Supporting Information

Arenes to anilines and arylethers by sequential iridium-catalyzed borylation and copper-catalyzed coupling

C. Christoph Tzschucke, Jaclyn M. Murphy, and John F. Hartwig*

*Department of Chemistry, Yale University, P.O. Box 208107, New Haven, CT 06520-8107 and
Department of Chemistry, University of Illinois, 600 S. Matthews Ave., Urbana, Illinois 61801 USA*

jhartwig@scs.uiuc.edu

General.

All the experiments were carried out in air, except where explicitly noted. Cyclohexane was distilled from sodium benzophenone solutions, and arenes were distilled from calcium hydride. All other commercially available chemicals and solvents were used as received. $[\text{Ir}(\text{COD})\text{OMe}]_2$ was prepared by a published procedure.¹ ^1H NMR spectra were recorded on samples in the indicated solvent at 400 or 500 MHz, with Me_4Si or residual protiated solvent as an internal chemical shift reference. Synthesis of aryl boronates and aryl boronic acids were carried out as described earlier.² The crude products were used as such without further purification for the coupling reactions.

Borylation of Benzene.²

In a nitrogen filled glovebox, a solution of pinacolborane (10 μl , 0.069 mmol) and $[(\text{COD})\text{Ir}(\text{OMe})]_2$ (2.6 mg, 0.0039 mmol) in benzene (2.0 ml) and a solution of 4,4'-di-tert-butyl-2,2'-bipyridine (2.3 mg, 0.0086 mmol) in benzene (2.0 ml) was added to a solution of bispinacolatodiboron (1.914 g, 7.53 mmol) in benzene (10.0 ml). The combined solution was heated at 80 °C in a sealed reaction vessel for 24 h. The volatile materials were removed *in vacuo* to give the crude 2-phenyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (phenylboronic acid pinacolester). 2.889 g, 14.16 mmol, 94%.

Borylation of Arenes. General Procedure:²

In a nitrogen filled glovebox, a solution of pinacolborane (10 μl , 0.069 mmol) and $[(\text{COD})\text{Ir}(\text{OMe})]_2$ (2.7 mg, 0.0041 mmol) in cyclohexane (2.5 ml) and a solution of 4,4'-di-tert-butyl-2,2'-bipyridine (2.5 mg, 0.0093 mmol) in cyclohexane (2.5 ml) was added to a solution of bispinacolatodiboron (1.91 g, 7.53 mmol) and arene (15.0 mmol) in cyclohexane (5.0 ml). The solution was heated at 80 °C in a sealed reaction vessel for 24 h. The volatile materials were removed *in vacuo* to give the crude product, together with

unreacted starting arene. The ratio of starting material to product was determined by ^1H -NMR spectroscopy.

Hydrolysis of boronic acid pinacol esters. General procedure:²

Crude arylboronic acid pinacol ester (8.00 mmol) and sodium periodate (5.16 g, 24.0 mmol) were stirred in 65 mL of a 4:1 mixture of THF and water for 30 min, at which time aqueous hydrochloric acid (1N, 5.6 mL, 5.6 mmol) was added to the suspension. The reaction mixture was stirred at ambient temperature for 17 h or until GC analysis showed complete consumption of the arylboronic acid ester. The reaction mixture was diluted with water (30 mL) and extracted with ethyl acetate (2 x 60 mL). The combined extracts were washed with water (2 x 30 mL) and brine (30 mL), dried over sodium sulfate, filtered, and concentrated to dryness by rotary evaporation. The residue was washed with small portions of hexane, to give a colourless, solid product.

Amination of arylboronic acid pinacol esters. General procedure:

A suspension of arylboronic acid pinacol ester (1.00 mmol), copper(II)acetate monohydrate (20.0 mg, 0.100 mmol), potassium fluoride (60.0 mg, 1.03 mmol) and powdered molecular sieves (4 Å, 800 mg) in acetonitrile (5.0 mL) was stirred under ambient conditions for 5 to 10 min. Alkylamine (2.00 mmol) was added, and the reaction was heated at 80 °C under oxygen for 24 h. The reaction mixture was diluted with diethylether (30 mL), filtered through a pad of Celite and concentrated in vacuo. The product was purified by column chromatography (silica gel, ethyl acetate/hexane gradient containing 0.1 vol% triethylamine). Yields of the coupling product between arylboronic esters and alkylamines are calculated based on ArBpin. Yields for the coupling of arylboronic esters and arylamines are based on arylamine.

N-Phenylcyclohexylamine (N-Phenylaminocyclohexane).³ The product was obtained starting from phenylboronic acid pinacol ester of 84% purity (main impurity pinBOBpin, 230 mg, 0.95 mmol) according to the general procedure. Yield 111 mg, 0.633 mmol, 67%.

^1H NMR (500 MHz, CDCl_3): 7.26 (2 H, t, $J = 7.9$ Hz), 6.75 (1 H, t, $J = 7.3$ Hz), 6.67 (2 H, d, $J = 8.3$ Hz), 3.57 (1 H, br), 3.34 (1 H, tt, $J = 10.3, 3.7$ Hz), 2.15 (2 H, dd, $J = 12.9, 3.3$ Hz), 1.85 (2 H, dt, $J = 13.4, 3.8$ Hz), 1.74 (1 H, dt, $J = 12.9, 3.8$ Hz), 1.46 (2 H, qt, $J = 12.4, 3.3$ Hz), 1.33 (1 H, tt, $J = 12.0, 3.5$ Hz), 1.23 (2 H, qd, $J = 11.4, 3.4$ Hz).

^{13}C NMR (125.7 MHz, CDCl_3): 147.3, 129.2, 116.8, 113.1, 51.7, 33.5, 25.9, 25.0.

N-Phenyl-2-aminoacetaldehyde diethylacetal.⁴ The product was obtained starting from phenylboronic acid pinacol ester of 84% purity (230 mg, 0.95 mmol). Yield 128 mg, 0.612 mmol, 64%.

^1H NMR (500 MHz, CDCl_3): 7.18 (2 H, dd, $J = 8.5, 7.6$ Hz), 6.72 (1 H, t, $J = 7.4$ Hz), 6.64 (2 H, d, $J = 7.5$ Hz), 4.69 (1 H, t, $J = 5.5$ Hz), 3.91 (1 H, br), 3.73 (2 H, dq, $J = 9.5, 7.0$), 3.58 (2 H, dq, $J = 9.5, 7.0$ Hz), 3.26 (2 H, d, $J = 5.6$ Hz), 1.25 (6 H, t, $J = 7.1$ Hz).
 ^{13}C NMR (125.7 MHz, CDCl_3): 148.0, 129.3, 117.7, 113.1, 100.9, 62.3, 46.4, 15.4.

N-Phenyl-1-aminooctane (N-Phenyl-1-aminooctane).⁵ The product was obtained starting from phenylboronic acid pinacolester of 84% purity (242 mg, 1.00 mmol). Yield 100 mg, 0.49 mmol, 49%.

^1H NMR (500 MHz, CDCl_3): 7.19 (2 H, t, $J = 7.9$ Hz), 6.71 (1 H, t, $J = 7.2$ Hz), 6.62 (2 H, d, $J = 8.2$ Hz), 3.12 (2 H, t, $J = 7.3$ Hz), 1.63 (2 H, quintet, $J = 7.4$ Hz), 1.28 – 1.44 (10 H, m), 0.92 (3 H, t, $J = 6.9$ Hz).
 ^{13}C NMR (125.7 MHz, CDCl_3): 148.5, 129.1, 117.0, 112.7, 44.0, 31.8, 29.5, 29.4, 29.2, 27.1, 22.6, 14.0.

N-(3,5-Dimethoxyphenyl)cyclohexylamine (N-(3,5-

Dimethoxyphenyl)aminocyclohexane).⁶ The product was obtained starting from (3,5-dimethoxyphenyl)boronic acid pinacolester of 80% purity (main impurity 1,3-dimethoxybenzene, 333 mg, 1.01 mmol). Yield 151 mg, 0.642 mmol, 64%.

^1H NMR (500 MHz, CDCl_3): 5.89 (1 H, t, $J = 2.0$ Hz), 5.82 (2 H, d, $J = 1.9$ Hz), 3.78 (6 H, s), 3.25 (1 H, tt, $J = 10.3, 3.7$ Hz), 2.09 (2 H, dd, $J = 12.7, 3.2$ Hz), 1.79 (2 H, dt, $J = 13.5, 3.8$ Hz), 1.68 (1 H, dt, $J = 12.9, 3.8$ Hz), 1.39 (2 H, qt, $J = 12.4, 3.3$ Hz), 1.26 (1 H, tt, $J = 12.3, 3.6$ Hz), 1.17 (2 H, qd, $J = 11.7, 3.5$ Hz).

^{13}C NMR (125.7 MHz, CDCl_3): 161.7, 149.2, 91.9, 89.1, 55.1, 51.7, 33.4, 25.9, 25.0.

N-(3,5-Dimethoxyphenyl)-2-aminoacetaldehyde diethylacetal.⁷ The product was obtained starting from (3,5-dimethoxyphenyl)boronic acid pinacolester of 80% purity (main impurity 1,3-dimethoxybenzene, 333 mg, 1.01 mmol). Yield 156 mg, 0.578 mmol, 57%.

^1H NMR (400 MHz, CDCl_3): 5.90 (1 H, t, $J = 2.2$ Hz), 5.84 (2 H, d, $J = 1.9$ Hz), 4.68 (1 H, t, $J = 5.6$ Hz), 3.76 (6 H, s), 3.74 (2 H, dq, $J = 9.7, 6.9$ Hz), 3.58 (2 H, dq, $J = 9.4, 7.1$ Hz), 3.24 (2 H, d, $J = 5.6$ Hz), 1.25 (6 H, t, $J = 7.0$ Hz).

^{13}C NMR (125.7 MHz, CDCl_3): 161.6, 149.8, 100.7, 91.8, 89.9, 62.2, 55.0, 46.3, 15.3.

***N*-(3,5-Dimethoxyphenyl)octylamine (*N*-(3,5-Dimethoxyphenyl)-1-aminooctane).**⁶

The product was obtained starting from (3,5-dimethoxyphenyl)boronic acid pinacolester of 80% purity (main impurity 1,3-dimethoxybenzene, 330 mg, 1.00 mmol). Yield 92 mg, 0.347 mmol, 35%.

¹H NMR (500 MHz, CDCl₃): 5.90 (1 H, t, *J* = 2.1 Hz), 5.82 (2 H, d, *J* = 1.9 Hz), 3.78 (6 H, s), 3.10 (2 H, t, *J* = 6.8 Hz), 1.62 (2 H, quintet, *J* = 7.4 Hz), 1.28 – 1.43 (10 H, m), 0.92 (3 H, t, *J* = 7.0 Hz).

¹³C NMR (125.7 MHz, CDCl₃): 161.7, 150.4, 91.4, 89.4, 55.0, 43.9, 31.8, 29.5, 29.3, 29.2, 27.1, 22.6, 14.0.

***N*-(3-Chloro-5-methoxyphenyl)cyclohexylamine (*N*-(3-Chloro-5-methoxyphenyl)aminocyclohexane).**

The product was obtained starting from (3-chloro-5-methoxyphenyl)boronic acid pinacolester of 84% purity (main impurity 3-chloroanisole, 319 mg, 1.00 mmol). Yield 134 mg, 0.559 mmol, 56%.

¹H NMR (500 MHz, CDCl₃): 6.25 (1 H, t, *J* = 2.0 Hz), 6.22 (1 H, t, *J* = 1.9 Hz), 6.03 (1 H, t, *J* = 2.1 Hz), 3.76 (3 H, s), 3.66 (1 H, br), 3.22 (1 H, tt, *J* = 10.1, 3.5 Hz), 2.05 (2 H, dd, *J* = 12.7, 3.2 Hz), 1.78 (2 H, dt, *J* = 13.6, 3.7 Hz), 1.68 (1 H, dt, *J* = 12.6, 3.7 Hz), 1.39 (2 H, qt, *J* = 11.3, 3.4 Hz), 1.26 (1 H, tt, *J* = 12.1, 3.6), 1.14 (2 H, qd, *J* = 11.7, 3.1 Hz).

¹³C NMR (125.7 MHz, CDCl₃): 161.2, 149.1, 135.3, 106.0, 102.3, 97.3, 55.2, 51.5, 33.2, 25.7, 24.9.

Elemental Analysis: C, 65.40; H, 7.65; N, 5.75 (calculated for C₁₃H₁₈ClNO: C, 65.13; H, 7.57; N, 5.84).

***N*-(3-Chloro-5-methoxyphenyl)-2-aminoacetaldehyde diethylacetal.** The product was obtained starting from (3-chloro-5-methoxyphenyl)boronic acid pinacolester of 84% purity (main impurity 3-chloroanisole, 319 mg, 1.00 mmol). Yield 157 mg, 0.574 mmol, 57%.

¹H NMR (500 MHz, CDCl₃): 6.27 (1 H, t, *J* = 1.9 Hz), 6.25 (1 H, t, *J* = 1.9 Hz), 6.05 (1 H, t, *J* = 2.1 Hz), 4.65 (1 H, t, *J* = 5.4 Hz), 4.04 (1 H, br), 3.74 (3 H, s), 3.73 (2 H, dq, *J* = 9.4, 7.1 Hz), 3.57 (2 H, dq, *J* = 9.4, 7.1 Hz), 3.21 (2 H, t, *J* = 5.4 Hz), 1.24 (6 H, t, *J* = 7.1 Hz).

¹³C NMR (125.7 MHz, CDCl₃): 161.1, 149.7, 135.3, 105.9, 103.3, 100.5, 97.2, 62.3, 55.1, 46.0, 15.2.

Elemental Analysis: C, 57.00; H, 7.33; N, 5.05 (calculated for C₁₃H₂₀ClNO₃: C, 57.04; H, 7.36; N, 5.12).

***N*-(3-Chloro-5-methoxyphenyl)octylamine (*N*-(3-Chloro-5-methoxyphenyl)-1-**

aminooctane). The product was obtained starting from (3-chloro-5-methoxyphenyl)boronic acid pinacolester of 84% purity (main impurity 3-chloroanisole, 319 mg, 1.00 mmol). Yield 127 mg, 0.471 mmol, 47%.

^1H NMR (500 MHz, CDCl_3): 6.28 (1 H, t, $J = 2.1$ Hz), 6.23 (1 H, t, $J = 1.9$ Hz), 6.04 (1 H, t, $J = 2.2$ Hz), 3.77 (3 H, s), 3.08 (2 H, q (coupling observed to the N-H), $J = 6.0$ Hz), 1.61 (2 H, quintet, $J = 7.4$ Hz), 1.30 – 1.43 (10 H, m), 0.95 (3 H, t, $J = 7.1$ Hz).

^{13}C NMR (125.7 MHz, CDCl_3): 161.1, 150.2, 135.3, 105.6, 102.6, 96.8, 55.1, 43.7, 31.7, 29.30, 29.28, 29.2, 27.0, 22.6, 14.0.

Elemental Analysis: C, 66.59; H, 8.59; N, 4.89 (calculated for $\text{C}_{15}\text{H}_{24}\text{ClNO}$: C, 66.77; H, 8.97; N, 5.19).

***N*-(3,5-Dimethylphenyl)cyclohexylamine (*N*-(3,5-**

Dimethylphenyl)aminocyclohexane).⁸ The product was obtained starting from (3,5-dimethylphenyl)boronic acid pinacolester (243 mg, 1.05 mmol). Yield 83 mg, 0.408 mmol, 39%.

^1H NMR (400 MHz, CDCl_3): 6.42 (1 H, s), 6.32 (2 H, s), 3.49 (1 H, br), 3.33 (1 H, tt, $J = 10.2, 3.8$ Hz), 2.33 (6 H, s), 2.12 – 2.16 (2 H, m), 1.85 (2 H, dt, $J = 13.4, 3.7$ Hz), 1.74 (1 H, dt, $J = 12.6, 3.8$ Hz), 1.47 (2 H, qt, $J = 12.2, 3.4$ Hz), 1.33 (1 H, tt, $J = 12.2, 3.5$ Hz), 1.22 (2 H, qd, $J = 11.5, 3.4$ Hz).

^{13}C NMR (100.6 MHz, CDCl_3): 147.4, 138.8, 118.9, 111.0, 51.5, 33.5, 25.9, 25.0, 21.5.

***N*-(3,5-Dimethylphenyl)-2-aminoacetaldehyde diethylacetal.**⁴ The product was obtained starting from (3,5-dimethylphenyl)boronic acid pinacolester (233 mg, 1.01 mmol). Yield 75 mg, 0.316 mmol, 31%.

^1H NMR (500 MHz, CDCl_3): 6.43 (1 H, s), 6.34 (2 H, s), 4.72 (1 H, t, $J = 5.5$ Hz), 3.83 (1 H, br), 3.76 – 3.79 (2 H, m), 3.61 – 3.64 (2 H, m), 3.29 (2 H, d, $J = 5.3$ Hz), 2.29 (6 H, s), 1.29 (6 H, t, $J = 7.1$ Hz).

^{13}C NMR (125.7 MHz, CDCl_3): 148.0, 138.8, 119.6, 111.0, 100.9, 62.1, 46.4, 21.4, 15.3.

***N*-(3,5-Dimethylphenyl)octylamine (*N*-(3,5-Dimethylphenyl)-1-aminooctane).** The product was obtained starting from (3,5-dimethylphenyl)boronic acid pinacolester (232 mg, 1.00 mmol). Yield 79 mg, 0.338 mmol, 34%.

^1H NMR (500 MHz, CDCl_3): 6.43 (1 H, s), 6.32 (2 H, s), 3.55 (1 H, br), 3.15 (2 H, t, $J = 7.1$ Hz), 2.32 (6 H, s), 1.67 (2 H, quintet, $J = 7.6$ Hz), 1.35 – 1.48 (10 H, m), 0.98 (3 H, t, $J = 7.1$ Hz).

^{13}C NMR (125.7 MHz, CDCl_3): 148.6, 138.7, 119.0, 110.6, 44.0, 31.8, 29.6, 29.4, 29.2, 27.2, 22.6, 21.4, 14.1.

Elemental Analysis: C, 82.26; H, 11.75; N, 5.62 (calculated for $\text{C}_{16}\text{H}_{27}\text{N}$: C, 82.34; H, 11.66; N, 6.00).

***N*-(3-Methoxycarbonyl-5-methylphenyl)-2-aminoacetaldehyde diethylacetal.** The product was obtained starting from (3-methoxycarbonyl-5-methylphenyl)boronic acid pinacolester of 70% purity (main impurity 3-methylbenzoic acid methyl ester, 395 mg, 1.00 mmol). Yield 186 mg, 0.661 mmol, 66%.

^1H NMR (500 MHz, CDCl_3): 7.19 (1 H, s), 7.10 (1 H, s), 6.62 (1 H, s), 4.65 (1 H, t, $J = 5.4$ Hz), 4.04 (1 H, br), 3.85 (3 H, s), 3.66 – 3.73 (2 H, m), 3.51 – 3.59 (2 H, m), 3.25 (2 H, d, $J = 5.3$ Hz), 2.28 (3 H, s), 1.21 (6 H, t, $J = 7.1$ Hz).

^{13}C NMR (125.7 MHz, CDCl_3): 167.4, 147.8, 138.8, 130.7, 119.4, 118.1, 110.7, 100.6, 62.2, 51.7, 46.1, 21.2, 15.1.

Elemental Analysis: C, 64.32; H, 8.19; N, 4.69 (calculated for $\text{C}_{15}\text{H}_{23}\text{NO}_4$: C, 64.03; H, 8.24; N, 4.98).

***N*-(5-Methoxy-3-trifluoromethylphenyl)-2-aminoacetaldehyde diethylacetal.** The product was obtained starting from (5-trifluoro-3-methoxyphenyl)boronic acid pinacolester (313 mg, 1.04 mmol). Yield 182 mg, 0.592 mmol, 57%.

^1H NMR (500 MHz, CDCl_3): 6.50 (2 H, t, $J = 2.0$ Hz), 6.32 (1 H, t, $J = 2.1$ Hz), 4.69 (1 H, t, $J = 5.4$ Hz), 4.17 (1 H, br), 3.80 (3 H, s), 3.76 (2 H, dq, $J = 9.5, 7.2$ Hz), 3.60 (2 H, dq, $J = 9.5, 6.8$ Hz), 3.28 (2 H, br), 1.27 (6 H, t, $J = 7.1$ Hz).

^{13}C NMR (125.7 MHz, CDCl_3): 161.0, 149.6, 132.3 (q, $J = 31.8$ Hz), 124.2 (q, $J = 272.5$ Hz), 102.7 (q, $J = 3.9$ Hz), 101.5, 100.7, 99.6 (q, 3.8 Hz), 62.5, 55.3, 46.2, 15.3.

Elemental Analysis: C, 54.92; H, 6.62; N, 4.31 (calculated for $\text{C}_{14}\text{H}_{20}\text{F}_3\text{NO}_3$: C, 54.72; H, 6.56; N, 4.56).

***N*-Phenyl-morpholine.**⁹ The product was obtained starting from phenylboronic acid pinacolester of 84% purity (231 mg, 0.95 mmol) using a stoichiometric amount of copper(II)acetate monohydrate (200 mg, 1.00 mmol). Yield 82 mg, 0.502 mmol, 50%.

^1H NMR (400 MHz, CDCl_3): 7.38 – 7.41 (2 H, m), 6.98 – 7.04 (3 H, m), 3.95 – 3.97 (4 H, m), 3.24 – 3.27 (4 H, m).

^{13}C NMR (125.7 MHz, CDCl_3): 151.2, 129.1, 119.9, 115.6, 66.8, 49.2.

Amination of Arylboronic acids. General Procedure:¹⁰

Arylboronic acid (1.50 mmol), arylamine (1.00 mmol), 2,6-lutidine (120 μl , 1.06 mmol), anhydrous copper(II)acetate (9.0 mg, 0.05 mmol) and decanoic acid (17.2 mg, 0.10 mmol) in toluene (3 ml) were stirred at room temperature under air in a rubber septum capped 100 ml round bottom flask for 24 h. The reaction mixture was loaded on a short plug of silica gel (ca. 3 cm^3) and eluted with ethyl acetate (ca. 20 ml). The solvent was removed by rotary evaporation, and the product isolated by column chromatography (silica gel, ethyl acetate/hexane gradient).

N-phenyl-3,5-dimethylphenylamine.¹¹ Starting from phenylboronic acid and 3,5-dimethylaniline, 187 mg, 0.948, 95% were obtained. Starting from 3,5-dimethylphenylboronic acid (226 mg, 1.51 mmol) and aniline (92 μl , 1.01 mmol), 179 mg, 0.907 mmol, 90% were obtained.

^1H NMR (500 MHz, CDCl_3): 7.38 (2 H, t, $J = 7.0$ Hz), 7.17 (2 H, d, $J = 7.6$ Hz), 7.04 (1 H, t, $J = 7.4$ Hz), 6.82 (2 H, s), 6.72 (2 H, s), 5.74 (1 H, br), 2.39 (6 H, s).

^{13}C NMR (125.7 MHz, CDCl_3): 143.3, 143.0, 138.8, 129.2, 122.8, 120.6, 117.8, 115.5, 21.3.

Bis-(3,5-dimethylphenyl)-amine.¹² The product was obtained from 3,5-dimethylphenylboronic acid (225 mg, 1.50 mmol) and 3,5-dimethylaniline (125 μl , 1.00 mmol). Yield 189 mg, 0.838 mmol, 84%.

^1H NMR (500 MHz, CDCl_3): 6.40 (4 H, s), 6.30 (2 H, s), 5.18 (1 H, br), 1.99 (12 H, s).

^{13}C NMR (125.7 MHz, CDCl_3): 143.2, 138.8, 122.6, 115.7, 21.3.

N-(3,5-dimethylphenyl)-2,4,6-trimethylphenylamine.¹³ The product was obtained from 3,5-dimethylphenylboronic acid (225 mg, 1.50 mmol) and 2,4,6-trimethylaniline (140 μl , 1.00 mmol). Yield 226 mg, 0.944 mmol, 94%.

^1H NMR (400 MHz, CDCl_3): 7.20 (2 H, s), 6.65 (1 H, s), 6.38 (2 H, s), 5.19 (1 H, br), 2.57 (3 H, s), 2.46 (6 H, s), 2.44 (6 H, s).

^{13}C NMR (100.6 MHz, CDCl_3): 146.5, 138.7, 135.8, 135.7, 135.0, 129.1, 119.8, 111.0, 21.3, 20.8, 18.2.

***N*-(4-chlorophenyl)-3,5-dimethylphenylamine.** The product was obtained from 3,5-dimethylphenylboronic acid (225 mg, 1.50 mmol) and 4-chloroaniline (126 mg, 0.99 mmol). Yield 209 mg, 0.902 mmol, 91%.

^1H NMR (400 MHz, CDCl_3): 7.30 (2 H, d, $J = 8.9$ Hz), 7.05 (2 H, d, $J = 8.9$ Hz), 6.78 (2 H, s), 6.74 (1 H, s), 2.39 (6 H, s).

^{13}C NMR (100.6 MHz, CDCl_3): 142.5, 142.0, 139.0, 129.1, 125.1, 123.3, 118.7, 115.9, 21.3.

Elemental Analysis: C, 72.70; H, 6.00; N, 5.83 (calculated for $\text{C}_{14}\text{H}_{14}\text{ClN}$: C, 72.57; H, 6.09; N, 6.04).

***N*-(2-*tert*-butylphenyl)-3,5-dimethylphenylamine.** The product was obtained from 3,5-dimethylphenylboronic acid (226 mg, 1.51 mmol) and 2-*tert*-butylaniline (155 μl , .99 mmol). Yield 231 mg, 0.912 mmol, 92%.

^1H NMR (500 MHz, CDCl_3): 7.74 (1 H, dd, $J = 7.9, 1.1$ Hz), 7.63 (1 H, dd, $J = 7.9, 0.9$ Hz), 7.48 (1 H, td, $J = 7.5, 1.3$ Hz), 7.37 (1 H, td, $J = 7.6, 1.2$ Hz), 6.81 (1 H, s), 6.79 (2 H, s), 5.63 (1 H, br), 2.56 (6 H, s), 1.76 (9 H, s).

^{13}C NMR (125.7 MHz, CDCl_3): 145.7, 143.0, 141.3, 138.7, 126.81, 126.75, 125.9, 123.6, 121.2, 113.8, 34.7, 30.5, 21.3.

Elemental Analysis: C, 85.28; H, 9.13; N, 5.44 (calculated for $\text{C}_{18}\text{H}_{23}\text{N}$: C, 85.32; H, 9.15; N, 5.53).

***N*-(3,5-dimethylphenyl)-3,5-dimethoxyphenylamine.** The product was obtained from 3,5-dimethoxyphenylboronic acid (272 mg, 1.49 mmol) and 3,5-dimethylaniline (125 μl , 1.00 mmol) using 30 mol% copper(II)acetate (55.3 mg, 0.304 mmol). Yield 209 mg, 0.812 mmol, 81%.

^1H NMR (400 MHz, CDCl_3): 6.79 (2 H, s), 6.67 (1 H, s), 6.29 (2 H, d, $J = 2.4$ Hz), 6.12 (1 H, t, $J = 2.2$ Hz), 5.72 (1 H, br), 3.81 (6 H, s), 2.33 (6 H, s).

^{13}C NMR (100.6 MHz, CDCl_3): 161.5, 145.4, 142.4, 138.9, 123.2, 116.5, 95.7, 92.6, 55.1, 21.3.

Elemental Analysis: C, 74.76; H, 7.30; N, 5.40 (calculated for $\text{C}_{16}\text{H}_{19}\text{NO}_2$: C, 74.68; H, 7.44; N, 5.44).

***N*-(3,5-dimethylphenyl)-3-methoxycarbonyl-5-methylphenylamine.** The product was obtained from (3-methoxycarbonyl-5-methylphenyl)boronic acid (292 mg, 1.51 mmol) and 3,5-dimethylaniline (125 μ l, 1.00 mmol). Yield 189 mg, 0.702 mmol, 70%.

^1H NMR (500 MHz, CDCl_3): 7.62 (1 H, s), 7.49 (1 H, s), 7.12 (1 H, s), 6.79 (2 H, s), 6.71 (1 H, s), 5.91 (1 H, br), 3.97 (3 H, s), 2.40 (3 H, s), 2.36 (6 H, s).

^{13}C NMR (125.7 MHz, CDCl_3): 167.2, 143.7, 142.4, 139.0, 138.9, 130.9, 123.3, 122.1, 122.0, 116.2, 112.4, 51.8, 21.22, 21.19.

Elemental Analysis: C, 75.89; H, 6.84; N, 5.09 (calculated for $\text{C}_{17}\text{H}_{19}\text{NO}_2$: C, 75.81; H, 7.11; N, 5.20).

***N*-(3,5-dimethylphenyl)-3-methoxy-5-trifluoromethylphenylamine.** The product was obtained from 5-trifluoromethyl-3-methoxyphenylboronic acid (330 mg, 1.50 mmol) and 3,5-dimethylaniline (125 μ l, 1.00 mmol) using 30 mol% copper(II)acetate (55.0 mg, 0.303 mmol). Yield 211 mg, 0.714 mmol, 71%.

^1H NMR (500 MHz, CDCl_3): 6.90 (1 H, s), 6.82 (2 H, s), 6.80 (1 H, s), 6.77 (1 H, s), 6.74 (1 H, s), 5.78 (1 H, br), 3.87 (3 H, s), 2.37 (6 H, s).

^{13}C NMR (125.7 MHz, CDCl_3): 160.9, 145.7, 141.4, 139.2, 132.5 (q, $J = 32.1$ Hz), 124.3, 124.0 (q, $J = 272.5$ Hz), 117.3, 106.1 (q, $J = 3.9$ Hz), 105.0, 102.0 (q, $J = 3.7$ Hz), 55.3, 21.3.

Elemental Analysis: C, 65.36; H, 5.23; N, 4.63 (calculated for $\text{C}_{16}\text{H}_{16}\text{F}_3\text{NO}$: C, 65.08; H, 5.46; N, 4.74).

***N*-(3,5-dimethylphenyl)-3-chloro-5-methoxyphenylamine.** The product was obtained from 5-trifluoromethyl-3-methoxyphenylboronic acid (283 mg, 1.52 mmol) and 3,5-dimethylaniline (125 μ l, 1.00 mmol) using 30 mol% copper(II)acetate (53.4 mg, 0.294 mmol). Yield 207 mg, 0.791 mmol, 79%.

^1H NMR (500 MHz, CDCl_3): 6.79 (2 H, s), 6.75 (1 H, s), 6.67 (1 H, t, $J = 2.0$ Hz), 6.53 (1 H, t, $J = 2.3$ Hz), 6.52 (1 H, t, $J = 1.9$ Hz), 5.71 (1 H, br), 3.82 (3 H, s), 2.37 (6 H, s).

^{13}C NMR (125.7 MHz, CDCl_3): 161.0, 145.8, 141.5, 139.0, 135.3, 124.1, 117.2, 103.4, 105.8, 100.8, 55.3, 21.3.

Elemental Analysis: C, 69.08; H, 6.41; N, 5.14 (calculated for $\text{C}_{15}\text{H}_{16}\text{ClNO}$: C, 68.83; H, 6.16; N, 5.35).

Copper-mediated coupling of aryl boronic acids and phenols to synthesize diaryl ethers. General procedure:

In a 100 mL roundbottom flask equipped with a stir bar, copper(II) acetate (1.00 mmol), aryl boronic acid (2.00 mmol), phenol (1.00 mmol), 4 Å powdered molecular sieves (1.00 g), and dry methylene chloride (10.0 mL) were combined. The reaction mixture was then stirred at room temperature for 16 h under ambient atmosphere. The reaction mixture was then filtered to remove the molecular sieves and copper salts. The resulting

solution was reduced under vacuum and purified using column chromatography on silica gel with hexanes as the elutant. Reported yields are based on amount of phenol used.

(3-chloro-5-methylphenyl)-4-tert-butylphenyl ether The product was obtained by combining 3-chloro-5-methylphenylboronic acid (0.348 g, 2.04 mmol), *p*-tert-butylphenol (0.154 g, 1.02 mmol), Cu(OAc)₂ (0.188 g, 1.04 mmol), triethylamine (0.70 mL, 5.0 mmol), and 4 Å powdered molecular sieves (0.990 g) in 10.0 mL of methylene chloride. 94% isolated yield.

¹H NMR (500 MHz, CDCl₃): 7.62 (2 H, m), 6.96 (2 H, m), 6.95 (1 H, m), 6.97 (1 H, m), 6.72 (1 H, m), 2.31 (3 H, s), 1.35 (9 H, s).

¹³C NMR (500 MHz, CDCl₃): 158.4, 153.9, 146.7, 134.5, 126.7, 123.6, 118.9, 117.3, 115.6, 34.3, 31.5, 21.5.

(3-trifluoromethyl-5-methoxyphenyl)-4-tert-butylphenyl ether The product was obtained by combining 3-trifluoromethyl-5-methoxyphenylboronic acid (0.418 g, 1.90 mmol), *p*-tert-butylphenol (0.161 g, 1.07 mmol), Cu(OAc)₂ (0.196 g, 1.08 mmol), triethylamine (0.70 mL, 5.0 mmol), and 4 Å powdered molecular sieves (1.00 g) in 10.0 mL of methylene chloride. 70% isolated yield.

¹H NMR (500 MHz, CD₂Cl₂): 7.42 (2 H, d, *J* = 5.5 Hz), 6.99 (2 H, d, *J* = 5.5 Hz), 6.88 (1 H, s), 6.72 (1 H, s), 6.71 (1 H, s), 3.81 (3 H, s), 1.35 (9 H, s).

¹³C NMR (500 MHz, CD₂Cl₂): 161.2, 159.5, 153.4, 147.4, 126.8, 119.0, 107.2, 107.0, 106.9, 105.1, 105.0, 55.63, 34.2, 31.1.

(3,5-dimethylphenyl)-4-tert-butylphenyl ether The product was obtained by combining 3,5-dimethylphenylboronic acid (0.244 g, 1.62 mmol), *p*-tert-butylphenol (0.185 g, 1.23 mmol), Cu(OAc)₂ (0.181 g, 0.998 mmol), triethylamine (0.70 mL, 5.0 mmol), and 4 Å powdered molecular sieves (1.05 g) in 10.0 mL of methylene chloride. 61% isolated yield.

¹H NMR (500 MHz, CDCl₃): 7.37 (2 H, d, *J* = 2.0 Hz), 6.94 (2 H, d, *J* = 2.7 Hz), 6.76 (1 H, s), 6.64 (s, 2 H), 2.29 (s, 6 H), 1.34 (s, 9 H).

¹³C NMR (500 MHz, CDCl₃): 157.5, 154.9, 145.9, 139.6, 126.5, 124.7, 118.3, 116.3, 34.2, 31.3, 21.0

(3,5-dimethylphenyl)-2-chlorophenyl ether The product was obtained by combining 3,5-dimethylphenylboronic acid (0.294 g, 1.96 mmol), *o*-chlorophenol (0.247 g, 1.92

mmol), Cu(OAc)₂ (0.182 g, 0.989 mmol), triethylamine (0.70 mL, 5.0 mmol), and 4 Å powdered molecular sieves (1.25 g) in 10.0 mL of methylene chloride. 39% isolated yield.

¹H NMR (500 MHz, CD₂Cl₂): 7.23 (1 H, d, *J* = 7 Hz), 7.12 (2 H, m), 7.11 (1 H, m), 7.01 (1 H, s), 6.81 (2 H, s), 2.32 (6 H, s).

¹³C NMR (500 MHz, CD₂Cl₂): 156.9, 152.6, 139.8, 130.7, 128.0, 125.6, 125.1, 124.5, 120.8, 115.5, 21.1.

(3,5-dimethylphenyl)-3-cyanophenyl ether The product was obtained by combining 3,5-dimethylphenylboronic acid (0.206 g, 1.37 mmol), 3-cyanophenol (0.122 g, 1.03 mmol), Cu(OAc)₂ (0.188 g, 1.03 mmol), triethylamine (0.70 mL, 5.0 mmol), and 4 Å powdered molecular sieves (1.01 g) in 10.0 mL of methylene chloride. 50% isolated yield.

¹H NMR (500 MHz, CDCl₃): 7.41 (1 H, m), 7.35 (1 H, m), 7.23 (1 H, m), 7.18 (1 H, m), 6.84 (1 H, s), 6.65 (2H, s), 2.32 (6H, s).

¹³C NMR (500 MHz, CDCl₃): 158.6, 155.6, 140.4, 130.8, 126.7, 126.4, 122.9, 121.1, 118.7, 117.7, 113.6, 21.5.

(3,5-dimethylphenyl)-4-chlorophenyl ether The product was obtained by combining 3,5-dimethylphenylboronic acid (0.207 g, 1.37 mmol), *p*-chlorophenol (0.138 g, 1.08 mmol), Cu(OAc)₂ (0.182 g, 0.989 mmol), triethylamine (0.70 mL, 5.0 mmol), and 4 Å powdered molecular sieves (1.05 g) in 10.0 mL of methylene chloride. 84% isolated yield.

¹H NMR (500 MHz, CDCl₃): 7.28 (2 H, d, *J* = 5.0 Hz), 6.94 (2 H, d, *J* = 5.5 Hz), 6.76 (1 H, s), 6.63 (s, 2 H), 2.29 (s, 6 H).

¹³C NMR (500 MHz, CDCl₃): 157.1, 156.4, 140.0, 129.9, 128.9, 125.6, 120.3, 116.9, 21.5.

References

- (1) Marigo, M.; Marsich, N.; Farnetti, E., *J. Mol. Catal. A*. **2002**, 187, 169.
- (2) Murphy, J. M.; Tzschucke, C. C.; Hartwig, J. F., *Org. Lett.* **2006**, in press.
- (3) Quach, T. D.; Batey, R. A., *Org. Lett.* **2003**, 5, 4397-4400.
- (4) Nordlander, J. E.; Catalane, D. B.; Kotian, K. D.; Stevens, R. M.; Haky, J. E., *J. Org. Chem.* **1981**, 46, 778-782.
- (5) Roy, A. H.; Hartwig, J. F., *J. Am. Chem. Soc.* **2003**, 125, 8704-8705.
- (6) Razzuk, A.; Biehl, E. R., *J. Org. Chem.* **1987**, 52, 2619-2622.
- (7) Hall, R. J.; Jackson, A. H.; Oliveira-Campos, A. M. F.; Shannon, P. V. R., *J. Chem. Res., Synop.* **1990**, 314-315.
- (8) Wolfe, J. P.; Wagaw, S.; Buchwald, S. L., *J. Am. Chem. Soc.* **1996**, 118, 7215-7216.
- (9) Kwong, F. Y.; Klapars, A.; Buchwald, S. L., *Org. Lett.* **2002**, 4, 581-584.
- (10) Antilla, J. C.; Buchwald, S. L., *Org. Lett.* **2001**, 3, 2077-2079.

- (11) Gajare, A. S.; Toyota, K.; Yoshifuji, M.; Ozawa, F., *J. Org. Chem.* **2004**, 69, 6504-6506.
- (12) Fritsch, A. J.; Moore, C. E.; Meyer, T. S., *Nature* **1968**, 217, 350.
- (13) Marcoux, J.-F.; Wagaw, S.; Buchwald, S. L., *J. Org. Chem.* **1997**, 62, 1568-1569.

Table 1, Entry 1

Table 1, Entry 2

Table 1, Entry 3

Table 1, Entry 4

Table 1, Entry 5

Table 1, Entry 6

Table 1, Entry 7

Table 1, Entry 8

Table 1, Entry 9

Table 1, Entry 10

Table 1, Entry 11

Table 1, Entry 12

Table 1, Entry 13

Table 1, Entry 14

Table 2, Entry 1

Table 2, Entry 2

Table 2, Entry 3

Table 2, Entry 4

Table 2, Entry 5

Table 2, Entry 7

Table 2, Entry 8

Table 2, Entry 9

Table 2, Entry 10

Table 3, Entry 1

Table 3, Entry 2

Table 3, Entry 3

Table 3, Entry 4

Table 3, Entry 6