Total Synthesis of (–)-Ratjadone

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Supporting Information

Experimental procedures and spectral data for all compounds of the synthesis pathway to (–)-ratjadone are provided. A proton NMR spectrum of (–)-ratjadone and diastereomers **9** and **10** are included. (52 pages)

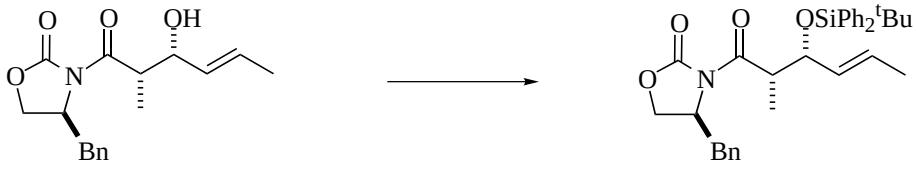
Experimental Procedures

General. Infrared (FT-IR) spectra were recorded on a Galaxy 4020 FT-IR or Nicolet Avator 360 FT-IR spectrometer and are reported in wavenumbers (cm^{-1}). Proton nuclear magnetic resonance (^{1}H NMR) spectra were measured on a Varian VXR-400 (400 MHz) spectrometer or on a Varian Inova 500 spectrometer (500 MHz). Carbon magnetic resonance (^{13}C NMR) were measured on a Varian VXR-400 (100 MHz) spectrometer or on a Varian Inova 500 spectrometer (125 MHz). NMR spectra were aquired in $CDCl_3$ solutions and are reported in parts per million (ppm) using the residual chloroform ($CHCl_3$) as a reference: δ 7.26 ppm for ^{1}H NMR; 77.0 ppm for ^{13}C NMR. Proton NMR data are reported in the form: δ (multiplicity, coupling constants, number of protons). Mass spectral data (MS and HRMS) were recorded on a Kratos MS 80 RFAQQ mass spectometer by use of chemical ionization (CI), electon impact (EI), or fast atom bombardment (FAB). Optical rotations were obtained on a Perkin Elmer 241 polarimeter at 589 nm (sodium D line) using a 10 cm path length and a 1.0 mL volume.

Analytical thin-layer chromatography (TLC) was performed on glass-backed silica gel plates precoated (0.25 mm thick) with 60 (F_{254}) from E. M. Scientific. Spots were visualized under UV light and/or staining with ethanolic *p*-anisaldehyde or ceric ammonium molybdate. Flash chromatography was performed using silica gel 60 (230-400 mesh) from E. M. Science. Ethyl acetate and hexanes for chromatography were distilled prior to use.

All reagents and solvents were used as received unless noted otherwise. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled under nitrogen from sodium/benzophenone ketyl. Methylene chloride (CH_2Cl_2), toluene, pivaloyl chloride, *N*,*N*-diisopropylethylamine, triethylamine, and pyridine were distilled from calcium hydride prior to use under dry air. Dimethyl sulfoxide, *N*,*N*-dimethyformamide, hexamethylphosphoramide, 1,8-diazabicyclo[5.4.0]undec-7-ene were distilled from calcium hydride and stored over 4 Å molecular sieves. Titanium(IV) isopropoxide was distilled and stored at –20 °C.

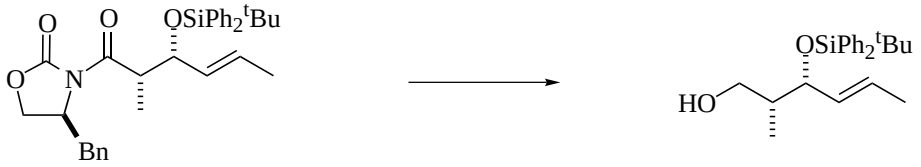
All reactions were conducted in flame or oven-dried glassware under an atmosphere of argon unless otherwise noted.



2 **29**

(4*S*)-3-[(*E*)-(2*S*,3*R*)-3-(*tert*-Butyldiphenylsilanoxy)-2-methyl-1-oxo-4-hexen-1-yl]-4-(phenylmethyl)-1,3-oxazolidin-2-one. (29)

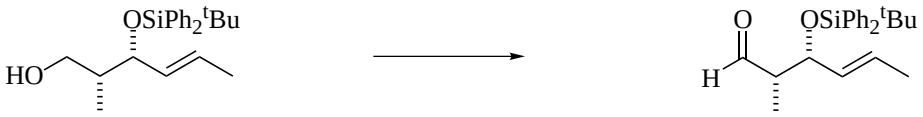
A solution of **2** (9.23 g, 30.6 mmol), *tert*-butyldiphenylsilyl chloride (8.74 mL, 33.6 mmol), imidazole (4.58 g, 67.2 mmol), and CH_2Cl_2 (100 mL) was stirred for 20 h. The reaction was partitioned between H_2O (250 mL) and Et_2O (250 mL). The organic layer was washed with H_2O (250 mL) and brine (250 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford a thick yellow oil. The crude product was purified by flash chromatography (375 g SiO_2, 10:1 hexanes : ethyl acetate) to afford 16.4 g (99%) of **29** as a thick, clear, colorless oil: R_f 0.58 (2:1 hexanes : ethyl acetate); $[\alpha]_D^{23}$ +35 (c 4.1, $CHCl_3$); IR (neat) ν = 3067, 3038, 2992, 2957, 2932, 2886, 2856, 2782, 1701, 1383, 1211, 1107, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.60 (m, 4H), 7.44 – 7.27 (m, 11H), 5.48 (dd, *J* = 16.9, 8.3 Hz, 1H), 5.13 (dq, *J* = 15.3, 6.4 Hz, 1H), 4.46 – 4.39 (m, 1H), 4.37 – 4.31 (m, 1H), 4.11 – 4.03 (m, 2H), 3.95 (dd, *J* = 8.3, 8.3 Hz, 1H), 3.25 (A of ABX, J_{AB} = 13.4 Hz, J_{AX} = 3.0 Hz, 1H), 2.73 (B of ABX, J_{AB} = 13.4 Hz, J_{BX} = 9.8 Hz, 1H), 1.41 (d, *J* = 6.5 Hz, 3H), 1.24 (d, *J* = 6.7 Hz, 3H), 1.05 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 153.1, 136.1, 136.0, 135.4, 134.8, 134.0, 131.1, 129.6, 129.5, 129.4, 128.9, 128.3, 127.7, 127.4, 127.3, 127.2, 76.8, 65.8, 55.5, 44.2, 37.7, 27.0, 19.4, 17.3, 12.6; MS(CI/CH_4) 415 (34), 414 (46), 308 (18), 307 (38), 201 (42), 198 (19), 181 (39), 152 (21), 83 (63); HRMS *m/e* calcd for $C_{29}H_{30}NO_4Si$ ($M^+ - C_4H_9$) 484.1944, found 484.1956.



29 **30**

(*E*)-(2*R*,3*R*)-3-(*tert*-Butyldiphenylsilanoxy)-2-methylhex-4-en-1-ol. (30)

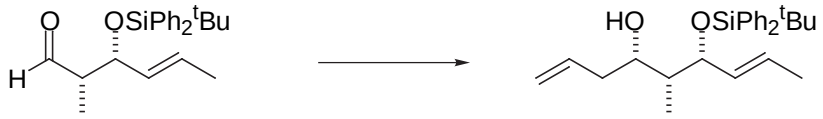
Lithium borohydride (0.887 g, 40.7 mmol) was added to a –20 °C solution of oxazolidinone **29** (20.1 g, 37.0 mmol) and Et_2O (100 mL). Water (0.750 mL, 40.7 mmol) was added dropwise. The reaction was slowly warmed to 5 °C. The reaction was diluted with saturated aqueous NH_4Cl (500 mL), H_2O (50 mL), and Et_2O (300 mL), and the layers were separated. The organic layer was washed with brine (250 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (250 g SiO_2, 9:1 hexanes : ethyl acetate) to afford 11.8 g (86%) of **30** as a clear, colorless oil: R_f 0.60 (2:1 hexanes : ethyl acetate); $[\alpha]_D^{23}$ –14 (c 1.7, $CHCl_3$); IR (neat) ν = 3389, 3071, 3050, 2999, 2965, 2936, 2859, 1107, 1026, 741, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.63 (m, 4H), 7.46 – 7.32 (m, 6H), 5.47 (ddq, *J* = 15.3, 7.8, 1.6 Hz, 1H), 5.17 (dqd, *J* = 15.3, 6.4, 1.2 Hz, 1H), 4.16 (A of ABX, J_{AB} = 7.8 Hz, J_{AX} = 3.8 Hz, 1H), 3.68 (B of ABX, J_{AB} = 7.8 Hz, J_{BX} = 9.1 Hz, 1H), 3.51 – 3.43 (m, 1H), 2.71 (br s, 1H), 2.05 – 1.94 (m, 1H), 1.50 (dd, *J* = 6.4, 1.5 Hz, 3H), 1.01 (s, 9H), 0.70 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1, 135.9, 133.7, 129.7, 129.6, 128.3, 127.6, 127.3, 78.5, 65.7, 41.0, 27.1, 19.3, 17.5, 12.6; MS(CI/CH_4) 200 (24), 199 (100), 167 (15), 139 (18), 135 (135), 91 (36), 78 (34), 77 (21), 75 (19); HRMS *m/e* calcd for $C_{19}H_{23}O_2Si$ ($M^+ - C_4H_9$) 311.1467, found 311.1470.



30 **3**

(*E*)-(2*S*,3*R*)-3-(*tert*-Butyldiphenylsilanoxy)-2-methylhex-4-enal. (3)

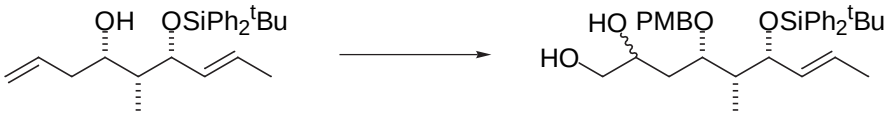
A solution of dimethylsulfoxide (2.81 mL, 39.6 mmol) and CH_2Cl_2 (130 mL) at –78 °C was treated with oxalyl chloride (1.88 mL, 19.8 mmol). After 15 min, a solution of alcohol **30** (4.86 g, 13.2 mmol) and CH_2Cl_2 (80.0 mL) was added dropwise. After 15 min, triethylamine (5.51 mL, 39.6 mmol) was added dropwise and the reaction was warmed to –30 °C. The reaction was diluted with pentane (150 mL), warmed to ambient temperature, and washed with H_2O (200 mL), saturated aqueous NH_4Cl (2 × 100 mL), H_2O (100 mL), and brine (100 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford 4.72 g (98% crude yield) of **3** as a clear, colorless oil which was used without further purification: R_f 0.76 (2:1 hexanes : ethyl acetate); $[\alpha]_D^{23}$ +25 (c 3.2, $CHCl_3$); IR (neat) ν = 2961, 2934, 2890, 2826, 1726, 1109, 1049, 822, 741, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.28 (d, *J* = 1.1 Hz, 1H), 7.67 – 7.61 (m, 4H), 7.44 – 7.33 (m, 6H), 5.39 (ddq, *J* = 15.3, 6.5, 1.6 Hz, 1H), 5.24 (dq, *J* = 15.3, 6.7 Hz, 1H), 4.38 (dd, *J* = 8.1, 4.6 Hz, 1H), 2.48 (dqd, *J* = 6.7, 4.6, 1.1 Hz, 1H), 1.49 (dd, *J* = 6.6, 1.6 Hz, 3H), 1.05 (s, 9H), 0.97 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.8, 136.0, 135.9, 133.8, 133.7, 130.0, 129.8, 129.5, 128.8, 127.6, 127.3, 75.5, 52.8, 27.0, 19.3, 17.4, 9.1; MS(CI/CH_4) 414 (67), 309 (80), 307 (47), 239 (65), 199 (100), 181 (49), 135 (51), 117 (43); HRMS *m/e* calcd for $C_{19}H_{21}O_2Si$ (M^+ – C_4H_9) 309.1311, found 309.1300. Anal. calcd. for $C_{23}H_{30}O_2Si$: C, 75.36; H, 8.25, found C, 75.49; H, 8.35.



3 **31**

(*E*)-(4*S*,5*R*,6*S*)-6-(*tert*-Butyldiphenylsilanoxy)-5-methylnon-1,7-diene-4-ol. (31)

A solution of aldehyde **3** (14.6 g, 39.7 mmol) and Et_2O (140 mL) was added dropwise to a solution of *B*-allyldiisocamphenylborane (13.8 mmol) from (+)-α-pinene and Et_2O (40 mL) at –78 °C. After 3h, a solution of aqueous 3 M sodium hydroxide (100 mL) and 30% aqueous H_2O_2 (100 mL) was added over 5 min and the reaction was warmed to 0 °C. The reaction was stirred for 30 min, warmed to ambient temperature, and stirred for 1.5 h. The layers were separated and the aqueous layer was extracted with Et_2O (1 × 200 mL). The combined organic layers were washed with H_2O (2 × 250 mL) and brine (1 × 250 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product (87% de by ^1H NMR) was purified by flash chromatography (375 g SiO_2, hexanes to 20:1 hexanes : ethyl acetate) to afford the desired alcohol **31** as a clear colorless oil (13.8 g, 85%): R_f 0.35 (10:1 hexanes : ethyl acetate); $[\alpha]_D^{26}$ –9.8 (c 0.85, $CHCl_3$); IR (neat) ν = 3484, 3073, 2951, 2932, 1857, 1670, 1655, 1427, 1111, 997, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.63 (m, 4H), 7.44 – 7.33 (m, 6H), 5.78 (ddt, *J* = 15.3, 8.1, 7.3 Hz, 1H), 5.39 (ddq, *J* = 15.3, 8.1, 4.3 Hz, 1H), 5.19 – 5.03 (m, 3H), 4.24 (dd, *J* = 7.8, 4.3 Hz, 1H), 4.01 – 3.94 (m, 1H), 2.40 (d, *J* = 2.7 Hz, 3H), 2.31 – 2.10 (m, 2H), 1.58 – 1.51 (m, 1H), 1.37 (dd, *J* = 6.4, 1.3 Hz, 3H), 1.05 (s, 9H), 0.98 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.0 135.8, 135.5, 134.3, 133.9, 131.7, 129.6, 129.4, 127.6, 127.5, 127.2, 117.1, 79.1, 72.2, 43.4, 39.7, 27.1, 19.3, 17.4, 7.8; MS(CI/CH_4) 414 (67), 309 (80), 307 (47), 239 (65), 199 (100), 181 (49), 135 (51), 117 (43); HRMS *m/e* calcd for $C_{22}H_{27}O_2Si$ ($M^+ - C_4H_9$) 351.1780, found 351.1787.



31 **32**

(*E*)-(4*S*,5*R*,6*S*)-6-(*tert*-Butyldiphenylsilanoxy)-4-(4-methoxybenzyloxy)-5-methylnon-7-ene-1,2-diol. (32)

4-Methoxybenzyl trichloroacetimidate (16.9 g, 72.8 mmol) was added dropwise to a solution of alcohol **31** (14.8 g, 36.4 mmol), camphorsulfonic acid (0.975 g, 3.64 mmol), and CH_2Cl_2 (150 mL). After 40 h, the reaction was diluted with Et_2O (300 mL) and washed with saturated aqueous $NaHCO_3$ (400 mL) and H_2O (100 mL). The organic layer was dried ($MgSO_4$), filtered , and concentrated *in vacuo*. The residue was triturated with hexanes (100 mL), filtered through cotton, and concentrated *in vacuo*. The crude product was purified by flash chromatography (250 g SiO_2, 20:1 hexanes : ethyl acetate) to afford a mixture of the desired ether **4** (12.8 g, 67% yield by ^{1}H NMR) and 4-methoxybenzyl alcohol as a clear oil which was used in the next step without further purification. Characteristic data for the desired ether: R_f 0.36 (10:1 hexanes : ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.62 (m, 4H), 7.43 – 7.31 (m, 6H), 7.16 (A of AB, J_{AB} = 8.6 Hz, 2H), 6.83 (B of AB, J_{AB} = 8.6 Hz, 2H), 5.75 (ddt, J = 17.7, 9.7, 7.0 Hz, 1H), 5.35 (ddq, J = 15.3, 8.3, 1.6 Hz, 1H), 5.05 - 4.89 (m, 3H), 4.47 (A of AB, J_{AB} = 11.1 Hz, 1H), 4.26 (B of AB, J_{AB} = 11.1 Hz, 1H), 4.07 (dd, J = 8.1, 5.9 Hz, 1H), 3.80 (s, 3H), 3.58 – 3.53 (m, 1H), 2.40 – 2.15 (m, 2H), 1.73 –1.64 (m, 1H), 1.38 (dd, J = 6.4, 1.3 Hz, 3H), 1.05 (s, 9H), 0.96 (d, J = 7.0 Hz, 3H).

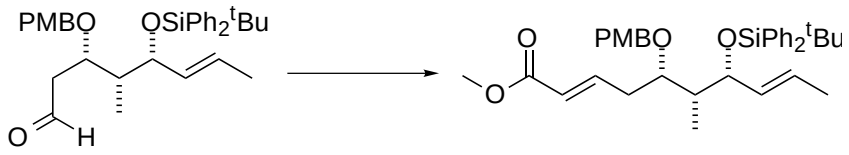
AD-mix-α (0.560 g) was added to a solution of the ether **4** in *tert*-butyl alcohol (2 mL) and H_2O (2 mL) under air. The reaction vessel was sealed. After 20 h, the reaction was cooled to 0 °C and sodium sulfite (1.68 g, 13.3 mmol) was added. The reaction was stirred at 0 °C for 30 min, warmed to ambient temperature, and stirred for 1 h. The mixture was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic layers were washed with 1 M sodium hyroxide (20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product (60 : 40

mixture of diastereomers) was purified by flash chromatography (625 g SiO_2, 4:1 to 2:1 hexanes : ethyl acetate) to afford 0.167 g (74%) of a diastereomeric mixture of diols **32** as a colorless oil: R_f 0.33 (1:1 hexanes : ethyl acetate); IR (neat) ν = 3416, 3071, 3048, 2934, 2857, 1613, 1514, 1427, 1248, 1109, 1038, 822, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.60 (m, 4H), 7.46 – 7.31 (m, 6H), 7.22 – 7.14 (m, 2H), 6.89 – 6.82 (m, 2H), 5.48 – 5.35 (m, 1H), 5.12 – 4.99 (m, 1H), 4.49 – 4.30 (m, 2H), 4.24 – 4.06 (m, 1H), 3.80 (s, 3H), 3.78 – 3.66 (m, 2H), 3.54 – 3.26 (m, 2H), 2.14 (br s, 1H), 2.09 (br s, 1H), 1.83 – 1.64 (m, 2H), 1.56 – 1.40 (m, 1H), 1.46 (dd, *J* = 7.6, 1.2 Hz, 1.5H), 1.41 (dd, *J* = 6.4, 1.6 Hz, 1.5H), 1.08 (s, 9H), 1.10 – 1.00 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 136.2, 136.1, 136.0, 134.4, 134.3, 132.5, 132.1, 130.2, 129.5, 129.4, 129.3, 127.5, 127.4, 127.1, 113.8, 79.8, 77.9, 76.1, 71.5, 71.3, 69.3, 67.0, 55.2, 44.1, 43.7, 27.1, 19.4, 17.4, 14.2, 10.9, 10.7; MS (FAB/Na) 585 (42), 309 (9), 241 (10), 199 (38), 176 (19), 135 (100); HRMS *m/e* calcd for $C_{34}H_{46}O_5SiNa$ (M^+ + Na) 585.3012, found 585.2989.

32 **33**

(*E*)-(4*S*,5*R*,6*S*)-5-(*tert*-Butyldiphenylsilanoxy)-3-(4-methoxybenzyloxy)-4-methyloct-6-enal. (33)

Sodium *meta*-periodate (1.47 g, 6.88 mmol) was added to a solution of diastereotopic diols **32** (1.29 g, 2.29 mmol), THF (50 mL), and H_2O (50 mL). After 30 min, the reaction was diluted with Et_2O (200 mL) and washed with H_2O (150 mL) and brine (100 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford 1.22 g (quant.) of **33** as a clear, colorless oil: R_f 0.82 (1:1 hexanes : ethyl acetate); $[\alpha]_D^{23}$ +6.9 (c 3.1, $CHCl_3$); IR (neat) ν = 3071, 3048, 2957, 2932, 2893, 2857, 1724, 1613, 1512, 1248, 1109, 1036, 822, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.74 (t, J = 2.0 Hz, 1H), 7.71 – 7.62 (m, 4H), 7.46 – 7.32 (m, 6H), 7.16 (A of AB, J_{AB} = 8.6 Hz, 2H), 6.85 (B of AB, J_{AB} = 8.6 Hz, 2H), 5.40 (ddq, J = 15.2, 8.0, 1.6 Hz, 1H), 5.06 (dq, J = 15.2, 6.4 Hz, 1H), 4.41 (A of AB, J_{AB} = 10.6 Hz, 1H), 4.33 (B of AB, J_{AB} = 10.6 Hz, 1H), 4.15 (dd, J = 8.0, 5.2 Hz, 1H), 4.03 (dt, J = 6.4, 5.2 Hz, 1H), 3.80 (s, 3H), 2.74 – 2.56 (m, 2H), 1.79 – 1.70 (m, 1H), 1.43 (dd, J = 6.4, 1.2 Hz, 3H), 1.07 (s, 9H), 1.02 (d, 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.6, 159.1, 136.1, 135.9, 134.2, 134.1, 131.7, 130.5, 129.5, 129.3, 129.1, 127.8, 127.4, 127.1, 76.7, 74.4, 71.4, 55.2, 47.3, 44.6, 27.1, 19.4, 17.4, 10.9; MS(CI/CH_4) 311 (30), 310 (31), 309 (43), 255 (32), 253 (31), 241 (37), 197 (34), 135 (44), 122 (46), 121 (100); HRMS *m/e* calcd for $C_{33}H_{41}O_4Si$ (M^+ – H) 529.2774, found 529.2767. Anal. calcd. for $C_{33}H_{42}O_4Si$: C, 74.68; H, 7.98, found C, 74.85; H, 8.03.



33 **34**

(2*E*,8*E*)-(5*S*,6*R*,7*S*)-7-(*tert*-Butyldiphenylsilanoxy)-5-(4-methoxybenzyloxy)-6-methyldeca-2,8-dienoic acid methyl ester. (34)

Methyl (triphenylphosphoranylidene)acetate (2.23 g, 6.67 mmol) was added to a solution of aldehyde **33** (1.18 g, 2.22 mmol) and CH_2Cl_2 (25 mL). After 1.5 h, the reaction was diluted with Et_2O (100 mL) and the organic layer was washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give a yellow residue. The residue was triturated with hexanes (50 mL), filtered, and and concentrated *in vacuo*. The crude material (≥95 : 5 *E* : *Z* by ^1H NMR) was purified by flash chromatography (375 g SiO_2, 20:1 hexanes : ethyl acetate) to afford 1.14 g (88%) of **34** as a clear, colorless oil: R_f 0.50 (4:1 hexanes : ethyl acetate); $[\alpha]_D^{22}$ +1.9 (c 1.1, $CHCl_3$); IR (neat) ν = 3069, 2998, 2953, 2934, 2857, 1724, 1657, 1613, 1514, 1248, 1171, 1038, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.61 (m, 4H), 7.46 – 7.32 (m, 6H), 7.16 (A of AB, J_{AB} = 8.7 Hz, 2H), 6.84 (B of AB, J_{AB} = 8.7 Hz, 2H), 6.93 (dt, *J* = 15.8, 7.5 Hz, 1H), 5.80 (d, *J* = 15.6 Hz, 1H), 5.37 (ddq, *J* = 15.3, 8.3, 1.6 Hz, 1H), 5.00 (dq, *J* = 15.3, 6.2 Hz, 1H), 4.43 (A of AB, J_{AB} = 11.0 Hz, 1H), 4.28, J_{AB} = 11.0 Hz, 1H), 4.07 (dd, *J* = 8.1, 5.6 Hz, 1H), 3.80 (s, 3H), 3.74 (s, 3H), 3.64 (td, *J* = 5.9, 4.6 Hz, 1H), 2.48 – 2.31 (m, 2H), 1.68 – 1.59 (m, 1H), 1.41(dd, *J* = 6.4, 1.3 Hz, 3H), 1.06 (s, 9H), 0.97 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 159.2, 146.3, 136.3, 136.1, 134.6, 134.4, 132.3, 130.9, 129.7, 129.4, 127.6, 127.3, 122.9, 113.8, 77.7, 77.5, 71.5, 55.4, 51.5, 44.0, 35.4, 27.3, 19.6, 17.6, 10.5; MS(CI/CH_4) 309 (46), 200 (41), 199 (84), 183 (36), 136 (45), 135 (68), 122 (44), 121 (100), 91 (42), 78 (54); HRMS *m/e* calcd for $C_{32}H_{37}O_5Si$ ($M^+ - C_4H_9$) 529.2410, found, 529.2413. Anal. calcd. for $C_{36}H_{46}O_5Si$: C, 73.68; H, 7.90, found C, 74.05; H, 8.08.

34 **35**

(2*E*, 8*E*)-(5*S*,6*R*,7*S*)-7-(*tert*-Butyldiphenylsilanoxy)-5-(4-methoxybenzyloxy)-6-methyldeca-2,8-dien-1-ol. (35)

Diisobutylaluminum hydride (4.13 mL of a 1.0 M solution in hexanes, 4.13 mmol) was added to a solution of ester **34** (1.10 g, 1.88 mmol) and CH_2Cl_2 (7.5 mL) at –78 °C. After 30 min, the reaction was quenched by addition of acetone. The mixture was warmed to ambient temperature and a 15% aqueous solution of potassium sodium tartrate (40 mL) was added. After 4 h, the mixture was diluted with Et_2O (100 mL) and the layers were separated. The organic layer was washed with H_2O (50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (250 g SiO_2, 4:1 hexanes : ethyl acetate) to afford 1.01 g (96%) of **35** as a clear, colorless oil: R_f 0.13 (4:1 hexanes : ethyl acetate); $[\alpha]_D^{22}$ +7.7 (c 1.1, $CHCl_3$); IR (neat) ν = 3389, 3071, 3046, 2998, 2932, 2857, 1613, 1512, 1248, 1107, 1036, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.61 (m, 4H), 7.46 – 7.31 (m, 6H), 7.16 (A of AB, J_{AB} = 8.7 Hz, 2H), 6.84 (B of AB, J_{AB} = 8.7 Hz, 2H), 5.67 – 5.55 (m, 2H), 5.37 (ddq, *J* = 15.3, 8.1, 1.3 Hz, 1H), 4.98 (dq, *J* = 15.3, 6.4 Hz, 1H), 4.44 (A of AB, J_{AB} = 11.0 Hz, 1H), 4.28 (B of AB, J_{AB} = 11.0 Hz, 1H), 4.09 (dd, *J* = 8.0, 5.9 Hz, 1H), 4.05 (bs, 2H), 3.80 (s, 3H), 3.56 (ddd, *J* = 5.6, 4.6, 1.3 Hz, 1H), 2.36 – 2.18 (m, 2H), 1.72 – 1.59 (m, 1H), 1.40 (dd, *J* = 6.4, 1.6 Hz, 3H), 1.05 (s, 9H), 0.97 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 136.1, 136.0, 134.5, 134.4, 132.4, 131.2, 129.4, 129.2, 127.4, 127.2, 127.1, 113.6, 78.1, 77.1, 71.1, 63.7, 55.3, 43.2, 34.8, 27.1, 19.4, 17.4, 10.2; MS(CI/CH_4) 309 (44), 239 (31), 199 (43), 183 (32), 136 (31), 135 (53), 122 (48), 121 (100), 78 (41), 77 (42); HRMS *m/e* calcd for $C_{31}H_{37}O_4Si$ ($M^+ - C_4H_9$) 501.2461, found 501.2478. Anal. calcd. for $C_{35}H_{46}O_4Si$: C, 75.23; H 8.30, found C 75.22; H, 8.42.

35 **5**

(*E*)-(2*S*,3*S*,5*S*,6*R*,7*S*)-7-(*tert*-Butyldiphenylsilanoxy)-2,3-epoxy-5-(4-methoxybenzyloxy)-6-methyldeca-8-en-1-ol. (5)

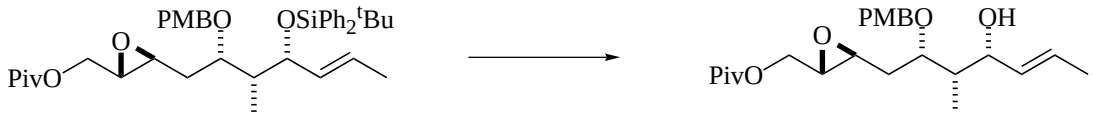
A solution of diethyl *L*-tartrate (87.0 μL, 0.509 mmol, ≥ 99% ee) and CH_2Cl_2 (40.0 mL) over 4Å molecular sieves (1.0 g) at –20 °C was treated dropwise with titanium isopropoxide (125 μL, 424 μmol). After 10 min, alcohol **35** (2.37 g, 4.24 mmol) in CH_2Cl_2 (10.0 mL) was added dropwise. After 40 min, *tert*-butylhydroperoxide (2.30 mL of a 3.71 M solution in toluene, 8.53 mmol) was added dropwise. The reaction was stirred for 30 min, sealed, and placed in a –20 °C freezer overnight. After 24 h, the reaction was treated with a 10 % aqueous solution of tartaric acid (100 mL) and was warmed to ambient temperature. The solution was stirred for 1 h and partitioned between Et_2O (400 mL) and H_2O (200 mL). The layers were separated and the organic layer was washed with saturated aqueous $NaHCO_3$ solution (400 mL) and brine (200 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product (95% de by ^1H NMR) was purified by flash chromatography (100 g SiO_2, 5:1 hexanes : ethyl acetate) to afford 2.31 g (95%) of **5** as a clear, colorless oil: R_f 0.18 (2:1 hexanes : ethyl acetate); $[\alpha]_D^{27}$ –3.2 (c 12.6, $CHCl_3$); IR (neat) ν = 3459, 3073, 2963, 2938, 2859, 1746, 1613, 1514, 1248, 1107, 1036, 822, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.60 (m, 4H), 7.46 – 7.30 (m, 4H), 7.17 (A of AB, J_{AB} = 8.4 Hz, 2H), 6.84 (B of AB, J_{AB} = 8.4 Hz, 2H), 5.38 (ddq, *J* = 15.2, 8.2, 1.2 Hz, 1H), 5.00 (dq, *J* = 15.2, 6.6 Hz, 1H), 4.45 (A of AB, J_{AB} = 11.4 Hz, 1H), 4.36 (B of AB, J_{AB} = 11.4 Hz, 1H), 4.11 (t, *J* = 5.8 Hz, 1H), 3.90 – 3.80 (m, 1H), 3.80 (s, 3H), 3.74 – 3.66 (m, 1H), 3.60 – 3.52 (m, 1H), 3.04 – 2.98 (m, 1H), 2.90 – 2.84 (m, 1H), 1.90 – 1.64 (m, 3H), 1.40 (d, *J* = 5.9 Hz, 3H), 1.05 (s, 9H), 1.00 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 136.1, 135.9, 134.4, 134.2, 132.2, 130.9, 129.4, 129.2, 128.9, 127.6, 127.4, 127.1, 113.6, 76.8, 72.0, 71.7, 61.6, 58.8, 55.2, 53.6, 44.5, 35.1, 27.1, 19.4, 17.4, 10.6; MS(CI/CH_4) 310 (34), 309 (52), 269 (29), 239 (31),

197 (44), 183 (38), 181 (29), 136 (28), 135 (61), 121 (100); HRMS *m/e* calcd for $C_{35}H_{45}O_5Si$ ($M^+ - H$) 573.3036, found 573.3012.

5 **36**

2,2-Dimethylpropionic acid (*E*)-(2*S*,3*S*,5*S*,6*R*,7*S*)-7-(*tert*-butyldiphenylsilanoxy)-2,3-epoxy-5-(4-methoxybenzyloxy)-6-methyldeca-8-enyl ester. (36)

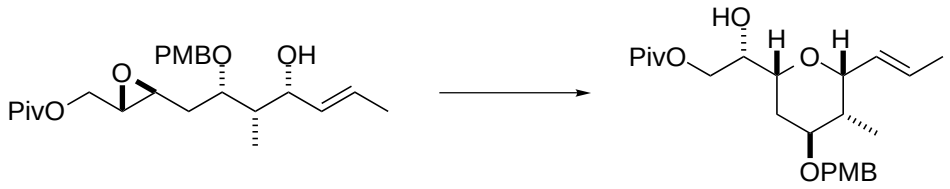
A solution of alcohol **5** (3.31 g, 5.76 mmol), CH_2Cl_2 (60 mL), and pyridine (0.606 mL, 7.49 mmol) at 0 °C was treated with pivaloyl chloride (0.780 mL, 6.33 mmol). The reaction was warmed to ambient temperature. After 5 h, the reaction was diluted with Et_2O (300 mL) and washed with saturated aqueous NH_4Cl (3 × 100 mL), H_2O (300 mL) and brine (100 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (150 g, SiO_2, 5:1 hexanes : ethyl acetate) to afford 3.60 g (95%) of **36** as a clear, colorless oil: R_f 0.57 (2:1 hexanes : ethyl acetate); $[\alpha]_D^{21}$ – 8.7 (c 1.2, $CHCl_3$); IR (neat) ν = 3067, 3044, 2961, 2932, 2857, 1734, 1514, 1248, 1154, 1101, 1086, 1035, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.61 (m, 4H), 7.46 – 7.32 (m, 6H), 7.17 (A of AB, J_{AB} = 8.6 Hz, 2H), 6.84 (B of AB, J_{AB} = 8.6 Hz, 2H), 5.37 (ddq, *J* = 15.3, 8.3, 1.5 Hz, 1H), 4.98 (dq, *J* = 15.3, 6.6 Hz, 1H), 4.45 (A of AB, J_{AB} = 10.9 Hz, 1H), 4.36 (B of AB, J_{AB} = 10.9 Hz, 1H), 4.34 (dd, *J* = 12.2, 2.6 Hz, 1H), 4.11 (dd, *J* = 8.2, 5.7 Hz, 1H), 3.87 (dd, *J* = 12.4, 6.3 Hz, 1H), 3.80 (s, 3H), 3.70 (td, *J* = 7.4, 4.8 Hz, 1H), 2.96 – 2.90 (m, 2H), 1.93 – 1.83 (m, 1H), 1.78 – 1.59 (m, 2H), 1.39 (dd, *J* = 6.4, 1.3 Hz, 3H), 1.23 (s, 9H), 1.05 (s, 9H), 1.01 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.2, 159.0, 136.1, 136.0, 134.4, 134.3, 132.2, 130.9, 129.5, 129.2, 128.9, 127.7, 127.4, 127.1, 113.7, 76.8, 71.9, 64.4, 56.0, 55.2, 53.8, 44.5, 35.2, 27.1, 26.9, 19.4, 17.4, 10.7; MS(CI/CH_4) 601 (31), 309 (51), 283 (45), 253 (47), 239 (44), 200 (30), 199 (45), 122 (47), 121 (100); HRMS *m/e* calcd for $C_{36}H_{46}O_6Si$ (M^+ – H) 602.3064, found 602.3074. Anal. calcd. for $C_{40}H_{55}O_6Si$: C, 72.80; H, 8.40, found C, 72.91; H, 8.30.



36 **37**

2,2-Dimethylpropionic acid (*E*)-(2*S*,3*S*,5*S*,6*R*,7*S*)-2,3-epoxy-7-hydroxy-5-(4-methoxybenzyloxy)-6-methyldeca-8-enyl ester. (37)

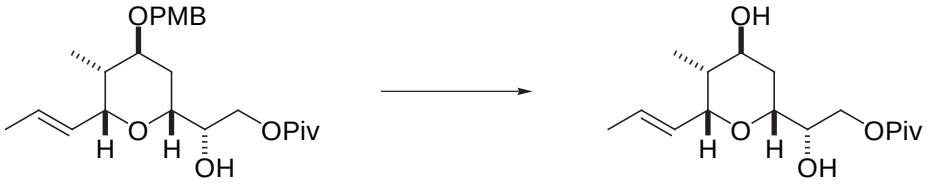
Silyl ether **36** (3.60 g, 5.46 mmol) was treated with *n*-tetrabutylammonium fluoride (13.1 mL of a 1.0 M solution in THF). The reaction was warmed to 40 °C for 24 h, cooled to ambient temperature, and diluted with Et_2O (400 mL). The organic layer was washed with saturated aqueous NH_4Cl (300 mL), H_2O (300 mL), and brine (250 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (50 g SiO_2, 5:1 hexanes : ethyl acetate) to afford 1.88 g (82%) of **37** as a clear, colorless oil: R_f 0.28 (2:1 hexanes : ethyl acetate); $[\alpha]_D^{23}$ –3.6 (c 1.2, $CHCl_3$); IR (neat) ν = 3455, 2965, 2934, 2880, 1730, 1613, 1450, 1263, 1248, 1155, 1088, 710 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (A of AB, J_{AB} = 8.9 Hz, 2H), 6.87 (B of AB, J_{AB} = 8.9 Hz, 2H), 5.66 (dqd, *J* = 15.2, 7.2, 0.8 Hz, 1H), 5.48 (ddq, *J* = 15.2, 6.0, 1.6 Hz, 1H), 4.55 (A of AB, J_{AB} = 11.0 Hz, 1H), 4.37 (B of AB, J_{AB} = 11.0 Hz, 1H), 4.30 (A of ABX, J_{AB} = 12.1 Hz, J_{AX} = 3.5 Hz, 1H), 3.95 (B of ABX, J_{AB} = 12.1 Hz, J_{BX} = 5.9 Hz, 1H), 4.27 – 4.23 (m, 1H), 3.80 (s, 3H), 3.80 – 3.73 (m, 1H), 3.04 – 2.98 (m, 1H), 2.91 – 2.86 (m, 1H), 2.67 (br s, 1H), 1.97 – 1.83 (m, 2H), 1.81 – 1.73 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.2, 159.3, 132.8, 130.0, 129.3, 126.7, 114.3, 80.1, 75.0, 71.6, 64.2, 55.8, 55.2, 53.9, 41.9, 38.8, 34.1, 27.1, 17.7, 7.6; MS(CI/NH_3) 201 (26), 155 (16), 136 (27), 97 (11), 95 (12), 91 (24); HRMS *m/e* calcd for $C_{24}H_{36}O_6$ (M^+) 420.2512, found 420.2508.



37 **6**

2,2-Dimethylpropionic acid 2*S*-hydroxy-2-(*E*)-[4*S*-(4-methoxybenzyloxy)-5*R*-methyl-6*S*-propenyltetrahydropyran-2*R*-yl]ethyl ester. (6)

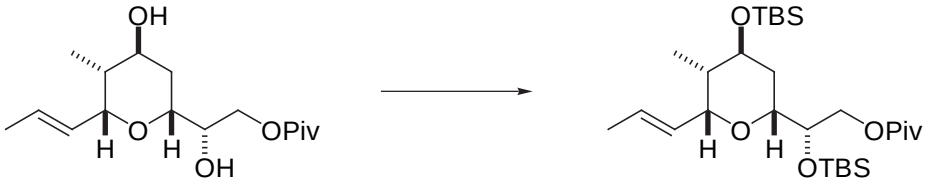
Camphorsulfonic acid (4.0 mg, 18μmol) was added to a solution of epoxyalcohol **37** (78 mg, 190 μmol) and CH_2Cl_2 (6.2 mL). After 4 h, the reaction was diluted with Et_2O (30 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (20 mL), and brine (15 mL). The layers were separated and the organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (0.8 g SiO_2, 5:1 hexanes : ethyl acetate) to afford 70 mg (90%) of **6** as a clear oil: R_f 0.28 (2:1 hexanes : ethyl acetate); $[\alpha]_D^{24}$ +13 (c 1.0, $CHCl_3$); IR (neat) ν = 3507, 2959, 2920, 2876, 1726, 1613, 1512, 1460, 1248, 1169, 1080, 1036, 822 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (A of AB, J_{AB} = 8.5 Hz, 2H), 6.87 (B of AB, J_{AB} = 8.5 Hz, 2H), 5.66 (dq, *J* = 15.4, 5.4 Hz, 1H), 5.41 (dd, *J* = 15.4, 1.5 Hz, 1H), 4.48 (s, 2H), 4.42 – 4.38 (m, 1H), 4.21 (A of ABX, J_{AB} = 11.6 Hz, J_{AX} = 3.7 Hz, 1H), 4.13 (B of ABX, J_{AB} = 11.6 Hz, J_{BX} = 6.7 Hz, 1H), 3.89 – 3.83 (m, 1H), 3.80 (s, 3H), 3.63 – 3.58 (m, 1H), 2.45 (s, 1H), 1.88 – 1.80 (m, 1H), 1.74 – 1.68 (m, 2H), 1.69 (d, *J* = 6.4 Hz, 3H), 1.20 (s, 9H), 0.88 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.8, 159.0, 130.8, 130.1, 128.7, 126.4, 113.7, 76.7, 76.6, 75.0, 72.9, 72.2, 65.3, 55.2, 38.8, 36.4, 27.1, 25.3, 17.8, 11.1; MS(CI/CH_4) 284 (31), 281 (31), 139 (31), 137 (48), 135 (41), 122 (48), 121 (100), 85 (30); HRMS *m/e* calcd for $C_{24}H_{37}O_6$ (M^+ + H) 421.2590, found 421.2585. Anal. calcd. for $C_{24}H_{36}O_6$: C, 68.55; H, 8.63, found C, 68.82; H, 8.68.



6 **7**

2,2-Dimethylpropionic acid 2*S*-hydroxy-2-(*E*)-[4*S*-hydroxy-5*R*-methyl-6*S*-propenyltetrahydropyran-2*R*-yl]ethyl ester. (7)

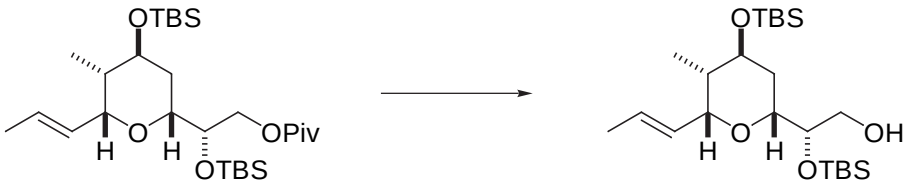
Ammonium cerium(IV) nitrate was added to a solution of tetrahydropyran **6** (1.38 g, 3.29 mmol), acetonitrile (15 mL), and H_2O (1.6 mL) under air. The reaction vessel was sealed. After 15 min, the reaction was diluted with Et_2O (150 mL) and washed with H_2O (150 mL). The layers were separated and the organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (50 g SiO_2, 2:1 hexanes : ethyl acetate) to afford 988 mg (quant) of **7** as a clear oil: R_f 0.28 (2:1 to 1:1 hexanes : ethyl acetate); $[\alpha]_D^{24}$ +2.6 (c 2.2, $CHCl_3$); IR (neat) ν = 3428, 3036, 2969, 2918, 2882, 1711, 1632, 1269, 1167, 1078, 966 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.67 (dqd, J = 15.3, 6.4, 1.1 Hz, 1H), 5.41 (ddq, J = 15.6, 5.9, 1.6 Hz, 1H), 4.41 (d, J = 5.6 Hz, 1H), 4.24 (A of ABX, J_{AB} = 11.6 Hz, J_{AX} = 3.5 Hz, 1H), 4.14 (B of ABX, J_{AB} = 11.6 Hz, J_{BX} = 6.4 Hz, 1H), 4.01 (dd, J = 5.5, 2.7 Hz,1H), 3.92 – 3.83 (m, 2H), 2.50 – 2.28 (m, 1H), 1.90 – 1.78 (m, 1H), 1.77 – 1.48 (m, 3H), 1.70 (d, J = 6.4 Hz, 3H), 1.21 (s, 9H), 0.90 (d, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.9, 130.0, 126.7, 74.6, 72.5, 72.3, 70.0, 65.4, 39.6, 38.8, 28.5, 27.2, 17.9, 11.1; MS(CI/CH_4) 210 (37), 194 (13), 193 (10), 180 (18), 175 (15), 157 (19), 155 (57), 149 (21), 137 (88), 85 (100); HRMS *m/e* calcd for $C_{16}H_{28}O_5$ (M^+) 300.1937, found 300.1945. Anal. calcd. for $C_{16}H_{28}O_5$: C, 63.97; H, 9.40, found C, 63.73; H, 9.47.



7 **38**

2,2-Dimethylpropionic acid 2*S*-(*tert*-butyldimethylsilanoxy)-2-(*E*)-[4*S*-(*tert*-butyldimethylsilanoxy)-5*R*-methyl-6*S*-propenyltetrahydropyran-2*R*-yl]ethyl ester. (38)

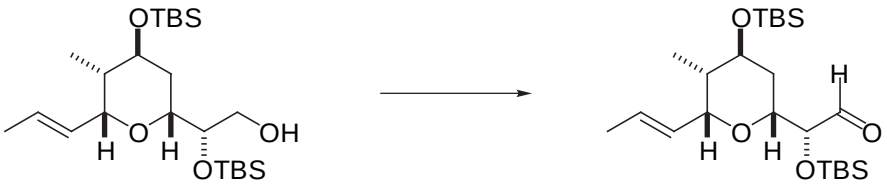
Imidazole (0.902 g, 6.63 mmol), *tert*-butyldimethylsilyl chloride (0.999 g, 6.63 mmol), and 4-*N*,*N*-dimethylaminopyridine (32 mg, 0.27 mmol) were respectively added to a solution of tetrahydropyran **7** (1.38 g, 3.29 mmol) and DMF (30 mL). After 16 h, the reaction was poured into saturated aqueous $NaHCO_3$ (75 mL) and extracted with Et_2O (3×50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (25 g SiO_2, 10:1 hexanes : ethyl acetate) to afford 1.25 g (91%) of **38** as a clear oil: R_f 0.46 (10:1 hexanes : ethyl acetate); $[\alpha]_D^{26}$ +16 (c 1.6, $CHCl_3$); IR (neat) ν = 3034, 2957, 2930, 2886, 2859, 1734, 1462, 1254, 1150, 1080, 1051, 837, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.67 (dqd, J = 15.4, 6.4, 1.3 Hz, 1H), 5.41 (ddq, J = 15.4, 5.6, 1.6 Hz, 1H), 4.38 (dd, J = 4.4, 1.1 Hz, 1H), 4.06 (A of ABX, J_{AB} = 11.4 Hz, J_{AX} = 4.7 Hz, 1H), 4.03 (B of ABX, J_{AB} = 11.6 Hz, J_{BX} = 4.2 Hz, 1H), 3.93 – 3.80 (m, 3H), 1.72 – 1.65 (m, 1H), 1.68 (ddd, J = 6.6, 1.4, 1.4 Hz, 3H), 1.55 – 1.40 (m, 2H), 1.19 (s, 9H), 0.88 (s, 9H), 0.87 (s, 9H), 0.85 (d, J = 7.3 Hz, 3H), 0.084 (s, 3H), 0.079 (s, 3H), 0.03 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.4, 130.9, 125.6, 74.7, 72.8, 72.6, 70.6, 65.4, 40.3, 38.8, 29.0, 27.2, 25.7, 25.7, 18.0, 17.9, 11.2, –4.5, –4.6, –4.9, –4.9; MS(CI/CH_4) 332 (10), 330 (10), 288 (11), 287 (42), 276 (46), 272 (43), 258 (40), 241 (18), 202 (50); HRMS *m/e* calcd for $C_{28}H_{57}O_5Si_2$ (M^+ + H) 529.3745, found 529.3730. Anal. calcd. for $C_{28}H_{56}O_5Si_2$: C, 63.58; H, 10.67, found C, 63.64; H, 10.60.



38 **39**

(*S*)-2-(*tert*-Butyldimethylsilanoxy)-2-[(*E*)-(2*R*,4*S*,5*S*,6*R*)-(*tert*-butyldimethylsilanoxy)-5-methyl-6-propenyltetrahydropyran-2-yl]-ethanol. (39)

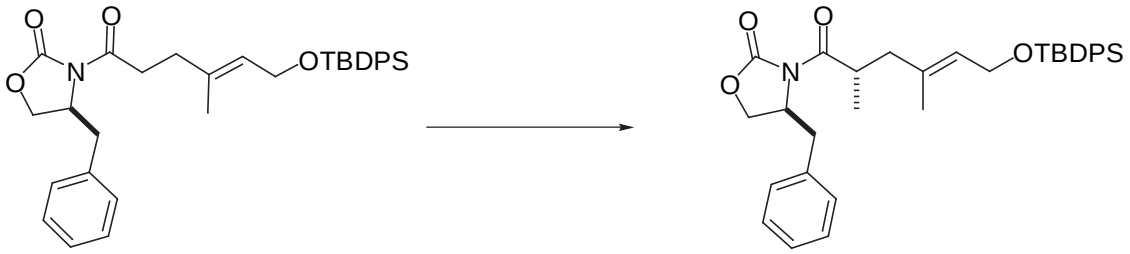
Diisobutylaluminum hydride (1.45 mL of a 1.0 M solution in hexanes, 1.45 mmol) was added dropwise to a –78 °C solution of ester **38** (1.38 g, 3.29 mmol) and CH_2Cl_2 (30 mL). After 10 min, the excess diisobutylaluminum hydride was reacted with acetone (0.1 mL). The reaction was warmed to ambient temperature. A 10% aqueous potassium sodium tartrate solution (40 mL) and Et_2O (20 mL) were added and the biphasic mixture was vigorously stirred for 3 h. The layers were separated and the aqueous layer was extracted with Et_2O (2×20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (7.5 g SiO_2, 4:1 hexanes : ethyl acetate) to afford 291 mg (99%) of **39** as a clear oil: R_f 0.65 (4:1 hexanes : ethyl acetate); $[\alpha]_D^{26}$ +15 (c 1.0, $CHCl_3$); IR (neat) ν = 3507, 3034, 2955, 2934, 2885, 2859, 1468, 1254, 1090, 837, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.60 (dqd, *J* = 15.4, 6.4, 1.2 Hz, 1H), 5.39 (ddq, *J* = 15.4, 5.9, 1.6 Hz, 1H), 4.40 (d, *J* = 2.8 Hz, 1H), 3.90 – 3.78 (m, 2H), 3.70 – 3.56 (m, 3H), 2.65 (dd, *J* = 7.5, 3.5 Hz, 1H), 1.68 (d, *J* = 6.4 Hz, 1H), 1.70 – 1.50 (m, 4H), 0.89 (s, 9H), 0.88 (s, 9H), 0.86 (d, *J* = 7.3 Hz, 3H), 0.08 (s, 6H), 0.04 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 130.5, 126.0, 75.4, 74.9, 74.4, 70.5, 65.7, 40.2, 31.1, 25.8, 25.8, 18.0, 18.0, 17.9, 11.2, -4.4, -4.6, -4.9, -4.9; MS(CI/CH_4) 331 (18), 288 (23), 287 (72), 256 (21), 255 (73), 237 (47), 231 (20), 227 (75), 225 (28), 219 (76), 213 (54), 185 (77); HRMS *m/e* calcd for $C_{19}H_{39}O_4Si_2$ ($M^+ - C_4H_9$) 387.2387, found 387.2406.



39 **8**

(*R*)-2-(*tert*-Butyldimethylsilanoxy)-2-[(*E*)-(2*R*,4*S*,5*S*,6*R*)-(*tert*-butyldimethylsilanoxy)-5-methyl-6-propenyltetrahydropyran-2-yl]-acetaldehyde. (8)

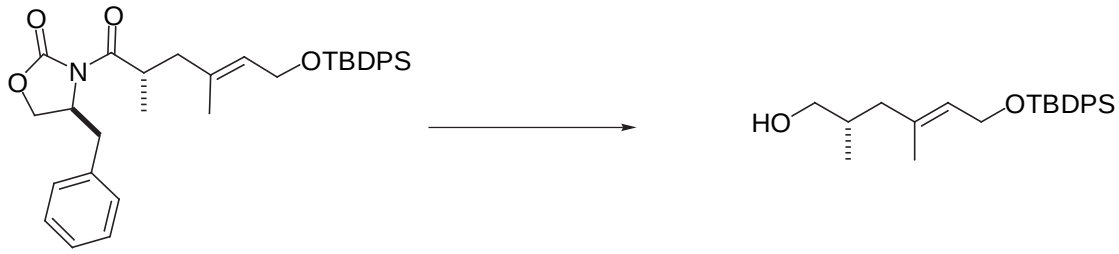
Solid $NaHCO_3$ (767 mg, 9.14 mmol) and Dess-Martin periodinane (517 mg, 1.22 mmol) were respectively added to a solution of alcohol **39** (271 mg, 609 mmol) and CH_2Cl_2 (6.1 mL). After 1.5 h, the mixture was diluted with Et_2O (15 mL) and 5% aqueous $NaHCO_3$ (15 mL). The layers were separated and the organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (7.5 g SiO_2, 10:1 hexanes : ethyl acetate) to afford 250 mg (93%) of **8** as a clear oil: R_f 0.35 (10:1 hexanes : ethyl acetate); $[\alpha]_D^{26}$ +23 (c 1.1, $CHCl_3$); IR (neat) ν = 3036, 2955, 2932, 2885, 2859, 2801, 1738, 1468, 1254, 1084, 1057, 837, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.63 (d, *J* = 1.2 Hz, 1H), 5.61 (dqd, *J* = 15.4, 6.6, 1.3 Hz, 1H), 5.38 (ddq, *J* = 15.4, 5.6, 1.6 Hz, 1H), 4.41 (d, *J* = 2.6 Hz, 1H), 4.14 – 4.04 (m, 2H), 3.87 (dd, *J* = 2.8, 2.8 Hz, 1H), 1.82 (ddd, *J* = 13.7, 11.4, 2.4 Hz, 1H), 1.68 (d, *J* = 6.4 Hz, 3H), 1.56 – 1.48 (m, 1H), 1.30 – 1.23 (m, 1H), 0.91 (s, 9H), 0.88 (s, 9H), 0.85 (d, *J* = 7.1 Hz, 3H), 0.09 (s, 6H), 0.04 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.6, 130.5, 125.7, 80.4, 74.7, 73.3, 70.4, 40.1, 29.3, 25.7, 25.6, 18.3, 18.0, 17.9, 11.1, –4.8, –4.9, –4.9, –4.9; MS(FAB/Na) 343 (24), 303 (26), 275 (17), 241 (19), 225 (40), 187 (100); HRMS *m/e* calcd for $C_{23}H_{46}O_4Si_2Na$ (M^+ + Na) 465.2832, found 465.2827.



12 **13**

(*S*)-4-Benzyl-3-[(2*S*)-(4*E*)-6-(*tert*-butyldiphenylsilanyloxy)-2,4-dimethyl-hex-4-enoyl]-oxazolidin-2-one. (13)

To a cold (–78 °C) solution of imide **12** (0.75 g, 1.38 mmol) in THF (1.5 mL) was added sodium *bis*(trimethylsilylamide) (1.0M in THF, 2.07 mL, 2.07 mmol) dropwise over 10 min. The dark yellow solution was stirred 1 h at –78 °C, and then methyl iodide (0.35 mL, 5.66 mmol) was added dropwise. The solution was stirred 1 h at –78 °C, and then warmed slowly to –20 °C over 45 min. The reaction mixture was quenched with aqueous saturated NH_4Cl (1 mL) and warmed to room temperature. The solution was poured into a mixture of Et_2O (30 mL) and aqueous saturated NH_4Cl (30 mL). The layers were separated, and the organic layer was washed with aqueous saturated NaCl (30 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromotography (50 g SiO_2, 10% EtOAc/hexanes) to yield 0.57 g (75%) of imide **13** and 0.05 g (6%) of minor diastereomer: $[\alpha]_D^{25}$ = +28.5 (c1.85, $CHCl_3$); R_f = 0.15 in 20% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.67 (m, 4H), 7.42-7.20 (m, 11H), 5.43 (t, *J*=5.9 Hz, 1H), 4.63-4.58 (m, 1H), 4.22 (d, *J*=6.1 Hz, 2H), 4.11-3.93 (m, 3H)**,** AB of ABX (δ_A = 3.27, δ_B = 2.77, J_{AB} = 13.3 Hz, J_{AX} = 3.0 Hz, J_{BX} = 9.7 Hz, 2H)**,** AB of ABX (δ_A = 2.45, δ_B = 2.07, J_{AB} = 13.4 Hz, J_{AX} = 7.0 Hz, J_{BX} = 7.4 Hz, 2H)**,** 1.49 (s, 3H), 1.19(d, *J*=6.7 Hz, 3H), 1.04 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 153.1, 135.5, 135.5, 135.3, 134.2, 134.0, 133.9, 129.5, 129.5, 129.4, 128.9, 127.6, 127.6, 127.3, 126.7, 66.0, 60.9, 55.4, 43.2, 37.9, 35.7, 26.8, 19.1, 16.9, 16.2; IR (neat) 3070, 3029, 2931, 2857, 1782, 1699, 1589, 1454, 1428, 1349, 1208, 1112, 1073 cm^{-1}; MS (DCI/CH_4) 498 (51), 322 (26), 321 (100), 243 (22), 199 (51), 135 (11), 95 (16), 91 (18); HRMS *m/e* calcd for $C_{30}H_{32}NO_4Si$ ($M^+ - C_4H_9$) 498.2101, found 498.2096.



13 **40**

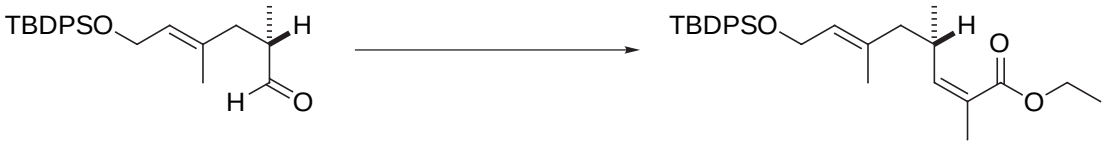
(2*S*)-(4*E*)-6-(*tert*-Butyldiphenylsilanyloxy)-2,4-dimethylhex-4-en-1-ol. (40)

To a 0 °C solution of imide **13** (7.38 g, 13.3 mmol) in Et_2O (66.5 mL) was added MeOH (1.08 mL, 26.6 mmol) and lithium borohydride (0.58 g, 26.6 mmol). The reaction mixture was stirred for 30 min at 0 °C, and then quenched carefully with aqueous saturated $NaHCO_3$ (5 mL). The solution was poured into a mixture of Et_2O (50 mL) and aqueous saturated $NaHCO_3$ (100 mL). The organic phase was partitioned and washed with aqueous saturated NaCl (100 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (250 g SiO_2, 15% EtOAc/hexanes) to yield 4.44 g (87%) of alcohol **40**: $[\alpha]_D^{24} = -2.1$ (c3.0, $CHCl_3$); $R_f = 0.50$ in 40% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.68 (m, 4H), 7.44-7.36 (m, 6H), 5.41 (t, *J*=6.3 Hz, 1H), 4.22 (d, *J*=6.3 Hz, 2H), 3.51-3.39 (m, 2H), 2.11-2.05 (m, 1H), 1.86-1.78 (m, 2H), 1.46 (s, 3H), 1.04 (s, 9H), 0.87 (d, *J*=6.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.2, 135.9, 134.3, 129.8, 127.9, 126.1, 68.6, 61.2, 44.3, 33.9, 27.1, 19.4, 16.9, 16.5; IR (neat) 3357, 3072, 2958, 1668, 1590, 1473, 1428, 1112, 1045 cm^{-1}; MS (DCI/CH_4) 325 (55), 229 (16), 217 (17), 181 (15), 139 (47), 135 (21), 109 (90), 91 (19), 83 (33), 77 (55); HRMS *m/e* calcd for $C_{20}H_{25}O_2Si$ ($M^+ - C_4H_9$) 325.1624, found 325.1630.

40 **14**

(2*S*)-(4*E*)-6-(*tert*-Butyldiphenylsilanyloxy)-2,4-dimethyl-hex-4-enal. (14)

To a cold (–78 °C) solution of oxalyl chloride (3.02 mL, 34.7 mmol) in CH_2Cl_2 (30 mL) was added dimethyl sulfoxide (4.10 mL, 57.8 mmol). After stirring for 10 min at –78 °C, a solution of alcohol **40** (4.42 g, 11.6 mmol) in CH_2Cl_2 (30 mL) was added dropwise to the reaction mixture. The solution was stirred for 15 minutes at –78 °C, and then triethylamine (12.0 mL, 86.6 mmol) was added dropwise. The reaction mixture was stirred at –78°C for 30 min, and then poured into a mixture of Et_2O (100 mL) and aqueous saturated NH_4Cl (100 mL). The organic phase was partitioned and washed with aqueous saturated $NaHCO_3$ (100 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (150 g SiO_2, 5% EtOAc/hexanes) to yield 4.13 g (94%) of aldehyde **14**: $[\alpha]_D^{24}$ = +0.8 (c1.2, $CHCl_3$); R_f = 0.50 in 20% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (d, *J*=1.8 Hz, 1H), 7.69-7.68 (m, 4H), 7.45-7.36 (m, 6H), 5.43 (t, *J*=6.1 Hz, 1H), 4.22 (d, *J*=6.1 Hz, 2H), 2.53-2.40 (m, 2H), 2.00-1.94 (m, 1H), 1.44 (s, 3H), 1.04-1.03 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.8, 135.6, 133.9, 133.4, 129.6, 127.6, 127.1, 60.8, 44.2, 40.4, 26.8, 19.1, 16.2, 13.1; IR (neat) 3071, 3049, 2892, 2710, 1727, 1589, 1462, 1428, 1112, 1079, 1049, 1007 cm^{-1}; MS (DCI/CH_4) 323(46), 246 (14), 199(100), 175 (3), 135 (16), 107 (53); HRMS *m/e* calcd for $C_{20}H_{23}O_2Si$ ($M^+ - C_4H_9$) 323.4869, found 323.1471.



14 **16**

(2*Z*,6*E*)-(4*S*)-8-(*tert*-Butyldiphenylsilanyloxy)-2,4,6-trimethylocta-2,6-dienoic acid ethyl ester. (16)

A solution of *bis*-trifluoroethyl 2-ethoxy-2-oxo-1-methyl-ethylphosphonate (8.26 g, 23.9 mmol) in THF (55 mL) was added to a flask containing 18-crown-6 (12.6 g, 47.7 mmol). The solution was cooled to 0 °C, and potassium *bis*(trimethylsilyl)amide (45.6 mL, 0.5 M solution in toluene, 22.8 mmol) was added to the mixture. After stirring at 0 °C for 30 min, the solution was cooled to –78 °C, and a solution of aldehyde **14** (4.13 g, 10.9 mmol) was added dropwise. The reaction mixture was stirred for 2 h at –78 °C, and then quenched with aqueous saturated NH_4Cl (10 mL). After warming to room temperature, the reaction mixture was poured into a mixture of Et_2O (100 mL) and aqueous saturated NH_4Cl (100 mL). The phases were separated, and the aqueous phase was extracted with Et_2O (2 x100 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (200 g SiO_2, hexanes to 3% EtOAc/hexanes) to yield 4.99 g (99%) of ester **16**: $[\alpha]_D^{24}$ = –22.6 (c1.56, $CHCl_3$); R_f = 0.60 in 20% EtOAc/Hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.67 (m 4H), 7.43-7.35 (m, 6H), 5.66 (dd, *J*=9.8, 1.3 Hz, 1H), 5.37 (ddd, *J*=6.2 Hz, 6.2 Hz, 1.1 Hz, 1H), 4.20-4.15 (m, 4H), 3.39-3.28 (m, 1H), AB of ABX(δ_A = 2.00, δ_B = 1.91, J_{AB} = 13.3 Hz, J_{AX} = 7.2 Hz, J_{BX} = 7.5 Hz, 2H)**,** 1.86 (d, *J*=1.4 Hz, 3H), 1.42 (s, 3H), 1.28 (t, *J*=7.1 Hz, 3H), 1.03 (s, 9H), 0.93 (d, *J*=6.6 Hz, 3H)**;** ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 148.3, 135.6, 135.2, 134.0, 129.5, 127.6, 125.9, 125.6, 61.0, 60.0, 47.3, 31.3, 26.8, 20.8, 20.0, 19.1, 16.1, 14.3; IR (neat) 3071, 2960, 2860, 1714, 1644, 1463, 1382, 1197, 1112, 1073 cm^{-1}; MS (DCI, CH4) 464 (1), 407 (57), 227 (23), 163 (17), 139 (11), 135 (30), 113 (17); HRMS *m/e* calcd for $C_{29}H_{40}O_3Si$ (M^+) 464.2747, found 464.2746.

16 **17**

(2*Z*,6*E*)-(4*S*)-8-(*tert*-Butyldiphenylsilanyloxy)-2,4,6-trimethylocta-2,6-dien-1-ol. (17)

To a solution of ester **16** (1.42 g, 3.06 mmol) in Et_2O (30 mL) was added diisobutylaluminum hydride (1 M in hexanes, 6.72 mL, 6.72 mmol) at –78 °C. The reaction mixture was stirred for 30 min at –78 °C, and then warmed to room temperature for 1 h. The solution was cooled to -78 °C and quenched with EtOAc (50 mL). The solution was warmed to room temperature and then stirred with aqueous saturated potassium sodium tartrate (50 mL) for 12 h. The organic phase was partitioned and washed with aqueous saturated NH_4Cl (50 mL) and aqueous saturated NaCl (50 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (50 g SiO_2, 10% EtOAc/Hexanes) to yield 1.26 g (98%) of alcohol **17**: $[\alpha]_D^{24}$ = –10.3 (c1.20, $CHCl_3$); R_f = 0.40 in 20% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.68 (m, 4), 7.44-7.37 (m, 6H), 5.32 (t, *J*=6.1 Hz, 1H), 5.03 (d, *J*=9.7 Hz, 1H), AB of ABX (δ_A = 4.20, δ_B = 3.99, J_{AB} = 11.7 Hz, J_{AX} = 6.8 Hz, J_{BX} = 7.1 Hz, 2H), 4.15-4.10 (m, 2H), 2.65-2.54 (m, 1H), AB of ABX (δ_A = 1.94, δ_B = 1.84, J_{AB} = 13.2 Hz, J_{AX} = 5.9 Hz, J_{BX} = 8.7 Hz, 2H), 1.79 (d, *J*=1.5 Hz, 3H), 1.48 (d, *J*=0.7 Hz, 3H), 1.48-1.42 (m, 1H) 1.05 (s, 9H), 0.93 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.0, 135.6, 134.2, 133.8, 133.4, 129.5, 127.6, 125.7, 61.8, 61.0, 47.6, 30.6, 26.8, 21.5, 21.2, 19.1, 16.7; IR (neat) 3365, 3072, 2957, 2860, 1670, 1590, 1467, 1428, 1111, 1079, 1007 cm^{-1}; MS (DCI, CH_4) 365 (1), 199 (100), 149 (61), 135 (13), 107 (68), 93 (22); HRMS *m/e* calcd for $C_{23}H_{29}O_2Si$ ($M^+ - C_4H_9$) 365.1937, found 365.1944.

17 **41**

(2*Z*,6*E*)-(4*S*)-8-(*tert*-Butyldiphenylsilanyloxy)-2,4,6-trimethylocta-2,6-dienal. (41)

To a cold (–78 °C) solution of oxalyl chloride (0.78 mL, 8.94 mmol) in CH_2Cl_2 (7.5 mL) was added dimethyl sulfoxide (1.06 mL, 14.9 mmol). After stirring for 10 min at –78 °C, a solution of alcohol **17** (1.26 g, 0.35 mmol) in CH_2Cl_2 (7.5 mL) was added dropwise to the reaction mixture. The solution was stirred for 15 min at –78 °C, and then triethylamine (3.10 mL, 22.4 mmol) was added dropwise. The reaction mixture was stirred at –78 °C for 45 min, and then poured into a mixture of Et_2O (10 mL) and aqueous saturated NH_4Cl (10 mL). The organic phase was partitioned and washed with aqueous saturated $NaHCO_3$ (10 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo* to yield 1.25 g (quant.) of crude aldehyde **41**: R_f = 0.50 in 20% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 7.69-7.66 (m, 4H), 7.44-7.36 (m, 6H), 6.26 (dd, *J*=10.7, 1.2 Hz, 1H), 5.38 (t, *J*=6.2 Hz, 1H), 4.18 (d, J=6.3 Hz, 2H), 3.41-3.30 (m, 1H), AB of ABX (δ_A = 2.06, δ_B = 2.01, J_{AB} = 13.4 Hz, J_{AX} = 6.5 Hz, J_{BX} = 8.0 Hz, 2H), 1.75 (d, *J*=1.2 Hz, 3H), 1.42 (s, 3H), 1.06-1.04 (m, 3H), 1.04 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.1, 155.0, 135.5, 134.7, 134.0, 133.8, 129.5, 127.6, 127.1, 60.8, 47.3, 29.3, 26.8, 21.1, 19.5, 19.1, 16.4; IR (neat) 3071, 2960, 2856, 1678, 1428, 1112, 1975 cm^{-1}; MS (DEI) 420 (1), 363 (65), 333 (10), 285 (41), 267 (17), 255 (10), 229 (11), 201 (39), 199 (100), 183 (26), 147 (75); HRMS *m/e* calcd for $C_{27}H_{36}O_2Si$ (M^+) 420.2485, found 420.2498.

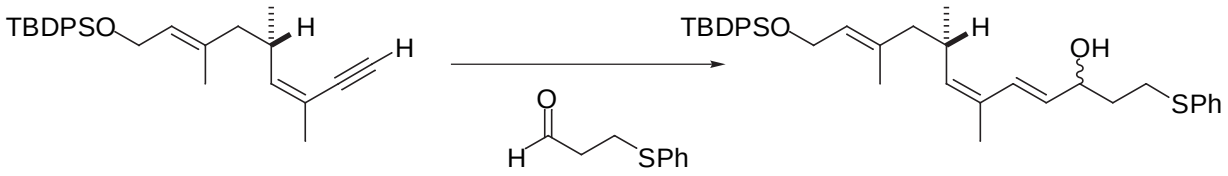
41 **18**

(3*Z*,7*E*)-(5*S*)-9-(*tert*-Butyldiphenylsilanyloxy)-3,5,7-trimethylnona-3,7-dien-1-yne. (18)

To a cold (0 °C) solution of triphenylphosphine (3.12 g, 11.9 mmol) in CH_2Cl_2 (15 mL) was added carbon tetrabromide (1.97 g , 5.94 mmol). After stirring for 15 min at 0 °C, a solution of crude aldehyde **41** (1.25 g, 2.97 mmol) in CH_2Cl_2 (15 mL) was added dropwise. The reaction mixture was stirred for 10 min at 0 °C, and then quenched with aqueous saturated $NaHCO_3$ (10 mL). After warming to room temperature, the reaction mixture was poured into a mixture of saturated aqueous $NaHCO_3$ (50 mL) and CH_2Cl_2 (50 mL). The phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 X 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The resulting yellow solid was diluted in hexanes (50 mL), and filtered through a pad of celite to yield 1.68g (98%) of crude dibromide: R_f = 0.60 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.67 (m, 4H), 7.42-7.36 (m, 6H), 7.02 (s, 1H), 5.34 (t, *J*=6.2 Hz, 1H), 5.17 (d, *J*=9.9 Hz, 1H), 4.20 (d, *J*=6.3 Hz, 2H), 2.45-2.39 (m, 1H), 2.00-1.84 (m, 2H), 1.84 (s, 3H), 1.43 (s, 3H), 1.04 (s, 9H), 0.91 (d, *J*=6.6 Hz, 3H).

To a cold (–78 °C) solution of crude dibromide (1.68g, 2.91 mmol) in THF (15 mL) was added *n*-BuLi (2.5 M in hexanes, 2.39 mL, 5.97 mmol). After stirring for 1 h at –78 °C, the reaction mixture was quenched with aqueous saturated NH_4Cl (10 mL) and warmed to room temperature. The reaction mixture was then poured into a mixture of saturated aqueous NH_4Cl (50 mL) and Et_2O (50 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (2 x 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (50 g SiO_2, 100% hexanes to 2% EtOAc/hexanes) to yield 1.05 g (85 %–3 steps from alcohol **17**) of alkyne **18**: $[\alpha]_D^{24}$ = –40.8 (c1.06, $CHCl_3$); R_f = 0.55 in 10% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.67 (m, 4H), 7.44-7.36 (m, 6H), 5.50, (d, *J*=9.5 Hz, 1H), 5.37 (t, *J*=6.2 Hz, 1H), 4.20 (d, *J*=6.3 Hz, 2H),

3.04 (s, 1H), 2.92-2.81 (m, 1H), AB of ABX(δ_A = 1.98, δ_B = 1.93, J_{AB} = 13.3 Hz, J_{AX} = 7.6 Hz, J_{BX} = 7.4 Hz, 2H), 1.81 (s, 3H), 1.44 (s, 3H), 1.04 (s, 9H), 0.93 (d, J=6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 135.8, 135.6, 134.3, 129.7, 127.8, 126.1, 115.7, 83.4, 80.3, 61.3, 47.3, 33.5, 27.1, 23.1, 20.2, 19.4, 16.4; IR (neat) 3304, 3072, 2957, 2858, 2075, 1961, 1891, 1822, 1590, 1473, 1428, 1112, 1073 cm^{-1}; MS (DCI/CH_4) 416 (1), 317 (10), 281 (17), 251 (14), 239 (30), 199 (100), 159 (15), 135 (30), 93 (19); HRMS *m/e* calcd for $C_{28}H_{36}OSi$ (M^+) 416.2535, found 416.1554.



18 **19** **20**

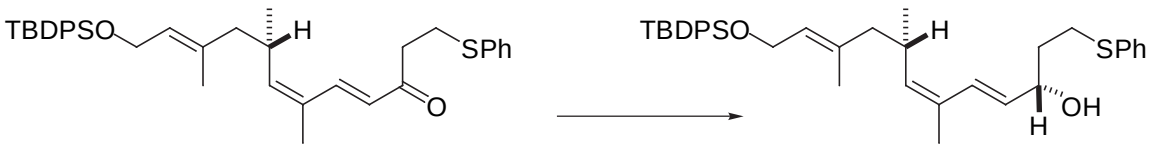
(6*S*)-(2*E*, 4*Z*, 8*E*)-1-(Benzenesulfanyl-ethyl)-10-(*tert*-butyldiphenylsilanyloxy)-4,6,8,-trimethyldeca-2,4,8-trien-1-ol. (20)

To a solution of alkyne **18** (0.50g, 1.20 mmol) in CH_2Cl_2 (6.0 mL) was added Schwartz reagent (0.40 g, 1.56 mmol) portionwise. The solution was stirred for 10 min at room temperature, and then cooled to –65 °C. Dimethylzinc (2.0 M in toluene, 0.78 mL, 1.56 mmol) was added dropwise, and the reaction mixture was stirred for 15 min at –65 °C. After warming the reaction mixture to 0 °C, a solution of aldehyde **19** (0.24 g, 1.44 mmol) and dimethylzinc (2.0 M in toluene, 0.60 mL, 1.20 mmol) in CH_2Cl_2 (2.0 mL) was added dropwise. The reaction mixture was stirred for 1.5 h at 0 °C, and then quenched with aqueous saturated NH_4Cl (10 mL). After warming to room temperature, the solution was poured into a mixture of Et_2O (50 mL) and aqueous saturated NH_4Cl (50 mL). The layers were separated, and the organic phase was washed with aqueous saturated NaCl (50 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (25 g SiO_2, 5% to 10% EtOAc/hexanes) to yield 0.64 g (92%) of a 1:1 mixture of diastereomeric alcohols **20**: R_f = 0.10 in 5% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.67 (m, 4H), 7.44-7.24 (m, 10H), 7.21-7.14 (m,1H), 6.61 (d, *J*=15.6 Hz, 0.5H), 6.60 (d, *J*=15.6 Hz, 0.5H), 5.62 (dd, *J*=15.6, 6.9 Hz, 0.5H), 5.62 (d, *J*=15.6, 6.9 Hz, 0.5H), 5.37 (t, *J*=6.2 Hz, 1H), 5.17 (d, *J*=9.5 Hz, 1H), 4.37-3.36 (m, 1H), 4.21-4.18 (m, 2H), 3.06-2.96 (m, 2H), 2.81-2.72 (m, 1H), 1.95-1.80 (m, 4H), 1.77 (s, 3H), 1.42 (s, 1.5H), 1.40 (s, 1.5H), 1.04 (s, 4.5H), 1.04 (s, 4.5H), 0.92 (d, *J*=6.7 Hz, 1.5H), 0.91 (d, *J*=6.7 Hz, 1.5H); IR (neat) 3408, 3072, 2958, 2858, 1652, 1567, 1428, 1112, 1067, 1048 cm^{-1}; MS (DCI/CH_4) 584 (1), 311 (10), 201 (33), 159 (21), 145 (12), 137 (27), 135 (31), 123 (95), 107 (33), 95 (55) 77 (14); HRMS *m/e* calcd for $C_{37}H_{48}O_2SSi$ (M^+) 584.3144, found 584.3132.

20 **21**

(6*S*)-(2*E*, 4*Z*, 8*E*)-1-(Benzenesulfanylethyl)-10-(*tert*-butyldiphenylsilanyloxy)-4,6,8,-trimethyldeca-2,4,8-trien-1-one. (21)

To a solution of alcohol **20** (0.48 g, 0.83 mmol) in CH_2Cl_2 (4.2 mL) was added sodium bicarbonate (0.70 g, 8.27 mmol) and Dess-Martin Periodinane (0.39 g, 0.91 mmol). After allowing the solution to stir for 15 min at room temperature, the reaction mixture was quenched with aqueous saturated $Na_2S_2O_3$ (1 mL). The quenched reaction mixture was then poured into a mixture of CH_2Cl_2 (15 mL) and aqueous saturated NH_4Cl (15 mL). The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (2 x 15 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (25 g SiO_2, 5% EtOAc/hexanes) to yield 0.40 g (84%) of ketone **21**: $[\alpha]_D^{24}$ = –48.5 (c 2.70, $CHCl_3$); R_f = 0.60 in 20% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.66 (m, 4H), 7.58 (d, *J*=15.7 Hz), 7.44-7.34 (m, 8H), 7.30-7.26 (m, 2H), 7.20-7.16 (m, 1H), 6.13 (d, *J*=15.7 Hz, 1H), 5.58 (d, *J*=9.8 Hz, 1H), 5.35 (m, 1H), 4.21-4.12 (m, 2H), 3.21 (t, *J*=7.4 Hz, 2H), 2.91-2.84 (m, 3H), 1.99-1.97 (m, 2H), 1.81 (s, 3H), 1.41 (s, 3H), 1.04 (s, 9H), 0.98-0.95 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 147.1, 139.4, 135.8, 135.7, 135.5, 134.6, 134.0, 129.5, 129.4, 129.0, 127.6, 126.5, 126.2, 125.6, 61.0, 47.4, 40.6, 30.5, 27.9, 26.8, 20.9, 20.0, 19.1, 16.3 ; IR (neat) 3071, 3052, 2959, 2857, 1735, 1686, 1590, 1427, 1267, 1112, 1076 cm^{-1}; MS (DCI, CH_4) 582 (1), 494 (21), 307 (14), 199 (22), 197 (12), 173 (12), 149 (15), 137 (24), 135 (43), 123 (81), 95 (19), 77 (18); HRMS *m/e* calcd for $C_{37}H_{46}O_2SiS$ (M^+) 582.2988, found 582.2982.



21 **22**

(1S,6*S*)-(2*E*, 4*Z*, 8*E*)-1-(Benzenesulfanylethyl)-10-(*tert*-butyldiphenylsilanyloxy)-4,6,8,-trimethyldeca-2,4,8-trien-1-ol. (22)

The Terashima reagent was prepared according to the following procedure: A flame-dried two-neck round bottom flask was equipped with a reflux condenser and charged with lithium aluminum hydride (0.10 g, 2.74 mmol) and dry Et_2O (3 mL). A solution of (–)–*N*–methyl ephedrine (0.49 g, 2.74 mmol) in Et_2O (8 mL) was added over 30 min. After heating the solution at reflux for 1 h, N-ethylaniline (0.69 mL, 5.48 mmol) was added dropwise. After an additional 1 h at reflux, the solution was cooled to ambient temperature.

Terashima reagent (0.25 M in Et_2O, 4.50 mL, 1.13 mmol) was added dropwise to a –78 °C solution of ketone **21** (0.33 g, 0.56 mmol) in Et_2O (5.6 mL). After stirring for 1.5 h at –78 °C, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (1 mL). After warming to room temperature, the quenched reaction mixture was poured into a mixture of Et_2O (25 mL) and aqueous saturated $NaHCO_3$ (25 mL). The layers were separated, and the organic phase was washed with aqueous 10% HCl (25 mL) and aqueous saturated NaCl (25 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (20 g SiO_2, 10% EtOAc/hexanes) to yield 0.32 g (98%) of a 4.5:1 mixture of diastereomeric alcohols: Major diastereomer **22**: $[\alpha]_D^{26}$ = –42.6 (c0.90, $CHCl_3$); R_f = 0.25 in 20% EtOAc/Hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.67 (m, 4H), 7.44 (m, 11H), 6.59 (d, *J*=15.6 Hz, 1H), 5.62 (dd, *J*=15.6, 6.8 Hz, 1H), 5.36 (t, *J*=5.2 Hz, 1H), 5.17 (d, *J*=9.5 Hz, 1H), 4.38-4.33 (m, 1H), 4.19 (d, *J*=6.2 Hz, 2H), 3.08-2.97 (m, 2H), 2.80-2.70 (m, 1H), 1.95-1.80 (m, 4H), 1.77 (d, *J*=1.1 Hz, 3H), 1.42 (s, 3H), 1.01 (s, 9H), 0.91 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.1, 136.3, 135.6, 135.2, 134.0, 131.2, 129.5, 126.0, 129.1, 128.9, 128.2, 127.6,

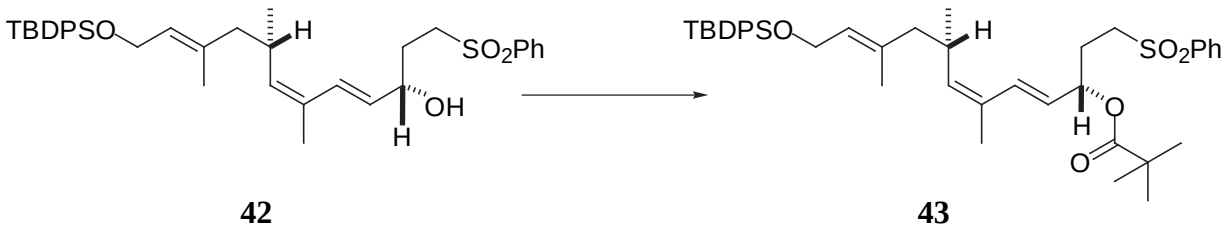
125.9, 121.8, 72.1, 61.1, 47.5, 36.5, 29.9, 29.8, 26.8, 20.8, 20.5, 19.2, 16.4; IR (neat) 3420, 3070, 2958, 2856, 1586, 1472, 1379, 1111, 1074, 1047 cm^{-1}; MS(DCI/CH_4) 584 (3), 509 (38), 349 (18), 311 (49), 265 (28), 261 (42), 243 (39), 201 (62), 181 (16), 159 (53), 149 (35), 145 (32), 123 (82), 121 (34), 95 (59); HRMS *m/e* calcd for $C_{37}H_{48}O_2SSi$ (M^+) 584.3144, found 584.3117.

22 **42**

(1S,6*S*)-(2*E*, 4*Z*, 8*E*)-1-(Benzenesulfonylethyl)-10-(tert-butyldiphenylsilanyloxy)-4,6,8,-trimethyldeca-2,4,8-trien-1-ol. (42)

Preparation of oxidant stock solution: To ammonium molybdate (0.32 g, 0.26 mmol) at 0°C was added 50% aqueous hydrogen peroxide (0.36 mL, 5.23 mmol). The yellow solution was stirred 10 min at 0°C.

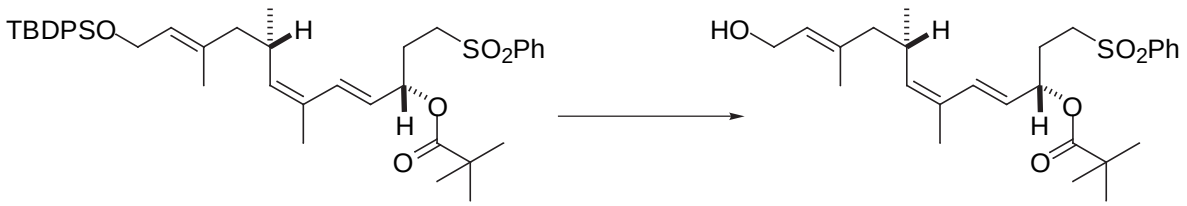
To a 0°C solution of sulfide **22** (64 mg, 0.11 mmol) in ethanol (1.1 mL) was added oxidant (60 μL) . The solution was stirred for 1h at 0°C, and then diluted in EtOAc (20 mL). The solution was washed with H_2O (20 mL) and aqueous saturated NaCl (20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (5 g SiO_2, 30% EtOAc/hexanes) to yield 60 mg (90%) of sulfone **42:** $[\alpha]_D^{24}$ = –37.6 (c1.15 $CHCl_3$); R_f = 0.35 in 40% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) 7.92-7.90 (m, 2H), 7.69-7.63 (m, 5H), 3.58-7.54 (m, 2H), 7.43-7.35 (m, 6H), 6.57 (d, *J*=15.6 Hz, 1H), 5.53 (dd, *J*=15.6, 6.9 Hz, 1H), 5.35 (t, *J*=5.4 Hz, 1H), 5.19 (d, *J*=9.5 Hz, 1H), 4.28-4.26 (m, 1H), 4.18 (d, *J*=6.2 Hz, 2H), 3.30-3.15 (m, 2H), 2.77-2.69 (m, 1H), 2.05-1.87 (m, 4H), 1.74 (d, *J*=0.7 Hz, 3H), 1.40 (s, 3H), 1.03 (s, 9H), 0.90 (d, *J*=6.6 Hz, 3H) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1, 138.7, 135.6, 135.1, 134.0, 133.7, 130.0, 129.5, 129.3, 129.2, 128.9, 128.0, 127.6, 126.0, 71.4, 61.1, 52.7, 47.5, 30.1, 29.9, 26.8, 20.8, 20.5, 19.1, 16.4; IR (neat) 3441, 3070, 2957, 2853, 1654, 1306, 1148, 1112, 1085, 1044 cm^{-1}; MS (DCI/NH_3) 559 (2), 263 (10), 201 (29), 199 (100), 159 (12), 135 (18), 133 (24), 199 (16), 95 (15), 77 (23); HRMS *m/e* calcd for $C_{33}H_{39}O_4SSi$ ($M^+ - C_4H_9$) 559.2338, found 559.2317.



42 **43**

2,2-Dimethylpropionic acid (1*S*,6*S*)-(2*E*,4*Z*,8*E*)-1-(2-benzenesulfonylethyl)-10-(*tert*-butyldiphenylsilanyloxy)-4,6,8-trimethyldeca-2,4,8-trienyl ester. (43)

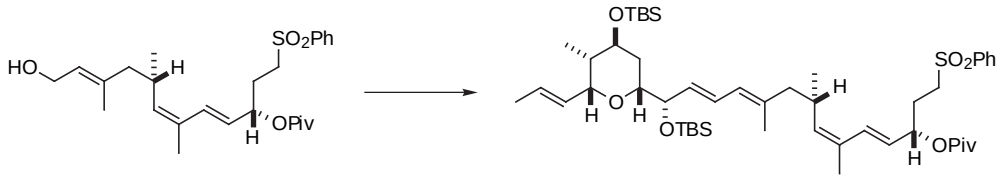
To a solution of alcohol **42** (0.31 g, 0.50 mmol) in CH_2Cl_2 (2.5 mL) was added pyridine (0.16 mL, 2.00 mmol), pivaloyl chloride (0.15 mL, 1.21 mmol), and DMAP (catalytic). The solution was stirred for 48 h at room temperature, and then poured into a mixture of Et_2O (10 mL) and aqueous saturated $NaHCO_3$ (10 mL). The phases were separated, and the organic phase was washed with aqueous 25% $CuSO_4$ (10 mL) and aqueous saturated NaCl (10 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (20 g SiO_2, 15% EtOAc/Hexanes) to yield 0.35 g (quantitative yield) of ester **43**: $[\alpha]_D^{20}$ – 14.2 (c 1.75, $CHCl_3$); R_f = 0.50 in 40% EtOAc/Hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90-7.88 (m, 2H), 7.69-7.64 (m, 5H), 7.59-7.52 (m, 2H), 7.43-7.21 (m, 6H), 6.56 (d, *J*=15.6 Hz, 1H), 5.43 (dd, *J*=15.6, 6.6 Hz, 1H), 5.37-5.34 (m, 1H), 5.19 (d, *J*=9.5 Hz, 1H), 4.18 (d, *J*= 6.2 Hz, 2H) 3.13-3.05 (m, 2H), 2.73-2.65 (m, 1H), 2.08-2.03 (m, 2H), AB of ABX (δ_A = 1.95, δ_B = 1.90, J_{AB} = 13.4 Hz, J_{AX} = 7.0 Hz, J_{BX} = 7.9 Hz, 2H), 1.71 (s, 3H), 1.38 (s, 3H), 1.15 (s, 9H), 1.03 (s, 9H), 0.87 (d, *J*=6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.2, 139.1, 138.8, 135.6, 135.0, 134.0, 133.8, 130.0, 129.5, 129.4, 129.0, 128.0, 127.6, 126.1, 125.3, 71.9, 61.0, 52.3, 47.5, 38.8, 29.7, 28.0, 27.0, 26.8, 20.6, 20.3, 19.1, 16.1; IR (neat) 3070, 2959, 2930, 2857, 1730, 1581, 1479, 1308, 1150, 1112, 1087 cm^{-1}; MS (DCI, CH_4) 700 (3), 643 (65), 541 (59), 343 (47), 283 (78), 223 (26), 201 (78), 199 (53), 159 (46), 145 (21), 133 (100), 107 (40); HRMS *m/e* calcd for $C_{42}H_{56}O_5SSi$ (M^+) 700.3618, found 700.3610.



43 **23**

2,2-Dimethylpropionic acid (1*S*,6*S*)-(2*E*,4*Z*,8*E*)-1-(2-benzenesulfonylethyl)-10-hydroxy-4,6,8-trimethyldeca-2,4,8-trienyl ester. (23)

To a solution of silyl ether **43** (0.31 g, 0.44 mmol) in THF (2.2 mL) was added tetrabutylammonium flouride (1M in THF, 0.52 mL, 0.52 mmol). The reaction mixture was stirred for 2 h at room temperature, and then poured into a mixture of Et_2O (25 mL) and aqueous saturated NaCl (25 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (2 x 25 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (15 g SiO_2, 30 to 40% EtOAc/hexanes) to yield 0.20 g (quantitative yield) of alcohol **23**; $[\alpha]_D^{23}$=–14.1 (c 1.65, $CHCl_3$); R_f = 0.25 in 40% EtOAc/hexanes; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91-7.89 (m,2H), 7.68 (t, *J*=7.4 Hz, 1H), 7.60-7.57 (m, 2H), 6.58 (d, *J*=15.4 Hz, 1H), 5.42-5.28 (m, 3H), 5.17 (d, *J*=9.7 Hz, 1H), 4.14-4.04 (m, 2H), 3.18-3.06 (m, 2H), 2.79-2.68 (m, 1H), 2.09-2.03 (m, 2H), AB of ABX (δ_A = 1.98, δ_B = 1.92, J_{AB} = 13.4 Hz, J_{AX} = 6.3 Hz, J_{BX} = 8.2 Hz, 2H). 1.73 (d, *J*=0.7 Hz, 3H), 1.61 (s, 3H), 1.16 (s, 9H), 0.91 (d, *J*=6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.4, 139.0, 138.8, 137.4, 133.9, 130.7, 129.4, 129.3, 128.0, 125.6, 125.2, 72.3, 59.2, 52.3, 47.3, 38.8, 30.4, 27.9, 27.0, 21.1, 20.3, 16.5; IR (neat) 3426, 2958, 2919, 2873, 1732, 1653, 1482, 1310, 1271, 1152, 1086 cm^{-1}; MS(DCI/CH_4) 445 (2), 343 (22), 331 (21), 276 (31), 275 (41), 218 (49), 200 (46), 188 (53), 185 (21), 151 (66), 134 (73), 133 (100), 125 (34), 107 (40), 95 (54), 85 (36); HRMS *m/e* calcd for $C_{26}H_{37}O_4S$ (M–OH) 445.2413, found 445.2435.



23 **26**

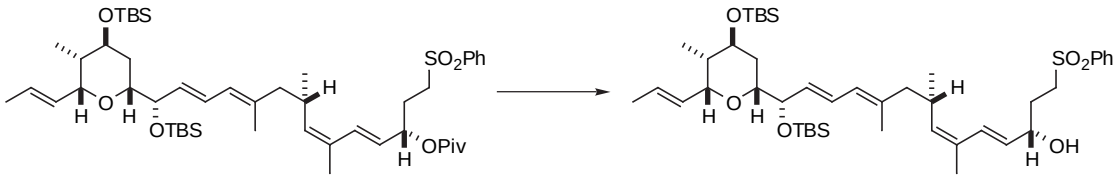
2,2-Dimethylpropionic acid (1*S*,6*S*,12*S*)-(2*E*,4*Z*,8*E*,10*E*)-1-(2-benzenesulfonylethyl)-12-(*tert*-butyldimethylsilanoxy)-12-((*E*)-(2*R*,4*S*,5*S*,6*R*)-5-methyl-6-propenyl-4-(*tert*-butyldimethylsilanoxy)-tetrahydropyran-2-yl)-4,6,8-trimethyldodeca-2,4,8,10-tetraenyl ester. (26)

Collidine (543 μL, 4.11 μmol) was added to a 0 °C solution of alcohol **23** (238 mg, 514 μmol) and CH_2Cl_2 (12.9 mL). Methanesulfonyl chloride (159 μL, 2.06 μmol) was added dropwise. After 3 h, the mixture was poured into EtOAc (75 mL) and saturated aqueous NH_4Cl (75 mL). The layers were separated and the organic layer was washed with saturated aqueous $CuSO_4$ (75 mL) and brine (50 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was used without further purification.

Solid, anhydrous lithium bromide (446 mg, 5.14 mmol) was added in one portion to a solution of the mesylate and THF (7.8 mL). After 15 min, the mixture was diluted with Et_2O (25 mL) and washed with H_2O (20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (7.5 g SiO_2, 2:1 hexanes : ethyl acetate) to afford 221 mg (82%) of a 2.5 : 1 mixture of the bromide **24** to the chloride as a pale, yellow oil: R_f 0.65 (3:2 hexanes : ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.9 Hz, 2H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.9 Hz, 2H), 6.53 (d, *J* = 15.3 Hz, 1H), 5.48 – 5.08 (m, 5H), 4.02 (dd, *J* = 7.9, 1.6 Hz, 0.6H), 3.94 (dd, *J* = 8.6, 1.9 Hz, 1.4H), 3,14 – 3.04 (m, 2H), 2.80 – 1.86 (m, 1H), 2.08 – 1.92 (m, 4H), 1.71 (s, 3H), 1.64 (s, 3H), 1.16 (s, 9H), 0.88 (d, *J* = 6.6 Hz, 3H).

Tributylphosphine (1.05 mL, 4.21 mmol) was added dropwise to the bromide. The reaction vessel was sealed for 48 h. The mixture was cooled to 0 °C and a solution of aldehyde **8** (186 mg,

421 μmol) and toluene (4.2 mL) was added. A solution of potassium *tert*-butoxide (62 mg, 550 μmol) and THF (0.89 mL) was slowly added dropwise. After completion of addition, the mixture was diluted with Et_2O (20 mL) and washed with H_2O (20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$), filtered, concentrated *in vacuo*, diluted with (5:1 hexanes : ethyl acetate), filtered through a plug of silica gel, and concentrated *in vacuo*. The crude product (16:1 ratio of olefin isomers) was purified by flash chromatography (20 g SiO_2, 10:1 hexanes : ethyl acetate) to afford 266 mg (72%) of **26** as a clear oil: R_f 0.43 (5:1 hexanes : ethyl acetate); $[\alpha]_D^{21}$ –36 (c 1.1, $CHCl_3$); IR (neat) ν = 3012, 2956, 2928, 2856, 1731, 1653, 1462, 1324, 1252, 1150, 1087, 1052, 1005, 836, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.3 Hz, 2H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.58 (t, *J* = 7.3 Hz, 2H), 6.58 (d, *J* = 15.3 Hz, 1H), 6.40 (ddd, *J* = 15.2, 11.0, 1.3 Hz, 1H), 5.76 (d, *J* = 11.0 Hz, 1H), 5.64 (dqd, *J* = 15.3, 6.4, 1.2 Hz, 1H), 5.55 – 5.31 (m, 4H), 5.18 (d, *J* = 9.4, 1H), 4.42 – 4.36 (m, 1H), 4.32 – 4.26 (m, 1H), 3.89 – 3.84 (m, 1H), 3.67 (ddd, *J* = 11.5, 3.6, 2.3, 1H), 3.20 – 3.02 (m 2H), 2.80 – 2.65 (m, 1H), 2.10 – 1.88 (m, 4H), 1.78 – 1.58 (m, 1H), 1.71 (s, 3H), 1.68 (d, *J* = 6.6 Hz, 3H), 1.66 (s, 3H), 1.54 – 1.44 (m, 1H), 1.35 – 1.28 (m, 1H), 1.16 (s, 9H), 0.91 (s, 9H), 0.87 (s, 9H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 7.1 Hz, 3H), 0.08 (s, 3H), 0.03 (s, 3H), 0.01 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.1, 139.0, 138.8, 135.8, 133.8, 131.7, 131.2, 130.0, 129.4, 129.0, 128.0, 126.3, 126.2, 125.3, 125.2, 75.9, 75.3, 74.5, 71.8, 70.9, 52.3, 47.8, 40.3, 38.8, 29.9, 27.9, 27.7, 27.0, 25.9, 25.7, 20.4, 20.2, 18.2, 18.0, 17.9, 16.3, 14.2, 11.1, –4.6, –4.6, –4.8, –5.0; MS(FAB/Na) 894 (56), 602 (18), 275 (33), 225 (70), 187 (100), 151 (57); HRMS *m/e* calcd for $C_{49}H_{82}O_7SSi_2Na$ (M^+ + Na) 893.5218, found 893.5218.

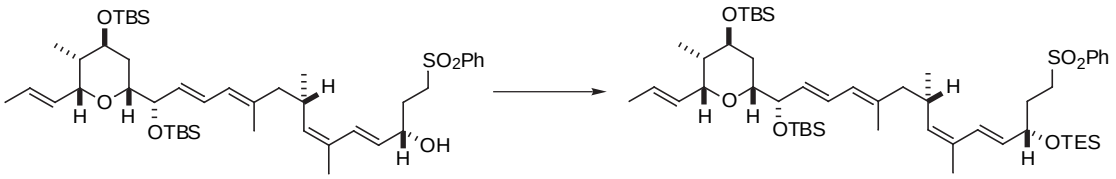


26 **44**

(1*S*,6*S*,12*S*)-(2*E*,4*Z*,8*E*,10*E*)-1-(2-Benzenesulfonylethyl)-12-(*tert*-butyldimethylsilanoxy)-12-[(*E*)-(2*R*,4*S*,5*S*,6*R*)-4-(*tert*-butyldimethylsilanoxy)-5-methyl-6-propenyl-tetrahydropyran-2-yl]-4,6,8-trimethyldodeca-2,4,8,10-tetraen-1-ol. (44)

Diisobutylaluminum hydride (475 μL of a 1.0 M in hexanes, 475 μmol) was added dropwise to a –78 °C solution of ester **26** (188 mg, 216 μmol) and CH_2Cl_2 (2.16 mL). After 10 min, acetone (0.1 mL) was added and the dry ice/acetone bath was removed. Five percent aqueous potassium sodium tartrate solution (30 mL) was added and the biphasic mixture was stirred vigorously. After 15 min, Et_2O (25 mL) was added and after 1.5 h, the layers were separated. The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (20 g SiO_2, 5:1 hexanes : ethyl acetate) to afford 152 mg (89%) of **44** as a sticky, white foam: R_f 0.57 (1:1 hexanes : ethyl acetate); $[\alpha]_D^{20}$ –53 (c 0.87, $CHCl_3$); IR (neat) ν = 3499, 3054, 3017, 2952, 2929, 2887, 2850, 1654, 1585, 1445, 1306, 1251, 1149, 1088, 1047, 963, 833 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.4 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.56 (t, *J* = 7.3 Hz, 2H), 6.56 (d, *J* = 15.6 Hz, 1H), 6.40 (ddd, *J* = 15.0, 11.0, 1.3 Hz, 1H), 5.76 (d, *J* = 10.9 Hz, 1H), 5.64 (dqd, *J* = 15.3, 6.6, 1.2 Hz, 1H), 5.57 – 5.48 (m, 2H), 5.40 (ddq, *J* = 15.3, 5.5, 1.5 Hz, 1H), 5.17 (d, *J* = 9.5 Hz, 1H), 4.42 – 4.36 (m, 1H), 4.32 – 4.24 (m, 2H), 3.89 – 3.84 (m, 1H), 3.67 (ddd, *J* = 11.7, 3.8, 2.3, 1H), 3.32 – 3.14 (m 2H), 2.84 – 2.68 (m, 1H), 2.06 – 1.86 (m, 4H), 1.78 – 1.58 (m, 1H), 1.73 (s, 3H), 1.68 (d, *J* = 6.3 Hz, 3H), 1.67 (s, 3H), 1.54 – 1.44 (m, 1H), 1.35 – 1.28 (m, 1H), 0.91 (s, 9H), 0.88 (d, *J* = 6.7 Hz, 3H), 0.87 (s, 9H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.08 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1, 138.5, 135.8, 133.7, 131.7, 131.2, 130.1, 129.3, 129.2, 128.8, 128.0, 126.3, 126.2, 125.2, 75.9, 75.3, 74.5, 71.3, 70.8, 55.8, 47.9, 40.3, 30.1, 30.0, 27.8, 25.9, 25.7, 20.6, 20.4, 18.2, 18.0, 17.9, 16.6, 11.1,

–4.6, –4.6, –4.8, –5.0; MS(FAB/Na) 810 (78), 518 (11), 316 (11), 225 (50), 187 (78), 151 (100); HRMS *m/e* calcd for $C_{44}H_{74}O_6SSi_2Na$ (M^+ + Na) 809.4643, found 809.4629.

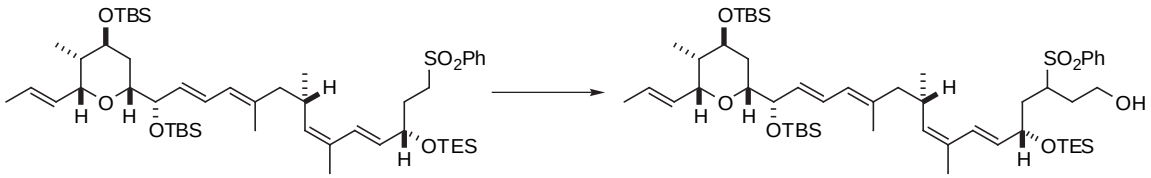


44 **27**

(2*R*,3*S*,4*S*,6*R*)-6-[(1*S*,7*S*,12*S*)-(2*E*,4*E*,8*Z*,10*E*)-14-Benzenesulfonyl-1-(*tert*-butyldimethylsilanoxy)-12-triethylsilanoxy-5,7,9-trimethyltetradeca-2,4,8,10-tetraenyl]-4-(*tert*-butyldimethylsilanoxy)-3-methyl-2-*E*-propenyltetrahydropyran. (27)

Pyridine (46 μL, 570 μmol) was added to a 0 °C solution of alcohol **44** (150 mg, 191 μmol) and CH_2Cl_2 (1.9 mL). Chlorotriethylsilane (38 μL, 230 μmol) was added dropwise and after 5 min, the ice bath was removed. After 3 h, Et_2O (20 mL) was added and the solution was washed with saturated aqueous $NaHCO_3$ (20 mL) and H_2O (20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (20 g SiO_2, 20:1 hexanes : ethyl acetate) to afford 162 mg (94%) of **27** as a clear, thick oil: R_f 0.43 (10:1 hexanes : ethyl acetate); $[\alpha]_D^{22}$ –37 (c=1.1, $CHCl_3$); IR (neat) ν = 3024, 2955, 2928, 2877, 2856, 1660, 1587, 1447, 1321, 1251, 1146, 1086, 1054, 1005, 965, 836, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.3 Hz, 2H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 2H), 6.53 (d, *J* = 15.6 Hz, 1H), 6.41 (ddd, *J* = 15.2, 11.0, 1.3 Hz, 1H), 5.78 (d, *J* = 11.0 Hz, 1H), 5.64 (dqd, *J* = 15.2, 6.6, 1.1 Hz, 1H), 5.55 – 5.36 (m, 3H), 5.14 (d, *J* = 9.5 Hz, 1H), 4.42 – 4.36 (m, 1H), 4.34 – 4.25 (m, 2H), 3.89 – 3.84 (m, 1H), 3.67 (ddd, *J* = 12.4, 3.2, 3.2 Hz, 1H), 3.32 – 3.12 (m 2H), 2.82 – 2.68 (m, 1H), 2.06 – 1.86 (m, 4H), 1.79 – 1.62 (m, 1H), 1.71 (s, 3H), 1.68 (d, *J* = 6.7 Hz, 3H), 1.67 (s, 3H), 1.55 – 1.45 (m, 1H), 1.36 – 1.28 (m, 1H), 0.91 (s, 9H), 0.89 (t, *J* = 8.2 Hz, 9H), 0.89 – 0.87 (m, 3H), 0.87 (s, 9H), 0.84 (d, *J* = 7.3 Hz, 3H), 0.59 (q, *J* = 8.1 Hz, 6H), 0.08 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1, 137.8, 135.8, 133.6, 131.7, 131.2, 130.6, 129.3, 129.2, 128.0, 127.9, 126.3, 126.1, 125.2, 76.0, 75.3, 74.5, 71.5, 70.9, 52.3, 48.1, 44.7, 40.3, 31.2, 29.8, 27.7, 25.9, 25.7, 20.4, 18.2, 18.0, 17.9, 16.3, 11.1, 6.7,

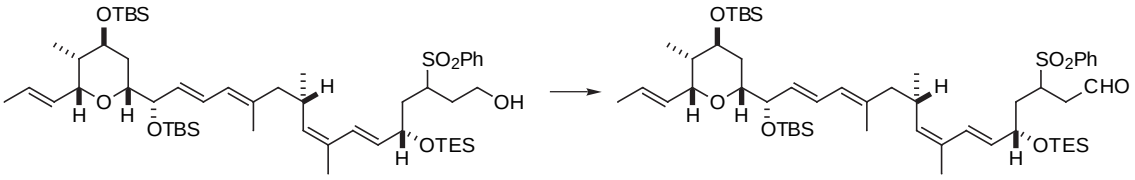
4.8, –4.6, –4.6, –4.8, –5.0; MS(FAB/Na) 924 (100), 632 (21), 408 (33), 331 (20), 265 (96), 225 (78), 171 (79); HRMS *m/e* calcd for $C_{50}H_{88}O_6SSi_3Na$ (M^+ + Na) 923.5508, found 923.5499.



27 **28**

(5*S*,10*S*,16*S*)-(6*E*,8*Z*,12*E*,14*E*)-3-Benzenesulfonyl-16-(*tert*-butyldimethylsilanoxy)-16-[-*E*-(2*R*,4*S*,5*S*,6*R*)-4-(*tert*-butyldimethylsilanoxy)-5-methyl-6-propenyltetrahydropyranyl]-5-triethylsilanoxy-8,10,12-trimethylhexadeca-6,8,12,14-tetraen-1-ol. (28)

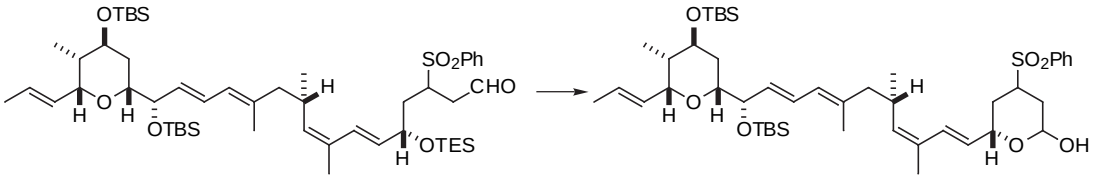
n-Butyllithium (11 μL of a 2.61 M in hexanes, 29 μmol)) was added dropwise to a solution of sulfone **27** (23 mg, 26 μmol), THF (255 μL), and HMPA (13 μL) at –78 °C. After 5 min, ethylene oxide (0.25 mL) was rapidly added to the light yellow solution. After 30 sec, the mixture was poured into Et_2O (15 mL) and 5% aqueous $NaHCO_3$ (15 mL). The layers were separated and the organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (5 g SiO_2, 1:1 hexanes : ethyl acetate) to afford 19 mg (78%) of **28** as a sticky, white foam: R_f 0.22 (3:1 hexanes : ethyl acetate); IR (neat) ν = 3499, 3024, 2955, 2928, 2856, 2877, 1653, 1469, 1305, 1251, 1146, 1054, 1005, 965, 836, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.80 (m, 2H), 7.70 – 7.50 (m, 3H), 6.53 (d, *J* = 15.4 Hz, 1H), 6.42 (ddd, *J* = 15.2, 11.0, 1.5 Hz, 1H), 5.80 (d, *J* = 11.1 Hz, 1H), 5.64 (dq, *J* = 15.2, 6.6 Hz, 1H), 5.57 – 5.36 (m, 3H), 5.17 (d, *J* = 9.5 Hz, 1H), 4.44 – 4.24 (m, 3H), 3.89 – 3.62 (m, 4H), 3.44 – 3.30 (m 1H), 2.84 – 2.68 (m, 1H), 2.18 – 1.88 (m, 6H), 1.79 – 1.62 (m, 1H), 1.73 (s, 3H), 1.68 (d, *J* = 7.6 Hz, 3H), 1.68 (s, 3H), 1.55 – 1.45 (m, 1H), 1.37 – 1.28 (m, 1H), 0.96 – 0.84 (m, 12H), 0.91 (s, 9H), 0.87 (s, 9H), 0.84 (d, *J* = 7.5 Hz, 3H), 0.60 – 0.51 (m, 6H), 0.08 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.00 (s, 3H); MS(FAB/Na) 968 (100), 810 (9), 383 (7), 309 (96), 275 (13), 225 (31), 133 (30); HRMS *m/e* calcd for $C_{52}H_{92}O_7SSi_3Na$ (M^+ + Na) 967.5770, found 967.5757. Anal. calcd. for $C_{52}H_{92}O_7SSi_3$: C, 66.05; H, 9.81; S, 3.39, found C, 66.04; H, 9.81; S, 3.27.



28 **45**

(5*S*,10*S*,16*S*)-(6*E*,8*Z*,12*E*,14*E*)-3-Benzenesulfonyl-16-(*tert*-butyldimethylsilanoxy)-16-[*E*-(2*R*,4*S*,5*S*,6*R*)-4-(*tert*-butyldimethylsilanoxy)-5-methyl-6-propenyltetrahydropyranyl]-5-triethylsilanoxy-8,10,12-trimethylhexadeca-6,8,12,14-tetraen-1-al. (45)

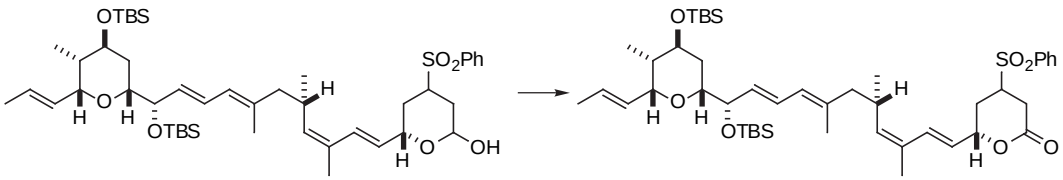
The Dess-Martin periodinane (8 mg, 20 mmol) was added in one portion to a solution of alcohol **28** (9.2 mg, 9.7 μmol), solid $NaHCO_3$ (12 mg, 150 μmol), and CH_2Cl_2 (100 μL). After 1 h, the mixture was diluted with Et_2O (10 mL) and 5% aqueous $NaHCO_3$ (10 mL). The layers were separated and the organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product **45** as a yellow oil was used without further purification: R_f 0.45 (3:1 hexanes : ethyl acetate); IR (neat) ν = 3005, 2952, 2932, 2873, 2846, 1732, 1673, 1449, 1304, 1251, 1146, 1073, 1001, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.70 (s, 1H), 7.94 – 7.80 (m, 2H), 7.70 – 7.54 (m, 3H), 6.49 (d, *J* = 15.7 Hz, 1H), 6.42 (dd, *J* = 15.0, 11.1 Hz, 1H), 5.79 (d, *J* = 10.7 Hz, 1H), 5.64 (dq, *J* = 15.3, 6.4 Hz, 1H), 5.52 (dd, *J* = 15.0, 5.1 Hz, 1H), 5.45 – 5.35 (m, 2H), 5.17 (d, *J* = 9.8 Hz, 1H), 4.44 – 4.24 (m, 3H), 3.96 – 3.84 (m, 2H), 3.72 – 3.64 (m 1H), 3.04 – 2.95 (m, 1H), 2.84 – 2.68 (m, 2H), 2.18 – 1.88 (m, 4H), 1.79 – 1.60 (m, 1H), 1.71 (s, 3H), 1.69 (d, *J* = 6.4 Hz, 3H), 1.68 (s, 3H), 1.55 – 1.45 (m, 1H), 1.36 – 1.26 (m, 1H), 0.96 – 0.82 (m, 15H), 0.91 (s, 9H), 0.87 (s, 9H), 0.57 – 0.46 (m, 6H), 0.08 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.00 (s, 3H); MS(FAB/Na) 965 (12), 307 (34), 263 (22), 225 (57), 187 (100); HRMS *m/e* calcd for $C_{52}H_{90}O_7SSi_3Na$ (M^+ + Na) 965.5613, found 965.5617.



45 **46**

(6*S*)-4-Benzenesulfonyl-6-{(5*S*,11*S*)-(1*E*,3*Z*,7*E*,9*E*)-11-(*tert*-butyldimethylsilanoxy)-11-[*E*-(2*R*,4*S*,5*S*,6*R*)-4-(*tert*-butyldimethylsilanoxy)-5-methyl-6-propenyltetrahydropyran-2-yl]-3,5,7-trimethylundeca-1,3,7,9-tetraenyl}-tetrahydropyran-2-ol. (46)

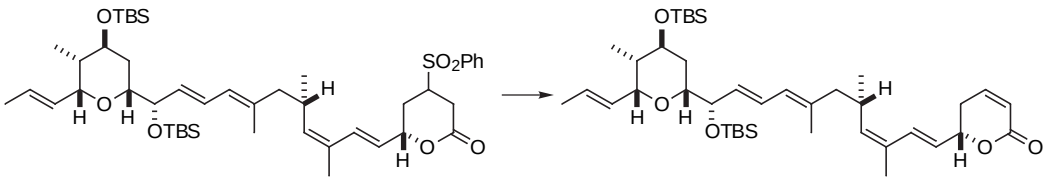
A solution of pyridinium *p*-toluenesulfonate (0.7 mg, 3 μmol) and ethanol (195 μL) was added to aldehyde **45** at 0 °C. After 3 h, the mixture was diluted with Et_2O (10 mL) and brine (10 mL). The layers were separated and the organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product **46** as a cloudy yellow oil was used without further purification: R_f 0.33 (2:1 hexanes : ethyl acetate); IR (neat) ν = 3420, 2952, 2925, 2879, 2853, 1660, 1449, 1297, 1258, 1146, 1080, 1047, 961, 829 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.80 (m, 2H), 7.74 – 7.54 (m, 3H), 6.70 – 6.54 (m, 1H), 6.50 – 6.32 (m, 1H), 5.82 – 5.35 (m, 5H), 5.24 – 5.10 (m, 1H), 4.84 – 4.62 (m, 0.5H), 4.44 – 4.24 (m, 2H), 3.96 – 3.84 (m, 1H), 3.72 – 3.64 (m 1H), 3.58 – 3.34 (m, 0.5H), 2.90 – 2.70 (m, 1H), 2.28 – 1.20 (m, 7H), 1.75 (s, 3H), 1.70 (s, 3H), 1.68 (s, 3H), 0.98 – 0.80 (m, 6H), 0.92 (s, 9H), 0.87 (s, 9H), 0.10 – 0.00 (m, 12H); MS(FAB/Na) 851 (76), 331 (20), 251 (17), 187 (100), 147 (66); HRMS *m/e* calcd for $C_{46}H_{76}O_7SSi_2Na$ (M^+ + Na) 851.4748, found 851.4724.



46 **47**

(6*S*)-4-Benzenesulfonyl-6-{(5*S*,11*S*)-(1*E*,3*Z*,7*E*,9*E*)-11-(*tert*-butyldimethylsilanoxy)-11-[*E*-(2*R*,4*S*,5*S*,6*R*)-4-(*tert*-butyldimethylsilanoxy)-5-methyl-6-propenyltetrahydropyran-2-yl]-3,5,7-trimethylundeca-1,3,7,9-tetraenyl}-tetrahydropyran-2-one. (47)

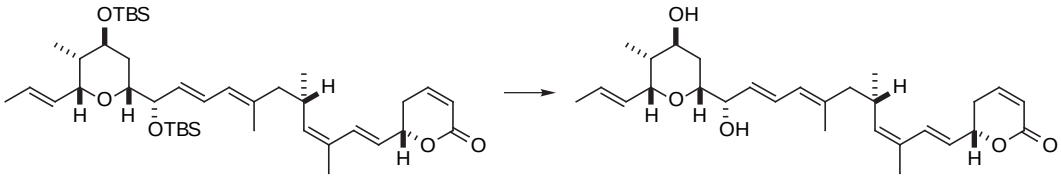
Powdered, activated 4 Å molecular sieves were added to a solution of lactol **46** and CH_2Cl_2 (165 μL). After 5 min, 4-methylmorpholine *N*-oxide (3 mg, 30 μmol) was added. After 10 min, *n*-tetrapropylammonium perruthenate (1 mg, 3 μmol) was added. After 20 min, the mixture was loaded directly onto a flash column (6 g, 2:1 hexanes : ethyl acetate) to afford 7 mg (86% for 3 steps) of **47** as a pale yellow oil: R_f 0.41 (2:1 hexanes : ethyl acetate); IR (neat) ν = 3018, 2952, 2925, 2886, 2853, 1745, 1653, 1607, 1310, 1244, 1152, 1093, 1047, 968, 836, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.4 Hz, 2H), 7.77 (t, *J* = 7.5 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 2H), 6.71 (d, *J* = 15.6 Hz, 1H), 6.41 (dd, *J* = 14.7, 12.1 Hz, 1H), 5.78 (d, *J* = 10.9 Hz, 1H), 5.70 – 5.36 (m, 4H), 5.26 (d, *J* = 9.8 Hz, 1H), 5.16 – 5.08 (m, 1H), 4.44 – 4.36 (m, 1H), 4.34 – 4.26 (m, 1H), 3.91 – 3.84 (m, 1H), 3.72 – 3.50 (m 2H), 2.97 – 2.38 (m, 4H), 2.18 – 1.88 (m, 3H), 1.79 – 1.24 (m, 3H), 1.76 (s, 3H), 1.69 (d, *J* = 7.1 Hz, 3H), 1.68 (s, 3H), 0.94 – 0.82 (m, 6H), 0.92 (s, 9H), 0.87 (s, 9H), 0.08 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H); MS(FAB/Na) 849 (92), 707 (54), 331 (13), 225 (69), 187 (100); HRMS *m/e* calcd for $C_{46}H_{74}O_7SSi_2Na$ (M^+ + Na) 849.4592, found 849.4629.



47 **48**

(*S*)-6-{(5*S*,11*S*)-(1*E*,3*Z*,7*E*,9*E*)-11-(*tert*-butyldimethylsilanoxy)-11-[*E*-(2*R*,4*S*,5*S*,6*R*)-4-(*tert*-butyldimethylsilanoxy)-5-methyl-6-propenyltetrahydropyran-2-yl]-3,5,7-trimethylundeca-1,3,7,9-tetraenyl}-5,6-dihydropyran-2-one. (48)

1,8-Diazabicyclo[5.4.0]undec-7-ene (17 μL, 120 μmol) was added to a solution of lactone **47** (32 mg, 39 μmol) and toluene (0.39 mL). After 10 min, the solution was diluted with Et_2O (15 mL) and washed with H_2O (10 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (7.5 g SiO_2, 2:1 hexanes : ethyl acetate) to afford 23 mg (87%) of **48** as a pale yellow oil: R_f 0.62 (2:1 hexanes : ethyl acetate); $[\alpha]_D^{25}$ –51 (c 1.1, $CHCl_3$); IR (neat) ν = 3018, 2952, 2925, 2892, 2846, 1732, 1469, 1376, 1251, 1126, 1080, 1060, 961, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.89 (ddd, *J* = 9.7, 4.3, 4.3, 1H), 6.72 (d, *J* = 15.6 Hz, 1H), 6.42 (ddd, *J* = 15.0, 12.4, 1.3 Hz, 1H), 6.06 (ddd, *J* = 9.8, 1.6, 1.6 Hz, 1H), 5.82 – 5.57 (m, 3H), 5.52 (dd, *J* = 15.2, 5.0 Hz, 1H), 5.24 (d, *J* = 9.4 Hz, 1H), 5.01 (dd, *J* = 14.2, 7.0 Hz, 1H), 4.44 – 4.36 (m, 1H), 4.33 – 4.26 (m, 1H), 3.90 – 3.84 (m, 1H), 3.72 – 3.63 (m 1H), 2.87 – 2.74 (m, 1H), 2.51 – 2.44 (m, 2H), 2.08 – 1.92 (m, 2H), 1.82 – 1.58 (m, 1H), 1.78 (s, 3H), 1.69 (d, *J* = 6.2 Hz, 3H), 1.70 (s, 3H), 0.86 (d, *J* = 6.3 Hz, 3H), 0.84 (d, *J* = 7.3 Hz, 3H), 0.92 (s, 9H), 0.87 (s, 9H), 0.08 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0, 144.6, 139.5, 135.8, 131.7, 131.2, 130.4, 129.1, 126.3, 125.3, 125.2, 121.7, 78.5, 76.0, 75.3, 74.5, 70.9, 47.9, 40.3, 30.1, 30.0, 27.8, 25.9, 25.8, 20.7, 20.3, 18.3, 18.0, 17.9, 16.6, 11.1, –4.5, –4.5, –4.8, –4.9; MS(FAB/Na) 707 (100), 421 (8), 305 (11), 225 (25), 187 (42); HRMS *m/e* calcd for $C_{40}H_{68}O_5Si_2Na$ (M^+ + Na) 707.4503, found 707.4557.

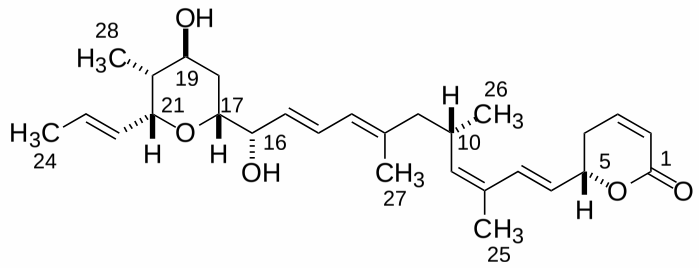


48 **1**

(–)-Ratjadone. (1)

A hydrogen fluoride•pyridine solution (940 μL from a stock solution of THF (10 mL), pyridine (5.7 mL), and Fluka brand hydrogen fluoride•pyridine (2.1 g)) was added slowly to a plastic vial containing silyl ether **48** (9.4 mg, 13.7 μmol) at 0 °C. After completion of addition, the vial was removed from the ice water bath and sealed. After 48 h, an additional portion of hydrogen fluoride•pyridine solution (100 μL) was added. After 12 h, the mixture was diluted with Et_2O (15 mL) and poured into saturated aqueous $NaHCO_3$ (10 mL). The layers were separated and the organic layer was washed with saturated aqueous NH_4Cl (10 mL). The aqueous layers were extracted with Et_2O (10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (5 g SiO_2, 1:1 to 1:1.5 hexanes : ethyl acetate) to afford 4.8 mg (76%) of **1** as an amorphous solid: R_f 0.24 (1:2 hexanes : ethyl acetate); $[\alpha]_D^{25}$ –48 (c 0.12, $CHCl_3$); IR (neat) ν = 3420, 2952, 2919, 2853, 1719, 1653, 1383, 1244, 1066, 1014, 968, 823 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.90 (ddd, *J* = 9.9, 4.2, 4.2, 1H), 6.72 (d, *J* = 15.7 Hz, 1H), 6.47 (ddd, *J* = 15.2, 12.2, 1.3 Hz, 1H), 6.07 (ddd, *J* = 9.8, 1.7, 1.7 Hz, 1H), 5.78 (d, *J* = 11.0 Hz, 1H), 5.71 (dd, *J* = 15.4, 6.6, 1H), 5.71 (dqd, *J* = 15.4, 6.6, 1.2 Hz, 1H), 5.52 (dd, *J* = 15.3, 6.4 Hz, 1H), 5.47 (ddq, *J* = 15.4, 6.3, 1.6 Hz, 1H), 5.23 (d, *J* = 9.80 Hz, 1H), 5.01 (qd, *J* = 6.9, 0.9 Hz, 1H), 4.47 (d, *J* = 5.9 Hz, 1H), 4.38 – 4.32 (m, 1H), 4.00 (d, *J* = 2.3 Hz, 1H), 3.87 (ddd, *J* = 12.4, 2.8, 2.8 Hz), 2.86 – 2.74 (m, 1H), 2.51 – 2.45 (m, 2H), 2.38 (d, *J* = 3.3 Hz, 1H), 2.03 (d, *J* = 12.4 Hz, 2H), 1.89 (ddd, *J* = 14.4, 12.2, 2.8 Hz, 1H), 1.79 (d, *J* = 1.1 Hz, 3H), 1.73 – 1.58 (m, 7H), 1.42 – 1.35 (m, 1H), 1.27 – 1.24 (m, 1H), 0.92 (d, *J* = 6.0 Hz, 3H), 0.91 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 1164.1, 144.7, 139.3, 137.5, 130.6, 130.1, 129.2, 128.4, 128.3, 126.9, 125.8, 125.3, 121.6, 78.6, 74.7, 74.6, 74.3, 70.2, 47.7, 39.6, 30.5, 30.0,

26.7, 20.8, 20.4, 17.9, 17.0, 11.1; MS(FAB/Na) 479 (100), 227 (6), 191 (13), 176 (49), 136 (19); HRMS *m/e* calcd for $C_{28}H_{40}O_5Na$ (M^+ + Na) 479.2773, found 479.2780.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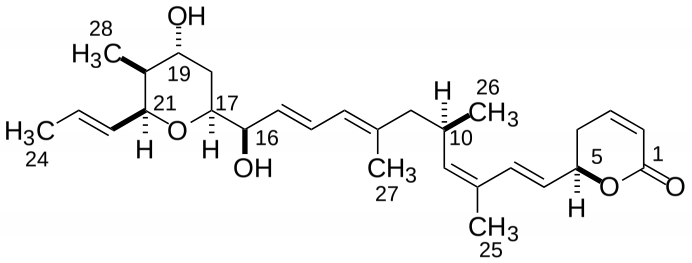
28
H3C
19
21
17
H
26
CH3
H3C
24
O
H
H
16
OH
10
CH3
27
5
1
O
O
H
CH3
25

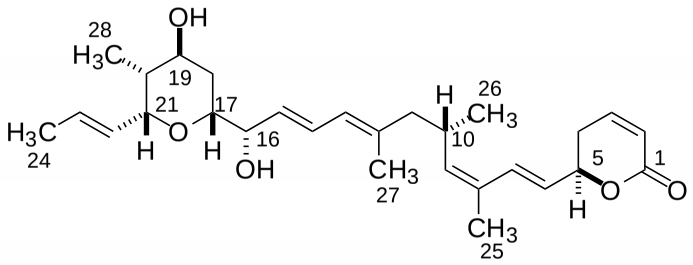
(–)-Ratjadone **(1)**

H27
H25
H26
H28
H24
H18a
H11
H4
H18b
H20
OH
H6 & H23
H7
H3
H2
H13
H15
H9
H5
H21
H19
H14
H22
H16
H17
H10
7
6
5
4
3
2
1
ppm



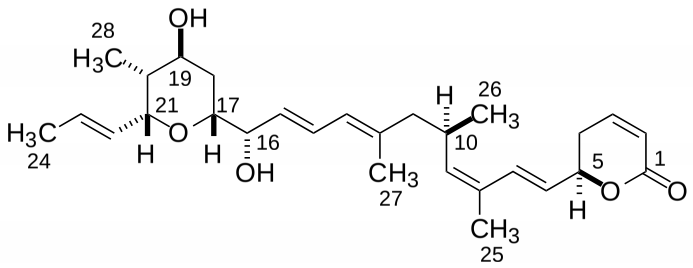
(+)-Ratjadone **((+)-1)**

Partial spectrum of (–)-ratjadone



5*R* diastereomer of (–)-ratjadone **(9)**

Partial spectrum of (–)-ratjadone



5*R*,10*R* diastereomer of (–)-ratjadone **(10)**

Partial spectrum of (–)-ratjadone