Total Synthesis of (+)-Amphidinolide A. Assembly of the Fragments

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To a solution of acid **14** (2.202 g, 26.2 mmol) and 9-fluorenylmethanol (5.164 g, 26.3 mmol) in benzene (60 mL) was added CSA (600 mg, 2.58 mmol). The reaction mixture was heated to reflux in a Dean-Stark trap. After 24 h, the reaction mixture was diluted with ether, washed with saturated NaHCO_3 (1 x) and brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (10% to 15% to 20% EtOAc in petroleum ether) gave ester **8** (6.627 g, 96%) as a low melting white solid: R_f = 0.55 (30% Et_2O /70% petroleum ether); IR (film from CH_2Cl_2) 3058, 2958, 2243, 1709 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.77 (d, J = 7.6 Hz, 2H), 7.63 (d, J = 7.3 Hz, 2H), 7.42 (t, J = 7.4 Hz, 2H), 7.33 (t, J = 7.4 Hz, 2H), 4.42 (d, J = 7.6 Hz, 2H), 4.25 (t, J = 7.6 Hz, 1H), 2.05 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 153.7, 143.3, 141.2, 127.9, 127.1, 125.1, 120.0, 80.1, 72.3, 67.6, 46.4, 3.9. Anal calcd for $\text{C}_{18}\text{H}_{14}\text{O}_2$: C, 82.42 H, 5.38. Found: C, 82.37, H, 5.47.

To a solution of allyltributyltin (11.0 mL, 11.7 g, 35.5 mmol) in THF (100 mL) at -78°C was added $n\text{-BuLi}$ (15.5 mL, 2.37 M in hexanes, 36.7 mmol). After 30 min, the solution was added to a suspension of CuI (6.651 g, 34.9 mmol) in THF (50 mL) at -78°C . The solution was warmed to -30°C over 45 min, cooled to -78°C and a solution of ester **8** (6.008 g, 22.9 mmol) in THF (70 mL) at -78°C was added via cannula. After 15 min, the reaction mixture was quenched with saturated NH_4Cl , warmed to room temperature, and diluted with ether and water. The aqueous phase was extracted with ether (5 x) followed by EtOAc (4 x) and the combined organic extracts were washed with saturated NH_4Cl (1 x) and brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (3% to 6% EtOAc in

petroleum ether) gave alkene **5** (6.73 g, 97%) as a colorless oil: R_f = 0.41 (10% Et₂O/90% petroleum ether); IR (film from CH₂Cl₂) 3067, 2940, 1954, 1908, 1714 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.76 (d, J = 7.3 Hz, 2H), 7.61 (d, J = 7.6 Hz, 2H), 7.40 (t, J = 6.8 Hz, 2H), 7.31 (t, J = 7.3 Hz, 2H), 5.75-5.86 (m, 2H), 5.17 (s, 1H), 5.12 (d, J = 7.1 Hz, 1H), 4.40 (d, J = 7.1 Hz, 2H), 4.24 (t, J = 7.1 Hz, 1H), 2.91 (d, J = 6.6 Hz, 2H), 2.14 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 166.6, 158.8, 144.0, 141.3, 134.1, 127.7, 127.0, 125.0, 120.0, 117.9, 116.0, 65.7, 46.8, 45.0, 18.8. Anal calcd for C₂₁H₂₀O₂: C, 82.86 H, 6.62. Found: C, 83.05, H, 6.49.

To a solution of **39** (55.2 g, 313 mmol) in 350 mL of THF at -78 °C was added 115 mL (297 mmol) of a 2.58 M solution of *n*-butyllithium in hexanes over 15 minutes. The resulting clear, pale yellow reaction mixture was allowed to stir at -78 °C for 3.5 h whereupon 10.5 g (142 mmol) of ethyl formate was added dropwise via syringe over 5 min and the resulting mixture was stirred at -78 °C for 1 h then allowed to warm to rt over 1 h. The reaction mixture was diluted with 300 mL of diethyl ether and 30 mL of saturated aqueous sodium bicarbonate was added dropwise followed by addition of 250 mL of water. The resulting layers were separated and the aqueous portion was extracted with additional diethyl ether (3 x 150 mL) and the combined organic extracts were washed with brine (3 x 100 mL), dried (MgSO₄), filtered, and concentrated *in vacuo* to afford 65 g of the crude bispropargylic alcohol intermediate (TLC R_f = 0.58 in 75% Et₂O in petroleum ether) as a dark red/orange oil. This material was subjected to the next step without further purification due to its instability.

The crude propargyl alcohol was dissolved in 600 mL of THF and cooled to -40 °C whereupon 149 mL (497 mmol) of 65% w/w solution of Red-Al in toluene was added dropwise via syringe over 30 min with concomitant hydrogen gas evolution. The resulting clear, reddish-orange mixture was allowed to stir while warming from -40 °C to 0 °C over 4.5 h. The reaction was then carefully quenched at 0 °C by dropwise addition of 30 mL of a 1 M aqueous solution of Rochelle's salts causing vigorous gas evolution. The mixture was allowed to warm to rt whereupon and additional 150 mL of 1 M aqueous Rochelle's salts, 100 mL of water, and 500 mL of diethyl ether were added followed by vigorous stirring for 2 h. The resulting

homogeneous layers were then separated and the aqueous phase was diluted with 200 mL of additional water before being extracted with diethyl ether (3 x 150 mL). The combined organic extracts were washed with brine (3 x 100 mL), dried (MgSO₄), filtered, and concentrated on a rotary evaporator to afford 69.5 g of the crude alcohol **40** containing residual solvents and 2-methoxyethanol from quenching of the Red-Al reagent. The residual solvents and 2-methoxyethanol were removed via Kugelrohr distillation at 70 °C at 1 Torr over 20-30 min to afford 59.4 g of a dark yellow/brown oil which was purified by flash chromatography on silica gel (elution with 75% Et₂O/petroleum ether) to deliver 33.2 g (61%) of pure **40** as a yellow oil. Due to the apparent instability of **40**, this material was not stored for prolonged periods but was converted to its more stable silyl ether derivative **41**. Physical data for **40**: TLC R_f = 0.35 (75% Et₂O in petroleum ether). IR (film): 3414.6, 3001.4, 2838.7, 1612.3, 1585.9, 1246.6, 1033.3, 971.6, 818.5 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 7.24 (d, *J* = 8.8 Hz, 4 H), 6.86 (d, *J* = 8.8 Hz, 4 H), 5.85-5.71 (m, 4 H), 4.64 (br d, *J* = 3.9 Hz, 1 H), 4.42 (s, 4 H), 3.98 (d, *J* = 3.9 Hz, 4 H), 3.77 (s, 6 H), 2.24 (d, *J* = 3.9 Hz, 1 H). ¹³C NMR (75 MHz, CDCl₃) δ 159.04, 133.77, 130.08, 129.28, 127.62, 113.65, 72.11, 71.82, 69.59, 55.13.

To a solution of alcohol **40** (29.3 g, 0.076 mmol) in 100 mL of DMF at 0°C were successively added 15.5 g (0.228 mmol) of imidazole and 14.9 g (0.099 mmol) of *t*-butyldimethylsilyl chloride. The resulting mixture was allowed to warm to rt and stir for 48 h then poured into 300 mL of saturated aqueous ammonium chloride and 300 mL of diethyl ether. The mixture was stirred until two homogeneous layers resulted (~ 2 min) and the layers were separated. The aqueous phase was extracted with diethyl ether (3 x 150 mL) and the combined organic extracts were washed with water (3 x 80 mL), brine (3 x 50 mL), then dried (MgSO₄), filtered, and concentrated *in vacuo* to give 39.4 g of crude **41** as a golden yellow oil. Flash chromatography on silica gel (elution with 20% Et₂O in petroleum ether) afforded 33.7 g (89%) of pure **41** as pale yellow oil. TLC R_f = 0.40 (20% Et₂O in petroleum ether). IR (film): 2930.6, 2855.1, 1613.0, 1585.9, 1513.7, 1249.0, 1102.6, 835.9, 776.8 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 7.26 (d, *J* = 8.8 Hz, 4 H), 6.86 (d, *J* = 8.8 Hz, 4 H), 5.76 (dt, *J* = 15.6, 4.9 Hz, 2 H), 5.69 (dd, *J*

= 15.6, 4.4 Hz, 2 H), 4.68 (app t, J = 4.4 Hz, 1 H), 4.43 (s, 4 H), 3.99 (d, J = 4.9 Hz, 4 H), 3.79 (s, 6 H), 0.91 (s, 9 H), 0.07 (s, 6 H). ^{13}C NMR (75 MHz, CDCl_3) δ 159.08, 134.94, 130.29, 129.31, 126.15, 113.68, 72.83, 71.56, 69.77, 55.19, 25.84, 18.30, -4.66. Anal. Calcd for $\text{C}_{29}\text{H}_{42}\text{SiO}_5$: C, 69.84; H, 8.49. Found: C, 69.70; H, 8.34.

To a mixture of potassium hexaferrocyanide (59.1 g, 179 mmol), potassium carbonate (24.8 g, 179 mmol), sodium bicarbonate (15.1 g, 179 mmol), methanesulfonamide (5.69 g, 59.8 mmol), (DHQD)₂-PHAL (0.935 g, 1.20 mmol), potassium osmate(VI) dihydrate (0.220 g, 0.598 mmol) was added 300 mL of water and 250 mL of *tert*-butanol and the resulting mixture was stirred at rt for 15 min to afford a homogeneous solution. The mixture was then cooled to 0°C at which time a suspension of 29.8 g (59.8 mmol) of **41** in 50 mL of *tert*-butanol was added *via* pipette. The reaction mixture was vigorously stirred at 0°C for 38 h then quenched at 0°C by the addition of 82 g of sodium sulfite. The resulting mixture was allowed to warm to rt with stirring over 1 h then 250 mL of water and 500 mL of ethyl acetate were added. The resulting layers were separated and the aqueous portion was extracted with additional ethyl acetate (3 x 200 mL). The combined organic layers were then washed with 2 N aqueous sodium hydroxide solution (2 x 200 mL), water (2 x 150 mL), and brine (2 x 200 mL), then dried over MgSO_4 , filtered, and concentrated *in vacuo* to afford 31.5 g of the crude diol as a dark yellow/green oil. Purification of the product by flash chromatography on silica gel (elution with 70% Et_2O in petroleum ether) yielded 25.02 g (79%) of a pale yellow oil as the inseparable diols **42** and **43** in a >15:1 diastereoselectivity. Physical data for **42** (major diastereomer): TLC R_f = 0.21 (50% Et_2O in petroleum ether). IR (film): 3474.6, 2953.9, 2856.6, 1613.2, 1586.3, 1248.8, 1099.8, 837.2, 778.9 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 7.24 (d, J = 8.8 Hz, 2 H), 7.22 (overlapping d, J = 8.8 Hz, 2 H), 6.86 (d, J = 8.8 Hz, 2 H), 6.84 (overlapping d, J = 8.8 Hz, 2 H), 5.82 (dt, J = 15.6, 4.9 Hz, 1 H), 5.72 (dd, J = 15.6, 5.9 Hz, 1 H), 4.46 (m, 2 H), 4.42 (s, 2 H), 4.36 (app t, J = 4.9 Hz, 1 H), 4.28 (br m, 1 H), 3.99 (d, J = 4.9 Hz, 2 H), 3.78 (s, 3 H), 3.77 (s, 3 H), 3.54 (dd, J = 5.9, 1.5 Hz, 2 H), 3.48 (app t, J = 5.9 Hz, 1 H), 3.17 (d, J = 3.4 Hz, 1 H), 2.88 (d, J = 6.8 Hz, 1 H), 0.90

(s, 9 H), 0.11 (s, 3 H), 0.06 (s, 3 H). ^{13}C NMR (75 MHz, CDCl_3) δ 159.17, 159.08, 131.99, 130.13, 129.79, 129.36, 129.23, 129.03, 113.71, 113.68, 93.94, 75.75, 73.52, 73.13, 71.98, 71.56, 69.46, 68.62, 55.14, 22.74, 18.00, -4.46, -5.08. Anal. Calcd for $\text{C}_{29}\text{H}_{44}\text{SiO}_7$: C, 65.38; H, 8.32. Found: C, 65.16; H, 8.18.

Physical data for **43** (minor diastereomer): TLC R_f = 0.21 (50% Et_2O in petroleum ether). ^1H NMR (300 MHz, CDCl_3) δ 7.24 (d, J = 8.8 Hz, 4 H), 6.86 (d, J = 8.8 Hz, 2 H), 6.84 (overlapping d, J = 8.8 Hz, 2 H), 5.82 (dt, J = 15.6, 4.9 Hz, 1 H), 5.72 (dd, J = 15.6, 5.9 Hz, 1 H), 4.46 (m, 2 H), 4.42 (m, 2 H), 4.27 (app t, J = 5.9 Hz, 1 H), 3.98 (d, J = 4.4 Hz, 2 H), 3.82 (m, 1 H), 3.78 (s, 3 H), 3.77 (s, 3 H), 3.53 (m, 2 H), 3.48-3.44 (m, 1 H), 3.17 (br s, 1 H), 2.80 (br s, 1 H), 0.88 (s, 9H), 0.06 (s, 3 H), 0.04 (s, 3 H).

A solution of the inseparable diastereomeric diols **42/43** (25.2 g, 47.5 mmol) in 150 mL of CH_2Cl_2 and 61.8 g (475 mmol) of 1,1-dimethoxycyclopentane at 0°C was treated with *p*-toluenesulfonic acid (0.270 g, 1.42 mmol). After stirring at 0°C for 1.75 h, the reaction mixture was neutralized by the addition of solid NaHCO_3 (ca. 2 g) and allowed to warm to rt and stir overnight. Filtration of the mixture through a short pad of silica gel (3 x 7 cm) washing with 200 mL of additional diethyl ether then provided a clear filtrate which was concentrated *in vacuo* on a rotary evaporator to provide approximately 75 mL of the crude acetal intermediate (TLC R_f = 0.90, 70% Et_2O in petroleum ether) as a pale yellow liquid which contained some residual 1,1-dimethoxycyclopentane.

The crude material was dissolved in 100 mL of anhydrous THF and the solution was cooled to 0°C whereupon 57 mL (57.0 mmol) of a 1.0 M solution of TBAF in THF was added dropwise. The resulting mixture was stirred at 0°C for 2 h and at rt for 14 h then the mixture was partitioned between 50 mL of saturated aqueous ammonium chloride solution and 50 mL of diethyl ether and the layers were separated. The aqueous phase was extracted with additional diethyl ether (3 x 50 mL) and the combined organic extracts were washed with brine (3 x 30

mL), dried over MgSO₄, filtered, and concentrated *in vacuo* on a rotary evaporator to afford the crude product as an orange liquid which contained residual 1,1-dimethoxycyclopentane.

Purification by flash chromatography on silica gel initially eluting with 70% Et₂O in petroleum ether then increasing to 80% Et₂O in petroleum ether provided 21.5 g (94%) of an inseparable 13 : 1 diastereomeric mixture of as a pale yellow oil.

Physical data for the major diastereomer: TLC R_f = 0.31 (70% Et₂O in petroleum ether). IR (film): 3442.1, 2954.8, 2869.3, 1612.7, 1586.0, 1513.8, 1248.4, 1107.7, 1035.0, 975.3, 820.0 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 7.24 (d, *J* = 8.3 Hz, 2 H), 7.22 (overlapping d, *J* = 8.3 Hz, 2 H), 6.84 (d, *J* = 8.3 Hz, 4 H), 5.90 (dt, *J* = 15.6, 5.9 Hz, 1 H), 5.74 (dd, *J* = 15.6, 5.4 Hz, 1 H), 4.48 (s, 2H), 4.40 (s, 2 H), 4.21 (br m, 1 H), 4.06 (dd, *J* = 12.2, 5.4 Hz, 1 H), 3.96 (d, *J* = 5.4 Hz, 2 H), 3.76 (s, 6 H), 3.69 (dd, *J* = 7.3, 5.9 Hz, 1 H), 3.57 (dd, *J* = 10.3, 5.4 Hz, 1 H), 3.50 (dd, *J* = 10.3, 5.4 Hz, 1 H), 2.91 (br s, 1 H), 1.89-1.71 (m, 4 H), 1.71-1.64 (m, 4 H). ¹³C NMR (75 MHz, CDCl₃) δ 159.12, 159.00, 130.99, 130.15, 129.48, 129.29, 129.21, 128.71, 119.20, 113.65, 113.58, 80.96, 76.81, 73.02, 71.56, 71.52, 70.30, 69.56, 55.06, 37.22, 37.07, 36.97, 23.42, 23.24. Anal. Calcd for C₂₈H₃₆O₇: C, 69.40; H, 7.49. Found: C, 69.19; H, 7.30.

To a mixture of the alcohols (21.5 g, 44.6 mmol) and 26.2 g (313 mmol) of sodium bicarbonate in 250 mL of methylene chloride at 0°C was added 24.6 g (57.9 mmol) of Dess-Martin periodinane as a solid over 1 minute. The resulting heterogeneous mixture was allowed to warm to rt and stir for 30 min, then the mixture was cooled to 0°C whereupon three 50 mL portions of 1 N aqueous sodium sulfite solution was slowly added over 15 minutes. After warming to rt and stirring vigorously for an additional 2 h, 50 mL of water was added and the resulting layers were separated. The aqueous portion was extracted with diethyl ether (3 x 75 mL). The combined extracts were washed with brine (2 x 75 mL), dried over MgSO₄, filtered, and concentrated *in vacuo* to afford 22.8 g of the crude enone as a yellow oil. Purification by flash chromatography (elution with 40% Et₂O in petroleum ether) provided 19.5 g (91%) of pure

44 as a pale yellow oil. Enantiomeric purity of **44** was determined to be 90% ee by chiral HPLC analysis : Chiralpak AD at 23°C, 1.0 mL/min flow rate, 20% isopropanol-heptane, 254 nm, retention times for enantiomers of **44** : 12.03 min (minor), 13.20 min (major) as compared to a racemic standard of **44**. TLC R_f = 0.65 (60% Et₂O in petroleum ether). IR (film): 2955.9, 2869.4, 1691.8, 1629.7, 1612.7, 1513.9, 1248.4, 1110.8, 1034.7, 819.4 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 7.24 (d, J = 8.3 Hz, 4 H), 7.04 (dt, J = 15.6, 3.9 Hz, 1 H), 6.88-6.78 (m, 5 H), 4.52 (s, 2 H), 4.47 (s, 2 H), 4.32 (d, J = 7.3 Hz, 1 H), 4.25-4.20 (m, 1 H), 4.16-4.14 (m, 2 H), 3.78 (s, 3 H), 3.77 (s, 3 H), 3.68 (dd, J = 10.7, 3.9 Hz, 1 H), 3.59 (dd, J = 10.7, 5.4 Hz, 1 H), 1.91-1.86 (m, 2 H), 1.83-1.76 (m, 2 H), 1.73-1.68 (m, 4 H). ¹³C NMR (75 MHz, CDCl₃) δ 197.58, 159.22, 159.11, 145.15, 129.81, 129.57, 129.28, 129.19, 123.98, 120.86, 113.73, 113.65, 80.90, 77.31, 73.05, 72.37, 69.77, 68.51, 55.14 (two carbons), 36.73, 36.57, 23.56, 23.16. Anal. Calcd for C₂₈H₃₄O₇: C, 69.69; H, 7.10. Found: C, 69.72; H, 6.88. $[\alpha]_D^{26}$ = +8.43 (c 1.79, CH₂Cl₂).

A 1-L round-bottomed flask was charged with potassium hexaferriocyanide (40.2 g, 122 mmol), potassium carbonate (16.9 g, 122 mmol), sodium bicarbonate (10.2 g, 122 mmol), methanesulfonamide (3.86 g, 40.6 mmol), (DHQD)₂-PHAL (0.950 g, 1.22 mmol), and potassium osmate(VI) dihydrate (0.450 g, 1.22 mmol) and 175 mL of water and 100 mL of *tert*-butanol was added. The mixture was stirred vigorously at rt for 10 min then cooled to 0°C and stirred for an additional 15 minutes. At this time, a suspension of 19.5 g (40.6 mmol) of **44** in 50 mL of *tert*-butanol was added *via* pipette. The flask was rinsed with 25 mL of additional *tert*-butanol and the rinse was added. The resulting orange, heterogeneous reaction mixture was vigorously stirred at 0-3°C for 24 h then quenched by the addition of 70 g of sodium sulfite along with 300 mL of water followed by warming to rt over 1 h with vigorous stirring. After adding 400 mL of ethyl acetate, the layers were separated and the aqueous portion was extracted with additional ethyl acetate (3 x 350 mL). The combined organic extracts were washed with 1 N aqueous

sodium hydroxide (2 x 300 mL), water (4 x 300 mL), and brine (3 x 200 mL), then dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo* to afford a yellow-green oil as the crude diol. This material was dissolved in diethyl ether (~300 mL) and the solution was filtered through a short pad of silica gel (3 x 8 cm) eluting with an additional liter of diethyl ether. The resulting clear filtrate was concentrated *in vacuo* to afford 18.03 g of a white solid as the partially purified diol intermediate (TLC R_f = 0.25, 50% Et₂O in petroleum ether).

The diol mixture was dissolved in 400 mL of anhydrous methylene chloride and 52.8 g (406 mmol) of 1,1-dimethoxycyclopentane was added. After cooling the mixture to 0°C, 0.463 g (2.44 mmol) of *p*-toluenesulfonic acid hydrate was added and the resulting mixture was stirred at 0°C for 4 h then ca. 3 g of solid sodium bicarbonate was added and the mixture was warmed to rt and stirred overnight (14 h). The contents were filtered and concentrated on a rotary evaporator to remove the solvents to give the desired product which contained the excess 1,1-dimethoxycyclopentane. Since the desired product appeared to be unstable to silica gel chromatography due to significant “streaking” of the product when analyzed by TLC (50% Et₂O in petroleum ether, R_f = 0.63), the 1,1-dimethoxypentane was removed by Kugelrohr distillation by heating the crude mixture to 60°C at 0.2 Torr for 30 minutes. The purified product (20.6 g, 88%) was then recovered from the distillation pot as an 8 : 1 diastereomeric mixture of **45** and **46** respectively, as a yellow oil. The diastereomeric ratio of 8:1 was determined by the relative integration areas of the major diastereomer resonance at 4.29 ppm (m, 2 H) compared to the minor diastereomer resonance at 4.21 ppm (m, 2 H). Due to the apparent instability of the product, a satisfactory elemental analysis was not obtained. Physical data for **45** (major diastereomer) : TLC R_f = 0.63 (50% Et₂O in petroleum ether). IR (film): 2956.6, 2872.0, 1730.3, 1612.7, 1586.1, 1513.9, 1248.5, 1106.0, 973.8, 820.3 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 7.22 (d, J = 8.8 Hz, 4 H), 6.84 (d, J = 8.8 Hz, 4 H), 4.56 (d, J = 6.8 Hz, 2 H), 4.48 (s, 4 H), 4.29 (m, 2 H), 3.77 (s, 6 H), 3.63 (dd, J = 10.2, 4.4 Hz, 2 H), 3.57 (dd, J = 10.2, 5.4 Hz, 2 H), 1.83-1.81 (m, 4 H), 1.78-1.71 (m, 4 H), 1.64 (br s, 8 H). ¹³C NMR (75 MHz, CDCl₃) δ 205.51, 159.19, 129.78, 129.34, 121.18, 113.69, 79.62, 76.68, 73.10, 69.75, 55.19, 36.86, 36.65, 23.56, 23.24.

To a solution of 20.6 g (35.4 mmol) of **45/46** in 100 mL of THF at 0°C was added 106 mL (106 mmol) of a 1.0 M solution of trimethylsilylmethylmagnesium chloride in diethyl ether over 15 minutes. The resulting clear yellow solution was allowed to warm to rt and stir for 4 h then carefully quenched by a slow, dropwise addition of 50 mL of water causing vigorous bubbling of the reaction mixture. After 30 min, 200 mL of saturated aqueous ammonium chloride and 200 mL of diethyl ether were then added and the mixture was stirred vigorously for 1 h. The resulting layers were separated and the aqueous portion was extracted with additional diethyl ether (3 x 200 mL). The combined organic extracts were washed with brine (3 x 50 mL), dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford 23.6 g of the crude hydroxysilane intermediate as a yellow oil.

The crude hydroxysilane was dissolved in 200 mL of anhydrous THF and 141.4 mL (70.7 mmol) of a 0.5 M solution of potassium hexamethyldisilazide (KHMDs) in toluene was added. The resulting mixture was stirred at rt for 18 h then partitioned between 300 mL of water and 200 mL of diethyl ether. The aqueous portion was extracted with diethyl ether (3 x 150 mL) and the combined organic extracts were washed with brine (3 x 100 mL), dried over magnesium sulfate, filtered, and concentrated *in vacuo* to give 20.3 g of a yellow oil as the crude product. Purification by flash chromatography on silica gel eluting with 35% diethyl ether in petroleum ether afforded 14.8 g (72%) of pure **47/48** in an 8:1 diastereomeric mixture as a pale yellow oil. The diastereomeric ratio was determined by the relative integration areas of the major diastereomer resonance at 5.36 ppm (s, 2 H) compared to the minor diastereomer resonance at 5.31 ppm (s, 2 H). Physical data for **47** (major diastereomer): TLC R_f = 0.70 (60% Et₂O in petroleum ether). IR (film): 2956.1, 2871.4, 1650.6, 1612.8, 1586.1, 1513.9, 1248.1, 1101.8, 1035.4, 820.2 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 7.22 (d, J = 8.8 Hz, 4 H), 6.84 (d, J = 8.8 Hz, 4 H), 5.36 (s, 2 H), 4.46 (s, 4 H), 4.22 (d, J = 7.8 Hz, 2 H), 4.07-4.02 (m, 2 H), 3.76 (s, 6 H), 3.56 (dd, J = 10.3, 3.4 Hz, 2 H), 3.48 (dd, J = 10.7, 5.4 Hz, 2 H), 1.86-1.82 (m, 4 H), 1.80-1.72 (m, 4 H), 1.66-1.58 (m, 8 H). ¹³C NMR (75 MHz, CDCl₃) δ 159.09, 143.14, 129.94, 129.26,

119.07, 115.76, 113.61, 79.91, 78.00, 72.99, 69.36, 55.13, 37.34, 37.04, 23.53, 23.32. Anal. Calcd for C₃₄H₄₄O₈: C, 70.32; H, 7.64. Found: C, 70.34; H, 7.80.

To a 0°C solution of 11.5 g (19.8 mmol) of **47/48** in 250 mL of methylene chloride at rt were successively added 7.6 mL of water and 13.5 g (59.4 mmol) of DDQ. The resulting dark green mixture was allowed to warm to rt and stir for 1.25 h and the resulting tan, heterogeneous mixture was filtered through a pad of celite to remove the solids and the pad was washed with 200 mL of additional methylene chloride. The resulting filtrate was washed with saturated aqueous sodium sulfite (3 x 80 mL), saturated aqueous sodium bicarbonate (80 mL), and brine (100 mL). The solution was dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to provide approximately 13 g of the crude diol mixture as a yellow liquid. Purification by flash chromatography (gradient elution from 80% Et₂O in petroleum ether to 100% Et₂O) initially afforded fractions containing the less polar minor diastereomer **70** (TLC R_f = 0.48, 100% Et₂O) with later fractions providing 5.6 g (83%) of the pure major diastereomer **57** as a pale yellow oil. Physical data for **57** (major diastereomer): TLC R_f = 0.36 (100% Et₂O). IR (film): 3431.3, 2958.6, 2874.4, 1649.8, 1334.5, 1112.0, 1039.7, 985.6 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 5.42 (s, 2 H), 4.32 (d, *J* = 8.3 Hz, 2 H), 3.98 (app dt, *J* = 7.8, 3.9 Hz, 2 H), 3.82 (dd, *J* = 12.2, 3.4 Hz, 2 H), 3.64 (dd, *J* = 12.2, 3.9 Hz, 2 H), 2.46 (br s, 2 H), 1.86-1.76 (m, 8 H), 1.71-1.57 (m, 8 H). ¹³C NMR (75 MHz, CDCl₃) δ 142.61, 118.98, 115.66, 80.98, 77.26, 61.43, 37.23, 37.02, 23.23, 23.20. Anal. Calcd for C₁₈H₂₈O₆: C, 63.51; H, 8.29. Found: C, 63.67, H, 8.14. [α]_D²⁴ = + 6.44 (c 1.79, CH₂Cl₂).

To a suspension of 0.73 g (18.2 mmol) of 60% sodium hydride dispersion in mineral oil in 80 mL of THF at rt was added a solution of 5.9 g (17.3 mmol) of diol **9** in 30 mL of THF via cannula. The resulting mixture was allowed to stir at rt for 5 h affording a thick, heterogeneous mixture which became difficult to stir. As a result, 20 mL of additional THF was added to aid in stirring the mixture followed by the addition of 2.61 g (17.3 mmol) of *t*-butyldimethylsilyl chloride. After stirring at rt for 48 h, the mixture was partitioned between 100 mL of saturated aqueous ammonium chloride and 100 mL of diethyl ether. The aqueous portion was extracted with additional diethyl ether (3 x 70 mL) and the combined organic extracts were washed with brine (2 x 50 mL), dried over magnesium sulfate, and concentrated *in vacuo* to provide approximately 8 g of the crude product as a yellow oil. Purification by flash chromatography (elution with 35% Et₂O in petroleum ether) afforded 6.34 g (80%) of pure **50** as a colorless oil. TLC R_f = 0.38 (30% Et₂O in petroleum ether). IR (film): 3483.1, 2956.3, 2858.1, 1648.8, 1471.9, 1334.3, 1111.4, 836.5, 778.6 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 5.42 (s, 1 H), 5.36 (s, 1 H), 4.35 (d, *J* = 7.8 Hz, 1 H), 4.31 (d, *J* = 7.8 Hz, 1 H), 3.98-3.90 (m, 2 H), 3.83-3.75 (m, 2 H), 3.70-3.59 (m, 2 H), 2.33 (dd, *J* = 13.2, 7.3 Hz, 1 H), 1.83-1.73 (m, 8 H), 1.70-1.61 (m, 8 H), 0.85 (s, 9 H), 0.02 (s, 6 H). ¹³C NMR (75 MHz, CDCl₃) δ 142.96, 118.89, 118.82, 115.88, 81.27, 80.77, 77.52 (two carbons), 62.42, 61.52, 37.39, 37.36, 37.17, 36.94, 25.81, 23.45, 23.32, 23.22 (two carbons), 18.29, -5.38, -5.53. Anal. Calcd for C₂₄H₄₂SiO₆: C, 63.40; H, 9.31. Found: C, 63.21; H, 9.52. [α]_D²⁴ = +8.80 (c 1.95, CH₂Cl₂).

To a solution of 4.06 g (11.6 mmol) of alkyne **51** in 80 mL of ethyl acetate at rt were successively added 2.26 mL (2.06 mL, 17.5 mmol) of quinoline and 0.50 g of Lindlar's catalyst (5 wt% of palladium/CaCO₃/Pb) and the resulting mixture was cooled to 0°C. The flask was purged with hydrogen gas using a balloon and the mixture was allowed to stir under a hydrogen atmosphere while closely monitoring the progress of the reaction by TLC analysis (50% diethyl ether in petroleum ether). After stirring at 0°C for 1.5 h, TLC analysis showed the complete

conversion of the starting alkyne **51** ($R_f \sim 0.34$) to the slightly less polar alkene ($R_f \sim 0.42$). The reaction mixture was immediately filtered through a pad of celite to remove the catalyst and the resulting clear filtrate was washed with ice-cold 1 N HCl (3 x 25 mL), saturated aqueous sodium bicarbonate (2 x 25 mL), and brine (25 mL). The solution was dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford 4.2 g of the crude product as a pale yellow oil. Flash chromatography on silica gel (elution with 45% Et₂O in petroleum ether) afforded 3.92 g (96%) of pure alkene as a pale yellow oil. TLC $R_f = 0.42$ (50% Et₂O in petroleum ether). IR (film): 3473.3, 2960.0, 2874.3, 1642.6, 1433.4, 1334.5, 1204.5, 1109.1, 1037.7, 988.2, 917.1 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 5.85 (ddt, $J = 17.1, 10.2, 6.8$ Hz, 1 H), 5.46 (s, 1 H), 5.38 (s, 1 H), 5.14-5.07 (m, 2 H), 4.32 (d, $J = 8.3$ Hz, 1 H), 4.08 (d, $J = 7.8$ Hz, 1 H), 4.03-3.97 (m, 2 H), 3.84 (dd, $J = 11.7, 2.9$ Hz, 1 H), 3.67 (dd, $J = 12.2, 3.9$ Hz, 1 H), 2.48-2.43 (m, 1 H), 2.31 (app dt, $J = 15.1, 5.9$ Hz, 1 H), 2.02 (br s, 1 H), 1.87-1.73 (m, 8 H), 1.69-1.64 (m, 8 H). ¹³C NMR (75 MHz, CDCl₃) δ 142.57, 133.82, 118.94, 118.63, 117.45, 116.48, 81.24, 80.77, 79.26, 77.56, 61.50, 37.49, 37.43, 37.20 (2), 36.46, 23.45, 23.37, 23.33(2). Anal. Calcd for C₂₀H₃₀O₅: C, 68.55; H, 8.63. Found: C, 68.70; H, 8.78. $[\alpha]_D^{24} = +19.7$ (c 2.50, CH₂Cl₂).

To a solution of 0.330 g (0.227 mL, 2.60 mmol) of oxalyl chloride in 7 mL of methylene chloride at -78°C was slowly added 0.406 g (0.369 mL, 5.20 mmol) of anhydrous DMSO dropwise with concomitant gas evolution. After stirring at -78°C for 10 minutes, a solution of 0.700 g (2.00 mmol) of the alcohol in 5 mL of methylene chloride was added dropwise *via* cannula and the resulting heterogeneous mixture was stirred for 1 h at -78°C, then 2.09 mL (12.0 mmol) of diisopropylethylamine was added to afford a clear homogeneous solution which was stirred at -78°C for 5 min then warmed to -20°C for 45 minutes. The reaction was quenched at -20°C by the addition of saturated aqueous ammonium chloride (10 mL) followed by warming to rt. The resulting mixture was partitioned between 10 mL of water and 20 mL of methylene chloride and the aqueous portion was extracted with additional methylene chloride (2 x 20 mL).

The combined organic extracts were successively washed with 1 N aqueous HCl (3 x 25 mL), saturated aqueous sodium bicarbonate (25 mL), and brine (25 mL), then dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to afford 0.711 g of crude aldehyde **52** intermediate as a clear, colorless oil. Due to the instability of **52**, this material was not purified further but was immediately dissolved in 8 mL of anhydrous THF and subjected directly to the next transformation. Data for **52**: IR (film): 2961.2, 2874.7, 1737.7, 1643.6, 1335.8, 1107.0, 1035.3, 918.7 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 9.74 (s, 1 H), 5.84 (ddt, $J = 17.1, 10.2, 6.8$ Hz, 1 H), 5.47 (s, 1 H), 5.37 (s, 1 H), 5.14-5.07 (m, 2 H), 4.56 (d, $J = 6.8$ Hz, 1 H), 4.35 (dd, $J = 7.3, 1.9$ Hz, 1 H), 4.12 (d, $J = 7.8$ Hz, 1 H), 4.02-3.95 (m, 1 H), 2.48-2.39 (m, 1 H), 2.30 (dt, $J = 14.2, 7.3$ Hz, 1 H), 1.82-1.56 (m, 14 H).

A solution of 0.745 g (5.00 mmol) of dimethyldiazomethylphosphonate in 8 mL of THF was transferred *via* cannula into 0.565 mL (0.565 mmol) of a 1.0 M solution of sodium hexamethyldisilazide in THF at -78°C . The resulting bright yellow mixture was stirred at -78°C for 20 min whereupon the solution of the previously prepared aldehyde in 8 mL of THF was added dropwise *via* cannula over 10 min (1 mL THF rinse). The resulting mixture was stirred at -78°C for 30 min then warmed to rt and quenched with 10 mL of water. The layers were separated and the aqueous portion was extracted with additional diethyl ether (3 x 25 mL) and the combined extracts were washed with brine (25 mL), dried over anhydrous magnesium, filtered, and concentrated *in vacuo* to afford 0.708 g of the crude alkyne as a yellow oil. Flash chromatography on silica gel (elution with 5% diethyl ether in petroleum ether) provided 0.578 g (84%) of pure **6** as a pale yellow oil. TLC $R_f = 0.28$ (5% Et_2O in petroleum ether). IR (film): 3268.0, 3077.8, 2961.9, 2874.8, 2116.2, 1643.1, 1433.6, 1335.5, 1205.5, 1107.2, 1037.8, 919.5 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 5.84 (ddt, $J = 17.1, 10.3, 6.8$ Hz, 1 H), 5.47 (s, 1 H), 5.39 (s, 1 H), 5.14-5.06 (m, 2 H), 4.46 (s, 2 H), 4.14 (d, $J = 8.3$ Hz, 1 H), 3.98 (ddd, $J = 11.7, 7.3, 4.4$ Hz, 1 H), 2.53 (s, 1 H), 2.42 (app dt, $J = 14.6, 5.9$ Hz, 1 H), 2.30 (app dt, $J = 14.6, 6.8$ Hz, 1 H), 1.98-1.76 (m, 8 H), 1.74-1.61 (m, 8 H). ^{13}C NMR (75 MHz, CDCl_3) δ 141.73, 133.79, 120.31, 118.71, 117.50, 117.24, 81.27, 81.17, 80.75, 79.28, 75.04, 70.32, 37.49, 37.26, 36.63(2), 36.36, 23.80, 23.46, 23.42, 23.12. Anal. Calcd for $\text{C}_{21}\text{H}_{28}\text{O}_4$: C, 73.23; H, 8.19. Found: C, 73.40; H, 8.33. $[\alpha]_D^{24} = +27.9$ (c 1.78, CH_2Cl_2).

To a solution of 0.564 g (1.64 mmol) of alkyne **6** in 4 mL of THF at -78°C was added 3.28 mL (3.28 mmol) of a 1.0 M solution of sodium hexamethyldisilazide in THF. The resulting mixture was stirred at -78°C for 45 min, warmed to 0°C for 20 min, then recooled to -78°C whereupon 0.69 g (0.72 mL, 4.92 mmol) of freshly distilled trimethylsilylchloride was added. After stirring at -78°C for 45 min, the mixture was warmed to 0°C then rapidly quenched by pouring in 10 mL of saturated aqueous sodium bicarbonate all at once. Diethyl ether (20 mL) was added and the resulting layers were separated. The aqueous portion was extracted with additional diethyl ether (3 x 20 mL) and the combined organic extracts were washed with brine (20 mL), dried over anhydrous magnesium, filtered, and concentrated *in vacuo* to afford 0.686 g of the crude product mixture as a golden-yellow oil. Flash chromatography on silica gel (elution with 5% diethyl ether in petroleum ether) provided 0.621 g (91%) of pure **53** as a pale yellow oil. TLC R_f = 0.84 (15% Et₂O in petroleum ether). IR (film): 2960.8, 2875.0, 2176.9, 1642.0, 1432.9, 1334.8, 1105.8, 844.3, 760.3 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 5.84 (ddt, J = 17.1, 10.2, 6.8 Hz, 1 H), 5.47 (s, 1 H), 5.39 (s, 1 H), 5.14-5.06 (m, 2 H), 4.39 (app s, 2 H), 4.16 (d, J = 8.3 Hz, 1 H), 3.94 (ddd, J = 11.7, 7.3, 4.4 Hz, 1 H), 2.44 (app dt, J = 14.6, 8.8 Hz, 1 H), 2.30 (dt, J = 14.6, 7.3 Hz, 1 H), 2.01-1.74 (m, 8 H), 1.721.50 (m, 8 H), 0.15 (s, 9 H). ^{13}C NMR (75 MHz, CDCl_3) δ 142.38, 133.79, 120.18, 118.73, 117.58, 116.20, 101.87, 92.40, 81.01, 80.72, 79.64, 71.39, 37.49, 37.33, 36.80, 36.71, 36.49, 23.80, 23.45(2), 23.25, -0.30. Anal. Calcd for $\text{C}_{24}\text{H}_{36}\text{SiO}_4$: C, 69.19; H, 8.71. Found: C, 69.16; H, 8.83. $[\alpha]_D^{24}$ = +43.4 (c 1.00, CH_2Cl_2).

To a solution of oxalyl chloride (1.50 mL, 2.18 g, 17.2 mmol) in CH_2Cl_2 (40 mL) at -78°C was added DMSO (2.50 mL, 2.75 g, 35.2 mmol), stirred for 15 min, and a solution of alcohol **55** (3.264 g, 10.6 mmol) in CH_2Cl_2 (35 mL) at -78°C was added via cannula. After 1 h at -78°C

°C, triethylamine (7.4 mL, 5.4 g, 53 mmol) was added, the reaction mixture was stirred at -78 °C for 15 min, warmed to room temperature, diluted with CH₂Cl₂, washed with saturated NH₄Cl (2 x), brine (1 x), dried over MgSO₄, filtered through a pad of silica gel, and concentrated to give aldehyde **64** which was used in the next step without further purification: ¹H NMR (500 MHz, CDCl₃) δ 9.75 (d, *J* = 1.7 Hz, 1H), 7.26 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 4.53 (s, 2H), 4.51 (m, 1H), 4.21 (m, 1H), 4.17 (dd, *J* = 7.1, 1.7 Hz, 1H), 3.81 (s, 3H), 3.79 (m, 1H), 3.62 (d, *J* = 4.9 Hz, 1H), 1.92-1.62 (m, 8H). To a solution of HC≡CCH₂CH₂OTBS (4.849 g, 26.3 mmol) in THF (100 mL) at 0 °C was added *n*-BuLi (10.5 mL, 2.5 M in hexanes, 26.3 mmol), stirred for 15 min, cooled to -60 °C, and ClTi(*Oi*-Pr)₃ (6.25 mL, 6.82 g, 26.2 mmol) was added. The solution was stirred at -60 °C for 1.5 h, cooled to -78 °C, and a solution of aldehyde **64**, prepared in the previous step, in THF (80 mL) at -78 °C was added via cannula. The reaction mixture was stirred at -78 °C for 1 h, warmed from -78 °C to -50 °C over 1 h, quenched with saturated NH₄Cl, warmed to room temperature, and diluted with ether and water. The aqueous phase was extracted with ether (6 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄, concentrated, to give alkyne **56** which was used without further purification: ¹H NMR (500 MHz, CDCl₃) δ 7.26 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 4.55-4.52 (m, 2H), 4.49 (m, 1H), 3.86 (dd, *J* = 7.3, 4.4 Hz, 1H), 3.81-3.78 (m, 3H), 3.80 (s, 3H), 3.69 (t, *J* = 7.3 Hz, 2H), 3.62 (d, *J* = 5.1 Hz, 1H), 2.45 (d, *J* = 4.6 Hz, 1H), 2.38 (dddd, *J* = 7.1, 7.1, 2.0, 2.0 Hz, 1H), 1.88-1.65 (m, 8H), 0.89 (s, 9H), 0.08 (s, 6H). To a solution of alkyne **56**, prepared in the previous step, in THF (33 mL) at 0 °C was added Red-Al[®] (5.6 mL, 65% wt in toluene, 18.7 mmol). The reaction mixture was warmed to room temperature, stirred for 6 h, quenched with aqueous potassium sodium tartrate, stirred for 20 min, and diluted with ether and water. The aqueous phase was extracted with Et₂O (5 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄, and concentrated. Purification by flash column chromatography on silica gel (20% to 30% to 50% EtOAc in petroleum ether) gave alkene **65** (2.636 g, 51%) and recovered alcohol **55** (747 mg, 23%) as colorless oils. Data for **65**: R_f = 0.29 (20% EtOAc in petroleum ether); ¹H NMR (500 MHz, CDCl₃) δ 7.25 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.76 (dddd, *J* = 13.9, 6.8, 6.8, 1.2 Hz, 1H), 5.51 (ddd, *J* = 15.4, 6.1, 1.2 Hz, 1H), 4.51 (s, 2H), 4.18 (m, 1H), 4.07 (ddd, *J* = 7.3, 5.4, 5.4 Hz, 1H), 3.80 (s, 3H), 3.70 (dd, *J* = 7.6, 5.6 Hz, 1H), 3.62 (t, *J* = 6.8 Hz, 2H), 3.58 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.51 (dd, *J* = 10.0, 5.1 Hz, 1H), 2.57 (d, *J* = 2.9 Hz, 1H), 2.25 (q br, *J* = 6.8 Hz, 2H), 1.88-1.62 (m, 8H), 0.89 (s, 9H),

0.04 (s, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 159.3, 130.1, 129.8, 129.7, 129.4, 119.3, 113.8, 81.2, 76.7, 73.2, 72.2, 70.4, 68.2, 55.2, 37.2, 37.1, 36.0, 25.9, 23.6, 23.3, 18.3, -5.3; IR (neat) 3458 (br), 2955, 1614, 1515, 1250, 1102 cm^{-1} ; MALDIMS m/z 515.3 $[\text{M} + \text{Na}]^+$; optical rotation $[\alpha]_{\text{D}}^{27} +9.5^\circ$ (c 1.0, CH_2Cl_2). Anal. Calcd for $\text{C}_{27}\text{H}_{44}\text{O}_6\text{Si}$: C, 65.82; H, 9.00. Found: C, 65.66; H, 8.87.

To a solution of alcohol **65** (3.038 g, 6.17 mmol) in CH_2Cl_2 (40 mL) at 0°C was added NaHCO_3 (3.668 g, 43.7 mmol) and Dess-Martin reagent (3.559 g, 8.39 mmol). The reaction mixture was warmed to room temperature, stirred for 2 h, quenched with saturated Na_2SO_3 , stirred for 15 min, and diluted with water. The aqueous phase was extracted with CH_2Cl_2 (5 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (5% to 10% to 15% EtOAc in petroleum ether) gave ketone **57** (2.613 g, 86%) as a colorless oil: R_f = 0.20 (10% EtOAc in petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.27 (d, J = 8.4 Hz, 2H), 7.05 (ddd, J = 15.9, 7.2, 7.2 Hz, 1H), 6.87 (d, J = 8.7 Hz, 2H), 6.58 (ddd, J = 15.9, 1.5, 1.5 Hz, 1H), 4.54 (s, 2H), 4.30 (d, J = 7.0 Hz, 1H), 4.23 (ddd, J = 7.0, 5.8, 3.5 Hz, 1H), 3.80 (s, 3H), 3.73 (t, J = 6.4 Hz, 2H), 3.70 (dd, J = 10.7, 3.5 Hz, 1H), 3.60 (dd, J = 10.5, 5.6 Hz, 1H), 2.44 (ddd, J = 13.6, 6.6, 1.5 Hz, 2H), 1.91-1.67 (m, 8H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 197.7, 159.2, 147.1, 130.0, 129.4, 126.5, 120.9, 113.8, 80.8, 77.5, 73.2, 69.9, 61.4, 55.3, 36.8, 36.7, 36.2, 25.9, 23.7, 23.3, 18.3, -5.3; IR (neat) 2959, 1691, 1252, 1103, 836 cm^{-1} ; EIMS m/z 277 (1), 213 (1), 145 (1), 137 (1), 121 (100); HREIMS calcd for $\text{C}_{27}\text{H}_{42}\text{O}_6\text{Si}$ 490.2751, found 490.2751; optical rotation $[\alpha]_{\text{D}}^{27} +6.0^\circ$ (c 1.0, CH_2Cl_2). Anal. Calcd for $\text{C}_{27}\text{H}_{42}\text{O}_6\text{Si}$: C, 66.09; H, 8.63. Found: C, 66.40; H, 8.62.

To a mixture of $\text{K}_3\text{Fe}(\text{CN})_6$ (17.96 g, 54.5 mmol), K_2CO_3 (7.57 g, 54.8 mmol), NaHCO_3 (4.62 g, 55.0 mmol), methanesulfonamide (1.720 g, 18.1 mmol), and $(\text{DHQ})_2\text{-PHAL}$ (369 mg, 0.47 mmol) at room temperature was added water (85 mL) and *tert*-butyl alcohol (45 mL). The reaction mixture was cooled to 0 °C, $\text{K}_2\text{OsO}_4 \cdot 2\text{H}_2\text{O}$ (171 mg, 0.46 mmol) was added followed by a solution of alkene **57** (8.871 g, 18.1 mmol) in *tert*-butyl alcohol (40 mL). The reaction mixture was stirred at 0 °C for 22 h, quenched with Na_2SO_3 (80 g), warmed to room temperature, stirred for 1 h, and diluted with EtOAc and water. The aqueous phase was extracted with EtOAc (4 x) and the combined organic extracts were washed with 2 M NaOH (1 x), brine (1 x), dried over MgSO_4 , and concentrated to give diol **58** which was used in the next step without further purification: R_f = 0.46 (30% EtOAc in petroleum ether); ^1H NMR (500 MHz, CDCl_3) δ 7.27 (d, J = 7.8 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 4.55 (s, 2H), 4.52 (d br, J = 7.3 Hz, 1H), 4.48 (d, J = 6.8 Hz, 1H), 4.34 (ddd, J = 5.9, 5.9, 3.2 Hz, 1H), 3.95-3.85 (m, 3H), 3.80 (s, 3H), 3.75 (dd, J = 11.0, 3.2 Hz, 1H), 3.62 (dd, J = 10.8, 5.9 Hz, 1H), 3.45 (d, J = 6.8 Hz, 1H), 3.14 (d, J = 4.9 Hz, 1H), 2.03-1.66 (m, 10H), 0.89 (s, 9H), 0.08 (s, 6H). To a solution of diol **58**, prepared in the previous step, and 1,1-dimethoxycyclopentane (25 mL) in CH_2Cl_2 (190 mL) at 0 °C was added $\text{TsOH} \cdot \text{H}_2\text{O}$ (562 mg, 2.95 mmol). The reaction mixture was stirred at 0 °C for 2 h, diluted with ether, washed with saturated NaHCO_3 (1 x), brine (1 x), dried over MgSO_4 , and concentrated to give ketal **59** which was used in the next step without further purification: R_f = 0.68 (30% EtOAc in petroleum ether); ^1H NMR (500 MHz, CDCl_3) δ 7.27 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 4.57-4.51 (m, 3H), 4.41 (d, J = 7.1 Hz, 1H), 4.26 (ddd, J = 9.3, 6.1, 3.2 Hz, 1H), 4.18 (ddd, J = 8.8, 7.1, 3.7 Hz, 1H), 3.80 (s, 3H), 3.79-3.72 (m, 3H), 3.62 (dd, J = 10.7, 6.1 Hz, 1H), 2.07-1.63 (m, 20H), 0.87 (s, 9H), 0.04 (s, 6H). To a suspension of methyltriphenylphosphonium bromide (13.08 g, 36.6 mmol) in THF (150 mL) at 0 °C was added NaHMDS (37 mL, 1.0 M in THF, 37 mmol), stirred at 0 °C for 15 min, warmed to room temperature, stirred for 1 h, cooled to 0 °C, and a solution of ketone **59**, prepared in the previous step, in THF (150 mL) at 0 °C was added via cannula. The reaction mixture was stirred at 0 °C for 11 h and diluted with ether and water. The aqueous phase was extracted with ether (3 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (5% to 10% EtOAc in petroleum ether) gave alkene **60** (6.351 g, 60%) as a colorless oil: R_f = 0.38 (10% EtOAc in petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.26 (d, J = 8.2 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 5.34 (s, 2H), 4.55-4.49 (m, 2H), 4.25 (d, J =

7.9 Hz, 1H), 4.11 (d, $J = 8.1$ Hz, 1H), 4.03 (ddd, $J = 9.0, 6.4, 2.3$ Hz, 1H), 3.89 (ddd, $J = 8.9, 8.9, 2.6$ Hz, 1H), 3.80 (s, 3H), 3.78-3.66 (m, 3H), 3.50 (dd, $J = 10.8, 6.6$ Hz, 1H), 1.97-1.56 (m, 18H), 0.88 (s, 9H), 0.042 (s, 3H), 0.038 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 159.2, 143.4, 130.2, 129.3, 119.4, 118.6, 116.5, 113.7, 80.9, 80.6, 77.6, 77.2, 73.1, 69.4, 60.1, 55.2, 37.5, 37.4, 37.1 (2 carbons), 35.3, 25.9, 23.6, 23.4, 23.3 (2 carbons), 18.3, -5.3, -5.4; IR (neat) 2949, 1614, 1510, 1334, 1103 cm^{-1} ; MALDIMS m/z 611.3 $[\text{M} + \text{Na}]^+$; optical rotation $[\alpha]_{\text{D}}^{25} -5.9^\circ$ (c 1.0, CH_2Cl_2). Anal. Calcd for $\text{C}_{33}\text{H}_{52}\text{O}_7\text{Si}$: C, 67.31; H, 8.90. Found: C, 67.15; H, 8.70.

To a solution of ether **60** (7.987 g, 13.6 mmol) in THF (90 mL) at room temperature was added TBAF (20.4 mL, 1 M in THF, 20.4 mmol). The reaction mixture was stirred for 24 h, and diluted with ether and water. The aqueous phase was extracted with ether (4 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (30% to 50% EtOAc in petroleum ether) gave alcohol **61** (5.024 g, 78%) as a colorless oil: $R_f = 0.38$ (50% EtOAc in petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.25 (d, $J = 8.7$ Hz, 2H), 6.86 (d, $J = 8.7$ Hz, 2H), 5.38 (s, 1H), 5.36 (s, 1H), 4.51 (s, 2H), 4.27 (d, $J = 8.1$ Hz, 1H), 4.15 (d, $J = 8.2$ Hz, 1H), 4.02 (ddd, $J = 8.2, 6.3, 2.7$ Hz, 1H), 3.91 (ddd, $J = 8.4, 8.4, 3.4$ Hz, 1H), 3.79 (s, 3H), 3.78-3.75 (m, 2H), 3.66 (dd, $J = 10.7, 2.7$ Hz, 1H), 3.50 (dd, $J = 10.8, 6.3$ Hz, 1H), 2.44 (t, $J = 5.6$ Hz, 2H), 1.99-1.59 (m, 17H); ^{13}C NMR (101 MHz, CDCl_3) δ 159.1, 143.0, 130.1, 129.35, 129.30, 119.5, 118.9, 117.2, 113.7, 80.9, 80.32, 80.30, 77.2, 73.1, 69.1, 60.8, 55.2, 37.5, 37.4, 37.1, 34.0, 23.5, 23.4, 23.2 (2 carbons); IR (neat) 3486 (br), 2951, 1611, 1516, 1108 cm^{-1} ; MALDIMS m/z 497.3 $[\text{M} + \text{Na}]^+$; optical rotation $[\alpha]_{\text{D}}^{26} +4.4^\circ$ (c 1.0, CH_2Cl_2); Anal. Calcd for $\text{C}_{27}\text{H}_{38}\text{O}_7$: C, 68.33; H, 8.07. Found: C, 68.17; H, 7.90.

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69.6, 55.5, 37.8, 37.7, 37.41, 37.38, 36.5, 23.8, 23.7, 23.6 (2 carbons); IR (neat) 2959, 1614, 1515, 1103 cm^{-1} ; EIMS m/z 137 (2), 123 (2), 122 (4), 121 (100); HREIMS calcd for $\text{C}_{28}\text{H}_{38}\text{O}_6$ 470.2663, found 470.2668; optical rotation $[\alpha]_{\text{D}}^{24} +0.5^\circ$ (c 1.0, CH_2Cl_2). Anal. Calcd for $\text{C}_{28}\text{H}_{38}\text{O}_6$: C, 71.46; H, 8.14. Found: C, 71.65; H, 7.98.

To a solution of ether **62** (3.990 g, 8.48 mmol) in CH_2Cl_2 (55 mL) and water (20 mL) at room temperature was added DDQ (2.359 g, 10.4 mmol). The reaction mixture was stirred at room temperature for 2 h and diluted with ether, water, and saturated NaHCO_3 . The aqueous phase was extracted with ether (4 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (0% to 50% EtOAc in CH_2Cl_2) gave the corresponding alcohol (2.918 g, 98%) as a colorless oil: R_f = 0.32 (30% EtOAc in petroleum ether); ^1H NMR (500 MHz, CDCl_3) δ 5.86 (dddd, J = 17.1, 13.7, 10.3, 7.0 Hz, 1H), 5.51 (s, 1H), 5.36 (s, 1H), 5.15-5.09 (m, 2H), 4.27 (d, J = 7.2 Hz, 1H), 4.19 (d, J = 8.2 Hz, 1H), 3.86 (ddd, J = 7.7, 7.7, 3.7 Hz, 1H), 3.83-3.75 (m, 3H), 2.68 (s br, 1H), 2.48 (dm, J = 14.8 Hz, 1H), 2.28 (ddd, J = 14.8, 7.3, 7.3 Hz, 1H), 1.90-1.61 (m, 16H); ^{13}C NMR (126 MHz, CDCl_3) δ 142.7, 133.8, 119.1, 118.7, 117.60, 117.59, 83.2, 81.8, 79.3, 77.1, 62.0, 37.4 (2 carbons), 37.3, 37.1, 36.0, 23.43, 23.39, 23.37, 23.2; IR (neat) 3484 (br), 2959, 1642, 1107 cm^{-1} ; EIMS m/z 277 350 (13), 322 (17), 321 (37), 225 (15); HREIMS calcd for $\text{C}_{20}\text{H}_{30}\text{O}_5$ 350.2093, found 350.2090; optical rotation $[\alpha]_{\text{D}}^{24} -22^\circ$ (c 1.0, CH_2Cl_2). Anal. Calcd for $\text{C}_{20}\text{H}_{30}\text{O}_5$: C, 68.54; H, 8.63. Found: C, 68.70; H, 8.66.

To a solution of oxalyl chloride (40 μL , 58 mg, 0.46 mmol) in CH_2Cl_2 (2 mL) at -78°C was added DMSO (65 μL , 72 mg, 0.92 mmol), stirred for 15 min, and a solution of the alcohol

(101 mg, 0.29 mmol) in CH₂Cl₂ (2 mL) at -78 °C was added via cannula. After 1 h at -78 °C, triethylamine (200 µL, 145 mg, 1.4 mmol) was added, the reaction mixture was stirred at -78 °C for 15 min, warmed to 0 °C, diluted with ether, washed with saturated NH₄Cl (2 x), brine (1 x), dried over MgSO₄, filtered through a pad of silica gel, and concentrated to give the aldehyde which was used in the next step without further purification: *R*_f = 0.19 (20% EtOAc in petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 9.72 (d, *J* = 2.0 Hz, 1H), 5.87 (dddd, *J* = 16.9, 13.6, 10.2, 6.9 Hz, 1H), 5.51 (s, 1H), 5.32 (s, 1H), 5.16-5.10 (m, 2H), 4.66 (d, *J* = 6.6 Hz, 1H), 4.23 (dd, *J* = 6.7, 2.0 Hz, 1H), 4.20 (d, *J* = 8.2 Hz, 1H), 3.86 (ddd, *J* = 7.6, 7.6, 3.8 Hz, 1H), 2.46 (dm, *J* = 14.8 Hz, 1H), 2.28 (ddd, *J* = 14.6, 6.9, 6.9 Hz, 1H), 2.00-1.62 (m, 16H). To a solution of (MeO)₂POC(=N₂)COMe (277 mg, 1.44 mmol) in MeOH (1 mL) at 0 °C was added K₂CO₃ (204 mg, 1.48 mmol). After 30 min, a solution of the aldehyde, prepared in the previous step, in MeOH (1.5 mL) at 0 °C was added via cannula. The reaction mixture was warmed to room temperature over 1 h, stirred at room temperature for 24 h, and diluted with ether and water. The aqueous phase was extracted with ether (4 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄, and concentrated. Purification by flash column chromatography on silica gel (5% to 10% EtOAc in petroleum ether) gave alkyne **63** (86 mg, 87%) as a colorless oil: *R*_f = 0.45 (10% EtOAc in petroleum ether); ¹H NMR (500 MHz, CDCl₃) δ 5.87 (dddd, *J* = 17.1, 13.7, 10.1, 6.8 Hz, 1H), 5.44 (s, 1H), 5.33 (s, 1H), 5.15-5.08 (m, 2H), 4.58 (d, *J* = 6.1 Hz, 1H), 4.52 (dd, *J* = 6.2, 2.2 Hz, 1H), 4.17 (d, *J* = 7.9 Hz, 1H), 3.89 (ddd, *J* = 7.7, 7.7, 3.8 Hz, 1H), 2.50 (d, *J* = 2.1 Hz, 1H), 2.47 (m, 1H), 2.29 (dddd, *J* = 14.7, 7.3, 7.3, 1.3, 1.3 Hz, 1H), 2.06-1.61 (m, 16H); ¹³C NMR (126 MHz, CDCl₃) δ 142.9, 134.1, 120.7, 119.1, 117.4, 116.1, 81.7, 81.2, 80.4, 79.5, 74.4, 70.6, 37.6, 37.1, 36.7, 36.6, 36.3, 23.9, 23.5, 23.4, 22.9; IR (neat) 3303, 2959, 1642, 1334, 1207, 1107 cm⁻¹; ESIMS *m/z* 367.4 [M + Na]⁺; optical rotation [α]_D²⁴ +1.6° (*c* 1.0, CH₂Cl₂); Anal. Calcd for C₂₁H₂₈O₄: C, 73.23; H, 8.19. Found: C, 73.35; H, 8.28.

To a suspension of 27 g of freshly activated 3 Å powdered molecular sieves (heated to 140°C at 1 Torr for 14 h then cooled to rt) in 250 mL of methylene chloride was added a solution

of 17.7 g (86 mmol) of freshly distilled (+)-diethyltartrate in 40 mL of methylene chloride. The resulting mixture was cooled to -30°C whereupon 20.5 g (21.2 mL, 72 mmol) of distilled titanium tetraisopropoxide and 145 mL (72-86 mmol) of a 5-6 M stock solution of *t*BuOOH in decane (NOTE: the *t*BuOOH decane solution was predried over 4Å molecular sieve pellets for 20 minutes just prior to use) were successively added and the resulting yellow mixture was stirred at -30°C for 30 minutes. During this time, a solution of 30.0 g (144 mmol) of allylic alcohol **67** in 150 mL of methylene chloride was predried over 4Å molecular sieve pellets for 20 min, then the solution was transferred *via* cannula over 30 min into the previously prepared reaction mixture at -30°C . The reaction flask was then placed into a -20°C freezer and allowed to remain at that temperature without stirring for 40 h whereupon the mixture was filtered to remove the sieves and *slowly* poured into a well-stirred 0°C solution of 236 g (86 mmol) of iron sulfate heptahydrate and 143 g (86 mmol) of tartaric acid in 800 mL of water. After stirring at 0°C for 15 min, the layers were separated and the aqueous portion was extracted with diethyl ether (3 x 500 mL). The combined organic extracts were cooled to 0°C whereupon 140 mL of 30% aqueous sodium hydroxide was added. After stirring at 0°C for 1 h, 500 mL of water was added and the layers were separated. The aqueous portion was extracted with diethyl ether (3 x 300 mL) and the combined extracts were washed with brine (2 x 200 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated on a rotary evaporator to afford approximately 100 mL of the crude product as a colorless suspension in residual decane. This material was purified by flash chromatography on silica gel beginning with 80% Et₂O in petroleum ether mixture as the eluant to remove the decane and less polar impurities. Finally, elution with 100% Et₂O afforded after concentration *in vacuo* 23.01 g (71%) of pure epoxide **68** as a yellow oil. The enantiomeric purity of **68** was determined to be 84% ee by chiral HPLC analysis : Chiralcel OD at 23°C , 1.0 mL/min flow rate, 15% isopropanol-heptane, 254 nm, retention times for enantiomers of **68**: 13.66 min (minor), 16.17 min (major) as compared to a racemic standard of **68**. TLC R_f = 0.22 (80% Et₂O in petroleum ether). IR (film): 3440.2, 2934.4, 1612.3, 1585.9, 1513.2, 1246.4, 1085.9, 1033.1, 821.4 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 7.26 (d, *J* = 8.5 Hz, 2 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 4.55 (d, *J* = 11.3 Hz, 1 H), 4.46 (d, *J* = 11.3 Hz, 1 H), 3.81 (s, 3 H), 3.78-3.67 (m, 3 H), 3.60 (dd, *J* = 6.0, 5.1 Hz, 1 H), 3.30-3.20 (m, 2 H), 1.76 (br s, 1 H). $[\alpha]_{\text{D}}^{25} = -17.0$ (c 2.15, CH₂Cl₂).

To a slurry of 32.0 g (357 mmol) of copper cyanide in 350 mL of diethyl ether at -40°C was added 422.3 mL (663 mmol) of a 1.57 M solution of methyllithium-lithium bromide complex in diethyl ether affording a cloudy, off-white colored mixture which was allowed to slowly warm from -40°C to -20°C over 1.5 h. The reaction mixture was then cooled to -50°C and a solution of 22.94 g (102 mmol) of epoxide **68** in 50 mL of diethyl ether was added *via* cannula and the resulting mixture was allowed to slowly warm from -50°C to -20°C over 3.5 h. At this time, the reaction was carefully quenched at -20°C by a slow, dropwise addition of 100 mL of an aqueous solution of saturated ammonium chloride which had been buffered to a pH~9 with conc ammonium hydroxide. After allowing to warm to rt with vigorous stirring for 1 h, the mixture was partitioned between 400 mL of the ammonium chloride/ammonium hydroxide solution, 200 mL of water, and 300 mL of diethyl ether. The aqueous portion was extracted with additional diethyl ether (2 x 400 mL) and the combined cloudy organic extracts were filtered through a pad of celite and the resulting clear filtrate was concentrated *in vacuo* to afford the crude diol mixture as a 2-3:1 regioisomeric mixture of the 1,2-diol and 1,3-diol **69** as determined by ^1H NMR analysis. Separation of the desired regioisomeric 1,3-diol from the 1,2-diol was accomplished by dissolving the crude mixture in 400 mL of 10% aqueous THF, cooling the resulting solution to 0°C , and adding 21.8 g (102 mmol) of sodium periodate. The mixture was warmed to rt and stirred for 1.5 h giving a thick, white heterogeneous mixture. After dilution with 1 L of chloroform, the mixture was decanted away from the white insoluble precipitate which had formed and the resulting solution was washed with brine (200 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to a yellow oil as the crude product mixture. Flash chromatography on silica gel initially eluting with 80% ethyl acetate in petroleum ether mixtures removed the aldehyde byproduct followed by eluting with 100% ethyl acetate to provide 16.7 g (68%) of pure **69** as a yellow oil. TLC R_f = 0.42 (80% EtOAc in petroleum ether). IR (film): 3405.6, 2910.9, 1612.8, 1514.0, 1248.6, 1096.6, 1033.8, 819.1 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 7.22 (d, J = 8.3 Hz, 2 H), 6.86 (d, J = 8.3 Hz, 2 H), 4.50-4.41 (m, 2 H), 3.98-3.92 (m, 1 H), 3.78 (s, 3 H), 3.60-3.58 (m, 2 H), 3.46 (d, J = 5.9 Hz, 2 H),

2.82 (br s, 2 H), 1.85-1.78 (br m, 1 H), 0.88 (d, $J = 7.3$ Hz, 3 H). ^{13}C NMR (75 MHz, CDCl_3) δ 159.24, 129.78, 129.39, 113.78, 73.02, 72.39, 72.05, 66.06, 55.19, 37.28, 11.00. Anal. Calcd for $\text{C}_{13}\text{H}_{20}\text{O}_4$: C, 64.98; H, 8.39. Found: C, 64.61; H, 8.32. $[\alpha]_{\text{D}}^{25} = +2.77$ (c 1.70, CH_2Cl_2).

To a solution of 14.4 g (60 mmol) of diol **69** in 280 mL of pyridine at 0°C was added 11.4 g (60 mmol) of freshly purified tosyl chloride in three portions over 15 min followed by stirring at 0-4°C (cold room temp) for 40 h. The cold mixture was then slowly poured into a well-stirred 0°C mixture of 10% aqueous HCl (400 mL) and diethyl ether (400 mL) and the resulting layers were separated. The organic layer was washed with additional ice-cold aqueous 10% HCl (300 mL) and the combined aqueous acidic portions were extracted with diethyl ether (3 x 300 mL). The combined organic extracts were successively washed with 300 mL of 10% aqueous HCl, 300 mL of 0.2 M aqueous copper sulfate solution, and brine (2 x 200 mL), then dried over anhydrous magnesium sulfate, filtered, and concentrated on a rotary evaporator to a total volume of approximately 500 mL. This solution which still contained residual pyridine was washed again with 10% aqueous HCl (3 x 100 mL), 100 mL of 0.2 aqueous copper sulfate solution, and brine (2 x 100 mL), then dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to afford a pale yellow oil as the crude tosylate intermediate. Due to the apparent instability of the tosylate, this intermediate was not purified further but was immediately dissolved in 50 mL of anhydrous THF and subjected directly to the next reaction. A relatively pure sample of the tosylate could be obtained by rapid flash chromatography on silica gel (50% Et_2O in petroleum ether): TLC $R_f = 0.37$ (50% Et_2O in petroleum ether). IR (film): 3447.9, 2909.5, 1612.1, 1513.7, 1357.6, 1248.2, 1176.1, 965.7, 815.7 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 7.76 (d, $J = 7.8$ Hz, 2 H), 7.32 (d, $J = 7.8$ Hz, 2 H), 7.22 (d, $J = 8.8$ Hz, 2 H), 6.88 (d, $J = 8.8$ Hz, 2 H), 4.43 (app s, 2 H), 4.03 (dd, $J = 9.3, 6.8$ Hz, 1 H), 3.90 (dd, $J = 9.8, 5.9$ Hz, 1 H), 3.85-3.82 (m, 1 H), 3.80 (s, 3 H), 3.43-3.33 (m, 2 H), 2.43 (s, 3 H), 2.35 (br s, 1 H), 2.04-1.93 (br m, 1 H), 0.87 (d, $J = 6.8$ Hz, 3 H). ^{13}C NMR (75 MHz, CDCl_3) δ 159.25, 144.72, 132.78, 129.79 (2), 129.34, 127.82, 113.79, 72.95, 72.14, 71.88, 69.49, 55.20, 35.42, 21.57, 10.63.

The THF solution of the crude tosylate was transferred *via* cannula into a suspension of 4.80 g (120 mmol) of 60% dispersion of sodium hydride in mineral oil in 100 mL of THF at rt and the resulting heterogeneous mixture was stirred at rt for 4 h. At this time, the reaction mixture was carefully quenched by a slow, dropwise addition of 20 mL of methanol followed by the addition of 100 mL of water and 100 mL of diethyl ether. The resulting layers were separated and the aqueous portion was extracted with diethyl ether (3 x 75 mL). The combined extracts were washed with brine (2 x 25 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to afford a 15.2 g of a yellow oil as the crude oxetane. Flash chromatography on silica gel (50% diethyl ether in petroleum ether) afforded 10.9 g (82%) of pure **70** as a pale yellow oil. TLC R_f = 0.57 (50% Et₂O in petroleum ether). IR (film): 2872.2, 1612.5, 1513.3, 1457.2, 1247.6, 1094.3, 1033.8, 969.6, 818.8 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 7.26 (d, *J* = 8.3 Hz, 2 H), 6.87 (d, *J* = 8.3 Hz, 2 H), 4.97-4.91 (m, 1 H), 4.76 (dd, *J* = 8.3, 5.9 Hz, 1 H), 4.50 (app q, *J* = 7.8 Hz, 2 H), 4.18 (app t, *J* = 6.3 Hz, 1 H), 3.79 (s, 3 H), 3.69 (d, *J* = 5.9 Hz, 2 H), 3.15 (app sextet, *J* = 6.8 Hz, 1 H), 1.16 (d, *J* = 7.3 Hz, 3 H).

To a solution of 20.8 mL (14.4 g, 147 mmol) of trimethylsilylacetylene in 230 mL of THF at -78°C was added 92 mL (147 mmol) of a 1.6 M solution of *n*-butyllithium in hexanes and the resulting clear, colorless solution was stirred at -78°C for 30 min then at 0°C for 45 minutes. The mixture was cooled to -78°C and 18.1 mL (20.9 g, 147 mmol) of freshly distilled boron trifluoride etherate was added followed by stirring for 10 min whereupon a solution of 10.9 g (49 mmol) of **70** in 30 mL of THF was added *via* cannula. After stirring at -78°C for 45 min, 100 mL of saturated aqueous ammonium chloride was added and the reaction mixture was allowed to warm to rt whereupon 100 mL of water and 100 mL of diethyl ether were added. The resulting layers were separated and the organic portion was washed with 5% aqueous HCl (2 x 100 mL). The aqueous portions were combined and extracted with diethyl ether (2 x 150 mL) and the combined organic extracts were washed with saturated aqueous sodium bicarbonate (100 mL), brine (100 mL), then dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to afford 15.5 g of a yellow oil as the crude product. Flash chromatography on silica gel (40% diethyl ether in petroleum ether) then afforded 10.57 g (62%) of pure **71** as a pale yellow oil. TLC R_f = 0.43 (50% Et₂O in petroleum ether). IR (film): 3463.3, 2959.4, 2902.6, 2173.1, 1612.9, 1514.0, 1249.4, 843.4 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 7.24 (d, *J* = 8.3 Hz, 2 H),

6.86 (d, $J = 8.8$ Hz, 2 H), 4.46 (s, 2 H), 3.82 (m, 1 H), 3.78 (s, 3 H), 3.49 (dd, $J = 9.8, 3.4$ Hz, 1 H), 3.41 (apparent t, $J = 9.8$ Hz, 1 H), 2.41 (br m, 1 H), 2.31 (dd, $J = 17.1, 6.4$ Hz, 1 H), 2.17 (dd, $J = 17.1, 6.8$ Hz, 1 H), 1.80 (m, 1 H), 1.00 (d, $J = 6.8$ Hz, 3 H), 0.13 (s, 9 H). ^{13}C NMR (75 MHz, CDCl_3) δ 159.21, 129.94, 129.31, 113.76, 105.70, 85.92, 72.92, 72.42, 72.28, 55.17, 35.06, 23.98, 14.22, 0.05. Anal. Calcd for $\text{C}_{18}\text{H}_{28}\text{O}_3\text{Si}$: C, 67.46; H, 8.81. Found: C, 67.59; H, 8.83. $[\alpha]_{\text{D}}^{26} = +11.5$ (c 3.8, CH_2Cl_2).

Alcohol **71** (75 mg, 0.234 mmol) was dissolved in 2 mL of DMF. Imidazole (21 mg, 0.304 mmol) was then added followed by TBDMSCl (46 mg, 0.304 mmol). After 22 h the reaction was taken up in diethyl ether and washed with water (1x) and brine (2x). The organic layer was then dried (MgSO_4) and concentrated. Purification by silica gel chromatography (2-6% Et_2O /petroleum ether) provided 94 mg (93%) of the silyl ether as an oil: $R_f = 0.37$ (5% Et_2O /95% petroleum ether); IR (film from CH_2Cl_2) 2959, 2859, 2170, 1609 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.35 (d, $J = 8.5$ Hz, 2H), 6.97 (d, $J = 8.5$ Hz, 2H), 4.54 (q, $J = 11.5$ Hz, 2H), 4.05-4.10 (m, 1H), 3.91 (s, 3H), 3.47 (d, $J = 6.1$ Hz, 2H), 2.30 (qd, $J = 16.8, 7.8$, 2H), 1.97-2.05 (m, 1H), 0.98 (d, $J = 6.8$ Hz, 3H), 0.96 (s, 9H), 0.24 (s, 9H), 0.17 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.0, 130.4, 129.2, 113.6, 106.7, 85.4, 72.7, 72.6, 72.0, 55.2, 35.7, 25.9, 24.5, 18.1, 13.0, 0.1, -4.2, -5.0. $[\alpha]_{\text{D}}^{23} = -4.8$ (c 1.2, CH_2Cl_2). Anal calcd for $\text{C}_{24}\text{H}_{42}\text{O}_3\text{Si}_2$: C, 66.30; H, 9.74. Found: C, 66.49; H, 9.62.

The protected alcohol (155 mg, 0.357 mmol) was dissolved in 3 mL of dichloromethane, 1 mL of water was then added followed by DDQ (97 mg, 0.428 mmol). The reaction was then stirred for 1 h, after which it was poured into diethyl ether and washed with sat. aq. NaHCO_3 (3x). The organic layer was then dried (MgSO_4) and concentrated. Purification by silica gel chromatography (20-40% Et_2O /petroleum ether) provided **72** (104 mg, 93%) as a clear oil: $R_f = 0.58$ (30% Et_2O /70% petroleum ether); IR (neat) 3402, 2949, 2170 cm^{-1} ; ^1H NMR (500 MHz,

CDCl₃) δ 3.79 (q, J = 4.7 Hz, 1H), 3.54-3.60 (m, 2H), 2.29 (dd, J = 16.8, 6.0, 1H), 2.16 (dd, J = 16.8, 6.8 Hz, 1H), 1.86-1.91 (m, 1H), 1.70 (s, 1H), 0.97 (d, J = 7.1 Hz, 3H), 0.90 (s, 9H), 0.14 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 106.0, 85.8, 74.5, 64.5, 35.6, 25.8, 23.8, 18.1, 14.6, 0.1, -4.3, -4.7. $[\alpha]_D^{23}$ = -5.7 (c 1.0, CH₂Cl₂).

Alkene **11** (650 mg, 1.71 mmol) was dissolved in 8 mL of THF. Tetrabutylammonium fluoride (1M in THF, 3.76 mL, 3.76 mmol) was then added. After approximately 24 h the reaction was poured into sat. aq. NaHCO₃ and extracted with ethyl ether (4x). The combined organic extracts were then dried (MgSO₄) and concentrated. Purification by silica gel chromatography (20-30% Et₂O/petroleum ether) provided **73** (305 mg, 92%) as a clear oil: R_f = 0.43 (20% Et₂O/80% petroleum ether); IR (film from CH₂Cl₂) 3402, 3312, 2958, 2116 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.55 (dd, J = 15.6, 7.6 Hz, 1H), 5.40 (dd, J = 15.6, 7.0 Hz, 1H), 4.08 (t, J = 5.9 Hz, 1H), 2.33 (ddd, J = 16.6, 5.9, 2.7 Hz, 1H), 2.12-2.17 (m, 1H), 2.08 (ddd, J = 16.6, 7.3, 2.4 Hz, 1H), 1.98 (t, J = 2.4 Hz, 1H), 1.74-1.86 (m, 1H), 1.22-1.32 (m, 4H), 1.02 (d, J = 6.8 Hz, 3H), 0.97 (d, J = 6.6 Hz, 3H), 0.88 (t, J = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 139.0, 128.6, 83.3, 75.5, 69.4, 39.1, 38.2, 36.2, 25.6, 22.1, 20.5, 14.5, 14.1. $[\alpha]_D^{23}$ = +2.7 (c 0.7, CH₂Cl₂).

Alkene **73** (125 mg, 0.643 mmol) was dissolved in 5 mL of methylene chloride and cooled to 0 °C. mCPBA (68%, 171 mg, 0.675 mmol) was then added in small portions over 5 min. After approximately 2 h the reaction was poured into 40 mL of sat. aq. NaHCO₃ and extracted with ethyl ether (3x). The combined organic extracts were then dried (MgSO₄) and concentrated. Purification by silica gel chromatography (25% Et₂O/petroleum ether) provided 50 mg (37%) of the trans epoxide (**74**) and 56 mg (41%) of the cis epoxide (**7**) as clear oils. Data for

74: R_f = 0.41 (30% Et₂O/70% petroleum ether); IR (film from CH₂Cl₂) 3465, 3302, 2959, 2116 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 3.85-3.91 (m, 1H), 2.80-2.87 (m, 2H), 2.38 (ddd, J = 16.8, 6.8, 2.7 Hz, 1H), 2.24 (ddd, J = 16.8, 7.1, 2.7 Hz, 1H), 2.00 (t, J = 2.7 Hz, 1H), 1.87-1.98 (m, 2H), 1.20-1.49 (m, 5H), 1.06 (d, J = 6.8 Hz, 3H), 1.00 (d, J = 6.3 Hz, 3H), 0.91 (t, J = 6.8 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 82.7, 70.8, 69.7, 60.1, 58.9, 35.6, 35.5, 34.9, 22.7, 20.1, 16.6, 14.2, 14.0. HRMS calcd for C₁₀H₁₅O₂ (M-C₃H₇): 167.1072. Found: 167.1074. $[\alpha]_D^{23}$ = +1.0 (c 1.0, CH₂Cl₂). Data for **7**: R_f = 0.32 (30% Et₂O/70% petroleum ether); IR (film from CH₂Cl₂) 3457, 3311, 2958, 2116 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 3.54-3.61 (m, 1H), 2.82 (dd, J = 4.6, 2.2 Hz, 1H), 2.73 (dd, J = 7.1, 2.2 Hz, 1H), 2.36 (ddd, J = 16.8, 6.8, 2.7 Hz, 1H), 2.22 (ddd, J = 16.8, 6.8, 2.7 Hz, 1H), 2.11 (d, J = 5.1 Hz, 1H), 1.99 (t, J = 2.7 Hz, 1H), 1.86-1.94 (m, 2H), 1.20-1.53 (m, 4H), 1.07 (d, J = 6.8 Hz, 3H), 0.88-0.97 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 82.6, 72.7, 69.7, 61.0, 58.8, 37.0, 36.7, 35.0, 22.4, 20.0, 15.7, 14.2, 14.1. HRMS calcd for C₁₀H₁₅O₂ (M-C₃H₇): 167.1072. Found: 167.1076 $[\alpha]_D^{23}$ = +34.7 (c 1.1, CH₂Cl₂).

To a solution of alcohol **7** (127 mg, 0.604 mmol) in PhMe (5 mL) at room temperature was added triphenylphosphine (193 mg, 0.736 mmol), *p*-nitrobenzoic acid (128 mg, 0.766 mmol), and DIAD (145 μ L, 149 mg, 0.736 mmol). The reaction mixture was stirred at room temperature for 4 h, concentrated, and filtered through silica gel (2.5% to 5% EtOAc in petroleum ether) to give the ester which was used in the next step without purification. PH8-15: To a solution of the ester, prepared in the previous step, in MeOH (6 mL) at 0°C was added NaOMe (62 mg, 1.1 mmol). The reaction mixture was stirred at 0°C for 1 h and diluted with ether, pH 7 buffer, and water. The aqueous phase was extracted with ether (5 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄, and concentrated. Purification by flash column chromatography on silica gel (CH₂Cl₂) gave alcohol **82** (31 mg, 24%) as a colorless oil: R_f = 0.27 (CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 3.69 (dt, J = 7.3, 3.1 Hz, 1H), 2.89 (dd, J = 3.4, 2.4 Hz, 1H), 2.80 (dd, J = 7.3, 2.4 Hz, 1H), 2.43 (ddd, J = 16.8, 4.4, 2.6 Hz, 1H), 2.32 (ddd, J = 16.8, 7.5, 2.7 Hz, 1H), 1.99 (t, J = 2.3 Hz, 1H), 1.84 (m, 1H), 1.55-1.26 (m, 6H), 1.13 (d, J = 6.9 Hz, 3H), 0.93 (t, J = 7.3 Hz, 3H), 0.90 (d, J = 7.2 Hz, 3H); ¹³C

NMR (101 MHz, CDCl₃) δ 82.5, 70.9, 69.8, 59.3, 57.9, 36.7, 36.4, 35.1, 22.0, 20.0, 15.9, 15.1, 14.2; IR (neat) 3457 (br), 3303, 2959, 2352, 1460 cm⁻¹; CIMS calcd for C₁₃H₂₃O₂ (M⁺ + H) 211.2, found 211.1; optical rotation [α]_D²⁷ +7.8° (*c* 0.50, CH₂Cl₂).

To a solution of alcohol **74** (323 mg, 1.54 mmol) in PhMe (12 mL) at room temperature was added triphenylphosphine (486 mg, 1.85 mmol), *p*-nitrobenzoic acid (308 mg, 1.84 mmol), and DIAD (365 μ L, 375 mg, 1.85 mmol). The reaction mixture was stirred at room temperature for 3 h, concentrated, and filtered through silica gel (2.5% to 5% to 10% EtOAc in petroleum ether) to give the ester which was used in the next step without purification. PH9-30: To a solution of the ester, prepared in the previous step, in MeOH (28 mL) at 0°C was added NaOMe (300 mg, 5.55 mmol). The reaction mixture was stirred at 0°C for 2.5 h and diluted with ether, pH 7 buffer, and water. The aqueous phase was extracted with ether (6 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄, and concentrated. Purification by flash column chromatography on silica gel (CH₂Cl₂ to 50% EtOAc in CH₂Cl₂) gave alcohol **83** (273 mg, 85%) as a colorless oil: *R*_f = 0.30 (20% EtOAc in petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 3.36 (dd, *J* = 12.7, 5.5 Hz, 1H), 2.88 (dd, *J* = 4.9, 2.3 Hz, 1H), 2.75 (dd, *J* = 6.9, 2.3 Hz, 1H), 2.41 (ddd, *J* = 16.8, 4.9, 2.7 Hz, 1H), 2.34 (ddd, *J* = 16.8, 7.0, 2.6 Hz, 1H), 2.12 (d br, *J* = 5.8 Hz, 1H), 1.98 (t, *J* = 2.6 Hz, 1H), 1.90 (m, 1H), 1.43-1.20 (m, 5H), 1.10 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.6 Hz, 3H), 0.90 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 82.4, 73.6, 69.8, 61.8, 59.6, 36.5, 35.4, 35.0, 21.8, 20.2, 16.7, 15.5, 14.2; IR (neat) 3457 (br), 3312, 2959, 2361, 1460 cm⁻¹; CIMS calcd for C₁₃H₂₃O₂ (M⁺ + H) 211.2, found 211.2; optical rotation [α]_D²⁶ -23° (*c* 2.0, CH₂Cl₂); Anal. Calcd for C₁₃H₂₂O₂: C, 74.24; H, 10.54. Found: C, 74.38; H, 10.34.

To KN(TMS)₂ (6.4 mL, 0.47 M in DME, 3.0 mmol) at -78°C was added a solution of **ent-13** (823 mg, 2.80 mmol) in DME (6 mL) at -78°C. The solution was stirred at -78°C for 1 h and a solution of aldehyde **12** (677 mg, 2.17 mmol) in DME (6 mL) at -78°C was added via cannula. The reaction mixture was warmed from -78°C to room temperature over 3 h, stirred at room temperature for 10 h, partially concentrated, and diluted with ether and water. The aqueous phase was extracted with ether (5 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄, and concentrated. Purification by flash column chromatography on silica gel (1% to 2% EtOAc in petroleum ether) gave the alkene (614 mg, 74%) as a colorless oil: *R*_f = 0.71 (5% EtOAc in petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 5.39 (dd, *J* = 15.4, 7.3 Hz, 1H), 5.30 (dd, *J* = 15.4, 6.9 Hz, 1H), 4.04 (dd, *J* = 6.9, 4.9 Hz, 1H), 2.30 (dd, *J* = 16.8, 5.8 Hz, 1H), 2.10 (m, 1H), 2.05 (dd, *J* = 16.9, 7.8 Hz, 1H), 1.68 (m, 1H), 1.32-1.21 (m, 4H), 0.963 (d, *J* = 6.7 Hz, 3H), 0.957 (d, *J* = 6.7 Hz, 3H), 0.89-0.86 (m, 3H), 0.88 (s, 9H), 0.15 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 137.7, 129.8, 106.9, 85.3, 76.0, 39.6, 39.2, 36.3, 25.9, 23.7, 20.6, 20.5, 18.2, 14.4, 14.1, 0.17, -4.0, -4.9; IR (neat) 2953, 2176, 1247, 1032, 842 cm⁻¹; EIMS *m/z* 147 (57), 81 (50), 73 (97), 71 (69), 69 (100); HREIMS calcd for C₁₈H₃₅OSi₂ (M⁺ - *tert*-butyl) 323.2226, found 323.2191; optical rotation [α]_D²⁶ +24° (*c* 1.0, CH₂Cl₂).

To a solution of the silyl ether (608 mg, 1.60 mmol) in THF (3.5 mL) at room temperature was added TBAF (3.5 mL, 1 M in THF, 3.5 mmol). The reaction mixture was stirred at room temperature for 24 h and concentrated. Purification by flash column chromatography on silica gel (5% to 10% to 20% EtOAc in petroleum ether) gave the alcohol (272 mg, 88%) as a colorless oil: *R*_f = 0.41 (20% EtOAc in petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 5.53 (ddd, *J* = 15.4, 7.8, 0.9 Hz, 1H), 5.40 (ddd, *J* = 15.4, 7.0, 0.9 Hz, 1H), 4.06 (m, 1H), 2.32 (ddd, *J* = 16.8, 5.8, 2.6 Hz, 1H), 2.13 (m, 1H), 2.08 (ddd, *J* = 16.8, 7.6, 2.8 Hz, 1H), 1.97 (t, *J* = 2.6 Hz, 1H), 1.80 (m, 1H), 1.60 (d br, *J* = 3.8 Hz, 1H), 1.30-1.23 (m, 4H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.87 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 139.3, 128.6, 83.2, 75.7, 69.4, 39.1, 38.2, 36.3, 22.1, 20.5, 20.4, 14.5, 14.1; IR (neat) 3420 (br), 3312, 2949, 2361, 1456, 989 cm⁻¹; EIMS *m/z* 163 (29), 149 (36), 105 (100), 77 (38), 69 (34); HREIMS calcd for

$C_8H_{15}O$ ($M^+ - HC\equiv CCH_2(CH_3)CH\cdot$) 127.1123, found 127.1119; optical rotation $[\alpha]_D^{27} +41^\circ$ (c 1.0, CH_2Cl_2).

To a solution of the alkene (272 mg, 1.39 mmol) in CH_2Cl_2 (11 mL) at $-10^\circ C$ was added $VO(acac)_2$ (26 mg, 0.098 mmol) and *tert*-butyl hydroperoxide (840 μL , 5-6 M in decane, 4.2-5.0 mmol). The reaction mixture was stirred at $-10^\circ C$ for 6 h and quenched with saturated Na_2SO_3 . After stirring for 15 min, the reaction mixture was diluted with ether and water. The aqueous phase was extracted with ether (3 x) and the combined organic extracts were washed with brine (1 x), dried over $MgSO_4$, and concentrated. Purification by flash column chromatography on silica gel (5% to 7.5% to 10% to 15% to 20% EtOAc in petroleum ether) gave a mixture of epoxides **85** (231 mg, 78%) and **84** (45 mg, 15%) as colorless oils. Data for **85**: R_f = 0.44 (20% EtOAc in petroleum ether); 1H NMR (400 MHz, $CDCl_3$) δ 3.92 (t, J = 3.5 Hz, 1H), 2.85 (dd, J = 6.9, 1.8 Hz, 1H), 2.82 (t, J = 2.9 Hz, 1H), 2.39 (ddd, J = 16.8, 6.9, 2.6 Hz, 1H), 2.23 (ddd, J = 16.8, 7.2, 2.8 Hz, 1H), 2.00 (dd, J = 2.6, 2.1 Hz, 1H), 1.94 (m, 1H), 1.54-1.19 (m, 6H), 1.07 (d, J = 6.9 Hz, 3H), 0.95 (d, J = 6.9 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 82.8, 70.3, 67.9, 59.8, 58.2, 36.7, 35.7, 35.2, 22.8, 20.0, 15.9, 14.2, 14.0; IR (neat) 3466 (br), 3312, 2959, 2361, 1460 cm^{-1} ; CIMS m/z 211.2 $[M + H]^+$; optical rotation $[\alpha]_D^{26} +2.0^\circ$ (c 0.25, CH_2Cl_2); Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.24; H, 10.68. Data for **84**: R_f = 0.39 (20% EtOAc in petroleum ether); 1H NMR (400 MHz, $CDCl_3$) δ 3.64 (t, J = 4.4 Hz, 1H), 2.91 (dd, J = 4.1, 2.4 Hz, 1H), 2.75 (dd, J = 6.9, 2.3 Hz, 1H), 2.37 (ddd, J = 16.8, 6.9, 2.6 Hz, 1H), 2.24 (ddd, J = 16.8, 6.6, 2.4 Hz, 1H), 2.00 (t, J = 2.4 Hz, 1H), 1.93 (m, 1H), 1.43-1.20 (m, 6H), 1.09 (d, J = 6.9 Hz, 3H), 1.01 (d, J = 6.4 Hz, 3H), 0.90 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 82.7, 72.1, 69.7, 61.0, 60.1, 37.1, 35.5, 35.1, 22.6, 20.2, 16.8, 14.2, 14.1; IR (neat) 3464 (br), 3310, 2951, 2353, 1462, 902 cm^{-1} ; CIMS m/z 211.2 $[M + H]^+$; optical rotation $[\alpha]_D^{27} +39^\circ$ (c 0.50, CH_2Cl_2); Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 73.99; H, 10.44.

To a suspension of activated 3Å powdered molecular sieves (19 g) in CH₂Cl₂ (150 mL) was added a solution of freshly distilled (-)-diethyl tartrate (9.5 mL, 11 g, 56 mmol) in CH₂Cl₂ (25 mL). The solution was cooled to -30°C and distilled Ti(Oi-Pr)₄ (13.5 mL, 13.0 g, 46 mmol) and *tert*-butyl hydroperoxide (93 mL, 5-6 M in decane, 465-558 mmol, solution dried for 20 min over activated 4Å molecular sieves before addition) were added. The solution was stirred at -30°C for 30 min, and a solution of alcohol **66** (19.250 g, 92.4 mmol) in CH₂Cl₂ (100 mL, solution dried for 20 min over activated 4Å molecular sieves before addition) at -30°C was added. The reaction mixture was maintained without stirring at -20°C for 48 h, and quenched by slow addition to a solution of FeSO₄·7H₂O (153 g) and tartaric acid (96 g) in water (500 mL) at 0°C. The mixture was stirred for 15 min and extracted with ether (3 x). The combined extracts were cooled to 0°C, 30% aqueous NaOH (100 mL) was added, stirred for 1 h, and diluted with water. The aqueous phase was extracted with ether (3 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄, and concentrated. Purification by crystallization from a mixture of CH₂Cl₂ and petroleum ether followed by filtration of an EtOAc solution through a pad of silica gel (washed with 10% to 50% EtOAc in petroleum ether) gave epoxide **ent-68** (15.146 g, 73%) as a low melting white solid that matched the spectroscopic data for **68**: optical rotation [α]_D²⁵ +16° (*c* 2.15, CH₂Cl₂).

To a suspension of CuCN (5.645 g, 63.0 mmol) in ether (60 mL) at -40°C was added MeLi·LiBr (80 mL, 1.5 M in ether, 120 mmol). The solution was warmed from -40°C to -20°C over 1 h, cooled to -50°C, and a solution of epoxide **ent-68** (4.030 g, 18.0 mmol) in ether (20 mL) was added via cannula. The reaction mixture was warmed from -50°C to -15°C over 1 h, quenched with pH 9 saturated NH₄Cl/concentrated NH₄OH, warmed to room temperature, and stirred for several hours until all the solids dissolved. The aqueous phase was extracted with EtOAc (8 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄,

and concentrated to give a mixture of **ent-69** and the 1,2-diol which was used in the next step without purification. To a solution of alcohol **ent-69**, prepared in the previous step, and the 1,2-diol in THF (60 mL) and water (6 mL) at 0°C was added NaIO₄ (4.004 g, 18.7 mmol). The reaction mixture was warmed to room temperature, stirred for 1.5 h, diluted with CH₂Cl₂ (200 mL), filtered through a glass frit, washed with brine, dried over MgSO₄, and concentrated. Purification by flash column chromatography on silica gel (50% to 75% to 100% EtOAc in petroleum ether) gave 1,3-diol **ent-69** (2.91 g, 67%) as a colorless oil that matched the spectroscopic data for **69**.

To a solution of diol **ent-69** (6.437 g, 26.8 mmol) in pyridine (125 mL) at 0°C was added TsCl (5.2 g, 27 mmol). The reaction mixture was stirred at 0°C for 2 d, partially concentrated, and diluted with 1 M HCl and ether. The aqueous phase was extracted with ether (4 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄, and concentrated to give the tosylate which was used in the next step without purification. To a suspension of NaH (2.5 g, 60% dispersion in mineral oil, 63 mmol) in THF (10 mL) at room temperature was added a solution of the tosylate, prepared in the previous step, in THF (55 mL). The reaction mixture was stirred at room temperature for 10 h, quenched with water, and diluted with ether and water. The aqueous phase was extracted with ether (5 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄, and concentrated. Purification by flash column chromatography on silica gel (20% to 30% to 40% EtOAc in petroleum ether) gave ether **ent-70** (4.22 g, 69%) as a colorless oil that matched the spectroscopic data for **70**.

To a solution of (trimethylsilyl)acetylene (12.4 mL, 8.62 g, 87.7 mmol) in THF (125 mL) at -78°C was added *n*-BuLi (62 mL, 1.3 M in hexanes, 81 mmol). The solution was warmed to room temperature, cooled to -78°C, and BF₃·Et₂O (10.3 mL, 11.4 g, 80.6 mmol) was added. After 10 min, a solution of oxetane **ent-70** (6.026 g, 26.4 mmol) in THF (20 mL) was added via

cannula. The reaction mixture was stirred at -78°C for 45 min, quenched with saturated NH_4Cl , warmed to room temperature, and diluted with ether and water. The aqueous phase was extracted with ether (3 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (15% to 30% EtOAc in petroleum ether) gave alcohol **ent-71** (7.284 g, 86%) as a colorless oil that matched the spectroscopic data reported for **71**: Anal. Calcd for $\text{C}_{18}\text{H}_{28}\text{O}_3\text{Si}$: C, 74.24; H, 10.54. Found: C, 74.16; H, 10.36.

To a solution of alcohol **ent-71** (3.410 g, 10.6 mmol) in DMF (20 mL) at room temperature was added a small amount of DMAP (spatula tip), imidazole (1.42 g, 20.9 mmol), and TBSCl (2.11 g, 14.0 mmol). The reaction mixture was stirred at room temperature for 2 h and diluted with ether and water. The aqueous phase was extracted with ether (4 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (1% to 2% to 4% EtOAc in petroleum ether) gave the ether (3.612 g, 78%) as a colorless oil that matched the spectroscopic data reported for the corresponding enantiomer: optical rotation $[\alpha]_{\text{D}}^{26} +7.7^{\circ}$ (c 1.0, CH_2Cl_2).

To a solution of the ether (3.586 g, 8.25 mmol) in CH_2Cl_2 (60 mL) and water (20 mL) at room temperature was added DDQ (2.316 g, 10.2 mmol). After 1 h at room temperature, the reaction mixture was diluted with CH_2Cl_2 , saturated NaHCO_3 , and water. The aqueous phase was extracted with CH_2Cl_2 (5 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (3% to 6% to 10% EtOAc in petroleum ether) gave alcohol **ent-72** (2.522 g, 97%) as a colorless oil that matched the spectroscopic data reported for **72**: optical rotation $[\alpha]_{\text{D}}^{25} +11^{\circ}$ (c 1.0, CH_2Cl_2); Anal. Calcd for $\text{C}_{16}\text{H}_{34}\text{O}_2\text{Si}_2$: C, 61.08; H, 10.89. Found: C, 61.19; H, 10.81.

To a solution of alcohol **ent-72** (1.278 g, 4.06 mmol) in CH_2Cl_2 (33 mL) at room temperature was added DMP (9.4 mL, 15% wt. in CH_2Cl_2 , 4.5 mmol). After 1.5 h at room temperature, the reaction mixture was quenched with saturated sodium thiosulfate and saturated NaHCO_3 , stirred for 15 min, and diluted with water. The aqueous phase was extracted with CH_2Cl_2 (3 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (3% EtOAc in petroleum ether) gave aldehyde **ent-12** (926 mg, 73%) as a colorless oil: R_f = 0.41 (5% EtOAc in petroleum ether); ^1H NMR (500 MHz, CDCl_3) δ 9.67 (d, J = 1.1 Hz, 1H), 4.21 (dd, J = 3.1, 1.1 Hz, 1H), 2.32-2.16 (m, 3H), 0.94 (s, 9H), 0.91 (d, J = 6.7 Hz, 3H), 0.14 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (126 MHz, CDCl_3) δ 204.9, 105.2, 86.7, 78.8, 36.2, 25.8, 23.9, 18.2, 13.7, 0.0, -4.5, -5.2; IR (neat) 2957, 2796, 2171, 1737, 1248, 840 cm^{-1} ; CIMS m/z 313 $[\text{M} + \text{H}]^+$; HREIMS calcd for $\text{C}_{15}\text{H}_{31}\text{OSi}_2$ ($\text{M}^+ - \text{CHO}$) 283.1913, found 283.1918.

To $\text{KN}(\text{TMS})_2$ (7.5 mL, 0.46 M in DME, 3.5 mmol) at -78°C was added a solution of **13** (984 mg, 3.34 mmol) in DME (7 mL) at -78°C . The solution was stirred at -78°C for 1 h and a solution of aldehyde **ent-12** (781 mg, 2.50 mmol) in DME (7 mL) at -78°C was added via cannula. The reaction mixture was warmed from -78°C to room temperature over 3 h, stirred at room temperature for 10 h, partially concentrated, and diluted with ether and water. The aqueous phase was extracted with ether (5 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (1% to 2% EtOAc in petroleum ether) gave the alkene (880 mg, 93%) as a colorless oil: R_f = 0.71 (5% EtOAc in petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 5.39 (dd, J = 15.4, 7.3 Hz, 1H), 5.30 (dd, J = 15.4, 6.9 Hz, 1H), 4.04 (dd, J = 6.9, 4.9 Hz, 1H), 2.30 (dd, J = 16.8, 5.8 Hz, 1H), 2.10 (m, 1H), 2.05 (dd, J = 16.9, 7.8 Hz, 1H), 1.68 (m, 1H), 1.32-1.21 (m, 4H), 0.963

(d, $J = 6.7$ Hz, 3H), 0.957 (d, $J = 6.7$ Hz, 3H), 0.89-0.86 (m, 3H), 0.88 (s, 9H), 0.15 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 137.7, 129.8, 106.9, 85.3, 76.0, 39.6, 39.2, 36.3, 25.9, 23.7, 20.6, 20.5, 18.2, 14.4, 14.1, 0.17, -4.0, -4.9; IR (neat) 2953, 2176, 1247, 1032, 842 cm^{-1} ; EIMS m/z 147 (57), 81 (50), 73 (97), 71 (69), 69 (100); HREIMS calcd for $\text{C}_{18}\text{H}_{35}\text{OSi}_2$ ($\text{M}^+ - \text{tert-Bu}$) 323.2226, found 323.2191; optical rotation $[\alpha]_{\text{D}}^{25} -23^\circ$ (c 1.0, CH_2Cl_2).

To a solution of the silyl ether (859 mg, 2.26 mmol) in THF (5 mL) at room temperature was added TBAF (5.0 mL, 1 M in THF, 5.0 mmol). The reaction mixture was stirred at room temperature for 24 h and concentrated. Purification by flash column chromatography on silica gel (10% to 20% to 40% EtOAc in petroleum ether) gave the alcohol (415 mg, 95%) as a colorless oil: $R_f = 0.41$ (20% EtOAc in petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 5.53 (ddd, $J = 15.4, 7.8, 0.9$ Hz, 1H), 5.40 (ddd, $J = 15.4, 7.0, 0.9$ Hz, 1H), 4.06 (m, 1H), 2.32 (ddd, $J = 16.8, 5.8, 2.6$ Hz, 1H), 2.13 (m, 1H), 2.08 (ddd, $J = 16.8, 7.6, 2.8$ Hz, 1H), 1.97 (t, $J = 2.6$ Hz, 1H), 1.80 (m, 1H), 1.60 (d br, $J = 3.8$ Hz, 1H), 1.30-1.23 (m, 4H), 1.02 (d, $J = 6.9$ Hz, 3H), 0.97 (d, $J = 6.7$ Hz, 3H), 0.87 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 139.3, 128.6, 83.2, 75.7, 69.4, 39.1, 38.2, 36.3, 22.1, 20.5, 20.4, 14.5, 14.1; IR (neat) 3420 (br), 3312, 2949, 2361, 1456, 989 cm^{-1} ; EIMS m/z 163 (29), 149 (36), 105 (100), 77 (38), 69 (34); HREIMS calcd for $\text{C}_8\text{H}_{15}\text{O}$ ($\text{M}^+ - \text{HC}\equiv\text{CCH}_2(\text{CH}_3)\text{CH}\cdot$) 127.1123, found 127.1119; optical rotation $[\alpha]_{\text{D}}^{26} -39^\circ$ (c 1.0, CH_2Cl_2).

To a solution of the alkene (415 mg, 2.14 mmol) in CH_2Cl_2 (20 mL) at 0°C was added MCPBA (649 mg, 68% pure, 2.6 mmol). The reaction mixture was stirred at 0°C for 5 h and quenched with saturated Na_2SO_3 and saturated NaHCO_3 . After stirring for 10 min, the reaction mixture was diluted with water. The aqueous phase was extracted with CH_2Cl_2 (5 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated.

Purification by flash column chromatography on silica gel (5% to 10% to 20% EtOAc in petroleum ether) gave a mixture of epoxides **ent-85** (122 mg, 27%), **ent-84** (258 mg, 57%), and a mixture of **ent-85** and **ent-84** (48 mg, 11%) as colorless oils. Data for **ent-85**: optical rotation $[\alpha]_D^{23} +3.5^\circ$ (*c* 0.5, CH₂Cl₂); Anal. Calcd for C₁₃H₂₂O₂: C, 74.24; H, 10.54. Found: C, 74.24; H, 10.68. Data for **ent-84**: optical rotation $[\alpha]_D^{24} -39^\circ$ (*c* 1.0, CH₂Cl₂); Anal. Calcd for C₁₃H₂₂O₂: C, 74.24; H, 10.54. Found: C, 74.16; H, 10.36.

To a solution of KN(TMS)₂ (8.0 mL, 0.47 M in DME, 3.8 mmol) at -78°C was added a solution of sulfone **ent-13** (1.106 g, 3.76 mmol) in DME (8 mL) at -78°C. The solution was stirred at -78°C for 1 h and a solution of aldehyde **ent-12** (853 mg, 2.73 mmol) in DME (8 mL) at -78°C was added via cannula. The reaction mixture was warmed from -78°C to room temperature over 2 h, stirred at room temperature for 12 h, partially concentrated, and diluted with ether and water. The aqueous phase was extracted with ether (4 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄, and concentrated. Purification by flash column chromatography on silica gel (1% to 2% EtOAc in petroleum ether) gave alkene **ent-11** (633 mg, 61%) as a colorless oil that matched the spectroscopic data for **11**.

To a solution of silyl ether **ent-11** (633 mg, 1.66 mmol) in THF (3.7 mL) at room temperature was added TBAF (3.7 mL, 1 M in THF, 3.7 mmol). The reaction mixture was stirred at room temperature for 24 h and concentrated. Purification by flash column chromatography on silica gel (10% to 20% to 30% EtOAc in petroleum ether) gave alcohol **ent-73** (319 mg, 99%) as a colorless oil that matched the spectroscopic data for **73**: optical rotation $[\alpha]_D^{25} -3.1^\circ$ (*c* 0.5, CH₂Cl₂).

To a solution of alkene **ent-73** (319 mg, 1.64 mmol) in CH_2Cl_2 (15 mL) at 0°C was added MCPBA (542 mg, 68% pure, 3.14 mmol). The reaction mixture was stirred at 0°C for 5 h and quenched with saturated Na_2SO_3 and saturated NaHCO_3 . After stirring for 15 min, the reaction mixture was diluted with water and ether. The aqueous phase was extracted with ether (3 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (5% to 10% to 20% EtOAc in petroleum ether) gave a mixture of epoxides **ent-74** (136 mg, 39%) and **ent-7** (183 mg, 53%) as colorless oils that matched the spectroscopic data reported for **74** and **7**. Data for **ent-74**: optical rotation $[\alpha]_D^{25} +2.9^\circ$ (c 0.5, CH_2Cl_2). Data for **ent-7**: optical rotation $[\alpha]_D^{25} -27^\circ$ (c 0.5, CH_2Cl_2).

To a solution of alcohol **ent-71** (107 mg, 0.33 mmol) in PhH (6.5 mL) at room temperature was added triphenylphosphine (325 mg, 1.24 mmol), *p*-nitrobenzoic acid (166 mg, 0.993 mmol), and DIAD (235 μL , 241 mg, 1.19 mmol). The reaction mixture was stirred at room temperature for 4 h, concentrated, and filtered through silica gel (10% to 15% to 20% EtOAc in petroleum ether) to give the ester which was used in the next step without purification. PH9-39: To a solution of the ester, prepared in the previous step, in CH_2Cl_2 (3 mL) at -78°C was added DIBAL (790 μL , 1 M in heptane, 0.79 mmol). The reaction mixture was stirred at -78°C for 10 min, quenched with EtOAc, warmed to room temperature, diluted with aqueous sodium potassium tartrate, stirred for 15 min, and diluted with ether and water. The aqueous phase was extracted with ether (3 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (20% EtOAc in petroleum ether) gave the alcohol (88 mg, 82%) as a colorless oil: $R_f = 0.31$ (15% EtOAc in petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.26 (d, $J = 8.9$ Hz, 2H), 6.89 (d, $J = 8.7$ Hz, 2H), 4.52-4.45 (m, 2H), 3.81 (s, 3H), 3.63 (ddd, $J = 7.5, 7.5, 2.9$ Hz, 1H), 3.57 (dd, $J =$

9.5, 3.1 Hz, 1H), 3.40 (dd, $J = 9.3, 7.3$ Hz, 1H), 2.45 (s br, 1H), 2.44 (dd, $J = 16.9, 4.6$ Hz, 1H), 2.29 (dd, $J = 17.1, 7.5$ Hz, 1H), 1.80 (m, 1H), 0.98 (d, $J = 6.9$ Hz, 3H), 0.14 (s, 9H); ^{13}C NMR (101 MHz, CDCl_3) δ 159.3, 129.9, 129.4, 113.8, 105.8, 85.9, 73.2, 73.0, 72.1, 55.3, 35.4, 23.2, 15.6, 0.12; optical rotation $[\alpha]_{\text{D}}^{27} +1.4^\circ$ (c 1.0, CH_2Cl_2).

To a solution of the alcohol (2.909 g, 9.08 mmol) in THF (13 mL) and DMF (13 mL) at room temperature was added a small amount of DMAP (spatula tip), imidazole (1.918 g, 28.2 mmol), and TBSCl (1.986 g, 13.2 mmol). The reaction mixture was stirred at room temperature for 15 h and diluted with petroleum ether and water. The aqueous phase was extracted with petroleum ether (3 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (1% to 2% to 5% EtOAc in petroleum ether) gave the ether (3.483 g, 88%) as a colorless oil: $R_f = 0.38$ (5% EtOAc in petroleum ether); ^1H NMR (500 MHz, CDCl_3) δ 7.26 (d, $J = 8.8$ Hz, 2H), 6.87 (d, $J = 8.7$ Hz, 2H), 4.44 (s, 2H), 3.81 (s, 3H), 3.74 (q br, $J = 5.2$ Hz, 1H), 3.44 (dd, $J = 10.0, 4.6$ Hz, 1H), 3.38 (dd, $J = 10.0, 5.5$ Hz, 1H), 2.31 (dd, $J = 16.9, 5.3$ Hz, 1H), 2.21 (dd, $J = 17.0, 7.8$ Hz, 1H), 1.93 (m, 1H), 0.99 (d, $J = 6.8$ Hz, 3H), 0.88 (s, 9H), 0.14 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 159.1, 130.4, 129.2, 113.7, 106.7, 85.4, 74.2, 72.9, 72.5, 55.2, 36.1, 25.9, 22.4, 18.2, 16.1, 0.2, -4.2, -4.9; IR (neat) 2945, 2174, 1612, 1249, 1092, 1038, 845 cm^{-1} ; EIMS m/z 283 (4), 121 (100), 147 (3); HREIMS calcd for $\text{C}_{24}\text{H}_{42}\text{O}_3\text{Si}_2$ 434.2673, found 434.2692; optical rotation $[\alpha]_{\text{D}}^{26} -5.3^\circ$ (c 1.0, CH_2Cl_2). Anal. Calcd for $\text{C}_{24}\text{H}_{42}\text{O}_3\text{Si}_2$: C, 61.08; H, 10.89. Found: C, 61.31; H, 10.67.

To a solution of the ether (3.588 g, 8.25 mmol) in CH_2Cl_2 (60 mL) and water (20 mL) at room temperature was added DDQ (2.377 g, 10.5 mmol). After 2 h at room temperature, the reaction mixture was diluted with CH_2Cl_2 , saturated NaHCO_3 , and water. The aqueous phase was

extracted with CH₂Cl₂ (4 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄, and concentrated. Purification by flash column chromatography on silica gel (5% to 7% to 12% EtOAc in petroleum ether) gave the alcohol (2.577 g, 99%) as a colorless oil: *R_f* = 0.46 (20% EtOAc in petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 3.68-3.56 (m, 3H), 2.31 (dd, *J* = 16.9, 5.8 Hz, 1H), 2.23 (dd, *J* = 16.9, 6.4 Hz, 1H), 1.97 (sept br, *J* = 6.6 Hz, 1H), 1.84 (dd, *J* = 7.2, 5.5 Hz, 1H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.91 (s, 9H), 0.14 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 105.9, 86.0, 75.1, 63.7, 35.1, 25.9, 23.1, 18.1, 15.7, 0.1, -4.4, -4.7; IR (neat) 3447, 2954, 2165, 1249, 1047, 841 cm⁻¹; CIMS *m/z* 315 (51) [M + H]⁺, 183 (29), 147 (60); HREIMS calcd for C₁₅H₃₁OSi₂ (M⁺ - CH₂OH) 283.1913, found 283.1909; optical rotation [α]_D²⁷ -21° (*c* 1.0, CH₂Cl₂).

To a solution of the alcohol (1.261 g, 4.01 mmol) in CH₂Cl₂ (33 mL) at 0°C was added DMP (9.2 mL, 15% wt. in CH₂Cl₂, 4.4 mmol). The reaction mixture was warmed to room temperature, stirred at room temperature for 1 h, quenched with saturated sodium thiosulfate and saturated NaHCO₃, stirred for 30 min, and diluted with water and CH₂Cl₂. The aqueous phase was extracted with CH₂Cl₂ (3 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO₄, and concentrated. Purification by flash column chromatography on silica gel (2.5% EtOAc in petroleum ether) gave the aldehyde (859 mg, 69%) as a colorless oil: *R_f* = 0.48 (5% EtOAc in petroleum ether); ¹H NMR (500 MHz, CDCl₃) δ 9.62 (d, *J* = 2.2 Hz, 1H), 3.84 (dd, *J* = 5.6, 2.3 Hz, 1H), 2.33 (dd, *J* = 16.9, 6.5 Hz, 1H), 2.27 (dd, *J* = 16.9, 6.5 Hz, 1H), 2.11 (sept br, *J* = 6.6 Hz, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.92 (s, 9H), 0.14 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 203.9, 105.2, 86.9, 80.2, 36.4, 25.7, 22.1, 18.1, 15.8, 0.0, -4.5, -5.1; IR (neat) 2959, 2850, 2180, 1737, 1252, 841 cm⁻¹; CIMS *m/z* 313 (31) [M + H]⁺, 283 (19), 181 (19), 147 (28); HREIMS calcd for C₁₅H₃₁OSi₂ (M⁺ - CHO) 283.1913, found 283.1917; optical rotation [α]_D²⁷ -21° (*c* 1.0, CH₂Cl₂).

To $\text{KN}(\text{TMS})_2$ (7.10 mL, 0.47 M in DME, 3.34 mmol) at -78°C was added a solution of **13** (982 mg, 3.33 mmol) in DME (7 mL) at -78°C . The solution was stirred at -78°C for 1 h and a solution of the aldehyde (834 mg, 2.67 mmol) in DME (7 mL) at -78°C was added via cannula. The reaction mixture was warmed from -78°C to room temperature over 3 h, stirred at room temperature for 12 h, partially concentrated, and diluted with petroleum ether and water. The aqueous phase was extracted with petroleum ether (3 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (1% to 2% EtOAc in petroleum ether) gave the alkene (834 mg, 82%) as a colorless oil: R_f = 0.65 (2.5% EtOAc in petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 5.42 (dd, J = 15.6, 7.6 Hz, 1H), 5.28 (dd, J = 15.4, 7.3 Hz, 1H), 3.93 (dd, J = 6.9, 6.9 Hz, 1H), 2.28 (dd, J = 16.9, 5.5 Hz, 1H), 2.20 (dd, J = 16.8, 7.3 Hz, 1H), 2.12 (m, 1H), 1.70 (sept br, J = 6.9 Hz, 1H), 1.32-1.22 (m, 4H), 0.96 (d, J = 6.9 Hz, 3H), 0.91 (d, J = 6.9 Hz, 3H), 0.90-0.86 (m, 3H), 0.88 (s, 9H), 0.15 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 138.2, 129.3, 106.6, 85.4, 76.6, 39.2, 39.1, 36.1, 25.9, 23.1, 20.6, 20.4, 18.2, 15.3, 14.2, 0.17, -4.0, -4.9; IR (neat) 2959, 2171, 1460, 1252, 1062, 840 cm^{-1} ; CIMS m/z 381 (16) $[\text{M} + \text{H}]^+$, 365 (24), 323 (22), 249 (88), 241 (88), 175 (42), 147 (61); HREIMS calcd for $\text{C}_{18}\text{H}_{35}\text{OSi}_2$ ($\text{M}^+ - \text{tert-butyl}$) 323.2226, found 323.2236; optical rotation $[\alpha]_{\text{D}}^{25}$ -2.3° (c 1.0, CH_2Cl_2).

To a solution of the silyl ether (834 mg, 2.19 mmol) in THF (5 mL) at room temperature was added TBAF (5.0 mL, 1 M in THF, 5.0 mmol). The reaction mixture was stirred at room temperature for 24 h, concentrated, and diluted with ether and water. The aqueous phase was extracted with ether (3 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (5% to 10% to 20% EtOAc in petroleum ether) gave the alcohol (352 mg, 83%) as a colorless oil: R_f = 0.65 (2.5% EtOAc in petroleum ether); ^1H NMR (500 MHz, CDCl_3) δ 5.56 (ddd, J = 15.5, 7.7,

0.9 Hz, 1H), 5.39 (ddd, $J = 15.4, 7.4, 1.0$ Hz, 1H), 3.95 (ddd, $J = 7.2, 7.2, 3.5$ Hz, 1H), 2.32 (ddd, $J = 16.7, 5.0, 2.7$ Hz, 1H), 2.24 (ddd, $J = 16.7, 7.2, 2.7$ Hz, 1H), 2.15 (m, 1H), 1.97 (t, $J = 2.7$ Hz, 1H), 1.78 (ddd, $J = 14.0, 7.1, 5.1$ Hz, 1H), 1.57 (d br, $J = 3.5$ Hz, 1H), 1.31-1.24 (m, 4H), 0.974 (d, $J = 7.0$ Hz, 3H), 0.972 (d, $J = 6.7$ Hz, 3H), 0.88 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 139.7, 128.7, 83.1, 76.1, 69.4, 39.0, 38.0, 36.1, 21.8, 20.5, 20.4, 15.4, 14.1; IR (neat) 3384, 3312, 2949, 1451, 1008, 971 cm^{-1} ; CIMS m/z 195 (5) $[\text{M} + \text{H}]^+$, 177 (14), 137 (36), 109 (35); HREIMS calcd for $\text{C}_8\text{H}_{15}\text{O}$ ($\text{M}^+ - \text{HC}\equiv\text{CCH}_2(\text{CH}_3)\text{CH}$) 127.1123, found 127.1128; optical rotation $[\alpha]_{\text{D}}^{24} -7.3^\circ$ (c 1.0, CH_2Cl_2).

To a solution of the alkene (352 mg, 1.81 mmol) in CH_2Cl_2 (17 mL) at 0°C was added MCPBA (562 mg, 68% pure, 2.2 mmol). The reaction mixture was stirred at 0°C for 5 h and quenched with saturated Na_2SO_3 and saturated NaHCO_3 . After stirring for 10 min, the reaction mixture was diluted with water. The aqueous phase was extracted with CH_2Cl_2 (4 x) and the combined organic extracts were washed with brine (1 x), dried over MgSO_4 , and concentrated. Purification by flash column chromatography on silica gel (5% to 10% to 20% EtOAc in petroleum ether) gave a mixture of epoxides **87** (116 mg, 30%), **86** (201 mg, 53%), and a mixture of **87** and **86** (54 mg, 14%) as colorless oils. Data for **87**: $R_f = 0.37$ (20% EtOAc in petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 3.63 (dd, $J = 7.5, 3.2, 3.2$ Hz, 1H), 2.92 (dd, $J = 3.5, 2.4$ Hz, 1H), 2.76 (dd, $J = 7.0, 2.4$ Hz, 1H), 2.41 (ddd, $J = 16.8, 4.6, 2.7$ Hz, 1H), 2.31 (ddd, $J = 16.7, 7.3, 2.7$ Hz, 1H), 2.13 (d, $J = 2.4$ Hz, 1H), 1.98 (t, $J = 2.6$ Hz, 1H), 1.83 (m, 1H), 1.40-1.20 (m, 5H), 1.11 (d, $J = 6.9$ Hz, 3H), 1.00 (d, $J = 6.4$ Hz, 3H), 0.89 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 82.4, 71.3, 69.8, 59.5, 59.0, 36.3, 35.5, 34.9, 22.0, 20.1, 16.8, 15.2, 14.2; IR (neat) 3457, 3303, 2958, 1460, 903 cm^{-1} ; CIMS m/z 211 (8) $[\text{M} + \text{H}]^+$, 193 (53), 153 (27), 127 (65), 109 (51); HREIMS calcd for $\text{C}_8\text{H}_{15}\text{O}_2$ ($\text{M}^+ - \text{HC}\equiv\text{CCH}_2(\text{CH}_3)\text{CH}$) 143.1072, found 143.1076; optical rotation $[\alpha]_{\text{D}}^{26} -6.9^\circ$ (c 0.50, CH_2Cl_2). Data for **86**: $R_f = 0.30$ (20% EtOAc in petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 3.25 (ddd, $J = 7.9, 5.3, 5.3$ Hz, 1H), 2.80 (dd, $J = 5.8, 2.3$ Hz, 1H), 2.73 (dd, $J = 7.3, 2.4$ Hz, 1H), 2.47 (d br, $J = 5.2$ Hz, 1H), 2.39 (ddd, $J = 16.8, 4.7, 2.6$ Hz, 1H), 2.32 (ddd, $J = 16.8, 6.9, 2.6$ Hz, 1H), 1.95 (t, $J = 2.8$ Hz, 1H),

1.88 (m, 1H), 1.52-1.19 (m, 5H), 1.06 (d, $J = 6.9$ Hz, 3H), 0.92 (d, $J = 6.9$ Hz, 3H), 0.88 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 82.3, 74.3, 69.7, 62.3, 59.1, 36.6, 36.2, 35.1, 21.8, 19.9, 15.7, 15.4, 14.2; IR (neat) 3457, 3303, 2945, 1456, 908 cm^{-1} ; CIMS m/z 211 (13) $[\text{M} + \text{H}]^+$, 193 (75), 153 (21), 135 (29), 127 (26), 109 (61); HREIMS calcd for $\text{C}_8\text{H}_{15}\text{O}_2$ ($\text{M}^+ - \text{HC}\equiv\text{CCH}_2(\text{CH}_3)\text{CH}$) 143.1072, found 143.1060; optical rotation $[\alpha]_{\text{D}}^{27} +24^\circ$ (c 0.50, CH_2Cl_2); Anal. Calcd for $\text{C}_{13}\text{H}_{22}\text{O}_2$: C, 74.24; H, 10.54. Found: C, 74.50; H, 10.36.