Palladium-Catalyzed C–O Cross-Coupling of Primary Alcohols

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Supporting Information

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I. General Information

A) General Reagent Information

Tetrahydrofuran (THF), toluene and dichloromethane (CH_2Cl_2) were purchased from J.T. Baker in CYCLE-TAINER® solvent-delivery kegs and vigorously purged with argon for 2 h, followed by passing it under argon pressure through two packed columns of neutral alumina. Anhydrous 1,4-dioxane was purchased from Sigma-Aldrich in Sure-Seal^{TM} bottles and used as received. Sodium *tert*-butoxide (NaO*t*-Bu) was purchased from Sigma-Aldrich and stored in a nitrogen-filled glovebox. Small quantities were stored on the bench in a desiccator and used within a week. *t*-BuBrettPhos (**L2**), BrettPhos (**L4**), 2-iodo-2',4',6'-triisopropyl-3,6-dimethoxybiphenyl (**S2**) and 1-adamantylzinc bromide solution (0.5 M in THF) were received as gifts from Sigma-Aldrich, which we are grateful for. RockPhos (**L1**),[1] AdBrettPhos (**L3**),[2] *t*-BuAdBrettPhos (**L6**),[2] 2-aminobiphenylpalladium methanesulfonate dimer (**S5**),[3a] precatalysts **P1–4**[3] were prepared following the literature procedures. All other reagents were purchased from Sigma-Aldrich, Strem Chemicals, Acros Organics, Alfa Aesar, TCI America, Combi Blocks, Oakwood Chemical and Matrix Scientific and used as received. Compounds were purified by flash chromatography with manually loaded Silicycle SiliaFlash® F60 silica gel (40–63 µm, 230–400 mesh, 60 Å pore) or with the aid of a Biotage® Isolera system, employing polypropylene cartridges preloaded with silica gel (Silicycle SiliaFlash® F60 silica gel) or with new Biotage® SNAP cartridges.

B) General Analytical Information

All compounds were characterized by ^1H and ^{13}C NMR, as well as ^{19}F and ^{31}P NMR where applicable. New compounds were also characterized by IR spectroscopy, melting point (if solid) and elemental analysis or high-resolution mass spectrometry. Copies of ^1H, ^{13}C, ^{19}F and ^{31}P NMR spectra can be found at the end of the Supporting Information. NMR experiments were performed on a Varian 500 MHz, a JEOL 500 MHz, or a Varian 300 MHz spectrometer. All chemical shifts are reported in δ, parts per million (ppm). ^1H and ^{13}C NMR signals were calibrated with the residual chloroform signal (δ 7.26 ppm and δ 77.23 ppm, respectively). ^{19}F and ^{31}P NMR spectra were referenced to an external standard of neat trifluorotoluene (δ –63.72 ppm) and H_3PO_4 (δ 0.00 ppm), respectively. Both ^{13}C and ^{31}P NMR experiments were carried out with decoupling on the ^1H channel. IR spectra were obtained on a Thermo Scientific iD5 ATR Nicolet iS5 FT-IR spectrometer. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA, USA. Melting points were obtained on a Mel-Temp capillary melting point apparatus. High Resolution Mass Spectra were obtained on a Bruker Daltonics APEXIV 4.7 Tesla Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR-MS). 1,1,2,2-tetrachloroethane and dodecane were used as standards for yields determined by ^{1}H NMR analysis and conversions determined by GC analysis, respectively. All isolated yields reported in Tables 2 and 3 of the manuscript represent an average value from two experiments.

II. Experimental Procedures and Characterization Data

A) Ligand Synthesis and Characterization

General Procedure A:

An oven-dried Schlenk tube, equipped with a magnetic stir bar and fitted with a rubber septum, was charged with 2-iodo-2',4',6'-triisopropyl-3,6-dimethoxybiphenyl (**S2**) (1.00 equiv). The Schlenk tube was evacuated and backfilled with argon (this process was repeated a total of three times). THF was added via syringe and the reaction mixture was cooled to −78 °C in a dry ice/acetone bath. *t*-BuLi (1.7 M in pentane, 2.1 equiv) was added dropwise via syringe. An additional 2–5 mL of THF was used to rinse the reaction vessel. The resulting solution was stirred at –78 °C for 1 h. After 1 h, the septum was replaced with a Teflon stopper under a positive pressure of argon, and pentane from the *t*-BuLi solution was removed under vacuum with the aid of an external trap (Figure S1). When the solvent level reached 2/3 of the initial volume, the Schlenk tube was backfilled with argon and CuCl (1.50 equiv) was added rapidly under a positive pressure of argon. The tube was sealed with a rubber septum and slowly warmed to rt over 30 min. Then, a solution of chlorophosphine (**S1, S3** or **S4)** in toluene was transferred via cannula into the reaction mixture (Note: when toluene was added to the crude mixture of chlorophosphine, the insoluble

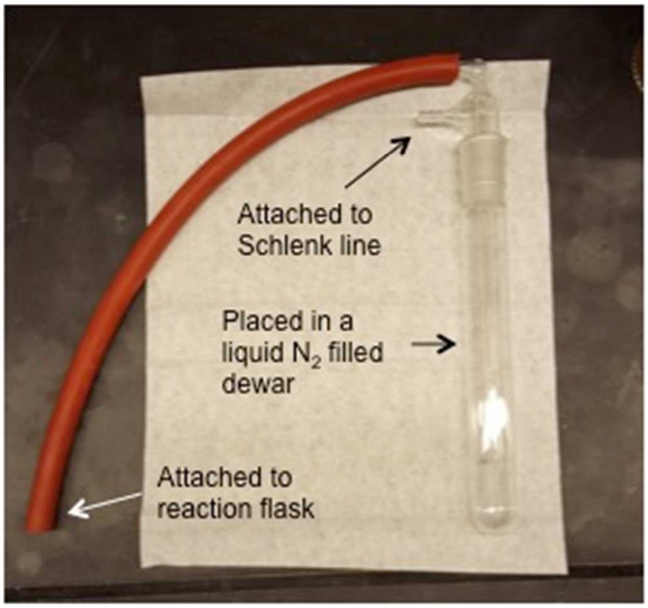
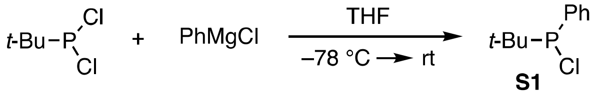


Figure S1. External trap for solvent removal.

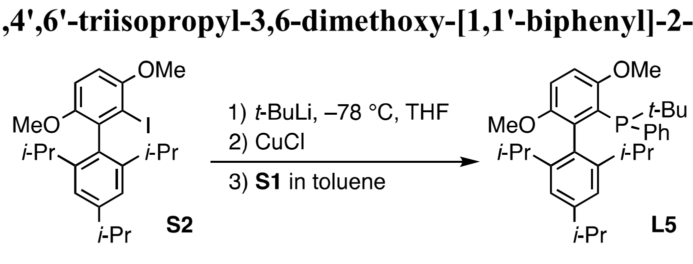
solids were allowed to settle at the bottom of the flask and the precipitate was not transferred into the reaction flask). An additional 5 mL of toluene was used to rinse the reaction vessel. The rubber septum was replaced with the Teflon stopper under a flow of argon and the reaction vessel was heated to 140 °C in an oil bath. The mixture was vigorously stirred for 24 h, turning from dark grey to a pinkish brown color. The reaction mixture was cooled to rt, diluted with EtOAc, and washed with a mixture of 30% NH_4OH and brine, until the aqueous layer was no longer blue. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The resulting solid was triturated in MeOH, filtered and purified by silica gel chromatography (gradient elution: 100% CH_2Cl_2 to 50% EtOAc in CH_2Cl_2).

a) Synthesis of **L5**:



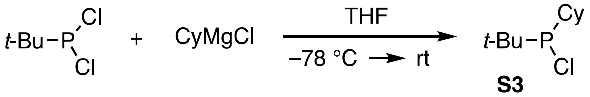
An oven-dried 50 mL round-bottom flask, equipped with a magnetic stir bar and fitted with a rubber septum, was brought into a nitrogen-filled glovebox. *t*-$BuPCl_2$ (318 mg, 2.00 mmol, 1.00 equiv) was added, and the reaction flask was recapped with the septum, taken outside the glovebox and cooled to –78 °C in a dry ice/acetone bath. A separate oven-dried 25 mL round-bottom flask equipped with a stir bar was evacuated and backfilled with argon (this process was repeated a total of three times). PhMgCl (2.0 M in THF, 1.2 mL, 2.4 mmol, 1.2 equiv) and THF (8.4 mL) were added via syringe. The combined solution was transferred via cannula to the 50-mL reaction flask. The resulting mixture was stirred at –78 °C for 30 min, warmed to rt and stirred for an additional 3 h. An aliquot was taken for ^{31}P NMR analysis to confirm the completion of the reaction (*Caution: **S1** is air- and moisture-sensitive). The solvent was removed under vacuum with the aid of an external trap (Figure S1) and the reaction flask was backfilled with argon and stored in the glovebox.

***tert*-butyl(phenyl)(2',4',6'-triisopropyl-3,6-dimethoxy-[1,1'-biphenyl]-2-yl)phosphane (L5):**



Following General Procedure A, a mixture of **S2** (622 mg, 1.33 mmol, 1.00 equiv), THF (8 mL), *t*-BuLi (1.7 M in pentane, 1.7 mL, 2.8 mmol, 2.1 equiv), CuCl (198 mg, 2.00 mmol, 1.50 equiv), a solution of **S1** in toluene (20 mL) was stirred at 140 °C for 24 h. The crude mixture was purified by silica gel chromatography (gradient elution: 100% CH_2Cl_2 to 50% EtOAc in CH_2Cl_2) to provide a white solid (214 mg, 32% yield). **mp** = 160–162 °C. **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.17–7.13 (m, 5H), 6.99–6.94 (m, 3H), 6.77 (s, 1H), 3.79 (s, 3H), 3.61 (s, 3H), 2.90 (hept, *J* = 6.5 Hz, 1H), 2.58 (hept, *J* = 7.0 Hz, 1H), 2.00 (hept, *J* = 7.0 Hz, 1H), 1.27 (d, *J* = 7.0 Hz, 6H), 1.25 (d, *J* = 7.0 Hz, 3H), 1.08 (d, *J* = 13.5 Hz, 9H), 1.03 (d, *J* = 7.0 Hz, 3H), 0.76 (d, *J* = 6.5 Hz, 3H), 0.19 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 155.7, 155.7, 152.7, 152.6, 147.0, 146.9, 146.8, 145.4, 145.4, 140.5, 138.7, 138.5, 133.0, 132.8, 132.7, 127.4, 127.4, 126.8, 125.6, 125.3, 120.2, 120.0, 111.9, 108.9, 55.2, 54.5, 34.0, 31.7, 31.5, 31.0, 30.8, 30.7, 25.1, 25.0, 24.2, 24.2, 23.8, 22.0 ppm (the observed complexity is due to C–P coupling). **^{31}P NMR** (203 MHz, Chloroform-d) δ 11.4 ppm. **IR** (neat, cm^{-1}) 2954, 1458, 1422, 1253, 1089, 1047, 1019, 872, 798, 747 711. **EA** Calcd. for $C_{33}H_{45}O_2P$: C, 78.54; H, 8.99, Found: C, 77.88; H, 8.90.

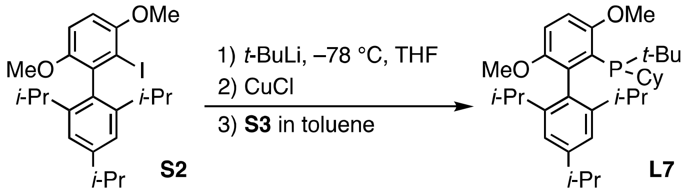
b) Synthesis of **L7**:



S3

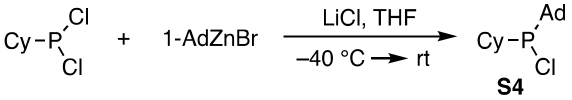
An oven-dried 50 mL round-bottom flask, equipped with a magnetic stir bar and fitted with a rubber septum, was brought into a nitrogen-filled glovebox. *t*-$BuPCl_2$ (318 mg, 2.00 mmol, 1.00 equiv) was added, and the reaction flask was recapped with the septum, taken outside the glovebox and cooled to –78 °C in a dry ice/acetone bath. A separate oven-dried 25 mL round-bottom flask equipped with a stir bar was evacuated and backfilled with argon (this process was repeated a total of three times). CyMgCl (1.0 M in 2-MeTHF, 2.40 mL, 2.40 mmol, 1.20 equiv) and THF (7.2 mL) were added via syringe. The combined solution was transferred via cannula to the 50-mL reaction flask. The resulting mixture was stirred at –78 °C for 30 min, warmed to rt and stirred for an additional 3 h. An aliquot was taken for ^{31}P NMR analysis to confirm the completion of the reaction (*Caution: **S3** is air- and moisture-sensitive). The solvent was removed under vacuum with the aid of an external trap (Figure S1) and the reaction flask was backfilled with argon and stored in the glovebox.

***tert*-butyl(cyclohexyl)(2',4',6'-triisopropyl-3,6-dimethoxy-[1,1'-biphenyl]-2-yl)phosphane (L7):**



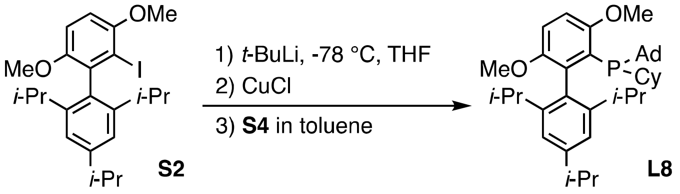
Following General Procedure A, a mixture of **S2** (622 mg, 1.33 mmol, 1.00 equiv), THF (8 mL), *t*-BuLi (1.7 M in pentane, 1.7 mL, 2.8 mmol, 2.1 equiv), CuCl (198 mg, 2.00 mmol, 1.50 equiv), and a solution of **S3** in toluene (20 mL) was stirred at 140 °C for 24 h. The crude mixture was purified by silica gel chromatography (gradient elution: 100% CH_2Cl_2 to 50% EtOAc in CH_2Cl_2) to provide a white solid (340 mg, 50% yield). **mp** = 129–131 °C. ^{1}**H NMR** (500 MHz, Chloroform-d) δ 6.96 (d, *J* = 2.0 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.77 (d, *J* = 8.9 Hz, 1H), 3.81 (s, 3H), 3.56 (s, 3H), 2.93 (hept, *J* = 7.0 Hz, 1H), 2.48–2.43 (m, 2H), 2.43–2.41 (m, 1H), 1.71–1.64 (m, 4H), 1.31 (dd, *J* = 6.9, 1.5 Hz, 6H), 1.28–1.27 (m, 1H), 1.24 (d, *J* = 6.8 Hz, 3H), 1.21–1.19 (m, 1H), 1.19–1.10 (m, 6H), 1.03 (d, *J* = 11.7 Hz, 9H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.93–0.92 (m, 1H), 0.89 (d, *J* = 6.7 Hz, 3H). ^{13}**C NMR** (126 MHz, Chloroform-d) δ 156.2, 152.6, 152.5, 147.1, 146.3, 146.2, 140.0, 139.7, 132.8, 132.8, 127.5, 127.3, 120.3, 110.8, 108.0, 54.8, 54.7, 34.1, 34.0, 33.8, 33.7, 31.9, 31.8, 30.7, 30.7, 29.7, 29.6, 29.5, 28.3, 28.2, 27.3, 27.2, 26.8, 25.6, 25.3, 24.4, 24.2, 24.0, 23.7 ppm (the observed complexity is due to C–P coupling). ^{31}**P NMR** (203 MHz, Chloroform-d) δ 10.1 ppm. **IR** (neat, cm^{-1}) 2954, 1458, 1422, 1253, 1089, 1047, 1019, 872, 798, 760, 747. **EA** Calcd. for $C_{33}H_{51}O_2P$: C, 77.61; H, 10.07, Found: C, 77.43; H, 10.06.

c) Synthesis of **L8**:



An oven-dried 250 mL three-neck round-bottom flask, equipped with a magnetic stir bar and fitted with a glass stopper and two rubber septa, was evacuated and backfilled with argon (this process was repeated a total of three times). $CyPCl_2$ (1.25 g, 6.76 mmol, 1.00 equiv, stored in a nitrogen-filled glovebox) was added via syringe and the reaction flask was cooled to –40 °C in a dry ice/acetonitrile bath. A separate oven-dried 100 mL round-bottom flask equipped with a stir bar was evacuated and backfilled with argon (this process was repeated a total of three times). A solution of AdZnBr (0.5 M in THF, 14.9 mL, 7.43 mmol, 1.10 equiv) and a solution of LiCl (0.5 M in THF, 14.9 mL, 7.43 mmol, 1.10 equiv) were added via syringe. The combined solution was transferred via cannula to the three-neck reaction flask. The resulting mixture was stirred at –40 °C for 30 min, warmed to rt and stirred for an additional 3 h. An aliquot was taken for ^{31}P NMR analysis to confirm the completion of the reaction (*Caution: **S4** is air- and moisture-sensitive). The solvent was removed under vacuum with the aid of an external trap (Figure S1) and the reaction flask was backfilled with argon and stored in the glovebox.

((3*r*)-adamantan-1-yl)(cyclohexyl)(2',4',6'-triisopropyl-3,6-dimethoxy-[1,1'-biphenyl]-2-yl)phosphane (L8):

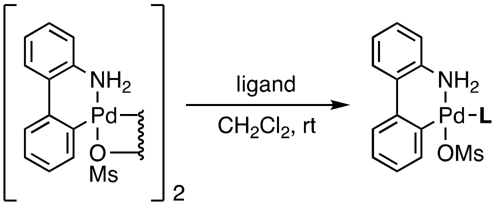


Following General Procedure A, a mixture of **S2** (2.63 g, 5.63 mmol, 1.00 equiv), THF (30 mL), *t*-BuLi (1.7 M in pentane, 7.0 mL, 11.8 mmol, 2.1 equiv), CuCl (836 mg, 8.45 mmol, 1.5 equiv), and a solution of **S4** in toluene (75 mL) was stirred at 140 °C for 24 h. The crude mixture was purified by silica gel chromatography (gradient elution: 100% CH_2Cl_2 to 50% EtOAc in CH_2Cl_2) to provide a white solid (2.33 g, 70% yield). **mp** = 224–226 °C. **^{1}H NMR** (500 MHz, Chloroform-d) δ 6.96 (s, 2H), 6.85 (d, *J* = 8.7 Hz, 1H), 6.78 (d, *J* = 8.8 Hz, 1H), 3.83 (s, 3H), 3.55 (s, 3H), 2.94 (p, *J* = 6.9 Hz, 1H), 2.52 (ddq, *J* = 8.9, 5.8, 3.1 Hz, 1H), 2.43 (dq, *J* = 20.3, 6.8 Hz, 2H), 1.91-1.76 (m, 6H), 1.73-1.55 (m, 13H), 1.31 (dt, *J* = 7.1, 1.4 Hz, 6H), 1.24 (d, *J* = 6.7 Hz, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.20-1.06 (m, 4H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ 156.2, 152.6, 152.6, 147.0, 146.4, 146.1, 140.2, 139.9, 132.9, 132.8, 126.7, 126.4, 120.3, 120.2, 110.7, 107.9, 54.9, 54.7, 42.5, 42.4, 37.2, 34.8, 34.5, 34.0, 33.2, 33.0, 31.8, 31.6, 30.7, 30.6, 30.0, 29.8, 29.6, 28.3, 28.3, 27.3, 27.2, 26.9, 25.5, 25.3, 24.4, 24.3, 24.0, 23.8 ppm (the observed complexity is due to C–P coupling). **^{31}P NMR** (203 MHz, Chloroform-d) δ 12.4 ppm. **IR** (neat, cm^{-1}) 2899, 1582, 1458, 1421, 1302, 1249, 1169, 1086, 1043, 1017, 873, 798, 760, 713. **HRMS** Calcd. for $C_{39}H_{57}O_2P$: 588.41, Found: [M+H] = 589.41.

B) Precatalyst Synthesis and Characterization

All precatalysts were synthesized according to a modified literature procedure.[3b]

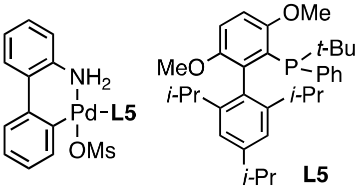
General Procedure B:



S5

A 25 mL screw-top oven-dried test tube (Fisher Scientific 20 × 125 mm tubes, Cat. No. 1495937A) equipped with a stir bar and sealed with a screw cap (Kimble Chase Open Top S/T Closure, Cat. No. 73804-18400) and a Teflon septum (Thermo Scientific PTFE: 0.010” silicone: 0.090”, Cat. No. B7995-18) was charged with 2-aminobiphenylpalladium methanesulfonate dimer (**S5**, 0.45 equiv) and ligand (1.00 equiv). The reaction tube was recapped. The septum was pierced with a needle attached to a Schlenk line, and the tube was evacuated and backfilled with argon (this process was repeated a total of three times). CH_2Cl_2 was added via syringe. The slurry mixture became a colored homogeneous solution within 30 min and was stirred at rt overnight. The crude mixture was concentrated *in vacuo* and triturated with diethyl ether with the aid of sonication until a free-flowing powder resulted. The solid was isolated by filtration and dried under high vacuum.

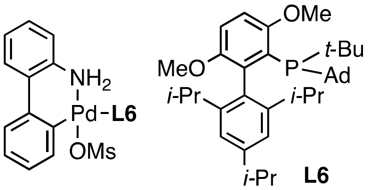
L5-OMs precatalyst (P5):



Following General Procedure B, a mixture of **S5** (33 mg, 0.045 mmol, 0.45 equiv), **L5** (50 mg, 0.010 mmol, 1.0 equiv), CH_2Cl_2 (3.0 mL) was stirred at rt overnight. The reaction mixture became a light brown homogeneous solution. The crude mixture was purified by trituation with diethyl ether to provide an off-white solid (52 mg, 60%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.51 (t, J = 7.5 Hz, 1H), 7.39–7.35 (m, 4H), 7.18–7.13 (m, 3H), 7.12–7.00 (m, 5H), 6.83–6.76 (m, 1H), 6.70 (td, J = 7.5 Hz, 2.0 Hz, 1H), 5.88 (dd, J = 7.5 Hz, 5.0 Hz, 1H), 5.74 (dd, J = 10.0 Hz, 4.0 Hz, 1H), 3.50 (s, 3H), 3.48 (s, 3H), 3.31 (heptet, J = 7.0 Hz, 1H), 2.69 (heptet, J = 7.0

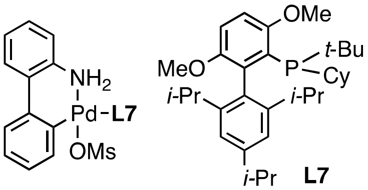
Hz, 1H), 2.47 (heptet, *J* = 7.0 Hz, 1H), 2.36 (s, 3H), 1.54 (d, *J* = 7.0 Hz, 3H), 1.51 (d, *J* = 7.0 Hz, 3H), 1.46 (d, *J* = 7.0 Hz, 3H), 1.05 (d, *J* = 17 Hz, 9H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 157.1, 155.9, 154.3, 154.0, 151.9, 151.8, 145.1, 140.4, 139.3, 136.3, 136.0, 135.9, 135.5, 135.5, 130.6, 128.5, 128.4, 128.1, 127.3, 126.8, 126.1, 125.9, 125.2, 122.4, 120.5, 118.5, 118.5, 116.0, 115.9, 113.3, 113.2, 55.3, 39.2, 37.3, 37.1, 34.4, 33.0, 32.0, 31.9, 31.5, 26.7, 24.9, 24.8, 24.7, 24.6, 24.6 ppm (the observed complexity is due to C–P coupling). **^{31}P NMR** (203 MHz, Chloroform-d) δ 52.5 ppm. **IR** (neat, cm^{-1}) 1460, 1426, 1221, 1181, 1034, 1009, 890, 825, 756, 746.

L6-OMs precatalyst (P6):



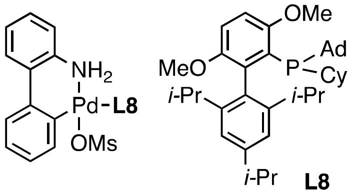
Following General Procedure B, a mixture of **S5** (30 mg, 0.040 mmol, 0.45 equiv), **L6** (50 mg, 0.089 mmol, 1.0 equiv), CH_2Cl_2 (3.0 mL) was stirred at rt overnight. The reaction mixture became a dark red homogeneous solution. The crude mixture was purified by trituation with diethyl ether to provide a dark red solid (50 mg, 60%). **^{1}H NMR** (500 MHz, Chloroform-d) complex spectrum – see attached. **^{13}C NMR** (126 MHz, Chloroform-d) δ 150.5, 147.7, 139.9, 126.7, 126.3, 125.7, 123.2, 121.5, 121.4, 120.1, 120.0, 119.0, 111.1 57.3, 55.2, 42.2, 41.6, 39.7, 39.6, 37.1, 36.9, 36.0, 35.5, 34.2, 34.2, 31.4, 31.3, 29.8, 29.2, 28.7, 28.2, 28.1, 25.9, 24.9, 24.7, 24.0, 24.0, 23.3, 23.2, 22.4, 14.2 ppm (the observed complexity is due to C–P coupling). **^{31}P NMR** (203 MHz, Chloroform-d) δ 82.7, 42.0 ppm. **IR** (neat, cm^{-1}) 1461, 1420, 1253, 1174, 1146, 1037, 1008, 887, 806, 754, 733.

L7-OMs precatalyst (P7):



Following General Procedure B, a mixture of **S5** (33 mg, 0.044 mmol, 0.45 equiv), **L7** (50 mg, 0.098 mmol, 1.0 equiv), CH_2Cl_2 (3.0 mL) was stirred at rt overnight. The reaction mixture became a light brown homogenous solution. The crude mixture was purified by trituation with diethyl ether to provide an off-white solid (47 mg, 55%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.45 (d, *J* = 1.5 Hz, 1H), 7.37 (dd, *J* = 5.5 Hz, 2.0 Hz, 1H), 7.32 (d, *J* = 1.5 Hz, 1H), 7.17–7.12 (m, 3H), 7.12–7.05 (m, 3H), 7.01 (d, *J* = 9.0 Hz, 1H), 6.72 (d, *J* = 6.5 Hz, 1H), 5.93 (d, *J* = 6.0 Hz, 1H), 3.84 (s, 3H), 3.47 (q, *J* = 7.0 Hz, 2H), 3.40 (s, 3H), 3.33 (heptet, *J* = 7.0 Hz, 1H), 2.63 (heptet, *J* = 6.5 Hz, 1H), 2.43 (s, 3H), 2.29 (heptet, *J* = 6.5 Hz, 1H), 1.19–1.75 (m, 6H), 1.55 (d, *J* = 6.5 Hz, 3H), 1.47 (d, *J* = 7.0 Hz, 3H), 1.32–1.23 (m, 2H), 1.23–1.11 (m, 4H), 0.91 (d, *J* = 15.5 Hz, 9H), 0.88–0.81 (m, 9H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 158.7, 156.1, 154.4, 151.5, 151.4, 140.3, 139.3, 136.6, 136.1, 128.0, 127.0, 126.8, 126.5, 125.8, 125.4, 122.7, 120.6, 117.8, 115.1, 112.2, 66.0, 54.8, 54.6, 39.2, 34.3, 32.9, 31.7, 30.3, 28.9, 28.2, 28.1, 27.6, 27.5, 26.3, 25.4, 25.2, 24.9, 24.8, 24.5, 13.4 ppm (the observed complexity is due to C–P coupling). **^{31}P NMR** (203 MHz, Chloroform-d) δ 58.8 ppm. **IR** (neat, cm^{-1}) 1461, 1429, 1219, 1182, 1035, 1008, 1002, 890, 819, 754, 736.

L8-OMs precatalyst (P8):



Following General Procedure B, a mixture of **S5** (233 mg, 0.315 mmol, 0.450 equiv), **L8** (412 mg, 0.700 mmol, 1.00 equiv), CH_2Cl_2 (5.0 mL) was stirred at rt overnight. The reaction mixture became a light brown clear solution. The crude mixture was purified by trituation with diethyl ether to provide an off-white solid (507 mg, 76%). **^{1}H NMR** (500 MHz, Chloroform-d) 7.44 (t, *J* = 3.6 Hz, 2H), 7.33 (d, *J* = 1.8 Hz, 1H), 7.22–7.11 (m, 4H), 7.11–7.06 (m, 2H), 7.02 (d, *J* = 8.9 Hz, 1H), 6.77–6.71 (m, 1H), 5.82 (s, 1H), 3.87 (s, 3H), 3.41 (s, 3H), 3.31 (heptet, *J* = 6.5 Hz, 1H), 2.70–2.57 (m, 1H), 2.48 (s, 3H), 2.33 (heptet, *J* = 6.5 Hz, 1H), 2.13–1.77 (m, 10H), 1.77–1.63 (m, 5H), 1.61–1.55 (m, 3H), 1.54 (d, *J* = 7.0 Hz, 3H), 1.52–1.43 (m, 6H), 1.43–1.33 (m, 3H), 1.33–1.13 (m, 5H), 0.99–0.85 (m, 6H), 0.83 (d, *J* = 7.0 Hz, 3H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ 159.3, 156.3, 154.6, 154.1, 151.6, 151.4, 139.3, 136.5, 136.1, 135.9, 128.1, 127.2, 126.9, 126.6, 125.8, 125.2, 122.8, 120.6, 117.8, 115.1, 112.5, 55.0, 54.7, 40.5, 39.3, 36.1, 34.4, 34.0, 33.8, 32.9, 31.9, 29.2, 28.8, 28.7, 28.3, 27.7, 27.6, 26.4, 25.5, 25.2, 25.0, 24.8, 24.6

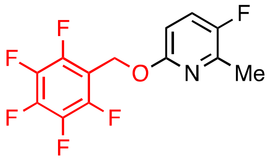
ppm (the observed complexity is due to C–P coupling). **^{31}P NMR** (203 MHz, Chloroform-d) δ 58.9 ppm. **IR** (neat, cm^{-1}) 1461, 1224, 1183, 1036, 1008, 1001, 822, 753, 739.

C) *O*-Arylation of Primary Alcohols

General Procedure C:

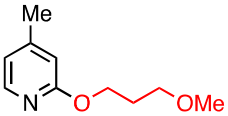
A 25 mL screw-top oven-dried test tube (Fisher Scientific 20 × 125 mm tubes, Cat. No. 1495937A) equipped with a stir bar and sealed with a screw cap (Kimble Chase Open Top S/T Closure, Cat. No. 73804-18400) and two Teflon septa (Thermo Scientific PTFE: 0.010" silicone: 0.090", Cat. No. B7995-18) was charged with aryl halide (if solid, 1.00 mmol, 1.00 equiv), alkyl alcohol, (if solid, 2.00 mmol, 2.00 equiv), precatalyst **P2** (8.5–17 mg, 1.0–2.0 mol %) or **P8** (9.6––24 mg, 1.0–2.5 mol %), and NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv). The reaction tube was recapped. The septum was pierced with a needle attached to a Schlenk line, and the tube was evacuated and backfilled with argon (this process was repeated a total of three times). Aryl halide and/or alkyl alcohol (if liquid) followed by 1,4-dioxane (1.0 mL) were added via syringe. The screw cap and the Teflon septum were wrapped completely with parafilm®. The reaction mixture was sonicated until there were no visible chunks of NaO*t*-Bu. The reaction was stirred at the time and temperature as indicated for each substrate. If heated, the reaction was allowed to cool to rt before addition of EtOAc (2 mL). The reaction slurry was then filtered through a pad of Celite® and rinsed with EtOAc. The crude material was concentrated *in vacuo* and purified via silica gel chromatography. In cases where the excess alcohol and the product were inseparable as determined by TLC analysis after workup, the crude reaction mixture was further treated successively with *N*,*N*-dimethylpyridin-4-amine (DMAP, 1.0–2.0 mg), triethylamine (Et_3N, 140–167 µL, 1.00–1.20 mmol, 1.00–1.20 equiv), acetic anhydride (Ac_2O, 56–113 µL, 0.65–1.20 mmol, 0.65–1.20 equiv). The resulting solution was stirred for 1 h at rt, concentrated *in vacuo*, and purified by silica gel chromatography.

3-fluoro-2-methyl-6-((perfluorophenyl)methoxy)pyridine (5):



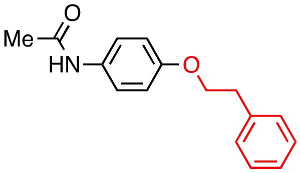
Following General Procedure C, a mixture of 6-bromo-3-fluoro-2-methylpyridine (190 mg, 1.00 mmol, 1.00 equiv), (perfluorophenyl)methanol (396 mg, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (8.5 mg, 1.0 mol %), and 1,4-dioxane (1.0 mL) was stirred at rt for 6 h. The crude mixture was purified by flash column chromatography (gradient elution: 100% hexanes to 5% EtOAc in hexanes) to provide the title compound as a colorless low melting solid (1st run: 289 mg, 94%; 2nd run: 271 mg, 88%). **mp** = 39–41 °C. **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.24 (t, *J* = 10.0 Hz, 1H), 6.52 (d, *J* = 10.0 Hz, 1H), 5.39 (s, 2H), 2.40 (s, 3H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ 157.7, 154.9–153.0 (d, *J* = 239.4 Hz), 147.0–145.1 (dm, *J* = 239.4 Hz), 142.7–140.7 (dm, *J* = 252 Hz), 142.6–142.4 (d, *J* = 25.2 Hz), 138.7–136.7 (dtd, *J* = 252 Hz), 126.6–126.4 (d, *J* = 25.2 Hz), 111.3 (td, *J* = 17.5 Hz, 3.5 Hz), 108.9 (d, *J* = 3.8 Hz), 55.4, 17.6 ppm. **^{19}F NMR** (470 MHz, Chloroform-d) δ –136.4 (m), –141.8 (dd, *J* = 23.5, 9.4 Hz), –153.7 (t, *J* = 23.5 Hz), –162.3 (td, *J* = 23.5 Hz, 9.4 Hz) ppm. **IR** (neat, cm^{-1}) 1499, 1317, 1226, 1046, 932, 830, 798. **EA** Calcd. for $C_{13}H_7F_6NO$: C, 50.83; H, 2.30, Found: C, 50.66; H, 2.46.

2-(3-methoxypropoxy)-4-methylpyridine (6):



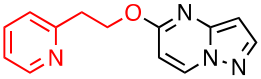
Following General Procedure C, a mixture of 2-chloro-4-methylpyridine (112 µL, 1.00 mmol, 1.00 equiv), 3-methoxypropan-1-ol (95 µl, 1.0 mmol, 1.0 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (8.5 mg, 1.0 mol %), and 1,4-dioxane (1.0 mL) was stirred at rt for 6 h. The crude mixture was purified by flash column chromatography (gradient elution: 100% hexanes to 25% EtOAc in hexanes) to provide the title compound as a yellow liquid (1st run: 147 mg, 82%; 2nd run: 156 mg, 86%). Note: due to the high volatility of the final compound, the use of high vacuum was avoided in the isolation process. **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.95 (d, *J* = 5.2 Hz, 1H), 6.63 (d, *J* = 5.2 Hz, 1H), 6.49 (s, 1H), 4.30 (t, *J* = 6.4 Hz, 2H), 3.49 (t, *J* = 6.4 Hz, 2H), 3.29 (s, 3H), 2.22 (s, 3H), 1.99 (quintet, *J* = 6.4 Hz, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ 164.4, 150.0, 146.6, 118.4, 111.2, 69.7, 63.0, 28.9, 29.6, 21.1 ppm. **IR** (neat, cm^{-1}) 2925, 2872, 1610, 1562, 1415, 1314, 1289, 1159, 1115, 1051, 811. **EA** Calcd. for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34, Found: C, 66.14; H, 8.48.

N-(4-phenethoxyphenyl)acetamide (7):



Following General Procedure C, a mixture of *N*-(4-chlorophenyl)acetamide (169 mg, 1.00 mmol, 1.00 equiv), 2-phenylethanol (240 µl, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (230 mg, 2.40 mmol, 2.40 equiv), **P2** (17 mg, 2.0 mol %), and dioxane (1.5 mL) was stirred at 40 °C for 15 h. The crude mixture was purified by flash column chromatography (gradient elution: 100% hexanes to 50% EtOAc in hexanes) to provide the title compound as a pale brown solid (1st run: 212 mg, 83%; 2nd run: 209 mg, 82%). **mp** = 96–98 °C. **^{1}H NMR** (500 MHz, Chloroform-d) δ 8.27 (s, 1H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.39–7.23 (m, 5H), 6.84 (d, *J* = 8.5 Hz, 2H), 4.14 (t, *J* = 7.0 Hz, 2H), 3.09 (t, *J* = 7.0 Hz, 2H), 2.12 (s, 3H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ 168.8, 155.7, 138.3, 131.3, 129.1, 128.6, 126.6, 122.2, 114.9, 69.0, 35.9, 24.3 ppm. **IR** (neat, cm^{-1}) 1657, 1605, 1556, 1510, 1474, 1371, 1241, 1173, 1031, 830, 726, 696, 611. **EA** Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71, Found: C, 75.55; H, 6.77.

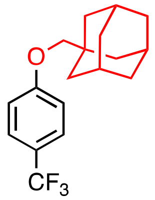
5-(2-(pyridin-2-yl)ethoxy)pyrazolo[1,5-*a*]pyrimidine (8):[4]



Following General Procedure C, a mixture of 5-chloropyrazolo[1,5-*a*]pyrimidine (154 mg, 1.00 mmol, 1.00 equiv), 2-pyridineethanol (169 µl, 1.50 mmol, 1.50 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (8.5 mg, 1.0 mol %), and dioxane (1.0 mL) was stirred at 40 °C for 15 h. The crude reaction mixture was diluted with EtOAc (1.0 mL), and DMAP (1.0 mg), Et_3N (139 µL, 1.00 mmol, 1.00 equiv) and Ac_2O (56 µL, 0.65 mmol, 0.65 equiv) were sequentially added. The new reaction mixture was stirred at rt and the reaction progress was monitored by TLC analysis (1:1 hexanes:EtOAc) until the excess alcohol was consumed (additional Ac_2O was added after 15 min). The resulting crude product was purified by flash column chromatography (gradient elution: 10% EtOAc in hexanes to 80% EtOAc in hexanes) to provide the title compound as a pale orange solid (1st run: 184 mg, 77%; 2nd run: 174 mg, 72%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 8.55 (ddd, *J* = 5.0, 1.9, 1.0 Hz, 1H), 8.37 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.93 (d, *J* = 2.2 Hz, 1H), 7.61 (td, *J* = 7.7, 1.9 Hz, 1H), 7.23 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.14 (ddd, *J* =

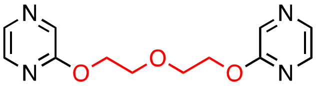
7.5, 4.8, 1.1 Hz, 1H), 6.30 (dd, *J* = 2.2, 0.8 Hz, 1H), 6.26 (d, *J* = 7.5 Hz, 1H), 4.77 (t, *J* = 6.7 Hz, 2H), 3.28 (t, *J* = 6.7 Hz, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ 161.3, 158.3, 149.6, 147.3, 145.0, 136.8, 136.5, 123.6, 121.7, 100.3, 94.6, 65.9, 37.5 ppm.

1-((4-(trifluoromethyl)phenoxy)methyl)adamantine (9):



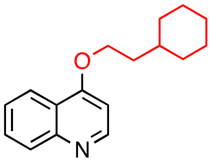
Following General Procedure C, a mixture of 1-bromo-4-(trifluoromethyl)benzene (140 µL, 1.00 mmol, 1.00 equiv), 1-adamantanemethanol (332 mg, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (8.5 mg, 1.0 mol %), and dioxane (1.0 mL) was stirred at rt for 6 h. The crude mixture was purified by flash column chromatography with 100% hexanes to provide the title compound as a white solid (1st run: 275 mg, 88%; 2nd run: 262 mg, 84%). **mp** = 133–134 °C. **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.53 (d, *J* = 8.6 Hz, 2H), 6.95 (d, *J* = 8.6 Hz, 2H), 3.53 (s, 2H), 2.03 (m, 3H), 1.77 (d, *J* = 12.0 Hz, 3H), 1.71 (d, *J* = 12.0 Hz, 3H), 1.66 (s, 6H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ 162.3, 128.0–121.5 (q, *J* = 264.6 Hz), 123.0–122.2 (q, *J* = 37.8 Hz), 126.9 (q, *J* = 3.8 Hz), 114.6, 78.6, 39.6, 37.3, 34.0, 28.4 ppm. **^{19}F NMR** (282 MHz, Chloroform-d) δ –62.7 ppm. **IR** (neat, cm^{-1}): 2902, 1320, 1309, 1264, 1162, 1155, 1108, 1067, 1024, 1008, 834, 812. **EA** Calcd. for $C_{18}H_{21}F_3O$: C, 69.66; H, 6.82, Found: C, 69.80; H, 6.81.

2,2'-((oxybis(ethane-2,1-diyl))bis(oxy))dipyrazine (10):



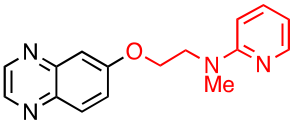
Following General Procedure C, a mixture of 2-chloropyrazine (196 µl, 2.20 mmol, 2.20 equiv), 2,2'-oxybis(ethan-1-ol) (95 µL, 1.0 mmol, 1.0 equiv), NaO*t*-Bu (269 mg, 2.80 mmol, 2.80 equiv), **P2** (17 mg, 2.0 mol %), and dioxane (1.5 mL) was stirred at 60 °C for 12 h. The crude mixture was purified by flash column chromatography (gradient elution: 5% acetone in hexanes to 30% acetone in hexanes) to provide the title compound as a beige solid (1st run: 200 mg, 76%; 2nd run: 175 mg, 67%). **mp** = 73–74 °C. **^{1}H NMR** (500 MHz, Chloroform-d) δ 8.11 (s, 2H), 7.97 (d, *J* = 3.0 Hz, 2H), 7.91 (m, 2H), 4.38 (t, *J* = 5.0 Hz, 4H), 3.78 (t, *J* = 5.0 Hz, 4H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 159.8, 140.3, 136.6, 136.0, 69.3, 65.2 ppm. **IR** (neat, cm^{-1}): 1527, 1403, 1293, 1125, 1062, 1007, 935, 845. **EA** Calcd. for $C_{12}H_{14}N_4O_3$: C, 54.96; H, 5.38, Found: C, 55.17; H, 5.61.

4-(2-cyclohexylethoxy)quinoline (11):



Following General Procedure C, a mixture of 4-chloroquinoline (131 μL, 1.00 mmol, 1.00 equiv), 2-cyclohexylethan-1-ol (279 μL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (17 mg, 2.0 mol %), and dioxane (1.0 mL) was stirred at 60 °C for 15 h. The crude mixture was purified by flash column chromatography (gradient elution: 5% EtOAc in hexanes to 30% EtOAc in hexanes) to provide the title compound as a white solid (1st run: 203 mg, 80%; 2nd run: 184 mg, 72%). **mp** = 88–90 °C. **^{1}H NMR** (500 MHz, Chloroform-d) δ 8.65 (d, *J* = 5.0 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 6.58 (d, *J* = 5.0 Hz, 1H), 4.06 (t, *J* = 5.0 Hz, 2H), 1.72–1.59 (m, 7H), 1.49 (m, 1H), 1.21–1.07 (m, 3H), 0.97–0.90 (m, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ 161.6, 151.4, 149.2, 129.6, 128.8, 125.4, 122.0, 121.5, 100.6, 66.5, 36.2, 34.7, 33.2, 26.4, 26.2 ppm. **IR** (neat, cm^{-1}): 2919, 1598, 1569, 1503, 1382, 1314, 1159, 1110, 977, 829, 765, 737, 652. **EA** Calcd. for $C_{17}H_{21}NO$: C, 79.96; H, 8.29, Found: C, 79.56; H, 8.52.

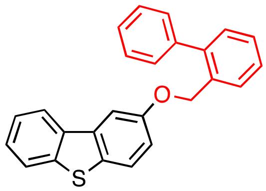
***N*-methyl-*N*-(2-(quinoxalin-6-yloxy)ethyl)pyridin-2-amine (12):**



Following General Procedure C, a mixture of 6-bromoquinoxaline (209 mg, 1.00 mmol, 1.00 equiv), 2-(methyl-2-pyridinylamino)-ethanol (203 μL, 1.50 mmol, 1.50 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (8.5 mg, 1.0 mol %), and dioxane (1.0 mL) was stirred at 40 °C for 15 h. The crude reaction mixture was diluted with EtOAc (1.0 mL), and DMAP (1.0 mg), Et_3N (140 μL, 1.00 mmol, 1.00 equiv) and Ac_2O (80 μL, 0.85 mmol, 0.85 equiv) were sequentially added. The new reaction mixture was stirred at rt for 15 min. The resulting crude product was purified by flash column chromatography (gradient elution: 100% hexanes to 80% EtOAc in hexanes) to provide the title compound as a pale yellow solid (1st run: 181 mg, 65%;

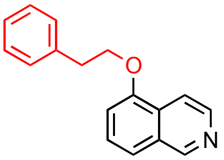
2nd run: 197 mg, 70%). **mp** = 102–104 °C. **^{1}H NMR** (500 MHz, Chloroform-d) δ 8.74 (d, *J* = 1.9 Hz, 1H), 8.67 (d, *J* = 1.9 Hz, 1H), 8.18 (ddd, *J* = 5.0, 2.0, 0.9 Hz, 1H), 7.96 (d, *J* = 9.0 Hz, 1H), 7.48–7.44 (m, 1H), 7.42–7.38 (m, 2H), 6.58–6.56 (m, 1H), 6.54 (d, 1H), 4.37 (t, *J* = 5.6 Hz, 2H), 4.08 (t, *J* = 5.6 Hz, 2H), 3.18 (s, 3H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 160.0, 158.3, 148.0, 145.0, 144.7, 142.4, 139.2, 137.4, 130.4, 123.5, 112.0, 107.6, 105.7, 67.0, 49.2, 37.9 ppm. **IR** (neat, cm^{-1}): 1594, 1499, 1421, 1359, 1303, 1227, 1123, 1036, 949, 880, 766, 732, 614. **EA** Calcd. for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75, Found: C, 68.29; H, 5.90.

2-([1,1'-biphenyl]-2-ylmethoxy)dibenzo[*b*,*d*]thiophene (13):



Following General Procedure C, a mixture of 2-bromodibenzo[*b*,*d*]thiophene (263 mg, 1.00 mmol, 1.00 equiv), 2-bephenylmethanol (368 mg, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (8.5 mg, 1.0 mol %), and dioxane (1.0 mL) was stirred at rt for 15 h. The crude product was purified by flash column chromatography (gradient elution: 100% hexanes to 50% CH_2Cl_2 in hexanes) to provide the title compound as a viscous oil (1st run: 290 mg, 79%; 2nd run: 291 mg, 79%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 8.11–8.10 (m, 1H), 7.92–7.91 (m, 1H), 7.84–7.82 (m, 1H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.68 (d, *J* = 2.5 Hz, 1H), 7.63–7.61 (m, 2H), 7.58–7.48 (m, 8H), 7.20 (dd, *J* = 8.7, 2.5 Hz, 1H), 5.21 (s, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ 156.7, 142.2, 140.6, 136.7, 135.5, 134.1, 131.7, 130.3, 129.7, 129.4, 128.5, 128.4, 127.9, 127.6, 126.8, 124.2, 123.5, 123.1, 121.7, 116.6, 106.5, 68.8 ppm. **IR** (neat, cm^{-1}): 1601, 1556, 1464, 1432, 1193, 1005, 905, 837, 745, 729, 701, 683. **HRMS** Calcd. for $C_{25}H_{18}OS$: 366.11 Found: [M+H] = 367.11.

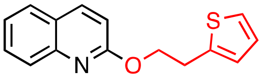
5-phenethoxyisoquinoline (14):[4]



Following General Procedure C, a mixture of 5-bromoisoquinoline (208 mg, 1.00 mmol, 1.00

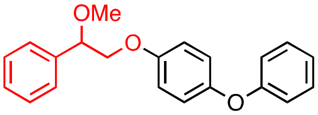
equiv), 2-phenylethan-1-ol (240 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (8.5 mg, 1.0 mol %), and dioxane (1.0 mL) was stirred at 40 °C for 15 h. The crude reaction mixture was diluted with CH_2Cl_2 (1.0 mL), and DMAP (2.0 mg), Et_3N (167 µL, 1.20 mmol, 1.20 equiv) and Ac_2O (113 µL, 1.20 mmol, 1.20 equiv) were sequentially added. The new reaction mixture was stirred at rt for 1 h. The resulting crude product was purified by flash column chromatography (gradient elution: 100% hexanes to 20% acetone in hexanes) to provide the title compound as a orange solid (1st run: 212 mg, 85%; 2nd run: 212 mg, 85%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 9.18 (s, 1H), 8.52 (d, *J* = 5.8 Hz, 1H), 7.98 (d, *J* = 5.9 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 1H), 7.44 (t, *J* = 7.9 Hz, 1H), 7.42–7.32 (m, 4H), 7.27–7.24 (m, 1H), 6.95 (d, *J* = 7.5 Hz, 1H), 4.33 (t, *J* = 6.8 Hz, 2H), 3.23 (t, *J* = 6.8 Hz, 2H) ppm. **^{13}C NMR** (126 MHz, Chloroform-d) δ 153.7, 151.9, 142.8, 138.3, 129.6, 129.2, 128.7, 128.6, 127.5, 126.8, 119.5, 115.2, 108.5, 69.2, 35.9 ppm.

2-(2-(thiophen-2-yl)ethoxy)quinolone (15):



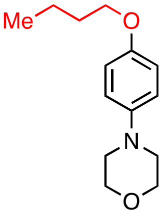
Following General Procedure C, a mixture of 2-chloroquinoline (164 mg, 1.00 mmol, 1.00 equiv), 2-(thiophen-2-yl)ethan-1-ol (222 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (8.5 mg, 1.0 mol %), and dioxane (1.5 mL) was stirred at rt for 12 h. The crude mixture was purified by flash column chromatography (gradient elution: 100% hexanes to 10% EtOAc in hexanes) to provide the title compound as a light yellow oil (1st run: 238 mg, 93%; 2nd run: 232 mg, 91%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.99 (d, *J* = 8.5 Hz, 1H), 7.85 (d, *J* = 8.5, 1H), 7.72 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.63 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H), 7.39 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 7.18 (dd, *J* = 5.0, 1.4 Hz, 1H), 6.98–6.92 (m, 3H), 4.73 (t, *J* = 6.8 Hz, 2H), 3.38 (td, *J* = 6.8, 0.8 Hz, 2H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 161.9, 146.7, 141.0, 138.8, 129.6, 127.5, 127.4, 126.9, 125.5, 125.2, 124.1, 123.9, 113.3, 66.3, 29.8 ppm. **IR** (neat, cm^{-1}): 1617, 1604, 1572, 1506, 1427, 1393, 1311, 1275, 1256, 1237, 1111, 1010, 819, 755, 694. **EA** Calcd. for $C_{15}H_{13}NOS$: C, 70.56; H, 5.13, Found: C, 70.83; H, 5.11.

1-(2-methoxy-2-phenylethoxy)-4-phenoxybenzene (16):



Following General Procedure C, a mixture of 1-bromo-4-phenoxybenzene (175 µL, 1.00 mmol, 1.00 equiv), 2-methoxy-2-phenylethan-1-ol (222 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (17 mg, 2.0 mol %), and dioxane (1.5 mL) was stirred at 60 °C for 15 h. The crude mixture was purified by flash column chromatography (gradient elution: 100% hexanes to 15% EtOAc in hexanes) to provide the title compound as a viscous oil (1st run: 232 mg, 72%; 2nd run: 230 mg, 72%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.42 (d, *J* = 4.3 Hz, 4H), 7.38–7.34 (m, 1H), 7.30 (t, *J* = 8.0 Hz, 2H), 7.05 (t, *J* = 7.0 Hz, 1H), 6.97–6.92 (m, 4H), 6.91–6.89 (m, 2H), 4.61 (dd, *J* = 7.9, 3.6 Hz, 1H), 4.17 (dd, *J* = 10.2, 7.9 Hz, 1H), 4.00 (dd, *J* = 10.2, 3.6 Hz, 1H), 3.38 (s, 3H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 158.6, 155.2, 150.5, 138.6, 129.8, 128.8, 128.5, 127.2, 122.6, 120.9, 117.8, 116.0, 82.5, 73.1, 57.4 ppm. **IR** (neat, cm^{-1}): 1588, 1495, 1487, 1453, 1216, 1118, 1067, 1024, 839, 757, 700, 691. **HRMS** Calcd. for $C_{21}H_{20}O_3$: 320.39, Found: [M+H] = 321.15.

4-(4-butoxyphenyl)morpholine (3):[1]

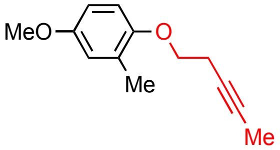


Following General Procedure C, a mixture of 4-(4-bromophenyl)morpholine (242 mg, 1.00 mmol, 1.00 equiv), butan-1-ol (183 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P8** (9.6 mg, 1.0 mol %), and dioxane (1.0 mL) was stirred at rt for 4 h. The crude mixture was purified by flash column chromatography (gradient elution: 100% hexanes to 6% acetone in hexanes with an increment of 1% acetone in hexanes) to provide the title compound as a white solid (1st run: 192 mg, 82%; 2nd run: 216 mg, 92%).

Following General Procedure B, a mixture of 4-(4-chlorophenyl)morpholine (198 mg, 1.00 mmol, 1.00 equiv), butan-1-ol (183 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P8** (12 mg, 1.2 mol %), and dioxane (1.0 mL) was stirred at rt for 15 h. The crude mixture was purified by flash column chromatography (gradient elution: 100% hexanes to 6% acetone in hexanes with an increment of 1% acetone in hexanes) to provide the title compound as a white solid (1st run: 207 mg, 88%; 2nd run: 223 mg, 95%).

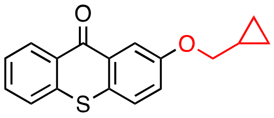
^{1}H NMR (500 MHz, Chloroform-d) δ 6.89–6.84 (m, 4H), 3.92 (t, J = 6.5 Hz, 2H), 3.86 (t, J = 4.5 Hz, 4H), 3.05 (t, J = 5.0 Hz, 4H), 1.77–1.72 (m, 2H), 1.49 (sextet, J = 7.4 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 153.7, 145.7, 118.0, 115.4, 68.3, 67.3, 51.0, 31.6, 19.5, 14.1 ppm.

4-methoxy-2-methyl-1-(pent-3-yn-1-yloxy)benzene (17):



Following General Procedure C, a mixture of 1-chloro-4-methoxy-2-methylbenzene (134 µL, 1.00 mmol, 1.00 equiv), pent-3-yn-1-ol (184 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P8** (19 mg, 2.0 mol %), and dioxane (1.0 mL) was stirred at 80 °C for 15 h. The crude mixture was purified by flash column chromatography (gradient elution: 100% hexanes to 15% EtOAc in hexanes) to provide the title compound as a clear oil (1st run: 128 mg, 63%; 2nd run: 112 mg, 55%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 6.77 (d, J = 8.8 Hz, 1H), 6.74 (d, J = 3.1 Hz, 1H), 6.67 (dd, J = 8.8, 3.2 Hz, 1H), 4.00 (t, J = 7.1 Hz, 2H), 3.76 (s, 3H), 2.61 (tq, J = 7.3, 2.5 Hz, 2H), 2.23 (s, 3H), 1.81 (t, J = 2.6 Hz, 3H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 153.9, 151.2, 128.8, 117.1, 113.3, 111.1, 75.6, 68.0, 55.9, 29.9, 20.2, 16.6, 3.7 ppm. **IR** (neat, cm^{-1}): 2919, 1499, 1466, 1280, 1217, 1159, 1128, 1046, 866, 793, 717, 704. **EA** Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90, Found: C, 76.72; H, 7.74.

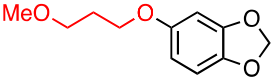
2-(cyclopropylmethoxy)-9*H*-thioxanthen-9-one (18):



Following General Procedure C, a mixture of 2-chloro-9*H*-thioxanthen-9-one (247 mg, 1.00 mmol, 1.00 equiv), cyclopropylmethanol (162 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P8** (19 mg, 2.0 mol %), and dioxane (1.0 mL) was stirred at 40 °C for 15 h. The crude mixture was purified by flash column chromatography (gradient elution: 100%

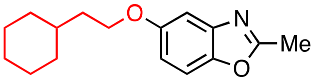
hexanes to 6% EtOAc in hexanes with an increment of 1% EtOAc in hexanes) to provide the title compound as a bright yellow solid (1st run: 202 mg, 71%; 2nd run: 221 mg, 78%). **mp** = 95–96 °C. **^{1}H NMR** (500 MHz, Chloroform-d) δ 8.63 (d, *J* = 8.5 Hz, 1H), 8.04 (d, *J* = 3.0 Hz, 1H), 7.63–7.58 (m, 2H), 7.51–7.46 (m, 2H), 7.30 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H), 3.96 (d, *J* = 7.0 Hz, 2H), 1.37–1.29 (m, 1H), 0.68 (dd, *J* = 8.0 Hz, 5.0 Hz, 2H), 0.40 (dd, *J* = 5.0 Hz, 5.0 Hz, 2H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 179.9, 158.0, 137.7, 132.2, 130.3, 130.1, 129.2, 128.8, 127.5, 126.2, 126.2, 123.4, 111.2, 73.4, 10.3, 3.5 ppm. **IR** (neat, cm^{-1}): 1629, 1600, 1589, 1477, 1459, 1437, 1406, 1341, 1317, 1293, 1261, 1228, 1217, 1153, 1115, 1009, 881, 820, 746, 741, 708, 677, 631. **EA** Calcd. for $C_{17}H_{14}O_2S$: C, 72.32; H, 5.00, Found: C, 72.06; H, 4.87.

5-(3-methoxypropoxy)benzo[*d*][1,3]dioxole (19):



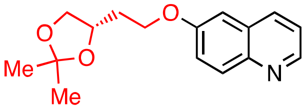
Following General Procedure C, a mixture of 5-chlorobenzo[*d*][1,3]dioxole (117 μL, 1.00 mmol, 1.00 equiv), 3-methoxypropan-1-ol (191 μL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P8** (24 mg, 2.5 mol %), and dioxane (1.0 mL) was stirred at 60 °C for 18 h. The crude mixture was purified by flash column chromatography (gradient elution: 100% hexanes to 25% Et_2O in hexanes with an increment of 3% Et_2O in hexanes) to provide the title compound as a light yellow oil (1st run: 170 mg, 81%; 2nd run: 184 mg, 87%). Note: due to the high volatility of the final compound, the use of high vacuum was avoided in the isolation process. **^{1}H NMR** (500 MHz, Chloroform-d) δ 6.69 (d, *J* = 8.5 Hz, 1H), 6.50 (d, *J* = 2.0 Hz, 1H), 6.32 (dd, *J* = 8.5 Hz, 2.0 Hz, 1H), 5.90 (s, 2H), 3.97 (t, *J* = 6.5 Hz, 2H), 3.54 (t, *J* = 6.5 Hz, 2H), 3.35 (s, 3H), 2.01 (quintet, *J* = 6.5 Hz, 2H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 154.7, 148.4, 141.7, 108.1, 105.8, 101.3, 98.3, 69.4, 65.9, 58.9, 29.8 ppm. **IR** (neat, cm^{-1}): 2877, 1502, 1487, 1471, 1394, 1241, 1180, 1116, 1035, 937, 924, 815. **EA** Calcd. for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71, Found: C, 62.99; H, 6.70.

5-(2-cyclohexylethoxy)-2-methylbenzo[*d*]oxazole (20):



Following General Procedure C, a mixture of 5-chloro-2-methylbenzo[*d*]oxazole (168 mg, 1.00 mmol, 1.00 equiv), 2-cyclohexylethan-1-ol (279 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P8** (14 mg, 1.5 mol %), and dioxane (1.5 mL) was stirred at 60 °C for 15 h. The crude mixture was purified by flash column chromatography (gradient elution: 100% hexanes to 10% EtOAc in hexanes) to provide the title compound as an orange oil (1st run: 197 mg, 76%; 2nd run: 202 mg, 78%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.32 (d, *J* = 8.9 Hz, 1H), 7.12 (d, *J* = 2.5 Hz, 1H), 6.87 (dd, *J* = 8.9, 2.5 Hz, 1H), 4.01 (t, *J* = 6.7 Hz, 2H), 2.60 (s, 3H), 1.78–1.64 (m, 7H), 1.52 (ttt, *J* = 10.6, 6.9, 3.5 Hz, 1H), 1.30–1.12 (m, 3H), 0.97 (qd, *J* = 12.2, 3.3 Hz, 2H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 164.6, 156.6, 145.6, 142.4, 113.3, 110.2, 103.6, 66.9, 36.8, 34.7, 33.4, 26.6, 26.4, 14.7 ppm. **IR** (neat, cm^{-1}): 2920, 2849, 1577, 1468, 1439, 1282, 1270, 1172, 1155, 947, 819, 802. **EA** Calcd. for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16, Found: C, 74.40; H, 8.36.

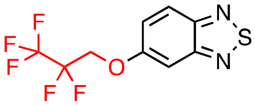
(*S*)-6-(2-(2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)quinolone (21):



Following General Procedure C, a mixture of 6-chloroquinoline (164 mg, 1.00 mmol, 1.00 equiv), (*S*)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)ethan-1-ol (285 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P8** (19 mg, 2.0 mol %), and dioxane (1.0 mL) was stirred at rt for 15 h. The crude reaction mixture was diluted with CH_2Cl_2 (1.0 mL), and DMAP (2.0 mg), Et_3N (167 µL, 1.20 mmol, 1.20 equiv) and Ac_2O (113 µL, 1.20 mmol, 1.20 equiv) were sequentially added. The new reaction mixture was stirred at rt for 1 h. The resulting crude produt was purified by flash column chromatography (gradient elution: 100% hexanes to 30% acetone in hexanes) to provide the title compound as a dark orange oil (1st run: 252 mg, 92%; 2nd run: 257 mg, 94%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 8.77 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 9.2 Hz, 1H), 7.35 (dt, *J* = 8.3, 3.3 Hz, 2H), 7.08 (d, *J* = 2.8 Hz, 1H), 4.35 (quintet, *J* = 6.4 Hz, 1H), 4.25–4.19 (m, 2H), 4.16 (dd, *J* = 8.1, 5.9 Hz, 1H), 3.69 (t, *J* = 7.5 Hz, 1H), 2.12 (q, *J* = 6.3 Hz, 2H), 1.44 (s, 3H), 1.37 (s, 3H). **^{13}C NMR** (126 MHz, Chloroform-

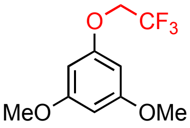
d) δ 157.0, 148.2, 144.6, 135.0, 131.1, 129.5, 122.6, 121.6, 109.1, 106.1, 73.5, 69.7, 65.2, 33.7, 27.2, 25.9 ppm. **IR** (neat, cm^{-1}): 2984, 2930, 2874, 1622, 1595, 1499, 1464, 1378, 1369, 1323, 1224, 1169, 1157, 1057, 832. **EA** Calcd. for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01, Found: C, 70.03; H, 7.13.

5-(2,2,3,3,3-pentafluoropropoxy)benzo[*c*][1,2,5]thiadiazole (22):



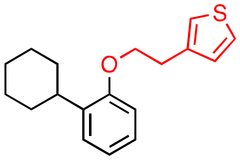
Following General Procedure C, a mixture of 5-chlorobenzo[*c*][1,2,5]thiadiazole (171 mg, 1.00 mmol, 1.00 equiv), 2,2,3,3,3-pentafluoropropan-1-ol (199 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P8** (19 mg, 2.0 mol %), and dioxane (1.0 mL) was stirred at 40 °C for 2.5 h. The crude mixture was purified by flash column chromatography (gradient elution: 100% hexanes to 5% EtOAc in hexanes with an increment of 1% EtOAc in hexanes) to provide the title compound as a white solid (1st run: 236 mg, 83%; 2nd run: 243 mg, 85%). **mp** = 62–64 °C. **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.85 (d, $J = 9.5$ Hz, 1H), 7.31 (dd, $J = 9.5, 2.5$ Hz 1H), 7.20 (d, $J = 2.5$ Hz, 1H), 4.51 (t, $J = 12$ Hz, 2H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 158.9, 155.6, 151.8, 124.7, 122.6, 99.6, 64.9 (t, $J = 28.4$ Hz) ppm (perfluorinated carbons are not reported due to low signal intensities). **^{19}F NMR** (376 MHz, Chloroform-d) δ –83.4 (s, 3F), –123.1 (t, $J = 12.0$ Hz, 2F) ppm. **IR** (neat, cm^{-1}): 1615, 1489, 1450, 1378, 1280, 1182, 1143, 1099, 1070, 964, 947, 929, 846, 822. **EA** Calcd. for $C_9H_5F_5N_2OS$: C, 38.04; H, 1.77, Found: C, 38.31; H, 1.70.

1,3-dimethoxy-5-(2,2,2-trifluoroethoxy)benzene (23):[5]



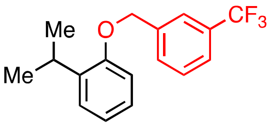
Following General Procedure C, a mixture of 1-bromo-3,5-dimethoxybenzene (217 mg, 1.00 mmol, 1.00 equiv), 2,2,2-trifluoroethan-1-ol (146 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P8** (14 mg, 1.5 mol %), and dioxane (1.0 mL) was stirred at 60 °C for 15 h. The crude mixture was purified by flash column chromatography (gradient elution: 100% hexanes to 10% Et_2O in hexanes) to provide the title compound as a light yellow oil (1st run: 208 mg, 88%; 2nd run: 205 mg, 87%). Note: due to the high volatility of the final compound, the use of high vacuum was avoided in the isolation process. **^{1}H NMR** (500 MHz, Chloroform-d) δ 6.16 (t, J = 2.1 Hz, 1H), 6.11 (d, J = 2.1 Hz, 2H), 4.30 (q, J = 8.1 Hz, 2H), 3.78 (s, 6H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 161.8, 159.4, 126.8–120.2 (q, J = 277.2 Hz), 94.7, 93.9, 66.4–65.5 (q, J = 36.5 Hz), 55.6 ppm. **^{19}F NMR** (282 MHz, Chloroform-d) δ –75.3 ppm.

3-(2-(2-cyclohexylphenoxy)ethyl)thiophene (24):



Following General Procedure C, a mixture of 1-bromo-2-cyclohexylbenzene (185 µL, 1.00 mmol, 1.00 equiv), 2-(thiophen-3-yl)ethan-1-ol (224 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P8** (19 mg, 2.0 mol %), and dioxane (1.0 mL) was stirred at rt for 15 h. Celite® (~ 2 g) and diethyl ether (Et_2O, 3 mL) were added to the crude reaction mixture, which was briefly sonicated to ensure full suspension of Celite® in the solution. Et_2O was carefully removed *in vacuo* to afford a dry Celite® powder absorbed with the crude reaction mixture. The resulting powder was loaded onto a column for purification by flash chromatography (gradient elution: 100% hexanes to 5% EtOAc in hexanes with an increment of 1% EtOAc in hexanes) to provide the title compound as a yellow oil (1st run: 191 mg, 67%; 2nd run: 215 mg, 75%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.30 (dd, J = 4.9, 2.9 Hz, 1H), 7.21 (dd, J = 7.6, 1.7 Hz, 1H), 7.19–7.10 (m, 2H), 7.08 (dd, J = 4.9, 1.2 Hz, 1H), 6.94 (td, J = 7.5, 1.0 Hz, 1H), 6.86 (dd, J = 8.2, 1.0 Hz, 1H), 4.20 (t, J = 6.5 Hz, 2H), 3.18 (t, J = 6.5 Hz, 2H), 2.96 (tt, J = 11.3, 3.2 Hz, 1H), 1.86–1.77 (m, 5H), 1.48–1.24 (m, 5H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 156.0, 139.1, 136.5, 128.6, 126.7, 126.5, 125.4, 121.7, 120.8, 111.3, 68.2, 37.1, 33.2, 30.6, 27.3, 26.6 ppm. **IR** (neat, cm^{-1}): 2920, 2849, 1491, 1447, 1232, 1139, 1101, 1051, 1030, 999, 854, 840, 772. **EA** Calcd. for $C_{18}H_{22}OS$: C, 75.48; H, 7.74, Found: C, 75.77; H, 7.72.

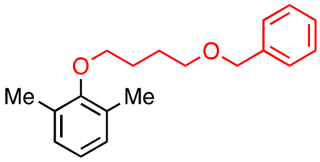
1-isopropyl-2-((3-(trifluoromethyl)benzyl)oxy)benzene (25):



Following General Procedure C, a mixture of 1-bromo-2-isopropylbenzene (153 µL, 1.00 mmol, 1.00 equiv), (3-(trifluoromethyl)phenyl)methanol (272 µL, 2.00 mmol, 2.00 equiv), NaO*t*-Bu

(115 mg, 1.20 mmol, 1.20 equiv), **P8** (14 mg, 1.5 mol %), and dioxane (1.0 mL) was stirred at rt for 12 h. Celite® (~ 2 g) and diethyl ether (Et_2O, 3 mL) were added to the crude reaction mixture, which was briefly sonicated to ensure full suspension of Celite® in the solution. Et_2O was carefully removed *in vacuo* to afford a dry Celite® powder absorbed with the crude reaction mixture. The resulting powder was loaded onto a column for purification by flash chromatography (gradient elution: 100% hexanes to 5% EtOAc in hexanes with an increment of 1% EtOAc in hexanes) to provide the title compound as a light yellow oil (1st run: 273 mg, 93%; 2nd run: 275 mg, 93%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.80 (s, 1H), 7.71 (d, *J* = 7.7 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.35 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.25–7.22 (m, 1H), 7.05 (td, *J* = 7.5, 1.1 Hz, 1H), 6.96 (dd, *J* = 8.2, 1.2 Hz, 1H), 5.18 (s, 2H), 3.50 (hept, *J* = 6.9 Hz, 1H), 1.34 (d, *J* = 7.1 Hz, 6H).**^{13}C NMR** (126 MHz, Chloroform-d) δ 155.7, 138.8, 137.6, 131.5–139.7 (q, *J* = 32.8 Hz), 130.5, 129.2, 127.6–121.1 (q, *J* = 272.2 Hz), 126.8, 126.5, 124.8 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 3.8 Hz), 121.5, 111.8, 69.4, 27.1, 22.9 ppm. **^{19}F NMR** (282 MHz, Chloroform-d) δ –64.0 ppm. **IR** (neat, cm^{-1}): 2966, 1599, 1584, 1490, 1447, 1362, 1328, 1233, 1164, 1122, 1073, 831, 794, 750. **HRMS** Calcd. for $C_{17}H_{17}F_3O$: 294.32, Found: [M+H] = 295.13.

2-(4-(benzyloxy)butoxy)-1,3-dimethylbenzene (26):

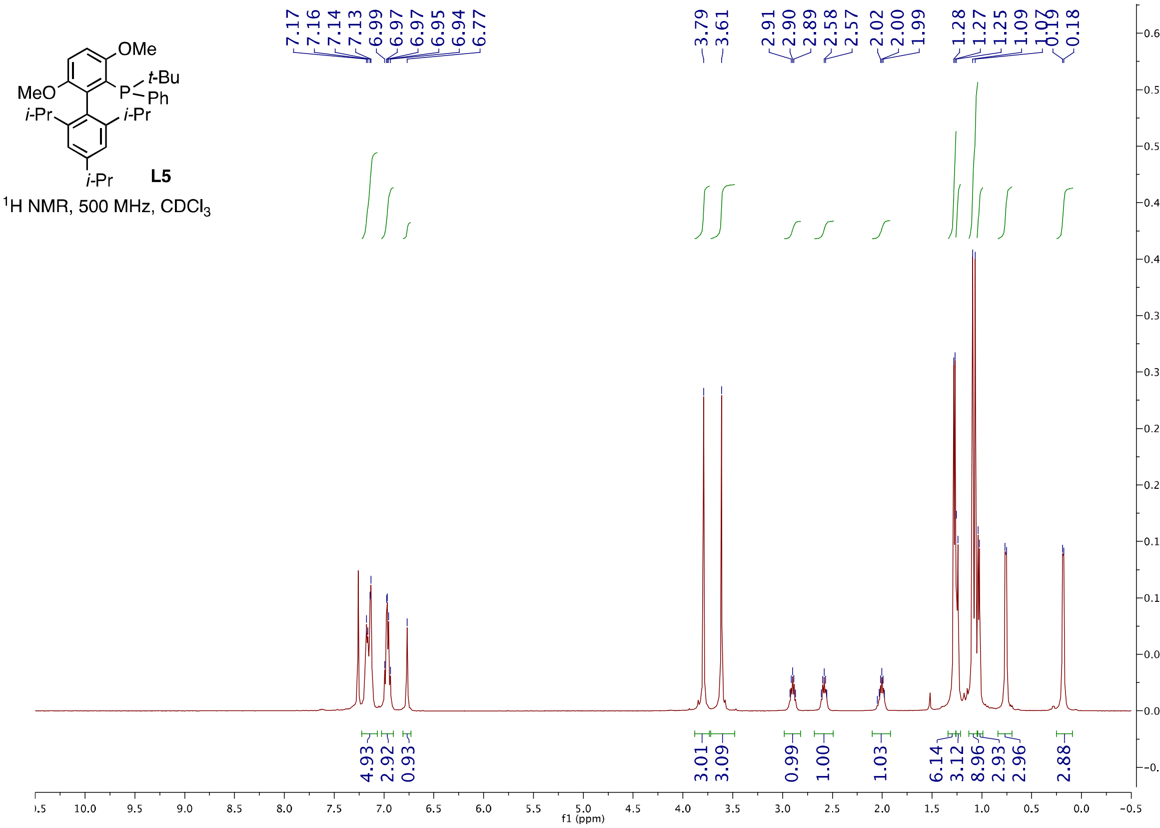


Following General Procedure C, a mixture of 2-bromo-1,3-dimethylbenzene (133 µL, 1.00 mmol, 1.00 equiv), 4-(benzyloxy)butan-1-ol (352 µL, 2.00 mmol, 2.00 equiv), **P1** (24 mg, 2.5 mol %), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), 1,4-dioxane (1 mL) was stirred at rt for 18 h. Celite® (~ 2 g) and diethyl ether (Et_2O, 3 mL) were added to the crude reaction mixture, which was briefly sonicated to ensure full suspension of Celite® in the solution. Et_2O was carefully removed *in vacuo* to afford a dry Celite® powder absorbed with the crude reaction mixture. The resulting powder was loaded onto the column for purification by silica gel chromatography (gradient elution: 100% hexanes to 7% EtOAc in hexanes with an increment of 1% EtOAc in hexanes) to provide the title compound as a light yellow oil (1st run: 216 mg, 76%; 2nd run: 239 mg, 84%). **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.38–7.36 (m, 4H), 7.32–7.28 (m, 1H), 7.02 (dd, *J* = 7.6, 3.0 Hz, 2H), 6.92 (ddd, *J* = 8.0, 6.7, 3.0 Hz, 1H), 4.56 (d, *J* = 2.8 Hz, 2H), 3.79 (td, *J* = 6.1, 3.0 Hz, 2H), 3.58 (td, *J* = 5.8, 2.9 Hz, 2H), 2.29 (d, *J* = 3.2 Hz, 6H), 1.96–1.84 (m, 4H). **^{13}C NMR** (126 MHz, Chloroform-d) δ 156.1, 138.8, 131.1, 129.0, 128.6, 127.8, 127.8, 123.8, 73.2, 72.1, 70.3, 27.4, 26.8, 16.5. **IR** (neat, cm^{-1}): 2921, 2856, 1475, 1453, 1262, 1202, 1090, 1055, 1028, 1100, 766, 733. **EA** Calcd. for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51, Found: C, 80.35; H, 8.50.

References:

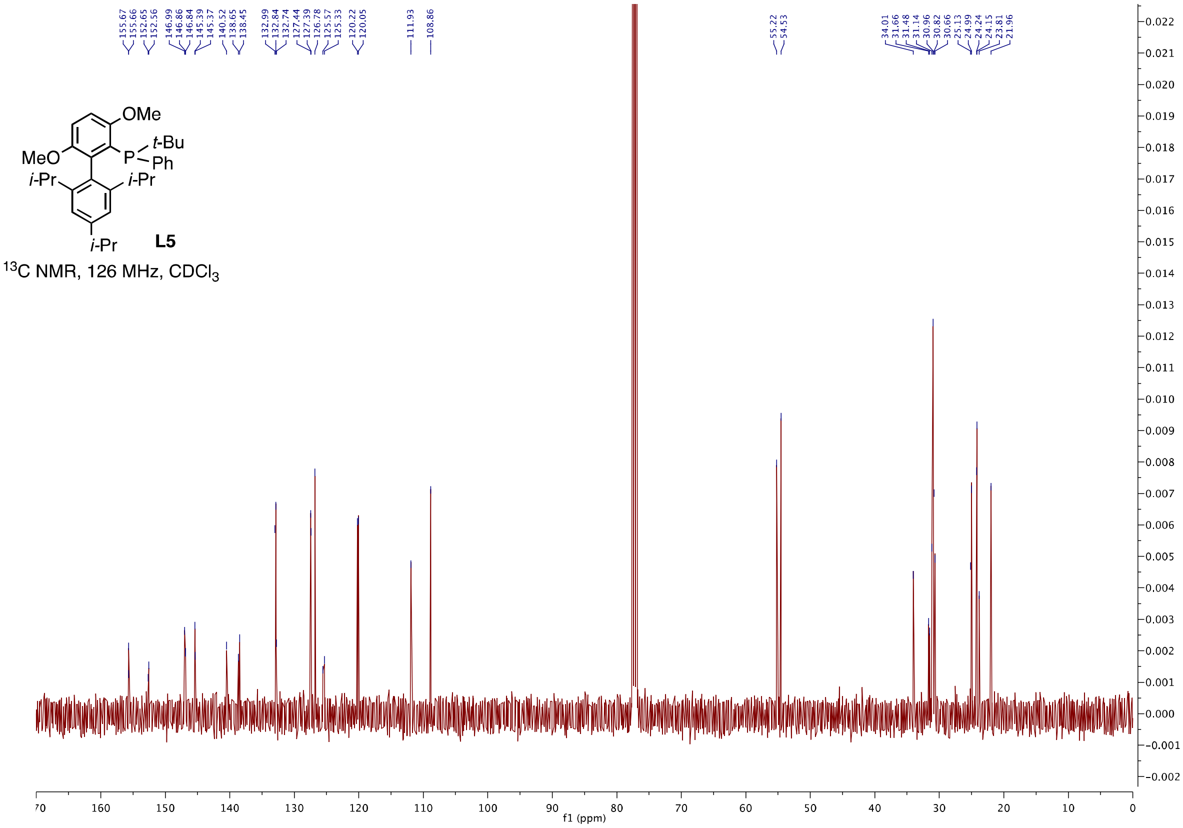
1. Wu, X.; Fors, B. P.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2011,** *50*, 9943.
2. Su, M.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2012,** *51*, 4710.
3. (a) Bruno, N. C.; Tudge, M. T.; Buchwald, S. L. *Chem. Sci.* **2013**, *4*, 916. (b) Bruno, N. C.; Buchwald, S. L. *Org. Lett.* **2013**, *15*, 2876.
4. Maligres, P. E.; Li, J.; Krska, S. W.; Schreier, J. D.; Raheem, I. T. *Angew. Chem. Int. Ed.* **2012**, *51*, 9071.
5. Fujita, M.; Mishima, E.; Okuyama, T. *J. Phys. Org. Chem.* **2007**, *20*, 241.

III. Copies of NMR Spectra



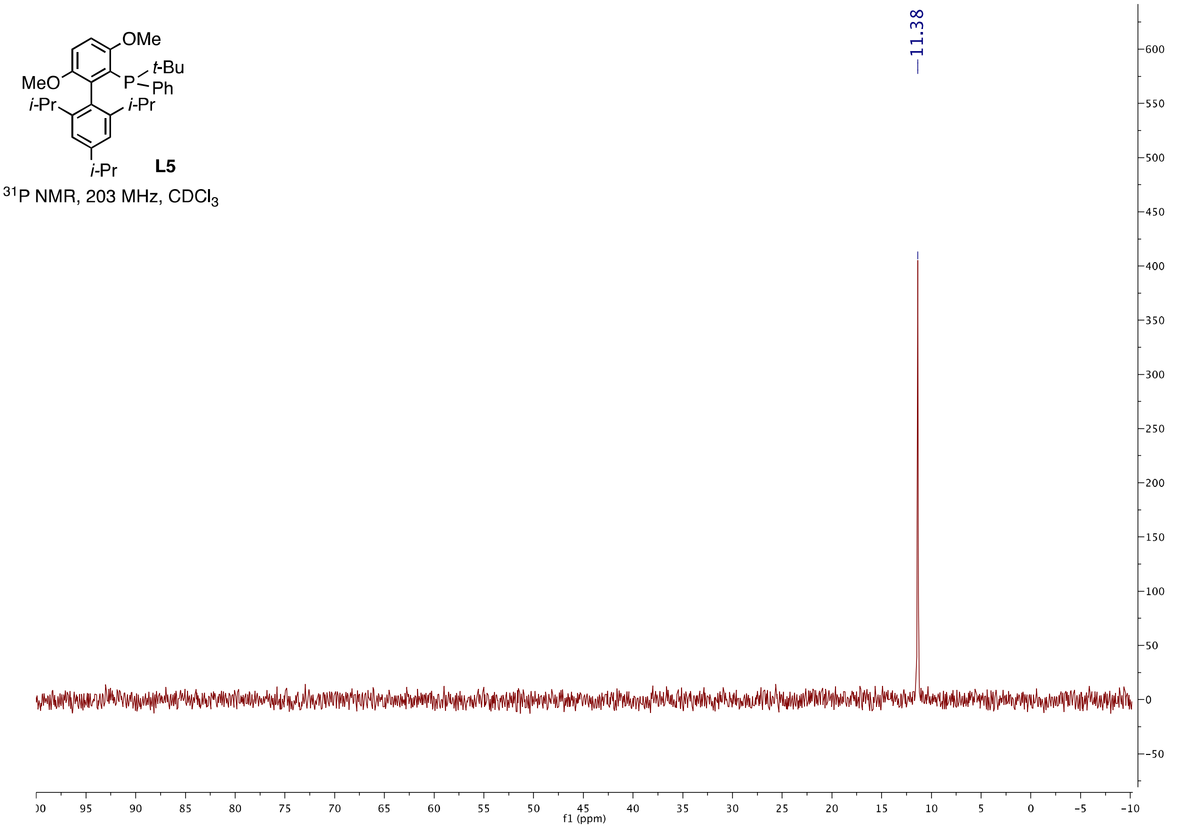
L5

^{1}H NMR, 500 MHz, CDCl$_3$



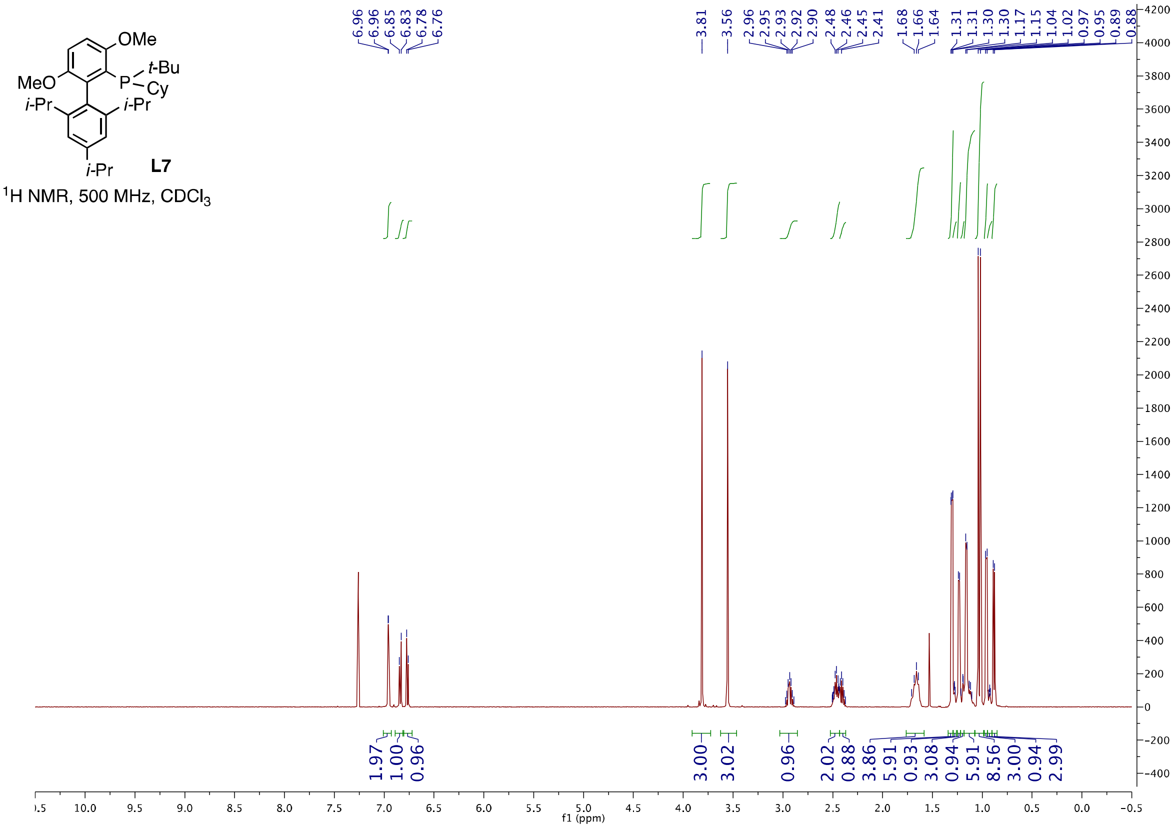
L5

^{13}C NMR, 126 MHz, $CDCl_3$



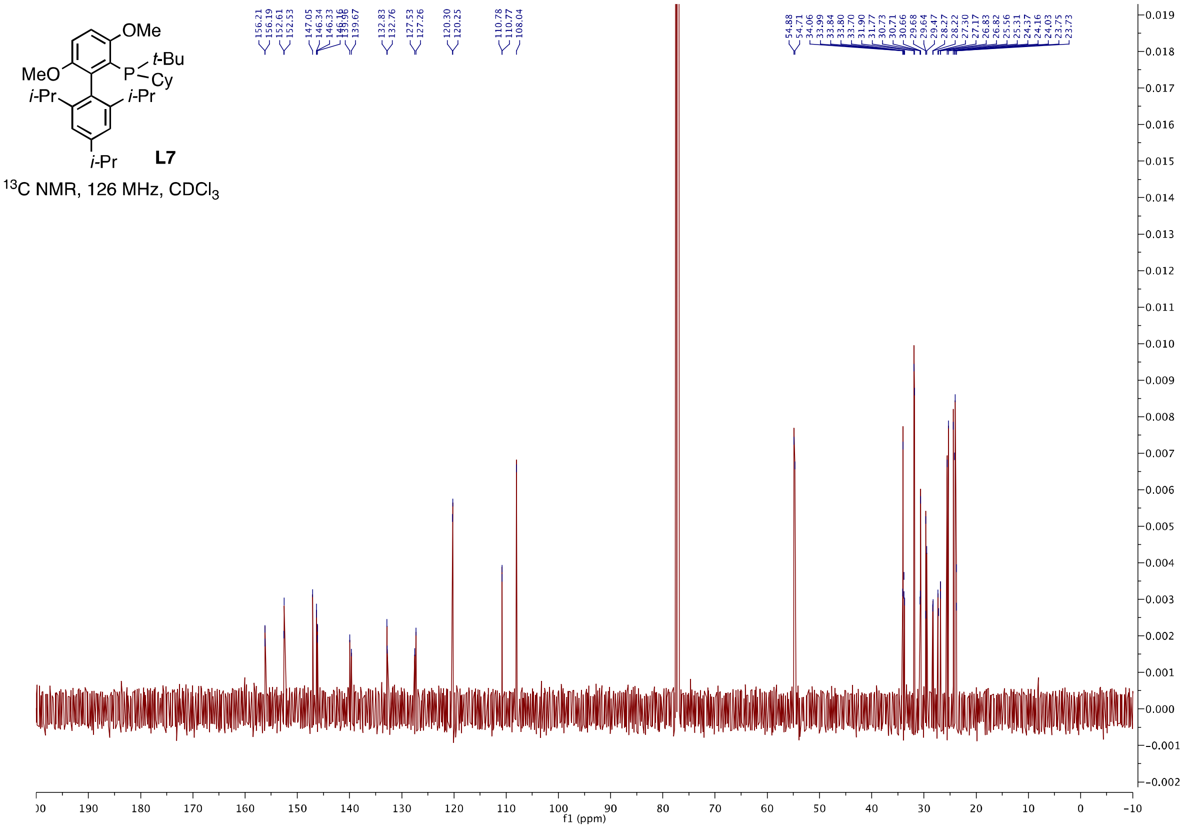
L5

^{31}P NMR, 203 MHz, $CDCl_3$



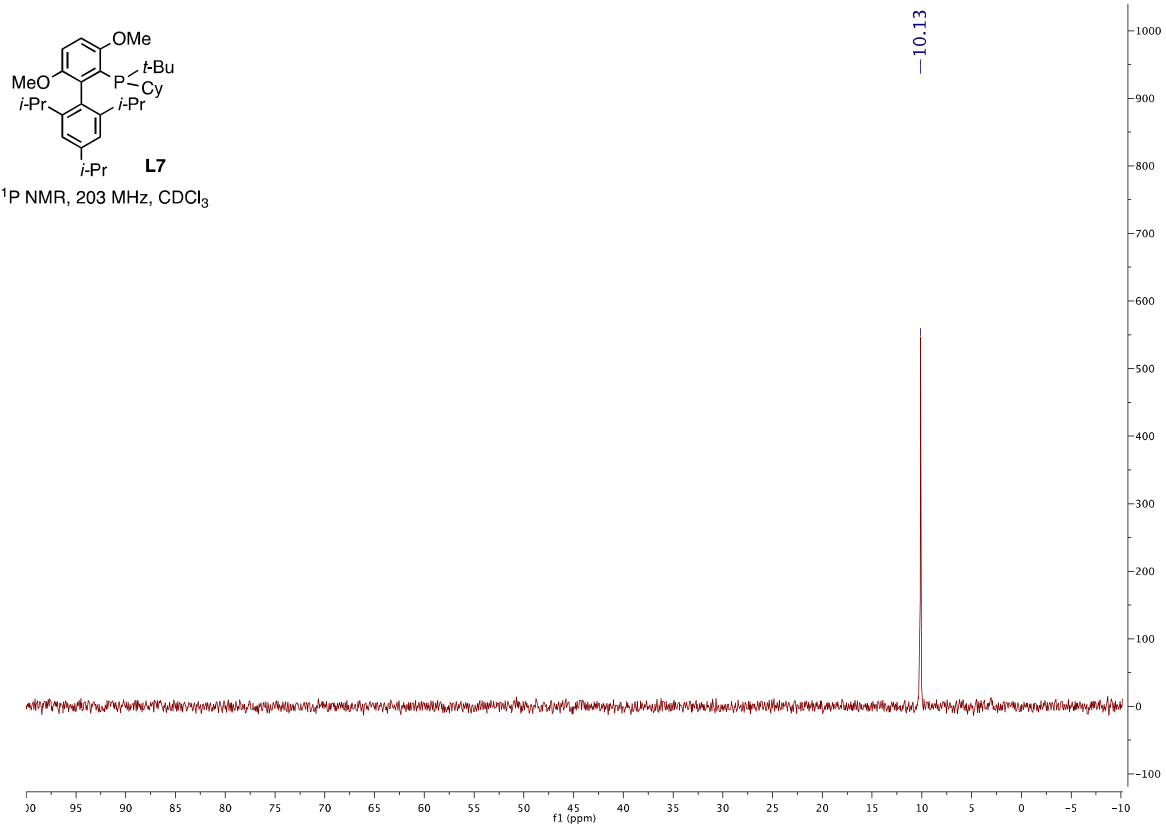
L7

^{1}H NMR, 500 MHz, CDCl$_3$



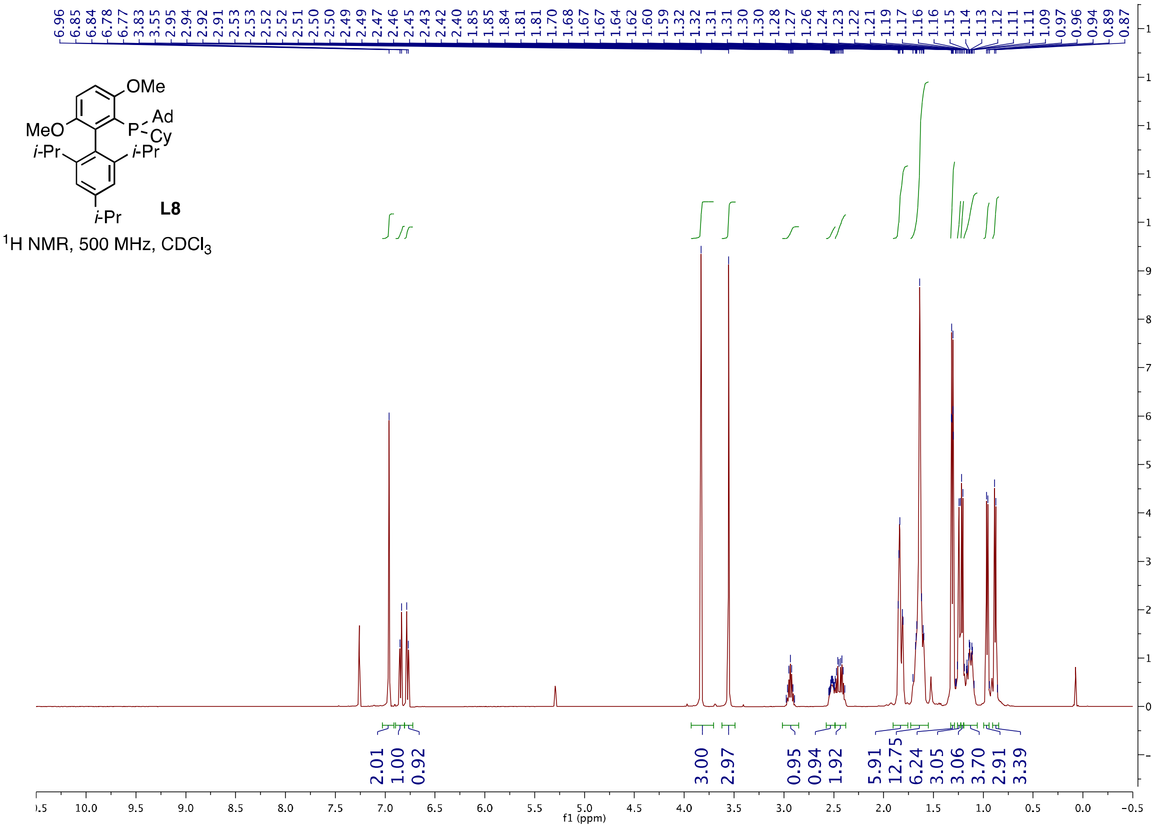
L7

^{13}C NMR, 126 MHz, CDCl$_3$



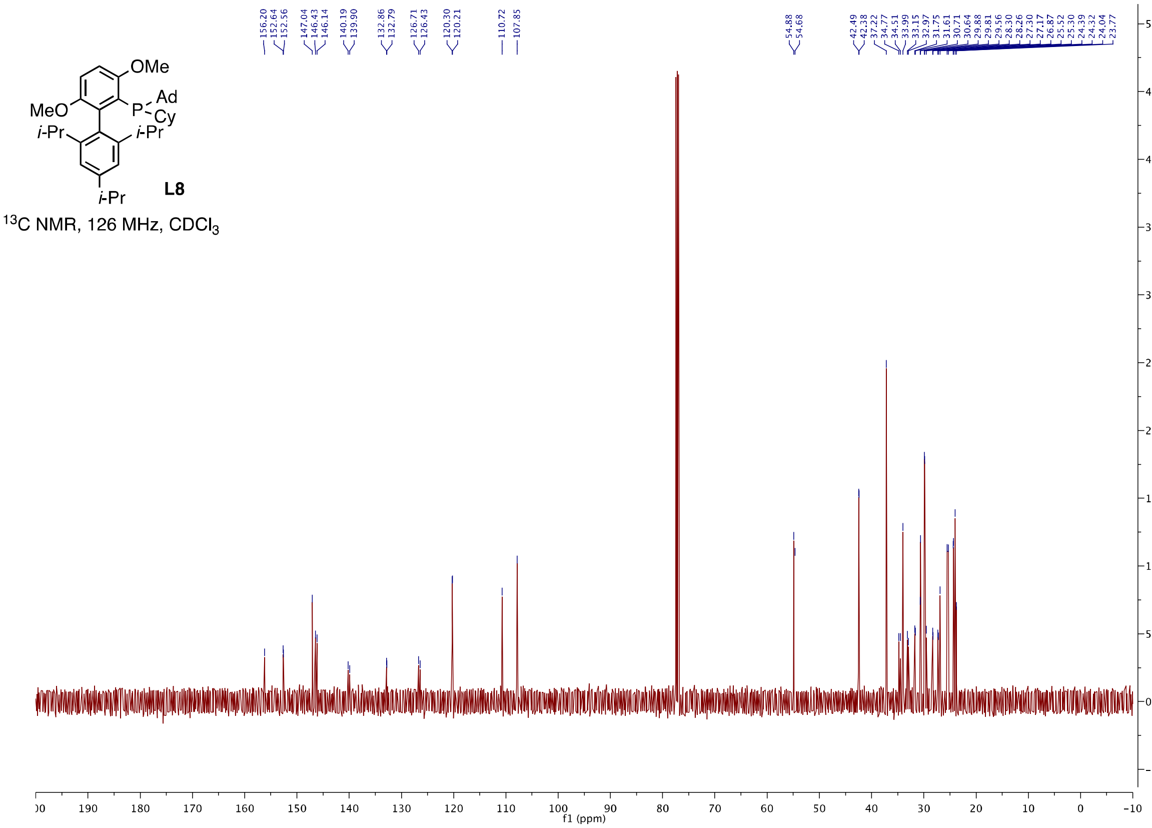
L7

^{31}P NMR, 203 MHz, CDCl$_3$



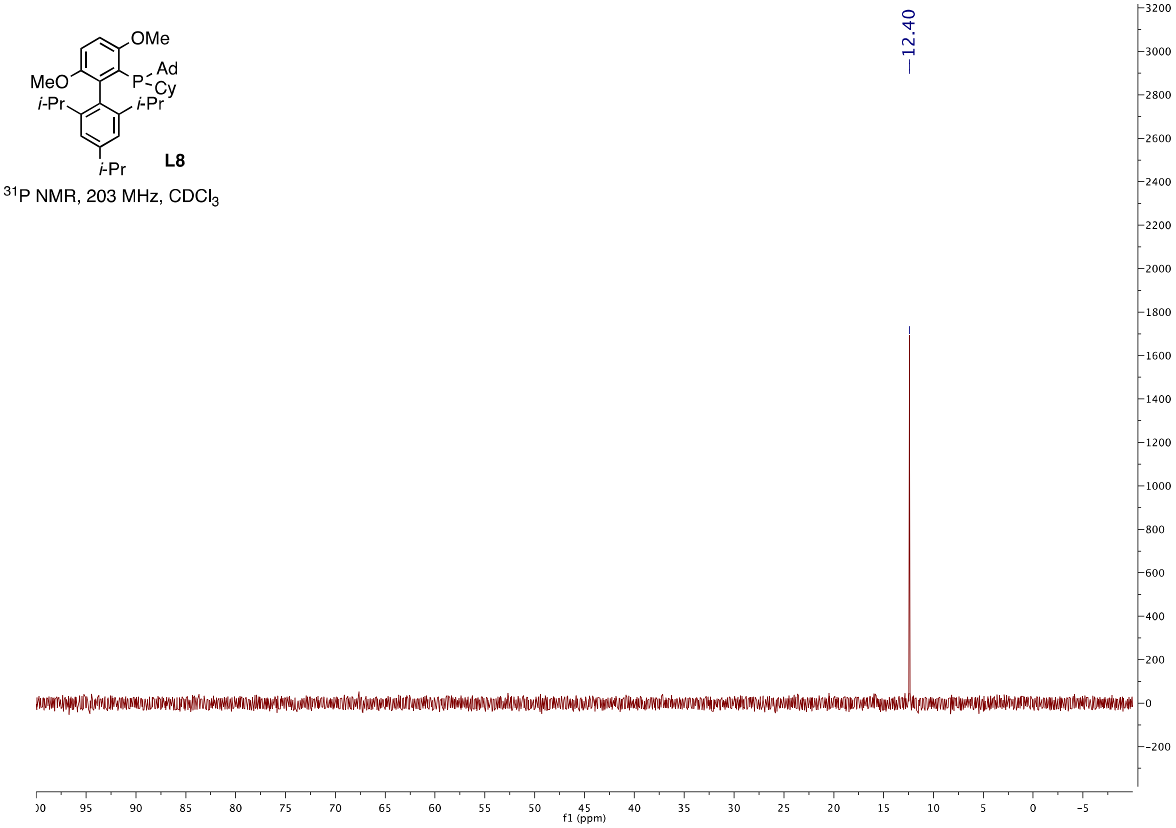
L8

^{1}H NMR, 500 MHz, CDCl$_3$



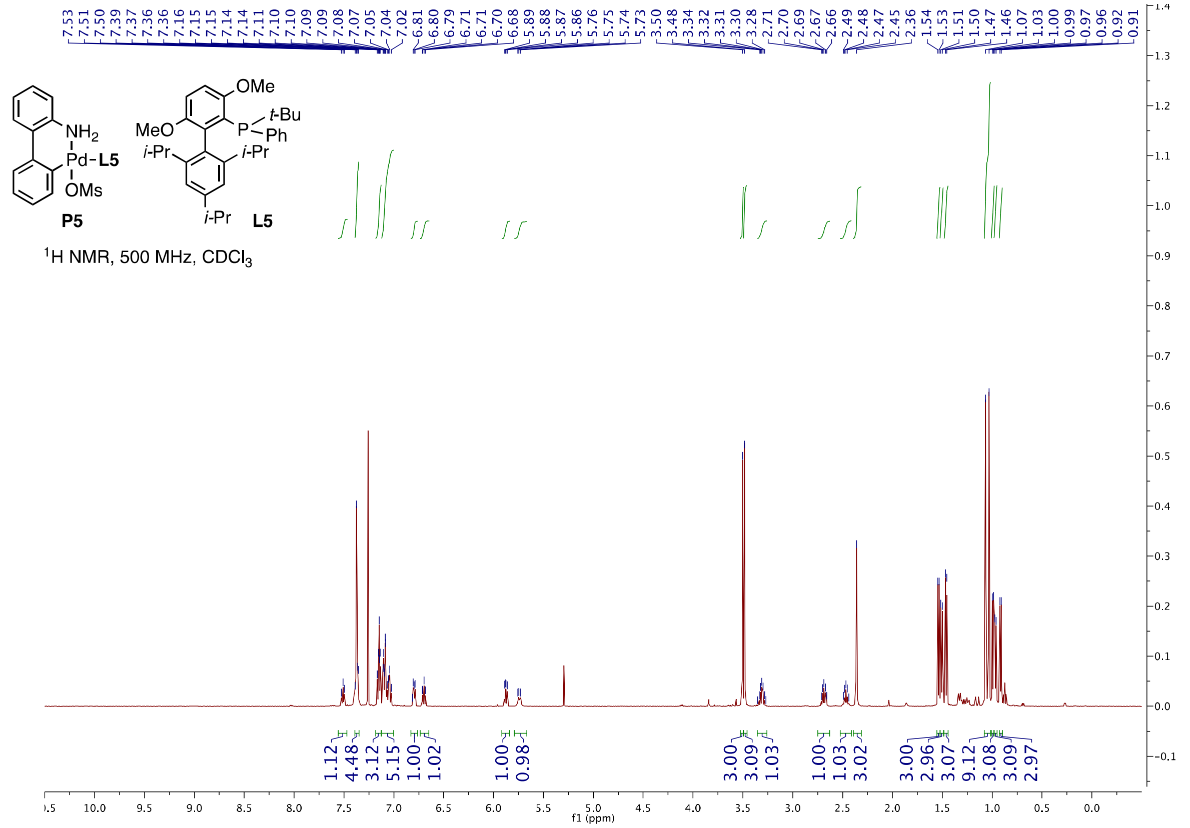
L8

^{13}C NMR, 126 MHz, CDCl$_3$



L8

^{31}P NMR, 203 MHz, $CDCl_3$


7.53
7.51
7.50
7.39
7.37
7.36
7.36
7.16
7.15
7.15
7.14
7.14
7.11
7.10
7.10
7.09
7.09
7.08
7.07
7.05
7.04
7.02
6.81
6.80
6.79
6.71
6.71
6.70
6.68
5.89
5.88
5.87
5.86
5.76
5.75
5.74
5.73
3.50
3.48
3.34
3.32
3.31
3.30
3.28
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2.70
2.69
2.67
2.66
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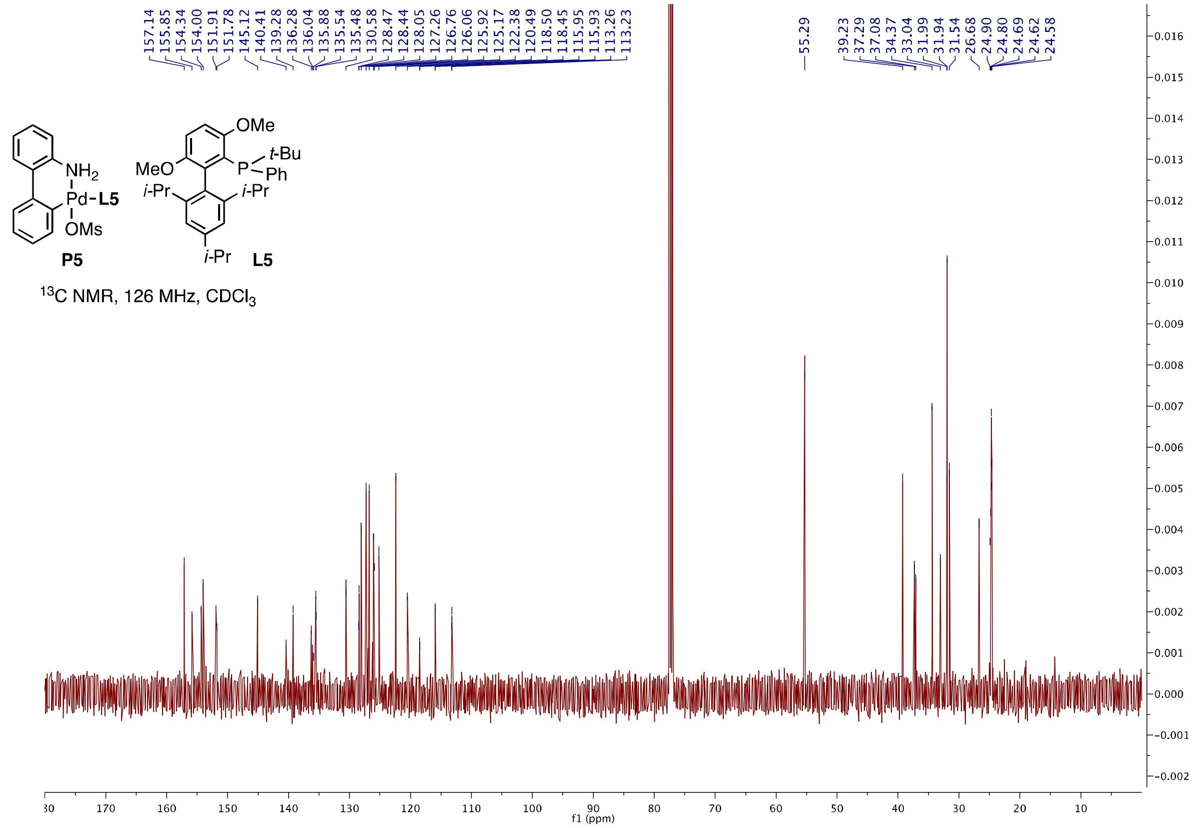
2.47
2.45
2.36
1.54
1.53
1.51
1.50
1.47
1.46
1.07
1.03
1.00
0.97
0.96
0.92
0.91
NH2
Pd-L5
OMs
P5
OMe
MeO
t-Bu
P
Ph
i-Pr
i-Pr
i-Pr
L5
¹H NMR, 500 MHz, CDCl3
1.12
4.48
3.12
5.15
1.00
1.02
1.00
0.98
3.00
3.09
1.03
1.00
1.03
3.02
3.00
2.96
3.07
9.12
3.08
3.09
2.97
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
f1 (ppm)
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
−0.1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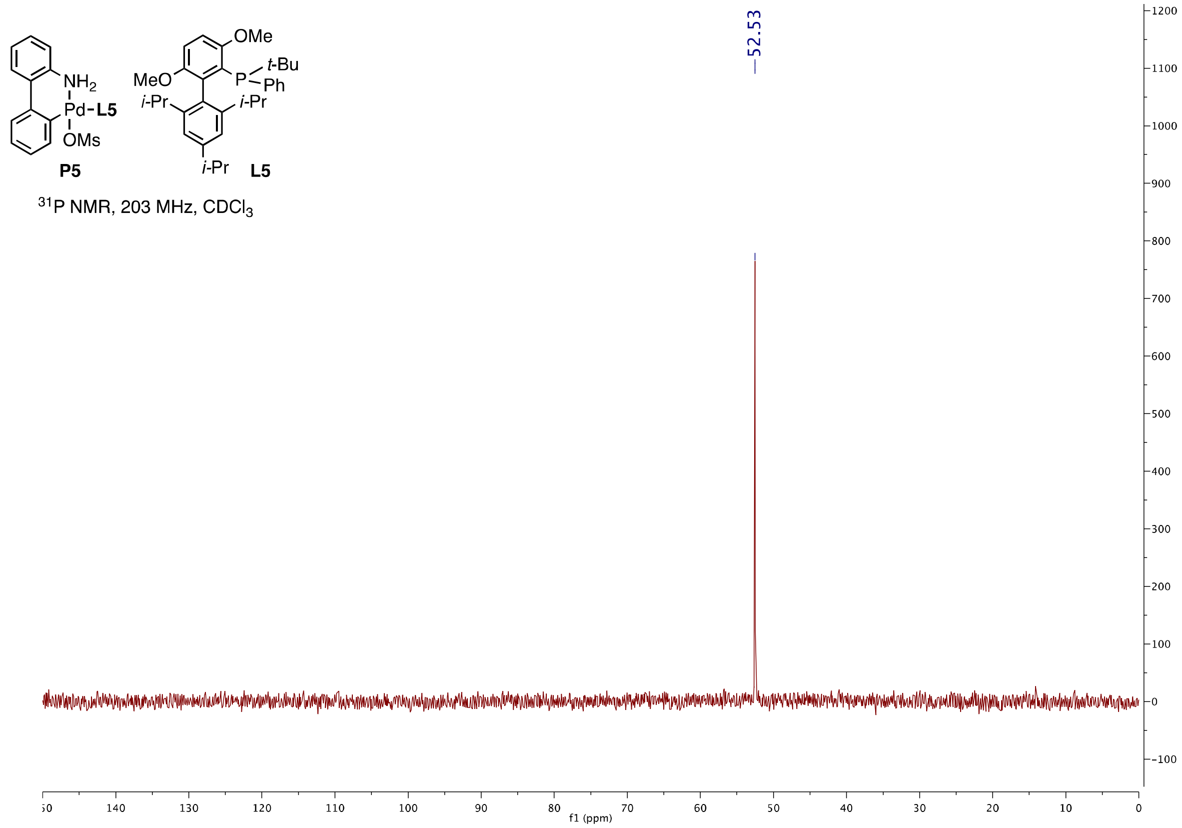
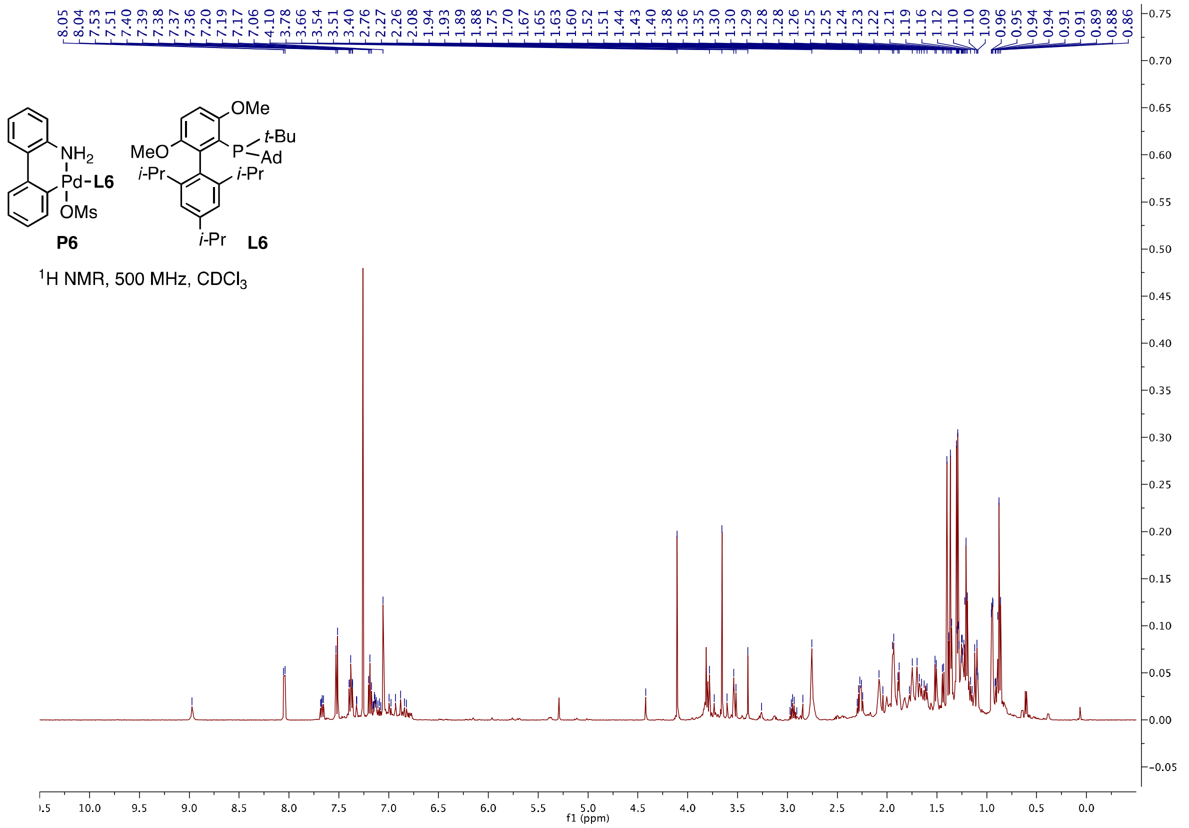
154.34
154.00
151.91
151.78
145.12
140.41
139.28
136.28
136.04
135.88
135.54
135.48
130.58
128.47
128.44
128.05
127.26
126.76
126.06
125.92
125.17
122.38
120.49
118.50
118.45
115.95
115.93
113.26
113.23
55.29
39.23
37.29
37.08
34.37
33.04
31.99
31.94
31.54
26.68
24.90
24.80
24.69
24.62
24.58
NH2
Pd-L5
OMs
P5
OMe
MeO
t-Bu
P
Ph
i-Pr
i-Pr
i-Pr
L5
¹³C NMR, 126 MHz, CDCl3
170
160
150
140
130
120
110
100
90
f1 (ppm)
80
70
60
50
40
30
20
10
0.016
0.015
0.014
0.013
0.012
0.011
0.010
0.009
0.008
0.007
0.006
0.005
0.004
0.003
0.002
0.001
0.000
−0.001
−0.002

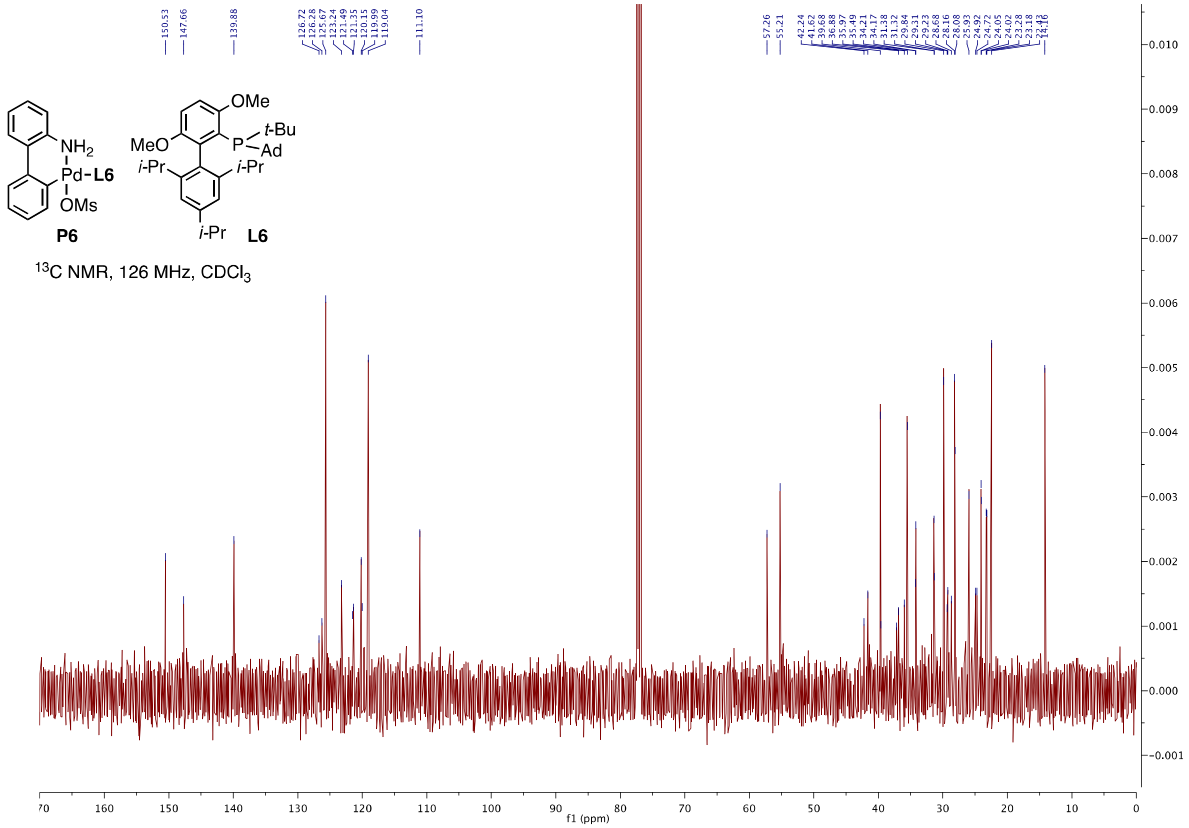


^{31}P NMR, 203 MHz, CDCl$_3$



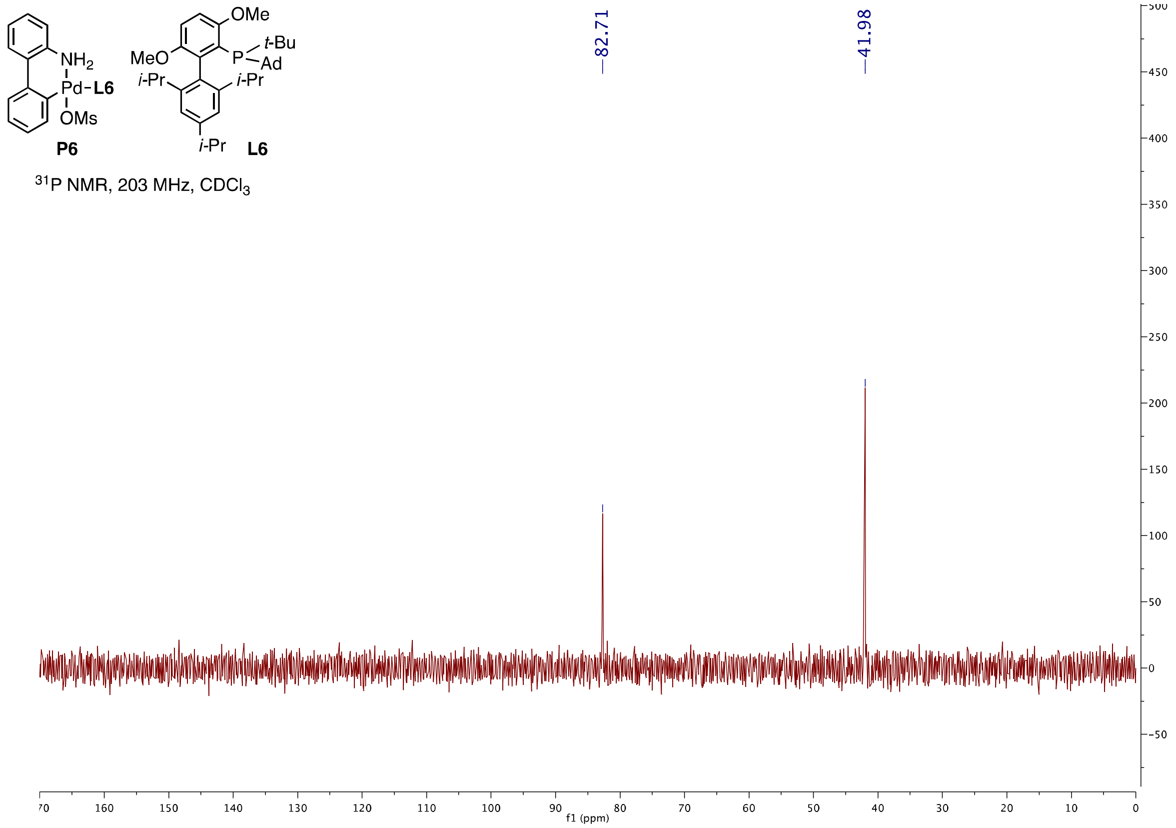
P6 **L6**

^{1}H NMR, 500 MHz, CDCl$_3$

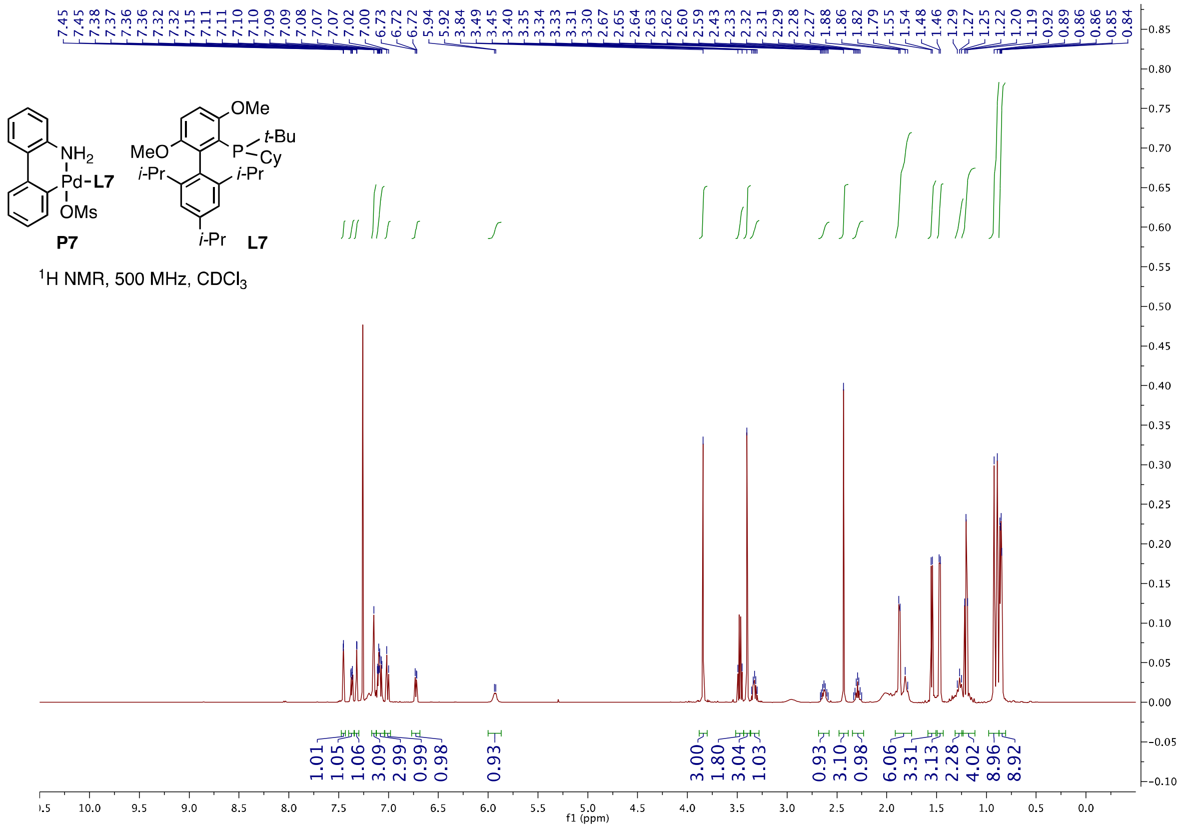


P6 **L6**

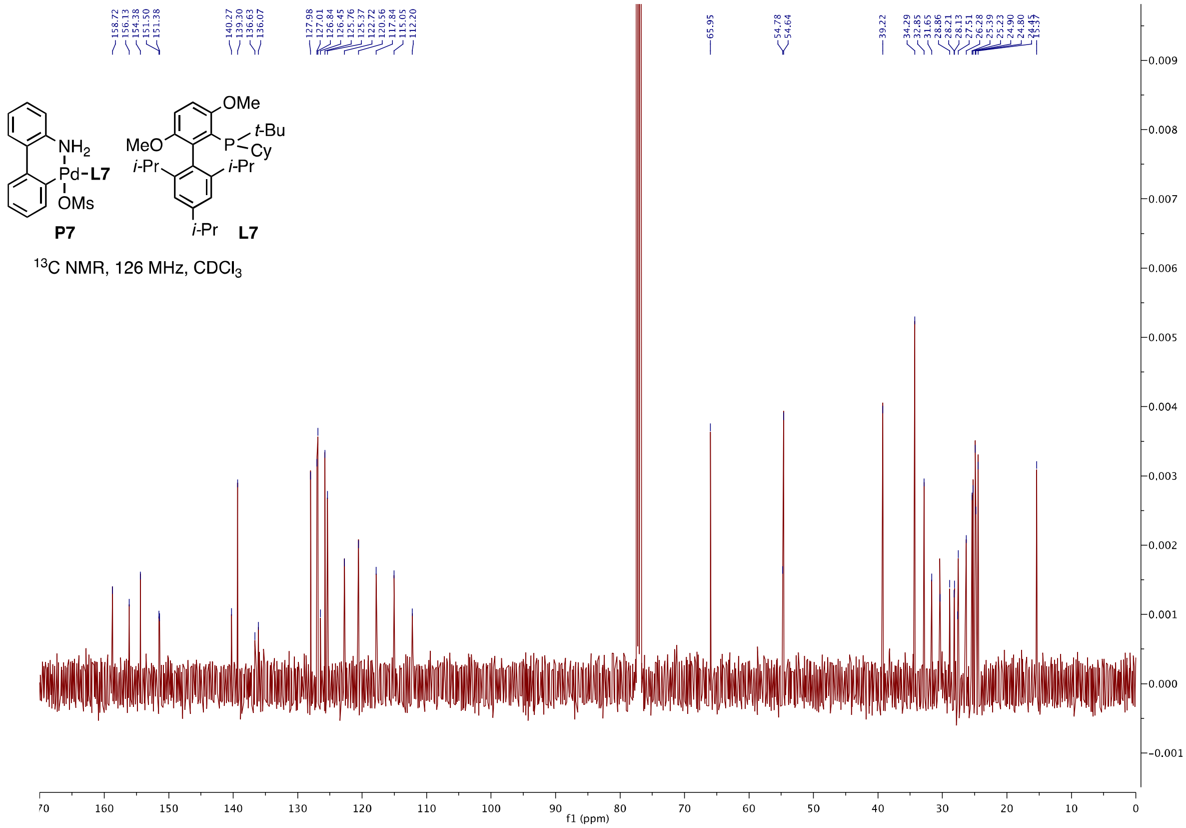
^{13}C NMR, 126 MHz, CDCl$_3$



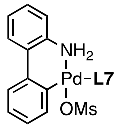
^{31}P NMR, 203 MHz, CDCl$_3$



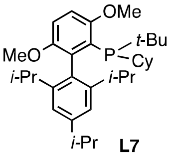
^{1}H NMR, 500 MHz, CDCl$_3$



^{13}C NMR, 126 MHz, CDCl$_3$

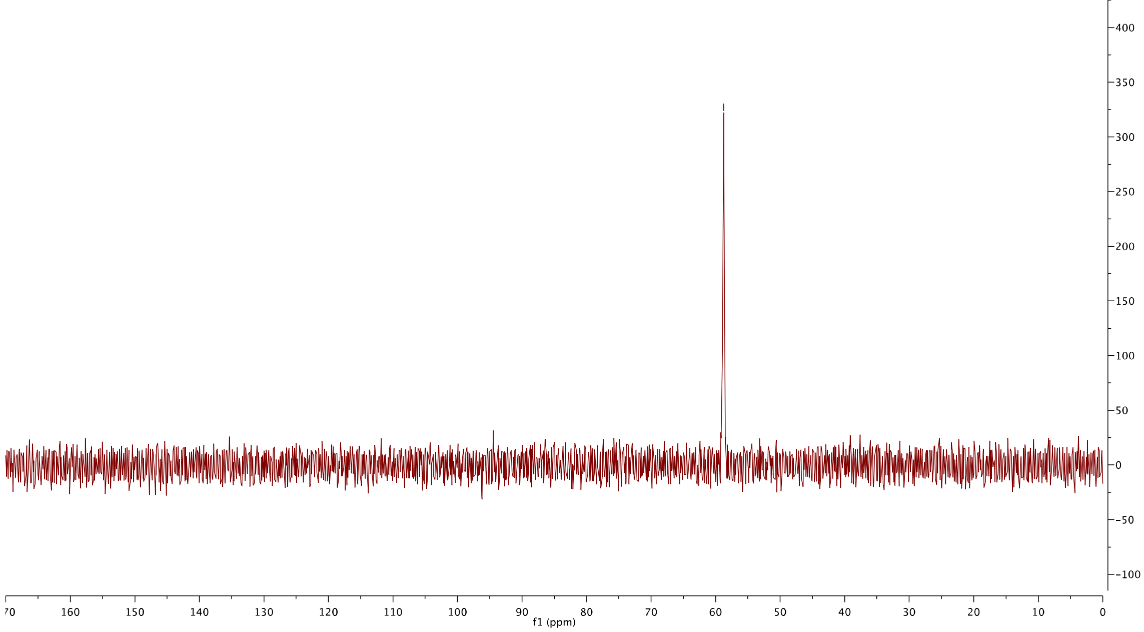


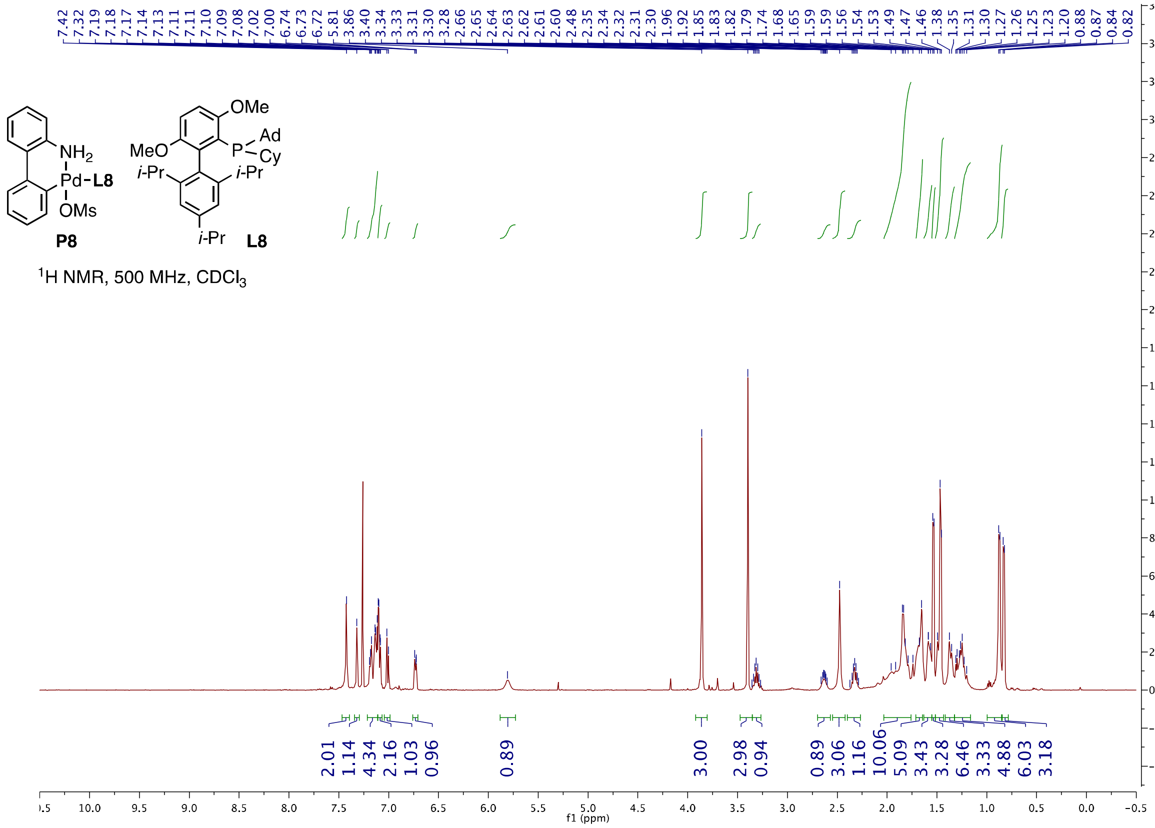
P7



L7

^{31}P NMR, 203 MHz, $CDCl_3$

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7.02
7.00
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6.73
6.72
5.81
3.86
3.40
3.34
3.33
3.31
3.30
3.28
2.66
2.65
2.64
2.63
2.62
2.61
2.60
2.48
2.35
2.34
2.32
2.31
2.30
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1.85
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1.82
1.79
1.74
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1.59
1.59
1.56
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1.49
1.47
1.46
1.38
1.35
1.31
1.30
1.27
1.26
1.25
1.23
1.20
0.88
0.87
0.84
0.82
NH2
Pd-L8
OMs
P8
OMe
MeO
P
Ad
Cy
i-Pr
i-Pr
i-Pr
L8
¹H NMR, 500 MHz, CDCl3
2.01
1.14
4.34
2.16
1.03
0.96
0.89
3.00
2.98
0.94
0.89
3.06
1.16
10.06
5.09
3.43
3.28
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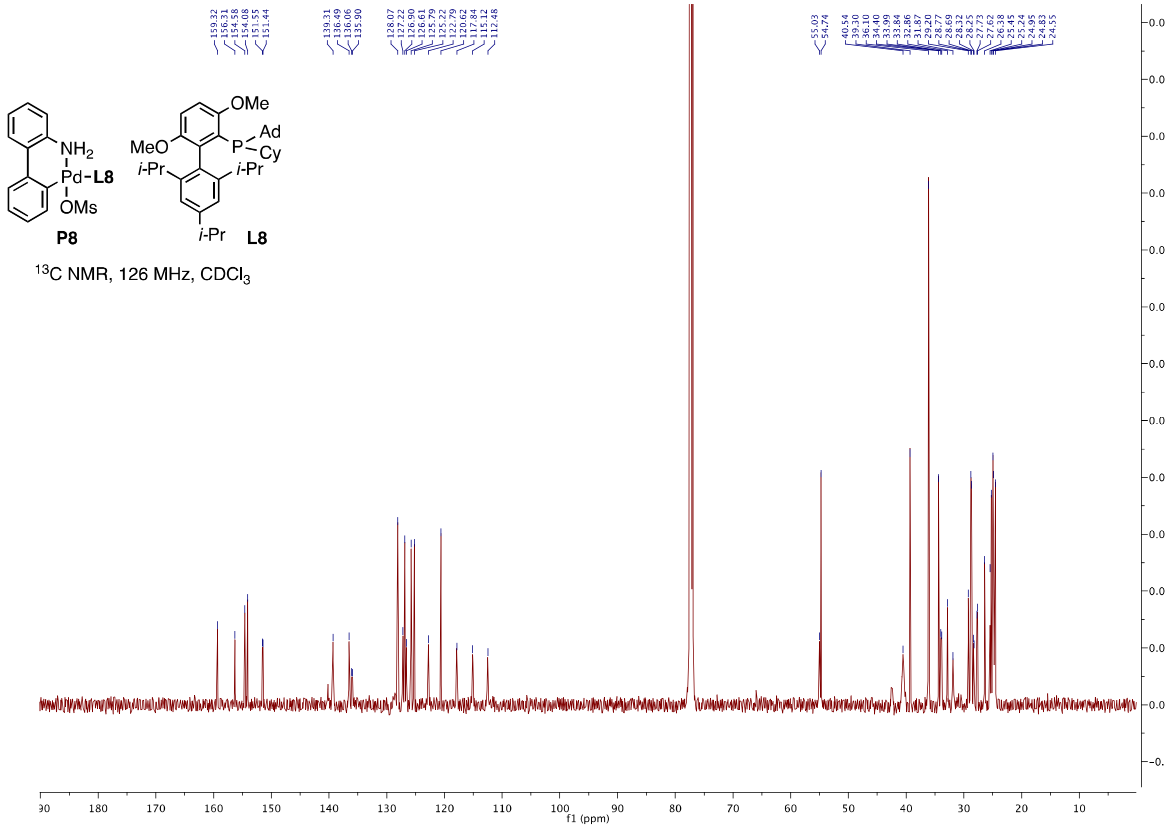
3.33
4.88
6.03
3.18
f1 (ppm)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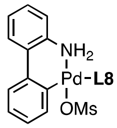
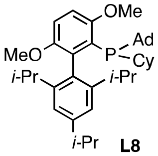
151.44
139.31
136.49
136.06
135.90
128.07
127.22
126.90
126.61
125.79
125.22
122.79
120.62
117.84
115.12
112.48
55.03
54.74
40.54
39.30
36.10
34.40
33.99
33.84
32.86
31.87
29.20
28.77
28.69
28.32
28.25
27.73
27.62
26.38
25.45
25.24
24.95
24.83
24.55
NH2
Pd-L8
OMs
P8
OMe
MeO
P
Ad
Cy
i-Pr
i-Pr
i-Pr
L8
¹³C NMR, 126 MHz, CDCl3
f1 (ppm)

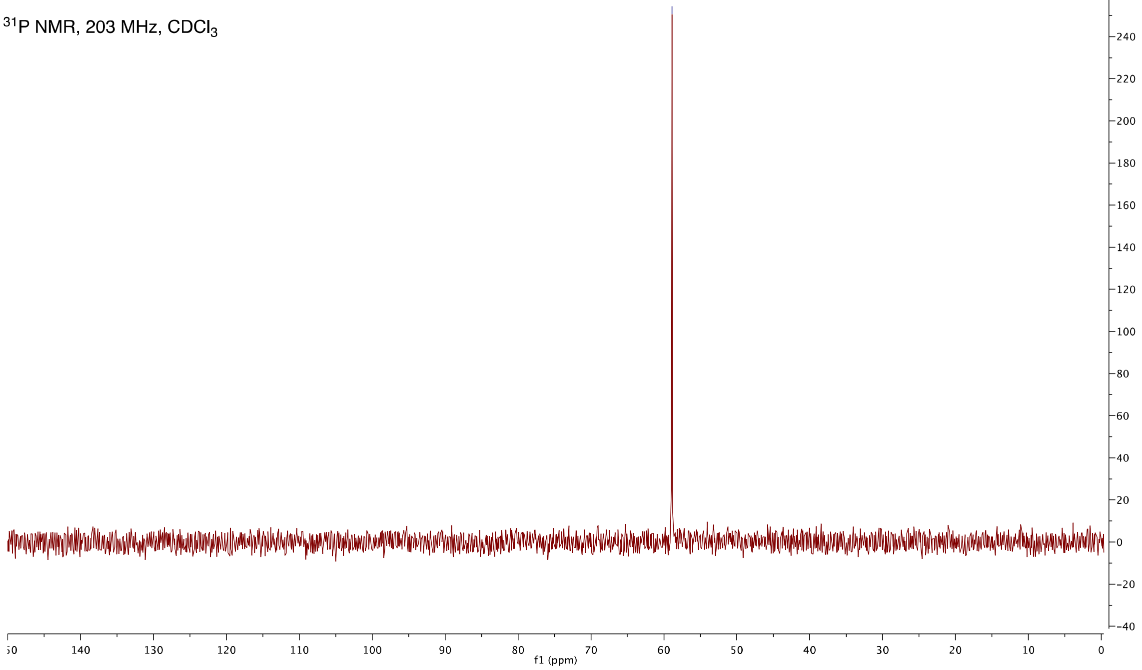


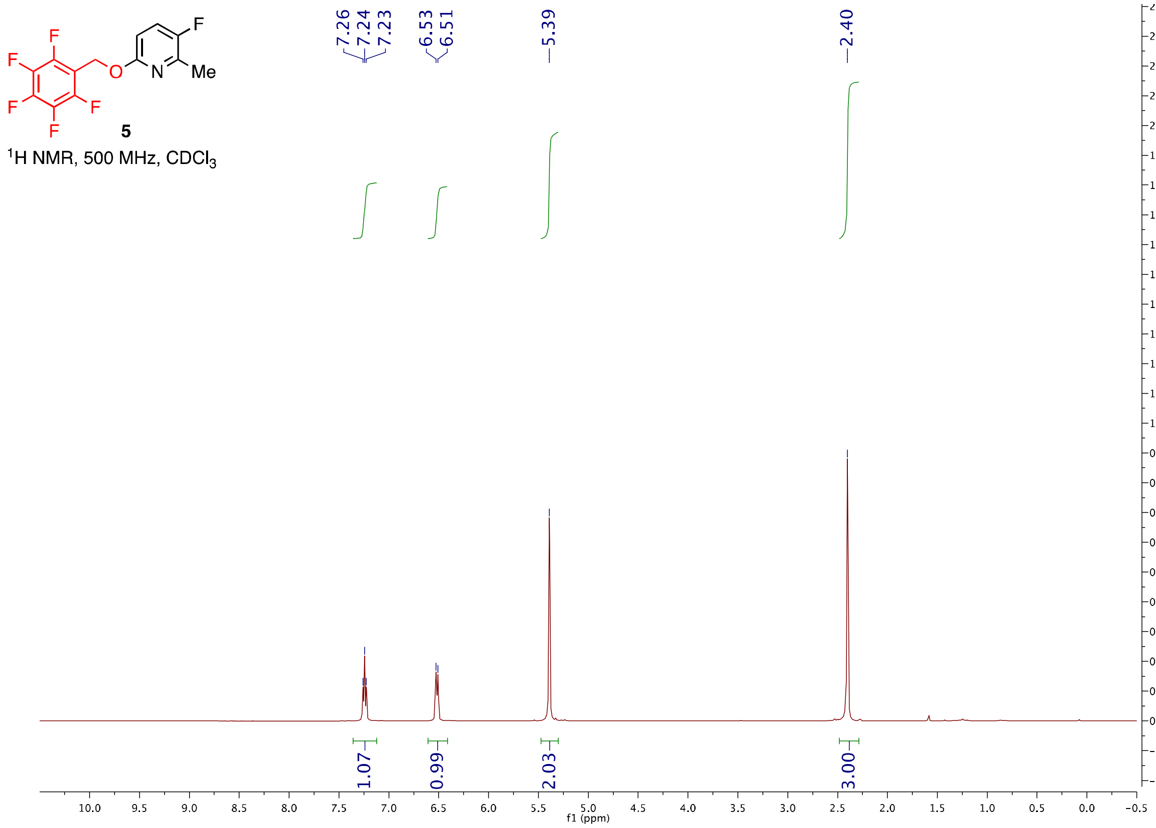
P8



L8

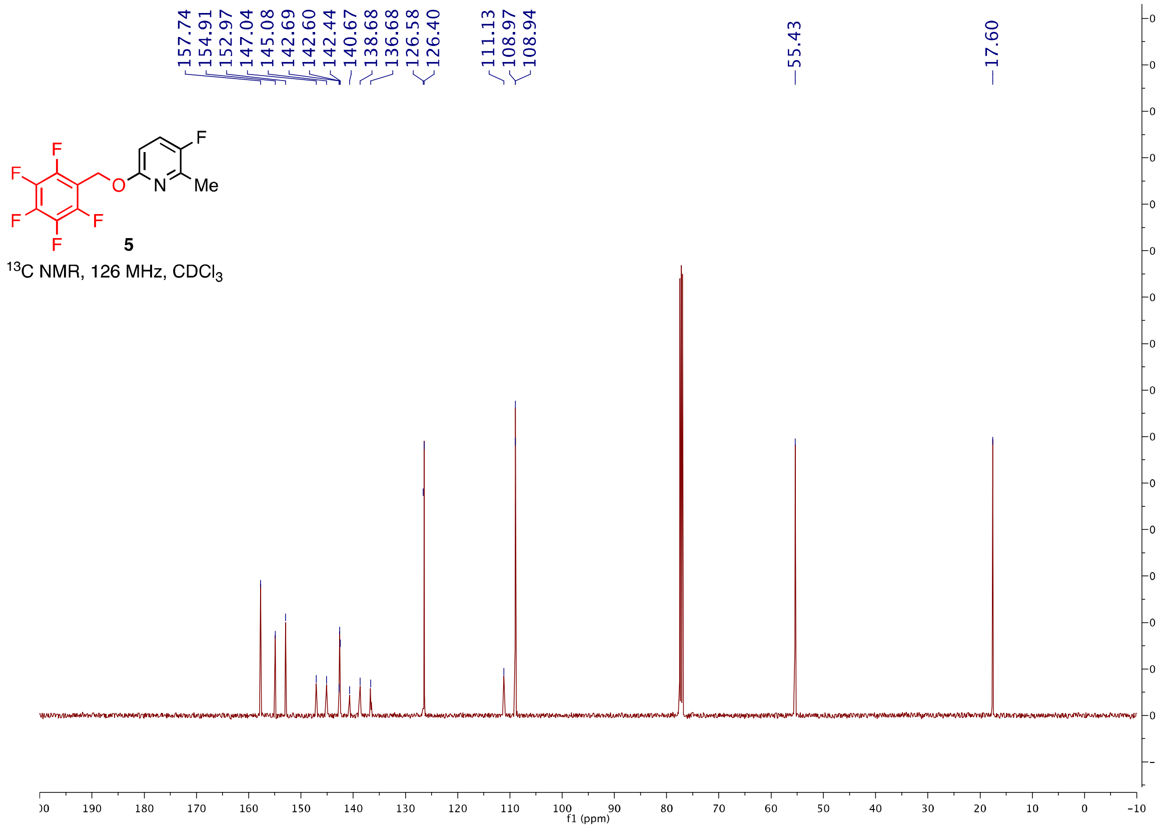
^{31}P NMR, 203 MHz, CDCl$_3$





5

^{1}H NMR, 500 MHz, $CDCl_3$



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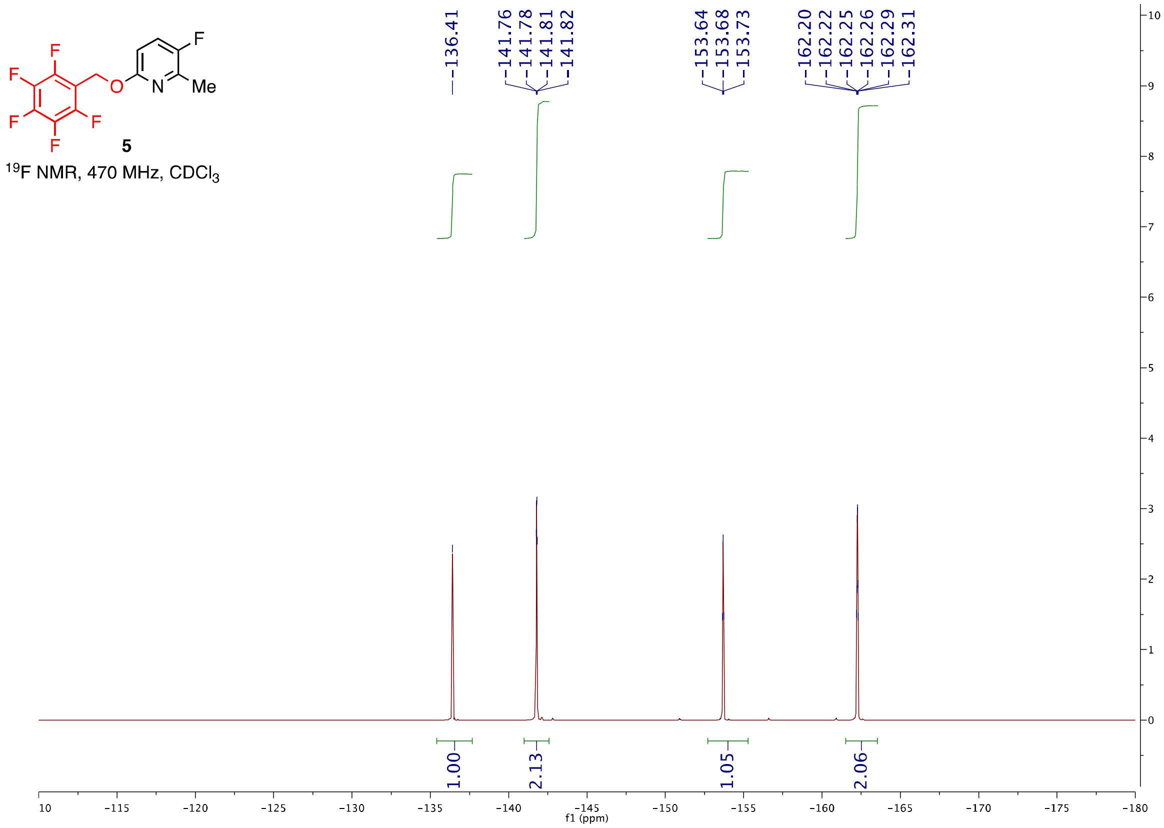
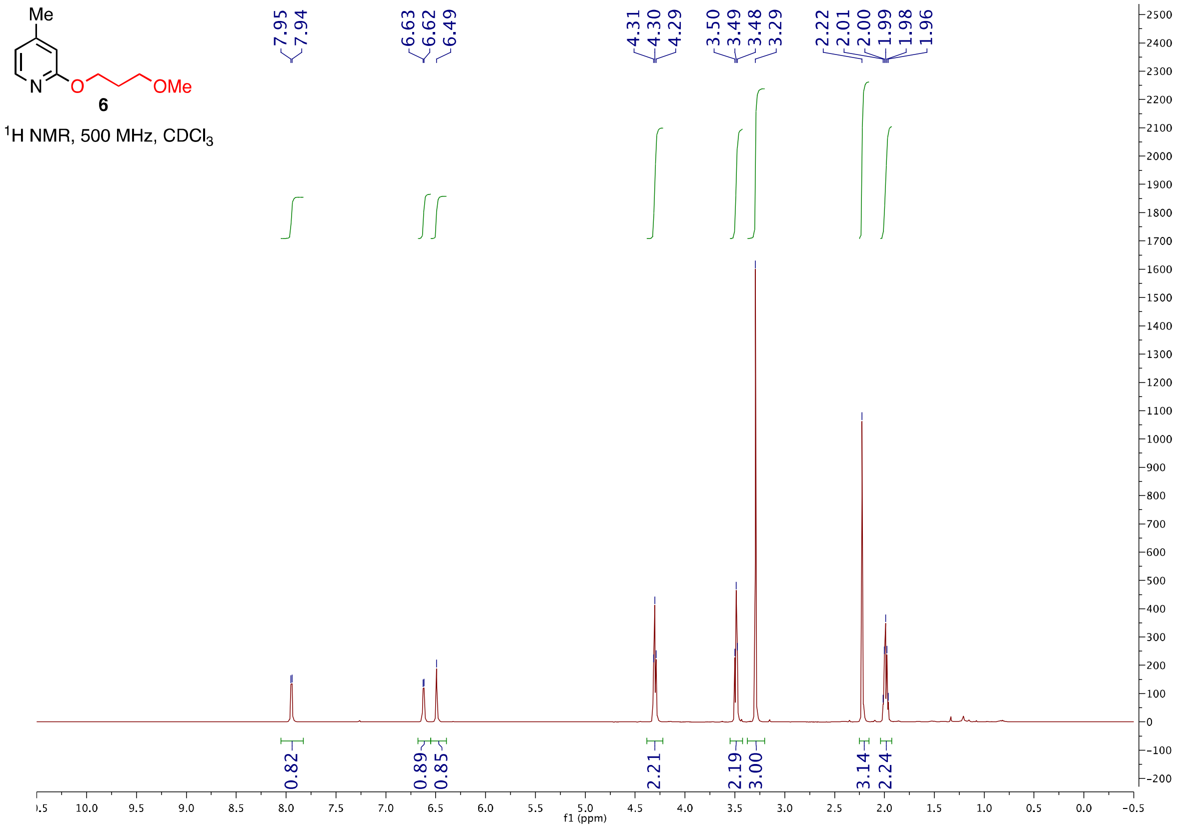
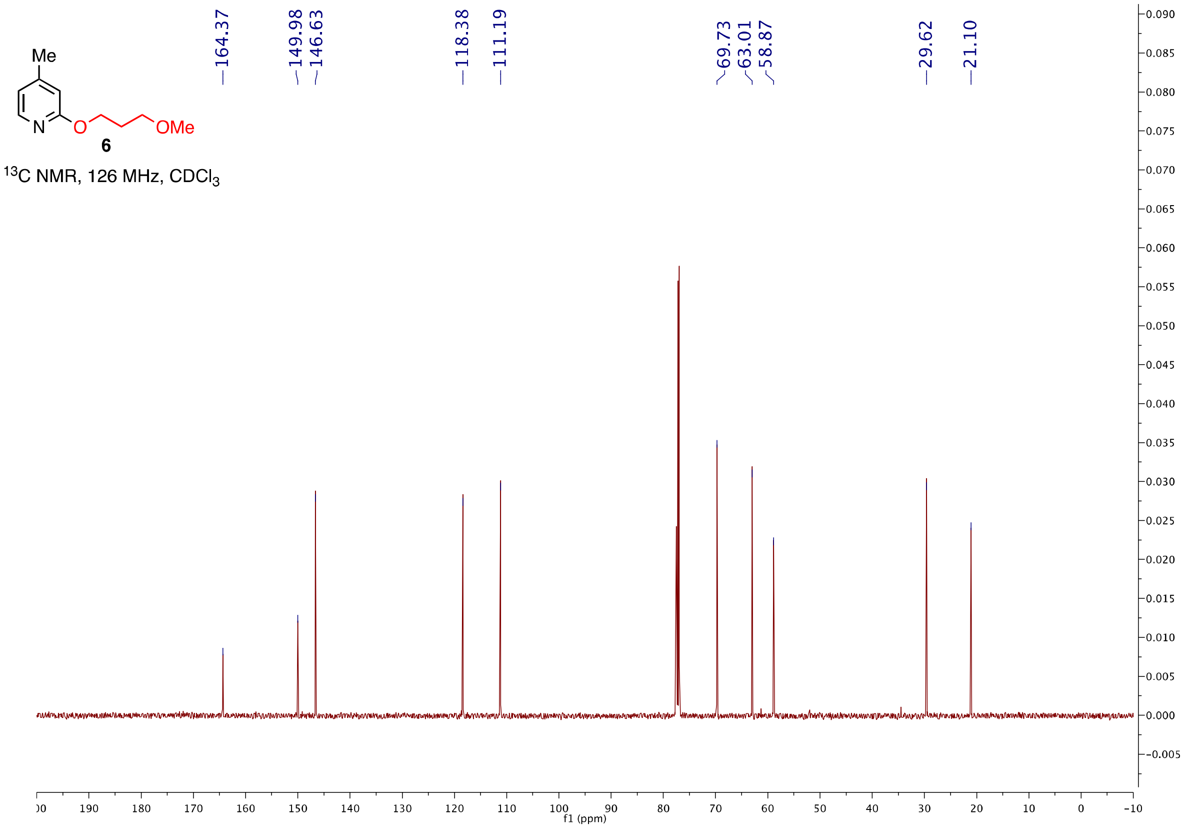
^{13}C NMR, 126 MHz, $CDCl_3$



5

^{19}F NMR, 470 MHz, CDCl$_3$


Me
N
O
OMe
6
^{1}H NMR, 500 MHz, CDCl$_3$
7.95
7.94
6.63
6.62
6.49
4.31
4.30
4.29
3.50
3.49
3.48
3.29
2.22
2.01
2.00
1.99
1.98
1.96
0.82
0.89
0.85
2.21
2.19
3.00
3.14
2.24
f1 (ppm)


Me
N
O
OMe
6
^{13}C NMR, 126 MHz, CDCl$_3$
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111.19
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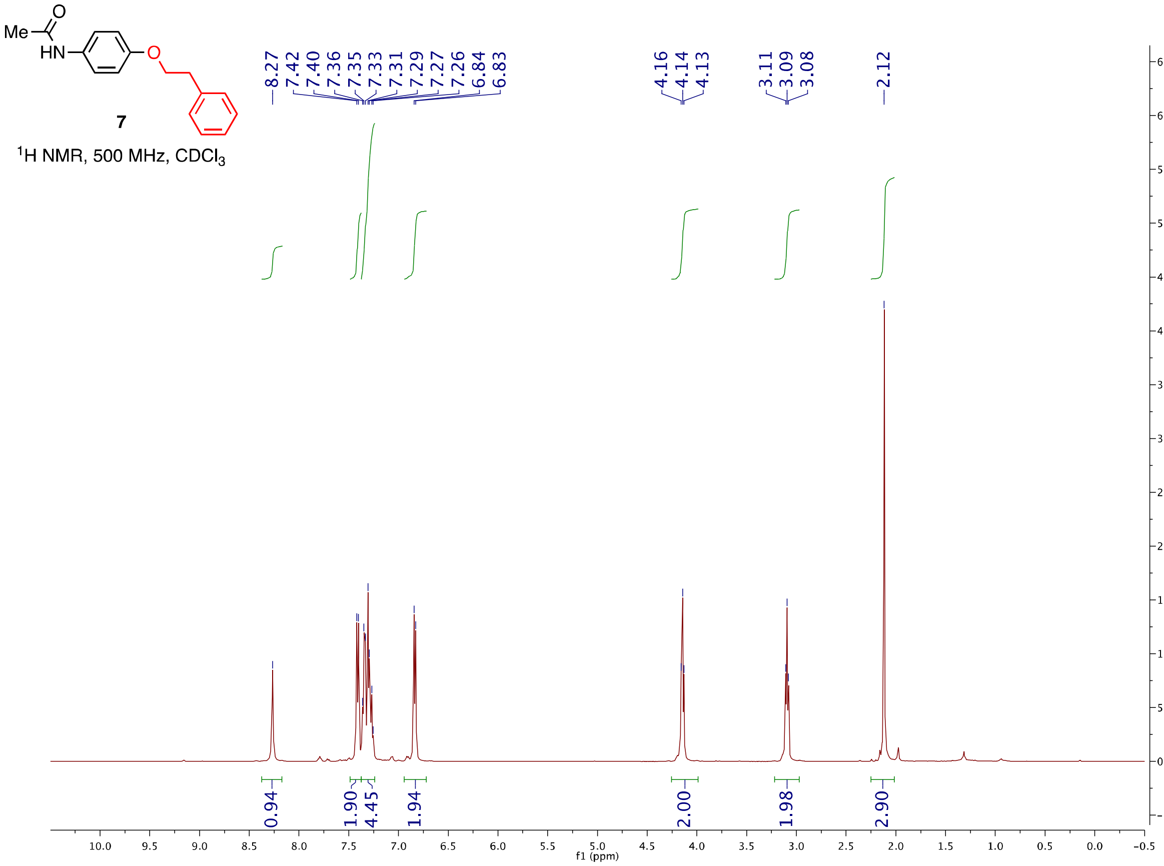
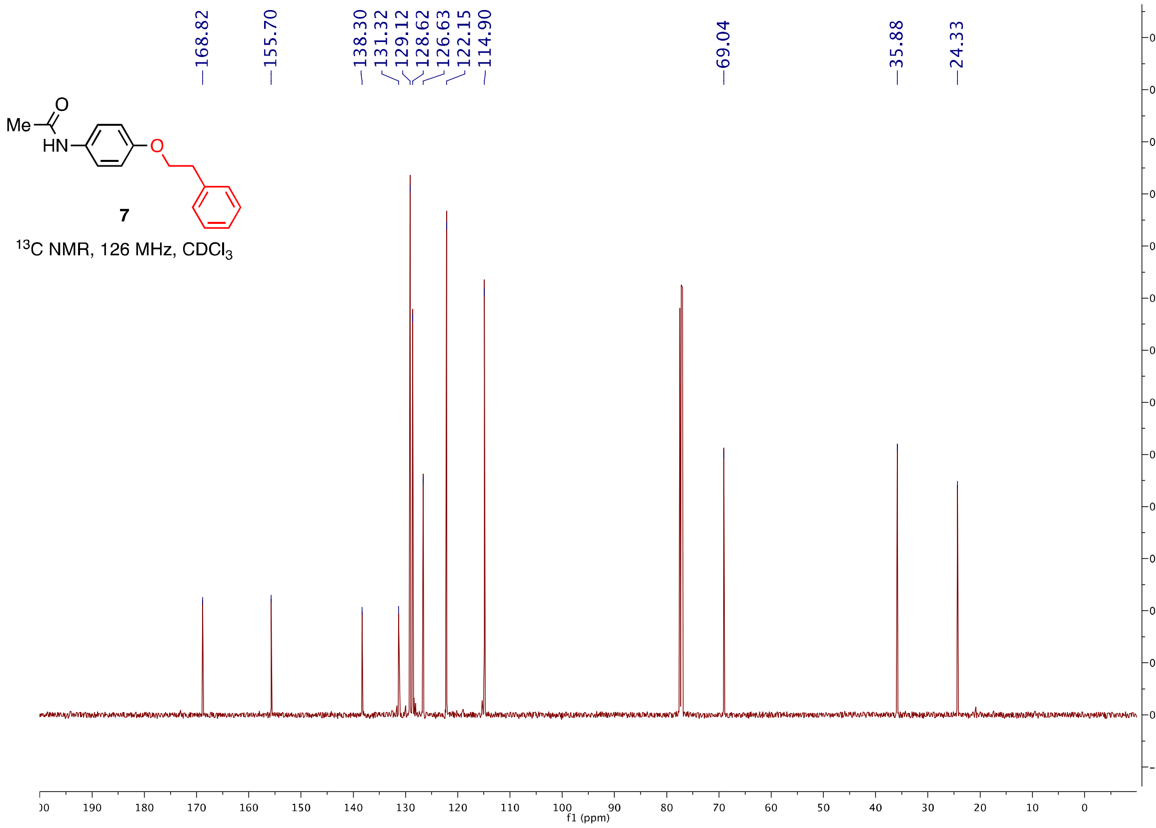
29.62
21.10
f1 (ppm)



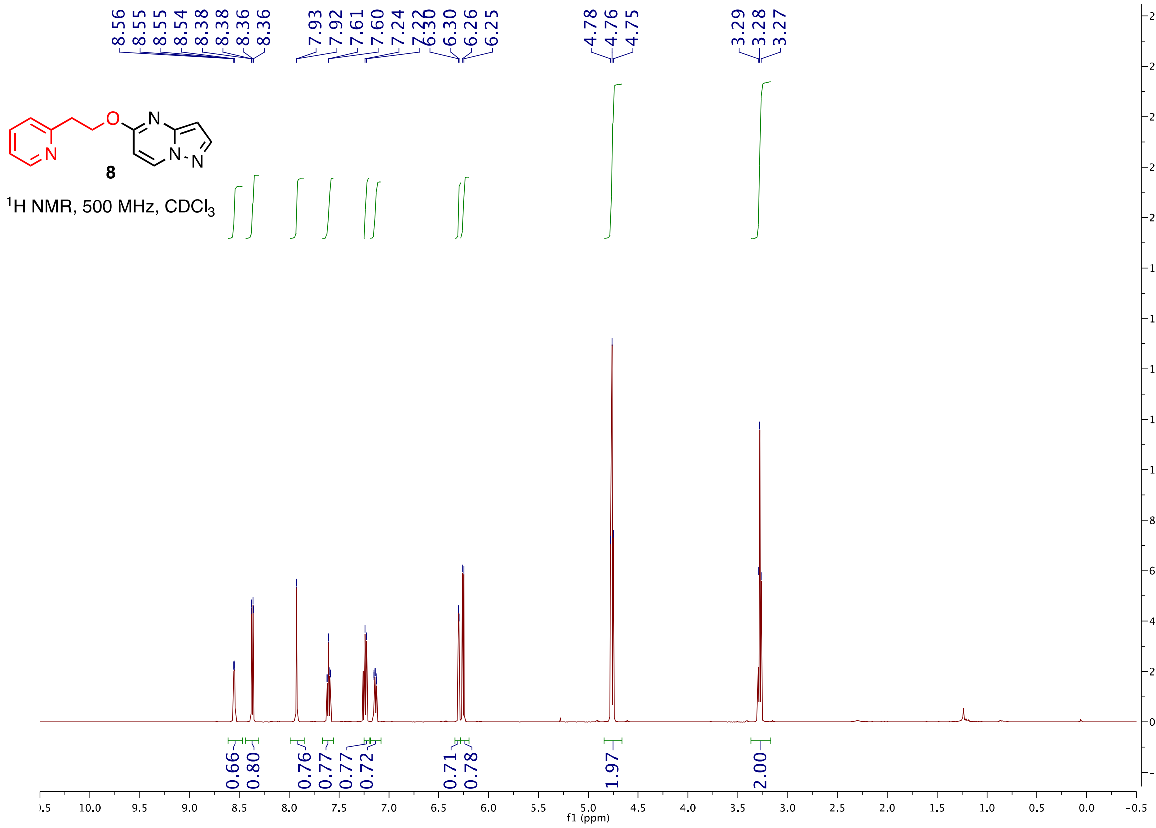
7

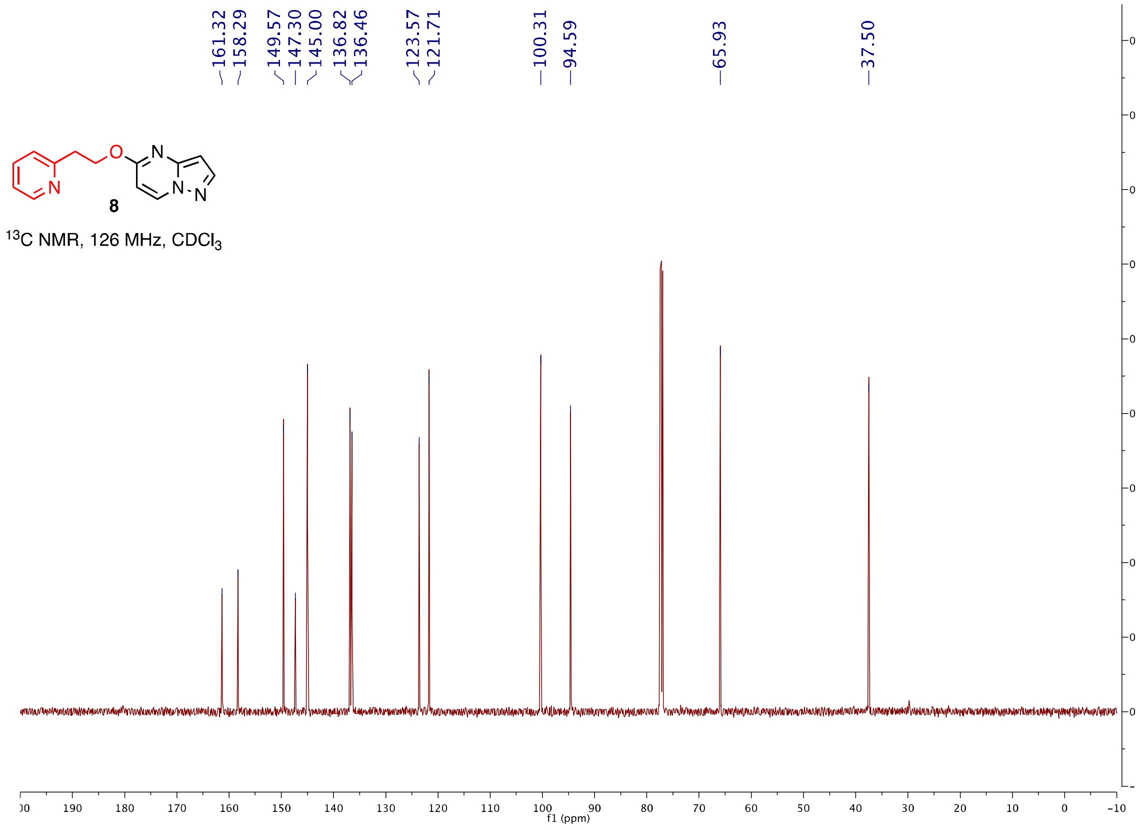
^{1}H NMR, 500 MHz, CDCl$_3$

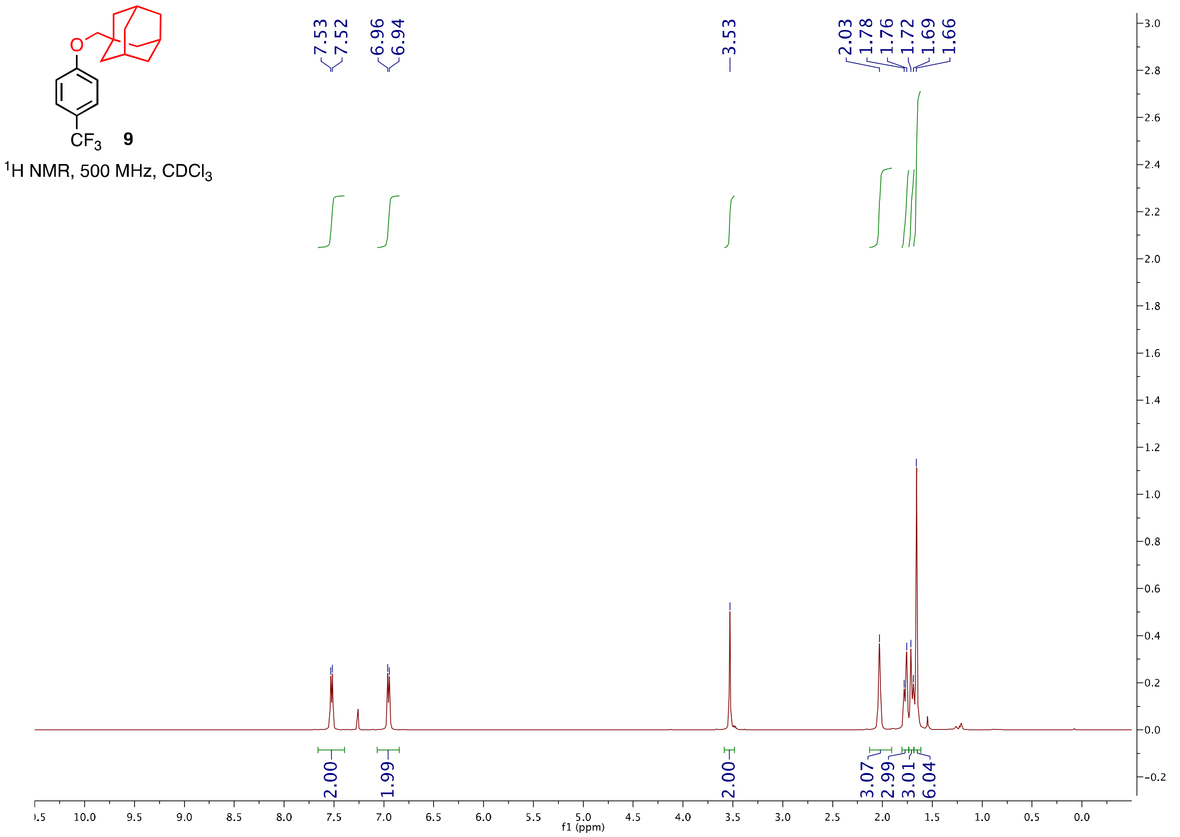


7

^{13}C NMR, 126 MHz, CDCl$_3$

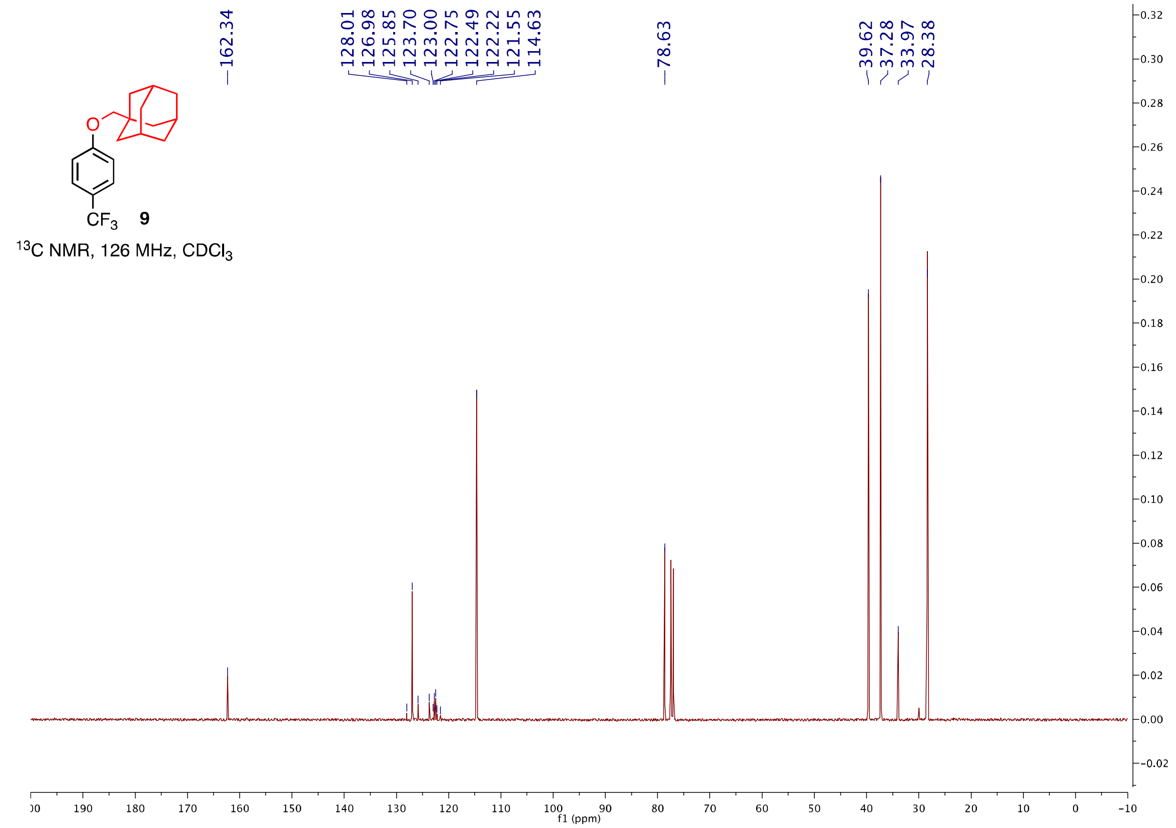

8.56
8.55
8.55
8.54
8.38
8.38
8.36
8.36
7.93
7.92
7.61
7.60
7.24
7.22
6.30
6.30
6.26
6.25
4.78
4.76
4.75
3.29
3.28
3.27
8
¹H NMR, 500 MHz, CDCl₃
0.66
0.80
0.76
0.77
0.77
0.72
0.71
0.78
1.97
2.00
f1 (ppm)
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
−200
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5


161.32
158.29
149.57
147.30
145.00
136.82
136.46
123.57
121.71
100.31
94.59
65.93
37.50
8
¹³C NMR, 126 MHz, CDCl₃
f1 (ppm)
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
−0.01
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10



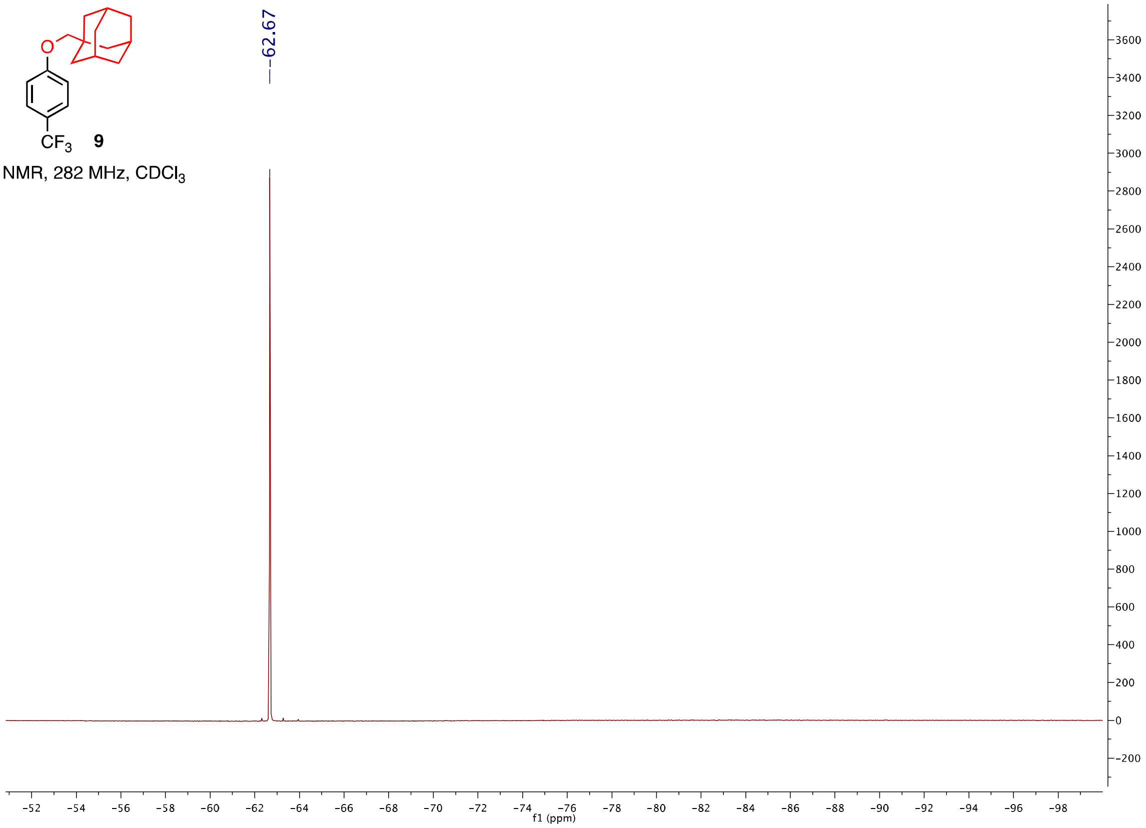
9

^{1}H NMR, 500 MHz, CDCl$_3$



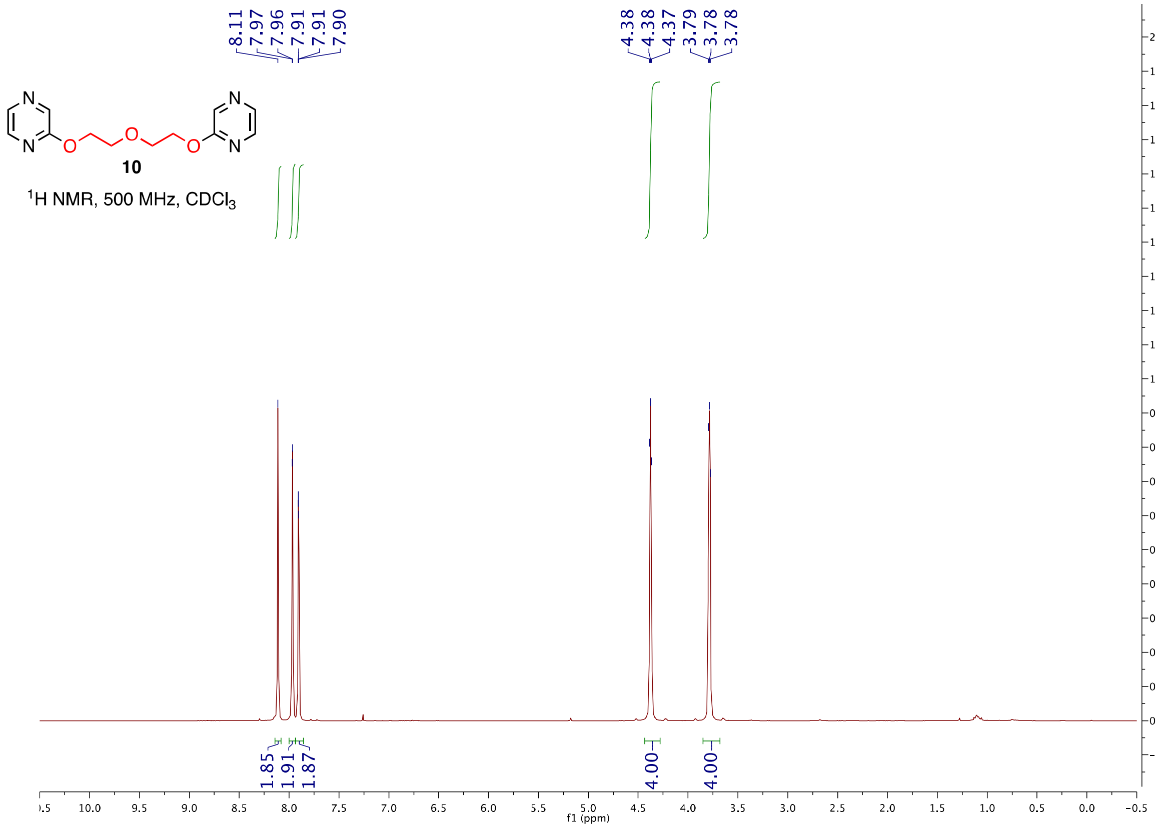
9

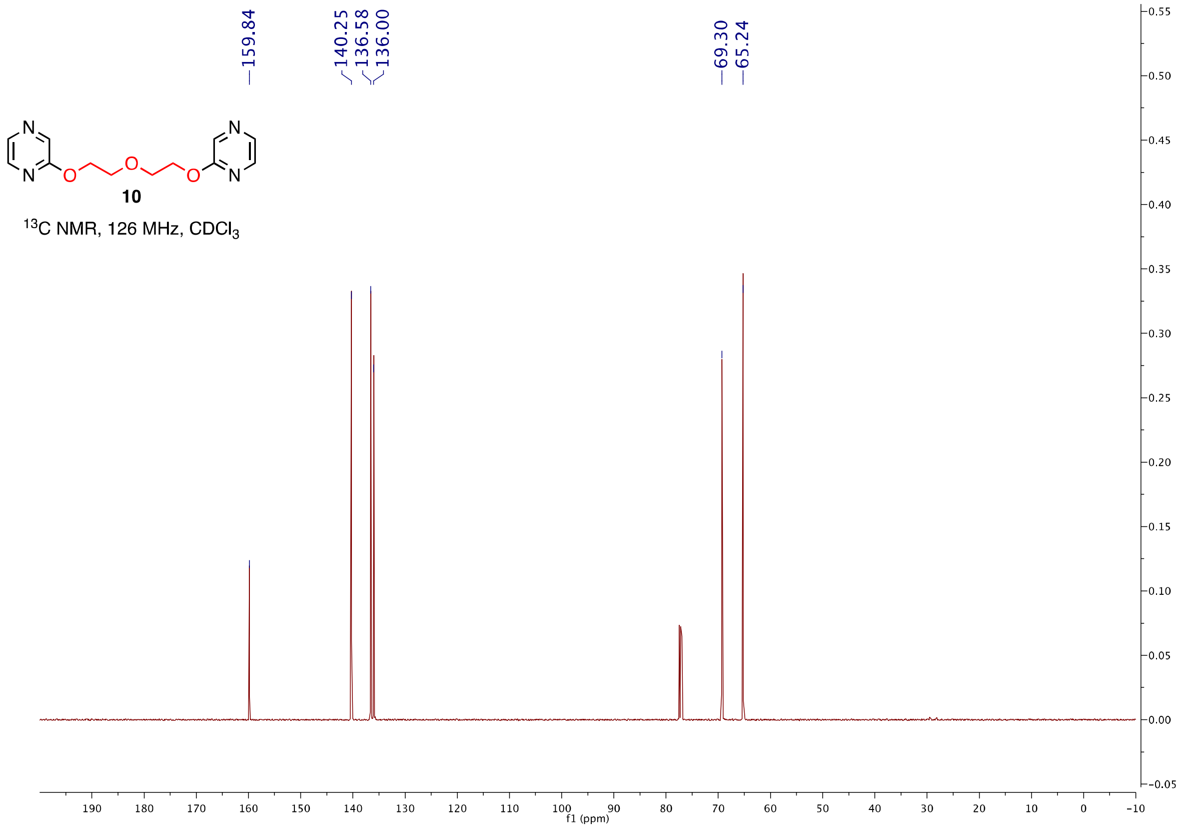
^{13}C NMR, 126 MHz, CDCl$_3$

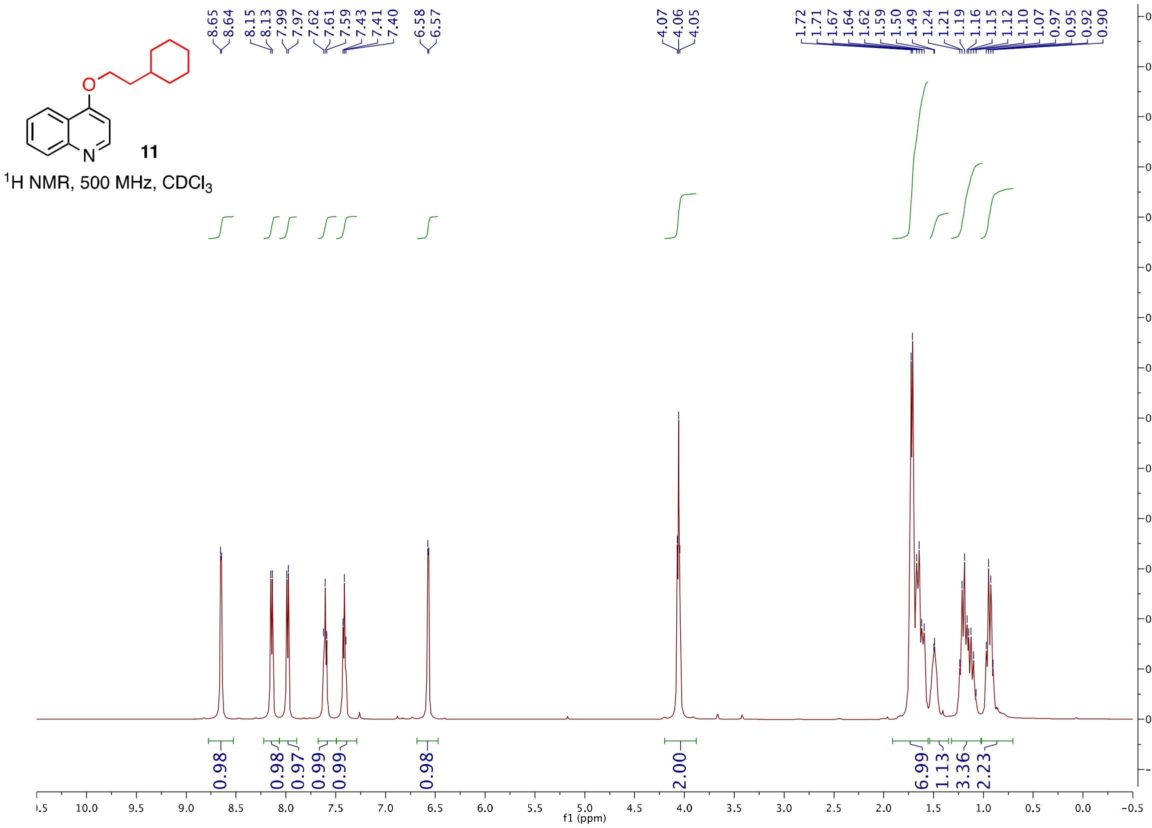


9

^{19}F NMR, 282 MHz, $CDCl_3$

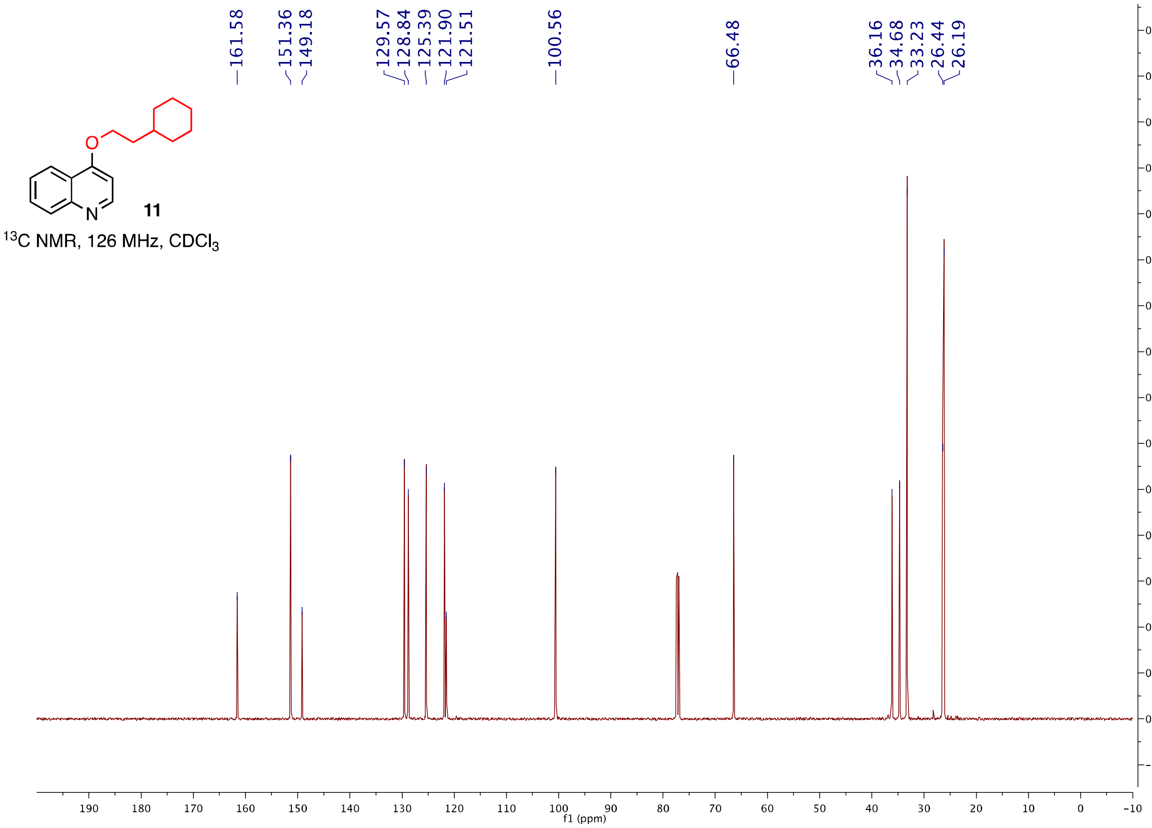

8.11
7.97
7.96
7.91
7.91
7.90
4.38
4.38
4.37
3.79
3.78
3.78
N
O
O
O
10
^{1}H NMR, 500 MHz, CDCl$_3$
1.85
1.91
1.87
4.00
4.00
f1 (ppm)
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6 0.5 0.4 0.3 0.2 0.1 0.0 −0.1


159.84
140.25
136.58
136.00
69.30
65.24
N
O
O
O
10
^{13}C NMR, 126 MHz, CDCl$_3$
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
0.55 0.50 0.45 0.40 0.35 0.30 0.25 0.20 0.15 0.10 0.05 0.00 −0.05



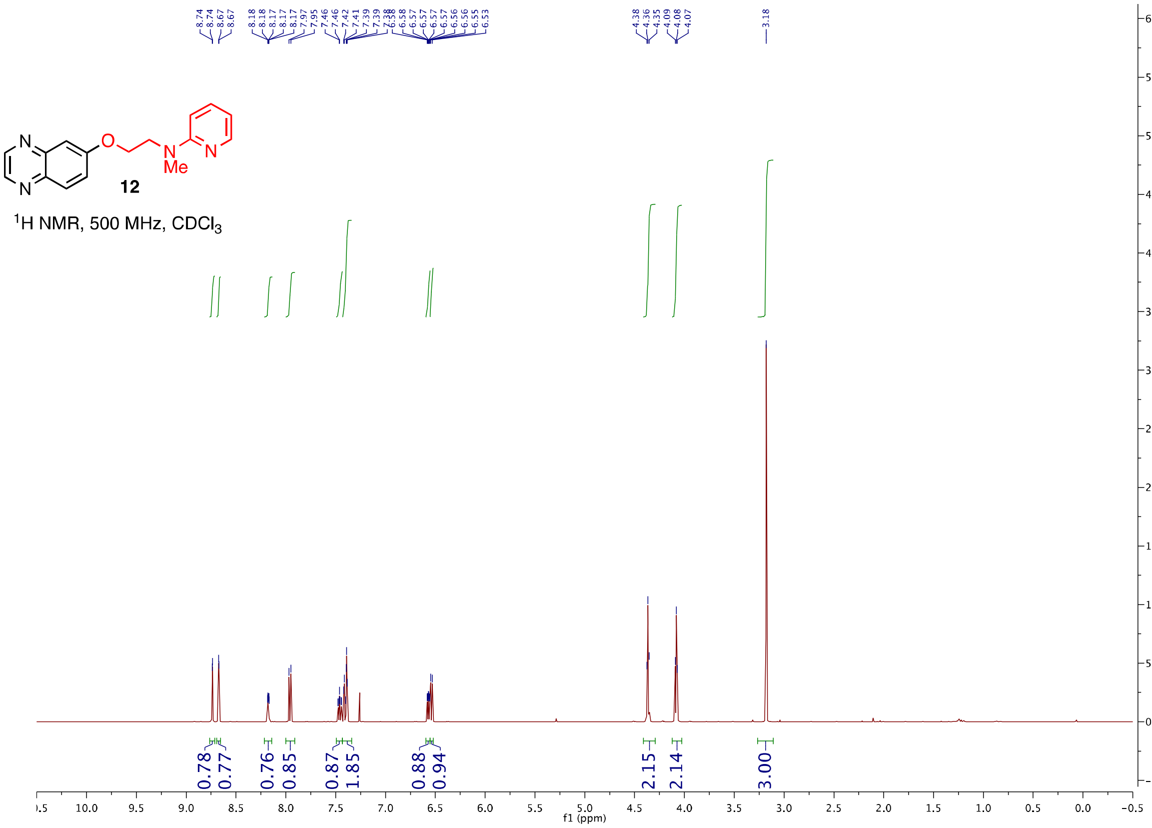
11

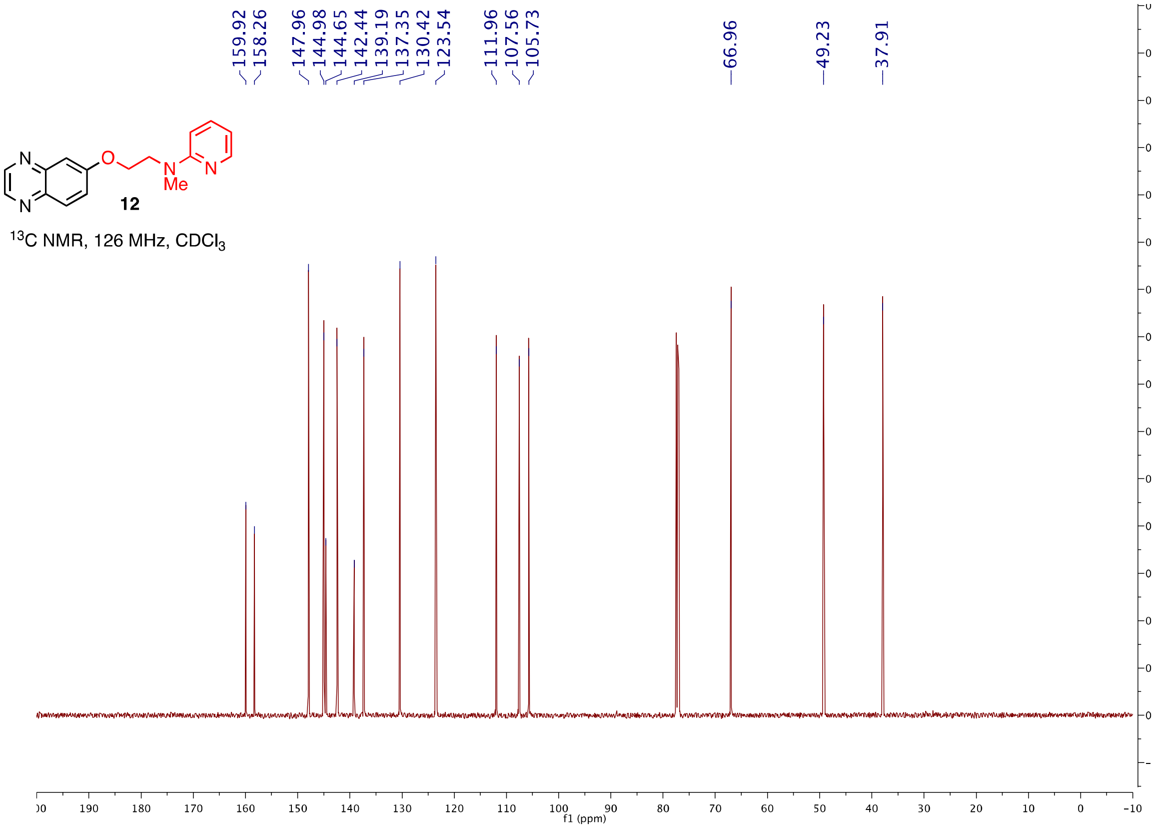
^{1}H NMR, 500 MHz, $CDCl_3$

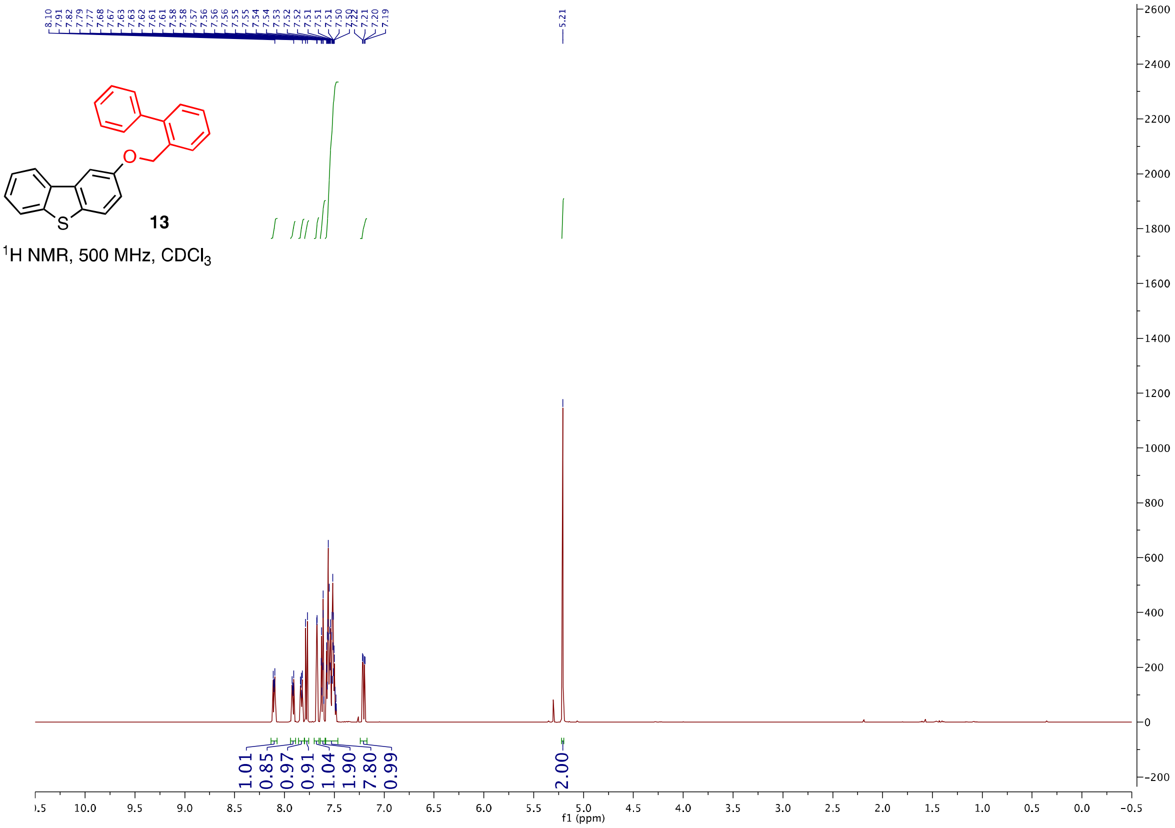


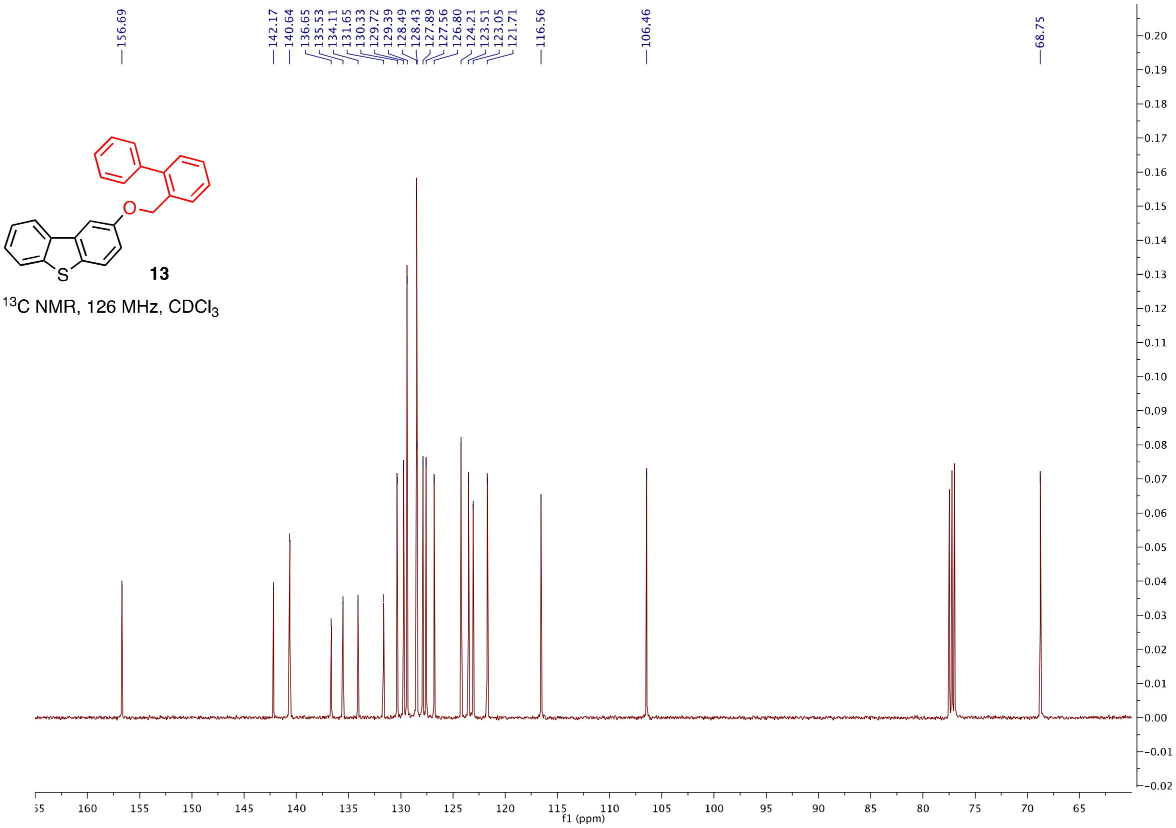
11

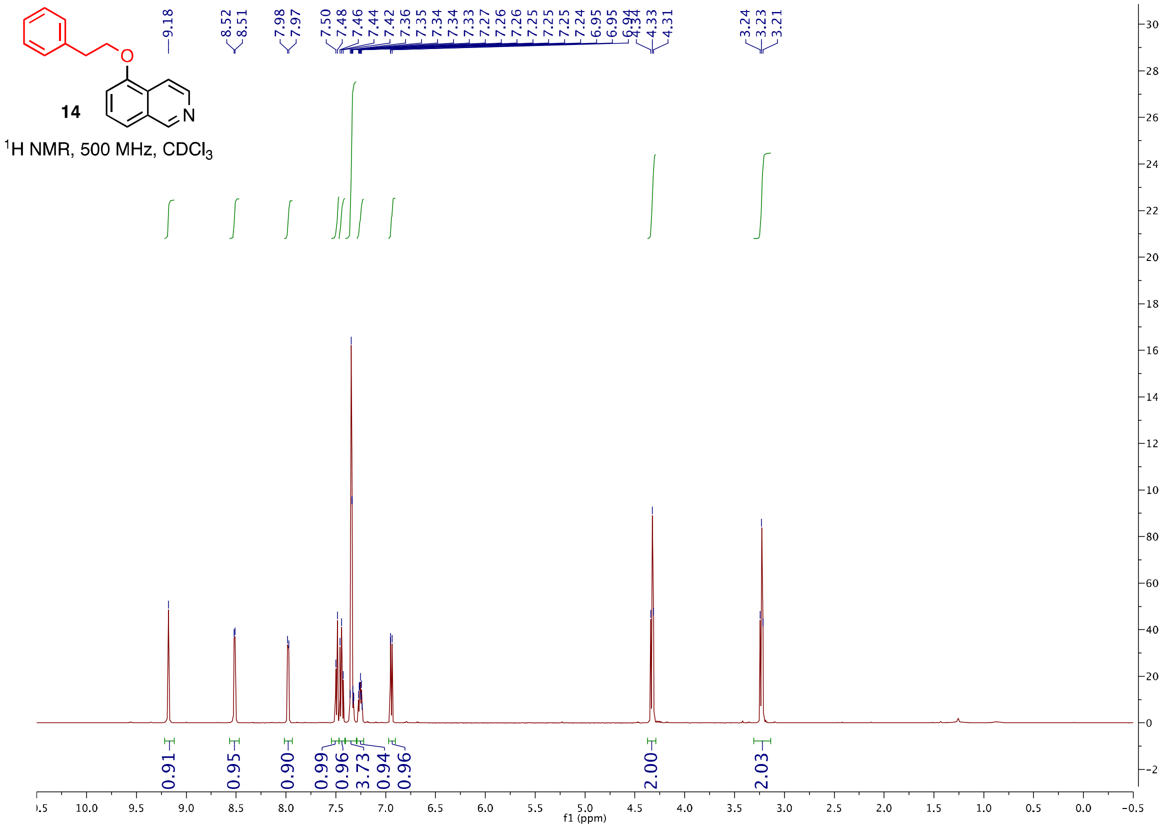
^{13}C NMR, 126 MHz, $CDCl_3$


8.74
8.74
8.67
8.67
8.18
8.18
8.17
8.17
8.17
7.97
7.95
7.46
7.46
7.42
7.41
7.39
7.39
7.38
6.58
6.58
6.57
6.57
6.57
6.57
6.56
6.56
6.55
6.53
4.38
4.36
4.35
4.09
4.08
4.07
3.18
N
N
O
N
Me
N
12
^{1}H NMR, 500 MHz, CDCl$_3$
0.78
0.77
0.76
0.85
0.87
1.85
0.88
0.94
2.15
2.14
3.00
f1 (ppm)


159.92
158.26
147.96
144.98
144.65
142.44
139.19
137.35
130.42
123.54
111.96
107.56
105.73
66.96
49.23
37.91
N
N
O
N
Me
N
12
^{13}C NMR, 126 MHz, CDCl$_3$
f1 (ppm)

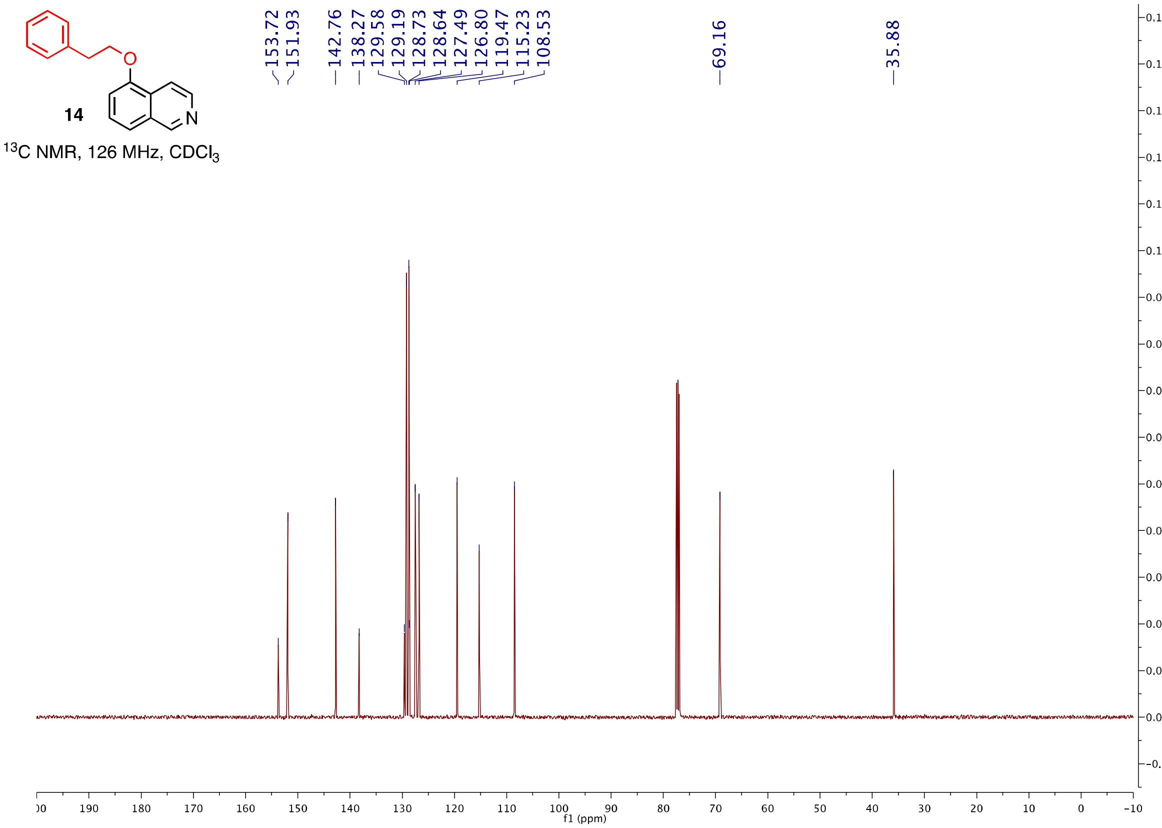

8.10
7.91
7.82
7.79
7.77
7.68
7.67
7.63
7.63
7.62
7.61
7.61
7.58
7.58
7.57
7.56
7.56
7.56
7.55
7.55
7.54
7.54
7.53
7.52
7.52
7.51
7.51
7.51
7.50
7.50
7.22
7.21
7.20
7.19
5.21
O
S
13
^{1}H NMR, 500 MHz, CDCl$_3$
1.01
0.85
0.97
0.91
1.04
1.90
7.80
0.99
2.00
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
−200
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)


156.69
142.17
140.64
136.65
135.53
134.11
131.65
130.33
129.72
129.39
128.49
128.43
127.89
127.56
126.80
124.21
123.51
123.05
121.71
116.56
106.46
68.75
O
S
13
^{13}C NMR, 126 MHz, CDCl$_3$
0.20
0.19
0.18
0.17
0.16
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
−0.01
−0.02
55
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
f1 (ppm)



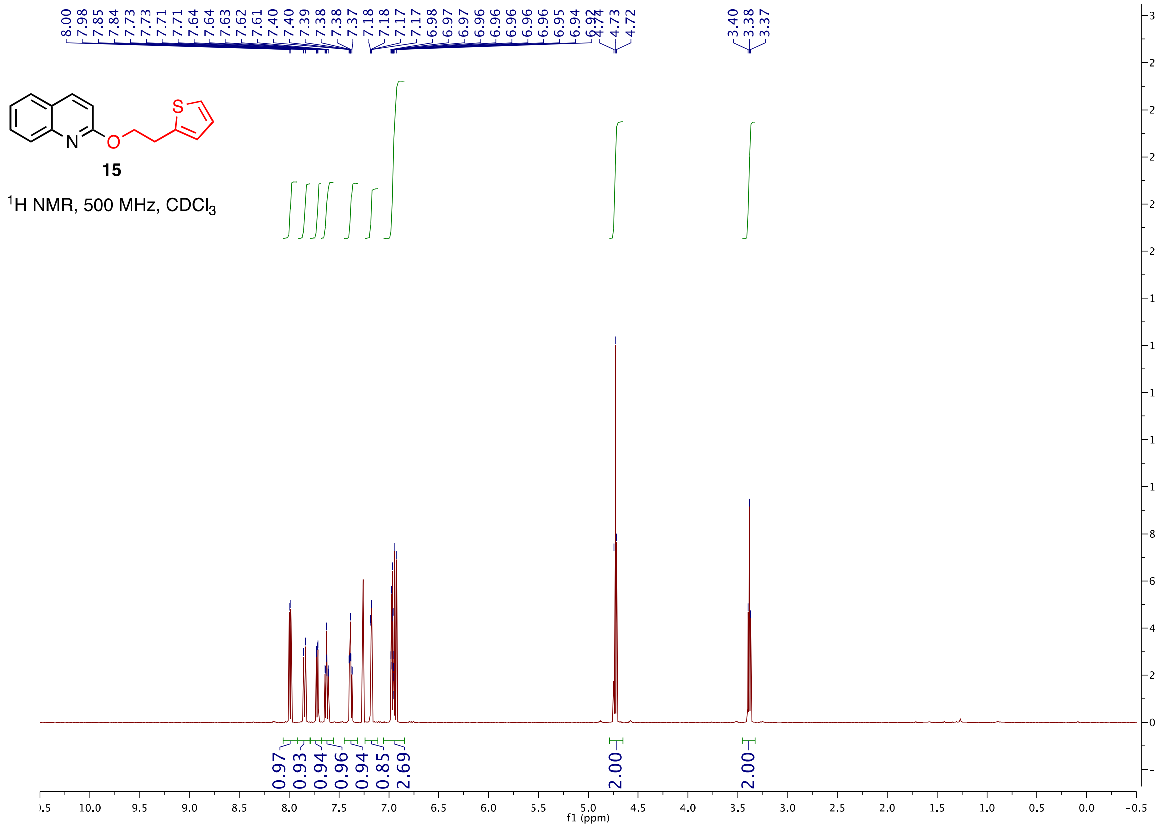
14

^{1}H NMR, 500 MHz, CDCl$_3$



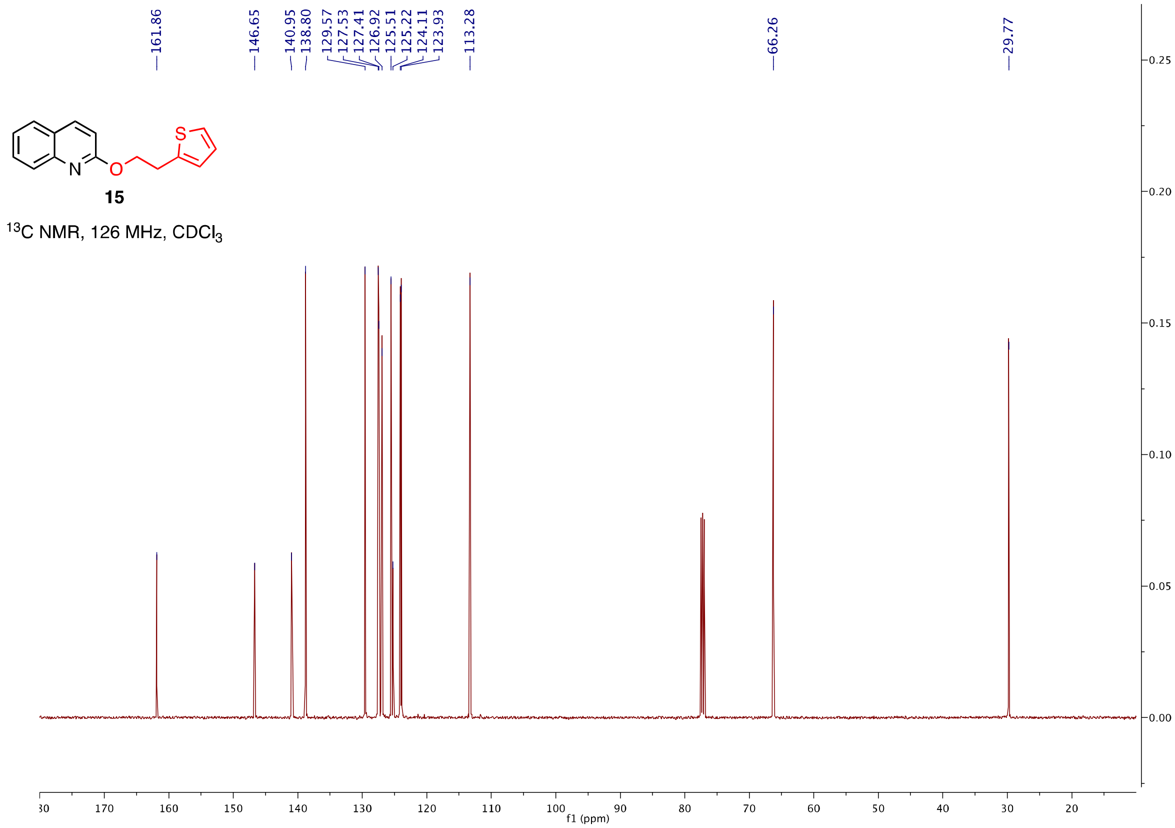
14

^{13}C NMR, 126 MHz, CDCl$_3$



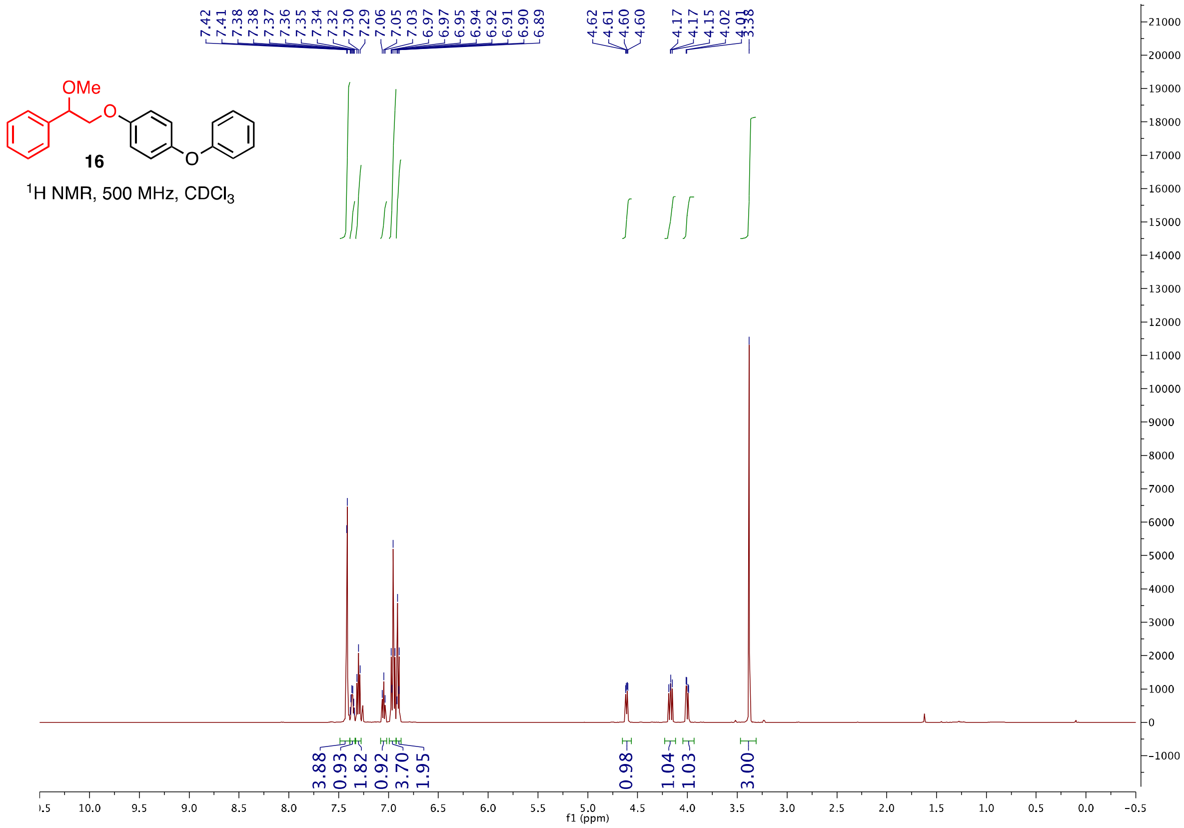
15

^{1}H NMR, 500 MHz, CDCl$_3$



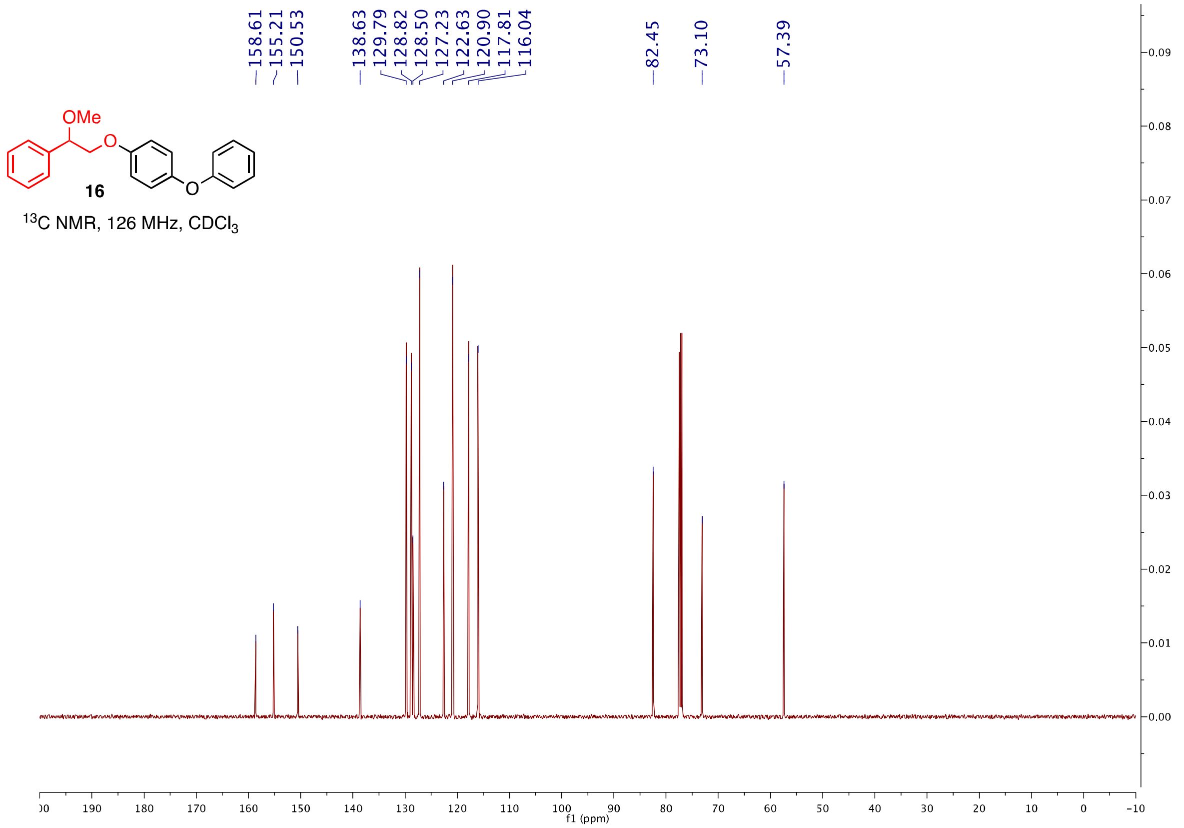
15

^{13}C NMR, 126 MHz, CDCl$_3$



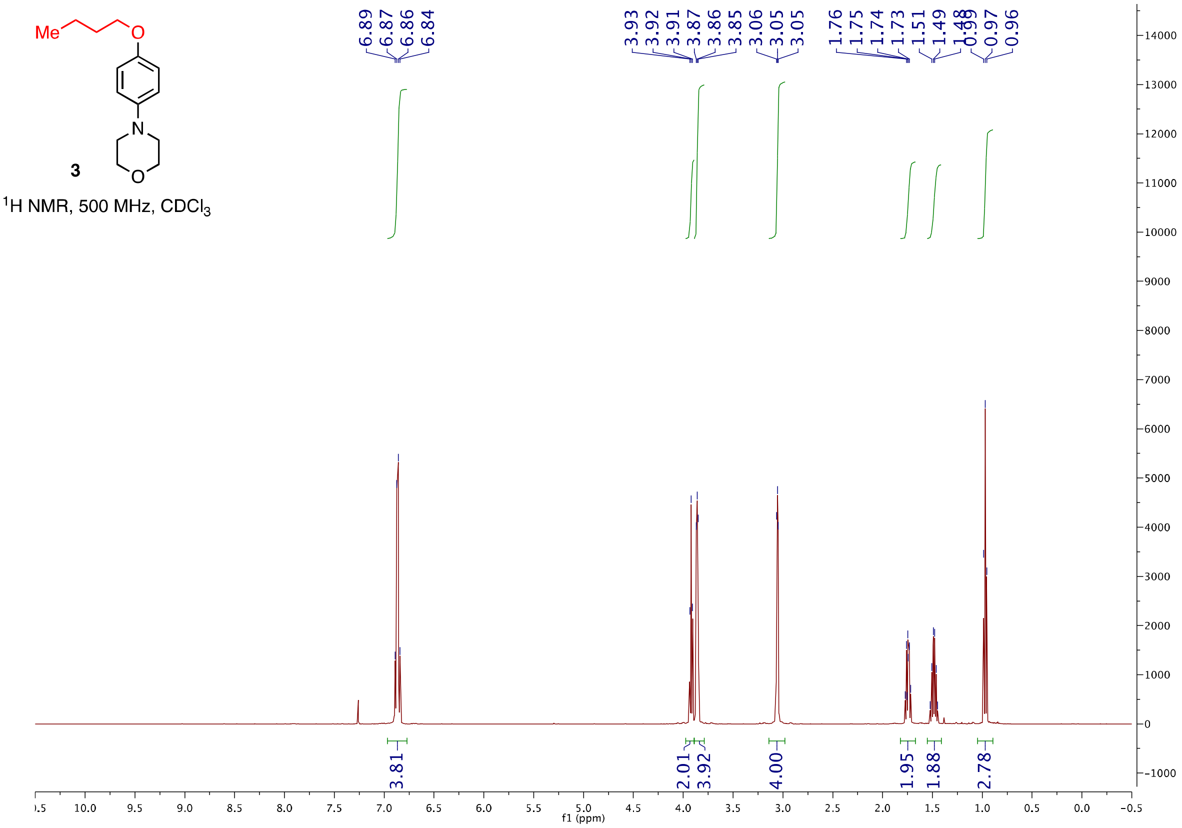
16

^{1}H NMR, 500 MHz, $CDCl_3$



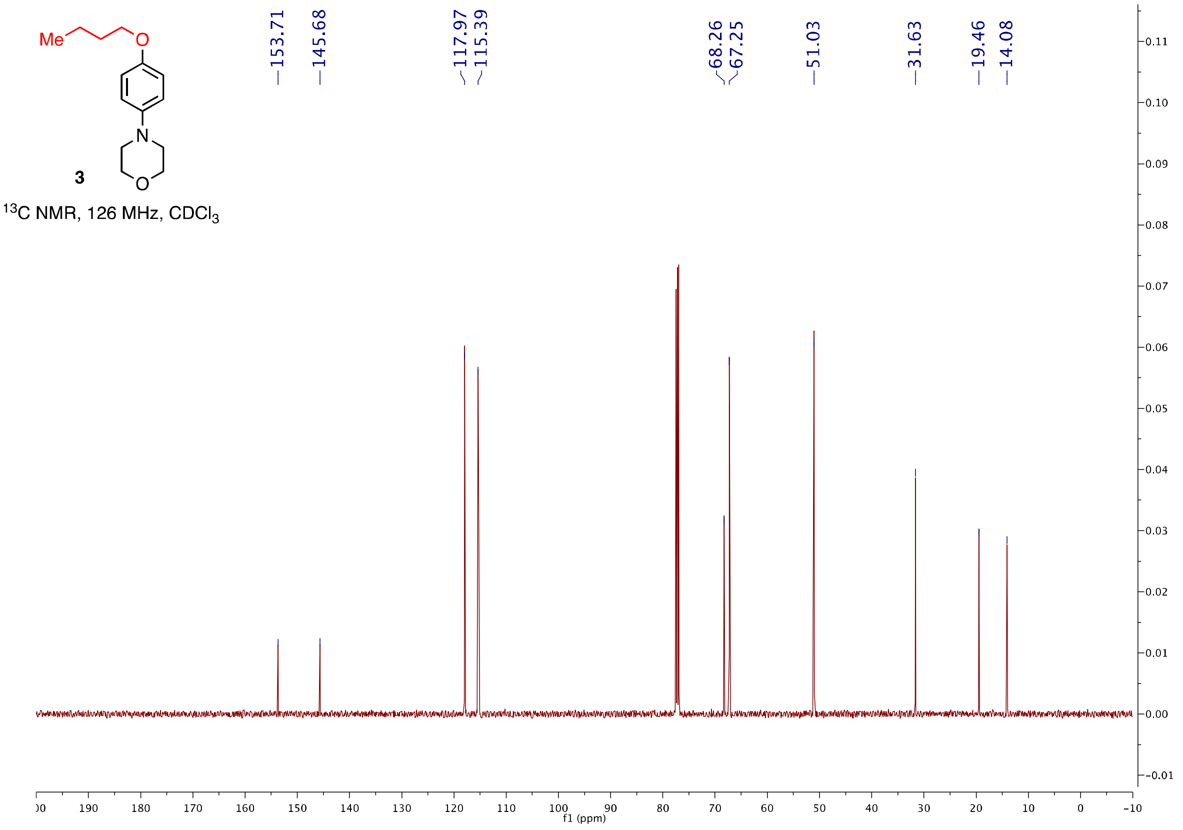
16

^{13}C NMR, 126 MHz, $CDCl_3$



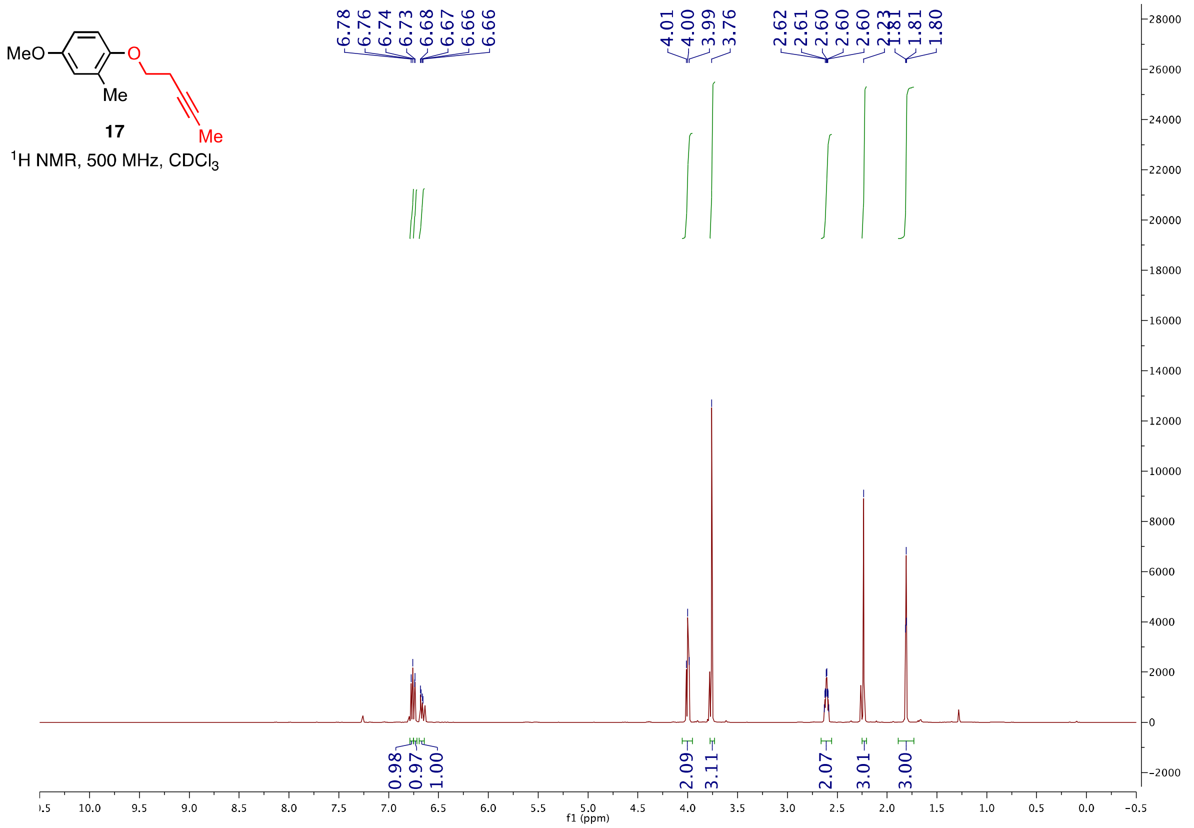
3

^{1}H NMR, 500 MHz, CDCl$_3$



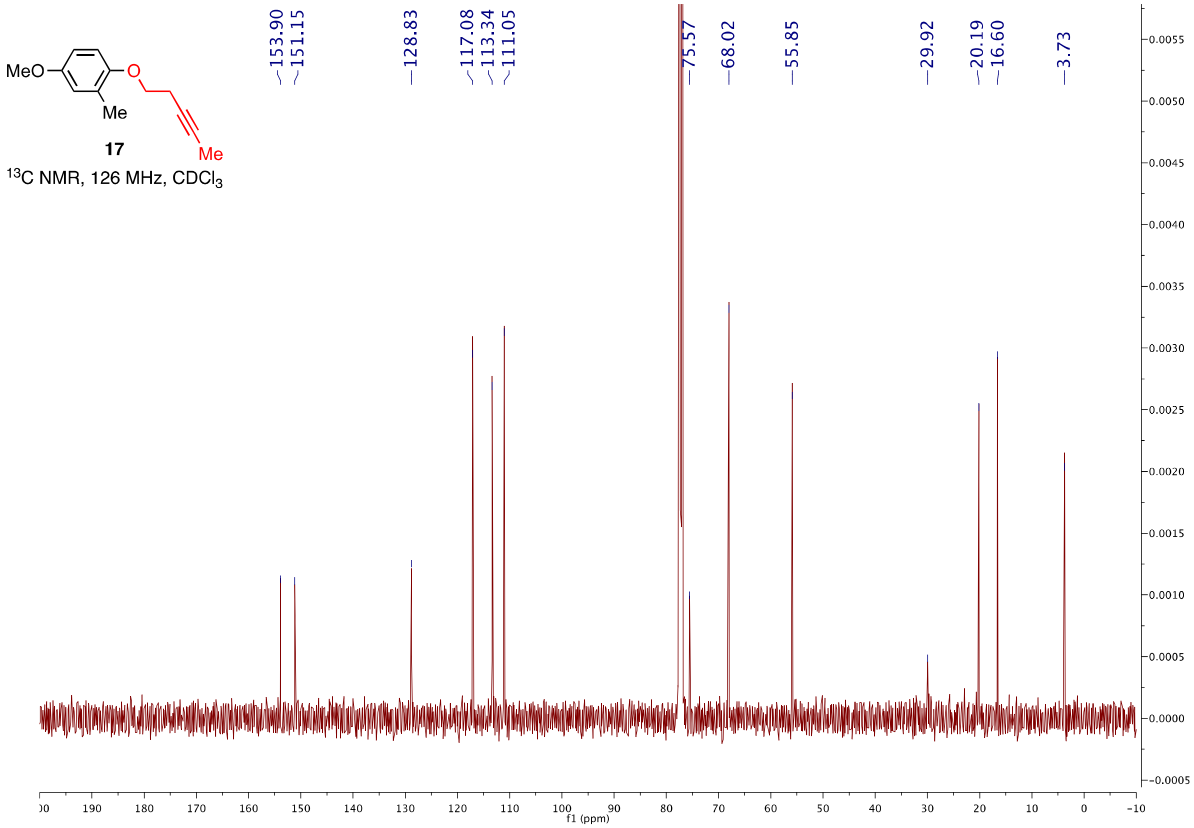
3

^{13}C NMR, 126 MHz, CDCl$_3$



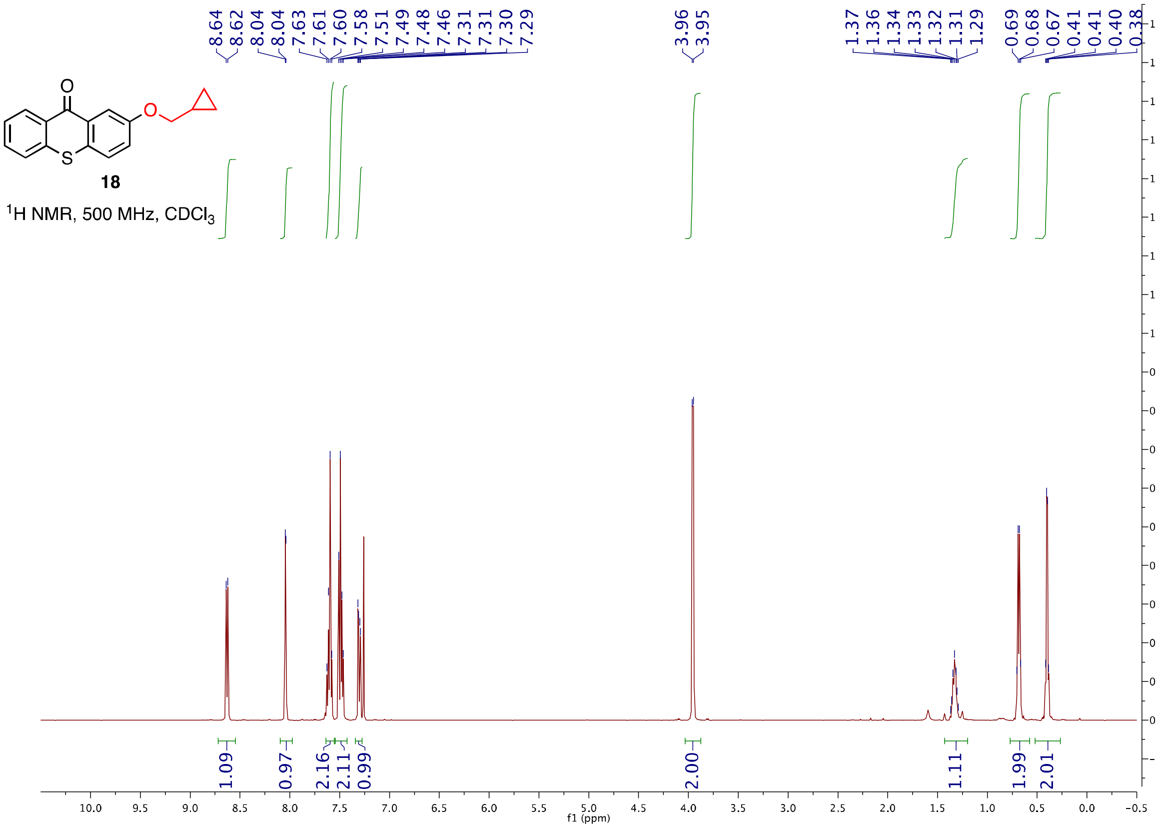
17

^{1}H NMR, 500 MHz, CDCl$_3$



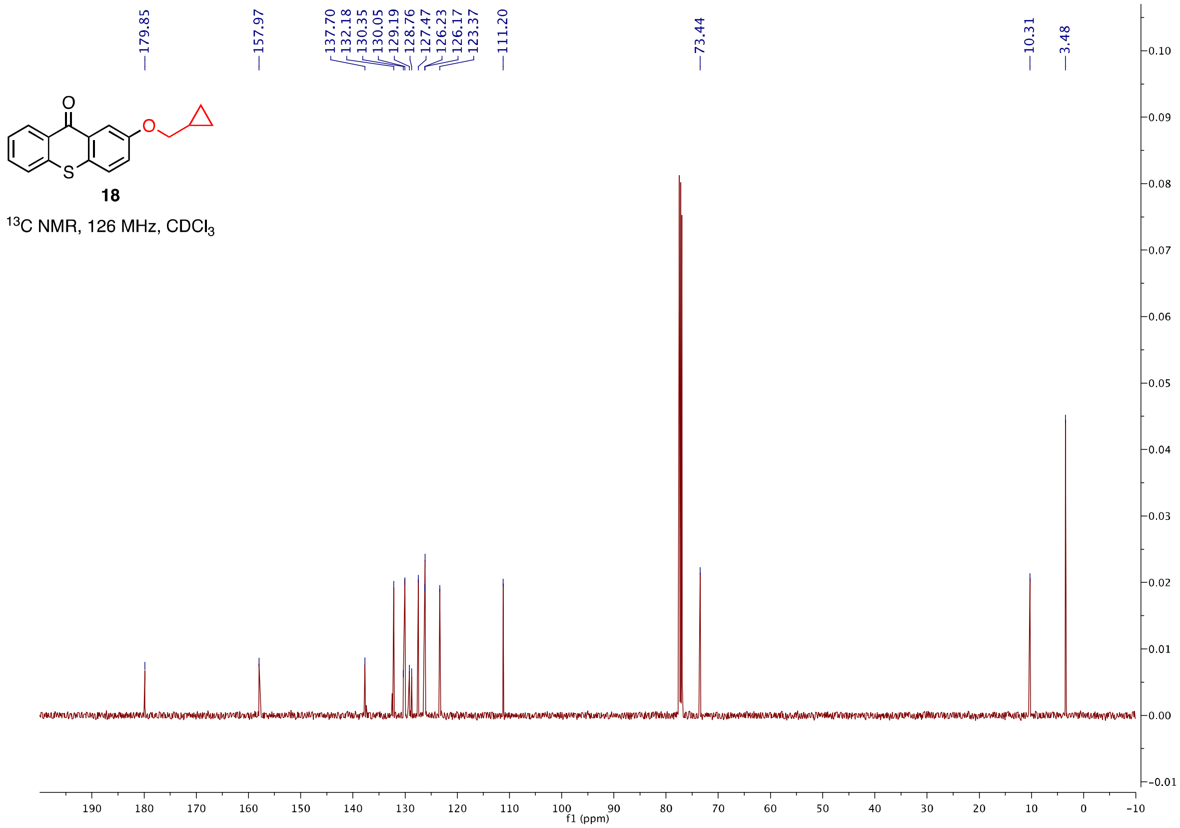
17

^{13}C NMR, 126 MHz, CDCl$_3$



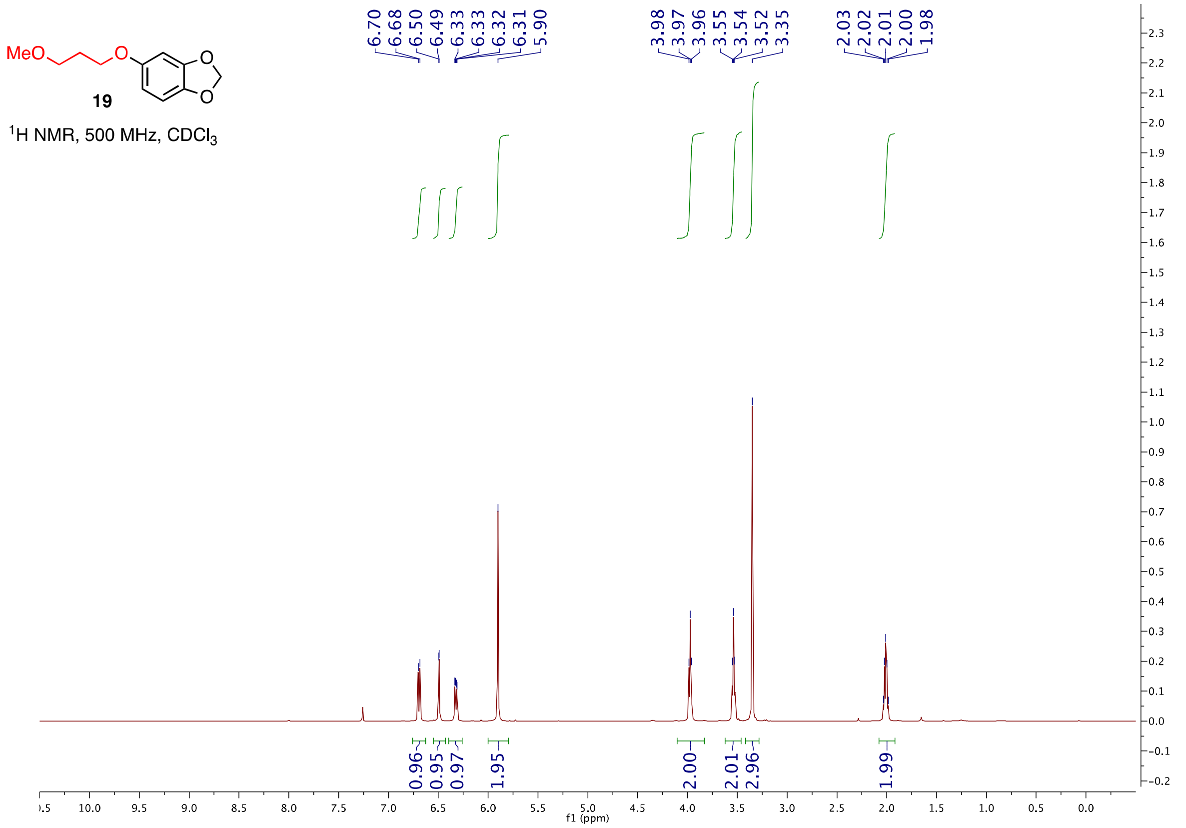
18

^{1}H NMR, 500 MHz, $CDCl_3$



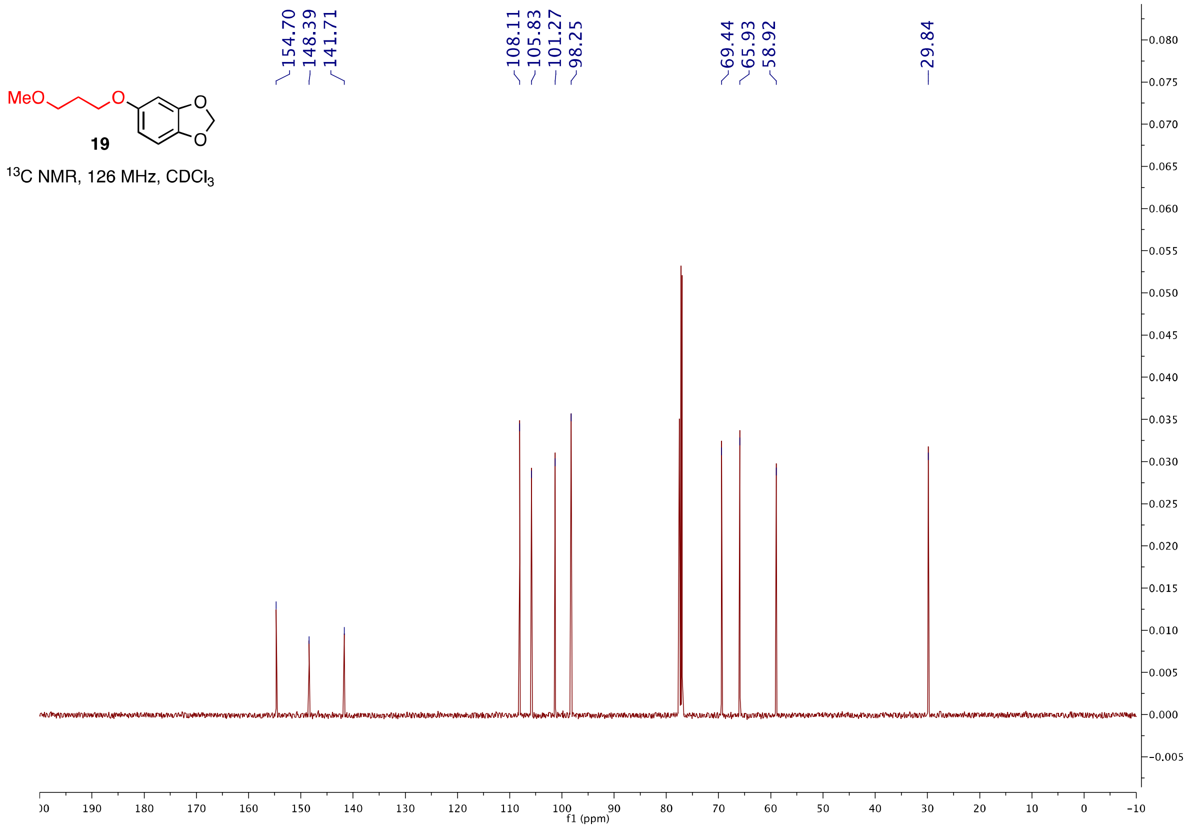
18

^{13}C NMR, 126 MHz, $CDCl_3$



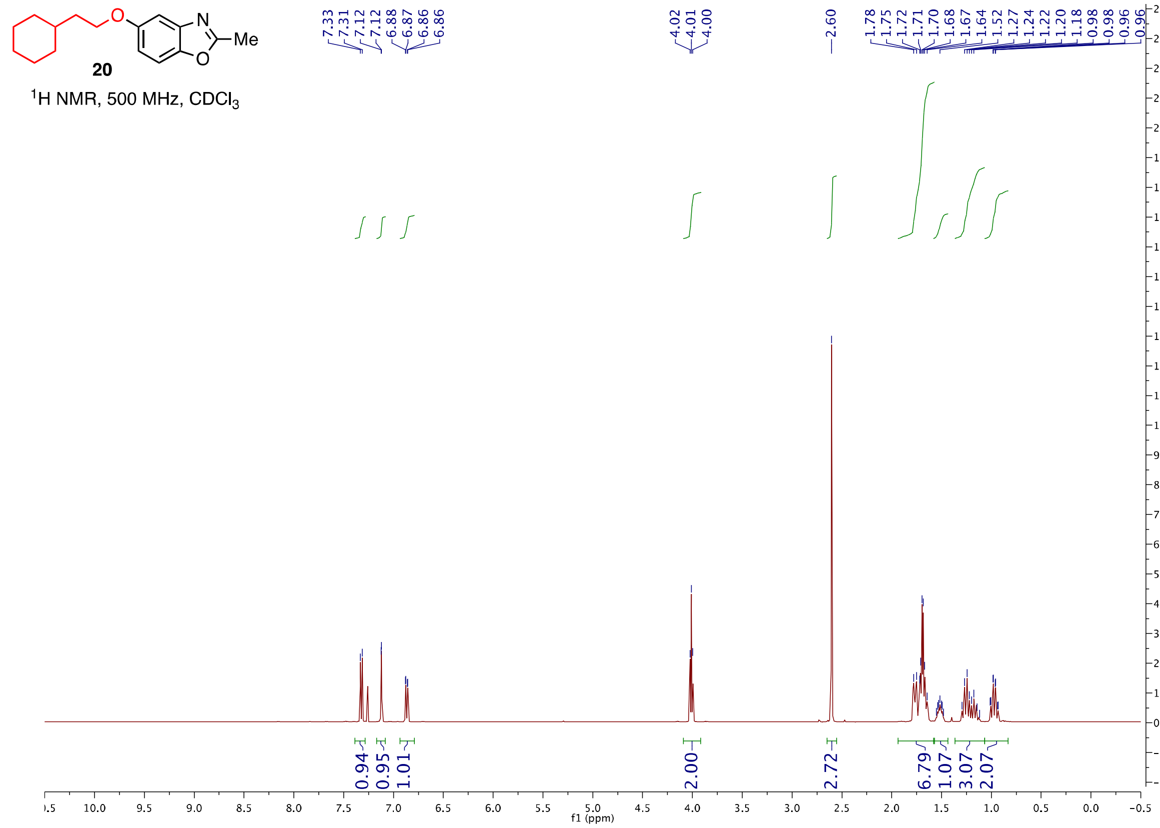
19

^{1}H NMR, 500 MHz, $CDCl_3$



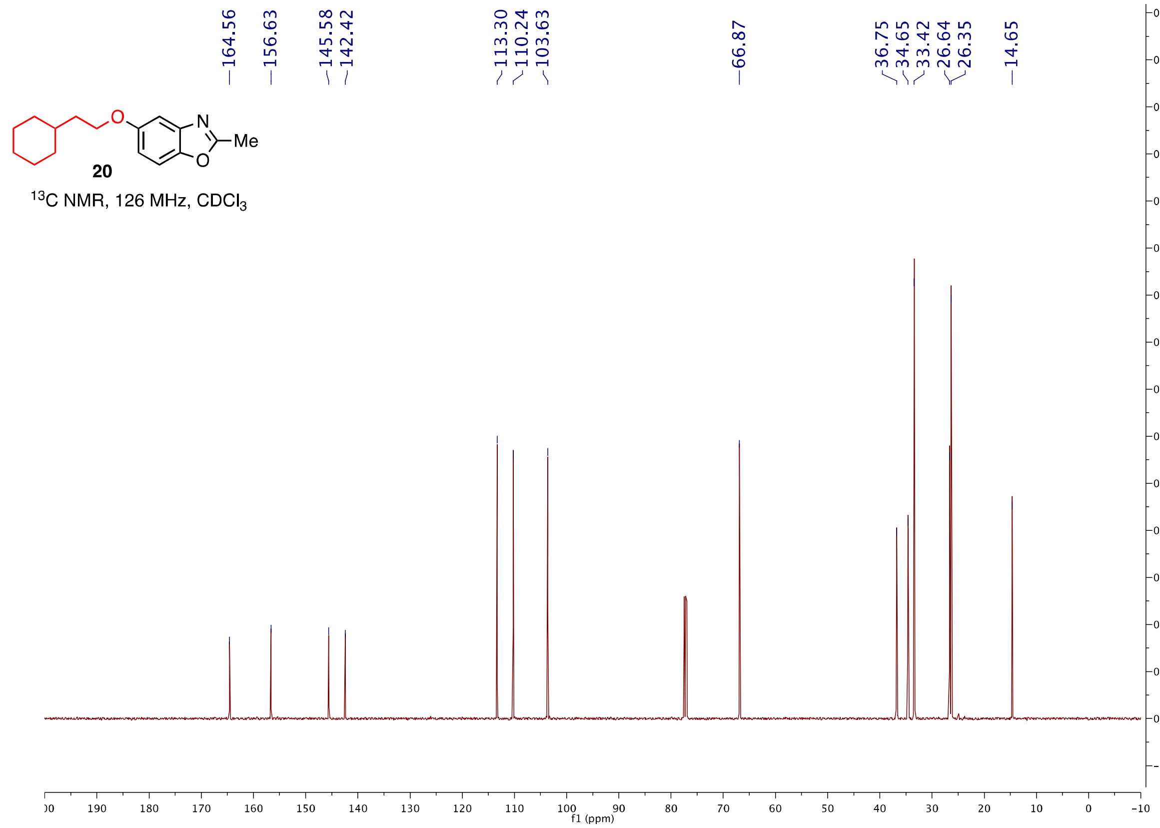
19

^{13}C NMR, 126 MHz, $CDCl_3$



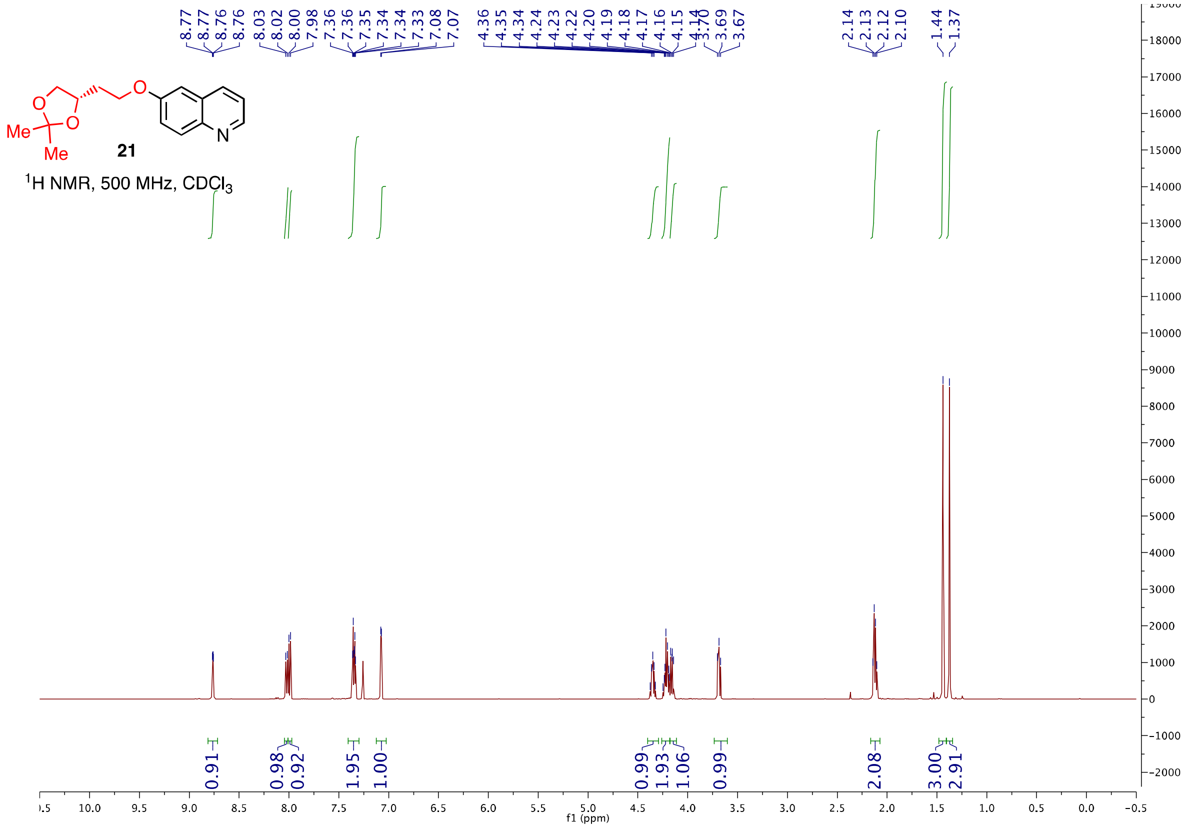
20

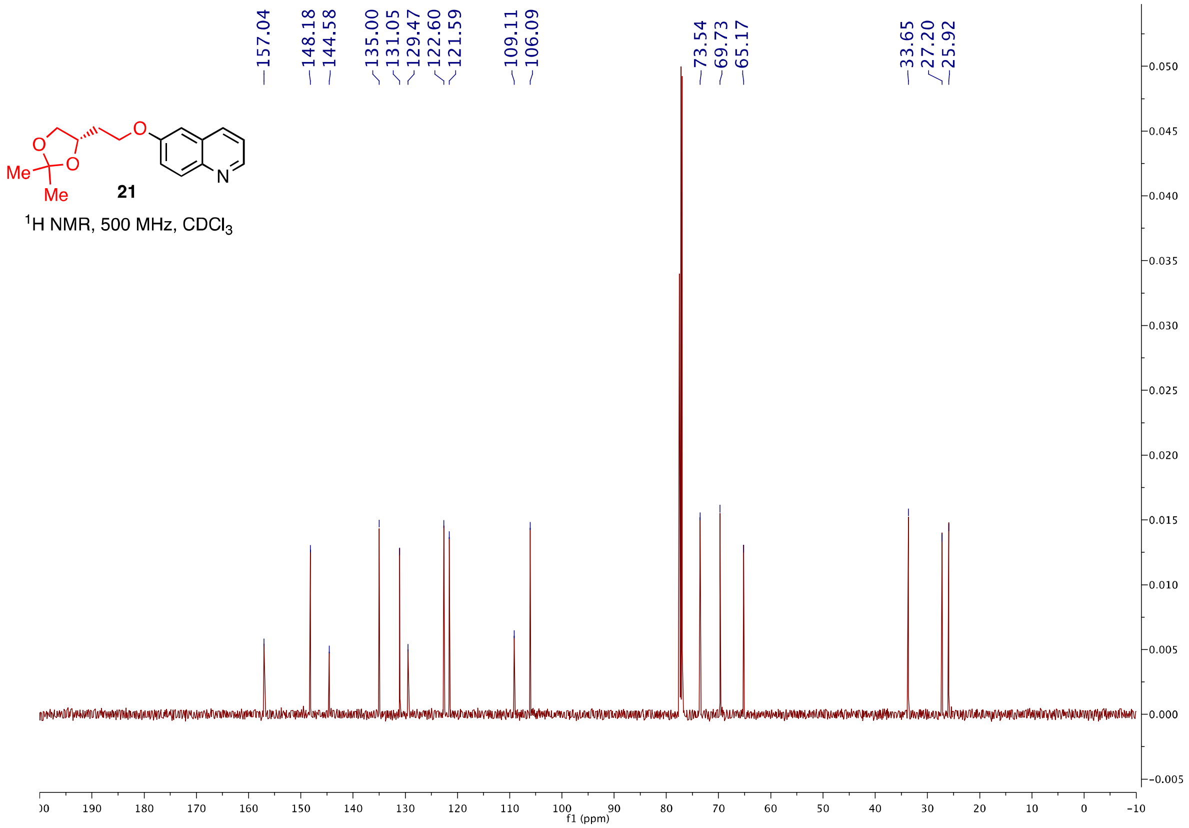
^{1}H NMR, 500 MHz, CDCl$_3$

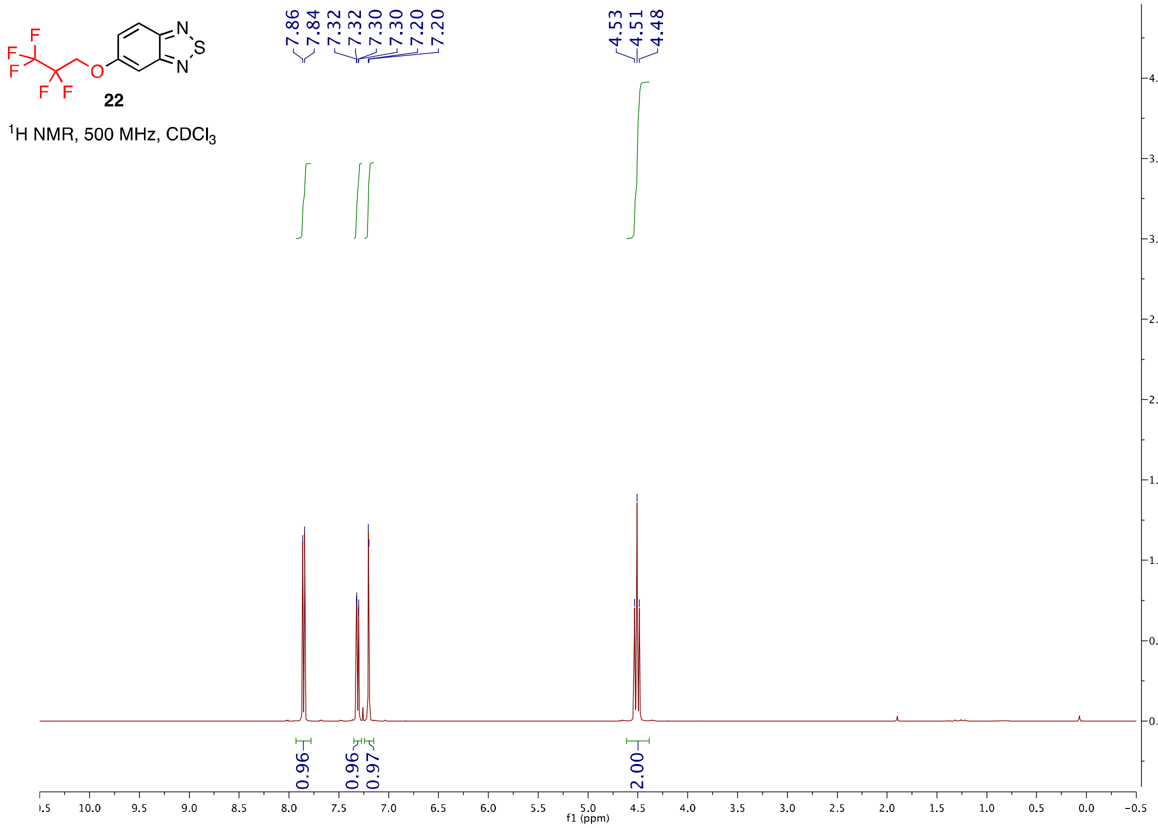


20

^{13}C NMR, 126 MHz, CDCl$_3$

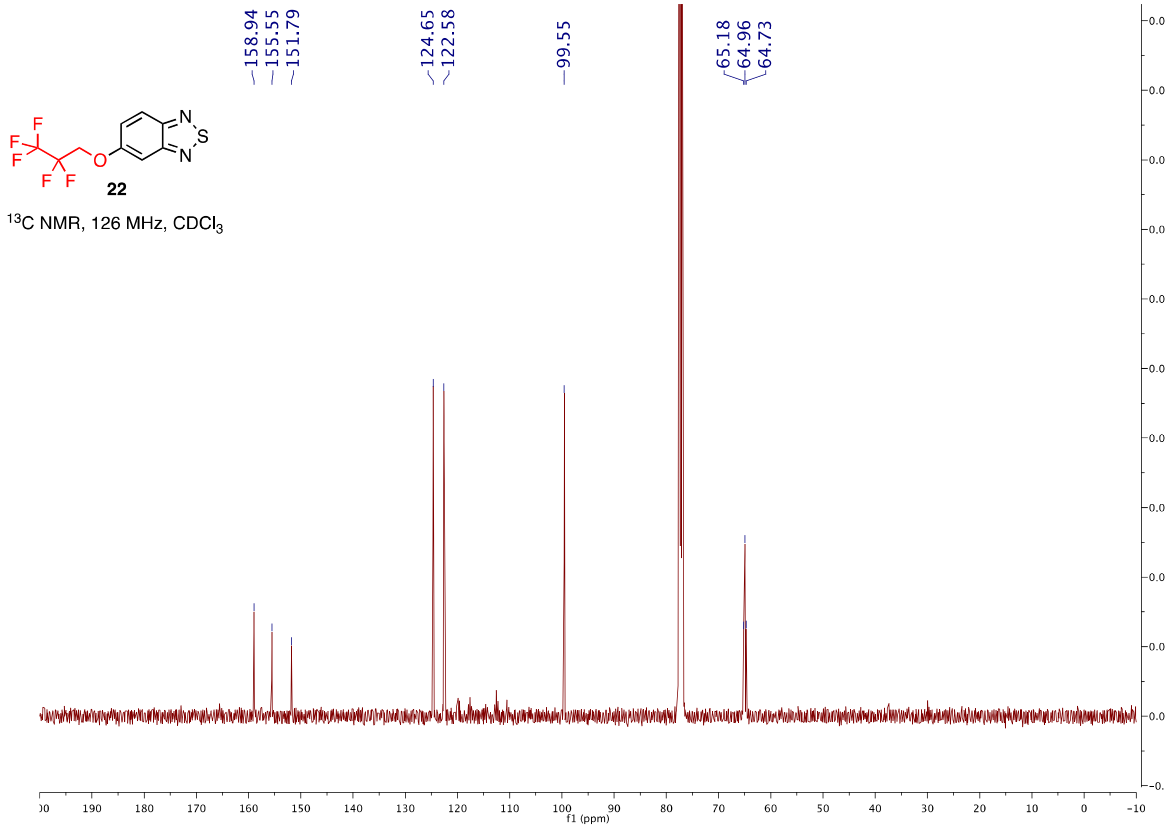

8.77
8.77
8.76
8.76
8.03
8.02
8.00
7.98
7.36
7.36
7.35
7.34
7.34
7.33
7.08
7.07
4.36
4.35
4.34
4.24
4.23
4.22
4.20
4.19
4.18
4.17
4.16
4.15
4.14
3.70
3.69
3.67
2.14
2.13
2.12
2.10
1.44
1.37
O
O
O
Me
Me
N
21
¹H NMR, 500 MHz, CDCl₃
0.91
0.98
0.92
1.95
1.00
0.99
1.93
1.06
0.99
2.08
3.00
2.91
f1 (ppm)


157.04
148.18
144.58
135.00
131.05
129.47
122.60
121.59
109.11
106.09
73.54
69.73
65.17
33.65
27.20
25.92
O
O
O
Me
Me
N
21
¹H NMR, 500 MHz, CDCl₃
f1 (ppm)



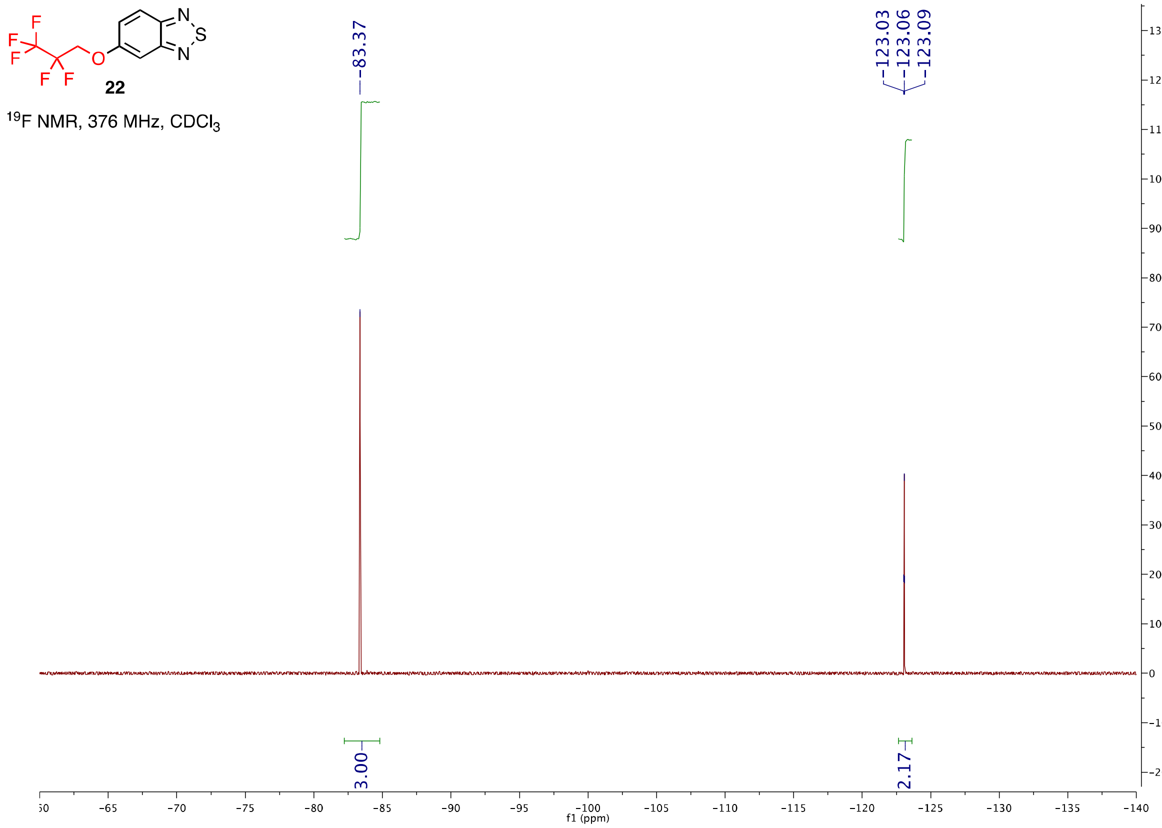
22

^{1}H NMR, 500 MHz, CDCl$_3$



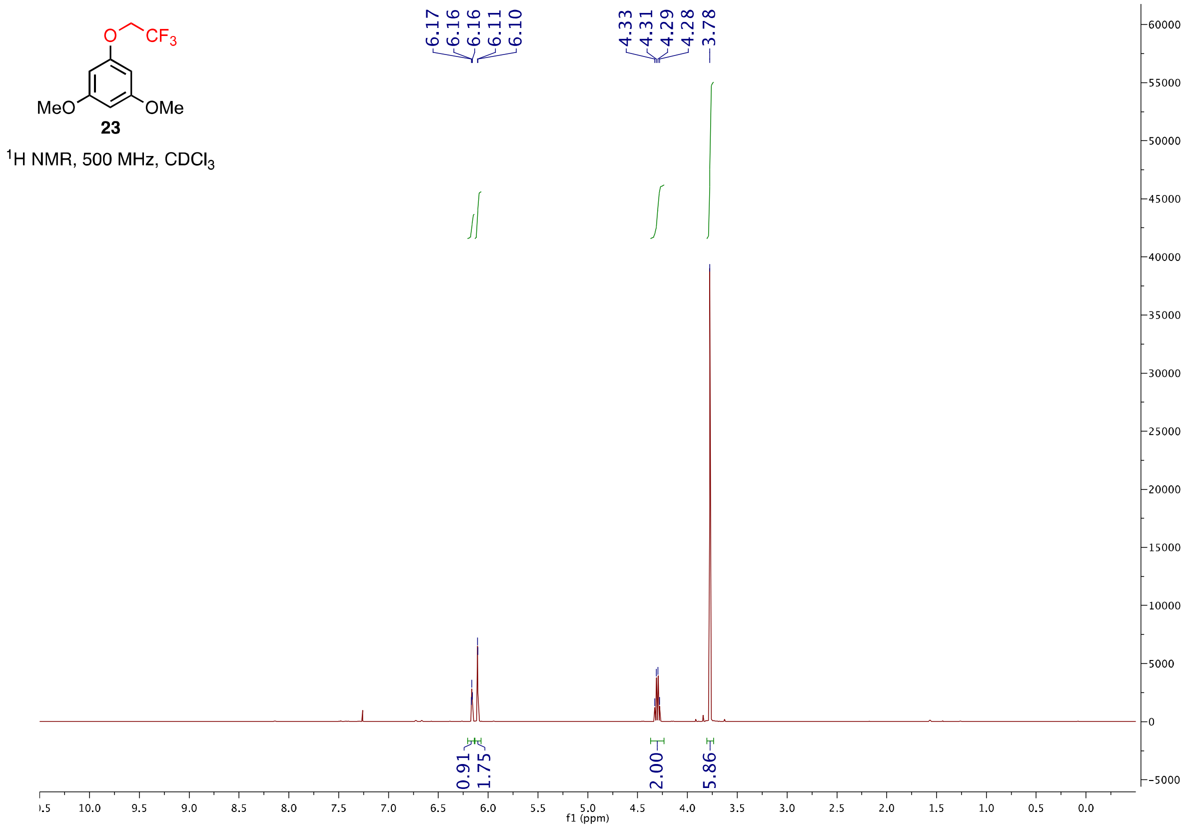
22

^{13}C NMR, 126 MHz, CDCl$_3$



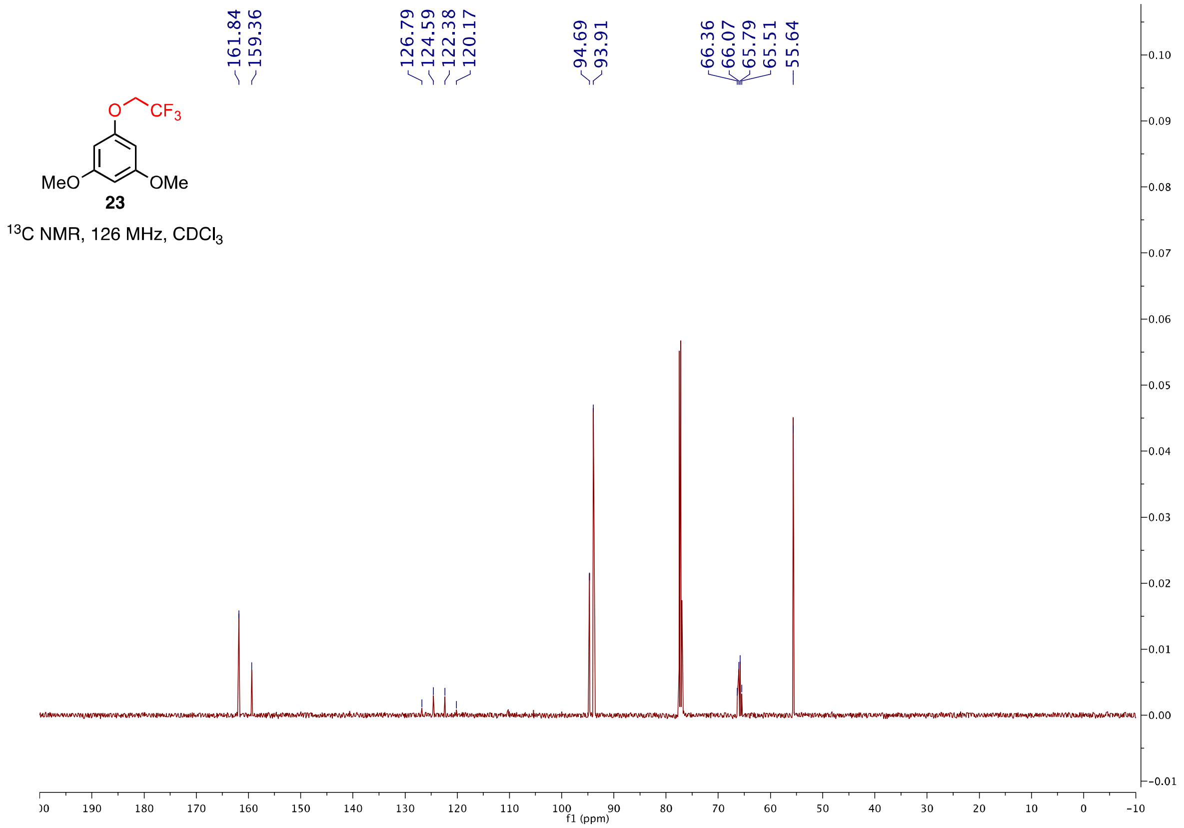
22

^{19}F NMR, 376 MHz, $CDCl_3$



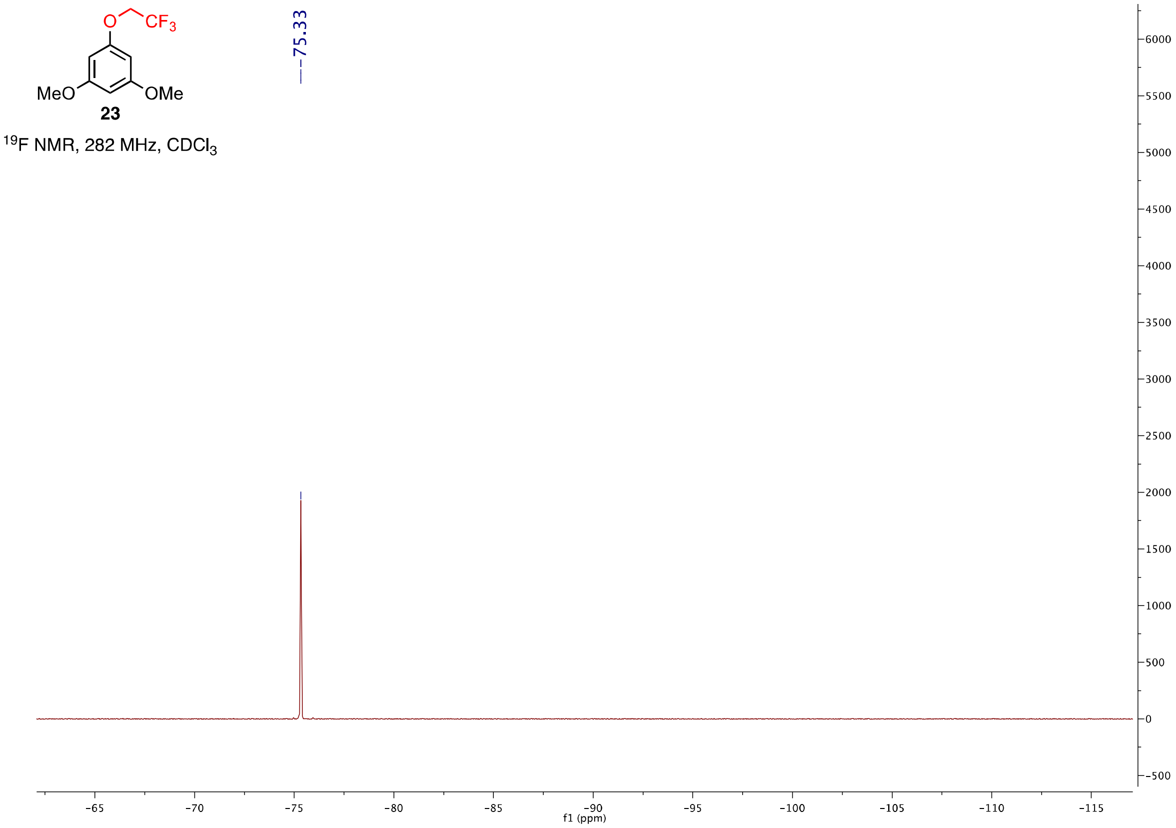
23

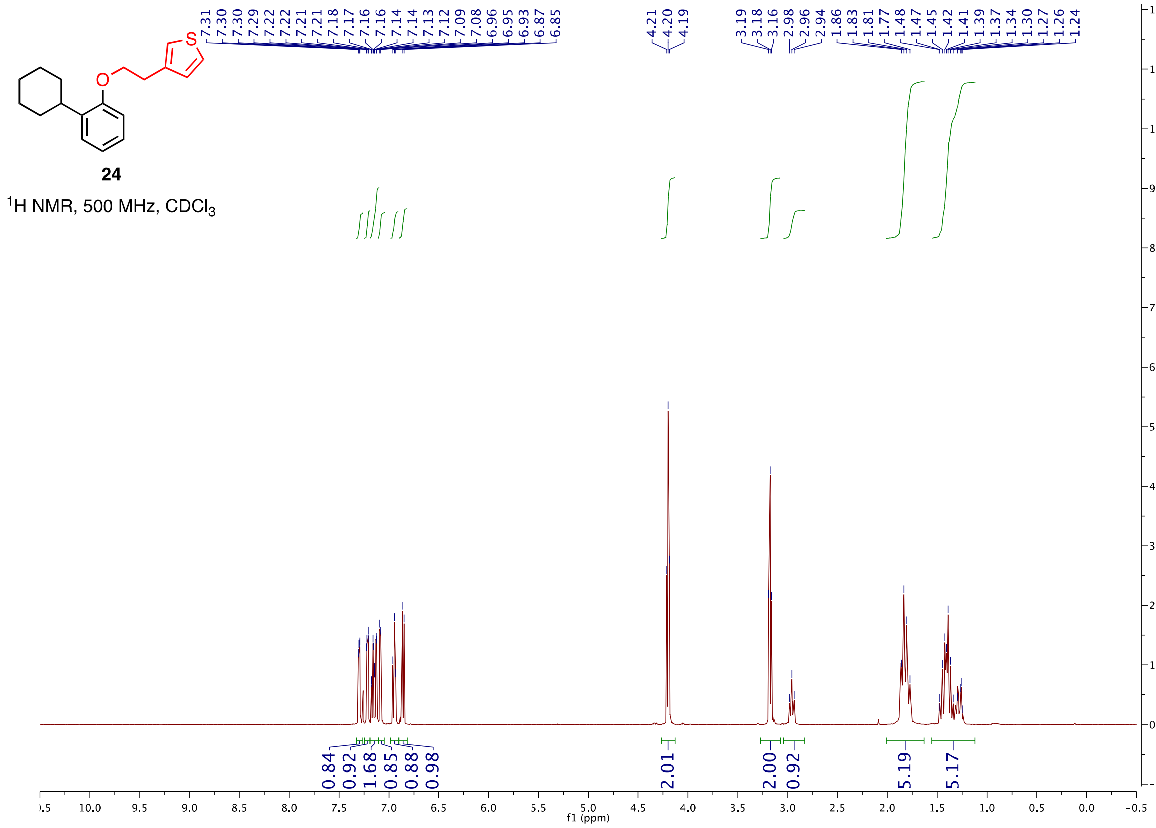
^{1}H NMR, 500 MHz, $CDCl_3$



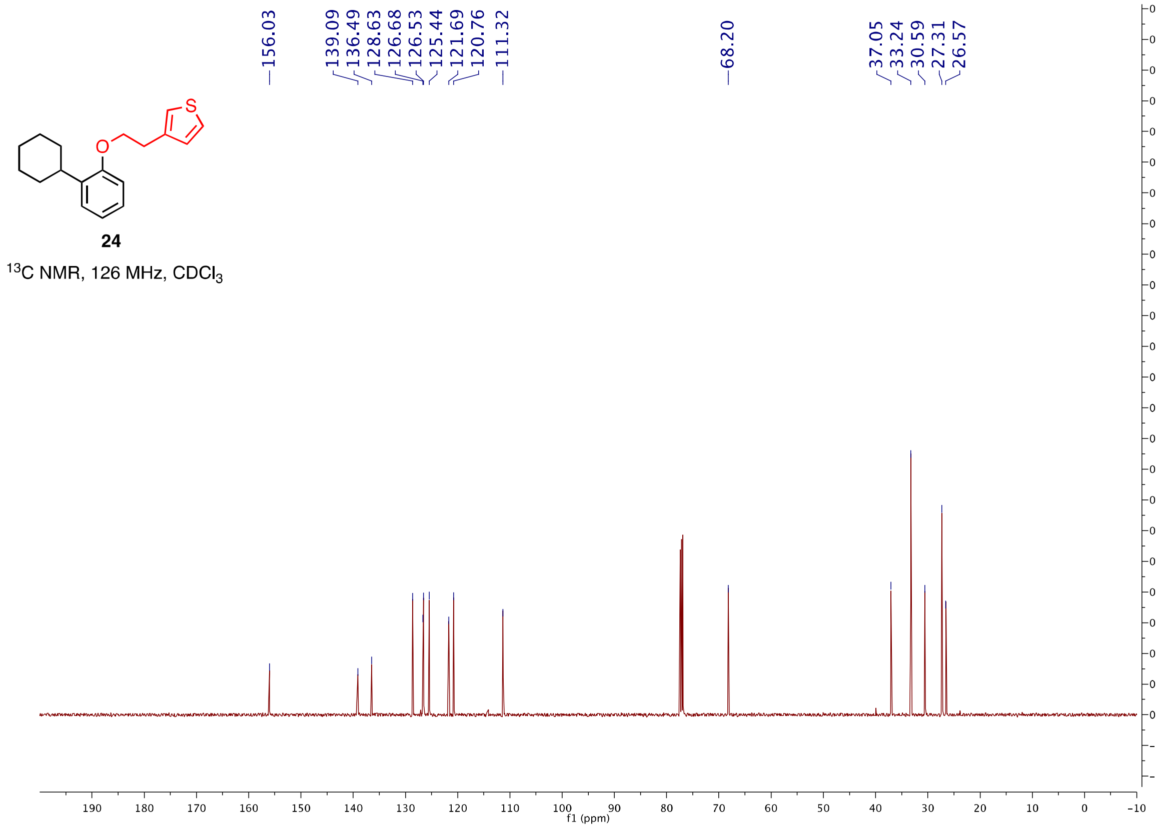
23

^{13}C NMR, 126 MHz, $CDCl_3$

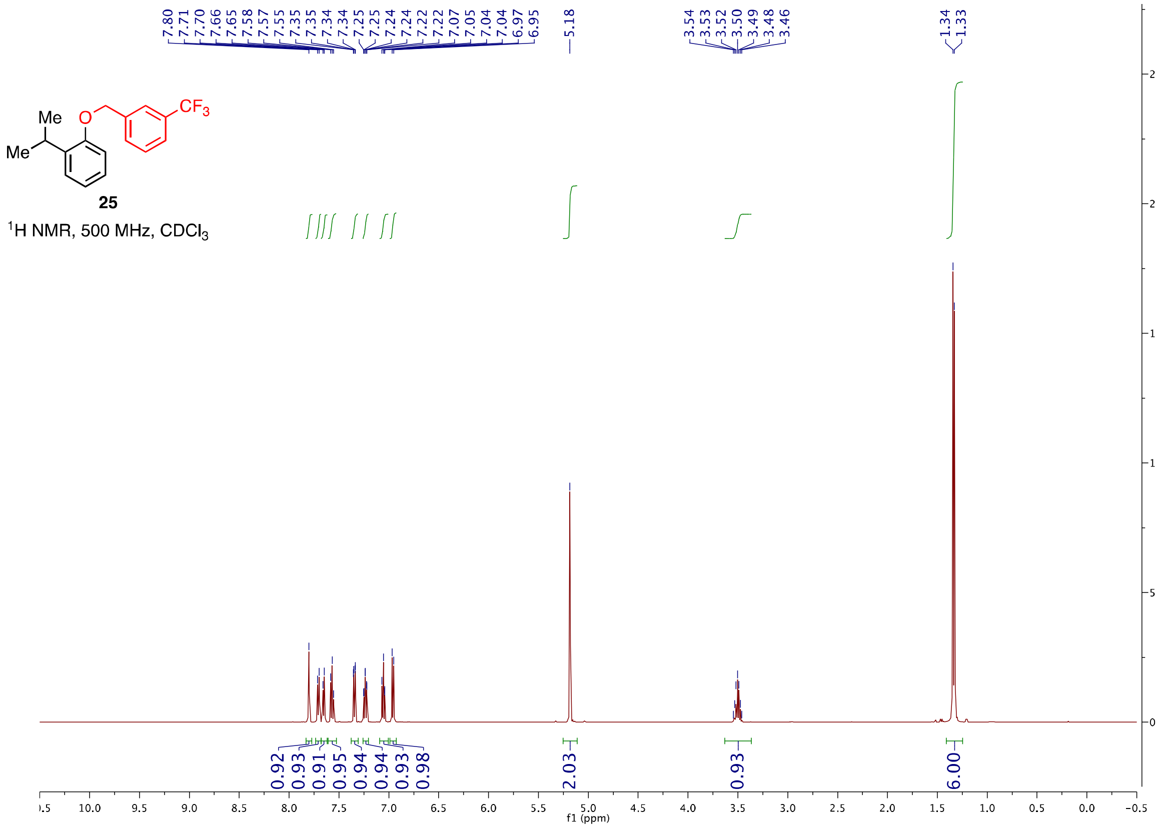

23
^{19}F NMR, 282 MHz, CDCl$_3$
MeO
OMe
O
CF$_3$
-75.33
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
f1 (ppm)


24

^{1}H NMR, 500 MHz, CDCl$_3$

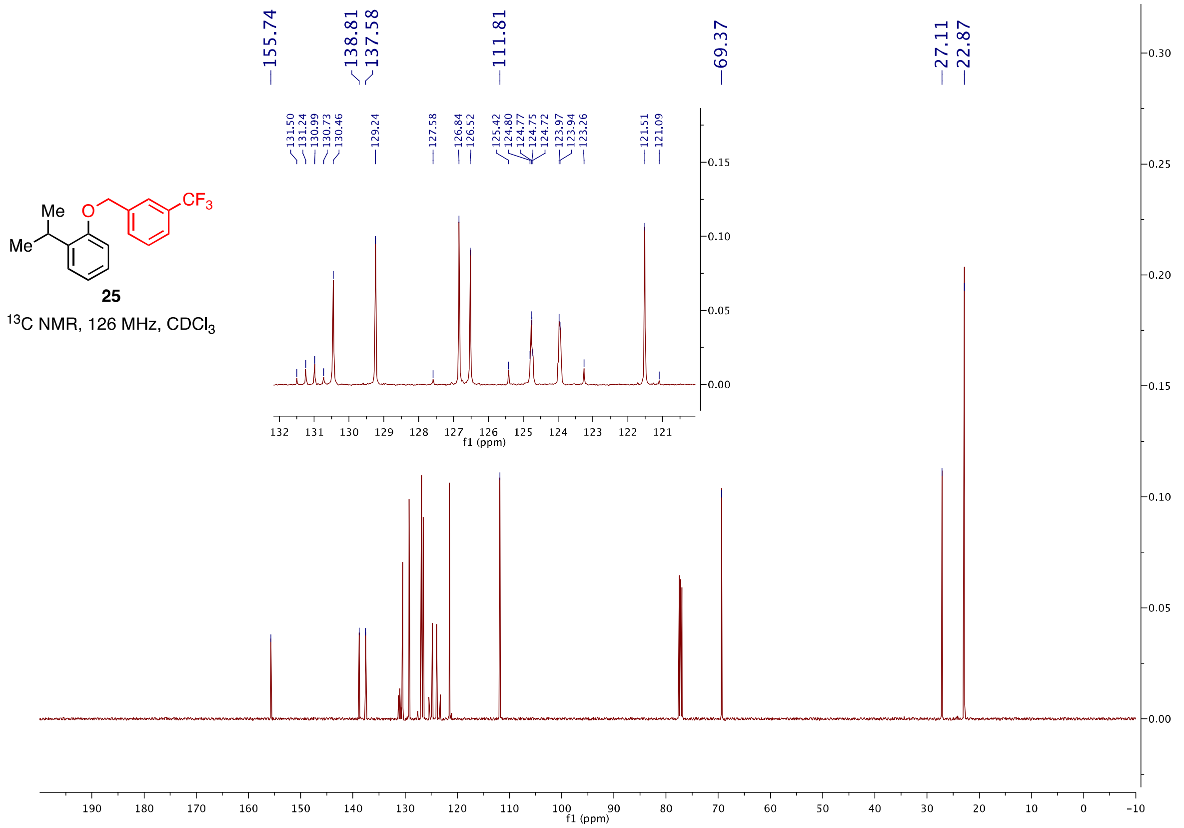

24

^{13}C NMR, 126 MHz, CDCl$_3$



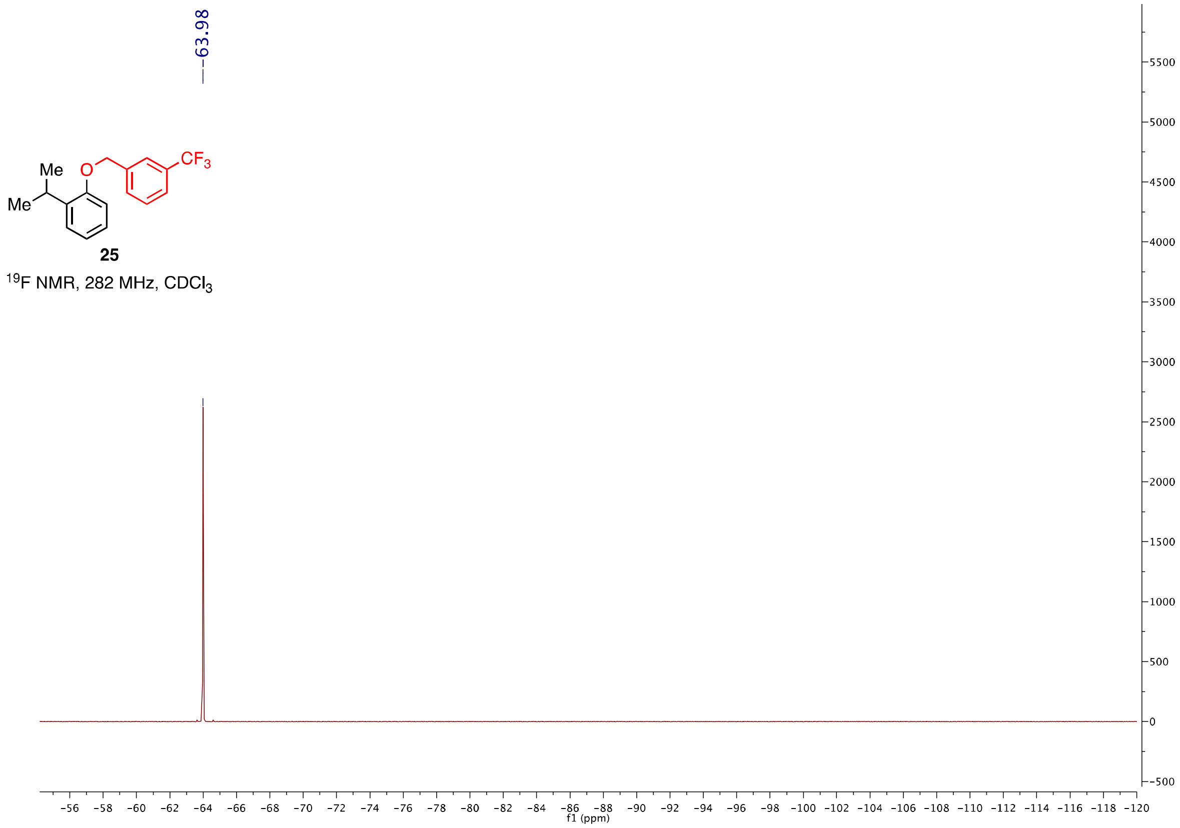
25

^{1}H NMR, 500 MHz, $CDCl_3$



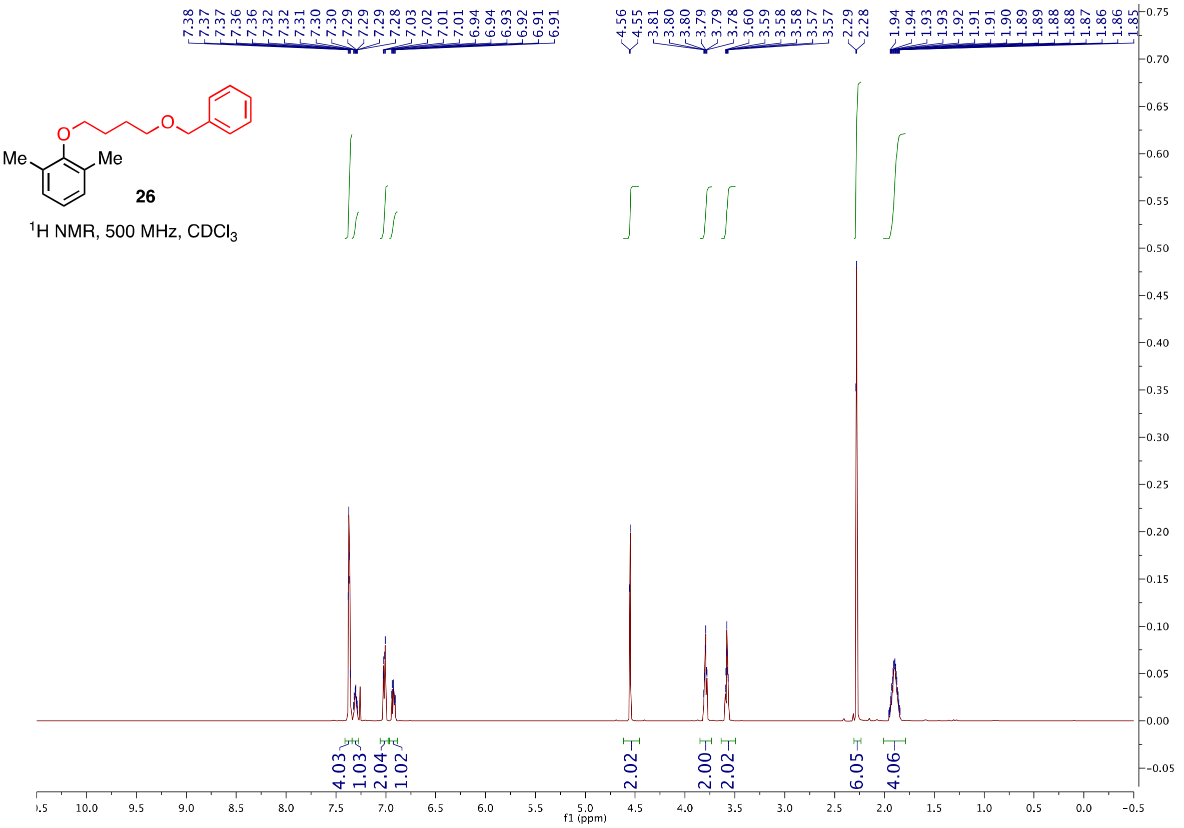
25

^{13}C NMR, 126 MHz, $CDCl_3$



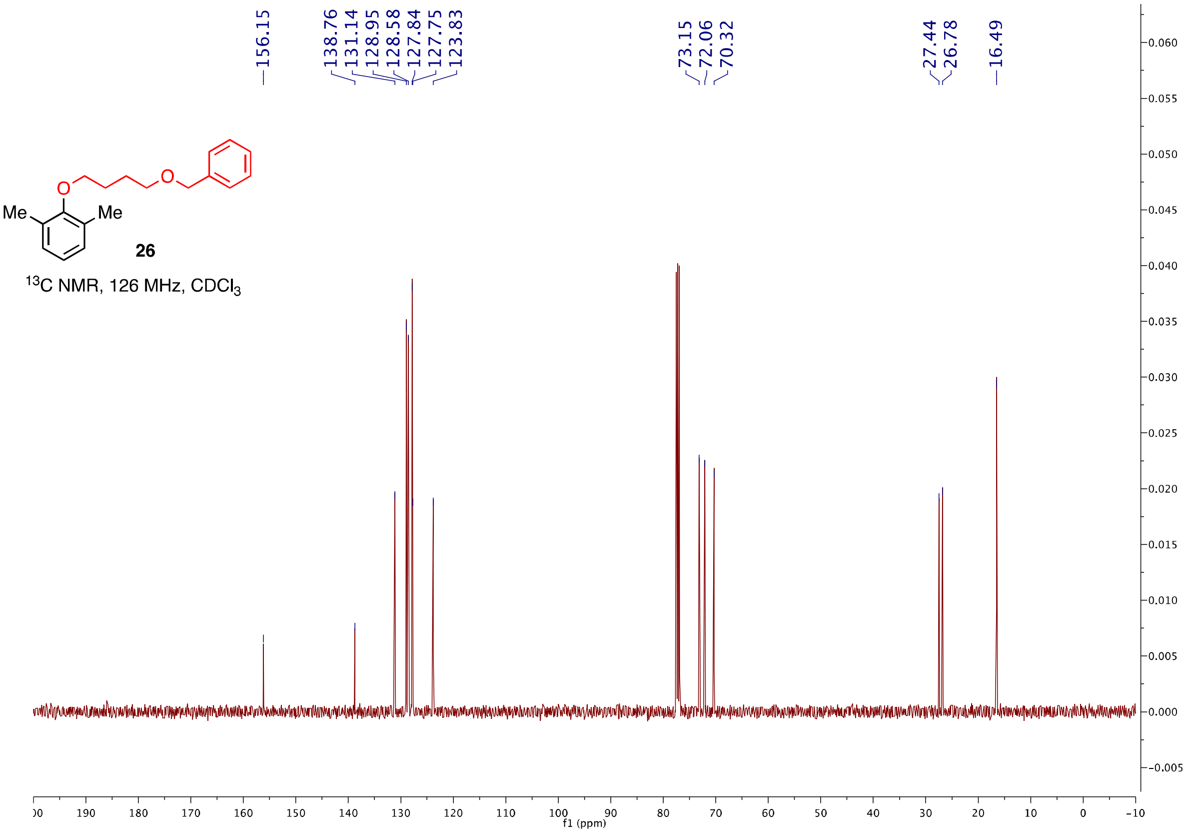
25

^{19}F NMR, 282 MHz, $CDCl_3$



26

^{1}H NMR, 500 MHz, CDCl$_3$



26

^{13}C NMR, 126 MHz, CDCl$_3$