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Regioselective Suzuki Couplings of Non-Symmetric Dibromobenzenes

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Supporting Information

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Supporting Information

General Experimental Details:

All reactions were carried out under an inert Ar atmosphere in oven-dried glassware. Flash column chromatography (FCC) was carried out with SiliaFlash P60, 60 Å silica gel. Reactions and column chromatography were monitored with EMD silica gel 60 F254 plates and visualized with potassium permanganate, ceric ammonium molybdate, iodine, or vanillin stains. Tetrahydrofuran (THF), methylene chloride (CH₂Cl₂), acetonitrile (MeCN) and diethyl ether (Et₂O) were dried by passage through activated alumina columns. DMSO was stored over 3 Å molecular sieves. All other reagents and solvents were used without further purification from commercial sources.

Instrumentation: FT-IR spectra were obtained on NaCl plates with a PerkinElmer Spectrum II spectrometer. HRMS data was collected using a TOF mass spectrometer. Proton and carbon NMR spectra (¹H NMR and ¹³C NMR) were recorded in deuterated chloroform (CDCl₃) unless otherwise noted on a Bruker 700 MHz Avance III spectrometer with carbon-optimized cryoprobe and Bruker 400 MHz DPX-400 spectrometer. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, br = broad, m = multiplet. Melting points were determined with a Cole–Parmer instrument and are uncorrected.



1,5-dibromo-2-methoxy-4-(2,2,2-trifluoroethoxy)benzene (6a). To a solution of phenol **S1**¹ (200 mg, 0.71 mmol) in MeOH (5 ml, 0.14 M) was added KF (49 mg, 0.85 mmol). The mixture was stirred at 19 °C for 30 min and concentrated to remove solvent. The resulting solid was mixed with CF_3CH_2I (447 mg, 2.13 mmol) and DMSO (2.5 ml) in a sealed tube. The mixture was heated to 120 °C for 24 h upon which time TLC indicated consumption of the starting material. The reaction mixture was quenched by adding water (5 mL). The mixture was diluted with H₂O and extracted with EtOAc (10 mL x 3). The organic layers were combined, washed with H₂O, saturated aqueous NaCl, dried over Na₂SO₄, filtered, and concentrated. Purification by FCC (5:1 hexane:EtOAc) yielded **6a** (125 mg, 0.34 mmol, 48%) as a white solid.

Data for **6a**: $R_f 0.7$ (5:1 Hexanes:EtOAc); mp = 68-69 °C; IR (thin film) 3457, 1586, 1488, 1442, 1378 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.74 (s, 1 H), 6.58 (s, 1 H), 4.43 (q, *J* = 8.4 Hz, 2 H), 3.92 (s, 3 H); ¹³C NMR (176 MHz, CDCl₃) δ C 156.2, 154.5, 123.0 (q, *J* = 281.6 Hz), 106.1, 104.3; CH 136.5, 101.6; CH₂ 68.1 (q, *J* = 35.2 Hz); CH₃ 56.7; HRMS (ESI) calcd for C₉H₈O₂F₃Br₂ [M+H]: 362.8843, found 362.8844.



5-bromo-4,4'-dimethoxy-2-(2,2,2-trifluoroethoxy)-1,1'-biphenyl (7a) and **5-bromo-2,4'-dimethoxy-4-(2,2,2-trifluoroethoxy)-1,1'-biphenyl (8a)**. To a solution of boronic ester **S2** (183 mg, 0.79 mmol) in dioxane (15 mL, 0.05 M) were added aryl bromide **6a** (358 mg, 0.98 mmol), KBr (466 mg, 3.92 mmol), K₃PO₄ (866 mg, 3.92 mmol), H₂O (1.5 ml) and Pd(PPh₃)₄ (113 mg, 0.098 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and heated to 65 °C for 24 h upon which time TLC indicated consumption of the boronic ester. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (10:1 hexanes:EtOAc) yielded **7a** (51 mg, 0.13 mmol, 16%) as an amorphous solid and **8a** (144 mg, 0.368 mmol, 47%) as a white solid.

Data for **7a**: $R_f 0.2$ (5:1 Hexanes:EtOAc); IR (thin film) 3435, 2942, 1606, 1495, 1443 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.56 (s, 1 H), 7.44 (d, J = 7.4 Hz, 2 H), 6.98 (d, J = 7.4 Hz, 2 H), 6.62 (s, 1 H), 4.18 (q, J = 8.4 Hz, 2 H), 3.96 (s, 3 H), 3.88 (s, 3 H); ¹³C NMR (176 MHz, CDCl₃) δ C 159.0, 155.6, 154.7, 130.2, 128.4, 125.8 (q, J = 280.2 Hz), 105.6; CH 134.8, 130.2 (2 C), 113.9 (2 H), 101.4; CH₂ 67.6 (q, J = 35.2 Hz); CH₃ 56.6, 55.3. HRMS (EI) calcd for C₁₆H₁₄O₃F₃Br [M+]: 390.0078, found 390.0071.

¹ Zhao, P.; Beaudry, C. M. Org. Lett. 2013, 15, 402-405.

Data for **8a**: $R_f 0.2$ (5:1 Hexanes:EtOAc);); mp = 70-71 °C; IR (thin film) 2940, 1609, 1597, 1493, 1380 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.50 (s, 1 H), 7.43 (d, J = 8.6 Hz, 2 H), 6.97 (d, J = 8.6 Hz, 2 H), 6.65 (s, 1 H), 4.48 (q, J = 8.3 Hz, 2 H), 3.87 (s, 3 H), 3.83 (s, 3 H); ¹³C NMR (176 MHz, CDCl₃) δ C 159.0, 156.7, 154.0, 128.9, 127.4, 123.2 (q, J = 278.1 Hz), 103.9; CH 134.6, 130.5 (2 C), 113.7 (2 H), 101.3; CH₂ 68.2 (q, J = 40.0 Hz); CH₃ 56.1, 55.3. HRMS (EI) calcd for C₁₆H₁₄O₃F₃Br [M+]: 390.0078, found 390.0076.



1,5-dibromo-2-methoxy-4-(methoxymethoxy)benzene (6b). To a solution of phenol **S1** (1.5 g, 5.32 mmol) in CH_2Cl_2 (40 mL, 0.13 M) was added Et_3N (1.47 ml, 10.64 mmol). The mixture was stirred at 0 °C while MOMCl (851 mg, 10.64 mmol) was added slowly. The resulting mixture was stirred at 19 °C overnight upon which time TLC indicated consumption of the starting material. The reaction mixture was quenched by adding water (15 mL). The mixture was diluted with H_2O and extracted with CH_2Cl_2 (20 mL x 3). The organic layers were combined, washed with H_2O , saturated aqueous NaCl, dried over Na₂SO₄, filtered, and concentrated. Purification by FCC (5:1 hexane:EtOAc) yielded **6b** (1.16 mg, 3.56 mmol, 67%) as an orange oil.

Data for **6b**: $R_f 0.6$ (5:1 Hexanes:EtOAc); IR (thin film) 2957, 2932, 1581, 1475, 1362 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.69 (s, 1 H), 6.82 (s, 1 H), 5.26 (s, 2 H), 3.90 (s, 3 H), 3.55 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ C 156.1, 154.1, 104.2, 103.5; CH 135.9, 101.2; CH₂ 95.5; CH₃ 56.52, 56.49. HRMS (EI) calcd for C₉H₁₀O₃Br₂ [M+]: 323.8997, found 323.9008.



5-bromo-4,4'-dimethoxy-2-(methoxymethoxy)-1,1'-biphenyl (7b) and 5-bromo-2,4'-dimethoxy-4-(methoxymethoxy)-1,1'-biphenyl (8b). To a solution of boronic ester S2 (286 mg, 1.23 mmol) in dioxane (20 mL, 0.04 M) were added aryl bromide 6b (500 mg, 1.53 mmol), KBr (730 mg, 6.12 mmol), K₃PO₄ (1.35 g, 6.12 mmol), H₂O (2 ml) and Pd(PPh₃)₄ (177 mg, 0.15 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and heated to 65 °C for 24 h upon which time TLC indicated consumption of the boronic ester. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (10:1 hexanes:EtOAc) yielded 7b and 8b (278 mg, 0.79 mmol, 53%, 7b:8b = 2.5:1) as an inseparable mixture.

Data for **7b** and **8b mixture**: $R_f 0.35$ (5:1 Hexanes:EtOAc); IR (thin film) 2930, 2836, 1637, 1515, 1455 cm⁻¹; ¹H NMR of **7b** (700 MHz, CDCl₃) δ 7.49 (s, 1 H), 7.44 (d, J = 9.2 Hz, 2H), 6.97 (d, J = 9.2 Hz, 2 H), 6.88 (s, 1 H), 5.32 (s, 2 H), 3.87 (s, 3 H), 3.83 (s, 3 H), 3.60 (s, 3 H); ¹³C NMR of **7b** (176 MHz, CDCl₃) C 158.8, 156.6, 153.6, 129.4, 125.9, 103.3; CH 134.1, 130.5, 113.6, 100.9; CH₂ 95.6; CH₃ 56.5, 56.0, 55.3; ¹H NMR of **8b** (700 MHz, CDCl₃) δ 7.51 (s, 1 H), 7.44 (d, J = 9.3 Hz, 2H), 6.97 (d, J = 9.3 Hz, 2 H), 6.89 (s, 1 H), 5.14 (s, 2 H), 3.96 (s, 3 H), 3.88 (s, 3 H), 3.46 (s, 3 H); ¹³C NMR of **8b** (176 MHz, CDCl₃) C 158.7, 155.6, 154.5, 129.5, 125.4, 104.0; CH 134.2, 130.5, 113.6, 101.1; CH₂ 95.5; CH₃ 56.5, 56.2, 55.3; HRMS (ESI) calcd for C₁₆H₁₇O₄Br [M+]: 352.0310, found 352.0298.



2,4-dibromo-5-(*tert*-butyl)phenol (S4). To the solution of phenol S3 (2 g, 13.3 mmol) in AcOH (33 ml, 0.4 M) was added Br₂ (4.26 g, 26.6 mmol) in AcOH (3 ml) slowly. The reaction mixture was stirred at 19 °C for 24 h upon which time TLC indicated consumption of the starting material. The mixture was diluted with H₂O and extracted with CH₂Cl₂ (20 mL x 3). The organic layers were combined, washed with H₂O, saturated aqueous NaCl, dried over Na₂SO₄, filtered, and concentrated. Purification by FCC (10:1 hexane:EtOAc) yielded S4 (3.23 g, 10.5 mmol, 79%) as a yellow oil.

Data for **S4**: $R_f 0.5$ (10:1 Hexanes:EtOAc); IR (thin film) 2963, 1740, 1555, 1461, 1446 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.69 (s, 1 H), 7.15 (s, 1H), 5.41 (br, 1 H), 1.50 (s, 9 H); ¹³C NMR (176 MHz, CDCl₃) C 151.3, 149.4, 112.9, 107.4, 36.6; CH 137.3, 115.8; CH₃ 29.5 (3 C); HRMS (EI) calcd for $C_{10}H_{12}OBr_2$ [M+]: 305.9255, found 305.92470.



1,5-dibromo-2-(*tert*-butyl)-4-methoxybenzene (6c). To the solution of phenol S4 (1.61 g, 5.22 mmol) in DMF (13 ml, 0.4 M) were added K_2CO_3 (1.44 g, 0.4 mmol) and MeI (888 mg, 6.26 mmol). The reaction mixture was stirred at 19 °C overnight upon which time TLC indicated consumption of the starting material. The mixture was diluted with H₂O and extracted with EtOAc (20 mL x 3). The organic layers were combined, washed with H₂O, saturated aqueous LiCl, dried over Na₂SO₄, filtered, and concentrated. The crude 6c (1.76 g, quant) as a white solid could be used for next step without further purification.

Data for **6c**: $R_f 0.6$ (10:1 Hexanes:EtOAc); mp = 84-85 °C; IR (thin film) 2956, 2923, 1633, 1473, 1454 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.76 (s, 1 H), 7.01 (s, 1H), 3.92 (s, 3 H), 1.53 (s, 9 H); ¹³C NMR (176 MHz, CDCl₃) C 154.9, 148.4, 113.2, 109.3, 36.9; CH 138.8, 111.8; CH₃ 56.3, 29.5 (3 C); HRMS (EI) calcd for C₁₁H₁₄OBr₂ [M+]: 319.94117, found 319.9368.



5-bromo-2-(*tert*-butyl)-4,4'-dimethoxy-1,1'-biphenyl (7c) and 5-bromo-4-(*tert*-butyl)-2,4'-dimethoxy-1,1'-biphenyl (8c). To a solution of boronic ester S2 (87 mg, 0.376 mmol) in dioxane (5 mL, 0.08 M) were added aryl bromide 6c (150 mg, 0.47 mmol), KBr (223 mg, 1.88 mmol), K_3PO_4 (415 mg, 1.88 mmol), H_2O (0.5 ml) and Pd(PPh₃)₄ (54 mg, 0.047 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and heated to 65 °C for 24 h upon which time TLC indicated consumption of the boronic ester. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (10:1 hexanes:EtOAc) yielded 7c (5.2 mg, 0.015 mmol, 4 %) as a white solid and 8c (38 mg, 0.11 mmol, 29 %) as a white solid.

Data for **7c**: $R_f 0.6$ (10:1 Hexanes:EtOAc); mp = 67-68 °C; IR (thin film) 2959, 1634, 1588, 1484, 1236 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.22 (s, 1 H), 7.17 (d, *J* = 9.1 Hz, 2 H), 7.07 (s, 1H) 6.89 (d, *J* = 9.1 Hz, 2 H), 3.97 (s, 3 H), 3.88 (s, 3 H), 1.22 (s, 9 H); ¹³C NMR (176 MHz, CDCl₃) C 158.5, 154.5, 149.0, 135.8 (2 C), 107.5, 36.8; CH 137.0, 131.4 (2 C), 112.7 (2 C), 110.7; CH₃ 56.2, 55.3, 32.4 (3 C); HRMS (EI) calcd for C₁₈H₂₁O₂Br [M+]: 348.0725, found 348.0723.

Data for **8c**: $R_f 0.6$ (10:1 Hexanes:EtOAc); mp = 68-69 °C; IR (thin film) 2958, 1609, 1516, 1483, 1462 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.55 (s, 1 H), 7.48 (d, *J* = 9.1 Hz, 2 H), 7.09 (s, 1H) 6.98 (d, *J* = 9.1 Hz, 2 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 1.59 (s, 9 H); ¹³C NMR (176 MHz, CDCl₃) C 158.9, 155.2, 147.4, 129.5, 129.1, 113.3, 36.8; CH 137.0, 130.4 (2 C), 113.6 (2 C), 111.7; CH₃ 55.8, 55.3, 29.7 (3 C); HRMS (EI) calcd for C₁₈H₂₁O₂Br [M+]: 348.0725, found 348.0723.



3-bromo-4,4'-dimethoxy-1,1'-biphenyl (7d) and 5-bromo-2,4'-dimethoxy-1,1'-biphenyl (8d). To a solution of boronic ester **S2** (166 mg, 0.72 mmol) in dioxane (5.4 mL, 0.13 M) were added aryl bromide **6d** (200 mg, 0.75 mmol), KBr (358 mg, 3 mmol), K₃PO₄ (638 mg, 3 mmol), H₂O (0.6 ml) and Pd(PPh₃)₄ (173 mg, 0.15 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and heated to 65 °C for 24 h upon which time TLC indicated consumption of the boronic ester. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (10:1 hexanes:EtOAc) yielded **7d** (31 mg, 0.106 mmol, 31 %) both as amorphous solid.

Data for **7d**: $R_f 0.2$ (30:1 Hexanes:EtOAc); IR (thin film) 3000, 2934, 1609, 1514, 1484 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.77 (s, 1 H), 7.76-7.46 (m, 3 H), 6.99-6.97 (m, 3 H), 3.96 (s, 3 H), 3.87 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) C 159.1, 154.9, 134.9, 132.1, 112.0; CH 131.5, 127.8 (2 C), 126.6, 114.3 (2 C), 112.1; CH₃ 56.4, 55.4; HRMS (EI) calcd for C₁₄H₁₃O₂Br [M+]: 292.0099, found 292.0106.

Data for **8d**: $R_f 0.18$ (30:1 Hexanes:EtOAc); IR (thin film) 3018, 2960, 1606, 1493, 1275 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.46 (d, J = 9.2 Hz, 2 H), 7.44 (d, J = 2.6 Hz, 1 H), 7.40 (dd, J = 8.1, 2.6 Hz, 1 H), 6.98 (d, J = 9.2 Hz, 2 H), 6.87 (d, J = 8.1 Hz, 1 H), 3.88 (s, 3 H), 3.82 (s, 3 H); ¹³C NMR (176 MHz, CDCl₃) C 159.0, 155.6, 132.3, 129.4, 113.0; CH 133.2, 130.62, 130.56 (2 C), 113.6 (2 C), 112.9; CH₃ 55.8, 55.3; HRMS (EI) calcd for C₁₄H₁₃O₂Br [M+]: 292.0099, found 292.0089.



5-bromo-4,4'-dimethoxy-[1,1'-biphenyl]-2-carbaldehyde (7e) and 5-bromo-2,4'-dimethoxy-[1,1'-biphenyl]-4-carbaldehyde (8e). To a solution of boronic ester S2 (39.6 mg, 0.17 mmol) in dioxane (0.9 mL, 0.19 M) were added aryl bromide **6e** (50 mg, 0.17 mmol), KBr (81 mg, 0.68 mmol), K₃PO₄ (150 mg, 0.68 mmol), H₂O (0.1 ml) and Pd(PPh₃)₄ (20 mg, 0.017 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and heated to 55 °C for 24 h upon which time TLC indicated consumption of the boronic ester. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (25:1 hexanes:EtOAc) yielded **7e** (9.1 mg, 0.028mmol, 21 % *brsm*) and **8e** (11 mg, 0.034 mmol, 26 % *brsm*) both as white solid.

Data for **7e**: $R_f 0.25$ (20:1 Hexanes:EtOAc); mp = 72 °C; IR (thin film) 3010, 2961, 1690, 1445, 1412 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 9.93 (s, 1 H), 7.69 (s, 1 H), 7.51 (s, 1 H), 7.28 (d, *J* = 7.9 Hz, 2 H), 7.01 (d, *J* = 7.9 Hz, 2 H), 4.02 (s, 3 H), 3.89 (s, 3 H); ¹³C NMR (176 MHz, CDCl₃) C 159.8, 155.4, 139.6, 133.5, 128.3, 118.6; CH 191.7, 135.6, 131.4 (2 C), 114.0 (2 C), 109.1; CH₃ 56.6, 55.4; HRMS (ESI) calcd for C₁₅H₁₄O₃Br [M+H]: 321.0126, found 321.0128.

Data for **8e**: $R_f 0.23$ (20:1 Hexanes:EtOAc); mp = 78 °C; IR (thin film) 2991, 2940, 1693, 1534, 1490 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 10.34 (s, 1 H), 7.60 (s, 1 H), 7.53-7.51 (m, 3 H), 6.99 (d, *J* = 8.5 Hz, 2 H), 3.90 (s, 3 H), 3.89 (s, 3 H); ¹³C NMR (176 MHz, CDCl₃) C 159.8, 156.2, 138.2, 132.4, 128.2, 118.6; CH 191.6, 135.0, 130.7 (2 C), 113.8 (2 C), 111.1; CH₃ 56.0, 55.4; HRMS (ESI) calcd for C₁₅H₁₄O₃Br [M+H]: 321.0126, found 321.0133.



3-bromo-4'-methoxy-4-vinyl-1,1'-biphenyl (10a). To a solution of boronic ester **S2** (91 mg, 0.39 mmol) in dioxane (4 mL, 0.1 M) were added aryl bromide **9a** (102 mg, 0.39 mmol), KBr (186 mg, 1.56 mmol), K_3PO_4 (330 mg, 1.56 mmol), H_2O (0.4 ml) and $Pd(PPh_3)_4$ (45 mg, 0.039 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and heated to 65 °C for 24 h upon which time TLC indicated consumption of the boronic ester. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (50:1 hexanes:EtOAc) yielded **10a** (58 mg, 0.20 mmol, 52 %, white solid) as the only isolated regioisomer.

Data for **10a**: $R_f 0.57$ (10:1 Hexanes:EtOAc); mp = 87-89 °C; IR (thin film) 2962, 2933, 1606, 1259, 825 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.78 (d, *J* = 2.9 Hz, 1 H), 7.63 (d, *J* = 8.3Hz, 1 H), 7.54 (d, *J* = 9.1 Hz, 2 H), 7.50 (dd, *J* = 8.3, 2.9 Hz, 1 H), 7.11 (dd, *J* = 18.4, 11.2 Hz), 7.00(d, *J* = 9.1 Hz, 2 H), 5.77 (dd, *J* = 18.4, 1.2 Hz, 1 H), 5.40 (dd, *J* = 11.2, 1.2 Hz, 1 H), 3.89 (s, 3 H); ¹³C NMR (176 MHz, CDCl₃) C 159.6, 141.8, 135.5, 131.7, 124.1; CH 135.4, 130.8, 128.0 (2 C), 126.9, 125.7, 114.4 (2 C); CH₂ 116.4; CH₃ 55.4; HRMS (ESI) calcd for C₁₅H₁₄OBr [M+H]: 289.0228, found 289.0241.



(*E*)-methyl 3-(2,4-dibromo-5-methoxyphenyl)acrylate (9b). To a solution of styrene 1 (500 mg, 1.7 mmol) and methyl acrylate (295 mg, 3.42 mmol) in CH_2Cl_2 (10 mL, 1.7 M) was added Grbbs catalyst 2nd (72 mg, 0.0856 mmol). The mixture was heated to 40 °C for 2h upon which time TLC indicated consumption of the starting material. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (5:1 hexanes:EtOAc) yielded **9b** (295 mg, 0.84 mmol, 49 %) as a white solid.

Data for **9b**: $R_f 0.25$ (10:1 Hexanes:EtOAc); mp = 133-140 °C; IR (thin film) 2951, 1709, 1580, 1373, 1288 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.97 (d, *J* = 16.1 Hz, 1 H), 7.81 (s, 1 H), 7.08 (s, 1 H), 6.42 (d, *J* = 16.1 Hz, 1 H), 3.95 (s, 3 H), 3.86 (s, 3 H); ¹³C NMR (176 MHz, CDCl₃) C 166.6, 155.5, 134.3, 116.1, 114.7; CH 142.6, 137.0, 121.0, 109.8; CH₃ 56.5, 52.1; HRMS (EI) calcd for C₁₅H₁₄OBr [M+]: 347.8997, found 347.8980.



(*E*)-methyl 3-(5-bromo-2,4'-dimethoxy-[1,1'-biphenyl]-4-yl)acrylate (10b). To a solution of boronic ester S2 (53 mg, 0.23 mmol) in dioxane (3 mL, 0.08 M) were added aryl bromide 9b (100 mg, 0.29 mmol), KBr (136 mg, 1.14 mmol), K_3PO_4 (242 mg, 1.14 mmol), H_2O (0.3 ml) and Pd(PPh_3)₄ (33 mg, 0.029 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and heated to 65 °C for overnight upon which time TLC indicated consumption of the boronic ester. To the reaction mixture was added boronic ester S2 (14 mg, 0.06 mmol) and stirred at 65 °C for 8h upon which time TLC indicated consumption of the boronic ester S2 (14 mg, 0.06 mmol) and stirred at 65 °C for 8h upon which time TLC indicated consumption of the boronic ester S2 (14 mg, 0.06 mmol) and stirred at 65 °C for 8h upon which time TLC indicated consumption of the boronic ester S2 (14 mg, 0.06 mmol) and stirred at 65 °C for 8h upon which time TLC indicated consumption of the aryl bromide 9b. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (30:1 hexanes:EtOAc) yielded 10b (47 mg, 0.125 mmol, 43 %, white solid) as the only isolated regioisomer.

Data for **10b**: $R_f 0.15$ (10:1 Hexanes:EtOAc); mp = 134-136 °C; IR (thin film) 2938, 2836, 1712, 1381, 1245 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (d, *J* = 16.2 Hz, 1 H), 7.56 (s, 1 H), 7.48 (d, *J* = 8.9 Hz, 2 H), 7.17 (s, 1 H), 6.98 (d, *J* = 8.9 Hz, 2 H), 6.44 (d, *J* = 16.2 Hz, 1 H), 3.872 (s, 3 H), 3.868 (s, 3 H), 3.861 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) C 167.0, 159.4, 155.9, 134.2, 133.2, 128.6, 116.7; CH 143.2, 134.6, 130.6 (2 C), 120.0, 113.7 (2 C), 109.7; CH₃ 55.9, 55.4, 52.0; HRMS (ESI) calcd for C₁₈H₁₈O₄Br [M+H]: 377.0388, found 377.0383.



1,5-dibromo-2-methoxy-4-(2-methoxyvinyl)benzene (9c). To a solution of (methoxymethyl)triphenylphosphonium chloride (1 g, 2.9 mmol) in THF (8 mL, 0.4 M) were added potassium *tert*-butoxide (325 mg, 2.9 mmol) portionwise. The mixture was stirred at 19 °C for 15 min before addition of aldehyde **6e** (429 mg, 1.46 mmol). The reaction mixture was stirred at 19 °C for 30 min upon which time TLC indicated consumption of th starting material. The mixture was diluted with H₂O and extracted with EtOAc (15 mL x 3). The organic layers were combined, washed with H₂O, saturated aqueous NaCl, dried over Na₂SO₄, filtered, and concentrated. Purification by FCC (15:1 hexanes:EtOAc) yielded **9c** (270 mg, 0.84 mmol, 57 %, *E*:*Z* = 1.8:1) as a colorless oil.

Data for **9c**: $R_f 0.4$ (7:1 Hexanes: EtOAc); IR (thin film) 3120, 2966, 1701, 1560, 1443 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.72 (s, 1 H), 7.71 (s, 1.8 H), 7.70 (s, 1 H), 7.03 (d, *J* = 13.0 Hz, 1.8 H), 6.86 (s, 1.8 H), 6.31 (d, *J* = 7.4 Hz, 1 H), 6.03 (d, *J* = 13.0 Hz, 1.8 H), 5.57 (d, *J* = 7.4 Hz, 1 H), 3.92 (s, 5.4 H), 3.90 (s, 3 H), 3.85 (s, 3 H), 3.77 (s, 5.4 H); ¹³C NMR (176 MHz, CDCl₃) δ C 155.3, 154.9, 136.5, 135.1, 113.6, 113.3, 109.4, 109.1; CH 150.8, 149.7, 136.2, 135.7, 113.1, 108.5, 104.2, 103.5; CH₃ 61.1, 56.7, 56.4, 56.3; HRMS (ESI) calcd for C₁₀H₁₀O₂Br₂ [M+]: 319.9047, found 319.9048.



5-bromo-2,4'-dimethoxy-4-(2-methoxyvinyl)-1,1'-biphenyl (10c). To a solution of boronic ester **S2** (87 mg, 0.37 mmol) in dioxane (5 mL, 0.07 M) were added aryl bromide **9c** (150 mg, 0.465 mmol), KBr (221 mg, 1.86 mmol), K_3PO_4 (411 mg, 1.86 mmol), H_2O (0.5 ml) and Pd(PPh₃)₄ (54 mg, 0.047 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and stirred at 65 °C for 24h upon which time TLC indicated consumption of the boronic ester. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (10:1 hexanes:EtOAc) yielded **10c** (75 mg, 0.22 mmol, 58 %) as the major regioisomer (regioselectivity 8:1). The minor regioisomer was not isolated but was detected through ¹H NMR.



2-(5-bromo-2,4'-dimethoxy-[1,1'-biphenyl]-4-yl)acetaldehyde (S5). To a solution of the vinyl ether **10c** (23 mg, 0.07 mmol) in acetone (0.5 mL, 0.14 M) were added H_2O (0.15 ml) and conc. HCl (0.15 ml). The mixture was stirred at 19 °C for 5h upon which time TLC indicated consumption of the starting material. The mixture was diluted with H_2O and extracted with EtOAc (5 mL x 3). The organic layers were combined, washed with H_2O , saturated aqueous NaCl, dried over Na₂SO₄, filtered, and concentrated. Purification by FCC (15:1 hexanes:EtOAc) yielded **S5** (13 mg, 0.04 mmol, 59%) as a yellow oil.

Data for **S5**: $R_f 0.15$ (10:1 Hexanes:EtOAc); IR (thin film) 2961, 2935, 1724, 1609, 1486 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 9.83 (d, J = 1.3 Hz, 1 H), 7.55 (s, 1 H), 7.46 (d, J = 8.1 Hz, 2 H), 6.98 (d, J = 8.1 Hz, 2 H), 6.83 (s, 1 H), 3.91 (d, J = 1.3 Hz, 2 H), 3.88 (s, 3 H), 3.82 (s, 3 H); ¹³C NMR (176 MHz, CDCl₃) C 159.2, 156.0, 131.8, 131.7, 128.9, 115.5; CH 198.3, 134.3, 130.5 (2 C), 114.4, 113.7 (2 C); CH₂ 50.7; CH₃ 55.9, 55.3; HRMS (ESI) calcd for C₁₆H₁₆O₃Br [M+H]: 335.0283, found 335.0299.



4-bromo-4'-methoxy-3-vinyl-1,1'-biphenyl (10d). To a solution of boronic ester **S2** (107 mg, 0.46 mmol) in dioxane (5.7 mL, 0.1 M) were added aryl bromide $9d^2$ (150 mg, 0.573 mmol), KBr (273 mg, 2.29 mmol), K₃PO₄ (506 mg, 2.29 mmol), H₂O (0.57 ml) and Pd(PPh₃)₄ (66 mg, 0.057 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and stirred at 65 °C for 24h upon which time TLC indicated consumption of the boronic ester. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (15:1 hexanes:EtOAc) yielded 10d (81 mg, 0.28 mmol, 61 %) as the major regioisomer (regioselectivity 10:1). The minor regioisomer was not isolated but was detected through ¹H NMR.

Data for **10d**: $R_f 0.35$ (15:1 Hexanes:EtOAc); IR (thin film) 3000, 2932, 1609, 1515, 1453 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.73 (d, J = 2.2 Hz, 1 H), 7.60 (d, J = 8.1 Hz, 1 H), 7.54 (d, J = 8.7 Hz, 2 H), 7.32 (dd, J = 8.1, 2.2 Hz, 1 H), 7.12 (dd, J = 17.1, 11.3 Hz, 1 H), 7.01 (d, J = 8.7 Hz, 2 H), 5.80 (dd, J = 17.1, 1.3 Hz, 1 H), 5.43 (dd, J = 11.3, 1.3 Hz, 1 H), 3.88 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) C 159.5, 140.4, 137.7, 132.6, 122.0; CH 135.9, 133.1, 128.1 (2 C), 127.5, 125.1, 114.3 (2 C); CH₂ 116.8; CH₃ 55.4; HRMS (EI) calcd for C₁₅H₁₃OBr [M+]: 288.0150, found 288.0137.



1,2-dibromo-3-vinylbenzene (9e). To a solution of NaH (65 mg, 2.27 mmol, 60% in mineral oil) in THF (10mL, 0.27 M) was added methyltriphenylphosphonium bromide (1.21 g, 3.4 mmol) portionwise. The mixture was stirred at 19 °C for 20 min before addition of aldehyde **S6** (180 mg, 0.68 mmol) in THF (2 ml, 0.34 mmol). The reaction mixture was stirred at 19 °C for 6h upon which time TLC indicated consumption of th starting material. The mixture was quenched with H₂O and extracted with EtOAc (15 mL x 3). The organic layers were combined, washed with H₂O, saturated aqueous NaCl, dried over Na₂SO₄, filtered, and concentrated. Purification by FCC (10:1 hexanes:EtOAc) yielded **9e** (124 mg, 0.47 mmol, 69%) as an amorphous solid.

Data for **9e**: $R_f 0.8$ (15:1 Hexanes: EtOAc); IR (thin film) 2917, 2849, 1642, 1578, 1544 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.57 (d, J = 8.2 Hz, 1 H), 7.48 (d, J = 8.2 Hz, 1 H), 7.19 (t, J = 8.2 Hz, 1 H), 7.11 (dd, J = 17.4, 11.1 Hz, 1 H), 5.68 (d, J = 17.4 Hz, 1 H), 5.40 (d, J = 11.1 Hz, 1 H); ¹³C NMR (176 MHz, CDCl₃) δ C 140.6, 126.1, 125.6; CH 137.0, 132.8, 128.3, 125.7; CH₂ 117.9; HRMS (ESI) calcd for C₈H₆Br₂ [M+]: 259.8836, found 259.8838.

² Grigg, D. R.; Hoveln, R. V.; Schomaker, J. M. J. Am. Chem. Soc. **2012**, 134, 16131-16134.



2-bromo-4'-methoxy-3-vinyl-1,1'-biphenyl (**10e**). To a solution of boronic ester **S2** (58 mg, 0.248 mmol) in dioxane (3.1 mL, 0.08 M) were added aryl bromide **9e** (81 mg, 0.31 mmol), KBr (148 mg, 1.24 mmol), K_3PO_4 (274 mg, 1.24 mmol), H_2O (0.31 ml) and $Pd(PPh_3)_4$ (36 mg, 0.031 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and stirred at 65 °C for 24h upon which time TLC indicated consumption of the boronic ester. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (20:1 hexanes:EtOAc) yielded **10e** (33 mg, 0.12 mmol, 47 %) as the major regioisomer (regioselectivity greater than10:1). The minor regioisomer was not isolated but was detected through ¹H NMR.

Data for **10e**: $R_f 0.45$ (15:1 Hexanes:EtOAc); IR (thin film) 2954, 2926, 1609, 1513, 1248 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 7.53 (t, J = 8.4 Hz, 1 H), 7.35-7.33 (m, 3 H), 7.24 (dd, J = 8.4, 1.2 Hz, 1 H), 7.20 (dd, J = 18.0, 11.3 Hz, 1 H), 6.99 (d, J = 8.6 Hz, 1 H), 5.73 (dd, J = 18.0, 1.2 Hz, 1 H), 5.42 (dd, J = 11.3, 1.2 Hz, 1 H), 3.89 (s, 3 H); ¹³C NMR (176 MHz, CDCl₃) C 159.0, 143.2, 138.8, 134.3, 124.3; CH 137.1, 130.61 (2 C), 130.57, 127.1, 125.8, 113.3 (2 C); CH₂ 117.0; CH₃ 55.3; HRMS (EI) calcd for C₁₅H₁₃OBr [M+]: 288.01498, found 288.01571.



4'-methoxy-2-vinyl-1,1'-biphenyl (**15**) and **2,4'-dimethoxy-1,1'-biphenyl** (**16**). To a solution of boronic ester **S2** (254 mg, 1.09 mmol) in dioxane (10 mL, 0.11 M) were added *o*-bromostyrene **S7** (200 mg, 1.09 mmol), *o*-bromoanisole **S8** (204 mg, 1.09 mmol), KBr (519 mg, 4.36 mmol), K₃PO₄ (964 mg, 4.36 mmol), H₂O (1 ml) and Pd(PPh₃)₄ (126 mg, 0.109 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and stirred at 65 °C for 24h upon which time TLC indicated consumption of the boronic ester. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (40:1 hexanes:EtOAc) yielded **15** (19 mg, 0.09 mmol, 8%) as a colorless oil and **16** (111 mg, 0.53 mmol, 49%) as a colorless oil.

Data for **15**: $R_f 0.4$ (16:1 Hexanes: EtOAc); IR (thin film) 3084, 2834, 1625, 1510, 1514 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.66 (m, 1H), 7.35-7.28 (m, 5 H), 6.99 (d, *J* = 8.1 Hz, 2 H), 6.76 (dd, *J* = 17.4, 11.1 Hz, 1 H), 5.72 (d, *J* = 17.4 Hz, 1 H), 5.22 (d, *J* = 11.1 Hz, 1 H), 3.89 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ C 158.8, 140.5, 135.9, 133.2; CH 136.1, 130.9, 130.2, 127.7, 127.2, 125.8, 113.5; CH₂ 114.5; CH₃ 55.3; HRMS (ESI) calcd for C₁₅H₁₄ONa [M+Na]: 233.0942, found 233.0938.

Data for **16**: $R_f 0.35$ (16:1 Hexanes: EtOAc); IR (thin film) 2958, 2834, 1517, 1487, 1245 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, J = 8.7 Hz, 2H), 7.36-7.32 (m, 2 H), 7.09-7.00 (m, 4 H), 3.89 (s, 3 H), 3.86 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ C 158.7, 156.5, 130.9, 130.4; CH 130.7, 130.6, 128.2, 120.9, 113.5, 111.2; CH₃ 55.6, 55.3; HRMS (ESI) calcd for C₁₄H₁₅O₂ [M+H]: 215.1072, found 215.1062.



4'-methoxy-3-vinyl-1,1'-biphenyl (17) and **3,4'-dimethoxy-1,1'-biphenyl (18)**. To a solution of boronic ester **S2** (128 mg, 0.55 mmol) in dioxane (5 mL, 0.11 M) were added *m*-bromostyrene **S9** (100 mg, 0.55 mmol), *m*-bromoanisole **S10** (103 mg, 0.55 mmol), KBr (262 mg, 2.2 mmol), K₃PO₄ (466 mg, 2.2 mmol), H₂O (0.5 ml) and Pd(PPh₃)₄ (64 mg, 0.055 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and stirred at 65 °C for 36h upon which time TLC indicated consumption of the boronic ester. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (40:1 hexanes:EtOAc) yielded **17** (46 mg, 0.22 mmol, 40%) as a white solid and **18** (36 mg, 0.17 mmol, 31%) as a colorless oil which showed identical spectroscopic properties to reported data.³

Data for **17**: $R_f 0.4$ (30:1 Hexanes: EtOAc); mp = 76-78 °C; IR (thin film) 2835, 2086, 1641, 1515 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.60-7.55 (m, 3H), 7.48-7.39 (m, 3 H), 7.01 (d, *J* = 8.1 Hz, 2 H), 6.81 (dd, *J* = 17.3, 11.0 Hz, 1 H), 5.84 (d, *J* = 17.3 Hz, 1 H), 5.31 (d, *J* = 11.0 Hz, 1 H), 3.88 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ C 159.2, 141.2, 138.0, 133.7; CH 136.9, 128.9, 128.2, 126.3, 124.8, 124.5, 114.2; CH₂ 114.1; CH₃ 55.4; HRMS (ESI) calcd for C₁₅H₁₄O [M+]: 210.10447, found 210.1035.



4-methoxy-4'-vinyl-1,1'-biphenyl (19) and 4,4'-dimethoxy-1,1'-biphenyl (20). To a solution of boronic ester S2 (254 mg, 1.09 mmol) in dioxane (10 mL, 0.11 M) were added *p*-bromostyrene S11 (200 mg, 1.09

³ Scheuermann, G.; Rumi, L.; Steurer, P.; Bannwarth, W and Mülhaupt, R. *J. Am. Chem. Soc.* **2009**, *131*, 8262–8270.

mmol), *p*-bromoanisole **S12** (204 mg, 1.09 mmol), KBr (519 mg, 4.36 mmol), K_3PO_4 (964 mg, 4.36 mmol), H_2O (1 ml) and $Pd(PPh_3)_4$ (126 mg, 0.109 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and stirred at 65 °C for 24h upon which time TLC indicated consumption of the boronic ester. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (40:1 hexanes:EtOAc) yielded **19** (89 mg, 0.43 mmol, 39%) as a white solid and **20** (109 mg, 0.51 mmol, 47%) as a white solid which showed identical spectroscopic properties to reported data.³

Data for **19**: $R_f 0.4$ (20:1 Hexanes: EtOAc); mp = 145-146 °C; IR (thin film) 2937, 2838, 1722, 1639, 1437 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.49-7.46 (m, 4H), 7.42-7.40 (m, 2 H), 6.92 (d, *J* = 8.1 Hz, 2 H), 6.70 (dd, *J* = 17.4, 11.1 Hz, 1 H), 5.73 (d, *J* = 17.4 Hz, 1 H), 5.21 (d, *J* = 11.1 Hz, 1 H), 3.78 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ C 159.3, 140.3, 136.1, 133.3; CH 136.5, 128.0, 126.8, 126.7, 114.3; CH₂ 113.4; CH₃ 55.4; HRMS (ESI) calcd for C₁₅H₁₄O [M+]: 210.1045, found 210.1037.



2-(3-benzylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**26**). To a solution of triflate **S13⁴** (185 mg, 0.58 mmol) in dioxane (5 mL, 0.12 M) were added 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (295 mg, 1.16 mmol), Et₃N (0.24 ml, 1.74 mmol) and Pd(PPh₃)₄ (67 mg, 0.058 mmol). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and stirred at 70 °C for 8h upon which time TLC indicated consumption of the starting material. The reaction mixture was cooled to 19 °C and concentrated. Purification by FCC (50:1 hexanes:EtOAc) yielded **26** (137 mg, 0.466 mmol, 80 %) as a white solid.

Data for **26**: $R_f 0.52$ (10:1 Hexanes:EtOAc); mp = 62 °C; IR 3026, 2978, 1605, 1453, 1359 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.77 (s, 1 H), 7.73 (d, *J* = 7.2 Hz, 1 H), 7.35-7.31 (m, 4 H), 7.26-7.24 (m, 3 H), 4.05 (s, 2 H), 1.40 (s, 12 H); ¹³C NMR (100 MHz, CDCl₃) C 141.3, 140.4, 83.8 (2 C); CH 135.4, 132.7, 132.0, 128.9 (2 C), 128.5 (2 C), 128.0, 126.0; CH₂ 41.9; CH₃ 24.9 (4 C); HRMS (EI) calcd for C₁₉H₂₃O₂B [M+]: 294.1791, found 294.1780.



⁴ Kutzki, O.; Park, H. S.; Ernst, J. T.; Orner, B. P.; Yin, H. and Hamilton, A. D. *J. Am. Chem. Soc.* **2002**, *124*, 11838-11839.

3-isopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenol (S15). To a solution of aryl bromide **S14**⁴ (4.88 g, 22.7 mmol) in THF (200 mL, 0.11 M) at -40 °C was added *n*-BuLi (44.2 ml, 1.54 M in THF) slowly. The mixture was warmed to -5 °C and stirred for 1h. The mixture was cooled down to -78 °C and 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (16.9 g, 90.8 mmol) was added slowly. The reaction mixture was warmed to 19 °C slowly. The mixture was quenched with H₂O and extracted with EtOAc (100 mL x 3). The organic layers were combined, washed with 1M HCl, saturated aqueous NaCl, dried over Na₂SO₄, filtered, and concentrated. Purification by FCC (15:1 hexanes:EtOAc) yielded **S15** (3.6 g, 13.7 mmol, 61%) as a colorless oil.

Data for **S15**: $R_f 0.3$ (10:1 Hexanes:EtOAc); IR (thin film) 2975, 2929, 1602, 1573, 1350 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, J = 8.4 Hz, 1 H), 6.80 (d, J = 2.0 Hz, 1 H), 6.64 (dd, J = 8.4, 2.0 Hz, 1 H), 5.02 (s, 1 H), 3.73 (sept, J = 7.3 Hz, 1 H), 1.35 (s, 12 H), 1.22 (d, J = 7.3 Hz, 6 H); ¹³C NMR (100 MHz, CDCl₃) C 158.6, 158.1, 83.2 (2 C); CH 138.1, 111.9, 111.7, 31.2; CH₃ 24.8 (4 C), 24.3 (2 C); HRMS (EI) calcd for C₁₅H₂₃O₃B [M+]: 262.1740, found 262.1748.



benzyl 2-(3-isopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)acetate (25). To a solution of phenol **S15** (301 mg, 1.15 mmol) in DMF (10 mL, 0.15 M) was added K_2CO_3 (555 mg, 4.03 mmol). The mixture was heated to 40 °C and benzyl 2-bromoacetate (303 mg, 1.32 mmol) was added slowly. The reaction mixture was stirred at 40 °C for 2h upon which time TLC indicated consumption of the starting material. The mixture was quenched with H₂O and extracted with EtOAc (30 mL x 3). The organic layers were combined, washed with saturated aqueous LiCl, saturated aqueous NaCl, dried over Na₂SO₄, filtered, and concentrated to give **25** (493 mg, quant.). The crude can be used for next step without further purification.

Data for **25**: $R_f 0.45$ (10:1 Hexanes: EtOAc); mp = 58-59 °C; IR (thin film) 2987, 2927, 1763, 1600, 1344 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, *J* = 8.3 Hz, 1 H), 7.38-7.36 (m, 5 H), 6.91 (d, *J* = 2.0 Hz, 1 H), 6.67 (dd, *J* = 8.3, 2.0 Hz, 1 H), 5.26 (s, 2 H), 4.70 (s, 2 H), 3.72 (sept, *J* = 7.2 Hz, 1 H), 1.35 (s, 12 H), 1.20 (d, *J* = 7.2 Hz, 6 H); ¹³C NMR (100 MHz, CDCl₃) δ C 168.7, 160.1, 158.3, 135.2, 83.2, 29.7; CH 137.9, 128.6, 128.5, 128.4, 111.8, 110.1, 31.3; CH₂ 70.0, 65.1; CH₃ 24.8, 24.2; HRMS (ESI) calcd for C₂₄H₃₁BO₅Na [M+Na]: 433.2162, found 433.2149.



benzyl 2-((3''-benzyl-2-isopropyl-3'-vinyl-[1,1':4',1''-terphenyl]-4-yl)oxy)acetate (27). To a solution of aryl bromide **9d** (50 mg, 0.19 mmol) in dioxane (2 mL, 0.1 M) were added boronic ester **25** (70 mg, 0.17 mmol), K_3PO_4 (168 mg, 0.76 mmol), KBr (90 mg, 0.76 mmol), $Pd(PPh_3)_4$ (22 mg, 0.019 mmol) and H_2O (0.03 mL). The mixture was degassed 3 times (evacuation followed by backfill with Ar) and heated to 50 °C for 24 h upon which time TLC indicated consumption of the boronic ester **25**. Boronic ester **25** (16 mg, 0.038 mmol) was added to the mixture and continued heating for another 6h upon which time TLC indicated consumption ester **25** (16 mg, 0.038 mmol) was added to the mixture and continued heating for another 5h upon which time TLC indicated consumption of the boronic ester **25**. Boronic ester **25** (23 mg, 0.057 mmol) was added to the mixture and continued heating for overnight upon which time TLC indicated consumption of the aryl bromide **9d**. To the reaction mixture was added boronic ester **26** (168 mg, 0.57 mmol) in three portions over 24h upon which time TLC indicated completion of the reaction. The reaction mixture was cooled to rt and concentrated. Purification by FCC (20:1 hexanes:EtOAc) yielded **27** (57 mg, 0.103 mmol, 54 %) as a colorless oil.

Data for **27**: $R_f 0.25$ (10:1 Hexanes: EtOAc); IR (thin film) 2961, 2925, 1761, 1604, 1473 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, J = 2.2 Hz, 1 H), 7.39-7.21 (m, 16 H), 7.17 (d, J = 8.3 Hz, 1 H), 7.00 (d, J = 2.8 Hz, 1 H), 6.80-6.72 (m, 2 H), 5.67 (dd, J = 17.3, 1.4 Hz, 1 H), 5.30 (s, 2 H), 5.18 (dd, J = 11.3, 1.4 Hz, 1 H), 4.75 (s, 2 H), 4.07 (s, 2 H), 3.13 (sept, J = 7.5 Hz, 1 H), 1.18 (d, J = 7.5 Hz, 6 H); ¹³C NMR (100 MHz, CDCl₃) δ C 168.9, 157.5, 148.3, 141.1, 140.9, 140.7, 140.6, 139.1, 135.3, 135.2, 134.5; CH 136.0, 131.0, 130.6, 129.7, 129.0, 128.8, 128.7, 128.6, 128.5, 128.2, 127.7, 127.6, 126.8, 126.1, 112.6, 111.0, 29.7; CH₂ 114.7, 67.0, 65.5, 42.0; CH₃ 24.3; HRMS (ESI) calcd for C₃₉H₃₆O₃Na [M+Na]: 575.2562, found 575.2591.



2-((3''-benzyl-3'-ethyl-2-isopropyl-[1,1':4',1''-terphenyl]-4-yl)oxy)acetic acid (21). To a solution of **27** (17 mg, 0.031 mmol) in MeOH (3 mL, 0.01 M) was added 5% Pd on carbon (3.2 mg, 0.0016 mmol). The

mixture was pressurized to 400 psi under a hydrogen atmosphere. After 12 h NMR of a concentrated aliquot indicated consumption of starting material. The reaction mixture was filtered through a silica gel/celite plug and concentrated to yield **21** (189 mg, 0.34 mmol, 84%) as a yellow oil.

Data for **21**: $R_f 0.1$ (10:1 Hexanes: EtOAc); IR (thin film) 2965, 2094, 1643, 1493, 1475 cm⁻¹; ¹H NMR (700 MHz, CD₃OD) δ 7.36 (dd, J = 7.9, 1.1 Hz, 1H), 7.30-7.15 (m, 10 H), 7.10-7.08 (m, 2 H), 7.00 (d, J = 2.9 Hz, 1 H), 6.81 (dd, J = 7.9, 2.9 Hz, 1 H), 4.49 (s, 1 H), 4.05 (s, 1 H), 3.11 (sept, J = 7.2 Hz, 1 H), 2.58 (q, J = 7.9 Hz, 2 H), 2.00 (s, 1 H), 1.19 (d, J = 7.2 Hz, 6 H), 1.05 (t, J = 7.9 Hz, 3 H); ¹³C NMR (176 MHz, CD₃OD) δ C 174.7, 158.3, 147.4, 142.0, 141.31, 141.28, 141.1, 140.9, 139.8, 133.8; CH 130.4, 129.6, 129.5, 129.1, 128.6, 128.1, 127.9, 127.0, 126.6, 126.5, 125.7, 111.6, 111.1, 29.5; CH₂ 66.8, 41.4, 25.8; CH₃ 23.1, 14.9; HRMS (ESI) calcd for C₃₂H₃₂O₃ [M+]: 464.2352, found 464.2349.


















































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PC	LB	SSB	WDW	SF	IS	SFO1	51.1	NUC1		TDO	11 1	ΠE	DE	DW	RG	AQ	FIDRES	SWH	DS	SN	SOLVENT	1	PULPROG	PROBHD	INSTRUM	Time	Date_	PROCNO	EXPNO	NAME
1.00	0.30 Hz	0	EM	400.1400000 MH:	16384	400.1428010 MH:		11 20	CHANNEL f1 =====:	1	2.00000000 se	298.4 K	6.50 usi	69.600 usi	128	2.2807028 se	0.219235 Hz	7183.908 Hz	2	10	CDC13	32768	Zg30	5 mm PABBO BB-	robinson	12.55	20140916	1	ц	PZ5022





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C13



