Synthesis and Application of Palladium Precatalysts that Accommodate Extremely Bulky di-*tert*-Butylphosphino Biaryl Ligands

Nicholas C. Bruno and Stephen L. Buchwald*

Department of Chemistry, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139, United States

Supporting Information

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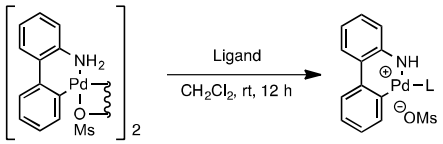
General: Reagent Information. THF and toluene were purchased from J.T. Baker in CYCLE-TAINER® solvent-delivery kegs and vigorously purged with argon for 2 h. The solvents were further purified by passing it under argon pressure through two packed columns of neutral alumina (for THF) or through neutral alumina and copper (II) oxide (for toluene). Anhydrous tribasic potassium phosphate was purchased from Acros Organics, stored in a nitrogen-filled glovebox and removed in small quantities. It was stored on the bench in a desiccator for up to two weeks. Cesium carbonate was purchased from Aldrich Chemical Co., stored in a nitrogen-filled glovebox and ground in a coffee grinder before use. Small quantities were stored on the bench in a desiccator for up to two weeks. Anhydrous *t*-butanol was purchased from Aldrich Chemical Co. in Sure-Seal™ bottles and used as received. $Pd(OAc)_2$ was purchased from Strem Chemicals Inc. or Johnson Matthey. The ligands *t*BuBrettPhos **(L1)**[1], RockPhos **(L2)**[1], AdBrettPhos **(L3)**[2], **L4**[3] and Me_4*t*BuXPhos **(L5)**[4] were prepared according to literature procedures. Palladium complexes **1** and **6** were synthesized according to a literature procedure.[5] All other reagents were purchased from Aldrich Chemical Co., Strem Chemicals, Acros Organics, Alfa Aesar, or TCI America and used as received. Flash chromatography was performed with SiliCycle *SiliaFlash® F60* silica gel.

General Analytical Information: Compounds were characterized by ^{1}H NMR, ^{13}C NMR, ^{19}F and ^{31}P NMR (where applicable). Copies of the ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra can be found at the end of the Supporting Information. ^{1}H and ^{13}C Nuclear Magnetic Resonance spectra were recorded on a Varian 500 MHz instrument. Fluorine and phosphorus Nuclear Magnetic Resonance spectra were recorded on a Varian 300 MHz instrument. All ^{1}H NMR experiments are reported in δ units, parts per million (ppm), and were measured relative to the signals for residual deuterochloroform (7.26 ppm), CD_2Cl_2 (5.32 ppm), or DMSO-d^6 (2.50 ppm) in the deuterated solvent. All ^{13}C NMR spectra are reported in ppm relative to deuterochloroform (77.23 ppm), CD_2Cl_2 (53.84 ppm) or DMSO-d^6 (39.52 ppm) and all were obtained with ^{1}H decoupling. All ^{19}F NMR spectra are reported in ppm relative to $CFCl_3$ (0.00 ppm). All ^{31}P NMR spectra are reported in ppm relative to 85% aq. phosphoric acid (0.00 ppm). All GC analyses were performed on an Agilent 6890 gas chromatograph with an FID detector using a J & W DB-1 column.

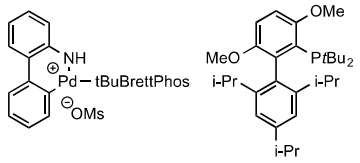
General Procedural Information



1 2

2-Aminobiphenylpalladium Methanesulfonate Precatalysts – General Procedure A

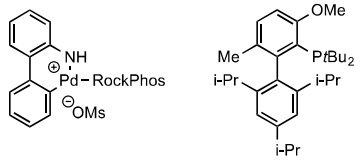
A 24 mL test tube equipped with a magnetic stir bar was charged with 2-aminobiphenylpalladium methanesulfonate dimer **1** (370 mg, 0.50 mmol, 0.50 equiv) and ligand (1.00 mmol, 1.00 equiv). Dichloromethane (5 mL) was added by syringe and the tube was sealed with a Teflon screw-top septum. The mixture was stirred overnight at ambient temperature, at which time it became dark red in appearance. The reaction progress was monitored by observing the disappearance of free-ligand and appearance of a new signal at ~45 ppm in the ^{31}P NMR spectrum. After the reaction was complete, the solvent was removed with the aid of a rotary evaporator and diethyl ether (25 mL) was added. The mixture was triturated with the aid of sonication until a dark powder results. The solid was isolated by filtration and dried under vacuum.



L1
tBuBrettPhos

OMs *t*BuBrettPhos Precatalyst (2a) – Large Scale

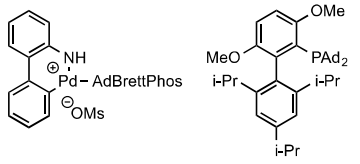
A 250 mL round-bottomed flask equipped with a magnetic stir bar was charged with **1** (4.07 g, 5.5 mmol, 0.50 equiv) and **L1** (5.33 g, 11.0 mmol, 1.00 equiv). Dichloromethane (55 mL) was added by syringe and the flask was sealed with a rubber septum. The mixture was stirred at room temperature overnight at which time it became dark red in appearance. The solvent was removed with the aid of a rotary evaporator and diethyl ether (150 mL) was added. The resulting slurry was triturated with the aid of sonication until a dark orange powder resulted. The solid was isolated by filtration and dried under vacuum to afford the title compound. Yield: 7.87 g, 90%. ^{1}H NMR (500 MHz, CD_2Cl_2) Complex Spectrum – See Attached.^{13}C NMR (126 MHz, CD_2Cl_2) δ 157.74, 147.97, 142.08, 140.84, 138.01, 128.72, 127.38, 126.84, 126.07, 124.37, 122.34, 120.45, 119.18, 111.99, 66.35, 57.13, 55.92, 55.27, 54.78, 35.18, 32.92, 32.87, 32.38, 32.34, 32.01, 31.04, 29.88, 29.86, 28.70, 26.93, 26.26, 25.12, 25.09, 24.89, 24.65, 24.32, 23.97, 23.52 ppm (Observed complexity due to C-P splitting). ^{31}P NMR (121 MHz, CD_2Cl_2) δ 77.22, 42.72 ppm. IR (neat, cm^{-1}): 1456, 1423, 1223, 1173, 1037, 761.



L2
RockPhos

OMs RockPhos Precatalyst (2b)

Following general procedure A, a mixture of **1** (370 mg, 0.50 mmol, 0.50 equiv) and **L4** (468 mg, 1.00 mmol, 1.00 equiv) was stirred at room temperature overnight. The solvent was removed with the aid of a rotary evaporator, diethyl ether (25 mL) was added. The resulting slurry was triturated with the aid of sonication until a dark brown solid resulted. The solid was isolated by filtration and dried under vacuum to afford the title compound. Yield: 762 mg, 91%. ^{1}H NMR (500 MHz, CD_2Cl_2) Complex Spectrum – See Attached. ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.4, 151.3, 146.7, 146.1, 139.8, 134.3, 134.3, 130.4, 122.6, 122.6, 122.2, 119.7, 111.4, 105.3, 104.7, 56.7, 37.6 37.3, 34.3, 32.6, 32.5, 31.2, 30.9, 29.7, 26.0, 25.8, 25.3, 24.5, 24.2, 22.6, 22.4, 14.3 ppm (observed complexity is due to C-P splitting). ^{31}P NMR (121 MHz, CD_2Cl_2) δ 79.06, 75.86, 44.44 ppm. IR (neat, cm^{-1}): 2959, 1569, 1455, 1262, 1147, 1030, 755, 637.

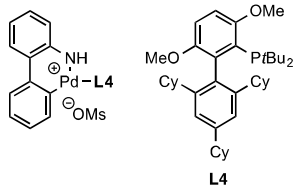


L3
AdBrettPhos

OMs AdBrettPhos Precatalyst (2c)

Following general procedure A, a mixture of **1** (370 mg, 0.50 mmol, 0.50 equiv) and **L3** (641 mg, 1.00 mmol, 1.00 equiv) was stirred at room temperature overnight. The solvent was removed with the aid of a rotary evaporator, and diethyl ether (25 mL) was added. The slurry was triturated with the aid of sonication until a deep red solid resulted. The solid was isolated by filtration and dried under vacuum to afford the title compound. Yield: 950 mg, 94%. ^{1}H NMR (500 MHz, CD_2Cl_2) Complex Spectrum – See Attached. ^{13}C

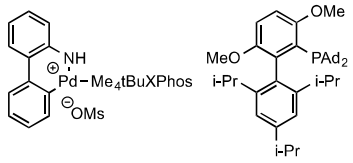
NMR (126 MHz, CD_2Cl_2) δ 155.86, 151.32, 148.10, 140.90, 126.03, 122.21, 120.42, 119.46, 119.12, 112.19, 112.05, 57.17, 55.83, 43.00, 42.75, 40.63, 40.61, 40.15, 38.22, 37.48, 36.08, 36.07, 34.82, 32.00, 31.79, 29.44, 29.36, 29.07, 28.99, 26.30, 25.82, 24.34, 23.83, 14.54 ppm (observed complexity is due to C-P). ^{31}P NMR (121 MHz, CD_2Cl_2) δ 83.25, 79.70, 41.11 ppm. IR (neat, cm^{-1}): 2907, 1456, 1283, 1149, 1030, 738, 636.



L4

OMs-L4 Precatalyst (2d)

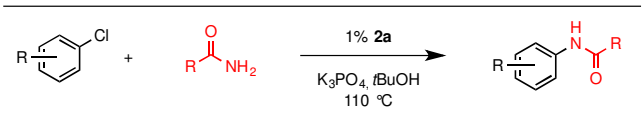
Following general procedure A, a mixture of **1** (370 mg, 0.50 mmol, 0.50 equiv) and **L4** (628 mg, 1.00 mmol, 1.00 equiv) was stirred at room temperature overnight. The solvent was removed with the aid of a rotary evaporator and diethyl ether (25 mL) was added. The resulting slurry was triturated with the aid of sonication until a deep red solid resulted. The solid was isolated by filtration and dried under vacuum to afford the title compound. Yield: 860 mg, 88%. ^{1}H NMR (500 MHz, CD_2Cl_2) Complex Spectrum – See Attached. ^{13}C NMR (126 MHz, CD_2Cl_2) δ 159.34, 159.19, 156.43, 154.78, 142.65, 141.40, 140.12, 137.85, 135.88, 128.60, 128.17, 127.61, 127.46, 127.35, 126.89, 126.02, 125.77, 125.74, 123.40, 120.82, 120.40, 119.10, 115.59, 112.62, 112.03, 100.50, 45.42, 43.45, 43.37, 41.41, 40.00, 39.91, 39.80, 39.67, 37.46, 36.53, 36.15, 35.84, 35.68, 35.43, 35.14, 35.05, 32.97, 32.92, 32.40, 32.36, 29.94, 29.92, 28.78, 27.81, 27.59, 27.44, 27.37, 27.34, 27.27, 27.06, 26.71, 26.58, 26.51, 26.28, 26.23, 26.02 ppm (Observed complexity due to C-P coupling). ^{31}P NMR (121 MHz, CD_2Cl_2) δ 76.89, 43.29 ppm. IR (neat, cm^{-1}): 2923, 1451, 1253, 1222, 1148, 1030, 738, 636.



L5
Me_4tBuXPhos

OMs Me_4*t*BuXPhos Precatalyst (2e)

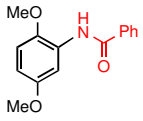
Following general procedure A, a mixture of **1** (370 mg, 0.50 mmol, 0.50 equiv) and **L5** (481 mg, 1.00 mmol, 1.00 equiv) was allowed to react at room temperature. The solvent was removed with the aid of a rotary evaporator and diethyl ether (25 mL) was added. The resulting slurry was triturated with the aid of sonication until a brown solid resulted. The solid was isolated by filtration and dried under vacuum to afford the title compound. Yield: 755 mg, 86%. ^{1}H NMR (500 MHz, CD_2Cl_2) Complex Spectrum – See Attached. ^{13}C NMR (126 MHz, CD_2Cl_2) δ 151.94, 147.64, 146.20, 145.31, 140.87, 137.94, 126.06, 123.22, 120.85, 120.44, 119.17, 112.03, 40.18, 39.07, 38.84, 34.94, 34.58, 31.57, 30.73, 30.72, 29.89, 28.19, 28.14, 26.09, 25.55, 25.25, 24.88, 24.59, 24.41, 22.88, 22.87, 21.28, 18.22, 17.13, 17.12 ppm (observed complexity is due to C-P coupling). ^{31}P NMR (121 MHz, CD_2Cl_2) δ 62.32, 47.37 ppm. IR (neat, cm^{-1}): 2962, 1456, 1262, 1151, 1029, 738, 639.



Arylation of Primary Amides, General Procedure B: A 24 mL screw-top test tube equipped with a stir bar and Teflon septum was charged with aryl chloride if solid (1.00 mmol, 1.00 equiv) amide (1.05 – 1.20 mmol, 1.05 – 1.20 equiv) **2a** (8.5 mg, 0.01 mmol, 1 mol %) and tribasic potassium phosphate (297 mg, 1.40 mmol, 1.40 equiv). The tube was evacuated and backfilled with argon. This sequence was repeated a total

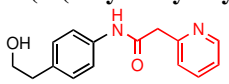
of three times, after which aryl halide was added by syringe if a liquid, followed by *t*-butanol (2 mL). Under positive pressure of argon, the Teflon septum was replaced with an unpunctured one and the reaction was placed in a preheated oil bath at 110 °C and stirred for 1.5 h. The reaction was monitored by thin layer chromatography. After completion the reaction was cooled to room temperature and diluted with ethyl acetate (5 mL) and water (5 mL). The phases were separated and the aqueous phase was extracted with ethyl acetate (3x5 mL). The combined organic phases were dried over magnesium sulfate, concentrated with the aid of a rotary evaporator and purified by flash chromatography.

_N_-(2,5-dimethoxyphenyl)benzamide (3a)[6]



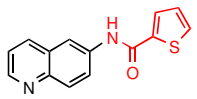
Following General Procedure B, a mixture of 2-chloro-1, 4-dimethoxybenzene (143 µL, 1.00 mmol, 1.00 equiv), benzamide (145 mg, 1.2 mmol, 1.20 equiv) K_3PO_4 (297 mg, 1.40 mmol, 1.40 equiv) **2a** (8.5 mg, 1 mol %), and *t*-butanol (2 mL) was stirred at 110 °C for 1.5 h. The crude product was purified via flash chromatography eluting with 20% EtOAc in hexanes to provide the title compound as a light-yellow solid. Yield: 249 mg, 97%. mp = 83 – 84 °C. ^{1}H NMR (500 MHz, DMSO-d^6) δ 9.37 (s, 1H), 8.01 - 7.92 (m, 2H), 7.62 - 7.55 (m, 2H), 7.52 (tt, *J* = 6.5, 1.4 Hz, 2H), 7.00 (d, *J* = 9.0 Hz, 1H), 6.73 (dd, *J* = 8.9, 3.1 Hz, 1H), 3.79 (s, 3H), 3.72 (s, 3H) ppm. ^{13}C NMR (126 MHz, DMSO-d^6) δ 166.05, 154.01, 146.29, 135.58, 132.87, 129.70, 128.79, 128.58, 113.16, 111.14, 110.60, 57.39, 56.56 ppm. IR (neat, cm^{-1}): 3325, 1652, 1535, 1485, 1445, 1420, 1224, 1046, 860, 810, 694, 674.

_N_-(4-(2-hydroxyethyl)phenyl)-2-(pyridin-2-yl)acetamide (3b)



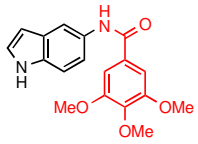
Following General Procedure B, a mixture of 4-chlorophenethyl alcohol (157 mg, 1.00 mmol, 1.00 equiv), 2-(pyridin-2-yl)acetamide (143 mg, 1.05 mmol, 1.05 equiv), K_3PO_4 (297 mg, 1.40 mmol, 1.40 equiv) **2a** (8.5 mg, 1 mol %), and *t*-butanol (2 mL) was stirred at 110 °C for 1.5 h. The crude product was purified via flash chromatography eluting with a gradient of 0 – 5 % methanol in dichloromethane to provide the title compound as an off-white solid. Yield: 228 mg, 92 %. mp = 96 – 97 °C. ^{1}H NMR (500 MHz, DMSO-d^6) δ 10.15 (s, 1H), 8.53 - 8.44 (m, 1H), 7.74 (td, *J* = 7.7, 1.9 Hz, 1H), 7.53 - 7.45 (m, 2H), 7.37 (dd, *J* = 7.8, 1.2 Hz, 1H), 3.86 - 3.76 (m, 2H), 7.30 - 7.20 (m, 1H), 7.17 - 7.06 (m, 2H), 4.60 (t, *J* = 5.2 Hz, 1H), 3.54 (td, *J* = 7.1, 5.2 Hz, 2H), 2.64 (t, *J* = 7.1 Hz, 2H) ppm. ^{13}C NMR (126 MHz, DMSO-d^6) δ 169.08, 157.28, 150.12, 138.27, 137.70, 135.49, 130.21, 125.11, 123.05, 120.17, 46.99, 39.65 ppm. IR (neat, cm^{-1}): 3258, 2924, 1695, 1606, 1538, 1439, 1171, 1064, 1003, 811, 755, 700. Anal. Calcd. for $C_{15}H_{15}N_2O_2$: C, 70.29; H, 6.29. Found: C, 69.89; H, 6.18.

_N_-(quinolin-6-yl)thiophene-2-carboxamide (3c)



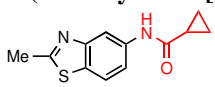
Following General Procedure B, a mixture of 6-chloroquinoline (163 mg, 1.00 mmol, 1.00 equiv), thiophene-2-carboxamide (134 mg, 1.05 mmol, 1.05 equiv), K_3PO_4 (297 mg, 1.40 mmol, 1.40 equiv) **2a** (8.5 mg, 1 mol %), and *t*-butanol (2 mL) was stirred at 110 °C for 2 h. The crude product was purified via flash chromatography eluting with 70% ethyl acetate in hexanes to provide the title compound as a yellow solid. Yield: 244 mg, 96%. mp = 185 °C. ^{1}H NMR (500 MHz, DMSO-d^6) δ 10.55 (s, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.50 - 8.42 (m, 1H), 8.31 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.10 (dd, *J* = 3.8, 1.2 Hz, 1H), 8.06 - 7.99 (m, 2H), 7.89 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.48 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.25 (dd, *J* = 5.0, 3.7 Hz, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d^6) δ 161.37, 150.43, 146.04, 140.93, 137.86, 136.74, 133.39, 130.61, 130.56, 129.36, 129.33, 125.33, 122.95, 117.52 ppm. IR (neat, cm^{-1}): 3272, 1657, 1549, 1419, 1367, 1277, 1221, 887, 826, 793, 721, 615. Anal. Calcd. for $C_{14}H_{10}N_2OS$: C, 66.12; H, 3.96. Found: C, 65.83; H, 4.12.

_N_-(1*H*-indol-5-yl)-3,4,5-trimethoxybenzamide (3d)



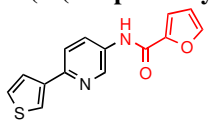
Following General Procedure B, a mixture of 5-chloroindole (152 mg, 1.00 mmol, 1.00 equiv), 3, 4, 5-trimethoxybenzamide (254 mg, 1.20 mmol, 1.20 equiv), K_3PO_4 (297 mg, 1.40 mmol, 1.40 equiv) **2a** (8.5 mg, 1 mol %), and *t*-butanol (2 mL) was stirred at 110 °C for 1.5 h. The crude product was purified via flash chromatography eluting with 80% ethyl acetate in hexanes to provide the title compound as a beige solid. Yield: 295 mg, 90%. mp = 190 – 191 °C. ^{1}H NMR (500 MHz, DMSO-d^6) δ 11.07 (s, 1H), 10.01 (s, 1H), 7.95 - 7.92 (s, 1H), 7.37 (m, 2H), 7.36 - 7.31 (m, 3H), 6.44 - 6.40 (m, 1H), 3.88 (s, 6H), 3.73 (s, 3H) ppm. ^{13}C NMR (126 MHz, DMSO-d^6) δ 165.17, 153.27, 140.60, 133.76, 131.40, 131.23, 128.11, 126.62, 117.16, 113.36, 111.72, 105.75, 101.83, 60.79, 56.72 ppm. IR (neat, cm^{-1}): 3281, 1623, 1583, 1505, 1414, 1330, 1231, 1123, 1003, 763, 726. Anal. Calcd. for $C_{18}H_{18}N_2O_4$: C, 66.25; H, 5.56. Found: C, 65.99; H, 5.74.

***N*-(2-methylbenzo[*d*]thiazol-5-yl)cyclopropanecarboxamide (3e)**

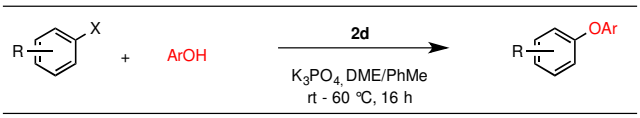


Following General Procedure B, a mixture of 5-chloro-2-methylbenzothiazole (183 mg, 1.00 mmol, 1.00 equiv), cyclopropylamide (90 mg, 1.05 mmol, 1.05 equiv), K_3PO_4 (297 mg, 1.40 mmol, 1.40 equiv) **2a** (8.5 mg, 1 mol %), and *t*-butanol (2 mL) was stirred at 110 °C for 1.5 h. The crude product was purified via flash chromatography eluting with ethyl acetate to provide the title compound as a light-yellow, crystalline solid. Yield: 214 mg, 92%. mp = 183 – 184 °C. ^{1}H NMR (500 MHz, DMSO-d^6) δ 10.38 (s, 1H), 8.27 (d, *J* = 2.0 Hz, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.53 (dd, *J* = 8.7, 2.1 Hz, 1H), 2.75 (s, 3H), 1.80 (tt, *J* = 7.7, 4.7 Hz, 1H), 0.90 - 0.76 (m, 4H) ppm. ^{13}C NMR (126 MHz, DMSO-d^6) δ 172.71, 168.73, 154.43, 138.80, 130.09, 122.67, 117.87, 112.72, 20.74, 15.62, 8.21 ppm. IR (neat, cm^{-1}): 3284, 1658, 1576, 1516, 1464, 1400, 1324, 1224, 1179, 908, 799, 656, 649. Anal. Calcd. for $C_{12}H_{12}N_2OS$: C, 62.04; H, 5.21. Found: C, 61.89; H, 4.99.

***N*-(6-(thiophen-3-yl)pyridin-3-yl)furan-2-carboxamide (3f)**

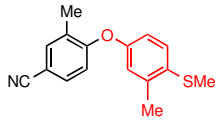


Following general procedure B, a mixture of 5-chloro-2-(thiophen-3-yl)pyridine (195 mg, 1.00 mmol, 1.00 equiv), 2-furamide (117 mg, 1.05 mmol, 1.05 equiv), K_3PO_4 (297 mg, 1.40 mmol, 1.40 equiv) **2a** (8.5 mg, 1 mol %), and *t*-butanol (2 mL) was stirred at 110 °C for 1.5 h. The crude reaction mixture was loaded directly onto silica and the product was purified via flash chromatography, eluting with 80% ethyl acetate in hexanes, to provide the title compound as a yellow solid. Yield: 217 mg, 81%. mp = 161 – 163 °C. ^{1}H NMR (500 MHz, DMSO-d^6) δ 10.50 (s, 1H), 8.94 (d, *J* = 2.5 Hz, 1H), 8.22 (dd, *J* = 8.6, 2.6 Hz, 1H), 8.09 (dd, *J* = 3.0, 1.3 Hz, 1H), 8.03 - 7.92 (m, 1H), 7.86 (d, *J* = 8.6 Hz, 1H), 7.81 - 7.69 (m, 1H), 7.67 - 7.58 (m, 1H), 7.43 - 7.33 (m, 1H), 6.77 - 6.68 (m, 1H) ppm. ^{13}C NMR (126 MHz, DMSO-d^6) - 157.56, 149.29, 148.31, 147.18, 142.76, 142.67, 134.96, 129.27, 128.12, 127.31, 124.20, 121.14, 116.47, 113.49 ppm. IR (neat, cm^{-1}): 3281, 1656, 1585, 1473, 1390, 1301, 1162, 798, 746, 607.



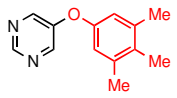
Arylation of Phenols – General Procedure C: A screw-top test tube equipped with a magnetic stir bar and fitted with a Teflon septum was charged with aryl halide (1.00 mmol, 1.00 equiv), phenol (1.50 mmol, 1.50 equiv), K_3PO_4 (318 mg, 1.50 mmol, 1.50 equiv) and **2d** (1 – 2 mol %). The tube was sealed and evacuated and backfilled with argon. This sequence was repeated a total of three times, after which toluene (0.6 mL) and 1, 2-dimethoxyethane (0.4 mL) were added by syringe. The reaction mixture was stirred at room temperature or 60° for 16 – 24 h. After completion the reaction mixture was cooled to room temperature, diluted with diethyl ether (5 mL) and eluted through a plug of silica with additional diethyl ether. The crude reaction mixture was concentrated with the aid of a rotary evaporator and purified by flash chromatography.

3-methyl-4-(3-methyl-4-(methylthio)phenoxy)benzonitrile (4a)

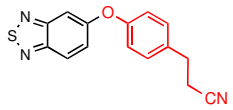


Following general procedure C, a mixture of 4-bromo-3-methylbenzonitrile (196 mg, 1.00 mmol, 1.00 equiv), 3-methyl-4-(methylthio)phenol (231 mg, 1.50 mmol, 1.50 equiv), K_3PO_4 (318 mg, 1.50 mmol, 1.50 equiv), **2d** (20 mg, 0.02 mmol, 2 mol %), toluene (0.6 mL) and 1, 2-dimethoxyethane (0.4 mL) was stirred at room temperature for 16 h. The crude reaction mixture was purified by flash chromatography, eluting with 0 – 5% diethyl ether in hexanes to provide the title compound as a yellow solid. Yield: 239 mg, 89%. mp = 54 – 56 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 2.1, 0.9 Hz, 1H), 7.42 - 7.38 (m, 1H), 7.21 - 7.18 (m, 1H), 6.87 - 6.83 (m, 2H), 6.76 (d, *J* = 8.5 Hz, 1H), 2.47 (s, 3H), 2.34 (m, *J* = 2.7 Hz, 6H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.01, 153.07, 138.70, 135.17, 133.72, 131.75, 129.93, 127.33, 121.56, 119.29, 118.03, 116.88, 106.01, 20.43, 16.35, 16.22 ppm. IR (neat, cm^{-1}): 2224, 1603, 1493, 1471, 1268, 1248, 1153, 1125, 1059, 955, 873, 819, 789, 689.

5-(3,4,5-trimethylphenoxy)pyrimidine (4b)

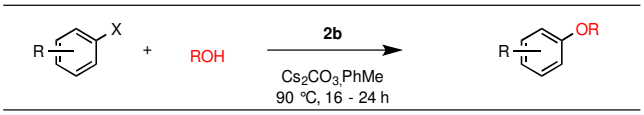


Following general procedure C, a mixture of 5-bromopyrimidine (159 mg, 1.00 mmol, 1.00 equiv), 3, 4, 5-trimethylphenol (204 mg, 1.50 mmol, 1.50 eq,) K_3PO_4 (318 mg, 1.50 mmol, 1.50 equiv), **2d** (15 mg, 0.015 mmol, 1.5 mol %), toluene (0.6 mL) and 1, 2-dimethoxyethane (0.4 mL) was stirred at 60 °C for 16 h. The crude reaction mixture was purified by flash chromatography, eluting with 10 – 25 % ethyl acetate in hexanes to provide the title compound as a yellow, crystalline solid. mp = 89 – 91 °C. Yield: 195 mg, 91%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 2.1, 0.9 Hz, 1H), 7.40 (ddd, *J* = 8.5, 2.2, 0.7 Hz, 1H), 7.21 - 7.17 (m, 1H), 6.87 - 6.83 (m, 2H), 6.76 (d, *J* = 8.5 Hz, 1H), 2.47 (s, 3H), 2.36 - 2.33 (m, 6H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.57, 153.34, 152.83, 147.19, 139.39, 132.72, 118.91, 21.47, 15.63 ppm. IR (neat, cm^{-1}): 1566, 1534, 1450, 1024, 787, 751, 620. Anal. Calcd. for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59. Found: C, 73.08; H, 6.74.



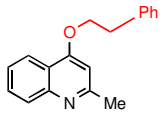
3-(4-(benzo[*c*][1,2,5]thiadiazol-5-yloxy)phenyl)propanenitrile (4c)

Following general procedure C, a mixture of 5-chloro-2, 1, 3-benzothiadiazole (170 mg, 1.00 mmol, 1.00 equiv), 3-(4-hydroxyphenyl)propionitrile (221 mg, 1.50 mmol, 1.50 equiv), **2d** (20 mg, 0.02 mmol, 2 mol %), toluene (0.6 mL) and 1, 2-dimethoxyethane (0.4 mL) were stirred at 60° for 24 h. The crude reaction mixture was purified by flash chromatography, eluting with 0 – 30 % ethyl acetate in hexanes to provide the title compound as a yellow solid. Yield: 281 mg, 78%. mp = 76 – 77 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 9.4, 0.7 Hz, 1H), 7.46 (ddd, *J* = 9.5, 2.4, 0.9 Hz, 1H), 7.31 (d, *J* = 6.6 Hz, 1H), 7.22 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.13 - 7.10 (m, 2H), 3.00 (t, *J* = 7.3 Hz, 2H), 2.67 (t, *J* = 7.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.41, 156.24, 155.08, 152.41, 135.45, 130.82, 125.55, 122.84, 121.48, 119.70, 105.25, 31.65, 20.23 ppm. IR (neat, cm^{-1}): 2232, 1606, 1508, 1483, 1423, 1270, 1219, 1175, 849, 816, 756.



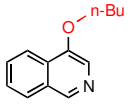
Arylation of Alkyl Alcohols – General Procedure D: A screw-top test tube equipped with a magnetic stir bar and fitted with a Teflon septum was charged with aryl halide (1.00 mmol, 1.00 equiv), alcohol (if a solid) (1.50 mmol, 1.50 equiv), Cs_2CO_3 (652 mg, 2.00 mmol, 2.00 equiv) and **2b** (1 – 2 mol %). The tube was sealed and evacuated and backfilled with argon. This sequence was repeated a total of three times, after which the aryl halide and alcohol, if liquids, were added by syringe, followed by toluene (1 mL) by syringe. The reaction mixture was stirred at 90 °C for 16 – 24 h. After completion the reaction mixture was cooled to room temperature, diluted with ethyl acetate (5 mL) and filtered. The crude reaction mixture was concentrated with the aid of rotary evaporation and purified by flash chromatography.

2-Methyl-4-phenethoxyquinoline (5a)[7]



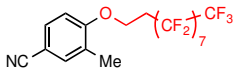
Following general prodecure D, a mixture of 4-chloro-2-methylquinoline (164 mg, 1.00 mmol, 1.00 equiv), phenethyl alcohol (180 µL, 1.50 mmol, 1.50 equiv), Cs_2CO_3 (652 mg, 2.00 mmol, 2.00 equiv), **2b** (9 mg, 0.01 mmol, 1 mol %) and toluene (1 mL) was heated with stirring at 90 °C for 16 h. The crude product mixture was purified by flash chromatography, eluting with 40% ethyl acetate in hexanes to provide the title compound as a light yellow solid. Yield: 240 mg, 91%. mp = 83 – 85 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.98 - 7.93 (m, 1H), 7.65 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.44 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.36 (s, 1H), 7.30 - 7.25 (m, 1H), 6.58 (s, 1H), 4.35 (t, *J* = 6.9 Hz, 2H), 3.24 (t, *J* = 6.9 Hz, 2H), 2.67 (s, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.11, 160.75, 138.51, 130.47, 129.75, 129.35, 128.77, 127.46, 125.48, 122.41, 120.54, 101.85, 69.65, 36.25, 26.67 ppm. IR (neat, cm^{-1}): 1598, 1567, 1510, 1423, 1345, 1251, 1184, 1114, 1023, 751, 701, 653.

4-Butoxyisoquinoline (5b)[8]



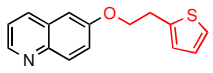
Following general prodecure D, a mixture of 4-bromoisoquinoline (207 mg, 1.00 mmol, 1.00 equiv), *n*-butanol (312 µL, 3.00 mmol, 3.00 equiv), Cs_2CO_3 (652 mg, 2.00 mmol, 2.00 equiv), **2b** (9 mg, 0.01 mmol, 1 mol %) and toluene (1 mL) was heated with stirring at 90 °C for 16 h. The crude product mixture was purified by flash chromatography, eluting with 50% ethyl acetate in hexanes to provide the title compound as a yellow oil. Yield: 178 mg, 89%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.23 (dt, *J* = 8.4, 1.4 Hz, 1H), 8.07 (d, *J* = 1.4 Hz, 1H), 7.96 - 7.88 (m, 1H), 7.68 (dddt, *J* = 8.2, 6.7, 2.4, 1.2 Hz, 1H), 7.61 (dddd, *J* = 9.4, 6.8, 2.9, 1.6 Hz, 1H), 4.22 (dtd, *J* = 6.3, 4.0, 2.0 Hz, 2H), 1.92 (tdd, *J* = 9.1, 6.5, 4.6 Hz, 2H), 1.68 - 1.54 (m, 2H), 1.04 (td, *J* = 7.4, 1.9 Hz, 3H) ppm.^{13}C NMR (126 MHz, $CDCl_3$) δ 150.73, 145.58, 130.13, 129.81, 129.01, 128.24, 127.54, 124.32, 121.89, 69.03, 32.05, 20.09, 14.61 ppm. IR (neat, cm^{-1}): 2957, 1578, 1502, 1458, 1399, 1279, 1156, 1121, 1091, 851, 779, 751, 619.

4-(1H, 1H, 2H, 2H-perfluorodecyloxy)-3-methylbenzonitrile (5c)



Following general prodecure E, a mixture of 4-bromo-3-methylbenzonitrile (207 mg, 1.00 mmol, 1.00 equiv), 1H, 1H, 2H, 2H-perfluorodecanol (487 mg, 1.05 mmol, 1.05 equiv), Cs_2CO_3 (652 mg, 2.00 mmol, 2.00 equiv), **2b** (9 mg, 0.01 mmol, 1 mol %) and toluene (1 mL) were heated with stirring at 90 °C for 16 h. The crude product mixture was purified by column chromatography, eluting with a gradient of 0 - 10% ethyl acetate in hexanes to provide the title compound as an light yellow solid. Yield: 469 mg, 81%. mp = 34 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.43 (dd, *J* = 2.1, 1.0 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 1H), 4.33 (t, *J* = 6.4 Hz, 2H), 2.68 (tt, *J* = 18.1, 6.4 Hz, 2H), 2.24 - 2.18 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.18, 136.17, 134.89, 132.59, 119.89, 118.85, 111.33, 60.98, 31.83 (t, *J* = 21.8 Hz), 16.56 ppm. ^{19}F NMR (282 MHz, $CDCl_3$) δ -81.23 (t, *J* = 9.9 Hz), -113.66 (p, *J* = 16.7 Hz), -121.03 - -122.83 (m), -122.83 – -123.53 (m), -123.89 (t, *J* = 13.9 Hz), -126.56 (t, *J* = 13.7 Hz). IR (neat, cm^{-1}): 2224, 1500, 1247, 1198, 1131, 808, 654.

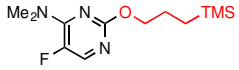
6-(2-(thiophen-2-yl)ethoxy)quinolone (5d)



Following general prodecure E, a mixture of 6-chloroquinoline (167 mg, 1.00 mmol, 1.00 equiv), 2-thiopheneethanol (167 µL, 1.50 mmol, 1.50 equiv), Cs_2CO_3 (652 mg, 2.00 mmol, 2.00 equiv), **2b** (18 mg, 0.02 mmol, 2 mol %) and toluene (1 mL) were heated with stirring at 90 °C for 16 h. The crude product mixture was purified by flash chromatography, eluting with a gradient of 0 - 20% ethyl acetate in hexanes to provide the title compound as an off-white solid. Yield: 245 mg, 96%. mp = 52 – 54 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.01 (dd, *J* = 8.8, 2.5 Hz, 2H), 7.40 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.33 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.19 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.06 (d, *J* = 2.8 Hz, 1H), 7.02 - 6.90 (m, 2H), 4.30 (t, *J* = 6.7 Hz, 2H), 3.45 - 3.31 (m, 2H) ppm. mp = 61 – 62 °C. ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.44, 148.73, 145.15, 140.83, 135.51, 131.63,

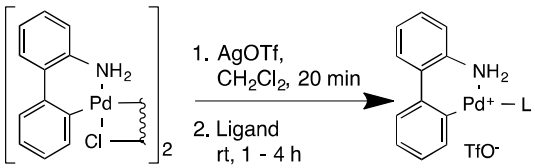
129.96, 127.60, 126.36, 124.81, 123.19, 122.09, 106.79, 69.36, 30.63 ppm. IR (neat, cm^{-1}): 1622, 1500, 1380, 1227, 1171, 1111, 1034, 927, 847, 828, 782, 768, 740, 701, 620.

5-fluoro-*N*,*N*-dimethyl-2-(3-(trimethylsilyl)propoxy)pyrimidin-4-amine (5e)



Following general prodecure D, a mixture of 2-chloro-5-fluoro-*N*,*N*-dimethylpyrimidin-4-amine (176 mg, 1.00 mmol, 1.00 equiv), 3-(trimethylsilyl)propan-1-ol (198 mg, 1.50 mmol, 1.50 equiv), Cs_2CO_3 (652 mg, 2.00 mmol, 2.00 equiv), **2b** (18 mg, 0.02 mmol, 2 mol %) and toluene (1 mL) were heated with stirring at 90 °C for 16 h. The crude product mixture was purified by column chromatography, eluting with 50% ethyl acetate in hexanes to provide the title compound as a yellow oil. Yield: 209 mg, 77%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 6.3 Hz, 1H), 4.16 (t, *J* = 7.1 Hz, 2H), 3.17 (d, *J* = 2.3 Hz, 6H), 1.80 - 1.68 (m, 2H), 0.61 - 0.50 (m, 2H), -0.07 (s, 9H) ppm. ^{13}C NMR (126 MHz, Chloroform-d) δ 160.92 , 153.98 (d, *J* = 6.6 Hz), 144.92, 143.26 (d, *J* = 26.9 Hz), 70.84 , 39.55 (d, *J* = 7.2 Hz), 24.18 , 13.13 , -1.07 ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.92 , 153.98 (d, *J* = 6.6 Hz), 144.92 , 143.26 (d, *J* = 26.9 Hz), 70.84 , 39.55 (d, *J* = 7.2 Hz), 24.18 , 13.13 , -1.07 . ^{19}F NMR (282 MHz, $CDCl_3$) δ -159.33 ppm. IR (neat, cm^{-1}): 2952, 1605, 1419, 1340, 1246, 1224, 1051, 855, 830, 769, 750. Anal. Calcd. for $C_{12}H_{22}FN_3OSi$: C, 53.10; H, 8.17. Found: C, 53.39; H, 8.02.

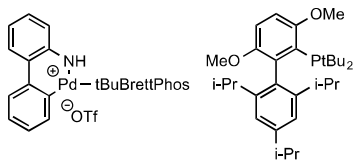
Triflate Palladacycle Precatalysts: Initially we were unable to prepare palladium methanesulfonate precatalysts of **L1 – L5**, so we prepared the triflate analogues. Upon synthesizing **2a** – **2e**, however, we compared the reactivities of **7a** and **2a** and found no significant differences.



6 **7**

2-Aminobiphenylpalladium Triflate Precatalysts – General Procedure

A 24 mL test tube equipped with a magnetic stir bar was charged with 2-aminobiphenylpalladium chloride dimer **6** (310 mg, 0.50 mmol, 0.50 equiv) and AgOTf (257 mg, 1.00 mmol, 1.00 equiv). Dichloromethane (10 mL) was added by syringe, the tube was sealed with a Teflon screw-top septum and wrapped in aluminum foil. The mixture was stirred at ambient temperature for 20 minutes, at which time a grey slurry formed. The slurry was filtered through a pad of celite into a 50 mL round-bottomed flask containing a magnetic stir bar and ligand (1.00 mmol, 1.00 eq). The pad of celite was further washed with additional dichloromethane (10 mL). The reaction mixture was stirred at room temperature for 1 – 4 h and the reaction progress was monitored by observing the disappearance of free-ligand and appearance of a new signal at ~45 ppm in the ^{31}P NMR spectrum. After completion, the solvent was removed with the aid of a rotary evaporator and pentane (25 mL) was added. The mixture was triturated with the aid of sonication until a dark powder resulted. The solid was isolated by filtration and dried under vacuum.



L1
tBuBrettPhos

OTf *t*BuBrettPhos Precatalyst (7a)

A 250 mL round-bottomed flask equipped with a stir bar and wrapped in aluminum foil was charged with μ-Cl dimer (3.41 g, 5.5 mmol, 0.50 equiv) and AgOTf (2.82 g, 11.0 mmol, 1.00 equiv). Dichloromethane

(100 mL) was added and the mixture was stirred at room temperature for 30 min. The mixture was then eluted through a plug of celite into a 500 mL round bottom flask equipped with a stir bar and tBuBrettPhos (5.33 g, 11.0 mmol, 1.00 equiv). The pad of celite was washed with additional dichloromethane (50 mL). The mixture was stirred at room temperature overnight and became dark red in appearance. At this time, the solvent was removed with the aid of a rotary evaporator and pentane (150 mL) was added. The mixture was sonicated and triturated until a dark orange powder resulted. The solid was filtered and dried under vacuum to afford the title compound. Yield: 9.59 g, 96%. ^{1}H NMR (500 MHz, $CDCl_3$) Complex Spectrum – See Attached ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.81, 159.52, 157.16, 155.20, 154.23, 154.04, 153.94, 151.68, 151.56, 150.85, 147.38, 141.30, 140.90, 139.41, 137.43, 136.21, 136.17, 135.27, 135.25, 135.15, 135.01, 128.24, 127.54, 126.83, 125.94, 125.76, 124.02, 123.89, 122.35, 121.76, 121.62, 120.28, 119.80, 117.64, 117.61, 117.25, 106.28, 105.70, 56.61, 55.37, 55.30, 54.94, 54.89, 54.49, 54.38, 39.80, 39.67, 39.49, 39.37, 37.24, 36.98, 34.58, 34.51, 34.30, 32.57, 32.52, 32.00, 31.49, 30.56, 29.51, 29.46, 26.50, 26.04, 26.02, 25.16, 24.94, 24.86, 24.61, 24.55, 24.11, 23.22, 22.53 ppm (observed complexity due to C-P and C-F splitting). ^{31}P NMR (121 MHz, $CDCl_3$) δ 78.53, 44.12 ppm. ^{19}F NMR (282 MHz, $CDCl_3$) δ -78.03 ppm. IR (neat, cm^{-1}): 2957, 1578, 1456, 1422, 1252, 1149, 1031, 755, 636.

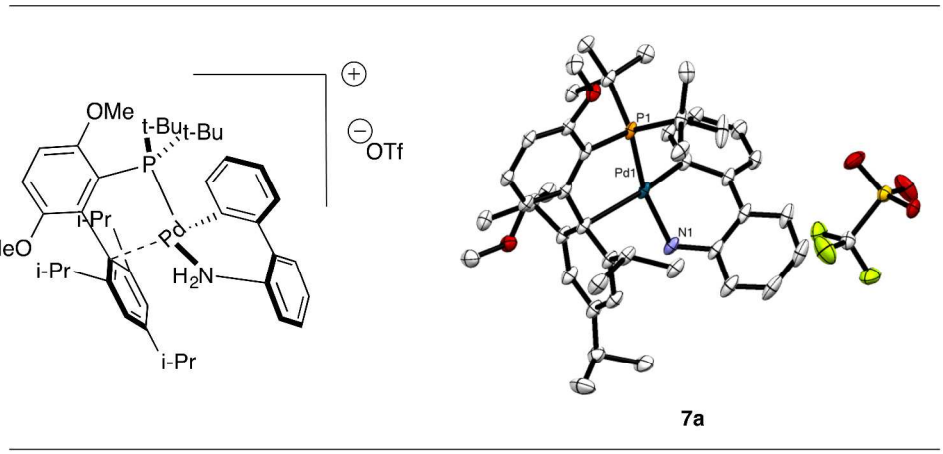
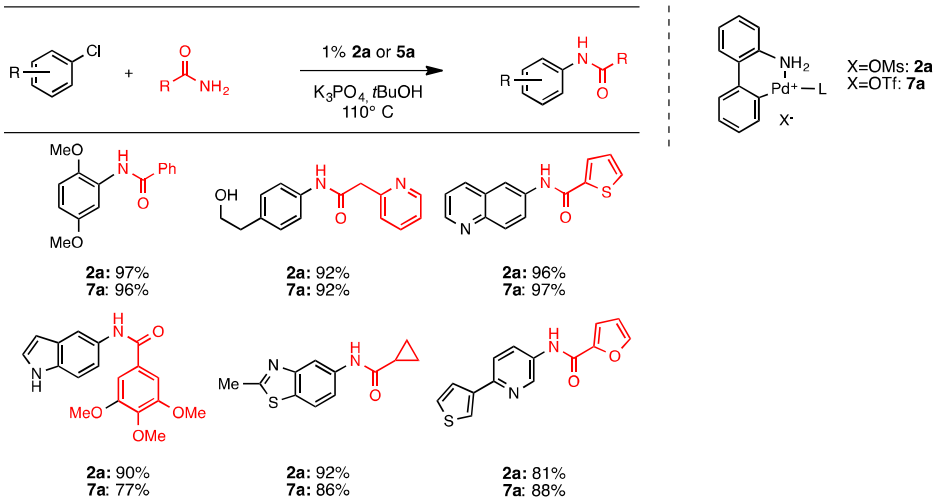


Figure 1. Crystallographically-determined X-ray structure of **7a** (thermal ellipsoid plot at 50% probability, hydrogen atoms are omitted for clarity).

Table 1: Arylation of Primary Amides with **2a** and **7a** comparing the reactivities of each.[a]



[a] ArCl (1 mmol), amide (1.05 – 1.2 mmol), K_3PO_4 (1.4 mmol), **2a** (1 mol %), tBuOH (2 mL), 110 °C, 1.5 h; isolated yields, average of two runs.

*No significant difference in reactivities was observed between methanesulfonate precatalyst **2a** and trifluoromenthanesulfonate precatalyst **7a** in the arylation of primary amides.

X-Ray Structure Determination

Low-temperature diffraction data (φ-and ω-scans) were collected on a Bruker-AXS X8 Kappa Duo diffractometer coupled to a Smart Apex2 CCD detector with Mo Kα radiation (λ = 0.71073 Å) from an IμS micro-source for the structure of compounds **2a** and **5a**. All structures were solved by direct methods using SHELXS[9] and refined against F^2 on all data by full-matrix least squares with SHELXL-97[10] using established refinement techniques.[11] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms they are linked to (1.5 times for methyl groups). All disordered atoms were refined with the help of similarity restraints on the 1,2- and 1,3-distances and displacement parameters as well as rigid bond restraints for anisotropic displacement parameters unless otherwise noted below.

Compound **2a** crystallizes in the monoclinic space group $P2_1/n$ with one molecule in the asymmetric unit.

Compound **7a** crystallizes in the monoclinic space group $P2_1/n$ with one molecule in the asymmetric unit. The hydrogen atoms on N1 correspond to the two highest residual density maxima. The nitrogen containing ligand (N1 to C52) shows higher than average motion. Attempts to refine a disorder failed.

Table 1. Crystal data and structure refinement for **2a**.

Identification code	x12164
Empirical formula	C44 H62 N O5 P Pd S
Formula weight	854.38
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/n

Unit cell dimensions	a = 15.5444(13) Å	a= 90°.
	b = 16.3387(14) Å	b= 96.6810(10)°.
	c = 16.8546(14) Å	g = 90°.
Volume	4251.6(6) $Å^3$	
Z	4	
Density (calculated)	1.335 Mg/m^3	
Absorption coefficient	0.567 mm^{-1}	
F(000)	1800	
Crystal size	0.16 x 0.15 x 0.12 mm^3	
Theta range for data collection	1.69 to 31.00°.	
Index ranges	-22<=h<=22, -23<=k<=23, -24<=l<=24	
Reflections collected	77171	
Independent reflections	13547 [R(int) = 0.0361]	
Completeness to theta = 31.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9351 and 0.9147	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	13547 / 2 / 499	
Goodness-of-fit on F^2	1.041	
Final R indices [I>2sigma(I)]	R1 = 0.0299, wR2 = 0.0737	
R indices (all data)	R1 = 0.0435, wR2 = 0.0824	
Largest diff. peak and hole	0.888 and -1.127 $e.Å^{-3}$	

Table 2. Crystal data and structure refinement for **7a**.

Identification code	x12124	
Empirical formula	C44 H59 F3 N O5 P Pd S	
Formula weight	908.35	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 11.4497(5) Å	a= 90°.
	b = 22.2598(9) Å	b= 102.1430(10)°.
	c = 17.1180(7) Å	g = 90°.
Volume	4265.2(3) $Å^3$	
Z	4	

Density (calculated)	1.415 Mg/m^3
Absorption coefficient	0.580 mm^{-1}
F(000)	1896
Crystal size	0.40 x 0.30 x 0.15 mm^3
Theta range for data collection	1.52 to 31.51°.
Index ranges	-16<=h<=16, -32<=k<=32, -25<=l<=24
Reflections collected	145732
Independent reflections	14208 [R(int) = 0.0539]
Completeness to theta = 31.51°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9181 and 0.8012
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	14208 / 494 / 617
Goodness-of-fit on F^2	1.047
Final R indices [I>2sigma(I)]	R1 = 0.0315, wR2 = 0.0739
R indices (all data)	R1 = 0.0447, wR2 = 0.0826
Largest diff. peak and hole	0.691 and -1.009 $e.Å^{-3}$

Supporting Information References:

1) Hoshiya, N.; Buchwald, S. L. *Adv. Syn. Catal.* **2012**, *354*, 2031 – 2037.

2) Su, M.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2012**, *51*, 4710.

3) Salvi, L.; Davis, N. R.; Ali, S. Z.; Buchwald, S. L. *Org. Lett.* **2012**, *14*, 170.

4) Vorogushin, A. V.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 8146.

5) Bruno, N. C.; Tudge, M. T.; Buchwald, S. L. *Chem. Sci.* **2013**, *4*, 916 – 920. It was found that complex **4** could be prepared in the presence of air.

6) Fors, B. P.; Dooleweerdt, K.; Zeng, Q.; Buchwald, S. L. *Tetrahedron*, **2009***, 65*, 6576.

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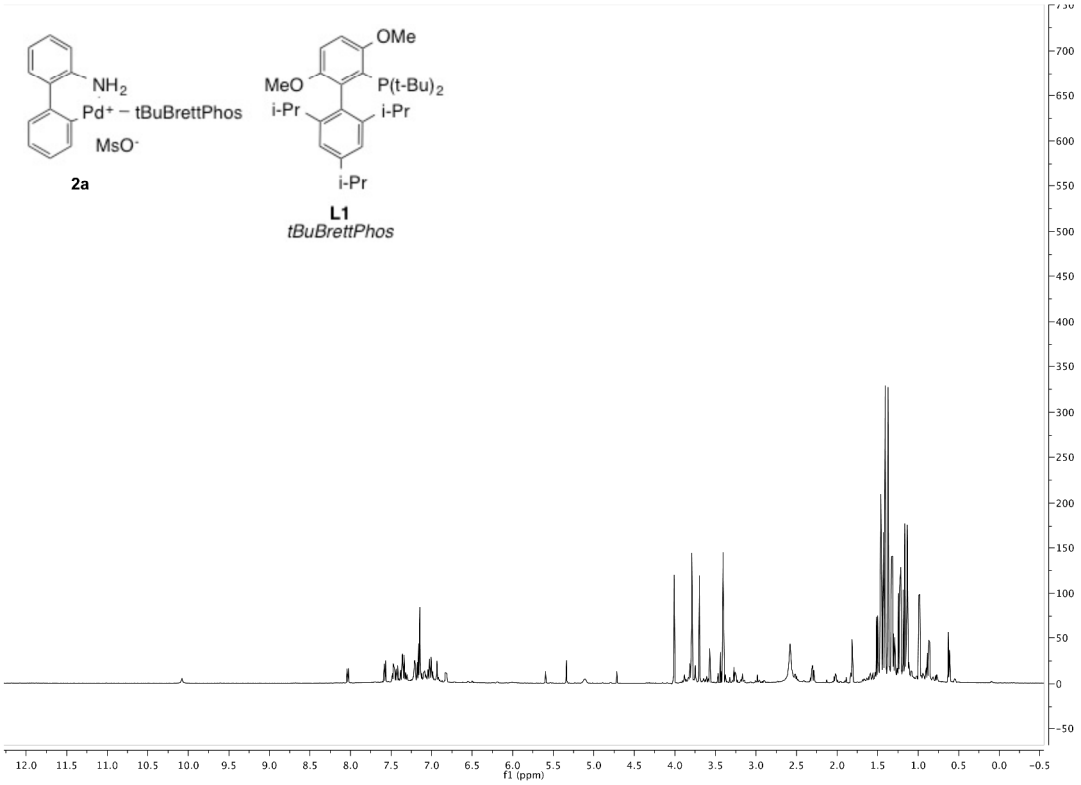
8) Wu, X.; Fors, B. P.; Buchwald, S. L.; *Angew. Chem. Int. Ed.* **2011,** *50*, 9943

9) Sheldrick, G. M. Acta Cryst. 1990, A46, 467-473.

10) Sheldrick, G. M. Acta Cryst. 2008, A64, 112-122.

11) Müller, P. Crystallography Reviews 2009, 15, 57-83.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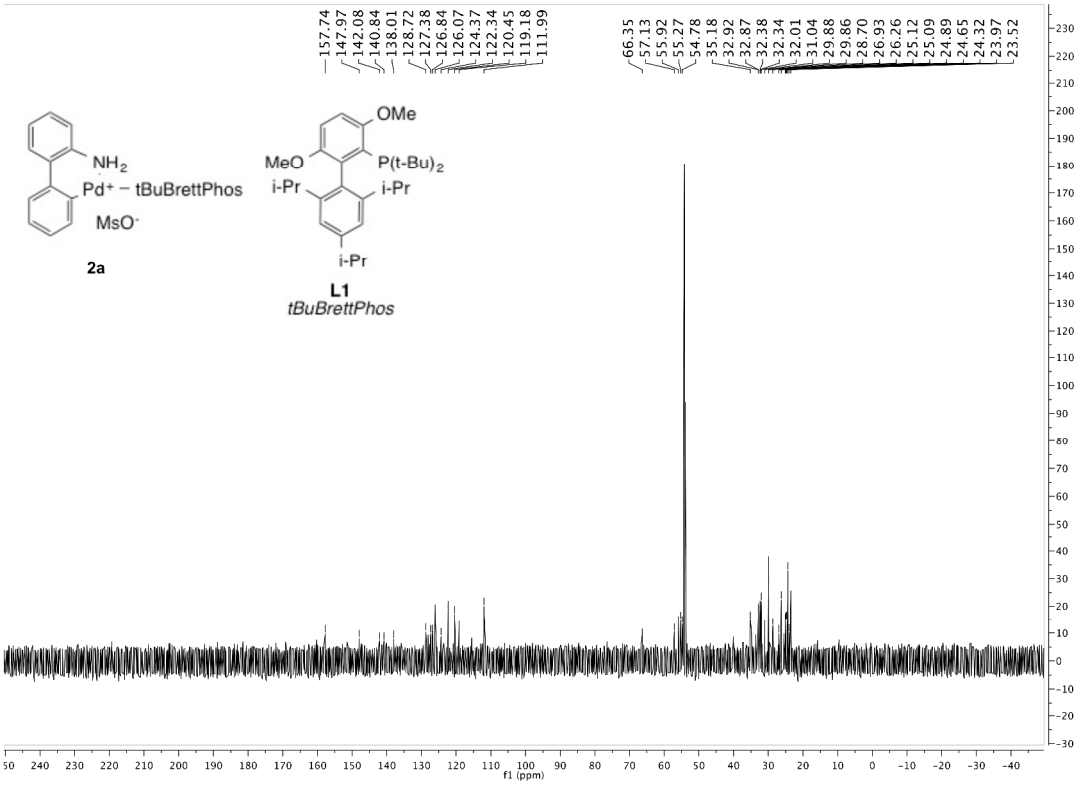
MsO-
2a
OMe
MeO
P(t-Bu)2
i-Pr
i-Pr
i-Pr
L1
tBuBrettPhos
f1 (ppm)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138.01
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126.07
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122.34
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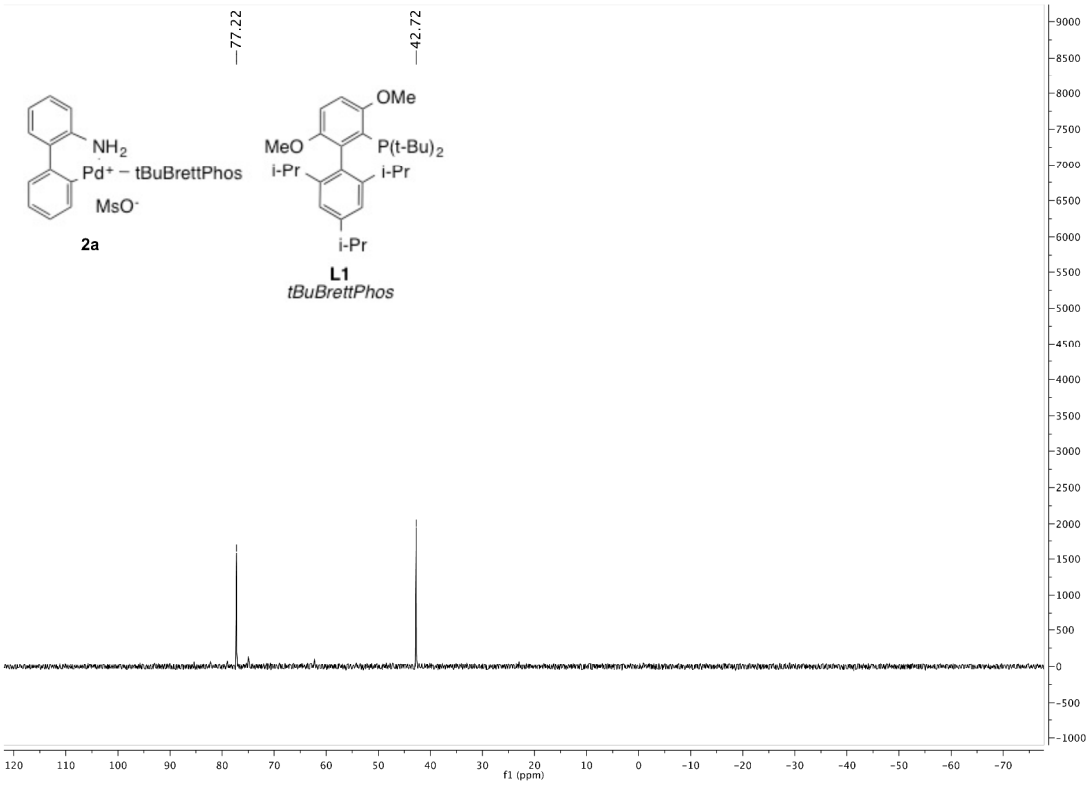
119.18
111.99
66.35
57.13
55.92
55.27
54.78
35.18
32.92
32.87
32.38
32.34
32.01
31.04
29.88
29.86
28.70
26.93
26.26
25.12
25.09
24.89
24.65
24.32
23.97
23.52
NH2
Pd+ – tBuBrettPhos
MsO-
2a
OMe
MeO
P(t-Bu)2
i-Pr
i-Pr
i-Pr
L1
tBuBrettPhos
f1 (ppm)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42.72
NH2
Pd+ – tBuBrettPhos
MsO-
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OMe
MeO
P(t-Bu)2
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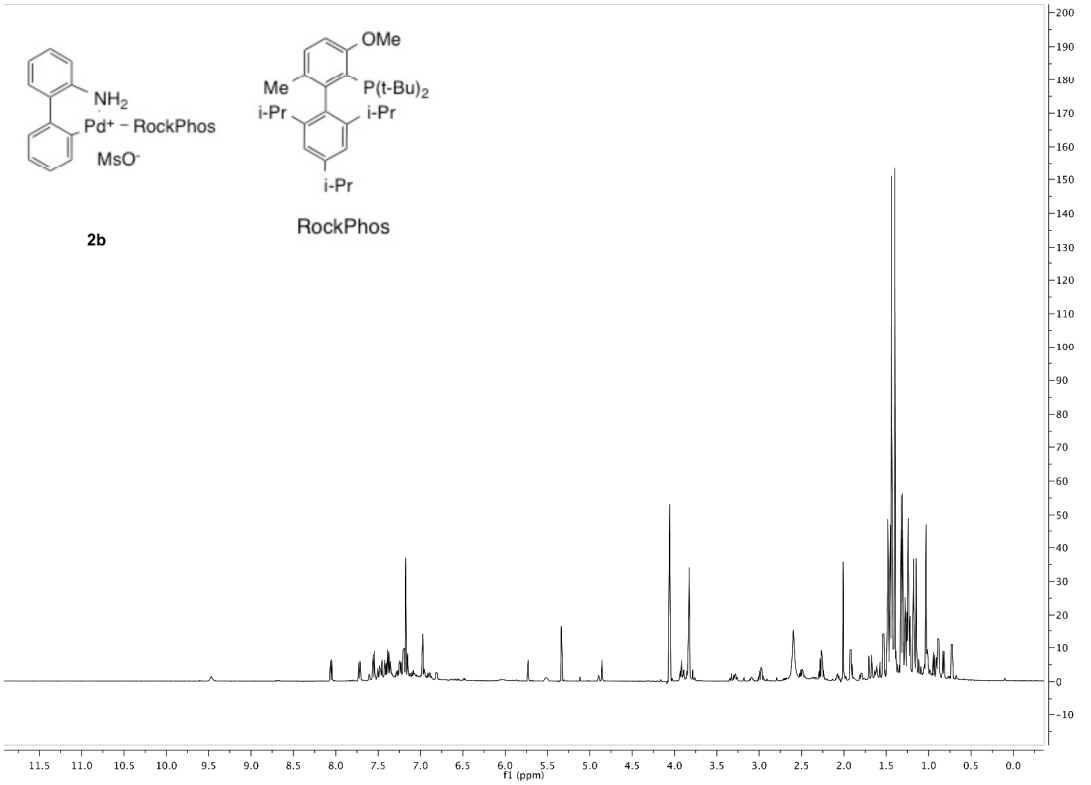
i-Pr
i-Pr
L1
tBuBrettPhos
f1 (ppm)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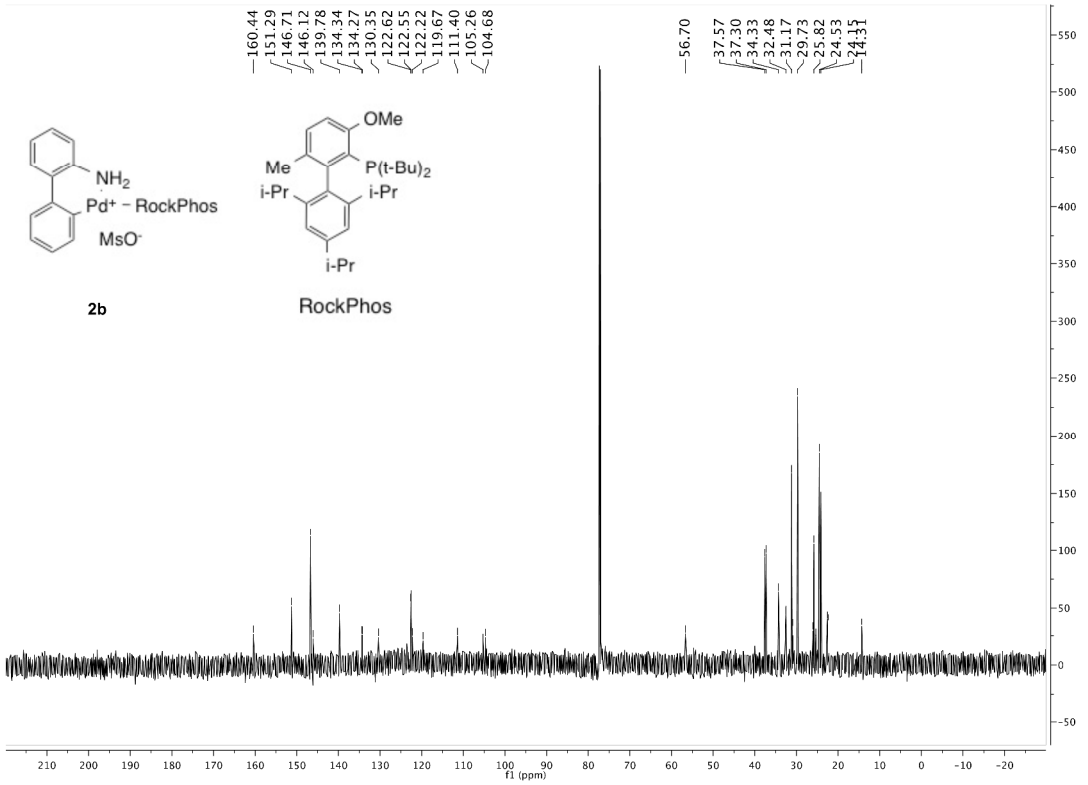
Pd+ – RockPhos
MsO-
2b
OMe
Me
P(t-Bu)2
i-Pr
i-Pr
i-Pr
RockPhos
f1 (ppm)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130.35
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122.55
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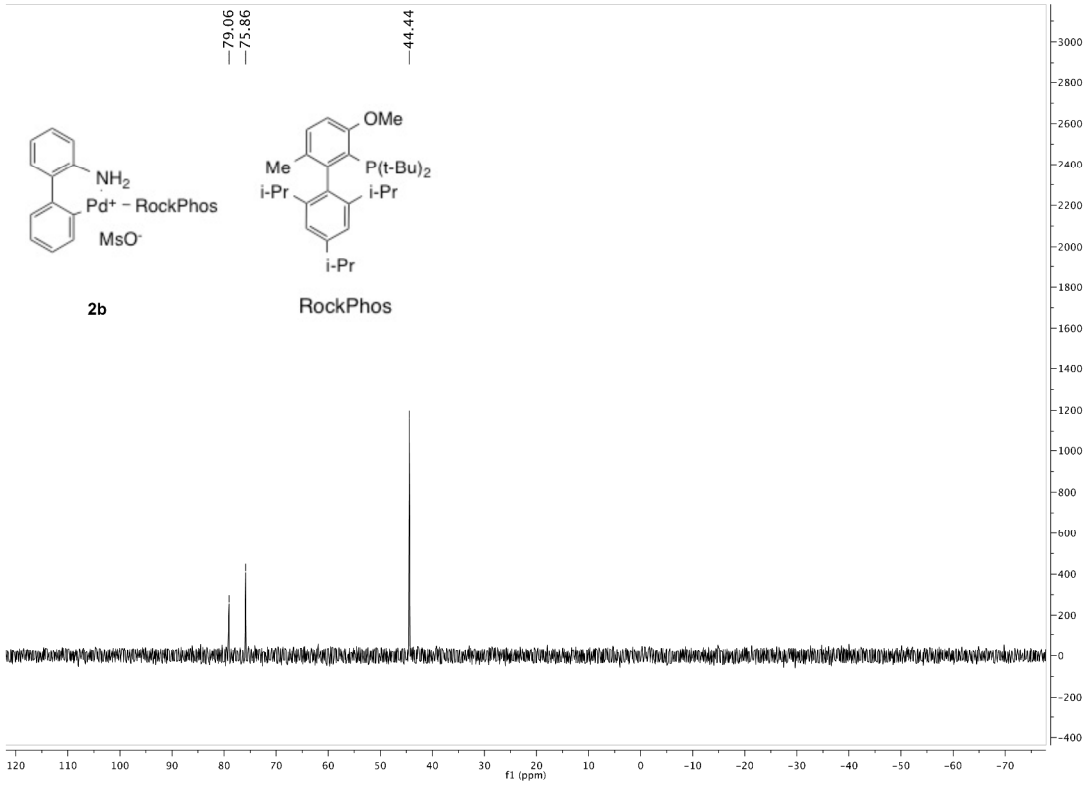
111.40
105.26
104.68
56.70
37.57
37.30
34.33
32.48
31.17
29.73
25.82
24.53
24.15
14.31
NH2
Pd+ – RockPhos
MsO-
2b
OMe
Me
P(t-Bu)2
i-Pr
i-Pr
i-Pr
RockPhos
f1 (ppm)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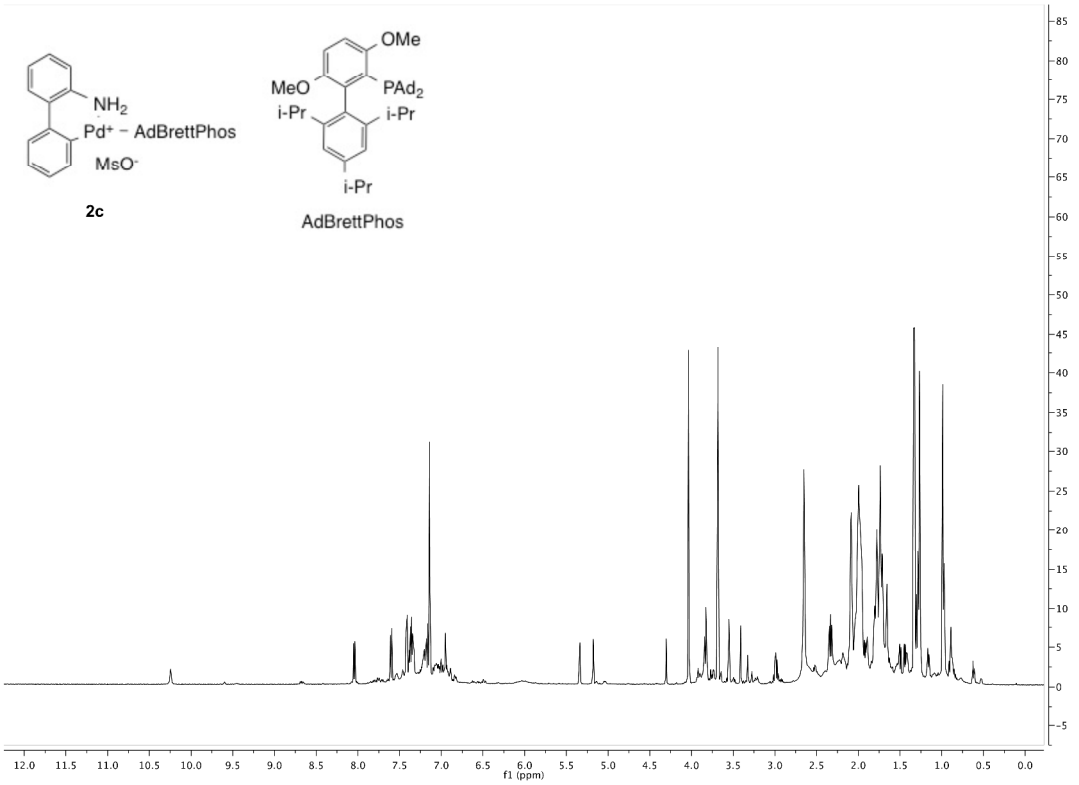
44.44
NH2
Pd+ – RockPhos
MsO-
2b
OMe
Me
P(t-Bu)2
i-Pr
i-Pr
i-Pr
RockPhos
f1 (ppm)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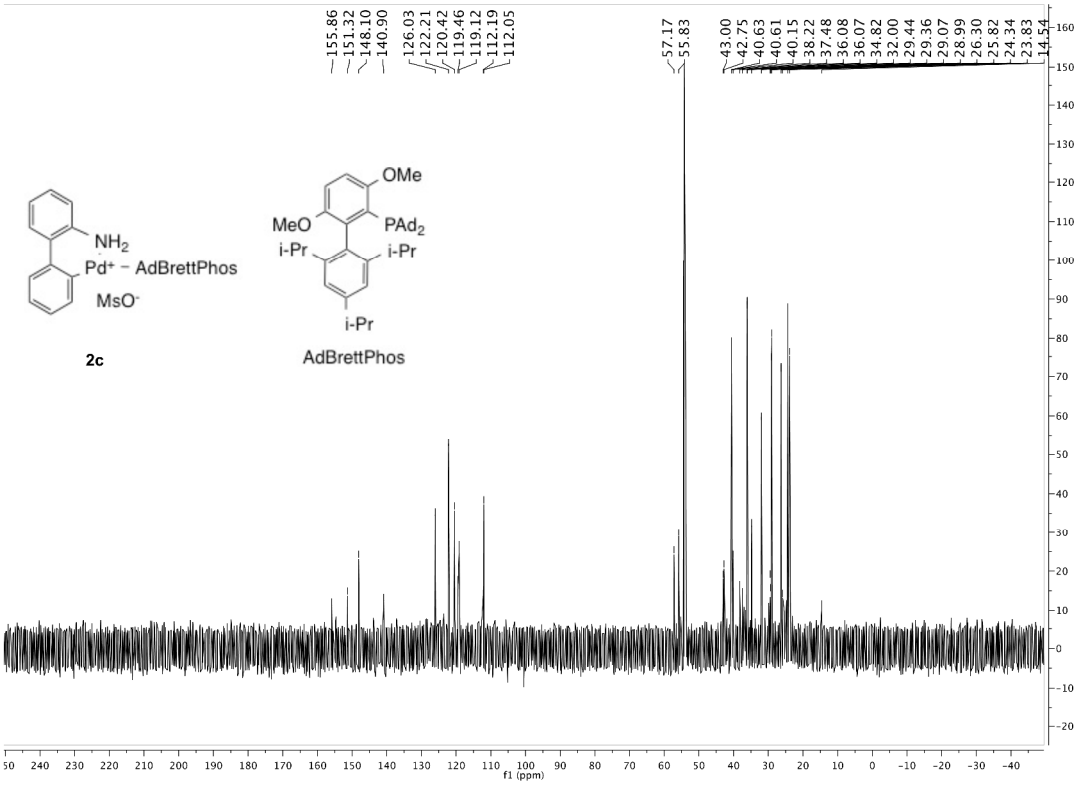
Pd+ – AdBrettPhos
MsO-
2c
OMe
MeO
PAd2
i-Pr
i-Pr
i-Pr
AdBrettPhos
f1 (ppm)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126.03
122.21
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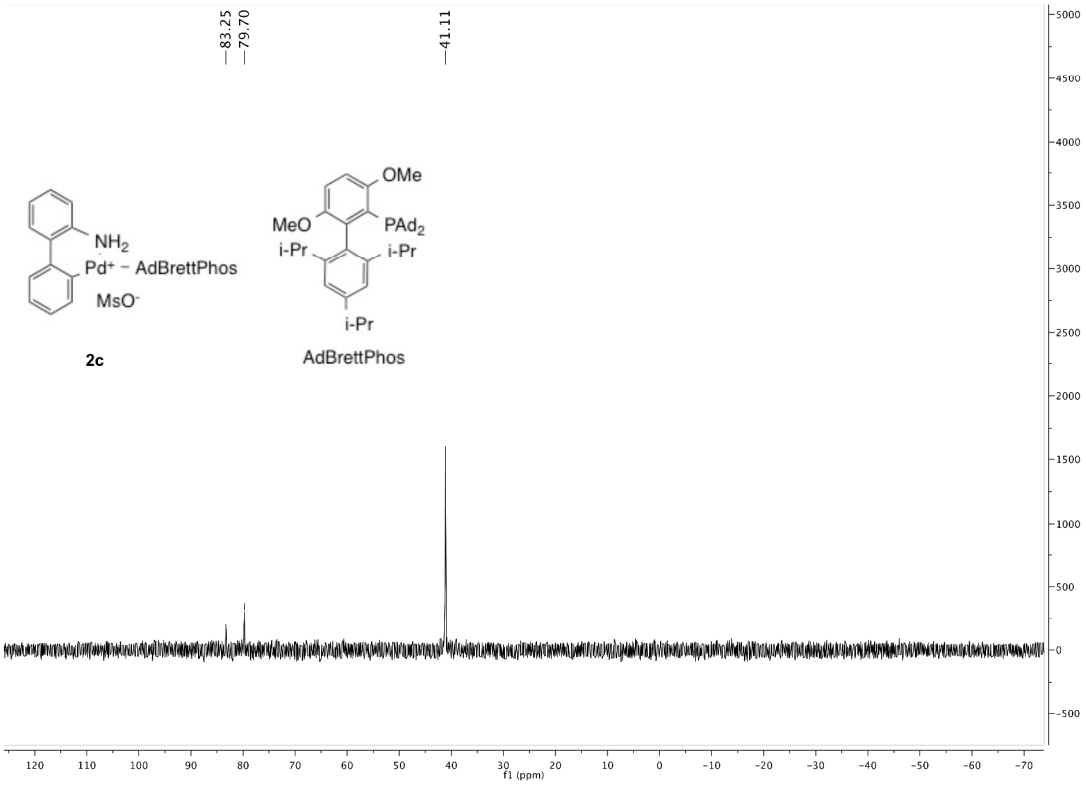
55.83
43.00
42.75
40.63
40.61
40.15
38.22
37.48
36.08
36.07
34.82
32.00
29.44
29.36
29.07
28.99
26.30
25.82
24.34
23.83
14.54
NH2
Pd+ – AdBrettPhos
MsO-
2c
OMe
MeO
PAd2
i-Pr
i-Pr
i-Pr
AdBrettPhos
f1 (ppm)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79.70
41.11
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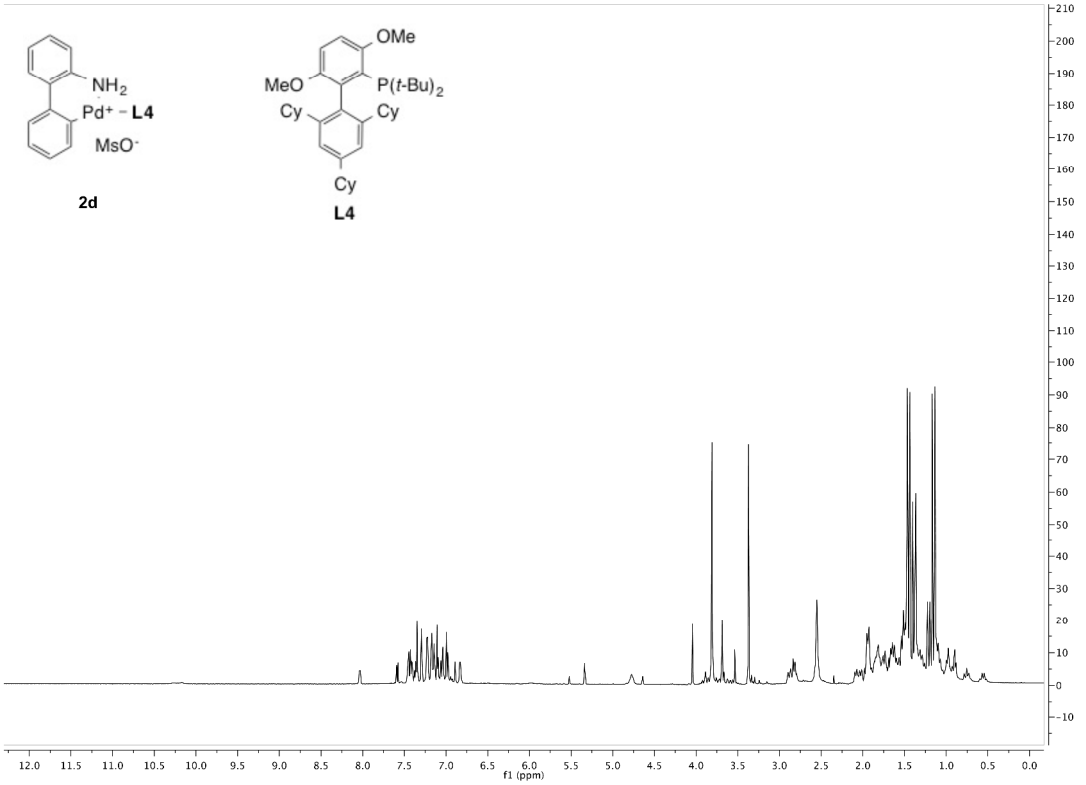
Pd+ – AdBrettPhos
MsO-
2c
OMe
MeO
PAd2
i-Pr
i-Pr
i-Pr
AdBrettPhos
f1 (ppm)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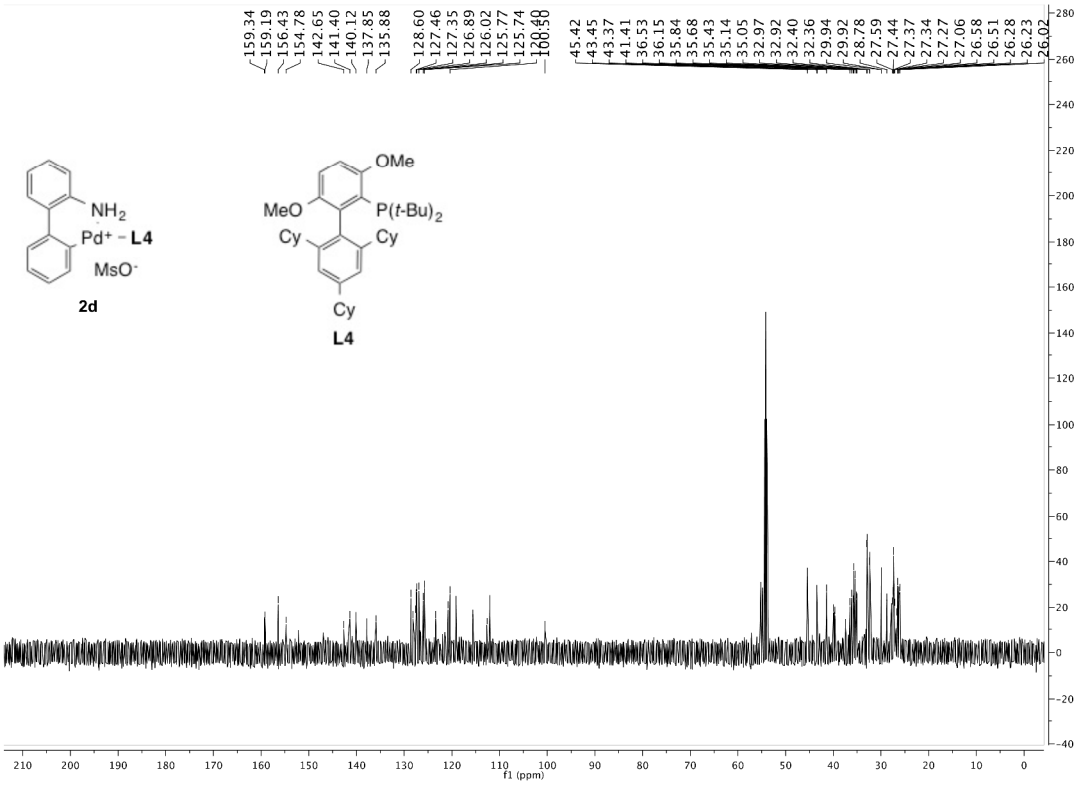
Pd+ – L4
MsO-
2d
OMe
MeO
P(t-Bu)2
Cy
Cy
Cy
L4
f1 (ppm)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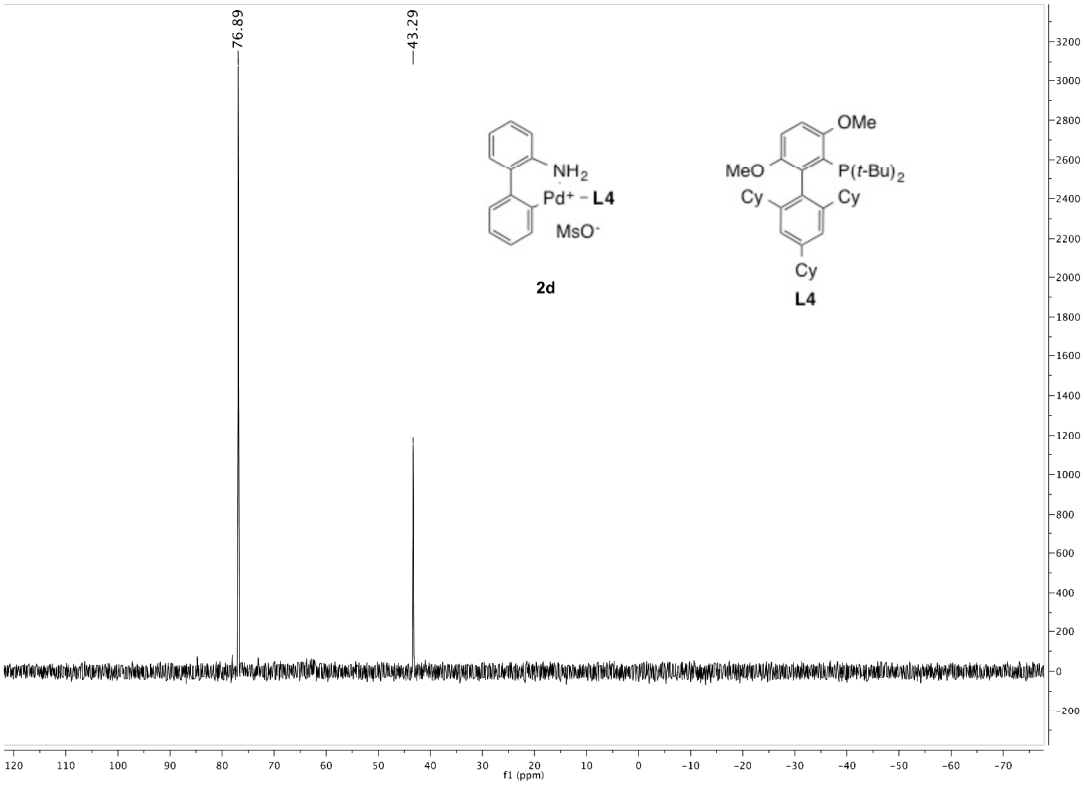
29.92
28.78
27.59
27.44
27.37
27.34
27.27
27.06
26.58
26.51
26.28
26.23
26.02
NH2
Pd+ – L4
MsO-
2d
OMe
MeO
P(t-Bu)2
Cy
Cy
Cy
L4
f1 (ppm)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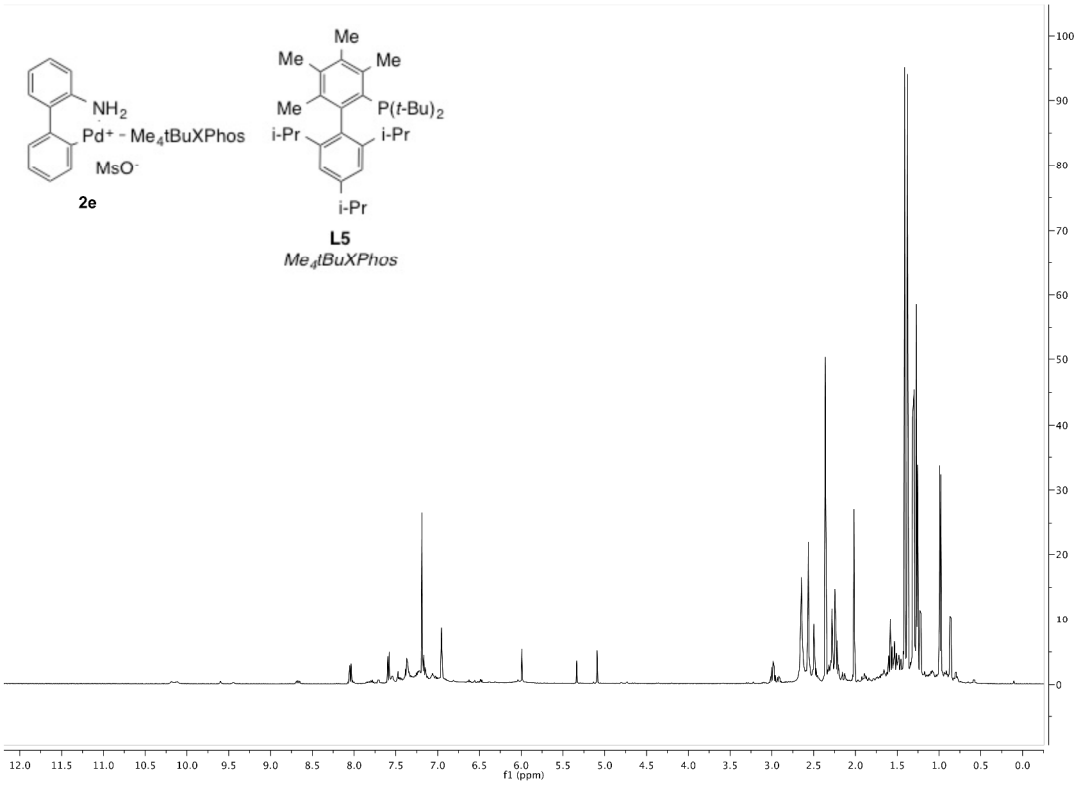
Cy
Cy
L4
f1 (ppm)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MsO-
2e
Me
Me
Me
Me
P(t-Bu)2
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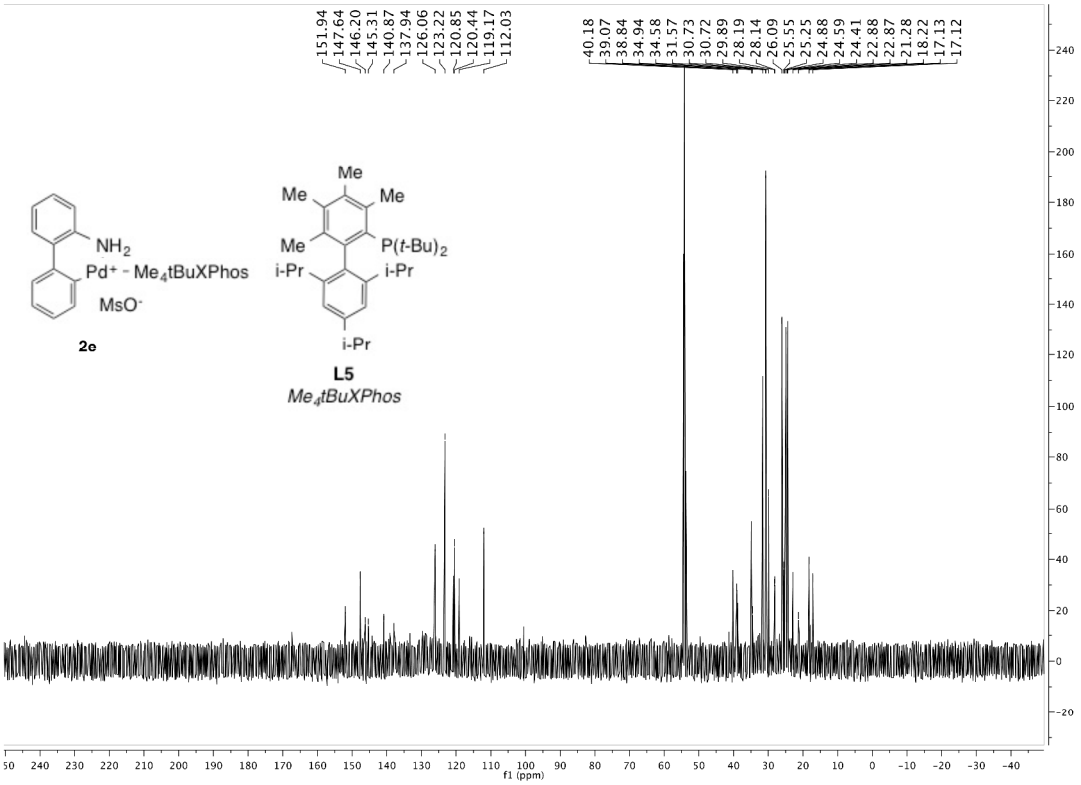
i-Pr
i-Pr
L5
Me4tBuXPhos
f1 (ppm)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34.94
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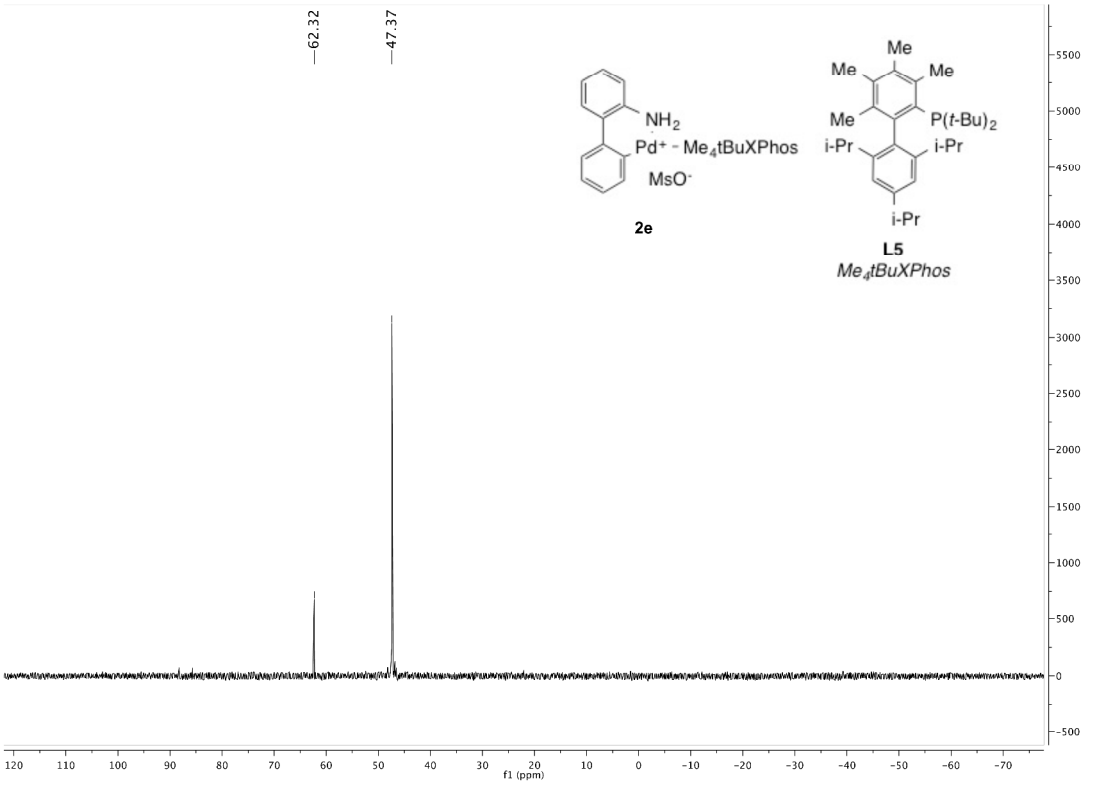
29.89
28.19
28.14
26.09
25.55
25.25
24.88
24.59
24.41
22.88
22.87
21.28
18.22
17.13
17.12
NH2
Pd+ - Me4tBuXPhos
MsO-
2e
Me
Me
Me
Me
P(t-Bu)2
i-Pr
i-Pr
i-Pr
L5
Me4tBuXPhos
f1 (ppm)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47.37
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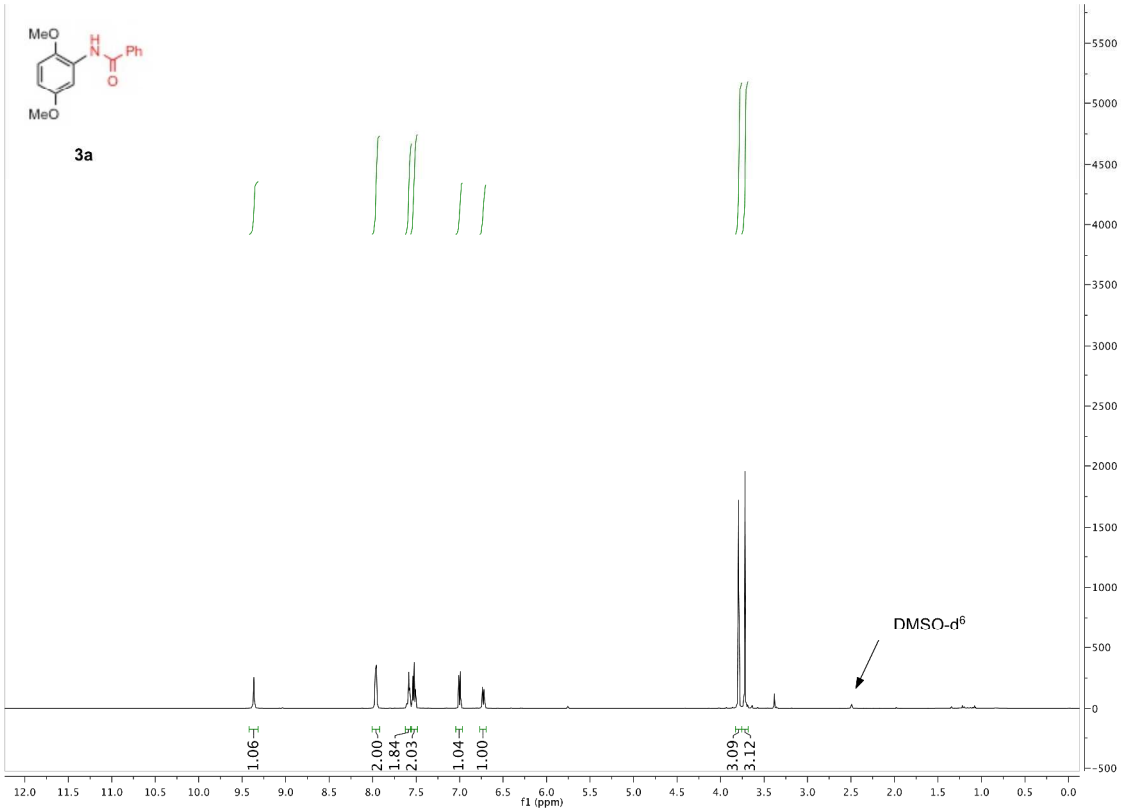
Pd+ - Me4tBuXPhos
MsO-
2e
Me
Me
Me
Me
P(t-Bu)2
i-Pr
i-Pr
i-Pr
L5
Me4tBuXPhos
f1 (ppm)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N
Ph
O
MeO
3a
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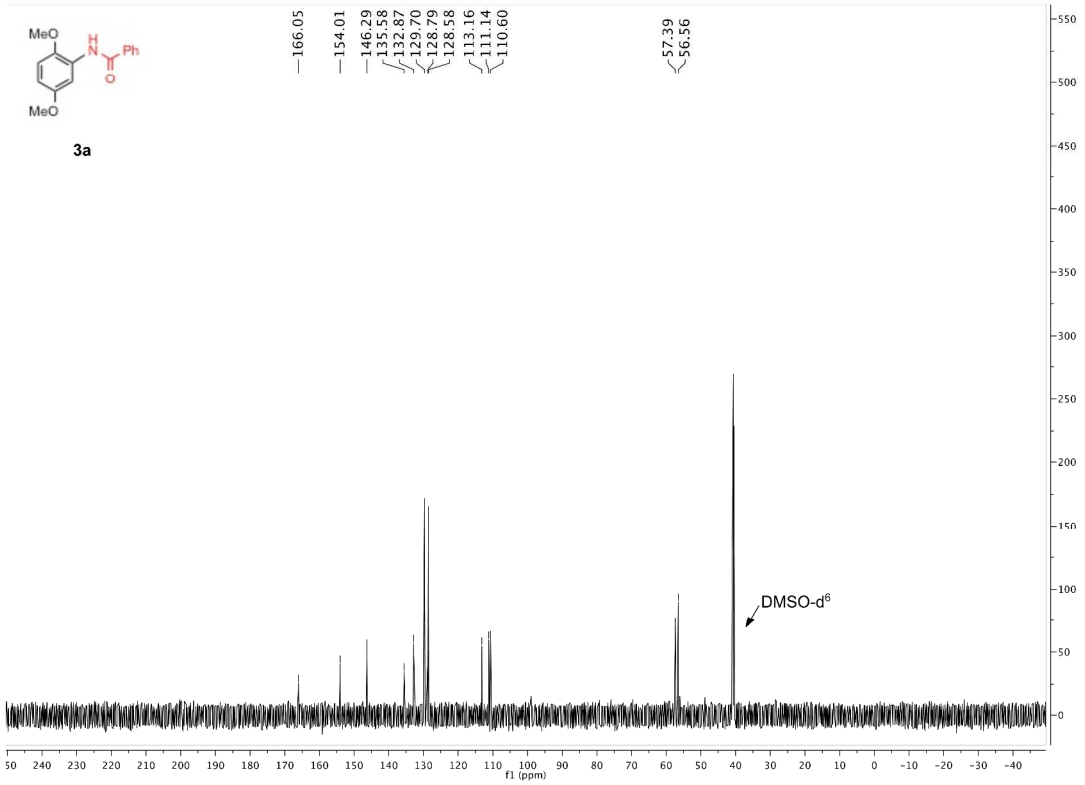
2.00
1.84
2.03
1.04
1.00
3.09
3.12
f1 (ppm)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H
N
Ph
O
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3a
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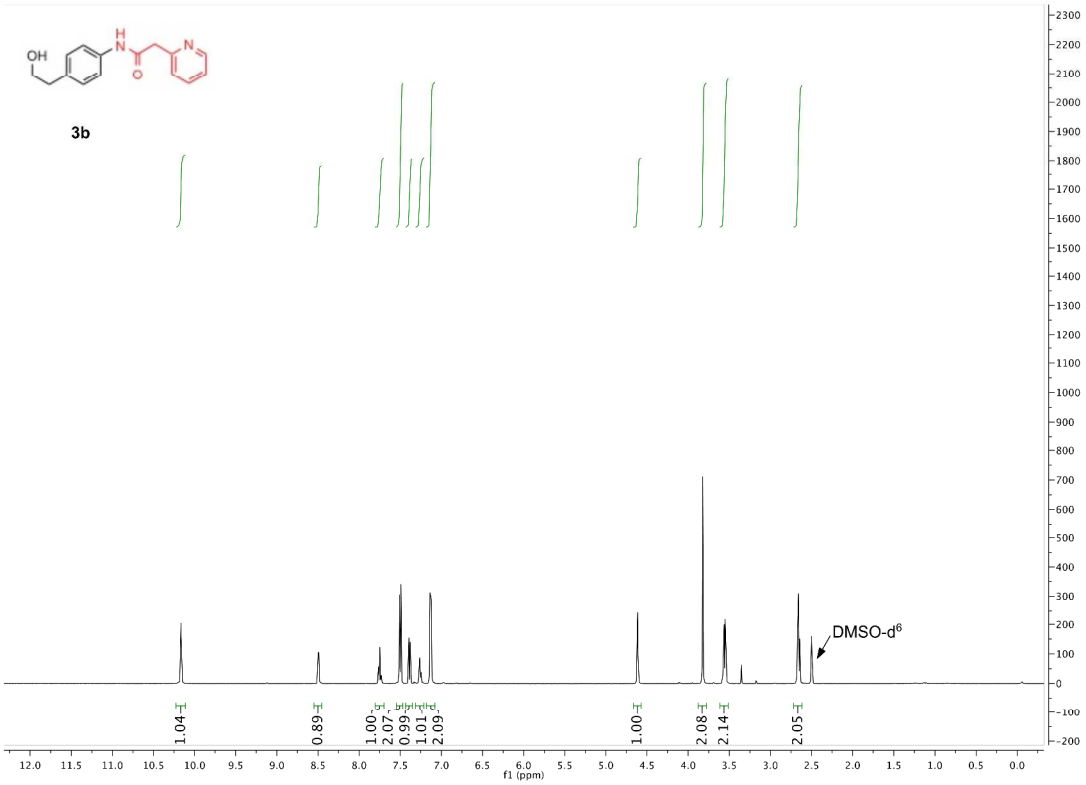
DMSO-d6
f1 (ppm)


OH
N
H
O
N
3b
DMSO-d6
1.04
0.89
1.00
2.07
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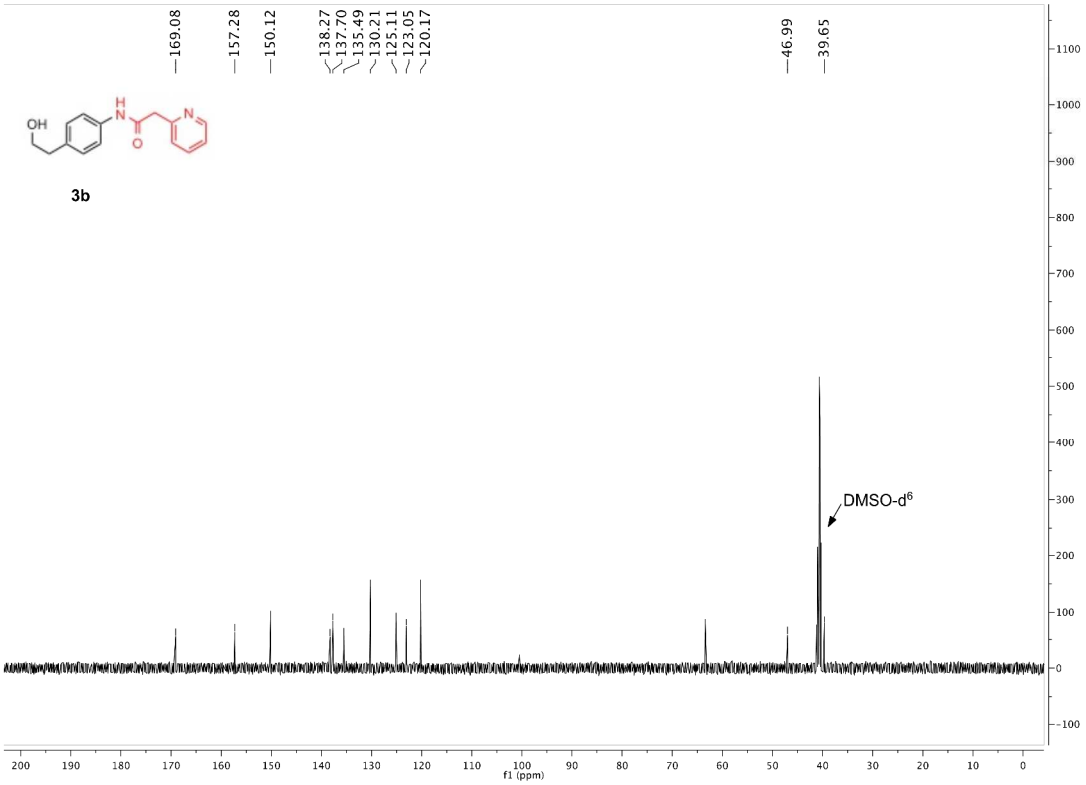
1.01
2.09
1.00
2.08
2.14
2.05
f1 (ppm)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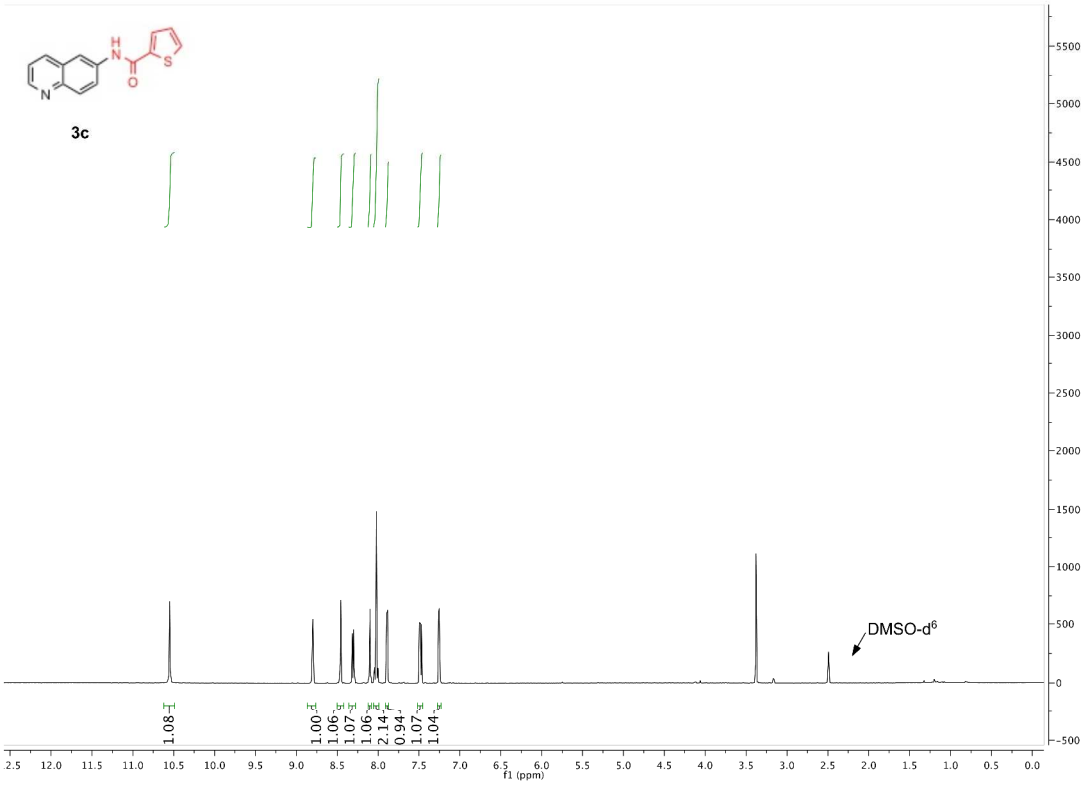
N
H
O
N
3b
DMSO-d6
f1 (ppm)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DMSO-d6
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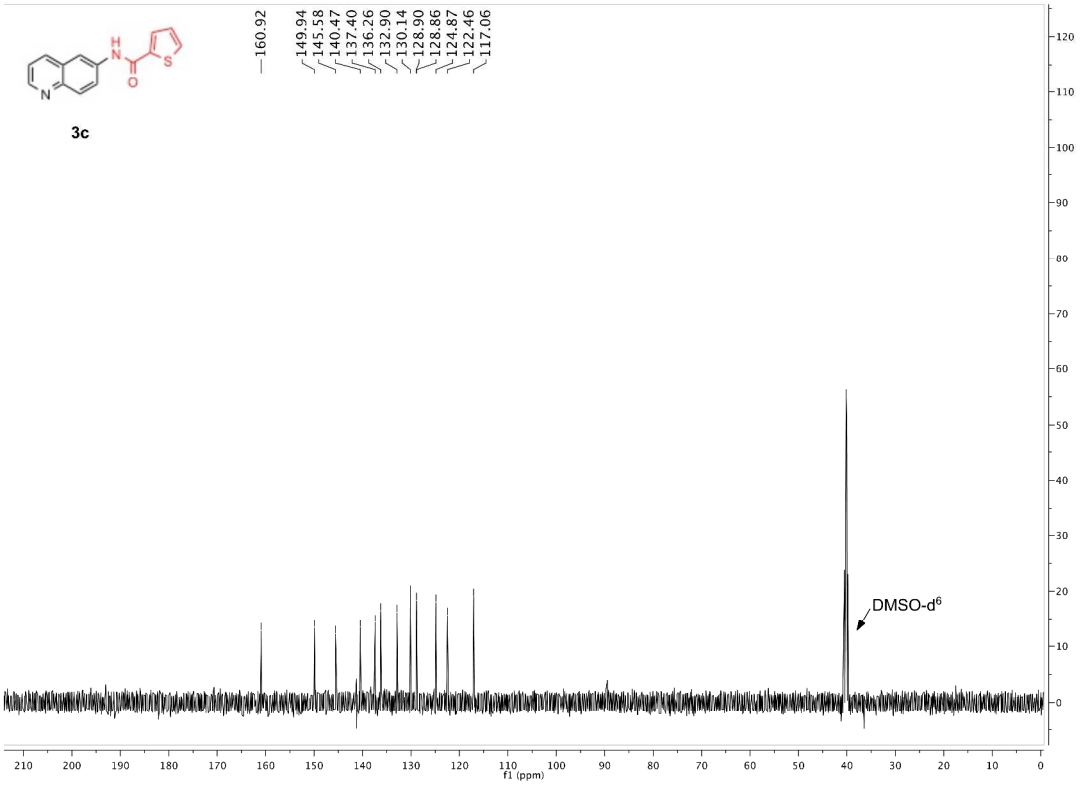
1.06
1.07
1.06
2.14
0.94
1.07
1.04
f1 (ppm)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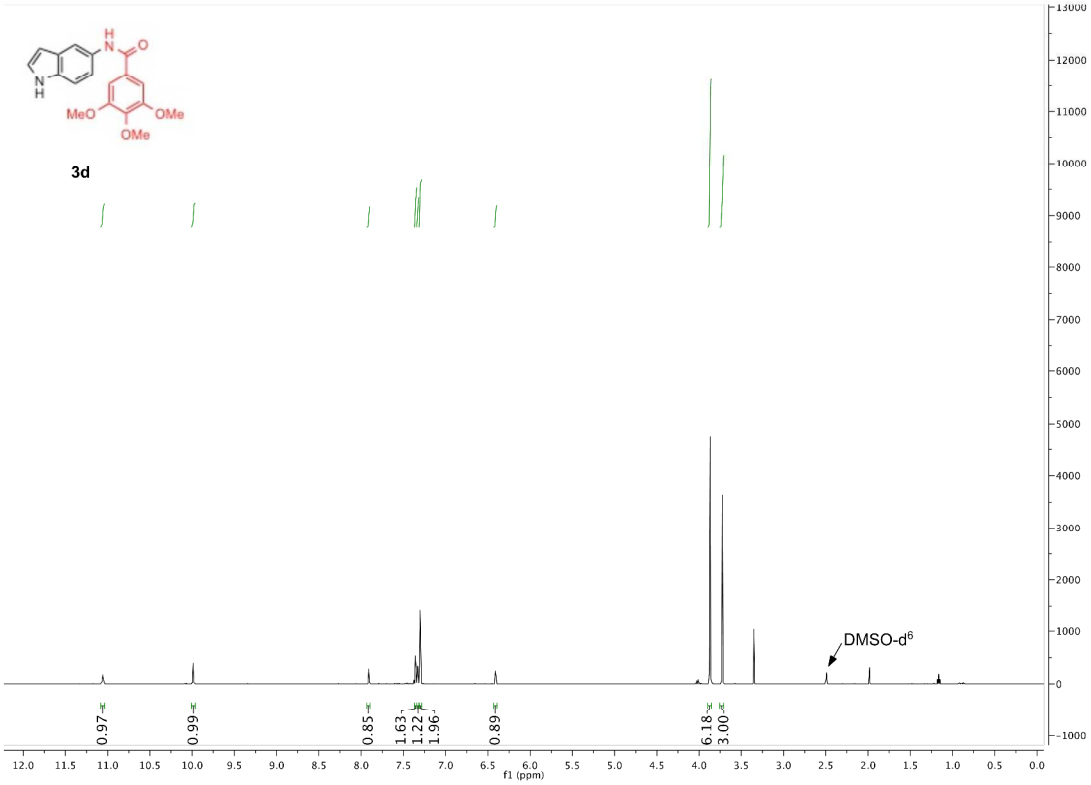
122.46
117.06
DMSO-d6
f1 (ppm)


3d
DMSO-d6
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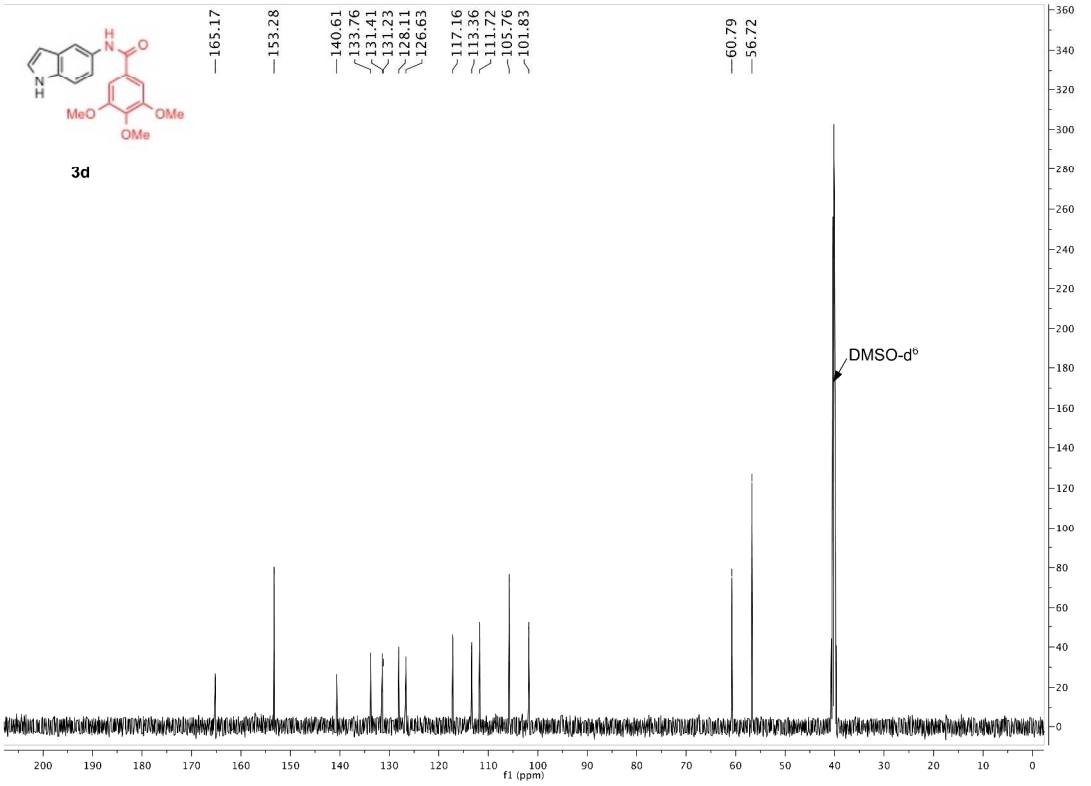
1.63
1.22
1.96
0.89
6.18
3.00
f1 (ppm)


3d
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133.76
131.41
131.23
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117.16
113.36
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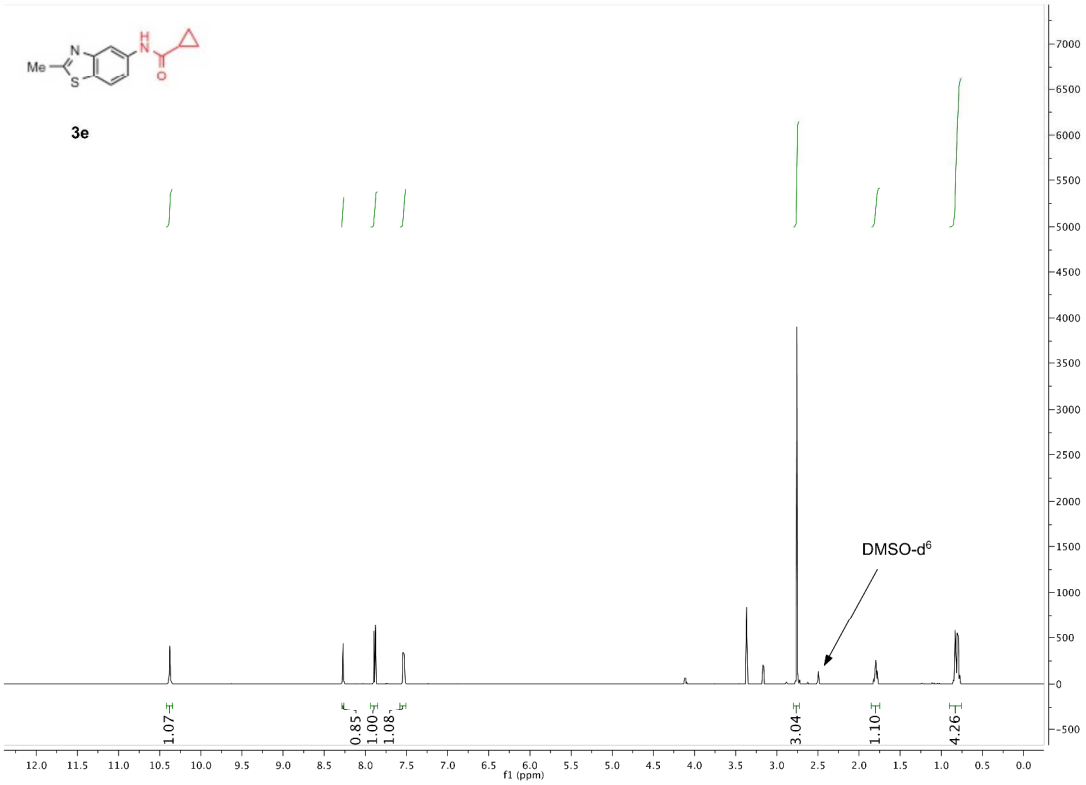
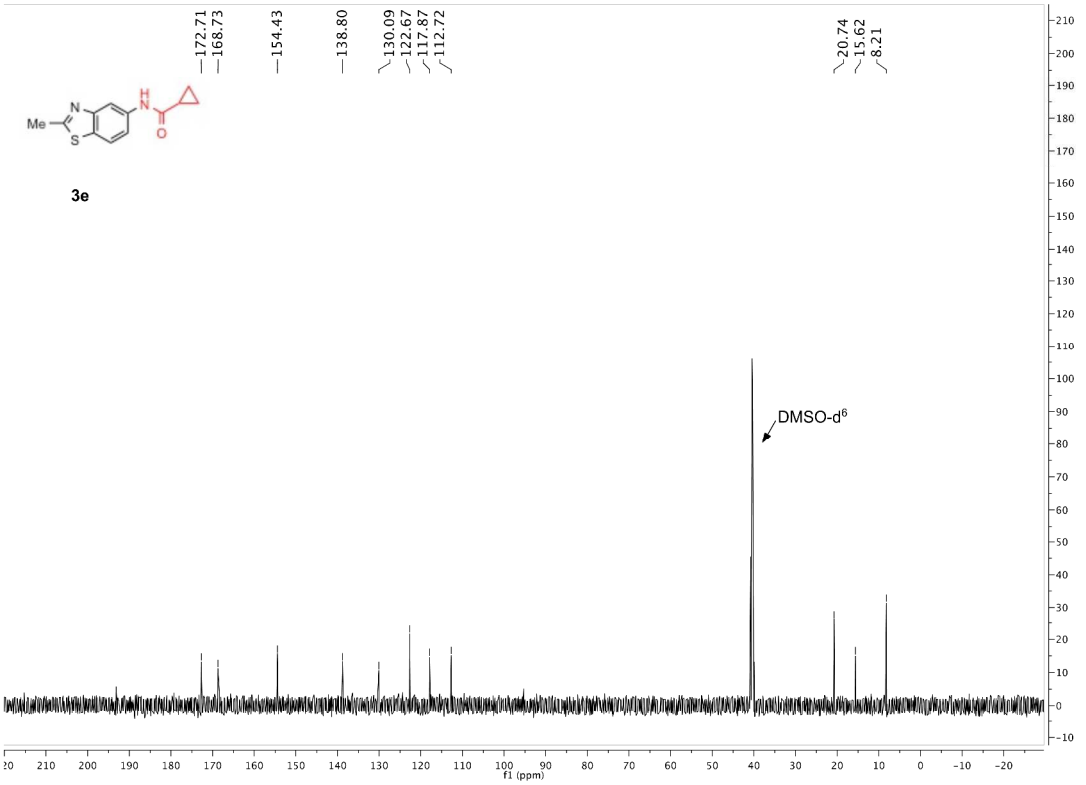
101.83
60.79
56.72
DMSO-d6
f1 (ppm)


Me
N
S
H
N
O
3e
DMSO-d6
1.07
0.85
1.00
1.08
3.04
1.10
4.26
f1 (ppm)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138.80
130.09
122.67
117.87
112.72
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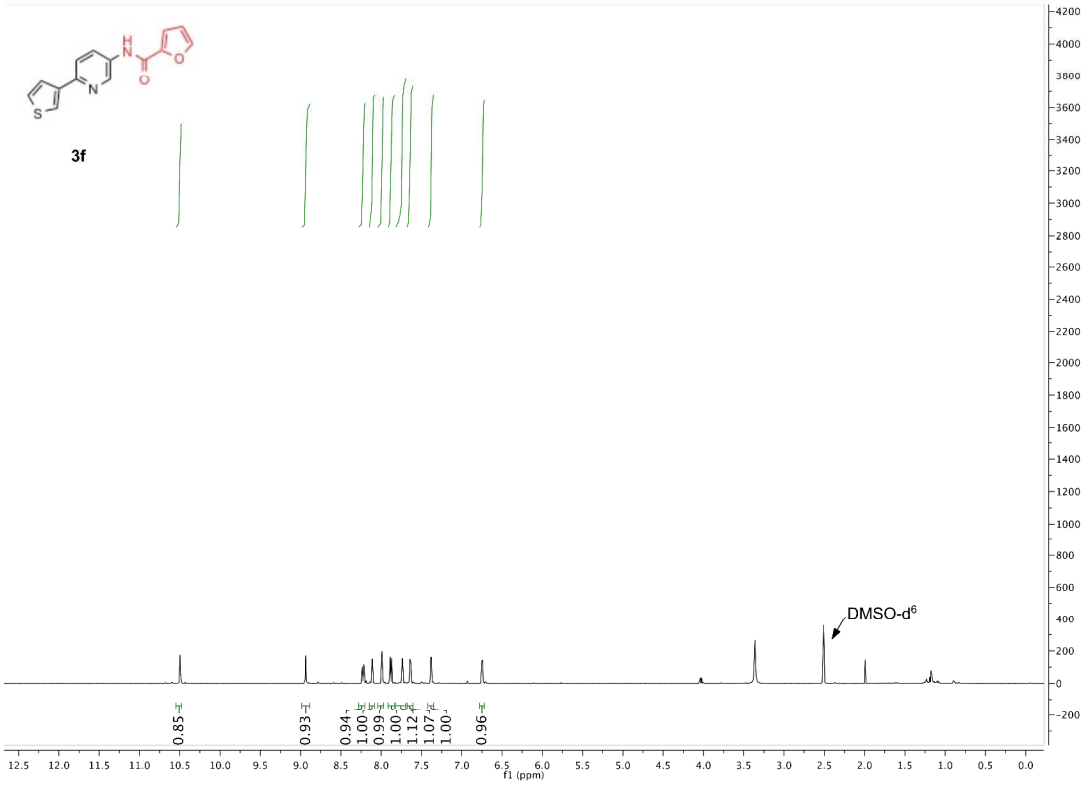
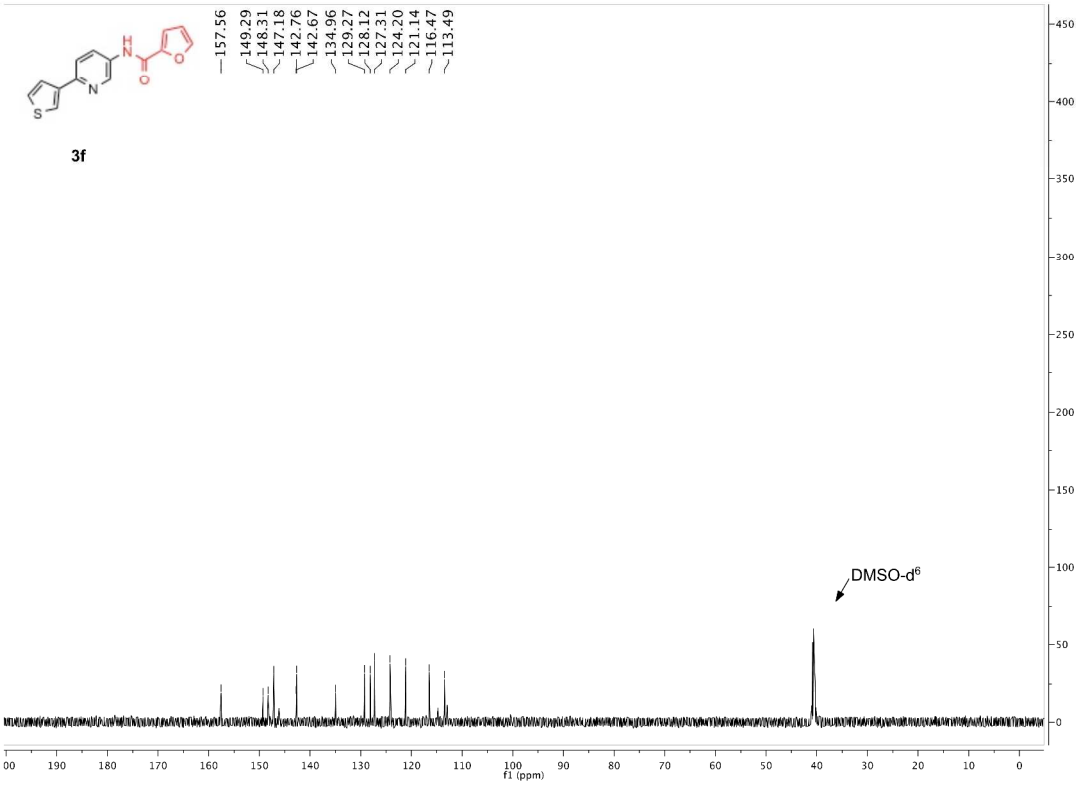
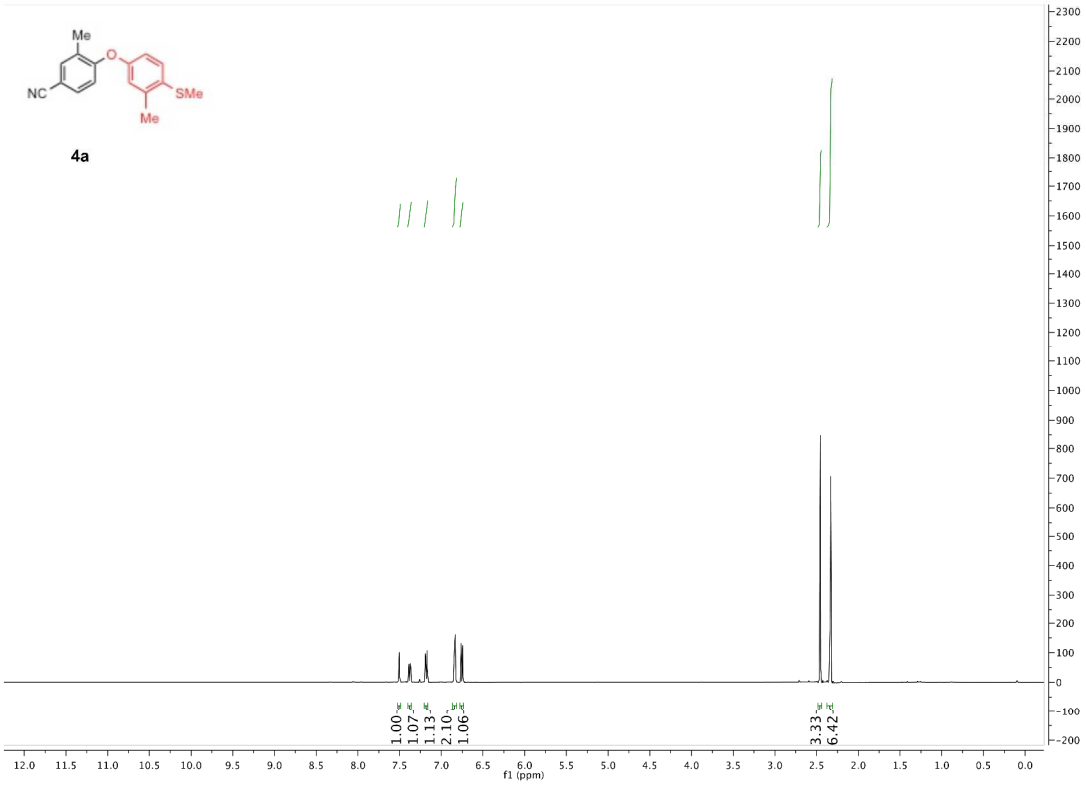
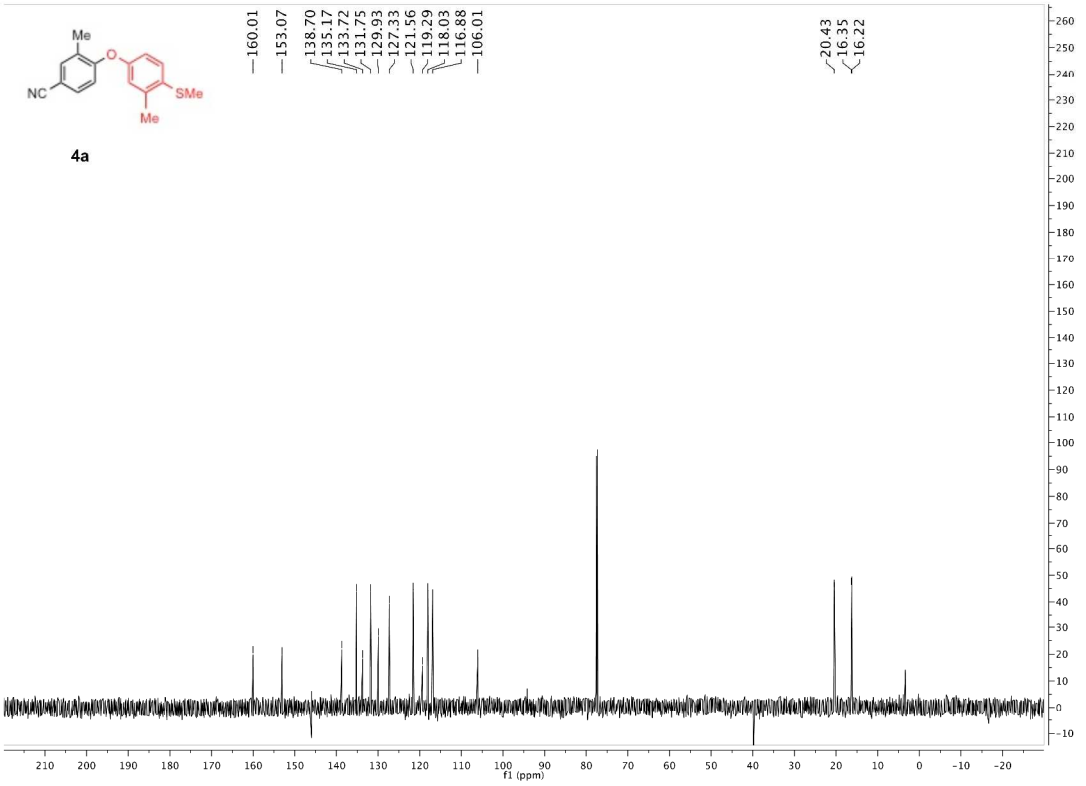
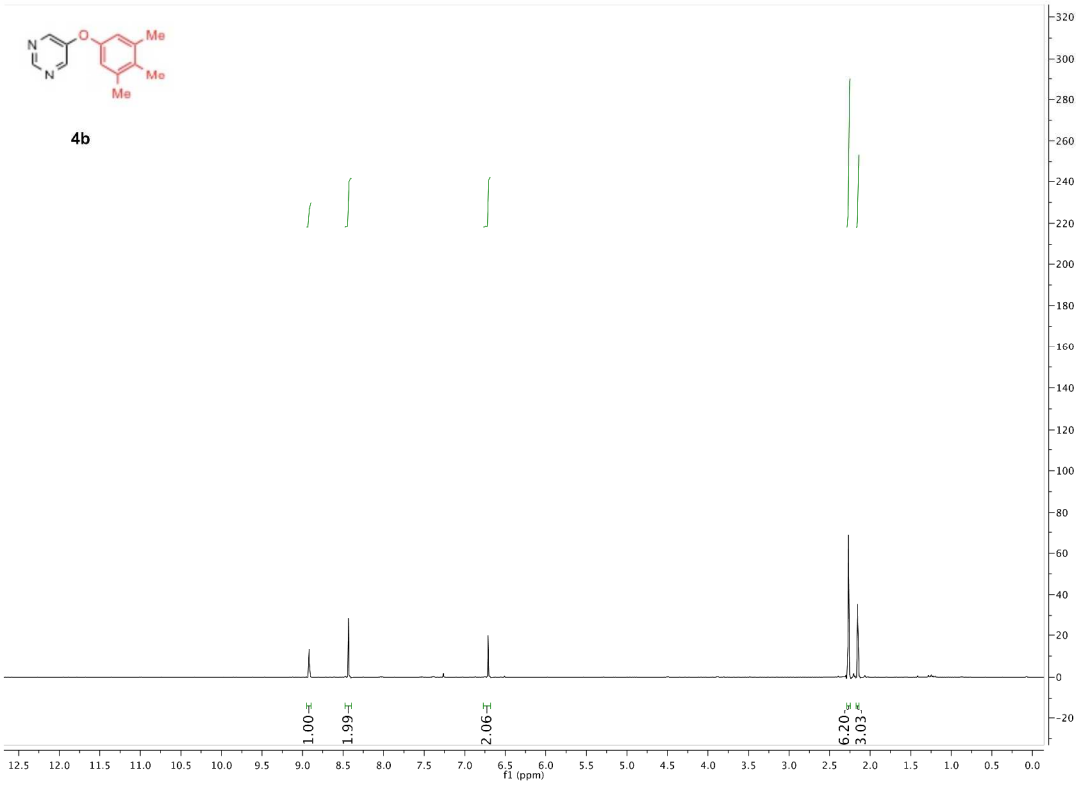
15.62
8.21
Me
N
S
H
N
O
3e
DMSO-d6
f1 (ppm)

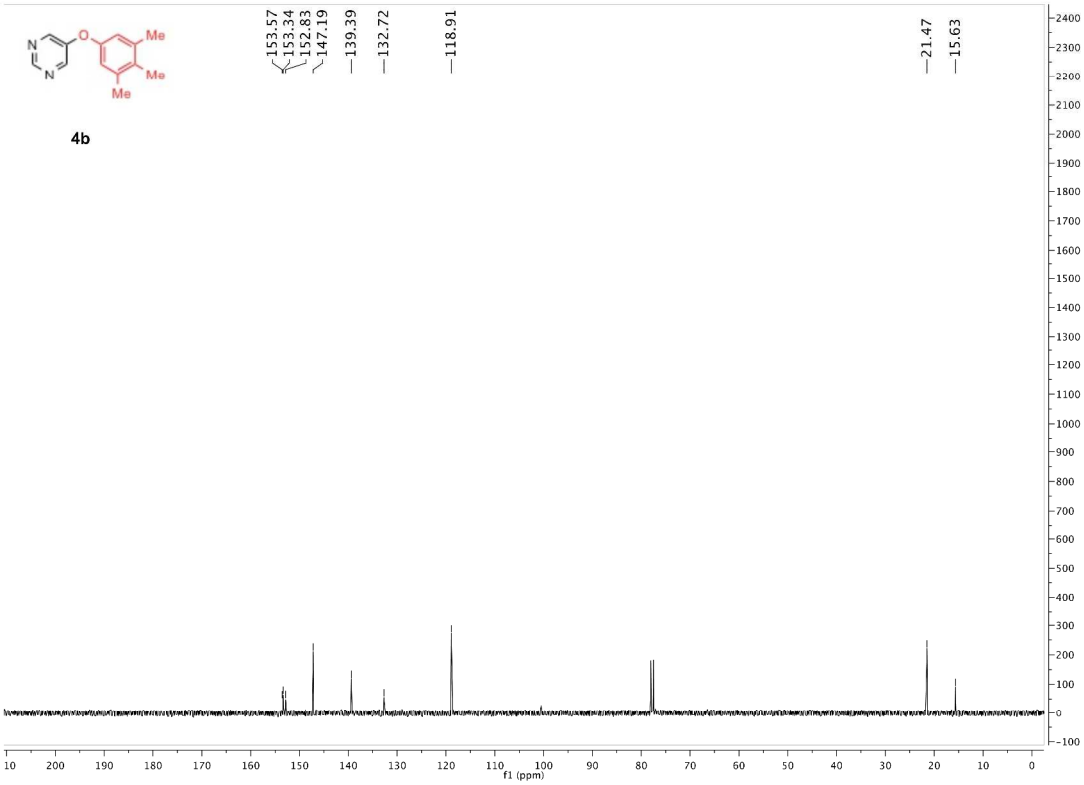

3f
DMSO-d6
0.85
0.93
0.94
1.00
0.99
1.00
1.12
1.07
1.00
0.96
f1 (ppm)

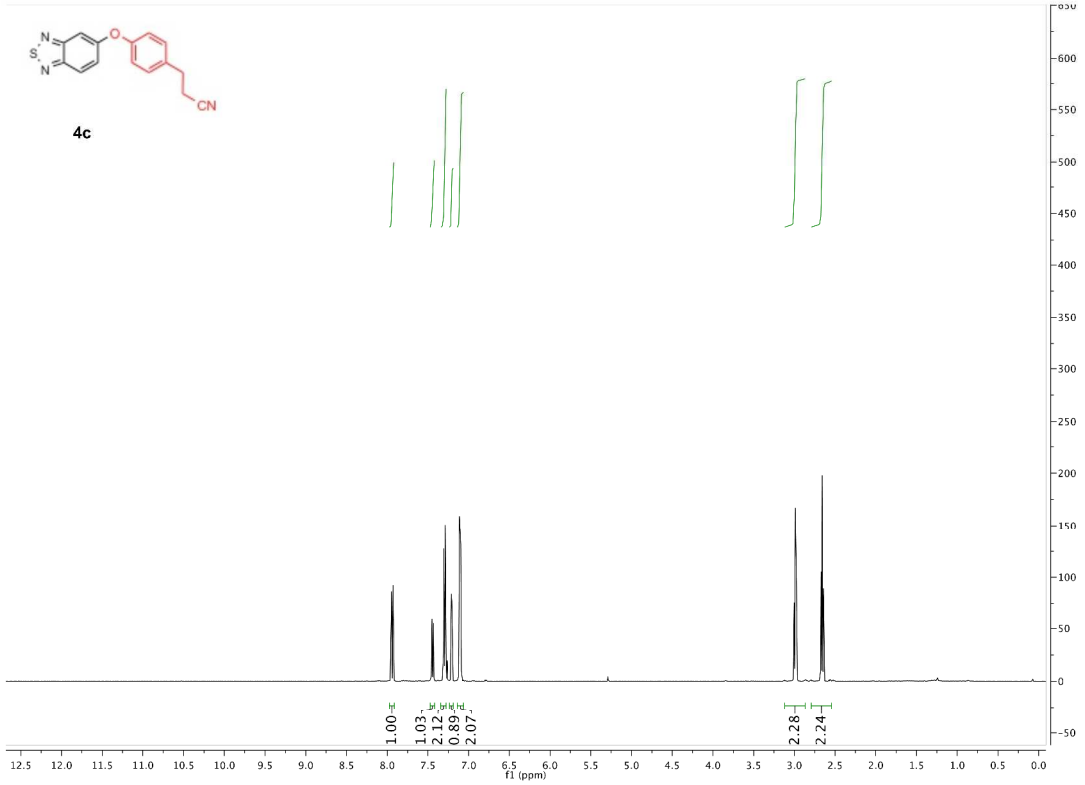

3f
157.56
149.29
148.31
147.18
142.76
142.67
134.96
129.27
128.12
127.31
124.20
121.14
116.47
113.49
DMSO-d6
f1 (ppm)

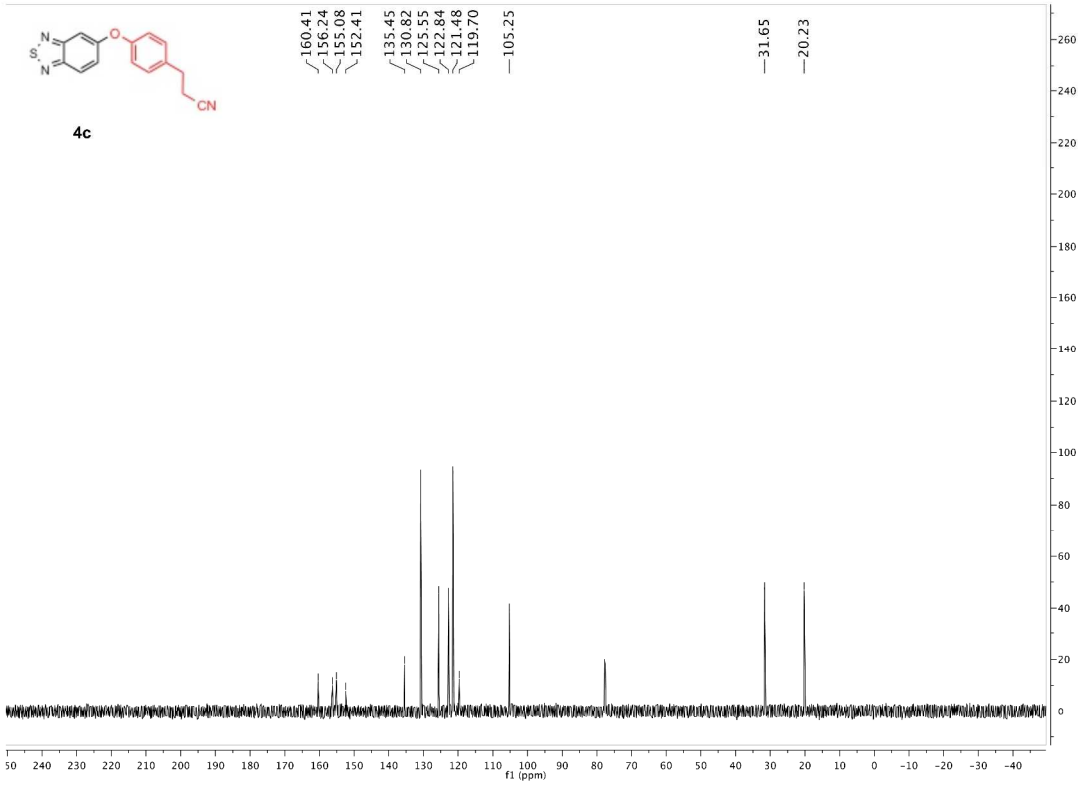

Me
O
NC
SMe
Me
4a
1.00
1.07
1.13
2.10
1.06
3.33
6.42
f1 (ppm)

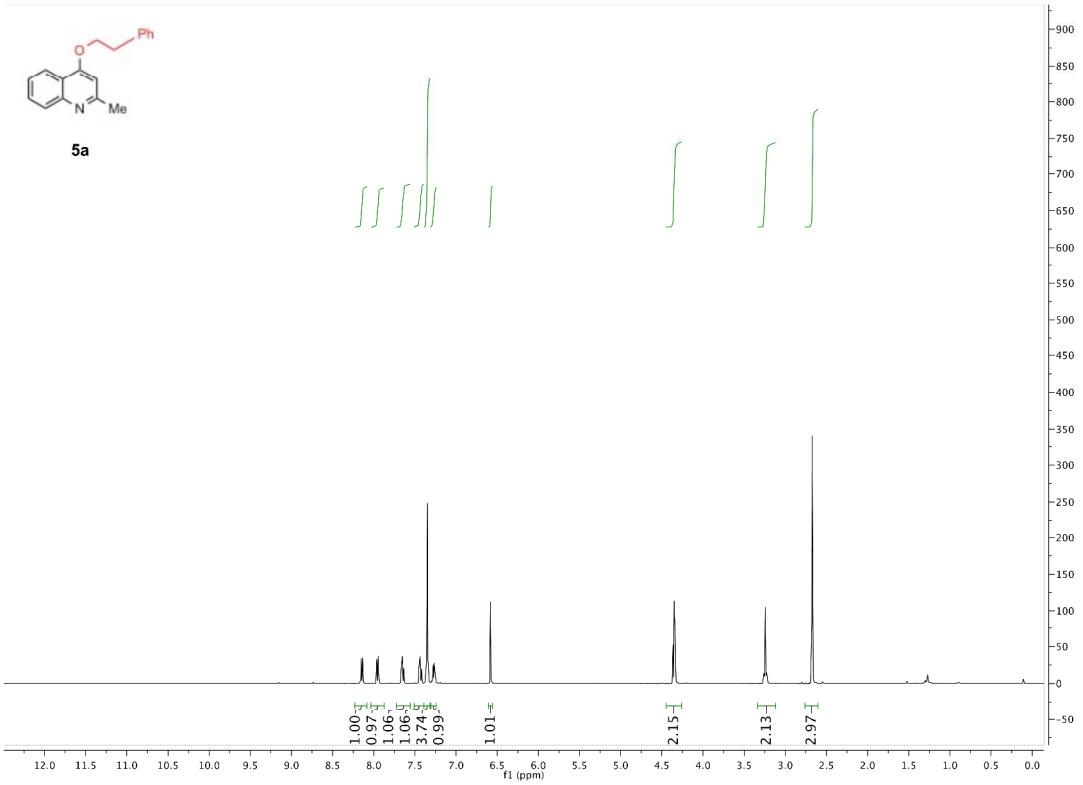

Me
O
NC
SMe
Me
4a
160.01
153.07
138.70
135.17
133.72
131.75
129.93
127.33
121.56
119.29
118.03
116.88
106.01
20.43
16.35
16.22
f1 (ppm)

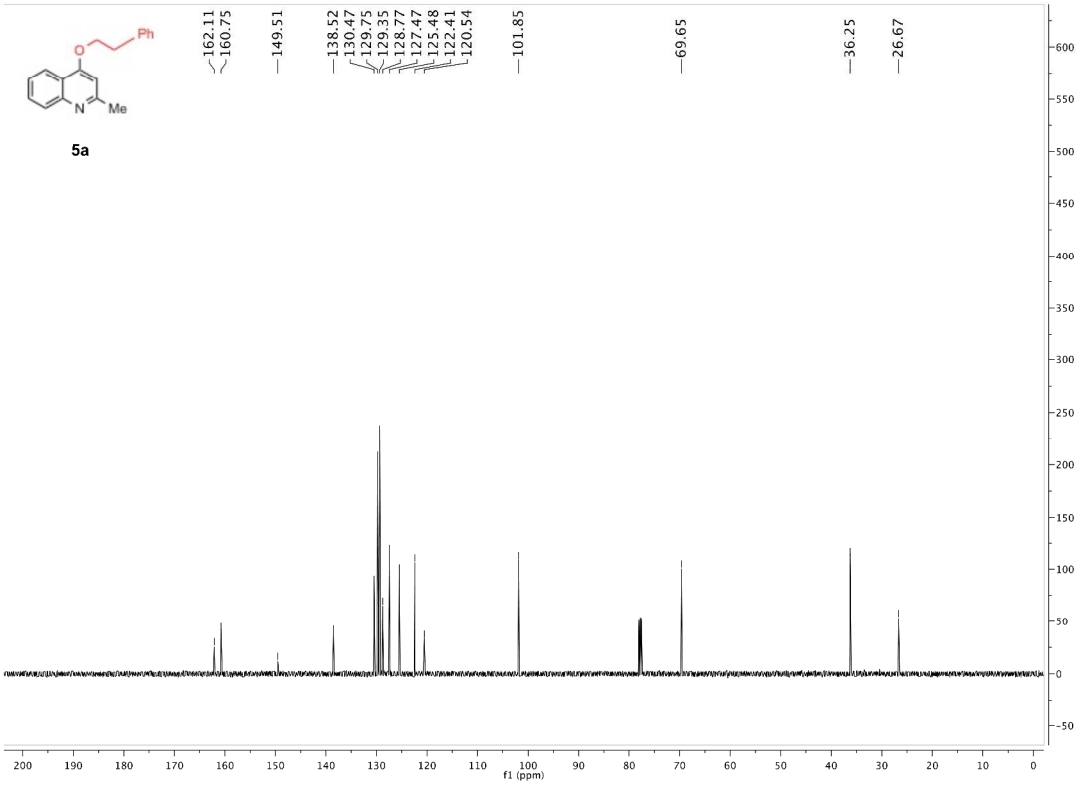

4b
1.00
1.99
2.06
6.20
3.03
f1 (ppm)

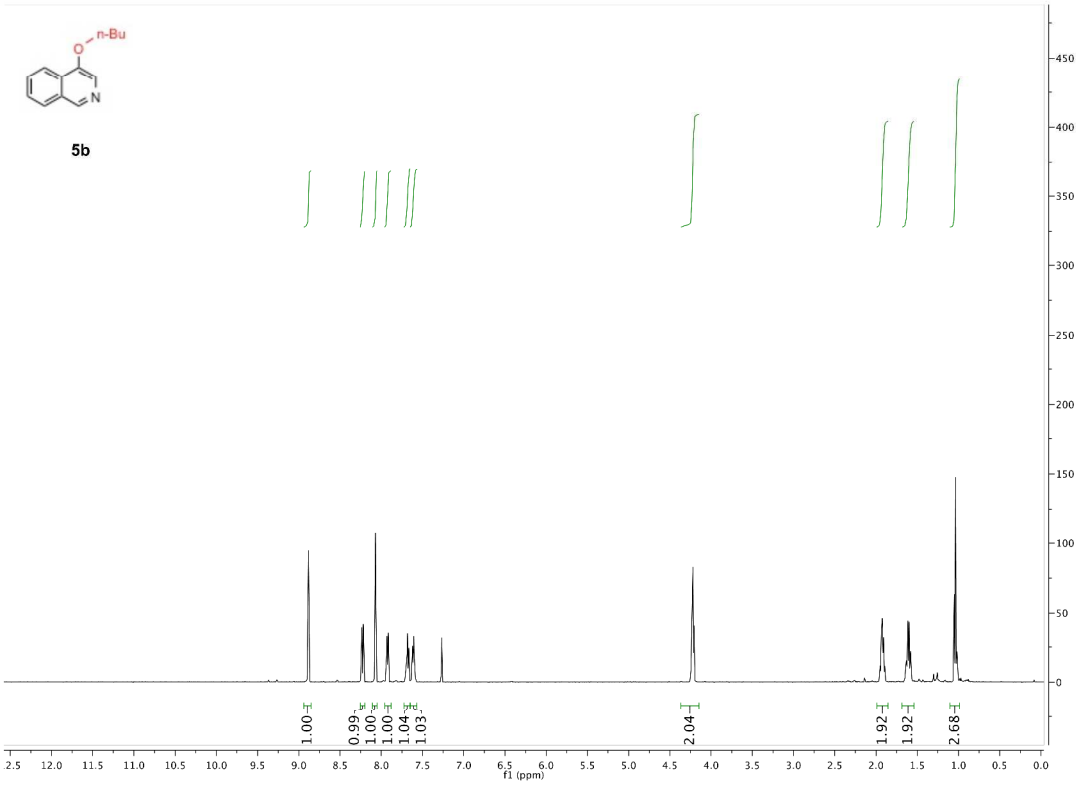

4b
153.57
153.34
152.83
147.19
139.39
132.72
118.91
21.47
15.63
f1 (ppm)

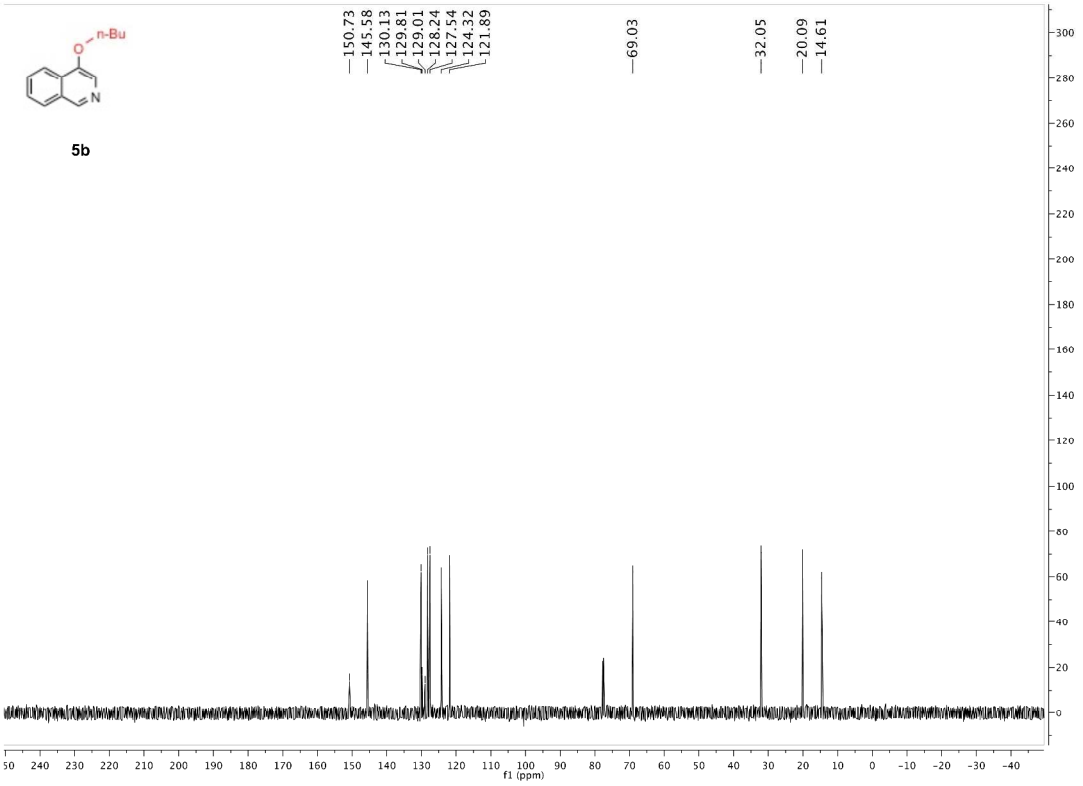

4c
1.00
1.03
2.12
0.89
2.07
2.28
2.24
f1 (ppm)

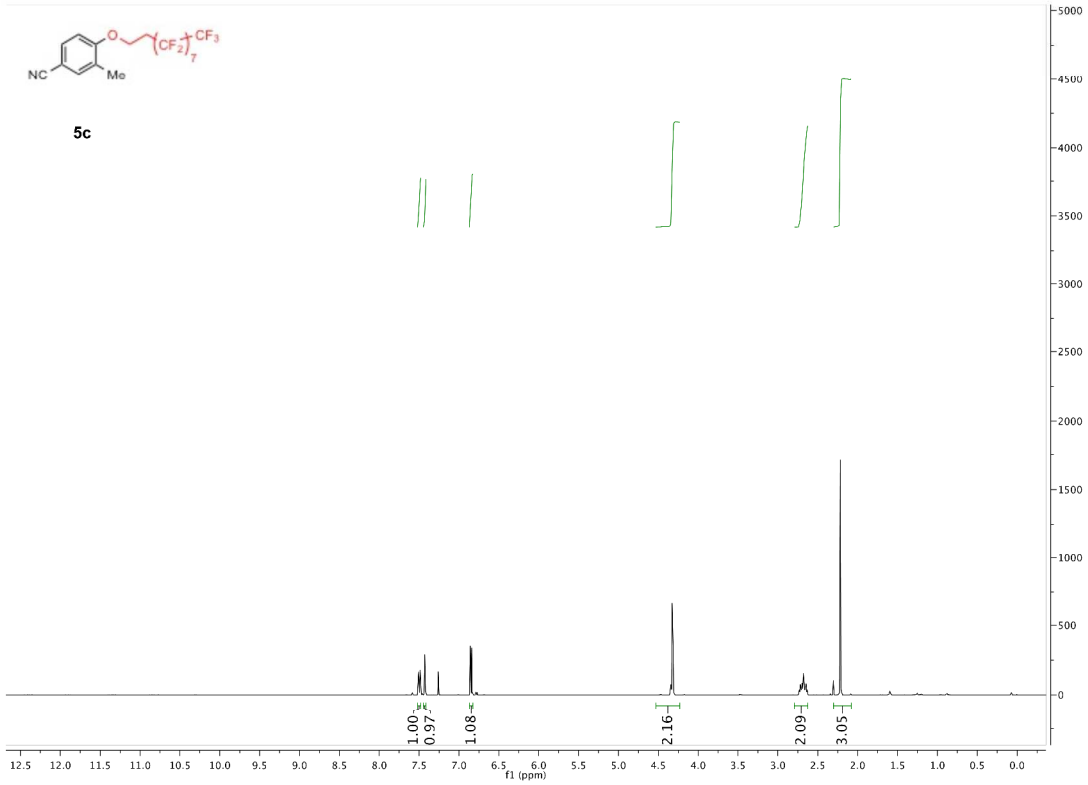

4c
160.41
156.24
155.08
152.41
135.45
130.82
125.55
122.84
121.48
119.70
105.25
31.65
20.23
f1 (ppm)

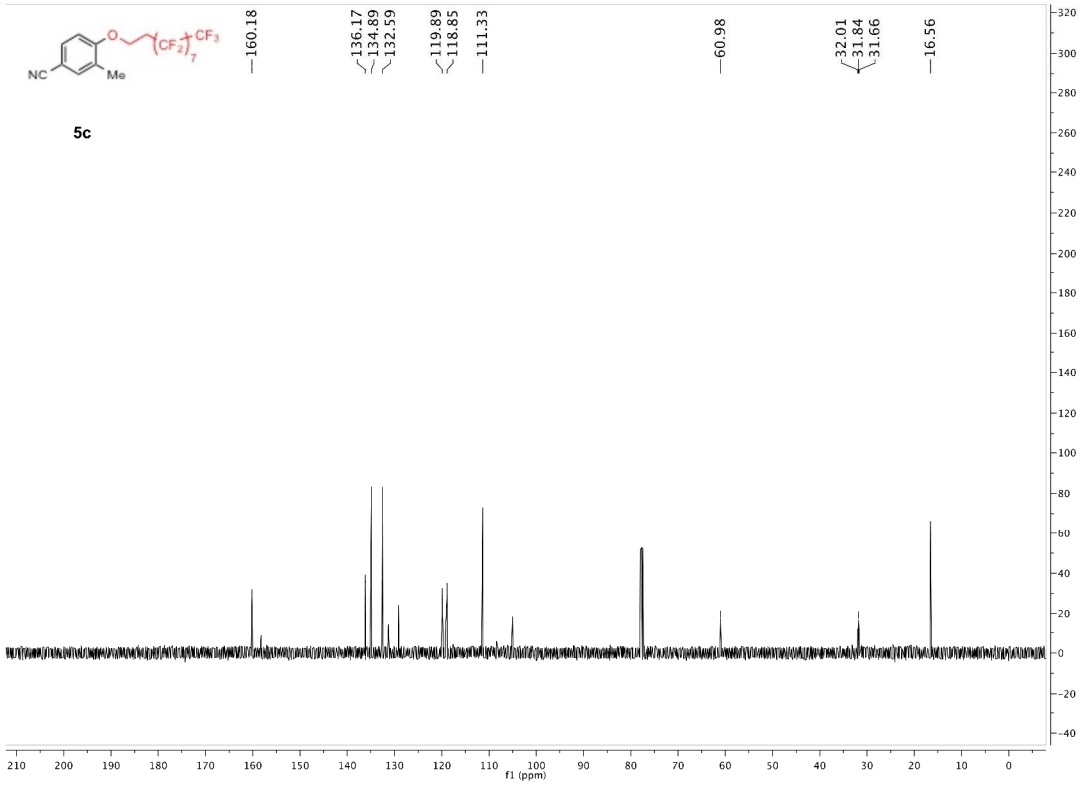

Ph
O
N
Me
5a
1.00
0.97
1.06
1.06
3.74
0.99
1.01
2.15
2.13
2.97
f1 (ppm)

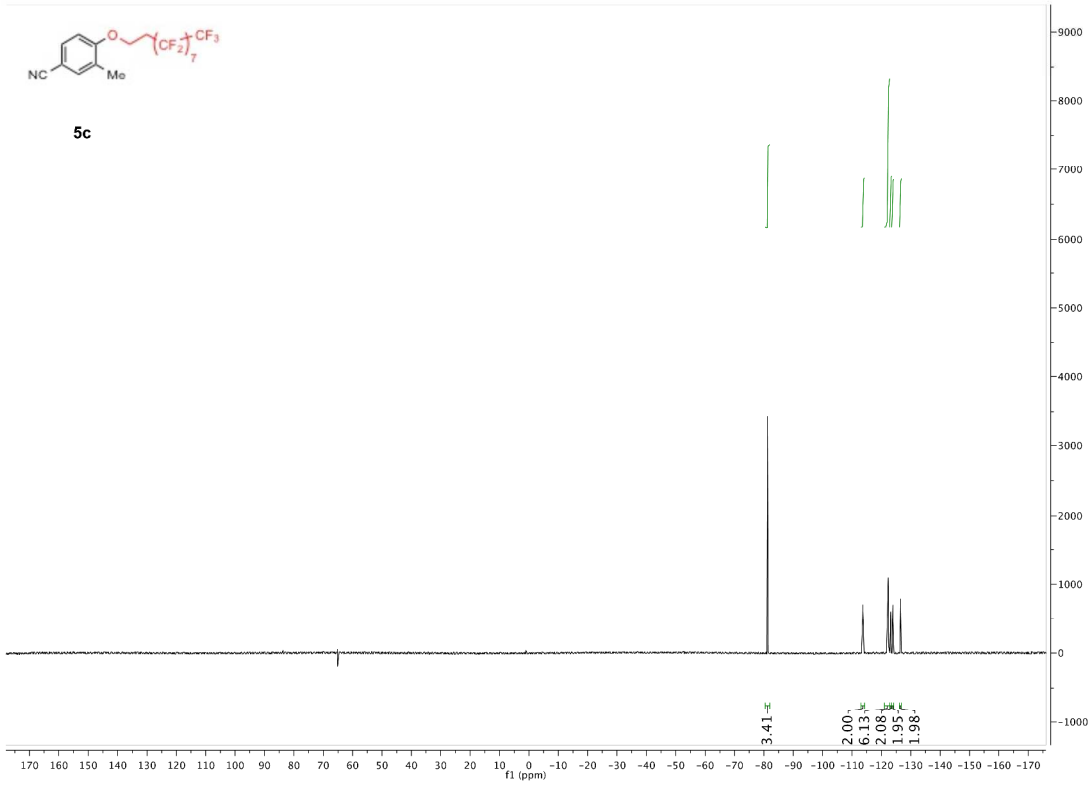

Ph
O
N
Me
5a
162.11
160.75
149.51
138.52
130.47
129.75
129.35
128.77
127.47
125.48
122.41
120.54
101.85
69.65
36.25
26.67
f1 (ppm)


n-Bu
O
N
5b
1.00
0.99
1.00
1.00
1.04
1.03
2.04
1.92
1.92
2.68
f1 (ppm)

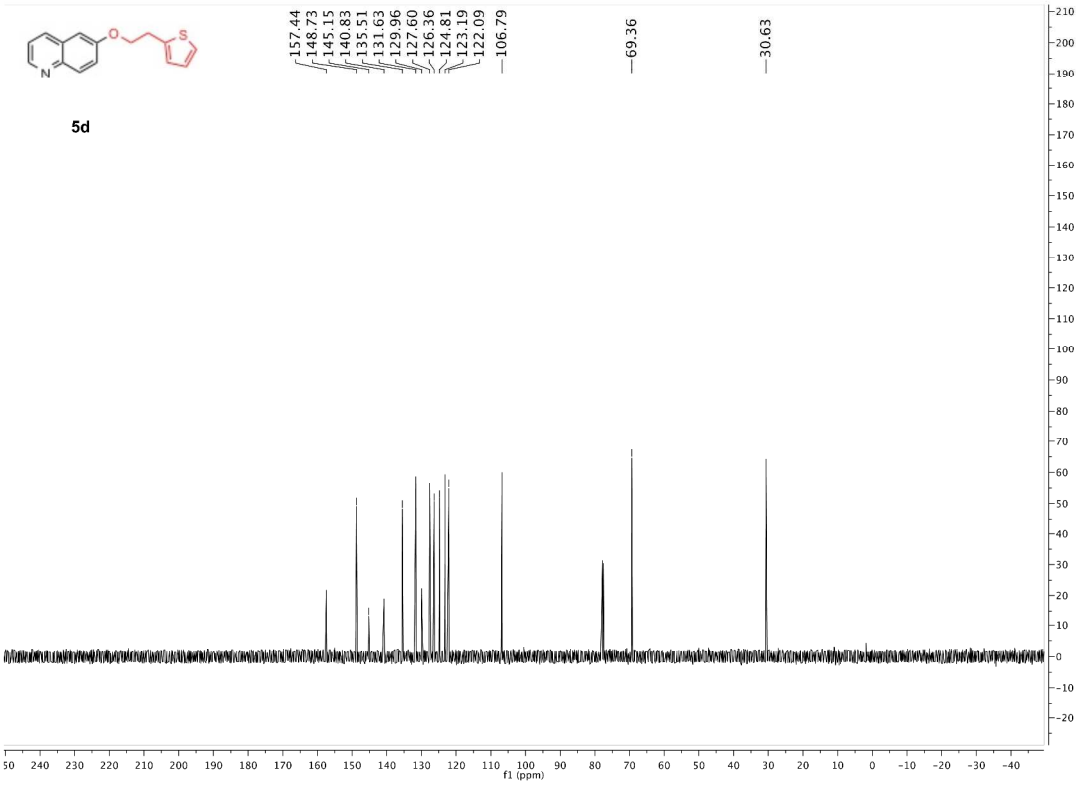

n-Bu
O
N
5b
150.73
145.58
130.13
129.81
129.01
128.24
127.54
124.32
121.89
69.03
32.05
20.09
14.61
f1 (ppm)

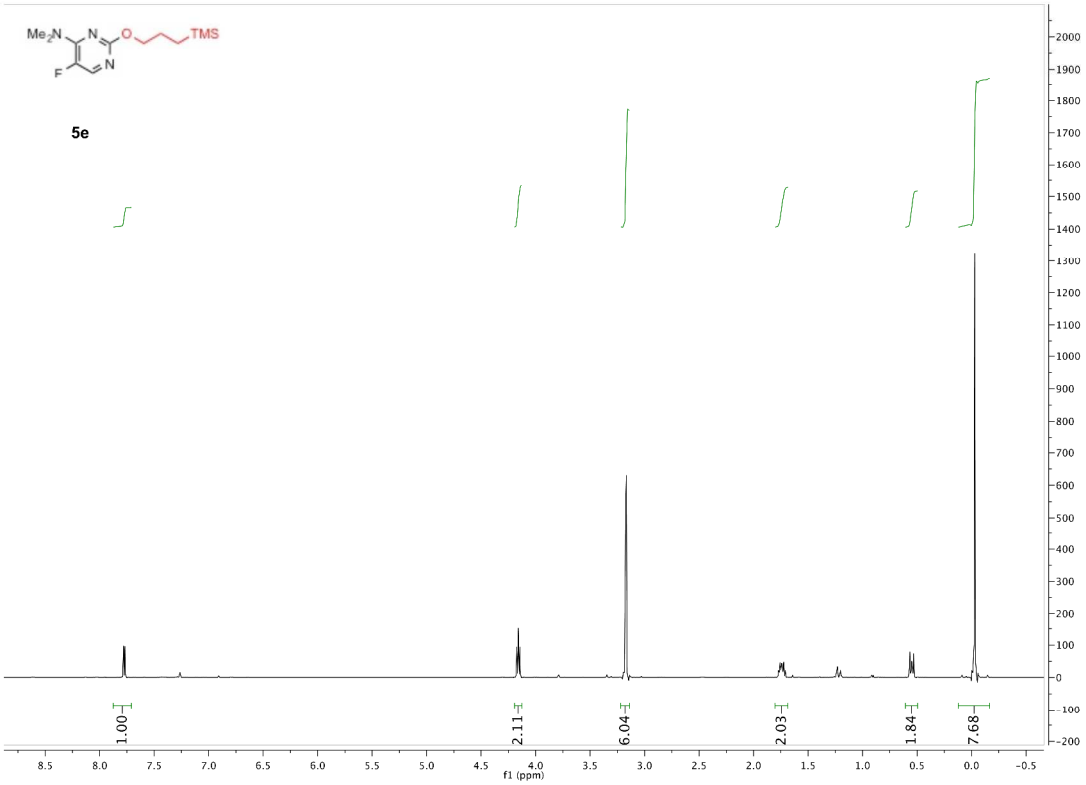

5c
1.00
0.97
1.08
2.16
2.09
3.05
f1 (ppm)

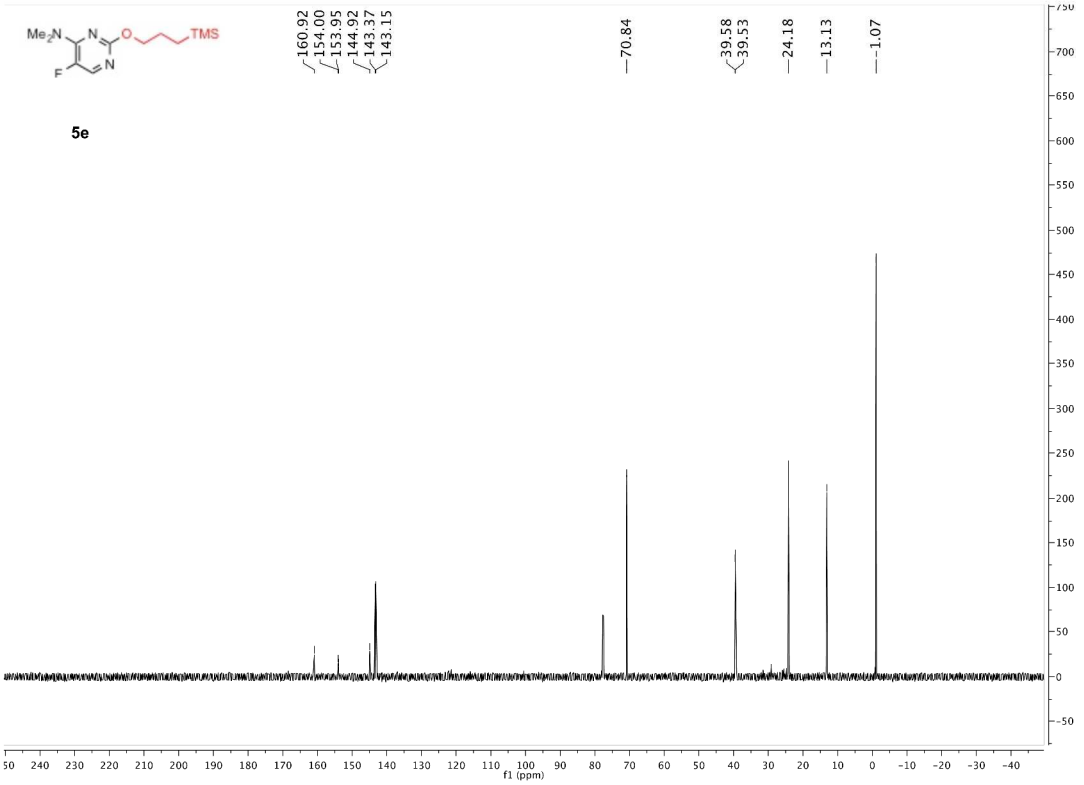

5c
160.18
136.17
134.89
132.59
119.89
118.85
111.33
60.98
32.01
31.84
31.66
16.56
f1 (ppm)

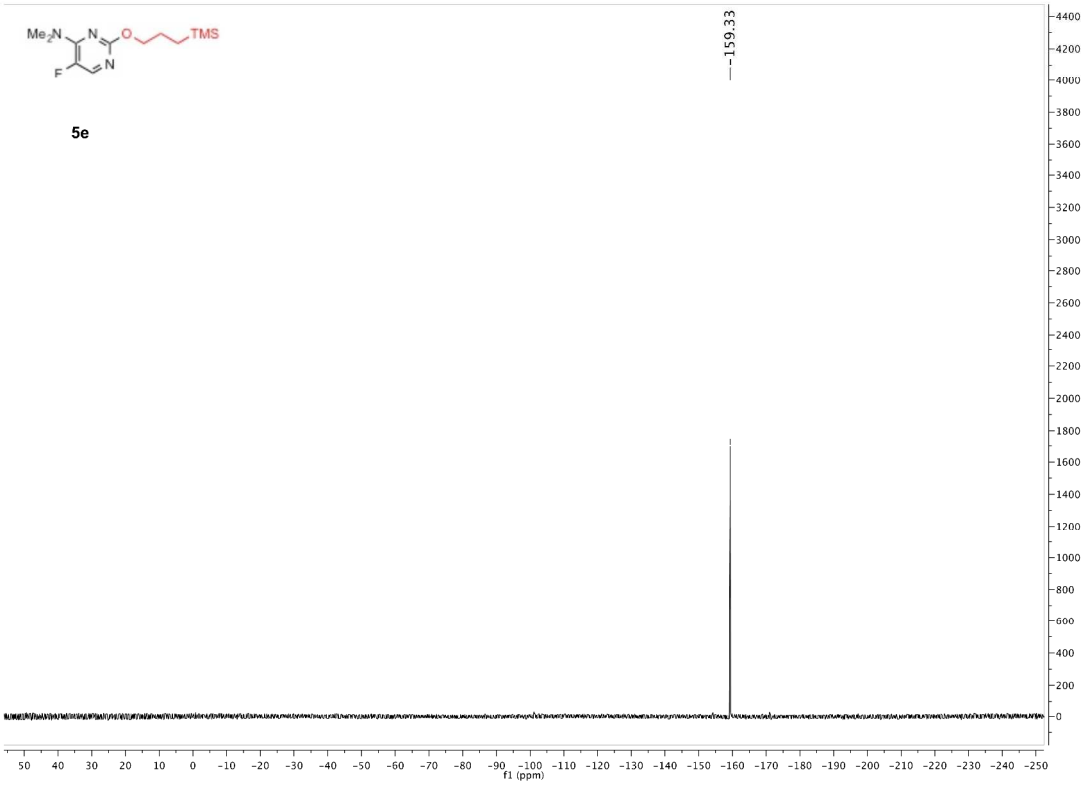

5c
3.41
2.00
6.13
2.08
1.95
1.98
f1 (ppm)

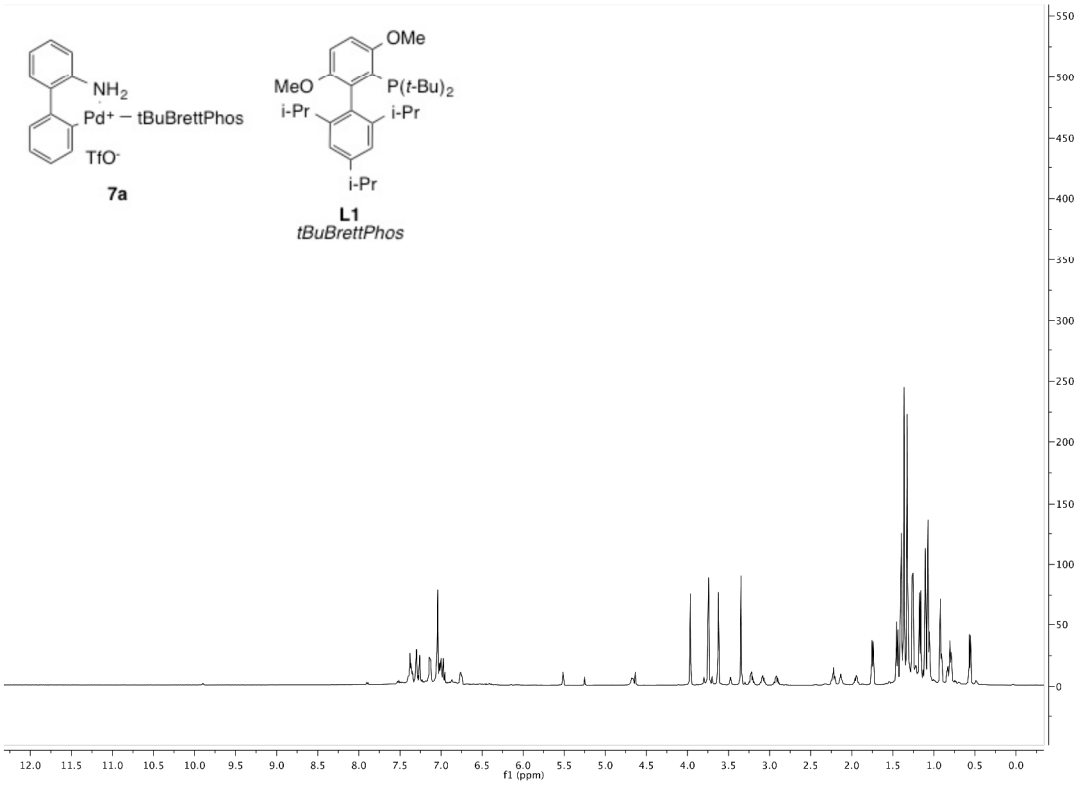

5d
1.00
2.13
1.00
1.14
0.96
1.13
2.13
2.28
2.29
f1 (ppm)

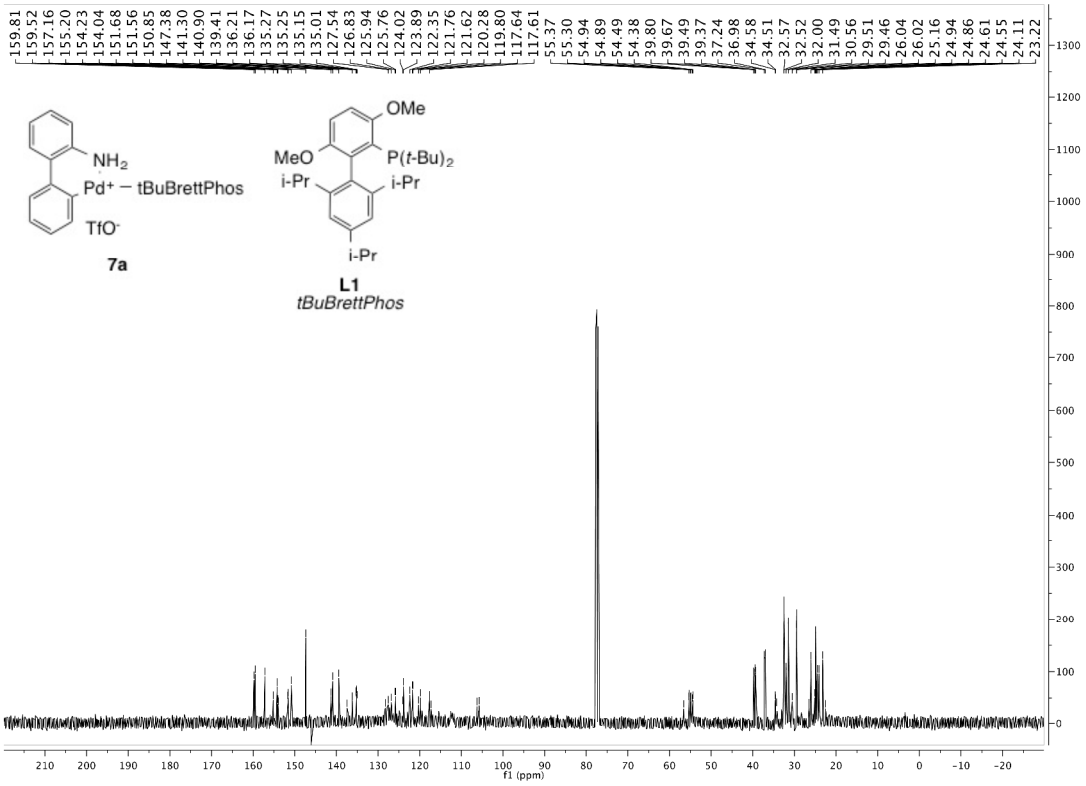

157.44
148.73
145.15
140.83
135.51
131.63
129.96
127.60
126.36
124.81
123.19
122.09
106.79
69.36
30.63
5d
f1 (ppm)

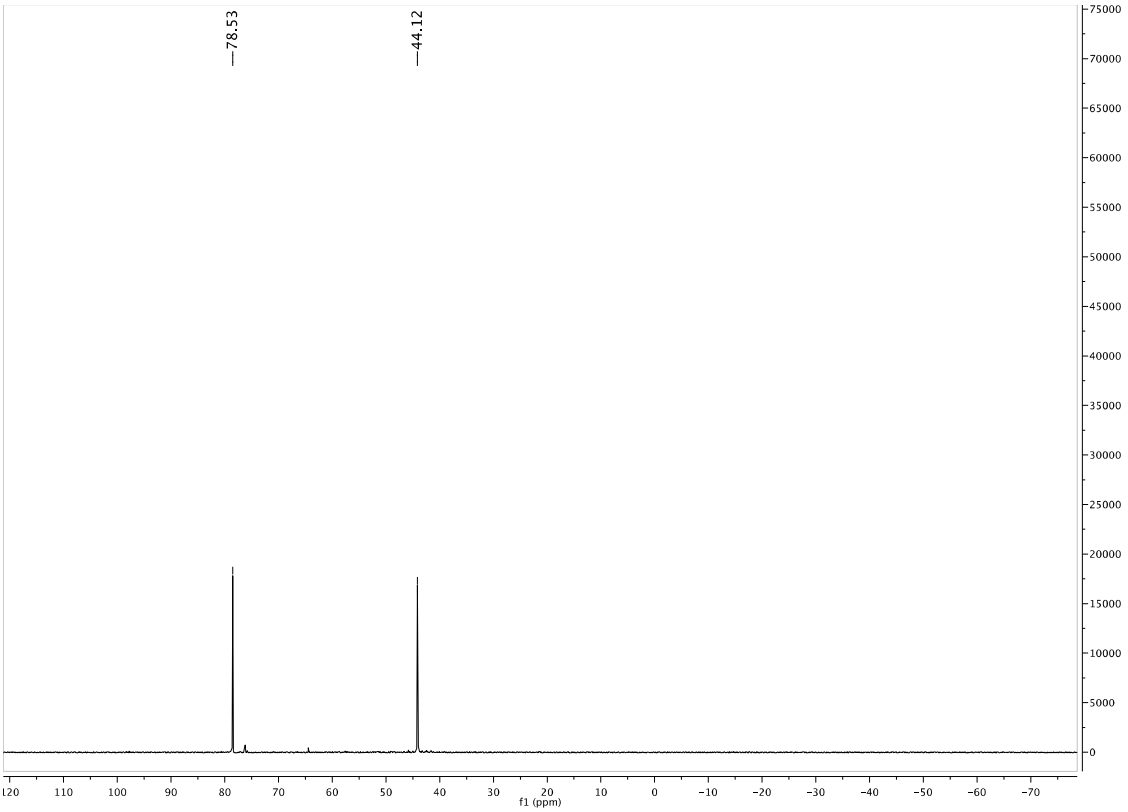

Me2N
TMS
F
5e
1.00
2.11
6.04
2.03
1.84
7.68
f1 (ppm)

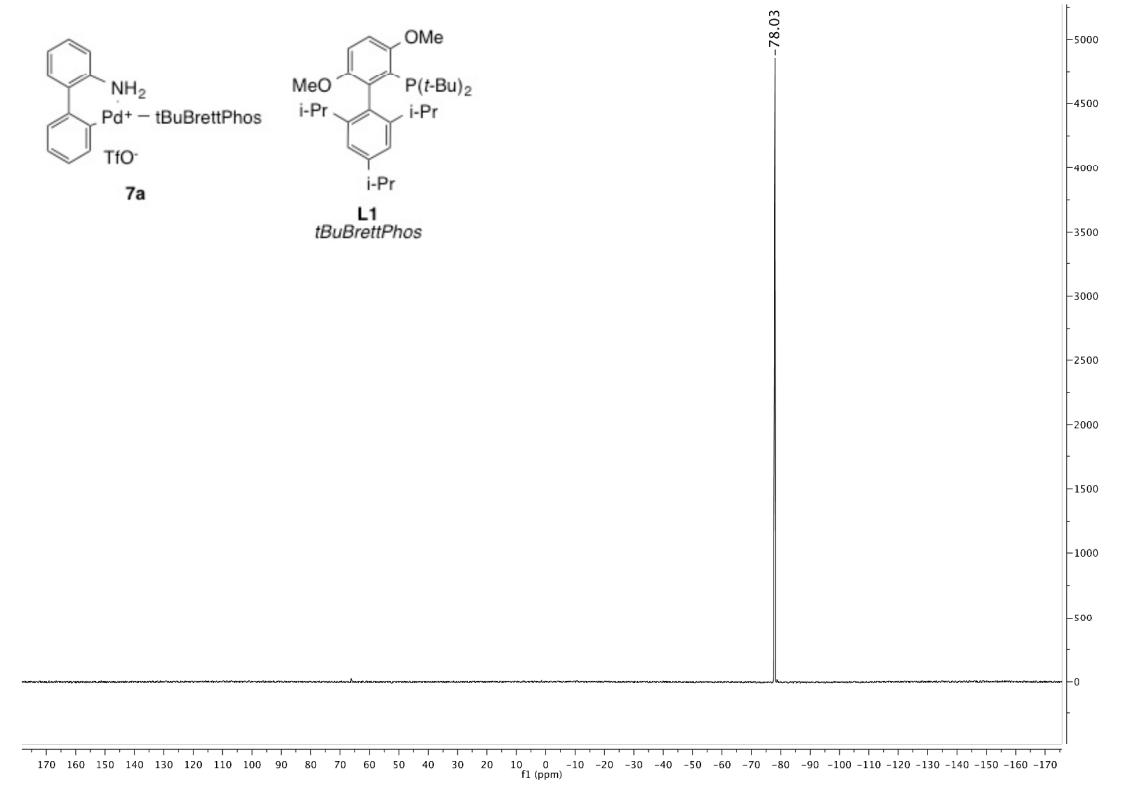

Me2N
N
O
TMS
F
N
160.92
154.00
153.95
144.92
143.37
143.15
70.84
39.58
39.53
24.18
13.13
1.07
5e
f1 (ppm)


Me2N
N
O
TMS
F
N
-159.33
5e
f1 (ppm)


NH2
Pd+ – tBuBrettPhos
TfO-
7a
OMe
MeO
P(t-Bu)2
i-Pr
i-Pr
i-Pr
L1
tBuBrettPhos
f1 (ppm)


159.81
159.52
157.16
155.20
154.23
154.04
151.68
151.56
150.85
147.38
141.30
140.90
139.41
136.21
136.17
135.27
135.25
135.15
135.01
127.54
126.83
125.94
125.76
124.02
123.89
122.35
121.76
121.62
120.28
119.80
117.64
117.61
55.37
55.30
54.94
54.89
54.49
54.38
39.80
39.67
39.49
39.37
37.24
36.98
34.58
34.51
32.57
32.52
32.00
31.49
30.56
29.51
29.46
26.04
26.02
25.16
24.94
24.86
24.61
24.55
24.11
23.22
NH2
Pd+ – tBuBrettPhos
TfO-
7a
OMe
MeO
P(t-Bu)2
i-Pr
i-Pr
i-Pr
L1
tBuBrettPhos
f1 (ppm)


78.53
44.12
f1 (ppm)


NH2
Pd+ – tBuBrettPhos
TfO-
7a
OMe
MeO
P(t-Bu)2
i-Pr
i-Pr
i-Pr
L1
tBuBrettPhos
78.03
f1 (ppm)