***Total Synthesis of Asimicin via Highly Stereoselective [3+2] Annulation
Reactions of Substituted Allylsilanes***

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Supporting Information

Part I. Experimental procedures and tabulated spectroscopic data for all new compounds.

General Experimental Details. All reaction solvents were purified before use. Tetrahydrofuran, dichloromethane, toluene, and diethyl ether were purified by passing through a solvent column composed of activated A-1 alumina. $\text{BF}_3 \cdot \text{OEt}_2$ and SnCl_4 were purified by fractional distillation and stored under nitrogen. Unless indicated, all other reagents and solvents were used as purchased without further purification.

Proton nuclear magnetic resonance (^1H NMR) spectra were conducted on a Varian VXR-400 spectrometer at 400 MHz or on an Inova-500 spectrometer at 500 MHz. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded on the aforementioned instruments at 100 MHz and 125 MHz, respectively. The proton signal of residual non-deuterated solvent (δ 7.26 ppm for CHCl_3) was used as an internal reference for ^1H NMR spectra. For ^{13}C NMR spectra, chemical shifts are reported relative to the δ 77.2 ppm resonance of CHCl_3 . Coupling constants are reported in Hz. Infrared (IR) spectra were recorded as films on a Perkin-Elmer Spectrum 1000 FTIR. Optical rotations were measured on a Rudolph Autopol III polarimeter using a quartz cell with 1 mL capacity and a 10 cm path length. Mass spectra were recorded on a ZVG 70-250-S spectrometer manufactured by Micromass Corp. (Manchester, UK). Optical rotations were measured on a Rudolph Autopol III polarimeter using a 1 mL capacity quartz cell with a 10 cm path length. Elemental analyses were performed by Atlantic Microlab, Inc. in Norcross, Georgia.

Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F_{254} glass plates pre-coated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and/or by staining with Hanessian solution (ceric sulfate and ammonium molybdate in aqueous sulfuric acid). Column chromatography was generally performed using Kieselgel 60 (230-400 mesh) silica gel, typically using a 50-100:1 weight ratio of silica gel to crude product.

(3S,4R)-3-(Dimethylphenylsilyl)-4-hydroxy-tridec-1-ene (8). To a solution of KO^tBu (2.3 g, 20.6 mmol) in THF (40 mL) at -78°C was added allyldimethylphenylsilane (4.0 g, 22.7 mmol). The mixture was stirred for 5 min, then $n\text{-BuLi}$ (2.4 M in hexanes, 8.6 mL, 20.6 mmol) was added slowly via syringe over 5 min. The reaction was stirred at -78°C for 10 min and then

warmed to -45 °C and stirred for 2 h. The reaction was recooled to -78 °C and (-)-Ipc₂BOMe (6.5 g, 20.6 mmol) was added as a solution in THF (26 mL) slowly over 5 min. The reaction was stirred for 30 min and then BF₃·OEt₂ (3.9 g, 27.4 mmol) was added in one portion. After 5 min, undecanal (4.2 g, 24.7 mmol) was added as a solution in hexanes (40 mL) slowly over 5 min. The reaction was stirred at -78 °C for 4 h and then diluted with KOH/KH₂PO₄ buffer (1 M solution of KH₂PO₄, adjusted to pH 6 with KOH, 20 mL) and warmed to room temperature. H₂O₂ (35%, 3 mL) was added and the two-phase mixture was stirred at ambient temperature for 16 h. The reaction mixture was partitioned between H₂O and 1:1 hexanes-Et₂O. The organic layer was dried over Na₂SO₄, concentrated, and purified by chromatography (SiO₂, 5% Et₂O-hexanes) to give 6.8 g (95%) of allylsilane **8** as a colorless oil: $[\alpha]_D^{23.0} = -0.7$ (c 1.5, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.57-7.54 (m, 2H), 7.40-7.34 (m, 3H), 5.84 (dt, *J* = 17.0, 10.5 Hz, 1H), 5.06 (dd, *J* = 10.5, 2.0 Hz, 1H), 4.91 (dd, *J* = 17.5, 2.0 Hz, 1H), 3.76-3.60 (m, 1H), 1.91 (dd, *J* = 10.5, 4.5 Hz, 1H), 1.56 (bs, 1H), 1.44-1.16 (m, 18H), 0.89 (t, *J* = 7.0 Hz, 3H), 0.37 (s, 3H), 0.34 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 138.3, 135.5, 134.3, 129.3, 128.0, 115.7, 71.7, 42.3, 37.4, 32.2, 29.9, 29.8, 29.8, 29.8, 29.6, 26.0, 23.0, 14.4, -3.1, -3.7; IR (thin film) 3468, 3070, 2956, 2930, 2854, 1624, 1466, 1428, 1248, 1113, 1000, 898, 833, 814, 792, 732, 700, 653 cm⁻¹; HRMS calcd for C₂₂H₃₈OSi, 833.5157 *m/z* (M+Na)⁺; observed 833.5178 *m/z*. *Anal.* Calcd for C₂₂H₃₈OSi; C, 74.01; H, 9.69. Found: C, 73.84; H, 9.68.

(3S,4R)-3-(Dimethylphenylsilyl)-4-(tert-butyl dimethylsilyloxy)-tridec-1-ene (9). To a solution of allylsilane **8** (6.1 g, 17.5 mmol) in DMF (17.5 mL) was added TBSCl (5.3 g, 35.0 mmol) and imidazole (3.6 g, 52.5 mmol) at ambient temperature. The reaction flask was flushed with nitrogen, sealed with a septum, and heated to 50 °C for 48 h. The mixture was cooled to ambient temperature and partitioned between H₂O and hexanes. The organic layer was dried over MgSO₄, and concentrated. The crude product was purified by chromatography (SiO₂, hexanes) to give 6.7 g (85%) of allylsilane **9** as a colorless oil: $[\alpha]_D^{23.0} = -2.9$ (c 1.2, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.49-7.43 (m, 2H), 7.31-7.26 (m, 3H), 5.80 (dt, *J* = 17.2, 10.8 Hz, 1H), 4.89 (dd, *J* = 10.0, 2.0 Hz, 1H), 4.69 (dd, *J* = 17.2, 2.0 Hz, 1H), 3.82-3.76 (m, 1H), 1.96 (dd, *J* = 10.4, 3.6 Hz, 1H), 1.50-1.41 (m, 1H), 1.38-1.00 (m, 20H), 0.83 (s, 9H), 0.30 (s, 3H), 0.35 (s, 3H), -0.04 (s, 3H), -0.06 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 139.0, 136.2, 134.3, 128.9, 127.7, 114.5, 73.6, 40.8, 37.0, 32.1, 29.8, 29.8, 29.5, 26.3, 25.9, 25.6, 22.9, 18.4, 14.3, -2.9, -3.5, -3.5, -3.7; IR (thin film) 2955, 2927, 2856, 1253, 1063, 835 cm⁻¹; HRMS calcd for C₂₈H₅₂OSi₂, 483.3454 *m/z* (M+Na)⁺; observed 483.3451 *m/z*.

(2S, 3R, 5R)-5-(Benzyloxymethyl)-2-[(1R)-1-(*tert*-butyldimethylsilanyloxy)-undecyl]-3-(dimethylphenylsilyl)-tetrahydrofuran (10**).** To a -45 °C solution of allylsilane **9** (1.0 g, 2.2 mmol), α -benzyloxyacetaldehyde (400 mg, 2.7 mmol), and flame-dried powdered 4Å molecular sieves (500 mg) in CH₂Cl₂ (4.4 mL) was added SnCl₄ (280 mg, 1.1 mmol) dropwise from a syringe over 2 min. The reaction mixture was stirred at -45 °C for 20 h and then quenched with Et₃N (1 mL) and warmed to ambient temperature. The mixture was diluted with hexanes (5 mL), Et₂O (5 mL), and saturated NaHCO₃ (5 mL) and stirred for 24 h. The layers were separated and the aqueous layer was washed with 1:1 hexanes-Et₂O (50 mL). The combined organic layers were dried over MgSO₄, concentrated, and purified by chromatography (SiO₂, 5% Et₂O-hexanes) to give 1.2 g (93%) of tetrahydrofuran **10** as a colorless oil: $[\alpha]_D^{23.0} = -0.8$ (c 2.4, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.51-7.48 (m, 2H), 7.39-7.26 (m, 8H), 4.60-4.52 (m, 2H), 4.10-4.04 (m, 1H), 3.95 (dd, *J* = 9.0, 2.0 Hz, 1H), 3.53 (A of ABX, *J*_{AB} = 10.5 Hz, *J*_{AX} = 5.5 Hz, 1H), 3.45 (B of ABX, *J*_{AB} = 10.0 Hz, *J*_{BX} = 5.0 Hz, 1H), 3.28-3.24 (m, 1H), 2.07-2.01 (m, 1H), 1.77-1.62 (m, 2H), 1.53-1.46 (m, 2H), 1.39-1.15 (m, 16H), 0.90 (s, 12H), 0.34 (s, 3H), 0.33 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H); ¹³C NMR (125MHz, CDCl₃) δ 138.9, 138.2, 134.1, 129.4, 128.5, 128.1, 128.0, 127.7, 83.1, 78.8, 75.1, 73.5, 72.9, 34.9, 33.5, 32.2, 30.1, 29.9, 29.9, 29.7, 26.8, 26.4, 26.2, 23.0, 18.5, 14.4, -3.7, -3.8, -4.1, -4.1; IR (thin film) 2954, 2920, 2855, 1462, 1428, 1360, 1251, 1112, 835, 773, 734, 698 cm⁻¹; HRMS calcd for C₃₇H₆₂O₃Si₂, 633.4135 *m/z* (M+Na)⁺; observed 633.4153 *m/z*. *Anal.* Calcd for C₃₇H₆₂O₃Si₂; C, 72.73; H, 10.23. Found: C, 72.84; H, 10.21.

(2R, 4R, 5S)-[5-[(1R)-1-(*tert*-Butyldimethylsilyloxy)-undecyl]-4-(dimethylphenylsilyl)-tetrahydrofuran-2-yl]-methanol (A**):** To a solution of tetrahydrofuran **10** (520 mg, 0.8 mmol) in THF (5 mL) was added 10% Pd(OH)₂ (250 mg). The reaction flask was evacuated and purged with H₂ three times and then the reaction was stirred at ambient temperature under a hydrogen atmosphere for 2 h. The reaction flask was then evacuated and purged with nitrogen three times. The catalyst was removed by filtration through Celite. The filtrate was concentrated and the crude product purified by chromatography (SiO₂, 10% EtOAc-hexanes) to give 380 mg (87%) of **A**.

as a colorless oil: $[\alpha]_D^{23.0} = -13.3$ (c 1.7, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.52-7.48 (m, 2H), 7.39-7.34 (m, 3H), 4.02-3.96 (m, 1H), 3.94 (dd, $J = 8.5, 2.0$ Hz, 1H), 3.73 (dd, $J = 11.5, 3.0$ Hz, 1H), 3.45 (dd, $J = 12.0, 4.5$ Hz, 1H), 3.26-3.20 (m, 1H), 1.95-1.89 (m, 1H), 1.81-1.74 (m, 1H), 1.68-1.56 (m, 3H), 1.37-1.13 (m, 20H), 0.89 (s, 9H), 0.34 (s, 6H), 0.02 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 137.9, 134.0, 129.5, 128.1, 83.0, 80.0, 75.0, 64.5, 34.9, 32.2, 31.5, 30.0, 29.9, 29.6, 27.0, 26.3, 26.1, 23.0, 18.4, 14.4, -3.7, -4.1, -4.2, -4.2; IR (thin film) 3448, 2955, 2925, 2855, 1462, 1428, 1376, 1252, 1112, 1067, 836, 773, 734, 700 cm^{-1} ; HRMS calcd for $\text{C}_{30}\text{H}_{56}\text{O}_3\text{Si}_2$, 543.3666 m/z ($\text{M}+\text{Na}$) $^+$; observed 543.3676 m/z . *Anal.* Calcd for $\text{C}_{30}\text{H}_{56}\text{O}_3\text{Si}_2$; C, 69.17; H, 10.84. Found: C, 69.20; H, 11.09.

(2R, 4R, 5S)-5-[(1R)-1-(*tert*-Butyldimethylsilanyloxy)-undecyl]-4-(dimethylphenylsilyl)-tetrahydrofuran-2-carbaldehyde (11). To a solution of alcohol **A** (260 mg, 0.5 mmol), diisopropyl ethyl amine (320 mg, 2.5 mmol), and DMSO (390 mg, 5.0 mmol) in CH_2Cl_2 (2.5 mL) at 0 °C was added SO_3 -pyridine complex (240 mg, 1.5 mmol) as a solid in one portion. The reaction was stirred at 0 °C for 1 h. The reaction was quenched with an aqueous solution of saturated $\text{Na}_2\text{S}_2\text{O}_3$ (5 mL) and warmed to ambient temperature. The aqueous layer was extracted with EtOAc (2 x 75 mL). The combined organic layers were dried over MgSO_4 , concentrated, and purified by chromatography (SiO_2 , 10% Et_2O -hexanes) to give 255 mg (99%) of aldehyde **11** as a colorless oil: $[\alpha]_D^{23.0} = 46.7$ (c 3.9, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 9.55 (d, $J = 2.5$ Hz, 1H), 7.50-7.46 (m, 2H), 7.42-7.35 (m, 3H), 4.21-4.16 (m, 1H), 4.08 (dd, $J = 8.5, 1.5$ Hz, 1H), 3.27-3.22 (m, 1H), 2.25-2.19 (m, 1H), 1.85-1.78 (m, 1H), 1.75-1.62 (m, 2H), 1.45-1.37 (m, 1H), 1.36-1.13 (m, 19H), 0.89 (s, 9H), 0.36 (s, 6H), 0.01 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 202.9, 137.1, 134.0, 129.7, 128.3, 84.3, 83.9, 74.6, 35.0, 32.2, 32.1, 30.0, 29.9, 29.8, 29.6, 26.8, 26.2, 26.0, 23.0, 18.4, 14.5, -3.6, -4.1, -4.2, -4.2; IR (thin film) 3070, 2955, 2920, 2856, 1736, 1463, 1428, 1376, 1253, 1113, 1067, 1006, 927, 884, 836, 774, 735, 700, 670, 648 cm^{-1} ; HRMS calcd for $\text{C}_{30}\text{H}_{54}\text{O}_3\text{Si}_2$, 573.3771 m/z ($\text{M}+\text{Na}$) $^+$; observed 573.3778 m/z . *Anal.* Calcd for $\text{C}_{30}\text{H}_{54}\text{O}_3\text{Si}_2$; C, 69.44; H, 10.49. Found: C, 69.42; H, 10.54.

10-(*tert*-Butyldiphenylsilyloxy)-decan-1-ol (12**).** To a suspension of commercially available 1,10-decanediol (10.0 g, 57.4 mmol), triethylamine (4.0 mL, 28.7 mmol), and DMAP (230 mg, 1.9 mmol) in CH₂Cl₂ (500 mL) was added TBDPSCl (5.0 mL, 19.1 mmol) dropwise over 10 min. The reaction mixture was stirred at room temperature for 20 h and then half of the CH₂Cl₂ was removed at reduced pressure. The remaining suspension was diluted with 250 mL of hexanes and the resulting precipitate was removed by filtration. The filtrate was concentrated and the crude product was purified by chromatography (SiO₂, 10% to 25% EtOAc-hexanes) to give 5.6 g (71%) of the monoprotected diol **12**: ¹H NMR (400 MHz, CDCl₃) δ 7.66-7.61 (m, 4H), 7.41-7.31 (m, 6H), 3.61 (t, *J* = 6.4 Hz, 2H), 3.60 (t, *J* = 6.4 Hz, 2H), 1.57-1.47 (m, 4H), 1.35-1.18 (m, 13H), 1.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 135.8, 134.4, 129.7, 127.8, 64.2, 63.3, 33.0, 32.8, 29.7, 29.6, 27.1, 26.0, 25.9, 19.4; HRMS calcd for C₂₆H₄₀O₂Si, 435.2695 *m/z* (M+Na)⁺; observed 435.2688 *m/z*.

10-(*tert*-Butyldiphenylsilyloxy)-1-iododecane (B**).** To a solution of triphenylphosphine (1.9 g, 7.4 mmol) and imidazole (500 mg, 7.4 mmol) in CH₂Cl₂ (30 mL) was added iodine (1.9 g, 7.4 mmol) in small portions over 10 min. After the addition of iodine was complete, the reaction was stirred at ambient temperature for 10 min. The alcohol **12** (2.6 g, 6.2 mmol) was then added slowly as a solution in CH₂Cl₂ (30 mL) over 5 min. The reaction mixture was stirred at ambient temperature for 30 min at which time TLC analysis showed the reaction to be complete. The mixture was diluted with hexanes (100 mL) and the solids were removed by filtration. The filtrate was concentrated and purified by chromatography (SiO₂, 1% to 3% Et₂O-hexanes) to give 2.9 g (89%) of **B**: ¹H NMR (400 MHz, CDCl₃) δ 7.65-7.61 (m, 4H), 7.41-7.31 (m, 6H), 3.61 (t, *J* = 6.8 Hz, 2H), 3.15 (t, *J* = 6.8 Hz, 2H), 1.78 (q, *J* = 7.2 Hz, 2H), 1.55-1.47 (m, 12H), 1.00 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 135.8, 134.4, 129.7, 127.8, 64.2, 33.8, 32.8, 30.7, 29.7, 29.6, 29.5, 28.7, 27.1, 26.0, 19.4, 7.6; HRMS calcd for C₂₆H₃₉IOSi, 523.1893 *m/z* (M+H)⁺; observed 523.1895 *m/z*.

portion at ambient temperature. The mixture was stirred for 20 h, then was diluted with hexanes (100 mL) and washed with 1M HCl (2 X 50 mL) and saturated NaHCO₃ (1 X 50 mL). The organic layer was dried over Na₂SO₄, concentrated, and the crude product was purified by chromatography (SiO₂, 10% to 20% to 25% EtOAc-hexanes) to give 3.9 g (92%) of **D** as a colorless oil: $[\alpha]_D^{23.0} = -4.9$ (c 3.5, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 5.67-5.61 (m, 1H), 5.43-5.38 (m, 1H), 4.88-4.83 (m, 1H), 4.07 (dd, *J* = 8.0, 6.0 Hz, 1H), 3.65 (t, *J* = 7.0 Hz, 2H), 3.52 (t, *J* = 8.0 Hz, 1H), 2.28-2.04 (m, 2H), 1.60-1.54 (m, 2H), 1.44 (s, 3H), 1.41 (s, 3H), 1.40-1.27 (m, 13H); ¹³C NMR (125 MHz, CDCl₃) δ 135.4, 127.2, 109.3, 72.2, 69.6, 63.1, 33.0, 29.8, 29.7, 29.6, 29.6, 29.3, 27.9, 27.0, 26.1, 26.0; IR (thin film) 3436, 2985, 2926, 2870, 1660, 1456, 1371, 1215, 1156, 1058, 860, 792, 723 cm⁻¹; HRMS calcd for C₁₆H₃₀O₃, 293.2093 *m/z* (M+Na)⁺; observed 293.2100 *m/z*. *Anal.* Calcd for C₁₆H₃₀O₃; C, 71.07; H, 11.18. Found: C, 70.80; H, 11.39.

(4R)-11-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-undecan-1-ol (E). To a solution of alcohol **D** (4.2 g, 15.5 mmol) in THF (75 mL) and EtOH (75 mL) was added 10% Pd/C (600 mg). The reaction flask was evacuated and purged with hydrogen three times. The reaction mixture was stirred under a H₂ atmosphere at ambient temperature for 2 h. The flask was then evacuated and purged with nitrogen three times and the catalyst was removed by filtration through Celite. The filtrate was concentrated and the crude product purified by chromatography (SiO₂, 10% to 15% to 20% to 25% EtOAc-hexanes) to give 3.6 g (85%) of alcohol **E** as a white solid: $[\alpha]_D^{23.0} = -12.5$ (c 10.8, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 4.12-4.02 (m, 2H), 3.65 (t, *J* = 6.5 Hz, 2H), 3.51 (t, *J* = 7.5 Hz, 1H), 1.69-1.24 (m, 21H), 1.42 (s, 3H), 1.37 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 108.8, 76.4, 69.8, 63.3, 33.8, 33.0, 29.9, 29.8, 29.8, 29.7, 29.7, 29.7, 27.2, 26.0, 26.0; IR (thin film) 3401, 2985, 2923, 2855, 1458, 1369, 1215, 1159, 1059, 857 cm⁻¹; HRMS calcd for C₁₆H₃₂O₃, 295.2249 *m/z* (M+Na)⁺; observed 295.2253 *m/z*. *Anal.* Calcd for C₁₆H₃₂O₃; C, 70.54; H, 11.84. Found: C, 70.33; H, 11.93.

(4R)-2,2-Dimethyl-propionic acid-11-(2,2-dimethyl-[1,3]dioxolan-4-yl)-undecyl ester (F). To a solution of alcohol **E** (1.3 g, 4.3 mmol), pyridine (1.0 g, 13.0 mmol), and DMAP (50 mg,

0.4 mmol) in CH₂Cl₂ (15 mL) at ambient temperature was added pivaloyl chloride (1.0 g, 8.7 mmol) in one portion. The reaction was stirred at ambient temperature for 20 h and then quenched with aqueous saturated NaHCO₃ (20 mL). The aqueous layer was extracted with hexanes (2 x 30 mL) and the combined organic layers were dried over MgSO₄, and concentrated. The crude product was purified by chromatography (SiO₂, 5% Et₂O-hexanes) to give 1.6 g (93%) of pivaloate **F** as a colorless oil: $[\alpha]_D^{23.0} = -8.9$ (c 14.2, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 4.12-4.02 (m, 4H), 3.51 (t, *J* = 7.5 Hz, 1H), 1.69-1.58 (m, 3H), 1.55-1.45 (m, 1H), 1.42 (s, 3H), 1.37 (s, 3H), 1.36-1.23 (m, 16H), 1.21 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 178.8, 108.7, 76.4, 69.7, 64.6, 38.9, 33.8, 29.9, 29.7, 29.7, 29.7, 29.4, 28.8, 27.4, 27.3, 27.2, 26.1, 26.0, 26.0; IR (thin film) 2981, 2929, 2856, 1730, 1481, 1461, 1398, 1378, 1368, 1284, 1247, 1215, 1157, 1104, 1062, 979, 939, 859, 792, 771, 722 cm⁻¹; HRMS calcd for C₂₁H₄₀O₄, 379.2824 *m/z* (M+Na)⁺; observed 379.2822 *m/z*. *Anal.* Calcd for C₂₁H₄₀O₄; C, 70.74; H, 11.31. Found: C, 70.81; H, 11.29.

(12R)-2,2-Dimethylpropionic acid-12,13-dihydroxytridecyl ester (15). To a solution of pivaloate **F** (580 mg, 1.5 mmol) in CHCl₃ (10 mL) was added FeCl₃·6H₂O·SiO₂ (1 g) at ambient temperature. The reaction was stirred for 7 d and then the catalyst was removed by filtration through Celite. The filtrate was concentrated and purified by chromatography (SiO₂, 3% MeOH-CH₂Cl₂) to give 470 mg (62%) of diol **15** as a white solid plus 175 mg (30%) of unreacted **F**: $[\alpha]_D^{23.0} = 0.4$ (c 8.2, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 4.06 (t, *J* = 6.5 Hz, 2H), 3.76-3.70 (m, 1H), 3.68 (A of ABX, *J*_{AB} = 11.0 Hz, *J*_{AX} = 3.0 Hz, 1H), 3.45 (B of ABX, *J*_{AB} = 11.0 Hz, *J*_{BX} = 8.0, 1H), 1.74 (bs, 2H), 1.63 (q, *J* = 8.0 Hz, 2H), 1.48-1.42 (m, 3H), 1.39-1.24 (m, 15H), 1.21 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 179.0, 72.6, 67.0, 64.7, 39.0, 33.4, 29.9, 29.7, 29.7, 29.7, 29.4, 28.8, 27.4, 26.1, 25.8; IR (thin film) 3369, 2920, 2855, 1731, 1480, 1463, 1398, 1366, 1285, 1158, 1067, 939, 869, 772, 722 cm⁻¹; HRMS calcd for C₁₈H₃₆O₄, 339.2511 *m/z* (M+Na)⁺; observed 339.2514 *m/z*. *Anal.* Calcd for C₁₈H₃₆O₄; C, 68.31; H, 11.47. Found: C, 68.01; H, 11.46.

(12R)-2,2-Dimethylpropionic acid-12-hydroxy-13-(toluene-4-sulfonyloxy)-tridecyl ester (G). To a solution of diol **15** (520 mg, 1.7 mmol), dibutyltin oxide (8 mg, 0.03 mmol), and triethylamine (170 mg, 1.7 mmol) in CH₂Cl₂ (5 mL) was added *p*-toluenesulfonyl chloride (320 mg,

1.7 mmol) as a solid in one portion. The reaction was stirred at ambient temperature for 16 h and then quenched with aqueous saturated NaHCO₃ (5 mL). The organic layer was dried over Na₂SO₄, concentrated, and the crude product purified by chromatography (SiO₂, 20% EtOAc-hexanes) to give 650 mg (83%) of tosylate **G** as a white solid: $[\alpha]_D^{23.0} = -5.0$ (c 1.8, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.82 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 4.07-4.04 (m, 3H), 3.91-3.82 (m, 2H), 2.47 (s, 3H), 2.02 (bs, 1H), 1.62 (q, *J* = 7.5 Hz, 2H), 1.46-1.23 (m, 18H), 1.21 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 178.9, 145.3, 132.9, 130.2, 128.2, 74.2, 69.7, 64.7, 39.0, 32.9, 29.7, 29.7, 29.7, 29.4, 28.8, 27.4, 26.1, 25.5, 21.9; IR (thin film) 3504, 2928, 2855, 2360, 1727, 1598, 1480, 1459, 1399, 1363, 1287, 1189, 1098, 1036, 969, 814, 667 cm⁻¹; HRMS calcd for C₂₅H₄₂O₆S, 493.2600 *m/z* (M+Na)⁺; observed 493.2614 *m/z*. *Anal.* Calcd for C₂₅H₄₂O₆S; C, 63.80; H, 8.99. Found: C, 63.72; H, 8.92.

(12R)-2,2-Dimethylpropionic acid-12,13-epoxytridecyl ester (16). To a solution of tosylate **G** (650 mg, 1.4 mmol) in MeOH (12 mL) and CH₂Cl₂ (1.2 mL) at 0 °C was added K₂CO₃ (290 mg, 2.1 mmol) as a solid in one portion. The reaction was stirred at 0 °C for 1 h and then quenched with HCl (1 M, 2.5 mL). The organic layer was washed with aqueous saturated NaHCO₃ (30 mL), dried over MgSO₄, and concentrated to give 410 mg (100%) of epoxide **16** as a colorless oil: $[\alpha]_D^{23.0} = 4.4$ (c 1.9, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 4.05 (t, *J* = 6.5 Hz, 2H), 2.94-2.89 (m, 1H), 2.76 (t, *J* = 3.0 Hz, 1H), 2.47 (dd, *J* = 5.0, 2.5 Hz, 1H), 1.66-1.26 (m, 20H), 1.20 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 178.8, 64.6, 52.6, 47.3, 38.9, 32.7, 29.7, 29.7, 29.7, 29.6, 29.4, 28.8, 27.4, 26.2, 26.1; IR (thin film) 2928, 2855, 1729, 1480, 1460, 1398, 1365, 1284, 1157, 1034, 836, 771 cm⁻¹; HRMS calcd for C₁₈H₃₄O₃, 321.2406 *m/z* (M+Na)⁺; observed 321.2401 *m/z*. *Anal.* Calcd for C₁₈H₃₄O₃; C, 72.44; H, 11.48. Found: C, 72.70; H, 11.73.

(12R, 16R)-2,2-Dimethylpropionic acid-16-(*tert*-butyldiphenylsilyloxy)-12-hydroxy-heptadec-14-ynyl ester (18). To a -78 °C solution of alkyne **17** (840 mg, 4.6 mmol) in THF (9 mL) was added *n*-BuLi (2.4 M in hexanes, 1.8 mL, 4.3 mmol). The reaction was stirred for 30 min and then BF₃·OEt₂ (610 mg, 4.3 mmol) was added in one portion. The reaction was stirred for 30 min and then epoxide **16** (1.0 g, 2.3 mmol) was added as a solution in THF (5 mL) slowly over 5

min. The reaction mixture was stirred at -78 °C for 1 h and then quenched with aqueous saturated NH₄Cl (5 mL) and warmed to room temperature. The aqueous layer was washed with Et₂O (2 x 30 mL) and the combined organic layers were dried over Na₂SO₄ and concentrated. The crude product was purified by chromatography (SiO₂, 10% Et₂O-hexanes) to give 1.3 g (88%) of **18** as a colorless oil: $[\alpha]_D^{23.0} = 55.2$ (c 3.9, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.78-7.75 (m, 2H), 7.72-7.69 (m, 2H), 7.46-7.37 (m, 6H), 4.54-4.48 (m, 1H), 4.07 (t, *J* = 7.0 Hz, 2H), 3.56-3.50 (m, 1H), 2.30 (A of ABXX', *J*_{AB} = 16.5 Hz, *J*_{AX} = 4.5 Hz, *J*_{AX'} = 2.0 Hz, 1H), 2.17 (B of ABXX', *J*_{AB} = 16.5 Hz, *J*_{BX} = 7.0 Hz, *J*_{BX'} = 2.0 Hz, 1H), 1.63 (q, *J* = 7.5 Hz, 2H), 1.42 (d, *J* = 6.5 Hz, 3H), 1.43-1.25 (m, 19H), 1.21 (s, 9H), 1.07 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 178.9, 136.2, 136.1, 136.0, 134.2, 134.0, 130.0, 129.9, 127.9, 127.7, 85.4, 80.7, 70.1, 64.7, 60.3, 40.0, 36.4, 29.8, 29.8, 29.8, 29.8, 29.5, 28.9, 27.9, 27.5, 27.1, 26.2, 25.9, 25.7, 19.4; IR (thin film) 3468, 3072, 2930, 2856, 1729, 1463, 1428, 1398, 1368, 1342, 1285, 1160, 1106, 1082, 1027, 955, 823, 740, 702, 613 cm⁻¹; HRMS calcd for C₃₈H₅₈O₄Si, 629.4002 *m/z* (M+Na)⁺; observed 629.4013 *m/z*. *Anal.* Calcd for C₃₈H₅₈O₄Si; C, 75.20; H, 9.63. Found: C, 75.13; H, 9.53.

(12R, 16R)-2,2-Dimethylpropionic acid-16-(tert-butyldiphenylsilyloxy)-12-(tert-butyl-dimethylsilyloxy)-heptadec-14-ynyl ester (H). To a solution of alcohol **18** (1.6 g, 2.6 mmol), triethylamine (1.1 g, 10.6 mmol), and DMAP (32 mg, 0.3 mmol) in CH₂Cl₂ (10 mL) was added TBSCl (1.2 g, 7.9 mmol) as a solid in one portion. The reaction was stirred at ambient temperature for 24 h and then diluted with hexanes (20 mL) and Et₂O (20 mL). The mixture was washed with HCl (1 M, 2 X 20 mL), aqueous saturated NaHCO₃ (20 mL), dried over MgSO₄, and concentrated. The residue was purified by chromatography (SiO₂, 5% Et₂O-hexanes) to give 1.8 g (93%) of **H** as a colorless oil: $[\alpha]_D^{23.0} = 60.3$ (c 3.2, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.78-7.75 (m, 2H), 7.71-7.68 (m, 2H), 7.45-7.35 (m, 6H), 4.49-4.44 (m, 1H), 4.05 (t, *J* = 7.0 Hz, 2H), 3.69-3.63 (m, 1H), 2.25 (A of ABXX', *J*_{AB} = 16.5 Hz, *J*_{AX} = 5.0 Hz, *J*_{AX'} = 2.0 Hz, 1H), 2.21 (B of ABXX', *J*_{AB} = 16.5 Hz, *J*_{BX} = 7.5 Hz, *J*_{BX'} = 2.0 Hz, 1H), 1.66-1.59 (m, 2H), 1.58-1.50 (m, 1H), 1.36 (d, *J* = 6.5 Hz, 3H), 1.45-1.23 (m, 17H), 1.21 (s, 9H), 1.08 (s, 9H), 0.88 (s, 9H), 0.05 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 178.9, 136.2, 136.0, 134.3, 134.1, 130.0, 129.9, 129.8, 127.9, 127.8, 127.6, 84.3, 81.6, 71.4, 64.7, 60.4, 39.0, 36.8, 31.9, 29.9, 29.9, 29.9, 29.8, 29.8, 29.5, 28.9, 27.9, 27.5, 27.1, 27.1, 26.2, 26.1, 26.0, 25.9, 25.7, 25.4, 22.9, 19.5, 18.3, 14.4, -4.2, -4.4; IR (thin film) 3072, 3050, 2930, 2857, 1730, 1472, 1463, 1428, 1390, 1362, 1344, 1284, 1256, 1160, 1099, 1027, 1006, 956, 940, 836, 824, 775, 739, 702, 613 cm⁻¹; HRMS calcd for C₄₄H₇₂O₄Si₂, 743.4867 *m/z* (M+Na)⁺;

observed 743.4874 m/z . *Anal.* Calcd for $C_{44}H_{72}O_4Si_2$; C, 73.28; H, 10.06. Found: C, 72.91; H, 10.23.

(12 R, 16 R)-12-(tert-Butyldimethylsilyloxy)-16-(tert-butyldiphenylsilyloxy)-heptadec-14-yn-1-ol (I). To a $-78\text{ }^{\circ}\text{C}$ solution of **H** (220 mg, 0.3 mmol) in CH_2Cl_2 (0.6 mL) at was added diisobutylaluminum hydride (1 M in hexanes, 0.9 mL, 0.9 mmol). The reaction was stirred at $-78\text{ }^{\circ}\text{C}$ for 30 min and then quenched with aqueous saturated sodium potassium tartrate (1 mL) and warmed to ambient temperature. The reaction was diluted with hexanes (5 mL) and stirred for 3 h. The aqueous layer was washed with hexanes (5 mL) and the combined organic layers were dried over Na_2SO_4 , and concentrated. The crude product was purified by chromatography (SiO_2 , 15% EtOAc-hexanes) to give 185 mg (97%) of alcohol **I** as a colorless solid: $[\alpha]_D^{23.0} = 72.3$ (c 2.6, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.78-7.75 (m, 2H), 7.71-7.68 (m, 2H), 7.45-7.35 (m, 6H), 4.50-4.44 (m, 1H), 3.69-3.63 (m, 3H), 2.25 (A of ABXX', $J_{AB} = 16.5\text{ Hz}$, $J_{AX} = 5.0\text{ Hz}$, $J_{AX'} = 2.0\text{ Hz}$, 1H), 2.21 (B of ABXX', $J_{AB} = 16.5\text{ Hz}$, $J_{BX} = 7.5\text{ Hz}$, $J_{BX'} = 2.0\text{ Hz}$, 1H), 1.61-1.49 (m, 5H), 1.37 (d, $J = 6.0\text{ Hz}$, 3H), 1.45-1.20 (m, 16H), 1.08 (s, 9H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 136.2, 136.0, 134.3, 134.1, 129.8, 129.8, 127.8, 127.6, 84.3, 81.6, 71.4, 63.3, 60.4, 36.8, 33.1, 29.9, 29.9, 29.9, 29.8, 29.7, 27.9, 27.1, 26.1, 26.0, 25.7, 25.4, 19.4, 18.3, -4.2, -4.4; IR (thin film) 3339, 2930, 2856, 1472, 1428, 1362, 1255, 1161, 1098, 1025, 955, 836, 775, 739, 701 cm^{-1} ; HRMS calcd for $\text{C}_{39}\text{H}_{64}\text{O}_3\text{Si}_2$, 659.4292 m/z ($\text{M}+\text{Na}^+$); observed 659.4280 m/z . *Anal.* Calcd for $\text{C}_{39}\text{H}_{64}\text{O}_3\text{Si}_2$; C, 73.52; H, 10.13. Found: C, 73.59; H, 10.18.

(12 R, 16 R)-12-(tert-Butyldimethylsilyloxy)-16-(tert-butyldiphenylsilyloxy)-heptadec-14-ynal (19). To a solution of alcohol **I** (190 mg, 0.3 mmol), DMSO (230 mg, 2.9 mmol), and diisopropylethylamine (190 mg, 1.5 mmol) in CH_2Cl_2 (1.5 mL) at $0\text{ }^{\circ}\text{C}$ was added SO_3 -pyridine complex (140 mg, 0.9 mmol) as a solid in one portion. The reaction was stirred at $0\text{ }^{\circ}\text{C}$ for 1 h and then quenched with aqueous saturated $\text{Na}_2\text{S}_2\text{O}_3$ (2 mL) and warmed to room temperature. The aqueous layer was washed with hexanes (10 mL) and the combined organic layers were dried over MgSO_4 , and concentrated. The crude product was purified by chromatography (SiO_2 , 5% EtOAc-hexanes) to give 180 mg (97%) of aldehyde **19** as a colorless oil: $[\alpha]_D^{23.0} = 63.2$ (c 5.6,

CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 9.72 (t, *J* = 2.4 Hz, 1H), 7.74-7.69 (m, 2H), 7.67-7.62 (m, 2H), 7.40-7.29 (m, 6H), 4.46-4.38 (m, 1H), 3.65-3.57 (m, 1H), 2.42 (dt, *J* = 7.0, 1.5 Hz, 2H), 2.26 (A of ABXX', *J*_{AB} = 16.5 Hz, *J*_{AX} = 5.5 Hz, *J*_{AX'} = 2.0 Hz, 1H), 2.19 (B of ABXX', *J*_{AB} = 16.5 Hz, *J*_{BX} = 7.5 Hz, *J*_{BX'} = 2.0 Hz, 1H), 1.62-1.44 (m, 4H), 1.31 (d, *J* = 8.5 Hz, 3H), 1.42-1.14 (m, 14H), 1.02 (s, 9H), 0.83 (s, 9H), -0.01 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 203.1, 136.2, 136.0, 134.3, 134.1, 129.9, 129.8, 127.8, 127.7, 84.3, 81.6, 71.4, 60.4, 44.2, 36.8, 29.9, 29.9, 29.8, 29.7, 29.6, 29.4, 27.9, 27.1, 26.1, 25.7, 25.4, 22.3, 19.5, 18.3, -4.2, -4.4; IR (thin film) 2930, 2856, 1728, 1472, 1463, 1428, 1390, 1362, 1255, 1161, 1098, 1025, 1006, 955, 836, 775, 739, 702, 612 cm⁻¹; HRMS calcd for C₃₉H₆₂O₃Si₂, 657.4135 *m/z* (M+Na)⁺; observed 657.4125 *m/z*. Anal. Calcd for C₃₉H₆₂O₃Si₂; C, 73.76; H, 9.84. Found: C, 73.81; H, 10.00.

(3S, 4R, 15R, 19R)-15-(*tert*-Butyldimethylsilanyloxy)-19-(*tert*-butyldiphenylsilanyloxy)-3-(dimethyl-phenyl-silanyl)-eicos-1-en-17-yn-4-ol (J). To a -78 °C solution of KO^{*t*}Bu (105 mg, 0.9 mmol) in THF (4 mL) was added allyldimethylphenylsilane (180 mg, 1.0 mmol). The mixture was stirred for 5 min, then *n*BuLi (2.6 M in hexanes, 0.33 mL, 0.9 mmol) was added slowly via syringe over 5 min. The reaction was stirred at -78 °C for 10 min and then warmed to -45 °C and stirred for 2 h. The mixture was cooled to -78 °C and (-)-Ipc₂BOMe (300 mg, 0.9 mmol) was added as a solution in THF (4 mL) slowly over 5 min. The reaction was stirred for 30 min and then BF₃·OEt₂ (180 mg, 1.3 mmol) was added in one portion. Five minutes later, a solution of aldehyde **19** (300 mg, 0.5 mmol) in hexanes (4 mL) was added slowly over 5 min. The reaction mixture was stirred at -78 °C for 4 h and then quenched with KOH/KH₂PO₄ buffer (1 M, 5 mL) and warmed to room temperature. H₂O₂ (35%, 1 mL) was added and the reaction was stirred at ambient temperature for 16 h. The mixture was partitioned between H₂O and 1:1 hexanes-Et₂O. The organic layer was dried over Na₂SO₄, concentrated, and purified by chromatography (SiO₂, 5% Et₂O-hexanes) to give 340g (88%) of allylsilane **J** as a colorless oil : [α]_D^{23.0} = 55.6 (c, 1.2, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.76 (dt, *J* = 6.5, 1.5 Hz, 2H), 7.70 (dt, *J* = 6.5, 1.5 Hz, 2H), 7.57-7.53 (m, 2H), 7.45-7.40 (m, 2H), 7.35-7.40 (m, 7H), 5.84 (dt, *J* = 17.0, 10.5 Hz, 1H), 5.06 (dd, *J* = 10.5, 2.0 Hz, 1H), 4.92 (ddd, *J* = 17.5, 2.0, 0.5 Hz, 1H), 4.50-4.44 (m, 1H), 3.76-3.70 (m, 1H), 3.69-3.63 (m, 1H), 2.26 (A of ABXX', *J*_{AB} = 16.5 Hz, *J*_{AX} = 5.0 Hz, *J*_{AX'} = 1.5 Hz, 1H), 2.20 (B of ABXX', *J*_{AB} = 16.5 Hz, *J*_{BX} = 7.5 Hz, *J*_{BX'} = 2.0 Hz, 1H), 1.92 (dd, *J* = 10.5, 5.0 Hz, 1H), 1.59-1.49 (m, 2H), 1.45-1.30 (m, 8H), 1.30-1.15 (m, 14H), 1.08 (s, 9H), 0.88 (s, 9H), 0.37 (s, 3H), 0.34 (s, 3H), 0.05 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 138.3, 136.2, 136.0, 135.4, 134.3, 134.1, 129.8,

129.7, 129.3, 128.0, 127.8, 127.6, 115.7, 84.3, 81.6, 71.7, 71.4, 67.2, 60.4, 42.3, 37.4, 36.6, 30.0, 29.9, 29.9, 29.8, 29.8, 29.8, 28.4, 27.9, 27.1, 26.1, 26.0, 25.7, 25.4, 19.5, 19.4, 18.3, -3.1, -3.7, -4.2, -4.4; IR (thin film) 2929, 2856, 1472, 1428, 1362, 1251, 1161, 1111, 1025, 955, 835, 775, 737, 700 cm^{-1} ; HRMS calcd for $\text{C}_{50}\text{H}_{78}\text{O}_3\text{Si}_3$, 833.5157 m/z ($\text{M}+\text{Na}$) $^{+}$; observed 833.5178 m/z . Anal. Calcd for $\text{C}_{50}\text{H}_{78}\text{O}_3\text{Si}_3$; C, 74.01; H, 9.69. Found: C, 73.84; H, 9.68.

(3S, 4R, 15R, 19R)-4,15-bis-(*tert*-Butyldimethylsilanyloxy)-19-(*tert*-butyldiphenylsilyloxy)-3-(dimethyl-phenyl-silanyl)-eicos-1-en-17-yne (2). To a solution of allylsilane **J** (190 mg, 0.2 mmol) in diethyl formamide (DEF, 1.0 mL) was added TBSCl (70 mg, 0.5 mmol) and imidazole (50 mg, 0.7 mmol). The reaction flask was flushed with nitrogen, sealed with a septum, and heated to 40 °C for 48 h. TLC analysis showed some remaining starting material and so an additional TBSCl (70 mg, 0.5 mmol) and imidazole (50 mg, 0.7 mmol) were added to the reaction mixture. After being heated for an additional 24 h, the mixture was partitioned between H_2O and hexanes. The organic layer was dried over MgSO_4 , concentrated, and purified by chromatography (SiO_2 , hexanes) to give 180 mg (85%) of allylsilane **2** as a colorless oil: $[\alpha]_{\text{D}}^{23.0} = 47.6$ (c 3.3, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.78-7.75 (m, 2H), 7.71-7.68 (m, 2H), 7.53-7.49 (m, 2H), 7.45-7.32 (m, 9H), 5.85 (dt, $J = 17.0, 10.5$ Hz, 1H), 4.95 (dd, $J = 10.5, 2.5$ Hz, 1H), 4.74 (dd, $J = 17.0, 2.0$ Hz, 1H), 4.50-4.44 (m, 1H), 3.86-3.81 (m, 1H), 3.69-3.63 (m, 1H), 2.65 (A of ABXX', $J_{\text{AB}} = 16.5$ Hz, $J_{\text{AX}} = 5.0$ Hz, $J_{\text{AX}'} = 1.5$ Hz, 1H), 2.19 (B of ABXX', $J_{\text{AB}} = 16.5$ Hz, $J_{\text{BX}} = 7.5$ Hz, $J_{\text{BX}'} = 2.0$ Hz, 1H), 2.02 (dd, $J = 10.5, 3.5$ Hz, 1H), 1.58-1.47 (m, 2H), 1.37 (d, $J = 6.0$ Hz, 3H), 1.45-1.30 (m, 2H), 1.30-1.11 (m, 16H), 1.08 (s, 9H), 0.88 (s, 18H), 0.35 (s, 3H), 0.31 (s, 3H), 0.05 (s, 6H), 0.01 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 139.1, 136.3, 136.3, 136.1, 134.4, 134.3, 134.1, 129.9, 129.8, 129.0, 127.8, 127.8, 127.7, 114.7, 84.3, 81.7, 73.7, 71.5, 60.5, 40.9, 37.2, 36.9, 30.0, 30.0, 29.9, 29.9, 28.0, 27.2, 26.5, 26.3, 26.2, 25.8, 25.8, 25.5, 19.5, 18.5, 18.4, -2.7, -3.3, -3.4, -3.5, -4.1, -4.3; IR (thin film) 3071, 3050, 2929, 2856, 1472, 1463, 1428, 1390, 1362, 1344, 1254, 1161, 1112, 1083, 1026, 1006, 955, 939, 898, 835, 774, 737, 701, 656, 613 cm^{-1} ; HRMS calcd for $\text{C}_{56}\text{H}_{92}\text{O}_3\text{Si}_4$, 947.6021 m/z ($\text{M}+\text{Na}$) $^{+}$; observed 947.6016 m/z . Anal. Calcd for $\text{C}_{56}\text{H}_{92}\text{O}_3\text{Si}_4$; C, 72.66; H, 10.02. Found: C, 72.86; H, 10.15.

(2R, 2'R, 4R, 4'R, 5S, 5'S)-4,4'-bis-(Dimethylphenylsilyl)-5-[(1R)-1-(*tert*-butyldimethylsilyloxy)-undecyl]-5'-[(1R, 12R, 16R)-1,12-bis-(*tert*-butyldimethylsilyloxy)-16-(*tert*-butyldiphenylsilyloxy)-heptadec-14-yne]-octahydro-2,2'-bifuran (**20**). To a solution of aldehyde **3** (74 mg, 0.14 mmol), allylsilane **2** (66 mg, 0.07 mmol), and flame-dried 4Å powdered molecular sieves (50 mg) in CH_2Cl_2 (0.35 mL) at 0 °C was added SnCl_4 (19 mg, 0.07 mmol) dropwise from a syringe. The reaction mixture was stirred at 0 °C for 4 h and then quenched with triethylamine (0.5 mL) and warmed to room temperature. The mixture was diluted with hexanes (1 mL), Et_2O (1 mL), and aqueous saturated NaHCO_3 (1 mL) and stirred for 20 h. The organic layer was dried over MgSO_4 and concentrated. Chromatographic purification of the crude product (SiO_2 , 5% Et_2O -hexanes) then gave 82 mg (80%) of **20** as a colorless oil: $[\alpha]_{\text{D}}^{23.0} = 26.8$ (c 0.2, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.76 (dt, $J = 6.5, 1.5$ Hz, 2H), 7.70 (dt, $J = 6.5, 1.5$ Hz, 2H), 7.51-7.47 (m, 4H), 7.45-7.32 (m, 12H), 4.50-4.44 (m, 1H), 3.89 (dd, $J = 8.5, 2.5$ Hz, 2H), 3.77-3.70 (m, 2H), 3.69-3.63 (m, 1H), 3.36-3.30 (m, 2H), 2.26 (A of ABXX', $J_{\text{AB}} = 16.0$ Hz, $J_{\text{AX}} = 5.0$ Hz, $J_{\text{AX}'} = 1.5$ Hz, 1H), 2.20 (B of ABXX', $J_{\text{AB}} = 16.0$ Hz, $J_{\text{BX}} = 7.0$ Hz, $J_{\text{BX}'} = 2.0$ Hz, 1H), 1.88-1.81 (m, 2H), 1.67-1.50 (m, 3H), 1.38 (d, $J = 6.5$ Hz, 3H), 1.45-1.12 (m, 42H), 1.08 (s, 9H), 0.88 (s, 27H), 0.31 (s, 6H), 0.30 (s, 6H), 0.05 (s, 6H), 0.02 (s, 6H), 0.01 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.6, 136.2, 136.0, 134.3, 134.1, 134.1, 129.8, 129.8, 129.3, 128.0, 127.8, 127.6, 84.3, 83.4, 83.4, 81.6, 81.4, 74.9, 71.4, 60.4, 36.9, 34.5, 32.4, 32.2, 30.2, 30.1, 30.0, 30.0, 30.0, 30.0, 29.9, 29.9, 29.6, 27.9, 27.1, 26.4, 26.4, 26.3, 26.3, 26.1, 26.0, 25.7, 25.5, 23.0, 19.5, 18.5, 18.3, 14.4, -3.4, -3.4, -3.8, -4.0, -4.0, -4.2, -4.4, -4.4; IR (thin film) 2925, 2856, 1472, 1428, 1361, 1251, 1111, 938, 835, 774, 735, 700 cm^{-1} ; HRMS calcd for $\text{C}_{86}\text{H}_{146}\text{O}_6\text{Si}_6$, 1465.9633 m/z ($\text{M}+\text{Na}$) $^+$; observed 1465.9636 m/z . Anal. Calcd for $\text{C}_{86}\text{H}_{146}\text{O}_6\text{Si}_6$; C, 71.50; H, 10.19. Found: C, 71.45; H, 10.26.

If the [3+2]-annulation was performed at temperatures below 0 °C, significant amounts of the allylation product **K** were obtained (especially at -40 °C or -78 °C).

(2R, 2'R, 5R, 5'R)-5-[(1R)-1-hydroxyundecyl]-5'-[(1R, 12R, 16R)-1,12,16-trihydroxyheptadec-14-yne]-octahydro-2,2'-bifuran (22**).** To a solution of bifuran **20** (44 mg, 0.045 mmol) in DMF (0.45 mL) was added TBAF (1 M in THF, 0.45 mL, 0.45 mmol). The reaction mixture was then heated to 90 °C for 6 h. The reaction was cooled to ambient temperature, diluted with hexanes (10 mL), washed with HCl (1 M, 2 x 10 mL), and aqueous saturated NaHCO₃ (10 mL). The organic layer was dried over Na₂SO₄ and concentrated. The crude product was purified by chromatography (SiO₂, 1% to 2% to 3% MeOH/CH₂Cl₂) to give 13 mg (60%) of the tetraol **22** as a white solid: $[\alpha]_D^{23.0} = 17.0$ (c 0.6, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 4.54 (tq, *J* = 6.5, 2.0 Hz, 1H), 3.92-3.82 (m, 4H), 3.77-3.71 (m, 1H), 3.41-3.37 (m, 2H), 2.72-2.28 (bs, 4H), 2.46 (A of ABXX', *J*_{AB} = 16.5 Hz, *J*_{AX} = 4.5 Hz, *J*_{AX'} = 2.0 Hz, 1H), 2.33 (B of ABXX', *J*_{AB} = 16.5 Hz, *J*_{BX} = 6.5 Hz, *J*_{BX'} = 2.0 Hz, 1H), 2.02-1.92 (m, 4H), 1.72-1.60 (m, 4H), 1.56-1.23 (m, 41H), 0.89 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 85.1, 83.5, 83.4, 82.1, 82.1, 81.1, 74.3, 70.1, 58.6, 36.4, 33.7, 33.7, 32.2, 30.0, 29.9, 29.9, 29.9, 29.7, 29.6, 29.5, 29.5, 29.5, 29.4, 29.3, 28.6, 27.9, 25.9, 25.7, 25.7, 24.9, 22.9, 14.4; IR (thin film) 3435, 2915, 2850, 1466, 1316, 1069, 959, 860 cm⁻¹; HRMS calcd for C₃₆H₆₆O₆, 617.4757 *m/z* (M+Na)⁺; observed 617.4760 *m/z*.

(+)-Asimicin (1**):** Compound **22** (10 mg, 0.0168 mmol) was dissolved in trifluoroacetic anhydride (0.5 ml) and stirred at ambient temperature under a nitrogen atmosphere for 30 minutes. The reaction was concentrated at reduced pressure and dried on a vacuum pump for 1 hour. The residue was dissolved in THF (0.25 ml) and water (0.02 ml) at ambient temperature under a CO atmosphere. Pd(PPh₃)₄ (0.4 mg, 0.00034 mmol) was added as a solution in THF (0.02 ml) and the

reaction was stirred for 2 hours. The reaction was diluted with Et₂O (5 ml) and dried over MgSO₄, then concentrated. The residue was dissolved in hexanes (0.2 ml) and CH₂Cl₂ (0.02 ml) and the flask was wrapped in aluminum foil to protect from light. AgNO₃/SiO₂ was added and the reaction was stirred for 2 hours. The reaction was filtered through Celite and concentrated and the residue was purified by chromatography (SiO₂, CH₂Cl₂). The purified material was dissolved in MeOH (0.5 ml) and KCN (1 mg, 0.02 mmol) was added to the reaction. After 20 minutes, the reaction was diluted with Et₂O (5 ml) and washed with water (1 ml). The organic layer was dried over MgSO₄, concentrated, and purified by chromatography (SiO₂, 20% acetone/CH₂Cl₂). The purified material was dissolved in freshly distilled CH₃CN (5 ml) and washed with hexanes (5 X 2 ml). The CH₃CN layer was concentrated to give 4.9 mg of (+)-asimicin **1** (47%): $[\alpha]_D^{23.0} = 13.6$ (c 0.3, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.18 (d, *J* = 1 Hz, 1H), 5.09-5.02 (m, 1H), 3.91-3.80 (m, 5H), 3.43-3.35 (m, 2H), 2.52 (d, *J* = 15.2 Hz, 1H), 2.43 (bs, 2H), 2.39 (dd, *J* = 15.2, 8.0 Hz, 1H), 2.24 (bs, 1H), 2.02-1.91 (m, 4H), 1.74-1.58 (m, 4H), 1.56-1.22 (m, 41H), 0.87 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 Mhz, CDCl₃) δ 151.8, 151.8, 131.2, 83.1, 81.8, 78.0, 74.1, 70.0, 69.9, 37.4, 33.4, 33.3, 29.9, 29.7, 29.7, 29.6, 29.5, 29.3, 29.0, 28.4, 25.6, 25.6, 25.5, 22.7, 19.1, 14.1; IR (thin film) 3436, 2929, 2854, 1753, 1465, 1319. 1068, 953, 668 cm⁻¹; HRMS calcd for C₃₇H₆₆O₇, 645.4706 *m/z* (M+Na)⁺; observed 645.4720 *m/z*.

Comparison of Published ¹H NMR Data for Synthetic Asimicin

Sinha & Keinan ^{3c}	Marshall ^{3d}	Roush (this study)
7.17 (s, 1H)	7.18 (bs, 1H)	7.18 (d, <i>J</i> = 1Hz, 1H)
5.06-5.01 (q, <i>J</i> = 6.6 Hz, 1H)	5.06 (q, <i>J</i> = 7.7 Hz, 1H)	5.06 (q, <i>J</i> = 6.4 Hz, 1H)
3.84-3.80 (m, 5H)	3.91-3.79 (m, 5H)	3.91-3.80 (m, 5H)
3.40-3.34 (m, 2H)	3.39 (q, <i>J</i> = 5.0 Hz, 1H)	3.43-3.35 (m, 2H)
2.52-2.48 (d, <i>J</i> = ?, 1H)	2.54 (d, <i>J</i> = 15.0 Hz, 1H)	2.52 (d, <i>J</i> = 15.2 Hz, 1H)
	2.45-2.34 (m, 1H)	2.43 (bs, 2H)
2.40-2.34 (d, <i>J</i> = ?, 1H)	2.11 (vbs, 3H)	2.39 (dd, <i>J</i> = 15.2, 8.0 Hz, 1H)
	2.04-1.91 (m, 2H)	2.24 (bs, 1H)
1.96-1.94 (m, 4H)	1.74-1.59 (m, 4H)	2.02-1.91 (m, 4H)
	1.43 (q, <i>J</i> = 6.9 Hz, 1H)	1.74-1.58 (m, 4H)
1.75-1.23 (m, 48H)	1.53-1.19 (m, 41H)	1.56-1.22 (m, 41H)
0.85 (t, <i>J</i> = 6.6 Hz, 3H)	0.88 (t, <i>J</i> = 6.9 Hz, 1H)	0.87 (t, <i>J</i> = 7.2 Hz, 3H)

Comparison of Published ^{13}C NMR Data for Synthetic Asimicin

Isolation ^{8c}	Marshall ^{3d}	Roush (this study)	Carbon Number ^{8c}
174.6	---	---	1
151.8	151.7	151.8	35
131.1	---	131.2	2
83.1	83.1	83.1	16, 23
81.8	81.8	81.8	19, 20
78.0	79.9	78.0	36
74.0	74.1	74.1	15, 24
69.9	70.0	70.0	4
37.4	37.4	37.4	3
33.4	33.4	33.4	14
33.3	33.3	33.3	25
31.9	31.9	31.9	5
29.7	---	29.7	32
29.6	29.6	29.6	26-30
29.5	29.5	29.5	7-13
29.3	29.3	29.3	31
28.9	29.0	29.0	6
28.4	28.4	28.4	17
25.5	25.6	25.6	18, 21, 22
22.7	22.7	22.7	33
19.1	19.1	19.1	37
14.1	14.1	14.1	34

Comparison of Published ^1H NMR Data for Mosher Ester Derivatives of Synthetic Asimicin

Roush – Observed for (S)-Ester	Literature Value for (S)-Mosher Esters ^{8d}	Carbon Number	Literature Value for (R)-Mosher Esters ^{8d}	Roush – Observed for (R)-Ester
2.57	2.56	3	2.66, 2.58	2.65, 2.58
Not clear	1.63	5	1.61	Not clear
1.57	1.56	14,25	1.45	1.46
3.93	3.93	16,23	3.97	3.98
3.77	3.76	19,20	3.92	3.92
6.71	6.70	35	6.96	6.96
4.84	4.84	36	4.88	4.88
1.27	1.26	37	1.29	1.30