An Extremely Active Catalyst for the Negishi Cross-Coupling Reaction

Supporting Information

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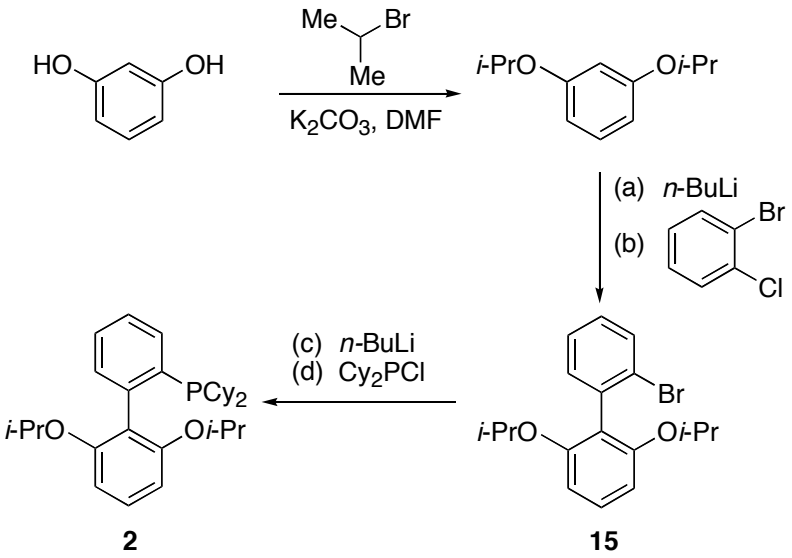
General. Unless otherwise noted all reactions were carried out under an argon or nitrogen atmosphere in oven-dried glassware. Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA. THF, Et_2O, CH_2Cl_2 and toluene were purchased from J.T. Baker in CYCLE-TAINER® solvent-delivery kegs and vigorously purged with argon for 2h. The solvents were further purified by passing them under argon pressure through two packed columns of neutral alumina (for THF and Et_2O) or through neutral alumina and copper (II) oxide (for toluene and CH_2Cl_2). Unless otherwise stated, commercially obtained materials were used without further purification. Aryl halides were purified by filtration through a thin pad of basic alumina prior to use. Zinc chloride, ultradry (H_2O, oxide, OH < 100ppm, 99.99%-Zn) PURATREM was purchased from Strem, stored and weighed out in the glove box.

All new compounds were characterized by ^1H NMR, ^{13}C NMR, and IR spectroscopy, in addition to elemental analysis (except **17f** and **17i**). Nuclear Magnetic Resonance spectra were recorded on either a 300 or 400 MHz instrument. All ^1H NMR experiments are reported in δ units, parts per million (ppm) downfield from tetramethylsilane (internal standard) and were measured relative to the signals for residual chloroform (7.27 ppm), DMSO (2.50 ppm) or benzene (7.16 ppm) in the deuterated solvents. All ^{13}C NMR spectra are reported in ppm relative to deuterochloroform (77.23 ppm), DMSO (39.51 ppm) or deuterobenzene (128.39 ppm), and all were obtained with ^1H decoupling. Infrared spectra were recorded on an ASI Applied Systems ReactIR 1000 (neat samples were placed directly on the DiComp probe). Melting points (uncorrected) were obtained on a Mel-Temp capillary melting point apparatus. Gas

Chromatographic analyses were performed on a Hewlett-Packard 6890 gas chromatography instrument with an FID detector using 25m x 0.20 mm capillary column with cross-linked methyl siloxane as a stationary phase.

The yields in Tables 1-3 refer to isolated yields (average of two runs) of compounds estimated to be ≥95% pure as determined by ^{1}H NMR and GC analysis and/or combustion analysis. The procedures described in this section are representative, and thus the yields may differ from those shown in Tables 1-3.

Preparation of Ligand 2



2 **15**

1,3-Diisopropoxybenzene[1] An oven-dried 500 mL round-bottomed flask equipped with a magnetic stirbar and a reflux condenser was charged with resorcinol (11.0 g, 100 mmol, 1 equiv.) and K_2CO_3 (55.2 g, 400 mmol, 4 equiv.), capped with a rubber septum, fitted with an argon inlet adapter, and then evacuated and backfilled with argon (this sequence was repeated three times). 2-Bromopropane (49.2 g, 37.7 mL, 400 mmol, 4 equiv.) and *N*,*N*-dimethylformamide (200 mL) were added and the reaction mixture was heated at 70 ºC for 24 h. The reaction mixture was then allowed to cool to room temperature, water (1 L) and diethyl ether (200 mL) were added and the layers were separated. The aqueous phase was extracted with diethyl ether (2 x 200 mL). The combined organic extracts were dried (Mg_2SO_4) and concentrated under reduced pressure. The crude product was purified by passage through a short plug of silica gel eluting with hexanes/EtOAc (9:1) until a yellow band reached the bottom of the column. The combined fractions were evaporated to yield 1,3-diisopropoxybenzene (18.5 g, 95%) as a colorless oil.[1]

2-(2',6'-Diisopropoxyphenyl)phenyldicyclohexylphosphine (2) An oven-dried 100 mL round-bottomed flask equipped with a magnetic stirbar and a reflux condenser was capped with a rubber septum, fitted with an argon inlet adapter, and then evacuated and backfilled with argon (this sequence was repeated three times). The reaction vessel was charged with 1,3-diisopropoxybenzene (1.5 g, 7.7 mmol, 1.1 equiv.), dry hexane (16 mL) and *n*-butyllithium (3.2 mL, 2.5 M solution in hexanes, 8.0 mmol, 1.2 equiv.). The reaction mixture was heated to reflux for 2.5 h (bath temperature of 80 ºC). Maintaining the reaction mixture at reflux, neat 2-bromochlorobenzene (0.8 mL, 6.8 mmol, 1.0 equiv) was added dropwise via syringe over 50 min with vigorous stirring. The resulting suspension was stirred at 80 °C for an additional 1 h. At this point the reaction mixture was cooled to room temperature. Analysis (GC) of a reaction aliquot (quenched by addition to ethanol) indicated that complete consumption of the 2-bromochlorobenzene and clean conversion to 2-bromo-2',6'-diisopropoxybiphenyl had occurred. Dry THF (16 mL) was added via syringe through the septum and the resulting reaction mixture was cooled to –78 ºC. *n*-Butyllithium (3.1 mL, 2.5 M solution in hexanes, 7.7 mmol, 1.1 equiv.) was added dropwise via syringe over 15 min. The resulting mixture was stirred at –78 °C for 1 h. Neat chlorodicyclohexylphosphine (1.5 mL, 6.8 mmol, 1.0 equiv) was then added via syringe. The reaction mixture was stirred at –78 °C for 1 h and then allowed to slowly warm to room temperature. The mixture was filtered through a pad of flash silica gel topped with a layer of celite, eluting with ethyl acetate (400 mL). The filtrate was concentrated under reduced pressure to provide a yellow solid. Recrystallization from ethanol provided (2.24 g, 71%) of **2** as a white solid, mp 123-124 ºC.

^{1}H NMR (400 MHz, C_6D_6) δ: 7.53 (d, J = 7.6 Hz, 1H), 7.30-7.14 (m, 4H), 6.49 (d, J = 8.3 Hz, 2H), 4.22 (sept, J = 6.0 Hz, 2H), 1.93-1.62 (m, 12H), 1.41-1.14 (m, 10H), 1.12 (d, J = 6.0 Hz, 6H), 0.96 (d, J = 6.0 Hz, 6H).

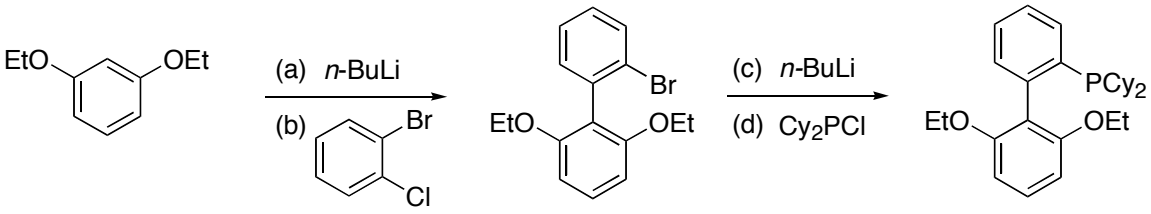
^{13}C NMR (100 MHz, C_6D_6) δ: 157.0, 144.7, 144.4, 137.8, 137.6, 132.4, 132.3, 131.9, 131.9, 126.4, 123.9, 123.9, 106.6, 70.3, 35.2, 35.0, 30.9, 30.8, 30.7, 30.6, 28.0, 28.0, 27.9, 27.3, 22.6, 22.3 (observed complexity due to P-C splitting; definitive assignments have not been made).

^{31}P NMR (121 MHz, C_6D_6) δ: –8.84.

IR (neat, cm^{-1}): 2919, 2848, 1594, 1461, 1447, 1380, 1246, 1135, 1113, 1061.

Anal. Calcd for $C_{30}H_{43}O_2P$: C, 77.22; H, 9.29. Found: C, 77.22; H, 9.41.

Preparation of Ligand 4



4

2-(2',6'-Diethoxyphenyl)phenyldicyclohexylphosphine (4) To a cold (0 °C) solution of 1,3-diethoxybenzene (2.5 g, 2.5 mL, 15.3 mmol, 1.1 equiv.) in dry THF (35 mL) was added *n*-butyllithium (6.20 mL, 2.5 M solution in hexanes, 15.5 mmol, 1.1 equiv.) dropwise via syringe over 5 min. The reaction mixture was allowed to warm to room temperature and then stirred at room temperature for 3.5 h. The mixture was recooled to 0 °C and neat 2-bromochlorobenzene (1.60 mL, 13.7 mmol, 1.0 equiv) was added dropwise via syringe over 15 min with vigorous stirring. The resulting burgundy colored mixture was stirred at 0 °C for an additional 15 min. At this point, GC analysis of a reaction aliquot (quenched by addition to ethanol) indicated that complete consumption of the 2-bromochlorobenzene and clean conversion to 2-bromo-2',6'-diethoxybiphenyl had occurred. The reaction mixture was cooled to -78 °C and *n*-butyllithium (6.20 mL, 2.5 M solution in hexanes, 15.5 mmol, 1.1 equiv.) was added dropwise via syringe over 5 min. The resulting mixture was stirred at -78 °C (periodic swirling of the reaction flask by hand was required as magnetic stirring became difficult) for 30 min. Neat chlorodicyclohexylphosphine (3.03 mL, 13.7 mmol, 1.0 equiv) was then added via syringe. The reaction mixture was stirred at -78 °C for 1 h and then allowed to slowly warm to room temperature. The mixture was filtered through a pad of flash silica gel topped with a layer of celite, eluting with ethyl acetate (400 mL). The filtrate was concentrated under reduced pressure to provide a yellow solid. Recrystallization from ethanol provided 2.4 g (40%) of **4** as a white solid, mp 107-108 °C.

^{1}H NMR (400 MHz, C_6D_6) δ: 7.55 (d, *J* = 7.6 Hz, 1H), 7.38 (ddd, *J* = 7.5, 3.4, 1.2 Hz, 1H), 7.25-7.14 (m, 3H), 6.46 (d, *J* = 8.4 Hz, 2H), 3.67 (q, J = 7.0 Hz, 4H), 1.91-1.60 (m, 12H), 1.36-1.09 (m, 10H), 0.99 (t, *J* = 7.0 Hz, 6H).

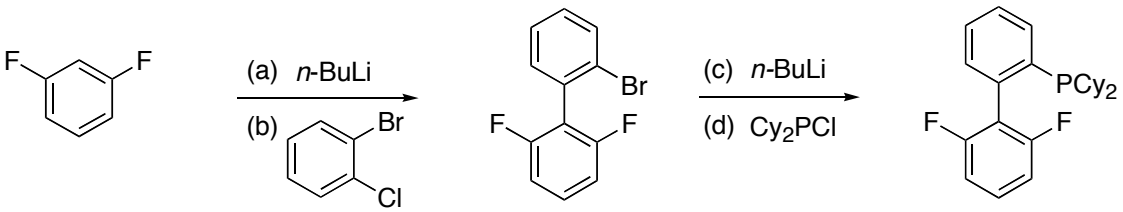
^{13}C NMR (100 MHz, C_6D_6) δ: 158.0, 144.5, 144.2, 137.4, 137.2, 132.5, 132.5, 132.3, 132.2, 129.0, 126.8, 121.6, 121.5, 104.7, 63.7, 35.0, 34.9, 30.9, 30.7, 30.6, 30.5, 28.2, 28.1, 28.1, 28.1, 27.4, 15.2 (observed complexity due to P-C splitting; definitive assignments have not been made).

^{31}P NMR (121 MHz, C_6D_6) δ: –10.4

IR (neat, cm^{-1}): 2979, 2926, 2862, 1688, 1469, 1389, 1241, 1121, 1088, 1003, 849.0.

Anal. Calcd for $C_{28}H_{39}O_2P$: C, 76.68; H, 8.96. Found: C, 76.60; H, 8.98.

Preparation of ligand 14



14

2-Bromo-2',6'-difluorobiphenyl To a cold (–78 °C), stirred solution of 1,3-difluorobenzene (1.5 mL, 15.3 mmol, 1.1 equiv.) in dry THF (35 mL) was added *n*-butyllithium (7.0 mL, 2.5 M solution in hexanes, 17.5 mmol, 1.1 equiv.) dropwise via syringe. The pale yellow reaction mixture was stirred for 1 h maintaining the reaction temperature at –78 ºC, then neat 2-bromochlorobenzene (1.60 mL, 13.7 mmol, 1.0 equiv) was added dropwise via syringe over 15 min with vigorous stirring. The resulting mixture was stirred at -78 °C for 1 h, then allowed to slowly warm to room temperature. The reaction was quenched by the addition of methanol (1 mL) and concentrated under reduced pressure. To the acquired residue was added diethyl ether (30 mL) and water (30 mL). The layers were separated and the aqueous phase extracted with diethyl ether (2 x 30 mL). The combined organic layers were dried (Mg_2SO_4) and

concentrated to provide a colourless oil. The crude product was purified by column chromatography on silica gel (hexanes) to provide 2-bromo-2',6'-difluorobiphenyl (2.6 g, 66%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.72 (dd, *J* = 8.0, 0.7 Hz, 1H), 7.42-7.22 (m, 4H), 7.00 (dd, *J* = 8.2, 7.2 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.4, 161.4, 159.0, 158.9, 133.0, 132.2, 131.1, 130.3, 130.2, 130.1, 130.0, 127.4, 124.6, 111.7, 111.6, 111.5, 111.4 (observed complexity due to F-C splitting; definitive assignments have not been made).

IR (neat, cm^{-1}): 2979, 2873, 1680, 1627, 1466, 1432, 1276, 1233, 1142, 1030, 1003.

Anal. Calcd for $C_{12}H_7BrF_2$: C, 53.56; H, 2.62. Found: C, 53.89; H, 2.69.

2-(2',6'-Difluorophenyl)phenyldicyclohexylphosphine (14) To a solution of 2-Bromo-2',6'-difluorobiphenyl (1.94 g, 7.2 mmol, 1 equiv.) in THF (20 mL) at -78 °C, *n*-butyllithium (3.40 mL, 2.5 M solution in hexanes, 7.2 mmol, 1.1 equiv.) was added dropwise via syringe over 5 min. The resulting mixture was stirred at -78 °C for 30 min. Neat chlorodicyclohexylphosphine (1.6 mL, 7.2 mmol, 1.0 equiv) was added dropwise via syringe. The resulting mixture was stirred at -78 °C for 1 h, then allowed to slowly warm to room temperature. The reaction was quenched by the addition of methanol (1 mL), then filtered through a pad of flash silica gel topped with a layer of celite, eluting with ethyl acetate (400 mL) and concentrated under reduced pressure to give a white solid. Recrystallization from ethanol provided 1.82 g (65%) of 2-(2',6'-difluorophenyl)phenyldicyclohexylphosphine as a white solid, mp = 131-134 °C.

^{1}H NMR (400 MHz, C_6D_6) δ: 7.51 (d, *J* = 7.5 Hz, 1H), 7.21-7.08 (m, 3H), 6.80-6.71 (m, 1H), 6.70-6.62 (t, *J* = 7.3 Hz, 2H), 1.85-1.45 (m, 12H), 1.28-0.90 (m, 10H).

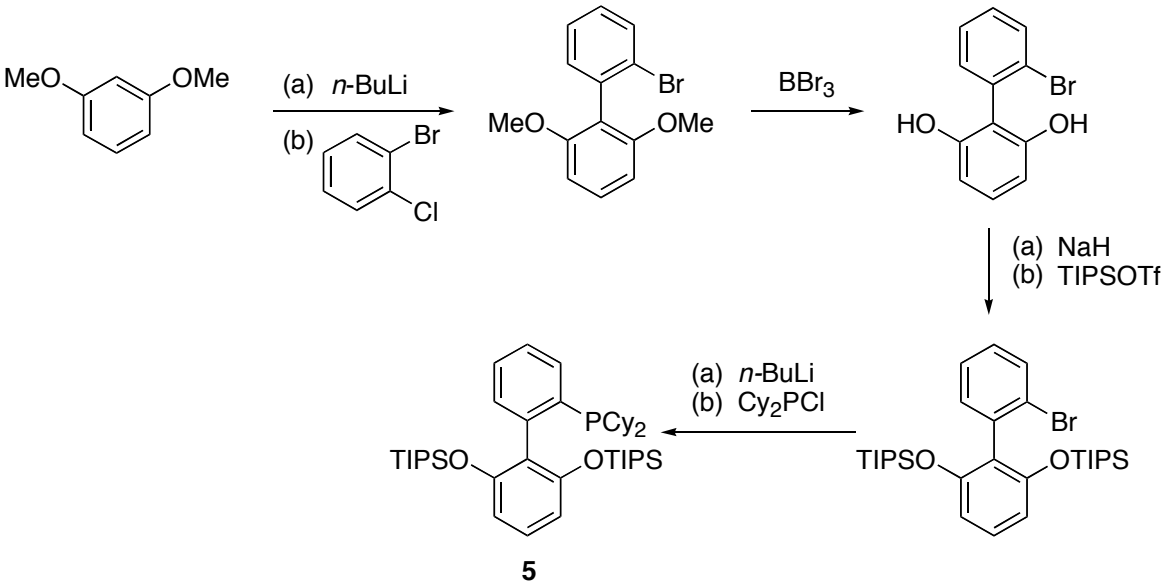
^{13}C NMR (100 MHz, C_6D_6) δ: 162.2, 162.2, 159.8, 159.7, 138.9, 138.6, 137.6, 137.4, 133.6, 133.5, 131.7, 131.6, 129.7, 129.6, 129.5, 129.3, 111.6, 111.5, 111.4, 111.3, 34.9, 34.8, 31.1, 30.9, 29.7, 29.6, 28.0, 27.8, 27.8, 27.1 (observed complexity due to P-C and F-C splitting; definitive assignments have not been made).

^{31}P NMR (121 MHz, C_6D_6) δ: –9.5 (t, J = 23.7 Hz).

IR (neat, cm^{-1}): 2923, 2862, 1682, 1626, 1466, 1447, 1266, 1231, 1133, 997.6.

Anal. Calcd for $C_{24}H_{29}F_2P$: C, 74.59; H, 7.56. Found: C, 74.52; H, 7.69.

Preparation of ligand 5



5

2-Bromo-2',6'-dimethoxybiphenyl To a cold (0 °C), stirred solution of 1,3-dimethoxybenzene (2.00 mL, 15.3 mmol, 1.2 equiv.) in dry THF (30 mL) was added *n*-butyllithium (9.60 mL, 1.6 M solution in hexanes, 15.4 mmol, 1.2 equiv.) dropwise via syringe over 5 min. The reaction mixture was allowed to warm to room temperature and then stirred at room temperature for 5 h. The mixture was recooled to 0 °C and neat 2-bromochlorobenzene (1.50 mL, 12.8 mmol, 1.0 equiv) was added dropwise via syringe over 15 min with vigorous stirring. The resulting burgundy colored mixture was stirred at 0 °C for an additional 15 min. Methanol (0.25 mL) was added via syringe and the resulting mixture was concentrated under reduced pressure. To the acquired residue was added diethyl ether (50 mL) and water (50 mL). The layers were separated and the aqueous phase was extracted with diethyl ether (2 x 25 mL). The combined organic

extracts were washed with brine (1 x 20 mL), dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to provide a yellow solid. The crude product was recrystallized from methanol to afford the title compound (3.03 g, 81% yield) as a pale yellow solid, mp = 141-142 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.69 (dd, *J* = 6.9, 1.1 Hz, 1H), 7.34-7.40 (m, 2H), 7.20-7.28 (m, 2H), 6.68 (d, *J* = 8.5 Hz, 2H), 3.76 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ: 157.8, 136.25, 132.52, 132.47, 129.6, 128.8, 127.1, 125.4, 119.0, 104.2, 56.2.

IR (neat, cm^{-1}): 2946, 1584, 1472, 1432, 1248, 1108, 1025, 783.

Anal. Calcd for $C_{14}H_{13}BrO_2$: C, 57.36; H, 4.47. Found: C, 57.11; H, 4.47.

2-Bromobiphenyl-2',6'-diol To a solution of 2-bromo-2',6'-dimethoxybiphenyl (0.59 g, 2 mmol, 1 equiv.) in CH_2Cl_2 (60 mL) at 0 ºC, boron tribromide (10 mL, 1 M in hexanes, 10 mmol) was added dropwise over 10 min via syringe. The reaction mixture was allowed to slowly warm to room temperature. After stirring for 4 h, methanol (1 mL) was added and the reaction was concentrated under reduced pressure to give the crude product. The product was purfied by column chromatography silica (hexanes/EtOAc gradient, 5:1 to 4:1) to give 2-bromobiphenyl-2',6'-diol (0.492 g, 93%) as a colorless solid, mp 156-158 ºC.

^{1}H NMR (400 MHz, DMSO) δ: 9.14 (s, 2H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.35 (dd, *J* = 7.8, 7.0 Hz, 1H), 7.23-7.16 (m, 2H), 6.95 (t, *J* = 8.0 Hz, 1H), 6.38 (d, *J* = 8.0 Hz, 2H).

^{13}C NMR (100 MHz, DMSO) δ: 155.6, 137.1, 132.8, 131.9, 128.7, 128.4, 127.0, 125.1, 115.7, 106.2.

IR (neat, cm^{-1}): 3426 (br), 2979, 2883, 1690, 1619, 1469, 1362, 1361, 1304, 1283, 1177, 1148, 1096, 1066, 1001.

Anal. Calcd for $C_{12}H_9BrO_2$: C, 54.37; H, 3.42. Found: C, 54.63; H, 3.43.

2-(2',6'-Di(triisopropylsilanyloxy)phenyl)phenyldicyclohexylphosphine (5) To a solution of 2-bromobiphenyl-2',6'-diol (0.5 g, 1.9 mmol, 1 equiv.) in THF (20 mL), NaH (0.54 g, 50% dispersion in oil, 11.3 mmol, 6 equiv.) was added in 5 portions at 0 ºC. After 15 min and maintaining the reaction temperature at 0 ºC, triisopropylsilyl trifluoromethanesulfonate (3 mL, 11.3 mmol, 6 equiv.) was added dropwise. The flask was removed from the ice bath and stirred at room temperature. Once the protection was complete (3 h), $NaHCO_3$ was carefully added followed by EtOAc (30 mL). The layers were separated and the aqueous phase was extracted with ethyl acetate (2 x 30 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure and passed through a short silica column (eluting with hexanes). The filtrate was concentrated under reduced pressure to provide crude 2-bromo-2',6'-di(triisopropylsilanyloxy)biphenyl as a colourless oil, which was dissolved in THF (12 mL) and cooled to –78 ºC. *n*-Butyllithium (0.84 mL, 2.5 M solution in hexanes, 2.1 mmol, 1.1 equiv.) was added dropwise and the resulting mixture was stirred at –78 ºC for 1 h. Maintaining the reaction temperature at –78 ºC, neat chlorodicyclohexylphosphine (0.42 mL, 1.9 mmol, 1.0 equiv) was then added via syringe. The reaction mixture was stirred at -78 °C for 1 h and then allowed to slowly warm to room temperature. The mixture was filtered through a pad of flash silica gel topped with a layer of celite, eluting with ethyl acetate (400 mL). The filtrate was concentrated under reduced pressure to give a colorless oil. The crude product was dissolved in hot ethanol, on cooling a white solid **5** (0.8 g, 62%) was collected, mp. = 126-127 ºC.

^{1}H NMR (400 MHz, C_6D_6) δ: 7.54 (d, *J* = 7.2 Hz, 1H), 7.39-7.34 (m, 1H), 7.24-7.14 (m, 2H), 7.00 (t, *J* = 8.2 Hz, 1H), 6.57 (d, *J* = 8.2 Hz, 2H), 1.92-1.62 (m, 12H), 1.38-1.10 (m, 16H), 0.99 (d, *J* = 5.5 Hz, 18H), 0.97 (d, *J* = 7.3 Hz, 18H).

^{13}C NMR (100 MHz, C_6D_6) δ: 155.3, 144.9, 144.6, 138.6, 138.4, 133.0, 133.0, 131.7, 131.6, 126.8, 126.4, 126.3, 112.3, 34.7, 34.5, 31.5, 31.3, 30.4, 30.3, 28.2, 28.2, 28.1, 28.1, 27.4, 18.7, 18.6, 13.5 (observed complexity due to P-C splitting; definitive assignments have not been made).

^{31}P NMR (121 MHz, C_6D_6) δ: –9.5.

IR (neat, cm^{-1}): 2939, 2923, 2869, 1671, 1467, 1331, 1301, 1246, 1142, 1069, 1016, 999.6.

Anal. Calcd for $C_{42}H_{71}O_2PSi_2$: C, 72.57; H, 10.29. Found: C, 72.65; H, 10.52.

General Procedure A: Pd-Catalyzed Negishi Couplings of Aryl Halides and Aryl Zinc Chlorides.

An oven-dried resealable Schlenk tube containing a magnetic stir bar was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was repeated three times). The Schlenk tube was charged with the aryl bromide (0.75 mmol, 1.5 equiv.) and dry THF (1.0 mL). The resulting solution was cooled to –78 ºC then *n*-butyllithium (0.825 mmol, 1.65 equiv.) was added dropwise *via* syringe through the septum and stirred at –78 ºC for 1 h. $ZnCl_2$ (0.9 mmol, 1.8 equiv.) was added in one solid portion by removal of the septum. After 30 min at –78 ºC, the Schlenk tube was removed from the cooling bath and the resulting solution stirred at room temperature for 1 h. $Pd_2(dba)_3$ (2.3 mg, 0.5 mol%), **2** (4.7 mg, 2.0 mol%) and the aryl chloride (0.5 mmol, 1.0 equiv.) were added with the aid of THF (0.5 mL) which was used to rinse the walls of the tube. The septum was replaced with a teflon screwcap and the Schlenk tube was sealed. The reaction mixture was placed in a preheated oil bath at 70 °C and magnetically stirred until the aryl halide had been completely consumed as judged by GC analysis. The reaction mixture was then cooled to room temperature, diluted with water (1 mL) and extracted with diethyl ether (4 x 10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel.

General Procedure B: Pd-Catalyzed Negishi Couplings of Aryl Halides and Aryl Zinc Chlorides at Low Catalyst Loading (≤0.5% Pd).

Procedure A was used with the following changes: A separate vial was charged with $Pd_2(dba)_3$ (2.3 mg, 0.5 mol%) and **2** (4.7 mg, 2.0 mol%). The vial was sealed with a teflon coated screwcap, a needle was

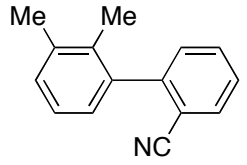
inserted through the cap and purged with argon. Dry THF (2 mL) was added and the mixture was sonicated for ~1 min to afford a homogeneous solution. The required quantity of catalyst solution (e.g., 20μL for reactions carried out at 0.01% Pd) was added to the reaction mixture.

General Procedure C: Pd-Catalyzed Negishi Couplings of Aryl Halides and Aryl Zinc Chlorides to Generate Hindered Biaryls.

Procedure A was used with the following changes: after the addition of the catalyst and the aryl halide, NMP (1.0 mL) was used to the rinse the walls of the tube. The septum was replaced with a teflon screwcap and the Schlenk tube was sealed. The reaction mixture was placed in a preheated oil bath at 100 °C and magnetically stirred until the aryl halide had been completely consumed as judged by GC analysis.

General Procedure D: Pd-Catalyzed Negishi Couplings of Aryl Halides and Aryl Zinc Chlorides to Generate Biaryls Combining a Directed-ortho-Metalation Approach.

Procedure A was used with the following changes to the preparation of the aryl zinc species: To a cold (0 °C), stirred solution of 1,3-dimethoxybenzene (98 μL, 0.75 mmol) in dry THF (1 mL) was added *n*-butyllithium (0.33 mL, 2.5 M in hexanes, 0.825 mmol) dropwise via syringe over 10 min. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. The aryllithium was cooled to –78 ºC and $ZnCl_2$ (0.9 mmol, 1.8 equiv.) was added in one solid portion by removal of the septum. After 30 min at –78 ºC, the reaction was removed from the cooling bath and the resulting solution stirred at room temperature for 1 h.



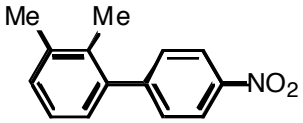
2-Cyano-2',3'-dimethylbiphenyl (3a) Following general procedure B, a mixture of 2,3-dimethylphenylzinc chloride (0.75 mmol) and 2-chlorobenzonitrile (69 mg, 0.5 mmol) was converted to product **3a**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 1:0 to 100:1) to provide the title compound as a colorless solid (104 mg, 100%), mp 80-81 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (dd, J = 7.8, 1.0 Hz, 1H), 7.64 (td, J = 7.7, 1.4 Hz, 1H), 7.46 (td, J = 7.7, 1.2 Hz, 1H), 7.38 (dd, J = 7.8, 0.6 Hz, 1H), 7.25 (d, J = 7.3 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.07 (d, J = 7.4 Hz, 1H), 2.36 (s, 3H), 2.09 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 146.6, 138.3, 137.5, 134.4, 132.8, 132.5, 130.7, 130.4, 127.5, 127.4, 125.6, 118.3, 113.1, 20.7, 16.8.

IR (neat, cm^{-1}): 3062, 2917, 2360, 1586, 1466, 1443, 1385, 1262.

Anal. Calcd for $C_{15}H_{13}O$: C, 86.92; H, 6.32. Found: C, 86.76; H, 6.35.



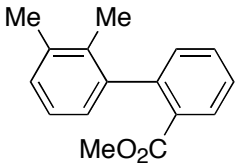
2,3-Dimethyl-4'-nitrobiphenyl (3b) Following general procedure B, except at room temperature, a mixture of 2,3-dimethylphenylzinc chloride (0.75 mmol) and 1-chloro-4-nitrobenzene (79 mg, 0.5 mmol) was converted to product **3b**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient) to provide the title compound as a colorless solid (107 mg, 94%), mp 93-95 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J = 8.8 Hz, 2H), 7.48 (d, J = 8.8 Hz, 2H), 7.24 (d, J = 7.2 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 7.07 (d, J = 7.2 Hz, 1H), 2.37 (s, 3H), 2.16 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 149.7, 146.9, 140.1, 137.9, 133.9, 130.5, 130.2, 127.4, 125.8, 123.5, 20.8, 17.2.

IR (neat, cm^{-1}): 2925, 1598, 1515, 1466, 1345, 1312, 1287.

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77. Found: C, 74.18; H, 5.86.



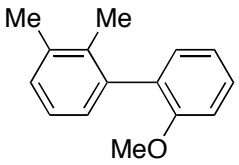
2-Carbomethoxy-2',3'-dimethylbiphenyl (3c) Following general procedure B, a mixture of 2,3-dimethylphenylzinc chloride (0.75 mmol) and methyl 2-chlorobenzoate (72 μL, 0.5 mmol) was converted to product **3c**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 1:0 to 100:1) to provide the title compound as a pale yellow oil (120 mg, 100%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (dd, J = 8.0, 1.2 Hz, 1H), 7.58 (td, J = 7.6, 1.2 Hz, 1H), 7.46 (td, J = Hz, 1H), 7.29 (dd, J = 7.6, 0.8 Hz, 1H), 7.24-7.13 (m, 2H), 7.00 (d, J = 7.2 Hz, 1H), 3.68 (s, 3H), 2.39 (s, 3H), 2.04 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.0, 143.7, 141.6, 136.4, 134.0, 131.6, 131.3, 130.6, 130.0, 129.0, 127.1, 126.5, 124.9, 52.0, 20.7, 16.8.

IR (neat, cm^{-1}): 3062, 2948, 1731, 1717, 1466, 1432, 1289, 1252.

Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.86; H, 6.86.



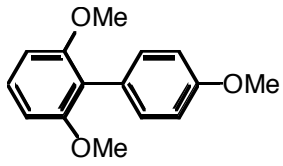
2-Methoxy-2',3'-dimethylbiphenyl (3d) Following general procedure B, a mixture of 2,3-dimethylphenylzinc chloride (0.75 mmol) and 2-chloroanisole (63 μL, 0.5 mmol) was converted to product **3d**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 1:0 to 100:1) to provide the title compound as a colorless solid (92 mg, 87%), mp 69-70 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (ddd, J = 8.4, 7.6, 1.6 Hz, 1H), 7.29-7.21 (m, 3H), 7.15 (dd, J = 6.6, 2.2 Hz, 1H), 7.10 (td, J = 7.4, 1.1 Hz, 1H), 7.05 (d, J = 8.0 Hz, 1H), 3.84 (s, 3H), 2.43 (s, 3H), 2.13 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 156.9, 138.8, 136.7, 135.6, 131.6, 131.3, 129.2, 128.6, 128.0, 125.3, 120.6, 110.7, 55.6, 20.9, 16.9.

IR (neat, cm^{-1}): 2939, 1600, 1580, 1495, 1461, 1272, 1235, 1028.

Anal. Calcd for $C_{15}H_{16}O$: C, 84.87; H, 7.60. Found: C, 84.87; H, 7.66.



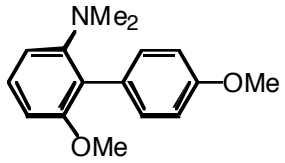
2,6,4'-Trimethoxybiphenyl (3e) Following general procedure D, a mixture of 2,6-dimethoxyphenylzinc chloride and 4-chloroanisole (61 μL, 0.5 mmol) was converted to product **3e**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 1:0 to 50:1) to provide the title compound as a colorless solid (122 mg, 100%), mp 116-117 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, J = 2.0 Hz, 2H), 7.34 (t, J = 8.4 Hz, 1H), 7.04 (d, J = 8.8 Hz, 2H), 6.73 (d, J = 8.4 Hz, 2H), 3.91 (s, 3H), 3.81 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4, 157.9, 132.1, 128.5, 126.2, 119.2, 113.4, 104.3, 56.1, 55.3.

IR (neat, cm^{-1}): 1588, 1519, 1470, 1433, 1289, 1246, 1111, 1100.

Anal. Calcd for $C_{15}H_{16}O_3$: C,73.75; H, 6.60. Found: C, 73.95; H, 6.85.



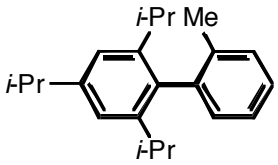
2-Dimethylamino-6,4'-dimethoxybiphenyl (3f) Following general procedure C, 2-*N*,*N*-dimethylamino-6-methoxyphenylzinc chloride (0.75 mmol) and 4-chloroanisole (61 μL, 0.5 mmol) was converted to product **3f**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 1:0 to 100:1) to provide the title compound as a colorless solid (103 mg, 80%), mp 88.5-90 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, J = 8.8 Hz, 2H), 7.30 (t, J = 8.2 Hz, 1H), 7.03 (d, J = 8.8 Hz, 2H), 6.80 (d, J = 8.2, 1H), 6.72 (d, J = 8.2 Hz, 1H), 3.92 (s, 3H), 3.78 (s, 3H), 2.55 (s, 6H).

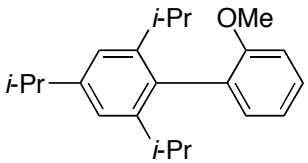
^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1, 157.8, 153.3, 132.0, 129.0, 128.2, 123.1, 113.5, 111.0, 104.9, 56.0, 55.2, 43.5.

IR (neat, cm^{-1}): 2937, 2906, 2833, 2780, 1590, 1571, 1515, 1465, 1243, 1175, 1075.

Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44. Found: C, 74.94; H, 7.44.



2,4,6-Triisopropyl-2'-methylbiphenyl (16a) Following general procedure A, a mixture of 2,4,6-triisopropylphenylzinc chloride (0.75 mmol) and 2-chlorotoluene (58 μL, 0.5 mmol) was converted to product **16a**. The crude product was purified by flash chromatography on silica gel (hexane) to provide the title compound as a colorless solid (144 mg, 98%), mp 93-95 °C, Lit. mp = 95.5-96.5 ºC.[3]



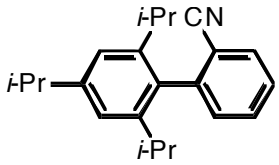
2,4,6-Triisopropyl-2'-methoxybiphenyl (16b) Following general procedure B, a mixture of 2,4,6-triisopropylphenylzinc chloride (0.75 mmol) and 2-chloroanisole (63 μL, 0.5 mmol) was converted to product **16b**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 1:0 to 100:1) to provide the title compound as a colorless solid (151 mg, 97%), mp 131-133 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (ddd, J = 8.2, 7.4, 1.9 Hz, 1H), 7.09-7.04 (m, 1H), 7.06 (s, 2H), 6.99 (td, J = 7.3, 1.0 Hz, 1H), 6.97 (d, J = 8.2, 1H), 3.73 (s, 3H), 2.95 (sept, J = 6.9 Hz, 1H), 2.55 (sept, J = 6.9 Hz, 2H), 1.32 (d, J = 7.0 Hz, 6H), 1.08 (d, J = 6.7 Hz, 6H), 1.06 (d, J = 6.7 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 157.6, 147.7, 146.9, 133.2, 131.8, 129.5, 128.3, 120.7, 120.3, 110.5, 55.3, 34.3, 30.8, 24.5, 24.2, 24.0.

IR (neat, cm^{-1}): 2958, 2865, 1596, 1578, 1497, 1461, 1432, 1360, 1246, 1025.

Anal. Calcd for $C_{22}H_{30}O$: C, 85.11; H, 9.74. Found: C, 84.91; H, 9.77.



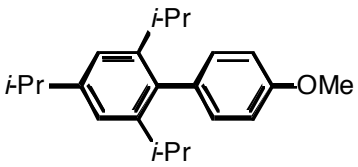
2-Cyano-2',4',6'-triisopropylbiphenyl (16c) Following general procedure B, a mixture of 2,4,6-triisopropylphenylzinc chloride (0.75 mmol) and 2-chlorobenzonitrile (69 mg, 0.5 mmol) was converted to product **16c**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 1:0 to 50:1) to provide the title compound as a colorless solid (147 mg, 96%), mp 133.5-135 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (dd, J = 7.7, 0.9 Hz, 1H), 7.65 (td, J = 7.6, 1.3 Hz, 1H), 7.48 (td, J = 7.7, 1.1 Hz, 1H), 7.36 (d, J = 7.7, 1H), 7.14 (s, 2H), 3.00 (sept, J = 6.9 Hz, 1H), 2.44 (sept, J = 6.8, 2H), 1.36 (d, J = 7.0 Hz, 6H), 1.23 (d, J = 6.9 Hz, 6H), 1.11 (d, J = 6.9 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 149.4, 146.4, 145.6, 132.9, 132.9, 132.4, 131.2, 127.5, 121.1, 118.2, 114.1, 34.4, 30.9, 24.6, 24.2, 24.1.

IR (neat, cm^{-1}): 2960, 2927, 2368, 1607, 1594, 1569, 1459, 1362.

Anal. Calcd for $C_{22}H_{27}N$: C, 86.51; H, 8.91. Found: C, 86.49; H, 8.99.



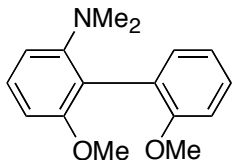
2,4,6-Triisopropyl-4'-methoxybiphenyl (16d) Following general procedure A, a mixture of 2,4,6-triisopropylphenylzinc chloride (0.75 mmol) and 4-chloroanisole (61 μL, 0.5 mmol) was converted to product **16d**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 1:0 to 100:1) to provide the title compound as a colorless solid (155 mg, 100%), mp 107-109 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (d, J = 8.7 Hz, 2H), 7.13 (s, 2H), 7.01 (d, J = 8.7 Hz, 2H), 3.92 (s, 3H), 3.01 (sept, J = 6.9 Hz, 1H), 2.73 (sept, J = 6.9 Hz, 2H), 1.38 (d, J = 6.9 Hz, 6H), 1.15 (d, J = 6.9 Hz, 12H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 147.9, 147.2, 136.9, 133.1, 130.9, 129.5, 120.7, 113.5, 55.3, 34.5, 30.4, 24.4.

IR (neat, cm^{-1}): 2958, 2929, 1737, 1607, 1513, 1466, 1281, 1237, 1183, 837.

Anal. Calcd for $C_{22}H_{30}O$: C, 85.11; H, 9.74. Found: C, 85.41; H, 9.91.



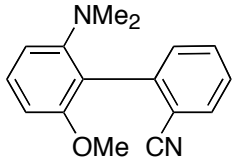
2-Dimethylamino-6,2'-dimethoxybiphenyl (16e) Following general procedure C, a mixture of 2-*N*,*N*-dimethylamino-6-methoxyphenylzinc chloride (0.75 mmol) and 2-chloroanisole (61 μL, 0.5 mmol), was converted to product **16e**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 100:1 to 20:1) to provide the title compound as a colorless solid (106 mg, 82%), mp. 83-84 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (td, J = 7.8 Hz, 1.5 Hz, 1H), 7.34 (t, J = 8.2 Hz, 1H), 7.27 (dd, J = 7.4, 1.4 Hz, 1H), 7.10 (t, J = 7.4 Hz, 1H), 7.07 (d, J = 8.1 Hz, 1H), 6.82 (d, J = 8.2 Hz, 1H), 6.72 (d, J = 8.2 Hz, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 2.57 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1, 157.7, 153.7, 131.9, 128.6, 128.3, 126.7, 120.7, 120.7, 111.2, 111.1, 104.9, 56.1, 55.8, 43.6.

IR (neat, cm^{-1}): 3215, 2989, 2871, 2870, 1573, 1465, 1428, 1252, 1142, 1075.

Anal. Calcd for $C_{16}H_{19}NO_2$: C,74.68; H, 7.44. Found: C, 74.64; H, 7.46.



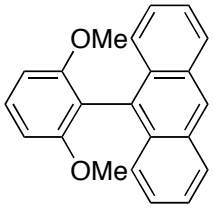
2-Cyano-6'-dimethylamino-2'-methoxybiphenyl (16f) Following general procedure B, a mixture of 2-*N*,*N*-dimethylamino-6-methoxyphenylzinc chloride (0.75 mmol) and 2-chlorobenzonitrile (69 mg, 0.5 mmol) was converted to product **16f**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 100:0 to 20:1) to provide the title compound as a colorless solid (76 mg, 60%), mp 101-103 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 7.7 Hz, 1H), 7.63 (td, J = 7.7, 1.1, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.39 (td, J = 7.6, 1.0 Hz, 1H), 7.34 (t, J = 8.2 Hz, 1H), 6.82 (d, J = 8.2 Hz, 1H), 6.71 (d, J = 8.3 Hz, 1H), 3.76 (s, 3H), 2.50 (s, 6H).

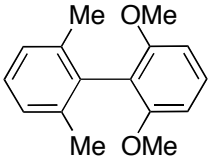
^{13}C NMR (100 MHz, $CDCl_3$): δ 157.4, 153.4, 141.3, 132.8, 132.3, 132.2, 130.2, 126.9, 120.2, 119.0, 114.7, 111.6, 105.2, 55.8, 43.5.

IR (neat, cm^{-1}): 2937, 2831, 2780, 2368, 1598, 1578, 1465, 1426, 1252, 1075.

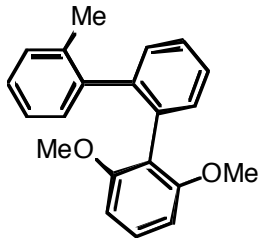
Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39. Found: C, 76.19; H, 6.49.



9-(2,6-Dimethoxyphenyl)anthracene (16g) Following general procedure D, a mixture of 2,6-dimethoxyphenylzinc chloride (0.75 mmol) and 9-chloroanthracene (106 mg, 0.5 mmol) were converted to product **16g**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 100:0 to 100:1) to provide the title compound as a colorless solid (144 mg, 92%), mp 172-174 ºC, Lit. mp = 172-174 ºC.[2]



2,6-Dimethoxy-2',6'-dimethylbiphenyl (16h) Following general procedure A, a mixture of 2,6-dimethylphenylzinc chloride (0.75 mmol) and 2-chloro-1,3-dimethoxybenzene (86 mg, 0.5 mmol), were converted to product **16h**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 100:0 to 50:1) to provide the title compound as a colorless solid (104 mg, 86%), mp 107-109 °C, Lit. mp = 107-109 ºC.[3]



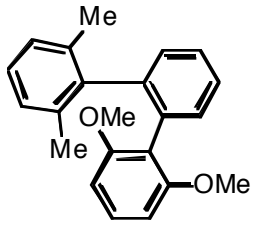
2'',6''-Dimethoxy-2-methyl-[1,1';2',1'']terphenyl (16i) Following general procedure A, a mixture of 2-methylphenylzinc chloride (0.75 mmol) and 2-bromo-2',6'-dimethoxybiphenyl (147 mg, 0.5 mmol), was converted to product **16i**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 100:0 to 100:1) to provide the title compound as a colorless solid (152 mg, 100%), mp 117-118 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45-7.31 (m, 4H), 7.12 (t, J = 8.4 Hz, 1H), 7.10-7.01 (m, 2H), 6.99-6.89 (m, 2H), 6.47 (d, J = 8.3 Hz, 1H), 6.36 (d, J = 8.3 Hz, 1H), 3.68 (s, 3H), 3.49 (s, 3H), 2.15 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 157.8, 157.3, 142.1, 141.5, 135.9, 133.9, 131.7, 130.1, 130.0, 129.4, 128.7, 126.8, 126.7, 126.6, 124.3, 118.9, 103.4, 103.4, 55.6, 55.2, 19.9.

IR (neat, cm^{-1}): 3054, 3018, 2933, 2834, 1590, 1470, 1430, 1246. 1108.

Anal. Calcd for $C_{21}H_{20}O_2$: C, 82.86; H, 6.62. Found: C, 82.84; H, 6.62.



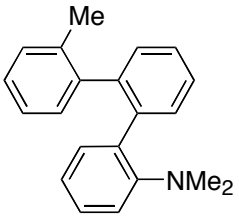
2'',6''-Dimethoxy-2,6-dimethyl-[1,1';2',1'']terphenyl (16j) Following general procedure A, a mixture of 2,6-dimethylphenylzinc chloride (0.75 mmol) and 2-bromo-2',6'-dimethoxybiphenyl (147 mg, 0.5 mmol) was converted to product **16j**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 100:0 to 100:1) to provide the title compound as a colorless solid (156 mg, 98%), mp 105-106.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.35 (m, 3H), 7.26-7.21 (m, 1H), 7.11 (t, J = 8.3 Hz, 1H), 7.01-6.94 (m, 1H), 6.89 (d, J = 7.4 Hz, 2H), 6.40 (d, J = 8.4 Hz, 2H), 3.54 (s, 6H), 1.99 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 157.6, 141.0, 140.9, 136.9, 134.2, 132.6, 130.7, 128.7, 126.9, 126.7, 126.4, 118.5, 103.4, 55.1, 20.6.

IR (neat, cm^{-1}): 3008, 2933, 2834, 1588, 1468, 1432, 1245, 1108.

Anal. Calcd for $C_{22}H_{22}O_2$: C, 82.99; H, 6.96. Found: C, 83.10; H, 7.05.



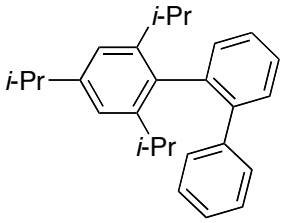
Dimethyl(2-methyl-[1,1';2',1'']terphenyl-2''-yl)amine (16 k) Following general procedure A, a mixture of 2-methylphenylzinc chloride (0.75 mmol) and 2-bromo-2'-dimethylaminobiphenyl (138 mg, 0.5 mmol) was converted to product **16k**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 100:0 to 100:1, 0.5% Et_3N) to provide the title compound as a colorless oil (142 mg, 99%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J = 7.6 Hz, 1H), 7.51 (td, J = 7.2, 1.3 Hz, 1H), 7.45 (td, J = 7.4, 1.2 Hz, 1H), 7.42-6.50 (br m, 9H), 2.60-1.80 (br m, 9H).

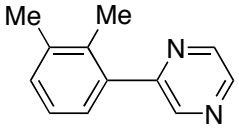
^{13}C NMR (100 MHz, $CDCl_3$): δ 151.4, 141.2, 140.7, 132.4, 130.8, 130.0, 129.6, 128.1, 127.5, 126.4, 124.1, 43.2, 20.4 (peaks are broad).

IR (neat, cm^{-1}): 3054, 3016, 2935, 2860, 2825, 2779, 1594, 1493, 1474, 1445, 1428, 1320, 1196, 1158, 1098, 1052, 1009, 947.

Anal. Calcd for $C_{21}H_{21}N$: C, 87.76; H, 7.36. Found: C, 87.51; H, 7.46.



2,4,6-Triisopropyl[1,1';2',1'']terphenyl (16l) Following general procedure C, a mixture of 2,4,6-triisopropylphenylzinc chloride (0.75 mmol) and 2-bromobiphenyl (85 μL, 0.5 mmol) was converted to product **16l**. The crude product was purified by flash chromatography on silica gel (hexane) to provide the title compound as a colorless solid (138 mg, 78%), mp 140-141.5 ºC, Lit. mp = 140-141.5 ºC.[3]



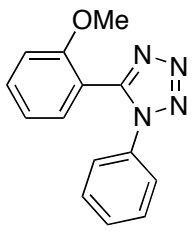
2-(2,3-Dimethylphenyl)pyrazine (17a) Following general procedure B, except at room temperature, a mixture of 2,3-dimethylphenylzinc chloride (0.75 mmol) and chloropyrazine (45 μL, 0.5 mmol) was converted to product **17a**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 1:0 to 50:1) to provide the title compound as a colorless oil (92 mg, 100%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70 (d, J = 1.5 Hz, 1H), 8.67 (dd, J = 2.5, 1.6 Hz, 1H), 8.54 (d, J = 2.5 Hz, 1H), 7.30-7.20 (m, 3H), 2.37 (s, 3H), 2.25 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 159.1, 146.4, 143.4, 140.0, 138.6, 135.4, 135.1, 132.1, 128.1, 126.3, 20.7, 17.0.

IR (neat, cm^{-1}): 3068, 3058, 2946, 2923, 1620, 1467, 1389, 1308, 1144, 1069, 1016.

Anal. Calcd for $C_{12}H_{12}N_2$: C,78.23; H, 6.57. Found: C, 78.32; H, 6.55.



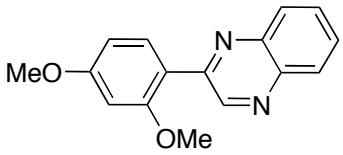
5-(2-Methoxyphenyl)1-phenyl-1*H*-tetrazole (17b) Following general procedure A, a mixture of 2-methoxyphenylzinc chloride (0.75 mmol) and 5-chloro-1-phenyl-1*H*-tetrazole (90 mg, 0.5 mmol) was converted to product **17b**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient, 100:1 to 4:1) to provide the title compound as a colorless solid (122 mg, 97%), mp 96-98 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 7.6 Hz, 1H), 7.52 (td, J = 7.8, 1.2 Hz, 1H), 7.47-7.40 (m, 3H), 7.37-7.31 (m, 2H), 7.13 (t, J = 7.6 Hz, 1H), 6.85 (d, J = 8.4 Hz, 1H), 3.33 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 156.7, 152.3, 135.7, 133.3, 131.7, 129.6, 129.4, 123.3, 121.4, 113.5, 111.6, 55.0.

IR (neat, cm^{-1}): 3070, 2931, 2844, 2368, 1609, 1586, 1534, 1499, 1476, 1443, 1270, 1250, 1115, 1021.

Anal. Calcd for $C_{14}H_{12}N_4$: C, 66.65; H, 4.79. Found: C, 66.92; H, 4.97.



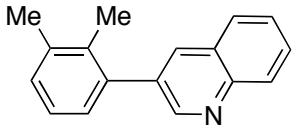
2-(2,4-Dimethoxyphenyl)quinoxaline (17c) Following general procedure B, except at room temperature, a mixture of 2,4-dimethoxyphenylzinc chloride (0.75 mmol) and 2-chloroquinoxaline (79 mg, 0.5 mmol) was converted to product **17c**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient 20:1 to 4:1) to provide the title compound as a colorless solid (130 mg, 98%), mp 60-62 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.35 (s, 1H), 8.15-8.08 (m, 2H), 7.92 (d, J = 8.5 Hz, 1H), 7.76 (td, J = 6.9, 1.8 Hz, 1H), 7.72 (td, J = 6.9, 1.7 Hz, 1H), 6.71 (dd, J = 8.6, 2.3 Hz, 1H), 6.62 (d, J = 2.3 Hz, 1H), 3.91 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6, 158.7, 151.9, 147.3, 142.7, 140.8, 132.6, 129.6, 129.3, 129.0, 128.9, 119.3, 105.9, 98.7, 55.6, 55.5.

IR (neat, cm^{-1}): 2939, 2838, 1609, 1580, 1509, 1281, 1210, 1162, 1129, 1032.

Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30. Found: C, 72.10; H, 5.36.



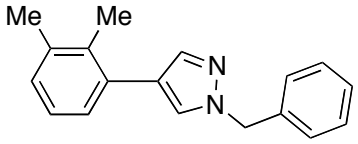
3-(2,3-Dimethylphenyl)quinoline (17d) Following general procedure B, a mixture of 2,3-dimethylphenylzinc chloride (0.75 mmol) and 3-bromoquinoline (68 μL, 0.5 mmol) was converted to product **17d**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc (0.5% Et_3N) gradient, 1:0 to 100:1) to provide the title compound as a colorless oil (114 mg, 97%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.96 (d, J = 2.4 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 8.11 (d, J = 2.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.77 (ddd, J = 8.0, 6.8, 1.3 Hz, 1H), 7.64-7.58 (m, 1H), 7.31-7.18 (m, 3H), 2.41 (s, 3H), 2.25 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 151.9, 147.0, 138.5, 137.7, 135.6, 135.5, 134.6, 129.9, 129.5, 129.4, 128.2, 128.0, 127.9, 127.0, 125.8, 20.8, 17.2.

IR (neat, cm^{-1}): 3060, 3031, 2923, 1567, 1492, 1459, 1412, 1358, 1339, 1025, 957.

Anal. Calcd for $C_{17}H_{15}N$: C,87.52; H, 6.48. Found: C, 87.22; H, 6.62.



1-Benzyl-4-(2,3-dimethylphenyl)-1*H*-pyrazole (17e) Following general procedure B, a mixture of 2,3-dimethylphenylzinc chloride (0.75 mmol) and *N*-benzyl-4-bromopyrazole (119 mg, 0.5 mmol) was

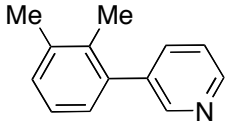
converted to product **17e**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc (0.5% Et_3N) gradient, 1:0 to 100:1) to provide the title compound as a colorless solid (131 mg, 100%), mp 101-103.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 0.5 Hz, 1H), 7.42 (d, J = 0.4 Hz, 1H), 7.40-7.26 (m, 5H), 7.16-7.08 (m, 3H), 5.37 (s, 2H), 2.33 (s, 3H), 2.28 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 139.5, 137.2, 136.6, 134.2, 132.5, 128.8, 128.6, 128.4, 128.0, 127.7, 127.6, 125.4, 123.0, 56.0, 20.9, 17.0.

IR (neat, cm^{-1}): 3218, 2989, 2979, 2871, 1584, 1559, 1457, 1376, 1353, 1142, 1121.

Anal. Calcd for $C_{18}H_{18}N_2$: C,82.41; H, 6.92. Found: C, 82.12; H, 6.98.

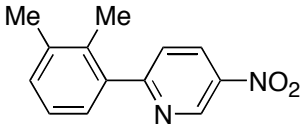


3-(2,3-Dimethylphenyl)pyridine (17f) Following general procedure B, a mixture of 2,3-dimethylphenylzinc chloride (0.75 mmol) and 3-chloropyridine (48 μL, 0.5 mmol) was converted to product **17f**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient) to provide the title compound as a colorless oil (92 mg, 100%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62-8.58 (m, 2H), 7.63 (dt, J = 8.0, 2.0 Hz, 1H), 7.34 (ddd, J = 7.8, 4.0, 0.6 Hz, 1H), 7.22 (d, J = 6.4 Hz, 1H), 7.19 (t, J = 7.4 Hz, 1H), 7.08 (d, J = 7.2 Hz, 1H), 2.36 (s, 3H), 2.17 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 150.2, 148.1, 138.5, 138.1, 137.6, 136.7, 134.3, 129.8, 127.8, 125.7, 123.0, 20.8, 17.0.

IR (neat, cm^{-1}): 3025, 2925, 2867, 1725, 1588, 1567, 1463, 1405, 1027.



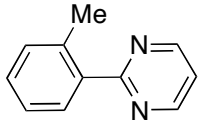
2-(2,3-Dimethylphenyl)-5-nitropyridine (17g) Following general procedure B, except at room temperature, a mixture of 2,3-dimethylphenylzinc chloride (0.75 mmol) and 2-chloro-5-nitropyridine (79 mg, 0.5 mmol) was converted to product **17g**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient) to provide the title compound as a colorless solid (106 mg, 93%), mp 68-69 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.53 (d, J = 2.6 Hz, 1H), 8.54 (dd, J = 8.6, 2.7 Hz, 1H), 7.61 (d, J = 8.6 Hz, 1H), 7.32-7.21 (m, 3H), 2.27 (s, 3H), 2.39 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 144.7, 142.6, 139.0, 138.2, 134.6, 131.4, 131.3, 127.7, 125.9, 124.6, 20.7, 16.9.

IR (neat, cm^{-1}): 3072, 2927, 2860, 1590, 1573, 1519, 1459, 1345, 1273, 1111.

Anal. Calcd for $C_{13}H_{12}N_2O_2$: C,68.41; H, 5.30. Found: C, 68.41; H, 5.40.



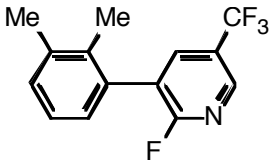
2-*o*-Tolylpyrimidine (17h) Following general procedure B, a mixture of 2-methylphenylzinc chloride (0.75 mmol) and 2-bromopyrimidine (79 mg, 0.5 mmol) was converted to product **17h**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient 100:1 to 4:1) to provide the title compound as a colorless oil (67 mg, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, J = 4.8 Hz, 2H), 7.83 (dd, J = 6.0, 2.0 Hz, 1H), 7.39-7.28 (m, 3H), 7.20 (t, J = 4.8 Hz, 1H), 2.57 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 156.9, 138.2, 137.3, 131.4, 130.5, 129.5, 126.0, 118.6, 21.1.

IR (neat, cm^{-1}): 3035, 2962, 2925, 1569, 1553, 1439, 1410, 1040.

Anal. Calcd for $C_{11}H_{10}N_2$: C, 77.62; H, 5.92. Found: C, 77.42; H, 5.98.

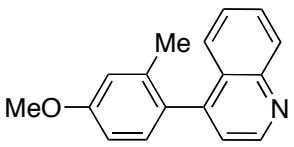


3-(2,3-Dimethylphenyl)-2-fluoro-5-trifluoromethylpyridine (17i) Following general procedure B, a mixture of 2,3-dimethylphenylzinc chloride (0.75 mmol) and 3-chloro-2-fluoro-5-trifluoromethylpyridine (65 μL, 0.5 mmol) was converted to **17i**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient) to provide the title compound as a colorless oil (124 mg, 92%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (m, 1H), 7.97 (ddd, J = 8.3, 2.4, 0.3 Hz, 1H), 7.29 (d, J = 8.1 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H), 7.07 (d, J = 7.5 Hz, 1H), 2.39 (s, 3H), 2.12 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 144.5, 144.5, 144.5, 144.4, 144.3, 139.5, 139.5, 139.5, 139.4, 137.8, 135.2, 132.5, 132.4, 131.0, 127.9, 127.4, 126.0, 125.7, 125.5, 125.4, 125.1, 125.1, 124.7, 122.0, 20.7, 16.9 (observed complexity due to F-C splitting; definitive assignments have not been made).

IR (neat, cm^{-1}): 2962, 2923, 2850, 1611, 1596, 1578, 1447, 1410, 1339, 1287, 1262, 1158, 1127.



4-(4-Methoxy-2-methylphenyl)quinoline (17j) Following general procedure B, except at room temperature, a mixture of 4-methoxy-2-methylphenylzinc chloride (0.75 mmol) and 4-chloroquinoline (82 mg, 0.5 mmol) was converted to product **17j**. The crude product was purified by flash chromatography on

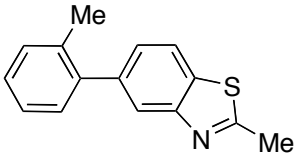
silica gel (hexane/EtOAc gradient, 100:1 to 4:1) to provide the title compound as a colorless solid (121 mg, 97%), mp 101-102 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (d, J = 4.4 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.67 (ddd, J = 8.4, 7.0, 1.3 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.22 (d, J = 4.4 Hz, 1H), 7.11 (d, J = 8.4 Hz, 1H), 6.89 (d, J = 2.4 Hz, 1H), 6.84 (dd, J = 8.4, 2.4 Hz, 1H), 3.84 (s, 3H), 2.00 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 150.1, 148.4, 148.4, 137.6, 130.8, 129.9, 129.8, 129.3, 127.8, 126.6, 126.1, 122.0, 115.7, 111.1, 55.3, 20.4.

IR (neat, cm^{-1}): 2998, 2956, 2836, 1607, 1495, 1387, 1295, 1239, 1162, 1109, 1042.

Anal. Calcd for $C_{17}H_{15}NO$: C,81.90; H, 6.06. Found: C, 82.04; H, 6.10.



2-Methyl-5-*o*-tolylbenzothiazole (17k) Following general procedure A, a mixture of 2-methylphenylzinc chloride (0.75 mmol) and 5-chloro-2-methylbenzothiazole (92 mg, 0.5 mmol) was converted to **17k**. The crude product was purified by flash chromatography on silica gel (hexane/EtOAc gradient) to provide the title compound as a yellow oil (84 mg, 70%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 1.3 Hz, 1H), 7.86 (d, J = 8.2 Hz, 1H), 7.34 (dd, J = 8.2, 1.6 Hz, 1H), 7.32-7.28 (m, 4H), 2.88 (s, 3H), 2.32 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 153.6, 141.6, 140.2, 135.7, 134.4, 130.6, 130.2, 127.7, 126.4, 126.1, 123.0, 121.1, 20.8, 20.4.

IR (neat, cm^{-1}): 3054, 3018, 2954, 2923, 1524, 1451, 1412, 1171, 1152, 1067.

Anal. Calcd for $C_{15}H_{13}NS$: C, 75.28; H, 5.47. Found: C, 75.25; H, 5.54.

(1) Ihara, E.; Adachi, Y.; Yasuda, H. Hashimoto, H.; Kanehisa, N.; Kai, Y. *J. Organomet. Chem.* **1998**, *569*, 147–157.

(2) Yin, J.; Rainka, M. P.; Zhang, X.-X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1162–1163.

(3) Walker, S. D.; Barder, T. E.; Martinelli, J. R.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2004**, *43*, 1871–1876.

Figure 1. [1]H NMR spectrum of 3-(2,3-Dimethylphenyl)pyridine (**17f**)

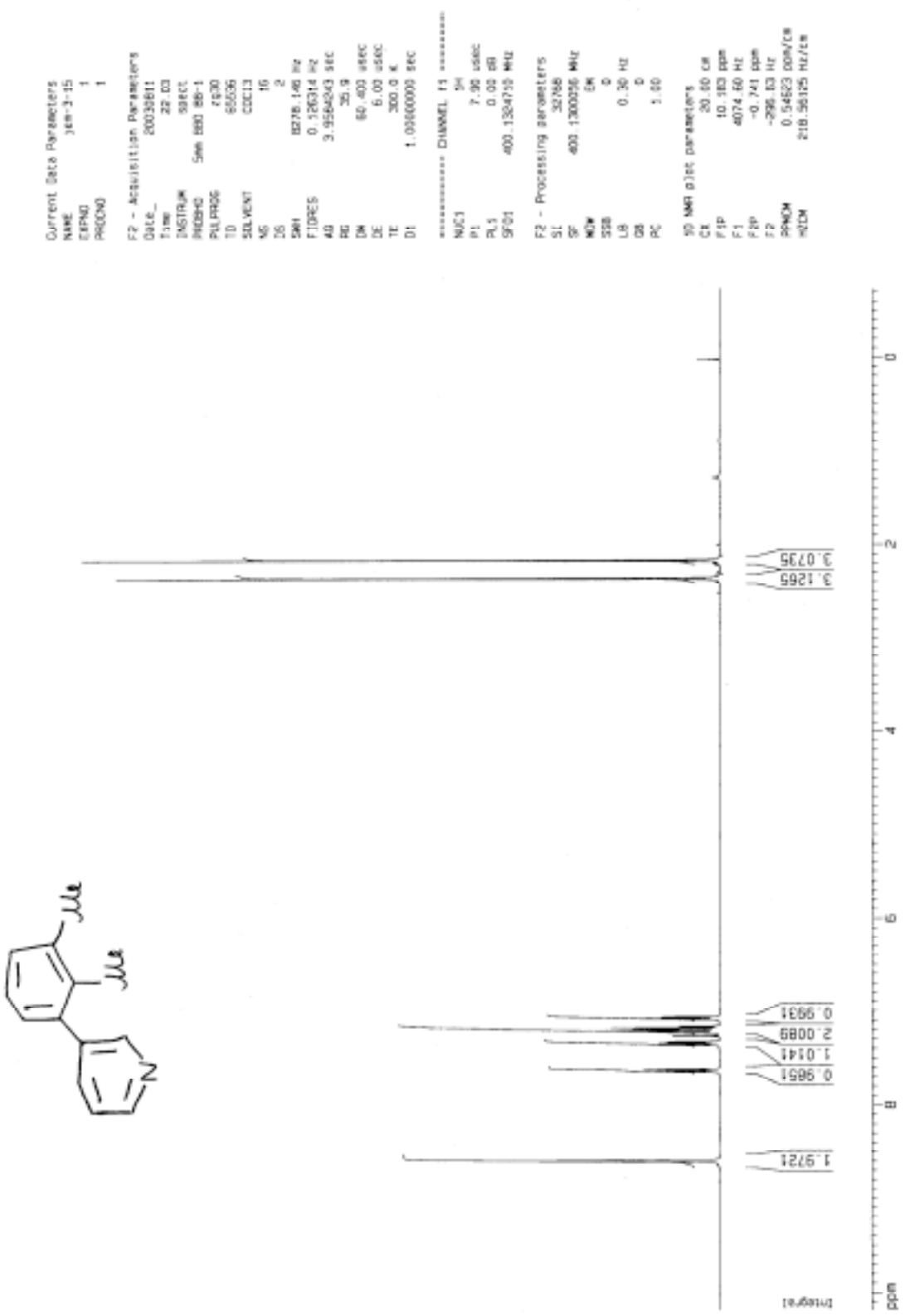


Figure 2. [1]H NMR spectrum of 3-(2,3-Dimethylphenyl)-2-fluoro-5-trifluoromethylpyridine (**17i**)