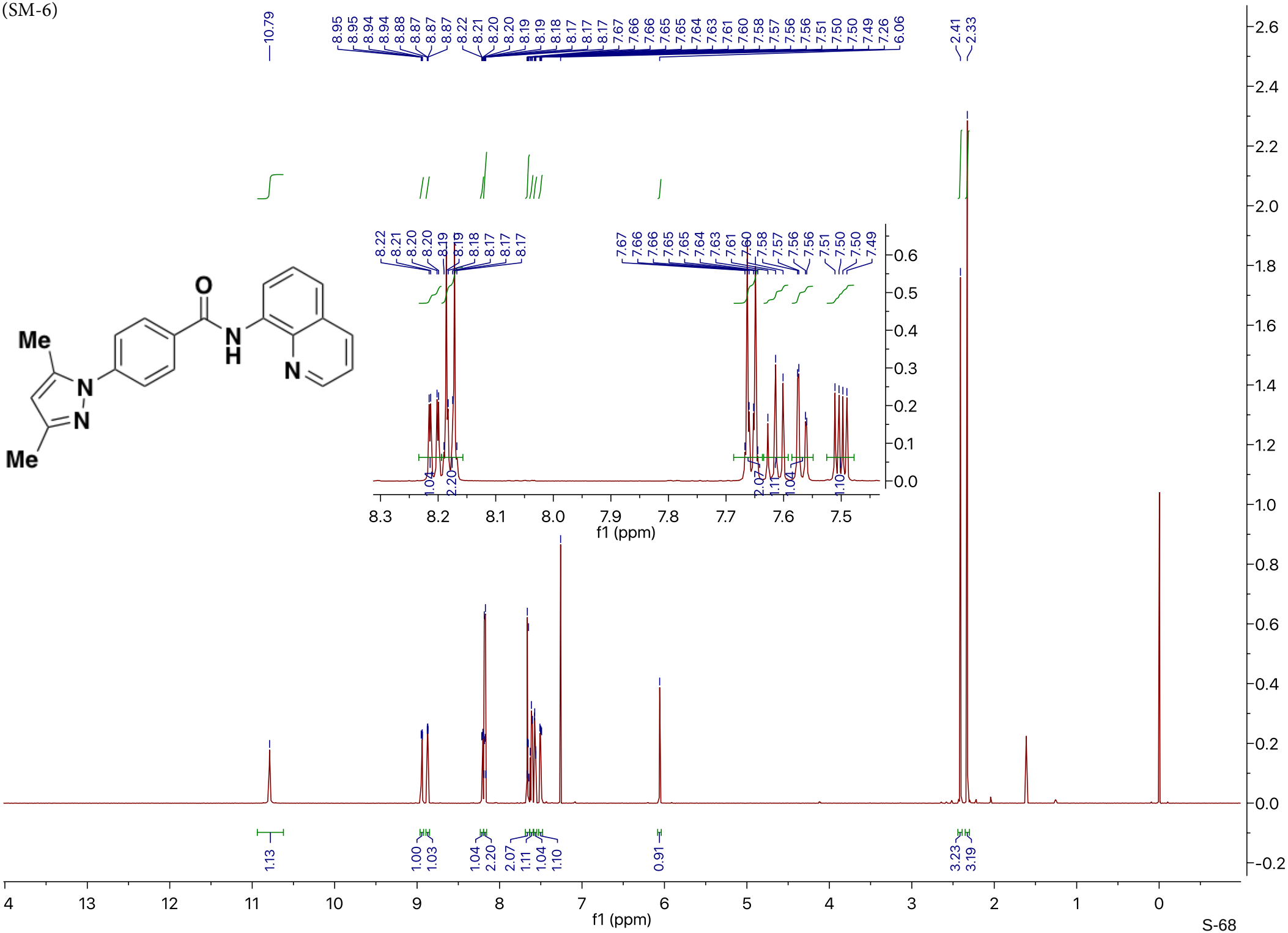
164.28
148.55
138.82
137.41
136.61
136.34
134.31
130.51
128.47
128.39
128.12
127.56
122.53
122.26
121.96
116.84
f1 (ppm)
S-66

(SM-5)

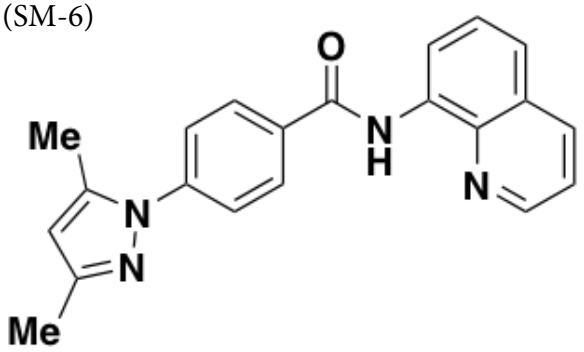

O
N
H
N
F3CS

-41.83
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
-2
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(SM-6)

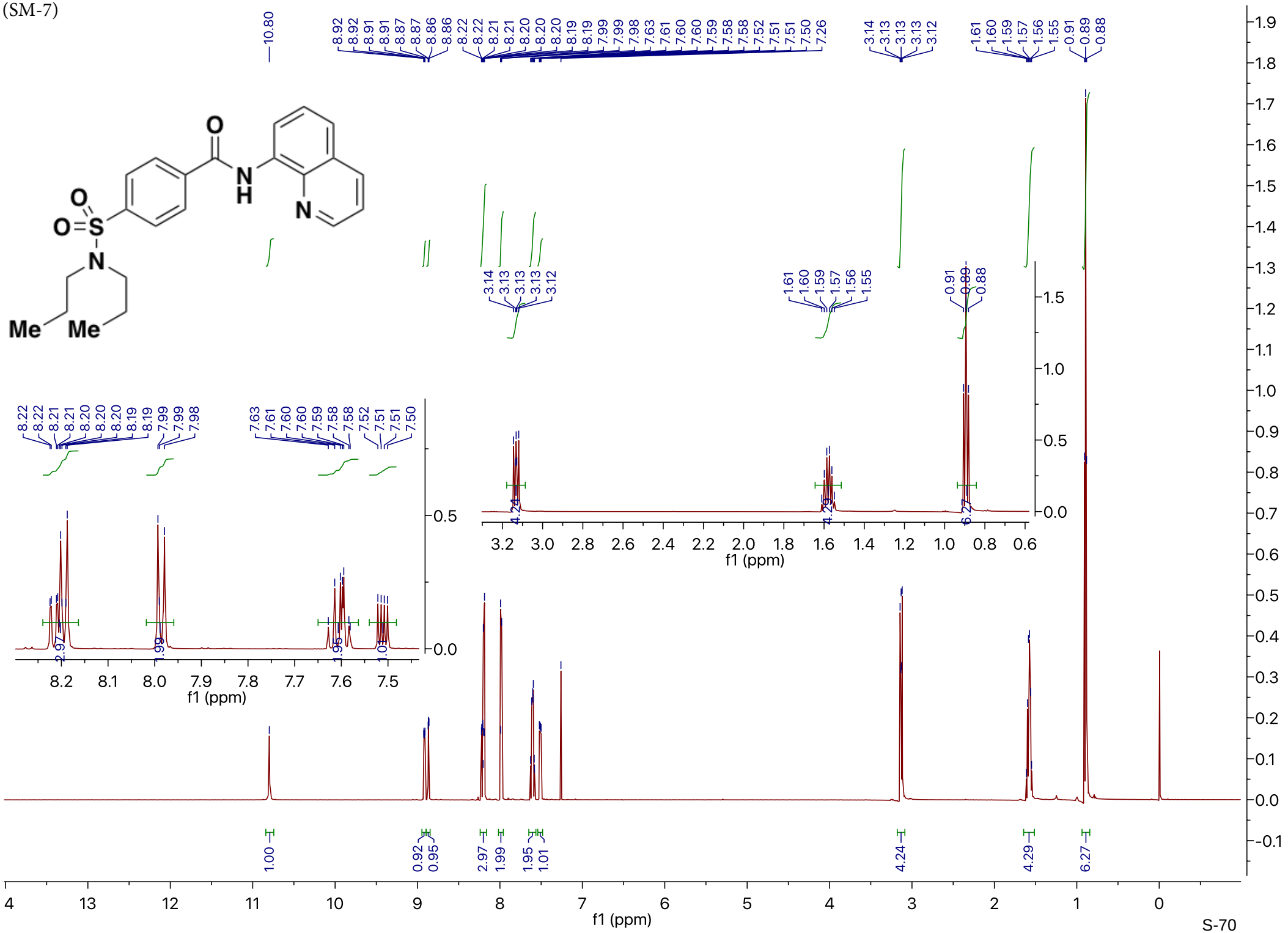

10.79
8.95 8.95 8.94 8.94 8.88 8.87 8.87 8.87 8.22 8.21 8.20 8.20 8.19 8.19 8.18 8.17 8.17 8.17 7.67 7.66 7.66 7.65 7.65 7.64 7.63 7.61 7.60 7.58 7.57 7.56 7.56 7.51 7.50 7.50 7.49 7.26 6.06
2.41 2.33
O
N
H
N
Me
N
N
Me
f1 (ppm)
1.13 1.00 1.03 1.04 2.20 2.07 1.11 1.04 1.10 0.91 3.23 3.19
f1 (ppm)

(SM-6)

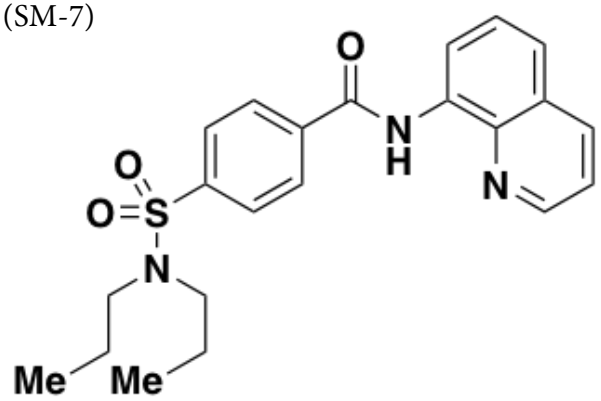

O
N
H
N
Me
N
N
Me

164.69
149.97
148.49
142.93
139.71
138.90
136.58
134.60
133.41
128.38
128.14
127.62
124.25
121.95
121.89
116.73
108.20
13.70
12.96
f1 (ppm)

(SM-7)

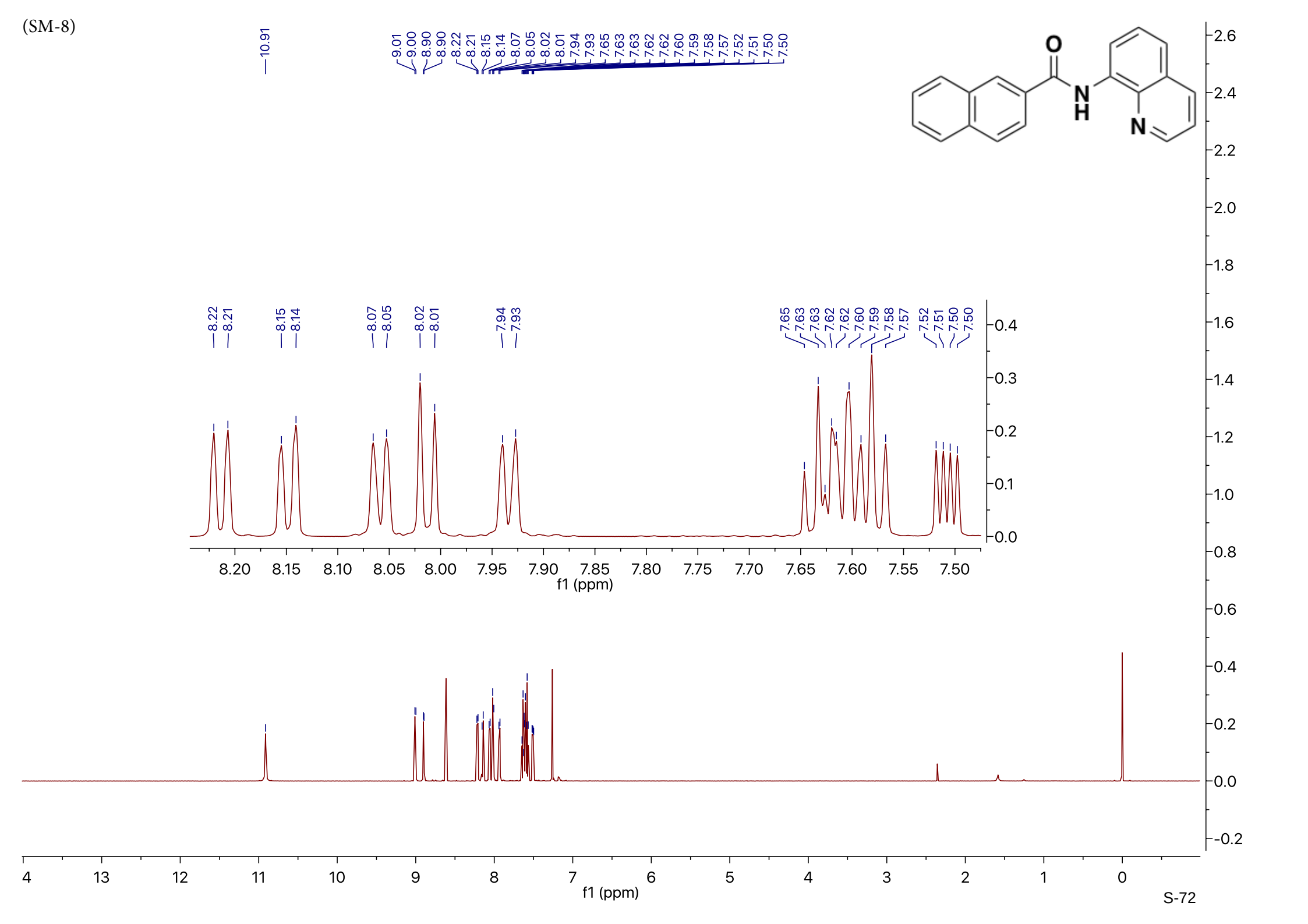

10.80
8.92 8.92 8.91 8.91 8.87 8.87 8.86 8.86 8.22 8.22 8.21 8.21 8.20 8.20 8.20 8.19 8.19 7.99 7.99 7.98 7.63 7.61 7.60 7.60 7.59 7.58 7.58 7.52 7.51 7.50 7.26
3.14 3.13 3.13 3.13 3.12
1.61 1.60 1.59 1.57 1.56 1.55
0.91 0.89 0.88
O
N
H
N
O
O=S
N
Me
Me
f1 (ppm)
1.00 0.92 0.95 2.97 1.99 1.95 1.01 4.24 4.29 6.27

(SM-7)

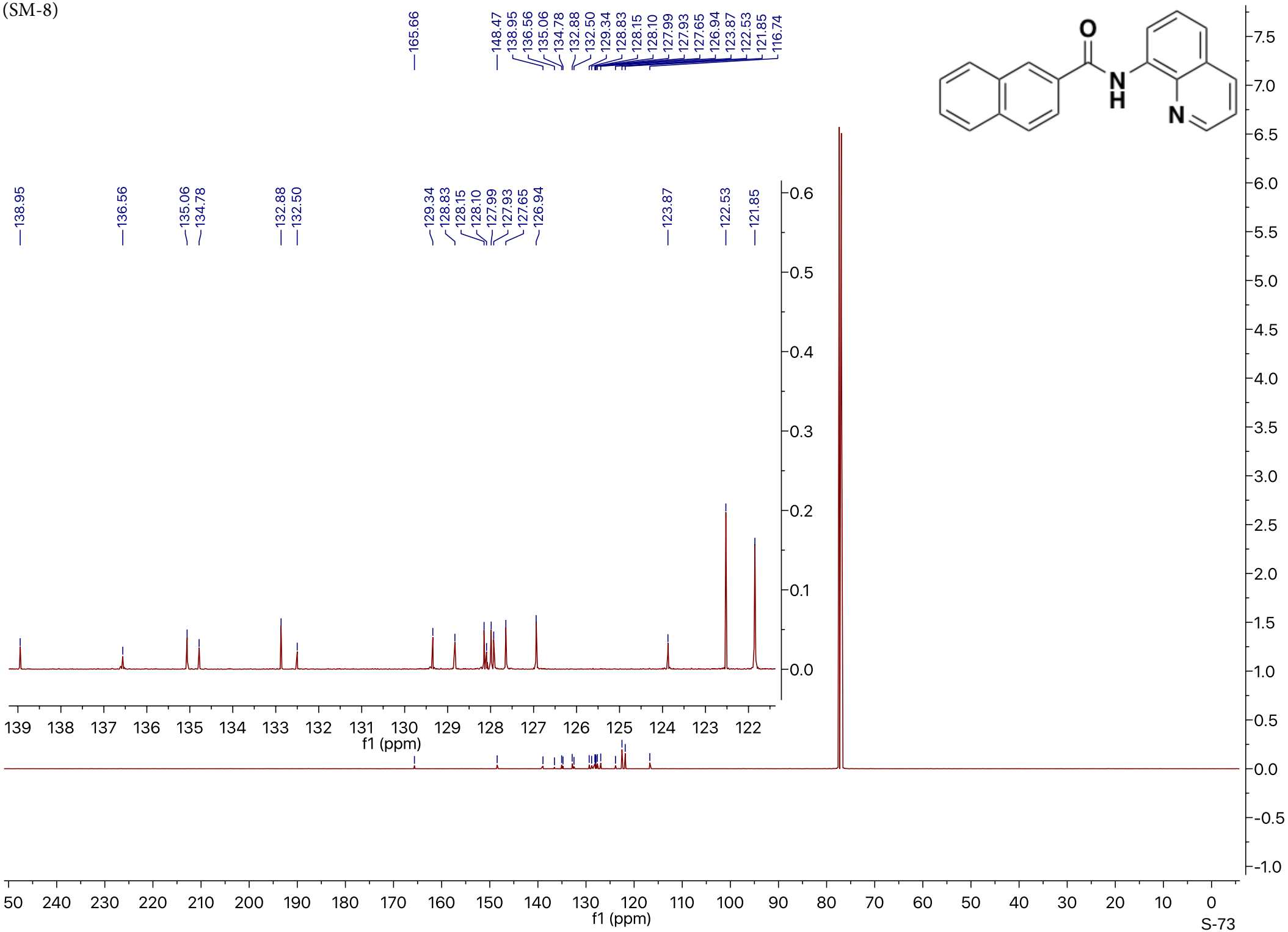

O
N
H
O
O
S
N
Me
Me
N

163.99
148.59
143.32
138.81
138.60
136.66
134.22
128.12
127.63
127.56
122.39
122.00
116.90
50.17
22.15
11.32
f1 (ppm)
S-71

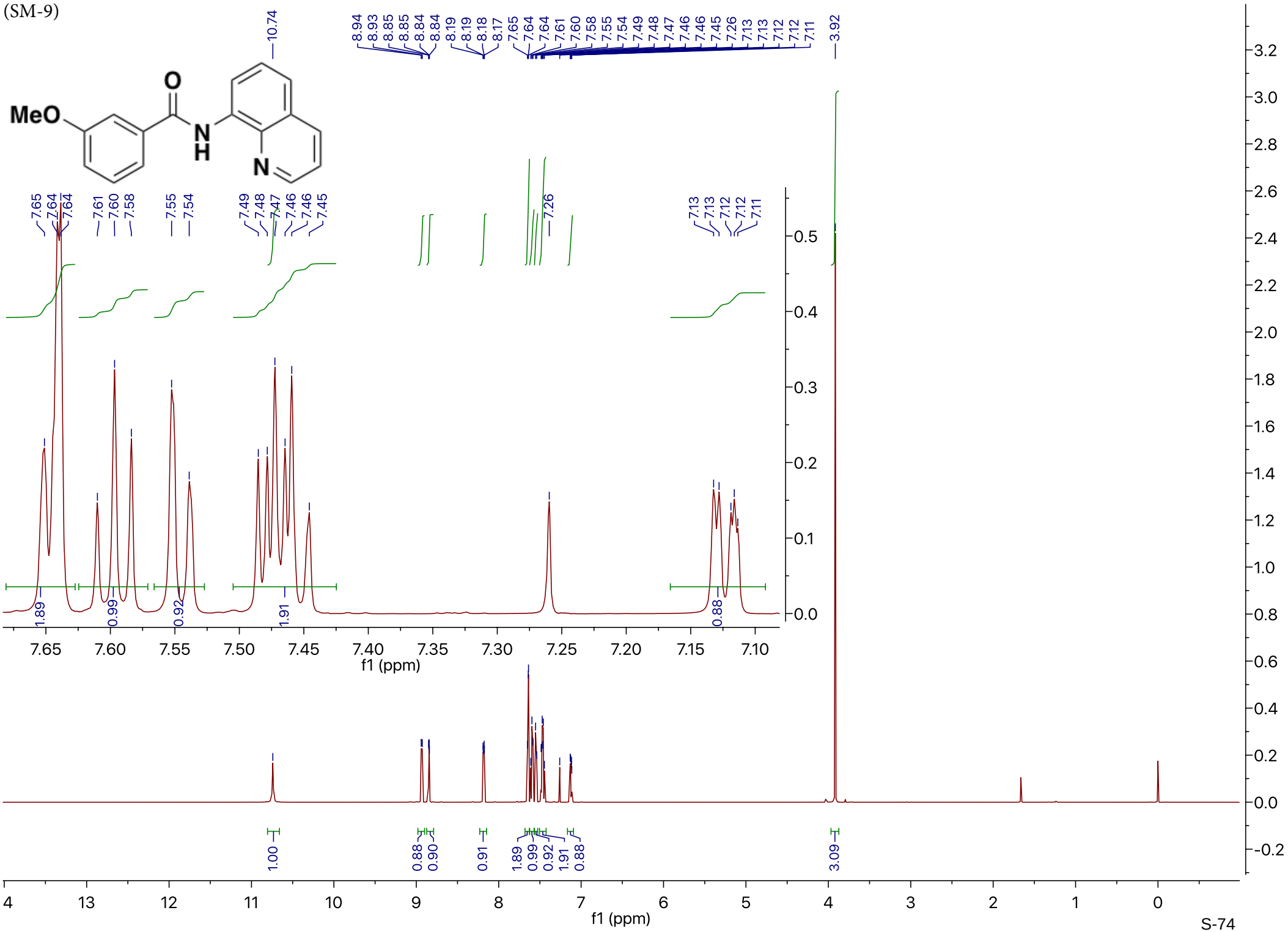
(SM-8)


10.91
9.01
9.00
8.90
8.90
8.22
8.21
8.15
8.14
8.07
8.05
8.02
8.01
7.94
7.93
7.65
7.63
7.63
7.62
7.62
7.60
7.59
7.58
7.57
7.52
7.51
7.50
7.50
O
N
H
N
f1 (ppm)
f1 (ppm)

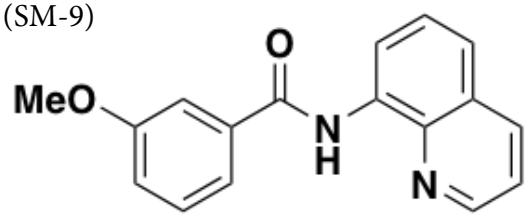
(SM-8)


165.66
148.47
138.95
136.56
135.06
134.78
132.88
132.50
129.34
128.83
128.15
128.10
127.99
127.93
127.65
126.94
123.87
122.53
121.85
116.74
O
N
H
N
f1 (ppm)
f1 (ppm)

(SM-9)

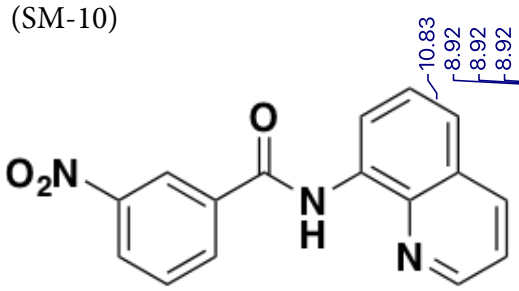

MeO
O
N
H
N
10.74
8.94
8.93
8.85
8.85
8.84
8.84
8.19
8.19
8.18
8.17
7.65
7.64
7.64
7.61
7.60
7.58
7.55
7.54
7.49
7.48
7.47
7.46
7.46
7.45
7.26
7.13
7.13
7.12
7.12
7.11
3.92
1.89
0.99
0.92
1.91
0.88
1.00
0.88
0.90
0.91
1.89
0.99
0.92
1.91
0.88
3.09
f1 (ppm)
f1 (ppm)

(SM-9)


MeO
O
N
H
N

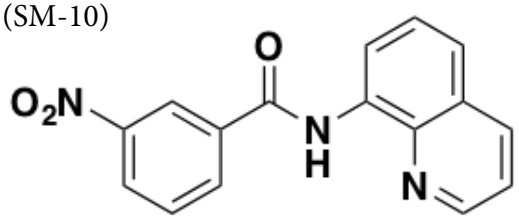
165.42
160.10
148.43
138.88
136.76
136.49
134.67
129.90
128.10
127.57
122.54
121.82
119.19
118.14
116.64
112.77
55.62
f1 (ppm)
S-75

(SM-10)


O
O_2N
N
H
N

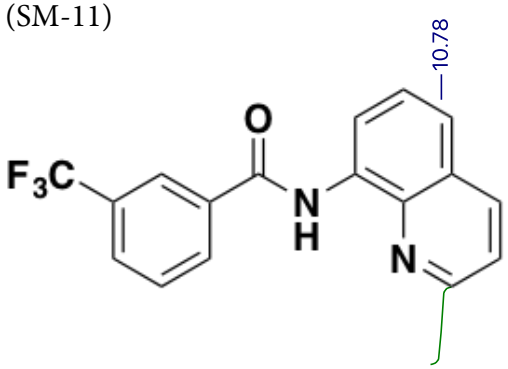
10.83
8.92 8.92 8.92 8.91 8.91 8.90 8.90 8.88 8.88 8.88 8.87
8.45 8.45 8.44 8.44 8.43 8.43 8.43 8.43 8.42 8.41 8.41 8.40 8.40 8.40 8.23 8.22 8.21 8.21
7.77 7.76 7.75 7.63 7.62 7.61 7.60 7.59 7.59 7.53 7.52 7.51 7.51
7.26
1.87 1.00 0.90 1.04 0.99 1.05 2.08 1.05
f1 (ppm)
1.12 1.87 1.00 0.90 1.04 0.99 1.05 2.08 1.05
f1 (ppm)

(SM-10)


O
O_2N
N
H
N

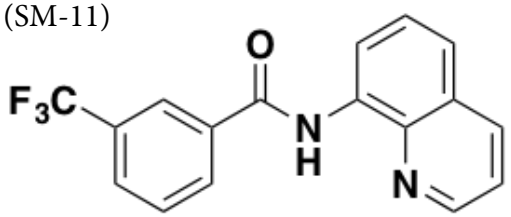
162.99
148.70
148.64
138.77
136.97
136.65
134.04
133.21
130.15
128.11
127.52
126.46
122.55
122.53
122.06
116.99
f1 (ppm)
f1 (ppm)

(SM-11)


O
F3C
N
H
N

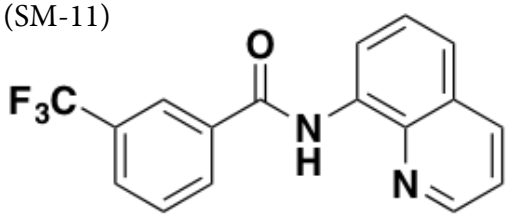
10.78
8.92 8.92 8.91 8.91 8.87 8.87 8.86 8.86 8.35 8.26 8.24 8.21 8.21 8.20 8.20 7.85 7.84 7.71 7.69 7.68 7.62 7.61 7.60 7.58 7.58 7.57 7.51 7.50 7.50 7.49 7.26
1.13 1.00 1.03 1.01 1.10 1.03 1.02 1.10 2.18 1.08
f1 (ppm)
S-78

(SM-11)


O
F3C
N
H
N

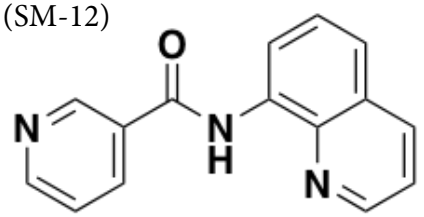
164.00
148.55
138.77
136.59
136.08
134.23
131.86
131.63
131.42
131.20
130.35
129.50
128.53
128.51
128.49
128.46
127.52
124.75
124.72
124.69
124.67
124.64
122.95
122.50
122.26
121.92
121.14
116.89
f1 (ppm)
f1 (ppm)

(SM-11)


O
F3C
N
H
N

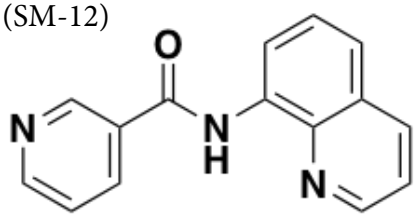
62.56
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
-2
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(SM-12)


O
N
N
H
N

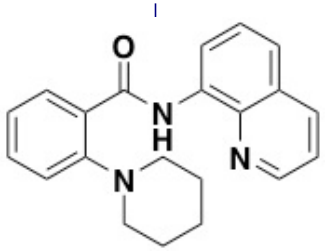
10.76
9.32 9.32 8.89 8.89 8.88 8.87 8.83 8.83 8.82 8.82 8.81 8.80 8.80 8.79 8.36 8.35 8.35 8.34 8.34 8.18 8.18 8.17 8.16 7.59 7.58 7.57 7.56 7.56 7.54 7.54 7.49 7.48 7.47 7.47 7.46
1.07 1.00 1.02 1.03 0.97 1.04 1.03 2.10 2.09
f1 (ppm)
S-81

(SM-12)


O
N
N
H
N

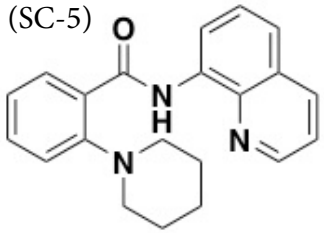
163.55
152.64
148.55
148.52
138.70
136.53
135.24
134.15
130.83
128.03
127.46
123.71
122.26
121.93
116.80
138.71
136.54
135.25
134.16
130.84
128.04
127.47
123.72
122.27
121.94
116.81
f1 (ppm)
f1 (ppm)

(SC-5)


O
N
H
N
N

12.85
9.15
9.14
8.84
8.83
8.83
8.18
8.16
8.16
8.15
7.60
7.58
7.57
7.52
7.51
7.47
7.45
7.44
7.43
7.24
7.23
7.20
7.19
7.18
3.07
1.82
1.81
1.49
1.48
1.46
1.00
1.08
2.05
1.13
1.07
2.17
1.41
1.10
4.56
4.59
2.31
f1 (ppm)
f1 (ppm)

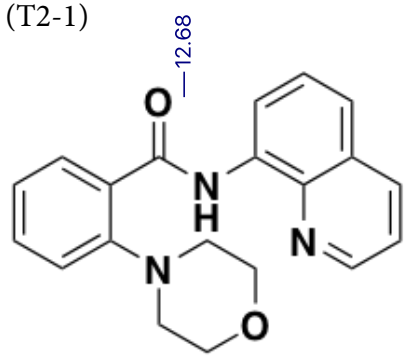
(SC-5)



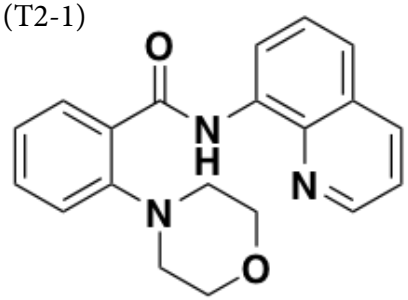
166.20
152.92
147.87
139.11
136.30
136.05
132.20
131.94
128.84
128.38
127.65
123.63
121.60
121.57
119.47
117.92
55.44
25.39
24.13

f1 (ppm)

(T2-1)

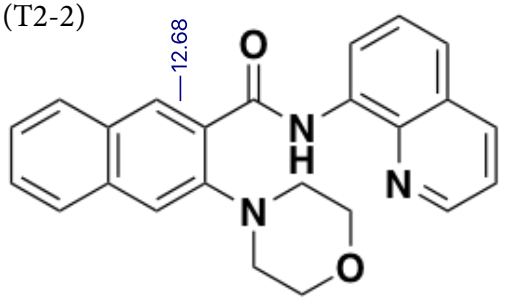


(T2-1)

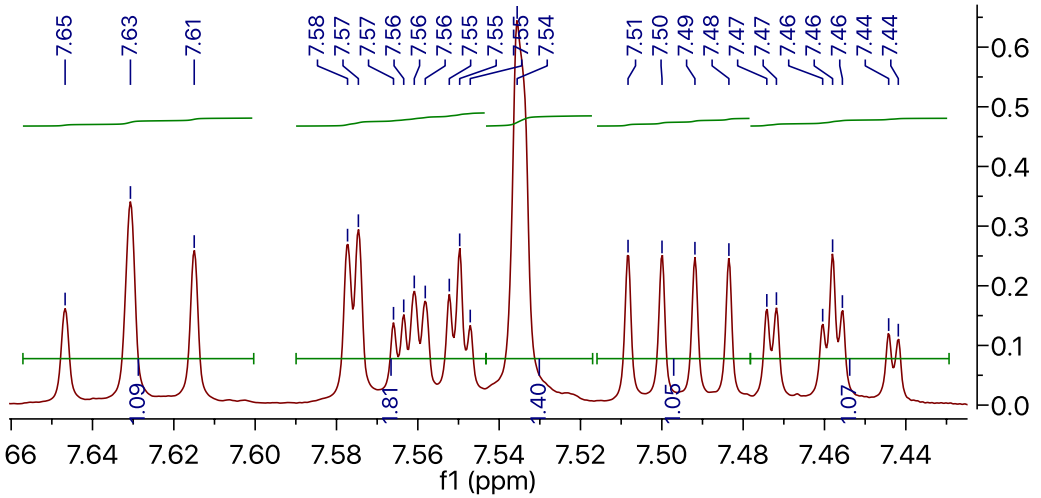

O
N
H
N
N
O

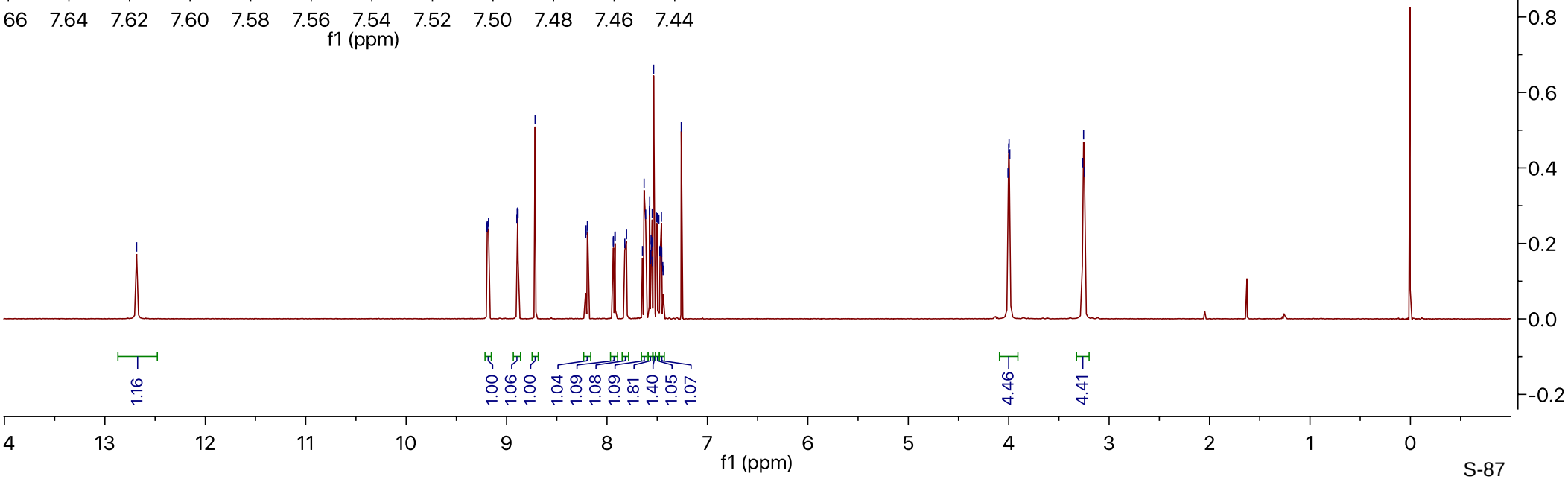
165.83
151.17
148.22
138.91
136.52
135.69
132.44
132.25
128.97
128.43
127.69
124.36
121.84
121.72
119.26
117.84
66.26
53.99
f1 (ppm)
f1 (ppm)

(T2-2)

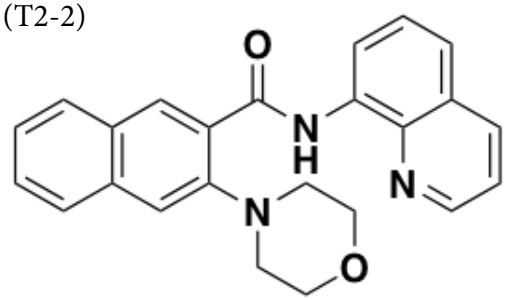


9.20 9.19 9.18 9.18 8.90 8.89 8.89 8.89 8.72 8.21 8.21 8.20 8.19 7.94 7.94 7.92 7.92 7.82 7.81 7.81 7.65 7.63 7.61 7.58 7.57 7.57 7.56 7.56 7.56 7.55 7.55 7.55 7.54 7.51 7.50 7.49 7.48 7.47 7.47 7.46 7.46 7.46 7.44 7.44 7.26 4.01 4.00 4.00 3.99 3.26 3.25 3.24

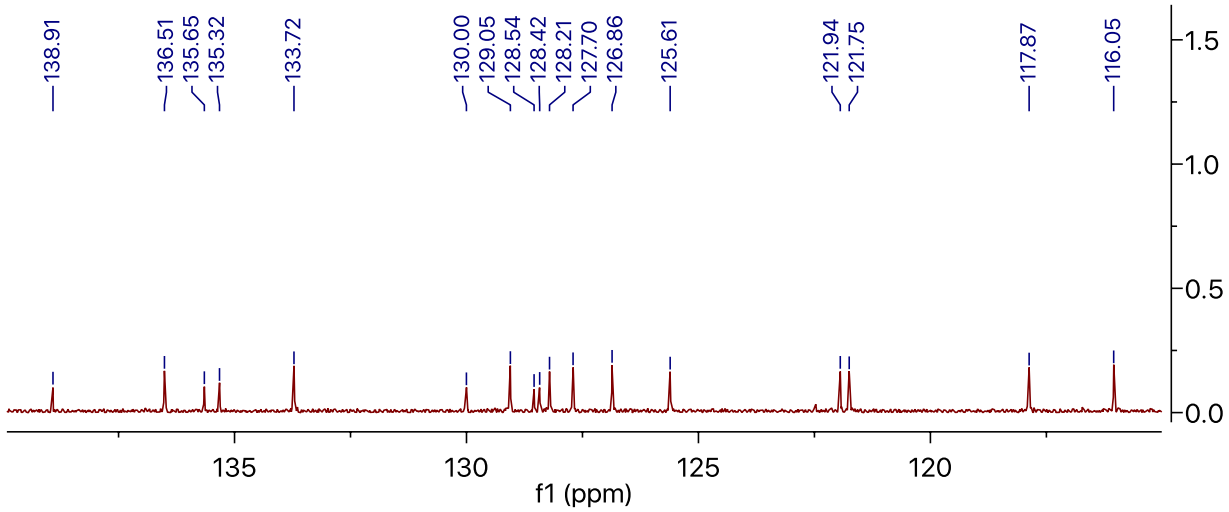




(T2-2)



165.76
148.29
147.92
138.91
136.51
135.65
135.32
133.72
130.00
129.05
128.54
128.42
128.21
127.70
126.86
125.61
121.94
121.75
117.87
116.05
66.23
54.14

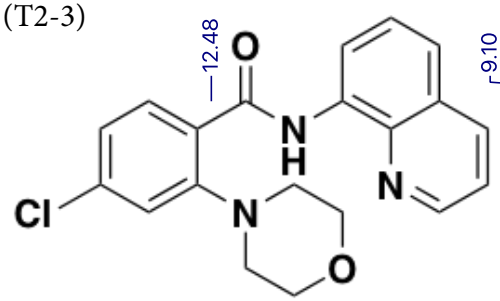


1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0

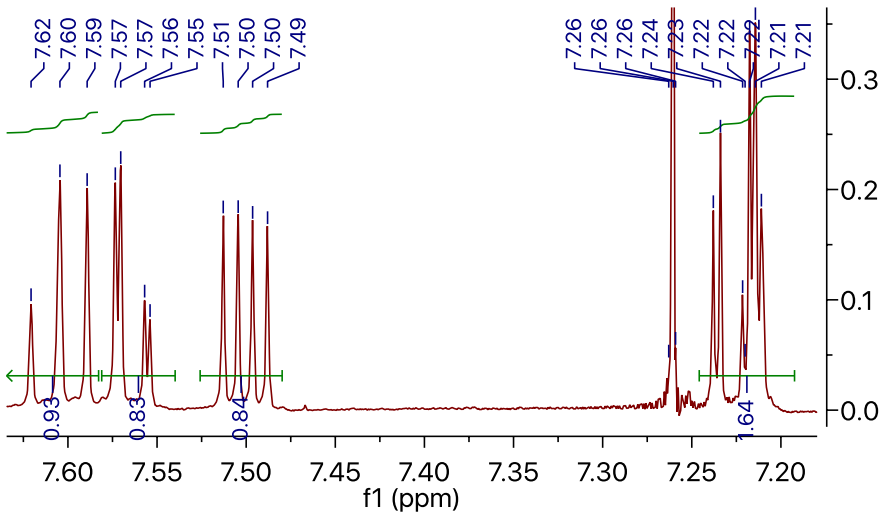
50 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

(T2-3)

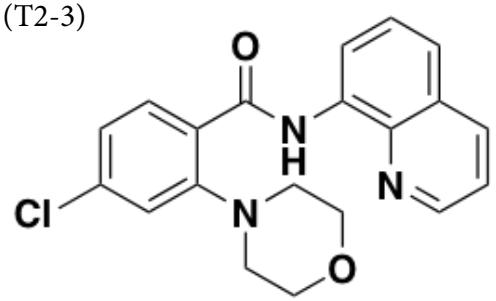

12.48
O
N
H
N
Cl
N
O


9.10
9.10
9.09
9.08
8.88
8.88
8.87
8.87
8.21
8.21
8.20
8.19
8.12
8.10
7.62
7.60
7.59
7.57
7.57
7.56
7.55
7.51
7.50
7.50
7.49
7.26
7.26
7.24
7.23
7.22
7.22
7.22
7.21
7.21
3.97
3.96
3.95
3.16
3.15
3.14


7.62
7.60
7.59
7.57
7.57
7.56
7.55
7.51
7.50
7.50
7.49
7.26
7.26
7.26
7.24
7.23
7.22
7.22
7.22
7.21
7.21
0.93
0.83
0.84
1.64
7.60
7.55
7.50
7.45
7.40
7.35
7.30
7.25
7.20
f1 (ppm)
0.3
0.2
0.1
0.0

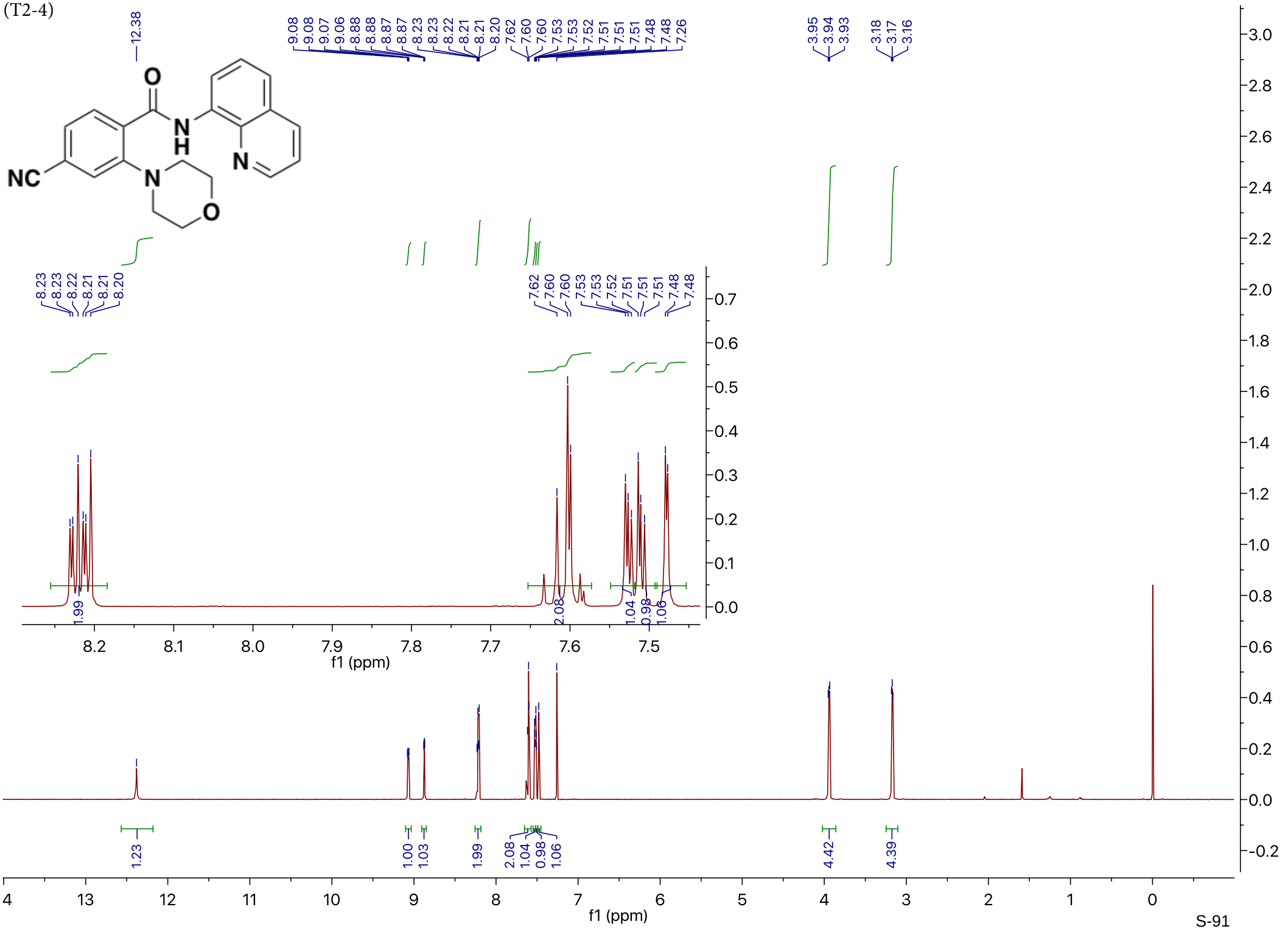
1.00
0.83
0.86
0.88
0.80
0.93
0.83
0.84
1.64
3.71
3.68
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-0.1

(T2-3)

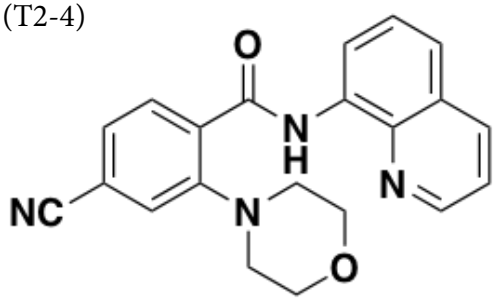

O
N
H
N
Cl
N
O

164.85
152.16
148.30
138.81
138.22
136.58
135.39
133.55
128.42
127.68
127.40
124.41
122.49
122.06
121.81
119.79
117.83
66.08
53.86
f1 (ppm)
S-90

(T2-4)


12.38
9.08
9.08
9.07
9.06
8.88
8.88
8.87
8.87
8.23
8.23
8.22
8.21
8.21
8.20
7.62
7.60
7.60
7.53
7.53
7.52
7.51
7.51
7.51
7.48
7.48
7.26
3.95
3.94
3.93
3.18
3.17
3.16
O
N
H
N
NC
N
O
1.99
2.08
1.04
0.98
1.06
f1 (ppm)
1.23
1.00
1.03
1.99
2.08
1.04
0.98
1.06
4.42
4.39
f1 (ppm)

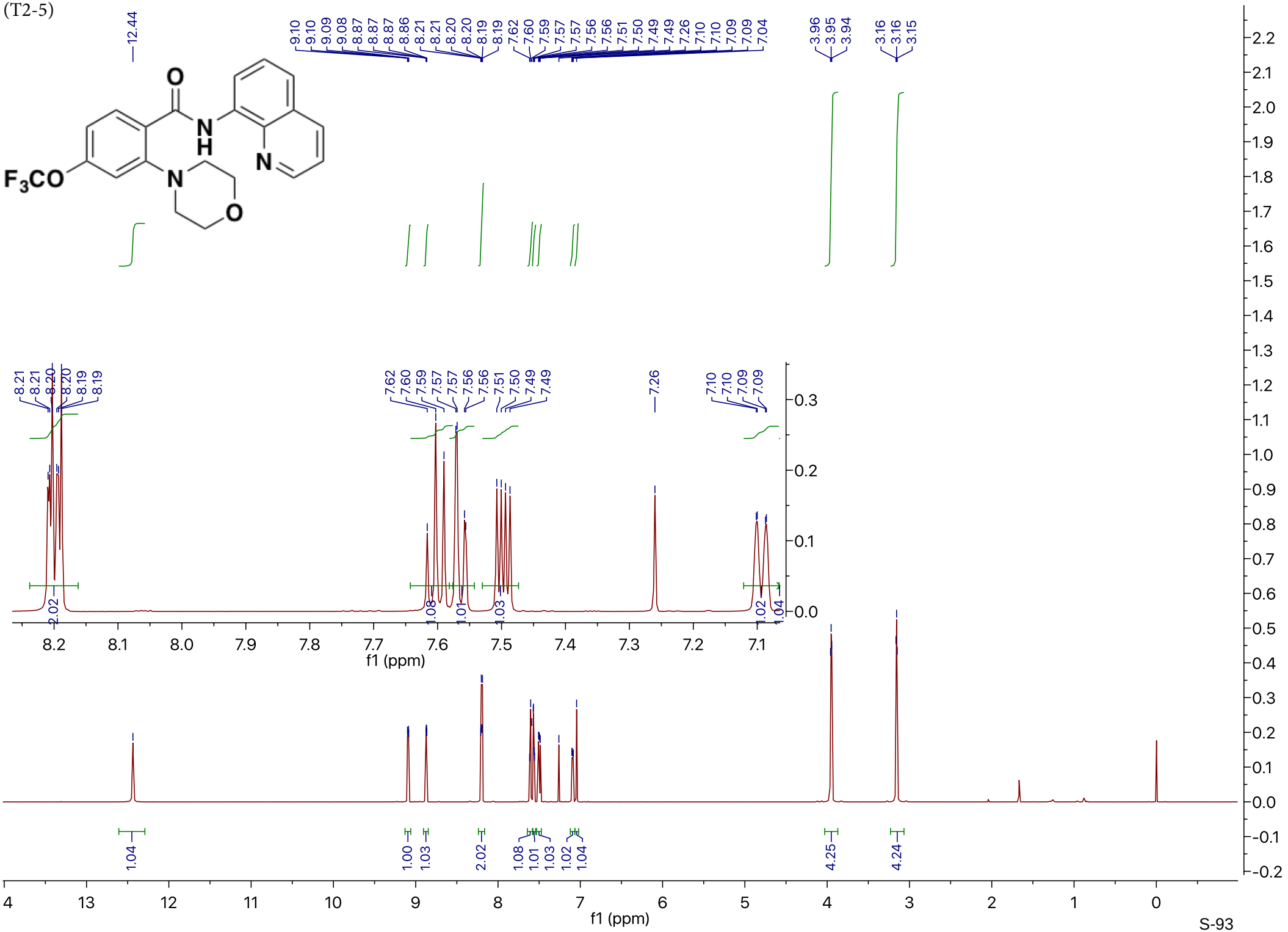
(T2-4)



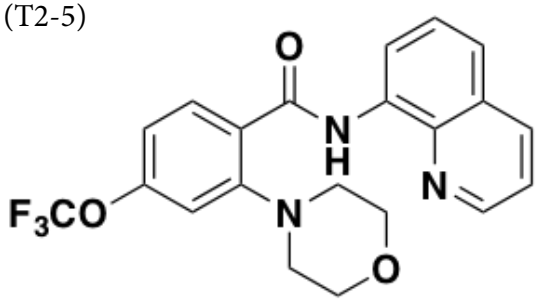
164.05
151.34
148.46
138.69
136.66
134.87
133.08
133.04
128.41
127.65
127.44
122.79
122.52
121.96
118.24
117.91
115.64
65.98
53.61

f1 (ppm)

(T2-5)

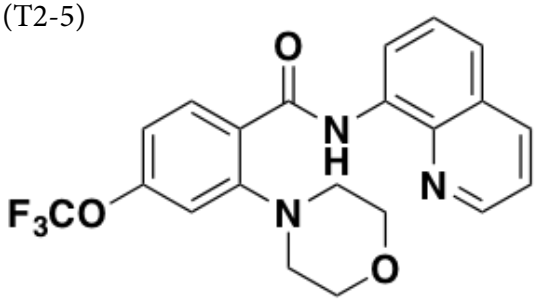

12.44
9.10 9.10 9.09 9.08 8.87 8.87 8.87 8.86 8.21 8.21 8.20 8.20 8.19 8.19 7.62 7.60 7.59 7.57 7.57 7.56 7.56 7.51 7.50 7.49 7.49 7.26 7.10 7.10 7.09 7.09 7.04
3.96 3.95 3.94 3.16 3.16 3.15
O
N
H
N
N
F3CO
O
8.21 8.21 8.20 8.20 8.19 8.19
7.62 7.60 7.59 7.57 7.57 7.56 7.56 7.51 7.50 7.49 7.49
7.26
7.10 7.10 7.09 7.09
2.02 1.08 1.01 1.03 1.02 1.04
f1 (ppm)
1.04 1.00 1.03 2.02 1.08 1.01 1.03 1.02 1.04 4.25 4.24
f1 (ppm)

(T2-5)


O
N
H
N
F3CO
N
O

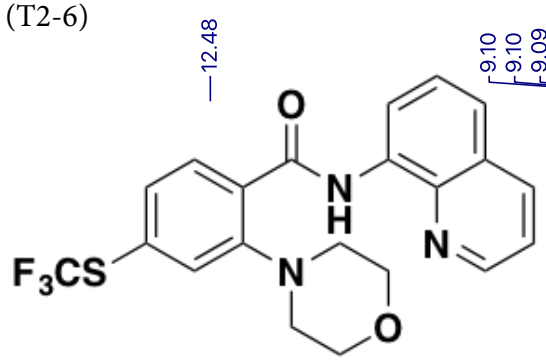
165.42
160.10
148.43
138.88
136.77
136.49
134.68
129.90
128.10
127.57
121.82
119.19
118.14
116.64
112.78
55.62
f1 (ppm)
f1 (ppm)

(T2-5)


O
N
H
N
F3CO
N
O

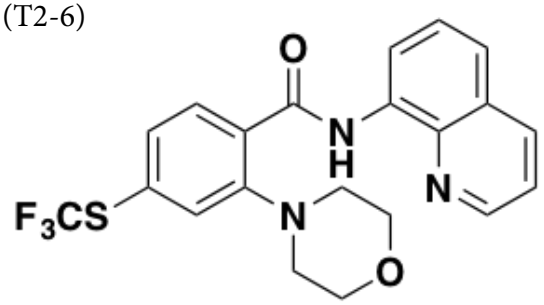
-57.37
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
-2
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(T2-6)


O
N
H
N
N
F3CS
O

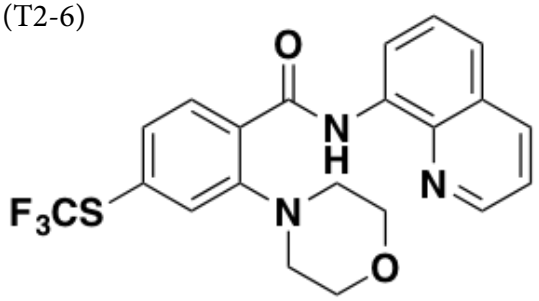
12.48
9.10 9.10 9.09 9.08 8.88 8.88 8.87 8.87 8.21 8.21 8.20 8.19 8.12 8.10 7.62 7.60 7.59 7.57 7.57 7.56 7.55 7.51 7.50 7.50 7.49 7.26 7.26 7.26 7.24 7.23 7.22 7.22 7.22 7.21 7.21 3.97 3.96 3.95 3.16 3.15 3.14
7.62 7.60 7.59 7.57 7.57 7.56 7.55 7.51 7.50 7.50 7.49 7.26 7.26 7.26 7.24 7.23 7.22 7.22 7.22 7.21 7.21
1.08 0.98 0.99 1.95
7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20
f1 (ppm)
1.06 0.97 1.00 1.01 0.94 1.08 0.98 0.99 1.95 4.41 4.37
4 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

(T2-6)


O
N
H
N
F3CS
N
O

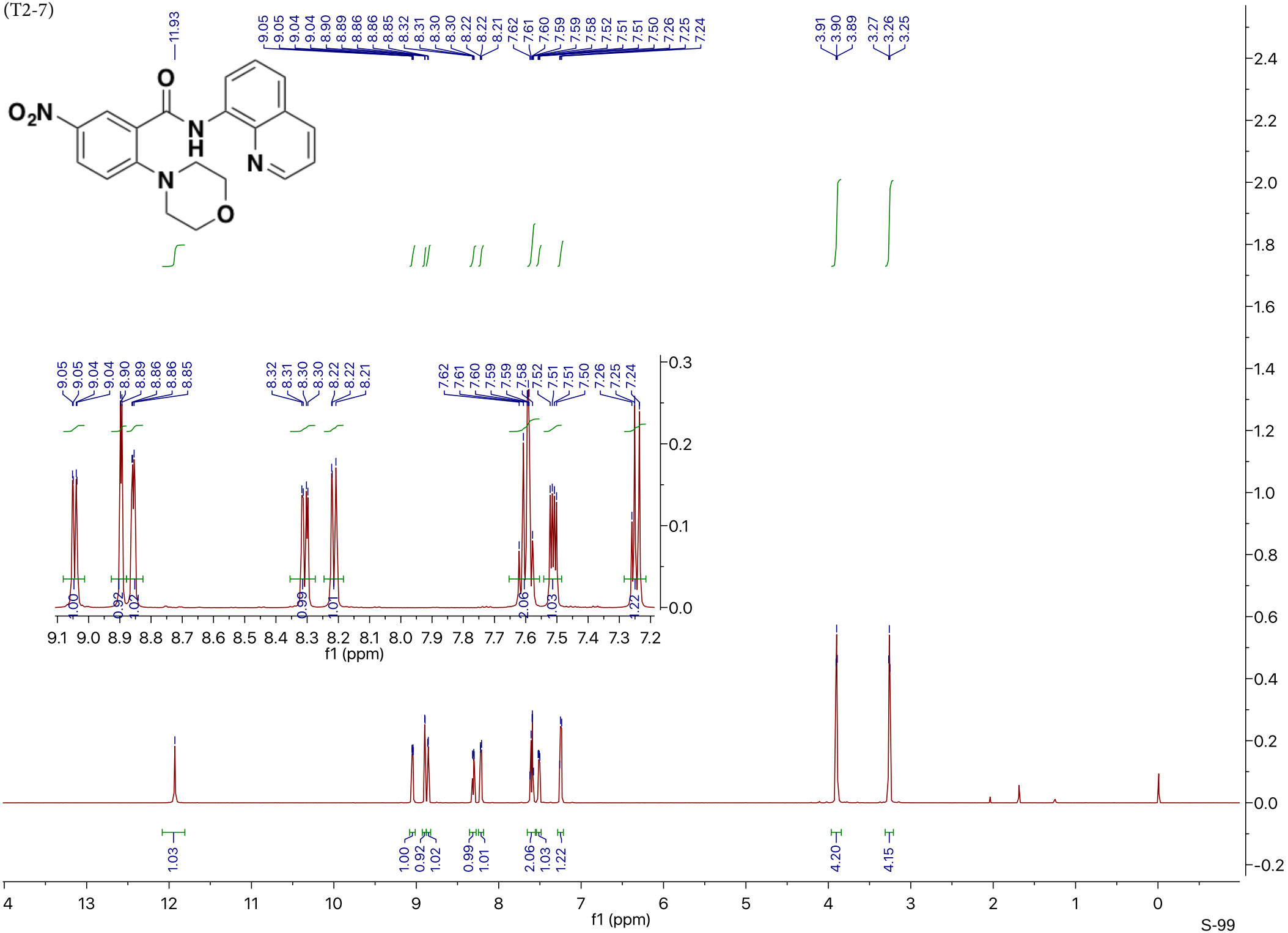
164.64
151.53
148.39
138.77
136.61
135.18
133.14
131.24
131.07
130.75
128.42
128.29
127.67
126.46
122.28
121.88
117.89
66.08
53.79
f1 (ppm)
f1 (ppm)

(T2-6)

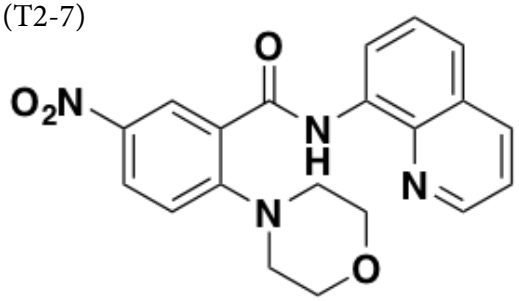

O
N
H
N
F3CS
N
O

-41.68
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(T2-7)

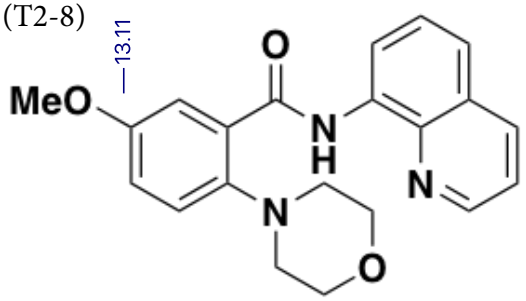

11.93
9.05 9.05 9.04 9.04 8.90 8.89 8.86 8.86 8.85 8.32 8.31 8.30 8.30 8.22 8.22 8.21 7.62 7.61 7.60 7.59 7.59 7.58 7.52 7.51 7.51 7.50 7.26 7.25 7.24
3.91 3.90 3.89 3.27 3.26 3.25
O
O2N
N
H
N
N
O
1.00 0.92 1.02 0.99 1.01 2.06 1.03 1.22
f1 (ppm)
1.03 1.00 0.92 1.02 0.99 1.01 2.06 1.03 1.22 4.20 4.15
f1 (ppm)

(T2-7)


O
O_2N
N
H
N
N
O

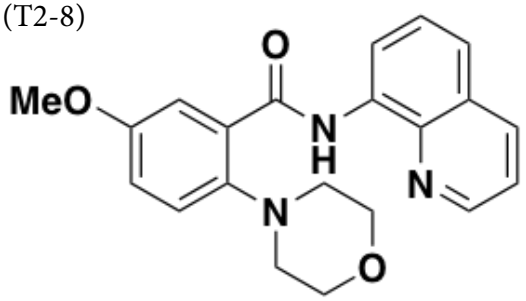
163.84
155.78
148.50
143.16
138.51
136.71
134.61
129.09
128.38
128.04
127.68
127.26
122.50
122.01
118.89
117.67
65.86
53.27
f1 (ppm)
S-100

(T2-8)

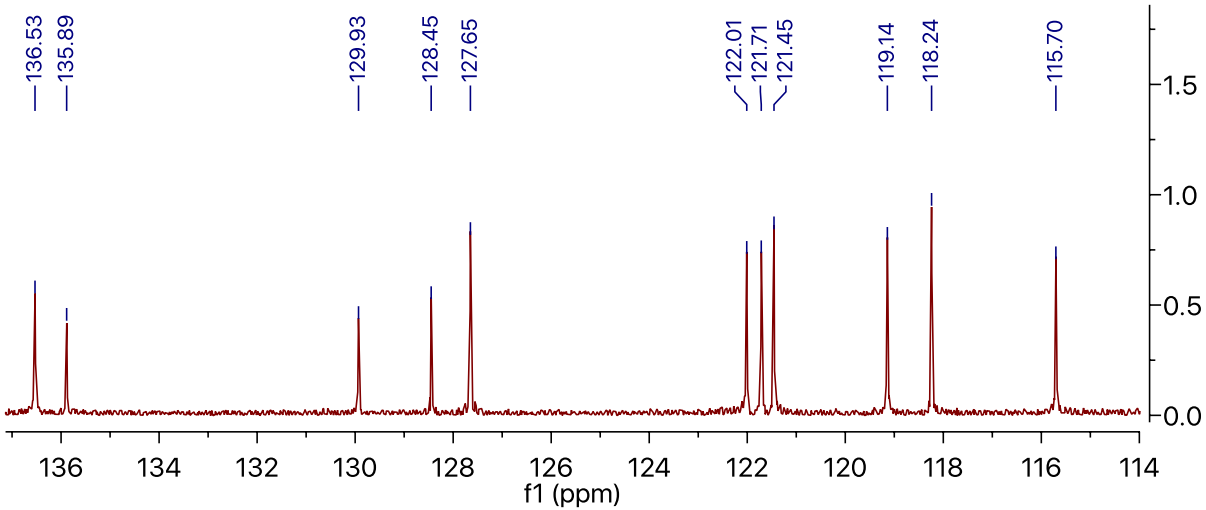

13.11
MeO
O
N
H
N
N
O

9.14
9.13
8.89
8.89
8.88
8.88
8.19
8.19
8.18
8.17
7.83
7.82
7.61
7.59
7.58
7.55
7.54
7.49
7.48
7.48
7.47
7.26
7.25
7.25
7.06
7.06
7.05
7.04
4.02
4.02
4.01
3.86
3.10
3.09
3.09
7.61
7.59
7.58
7.55
7.54
7.49
7.48
7.48
7.47
1.07
1.05
1.05
7.62 7.60 7.58 7.56 7.54 7.52 7.50 7.48 7.46
f1 (ppm)
1.04
1.00
1.03
1.05
0.99
1.07
1.05
1.05
1.30
1.05
4.35
3.20
4.30
f1 (ppm)

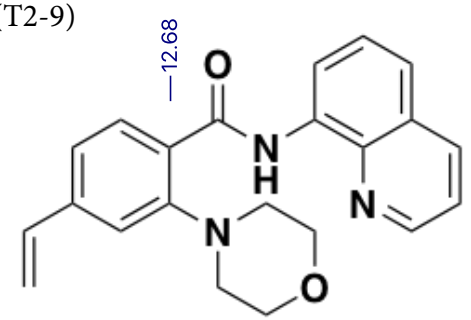
(T2-8)

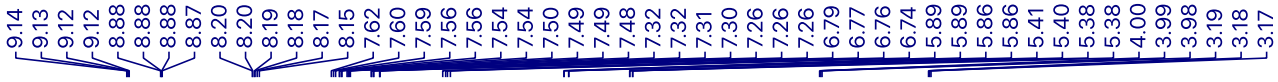


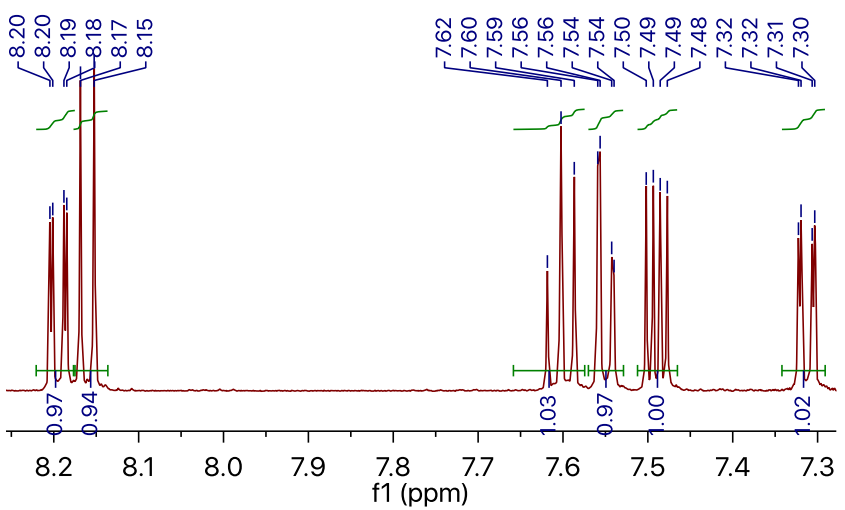
165.26
156.64
148.23
144.72
139.10
136.53
135.89
129.93
128.45
127.65
122.01
121.71
121.45
119.14
118.24
115.70
66.32
55.76
54.41



(T2-9)

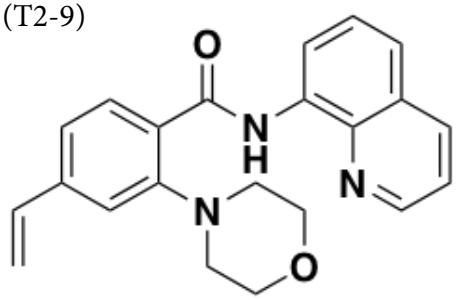

12.68
O
N
H
N
N
O


9.14
9.13
9.12
9.12
8.88
8.88
8.88
8.87
8.20
8.20
8.19
8.18
8.17
8.15
7.62
7.60
7.59
7.56
7.56
7.54
7.54
7.50
7.49
7.49
7.48
7.32
7.32
7.31
7.30
7.26
7.26
6.79
6.77
6.76
6.74
5.89
5.89
5.86
5.86
5.41
5.40
5.38
5.38
4.00
3.99
3.98
3.19
3.18
3.17


8.20
8.20
8.19
8.18
8.17
8.15
7.62
7.60
7.59
7.56
7.56
7.54
7.54
7.50
7.49
7.49
7.48
7.32
7.32
7.31
7.30
0.97
0.94
1.03
0.97
1.00
1.02
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
f1 (ppm)
0.4
0.3
0.2
0.1
0.0

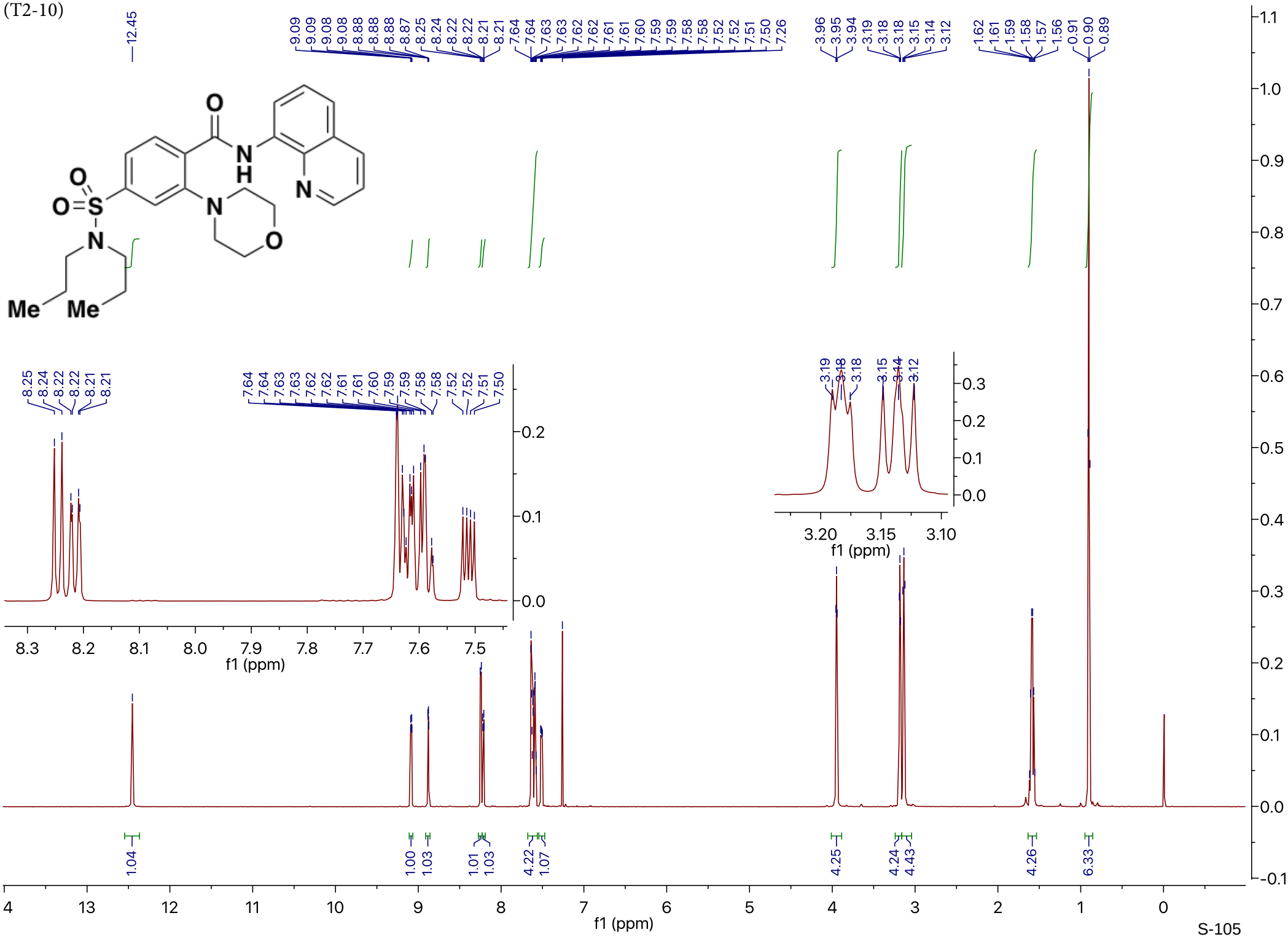
1.09
0.95
1.00
0.97
0.94
1.03
0.97
1.00
1.02
1.00
1.07
1.05
4.27
4.27
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-0.1

(T2-9)

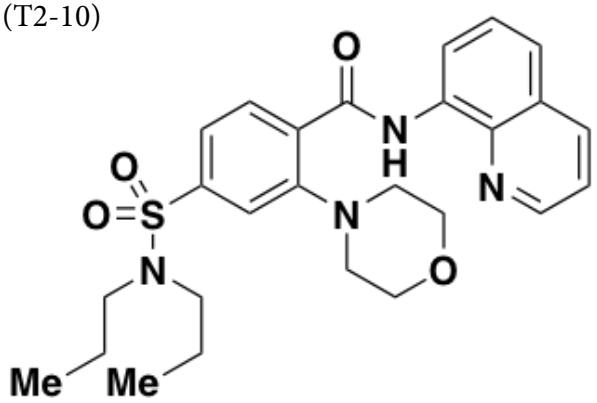

O
N
H
N
N
O

165.50
151.48
148.21
141.58
138.91
136.51
136.17
135.70
132.59
128.42
128.08
127.69
121.97
121.84
121.72
117.86
117.24
116.23
77.36
66.23
53.97
f1 (ppm)
S-104

(T2-10)

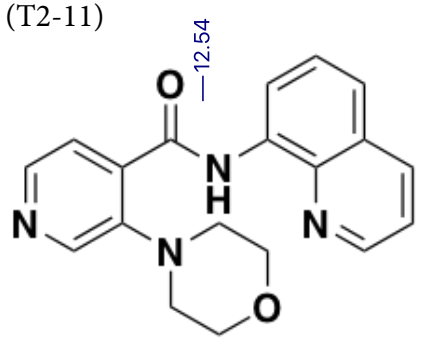

12.45
9.09 9.09 9.08 9.08 8.88 8.88 8.88 8.87 8.25 8.24 8.22 8.22 8.21 8.21
7.64 7.64 7.63 7.63 7.62 7.62 7.61 7.61 7.60 7.59 7.59 7.58 7.58 7.52 7.52 7.51 7.50 7.26
3.96 3.95 3.94 3.19 3.18 3.18 3.15 3.14 3.12
1.62 1.61 1.59 1.58 1.57 1.56 0.91 0.90 0.89
O
N
H
N
O
O
S
O
N
N
O
Me
Me
f1 (ppm)
1.04
1.00
1.03
1.01
1.03
4.22
1.07
4.25
4.24
4.43
4.26
6.33
S-105

(T2-10)


O
N
H
O
O=S
N
N
N
O
Me
Me

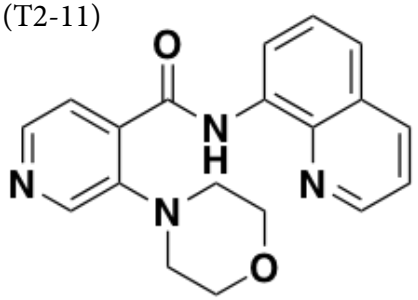
164.45
151.52
148.46
143.65
138.76
136.68
135.06
133.09
132.25
128.44
127.68
122.42
122.16
121.95
117.94
117.81
66.05
53.80
50.11
22.12
11.33
f1 (ppm)
S-106

(T2-11)


12.54
O
N
H
N
N
N
O

9.09 9.08 9.08 9.07 8.89 8.89 8.89 8.88 8.63 8.56 8.56 8.23 8.22 8.21 8.21 7.99 7.98 7.63 7.61 7.60 7.60 7.60 7.59 7.53 7.52 7.51 7.50 7.26
4.00 3.99 3.98 3.26 3.25 3.24
f1 (ppm)
1.07 0.96 1.00 1.03 0.97 0.98 0.94 2.00 1.00 4.32 4.32

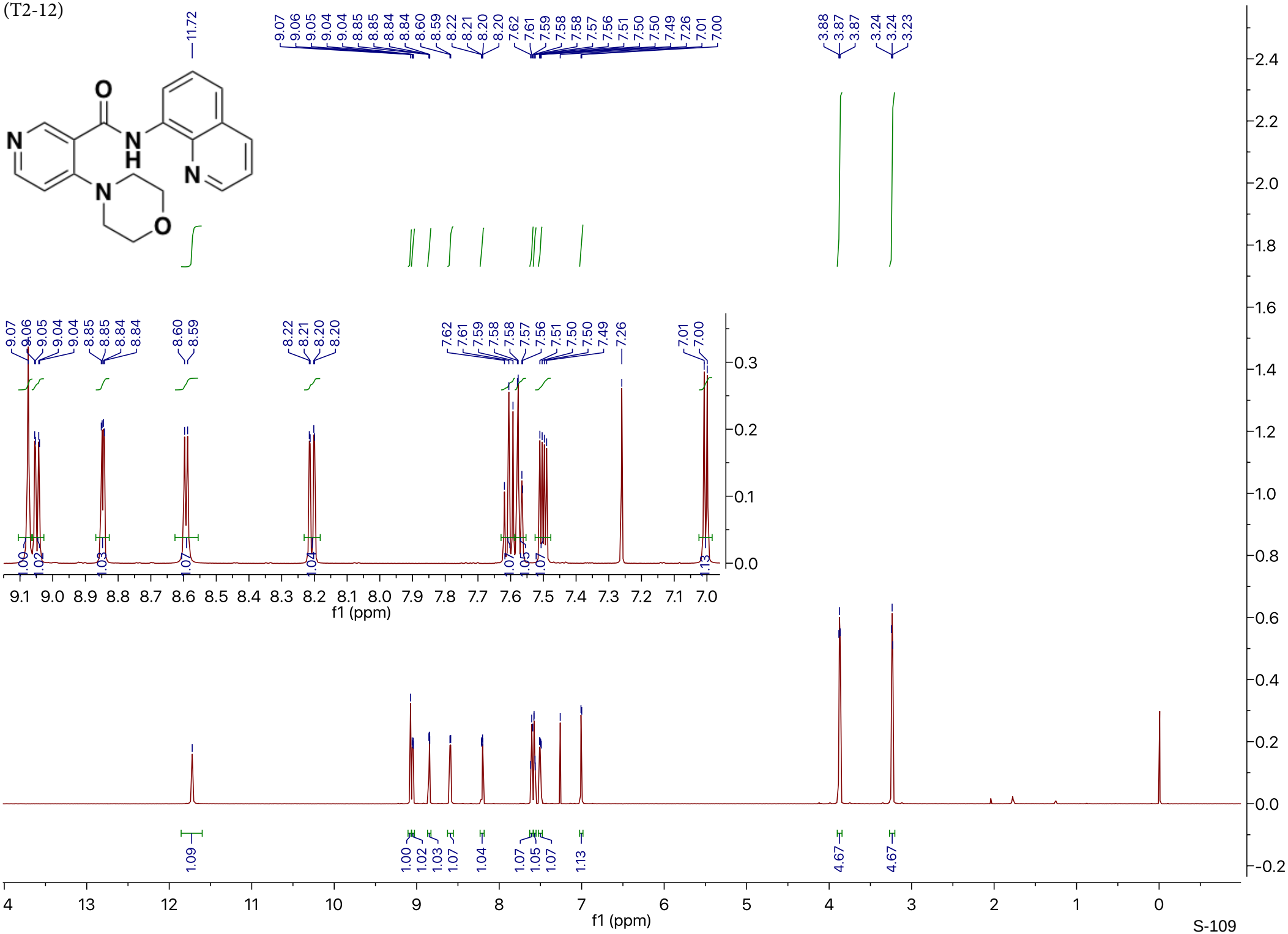
(T2-11)



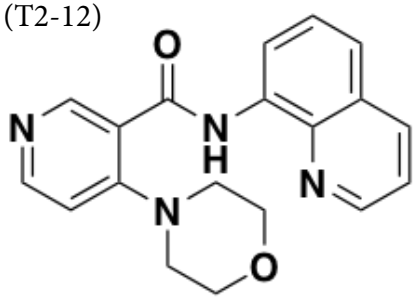
163.66
148.48
146.39
145.20
142.49
138.79
136.65
135.40
134.94
128.41
127.63
124.64
122.63
121.96
118.14
66.14
53.63

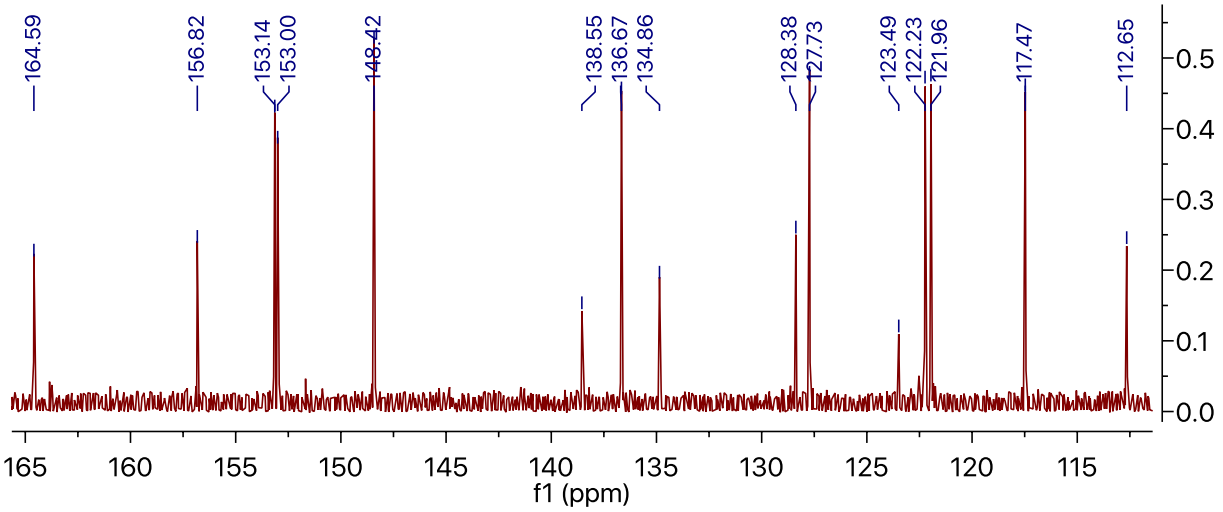
f1 (ppm)

(T2-12)


11.72
9.07 9.06 9.05 9.04 9.04 8.85 8.85 8.84 8.84 8.60 8.59 8.22 8.21 8.20 8.20 7.62 7.61 7.59 7.58 7.58 7.57 7.56 7.51 7.50 7.50 7.49 7.26 7.01 7.00
3.88 3.87 3.87 3.24 3.24 3.23
O
N
N
H
N
N
O
f1 (ppm)
1.09 1.02 1.03 1.07 1.04 1.07 1.05 1.07 1.13 4.67 4.67
S-109

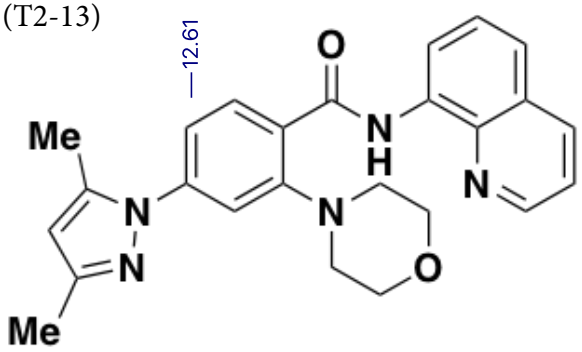
(T2-12)


O
N
N
H
N
N
O


164.59
156.82
153.14
153.00
148.42
138.55
136.67
134.86
128.38
127.73
123.49
122.23
121.96
117.47
112.65
0.5
0.4
0.3
0.2
0.1
0.0
165
160
155
150
145
140
135
130
125
120
115
f1 (ppm)

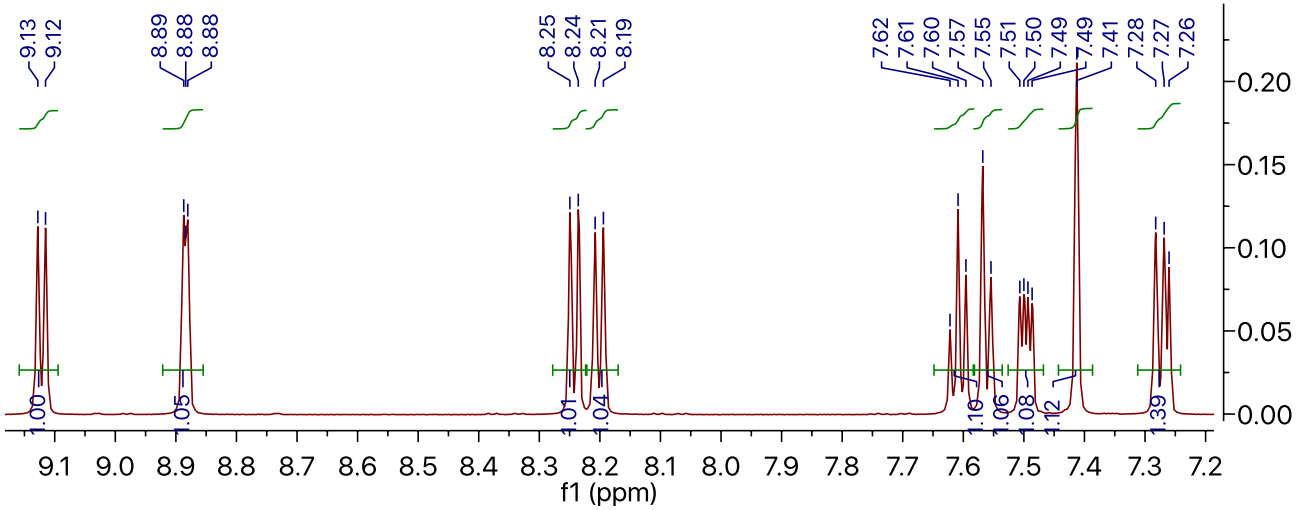
164.59
156.82
153.14
153.00
148.42
138.55
136.67
134.86
128.38
127.73
123.49
122.23
121.96
117.47
112.65
77.36
65.98
52.41
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
50
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

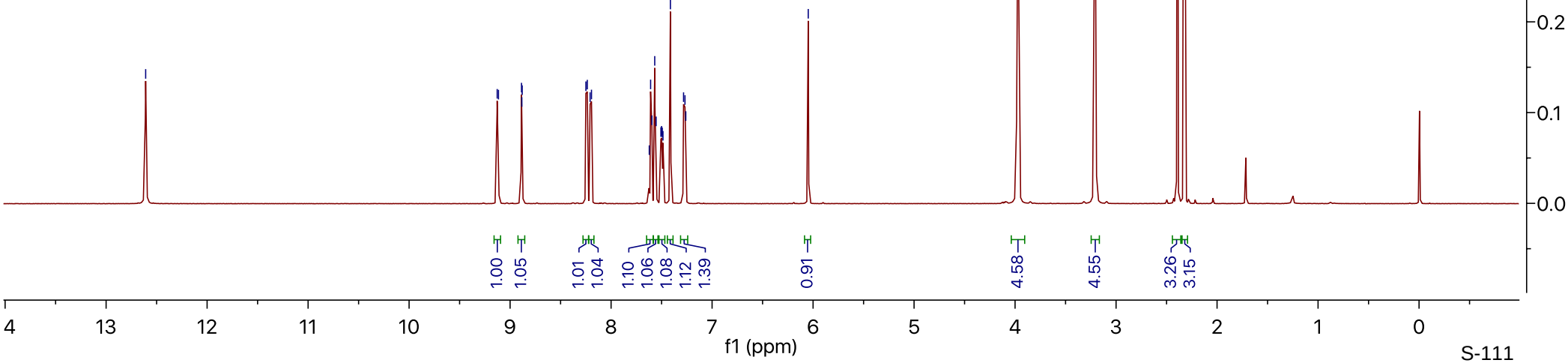
(T2-13)


12.61
O
N
H
N
N
N
N
O
Me
Me

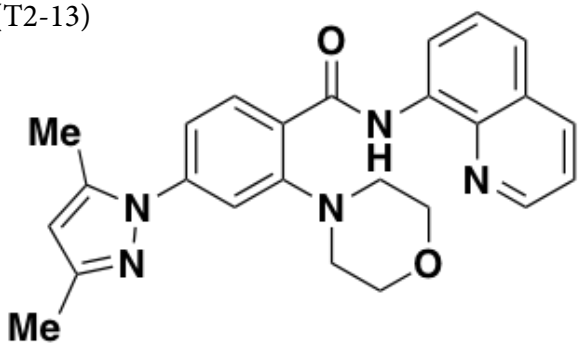

9.13
9.12
8.89
8.88
8.88
8.25
8.24
8.21
8.19
7.62
7.61
7.60
7.57
7.55
7.51
7.50
7.49
7.49
7.41
7.28
7.27
7.26
6.05


3.97
3.21
3.21
2.39
2.32


9.13
9.12
8.89
8.88
8.88
8.25
8.24
8.21
8.19
7.62
7.61
7.60
7.57
7.55
7.51
7.50
7.49
7.49
7.41
7.28
7.27
7.26
1.00
1.05
1.01
1.04
1.10
1.06
1.08
1.12
1.39
0.20
0.15
0.10
0.05
0.00
9.1 9.0 8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2
f1 (ppm)

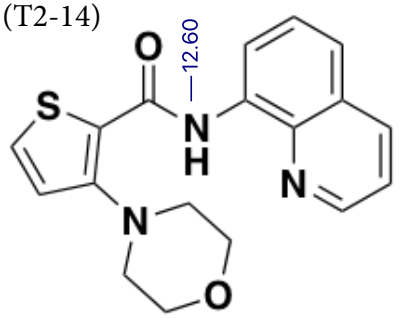

1.00
1.05
1.01
1.04
1.10
1.06
1.08
1.12
1.39
0.91
4.58
4.55
3.26
3.15
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
4 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

(T2-13)


O
N
H
N
Me
N
N
N
O
Me

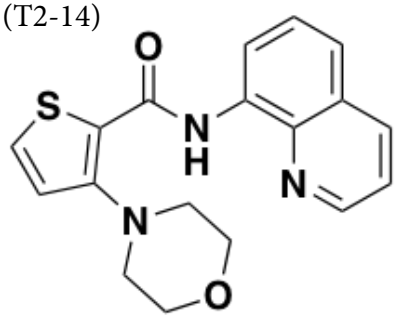
165.11
152.09
149.84
148.31
143.19
139.68
138.86
136.56
135.54
133.00
128.43
127.69
127.15
121.99
121.80
119.12
117.85
115.44
108.14
66.16
53.91
13.69
12.95
f1 (ppm)
S-112

(T2-14)

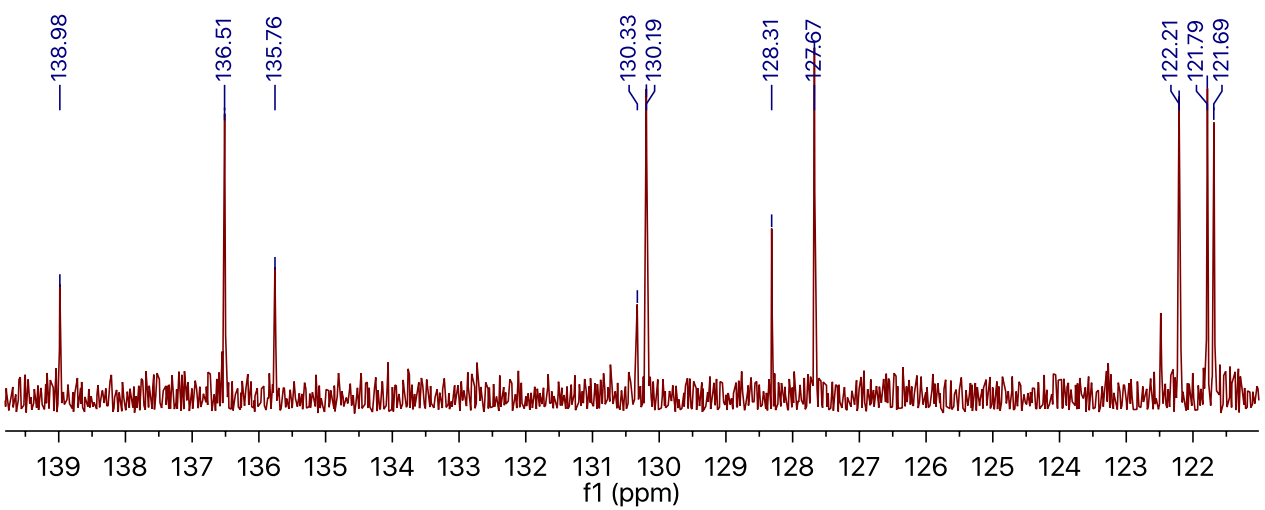

O
12.60
S
N
H
N
N
O

9.05 9.05 9.04 9.04 8.94 8.94 8.93 8.93 8.21 8.21 8.19 8.19 7.60 7.59 7.57 7.55 7.55 7.54 7.53 7.53 7.52 7.51 7.50 7.49 7.26 7.26 7.26 7.21 7.20 4.17 4.16 4.15 3.13 3.12 3.11
7.60 7.59 7.57 7.55 7.55 7.54 7.53 7.53 7.52 7.51 7.50 7.49
1.02
2.88
7.61 7.60 7.59 7.58 7.57 7.56 7.55 7.54 7.53 7.52 7.51 7.50 7.49
f1 (ppm)
1.11
0.94
1.00
0.98
1.02
2.88
1.00
4.19
4.26
f1 (ppm)

(T2-14)



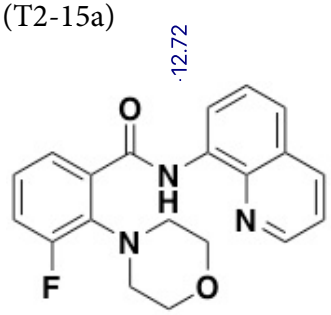
160.70
152.28
148.10
138.98
136.51
135.76
130.33
130.19
128.31
127.67
122.21
121.79
121.69
118.09
66.57
54.41



0.80 0.75 0.70 0.65 0.60 0.55 0.50 0.45 0.40 0.35 0.30 0.25 0.20 0.15 0.10 0.05 0.00 -0.05

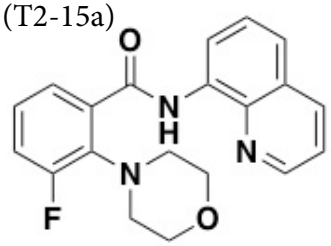
50 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

(T2-15a)


O
N
H
N
N
F
O

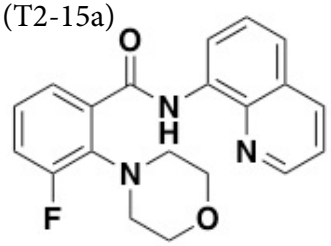
12.72
9.07
9.06
8.89
8.88
8.21
8.19
8.09
8.08
7.62
7.60
7.59
7.58
7.56
7.50
7.50
7.49
7.48
7.30
7.29
7.28
7.27
7.25
7.23
7.22
4.07
3.36
1.05
1.11
1.09
1.05
2.25
1.12
1.15
1.69
1.00
4.93
4.84
f1 (ppm)
f1 (ppm)

(T2-15a)


O
N
H
N
N
F
O

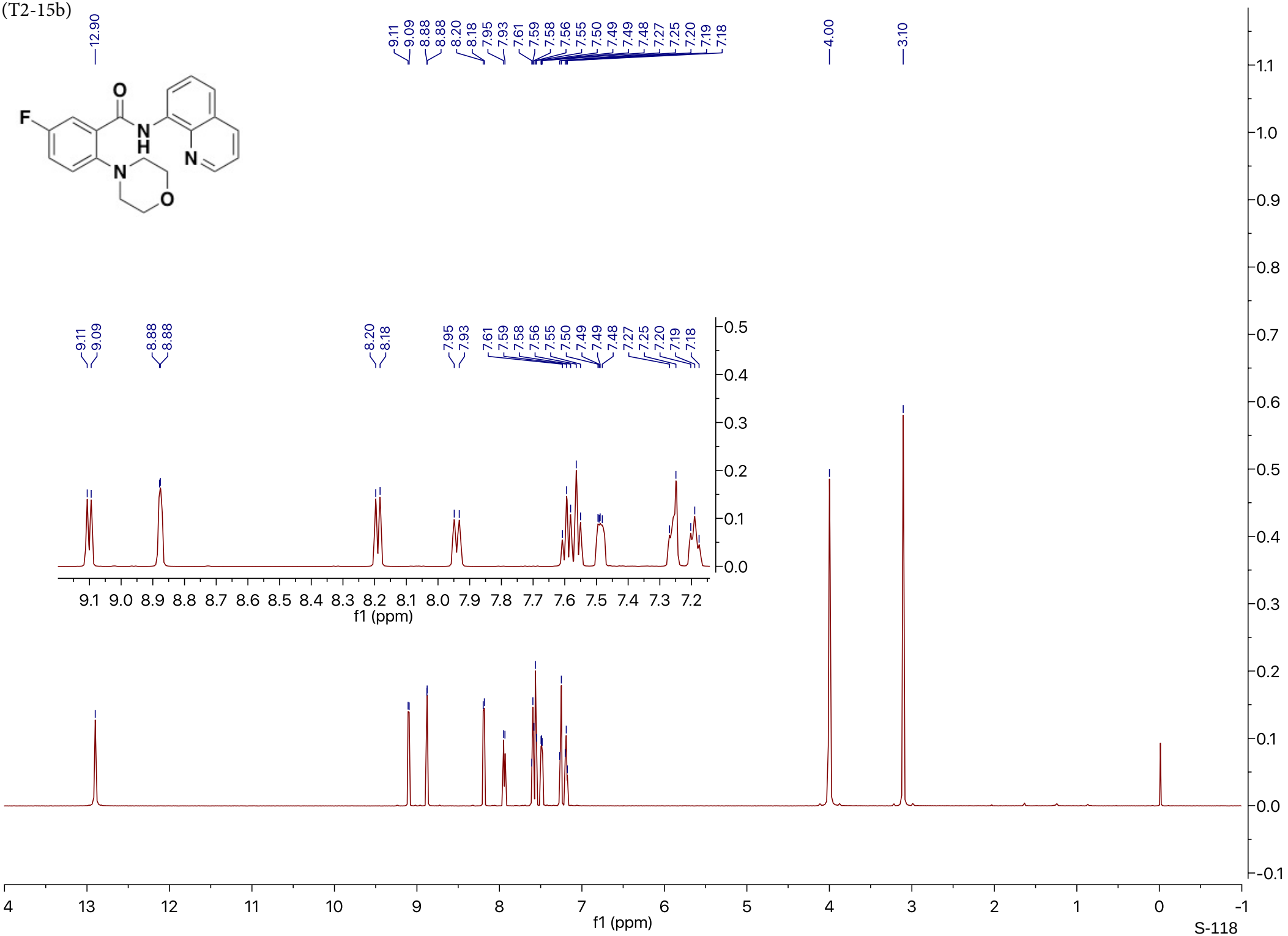
164.52
164.49
161.80
160.13
148.15
139.18
137.16
137.09
136.60
135.52
133.34
133.31
128.41
127.58
127.55
126.78
126.72
122.33
121.74
120.29
120.14
118.82
66.49
52.02
f1 (ppm)
S-116

(T2-15a)

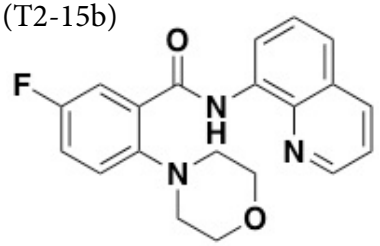

O
N
H
N
N
F
O

-117.58
-117.60
-117.64
-117.66
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-0.1
-117.58
-117.60
-117.64
-117.66
1.0
0.8
0.6
0.4
0.2
0.0
-117.50
-117.60
-117.70
-117.80
f1 (ppm)
150
100
50
0
-50
-100
-150
-200
f1 (ppm)

(T2-15b)

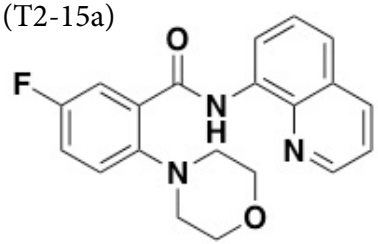

12.90
9.11
9.09
8.88
8.88
8.20
8.18
7.95
7.93
7.61
7.59
7.58
7.56
7.55
7.50
7.49
7.49
7.48
7.27
7.25
7.20
7.19
7.18
4.00
3.10
F
O
N
H
N
N
O
f1 (ppm)
f1 (ppm)

(T2-15b)


O
F
N
H
N
N
O

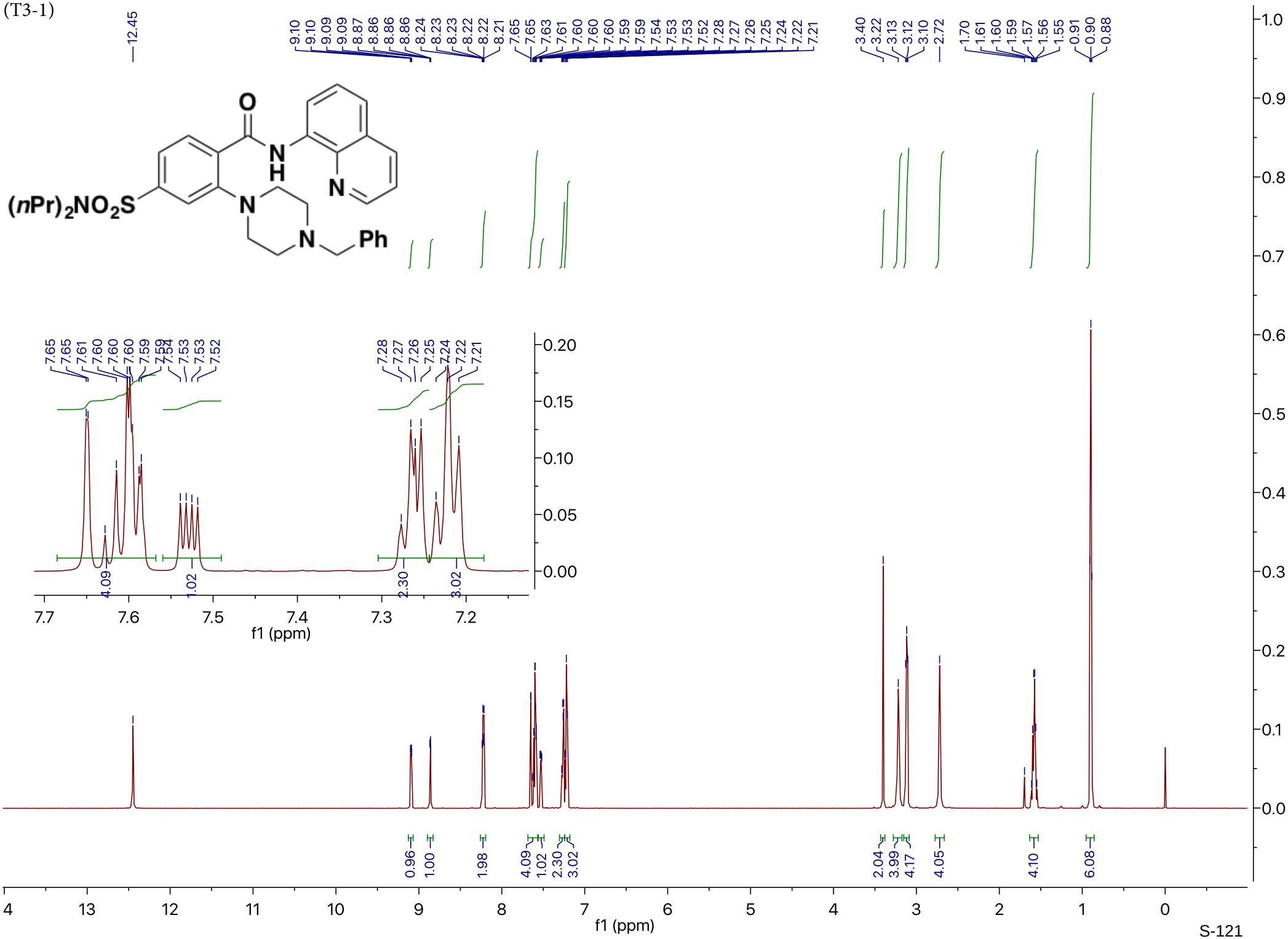
164.21
164.19
160.54
158.92
148.31
147.44
147.42
139.00
136.60
135.54
131.03
130.99
128.46
127.68
122.52
122.23
121.80
121.58
121.53
119.13
118.98
118.91
118.75
118.26
66.22
54.35
f1 (ppm)
S-119

(T2-15a)

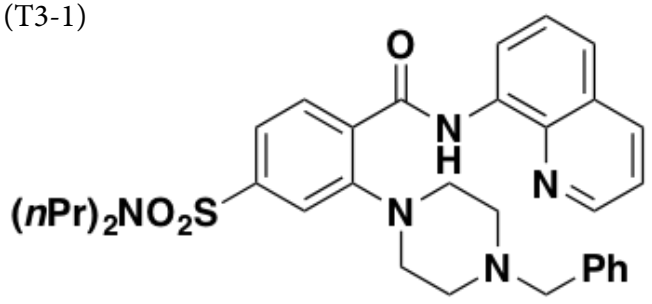

O
F
N
H
N
N
O

-117.52
-117.53
-117.54
-117.54
-117.55
-117.56
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)
-117.52
-117.53
-117.54
-117.54
-117.55
-117.56
0.8
0.6
0.4
0.2
0.0
-116.8
-117.0
-117.2
-117.4
-117.6
-117.8
-118.0
-118.2
f1 (ppm)

(T3-1)

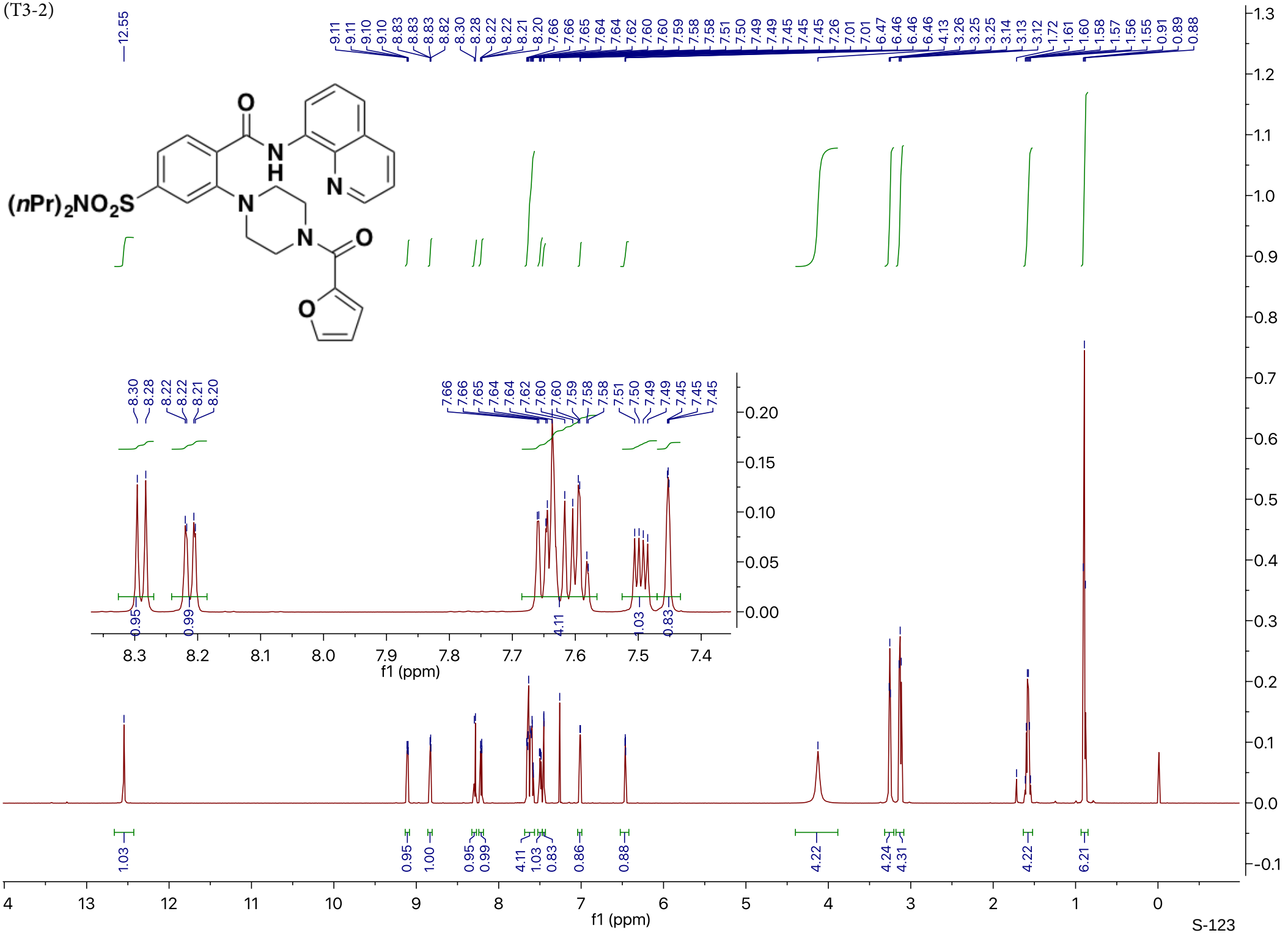

12.45
9.10 9.10 9.09 9.09 8.87 8.86 8.86 8.86 8.24 8.23 8.23 8.22 8.22 8.21
7.65 7.65 7.63 7.61 7.60 7.60 7.60 7.59 7.59 7.54 7.53 7.53 7.52 7.28 7.27 7.26 7.25 7.24 7.22 7.21
3.40 3.22 3.13 3.12 3.10 2.72
1.70 1.61 1.60 1.59 1.57 1.56 1.55 0.91 0.90 0.88
O
N
H
N
N
N
Ph
(nPr)2NO2S
0.96 1.00 1.98 4.09 1.02 2.30 3.02 2.04 3.99 4.17 4.05 4.10 6.08
f1 (ppm)
S-121

(T3-1)

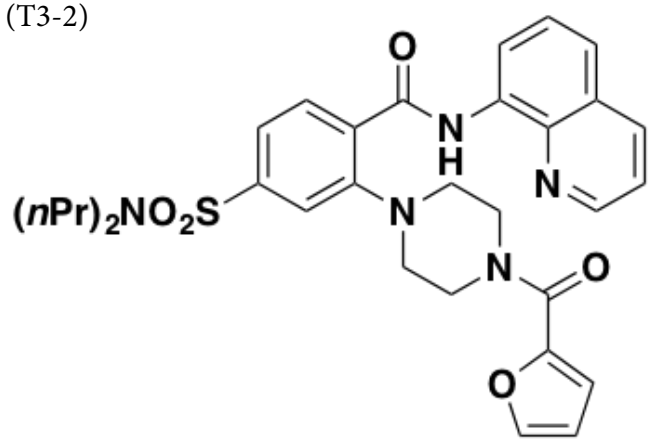

O
N
H
N
N
N
Ph
(nPr)2NO2S

164.67
151.90
148.42
143.40
138.88
137.84
136.51
135.23
132.86
132.15
129.11
128.42
128.37
127.69
127.31
122.28
121.85
121.80
117.94
117.83
62.77
53.66
51.94
50.16
22.15
11.34
f1 (ppm)
S-122

(T3-2)

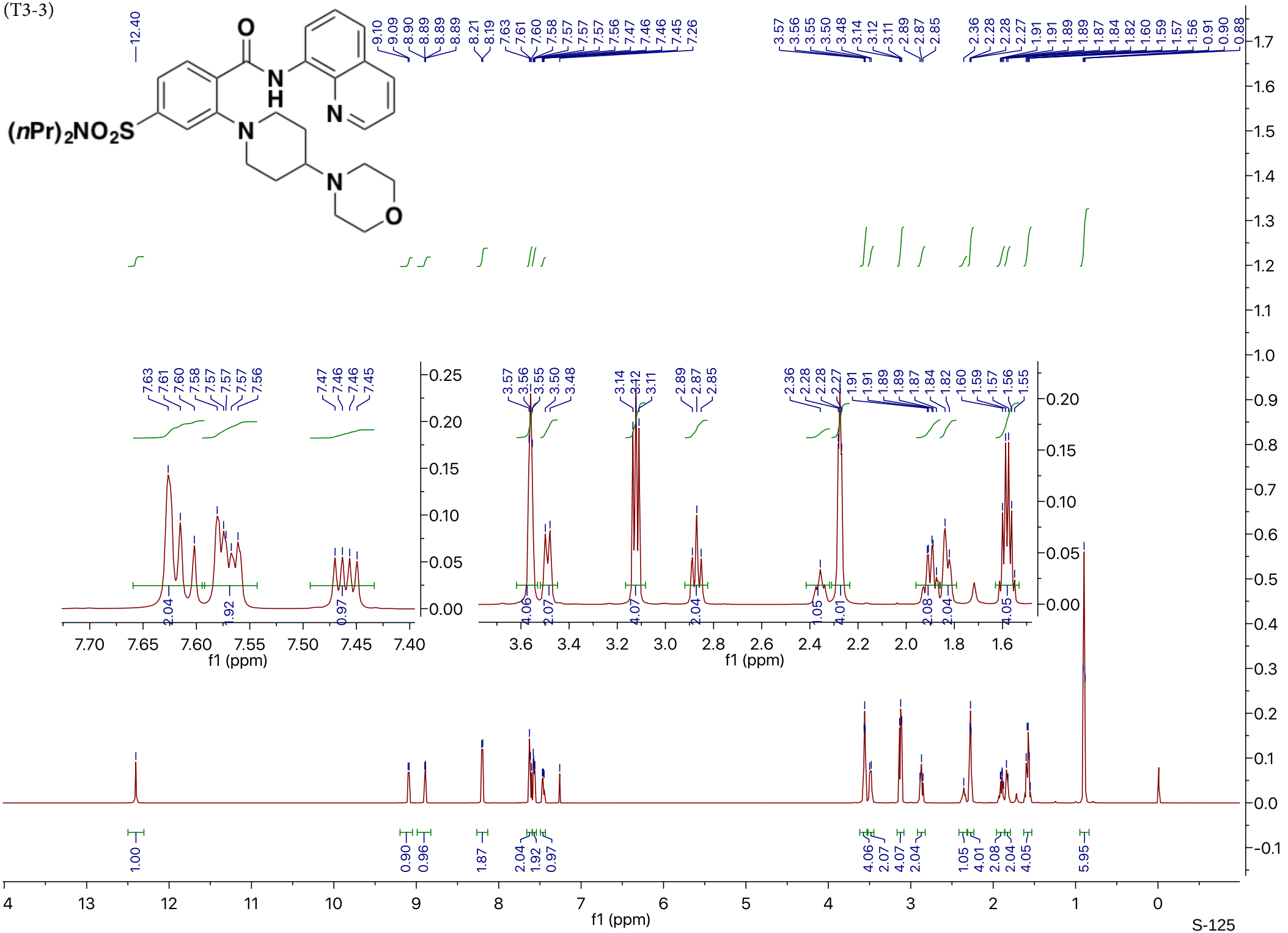

12.55
9.11 9.11 9.10 9.10 8.83 8.83 8.83 8.82 8.30 8.28 8.22 8.22 8.21 8.20 7.66 7.66 7.65 7.64 7.64 7.62 7.60 7.60 7.59 7.58 7.58 7.51 7.50 7.49 7.49 7.45 7.45 7.45 7.26 7.01 7.01 6.47 6.46 6.46 6.46 4.13 3.26 3.25 3.25 3.14 3.13 3.12 1.72 1.61 1.60 1.58 1.57 1.56 1.55 0.91 0.89 0.88
(nPr)2NO2S
O
N
H
N
N
N
O
O
8.30 8.28 8.22 8.22 8.21 8.20
7.66 7.66 7.65 7.64 7.64 7.62 7.60 7.60 7.59 7.58 7.58 7.51 7.50 7.49 7.49 7.45 7.45 7.45
0.95 0.99 4.11 1.03 0.83
f1 (ppm)
1.03 0.95 1.00 0.95 0.99 4.11 1.03 0.83 0.86 0.88 4.22 4.24 4.31 4.22 6.21
f1 (ppm)

(T3-2)

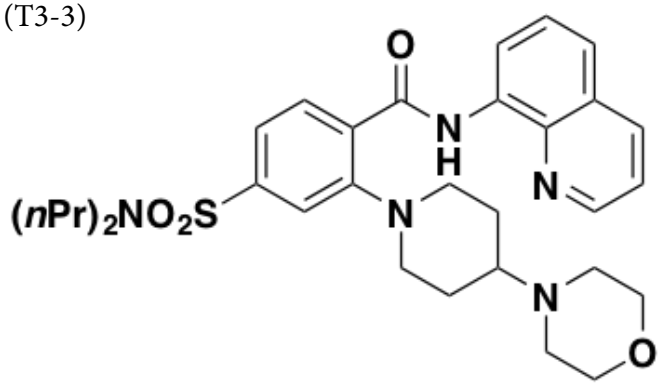

O
N
H
N
N
(nPr)2NO2S
N
O
O

164.19
159.20
151.12
148.31
147.83
143.91
143.82
138.73
136.83
135.00
133.19
132.36
128.49
127.73
122.65
122.53
122.03
118.24
118.12
117.12
111.55
53.73
50.10
22.12
11.33
f1 (ppm)
S-124

(T3-3)

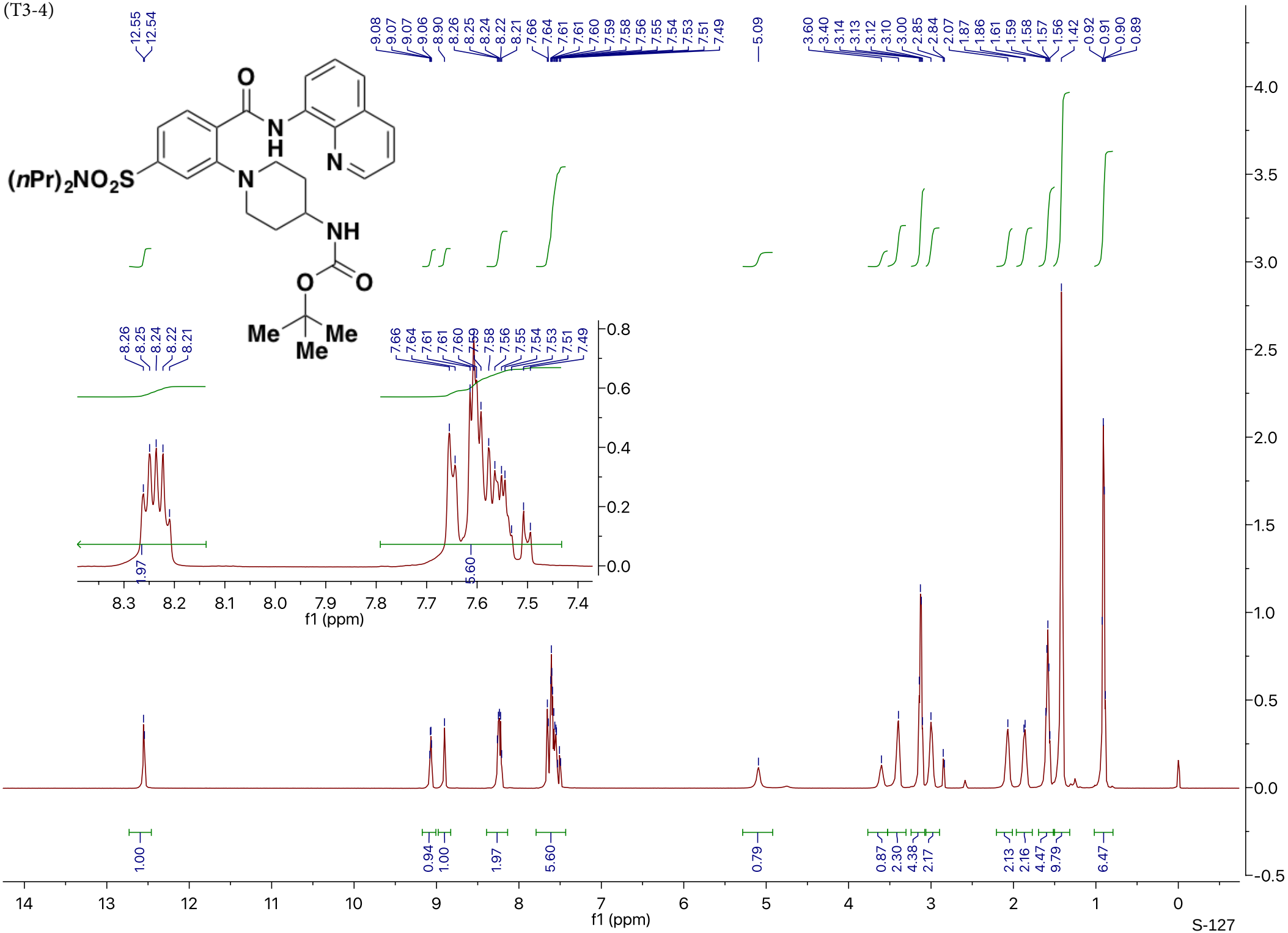


(T3-3)

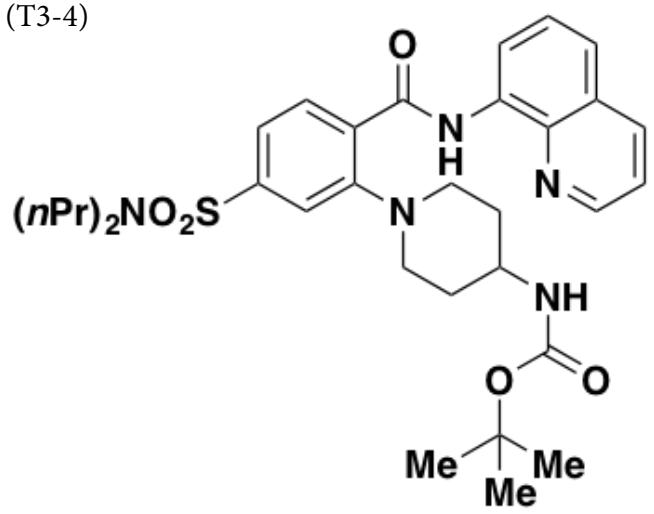

O
N
H
N
N
N
O
(nPr)2NO2S

163.72
151.15
147.51
142.32
137.92
135.68
134.21
131.74
131.19
127.39
126.75
121.52
121.28
120.60
120.50
116.94
116.91
66.39
60.24
52.65
49.15
48.44
26.34
21.15
10.34
f1 (ppm)
S-126

(T3-4)

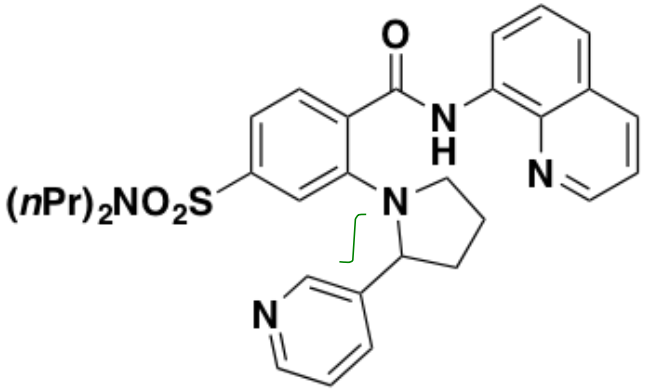

12.55
12.54
9.08
9.07
9.07
9.06
8.90
8.26
8.25
8.24
8.22
8.21
7.66
7.64
7.61
7.61
7.60
7.59
7.58
7.56
7.55
7.54
7.53
7.51
7.49
5.09
3.60
3.40
3.14
3.13
3.12
3.10
3.00
2.85
2.84
2.07
1.87
1.86
1.61
1.59
1.58
1.57
1.56
1.42
0.92
0.91
0.90
0.89
(nPr)2NO2S
O
N
H
N
N
NH
O
O
Me
Me
Me
1.97
5.60
f1 (ppm)
1.00
0.94
1.00
1.97
5.60
0.79
0.87
2.30
4.38
2.17
2.13
2.16
4.47
9.79
6.47
f1 (ppm)

(T3-4)

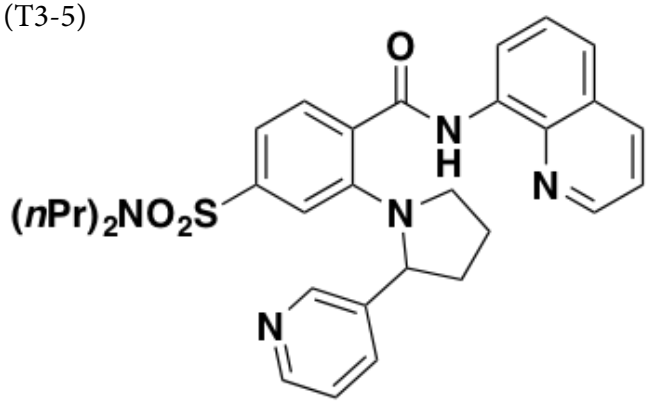

O
N
H
N
N
(nPr)2NO2S
NH
O
O
Me
Me
Me

162.19
153.18
150.13
146.15
141.10
136.62
134.51
133.00
130.58
129.98
126.23
125.39
120.20
119.83
119.56
115.91
115.73
75.76
50.52
47.96
44.74
29.25
26.36
19.93
9.16
f1 (ppm)
S-128

(T3-5)

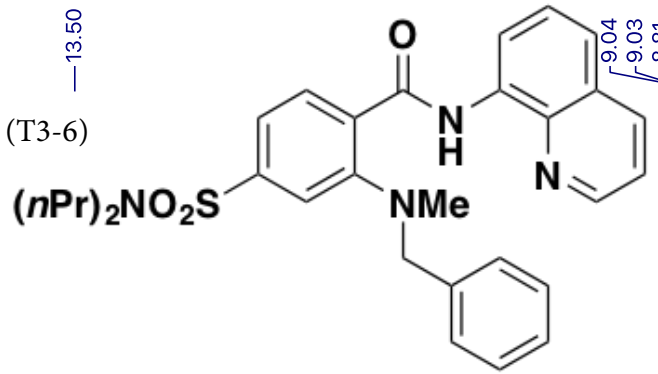


(T3-5)


O
N
H
N
N
N
(nPr)2NO2S

165.85
149.28
149.06
148.27
146.74
142.16
138.94
137.68
136.72
134.88
134.66
132.11
129.87
128.29
127.74
123.82
122.21
122.01
118.47
117.34
115.94
63.17
55.73
50.18
37.18
24.82
22.20
11.26
f1 (ppm)
S-130

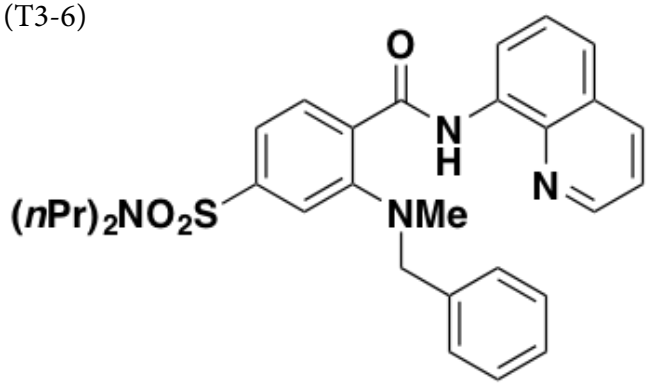
(T3-6)


O
N
H
N
(nPr)2NO2S
NMe

13.50
9.04 9.03 8.81 8.81 8.81 8.34 8.33 8.22 8.20 7.63 7.62 7.61 7.59 7.57 7.56 7.55 7.53 7.49 7.48 7.47 7.47 7.31 7.30 7.26 7.14 7.13 7.12 7.11 4.42
2.98 2.95 2.94 2.92 1.65 1.51 1.50 1.49 1.48 1.46 1.45 0.85 0.84 0.83
1.00 0.99 1.01 1.00 1.02 1.08 1.02 1.04 0.98 1.02 2.01 3.02 2.00 3.06 3.98 3.97 5.95
f1 (ppm)
S-131

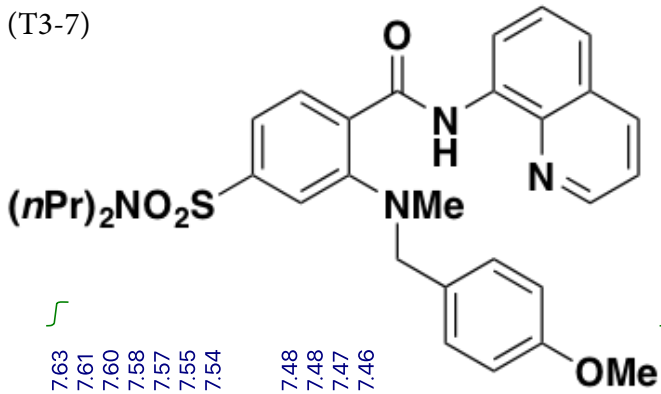
7.63 7.62 7.61 7.59 7.57 7.56 7.55 7.53 7.49 7.48 7.47 7.47 7.31 7.30 7.26 7.14 7.13 7.12 7.11
1.08 1.02 1.04 0.98 1.02 2.01 3.02
f1 (ppm)

(T3-6)


O
N
H
N
(nPr)2NO2S
NMe

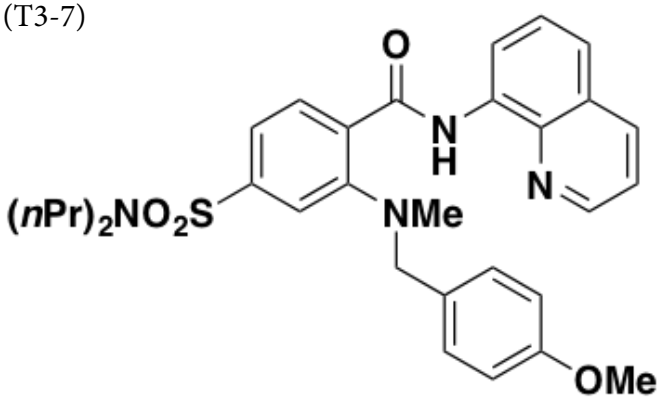
164.02
150.84
148.59
142.86
139.65
136.55
136.20
135.65
132.88
132.32
129.38
128.55
128.46
127.79
127.69
122.21
121.96
121.84
120.64
117.93
60.69
50.17
44.20
22.23
11.40
f1 (ppm)
f1 (ppm)

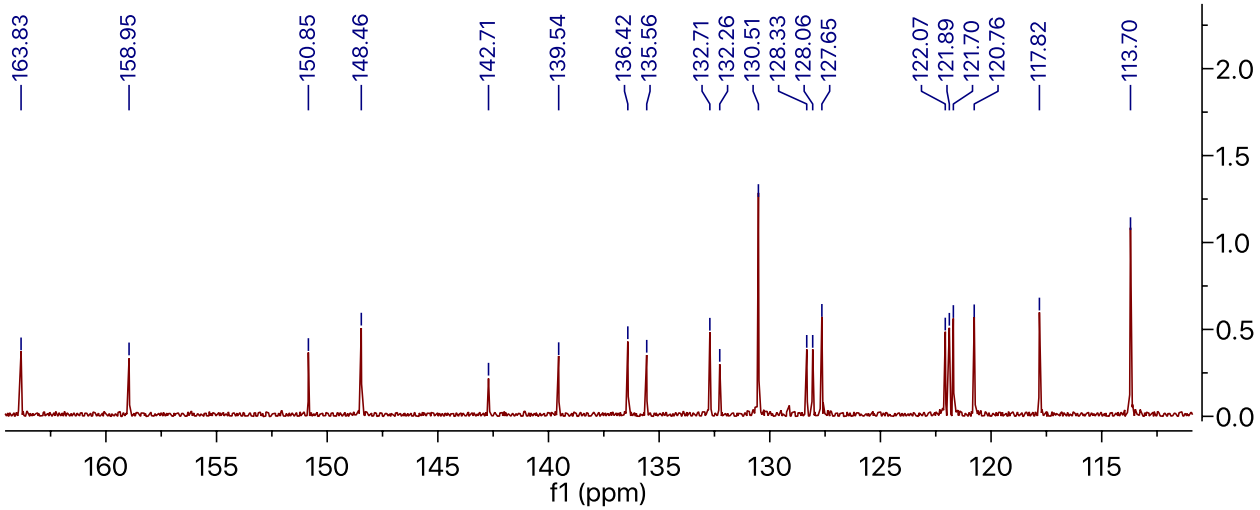
(T3-7)


O
N
H
N
(nPr)2NO2S
NMe
OMe

13.60
9.04
9.03
8.82
8.82
8.81
8.81
8.35
8.34
8.21
8.21
8.20
8.20
7.63
7.61
7.60
7.58
7.57
7.55
7.54
7.48
7.48
7.47
7.46
7.26
7.20
7.19
6.64
6.62
4.35
3.67
2.99
2.98
2.96
2.96
1.52
1.51
1.49
1.48
0.86
0.85
0.83
f1 (ppm)
S-133

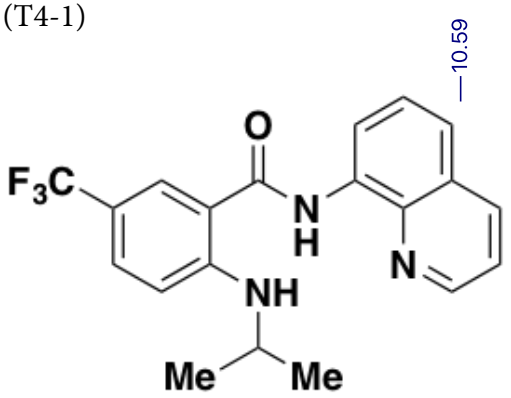
(T3-7)


O
N
H
N
(nPr)2NO2S
NMe
OMe


163.83
158.95
150.85
148.46
142.71
139.54
136.42
135.56
132.71
132.26
130.51
128.33
128.06
127.65
122.07
121.89
121.70
120.76
117.82
113.70
f1 (ppm)

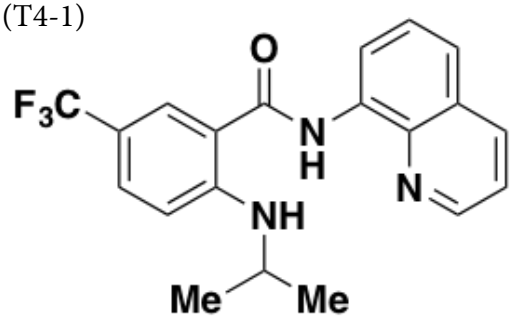
163.83
158.95
150.85
148.46
142.71
139.54
136.42
135.56
132.71
132.26
130.51
128.33
128.06
127.65
122.07
121.89
121.70
120.76
117.82
113.70
60.07
55.17
50.04
43.78
22.09
f1 (ppm)

(T4-1)


O
F3C
N
H
N
NH
Me
Me

10.59
8.86 8.86 8.86 8.78 8.77 8.76 8.76 8.19 8.19 8.18 8.18 8.07 8.06 7.99 7.60 7.58 7.57 7.56 7.56 7.56 7.56 7.55 7.54 7.50 7.49 7.48 7.48 7.26 6.80 6.79 3.79 3.78 3.77 3.76 3.75 3.74
1.59 1.32 1.31
7.60 7.58 7.57 7.56 7.56 7.56 7.56 7.55 7.55 7.54
7.50 7.49 7.48 7.48
0.4 0.3 0.2 0.1 0.0
7.62 7.60 7.58 7.56 7.54 7.52 7.50 7.48
f1 (ppm)
1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6 0.5 0.4 0.3 0.2 0.1 0.0 -0.1
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

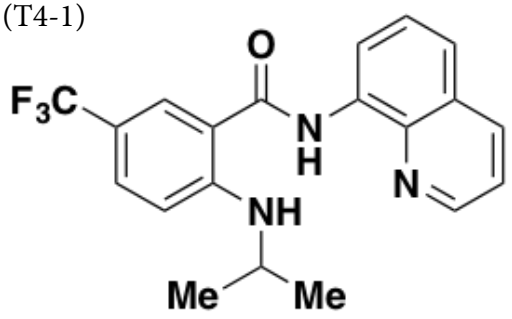
(T4-1)



167.51
151.43
148.60
138.92
136.46
134.51
129.89
129.87
128.12
127.36
125.92
125.73
125.70
123.77
121.89
116.55
116.27
116.00
115.74
115.48
114.40
111.96
43.68
22.68

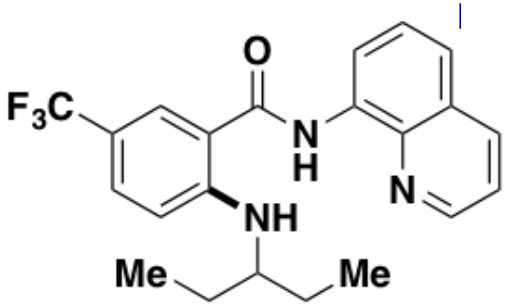
f1 (ppm)

(T4-1)


O
F3C
N
H
N
NH
Me
Me

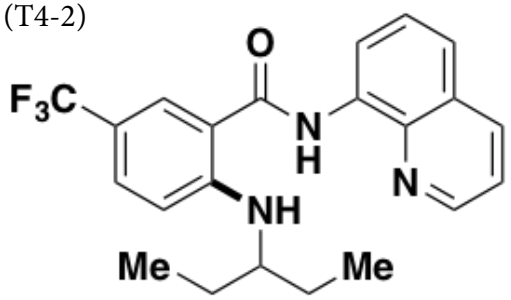
-60.85
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(T4-2)


O
F3C
N
H
N
NH
Me
Me

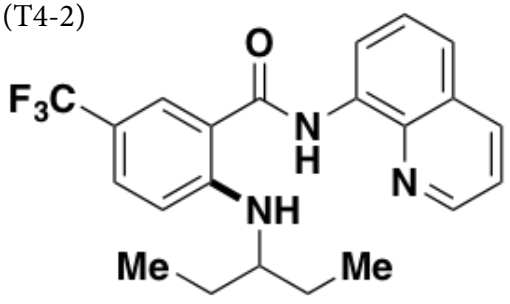
10.60
8.87 8.87 8.86 8.78 8.77 8.20 8.19 8.18 8.14 8.13 8.00 7.60 7.58 7.57 7.56 7.54 7.53 7.50 7.49 7.49 7.48 7.26 6.80 6.78
3.43 3.42 3.41 3.40 3.39 3.38 1.72 1.70 1.69 1.68 1.67 1.66 1.65 1.63 1.62 1.61 1.60 1.59 1.58 1.57 1.56 1.00 0.98 0.97
f1 (ppm)
1.00 0.91 0.89 0.93 0.98 1.00 0.96 1.86 0.97 1.03 1.01 4.30 6.03
S-138

(T4-2)


O
F3C
N
H
N
NH
Me
Me

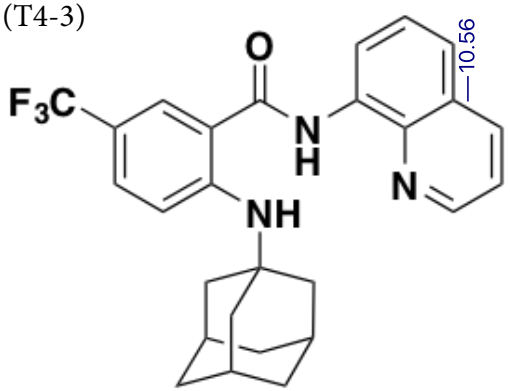
167.62
152.48
148.62
138.96
136.49
134.59
129.89
129.87
128.16
127.41
125.87
125.85
125.83
125.80
124.01
121.92
121.86
116.59
115.71
115.49
114.18
111.96
55.18
26.95
10.44
f1 (ppm)
S-139

(T4-2)

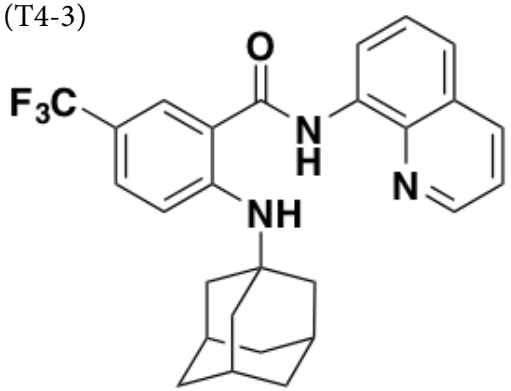

O
F3C
N
H
N
NH
Me
Me

-60.85
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(T4-3)



(T4-3)

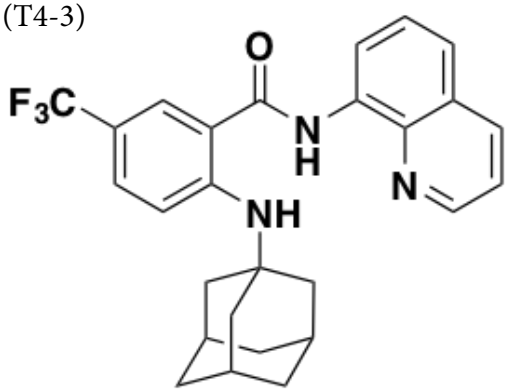


167.80
151.18
148.60
138.95
136.48
134.61
128.93
128.91
128.89
128.86
127.43
126.06
126.03
126.00
125.98
125.77
123.98
121.90
121.87
116.65
115.82
115.76
114.85
52.09
42.36
36.56
29.70

f1 (ppm)

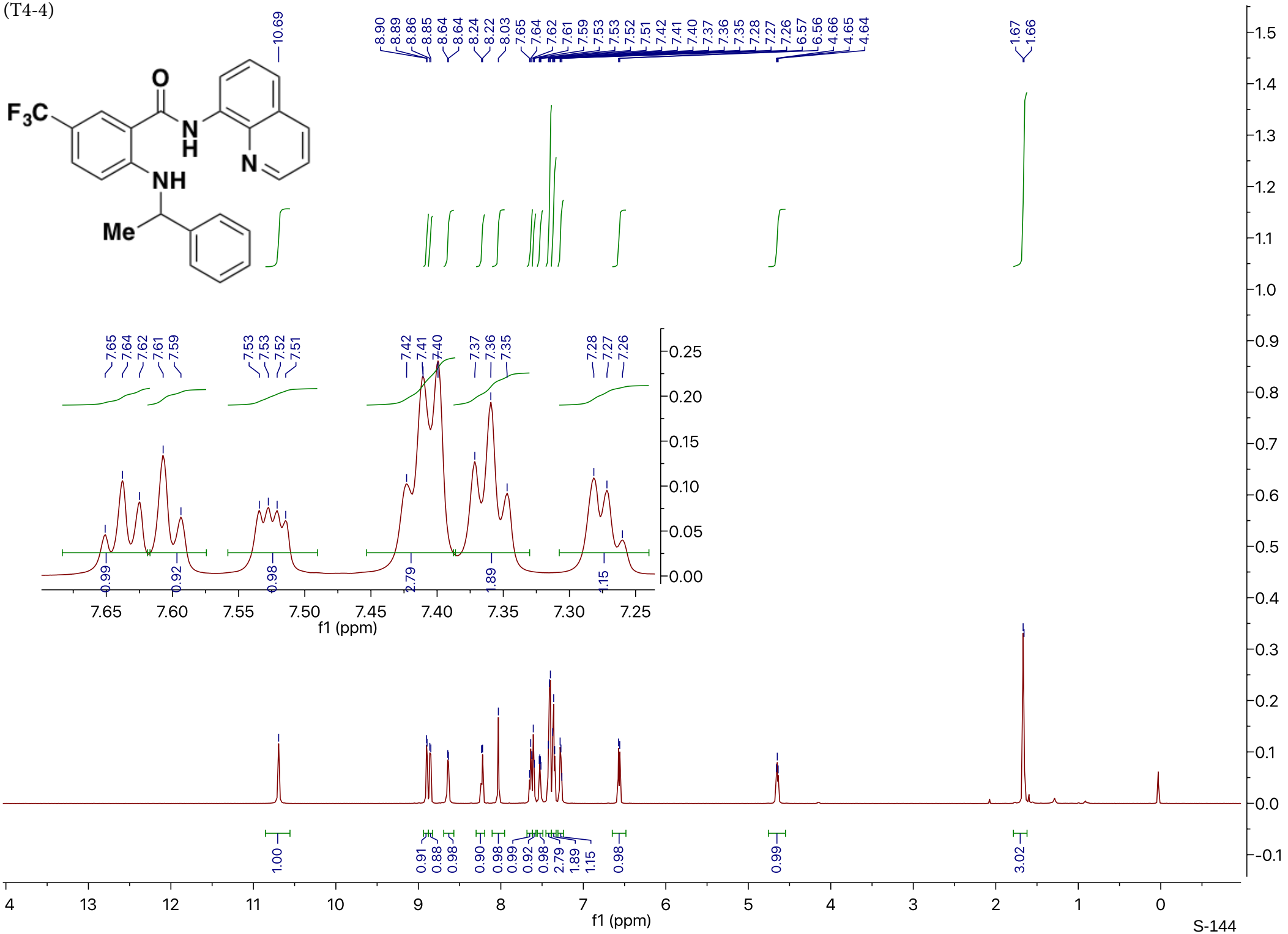
S-142

(T4-3)

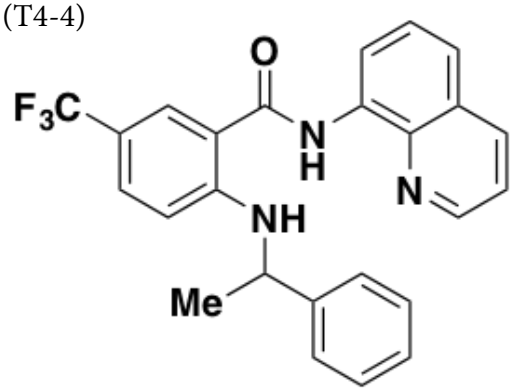

O
F3C
N
H
N
NH

-60.95
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(T4-4)

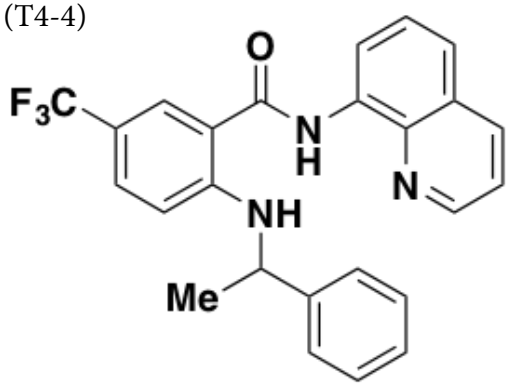

F3C
O
N
H
NH
N
Me
10.69
8.90
8.89
8.86
8.85
8.64
8.64
8.24
8.22
8.03
7.65
7.64
7.62
7.61
7.59
7.53
7.53
7.52
7.51
7.42
7.41
7.40
7.37
7.36
7.35
7.28
7.27
7.26
6.57
6.56
4.66
4.65
4.64
1.67
1.66
0.99
0.92
0.98
2.79
1.89
1.15
f1 (ppm)
1.00
0.91
0.88
0.98
0.90
0.98
0.99
0.92
0.98
2.79
1.89
1.15
0.98
0.99
3.02
f1 (ppm)

(T4-4)


O
F3C
N
H
N
NH
Me

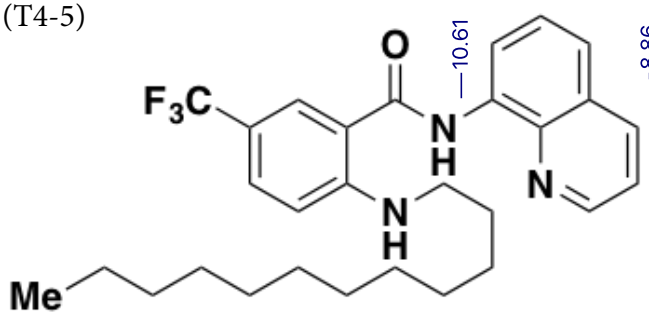
167.48
151.34
148.64
144.31
138.94
136.48
134.47
129.77
129.75
128.96
128.14
127.39
127.26
125.83
125.63
125.36
125.34
123.84
122.02
121.93
117.06
116.84
116.65
116.40
114.91
113.20
53.09
25.21
f1 (ppm)
S-145

(T4-4)


O
F3C
N
H
N
NH
Me

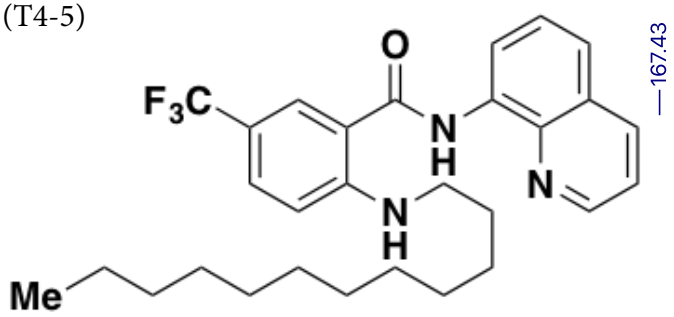
-60.98
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(T4-5)

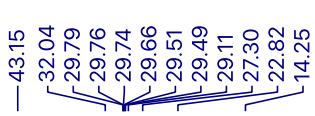

O
10.61
F3C
N
H
N
N
H
Me

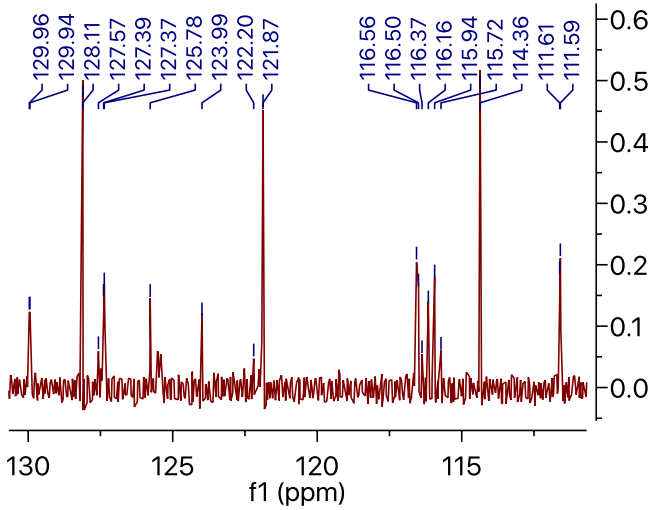
8.86 8.85 8.79 8.78 8.18 8.17 8.15 7.99 7.59 7.58 7.56 7.55 7.54 7.53 7.48 7.48 7.47 7.46 7.26 6.78 6.76
3.24 3.23 3.22 3.20 1.73 1.72 1.70 1.69 1.46 1.45 1.43 1.42 1.35 1.34 1.28 1.26 0.89 0.88 0.87
0.98 1.00 1.01 2.08 1.04 3.11 1.06 1.04 2.07 2.22 2.37 24.21 4.85
f1 (ppm)

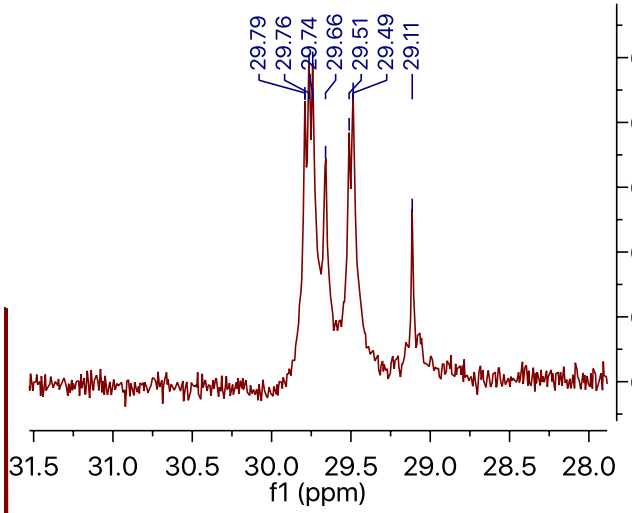
(T4-5)

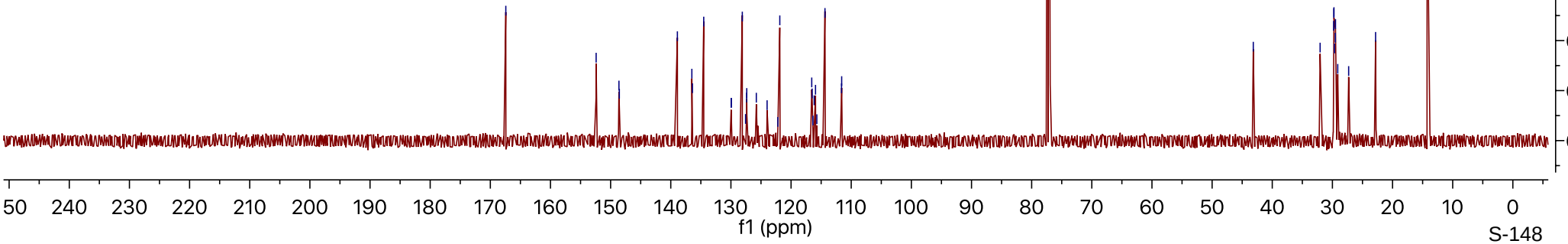

O
F3C
N
H
N
N
H
Me


152.41
148.62
148.55
138.90
136.50
136.40
134.52
129.96
129.94
128.11
127.57
127.39
127.37
125.78
123.99
122.20
121.87
116.56
116.50
116.37
116.16
115.94
115.72
114.36
111.61
111.59
167.43

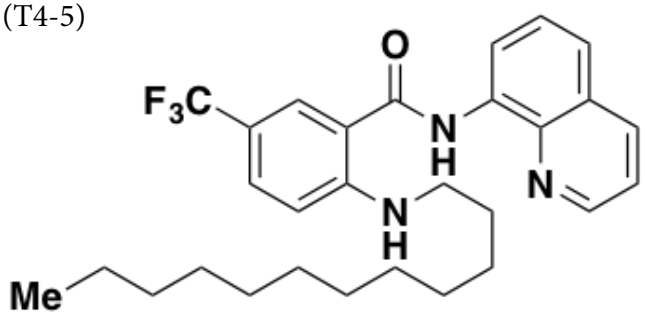

43.15
32.04
29.79
29.76
29.74
29.66
29.51
29.49
29.11
27.30
22.82
14.25


129.96
129.94
128.11
127.57
127.39
127.37
125.78
123.99
122.20
121.87
116.56
116.50
116.37
116.16
115.94
115.72
114.36
111.61
111.59
130
125
120
115
f1 (ppm)


29.79
29.76
29.74
29.66
29.51
29.49
29.11
31.5
31.0
30.5
30.0
29.5
29.0
28.5
28.0
f1 (ppm)

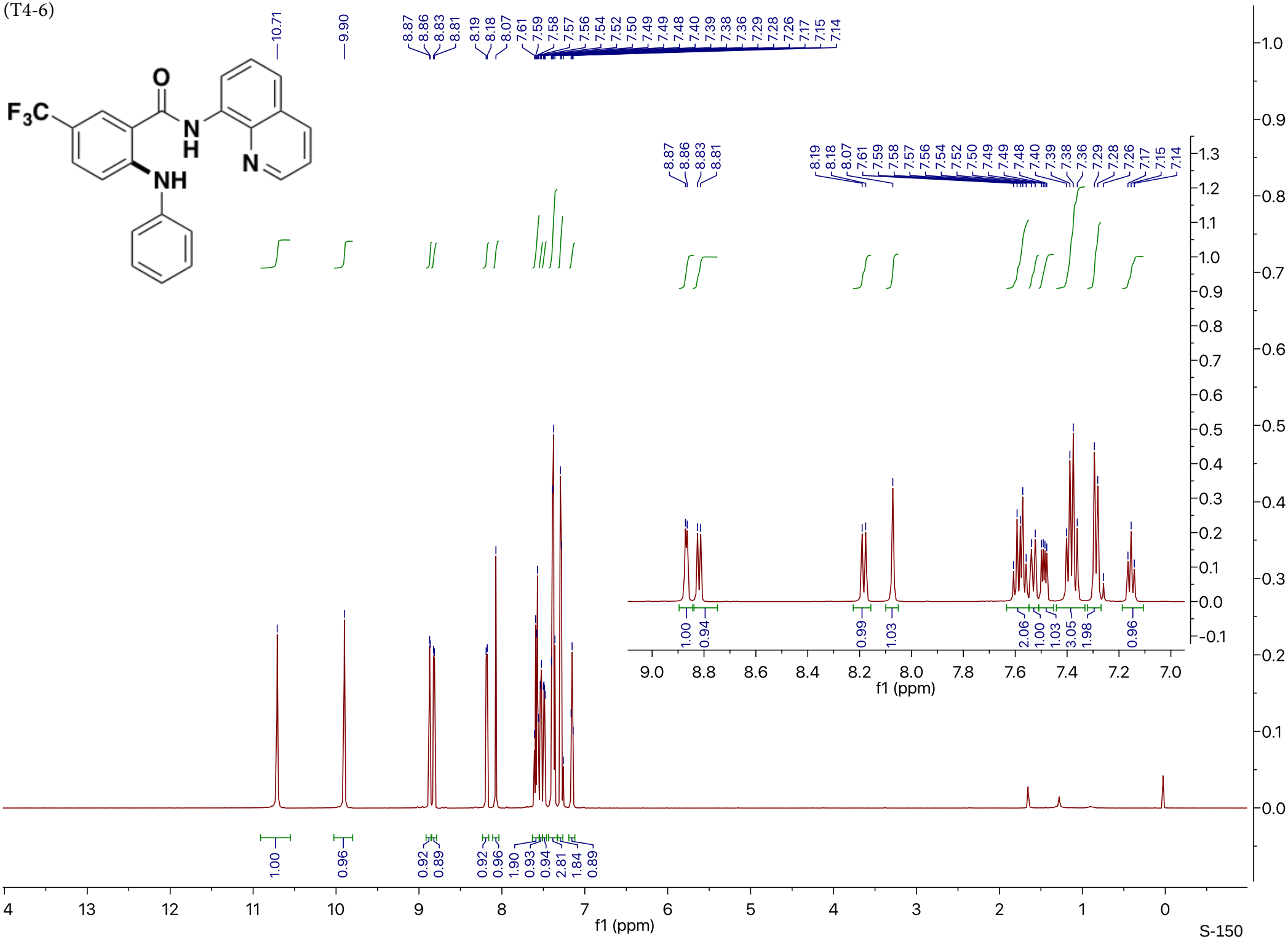

50
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

(T4-5)

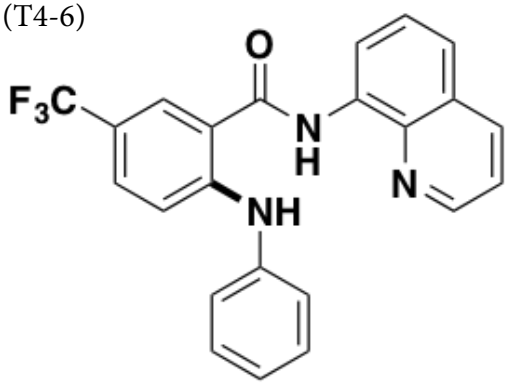

O
F3C
N
H
N
N
H
Me

-60.81
25
24
23
22
21
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(T4-6)


F3C
O
N
H
NH
N
10.71
9.90
8.87
8.86
8.83
8.81
8.19
8.18
8.07
7.61
7.59
7.58
7.57
7.56
7.54
7.52
7.50
7.49
7.49
7.48
7.40
7.39
7.38
7.36
7.29
7.28
7.26
7.17
7.15
7.14
1.00
0.96
0.92
0.89
0.92
0.96
1.90
0.93
0.94
2.81
1.84
0.89
f1 (ppm)
1.00
0.94
0.99
1.03
2.06
1.00
1.03
3.05
1.98
0.96
f1 (ppm)

(T4-6)



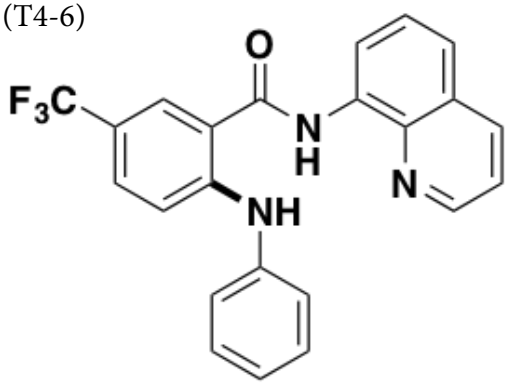
167.02

149.45 148.67 140.04 138.86 136.49 134.26 129.64 129.46 129.44 128.09 127.34 127.18 125.51 125.48 125.39 124.38 123.59 122.85 122.23 121.95 121.80 119.44 119.22 119.00 118.78 117.04 116.72 114.68

f1 (ppm)

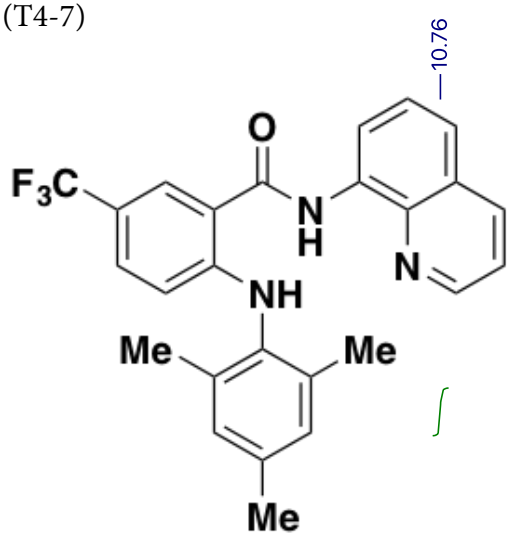
f1 (ppm)

(T4-6)


O
F3C
N
H
NH
N

30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
-2
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

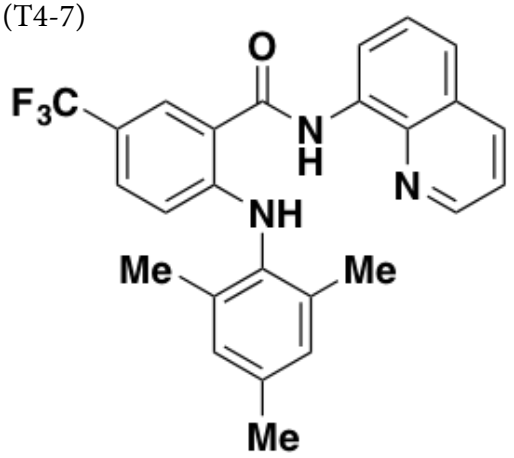
(T4-7)


O
F3C
N
H
N
NH
Me
Me
Me

10.76
9.44
8.90
8.90
8.90
8.89
8.85
8.85
8.84
8.84
8.22
8.22
8.21
8.21
8.08
7.62
7.61
7.59
7.59
7.58
7.57
7.57
7.53
7.52
7.51
7.51
7.42
7.40
7.26
6.98
6.35
6.33
2.33
2.20
1.14
1.09
1.02
1.00
1.03
1.14
2.14
1.08
1.05
2.08
1.04
3.36
6.77
f1 (ppm)

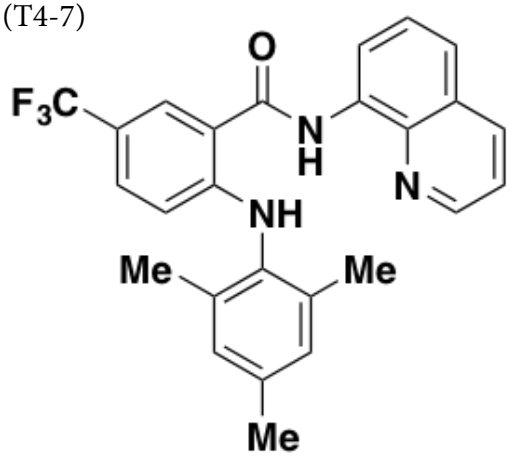
7.62
7.61
7.59
7.59
7.58
7.57
7.57
7.53
7.52
7.51
7.51
2.14
1.08
7.65
7.60
7.55
7.50
f1 (ppm)

(T4-7)


O
F3C
N
H
N
NH
Me
Me
Me

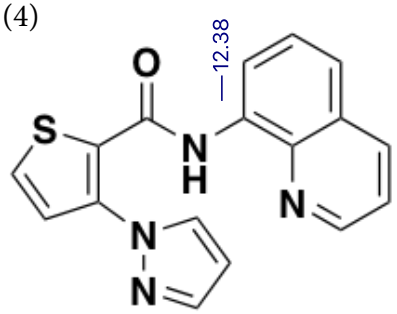
167.44
151.60
148.69
138.97
136.66
136.56
136.38
134.50
133.89
129.83
129.81
129.42
128.18
127.44
125.64
125.58
125.55
123.85
122.06
121.98
117.56
117.34
116.66
116.66
114.64
113.27
21.12
18.31
f1 (ppm)
f1 (ppm)

(T4-7)

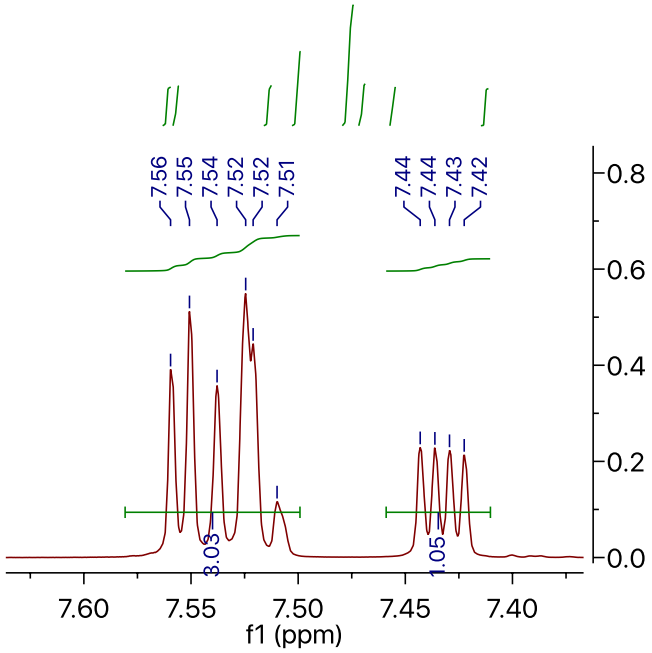

O
F3C
N
H
N
NH
Me
Me
Me

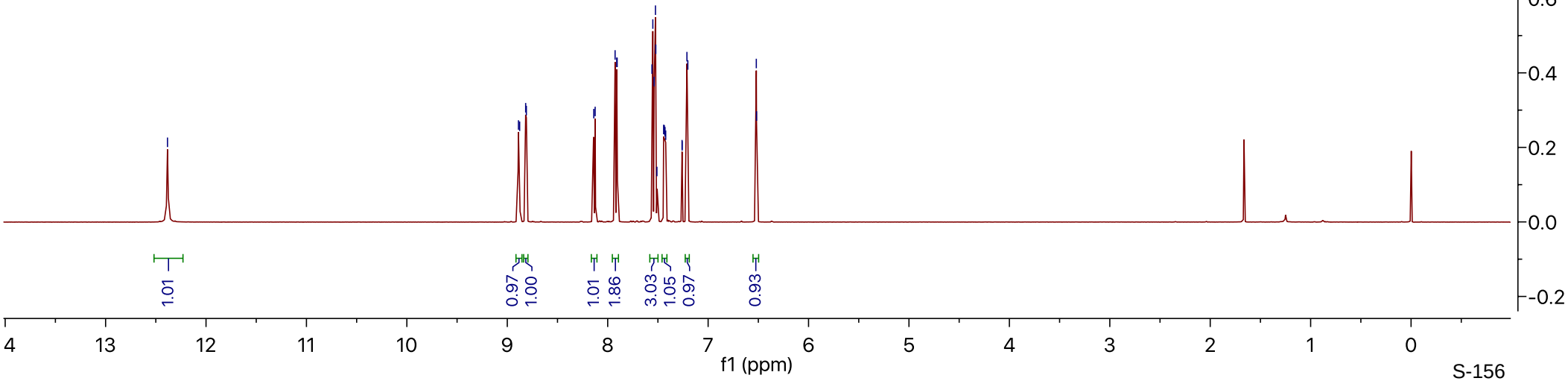
-60.97
11
10
9
8
7
6
5
4
3
2
1
0
-1
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(4)

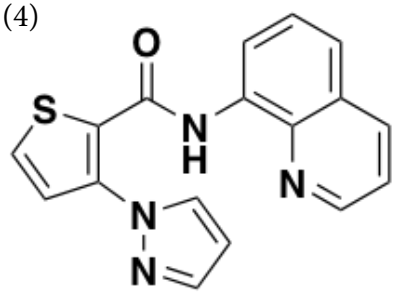

O
S
N
H
N
N
N


12.38
8.89
8.88
8.82
8.81
8.14
8.12
7.93
7.91
7.91
7.56
7.55
7.54
7.52
7.52
7.51
7.44
7.44
7.43
7.42
7.26
7.21
7.20
6.52
6.52


7.56
7.55
7.54
7.52
7.52
7.51
7.44
7.44
7.43
7.42
3.03
1.05
7.60
7.55
7.50
7.45
7.40
f1 (ppm)


1.01
0.97
1.00
1.01
1.86
3.03
1.05
0.97
0.93
f1 (ppm)

(4)

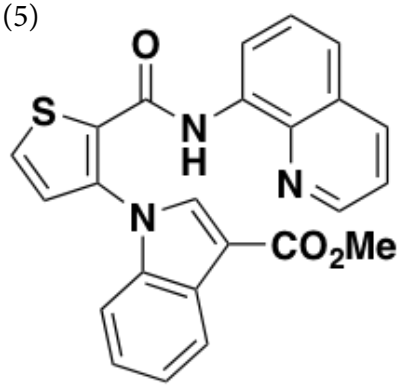


159.36
148.19
141.63
139.64
136.25
136.12
135.52
131.15
130.86
129.92
128.25
127.45
125.05
122.37
121.62
118.29
107.84

f1 (ppm)

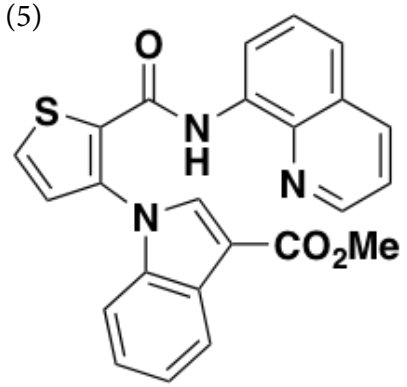
S-157

(5)


O
S
N
H
N
N
CO2Me

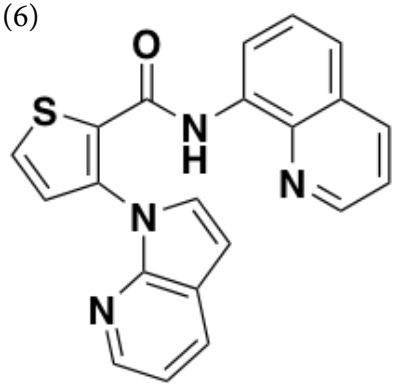
10.14
8.72
8.71
8.37
8.35
8.05
8.01
8.01
8.00
8.00
7.95
7.95
7.94
7.94
7.70
7.69
7.45
7.44
7.43
7.39
7.38
7.32
7.31
7.30
7.26
7.25
7.23
7.22
7.22
7.21
7.20
7.14
7.13
3.90
1.02
1.00
0.98
0.91
1.04
1.02
0.94
1.10
1.08
2.12
2.29
1.04
3.16
f1 (ppm)

(5)


O
S
N
H
N
N
CO2Me

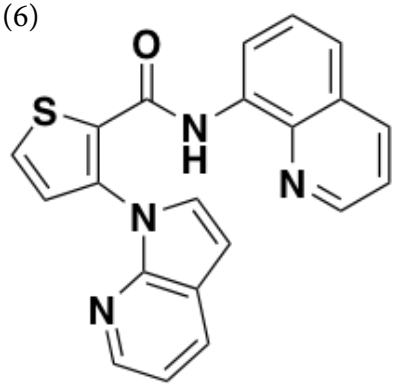
165.23
158.05
147.74
138.19
138.12
135.77
135.18
134.65
134.50
133.82
130.26
128.29
127.57
127.39
127.09
124.21
123.02
122.04
121.76
121.64
116.64
111.11
111.09
51.32
f1 (ppm)
f1 (ppm)

(6)


O
S
N
H
N
N
N

10.20
8.76 8.76 8.75 8.75 8.35 8.35 8.34 8.34 8.06 8.05 8.04 8.04 7.98 7.98 7.97 7.97 7.93 7.93 7.93 7.92 7.65 7.65 7.64 7.48 7.46 7.45 7.42 7.41 7.41 7.40 7.39 7.39 7.26 7.25 7.24 7.24 7.22 7.21 7.20 7.20 7.17 7.16 7.15 7.14 6.69 6.69
7.65 7.65 7.64 7.48 7.46 7.45 7.42 7.41 7.41 7.40 7.39 7.39 7.26 7.25 7.24 7.24 7.22 7.21 7.20 7.17 7.16 7.15 7.14
0.94 1.12 2.07 1.18 1.11 1.10
7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15
f1 (ppm)
1.04 1.00 0.98 1.02 1.06 1.05 0.94 1.12 2.07 1.18 1.11 1.10 0.99
13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

(6)



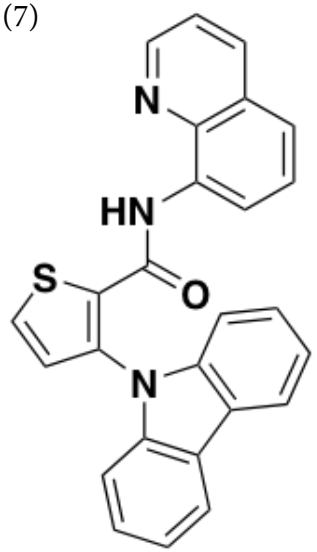
158.99
149.07
147.44
144.32
138.27
135.88
135.21
134.20
133.51
129.42
129.31
129.04
128.37
127.67
127.29
121.72
121.66
121.40
117.13
116.65
103.39

138.27
135.88
135.21
134.20
133.51
129.42
129.31
129.04
128.37
127.67
127.29
121.72
121.66
121.40
117.13
116.65

f1 (ppm)

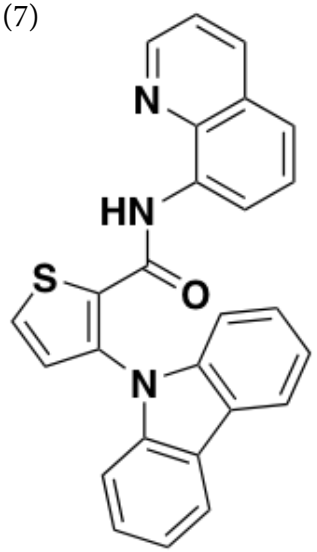
f1 (ppm)

(7)


N
HN
S
O
N

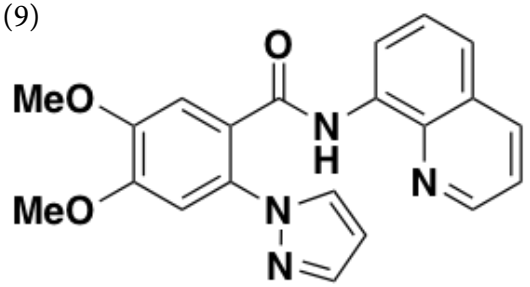
10.68
8.72
8.70
8.23
8.22
7.84
7.84
7.83
7.82
7.75
7.74
7.63
7.63
7.62
7.62
7.41
7.40
7.38
7.37
7.36
7.33
7.31
7.31
7.31
7.29
7.28
7.26
7.10
7.09
7.08
7.07
7.06
7.05
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-0.1
7.41
7.40
7.38
7.37
7.36
7.33
7.31
7.31
7.31
7.29
7.28
7.26
7.10
7.09
7.08
7.07
7.06
7.05
0.5
0.4
0.3
0.2
0.1
0.0
3.25
5.21
1.00
1.07
7.40
7.35
7.30
7.25
7.20
7.15
7.10
7.05
f1 (ppm)
1.05
1.00
2.09
1.05
0.97
1.03
3.25
5.21
1.00
1.07
4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

(7)


N
HN
S
O
N

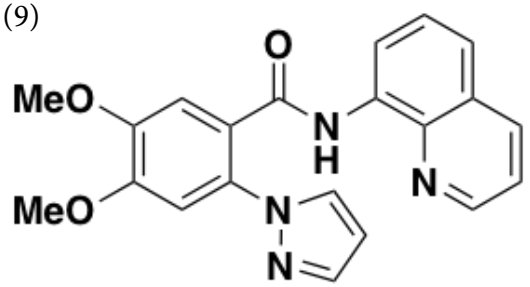
158.68
147.29
141.74
138.19
136.51
135.51
134.59
134.13
130.63
128.31
127.46
127.05
126.59
124.98
121.64
121.31
121.00
120.16
116.51
110.58
77.36
f1 (ppm)
S-163

(9)


O
MeO
MeO
N
H
N
N
N

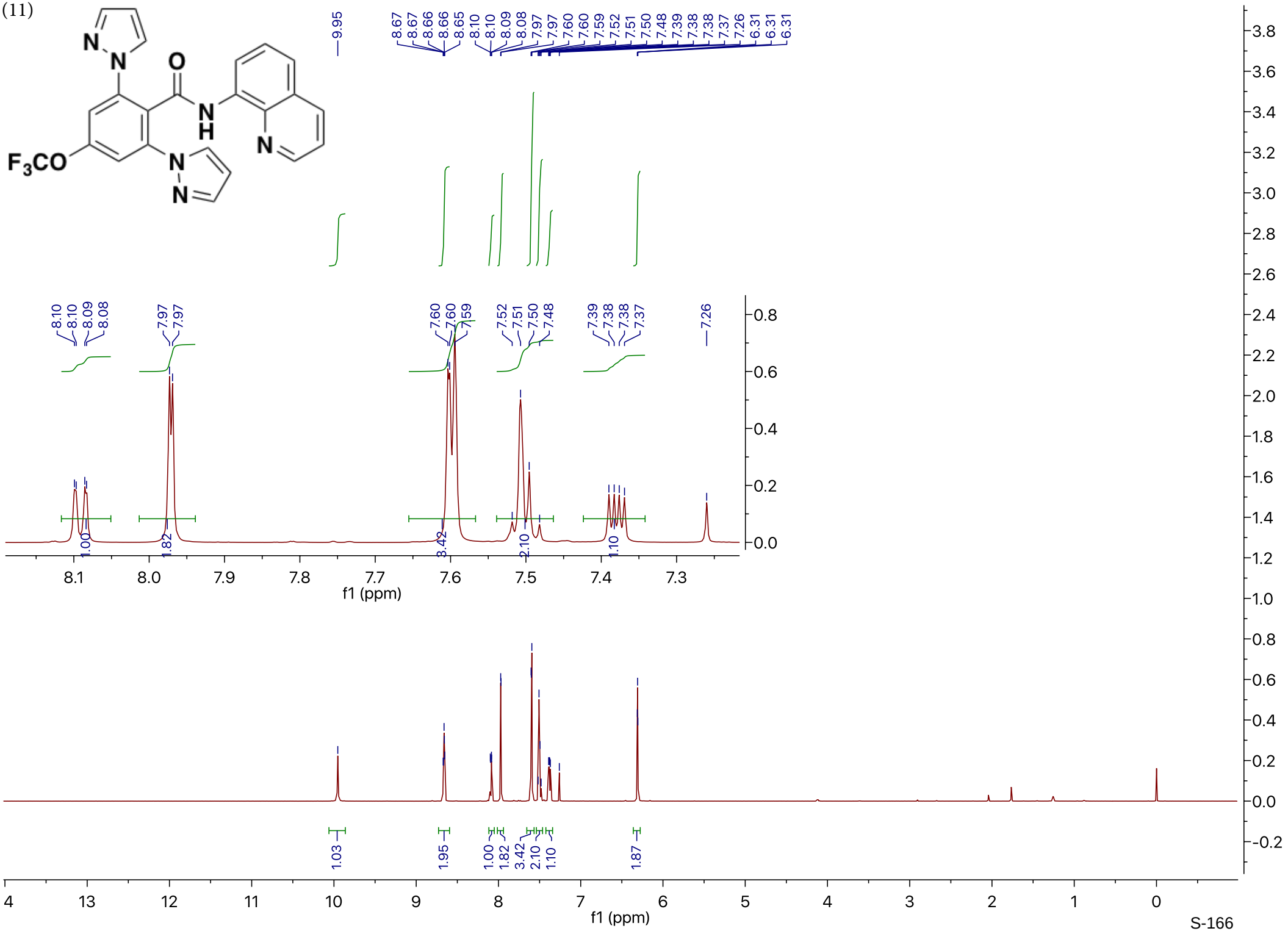
9.88 8.80 8.80 8.79 8.79 8.67 8.66 8.66 8.66 8.10 8.09 8.08 8.08 7.69 7.69 7.65 7.65 7.53 7.52 7.50 7.49 7.49 7.47 7.47 7.41 7.39 7.39 7.38 7.37 7.26 7.08 6.22 6.21 6.21 3.99 3.97
7.69 7.69 7.65 7.65 7.53 7.52 7.50 7.49 7.49 7.47 7.47 7.41 7.39 7.39 7.38 7.37
0.94 0.87 1.10 1.05 1.04 1.08
7.70 7.65 7.60 7.55 7.50 7.45 7.40
f1 (ppm)
1.03 0.98 1.00 1.02 0.94 0.87 1.10 1.05 1.04 1.08 1.05 0.95 3.48 3.35
4 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

(9)

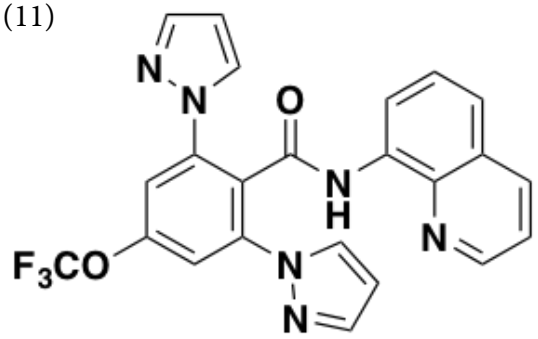

O
MeO
MeO
N
H
N
N
N

165.04
151.16
148.92
148.02
141.30
138.45
136.06
134.60
131.87
131.44
127.84
127.28
124.40
121.94
121.70
116.56
111.84
109.44
107.50
56.46
56.45
f1 (ppm)
S-165

(11)

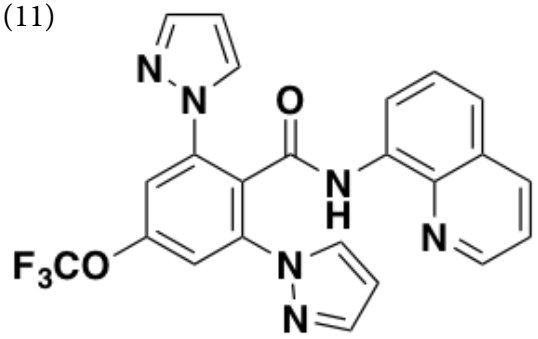


(11)


N
N
O
N
H
N
F3CO
N
N

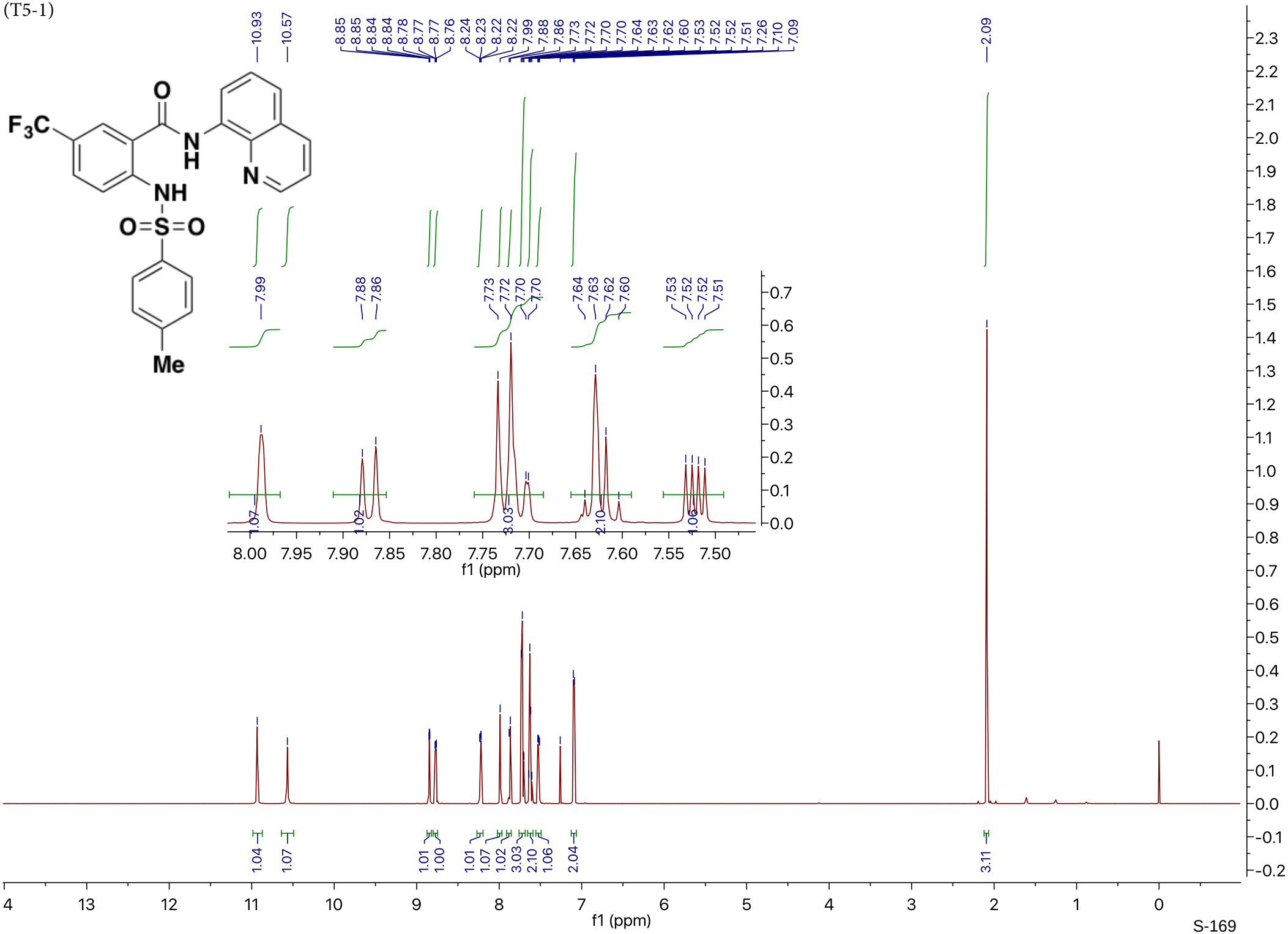
162.58
150.00
148.46
142.14
140.34
138.32
136.15
133.97
130.85
127.84
127.18
124.97
122.61
121.86
121.27
119.55
116.86
116.61
108.30
f1 (ppm)
S-167

(11)

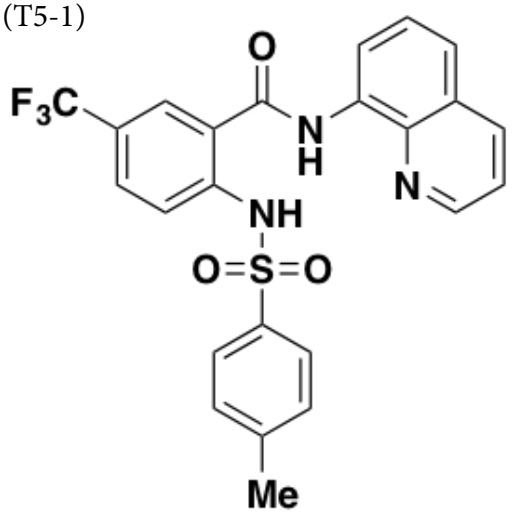

N
N
O
N
H
N
F3CO
N
N

-57.47
26
24
22
20
18
16
14
12
10
8
6
4
2
0
-2
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(T5-1)

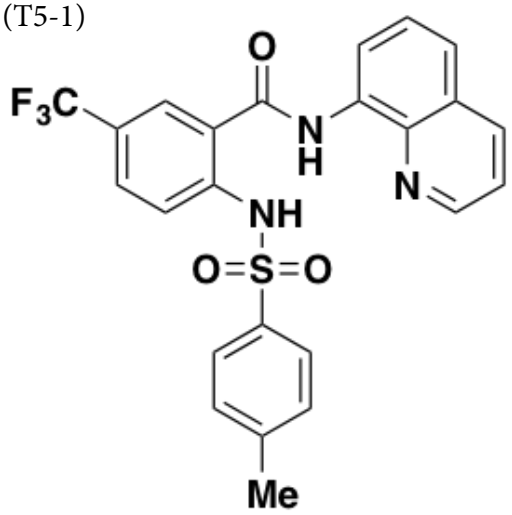

F3C
O
N
H
N
NH
O=S=O
Me
10.93
10.57
8.85
8.85
8.84
8.84
8.78
8.77
8.77
8.76
8.24
8.23
8.22
8.22
7.99
7.88
7.86
7.73
7.72
7.70
7.70
7.64
7.63
7.62
7.60
7.53
7.52
7.52
7.51
7.26
7.10
7.09
2.09
1.07
1.02
3.03
2.10
1.06
f1 (ppm)
1.04
1.07
1.01
1.00
1.01
1.07
1.02
3.03
2.10
1.06
2.04
3.11
f1 (ppm)

(T5-1)


O
F3C
N
H
N
NH
O=S=O
Me

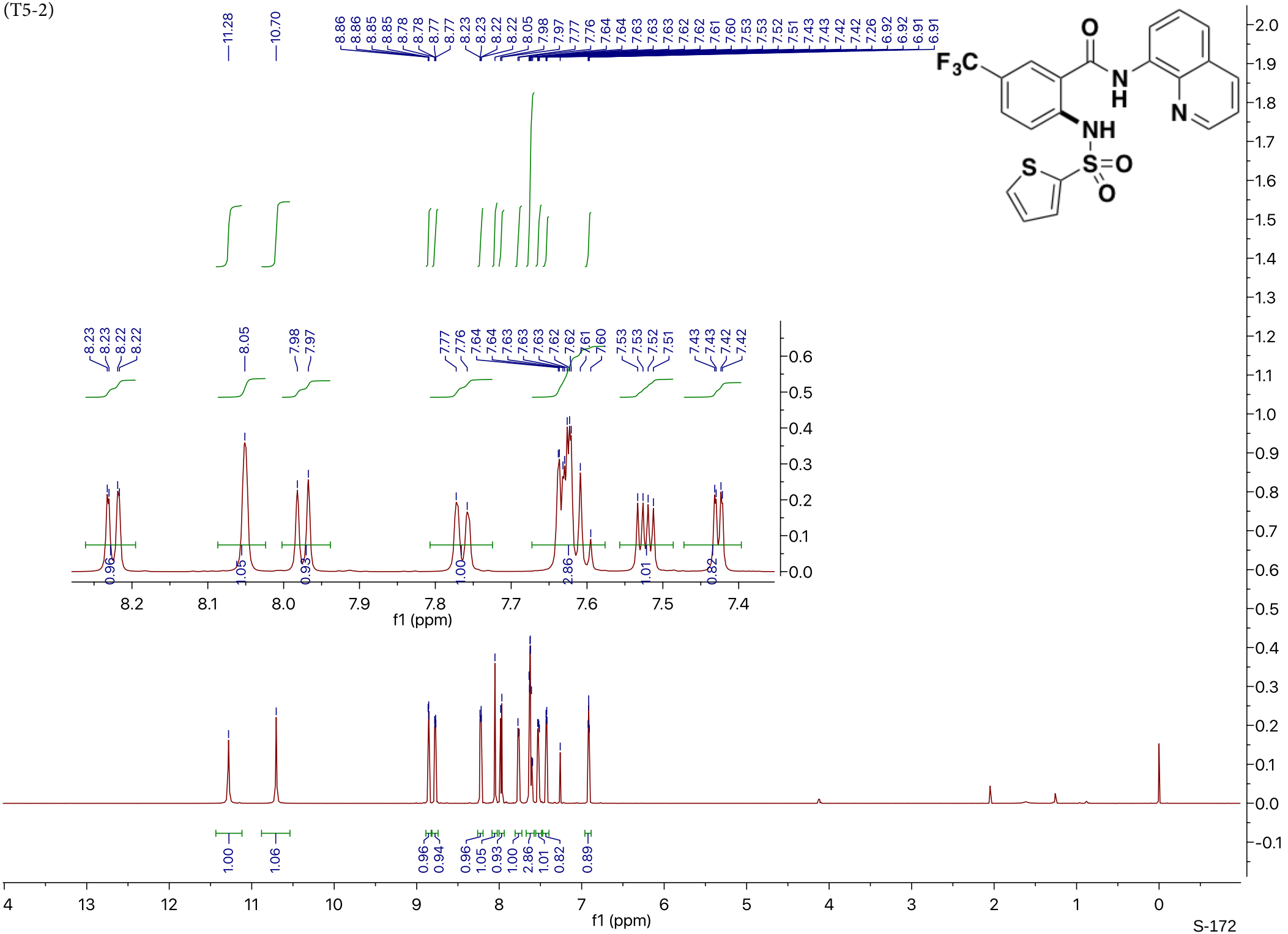
165.47
148.84
144.24
142.29
138.62
136.68
136.18
133.48
129.86
129.73
129.70
129.68
129.65
128.05
127.41
127.34
125.76
125.54
124.55
124.39
124.36
124.33
123.01
122.74
122.23
122.15
121.44
117.21
21.36
f1 (ppm)
S-170

(T5-1)

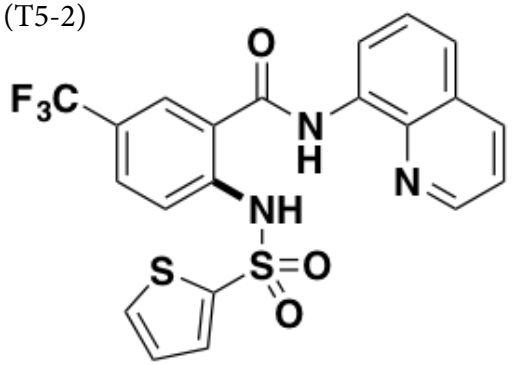

O
F3C
N
H
N
NH
O=S=O
Me

-62.10
26
24
22
20
18
16
14
12
10
8
6
4
2
0
-2
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(T5-2)

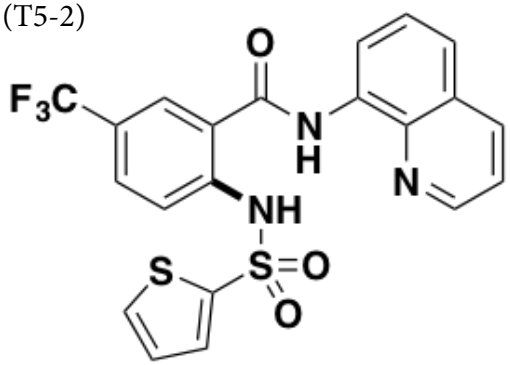

11.28
10.70
8.86 8.86 8.85 8.85 8.78 8.78 8.77 8.77 8.23 8.23 8.22 8.22 8.05 7.98 7.97 7.77 7.76 7.64 7.64 7.63 7.63 7.63 7.62 7.62 7.61 7.60 7.53 7.53 7.52 7.51 7.43 7.43 7.42 7.42 7.26 6.92 6.92 6.91 6.91
F3C
O
N
H
NH
S
S=O
O
N
8.23 8.23 8.22 8.22
8.05
7.98 7.97
7.77 7.76 7.64 7.64 7.63 7.63 7.63 7.62 7.62 7.61 7.60
7.53 7.53 7.52 7.51
7.43 7.43 7.42 7.42
0.96 1.05 0.93 1.00 2.86 1.01 0.82
f1 (ppm)
1.00 1.06 0.96 0.94 0.96 1.05 0.93 1.00 2.86 1.01 0.82 0.89
f1 (ppm)

(T5-2)


O
F3C
N
H
N
NH
S
S=O
O

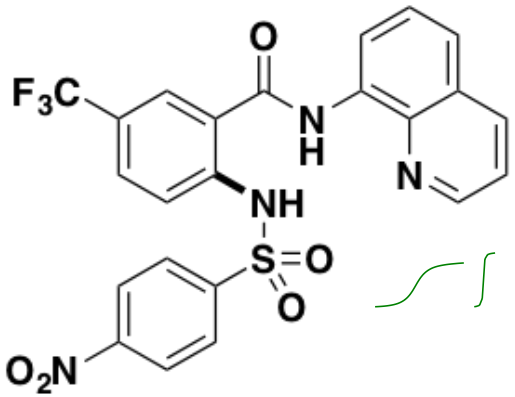
165.43
148.87
142.16
139.89
138.70
136.68
133.38
133.18
132.89
129.88
129.85
129.83
129.80
128.06
127.55
127.39
125.95
125.72
125.51
124.57
124.55
124.52
124.49
124.47
123.11
122.72
122.17
121.73
120.98
117.32
f1 (ppm)
f1 (ppm)

(T5-2)


O
F3C
N
H
N
NH
S
S=O
O

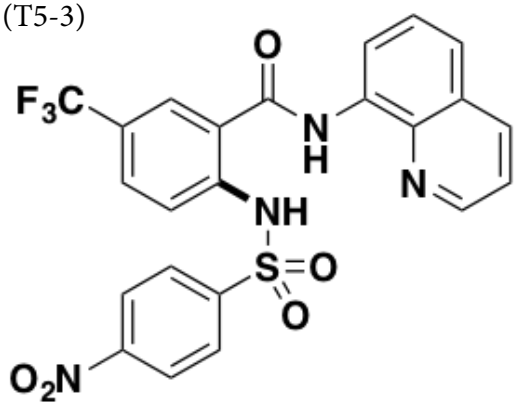
-62.10
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
-2
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(T5-3)

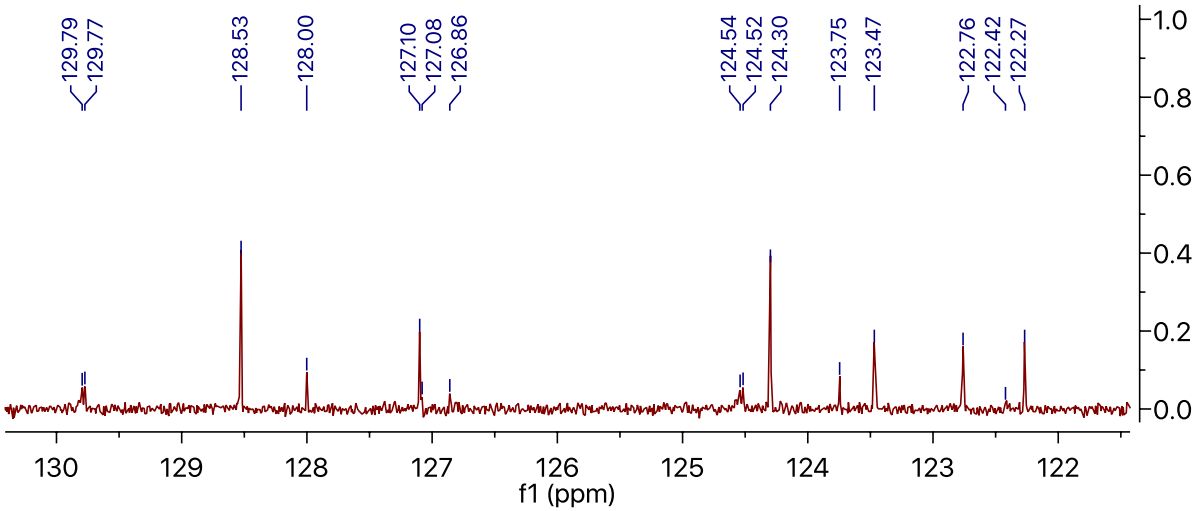

O
F3C
N
H
N
NH
S
O
O
O2N

10.92
10.41
8.71 8.71 8.70 8.70 8.59 8.58 8.16 8.15 8.14 8.14 7.97 7.97 7.96 7.96 7.90 7.88 7.88 7.87 7.87 7.80 7.78 7.69 7.67 7.57 7.57 7.56 7.53 7.52 7.51 7.50 7.45 7.44 7.43 7.43 7.26 7.26
0.87 1.07 1.00 0.98 1.01 1.90 1.05 1.98 1.01 1.02 1.02 1.07 1.04
f1 (ppm)
7.97 7.97 7.96 7.96 7.90 7.88 7.88 7.87 7.87 7.80 7.78 7.69 7.67 7.57 7.57 7.56 7.53 7.52 7.51 7.50 7.45 7.44 7.43 7.43
1.90 1.05 1.98 1.01 1.02 1.02 1.07 1.04
f1 (ppm)

(T5-3)

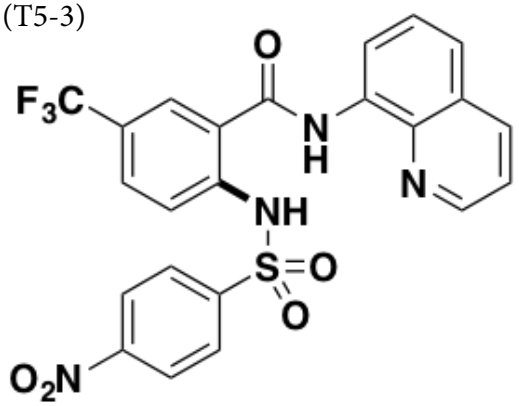

O
F3C
N
H
N
NH
S
O
O
O2N


165.06
150.00
149.00
144.58
140.75
138.36
136.70
132.95
129.79
129.77
128.53
128.00
127.10
127.08
126.86
124.54
124.52
124.30
123.75
123.47
122.76
122.42
122.27
117.27


129.79
129.77
128.53
128.00
127.10
127.08
126.86
124.54
124.52
124.30
123.75
123.47
122.76
122.42
122.27
1.0
0.8
0.6
0.4
0.2
0.0
130
129
128
127
126
125
124
123
122
f1 (ppm)

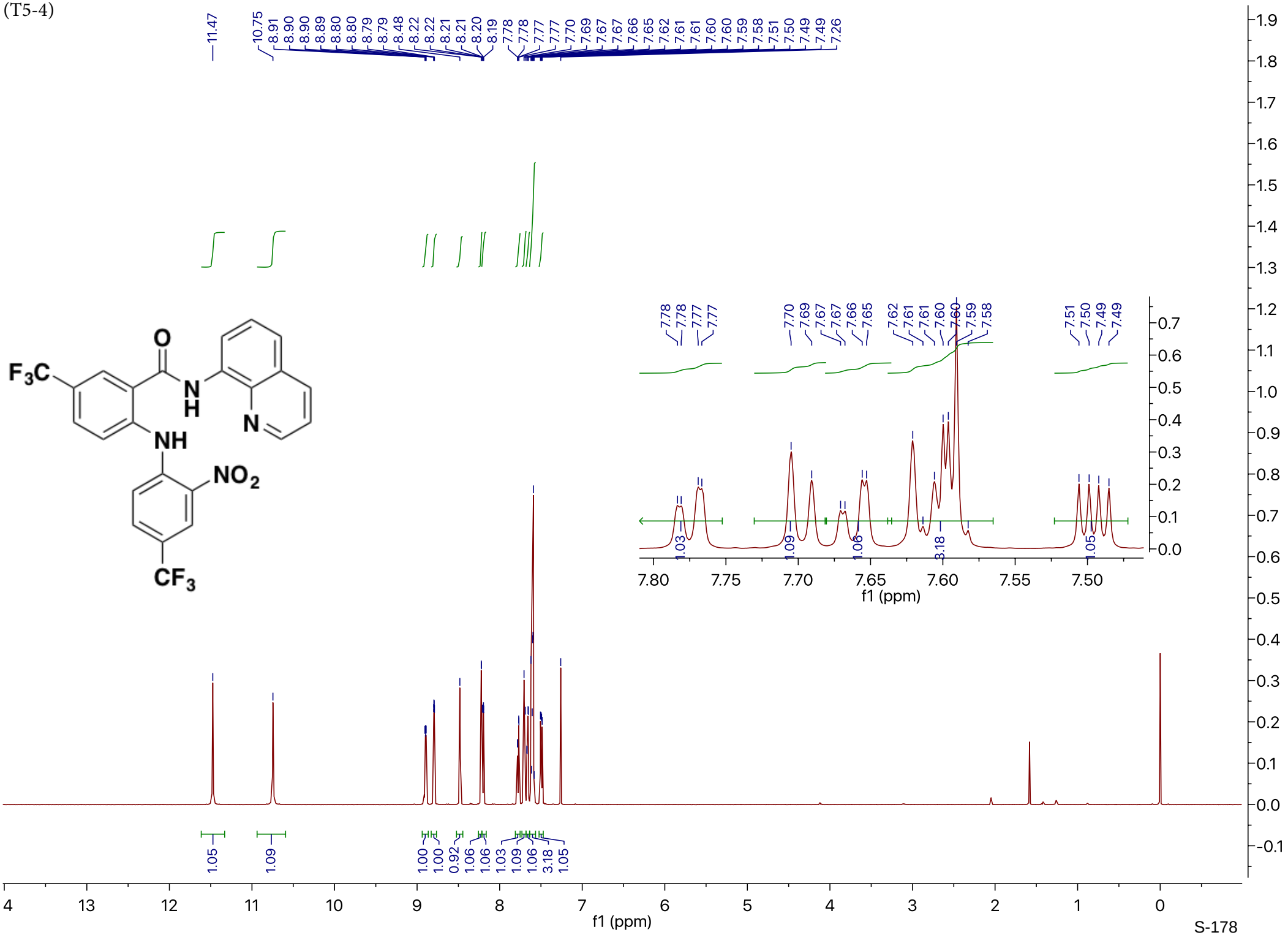
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
50
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

(T5-3)

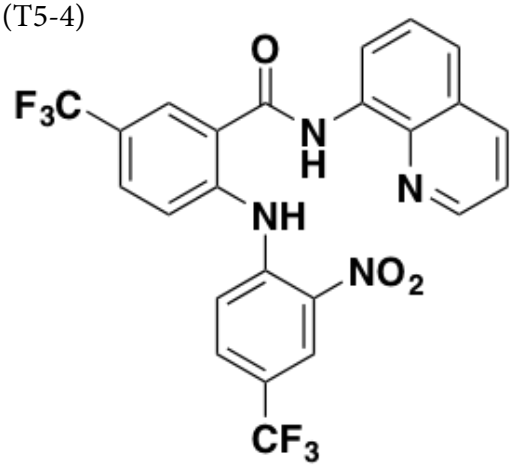

O
F3C
N
H
N
NH
S=O
O
O2N

62.25
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(T5-4)

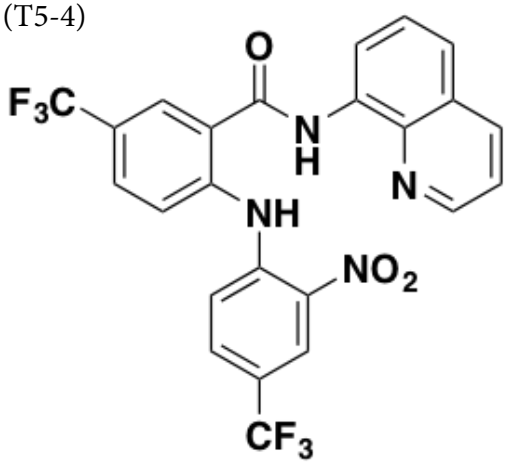

11.47
10.75
8.91
8.90
8.90
8.89
8.80
8.80
8.79
8.79
8.48
8.22
8.22
8.21
8.21
8.20
8.19
7.78
7.78
7.77
7.77
7.70
7.69
7.67
7.67
7.66
7.65
7.62
7.61
7.61
7.60
7.60
7.59
7.58
7.51
7.50
7.49
7.49
7.26
F3C
O
N
H
N
NH
NO2
CF3
1.05
1.09
1.00
1.00
0.92
1.06
1.06
1.03
1.09
1.06
3.18
1.05
f1 (ppm)
S-178

(T5-4)


O
F3C
N
H
N
NH
NO2
CF3

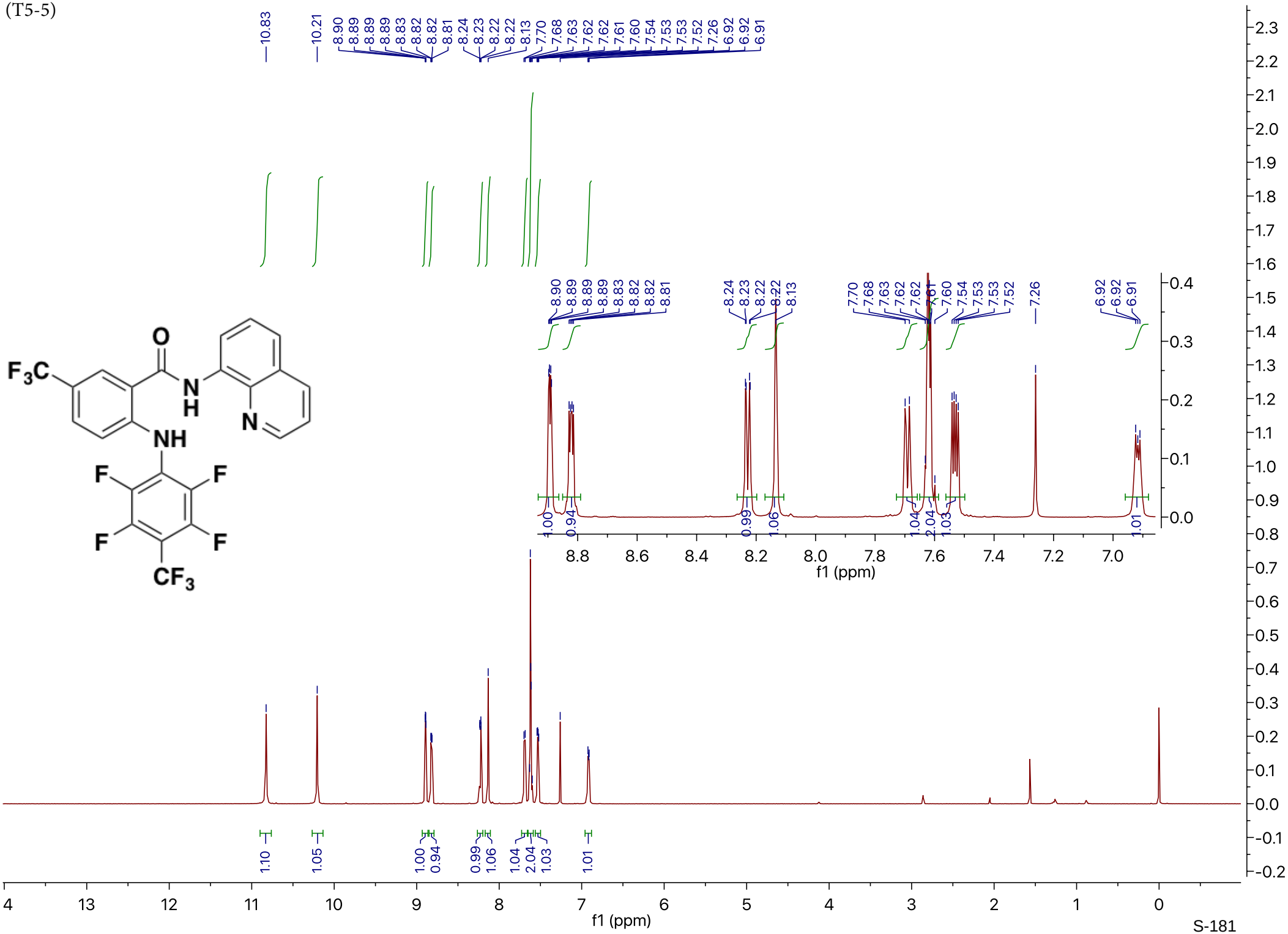
164.65
148.61
142.34
141.68
138.60
136.57
135.81
133.75
131.48
129.07
127.99
127.39
126.75
126.41
126.36
126.26
126.25
126.18
125.96
125.87
125.74
124.71
124.69
124.56
124.07
122.72
122.54
122.50
122.31
122.27
122.08
121.99
121.85
121.64
120.95
120.47
118.41
117.23
f1 (ppm)
f1 (ppm)

(T5-4)

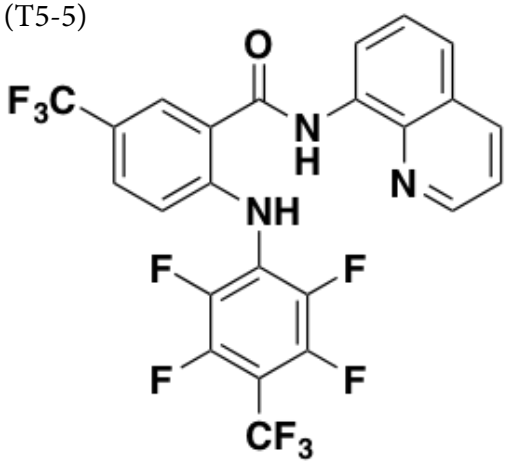

O
F3C
N
H
N
NH
NO2
CF3

-62.09
-62.21
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

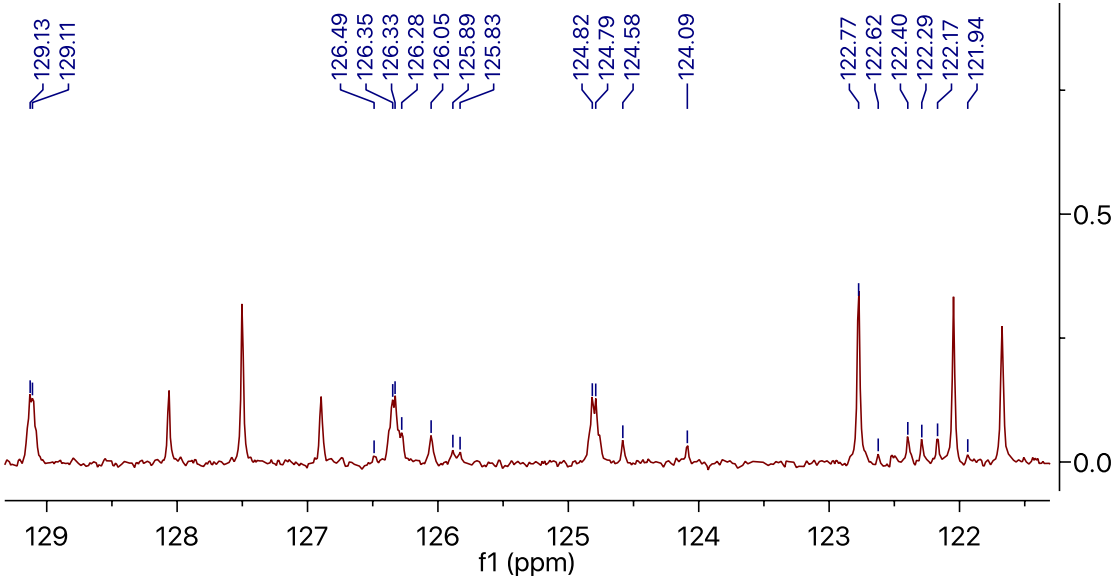
(T5-5)


10.83
10.21
8.90
8.89
8.89
8.89
8.83
8.82
8.82
8.81
8.24
8.23
8.22
8.22
8.13
7.70
7.68
7.63
7.62
7.62
7.61
7.60
7.54
7.53
7.53
7.52
7.26
6.92
6.92
6.91
O
F3C
N
H
N
NH
F
F
F
F
CF3
1.00
0.94
0.99
1.06
1.04
2.04
1.03
1.01
f1 (ppm)
1.10
1.05
1.00
0.94
0.99
1.06
1.04
2.04
1.03
1.01
f1 (ppm)

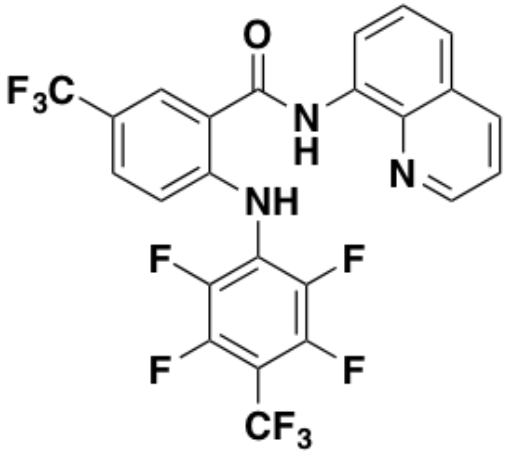
(T5-5)



137.69
131.53
131.51
129.13
129.11
126.49
126.35
126.33
126.28
126.05
125.89
125.83
124.82
124.79
124.58
124.09
122.77
122.62
122.40
122.29
122.17
121.94
120.49

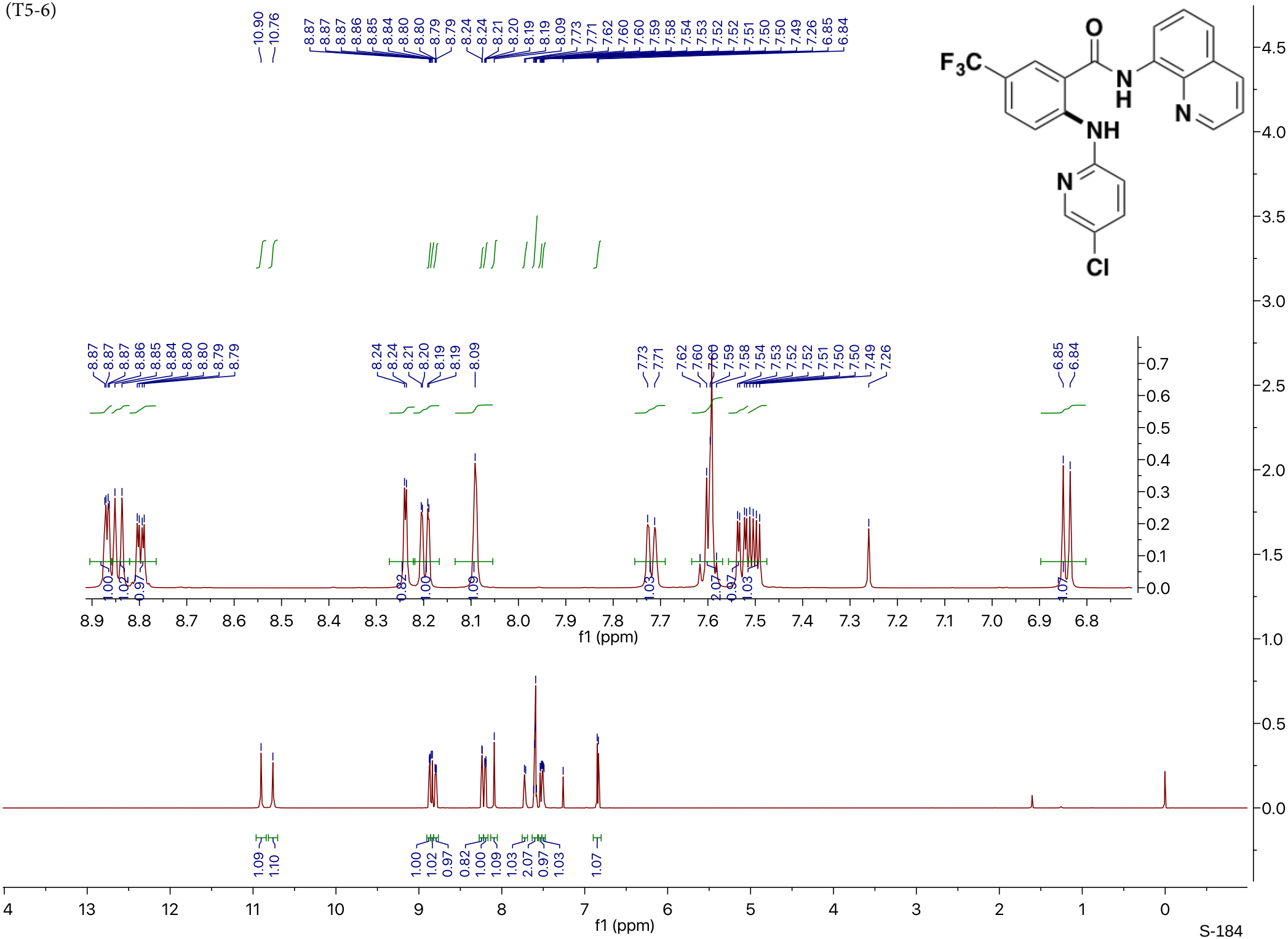


(T5-5)

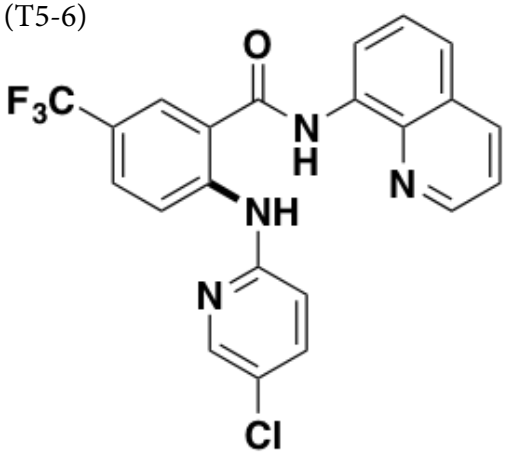


-55.42
-55.46
-55.49
-61.70
-140.57
-140.58
-140.59
-140.62
-140.63
-140.65
-140.67
-140.69
-140.70
-140.72
-140.74
-140.75
-144.87
-144.88
-144.89
-144.90
-144.91
-144.92
1.44
1.43
1.00
1.00
f1 (ppm)

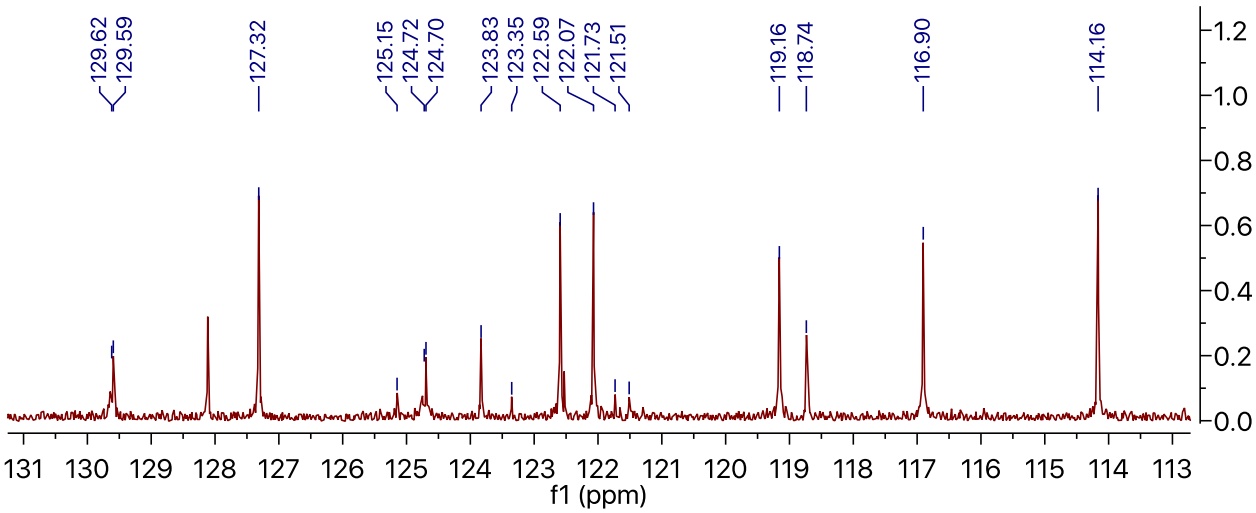
(T5-6)



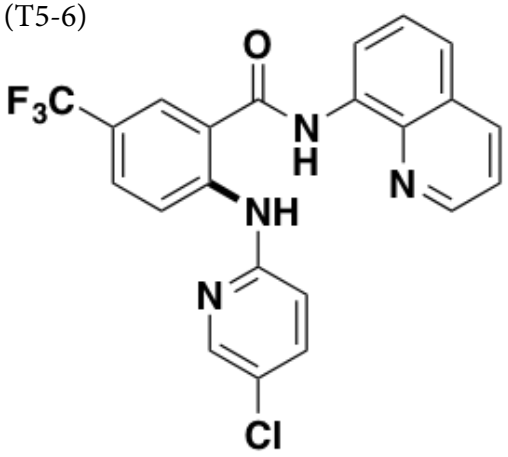
(T5-6)



167.03
152.71
148.82
146.05
145.68
138.87
137.63
136.54
134.03
129.62
129.59
127.32
125.15
124.72
124.70
123.83
123.35
122.59
122.07
121.73
121.51
119.16
118.74
116.90
114.16
77.36

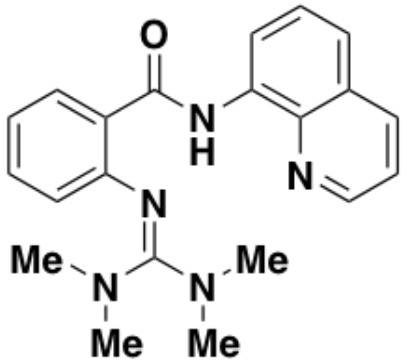


(T5-6)


O
F3C
N
H
N
NH
N
Cl

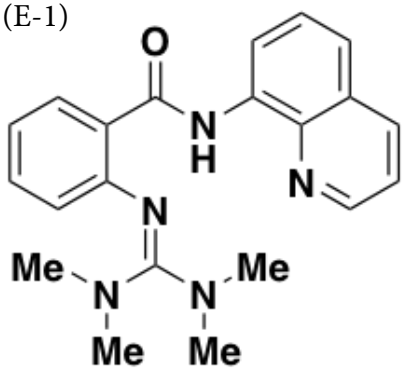
-61.61
25
24
23
22
21
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

(E-1)


O
N
H
N
N
Me
N
N
Me
Me
Me

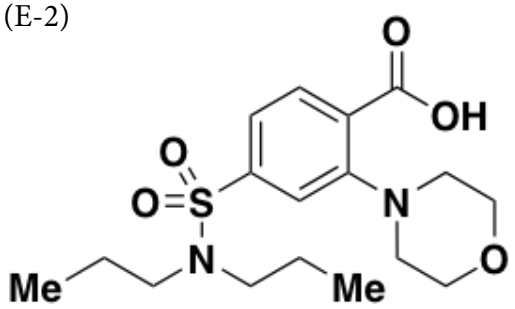
13.49
9.19
9.17
8.82
8.81
8.39
8.37
8.11
8.09
7.56
7.55
7.54
7.46
7.45
7.39
7.39
7.38
7.37
7.31
7.30
7.28
6.98
6.97
6.96
6.47
6.46
2.82
f1 (ppm)
1.00
0.98
1.08
0.99
1.09
1.13
1.07
1.11
1.08
1.07
1.01
13.56

(E-1)


O
N
H
N
N
Me
N
N
Me
Me
Me

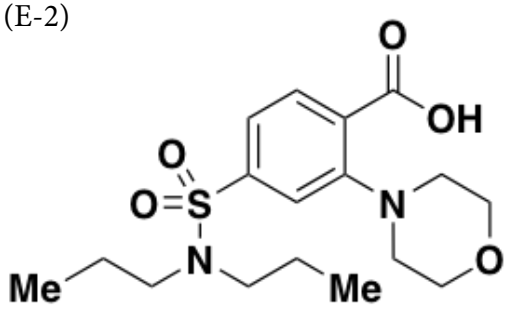
166.34
160.84
151.40
147.69
140.01
137.18
136.12
131.85
131.37
128.35
127.49
124.15
121.91
121.24
121.08
119.88
118.38
39.84
f1 (ppm)
f1 (ppm)

(E-2)


O
OH
O
O=S
N
N
O
Me
Me

8.39
8.38
7.87
7.77
7.76
3.95
3.11
3.10
3.09
1.55
1.54
1.53
1.52
1.51
1.49
0.85
0.84
0.83
1.00
1.02
0.96
3.98
8.03
4.03
5.95
f1 (ppm)

(E-2)


O
OH
O
O=S
N
N
O
Me
Me

165.24
150.87
145.92
133.64
128.34
125.69
121.59
66.82
53.69
49.87
21.92
11.22
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
50 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)