

# **An Improved Process for the Palladium-Catalyzed C–O Cross-Coupling of Secondary Alcohols**

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## I. General Information

### A) General Reagent Information

Tetrahydrofuran (THF) and dichloromethane ( $\text{CH}_2\text{Cl}_2$ ) 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 and methanol were purchased from Sigma-Aldrich in Sure-Seal™ bottles and used as received. Sodium *tert*-butoxide ( $\text{NaOt-Bu}$ ) was purchased from Strem and stored in a nitrogen-filled glovebox. Small quantities were stored on the bench in a desiccator and used within a week. 1-adamantylzinc bromide solution (0.5 M in THF) was received as a gift from Sigma-Aldrich, which we are grateful for. AdCyBrettPhos (**L2**),<sup>S1</sup> precatalyst (**P2**),<sup>S1</sup> (COD)Pd( $\text{CH}_2\text{TMS}$ )<sub>2</sub><sup>S2</sup> and alcohol **18**<sup>S3</sup> were prepared following 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 silica gel chromatography with manually loaded Silicycle SiliaFlash® F60 silica gel (40–63  $\mu\text{m}$ , 230–400 mesh, 60 Å pore) or with the aid of a Teledyne ISCO CombiFlash® Automated Flash Chromatography System using prepacked SNAP silica cartridges (50 or 100 g).

### B) General Analytical Information

All compounds were characterized by  $^1\text{H}$  and  $^{13}\text{C}$  NMR, as well as  $^{19}\text{F}$  and  $^{31}\text{P}$  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  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{19}\text{F}$  and  $^{31}\text{P}$  NMR spectra can be found at the end of the Supporting Information. NMR experiments were performed on a Bruker Avance 400 MHz or a JEOL 500 MHz spectrometer. All chemical shifts are reported in  $\delta$ , parts per million (ppm).  $^1\text{H}$  and  $^{13}\text{C}$  NMR signals were calibrated with the residual chloroform signal ( $\delta$  7.26 ppm and  $\delta$  77.16 ppm, respectively), dichloromethane signal ( $\delta$  5.32 ppm and  $\delta$  53.84 ppm, respectively).  $^{19}\text{F}$  and  $^{31}\text{P}$  NMR spectra were referenced to an external standard of neat trifluorotoluene ( $\delta$  –63.72 ppm) and  $\text{H}_3\text{PO}_4$  ( $\delta$  0.00 ppm), respectively. Both  $^{13}\text{C}$  and  $^{31}\text{P}$  NMR experiments were carried out with decoupling on the  $^1\text{H}$  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 recorded on a JEOL

AccuTOF LC-Plus 46 DART system. 1,1,2,2-tetrachloroethane and dodecane were used as standards for yields or conversions determined by  $^1\text{H}$  NMR analysis and by GC analysis, respectively. All isolated yields reported in Schemes 3 and 4 of the manuscript represent an average value from two experiments.

## II. Experimental Procedures and Characterization Data

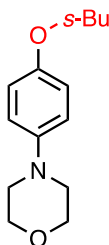
### A) O-Arylation of Secondary Alcohols

#### General Procedure A:

A 25 mL screw-top oven-dried test tube (Fisher Scientific 20 × 125 mm tubes, Cat. No. 1495937A) equipped with a stir bar was charged with aryl halide (if solid, 1.00 mmol, 1.00 equiv), alkyl alcohol, (if solid, 1.20 mmol, 1.20 equiv for aryl chlorides, or 2.00 mmol, 2.00 equiv for aryl bromides), precatalyst **P2** (19–38 mg, 2.0–4.0 mol %), and NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv). The reaction tube was sealed with a screw cap (Kimble Chase Open Top S/T Closure, Cat. No. 73804-18400), fitted with a Teflon septum (Thermo Scientific PTFE: 0.010" silicone: 0.090", Cat. No. B7995-18). 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 THF (1.0 mL) were added via syringe. The screw cap and the Teflon septum were wrapped completely with parafilm®. The reaction tube was sonicated until there were no visible solid pieces of NaO*t*-Bu. The reaction mixture was stirred for 18 h at the temperature as indicated for each substrate. If heated, the reaction vessel was placed in a preheated oil bath and upon completion the reaction mixture was allowed to cool to rt, after the reaction was complete, before addition of EtOAc (2 mL). The reaction mixture slurry was then filtered through a pad of Celite® and rinsed with EtOAc. The crude material was concentrated with the aid of a rotary evaporator. In cases where the excess alcohol and the product were inseparable, as determined by TLC analysis after workup, the crude reaction mixture was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL) and further treated successively with *N,N*-dimethylpyridin-4-amine (DMAP, 1.0 mg), triethylamine (Et<sub>3</sub>N, 70 μL, 0.50 mmol, 0.50 equiv), acetic anhydride (Ac<sub>2</sub>O, 47 μL, 0.50 mmol, 0.50 equiv). The resulting solution was stirred at rt overnight and then concentrated with the aid of a rotary evaporator. For compounds purified by flash chromatography, the concentrated crude mixture was dissolved in diethyl ether (Et<sub>2</sub>O, ~3 mL). Celite® (~2 g) was added to the crude mixture, which was briefly sonicated to ensure full suspension of Celite® in the solution. Et<sub>2</sub>O

was carefully removed with the aid of a rotary evaporator to afford a dry Celite® powder, which absorbed the crude reaction mixture. The resulting powder was loaded onto a column for purification by silica gel chromatography. For compounds purified via the CombiFlash® Automated System, the crude mixture was loaded in toluene (~3 mL).

#### 4-(4-(*sec*-butoxy)phenyl)morpholine (**3**)

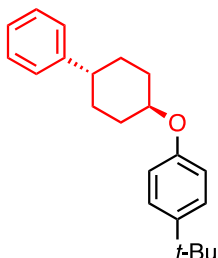


Following General Procedure A, a mixture of 4-(4-chlorophenyl)morpholine (198 mg, 1.00 mmol, 1.00 equiv), butan-2-ol (110  $\mu$ L, 1.20 mmol, 1.20 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (24 mg, 2.5 mol %), and THF (1.0 mL) was stirred at rt for 18 h. The crude mixture was purified by CombiFlash® Automated System (100 g silica gel, 100% hexane to 5% acetone in hexane over 18 column volumes (CV)) to provide the title compound as a light-yellow oil (1<sup>st</sup> run: 190 mg, 81%; 2<sup>nd</sup> run: 192 mg, 82%; average yield: 82%).

Following General Procedure A, a mixture of 4-(4-bromophenyl)morpholine (242 mg, 1.00 mmol, 1.00 equiv), butan-2-ol (183  $\mu$ L, 2.00 mmol, 2.00 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (24 mg, 2.5 mol %), and THF (1.0 mL) was stirred at rt for 18 h. The crude mixture was purified by CombiFlash® Automated System (100 g silica gel, 100% hexane to 5% acetone in hexane over 18 CV) to provide the title compound as a light-yellow oil (1<sup>st</sup> run: 152 mg, 65%; 2<sup>nd</sup> run: 148 mg, 63%; average yield: 64%).

**<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  6.93–6.80 (m, 4H), 4.18 (h,  $J$  = 6.1 Hz, 1H), 3.86 (t,  $J$  = 4.5 Hz, 4H), 3.06 (t,  $J$  = 4.8 Hz, 4H), 1.79–1.66 (m, 1H), 1.65–1.53 (m, 1H), 1.26 (d,  $J$  = 6.1 Hz, 3H), 0.97 (t,  $J$  = 7.5 Hz, 3H) ppm. **<sup>13</sup>C NMR** (101 MHz, Chloroform-*d*)  $\delta$  152.7, 145.7, 117.9, 117.3, 76.1, 67.2, 51.0, 29.4, 19.6, 10.0 ppm. **IR** (neat,  $\text{cm}^{-1}$ ) 2963, 2852, 2816, 1507, 1449, 1259, 1234, 1119, 926, 825. **EA** Calcd. for C<sub>14</sub>H<sub>21</sub>NO<sub>2</sub>: C, 71.46; H, 9.00, Found: C, 71.57; H, 8.83.

**1-(*tert*-butyl)-4-((*trans*-4-phenylcyclohexyl)oxy)benzene (5)**

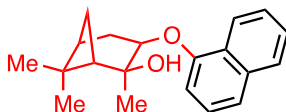


Following General Procedure A, a mixture of 1-(*tert*-butyl)-4-chlorobenzene (169 mg, 1.00 mmol, 1.00 equiv), *trans*-4-phenylcyclohexan-1-ol (212 mg, 1.20 mmol, 1.20 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (24 mg, 2.5 mol %), and THF (1.0 mL) was stirred at rt for 18 h. The crude mixture was purified by CombiFlash® Automated System (50 g silica gel, 100% hexane to 5% EtOAc in hexane over 12 CV) to provide the title compound as a colorless viscous oil (1<sup>st</sup> run: 277 mg, 90%; 2<sup>nd</sup> run: 262 mg, 85%; average yield: 88%).

Following General Procedure A, a mixture of 1-bromo-4-(*tert*-butyl)benzene (213 mg, 1.00 mmol, 1.00 equiv), *trans*-4-phenylcyclohexan-1-ol (264 mg, 1.50 mmol, 1.50 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (24 mg, 2.5 mol %), and THF (1.0 mL) was stirred at rt for 18 h. The crude mixture was purified by CombiFlash® Automated System (50 g silica gel, 100% hexane to 5% EtOAc in hexane over 12 CV) to provide the title compound as a colorless viscous oil (1<sup>st</sup> run: 255 mg, 83%; 2<sup>nd</sup> run: 254 mg, 82%; average yield: 83%).

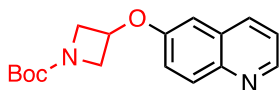
<sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.35 (dd, *J* = 8.2, 6.2 Hz, 4H), 7.29–7.21 (m, 3H), 6.95–6.89 (m, 2H), 4.28 (tq, *J* = 10.2, 4.6 Hz, 1H), 2.62 (ddt, *J* = 11.8, 7.0, 4.0 Hz, 1H), 2.42–2.25 (m, 2H), 2.13–1.98 (m, 2H), 1.74–1.57 (m, 4H), 1.35 (s, 9H) ppm. <sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 155.7, 146.6, 143.6, 128.6, 127.0, 126.4, 126.3, 115.7, 76.3, 43.8, 34.3, 32.7, 32.6, 31.8 ppm. IR (neat, cm<sup>-1</sup>) 2935, 2860, 1732, 1510, 1431, 1239, 1180, 1042, 1028, 827, 756, 698. EA Calcd. for C<sub>22</sub>H<sub>28</sub>O: C, 85.66; H, 9.15, Found: C, 85.86; H, 9.14.

**(1*S*,2*S*,5*S*)-2,6,6-trimethyl-3-(naphthalen-1-yloxy)bicyclo[3.1.1]heptan-2-ol (6)**



Following General Procedure A, a mixture of 1-chloronaphthalene (136  $\mu\text{L}$ , 1.00 mmol, 1.00 equiv), (1*S*,2*S*,3*S*,5*S*)-2,6,6-trimethylbicyclo[3.1.1]heptane-2,3-diol (204 mg, 1.20 mmol, 1.20 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (19 mg, 2.0 mol %), and THF (7.0 mL) was stirred at 80  $^{\circ}\text{C}$  for 18 h. The crude mixture was purified by CombiFlash<sup>®</sup> Automated System (50 g silica gel, 100% hexane to 10% acetone in hexane over 12 CV) to provide the title compound as an off-white solid (1<sup>st</sup> run: 247 mg, 84%; 2<sup>nd</sup> run: 229 mg, 77%; average yield: 81%). <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  8.29 (ddd,  $J = 7.4, 5.1, 2.9$  Hz, 1H), 7.90–7.81 (m, 1H), 7.59–7.47 (m, 3H), 7.42 (t,  $J = 7.9$  Hz, 1H), 6.94 (d,  $J = 7.6$  Hz, 1H), 4.82 (dd,  $J = 9.0, 5.1$  Hz, 1H), 3.73 (s, 1H), 2.75–2.63 (m, 1H), 2.35 (dtd,  $J = 10.4, 6.0, 2.3$  Hz, 1H), 2.18 (t,  $J = 5.8$  Hz, 1H), 2.04 (tt,  $J = 5.9, 3.1$  Hz, 1H), 1.92 (ddd,  $J = 14.0, 5.1, 2.6$  Hz, 1H), 1.80 (d,  $J = 10.4$  Hz, 1H), 1.46 (s, 3H), 1.38 (s, 3H), 1.10 (s, 3H) ppm. <sup>13</sup>C NMR (101 MHz, Chloroform-*d*)  $\delta$  153.1, 134.8, 127.8, 126.6, 126.3, 125.8, 125.6, 121.9, 121.2, 107.3, 76.0, 74.3, 53.9, 40.5, 38.6, 35.5, 30.8, 28.4, 28.0, 24.5 ppm. mp = 77–79  $^{\circ}\text{C}$ . IR (neat,  $\text{cm}^{-1}$ ) 2990, 2914, 1577, 1398, 1265, 1095, 1058, 785, 771. EA Calcd. for  $\text{C}_{20}\text{H}_{24}\text{O}_2$ : C, 81.04; H, 8.16, Found: C, 81.32; H, 7.97.

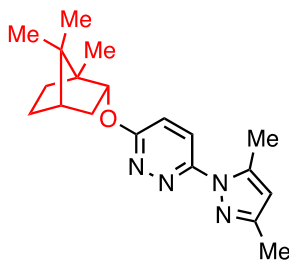
***tert*-butyl 3-(quinolin-6-yloxy)azetidine-1-carboxylate (7)**



Following General Procedure A, a mixture of 6-chloroquinoline (164 mg, 1.00 mmol, 1.00 equiv), *tert*-butyl 3-hydroxyazetidine-1-carboxylate (208 mg, 1.20 mmol, 1.20 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (38 mg, 4.0 mol %), and THF (3.0 mL) was stirred at rt for 18 h. The crude reaction mixture was dissolved in  $\text{CH}_2\text{Cl}_2$  (1.0 mL) and further treated successively with DMAP (1.0 mg),  $\text{Et}_3\text{N}$  (70  $\mu\text{L}$ , 0.50 mmol, 0.50 equiv), and  $\text{Ac}_2\text{O}$  (47  $\mu\text{L}$ , 0.50 mmol, 0.50 equiv). The resulting solution was stirred at rt overnight. The crude mixture was purified by CombiFlash<sup>®</sup> Automated System (50 g silica gel, 100% hexane to 25% acetone in hexane over 12 CV) to provide the title compound as a thick dark-yellow oil (1<sup>st</sup> run: 276 mg, 92%; 2<sup>nd</sup> run: 266 mg, 89%; average yield: 91%). <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  8.80 (dd,  $J = 4.3, 1.7$  Hz, 1H), 8.12–7.94 (m, 2H), 7.36 (ddd,  $J = 11.9, 8.8, 3.5$  Hz, 2H), 6.78 (d,  $J = 2.8$  Hz, 1H), 5.01 (tt,  $J = 6.4, 4.1$  Hz, 1H), 4.39 (ddd,  $J = 9.8, 6.4, 1.1$  Hz, 2H), 4.08 (ddd,  $J = 9.7, 4.1, 1.1$  Hz, 2H), 1.46 (s, 9H) ppm. <sup>13</sup>C NMR (101 MHz, Chloroform-*d*)  $\delta$  156.3, 154.9, 148.6, 144.8, 135.1, 131.7, 129.3, 122.4, 121.8,

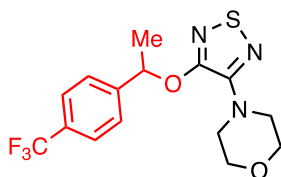
106.5, 80.2, 66.2, 56.5, 28.6 ppm. **IR** (neat,  $\text{cm}^{-1}$ ) 2974, 2884, 1695, 1392, 1364, 1224, 1136, 1112, 832. **HRMS** (DART)  $m/z$   $[M+H]^+$  Calcd. for  $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_3^+$ : 301.1547. Found: 301.1556.

**3-(3,5-dimethyl-1*H*-pyrazol-1-yl)-6-(((1*S*,2*R*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)oxy)pyridazine (8)**



Following General Procedure A, a mixture of 3-chloro-6-(3,5-dimethyl-1*H*-pyrazol-1-yl)pyridazine (209 mg, 1.00 mmol, 1.00 equiv), (1*S*,2*R*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (185 mg, 1.20 mmol, 1.20 equiv),  $\text{NaO}t\text{-Bu}$  (115 mg, 1.20 mmol, 1.20 equiv), **P2** (38 mg, 4.0 mol %), and THF (1.0 mL) was stirred at rt for 18 h. The crude mixture was purified by CombiFlash® Automated System (50 g silica gel, 100% hexane to 10% EtOAc in hexane over 12 CV) to provide the title compound as a white solid (1<sup>st</sup> run: 181 mg, 55%; 2<sup>nd</sup> run: 178 mg, 54%; average yield: 55%). **mp** = 128–130 °C. **<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  8.00 (d,  $J = 9.4$  Hz, 1H), 7.06 (d,  $J = 9.4$  Hz, 1H), 5.99 (s, 1H), 5.33–5.25 (m, 1H), 2.67 (s, 3H), 2.60 (ddt,  $J = 13.8, 9.0, 4.0$  Hz, 1H), 2.27 (s, 3H), 2.17 (ddd,  $J = 13.2, 9.4, 4.2$  Hz, 1H), 1.79 (dp,  $J = 11.7, 4.0$  Hz, 1H), 1.73 (t,  $J = 4.5$  Hz, 1H), 1.45–1.32 (m, 1H), 1.26 (ddd,  $J = 11.5, 9.4, 4.4$  Hz, 1H), 1.05 (dd,  $J = 13.8, 3.5$  Hz, 1H), 0.97 (s, 3H), 0.91 (d,  $J = 5.3$  Hz, 6H) ppm. **<sup>13</sup>C NMR** (101 MHz, Chloroform-*d*)  $\delta$  164.0, 153.1, 150.4, 141.8, 124.4, 120.5, 109.3, 82.8, 49.3, 47.8, 45.1, 37.1, 28.2, 27.1, 19.9, 19.1, 14.6, 13.8, 13.7 ppm. **IR** (neat,  $\text{cm}^{-1}$ ) 2953, 2870, 1572, 1432, 1305, 1295, 1015, 971, 852, 789. **HRMS** (DART)  $m/z$   $[M+H]^+$  Calcd. for  $\text{C}_{19}\text{H}_{27}\text{N}_4\text{O}^+$ : 327.2179. Found: 327.2187.

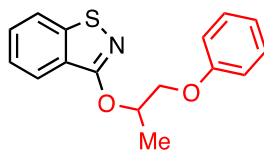
**4-(4-(1-(4-(trifluoromethyl)phenoxy)-1,2,5-thiadiazol-3-yl)morpholine (9)**



Following General Procedure, a mixture of 4-(4-chloro-1,2,5-thiadiazol-3-yl)morpholine (206 mg,

1.00 mmol, 1.00 equiv), 1-(4-(trifluoromethyl)phenyl)ethan-1-ol (184  $\mu\text{L}$ , 1.20 mmol, 1.20 equiv), NaOt-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (38 mg, 4.0 mol %), and THF (1.0 mL) was stirred at rt for 18 h. The crude mixture was purified by flash column chromatography (100% hexane to 10% EtOAc in hexane, with an increment of 1% EtOAc in hexane) to provide the title compound as a viscous orange oil (1<sup>st</sup> run: 307 mg, 85%; 2<sup>nd</sup> run: 308 mg, 86%; average yield: 86%). **<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  7.62 (d,  $J$  = 8.1 Hz, 2H), 7.50 (d,  $J$  = 8.1 Hz, 2H), 6.04 (q,  $J$  = 6.5 Hz, 1H), 3.83 (t,  $J$  = 4.0 Hz, 4H), 3.55 (t,  $J$  = 4.0 Hz, 4H), 1.71 (d,  $J$  = 6.6 Hz, 3H). **<sup>13</sup>C NMR** (101 MHz, Chloroform-*d*)  $\delta$  152.8, 150.2, 145.8, 130.8–129.8 (q,  $J$  = 30.3 Hz), 128.2–120.0 (q,  $J$  = 242.4 Hz), 126.3, 125.8–125.7 (q,  $J$  = 6.7 Hz), 78.3, 66.6, 48.1, 22.9 ppm. **<sup>19</sup>F NMR** (376 MHz, Chloroform-*d*)  $\delta$  -62.6 ppm. **IR** (neat,  $\text{cm}^{-1}$ ) 2584, 2463, 1483, 1322, 1116, 1067, 838. **EA** Calcd. for  $\text{C}_{15}\text{H}_{16}\text{F}_3\text{N}_3\text{O}_2\text{S}$ : C, 50.13; H, 4.49, Found: C, 50.30; H, 4.60.

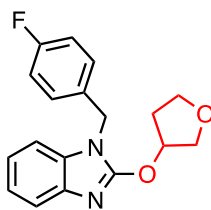
### 3-((1-phenoxypropan-2-yl)oxy)benzo[*d*]isothiazole (**10**)



Following General Procedure A, a mixture of 3-chlorobenzo[*d*]isothiazole (170 mg, 1.00 mmol, 1.00 equiv), 1-phenoxypropan-2-ol (172  $\mu\text{L}$ , 1.20 mmol, 1.20 equiv), NaOt-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (38 mg, 4.0 mol %), and THF (1.0 mL) was stirred at rt for 18 h. The crude mixture was purified by CombiFlash® Automated System (50 g silica gel, 100% hexane to 4% acetone in hexane over 12 CV) to provide the title compound as a colorless viscous oil (1<sup>st</sup> run: 232 mg, 81%; 2<sup>nd</sup> run: 218 mg, 76%; average yield: 79%). **<sup>1</sup>H NMR** (400 MHz, Methylene Chloride-*d*<sub>2</sub>)  $\delta$  7.91 (dt,  $J$  = 8.1, 1.0 Hz, 1H), 7.81 (dd,  $J$  = 8.2, 0.9 Hz, 1H), 7.53 (ddd,  $J$  = 8.1, 7.0, 1.2 Hz, 1H), 7.39 (ddd,  $J$  = 8.0, 6.9, 1.0 Hz, 1H), 7.32–7.23 (m, 2H), 6.98–6.89 (m, 3H), 5.64 (pd,  $J$  = 6.3, 4.5 Hz, 1H), 4.31 (dd,  $J$  = 10.2, 5.6 Hz, 1H), 4.22 (dd,  $J$  = 10.2, 4.4 Hz, 1H), 1.59 (d,  $J$  = 6.4 Hz, 3H) ppm. **<sup>13</sup>C NMR** (101 MHz, Methylene Chloride-*d*<sub>2</sub>)  $\delta$  162.7, 159.3, 152.0, 129.8, 129.1, 126.0, 124.8, 123.4, 121.3, 120.5, 115.0, 73.8, 70.7, 17.1 ppm. **IR** (neat,  $\text{cm}^{-1}$ ) 3061, 2978, 2932, 1597, 1495, 1240, 751, 733, 689. **EA** Calcd. for  $\text{C}_{16}\text{H}_{15}\text{NO}_2\text{S}$ : C, 67.34; H, 5.30, Found: C, 67.64; H, 5.25.

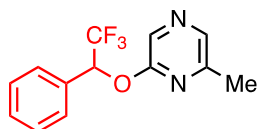
### 1-(4-fluorobenzyl)-2-((tetrahydrofuran-3-yl)oxy)-1*H*-benzo[*d*]imidazole (**11**)





Following General Procedure, a mixture of 2-chloro-1-(4-fluorobenzyl)-1*H*-benzo[*d*]imidazole (261 mg, 1.00 mmol, 1.00 equiv), tetrahydrofuran-3-ol (97.0  $\mu$ L, 1.20 mmol, 1.20 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (38 mg, 4.0 mol %), and THF (1.5 mL) was stirred at rt for 18 h. The crude mixture was purified by CombiFlash® Automated System (50 g silica gel, 100% hexane to 20% acetone in hexane over 14 CV) to provide the title compound as a thick dark-yellow oil (1<sup>st</sup> run: 203 mg, 65%; 2<sup>nd</sup> run: 199 mg, 64%; average yield: 65%). **<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  7.56 (d, *J* = 7.7 Hz, 1H), 7.22–7.14 (m, 3H), 7.14–7.06 (m, 2H), 6.99 (m, 2H), 5.74 (ddt, *J* = 5.9, 3.7, 1.7 Hz, 1H), 5.10 (s, 2H), 4.16–4.01 (m, 2H), 4.01–3.84 (m, 2H), 2.34 (dtd, *J* = 14.3, 8.5, 5.9 Hz, 1H), 2.23 (dt, *J* = 13.5, 5.4 Hz, 1H). **<sup>13</sup>C NMR** (101 MHz, Chloroform-*d*)  $\delta$  163.6, 161.2, 156.4, 136.9 (d, *J* = 673 Hz), 132.0, 129.0 (d, *J* = 21.7 Hz), 121.9, 121.3, 118.0, 115.8 (d, *J* = 8.2 Hz), 108.6, 80.7, 73.4, 67.1, 45.1, 33.3 ppm. **<sup>19</sup>F NMR** (376 MHz, Chloroform-*d*)  $\delta$  –114.2 ppm. **IR** (neat,  $\text{cm}^{-1}$ ) 2873, 1531, 1509, 1454, 1271, 1006, 899, 738. **EA** Calcd. for  $\text{C}_{18}\text{H}_{17}\text{FN}_2\text{O}_2$ : C, 69.22; H, 5.49, Found: C, 69.03; H, 5.45.

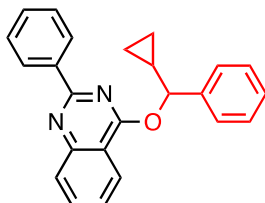
### 2-methyl-6-(2,2,2-trifluoro-1-phenylethoxy)pyrazine (**12**)



Following General Procedure A, a mixture of 2-chloro-6-methylpyrazine (129 mg, 1.00 mmol, 1.00 equiv), 2,2,2-trifluoro-1-phenylethan-1-ol (163  $\mu$ L, 1.20 mmol, 1.20 equiv), NaO*t*-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (19 mg, 2.0 mol %), and THF (1.0 mL) was stirred at 40 °C for 18 h. The crude mixture was purified by CombiFlash® Automated System (50 g silica gel, 100% hexane to 10% acetone in hexane over 14 CV) to provide the title compound as a colorless oil (1<sup>st</sup> run: 214 mg, 80%; 2<sup>nd</sup> run: 216 mg, 81%; average yield: 81%). Note: the final compound may be volatile under high vacuum. **<sup>1</sup>H NMR** (400 MHz, Chloroform-*d*)  $\delta$  8.21 (s, 1H), 8.05 (s, 1H), 7.59–7.58 (m, 2H), 7.44–7.34 (m, 3H), 6.61 (q, *J* = 6.9 Hz, 1H), 2.39 (s, 3H). **<sup>13</sup>C NMR** (101 MHz, Chloroform-*d*)  $\delta$  157.1, 150.4, 137.6, 132.3, 131.9, 129.8, 128.7, 128.4, 127.9–119.5 (q, *J* = 281.9

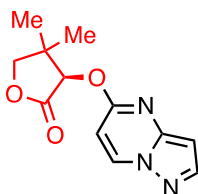
Hz), 73.5–72.5 (q,  $J = 33.4$  Hz), 21.0 ppm.  $^{19}\text{F}$  NMR (376 MHz, Chloroform- $d$ )  $\delta$  –75.8 ppm. IR (neat,  $\text{cm}^{-1}$ ) 1538, 1406, 1250, 1174, 1128, 1010, 699. HRMS (DART)  $m/z$   $[\text{M}+\text{H}]^+$  Calcd. for  $\text{C}_{13}\text{H}_{12}\text{F}_3\text{N}_2\text{O}^+$ : 269.0896. Found: 269.0902.

#### 4-(cyclopropyl(phenyl)methoxy)-2-phenylquinazoline (13)



Following General Procedure A, a mixture of 4-chloro-2-phenylquinazoline (241 mg, 1.00 mmol, 1.00 equiv), cyclopropyl(phenyl)methanol (172  $\mu\text{L}$ , 1.20 mmol, 1.20 equiv),  $\text{NaO}t\text{-Bu}$  (115 mg, 1.20 mmol, 1.20 equiv), **P2** (19 mg, 2.0 mol %), and THF (1.0 mL) was stirred at 40  $^\circ\text{C}$  for 18 h. The crude mixture was purified by silica gel chromatography (silica gel was pre-treated with 1%  $\text{Et}_3\text{N}$  in hexane prior to column assembly; 100% hexane to 5% acetone in hexane with an increment of 1% acetone in hexane) to provide the title compound as a thick off-white viscous oil (1<sup>st</sup> run: 301 mg, 85%; 2<sup>nd</sup> run: 284 mg, 81%; average yield: 83%).  $^1\text{H}$  NMR (400 MHz, Chloroform- $d$ )  $\delta$  8.46 (dd,  $J = 7.4, 2.3$  Hz, 2H), 8.33 (d,  $J = 8.1$  Hz, 1H), 7.97 (d,  $J = 8.4$  Hz, 1H), 7.82 (t,  $J = 7.7$  Hz, 1H), 7.60 (d,  $J = 7.5$  Hz, 2H), 7.55 (t,  $J = 7.6$  Hz, 1H), 7.52–7.44 (m, 3H), 7.37 (t,  $J = 7.5$  Hz, 2H), 7.29 (d,  $J = 7.3$  Hz, 1H), 6.11 (d,  $J = 8.3$  Hz, 1H), 1.66–1.56 (m, 1H), 0.76–0.55 (m, 4H) ppm.  $^{13}\text{C}$  NMR (101 MHz, Chloroform- $d$ )  $\delta$  166.3, 160.1, 152.2, 141.0, 138.4, 133.6, 130.5, 128.5, 128.5, 128.5, 128.1, 127.9, 126.8, 126.5, 123.8, 115.7, 81.7, 17.1, 4.4, 3.2 ppm. IR (neat,  $\text{cm}^{-1}$ ) 1618, 1571, 1556, 1498, 1487, 1356, 1161, 939, 765, 707. EA Calcd. for  $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}$ : C, 81.79; H, 5.72, Found: C, 81.67; H, 5.84.

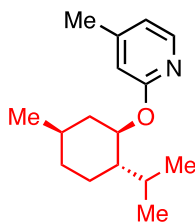
#### (*R*)-4,4-dimethyl-3-(pyrazolo[1,5-*a*]pyrimidin-5-yloxy)dihydrofuran-2(3*H*)-one (14)



Following General Procedure A, a mixture of 5-chloropyrazolo[1,5-*a*]pyrimidine (154 mg, 1.00 mmol, 1.00 equiv), (*R*)-3-hydroxy-4,4-dimethyldihydrofuran-2(3*H*)-one (156 mg, 1.20 mmol,

1.20 equiv), NaOt-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (19 mg, 2.0 mol %), and THF (1.0 mL) was stirred at 40 °C for 18 h. The crude reaction mixture was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL) and further treated successively with DMAP (1.0 mg), Et<sub>3</sub>N (70 μL, 0.50 mmol, 0.50 equiv), and Ac<sub>2</sub>O (47 μL, 0.50 mmol, 0.50 equiv). The resulting solution was stirred at rt overnight. The crude mixture was purified by silica gel chromatography (100% hexane to 20% acetone in hexane with an increment of 1% acetone in hexane) to provide the title compound as a yellow solid (1<sup>st</sup> run: 198 mg, 80%; 2<sup>nd</sup> run: 205 mg, 83%; average yield: 82%). mp = 167–168 °C. <sup>1</sup>H NMR (400 MHz, Chloroform-d) δ 8.49 (dd, *J* = 7.4, 0.9 Hz, 1H), 7.97 (d, *J* = 2.2 Hz, 1H), 6.46 (d, *J* = 7.4 Hz, 1H), 6.31 (dd, *J* = 2.2, 0.9 Hz, 1H), 5.97 (s, 1H), 4.10 (s, 2H), 1.28 (s, 3H), 1.20 (s, 3H) ppm. <sup>13</sup>C NMR (101 MHz, Chloroform-d) δ 172.7, 160.1, 146.5, 145.4, 137.6, 99.7, 95.0, 76.6, 76.3, 40.6, 23.3, 20.1 ppm. IR (neat, cm<sup>-1</sup>) 2966, 1633, 1412, 1306, 1214, 1075, 1008, 910, 804, 784. EA Calcd. for C<sub>12</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>: C, 58.29; H, 5.30, Found: C, 58.00; H, 5.38.

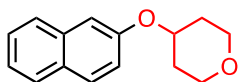
## 2-(((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)oxy)-4-methylpyridine (**15**)



Following General Procedure A, a mixture of 2-chloro-4-methylpyridine (112 μL, 1.00 mmol, 1.00 equiv), (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexan-1-ol (234 mg, 1.50 mmol, 1.50 equiv, due to the sublimation of alcohol under high vacuum), NaOt-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (19 mg, 2.0 mol %), and THF (1.0 mL) was stirred at 40 °C for 18 h. Note: acetylated menthol and the desired product were inseparable by silica gel chromatography. Therefore, CH<sub>2</sub>Cl<sub>2</sub>, instead of EtOAc, was used to dilute the reaction mixture. The crude mixture was purified by CombiFlash® Automated System (50 g silica gel, 100% hexane to 4% EtOAc in hexane over 14 CV) to provide the title compound as a colorless oil (1<sup>st</sup> run: 196 mg, 79%; 2<sup>nd</sup> run: 197 mg, 80%; average yield: 80%). Note: the final compound may be volatile under high vacuum. <sup>1</sup>H NMR (400 MHz, Chloroform-d) δ 7.98 (d, *J* = 5.2 Hz, 1H), 6.62 (dd, *J* = 5.3, 1.5 Hz, 1H), 6.48 (s, 1H), 4.97 (td, *J* = 10.7, 4.3 Hz, 1H), 2.25 (s, 3H), 2.19 (dtd, *J* = 12.1, 3.9, 1.8 Hz, 1H), 2.05 (heptd, *J* = 7.0, 4.0 Hz, 1H), 1.69 (dp, *J* = 12.9, 3.0 Hz, 2H), 1.57 (dddd, *J* = 12.0, 9.0, 6.4, 3.3 Hz, 1H), 1.49 (ddt, *J* = 12.4, 10.7, 3.2 Hz, 1H), 1.13 (qd, *J* = 13.5, 12.7, 3.7 Hz, 1H), 1.05–0.95 (m, 1H), 0.95–0.91

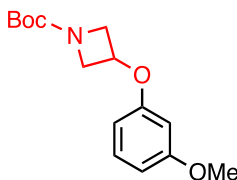
(m, 1H), 0.90 (d,  $J = 1.1$  Hz, 3H), 0.89 (d,  $J = 1.4$  Hz, 3H), 0.75 (d,  $J = 7.0$  Hz, 3H) ppm.  $^{13}\text{C}$  NMR (101 MHz, Chloroform-d)  $\delta$  164.3, 149.8, 146.6, 117.8, 111.6, 74.4, 48.0, 41.0, 34.7, 31.5, 26.5, 22.3, 21.0, 20.9, 16.8 ppm. IR (neat,  $\text{cm}^{-1}$ ) 2953, 2868, 1610, 1561, 1407, 1314, 1160, 1027, 807. EA Calcd. for  $\text{C}_{16}\text{H}_{25}\text{NO}$ : C, 77.68; H, 10.19, Found: C, 77.76; H, 10.07.

#### 4-(naphthalen-2-yloxy)tetrahydro-2H-pyran (16)



Following General Procedure A, a mixture of 2-bromonaphthalene (207 mg, 1.00 mmol, 1.00 equiv), tetrahydro-2H-pyran-4-ol (191  $\mu\text{L}$ , 2.00 mmol, 2.00 equiv), NaOt-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (24 mg, 2.5 mol %), and THF (1.0 mL) was stirred at rt for 18 h. The crude mixture was purified by CombiFlash® Automated System (50 g silica gel, 100% hexane to 10% acetone in hexane over 14 CV) to provide the title compound as a white solid (1<sup>st</sup> run: 181 mg, 80%; 2<sup>nd</sup> run: 197 mg, 87%; average yield: 84%). mp = 76–77 °C.  $^1\text{H}$  NMR (400 MHz, Chloroform-d)  $\delta$  7.85–7.70 (m, 3H), 7.48 (t,  $J = 7.5$  Hz, 1H), 7.38 (t,  $J = 7.5$  Hz, 1H), 7.21 (dq,  $J = 5.1, 2.6$  Hz, 2H), 4.65 (tt,  $J = 7.8, 3.8$  Hz, 1H), 4.06 (ddd,  $J = 10.8, 6.0, 3.9$  Hz, 2H), 3.65 (ddd,  $J = 11.6, 8.2, 3.2$  Hz, 2H), 2.12 (ddt,  $J = 13.5, 6.7, 3.8$  Hz, 2H), 1.90 (dtd,  $J = 12.4, 8.0, 3.8$  Hz, 2H) ppm.  $^{13}\text{C}$  NMR (101 MHz, Chloroform-d)  $\delta$  155.0, 134.6, 129.7, 129.1, 127.7, 126.7, 126.4, 123.8, 119.7, 108.9, 71.6, 65.2, 31.8 ppm. IR (neat,  $\text{cm}^{-1}$ ) 3056, 2863, 2836, 1626, 1521, 1464, 1214, 1182, 1089, 837, 742. EA Calcd. for  $\text{C}_{15}\text{H}_{16}\text{O}_2$ : C, 78.92; H, 7.06, Found: C, 78.63; H, 7.13.

#### tert-butyl 3-(3-methoxyphenoxy)azetidine-1-carboxylate (17)

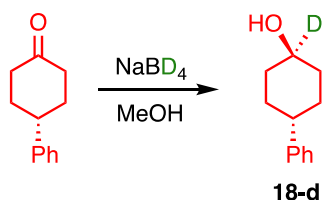


Following General Procedure, a mixture of 1-bromo-3-methoxybenzene (127  $\mu\text{L}$ , 1.00 mmol, 1.00 equiv), tert-butyl 3-hydroxyazetidine-1-carboxylate (346 mg, 2.00 mmol, 2.00 equiv), NaOt-Bu (115 mg, 1.20 mmol, 1.20 equiv), **P2** (19 mg, 2.0 mol %), and THF (5.0 mL) was stirred at 60 °C for 18 h. The crude mixture was purified by flash column chromatography (50%  $\text{CH}_2\text{Cl}_2$  in hexane isocratic to 10% acetone in hexane isocratic) to provide the title compound as a thick light-yellow oil (1<sup>st</sup> run: 252 mg, 90%; 2<sup>nd</sup> run: 249 mg, 89%; average yield: 90%).  $^1\text{H}$  NMR (400 MHz,

Chloroform-*d*)  $\delta$  7.17 (t,  $J = 8.5$  Hz, 1H), 6.54 (d,  $J = 7.8$  Hz, 1H), 6.31 (d,  $J = 6.8$  Hz, 2H), 4.84 (td,  $J = 6.4, 3.3$  Hz, 1H), 4.28 (dd,  $J = 9.7, 6.4$  Hz, 2H), 3.99 (dd,  $J = 9.8, 4.2$  Hz, 2H), 3.77 (s, 3H), 1.44 (s, 9H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  161.1, 157.9, 156.2, 130.3, 107.1, 106.7, 101.4, 79.9, 65.8, 56.5, 55.4, 28.5 ppm. IR (neat,  $\text{cm}^{-1}$ ) 2974, 1699, 1589, 1390, 1365, 1133, 1041, 762, 686. EA Calcd. for  $\text{C}_{15}\text{H}_{21}\text{NO}_4$ : C, 64.50; H, 7.58, Found: C, 64.68; H, 7.75.

## B) $\alpha$ -Deutero-Alcohol 18-*d* Synthesis and Characterization

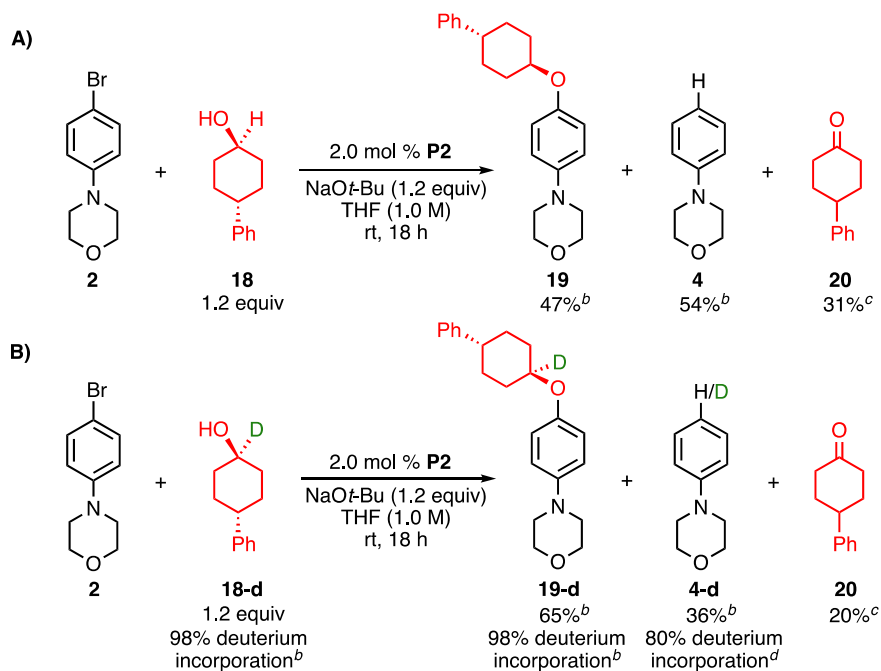
### *trans*-4-phenylcyclohexan-1-*d*-1-ol (18-*d*)



A 100 mL round bottom flask equipped with a stir bar was charged with 4-phenylcyclohexan-1-one (1.05 g, 6.00 mmol, 1.00 equiv). The round bottom flask was fitted with a rubber septum. Anhydrous methanol (10 mL) was added via syringe. The round bottom flask was cooled to 0 °C in an ice/water bath. The rubber septum was removed, and sodium borodeuteride (98% deuterium incorporation, 502 mg, 12.0 mmol, 2.00 equiv) was added portion wise. The reaction flask was refitted with the rubber septum and stirred at rt. The reaction progress was monitored by TLC analysis. Upon completion, water (2 mL) was added to the reaction mixture and a white precipitate was formed. The reaction mixture was transferred to a separatory funnel and was extracted with  $\text{Et}_2\text{O}$  (15 mL x 3). The organic layer was dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated with the aid of a rotary evaporator. The crude mixture was triturated in cyclohexane with the aid of sonication until a free-flowing white solid resulted. The desired product **18-*d*** was isolated (783 mg, 74% yield) by filtration and dried under high vacuum. Deuterium incorporation (98%) was determined by  $^1\text{H}$  NMR analysis. mp = 118.4–120.1 °C.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.30 (dd,  $J = 8.4, 6.9$  Hz, 2H), 7.25–7.16 (m, 3H), 3.75–3.64 (m, 0.2H), 2.51 (tt,  $J = 12.0, 3.5$  Hz, 1H), 2.10 (dd,  $J = 11.3, 2.5$  Hz, 2H), 2.01–1.87 (m, 2H), 1.63 (d,  $J = 5.1$  Hz, 1H), 1.61–1.48 (m, 2H), 1.49–1.38 (m, 2H) ppm.  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  146.7, 128.5, 126.9, 126.2, 70.3 (t,  $J = 21.5$  Hz), 43.5, 36.0, 32.6 ppm. IR (neat,  $\text{cm}^{-1}$ ) 3424, 3028, 2921, 2849, 1600, 1493, 1452, 1342, 1219, 1123, 1089, 1064, 945. HRMS (DART) Calcd.  $\text{C}_{12}\text{H}_{14}\text{D}$   $[\text{M}-\text{H}_2\text{O}]^+$ : 160.1237. Found: 160.1226.

Note: alcohol **18**, *trans*-4-phenylcyclohexan-1-ol, has been previously reported and was prepared as before.<sup>S3</sup> The <sup>1</sup>H NMR spectrum of alcohol **18-d** matches that of alcohol **18**, except for the attenuated signal intensity at ~3.7 ppm.

### C) Deuterium-Labeling Study



Following General Procedure A, a mixture of 4-(4-bromophenyl)morpholine (121 mg, 0.50 mmol, 1.0 equiv), alcohol **18** or **18-d** (106 mg, 0.60 mmol, 1.2 equiv), NaOt-Bu (58 mg, 0.60 mmol, 1.20 equiv), **P2** (9.6 mg, 2.0 mol %), and THF (0.5 mL) was stirred at rt for 18 h. The crude mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (2 mL), filtered through a pad of Celite® that was further rinsed with CH<sub>2</sub>Cl<sub>2</sub>. The crude material was concentrated with the aid of a rotary evaporator. Dodecane (50 μL) was added to the crude mixture as an internal standard for GC analysis to first determine the yield of **4**. The yield of **20** could not be determined at this point by GC analysis, due to the overlap of GC signals from **18** or **18-d** and **20**. The GC sample and the rest of the crude material were combined and concentrated with the aid of a rotary evaporator. 1,1,2,2-Tetrachloroethane (50 μL) was added to the crude material as an internal standard for <sup>1</sup>H NMR analysis to determine the yields of **19** or **19-d** and **4** or **4-d**. The NMR sample and the rest of the crude material were recombined and concentrated with the aid of a rotary evaporator. In order to obtain reliable data to determine the deuterium content of the samples, approximately 60% of the crude material was purified by preparative thin layer chromatography (15% acetone in hexane) to obtain <sup>1</sup>H NMR

spectra for **19** and **19-d**, and HRMS data for **4** and **4-d**. In order to determine the yield of ketone **20** by GC analysis, the rest of the crude mixture was re-dissolved in CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL), and the resulting solution was further treated successively with DMAP (1.0 mg), Et<sub>3</sub>N (69 μL, 0.50 mmol, 1.00 equiv), Ac<sub>2</sub>O (48 μL, 0.50 mmol, 1.00 equiv). The reaction solution was stirred at rt overnight to ensure full acetylation of **18** or **18-d**. An aliquot of the solution was then subjected to GC analysis to determine the yield of **20**.

*Analysis for determining deuterium incorporation for 19-d and 4-d*

The <sup>1</sup>H NMR spectra of aryl ether **19** and **19-d** contain signals from carbazole (a side product from the precatalyst), but the signal of interest (H<sub>α</sub>: 4.16 ppm, highlight in the blue boxes, Figure S1) used for determining deuterium incorporation can be unambiguously identified. Since the peak of interest in Figure S1B integrated to 0.02, 98% deuterium incorporation (1 – 0.02 = 0.98) was detected for **19-d**.

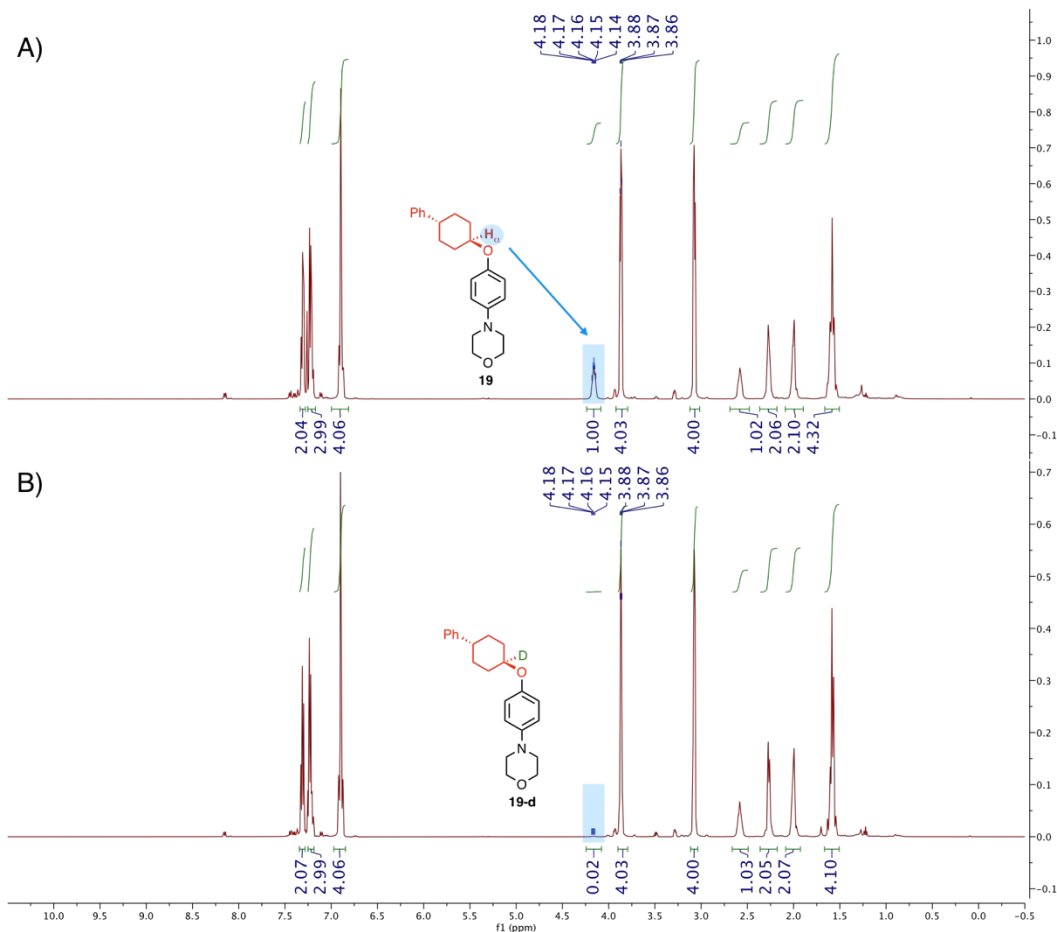


Figure S1. <sup>1</sup>H NMR spectra of **19** (A) and **19-d** (B).

In order to determine the percent deuterium incorporation of **4-d**, HRMS (DART) was used (Figure S2). The ratio of the relative intensities of **4:4-d** was considered along with the 10.8% isotope contribution of **4** to the parent mass of **4-d**. The raw data was analyzed using Mass Mountaineer and Excel.

The analysis for determining deuterium incorporation in **4-d** is as follows:

**4**  $m/z$   $[M+H]^+$  Calcd. for  $C_{10}H_{14}NO^+$ : 164.1070. Found: 164.1072. Relative intensity: 754769.1989. Isotope contribution (10.8%): 81515.0734.

**4-d**  $m/z$   $[M+H]^+$  Calcd. for  $C_{10}H_{13}DNO^+$ : 165.1133. Found: 165.1139. Relative intensity: 3187474.598.

Total contribution of **4-d** to parent mass peak:  $(3187474.598 - 81515.0734) = 3105959.5246$

Deuterium incorporation:  $3105959.5246 / (3105959.5246 + 754769.1989) = 0.804$ ; therefore 80% deuterium incorporation was detected in **4-d**.

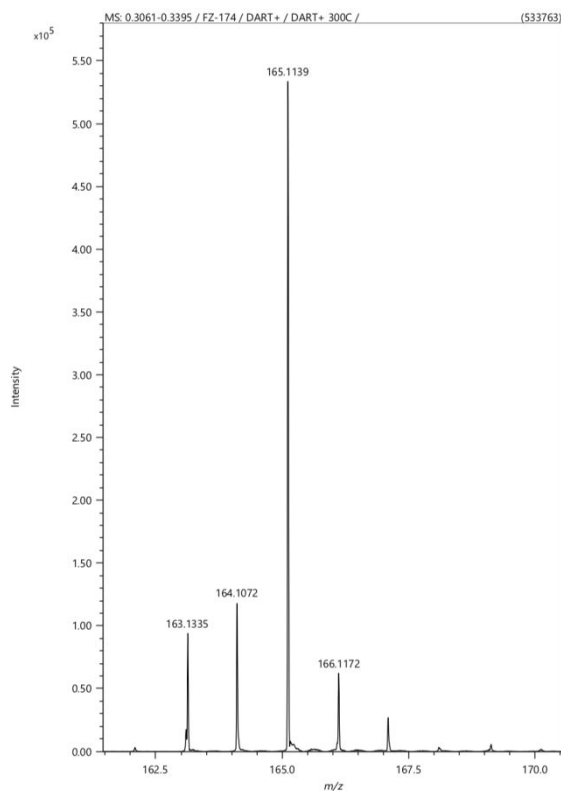


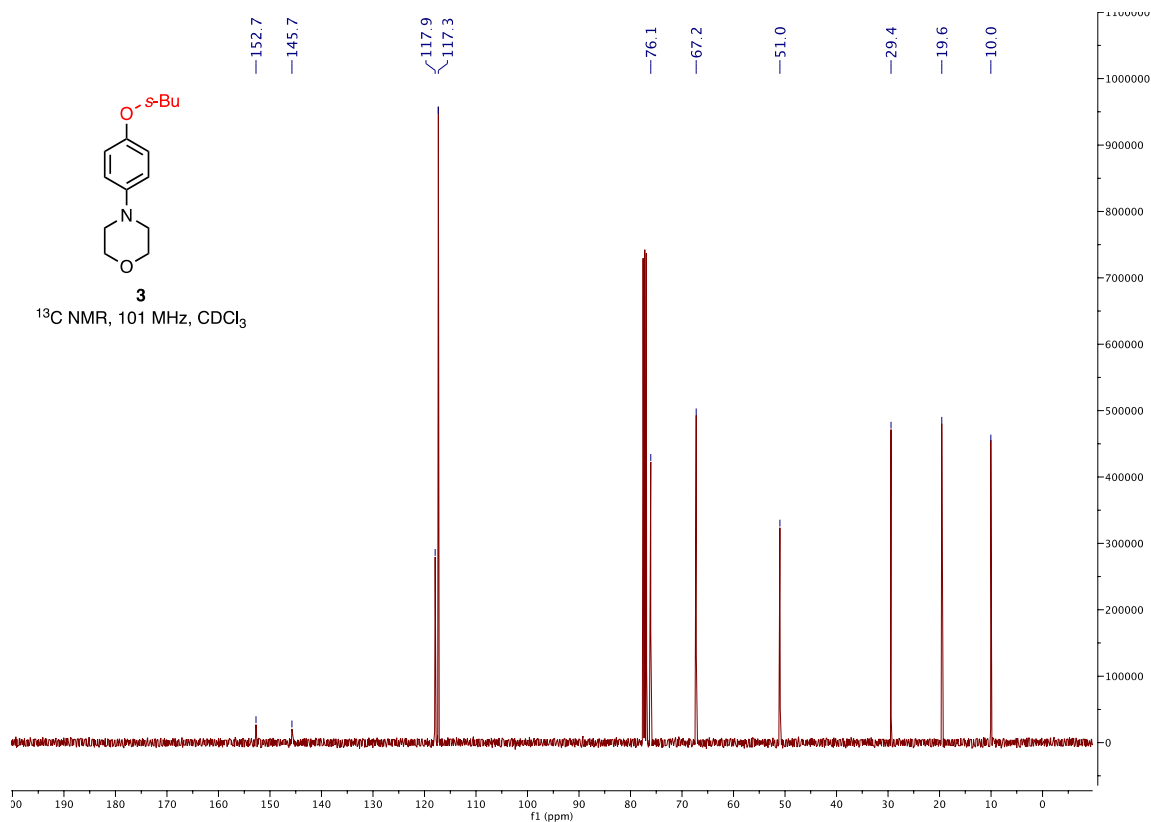
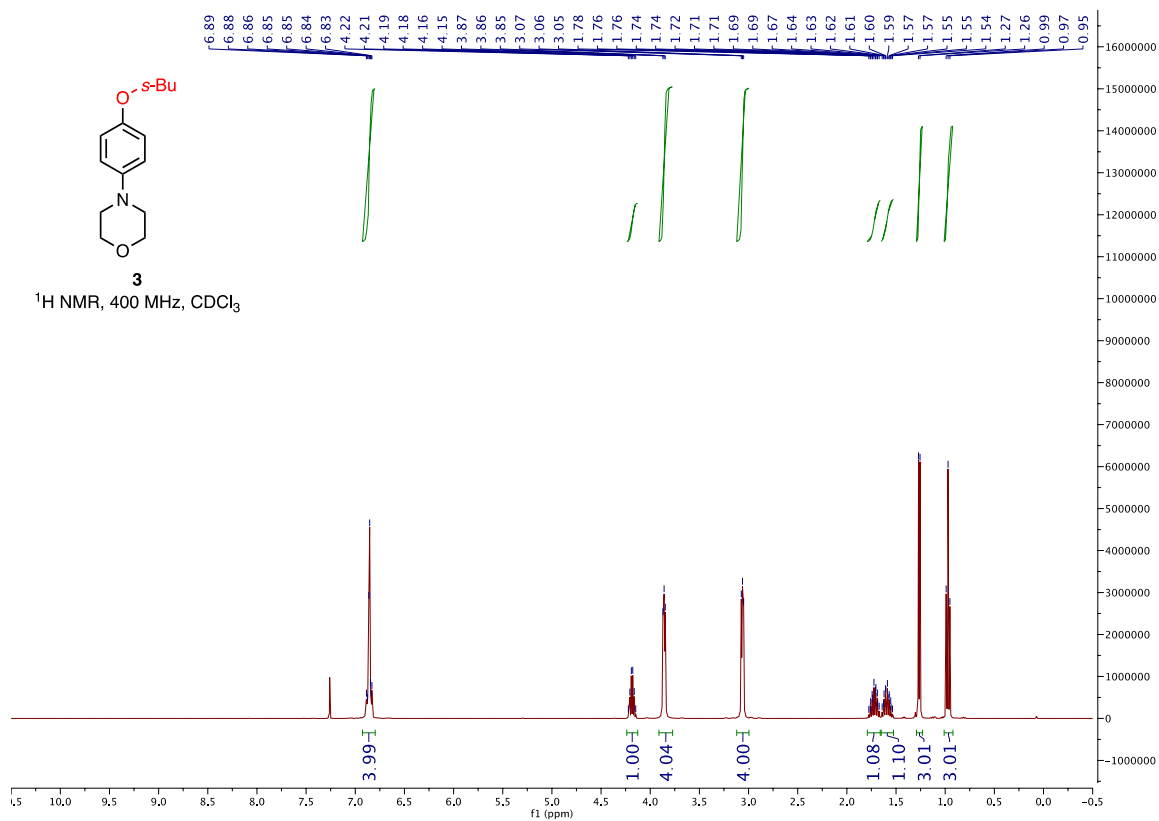
Figure S2. HRMS of **4-d**.

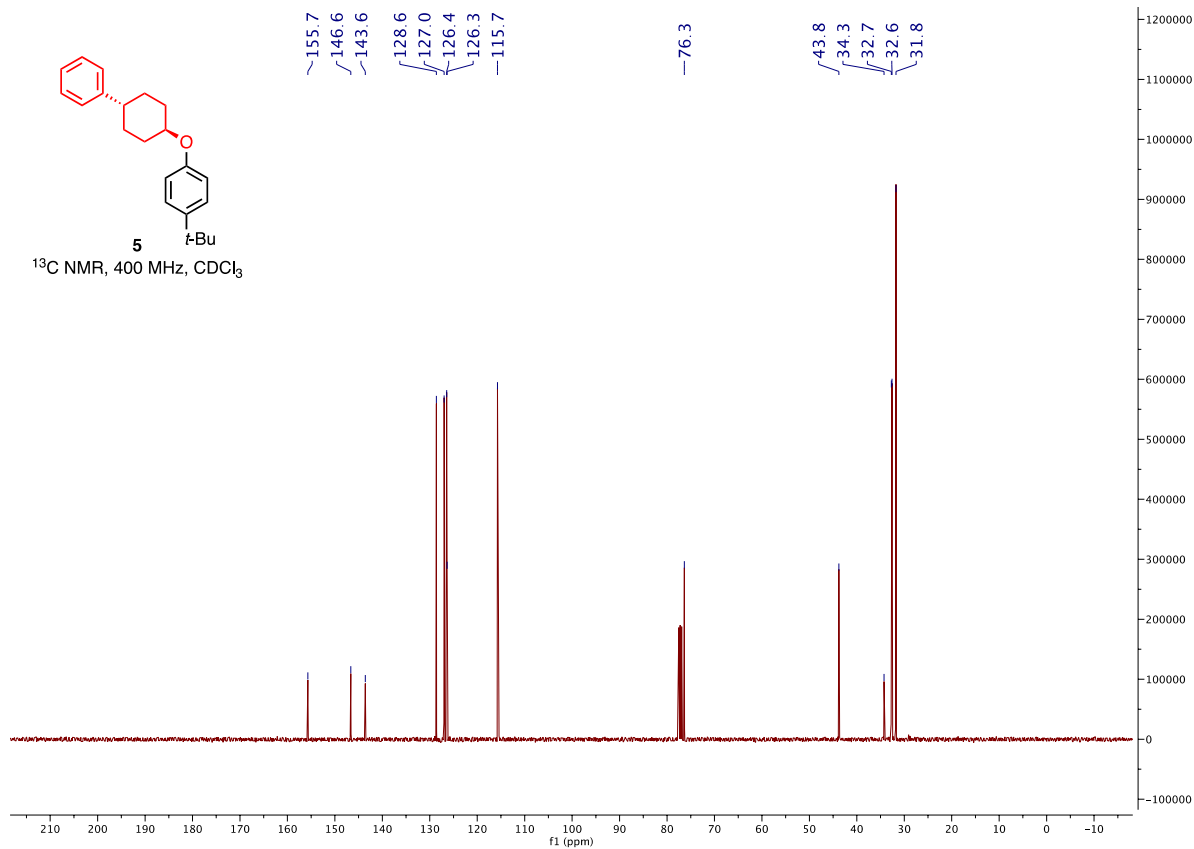
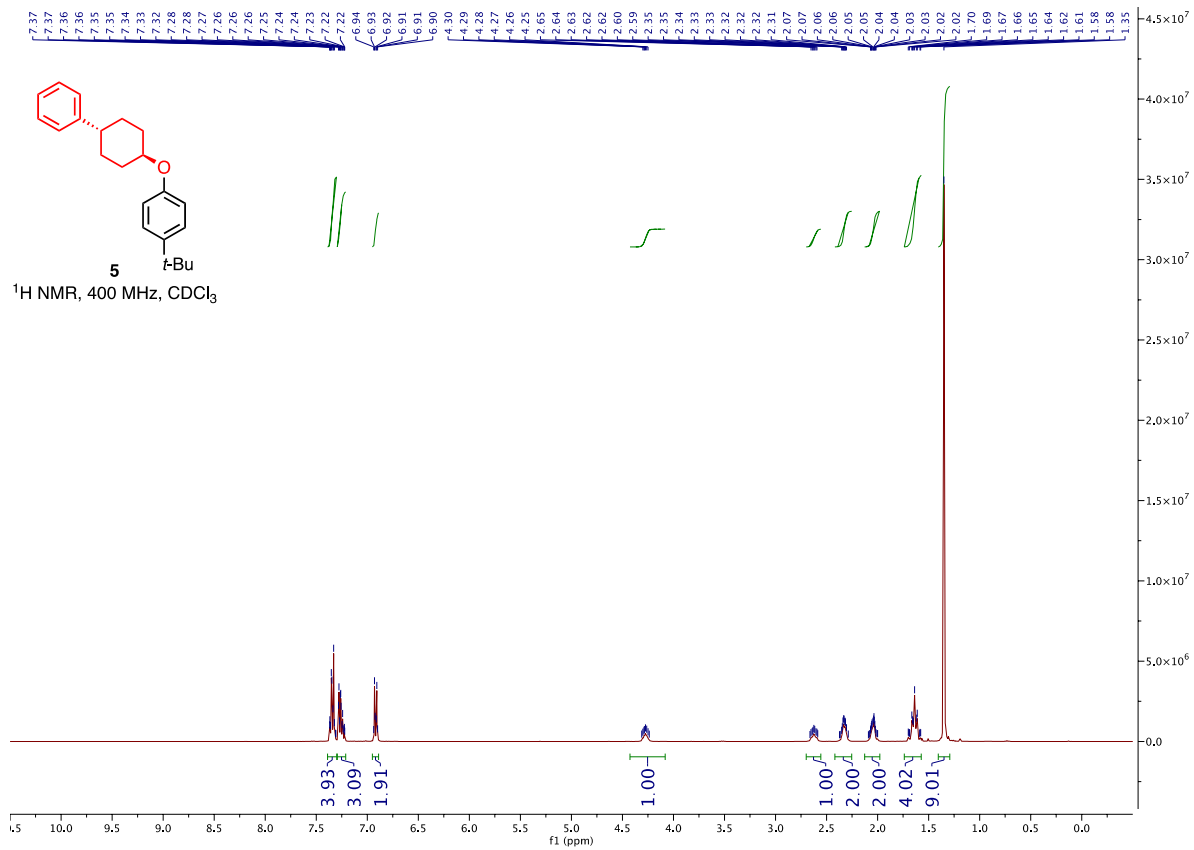
## References

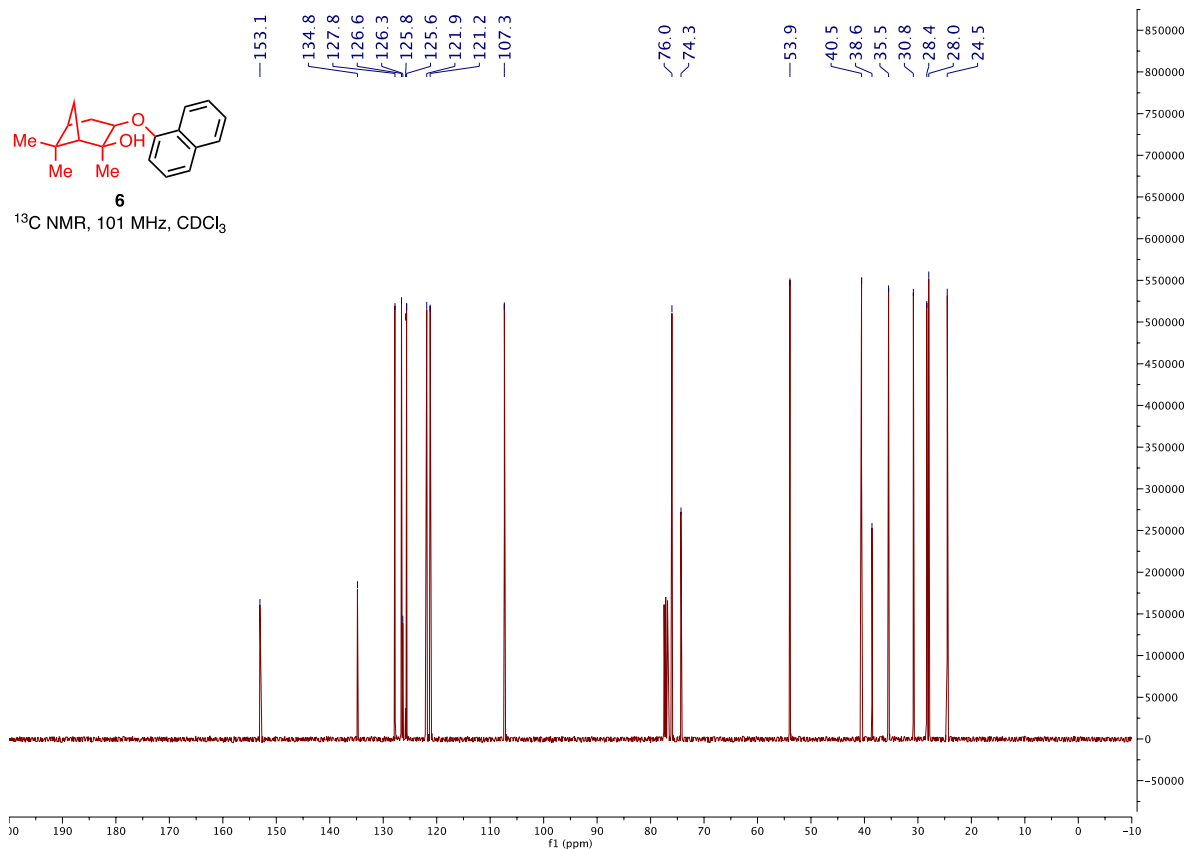
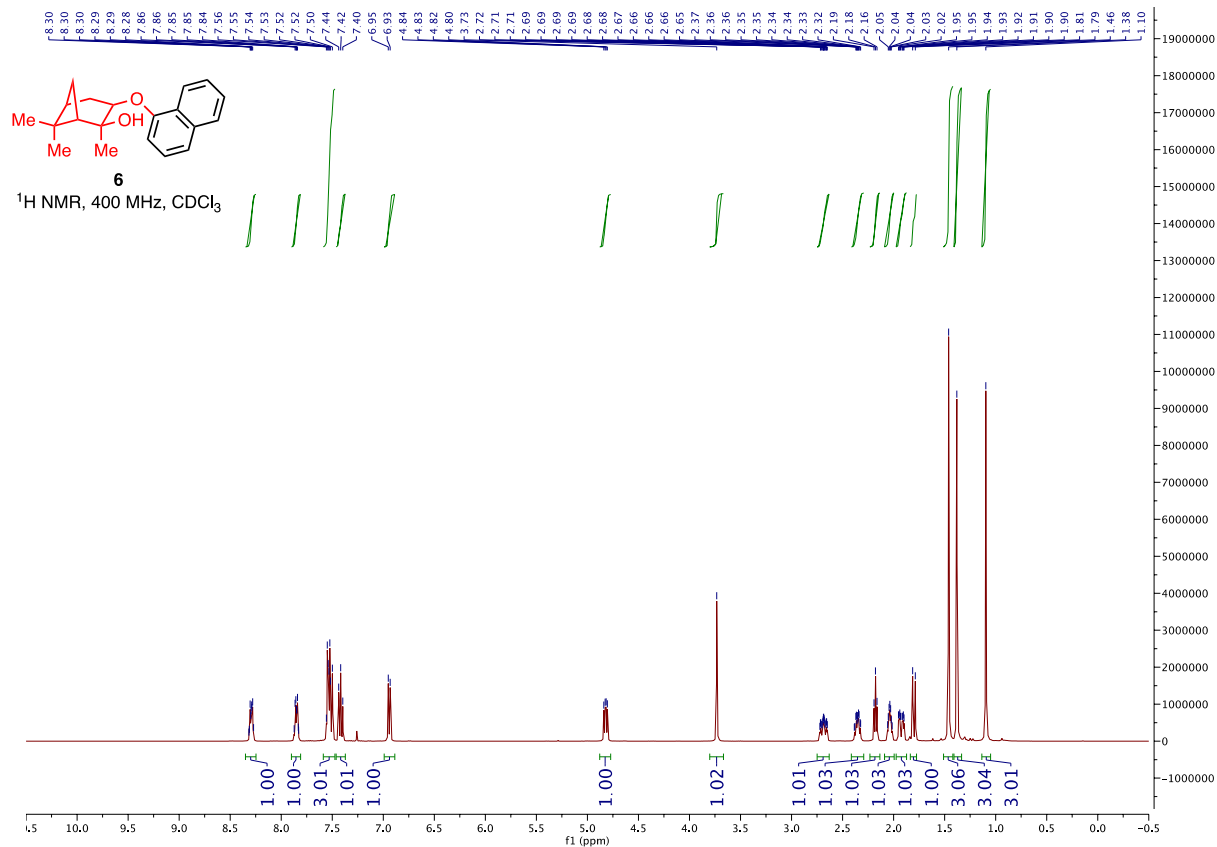


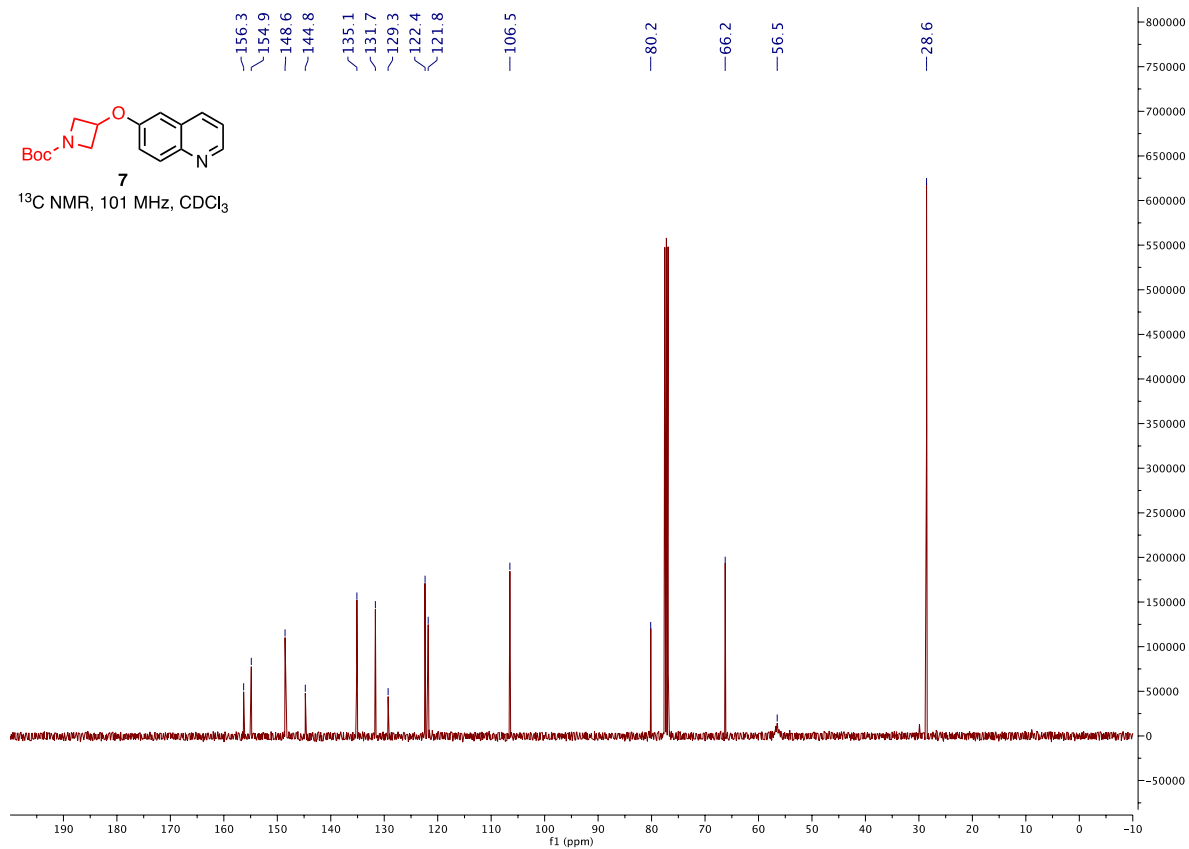
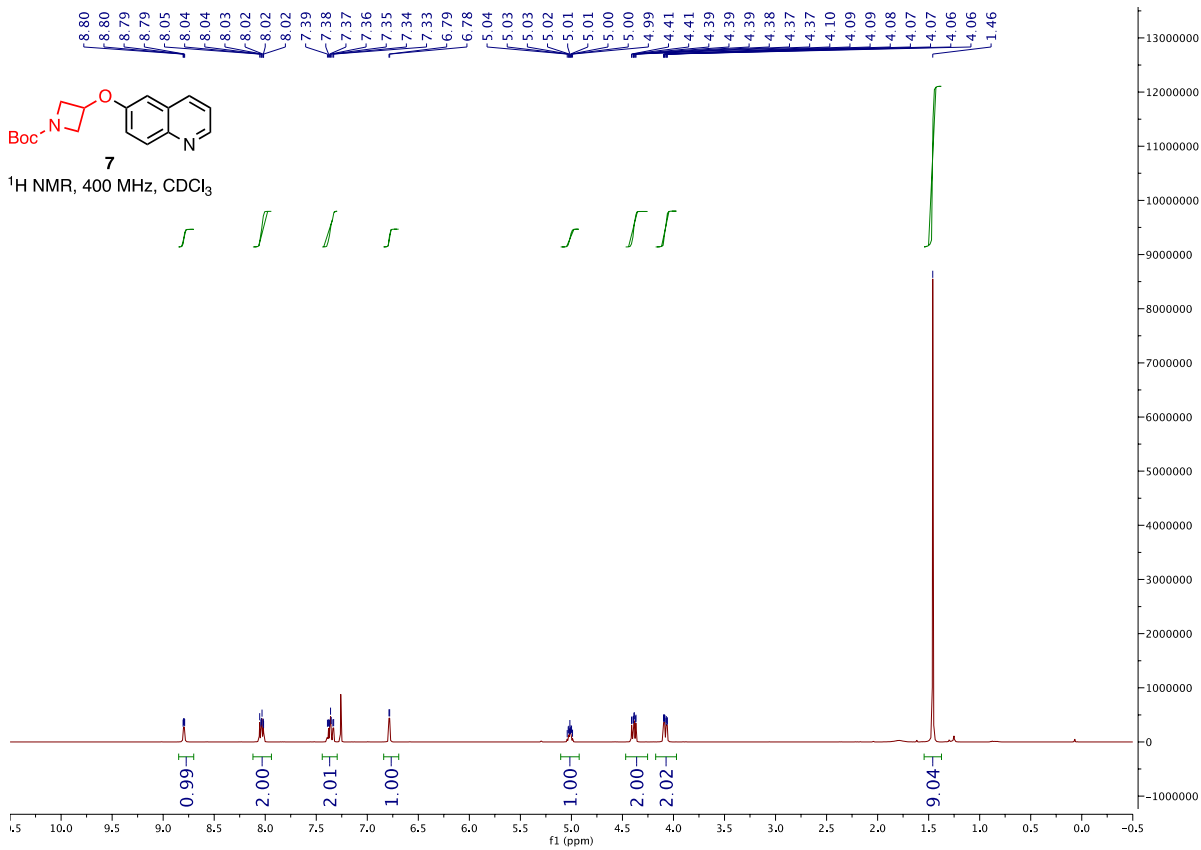
- S1. Zhang, H.; Ruiz-Castillo, P.; Buchwald, S. L. Palladium-Catalyzed C–O Cross-Coupling of Primary Alcohols. *Org. Lett.* **2018**, *20*, 1580–1583.
- S2. Lee, H. G.; Milner, P. J.; Buchwald, S. L. An Improved Catalyst System for the Pd-Catalyzed Fluorination of (Hetero)Aryl Triflates. *Org. Lett.* **2013**, *15*, 5602–5605.
- S3. Gärtner, D.; Stein, A.L.; Grupe, S.; Arp, J.; Jacobi von Wangelin, A. Iron-Catalyzed Cross-Coupling of Alkenyl Acetates. *Angew. Chem. Int. Ed.* **2015**, *54*, 10545–10549.

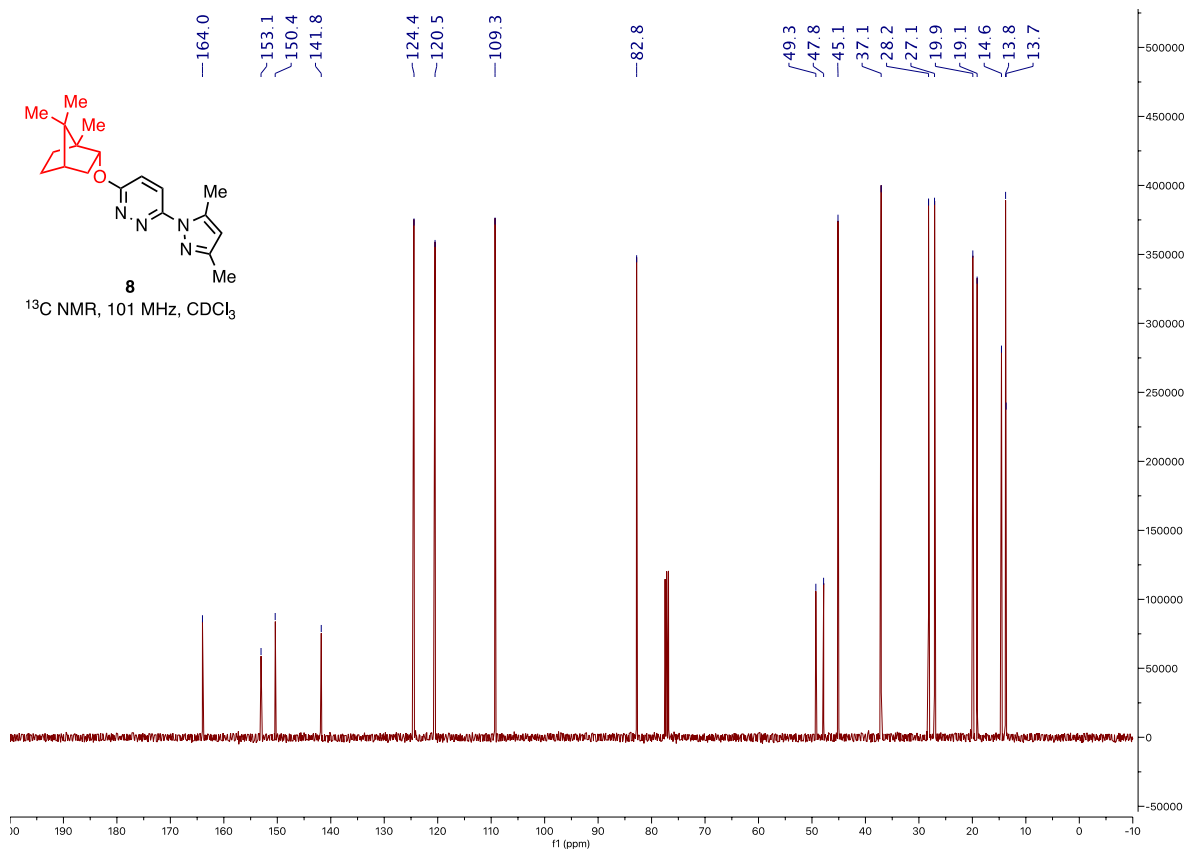
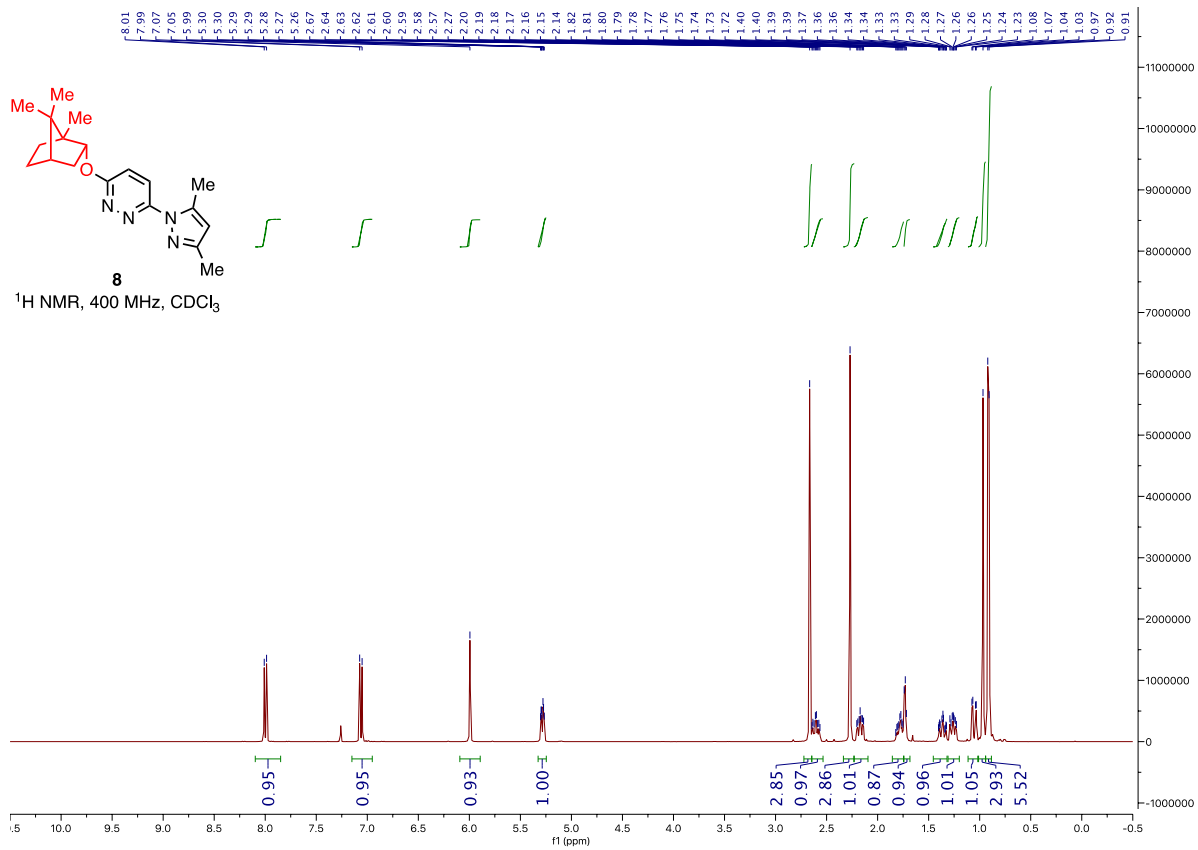
### III. Copies of NMR Spectra

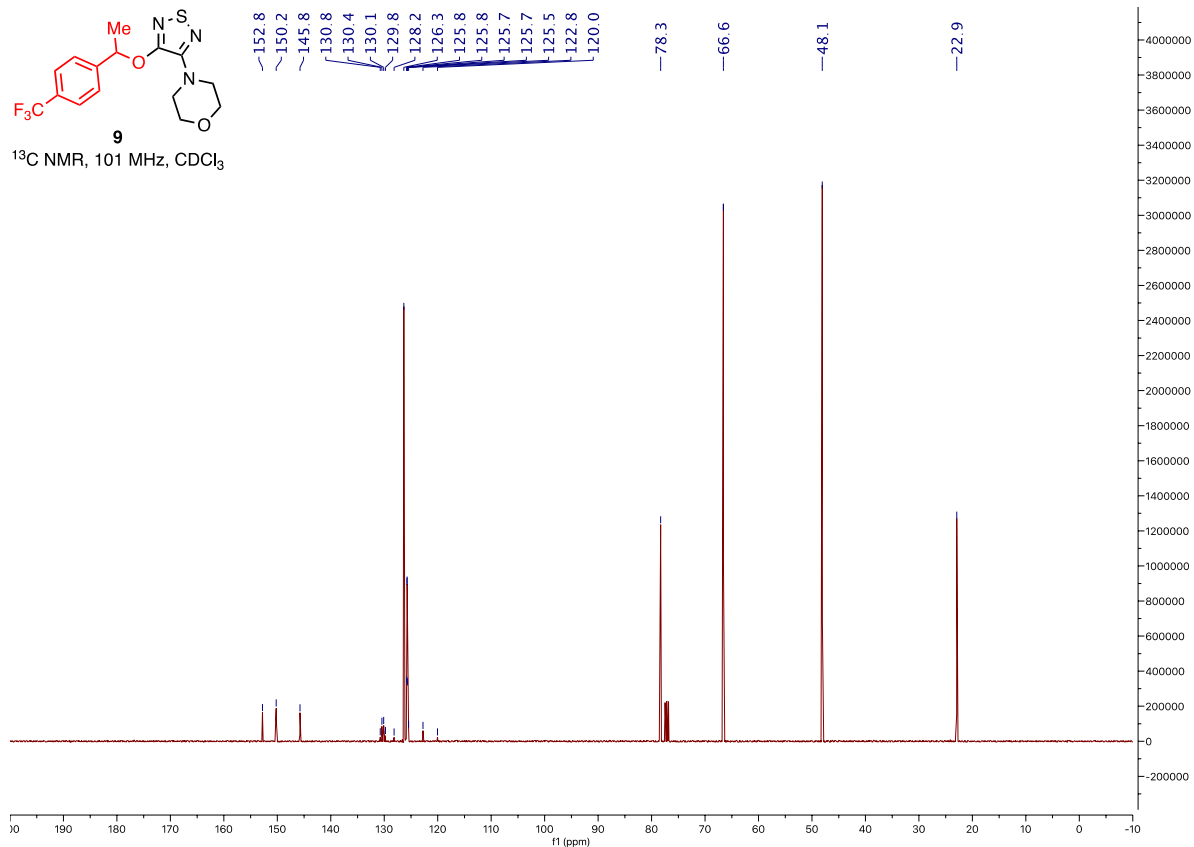
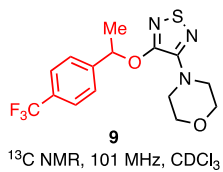
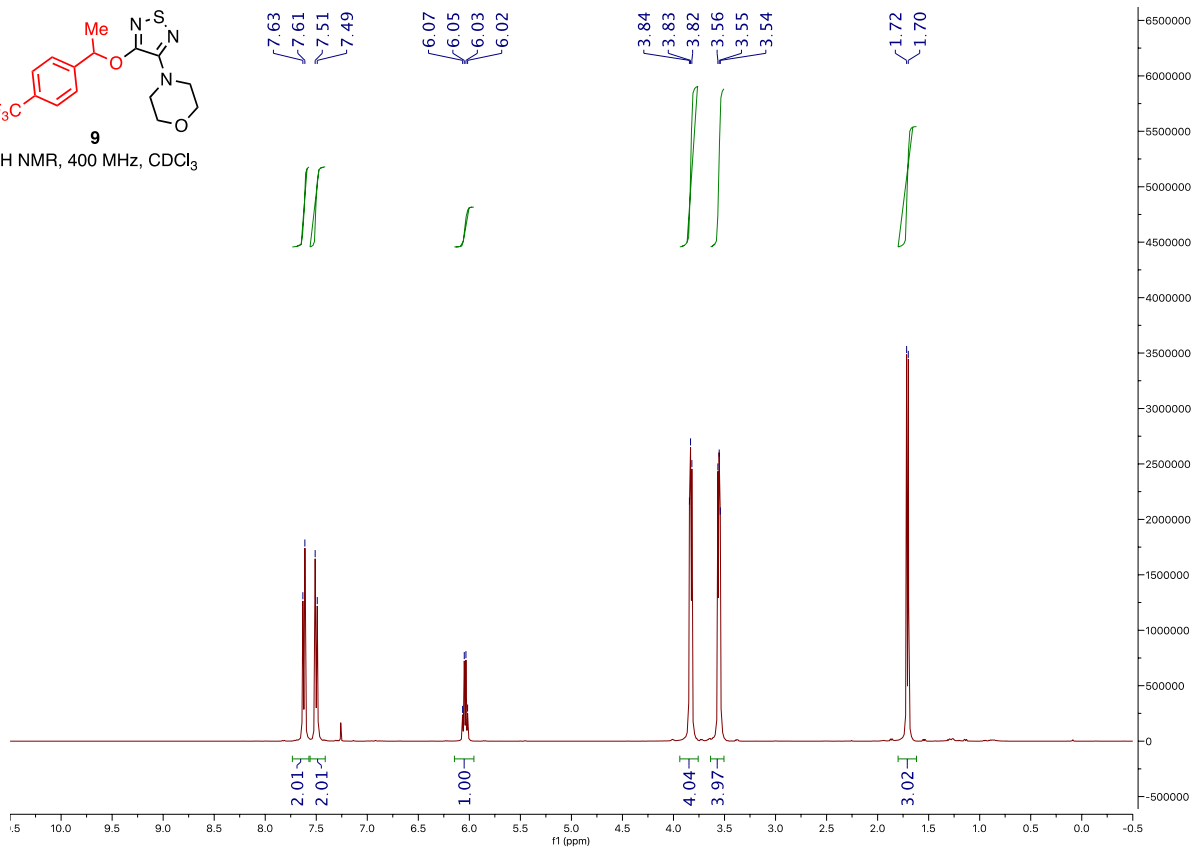
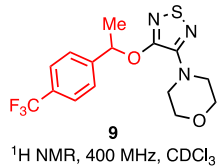


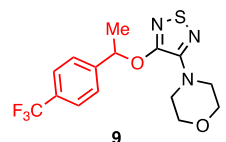




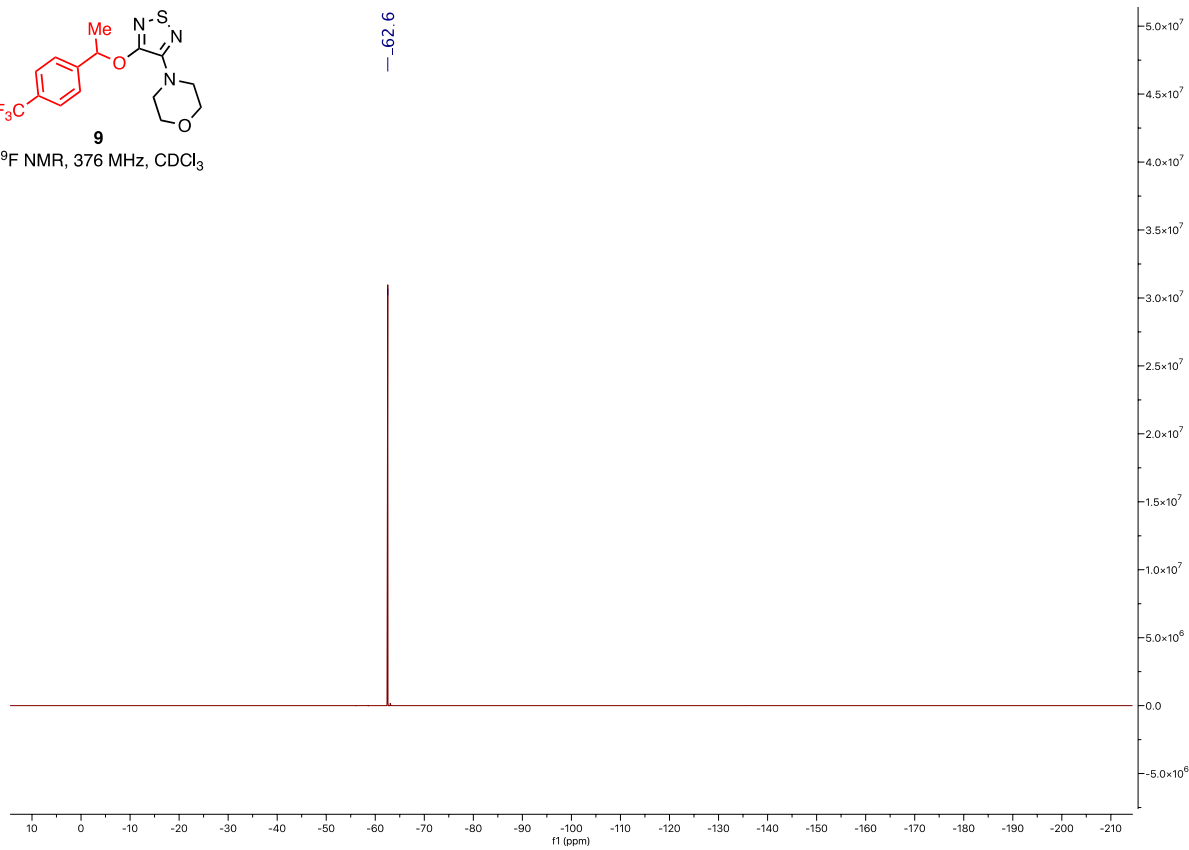






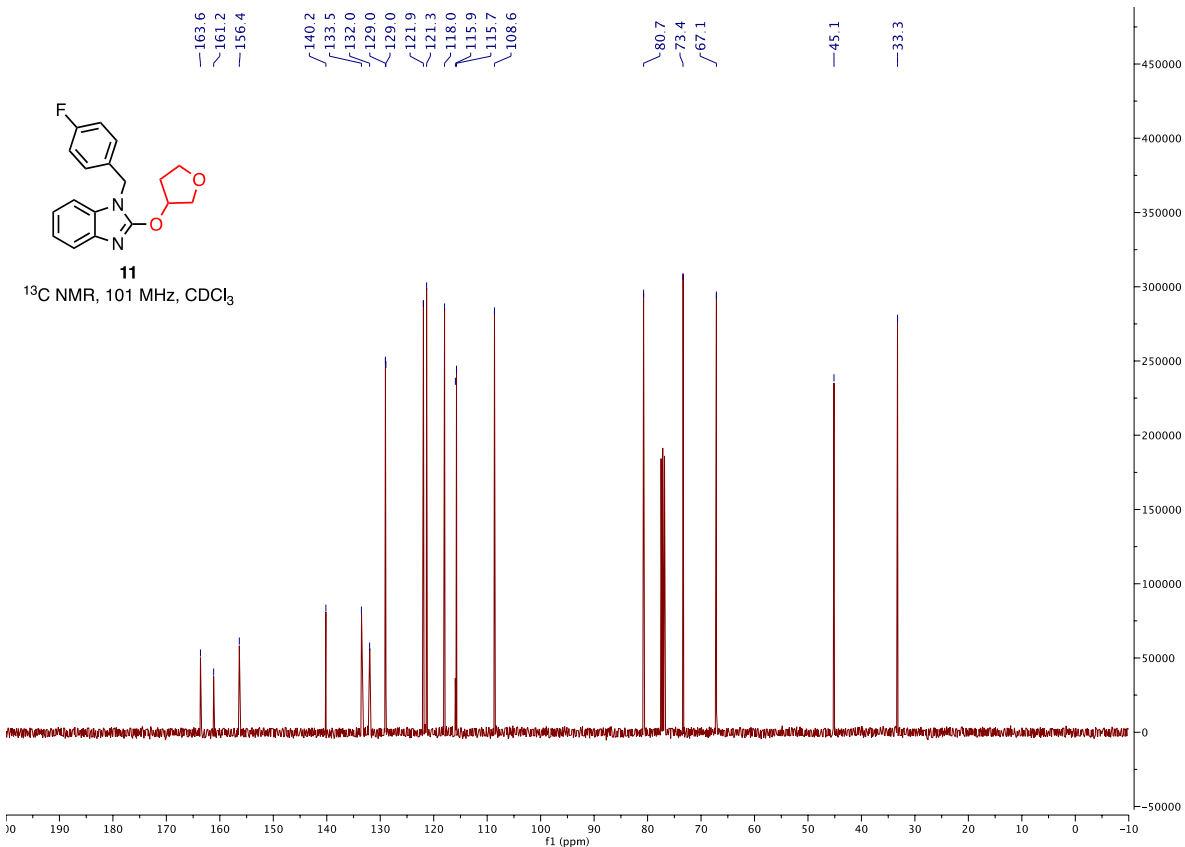
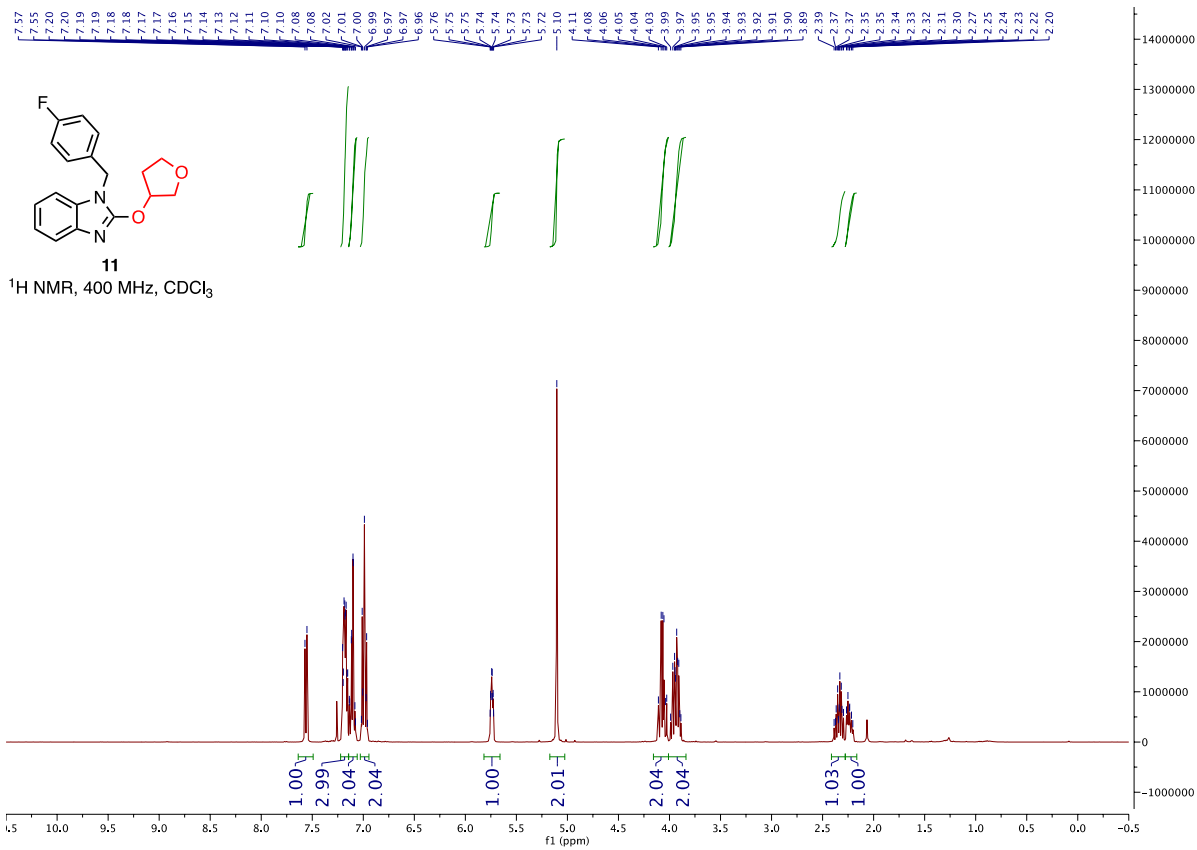


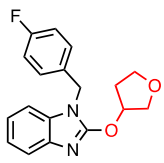
<sup>19</sup>F NMR, 376 MHz, CDCl<sub>3</sub>





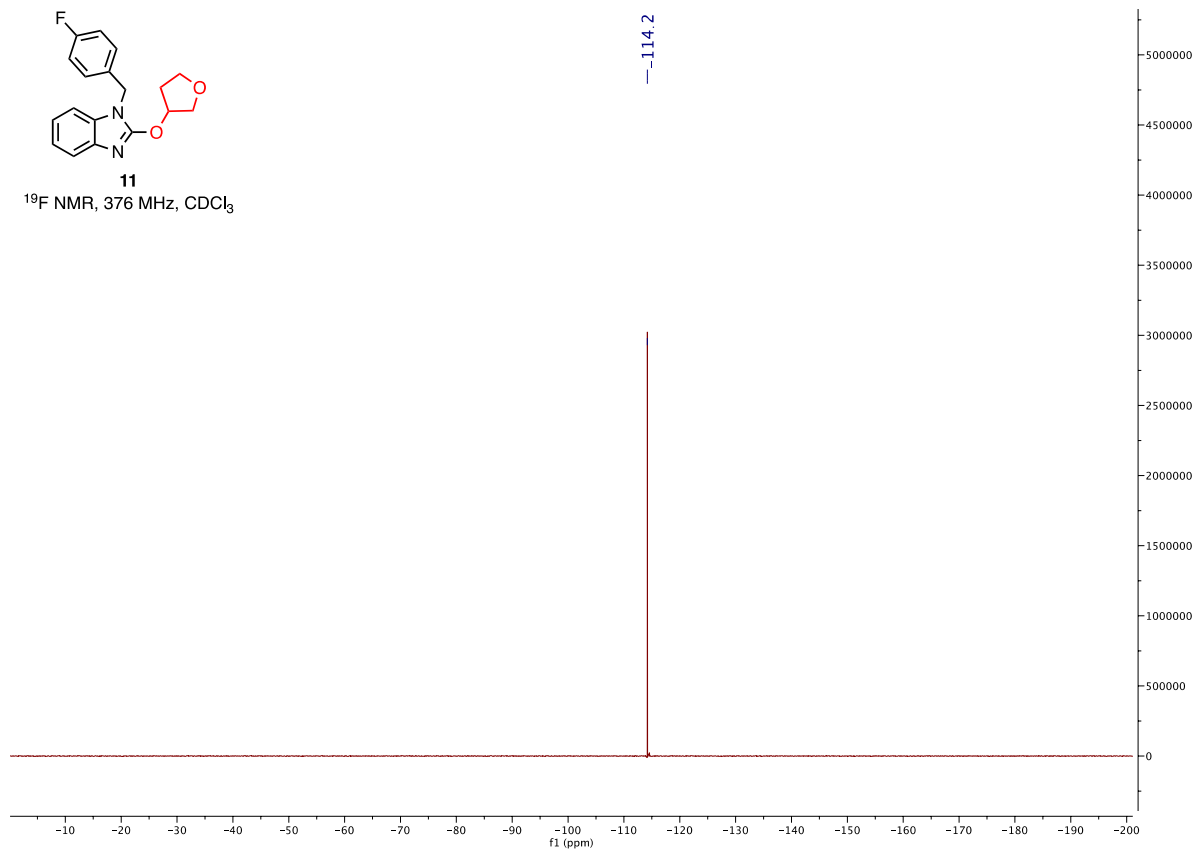


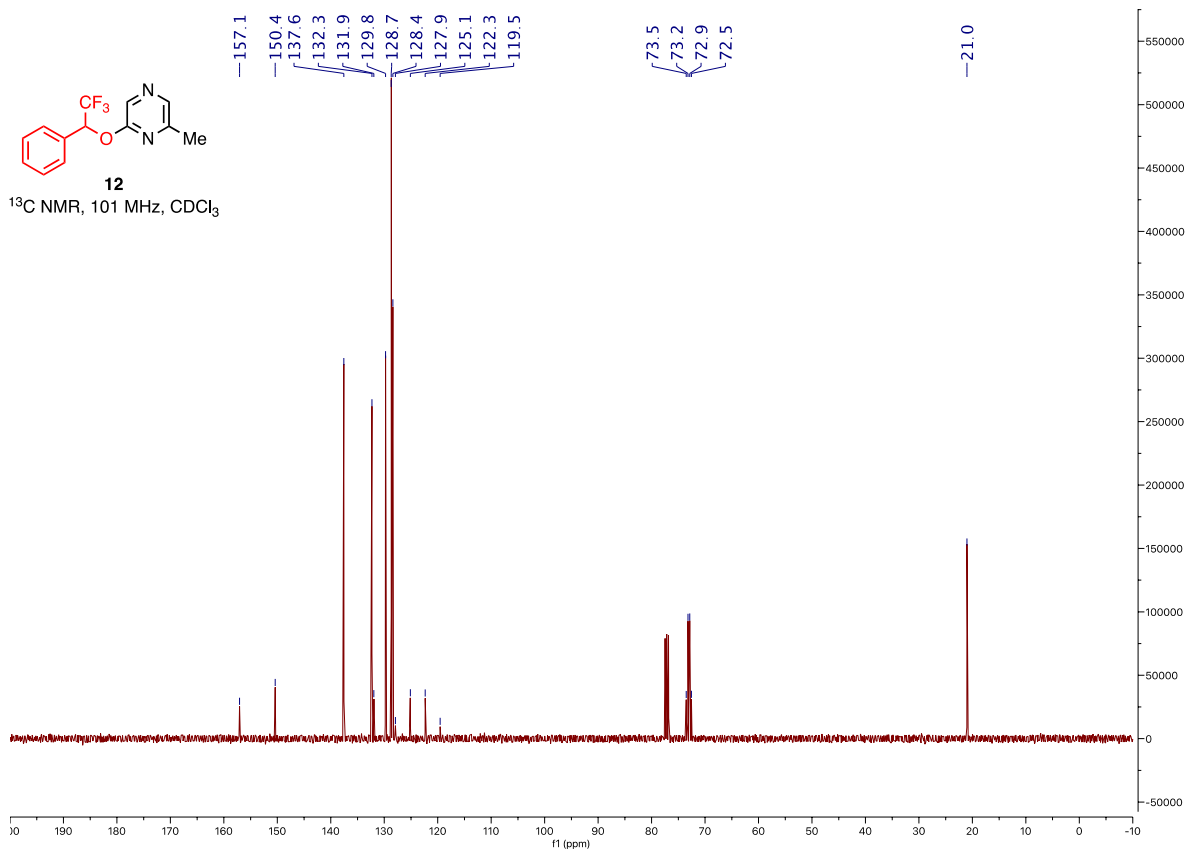
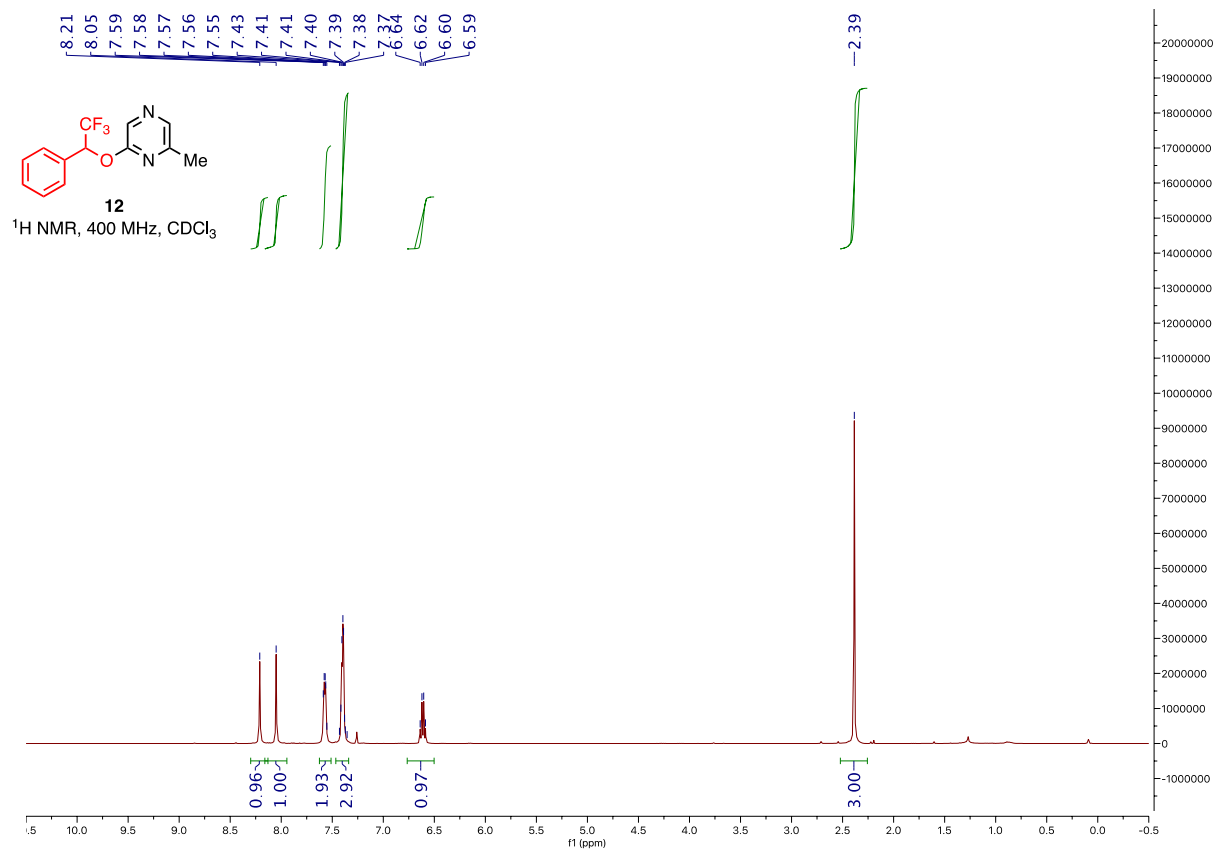


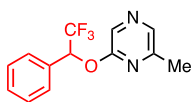


11

$^{19}\text{F}$  NMR, 376 MHz,  $\text{CDCl}_3$







**12**  
<sup>19</sup>F NMR, 376 MHz, CDCl<sub>3</sub>

