TOTAL SYNTHESIS OF CONSTANOLACTONE E, A MARINE EICOSANOID FROM THE ALGA CONSTANTINEA SIMPLEX; ABSOLUTE STRUCTURE OF CONSTANOLACTONE E†*

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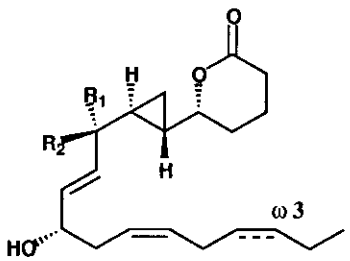
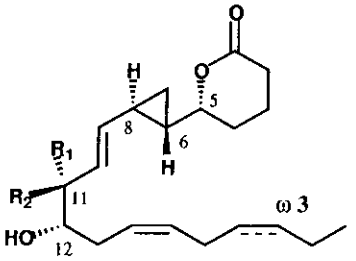
Abstract - Synthesis of marine eicosanoid constanolactone E was achieved through the one-pot formation of chiral cyclopropane derivative (**6**) using the anion of allyl phenyl sulfone and chiral epoxy mesylate (**5**). The absolute structure of constanolactone E was determined as **1** by the present synthesis.

Marine eicosanoids are of considerable interest for their unique structural features, peculiar biosynthetic pathways and biological activities.[1,2] Gerwick *et al.* isolated and determined the structures of constanolactones A-G, lactonized cyclopropyleicosanoids, from the marine red alga *Constantinea simplex* obtained off the Oregon coast.[3,4] Absolute structures of constanolactones A-G were determined through of degradative and spectroscopic methods except for absolute configurations of the C-5, -6 and -8 positions in constanolactones E-G. The synthesis of constanolactones A and B has been conducted by White *et al.*[5,6] The synthesis of marine eicosanoids such as clavulone,[7] chlorovulone[8] and punaglandin[9] was previously reported by the present authors. The stereoselective total synthesis of constanolactone E (**1**) involving the crucial step of one-pot formation of chiral cyclopropane derivative (**6**) using the anion of allyl phenyl sulfone and chiral epoxy mesylate (**5**) was conducted in the present study.[10]



constanolactone A : R_1=OH, R_2=H
constanolactone B : R_1=H, R_2=OH
constanolactone C : (ω 3) R_1=OH, R_2=H
constanolactone D : (ω 3) R_1=H, R_2=OH

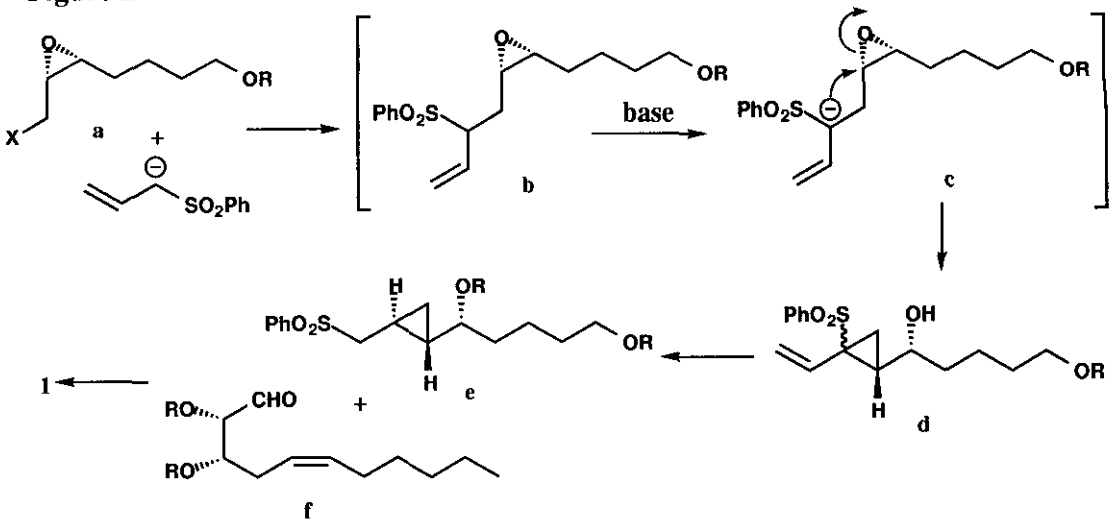


constanolactone E (1) : R_1=OH, R_2=H
constanolactone F : R_1=H, R_2=OH
constanolactone G : (ω 3) R_1=H, R_2=OH

† Dedicated to Professor Koji Nakanishi on the occasion of his 75th birthday.

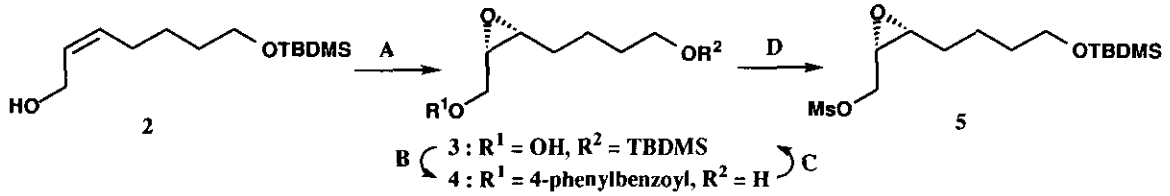
Chiral cyclopentane derivative was previously synthesized using the anion of allyl phenyl sulfone and chiral diepoxide[11] and through this reaction, stereocontrolled synthesis of natural product was carried out.[12] The reaction was applied to the synthesis of chiral cyclopropane derivative and synthesis of constanolactone E (Figure 1). Cyclopropane formation occurs in a one-pot process as follows: 1) an anion of allyl phenyl sulfone reacts with chiral epoxide **a** to give epoxy sulfone **b**, 2) deprotonation of **b** *in situ* generates the anion of epoxy sulfone **c** and 3) cyclization gives chiral cyclopropane derivative **d** possessing requisite chiral centers at C-5 and -6.[13,14] The cyclopropane derivative **d** was converted to sulfone **e**, corresponding to the C-1~9 segment of constanolactone E (**1**) by removal of the phenylsulfonyl group, oxidative cleavage of the double bond, reduction of formyl group, and conversion of hydroxyl group to phenylsulfonyl group. Coupling reaction of sulfone **e** with aldehyde **f**, corresponding to the C-10~20 segment, and following modifications gave constanolactone E (**1**).

Figure 1



Enantiomerically pure epoxy mesylate (**5**) was prepared from (*Z*)-7-*tert*-butyldimethylsiloxy-2-hepten-1-ol (**2**)[15] in the following manner (Scheme 1): Asymmetric epoxidation[16] of allylic alcohol (**2**) gave epoxy alcohol **3** (89% yield). Enantiomeric excess of **3** was 80% ee as determined by ^{1}H NMR analysis of the (*S*)-MTPA ester.[17] Enantiomeric excess of **3** was improved using phenylbenzoate (**4**) as follows: 1) esterification of hydroxyl group as 4-phenylbenzoate by treatment with 4-phenylbenzoic acid and DCC in the presence of DMAP (98% yield), 2) deprotection of the TBDMS group with Bu_4NF (95% yield) to give 4-phenylbenzoate (**4**), 3) recrystallization from $CHCl_3$-hexane (68% yield), 4) protection of the hydroxyl group as TBDMS ether by treatment of TBDMSCl in the presence of diisopropylethylamine (90% yield), and 5) hydrolysis of the 4-phenylbenzoate with K_2CO_3 (98% yield) to give enantiomerically pure epoxy alcohol (**3**), ~100% ee, $[\alpha]_D$ -4.7 ° (*c* 0.51, $CHCl_3$). Epoxy alcohol (**3**) was converted to epoxy mesylate (**5**), $[\alpha]_D$ -7.1° (*c* 0.86, $CHCl_3$), with methanesulfonyl chloride in the presence of DMAP (97% yield).

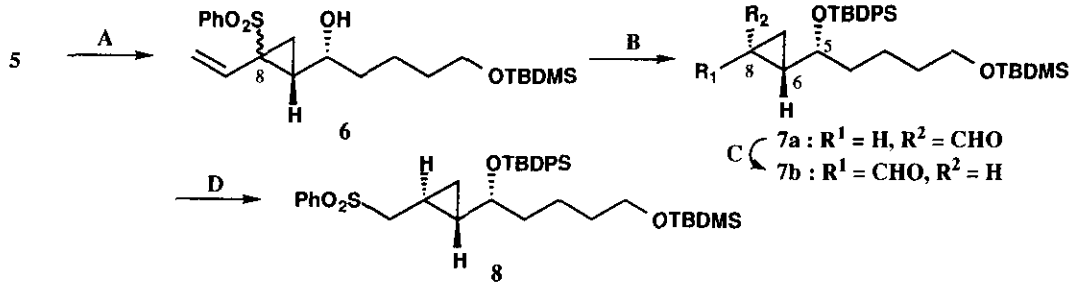
Scheme 1



Reagents and conditions : **A**. TBHP, L-(+)-DET, $Ti(O^iPr)_4$, 4AMS, CH_2Cl_2, -20°C; **B**. i) 4-phenylbenzoic acid, DCC, DMAP, CH_2ClCH_2Cl, rt, ii) Bu_4NF, THF, rt, iii) recrystalization from $CHCl_3$-hexane; **C**. i) TBDMSCl, $^iPr_2NEt$, CH_2ClCH_2Cl, rt, ii) K_2CO_3, MeOH, rt; **D**. MsCl, DMAP, CH_2Cl_2, rt

Reaction of the lithio derivative of allyl phenyl sulfone (2.4 equiv.) with chiral epoxy mesylate (**5**) (1.0 equiv.) in THF at -78°C to room temperature over 12 h, gave chiral cyclopropane (**6**) as a diastereomeric mixture at C-8 in a ratio of 8:1 in 83% yield (Scheme 2).[14,18] Without separating the diastereomers, the hydroxyl group in **6** was protected as *tert*-butyldiphenylsilyl(TBDPS) ether (81% yield), the phenylsulfonyl group was removed by treatment with SmI_2 in the presence of HMPA (92% yield) and the terminal olefin was oxidized by ozone to give a mixture of aldehydes (**7a**) and (**7b**) (**7a** : **7b** = 8 : 1) (80% yield). Epimerization of the C-8 position in **7a** was carried out by treatment with K_2CO_3 in MeOH at 55°C to afford aldehyde (**7b**) predominantly (**7a** : **7b** = 1 : 15)(99% yield), bearing the requisite chiral centers at C-5, C-6, and C-8 corresponding to the C-1~9 segment.[14] The stereochemistry of major aldehyde (**7b**) was confirmed by the NOESY spectrum of **7b**. NOE was observed between the formyl proton at C-9 position and cyclopropyl proton at C-6 position.[14] Aldehyde (**7b**) was converted to sulfone (**8**), $[\alpha]_D$ +25.0° (*c* 0.24, $CHCl_3$), in the following three steps: 1) $NaBH_4$ reduction to alcohol (98% yield), 2) thioetherification by treatment with diphenyl disulfide and tributylphosphine in the presence of pyridine (99% yield), and 3) *m*-CPBA oxidation of phenylthio ether in the presence of Na_2HPO_4 (99% yield).

Scheme 2

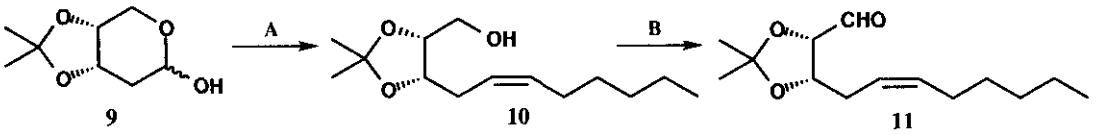


Reagents and conditions : **A**. allyl phenyl sulfone, BuLi, THF, -78°C ~ rt; **B**. i) TBDPSCl, imidazole, DMF, rt, ii) SmI_2, HMPA, THF, rt, iii) O_3, CH_2Cl_2-MeOH, -78°C, Me_2S, rt, C. K_2CO_3, MeOH, 55°C; **D**. i) $NaBH_4$, MeOH, 0°C, ii) PhSSPh, Bu_3P, Py, rt, iii) mCPBA, Na_2HPO_4, CH_2Cl_2, rt

Aldehyde (**11**), corresponding to C-10~20 segment **f**, was synthesized from 2-deoxy-D-ribose-3,4-acetonide (**9**)[19] as follows (Scheme 3): The Wittig reaction of 2-deoxy-D-ribose-3,4-acetonide (**9**) with the ylide, prepared from hexyltriphenylphosphonium bromide and *n*-butyllithium, in THF containing 4

equiv. HMPA gave Z-olefin (**10**) as the sole product in 90% yield. Alcohol (**10**) was oxidized by according to the method of Swern[20] to give aldehyde (**11**), $[\alpha]_D$ -12.3° (*c* 0.99, $CHCl_3$), corresponding to the C-10~20 segment, in quantitative yield.

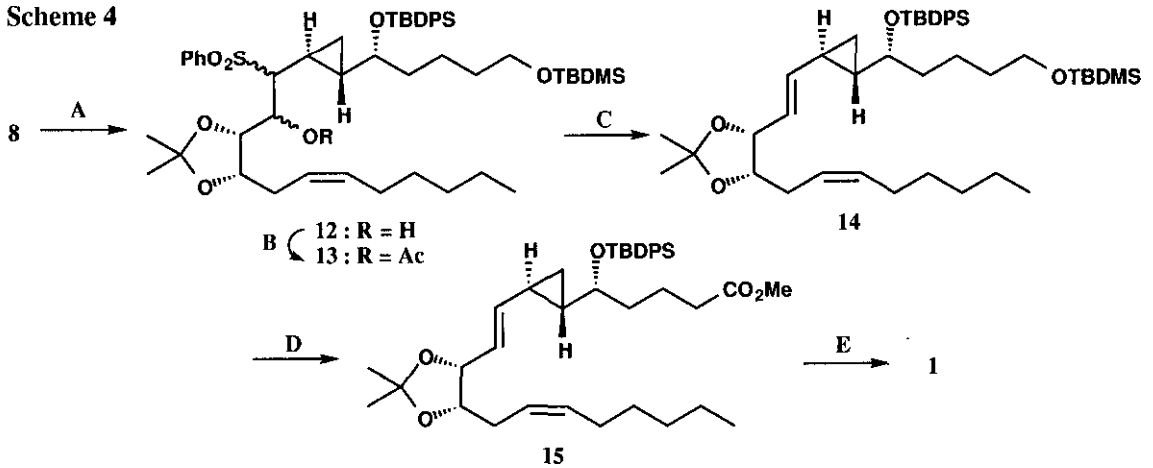
Scheme 3



Reagents and conditions : A. $Ph_3P{=}CH(CH_2)_4Me$, HMPA, THF, -78°C ~ 0°C; B. DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2, -78°C.

Coupling of two segments (**8**) with (**11**) to form olefin was carried out using Julia olefination reaction[21] (Scheme 4). Reaction of the anion of sulfone (**8**) with aldehyde (**11**) afforded alcohol (**12**), mixed with two diastereomers present at a 2 : 1 ratio in 80% yield. Without separation of the diastereomers, alcohol (**12**) was converted to acetate (**13**) with acetic anhydride and pyridine in the presence of DMAP (70% yield), followed by treatment with Na-Hg in THF-MeOH to afford *E*-olefin (**14**) as the sole product in 56% yield. Following the selective deprotection of TBDMS ether in **14** by treatment with AcOH-H_2O-THF = 2 : 1 : 1 (85% yield), the alcohol was converted to methyl ester (**15**) in three steps: 1) oxidation of hydroxyl group to formyl group with PDC, 2) oxidation of aldehyde to carboxylic acid with $NaClO_2$, and 3) esterification of carboxylic acid with CH_2N_2 in 85% yield (three steps). Deprotection of acetonide in **15** was done with AcOH-H_2O = 4 : 1 (77% yield) and the TBDPS group was removed by treatment with Bu_4NF in DMF at 45°C, lactonization by acid treatment completed the synthesis of constanolactone E (**1**), $[\alpha]_D$ +34° (*c* 0.18, MeOH), in 65% yield. The spectral data and optical rotation of **1** thus obtained were identical to those of reported data of natural constanolactone E, $[\alpha]_D$ +33° (*c* 0.22, MeOH),[4] in every respects. This synthesis confirmed the absolute configuration of constanolactone E to be 5*R*, 6*S*, 8*R*, 11*R*, and 12*S*.

Scheme 4



Reagents and conditions : A. BuLi, THF, -78°C, then **11**; B. Ac_2O, Py, DMAP, rt; C. i) Na-Hg, MeOH-THF, 0°C; D. i) AcOH-H_2O-THF, rt, ii) PDC, 4AMS, CH_2Cl_2, rt, iii) $NaClO_2$, ^tBuOH-H_2O, 0°C, iv) CH_2N_2, Et_2O, 0°C, E. i) AcOH-H_2O (4:1), rt, ii) Bu_4NF, DMF, 45°C, then 1*N* HCl.

EXPERIMENTAL

Melting points were measured on a Yazawa BY-2 micro melting point apparatus and uncorrected. Optical rotations were measured with a JASCO DIP-360 automatic polarimeter. IR spectra were recorded on a Perkin-Elmer FT-IR 1710 spectrophotometer. NMR spectra were recorded with a Bruker AM-400 (400 MHz) or a Varian Gemini-300 (300 MHz). Electron impact MS (EIMS) spectra and high resolution MS spectra (HRMS) were taken with a Hitachi M-80 or VG Auto Spec spectrometer. Elemental analysis was conducted using a Perkin-Elmer 242.

(2*S*,3*R*)-7-*tert*-Butyldimethylsiloxy-2,3-epoxyheptanol (3). A mixture of powdered 4A molecular sieves (300 mg) and CH_2Cl_2 (9.0 mL) was cooled to 0 °C, followed by the addition of D-(-)-diethyl tartrate (DET) (0.105 mL, 0.61 mmol) and Ti(*i*-PrO)$_4$ (0.12 mL, 0.407 mmol) in this order. After cooling the mixture to -20 °C, *tert*-butyl hydroperoxide (TBHP) (2.7 mL, 8.1 mmol, 3.0 M in CH_2Cl_2) was added, followed by stirring for 20 min, and then adding allylic alcohol (**2**) (1.0 g, 8.1 mmol) in CH_2Cl_2 (1.0 mL). Stirring was continued at -20 °C for 10 h. The reaction mixture was warmed to 0 °C, water (3.0 mL) was added and the mixture was stirred for 1 h and allowed to rt for 1 h. Aqueous solution of NaOH (30 %) saturated with NaCl (1.0 mL) was added and the mixture was stirred vigorously. After 1 h stirring, the mixture was filtered through celite. The filtrate was diluted with Et_2O, washed with 1*N* NaOH, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 3 : 1) to give epoxy alcohol (**3**) (942 mg, 89 %, enantiomeric excess was 80% ee as determined by ^{1}H-NMR analysis of the (*S*)-MTPA ester) as a colorless oil, $[\alpha]_D$ -4.1° (*c* 0.50, $CHCl_3$). IR ν_{max} (neat): 3418, 2931 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.05 (6H, s), 0.89 (9H, s), 1.45-1.65 (5H, m), 1.68 (1H, dd, *J* = 5.1, 7.1 Hz), 3.03 (1H, m), 3.15 (1H, td, *J* = 4.3, 6.7 Hz), 3.63 (2H, t, *J* = 6.0 Hz), 3.68 (1H, ddd, *J* = 5.1, 6.7, 11.9 Hz), 3.84 (1H, ddd, *J* = 4.3, 7.3, 11.9 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.3, 18.3, 23.0, 25.9, 27.7, 32.4, 56.8, 57.2, 60.8, 62.8. EIMS *m/z* (rel. intensity, %) 203 (1), 185 (9), 117 (100). HRMS Calcd for $C_9H_{17}O_2Si$ (M^+-^{t}BuOH): 185.0998. Found: 185.0983.

(2*S*,3*R*)-2,3-Epoxy-7-hydroxyheptyl 4-phenylbenzoate (4). To a solution of alcohol (**3**) (80% ee) (100 mg, 0.38 mmol) in CH_2Cl_2 (3.0 mL) were added DMAP (93 mg, 0.76 mmol), DCC (236 mg, 1.2 mmol) and 4-phenylbenzoic acid (150 mg, 0.76 mmol). The mixture was stirred at rt for 30 min, diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 14 : 1) to give 4-phenylbenzoate (164 mg, 98 %) as a colorless oil. IR ν_{max} (neat): 2931, 1723 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.90 (9H, s), 1.50-1.70 (6H, m), 3.10 (1H, m), 3.35 (1H, td, *J* = 4.3, 7.0 Hz), 3.64 (2H, t, *J* = 5.8 Hz), 4.32 (1H, dd, *J* = 7.0, 12.1 Hz), 4.60 (1H, dd, *J* = 4.3, 12.1 Hz), 7.40 (1H, m), 7.48 (2H, m), 7.65 (4H, m), 8.15 (2H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.3, 18.3, 23.1, 25.9, 27.9, 32.5, 53.8, 56.5,62.8, 63.4, 127.1, 127.3, 128.2, 128.4, 128.9, 130.3, 139.9, 145.9, 166.3. EIMS *m/z* (rel. intensity, %) 383 (M^+-^{t}Bu, 5), 255 (35), 181 (100). HRMS Calcd for $C_{22}H_{27}O_4Si$ (M^+-^{t}Bu): 383.1679. Found: 383.1661.

To a solution of the above 4-phenylbenzoate (200 mg, 0.454 mmol) in THF (1.0 mL) was added Bu_4NF (10 mL, 10 mmol, 1 M in THF), followed by stirring at rt for 3 h. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 5 : 1) to give crude crystals which were recrystallized from $CHCl_3$-hexane (about 1 : 1) to give alcohol (**4**) (99 mg, 67 %) as colorless rods, mp 85 - 89 °C, $[\alpha]_D$ -11.5° (*c* 0.70, $CHCl_3$). IR ν max (neat): 3329, 2927, 1713 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.60-1.75 (6H, m), 3.10 (1H, m), 3.36 (1H, td, *J* = 4.4, 6.8 Hz), 3.69 (2H, m), 4.34 (1H, dd, *J* = 6.8, 12.1 Hz), 4.60 (1H, dd, *J* = 4.4, 12.1 Hz), 7.41 (1H, m), 7.48 (2H, m), 7.63 (2H, m), 7.68 (2H, m), 8.15 (2H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 22.9, 27.7, 32.2, 53.8, 56.5, 62.4, 63.2, 127.0, 127.2, 128.2, 128.3, 128.9, 130.2, 139.8, 145.9, 166.3. EIMS *m/z* (rel. intensity, %) 326 (M^+, 6), 181 (75), 152 (100). HRMS Calcd for $C_{20}H_{22}O_4$ (M^+): 326.1522. Found: 326.1518.

(2*S*,3*R*)-7-*tert*-Butyldimethylsiloxy-2,3-epoxyheptanol (optically pure) (3). A solution of alcohol (**4**) (22 mg, 0.087 mmol) in $ClCH_2CH_2Cl$ (0.8 mL) following treatment with *i*-Pr_2NEt (0.044 mL, 0.256 mmol) and TBDMS-Cl (20 mg, 0.128 mmol) was stirred at rt for 3 h, diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue thus obtained was purified by silica gel column chromatography (eluted with hexane - EtOAc = 14 : 1) to give silyl ether (35 mg, 90 %) as a colorless oil, $[\alpha]_D$ -10.0° (*c* 1.09, $CHCl_3$).

A solution of the above 4-phenylbenzoate (200 mg, 0.45 mmol) in MeOH (10 mL) to which had been added K_2CO_3 (70 mg, 0.506 mmol) was stirred at rt for 30 min, diluted with Et_2O and filtered through silica gel. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 3 : 1) to give alcohol (**3**) (115 mg, 98 %, enantiomeric excess was 100% ee as determined by ^{1}H-NMR analysis of the (*S*)-MTPA ester) as a colorless oil, $[\alpha]_D$ -4.7° (*c* 0.51, $CHCl_3$).

(2*S*,3*R*)-7-*tert*-Butyldimethylsiloxy-2,3-epoxyheptyl (*S*)-2-methoxy-2-trifluoromethylphenylacetate. To a solution of alcohol (**3**) (purified) (20 mg, 0.077 mmol) in CH_2Cl_2 (1.5 mL) were added DMAP (20 mg, 0.15 mmol), DCC (48 mg, 0.15 mmol) and (*S*)-2-methoxy-2-trifluoromethylphenylacetic acid (MTPA) (150 mg, 0.76 mmol). The mixture was stirred at rt for 35 min, diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on silica gel column (eluted with hexane - EtOAc = 10 : 1) to give MTPA ester (36 mg, 97 %) as a colorless oil, $[\alpha]_D$ -44.0° (*c* 0.67, $CHCl_3$). Any diastereomer of the MTPA ester was not observed by ^{1}H-NMR. IR ν max (neat): 2931, 1753 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.04 (6H, s), 0.89 (9H, s), 1.50-1.60 (6H, m), 3.02 (1H, m), 3.23 (1H, td, *J* = 4.5, 6.8 Hz), 3.57 (3H, q, *J* = 1.2 Hz), 3.61 (2H, t, *J* = 5.8 Hz), 4.34 (1H, dd, *J* = 6.8, 12.0 Hz), 4.51 (1H, dd, *J* = 4.5, 12.0 Hz), 7.38-7.45 (3H, m), 7.50-7.60 (2H, m). EIMS *m/z* (rel.

intensity, %) 419 (M^+-^{t}Bu, 5), 290 (10), 189 (35), 57 (100). HRMS Calcd for $C_{19}H_{26}O_5F_3Si$ (M^+-^{t}Bu): 419.1501. Found: 419.1514.

(2*S*,3*R*)-7-*tert*-Butyldimethylsiloxy-2,3-epoxyheptyl methanesulfonate (5). A solution of alcohol (**3**) (100% ee) (3.0 g, 11.5 mmol) in CH_2Cl_2 (115 mL) containing DMAP (4.2 g, 34.6 mmol) and methanesulfonyl chloride (1.9 mL, 17.3 mmol) was stirred at 0 °C for 2 h, diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 4 : 1) to give mesylate (**5**) (3.8 g, 97 %) as a colorless oil, $[\alpha]_D$ -7.1° (*c* 0.86, $CHCl_3$). IR ν max (neat): 2932 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.05 (6H, s), 0.89 (9H, s), 1.50-1.65 (6H, m), 3.07 (1H, m), 3.09 (3H, s), 3.27 (1H, td, *J* = 4.1, 7.3 Hz), 3.63 (2H, t, *J* = 5.7 Hz), 4.23 (1H, dd, *J* = 7.3, 11.6 Hz), 4.45 (1H, dd, *J* = 4.1, 11.6 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.4, 18.3, 23.0, 25.9, 27.7, 32.3, 37.8, 53.3, 56.7, 62.6, 68.2. EIMS *m/z* (rel. intensity, %) 280 (M^+-^{t}Bu, 1), 152 (15), 79 (100). *Anal.* Calcd for $C_{14}H_{30}O_5SSi$: C, 49.67; H, 8.93. Found: C, 49.72; H, 8.86.

(1*RS*,2*R*,1'*R*)-2-(5'-*tert*-Butyldimethylsiloxy-1'-hydroxypentyl)-1-phenylsulfonyl-1-vinylcyclopropane (6). To a cold (-78 °C) solution of allyl phenyl sulfone (5.2 g, 28.8 mmol) in THF (90 mL) was added BuLi (18.5 mL, 27.8 mmol, 1.50 M in hexane). The mixture was stirred at -78 °C for 30 min, treated with a solution of epoxy mesylate (**5**) (3.8 g, 11.1 mmol) in THF (10 mL) and stirred for 30 min and warmed to rt over 5 h, and then stirred for 1 h at rt. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 4 : 1) to give an epimeric mixture of alcohol (**6**) (3.9 g, 83 %) in a ratio of 8 : 1. A part of a mixture of the alcohols was separated for the spectral analysis by silica gel column chromatography (eluted with hexane - EtOAc = 4 : 1). **major product**: $[\alpha]_D$ +58.1° (*c* 0.27, $CHCl_3$). IR ν max (neat): 3452, 2930 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.04 (6H, s), 0.89 (9H, s), 1.07 (1H, t, *J* = 6.2 Hz), 1.44 (1H, m), 1.52 (4H, m), 1.60-1.70 (2H, m), 1.74 (1H, dd, *J* = 5.7, 9.8 Hz), 2.24 (1H, dt, *J* = 6.7, 9.8 Hz), 3.07 (1H, m), 3.61 (2H, t, *J* = 6.2 Hz), 5.18 (1H, d, *J* = 17.0 Hz), 5.41 (1H, d, *J* = 10.3 Hz), 6.10 (1H, dd, *J* = 10.3, 17.0 Hz), 7.52 (2H, m), 7.62 (1H, m), 7.84 (2H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.3, 14.2, 18.4, 21.9, 26.0, 30.9, 32.6, 36.7, 48.5, 63.0, 70.9, 77.2, 124.7, 128.2, 128.8, 128.9, 133.4, 138.2. EIMS *m/z* (rel. intensity, %) 424 (M^+, 0.5), 407 (2), 367 (19), 57 (100). HRMS Calcd for $C_{22}H_{36}O_4SSi$ (M^+): 424.2116. Found: 424.2122. **minor product**: IR ν max (neat): 3501, 2928 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.90 (9H, s), 1.44 (1H, dd, *J* = 5.3, 9.1 Hz), 1.50-1.70 (6H, m), 1.83 (1H, dd, *J* = 5.3, 7.8 Hz), 2.84 (1H, d, *J* = 3.0 Hz), 3.64 (2H, t, *J* = 6.0 Hz), 4.25 (1H, m), 5.03 (1H, d, *J* = 17.0 Hz), 5.10 (1H, d, *J* = 10.2 Hz), 5.94 (1H, dd, *J* = 10.2, 17.0 Hz), 7.54 (2H, m), 7.64 (1H, m), 7.86 (2H, m).

(1*S*,2*R*,1'*R*)-1-(5'-*tert*-Butyldimethylsiloxy-1'-*tert*-butyldiphenylsiloxypentyl)-2-formylcyclopropane (7a) and (1*S*,2*S*,1'*R*)-1-(5'-*tert*-butyldimethylsiloxy-1'-*tert*-butyl-

diphenylsiloxypentyl)-2-formylcyclopropane (7b). A solution of alcohols (**6a**) and (**6b**) (4.9 g, 11.5 mmol) in DMF (12 mL) was treated with imidazole (2.4 g, 34.7 mmol) and *tert*-butyldiphenylsilyl chloride (TBDPS-Cl) (4.5 mL, 17.3 mmol), stirred at rt for 4 h, diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 10 : 1) to give a ratio of 8 : 1 silyl ether mixture (8.0 g, 96 %). A part of a mixture of the silyl ethers was separated for the spectral analysis by silica gel column chromatography (eluted with hexane - EtOAc = 10 : 1). **major product**: $[\alpha]_D$ +30.1° (*c* 0.71, $CHCl_3$). IR ν max (neat): 2931 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.01 (6H, s), 0.87 (9H, s), 0.95 (9H, s), 1.10-1.60 (7H, m), 1.64 (1H, dd, *J* = 5.8, 9.4 Hz), 2.41 (1H, dt, J = 6.8, 9.4 Hz), 3.13 (1H, m), 3.44 (2H, t, *J* = 6.3 Hz), 4.88 (1H, d, *J* = 17.0 Hz), 5.04 (1H, d, *J* = 10.2 Hz), 5.86 (1H, dd, *J* = 10.2, 17.0 Hz), 7.30-7.60 (13H, m), 7.82 (2H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.3, 13.1, 18.3, 19.1, 20.9, 25.9, 26.9, 30.6, 32.7, 37.6, 48.5, 62.9, 71.9, 123.5, 127.3, 127.5, 128.5, 128.7, 128.9, 129.0, 129.5, 133.2, 133.6, 134.3, 135.9, 138.6. EIMS *m/z* (rel. intensity, %) 605 (M^+-^{t}Bu, 30), 397 (20), 336 (25), 57 (100). HRMS Calcd for $C_{34}H_{45}O_4SSi_2$ (M^+-^{t}Bu): 605.2577. Found: 605.2560.

To a solution of SmI_2 (400 mL, 48.2 mmol, 0.12 M in THF), HMPA (65 mL) was added followed by stirring at rt for 15 min. The above diastereomeric mixture of sulfones (4.0 g, 6.00 mmol) in THF (25 mL) was then added and the mixture was stirred at rt for 30 min, diluted with Et_2O and H_2O and filtered through celite. The filtrate was washed with 1*N* NaOH, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 10 : 1) to give a diastereomeric mixture of olefins (2.9 g, 92 %) in a ratio of 8 : 1. A part of a mixture of the olefins was separated for the spectral analysis by silica gel column chromatography (eluted with hexane - EtOAc = 10 : 1). **major product**: IR ν max (neat): 2931 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.03 (6H, s), 0.22 (1H, m), 0.82 (1H, m), 0.89 (9H, s), 1.02 (9H, s), 1.26 (1H, m), 1.30-1.60 (7H, m), 3.37 (1H, td, *J* = 5.1, 8.8 Hz), 3.52 (2H, t, *J* = 6.1 Hz), 4.64 (1H, dd, *J* = 2.0, 10.2 Hz), 4.79 (1H, dd, *J* = 1.4, 17.0 Hz), 5.20 (1H, ddd, *J* = 8.4, 10.2, 17.0 Hz), 7.30-7.45 (6H, m), 7.65-75 (4H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.3, 9.6, 18.4, 19.4, 20.2, 21.3, 23.8, 25.4, 26.0, 26.8, 27.0, 33.0, 38.3, 63.2, 72.8, 114.1, 127.1, 127.2, 129.3, 134.5, 134.6, 136.0, 137.7. EIMS *m/z* (rel. intensity, %) 465 (M^+-^{t}Bu, 3), 199 (90), 135 (100). *Anal.* Calcd for $C_{31}H_{48}O_3Si_2$: C, 73.5; H, 9.64. Found: C, 73.35; H, 9.49.

A cold (-78 °C) solution of the above diastereomeric mixture of olefins (2.7 g, 5.20 mmol) in CH_2Cl_2 (80 mL) and MeOH (20 mL) was treated with ozone until blue color persisted. Excess ozone was removed by a flow of argon. The reaction mixture was treated with Me_2S (3.0 mL), allowed to warm slowly to rt over 2 h, stirred for 8 h at this temperature and concentrated under reduced pressure. The residue was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 14 : 1) to give a mixture of aldehydes (**7a**) and (**7b**) (2.6 g, 94 %) in a ratio of 8 : 1. Mixture of the aldehydes was separated by silica gel column chromatography (eluted with hexane - EtOAc = 14 : 1). **7a**: IR ν max (neat): 2930, 1707 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.01 (6H, s), 0.87

(9H, s), 1.02 (9H, s), 1.10-1.60 (8H, m), 1.68 (1H, m), 1.81 (1H, m), 3.47 (2H, t, J = 6.0 Hz), 3.75 (1H, m), 7.30-7.45 (6H, m), 7.60-7.70 (4H, m), 9.01 (1H, d, J = 5.3 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.3, 11.9, 18.3, 19.3, 21.3, 26.0, 27.0, 27.7, 30.5, 32.7, 38.4, 63.0, 71.1, 127.5, 127.6, 129.7, 133.7, 134.1, 135.9, 201.1. EIMS *m/z* (rel. intensity, %) 467 (M^+-^{t}Bu, 1), 251(20), 75 (100). *Anal.* Calcd for $C_{31}H_{48}O_3Si_2$: C, 70.94; H, 9.22. Found: C, 70.85; H, 9.29. **7b**: IR ν max (neat): 2953, 1709 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.04 (6H, s), 0.82 (1H, m), 0.89 (9H, s), 1.02 (9H, s), 1.16 (1H, m), 1.20-1.60 (7H, m), 1.67 (1H, m), 3.27 (1H, m), 3.54 (2H, t, J = 5.9 Hz), 7.35-7.45 (6H, m), 7.65-7.70 (4H, m), 8.89 (1H, dd, J = 0.7, 4.6 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.3, 12.5, 18.3, 19.3, 21.2, 26.0, 26.9, 28.2, 28.9, 32.9, 37.6, 63.0, 74.5, 127.6, 127.7, 129.7, 129.8, 133.8, 133.9, 135.8, 200.6. EIMS *m/z* (rel. intensity, %) 467 (M^+-^{t}Bu, 1), 251 (18), 75 (100). *Anal.* Calcd for $C_{31}H_{48}O_3Si_2$: C, 70.94; H, 9.22. Found: C, 70.70; H, 9.21.

Isomerization of aldehyde (7a) to aldehyde (7b). To a solution of diastereomeric mixture of aldehydes (**7a**) and (**7b**) (8 : 1) (2.4 g, 4.50 mmol) in MeOH (65 mL) was added K_2CO_3 (2.5 g, 18.1 mmol). The mixture was stirred at 55 °C for 16 h, diluted with Et_2O and filtered through silica gel. The filtrate was concentrated under reduced pressure and then the residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 10 : 1) to give a mixture of aldehydes (**7a**) and (**7b**) (2.30 g, 92 %) in a ratio of 1 : 15.

(1*S*,2*S*,1'*R*)-1-(5'-*tert*-Butyldimethylsiloxy-1'-*tert*-butyldiphenylsiloxypentyl)-2-phenylsulfonylmethylcyclopropane (8). To a solution of aldehyde (**7b**) (200 mg, 0.38 mmol) in MeOH (5.0 mL) was added $NaBH_4$ (30 mg, 0.76 mmol). The mixture was stirred at 0 °C for 30 min, treated with saturated aqueous NaCl and concentrated under reduced pressure. The residue was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 4 : 1) to give alcohol (184 mg, 92 %) as a colorless oil, $[\alpha]_D$ +6.2 ° (*c* 1.20, $CHCl_3$). IR ν max (neat): 3349, 2932 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.04 (6H, s), 0.21 (1H, td, J = 4.9, 8.5 Hz), 0.29 (1H, td, J = 4.9, 8.8 Hz), 0.57 (1H, m), 0.86 (1H, m), 0.89 (9H, s), 1.02 (9H, s), 1.40-1.50 (4H, m), 1.50-1.60 (2H, m), 3.05 (1H, m), 3.09 (1H, td, J = 5.4, 8.1 Hz), 3.21 (1H, dd, J = 6.2, 10.9 Hz), 3.56 (2H, t, J = 6.1 Hz), 7.35-7.45 (6H, m), 7.65-7.75 (4H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ –5.3, 7.6, 18.3, 19.4, 19.9, 21.4, 23.3, 26.0, 27.0, 33.0, 37.7, 63.1, 66.1, 76.6, 76.6, 127.5, 127.6, 129.5, 129.6, 133.9, 134.6, 135.8, 135.9. EIMS *m/z* (rel. intensity, %) 469 (M^+-^{t}Bu, 1), 339 (8), 199 (100). *Anal.* Calcd for $C_{31}H_{50}O_3Si_2$: C, 70.67; H, 9.56. Found: C, 70.51; H, 9.46.
To a solution of the above alcohol (4.5 g, 8.60 mmol) in pyridine (7.0 mL) were added PhSSPh (9.2 g, 42.0 mmol) and Bu_3P (10.5 mL, 42.0 mmol). The mixture was stirred at 0 °C for 3 h, diluted with Et_2O, washed with 5 % aqueous NaOH, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 14 : 1) to give sulfide (5.3 g, 99 %) as a colorless oil, $[\alpha]_D$ +56.0 ° (*c* 0.47, $CHCl_3$). IR ν max (neat): 2930 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.03 (6H, s), 0.24 (1H, m), 0.30

(1H, td, J = 5.0, 8.7 Hz), 0.56 (1H, m), 0.89 (9H, s), 0.91 (1H, m), 1.00 (9H, s), 1.35-1.60 (6H, m), 1.52 (2H, m), 2.12 (1H, dd, J = 9.4, 12.9 Hz), 2.84 (1H, dd, J = 4.7, 12.9 Hz), 3.01 (1H, m), 3.55 (2H, t, J = 6.1 Hz), 7.10-7.45 (11H, m), 7.60-7.75 (4H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ −5.3, 10.2, 16.8, 18.4, 19.4, 21.4, 26.0, 27.0, 33.0, 37.6, 37.8, 63.2, 125.5, 127.4, 127.5, 128.7, 128.7, 129.5, 129.5, 133.8, 134.5, 135.9, 136.0, 137.0, EIMS m/z (rel. intensity, %) 561 (M^+-^{t}Bu, 2), 213 (15), 199 (28), 135 (58), 123 (95), 57 (100). *Anal.* Calcd for $C_{37}H_{54}O_2SSi_2$: C, 71.79; H, 8.79. Found: C, 71.59; H, 8.75.

To a solution of the above sulfide (5.0 g, 8.09 mmol) in CH_2Cl_2 (90 mL) was added *m*-CPBA (4.57 g (70%), 18.5 mmol). The mixture was stirred at 0 °C for 1 h, diluted with Et_2O, washed with saturated aqueous NaOH, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 6 : 1) to give sulfone (**8**) (5.9 g, 99 %) as a colorless oil, $[\alpha]_D$ +25.0 ° (c 0.24, $CHCl_3$). IR ν max (neat): 2930 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.03 (6H, s), 0.20 (1H, m), 0.28 (1H, m), 0.34 (1H, m), 0.75 (1H, m), 0.88 (9H, s), 0.96 (9H, s), 1.35-1.60 (6H, m), 2.09 (1H, dd, J = 10.5, 14.4 Hz), 2.83 (1H, dd, J = 3.3, 14.4 Hz), 2.95 (1H, m), 3.55 (2H, t, J = 5.7 Hz), 7.25-7.75 (15H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ −5.3, 9.6, 11.1, 18.3, 19.3, 21.5, 24.3, 26.0, 26.1, 26.9, 32.9, 37.5, 59.7, 63.1, 76.5, 127.5, 127.6, 128.2, 129.0, 129.7, 133.4, 133.5, 134.3, 135.7, 135.8, 139.1. EIMS m/z (rel. intensity, %) 593 (M^+-^{t}Bu, 7), 323 (15), 259 (38), 199 (38), 57 (100). HRMS Calcd for $C_{33}H_{45}O_4SSi_2$ (M^+-^{t}Bu): 593.2577. Found: 593.2561.

(*Z*)-(2*R*,3*S*)-2,3-Dihydroxy-2,3-*O*-isopropylidene-5-undecen-1-ol (10). To a suspension of hexyltriphenylphosphonium bromide (10.3 g, 24.0 mmol) in THF (75 mL) was added BuLi (16.4 mL, 23.0 mmol, 1.40 M in hexane). The mixture was stirred at 0 °C for 30 min, cooled to -78°C, treated with HMPA (8.0 mL, 46.0 mmol) and stirred at -78°C for 30 min and then with a solution of acetonide (**9**)[19] (1.60 g, 11.1 mmol) in THF (5.0 mL) and stirred and warmed to 0 °C over 1 h, and then for 1 h at 0 °C. The reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 4 : 1) to give alcohol (**10**) (2.0 g, 90 %) as a colorless oil, $[\alpha]_D$ +7.5 ° (c 0.44, $CHCl_3$). IR ν max (neat): 3435, 2935 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 6.9 Hz), 1.20-1.40 (6H, m), 1.36 (3H, s), 1.48 (3H, s), 2.02 (2H, m), 2.29 (1H, m), 2.35 (1H, m), 3.64 (2H, m), 4.18 (2H, m), 5.36 (1H, m), 5.52 (1H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.0, 22.5, 25.4, 27.3, 27.5, 28.1, 29.1, 31.5, 61.7, 76.7, 77.8, 108.2, 124.2, 132.9. EIMS m/z (rel. intensity, %) 242 (M^+, 1), 227 (8), 131 (100). HRMS Calcd for $C_{13}H_{23}O_3$ (M^+-Me): 227.1647. Found: 227.1638.

(*Z*)-(2*S*,3*S*)-2,3-Dihydroxy-2,3-*O*-isopropylidene-5-undecenal (11). To a cold (-78°C) solution of oxalyl chloride (0.95 mL, 11.0 mmol) in CH_2Cl_2 (27 mL) was added DMSO (1.0 mL, 14.0 mmol) in CH_2Cl_2 (1.0 mL). The mixture was stirred at -78 °C for 30 min, treated with a solution of alcohol (**10**) (850 mg, 3.50 mmol) in CH_2Cl_2 (2 mL) and stirred for 15 min and then with Et_3N (2.5 mL,

17.5 mmol). The mixture was stirred for 15 min and warmed to rt over 1 h and stirred for 1 h. The reaction mixture was diluted with Et_2O - benzene (4 : 1), washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 2 : 1) to give aldehyde (**11**) (2.0 g, quantitative yield) as a colorless oil, $[\alpha]_D$ -12.3 ° (*c* 0.99, $CHCl_3$). IR ν max (neat): 2931, 1735 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.87 (3H, t, *J* = 6.8 Hz), 1.20-1.40 (6H, m), 1.40 (3H, s), 1.59 (3H, s), 1.99 (2H, m), 2.31 (2H, br t, *J* = 6.8 Hz), 4.30 (1H, dd, *J* = 3.1, 7.2 Hz), 4.37 (1H, m), 5.38 (1H, m), 5.53 (1H, m), 9.66 (1H, d, *J* = 3.1 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.0, 22.5, 25.2, 27.4, 27.5, 27.8, 29.0, 31.4, 78.4, 81.9, 123.4, 133.5, 201.6. EIMS *m/z* (rel. intensity, %) 241 (M^++1, 2), 225 (7), 129 (100). HRMS Calcd for $C_{13}H_{21}O_3$ (M^+-Me): 225.1491. Found: 225.1501.

(*Z*)-(1*S*,2*S*,3'*S*,4'*S*,1''*R*)-1-(5'-*tert*-Butyldimethylsiloxy-1'-*tert*-butyldiphenylsiloxypentyl)-2-(2',3',4'-trihydroxy-3',4'-*O*-isopropylidene-1'-phenylsulfonyl-6'-undecenyl)cyclopropane (12). To a cold (-78°C) solution of sulfone (**8**) (500 mg, 0.76 mmol) in THF (6.0 mL) was added BuLi (0.57 mL, 0.827 mmol, 1.45 M in hexane). The mixture was stirred at -78 °C for 1 h, treated with a solution of aldehyde (**11**) (288 mg, 1.2 mmol) in THF (5.0 ml), stirred for 1 h and warmed to rt over 1 h and stirred again for 1 h. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 4 : 1) to give two diastereomeric mixture of alcohol (**12**) (2.0 g, 80 %) in a ratio of 2 : 1. IR ν max (neat): 3470, 2931 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.03 (6H, s), 0.24 (1H, dt, *J* = 5.1, 8.3 Hz), 0.30 (1H, dt, *J* = 5.0, 8.7 Hz), 0.55 (1H, ddd, *J* = 5.0, 9.7, 18.5 Hz), 0.88 (3H, t, *J* = 6.9 Hz), 0.89 (9H, s), 0.91 (1H, m), 1.00 (6H, s), 1.29 (6H, m), 1.36 (3H, s), 1.41 (4H, m), 1.48 (3H, s), 1.52 (2H, m), 2.03 (2H, m), 2.12 (2H, dd, *J* = 9.4, 12.9 Hz), 2.29 (1H, m), 2.35 (1H, m), 3.01 (1H, dt, *J* = 5.0, 8.0 Hz), 3.55 (2H, t, *J* = 6.1 Hz), 3.64 (2H, m), 4.18 (1H, m), 5.36 (1H, m), 5.52 (1H, m), 7.22 (5H, m), 7.39 (6H, m), 7.68 (4H, m).

(*Z*)-(1*S*,2*S*,3'*S*,4'*S*,1''*R*)-1-(5'-*tert*-Butyldimethylsiloxy-1'-*tert*-butyldiphenylsiloxypentyl)-2-(2'-acetoxy-3',4'-dihydroxy-3',4'-*O*-isopropylidene-1'-phenylsulfonyl-6'-undecenyl)cyclopropane (13). To a solution of alcohol (**12**) (500 mg, 0.56 mmol) in pyridine (10 mL) was added acetic anhydride (10 mL) and DMAP (20 mg, 0.16 mmol). The mixture was stirred at rt for 12 h and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 5 : 1) to give two diastereomeric mixtures of acetate (**13**) (366 mg, 70 %) in a ratio of 2 : 1.

(1'*E*,6'*Z*)-(1*S*,2*R*,3'*S*,4'*S*,1''*R*)-1-(5'-*tert*-Butyldimethylsiloxy-1'-*tert*-butyldiphenylsiloxypentyl)-2-(3',4'-dihydroxy-3',4'-*O*-isopropylideneundec-1',6'-dienyl)cyclopropane (14). To a cold (0°C) solution of sulfone (**13**) (50 mg, 0.054 mmol) in MeOH (1.6 mL) and THF (0.4 mL) were added Na_2HPO_4 (500 mg) and 5% Na-Hg (500 mg). The mixture was stirred at 0 °C

for 1 h, diluted with Et_2O and filtered through silica gel. The filtrate was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 9 : 1) to give olefin (**14**) (22 mg, 56 %) as a colorless oil, $[\alpha]_D$ +20.4 ° (*c* 0.50, $CHCl_3$). IR ν max (neat): 2931 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.03 (6H, s), 0.44 (1H, td, *J* = 4.9, 8.7 Hz), 0.50 (1H, td, *J* = 4.9, 8.3 Hz), 0.87 (3H, t, *J* = 6.8 Hz), 0.88 (9H, s), 0.95 (1H, m), 1.02 (9H, s), 1.20-1.60 (12H, m), 1.34 (3H, s), 1.47 (3H, s), 2.03 (4H, m), 2.27 (1H, m), 3.10 (1H, m), 3.52 (2H, t, *J* = 6.1 Hz), 4.04 (1H, td, *J* = 5.8, 9.1 Hz), 4.38 (1H, dd, *J* = 5.8, 8.2 Hz), 5.14 (1H, dd, *J* = 8.2, 15.3 Hz), 5.31 (1H, dd, *J* = 8.2, 15.3 Hz), 5.37 (1H, m), 5.49 (1H,m), 7.30-7.45 (6H, m), 7.60-7.75 (4H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ -5.3, 11.4, 14.0, 18.3, 19.4, 19.7, 21.1, 22.5, 25.6, 25.9, 27.0, 27.1, 27.5, 28.2, 28.9, 29.2, 31.5, 33.0, 37.6, 63.1, 76.3, 77.2, 78.3, 79.5, 107.7, 122.5, 125.1, 127.3, 127.4, 129.4, 129.5, 132.2, 134.1, 134.4, 135.8, 136.0, 138.7. EIMS *m/z* (rel. intensity, %) 732 (M^+, 1), 675 (1), 617 (2), 411 (4), 135 (100). HRMS Calcd for $C_{45}H_{72}O_4Si_2$ (M^+): 732.4969. Found: 732.4938.

(1'*E*,6'*Z*)-(1*S*,2*R*,3'*S*,4'*S*,1''*R*)-1-(1'-*tert*-Butyldiphenylsiloxy-4'-methoxycarbonylbutyl)-2-(3',4'-dihydroxy-3',4'-*O*-isopropylideneundec-1',6'-dienyl)cyclopropane (15). A solution of silyl ether (**14**) (100 mg, 0.137 mmol) in AcOH-H_2O-THF (2 : 1 : 1, 10 mL) was stirred at rt for 1 h, diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 3 : 1) to give alcohol (72 mg, 85 %) as a colorless oil, $[\alpha]_D$ +28.1° (*c* 0.27, $CHCl_3$). IR ν max (neat): 3442, 2931 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.40-0.55 (2H, m), 0.87 (3H, t, *J* = 6.8 Hz), 0.98 (1H, m), 1.02 (9H, s), 1.20-1.60 (12H, m), 1.34 (3H, s), 1.47 (3H, s), 2.03 (4H, m), 2.28 (1H, m), 3.13 (1H, m), 3.53 (2H, m), 4.04 (1H, td, *J* = 5.0, 8.2 Hz), 4.38 (1H, dd, *J* = 6.6, 8.2 Hz), 5.15 (1H, dd, *J* = 8.2, 15.3 Hz), 5.32 (1H, dd, *J* = 8.2, 15.3 Hz), 5.38 (1H, m), 5.50 (1H, m), 7.30-7.45 (6H, m), 7.60-7.70 (4H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.2, 13.8, 19.1, 19.4, 20.7, 22.3, 25.4, 26.8, 26.9, 27.3, 28.0, 28.6, 29.0, 31.3, 32.6, 37.3, 62.5, 75.8, 76.4, 78.1, 79.2, 107.6, 122.5, 124.8, 127.2, 129.2, 129.3, 132.0, 133.8, 134.2, 135.6, 135.8, 138.4. EIMS *m/z* (rel. intensity, %) 618 (M^+, 1), 561 (1), 503 (2), 425 (4), 199 (100). HRMS Calcd for $C_{32}H_{43}O_3Si$ ((M^+-^{t}Bu)): 503.2981. Found: 503.2964.

To a solution of the above alcohol (70 mg, 0.137 mmol) in CH_2Cl_2 (2 mL) were added powdered molecular sieves 4A (130 mg) and PDC (63 mg, 0.17 mmol). The mixture was stirred at rt for 2 h, diluted with Et_2O and filtered through silica gel. The filtrate was concentrated under reduced pressure to give crude aldehyde for use in the reaction below without purification.

To a cold (0 °C) solution of the above aldehyde, 2-methyl-2-butene (39 mg, 0.55 mmol) and NaH_2PO_4 (17 mg, 0.11 mmol) in ^{t}BuOH-H_2O (3 : 1, 2 mL) was added $NaClO_2$ (20 mg, 0.22 mmol). The mixture was stirred at 0 °C for 30 min, treated with 1N HCl to attain pH 3, diluted with Et_2O-$CHCl_3$ (4 : 1), washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give crude carboxylic acid for use in the reaction below without purification.

To a cold (0°C) solution of the above crude carboxylic acid in Et_2O (2 mL) was added a solution of CH_2N_2 in Et_2O until the mixture took on yellow color. The reaction mixture was concentrated under reduced

pressure and the residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 5 : 1) to give methyl ester (**15**) (61 mg, 85 %) as a colorless oil, $[\alpha]_D$ +42.7 ° (*c* 0.60, $CHCl_3$). IR ν max (neat): 2956, 1742 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.43 (1H, td, *J* = 4.9, 8.9 Hz), 0.52 (1H, td, *J* = 4.9, 8.7 Hz), 0.87 (3H, t, *J* = 6.8 Hz), 0.96 (1H, m), 1.02 (9H, s), 1.20-1.40 (5H, m), 1.34 (3H, s), 1.47 (3H, s), 1.50-1.60 (3H, m), 1.70 (2H, m), 2.02 (4H, m), 2.18 (2H, t, *J* = 7.4 Hz), 2.24 (1H, m), 3.12 (1H, td, *J* = 5.3, 7.7 Hz), 3.64 (3H, s), 4.04 (1H, ddd, *J* = 5.2, 6.0, 8.9 Hz), 4.38 (1H, dd, *J* = 6.0, 8.1 Hz), 5.14 (1H, dd, *J* = 8.1, 15.3 Hz), 5.33 (1H, dd, *J* = 8.1, 15.3 Hz), 5.37 (1H, m), 5.49 (1H,m), 7.30-7.45 (6H, m), 7.60-7.70 (4H, m). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.3, 14.0, 19.3, 19.8, 20.3, 22.5, 25.6, 27.0, 27.5, 28.2, 28.9, 29.2, 31.5, 34.1, 37.0, 51.4, 75.9, 77.2, 78.2, 79.4, 107.7, 122.7, 125.1, 127.4, 127.5, 129.4, 129.6, 132.2, 133.9, 134.2, 135.8, 136.0, 138.4, 173.9. EIMS *m/z* (rel. intensity, %) 646 (M^+, 1), 631 (1), 589 (8), 325 (20), 213 (40), 199 (100). HRMS Calcd for $C_{40}H_{58}O_5Si$ (M^+): 646.4054. Found: 646.4058.

Constanolactone E (1). A solution of acetonide (**15**) (30 mg, 0.046 mmol) in AcOH-H_2O (4 : 1, 3 mL) was stirring at rt for 12 h. The mixture was diluted with Et_2O-$CHCl_3$ (4 : 1), washed with saturated aqueous $NaHCO_3$, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 2 : 1) to give diol (22 mg, 77 %) as a colorless oil, $[\alpha]_D$ +45.8 ° (*c* 0.24, $CHCl_3$). IR ν max (neat): 3359, 2954, 1740 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.45 (1H, td, *J* = 5.1, 8.5 Hz), 0.50 (1H, td, *J* = 4.9, 8.5 Hz), 0.88 (3H, t, *J* = 6.9 Hz), 0.96 (1H, m), 1.02 (9H, s), 1.20-1.40 (4H, m), 1.50-1.60 (4H, m), 1.70-1.80 (2H, m), 1.96 (1H, m), 2.03 (2H, m), 2.10-2.30 (2H, m), 2.20 (2H, t, *J* = 7.0 Hz), 3.17 (1H, td, *J* = 5.3, 7.5 Hz), 3.58 (1H, m), 3.65 (3H, s), 3.96 (1H, m), 5.14 (1H, dd, *J* = 8.3, 15.5 Hz), 5.33 (1H, dd, *J* = 7.1, 15.5 Hz), 5.40 (1H, m), 5.55 (1H,m), 7.30-7.45 (6H, m), 7.64-7.72 (4H, m). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 11.4, 14.1, 19.4, 19.8, 20.4, 22.6, 27.0, 27.5, 29.3, 30.1, 31.5, 34.2, 37.1, 51.5, 74.0, 75.1, 75.9, 77.2, 124.9, 125.1, 127.4, 127.5, 129.5, 129.6, 133.4, 135.9, 136.1, 137.2, 173.9. EIMS *m/z* (rel. intensity, %) 606 (M^+, 2), 571 (10), 549 (8), 531 (15), 325 (38), 210 (100). HRMS Calcd for $C_{33}H_{45}O_5Si$ (M^+-^{t}Bu): 549.3036. Found: 549.3010.

To a cold (0°C) solution of the above silyl ether (21 mg, 0.036 mmol) in DMF (1 mL) was added Bu_4NF (1.0 mL, 2.0 mmol, 2.0 M in DMF). The mixture was stirred at 0 °C for 12 h, poured into 1N HCl (2 mL) and extracted with $CHCl_3$. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - EtOAc = 1 : 5) to give constanolactone E (**1**) (8.0 mg, 65 %) as a colorless oil, $[\alpha]_D$ +34° (*c* 0.18, MeOH), (lit.,[4] $[\alpha]_D$ +33° (*c* 0.22, MeOH)). IR ν max (neat): 3434, 2956, 2924, 1733, 1244, 1050, 967 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.72 (1H, td, *J* = 5.2, 8.7 Hz), 0.77 (1H, td, *J* = 5.2, 8.4 Hz), 0.89 (3H, t, *J* = 6.8 Hz), 1.12 (1H, m), 1.25-1.40 (6H, m), 1.50-1.65 (4H, m), 1.67 (1H, m), 1.81 (1H, m), 1.90-2.10 (4H, m), 2.21 (1H, m), 2.29 (1H, m), 2.46 (1H, ddd, *J* = 7.0, 8.6, 17.6 Hz), 2.57 (1H, dt, *J* = 6.3, 17.6 Hz), 3.66 (1H, m), 3.79 (1H, ddd, *J* = 3.1, 7.8, 10.2 Hz), 4.10 (1H, m), 5.38 (1H, m), 5.42 (1H, dd, *J* = 8.2, 15.7 Hz), 5.57 (1H, m), 5.62 (1H, dd, *J* = 6.8, 15.7 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 10.6, 14.0, 18.5, 19.3, 22.6, 25.0, 27.4, 27.8, 29.3,

29.5, 30.0, 31.5, 73.9, 74.9, 83.2, 124.7, 126.4, 133.7, 135.7, 171.4. EIMS *m/z* (rel. intensity, %) 336 (M^+, 1), 196 (65), 55 (100). HRMS Calcd for $C_{20}H_{32}O_4$ (M^+): 336.2301. Found: 336.2297.

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