Enantio- and Diastereoselective Synthesis of Cyclic β -Hydroxy Allylsilanes via Sequential Aldehyde γ -Silylallylboration and Ring Closing Metathesis Reactions

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SUPPORTING INFORMATION

Experimental procedures for synthesis of **1-2**, **6-7**, **9-13**, and **15-21** (18 pages). This material is available free of charge via the Internet at <http://pubs.acs.org>

General. All reactions were conducted in flame-dried or oven dried glassware under an atmosphere of dry nitrogen. All solvents were purified before use unless otherwise indicated. Tetrahydrofuran, diethyl ether, toluene, and dichloromethane were purified by passage through a column of activated alumina (A-1)¹; benzene was distilled from sodium metal; methanol was distilled from magnesium turnings; pyridine and triethylamine were distilled from CaH₂. All other reagents were used without further purification. Solvent removal was performed using a rotary evaporator at reduced pressure via water aspiration.

Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F₂₅₄ glass plates precoated with a 0.25 mm thickness of silica gel. The TLC plates were visualized by shortwave UV light, potassium permanganate or ceric ammonium molybdate stain. Flash chromatography was performed according to the method of Still² on Kieselgel 60 (230-400 mesh) silica gel. Analytical and semi-preparative HPLC normal phase separations were performed using an HPLC system composed of two Ranin HXPL pumps, a Rheodyne 7125 injector, a Dynamax UV-C detector and Dynamax software on a Macintosh II SI computer for data processing.

Infrared spectra were recorded as thin films on NaCl plates using a Perkin-Elmer Spectrum 1000 FT-IR spectrophotometer. Optical rotations were measured on a Rudolph Autopol III polarimeter using a quartz cell with 1 mL capacity and a 10 cm path length. Melting points were determined on a Mel-Temp II hot stage melting point apparatus and are uncorrected. ¹H NMR spectra were measured at 500 MHz on a Varian Inova 500 instrument using CDCl₃ as solvent. Chemical shifts are reported in δ units to 0.01 ppm precision with coupling constants reported to 0.1 Hz precision using residual chloroform (δ 7.27 ppm) as an internal reference. ¹³C NMR spectra were measured at 125 MHz or 100 MHz using CDCl₃ (δ 77.0 ppm) as an internal reference. High resolution mass spectra were measured on a VG 70-250-S Micromass spectrometer at the University of Michigan Mass Spectrometry Laboratory.

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¹Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

²Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.

(3*R*,4*S*)-3-Dimethylphenylsilyl-4-hydroxy-1,7-octadiene (2). To a solution of [(*E*)- γ -(dimethylphenylsilyl)allyl]diisopinocampheylborane **3**³ (1.58 mmol, 1.0 equiv.) (derived from 500 mg (1.58 mmol) of (–)-Ipc₂BOMe) at –78 °C was added BF₃·OEt₂ (0.26 mL, 2.06 mmol, 1.33 equiv.) followed by aldehyde **4** (0.23 mL, 2.37 mmol, 1.5 equiv). After being stirred for 4 h at –78 °C, the mixture was warmed to 0 °C and treated with 3 N NaOH solution (2.64 mL) and 30% H₂O₂ (1.62 mL) for 2 h. The resulting mixture was extracted with EtOAc. The extracts were washed with aq. saturated NaHCO₃ solution, dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (5% EtOAc/hexanes) to provide 355 mg of β -hydroxy allylsilane **2** as a colorless oil in 86% yield (94% ee, determined by Mosher ester analysis⁴): [α]_D²⁴ = –2.3° (*c* 0.84, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.58–7.55 (m, 2H), 7.40–7.36 (m, 3H), 5.86 (dt, *J* = 17.3, 10.3 Hz, 1H), 5.75 (app ddt, *J* = 17.3, 10.3, 6.8 Hz, 1H), 5.08 (dd, *J* = 10.3, 2.0 Hz, 1H), 4.97 (ddd, *J* = 17.3, 3.4, 1.7 Hz, 1H), 4.96–4.91 (m, 2H), 3.80–3.76 (m, 1H), 2.08–2.02 (m, 2H), 1.93 (dd, *J* = 10.5, 4.4 Hz, 1H), 1.51 (app q, *J* = 7.3 Hz, 2H), 1.46 (d, *J* = 4.4 Hz, 1H), 0.38 (s, 3H), 0.36 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 138.7, 138.2, 135.3, 134.3, 129.4, 128.0, 115.9, 114.9, 71.2, 42.4, 36.5, 30.4, –3.2, –3.7; IR (thin film) ν_{max} 3570, 3458, 3071, 2956, 2932, 1640, 1624, 1428, 1249, 1113, 905, 834, 815, 733, 701 cm^{–1}; HRMS (CI, NH₃) calcd for C₁₆H₂₃OSi, 243.1569 *m/z* [M–OH]⁺, observed 243.1570 *m/z*.

³ Roush, W. R.; Pinchuk, A. N.; Micalizio, G. C. *Tetrahedron Lett.* **2000**, *41*, 9413.

⁴ Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092.

(1*S*,2*R*)-2-Dimethylphenylsilyl-cyclohex-3-enol (1). A solution of diene **2** (247 mg, 0.95 mmol, 1.0 equiv.) in CH₂Cl₂ (95 mL, 0.01 M) was degassed under argon bubbling with sonication for 10 min. The solution was treated with catalyst **8** (40 mg, 5 mol%) in one portion and stirred for 1 h at 40 °C. The mixture was cooled to 23 °C and concentrated under reduced pressure. The residue was purified by column chromatography (5% EtOAc/hexanes) to provide 206 mg (94%) of cyclohexenylsilane **1** as a colorless oil: $[\alpha]_D^{25} = -59.9^\circ$ (*c* 0.7, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.61-7.59 (m, 2H), 7.39-7.36 (m, 3H), 5.69-5.65 (m, 1H), 5.59-5.56 (m, 1H), 4.23-4.18 (m, 1H), 2.20-2.04 (m, 3H), 1.77-1.71 (m, 1H), 1.67-1.61 (m, 1H), 1.39 (d, *J* = 6.5 Hz, 1H), 0.41 (s, 3H), 0.40 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 139.1, 134.3, 129.2, 128.0, 125.4, 125.0, 68.3, 34.6, 30.0, 21.4, -2.8, -3.0; IR (thin film) $\nu_{\max}$ 3433, 3069, 3020, 2952, 2841, 1427, 1248, 1111, 1066, 832, 814, 773, 736, 700 cm⁻¹; HRMS (CI, NH₃) calcd for C₁₄H₂₄NOSi, 250.1627 *m/z* [M+NH₄]⁺, observed 250.1637 *m/z*.

(3*S*,4*R*)-3-Dimethylphenylsilyl-4-hydroxy-1,6-heptadiene (6). To a solution of [(*E*)-γ-(dimethylphenylsilyl)allyl]diisopinocampheylborane **3**³ (1.58 mmol, 1.0 equiv.) (derived from 500 mg (1.58 mmol) of (-)-Ipc₂BOMe) at -78 °C was added BF₃·OEt₂ (0.26 mL, 2.06 mmol, 1.33 equiv.) followed by aldehyde **5** (2.37 mmol, 1.5 equiv.). After being stirred for 4 h at -78 °C, the mixture was warmed to 0 °C and treated with 3 N NaOH solution (2.64 mL) and 30% H₂O₂ (1.62

mL). After being stirred for 2 h, the mixture was extracted with EtOAc (2 × 100mL). The extracts were washed with saturated NaHCO₃ solution, dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (5% EtOAc/hexanes) to provide 298 mg of β-hydroxy allylsilane **6** as a colorless oil in 77% yield (98% ee, determined by Mosher ester analysis⁴): $[\alpha]_D^{23} = -6.2^\circ$ (*c* 1.23, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.58-7.55 (m, 2H), 7.39-7.36 (m, 3H), 5.89 (dt, *J* = 17.0, 10.5 Hz, 1H), 5.73 (dddd, *J* = 17.0, 10.5, 8.0, 6.5 Hz, 1H), 5.09-5.03 (m, 3H), 4.91 (ddd, *J* = 17.5, 2.0, 1.0 Hz, 1H), 3.78 (d, *J* = 3.5 Hz, 1H), 2.19-2.14 (m, 2H), 1.92 (dd, *J* = 10.5, 4.0 Hz, 1H), 1.56 (d, *J* = 2.5 Hz, 1H), 0.38 (s, 3H), 0.35 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 138.2, 135.5, 135.1, 134.3, 129.3, 128.0, 118.1, 115.7, 70.5, 42.2, 41.9, -3.3, -3.7; IR (thin film) $\nu_{\max}$ 3577, 3468, 3071, 2957, 2902, 1428, 1247, 1113, 900, 815, 834, 791, 734, 701 cm⁻¹; HRMS (CI, NH₃) calcd for C₁₅H₂₄NSi, 246.1678 *m/z* [M+NH₄-H₂O]⁺, observed 246.1677 *m/z*.

(1R,2S)-2-(Dimethylphenylsilyl)-cyclopent-3-enol (7). A solution of diene **6** (80 mg, 0.32 mmol, 1.0 equiv.) in toluene (32 mL, 0.01 M) was degassed under argon bubbling with sonication for 10 min. The catalyst **8** (27 mg, 10 mol%) was added in one portion and stirred for 1 h at 80 °C. The mixture was cooled to 23 °C and concentrated under reduced pressure. The residue was purified by column chromatography (5% EtOAc/hexanes) to provide cyclopentene **7** (51 mg, 73%) as a colorless oil: $[\alpha]_D^{25} = +75.6^\circ$ (*c* 0.75, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.64-7.60 (m, 2H), 7.40-7.36 (m, 3H), 5.73-5.66 (m, 2H), 4.77-4.73 (m, 1H), 2.68 (dddd, *J* = 17.0, 7.0, 4.5, 2.0 Hz, 1H), 2.45-2.42 (m, 1H), 2.27 (dddd, *J* = 17.0, 4.0, 3.5, 2.0 Hz, 1H), 1.45 (d, *J* = 5.5 Hz, 1H), 0.42 (s, 3H), 0.40 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 139.8, 134.0, 130.8, 129.1, 128.0, 126.6, 75.3, 43.7, 32.5, -2.6 (2C); IR (thin film) $\nu_{\max}$ 3569, 3449, 3068, 3050, 2953, 2902, 1427, 1246,

2220, 1050, 833, 818, 787, 734, 700, 669 cm^{-1} ; HRMS (CI, NH_3) calcd for $\text{C}_{13}\text{H}_{22}\text{NOSi}$, 246.1471 m/z [$\text{M}+\text{NH}_4$] $^+$, observed 246.1462 m/z .

1-(Dimethylphenylsilyl)-1-propylallene (9). Methanesulfonyl chloride (1.01 mL, 13 mmol, 1.3 equiv.) was added to a solution of (dimethylphenylsilyl)propargyl alcohol⁵ (2.01 g, 10 mmol) and Et_3N (2.09 mL, 15 mmol, 1.5 equiv.) in CH_2Cl_2 at $-50\text{ }^\circ\text{C}$ via syringe pump over 30 min. The mixture was allowed to warm to $23\text{ }^\circ\text{C}$ and stirred for 2.5 h. The mixture was quenched by addition of water (20 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 ($2 \times 20\text{ mL}$). The organic extracts were washed with water (40 mL) and brine (40 mL), dried over MgSO_4 , filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (10% EtOAc/hexanes) to afford the mesylate (2.04 g, 82%) as an oil.

To a solution of LiBr (0.76 g, 8.7 mmol, 1.1 equiv.) and CuBr (1.18 g, 8.7 mmol, 1.1 equiv.) in THF (20 mL) at $-10\text{ }^\circ\text{C}$ was added $n\text{-PrMgCl}$ (4.4 mL of a 2.0 M solution in Et_2O , 8.7 mmol, 1.1 equiv.) via syringe pump over 1.5 h. The resulting suspension was stirred at $-10\text{ }^\circ\text{C}$ for 1 h, cooled to $-60\text{ }^\circ\text{C}$, and treated with a solution of the mesylate prepared above (2.04 g, 7.9 mmol) in THF (5 mL) via syringe pump over 30 min. After being stirred for additional 30 min at $-60\text{ }^\circ\text{C}$, the mixture was allowed to warm to $23\text{ }^\circ\text{C}$ over 1 h, kept at $23\text{ }^\circ\text{C}$ for an additional 1 h, and then poured into aq. saturated NH_4Cl solution (20 mL, adjusted to pH 8 using NH_4OH). The resulting mixture was stirred for 1 h, and the organic layer was separated and washed with sat. pH 8 NH_4Cl solution until the extracts were no longer blue. The combined organic layers were washed with water (30 mL) and brine (30 mL), dried over MgSO_4 , filtered, and concentrated in vacuum. The residue was purified by column chromatography (100% hexanes) to provide allene **9** (1.38 g, 80%) as an oil: ^1H NMR (500 MHz, CDCl_3) δ 7.55-7.53 (m, 2H), 7.38-7.36 (m, 3H), 4.41 (t, $J = 3.3\text{ Hz}$, 2H), 1.91-1.87 (m, 2H),

⁵ Danheiser, R. L.; Carini, D. J.; Fink, D. M.; Basik, A. *Tetrahedron* **1983**, 39, 935.

1.44 (sextet, $J = 7.5$ Hz, 2H), 0.87 (t, $J = 7.3$ Hz, 3H), 0.38 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 209.6, 138.4, 134.1, 129.2, 127.9, 93.4, 69.5, 31.3, 22.3, 14.0, -2.9; IR (thin film) ν_{max} 2958, 1927, 1427, 1248, 1112, 813, 776, 731, 699 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{14}\text{H}_{20}\text{Si}$, 216.1334 m/z [M] $^{+}$, observed 216.1331 m/z .

(3*R*,4*R*)-3-(Dimethylphenylsilyl)-4-hydroxy-3-propyl-1,7-octadiene (*syn*-**11**). A suspension of (–)-HB(Ipc) $_2$ ⁶ (143 mg, 0.5 mmol, 1.0 equiv.) in THF (2.5 mL) was stirred at 23 °C until it became homogeneous. The solution was cooled to –50 °C and a solution of allene **9** in THF (0.5 mL) was added via cannula. The mixture was stirred for 14 h at –50 °C and then cooled to –78 °C and treated with aldehyde **4** (74 μL , 0.75 mmol, 1.5 equiv.). After being stirred for 4 h, the mixture was quenched by addition of a solution of 30% H_2O_2 (0.5 mL) and 3 N NaOH (1.0 mL). The mixture was vigorously stirred for 2 h at 0 °C and diluted with EtOAc (10 mL). The two phases were separated and the aqueous layer was extracted with EtOAc (2 $\times$ 5 mL). The combined organic layers were washed with sat. NaHCO_3 (10 mL) and brine (10 mL), dried (MgSO_4), filtered, and concentrated under reduced pressure. The resulting residue was purified by chromatography (3% EtOAc/hexanes) to give a 10:1 diastereomeric mixture (101 mg, 67%) of *syn*-**11** and *anti*-**11** as a colorless oil. Data for *syn*-**11** as a mixture: ^1H NMR (500 MHz, CDCl_3) δ 7.59–7.55 (m, 2H), 7.37–7.33 (m, 3H), 5.84–5.76 (m, 2H), 5.11 (dd, $J = 11.0, 1.0$ Hz, 1H), 5.01 (ddd, $J = 17.0, 2.5, 1.7$ Hz, 1H), 4.95 (dd, $J = 10.0, 1.0$ Hz, 1H), 4.79 (dd, $J = 17.8, 2.2$ Hz, 1H), 3.70 (ddd, $J = 10.2, 6.6, 1.2$ Hz, 1H), 2.26–2.19 (m, 1H), 2.09–2.00 (m, 1H), 1.66–1.57 (m, 2H), 1.52 (td, $J = 12.0, 4.1$ Hz, 1H), 1.50–1.32 (m, 2H), 1.37 (d, $J = 6.6$ Hz, 1H), 0.89 (t, $J = 7.0$ Hz, 3H), 0.41 (s, 3H), 0.36 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 141.1, 138.9, 138.5, 135.1, 129.1, 127.6, 115.1, 112.8, 75.2, 42.3, 32.6,

⁶ Brown, H. C.; Joshi, N. N. *J. Org. Chem.* **1988**, 53, 4059.

32.5, 31.8, 19.0, 15.6, -2.4, -2.5; IR (thin film) $\nu_{\max}$ 3575, 3494, 3072, 3050, 2959, 2872, 1640, 1619, 1455, 1428, 1414, 1250, 1110, 1066, 1010, 910, 834, 816, 771, 737, 702 cm^{-1} ; HRMS (CI, NH_3) calcd for $\text{C}_{19}\text{H}_{29}\text{Si}$, 285.2039 m/z $[\text{M}-\text{OH}]^+$, observed 285.2037 m/z .

(1*R*,2*R*)-2-(Dimethylphenylsilanyl)-2-propyl-cyclohex-3-enol (12a). A solution of dienes *syn-11* and *anti-11* (dr 6:1, 933 mg, 3.1 mmol, 1.0 equiv.) in CH_2Cl_2 (300 mL, 0.01 M) was degassed under argon bubbling while being sonicated for 10 min. The catalyst **8** (131 mg, 5 mol%) was added in one portion and stirred for 1 h at 40 °C. The mixture was allowed to cool to 23 °C and concentrated under reduced pressure. The residue was purified by column chromatography (3% EtOAc/hexanes) to provide cyclohexenylsilane **12a** (697 mg, 82%) as a colorless oil along with the diastereomer **12b** (116 mg, 14%). Data for **12a**: $[\alpha]_{\text{D}}^{24} = +23.8^\circ$ (c 0.81, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.57-7.55 (m, 2H), 7.39-7.36 (m, 3H), 5.68 (ddd, $J = 10.0, 4.7, 2.7$ Hz, 1H), 5.45 (ddd, $J = 10.0, 2.4, 1.5$ Hz, 1H), 4.00 (t, $J = 6.5$ Hz, 1H), 2.08 (dddd, $J = 17.8, 10.0, 5.3, 1.5$ Hz, 1H), 1.94 (dt, $J = 10.0, 7.6, 2.7$ Hz, 1H), 1.71-1.67 (m, 2H), 1.55-1.33 (m, 4H), 1.23 (bs, 1H), 0.84 (t, $J = 7.1$ Hz, 3H), 0.37 (s, 3H), 0.36 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.0, 134.6, 131.2, 129.4, 128.0, 125.4, 70.5, 36.0, 35.0, 28.2, 23.6, 20.0, 15.5, -3.8, -3.9; IR (thin film) $\nu_{\max}$ 3468, 3014, 2956, 2871, 1428, 1249, 1109, 1054, 826, 807, 770, 736, 701 cm^{-1} ; HRMS (CI, NH_3) calcd for $\text{C}_{17}\text{H}_{28}\text{NSi}$, 274.1991 m/z $[\text{M}+\text{NH}_4-\text{H}_2\text{O}]^+$, observed 274.1991 m/z .

(1*R*,2*S*)-2-(Dimethylphenylsilyl)-2-propyl-cyclohex-3-en-1-ol (12b). $[\alpha]_D^{24} = -0.3^\circ$ (c 0.67, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.61-7.58 (m, 2H), 7.36-7.32 (m, 3H), 5.63 (dt, $J = 10.0, 3.6$ Hz, 1H), 5.30 (dt, $J = 10.0, 1.7$ Hz, 1H), 3.96 (dt, $J = 10.5, 4.5$ Hz, 1H), 2.08-1.94 (m, 2H), 1.71-1.61 (m, 2H), 1.56-1.50 (m, 1H), 1.43 (d, $J = 4.9$ Hz, 1H), 1.44-1.38 (m, 1H), 1.35-1.25 (m, 1H), 1.22-1.12 (m, 1H), 0.87 (t, $J = 7.3$ Hz, 3H), 0.42 (s, 3H), 0.39 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 139.6, 135.2, 131.7, 128.9, 127.7, 124.6, 72.5, 39.0, 36.6, 28.9, 23.7, 17.7, 15.1, -2.2, -2.3.

(2*R*,3*R*)-1-(*tert*-Butyldimethylsilyloxy)-2,3-dibenzyloxy-4-pentene. To a solution of (2*R*,3*R*)-4-(*tert*-butyldimethylsilyloxy)-2,3-dibenzyloxy-1-pentanol⁷ (7.47 g, 18 mmol) in CH_2Cl_2 at 0°C was added Dess-Martin periodinane (9.51 g, 22.4 mmol, 1.25 equiv.) in a single portion. After 5 min, the mixture was allowed to warm to 23°C and stirred for 1 h. The mixture was diluted with Et_2O (150 mL), poured into a saturated solution of $\text{Na}_2\text{S}_2\text{O}_3$ (100 mL), and then stirred until the layers became clear. The two phases were separated and the aqueous phase was extracted with Et_2O (2×100 mL). The combined organic layers were washed with aq. saturated NaHCO_3 solution (2×100 mL) and brine (100 mL), filtered, and concentrated under reduced pressure to give the crude aldehyde which was used for the next step without further purification. An analytical sample was obtained by column chromatography (5% EtOAc /hexanes): $[\alpha]_D^{24} = -39.5^\circ$ (c 1.23, CHCl_3) {lit.⁷ for *enantiomer* $[\alpha]_D^{27} = +38.1^\circ$ (c 1.08, CHCl_3)}; ^1H NMR (500 MHz, CDCl_3) δ 9.72 (d, $J = 1.2$ Hz, 1H), 7.36-7.29 (m, 10H), 4.76 (d, $J = 12.0$ Hz, 1H), 4.63 (d, $J = 12.0$ Hz, 2H), 4.57 (d, $J = 11.7$ Hz, 1H), 3.99 (dd, $J = 3.9, 1.2$ Hz, 1H), 3.84 (ddd, $J = 6.3, 4.9, 3.9$ Hz, 1H), 3.79 (dd, $J = 10.3, 6.1$ Hz,

⁷ Marshall, J. A.; Seletsky, B. M.; Luke, G. P. *J. Org. Chem.* **1994**, *59*, 3413.

1H), 3.74 (dd, $J = 10.2, 5.0$ Hz, 1H), 0.89 (s, 9H), 0.04 (s, 6H); IR (thin film) $\nu_{\max}$ 3032, 2929, 2857, 1732, 1497, 1471, 1455, 1362, 1255, 1208, 1094, 1006, 837 cm^{-1} ; HRMS (FAB) calcd for $\text{C}_{24}\text{H}_{35}\text{O}_4\text{Si}$, 415.2305 m/z $[\text{M} + \text{H}]^+$, observed 415.2305 m/z .

To a suspension of $\text{Ph}_3\text{PCH}_2\text{Br}$ (12.32 g, 34 mmol, 1.5 equiv.) in THF (300 mL) at -78°C was added $n\text{-BuLi}$ (2.4 M in hexane, 14.1 mL, 34 mmol, 1.5 equiv.) dropwise over 5 min. After 5 min, the mixture was allowed to warm to 23°C and stirred for 1.5 h. The mixture was recooled to -78°C , and treated with a solution of aldehyde prepared above in THF (50 mL) for 30 min. The reaction mixture was stirred at 23°C for 1.5 h. The resulting mixture was then poured into a saturated NH_4Cl solution (100 mL) and separated. The aqueous layer was extracted with Et_2O (2×50 mL) and the combined layers were washed with brine (100 mL). The extracts were dried over MgSO_4 , filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (5% EtOAc /hexanes) to give alkene (8.15 g, 85% for 2 steps) as an oil: $[\alpha]_D^{24} = -15.3^\circ$ (c 1.35, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.38-7.26 (m, 10H), 5.89 (ddd, $J = 17.3, 10.5, 7.3$ Hz, 1H), 5.31 (ddd, $J = 17.1, 2.0, 1.2$ Hz, 1H), 5.29 (ddd, $J = 10.5, 2.0, 1.0$ Hz, 1H), 4.75 (A of ABq, $J = 12.0$ Hz, 1H), 4.71 (B of ABq, $J = 12.0$ Hz, 1H), 4.64 (d, $J = 12.0$ Hz, 1H), 4.41 (d, $J = 12.0$ Hz, 1H), 3.97 (ddt, $J = 7.5, 5.1, 1.0$ Hz, 1H), 3.80 (dd, $J = 10.6, 4.2$ Hz, 1H), 3.68 (dd, $J = 10.7, 6.4$ Hz, 1H), 3.55 (ddd, $J = 6.4, 4.9, 4.4$ Hz, 1H), 0.90 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 145.4, 139.2, 138.8, 135.8, 128.5, 128.4, 128.2, 128.0, 127.6, 118.4, 82.6, 80.6, 73.8, 71.0, 63.5, 26.2, 18.5, -5.1, -5.2; IR (thin film) $\nu_{\max}$ 2928, 2857, 1497, 1455, 1253, 1092, 927, 836 cm^{-1} ; HRMS (FAB) calcd for $\text{C}_{25}\text{H}_{36}\text{NaO}_3\text{Si}$, 435.2331 m/z $[\text{M} + \text{Na}]^+$, observed 435.2330 m/z .

(2S,3R)-2,3-Dibenzyloxy-4-penten-1-al (13). To a solution of TBS ether (8.03 g, 19.5 mmol) in THF (80 mL) at 23°C was added tetrabutylammonium fluoride (29.6 mL of a 1.0 M in

THF, 29.6 mmol, 1.5 equiv.) over 10 min. After 1 h, the mixture was diluted with EtOAc (100 mL), poured into aq. saturated NaHCO_3 (100 mL), and the layers separated. The aqueous layer was extracted with EtOAc (2 x 50 mL) and the combined organic layers were washed with brine (100 mL). The extracts were dried over MgSO_4 , filtered, and concentrated under vacuum. The residue was purified by gradient column chromatography (20% $\rightarrow$ 50% EtOAc/hexanes) to give the corresponding alcohol (5.45 g, 93% yield) as an oil: $[\alpha]_D^{24} = -11.9^\circ$ (c 1.21, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.37-7.30 (m, 10H), 5.88 (ddd, 1H, $J = 16.8$ Hz, 10.7 Hz, 7.1 Hz), 5.37 (ddd, 1H, $J = 10.8$ Hz, 1.5 Hz, 0.7 Hz), 5.36 (ddd, 1H, $J = 16.9$ Hz, 1.7 Hz, 1.0 Hz), 4.82 (d, 1H, $J = 11.7$ Hz), 4.68 (d, 1H, $J = 11.7$ Hz), 4.67 (d, 1H, $J = 11.7$ Hz), 4.43 (d, 1H, $J = 12.0$ Hz), 4.03 (dd, 1H, $J = 7.5$ Hz, 5.8 Hz), 3.77-3.73 (m, 1H), 3.65-3.58 (m, 2H), 2.13 (dd, 1H, $J = 7.3$ Hz, 5.4 Hz); ^{13}C NMR (125 MHz, CDCl_3) δ 138.6, 138.4, 134.9, 128.7, 128.6, 128.2, 128.1, 128.0, 127.9, 119.6, 81.6, 81.2, 73.7, 70.9, 62.3; IR (thin film) ν_{max} 3437, 3064, 3030, 2927, 2871, 1496, 1454, 1351, 1207, 1068, 996, 931, 736, 697 cm^{-1} ; HRMS (CI, NH_3) calcd for $\text{C}_{19}\text{H}_{26}\text{NO}_3$, 316.1913 m/z [$\text{M} + \text{NH}_4$] $^+$, observed 316.1923 m/z .

To a solution of the alcohol prepared above (2.99 g, 10 mmol, 1.0 equiv.) in CH_2Cl_2 (40 mL) at 0 $^\circ\text{C}$ was added Dess-Martin periodinane (5.28 g, 12.5 mmol, 1.25 equiv.) in one portion. After 5 min, the mixture was allowed to warm to 23 $^\circ\text{C}$ and stirred for 1 h. The mixture was diluted with Et_2O (50 mL), poured into a saturated solution of $\text{Na}_2\text{S}_2\text{O}_3$ (30 mL), and then stirred until the mixture became clear. The two phases were separated and the aqueous layer was extracted with Et_2O (2 x 30 mL). The combined extracts were washed with aq. saturated NaHCO_3 solution (2 x 50 mL) and brine (50 mL), filtered, and concentrated under reduced pressure. The crude aldehyde was purified by gradient column chromatography (10% $\rightarrow$ 20% EtOAc/hexanes) to give aldehyde **13** (2.59 g, 88% yield) as an oil: $[\alpha]_D^{24} = -48.9^\circ$ (c 1.27, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 9.71 (d, $J = 1.5$ Hz, 1H), 7.37-7.27 (m, 10H), 5.97 (ddd, $J = 17.0$, 10.2, 7.5, 1H), 5.40 (ddd, $J = 10.3$, 1.5, 0.7 Hz, 1H), 5.37 (ddd, $J = 17.3$, 1.5, 0.8 Hz, 1H), 4.78 (d, $J = 12.2$ Hz, 1H), 4.66 (d, $J = 12.2$ Hz, 1H), 4.65 (d, $J = 12.0$ Hz, 1H), 4.38 (d, $J = 12.0$ Hz, 1H), 4.20 (ddt, $J = 7.6$, 3.9, 1.0 Hz, 1H), 3.86 (dd, $J = 4.2$, 1.5 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 202.8, 137.8, 137.3, 134.1, 128.7, 128.6,

128.4, 128.3, 128.2, 128.0, 120.2, 85.4, 80.2, 73.7, 70.9; IR (thin film) ν_{max} 3065, 3031, 2867, 1734, 1497, 1455, 1123, 1070, 1028, 996, 935, 738, 698 cm^{-1} ; HRMS (CI, NH_3) m/z calcd for $\text{C}_{19}\text{H}_{24}\text{NO}_3$, 314.1756 m/z [$\text{M} + \text{NH}_4$] $^+$, observed 314.1750 m/z .

(3*R*,4*R*,5*S*,6*R*)-5,6-Dibenzyloxy-3-(dimethylphenylsilyl)-4-hydroxy-3-propyl-1,7-octadiene (15a). (–)-HB(lpc) $_2$ ⁸ (487 mg, 1.7 mmol, 1.7 equiv.) was stirred in THF (5.0 mL) at 23 °C until the solution became clear. The solution was then placed in a –50 °C bath and a solution of allene **9** in THF (0.5 mL) was added via cannula. After being stirred for 6 h at –50 °C, the mixture was cooled to –78 °C and treated with a solution of aldehyde **13** (296 mg, 1.0 mmol, 1.0 equiv.) in THF (1.0 mL). After being stirred for 4 h at –78 °C, the mixture was quenched by addition of pH 7 buffer solution⁹ (3.0 mL) and 30% H_2O_2 (1.0 mL) sequentially. The heterogeneous mixture was vigorously stirred for 12 h at 23 °C and diluted with EtOAc (20 mL). The two phases were separated and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic extracts were washed with sat. NaHCO_3 (20 mL) and brine (20 mL), dried (MgSO_4), filtered, and concentrated under reduced pressure. The resulting residue was purified by column chromatography (3% EtOAc/hexanes) to give a diastereomeric mixture (408 mg, 79%) of **15a-c** (dr 77:16:7) as a colorless oil. An analytical sample of **15a** was obtained by HPLC (3% EtOAc/hexanes, 21mm Dynamax 60A column, 10 ml/min). Data for **15a**: Retention time 10.4 min; $[\alpha]_{\text{D}}^{24} = -18.9^\circ$ (c 1.57, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.63–7.62 (m, 2H), 7.36–7.22 (m, 13H), 5.70–5.62 (m, 2H),

⁸ Brown, H. C.; Joshi, N. N. *J. Org. Chem.* **1988**, 53, 4059.

⁹ Treatment of borane intermediate using $\text{H}_2\text{O}_2/3\text{ N NaOH}$ caused significant Peterson elimination reactions to provide corresponding olefinated side-products.

5.17 (dd, $J = 10.5, 1.5$ Hz, 1H), 5.11 (d, $J = 17.3$ Hz, 1H), 5.05 (dd, $J = 11.2, 1.2$ Hz, 1H), 4.87 (d, $J = 10.7$ Hz, 1H), 4.83 (dd, $J = 17.8, 1.5$ Hz, 1H), 4.54 (d, $J = 12.0$ Hz, 1H), 4.43 (d, $J = 10.7$ Hz, 1H), 4.33 (d, $J = 11.7$ Hz, 1H), 3.94 (app. t, $J = 7.1$ Hz, 1H), 3.82 (d, $J = 9.6$ Hz, 1H), 3.59 (dd, $J = 6.8, 0.5$ Hz, 1H), 2.90 (d, $J = 9.5$ Hz, 1H), 1.82-1.76 (m, 1H), 1.54-1.40 (m, 3H), 0.82 (app. t, $J = 7.6$ Hz, 3H), 0.45 (s, 3H), 0.34 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 141.2, 138.7, 138.6 (2C), 135.7, 135.4, 128.9, 128.5, 128.2, 127.9, 127.6, 127.4, 119.8, 112.8, 83.1, 78.0, 73.1, 72.1, 70.7, 43.3, 32.5, 19.9, 15.8, -2.0, -2.1; IR (thin film) ν_{max} 3555, 3069, 3031, 2959, 2870, 1497, 1453, 1426, 1405, 1249, 1109, 1070, 817, 772, 736, 699 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{33}\text{H}_{42}\text{NaO}_3\text{Si}$, 537.2801 m/z [$\text{M} + \text{Na}$] $^+$, observed 537.2808 m/z .

(1*R*,2*R*,3*R*,4*R*)-5,6-Dibenzyloxy-2-(dimethylphenylsilyl)-2-propyl-cyclohex-3-enol

(17a). A solution of dienes **15a** and **15c** (dr 10:1, 505 mg, 0.98 mmol, 1.0 equiv.) in toluene (100 mL, 0.01 M) was degassed under argon bubbling while being sonicated for 30 min. Grubbs' catalyst **8** (83 mg, 10 mol%) was added in one portion and the reaction mixture was stirred for 72 h at 80 °C. The mixture was allowed to cool to 23 °C and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (20 mL) and treated with silica gel (830 mg, 10 wt. equiv. of catalyst). The mixture was passed through a short silica gel pad, rinsed with 20% EtOAc/hexanes (100 mL), and then concentrated *in vacuo*. The residue was purified by column chromatography (3% EtOAc/hexanes) to provide cyclohexenylsilane **17a** (412 mg, 88%) as a colorless oil along with **17c** (33 mg, 5%). Data for **17a**: $[\alpha]_{\text{D}}^{23} = -60.3^\circ$ (c 0.33, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.54-7.51 (m, 2H), 7.40-7.29 (m, 13H), 5.67 (dd, $J = 10.0, 1.5$ Hz, 1H), 5.56 (dd, $J = 10.0, 2.0$ Hz, 1H), 5.01 (d, $J = 10.5$ Hz, 1H), 4.71 (d, $J = 11.5$ Hz, 1H), 4.70 (d, $J = 11.0$ Hz, 1H), 4.63 (d, $J = 11.5$ Hz, 1H), 3.94 (dt, $J = 7.6, 2.0$ Hz, 1H), 3.77 (dd, $J = 10.0, 1.5$ Hz, 1H), 3.70 (dd, $J = 10.0, 7.5$

Hz, 1H), 2.44 (d, $J = 2.0$ Hz, 1H), 1.78 (td, $J = 12.0, 4.5$ Hz, 1H), 1.42 (td, $J = 12.5, 3.5$ Hz, 1H), 1.39-1.31 (m, 1H), 1.29-1.23 (m, 1H), 0.82 (t, $J = 7.0$ Hz, 3H), 0.41 (s, 3H), 0.40 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.8, 138.7, 137.2, 134.9, 132.9, 129.4, 128.9, 128.7, 128.5, 128.2, 128.1, 128.0, 127.8, 124.9, 81.1, 80.9, 75.3, 71.8, 71.7, 37.0, 33.6, 20.5, 15.4, -4.0, -4.5; IR (thin film) ν_{max} 3568, 3067, 3028, 2957, 2870, 1497, 1454, 1427, 1249, 1110, 1058, 832, 815, 773, 736, 699 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{31}\text{H}_{38}\text{NaO}_3\text{Si}$, 509.2488 m/z $[\text{M} + \text{Na}]^+$, observed 509.2488 m/z .

(3*R*,4*R*,5*S*)-3-(Dimethylphenylsilyl)-4-hydroxy-5-methyl-3-propyl-1,7-octadiene

(16a). A suspension of (–)-HB(Ipc)₂⁸ (487 mg, 1.7 mmol, 1.7 equiv.) in THF (7.0 mL) was stirred at 23 °C until it became clear. The solution was placed in a –50 °C bath and a solution of allene **9** (216 mg, 1.0 mmol, 1.0 equiv.) in THF (1.0 mL) was added via cannula. After being stirred for 6 h at –50 °C, the mixture was cooled to –78 °C and treated with aldehyde **14**¹⁰ (755 mg of a 15.6 wt% solution in CH_2Cl_2 , 1.0 mmol, 1.0 equiv.). The mixture was stirred for 4 h at –78 °C and quenched by addition of a mixture of 30% H_2O_2 (2.0 mL) and 3 N NaOH (3.0 mL), then allowed to warm slowly to 0 °C. The mixture was vigorously stirred for 2 h and diluted with EtOAc (20 mL). The two phases were separated and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with aq. saturated NaHCO_3 (20 mL) and brine (20 mL), dried (MgSO_4), filtered, and concentrated under reduced pressure. The resulting residue was purified by chromatography (3% EtOAc/hexanes) to give the diastereomeric mixture (229 mg, 73%) of **16a-c** (dr 83:10:7) as a colorless oil, which was separated by HPLC (3% EtOAc/hexanes, 21mm Dynamax

¹⁰ Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737.

60A column, 10 ml/min). Data for **16a**: $[\alpha]_D^{24} = -5.2^\circ$ (c 0.83, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.61-7.59 (m, 2H), 7.37-7.32 (m, 3H), 5.79 (dd, $J = 16.5, 11.0$ Hz, 1H), 5.69 (ddt, $J = 16.0, 10.2, 7.0$ Hz, 1H), 5.08 (dd, $J = 11.2, 1.4$ Hz, 1H), 4.94 (dd, $J = 10.0, 1.2$ Hz, 1H), 4.90 (dd, $J = 17.0, 1.2$ Hz, 1H), 4.81 (dd, $J = 17.6, 1.2$ Hz, 1H), 3.66 (dd, $J = 7.3, 2.0$ Hz, 1H), 2.09-2.01 (m, 1H), 1.90-1.83 (m, 2H), 1.73-1.65 (m, 1H), 1.58-1.45 (m, 3H), 1.36 (d, $J = 7.3$ Hz, 1H), 0.92 (t, $J = 7.2$ Hz, 3H), 0.86 (d, $J = 6.6$ Hz, 3H), 0.44 (s, 3H), 0.35 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 141.5, 138.8, 137.3, 135.2, 129.0, 127.6, 116.6, 112.5, 77.1, 44.0, 42.2, 34.4, 32.8, 19.8, 15.7, 15.4, -2.0, -2.1; IR (thin film) ν_{max} 3582, 3072, 3050, 2961, 2873, 1647, 1618, 1458, 1427, 1412, 1380, 1250, 1109, 993, 910, 818, 770, 737, 702 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{20}\text{H}_{32}\text{NaOSi}$, 339.2120 m/z $[\text{M}+\text{Na}]^+$, observed 339.2126 m/z .

(1R,2R,6S)-2-(Dimethylphenylsilyl)-6-methyl-2-propyl-cyclohex-5-enol (18a). A solution of dienes **16a** and **16c** (dr 12:1, 172 mg, 0.54 mmol, 1.0 equiv.) in toluene (50 mL, 0.01 M) was degassed under argon bubbling while being sonicated for 10 min. The catalyst **8** (23 mg, 5 mol%) was added in one portion and stirred for 1 h at 80 °C. The mixture was allowed to cool to 23 °C and concentrated under reduced pressure. The resulting residue was purified by column chromatography (4% EtOAc/hexanes) to provide cyclohexenylsilane **18a** (117 mg, 81%) as a colorless oil along with **18c** (14 mg, 9%). Data for **18a**: $[\alpha]_D^{24} = +86.1^\circ$ (c 1.14, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.60-7.57 (m, 2H), 7.40-7.36 (m, 3H), 5.66 (ddd, $J = 10.0, 5.6, 2.0$ Hz, 1H), 5.48 (dd, $J = 10.0, 2.5$ Hz, 1H), 3.54 (d, $J = 10.8$ Hz, 1H), 2.05 (dt, $J = 7.4, 5.2$ Hz, 1H), 1.78-1.64 (m, 2H), 1.61-1.54 (m, 1H), 1.40 (td, $J = 12.2, 3.6$ Hz, 1H), 1.39-1.24 (m, 2H), 1.11 (bs, 1H), 0.96 (d, $J = 6.3$ Hz, 3H), 0.86 (t, $J = 7.4$ Hz, 3H), 0.37 (s, 3H), 0.35 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 137.9, 134.7, 131.6, 129.4, 128.1, 125.7, 77.0, 36.4, 34.2, 34.0, 31.8, 20.6, 18.5, 15.5, -

4.5, -4.6; IR (thin film) $\nu_{\max}$ 3586, 3070, 3014, 2956, 2871, 1454, 1428, 1249, 1110, 1040, 835, 820, 769, 736, 702 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{18}\text{H}_{28}\text{NaOSi}$, 311.1807 m/z $[\text{M}+\text{Na}]^+$, observed 311.1817;.

(1R,2R)-2-(Dimethylphenylsilyl)-2-propyl-1-(triethylsilyloxy)-3-cyclohexene (19). To a solution of alcohol **12a** (1.25 g, 4.5 mmol, 1.0 equiv.) in CH_2Cl_2 (20 mL) was added Et_3N (3.5 mL, 18.2 mmol, 4.0 equiv.), DMAP (111 mg, 0.9 mmol, 0.2 equiv.), and TES-Cl (2.3 mL, 13.6 mmol, 3.0 equiv.) sequentially at 23 °C. After being stirred for 15 h, the reaction was quenched with saturated aq. NaHCO_3 and diluted with EtOAc. The two phases were separated and the organic layer was washed with 1M KHSO_4 and brine, dried (MgSO_4), filtered, and concentrated *in vacuo*. The residue was purified by chromatography (3% EtOAc/hexanes) to provide TES ether **19** (1.73 g, 98%) as an oil: $[\alpha]_{\text{D}}^{23} = -1.3^\circ$ (c 0.86, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.54-7.51 (m, 2H), 7.37-7.31 (m, 3H), 5.63 (ddd, $J = 10.0, 4.7, 2.7$ Hz, 1H), 5.44 (ddd, $J = 10.0, 2.4, 1.5$ Hz, 1H), 4.06 (dd, $J = 7.3, 5.6$ Hz, 1H), 2.04 (dq, $J = 16.4, 5.2, 1.2$ Hz, 1H), 1.84-1.76 (m, 1H), 1.65-1.56 (m, 3H), 1.47-1.35 (m, 2H), 1.31-1.20 (m, 1H), 0.95 (t, $J = 7.8$ Hz, 9H), 0.82 (t, $J = 7.1$ Hz, 3H), 0.58 (q, $J = 7.8$ Hz, 6H), 0.35 (s, 3H), 0.34 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.6, 134.9, 132.0, 128.9, 127.6, 124.9, 72.0, 36.3, 35.2, 29.4, 23.8, 20.2, 15.5, 7.3, 6.0, -3.2, -3.8; IR (thin film) $\nu_{\max}$ 3070, 3051, 3015, 2956, 2876, 1458, 1428, 1414, 1247, 1110, 1091, 1003, 830, 812, 769, 735, 701 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{23}\text{H}_{40}\text{NaOSi}_2$, 411.2515 m/z $[\text{M}+\text{Na}]^+$, observed 411.2526 m/z .

(1*R*,4*R*,5*R*,7*S*,8*R*)-7-Benzyloxymethyl-8-(dimethylphenylsilyl)-5-propyl-4-

(triethylsilyloxy)-6-oxa-bicyclo[3.2.1]octane (20). To a mixture of cyclic allylsilane **19** (117 mg, 0.3 mmol, 1.0 equiv.) and activated molecular sieves (4Å, 30 mg) in CH₂Cl₂ (0.7 mL) at –78 °C was added α-benzyloxyacetaldehyde (84 μL, 0.45 mmol, 1.5 equiv.). The mixture was treated with SnCl₄ (42 μL, 0.36 mmol, 1.2 equiv.) and stirred for 1 h at –78 °C. The reaction was quenched with Et₃N (0.3 mL) and allowed to warm to 23 °C. The mixture was diluted with EtOAc (30 mL) and saturated aq. NaHCO₃. After separation of the two phases, the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined extracts were washed with brine, dried (MgSO₄), filtered, and concentrated *in vacuo*. The residue was purified by gradient chromatography (3% → 10% EtOAc/hexanes) to give a 9:1 diastereomeric mixture of **20** and **21** (123 mg, 71%), which was separated by HPLC (5% EtOAc/hexanes, 10 mm Dynamax 60A column, 5 ml/min). Data for **20**: Retention time 9.6 min; $[\alpha]_D^{24} = -2.7^\circ$ (*c* 1.16, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.52-7.51 (m, 2H), 7.39-7.30 (m, 8H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 3.94 (dd, *J* = 8.3, 4.3 Hz, 1H), 3.56 (dd, *J* = 9.0, 6.0 Hz, 1H), 3.41 (dd, *J* = 9.4, 4.3 Hz, 1H), 3.23 (dd, *J* = 9.4, 8.6 Hz, 1H), 2.35 (d, *J* = 1.5 Hz, 1H), 2.01-1.95 (m, 1H), 1.76-1.71 (m, 1H), 1.68-1.58 (m, 3H), 1.57-1.53 (m, 1H), 1.25-1.18 (m, 2H), 1.00-0.90 (m, 1H), 0.94 (t, *J* = 8.0 Hz, 9H), 0.68 (t, *J* = 7.2 Hz, 3H), 0.54 (q, *J* = 7.8 Hz, 6H), 0.45 (s, 3H), 0.43 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 138.7 (2C), 134.0, 129.4, 128.6, 128.2, 127.8 (2C), 88.9, 80.6, 73.8, 73.4, 72.3, 41.2, 34.7, 34.3, 30.4, 27.7, 15.9, 14.4, 7.2, 5.2, -0.8, -0.9; IR (thin film) $\nu_{\max}$ 3068, 3029, 2955, 2875, 1458, 1414, 1375, 1253, 1172, 1099, 1004, 970, 871, 811, 736, 700 cm⁻¹; HRMS (FAB) calcd for C₃₂H₅₀NaO₃Si₂, 561.3196 *m/z* [M+Na]⁺, observed 561.3209 *m/z*.

(1*R*,4*R*,5*R*,7*R*,8*R*)-7-Benzyloxymethyl-8-(dimethylphenylsilanyl)-5-propyl-4-(triethylsilyloxy)-6-oxa-bicyclo[3.2.1]octane (21). HPLC (5% EtOAc/hexanes, 10 mm Dynamax 60A column, 5 ml/min), Retention time 8.1 min; $[\alpha]_D^{24} = +8.9^\circ$ (*c* 0.57, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.55-7.53 (m, 2H), 7.39-7.28 (m, 8H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 12.2 Hz, 1H), 3.96 (ddd, *J* = 7.8, 5.4, 3.4 Hz, 1H), 3.77 (dd, *J* = 9.5, 5.5 Hz, 1H), 3.61-3.57 (m, 1H), 3.57 (dd, *J* = 9.5, 7.8 Hz, 1H), 2.27 (t, *J* = 3.0 Hz, 1H), 2.02 (td, *J* = 13.9, 3.9 Hz, 1H), 1.76 (d, *J* = 3.0 Hz, 1H), 1.69-1.54 (m, 4H), 1.39-1.33 (m, 1H), 1.11-1.04 (m, 1H), 1.02-0.97 (m, 1H), 0.94 (t, *J* = 8.0 Hz, 9H), 0.74 (t, *J* = 7.1 Hz, 3H), 0.53 (q, *J* = 8.0 Hz, 6H), 0.45 (s, 3H), 0.44 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 138.5 (2C), 133.9, 129.4, 128.5, 128.1, 128.0, 127.8, 88.7, 82.0, 74.1, 73.6, 69.1, 40.1, 38.9, 35.3, 30.8, 23.1, 16.0, 14.4, 7.2, 5.2, -1.0, -1.1; IR (thin film) $\nu_{\max}$ 2956, 2874, 1455, 1428, 1377, 1251, 1173, 1087, 1002, 967, 927, 872, 800, 735, 700 cm⁻¹; HRMS (FAB) calcd for C₃₂H₅₀NaO₃Si₂, 561.3196 *m/z* [M+Na]⁺, observed 561.3180 *m/z*.