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Supporting Information

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Significantly Improved Method for the Palladium-Catalyzed Coupling of Phenols and Aryl Halides: Understanding Ligand Effects in Phenol/Aryl Halide Coupling Reactions

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General Considerations

Reagents: $Pd(OAc)_2$ was purchased from Strem Chemical Co. and was used without further purification. Ligands **6**[1] and **9**[2] were prepared as previously described. Ligands **1**, **5** and **10** are commercially available from Strem Chemical Co. 1,2,3,4-Tetramethylbenzene was purchased from TCI America, Inc. Acetic acid was purchased from Mallinckrodt Chemicals, Inc. $ZnCl_2$ and Br_2 were purchased from Strem Chemicals, Inc. Copper(I) chloride was purchased from Strem Chemical, Inc. and stored in a Vacuum Atomspheres glovebox. Potassium phosphate (K_3PO_4) was purchased from Aldrich and was finely ground (with a mortar and pestle) prior to use. NaO*t*Bu was also purchased from Aldrich and stored under nitrogen in a Vacuum Atmospheres glovebox. Small quantities (2-3 g) were removed and used for a two to three week period and stored in a desiccator. Dialkylchlorophosphines and magnesium powder (50 mesh) were purchased from Aldrich and were used without further purification. Aryl halides and phenols were purchased from either Aldrich or Alfa Aesar and were used without further purification. Toluene was purchased from J. T. Baker in CYCLE-TAINER solvent delivery kegs, which were purged with argon for 2 h and purified by passing the toluene through two packed columns of neutral alumina and copper(II) oxide under argon pressure. Silica gel chromatography purifications were performed by flash chromatography using EM Science silica gel 60 (230-400 mesh). All other reagents were commercially available and were used without further purification.

Analytical methods: All new compounds were characterized by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy, in addition to elemental analysis (Atlantic Microlabs, Norcross, GA). Nuclear Magnetic Resonance spectra were recorded on a Varian Mercury 300, a Varian Unity 300 or a Bruker 400 instrument. Infrared spectra were recorded on an ASI Applied Systems ReactIR 1000 (neat samples were placed directly on the DiComp probe). All ^{1}H 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) in the deuterated solvents. All ^{13}C NMR spectra are reported in ppm relative to deuterochloroform (77.23 ppm) and all were obtained with ^{1}H decoupling. Melting points (uncorrected) were obtained on a Mel-Temp capillary melting point apparatus. Gas chromatography analyses were performed on a Hewlett Packard 5890 instrument with FID detector and a Hewlett Packard 25 m x 0.2 mm i.d. HP-5 capillary column or a Hewlett Packard 6890 instrument with a FID detector and a Hewlett Packard 10 m x 0.1 mm i.d. HP-1 column. Mass Spectra (GC/MS) were recorded on a Hewlett Packard model GCD.

1,2-Dibromo-3,4,5,6-tetramethylbenzene (8).[3] $ZnCl_2$ (23.12 g, 170 mmol) was added o a solution of 1,2,3,4-tetramethylbenzene (10.72 g, 80 mmol) in acetic acid (320 mL). To the above solution was added bromine (26.90 g, 8.8 mL, 168 mmol) dropwise, at room temperature. The reaction mixture was stirred for 14 h at room temperature, then a saturated solution of Na_2SO_3 was added to quench the excess Br_2. CH_2Cl_2 (400 mL) and H_2O (400 mL) were added to the resulting colorless mixture and stirring was continued for 30 min at room temperature until the white precipitate dissolved. The mixture was transferred to a separatory funnel. The lower organic layer was collected, washed with 3 x 200 mL 10% aqueous NaOH and 200 mL H_2O. The organic layer was separated, dried over $MgSO_4$ and concentrated *in vacuo* to afford crude product. Recrystallization was performed by dissolving the compound in THF and adding 50 mL hexane. Cooling the mixture to 0 ^{o}C resulted in the formation of a white solid, which was washed with pentane and dried. Two crops were collected. Combined Yield: 19.96 g, 85%. Mp: 199-201 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.50 (s, 6H), 2.25 (s, 6H).

Ligand Syntheses.

2-Di-*t*-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-triisopropylbiphenyl (7). An oven-dried Schlenk tube was charged with magnesium powder (0.280 g, 11.5 mmol), 1-bromo-2,4,6-triisopropylbenzene (1.3 mL, 5.0 mmol) and THF (6 mL). The Schlenk tube was suspended in a 60 °C oil bath with stirring, and 1,2-dibromoethane (20 µL, 0.23 mmol) was added dropwise via syringe over 15 min. The mixture was stirred at 60 °C for 1.5 h and then 1,2-dibromo-3,4,5,6-tetramethylbenzene (1.46 g, 5.00 mmol) was added portion-wise over 30 min. The resulting mixture was stirred at 60 °C for 1.5 h, and then was allowed to cool to room temperature. Anhydrous CuCl (0.50 g, 5.0 mmol) was added in a single portion, followed by the addition of di-*tert*-butylchlorophosphine (1.2 mL, 6.0 mmol) via syringe. The Schlenk tube was sealed with a Teflon screw cap and suspended in a 75 °C oil bath. The reaction mixture was stirred at 75 °C for 40 h. The mixture was allowed to cool to room temperature and then 30% aqueous NH_4OH was added. The resulting suspension was extracted with 4:1 ethyl acetate:ether. The organic layer was separated and washed three times with 30% aqueous NH_4OH and once with brin, dried over Na_2SO_4, filtered and concentrated *in vacuo*. Flash chromatography on a short silica gel column (4:1 hexane/ethyl acetate) followed by recrystallization of the acquired material from methanol/diethyl ether gave 1.49 g (62% yield) of the title compound as a white crystalline solid, mp 162-163 °C. ^{1}H NMR (300 MHz, C_6D_6) δ: 7.19 (s, 2H), 2.86 (septet, J = 6.9 Hz, 1H), 2.72 (septet, J = 6.6 Hz, 2H), 2.47 (s, 3H), 2.02 (s, 3H), 1.98 (s, 3H), 1.87 (s, 3H), 1.41 (d, J = 6.6 Hz, 6H), 1.26 (d, J = 6.9 Hz, 6H), 1.20 (d, J_{HP} = 12.0 Hz, 18H), 1.06 (d, J = 6.9 Hz, 6H). ^{13}C NMR (75 MHz, C_6D_6) δ: 148.7, 148.2, 148.1, 147.2, 147.1, 139.92, 139.87, 139.6, 139.5, 137.06, 137.04, 135.5, 134.9, 134.8, 134.7, 134.1, 121.3, 35.1, 34.9, 34.6, 33.3, 33.0, 31.8, 31.7, 27.30, 27.28, 26.0, 25.21, 25.18, 24.8, 22.4, 22.3, 17.4, 17.3 (observed complexity due to P-C splitting). ^{31}P NMR (121 MHz, C_6D_6) δ 38.7. Anal. Calcd for $C_{33}H_{53}P$: C, 82.45; H, 11.11. Found: C, 82.27; H, 11.11.

2-Di-*t*-butylphosphino-3-methyl-2',4',6'-triisopropylbiphenyl (9). An oven-dried Schlenk tube was charged with magnesium powder (0.276 g, 11.5 mmol, 50 mesh), 1-

bromo-2,4,6-triisopropylbenzene (1.3 mL, 5.0 mmol) and THF (6 mL). The mixture was heated to 60 °C, and 1,2-dibromoethane (40 µL, 0.46 mmol) was added dropwise via syringe. The mixture was heated at 60 °C for 1 h and then 3-chloro-2-iodotoluene (1.3 g, 5.0 mmol) in THF (2 mL) was added dropwise via syringe. The resulting mixture was heated for 2 h at 60 °C and subsequently allowed to cool to room temperature. Anhydrous CuCl (0.50 g, 5.0 mmol) was weighed out in glovebox and removed from the glovebox (only in this procedure) right before its addition into the above reaction mixture under a flow of argon, followed by the addition of di-*t*-butylchlorophosphine (1.5 mL, 7.5 mmol). The mixture was heated to 60 °C and stirred for 15 h, then was allowed to cool to room temperature. 100 mL 30 % aqueous NH_4OH was then added into the reaction mixture and the resulting suspension was extracted with a 1:1 ether:ethyl acetate (2 x 100 mL) mixture. The combined organic extracts were washed with 30% aqueous NH_4OH (3 x 100 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was passed through a silica gel column with 10:1 hexane:ethyl acetate. At this point the crude product consists of a mixture of regioisomeric phosphines. This material was recrystallized from a mixture of methanol/ether to yield **9** (394 mg, 18% yield) as a white crystalline solid, mp 117-119 °C. ^{1}H NMR (300 MHz, C_6D_6) δ: 7.17 (s, 2H), 7.02-6.97 (m, 3H), 2.88-2.74 (m, 3H), 2.51 (s, 3H), 1.39 (d, J = 6.6 Hz, 6H), 1.22 (d, J = 6.9 Hz, 6H), 1.17 (d, J_{HP} = 12.3 Hz, 18H), 1.10 (d, J = 6.6 Hz, 6H). ^{31}P NMR (121 MHz, C_6D_6) δ: 35.6. IR (neat, cm^{-1}) 2956, 1459, 1439, 1382, 1360, 1167, 872, 789. Anal. Calcd for $C_{30}H_{47}P$: C, 82.14; H, 10.80. Found: C, 82.21; H, 10.87.

2-Di-*t*-butylphosphino-2',4', 6'-trimethylbiphenyl (12). A flame-dried 100 mL, 3-neck, round bottom flask equipped with a magnetic stir bar, reflux condenser and a rubber septum was purged with argon and charged with Mg powder (50 mesh, 0.88 g, 36 mmol), THF (25 mL) and 2-bromomesitylene (2.3 mL, 15 mmol). The reaction mixture was stirred vigorously under argon and then heated to 65 ^{o}C in oil bath. After 60 min, Grignard formation was complete as judged by GC analysis, and 2-bromochlorobenzene (1.9 mL, 27.5 mmol) was added at 65 ^{o}C over 15 min. After an additional 1 h of stirring at 65 ^{o}C, the reaction mixture was cooled to room temperature. Anhydrous CuCl (1.48 g, 15 mmol) was rapidly added in a single portion and then Cl*P*tBu_2 (3.0 mL, 15 mmol) was

slowly added dropwise, via syringe (CAUTION: exotherm), over 15 minutes. The reaction mixture was stirred at 65 ^{o}C overnight. After 16 h the reaction mixture was allowed to cool to room temperature, the reaction flask was placed in an ice bath, and methanol (1mL) was added (CAUTION: exotherm). The mixture was filtered through a pad of celite, eluting with ethyl acetate (100 mL). The combined eluent was washed six times with 30% aqueous NH_4OH, once with brine, and dried over $MgSO_4$. Flash chromatography on silica gel (4:1 hexane/ethyl acetate) followed by recrystallization of the acquired material from methanol/diethyl ether provided 1.3 g (26% yield) of the title compound as a white crystalline solid, mp 85-88 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7,87 (dt, *J* = 7.5 Hz, *J* = 1.6 Hz, 1H), 7.40-7.31 (m, 2H), 7.12-7.09 (m, 1H), 6.90 (s, 2H), 2.33 (s, 3H), 2.06 (s, 6H), 1.18 (d, *J* = 11.5 Hz, 18 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 149.1, 148.7, 139.1, 139.0, 136.8, 136.5, 136.2, 136.1, 136.1, 135.8,131.5, 131.4, 128.4, 127.9, 125.4, 32.7, 32.5, 31.0, 30.9, 21.9, 21.1 (observed complexity due to P-C splitting). ^{31}P NMR (121 MHz, C_6D_6) δ: 24.5. IR (neat, cm^{-1}) 2983, 1459, 1362, 1015.

General Procedure for the Pd-Catalyzed Coupling Reaction of Aryl Halides and Phenols. An oven-dried screw-cap tube or Schlenk flask (no improvement in yield was observed using a Schlenk flask over a screw cap tube) was cooled to room temperature under argon or nitrogen pressure (no improvement in yield was observed using argon instead of nitrogen). The tube was charged with ligand (3 mol%), $Pd(OAc)_2$ (2 mol%, 0.02 mmol, 4.5 mg), K_3PO_4 (2.0 mmol, 424 mg), phenol (1.2 mmol) and the aryl halide (1.0 mmol). The tube was capped with a septum and under a positive pressure of argon or nitrogen, toluene (2 mL) was added via syringe through the septum. The reaction flask was sealed and was placed in a pre-heated oil bath at 100 ^{o}C and stirred for 5-24 h (reaction times were not optimized). At this time the reaction mixture was allowed to cool to room temperature and was then filtered through a small pad of Celite, washed with diethyl ether or ethyl acetate (25 mL) and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel.

4-(4'-Chlorophenoxy)benzonitrile (Table 1, Entry 1).[4] The general procedure was followed using ligand **6** at 100 °C for 18 h. The crude material was purified by flash chromatography on silica gel (50:1 hexanes:Et_2O) to afford 220 mg (96%) of the title compound as a white solid, mp 74-76 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.62 (d, 2H, *J* = 8.9 Hz), 7.38 (s, 2H, *J* = 8.9 Hz), 7.01 (d, 4H, *J* = 8.6 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 161.2, 153.4, 134.2, 130.4, 130.3, 121.6, 118.6, 118.0, 106.4.

4-(2'-Isopropylphenoxy)benzonitrile (Table 1, Entry 2). The general procedure was followed at 50% scale using ligand **6** for 17 h at 100 °C. The crude material was purified by flash chromatography column on silica gel (hexanes) to afford 99 mg (84%) of the title compound as white solid, mp 52-54 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.60-7.58 (m, 2H), 7.42-7.38 (m, 1H), 7.26-7.21 (m, 2H), 6.97-6.93 (m, 3H), 3.13 (sept, 1H, *J* = 6.9 Hz), 1.20 (d, 6H, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 162.2, 151.4, 140.8, 134.1, 127.5, 127.3, 125.9, 121.1, 118.9, 117.0, 105.2, 27.0, 23.0. IR (neat, cm^{-1}) 2962, 2250, 1598, 1233. Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37. Found: C, 80.72; H, 6.41.

4-Phenoxybenzonitrile (Table 1, Entry 3).[5] The general procedure was followed at 50% scale using ligand **6** for 22 h at 100 °C. The crude material was purified by flash chromatography column on silica gel (50:1 hexanes:Et_2O) to afford 98 mg (94%) of the title compound as a white solid, mp 28-31 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.60 (m, 2H), 7.42 (m, 2H), 7.23 (m, 1H), 7.07 (m, 2H), 7.00 (m, 2H).

2-Phenoxybenzaldehyde (Table 1, Entry 4).[6] The general procedure was followed at 110 °C using 5 mol % ligand **6** (21 mg) and 3 mol % $Pd(OAc)_2$ (6.7 mg). The crude material was purified by flash chromatography column on silica gel (30:1 hexanes:Et_2O) to afford 198 mg (81%) of the title compound as colorless liquid. Reaction with 2-chlorobenzaldehyde at 50% scale for 22 h at 110 °C afford 84 mg (85%) of the title compound. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 10.52 (s, 1H), 7.94 (dd, 1H, *J* = 7.8 Hz, *J* = 1.8 Hz), 7.53-7.49 (m, 1H), 7.41-7.37 (m, 2H), 7.21-7.16 (m, 2H), 7.08-7.06 (m, 2H), 6.89 (d, 1H, *J* = 8.4 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 189.4, 160.0, 156.3, 135.7,

130.1, 128.4, 126.8, 124.3, 123.3, 119.4, 118.4. IR (neat, cm^{-1}) 3066, 2858, 1686, 1600, 1229.

Methyl 2-(2'-Isopropylphenoxy)benzoate (Table 1, Entry 5). The general procedure was followed at 110 ^{o}C for 22 h using 5 mol % ligand **6** (21 mg) and 3 mol % $Pd(OAc)_2$ (6.7 mg). The crude material was purified by flash chromatography column on silica gel (50:1 hexanes:Et_2O) to afford 210 mg (78%) of the title compound as colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.91 (dd, 1H, *J* = 7.8 Hz, *J* = 1.8 Hz), 7.42-7.34 (m, 2H) 7.17-7.10 (m, 3H), 6.84-6.79 (m, 2H), 3.86 (s, 3H), 3.31 (hept, 1H, J = 6.9 Hz), 1.26 (d, 6H, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 166.5, 157.1, 153.5, 139.6, 133.3, 131.8, 126.9, 126.8, 124.1, 122.3, 122.0, 118.9, 118.3, 52.1, 27.2, 22.8. IR (neat, cm^{-1}) 2958, 1737, 1602, 1235. Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found C, 75.77; H, 6.74.

2-(2'-Methylphenoxy)benzonitrile (Table 1, Entry 6). The general procedure was followed using ligand **6** at 100 ^{o}C for 20 h. The crude material was purified by flash chromatography column on silica gel (50:1 hexanes:Et_2O) to afford 198 mg (91%) of the title compound as white solid, mp 61-63 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.65 (dd, 1H, *J* = 7.7, 1.6 Hz), 7.43 (ddd, 1H, *J* = 8.0, 8.0, 1.7 Hz), 7.29 (d, 1H, *J* = 7.5 Hz), 7.26-7.15 (m, 2H), 7.09 (ddd, 1H, *J* = 7.6, 7.6, 0.9 Hz), 6.99 (dd, 1H, *J* = 7.9, 1.1 Hz), 6.66 (d, 1H, *J* = 8.5 Hz), 2.22 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 159.9, 152.5, 134.2, 133.8, 131.8, 130.4, 127.4, 125.6, 122.1, 120.7, 116.1, 115.3, 102.6, 16.0. IR (neat, cm^{-1}) 2962, 2250, 1600, 1248. Anal. Calcd for $C_{14}H_{11}NO$: C, 80.36; H, 5.30. Found C, 80.25; H, 5.22.

2-(2'-Methylphenoxy)trifluoromethylbenzene (Table 1, Entry 7). The general procedure was followed at 110 ^{o}C for 22 h using 5 mol % ligand **6** (21 mg) and 3 mol % $Pd(OAc)_2$ (6.7 mg). The crude material was purified by flash chromatography column on silica gel (50:1 hexanes:Et_2O) to afford 214 mg (85%) of the title compound as a colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.65 (dd, 1H, *J* = 7.8 Hz, *J* = 0.8 Hz), 7.37 (td, 1H, *J* = 7.9 Hz, *J* = 1.1 Hz), 7.26 (dd, 1H, *J* = 7.4, *J* = 0.8 Hz), 7.19 (td, 1H, *J* = 7.5 Hz, *J* = 1.4 Hz), 7.14-7.06 (m, 2H), 6.94 (dd, 1H, *J* = 8.0 Hz, *J* = 1.0 Hz), 6.69 (d, 1H,

J = 8.4 Hz), 2.21 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 155.8, 153.2, 133.1, 131.7, 130.4, 127.3, 127.3 (q, *J* = 5.3 Hz), 124.9, 122.2, 121.6, 120.3, 119.8 (q, *J* = 31.3 Hz), 116.4, 15.9. IR (neat, cm^{-1}) 2971, 1609, 1488, 1459, 1243, 1131. Anal. Calcd for $C_{14}H_{11}F_3O$: C, 66.67; H, 4.40. Found C, 66.57; H, 4.28.

3-(2'-Methylphenoxy)acetophenone (Table 1, Entry 8).[7] The general procedure was followed using ligand 6 at 100 °C for 18 h. The crude material was purified by flash chromatography column on silica gel (50:1 hexanes:Et_2O) to afford 209 mg (92%) of the title compound as a colorless liquid.

Methyl 4-(3'-Methylphenoxy)benzoate (Table 1, Entry 9). The general procedure was followed using ligand 6 at 100 °C for 18 h to afford 223 mg (92%) of the title compound as colorless liquid. The crude material was purified by flash chromatography column on silica gel (50:1 hexanes:Et_2O). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.02 (d, 2H, *J* = 8.5 Hz), 7.29 (t, 1H, *J* = 7.7 Hz), 7.04-6.99 (m, 3H), 6.90-6.88 (m, 2H), 3.92 (s, 3H), 2.38 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 166.6, 161.9, 155.5, 140.2, 131.6, 129.7, 125.2, 124.2, 120.7, 117.2, 117.0, 51.9, 21.3.

4-(2'-Methylphenoxy)trifluoromethylbenzene (Table 1, Entry 10). The general procedure was followed using ligand **6** at 100 °C for 20 h. The crude material was purified by flash chromatography column on silica gel (hexane) to afford 238 mg (94%) of the title compound as colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.59 (d, 2H, *J* = 8.7 Hz), 7.34 (broad d, 1H, *J* = 7.4 Hz), 7.28 (broad t, 1H, *J* = 9.0 Hz), 7.20 (t, 1H, *J* = 7.4 Hz), 7.03 (d, 1H, *J* = 7.9 Hz), 6.98 (d, 2H, *J* = 8.6 Hz), 2.26 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 160.8, 153.1, 131.8, 130.5, 128.3, 127.5, 127.1 (q, *J* = 3.7 Hz), 125.2, 124.1 (q, *J* = 32.8 Hz), 120.8, 116.4, 16.0.

Methyl 3-phenoxybenzoate (Table 1, Entry 11).[5] The general procedure was followed using ligand **6** at 100 °C for 18 h. The crude material was purified by flash chromatography column on silica gel (50:1 hexanes:Et_2O) to afford 219 mg (96%) of the title compound as a colorless liquid.

1-Phenoxy-4-trifluoromethylbenzene (Table 1, Entry 12).[5] The general procedure was followed using ligand **6** at 100 °C for 20 h. The crude material was purified by flash chromatography column on silica gel (hexanes) to afford 215 mg (90%) of the title compound as a colorless liquid.

4-(4-Cyano-phenoxy)-benzoic acid methyl ester (Table 1, Entry 13). The general procedure was followed using ligand **6** at 100 °C for 21 h. The crude material was purified by flash chromatography column on silica (50:40 hexanes:Et_2O) to afford 208 mg (82%) of the title compound as colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.08 (d, 2H, *J* = 8.8 Hz), 7.66 (d, 2H, *J* = 8.9 Hz), 7.09 (d, 4H, *J* = 8.9 Hz), 3.90 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 166.2, 160.1, 159.1, 134.3, 131.9, 126.4, 119.1, 119.1, 118.5, 107.1, 52.2. IR (neat, cm^{-1}) 2251, 1710, 1596, 1239. Anal. Calcd for $C_{15}H_{11}NO_3$: C, 71.14; H 4.38. Found: C, 71.05; H 4.44.

4-(4-Acetyl-phenoxy)-benzonitrile (Table 1, Entry 14). The general procedure was followed at 115 °C for 20 h using 5 mol % ligand **6** (21 mg) and 4 mol % $Pd(OAc)_2$ (9.0 mg) to afford 176 mg (74%) of the title compound as white solid, mp 100-102 °C. The crude material was purified by flash chromatography column on silica (2:1 hexanes:Et_2O) followed by a second flash chromatography column (1:5 hexane:CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.02 (d, 2H, *J* = 8.5 Hz), 7.67 (d, 2H, *J* = 8.4 Hz), 7.10 (dd, 4H, *J* = 8.6 Hz, *J* = 3.1 Hz), 2.61 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 196.5, 160.0, 159.3, 134.3, 133.5, 130.8, 119.2, 118.5, 107.2, 26.5. IR (neat, cm^{-1}) 1667, 1592, 1497, 1245. Anal. Calcd for $C_{15}H_{11}NO_2$: C, 75.94; H 4.67. Found: C, 75.90; H 4.69.

2-Isopropyl-2'-methyldiphenyl Ether (Table 2, Entry 1). The general procedure was followed at 100 °C for 20 h. The crude material was purified by flash chromatography column on silica gel (75:1 hexanes:Et_2O) to afford 189 mg (84%) of the title compound as a colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.42 (dd, 1H, *J* = 7.2, 2.2 Hz), 7.32 (broad d, 1H, *J* = 7.4 Hz), 7.22-7.13 (m, 3H), 7.09 (dd, 1H, *J* = 7.4, 1.1 Hz), 6.83 (broad d, 1H, *J* = 8.0 Hz), 6.79 (dd, 1H, *J* = 7.8, 1.8 Hz), 3.45 (sept, 1H, *J* = 6.9 Hz), 2.40 (s,

3H), 1.37 (d, 6H, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 155.5, 154.4, 139.0, 131.2, 129.0, 127.0, 126.8, 126.7, 123.2, 123.0, 117.8, 117.6, 27.3, 22.9, 16.2.

2-Isopropyl-4'-methoxydiphenyl Ether (Table 2, Entry 2).[7] The general procedure was followed at 100 ^{o}C for 20 h to afford 178 mg (74%) of the title compound as a colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.34 (dd, 1H, *J* = 7.3, 1.9 Hz), 7.34-7.09 (m, 2H), 6.94-6.83 (m, 4H), 6.81 (dd, 1H, *J* = 7.8, 1.4 Hz), 3.82 (s, 3H), 3.40 (sept, 1H, *J* = 6.9 Hz), 1.29 (d, 6H, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 155.3, 154.9, 151.1, 139.4, 126.8, 126.7, 123.3, 119.4, 118.3, 114.8, 55.6, 27.1, 22.9.

3,3',4',5-Tetramethyldiphenyl Ether (Table 2, Entry 3).[7,9] The general procedure was followed at 50% scale for 19 h at 100 ^{o}C. The crude material was purified by flash chromatography column on silica gel (hexanes) to afford 103 mg (91%) of the title compound as colorless liquid.

3,5-Dimethyldiphenyl Ether (Table 2, Entry 4).[7,10] The general procedure was followed at 50% scale for 18 h at 100 ^{o}C. The crude material was purified by flash chromatography column on silica gel (hexanes) to afford 85 mg (86%) of the title compound as colorless liquid.

3-Methoxydiphenyl Ether (Table 2, Entry 5).[11] The general procedure was followed at 50% scale for 20 h at 100 ^{o}C. The crude material was purified by flash chromatography column on silica gel (hexanes) to afford 86 mg (86%) of the title compound as colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.35 (t, 2H, J = 7.4 Hz), 7.24 (t, 1H, J = 8.3 Hz), 7.12 (t, 1H, 7.4 Hz), 7.03 (dd, 2H, J = 8.7, 1.0 Hz), 6.69-6.66 (m, 1H), 6.62-6.59 (m, 2H), 3.79 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 160.9, 158.4, 156.9, 130.1, 129.7, 123.3, 119.0, 110.9, 108.8, 104.8, 55.3.

2,2',5-Trimethyldiphenyl Ether (Table 2, Entry 6).[7,9] The general procedure was followed at 100 ^{o}C for 24 h. The crude material was purified by flash chromatography

column on silica gel (hexanes) to afford 194 mg (92%) of the title compound as colorless liquid.

4-*tert*-Butyl-2'-methyldiphenyl Ether (Table 2, Entry 7).[7] The general procedure was followed at 100 ^{o}C for 20 h. The crude material was purified by flash chromatography column on silica gel (75:1 hexanes:Et_2O) to afford 240 mg (92%) of the title compound as colorless liquid.

4-Methoxy-2'-methyldiphenyl Ether (Table 2, Entry 8).[7,11] The general procedure was followed at 110 ^{o}C for 20 h. The crude material was purified by flash chromatography column on silica gel (50:1 hexanes:Et_2O) to afford 180 mg (84%) of the title compound as colorless liquid.

4-Methoxydiphenyl Ether (Table 2, Entry 9). The general procedure was followed at 50% scale for 16 h at 100 ^{o}C. The crude material was purified by flash chromatography column on silica gel (50:1 hexanes:Et_2O) to afford 89 mg (89%) of the title compound as colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.35-7.30 (m, 2H), 7.07 (t, 1H, J = 7.4 Hz), 7.02-6.96 (m, 4H), 6.91 (dt, 2H, J = 9.1, 2.4 Hz), 3.83 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 158.5, 155.8, 150.0, 129.6, 122.4, 120.8, 117.5, 114.8, 55.6.

4-*n*-Butyldiphenyl Ether (Table 2, Entry 10).[7] The general procedure was followed at 50% scale for 18 h at 100 ^{o}C. The crude material was purified by flash chromatography column on silica gel (hexanes) to afford 109 mg (96%) of the title compound as colorless liquid.

2,5-Dimethyldiphenyl Ether (Table 2, Entry 11).[7,13] The general procedure was followed at 50% scale for 16 h. The crude material was purified by flash chromatography column on silica gel (hexanes) at 100 ^{o}C to afford 88 mg (89%) of the title compound as colorless liquid.

2,5-Dimethyl-4'-methoxydiphenyl Ether (Table 2, Entry 12).[7] The general procedure was followed at 50% scale for 20 h. The crude material was purified by flash chromatography column on silica gel (50:1 hexanes:Et_2O) at 100 ^oC to afford 90 mg (79%) of the title compound as an off-white solid.

4-(2,5-Dimethyl-phenoxy)-benzoic acid methyl ester (Table 2, Entry 13). The general procedure was followed at 115 ^oC using 7 mol % ligand 1 (30 mg) and 5 mol % $Pd(OAc)_2$ (11 mg). The crude material was purified by flash chromatography column on silica gel (3:1 hexanes:Et_2O) to afford 196 mg (77%) of the title compound as a colorless liquid. ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.97 (d, 2H, *J* = 8.8 Hz), 7.15 (d, 1H, *J* = 7.7 Hz), 6.95 (d, 1H, *J* = 7.6 Hz), 6.87 (d, 2H, *J* = 8.8 Hz), 6.80 (s, 1H), 3.89 (s, 3H), 2.31 (s, 3H), 2.13 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 166.7, 162.2, 152.8, 137.5, 131.6, 131.4, 127.2, 125.9, 123.7, 121.5, 115.9, 51.9, 20.9, 15.6. IR (neat, cm^{-1}) 2985, 1737, 1374, 1233. Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37. Found: C, 80.72; H, 6.41.

4-*n*-Butyl-3',4'-dimethyldiphenyl Ether (Table 2, Entry 14).[7] The general procedure was followed at 50% scale for 20 h at 100 ^oC. The crude material was purified by flash chromatography column on silica gel (hexanes) to afford 119 mg (94%) of the title compound as a colorless liquid.

[3-(2-*tert*-Butylphenoxy)-phenyl]-dimethyl-amine (Table 2, Entry 15). The general procedure was followed at 100 ^oC for 18 h. The crude material was purified by flash chromatography column on silica gel (50:1 hexanes:Et_2O) to afford 238 mg (88%) of the title compound as white solid, mp 71-73 ^oC. ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.46 (dd, 1H, *J* = 7.7 Hz, *J* = 1.0 Hz), 7.27-7.17 (m, 2H), 7.09 (t, 1H, *J* = 7.8 Hz), 6.95 (d, 1H, *J* = 8.0 Hz), 6.52 (dd, 1H, *J* = 8.3 Hz, J = 2.4 Hz), 6.49 (broad s, 1H), 6.36 (dt, 1H, *J* = 8.1 Hz, *J* = 1.0 Hz), 2.99 (s, 6H), 1.52 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 158.6, 156.0, 152.0, 140.6, 129.8, 126.9, 126.9, 122.8, 120.0, 107.1, 106.8, 106.7, 103.3, 40.5, 34.7, 30.1. IR (neat, cm^{-1}) 2954, 1609, 1231. Anal. Calcd for $C_{18}H_{20}NO$: C, 80.26; H, 8.61. Found: C, 80.11; H, 8.73.

Dimethyl-(3-phenoxy-phenyl)-amine (Table 2, Entry 16). The general procedure was followed at 100 ^{o}C for 16 h. The crude material was purified by flash chromatography column on silica gel (5:1 hexanes:ethyl acetate) to afford 178 mg (84%) of the title compound as colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.35 (t, 2H, *J* = 7.2 Hz), 7.20 (td, 1H, *J* = 8.2 Hz, *J* = 1.6 Hz), 7.10 (t, 1H, *J* = 7.6 Hz), 7.05 (d, 2H, *J* = 7.7 Hz), 6.52 (broad d, 1H, *J* = 8.3 Hz), 6.45 (d, 1H, 2.2 Hz), 6.36 (broad d, 1H, *J* = 8.0 Hz), 2.96 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 158.0, 157.5, 152.1, 129.9, 129.5, 122.7, 118.5, 107.7, 106.8, 103.5, 40.5. IR (neat, cm^{-1}) 2877, 1592, 1488, 1229. Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 79.04; H, 6.86.

***N*-(4-Phenoxyphenyl)-acetamide (Table 2, Entry 17).**[5] The general procedure was followed at 100 ^{o}C for 20 h. The crude material was purified by flash chromatography column on silica gel (5:2 hexanes:Et_2O) to afford 216 mg (95%) of the title compound as colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.58 (broad s, 1H), 7.46 (d, 2H, *J* = 8.8 Hz), 7.32 (t, 2H, *J* = 7.6 Hz), 7.09 (t, 1H, *J* = 7.4 Hz), 6.99-6.95 (m, 4H), 2.17 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 168.5, 157.4, 153.4, 133.3, 129.7, 123.0, 121.8, 119.5, 118.4, 24.3.

2-Methoxy-2'-methyldiphenyl Ether (Table 2, Entry 18).[15] The general procedure was followed on a 0.4 equivalent scale for 20 h at 100 ^{o}C. The crude material was purified by flash chromatography column on silica gel (100:3 hexanes:Et_2O) to afford 77 mg (89%) of the title compound as colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.18 (d, 1H, *J* = 7.3 Hz), 7.10-7.04 (m, 4H), 6.89 (dt, 1H, *J* = 7.3, 1.6 Hz), 6.87-6.77 (m, 2H), 3.90 (s, 3H), 2.34 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 155.2, 150.5, 146.3, 131.2, 129.0, 126.9, 123.6, 123.2, 121.0, 118.7, 118.0, 114.8, 112.6, 56.0, 16.1.

3-(2-Isopropylphenoxy)quinoline (Table 3, Entry 1). The general procedure was followed at 115 ^{o}C for 24 h. The crude material was purified by flash chromatography column on silica gel (3:1 hexanes:Et_2O) to afford 238 mg (90%) of the title compound as white solid, mp 96-97 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.84 (d, 1H, *J* = 2.8 Hz), 8.10

(d, 1H, *J* = 8.4 Hz), 7.64-7.658 (m, 2H), 7.49 (t, 1H, *J* = 7.9 Hz), 7.43-7.41 (m, 1H), 7.32 (d, 1H, *J* = 2.7 Hz), 7.26-7.22 (m, 2H), 6.99-6.97 (m, 1H), 3.28 (hept, 1H, *J* = 6.9 Hz), 1.24 (d, 6H, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 152.5, 152.1, 144.6, 144.3, 140.5, 129.2, 128.6, 127.5, 127.4, 127.2, 127.2, 126.9, 125.2, 121.1, 118.0, 27.1, 23.0. IR (neat, cm^{-1}) 2964, 2362, 1600, 1223. Anal. Calcd for $C_{18}H_{17}NO$: C, 82.10; H 6.51. Found: C, 82.17; H 6.66.

3-Phenoxyquinoline (Table 3, Entry 2). The general procedure was followed at 50% scale for 24 h at 115 ^{o}C using 6 mol % ligand 2 (14 mg) and 5 mol % $Pd(OAc)_2$ (4.5 mg). The crude material was purified by flash chromatography column on silica gel (2:1 hexanes:Et_2O) to afford 82 mg (75%) of the title compound as white solid, mp 64-67 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.83 (d, 1H, *J* = 2.8 Hz), 8.12 (d, 1H, *J* = 8.2 Hz), 7.69-7.62 (m, 2H), 7.54-7.52 (m, 2H), 7.42 (t, 2H, *J* = 8.5 Hz), 27.21 (t, 1H, *J* = 7.4 Hz), 7.11 (d, 2H, *J* = 7.6 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 156.2, 151.1, 145.1, 144.6, 130.1, 129.2, 128.5, 127.8, 127.2, 127.0, 124.3, 120.1, 119.2. Anal. Calcd for $C_{15}H_{11}NO$: C, 81.43; H 5.01. Found: C, 81.31; H 5.06.

3-*o*-Tolyloxypyridine (Table 3, Entry 3). The general procedure was followed at 115 ^{o}C for 20 h using 10 mol % ligand 1 (42 mg) and 8 mol % $Pd(OAc)_2$ (18 mg). The crude material was purified by flash chromatography column on silica gel (2:1 hexanes:Et_2O) to afford 163 mg (88%) of the title compound as colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.34 (d, 1H, *J* = 2.7 Hz), 8.31 (dd, 1H, *J* = 4.6 Hz, *J* = 1.2 Hz), 7.28-7.11 (m, 5H), 6.91 (d, 1H, *J* = 7.9 Hz), 2.23 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 154.3, 153.5, 143.5, 140.1, 131.7, 129.9, 127.4, 123.9, 123.6, 119.7, 16.1. IR (neat, cm^{-1}) 3035, 1573,1231. Anal. Calcd for $C_{12}H_{11}NO$: C, 77.81; H 5.99. Found: C, 77.10; H 6.00.

2-*o*-Tolyloxypyrazine (Table 3. Entry 4). The general procedure was followed at 100 ^{o}C for 24 h. The crude material was purified by flash chromatography column on silica gel (2:1 hexanes:Et_2O) to afford 161 mg (87%) of the title compound as colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.44 (d, 1H, *J* = 1.4 Hz), 8.25 (d, 1H, *J* = 2.7 Hz), 8.09 (dd, 1 H, *J* = 2.7 Hz), 7.32-7.18 (m, 3H), 7.08 (dd, 1H, *J* = 7.8 Hz, 1.2 Hz), 2.19 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ: 160.1, 151.2, 141.2,138.1, 135.4, 131.5, 130.6, 127.2, 125.9, 121.7, 16.3. IR (neat, cm^{-1}) 3051, 1578, 1283. Anal. Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H 5.41. Found: C, 70.72; H 5.47.

4-Phenoxyquinoline (Table 3, Entry 5).[14] The general procedure was followed at 100 ^oC for 22 h. The crude material was purified by flash chromatography column on silica gel (2:1 hexanes:Et_2O) to afford 191 mg (86%) of the title compound as colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.68 (d, 1H, *J* = 5.1 Hz), 8.38 (d, 1H, *J* = 8.3 Hz), 8.10 (d, 1H, *J* = 8.5 Hz), 7.77 (t, 1H, *J* = 7,7 Hz), 7.59 (t, 1H, *J* = 7.6 Hz), 7.48 (t, 2H, *J* = 7.3 Hz), 7.31 (t, 1H, *J* = 7.4 Hz), 7.20 (d, 2H, *J* = 7.7 Hz), 6.56 (d, 1H, *J* = 5.1 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 161.8, 154.3, 151.1, 149.8, 130.3, 130.1, 129.1, 126.1, 125.6, 121.8, 121.5, 121.1, 104.3.

1-Phenoxyisoquinoline (**Table 3, Entry 6).**[5,15] The general procedure was followed at 50% scale for 20 h. The crude material was purified by flash chromatography column on silica gel (2:1 hexanes:Et_2O) at 100 ^oC to afford 100 mg (90%) of the title compound as white solid, mp 66-68 ^oC. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.44 (d, 1H, *J* = 8.3 Hz), 7.97 (d, 1H, *J* = 5.8 Hz), 7.79 (d, 1H, *J* = 8.1 Hz), 7.72 (dt, 1H, *J* = 8.1 Hz, *J* = 1.1 Hz), 7.62 (dt, 1H, *J* = 8.1 Hz, *J* = 1.1 Hz), 7.46 (t, 2H, *J* = 7.9 Hz), 7.31 (d, 1H, *J* = 5.9 Hz), 7.27-7.23 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 160.6, 153.8, 139.8, 138.4, 130.8, 129.6, 127.1, 126.2, 125.0, 124.2, 121.8, 119.8, 116.3.

2-Methyl-5-phenoxybenzooxazole (Table 3, Entry 7). The general procedure was followed at 50% scale for 19 h at 100 ^oC. The crude material was purified by flash chromatography column on silica gel (2:1 hexanes:Et_2O) to afford 103 mg (91%) of the title compound as brown liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.41-7.39 (m, 1H), 7.33-7.29 (m, 3H), 7.07 (t, 1H, *J* = 7.3 Hz), 7.01-6.97 (m, 3H), 2.62 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 165.1, 158.0, 153.6, 147.3, 142.4, 129.6, 122.9, 118.0, 116.6, 110.5, 110.1, 14.5. IR (neat, cm^{-1}) 3066, 1663, 1490, 1214. Anal. Calcd for $C_{14}H_{11}NO_2$: C, 74.65; H 4.92. Found: C, 74.35; H 4.85.

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