Use of Tunable Ligands Allows for Intermolecular Pd-Catalyzed C-O Bond

Formation

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Supporting Information.

General Considerations. All ligand syntheses and Pd-catalyzed cross-coupling reactions were carried out under an atmosphere of argon in oven-dried glassware. Unless otherwise indicated, all other reactions were carried out under an atmosphere of argon. Toluene, THF, and diethyl ether were purchased from J. T. Baker in CYCLE-TAINER® solvent delivery kegs, which were vigorously purged with argon for 2 h, and further purified by passing the solvent 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). Tributylamine was distilled over CaH_2 and stored under argon. 1-Butanol, 2-butanol, benzyl alcohol were purchased from Aldrich in Sure-Seal® bottles and used without further purification. All other alcohols were purchased from Alfa Aesar or Aldrich, dried by stirring with CaH_2 , filtered through a layer of Celite and stored under argon over 3Å molecular sieves. Di-*tert*-butylchlorophosphine was generously donated by FMC Lithium and distilled before use. Liquid aryl halides were purchased from Alfa Aesar or Aldrich and filtered through a thin pad of alumina prior to use. Magnesium powder (50 mesh) was purchased from Aldrich and used without further purification. A solution of neopentylmagnesium

chloride was purchased from Alfa Aesar. Anhydrous Cs_2CO_3 was generously donated by Chemetall GmbH; the bulk of the material was stored under nitrogen in a Vacuum Atmospheres glovebox. Small portions (1-2 g) were removed from the glovebox in glass vials, stored in the air in desiccators filled with anhydrous calcium sulfate, and weighed in the air. $\text{Pd}(\text{OAc})_2$, copper (I) chloride, ZnCl_2 and bromine were purchased from Strem chemical company and used without further purification. 1,2,3,4-Tetramethylbenzene was purchased from TCI America, Inc. GC yields (Table 1) were determined using dodecane as an internal standard. Yields refer to isolated yields of compounds greater than 95 % purity as determined by capillary gas chromatography (GC), and proton Nuclear Magnetic Resonance spectroscopy (^1H NMR) analysis. New compounds were also characterized by elemental analysis (Atlantic Microlabs, Norcross, GA). Yields reported in this section refer to a single experiment whereas those reported for Pd-catalyzed coupling of aryl halides with alcohols are an average of two runs. IR spectra were recorded on a Perkin Elmer system 2000 FT-IR. Specific rotations were measured on a Jasco P-1010 polarimeter. Mass spectra were recorded on Bruker Apex IV FT-MS with 4.7 T magnet and EI or ESI ion source. ^1H NMR, ^{13}C NMR, ^{31}P NMR spectra were recorded on Varian 300 MHz, Varian 500 MHz or Bruker 400 MHz instruments with chemical shifts reported in ppm relative to the residual deuterated solvent or TMS as an internal standard. Gas chromatography analyses were performed on a Hewlett Packard 6890 instrument with a FID detector and a Hewlett Packard 10 m x 0.1 mm i.d. HP-1 column. Melting points (uncorrected) were obtained on a Mel-Temp capillary melting

point apparatus. The procedures described in this section are representative; thus, the yields may differ slightly from those given in Tables 1, 2, 3 and eq. 2.

Synthesis of Ligands.

Ligands **L1**,¹ **L2**,² **L3**,³ **L5**⁴ have been previously reported by our group.

1,2-Dibromo-3,4,5,6-tetramethylbenzene.

The reaction was performed using a modification of the known procedure.⁵ ZnCl₂ (23.12 g, 170 mmol) was added to 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. After the addition was complete the formation of a white precipitate was observed. The reaction mixture was stirred for 14 h at room temperature, then a saturated solution of Na₂SO₃ (50 mL) was added to quench the excess of bromine. CH₂Cl₂ (400 mL) and water (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 organic layer was collected, washed with 10 % aqueous NaOH (3 x 200 mL) and water (200 mL). The organic layer was separated, dried over MgSO₄ and concentrated *in vacuo* to afford crude product. Crystallization was performed by dissolving the compound in THF and adding hexane (50 mL). Cooling the solution to 0 °C resulted in the formation of a white solid, which was washed with pentane and dried. Two crops were collected. Combined

yield of the title compound: 19.96 g, 85 %. M.p. 204 - 206 °C (lit.⁶ 208 °C). ¹H NMR (300 MHz, CDCl₃) δ 2.50 (s, 6H), 2.25 (s, 6H).

Synthesis of Ligands. General procedure.

An oven-dried Schlenk tube was charged with magnesium powder (0.280 g, 11.5 mmol), aryl bromide (5.0 mmol) and THF (6 mL). The Schlenk tube was put into a 60 °C oil bath and 1,2-dibromoethane (43 mg, 20 µl, 0.23 mmol) was added dropwise via syringe over 15 min. The mixture was stirred at 60 °C for 15 min and then 1,2-dibromo-3,4,5,6-tetramethylbenzene (1.46 g, 5.00 mmol) was added portionwise over 30 min. The resulting mixture was stirred at 60 °C for 1.5 h, and then allowed to cool to room temperature. Copper(I) chloride (0.50 g, 5.0 mmol) was weighed in the glovebox and removed from the glovebox right before its addition into the above reaction mixture under a flow of argon. This was followed by the addition of di-*tert*-butylchlorophosphine (1.083 g, 1.2 mL, 6.0 mmol). The Schlenk tube was sealed with a Teflon screw cap and put into a 75 °C oil bath. The reaction mixture was stirred at 75 °C for 40 h. The Schlenk tube was taken out of the 75 °C oil bath and allowed to cool to room temperature. The reaction mixture was quenched with 30 % aqueous NH₄OH solution (50 mL). The resulting suspension was extracted with 4 : 1 ethyl acetate : diethyl ether (100 mL). The organic layer was separated and washed with 30 % aqueous NH₄OH (3 x 50 mL) and brine once (50 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. The product was purified as indicated below.

2-Di-*tert*-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-tri-*iso*-propylbiphenyl (L4).

The general procedure for ligand synthesis was followed. The product was crystallized from a mixture of ethanol and methyl *iso*-propyl ketone to give 1.214 g of the title compound as a white crystalline solid. The solvent was removed from the filtrate *in vacuo* and the residue was crystallized from ethanol to give 0.320 g of the title compound. Combined yield 1.534 g (64 %). Colorless crystals. M.p. 162 - 163 °C. ¹H NMR (300 MHz, C₆D₆) 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). ¹³C NMR (75 MHz, C₆D₆) 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). ³¹P NMR (121 MHz, C₆D₆) δ 38.7. IR (neat, cm⁻¹) 2957, 1459, 1382, 1361, 1067, 875, 802, 742. Anal. Calcd for C₃₃H₅₃P: C, 82.45; H, 11.11. Found: C, 82.27; H, 11.11.

1-(2-Di-*tert*-butylphosphino-3,4,5,6-tetramethylphenyl)-2-*iso*-propylnaphthalene (L6).

Step 1. 1-Bromo-2-*iso*-propylnaphthalene (99 % isomeric purity).

Bromination of 2-*iso*-propylnaphthalene was carried out according to the known procedure.⁷ A 100 mL round-bottom flask was charged with 2-*iso*-propylnaphthalene (11.3 g, 66.5 mmol) and CS₂ (20 mL). To the resulting solution, bromine (11.7 g, 73 mmol, 3.76 mL) was added dropwise with stirring. After the addition was complete, the mixture was stirred at room temperature for 17 h, then the excess of bromine was quenched by the addition of saturated aqueous Na₂SO₃ solution (25 mL). Water (50 mL) was added and the mixture was transferred to a separatory funnel. The organic layer was isolated and the aqueous layer was further extracted with diethyl ether (2 x 25 mL). The combined organic extracts were dried over MgSO₄. The solvent was removed and the residue was distilled *in vacuo* to give 14.99 g of yellowish liquid, which was analyzed by GC. Composition of the mixture: 2-*iso*-propylnaphthalene (2 %), 1-bromo-2-*iso*-propylnaphthalene (87 %), isomeric bromo-2-*iso*-propylnaphthalenes (11 %). The isomeric purity of 1-bromo-2-*iso*-propylnaphthalene was improved using a Ni-catalyzed Kumada coupling procedure.⁸ The above mixture was dissolved in diethyl ether (3.4 mL). NiCl₂(PPh₃)₂ (235 mg, 0.36 mmol) was added to the solution and the mixture was cooled to 0 °C. Next, MeMgBr (3 M, 18 mmol, 6 mL) was added dropwise. When the addition was complete the reaction mixture was heated to reflux for 12 h, then cooled to room temperature and quenched by the dropwise addition of 10 % HCl (3.5 mL). The resulting mixture was transferred to a separatory funnel and shaken with 10 % HCl (70 mL). The organic layer was separated and the aqueous layer was back extracted with diethyl ether (2 x 25 mL). The combined organic layers were dried over MgSO₄, the solvent was removed and the residue was filtered through a plug of silica gel (hexane) to give, after

evaporation of the solvent, 13.73 g of a colorless oil. The product mixture was analyzed by GC and ^1H NMR and found to consist of 1-bromo-2-*iso*-propylnaphthalene (99 % isomeric purity, ~ 75 % of the mixture), 2-*iso*-propylnaphthalene and isomeric methyl-2-*iso*-propylnaphthalenes. The yield of 1-bromo-2-*iso*-propylnaphthalene was approximately 62 %. The mixture was used in the next step without further purification.

Step 2. 1-(2-Di-*tert*-butylphosphino-3,4,5,6-tetramethylphenyl)-2-*iso*-propylnaphthalene.

An oven-dried two-neck 250 mL round-bottom flask was charged with magnesium powder (2.256 g, 94 mmol), 1-bromo-2-*iso*-propylnaphthalene (13.722 g of the mixture, step 1) and THF (50 mL). One neck was fitted with a rubber septum and another equipped with a pressure-equalizing dropping funnel. The dropping funnel was charged with 1,2-dibromo-3,4,5,6-tetramethylbenzene (13.14 g, 45 mmol) and diethyl ether (50 mL) and equipped with a reflux condenser. The apparatus was flushed with argon and the flask was put into a 60 °C oil bath and 1,2-dibromoethane (107 mg, 50 μL , 0.57 mmol) was added dropwise via syringe over 15 min. The mixture was stirred at 60 °C for an additional 15 min. Then the temperature of the oil bath was raised to 65 °C and the stopcock of the dropping funnel was opened. Throughout the addition of 1,2-dibromo-3,4,5,6-tetramethylbenzene (~ 4 h) the level of diethyl ether in the dropping funnel was kept constant by adjusting the stopcock. After the addition was complete the stopcock was closed and the reaction mixture was stirred at 65 °C for 1 h. Diethyl ether was distilled out of the reaction flask and collected in the dropping funnel. THF (30 mL) was

added into the flask and the hot solution was transferred via cannula into a 200 mL Schlenk tube, which contained copper(I) chloride (4.059 g, 41 mmol) under argon, followed by the addition of di-*tert*-butylchlorophosphine (8.88 g, 9.84 mL, 49 mmol) into the reaction mixture. The Schlenk tube was sealed with a Teflon screw cap and put into a 75 °C oil bath. The reaction mixture was stirred at 75 °C for 48 h. The Schlenk tube was taken out of the 75 °C oil bath and allowed to cool to room temperature. The reaction mixture was quenched with 30 % aqueous NH₄OH solution (400 mL, first 30 mL dropwise, with stirring). The resulting suspension was extracted with 4 : 1 ethyl acetate : diethyl ether (800 mL). The organic layer was separated and washed with 30 % aqueous NH₄OH (3 x 200 mL), then phosphines were extracted into the aqueous layer by 10 % HCl (2 x 400 mL). The combined organic layers were basified by the addition of 10 % NaOH. The crude product precipitated as yellow solid. It was filtered, washed with water, then with 4 : 1 ethyl acetate : diethyl ether (200 mL). The filtrate was transferred into a separatory funnel and shaken. The organic layer was isolated and the aqueous layer was extracted with 4 : 1 ethyl acetate : diethyl ether (200 mL). The combined organic extracts were dried over MgSO₄, the solvent was removed and the residue was combined with the previously isolated solid. This mixture was recrystallized from methyl *iso*-propyl ketone to give a white solid, which was washed with methanol. The mother liquor was concentrated and filtered through a plug of silica gel (25 % ethyl acetate in hexane). Two additional crops of crystals were collected and the combined product was dried *in vacuo*. The yield of the title compound was 13.32 g (73 %). Colorless crystals. M.p. 165 - 167 °C. ¹H NMR (400 MHz, C₆D₆) δ 7.75 (d, 1H, J = 8.6 Hz), 7.71 (d, 1H, J = 8.2 Hz), 7.51

(d, 1H, $J = 8.6$ Hz), 7.19-7.26 (m, 2H), 7.05-7.10 (m, 1H), 3.25 (septet, 1H, $J = 6.9$ Hz), 2.52 (s, 3H), 2.13 (s, 3H), 2.07 (s, 3H), 1.77 (s, 3H), 1.55 (d, 3H, $J = 7.0$ Hz), 1.32 (d, 9H, $J_{\text{HP}} = 11.7$ Hz), 1.05 (d, 3H, $J = 7.0$ Hz), 0.87 (d, 9 H, $J_{\text{HP}} = 11.7$ Hz). ^{13}C NMR (100 MHz, C_6D_6) δ 143.10, 143.06, 139.91, 139.87, 137.4, 135.12, 135.10, 134.42, 134.40, 133.0, 129.2, 128.5, 128.3, 125.2, 125.0, 124.2, 35.1, 34.7, 34.0, 33.6, 33.2, 33.0, 32.9, 32.7, 31.74, 31.71, 27.1, 24.5, 23.8, 20.4, 20.3, 17.6, 17.5 (observed complexity due to P-C splitting). ^{31}P NMR (161 MHz, C_6D_6) δ 38.7. IR (neat, cm^{-1}) 2959, 1461, 1386, 1360, 1166, 816, 748. Anal. Calcd for $\text{C}_{31}\text{H}_{43}\text{P}$: C, 83.36; H, 9.70. Found: C, 83.15; H, 9.68.

1-(2-Di-*tert*-butylphosphinophenyl)-2-*iso*-propylnaphthalene (L5).

The reaction was performed using a modification of the known procedure.⁴ An oven-dried Schlenk tube was charged with magnesium powder (0.312 g, 13.0 mmol), 1-bromo-2-*iso*-propylnaphthalene (99 % isomeric purity, from **L6**, step 1) (1.705 g of the mixture, ~ 1.245 g, ~ 5.0 mmol) and THF (6 mL). The Schlenk tube was put into a 60 °C oil bath and 1,2-dibromoethane (43 mg, 20 μl , 0.23 mmol) was added dropwise via syringe over 15 min. The mixture was stirred at 60 °C for 15 min and then the solution of 1-bromo-2-chlorobenzene (1.245 g, 6.5 mmol) in THF (9 mL) was added over 3.5 h via syringe with the help of a syringe pump. The resulting mixture was stirred at 60 °C for 1 h, and then allowed to cool to room temperature. Copper(I) chloride (0.50 g, 5.0 mmol) was weighed in the glovebox and removed from the glovebox right before its addition into the above reaction mixture under a flow of argon. This was followed by the addition of di-*tert*-butylchlorophosphine (1.083 g, 1.2 mL, 6.0 mmol). The Schlenk tube was sealed with a

Teflon screw cap and put into a 75 °C oil bath. The reaction mixture was stirred at 75 °C for 40 h. The Schlenk tube was taken out of the 75 °C oil bath and allowed to cool to room temperature. The reaction mixture was quenched with 30 % aqueous NH_4OH solution (50 mL). The resulting suspension was extracted with 4 : 1 ethyl acetate : diethyl ether (100 mL). The organic layer was separated and washed with 30 % aqueous NH_4OH (3 x 50 mL), then phosphines were extracted into the aqueous layer by 10 % HCl (2 x 50 mL). The combined organic layers were basified by the addition of 10 % NaOH . The product was extracted with 4 : 1 ethyl acetate : diethyl ether (2 x 50 mL). The combined organic extracts were dried over MgSO_4 , the solvent was removed to give the crude product as a colorless solid, which was recrystallized from ethanol. Two crops were collected, the combined product was dried *in vacuo*. The yield of the title compound was 1.186 g (61 %). Colorless crystals. M.p. 147 - 149 °C (lit.⁴ 141 - 142 °C). ^1H and ^{31}P NMR data were consistent with those of the previously reported compound.

1-(2-Di-*tert*-butylphosphino-3,4,5,6-tetramethylphenyl)-2-methoxynaphthalene (L7).

The general procedure for ligand synthesis was followed. The crude product was purified chromatographically (silica gel). First, a mixture of side products was washed out with 10 % ethyl acetate in hexane. Then the product phosphine was eluted with pure ethyl acetate. The solvent was evaporated and the residue was crystallized from methyl *iso*-propyl ketone, dried *in vacuo* to give 0.310 g of the title compound (14 %). Yellowish crystals. M.p. 208 - 210 °C. ^1H NMR (400 MHz, C_6D_6) δ 7.68-7.75 (m, 2H), 7.40-7.45 (m, 1H), 7.14-7.22 (m, 2H), 7.00 (d, 1H, $J = 8.8$ Hz), 3.38 (s, 3H), 2.55 (s, 3H), 2.14 (s, 3H), 2.05

(s, 3H), 1.93 (s, 3H), 1.28 (d, 9H, $J_{\text{HP}} = 12.2$ Hz), 1.02 (d, 9H, $J_{\text{HP}} = 12.2$ Hz). ^{13}C NMR (125 MHz, C_6D_6) δ 153.6, 145.0, 139.2, 139.1, 137.17, 137.16, 135.1, 134.9, 134.8, 129.7, 128.8, 128.69, 128.67, 127.6, 125.9, 123.5, 112.6, 55.0, 33.9, 33.6, 32.9, 32.8, 32.7, 32.5, 26.82, 26.81, 19.02, 19.00, 17.6, 17.5 (observed complexity due to P-C splitting). ^{31}P NMR (161 MHz, C_6D_6) δ 38.5. IR (neat, cm^{-1}) 2891, 1593, 1465, 1360, 1264, 1087, 802, 746. HRMS (ESI) calcd for $\text{C}_{29}\text{H}_{39}\text{OP}$ $[\text{M}+\text{H}^+]$: 435.2811. Found: 435.2806

¹H-NMR spectrum of L7

1-(2-Di-*tert*-butylphosphino-3,4,5,6-tetramethylphenyl)-2-phenylnaphthalene (L8).

The general procedure for ligand synthesis was followed. Magnesium powder (0.341 g, 14.20 mmol), 1-bromo-2-phenylnaphthalene⁹ (1.75 g, 6.18 mmol), 1,2-dibromoethane (43 mg, 20 μ l, 0.23 mmol), 1,2-dibromo-3,4,5,6-tetramethylbenzene (1.806 g, 6.18 mmol), copper(I) chloride (0.612 g, 6.18 mmol), di-*tert*-butylchlorophosphine (1.339 g, 1.48 mL, 7.42 mmol) and THF (7 mL) were used. The crude product was purified chromatographically (silica gel). First, a mixture of side products was washed out with hexane. Then the product phosphine was eluted with 20 % ethyl acetate in hexane. The solvent was evaporated and the residue was crystallized from a methyl *iso*-propyl ketone / ethanol mixture. The crystals were washed with methanol, dried *in vacuo* to give 0.852 g of the title compound (29 %). Colorless crystals. M.p. 165 - 167 °C. ¹H NMR (400 MHz, C₆D₆) δ 7.72 (t, 2H, J = 9.4 Hz), 7.66 (d, 1H, J = 8.5 Hz), 7.55 (d, 2H, J = 8.3 Hz), 7.38 (d, 1H, J = 8.7 Hz), 7.20-7.25 (m, 1H), 7.05-7.13 (m, 3H), 6.93-6.99 (m, 1H), 2.40 (s, 3H), 2.14 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 0.88 (d, 9H, J_{HP} = 12.2 Hz), 0.82 (d, 9H, J_{HP} = 11.9 Hz). ¹³C NMR (125 MHz, C₆D₆) δ 147.3, 146.9, 143.9, 140.3, 140.2, 140.0, 137.7, 137.6, 136.66, 136.65, 136.4, 136.3, 135.5, 135.1, 134.8, 134.68, 134.67, 133.5, 131.4, 129.7, 129.5, 128.7, 128.0, 127.0, 125.8, 125.6, 34.9, 34.6, 32.71, 32.66, 32.57, 32.4, 32.2, 26.89, 26.88, 20.25, 20.22, 17.6, 17.5 (observed complexity due to P-C splitting). ³¹P NMR (161 MHz, C₆D₆) δ 38.0. IR (neat, cm⁻¹) 2890, 1496, 1465, 1359, 1265, 1169, 821.5, 762, 740, 702. Anal. Calcd for C₃₄H₄₁P: C, 84.96; H, 8.60. Found: C, 84.69; H, 8.56.

1-(2-Di-*tert*-butylphosphino-3,4,5,6-tetramethylphenyl)-2-methylnaphthalene (L9).

The general procedure for ligand synthesis was followed. The crude product was dissolved in 25 % ethyl acetate in hexane, filtered through a plug of silica gel (25 % ethyl acetate in hexane). The solvent was evaporated and the residue was crystallized from a methyl *iso*-propyl ketone / methanol mixture, washed with methanol, dried *in vacuo* to give 0.655 g of the title compound (32 %). Colorless crystals. M.p. 147 - 148 °C. ¹H NMR (500 MHz, C₆D₆) δ 7.71 (d, 1H, J = 8.2 Hz), 7.64 (d, 1H, J = 8.2 Hz), 7.41 (d, 1H, J = 8.2 Hz), 7.29 (d, 1H, J = 8.2 Hz), 7.23 (t, 1H, J = 7.5 Hz), 7.14-7.18 (m, 1H), 2.50 (s, 3H), 2.20 (s, 3H), 2.16 (s, 3H), 2.09 (s, 3H), 1.83 (s, 3H), 1.17 (d, 9H, J_{HP} = 12.2 Hz), 1.01 (d, 9H, J_{HP} = 12.2 Hz). ¹³C NMR (125 MHz, C₆D₆) δ 147.8, 147.4, 141.6, 141.5, 139.8, 139.7, 137.22, 137.20, 135.9, 135.5, 135.1, 134.85, 134.81, 134.6, 134.5, 133.5, 133.4, 132.8, 128.9, 128.7, 128.6, 128.5, 127.3, 125.5, 124.9, 34.4, 34.1, 33.6, 33.0, 32.9, 32.7, 26.77, 26.75, 22.15, 22.14, 18.62, 18.60, 17.6, 17.5 (observed complexity due to P-C splitting). ³¹P NMR (161 MHz, C₆D₆) δ 36.3. IR (neat, cm⁻¹) 2891, 1454, 1359, 1165, 808, 742. Anal. Calcd for C₂₉H₃₉P: C, 83.21; H, 9.39. Found: C, 82.92; H, 9.52.

1-(2-Di-*t*-butylphosphino-3,4,5,6-tetramethylphenyl)-2-neopentyl-naphthalene (L10).

Step 1. 1-Bromo-2-neopentyl-naphthalene.

An oven-dried two-neck 250 mL round-bottom flask was cooled *in vacuo*, back-filled with argon. One neck was fitted with a rubber septum, another equipped with a reflux

condenser. The flask was charged with $\text{PdCl}_2(\text{dppp})^{10}$ (442 mg, 0.75 mmol), LiBr (1.305 g, 15 mmol) and trifluoromethanesulfonic acid 1-bromonaphthalen-2-yl ester⁹ (5.325 g, 15 mmol). The top of the condenser was closed by rubber septum and the apparatus was flushed with argon. Diethyl ether (132 mL) was added and the stirring was started. The reaction was performed under 1 atmosphere of argon maintained by a balloon. A solution of neopentylmagnesium chloride (1 M, 18 mL, 18 mmol) was added to the reaction mixture at room temperature and the flask was put into a 50 °C oil bath. The reaction mixture was refluxed for 36 h and was monitored by TLC for the disappearance of the starting material. Then the mixture was cooled to room temperature and quenched by the dropwise addition of methanol (5 mL, exothermic!). 5 % HCl (100 mL) was added and the mixture was transferred into a separatory funnel. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were dried over MgSO_4 . The residue after the solvent removal was filtered through a plug of silica gel (hexane), giving, after solvent removal, a yellowish solid (4.047 g). GC analysis: 96 % title compound, 4 % 2-neopentyl-naphthalene. Estimated yield of 1-bromo-2-neopentyl-naphthalene: 3.89 g (94 %). The material can be used in the next step without further purification. To obtain the pure product, the solid was stirred with 20 mL of methanol at room temperature for 1 h. Then the precipitate was isolated by filtration, washed with methanol, dried *in vacuo*. Obtained 2.646 g of colorless crystals. M.p. 78 – 79 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.36 (d, 1H, $J = 8.9$ Hz), 7.78 (d, 1H, $J = 7.8$ Hz), 7.68 (d, 1H, $J = 8.3$ Hz), 7.53-7.58 (m, 1H), 7.44-7.49 (m, 1H), 7.32 (d, 1H, $J = 8.4$ Hz), 3.00 (s, 2H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 137.8, 133.1, 132.7, 129.9,

127.91, 127.86, 127.1, 126.4, 125.8, 125.4, 49.2, 33.8, 29.9. IR (neat, cm^{-1}) 2960, 1476, 1365, 1265, 821, 740. MS (EI) 278 [M^+ , $\{^{81}\text{Br}\}$], 276 [M^+ , $\{^{79}\text{Br}\}$], 222, 220, 141. HRMS (EI) calcd for $\text{C}_{15}\text{H}_{17}\text{Br}$: 276.0508 $\{^{79}\text{Br}\}$. Found: 276.0511 $\{^{79}\text{Br}\}$.

¹H NMR spectrum of 1-bromo-2-neopentyl-naphthalene

Current Data Parameters
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 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
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 Time 9.22
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 PULPROG zg30
 TO 65336
 SOLVENT CDCl3
 NS 16
 DS 2
 SMH 8278.146 Hz
 FIDRES 0.126314 Hz
 AQ 3.5584243 sec
 RG 57
 DM 60.400 usec
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 TE 300.0 K
 D1 1.00000000 sec

===== CHANNEL f1 =====
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 P1 7.90 usec
 PL1 0.00 dB
 SFO1 400.1324710 MHz

F2 - Processing parameters
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 LB 0.30 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
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 F1 3528.68 Hz
 F2P -0.198 ppm
 F2 -79.06 Hz
 PPMCM 0.45082 ppm/cm
 HZCM 180.38678 Hz/cm

Step 2. 1-(2-Di-*tert*-butylphosphino-3,4,5,6-tetramethylphenyl)-2-neopentyl-naphthalene.

The procedure used for the synthesis of **L6** was followed. Magnesium powder (2.16 g, 90 mmol), 1-bromo-2-neopentyl-naphthalene (10.82 g, 39 mmol), 1,2-dibromo-3,4,5,6-tetramethylbenzene (12.556 g, 43 mmol), 1,2-dibromoethane (107 mg, 50 μ l, 0.57 mmol), copper(I) chloride (3.861 g, 39 mmol) and di-*tert*-butylchlorophosphine (8.525 g, 9.45 mL, 47 mmol) were used. The crude product precipitated as yellow solid. It was filtered, washed with water, dried. The filtrate was extracted with 4 : 1 ethyl acetate : diethyl ether (2 x 200 mL). The organic layer was isolated and the aqueous layer was extracted with 4 : 1 ethyl acetate : diethyl ether (200 mL). The combined organic extracts were dried over MgSO_4 , the solvent was removed and the residue was united with the previously isolated solid. The product was crystallized from a toluene / ethanol mixture to give white solid, which was washed with methanol. The mother liquor was concentrated and filtered through a plug of silica gel (25 % ethyl acetate in hexane). Two additional crops of crystals were collected and the combined product was dried *in vacuo*. The yield of the title compound was 10.673 g (58 %). Colorless crystals. M.p. 184 - 185 °C. ^1H NMR (400 MHz, C_6D_6) δ 7.71 (d, 1H, J = 8.2 Hz), 7.68 (d, 1H, J = 8.5 Hz), 7.60 (d, 1H, J = 8.8 Hz), 7.31 (d, 1H, J = 8.5 Hz), 7.20-7.25 (m, 1H), 7.07-7.12 (m, 1H), 2.96 (d, 1H, J = 13.5 Hz), 2.84 (d, 1H, J = 13.6 Hz), 2.51 (s, 3H), 2.10 (s, 6H), 1.92 (s, 3H), 1.40 (d, 9H, J_{HP} = 12.1 Hz), 0.97 (s, 9H), 0.80 (d, 9H, J_{HP} = 12.1 Hz). ^{13}C NMR (100 MHz, C_6D_6) δ 139.9, 139.8, 137.3, 136.50, 136.45, 135.4, 135.2, 134.5, 132.8, 129.6, 129.3, 126.7, 125.2, 124.9, 50.6, 50.5, 35.2, 34.8, 34.0, 33.6, 33.5, 33.3, 33.2, 32.7, 32.5, 31.5, 27.0,

21.61, 21.57, 17.7, 17.5 (observed complexity due to P-C splitting). ^{31}P NMR (161 MHz, C_6D_6) δ 39.1. IR (neat, cm^{-1}) 2951, 1465, 1362, 1166, 819, 756, 741. Anal. Calcd for $\text{C}_{33}\text{H}_{47}\text{P}$: C, 83.50; H, 9.98. Found: C, 83.24; H, 9.94.

1-(2-Di-*tert*-butylphosphinophenyl)-2-neopentyl-naphthalene (L11).

An oven-dried Schlenk tube was charged with 1-bromo-2-neopentyl-naphthalene (0.723 g, 2.61 mmol), 2-chlorophenylboronic acid (0.6 g, 3.834 mmol), K_3PO_4 (1.219 g, 5.751 mmol), $\text{Pd}(\text{OAc})_2$ (8.6 mg, 0.038 mmol), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (19 mg, 0.046 mmol) and toluene (5 mL). The Schlenk tube was sealed with a Teflon screw cap and placed into a 90 °C oil bath. The mixture was stirred at 90 °C for 7 h and then cooled to room temperature and then quenched by the addition of water. The product was extracted with diethyl ether (2 x 25 mL). The combined organic layers were dried over MgSO_4 . The solvent was removed and the residue was filtered through a plug of silica gel (hexane). A colorless oil was obtained after the removal of solvent, which was analyzed by GC and GC-MS. The coupling product 1-(2-chlorophenyl)-2-neopentyl-naphthalene was about 90 % pure and was used without further purification. An oven-dried Schlenk tube was charged with magnesium powder (0.081 g, 3.4 mmol), 1-(2-chlorophenyl)-2-neopentyl-naphthalene (90 % pure) and THF (3 mL). The Schlenk tube was put into a 60 °C oil bath and 1,2-dibromoethane (22 mg, 10 μl , 0.12 mmol) was added dropwise via syringe over 5 min. The mixture was stirred at 60 °C for 20 min and then 1,2-dibromoethane (43 mg, 20 μl , 0.23 mmol) was added. The tube was sealed with a Teflon screw cap, then the mixture was stirred at 75 °C for 17 h.

The mixture was then cooled to room temperature. Copper(I) chloride (0.258 g, 2.61 mmol) was weighed in the glovebox and removed from the glovebox right before its addition into the above reaction mixture under a flow of argon, followed by the addition of di-*tert*-butylchlorophosphine (0.471 g, 0.52 mL, 2.61 mmol). The Schlenk tube was sealed with a Teflon screw cap and put into a 75 °C oil bath. The reaction mixture was stirred at 75 °C for 30 h. The Schlenk tube was taken out of the 75 °C oil bath and allowed to cool to room temperature. The reaction mixture was quenched with 30 % aqueous NH₄OH solution (25 mL). The resulting suspension was extracted with 4 : 1 ethyl acetate : diethyl ether (50 mL). The organic layer was separated and washed with 30 % aqueous NH₄OH (3 x 25 mL) and the phosphine products were extracted into the aqueous layer by 10 % HCl (2 x 50 mL). The combined organic layers were basified by the addition of 10 % NaOH, extracted with 4 : 1 ethyl acetate : diethyl ether (2 x 25 mL). The crude product was isolated by solvent removal, filtered through a plug of silica gel (hexane), crystallized from methanol by passing the flow of N₂ over the solution, washed with methanol, dried *in vacuo* to give 0.339 g of the title compound (31 %). Colorless crystals. M.p. 109 - 110 °C. ¹H NMR (400 MHz, C₆D₆) δ 7.87-7.92 (m, 1H), 7.70 (d, 1H, J = 8.0 Hz), 7.67 (d, 1H, J = 8.5 Hz), 7.50 (d, 1H, J = 8.5 Hz), 7.47 (d, 1H, J = 8.0 Hz), 7.36-7.42 (m, 1H), 7.17-7.25 (m, 3H), 7.11-7.16 (m, 1H), 2.98 (d, 1H, J = 12.9 Hz), 2.70 (d, 1H, J = 13.2 Hz), 1.29 (d, 9H, J_{HP} = 11.2 Hz), 0.88 (s, 9H), 0.81 (d, 1H, J_{HP} = 11.2 Hz). ¹³C NMR (125 MHz, C₆D₆) δ 148.5, 148.3, 139.9, 139.8, 139.2, 138.9, 136.58, 136.56, 136.00, 135.98, 135.02, 134.97, 134.6, 133.2, 129.8, 128.7, 127.2, 126.6, 125.5, 125.1, 49.30, 49.26, 33.8, 33.1, 32.9, 32.8, 32.7, 32.4, 32.3, 31.1, 30.9 (observed

complexity due to P-C splitting). ^{31}P NMR (161 MHz, C_6D_6) δ 23.7. IR (neat, cm^{-1}) 3052, 2951, 1475, 1385, 1363, 1173, 822, 756. Anal. Calcd for $\text{C}_{29}\text{H}_{39}\text{P}$: C, 83.21; H, 9.39. Found: C, 83.05; H, 9.57.

Coupling of 5-bromo-*m*-xylene with 2-butanol. Ligand evaluation (Table 1).

Ten oven-dried Schlenk tubes were cooled *in vacuo* and then back-filled with argon. Each tube was charged with $\text{Pd}(\text{OAc})_2$ (2.2 mg, 0.01 mmol), appropriate ligand **L1** – **L10** (1.2 mmol) and Cs_2CO_3 (245 mg, 0.75 mmol). The Schlenk tubes were fitted with rubber septa, evacuated and back-filled with argon. 5-Bromo-*m*-xylene (**1a**) (93 mg, 0.5 mmol), 2-butanol (74 mg, 1 mmol) and dodecane (85 mg, 0.5 mmol) were added into each tube through the septum via syringe, followed by dry toluene (1 mL). Then the septa were replaced with Teflon screw caps under argon, the tubes were sealed and placed in an oil bath (90 °C) for 24 h. After this time the reaction mixtures were cooled to room temperature, filtered through a layer of Celite with the aid of ethyl acetate and analyzed by GC. The corrected GC yields of the starting **1a** and the products 1-*sec*-butoxy-3,5-dimethylbenzene (**2a**), *m*-xylene (**3**), di-(3,5-dimethylphenyl)ether¹¹ (**4**) and 3,3',5,5'-tetramethylbiphenyl¹² (**5**) were measured. The results are reported in table 1.

General Procedure for the Intermolecular Coupling of Alcohols with Aryl Halides.

An oven-dried Schlenk tube was cooled *in vacuo*, back-filled with argon and charged with $\text{Pd}(\text{OAc})_2$, ligand and Cs_2CO_3 . The Schlenk tube was fitted with rubber septum, evacuated, and back-filled with argon. The aryl halide and alcohol were added through

the septum via syringe, followed by the solvent. The septum was replaced with a Teflon screw cap under a counterflow of argon, the tube was sealed and was placed in an oil bath. The reaction was conducted under the conditions indicated below. After the reaction mixture was allowed to cool to room temperature, it was filtered through a layer of Celite with the aid of ethyl acetate. In the cases where toluene was used as the solvent, the filtrate was concentrated *in vacuo* and the crude product was purified chromatographically (silica gel). In the cases where Bu₃N was used as the solvent, the filtrate was extracted with 10 % HCl. The organic layer was isolated and the aqueous layer was back extracted with diethyl ether. The combined organic extracts were dried over MgSO₄ and the crude product was purified chromatographically (silica gel). The yields of the coupling products are indicated below.

1-*sec*-butoxy-3,5-dimethylbenzene (2a)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), 5-bromo-*m*-xylene (185 mg, 1 mmol), 2-butanol (148 mg, 2 mmol) with Bu₃N (1 mL) as solvent for 24 h at 90 °C. The filtrate was extracted with 10 % HCl (2 x 20 mL). The combined organic extracts were concentrated to exactly 5 mL, 0.5 mL of this solution was taken, mixed with 0.1 M solution of dodecane in ethyl acetate (1 mL) and the resulting solution was analyzed by GC. GC yields: **2a** (76 %), **3** (5 %), **4** (4 %), **5** (6 %). Chromatographic purification (hexane, followed by 5 % ethyl acetate in hexane) provided **2a** (colorless liquid, 132 mg, 74 %). ¹H NMR (400 MHz, CDCl₃) δ 6.57 (s, 1H), 6.52 (s, 2H), 4.26 (sextet, 1H, J = 6.1 Hz),

2.28 (s, 6H), 1.67-1.78 (m, 1H), 1.56-1.65 (m, 1H), 1.27 (d, 3H, $J = 6.0$ Hz), 0.97 (t, 3H, $J = 7.5$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 158.2, 139.1, 122.2, 113.6, 74.7, 29.3, 21.4, 19.3, 9.9. IR (neat, cm^{-1}) 2972, 2922, 1594, 1465, 1321, 1294, 1180, 1153, 1125, 1052, 828, 690. Anal. Calcd for $\text{C}_{12}\text{H}_{18}\text{O}$: C, 80.85; H, 10.18. Found: C, 81.02; H, 10.27.

1-Cyclopentyloxy-3,5-dimethylbenzene (2b)

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 5-bromo-*m*-xylene (185 mg, 1 mmol) and cyclopentanol (172 mg, 2 mmol) with Bu_3N (2 mL) as solvent for 24 h at 90 °C. The filtrate was extracted with 10 % HCl (2 x 35 mL). Chromatographic purification (hexane, followed by 5 % ethyl acetate in hexane) provided **2b** (colorless liquid, 144 mg, 76 %). ^1H NMR (400 MHz, CDCl_3) δ 6.56 (s, 1H), 6.51 (s, 2H), 4.70-4.75 (m, 1H), 2.27 (s, 6H), 1.73-1.93 (m, 6H), 1.56-1.64 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 158.1, 139.0, 122.0, 113.2, 78.8, 32.9, 24.0, 21.5. IR (neat, cm^{-1}) 2961, 1594, 1471, 1325, 1294, 1155, 1053, 829, 689. Anal. Calcd for $\text{C}_{13}\text{H}_{18}\text{O}$: C, 82.06; H, 9.53. Found: C, 82.09; H, 9.66.

1,3-Dimethyl-5-(1-methyl-2-phenylethoxy)-benzene (2c)

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6.7 mg, 0.03 mmol), **L10** (17.1 mg, 0.036 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 5-bromo-*m*-xylene (185 mg, 1 mmol), 1-phenylpropan-2-ol (272 mg, 2 mmol) with Bu_3N (4 mL) as solvent for 24 h at 90 °C. The filtrate was extracted with 10 % HCl (2 x 50 mL). Chromatographic purification (hexane)

provided **2c** (colorless liquid, 164 mg, 68 %). ^1H NMR (400 MHz, CDCl_3) δ 7.19-7.33 (m, 5H), 6.58 (s, 1H), 6.52 (s, 2H), 4.55 (sextet, 1H, $J = 6.0$ Hz), 3.09 (dd, 1H, $J = 13.6$, 6.0 Hz), 2.80 (dd, 1H, $J = 13.6$, 6.7 Hz), 2.27 (s, 6H), 1.28 (d, 3H, $J = 6.0$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 157.8, 139.1, 138.3, 129.5, 128.3, 126.3, 122.4, 113.7, 74.3, 42.7, 21.4, 19.4. IR (neat, cm^{-1}) 2919, 1593, 1454, 1377, 1295, 1155, 1077, 829, 745, 700. Anal. Calcd for $\text{C}_{17}\text{H}_{20}\text{O}$: C, 84.96; H, 8.39. Found: C, 84.70; H, 8.35.

1,3-Dimethyl-5-(1,2,2-trimethylpropoxy)-benzene (2d)

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 5-bromo-*m*-xylene (185 mg, 1 mmol), 3,3-dimethylbutan-2-ol (204 mg, 2 mmol) with Bu_3N (1 mL) as solvent for 24 h at 90 °C. The filtrate was extracted with 10 % HCl (2 x 25 mL). Chromatographic purification (hexane) provided a colorless liquid (124 mg), which was a mixture of **2d** and a small amount of **5** that could not be fully separated. The amount of **2d** in the mixture was estimated using GC and ^1H -NMR: 117 mg (57 %). Further chromatographic purification (2 % methylene chloride in hexane) of the small amount of the mixture (50 mg) provided pure **2d**. ^1H NMR (400 MHz, CDCl_3) δ 6.56 (s, 1H), 6.53 (s, 2H), 3.99 (q, 1H, $J = 6.3$ Hz), 2.28 (s, 6H), 1.18 (d, 3H, $J = 6.3$ Hz), 0.98 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 158.9, 139.1, 122.0, 113.5, 80.8, 35.0, 25.9, 21.4, 14.2. IR (neat, cm^{-1}) 2959, 1595, 1470, 1376, 1321, 1295, 1155, 1082, 954, 829, 689. Anal. Calcd for $\text{C}_{14}\text{H}_{22}\text{O}$: C, 81.50; H, 10.75. Found: C, 81.61; H, 10.85.

1-(1,3-Dimethylbut-2-enyloxy)-3,5-dimethylbenzene (2e)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), 5-bromo-*m*-xylene (185 mg, 1 mmol), 4-methylpent-3-en-2-ol (200 mg, 2 mmol) with Bu₃N (2 mL) as solvent for 18 h at 50 °C. The filtrate was extracted with 10 % HCl (2 x 35 mL). Chromatographic purification (1 % ethyl acetate in hexane) provided **2e** (colorless liquid, 165 mg, 81 %). ¹H NMR (400 MHz, CDCl₃) δ 6.56 (s, 1H), 6.50 (s, 2H), 5.20-5.24 (m, 1H), 4.93-5.01 (m, 1H), 2.26 (m, 6H), 1.73 (d, 3H, J = 1.3 Hz), 1.72 (d, 3H, J = 1.3 Hz), 1.35 (d, 3H, J = 6.2 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 158.0, 138.9, 134.0, 127.1, 122.1, 113.5, 70.7, 25.6, 21.4, 21.3, 18.2. IR (neat, cm⁻¹) 2975, 1595, 1448, 1292, 1155, 1067, 827, 688. Anal. Calcd for C₁₄H₂₀O: C, 82.30; H, 9.87. Found: C, 81.95; H, 9.84.

(R)-1,3-Dimethyl-5-(1-phenylethoxy)-benzene (2f)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), 5-bromo-*m*-xylene (185 mg, 1 mmol), (*R*)-1-phenylethanol (98 % ee) (244 mg, 2 mmol) with Bu₃N (4 mL) as solvent for 24 h at 90 °C. The filtrate was extracted with 10 % HCl (2 x 50 mL). Chromatographic purification (hexane, followed by 2 % ethyl acetate in hexane) provided (*R*)-**2f** (colorless liquid, 158 mg, 70 %). [α]_D²⁰ = 12.17° (c = 1, CH₂Cl₂). HPLC: Chiralcel OJ Column, t[*major*] = 9.5 min, t[*minor*] = 11.0 min (10 % isopropanol in hexane, 1 mL/min), 98 % ee. ¹H NMR

(400 MHz, CDCl_3) δ 7.30-7.39 (m, 4H), 7.22-7.27 (m, 1H), 6.53 (s, 1H), 6.50 (s, 2H), 5.29 (q, 1H, $J = 6.5$ Hz), 2.22 (s, 6H), 1.60 (d, 3H, $J = 6.4$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 158.0, 143.4, 139.0, 128.5, 127.3, 125.5, 122.4, 113.6, 75.5, 24.4, 21.4. IR (neat, cm^{-1}) 2978, 1595, 1451, 1321, 1293, 1154, 1071, 828, 760, 700. Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{O}$: C, 84.91; H, 8.02. Found: C, 84.76; H, 8.07.

1-sec-butoxy-4-butylbenzene (2g)

A. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 1-bromo-4-butylbenzene (214 mg, 1 mmol), 2-butanol (148 mg, 2 mmol) with Bu_3N (1 mL) as solvent for 24 h at 90 °C. The filtrate was extracted with 10 % HCl (2 x 20 mL). Chromatographic purification (hexane, followed by 5 % ethyl acetate in hexane) provided **2g** (colorless liquid, 149 mg, 72 %).

B. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 1-chloro-4-butylbenzene (169 mg, 1 mmol), 2-butanol (148 mg, 2 mmol) with Bu_3N (1 mL) as solvent for 24 h at 100 °C. The filtrate was extracted with 10 % HCl (2 x 20 mL). Chromatographic purification (hexane, followed by 5 % ethyl acetate in hexane) provided **2g** (colorless liquid, 144 mg, 70 %). ^1H NMR (400 MHz, CDCl_3) δ 7.07 (d, 2H, $J = 8.6$ Hz), 6.80 (d, 2H, $J = 8.7$ Hz), 4.24 (sextet, 1H, $J = 6.3$ Hz), 2.54 (t, 2H, $J = 7.7$ Hz), 1.68-1.79 (m, 1H), 1.52-1.65 (m, 3H), 1.34 (sextet, 2H, $J = 7.5$ Hz), 1.28 (d, 3H, $J = 6.1$ Hz), 0.97 (t, 3H,

$J = 7.5$ Hz), 0.92 (t, 3H, $J = 7.3$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 156.2, 134.8, 129.2, 115.7, 75.0, 34.7, 33.9, 29.2, 22.3, 19.3, 14.0, 9.8. IR (neat, cm^{-1}) 2930, 1612, 1509, 1465, 1377, 1241, 1128, 989, 827. Anal. Calcd for $\text{C}_{14}\text{H}_{22}\text{O}$: C, 81.50; H, 10.75. Found: C, 81.36; H, 10.81.

1-Butyl-4-(1,3-dimethylbut-2-enyloxy)-benzene (**2h**)

- A. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 1-bromo-4-butylbenzene (214 mg, 1 mmol), 4-methylpent-3-en-2-ol (200 mg, 2 mmol) with Bu_3N (2 mL) as solvent for 18 h at 50 °C. The filtrate was extracted with 10 % HCl (2 x 35 mL). Chromatographic purification (1 % ethyl acetate in hexane) provided **2h** (colorless liquid, 176 mg, 76 %).
- B. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (11.2 mg, 0.05 mmol), **L10** (28.4 mg, 0.06 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 1-chloro-4-butylbenzene (169 mg, 1 mmol), 4-methylpent-3-en-2-ol (200 mg, 2 mmol) with Bu_3N (2 mL) as solvent for 18 h at 50 °C. The filtrate was extracted with 10 % HCl (2 x 35 mL). Chromatographic purification (1 % ethyl acetate in hexane) provided **2h** (colorless liquid, 183 mg, 79 %). ^1H NMR (400 MHz, CDCl_3) δ 7.05 (d, 2H, $J = 8.7$ Hz), 6.78 (d, 2H, $J = 8.6$ Hz), 5.20-5.25 (m, 1H), 4.91-4.99 (m, 1H), 2.53 (t, 2H, $J = 7.7$ Hz), 1.72 (s, 3H), 1.71 (s, 3H), 1.51-1.60 (m, 2H), 1.36 (d, 3H, $J = 6.4$ Hz), 1.29-1.40 (m, 2H), 0.91 (t, 3H, $J = 7.4$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 156.5, 135.2, 134.5, 129.5, 127.7, 116.1, 71.6, 35.2, 34.3, 26.1, 22.8, 21.8, 18.7, 14.4. IR (neat, cm^{-1}) 2929,

2858, 1612, 1509, 1447, 1376, 1239, 1065, 950, 828. Anal. Calcd for C₁₆H₂₄O: C, 82.70; H, 10.41. Found: C, 82.64; H, 10.65.

1-*sec*-butoxy-3-trifluoromethylbenzene (2i)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), 1-chloro-3-trifluoromethylbenzene (181 mg, 1 mmol), 2-butanol (148 mg, 2 mmol) with Bu₃N (1 mL) as solvent for 24 h at 90 °C. The filtrate was extracted with 10 % HCl (2 x 20 mL). Chromatographic purification (hexane) provided **2i** (colorless liquid, 175 mg, 80 %). ¹H NMR (400 MHz, CDCl₃) δ 7.37 (t, 1H, J = 8.1 Hz), 7.17 (d, 1H, J = 7.8 Hz), 7.11 (s, 1H), 7.04 (d, 1H), 4.34 (sextet, 1H, J = 6.0 Hz), 1.70-1.82 (m, 1H), 1.59-1.70 (m, 1H), 1.31 (d, 3H, J = 6.1 Hz), 0.99 (t, 3H, J = 7.5 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 158.3, 132.3, 132.0, 131.6, 131.3, 129.9, 128.1, 125.4, 122.7, 120.0, 119.0, 117.0, 112.5, 75.4, 29.1, 19.1, 9.7 (observed complexity due to P-C splitting). IR (neat, cm⁻¹) 2977, 1591, 1492, 1454, 1328, 1235, 1168, 1127, 1066, 785, 698. Anal. Calcd for C₁₁H₁₃F₃O: C, 60.54; H, 6.00. Found: C, 60.57; H, 6.14.

1-(1,3-Dimethylbut-2-enyloxy)-3-trifluoromethylbenzene (2j)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs₂CO₃ (391 mg, 1.2 mmol), 1-chloro-3-trifluoromethylbenzene (181 mg, 1 mmol), 4-methylpent-3-en-2-ol (200 mg, 2 mmol) with toluene (2 mL) as solvent for 8 h at 50 °C. Chromatographic purification (hexane) provided **2j** (colorless liquid, 201 mg, 82 %). ¹H NMR (400 MHz, CDCl₃) δ 7.34 (t, 1H, J = 8.1 Hz), 7.15 (d, 1H, J = 7.6 Hz),

7.08 (s, 1H), 7.01 (dd, 1H, $J = 8.3, 2.6$ Hz), 5.15-5.20 (m, 1H), 4.98-5.05 (m, 1H), 1.75 (d, 3H, $J = 1.3$ Hz), 1.72 (d, 3H, $J = 1.3$ Hz), 1.40 (d, 3H, $J = 6.2$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 158.2, 135.1, 132.0, 131.7, 131.4, 131.1, 129.7, 128.1, 126.2, 125.4, 122.7, 120.0, 119.2, 117.0, 112.6, 71.7, 25.6, 21.3, 18.2. IR (neat, cm^{-1}) 2979, 1591, 1491, 1450, 1336, 1235, 1127, 1065, 960, 792. Anal. Calcd for $\text{C}_{13}\text{H}_{15}\text{F}_3\text{O}$: C, 63.93; H, 6.19. Found: C, 64.16; H, 6.42.

3-(1,2,2-Trimethylpropoxy)-biphenyl (2k)

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 3-bromobiphenyl (233 mg, 1 mmol), 3,3-dimethylbutan-2-ol (204 mg, 2 mmol) with Bu_3N (1 mL) as solvent for 24 h at 90 °C. The filtrate was extracted with 10 % HCl (2 x 20 mL). Chromatographic purification (hexane, followed by 1 % ethyl acetate in hexane) provided **2k** (colorless liquid, 158 mg, 62 %). ^1H NMR (400 MHz, CDCl_3) δ 7.57-7.62 (m, 2H), 7.41-7.46 (m, 2H), 7.30-7.37 (m, 2H), 7.11-7.16 (m, 2H), 6.89 (ddd, 1H, $J = 8.2, 2.5, 1.0$ Hz), 4.08 (q, 1H, $J = 6.4$ Hz), 1.24 (d, 3H, $J = 6.3$ Hz), 1.01 (s, 9H). ^{13}C NMR (125 MHz, CDCl_3) δ 159.2, 142.7, 141.2, 129.7, 128.6, 127.3, 127.2, 119.2, 114.9, 114.5, 81.3, 35.1, 25.9, 14.2. IR (neat, cm^{-1}) 2960, 1597, 1477, 1420, 1375, 1295, 1202, 1079, 1008, 931, 757. Anal. Calcd for $\text{C}_{18}\text{H}_{22}\text{O}$: C, 84.99; H, 8.72. Found: C, 85.05; H, 8.84.

3-(1,3-Dimethylbut-2-enyloxy)-biphenyl (2l)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), 3-bromobiphenyl (233 mg, 1 mmol), 4-methylpent-3-en-2-ol (200 mg, 2 mmol) with Bu₃N (2 mL) as solvent for 18 h at 50 °C. The filtrate was extracted with 10 % HCl (2 x 35 mL). Chromatographic purification (1 % ethyl acetate in hexane) provided **2l** (colorless liquid, 209 mg, 83 %). ¹H NMR (400 MHz, CDCl₃) δ 7.55-7.58 (m, 2H), 7.40-7.45 (m, 2H), 7.29-7.36 (m, 2H), 7.13-7.16 (m, 1H), 7.10-7.12 (m, 1H), 6.85 (ddd, 1H, J = 8.2, 2.6, 1.0 Hz), 5.24-5.28 (m, 1H), 5.02-5.10 (m, 1H), 1.75 (d, 3H, J = 1.3 Hz), 1.73 (d, 3H, J = 1.3 Hz), 1.41 (d, 3H, J = 6.3 Hz). ¹³C NMR (125 MHz, CDCl₃) δ 158.4, 142.5, 141.2, 134.4, 129.6, 128.7, 127.2, 127.1, 127.0, 119.4, 114.8, 114.5, 71.2, 25.7, 21.4, 18.3. IR (neat, cm⁻¹) 2975, 2930, 1597, 1477, 1420, 1294, 1202, 1064, 757, 698. Anal. Calcd for C₁₈H₂₀O: C, 85.67; H, 7.99. Found: C, 85.65; H, 8.07.

1-sec-butoxy-3-methoxybenzene (2m)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), 1-bromo-3-methoxybenzene (187 mg, 1 mmol), 2-butanol (148 mg, 2 mmol) with Bu₃N (1 mL) as solvent for 24 h at 90 °C. The filtrate was extracted with 10 % HCl (2 x 20 mL). Chromatographic purification (2 % ethyl acetate in hexane) provided **2m** (colorless liquid, 114 mg, 63 %). ¹H NMR (400 MHz, CDCl₃) δ 7.16 (t, 1H), 6.45-6.51 (m, 3H), 4.28 (sextet, 1H, J = 6.2 Hz), 3.79 (s, 3H), 1.69-1.80 (m, 1H), 1.56-1.67 (m, 1H), 1.29 (d, 3H, J = 6.1 Hz), 0.97 (t, 3H, J = 7.5

Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 160.8, 159.4, 129.8, 107.9, 105.9, 102.2, 74.9, 55.1, 29.1, 19.2, 9.8. IR (neat, cm^{-1}) 2972, 1601, 1492, 1377, 1286, 1201, 1150, 1043, 1001, 837, 763, 688. Anal. Calcd for $\text{C}_{11}\text{H}_{16}\text{O}_2$: C, 73.30; H, 8.95. Found: C, 73.44; H, 9.11.

1-(1,3-Dimethylbut-2-enyloxy)-3-methoxybenzene (2n)

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 1-bromo-3-methoxybenzene (187 mg, 1 mmol), 4-methylpent-3-en-2-ol (200 mg, 2 mmol) with toluene (2 mL) as solvent for 18 h at 50 °C. Chromatographic purification (2 % ethyl acetate in hexane) provided **2n** (colorless liquid, 187 mg, 91 %). ^1H NMR (400 MHz, CDCl_3) δ 7.14 (t, 1H, J = 8.2 Hz), 6.42-6.51 (m, 3H), 5.19-5.25 (m, 1H), 4.94-5.02 (m, 1H), 3.77 (s, 3H), 1.73 (d, 3H, J = 1.3 Hz), 1.72 (d, 3H, J = 1.3 Hz), 1.37 (d, 3H, J = 6.3 Hz). ^{13}C NMR (125 MHz, CDCl_3) δ 160.6, 159.3, 134.2, 129.6, 126.9, 107.9, 106.0, 102.0, 71.1, 55.1, 25.6, 21.3, 18.2. IR (neat, cm^{-1}) 2975, 1599, 1491, 1452, 1284, 1263, 1200, 1152, 1044, 976, 834, 762, 687. Anal. Calcd for $\text{C}_{13}\text{H}_{18}\text{O}_2$: C, 75.69; H, 8.80. Found: C, 75.39; H, 8.87.

1-Methoxy-3-(1-vinylbutoxy)-benzene (2o)

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (11.2 mg, 0.05 mmol), **L10** (28.4 mg, 0.06 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 1-bromo-3-methoxybenzene (187 mg, 1 mmol), hex-1-en-3-ol (120 mg, 1.2 mmol) with Bu_3N (2 mL) as solvent for 18 h at 70 °C. The filtrate was extracted with 10 % HCl (2 x 35 mL). Chromatographic purification (1.5 % ethyl acetate in hexane) provided **2o** (colorless liquid, 129 mg, 63 %). ^1H NMR (400

MHz, CDCl₃) δ 7.14 (t, 1H), 6.46-6.54 (m, 3H), 5.84 (ddd, 1H, J = 17.4, 10.6, 6.3 Hz), 5.25 (dt, 1H, J = 17.4, 1.2 Hz), 5.19 (dt, 1H, J = 10.6, 1.2 Hz), 4.56-4.63 (m, 1H), 3.78 (s, 3H), 1.72-1.83 (m, 1H), 1.58-1.68 (m, 1H), 1.37-1.57 (m, 2H), 0.95 (t, 3H, J = 7.4 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 160.6, 159.6, 138.1, 129.6, 116.2, 108.1, 106.1, 102.2, 78.7, 55.1, 37.6, 18.5, 13.9. IR (neat, cm⁻¹) 2960, 1600, 1491, 1284, 1200, 1151, 1044, 989, 926, 836, 762, 687. Anal. Calcd for C₁₃H₁₈O₂: C, 75.69; H, 8.80. Found: C, 75.68; H, 8.85.

1-sec-butoxy-2,5-dimethylbenzene (2p)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L11** (10.0 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), bromo-*p*-xylene (185 mg, 1 mmol), 2-butanol (148 mg, 2 mmol) with toluene (2 mL) as solvent for 24 h at 90 °C. Chromatographic purification (0.5 % ethyl acetate in hexane) provided **2p** (colorless liquid, 82 mg, 46 %). ¹H NMR (400 MHz, CDCl₃) δ 7.01 (d, 1H, J = 8.0 Hz), 6.63-6.66 (m, 2H), 4.28 (sextet, 1H, J = 6.0 Hz), 2.30 (s, 3H), 2.17 (s, 3H), 1.69-1.80 (m, 1H), 1.58-1.68 (m, 1H), 1.28 (d, 3H), 0.98 (t, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 156.2, 136.2, 130.4, 124.6, 120.5, 113.7, 74.9, 29.4, 21.4, 19.4, 16.0, 9.8. IR (neat, cm⁻¹) 2971, 2925, 1584, 1507, 1462, 1412, 1378, 1263, 1129, 1004, 802. Anal. Calcd for C₁₂H₁₈O: C, 80.85; H, 10.18. Found: C, 80.91; H, 10.27.

1-(1,3-Dimethylbut-2-enyloxy)-2,5-dimethylbenzene (2q)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L11** (10.0 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), bromo-*p*-xylene (185 mg, 1 mmol), 4-methylpent-3-en-2-ol (200 mg, 2 mmol) with Bu₃N (2 mL) as solvent for 18 h at 70 °C. The filtrate was extracted with 10 % HCl (2 x 35 mL). Chromatographic purification (1 % ethyl acetate in hexane) provided **2q** (colorless liquid, 123 mg, 60 %). ¹H NMR (400 MHz, CDCl₃) δ 6.99 (d, 1H, J = 7.5 Hz), 6.64 (d, 1H, J = 7.5 Hz), 6.61 (s, 1H), 5.21-5.26 (m, 1H), 4.91-4.99 (m, 1H), 2.28 (s, 3H), 2.17 (s, 3H), 1.71 (s, 6H), 1.36 (d, 3H, J = 6.3 Hz). ¹³C NMR (125 MHz, CDCl₃) δ 156.2, 136.0, 133.6, 130.2, 127.5, 124.4, 120.7, 114.4, 71.4, 25.6, 21.5, 21.4, 18.2, 16.0. IR (neat, cm⁻¹) 2976, 1614, 1584, 1507, 1448, 1376, 1261, 1127, 1064, 1001, 802. Anal. Calcd for C₁₄H₂₀O: C, 82.30; H, 9.87. Found: C, 82.08; H, 9.93.

(2,4,4-Trimethylcyclohex-2-enyloxy)-benzene (2r)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), bromobenzene (157 mg, 1 mmol), 2,4,4-trimethylcyclohex-2-enol (280 mg, 2 mmol) with toluene (2 mL) as solvent for 24 h at 70 °C. Chromatographic purification (0.5 % ethyl acetate in hexane) provided **2r** (colorless liquid, 180 mg, 84 %). ¹H NMR (400 MHz, CDCl₃) δ 7.26-7.31 (m, 2H), 6.91-6.98 (m, 3H), 5.42 (s, 1H), 4.52 (t, 1H, J = 4.3 Hz), 1.82-1.99 (m, 2H), 1.77 (s, 3H), 1.61 (ddd, 1H, J = 13.3, 11.0, 3.7 Hz), 1.37 (ddd, 1H, J = 13.1, 6.6, 3.3 Hz), 1.05 (s, 3H), 0.97 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 158.6, 137.5, 130.3, 129.4, 120.6, 116.0, 74.2, 32.5, 32.0,

30.0, 28.0, 24.8, 20.8. IR (neat, cm^{-1}) 2955, 1597, 1493, 1360, 1297, 1237, 1171, 1032, 1002, 966, 880, 752, 692. Anal. Calcd for $\text{C}_{15}\text{H}_{20}\text{O}$: C, 83.28; H, 9.32. Found: C, 83.42; H, 9.42.

3-*sec*-Butoxybenzoic acid *tert*-butyl ester (2s)

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 3-bromobenzoic acid *tert*-butyl ester¹³ (257 mg, 1 mmol), 2-butanol (148 mg, 2 mmol) with Bu_3N (2 mL) as solvent for 24 h at 90 °C. The filtrate was extracted with 10 % HCl (2 x 35 mL). Chromatographic purification (1.5 % ethyl acetate in hexane) provided **2s** (colorless liquid, 203 mg, 81 %). ^1H NMR (400 MHz, CDCl_3) δ 7.55 (dt, 1H, $J = 7.8, 1.3$ Hz), 7.51 (dd, 1H, $J = 2.6, 1.5$ Hz), 7.30 (t, 1H, $J = 7.9$ Hz), 7.05 (ddd, 1H, $J = 8.3, 2.6, 1.0$ Hz), 4.35 (sextet, 1H, $J = 6.0$ Hz), 1.70-1.81 (m, 1H), 1.59-1.69 (m, 1H), 1.59 (s, 9H), 1.30 (d, 3H, $J = 6.1$ Hz), 0.98 (t, 3H, $J = 7.5$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 165.6, 158.0, 133.2, 129.1, 121.4, 120.3, 116.1, 80.8, 75.1, 29.0, 28.1, 19.1, 9.7. IR (neat, cm^{-1}) 2976, 1716, 1584, 1440, 1294, 1171, 1003, 952, 757, 685. Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{O}_3$: C, 71.97; H, 8.86. Found: C, 71.86; H, 8.81.

3-(1,3-Dimethylbut-2-enyloxy)-benzoic acid *tert*-butyl ester (2t)

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (4.5 mg, 0.02 mmol), **L10** (11.4 mg, 0.024 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 3-bromobenzoic acid *tert*-butyl ester (257 mg, 1 mmol), 4-methylpent-3-en-2-ol (200 mg, 2 mmol) with toluene (2 mL) as solvent for 18 h at 50 °C. Chromatographic purification (2 % ethyl acetate in hexane) provided **2t**

(colorless liquid, 254 mg, 92 %). ^1H NMR (400 MHz, CDCl_3) δ 7.55 (dt, 1H, $J = 7.7, 1.3$ Hz), 7.48 (dd, 1H, $J = 2.5, 1.5$ Hz), 7.28 (t, 1H, $J = 8.0$ Hz), 7.02 (ddd, 1H, $J = 8.2, 2.7, 1.0$ Hz), 5.18-5.22 (m, 1H), 5.00-5.08 (m, 1H), 1.76 (d, 3H, $J = 1.3$ Hz), 1.72 (d, 3H, $J = 1.3$ Hz), 1.58 (s, 9H), 1.39 (d, 3H, $J = 6.3$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 165.6, 157.9, 134.7, 133.1, 129.0, 126.5, 121.5, 120.4, 116.0, 80.8, 71.3, 28.1, 25.6, 21.3, 18.3. IR (neat, cm^{-1}) 2977, 1714, 1583, 1485, 1441, 1369, 1294, 1107, 1000, 969, 851, 757, 683. Anal. Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_3$: C, 73.88; H, 8.75. Found: C, 73.83; H, 8.88.

5-sec-Butoxy-1-tosylindole (2u)

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (11.2 mg, 0.05 mmol), **L10** (28.4 mg, 0.06 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 5-bromo-1-tosylindole¹⁴ (350 mg, 1 mmol), 2-butanol (148 mg, 2 mmol) with Bu_3N (2 mL) as solvent for 24 h at 90 °C. The filtrate was concentrated and Bu_3N was distilled out *in vacuo*. Chromatographic purification (2 : 1 hexane : CH_2Cl_2 , followed by 1 : 1 hexane : CH_2Cl_2) provided **2u** (colorless oil, 244 mg, 71 %). Crystallized on storage to give the colorless crystals. M.p. 80 – 81 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, 1H, $J = 8.9$ Hz), 7.73 (d, 2H, $J = 8.5$ Hz), 7.50 (d, 1H, $J = 3.7$ Hz), 7.19 (d, 2H, $J = 8.4$ Hz), 6.96 (d, 1H, $J = 2.4$ Hz), 6.91 (dd, 1H, $J = 9.0, 2.5$ Hz), 6.55 (dd, 1H, $J = 3.7, 0.7$ Hz), 4.25 (sextet, 1H, $J = 6.1$ Hz), 2.32 (s, 3H), 1.68-1.79 (m, 1H), 1.54-1.65 (m, 1H), 1.27 (d, 3H, $J = 6.1$ Hz), 0.96 (t, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 154.8, 144.7, 135.2, 131.7, 129.8, 129.4, 126.9, 126.7, 115.4, 114.3, 109.1, 106.4, 75.8, 29.1, 21.5, 19.2, 9.8. IR (neat, cm^{-1}) 2973, 1597, 1458, 1371,

1223, 1151, 996, 813, 676. Anal. Calcd for $C_{19}H_{21}NO_3S$: C, 66.45; H, 6.16. Found: C, 66.31; H, 6.15.

5-(1,3-Dimethylbut-2-enyloxy)-1-tosylindole (2v)

The general procedure was followed using $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), **L10** (28.4 mg, 0.06 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 5-bromo-1-tosylindole (350 mg, 1 mmol), 4-methylpent-3-en-2-ol (200 mg, 2 mmol) with toluene (2 mL) as solvent for 18 h at 50 °C. Chromatographic purification (2 : 1 hexane : CH_2Cl_2 , followed by 1 : 1 hexane : CH_2Cl_2) provided **2v** (colorless oil, 281 mg, 76 %). Crystallized from ethanol to give the colorless crystals. M.p. 102 – 103 °C. 1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, 1H, J = 8.9 Hz), 7.73 (d, 2H, J = 8.4 Hz), 7.49 (d, 1H, J = 3.7 Hz), 7.20 (d, 2H, J = 8.4 Hz), 6.92 (d, 1H, J = 2.2 Hz), 6.89 (dd, 1H, J = 8.9, 2.5 Hz), 6.54 (dd, 1H, J = 3.7, 0.8 Hz), 5.19-5.24 (m, 1H), 4.91-4.98 (m, 1H), 2.33 (s, 3H), 1.701 (s, 3H), 1.697 (s, 3H), 1.36 (d, 3H, J = 6.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 144.7, 135.2, 134.4, 131.6, 129.7, 129.5, 127.0, 126.8, 126.7, 115.3, 114.2, 109.2, 106.4, 71.9, 25.6, 21.5, 21.3, 18.2. IR (neat, cm^{-1}) 3119, 2983, 1610, 1459, 1371, 1226, 1157, 816, 719, 673. Anal. Calcd for $C_{21}H_{23}NO_3S$: C, 68.27; H, 6.27. Found: C, 68.11; H, 6.25.

1-Butoxy-3,5-dimethylbenzene (12a)

The general procedure was followed using $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), **L6** (10.7 mg, 0.024 mmol), Cs_2CO_3 (489 mg, 1.5 mmol), 5-bromo-*m*-xylene (185 mg, 1 mmol), butanol (148 mg, 2 mmol) with Bu_3N (2 mL) as solvent for 18 h at 70 °C. The filtrate was

extracted with 10 % HCl (2 x 35 mL). Chromatographic purification (hexane, followed by 2 % ethyl acetate in hexane) provided **12a**⁴ (colorless liquid, 161 mg, 90 %). ¹H and ¹³C NMR data were consistent with those of the previously reported compound.

1-Benzyloxy-3,5-dimethylbenzene (12b)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L6** (10.7 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), 5-bromo-*m*-xylene (185 mg, 1 mmol), benzylic alcohol (216 mg, 2 mmol) with toluene (2 mL) as solvent for 18 h at 70 °C. Chromatographic purification (0.5 % ethyl acetate in hexane) provided **12b**¹⁵ (colorless liquid, 203 mg, 96 %). ¹H NMR (400 MHz, CDCl₃) δ 7.29-7.45 (m, 5H), 6.62 (s, 3H), 5.03 (s, 2H), 2.29 (s, 6H). ¹³C NMR (125 MHz, CDCl₃) δ 158.8, 139.2, 137.2, 128.5, 127.8, 127.4, 122.7, 112.5, 69.7, 21.4.

1-Butoxy-2,5-dimethylbenzene (12c)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L5** (9.4 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), bromo-*p*-xylene (185 mg, 1 mmol), butanol (148 mg, 2 mmol) with toluene (2 mL) as solvent for 18 h at 70 °C. Chromatographic purification (hexane) provided **12c**⁴ (colorless liquid, 141 mg, 80 %). ¹H and ¹³C NMR data were consistent with those of the previously reported compound.

1-Butoxy-4-methoxybenzene (12d)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L4** (11.5 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), *p*-bromoanisole (187 mg, 1 mmol), 2-butanol (148 mg, 2 mmol) with toluene (2 mL) as solvent for 18 h at 70 °C. Chromatographic purification (2 % ethyl acetate in hexane) provided **12d**⁴ (colorless liquid, 126 mg, 70 %). ¹H and ¹³C NMR data were consistent with those of the previously reported compound.

1-Butoxy-2-methoxybenzene (**12e**)

The general procedure was followed using Pd₂(dba)₃ (9.2 mg, 0.01 mmol) instead of Pd(OAc)₂, **L4** (11.5 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), *o*-bromoanisole (187 mg, 1 mmol), 2-butanol (148 mg, 2 mmol) with toluene (2 mL) as solvent for 18 h at 70 °C. Chromatographic purification (2 % ethyl acetate in hexane) provided **12e**⁴ (colorless liquid, 131 mg, 73 %). ¹H and ¹³C NMR data were consistent with those of the previously reported compound.

3-Butoxybenzoic acid *tert*-butyl ester (**12f**)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L6** (10.7 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), 3-bromobenzoic acid *tert*-butyl ester (257 mg, 1 mmol), butanol (148 mg, 2 mmol) with Bu₃N (2 mL) as solvent for 18 h at 70 °C. The filtrate was extracted with 10 % HCl (2 x 35 mL). Chromatographic purification (1.5 % ethyl acetate in hexane) provided **12f**⁴ (colorless liquid, 223 mg, 89 %). ¹H and ¹³C NMR data were consistent with those of the previously reported compound.

Butoxybenzene (12g)

The general procedure was followed. Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L6** (10.7 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), bromobenzene (157 mg, 1 mmol) and butanol (148 mg, 2 mmol) were used. Bu₃N (2 mL) was utilized as a solvent. The reaction was performed at 70 °C for 18 h. The filtrate was extracted with 10 % HCl (2 x 35 mL). The organic layer was isolated and the aqueous layer was extracted with diethyl ether. The combined organic extracts were dried over MgSO₄ and the crude product was purified chromatographically (silica gel, pentane) to give after the solvent removal **12g**¹⁶ as a colorless liquid (128 mg, 86 %). ¹H and ¹³C NMR data were consistent with those of the commercially available compound.

1-Butoxy-3,5-dimethylbenzene (12h)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L6** (10.7 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), 1-bromo-3-ethylbenzene (185 mg, 1 mmol), butanol (148 mg, 2 mmol) with Bu₃N (2 mL) as solvent for 18 h at 70 °C. The filtrate was extracted with 10 % HCl (2 x 35 mL). Chromatographic purification (hexane, followed by 2 % ethyl acetate in hexane) provided **12h**⁴ (colorless liquid, 162 mg, 91 %). ¹H and ¹³C NMR data were consistent with those of the previously reported compound.

1,3-Dimethyl-5-prop-1-ynyloxybenzene (12i)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L6** (10.7 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), 5-bromo-*m*-xylene (185 mg, 1 mmol),

propyn-1-ol (140 mg, 2 mmol). The solution of the alcohol in 1 mL of toluene was added under argon over 10 h to the stirred at 70 °C reaction mixture in 1 mL of toluene via syringe with the help of a syringe pump. Chromatographic purification (0.5 % ethyl acetate in hexane) provided **12i**¹⁷ (colorless liquid, 157 mg, 90 %). ¹H NMR (400 MHz, CDCl₃) δ 6.62 (s, 1H), 6.58 (s, 2H), 4.60 (q, 2H, J = 2.3 Hz), 2.28 (s, 6H), 1.86 (t, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 157.8, 139.1, 122.9, 112.4, 83.4, 74.2, 56.1, 21.4, 3.7.

1,3-Dimethyl-5-(3-methylbut-2-enyloxy)-benzene (12j)

The general procedure was followed using Pd(OAc)₂ (4.5 mg, 0.02 mmol), **L6** (10.7 mg, 0.024 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), 5-bromo-*m*-xylene (185 mg, 1 mmol), 3-methylbut-2-en-1-ol (172 mg, 2 mmol) with toluene (2 mL) as solvent for 18 h at 50 °C. Chromatographic purification (1 % ethyl acetate in hexane) provided **12j** (colorless liquid, 159 mg, 84 %). ¹H NMR (300 MHz, CDCl₃) δ 6.60 (s, 1H), 6.57 (s, 2H), 5.60-5.42 (m, 1H), 4.49 (d, J = 6.6 Hz, 2H), 2.31 (s, 6H), 1.82 (s, 3H), 1.76 (s, 3H); ³¹C NMR (75 MHz, CDCl₃) δ 158.9, 139.2, 138.0, 122.4, 119.9, 112.5, 64.7, 26.2, 21.8, 18.5; IR (neat, cm⁻¹) 2917, 1594, 1293, 1154, 1055, 826, 687. Anal. Calcd for C₁₃H₁₈O: C, 82.06; H, 9.53. Found: C, 81.91; H, 9.61.

4-(3,5-Dimethylphenoxy)-butan-2-ol (12k)

The general procedure was followed using Pd(OAc)₂ (11.2 mg, 0.05 mmol), **L4** (28.8 mg, 0.06 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), 5-bromo-*m*-xylene (185 mg, 1 mmol) and 1,3-

butandiol (108 mg, 2 mmol) with toluene (2 mL) as solvent for 24 h at 70 °C. Chromatographic purification (20 % ethyl acetate in hexane) provided a yellowish oil, which was found by TLC and NMR to contain the coupling product contaminated by a small amount of **L4**. To remove **L4**, the oil was dissolved in 3 mL of diethyl ether, HBF₄ monoetherate (0.12 mmol, 23 mg of 85 % solution) was added, the solvent was removed and the residue was filtered through a short plug of silica gel (25 % ethyl acetate in hexane), giving **12k** (colorless oil, 0.128 g, 66 %). ¹H NMR (400 MHz, CDCl₃) δ 6.60 (s, 1H), 6.54 (s, 2H), 4.02-4.15 (m, 3H), 2.36-2.41 (br. s, 1H), 2.28 (s, 6H), 1.87-1.92 (m, 2H), 1.25 (d, 3H, J = 6.2 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 158.7, 139.1, 122.8, 112.1, 66.2, 65.7, 38.0, 23.3, 21.4. IR (neat, cm⁻¹) 3381, 2967, 1740, 1595, 1469, 1324, 1156, 830, 689. HRMS (ESI) calcd for C₁₂H₁₈O₂ [M+Na⁺]: 217.1199. Found: 217.1195

¹H NMR spectrum of 12k

CDCl₃

Current Data Parameters
 NAME av-2-159-H-a
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20040730
 Time 11.21
 INSTRUM spect
 PROBD 5mm BBO BB-1
 PULPROG zg30
 TO 65536
 SOLVENT CDCl₃
 NS 16
 DS 2
 SWH 8278.146 Hz
 FIDRES 0.126314 Hz
 AQ 3.9584243 sec
 RG 45.3
 DM 60.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== CHANNEL f1 =====
 NUC1 ¹H
 P1 7.50 usec
 PL1 0.00 dB
 SF01 400.1324710 MHz

F2 - Processing parameters
 SI 32768
 SF 400.1300174 MHz
 MDW EM
 SSB 0
 LB 0.30 Hz
 SB 0
 PC 1.00

1D NMR plot parameters
 CX 20.00 cm
 F1P 8.080 ppm
 F1 3233.09 Hz
 F2P -0.293 ppm
 F2 -117.15 Hz
 PPMKHZ 0.41864 ppm/cm
 HZCM 167.51180 Hz/cm

1-Bromo-3-*iso*-propoxybenzene (7)

The general procedure¹⁸ for the Cu-catalyzed intermolecular coupling of alcohols with aryl iodides was followed. An oven-dried Schlenk tube was charged with CuI (191 mg, 1 mmol), 1,10-phenanthroline (360 mg, 2 mmol) and Cs₂CO₃ (6.52 g, 20 mmol). The solution of 1-bromo-3-iodobenzene (2.83 g, 10 mmol) in isopropanol (10 mL) was added. The Schlenk tube was sealed with Teflon screw cap and placed in an oil bath (110 °C) for 24 h. After the reaction mixture was allowed to cool to room temperature, it was filtered through a layer of silica gel (diethyl ether). The solution was concentrated, filtered through a short plug of silica gel (5 % ethyl acetate in hexane). The solvent was removed to provide **7**¹⁹ (colorless oil, 1.742 g, 81 %). ¹H and ¹³C NMR data were consistent with those of the commercially available compound.

1-(1,3-Dimethylbut-2-enyloxy)-3-*iso*-propoxybenzene (8)

The general procedure for the Pd-catalyzed intermolecular coupling of alcohols with aryl halides was followed using Pd(OAc)₂ (6.7 mg, 0.03 mmol), **L10** (17.1 mg, 0.036 mmol), Cs₂CO₃ (489 mg, 1.5 mmol), **7** (215 mg, 1 mmol), 4-methylpent-3-en-2-ol (200 mg, 2 mmol) with Bu₃N (2 mL) as solvent for 18 h at 50 °C. A mixture of 10 % HCl (5 mL) and water (15 mL) was used for the extraction. Chromatographic purification (2 % ethyl acetate in hexane) provided **8** (colorless liquid, 195 mg, 83 %). ¹H NMR (400 MHz, CDCl₃) δ 7.11 (t, 1H, J = 8.0 Hz), 6.42-6.49 (m, 3H), 5.20-5.26 (m, 1H), 4.93-5.00 (m, 1H), 4.49 (septet, 1H, J = 6.1 Hz), 1.72 (s, 6H), 1.36 (d, 3H, J = 6.2 Hz), 1.32 (d, 6H, J =

6.0 Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 159.3, 158.9, 134.1, 129.6, 127.0, 108.2, 107.8, 103.7, 71.1, 69.7, 25.6, 22.1, 22.0, 21.3, 18.2. IR (neat, cm^{-1}) 2977, 1588, 1489, 1373, 1282, 1145, 1006, 836, 762, 688. Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{O}_2$: C, 76.88; H, 9.46. Found: C, 76.61; H, 9.51.

Synthesis of ^{18}O -labeled 1-phenylethanol.

To the CH_2Cl_2 solution of acetophenone (1.2 g, 10 mmol) and $\text{CH}_3\text{SO}_2\text{OH}$ (1.056 g, 11 mmol) H_2O^{18} (95 % ^{18}O , 200 mg, 10 mmol) was added and the mixture was stirred at room temperature for 15 h. Then it was filtered through a plug of silica gel (CH_2Cl_2). The solvent was removed to give ^{18}O -enriched acetophenone (1.149 g). This was dissolved in dry THF, NaBH_4 (361 mg, 9.496 mmol) was added and the mixture was stirred under N_2 for 3 h at 70 °C. Then it was cooled to room temperature, water (20 mL) was added, followed by 10 % HCl. The mixture was transferred to a separatory funnel, shaken, the organic layer was isolated and the aqueous layer was extracted with diethyl ether (2 x 25 mL). The combined organic layers were united, dried over MgSO_4 . The solvent was evaporated and the crude product was purified chromatographically (silica gel, 20 % ethyl acetate in hexane) to give after the solvent removal 0.856 g of the product (73 %). The isotopic composition was determined by MS analysis (40 % ^{18}O).

Coupling of 5-bromo-*m*-xylene with ^{18}O -1-phenylethanol.

The general procedure for the Pd-catalyzed intermolecular coupling of alcohols with aryl halides was followed using $\text{Pd}(\text{OAc})_2$ (2.2 mg, 0.01 mmol), **L4** (5.8 mg, 0.012 mmol),

Cs₂CO₃²⁰ (245 mg, 0.75 mmol), 5-bromo-*m*-xylene (93 mg, 0.5 mmol), ¹⁸O-1-phenylethanol (40 % ¹⁸O, 123 mg, 1 mmol) with toluene (1 mL) as solvent for 24 h at 90 °C. Chromatographic purification (1 % ethyl acetate in hexane) provided **5** (8 mg, 8 %), **4** (51 mg, 45 %), (rac)-**2f** (18 mg, 8 %). The isotopic composition of **4** and **2f** was determined by MS analysis. The latter contained 40 % ¹⁸O, the former showed no ¹⁸O enrichment.

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²⁰ weighed and added into the Schlenk tube in the glove box