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Synthesis of C-1 ~ C-13 Segment of Amphidinolide B

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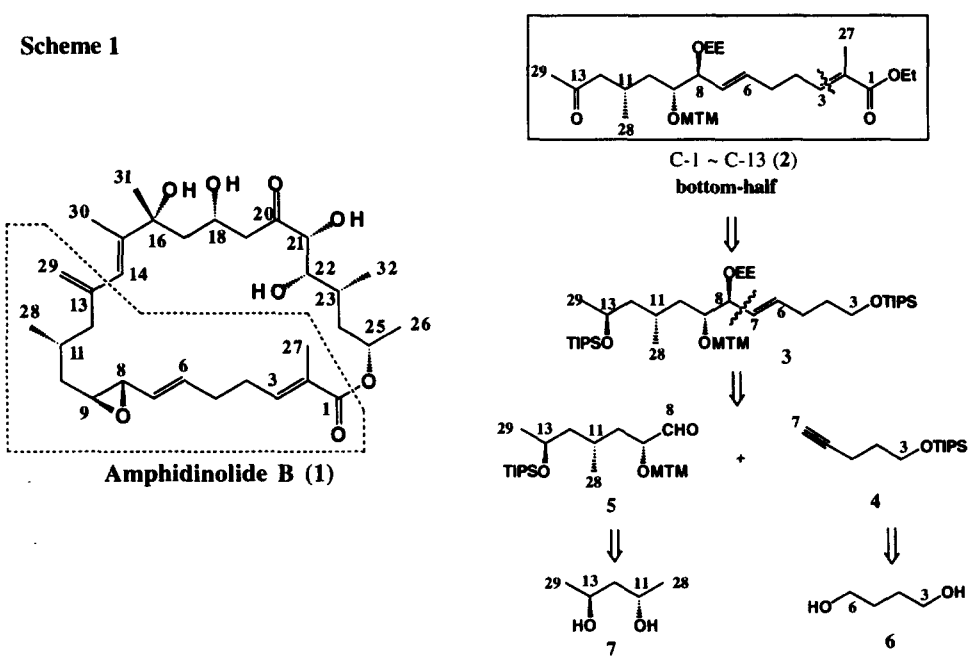
Abstract; The C-1 ~ C-13 segment (**2**) of amphidinolide B (**1**), a potent cytotoxic 26-membered macrolide, has been synthesized.

Amphidinolide B[1,2] (**1**), a 26-membered macrolide isolated from culture of the symbiotic marine dinoflagellate *Amphidinium* sp. (strain Y-5), exhibits potent cytotoxicity against L1210 murine leukemia and KB human epidermoid carcinoma cells in vitro (IC_{50} 0.00014 and 0.0042 μg/mL, respectively). The relative stereochemistry of nine chiral centers in **1** was determined by X-ray crystal analysis,[3] and their absolute configurations were established on the basis of synthesis of the C-22 ~ C-26 segment.[4] Amphidinolide B (**1**) has attracted great interests as one of challenging targets for total synthesis, and some syntheses of the segments have been recently reported.[5-8] In this paper we describe the synthesis of the C-1 ~ C-13 segment (**2**) toward the total synthesis of amphidinolide B (**1**).

Scheme 1



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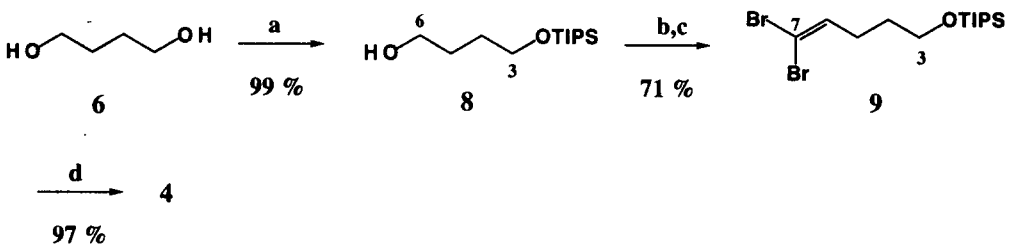
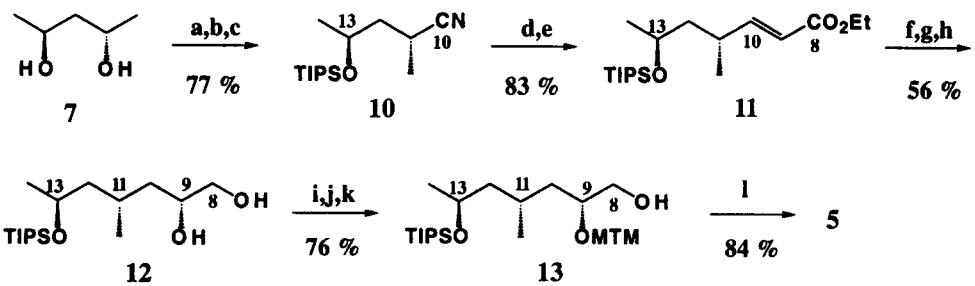
Scheme 2



[a] NaH, THF, 0 °C ~ rt, 45 min, then TIPSCl, 0 °C ~ rt, rt, 30 min; [b] $(COCl)_2$, DMSO, CH_2Cl_2, -78 °C, 45 min, then Et_3N, -78 °C ~ -50 °C; [c] CBr_4, Ph_3P, Et_3N, CH_2Cl_2, 0 °C, 1 h; [d] *n*-BuLi, THF, -78 °C, 2 h.

Scheme 3

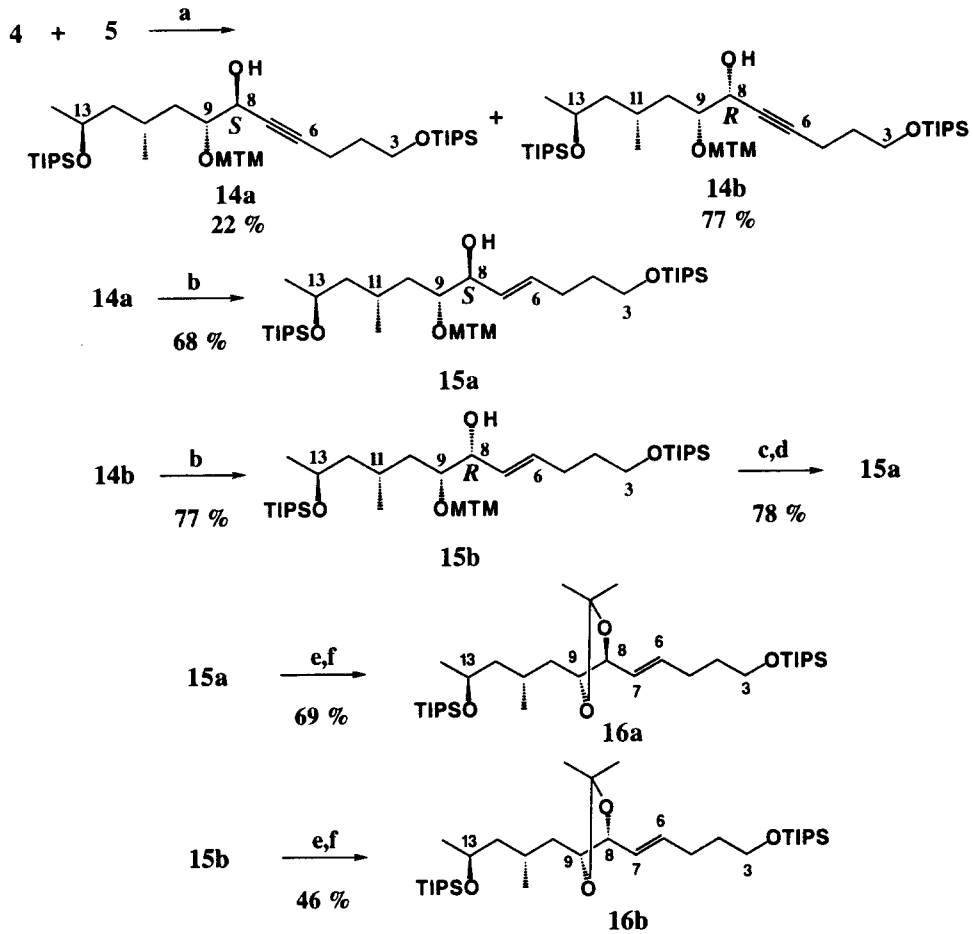


[a] NaH, THF, rt, 1 h, then TIPSCl, rt, 24 h; [b] TsCl, pyridine, 4 °C, 6 days; [c] NaCN, DMSO, 60 °C, 3 h; [d] DIBAL, CH_2Cl_2, -20 °C, 30 min, then NH_4Cl aq., rt, 20 min; [e] $Ph_3P{=}CHCO_2Et$, benzene, rt, 24 h; [f] DIBAL, CH_2Cl_2, -78 °C, 30 min; [g] (+)-DET, Ti(*i*-PrO)$_4$, *t*-BuOOH, CH_2Cl_2, MS-4Å, -20 °C, 14 h; [h] DIBAL, toluene, rt, 3 h and then separation; [i] PivCl, pyridine/CH_2Cl_2 (1:1), 0 °C ~ rt, then rt, 30 min; [j] DMSO, Ac_2O, AcOH, rt, 48 h; [k] DIBAL, CH_2Cl_2, -78 °C, 30 min; [l] Dess-Martin periodinane, pyridine/CH_2Cl_2 (1:1), rt, 2 h.

Our synthetic route of the C-1 ~ C-13 segment (**2**) was based on the convergent strategy through cross-coupling reaction between two segments C-3 ~ C-7 (**4**) and C-8 ~ C-13 (**5**) as shown in Scheme 1. The segments **4** and **5** could be derived from 1,4-butanediol (**6**) and (2*S*,4*S*)-2,4-pentanediol (**7**), respectively. Since the allyl epoxide moiety of amphidinolide B (**1**) was labile under acidic or basic conditions, we planned to synthesize the C-1 ~ C-13 segment as a 8,9-diol, which would be converted into the 8,9-epoxide unit, protected by an ethoxyethyl and a methylthiomethyl (MTM) groups at 8-OH and 9-OH, respectively.

The monoprotected diol (**8**) derived from 1,4-butanediol (**6**) was subjected to Swern oxidation and then homologation using carbon tetrabromide and triphenylphosphine to afford the dibrominated olefin **9** (71 %)[9] (Scheme 2). The acetylene **4**, correpsonding to the C-3 ~ C-7 segment, was obtained by treatment of **9** with *n*-BuLi in 97 % yield.

Scheme 4



[a]*n*-BuLi, $CeCl_3$, THF, -78 °C, 90 min, and then separation; [b]Red-Al®, Et_2O, rt, 3 h; [c]Dess-Martin periodinane, pyridine/CH_2Cl_2 (1:1), rt, 2 h; [d]$Zn(BH_4)_2$, Et_2O, 0 °C, 1 h; [e]$AgNO_3$, 2,6-lutidine, THF/H_2O (4:1), rt, 90 min; [f]2,2-dimethoxypropane, PPTS, CH_2Cl_2, rt, 2h.

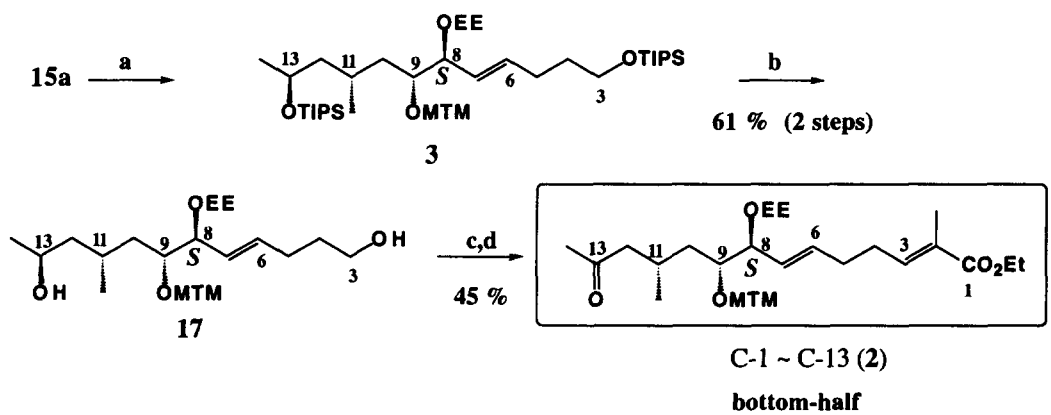
On the other hand, the cyanide **10** prepared from (2*S*,4*S*)-2,4-pentanediol (**7**) in three steps was converted into the α,β-unsaturated ester **11** by DIBAL reduction and then Wittig reaction with triphenyl(ethoxycarbonylmethylene)phosphorane in 83 % yield (Scheme 3). After reduction of **11** with DIBAL (99 %), Sharpless asymmetric epoxidation[10] of the corresponding allyl alcohol with (+)-diethyl tartrate afforded the 9*S*,10*R*-epoxyalcohol in 77 % yield with 95 % de. Regioselective ring opening reaction[11] of the epoxide with DIBAL followed by separation gave the 1,2-diol **12** (73 %) and its 1,3-regioisomer (9 %). After protection of primary and secondary hydroxyl groups as a pivaloyl ester and an MTM ether, respectively, the pivaloyl ester was deprotected by DIBAL reduction, and compound **13** was

Figure 1. Stereochemistry at C-8 and C-9 of **16a** and **16b**.
Allows showed NOESY correlations.

obtained in 76 % yield. Oxidation of **13** with Dess-Martin periodinane[12] in pyridine/CH_2Cl_2 (1:1) afforded the C-8 ~ C-13 segment (**5**) in 84 % yield.

Coupling reaction of the acetylene **4** and the aldehyde **5** with *n*-BuLi and $CeCl_3$ followed by separation by column chromatography (SiO_2) gave the coupling products **14a** (22 %) and **14b** (77 %) (Scheme 4). Compounds **14a** and **14b** were converted into the allyl alcohols **15a** (68 %) and **15b** (77 %), respectively, by Red-Al® reduction. Absolute configurations at C-8 of **15a** and **15b** were determined as *S* and *R*, respectively, on the basis of NOE data of the acetonides (**16a** and **16b**) derived from **15a** and **15b**, respectively (Figure 1). On the other hand, the undesired **15b** was converted into **15a** in 78 % yield by two steps: Dess-Martin oxidation of the hydroxyl group at C-8 and reduction of the ketone with $Zn(BH_4)_2$.[13,14] Protection of the hydroxyl group at C-8 with an ethoxyethyl group afforded compound **3**, which was converted into the 3,13-diol **17** in 61 % yield by deprotection of two triisopropylsilyl groups with TBAF (Scheme 5). Dess-Martin oxidation of **17** followed by Wittig reaction yielded the C-1 ~ C-13 segment (**2**) in 45 % yield for the two steps, and the 13-ketoaldehyde of **17** was recovered (41 %).

Scheme 5



[a]ethyl vinyl ether, PPTS, CH_2Cl_2, rt, 2 h; [b]TBAF, THF, rt, 3 h; [c]Dess-Martin periodinane, pyridine/CH_2Cl_2 (1:1), rt, 2.5 h; [d]$Ph_3P{=}C(Me)CO_2Et$, benzene, rt, 12 h.

Thus the synthesis of the C1 ~ C-13 segment (**2**), corresponding to the bottom-half of amphidinolide B (**1**), has been completed using the convergent route. Synthesis of the top-half of amphidinolide B (**1**) and its total synthesis are under investigation.

Experimental Section

General Methods. All moisture and air sensitive reactions were performed in flamed dried glassware equipped with rubber septa under a positive pressure of nitrogen or argon. Et_2O and THF were distilled from sodium benzophenone ketyl prior to use. CH_2Cl_2, toluene, benzene, and pyridine were distilled from CaH_2, while DMSO was dried over molecular sieves 4Å. All yields reported refer to isolated material judged to be homogeneous by tlc and NMR spectroscopy. Wakogel® C-200 (75 ~ 150 μm) was used for column chromatography. Optical rotations were measured on a JASCO DIP-360 polarimeter. IR spectra were recorded on a JASCO FT/IR-5300 spectrophotometer. ^1H and ^{13}C NMR spectra were measured on Bruker ARX-500 or JEOL EX-400 spectrometers in $CDCl_3$, ^1H NMR spectra were recorded in ppm using the residual $CHCl_3$ signal (δ 7.26) as an internal standard, while ^{13}C NMR spectra were recorded in ppm relative to the $CDCl_3$ signal (δ 77.0). Multiplicity of each carbon signal was assigned on the basis of DEPT spectra. EI and FAB mass spectra were obtained on JEOL DX-303 and JMX-HX110 spectrometers, respectively.

1,1-Dibromo-5-triisopropylsilyloxy-1-pentene (9). To a stirred suspension of 60 % oil dispersion of sodium hydride (271 mg, 6.8 mmol) in THF (6 mL) was added 1,4-butanediol (**6**, 495 mg, 5.5 mmol) at 0 °C, and the mixture was stirred at room temperature for 45 min. Triisopropylsilyl chloride (1.3 mL, 6.1 mmol) was added to this mixture at 0 °C, and stirring was continued for 30 min. The reaction mixture was partitioned between Et_2O (40 mL x 3) and 10 % aqueous K_2CO_3 (20 mL), and the organic phase was washed with water and brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/EtOAc, 8:1 → 4:1) to afford a TIPS alcohol (1.33 g, 5.4 mmol, 99 %). To a stirring solution containing oxalyl chloride (1.8 mL, 20.8 mmol) and DMSO (2.2 mL, 25.2 mmol) in CH_2Cl_2 (32 mL) was added dropwise a solution of the TIPS alcohol (2.57 g, 10.4 mmol) in CH_2Cl_2 (14 mL) at -78 °C. After being stirred at -78 °C for 45 min, the mixture was treated with triethylamine (7 mL, 49 mmol) and allowed to warm to -50 °C. After addition of saturated aqueous NH_4Cl (50 mL), the reaction mixture was extracted with Et_2O (60 mL x 3). The organic phase was washed with water and brine, and dried over $MgSO_4$. The solvent was evaporated *in vacuo*, and a crude aldehyde was obtained, which was used for the following reaction without separation. To a solution of carbon tetrabromide (13.8 g, 40 mmol) in CH_2Cl_2 (56 mL) was added triphenylphosphine (21.4 g, 81.5 mmol) at 0 °C, and stirring was continued for 10 min. To the reaction mixture was added triethylamine (11.2 mL, 80.4 mmol) and then a solution of the crude aldehyde (2.62 g) in CH_2Cl_2 (28 mL). After being stirred at 0 °C for 1 h, the reaction mixture was partitioned between water (100 mL) and $CHCl_3$ (200 mL x 3), and the organic phase was washed with saturated aqueous $NaHCO_3$, water, and brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was subjected to a silica gel column (hexane/EtOAc, 40:1), and a dibrominated olefin **9** (2.92 g, 7.28 mmol) was obtained in 71 % yield by two steps. **9**: colorless oil; IR (neat) ν_{max} 1460 and 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (18 H, s), 1.08 (3H, m), 1.69 (2H, dt, J = 13.9 and 6.2 Hz), 2.20 (2H, dt, J = 14.8 and 7.4 Hz), 3.71 (2H, t, J = 6.2 Hz), and 6.45 (1H, t, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ 12.0 (3C, d), 18.0 (6C, q), 29.8 (t), 31.0 (t), 62.5 (t), 88.7 (s), and 138.6 (d);

FABMS *m/z* 399, 401, and 403 $(M+H)^+$; HRFABMS *m/z* 399.0344 $(M+H)^+$, calcd for $C_{14}H_{29}OSi^{79}Br_2$, 399.0354.

5-Triisopropylsilyloxy-1-pentyne (4). A solution of compound **9** (743 mg, 1.86 mmol) in THF (7 mL) was treated with 1.6 M hexane solution of *n*-BuLi (3.5 mL, 5.6 mmol) at -78 °C for 2 h. After addition of saturated aqueous NH_4Cl (10 mL), the reaction mixture was extracted with EtOAc (20 mL x 3). The organic phase was washed with water and brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/Et_2O, 20:1), and an acetylene **4** (434 mg, 1.80 mmol) was obtained in 97 % yield. **4:** colorless oil; IR (neat) ν_{max} 2120 and 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (21H, m), 1.74 (2H, m), 1.92 (1H, t, *J* = 2.4 Hz), 2.30 (2H, m), and 3.76 (2H, t, *J* = 6.1 Hz); FABMS *m/z* 241 $(M+H)^+$; HRFABMS *m/z* 241.1981 $(M+H)^+$, calcd for $C_{14}H_{29}OSi$, 241.1988.

(2*R*,4*S*)-2-Methyl-4-triisopropylsilyloxypentanenitrile (10). To a stirred suspension of 60 % oil dispersion of sodium hydride (2.31 g, 57.8 mmol) in THF (43.5 mL) was added (2*S*,4*S*)-2,4-pentanediol (**5**, 5.03 g, 48.4 mmol) in THF (34 mL). After being stirred at room temperature for 1 h, the reaction mixture was treated with triisopropylsilyl chloride (12.3 mL, 63.8 mmol) at room temperature for 24 h. After addition of water (125 mL), the reaction mixture was extracted with Et_2O (450 mL x 3), and the organic phase was washed with brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/EtOAc, 5:1) to afford a crude TIPS alcohol (13.2 g). A solution of the alcohol (5.25 g) in pyridine (46 mL) was treated with *p*-toluenesulfonyl chloride (5.39 g, 28.3 mmol) at 4 °C for 6 days. After addition of water (50 mL), the reaction mixture was extracted with Et_2O (400 mL x 3), and the organic phase was washed with brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was subjected to a silica gel column (hexane/EtOAc, 8:1), and a tosylate (7.37 g, 17.8 mmol) was obtained in 90 % yield by two steps. To a solution of the tosylate (7.37 g, 17.8 mmol) in DMSO (126 mL) was added sodium cyanide (2.62 g, 53.4 mmol), and the mixture was stirred at 60 °C for 3 h. The reaction mixture was partitioned between water (380 mL) and Et_2O (400 mL x 3), and the organic phase was washed with brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/Et_2O, 8:1 → 5:1), and a cyanide **10** (3.44 g, 15.1 mmol) was obtained in 85 % yield. **10:** $[\alpha]_D^{27}$ -4.7° (*c* 1.1, $CHCl_3$); IR (neat) ν_{max} 2240, 1135, and 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (21H, s), 1.22 (3H, d, *J* = 6.1 Hz), 1.31 (3H, d, *J* = 7.1 Hz), 1.57 (1H, m), 1.90 (1H, m), 2.74 (1H, m), and 4.08 (1H, m); ^{13}C NMR ($CDCl_3$) δ 12.4 (3C, d), 18.0 (d), 18.1 (6C, q), 21.3 (q), 23.3 (q), 43.7 (d), 65.8 (d), and 123.2 (s); FABMS *m/z* 270 $(M+H)^+$; HRFABMS *m/z* 270.2223 $(M+H)^+$, calcd for $C_{15}H_{32}NOSi$, 270.2253.

Ethyl (2*E*,4*R*,6*S*)-4-Methyl-6-triisopropylsilyloxy-2-heptenoate (11). To a solution of the cyanide **10** (3.85 g, 14.3 mmol) in CH_2Cl_2 (70 mL) was added 0.95 M hexane solution of DIBAL (16.5 mL, 15.7 mmol) at -20 °C, and the mixture was stirred at -20 °C for 30 min. MeOH (1 mL) was added to the reaction mixture, and stirring was continued at 0 °C for 10 min. After addition of saturated aqueous NH_4Cl (10 mL), the mixture was stirred at room temperature for 20 min. After addition of saturated aqueous potassium sodium tartrate (40 mL) and then Et_2O (120 mL), the reaction mixture was stirred vigorously at room temperature for 1 h. The reaction mixture was extracted with EtOAc (10 mL x 3), and the organic phase was washed with water and brine, dried over $MgSO_4$, and evaporated *in vacuo* to afford a crude aldehyde (3.84 g), which was used for the following reaction without separation. To a solution of the crude aldehyde in benzene (20 mL) was added triphenyl(ethoxycarbonylmethylene)phosphorane (9.96 g, 28.6 mmol), and the reaction mixture was stirred at room temperature for 24 h. After filtration of insoluble materials, the reaction mixture was evaporated *in vacuo*. The residue was

purified by a silica gel column (hexane/EtOAc, 20:1), and an ester **11** (4.08 g, 11.9 mmol) was obtained in 83 % yield by two steps. **11:** colorless oil; $[\alpha]_D^{27}$ -4.7° (*c* 1.1, $CHCl_3$); IR (neat) ν_{max} 1710 and 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (27H, m), 1.16 (3H, d, *J* = 7.1 Hz), 1.38 (1H, dt, *J* = 13.4 and 6.6 Hz), 1.63 (1H, m), 2.45 (1H, m), 3.92 (1H, m), 4.17 (2H, q, *J* = 7.1 Hz), 5.75 (1H, d, *J* = 15.7 Hz), and 6.85 (1H, dd, *J* = 8.0 and 15.7 Hz); ^{13}C NMR ($CDCl_3$) δ 12.5 (3C, d), 14.2 (q), 18.1 (6C, q), 19.8 (q), 23.7 (q), 33.3 (d), 46.4 (t), 60.1 (t), 66.4 (d), 119.6 (d), 154.4 (d), and 166.7 (s); FABMS *m/z* 343 $(M+H)^+$; HRFABMS *m/z* 343.2689 $(M+H)^+$, calcd for $C_{19}H_{39}O_3Si$, 343.2668.

(2*R*,4*S*,6*S*)-4-Methyl-6-triisopropylsilyloxy-1,2-heptanediol (12). To a solution of the ester **11** (10.3 g, 30 mmol) in CH_2Cl_2 (80 mL) was slowly added 0.95 M hexane solution of DIBAL (76 mL, 72 mmol) at -78 °C, and the mixture was stirred at -78 °C for 30 min. After addition of saturated aqueous potassium sodium tartrate (100 mL), the reaction mixture was extracted with EtOAc (200 mL x 2), and the organic phase was washed with water and brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was subjected to a silica gel column (hexane/Et_2O, 8:1 → hexane/EtOAc, 8:1 → 4:1), and an allyl alcohol (8.96 g, 29.8 mmol) was obtained in 99 % yield. To a stirred suspension of molecular sieves 4Å (5 g) in CH_2Cl_2 (24 mL) containing diethyl (+)-tartrate (1.96 g, 9.5 mmol) was added titanium tetraisopropoxide (2.4 mL, 8.72 mmol) at -20 °C and then, dropwise, a solution of the allyl alcohol (5.38 g, 17.9 mmol) in CH_2Cl_2 (12 mL). After being stirred for 30 min, 3.2 M toluene solution of *tert*-butyl hydroperoxide (16.8 mL, 53 8 mmol) was added to the mixture, and stirring was continued at -20 °C for 14 h. After filtration of insoluble materials, it was then poured into a cold and stirred solution of $FeSO_4 \cdot 7H_2O$ (10 g) and tartaric acid (3 g) in water (40 mL), and the mixture was stirred at 0 °C for 15 min. The mixture was extracted with $CHCl_3$ (100 mL x 3), and the organic phase was concentrated to 50 mL. To the mixture was added Et_2O (70 mL) and an aqueous solution (40 mL) of NaOH (10.2 g) and NaCl (2.28 g), and stirring was continued at 0 °C for 1 h. The mixture was extracted with EtOAc (200 mL x 3), and the organic phase was washed with water and brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was subjected to a silica gel column (hexane/EtOAc, 5:1), and an epoxy alcohol (4.35 g, 13.7 mmol, 77 %) was yielded. A solution of the epoxy alcohol in toluene (40 mL) was treated with 1.05 M toluene solution of DIBAL (41.2 mL, 43.3 mmol) at room temperature for 3 h. After addition of MeOH (1.2 mL) at 0 °C to decompose excess of reagent, saturated aqueous potassium sodium tartrate (40 mL) and Et_2O (120 mL) were added to the mixture, and the reaction mixture was stirred vigorously at room temperature for 1 h. The reaction mixture was extracted with EtOAc (80 mL x 3), and the organic phase was washed with water and brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was subjected to a silica gel column (hexane/EtOAc, 3:1), and a 1,2-diol **12** (3.19 g, 10.0 mmol) and its 1,3-regioisomer (393 mg, 1.23 mmol) were obtained in 73 % and 9 % yield, respectively. **12:** colorless amorphous solid; $[\alpha]_D^{23}$ +12.9° (*c* 1.16, $CHCl_3$); IR (neat) ν_{max} 3310 and 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (3H, d, *J* = 6.6 Hz), 1.07 (21H, m), 1.14 (1H, m), 1.18 (3H, d, *J* = 6.0 Hz), 1.35 (2H, m), 1.57 (1H, m), 1.81 (1H, m), 1.90 (1H, m), 2.07 (1H, brd, *J* = 7.0 Hz), 3.41 (1H, m), 3.65 (1H, m), 3.84 (1H, m), and 4.04 (1H, m); ^{13}C NMR ($CDCl_3$) δ 12.7 (3C, d), 18.2 (6C, q), 20.7 (q), 24.5 (q), 26.1 (d), 40.9 (t), 47.4 (t), 66.7 (d), 66.8 (t), and 70.3 (d); FABMS *m/z* 319 $(M+H)^+$; HRFABMS *m/z* 319.2665 $(M+H)^+$, calcd for $C_{17}H_{39}O_3Si$, 319.2668.

(2*R*,4*S*,6*S*)-4-Methyl-2-methylthiomethoxy-6-triisopropylsilyloxy-1-heptanol (13). To a solution of the 1,2-diol **12** (1.53 g, 4.79 mmol) in CH_2Cl_2 (5 mL) and pyridine (5 mL) was added pivaloyl chloride (590 μL, 4.79 mmol) at 0 °C, and stirring was continued at room temperature for 30 min. After addition of saturated aqueous NH_4Cl (30 mL), the mixture was extracted with EtOAc (40 mL x 3), and the organic phase was washed with water and brine, dried over Na_2SO_4, and evaporated *in vacuo*. The

residue was purified by silica gel column chromatography (hexane/EtOAc, 8:1), and a pivaloyl ester (1.66 g, 4.11 mmol) was obtained in 86 % yield. To a solution of the pivaloyl ester (4.26g, 10.6 mmol) in DMSO (10 mL) was added AcOH (9 mL, 157 mmol) and then acetic anhydride (29 mL, 307 mmol), and the reaction mixture was standed at room temperature for 48 h. The mixture was partitioned between saturated aqueous $NaHCO_3$ (100 mL) and Et_2O (200 mL x 3), and the organic phase was washed with water and brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was purified by a silica gel column (hexane/EtOAc, 10:1), and an MTM ether (4.62 g, 9.98 mmol, 94 %) was yielded. A solution of the MTM ether (2.00 g, 4.32 mmol) in CH_2Cl_2 (20 mL) was treated with 0.95 M hexane solution of DIBAL (13 mL, 12.4 mmol) at -78 °C for 30 min. After addition of saturated aqueous potassium sodium tartrate (15 mL) and Et_2O (30 mL), stirring was continued at room temperature for 1 h. The reaction mixture was extracted with EtOAc (30 mL x 3), and the organic phase was washed with water and brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by a silica gel column (hexane/EtOAc, 10:1 → 4:1), and compound **13** (1.88 g, 6.56 mmol) was obtained in 94 % yield. **13:** colorless oil; $[\alpha]_D^{25}$ -30.7° (*c* 1.05 $CHCl_3$); IR (neat) ν_{max} 3445 and 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (3H, d, *J* = 6.5 Hz), 1.05 (21H, m), 1.16 (3H, d, *J* = 6.0 Hz), 1.17 (1H, m), 1.40 (2H, t, *J* = 6.9 Hz), 1.54 (1H, ddd, *J* = 5.5, 7.7, and 13.4 Hz), 1.72 (1H, m), 2.03 (1H, brt, *J* = 6.3 Hz), 2.19 (3H, s), 3.46 (1H, m), 3.68 (1H, m), 3.76 (1H, dq, *J* = 2.9 and 6.5 Hz), 4.02 (1H, m), 4.62 (1H, d, *J* = 11.7 Hz), and 4.77 (1H, d, *J* = 11.7 Hz); ^{13}C NMR ($CDCl_3$) δ 12.7 (3C, d), 14.2 (q), 18.2 (6C, q), 20.3 (q), 24.4 (q), 26.0 (d), 38.7 (t), 48.0 (t), 64.3 (t), 66.4 (d), 74.1 (t), and 77.3 (t); FABMS *m/z* 379 $(M+H)^+$; HRFABMS *m/z* 379.2713 $(M+H)^+$, calcd for $C_{19}H_{43}O_3SSi$, 379.2702.

(2*R*,4*S*,6*S*)-4-Methyl-2-methylthiomethoxy-6-triisopropylsilyloxyheptanal (5). To a solution of compound **13** (1.53 g, 4.04 mmol) in pyridine and CH_2Cl_2 (1:1, 40 mL) was added Dess-Martin periodinane (2.8 g, 6.57 mmol), and the mixture was stirred at room temperature for 2 h. The reaction was quenched by addition of saturated aqueous $Na_2S_2O_3$ (25 mL), and then the reaction mixture was partitioned between EtOAc (100 mL x 3) and water (25 mL). The organic phase was washed with water and brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/EtOAc, 20:1), and an aldehyde **5** (1.28 g, 3.40 mmol) was obtained in 84 % yield. **5:** colorless oil; $[\alpha]_D^{22}$ +42° (*c* 0.81 $CHCl_3$); IR (neat) ν_{max} 1730 and 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (3H, d, *J* = 6.7 Hz), 1.06 (21H, m), 1.15 (1H, m), 1.18 (3H, d, *J* = 6.0 Hz); 1.55 (3H, m), 2.18 (3H, s), 4.04 (2H, m), 4.68 (1H, d, *J* = 11.9 Hz), 4.77 (1H, d, *J* = 11.9 Hz), and 9.67 (1H, d, *J* = 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 12.7 (3C, d), 14.3 (q), 18.6 (6C, q), 20.6 (q), 24.6 (q), 25.7 (d), 37.6 (t), 47.0 (t), 66.4 (d), 75.5 (t), 80.6 (d), and 202.8 (d); FABMS *m/z* 377 $(M+H)^+$; HRFABMS *m/z* 377.2523 $(M+H)^+$, calcd for $C_{19}H_{41}O_3SSi$, 377.2546.

(6*S*,7*R*,9*S*,11*S*)-9-Methyl-7-methylthiomethoxy-1,11-bis(triisopropylsilyloxy)-4-dodecyn-6-ol (14a) and (6*R*,7*R*,9*S*,11*S*)-9-Methyl-7-methylthiomethoxy-1,11-bis(triisopropylsilyloxy)-4-dodecyn-6-ol (14b). A solution of the acetylene **4** (1.7 g, 4.0 mmol) in THF (8 mL) was treated with 1.6 M hexane solution of *n*-BuLi (4.1 mL, 6.56 mmol) at -78 °C for 30 min. The reaction mixture was added to a suspension of $CeCl_3$ (1.634 g, 6.63 mmol) in THF (20 mL) at -78 °C. After being stirred at -78 °C for 30 min, a solution of the aldehyde **5** (1.28 g, 3.40 mmol) in THF (5 mL) was added dropwise to the reaction mixture at -78 °C, and stirring was continued for 90 min. After addition of saturated aqueous NH_4Cl (40 mL), the reaction mixture was extracted with EtOAc (80 mL x 3), and the organic phase was washed with water and then brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was subjected to a silica gel column (hexane/Et_2O, 20:1 → 10:1 → 5:1), and a 1:3.5 mixture of

coupling products **14a** and **14b** (2.07 g, 3.35 mmol) were obtained in 99 % yield. The mixture was repeatedly separated by a silica gel column (hexane/Et_2O, 20:1 → 10:1), and compounds **14a** (473 mg, 780 μmol, 22 %) and **14b** (1.58 g, 2.57 mmol, 77 %) were obtained. **14a:** a colorless oil; $[\alpha]_D^{22}$ +3.0° (*c*, 1.05, $CHCl_3$); IR (neat) ν_{max} 3445 and 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (3H, d, *J* = 6.5 Hz), 1.06 (42H, m), 1.16 (1H, m), 1.18 (3H, d, *J* = 5.9 Hz), 1.40 (1H, m), 1.62 (2H, t, *J* = 6.9 Hz), 1.73 (2H, m), 1.82 (1H, m), 2.20 (3H, s), 2.33 (2H, dt, *J* = 1.8 and 7.0 Hz), 2.44 (1H, d, *J* = 6.4 Hz), 3.73 (1H, m), 3.74 (2H, t, *J* = 6.0 Hz), 4.05 (1H, m), 4.31 (1H, m), 4.73 (1H, d, *J* = 11.5 Hz), and 4.87 (1H, d, *J* = 11.5 Hz); ^{13}C NMR ($CDCl_3$) δ 12.1 (3C, d), 12.8 (3C, d), 14.2 (q), 15.4 (t), 18.2 (6C, q), 18.3 (6C, q), 20.8 (q), 24.5 (q), 26.0 (d), 31.9 (t), 38.9 (t), 47.5 (t), 61.9 (t), 64.4 (d), 66.4 (d), 75.2 (t), 79.0 (d), 79.2 (s), and 86.3 (s); FABMS *m/z* 617 $(M+H)^+$; HRFABMS *m/z* 617.4483, $(M+H)^+$, calcd for $C_{33}H_{69}O_4SSi_2$, 617.4455. **14b:** a colorless oil; $[\alpha]_D^{22}$ -8.3° (*c*, 1.01, $CHCl_3$); IR (neat) ν_{max} 3445 and 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (6H, d, *J* = 6.5 Hz), 1.06 (39H, m), 1.15 (1H, m), 1.18 (3H, d, *J* = 5.8 Hz), 1.49 (1H, m), 1.59 (2H, m), 1.74 (3H, m), 2.21 (3H, s), 2.33 (2H, m), 2.70 (1H, d, *J* = 7.4 Hz), 3.74 (2H, t, *J* = 6.0 Hz), 3.77 (1H, m), 4.05 (1H, m), 4.46 (1H, m), 4.65 (1H, d, *J* = 11.7 Hz), and 4.85 (1H, d, *J* = 11.7 Hz); ^{13}C NMR ($CDCl_3$) δ 12.0 (3C, d), 12.6 (3C, d), 14.2 (q), 15.3 (t), 18.0 (6C, q), 18.2 (6C, q), 20.6 (q), 24.3 (q), 26.0 (d), 32.0 (t), 38.2 (t), 47.7 (t), 61.9 (t), 64.4 (d), 66.4 (d), 74.9 (t), 77.6 (s), 79.3 (s), and 86.9 (s); FABMS *m/z* 617 $(M+H)^+$; HRFABMS *m/z* 617.4483, $(M+H)^+$, calcd for $C_{33}H_{69}O_4SSi_2$, 617.4455.

(4*E*,6*S*,7*R*,9*S*,11*S*)-9-Methyl-7-methylthiomethoxy-1,11-bis(triisopropylsilyloxy) -4-dodecen-6-ol (15a) and (4*E*,6*R*,7*R*,9*S*,11*S*)-9-Methyl-7-methylthiomethoxy-1,11-bis(triisopropylsilyloxy)-4-dodecen-6-ol (15b). To a solution of compound **14a** (395 mg, 640 μmol) in Et_2O (3 mL) was added 65 % Red-Al® in toluene (660 μL, 2.2 mmol) at 0 °C. After being stirred at room temperature for 3 h, the reaction mixture was quenched by addition of saturated aqueous potassium sodium tartrate (5 mL) and Et_2O (10 mL), and stirred vigorously at room temperature for 1 h. The mixture was extracted with EtOAc (10 mL x 3), and the organic phase was washed with water and brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was subjected to silica gel column chromatography (hexane/Et_2O, 4:1), and an allyl alcohol **15a** (269 mg, 434 μmol) was obtained in 68 % yield. **15a:** a colorless oil; $[\alpha]_D^{23}$ -9.6° (*c* 1.17, $CHCl_3$); IR (neat) ν_{max} 3445, 2945 and 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (6H, d, *J* = 6.6 Hz), 1.06, (39H, m), 1.16 (3H, d, *J* = 5.9 Hz), 1.36 (2H, t, *J* = 6.8 Hz), 1.56 (2H, m), 1.63 (2H, m), 1.74 (1H, m), 2.17 (2H, m), 2.21 (3H, m), 2.40 (1H, d, *J* = 6.6 Hz), 3.69 (2H, t, *J* = 6.4 Hz), 3.75 (1H, m), 4.02 (1H, m), 4.13 (1H, m), 4.64 (1H, d, *J* = 11.6 Hz), 4.82 (1H, d, *J* = 11.6 Hz), 5.51 (1H, dd, *J* = 7.3 and 15.5 Hz), and 5.73 (1H, dt, *J* = 15.5 and 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 12.0 (3C, d), 12.7 (3C, d), 14.3 (q), 18.0 (6C, q), 18.2 (6C, q), 20.6 (q), 24.5 (q), 25.9 (d), 28.8 (t), 32.5 (t), 38.1 (t), 47.7 (t), 62.8 (t), 66.4 (d), 73.8 (d), 74.8 (t), 79.8 (d), 127.9 (d), and 134.0 (d); FABMS *m/z* 641 $(M+Na)^+$; HRFABMS, *m/z* 641.4429 $(M+Na)^+$, calcd for $C_{33}H_{70}O_4SSi_2Na$, 641.4432. Compound **15b** (1.14 g, 1.85 mmol) was obtained by the same procedure described above from **14b** (1.49 g, 2.4 mmol) in 77 % yield. **15b:** a colorless oil; $[\alpha]_D^{25}$ -26.1° (*c* 1.69, $CHCl_3$); IR (neat) ν_{max} 3445 and 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (6H, d, *J*= 6.5 Hz), 1.05, (39H, m), 1.14 (1H, m), 1.18 (3H, d, *J*= 6.0 Hz), 1.31 (1H, m), 1.57 (2H, m), 1.63 (2H, m), 1.79 (1H, m), 2.14 (2H, m), 2.19 (3H, s), 2.34 (1H, br d, *J*= 5.0 Hz), 3.58 (1H, m), 3.69 (2H, t, *J*= 6.9 Hz), 4.01 (1H, m), 4.04 (1H, m), 4.63 (1H, d, *J*= 11.5 Hz), 4.79 (1H, d, *J*= 11.5 Hz), 5.51 (1H, dd, *J*= 5.8 and 15.5 Hz), and 5.77 (1H, dt, *J*= 15.5 and 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 12.0 (3C, d), 12.7 (3C, d), 14.3 (q), 18.0 (6C, q), 18.2 (6C, q), 20.7 (q), 24.4 (q), 26.0 (d), 28.7 (t), 32.4 (t), 38.5 (t), 47.7 (t), 62.8 (t), 66.4 (d), 74.1 (d), 74.8 (t), 79.4 (d),

129.7 (d), and 133.2 (d); FABMS *m/z* 641 $(M+Na)^+$; HRFABMS *m/z* 641.4432 $(M+Na)^+$, calcd for $C_{33}H_{70}O_4SSi_2Na$, 641.4432.

Inversion of the Hydroxy Group at C-8 of Compound 15b. To a solution of the allyl alcohol **15b** (1.127 g, 1.82 mmol) in pyridine/CH_2Cl_2 (1:1, 16 mL) was added Dess-Martin periodinane (1.16 g, 2.74 mmol), and stirring was continued at room temperature for 1 h. After addition of saturated aqueous Na_2SO_3 (10 mL), the reaction mixture was partitioned between Et_2O (40 mL x 3) and water (10 mL). The organic phase was washed with 2N HCl and brine, dried over Na_2SO_4, and evaporated *in vacuo*, and a crude ketone (1.164 g) was obtained. To a solution of the crude ketone in Et_2O (16 mL) was added 112 mM Et_2O solution of $Zn(BH_4)_2$ (16 mL, 1.8 mmol) at 0 °C, and stirring was continued at 0 °C for 1 h. The reaction mixture was partitioned between EtOAc (40 mL x 3) and saturated aqueous NH_4Cl (20 mL), and the organic phase was washed with water and brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane/Et_2O, 5:1), and **15a** (880 mg, 1.42 mmol) was obtained in 78 % by two steps.

(4*E*,6*S*,7*R*,9*S*,11*S*)-6,7-Isopropylidenedioxy-9-methyl-1,11-bis(triisopropylsilyl oxy)-4-dodecene (16a) and (4*E*,6*R*,7*R*,9*S*,11*S*)-6,7-Isopropylidenedioxy-9-methyl-1,11-bis(triisopropylsilyloxy)-4-dodecene (16b). To a solution of **15a** (20 mg, 32 μmol) in THF and water (4:1, 200 μL) were added 2,6-lutidine (12 μL, 103 μmol) and $AgNO_3$ (29 mg, 170 μmol), and the reaction mixture was stirred at room temperature for 90 min. After evaporation *in vacuo*, the residue was subjected to a silica gel column (hexane/EtOAc, 8:1), and an 8,9-diol (13 mg, 24 μmol) was obtained in 75 % yield. To a solution of the diol in CH_2Cl_2 (500 μL) were added 2,2-dimethoxypropane (200 μL, 1.6 mmol) and pyridinium *p*-toluenesulfonate (2 mg, 8 μmol). After being stirred at room temperature for 2 h, the reaction mixture was partitioned between Et_2O (10 mL x 3) and saturated aqueous $NaHCO_3$ (5 mL). The organic phase was washed with water and brine, dried over Na_2SO_4. The solvent was evaporated *in vacuo*, and an 8,9-acetonide **16a** (13 mg, 22 μmol) was obtained in 69 %. **16a:** a colorless oil; $[\alpha]_D^{23}$ -4.8° (*c* 0.47, $CHCl_3$); IR (neat) ν_{max} 1465 and 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (3H, d, *J* = 6.6 Hz), 1.05 (42H, m), 1.15 (3H, d, *J* = 6.0 Hz), 1.34 (3H, s), 1.37 (2H, t, *J* = 6.6 Hz), 1.46 (3H, s), 1.57 (2H, m), 1.63 (2H, m), 1.73 (1H, m), 2.14 (2H, m), 3.68 (2H, t, *J* = 6.3 Hz), 4.00 (1H, m), 4.20 (1H, dd, *J* = 6.0 and 6.6 Hz), 4.40 (1H, dd, *J* = 6.0 and 8.6 Hz), 5.54 (1H, dd, *J* = 8.6 and 15.4 Hz), and 5.70 (1H, dt, *J* = 15.4 and 6.6 Hz); FABMS *m/z* 621 $(M+Na)^+$; HRFABMS *m/z* 621.4706 $(M+Na)^+$, calcd for $C_{34}H_{70}O_4Si_2Na$, 621.4710. Compound **15b** (20 mg, 32 μmol) was treated under the same procedure as described above, and an 8,9-acetonide **16b** (8.6 mg, 15 μmol) was obtained in 46 % yield. **16b:** a colorless oil; $[\alpha]_D^{22}$ +8.8° (*c* 0.38, $CHCl_3$); IR (neat) ν_{max} 1465 and 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (3H, d, *J* = 6.6 Hz), 1.06 (42H, m), 1.16 (3H, d, *J* = 6.1 Hz), 1.38 (3H, s), 1.39 (3H, s), 1.43 (2H, m), 1.56 (2H, m), 1.63 (2H, m), 1.78 (1H, m), 2.14 (2H, m), 3.68(2H, t, *J* = 6.3 Hz), 3.72 (1H, m), 3.89 (1H, t, *J* = 8.1 Hz), 4.01 (1H, m), 5.42 (1H, dd, *J* = 8.1 and 15.4 Hz), and 5.81 (1H, dt, *J* = 15.4 and 7.0 Hz); FABMS *m/z* 621 $(M+Na)^+$; HRFABMS *m/z* 621.4705 $(M+Na)^+$, calcd for $C_{34}H_{70}O_4Si_2Na$, 621.4710.

(4*E*,6*S*,7*R*,9*R*,11*S*)-6-[1-(Ethoxy)ethoxy]-9-methyl-7-methylthiomethoxy-4-dodecene-1,11-diol (17). To a solution of **15a** (880 mg, 1.42 mmol) in CH_2Cl_2 (12 mL) were added ethyl vinyl ether (600 μL, 6.27 mmol) and pyridinium *p*-toluenesulfonate (58 mg, 231 μmol), and stirring

was continued at room temperature for 2 h. After addition of saturated aqueous $NaHCO_3$ (20 mL), the mixture was extracted with Et_2O (40 mL x 3). The organic phase was washed with water and brine, dried over Na_2SO_4, and evaporated *in vacuo*, and the crude C-3 ~ C-13 segment (**3**, 997 mg) was obtained. The crude compound **3** in THF (9 mL) was treated with 1 M THF solution of TBAF (9 mL, 9 mmol) at room temperature for 3 h. After addition of saturated aqueous $NaHCO_3$ (20 mL), the mixture was extracted with Et_2O (40 mL x 3). The organic phase was washed with water and brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was subjected to a silica gel column (hexane/acetone, 4:1 → 2:1), and a 3,13-diol (**17**, 330 mg, 874 μmol) was obtained in 61 %. **17:** colorless oil; $[\alpha]_D^{26}$ +10.1° (*c* 1.03, $CHCl_3$); IR (neat) ν_{max} 3420 and 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (3H, d, *J* = 6.7 Hz), 1.19 (7H, m), 1.27 (1.5H, d, *J* = 5.5 Hz), 1.29 (1.5H, d, *J* = 5.3 Hz), 1.40 (1H, m), 1.56 (2H, m), 1.68 (2H, m), 2.17 (2H, m), 2.19 (3H, s), 3.42 (0.5H, m), 3.52 (2H, m), 3.65 (0.5H, m), 3.67 (2H, t, *J* = 6.4 Hz), 3.78 (0.5H, m), 3.83 (0.5H, m), 3.88 (1H, m), 4.01 (0.5H, dd, *J* = 1.9 and 7.6 Hz), 4.05 (0.5H, dd, *J* = 2.5 and 8.4 Hz), 4.69 (0.5H, q, *J* = 5.3 Hz), 4.77 (0.5H, d, *J* = 11.5 Hz), 4.78 (0.5H, q, *J* = 5.5 Hz), 4.79 (0.5H, d, *J* = 11.5 Hz), 4.83 (0.5H, d, *J* = 11.5 Hz), 4.86 (0.5H, d, *J* = 11.5 Hz), 5.46 (0.5H, dd, *J* = 8.3 and 15.5 Hz), 5.55 (0.5H, dd, *J* = 7.8 and 15.5 Hz), and 5.68 (1H, dt, *J* = 15.5 and 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 14.26 (0.5C, q), 14.28 (0.5C, q), 15.1 (0.5C, q), 15.4 (0.5C, q), 20.18 (0.5C, q), 20.26 (0.5C, q), 20.28 (0.5C, q), 20.33 (0.5C, q), 24.5 (q), 25.98 (0.5C, d), 26.02 (0.5C, d), 28.73 (0.5C, t), 28.78 (0.5C, t), 31.95 (0.5C, t), 32.00 (0.5C, t), 38.87 (0.5C, t), 39.31 (0.5C, t), 46.49 (0.5C, t), 45.52 (0.5C, t), 59.19 (0.5C, t), 60.44 (0.5C, t), 62.06 (0.5C, t), 62.09 (0.5C, t), 65.68 (d), 74.65 (0.5C, t), 74.89 (0.5C, t), 77.1 (d), 78.83 (0.5C, d), 78.98 (0.5C, d), 96.60 (0.5C, d), 98.84 (0.5C, d), 126.7 (0.5C, d), 127.9 (0.5C, d), 133.7 (0.5C, d), and 135.6 (0.5C, d); FABMS *m/z* 401 $(M+Na)^+$; HRFABMS *m/z* 401.2347 $(M+Na)^+$, calcd for $C_{19}H_{38}O_5SNa$, 401.2336.

C-1 ~ C-13 Segment: Ethyl (2*E*,6*E*,8*S*,9*R*,11*S*)-8-[1-(Ethoxy)ethoxy]-2,11-dimethyl-9-methylthiomethoxy-13-oxo-2,6-tetradecadienoate (2). The 3,13-diol (**17**, 330 mg, 874 μmol) in pyridine/CH_2Cl_2 (1:1, 30 mL) was treated with Dess-Martin periodinane (2.1g, 5 mmol) at room temperature for 2.5 h. After addition of saturated aqueous Na_2SO_3 (10 mL), the reaction mixture was partitioned between Et_2O (40 mL x 3) and water (10 mL). The organic phase was washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*, and then a crude aldehyde (390 mg) was obtained. To a solution of the crude aldehyde in benzene (7 mL) was added (1-ethoxycarbonylethyl)triphenylphosphine (953 mg, 2.63 mmol). After being stirred at room temperature for 12 h, the reaction mixture was evaporated *in vacuo*. The residue was subjected to a silica gel column (hexane/EtOAc, 4:1 → 2:1), and the C-1 ~ C-13 segment (**2**, 181 mg, 394 μmol) was obtained in 45 % yield by two steps, and the aldehyde (138 mg, 364 μmol, 41 %) was recovered. **2:** colorless oil; $[\alpha]_D^{24}$ +99.8° (*c* 0.43, $CHCl_3$); IR (neat) ν_{max} 1710 and 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (3H, d, *J* = 5.9 Hz), 1.16 (1.5H, t, *J* = 7.1 Hz), 1.18 (1.5H, t, *J* = 6.9 Hz), 1.27 (1.5H, d, *J* = 5.9 Hz), 1.28 (1.5H, d, *J* = 7.0 Hz), 1.29 (3H, t, *J* = 7.1 Hz), 1.32 (1H, m), 1.41 (1H, m), 1.56 (3H, s), 1.82 (3H, s), 2.12 (1.5H, s), 2.15 (2H, m), 2.17 (1.5H, s), 2.19 (2H, m), 2.25 (2H, m), 2.62 (1H, m), 3.40 (0.5H, m), 3.51 (1H, m), 3.64 (0.5H, m), 3.78 (0.5H, m), 3.82 (0.5H, m), 4.02 (1H, m), 4.18 (2H, q, *J* = 7.1Hz), 4.66 (0.5H, q, *J* = 5.9 Hz), 4.72 (0.5H, d, *J* = 11.3 Hz), 4.73 (0.5H, m), 4.74 (0.5H, d, *J* = 11.6 Hz), 4.81 (0.5H, d, *J* = 11.6 Hz), 4.83 (0.5H, d, *J* = 11.3 Hz), 5.42 (0.5H, dd, *J* = 8.6 and 15.6 Hz), 5.51 (0.5H, d, 11.3 Hz), 5.62 (1H, m), and 6.70 (1H, m); ^{13}C NMR ($CDCl_3$) δ 12.38 (0.5C, q), 12.40 (0.5C, q), 13.94 (0.5C, q), 14.27 (0.5C, q), 14.31 (0.5C, q), 15.1 (0.5C, q), 15.4 (0.5C, q), 15.6 (0.5C, q), 20.22 (0.5C, q), 20.28 (0.5H, q), 20.57

(0.5C, q), 20.65 (0.5C, q), 25.63 (0.5C, d), 25.66 (0.5C, d), 28.2 (t), 30.37 (0.5C, q), 30.42 (0.5C, q), 31.23 (0.5C, t); 31.25 (0.5C, t), 37.9 (0.5C, t), 38.4 (0.5C, t), 50.2 (t), 59.4 (0.5C, t), 60.4 (0.5C, t), 60.7 (0.5C, t), 61.0 (0.5C, t), 74.5 (0.5C, t), 74.8 (0.5C, t), 76.3 (d), 78.4 (0.5C, d), 78.9 (0.5C, d), 96.7 (0.5C, d), 98.9 (0.5C, d), 127.1 (0.5C, d), 128.3 (0.5C, d), 133.1 (0.5C, d), 133.2 (s), 134.9 (0.5C, d), 140.91 (0.5C, d), 140.94 (0.5C, d), 167.93 (0.5C, s), 167.95 (0.5C, s), 208.4 (0.5C, s), and 208.5 (0.5C, s); FABMS *m/z* 481 $(M+Na)^+$; HRFABMS *m/z* 481.2631 $(M+Na)^+$, calcd for $C_{24}H_{42}O_6SNa$, 481.2600.

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