Supporting Information

Copper-Catalyzed Etherification of Arene C-H Bonds

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General Considerations:

Reactions were preformed using standard glassware. Column chromatography was performed on 60Å silica gel (Dynamic Adsorbents Inc.). ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR were recorded on JEOL EC-400 or JEOL EC-500 spectrometers using residual solvent peak as a reference. IR- spectra were obtained using a Perkin Elmer Spectrum 100 FT-IR spectrometer. Compounds for HRMS were analyzed by positive mode electrospray ionization (+ESI) using Agilent QTOF mass spectrometer in the Mass Spectrometry Facility (MSF) of the Department of Chemistry and Biochemistry of University of Texas-Austin. Analytical thin layer chromatography was performed on silica gel. All procedures were performed under ambient air unless otherwise noted.

Materials:

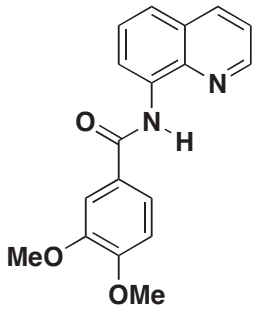
The following chemicals were obtained from commercial sources and used without further purification:

8-Aminoquinoline, 3-trifluoromethylbenzoyl chloride, 4-*tert*-butyl phenol, copper (II) carbonate basic, potassium carbonate, dimethylformamide, 4-(methylmercapto)-phenol, 3-hydroxybenzotrifluoride, 3-chloro-4-methylphenol, ethyl 3-hydroxybenzoate, 4-bromophenol, 3-iodophenol, triethylamine, 3,4-dimethoxybenzoyl chloride, 2,2-bis(4-hydroxyphenyl)propane, 4-cyanobenzoyl chloride, thionyl chloride, potassium acetate, 4-trifluoromethylbenzoyl chloride, 4-nitrobenzoyl chloride, 2,2,2-trifluoroethanol, pyridine, oxygen, 1-aminonapthalene, potassium phosphate tribasic, 2-picolinic acid, triphenyl phosphite, pyridine, carbitol, tetramethylguanidine, cyclopropanemethanol, cinchonine*, allyl alcohol, cumylamine, ethyl chloroformate, (-)-ethyl L-lactate, isonicotinic acid.

* - NMR of cinchonine revealed an impurity and therefore this chemical was recrystalized three times from toluene before use.

Synthesis of Amides

The following amides were synthesized according to literature procedures:
3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide, 4-cyano-*N*-(quinolin-8-yl)benzamide, 4-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide, 4-nitro-*N*-(quinolin-8-yl)benzamide, and *N*-(quinolin-8-yl)isonicotinamide.[1,2]



3,4-Dimethoxy-*N*-(quinolin-8-yl)benzamide

A 250 mL round bottom flask was equipped with a magnetic stirbar and charged with 8-aminoquinoline (2.39 g, 16.6 mmol), triethylamine (2.78 mL, 20 mmol), and CH_2Cl_2 (150 mL). A vigreux condenser was attached to the flask and the stirring solution was purged with nitrogen for 10 minutes. After the mixture had been cooled in an ice-bath to 5 °C, 3,4-dimethoxybenzoyl chloride (4.01 g, 20 mmol) was added dropwise over 5 minutes. The reaction was stirred at 5 °C for one hour followed by heating to reflux for 16 hours. The reaction mixture was cooled to room temperature, concentrated by rotary evaporation, and dry-absorbed on SiO_2 (100 mL). Column chromatography on SiO_2 (500 mL) with toluene/ethyl acetate (30:1 to 10:1) gave the pure product as a light beige solid. R_f = 0.23 (SiO_2, toluene/ethyl acetate, 30:1). MP = 143 – 144 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 10.67 (*s*, 1H) 8.89 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.80 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.13 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.63 (*m*, 2H) 7.55 (*t*, *J* = 8.0 Hz, 1H) 7.48 (*d*, *J* = 8.6 Hz, 1H) 7.42 (*dd*, *J* = 8.0, *J* = 4.0 Hz, 1H) 6.95 (*d*, *J* = 8.0, 1H) 3.98 (*s*, 3H) 3.93 (*s*, 3H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 165.1, 152.1, 149.2, 148.3, 138.8, 136.5, 134.8, 128.1, 127.9, 127.6, 121.7, 121.5, 119.9, 116.4, 110.9, 110.5, 56.2. FT-IR (neat, cm^{-1}) υ. HRMS (+ESI): Calculated for $C_{18}H_{16}N_2O_3$ $[M+H]^+$ 309.12340, Found 309.12320.

The following picoline amides were synthesized according to literature procedures. *N*-(2-phenylpropan-2-yl)picolinamide and *N*-(naphthalen-8-yl)picolinamide.[3,4]

Optimization of Reaction Conditions

Entries 1-4

A 4-dram screw-cap vial was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.032 g, 0.1 mmol), copper catalyst (0.1 mmol), and K_2CO_3 (0.028 g, 0.2 mmol). The vial was flushed with N_2 and, inside the glovebox, NMO (0.023 g, 0.2 mmol) was added (entries 1-3 only). Outside the glovebox DMF (1 mL) was added and the resulting mixture was stirred at room temperature (20 °C) for 5 minutes. 4-*tert*-Butylphenol (0.030 g, 0.2 mmol) was added and the vial was allowed to stir for 5 minutes at room temperature. The vessel was then flushed with the appropriate gas, sealed (entries 1-3 only), and placed in a reaction block that had been pre-heated to 110 °C. After 12 hours the resulting dark-brown mixture was allowed to

cool to room temperature and dissolved in ethyl acetate (15 mL). The diluted solution was washed with de-ionized water (2x 10 mL), saturated sodium bicarbonate solution (10 mL), and brine (10 mL). The remaining organic portion was dried over sodium sulfate, filtered through a pad of Celite®, and concentrated under reduced pressure. After drying under vacuum for 12 hours 1,3,5-trimethoxybenzene (1.9 mg, 0.102 mmol) was added as an internal standard. The yield was determined using NMR spectroscopy by comparing the sums of the integrals for the amide N-H bond with the methoxy CH_3 of the internal standard.

Entry 5

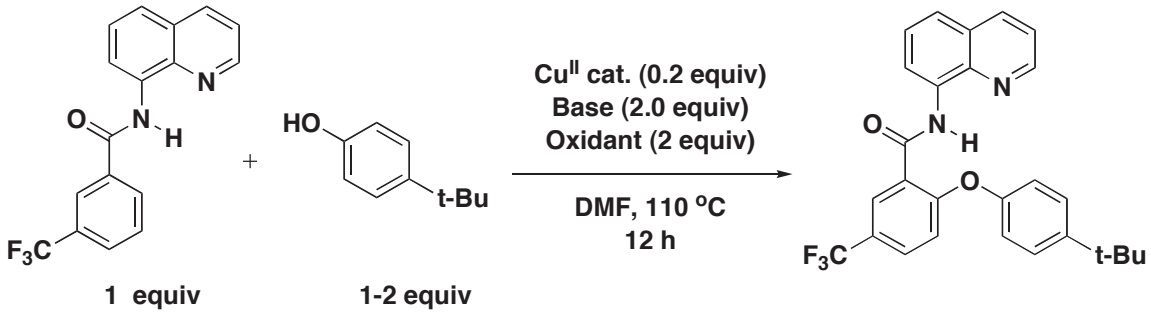
A 4-dram screw-cap vial was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol $Cu(OPiv)_2$ (0.027 g, 0.1 mmol), and Rb_2CO_3 (0.231 g, 1.0 mmol). The vial was flushed with N_2 and, inside the glovebox, NMO (0.117 g, 1.0 mmol) was added. Outside the glovebox DMF (2.5 mL) was added and the resulting mixture was stirred at room temperature (20 °C) for 5 minutes. 4-*tert*-Butylphenol (0.030 g, 0.2 mmol) was added and the vial was allowed to stir for 5 minutes at room temperature. After flushing with air, the vial was placed in a reaction block that had been pre-heated to 110 °C for 12 hours. The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (15 mL). The diluted solution was washed with de-ionized water (2x 10 mL), saturated sodium bicarbonate solution (10 mL), and brine (10 mL). The remaining organic portion was dried over sodium sulfate, filtered through a pad of Celite®, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 and subjected to column chromatography to obtain 0.149 g (64%) of the pure product.

Entry 6

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $Cu(OPiv)_2$ (0.027 g, 0.1 mmol), Rb_2CO_3 (0.231 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.075 g, 0.5 mmol) and stirring for an additional 5 minutes. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. After 12 hours the resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with deionized water (2× 15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 and subjected to column chromatography to obtain 0.169 g (73%) of the pure product.

Entry 7

Refer to procedure for **Table 2, Entry 1**.

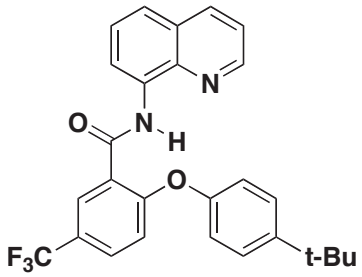


Entry	Cu Catalyst	Oxidant	Additive	Base	Time	Yield
1	$Cu(OAc)_2$ (.2 equiv)	NMO (2 equiv) Under Air	Ag_2CO_3 (.2 equiv)	-	12 h	21%*
2	$Cu(OAc)_2$ (.2 equiv)	NMO (2 equiv) Under N_2	-	K_2CO_3 (2 equiv)	12 h	64%*
3	$Cu(OAc)_2$ (.2 equiv)	NMO (2 equiv) O_2 (1 atm)	-	K_2CO_3 (2 equiv)	12 h	67%*
4	$CuCO_3$•$Cu(OH)_2$ (.11 equiv)	Open Air	-	K_2CO_3 (2 equiv)	12 h	68%*
5	$Cu(OPiv)_2$ (.2 equiv)	NMO (2 equiv)	-	Rb_2CO_3 (2 equiv)	12 h	64%
6	$Cu(OPiv)_2$ (.2 equiv)	NMO (2 equiv) Open Air	-	Rb_2CO_3 (2 equiv)	12 h	73%
7	$CuCO_3$•$Cu(OH)_2$ (.11 equiv)	Open Air	-	K_2CO_3 (2 equiv)	6 h	88%

*** - yields determined by NMR spectroscopy.**

General Etherification Procedure Employing Phenols

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with amide (0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.054 mmol, 0.12 equiv), K_2CO_3 (1.0 mmol, 2.0 equiv), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of phenol (0.5 mmol, 1.0 equiv) and stirring for an additional 5 minutes. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath only after the starting amide was no longer visible. The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with deionized water (2× 15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 and subjected to column chromatography to obtain the pure product.



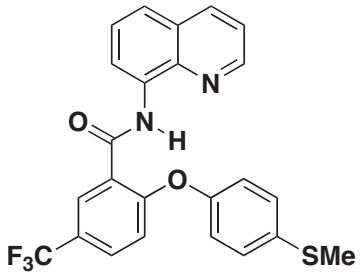
2-(4-*tert*-Butylphenoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 2, Entry 1)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), K_2CO_3 (0.138 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.075 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (6 hours. The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2× 15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene (100%) to obtain 0.204 g (88%) the pure product as a white solid. R_f = 0.29 (SiO_2, hexanes/ethyl acetate, 10:1). MP =165 – 166 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 112.29 (*s*, 1H) 8.99 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.70 (*d*, *J* = 2.3 Hz, 1H) 8.56 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.13 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.65 (*dd*, *J* = 9.2 Hz, *J* = 2.3 Hz, 1H) 7.59 (*t*, *J* = 8.0 Hz, 1H) 7.52 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.49 (*dt*, *J* = 9.2 Hz, *J* = 2.3 Hz 2H) 7.39 (*dd*, *J* = 8.6 Hz, *J* = 4.0 Hz, 1H) 7.23 (*dt*, *J* = 8.6 Hz, *J* = 1.7 Hz, 2H) 7.09 (*d*, *J* = 8.6 Hz, 1H) 1.37 (*s*, 9H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.9, 158.6, 152.2, 148.5, 148.3, 139.2, 136.2, 135.3, 130.3, 129.7, 128.1, 127.6, 127.2, 125.4 (*q*, $J_{C\text{-}F}$ = 32.9 Hz),124.6, 124.0 (*q*, $J_{C\text{-}F}$ = 271.0 Hz), 122.1, 121.7, 119.9, 117.5, 117.4, 34.7, 31.6. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -61.9. FT-IR (neat, cm^{-1}) υ 1666, 1541, 1490, 1327, 1270, 1242, 1166, 1115. HRMS (+ESI): Calculated for $C_{27}H_{24}F_3N_2O_2$ $[M+H]^+$ 465.17840, Found 465.17850.

Large Scale Synthesis

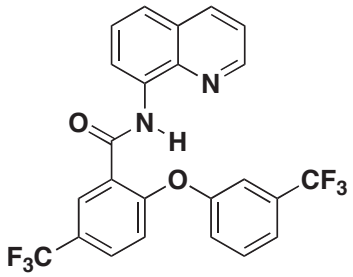
A 100 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (1.01 g, 3.2 mmol), $CuCO_3$•$Cu(OH)_2$ (0.040 g, 0.19 mmol), K_2CO_3 (0.88 g, 6.4 mmol), and DMF (16 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.48 g, 3.2 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at

regular intervals and removed from the oil bath after full consumption of the amide starting material (10 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×25 mL), saturated sodium bicarbonate solution (25 mL), and brine (25 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (20 mL) and subjected to column chromatography on SiO_2 (400 mL) with toluene (100%) to obtain 1.08 g (73%) of the pure product as a white solid.



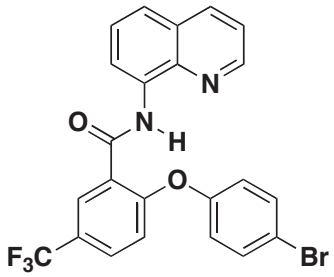
2-(4-(Methylthio)phenoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 2, Entry 2)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), K_2CO_3 (0.138 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-methylthiophenol (0.070 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (2.5 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene (100%) to obtain 0.184 g (78%) of the pure product as a white solid. R_f = 0.47 (SiO_2, toluene/ethyl acetate, 30:1). MP =155 – 156 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.25 (*s*, 1H) 8.97 (*d*, *J* = 8.0 Hz, 1H) 8.69 (*d*, *J* = 2.3 Hz, 1H) 8.52 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.09 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 7.64 (*dd*, *J* = 8.6 Hz, *J* = 1.72 Hz, 1H) 7.55 (*t*, *J* = 7.45 Hz, 1H) 7.49 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.37 (*dt*, *J* = 9.2 Hz, *J* = 3.4 Hz, 2H) 7.35 (*d*, *J* = 4.0 Hz, 1H) 7.23 (*dt*, *J* = 9.2 Hz, *J* = 2.3 Hz, 2H) 7.04 (*d*, *J* = 8.6 Hz, 1H) 2.52 (*s*, 3H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.6, 158.2, 152.3, 148.3, 139.0, 136.2, 135.5, 135.1, 130.3, 129.7, 128.6, 128.0, 127.5, 125.6 (*q*, J_{C-F} = 33.6 Hz), 124.6, 123.9 (*q*, J_{C-F} = 272.3 Hz), 122.1, 121.7, 121.1, 117.4, 117.3 16.5 ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -61.9. FT-IR (neat, cm^{-1}) υ 1667, 1542, 1487, 1328, 1268, 1245, 1110. HRMS (+ESI): Calculated for $C_{24}H_{18}F_3N_2O_2S$ $[M+H]^+$ 455.10360, Found 455.10350.



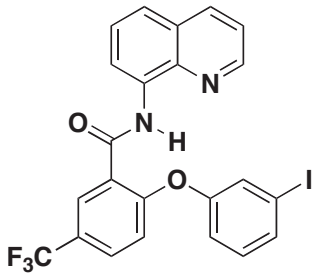
2-(3-(Trifluoromethyl)phenoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 2, Entry 3)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), K_2CO_3 (0.138 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 3-hydroxybenzotrifluoride (0.081 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (6 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene (100%) to obtain 0.132 g (55%) of the pure product as a white solid. R_f = 0.18 (SiO_2, hexanes/ethyl acetate, 10:1). MP =150 – 151 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.10 (*s*, 1H) 8.97 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.72 (*d*, *J* = 1.7 Hz, 1H) 8.54 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.14 (*dd*, *J* = 8.0 Hz, *J* = 1.2, 1H) 7.73 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H), 7.67 (*brs*, 1H) 7.59 (*t*, *J* = 8.0 Hz, 2H) 7.54 (*d*, *J* = 8.0 Hz, 2H) 7.41 (*m*, 2H) 7.12 (*d*, *J* = 8.6 Hz, 1H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.3, 156.9, 155.2, 148.2, 139.0, 136.4, 134.9, 133.0 (*q*, $J_{C\text{-}F}$ = 34.8 Hz), 130.9, 130.6, 130.0, 128.1, 127.6, 126.7 (*q*, $J_{C\text{-}F}$ = 33.6 Hz), 125.6, 124.8 (*q*, $J_{C\text{-}F}$ = 273.1 Hz), 124.6 (*q*, $J_{C\text{-}F}$ = 273.1 Hz), 122.9, 122.3, 121.9, 121.8, 118.2, 117.4. The signal for one carbon could not be located. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -62.1, -62.5. HRMS (+ESI): Calculated for $C_{24}H_{15}F_6N_2O_2$ $[M+H]^+$ 477.10320, Found 477.10300.



2-(4-Bromophenoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 2, Entry 4)

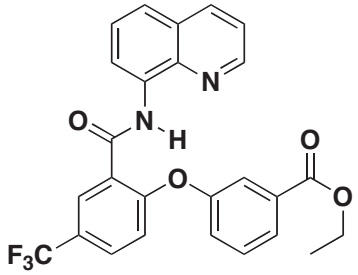
A 10 mL round-bottom flask was equiped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), K_2CO_3 (0.138 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-bromophenol (0.087 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (2 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene (100%) to obtain 0.190 g (78%) of the pure product as a white solid. R_f = 0.25 (SiO_2, hexanes/ethyl acetate, 10:1). MP =196 – 197 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.14 (*s*, 1H) 8.96 (*d*, *J* = 7.5 Hz, 1H) 8.69 (*d*, *J* = 1.7 Hz, 1H) 8.52 (*dd*, *J* = 4.0 Hz, *J* = 1.2 Hz, 1H) 8.11 (*dd*, *J* = 8.6 Hz, *J* = 1.2 Hz, 1H) 7.67 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H) 7.59 (*d*, *J* = 8.6 Hz, 2H) 7.56 (*d*, *J* = 7.5 Hz, 1H) 7.51 (*d*, *J* = 7.5 Hz, 1H) 7.38 (*dd*, *J* = 8.0 Hz, *J* = 3.7 Hz, 1H) 7.18 (*d*, *J* = 9.2 Hz, 2H) 7.05 (*d*, *J* = 8.6 Hz, 1H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.4, 157.6, 154.0, 148.3, 139.0, 136.3, 135.0, 133.4, 130.4, 129.8, 128.0, 127.6, 126.2 (*q*, $J_{C\text{-}F}$ = 33.6 Hz), 125.1, 123.8 (*q*, $J_{C\text{-}F}$ = 271.1 Hz), 122.2, 122.0, 121.7, 118.3, 117.8, 117.4 ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -61.9. FT-IR (neat, cm^{-1}) υ 1668, 1543, 1480, 1336, 1329, 1270, 1248, 1107. HRMS (+ESI): Calculated for $C_{23}H_{15}BrF_3N_2O_2$ $[M+H]^+$ 489.02430, Found 489.02460.



2-(3-Iodophenoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 2, Entry 5)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$

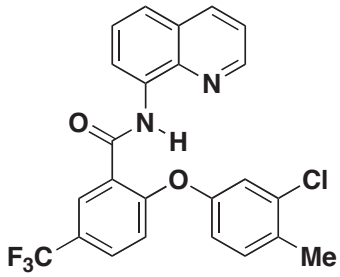
(0.012 g, 0.054 mmol), K_2CO_3 (0.138 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 3-iodophenol (0.110 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (2 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene (100%) to obtain 0.148 g (56%) of the pure product as a light yellow solid. R_f = 0.23 (SiO_2, hexanes/ethyl acetate, 10:1). MP =160 – 161 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.12 (*s*, 1H) 8.96 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.70 (*d*, *J* = 2.3 Hz, 1H) 8.59 (*dd*, *J* = 4.6 Hz, *J* = 1.7 Hz, 1H) 8.13 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 7.74 (*t*, *J* = 1.7 Hz, 1H) 7.70 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H) 7.62 (*dt*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.58 (*t*, *J* = 8.0 Hz, 1H) 7.53 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.41 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 7.24 (*ddd*, *J* = 8.6 Hz, *J* = 2.3 Hz, *J* = 1.2 Hz, 1H) 7.18 (*t*, *J* = 8.0 Hz, 1H) 7.11 (*d*, *J* = 8.6 Hz, 1H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.4, 157.2, 155.3, 148.4, 139.0, 136.3 135.0, 134.4, 131.5, 130.4, 129.9, 129.5, 128.1, 127.6, 126.4 (*q*, $J_{C\text{-}F}$ = 33.6 Hz), 125.2, 123.8 (*q*, $J_{C\text{-}F}$ = 271.1 Hz) 122.2, 121.8, 119.2, 118.2, 117.4, 94.5. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -62.0. FT-IR (neat, cm^{-1}) υ 1667, 1543, 1327, 1055, 1033, 1012. HRMS (+ESI): Calculated for $C_{23}H_{15}F_3N_2O_2I$ $[M+H]^+$ 535.01250, Found 535.01240.



Ethyl 3-(2-(quinolin-8-ylcarbamoyl)-4-(trifluoromethyl)phenoxy)benzoate (Table 2, Entry 6)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), K_2CO_3 (0.138 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of ethyl 3-hydroxybenzoate (0.083 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (2.5 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15

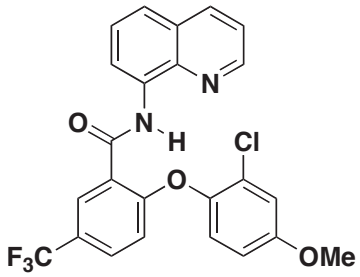
mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene (100%) to obtain 0.202 g (84%) of the pure product as a light pink solid. R_f = 0.35 (SiO_2, toluene 100%). MP 128 – 129 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.22 (*s*, 1H) 8.97 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.72 (*d*, *J* = 2.3 Hz, 1H) 8.58 (*dd*, *J* = 4.0 Hz, *J* = 1.2 Hz, 1H) 8.11 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 8.05 (*t*, *J* = 1.7 Hz, 1H) 7.97 (*d*, *J* = 7.5 Hz, 1H) 7.69 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H) 7.57 (*t*, *J* = 8.0 Hz, 1H) 7.55 (*t*, *J* = 8.0 Hz, 1H) 7.52 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.47 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.38 (*dd*, *J* = 8.6 Hz, *J* = 4.0 Hz, 1H) 7.09 (*d*, *J* = 8.6 Hz, 1H) 4.41 (*q*, *J* = 7.5 Hz, 2H) 1.41 (*t*, *J* = 6.9 Hz, 3H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 165.7, 161.5, 157.5, 154.8, 148.4, 139.1, 136.3, 135.1, 133.0, 130.5, 130.3, 129.9, 128.0, 127.6, 126.5, 126.2 (*q*, $J_{C\text{-}F}$ = 33.6 Hz), 125.5, 124.3, 123.8 (*q*, $J_{C\text{-}F}$ = 272.3 Hz) 122.2, 121.7, 121.4, 117.9, 117.4, 61.6, 14.4. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -62.0. FT-IR (neat, cm^{-1}) υ 1722, 1671, 1544, 1330, 1271, 1171, 1110. HRMS (+ESI): Calculated for $C_{26}H_{20}F_3N_2O_4$ $[M+H]^+$ 481.13750, Found 481.13750.



2-(3-Chloro-4-methylphenoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 2, Entry 7)

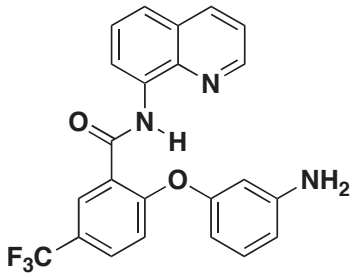
A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), K_2CO_3 (0.138 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 3-chloro-4-methylphenol (0.071 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (2.5 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene (100%) to obtain 0.177 g (77%) of the pure product as a white solid. R_f = 0.40 (SiO_2, toluene 100%). MP =163 – 164 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.17 (*s*, 1H) 8.97 (*dd*, *J* = 7.45 Hz, *J* = 1.2 Hz, 1H) 8.70 (*d*, *J* = 2.3 Hz, 1H) 8.58 (*dd*, *J* = 4.6 Hz, *J* = 1.7 Hz, 1H) 8.11 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.67 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H) 7.57 (*t*, *J* = 7.6 Hz, 1H) 7.51 (*dd*, *J* = 8.0, *J* = 1.2 Hz, 1H)

7.39 (*t*, *J* = 5.7 Hz, 1H) 7.39 (*d*, *J* = 4.0 Hz, 1H) 7.31 (*d*, *J* = 8.6 Hz, 1H) 7.09 (*d*, *J* = 8.6 Hz, 1H) 7.08 (*d*, *J* = 8.0 Hz, 1H) 2.41 (*s*, 3H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.5, 157.7, 153.1, 148.4, 139.1, 136.3, 135.4, 135.1, 133.3, 132.0, 130.4 129.8, 128.0, 127.6, 126.0 (*q*, $J_{C\text{-}F}$ = 33.6 Hz), 124.9, 123.8 (*q*, $J_{C\text{-}F}$ = 272.3 Hz), 122.2, 121.8, 121.3, 118.4, 117.7, 117.4, 19.6. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -61.9. FT-IR (neat, cm^{-1}) υ 1668, 1542, 1486, 1336, 1328, 1270, 1108. HRMS (+ESI): Calculated for $C_{24}H_{17}ClF_3N_2O_2$ $[M+H]^+$ 457.09250, Found 457.09250.



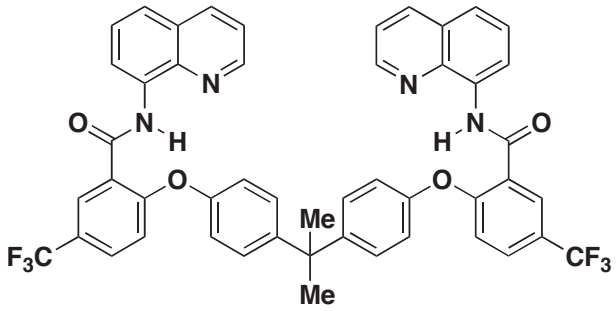
2-(2-Chloro-4-methoxyphenoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 2, Entry 8)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), K_2CO_3 (0.138 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 2-chloro-4-methoxyphenol (0.079 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (2.5 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene (100%) to obtain 0.184 g (78%) of the pure product as a white solid. R_f = 0.42 (SiO_2, hexanes/ethyl acetate, 6:1). MP =158 – 159 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.24 (*s*, 1H) 8.99 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.67 (*d*, *J* = 2.3 Hz, 1H) 8.53 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.13 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.63 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H) 7.60 (*t*, *J* = 7.5, 1H) 7.53 (*dd*, *J* = 8.0 Hz, *J* = 1.2Hz, 1H) 7.37 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 7.28 (*d*, *J* = 9.2 Hz, 1H) 7.12 (*d*, *J* = 2.9 Hz, 1H) 6.94 (*dd*, *J* = 9.2 Hz, *J* = 3.4 Hz, 1H) 6.80 (*d*, *J* = 8.6 Hz, 1H) 3.87 (*s*, 3H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.8, 158.4, 158.0, 148.3, 143.1, 139.1, 136.2, 135.3, 130.3, 129.7, 128.0, 127.9, 127.5, 125.35 (*q*, $J_{C\text{-}F}$ = 33.6 Hz), 124.0, 123.9 (*q*, $J_{C\text{-}F}$ = 273.5 Hz) 123.8, 122.0, 121.6, 117.3, 116.1, 115.4, 114.3, 56.0. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -61.8. FT-IR (neat, cm^{-1}) υ 1668, 1544, 1487, 1327, 1266, 1211, 1113. HRMS (+ESI): Calculated for $C_{24}H_{17}ClF_3N_2O_3$ $[M+H]^+$ 473.08740, Found 473.08740.



2-(3-Aminophenoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 2, Entry 9)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), K_2CO_3 (0.138 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 3-aminophenol (0.109 g, 1.0 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 120 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (6 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene (100%) to obtain 0.121 g (57%) the pure product as a light tan solid. R_f = 0.21 (SiO_2, 4:1 hexanes/ethyl acetate MP 181 – 182 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.27 (*s*, 1H) (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.68 (*d*, *J* = 2.3 Hz, 1H) 8.56 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.10 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.64 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H) 7.56 (*t*, *J* = 8.0 Hz, 1H) 7.50 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.36 (*dd*, *J* = 8.6 Hz, *J* = 4.6 Hz, 1H) 7.23 (*t*, *J* = 8.6 Hz, 1H) 7.11 (*d*, *J* = 8.6 Hz, 1H) 6.67 (*dd*, *J* = 7.5 Hz, *J* = 1.7 Hz, 1H) 6.59 (*d*, *J* = 4.6 Hz, 1H) 6.58 (*d*, *J* = 1.7 Hz, 1H) 3.85 (*s*, 2H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.8, 158.4, 155.8, 148.5, 148.3, 139.1, 136.2, 135.2, 130.9, 130.1, 129.7, 128.0, 127.5, 125.4 (*q*, $J_{C\text{-}F}$ = 33.6 Hz), 124.5 123.9 (*q*, $J_{C\text{-}F}$ = 272.3 Hz) 122.0, 121.7, 117.9, 117.4, 112.1, 110.2, 106.9. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -61.8. FT-IR (neat, cm^{-1}) υ 1664, 1540, 1490, 1275, 1146, 1110. HRMS (+ESI): Calculated for $C_{23}H_{17}F_3N_3O_2$ $[M+H]^+$ 424.12670, Found 424.12770.



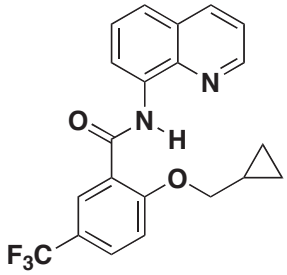
Compound 2

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), K_2CO_3 (0.138 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of bisphenol-A (0.057 g, 0.25 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (12 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene/etyl acetate (30:1) to obtain 0.142 g (66%) the pure product as a tan solid. R_f = 0.35 (SiO_2, hexanes/ethyl acetate, 6:1). MP =258 – 259 °C (from 1:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.20 (*s*, 2H) 8.98 (*d*, *J* = 7.5 Hz, 2H) 8.69 (*d*, *J* = 1.7 Hz, 2H) 8.50 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 2H) 8.09 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 2H) 7.66 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 2H) 7.58 (*t*, *J* = 8.0 Hz, 2H) 7.51 (*d*, *J* = 7.5 Hz, 2H) 7.36 (*d*, *J* = 8.6 Hz, 4H) 7.31 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 2H) 7.22 (*d*, *J* = 9.2 Hz, 4H) 7.12 (*d*, *J* = 8.6 Hz, 2H) 1.78 (*s*, 6H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.8, 158.2, 152.8, 148.2, 147.6, 139.1, 136.3, 135.2, 130.3, 129.7, 128.6, 128.1, 127.7, 125.7 (*q*, $J_{C\text{-}F}$ = 33.6 Hz), 125.0, 123.9 (*q*, $J_{C\text{-}F}$ = 272.3 Hz) 122.1, 121.6, 119.8, 117.9, 117.5, 42.7, 31.1. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -61.9. FT-IR (neat, cm^{-1}) υ 1667, 1536, 1492, 1328, 1270, 1241, 1165, 1119. HRMS (+ESI): HRMS (+ESI): Calculated for $C_{49}H_{34}F_6N_4O_4Na$ $[M+Na]^+$ 879.23760, Found 879.23810.

General Etherification Procedure Employing Aliphatic Alcohols

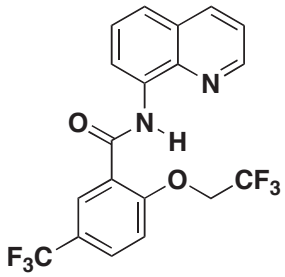
A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), tetramethylguanidine (0.115 g, 1.0 mmol), and pyridine (2.0 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 5 equivalents of alcohol and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath only after the starting amide was no

longer visible. The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 to give the pure product.



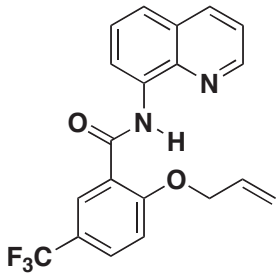
2-(Cyclopropylmethoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 3, Entry 1)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), tetramethylguanidine (0.115 g, 1.0 mmol), and pyridine (2.0 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of cyclopropanemethanol (0.180 g, 2.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (12 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with hexane/ethyl acetate (10:1) to obtain 0.145 g (75%) the pure product as a white solid. R_f = 0.21 (SiO_2, hexanes/ethyl acetate, 8:1). MP =154 – 155 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.10 (*s*, 1H) 9.06 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.74 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.65 (*d*, *J* = 2.3 Hz, 1H) 8.16 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.69 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H) 7.59 (*t*, *J* = 8.0 Hz, 1H) 7.54 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.44 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 7.12 (*d*, *J* = 8.6 Hz, 1H) 4.22 (*d*, *J* = 6.9 Hz, 2H) 1.64 (*m*, 1H) 0.66 (*q*, *J* = 9.2 Hz, 2H) 0.48 (*q*, *J* = 5.7 Hz, 2H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.6, 159.3, 148.0, 139.3, 136.4, 135.6, 130.3, 129.9, 128.2, 127.6, 124.2 (*q*, $J_{C\text{-}F}$ = 272.3 Hz), 123.6 (*q*, $J_{C\text{-}F}$ = 33.6 Hz) 123.2, 122.1, 121.6, 118.0, 113.1, 75. 2, 10.2, 4.1. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -61.6. FT-IR (neat, cm^{-1}) υ 1659, 1536, 1340, 1278, 1113, 1055, 1032, 1012. HRMS (+ESI): Calculated for $C_{21}H_{18}F_3N_2O_2$ $[M+H]^+$ 387.13150, Found 387.13240.



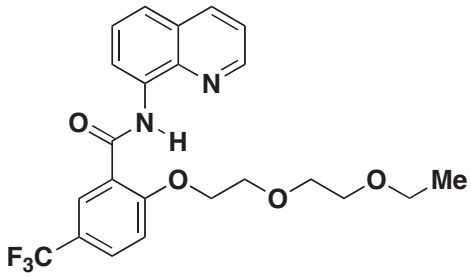
2-(2,2,2-Trifluoroethoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 3, Entry 2)

A 20 mL vial affixed with a pressure-relief cap and silicon/TFE septa was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), tetramethylguanidine (0.115 g, 1.0 mmol), and pyridine (2.0 mL). The vial was then purged with oxygen for 30 seconds and allowed to stir at room temperature (20 °C) for 10 minutes. Addition of 2,2,2-trifluoroethanol (0.250 g, 0.19 mL, 2.5 mmol) was followed by a second 30-second purge with oxygen and an additional 10-minute stir at room temperature. The vial was then placed in an oil-bath that had been pre-heated to 110 °C and the reaction was assessed by TLC analysis after 8 hours. After TLC the vial was once again charged with oxygen and returned to 110 °C for an additional 8 hours. The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with hexane/ethyl acetate (6:1) to obtain 0.151 g (73%) of the pure product as a white solid. R_f = 0.19 (SiO_2, hexanes/ethyl acetate, 8:1). MP =138 – 139 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 11.69 (*s*, 1H) 8.97 (*dd*, *J* = 7.5 Hz, *J* = 1.7 Hz, 1H) 8.79 (*J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.60 (*J* = 1.7 Hz, 1H) 8.14 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.73 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H) 7.57 (*t*, *J* = 8.0 Hz, 1H) 7.53 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.44 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 7.14 (*d*, *J* = 8.6 Hz, 1H) 4.76 (*q*, $J_{H\text{-}F}$ 8.0 Hz, 2H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.5, 157.4, 148.4, 139.0, 136.3, 135.0, 130.6, 130.1, 128.1, 127.4, 125.9 (*q*, $J_{C\text{-}F}$ = 33.6 Hz), 124.6, 123.8 (*q*, $J_{C\text{-}F}$ = 272.3 Hz), 123.0 (*q*, $J_{C\text{-}F}$ = 279.5 Hz), 122.4, 121.8, 117.6, 113.7, 67.2. (*q*, $J_{C\text{-}F}$ = 37.2 Hz) ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -62.0, -72.7 (*t*, $J_{H\text{-}F}$ = 8.7 Hz). FT-IR (neat, cm^{-1}) υ 1663, 1547, 1329, 1264, 1171, 1146, 1118. HRMS (+ESI): Calculated for $C_{19}H_{13}F_6N_2O_2$ $[M+H]^+$ 415.08760, Found 415.08860.



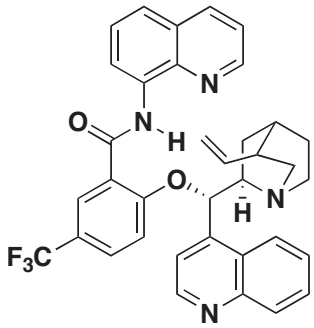
2-(Allyloxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 3, Entry 3)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), tetramethylguanidine (0.115 g, 1.0 mmol), and pyridine (2.0 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of allyl alcohol (0.145 g, 2.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (16 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with hexane/ethyl acetate (6:1) to obtain 0.127 g (68%) of the pure product as a clear oil which solidified after some time under vacuum. R_f = 0.38 (SiO_2, toluene/ethyl acetate, 30:1). MP =101 – 102 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.09 (*s*, 1H) 7.45 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.78 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.64 (*d*, *J* = 2.3 Hz, 1H) 8.13 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.67 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H) 7.57 (*t*, *J* = 8.0 Hz, 1H) 7.51 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.43 (*dd*, *J* = 8.6 Hz, *J* = 4.6 Hz, 1H) 7.09 (*d*, *J* = 8.6 Hz, 1H) 6.37 (*ddt*, *J* = 17.2 Hz, *J* = 10.3 Hz, *J* = 5.7 Hz, 1 H) 5.50 (*dd*, *J* = 17.2 Hz, *J* = 1.2 Hz, 1H) 5.40 (*dd*, *J* = 10.3 Hz, *J* = 1.2 Hz, 1H) 4.93 (*d*, *J* = 5.7 Hz, 2H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.3, 158.9, 148.1, 139.2, 136.3, 135.5, 132.5, 130.3, 129.9, 128.1, 127.6, 125.2, 124.1 (*q*, $J_{C\text{-}F}$ = 271.1 Hz), 123.8 (*q*, $J_{C\text{-}F}$ = 33.6 Hz) 122.0, 121.7, 119.1, 117.7, 113.1, 71.1. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -61.7. FT-IR (neat, cm^{-1}) υ 1662, 1539, 1329, 1272, 1146, 1111. HRMS (+ESI): Calculated for $C_{20}H_{16}F_3N_2O_2$ $[M+H]^+$ 373.11580, Found 373.11620.



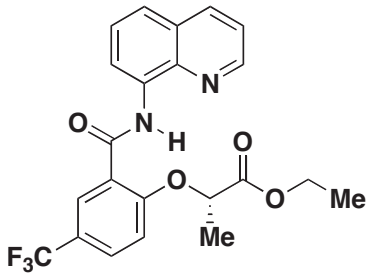
2-(2-(2-Ethoxyethoxy)ethoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 3, Entry 4)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), tetramethylguanidine (0.115 g, 1.0 mmol), and pyridine (2.0 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of carbitol (0.335 g, 2.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (16 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene/ethyl acetate (10:1) to obtain 0.162 g (72%) of the pure product as a clear oil which solidified after some time under vacuum. R_f = 0.21 (SiO_2, toluene/ethyl acetate, 10:1). MP =103 – 104 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 11.85 (*s*, 1H) 9.00 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.80 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.59 (*d*, *J* = 2.3 Hz, 1H) 8.10 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.64 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H) 7.53 (*t*, *J* = 8.0 Hz, 1H) 7.47 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.40 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 7.11 (*d*, *J* = 8.6 Hz, 1H) 4.52 (*t*, *J* = 5.7 Hz, 2H) 4.19 (*t*, *J* = 5.7 Hz, 2H) 3.58 (*t*, *J* = 4.6 Hz, 2H) 3.40 (*t*, *J* = 4.6 Hz, 2H) 3.35 (*q*, *J* = 6.9 Hz, 2H) 1.08 (*t*, *J* = 6.9 Hz, 3H) (^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.3, 159.2, 148.1, 139.1, 136.5, 135.5, 130.2, 130.0, 128.2, 127.6, 125.2, 123.8 (*q*, $J_{C\text{-}F}$ = 32.4 Hz), 123.0,122.1 122.0 (*q*, $J_{C\text{-}F}$ = 271.1 Hz) 117.9, 113.3, 71.0, 69.8, 69.4, 69.2, 66.7, 15.2. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -61.6. FT-IR (neat, cm^{-1}) υ 1533, 1275, 1112, 1055, 1032, 1021, 1009. HRMS (+ESI): Calculated for $C_{23}H_{24}F_3N_2O_4$ $[M+H]^+$ 449.16830, Found 449.16950.



2-((*S*)-(Quinolin-4-yl)((2*R*)-8-vinylquinuclidin-2-yl)methoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 3, Entry 5)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), tetramethylguanidine (0.115 g, 1.0 mmol), and pyridine (6.0 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of cinchonine (0.736 g, 2.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (14 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with ethyl acetate (5% triethylamine) to obtain 0.259 g (85%) of the pure product as a yellow oil. R_f = 0.36 (SiO_2, ethyl acetate/triethylamine, 95:5). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 11.96 (*s*, 1H), 9.16 (*dd*, *J* = 7.5 Hz, *J* = 1.7 Hz, 1H) 8.98 (*d*, *J* = 4.0 Hz, 1H) 8.94 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.55 (*d*, *J* = 2.3 Hz, 1H) 8.48 (*d*, *J* = 8.0 Hz, 1H) 8.30 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 8.22 (*d*, *J* = 8.0 Hz, 1H) 8.18 (*d*, *J* = 4.6 Hz, 1H) 7.79 (*t*, *J* = 7.5 Hz, 1H) 7.67 (*m*, 3H) 7.56 (*dd*, *J* = 8.6 Hz, *J* = 4.6 Hz, 1H) 7.45 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H) 6.86 (*d*, *J* = 8.6 Hz, 1H) 6.07 (*d*, *J* = 8.0 Hz, 1H) 5.82 (*ddd*, *J* = 17.2 Hz, *J* = 10.3 Hz, *J* = 7.5 Hz, 1H) 4.95 (*d*, *J* = 17.2 Hz, 1H) 4.88 (*d*, *J* = 10.3 Hz, 1H) 3.98 (*q*, *J* = 8.6 Hz, 1H) 2.91 (*m*, 2H) 2.71 (*m*, 1H) 2.63 (*m*, 1H) 2.18 (*q*, *J* = 8.6 Hz, 1H) 1.78 (*m*, 1H) 1.70 (*m*, 1H) 1.57 (*s*, 1H) 1.37 (*t*, *J* = 10.9 Hz, 1H) 1.15 (*q*, *J* = 12.0 Hz, 1H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.6, 158.0, 150.6, 148.6, 147.6, 146.0, 139.8, 139.2, 137.1, 135.3, 131.2, 130.3, 120.1, 129.6, 128.4, 128.0, 127.5, 126.5, 124.2 (*q*, $J_{C\text{-}F}$ = 32.9 Hz), 123.9 (*q*, $J_{C\text{-}F}$ = 272.0 Hz) 123.8, 122.6, 122.4, 122.0, 119.0, 118.2, 115.0, 113.7, 62.4, 50.0, 49.6, 39.8, 29.8, 27.6, 26.4, 25.7. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -61.9. HRMS (+ESI): Calculated for $C_{36}H_{32}F_3N_4O_2$ $[M+H]^+$ 609.24720, Found 609.24780.



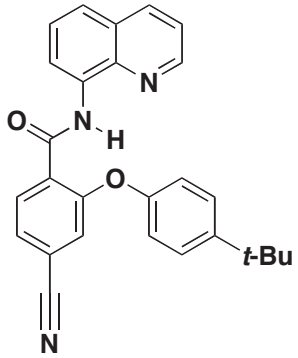
(*S*)-Ethyl 2-(2-(quinolin-8-ylcarbamoyl)-4-(trifluoromethyl)phenoxy)propanoate (Table 3, Entry 6)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), tetramethylguanidine (0.115 g, 1.0 mmol), and pyridine (6.0 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of ethyl-(L)-lactate (0.295 g, 2.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (16 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with ethyl acetate/hexanes (10:1 to 4:1) to obtain 0.084 g (39%) of the pure product as a faint pink solid. R_f = 0.20 (SiO_2, 8:1 hexanes/ethyl acetate). MP 159 – 160 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 11.89 (*s*, 1H) 9.07 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.76 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.65 (*d*, *J* = 1.7 Hz, 1H) 8.17 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.69 (*dd*, *J* = 8.6 Hz, *J* = 2.3 Hz, 1H) 7.59 (*t*, *J* = 8.0 Hz, 1H) 7.55 (*dd*, *J* = 8.6 Hz, *J* = 1.2 Hz, 1H) 7.45 (*dd*, *J* = 8.6 Hz, *J* = 4.6 Hz, 1H) 7.00 (*d*, *J* = 8.6 Hz, 1H) 5.17 (*q*, *J* = 6.9 Hz, 1H) 4.18 (*m*, 2H) 2.01 (*d*, *J* = 6.9 Hz, 3H) 1.15 (*t*, *J* = 7.5 Hz, 3H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 170.8, 162.4, 158.1, 147.9, 139.2, 136.5, 135.5, 130.7, 129.8, 128.2, 127.7, 124.5 (*q*, $J_{C\text{-}F}$ = 36.0 Hz), 124.0 (*q*, $J_{C\text{-}F}$ = 273.5 Hz), 123.9, 122.2, 121.7, 118.0, 113.0, 74.3, 61.9, 18.6, 14.1. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -61.8. FT-IR (neat, cm^{-1}) υ. 1743, 1668, 1533, 1324, 1274, 1210, 1147, 1107. HRMS (+ESI): Calculated for $C_{22}H_{20}F_3N_2O_4$ $[M+H]^+$ 433.13700, Found 433.13750.

General Etherification Procedure for Amides

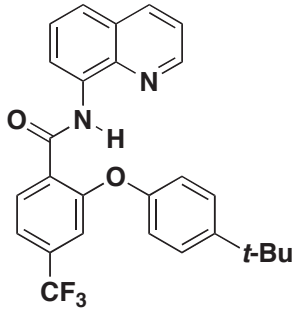
A 10 mL round-bottom flask was charged with amide, (0.5 mmol, 1.0 equiv), $CuCO_3$•$Cu(OH)_2$ (0.054 mmol, 0.12 eq), base (1.0 mmol, 2.0 eq) and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.5 mmol, 1 equiv) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to between (70-110) °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath only after

the starting amide was no longer visible. The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was dry-absorbed on silica and purified by column chromatography to give the pure product.



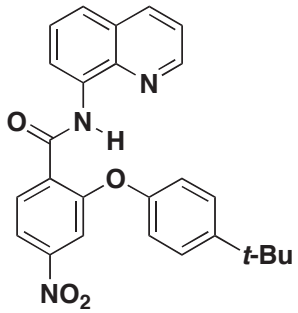
2-(4-*tert*-Butylphenoxy)-4-cyano-*N*-(quinolin-8-yl)benzamide (Table 4, Entry 1)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 4-(cyano)-*N*-(quinolin-8-yl)benzamide (0.137 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), KOAc (0.098 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.075 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 70 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (12 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with hexane/ethyl acetate (6:1) to obtain 0.116 g (55%) the pure product as a white solid. R_f = 0.24 (SiO_2, hexanes/ethyl acetate, 6:1). MP =207 – 208 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.26 (*s*, 1H) 8.96 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.56 (*dd*, *J* = 4.6 Hz, *J* = 1.7 Hz, 1H) 8.46 (*t*, *J* = 8.0 Hz, 1H) 8.13 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 7.59 (*t*, *J* = 8.6 Hz, 1H) 7.54 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.51 (*d*, *J* = 8.6 Hz, 2H) 7.48 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.39 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 7.25 (*d*, *J* = 1.2 Hz, 1H) 7.21 (*d*, *J* = 8.6 Hz, 2H) 1.39 (*s*, 9H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.5, 156.4, 151.9, 148.9, 148.4, 139.1, 136.3, 135.0, 133.4, 128.3, 128.0, 127.5, 127.4, 126.2, 122.3, 121.8, 120.5, 119.9, 117.8, 117.5, 115.9, 34.7, 31.6. FT-IR (neat, cm^{-1}) υ 1656, 1536, 1505, 1485, 1253. HRMS (+ESI): Calculated for $C_{27}H_{24}N_3O_2$ $[M+H]^+$ 422.18630, Found 428.18650.



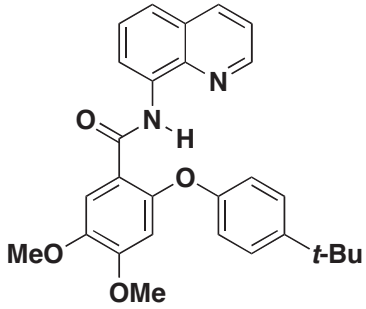
2-(4-*tert*-Butylphenoxy)-4-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (Table 4, Entry 2)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 4-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.158 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), KOAc (0.098 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.075 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 90 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (12 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene/ethyl acetate (100:1) to obtain 0.172 g (74%) the pure product as a faintly yellow solid. R_f = 0.40 (SiO_2, hexanes/ethyl acetate, 8:1). MP 181 – 182 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.25 (*s*, 1H) 8.98 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.57 (*dd*, *J* = 4.0 Hz, *J* = 1.2 Hz, 1H) 8.50 (*d*, *J* = 8.0 Hz, 1H) 8.11 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 7.57 (*t*, *J* = 8.0 Hz, 1H) 7.52 (*d*, *J* = 1.2 Hz, 1H) 7.50 (*m*, 1H) 7.48 (*d*, *J* = 9.2 Hz, 2H) 7.38 (*dd*, *J* = 8.6 Hz, *J* = 5.6 Hz, 1H) 7.29 (*s*, 1H) 7.21 (*d*, *J* = 8.6 Hz, 2H) 1.37 (*s*, 9H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.0, 156.0, 152.6, 148.3, 148.2, 139.1, 136.2, 135.2, 134.5 (*q*, J_{C-F} = 32.4 Hz), 133.3, 128.0, 127.7, 127.2, 123.4 (*q*, J_{C-F} = 272.3 Hz) 122.3, 121.7, 119.8, 119.3, 117.4, 114.8, 34.6, 31.6. The signal for one carbon could not be located. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -62.8. FT-IR (neat, cm^{-1}) υ 1667, 1543, 1326, 1056, 1032, 1011. HRMS (+ESI): Calculated for $C_{27}H_{24}F_3N_2O_2$ $[M+H]^+$ 465.17840, Found 465.17880.



2-(4-*tert*-Butylphenoxy)-4-nitro-*N*-(quinolin-8-yl)benzamide (Table 4, Entry 3)

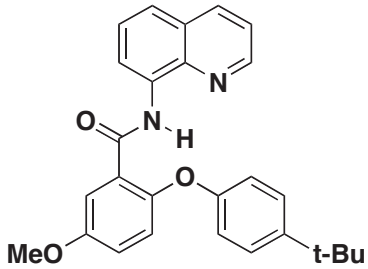
A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 4-(nitro)-*N*-(quinolin-8-yl)benzamide (0.147 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), KOAc (0.098 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.075 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 90 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (12 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with hexane/ethyl acetate (6:1) to obtain 0.130 g (59%) the pure product. R_f = 0.42 (SiO_2, hexanes/ethyl acetate, 6:1). MP =208 – 209 °C (from 2:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.29 (*s*, 1H) 8.97 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.57 (*dd*, *J* = 4.0 Hz, *J* = 1.2 Hz, 1H) 8.54 (*d*, *J* = 8.6 Hz, 1H) 8.14 (*d*, *J* = 6.9 Hz, 1H) 8.03 (*dt*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 7.85 (*d*, *J* = 2.3 Hz, 1H) 7.59 (*t*, *J* = 8.0 Hz, 1H) 7.55 (*d*, *J* = 7.5 Hz, 1H) 7.51 (*d*, *J* = 8.6 Hz, 2H) 7.41 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 7.24 (*d*, *J* = 8.6 Hz, 2H) 1.39 (*s*, 9H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.3, 156.5, 152.0, 150.4 148.9, 148.4, 139.1, 136.3, 135.0, 133.8, 129.7, 128.1, 127.6, 127.5, 122.4, 121.8, 119.7, 117.6, 117.5, 112.3, 34.7, 31.6. FT-IR (neat, cm^{-1}) υ 1667, 1529, 1242. HRMS (+ESI): Calculated for $C_{26}H_{23}N_3O_4Na$ $[M+Na]^+$ 464.15810, Found 464.15790.



2-(4-*tert*-Butylphenoxy)-4,5-dimethoxy-*N*-(quinolin-8-yl)benzamide (Table 4, Entry 4)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3,4-(dimethoxy)-*N*-(quinolin-8-yl)benzamide (0.154 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g,

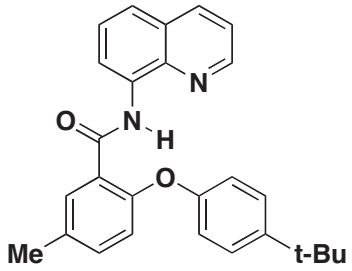
0.054 mmol), K_3PO_4 (0.212 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.075 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (12 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with toluene/ethyl acetate (30:1 to 10:1) to obtain 0.131 g (57%) of the pure product. R_f = 0.35 (SiO_2, hexanes/ethyl acetate, 6:1). MP =199 – 200 °C (from 2:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.18 (*s*, 1H) 8.96 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.61 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.07 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 7.90 (*s*, 1H) 7.53 (*t*, *J* = 8.0 Hz, 1H) 7.45 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.37 (*d*, *J* = 9.2 Hz, 2H) 7.36 (*m*, 1H) 7.13 (*d*, *J* = 9.2 Hz, 2H) 6.61 (*s*, 1H) 4.01 (*s*, 3H) 3.81 (*s*, 3H) 1.31 (*s*, 9H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 163.0, 154.7, 152.7, 149.2, 148.0, 146.4, 145.6, 139.2, 136.1, 135.7, 128.0, 127.5, 126.6, 121.5, 121.4, 117.7, 117.4, 117.0, 113.0, 103.6, 56.4, 56.3, 34.4, 31.6. FT-IR (neat, cm^{-1}) υ 1660, 1509, 1484, 1272, 1214. HRMS (+ESI): Calculated for $C_{28}H_{29}N_2O_4$ $[M+H]^+$ 457.21220, Found 457.21190.



2-(4-*tert*-Butylphenoxy)-5-methoxy-*N*-(quinolin-8-yl)benzamide (Table 4, Entry 5)

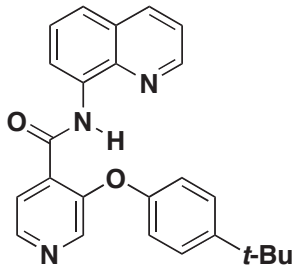
A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3,4-(dimethoxy)-*N*-(quinolin-8-yl)benzamide (0.154 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), K_3PO_4 (0.212 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.075 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (12 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with

toluene/ethyl acetate (30:1 to 10:1) to obtain 0.116 g (54%) of the pure product. R_f = 0.26 (SiO_2, hexanes/ethyl acetate, 6:1). MP = 133 – 134 °C (from 2:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.26 (*s*, 1H) 8.98 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 8.63 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.11 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.91 (*t*, *J* = 1.7 Hz, 1H) 7.56 (*t*, *J* = 8.0 Hz, 1H) 7.49 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 7.39 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 7.36 (*d*, *J* = 8.6 Hz, 2H) 7.12 (*d*, *J* = 9.2 Hz, 2H) 7.03 (*d*, 2H) 3.91 (*s*, 3H) 1.31 (*s*, 9H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 163.1, 155.8, 154.7, 149.0, 148.2, 146.5, 139.3, 136.1, 135.6, 128.1, 127.5, 126.6, 126.0, 121.8, 121.6, 121.1, 120.3, 118.2, 117.3, 114.8, 56.0, 34.4, 31.6. FT-IR (neat, cm^{-1}) υ 1652, 1535, 1486, 1217. HRMS (+ESI): Calculated for $C_{27}H_{27}N_2O_3$ $[M+H]^+$ 427.20160, Found 427.20270.



2-(4-*tert*-Butylphenoxy)-5-methyl-*N*-(quinolin-8-yl)benzamide (Table 4, Entry 6)

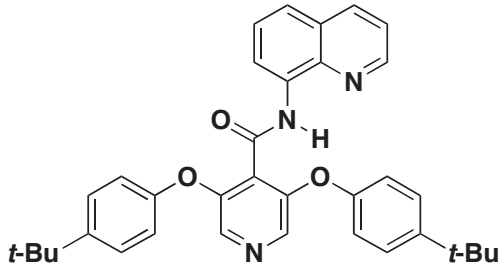
A 100 mL round-bottom flask was equipped with a magnetic stir bar and charged with 3-(methoxy)-*N*-(quinolin-8-yl)benzamide (1.34 g, 5.0 mmol), $CuCO_3$•$Cu(OH)_2$ (0.110 g, 0.50 mmol), K_3PO_4 (2.12 g, 1.0 mmol), and DMF (25 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.758 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (12 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (150 mL). The diluted solution was washed with de-ionized water (2×100 mL), saturated sodium bicarbonate solution (100 mL), and brine (100 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (30 mL) and subjected to column chromatography on SiO_2 (500 mL) with hexane/ethyl acetate (12:1) to obtain 1.25 g (60%) of the pure product. R_f = 0.34 (SiO_2, hexanes/ethyl acetate, 12:1). MP = 136 – 137 °C (from 2:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.22 (*s*, 1H) 9.00 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.61 (*dd*, *J* = 4.0 Hz, *J* = 1.7 Hz, 1H) 8.19 (*d*, *J* = 1.7 Hz, 1H) 8.10 (*dd*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.56 (*t*, *J* = 8.0 Hz, 1H) 7.48 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 7.39 (*d*, *J* = 9.2 Hz, 2H) 7.37 (*dd*, *J* = 8.0 Hz, 4.0 Hz, 1H) 7.25 (*dd*, *J* = 6.3 Hz, 1.7 Hz, 1H) 7.16 (*d*, *J* = 9.2 Hz, 2H) 6.96 (*d*, *J* = 8.0 Hz, 1H) 2.42 (*s*, 3H) 1.33 (*s*, 9H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 163.5, 154.0, 153.4, 148.2, 146.8, 139.2, 136.1, 135.7, 133.6, 133.3, 132.5, 128.0, 127.6, 126.7, 124.6, 121.6, 121.5, 118.8, 118.7, 117.2, 34.5, 31.6, 20.8. FT-IR (neat, cm^{-1}) υ 1661, 1533, 1486, 1236. HRMS (+ESI): Calculated for $C_{27}H_{27}N_2O_2$ $[M+H]^+$ 411.20670, Found 411.20710.



3-(4-*tert*-Butylphenoxy)-*N*-(quinolin-8-yl)pyridine-4-carboxamide (Table 4, Entry 7)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with *N*-(quinolin-8-yl)isonicotinamide (0.125 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), KOAc (0.098 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.225 g, 1.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 90 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (9 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with hexane/ethyl acetate (6:1 to 5:1) to obtain 0.102 g (51%) the pure product as a light yellow oil. R_f = 0.17 (SiO_2, hexanes/ethyl acetate, 6:1). MP 169 – 170 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 12.17 (*s*, 1H) 8.93 (*dd*, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H) 8.54 (*dd*, *J* = 4.6 Hz, *J* = 1.7 Hz, 1H) 8.52 (*d*, *J* = 5.2 Hz, 1H) 8.44 (*s*, 1H) 8.17 (*d*, *J* = 4.6 Hz, 1H) 8.04 (*dd*, *J* = 8.6 Hz, *J* = 1.7 Hz, 1H) 7.50 (*t*, *J* = 8.0 Hz, 1H) 7.45 (*dd*, *J* = 8.6 Hz, *J* = 1.2 Hz, 1H) 7.43 (*d*, *J* = 8.6 Hz, 2H) 7.32 (*dd*, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H) 7.18 (*d*, *J* = 8.6 Hz, 2H) 1.32 (*s*, 9H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.0, 153.0, 150.8, 148.3, 147.8, 144.9, 141.5, 138.9, 136.1, 134.8 130.9, 127.8, 127.3, 127.0, 124.5, 122.3, 121.6, 118.7, 117.4, 34.5, 31.5. 1663, 1542, 1507, 1483, 1223. HRMS (+ESI): Calculated for $C_{25}H_{23}N_3O_2Na$ $[M+Na]^+$ 420.16820, Found 420.16890.

Di-phenoxylation of *N*-(quinolin-8-yl)isonicotinamide.

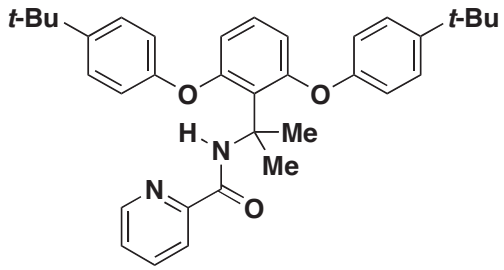


3,5-bis(4-*tert*-Butylphenoxy)-*N*-(quinolin-8-yl)pyridine-4-carboxamide (Table 4, Entry 6)

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with *N*-(quinolin-8-yl)isonicotinamide (0.125 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054

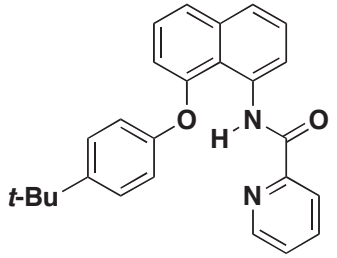
mmol), K_3PO_4 (0.424 g, 2.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.225 g, 1.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (9 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with hexane/ethyl acetate (10:1 to 5:1) to obtain 0.130 g (47%) the pure product as a light yellow oil. R_f = 0.47 (SiO_2, hexanes/ethyl acetate, 10:1). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 10.42 (*s*, 1H) 8.83 (*dd*, *J* = 6.3 Hz, *J* = 1.7 Hz, 1H) 8.74 (*dd*, *J* = 4.0 Hz, *J* = 1.2 Hz, 1H) 8.11 (*s*, 2H) 8.08 (*d*, *J* = 8.0 Hz, 1H) 7.47 (*t*, *J* = 6.9 Hz, 2H) 7.38 (*dd*, *J* = 8.0 Hz, *J* = 3.9 Hz, 1H) 7.34 (*d*, *J* = 8.6 Hz, 4H) 7.11 (*d*, *J* = 8.6 Hz, 4H) 1.27 (*s*, 18H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 160.2, 153.7, 151.5, 148.2, 147.5, 138.3, 136.3, 135.1, 134.1, 127.8, 127.3, 126.8, 126.3, 122.2, 121.6, 118.9, 117.0, 34.4, 31.4. HRMS (+ESI): Calculated for $C_{35}H_{36}N_3O_3$ $[M+H]^+$ 546.27510, Found 546.27460.

Phenoxylation of Picolinamide



***N*-(2-(2,6-bis(4-*tert*-Butylphenoxy)phenyl)propan-2-yl)picolinamide (Compound 3)**
A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with *N*-(2-phenylpropan-2-yl)picolinamide (0.120 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), K_3PO_4 (0.424 g, 2.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.150 g, 1.0 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 130 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (8 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on

SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with hexane/ethyl acetate (10:1 to 6:1) to obtain 0.130 g (48%) of the pure product as a light tan oil. R_f = 0.37 (SiO_2, hexanes/ethyl acetate, 10:1). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.75 (*s*, 1H) 8.23 (*d*, *J* = 4.6 Hz, 1H) 8.04 (*d*, *J* = 8.0 Hz, 1H) 7.69 (*td*, *J* = 8.0 Hz, *J* = 1.7 Hz, 1H) 7.21 (*m*, 1H) 7.19 (*d*, *J* = 9.2 Hz, 4H) 7.05 (*t*, *J* = 8.0 Hz, 1H) 6.90 (*d*, *J* = 8.6 Hz, 4H) 6.68 (*d*, *J* = 8.0 Hz, 2H) 2.05 (*s*, 6H) 1.26 (*s*, 18H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.8, 156.2, 155.6, 150.7, 147.5, 145.0, 136.8, 129.0, 127.7, 126.3, 125.4, 121.5, 117.7, 116.9, 55.2, 34.2, 31.6, 29.9. HRMS (+ESI): Calculated for $C_{35}H_{40}N_3O_3Na$ $[M+Na]^+$ 559.29310, Found 559.29370.



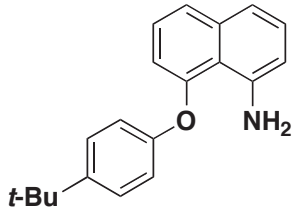
***N*-(1-(4-*tert*-butylphenoxy)naphthalen-8-yl)picolinamide (Compound 4)**

A 10 mL round-bottom flask was equipped with a magnetic stir bar and charged with *N*-(naphthalen-8-yl)picolinamide (0.160 g, 0.5 mmol), $CuCO_3$•$Cu(OH)_2$ (0.012 g, 0.054 mmol), K_3PO_4 (0.212 g, 1.0 mmol), and DMF (2.5 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.075 g, 0.5 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (6 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (25 mL). The diluted solution was washed with de-ionized water (2×15 mL), saturated sodium bicarbonate solution (15 mL), and brine (15 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (10 mL) and subjected to column chromatography on SiO_2 (150 mL) with hexane/ethyl acetate (6:1) to obtain 0.159 g (70%) of the pure product as a beige solid. R_f =0.28 (SiO_2, hexanes/ethyl acetate, 8:1). MP =135 – 136 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 13.08 (*s*, 1H) 9.07 (*dd*, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H) 8.26 (*m*, 2H) 7.79 (*td*, *J* = 7.5 Hz, *J* = 1.7 Hz, 1H) 7.63 (*d*, *J* = 7.5 Hz, 1H) 7.57 (*t*, *J* =8.0 Hz, 2H) 7.41 (*d*, *J* = 9.2 Hz, 2H) 7.31 (*m*, 2H) 7.16 (*d*, *J* = 8.6 Hz, 2H) 6.97 (*d*, *J* = 8.6 Hz, 1H) 1.35 (*s*, 9H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.7, 154.4, 154.1, 150.6, 147.8, 146.9, 137.3, 136.6, 134.7, 126.9, 126.5, 126.0, 125.7, 124.0, 123.9, 122.1, 119.5, 117.8, 116.9, 113.7, 34.4, 31.6. FT-IR (neat, cm^{-1}) υ 1681, 1540, 1497, 1227. HRMS (+ESI): Calculated for $C_{26}H_{25}N_2O_2$ $[M+H]^+$ 397.19110, Found 397.19220.

Large Scale Synthesis

A 100 mL round-bottom flask was equipped with a magnetic stir bar and charged with *N*-(naphthalen-8-yl)picolinamide (1.24 g, 5.0 mmol), $CuCO_3 \bullet Cu(OH)_2$ (0.124 g, 0.56 mmol mmol), K_3PO_4 (2.12 g, 10.0 mmol), and DMF (25 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes followed by addition of 4-*tert*-butylphenol (0.758 g, 5.0 mmol) and stirring for an additional 5 minutes at room temperature. The flask was then equipped with a reflux condenser and placed in an oil-bath that had been pre-heated to 110 °C. The reaction was monitored by TLC analysis at regular intervals and removed from the oil bath after full consumption of the amide starting material (12 hours). The resulting dark-brown mixture was allowed to cool to room temperature and dissolved in ethyl acetate (100 mL). The diluted solution was washed with de-ionized water (2×25 mL), saturated sodium bicarbonate solution (25 mL), and brine (25 mL). The remaining organic portion was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (20 mL) and subjected to column chromatography on SiO_2 (400 mL) with hexane/ethyl acetate (6:1) to obtain 1.98 g (73%) of the pure product as a beige solid.

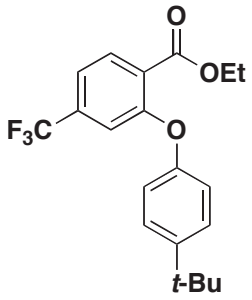
Clevage of Picolinamide Auxiliary



8-(4-*tert*-Butylphenoxy)naphthalen-1-amine (Compound 5)

A 50 mL pressure-bomb equipped with a magnetic stir bar was charged with *N*-(1-(4-*tert*-butylphenoxy)naphthalen-8-yl)picolinamide (1.38 g, 3.48 mmol), NaOH (1.39 g, 34.8 mmol) and 15 mL of a 10:1 mixture of ethanol and water. The vessel was sealed and placed in an oil bath, which had been that had been pre-heated to 130 °C, for 8 hours. After cooling to room temperature, the reaction mixture was diluted with de-ionized water (30 mL) and extracted with CH_2Cl_2 (4×40 mL). The combined organic portions were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was absorbed on SiO_2 (30 mL) and subjected to column chromatography on SiO_2 (300 mL) with toluene/ethyl acetate (30:1) to obtain 1.01 g (88%) of the pure product as a beige solid. R_f = 0.47 (SiO_2, toluene/ethyl acetate, 30:1). MP =126 – 127 °C (from 6:1 hexanes/ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.49 (*d*, *J* = 8.0 Hz, 1H) 7.42 (*d*, *J* = 8.6 Hz, 2H) 7.22 (*m*, 3H) 7.03 (*d*, *J* = 8.6 Hz, 2H) 6.68 (*d*, *J* = 7.5 Hz, 1H) 6.62 (*d*, *J* = 7.6 Hz, 1H) 5.22 (*s*, 2H) 1.33 (*s*, 9H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 155.9, 154.3, 147.0, 144.1, 137.5, 127.3, 127.0, 125.7, 123.7, 119.4, 117.4, 116.4, 112.3, 110.2, 34.5, 31.6. FT-IR (neat, cm^{-1}) υ 1593, 1578, 1504, 1396, 1231. HRMS (+ESI): Calculated for $C_{20}H_{22}NO$ $[M+H]^+$ 292.16960, Found 292.16870.

Cleavage of 8-Aminoquinoline Auxiliary



2-(4-*tert*-Butylphenoxy)-4-(trifluoromethyl)benzoic acid Ethyl Ester (Compound 6)

A 2-dram screw-cap vial was equipped with a magnetic stir bar and charged with 2-(4-*tert*-butylphenoxy)-5-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.116 g, 0.25 mmol). Sequential addition of NaOH (0.150 g, 3.75 mmol) and ethanol (1.0 mL) resulted in a tan suspension. The suspension was heated at 120 °C for 24 hours giving a light-yellow mixture. After cooling to room temperature (22 °C) the solution was diluted with 25 mL of ethyl acetate and washed with 1M HCl (4×20 mL). The combined aqueous layers were washed with ethyl acetate (4×25 mL) and the organic portions were collected and dried over Na_2SO_4. Rotary evaporation resulted in isolation of 0.084 g (91%) of product as a yellow oil. R_f = 0.27 (SiO_2, hexane/ethyl acetate, 12:1). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.42 (*d*, *J* = 1.7 Hz, 1H) 7.89 (*dd*, *J* = 9.2 Hz, *J* = 2.3 Hz, 1H) 7.24 (*d*, *J* = 8.6 Hz, 2H) 7.14 (*d*, *J* = 8.6 Hz, 1H) 6.82 (*d*, *J* = 8.6 Hz, 1H) 4.36 (*q*, *J* = 7.5 Hz, 2H) 1.58 (*t*, *J* = 6.9 Hz, 3H) 1.28 (*s*, 9H) ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 165.2, 159.9, 153.5, 143.3, 132.1, 131.1, 126.4 124.5 (*q*, J_{C-F} = 33.6 Hz), 123.6 (*q*, J_{C-F} = 271.1 Hz) 118.2, 114.9, 113.2, 66.7, 34.1, 31.6, 14.6. ^{19}F NMR (470 MHz, $CDCl_3$, ppm) δ -62.0.

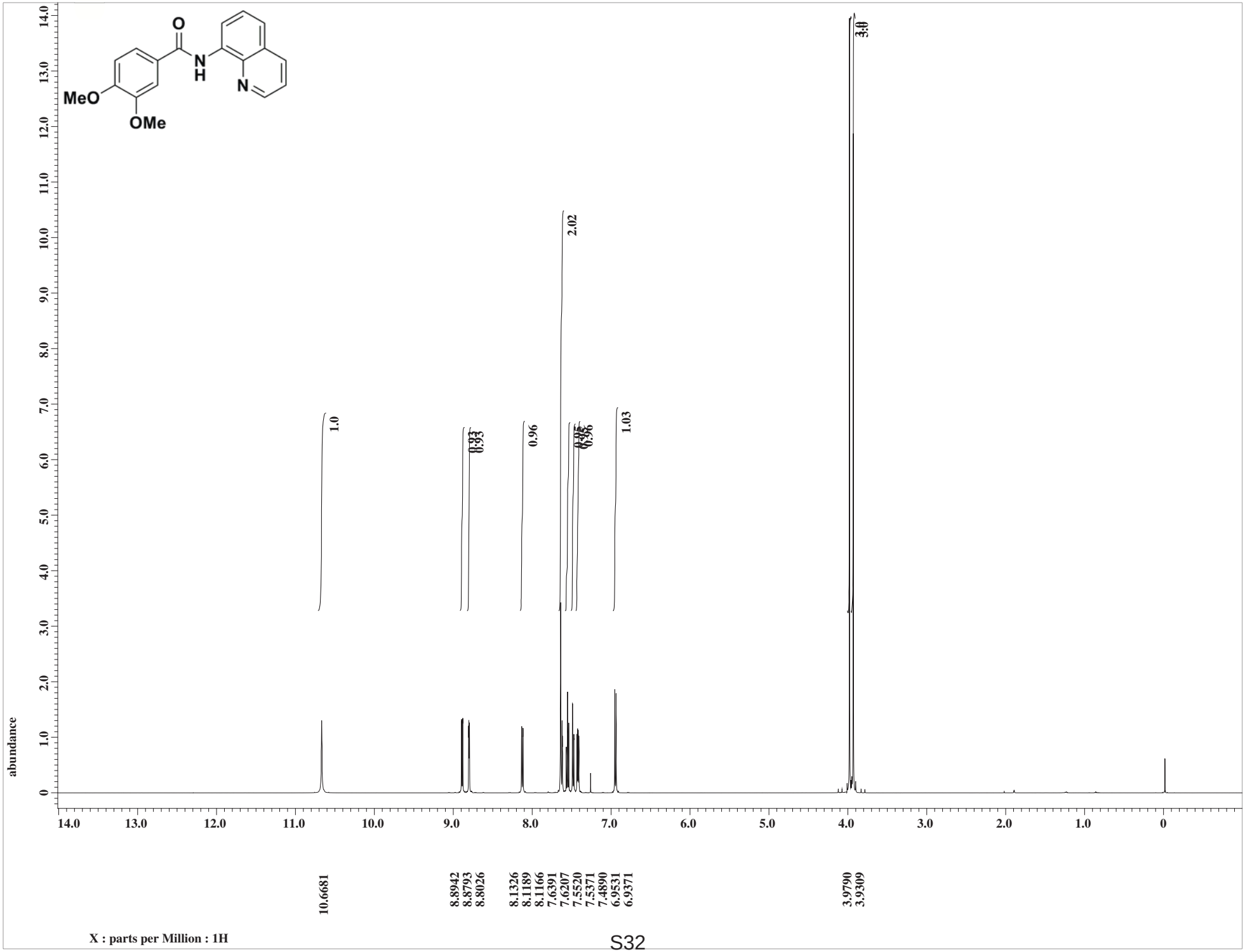
Control Experiment

Standard Conditions Without Copper Catalyst.

A 4-dram screw-cap vial was equipped with a magnetic stir bar and charged with 3-(trifluoromethyl)-*N*-(quinolin-8-yl)benzamide (0.032 g, 0.1 mmol), K_2CO_3 (0.028 g, 0.2 mmol), and DMF (1 mL). The resulting mixture was stirred at room temperature (20 °C) for 5 minutes. 4-*tert*-butylphenol (0.030 g, 0.2 mmol) was added and the vial was allowed to stir for 5 minutes at room temperature. The vial was placed in a reaction block that had been pre-heated to 110 °C for 12 hours. The resulting mixture was allowed to cool to room temperature then dissolved in 15 mL of ethyl acetate. The diluted solution was washed with de-ionized water (2×10 mL), saturated sodium bicarbonate solution (10 mL), and brine (10 mL). The remaining organic portion was dried over sodium sulfate, filtered through a pad of celite®, and concentrated under reduced pressure. After drying under vacuum for 12 hours 0.1 eq of 1,3,5-trimethoxybenzene was added as an internal standard and the yield was determined by NMR spectroscopy. No detectable amount of product was observed.

References:

1: Tran, L. D.; Roane, J.; Daugulis, O. *Angew. Chem. Int. Ed*. **2013**, *52*, 6043.
2: Truong, T; Klimovica, K.; Daugulis, O. *J. Am. Chem. Soc*. **2013**, *135*, 9342.
3: Tran, L. D.; Popov, I.; Daugulis, O. *J. Am. Chem. Soc*. **2012**, *134*, 18237.
4: Lehao, H.; Qian, L.; Chen, W.; Chenze, Q. *J. Org. Chem.* **2013**, *78*, 3030.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8.8026
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8.1189
8.1166
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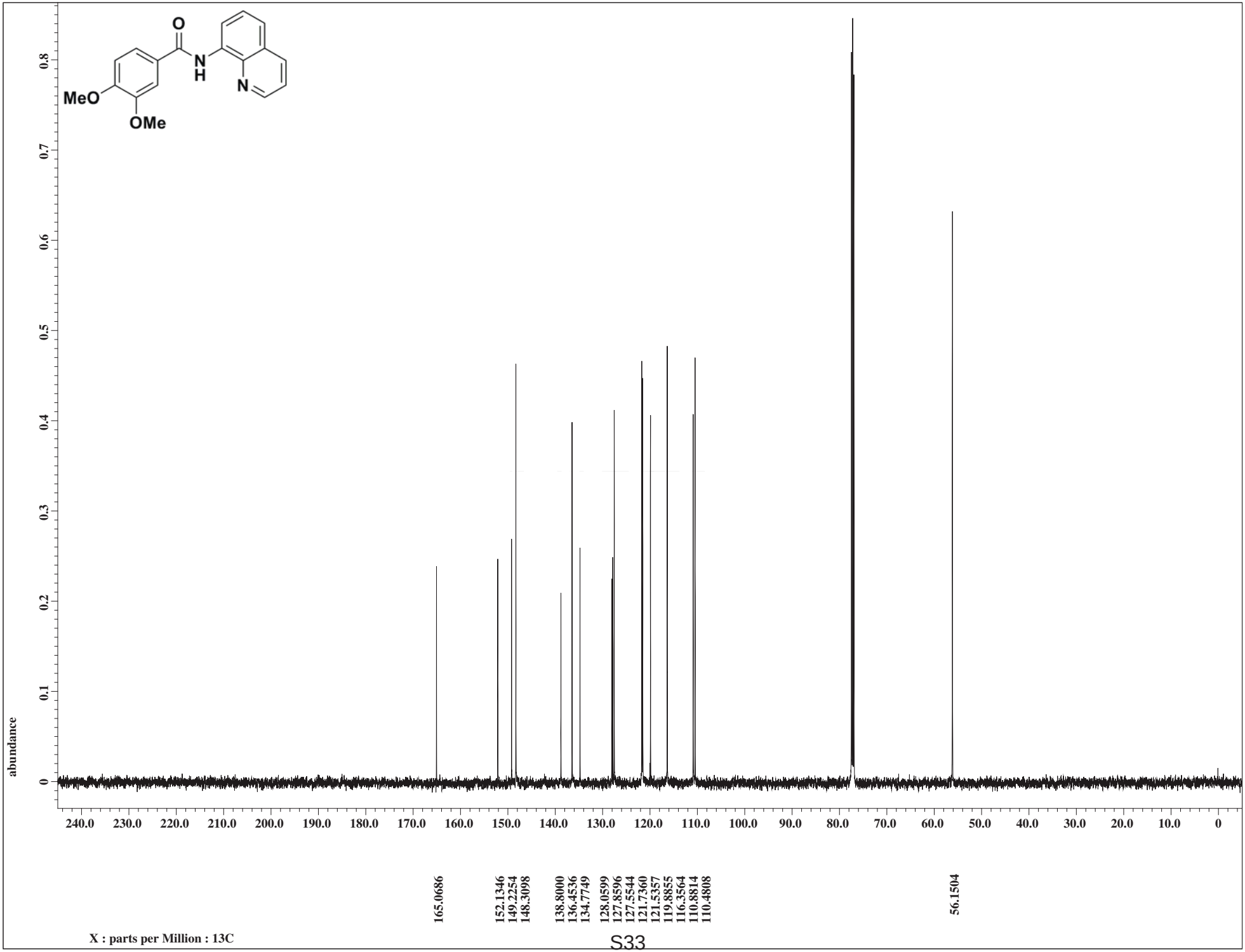
3.9309
X : parts per Million : 1H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200.0
190.0
180.0
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160.0
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140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
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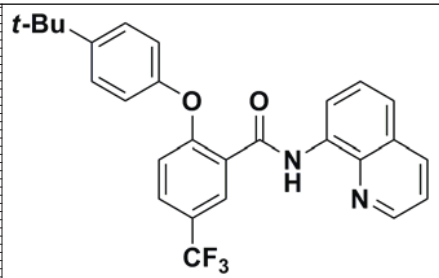

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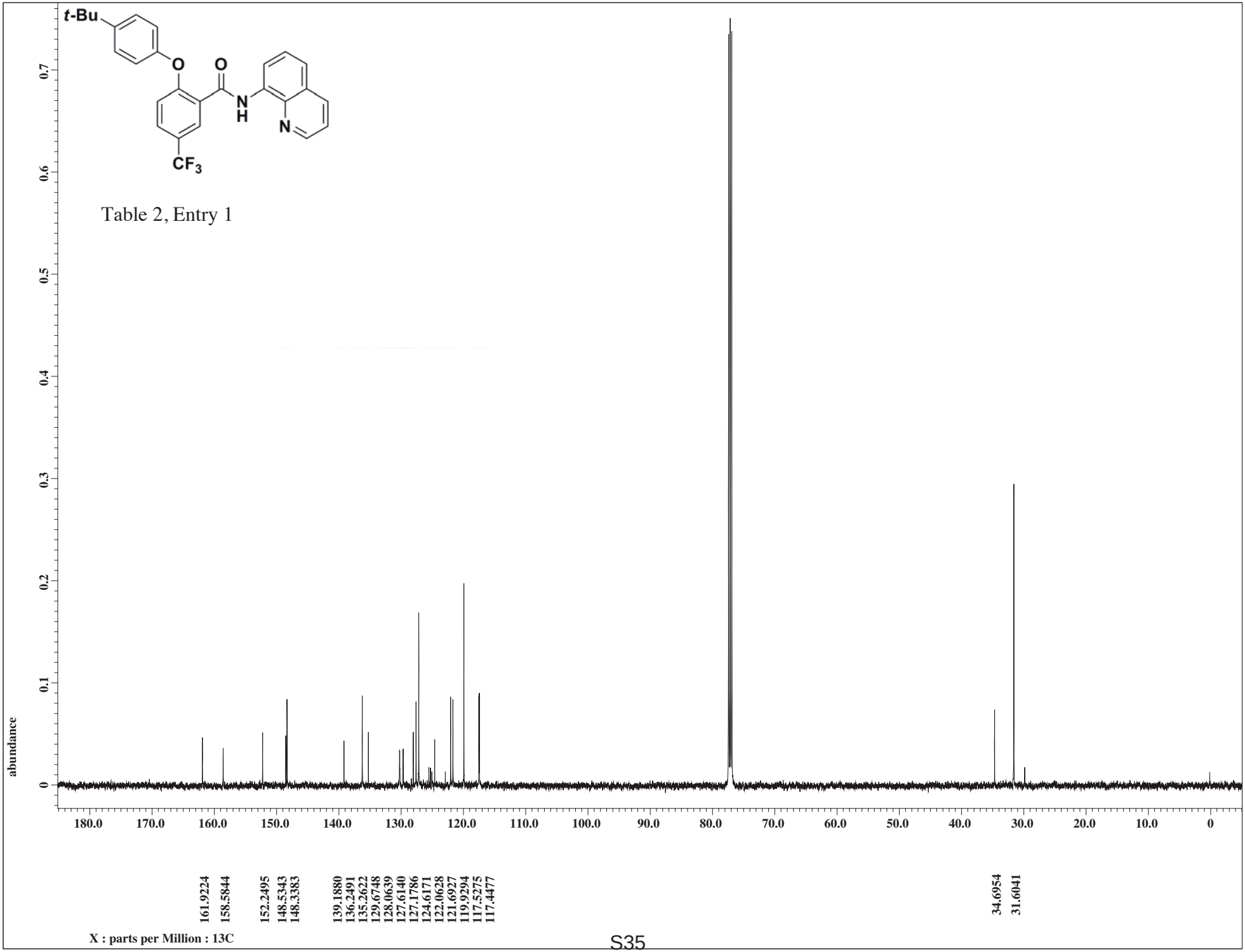
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110.0
100.0
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20.0
10.0
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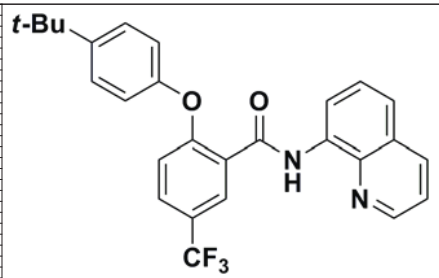

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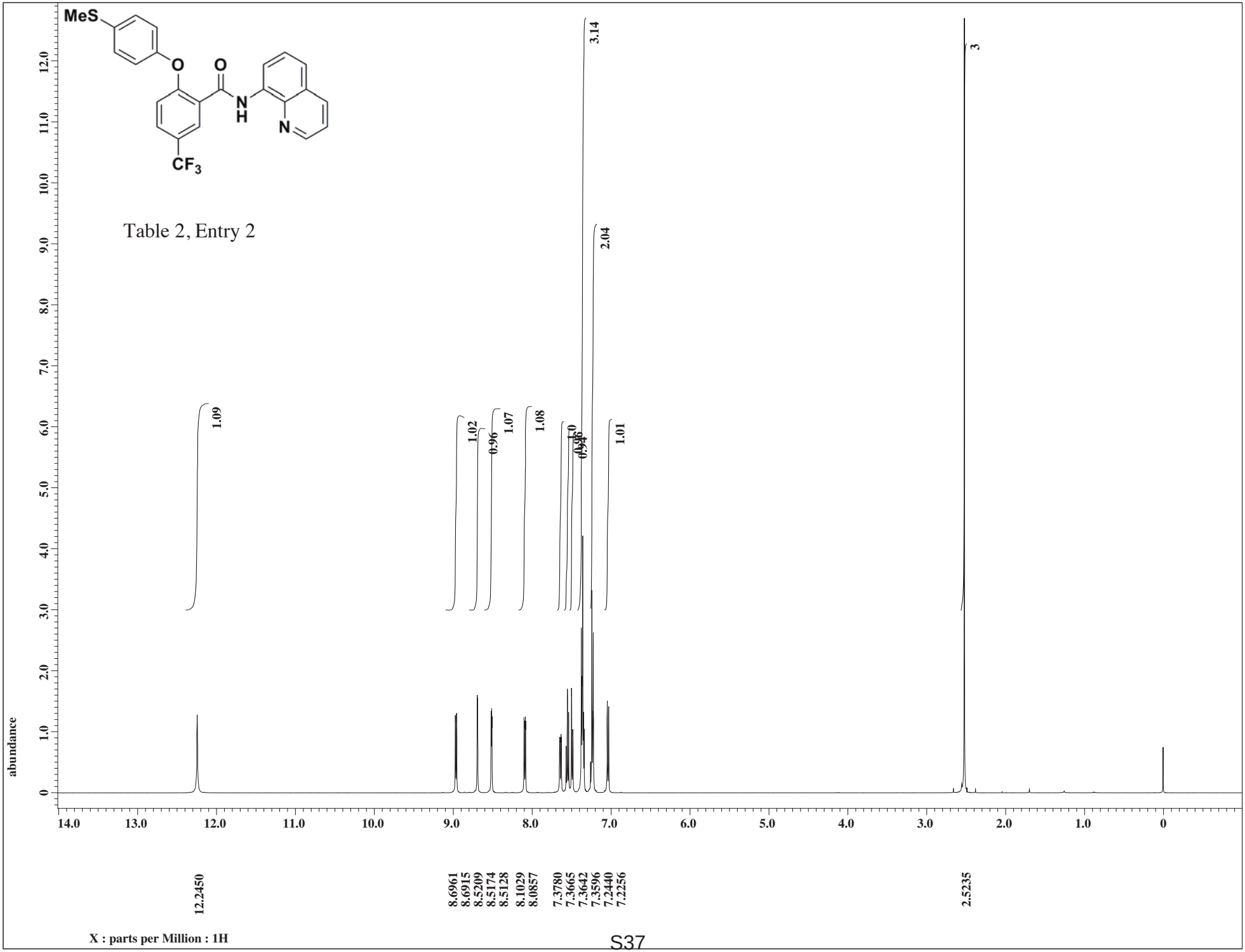
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H
N
CF3
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7.3642
7.3596
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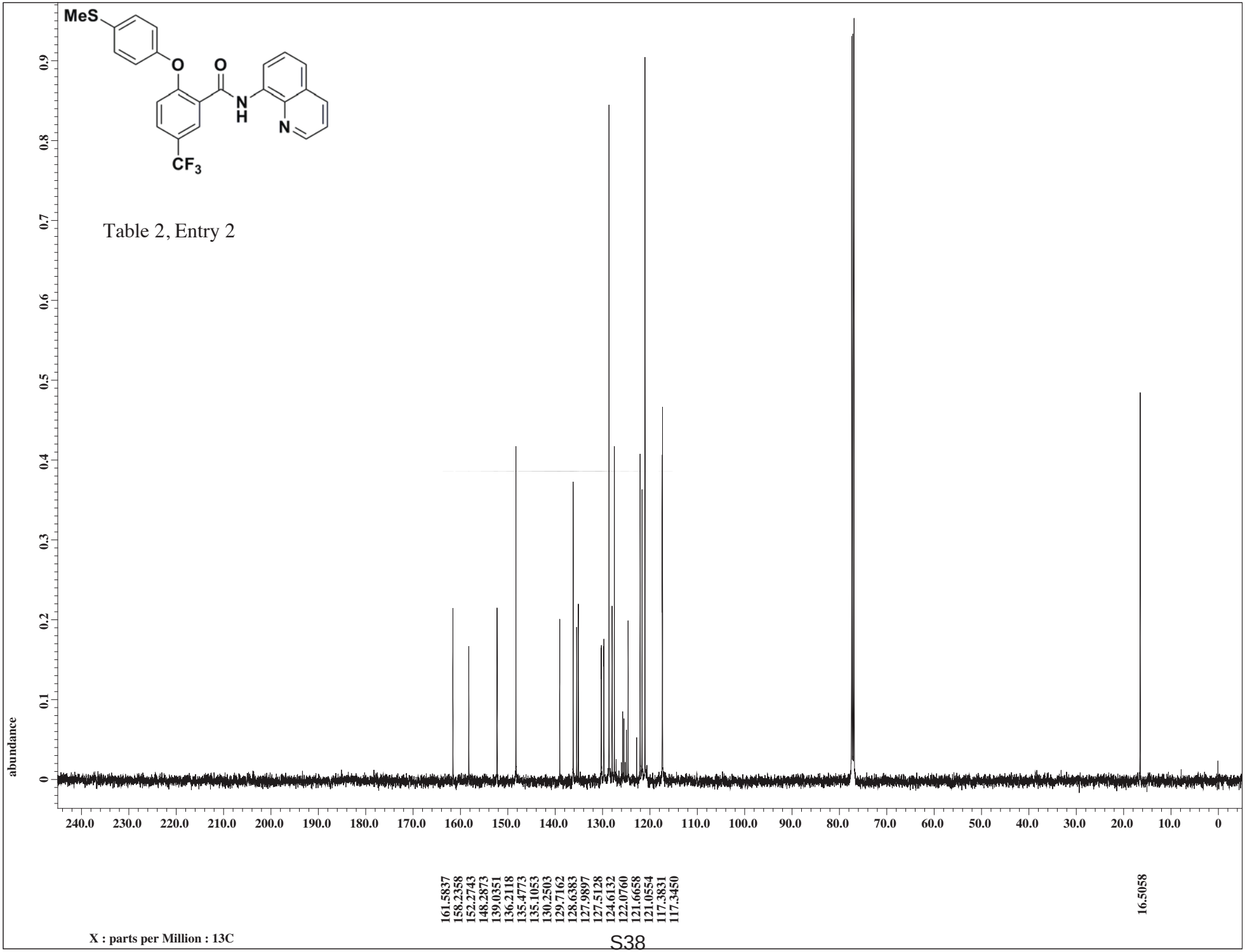
1.02
0.96
1.07
1.08
1.01
2.04
3.14
3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O
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H
N
CF3
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0.6
0.7
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0.9
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220.0
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200.0
190.0
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170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
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60.0
50.0
40.0
30.0
20.0
10.0
0
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139.0351
136.2118
135.4773
135.1053
130.2503
129.7162
128.6383
127.9897
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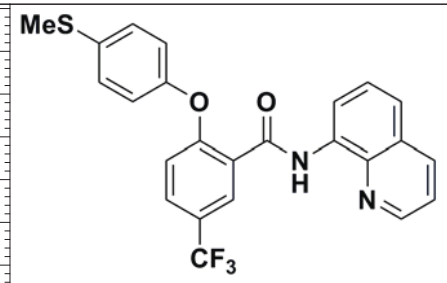
X : parts per Million : 13C



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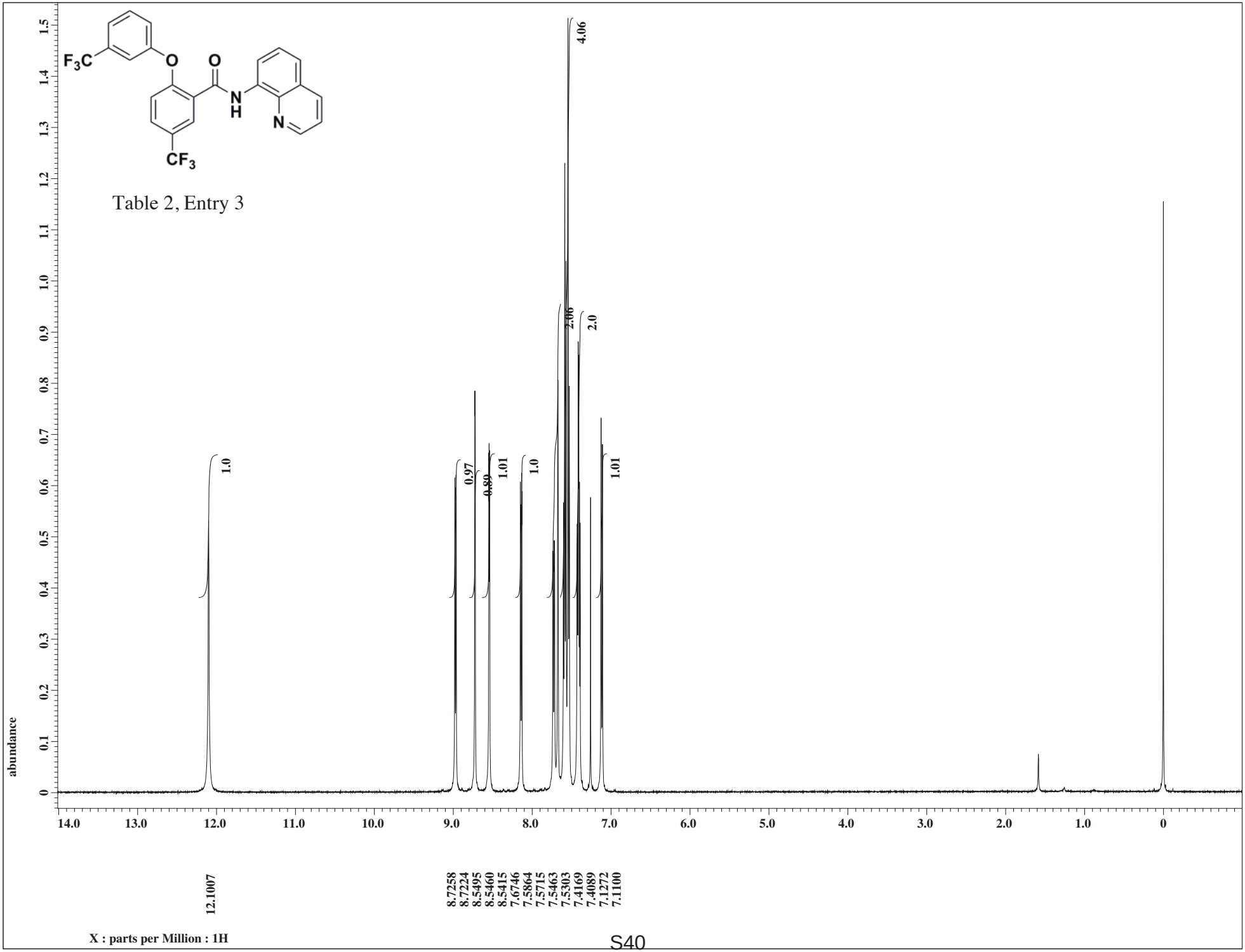
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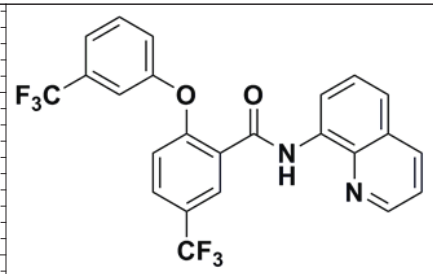
X : parts per Million : 1H



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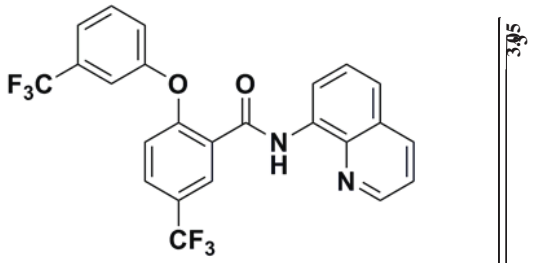

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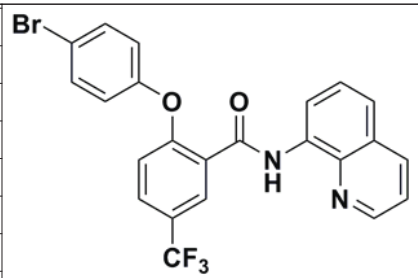

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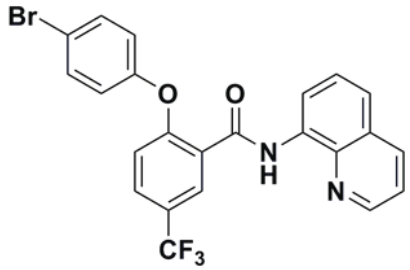

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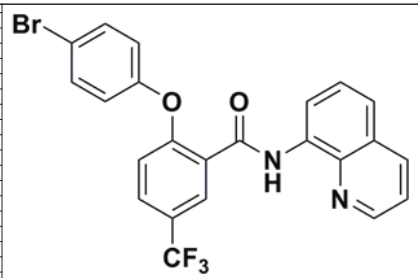

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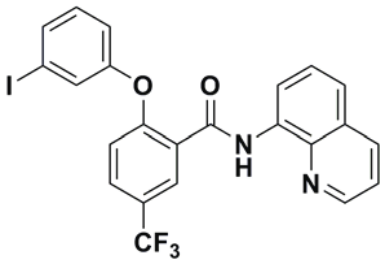

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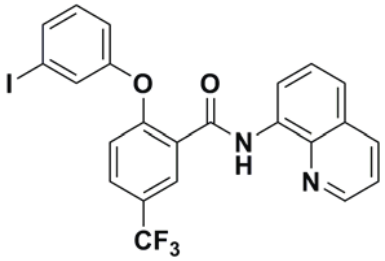

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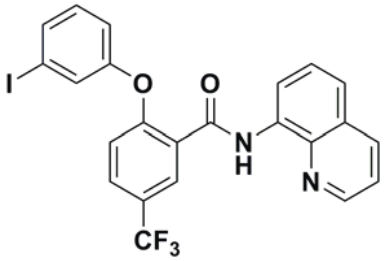

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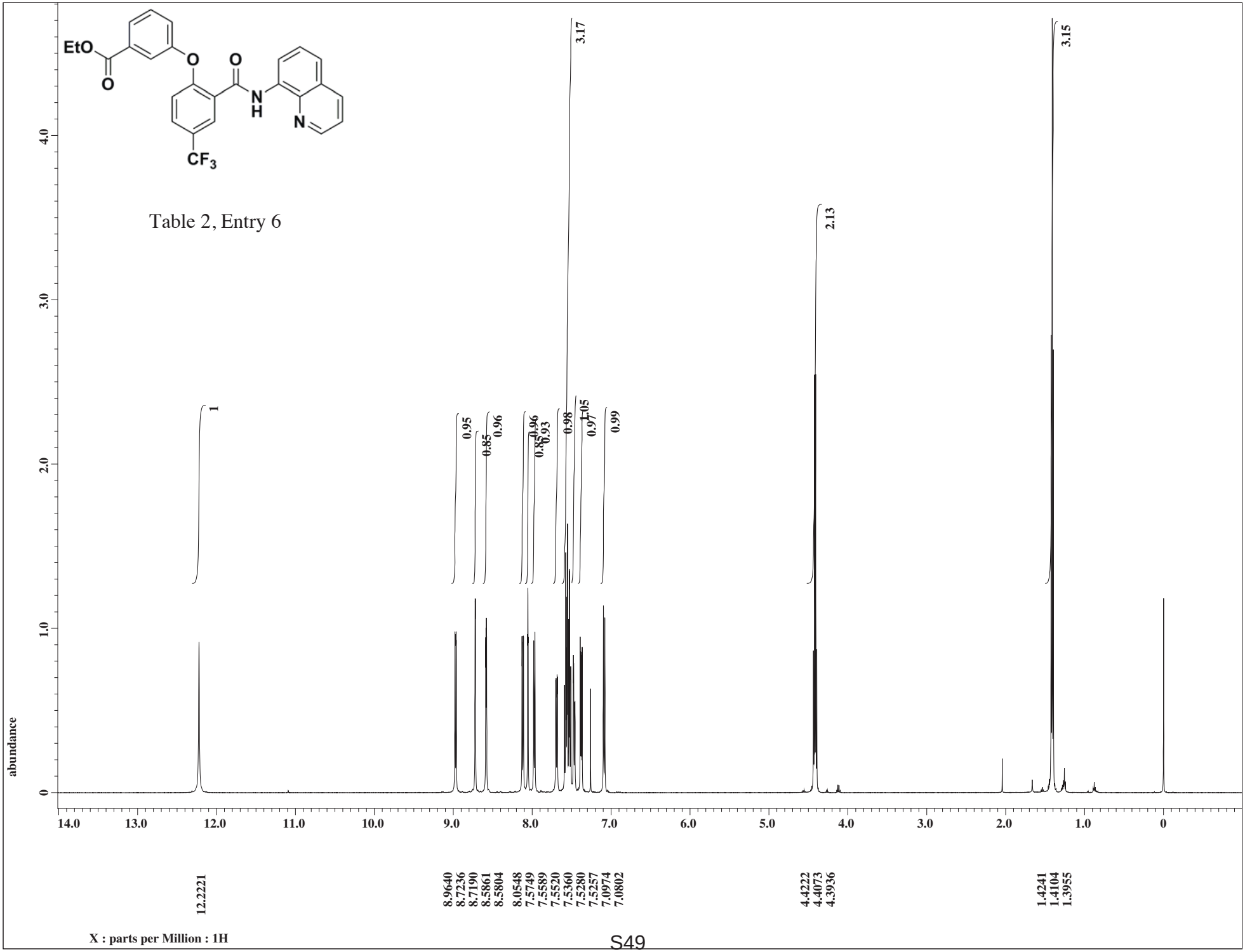
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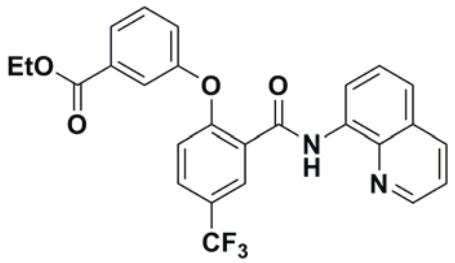

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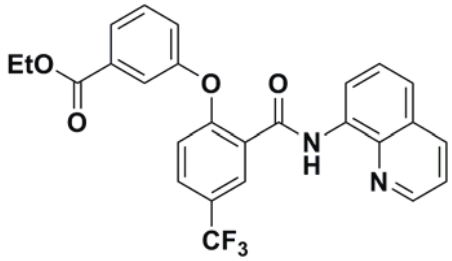

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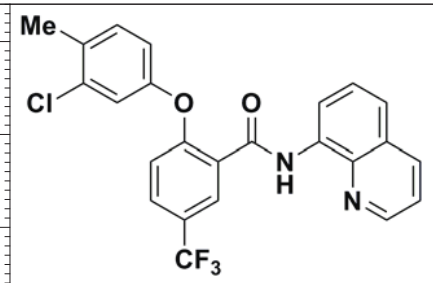

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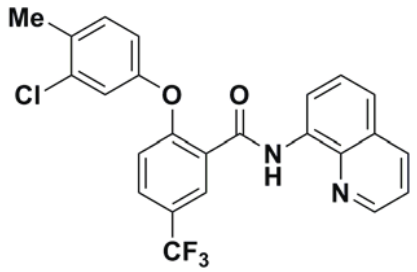

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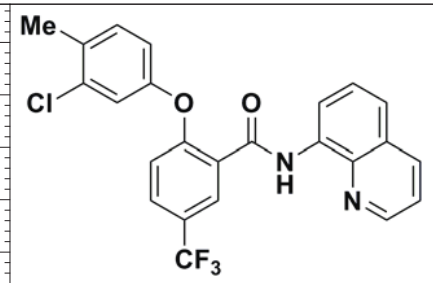

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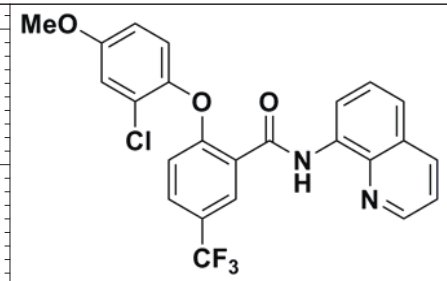

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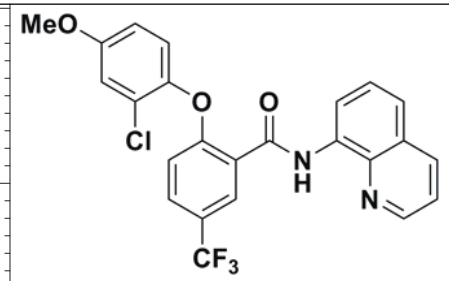


Table 2, Entry 8

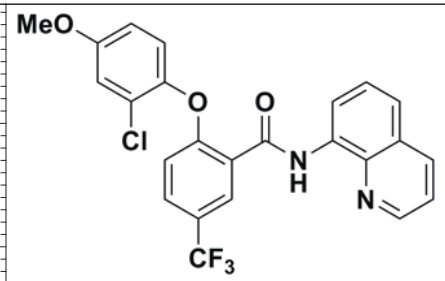


Table 2, Entry 8

abundance

9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0

−30.0 −40.0 −50.0 −60.0 −70.0 −80.0 −90.0 −100.0 −110.0 −120.0 −130.0 −140.0 −150.0

−61.8351

X : parts per Million : 19F

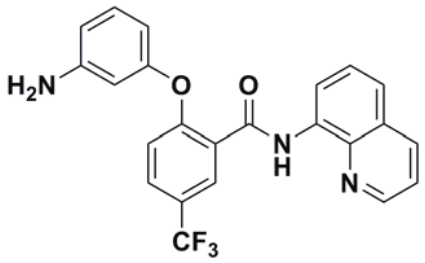


Table 2, Entry 9

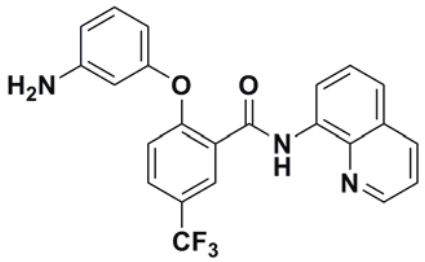


Table 2, Entry 9

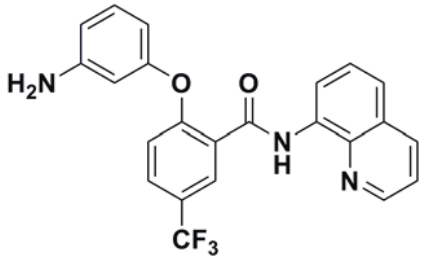
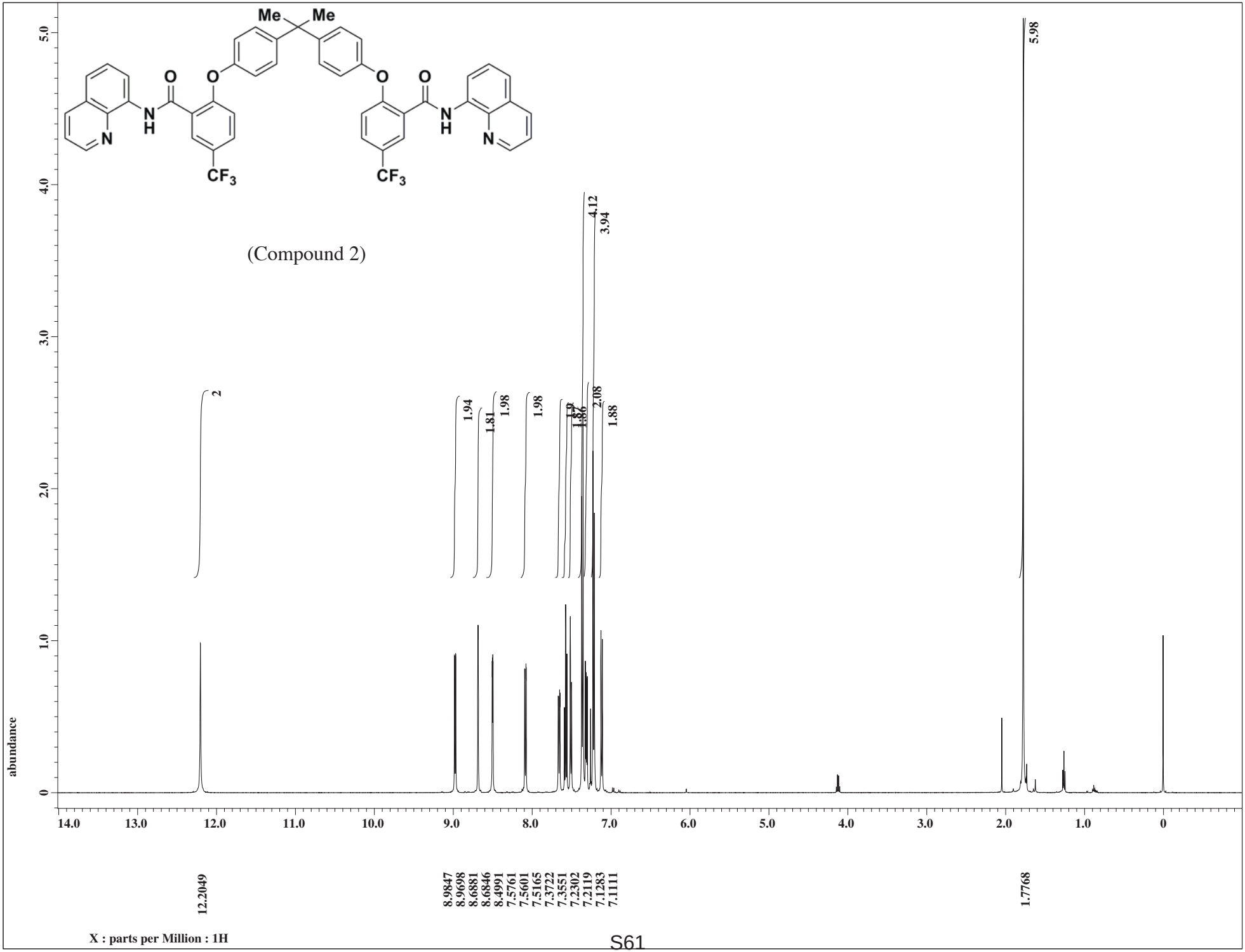
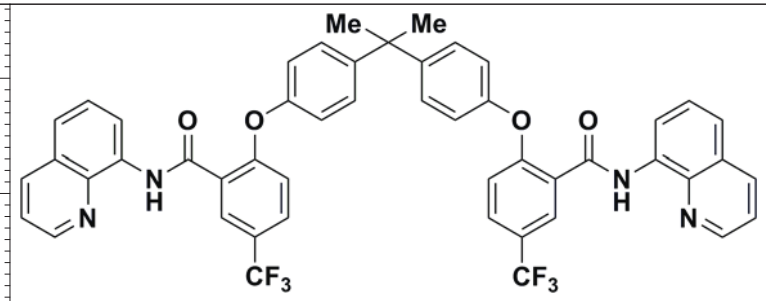


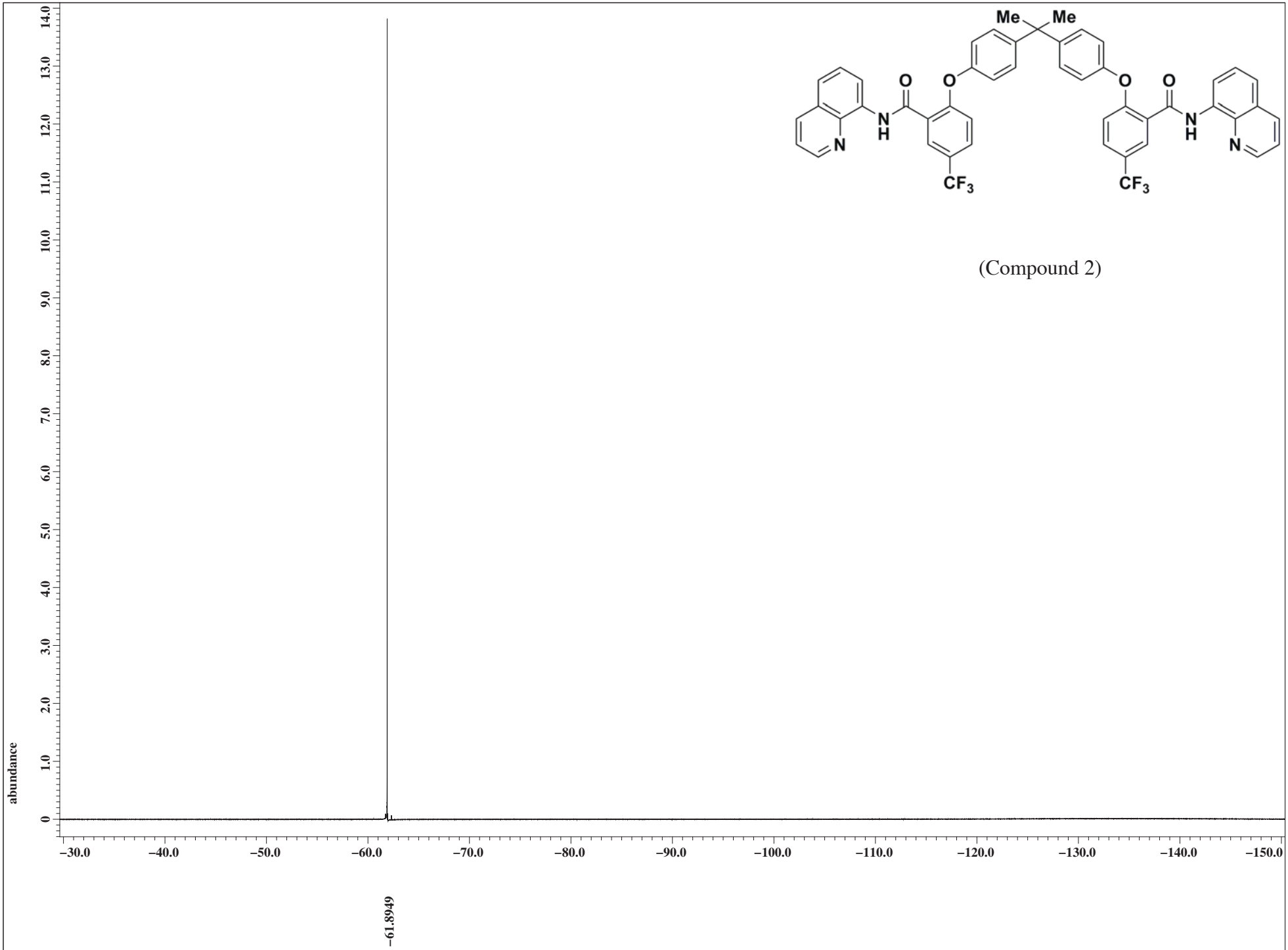
Table 2, Entry 9


Me
Me
O
O
O
O
N
H
N
H
N
N
CF3
CF3
(Compound 2)
5.98
4.12
3.94
2.08
1.98
1.98
1.94
1.88
1.86
1.81
2
abundance
0
1.0
2.0
3.0
4.0
5.0
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
12.2049
8.9847
8.9698
8.6881
8.6846
8.4991
7.5761
7.5601
7.5165
7.3722
7.3551
7.2302
7.2119
7.1283
7.1111
1.7768
X : parts per Million : 1H

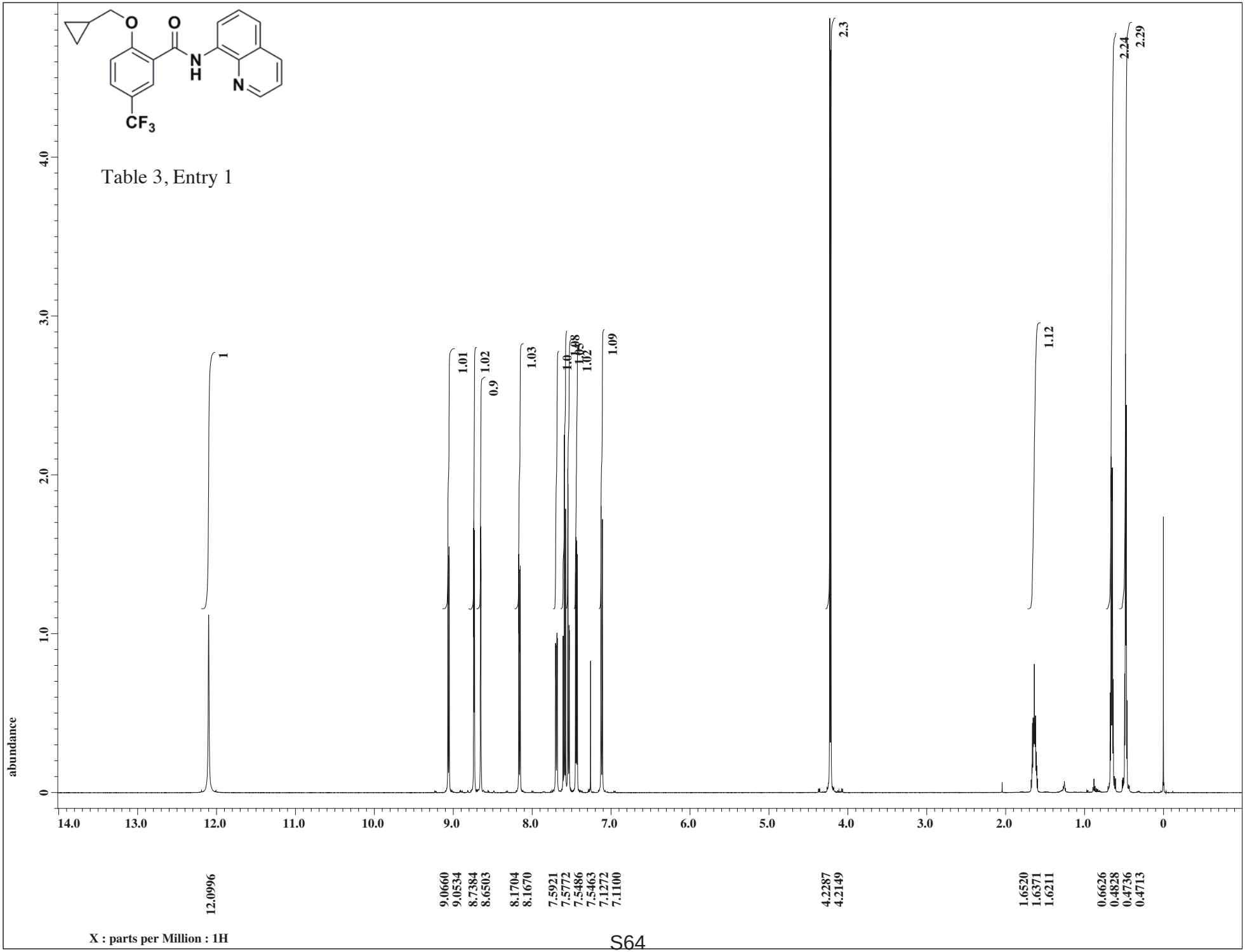

Me
Me
O
O
O
O
N
H
N
H
N
N
CF3
CF3

(Compound 2)

abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
240.0
230.0
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
161.8128
158.1787
152.8277
148.1825
147.5530
139.1211
136.2977
135.1532
130.2504
129.6972
128.6194
128.0566
127.6369
124.9853
122.1238
121.6469
119.8155
117.9269
117.4691
42.6695
31.0900
X : parts per Million : 13C


Me
Me
O
O
O
O
N
H
N
H
N
N
CF3
CF3
abundance
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
−30.0
−40.0
−50.0
−60.0
−70.0
−80.0
−90.0
−100.0
−110.0
−120.0
−130.0
−140.0
−150.0
−61.8949
X : parts per Million : 19F

(Compound 2)


O
O
N
H
N
CF3
Table 3, Entry 1
abundance
4.0
3.0
2.0
1.0
0
1
1.01
1.02
0.9
1.03
1.0
1.08
1.03
1.02
1.09
1.12
2.3
2.24
2.29
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
12.0996
9.0660
9.0534
8.7384
8.6503
8.1704
8.1670
7.5921
7.5772
7.5486
7.5463
7.1272
7.1100
4.2287
4.2149
1.6520
1.6371
1.6211
0.6626
0.4828
0.4736
0.4713
X : parts per Million : 1H

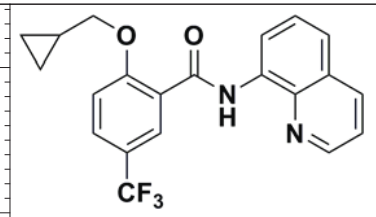


Table 3, Entry 1

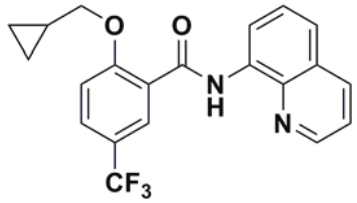
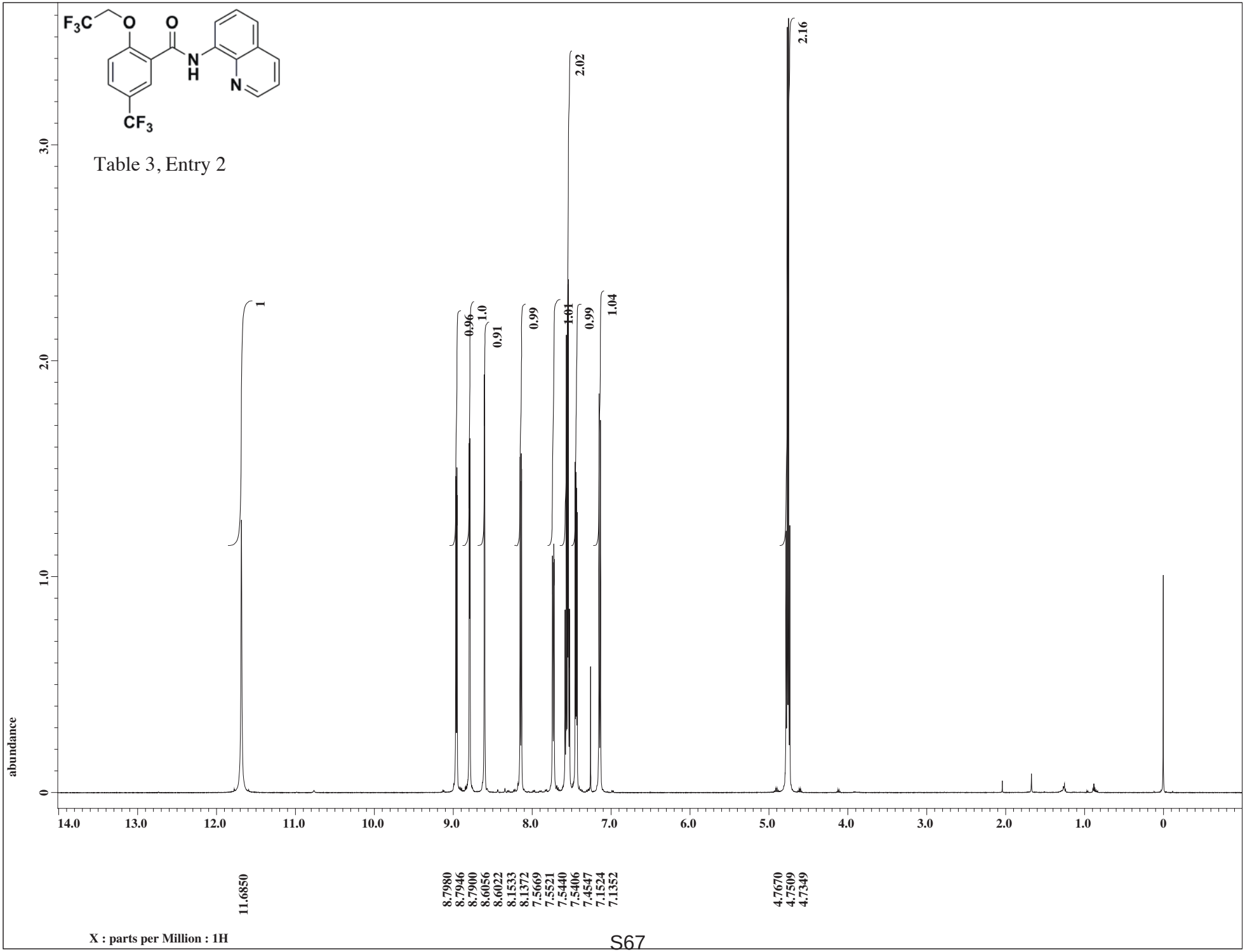


Table 3, Entry 1


F3C
O
O
N
H
N
CF3
Table 3, Entry 2
abundance
X : parts per Million : 1H
11.6850
8.7980
8.7946
8.7900
8.6056
8.6022
8.1533
8.1372
7.5669
7.5521
7.5440
7.5406
7.4547
7.1524
7.1352
4.7670
4.7509
4.7349

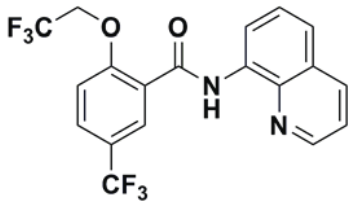
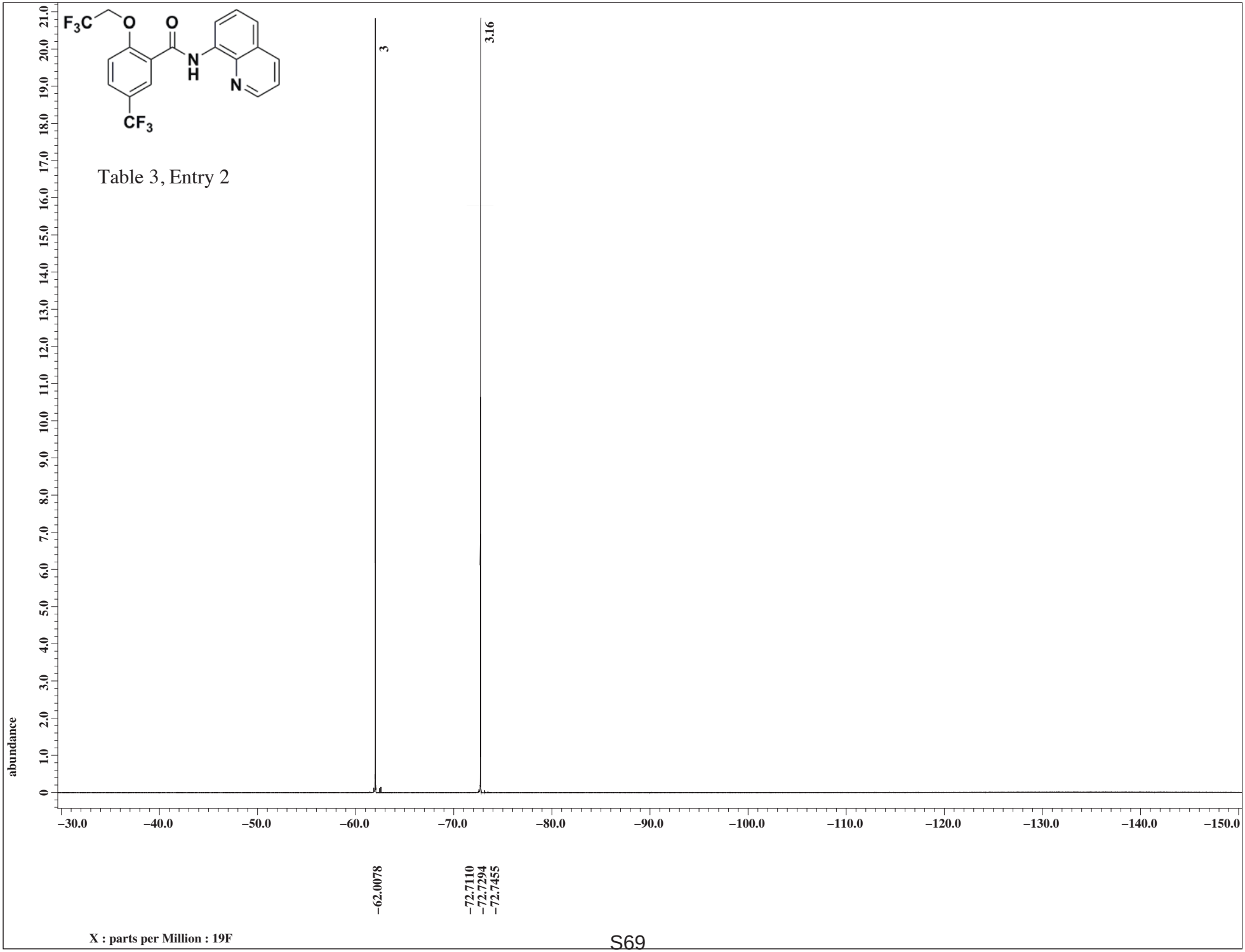


Table 3, Entry 2


F3C
O
O
N
H
N
CF3
Table 3, Entry 2
3
3.16
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
15.0
16.0
17.0
18.0
19.0
20.0
21.0
−30.0
−40.0
−50.0
−60.0
−70.0
−80.0
−90.0
−100.0
−110.0
−120.0
−130.0
−140.0
−150.0
−62.0078
−72.7110
−72.7294
−72.7455
X : parts per Million : 19F

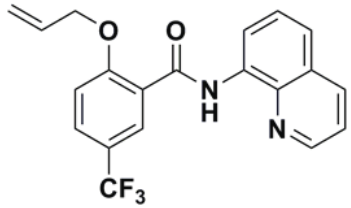


Table 3, Entry 3

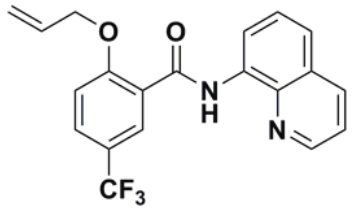


Table 3, Entry 3

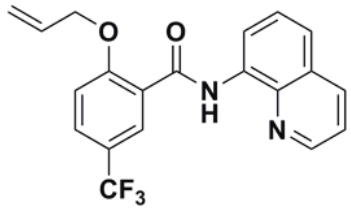
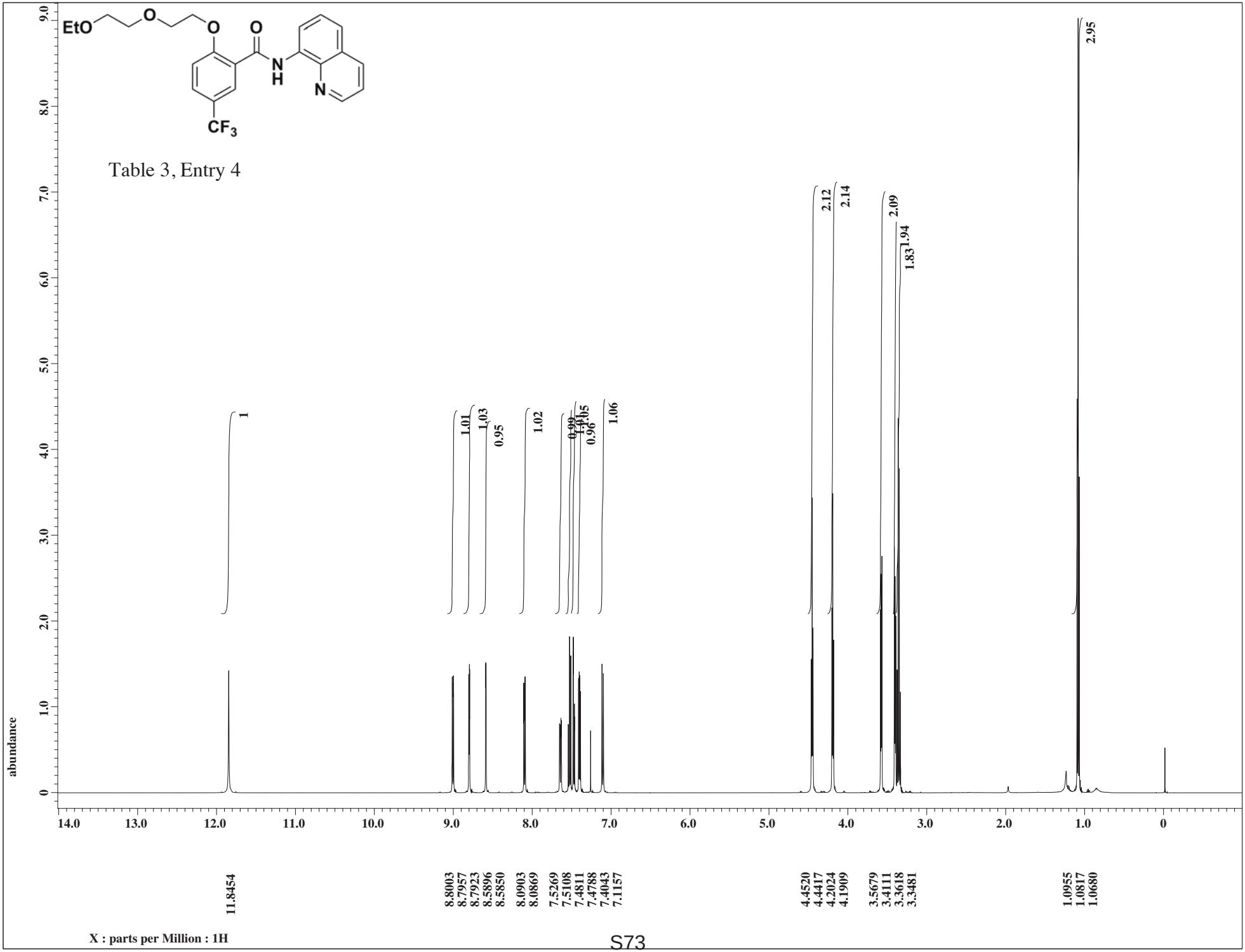
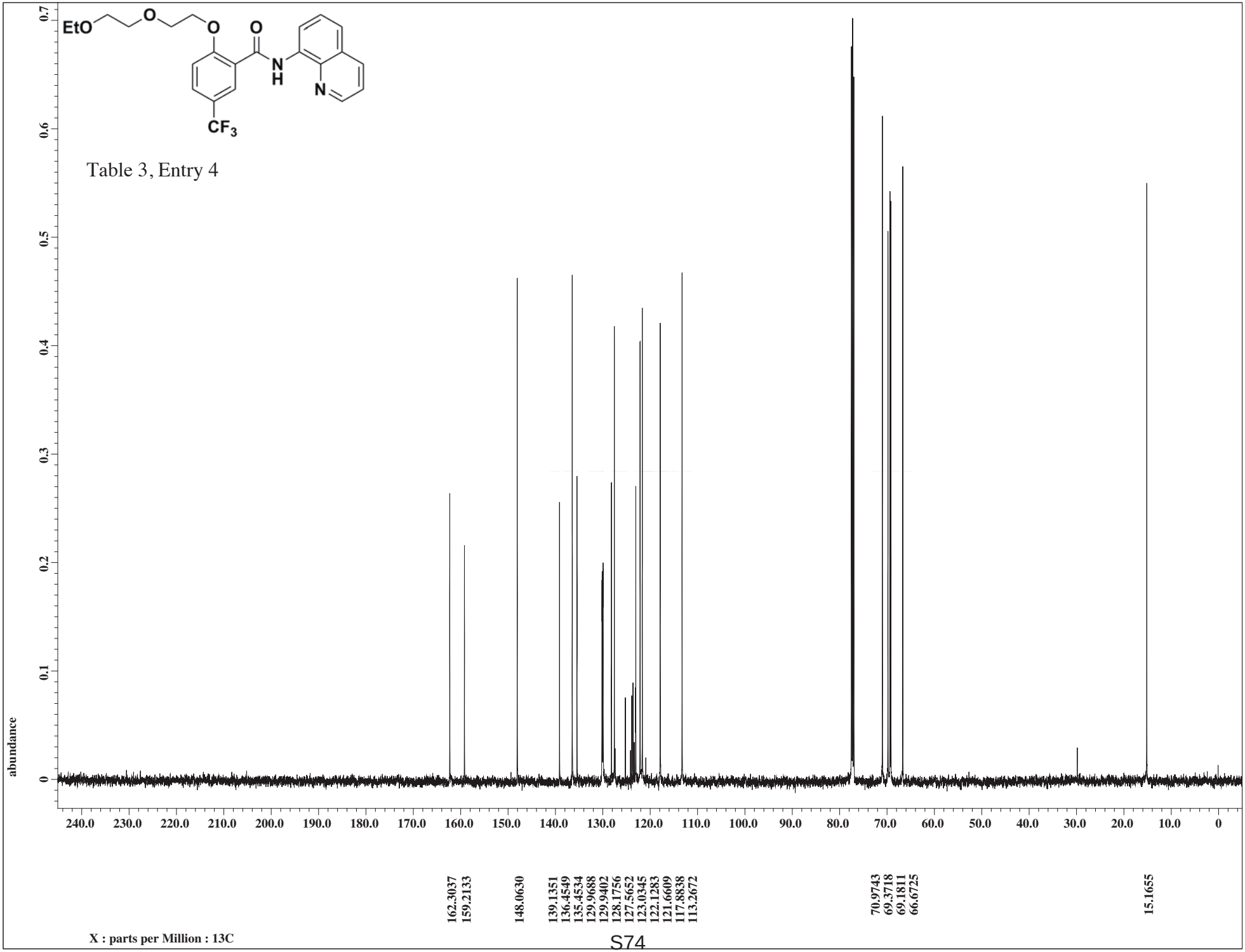


Table 3, Entry 3


EtO
O
O
O
N
H
N
CF3
Table 3, Entry 4
abundance
X : parts per Million : 1H
11.8454
8.8003
8.7957
8.7923
8.5896
8.5850
8.0903
8.0869
7.5269
7.5108
7.4811
7.4788
7.4043
7.1157
4.4520
4.4417
4.2024
4.1909
3.5679
3.4111
3.3618
3.3481
1.0955
1.0817
1.0680


EtO
O
O
O
N
H
N
CF3
Table 3, Entry 4
abundance
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
240.0 230.0 220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.3037
159.2133
148.0630
139.1351
136.4549
135.4534
129.9688
129.9402
128.1756
127.5652
123.0345
122.1283
121.6609
117.8838
113.2672
70.9743
69.3718
69.1811
66.6725
15.1655
X : parts per Million : 13C

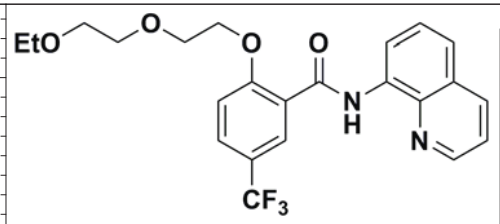


Table 3, Entry 4

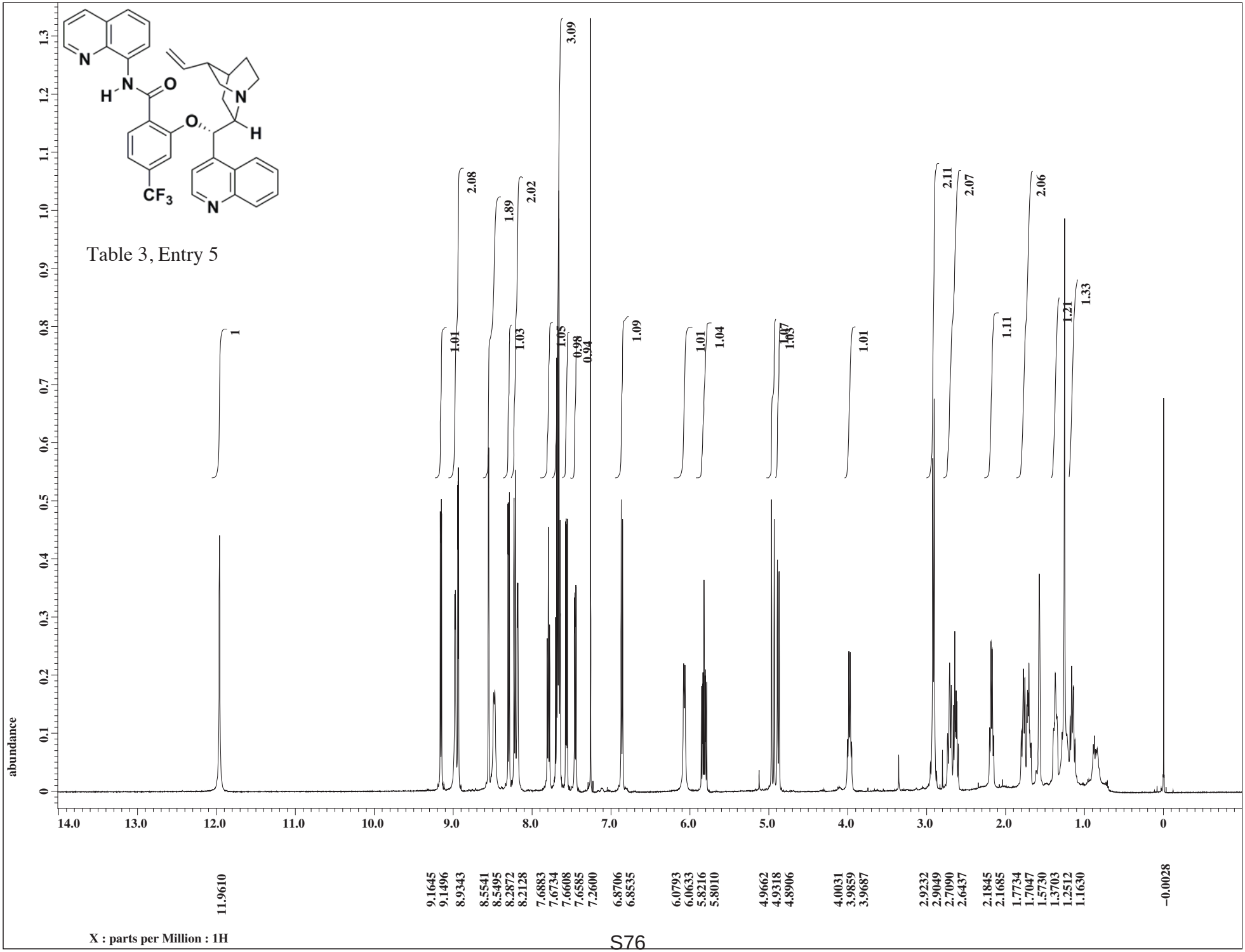


Table 3, Entry 5
abundance
X : parts per Million : 1H
11.9610
9.1645
9.1496
8.9343
8.5541
8.5495
8.2872
8.2128
7.6883
7.6734
7.6608
7.6585
7.2600
6.8706
6.8535
6.0793
6.0633
5.8216
5.8010
4.9662
4.9318
4.8906
4.0031
3.9859
3.9687
2.9232
2.9049
2.7090
2.6437
2.1845
2.1685
1.7734
1.7047
1.5730
1.3703
1.2512
1.1630
−0.0028

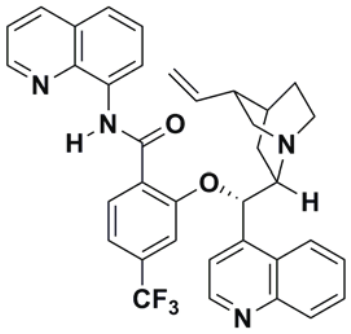


Table 3, Entry 5

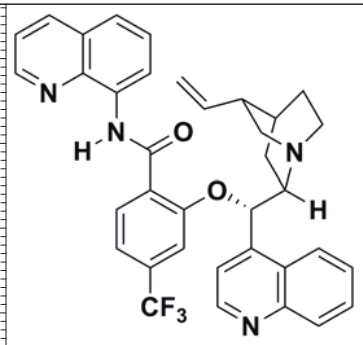
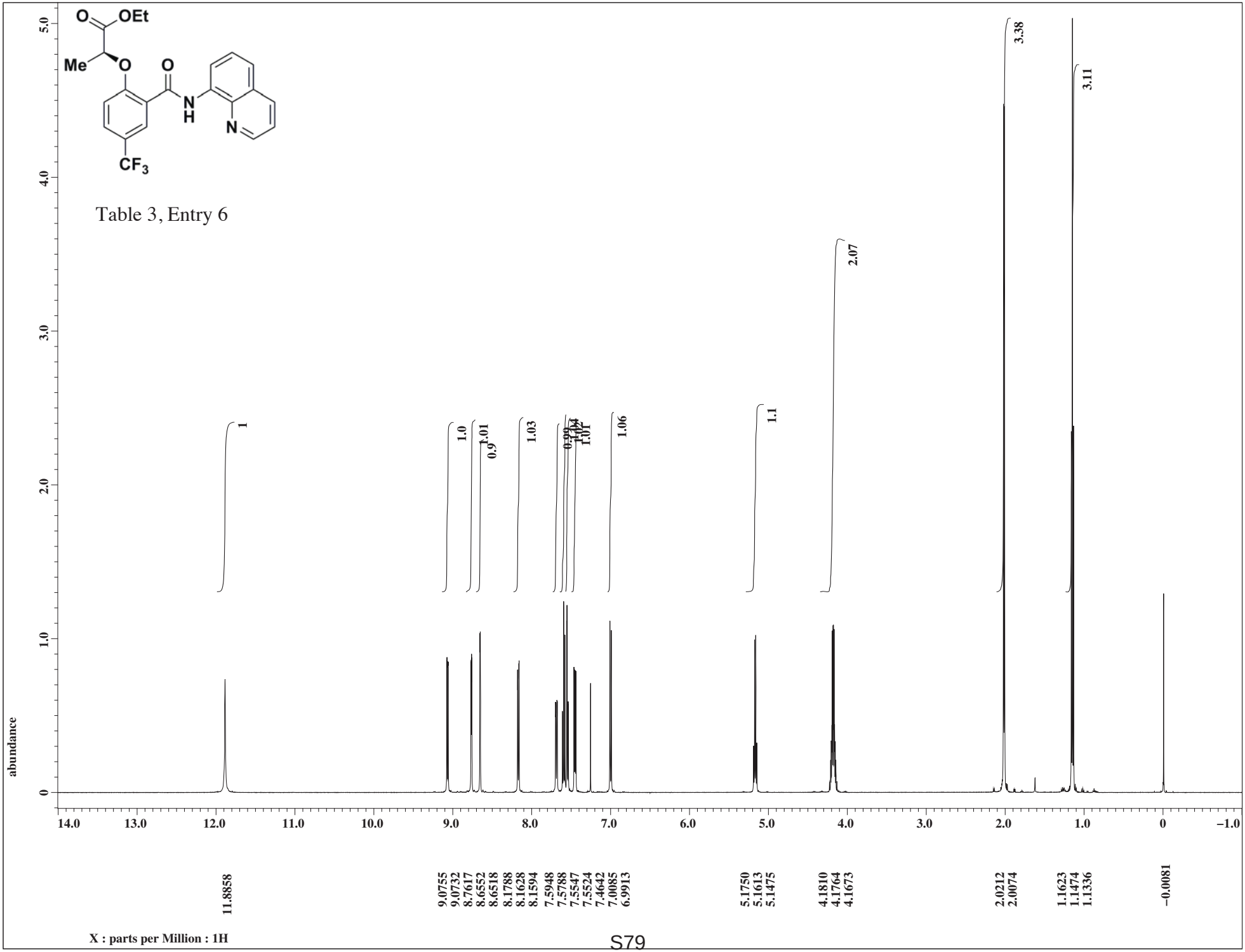


Table 3, Entry 5


O
OEt
Me
O
O
N
H
N
CF3
Table 3, Entry 6
abundance
1
1.0
1.01
0.9
1.03
1.06
1.1
2.07
3.38
3.11
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
−1.0
11.8858
9.0755
9.0732
8.7617
8.6552
8.6518
8.1788
8.1628
8.1594
7.5948
7.5788
7.5547
7.5524
7.4642
7.0085
6.9913
5.1750
5.1613
5.1475
4.1810
4.1764
4.1673
2.0212
2.0074
1.1623
1.1474
1.1336
−0.0081
X : parts per Million : 1H

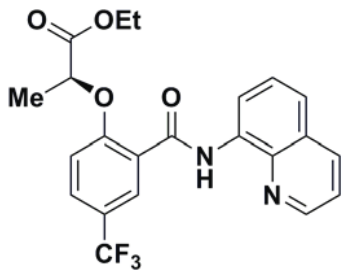


Table 3, Entry 6

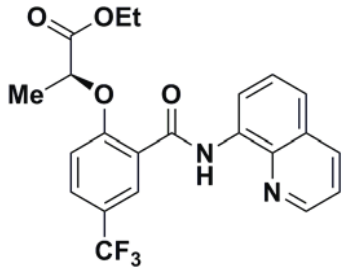


Table 3, Entry 6

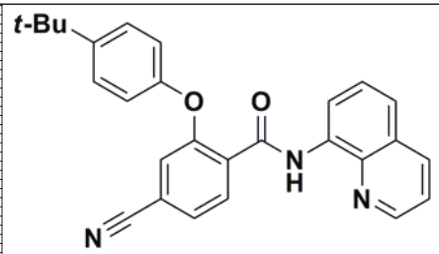


Table 4, Entry 1

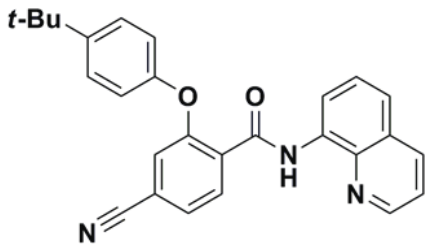


Table 4, Entry 1

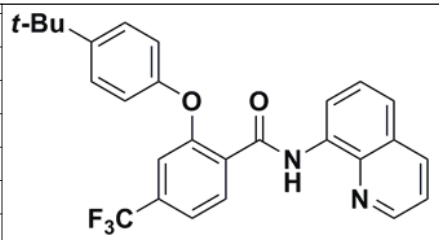


Table 4, Entry 2

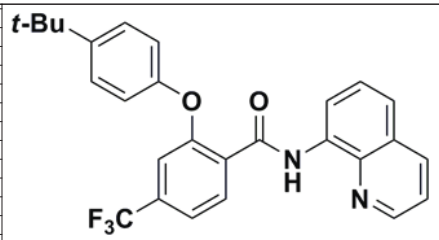


Table 4, Entry 2

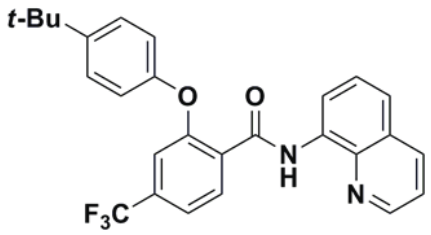


Table 4, Entry 2

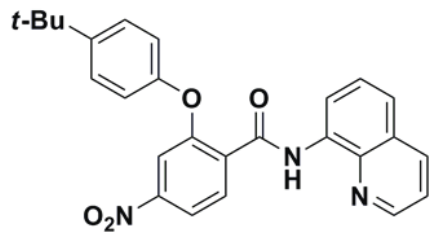


Table 4, Entry 3

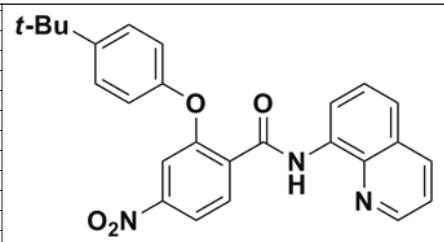


Table 4, Entry 3

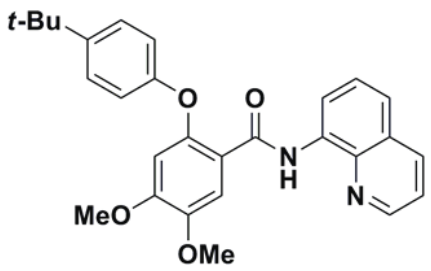


Table 4, Entry 4

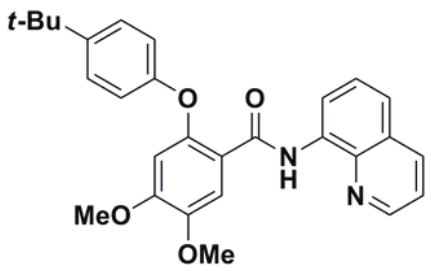


Table 4, Entry 4

abundance

0 0.1 0.2 0.3 0.4 0.5 0.6

240.0 230.0 220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0

163.0240
154.7161
152.6749
149.2030
148.0393
146.3987
145.6357
139.1591
136.0687
135.7349
128.0088
127.5033
126.5971
121.5037
121.4274
117.7360
117.4690
117.0493
112.9860
103.6289
56.4046
56.3474
34.4092
31.5573

X : parts per Million : 13C

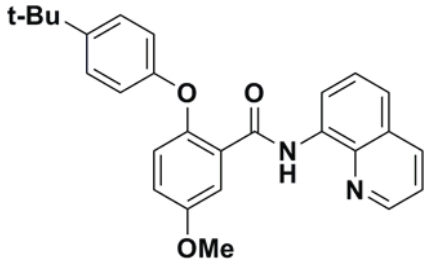


Table 4, Entry 5

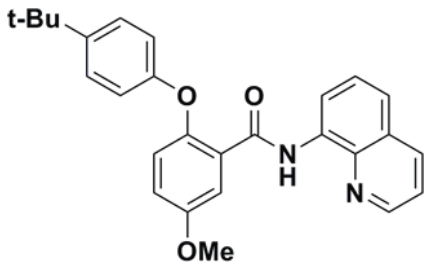


Table 4, Entry 5

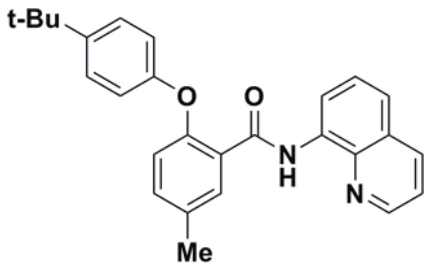


Table 4, Entry 6

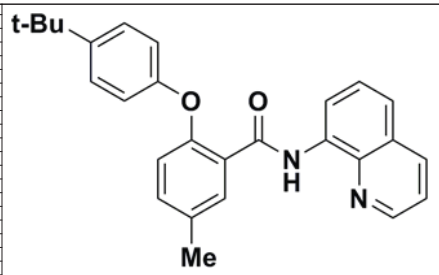


Table 4, Entry 6

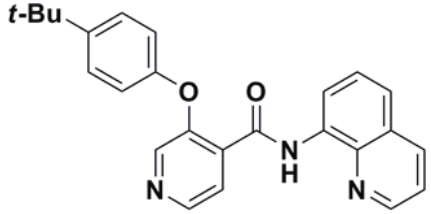


Table 4, Entry 7

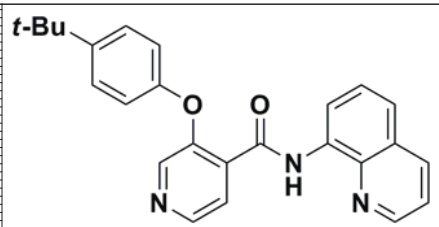


Table 4, Entry 7

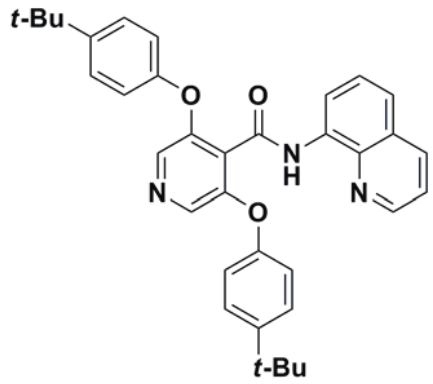


Table 4, Entry 8

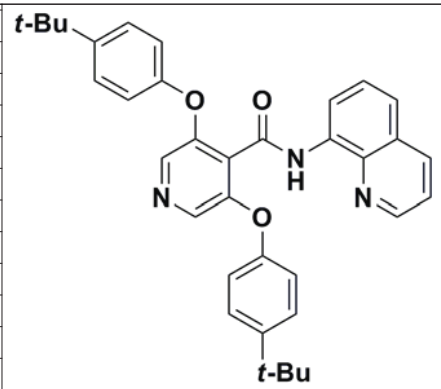
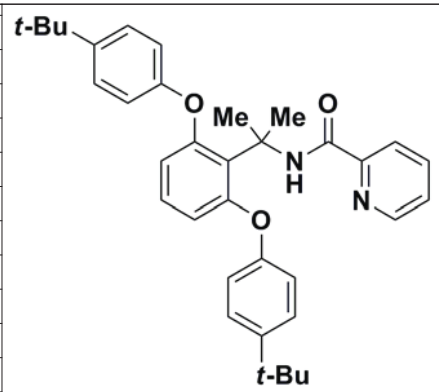
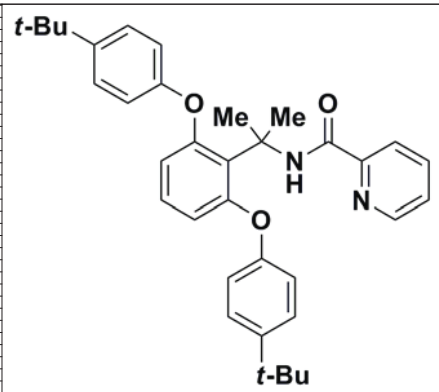


Table 4, Entry 8


t-Bu
O
Me
Me
O
N
H
N
O
t-Bu

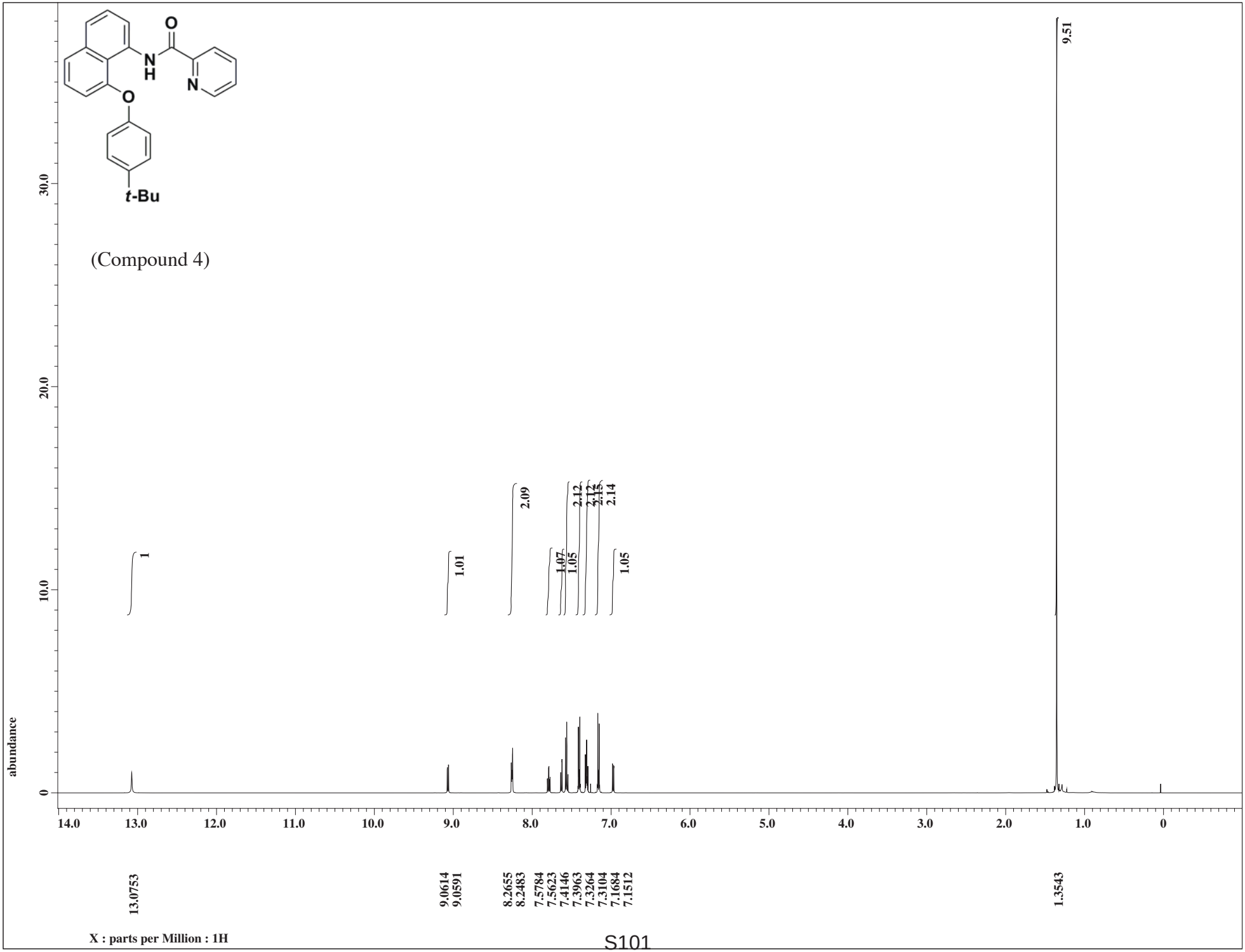
(Compound 3)

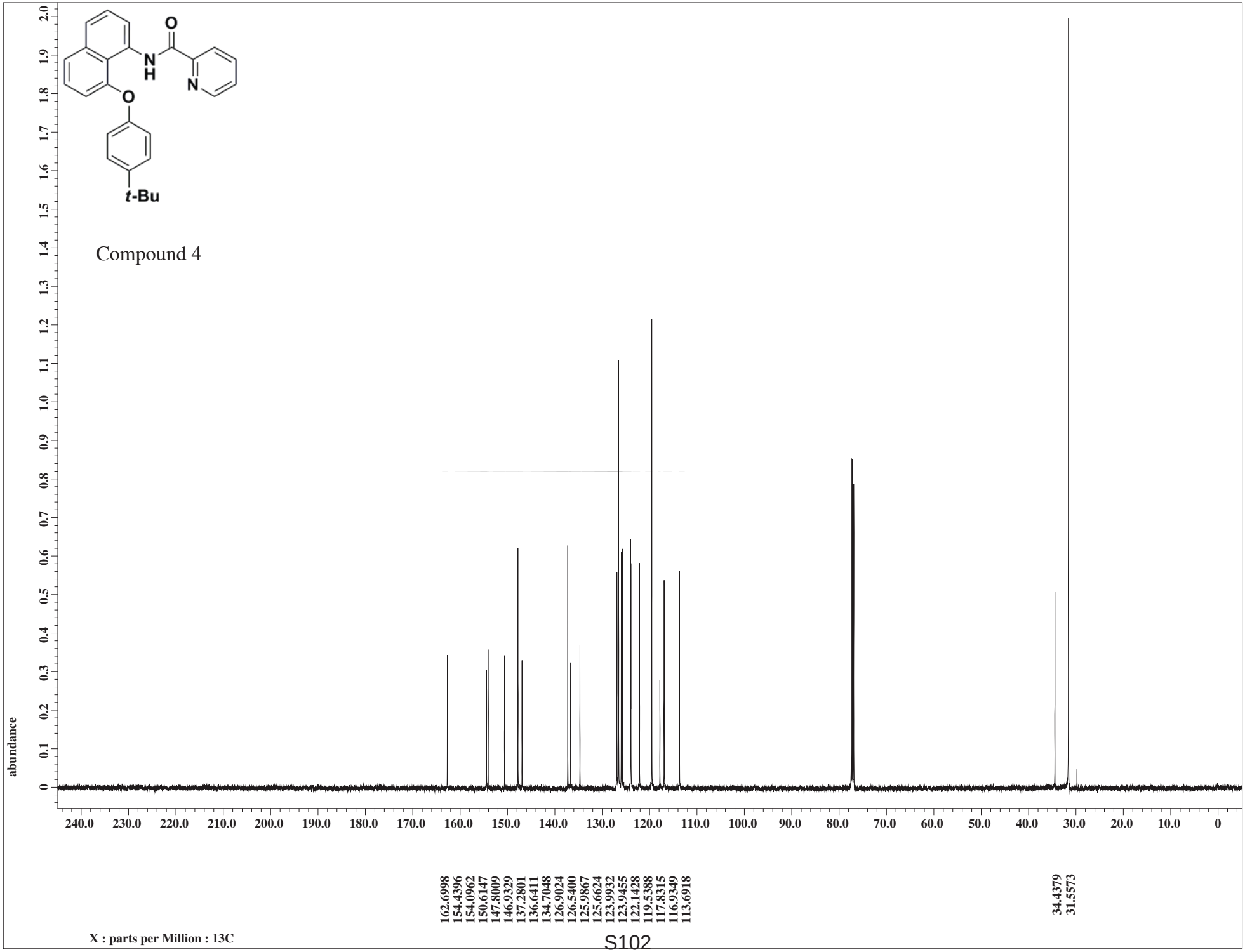
abundance
30.0
20.0
10.0
0
18.47
6.12
5.27
3.89
1.87
1
0.96
0.92
0.99
1.03
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.7476
8.0433
8.0273
7.2600
7.2085
7.1982
7.1936
7.1844
7.1798
7.0504
6.9073
6.8935
6.8901
6.6874
6.6714
2.0460
1.2562
X : parts per Million : 1H

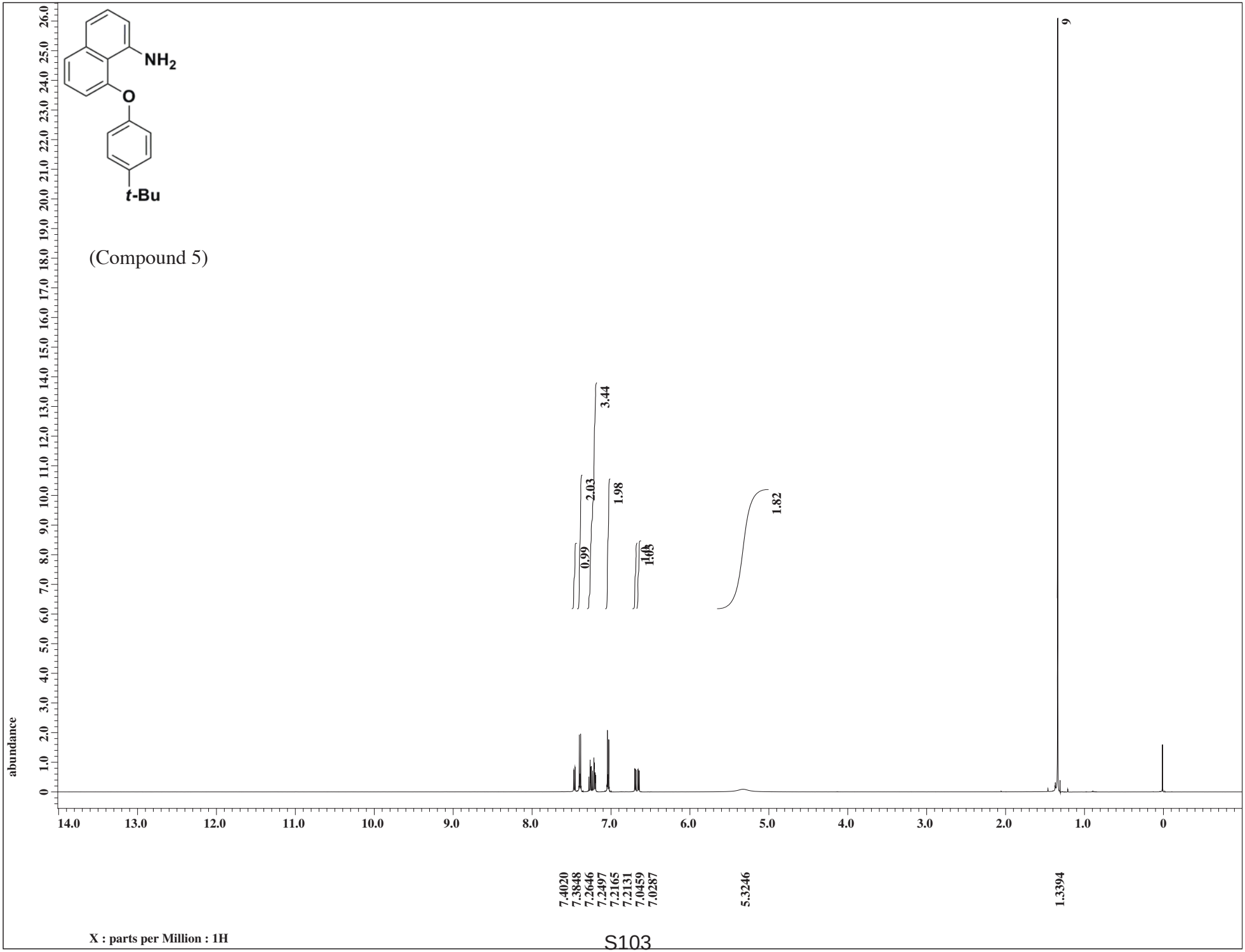

t-Bu
O
Me
Me
O
N
H
N
O
t-Bu

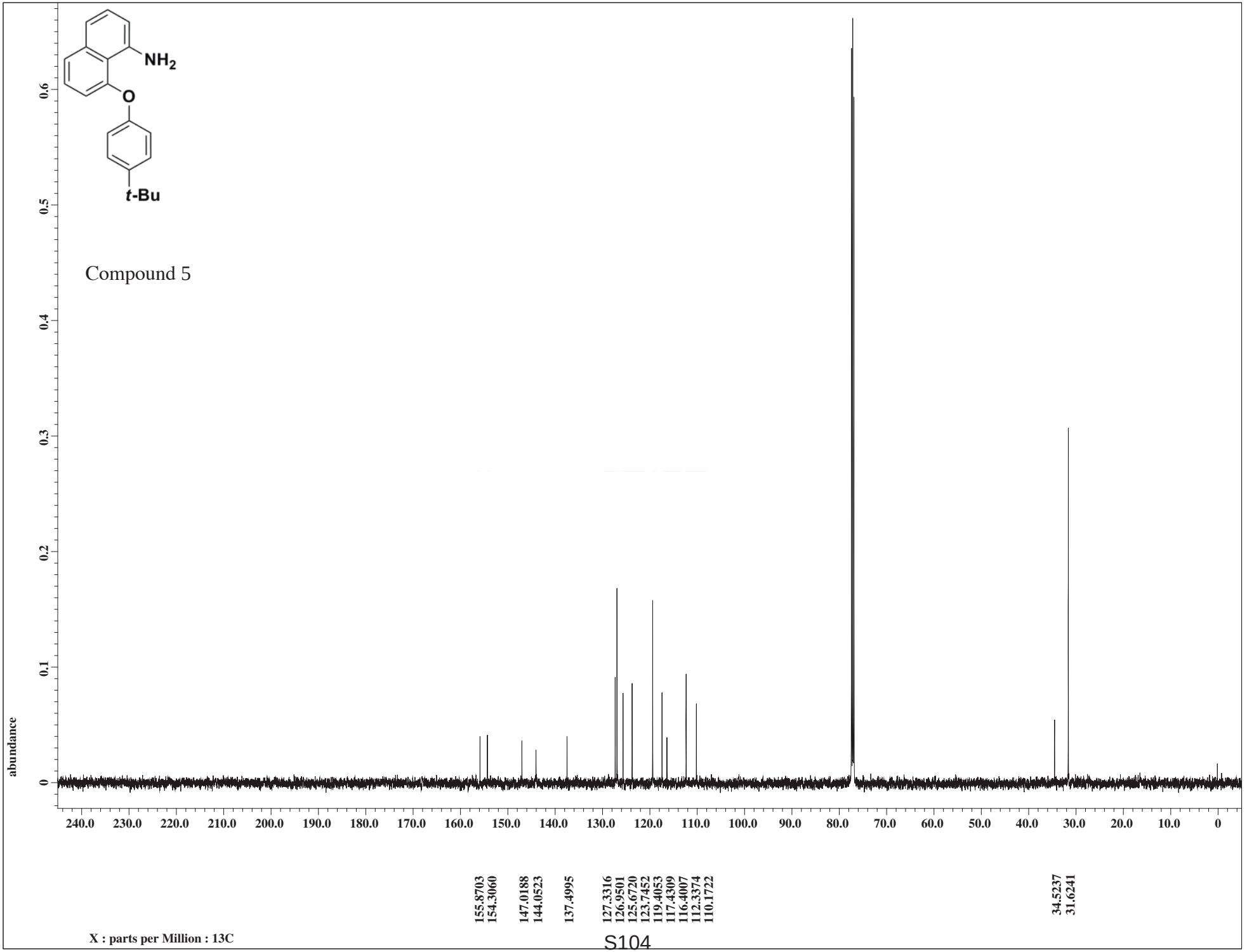
(Compound 3)

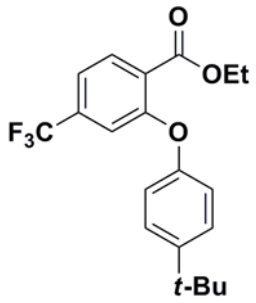
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
1.9
2.0
240.0
230.0
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
162.7951
156.2041
155.6127
150.7482
147.4575
145.0157
136.7841
128.9913
127.7418
126.2729
125.3953
121.5419
117.6502
116.8967
55.2219
34.2090
31.5859
29.9358
X : parts per Million : 13C


O
N
H
N
O
t-Bu
(Compound 4)
abundance
30.0
20.0
10.0
0
1
1.01
2.09
1.07
1.05
2.12
2.13
2.15
2.14
1.05
9.51
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
13.0753
9.0614
9.0591
8.2655
8.2483
7.5784
7.5623
7.4146
7.3963
7.3264
7.3104
7.1684
7.1512
1.3543
X : parts per Million : 1H


O
N
H
N
O
t-Bu
Compound 4
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
1.9
2.0
240.0
230.0
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
162.6998
154.4396
154.0962
150.6147
147.8009
146.9329
137.2801
136.6411
134.7048
126.9024
126.5400
125.9867
125.6624
123.9932
123.9455
122.1428
119.5388
117.8315
116.9349
113.6918
34.4379
31.5573
X : parts per Million : 13C

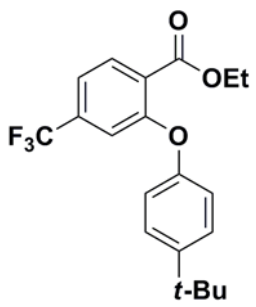

NH2
O
t-Bu
(Compound 5)
abundance
X : parts per Million : 1H
7.4020
7.3848
7.2646
7.2497
7.2165
7.2131
7.0459
7.0287
5.3246
1.3394
0.99
2.03
3.44
1.98
1.82


NH2
O
t-Bu
Compound 5
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
240.0 230.0 220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
155.8703
154.3060
147.0188
144.0523
137.4995
127.3316
126.9501
125.6720
123.7452
119.4053
117.4309
116.4007
112.3374
110.1722
34.5237
31.6241
X : parts per Million : 13C


O
OEt
F3C
O
t-Bu

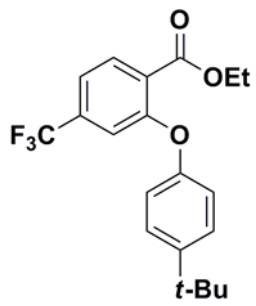
Compound 6

abundance
0.97
1.0
1.01
1.69
1.65
2
2.99
8.25
8.4212
8.4178
7.7971
7.7925
7.7788
7.7742
7.2485
7.2314
7.1489
7.1317
6.8271
6.8099
4.3695
4.3547
4.3409
1.5890
1.5753
1.5615
1.2844
X : parts per Million : 1H


O
OEt
F3C
O
t-Bu

Compound 6

abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
1.2
1.3
1.4
240.0
230.0
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
165.1797
159.8668
153.5143
143.2701
132.0531
132.0244
131.2423
131.2137
126.4445
124.6322
118.1843
114.9032
113.1862
66.6678
34.1135
31.6145
14.5695
X : parts per Million : 13C



Compound 6

abundance

0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0 15.0 16.0 17.0 18.0 19.0 20.0 21.0 22.0 23.0 24.0 25.0 26.0 27.0 28.0

−30.0 −40.0 −50.0 −60.0 −70.0 −80.0 −90.0 −100.0 −110.0 −120.0 −130.0 −140.0 −150.0

−61.9917

X : parts per Million : 19F