Aminoalcohols as Ligands for Nickel-Catalyzed Suzuki Reactions of Unactivated Alkyl Halides, Including Secondary Alkyl Chlorides, with Arylboronic Acids

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Supporting Information

I. General

The following chemicals were purchased and used as received: NiI_2 (Strem, Alfa-Aesar), $\text{NiCl}_2\cdot\text{glyme}$ (Strem), ($\pm$)-*trans*-2-aminocyclohexanol hydrochloride (Alfa-Aesar), (*S*)-(+)-prolinol (Lancaster, Aldrich), NaHMDS (Strem, Aldrich, Alfa-Aesar; stored under argon in a desiccator, with CaCl_2 as a desiccant), KHMDS (Aldrich; stored under argon in a desiccator, with CaCl_2 as a desiccant), 2-propanol (Fluka; stored over molecular sieves), cyclopentyl bromide (Aldrich), cyclohexyl bromide (Aldrich), 4-bromopiperidine hydrobromide (Aldrich), cycloheptyl bromide (Aldrich, Alfa-Aesar), cyclooctyl bromide (Aldrich), 1-bromobenzocyclobutane (Aldrich), *exo*-2-bromonorbornane (Aldrich), propylene oxide (Aldrich), benzyl alcohol (Aldrich), 3-phenylpropanal (Acros), allyl alcohol (Aldrich), 2,3-dihydrofuran (Aldrich), cyclohexyl iodide (Lancaster), 1-bromo-6-chlorohexane (Alfa-Aesar), furfuryl bromide (TCI), cyclohexyl chloride (Alfa-Aesar, Aldrich), 4-chlorotetrahydropyran (Aldrich), 2-chlorohexane (TCI), 2-chlorocyclohexanol (TCI), 1-chlorodecane (Alfa-Aesar), 6-chloro-1-hexanol (Alfa-Aesar), phenylboronic acid (Frontier, Strem). All other boronic acids were obtained from Frontier Scientific.

II. Preparation of Alkyl Halides

4-Bromo-1-[(4-methylphenyl)sulfonyl]-piperidine [347885-68-1]. *p*-TsCl (580 mg, 3.05 mmol) was added to a stirred solution of 4-bromopiperidine hydrobromide (575 mg, 2.35 mmol) in pyridine (5 mL). The resulting orange mixture was stirred for 20 h, and then it was poured into a separation funnel that contained CH₂Cl₂ (50 mL) and HCl (1N; 50 mL). The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3x30 mL). The combined organic layers were sequentially washed with HCl (1N; 75 mL) and brine (100 mL), then dried over anhydrous Na₂SO₄, filtered, and concentrated under vacuum. The residue was purified by column chromatography (hexanes/EtOAc gradient from 10:1 to 3:1), furnishing the title compound as a white solid (710 mg, 95%).

***cis*-1-Bromo-4-chlorocyclohexane [16661-98-6].** This compound was prepared according to a literature procedure.¹ Analysis by ¹H NMR spectroscopy showed a diastereomeric purity of >95:5. The relative stereochemistry was assigned on the basis of the melting point of the compound (m.p.<25 °C) (*trans* isomer, m.p. 101 °C; *cis* isomer, m.p.<25 °C).²

***endo*-2-Bromonorbornane [13237-81-1].** This compound was prepared according to a literature procedure (endo:exo = 96:4).³

3-Benzyloxy-2-propanol [13807-91-5]. A mixture of sodium hydroxide (100 mg, 1.00 mmol) and benzyl alcohol (19.0 g, 176 mmol) was heated in an oil bath at 125 °C. Propylene oxide (3.0 mL, 44 mmol) was added drop-wise over 2 hours. After 4 hours at 125 °C, the reaction mixture was allowed to cool to room temperature. The crude reaction mixture was distilled under reduced pressure (75 °C, 0.25 Torr), which furnished the product as a colorless oil (3.5 g, 49%).

3-Benzyloxy-2-bromopropane. Bromine (1.13 mL, 22 mmol) was added to a suspension of PPh₃ (5.26 g, 22 mmol) and imidazole (1.5 g, 22 mmol) in anhydrous CH₂Cl₂ (100 mL) at 0 °C. 3-Benzyloxy-2-propanol (3.00 g, 18.3 mmol) was then added slowly by syringe. The resulting mixture was allowed to warm to room temperature. After 14 hours, the reaction mixture was concentrated under vacuum to remove the CH₂Cl₂, diluted with hexanes/EtOAc (4:1; 650 mL), filtered through a short pad of silica gel, and concentrated (3.4 g, 82%).

¹H NMR (400 MHz, CDCl₃) δ 7.44-7.32 (5H, m), 4.62 (2H, s), 4.23 (1H, sextet, *J* = 6.6 Hz), 3.72 (1H, dd, *J* = 10.2, 6.1 Hz), 3.62 (1H, dd, *J* = 10.2, 6.6 Hz), 1.64 (3H, t, *J* = 6.6 Hz).

¹³C NMR (100 MHz, CDCl₃) δ 137.7, 128.3, 127.7, 127.6, 75.5, 73.0, 46.7, 22.6.

IR (neat) 3030, 2861, 1496, 1453, 1363, 1203 cm⁻¹.

MS (EI) calcd for C₁₀H₁₃BrO: 228, found: 228.

4-Phenyl-2-butanol [2344-70-9]. MeMgBr (3.0 N in ether; 40 mL, 120 mmol) was carefully added to a $-50\text{ }^{\circ}\text{C}$ solution of 3-phenylpropanal (13.4 g, 100 mmol) in THF (100 mL). The mixture was allowed to warm to room temperature overnight, and then it was carefully quenched with a saturated solution of NH_4Cl (200 mL). The aqueous layer was separated and extracted with ether (2x100 mL). The combined organic layers were washed with a saturated solution of NaCl (2x100 mL) and dried over anhydrous Na_2SO_4 . Evaporation of the volatiles afforded 14.5 g (96%) of the title compound, which was used without purification in the next step.

4-Phenyl-2-bromobutane [21953-83-3]. 4-Phenyl-2-butanol (7.5 g, 50 mmol) was brominated with $\text{Br}_2/\text{PPh}_3/\text{imidazole}$ according to the general protocol disclosed above for 3-benzyloxy-2-bromopropane. The product was purified by column chromatography (eluant: hexanes), which furnished a colorless liquid that turned pale yellow upon standing (8.2 g, 77%).

***trans*-1-Allyloxy-2-bromocyclopentane [174619-43-3].** This compound was prepared according to a literature procedure.⁴

***trans*-2-Allyloxy-3-bromotetrahydrofuran [143037-46-1].** This compound was prepared according to a literature procedure.⁴

1-(6-Iodohexyl)-1*H*-pyrrole [838821-68-4]. This compound was prepared according to a literature procedure.⁴

***trans*-[(2-Chlorocyclohexyl)oxy](1,1-dimethylethyl)dimethylsilane [148494-11-5].** TBSCl (1.83 g, 12.2 mmol) was added to a mixture that contained *trans*-2-chlorocyclohexanol (1.26 g, 9.4 mmol), imidazole (0.96 g, 14 mmol), and CH_2Cl_2 (50 mL), resulting in the immediate formation of a white solid. After 6 hours, the reaction mixture was filtered through Celite and washed with CH_2Cl_2 (2x25 mL). The filtrate was concentrated under vacuum, and the residue was purified by flash chromatography (eluant: hexanes), which furnished the product as a colorless oil (2.1 g, 89%).

^1H NMR (400 MHz, CDCl_3) δ 3.76 (1H, ddd, $J = 9.5, 7.6, 4.1$ Hz), 3.60 (1H, ddd, $J = 11.8, 7.6, 4.1$ Hz), 2.22 (1H, s), 2.00-1.95 (1H, m), 1.74-1.58 (3H, m), 1.43-1.27 (m, 3H), 0.92 (9H, s), 0.12 (3H, s), 0.09 (3H, s).

^{13}C NMR (100 MHz, CDCl_3) δ 74.6, 64.6, 33.8, 25.7, 24.1, 22.9, 18.0, -2.9 , -5.5 , -4.6 .

IR (neat) 2937, 2859, 1472, 1450, 1256 cm^{-1} .

MS (EI) calcd for $\text{C}_{12}\text{H}_{25}\text{ClOSi}$: 248, found: 191 ($\text{M}-t\text{-Bu}$).

1-*tert*-Butyldimethylsilyloxy-6-chlorohexane [59431-24-2]. TBSCl (1.83 g, 12.2 mmol) was added to a mixture that contained 6-chloro-1-hexanol (1.28 g, 9.4 mmol), imidazole (0.96 g, 14 mmol), and CH₂Cl₂ (50 mL), resulting in the immediate formation of a white solid. After 14 hours, the mixture was filtered through a short pad of silica gel and washed with CH₂Cl₂. The filtrate was sequentially washed with HCl (1N; 100 mL), saturated NaHCO₃ (100 mL), and brine (100 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under vacuum, yielding a colorless oil (2.2 g, 93%).

III. Suzuki Cross-Coupling Reactions

Cross-coupling of alkyl bromides: General protocol (Table 1, Table 2, and eq 4). In the air, NiI_2 (18.8 mg, 0.060 mmol, 6.0 mol%), *trans*-2-aminocyclohexanol hydrochloride (9.3 mg, 0.060 mmol, 6.0 mol%), the boronic acid (1.2 or 2.0 equiv), and NaHMDS (366 mg, 2.0 mmol, 2.0 equiv) were placed in a 4-mL vial equipped with a stir bar. The vial was capped and purged with argon for 5 minutes. 2-PrOH (2 mL) was added by syringe, and the resulting mixture was stirred for 5 minutes at room temperature. The alkyl halide (1.00 mmol) was then added by syringe and the vial was heated at 60 °C in an oil bath. After 6 hours, the reaction mixture was allowed to cool to room temperature, and then it was filtered through a short pad of silica gel (washing with 200 mL of 1:1 hexanes:ether). The filtrate was concentrated under vacuum, and then the residue was purified by column chromatography.

1-Cyclopentyl-4-methoxybenzene (Table 1, entry 1) [1507-97-7].⁵ Equivalents of $\text{ArB}(\text{OH})_2$: 2.0. Solvent used for chromatography: 10:1 hexanes:EtOAc. Colorless liquid. First run: 125 mg (71%). Second run: 128 mg (73%).

^1H NMR (400 MHz, CDCl_3) δ 7.24 (2H, d, J = 8.8 Hz), 6.91 (2H, d, J = 8.8 Hz), 3.85 (3H, s), 3.01 (1H, tt, J = 9.8, 7.5 Hz), 2.15-2.08 (2H, m), 1.92-1.37 (6H, m).

1-Cyclohexyl-2-methylbenzene (Table 1, entry 2) [4501-35-3].⁴ Equivalents of $\text{ArB}(\text{OH})_2$: 1.2. Solvent used for chromatography: 100% hexanes. Colorless oil. First run: 120 mg (69%). Second run: 118 mg (68%).

^1H NMR (400 MHz, CDCl_3) δ 7.28-7.09 (4H, m), 2.80-2.70 (1H, m), 2.44 (3H, s), 1.91-1.69 (5H, m), 1.54-1.38 (5H, m).

1-Cyclohexyl-4-(methylthio)benzene (Table 1, entry 3) [56354-58-6]. Equivalents of $\text{ArB}(\text{OH})_2$: 1.2. Solvent used for chromatography: 15:1 hexanes: CH_2Cl_2 . White solid. First run: 144 mg (70%). Second run: 146 mg (71%).

^1H NMR (400 MHz, CDCl_3) δ 7.23 (2H, d, J = 8.3 Hz), 7.18 (2H, d, J = 8.3 Hz), 2.53-2.47 (1H, m), 2.51 (3H, s), 1.90-1.84 (4H, m), 1.81-1.77 (1H, m), 1.49-1.20 (5H, m).

^{13}C NMR (100 MHz, CDCl_3) δ 145.2, 134.9, 127.3, 127.0, 43.9, 34.3, 26.8, 26.0, 16.2.

IR (CH_2Cl_2) 3053, 2927, 2853, 1495, 1265 cm^{-1} .

MS (EI) calcd for $\text{C}_{13}\text{H}_{18}\text{S}$: 206, found: 206.

m.p. (from hexanes/ CH_2Cl_2) 44-45 $^\circ\text{C}$.

4-(4-*tert*-Butylphenyl)-*N*-tosylpiperidine (Table 1, entry 4). Equivalents of $\text{ArB}(\text{OH})_2$: 1.2. The alkyl halide (a solid) was added after the NaHMDS. Solvent used for chromatography: 5:1 hexanes:ether. White solid. First run: 249 mg (67%). Second run: 245 mg (66%).

^1H NMR (400 MHz, CDCl_3) δ 7.70 (2H, d, J = 8.0 Hz), 7.36 (2H, d, J = 8.2 Hz), 7.34 (2H, d, J = 8.2 Hz), 7.10 (2H, d, J = 8.0 Hz), 3.95 (2H, d, J = 11.4 Hz), 2.47 (3H, s), 2.44-2.31 (3H, m), 1.94-1.79 (4H, m), 1.32 (9H, s).

^{13}C NMR (100 MHz, CDCl_3) δ 149.3, 143.4, 141.7, 132.9, 129.5, 127.7, 126.2, 125.3, 46.8, 41.1, 34.3, 32.4, 31.2, 21.4.

IR (CH_2Cl_2) 2946, 2852, 1913, 1596, 1463, 1441, 1349, 1158 cm^{-1} .

MS (ESI) calcd for $\text{C}_{22}\text{H}_{29}\text{NO}_2\text{S}$: 371, found: 394 ($\text{M}+\text{Na}$).

m.p. (from hexanes/ether) 150-151 $^\circ\text{C}$.

(4-Cyclohexyl)benzene (Table 1, entry 5) [394704-02-0].¹ Equivalents of $\text{ArB}(\text{OH})_2$: 1.2. Run on a 0.50-mmol scale. Solvent used for chromatography: 100% hexanes. The *cis* and *trans* diastereomers were separated by column chromatography.

Cis diastereoisomer: Colorless oil. First run: 25.3 mg (26%). Second run: 23.3 mg (24%).

^1H NMR (400 MHz, CDCl_3) δ 7.37-7.20 (5H, m), 4.58 (1H, t, J = 3.0 Hz), 2.57 (1H, tt, J = 11.5, 3.5 Hz), 2.19-1.88 (6H, m), 1.79-1.72 (2H, m).

Trans diastereoisomer: Colorless oil. First run: 43.8 mg (45%). Second run: 44.2 mg (45%).

^1H NMR (400 MHz, CDCl_3) δ 7.33-7.18 (5H, m), 3.96 (1H, tt, J = 11.7, 4.2 Hz), 2.58 (1H, tt, J = 12.1, 3.4 Hz), 2.37-2.33 (2H, m), 2.14-1.93 (2H, m), 1.83 (2H, qd, J = 12.7, 3.0 Hz), 1.65-1.55 (2H, m).

(4-Methylphenyl)cycloheptane (Table 1, entry 6) [92298-88-9].⁶ Equivalents of ArB(OH)_2 : 1.2. Solvent for chromatography: 100% hexanes. Colorless oil. First run: 155 mg (83%). Second run: 160 mg (85%).

^1H NMR (400 MHz, CDCl_3) δ 7.20 (4H, s), 2.75 (1H, tt, $J = 10.4, 3.5$ Hz), 2.40 (3H, s), 2.01 (2H, s), 1.84-1.64 (m, 10H).

Phenylcyclooctane (Table 1, entry 7) [16538-85-5].¹ Equivalents of ArB(OH)_2 : 1.2. Reaction time: 12 h. Solvent used for chromatography: 100% hexanes. Colorless oil. First run: 149 mg (79%). Second run: 144 mg (76%).

^1H NMR (400 MHz, CDCl_3) δ 7.36-7.19 (5H, m), 2.97-2.78 (1H, m), 1.93-1.61 (14H, m).

7-(2-Methylphenyl)bicyclo[4.2.0]octa-1,3,5-triene (Table 1, entry 8) [733810-61-2].⁴ Equivalents of ArB(OH)_2 : 1.2. Solvent used for chromatography: 100% hexanes. Colorless oil. First run: 181 mg (93%). Second run: 177 mg (91%).

^1H NMR (400 MHz, CDCl_3) δ 7.42-7.30 (4H, m), 7.29-7.17 (4H, m), 4.88 (1H, dd, $J = 5.6, 3.1$ Hz), 3.83 (1H, dd, $J = 13.6, 5.6$ Hz), 3.00 (1H, dd, $J = 13.6, 3.1$ Hz), 2.4 (3H, s).

5-Bicyclo[4.2.0]octa-1,3,5-trien-7-yl-1-methyl-1H-indole (Table 1, entry 9). Equivalents of ArB(OH)_2 : 2.0. Solvent used for chromatography: 15:1 hexanes: CH_2Cl_2 . Colorless oil (turns red upon standing). First run: 210 mg (90%). Second run: 218 mg (94%).

^1H NMR (400 MHz, CDCl_3) δ 7.68-7.66 (1H, m), 7.44-7.26 (6H, m), 7.12 (1H, d, $J = 3.0$ Hz), 6.55 (1H, d, $J = 3.0$ Hz), 4.94 (1H, dd, $J = 5.5, 2.7$ Hz), 3.89 (1H, dd, $J = 13.8, 5.5$ Hz), 3.85 (3H, s), 3.26 (1H, dd, $J = 13.8, 2.7$ Hz).

^{13}C NMR (100 MHz, CDCl_3) δ 148.7, 144.3, 135.6, 133.7, 129.0, 128.4, 127.3, 126.9, 123.2, 122.7, 120.9, 118.6, 109.1, 100.6, 47.7, 40.6, 32.7.

IR (neat) 3065, 2920, 1720, 1684, 1512, 1457, 1244, 1080 cm^{-1} .

MS (ESI) calcd for $\text{C}_{17}\text{H}_{15}\text{N}$: 233, found: 234.

***exo*-2-Phenylbicyclo[2.2.1]heptane (Table 1, entry 10) [52752-81-5].⁴** Equivalents of $\text{ArB}(\text{OH})_2$: 1.2. Solvent used for chromatography: 100% hexanes. Colorless oil. First run: 146 mg (85%). Second run: 143 mg (83%).

***exo*-2-Phenylbicyclo[2.2.1]heptane (Table 1, entry 11) [52752-81-5].⁴** Equivalents of $\text{ArB}(\text{OH})_2$: 1.2. Solvent used for chromatography: 100% hexanes. Colorless oil. First run: 156 mg (91%). Second run: 158 mg (92%).

^1H NMR (400 MHz, CDCl_3) δ 7.35-7.17 (5H, m), 2.79 (1H, dd, $J = 8.5, 6.0$ Hz), 2.44-2.37 (2H, m), 1.86-1.55 (6H, m), 1.44-1.20 (2H, m).

exo-2-(3-Methoxyphenyl)bicyclo[2.2.1]heptane (Table 1, entry 12) [62226-58-8].⁷ Equivalents of ArB(OH)₂: 2.0. Solvent used for chromatography: 10:1 hexanes:CH₂Cl₂. Colorless liquid. First run: 135 mg (67%). Second run: 139 mg (69%).

¹H NMR (400 MHz, CDCl₃) δ 7.26 (1H, t, *J* = 7.9 Hz), 6.88 (1H, dd, *J* = 7.7, 0.7 Hz), 6.84 (1H, t, *J* = 1.8 Hz), 6.76 (1H, dd, *J* = 7.9, 1.8 Hz), 3.85 (3H, s), 2.78 (1H, dd, *J* = 9.0, 5.8 Hz), 2.43-2.38 (2H, m), 1.82 (1H, ddd, *J* = 11.7, 9.0, 2.2 Hz), 1.74-1.58 (4H, m), 1.46-1.23 (3H, m).

1-(2-Benzyloxy-1-methylethyl)-3-chlorobenzene (Table 1, entry 13). Equivalents of ArB(OH)₂: 1.2. Solvent used for chromatography: 3:1 hexanes:CH₂Cl₂. Colorless oil. First run: 220 mg (85%). Second run: 221 mg (85%).

¹H NMR (400 MHz, CDCl₃) δ 7.42-7.24 (8H, m), 7.17 (1H, dt, *J* = 6.9, 1.7 Hz), 4.57 (2H, s), 3.63 (1H, dd, *J* = 9.2, 7.0 Hz), 3.57 (1H, dd, *J* = 9.2, 7.0 Hz), 3.11 (1H, sextet, *J* = 7.0 Hz), 1.36 (3H, d, *J* = 7.0 Hz).

¹³C NMR (100 MHz, CDCl₃) δ 146.5, 138.2, 134.0, 129.5, 128.3 (2), 127.4 (2), 126.4, 125.6, 75.4, 72.9, 39.8, 18.2.

IR (neat) 3064, 2929, 2855, 1597, 1571, 1477, 1453, 1360 cm⁻¹.

MS (EI) calcd for C₁₆H₁₇ClO: 260, found: 260.

5-(1-Methyl-3-phenylpropyl)-benzo[1,3]dioxolane (Table 1, entry 14). Equivalents of ArB(OH)₂: 2.0. Solvent used for chromatography: 10:1 hexanes:CH₂Cl₂. Colorless oil. First run: 185 mg (73%). Second run: 188 mg (73%).

¹H NMR (400 MHz, CDCl₃) δ 7.33-7.28 (2H, m), 7.24-7.16 (3H, m), 6.80 (1H, d, *J* = 7.9 Hz), 6.78 (1H, s), 6.76 (1H, d, *J* = 1.7 Hz), 5.90 (2H, s), 2.70 (1H, sextet, *J* = 7.0 Hz), 2.57-2.53 (2H, m), 1.93-1.87 (2H, m), 1.27 (3H, d, *J* = 7.0 Hz).

¹³C NMR (100 MHz, CDCl₃) δ 147.5, 145.3, 142.4, 141.2, 128.3, 128.2, 125.6, 119.9, 108.0, 107.1, 100.6, 40.1, 39.2, 33.8, 22.7.

IR (neat) 3026, 2924, 1603, 1439, 1374, 1242, 1040 cm⁻¹.

MS (EI) calcd for C₁₇H₁₈O₂: 254, found: 254.

Procedure for 10-mmol Suzuki reactions (footnote 7). In the air, NiI₂ (188 mg, 0.60 mmol, 6.0 mol%), *trans*-2-aminocyclohexanol hydrochloride (93 mg, 0.60 mmol, 6.0 mol%), *p*-tolylboronic acid (1.63 g, 12.0 mmol, 1.2 equiv), and NaHMDS (3.66 g, 20.0 mmol, 2.0 equiv) were placed in a 50-mL round-bottomed flask equipped with a stir bar. The flask was capped with a septum and purged with argon for 10 minutes. The flask was then cooled to 0 °C, and 2-PrOH (20 mL) was added. The resulting green mixture was taken out of the cold bath and stirred for 5 minutes at room temperature. Cycloheptyl bromide (1.77 g, 10.0 mmol, 1.0 equiv) was then added by syringe, and the reaction mixture was heated at 60 °C (oil bath) for 6 hours. The resulting white suspension was allowed to cool to room temperature, and then it was filtered through a short pad of silica gel (washing with 500 mL of 1:1 hexanes:ether). The filtrate was concentrated under vacuum, and the product was isolated by column chromatography (100% hexanes) as a colorless oil. First run: 1.61 g (86%). Second run: 1.58 g (84%).

Procedure for microwave experiments (footnote 7). In the air, NiI₂ (18.8 mg, 0.060 mmol, 6.0 mol%), *trans*-2-aminocyclohexanol hydrochloride (9.3 mg, 0.060 mmol, 6.0 mol%), PhB(OH)₂ (146 mg, 1.2 mmol, 1.2 equiv), and NaHMDS (366 mg, 2.0 mmol, 2.0 equiv) were placed in a microwave vial. The resulting green mixture was magnetically stirred for 5 minutes. Cyclohexyl bromide was then added (114 µL, 1.0 mmol, 1.0 equiv), and the vessel was capped and introduced into a CEM Discover microwave apparatus. The following parameters were set: temperature: 80 °C; power: 250 W; reaction time: 5 minutes; hold time: 5 minutes; maximum pressure: 150 psia; stirring and cooling: both on.

The resulting black reaction mixture was diluted with EtOH (2 mL), and an internal standard was added (*n*-tetradecane; 65 µL, 0.25 mmol). An aliquot was filtered through a short pad of silica gel (eluant: ether) and analyzed by GC. First run: 56%. Second run: 57%.

3-Benzylhexahydrocyclopenta[b]furan (eq 4) [838821-72-0]. Equivalents of ArB(OH)₂: 1.2. GC analysis of the unpurified reaction mixture revealed a 68:32 ratio of diastereomers. Solvent used for chromatography: hexanes:ether gradient from 20:1 to 3:1. Pale-yellow oil. First run: 139 mg (69%). Second run: 141 mg (70%).

Isomerically pure compounds could be obtained via preparative HPLC. The structural assignments were made as previously described.⁴

(3*R, 3*aS**, 6*aR**)-3-Benzylhexahydrocyclopenta[*b*]furan (major diastereomer) [838821-71-9].**⁴

¹H NMR (400 MHz, CDCl₃) δ 7.39-7.19 (5H, m), 4.55 (1H, td, *J* = 5.9, 2.0 Hz), 3.84 (1H, dd, *J* = 8.2, 6.9 Hz), 3.49 (1H, dd, *J* = 9.5, 8.2 Hz), 2.80-2.75 (1H, m), 2.69-2.65 (2H, m), 2.57-2.52 (1H, m), 1.86-1.51 (6H, m).

(3*R, 3*aR**, 6*aR**)-3-Benzylhexahydrocyclopenta[*b*]furan (minor diastereomer) [838821-73-1].**⁴

¹H NMR (400 MHz, CDCl₃) δ 7.39-7.19 (5H, m), 4.53-4.49 (1H, m), 3.88 (1H, dd, *J* = 8.3, 6.2 Hz), 3.36 (1H, t, *J* = 8.3 Hz), 2.80-2.72 (1H, m), 2.71-2.63 (1H, m), 2.37-2.33 (1H, m), 2.11-2.05 (1H, m), 1.84-1.36 (6H, m).

(3*R, 3*aS**, 6*aR**)-Benzylhexahydrofuro[2,3-*b*]furan (eq 4) [838821-72-0].**⁴ Equivalents of ArB(OH)₂: 1.2. GC analysis of the unpurified reaction mixture revealed a 96:4 ratio of diastereomers. Solvent used for chromatography: 3:1 hexanes:EtOAc. Pale-yellow oil. First run: 176 mg (86%). Second run: 180 mg (88%).

¹H NMR (400 MHz, CDCl₃) δ 7.33-7.30 (2H, m), 7.25-7.18 (3H, m), 5.74 (1H, d, *J* = 4.9 Hz), 4.02-3.95 (1H, m), 3.93-3.85 (2H, m), 3.58 (1H, dd, *J* = 10.6, 8.5 Hz), 2.82-2.63 (4H, m), 2.06-1.97 (1H, m), 1.92-1.83 (1H, m).

1-Cyclohexyl-4-methoxybenzene (Table 2, entry 1) [613-36-5].⁸ Equivalents of ArB(OH)₂: 2.0. Solvent used for chromatography: 20:1 hexanes:EtOAc. Pale-yellow solid. First run: 145 mg (76%). Second run: 150 mg (78%).

¹H NMR (400 MHz, CDCl₃) δ 7.21 (2H, d, *J* = 8.7 Hz), 6.92 (2H, d, *J* = 8.7 Hz), 3.86 (3H, s), 2.57-2.50 (1H, m), 2.00-1.88 (4H, m), 1.85-1.80 (1H, m), 1.53-1.41 (4H, m), 1.39-1.18 (1H, m).

m.p. (from hexanes/EtOAc) 57-59 °C (literature: 56-57 °C).⁹

1-(6-Phenylhexyl)-1H-pyrrole (Table 2, entry 2) [838821-69-5].⁴ Equivalents of ArB(OH)₂: 1.2. Solvent used for chromatography: 3:1 hexanes:CH₂Cl₂. Pale-yellow oil. First run: 218 mg (96%). Second run: 222 mg (98%).

¹H NMR (400 MHz, CDCl₃) δ 7.35-7.21 (5H, m), 6.72-6.68 (2H, m), 6.22-6.17 (2H, m), 3.90 (2H, t, *J* = 7.2 Hz), 2.65 (2H, t, *J* = 7.7 Hz), 1.86-1.76 (2H, m), 1.71-1.61 (2H, m), 1.45-1.33 (4H, m).

2-[(4-Chlorophenyl)methyl]tetrahydrofuran (Table 2, entry 3) [60278-53-7].¹⁰ Equivalents of ArB(OH)₂: 1.2. Solvent used for chromatography: 10:1 hexanes:EtOAc. Colorless oil. First run: 179 mg (91%). Second run: 186 mg (94%).

¹H NMR (400 MHz, CDCl₃) δ 7.27 (2H, d, *J* = 8.3 Hz), 7.18 (2H, d, *J* = 8.3 Hz), 4.05 (1H, pentet, *J* = 6.7 Hz), 3.89 (1H, dt, *J* = 8.1, 6.7 Hz), 3.77-3.72 (1H, m), 2.86 (1H, dd, *J* = 13.7, 6.7 Hz), 2.76 (1H, dd, *J* = 13.7, 5.9 Hz), 1.98-1.82 (3H, m), 1.59-1.50 (1H, m).

2-(6-Chlorohexyl)naphthalene (Table 2, entry 4). Equivalents of ArB(OH)₂: 1.2. Solvent used for chromatography: 100% hexanes. Pale-yellow oil. First run: 207 mg (84%). Second run: 210 mg (85%).

¹H NMR (400 MHz, CDCl₃) δ 7.86-7.80 (3H, m), 7.65 (1H, s), 7.52-7.44 (2H, m), 7.37 (1H, dd, *J* = 8.4, 1.7 Hz), 3.57 (2H, t, *J* = 6.7 Hz), 2.82 (2H, t, *J* = 7.6 Hz), 1.85-1.77 (4H, m), 1.56-1.39 (4H, m).

¹³C NMR (100 MHz, CDCl₃) δ 140.0, 133.5, 131.8, 127.7, 127.6, 127.5, 127.3, 126.2, 125.8, 125.0, 45.0, 35.9, 32.5, 31.1, 28.4, 26.7.

IR (neat) 3052, 2932, 2856, 1600, 1507, 1463 cm⁻¹.

MS (EI) calcd for C₁₆H₁₉Cl: 246, found: 246.

Cross-coupling of alkyl chlorides: General protocol (Table 3). In the air, (*S*)-(+)-prolinol (12 mg, 0.12 mmol, 12 mol%), NiCl₂·glyme (13.3 mg, 0.060 mmol, 6.0 mol%), the boronic acid (1.5 or 2.0 equiv), and KHMDS (400 mg, 2.0 mmol, 2.0 equiv) were placed in a 4-mL vial equipped with a stir bar. The vial was capped and then purged with

argon (three evacuation/refill cycles). 2-PrOH (1.2 mL) was added, and the resulting mixture was stirred for 5 minutes at room temperature. The alkyl halide (1.0 mmol) was then added by syringe, and the vial was heated at 60 °C (oil bath). After 24 hours, the reaction mixture was allowed to cool to room temperature, and then it was filtered through a short pad of silica gel (washing with 200 mL of 1:1 hexanes:ether). The filtrate was concentrated under vacuum, and the residue was purified by column chromatography.

Cyclohexylbenzene (Table 3, entry 1) [827-52-1].¹ Equivalents of ArB(OH)₂: 1.5. Solvent used for chromatography: 100% hexanes. Colorless liquid. First run: 130 mg (80%). Second run: 127 mg (79%).

¹H NMR (400 MHz, CDCl₃) δ 7.38-7.21 (5H, m), 2.60-2.53 (1H, m), 1.96-1.79 (5H, m), 1.56-1.28 (5H, m).

4-Phenyltetrahydropyran (Table 3, entry 2) [20638-52-2].¹¹ Equivalents of ArB(OH)₂: 1.5. Solvent used for chromatography: 10:1 hexanes:EtOAc. White solid. First run: 135 mg (83%). Second run: 137 mg (84%).

¹H NMR (400 MHz, CDCl₃) δ 7.39-7.35 (2H, m), 7.19-7.24 (3H, m), 4.17-4.10 (2H, m), 3.58 (2H, td, *J* = 11.6, 2.7 Hz), 2.80 (1H, tt, *J* = 11.6, 4.2 Hz), 1.93-1.79 (4H, m).

m.p. (from hexanes/EtOAc) 49-50 °C (literature: 48-49 °C).¹¹

2-(4-Methylphenyl)hexane (Table 3, entry 3) [51770-85-5]. Equivalents of ArB(OH)₂: 1.2. Solvent used for chromatography: 100% hexanes. Colorless liquid. First run: 130 mg (74%). Second run: 133 mg (75%).

¹H NMR (400 MHz, CDCl₃) δ 7.22-7.14 (4H, m), 2.77-2.68 (1H, m), 2.41 (3H, s), 1.67-1.61 (2H, m), 1.42-1.21 (4H, m), 1.31 (3H, d, *J* = 6.9 Hz), 0.94 (3H, t, *J* = 7.2 Hz).

¹³C NMR (100 MHz, CDCl₃) δ 144.9, 135.0, 128.9, 126.8, 39.5, 38.2, 30.0, 22.8, 22.4, 21.0, 14.0.

IR (neat) 2958, 2953, 1893, 1514, 1457, 1376 cm⁻¹.

MS (EI) calcd for C₁₃H₂₀: 176, found: 176.

***trans*-tert-Butyl-[2-(4-fluorophenyl)cyclohexyloxy]dimethylsilane (Table 3, entry 4) [838821-67-3].**⁴ Equivalents of ArB(OH)₂: 1.5. GC analysis of the unpurified reaction mixture revealed a 78:22 ratio of diastereomers and a 65% yield (both isomers). Solvent used for chromatography: 10:1 hexane:CH₂Cl₂. Colorless liquid. First run: 140 mg of the trans isomer (46%). Second run: 140 mg of the trans isomer (46%).

¹H NMR (400 MHz, CDCl₃) δ 7.17-7.12 (2H, m), 6.98-6.93 (2H, m), 3.47 (1H, td, *J* = 10.0 Hz, 4.5 Hz), 2.44 (1H, ddd, *J* = 12.5, 10.0, 3.3 Hz), 2.00-1.97 (1H, m), 1.86-1.72 (3H, m), 1.60-1.46 (1H, m), 1.42-1.26 (3H, m), 0.68 (9H, s), -0.17 (3H, s), -0.50 (3H, s).

4-(4-Trifluoromethylphenyl)tetrahydropyran (Table 3, entry 5). Equivalents of ArB(OH)₂: 1.5. Solvent used for chromatography: 20:1 hexane:EtOAc. Colorless liquid. First run: 181 mg (79%). Second run: 182 mg (79%).

¹H NMR (400 MHz, CDCl₃) δ 7.66-7.52 (2H, m), 7.42-7.30 (2H, m), 4.15-4.09 (2H, m), 3.56 (2H, td, *J* = 11.6, 2.8 Hz), 2.85 (1H, tt, *J* = 11.6, 4.4 Hz), 1.90-1.70 (4H, m).

¹³C NMR (100 MHz, CDCl₃) δ 149.7, 128.5 (q, ²*J*_{C-F} = 32), 127.0, 125.4 (q, ³*J*_{C-F} = 3.7 Hz), 124.2 (q, ¹*J*_{C-F} = 272 Hz), 68.1, 41.4, 33.5.

IR (neat) 2939, 2846, 1619, 1443, 1420, 1387, 1238 cm⁻¹.

MS (EI) calcd for C₁₂H₁₃F₃O: 230, found: 230.

1-Decyl-4-methoxybenzene (Table 3, entry 6) [848737-04-2].¹² Equivalents of ArB(OH)₂: 2.0. Solvent used for chromatography: 10:1 hexanes:CH₂Cl₂. Colorless liquid. First run: 205 mg (83%). Second run: 200 mg (80%).

¹H NMR (400 MHz, CDCl₃) δ 7.16 (2H, d, *J* = 8.4 Hz), 6.89 (2H, d, *J* = 8.4 Hz), 3.84 (3H, s), 2.61 (2H, t, *J* = 7.7 Hz), 1.70-1.61 (2H, m), 1.43-1.30 (14H, m), 0.96 (3H, t, *J* = 6.8 Hz).

***tert*-Butyldimethyl-(6-phenylhexyloxy)silane (Table 3, entry 7).** Equivalents of ArB(OH)₂: 1.5. Solvent used for chromatography: hexanes/EtOAc gradient from 100:0 to 20:1. Colorless oil. First run: 250 mg (86%). Second run: 256 mg (87%).

¹H NMR (400 MHz, CDCl₃) δ 7.33-7.19 (5H, m), 3.63 (2H, t, *J* = 6.5 Hz), 2.64 (2H, t, *J* = 7.7 Hz), 1.69-1.62 (2H, m), 1.58-1.51 (2H, m), 1.40-1.37 (4H, m), 0.93 (9H, s), 0.08 (6H, s).

¹³C NMR (100 MHz, CDCl₃) δ 142.8, 128.3, 128.1, 125.5, 63.2, 35.9, 32.7, 31.5, 29.0, 25.9, 25.6, 18.3, -5.2.

IR (neat) 3027, 2930, 1604, 1471, 1387, 1255, 1100 cm⁻¹.

MS (EI) calcd for C₁₈H₃₂OSi: 292, found: 235 (M-*t*-Bu).

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ppm (t1)

150

100

50

ppm (t1)

150

100

50

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33.627
27.162
26.328
19.330

145.844
135.045
130.143
126.051
125.415
125.313

ppm (t1)

150

100

50

50

100

150

ppm (t1)

19.279

39.160

45.310

123.430

125.695

125.800

126.401

126.944

127.560

129.943

135.849

140.335

143.679

146.488

from endo-bromonorbornane

ppm (f1)

150

100

50

(from endo-bromonorbornane)

ppm (t1)

100

50

150
ppm (t1)

100

50

65:35 endo:exo

96:4 endo:exo

ppm (t1)

100

50

96:4 endo:exo

ppm (t1)

50

100

ppm (t1)

100

50

ppm (t1)

50

100

26.708
28.461
31.102
32.502
35.897

45.087

125.003
125.807
126.272
127.307
127.340
127.551
127.625
127.745
131.888
133.558
140.019

150
ppm (f1)

100

50

2.0

3.0

4.0

5.0

6.0

7.0

8.0

ppm (f1)

150
ppm (f1)

100

50