Supporting Information 1

Total Synthesis of Methyl Sarcophytoate, a Marine Natural Biscembranoid

Takahiro Ichige, Yusuke Okano, Naoki Kanoh, and Masaya Nakata*

Department of Applied Chemistry, Faculty of Science and Technology, Keio University, 3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223-8522, Japan

Corresponding Author E-mail Address: msynktxa@applc.keio.ac.jp

Experimental Section

General.

The IR spectra were obtained on a NaCl or KBr cell. The ^{1}H NMR spectra were recorded at 300 and 500 MHz, and the ^{13}C NMR spectra were recorded at 75 and 125 MHz at ambient temperature. Chemical shifts of the ^{1}H NMR spectra are expressed in ppm relative to the solvent residual signal 7.26 in $CDCl_3$ or to tetramethylsilane ($\delta = 0.00$). Chemical shifts of the ^{13}C NMR spectra are expressed in ppm relative to the solvent signal 77.16 in $CDCl_3$ unless otherwise noted. The high and low resolution mass spectra were obtained with EI. Analytical thin layer chromatography (TLC) was performed using pre-coated (60F-254) plates (0.25 mm), and visualization was accomplished with ethanolic phosphomolybudic acid. Column chromatography was performed on spherical silica gel (particle size 100 μm). All reactions requiring anhydrous conditions were carried out in oven-dried glassware under an argon atmosphere. Organic solvents were distilled by appropriate procedures and stored under argon atmosphere.

Synthesis of the C1–C3, C14 Segment 7

Oxetane Ester 13. To a suspension of mesaconic acid (**10**) (2.99 g, 23.0 mmol) in dry toluene (30 mL) were added $(COCl)_2$ (4.95 mL, 57.8 mmol) and dry DMF (0.179 mL, 2.31 mmol) at 0 °C. After 3 h at rt, the resulting yellow solution was carefully evaporated at 130 hpa for about 0.5 h to remove excess $(COCl)_2$. The resulting solution of acid chloride in toluene was cooled to 0 °C and to this was added with a cannula a solution of (3-methyloxetan-3-yl)methanol (5.34 mL, 46.2 mmol) and dry pyridine (8.0 mL) in dry toluene (9.0 mL). The resulting dark brown mixture was stirred at rt for 12 h and water (50 mL) was added. The mixture was extracted with EtOAc (50 mL × 3) and the extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (200 g, 4:1 hexane–EtOAc including 1% Et_3N) to afford **13** (6.31 g, 92%) as a pale yellow oil: R_f = 0.34 (1:1 hexane–EtOAc); IR (neat, cm^{-1}) 2960, 2940, 2870, 1720, 1650, 1460, 1390, 1380, 1350, 1255, 1195, 1120, 1035, 980, 945, 835, 775; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (3H, s), 1.38 (3H, s), 2.33 (3H, d, J = 2.0 Hz), 4.28 and 4.31 (each 2H, each s), 4.41 and 4.43 (each 2H, each d, J = 5.0 Hz), 4.54 and 4.56 (each 2H, each d, J = 6.5 Hz), 6.82 (1H, q, J = 1.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.6, 21.2, 21.3, 39.1, 39.3, 69.1, 69.9, 79.5, 79.6, 126.6, 144.1, 165.8, 167.0; MS (EI) *m*/*z* 298 (M^+); HRMS (EI) *m*/*z* calcd for $C_{15}H_{22}O_6$ (M^+) 298.1416, found 298.1414.

Ortho Ester 14. To a solution of **13** (8.00 g, 26.8 mmol) in dry CH_2Cl_2 (268 mL) was added BF_3•OEt_2 (1.70 mL, 13.4 mmol) at 0 °C. After 24 h at rt, the reaction mixture was cooled to 0 °C and dry Et_3N (15.0 mL, 0.107 mol) was added. After 1 h at rt, the resulting orange

mixture was filtered through a column of silica gel (240 g, 1:1 hexane–EtOAc including 1% Et_3N). The filtrate was concentrated under reduced pressure to afford **14** (4.87 g, 61%) as colorless solids: R_f = 0.47 (1:1 hexane–EtOAc); IR (KBr, cm^{-1}) 2960, 2935, 2880, 1475, 1460, 1400, 1360, 1350, 1310, 1195, 1125, 1050, 1040, 995, 980, 925, 885, 850, 760, 740, 690; ^1H NMR (300 MHz, $CDCl_3$) δ 0.79 (6H, s), 1.90 (3H, d, J = 1.5 Hz), 3.91 and 3.92 (each 6H, each s), 5.88 (1H, q, J = 1.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.0, 14.5, 14.7, 30.3, 30.5, 72.7, 72.9, 107.3, 124.7, 139.1; MS (EI) *m*/*z* 298 (M^+); HRMS (EI) *m*/*z* calcd for $C_{15}H_{22}O_6$ (M^+) 298.1416, found 298.1410.

The C1–C3, C14 Segment 7. To a solution of **14** (4.80 g, 16.1 mmol) in dry benzene (96 mL) were added NBS (3.40 g, 19.3 mmol) and BPO (39.0 mg, 0.161 mmol). After 3 h at 70 °C, the resulting orange solution was cooled to rt and Et_3N (2.2 mL) was added. The mixture was diluted with water (100 mL) and the aqueous layer was extracted with EtOAc (100 mL × 3). The extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (304 g, 2:1 hexane–EtOAc including 1% Et_3N) to afford **7** (4.56 g, 75%) as colorless solids: R_f = 0.60 (1:1 hexane–EtOAc); IR (KBr, cm^{-1}) 2965, 2930, 2880, 1470, 1435, 1400, 1350, 1320, 1220, 1190, 1175, 1130, 1100, 1045, 1020, 1000, 980, 900, 760, 740, 690; ^1H NMR (300 MHz, $CDCl_3$) δ 0.81 (6H, br s), 3.94 and 3.95 (each 6H, each s), 4.34 (1H, s), 6.10 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 14.6, 23.8, 30.4, 30.5, 72.8, 73.0, 106.9, 107.2, 130.7, 138.1; MS (EI) *m*/*z* 378 (M^+); HRMS (EI) *m*/*z* calcd for $C_{15}H_{21}O_6Br$ (M^+) 376.0521 and 378.0503, found 376.0524 and 378.0493.

Synthesis of the C10–C13 Segment 8

Aldehyde 15.[18] To a mixture of aminal **11**[18] (4.68 g, 17.2 mmol) and CuI (164 mg, 0.861 mmol) in dry ether (282 mL) was added 2.0 M THF solution of *i*-PrMgCl (17.2 mL, 34.4 mmol) at −78 °C over 15 min. After 4 h at −78 °C, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl (50 mL) and neutralized with saturated aqueous solution of $NaHCO_3$. The mixture was extracted with ether (200 mL × 2) and the combined ethereal solution was hydrolyzed with 2% aqueous solution of HCl (170 mL) at rt for 1 h. The mixture was extracted with EtOAc (200 mL × 3) and the extracts were washed with brine (200 mL), dried over Na_2SO_4, and concentrated under reduced pressure to afford **15**[18] (1.63 g, 60%) as a colorless oil. This product was used in the next reaction without further purification. R_f = 0.50 (1:1 hexane–EtOAc); $[\alpha]_D^{24}$ +119 (*c* 5.01, ether); ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (3H, d, J = 7.0 Hz), 0.99 (3H, d, J = 7.0 Hz), 2.17 (1H, dquint, J = 7.0 Hz, 4.5 Hz), 2.29 (1H, dd, J = 16.5 Hz, 4.0 Hz), 2.69 (1H, dd, J = 16.5 Hz, 9.0 Hz), 2.76–2.86 (1H, m), 3.65 (3H, s), 9.73 (1H, s).

Dithiane 16. To a solution of **15** (2.50 g, 15.8 mmol) in dry CH_2Cl_2 (25 mL) were added 1,3-propanedithiol (2.38 mL, 23.7 mmol) and BF_3•OEt_2 (0.401 mL, 3.16 mmol) at 0 °C. After 2 h at 0 °C, saturated aqueous solution of $NaHCO_3$ (10 mL) and water (10 mL) were added. This mixture was extracted with $CHCl_3$ (15 mL × 3) and the extracts were washed with brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (200 g, 15:1 hexane–EtOAc) to afford **16** (2.94 g, 75%) as a colorless oil: R_f = 0.50 (5:1 hexane–EtOAc); $[\alpha]_D^{25}$ +9.60 (*c* 1.21, $CHCl_3$); IR (neat, cm^{-1}) 2960, 2900, 1740, 1730, 1460, 1435, 1425, 1390, 1370, 1340, 1280, 1255, 1235, 1195, 1165, 1120, 1020, 990, 910, 890, 865, 850, 840, 815, 770, 730; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (3H, d, *J* = 7.0 Hz), 1.00 (3H, d, *J* = 7.0 Hz), 1.76–1.97 (1H, m), 1.97–2.15 (2H, m), 2.28 (1H, q, *J* = 6.4 Hz), 2.36 (1H, dd, *J* = 17.5 Hz, 5.8 Hz), 2.68 (1H, dd, *J* = 17.5 Hz, 5.8 Hz), 2.58–2.98 (4H, m), 3.69 (3H, s), 4.19 (1H, d, *J* = 6.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 21.4, 26.1, 29.6, 30.2, 30.5, 34.0, 45.5, 51.88, 51.94, 174.0; MS (EI) *m*/*z* 248 (M^+); HRMS (EI) *m*/*z* calcd for $C_{11}H_{20}O_2S_2$ (M^+) 248.0905, found 248.0879.

(3*S*)-3-(1,3-Dithian-2-yl)-4-methylpentan-1-ol. To a solution of **16** (2.80 g, 11.3 mmol) in dry THF (38 mL) was added $LiAlH_4$ (514 mg, 13.6 mmol) at 0 °C. After 1 h at 0 °C, saturated aqueous solution of NH_4Cl (10 mL) and water (10 mL) were added and the mixture was extracted with EtOAc (20 mL × 3). The extracts were washed with brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (125 g, 4:1 hexane–EtOAc) to afford the title compound (2.40 g, 96%) as a colorless oil: R_f = 0.20 (3:1 hexane–EtOAc); $[\alpha]_D^{26}$ +13.9 (*c* 1.12, $CHCl_3$); IR (neat, cm^{-1}) 3380, 2960, 2900, 1465, 1420, 1390, 1370, 1280, 1245, 1190, 1050, 910, 870, 760; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (3H, d, *J* = 7.0 Hz), 0.99 (3H, d, *J* = 7.0 Hz), 1.49 (1H, t, *J* = 6.0 Hz), 1.54–2.20 (6H, m), 2.74–3.00 (4H, m), 3.66–3.84 (2H, m), 4.27 (1H, d, *J* = 4.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.5, 21.5, 26.3, 30.0, 30.9, 31.5, 31.8, 46.3, 53.2, 62.5; MS (EI) *m*/*z* 220 (M^+); HRMS (EI) *m*/*z* calcd for $C_{10}H_{20}OS_2$ (M^+) 220.0956, found 220.0966.

The C10–C13 Segment 8. To a solution of the above alcohol (4.30 g, 19.5 mmol) in dry CH_2Cl_2 (49 mL) were added imidazole (1.99 g, 29.3 mmol) and TBSCl (3.53 g, 23.4 mmol) at 0 °C. After 1 h at 0 °C, water (40 mL) was added and the mixture was extracted with $CHCl_3$ (40 mL × 3). The extracts were washed with brine (40 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (196 g, 20:1 hexane–EtOAc) to afford **8** (6.31 g, 97%) as a colorless oil: R_f = 0.67 (5:1 hexane–EtOAc); $[\alpha]_D^{26}$ −1.59 (*c* 1.23, $CHCl_3$); IR (neat, cm^{-1}) 2960, 2930, 2900, 2860, 1475, 1465, 1420, 1390, 1360, 1280, 1255, 1190, 1095, 1005, 940, 920, 910, 840, 810, 780, 680, 660; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.06 (3H, s), 0.07 (3H, s), 0.90 (9H, s), 0.94

(3H, d, J = 7.5 Hz), 0.97 (3H, d, J = 7.5 Hz), 1.52–2.20 (6H, m), 2.76–2.98 (4H, m), 3.58–3.78 (2H, m), 4.23 (1H, d, J = 5.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.12, −5.08, 18.5, 19.5, 21.7, 26.1, 26.5, 29.8, 31.2, 31.7, 46.0, 53.8, 63.0; MS (EI) m/z 334 (M^+); HRMS (EI) m/z calcd for $C_{16}H_{34}OS_2Si$ (M^+) 334.1821, found 334.1848.

Structure Determination of Aldehyde 15

Alcohol 18a. To a solution of 1-pentyne (0.187 mL, 1.90 mmol) in dry CH_2Cl_2 (3.16 mL) was added $Cp_2Zr(H)Cl$ (244 mg, 0.948 mmol) and the mixture was stirred at rt for 10 min to give a clear solution. This was cooled to −65 °C and 1.0 M hexane solution of Me_2Zn (0.948 mL, 0.948 mmol) was added. The mixture was then warmed to 0 °C and a solution of **15** (100 mg, 0.632 mmol) in dry CH_2Cl_2 (0.316 mL) was added. After stirring at rt for 2 h, saturated aqueous solution of NH_4Cl (1.5 mL) was added and the mixture was extracted with hexane (1.5 mL × 3). The extracts were washed with brine (1.5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (6.2 g, 5:1 hexane–EtOAc) to afford a 4:1 inseparable mixture of **17** (102 mg, 82%) [**17** (major): R_f = 0.73 (1:1 hexane–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82–1.04 (9H, m), 1.32–1.82 (3H, m), 1.96–2.64 (5H, m), 4.60 (1H, t, J = 8.0 Hz), 5.45 (1H, dd, J = 15.5 Hz, 8.0 Hz), 5.72-5.88 (1H, m). In addition, there is a signal of the minor diastreomer of **17** at δ 4.94 (1H, t, J = 7.0 Hz)]. To a solution of **17** (10.7 mg, 0.055 mmol, a 4:1 mixture of diastereomers) in dry THF (0.275 mL) was added $LiAlH_4$ (2.5 mg, 0.065 mmol) at 0 °C and the mixture was stirred at 0 °C for 1 h. Saturated aqueous solution of NH_4Cl (0.5 mL) and water (0.5 mL) were added and the mixture was extracted with EtOAc (1.0 mL × 3). The extracts were washed with brine (1.0 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (1.1 g, 1:1 hexane–EtOAc) to afford diol (9.9 mg, 90%) as a 4:1 mixture of diastereomers. To a solution of this diol (9.9 mg, 0.0497 mmol, a 4:1 mixture of diastereomers) and imidazole (5.1 mg, 0.075 mmol) in dry CH_2Cl_2 (0.250 mL) was added TBSCl (9.0 mg, 0.060 mmol) at 0 °C, and the mixture was stirred at 0 °C for 1 h. Water (1.0 mL) was added and the organic layer was separated. The aqueous layer was extracted with hexane (1.0 mL × 3) and the combined organic layers were washed with brine (1.0 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (6.2 g, 15:1 hexane–EtOAc) to afford the major diastereomer **18a** (8.0 mg, 51%) and its minor diasteromer **18b** (3.6 mg, contaminated with a small amount of **18a**). **18a**: R_f = 0.41 (10:1 hexane–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.09 (6H, s), 0.77 (3H, d, J = 6.5 Hz), 0.84–0.96 (6H, m), 0.91 (9H, s), 1.20–1.48 (3H, m), 1.50–1.76 (2H, m), 1.78–1.92 (1H, m), 1.94–2.12 (2H, m), 3.54 (1H, dt, J = 4.5 Hz, 9.5 Hz), 3.74–3.84 (1H, m), 3.80 (1H, d, J = 4.5 Hz), 3.86–3.96 (1H, m), 5.42 (1H, dd, J = 15.5 Hz, 7.0 Hz), 5.62 (1H, dt, J = 15.5 Hz, 6.5

Hz).

(*S*)-MTPA Ester 19a and (*R*)-MTPA Ester 19b. To a stirred solution of **18a** (4.0 mg, 0.0128 mmol), Et_3N (0.0089 mL, 0.064 mmol), and DMAP (1.6 mg, 0.0128 mmol) in dry CH_2Cl_2 (0.128 mL) was added (*R*)-(−)-MTPACl (0.0029 mL, 0.0154 mmol) at 0 °C. After 2 h at rt, the reaction mixture was diluted with hexane (1.0 mL) and this was washed with water (0.5 mL × 3) and brine (0.5 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to afford the crude (*S*)-MTPA ester **19a** (quantitative yield). (*R*)-MTPA ester **19b** was prepared in the same way by using (*S*)-(+)-MTPACl (quantitative yield). **19a**: R_f = 0.69 (5:1 hexane–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.01 (3H, s), −0.003 (3H, s), 0.81 (6H, br d, *J* = 7.0 Hz), 0.86 (9H, s), 0.88 (3H, t, *J* = 7.0 Hz), 1.30–1.76 (4H, m), 1.39 (2H, m), 2.03 (2H, br q, *J* = 7.0 Hz), 3.37 (2H, t, *J* = 6.0 Hz), 3.55 (3H, s), 5.38–5.56 (2H, m), 5.83 (1H, dt, *J* = 14.0 Hz, 6.5 Hz), 7.30–7.56 (5H, m). **19b**: R_f = 0.69 (5:1 hexane–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.002 (6H, br s), 0.82–0.92 (9H, m), 0.86 (9H, s), 1.14–1.82 (4H, m), 1.38 (2H, m), 1.99 (2H, br q, *J* = 7.0 Hz), 3.50 (3H, s), 3.54 (2H, m), 5.31 (1H, dd, *J* = 15.0 Hz, 8.0 Hz), 5.46 (1H, dd, *J* = 8.0 Hz, 5.0 Hz), 5.73 (1H, dt, *J* = 15.0 Hz, 8.0 Hz), 7.30–7.56 (5H, m). The Δδ ($\delta_S - \delta_R$) values are shown in Scheme 6.

γ-Lactones 20a[21] **and 20b.**[22] A solution of **17** (18.0 mg, 0.0917 mmol, a 4:1 mixture of diastereomers) in dry MeOH (3.1 mL) was cooled to −78 °C, and O_3/O_2 gas was bubbled into this solution for ca. 20 min. Me_2S (0.0680 mL, 0.920 mmol) was added and this was warmed to 0 °C over 2 h. To this was added $NaBH_4$ (7.0 mg, 0.184 mmol) and the mixture was stirred at 0 °C for 1 h. The reaction was quenched with saturated aqueous solution of NH_4Cl (3.0 mL) at 0 °C. This was diluted with water (3.0 mL), and the mixture was extracted with ether (3.0 mL × 3). The extracts were washed with brine (3.0 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (2 g, 1:1 hexane–EtOAc) to afford **20a**[21] (8.0 mg, 55%) as a colorless syrup and **20b**[22] (2.1 mg, 14%) as colorless solids. **20a**:[21] R_f = 0.36 (1:1 hexane–EtOAc); $[\alpha]_D^{28}$ −40.5 (*c* 1.67, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (3H, d, *J* = 7.0 Hz), 0.95 (3H, d, *J* = 7.0 Hz), 1.74 (1H, octet, *J* = 8.5 Hz), 2.18–2.50 (2H, m), 2.34 (1H, dd, *J* = 17.5 Hz, 7.0 Hz), 2.70 (1H, dd, *J* = 17.5 Hz, 9.0 Hz), 3.63 (1H, br d, *J* = 12.5 Hz), 3.92 (1H, br d, *J* = 12.5 Hz), 4.37 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.5, 20.2, 31.1, 32.7, 42.2, 64.5, 84.2, 177.2. **20b**:[22] R_f = 0.44 (1:1 hexane–EtOAc); $[\alpha]_D^{25}$ +19.8 (*c* 0.48, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (3H, d, *J* = 6.5 Hz), 0.99 (3H, d, *J* = 6.5 Hz), 1.76–1.94 (1H, m), 2.10 (1H, t, *J* = 6.0 Hz), 2.24–2.58 (3H, m), 3.76–4.01 (2H, m), 4.59 (1H, ddd, *J* = 7.5 Hz, 4.5 Hz, 3.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 22.0, 28.2, 33.7, 46.1, 61.8, 82.3, 177.6.

Synthesis of the C4–C8 Segment 6

Vinyl Iodide 21. To a slurry of Cp_2ZrCl_2 (0.868 mg, 2.97 mmol) in 1,2-dichloroethane (14.9 mL) was added 2.0 M toluene solution of Me_3Al (8.91 mL, 17.8 mmol) at rt. After stirring for 10 min at rt, 4-pentyn-1-ol (**12**) (500 mg, 5.94 mmol) was slowly added to the above mixture at 0 °C. After 24 h at rt, the reaction mixture was cooled to 0 °C and treated with a solution of I_2 (1.81 g, 7.13 mmol) in dry THF (8.91 mL). After 0.5 h at 0 °C, water (20 mL) was slowly added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with EtOAc (20 mL × 3). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (67 g, 1:1 hexane–EtOAc) to afford **21** (1.21 g, 90%) as a colorless oil: R_f = 0.44 (1:1 hexane–EtOAc); IR (neat, cm^{-1}) 3330, 3060, 2940, 2880, 1615, 1450, 1435, 1375, 1350, 1285, 1270, 1170, 1140, 1060, 1020, 1000, 920, 830, 770, 730, 665; ^1H NMR (300 MHz, $CDCl_3$) δ 1.20 (1H, t, J = 5.0 Hz), 1.64–1.78 (2H, m), 1.85 (3H, d, J = 1.0 Hz), 2.31 (2H, t, J = 7.0 Hz), 3.65 (2H, q, J = 5.0 Hz), 5.93 (1H, q, J = 1.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.9, 30.6, 35.9, 62.1, 75.1, 147.6; MS (EI) m/z 226 (M^+); HRMS (EI) m/z calcd for $C_6H_{11}OI$ (M^+) 225.9855, found 225.9831.

Vinyl Stannane 22. To a solution of **21** (1.10 g, 4.87 mmol) in dry ether (22 mL) was added 1.57 M hexane solution of *n*-BuLi (7.45 mL, 11.7 mmol) at −78 °C and the reaction mixture was stirred at −78 °C for 6 h. To this slurry was added Bu_3SnCl (3.40 mL, 11.7 mmol) and the mixture was allowed to warm to rt over 1.5 h. Water (25 mL) was added and the mixture was extracted with EtOAc (25 mL × 3). The extracts were washed with brine (25 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (57 g, 10:1 hexane–EtOAc including 1% Et_3N) to afford **22** (1.37 g, 72%) as a colorless oil: R_f = 0.59 (3:1 hexane–EtOAc); IR (neat, cm^{-1}) 3330, 2960, 2930, 2870, 2850, 1605, 1465, 1455, 1420, 1380, 1340, 1290, 1260, 1250, 1180, 1150, 1130, 1070, 1050, 1020, 960, 920, 875, 865, 840, 795, 770, 740; ^1H NMR (300 MHz, $CDCl_3$) δ 0.75–1.03 (15H, m), 1.20–1.56 (12H, m), 1.66–1.82 (2H, m), 1.78 (3H, s), 2.22 (2H, t, J = 8.0 Hz), 3.58–3.74 (2H, m), 5.01 (1H, t, $J_{H–Sn}$ = 36.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2, 13.8, 24.6, 27.4, 29.4, 31.1, 38.5, 63.0, 122.4, 154.7; MS (EI) m/z 333 [(M−*n*-Bu)$^+$]; HRMS (EI) m/z calcd for $C_{14}H_{29}OSn$ [(M−*n*-Bu)$^+$] 333.1240, found 333.1226.

The C4–C8 Segment 6. To a solution of **22** (586 mg, 1.51 mmol) in dry CH_2Cl_2 (30.2 mL) were added MS4A powder (290 mg), NMO (531 mg, 4.53 mmol), and TPAP (26.5 mg, 0.0753 mmol). The resulting mixture was stirred at rt for 30 min and filtered through a short column of silica gel (50 g, 10:1 hexane–EtOAc including 1% Et_3N). The filtrate was concentrated under reduced pressure to afford aldehyde (472 mg, 81%) [R_f = 0.62 (10:1 hexane–EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ 0.75–1.03 (15H, m), 1.15–1.60 (12H, m),

1.78 (3H, t, J = 4.0 Hz), 2.35–2.67 (4H, m), 5.47 (1H, t, $J_{H–Sn}$ = 30.0 Hz), 9.77 (1H, s)]. To a suspension of methyl triphenylphosphonium bromide (386 mg, 1.08 mmol) in dry THF (1.05 mL) was added 1.57 M hexane solution of *n*-BuLi (0.758 mL, 1.19 mmol) at rt. After 10 min at rt, the resulting red solution was cooled to −30 °C and a solution of the above aldehyde (210 mg, 0.542 mmol) in dry THF (1.05 mL) was added. The reaction mixture was allowed to warm to 0 °C over 1.5 h and water (2.0 mL) was added. The mixture was extracted with hexane (2.0 mL × 3) and the extracts were washed with brine (2.0 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (15 g, 100:1 hexane–Et_3N) to afford **6** (190 mg, 91%) as a colorless oil: R_f = 0.93 (10:1 hexane–EtOAc); IR (neat, cm^{-1}) 3080, 2960, 2920, 2870, 2850, 1640, 1605, 1465, 1460, 1420, 1375, 1340, 1290, 1250, 1180, 1150, 1130, 1070, 1045, 1020, 990, 960, 910, 875, 865, 845, 805, 770; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.75–1.03 (15H, m), 1.20–1.60 (12H, m), 1.76 (3H, t, J = 5.0 Hz), 2.14–2.28 (4H, m), 4.94 (1H, dd, J = 10.0 Hz, 2.0 Hz), 5.01 (1H, d, J = 17.0 Hz), 5.46 (1H, t, J = 35.0 Hz), 5.70–5.94 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2, 13.9, 24.7, 27.5, 29.4, 32.7, 41.5, 114.5, 122.0, 138.8, 154.4; MS (EI) *m*/*z* 329 [(M−*n*-Bu)$^+$]; HRMS (EI) *m*/*z* calcd for $C_{15}H_{29}Sn$ [(M−*n*-Bu)$^+$] 329.1291, found 329.1273.

Transformation of 23 into Carboxylic Acid 27

Methyl Ester 24. To a solution of **23** (170 mg, 0.269 mmol) in MeOH (1.7 mL) was added 1.5 mM aqueous solution of H_2SO_4 (3.4 mL) and the resulting mixture was stirred at rt for 3 h. This was neutralized with saturated aqueous solution of $NaHCO_3$ and the mixture was extracted with EtOAc (3.0 mL × 3). The extracts were washed with brine (3.0 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (7.5 g, 10:1 $CHCl_3$–MeOH) to afford diester (144 mg, 97%) as colorless solids [R_f = 0.15 (10:1 $CHCl_3$–MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 and 0.91 (each 3H, each s), 1.00 (3H, d, J = 7.0 Hz), 1.04 (3H, d, J = 7.0 Hz), 1.64–2.24 (4H, m), 2.50–3.02 (8H, m), 3.43 (2H, s), 3.52–3.88 (10H, m), 4.28 and 4.39 (each 1H, each d, J = 12.0 Hz), 4.31 and 4.40 (each 1H, each d, J = 12.0 Hz), 6.83 (1H, s)]. To a mixture of the above diester (970 mg, 1.75 mmol) in MeOH (9.7 mL) and H_2O (9.7 mL) was added LiOH (462 mg, 19.3 mmol). After 30 h at rt, the reaction mixture was acidified with 1 M aqueous solution of HCl and this was extracted with EtOAc (15 mL × 3). The extracts were washed with brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure to afford crude dicarboxylic acid. This crude acid was dissolved in MeOH (2.5 mL) and ethereal solution of CH_2N_2 was added until all the starting material disappeared (monitored by TLC). The resulting yellow solution was concentrated under reduced pressure and the residue was purified with silica-gel column chromatography (33 g, 1:1 hexane–EtOAc) to afford **24** (575 mg, 87%) as a yellow syrup: R_f = 0.39 (1:1 hexane–EtOAc); $[\alpha]_D^{25}$ +11.6 (*c* 1.20, $CHCl_3$); IR

(neat, cm^{-1}) 3420, 2950, 2910, 2870, 1730, 1715, 1645, 1435, 1370, 1285, 1230, 1205, 1100, 1050, 1030, 910, 850, 785, 760; ^1H NMR (300 MHz, $CDCl_3$) δ 1.02 (3H, d, J = 7.0 Hz), 1.05 (3H, d, J = 7.0 Hz), 1.62–3.12 (10H, m), 3.35 (1H, d, J = 14.0 Hz), 3.45 (1H, d, J = 14.0 Hz), 3.60–3.94 (2H, m), 3.78 (3H, s), 3.83 (3H, s), 6.79 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 23.9, 25.8, 26.4, 26.5, 28.3, 29.7, 32.1, 44.5, 52.0, 52.9, 61.5, 63.6, 128.5, 144.2, 166.5, 168.7; MS (EI) m/z 376 (M^+); HRMS (EI) m/z calcd for $C_{17}H_{28}O_5S_2$ (M^+) 376.1378, found 376.1364.

Aldehyde 25. To a solution of **24** (109 mg, 0.289 mmol) in dry DMSO (0.576 mL) and dry THF (1.92 mL) was added IBX (242 mg, 0.864 mmol) at 0 °C. The resulting mixture was shielded from the light and stirred at rt for 2 h. The reaction was quenched with 1:1 solution of saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$ (1.5 mL) at 0 °C. The mixture was extracted with EtOAc (2.0 mL × 3) and the extracts were washed with brine (1.5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (5.39 g, 1:1 hexane–EtOAc) to afford **25** (105 mg, 97%) as a yellow syrup: R_f = 0.70 (1:1 hexane–EtOAc); $[\alpha]_D^{29}$ +8.36 (*c* 1.60, $CHCl_3$); IR (neat, cm^{-1}) 2950, 2910, 2840, 1720, 1650, 1435, 1390, 1370, 1290, 1260, 1230, 1200, 1180, 1100, 1025, 910, 780, 760; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (3H, d, J = 7.0 Hz), 1.00 (3H, d, J = 7.0 Hz), 1.65–1.80 (1H, m), 1.86–2.00 (1H, m), 2.26–2.60 (4H, m), 2.69 (1H, ddd, J = 3.0 Hz, 12.0 Hz, 15.0 Hz), 2.84–3.04 (3H, m), 3.36 (1H, d, J = 14.5 Hz), 3.42 (1H, d, J = 14.5 Hz), 3.79 and 3.83 (each 3H, each s), 6.81 (1H, s), 9.90 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.5, 23.6, 25.2, 26.3, 26.4, 27.9, 31.8, 40.3, 45.4, 52.1, 52.9, 59.5, 128.7, 143.7, 166.5, 168.5, 199.8; MS (EI) m/z 374 (M^+); HRMS (EI) m/z calcd for $C_{17}H_{26}O_5S_2$ (M^+) 374.1222, found 374.1216.

Ketone 26. To a solution of **25** (292 mg, 0.780 mmol) in dry ether (5.8 mL) was added 1.0 M THF solution of isopropenyl magnesium bromide (1.56 mL, 1.56 mmol) at −40 °C. After 0.5 h at −40 °C, saturated aqueous solution of NH_4Cl (3.0 mL) and water (3.0 mL) were added and the mixture was allowed to warm to rt. This was extracted with EtOAc (3.0 mL × 3) and the extracts were washed with brine (3.0 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (26 g, 2:1 hexane–EtOAc) to afford allyl alcohol (241 mg, 74%) as a 2:1 mixture of diastereomers [the major diastereomer: R_f = 0.57 (1:1 hexane–EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ 1.04 (3H, d, J = 7.0 Hz), 1.09 (3H, d, J = 7.0 Hz), 1.50–1.94 (2H, m), 1.83 (3H, s), 2.14–2.96 (10H, m), 3.30 (1H, d, J = 14.0 Hz), 3.43 (1H, d, J = 14.0 Hz), 3.78 (3H, s), 3.83 (3H, s), 4.32–4.43 (1H, m), 4.92 (1H, br s), 5.00 (1H, s), 6.80 (1H, s). In addition, there are two signals of the minor diastreomer at δ 1.13 (3H, d, J = 7.0 Hz) and 4.83 (1H, br s)]. To a solution of the above diastereomers (260 mg, 0.624 mmol) in dry DMSO (1.25 mL) and dry THF (4.16 mL) was

added IBX (524 mg, 1.87 mmol). The mixture was shielded from light and stirred at rt for 5 h. A 1:1 solution of saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$ (1.0 mL) was added at 0 °C and the mixture was diluted with water (3.0 mL). This was extracted with EtOAc (3.0 mL × 3) and the extracts were washed with brine (3.0 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (20.6 g, 3:1 hexane–EtOAc) to afford **26** (217 mg, 84%) as a yellow syrup: R_f = 0.69 (1:1 hexane–EtOAc); $[\alpha]_D^{25}$ +29.6 (*c* 1.03, $CHCl_3$); IR (neat, cm^{-1}) 2950, 1730, 1720, 1675, 1435, 1370, 1290, 1235, 1200, 1180, 1100, 1030, 930, 910, 875, 850, 760; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (3H, d, *J* = 7.0 Hz), 0.96 (3H, d, *J* = 7.0 Hz), 1.65–1.80 (1H, m), 1.84–1.98 (1H, m), 1.91 (3H, q, *J* = 1.0 Hz), 2.30–2.44 (1H, m), 2.48–2.68 (3H, m), 2.91 (1H, ddd, *J* = 15.0 Hz, 13.0 Hz, 3.0 Hz), 2.99 (1H, ddd, *J* = 15.0 Hz, 13.0 Hz, 3.0 Hz), 3.15 (1H, dt, *J* = 2.0 Hz, 6.0 Hz), 3.28 (1H, dd, *J* = 17.0 Hz, 6.0 Hz), 3.40 (2H, s), 3.77 (3H, s), 3.83 (3H, s), 5.76 (1H, br s), 6.13 (1H, s), 6.79 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.4, 19.5, 23.9, 25.1, 26.5, 26.7, 28.0, 32.2, 34.2, 44.2, 52.0, 52.8, 60.4, 124.0, 128.5, 143.9, 144.8, 166.5, 168.5, 200.8; MS (EI) *m*/*z* 414 (M^+); HRMS (EI) *m*/*z* calcd for $C_{20}H_{30}O_5S_2$ (M^+) 414.1535, found 414.1546.

Carboxylic Acid 27. To a solution of **26** (100 mg, 0.241 mmol) in THF (2.0 mL) was added a solution of LiOH (11.6 mg, 0.482 mmol) in water (1.0 mL). After 2 h at rt, the reaction mixture was extracted with hexane (2.0 mL). The aqueous layer was acidified to pH 3 using 1 M aqueous solution of HCl and this was extracted with EtOAc (2.0 mL × 3). The extracts were washed with brine (2.0 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (6.9 g, 1:1 hexane–EtOAc) to afford **27** (76.2 mg, 78%) as a yellow syrup: R_f = 0.22–0.56 (1:2 hexane–EtOAc); $[\alpha]_D^{24}$ +20.0 (*c* 2.60, $CHCl_3$); IR (neat, cm^{-1}) 3200, 2955, 1720, 1700, 1670, 1645, 1435, 1370, 1285, 1230, 1170, 1095, 930, 910; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (3H, d, *J* = 7.0 Hz), 0.96 (3H, d, *J* = 7.0 Hz), 1.60–1.78 (1H, m), 1.82–2.00 (4H, m), 2.36–2.42 (1H, m), 2.42–2.80 (3H, m), 2.82–3.08 (2H, m), 3.10–3.19 (1H, m), 3.25 (1H, dd, *J* = 16.0 Hz, 6.0 Hz), 3.37 (1H, d, *J* = 14.0 Hz), 3.44 (1H, d, *J* = 14.0 Hz), 3.84 (3H, s), 5.75 (1H, br s), 6.08 (1H, br s), 6.81 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.4, 19.6, 23.8, 25.1, 26.5, 26.8, 28.0, 32.4, 34.2, 44.4, 53.0, 60.3, 124.0, 127.6, 144.8, 146.3, 168.3, 170.8, 200.7; MS (EI) *m*/*z* 400 (M^+); HRMS (EI) *m*/*z* calcd for $C_{19}H_{28}O_5S_2$ (M^+) 400.1378, found 400.1387.

Entry 2 in Table 2

Decarbonylative Product 28. To a solution of **27** (4.7 mg, 0.0116 mmol) in dry THF (0.094 mL) was added 1.57 M hexane solution of *n*-BuLi (0.0074 mL, 0.0116 mmol) at −78 °C. After 5 min at −78 °C, the solution was warmed to 0 °C and oxalyl chloride (0.0031 mL,

0.0348 mmol) was added. After 0.5 h at rt, solvents and excess oxalyl chloride were carefully evaporated under reduced pressure to afford the crude acid chloride **5**. To a solution of this crude **5** in dry THF (0.094 mL) were added a solution of **6** (12.2 mg, 0.0348 mmol) in dry THF (0.047 mL) and $Pd(PPh_3)_4$ (1.34 mg, 0.00116 mmol). The solution was degassed with CO gas and then stirred at 50 °C for 16 h under CO atmosphere. Saturated aqueous solution of $NaHCO_3$ (0.1 mL) and water (1.0 mL) were added and the mixture was extracted with EtOAc (1.0 mL × 3). The extracts were washed with brine (1.0 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (1.0 g, 10:1 hexane–EtOAc including 1% Et_3N) to afford **28** (1.4 mg, 27%) as a yellow syrup: R_f = 0.53 (2:1 hexane–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (3H, d, J = 7.0 Hz), 1.00 (3H, d, J = 7.0 Hz), 1.66–1.80 (1H, m), 1.84–1.98 (7H, m), 2.20–2.40 (5H, m), 2.46–2.72 (2H, m), 2.62 (1H, dd, J = 16.5 Hz, 5.0 Hz), 2.83 (2H, s), 2.85–3.08 (2H, m), 3.12–3.22 (1H, m), 3.30 (1H, dd, J = 16.5 Hz, 6.0 Hz), 3.78 (3H, s), 4.97 (1H, dd, J = 10.5 Hz, 2.0 Hz), 5.05 (1H, br d, J = 17.0 Hz), 5.75 (1H, br s), 5.72–5.92 (1H, m), 6.08 (1H, s), 6.26 (1H, br d, J = 12.5 Hz), 7.59 (1H, d, J = 12.5 Hz); MS (EI) m/z 450 (M^+); HRMS (EI) m/z calcd for $C_{25}H_{38}O_3S_2$ (M^+) 450.2263, found 450.2264.

Synthesis of Aldehyde 36

Allyl Alcohol 42.[36] To a stirred solution of geraniol (**41**) (30.0 g, 0.195 mol) in dry DMF (648 mL) were added NaH (7.47 g, 0.311 mol) and PMBCl (34.3 mL, 0.253 mol) at 0 °C. After 5 h at 0 °C, saturated aqueous solution of NH_4Cl (100 mL) and water (500 mL) were added and the mixture was extracted with 1:1 hexane–EtOAc (500 mL × 3). The extracts were washed with brine (300 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (65 mL) and to this solution were added SeO_2 (648 mg, 5.84 mmol), 70% aqueous TBHP (93.3 mL, 0.681 mol), and salicylic acid (2.69 g, 19.5 mmol). After 4 days at rt, SeO_2 (648 mg, 5.84 mmol) was added and the mixture was stirred for another 3 days. $CHCl_3$ (100 mL) and water (100 mL) were added to the reaction mixture and the separated organic layer was washed with water (100 mL × 3). To this organic layer was added saturated aqueous solution of $Na_2S_2O_3$ (200 mL) and the mixture was stirred at rt for 1 h. Organic layer was separated and the aqueous layer was extracted with EtOAc (200 ml × 3). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (1.94 kg, 2:1 hexane–EtOAc) to afford **42**[36] (23.0 g, 41%) as a pale yellow oil: R_f = 0.18 (5:1 hexane–EtOAc); IR (neat, cm^{-1}) 3410, 2910, 2860, 1615, 1575, 1515, 1460, 1360, 1300, 1250, 1175, 1070, 1040, 820, 760; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.64 (3H, s), 1.65 (3H, s), 2.01–2.23 (4H, m), 3.80 (3H, s), 3.96 (2H, s), 3.99 (2H, d, J = 7.0 Hz), 4.43 (2H, s), 5.33–5.42 (2H, m), 6.87 (2H, d, J = 9.0 Hz), 7.27 (2H, d, J = 9.0 Hz); ^{13}C NMR (75 MHz,

$CDCl_3$) δ 13.8, 16.5, 25.8, 39.2, 55.3, 66.3, 68.8, 71.8, 113.8, 121.2, 125.5, 129.5, 130.6, 135.2, 139.9, 159.2; MS (EI) *m*/*z* 290 (M^+); HRMS (EI) *m*/*z* calcd for $C_{18}H_{26}O_3$ (M^+) 290.1882, found 290.1862.

Epoxy Alcohol 43. To a mixture of L-(+)-DET (1.97 g, 9.56 mmol) and MS4A powder (18.5 g) in dry CH_2Cl_2 (212 mL) was added (*i*-PrO)$_4$Ti (1.89 mL, 6.37 mmol) at 0 °C and the resulting mixture was stirred at 0 °C for 0.5 h. This was cooled to −30 °C and a 4.89 M CH_2Cl_2 solution of TBHP (39.1 mL, 0.191 mol) was added. After 0.5 h at −30 °C, a solution of **42** (18.5 g, 63.7 mmol) in dry CH_2Cl_2 (106 mL) was added and the resulting mixture was stirred at −30 °C for 3 h. The reaction mixture was passed through a pad of celite and 30% aqueous soloution of NaOH saturated with NaCl (20 mL) was added to the filtrate. After 20 min at rt, water (300 mL) was added and the mixture was extracted with $CHCl_3$ (300 ml × 3). The extracts were washed with brine (300 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (975 g, 1:1 hexane–EtOAc) to afford **43** (14.5 g, 75%) as a colorless oil: R_f = 0.21 (2:1 hexane–EtOAc); $[\alpha]_D^{28}$ −3.29 (*c* 1.94, $CHCl_3$); IR (neat, cm^{-1}) 3430, 3000, 2930, 2860, 1615, 1585, 1515, 1460, 1385, 1300, 1250, 1175, 1070, 1040, 820, 760; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (3H, s), 1.62–1.82 (2H, m), 1.66 (3H, s), 2.08–2.30 (3H, m), 3.01 (1H, t, *J* = 6.0 Hz), 3.56 (1H, dd, *J* = 12.0 Hz, 8.0 Hz), 3.63 (1H, dd, *J* = 12.0 Hz, 5.0 Hz), 3.80 (3H, s), 3.99 (2H, d, *J* = 7.0 Hz), 4.44 (2H, s), 5.43 (1H, tq, *J* = 7.0 Hz, 1.0 Hz), 6.88 (2H, d, *J* = 8.5 Hz), 7.27 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 16.6, 26.4, 36.2, 55.4, 60.1, 61.1, 65.7, 66.2, 72.0, 113.8, 121.7, 129.6, 130.5, 139.2, 159.2; MS (EI) *m*/*z* 306 (M^+); HRMS (EI) *m*/*z* calcd for $C_{18}H_{26}O_4$ (M^+) 306.1831, found 306.1832. Enantiomeric excess was determined to be 94% ee by comparing the ^{1}H NMR of (*S*)-MTPA and (*R*)-MTPA esters of **43** which were easily synthesized using the already described method.

Epoxy Iodide 44. To a stirred solution of **43** (13.5 g, 44.1 mmol), PPh_3 (23.1 g, 88.2 mmol), and imidazole (12.0 g, 0.176 mol) in dry CH_2Cl_2 (221 mL) was added I_2 (22.4 g, 88.2 mmol) at 0 °C. The resulting mixture was shielded from light and stirred at 0 °C for 3 h. Saturated aqueous solution of $Na_2S_2O_3$ (40 mL), saturated aqueous solution of $NaHCO_3$ (40 mL), and water (200 mL) were added and the organic layer was separated. The aqueous layer was extracted with EtOAc (200 mL × 3) and the combined organic layers were washed with brine (200 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (920 g, 5:1 hexane–EtOAc) to afford **44** (14.5 g, 79%) as a pale yellow syrup: R_f = 0.73 (1:1 hexane–EtOAc); $[\alpha]_D^{27}$ +8.59 (*c* 2.32, $CHCl_3$); IR (neat, cm^{-1}) 3000, 2960, 2940, 2850, 1615, 1585, 1515, 1460, 1385, 1300, 1250, 1175, 1120, 1080, 1070, 1040, 820; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (3H, s), 1.60–1.78 (2H, m), 1.66 (3H, s), 2.08–2.30 (2H, m), 2.87 (1H, t, *J* = 6.0 Hz), 3.08 (1H, d, *J* = 10.0 Hz), 3.21 (1H,

d, J = 10.0 Hz), 3.80 (3H, s), 4.00 (2H, d, J = 7.0 Hz), 4.44 (2H, s), 5.44 (1H, tq, J = 7.0 Hz, 1.0 Hz), 6.88 (2H, d, J = 9.0 Hz), 7.27 (2H, d, J = 9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 16.2, 16.6, 27.4, 36.1, 55.4, 60.2, 66.2, 66.3, 72.0, 113.9, 121.9, 129.5, 130.6, 138.9, 159.2; MS (EI) m/z 416 (M^+); HRMS (EI) m/z calcd for $C_{18}H_{25}O_3I$ (M^+) 416.0849, found 416.0841.

Ester 45. To a solution of **39b** (6.50 g, 22.4 mmol) in dry CH_2Cl_2 (75 mL) were added vinylacetic acid (**40**) (2.87 mL, 33.8 mmol), DMAP (825 mg, 6.75 mmol), and DCC (6.91 g, 33.8 mmol) at 0 °C. After 1.5 h at 0 °C, EtOAc (200 mL) was added and the mixture was filtered through a pad of celite. Water (200 ml) was added to the filtrate and this mixture was extracted with EtOAc (200 ml × 3). The extracts were washed with brine (100 ml), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (400 g, 8:1 hexane–EtOAc) to afford **45** (7.78 g, 97%) as a colorless oil: R_f = 0.67 (2:1 hexane–EtOAc); $[\alpha]_D^{27}$ −6.25 (c 1.93, $CHCl_3$); IR (neat, cm^{-1}) 3080, 2940, 2860, 1740, 1615, 1585, 1515, 1440, 1300, 1250, 1175, 1075, 1040, 995, 920, 820, 760; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.64 (3H, s), 1.71 (3H, s), 1.68–1.88 (2H, m), 1.90–2.12 (2H, m), 3.10 (2H, dt, J = 7.0 Hz, 1.5 Hz), 3.80 (3H, s), 3.90 (2H, d, J = 7.0 Hz), 4.43 (2H, s), 4.89 (1H, br s), 4.49 (1H, br s), 5.10–5.22 (3H, m), 5.38 (1H, tq, J = 7.0 Hz, 1.0 Hz), 5.93 (1H, ddt, J = 17.0 Hz, 10.0 Hz, 7.0 Hz), 6.87 (2H, d, J = 8.5 Hz), 7.27 (2H, d, J = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.7, 18.2, 30.7, 35.2, 39.5, 55.4, 66.3, 71.9, 77.3, 113.1, 113.8, 118.7, 121.5, 129.6, 130.4, 130.7, 139.3, 142.9, 159.2, 170.8; MS (EI) m/z 358 (M^+); HRMS (EI) m/z calcd for $C_{22}H_{30}O_4$ (M^+) 358.2144, found 358.2169.

δ-Lactone 37. To a solution of **45** (207 mg, 0.578 mmol) in dry CH_2Cl_2 (115 mL) was added Grubbs second generation catalyst **29** (2.45 mg, 0.00289 mmol). The resulting purple solution was refluxed for 1.5 h and additional Grubbs second generation catalyst **29** (9.8 mg, 0.0116 mmol) was added. After refluxing for 4 h, the resulting light brown solution was cooled to rt. The solvent was removed under reduced pressure and the residue was purified with silica-gel column chromatography (9.6 g, 3:1 hexane–EtOAc) to afford **37** (141 mg, 74%) as a yellow oil: R_f = 0.25 (2:1 hexane–EtOAc); $[\alpha]_D^{27}$ +36.9 (c 1.87, $CHCl_3$); IR (neat, cm^{-1}) 2940, 2860, 1740, 1615, 1585, 1515, 1440, 1390, 1360, 1300, 1250, 1215, 1180, 1070, 1040, 930, 820, 755; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.62 (3H, s), 1.65–1.79 (1H, m), 1.71 (3H, d, J = 2.0 Hz), 1.88–2.28 (3H, m), 2.95–3.04 (2H, m), 3.77 (3H, s), 3.97 (2H, d, J = 7.0 Hz), 4.41 (2H, s), 4.76 (1H, dd, J = 7.5 Hz, 3.0 Hz), 5.39 (1H, tq, J = 7.0 Hz, 1.0 Hz), 5.48 (1H, br s), 6.85 (2H, d, J = 9.0 Hz), 7.24 (2H, d, J = 9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.7, 18.8, 29.9, 32.0, 33.8, 55.3, 66.2, 71.9, 82.6, 113.7, 116.6, 121.7, 129.4, 130.5, 132.7, 138.8, 159.1, 169.4; MS (EI) m/z 330 (M^+); HRMS (EI) m/z calcd for $C_{20}H_{26}O_4$ (M^+) 330.1831, found 330.1845.

Allyl Alcohol 46. To a −78 °C solution of **37** (1.37 g, 4.15 mmol) in dry CH_2Cl_2 (20.8 mL)

was added 1.0 M toluene solution of DIBAL (6.2 mL, 6.22 mmol). After 1 h at −78 °C, 10% aqueous solution of potassium sodium tartrate (8 mL) was added and the mixture was gradually warmed to rt. After 3 h at rt, water (30 mL) was added and the mixture was extracted with $CHCl_3$ (30 mL × 3). The extracts were washed with brine (30 ml), dried over Na_2SO_4, and concentrated under reduced pressure to afford the crude lactol. This was dissolved in dry toluene (20.8 mL) and Wittig reagent **38** (4.50 g, 12.5 mmol) was added. After 3 h at 80 °C, the mixture was cooled to rt and the solvent was removed under reduced pressure. The residue was purified with silica-gel column chromatography (69 g, 2:1 hexane–EtOAc) to afford ester (1.63 g, 2 steps 94%) as a colorless syrup [R_f = 0.58 (1:1 hexane–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (3H, t, J = 7.0 Hz), 1.42 (1H, d, J = 4.0 Hz), 1.50–2.20 (4H, m), 1.65 (3H, s), 1.71 (3H, d, J = 1.5 Hz), 1.84 (3H, d, J = 1.5 Hz), 2.78–3.04 (2H, m), 3.80 (3H, s), 3.99 (2H, d, J = 7.0 Hz), 4.18 (2H, q, J = 7.0 Hz), 4.43 (2H, s), 4.47–4.58 (1H, m), 5.26 (1H, br t, J = 7.0 Hz), 5.42 (1H, tq, J = 6.0 Hz, 1.5 Hz), 6.66 (1H, tq, J = 7.0 Hz, 1.5 Hz), 6.87 (2H, d, J = 9.0 Hz), 7.26 (2H, d, J = 9.0 Hz)]. To a solution of this ester (590 mg, 1.42 mmol) and imidazole (289 mg, 4.25 mmol) in dry CH_2Cl_2 (14.2 mL) was added TESCl (0.475 mL, 2.83 mmol) at 0 °C. After 1 h at rt, water (30 mL) was added and the mixture was extracted with $CHCl_3$ (30 mL × 3). The extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (38 g, 5:1 hexane–EtOAc) to afford TES ether (751 mg, 100%) as a colorless syrup [R_f = 0.75 (2:1 hexane–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.46–0.64 (6H, m), 0.84–1.02 (9H, m), 1.28 (3H, t, J = 7.0 Hz), 1.46–2.16 (4H, m), 1.63 (3H, br s), 1.68 (3H, br s), 1.86 (3H, br s), 2.76–3.05 (2H, m), 3.80 (3H, s), 3.98 (2H, d, J = 7.0 Hz), 4.18 (2H, q, J = 7.0 Hz), 4.39–4.50 (1H, m), 4.43 (2H, s), 5.14 (1H, br t, J = 7.0 Hz), 5.40 (1H, br t, J = 7.0 Hz), 6.67 (1H br t, J = 7.0 Hz), 6.87 (2H, d, J = 8.5 Hz), 7.27 (2H, d, J = 8.5 Hz)]. To a –78 °C solution of the above TES ether (714 mg, 1.34 mmol) in dry CH_2Cl_2 (13.4 mL) was added 0.94 M hexane solution of DIBAL (3.86 mL, 3.63 mmol). After 1 h at –78 °C, 10% aqueous solution of potassium sodium tartrate (5 mL) was added and the mixture was gradually warmed to rt. After 12 h at rt, water (30 mL) was added and the mixture was extracted with $CHCl_3$ (30 mL × 3). The extracts were washed with brine (30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (34 g, 3:1 hexane–EtOAc) to afford **46** (617 mg, 90%) as a colorless oil: R_f = 0.25 (3:1 hexane–EtOAc); $[\alpha]_D^{28}$ −4.98 (*c* 1.82, $CHCl_3$); IR (neat, cm^{-1}) 3420, 2950, 2910, 2880, 1615, 1585, 1515, 1460, 1380, 1300, 1250, 1175, 1075, 1040, 1010, 820, 745; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.57 (6H, q, J = 8.0 Hz), 0.94 (9H, t, J = 8.0 Hz), 1.38–1.80 (3H, m), 1.63 (3H, br s), 1.66 (3H, d, J = 1.0 Hz), 1.68 (3H, br s), 1.82–1.98 (1H, m), 2.00–2.14 (1H, m), 2.64–2.88 (2H, m), 3.80 (3H, s), 3.95–4.02 (4H, m), 4.43 (2H, s), 4.49 (1H, t, J = 6.5 Hz), 5.10 (1H, br t, J = 7.0 Hz), 5.34 (1H, tq, J = 7.0 Hz, 1.0 Hz), 5.39 (1H, tq, J = 7.0 Hz, 1.0 Hz), 6.87 (2H, d, J = 9.0 Hz), 7.27 (2H, d, J = 9.0 Hz); ^{13}C NMR (75 MHz,

$CDCl_3$) δ 4.9, 7.0, 13.9, 16.8, 17.8, 26.2, 34.6, 36.0, 55.4, 66.4, 68.9, 70.1, 71.9, 113.9, 120.8, 123.6, 124.7, 129.5, 130.7, 135.0, 138.5, 140.4, 159.2; MS (EI) *m*/*z* 488 (M^+); HRMS (EI) *m*/*z* calcd for $C_{29}H_{48}O_4Si$ (M^+) 488.3322, found 488.3299.

Epoxy Alcohol 47. To a mixture of L-(+)-DET (304 mg, 1.47 mmol) and MS4A powder (4.8 g) in dry CH_2Cl_2 (33.0 mL) was added (*i*-PrO)$_4$Ti (0.292 mL, 0.982 mmol) at 0 °C. After 0.5 h at 0 °C, the mixture was cooled to −30 °C and 3.99 M CH_2Cl_2 solution of TBHP (4.93 mL, 19.6 mmol) was added. After 0.5 h at −30 °C, a solution of **46** (4.80 g, 9.82 mmol) in dry CH_2Cl_2 (16.0 mL) was added and the mixture was stirred at −20 °C for 12 h. The reaction mixture was passed through a pad of celite and 30% aqueous solution of NaOH saturated with NaCl (3 ml) was added to the filtrate. After 20 min at rt, water (30 mL) was added and the mixture was extracted with $CHCl_3$ (50 mL × 3). The extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (400 g, 2:1 hexane–EtOAc) to afford **47** (4.57 g, 92%) as a colorless syrup: R_f = 0.37 (2:1 hexane–EtOAc); $[\alpha]_D^{26}$ −9.94 (*c* 2.11, $CHCl_3$); IR (neat, cm^{-1}) 3440, 2950, 2910, 2880, 1615, 1585, 1515, 1460, 1380, 1300, 1250, 1175, 1075, 1040, 1010, 820, 750; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.56 (6H, q, *J* = 8.0 Hz), 0.94 (9H, t, *J* = 8.0 Hz), 1.30 (3H, s), 1.44–1.66 (1H, m), 1.63 (3H, br s), 1.70 (3H, d, *J* = 1.0 Hz), 1.74 (1H, dd, *J* = 8.5 Hz, 4.5 Hz), 1.83–1.98 (1H, m), 2.01–2.17 (1H, m), 2.18–2.32 (1H, m), 2.32–2.50 (1H, m), 3.01 (1H, t, *J* = 7.0 Hz), 3.57 (1H, dd, *J* = 12.0 Hz, 8.5 Hz), 3.68 (1H, dd, *J* = 12.0 Hz, 4.5 Hz), 3.80 (3H, s), 3.98 (2H, d, *J* = 7.0 Hz), 4.40–4.47 (1H, m), 4.43 (2H, s), 5.16 (1H, br t, *J* = 7.0 Hz), 5.39 (1H, tq, *J* = 7.0 Hz, 1.0 Hz), 6.87 (2H, d, *J* = 9.0 Hz), 7.27 (2H, d, *J* = 9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.0, 7.0, 14.4, 16.8, 18.1, 27.0, 34.7, 36.0, 55.4, 59.5, 61.1, 65.4, 66.4, 70.3, 71.9, 113.9, 119.6, 120.8, 129.5, 140.3, 141.2, 159.2; MS (EI) *m*/*z* 504 (M^+); HRMS (EI) *m*/*z* calcd for $C_{29}H_{48}O_5Si$ (M^+) 504.3271, found 504.3259.

Aldehyde 36. To a 0 °C solution of **47** (4.50 g, 8.91 mmol) and dry Et_3N (7.5 mL, 53.5 mmol) in dry CH_2Cl_2 (89.0 mL) and dry DMSO (18.0 mL) was added SO_3•Py (4.3 g, 26.7 mmol). After 3.5 h at 0 °C, water (50 mL) was added and the mixture was extracted with $CHCl_3$ (50 mL × 3). The extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (180 g, 3:1 hexane–EtOAc) to afford **36** (4.45 g, 99%) as a colorless syrup: R_f = 0.78 (2:1 hexane–EtOAc); $[\alpha]_D^{27}$ +41.5 (*c* 2.27, $CHCl_3$); IR (neat, cm^{-1}) 2950, 2910, 2880, 1730, 1615, 1585, 1515, 1460, 1380, 1300, 1250, 1175, 1080, 1040, 1010, 820, 740; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.56 (6H, q, *J* = 8.0 Hz), 0.94 (9H, t, *J* = 8.0 Hz), 1.43 (3H, s), 1.46–1.61 (1H, m), 1.64 (3H, br s), 1.71 (3H, br s), 1.66–1.80 (1H, m), 1.82–1.98 (1H, m), 2.00–2.16 (1H, m), 2.20–2.40 (1H, m), 2.40–2.60 (1H, m), 3.01 (1H, t, *J* = 7.0 Hz), 3.80 (3H, s), 3.98 (2H, d, *J* = 7.0 Hz), 4.36–4.46 (1H, m), 4.43 (2H, s), 5.16 (1H, br t, *J* = 7.0 Hz), 5.39

(1H, br t, J = 7.0 Hz), 6.87 (2H, d, J = 9.0 Hz), 7.27 (2H, d, J = 9.0 Hz), 8.85 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.0, 7.0, 10.2, 16.8, 18.3, 26.8, 34.7, 36.0, 55.4, 59.5, 62.5, 66.4, 70.4, 72.0, 113.9, 118.4, 121.0, 129.5, 130.7, 140.1, 142.5, 159.3, 200.0; MS (EI) m/z 502 (M^+); HRMS (EI) m/z calcd for $C_{29}H_{46}O_5Si$ (M^+) 502.3115, found 502.3136.

Second-generation Synthesis of Epoxy Allyl Sulfide 33

Homoallyl Alcohols 48a and 48b. To a −78 °C solution of (−)-DIPCl (1.8 M hexane solution, 4.9 mL, 8.64 mmol) in dry ether (22.0 mL) was added 1.0 M ether solution of allylmagnesium bromide (8.64 mL, 8.64 mmol). After 15 min at −78 °C, the reaction mixture was warmed to rt and stirred at rt for 2 h. The reaction mixture was cooled to −78 °C and this was added a solution of **36** (2.17 g, 4.32 mmol) in dry ether (22.0 mL) over 10 min. After 12 h at −40 °C, saturated aqueous solution of $NaHCO_3$ (20 mL) and water (100 mL) were added and the mixture was extracted with ether (100 mL × 3). The extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (118 g, 7:1 toluene–EtOAc) to afford **48a** (2.35 g, 83%) as a colorless oil and **48b** (contaminated with DIP derived by-product). **48b** was further purified with silica-gel column chromatography (100 g of silica gel, 5:1 hexane–EtOAc) to afford **48b** (231 mg, 10%) as a colorless oil. **48a**: R_f = 0.62 (2:1 hexane–EtOAc); $[\alpha]_D^{25}$ –2.54 (c 3.02, $CHCl_3$); IR (neat, cm^{-1}) 3450, 2955, 2910, 2875, 1615, 1515, 1455, 1380, 1300, 1250, 1175, 1075, 1040, 1005, 915, 820, 740; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.57 (6H, q, J = 8.0 Hz), 0.94 (9H, t, J = 8.0 Hz), 1.30 (3H, s), 1.46–1.82 (2H, m), 1.63 (3H, s), 1.70 (3H, d, J = 1.0 Hz), 1.82–2.00 (1H, m), 2.00–2.52 (6H, m), 3.00 (1H, t, J = 6.5 Hz), 3.68 (1H, dd, J = 8.0 Hz, 3.5 Hz), 3.80 (3H, s), 3.98 (2H, d, J = 7.0 Hz), 4.40–4.48 (1H, m), 4.43 (2H, s), 5.04–5.23 (3H, m), 5.40 (1H, t, J = 7.0 Hz, 1.0 Hz), 5.86 (1H, m), 6.87 (2H, d, J = 8.5 Hz), 7.27 (2H, d, J = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.0, 7.0, 14.5, 16.8, 18.1, 27.0, 34.7, 36.0, 37.4, 55.4, 59.0, 62.6, 66.4, 70.3, 71.9, 72.2, 113.9, 117.6, 119.6, 120.9, 129.5, 130.8, 134.4, 140.2, 141.1, 159.2; MS (EI) m/z 544 (M^+); HRMS (EI) m/z calcd for $C_{32}H_{52}O_5Si$ (M^+) 544.3584, found 544.3561. **48b**: R_f = 0.42 (2:1 hexane–EtOAc); $[\alpha]_D^{29}$ −2.03 (c 1.75, $CHCl_3$); IR (neat, cm^{-1}) 3440, 2955, 2910, 2875, 1615, 1515, 1460, 1380, 1300, 1250, 1175, 1075, 1040, 1005, 915, 850, 820, 750; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.56 (6H, q, J = 8.0 Hz), 0.93 (9H, t, J = 8.0 Hz), 1.30 (3H, s), 1.46–1.60 (1H, m), 1.63 (3H, s), 1.70 (3H, br s), 1.66–1.80 (1H, m), 1.82–1.98 (1H, m), 1.93 (1H, d, J = 4.0 Hz), 2.00–2.50 (5H, m), 2.83 (1H, t, J = 6.0 Hz), 3.32 (1H, dt, J = 4.0 Hz, 7.0 Hz), 3.80 (3H, s), 3.98 (2H, d, J = 7.0 Hz), 4.38–4.47 (1H, m), 4.43 (2H, s), 5.05–5.22 (3H, m), 5.39 (1H, tq, J = 7.0 Hz, 1.0 Hz), 5.77 (1H, ddt, J = 17.0 Hz, 10.0 Hz, 7.0 Hz), 6.87 (2H, d, J = 8.5 Hz), 7.27 (2H, d, J = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.0, 7.0, 11.7, 16.8, 18.1, 27.0, 34.7, 36.0, 37.9, 55.4, 61.3, 63.3, 66.4, 70.3, 71.9, 75.9, 113.9, 118.1, 119.6, 120.9, 129.5, 130.7, 134.0, 140.3, 141.2, 159.2; MS (EI) m/z 544 (M^+); HRMS

(EI) *m*/*z* calcd for $C_{32}H_{52}O_5Si$ (M^+) 544.3584, found 544.3559.

Dihydropyran 49. To a −78 °C solution of **48a** (1.45 g, 2.66 mmol) in dry MeOH (53.2 mL) was added BF_3•OEt_2 (1.00 mL, 7.98 mmol) and the resulting solution was warmed to 0 °C over 2 h. After 1 h at 0 °C, saturated aqueous solution of $NaHCO_3$ (10 mL) and water (100 mL) were added and the mixture was extracted with EtOAc (200 mL × 3). The extracts were washed with brine (100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (57 g, 2:1 hexane–EtOAc) to afford **49** (1.02 g, 89%) as a colorless syrup: R_f = 0.35 (2:1 hexane–EtOAc); $[\alpha]_D^{29}$ +27.4 (*c* 2.47, $CHCl_3$); IR (neat, cm^{-1}) 3460, 2940, 2860, 1615, 1585, 1515, 1440, 1370, 1300, 1250, 1175, 1075, 1040, 925, 820, 760; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (3H, s), 1.58–1.78 (2H, m), 1.63 (3H, br s), 1.66 (3H, br s), 1.92–2.38 (6H, m), 2.42 (1H, s), 2.50–2.61 (1H, m), 3.57–3.64 (1H, m), 3.67 (1H, dd, *J* = 11.0 Hz, 3.5 Hz), 3.80 (3H, s), 3.93–4.04 (1H, m), 4.00 (2H, d, *J* = 7.0 Hz), 4.44 (2H, s), 5.17 (1H, d, *J* = 17.5 Hz), 5.18 (1H, d, *J* = 8.0 Hz), 5.43 (1H, tq, *J* = 7.0 Hz, 1.0 Hz), 5.51 (1H, br s), 5.87 (1H, dddd, *J* = 17.5 Hz, 10.5 Hz, 8.0 Hz, 6.0 Hz), 6.88 (2H, d, *J* = 9.0 Hz), 7.27 (2H, d, *J* = 9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.8, 19.5, 20.0, 25.0, 29.5, 36.2, 36.5, 55.4, 66.4, 70.9, 72.0, 73.9, 74.8, 77.0, 113.9, 118.3, 119.7, 121.5, 129.6, 130.7, 135.1, 136.0, 139.9, 159.3; MS (EI) *m*/*z* 430 (M^+); HRMS (EI) *m*/*z* calcd for $C_{26}H_{38}O_5$ (M^+) 430.2719, found 430.2717.

Acetonide 50. To a solution of **49** (1.34 g, 3.11 mmol) in dry CH_2Cl_2 (31.1 mL) were added 2,2-dimethoxypropane (3.8 mL, 31.1 mmol) and PPTS (78.2 mg, 0.311 mmol). After 12 h at rt, saturated aqueous solution of $NaHCO_3$ (5 mL) and water (100 mL) were added at 0 °C. The resulting mixture was extracted with $CHCl_3$ (100 mL × 3) and the extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (284 g, 6:1 hexane–EtOAc) to afford **50** (1.42 g, 97%) as a colorless syrup: R_f = 0.77 (2:1 hexane–EtOAc); $[\alpha]_D^{27}$ +22.5 (*c* 2.14, $CHCl_3$); IR (neat, cm^{-1}) 3080, 2980, 2940, 2860, 1640, 1615, 1585, 1515, 1440, 1380, 1300, 1250, 1220, 1190, 1175, 1100, 1070, 1040, 920, 850, 820, 760; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (3H, s), 1.35 (3H, s), 1.39 (3H, s), 1.60–1.74 (2H, m), 1.62 (3H, br s), 1.64 (3H, br s), 1.92–2.42 (5H, m), 2.57 (1H, dddd, *J* = 15.0 Hz, 6.5 Hz, 4.0 Hz, 1.5 Hz), 3.74 (1H, dd, *J* = 10.0 Hz, 4.0 Hz), 3.80 (3H, s), 3.82 (1H, dd, *J* = 10.0 Hz, 4.0 Hz), 3.90 (1H, br d, *J* = 8.0 Hz), 3.99 (2H, d, *J* = 7.0 Hz), 4.43 (2H, s), 5.09 (1H, br d, *J* = 10.0 Hz), 5.15 (1H, dd, *J* = 17.0 Hz, 1.5 Hz), 5.41 (1H, tq, *J* = 7.0 Hz, 1.0 Hz), 5.55 (1H, br s), 5.92 (1H, ddt, *J* = 17.0 Hz, 10.0 Hz, 7.0 Hz), 6.87 (2H, d, *J* = 9.0 Hz), 7.27 (2H, d, *J* = 9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.8, 19.0, 20.2, 25.9, 26.7, 28.4, 29.3, 33.8, 37.5, 55.4, 66.4, 67.1, 71.9, 82.9, 83.9, 107.2, 113.9, 116.9, 120.2, 121.3, 129.6, 130.7, 134.7, 135.8, 140.0, 159.2; MS (EI) *m*/*z* 470 (M^+); HRMS (EI) *m*/*z* calcd for $C_{29}H_{42}O_5$ (M^+) 470.3032, found 470.3021.

Olefin 34. To a stirred solution of **50** (1.05 g, 2.23 mmol) in dry 2-methyl-2-butene (11.2 mL) was added Grubbs second generation catalyst **29** (95 mg, 0.112 mmol) and the resulting purple solution was stirred at rt for 1.5 h. This solution was passed through a short column of silica gel and the filtrate was concentrated under reduced pressure. The residue was further purified with silica-gel column chromatography (56 g, 8:1 hexane–EtOAc) to afford **34** (868 mg, 78%) as a slightly brown syrup: R_f = 0.53 (4:1 hexane–EtOAc); $[\alpha]_D^{24}$ +18.9 (*c* 2.90, $CHCl_3$); IR (neat, cm^{-1}) 2980, 2940, 2860, 1615, 1585, 1515, 1455, 1380, 1300, 1250, 1220, 1180, 1170, 1095, 1070, 1040, 930, 855, 820, 760; ^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (3H, s), 1.35 (3H, s), 1.39 (3H, s), 1.54–1.78 (2H, m), 1.62 (6H, s), 1.63 (3H, s), 1.72 (3H, s), 1.90–2.38 (5H, m), 2.42–2.56 (1H, m), 3.70–3.78 (2H, m), 3.80 (3H, s), 3.98 (2H, d, *J* = 7.0 Hz), 4.42 (2H, s), 5.26 (1H, br t, *J* = 7.0 Hz), 5.40 (1H, tq, *J* = 7.0 Hz, 1.0 Hz), 5.55 (1H, br s), 6.87 (2H, d, *J* = 9.0 Hz), 7.27 (2H, d, *J* = 9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.7, 18.1, 19.4, 20.2, 25.96, 26.03, 26.7, 28.1, 28.3, 29.3, 37.3, 55.4, 66.4, 67.3, 71.8, 77.1, 82.9, 84.6, 106.9, 113.9, 120.2, 121.3, 121.5, 129.5, 130.7, 133.5, 134.1, 139.9, 159.2; MS (EI) *m*/*z* 498 (M^+); HRMS (EI) *m*/*z* calcd for $C_{31}H_{46}O_5$ (M^+) 498.3345, found 498.3346.

A 2:1 Mixture of 33a and 33b. To a solution of **34** (450 mg, 0.902 mmol) in dry CH_2Cl_2 (36 mL) was added 65% *m*CPBA (192 mg, 0.722 mmol) at −78 °C and the resulting mixture was gradually warmed to 0 °C over 3 h. Saturated aqueous solution of $Na_2S_2O_3$ (10 mL), saturated aqueous solution of $NaHCO_3$ (10 mL), and water (30 mL) were added and this mixture was extracted with $CHCl_3$ (50 mL × 3). The extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (46 g, 5:1 hexane–EtOAc) to afford a 2:1 inseparable mixture of **51a** and **51b** (160 mg, 34%) along with the recovered **34** (203 mg, 45%). This mixture of **51a** and **51b** (587 mg, 1.14 mmol) in dry CH_2Cl_2 (34.5 mL) and 1.0 M pH 7 phosphate buffer (3.5 mL, prepared by mixing 1.75 mL of 1 M aqueous solution of NaH_2PO_4 and 1.75 mL of 1 M aqueous solution of Na_2HPO_4) was cooled to 0 °C and DDQ (631 mg, 2.28 mmol) was added. After 2 h at 0 °C, saturated aqueous solution of $Na_2S_2O_3$ (10 mL), saturated aqueous solution of $NaHCO_3$ (10 mL), and water (20 mL) were added. The mixture was extracted with ether (50 mL × 3) and the extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (45 g, 2:1 hexane–EtOAc) to afford allyl alcohol (364 mg, 81%) as a 2:1 mixture of diastereomers. To a stirred solution of the above allyl alcohol (364 mg, 0.923 mmol) in 10:1 CH_2Cl_2–pyridine (18.5 mL) were added at 0 °C diphenyldisulfide (604 mg, 2.77 mmol) and tri-*n*-butylphosphine (0.683 mL, 2.77 mmol). After 16 h at rt, the solution was diluted with ether (30 mL) and water (30 mL). The mixture was extracted with ether (30 mL × 3) and the extracts were washed with brine (30 mL), dried over Na_2SO_4, and

concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (45 g, 8:1 hexane–EtOAc) to afford a 2:1 mixture of **33a** and **33b** (397 mg, 91%) as a colorless syrup. These mixture of **33a** and **33b** was identical to our previous sample of **33a** and **33b** in all respects.[12a,12b]

Third-generation Synthesis of Epoxy Allyl Sulfide 33

***tert*-Butyl Ester 52a and 52b.** To a −40 °C solution of LDA (12.6 mmol) in ether (10.5 mL) was added *tert*-BuOAc (1.91 mL, 14.2 mmol) and the resulting solution was stirred at −40 °C for 1 h. This was cooled to −78 °C and a solution of **36** (1.58 g, 3.14 mmol) in ether (15.8 mL) was added. After 1 h at −78 °C, saturated aqueous solution of NH_4Cl (10 mL) and water (10 mL) were added and the mixture was allowed to warm to rt. This was extracted with ether (20 mL × 3) and the extracts were washed with brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (195 g, 7:1 hexane–EtOAc) to afford **52a** (1.23 g, 63%, a colorless syrup) and its diastereomer **52b** (525 mg, 27%, a colorless syrup). **52a**: R_f = 0.53 (3:1 hexane–EtOAc); $[\alpha]_D^{27}$ −15.3 (*c* 2.41, $CHCl_3$); IR (neat, cm^{-1}) 3470, 2955, 2880, 1730, 1615, 1515, 1455, 1370, 1250, 1155, 1070, 1040, 1010, 820, 745; ^1H NMR (300 MHz, $CDCl_3$) δ 0.56 (6H, q, *J* = 8.0 Hz), 0.93 (9H, t, *J* = 8.0 Hz), 1.29 (3H, s), 1.46 (9H, s), 1.63 (3H, br s), 1.70 (3H, br s), 1.40–1.78 (1H, m), 1.80–2.16 (2H, m), 2.16–2.46 (2H, m), 2.37 (1H, dd, *J* = 16.5 Hz, 9.5 Hz), 2.52 (1H, dd, *J* = 16.5 Hz, 3.0 Hz), 2.87 (1H, d, *J* = 2.0 Hz), 2.95 (1H, t, *J* = 6.5 Hz), 3.80 (3H, s), 3.85 (1H, dt, *J* = 9.0 Hz, 2.0 Hz), 3.98 (2H, d, *J* = 6.5 Hz), 4.42 (1H, t, *J* = 6.8 Hz), 4.43 (2H, s), 5.15 (1H, br t, *J* = 7.5 Hz), 5.39 (1H, tq, *J* = 6.5 Hz, 1.0 Hz), 6.87 (2H, d, *J* = 8.5 Hz), 7.27 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.0, 7.0, 13.3, 16.8, 18.1, 27.0, 28.2, 34.7, 36.0, 38.6, 55.4, 60.7, 61.9, 66.4, 70.4, 71.2, 71.9, 81.5, 113.9, 119.5, 120.8, 129.5, 130.8, 140.3, 141.3, 159.2, 171.6; MS (EI) *m*/*z* 561 [(M−*tert*-Bu)$^+$]; HRMS (EI) *m*/*z* calcd for $C_{31}H_{49}O_7Si$ [(M−*tert*-Bu)$^+$] 561.3248, found 561.3247. **52b**: R_f = 0.42 (3:1 hexane–EtOAc), $[\alpha]_D^{27}$ −1.07 (*c* 2.43, $CHCl_3$); IR (neat, cm^{-1}) 3450, 2950, 2910, 2880, 1730, 1615, 1585, 1515, 1460, 1415, 1370, 1300, 1250, 1170, 1150, 1070, 1040, 1010, 980, 955, 850, 820, 745; ^1H NMR (300 MHz, $CDCl_3$) δ 0.56 (6H, q, *J* = 8.0 Hz), 0.93 (9H, t, *J* = 8.0 Hz), 1.29 (3H, s), 1.47 (9H, s), 1.48–1.78 (2H, m), 1.63 (3H, br s), 1.69 (3H, br s), 1.82–1.97 (1H, m), 1.98–2.28 (2H, m), 2.30–2.50 (3H, m), 2.86 (1H, d, *J* = 4.0 Hz), 2.94 (1H, t, *J* = 6.5 Hz), 3.72–3.82 (1H, m), 3.80 (3H, s), 3.98 (2H, d, *J* = 6.5 Hz), 4.38–4.46 (1H, m), 4.42 (2H, s), 5.13 (1H, br t, *J* = 6.5 Hz), 5.38 (1H, tq, *J* = 6.5 Hz, 1.0 Hz), 6.87 (2H, d, *J* = 8.5 Hz), 7.27 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.0, 7.0, 12.6, 16.8, 18.1, 26.9, 28.2, 34.7, 36.0, 38.9, 55.4, 60.5, 62.6, 66.4, 70.3, 71.9, 72.3, 81.6, 113.9, 119.5, 120.8, 129.5, 130.7, 140.3, 141.3, 159.2, 171.3; MS (EI) *m*/*z* 561 [(M−*tert*-Bu)$^+$]; HRMS (EI) *m*/*z* calcd for $C_{31}H_{49}O_7Si$ [(M−*tert*-Bu)$^+$] 561.3248, found 561.3257.

Acetonide 53a and Its Diastereomer 53b. To a stirred solution of **52a** (26.6 mg, 0.0430 mmol) in dry THF (0.215 mL) was added 1.0 M THF solution of TBAF (0.0860 mL, 0.0860 mmol) at rt. After 1 h at rt, saturated aqueous solution of NH_4Cl (0.5 mL) and water (1 mL) were added and the mixture was extracted with EtOAc (1 mL × 3). The extracts were washed with brine (1 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (1.0 g, 1:1 hexane–EtOAc) to afford alcohol (21.6 mg, 99%) as a colorless syrup. To a stirred solution of this alcohol (6.1 mg, 0.0121 mmol) in dry toluene (0.605 mL) was added (*i*-PrO)$_4$Ti (0.0036 mL, 0.0121 mmol) in dry toluene (0.806 mL) and the solution was heated at 50 °C for 3 h. After cooling to rt, water (2 mL) was added and the mixture was extracted with EtOAc (2 mL × 3). The extracts were washed with brine (2 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (1.0 g, 3:1 hexane–EtOAc) to afford pyran (2.4 mg, 40%) as a colorless syrup. A solution of this pyran (8.2 mg, 0.0162 mmol) in dry CH_2Cl_2 (0.0810 mL) were added 2,2-dimethoxypropane (0.0199 mL, 0.162 mmol) and PPTS (0.4 mg, 0.00162 mmol) at rt. After 22 h at rt, saturated aqueous solution of $NaHCO_3$ (0.5 mL) and water (1 mL) were added. The mixture was extracted with $CHCl_3$ (1 mL × 3) and the extracts were washed with brine (1 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (1.0 g, 3:1 hexane–EtOAc) to afford pyran **53a** (5.0 mg, 56%) as a colorless syrup: R_f = 0.71 (2:1 hexane–EtOAc); $[\alpha]_D^{27}$ +17.5 (*c* 0.92, $CHCl_3$); IR (neat, cm^{-1}) 2980, 2935, 2860, 1735, 1610, 1515, 1460, 1370, 1310, 1250, 1155, 1100, 1070, 1045, 1000, 935, 850, 820; ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (3H, s), 1.38 (6H, s), 1.46 (9H, s), 1.50–1.78 (2H, m), 1.62 (3H, br s), 1.68 (3H, br s), 1.90–2.24 (3H, m), 2.26–2.44 (1H, m), 2.52 (1H, dd, *J* = 16.5 Hz, 9.0 Hz), 2.84 (1H, dd, *J* = 16.5 Hz, 3.0 Hz), 3.70 (1H, dd, *J* = 10.0 Hz, 3.5 Hz), 3.80 (3H, s), 3.91 (1H, br s), 4.00 (2H, d, *J* = 6.5 Hz), 4.25 (1H, dd, *J* = 9.5 Hz, 3.0 Hz), 4.44 (2H, s), 5.46 (1H, t, *J* = 6.5 Hz), 5.54 (1H, m), 6.87 (2H, d, *J* = 8.5 Hz), 7.27 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.8, 18.7, 20.2, 25.6, 26.7, 28.3, 28.4, 29.7, 35.7, 37.6, 55.4, 66.4, 67.2, 71.9, 79.9, 81.0, 82.7, 107.4, 113.9, 120.0, 121.4, 129.6, 130.7, 134.6, 140.0, 159.3, 170.8; MS (EI) *m*/*z* 544 (M^+); HRMS (EI) *m*/*z* calcd for $C_{32}H_{48}O_7$ (M^+) 544.3400, found 544.3418. **53b** was synthesized from **52b** (3 steps 24%) using the same procedure. **53b**: R_f = 0.63 (2:1 hexane–EtOAc); $[\alpha]_D^{27}$ +16.4 (*c* 1.76, $CHCl_3$); IR (neat, cm^{-1}) 2980, 2935, 2860, 1735, 1610, 1515, 1455, 1370, 1305, 1250, 1155, 1100, 950, 850; ^1H NMR (300 MHz, $CDCl_3$) δ 1.11 (3H, s), 1.36 (3H, s), 1.44 (9H, s), 1.52–1.76 (2H, m), 1.61 (3H, br s), 1.66 (3H, br s), 1.88–2.34 (4H, m), 2.49 (1H, dd, *J* = 16.0 Hz, 9.5 Hz), 2.68 (1H, dd, *J* = 16.0 Hz, 2.5 Hz), 3.54 (1H, dd, *J* = 10.5 Hz, 3.0 Hz), 3.80 (3H, s), 3.92 (1H, d, *J* = 9.5 Hz), 4.00 (2H, d, *J* = 6.5 Hz), 4.32 (1H, dd, *J* = 9.5 Hz, 2.5 Hz), 4.42 (2H, s), 5.42 (1H, t, *J* = 6.5 Hz), 5.51 (1H, m), 6.87 (2H, d, *J* = 8.5 Hz), 7.27 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.7,

17.2, 20.1, 25.5, 26.9, 28.2, 28.8, 29.2, 36.2, 37.1, 55.4, 66.4, 71.8, 72.0, 76.5, 78.8, 80.9, 82.3, 107.9, 113.8, 119.3, 121.6, 129.5, 130.8, 135.3, 139.9, 159.2, 170.5; MS (EI) *m*/*z* 544 (M^+); HRMS (EI) *m*/*z* calcd for $C_{32}H_{48}O_7$ (M^+) 544.3400, found 544.3425.

Conversion of 52b into 52a. To a solution of **52b** (181 mg, 292 mmol) in dry CH_2Cl_2 (2.92 mL) was added at 0 °C DMP (187 mg, 438 mmol). After 1h at rt, saturated aqueous solution of $Na_2S_2O_3$ and saturated aqueous solution of $NaHCO_3$ were added. The mixture was extracted with $CHCl_3$ and the extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (9 g, 4:1 hexane–EtOAc) to afford ketone (174 mg, 97%) as a colorless syrup [R_f = 0.71 (3:1 hexane–EtOAc); $[\alpha]_D^{28}$ +41.0 (*c* 2.30, $CHCl_3$); IR (neat, cm^{-1}) 2955, 2910, 2880, 1735, 1715, 1615, 1585, 1515, 1460, 1395, 1370, 1330, 1300, 1255, 1170, 1155, 1075, 1040, 1005, 980, 950, 820, 745; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.56 (6H, q, *J* = 8.0 Hz), 0.93 (9H, t, *J* = 8.0 Hz), 1.44 (9H, s), 1.48 (3H, br s), 1.63 (3H, br s), 1.70 (3H, br s), 1.38–1.80 (2H, m), 1.80–1.97 (1H, m), 2.00–2.15 (1H, m), 2.20–2.50 (2H, m), 3.00 (1H, dd, *J* = 6.5 Hz, 6.5 Hz), 3.26 (2H, q, *J* = 15.5 Hz), 3.80 (3H, s), 3.98 (2H, d, *J* = 7.0 Hz), 4.40 (1H, dd, *J* = 7.0 Hz, 7.0 Hz), 4.43 (2H, s), 5.15 (1H, dd, *J* = 7.5 Hz, 7.5 Hz), 5.39 (1H, dd, *J* = 7.0 Hz, 7.0 Hz). 6.87 (2H, d, *J* = 8.5 Hz), 7.27 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.0, 7.0, 12.8, 16.8, 18.3, 27.1, 28.1, 28.4, 34.7, 35.9, 44.0, 55.4, 60.3, 64.0, 66.4, 70.4, 71.9, 77.4, 82.2, 113.9, 118.5, 120.9, 129.5, 130.7, 140.2, 142.2, 159.3, 166.3, 203.8; MS (EI) *m*/*z* 616 (M^+); HRMS (EI) *m*/*z* calcd for $C_{31}H_{49}O_7Si$ [(M−*tert*-Bu)$^+$] 561.3248, found 561.3247]. To this ketone (588 mg, 0.953 mmol) in MeOH (4.8 mL) was added at −78 °C $NaBH_4$ (54.1 mg, 1.43 mmol). After −78 °C for 1 h, water was added and the mixture was extracted with 1:1 hexane–EtOAc. The extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (59 g, 8:1 hexane–EtOAc) to afford **52a** (380 mg, 64%) and **52b** (155 mg, 26%).

TES Ether 54. To a solution of **52a** (75.3 mg, 0.122 mmol) and imidazole (33.0 mg, 0.486 mmol) in dry CH_2Cl_2 (1.21 mL) was added TESCl (0.061 mL, 0.365 mmol) at 0 °C. After 1 h at rt, water (3 mL) was added and the mixture was extracted with $CHCl_3$ (3 mL × 3). The extracts were washed with brine (3 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (4.5 g, 5:1 hexane–EtOAc) to afford **54** (86.1 mg, 97%) as a colorless syrup: R_f = 0.63 (5:1 hexane–EtOAc); $[\alpha]_D^{27}$ −20.4 (*c* 1.25, $CHCl_3$); IR (neat, cm^{-1}) 2955, 2910, 2880, 1735, 1615, 1515, 1460, 1415, 1380, 1370, 1330, 1300, 1250, 1155, 1110, 1080, 1040, 1005, 975, 955, 855, 820, 745; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.46-0.64 (12H, m), 0.88-0.98 (18H, m), 1.25 (3H, s), 1.42-1.80 (2H, m), 1.44 (9H, s), 1.63 (3H, br s), 1.69 (3H, br s), 1.82–1.98 (1H, m),

2.00–2.15 (1H, m), 2.15–2.36 (1H, m), 2.42 (1H, dd, J = 15.0 Hz, 8.5 Hz), 2.53 (1H, dd, J = 15.0 Hz, 3.5 Hz), 2.80 (1H, t, J = 6.5 Hz), 3.71 (1H, dd, J = 8.5 Hz, 3.5 Hz), 3.80 (3H, s), 3.98 (2H, d, J = 7.0 Hz), 4.40–4.48 (1H, m), 4.43 (2H, s), 5.17 (1H, br t, J = 7.0 Hz), 5.39 (1H, br t, J = 7.0 Hz), 6.87 (2H, d, J = 8.5 Hz), 7.27 (2H, d, J = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.0, 5.1, 6.5, 6.95, 7.01, 11.8, 16.8, 18.0, 27.4, 28.2, 34.7, 36.0, 40.6, 55.4, 62.1, 63.6, 66.4, 70.3, 71.9, 73.9, 80.6, 113.9, 119.9, 120.9, 129.5, 130.8, 140.3, 141.0, 170.7; MS (EI) m/z 675 [(M−*tert*-Bu)$^+$]; HRMS (EI) m/z calcd for $C_{37}H_{63}O_7Si_2$ [(M−*tert*-Bu)$^+$] 675.4113, found 675.4114.

Allyl Alcohol 57. To a −78 °C solution of **54** (86.1 mg, 0.117 mmol) in dry CH_2Cl_2 (1.17 mL) was added 0.94 M hexane solution of DIBAL (0.187 mL, 0.176 mmol). After 1 h at −78 °C, 10% aqueous solution of potassium sodium tartrate (2 mL) was added and the reaction mixture was allowed to warm to rt. After 1 h at rt, water (2 mL) was added and the mixture was extracted with hexane (4 mL × 3). The extracts were washed with brine (4 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (3.9 g, 7:1 hexane–EtOAc) to afford aldehyde **55** (58.4 mg, 75%) as a colorless syrup [R_f = 0.56 (5:1 hexane–EtOAc); $[\alpha]_D^{27}$ −6.41 (c 2.34, $CHCl_3$); IR (neat, cm^{-1}) 2955, 2910, 2880, 1725, 1615, 1515, 1460, 1415, 1380, 1300, 1250, 1175, 1110, 1085, 1040, 1005, 820; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.56 (6H, q, J = 8.0 Hz), 0.58 (6H, q, J = 8.0 Hz), 0.83 (9H, t, J = 8.0 Hz), 0.84 (9H, t, J = 8.0 Hz), 1.28 (3H, s), 1.63 (3H, br s), 1.70 (3H, br s), 1.44–1.80 (2H, m), 1.80–1.98 (1H, m), 2.00–2.15 (1H, m), 2.16–2.40 (2H, m), 2.65 (2H, dd, J = 6.0 Hz, 2.5 Hz), 2.81 (1H, t, J = 6.5 Hz), 3.79 (1H, t, J = 6.0 Hz), 3.80 (3H, s), 3.98 (2H, d, J = 7.0 Hz), 4.43 (2H, s), 4.44 (1H, t, J = 6.5 Hz), 5.16 (1H, br t, J = 7.0 Hz), 5.39 (1H, tq, J = 7.0 Hz, 1.0 Hz), 6.87 (2H, d, J = 8.5 Hz), 7.27 (2H, d, J = 8.5 Hz), 9.76 (1H, t, J = 2.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.96, 5.02, 6.9, 7.0, 11.9, 16.8, 18.1, 27.3, 34.7, 36.0, 48.1, 55.4, 62.1, 63.8, 66.4, 70.3, 71.9, 72.3, 113.9, 119.5, 120.9, 129.5, 130.8, 140.3, 141.3, 159.2, 200.8; MS (EI) m/z 660 (M$^+$); HRMS (EI) m/z calcd for $C_{37}H_{64}O_6Si_2$ (M$^+$) 660.4241, found 660.4231]. A mixture of **55** (135 mg, 0.204 mmol) and Wittig reagent **38** (296 mg, 0.816 mmol) in dry toluene (1.36 mL) was stirred at 80 °C for 2 h. The solvent was removed under reduced pressure and the residue was purified with silica-gel column chromatography (7.6 g, 5:1 hexane–EtOAc) to afford ethyl ester **56** (146 mg, 96%) as a colorless syrup [R_f = 0.62 (5:1 hexane–EtOAc); $[\alpha]_D^{28}$ −11.9 (c 2.32, $CHCl_3$); IR (neat, cm^{-1}) 2955, 2910, 2880, 1715, 1615, 1515, 1460, 1415, 1380, 1365, 1300, 1280, 1250, 1210, 1175, 1085, 1040, 1010, 975, 950, 820, 745; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.56 (12H, br q, J = 8.0 Hz), 0.93 (9H, t, J = 8.0 Hz), 0.94 (9H, t, J = 8.0 Hz), 1.27 (3H, t, J = 7.5 Hz), 1.28 (3H, s), 1.44–1.78 (2H, m), 1.63 (3H, br s), 1.69 (3H, br s), 1.84 (3H, d, J = 1.0 Hz), 1.80–1.97 (1H, m), 2.01–2.16 (1H, m), 2.16–2.43 (4H, m), 2.77 (1H, t, J = 6.5 Hz), 3.29 (1H, dd, J = 8.0 Hz, 4.0 Hz), 3.80 (3H, s), 3.98 (2H, d, J = 6.5 Hz), 4.18 (2H, q, J = 7.5 Hz), 4.42 (2H, s), 4.44 (1H,

br t, J = 7.0 Hz), 5.17 (1H, br t, J = 7.5 Hz), 5.39 (1H, tq, J = 6.5 Hz, 1.0 Hz), 6.87 (2H, d, J = 8.5 Hz), 7.27 (2H, d, J = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.0, 5.1, 6.95, 7.01, 11.8, 12.7, 14.4, 16.8, 18.0, 27.3, 33.3, 34.7, 36.0, 55.4, 60.5, 62.5, 63.3, 66.4, 70.3, 71.9, 76.4, 113.9, 119.8, 120.9, 129.3, 129.5, 130.8, 138.7, 140.3, 141.1, 159.2, 168.1; MS (EI) m/z 744 (M^+); HRMS (EI) m/z calcd for $C_{42}H_{72}O_7Si_2$ (M^+) 744.4817, found 744.4823]. To a −78 °C solution of **56** (146 mg, 0.196 mmol) in dry CH_2Cl_2 (1.96 mL) was added 0.94 M hexane solution of DIBAL (0.562 mL, 0.528 mmol). After 1 h at −78 °C, 10% aqueous solution of potassium sodium tartrate (3 mL) was added and the reaction mixture was allowed to warm up to rt. After 1 h at rt, water (3 mL) was added and the mixture was extracted with hexane (6 mL × 3). The extracts were washed with brine (6 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (6.9 g, 4:1 hexane–EtOAc) to afford **57** (129 mg, 94%) as a colorless syrup: R_f = 0.20 (5:1 hexane–EtOAc); $[\alpha]_D^{31}$ −8.70 (c 2.03, $CHCl_3$); IR (neat, cm^{-1}) 3450, 2955, 2910, 2875, 1615, 1510, 1460, 1420, 1380, 1300, 1255, 1175, 1080, 1040, 1010, 940, 820, 745, 725; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.55 (6H, q, J = 8.0 Hz), 0.56 (6H, q, J = 8.0 Hz), 0.93 (9H, t, J = 8.0 Hz), 0.94 (9H, t, J = 8.0 Hz), 1.27 (3H, s), 1.30 (1H, br t, J = 6.0 Hz), 1.46–1.82 (2H, m), 1.63 (3H, br s), 1.68 (3H, br s), 1.70 (3H, br s), 1.83–1.98 (1H, m), 1.98-2.46 (5H, m), 2.74 (1H, t, J = 6.5 Hz), 3.24 (1H, dd, J = 7.5 Hz, 5.0 Hz), 3.80 (3H, s), 3.94–4.05 (4H, m), 4.42 (2H, s), 4.44 (1H, br), 5.18 (1H, br t, J = 7.0 Hz), 5.39 (1H, br t, J = 6.5 Hz), 5.48 (1H, br t, J = 7.5 Hz), 6.87 (2H, d, J = 8,5 Hz), 7.27 (2H, d, J = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.0, 5.2, 7.0, 11.9, 14.0, 16.8, 18.0, 27.3, 32.4, 34.7, 36.0, 55.4, 62.67, 62.72, 66.4, 69.1, 70.3, 71.9, 76.8, 113.9, 112.0, 120.8, 122.3, 129.5, 130.8, 136.5, 140.3, 141.0, 159.2; MS (EI) m/z 702 (M^+); HRMS (EI) m/z calcd for $C_{40}H_{70}O_6Si_2$ (M^+) 702.4711, found 702.4726.

Acetonide 35. To a solution of **58** (121 mg, 0.255 mmol) in dry CH_2Cl_2 (2.6 mL) were added 2,2-dimethoxypropane (0.313 mL, 2.55 mmol) and PPTS (6.4 mg, 0.0255 mmol). After 1 h at rt, dry MeOH (2.6 mL) was added and the solution was stirred for 5 min. This was cooled to 0 °C and saturated aqueous solution of $NaHCO_3$ (1 mL) and water (3 mL) were added. The mixture was extracted with 1:1 hexane–EtOAc (4 mL × 3) and the extracts were washed with brine (4 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (7.3 g, 2:1 hexane–EtOAc) to afford **35** (134 mg, 91%) as a colorless syrup: R_f = 0.55 (1:1 hexane–EtOAc); $[\alpha]_D^{26}$ +9.58 (c 1.16, $CHCl_3$); IR (neat, cm^{-1}) 3440, 2985, 2935, 2860, 1615, 1515, 1450, 1380, 1300, 1250, 1180, 1095, 1070, 1040, 930, 855, 820; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (3H, s), 1.34 (3H, s), 1.38 (3H, s), 1.56–1.76 (2H, m), 1.60 (3H, br s), 1.62 (3H, br s), 1.70 (3H, br s), 1.87–2.44 (6H, m), 2.57 (1H, ddd, J = 15.0 Hz, 8.0 Hz, 3.5 Hz), 3.70–3.82 (2H, m), 3.80 (3H, s), 3.90 (1H, br d, J = 8.0 Hz), 3.94–4.04 (4H, m), 4.42 (2H, s), 5.35 (1H, br t, J = 6.0 Hz), 5.56 (2H, br s), 6.87 (2H, d, J = 8.5 Hz), 7.27 (2H, d, J = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 16.6, 19.2,

20.2, 25.9, 26.7, 27.9, 28.4, 29.4, 37.6, 55.4, 66.5, 67.2, 68.9, 71.9, 77.3, 82.9, 84.1, 107.1, 113.9, 120.2, 121.7, 122.8, 129.7, 130.4, 134.6, 137.0, 139.3, 159.3; MS (EI) *m*/*z* 514 (M^+); HRMS (EI) *m*/*z* calcd for $C_{31}H_{46}O_6$ (M^+) 514.3294, found 514.3294.

Epoxy Alcohol 59. To a mixture of L-(+)-DET (2.35 mg, 0.0114 mmol) and MS4A powder (78.4 mg) in dry CH_2Cl_2 (0.381 mL) was added (*i*-PrO)$_4$Ti (0.00227 mL, 0.00762 mmol) at 0 °C. After 0.5 h at 0 °C, the mixture was cooled to −40 °C and 3.98 M CH_2Cl_2 solution of TBHP (0.0382 mL, 0.152 mmol) was added. After 0.5 h at −40 °C, a solution of **35** (39.2 mg, 0.0762 mmol) in dry CH_2Cl_2 (0.254 mL) was added and the resulting mixture was stirred at −40 °C for 17 h. The reaction was quenched with water (1 mL) and the organic layer was separated. The aqueous layer was extracted with EtOAc (1 mL × 3) and the combined organic layers were washed with brine (1 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (2.0 g, 4:1 hexane–EtOAc to 3:1 hexane–EtOAc) to afford **59** (38.2 mg, 95%) as a colorless syrup: R_f = 0.44 (1:1 hexane–EtOAc); $[\alpha]_D^{27}$ +7.30 (*c* 1.89, $CHCl_3$); IR (neat, cm^{-1}) 3450, 2985, 2935, 2860, 1615, 1515, 1455, 1380, 1300, 1250, 1220, 1180, 1095, 1070, 1040, 930, 870, 850, 820; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (3H, s), 1.32 (3H, s), 1.37 (3H, s), 1.39 (3H, s), 1.54–1.74 (8H, m), 1.86–2.38 (6H, m), 3.24 (1H, dd, *J* = 7.5 Hz, 5.0 Hz), 3.54 (1H, d, *J* = 12.0 Hz), 3.59 (1H, d, *J* = 12.0 Hz), 3.74 (1H, dd, *J* = 10.0 Hz, 4.0 Hz), 3.80 (3H, s), 3.89 (1H, br), 3.96 (1H, dd, *J* = 9.0 Hz, 4.5 Hz), 4.00 (2H, d, *J* = 7.0 Hz), 4.43 (2H, s), 5.37 (1H, br t, *J* = 7.0 Hz), 5.55 (1H, m), 6.88 (2H, d, *J* = 8.5 Hz), 7.27 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.8, 16.8, 18.5, 20.2, 25.7, 26.8, 28.4, 28.6, 29.4, 37.5, 55.4, 58.7, 61.5, 66.0, 66.5, 67.0, 72.1, 81.2, 82.9, 107.4, 113.9, 120.1, 121.4, 129.7, 130.4, 134.6, 139.5, 159.3; MS (EI) *m*/*z* 530 (M^+); HRMS (EI) *m*/*z* calcd for $C_{31}H_{46}O_7$ (M^+) 530.3243, found 530.3253.

Iodide 60. To a solution of **59** (212 mg, 0.399 mmol), PPh_3 (209 mg, 0.797 mmol), and imidazole (108 mg, 1.59 mmol) in dry CH_2Cl_2 (9.5 mL) was added I_2 (181 mg, 0.718 mmol) at 0 °C. The resulting mixture was shielded from light and stirred at 0 °C for 3 h. Saturated aqueous solution of $Na_2S_2O_3$ (2 mL) and saturated aqueous solution of $NaHCO_3$ (2.0 mL) were added and the organic layer was separated. The aqueous layer was extracted with hexane (4 mL × 3) and the combined organic layers were washed with brine (4 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (12.8 g, 4:1 hexane–EtOAc) to afford **60** (238 mg, 93%) as a colorless syrup: R_f = 0.83 (2:1 hexane–EtOAc); $[\alpha]_D^{27}$ +8.61 (*c* 2.13, $CHCl_3$); IR (neat, cm^{-1}) 2985, 2935, 2860, 1735, 1615, 1585, 1515, 1455, 1380, 1300, 1250, 1220, 1185, 1170, 1095, 1070, 1045, 930, 870, 850, 820; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (3H, s), 1.36 (3H, s), 1.39 (3H, s), 1.47 (3H, s), 1.61 (3H, br s), 1.66 (3H, br s), 1.56–1.72 (2H, m), 1.82-2.36 (6H, m), 3.12 (1H, d, *J* = 10.0 Hz), 3.14 (1H, dd, *J* = 5.5 Hz, 2.5 Hz), 3.19 (1H, d, *J* = 10.0 Hz),

3.73 (1H, dd, J = 10.5 Hz, 4.0 Hz), 3.80 (3H, s), 3.85–3.93 (1H, m), 3.93 (1H, dd, J = 9.5 Hz, 4.5 Hz), 4.00 (2H, d, J = 6.5 Hz), 4.43 (2H, s), 5.39 (1H, tq, J = 6.5 Hz, 1.0 Hz), 5.55 (1H, m), 6.88 (2H, d, J = 8.5 Hz), 7.27 (2H, d, J = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 16.7, 17.1, 18.6, 20.2, 25.7, 26.8, 28.4, 29.3, 29.5, 37.4, 55.4, 60.6, 64.7, 66.5, 67.0, 72.1, 81.0, 82.9, 107.5, 113.9, 120.0, 121.5, 129.6, 130.6, 134.6, 139.6, 159.3; MS (EI) m/z 640 (M^+); HRMS (EI) m/z calcd for $C_{31}H_{45}O_6I$ (M^+) 640.2261, found 640.2268.

β-Epoxide 51a. To a solution of **60** (65.6 mg, 0.102 mmol) in dry THF (1.0 mL) was added $NaBH_3CN$ (96.5 mg, 1.54 mmol) and the mixture was stirred at 50 °C for 18 h. After cooling to 0 °C, water (2 mL) was added and the mixture was extracted with EtOAc (2 mL × 3). The extracts were washed with brine (2 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (2.95 g, 7:1 hexane–EtOAc) to afford **51a** (38.6 mg, 73%) as a colorless syrup: R_f = 0.48 (4:1 hexane–EtOAc); $[\alpha]_D^{27}$ +9.55 (c 0.94, $CHCl_3$); IR (neat, cm^{-1}) 2985, 2930, 2855, 1735, 1610, 1515, 1460, 1380, 1300, 1250, 1220, 1185, 1170, 1095, 1070, 1040, 1010, 930, 870, 850, 815; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (3H, s), 1.29 (3H, s), 1.31 (3H, s), 1.37 (3H, s), 1.39 (3H, s), 1.54–1.72 (2H, m), 1.62 (3H, br s), 1.64 (3H, br s), 1.76-2.38 (6H, m), 2.99 (1H, dd, J = 8.5 Hz, 4.0 Hz), 3.73 (1H, dd, J = 10.5 Hz, 4.0 Hz), 3.80 (3H, s), 3.89 (1H, br s), 3.94–4.02 (1H, m), 3.99 (2H, d, J = 6.0 Hz), 4.43 (2H, s), 5.39 (1H, tq, J = 6.0 Hz, 1.0 Hz), 5.55 (1H, m), 6.88 (2H, d, J = 8.5 Hz), 7.27 (2H, d, J = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.8, 18.6, 19.2, 20.2, 24.9, 25.8, 26.7, 28.4, 29.2, 29.3, 37.4, 55.4, 58.9, 62.2, 66.4, 67.1, 71.9, 77.1, 81.3, 82.9, 107.3, 113.8, 120.1, 121.5, 129.5, 130.6, 134.6, 139.7, 159.2; MS (EI) m/z 514 (M^+); HRMS (EI) m/z calcd for $C_{31}H_{46}O_6$ (M^+) 514.3294, found 514.3276.

Allyl Alcohol 61. A mixture of **51a** (78.2 mg, 0.152 mmol) in dry CH_2Cl_2 (2.1 mL) and water (0.210 mL) was cooled to 0 °C and DDQ (41.4 mg, 0.150 mmol) was added. The resulting dark brown mixture was stirred at 0 °C for 0.5 h and saturated aqueous solution of $Na_2S_2O_3$ (0.5 mL), saturated aqueous solution of $NaHCO_3$ (0.5 mL), and water (2.0 mL) were added. The mixture was extracted with hexane (2 mL × 3) and the extracts were washed with brine (2 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (2.7 g, 2:1 hexane–EtOAc) to afford **61** (53.1 mg, 89%) as a colorless syrup: R_f = 0.10 (4:1 hexane–EtOAc); $[\alpha]_D^{28}$ +11.5 (c 0.69, $CHCl_3$); IR (neat, cm^{-1}) 3450, 2985, 2935, 2870, 1450, 1380, 1260, 1190, 1095, 1060, 1045, 1010, 930, 915, 870, 845, 810; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (3H, s), 1.30 (3H, s), 1.34 (3H, s), 1.37 (3H, s), 1.39 (3H, s), 1.50–1.76 (2H, m), 1.62 (3H, br s), 1.68 (3H, br s), 1.80–2.40 (6H, m), 2.98 (1H, dd, J = 7.5 Hz, 5.5 Hz), 3.73 (1H, dd, J = 10.0 Hz, 3.5 Hz), 3.89 (1H, br), 3.97 (1H, dd, J = 9.5 Hz, 4.0 Hz), 4.16 (2H, d, J = 7.0 Hz), 5.43 (1H, tq, J = 7.0 Hz, 1.0 Hz), 5.56 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.5, 18.7, 19.2, 20.2, 24.9, 25.8, 26.8, 28.4, 29.1,

29.2, 37.3, 59.0, 59.4, 62.5, 67.2, 77.1, 81.4, 82.9, 107.3, 120.2, 124.0, 134.5, 139.0; MS (EI) *m*/*z* 394 (M^+); HRMS (EI) *m*/*z* calcd for $C_{23}H_{38}O_5$ (M^+) 394.2719, found 394.2716.

Epoxy Allyl Sulfide 33a. To a stirred solution of **61** (53.1 mg, 0.135 mmol) in 10:1 CH_2Cl_2–pyridine (2.69 mL) were added at 0 °C diphenyldisulfide (88.1 mg, 0.404 mmol) and tri-*n*-butylphosphine (0.129 mL, 0.404 mmol). After 2.5 h at rt, the solution was diluted with hexane (10 mL) and water (10 mL). The organic layer was separated and the aqueous layer was extracted with hexane (10 mL × 3). The combined organic layers were washed with brine (10 mL), and dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified with silica-gel column chromatography (3.3 g, 7:1 hexane–EtOAc) to afford **33a** (58.1 mg, 89%) as a colorless syrup: R_f = 0.54 (4:1 hexane–EtOAc); $[\alpha]_D^{29}$ +8.45 (*c* 1.18, $CHCl_3$); IR (neat, cm^{-1}) 3060, 2985, 2935, 2870, 1585, 1480, 1450, 1440, 1380, 1260, 1220, 1190, 1095, 1050, 1010, 870, 845; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (3H, s), 1.28 (3H, s), 1.33 (3H, s), 1.37 (3H, s), 1.39 (3H, s), 1.51–1.65 (8H, m), 1.82 (1H, ddd, *J* = 15.0 Hz, 8.0 Hz, 3.0 Hz), 1.92 (1H, ddd, *J* = 15.0 Hz, 10.5 Hz, 4.0 Hz), 1.84–2.38 (4H, m), 2.99 (1H, dd, *J* = 8.0 Hz, 4.0 Hz), 3.55 (2H, d, *J* = 7.5 Hz), 3.72 (1H, dd, *J* = 10.5 Hz, 4.0 Hz), 3.84 (1H, br d, *J* = 7.0 Hz), 3.97 (1H, dd, *J* = 10.5 Hz, 3.0 Hz), 5.31 (1H, br t, *J* = 7.5 Hz), 5.54 (1H, m), 7.12–7.38 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.3, 18.6, 19.2, 20.2, 24.9, 25.8, 26.7, 28.4, 29.3, 32.3, 37.3, 58.9, 62.2, 67.0, 76.9, 81.4, 82.9, 107.3, 119.9, 120.1, 126.3, 128.9, 130.1, 134.6, 136.7, 139.5; MS (EI) *m*/*z* 486 (M^+); HRMS (EI) *m*/*z* calcd for $C_{29}H_{42}O_4S$ (M^+) 486.2804, found 486.2796.

Isomerization Experiments

Isomerization of 72 to 71. 72 (1.1 mg, 0.00153 mmol) was dissolved in AcOH (0.220 mL) and the solution was stirred at rt for 6.5 days. This solution was concentrated under reduced pressure to afford a 52:48 mixture of **72** and **71** (determined by the ^{1}H NMR analysis). This crude mixture was purified with silica-gel column chromatography (1 g, 2:1 hexane–EtOAc) to afford the desired isomer **71** (0.5 mg, 45%) as a colorless syrup.

4*Z*-Isomer 73 of Methyl Sarcoate (2). A solution of methyl sarcoate (**2**) (1.3 mg, 0.00361 mmol) in dry toluene (0.130 mL) was heated at 100 °C for 12 h. After cooling to rt, the solution was concentrated under reduced pressure to afford a 71:29 mixture of **2** and its 4*Z*-isomer **73** (contaminated with some unidentified products). This crude mixture was purified with preparative TLC on silica gel (2:1 hexane–EtOAc) to afford **73** (contaminated with an unidentified product). This was further purified with preparative TLC on silica gel (5:1 toluene–EtOAc) to afford the pure **73** (0.3 mg, 23%) as a pale yellow syrup: R_f = 0.36 (2:1 hexane–EtOAc), 0.43 (5:1 toluene–EtOAc); $[\alpha]_D^{28}$ +78.4 (*c* 0.30, $CHCl_3$); ^{1}H NMR (300

MHz, $CDCl_3$) δ 0.94 (3H, d, *J* = 6.5 Hz), 0.97 (3H, d, *J* = 6.5 Hz), 1.76 (3H, s), 1.98 (3H, d, *J* = 1.5 Hz), 1.94–2.08 (1H, m), 2.19 (1H, dd, *J* = 13.5 Hz, 3.5 Hz), 2.28–2.42 (1H, m), 2.51–2.68 (2H, m), 2.82 (1H, ddd, *J* = 11.0 Hz, 8.5 Hz, 3.5 Hz), 3.20 (1H, dd, *J* = 13.5 Hz, 8.5 Hz), 3.36–3.50 (1H, m), 3.75 (1H, dd, *J* = 18.0 Hz, 1.5 Hz), 3.77 (3H, s), 3.95 (1H, d, *J* = 18.0 Hz), 6.22 (1H, d, *J* = 1.0 Hz), 6.40–6.52 (1H, m), 7.27 (1H, d, *J* = 1.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.5, 19.7, 20.9, 25.5, 27.3, 30.3, 31.5, 35.3, 41.1, 52.7, 56.7, 124.8, 132.7, 138.4, 140.4, 141.9, 160.5, 167.4, 191.7, 202.2, 208.3; MS (EI) *m*/*z* 360 (M^+); HRMS (EI) *m*/*z* calcd for $C_{21}H_{28}O_5$ (M^+) 360.1937, found 360.1908. Results of NOE and HMBC experiments are shown in Scheme 19.

^{1}H NMR Data of Methyl Sarcoate (2) and Diene 64 in Toluene-d_8.

Methyl Sarcoate (2): ^{1}H NMR (300 MHz, toluene-d_8, 50 °C) δ 0.85 (3H, d, *J* = 6.5 Hz), 0.99 (3H, d, *J* = 6.5 Hz), 1.63 (3H, s), 1.70–2.15 (5H, m), 1.96 (3H, d, *J* = 1.5 Hz), 1.98 (1H, dd, *J* = 13.0 Hz, 3.0 Hz), 2.67 (1H, ddd, *J* = 9.0 Hz, 6.0 Hz, 3.0 Hz), 2.77 (1H, d, *J* = 17.0 Hz), 3.16 (1H, dd, *J* = 13.0 Hz, 9.0 Hz), 3.26 (3H, s), 3.33 (1H, d, *J* = 17.0 Hz), 5.96 (1H, br dd, *J* = 9.0 Hz, 4.0 Hz), 5.98 (1H, br s), 7.15 (1H, s).

Diene 64: ^{1}H NMR (300 MHz, toluene-d_8, 50 °C) δ 1.22 (3H, s), 1.30 (3H, s), 1.34 (3H, s), 1.49 (3H, br s), 1.58 (3H, s), 1.47–1.72 (2H, m), 1.91 (3H, s), 1.87–2.36 (4H, m), 2.68 (1H, dd, *J* = 14.5 Hz, 1.5 Hz), 3.35 (1H, dd, *J* = 14.5 Hz, 8.5 Hz), 3.90–3.99 (1H, br d), 3.99 (1H, dd, *J* = 9.5 Hz, 4.5 Hz), 4.05 (1H, dd, *J* = 8.5 Hz, 1.5 Hz), 5.05 (1H, s), 5.42 (1H, s), 5.52 (1H, m), 6.09 (1H, d, *J* = 5.5 Hz), 6.28 (1H, d, *J* = 5.5 Hz).