Supporting Information for:

Synthesis and Reactivity of Conformationally Locked α-Aminoorganostannanes and α-Aminoorganolithiums. Discovery of a Surprising Configurational Requirement for Transmetalation

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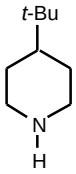
GENERAL EXPERIMENTAL

The ^{1}H nuclear magnetic resonance spectra were recorded at 300 MHz. Chemical shifts are reported in parts per million (δ) relative to tetramethylsilane (δ = 0.0). The ^{1}H NMR spectra are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad), coupling constant in Hz, integration]. The ^{13}C nuclear magnetic spectra were recorded at 75 MHz and are reported with multiplicities (s = singlet, d = doublet, t = triplet, q = quartet, b = broad) determined by ^{13}C DEPT45, ^{13}C DEPT90 and ^{13}C DEPT135 experiments. Chemical shifts are reported in parts per million (δ) relative to tetramethylsilane (δ = 0.0). FAB Mass spectra were recorded on a single stage quadropole instrument; molecular weights of tin-containing compounds are calculated using ^{119}Sn isotope. Compounds for which molecular ion mass is reported exhibited no significant peak at *m/z* greater than the parent. All melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected as are all boiling points. Combustion analyses were performed by Atlantic Microlab, Inc., Norcross, Georgia.

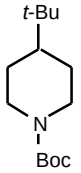
Column chromatography was performed over silica gel 60 (230-400 mesh). Analytical thin layer chromatography was carried out on aluminum plates coated with 0.25 mm of silica gel 60 F-254.

Solvents were dried and purified as follows: tetrahydrofuran and diethyl ether were distilled from sodium-benzophenone ketyl; dichloromethane was distilled from calcium hydride; hexanes and ethyl acetate were distilled. Commercially available reagents were purchased from the Aldrich company and used as received or purified as follows: acetone and cyclohexanone were distilled at atmospheric pressure from 4Å molecular sieves, *N*,*N*′-tetramethylethylenediamine was distilled from calcium hydride at atmospheric pressure. Reactions requiring an inert atmosphere were run under an argon or nitrogen atmosphere in flame dried glassware. *n*-Butyllithium was titrated before use with 1,3-diphenylacetone *p*-tosylhydrazone as the acid and indicator.[12] *sec*-Butyllithium was filtered over a bed of oven dried

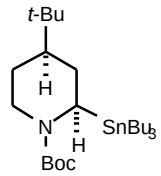
Celite® 545 in a Schlenck tube under nitrogen and titrated prior to use with 1,3-diphenylacetone *p*-tosylhydrazone as the acid and indicator.[12] All chiral compounds are racemic.



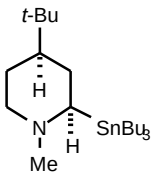
4-*tert*-Butylpiperidine. To a 500 mL Parr bottle was added 10 g (74.7 mmol) of 4-*tert*-butylpyridine, 200 mL of 95 % ethanol, 20 mL of chloroform and 0.5 g (2.2 mmol) of platinum dioxide. The heterogenous mixture was shaken under a 50 psi atmosphere of hydrogen for 2 days. The catalyst was gravity filtered, and the resulting colorless filtrate was concentrated in vacuo. The resulting white solid was dissolved in 100 mL of dichloromethane and washed with 100 mL of 2M aqueous potassium hydroxide. The aqueous layer was reextracted with 100 mL of dichloromethane. The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was distilled under reduced pressure to afford 8.4 g (80.5 %) of the product amine as a colorless liquid: bp 61-64 °C, 5 torr, (lit[13] 83 °C, 31 torr); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.81 (s, 9H), 1.00-1.19 (m, 3H), 1.53 (bs, 1H, NH), 1.62 (d, *J* = 11.3 Hz, 2H), 2.51 (t, *J* = 11.5 Hz, 2H), 3.07 (d, *J* = 12.0 Hz, 2H). The product was spectroscopically comparable by ^{1}H NMR to literature data.[13]



4-*tert*-Butyl-piperidine-1-carboxylic acid *tert*-butyl ester (2). To a solution of 11.8 g (54.0 mmol) of di-*t*-butyl dicarbonate in 50 mL of dichloromethane at 0 °C was added a solution of 6.70 g (47.5 mmol) of 4-*tert*-butylpiperidine in 50 mL of dichloromentane over 45 min via addition funnel. The cold bath was removed allowing the mixture to gradually warm to rt where it was stirred for 12 h. The mixture was concentrated in vacuo, and the residue was purified by column chromatography over 80 g of flash silica [eluted with hexanes/ethyl acetate (10:1)] to afford 13.25 g (97 %) of carbamate **2** as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.84 (s, 9H), 1.07-1.17 (m, 3H), 1.44 (s, 9H,), 1.63 (d, *J* = 9.8 Hz, 2H), 2.58 (bt, *J* = 11.1 Hz, 2H), 4,14 (bd, *J* = 9.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.2 (t), 27.6 (q), 28.8 (q), 32.5 (s), 45.0 (bt), 47.1 (d), 79.4 (s), 155.2 (s). This compound has already been reported but experimental details were not provided.[5]

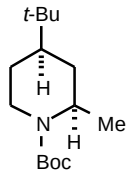


***cis*-4-*tert*-Butyl-2-(tributylstannanyl)-piperidine-1-carboxylic acid *tert*-butyl ester.** To a stirred solution of 8.28 g (34.3 mmol) of carbamate **2** in 80 mL of dry diethyl ether under nitrogen at -78 °C was added 6.0 g (51.5 mmol, 7.8 mL) of *N*,*N'*-tetramethylethylenediamine in one portion via syringe, and 37.2 mL (44.7 mmol) of a 1.2 M solution of *sec*-butyllithium in cyclohexane over 30 min via canula. The mixture turned yellow, then milky during the addition. The mixture was stirred for 5 h at -78 °C, and 17.9 g (55 mmol, 15 mL) of neat tri-*n*-butyltin chloride was added over 5 min via syringe. The cold bath was removed allowing the mixture to warm gradually to rt where it was stirred for 15 h. The mixture was diluted with 100 mL of ethyl acetate and washed with 100 mL of water. The aqueous layer was reextracted with two 100-mL portions of ethyl acetate. The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by column chromatography over 250 g of flash silica [eluted with hexanes] to afford 11.1 g (61 %) of product as a colorless oil: IR (neat) 1670 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.44-1.42 (m, 49 H), 1.51 (bd, *J* = 12.4 Hz, 1 H), 2.25 (bd, *J* = 12.2 Hz, 1H), 2.48 (bt, *J* = 11.3 Hz, 1H), 3.92 (bd, *J* = 12.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.3 (t), 14.2 (q), 27.7 (q), 27.9 (t), 28.0 (t), 28.8 (q), 29.7 (t), 32.0 (t), 32.7 (s), 46.7 (d), 48.0 (t), 50.0 (d), 79.4 (s), 156.4 (s); mass calculated for $C_{26}H_{53}NO_2Sn$ (M^+) *m/z* 530, found *m/z* 530. Anal. Calcd. for $C_{26}H_{53}NO_2Sn$: C 58.87, H 10.07. Found C 58.71, H 9.98.

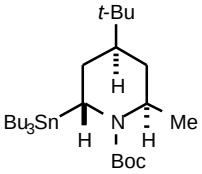


***cis*-4-*tert*-Butyl-1-methyl-2-(tributylstannanyl)-piperidine (3).** To a stirred solution of 4.47 g (8.43 mmol) of the above carbamate in 50 mL of dry THF at 0 °C was added 7.19 g (50.6 mmol, 9.0 mL) of neat diisobutylaluminum hydride over 5 min via syringe. The mixture was heated to reflux for 60 h. The mixture was cooled to -78 °C, and 20 mL of methanol was added to quench the excess hydride. The mixture was treated with 50 mL of aqueous saturated potassium, sodium tartrate. The cold bath was removed allowing the mixture to warm to rt where it was stirred for 12 h. The layers of the resulting biphasic mixture were separated, and the aqueous layer was reextracted with three 50-mL portions of diethyl ether. The combined organic extracts were dried ($MgSO_4$) and concentrated in

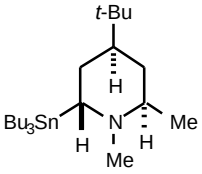
vacuo. The residue was purified by column chromatography over 100 g of flash silica [eluted with hexanes/ethyl acetate (20:1) progressing to hexanes/ethyl acetate (5:1)] to afford 2.81 g (75 %) of amine **3** as a slightly yellow liquid: IR (neat) 1363 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85-0.95 (m, 25 H), 1.22-1.56 (m, 14H), 1.60 (dt, *J* = 12.8, 2.82 Hz, 1H), 1.74 (dd, *J* = 12.9, 2.9 Hz, 1H), 1.80 (td, *J* = 11.6, 1.7 Hz, 1H), 2.05 (dd, *J* = 12.8, 2.2 Hz, 1H), 2.20 (s, 3H), 2.98 (dt, *J* = 11.0, 3.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.66 (t), 14.1 (q), 27.5 (t), 27.7 (q), 27.9 (t), 29.6 (t), 32.6 (t), 32.7 (s), 48.3 (d), 48.7 (q), 59.7 (d), 60.2 (t); mass calculated for $C_{22}H_{47}NSn$ (M^+) *m/z* 444, found *m/z* 444. Anal. Calcd. for $C_{22}H_{47}NSn$: C 59.47, H 10.66, N 3.15. Found C 59.75, H 10.71, N 3.10.



***cis*-4-*tert*-Butyl-2-methylpiperidine-1-carboxylic acid *tert*-butyl ester (4).**[5b] To a stirred solution of 6.0 g (24.9 mmol) of carbamate **2** in 50 mL of dry diethyl ether under nitrogen at –78 °C (acetone/dry ice bath) was added 3.75 g (32.4 mmol, 4.9 mL) of *N,N'*-tetramethylethylenediamine via syringe in one portion, and 27 mL (32.4 mmol) of a 1.2 M solution of *sec*-butyllithium in cyclohexane over 15 min via syringe. The mixture was stirred at –78 °C for 6h, and 4.1 g (32.4 mmol, 3.1 mL) of neat dimethylsulfate was added over 1 min via syringe. The resulting mixture was stirred for 10 min at –78 °C, and the cold bath was removed allowing the mixture to gradually warm to rt where it was stirred for 15 h. The resulting white solution was diluted with 100 mL of ethyl acetate, and washed with 75 mL of water. The aqueous layer was extracted with two 50mL-portions of ethyl acetate. The combined organic extracts were dried ($MgSO_4$), and concentrated in vacuo. The crude residue was chromatographed over 150 g of flash silica [eluted with hexanes/ethyl acetate (20:1)] to afford 4.81 g (76 %) of carbamate **4** as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.83 (s, 9H), 0.91-1.09 (m, 1H), 1.13 (d, *J* = 5.9 Hz, 3H), 1.20-1.28 (m, 2H), 1.45 (s, 9H), 1.87-1.60 (m, 2H), 2.91 (dq, *J* = 10.8, 5.9 Hz, 1H), 3.75 (m, 2H). The product was spectroscopically comparable ^{1}H NMR to literature data.[5b]

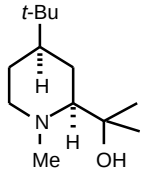


(2*R, 4*S**, 6*R**)-4-*tert*-Butyl-2-methyl-6-(tributylstannanyl)-piperidine-1-carboxylic acid *tert*-butyl ester (5).**[5b] To a stirred solution of 2.0 g (7.84 mmol) of carbamate **4** in 25 mL of dry diethyl ether at –78 °C (acetone/dry ice bath) was added 1.18 g (10.2 mmol, 1.6 mL) of *N*,*N*′-tetramethylethylenediamine via syringe in one portion and 8.5 mL (10.2 mmol) of a 1.2 M solution of *sec*-butyllithium in cyclohexane over 15 min via syringe. The resulting mixture was stirred for 5.5 h at –78 °C, and 3.32 g (10.2 mmol, 2.8 mL) of neat tri-*n*-butyltin chloride was added over 1 min via syringe. The mixture was stirred for 10 min at –78 °C, and the cold bath was removed allowing the mixture to gradually warm to rt where it was stirred for 12 h. The mixture was diluted with 50 mL of ethyl acetate and washed with 50 mL of water. The aqueous layer was extracted with two 50 mL-portions of ethyl acetate. The combined organic extracts were dried ($MgSO_4$), and concentrated in vacuo. The crude residue was purified by column chromatography over 160 g of flash silica [eluted with hexanes] to afford 3.48 g (82 %) of carbamate **5** as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.75-0.91 (m, 24H), 1.07 (d, *J* = 6.1 Hz, 3 H), 1.08-1.68 (m, 25 H), 1.89 (m, 1H), 2.73 (dd, *J* = 13.0, 5.6 Hz, 1H), 3.75 (m, 1H). The product was spectroscopically comparable to ^{1}H NMR reported data.[5b]

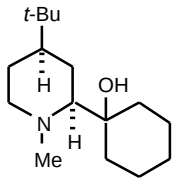


(2*R, 4*S**, 6*R**)-4-*tert*-Butyl-1,2-dimethyl-6-(tributylstannanyl)-piperidine (6).** To a solution of 3.0 g (5.51 mmol) of carbamate **5** in 50 mL of dry THF under nitrogen was added 33 mL (33.0 mmol) of a 1.0 M solution of diisobutylaluminum hydride in hexanes over 5 min via syringe. The resulting mixture was heated to reflux for 36 h. The mixture was cooled to rt, and 25 mL of methanol was added over 5 min via Pasteur pipette to quench the excess hydride. The mixture was stirred for 1 h at rt, and 50 mL of aqueous saturated sodium potassium tartrate was added over 5 min via Pasteur pipette. The resulting biphasic mixture was stirred for 2 h at rt, and diluted with 100mL of ethyl acetate. The aqueous layer was extracted with two 50 mL-portions of ethyl acetate. The combined organic extracts were washed with 100 mL of brine, dried ($MgSO_4$), and concentrated in vacuo. The

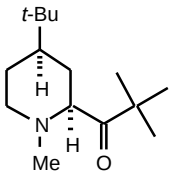
crude residue was chromatographed over 150 g of flash silica [eluted with hexanes/ethyl acetate (10:1) progressing to hexanes/ethyl acetate (2:1)] to afford 1.51 g (60 %) of **6** as a slightly yellow oil: IR (neat) 1366 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.78-1.07 (m, 25H), 1.11 (d, *J* = 6.1 Hz, 3H), 1.27-1.86 (m, 17H), 2.28 (s, 3H), 3.50 (t, *J* = 3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.3 (t), 14.0 (q), 21.4 (q), 27.7 (q), 28.0 (t), 29.8 (t), 32.4 (t), 32.7 (s), 36.7 (t), 43.7 (q), 47.4 (d), 58.8 (d), 64.7 (d); mass calcd for $C_{23}H_{49}NSn$ (M^+) *m/z* 458, found *m/z* 458. Anal. Calcd. for $C_{23}H_{49}NSn$: C 60.27, H 10.78. Found: C 60.16, H 10.70.



2-(cis-4-*tert*-Butyl-1-methylpiperidin-2-yl)-propan-2-ol (8a). To a stirred solution of 1.0 g (2.25 mmol) of piperidine **3** in 15 mL of dry THF under argon at -78 °C was added 2.0 mL (2.92 mmol) of a 1.45 M solution of *n*-butyllithium in hexanes over 3 min via syringe. The straw yellow mixture was stirred for 20 min at -78 °C, and 0.17 g (2.92 mmol, 0.22 mL) of dry acetone was then added in one portion via syringe. The resulting colorless mixture was stirred for 15 h during which time it gradually warmed to rt. The mixture was diluted with 50 mL of diethyl ether, and the resulting mixture was extracted with three 30-mL portions of aqueous 2M HCl. The combined aqueous extracts were basified to pH 14 with potassium hydroxide pellets, and extracted with five 25-mL portions of diethyl ether. The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The crude residue was bulb-to-bulb distilled under reduced pressure (140-150 °C, 3 torr) to afford 0.377 g (79 %) of amino alcohol **8a** as a colorless oil: IR (neat) 3343, 1364 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85 (s, 9H), 1.06-1.17 (m, 2H), 1.19 (s, 3H), 1.24 (s, 3H), 1.29-1.42 (m, 1H), 1.53-1.62 (m, 2H), 2.31 (dd, *J* = 11.4, 3.0 Hz, 1H), 2.48 (s, 3H, NCH_3), 2.61 (ddd, *J* = 13.3, 9.6, 3.8 Hz, 1H), 2.95 (dt, *J* = 13.3, 4.7 Hz, 1H), 3.05 (bs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.5 (t), 24.1 (t), 25.3 (q), 27.5 (q), 30.3 (q), 32.9 (s), 42.05 (q), 45.8 (d), 55.9 (t), 71.3 (d), 72.9 (s); mass calculated for $C_{13}H_{28}NO$ (MH^+) *m/z* 214, found *m/z* 214. Anal. Calcd. for $C_{13}H_{27}NO$: C 73.18, H 12.76. Found C 72.89, H 12.78.

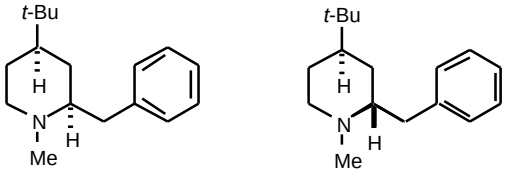


1-(cis-4-*tert*-Butyl-1-methylpiperidin-2-yl)-cyclohexanol (8b). To a stirred solution of 0.95 g (2.13 mmol) of piperidine **3** in 15 mL of dry THF under argon at -78 °C was added 1.9 mL (2.78 mmol) of a 1.45 M solution of *n*-butyllithium in hexanes over 3 min via syringe. The straw yellow mixture was stirred for 20 min at -78 °C, and 0.172 g (2.78 mmol, 0.29 mL) of dry cyclohexanone was added in one portion via syringe. The resulting colorless mixture was stirred for 15 h during which time it gradually warmed to rt. The mixture was diluted with 25 mL of diethyl ether, and extracted with three 25-mL portions of aqueous 2M HCl. The combined aqueous extracts were basified to pH 14 with potassium hydroxide pellets, and extracted with five 25-mL portions of diethyl ether. The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The crude residue was bulb-to-bulb distilled under reduced pressure (140-150 °C, 3 torr) to afford 0.45 g (84 %) of amino alcohol **8b** as a slightly yellow oil: IR (neat) 3406, 3261, 1364 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86 (s, 9H), 1.15-1.71 (m, 15H), 2.31 (dd, *J* = 11.6, 3.3 Hz, 1H), 2.44 (s, 3H, NCH_3), 2.67 (ddd, *J* =13.5, 7.8, 4.7 Hz, 1H), 2.93 (dt, *J* = 13.5, 5.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3 (t), 21.6 (t), 22.2 (t), 22.5 (t), 26.3 (t), 27.5 (q), 33.1 (s), 33.5 (t), 37.1 (t), 41.8(q), 45.5 (d), 54.4 (t), 70.6 (d), 73.3 (s); mass calculated for $C_{16}H_{32}NO$ (MH^+) *m/z* 254, found *m/z* 254. Anal. calcd. for $C_{16}H_{31}NO$: C 75.83, H 12.33. Found C 75.75, H12.37.



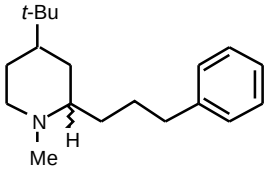
1-(cis-4-*tert*-Butyl-1-methylpiperidin-2-yl)-2,2-dimethylpropan-1-one (8c). To a stirred solution of 0.608 g (1.37 mmol) of piperidine **3** in 15 mL of dry THF under argon at -78 °C was added 1.35 mL (1.78 mmol) of a 1.35 M solution of *n*-butyllithium in hexanes over 3 min via syringe. The straw yellow mixture was stirred for 20 min at -78 °C, and 0.215 g (1.78 mmol, 0.22 mL) of neat trimethylacetyl chloride was added in one portion via syringe. The resulting colorless mixture was stirred for 15 h during which time it gradually warmed to rt. The mixture was diluted with 30 mL of diethyl ether, and the mixture was extracted with three 30-mL portions of aqueous 2M HCl. The combined aqueous extracts were cooled to 0°C, and basified to pH 9 with solid potassium carbonate. The

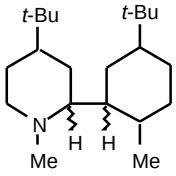
basic mixture was extracted with five 30-mL portions of diethyl ether. The combined organic extracts were dried ($MgSO_4$), and concentrated in vacuo. The crude residue was bulb-to-bulb distilled under reduced pressure (130-140°C, 3 torr) to afford 0.272 g (83 %) of amino ketone **8c** as a colorless oil: IR (neat) 1711, 1364 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.80 (s, 9H), 0.87-1.10 (m, 2H), 1.14 (s, 9H), 1.44 (qd, *J* =12.4, 3.9 Hz, 1H), 1.60 (dm, *J* = 12.5 Hz, 1H), 1.71 (dm, *J* = 12.1 Hz, 1H), 2.02 (td, *J* = 11.6 Hz, 1H), 2.05 (s, 3H,), 2.97 (dt, *J* = 11.4, 3.0 Hz, 1H), 3.06 (dd, *J* = 10.7, 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.8 (t), 27.0 (q), 27.6 (q), 32.0 (t), 32.5 (s), 44.4 (q), 44.7 (s), 46.5 (d), 57.2 (t), 69.3 (d), 215.7 (s); mass calculated for $C_{15}H_{30}NO$ (MH^+) *m/z* 240, found *m/z* 240. Anal. calcd. for $C_{15}H_{29}NO$: C 75.26, H 12.21. Found C 75.09, H 12.17.



***cis*-2-Benzyl-4-*tert*-butyl-1-methylpiperidine (9) and *trans*-2-Benzyl-4-*tert*-butyl-1-methyl-piperidine (10).** To a stirred solution of 0.5 g (1.13 mmol) of piperidine **3** in 12 mL of dry THF under nitrogen at -78 °C (acetone/dry ice bath) was added 0.17 g (1.46 mmol, 0.22 mL) of *N*,*N'*-tetramethylethylenediamine in one portion via syringe, and 1.62 mL (1.46 mmol) of a 0.9 M solution of *n*-butyllithium in hexanes over 5 min via syringe. The straw yellow mixture was stirred for 20 min at -78 °C, and 0.25 g (1.46 mmol, 0.2 mL) of neat benzyl bromide was then added over 2 min via syringe. The mixture took a bright yellow color, which disappeared within 30 sec. The resulting colorless mixture was stirred for 1.5 h at -78 °C and quenched with 5 mL of water. The cold bath was removed allowing the mixture to gradually warm to rt. The mixture was diluted with 20 mL of diethyl ether and extracted with three 20-mL portions of aqueous 2M HCl. The combined aqueous extracts were basified to pH 14 with 2M aqueous potassium hydroxide , and then extracted with three 20-mL portions of diethyl ether. The combined organic extracts were dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by column chromatography over 40 g of flash silica [eluted with hexanes/ethyl acetate/ethanol (5:1:0.5)] to afford an amber oil. Bulb to bulb distillation of the oil (130-140 °C, 1.5-2 mmHg) afforded 98 mg (35 %) of an

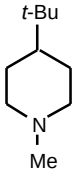
impure (1:1) mixture (by ^{1}H NMR) of piperidines **9** and **10** as a thick yellow oil: IR (neat) 1671, 1364 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.77 (s, 9H), 0.83 (s, 9H), 0.87-1.04 (m, 2H), 1.23-1.71 (m, 8H), 2.02-2.17 (m, 2H), 2.26-2.73 (m, 4H), 2.42 (s, 3H), 2.52 (s, 3H), 2.90 (dd, *J* =12.8, 3.5 Hz, 1H), 3.00 (dt, *J* = 11.2, 3.3 Hz, 1H), 3.12 (dm, *J* = 11.1 Hz, 1H), 3.23 (dd, *J* = 13.3, 4.0 Hz, 1H), 7.15-7.32 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.9 (t), 27.0 (t), 27.6 (q), 27.7 (q), 27.9 (t), 28.8 (t), 32.4 (t), 32.5 (s), 32.6 (s), 39.5 (d), 41.3 (t), 43.1 (q), 43.6 (q), 46.7 (d), 49.2 (t), 58.5 (t), 62.1 (d), 66.2 (d); exact mass calculated for $C_{17}H_{26}N$ (M-H$^+$) *m/z* 244.2067, found *m/z* 244.2061. Anal. Calcd. for $C_{17}H_{27}N$: C 83.20, H 11.09. Found C 82.96, H 11.13.



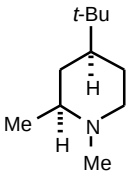


4-*tert*-Butyl-1-methyl-2-(3-phenylpropyl)-piperidine (14) and 4,4'-Di-*tert*-butyl-1,1'-dimethyl-[2,2']-bipiperidinyl (15). To a stirred solution of 1.0 g (22.26 mmol) of piperidine **3** in 12 mL of dry THF under nitrogen at -78 °C was added 0.34 g (2.92 mmol, 0.44mL) of *N*,*N'*-tetramethylethylenediamine in one portion via syringe, and 2.0 mL of a 1.45 M solution of *n*-butyllihium in hexanes. The resulting straw yellow mixture was stirred for 20 min at -78 °C, and 0.58 g (2.92 mmol, 0.44 mL) of 3-phenyl-1-bromo propane was added in 2mL of dry THF. The mixture was stirred for 1 h at -78 °C, and was quenched with 5 mL of water. The cold bath was removed, and the mixture was allowed to gradually warm to rt where it was stirred for 10 h. The mixture was diluted with 25 mL of diethyl ether, and was extracted with two 25-mL portions of aqueous 2M HCl. The combined aqueous extracts were basified to pH 9 with solid potassium carbonate. The basic mixture was extracted with three 25-mL portions of diethyl ether. the combined organic extracts were dried ($MgSO_4$), and concentrated in vacuo. The crude residue was purified by column chromatography over 60 g of flash silica [eluted with hexanes/ethyl acetate/ ethanol (5:1:0.5)] to yield 27 mg (3.9 %) of a white solid whose structure was tentatively assigned to bipiperidine **15**, based on the following data: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85 (s, 18H,), 1.05-1.44 (m, 8H), 1.77 (bd, *J* = 12.6 Hz, 2H), 2.50 (s, 6H), 2.65 (dm, *J* = 13.2 Hz, 2H),

2.77 (td, *J* = 13.2, 2.8 Hz, 2H), 2.85 (bs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.5 (t), 20.8 (t), 27.5 (q), 32.7 (s), 42.1 (q), 43.7 (d), 48.9 (t), 58.0 (d); mass calcd. for $C_{20}H_{41}N_2$ (MH^+) *m/z* 309, found *m/z* 309. Further elution with hexanes/ethyl acetate/ethanol (5:1:0.5) afforded an amber oil which was bulb to bulb distilled under reduced pressure (90-100 °C, 1-2 mmHg) to afford 28 mg (4.9%) of piperidine **14** as a colorless oil: IR (neat) 1364 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ, 0.86 (s, 9H), 0.93-1.13 (m, 2H), 1.28-1.86 (m, 8H), 2.07 (td, *J* = 12.0, 2.5 Hz, 1H), 2.58-2.66 (m, 2H), 2.97 (td, *J* = 12.0, 3.2 Hz, 1H), 7.16-7.32 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.0 (t), 27.4 (t), 27.7 (q), 32.3 (t), 32.6 (s), 33.9 (t), 36.8 (t), 42.8 (q), 47.0 (d), 58.4 (t), 64.5 (d), 126.1 (d), 128.7 (d), 128.8 (d), 142.9 (s); mass calcd. for $C_{19}H_{32}N$ (MH^+) *m/z* 274, found *m/z* 274. Anal.calcd. for $C_{19}H_{31}N$: C 83.45, H 11.43. Found C 83.41, H 11.58.



4-*tert*-Butyl-1-methylpiperidine (12). To a stirring solution of 3.2 g (85.1 mmol) of lithium aluminum hydride in 50 mL of dry diethyl ether at rt was added 2.0 g (8.30 mmol) of carbamate **2** in 50 mL of dry diethyl ether over 45 min via addition funnel. The resulting mixture was heated to reflux for 15 h. The mixture was cooled to 0 °C, and 20 mL of methanol was cautiously added via Pasteur pipette to quench the excess hydride. The mixture was stirred for 1 h at rt, and 50 mL of aqueous saturated sodium potassium tartrate was added over 5 min via Pasteur pipette. The resulting biphasic mixture was stirred for 15 h at rt, and diluted with 50mL of diethyl ether. The aqueous layer was extracted with three 25 mL-portions of diethyl ether. The combined organic extracts were washed with 50 mL of brine, dried ($MgSO_4$), and concentrated in vacuo to afford 0.91 g (70 %) of piperidine **10** as a slightly yellow liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (s, 9H), 0.94 (tt, *J* = 12.1, 3.5 Hz, 1H), 1.33 (qd, *J* = 12.6, 3.5 Hz, 2H), 1.65 (bd, *J* = 13.0 Hz, 2H), 1.83 (td, *J* = 12.1, 2.2 Hz, 2H), 2.24 (s, 3H), 2.91 (bd, *J* = 11.4 Hz, 2H). The product was spectroscopically comparable by ^{1}H NMR to literature value[13].



***cis*-4-*tert*-Butyl-1,2-dimethylpiperidine (17).** To a stirring solution of 1.5 g (39.5 mmol) of lithium aluminum hydride in 50 mL of dry THF at rt was added 1.68 g (6.59 mmol) of carbamate **4** in 50 mL of dry THF over 45 min via addition funnel. The resulting mixture was heated to reflux for 15 h. The mixture was cooled to 0 °C, and 20 mL of methanol was cautiously added via Pasteur pipette to quench the excess hydride. The mixture was stirred for 1 h at rt, and 50 mL of aqueous saturated sodium potassium tartrate was added over 5 min via Pasteur pipette. The resulting biphasic mixture was stirred for 15 h at rt, and diluted with 50mL of diethyl ether. The aqueous layer was extracted with three 25 mL-portions of diethyl ether. The combined organic extracts were washed with 50 mL of brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was bulb-to-bulb distilled under reduced pressure (70-80 °C, 5 mmHg) to afford 0.51 g (47 %) of piperidine **17** as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (s, 9H), 0.84-1.06 (m,2H), 1.08 (d, *J* = 6.2 Hz, 3H), 1.22-1.45 (m, 1H), 1.53-1.66 (m, 2H), 1.75-1.87 (m, 1H), 1.98 (td, *J* = 11.6, 2.6 Hz, 1H), 2.23 (s, 3H), 2.89 (dm, *J* = 11.3 Hz, 1H). The compound was previously published but experimental details were not provided.[14]

References for Supporting Information

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