A dual Pd- and CuH-catalyzed approach for alkyl-aryl cross-coupling of aryl halides and olefins

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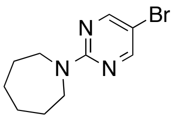
Contents

I. General Information

General reagent information. All reactions were set up on the bench-top unless otherwise indicated, using oven-dried (140 °C) glassware. 21G or 22G needles were used. Tetrahydrofuran (THF) was dried and deoxygenated by passage through two packed columns of neutral alumina and copper(II) oxide under a positive pressure of argon. (*R*)- and (*S*)-DTBM-SEGPHOS ligands were purchased from Strem Chemicals Inc. and Takasago International Co. and used as received. [Pd(cinnamyl)Cl]$_2$ and CuCl were purchased from Strem Chemicals Inc. Dimethylphenylsilane was purchased from Tokyo Chemical Industry Co. (TCI) or Alfa Aesar. *d*$_1$-Dimethylphenylsilane was prepared according to literature procedure.[1] Sodium trimethylsilanolate was purchased from Sigma Aldrich. Sodium trimethylsilanolate and CuCl were stored in a nitrogen-filled glovebox. CuCl[(R)-DTBM-SEGPHOS] was kept in a nitrogen-filled glovebox for long term storage. Other commercial reagents were purchased from Sigma Aldrich, Alfa Aesar, Acros Organics, Combi-Blocks, or ChemImpex. All commercial reagents were used as received. Flash column chromatography was performed using 40-63 µm silica gel (SiliaFlash® F60 from Silicycle) or with SNAP silica gel columns on a Biotage Isolera 4.

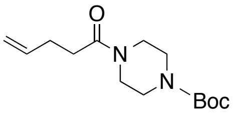
General analytical information. All new compounds were characterized by NMR spectroscopy, IR spectroscopy, elemental analysis (or high-resolution mass spectrometry), and melting point analysis (if solid). ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AMX-400 spectrometer. Data for ^{1}H NMR are reported as follows: chemical shift in reference to residual $CHCl_3$ at 7.26 ppm (δ ppm), multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, m = multiplet), coupling constant (Hz), and integration. Data for ^{13}C NMR are reported in terms of chemical shift in reference to the $CDCl_3$ solvent signal (77.16 ppm). ^{19}F and ^{31}P NMR spectroscopy were performed on a Varian Inova 500 MHz and spectra are referenced to neat α,α,α-trifluorotoluene at -63.7 (δ ppm) and 85% H_3PO_4 in water at 0.0 ppm (δ ppm), respectively. IR spectra were recorded on a Thermo Scientific Nicolet iS5 spectrometer (iD5 ATR, diamond) and are reported in terms of frequency of absorption (cm^{-1}). Melting points were measured on a Mel-Temp capillary melting point apparatus. Optical rotations were measured using a Jasco P-1010 digital polarimeter. Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA. Chiral HPLC analysis was performed on an Agilent Technologies 1200 series instrument with Chiralcel chiral columns (25 cm) using the conditions detailed for each substrate. Achiral gas chromatography (GC) analyses were performed on an Agilent 7890A gas chromatograph with an FID detector using a J&W DB-1 column (10 m, 0.1 I.D.). HPLC-MS analysis was preformed in an Agilent Technologies 1260 Infinity, 6120 Quadrupole instrument with a Thermo Scientific Accucore C18 HPLC column (2.6 µm, 30 × 2.1 mm I.D). Thin-layer chromatography (TLC) was performed on silica gel 60Å F_{254} plates (SiliaPlate from Silicycle) and visualized under UV light or with potassium permanganate stain. Preparatory thin-layer chromatography (Prep-TLC) was performed on silica gel GF with UV 254 (20 x 20 cm, 1000 microns, catalog # 02013 from Analtech) and visualized under UV light.

II. Preparation of starting materials



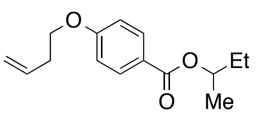
1-(5-bromopyrimidin-2-yl)azepane (1l) was prepared by adding hexamethyleneimine (2.8 mL, 25 mmol) to a flask charged with 5-bromo-2-chloropyrimidine (1.93 g, 10 mmol) and CH_2Cl_2 (20 mL). After stirring at ambient temperature for 2 h, GC analysis showed full conversion of the starting material. The reaction mixture was poured into a separatory funnel containing 1 M NaOH (25 mL) and the product was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The product was purified by automated flash column chromatography (0-10% EtOAc in hexanes, 100 g silica gel) and isolated as a colorless solid (2.51 g, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.25 (s, 2H), 3.72-3.65 (m, 4H), 1.80-1.71 (m, 4H), 1.56-1.49 (m, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 159.8, 157.9 (2C), 104.9, 47.5 (2C), 27.8 (2C), 27.3 (2C). **IR** (neat, cm^{-1}): 2920, 2847, 1571, 1497, 1317, 783, 644. **M.p.** 76-78 °C. **Elemental Anal.** Calcd. for $C_{10}H_{14}BrN_3$: C, 46.89; H, 5.51; found: C, 46.93; H, 5.37.



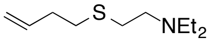
***tert*-butyl 4-(pent-4-enoyl)piperazine-1-carboxylate (2c)** was prepared by dropwise addition of pent-4-enoyl chloride (1.9 mL, 16.8 mmol) to a flask charged with *tert*-butyl piperazine-1-carboxylate (3.8 g, 20.2 mmol), triethylamine (2.8 mL, 20.2 mmol), *N*,*N*-dimethylpyridine-4-amine (5 mg, 0.04 mmol), and CH_2Cl_2 (35 mL). The mixture was stirred at ambient temperature for 2 h, and the crude reaction mixture was subsequently transferred to a separatory funnel containing a saturated aqueous solution of $NaHCO_3$ (30 mL). The organic layer was separated and concentrated *in vacuo*. Purification by flash column chromatography (25-100% EtOAc in hexanes, silica gel) provided the isolated product as a colorless solid (3.5 g, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.93-5.78 (m, 1H), 5.05 (d, *J* = 17.2 Hz, 1H), 5.00 (d, *J* = 10.4 Hz, 1H), 3.62-3-55 (m, 2H), 3.46-3.34 (m, 6H), 2.45-2.35 (m, 4H), 1.46 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 171.0, 154.7, 137.4, 115.5, 80.4, 45.5, 43.7 (br s, 2C), 41.5, 32.7, 29.3, 28.5 (3C). **IR** (neat, cm^{-1}): 2981, 2857, 1695, 1631, 1416, 1158, 766. **M.p.** 73-75 °C. **Elemental Anal.** Calcd. for $C_{14}H_{24}N_2O_3$: C, 62.66; H, 9.01; found: C, 62.69; H, 9.02.



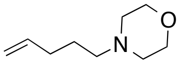
***sec*-butyl 4-(but-3-en-1-yloxy)benzoate (2e)** was prepared by charging a flask with *sec*-butyl 4-hydroxybenzoate (2.91 g, 15 mmol) and K_2CO_3 (4.15 g, 30 mmol). The flask was closed with a septum, evacuated, and backfilled with N_2. Dry DMF (20 mL) was added followed by 4-bromobut-1-ene (3.0 mL, 30 mmol). The reaction mixture was stirred at 70 °C for 21 h, before it was allowed to cool to ambient temperature. The solution was transferred into a separatory funnel containing EtOAc (40 mL), and washed with water (3 × 30 mL) and brine (30 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by automated flash column chromatography (0-60% CH_2Cl_2 in hexanes, 100 g silica gel) provided the isolated product as a colorless liquid (1.90 g, 51%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.99 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 5.90 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.17 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.12 (dq, *J* = 10.0, 1.6 Hz, 1H), 5.05 (sextet, *J* = 6.0 Hz, 1H), 4.06 (t, *J* = 6.7 Hz, 2H), 2.56 (qt, *J* = 6.7, 1.4 Hz, 2H), 1.80-1.56 (m, 2H), 1.31 (d, *J* = 6.3 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 166.1, 162.6, 134.2, 131.6 (2C), 123.4, 117.4, 114.1 (2C), 72.5, 67.4, 33.6, 29.1, 19.7, 9.9. **IR** (neat, cm^{-1}): 2972, 2937, 1706, 1605, 1247, 1166, 1099, 769. **Elemental Anal.** Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12; found: C, 72.54; H, 8.17.



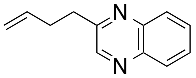
2-(but-3-en-1-ylthio)-*N,N*-diethylethan-1-amine (2g) was prepared by adding 4 M NaOH (20 mL, 80 mmol) to a flask charged with 2-(dimethylamino)ethanethiol hydrochloride (6.80 g, 40 mmol) and MeOH (40 mL). This mixture was cooled in an ice bath before 4-bromobut-1-ene (6.5 mL, 65 mmol) was added. After complete addition, the ice bath was removed and the reaction mixture was stirred at ambient temperature. After 18 h, the product was extracted with CH_2Cl_2 (3 × 30 mL). The organic phase was dried over $MgSO_4$, filtered, and concentration *in vacuo*. Purification by automated flash column chromatography (0-8% MeOH in CH_2Cl_2, 100 g silica gel) provided the isolated product as a slightly yellow liquid (5.83 g, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.81 (ddt, *J* = 16.9, 10.1, 6.7 Hz, 1H), 5.05 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.00 (dq, *J* = 10.4, 1.6 Hz, 1H), 2.68-2.56 (m, 6H), 2.53 (q, *J* = 7.1 Hz, 4H), 2.32 (q, *J* = 7.2 Hz, 2H), 1.00 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 136.8, 116.0, 53.0, 47.1 (2C), 34.2, 31.8, 29.8, 12.0 (2C). **IR** (neat, cm^{-1}): 2968, 2922, 2799,1444, 1200, 1068, 913. **Elemental Anal.** Calcd. for $C_{10}H_{21}NS$: C, 64.11; H, 11.30; found: C, 63.99; H, 11.29.



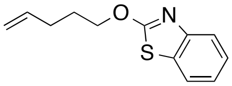
4-(pent-4-en-1-yl)morpholine (2h) 4-(pent-4-en-1-yl)morpholine (2h) was prepared by adding sodium triacetoxyborohydride (6.6 g, 31.5 mmol) to a flask charged with morpholine (2.5 mL, 29.1 mmol), pent-4-enal (2.4 mL, 16.3 mmol), and THF (48 mL). The reaction mixture was stirred at ambient temperature for 22 h, and then transferred to a separatory funnel containing a saturated aqueous solution of $NaHCO_3$ (30 mL) and EtOAc (30 mL). The organic layer was collected and concentrated *in vacuo*. Purification by flash column chromatography (50-100% EtOAc in hexanes with 5% NEt_3) provided the isolated product as a slightly yellow liquid (0.5 g, 20%). Please note that the product is volatile.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.79 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.00 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.94 (dq, *J* = 10.2, 1.6 Hz, 1H), 3.75-3.68 (m, 4H), 2.49-2.41 (m, 4H), 2.38-2.31 (m, 2H), 2.06 (qt, *J* = 6.8, 1.6 Hz, 2H), 1.59 (quintet, *J* = 7.6 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 138.5, 114.8, 67.1 (2C), 58.6, 53.9 (2C), 31.7, 25.9. **IR** (neat, cm^{-1}): 2936, 2854, 2805, 1445, 1117, 915. **HRMS** $C_9H_{17}NO$; calcd. for (M+H): 156.1383, found: 156.1379.



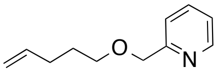
2-(but-3-en-1-yl)quinoxaline (2i) was prepared according to literature procedure, using 2-chloroquinoxaline (1.32 g, 8.0 mmol), but-3-en-1-ylzinc bromide lithium chloride complex in THF (≤ 0.75 M, 20 mL, ≤ 15 mmol), CPhos-Pd-G3 Precatalyst (64 mg, 0.08 mmol), and CPhos (35 mg, 0.08 mmol).[2] After having stirred at ambient temperature for 17 h, the reaction mixture was diluted with EtOAc (20 mL), and washed with water (2 × 30 mL) and brine (30 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by automated flash column chromatography (0-15% EtOAc in hexanes, 100 g silica gel) provided the isolated product as a slightly yellow liquid (746 mg, 51%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.73 (s, 1H), 8.10-7.99 (m, 2H), 7.77-7.65 (m, 2H), 5.91 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.05 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.00 (dq, *J* = 10.0, 1.6 Hz, 1H), 3.11 (dd, *J* = 8.6, 6.8 Hz, 2H), 2.62 (dtt, *J* = 7.9, 6.6, 1.4 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 156.8, 145.9, 142.3, 141.4, 137.1, 130.1, 129.3, 129.1, 129.0, 116.0, 35.8, 33.3. **IR** (neat, cm^{-1}): 3066, 2921, 1640, 1559, 1491, 1126, 911, 756. **HRMS** $C_{12}H_{12}N_2$; calcd. for (M+H): 185.1073, found: 185.1062.



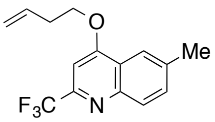
2-(pent-4-en-1-yloxy)benzo[*d*]thiazole (2j) was prepared by charging a flask with NaH (312 mg, 13 mmol). The flask was closed with a septum, evacuated, and backfilled with N_2. Dry DMF (20 mL) was added and a needle connected to a gas bubbler was inserted into the septum before pent-4-en-1-ol (1.2 mL, 12 mmol) was carefully added in two portions. [Caution! Gas evolution.]. After 15 min, 2-chlorobenzo[*d*]thiazole (1.3 mL, 10 mmol) was added [Caution! Exothermic.] and the solution was stirred at ambient temperature. After 17 h, the reaction mixture was carefully quenched with water (10 mL) [Caution! Gas evolution], before EtOAc (30 mL) was added. The organic phase was washed with water (3 × 20 mL) and brine (30 mL), and then dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by automated flash column chromatography (0-10% EtOAc in hexanes, 100 g silica gel) provided the isolated product as an amber liquid (2.19 g, 100%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.68 (d, *J* = 8.1 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.36 (td, *J* = 7.4, 1.3 Hz, 1H), 7.22 (td, *J* = 7.7, 1.2 Hz, 1H), 5.85 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H), 5.08 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.03 (dq, *J* = 10.0, 1.6 Hz, 1H), 4.58 (t, *J* = 6.5 Hz, 2H), 2.25 (q, *J* = 6.8 Hz, 2H), 1.96 (dq, *J* = 8.6, 6.6 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 173.1, 149.5, 137.4, 132.0, 126.1, 123.5, 121.3, 120.8, 115.7, 71.4, 30.0, 28.1. **IR** (neat, cm^{-1}): 2951, 1533, 1442, 1248, 1213, 911, 751. **Elemental Anal.** Calcd. for $C_{12}H_{13}NOS$: C, 65.72; H, 5.98; found: C, 65.94; H, 6.04.



2-((pent-4-en-1-yloxy)methyl)pyridine (2k) was prepared by charging a flask with NaH (0.84 g, 35 mmol). The flask was closed with a septum, evacuated, and backfilled with N_2. Dry DMF (40 mL) was added and the solution was cooled in an ice bath. A needle connected to a gas bubbler was inserted into the septum before pent-4-en-1-ol (1.75 mL, 17 mmol) was carefully added. [Caution! Gas evolution.] The reaction mixture was allowed to warm to ambient temperature. After 1 h, 2-(chloromethyl)pyridine hydrochloride (2.46 g, 15 mmol) was added in small portions by quickly removing the septum. [Caution! Gas evolution.] The solution was stirred at ambient temperature. After 2 h, the reaction mixture was carefully quenched with water (10 mL) [Caution! Gas evolution.] before EtOAc (50 mL) was added. The organic phase was washed with water (3 × 40 mL) and brine (40 mL), and then dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by automated flash column chromatography (0-35% EtOAc in hexanes, 100 g silica gel) provided the isolated product as a colorless liquid (2.16 g, 81%).

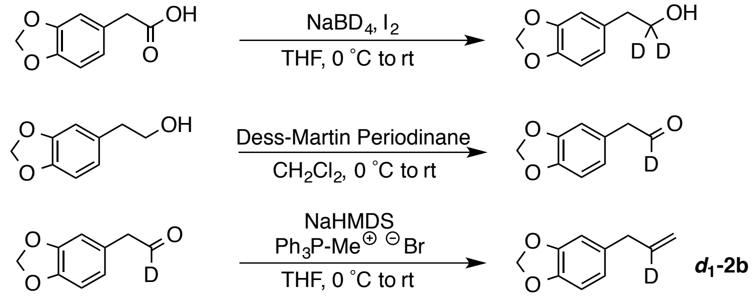
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.52 (d, *J* = 4.9 Hz, 1H), 7.66 (td, *J* = 7.7, 1.8 Hz, 1H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.18-7.12 (m, 1H), 5.80 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H), 5.00 (dq, *J* = 17.2, 1.6 Hz, 1H), 4.94 (dq, *J* = 10.0, 1.6 Hz, 1H), 4.60 (s, 2H), 3.55 (t, *J* = 6.5 Hz, 2H), 2.15 (q, *J* = 6.8 Hz, 2H), 1.74 (quintet, *J* = 6.4 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 158.9, 149.1, 138.3, 136.7, 122.3, 121.3, 114.9, 73.8, 70.5, 30.4, 29.0. **IR** (neat, cm^{-1}): 2936, 2856, 1590, 1434, 1116, 911, 755. **HRMS** $C_{11}H_{15}NO$; calcd. for (M+H): 178.1226, found: 178.1219.

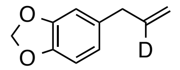


4-(but-3-en-1-yloxy)-6-methyl-2-(trifluoromethyl)quinolone (2n) was prepared by charging a flask with 6-methyl-2-(trifluoromethyl)quinolin-4-ol (3.11 g, 13.6 mmol) and K_2CO_3 (4.15 g, 30 mmol). The flask was closed with a septum, evacuated, and backfilled with N_2. Dry DMF (20 mL) was added followed by 4-bromobut-1-ene (3.0 mL, 30 mmol). The reaction mixture was stirred at 70 °C for 21 h, before the reaction mixture was allowed to cool to ambient temperature. The solution was poured into EtOAc (40 mL), and washed with water (3 × 30 mL) and brine (30 mL). Drying the organic phase over $MgSO_4$, filtration, and concentration *in vacuo* afforded the crude product, which was purified by automated flash column chromatography (0-60% CH_2Cl_2 in hexanes, 100 g silica gel). Isolated as a colorless solid (3.18 g, 83%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.06-7.95 (m, 2H), 7.59 (dd, *J* = 8.7, 2.0 Hz, 1H), 6.98 (s, 1H), 5.97 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.27 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.19 (dq, *J* = 10.0, 1.6 Hz, 1H), 4.28 (t, *J* = 6.6 Hz, 2H), 2.73 (qt, *J* = 6.6, 1.3 Hz, 2H), 2.56 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 162.5, 148.2 (q, $J_{C\text{-}F}$ = 34 Hz), 146.8, 137.8, 133.7, 133.2, 129.4, 121.8 (q, $J_{C\text{-}F}$ = 273 Hz), 121.7, 120.8, 118.0, 96.7 (q, $J_{C\text{-}F}$ = 2 Hz), 68.2, 33.3, 22.0. **^{19}F NMR** (471 MHz, $CDCl_3$) δ (ppm) -67.9 (s). **IR** (neat, cm^{-1}): 2930, 1593, 1576, 1364, 1130, 1094, 837. **M.p.** 93-95 °C. **Elemental Anal.** Calcd. for $C_{15}H_{14}F_3NO$: C, 64.05; H, 5.02; found: C, 64.00; H, 5.14.

Synthetic route to ***d*$_1$-2b**:



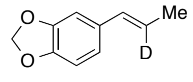


5-(Allyl-2-*d*)benzo[*d*][1,3]dioxole (*d*$_1$-2b) was prepared by charging a dry flask with 2-(benzo[*d*][1,3]dioxol-5-yl)acetic acid (1.80 g, 10 mmol), NaBD$_4$ (837 mg, 20 mmol). The flask was closed with a septum, evacuated, and backfilled with N$_2$. Dry THF (30 mL) was then added via syringe. The solution was stirred for 10 min before being cooled to 0 °C in an ice/water bath. Iodine (1.78 g, 7.0 mmol) was dissolved in dry THF (10 mL) and added dropwise while stirring under a N$_2$-flow. After addition was complete, the reaction mixture was allowed to slowly warm to rt. After 40 h, the reaction was carefully quenched with water (5 mL), and 2 M HCl (20 mL) and EtOAc (20 mL) were subsequently added. After phase separation, the organic phase was washed with 2 M HCl (20 mL), a saturated solution of NaHCO$_3$ (2 × 20 mL), and brine (20 mL). The combined organic layers were then dried over MgSO$_4$, filtered, and concentrated *in vacuo*. Purification by automated flash column chromatography (0-60% EtOAc in hexanes, 100 g silica gel) yielded an orange liquid, which was used directly in the next step.

The orange liquid, which consisted mainly of the desired d_2-alcohol, was dissolved in CH$_2$Cl$_2$ (50 mL), and the solution was cooled to 0 °C in an ice/water bath. Dess-Martin Periodinane (5.00 g, 11.8 mmol) was then added in small portions. After addition was complete, the reaction mixture was stirred at 0 °C for 5 min and subsequently allowed to warm to rt. Analysis by GC showed complete consumption of starting material after 4 h, at which point a saturated solution of NaHCO$_3$ (30 mL) was added. The phases were separated, and the aqueous phase was extracted with CH$_2$Cl$_2$ (3× 30 mL). The combined organic phases were dried over MgSO$_4$, filtered, and concentrated *in vacuo*. Purification by automated flash column chromatography (0-25% EtOAc in hexanes, 100 g silica gel) yielded a colorless liquid, which was used directly in the next step.

A flask was charged with methyltriphenylphosphonium bromide (7.10 g, 20 mmol). The flask was closed with a septum, evacuated, and backfilled with N$_2$. Dry THF (40 mL) was added and the mixture was cooled to 0 °C in an ice/water bath. NaHMDS (3.30 g, 18 mml) was subsequently added by quickly removing the septum. The resulting yellow solution was stirred for 1 h before the d_1-aldehyde from the previous step was added dropwise at 0 °C via syringe. After addition was complete, the reaction mixture was allowed to slowly warm to rt. After 16 h, the reaction was quenched with water (50 mL), and EtOAc (20 mL) was then added. After phase separation, the organic phase was washed with water (2 × 30 mL) and brine (20 mL). The combined organic layers were then dried over MgSO$_4$, filtered, and concentrated *in vacuo*. Purification by automated flash column chromatography (0-50% CH$_2$Cl$_2$ in hexanes, 100 g silica gel) provided the isolated product as a colorless liquid (492 mg, 30% over three steps).

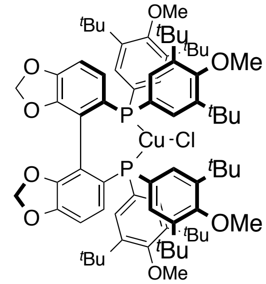
This colorless liquid was the desired product contaminated with approximately 5 mol% of (*E*)-5-(prop-1-en-1-yl-2-*d*)benzo[*d*][1,3]dioxole.



(*E*)-5-(prop-1-en-1-yl-2-*d*)benzo[*d*][1,3]dioxole

^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm) 6.75 (d, J = 7.8 Hz, 1H), 6.69 (s, 1H), 6.65 (d, J = 8.0 Hz, 1H), 5.93 (s, 2H), 5.07 (s, 2H), 3.31 (s, 2H). **^{13}C NMR** (100 MHz, CDCl$_3$) δ (ppm) 147.8, 146.0, 137.4 (t, $J_{\text{C-D}}$ = 23.5 Hz), 134.0, 121.4, 115.7, 109.2, 108.3, 100.9, 39.9. **IR** (neat, cm^{-1}): 2890, 1501, 1487, 1442, 1243, 1038. **Elemental Anal.** Calcd. for C$_{10}$H$_9$DO$_2$: C, 73.60; H+D, 6.18; found: C, 73.13; H+D, 6.19.

III. Catalyst preparation



CuCl-[(*R*)-DTBM-SEGPHOS] (P1) was prepared by charging a screw-cap reaction tube (Fisher Scientific, 20 x 150 mm, Cat. No. 1495937C) equipped with a stir bar with CuCl (416 mg, 4.2 mmol) and (*R*)-DTBM-SEGPHOS (4.72 g, 4.0 mmol). The reaction tube was capped with a phenolic screw cap and septum (Cap: Fisher Scientific, Closure OT S/T 18-400, Cat. No. 033407G; Septa: Thermo Scientific, Septa T/S for 18-400Cap, Cat. No. B7995-18). The reaction tube was evacuated and backfilled with N_2. (this process was repeated at total of three times), before dry THF (15 mL) was added via syringe. The reaction mixture was stirred at ambient temperature. After 16 h, the solids were removed by filtration through a plug of Celite. The plug was rinsed with CH_2Cl_2 and the volatiles were removed *in vacuo*. PhMe (15 mL) was added and the volatiles were removed *in vacuo* to give the complex as a gray to slightly yellow solid (5.07 g, 99%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.88 (t, *J* = 5.9 Hz, 4H), 7.41 (t, *J* = 5.8 Hz, 4H), 6.46 (d, *J* = 8.0 Hz, 2H), 6.43-6.36 (m, 2H) 5.58 (s, 2H), 5.47 (s, 2H), 3.71 (s, 6H), 3.60 (s, 6H), 1.45 (s, 36H), 1.28 (s, 36H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) *Complex spectrum observed due to hindered rotation and C-P coupling, number of carbons are not given for aromatic signals (see the end of Supporting Information for the spectra observed)*. 161.7, 161.6, 147.4, 147.0 (t, *J* = 6 Hz), 144.4 (t, *J* = 6 Hz), 143.4 (t, *J* = 6 Hz), 134.4 (br s), 133.0 (br s), 128.4 (t, *J* = 14 Hz), 126.4 (t, *J* = 17 Hz), 125.3 (t, *J* = 4 Hz), 124.4 (t, *J* = 21 Hz), 118.4 (t, *J* = 11 Hz), 107.87 (t, *J* = 3.8 Hz), 100.4 (2C), 64.4 (2C), 64.2 (2C), 36.2 (4C), 35.8 (4C), 32.3 (12C), 32.0 (12C). **^{31}P NMR** (203 MHz, $CDCl_3$) δ (ppm) -3.9 (s). **IR** (neat, cm^{-1}): 2958, 1436, 1224, 1115, 1051, 1007. **M.p.** 315-319 °C (dec.). **HRMS** $C_{74}H_{100}ClCuO_8P_2$; calcd. for (M–Cl): 1241.6189, found: 1241.6221.

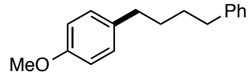
IV. General experimental procedures

General Procedure A: A screw-cap reaction tube (Fisher Scientific, 16 x 125 mm, Cat. No. 1495935A) equipped with a stir bar was charged with CuCl-[(R)-DTBM-SEGPHOS] (77 mg, 0.060 mmol) and TMSONa (224 mg, 2.0 mmol). [*See note below and section VI on the importance of using dry TMSONa*] If the aryl bromide (1.5 mmol) was a solid, it was also weighed and added into the reaction tube at this point. A separate 8 mL vial (VWR, Cat. No. 66030-722) equipped with a stir bar was charged with $[Pd(cinnamyl)Cl]_2$ (10.4 mg, 0.020 mmol) and BrettPhos (23.6 mg, 0.044 mmol). The reaction tube and vial were capped with a phenolic screw cap and septum (Cap: Fisher Scientific, Closure OT S/T 15-425TH 14, Cat. No. 033407E; Septa: Thermo Scientific, Septa T/S for 15-425Cap, Cat. No. B7995-15). Both the reaction tube and vial were evacuated and backfilled with N_2 (this process was repeated a total of three times). The N_2 inlet needles were left in the septa. Dry THF (0.5 mL) was added to the reaction tube and dry THF (0.5 mL) was added to the vial containing the palladium. A needle was inserted into the septum of the reaction tube before dimethylphenylsilane (0.4 mL, 2.6 mmol) was added via syringe to the reaction tube. [Caution! Gas evolution.] The solutions in both the reaction tube and vial were stirred for 5 min with a positive pressure of N_2 flowing through the reaction tube. Subsequently, the alkene (1.0 mmol) was added to the reaction tube through the septum using a microsyringe, along with the aryl bromide (1.5 mmol, if liquid). The solution in the reaction tube was stirred for another 5 min under N_2-flow before the palladium-THF solution from the vial was added through the septum via a syringe. After stirring for another 2 min under N_2-flow, the N_2 in- and outlet needles were removed and the reaction tube was placed in an oil bath preheated to 45 °C. After stirring for 18 h, the reaction mixture was allowed to cool to ambient temperature before the solids were removed by filtration through a plug of Celite. The plug was rinsed with CH_2Cl_2 (15 mL), the volatiles were removed *in vacuo*, and the product was purified by flash column chromatography.

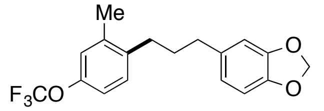
Note: Thorough flushing with N_2 is important to remove H_2 formed by silylation of adventitious water in the reaction tube. If not flushed properly with N_2, undesired reduction of both starting materials is observed. Also, excessively moist reagents will cause increased consumption of silane, which may lead to incomplete conversion of the starting materials (see section VI, page S15).

For solid alkenes: If the alkene is a solid, the reaction may be set up on the bench top as described for the preparation of compound **3n** and **3m**, or in a glovebox as described for the preparation of compound **3c**. If the alkene is weighed into the reaction tube along with CuCl-[(R)-DTBM-SEGPHOS] and TMSONa, lower yields were obtained due to alkene reduction.

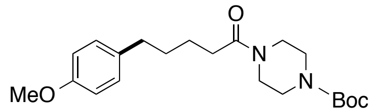
V. Experimental and analytical data for products



1-Methoxy-4-(3-phenylpropyl)benzene (3a) was prepared according to General Procedure A, with the modification of using 1 mol% [Pd(cinnamyl)Cl]$_2$ (5.2 mg, 0.01 mmol), 2.2 mol% BrettPhos (11.8 mmol, 0.022 mmol), and 3 mol% CuCl-[(R)-DTBM-SEGPHOS] (38 mg, 0.03 mmol) coupling 4-bromoanisole (188 μL, 1.5 mmol) and but-3-en-1-ylbenzene (150 μL, 1.0 mmol). Purified by automated flash column chromatography (0-35% CH$_2$Cl$_2$ in hexanes, 100 g silica gel). Isolated as a colorless solid (1st run 184 mg, 77%; 2nd run 177 mg, 74%). The product isolated matched previously reported spectra for this structure.[3]
^{1}**H NMR** (400 MHz, CDCl$_3$) δ (ppm) 7.30-7.21 (m, 2H), 7.19-7.13 (m, 3H), 7.07 (d, J = 8.8 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 3.77 (s, 3H), 2.66-2.53 (m, 4H), 1.70-1.57 (m, 4H). ^{13}**C NMR** (100 MHz, CDCl$_3$) δ (ppm) 157.8, 142.8, 134.8, 129.4 (2C), 128.5 (2C), 128.4 (2C), 125.8, 113.8 (2C), 55.4, 36.0, 35.0, 31.5, 31.2. **IR** (neat, cm^{-1}): 2934, 2852, 1611, 1511, 1248, 1180, 834, 742, 699. **M.p.** 35-37 °C. **Elemental Anal.** Calcd. for C$_{17}$H$_{20}$O: C, 84.96; H, 8.39; found: C, 84.90; H, 8.39.

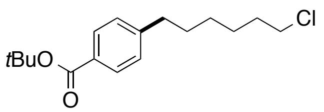


5-(3-(2-Methyl-4-(trifluoromethoxy)phenyl)propyl)benzo[*d*][1,3]dioxole (3b) was prepared according to General Procedure A, using 1-bromo-2-methyl-4-(trifluoromethoxy)benzene (383 mg, 1.5 mmol) and safrole (148 μL, 1.0 mmol). Purified by automated flash column chromatography (0-25% CH$_2$Cl$_2$ in hexanes, 100 g silica gel). Isolated as a colorless liquid (1st run 266 mg, 79%; 2nd run 284 mg, 84%).
^{1}**H NMR** (400 MHz, CDCl$_3$) δ (ppm) 7.14 (d, J = 8.0 Hz, 1H), 7.00 (d, J = 9.0 Hz, 2H), 6.76 (d, J = 7.9 Hz, 1H), 6.71 (d, J = 1.7 Hz, 1H), 6.66 (dd, J = 7.9, 1.7 Hz, 1H), 5.94 (s, 2H), 2.62 (q, J = 7.5 Hz, 4H), 2.29 (s, 3H), 1.92-1.81 (m, 2H). ^{13}**C NMR** (100 MHz, CDCl$_3$) δ (ppm) 147.7, 147.3 (q, $J_{C\text{-}F}$ = 1.9 Hz), 145.8, 139.3, 138.0, 136.0, 129.9, 122.6, 121.2, 120.7 (q, $J_{C\text{-}F}$ = 254 Hz), 118.3, 108.9, 108.3, 100.9, 35.6, 32.2, 32.0, 19.5. ^{19}**F NMR** (471 MHz, CDCl$_3$) δ (ppm) -58.0. **IR** (neat, cm^{-1}): 2938, 2870, 1489, 1442, 1242, 1217, 1151, 1039, 808. **Elemental Anal.** Calcd. for C$_{18}$H$_{17}$F$_3$O$_3$: C, 63.90; H, 5.06; found: C, 64.09; H, 5.08.



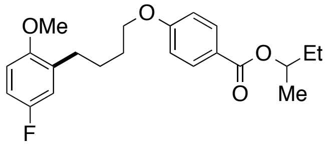
***tert*-Butyl 4-(5-(4-methoxyphenyl)pentanoyl)piperazine-1-carboxylate (3c)** was prepared using a reaction tube (Fisher Scientific, 16 x 125 mm, Cat. No. 1495935A) equipped with a stir bar, which was charged with CuCl-[(R)-DTBM-SEGPHOS] (38 mg, 0.030 mmol) and TMSONa (224 mg, 2.0 mmol) in a nitrogen filled glovebox. A separate 8 mL vial (VWR, Cat. No. 66030-722) equipped with a stir bar was charged with [Pd(cinnamyl)Cl]$_2$ (5.2 mg, 0.010 mmol) and BrettPhos (11.8 mg, 0.022 mmol). Dry THF (0.6 mL) was added to the reaction tube and dry THF (0.4 mL) was added to the vial. Dimethylphenylsilane (0.31 mL, 2.0 mmol) was added to the reaction tube. [Caution! Gas evolution.] The solutions in both the reaction tube and vial were stirred for 5 min, and the palladium-THF solution from the vial was subsequently added. After the solution in the reaction tube was stirred for 5 min, 4-bromoanisole (188 μL, 1.5 mmol) and *tert*-butyl 4-(pent-4-enoyl)piperazine-1-carboxylate (268 mg, 1.0 mmol) were also added to the reaction tube. The reaction tube was capped with a phenolic screw cap and septum (Cap: Fisher Scientific, Closure OT S/T 15-425TH 14, Cat. No. 033407E; Septa: Thermo Scientific, Septa T/S for 15-425Cap, Cat. No. B7995-15). At this point, the reaction tube was removed from the glovebox and placed in an oil bath preheated to 45 °C. After stirring for 18 h, the reaction mixture was allowed to cool to ambient temperature before the solids were removed by filtration through a plug of Celite. The plug was rinsed with CH$_2$Cl$_2$ (15 mL), the volatiles were removed *in vacuo*, and the product was purified by automated flash column chromatography (0-30% EtOAc in CH$_2$Cl$_2$, 100 g silica gel). Isolated as a colorless solid (1st run 347 mg, 92%; 2nd run 339 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.08 (d, *J* = 8.4 Hz, 2H), 6.81 (d, *J* = 8.4 Hz, 2H), 3.77 (s, 3H), 3.59-3.53 (m, 2H), 3.42-3.34 (m, 6H), 2.58 (t, *J* = 6.8 Hz, 2H), 2.32 (t, *J* = 6.8 Hz, 2H), 1.70-1.60 (m, 4H), 1.46 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 171.6, 157.7, 154.6, 134.2, 129.3 (2C), 113.7 (2C), 80.3, 55.3, 45.4, 43.6 (br s, 2C), 41.3, 34.8, 33.2, 31.4, 28.4 (3C), 24.8. **IR** (neat, cm^{-1}): 2977, 2929, 2865, 1684, 1626, 1423, 1236, 1173, 1030. **M.p.** 52-54 °C. **Elemental Anal.** Calcd. for $C_{21}H_{32}N_2O_4$: C, 66.99; H, 8.57; found: C, 66.69; H, 8.62.



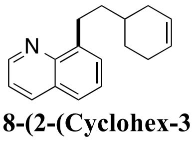
***tert*-Butyl 4-(6-chlorohexyl)benzoate (3d)** was prepared according to General Procedure A, using *tert*-butyl 4-bromobenzoate (386 mg, 1.5 mmol) and 6-chlorohex-1-ene (132 μL, 1.0 mmol). Purified by automated flash column chromatography (10-25% CH_2Cl_2 in hexanes, 100 g silica gel). Isolated as a colorless liquid (1st run 202 mg, 68%; 2nd run 193 mg, 65%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.90 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 3.52 (t, *J* = 6.7 Hz, 2H), 2.66 (t, *J* = 7.6 Hz, 2H), 1.81-1.71 (m, 2H), 1.69-1.61 (m, 2H), 1.59 (s, 9H), 1.51-1.41 (m, 2H), 1.40-1.29 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 166.0, 147.6, 129.7, 129.6 (2C), 128.4 (2C), 80.8, 45.2, 35.9, 32.6, 31.1, 28.5, 28.4 (3C), 26.8. **IR** (neat, cm^{-1}): 2932, 2858, 1708, 1289, 1163, 1112, 849. **Elemental Anal.** Calcd. for $C_{17}H_{25}ClO_2$: C, 68.79; H, 8.49; found: C, 69.04; H, 8.57.



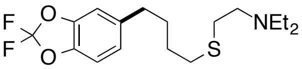
***sec*-Butyl 4-(4-(5-fluoro-2-methoxyphenyl)butoxy)benzoate (3e)** was prepared according to General Procedure A, using 2-bromo-4-fluoro-1-methoxybenzene (195 μL, 1.5 mmol) and *sec*-butyl 4-(but-3-en-1-yloxy)benzoate (248 mg, 1.0 mmol). Purified by automated flash column chromatography (30-60% CH_2Cl_2 in hexanes, 100 g silica gel). Isolated as a colorless liquid (1st run 316 mg, 84%; 2nd run 305 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.99 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.88-6.81 (m, 2H), 6.75 (dd, *J* = 8.7, 4.5 Hz, 1H), 5.07 (sextet, *J* = 6.3 Hz, 1H), 4.03 (t, *J* = 6.2 Hz, 2H), 3.78 (s, 3H), 2.67 (t, *J* = 7.4 Hz, 2H), 1.91-1.58 (m, 6H), 1.32 (d, *J* = 6.3 Hz, 3H), 0.97 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 166.2, 162.9, 157.0 (d, J_{C-F} = 237 Hz), 153.7 (d, J_{C-F} = 2 Hz), 132.4 (d, J_{C-F} = 7 Hz), 131.6 (2C), 123.3, 116.5 (d, J_{C-F} = 22 Hz), 114.1 (2C), 112.7 (d, J_{C-F} = 22 Hz), 111.1 (d, J_{C-F} = 8 Hz), 72.5, 68.1, 56.0, 29.8, 29.1, 28.9, 26.1, 19.7, 9.9. **^{19}F NMR** (471 MHz, $CDCl_3$) δ (ppm) -124.78 (td, *J* = 8.5, 4.5 Hz). **IR** (neat, cm^{-1}): 2939, 1704, 1605, 1496, 1249, 1165, 1100, 770. **Elemental Anal.** Calcd. for $C_{22}H_{27}FO_4$: C, 70.57; H, 7.27; found: C, 70.48; H, 7.27.



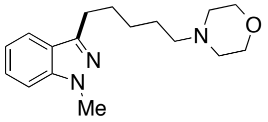
8-(2-(Cyclohex-3-en-1-yl)ethyl)quinolone (3f) was prepared according to General Procedure A, using 8-bromoquinoline (312 mg, 1.5 mmol) and 4-vinylcyclohex-1-ene (130 μL, 1.0 mmol). Purified by automated flash column chromatography (0-3% EtOAc in CH_2Cl_2, 100 g silica gel). Isolated as a colorless liquid (1st run 184 mg, 77%; 2nd run 178 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.94 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.65 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.57 (dd, *J* = 7.1, 1.5 Hz, 1H), 7.46 (dd, *J* = 8.1, 7.1 Hz, 1H), 7.38 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.74-5.63 (m, 2H), 3.35 (dd, *J* = 9.0, 6.8 Hz, 2H), 2.32-2.20 (m, 1H), 2.13-1.97 (m, 2H), 1.95-1.86 (m, 1H), 1.86-1.61 (m, 4H), 1.39-1.26 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 149.4, 147.0, 141.9, 136.4, 128.6 128.5, 127.2, 126.8, 126.4, 125.9, 120.9, 37.6, 33.6, 32.2, 29.1, 28.7, 25.4. **IR** (neat, cm^{-1}): 3018, 2909, 2834, 1497, 792, 653. **Elemental Anal.** Calcd. for $C_{17}H_{19}N$: C, 86.03; H, 8.07; found: C, 85.80; H, 8.13.



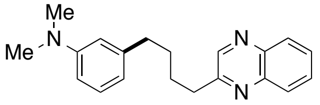
2-((4-(2,2-Difluorobenzo[*d*][1,3]dioxol-5-yl)butyl)thio)-*N*,*N*-diethylethan-1-amine (3g) was prepared according to General Procedure A, using 5-bromo-2,2-difluorobenzo[*d*][1,3]dioxole (204 µL, 1.5 mmol) and 2-(but-3-en-1-ylthio)-*N*,*N*-diethylethan-1-amine (187 mg, 1.0 mmol). Purified by manual flash column chromatography (1% Et_3N in EtOAc, 100 g silica gel). Isolated as an amber liquid (1st run 304 mg, 88%; 2nd run 306 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.92 (d, *J* = 8.1 Hz, 1H), 6.88-6.81 (m, 2H), 2.66-2.50 (m, 8H), 2.52 (q, *J* = 7.2 Hz, 4H), 1.73-1.64 (m, 2H), 1.64-1.54 (m, 2H), 1.01 (t, *J* = 7.2 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 143.9, 142.0, 138.4, 131.7 (t, $J_{C\text{-}F}$ = 253 Hz) 123.2, 109.6, 109.1, 53.1, 47.1 (2C), 35.4, 32.2, 30.7, 29.8, 29.1, 11.9 (2C). **^{19}F NMR** (471 MHz, $CDCl_3$) δ (ppm) -50.3 (s). **IR** (neat, cm^{-1}): 2968, 2934, 1498, 1447, 1233, 1146, 1034, 703. **Elemental Anal.** Calcd. for $C_{17}H_{25}F_2NO_2S$: C, 59.11; H, 7.29; found: C, 59.37; H, 7.26.



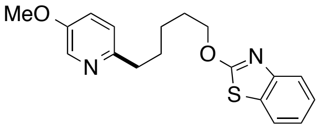
4-(5-(1-Methyl-1*H*-indazol-3-yl)pentyl)morpholine (3h) was prepared according to General Procedure A, using 3-bromo-1-methyl-1*H*-indazole (317 mg, 1.5 mmol) and 4-(pent-4-en-1-yl)morpholine (155 mg, 1.0 mmol). Purified by automated flash column chromatography (0-14% MeOH in EtOAc, 100 g silica gel). Isolated as an amber liquid (1st run (169 mg, 1.09 mmol of alkenes was used) 227 mg, 72%; 2nd run 211 mg, 73%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.65 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.38-7.28 (m, 2H), 7.09 (ddd, *J* = 7.9, 6.5, 1.3 Hz, 1H), 3.99 (s, 3H), 3.69 (t, *J* = 4.7 Hz, 4H), 2.99-2.92 (m, 2H), 2.41 (br s, 4H), 2.35-2.27 (m, 2H), 1.82 (quint, *J* = 7.6 Hz, 2H), 1.60-1.49 (m, 2H), 1.47-1.36 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 145.4, 140.9, 126.2, 122.8, 120.5, 119.6, 108.9, 67.0 (2C), 59.1, 53.8 (2C), 35.2, 29.4, 27.5, 27.1, 26.3. **IR** (neat, cm^{-1}): 2932, 2854, 1505, 1444, 1115, 867, 741. **Elemental Anal.** Calcd. for $C_{17}H_{25}N_3O$: C, 71.04; H, 8.77; found: C, 71.06; H, 8.90.



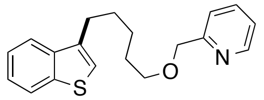
***N*,*N*-Dimethyl-3-(4-(quinoxalin-2-yl)butyl)aniline (3i)** was prepared according to General Procedure A, using 3-bromo-*N*,*N*-dimethylaniline (214 µL, 1.5 mmol) and 2-(but-3-en-1-yl)quinoxaline (184 mg, 1.0 mmol). Purified by automated flash column chromatography (5-20% EtOAc in CH_2Cl_2, 100 g silica gel). Isolated as an amber liquid (1st run 224 mg, 73%; 2nd run 219 mg, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.73 (s, 1H), 8.11-8.02 (m, 2H), 7.78-7.66 (m, 2H), 7.15 (t, *J* = 8.0 Hz, 1H), 6.61-6.54 (m, 3H), 2.66 (t, *J* = 8.0 Hz, 2H), 2.93 (s, 6H), 2.66 (t, *J* = 7.6 Hz, 2H), 1.98-1.87 (m, 2H), 1.83-1.73 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 157.6, 150.9, 145.9, 143.2, 142.3, 141.3, 130.0, 129.3, 129.1, 129.0, 128.9, 117.0, 112.9, 110.4, 40.8 (2C), 36.5, 36.3, 31.4, 29.3. **IR** (neat, cm^{-1}): 2930, 2855, 1602, 1492, 1351, 908, 728. **HRMS** $C_{20}H_{23}N_3$; calcd. for (M+H): 306.1965, found: 306.1976.



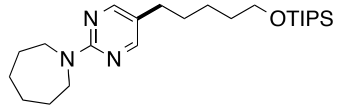
2-((5-(5-Methoxypyridin-2-yl)pentyl)oxy)benzo[*d*]thiazole (3j) was prepared according to General Procedure A, using 2-bromo-5-methoxypyridine (284 mg, 1.5 mmol) and 2-(pent-4-en-1-yloxy)benzo[*d*]thiazole (219 mg, 1.0 mmol). Purified by automated flash column chromatography (10-35% EtOAc in CH_2Cl_2, 100 g silica gel). Isolated as a slightly yellow liquid (1st run 191 mg, 58%; 2nd run 202 mg, 61%).

^{1}**H NMR** (400 MHz, $CDCl_3$) δ (ppm) 8.22 (d, J = 3.2 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H). 7.63 (d, J = 8.0 Hz, 1H), 7.35 (td, J = 7.6, 1.3 Hz, 1H), 7.21 (td, J = 7.6, 1.2 Hz, 1H), 7.13 (dd, J = 8.5, 3.0 Hz, 1H), 7.06 (d, J = 8.5 Hz, 1H), 4.55 (t, J = 6.6 Hz, 2H), 3.84 (s, 3H), 2.77 (t, J = 7.6 Hz, 2H), 1.93-1.84 (m, 2H), 1.84-1.73 (m, 2H), 1.58-1.47 (m, 2H). ^{13}**C NMR** (100 MHz, $CDCl_3$) δ (ppm) 173.1, 154.1, 153.9, 149.5, 136.5, 131.9, 126.0, 123.5, 122.9, 121.4, 121.3, 120.8, 72.1, 55.7, 37.2, 29.7, 28.8, 25.6. **IR** (neat, cm^{-1}): 2936, 1533, 1442, 1248, 1214, 1032, 753. **Elemental Anal.** Calcd. for $C_{18}H_{20}N_2O_2S$: C, 65.83; H, 6.14; found: C, 66.03; H, 6.29.



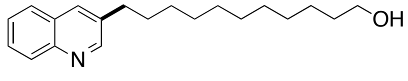
2-(((5-(Benzo[*b*]thiophen-3-yl)pentyl)oxy)methyl)pyridine (3k) was prepared according to General Procedure A, using 3-bromobenzo[*b*]thiophene (196 μL, 1.5 mmol) and 2-((pent-4-en-1-yloxy)methyl)pyridine (177 mg, 1.0 mmol). Purified by automated flash column chromatography (5-15% EtOAc in CH_2Cl_2, 100 g silica gel). Isolated as a slightly yellow liquid (1st run 239 mg, 77%; 2nd run 246 mg, 79%).

^{1}**H NMR** (400 MHz, $CDCl_3$) δ (ppm) 8.55 (d, J = 4.3 Hz, 1H), 7.85 (d, J = 7.6 Hz, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.67 (td, J = 7.7, 1.8 Hz, 1H), 7.43 (d, J = 7.9 Hz, 1H), 7.40-7.30 (m, 2H), 7.20-7.14 (m, 1H), 7.08 (s, 1H), 4.64 (s, 2H), 3.58 (t, J = 6.5 Hz, 2H), 2.89 (t, J = 7.6 Hz, 2H), 1.85-1.69 (m, 4H), 1.59-1.48 (m, 2H). ^{13}**C NMR** (100 MHz, $CDCl_3$) δ (ppm) 158.9, 149.1, 140.6, 139.2, 137.0, 136.7, 124.2, 123.8, 122.9, 122.3, 121.8, 121.4, 121.0, 73.9, 71.1, 29.7, 29.1, 28.6, 26.2. **IR** (neat, cm^{-1}): 2932, 2856, 1589, 1433, 1116, 756, 730. **Elemental Anal.** Calcd. for $C_{19}H_{21}NOS$: C, 73.27; H, 6.80; found: C, 73.22; H, 6.76.



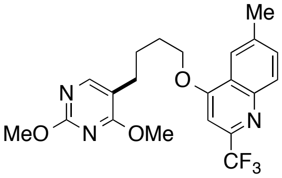
1-(5-(5-((Triisopropylsilyl)oxy)pentyl)pyrimidin-2-yl)azepane (3l) was prepared according to General Procedure A, using 1-(5-bromopyrimidin-2-yl)azepane (384 mg, 1.5 mmol) and triisopropyl(pent-4-en-1-yloxy)silane (242 mg, 1.0 mmol). Purified by automated flash column chromatography (0-8% EtOAc in hexanes, 100 g silica gel). Isolated as a colorless liquid (1st run 318 mg, 76%; 2nd run 308 mg, 73%).

^{1}**H NMR** (400 MHz, $CDCl_3$) δ (ppm) 8.12 (s, 2H), 3.71 (t, J = 6.0 Hz, 4H), 3.66 (t, J = 6.5 Hz, 2H), 2.39 (t, J = 7.6 Hz, 2H), 1.81-1.73 (m, 4H), 1.60-1.50 (m, 8H), 1.43-1.34 (m, 2H), 1.10-1.01 (m, 21H). ^{13}**C NMR** (100 MHz, $CDCl_3$) δ (ppm) 160.7, 157.6 (2C), 121.8, 63.5, 47.1 (2C), 32.9, 31.3, 29.7, 28.2 (2C), 27.5 (2C), 25.4, 18.2 (6C), 12.1 (3C). **IR** (neat, cm^{-1}): 2925, 2863, 1603, 1505, 1431, 1105, 796, 679. **Elemental Anal.** Calcd. for $C_{24}H_{45}N_3OSi$: C, 68.68; H, 10.81; found: C, 68.80; H, 10.75.



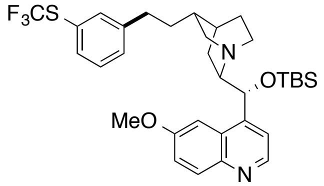
11-(Quinolin-3-yl)undecan-1-ol (3m) was prepared using a reaction tube (Fisher Scientific, 16 x 125 mm, Cat. No. 1495935A) equipped with a stir bar, which was charged with CuCl-[(R)-DTBM-SEGPHOS] (77 mg, 0.060 mmol) and TMSONa (224 mg, 2.0 mmol). A separate 8 mL vial (VWR, Cat. No. 66030-722) equipped with a stir bar was charged with $[Pd(cinnamyl)Cl]_2$ (10.4 mg, 0.020 mmol) and BrettPhos (23.6 mg, 0.044 mmol). The reaction tube and vial were capped with a phenolic screw cap and septum (Cap: Fisher Scientific, Closure OT S/T 15-425TH 14, Cat. No. 033407E; Septa: Thermo Scientific, Septa T/S for 15-425Cap, Cat. No. B7995-15). The reaction tube and vial were evacuated and backfilled with N_2 (this process was repeated a total of three times). The N_2 inlet needles were left in the septa. Dry THF (0.5 mL) was added to the reaction tube and dry THF (0.5 mL) was added to the vial via syringes. A needle was inserted into the septum of the reaction tube before dimethylphenylsilane (0.55 mL, 3.6 mmol) was added to the reaction tube. [Caution! Gas evolution.] The solutions in both the reaction tube and vial were stirred for 5 min, with a flow of N_2 through the reaction tube. Subsequently, undec-10-en-1-ol (200 μL, 1.0 mmol) was added through the septum using a syringe. [Caution! Gas evolution.] The solution in the reaction tube was stirred for another 20 min under N_2-flow and 3-bromoquinoline (204 μL, 1.5 mmol) was then added. The solution was stirred for 5 min under N_2-flow. At this point, the palladium-THF solution from the vial was added through the septum using a syringe. After stirring for another 2 min under N_2-flow, the N_2 in- and outlet needles were removed and the reaction tube was placed in an oil bath preheated to 45 °C. After stirring for 18 h, the reaction mixture was allowed to cool to ambient temperature before TBAF in THF (1 M, 4.0 mL, 4.0 mmol) was added. The solution was stirred at ambient temperature for 2 h before a solution of saturated $NaHCO_3$ (10 mL) was added and the product was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried over $MgSO_4$ and filtered, and the volatiles were removed *in vacuo*. The product was purified by automated flash column chromatography (10-50% EtOAc in CH_2Cl_2, 100 g silica gel). Isolated as a slightly yellow solid (1st run 105 mg, 35%; 2nd run 104 mg, 35%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.76 (s, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 2.0 Hz, 1H), 7.75 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.64 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 3.63 (t, *J* = 6.6 Hz, 2H), 2.78 (t, *J* = 7.7 Hz, 2H), 2.07 (br s, 1H), 1.70 (quint, *J* = 7.4 Hz, 2H), 1.55 (quint, *J* = 6.8 Hz, 2H), 1.43-1.19 (m, 14H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 152.2, 146.8, 135.5, 134.3, 129.2, 128.6, 128.3, 127.4, 126.6, 63.0, 33.3, 32.9, 31.2, 29.7, 29.6 (2C), 29.5, 29.5, 29.2, 25.9. **IR** (neat, cm^{-1}): 3334, 2917, 2851, 1467, 1051, 755. **M.p.** 50-52 °C. **Elemental Anal.** Calcd. for $C_{20}H_{29}NO$: C, 80.22; H, 9.76; found: C, 80.25; H, 9.79.



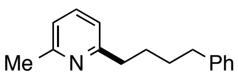
4-(4-(2,4-Dimethoxypyrimidin-5-yl)butoxy)-6-methyl-2-(trifluoromethyl)quinolone (3n) was prepared using a screw-cap reaction tube (A) (Fisher Scientific, 16 x 125 mm, Cat. No. 1495935A) equipped with a stir bar, which was charged with 4-(but-3-en-1-yloxy)-6-methyl-2-(trifluoromethyl)quinoline (281 mg, 1.0 mmol) and 5-bromo-2,4-dimethoxypyrimidine (329 mg, 1.5 mmol). A separate 8 mL vial (B) (VWR, Cat. No. 66030-722) equipped with a stir bar was charged with [Pd(cinnamyl)Cl]$_2$ (10.4 mg, 0.020 mmol) and BrettPhos (23.6 mg, 0.044 mmol). Similarly, another 8 mL vial (C) (VWR, Cat. No. 66030-722) equipped with a stir bar was charged with CuCl-[(R)-DTBM-SEGPHOS] (77 mg, 0.060 mmol) and TMSONa (224 mg, 2.0 mmol). The reaction tube (A) and vials (B and C) were capped with a phenolic screw cap and septum (Cap: Fisher Scientific, Closure OT S/T 15-425TH 14, Cat. No. 033407E; Septa: Thermo Scientific, Septa T/S for 15-425Cap, Cat. No. B7995-15). The reaction tube (A) and vials (B and C) were evacuated and backfilled with N_2 (this process was repeated a total of three times). The N_2 inlet needles were left in the septa. Dry THF (0.5 mL) was added to the vial (B) containing the Pd catalyst mixture and dry THF (0.5 mL) was added to the vial (C) containing the Cu catalyst mixture. A needle was inserted into the septum of the vial (C) containing the Cu solution, and dimethylphenylsilane (0.4 mL, 2.6 mmol) was subsequently added to this vial (C). [Caution! Gas evolution.] The solutions in both vials (B and C) were stirred for 5 min, with a flow of N_2 through the vial (C) containing the Cu solution. Subsequently, the solution in the vial (C) with the Cu solution was transferred to the reaction tube (A) using a syringe and dry THF (3.0 mL) was added. A needle was inserted into the septum of the reaction tube (A), and this solution was stirred for another 5 min under N_2-flow. The contents of the vial (B) with the Pd solution were then added through the septum using a syringe. After stirring for another 2 min under N_2-flow, the N_2 in- and outlet needles were removed and the reaction tube (A) was placed in an oil bath preheated to 45 °C. After stirring for 18 h, the reaction mixture was allowed to cool to ambient temperature before it was diluted with CH_2Cl_2 (15 mL) and concentrated onto silica gel *in vacuo*. The product was purified by automated flash column chromatography (0-15% EtOAc in CH_2Cl_2, 100 g silica gel). Isolated as an orange solid (1st run 392 mg, 93%; 2nd run 403 mg, 96%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.07-8.00 (m, 2H), 8.00-7.93 (m, 1H), 7.61 (dd, *J* = 8.7, 2.0 Hz, 1H), 6.99 (s, 1H), 4.27 (t, *J* = 6.3 Hz, 2H), 3.98 (s, 6H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.57 (s, 3H), 2.06-1.95 (m, 2H), 1.90-1.80 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 169.6, 164.3, 162.6, 157.0, 148.2 (q, $J_{C\text{-}F}$ = 33 Hz), 146.8, 137.8, 133.2, 129.5, 121.8 (q, $J_{C\text{-}F}$ = 273 Hz), 121.8, 120.7, 114.9, 96.7 (q, $J_{C\text{-}F}$ = 2 Hz), 68.7, 54.8, 54.0, 28.5, 26.4, 25.6, 22.0. **IR** (neat, cm^{-1}): 2957, 1568, 1454, 1368, 1132, 837. **M.p.** 156-158 °C. **Elemental Anal.** Calcd. for $C_{21}H_{22}F_3N_3O_3$: C, 59.85; H, 5.26; found: C, 59.56; H, 5.33.



2-((*R*)-((*tert*-Butyldimethylsilyl)oxy)(6-methoxyquinolin-4-yl)methyl)-5-(3-((trifluoromethyl)thio)phenethyl)quinuclidine (3o) was prepared using a screw-cap reaction tube (A) (Fisher Scientific, 16 x 125 mm, Cat. No. 1495935A) equipped with a stir bar, which was charged with 2-((*R*)-((*tert*-butyldimethylsilyl)oxy)(6-methoxyquinolin-4-yl)methyl)-5-vinylquinuclidine (439 mg, 1.0 mmol). A separate 8 mL vial (B) (VWR, Cat. No. 66030-722) equipped with a stir bar was charged with [Pd(cinnamyl)Cl]$_2$ (10.4 mg, 0.020 mmol) and BrettPhos (23.6 mg, 0.044 mmol). Similarly, another 8 mL vial (C) (VWR, Cat. No. 66030-722) equipped with a stir bar was charged with CuCl-[(R)-DTBM-SEGPHOS] (77 mg, 0.060 mmol) and TMSONa (224 mg, 2.0 mmol). The reaction tube (A) and vials (B and C) were capped with a phenolic screw cap and septum (Cap: Fisher Scientific, Closure OT S/T 15-425TH 14, Cat. No. 033407E; Septa: Thermo Scientific, Septa T/S for 15-425Cap, Cat. No. B7995-15). The reaction tube (A) and vials (B and C) were evacuated and backfilled with N$_2$. This process was repeated three times. The N$_2$ inlet needles were left in the septa. Dry THF (0.5 mL) was added to the vial (B) containing the Pd catalyst mixture, and dry THF (0.5 mL) was also added to the vial (C) containing the Cu catalyst mixture. Dry THF (1.0 mL) was also added to the reaction tube (A) with the alkene starting material. A needle was inserted into the septum of the vial (C) containing the Cu solution, and dimethylphenylsilane (0.4 mL, 2.6 mmol) was subsequently added to this vial (C). [Caution! Gas evolution.] The solutions in both vials (B and C) were stirred for 5 min, with a flow of N$_2$ through the vial (C) containing the Cu solution. Subsequently, the Cu solution (from vial C) was transferred to the reaction tube (A) using a syringe, and (3-bromophenyl)(trifluoromethyl)sulfane (386 mg, 1.5 mmol) was then added to the reaction tube (A). A needle was inserted into the septum of the reaction tube (A), and this solution was stirred for another 5 min under N$_2$-flow. The Pd solution (from vial B) was subsequently added through the septum using a syringe and needle. After stirring for another 2 min under N$_2$-flow, the N$_2$ in- and outlet needles were removed and the reaction tube (A) was placed in an oil bath preheated to 45 °C. After stirring for 18 h, the reaction mixture was allowed to cool to ambient temperature before the solids were removed by filtration through a plug of Celite. The plug was rinsed with CH$_2$Cl$_2$ (15 mL), the volatiles were removed *in vacuo*, and the product was purified by preparative TLC (7% MeOH in EtOAc, four preparative TLC plates). Isolated as a colorless wax (1st run 269 mg, 44%; 2nd run 278 mg, 45%).

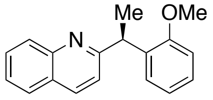
^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm) *Complex spectrum observed due to hindered rotation (see the end of the Supporting Information for the spectra observed)*. Characteristic peaks: *major rotamer (approx. 75%)* 8.75 (d, *J* = 4.6 Hz, 1H), 8.03 (d, *J* = 9.2 Hz, 1H), 3.95 (br s, 3H), 0.98 (s, 9H), 0.13 (br s, 3H), -0.37 (s, 3H); *minor rotamer (approx. 25%)* 8.65 (d, *J* = 4.3 Hz, 1H), 7.99 (d, *J* = 9.2 Hz, 1H), 3.88 (s, 3H), 0.84 (s, 9H), 0.10 (s, 3H), -0.45 (s, 3H). **^{13}C NMR** (100 MHz, CDCl$_3$) δ (ppm) *Complex spectrum observed due to hindered rotation and C-F coupling, number of carbons are not given (see the end of the Supporting Information for the spectra observed)*. 156.7, 147.4, 147.3, 145.6, 144.6, 144.1, 136.2, 133.9, 133.8, 132.0, 131.7, 130.9, 129.6, 128.2, 127.2, 126.3, 124.4, 121.5, 121.2, 118.9, 104.7, 100.8, 80.3, 61.1, 60.9, 58.1, 55.5, 43.3, 41.4, 36.9, 36.3, 35.2, 33.7, 33.4, 28.9, 27.0, 26.1, 25.9, 18.3, 18.2, -4.1, -4.5, -4.9, -5.1. **^{19}F NMR** (471 MHz, CDCl$_3$) δ (ppm) -42.9 (s). **IR** (neat, cm^{-1}): 2929, 2858, 1619, 1506, 1110, 836, 777. **Elemental Anal.** Calcd. for $C_{33}H_{34}F_3N_2O_2SSi$: C, 64.26; H, 7.03; found: C, 64.00; H, 7.00.



2-Methyl-6-(4-phenylbutyl)pyridine (3p) was prepared according to General Procedure A, using 2-chloro-6-methylpyridine (164 μL, 1.5 mmol) or 2-bromo-6-methylpyridine (171 μL, 1.5 mmol) and pent-4-en-1-ylbenzene (150 μL, 1.0 mmol). Purified by automated flash column chromatography (0-30% EtOAc in CH$_2$Cl$_2$, 100 g silica gel). Isolated as a slightly yellow liquid (for 2-chloro-6-methylpyridine 1st run 163 mg, 72%; 2nd run 168 mg, 75%; for 2-bromo-6-methylpyridine 1st run 96 mg, 43%; 2nd run 95 mg, 42%). The product isolated matched previously reported spectra for this structure.[4]

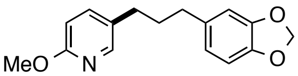
^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.46 (t, *J* = 7.6 Hz, 1H), 7.31-7.23 (m, 2H), 7.21-7.13 (m, 3H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.92 (d, *J* = 7.6 Hz, 1H), 2.79 (t, *J* = 7.4 Hz, 2H), 2.65 (t, *J* = 7.4 Hz, 2H), 2.53 (s, 3H), 1.83-1.65 (m, 4H). **^{13}C NMR** (100 MHz, CDCl$_3$) δ (ppm) 161.7, 157.8, 142.7, 136.6, 128.5 (2C), 128.4

(2C), 125.7, 120.5, 119.6, 38.5, 36.0, 31.4, 30.0, 24.7. **IR** (neat, cm^{-1}): 2926, 2856, 1577, 1453, 745, 698. **HRMS** $C_{16}H_{19}N$; calcd. for (M+H): 226.1590, found: 226.1583.



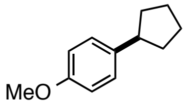
(*S*)-2-(1-(2-Methoxyphenyl)ethyl)quinolone (4a) was prepared according to General Procedure A, using either 2-chloroquinoline (245 mg, 1.5 mmol) or 2-bromoquinoline (312 mg, 1.5 mmol) and 2-vinylanisole (134 µL, 1.0 mmol). Purified by automated flash column chromatography (0-10% EtOAc in CH_2Cl_2, 100 g silica gel). Isolated as a brown liquid (for 2-chloroquinoline 1st run 215 mg, 82%; 2nd run 219 mg, 83%; for 2-bromoquinoline 1st run 140 mg, 53%; 2nd run 131 mg, 50%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.14 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 8.5 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.69 (t, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 8.1 Hz, 1H), 7.29 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.23 (td, *J* = 8.1, 1.7 Hz, 1H), 7.19 (d, *J* = 8.5 Hz, 1H), 6.94 (t, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 4.91 (q, *J* = 7.2 Hz, 1H), 3.77 (s, 3H), 1.77 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 165.6, 157.1, 147.9, 135.9, 133.4, 129.4, 129.1, 128.3, 127.6, 127.5, 126.9, 125.7, 121.1, 120.7, 110.7, 55.5, 40.9, 19.8. **IR** (neat, cm^{-1}): 2964, 2932, 2834, 1597, 1490, 1239, 748. **Specific rotation** $[\alpha]_D^{23.9}$ = 138 (c = 1.0, $CHCl_3$); **Chiral HPLC** analysis: Chiralpak OJH (hexanes/IPA = 90/10, 1.0 mL/min), 8.3 min (major), 13.1 min (minor), for 2-chloroquinoline: 1st run 96% ee, 2nd run 93% ee, for 2-bromoquinoline: 1st run 83% ee, 2nd run 81% ee. **HRMS** $C_{18}H_{17}NO$; calcd. for (M+H): 264.1383, found: 264.1361.



5-(3-(Benzo[*d*][1,3]dioxol-5-yl)propyl)-2-methoxypyridine (3q) was prepared using a screw-cap reaction tube (Fisher Scientific, 20 x 150 mm, Cat. No. 1495937C) equipped with a stir bar, which was charged with CuCl-[(R)-DTBM-SEGPHOS] (384 mg, 0.30 mmol) and TMSONa (2.24 g, 20.0 mmol). A separate 8 mL vial (VWR, Cat. No. 66030-722) equipped with a stir bar was charged with $[Pd(cinnamyl)Cl]_2$ (118 mg, 0.10 mmol) and BrettPhos (52 mg, 0.22 mmol). The reaction tube and vial were capped with a phenolic screw cap and septum (Cap for vial: Fisher Scientific, Closure OT S/T 15-425TH 14, Cat. No. 033407E; Septa for vial: Thermo Scientific, Septa T/S for 15-425Cap, Cat. No. B7995-15; Cap for reaction tube: Fisher Scientific, Closure OT S/T 18-400, Cat. No. 033407G; Septa for vial: Thermo Scientific, Septa T/S for 18-400Cap, Cat. No. B7995-18). The reaction tube and vial were evacuated and backfilled with N_2 (this process was repeated a total of three times). The N_2 inlet needles were left in the septa. Dry THF (6.0 mL) was added to the reaction tube and dry THF (4.0 mL) was added to the vial via syringes. A needle was inserted into the septum of the reaction tube, and dimethylphenylsilane (4.0 mL, 26.0 mmol) was then carefully added to the reaction tube. [Caution! Gas evolution.] The solutions in both the reaction tube and vial were stirred for 10 min, with a flow of N_2 through the reaction tube. Subsequently, safrole (1.5, 10.1 mmol) and 5-bromo-2-methoxypyridine (2.0 mL, 15.5 mmol) were added to the reaction tube through the septum using a syringe. The solution in the reaction tube was stirred for another 10 min under N_2-flow, and the THF solution from the vial was added through the septum using a syringe. After stirring for another 2 min under N_2-flow, the N_2 in- and outlet needles were removed and the reaction tube was placed in an oil bath preheated to 45 °C. After stirring for 18 h, the reaction mixture was allowed to cool to ambient temperature before the solids were removed by filtration through a plug of Celite. The plug was rinsed with CH_2Cl_2 (40 mL), the volatiles were removed *in vacuo*, and the product was purified by manual flash column chromatography (0-7% EtOAc in hexanes with 1% Et_3N, 200 g silica gel). Isolated as a slightly yellow liquid (1st run 2.40 g, 87%; 2nd run 2.47 g, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.04-7.87 (d, *J* = 2.4 Hz, 1H), 7.38 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.72 (d, *J* = 7.9 Hz, 1H), 6.69-6.65 (m, 2H), 6.61 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.91 (s, 2H), 3.91 (s, 3H), 2.68-2.43 (m, 4H), 2.00-1.72 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 162.7, 147.7, 146.2, 145.7, 139.0, 135.8, 130.0, 121.2, 110.5, 108.9, 108.2, 100.9, 53.4, 35.0, 33.2, 31.44. **IR** (neat, cm^{-1}): 2939, 1607, 1487, 1241, 1026, 808. **Elemental Anal.** Calcd. for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; found: C, 70.55; H, 6.21.



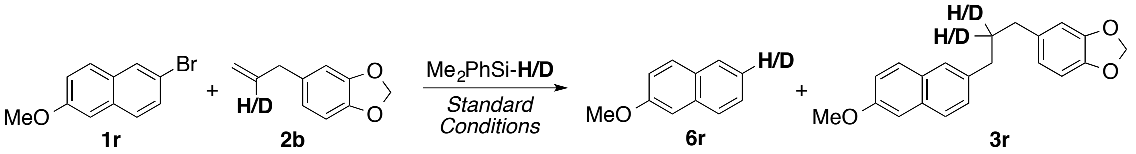
1-cyclopentyl-4-methoxybenzene 1-cyclopentyl-4-methoxybenzene (5a) was prepared in a nitrogen-filled glovebox using a reaction tube (Fisher Scientific, 16 x 125 mm, Cat. No. 1495935A) equipped with a stir bar, which was charged with CuOAc (12.4 mg, 0.10 mmol), (*S*)-DTBM-SEGPHOS] (130 mg, 0.11 mmol), and TMSONa (224 mg, 2.0 mmol). A separate 8 mL vial (VWR, Cat. No. 66030-722) equipped with a stir bar was charged with [Pd(cinnamyl)Cl]$_2$ (5.2 mg, 0.010 mmol) and BrettPhos (11.8 mg, 0.022 mmol). Dry THF (0.6 mL) was added to the reaction tube and dry THF (0.4 mL) was added to the vial. Dimethylphenylsilane (0.32 mL, 2.0 mmol) was added to the reaction tube. [Caution! Gas evolution.] The solutions in both the reaction tube and vial were stirred for 5 min, and the THF solution from the vial was subsequently added via syringe. After the solution in the reaction tube was stirred for 5 min, 4-bromoanisole (125 μL, 1.0 mmol) and cyclopentene (1.8 mL, 20.0 mmol) were then added to the reaction tube as well via syringe. The reaction tube was capped with a phenolic screw cap and septum (Cap: Fisher Scientific, Closure OT S/T 15-425TH 14, Cat. No. 033407E; Septa: Thermo Scientific, Septa T/S for 15-425Cap, Cat. No. B7995-15). At this point, the reaction tube was removed from the glovebox and placed in an oil bath preheated to 45 °C. After stirring for 18 h, the reaction mixture was allowed to cool to ambient temperature before the solids were removed by filtration through a plug of Celite. The plug was rinsed with CH_2Cl_2 (15 mL), the volatiles were removed *in vacuo*, and the product was purified by automated flash column chromatography (0-30% CH_2Cl_2 in hexanes, 100 g silica gel). Isolated as a colorless liquid (1st run 146 mg, 83%; 2nd run 147 mg, 84%). The product isolated matched previously reported spectra for this structure.[5]

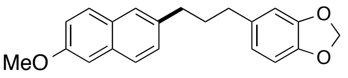
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.16 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 3.79 (s, 3H), 2.94 (tt, *J* = 9.8, 7.4 Hz, 1H), 2.10-1.97 (m, 2H), 1.85-1.73 (m, 2H), 1.73-1.60 (m, 2H), 1.60-1.46 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 157.8, 138.7, 128.1 (2C), 113.8 (2C), 55.4, 45.3, 34.9 (2C), 25.6 (2C).

Reactions using cyclohexene, cycloheptene, or cyclooctene were conducted in a similar manner, but provided only low yields of the desired products (**5b**-**5d**). ^{1}H NMR yields were obtained using 1,3-benzodioxole (26 μL, 0.25 mmol) as an internal standard, and comparing to previously reported spectra.[5] The identity of the products were confirmed by GC-MS.

VI. Deuterium experiments

Four reactions were performed using all combinations of *protio*- or *deutero*-safrole (**2b** or ***d_1*-2b**) and Me_2PhSiH or Me_2PhSiD.





5-(3-(6-methoxynaphthalen-2-yl)propyl)benzo[*d*][1,3]dioxole (3r) was prepared according to General Procedure A to couple 2-bromo-6-methoxynaphthalene (178 mg, 0.75 mmol) and safrole (74 µL, 0.5 mmol) with the modification of the silane used . The volume of solvent was also increased to 1 mL of THF to fully dissolve the 2-bromo-6-methoxynaphthalene. Cross-coupled product **3r** and 2-methoxynaphthalene were purified by automated flash column chromatography (0-50% CH_2Cl_2 in hexanes, 50 g silica gel). Both compounds are isolated as colorless solids (2-methoxynaphthalene: 68 mg, 57%; **3r**: 122 mg, 76%). The spectroscopic data for the isolated 2-methoxynaphthalene matches the previously reported spectra for this structure.[6]

2-methoxynaphthalene (6r): ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.80-7.70 (m, 3H), 7.44 (t, *J* = 6.8 Hz, 1H), 7.34 (t, *J* = 6.8 Hz, 1H), 7.18-7.12 (m, 2H), 3.93 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 157.6, 134.6, 129.4, 128.9, 127.6, 126.7, 126.4, 123.6, 118.7, 105.7, 55.3.

3r: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.70-7.63 (m, 2H), 7.54 (s, 1H), 7.29 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.15-7.10 (m, 2H), 6.73 (d, *J* = 7.9 Hz, 1H), 6.69 (d, *J* = 1.7 Hz, 1H), 6.64 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.92 (s, 2H), 3.91 (s, 3H), 2.76 (t, *J* = 7.6 Hz, 2H), 2.60 (t, *J* = 7.6 Hz, 2H), 1.99 (pent, *J* = 7.6 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 157.1, 147.5, 145.5, 137.4, 136.2, 132.9, 129.1, 128.9, 127.8, 126.7, 126.3, 121.1, 118.6, 108.9, 108.1, 105.6, 100.7, 55.3, 35.2, 35.1, 33.2. **IR** (neat, cm^{-1}): 2932, 2853, 1605, 1502, 1484, 1245, 1027. **Elemental Anal.** Calcd. for $C_{21}H_{20}O_3$: C, 78.73; H, 6.29; found: C, 78.88; H, 6.29.

Similarly, reactions using Me_2PhSiD and/or d_1-safrole (***d_1*-2b**) were performed. The products were purified as described above giving the following yields (identity of major product given).

Me_2PhSiH and ***d_1*-2b**:	2-methoxynaphthalene (**6r**): 71 mg, 60%	***d_1*-3r**: 119 mg, 74%
Me_2PhSiD and **2b**:	d_1-2-methoxynaphthalene (***d_1*-6r**): 65 mg, 54%	***d_1*-3r**: 120 mg, 74%
Me_2PhSiD and ***d_1*-2b**:	d_1-2-methoxynaphthalene (***d_1*-6r**): 68 mg, 57%	***d_2*-3r**: 118 mg, 73%

Deuterium-labeling results with 2-bromo-6-methoxynaphthalene (**1r**) and 5-(Allyl-2-*d*)benzo[*d*][1,3]dioxole or 5-benzo[*d*][1,3]dioxole (**2b** or ***d_1*-2b**)

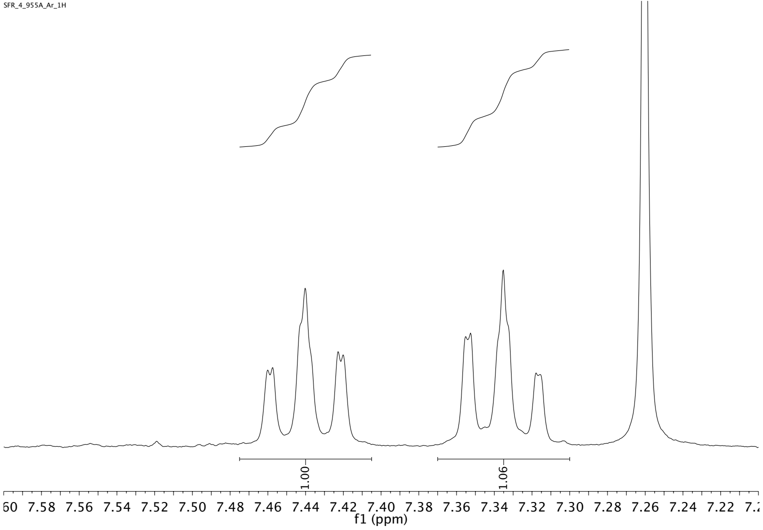
Silane **2b (alkene)**	**H**	**D**
H	**3r** - 0%D **6r** – 0%D	**3r** - 48%D **6r** – 96%D
D	**3r** - 50%D **6r** – 0%D	**3r** - 93%D **6r** – 96%D

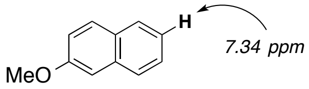
Analysis by GC-MS of samples of d_1-2-methoxynaphthalene (***d_1*-6r**) prepared with Me_2PhSiD and **2b** or Me_2PhSiD and ***d_1*-2b** showed a ratio of 4:96 (2-methoxynaphthalene (**6r**) : d_1-2-methoxynaphthalene(***d_1*-6r**)) in both cases. The ^{1}H NMR data indicates a ratio of 10:90 and 8:92 (2-methoxynaphthalene (**6r**) : d_1-2-methoxynaphthalene (***d_1*-6r**)). See comment below regarding this enlarged ^{1}H NMR integral for 2-methoxynaphthalene (**6r**).

^{1}H NMR spectra of products from the reaction with Me_2PhSiH and 5-allylbenzo[*d*][1,3]dioxole (2b):

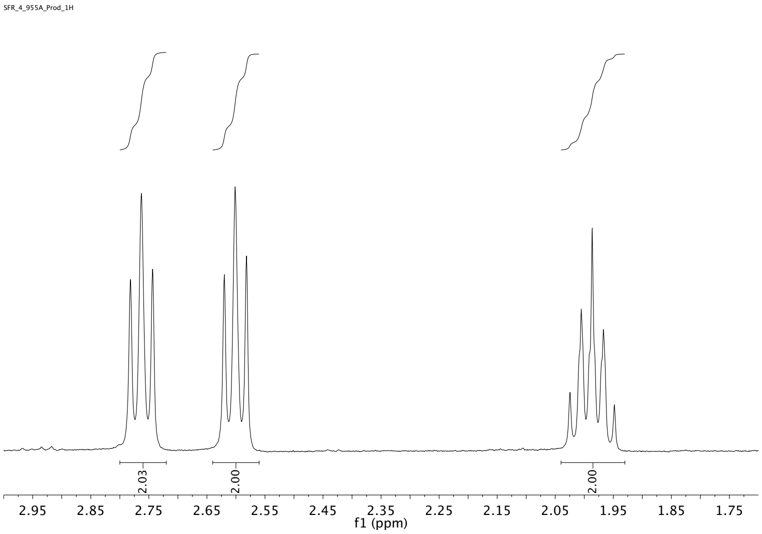
For full spectra see section IX. NMR spectra and HPLC chromatograms.

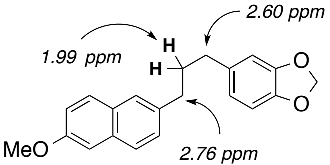
Key regions





6r

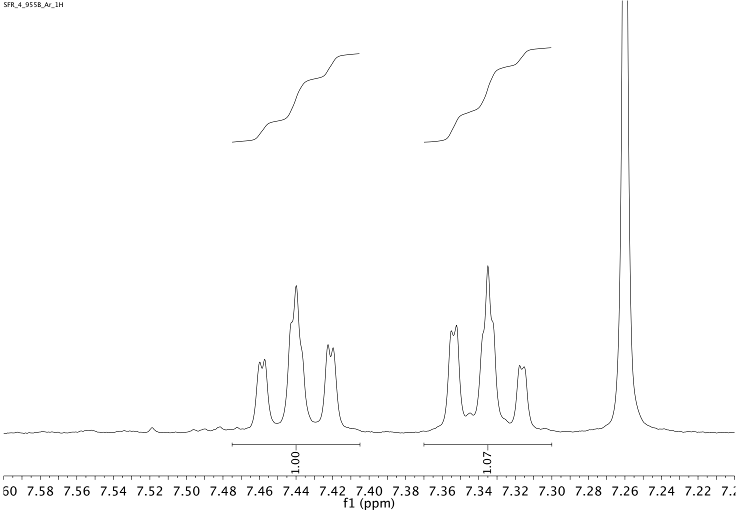


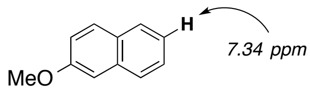


3r

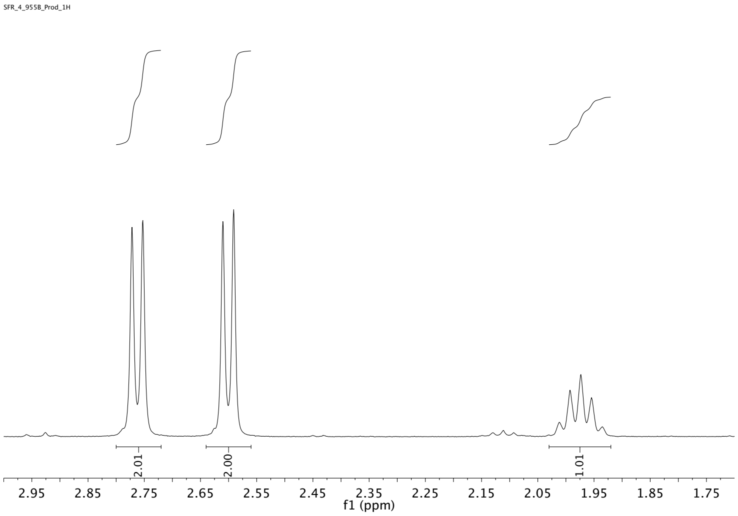
^{1}H NMR spectra of products from the reaction with Me$_2$PhSiH and 5-(Allyl-2-*d*)benzo[*d*][1,3]dioxole (*d$_1$*-2b):

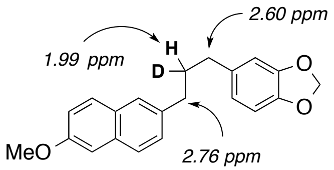
Key regions





6r

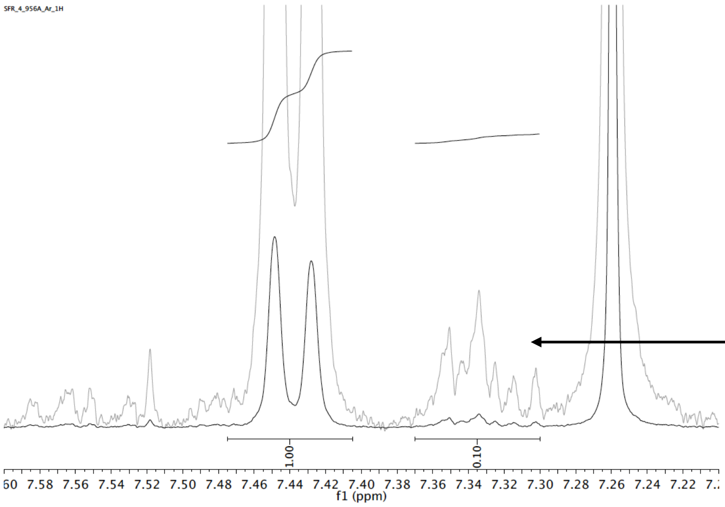


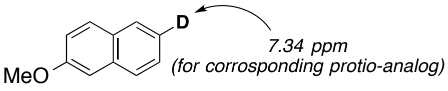


***d$_1$*-3r**

^{1}H NMR spectra of products from the reaction with Me_2PhSiD and 5-allylbenzo[*d*][1,3]dioxole (2b):

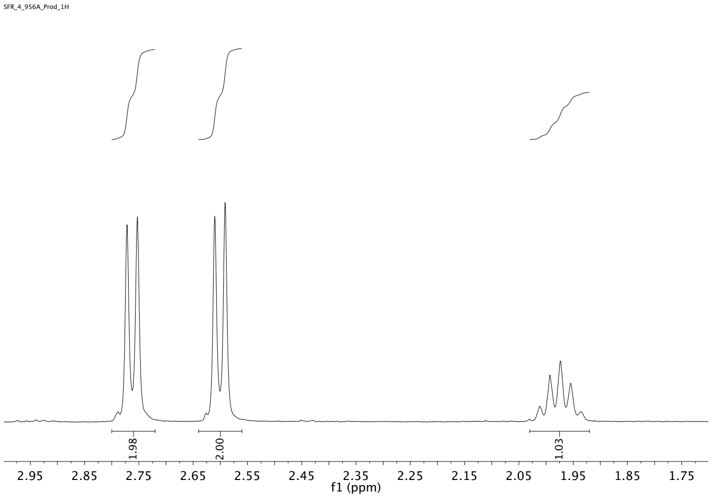
Key regions

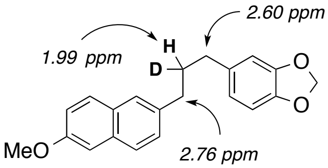




***d*₁-6r**

*Protio-**6r** and unknown impurity*
(key region shown with increased intensity in gray)

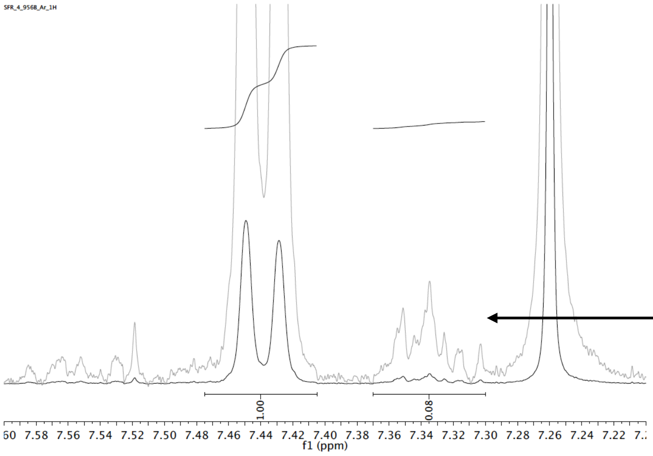


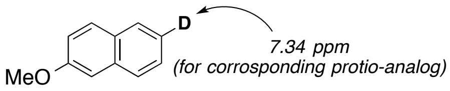


***d*₁-3r**

^{1}H NMR spectra of products from the reaction with Me$_2$PhSiD and 5-(Allyl-2-*d*)benzo[*d*][1,3]dioxole (*d$_1$*-2b):

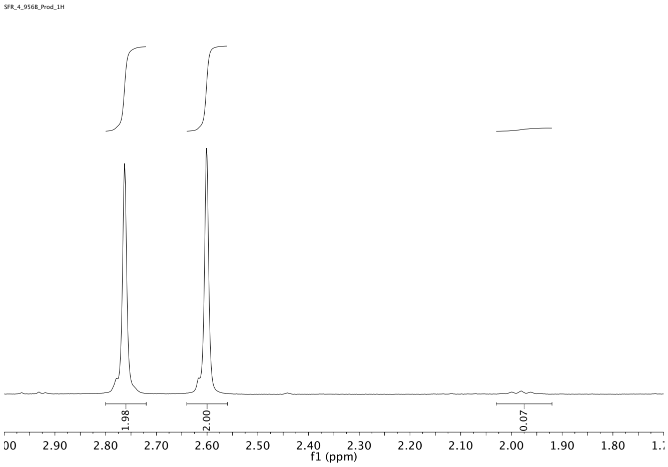
Key regions

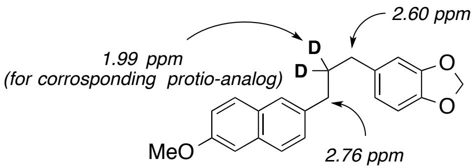




***d$_1$*-6r**

*Protio-**6r** and unknown impurity*
(key region shown with increased intensity in gray)

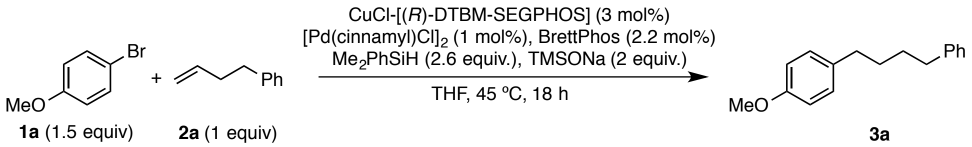




***d$_2$*-3r**

VII. Water sensitivity

The reactions presented in the manuscript were performed with Me_3SiONa that was kept outside the glovebox for up to two weeks in a capped 20 mL vial, which was stored in a desiccator. We found that using dry Me_3SiONa was important for obtaining optimal results.



Entry	Conditions	Yield (3a)*	Alkene (2a) left*
1	Dry base + new silane	76%	0%
2	Dry base + old silane	78%	0%
3	Wet base + old silane	0%	98%
4	Wet base + old silane (3.9 equiv.)	0%	98%
5	Dry base + old silane + H_2O (10 μL, 0.56 equiv)	65%	13%
6	Dry base + old silane + H_2O (20 μL, 1.1 equiv)	0%	86%

*Yields determined by GC analysis of the crude reaction mixture using tetradecane as an internal standard

Dry base:	The base was removed from a nitrogen filled glovebox before the reaction was set up.
Wet base:	The base was removed from a nitrogen filled glovebox and aged for 20 h on the bench top with no cap.
New silane:	The silane was stored in a nitrogen filled glovebox and removed before the reaction was set up.
Old silane:	The silane had been stored on the bench top for more than two months.

VIII. References

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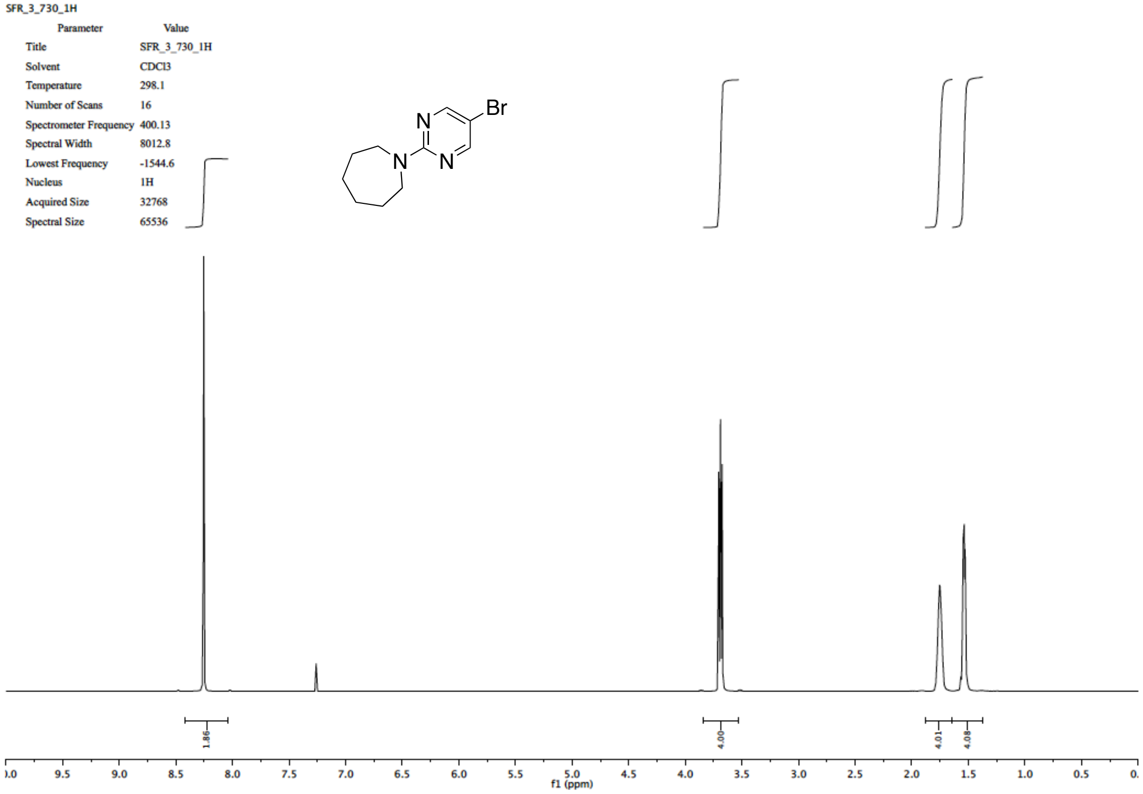
S2. Y. Yang, K. Niedermann, C. Han, S. L. Buchwald, *Org. Lett.* **2014**, *16*, 4638.
S3. G. A. Mirafzal, J. Liu, N. L. Bauld, *J. Am. Chem. Soc.*, **1993**, *115*, 6072.
S4. I. Kawasaki, I. Kusumoto, T. Kaneko, *Bull. Chem. Soc. Jpn.* **1971**, *44*, 2861.
S5. Y-P. Xiao, X-Y. Liu, C-M. Che, *J. Organomet. Chem.* **2009**, *694*, 494.
S6. S. Bhadra, W. I. Dzik, L. J. Goossen, *Angew. Chem. Int. Ed.* **2013**, *125*, 3031.

IX. NMR spectra and HPLC chromatograms

1-(5-bromopyrimidin-2-yl)azepane (1l)


SFR_3_730_1H

Parameter	Value
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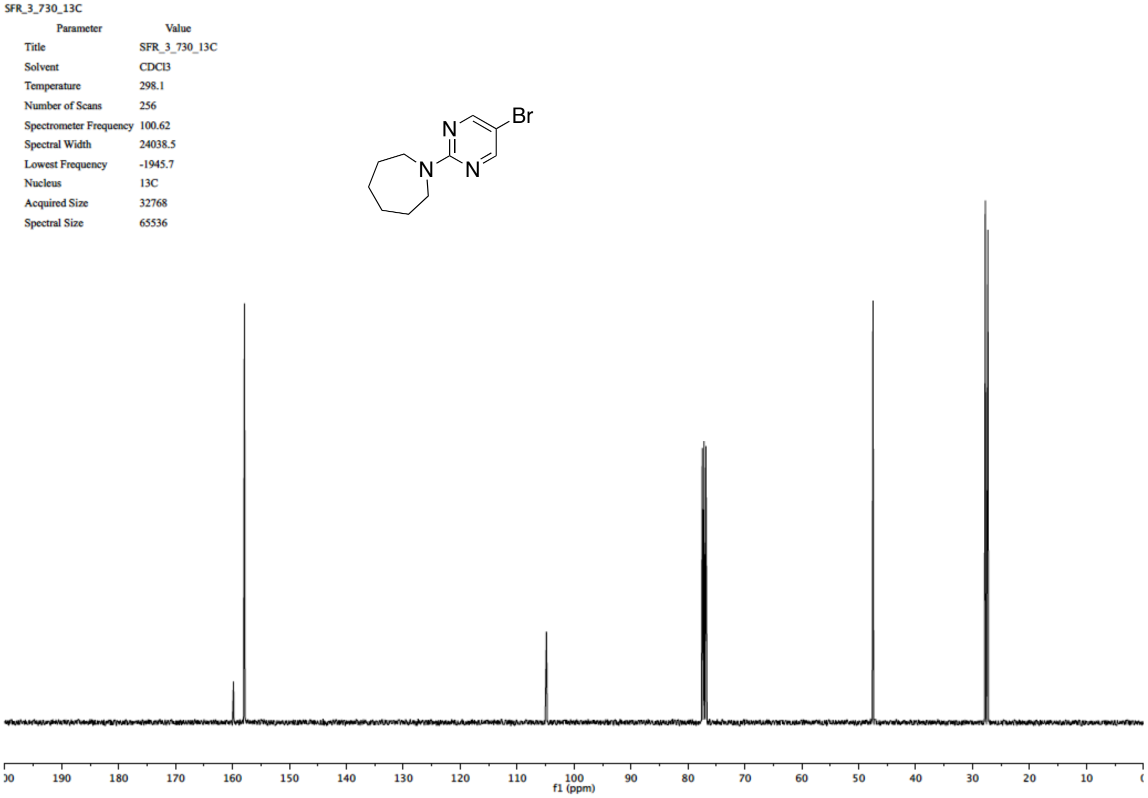
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


SFR_3_730_13C

Parameter	Value
Title	SFR_3_730_13C
Solvent	CDCl3
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Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
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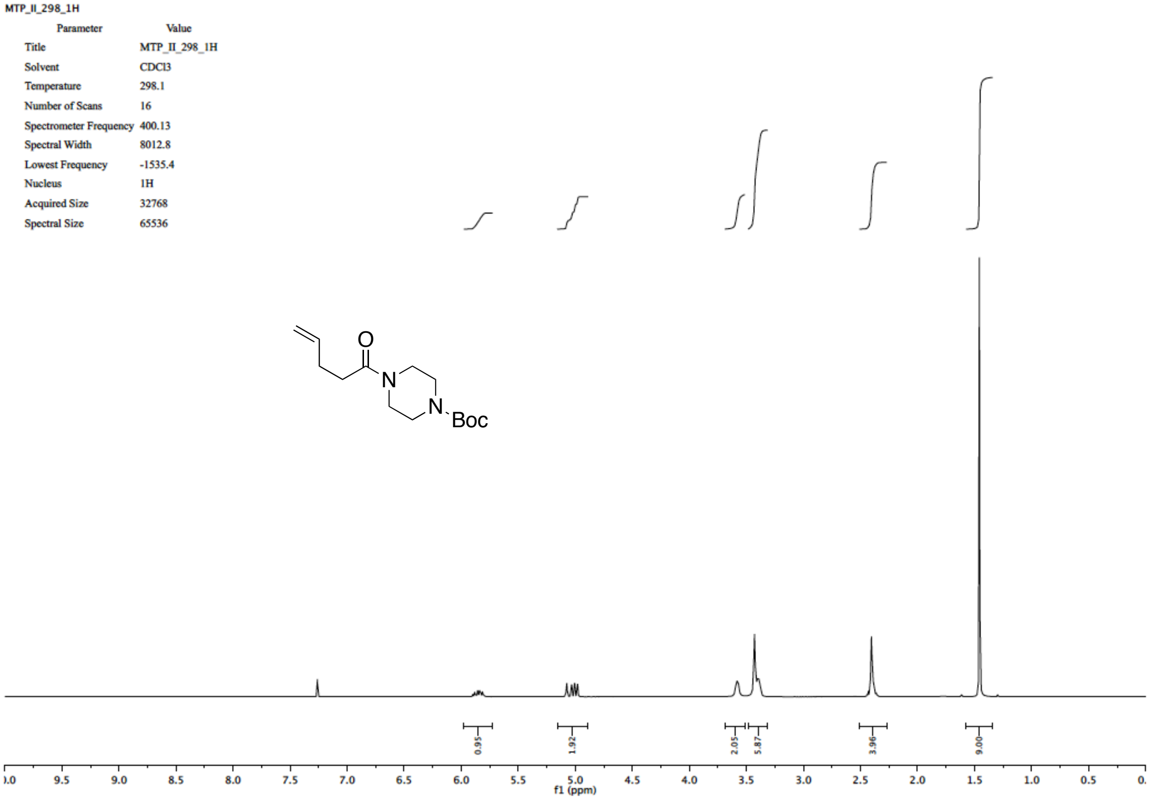
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

tert-butyl 4-(pent-4-enoyl)piperazine-1-carboxylate (2c)



MTP_II_298_1H

Parameter	Value
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Temperature	298.1
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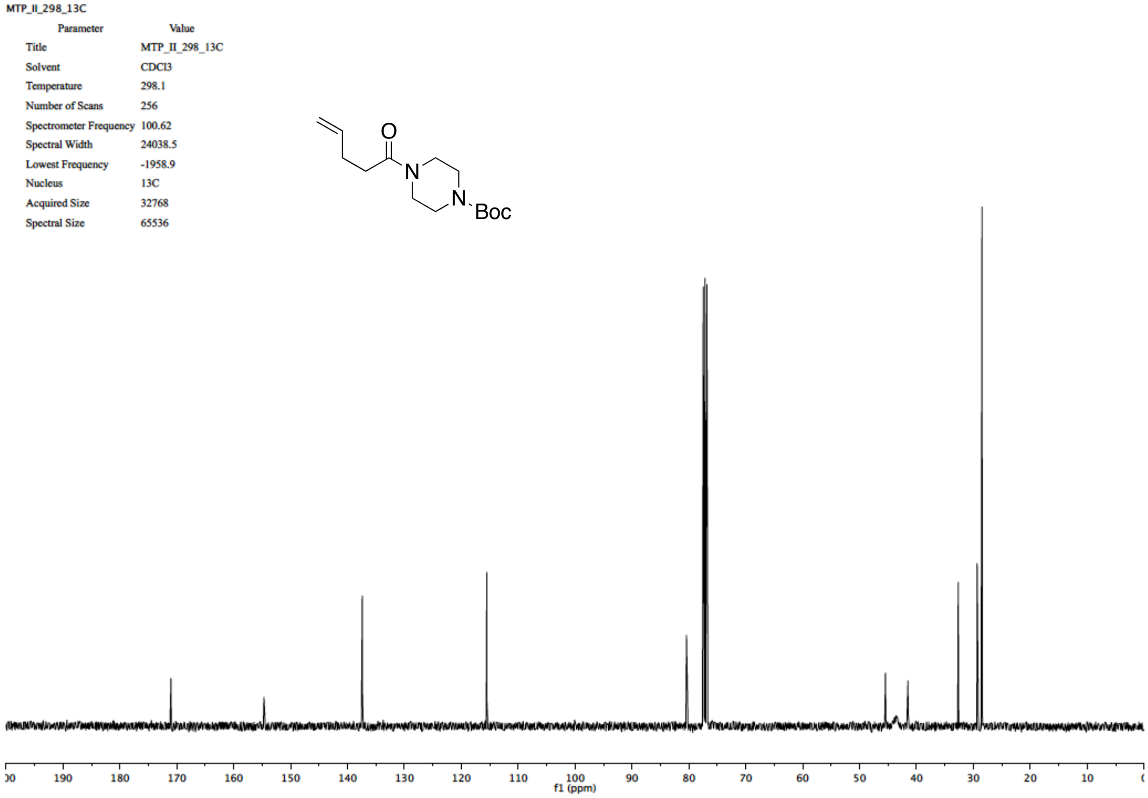
Spectral Width	8012.8
Lowest Frequency	-1535.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



MTP_II_298_13C

Parameter	Value
Title	MTP_II_298_13C
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Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
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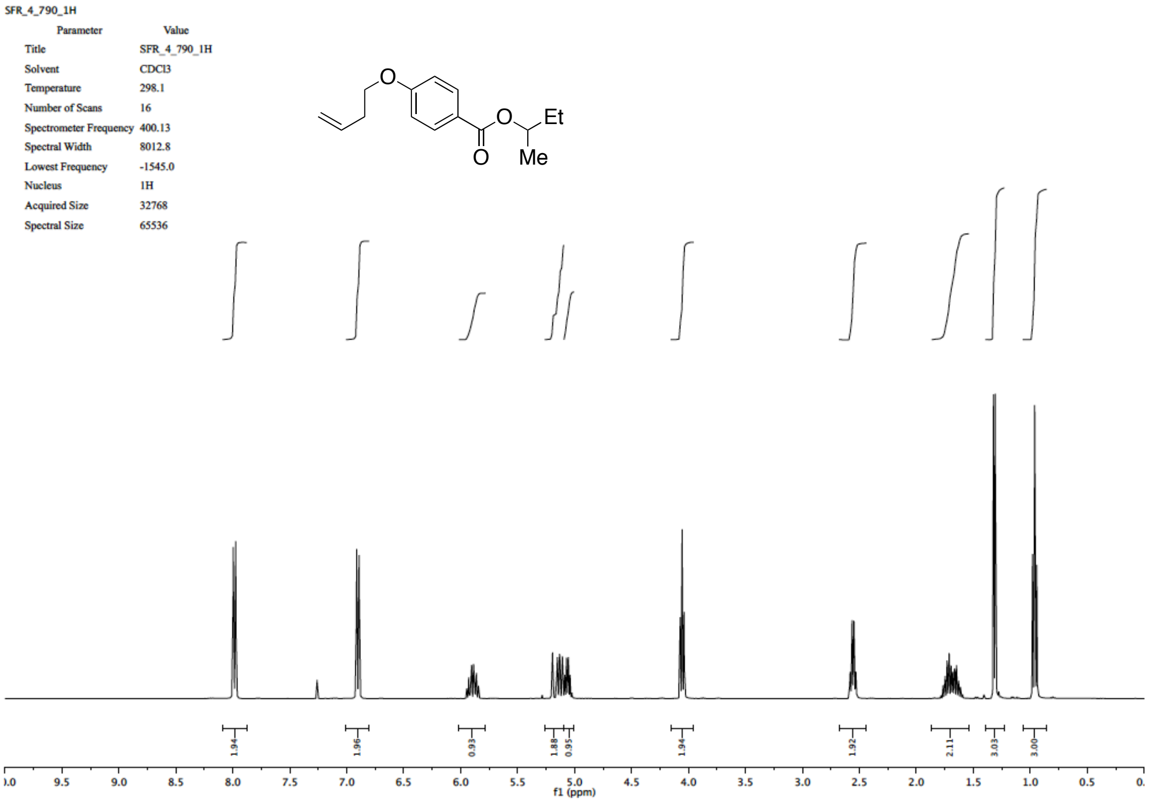
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

***sec*-butyl 4-(but-3-en-1-yloxy)benzoate (2e)**



SFR_4_790_1H

Parameter	Value
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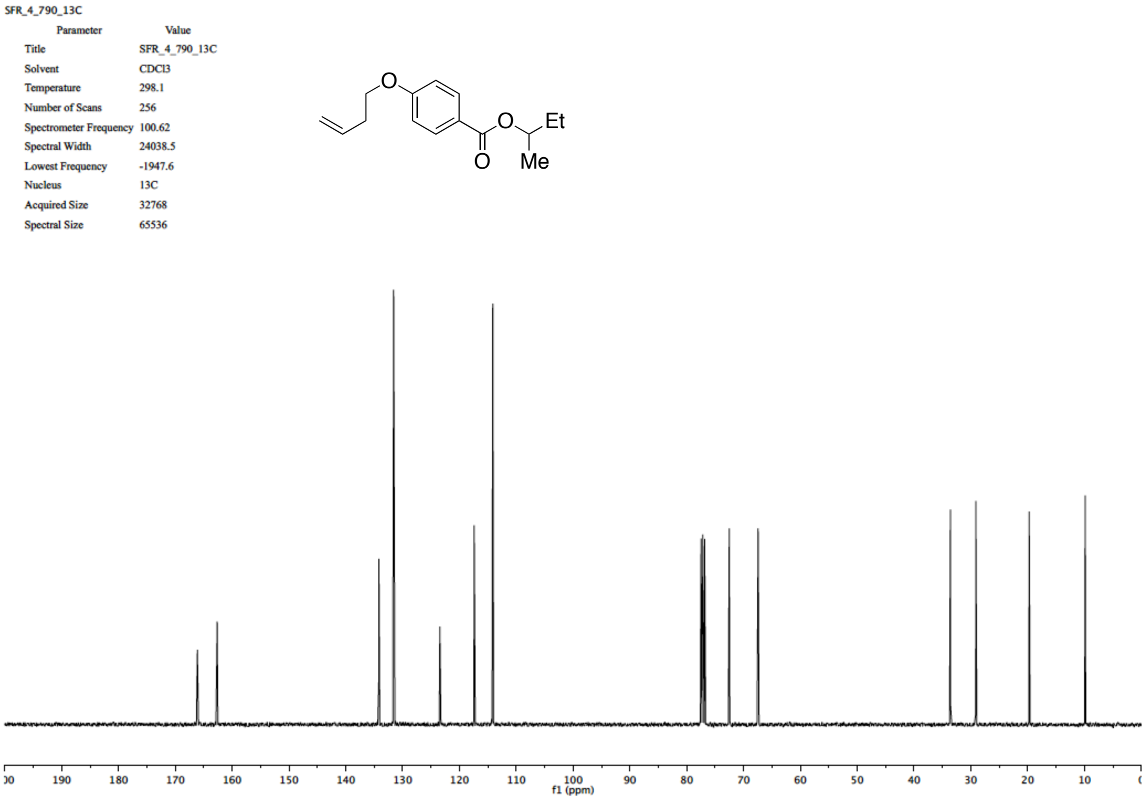
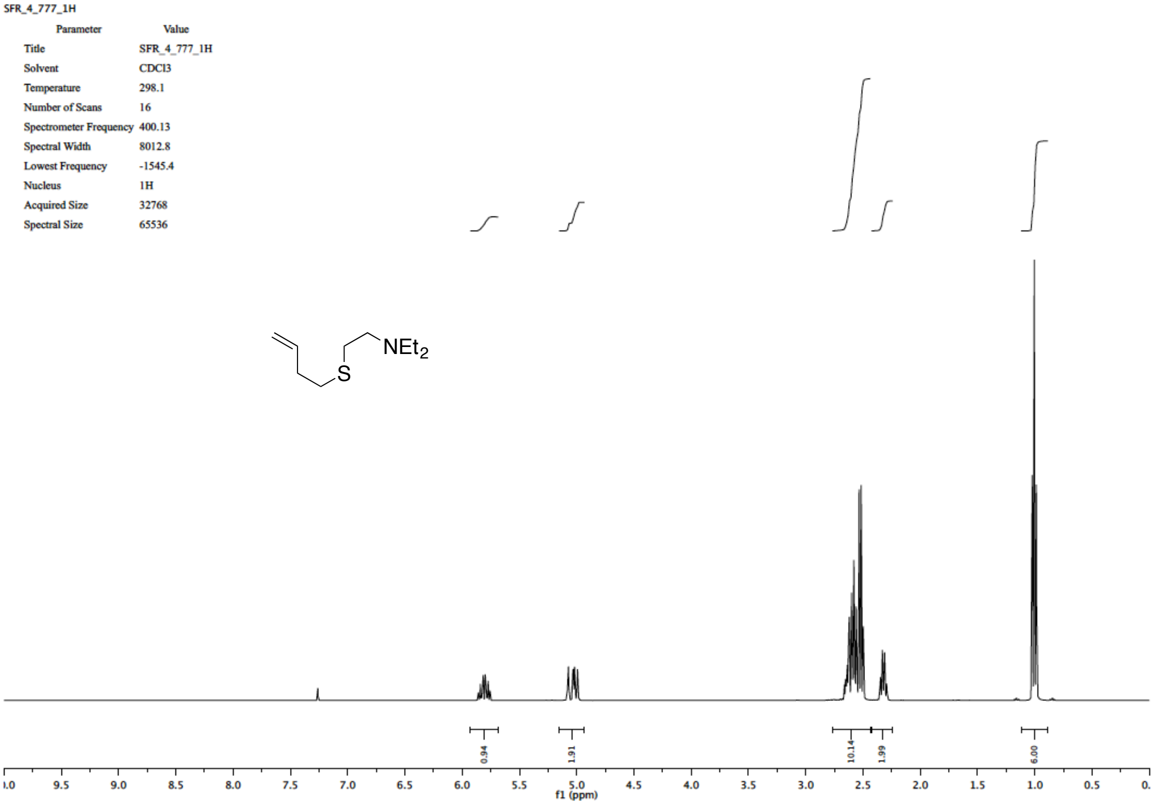
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



SFR_4_790_13C

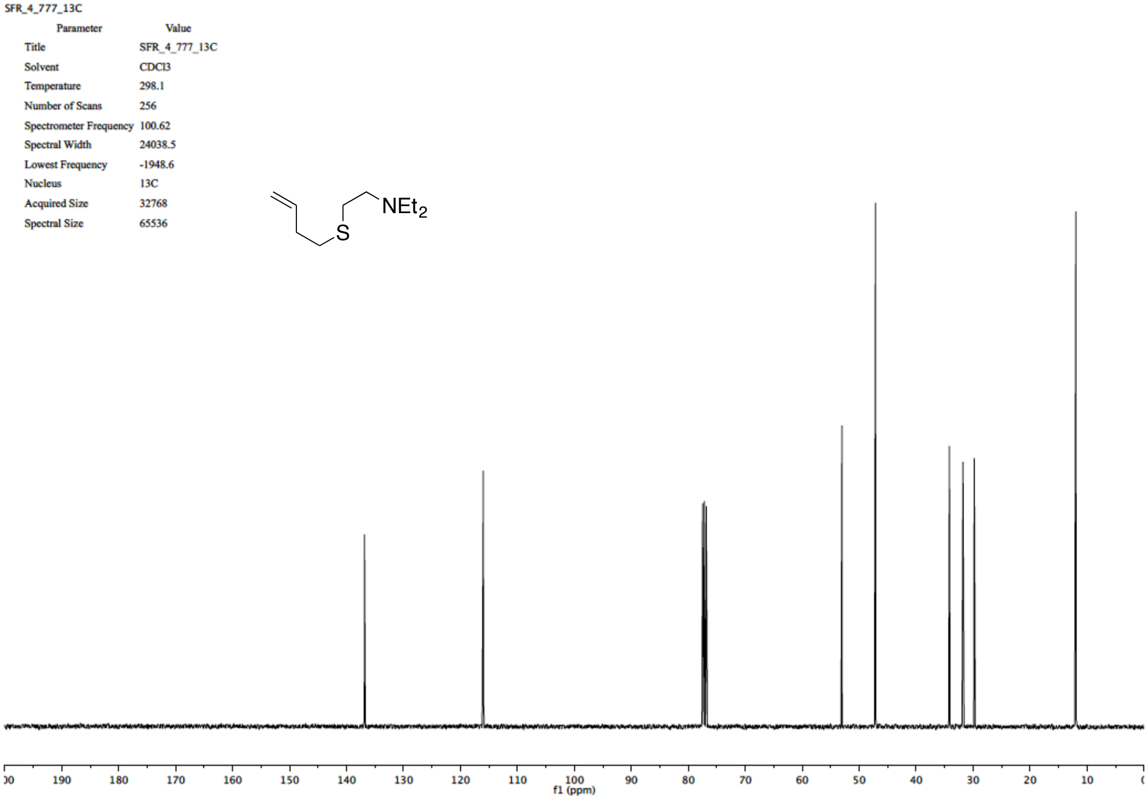
Parameter	Value
Title	SFR_4_790_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1947.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

2-(but-3-en-1-ylthio)-*N*,*N*-diethylethan-1-amine (2g)



SFR_4_777_1H

Parameter	Value
Title	SFR_4_777_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



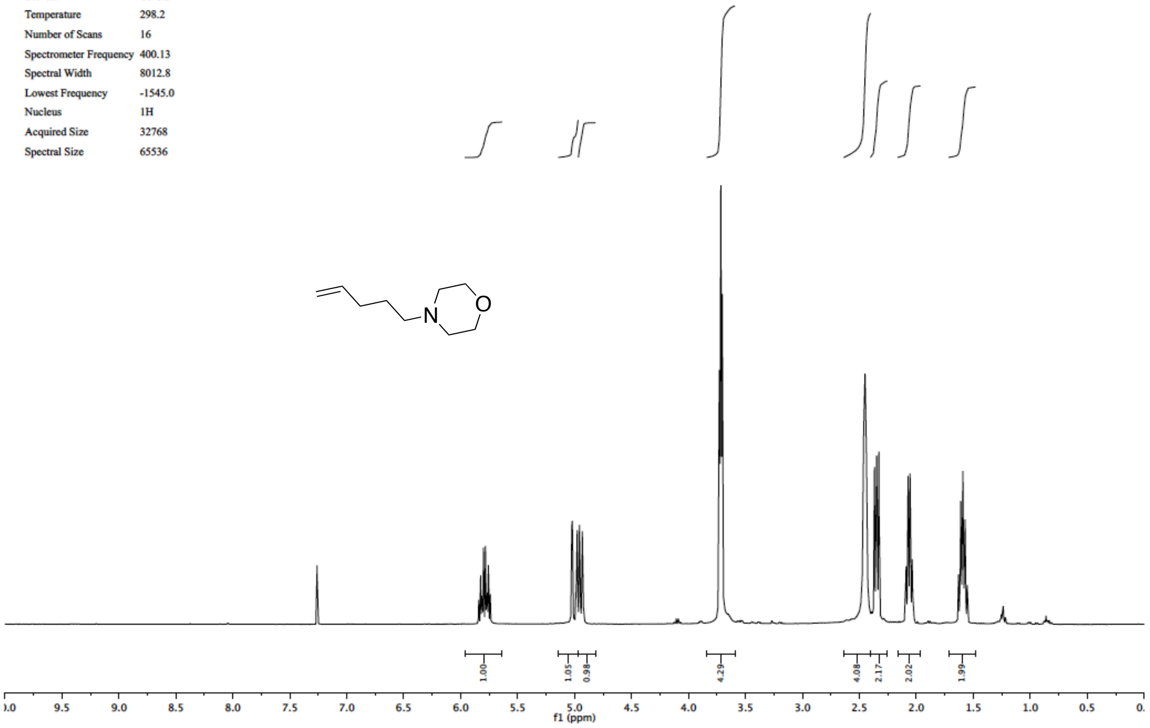
SFR_4_777_13C

Parameter	Value
Title	SFR_4_777_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1948.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

4-(pent-4-en-1-yl)morpholine (2h)

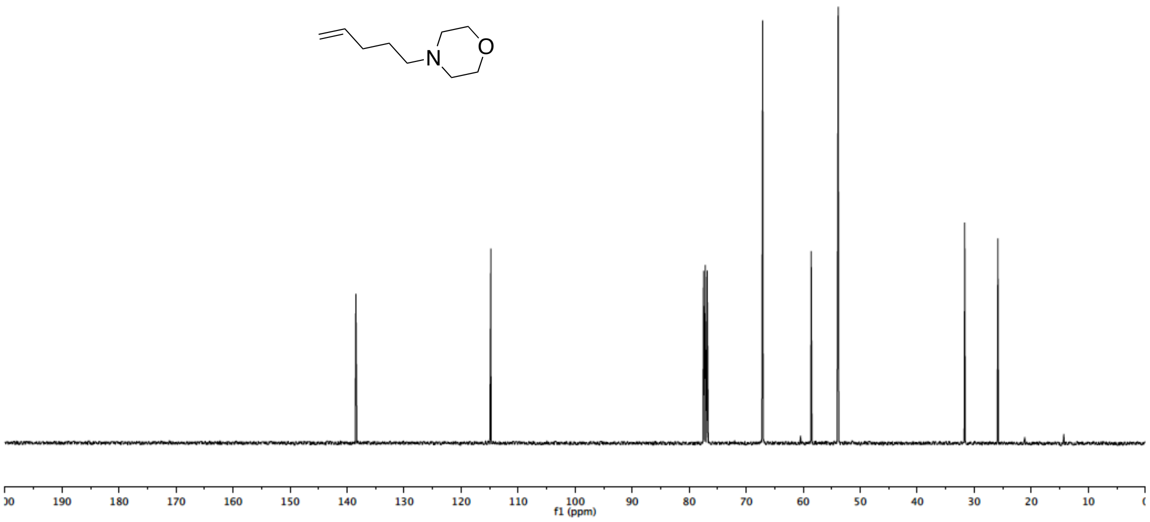
MTP_III_58A_1H

Parameter	Value
Title	MTP_III_58A_1H
Solvent	CDCl3
Temperature	298.2
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



MTP_III_58A_13C

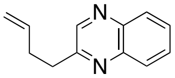
Parameter	Value
Title	MTP_III_58A_13C
Solvent	CDCl3
Temperature	298.2
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1947.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

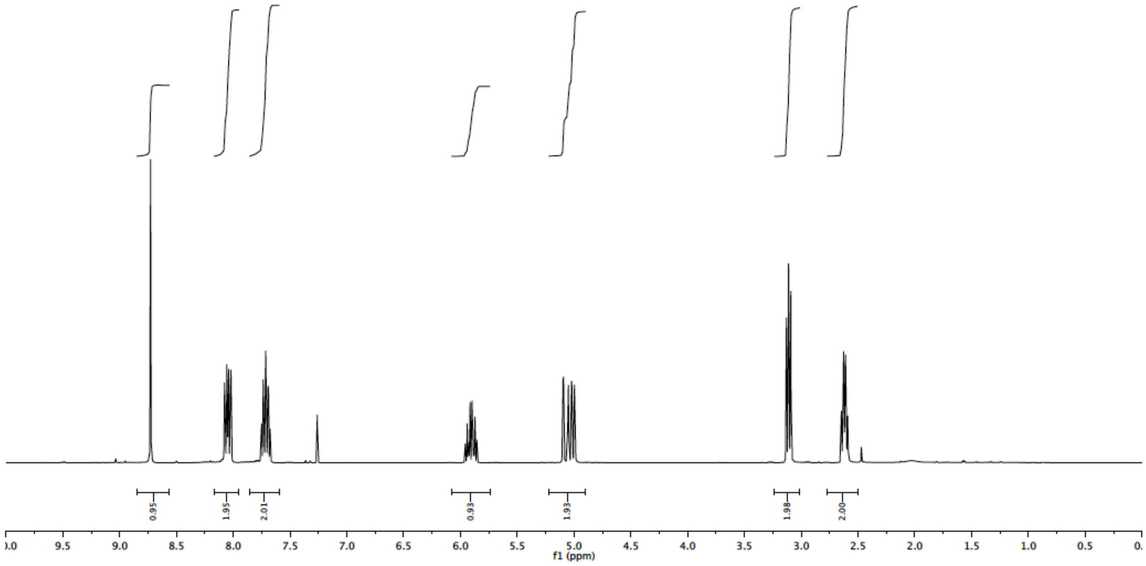


2-(but-3-en-1-yl)quinoxaline (2i)

SFR_4_787_1H

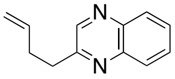
Parameter	Value
Title	SFR_4_787_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

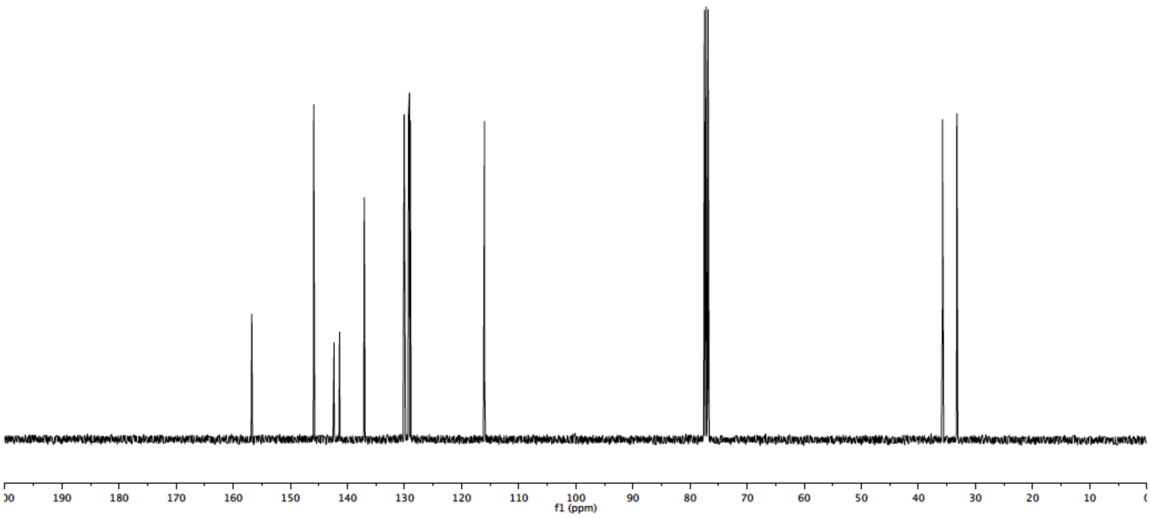




SFR_4_787_13C

Parameter	Value
Title	SFR_4_787_13C
Solvent	CDCl3
Temperature	298.2
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1946.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

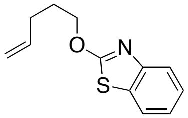


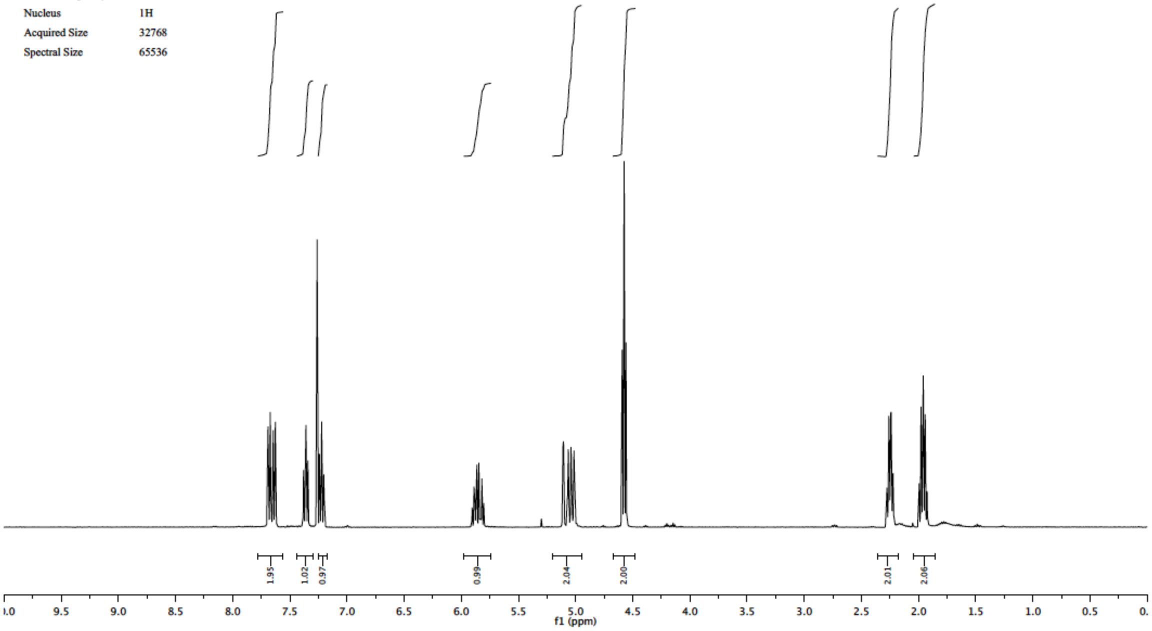


2-(pent-4-en-1-yloxy)benzo[*d*]thiazole (2j)

SFR_3_743_1H

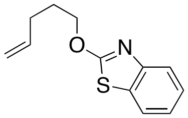
Parameter	Value
Title	SFR_3_743_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

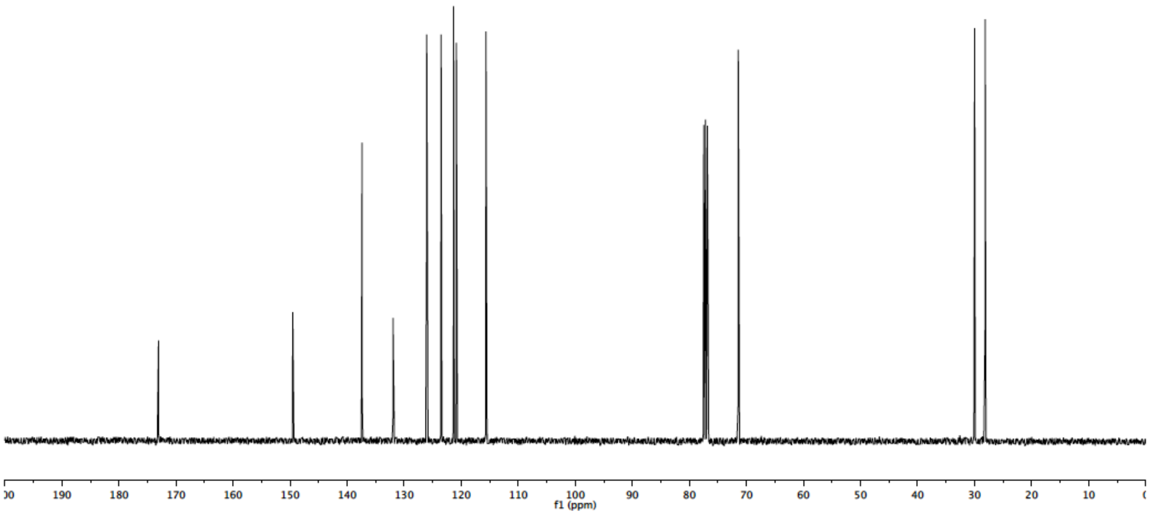




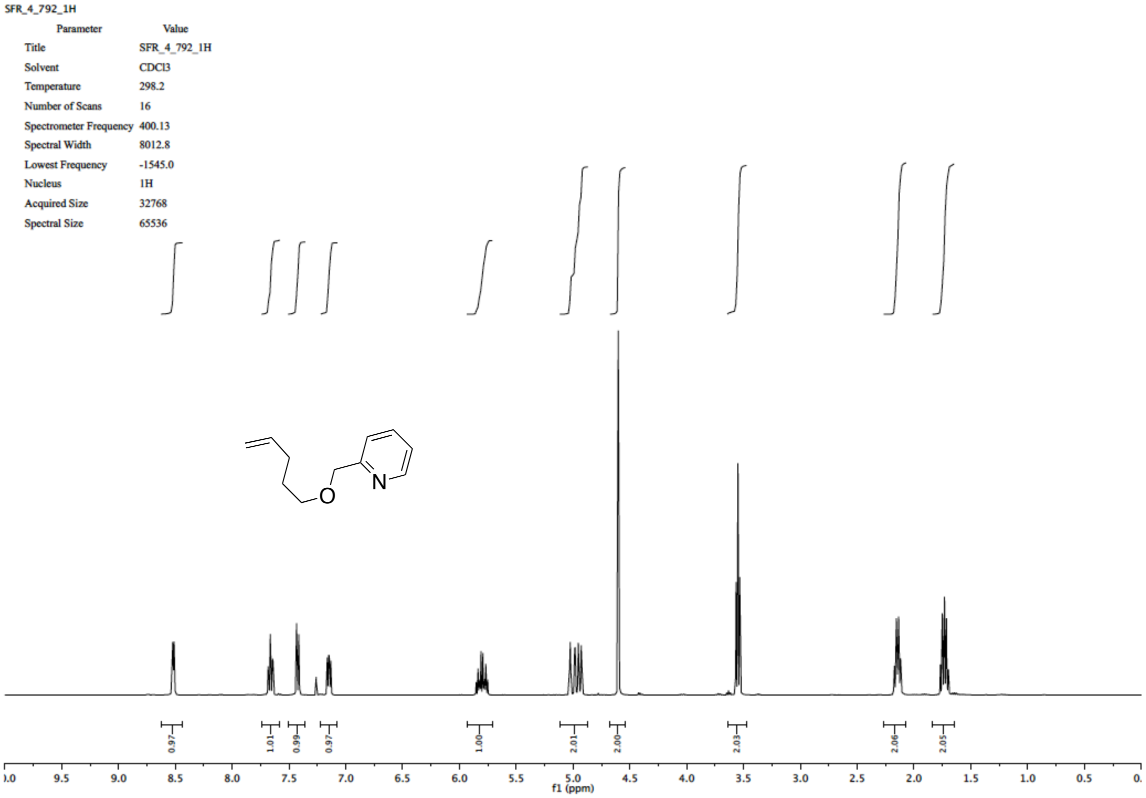
SFR_3_743_13C

Parameter	Value
Title	SFR_3_743_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1949.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



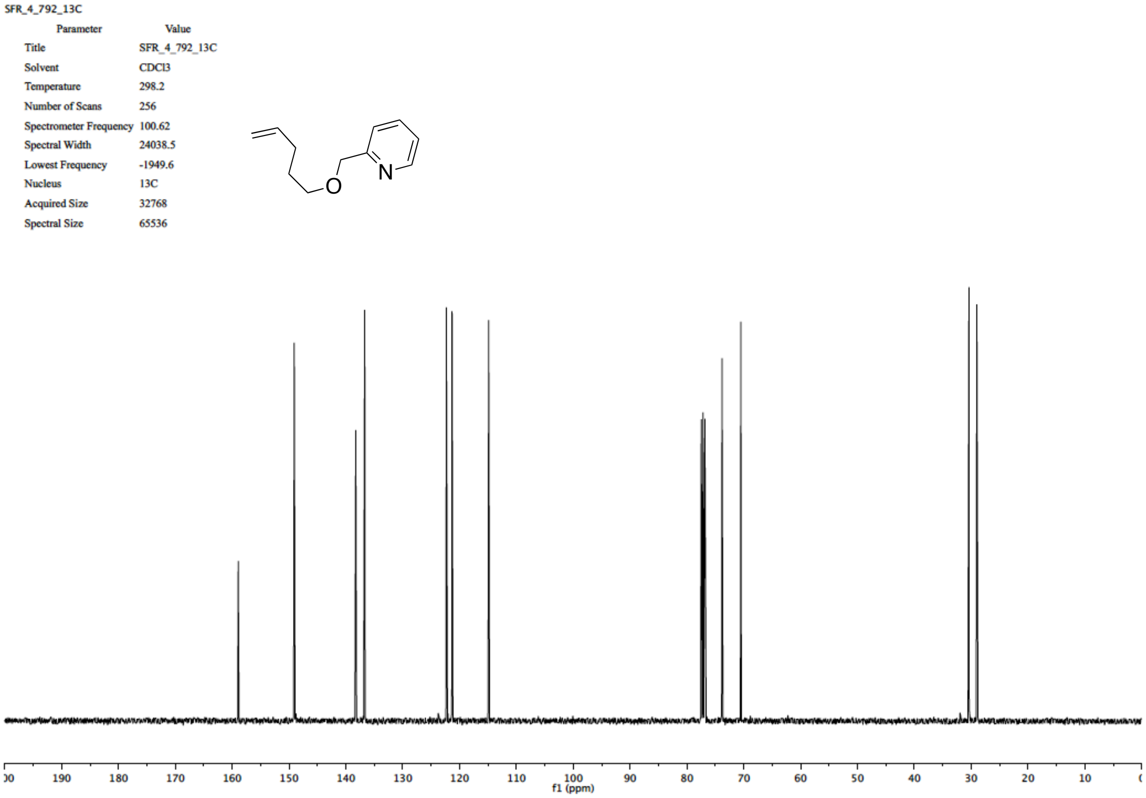


2-((pent-4-en-1-yloxy)methyl)pyridine (2k)



SFR_4_792_1H

Parameter	Value
Title	SFR_4_792_1H
Solvent	CDCl3
Temperature	298.2
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



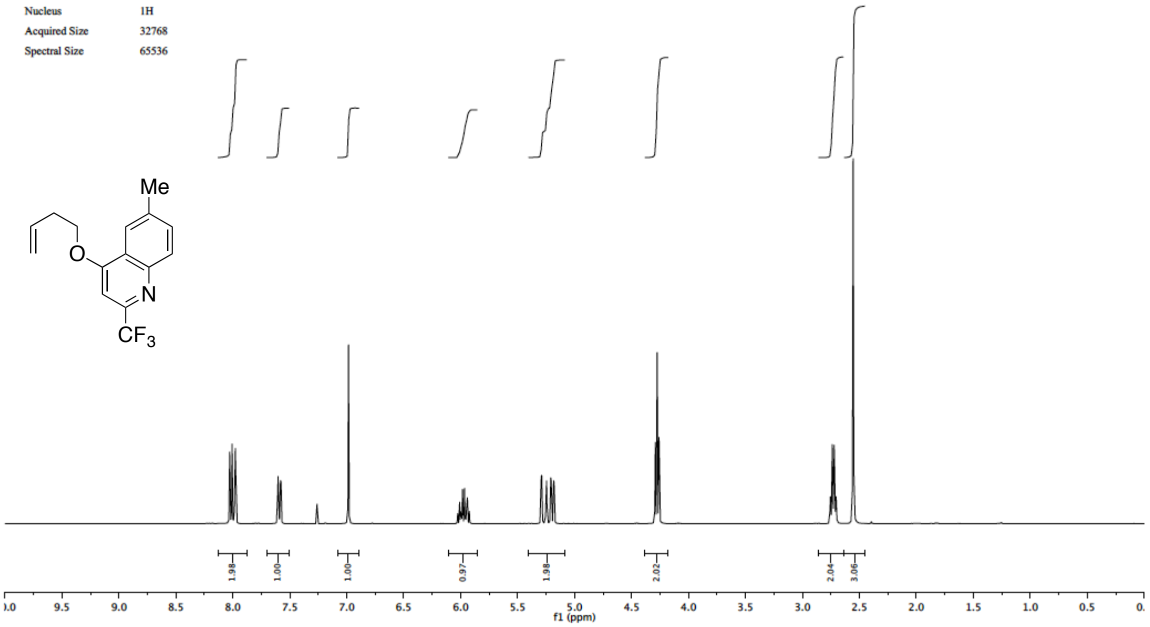
SFR_4_792_13C

Parameter	Value
Title	SFR_4_792_13C
Solvent	CDCl3
Temperature	298.2
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1949.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

4-(but-3-en-1-yloxy)-6-methyl-2-(trifluoromethyl)quinoline (2n)

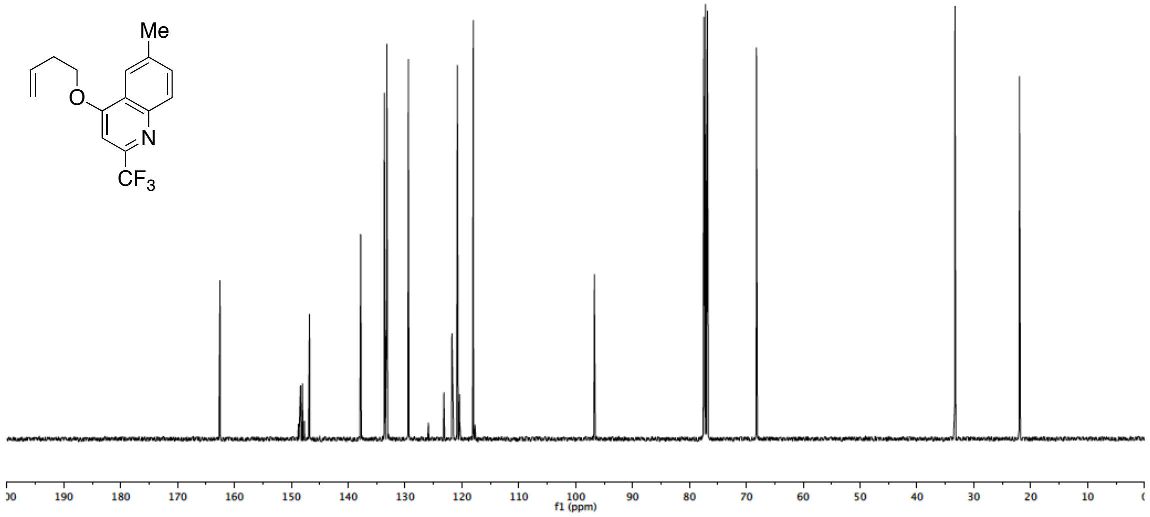
SFR_4_789_1H

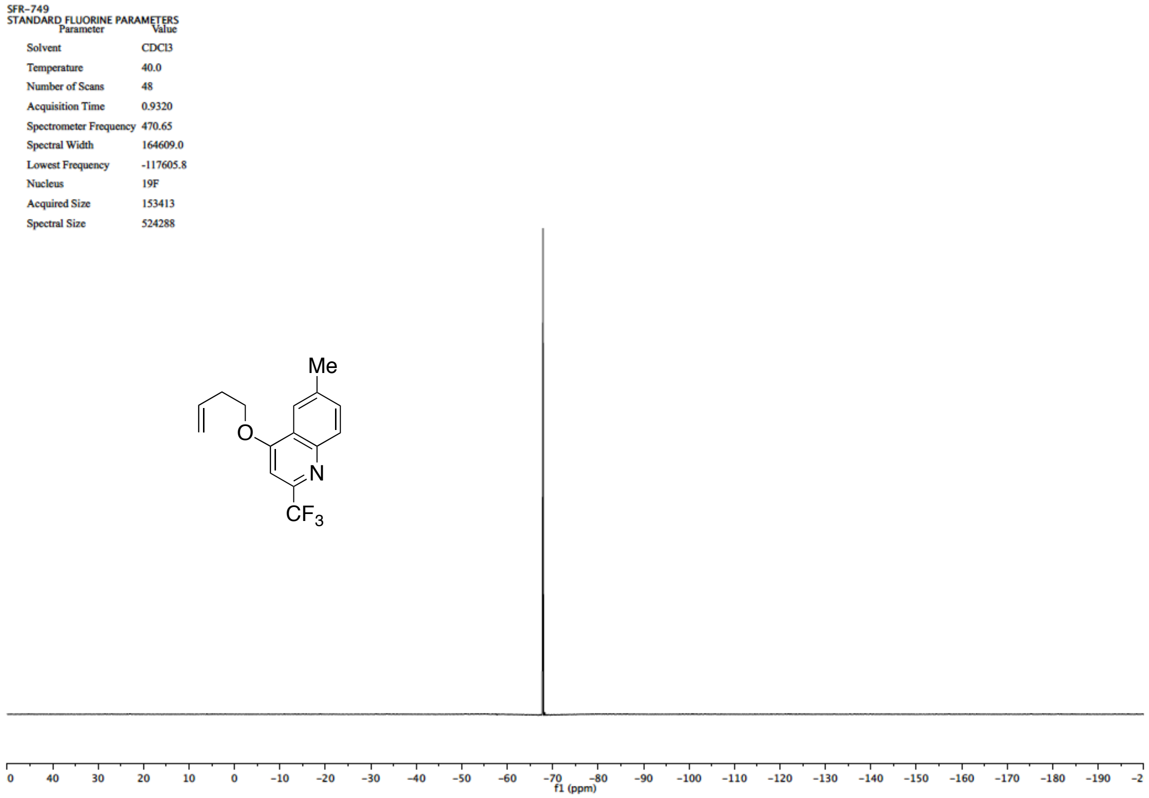
Parameter	Value
Title	SFR_4_789_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



SFR_4_789_13C

Parameter	Value
Title	SFR_4_789_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	1024
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1946.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

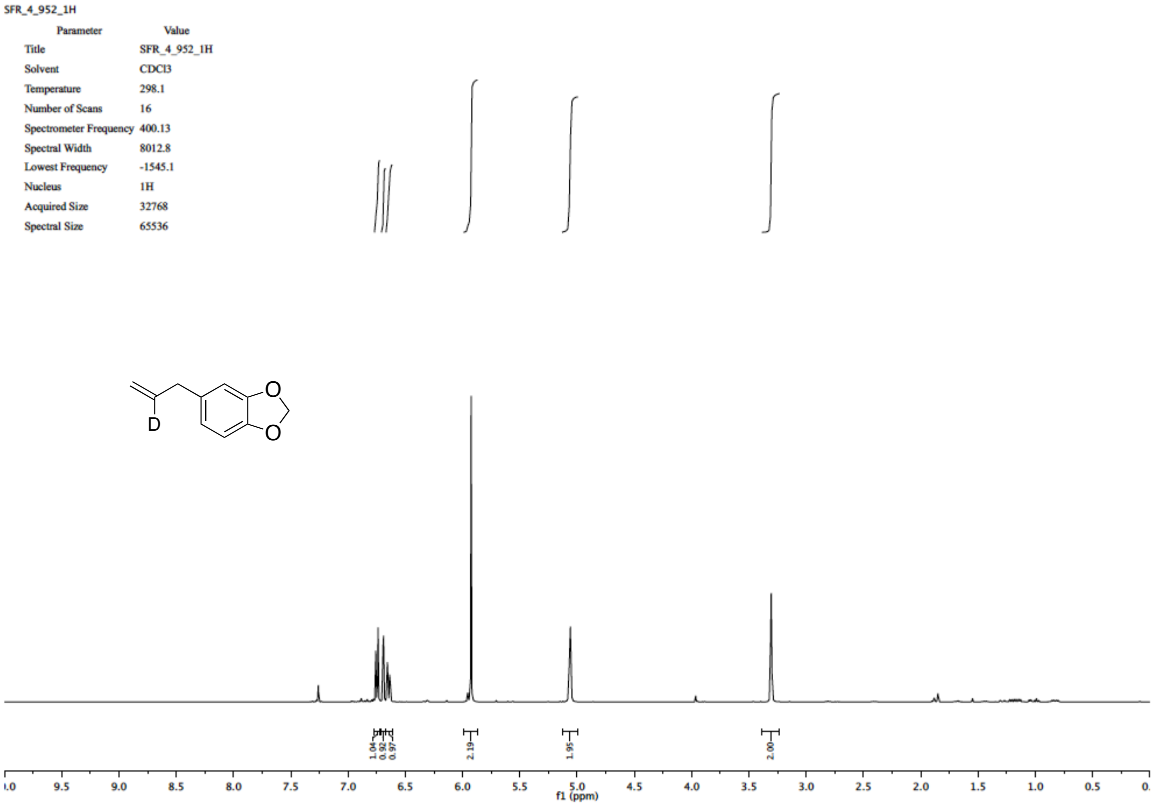




SFR-749
STANDARD FLUORINE PARAMETERS

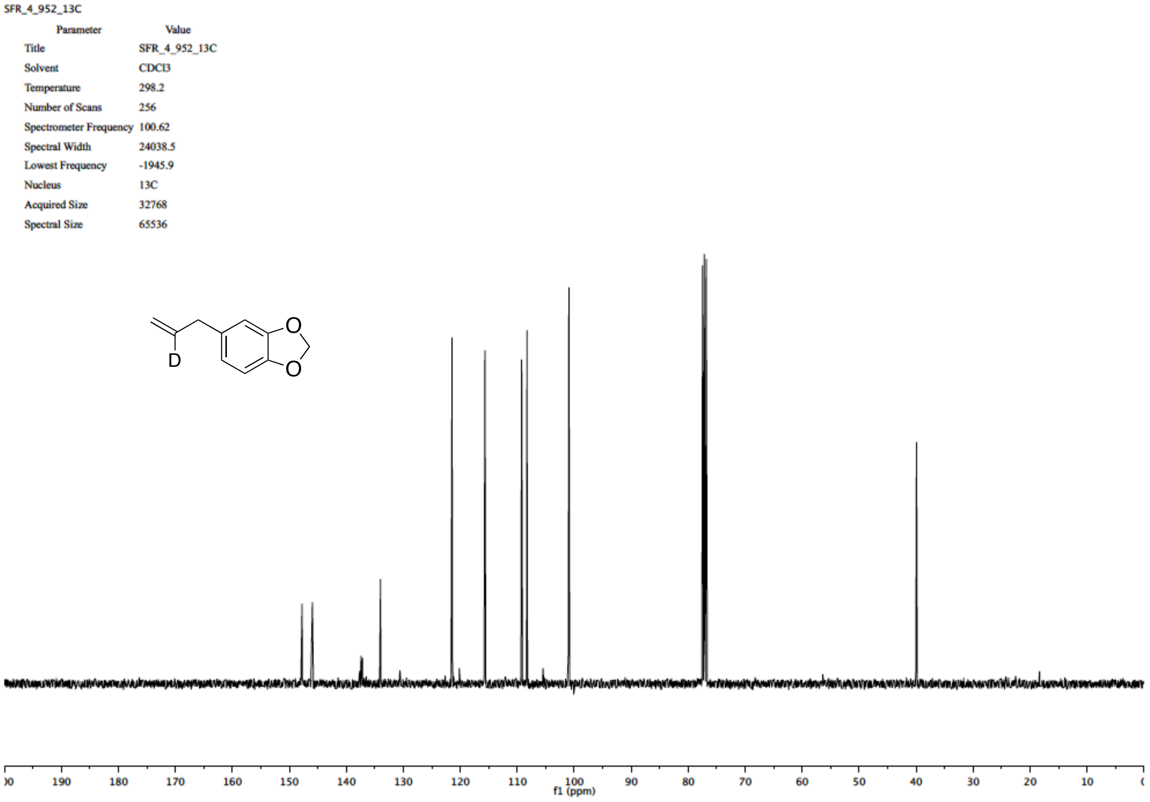
Parameter	Value
Solvent	CDCl3
Temperature	40.0
Number of Scans	48
Acquisition Time	0.9320
Spectrometer Frequency	470.65
Spectral Width	164609.0
Lowest Frequency	-117605.8
Nucleus	19F
Acquired Size	153413
Spectral Size	524288

5-(Allyl-2-*d*)benzo[*d*][1,3]dioxole (d_1-2b)



SFR_4_952_1H

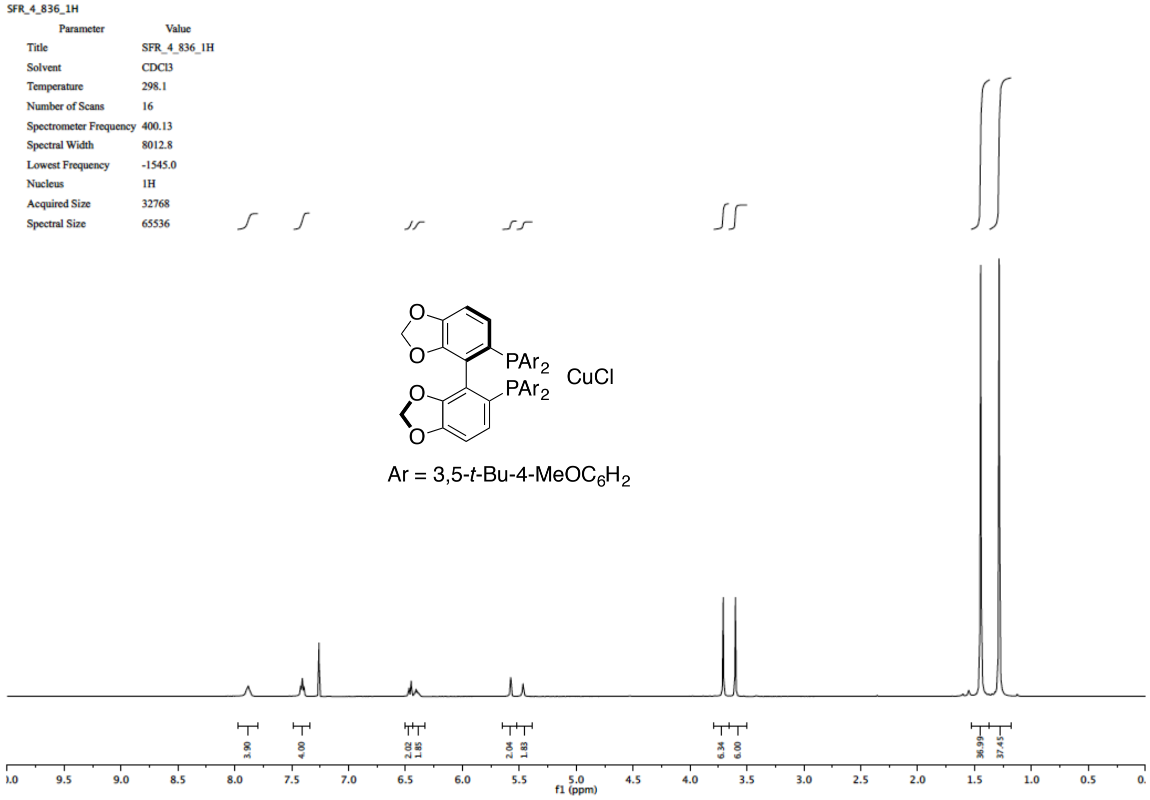
Parameter	Value
Title	SFR_4_952_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



SFR_4_952_13C

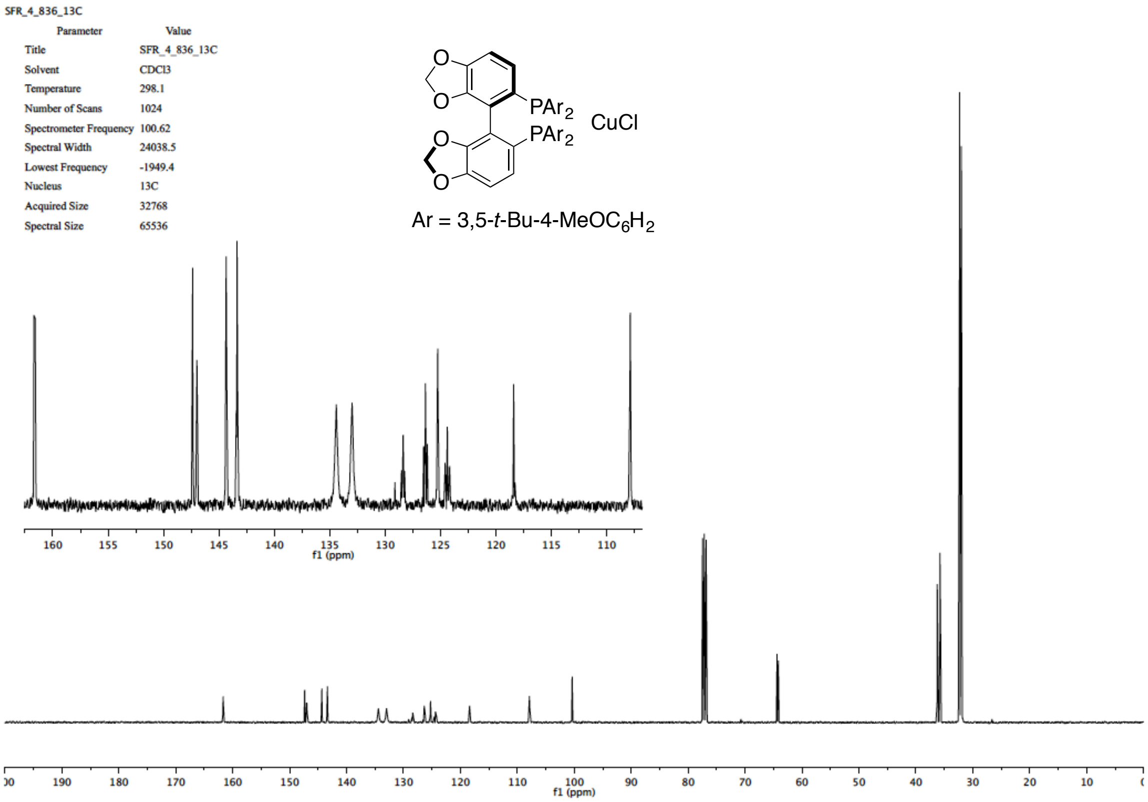
Parameter	Value
Title	SFR_4_952_13C
Solvent	CDCl3
Temperature	298.2
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1945.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

CuCl-[(*R*)-DTBM-SEGPHOS] (P1)



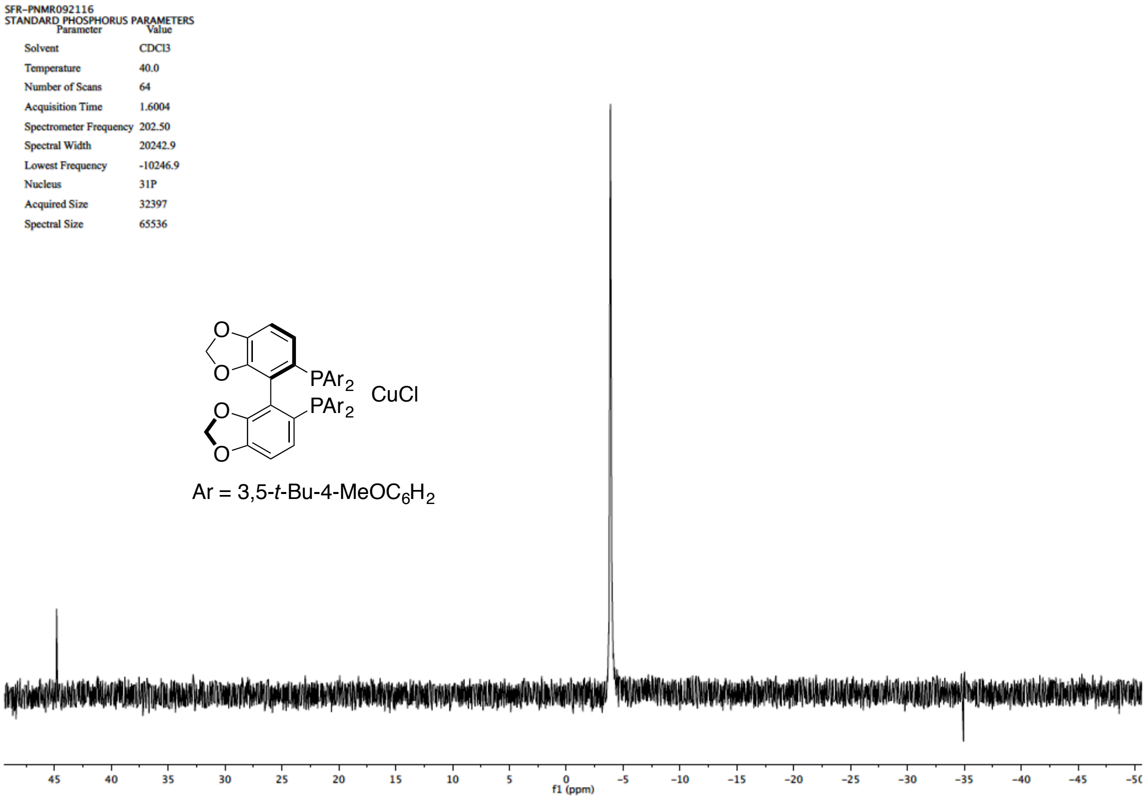
SFR_4_836_1H

Parameter	Value
Title	SFR_4_836_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



SFR_4_836_13C

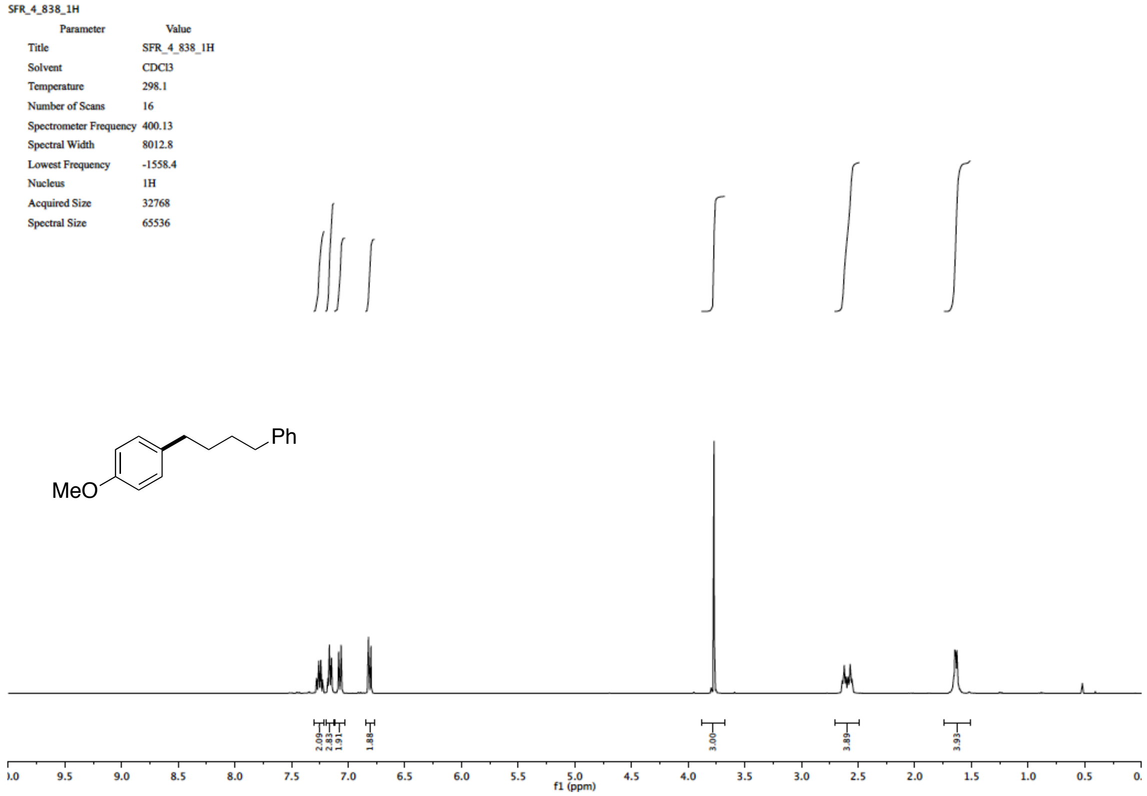
Parameter	Value
Title	SFR_4_836_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	1024
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1949.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



SFR-PNMR092116
STANDARD PHOSPHORUS PARAMETERS

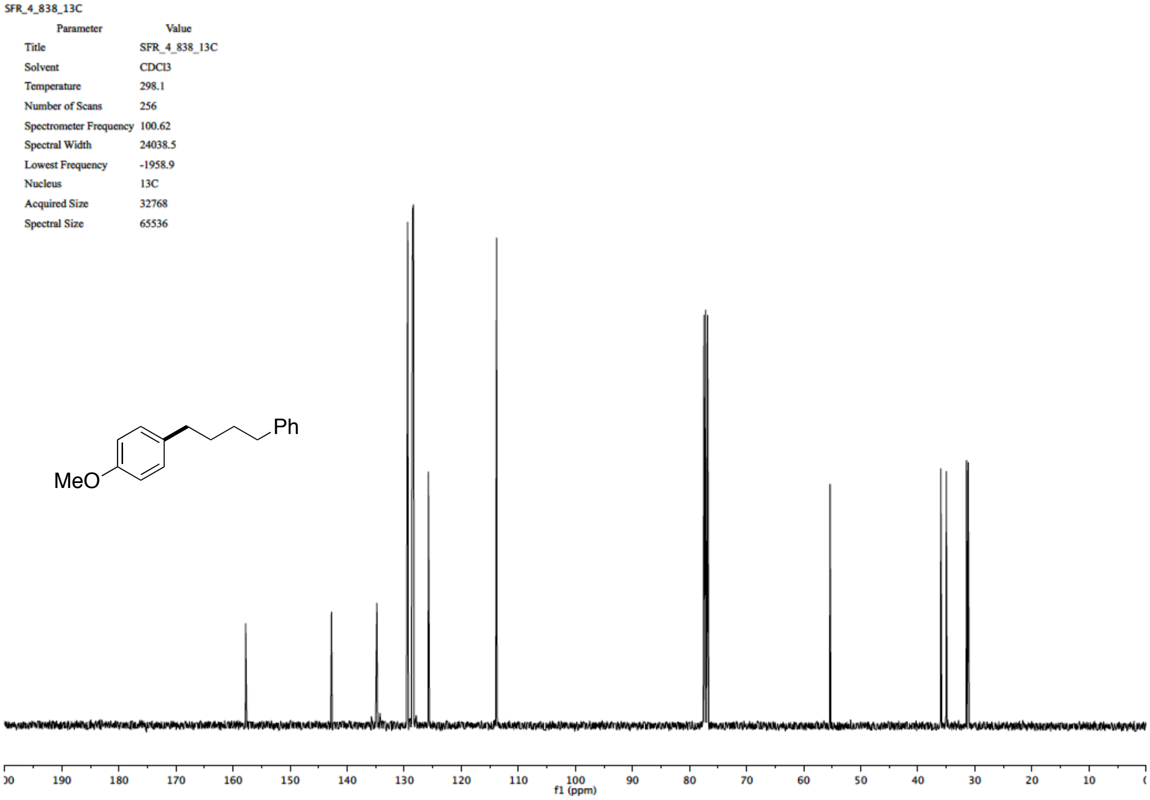
Parameter	Value
Solvent	CDCl3
Temperature	40.0
Number of Scans	64
Acquisition Time	1.6004
Spectrometer Frequency	202.50
Spectral Width	20242.9
Lowest Frequency	-10246.9
Nucleus	31P
Acquired Size	32397
Spectral Size	65536

1-Methoxy-4-(4-phenylbutyl)benzene (3a)



SFR_4_838_1H

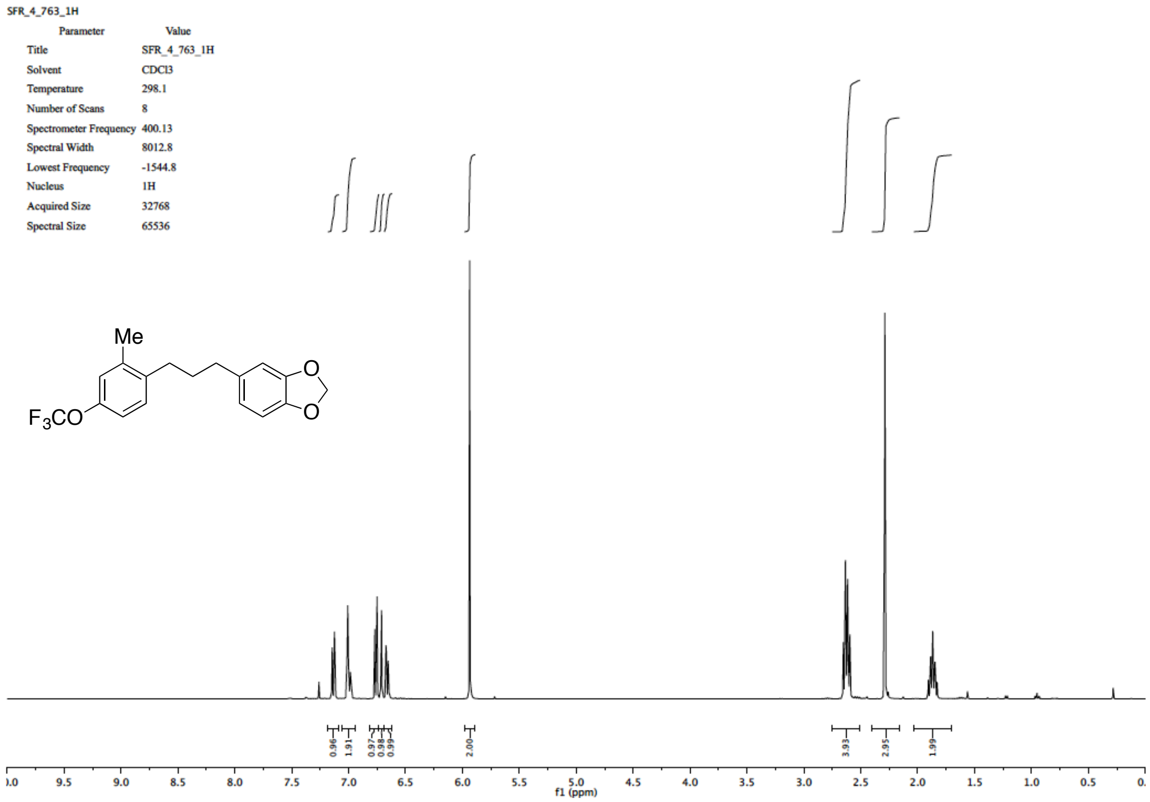
Parameter	Value
Title	SFR_4_838_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1558.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



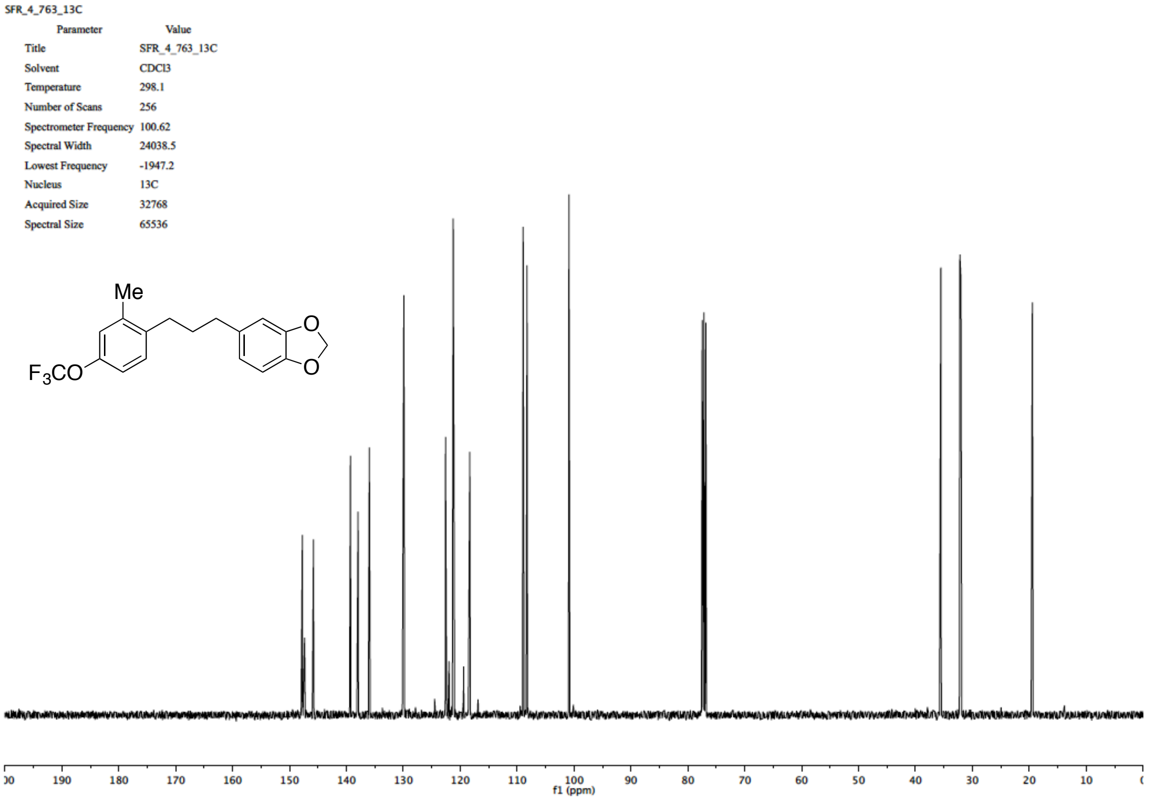
SFR_4_838_13C

Parameter	Value
Title	SFR_4_838_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1958.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

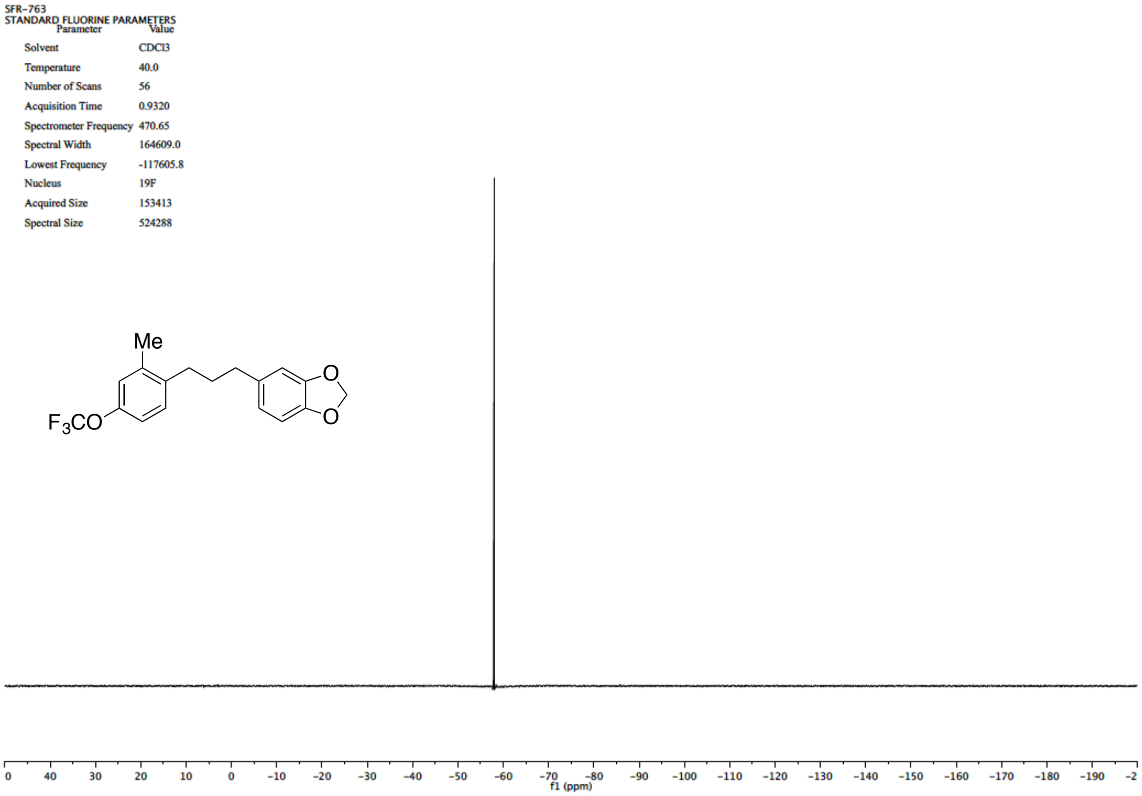
5-(3-(2-Methyl-4-(trifluoromethoxy)phenyl)propyl)benzo[*d*][1,3]dioxole (3b)


SFR_4_763_1H

Parameter	Value
Title	SFR_4_763_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	8
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.8
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


SFR_4_763_13C

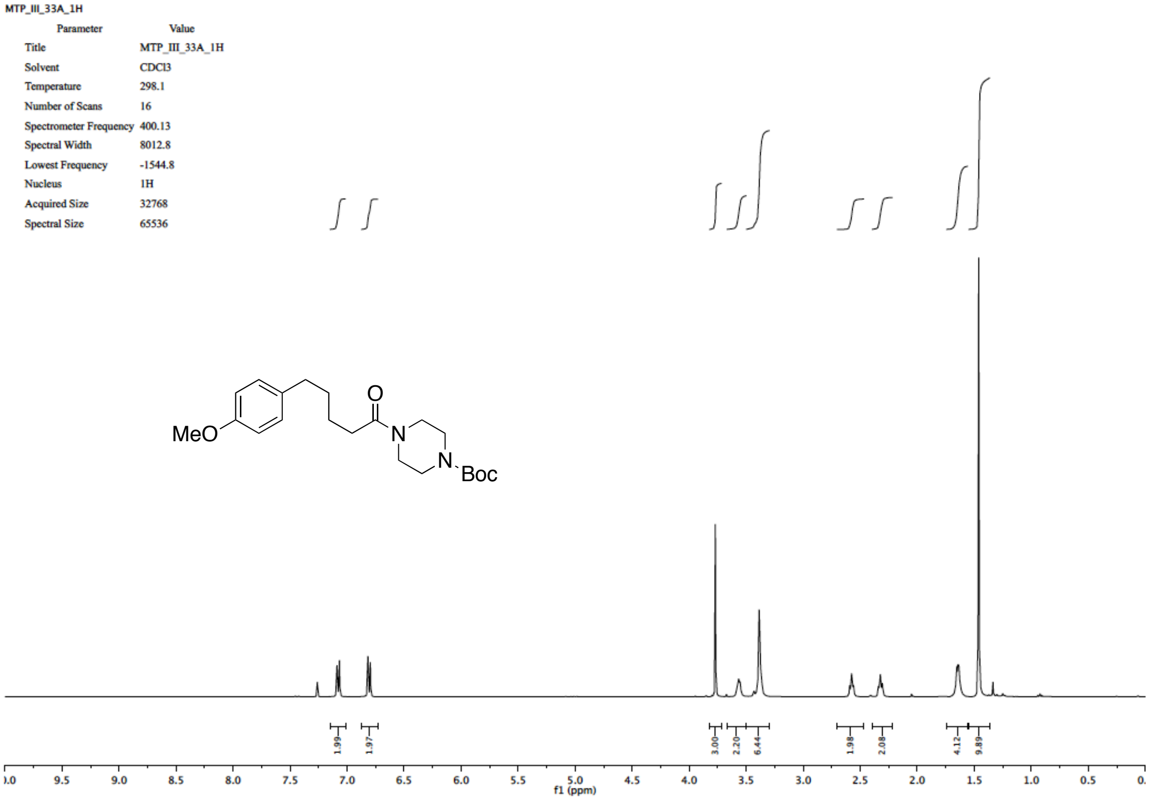
Parameter	Value
Title	SFR_4_763_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1947.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



SFR-763
STANDARD FLUORINE PARAMETERS

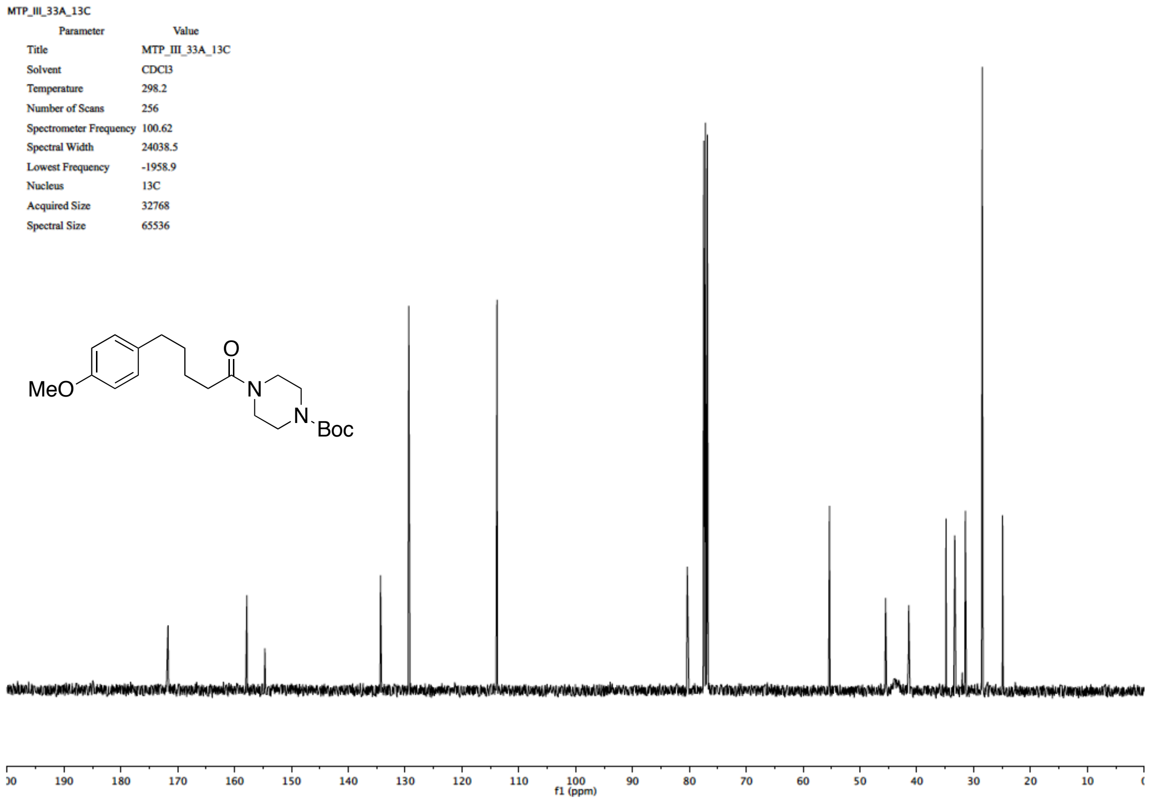
Parameter	Value
Solvent	CDCl3
Temperature	40.0
Number of Scans	56
Acquisition Time	0.9320
Spectrometer Frequency	470.65
Spectral Width	164609.0
Lowest Frequency	-117605.8
Nucleus	19F
Acquired Size	153413
Spectral Size	524288

tert-Butyl 4-(5-(4-methoxyphenyl)pentanoyl)piperazine-1-carboxylate (3c)



MTP_III_33A_1H

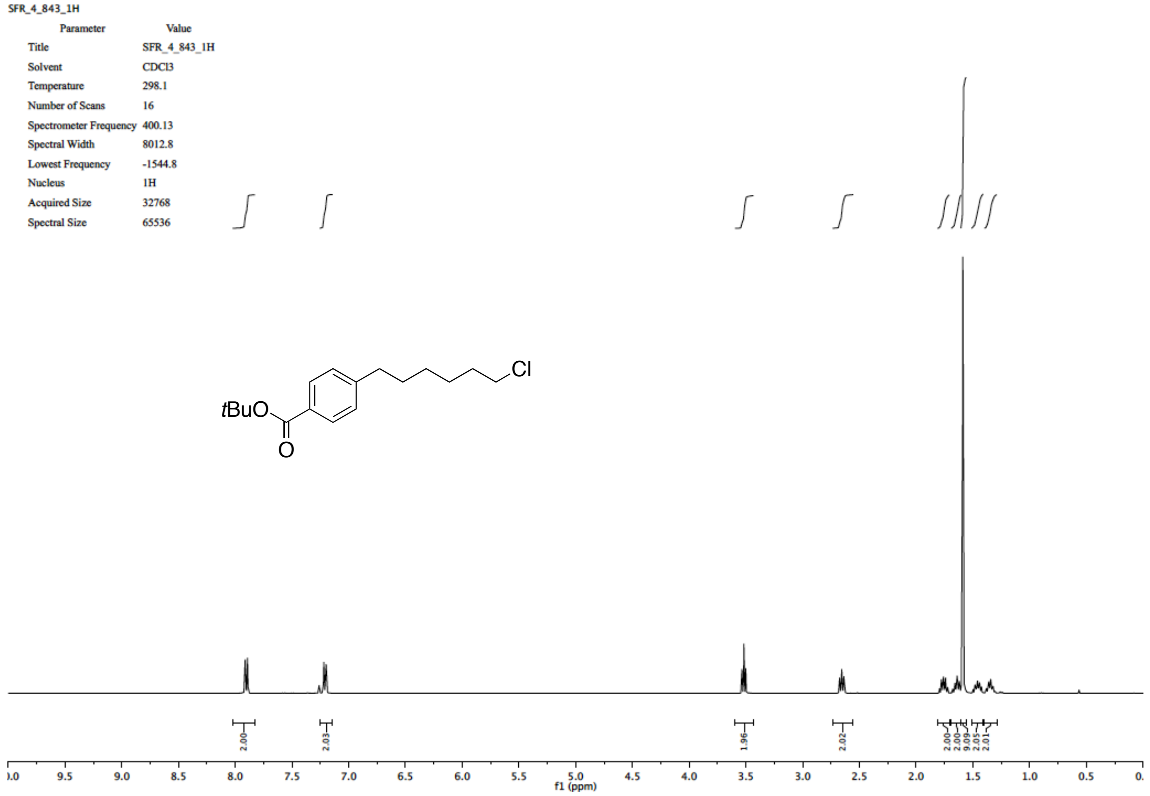
Parameter	Value
Title	MTP_III_33A_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.8
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



MTP_III_33A_13C

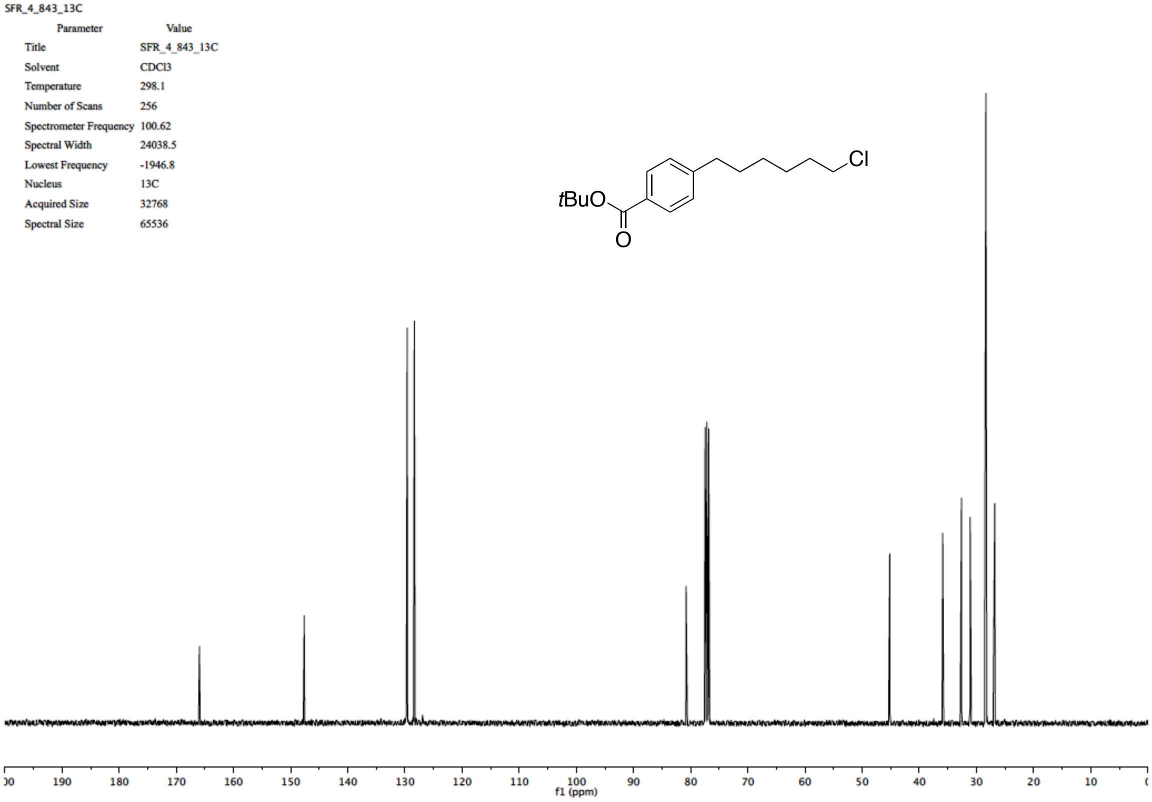
Parameter	Value
Title	MTP_III_33A_13C
Solvent	CDCl3
Temperature	298.2
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1958.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

tert-Butyl 4-(6-chlorohexyl)benzoate (3d)



SFR_4_843_1H

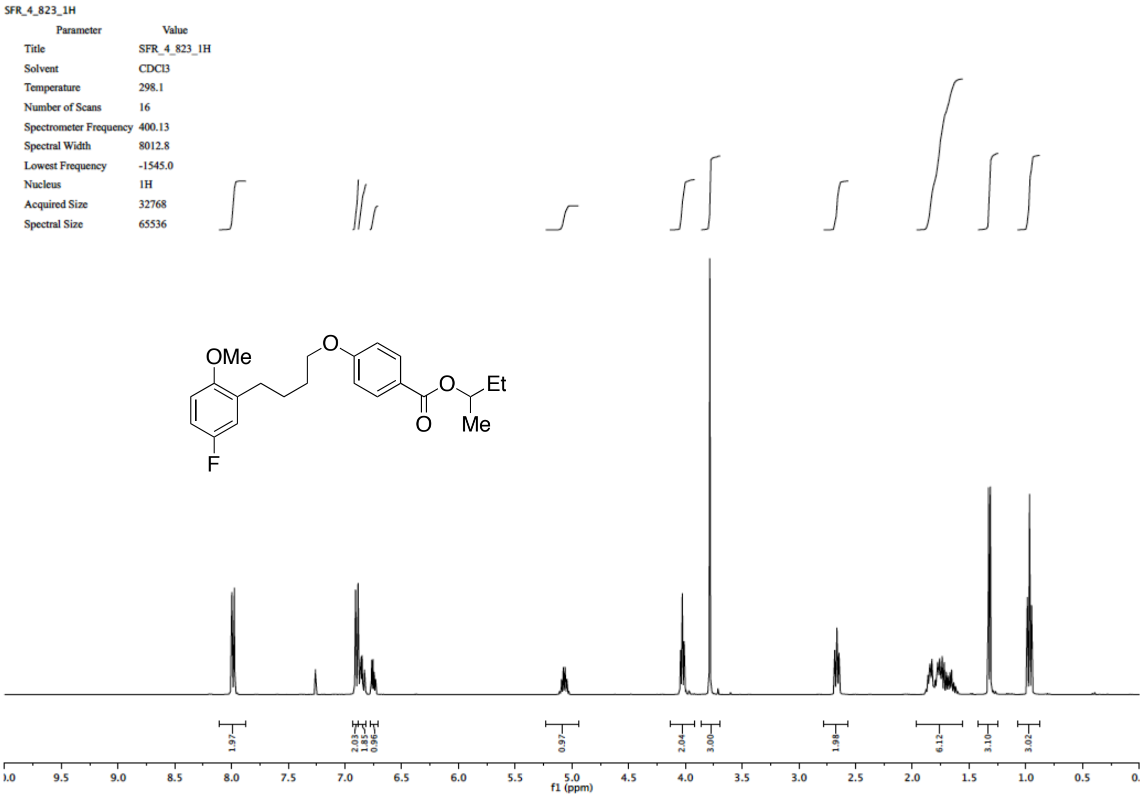
Parameter	Value
Title	SFR_4_843_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.8
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



SFR_4_843_13C

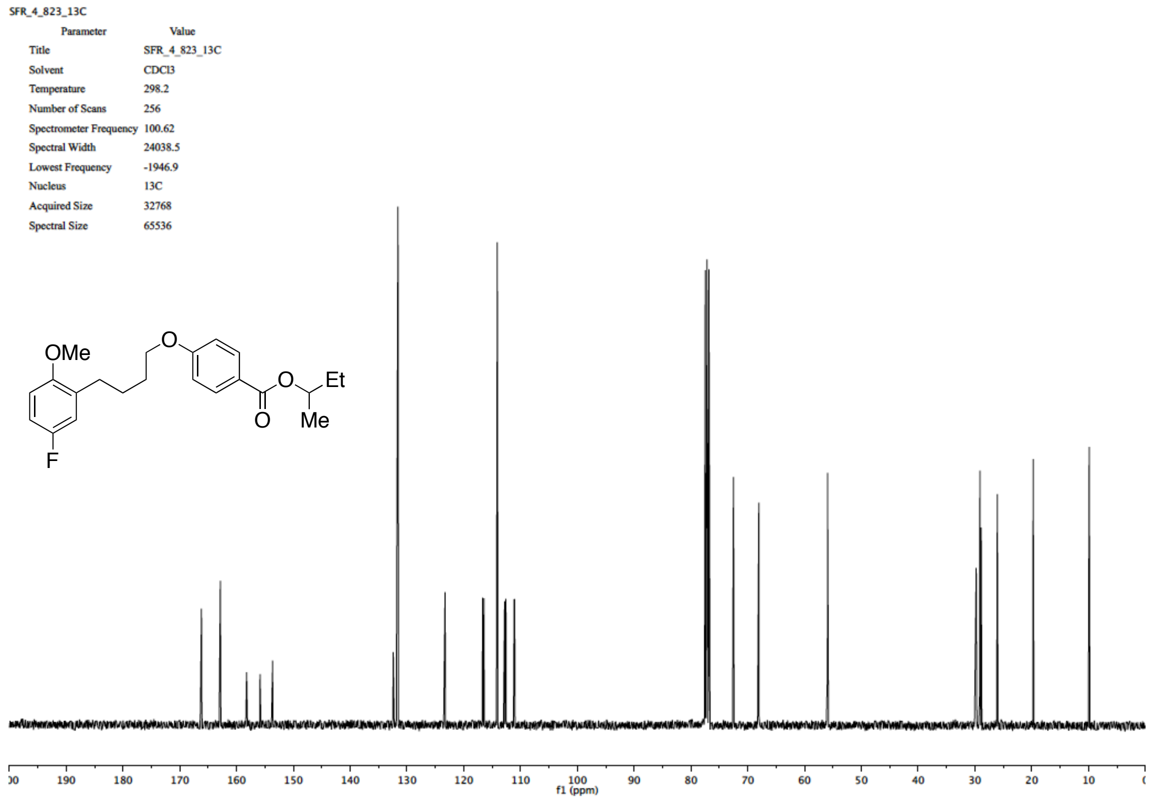
Parameter	Value
Title	SFR_4_843_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1946.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

sec-Butyl 4-(4-(5-fluoro-2-methoxyphenyl)butoxy)benzoate (3e)



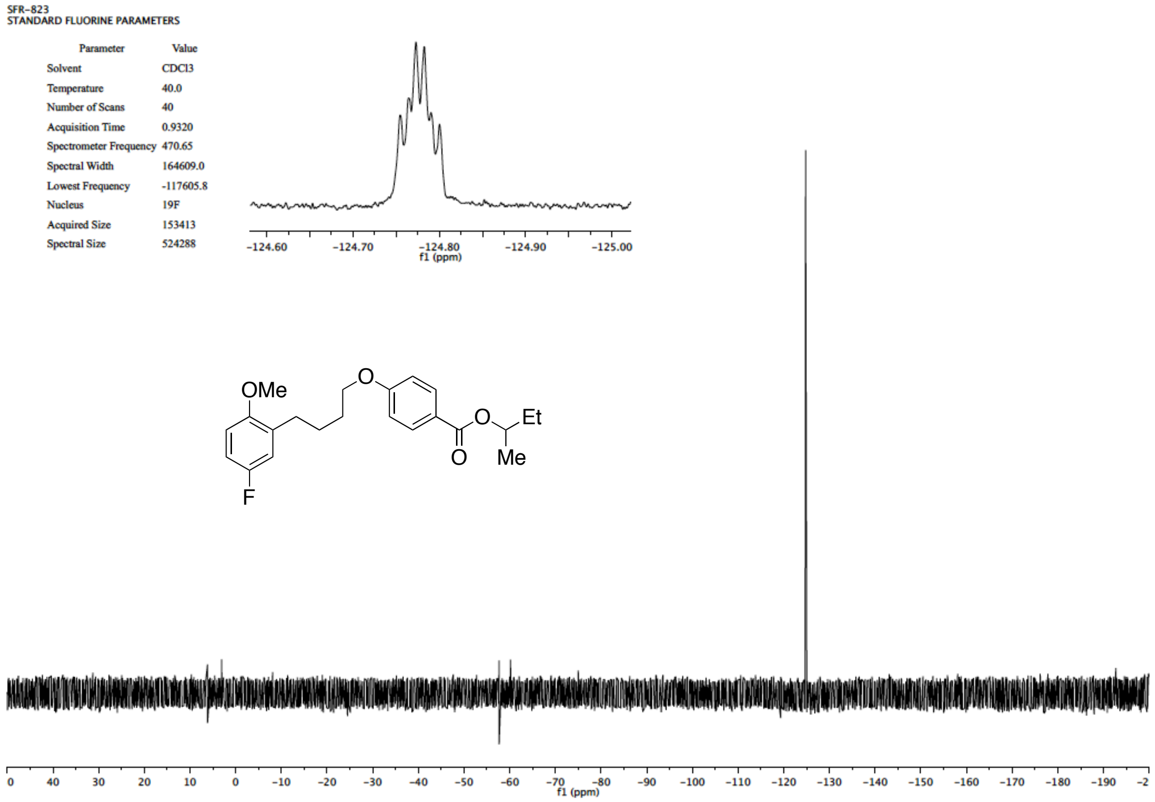
SFR_4_823_1H

Parameter	Value
Title	SFR_4_823_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



SFR_4_823_13C

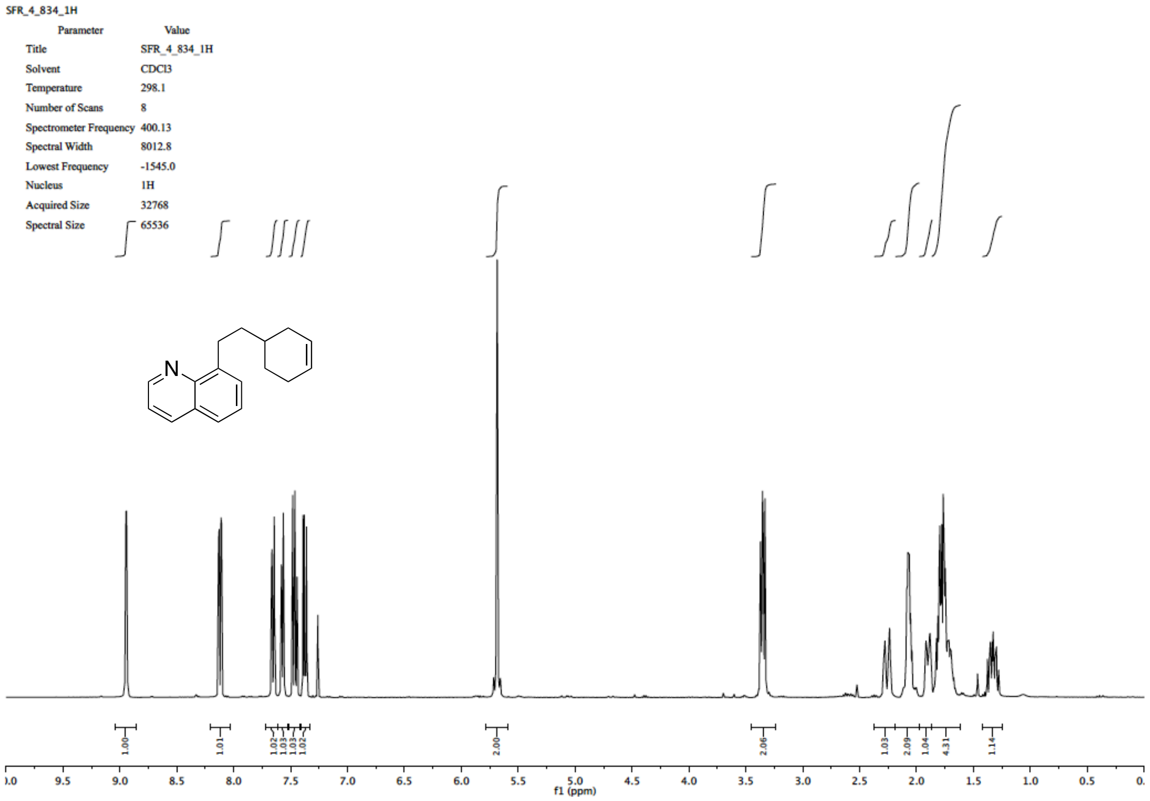
Parameter	Value
Title	SFR_4_823_13C
Solvent	CDCl3
Temperature	298.2
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1946.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



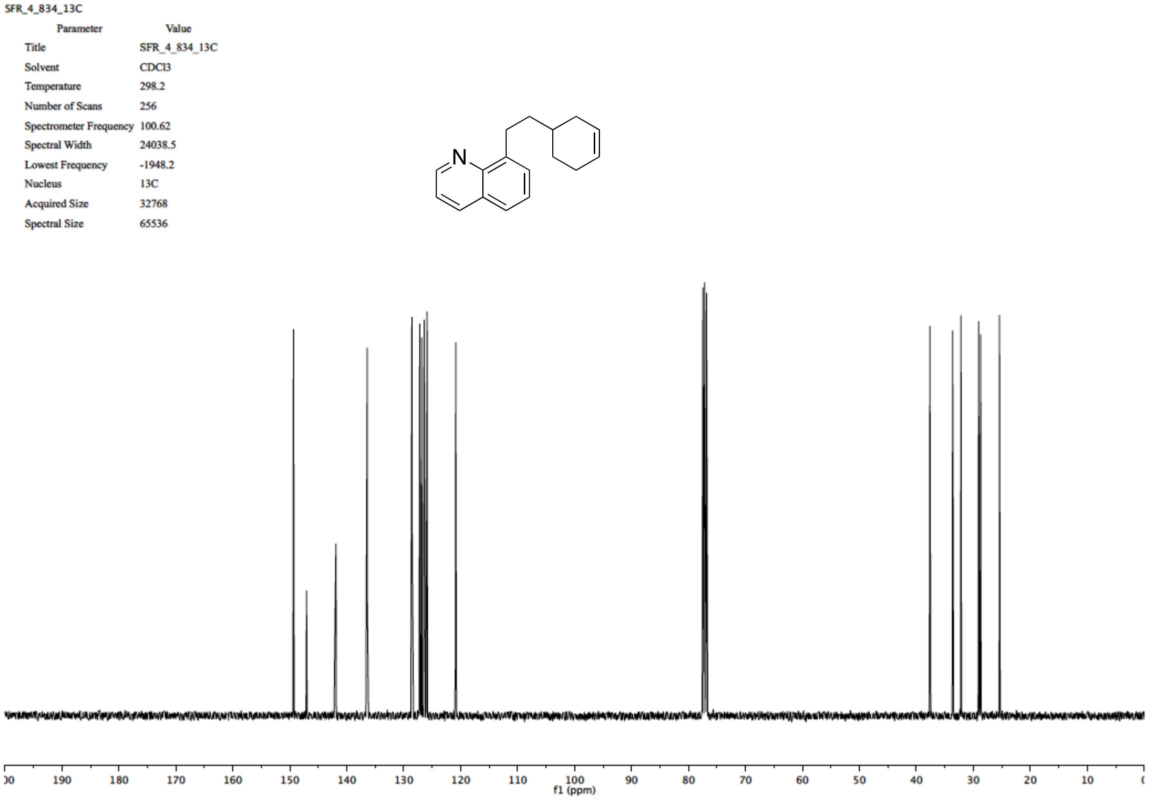
SFR-823
STANDARD FLUORINE PARAMETERS

Parameter	Value
Solvent	CDCl3
Temperature	40.0
Number of Scans	40
Acquisition Time	0.9320
Spectrometer Frequency	470.65
Spectral Width	164609.0
Lowest Frequency	-117605.8
Nucleus	19F
Acquired Size	153413
Spectral Size	524288

8-(2-(Cyclohex-3-en-1-yl)ethyl)quinoline (3f)

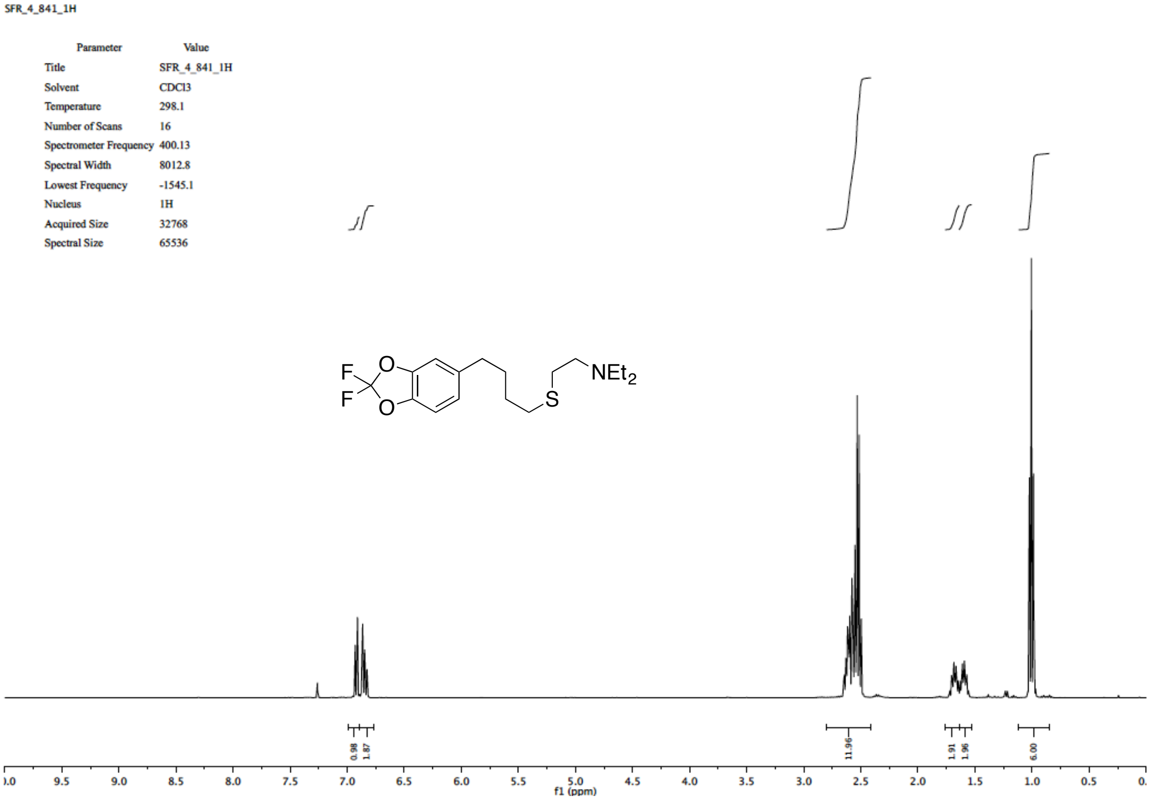


Parameter	Value
Title	SFR_4_834_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	8
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

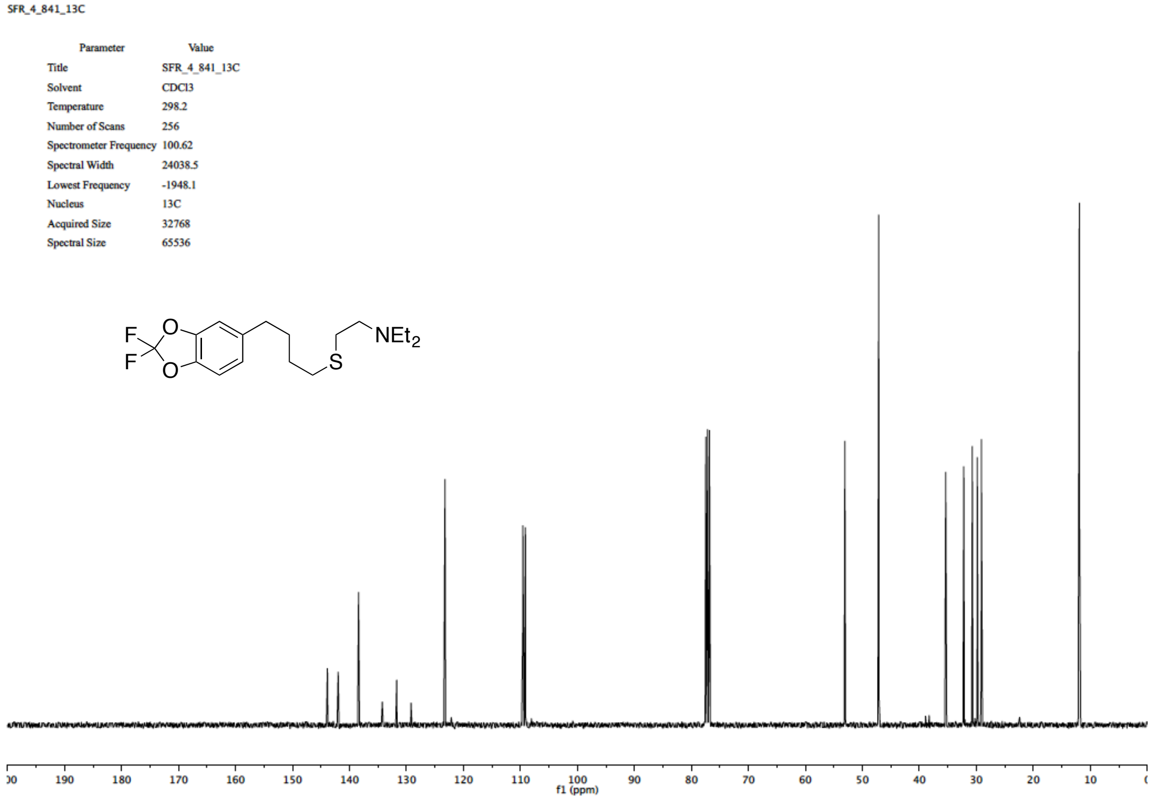


Parameter	Value
Title	SFR_4_834_13C
Solvent	CDCl3
Temperature	298.2
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1948.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

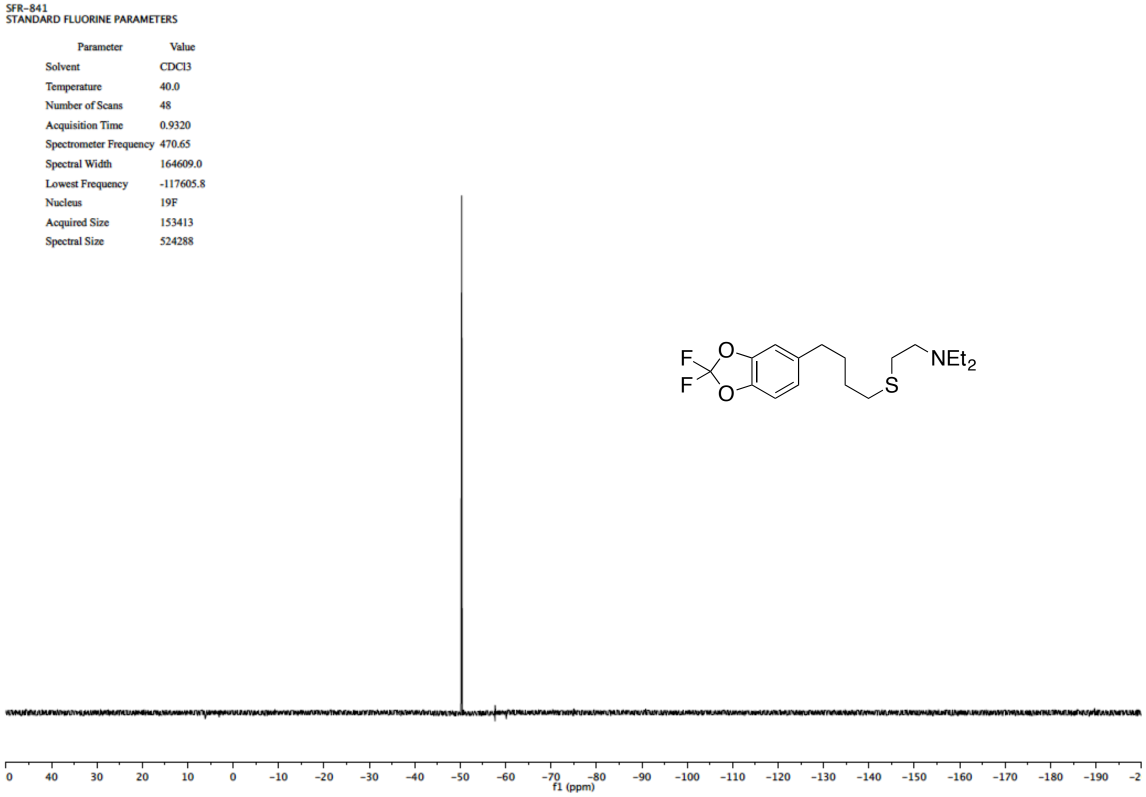
2-((4-(2,2-Difluorobenzo[*d*][1,3]dioxol-5-yl)butyl)thio)-*N*,*N*-diethylethan-1-amine (3g)



Parameter	Value
Title	SFR_4_841_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

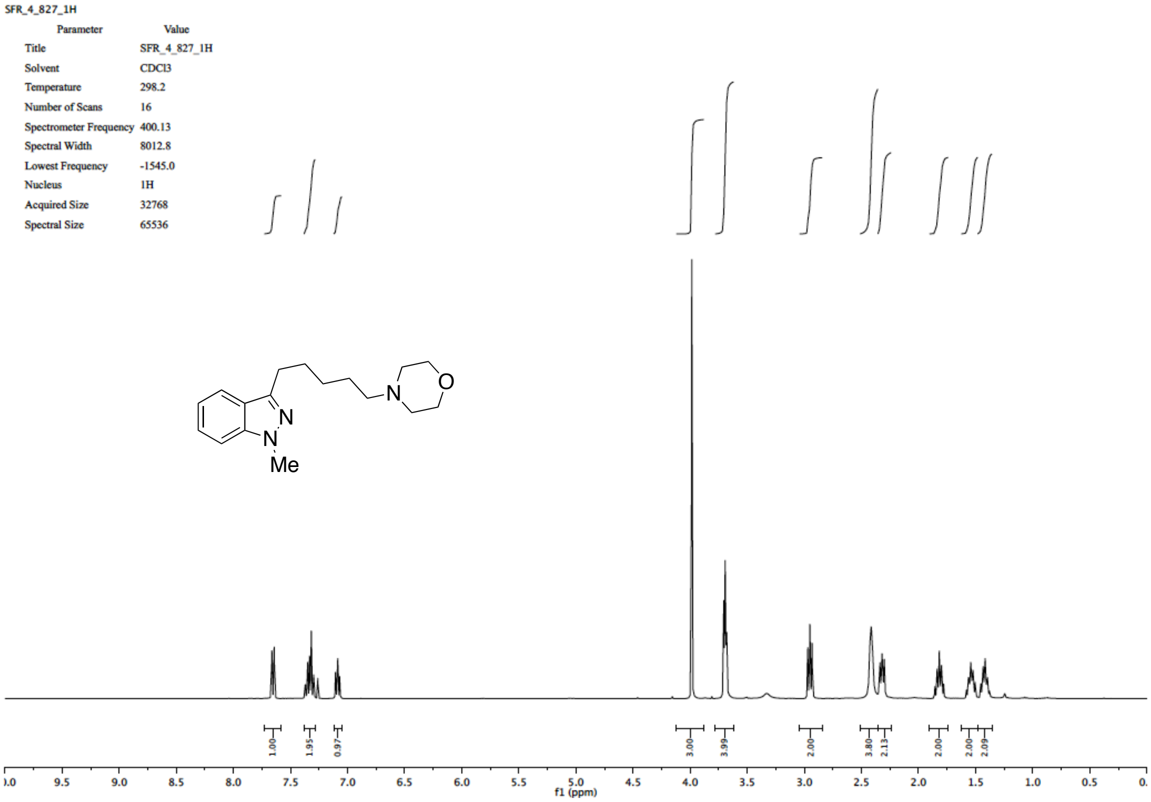


Parameter	Value
Title	SFR_4_841_13C
Solvent	CDCl3
Temperature	298.2
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1948.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536


SFR-841
STANDARD FLUORINE PARAMETERS

Parameter	Value
Solvent	CDCl3
Temperature	40.0
Number of Scans	48
Acquisition Time	0.9320
Spectrometer Frequency	470.65
Spectral Width	164609.0
Lowest Frequency	-117605.8
Nucleus	19F
Acquired Size	153413
Spectral Size	524288

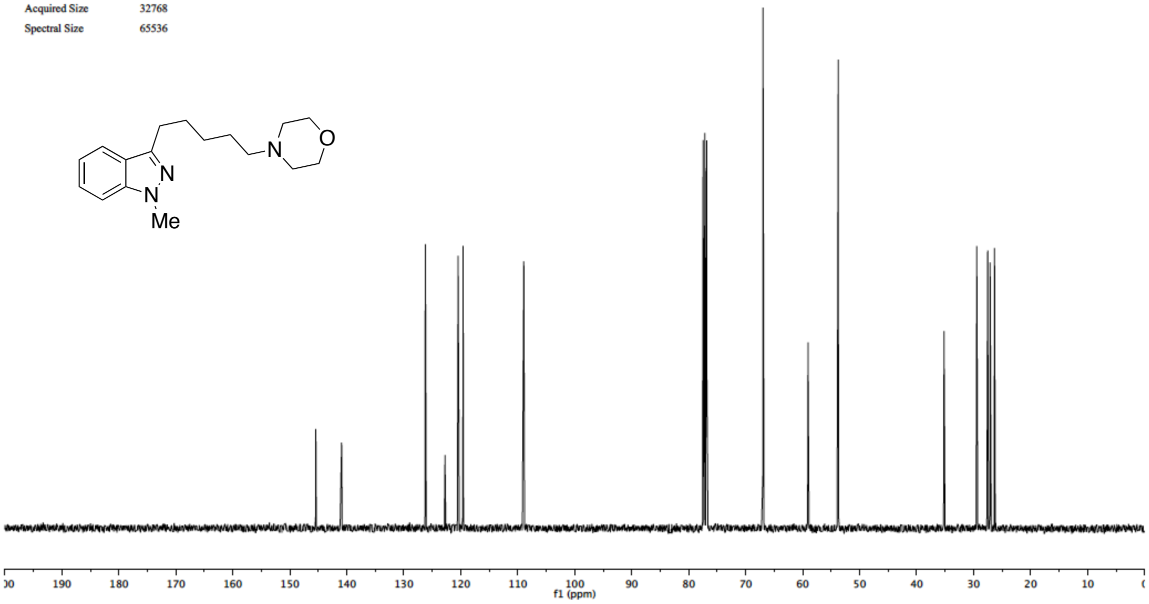
4-(5-(1-Methyl-1*H*-indazol-3-yl)pentyl)morpholine (3h)


SFR_4_827_1H

Parameter	Value
Title	SFR_4_827_1H
Solvent	CDCl3
Temperature	298.2
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

SFR_4_827_13C

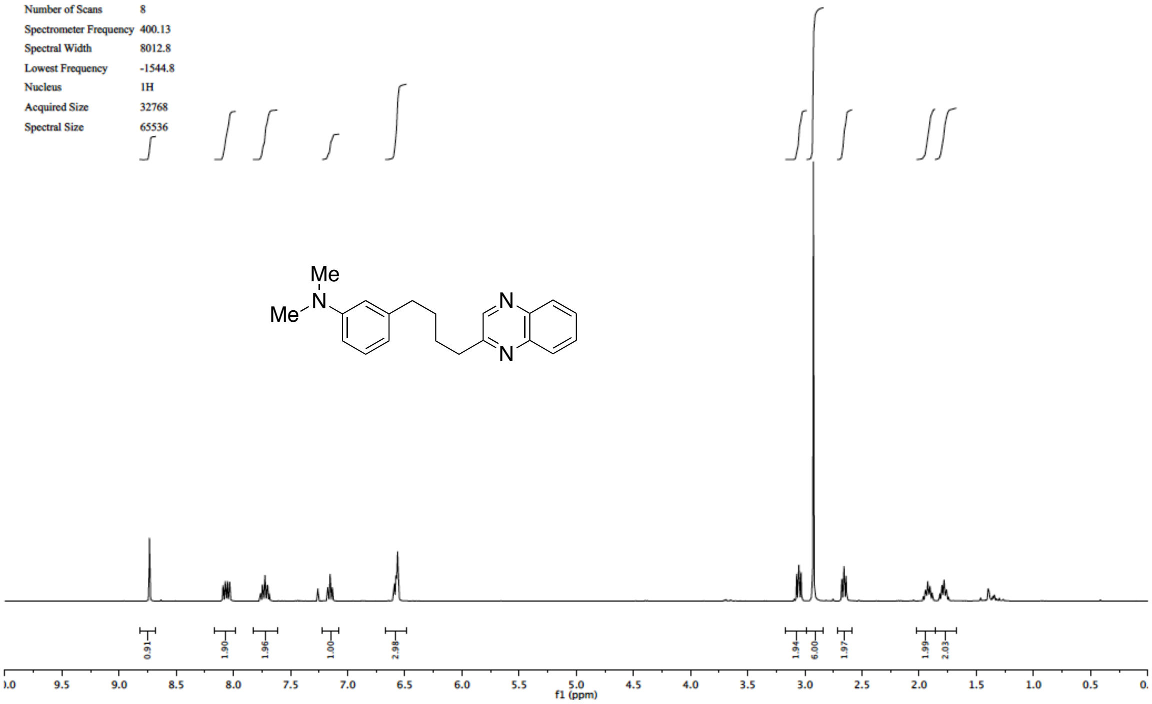
Parameter	Value
Title	SFR_4_827_13C
Solvent	CDCl3
Temperature	298.2
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1951.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

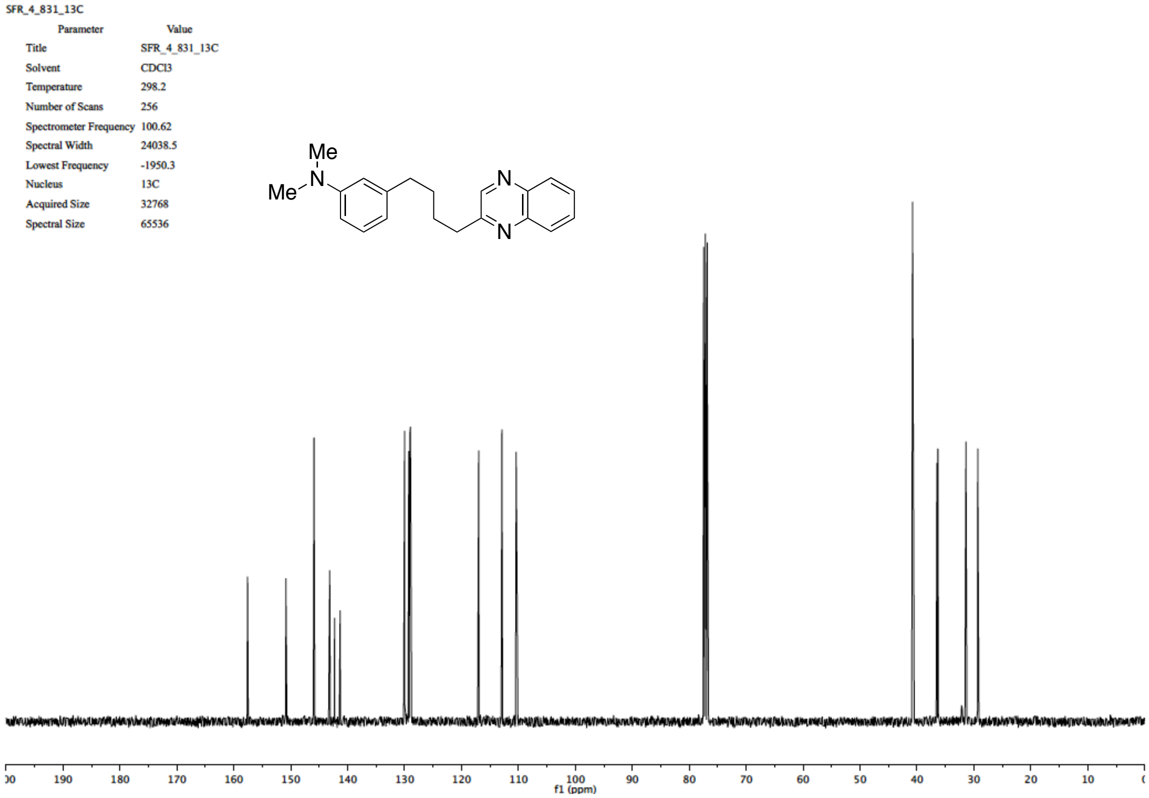


N,*N*-Dimethyl-3-(4-(quinoxalin-2-yl)butyl)aniline (3i)

SFR_4_831_1H

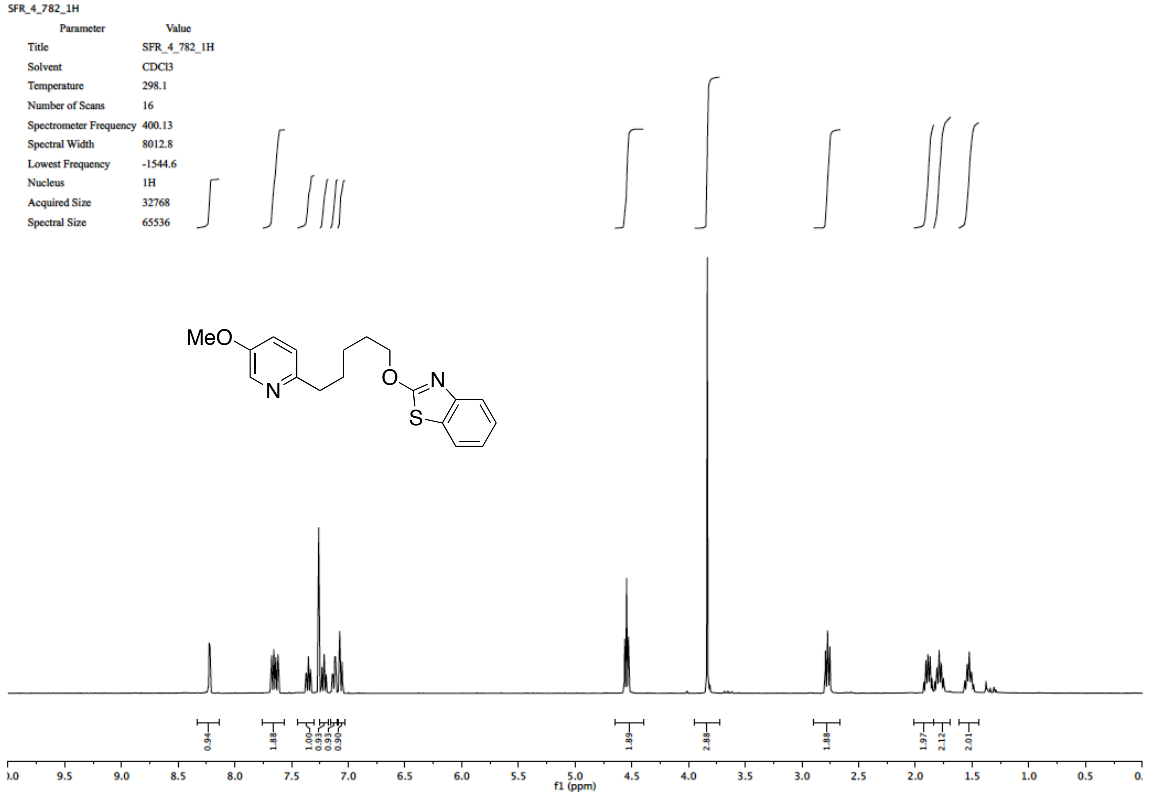
Parameter	Value
Title	SFR_4_831_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	8
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.8
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



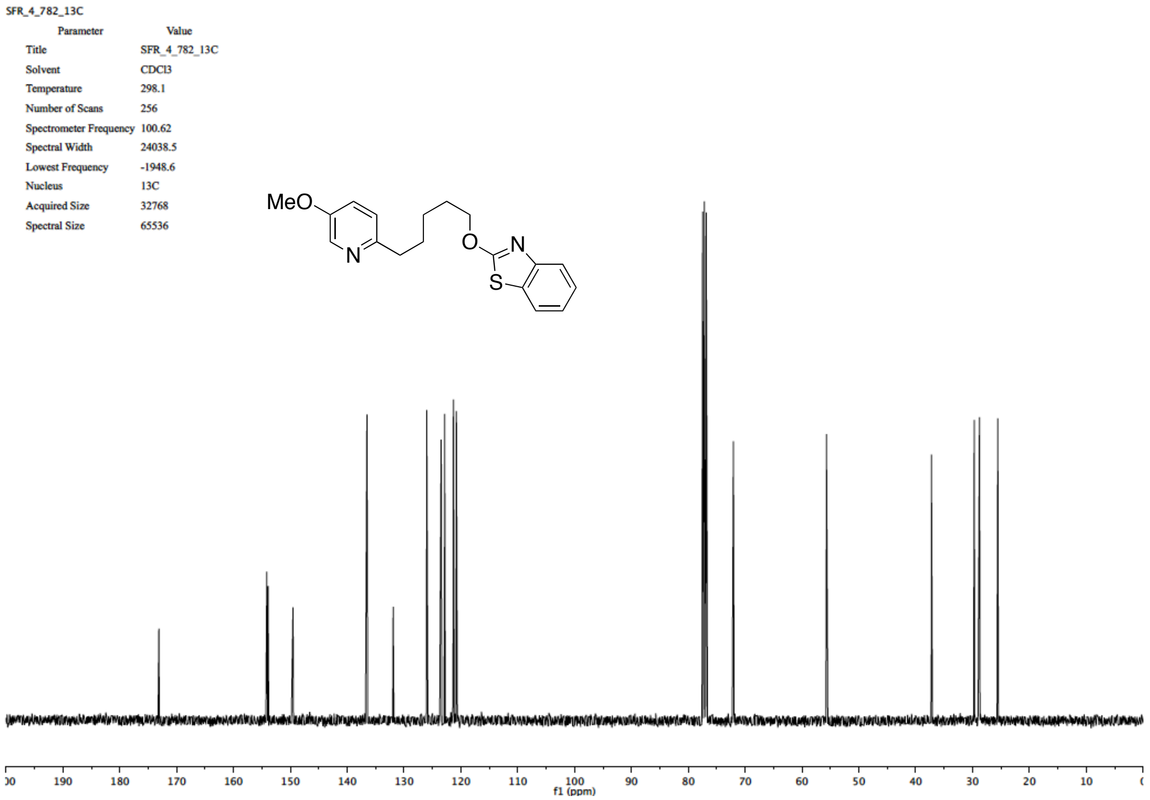

SFR_4_831_13C

Parameter	Value
Title	SFR_4_831_13C
Solvent	CDCl3
Temperature	298.2
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1950.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

2-((5-(5-Methoxypyridin-2-yl)pentyl)oxy)benzo[*d*]thiazole (3j)


SFR_4_782_1H

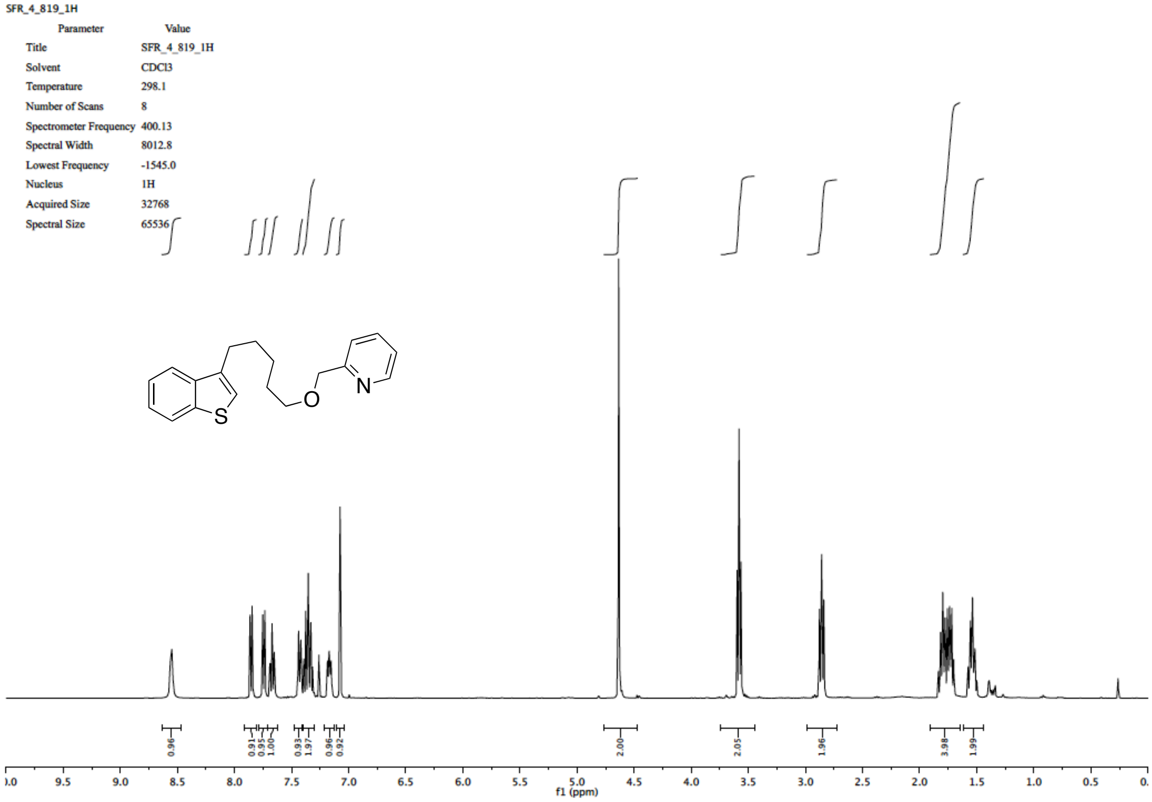
Parameter	Value
Title	SFR_4_782_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



SFR_4_782_13C

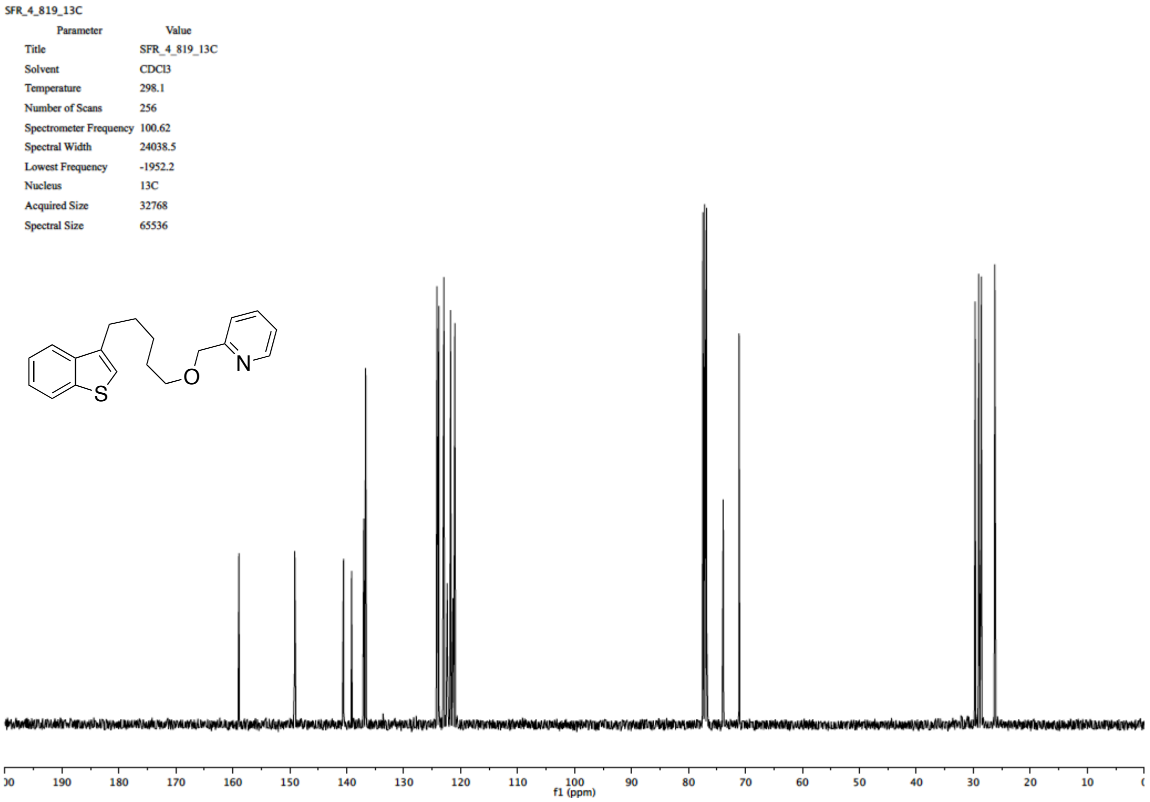
Parameter	Value
Title	SFR_4_782_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1948.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

2-(((5-(Benzo[*b*]thiophen-3-yl)pentyl)oxy)methyl)pyridine (3k)



SFR_4_819_1H

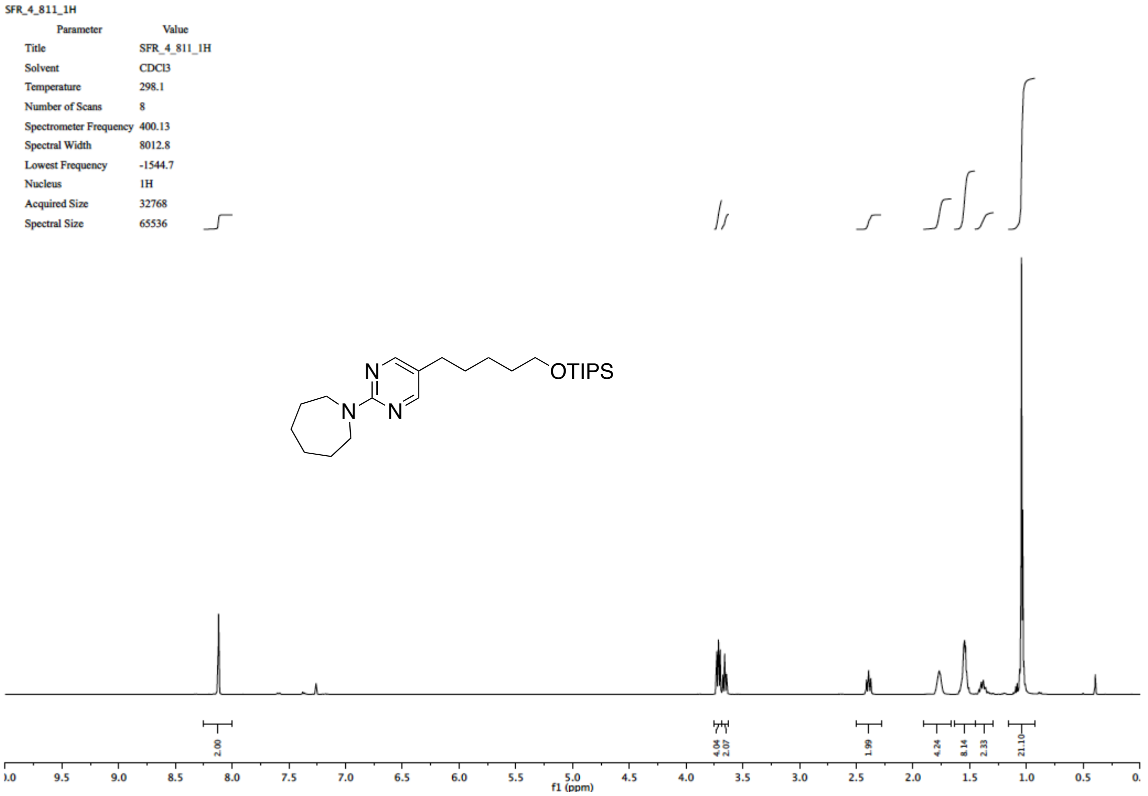
Parameter	Value
Title	SFR_4_819_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	8
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



SFR_4_819_13C

Parameter	Value
Title	SFR_4_819_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1952.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

1-(5-(5-((Triisopropylsilyl)oxy)pentyl)pyrimidin-2-yl)azepane (3l)

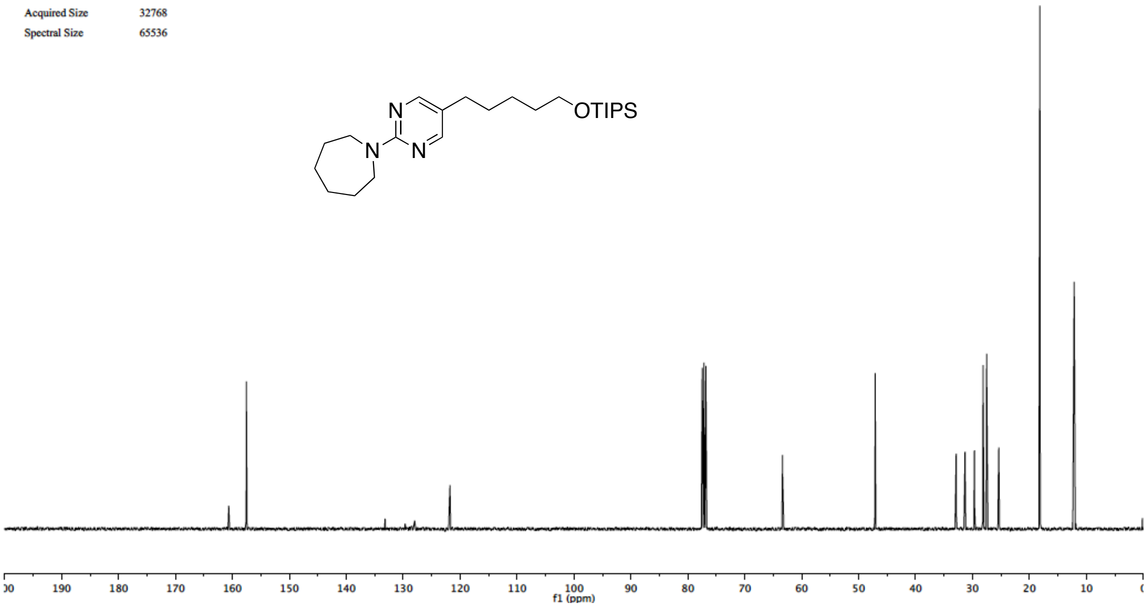


SFR_4_811_1H

Parameter	Value
Title	SFR_4_811_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	8
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.7
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

SFR_4_811_13C

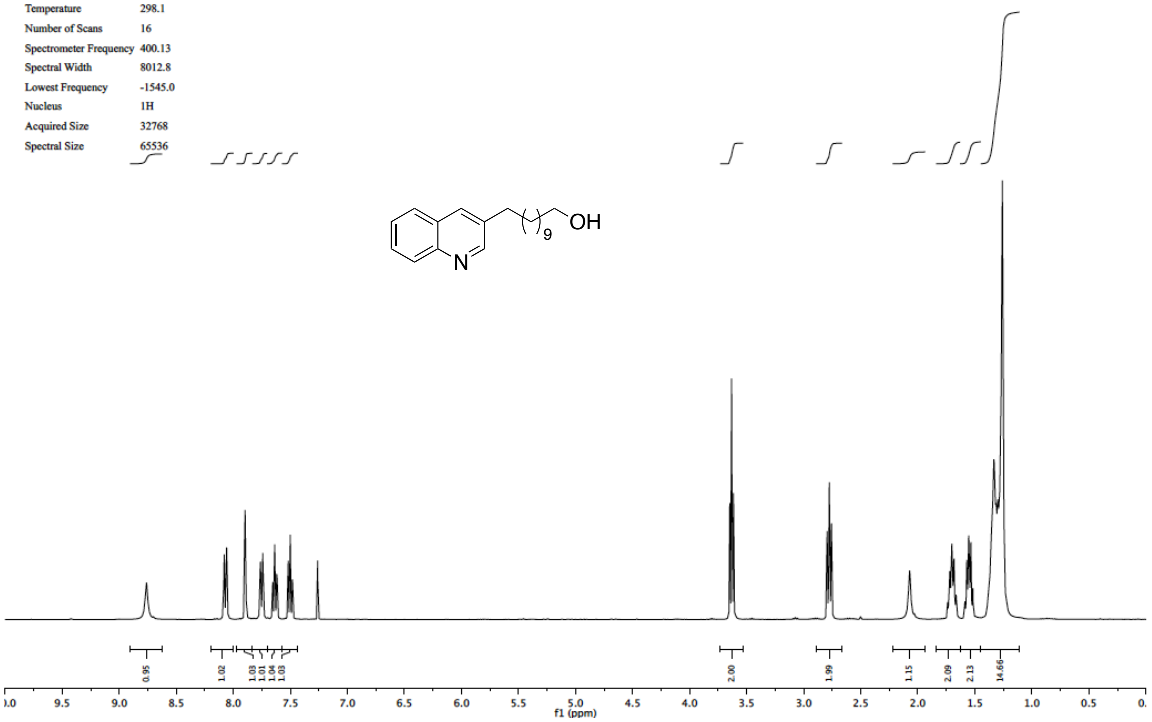
Parameter	Value
Title	SFR_4_811_13C
Solvent	CDCl3
Temperature	298.2
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1945.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



11-(Quinolin-3-yl)undecan-1-ol (3m)

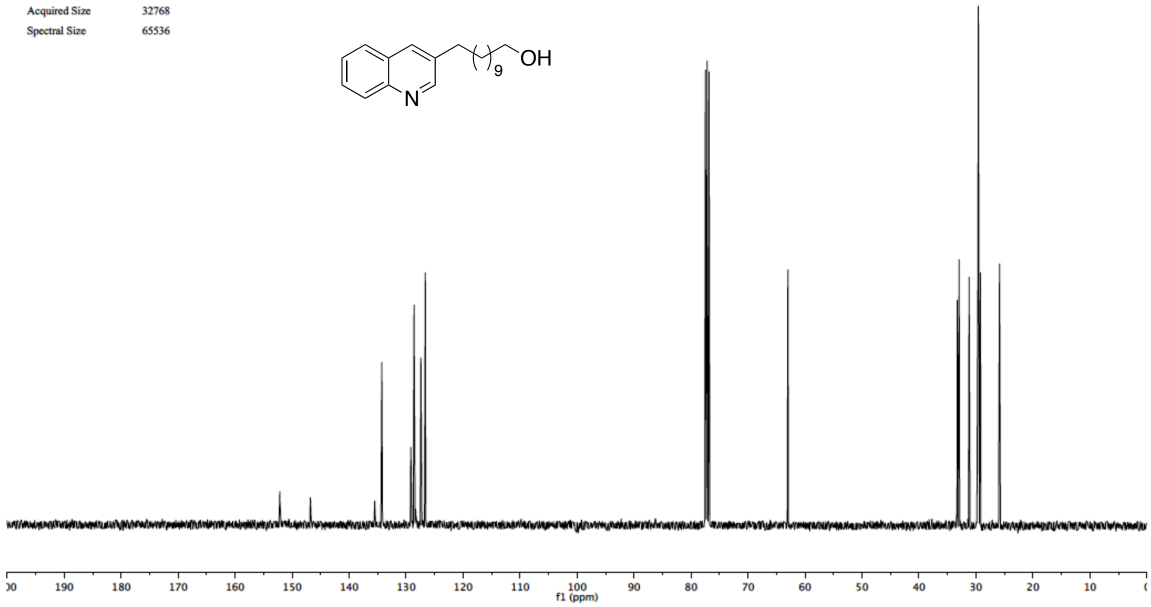
SFR_4_846_1H

Parameter	Value
Title	SFR_4_846_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



SFR_4_846_13C

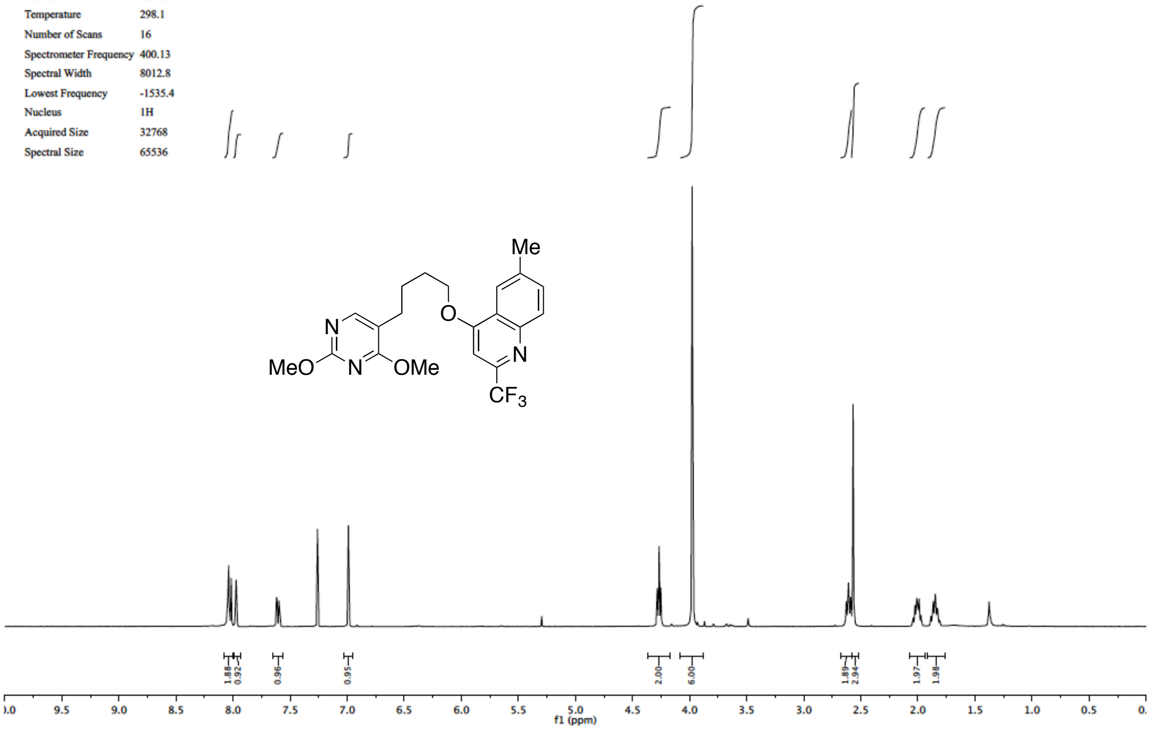
Parameter	Value
Title	SFR_4_846_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1948.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

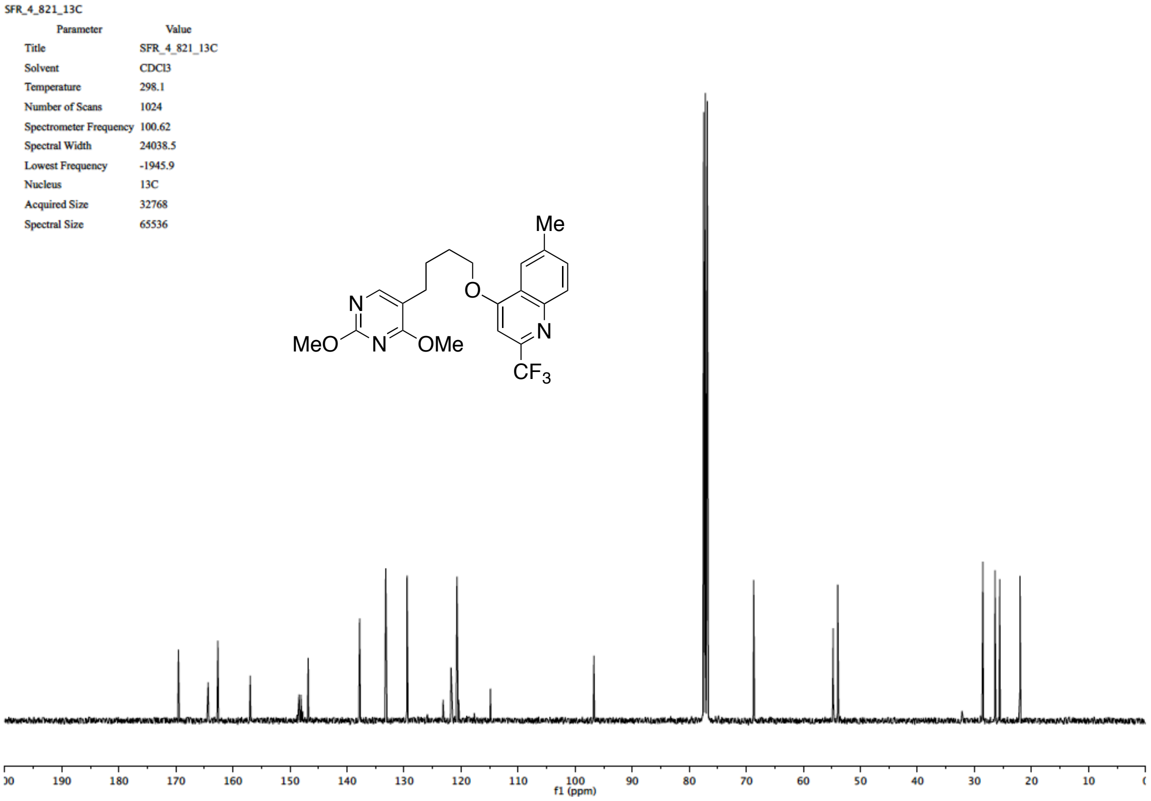


4-(4-(2,4-Dimethoxypyrimidin-5-yl)butoxy)-6-methyl-2-(trifluoromethyl)quinolone (3n)

SFR_4_821_1H

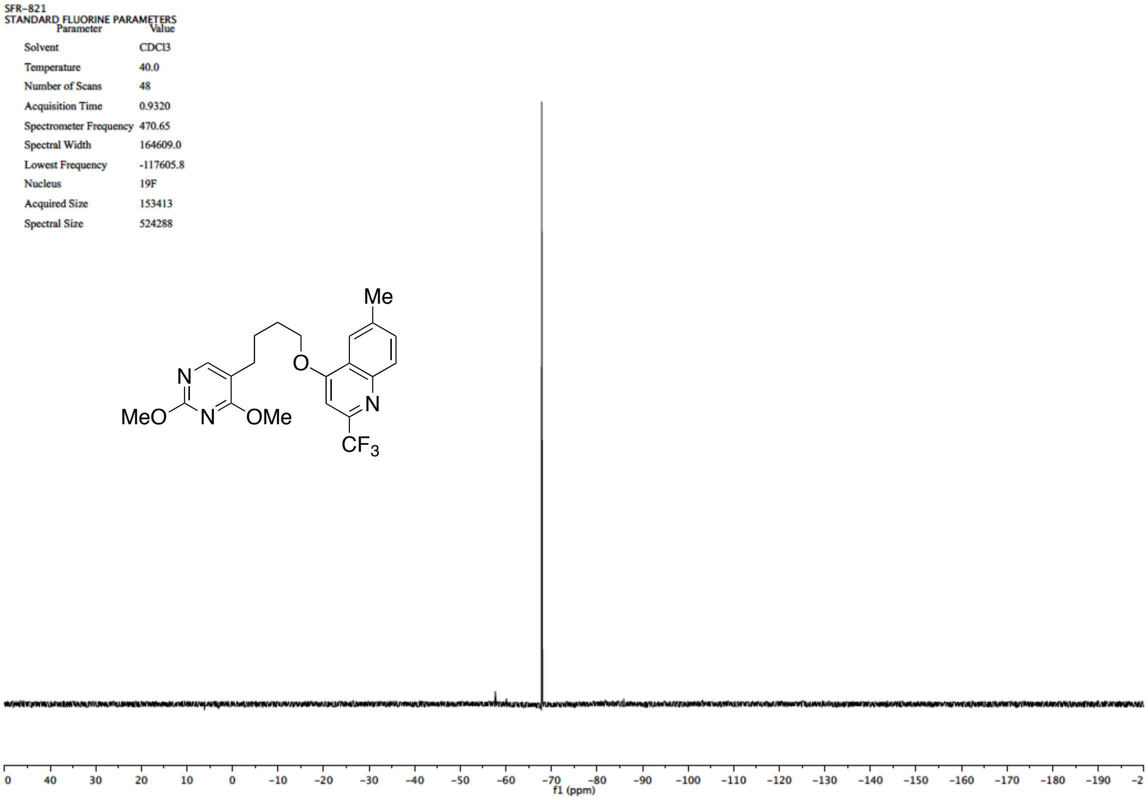
Parameter	Value
Title	SFR_4_821_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1535.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536





SFR_4_821_13C

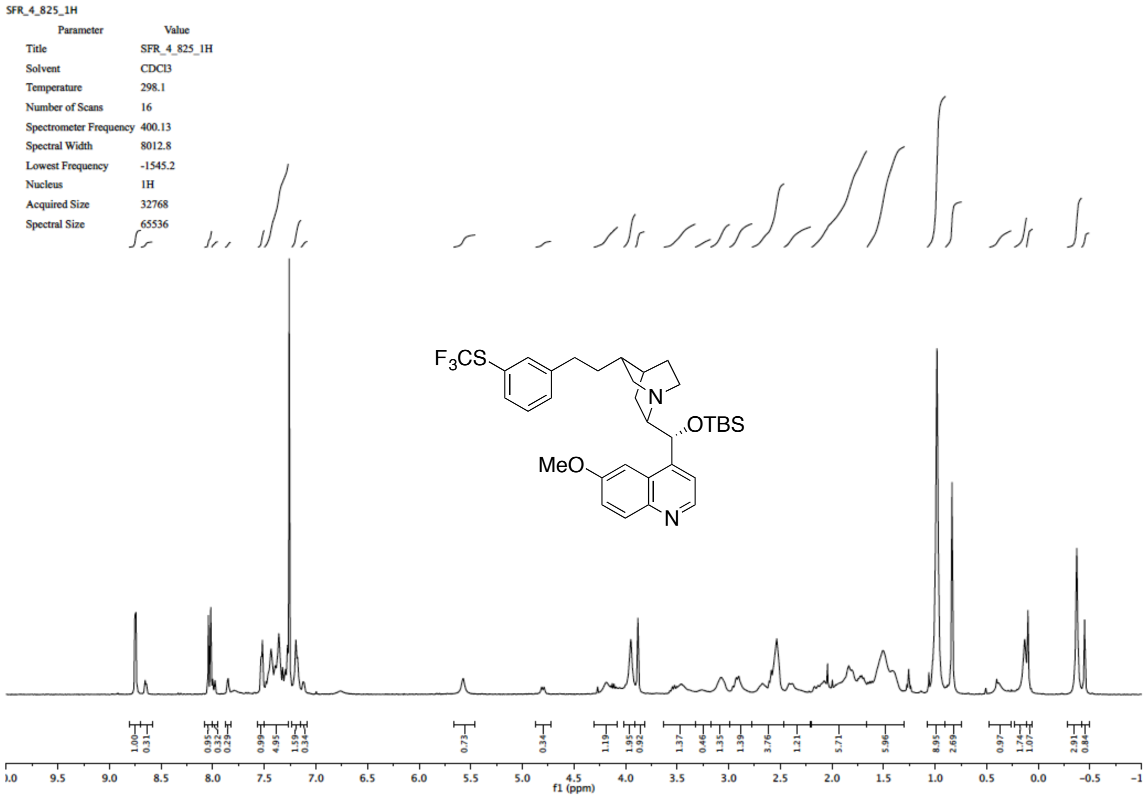
Parameter	Value
Title	SFR_4_821_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	1024
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1945.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



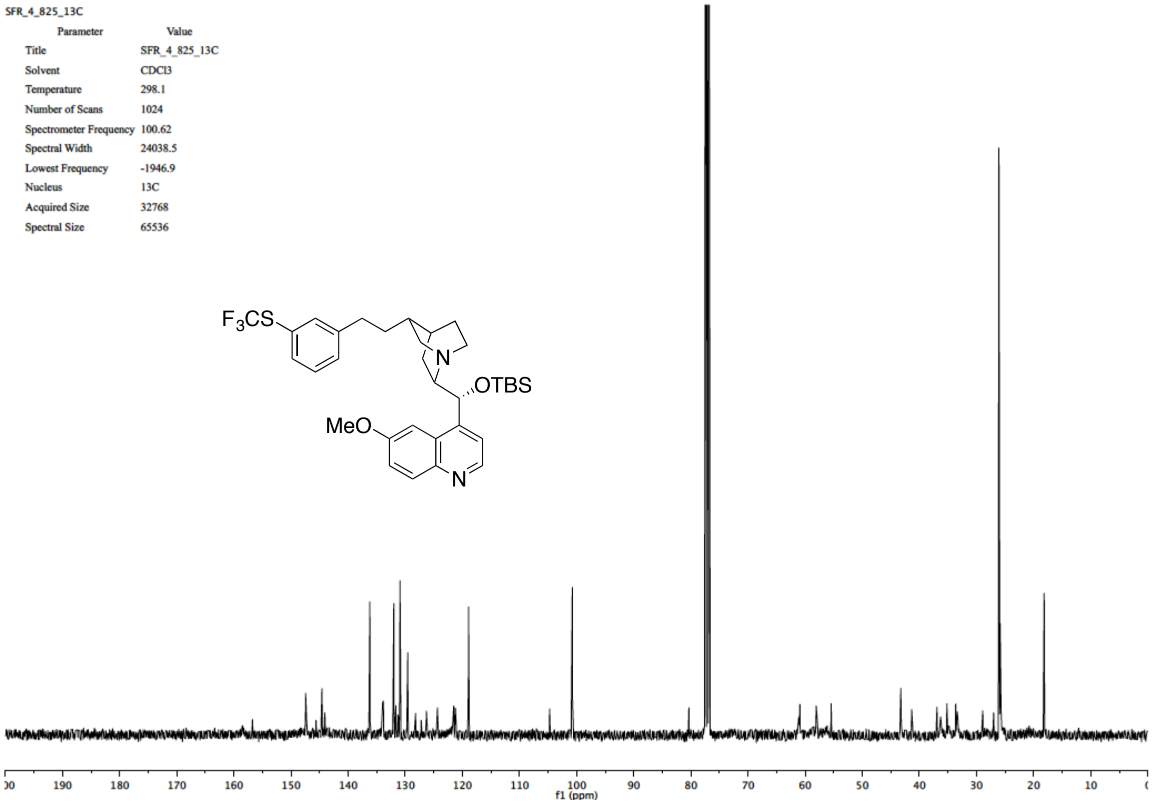
SFR-821
STANDARD FLUORINE PARAMETERS

Parameter	Value
Solvent	CDCl3
Temperature	40.0
Number of Scans	48
Acquisition Time	0.9320
Spectrometer Frequency	470.65
Spectral Width	164609.0
Lowest Frequency	-117605.8
Nucleus	19F
Acquired Size	153413
Spectral Size	524288

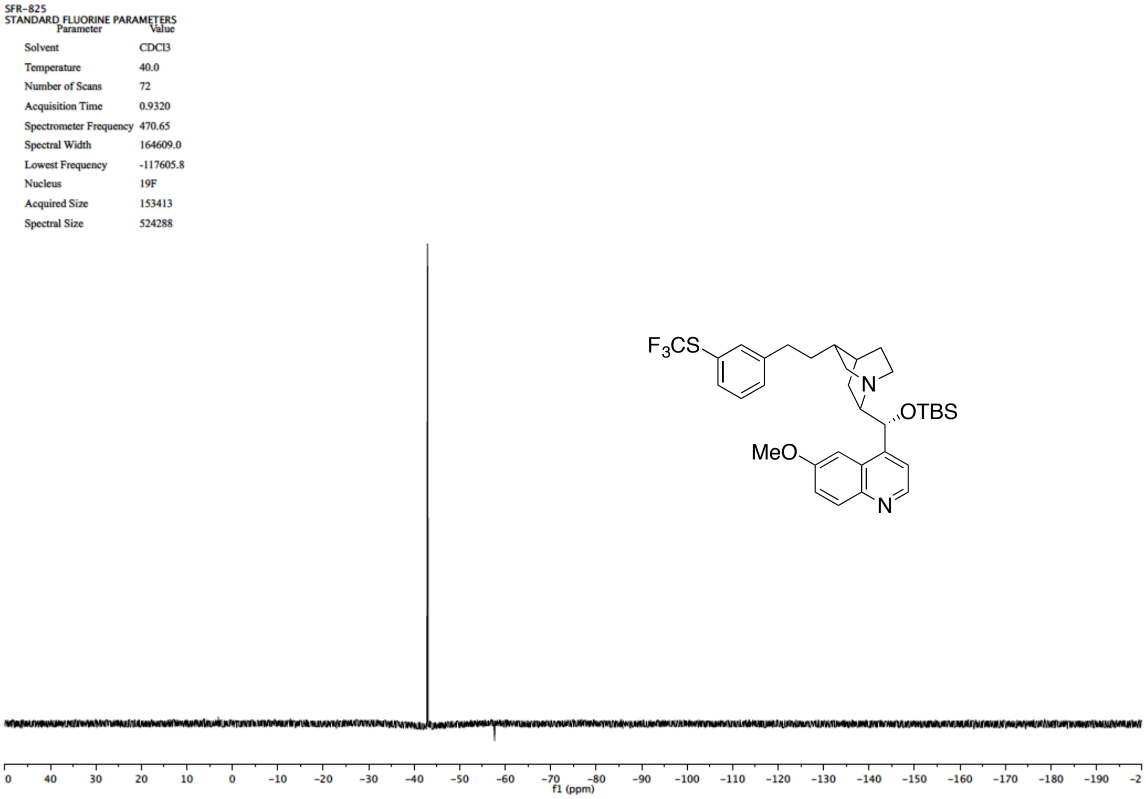
2-((*R*)-((*tert*-Butyldimethylsilyl)oxy)(6-methoxyquinolin-4-yl)methyl)-5-(3-((trifluoromethyl)thio)phenethyl)quinuclidine (3o)


SFR_4_825_1H

Parameter	Value
Title	SFR_4_825_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


SFR_4_825_13C

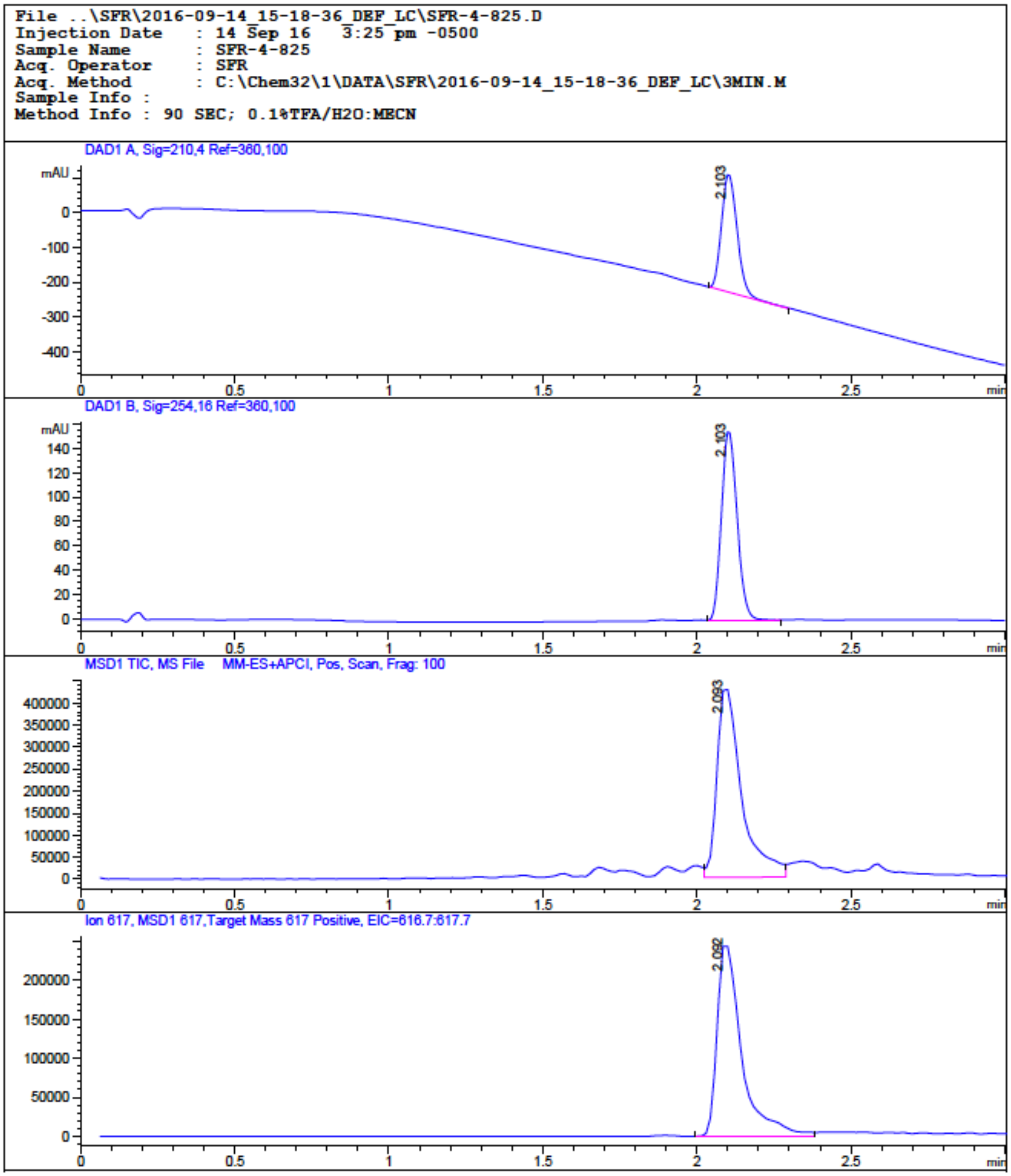
Parameter	Value
Title	SFR_4_825_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	1024
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1946.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



SFR-825
STANDARD FLUORINE PARAMETERS

Parameter	Value
Solvent	CDCl3
Temperature	40.0
Number of Scans	72
Acquisition Time	0.9320
Spectrometer Frequency	470.65
Spectral Width	164609.0
Lowest Frequency	-117605.8
Nucleus	19F
Acquired Size	153413
Spectral Size	524288

HPLC-MS analysis: Accucore C18 column (7-95 % MeCN in water w. 0.1% TFA, 2.5 min, 0.9 mL/min, 40 °C, positive ionization)



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File ..\SFR\2016-09-14_15-18-36_DEF_LC\SFR-4-825.D
Injection Date     : 14 Sep 16    3:25 pm -0500
Sample Name        : SFR-4-825
Acq. Operator      : SFR
Acq. Method        : C:\Chem32\1\DATA\SFR\2016-09-14_15-18-36_DEF_LC\3MIN.M
Sample Info :
Method Info : 90 SEC; 0.1%TFA/H2O:MECN
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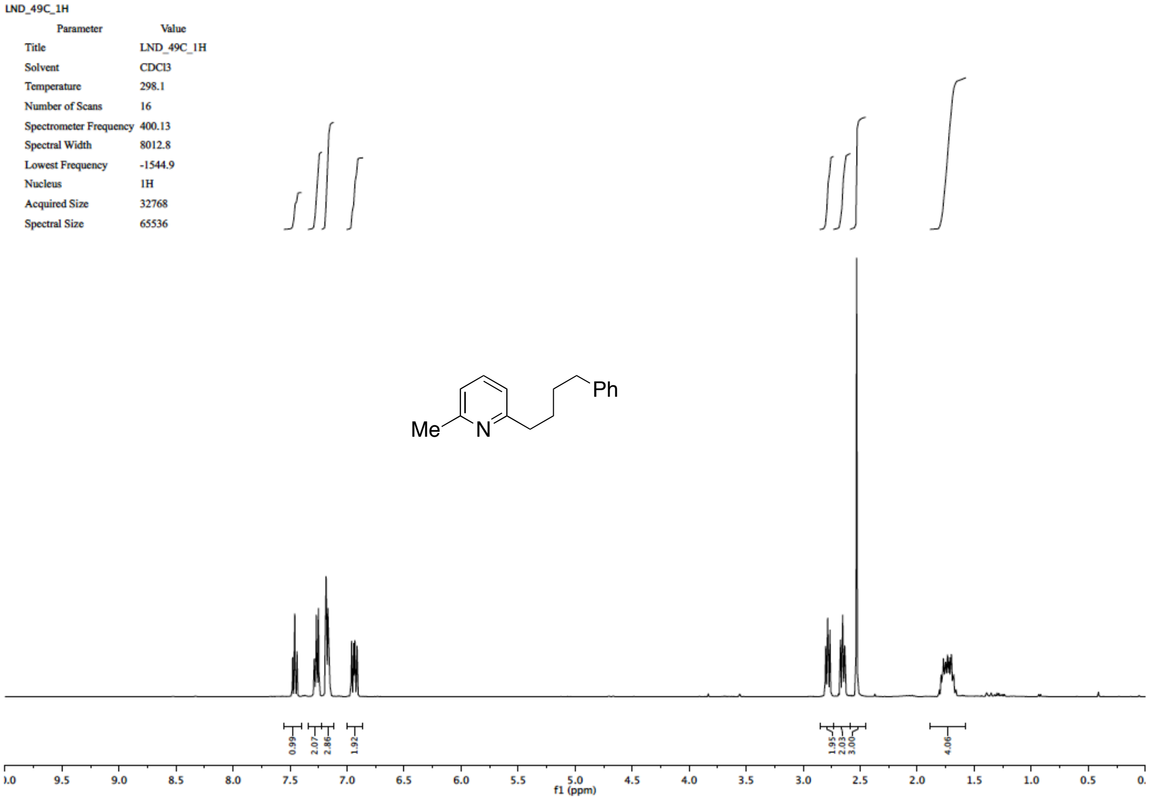
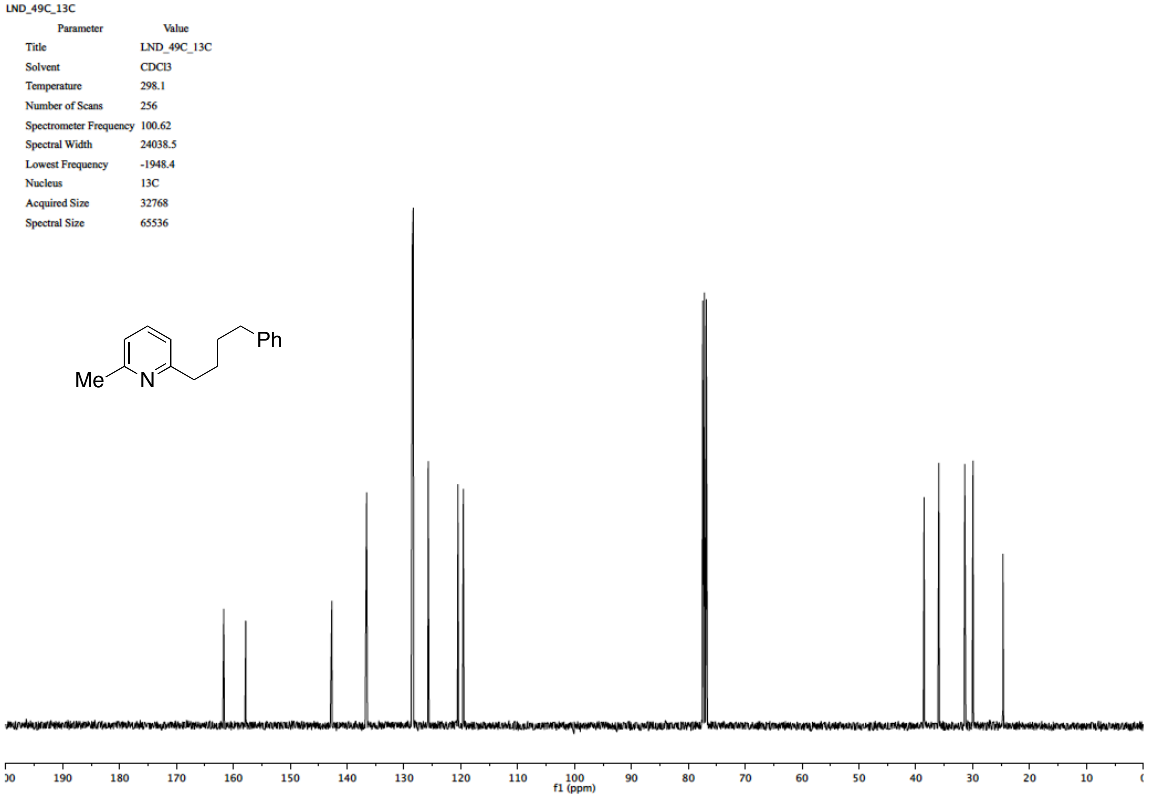
2-Methyl-6-(4-phenylbutyl)pyridine (3p)

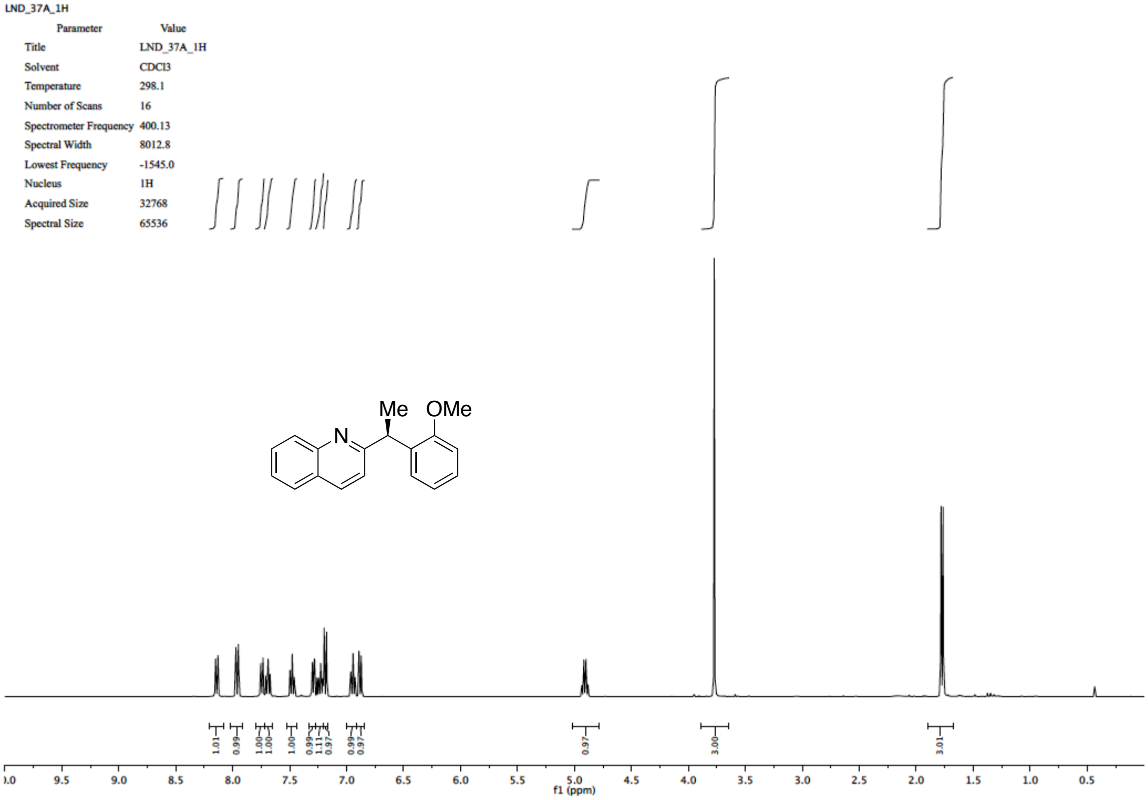

LND_49C_1H

Parameter	Value
Title	LND_49C_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.9
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

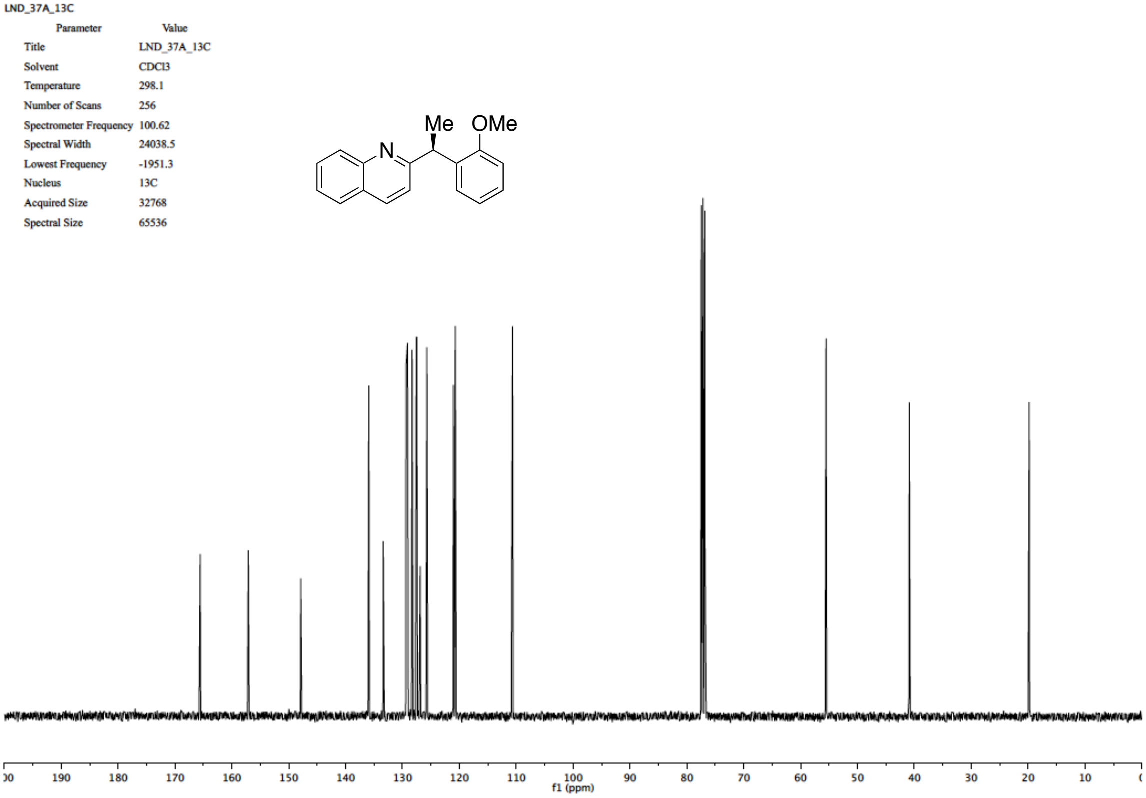

LND_49C_13C

Parameter	Value
Title	LND_49C_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1948.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

(*S*)-2-(1-(2-Methoxyphenyl)ethyl)quinoline (4a)


LND_37A_1H

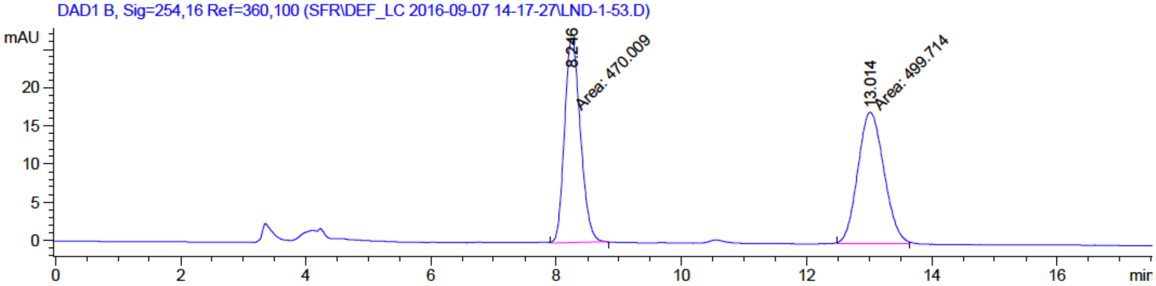
Parameter	Value
Title	LND_37A_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536


LND_37A_13C

Parameter	Value
Title	LND_37A_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1951.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

Chiral HPLC: Chiracel OJ-H (Hexanes/*i*PrOH = 90/10, 1.0 mL/min, 254 nm)

Racemic:



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Signal 2: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.246 MM    0.2931  470.00867   26.72714  48.4683
   2  13.014 MM    0.4842  499.71426   17.20137  51.5317

Totals :                   969.72293   43.92851
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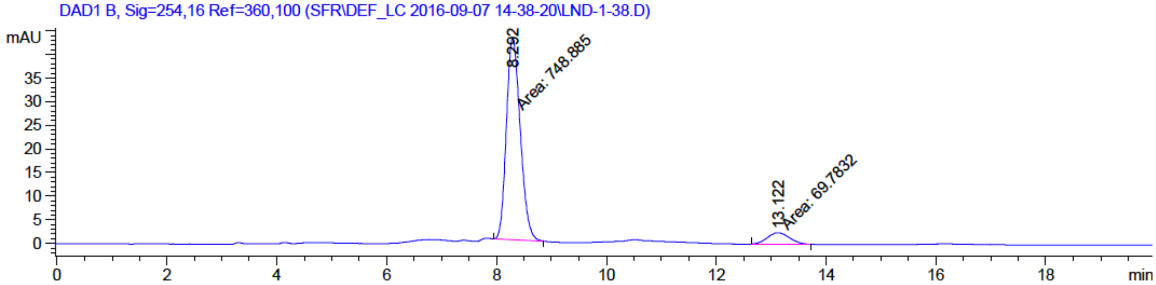
From ArBr:



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Signal 2: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.292 MM    0.2933  748.88513   42.55324  91.4760
   2  13.122 MM    0.4752   69.78320    2.44773   8.5240

Totals :                   818.66833   45.00097
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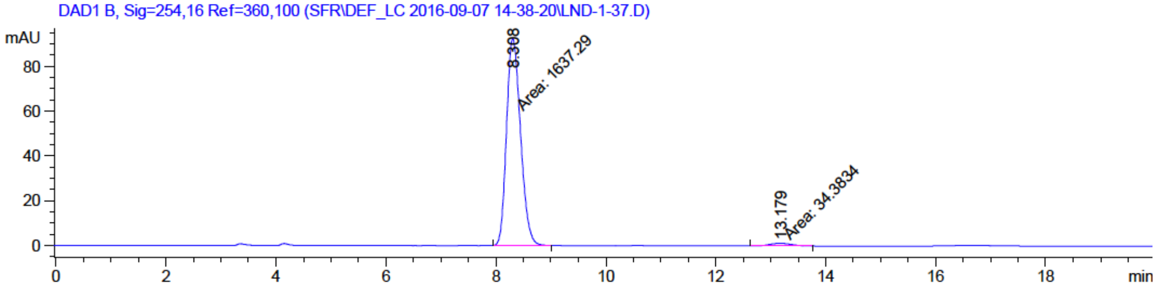
From ArCl:

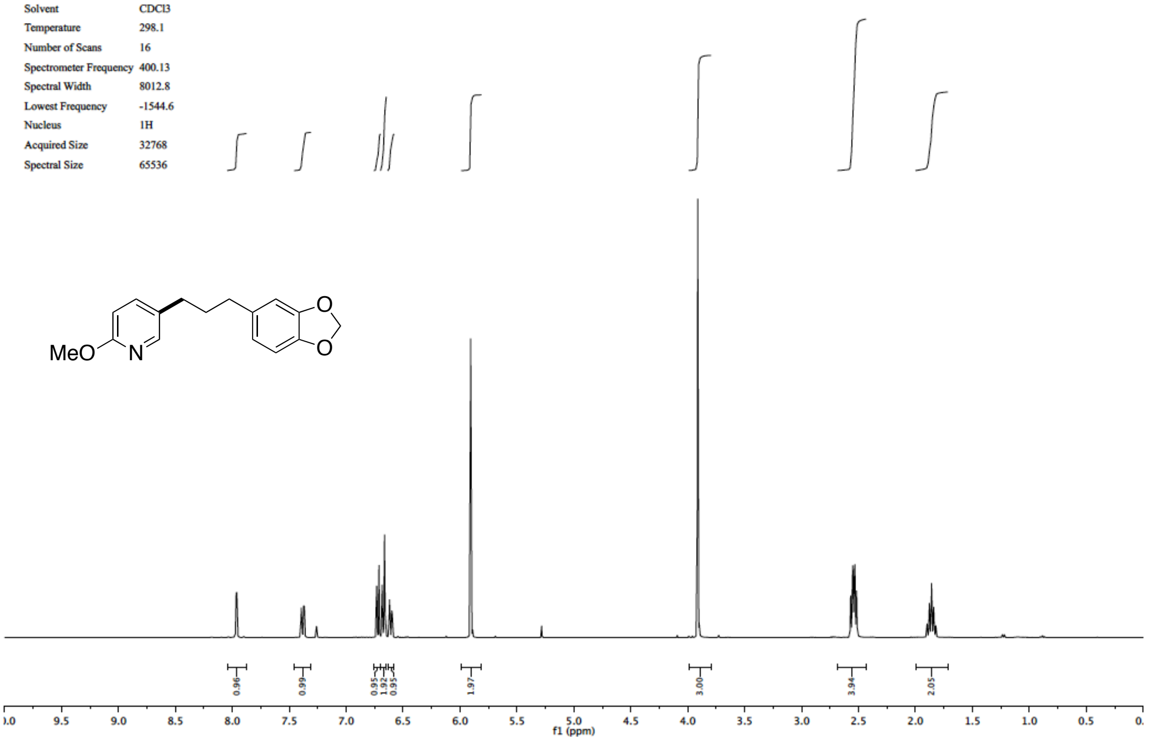


```
Signal 2: DAD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.308 MM    0.2948 1637.29407   92.56232  97.9432
   2  13.179 MM    0.4788   34.38338    1.19681   2.0568

Totals :                  1671.67744   93.75914
```

5-(3-(Benzo[*d*][1,3]dioxol-5-yl)propyl)-2-methoxypyridine (3q)

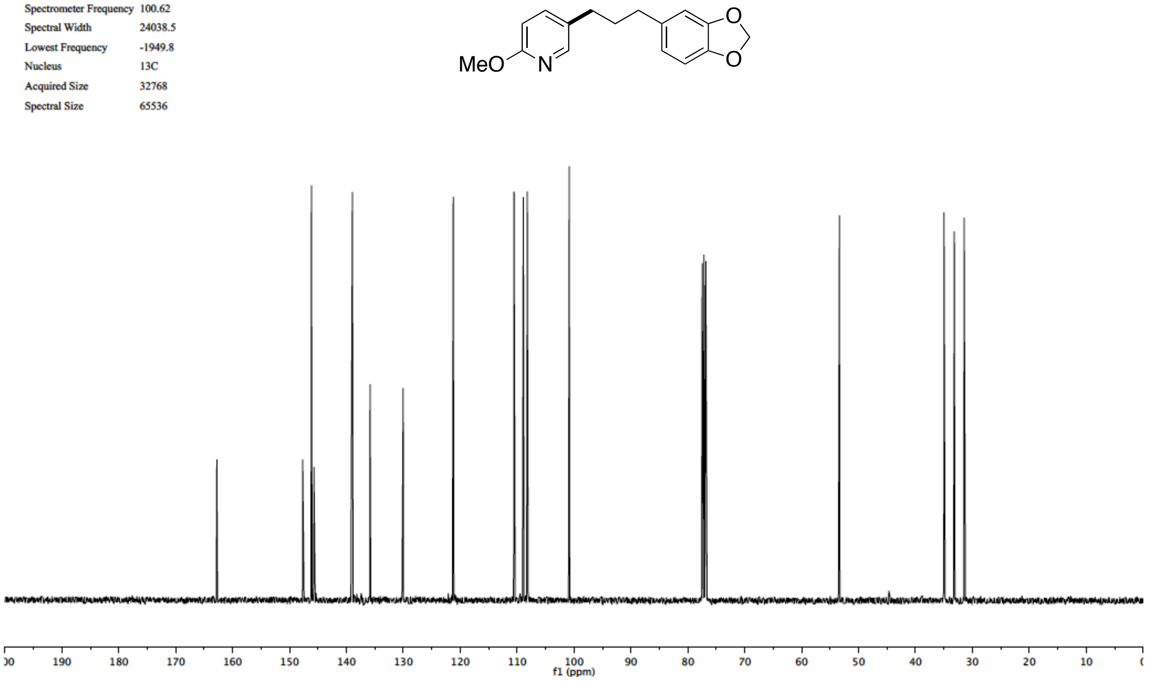
SFR_4_816_1H

Parameter	Value
Title	SFR_4_816_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

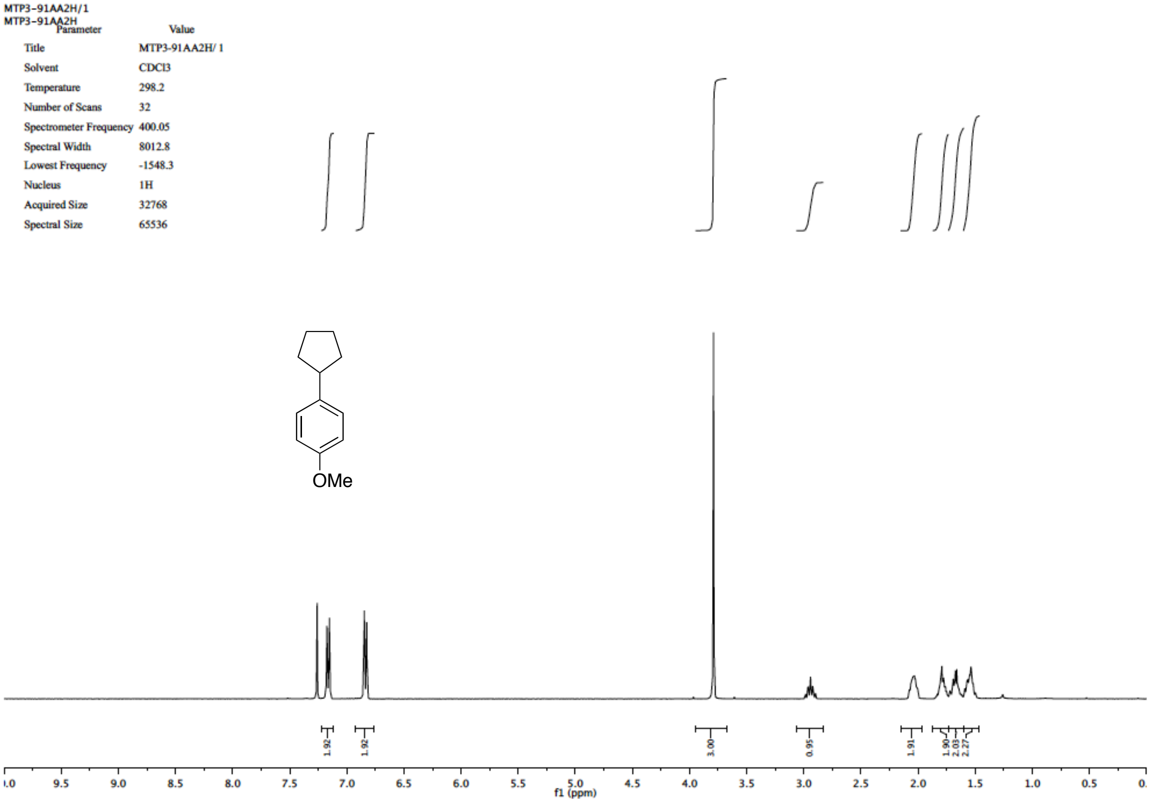


SFR_4_816_13C

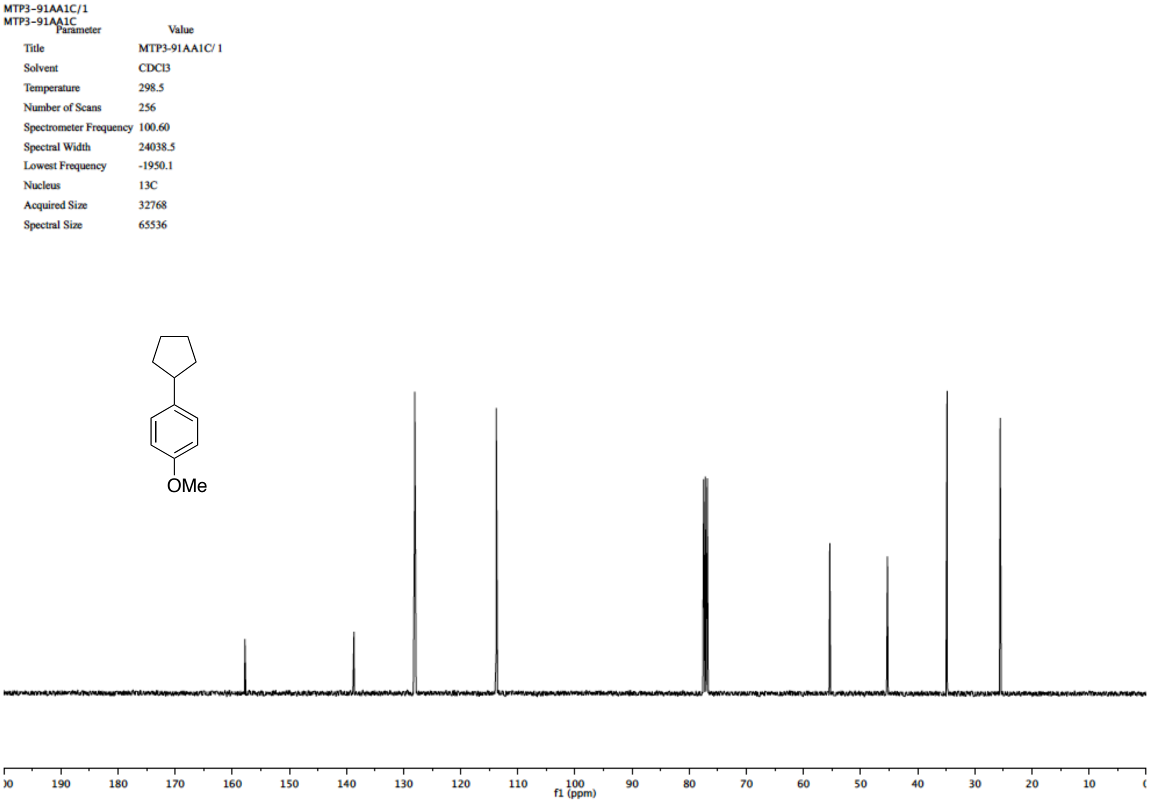
Parameter	Value
Title	SFR_4_816_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	256
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1949.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



1-cyclopentyl-4-methoxybenzene (5a)

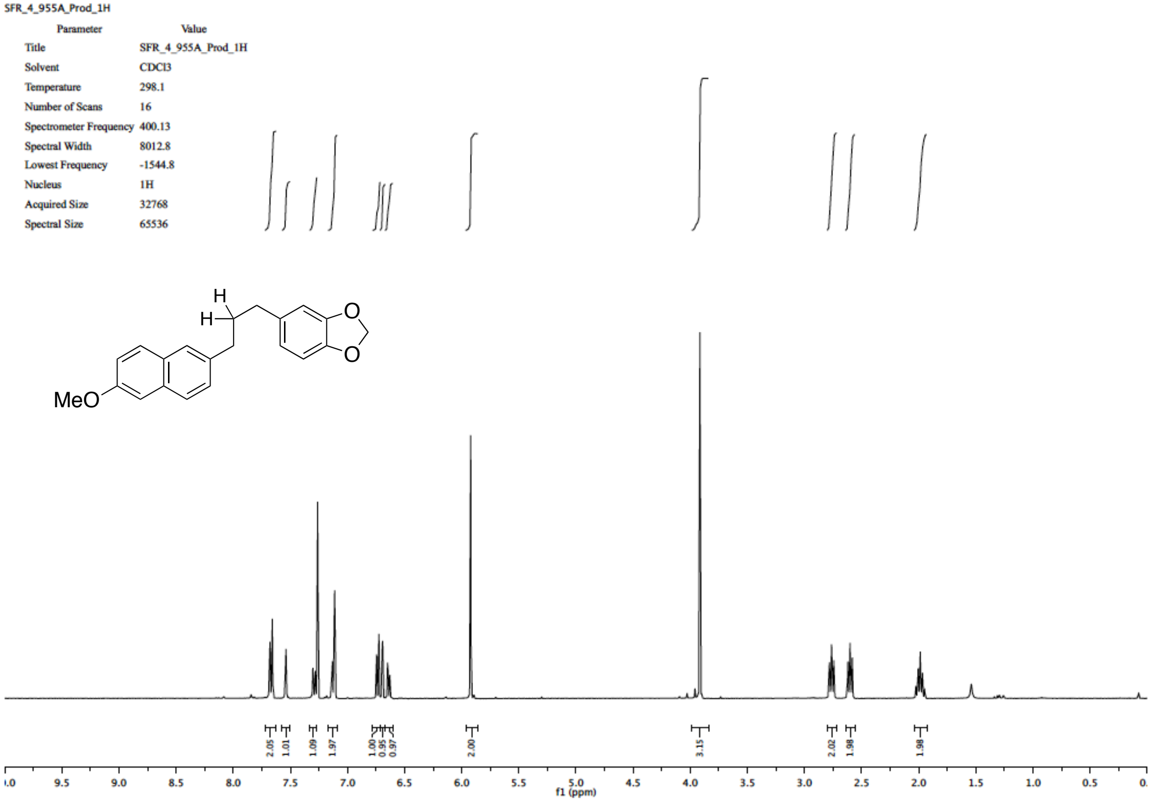


Parameter	Value
Title	MTP3-91AA2H/ 1
Solvent	CDCl3
Temperature	298.2
Number of Scans	32
Spectrometer Frequency	400.05
Spectral Width	8012.8
Lowest Frequency	-1548.3
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



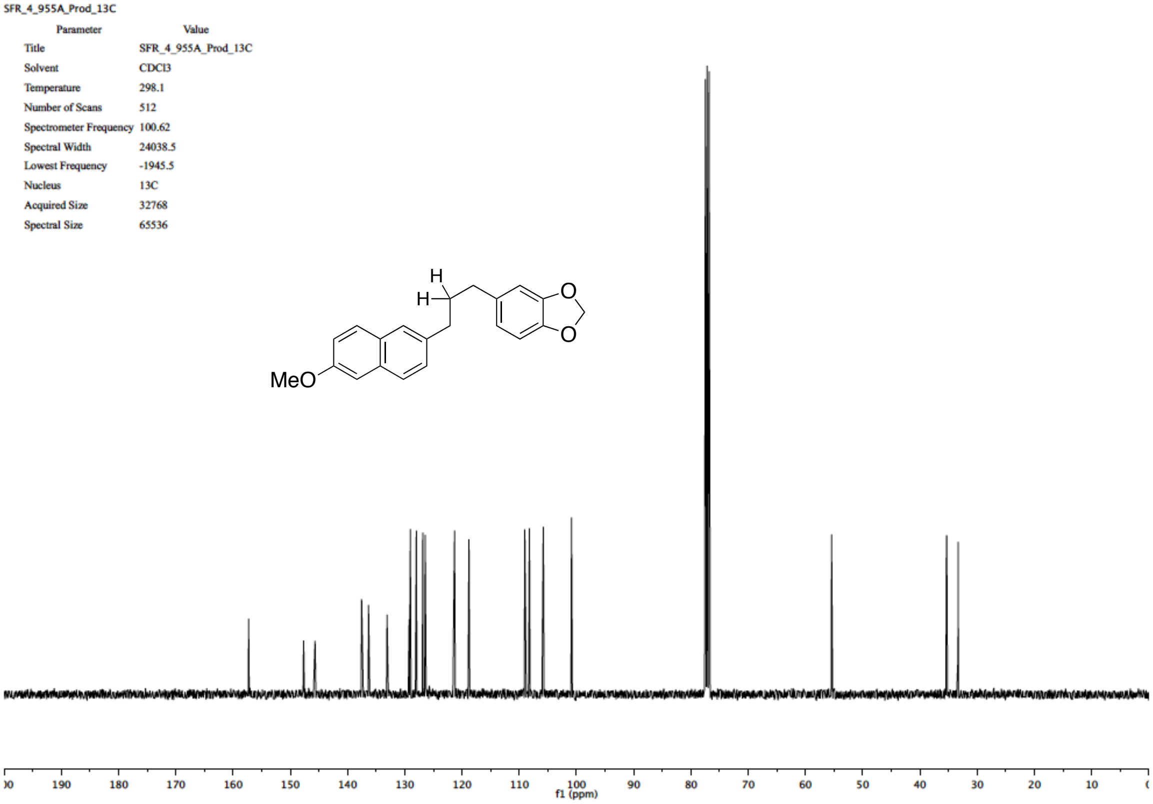
Parameter	Value
Title	MTP3-91AA1C/ 1
Solvent	CDCl3
Temperature	298.5
Number of Scans	256
Spectrometer Frequency	100.60
Spectral Width	24038.5
Lowest Frequency	-1950.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

5-(3-(6-methoxynaphthalen-2-yl)propyl)benzo[*d*][1,3]dioxole (3r)



SFR_4_955A_Prod_1H

Parameter	Value
Title	SFR_4_955A_Prod_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1544.8
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



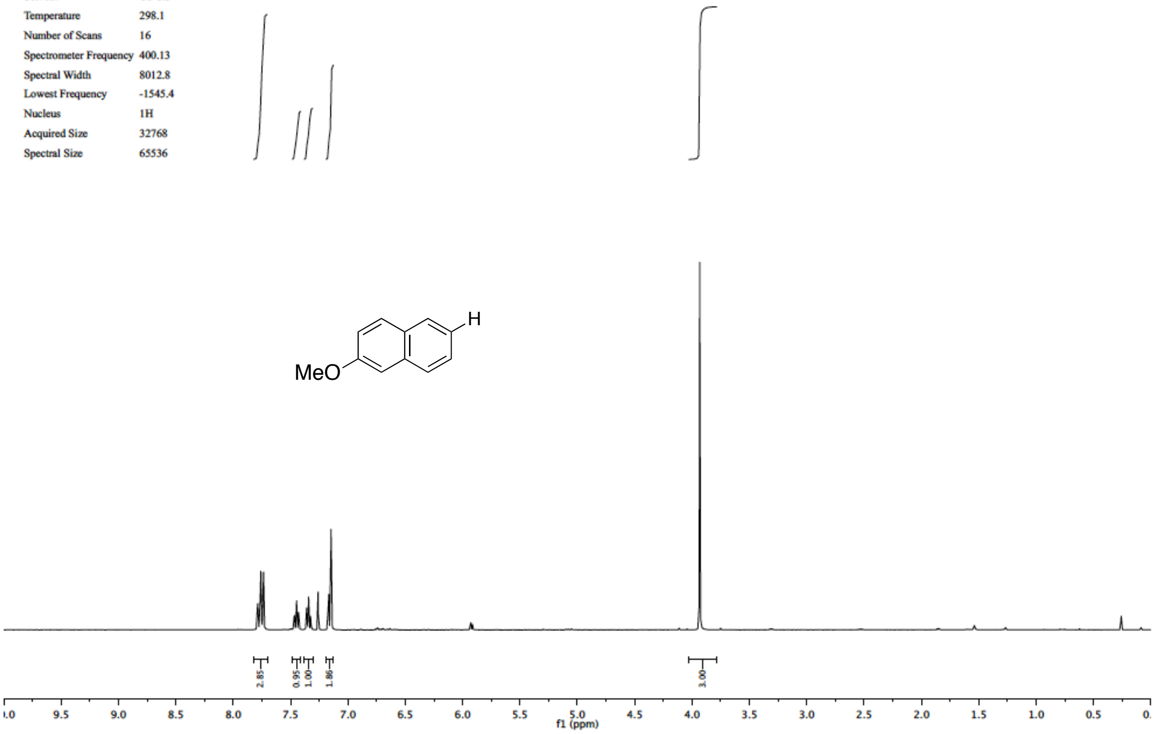
SFR_4_955A_Prod_13C

Parameter	Value
Title	SFR_4_955A_Prod_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	512
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1945.5
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

2-methoxynaphthalene (6r)

SFR_4_955A_Ar_1H

Parameter	Value
Title	SFR_4_955A_Ar_1H
Solvent	CDCl3
Temperature	298.1
Number of Scans	16
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



SFR_4_955A_Ar_13C

Parameter	Value
Title	SFR_4_955A_Ar_13C
Solvent	CDCl3
Temperature	298.1
Number of Scans	512
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1945.0
Nucleus	13C
Acquired Size	32768
Spectral Size	65536