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Highly Stereocontrolled Total Synthesis of the Polyether Antibiotic Salinomycin. II. Synthesis of Right (C18—C30) Segments from D-Glucose, D-Mannitol, and Ethyl L-Lactate[1]

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(*S*)-4-[(2*R*,5*R*,6*S*)-5-Ethyl-5-hydroxy-6-methyltetrahydropyran-2-yl]pentan-4-olide (5), an alkaline degradation product of salinomycin (1), was synthesized with complete stereoselectivity from D-mannitol and ethyl L-lactate. Compound 5 was then converted to (3*R*,4*S*,7*S*)-7-[(2*R*,5*R*,6*S*)]-5-ethyl-5-methoxymethoxy-6-methyltetrahydropyran-2-yl]-4,7-bismethoxymethoxy-3-(tetrahydropyran-2-yloxy)oct-1-yne (3), a C18—C30 segment of 1, *via* Sharpless asymmetric epoxidation. Another C18—C30 segment, (*R*)-3-[(2*RS*,5*S*)-5-[(2*R*,5*R*,6*S*)-5-benzyloxy-5-ethyl-6-methyltetrahydropyran-2-yl]-2-methoxy-5-methyltetrahydrofuran-2-yl]-3-(4-methoxybenzyloxy)prop-1-yne (4), was synthesized more conveniently *via* coupling between a C19—C22 fragment prepared starting from D-glucose and a C23—C30 fragment prepared starting from D-mannitol and ethyl L-lactate.

Keywords polyether antibiotic; salinomycin; stereoselective synthesis; tetrahydropyran ring formation; chelation controlled Grignard reaction; Sharpless asymmetric epoxidation; Wittig–Horner coupling; 4-methoxybenzyl protection

In the preceding paper,[1] we reported a highly stereoselective synthesis of the left (C1—C9) and middle (C10—C17) segments of the polyether antibiotic salinomycin (1), one of target molecules in our studies on the stereoselective synthesis of complex natural products such as macrolide and polyether antibiotics by means of a common methodology recently established in the synthesis of some macrolide aglycones.[2] We report here stereoselective syntheses of two compounds, 3 and 4,[3] corresponding to the right segment (C18—C30) (2) of 1 starting from D-glucose, D-mannitol, and ethyl L-lactate.

Synthesis of 5 First, we planned to synthesize 3 *via* a stereoselective introduction of a three-carbon unit (C18—C20) into the lactone (5), an alkaline degradation product of 1.[4] For the construction of two 1,2-diol systems at C24—C25 and C28—C29,[5] the chelation-controlled Grignard reaction of acyclic α-alkoxyketones[6] was applied, and the Sharpless asymmetric epoxidation[7] was applicable to the introduction of the C20 chiral center.

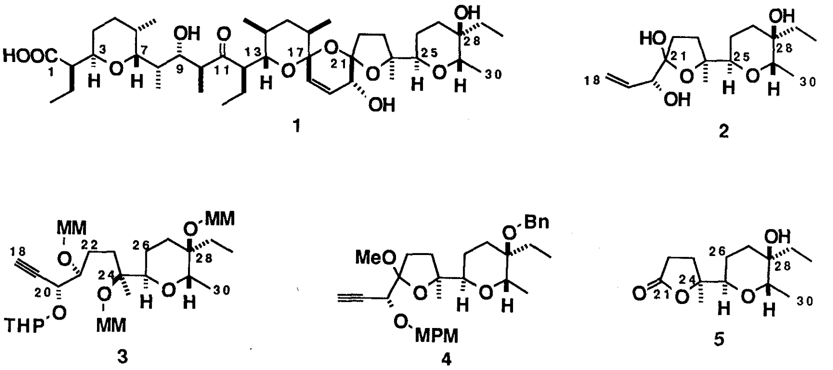
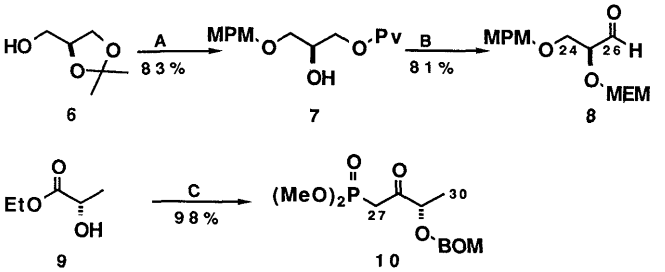


Chart 1

After protection of the alcohol (6)[8] derived from D-mannitol with a 4-methoxybenzyl (MPM) group,[9] the isopropylidene protection was removed with hydrochloric acid, and then the primary alcohol of the resulting diol was selectively protected with a pivaloyl group to give 7. Three consecutive reactions, *i.e.*, protection of the secondary alcohol of 7 with a methoxyethoxymethyl (MEM) group, removal of the pivaloyl group with lithium aluminum hydride (LAH), and Swern oxidation[10] of the resulting primary alcohol, gave the C24—C26 aldehyde (8).

Ethyl L-lactate (9) was protected with a benzyloxymethyl (BOM) group and then treated with the lithium salt of dimethyl methanephosphonate[11] to give the β-ketophosphonate (10).



(A) 1) MPMCl, NaH, DMSO–THF, r.t.; 2) 1 N HCl, THF, r.t.; 3) PvCl, Py, 0 °C (B) 1) MEMCl, iso-Pr$_2$EtN, CH_2Cl_2, r.t.; 2) $LiAlH_4$, Et_2O–THF; 3) DMSO, $(COCl)_2$, Et_3N (C) 1) BOMCl, iso-Pr$_2$EtN, CH_2Cl_2, 0 °C; 2) MePO(OMe)$_2$, *n*-BuLi, THF, $-78\,^{\circ}C$

r.t. = room temperature

Chart 2

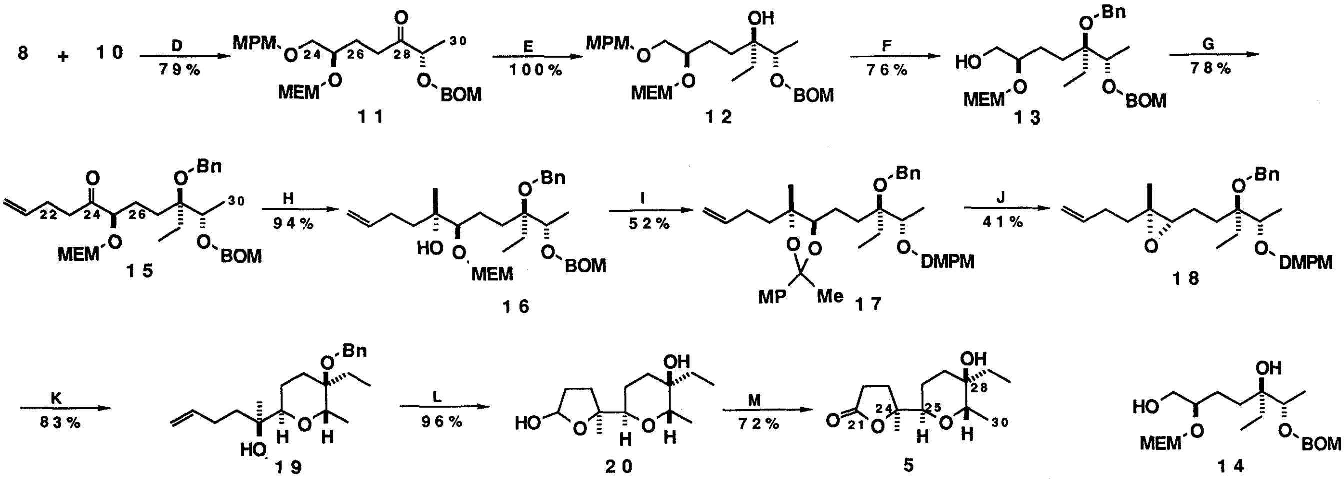
The Wittig–Horner reaction of 8 and 10 gave an enone, which was reduced to give the α-alkoxyketone (11). When 11 was treated with ethylmagnesium bromide at $-78\,^{\circ}C$, a highly stereocontrolled reaction *via* a five-membered cyclic transition state,[6] formed by a chelation of magnesium with the carbonyl and BOM-oxy group, proceeded smoothly to give the alcohol (12) with complete stereoselectivity ($>100:1$) in quantitative yield. After protection of the hydroxy group of 12 with a benzyl (Bn) group, the MPM group of the resulting ether was removed in the usual way [2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) (1.3 eq) in dichloromethane–water (20 : 1) at room temperature for 2 h].[9a] However, the deprotection of the MPM group was unfortunately accompanied with loss of the Bn group to give a 1 : 1.25 mixture of the expected alcohol (**13**) and the diol (**14**) in 90% yield, because the tertiary *O*-Bn group was unusually sensitive to DDQ. The DDQ oxidation at lower temperature slightly improved the result (**13** : **14** = 2.2 : 1). In benzene containing a small amount of water (1/10) a better result was obtained, and **13** and **14** were isolated in 66 and 11% yields, respectively. Swern oxidation[10] of **13** gave an aldehyde, which was treated with excess 1-butenylmagnesium bromide, and the resulting secondary alcohol was again oxidized under Swern's conditions to give the second α-alkoxyketone (**15**).

The chelation-controlled Grignard reaction[6] with methylmagnesium bromide proceeded quite smoothly to give **16** (stereoselection > 100 : 1). Thus the two 1,2-diol systems at C24—C25 and C28—C29 were constructed with complete stereoselectivity in excellent yield. After the MEM and BOM protecting groups were removed with hydrochloric acid, the vicinal diol group of the resulting triol was protected as a *p*-methoxyphenyl (MP)-ethylidene ketal, and the remaining secondary alcohol was protected with a 3,4-dimethoxybenzyl (DMPM) group[9b,12] to give **17**. The ketal was hydrolyzed to recover the diol group, whose secondary alcohol was selectively mesylated by treatment with a slight excess of mesyl chloride at 0 °C, and then treatment of the mesylate with excess potassium carbonate gave the epoxide (**18**).

After removal of the DMPM group with DDQ at 0 °C,[9b,12] the resulting epoxyalcohol was treated with 10-camphorsulfonic acid (CSA) at 0 °C. A quite smooth recyclization proceeded with complete regio- and stereoselectivities and was completed within 15 min to give the expected tetrahydropyran (**19**). The double bond of **19** was oxidized with a catalytic amount of osmium tetroxide in the presence of *N*-methylmorpholine *N*-oxide (NMO)[13] to a diol, then the Bn protecting group was removed by means of catalytic hydrogenation over palladium-black, and finally oxidation of the vicinal diol group with periodic acid resulted in a spontaneous cyclization to the hemiacetal (**20**), which was converted to the C21—C30 lactone (**5**) by pyridinium chlorochromate (PCC) oxidation in the presence of powdered 3 Å molecular sieves. This synthetic γ-lactone (**5**) was identical, in terms of its infrared (IR), nuclear magnetic resonance (NMR), and mass spectra (MS) and specific rotation, with the degradation product of natural salinomycin (**1**).[4]

Synthesis of 3 *via* 5 In the conversion of **5** or its synthetic equivalent hemiacetal (**20**) into **3**, stereoselective introduction of the C20 hydroxy group and functionalization at the C18 position were very important. After reduction of **5** with LAH, two tertiary hydroxy groups of the resulting triol were protected with MPM groups to give the alcohol (**21**). Swern oxidation of **21** followed by the Wittig reaction with ethoxycarbonylmethylenetriphenylphosphorane and then diisobutylaluminum hydride (DIBAH) reduction gave the allyl alcohol (**22**), which was subjected to the Sharpless asymmetric epoxidation using diethyl (+)-tartrate.[7] However, the reaction proceeded very slowly to give only the unexpected tetrahydrofuran derivative (**23**) formed by recyclization of the initially formed expected epoxy compound. Similar compounds, protected with Bn and methoxymethyl (MM) groups instead of the MPM groups, gave almost the same results. Therefore, protection of the C24-hydroxy group with an electron-withdrawing group seemed to be required.

The Wittig reaction of **20** with the phosphorane gave the α,β-unsaturated ester (**24**), which was converted to **25** *via* DIBAH reduction of the ester, *tert*-butyldimethylsilyl (TBDMS) protection of the resulting primary alcohol, acetylation of the two tertiary hydroxy groups, and recovery of the primary alcohol with the fluoride anion. The Sharpless reaction[7] of **25** proceeded quite smoothly, and



(D) 1) NaH, DMF–THF, r.t.; 2) Pd–C, H_2, EtOAc, r.t. (E) EtMgBr, THF, −78 °C (F) 1) BnBr, NaH, DMF–THF, 60 °C; 2) DDQ, C_6H_6–H_2O, r.t. (G) 1) DMSO, $(COCl)_2$, Et_3N; (2) $CH_2{=}CHCH_2CH_2MgBr$, THF, 0 °C; 3) DMSO, $(COCl)_2$, Et_3N (H) MeMgBr, THF, −78 °C (I) 1) 4 N HCl, THF, 50 °C; 2) 4-$MeOC_6H_4C(OMe)_2Me$, CSA, CH_2Cl_2, r.t.; 3) DMPMCl, NaH, DMSO–THF, r.t. (J) 1) 1 N HCl, THF, 45 °C; 2) MsCl, Et_3N, toluene, 0 °C; 3) K_2CO_3, MeOH, r.t. (K) 1) DDQ, CH_2Cl_2–H_2O, 0 °C; 2) CSA, CH_2Cl_2, 0 °C (L) 1) OsO_4, NMO, H_2O–MeCOMe, r.t.; 2) Pd, H_2, EtOH; 3) $NaIO_4$, THF–H_2O, r.t. (M) PCC, MS, CH_2Cl_2, r.t.
r.t. = room temperature

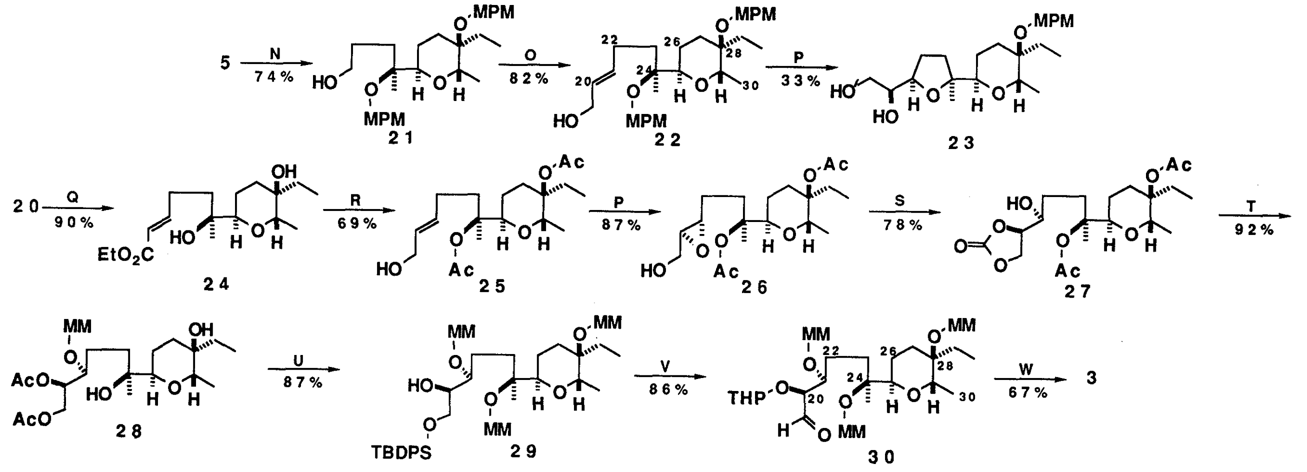
Chart 3

the expected epoxide (**26**) was isolated in high yield. Compound **26** was then converted to the carbonate (**27**), in which the configuration at C20 was inverted, by Masamune's method,[14] namely, treatment of **26** with phenyl isocyanate gave the urethane, which, without purification, was treated with perchloric acid to give **27**. Almost completely stereoselective introduction of the C20 chiral center was thus achieved.

The secondary alcohol of **27** was protected with an MM group followed by LAH reduction to give the tetraol, whose primary and secondary alcohols were then protected as the diacetate (**28**). The remaining two tertiary hydroxy groups were also protected with MM groups and then the diacetate was hydrolyzed with potassium carbonate to recover the primary and secondary hydroxy groups. The primary alcohol was selectively protected with a *tert*-butyldiphenylsilyl (TBDPS) group to give **29**. Tetrahydropyranyl (THP) protection of the secondary alcohol of **29** followed by desilylation with the fluoride anion again recovered the primary alcohol, which was oxidized to **30** under Swern's conditions.[10] Conversion from the aldehyde (**30**) into the acetylene (**3**) was readily carried out by Corey's method[15] *via* the dibromoolefin, which was formed by treatment of **30** with carbon tetrabromide and triphenylphosphine in the presence of zinc dust.[16] In this manner, the stereoselective synthesis of **3** was completed, but many steps, *e.g.*, nineteen steps from **20** to **3**, were required mainly because of the need for repeated protection and deprotection of hydroxy groups.[17]

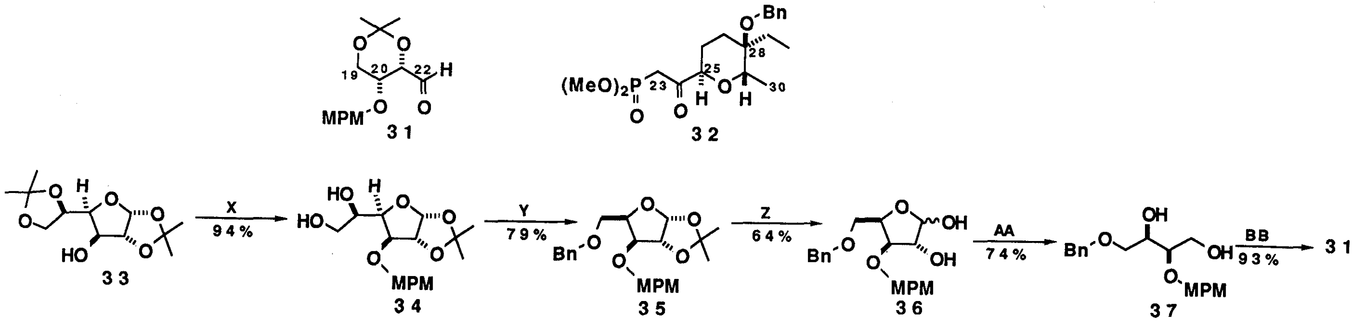
Synthesis of 4 *via* Coupling of 31 and 32[3] As a more convenient and efficient synthesis of a right segment, next we planned to synthesize **4** from **31** and **32**. Three advantages were expected. 1) Compound **4** would be much better than **3** for further reactions in order to complete the total synthesis of **1**. 2) The C20 chiral center is already present in **31**. 3) A considerable reduction in the number of reaction steps was expected.

Compound **31** was easily synthesized from diacetone-glucose (**33**) in a conventional sequence of reactions. Protection of the secondary alcohol of **33** with an MPM group[9] followed by treatment with 2% sulfuric acid to hydrolyze one of the acetonides gave the diol (**34**), which



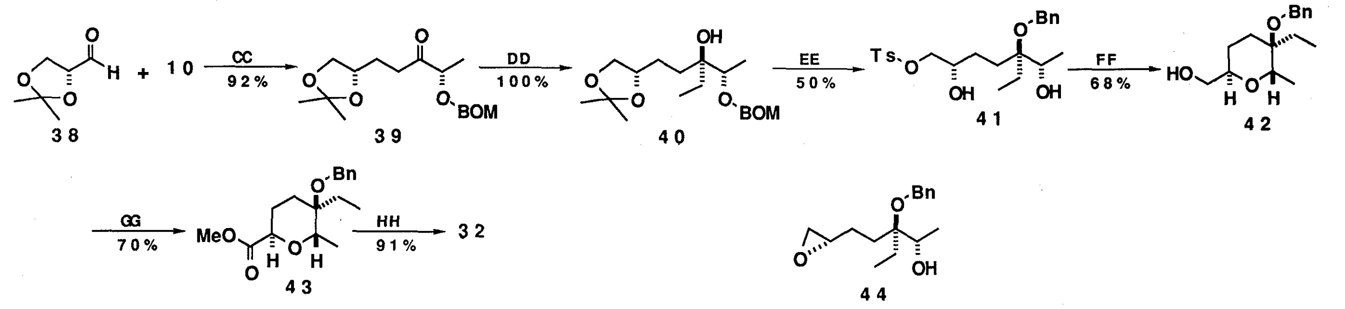
(N) 1) LiAlH$_4$, THF, 0 °C; 2) Me$_2$C(OMe)$_2$, CSA, CH$_2$Cl$_2$, r.t.; 3) MPMCl, NaH, DMSO–THF, r.t.; 4) 1 N HCl, MeOH, r.t. (O) 1) DMSO, (COCl)$_2$, Et$_3$N; 2) Ph$_3$P=CHCO$_2$Et, (CH$_2$Cl)$_2$, 70 °C; 3) DIBAH, CH$_2$Cl$_2$, −78 °C (P) TBHP, (+)-DET, Ti(iso-PrO)$_4$, CH$_2$Cl$_2$, −20 °C (Q) Ph$_3$P=CHCO$_2$Et, (CH$_2$Cl)$_2$, 60 °C (R) 1) DIBAH, CH$_2$Cl$_2$, −78 °C; 2) TBDMSCl, imidazole, CH$_2$Cl$_2$, r.t.; 3) Ac$_2$O, DMAP, Et$_3$N, toluene, 70 °C; 4) *n*-Bu$_4$NF, THF, r.t. (S) 1) PhNCO, Et$_3$N, CH$_2$Cl$_2$, r.t.; 2) 5% HClO$_4$, MeCN, r.t. (T) 1) MMCl, iso-Pr$_2$EtN, CH$_2$Cl$_2$, r.t.; 2) LiAlH$_4$, THF; 3) Ac$_2$O, DMAP, Et$_3$N, CH$_2$Cl$_2$ (U) 1) MMCl, iso-Pr$_2$EtN, CH$_2$Cl$_2$, r.t.; 2) K$_2$CO$_3$, MeOH, r.t.; 3) TBDPSCl, imidazole, CH$_2$Cl$_2$, r.t. (V) 1) DHP, PPTS, CH$_2$Cl$_2$, r.t.; 2) *n*-Bu$_4$NF, THF, r.t.; 3) DMSO, (COCl)$_2$, Et$_3$N (W) 1) CBr$_4$, Ph$_3$P, Zn dust, CH$_2$Cl$_2$, r.t.; 2) *n*-BuLi, THF, −78—0 °C
r.t. = room temperature

Chart 4



(X) 1) MPMCl, NaH, DMSO–THF, r.t.; 2) 2% H$_2$SO$_4$, MeOH, r.t. (Y) 1) NaIO$_4$, MeOH–H$_2$O, 0 °C; 2) NaBH$_4$, r.t.; 3) BnCl, NaH, DMSO–THF (Z) 4 N HCl, THF, 55 °C (AA) 1) NaIO$_4$, THF–MeOH–H$_2$O, 0 °C; 2) LiAlH$_4$, THF, 0 °C (BB) 1) (MeO)$_2$CMe$_2$; 2) Raney Ni, H$_2$, EtOH, r.t.; 3) DMSO, (COCl)$_2$, Et$_3$N
r.t. = room temperature

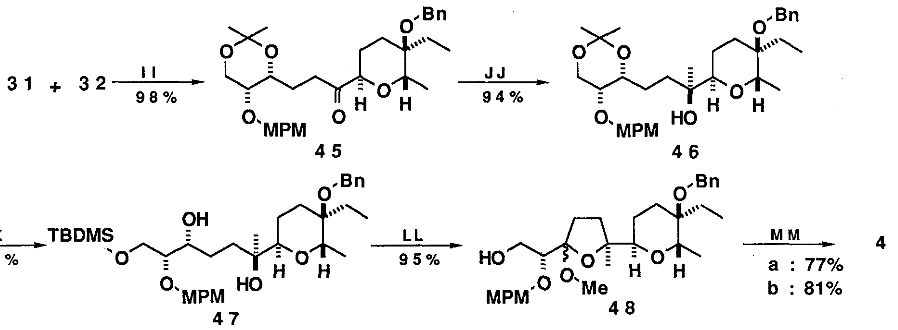
Chart 5



(CC) 1) NaH, DMSO–THF, 0 °C; 2) Pd–C, H_2, EtOAc, r.t. (DD) EtMgBr, THF, −93 °C (EE) 1) BnBr, NaH, DMF, r.t.; 2) 4 N HCl, THF, 50 °C; 3) TsCl, pyridine, r.t. (FF) NaH, DMSO–THF, r.t. (GG) 1) CrO_3, H_2SO_4, MeCOMe, 0 °C; 2) CH_2N_2, Et_2O (HH) $MePO(OMe)_2$, *n*-BuLi, THF, −93 °C

r.t. = room temperature

Chart 6



(II) 1) NaH, DMSO–THF, 0 °C; 2) Pd–C, H_2, EtOAc (JJ) MeLi, Et_2O, −93 °C (KK) 1) 1 N HCl, THF, r.t.; 2) TBDMSCl, imidazole, CH_2Cl_2, r.t. (LL) 1) DMSO, $(COCl)_2$, Et_3N; 2) CSA, MeOH, r.t. (MM) 1) DMSO, $(COCl)_2$, Et_3N; 2) $PhHgCBrCl_2$, Ph_3P, C_6H_6, reflux; 3) *n*-BuLi, THF, −78 °C

r.t. = room temperature

Chart 7

was converted to **35** *via* three conventional steps, sodium periodate oxidation, sodium borohydride reduction, and protection of the resulting primary hydroxy group with a Bn group. After hydrolysis of the acetonide of **35**, the resulting diol (**36**) was cleaved again with sodium periodate, and then reduced with LAH to give the 1,3-diol (**37**), which was protected with an isopropylidene group. Selective deprotection of the Bn group by hydrogenolysis over Raney nickel[9b,18] followed by Swern oxidation gave **31** in excellent yield.

Another fragment (**32**) was synthesized from **38**, derived from D-mannitol,[8,19] and **10** as follows. Wittig–Horner condensation of **38** and **10** gave the *E*-olefin, which was reduced to the α-alkoxyketone (**39**) in excellent yield. The chelation-controlled Grignard reaction of **39** with ethylmagnesium bromide proceeded with complete stereoselectivity *via* a five-membered transition state[6] to give **40** in quantitative yield. Benzyl protection of the tertiary alcohol of **40** followed by hydrolysis of the acetonide and BOM groups gave the triol, whose primary alcohol was selectively tosylated to give **41**. When **41** was treated with a large excess of sodium hydride, a base-catalyzed pyran ring formation *via* recyclization of the initially formed epoxide (**44**) took place to afford the expected tetrahydropyran (**42**).[20] Jones oxidation of **42** followed by treatment with diazomethane gave the ester (**43**), which was finally condensed with the lithio derivative of dimethyl methanephosphonate[11] to give the β-ketophosphonate (**32**).

Wittig–Horner condensation between **31** and **32** quantitatively gave an *E*:*Z* (5 : 1) mixture of enones, which, without separation, was readily reduced to the ketone (**45**). Although no reaction of **45** occurred with methylmagnesium bromide or lithium dimethyl cuprate, the five-membered chelation-controlled addition of methyllithium proceeded quite smoothly in ether at −93 °C to give **46** in excellent yield and stereoselectivity (33 : 1).[21] All the chiral centers required for **4** were thus constructed almost completely stereoselectively. The acetonide protection of **46** was removed with HCl, and the resulting primary alcohol was selectively protected by a TBDMS group to afford **47**. Swern oxidation of the remaining secondary alcohol gave the five-membered hemiacetal. On treatment of the hemiacetal with CSA in methanol, methylation of the hemiacetal and deprotection of the TBDMS group occurred simultaneously to give the acetal (**48**) as a *ca.* 1 : 1 stereoisomeric mixture, which was easily separated into its components, **48a** and **48b**.[22] Swern oxidation of **48a** gave the aldehyde, which was converted to the expected acetylene (C18—C30 segment) (**4**) *via* the dichloroolefin.[23,24] Compound **48b** gave almost the same result.[25]

Experimental

Physical data were measured as described in the preceding paper.[1]

(*S*)-1-(4-Methoxybenzyloxy)-3-pivaloyloxypropan-2-ol (7) A solution of **6** (5.7 g, 43.1 mmol) in tetrahydrofuran (THF, 15 ml) was added to a stirred suspension of NaH (1.6 g, 64.7 mmol) in dimethyl sulfoxide (DMSO, 50 ml) at room temperature under argon. After evolution of H_2 had ceased, MPM chloride (6.8 g, 45.3 mmol) was added, and the stirring was continued for 2 h. Et_2NH (4 ml) was added to quench excess MPM chloride, and the reaction mixture was poured into cold aqueous NH_4Cl, and extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 4) to give an MPM ether as a colorless oil (10.9 g, 100%). $[\alpha]_D^{18}$ +23° (c=2.00). ^{1}H-NMR δ: 1.36 (3H, s), 1.42 (3H, s), 3.43 (1H, dd, J=10.5, 5.5 Hz), 3.53 (1H, dd, J=10.5, 5.5 Hz), 3.72 (1H, dd, J=8.5, 6.5 Hz), 3.80 (3H, s), 4.04 (1H, dd, J=8.5, 6.5 Hz), 4.28 (1H, quintet, J=6.5 Hz), 4.47 (1H, d, J=11.5 Hz), 4.54 (1H, d, J=11.5 Hz), 6.88 (2H, d, J=8.5 Hz), 7.26 (2H, d, J=8.5 Hz). MS m/z (relative intensity): 252 (M^+, 4.8), 237 (5.6), 194 (22), 121 (100). Exact MS m/z Calcd for $C_{14}H_{20}O_4$ (M^+): 252.1363. Found: 252.1349.

A 1 N HCl solution (25 ml) was added to a stirred solution of the above MPM ether (10.9 g, 43.2 mmol) in THF (50 ml) at room temperature. After 16 h, the reaction mixture was neutralized with $NaHCO_3$ and evaporated *in vacuo*. The residue was extracted with CH_2Cl_2, and the extract was dried, and evaporated *in vacuo* to give the diol as a colorless oil (9.1 g, 99%). $[\alpha]_D^{18}$ −0.7° (c=2.44). ^{1}H-NMR δ: 2.06 (1H, t, J=6.0 Hz), 2.55 (1H, d, J=5.0 Hz), 3.45—3.78 (5H, m), 3.81 (3H, s), 4.49 (2H, s), 6.89 (2H, d, J=8.5 Hz), 7.25 (2H, d, J=8.5 Hz). MS m/z (relative intensity): 212 (M^+, 9.7), 137 (31), 121 (100). Exact MS m/z Calcd for $C_{11}H_{16}O_4$ (M^+): 212.1050. Found: 212.1050.

Pivaloyl chloride (5.4 ml, 43.7 mmol) was added dropwise to a stirred solution of the above diol (9.0 g, 42.4 mmol) in pyridine (80 ml) at 0 °C. After 1.5 h, crushed ice was added and the stirring was continued for 30 min. The reaction mixture was extracted with ether, and the extract was washed successively with 4 N HCl, brine, 10% $NaHCO_3$, and brine, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 3) to give **7** as a colorless oil (10.5 g, 84%). $[\alpha]_D^{18}$ +0.6° (c=2.16). IR ν_{max} cm^{-1}: 3450, 1720, 1610, 1590. ^{1}H-NMR δ: 1.19 (9H, s), 2.32 (1H, br s), 3.45 (1H, dd, J=9.5, 6.0 Hz), 3.55 (1H, dd, J=9.5, 4.5 Hz), 3.81 (3H, s), 3.95—4.07 (1H, m), 4.12 (1H, dd, J=6.5, 1.0 Hz), 4.17 (1H, dd, J=6.5, 1.5 Hz), 4.49 (2H, s), 6.88 (2H, d, J=8.5 Hz), 7.25 (2H, d, J=8.5 Hz). MS m/z (relative intensity): 296 (M^+, 4.7), 211 (9), 121 (100). Exact MS m/z Calcd for $C_{16}H_{24}O_5$ (M^+): 296.1625. Found: 296.1614.

(*S*)-3-(4-Methoxybenzyloxy)-2-methoxyethoxymethoxypropanal (8) Diisopropylethylamine (6.0 g, 48.1 mmol) and MEM chloride (6.4 ml) were added to a stirred solution of **7** (9.5 g, 32.0 mmol) in CH_2Cl_2 (20 ml) at room temperature. After 48 h, Et_2NH (10 ml) was added, and the reaction mixture was diluted with ether (200 ml), washed with 1 N HCl, brine, 10% $NaHCO_3$, and brine, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was chromatographed on silica gel (ether–hexane, 1 : 1) to give (*S*)-3-(4-methoxybenzyloxy)-2-methoxyethoxymethoxy-1-pivaloyloxypropane as a colorless oil (10.8 g, 88%). $[\alpha]_D^{18}$ −0.6° (c=2.24). IR ν_{max} cm^{-1}: 1720, 1610, 1590, 1510. ^{1}H-NMR δ: 1.17 (9H, s), 3.37 (3H, s), 3.59—3.66 (4H, m), 3.69—3.75 (2H, m), 3.80 (3H, s), 3.97—4.05 (1H, m), 4.13 (1H, dd, J=11.5, 5.5 Hz), 4.25 (1H, dd, J=11.5, 4.5 Hz), 4.47 (2H, s), 4.82 (2H, s), 6.87 (2H, d, J=8.5 Hz), 7.24 (2H, d, J=8.5 Hz). MS m/z (relative intensity): 295 (M^+−89, 16.4), 159 (95), 121 (100). Exact MS m/z Calcd for $C_{16}H_{23}O_5$ (M^+−89): 295.1547. Found: 295.1550.

A THF–ether (1 : 2) solution of the above compound (10.7 g, 27.8 mmol) was reduced with $LiAlH_4$ (1.6 g) in the usual way to give (*S*)-3-(4-methoxybenzyloxy)-2-methoxyethoxymethoxypropanol as a colorless oil (7.7 g, 92%).

A solution of DMSO (3.47 ml, 48.9 mmol) in CH_2Cl_2 (10 ml) was added dropwise to a stirred solution of $(COCl)_2$ (2.85 ml, 32.7 mmol) in CH_2Cl_2 (40 ml) at −70 °C under argon. After 8 min, a solution of the above alcohol (4.9 g, 16.3 mmol) in CH_2Cl_2 (10 ml) was added, and the reaction mixture was stirred for 10 min at −70 °C. Et_3N (13.6 ml, 97.6 mmol) was then added. The mixture was allowed to warm to −10 °C, diluted with CH_2Cl_2 (50 ml), washed with brine, dried (Na_2SO_4), and evaporated *in vacuo*, and the residue was chromatographed on a short silica gel column (EtOAc–hexane, 3 : 1) to give **8** as a colorless oil (4.9 g, 100%). IR ν_{max} cm^{-1}: 3500, 1730, 1610, 1590, 1510. ^{1}H-NMR δ: 3.37 (3H, s), 3.39—3.57 (2H, m), 3.73—3.79 (4H, m), 3.81 (3H, s), 4.15—4.20 (1H, m), 4.48 (2H, s), 4.89 (2H, s), 6.86 (2H, d, J=8.5 Hz), 7.23 (2H, d, J=9.5 Hz), 9.71 (1H, d, J=1.0 Hz).

Dimethyl (*S*)-3-Benzyloxymethoxy-2-oxobutylphosphonate (10) BOM chloride (10.7 g, 68.3 mmol) was added to a stirred solution of ethyl (−)-lactate (6.5 g, 55.0 mmol) and diisopropylethylamine (8.9 g, 69.0 mmol) in CH_2Cl_2 (4 ml) at 0 °C under argon. After 1 h, the solution was allowed to warm to room temperature and the stirring was continued for 24 h. The reaction mixture was diluted with CH_2Cl_2 (180 ml), washed with brine, dried (Na_2SO_4), and evaporated *in vacuo*, and the residue was chromatoraphed on a silica gel column (EtOAc–hexane, 1 : 8) to give ethyl (*S*)-2-benzyloxymethoxypropanate as a colorless oil (13.1 g, 100%). IR ν_{max} cm^{-1}: 1740, 1490. ^{1}H-NMR δ: 1.26 (3H, t, J=7.0 Hz), 1.43 (3H, d, J=7.0 Hz), 4.18 (2H, q, J=7.0 Hz), 4.29 (1H, q, J=7.0 Hz), 4.65 (2H, s), 4.83 (2H, s), 7.33 (5H, s). FD-MS m/z (relative intensity): 238 (M^+, 100).

A 1.6 M n-BuLi solution (11.5 ml, 18.4 mmol) in hexane was added dropwise to a stirred solution of dimethyl methanephosphonate (2.6 g, 21.0 mmol) in THF (30 ml) at −78 °C under argon. After 5 min, a solution of the above ester (2.0 g, 8.39 mmol) in THF (7 ml) was added dropwise, and the stirring was continued for 35 min at −78 °C. The reaction mixture was poured into cold aqueous NH_4Cl, and extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOAc) to give **10** as a colorless oil (2.6 g, 98%). $[\alpha]_D^{15}$ −27° (c=7.68). IR ν_{max} cm^{-1}: 1720, 1490. ^{1}H-NMR δ: 1.37 (3H, d, J=7.0 Hz), 3.16 (1H, d, J=1.0 Hz), 3.38 (1H, d, J=1.5 Hz), 3.72 (3H, s), 3.83 (3H, s), 4.30 (1H, q, J=7.0 Hz), 4.64 (2H, s), 4.80 (1H, d, J=7.0 Hz), 4.88 (1H, d, J=7.0 Hz), 7.34 (5H, s). FD-MS m/z (relative intensity): 317 (M^+, 100).

(2*S*,6*R*)-2-Benzyloxymethoxy-7-(4-methoxybenzyloxy)-6-methoxyethoxymethoxyheptan-3-one (11) A solution of **10** (393 mg, 1.24 mmol) in THF (2.0 ml) was added dropwise to a stirred suspension of NaH (24 mg, 1.01 mmol) in N,N-dimethylformamide (DMF, 4 ml) at 0 °C. The mixture was stirred at 0 °C for 10 min and at room temperature for 30 min. A solution of **8** (232 mg, 0.778 mmol) in THF (3.0 ml) was then added at 0 °C. After 3.5 h, the reaction mixture was stirred at room temperature for 16 h, poured into cold aqueous NH_4Cl, and extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 1) to give (2*S*,6*S*)-2-benzyloxymethoxy-7-(4-methoxybenzyloxy)-6-methoxyethoxymethoxyhept-3-en-3-one as a colorless oil (322 mg, 85%). IR ν_{max} cm^{-1}: 1700, 1640, 1620, 1590, 1520. ^{1}H-NMR δ: 1.35 (3H, d, J=7.0 Hz), 3.35 (3H, s), 3.38—3.53 (4H, m), 3.68—3.74 (2H, m), 3.79 (3H, s), 4.36 (1H, q, J=7.0 Hz), 4.40—4.52 (1H, m), 4.46 (2H, s), 4.61 (2H, s), 4.70—4.89 (4H, m), 6.63 (1H, dd, J=16.0, 1.0 Hz), 6.85 (1H, dd, J=16.0, 5.0 Hz), 6.93 (2H, d, J=8.5 Hz), 7.22 (2H, d, J=8.5 Hz), 7.31 (5H, s). MS m/z (relative intensity): 399 (M^+−89, 0.5), 121 (100). Exact MS m/z Calcd for $C_{23}H_{27}O_6$ (M^+−89): 399.1809. Found: 399.1783.

A solution of the above enone (300 mg, 0.614 mmol) in EtOAc (5 ml) was hydrogenated in the presence of 10% Pd–C (100 mg) at ordinary temperature and pressure for 1.5 h. After removal of the catalyst, the filtrate was evaporated *in vacuo* to leave **11** as a colorless oil (278 mg, 93%). IR ν_{max} cm^{-1}: 1720, 1620, 1590, 1520, 1500. ^{1}H-NMR δ: 1.32 (3H, d, J=7.0 Hz), 1.79—1.93 (2H, m), 2.62 (2H, t, J=7.5 Hz), 3.36 (3H, s), 3.40 (2H, d, J=4.5 Hz), 3.42—3.49 (2H, m), 3.52—3.77 (3H, m), 3.79 (3H, s), 4.19 (1H, q, J=7.0 Hz), 4.44 (2H, s), 4.61 (2H, s), 4.68—4.87 (4H, m), 6.86 (2H, d, J=9.0 Hz), 7.23 (2H, d, J=9.0 Hz), 7.32 (5H, s). MS m/z (relative intensity): 401 (M^+−89, 1.1), 369 (0.7), 121 (100), 91 (80). Exact MS m/z Calcd for $C_{23}H_{29}O_6$ (M^+−89): 401.1966. Found: 401.1972.

(2*S*,3*R*,6*R*)-2-Benzyoxymethoxy-3-ethyl-7-(4-methoxybenzyloxy)-6-methoxyethoxymethoxyheptan-3-ol (12) A solution of **11** (2.0 g, 4.16 mmol) in THF (10 ml) was added dropwise to a stirred EtMgBr solution prepared from EtBr (2.5 ml, 33.7 mmol) and Mg (734 mg, 30 matom) in THF (40 ml) at −78 °C. After 2 h, the reaction mixture was poured into cold aqueous NH_4Cl, and extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated *in vacuo*, and the residue was chromatographed on silica gel (EtOAc–hexane, 1 : 2) to give **12** as a colorless oil (2.3 g, 100%). $[\alpha]_D^{17}$ +20° (c=1.2). ^{1}H-NMR δ: 0.90 (3H, t, J=7.0 Hz), 1.17 (3H, d, J=6.5 Hz), 1.28—1.66 (6H, m), 2.31 (1H, br s), 3.39 (3H, s), 3.50 (2H, d, J=4.5 Hz), 3.47—3.57 (2H, m), 3.69—3.75 (4H, m), 3.81 (3H, s), 4.48 (2H, s), 4.65 (2H, s), 4.74—4.84 (4H, m), 6.87 (2H, d, J=8.5 Hz), 7.27 (2H, d, J=8.5 Hz), 7.36 (5H, s). FD-MS m/z (relative intensity): 520 (M^+, 9.1), 121 (100).

(2*R*,5*R*,6*S*)-5-Benzyloxy-6-benzyloxymethoxy-5-ethyl-2-methoxyethoxymethoxyheptan-1-ol (13) A solution of **12** (5.4 g, 10.4 mmol) in THF (30 ml) was added to a stirred suspension of NaH (745 mg, 31.0 mmol) in DMF (10 ml) at room temperature. After evolution of H_2 had ceased, benzyl bromide (3.3 ml, 28.0 mmol) was added. The reaction mixture was stirred at 60 °C for 6.5 h, poured into cold aqueous NH_4Cl, and extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 3) to give (2*S*,3*R*,6*R*)-3-benzyloxy-2-benzyloxymethoxy-3-ethyl-7-(4-methoxybenzyloxy)-6-methoxyethoxymethoxyheptane as a colorless oil (6.4 g, 100%). $[\alpha]_D^{17}$ +6.4° (c=2.40). ^{1}H-NMR δ: 0.92 (3H, t, J=7.5 Hz), 1.27 (3H, d, J=6.5 Hz), 1.50—1.90 (6H, m), 3.35 (3H, s), 3.44—3.51 (4H, m), 3.78 (3H, s), 3.65—3.85 (4H, m), 4.44 (2H, s), 4.44 (1H, d, J=12.0 Hz), 4.62 (1H, d, J=12.0 Hz), 4.62 (2H, s), 4.70—4.87

(4H, m), 6.83 (2H, d, $J=9.0$ Hz), 7.23 (2H, d, $J=9.0$ Hz), 7.31—7.33 (10H, m). FD-MS m/z (relative intensity): 611 ($M^+ + 1$, 100), 610 (M^+, 56). *Anal.* Calcd for $C_{36}H_{50}O_8$: C, 70.79; H, 8.25. Found: C, 70.55; H, 8.27.

DDQ (2.9 g, 12.8 mmol) and H_2O (15 ml) were added to a stirred solution of the above compound (7.1 g, 11.6 mmol) in benzene (150 ml) at room temperature. After 3 h, the reaction mixture was diluted with ether, washed with 10% $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 2 : 1). The first fraction gave **13** as a colorless oil (3.78 g, 66%). $[\alpha]_D^{17}$ $-5.1°$ ($c=1.64$). ^{1}H-NMR δ: 0.93 (3H, t, $J=7.5$ Hz), 1.28 (3H, d, $J=6.5$ Hz), 1.53—1.82 (6H, m), 3.02—3.32 (1H, m), 3.38 (3H, s), 3.47—3.90 (8H, m), 4.45 (1H, d, $J=11.5$ Hz), 4.61 (1H, d, $J=11.5$ Hz), 4.63 (2H, s), 4.72 (1H, d, $J=7.5$ Hz), 4.70—4.86 (8H, m), 7.21—7.33 (5H, m). FD-MS m/z (relative intensity): 491 ($M^+ + 1$, 81), 391 (33), 165 (33), 121 (100). *Anal.* Calcd for $C_{28}H_{42}O_7$: C, 68.54; H, 8.63. Found: C, 68.24; H, 8.68.

The second fraction gave (2*S*,5*R*,6*R*)-6-benzyloxymethoxy-5-ethyl-2-methoxyethoxymethoxyheptane-1,5-diol (**14**) as a colorless oil (520 mg, 11%). ^{1}H-NMR δ: 0.89 (3H, t, $J=7.5$ Hz), 1.18 (3H, d, $J=6.5$ Hz), 1.30—1.64 (6H, m), 2.36 (2H, br s), 3.39 (3H, s), 3.56—3.88 (8H, m), 4.64 (2H, s), 4.72—4.89 (4H, m), 7.34 (5H, s).

(6*R*,9*R*,10*S*)-9-Benzyloxy-10-benzyloxymethoxy-9-ethyl-6-methoxyethoxymethoxyundec-1-en-5-one (15) Swern oxidation of **13** (3.8 g, 7.71 mmol) as described for **8** gave the aldehyde as a colorless oil (3.7 g, 98%). IR ν_{max} cm^{-1}: 1730, 1610, 1590, 1490. ^{1}H-NMR δ: 0.92 (3H, t, $J=7.5$ Hz), 1.27 (3H, d, $J=6.5$ Hz), 1.69—1.80 (6H, m), 3.36 (3H, s), 3.50 (2H, t, $J=4.5$ Hz), 3.64—3.95 (4H, m), 4.44 (1H, d, $J=11.5$ Hz), 4.58 (1H, d, $J=11.5$ Hz), 4.62 (2H, s), 4.76 (1H, d, $J=7.0$ Hz), 4.77 (1H, d, $J=7.0$ Hz), 4.82 (1H, d, $J=7.0$ Hz), 4.84 (1H, d, $J=7.0$ Hz), 7.23—7.33 (10H, m), 9.61 (1H, d, $J=1.5$ Hz). FD-MS m/z (relative intensity): 489 ($M^+ + 1$, 21), 488 (M^+, 15), 487 (21), 323 (100).

A solution of the aldehyde (430 mg, 0.88 mmol) in THF (3 ml) was added dropwise to a stirred solution of the Grignard reagent prepared from 4-bromo-1-butene (503 mg, 3.73 mmol) and Mg (60 mg) in THF (2.5 ml) at 0 °C under argon. After 1 h, work-up as described for **12** gave the alcohol as a colorless oil (460 mg, 96%). FD-MS m/z (relative intensity): 545 ($M^+ + 1$, 41), 323 (11.5), 308 (14), 271 (22), 165 (46), 135 (36), 121 (100).

Swern oxidation of the alcohol (3.7 g, 6.77 mmol) as described for **8** gave **15** as a colorless oil (3.1 g, 83%). IR ν_{max} cm^{-1}: 1720, 1640, 1610, 1580, 1490. ^{1}H-NMR δ: 0.91 (3H, t, $J=7.5$ Hz), 1.26 (3H, d, $J=6.5$ Hz), 1.60—1.85 (6H, m), 2.27 (1H, t, $J=7.5$ Hz), 2.32 (1H, t, $J=7.0$ Hz), 2.57 (2H, t, $J=7.0$ Hz), 3.35 (3H, s), 3.45—3.50 (2H, m), 3.66—3.70 (2H, m), 3.83 (1H, q, $J=6.5$ Hz), 4.05 (1H, dd, $J=6.5$, 4.5 Hz), 4.44 (1H, d, $J=12.5$ Hz), 4.58 (2H, d, $J=12.5$ Hz), 4.65 (1H, d, $J=12.5$ Hz), 4.69 (1H, d, $J=7.0$ Hz), 4.74 (1H, d, $J=7.0$ Hz), 4.76 (1H, d, $J=7.0$ Hz), 4.83 (1H, d, $J=7.0$ Hz), 4.95 (1H, dq, $J=17.0$, 1.5 Hz), 5.02 (1H, dq, $J=10.0$, 1.5 Hz), 5.78 (1H, ddt, $J=17.0$, 10.0, 6.5 Hz), 7.20—7.33 (10H, m). FD-MS m/z (relative intensity): 543 ($M^+ + 1$, 23), 542 (7), 467 (14), 435 (31), 377 (100).

(5*S*,6*R*,9*R*,10*S*)-9-Benzyloxy-10-benzyloxymethoxy-9-ethyl-6-methoxyethoxymethoxy-5-methylundec-1-en-5-ol (16) A solution of **15** (336 mg, 0.619 mmol) in THF (3 ml) was added dropwise to a stirred MeMgBr solution prepared from MeBr (0.51 ml, 9.29 mmol) and Mg (150 mg, 6.19 matom) in THF (10 ml) at -78 °C. After 1.5 h, work-up as described for **12** gave **16** as a colorless oil (325 mg, 94%). $[\alpha]_D^{16.5}$ $-2.2°$ ($c=4.12$). ^{1}H-NMR δ: 0.93 (3H, t, $J=7.5$ Hz), 1.08 (3H, s), 1.29 (3H, d, $J=6.5$ Hz), 1.36—2.38 (11H, m), 3.24 (1H, t, $J=6.0$ Hz), 3.36 (3H, s), 3.50—3.86 (5H, m), 4.43 (1H, d, $J=11.0$ Hz), 4.61 (1H, d, $J=11.0$ Hz), 4.64 (2H, s), 4.72 (1H, d, $J=7.5$ Hz), 4.77 (1H, d, $J=7.5$ Hz), 4.85 (1H, d, $J=7.5$ Hz), 4.87 (1H, d, $J=7.5$ Hz), 4.93 (1H, dq, $J=10.0$, 1.5 Hz), 5.01 (1H, dq, $J=16.5$, 2.0 Hz), 5.84 (1H, ddt, $J=16.5$, 10.0, 6.5 Hz), 7.23—7.33 (10H, m). FD-MS m/z (relative intensity): 559 ($M^+ + 1$, 66), 165 (100). *Anal.* Calcd for $C_{33}H_{50}O_7$: C, 70.93; H, 9.02. Found: C, 70.93; H, 9.06.

(5*S*,6*R*,9*R*,10*S*)-9-Benzyloxy-9-ethyl-10-(3,4-dimethoxybenzyloxy)-5,6-[1-(4-methoxyphenyl)ethylidenedioxy)]-5-methylundec-1-ene (17) A solution of **16** (270 mg, 0.483 mmol) in THF (4 ml) and 4 N HCl (2 ml) was stirred at 50 °C for 6 h. The reaction mixture was neutralized with $NaHCO_3$ and evaporated *in vacuo*. The residue was extracted with CH_2Cl_2, dried, evaporated, and chromatographed on a silica gel column (EtOAc–hexane, 2 : 3 then MeOH–CH_2Cl_2, 1 : 10) to give (2*S*,3*R*,6*R*,7*S*)-3-benzyloxy-3-ethyl-7-methylundec-10-ene-2,6,7-triol as a colorless oil (105 mg, 62%). $[\alpha]_D^{21}$ $+15°$ ($c=2.44$). ^{1}H-NMR δ: 0.94 (3H, t, $J=7.5$ Hz), 1.14 (3H, s), 1.22 (3H, d, $J=6.5$ Hz), 1.34—2.74 (13H, m), 3.30 (1H, t, $J=6.5$ Hz), 3.99 (1H, q, $J=6.5$ Hz), 4.39 (1H, d, $J=11.0$ Hz), 4.53 (1H, d, $J=11.0$ Hz), 4.97 (1H, dq, $J=10.0$, 1.0 Hz), 5.01 (1H, dq, $J=16.5$, 1.5 Hz), 5.85 (1H, ddt, $J=16.5$, 10.0, 6.5 Hz), 7.34 (5H, s). FD-MS m/z (relative intensity): 351 ($M^+ + 1$, 100).

CSA (30 mg) and 4-methoxyacetophenone dimethyl acetal (836 mg, 4.26 mmol) were added to a stirred solution of the above triol (995 mg, 2.84 mmol) in CH_2Cl_2 (10 ml) at room temperature. After 30 min, the reaction mixture was neutralized with Et_3N and evaporated *in vacuo*. The residue was chromatographed on a silica gel column (ether–benzene, 1 : 10) to give the acetal as a colorless oil (1.18 g, 86%). ^{1}H-NMR δ: 0.96 (3H, t, $J=7.5$ Hz), 1.23 (3H, d, $J=6.5$ Hz), 1.24 (3H, s), 1.58 (3H, s), 1.31—2.07 (10H, m), 2.47 (1H, br s), 3.75 (1H, dd, $J=11.0$, 3.0 Hz), 3.79 (3H, s), 3.99 (1H, q, $J=6.5$ Hz), 4.42 (1H, d, $J=11.0$ Hz), 4.51 (1H, d, $J=11.0$ Hz), 4.73 (1H, br d, $J=17.5$ Hz), 4.74 (1H, br d, $J=9.0$ Hz), 5.44 (1H, ddt, $J=17.5$, 9.0, 7.0 Hz), 6.82 (2H, d, $J=9.0$ Hz), 7.27—7.34 (5H, m), 7.43 (2H, d, $J=9.0$ Hz). MS m/z (relative intensity): 467 ($M^+ - 15$, 10), 359 (7), 241 (5.7), 135 (100). Exact MS m/z Calcd for $C_{29}H_{39}O_5$ ($M^+ - 15$): 467.2800. Found: 467.2770.

A solution of the above acetal (1.2 g, 2.45 mmol) in THF (9.5 ml) was added to a stirred suspension of NaH (176 mg, 7.34 mmol) in DMSO (3.2 ml) at room temperature. After evolution of H_2 had ceased, DMPM chloride (910 mg, 4.89 mmol) was added, and the reaction mixture was stirred at room temperature under argon overnight and then quenched with Et_2NH. Work-up as described for **7** gave **17** as a colorless oil (1.5 g, 97%). ^{1}H-NMR δ: 0.96 (3H, t, $J=7.5$ Hz), 1.24 (3H, s), 1.29 (3H, d, $J=6.5$ Hz), 1.56 (3H, s), 1.37—2.15 (10H, m), 3.64 (1H, q, $J=6.5$ Hz), 3.77—3.88 (1H, m), 3.77 (3H, s), 3.83 (3H, s), 3.86 (3H, s), 4.36 (1H, d, $J=11.5$ Hz), 4.48 (1H, d, $J=11.5$ Hz), 4.62 (1H, d, $J=11.5$ Hz), 4.66 (1H, d, $J=11.5$ Hz), 4.72 (1H, d, $J=18.0$ Hz), 4.73 (1H, d, $J=10.0$ Hz), 5.42 (1H, ddt, $J=18.0$, 10.0, 6.5 Hz), 6.75—6.90 (5H, m), 7.20—7.43 (7H, m). MS m/z (relative intensity): 632 (M^+, 0.2), 617 (1.4), 467 (1.5), 287 (19), 151 (100), 91 (89). Exact MS m/z Calcd for $C_{39}H_{52}O_7$ (M^+): 632.3716. Found: 632.3706. Calcd for $C_{38}H_{49}O_7$ ($M^+ - 15$): 617.3481. Found: 617.3472.

(5*S*,6*R*,9*R*,10*S*)-9-Benzyloxy-9-ethyl-10-(3,4-dimethoxybenzyloxy)-5-methyl-5,6-epoxyundec-1-ene (18) A solution of **17** (1.46 g, 2.32 mmol) in THF (45 ml) and 1 N HCl (15 ml) was stirred at 45 °C for 7.5 h. After neutralization with $NaHCO_3$, the mixture was evaporated *in vacuo*. The residue was extracted with CH_2Cl_2, dried, and evaporated, and this residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 1) to give the diol as a colorless oil (937 mg, 81%). $[\alpha]_D^{22}$ $+26°$ ($c=1.96$). ^{1}H-NMR δ: 0.90 (3H, t, $J=7.5$ Hz), 1.09 (3H, s), 1.30 (3H, d, $J=6.5$ Hz), 1.39—2.20 (12H, m), 3.31 (1H, dd, $J=10.0$, 2.5 Hz), 3.62 (1H, q, $J=6.5$ Hz), 3.84 (3H, s), 3.88 (3H, s), 4.34 (1H, d, $J=11.5$ Hz), 4.50 (1H, d, $J=11.0$ Hz), 4.63 (1H, d, $J=11.0$ Hz), 4.68 (1H, d, $J=11.5$ Hz), 4.94 (1H, dq, $J=10.5$, 1.0 Hz), 5.00 (1H, dq, $J=16.5$, 2.0 Hz), 5.82 (1H, ddt, $J=16.5$, 10.5, 6.0 Hz), 6.80—6.89 (3H, m), 7.29—7.34 (5H, m). MS m/z (relative intensity): 500 (M^+, 0.1), 287 (4.3), 197 (21), 151 (87), 91 (100). Exact MS m/z Calcd for $C_{30}H_{44}O_6$ (M^+): 500.3140. Found: 500.3138.

Mesyl chloride (25 mg) was added to a stirred solution of the above diol (77 mg, 0.154 mmol) and Et_3N (25 mg) in toluene (0.8 ml) at 0 °C. After 2 h, the reaction mixture was diluted with ether (10 ml), washed successively with 1 N HCl, brine, 10% $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. The residue was dissolved in MeOH (4 ml) and K_2CO_3 (42 mg) was added at room temperature. After 30 min, the precipitates were removed by filtration, the filtrate was evaporated, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 3) to give **18** as a colorless oil (41 mg, 55%). ^{1}H-NMR δ: 0.92 (3H, t, $J=7.5$ Hz), 1.21 (3H, s), 1.28 (3H, d, $J=6.5$ Hz), 1.46—1.88 (8H, m), 2.08—2.20 (2H, m), 2.69 (1H, dd, $J=5.5$, 5.0 Hz), 3.61 (1H, q, $J=6.5$ Hz), 3.84 (3H, s), 3.88 (3H, s), 4.33 (1H, d, $J=11.5$ Hz), 4.49 (1H, d, $J=11.5$ Hz), 4.62 (1H, d, $J=11.5$ Hz), 4.63 (1H, d, $J=11.5$ Hz), 4.95 (1H, dq, $J=10.5$, 1.5 Hz), 5.01 (1H, dq, $J=17.0$, 2.0 Hz), 5.79 (1H, ddt, $J=17.0$, 10.5, 6.5 Hz), 6.84—6.89 (3H, m), 7.22—7.33 (5H, m).

(*S*)-2-[(2*R*,5*R*,6*S*)-5-Benzyloxy-5-ethyl-6-methyltetrahydropyran-2-yl]-hex-5-en-2-ol (19) DDQ (19 mg, 0.085 mmol) and H_2O (0.01 ml) were added to a stirred solution of **18** (39 mg, 0.081 mmol) in CH_2Cl_2 (2 ml) at 0 °C. After 20 min, 10% $NaHCO_3$ (1 ml) was added. The mixture was extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 4) to give the epoxy alcohol as a colorless oil (25 mg, 92%). $[\alpha]_D^{21.5}$ $+5.9°$ ($c=2.08$). ^{1}H-NMR δ: 0.94 (3H, t, $J=7.5$ Hz), 1.20 (3H, d, $J=6.5$ Hz), 1.26 (3H, s), 1.43—1.93 (8H, m), 2.13—2.22 (2H, m), 2.46 (1H, d, $J=1.0$ Hz), 2.70 (1H, dd, $J=7.0$, 5.5 Hz), 3.98 (1H, dq, $J=1.0$, 6.5 Hz), 4.46 (2H, s), 4.96 (1H, d, $J=10.5$ Hz), 5.03 (1H, dq, $J=17.0$, 1.5 Hz), 5.86 (1H, ddt, $J=17.0$, 10.5, 6.5 Hz), 7.28—7.36 (5H, m).

CSA (6 mg) was added to a stirred solution of the above alcohol (25 mg, 0.075 mmol) in CH_2Cl_2 (5 ml) at 0 °C. After 15 min, Et_3N was added, and the mixture was evaporated *in vacuo*. The residue was chromatographed on a silica gel column (EtOAc–hexane, 1:4) to give **19** as a colorless oil (22 mg, 90%). $[\alpha]_D^{22}$ $-5.1°$ ($c=3.04$). ^{1}H-NMR δ: 0.89 (3H, t, $J=7.5$ Hz), 1.14 (3H, s), 1.26 (3H, d, $J=7.0$ Hz), 1.32—2.26 (11H, m), 3.44 (1H, dd, $J=11.5$, 2.5 Hz), 4.14 (1H, q, $J=7.0$ Hz), 4.31 (1H, d, $J=11.0$ Hz), 4.41 (1H, d, $J=11.0$ Hz), 4.93 (1H, d, $J=11.0$ Hz), 5.01 (1H, dq, $J=17.0$, 1.5 Hz), 5.85 (1H, ddq, $J=17.0$, 11.0, 6.5 Hz), 7.21—7.43 (5H, m). MS *m/z* (relative intensity): 314 (M^+-18, 0.1), 273 (0.5), 233 (0.9), 223 (1.0), 208 (3), 91 (100). Exact MS *m/z* Calcd for $C_{21}H_{30}O_2$ (M^+-18): 314.2247. Found: 314.2233.

(2*S*,3*R*,6*R*)-3-Ethyl-6-[(2*S*)-5-hydroxytetrahydrofuran-2-yl]-2-methyltetrahydropyran-3-ol (20) NMO (90 mg) and OsO_4 (9 mg) were added to a stirred solution of **19** (22 mg, 0.066 mmol) in H_2O–acetone (1:2) (1.5 ml) at room temperature. After 30 min, aqueous $Na_2S_2O_4$ and celit were added and the mixture was vigorously stirred at room temperature for 30 min, and then filtered. The filtrate was concentrated *in vacuo*, and the residue was extracted with ether. The extract was washed with 0.1 N HCl and brine, dried ($MgSO_4$), and evaporated, and the residue was chromatographed on a silica gel column (MeOH–CH_2Cl_2, 1:8) to give the triol as a colorless oil (24 mg, 96%). ^{1}H-NMR δ: 0.89 (3H, t, $J=7.5$ Hz), 1.15 (1.5H, s), 1.16 (1.5H, s), 1.25 (3H, d, $J=7.0$ Hz), 1.29—2.05 (13H, m), 3.35—3.66 (4H, m), 4.07—4.16 (1H, m), 4.31 (1H, d, $J=11.0$ Hz), 4.40 (1H, d, $J=11.0$ Hz), 7.29—7.43 (5H, m).

A solution of the above triol (109 mg, 0.297 mmol) in EtOH (2 ml) was hydrogenated over Pd–black (30 mg) at ordinary temperature and pressure for 3 d. Work-up as usual gave the tetraol as a colorless oil (82 mg). ^{1}H-NMR δ: 0.92 (3H, t, $J=7.5$ Hz), 1.16 (1.5H, s), 1.17 (1.5H, s), 1.23 (3H, d, $J=7.0$ Hz), 1.30—1.69 (10H, m), 2.58 (4H, br s), 3.38—3.85 (5H, m).

An aqueous solution (1 ml) of $NaIO_4$ (64 mg, 0.30 mmol) was added to a stirred solution of the above tetraol (78 mg, 0.282 mmol) in THF (4 ml) at room temperature. After 30 min, the reaction mixture was filtrated, and the filtrate was evaporated *in vacuo*. The residue was extracted with CH_2Cl_2. The extract was dried (Na_2SO_4), and evaporated *in vacuo* to give **20** as a colorless oil (66 mg, 96%). MS *m/z* (relative intensity): 226 (M^+-18, 8.5), 208 (5.7), 181 (9.2), 143 (40), 125 (42), 107 (46), 83 (95), 57 (100). Exact MS *m/z* Calcd for $C_{13}H_{22}O_3$ (M^+-18): 226.1566. Found: 226.1570.

(*S*)-4-[(2*R*,5*R*,6*S*)-5-Ethyl-5-hydroxy-6-methyltetrahydropyran-2-yl]pentan-4-olide (5) PCC (123 mg, 0.57 mmol) and powdered molecular sieves 3 Å (85 mg) were added to a stirred solution of **20** (63 mg, 0.258 mmol) in CH_2Cl_2 (1 ml) at room temperature. After 40 min, the reaction mixture was filtered, and the filtrate was evaporated *in vacuo*. The residue was purified by a silica gel column chromatography and TLC (EtOAc–hexane, 2:1) to give **5** as a colorless oil (45 mg, 72%). $[\alpha]_D^{21.5}$ $-31°$ ($c=1.4$). IR ν_{max} cm^{-1}: 3450, 1760. ^{1}H-NMR δ: 0.95 (3H, t, $J=7.5$ Hz), 1.23 (3H, d, $J=7.0$ Hz), 1.36 (3H, s), 1.03—1.93 (8H, m), 2.17—2.77 (3H, m), 3.64 (1H, dd, $J=8.0$, 3.0 Hz), 3.80 (1H, q, $J=7.0$ Hz). MS *m/z* (relative intensity): 242 (M^+, 3.7), 224 (6.6), 198 (4.4), 180 (35), 158 (36), 143 (54), 125 (63), 123 (46), 99 (79), 57 (100). Exact MS *m/z* Calcd for $C_{13}H_{22}O_4$ (M^+): 242.1519. Found: 242.1536.

(*S*)-4-[(2*R*,5*R*,6*S*)-5-Ethyl-5-(4-methoxybenzyloxy)-6-methyltetrahydropyran-2-yl]-4-(4-methoxybenzyloxy)pentan-1-ol (21) A solution of **5** (3.04 g, 12.6 mmol) in THF (20 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (1.10 g, 29.0 mmol) in THF (20 ml) at 0°C. The reaction mixture was stirred at room temperature for 1.5 h and then quenched with MeOH at 0°C. H_2O (4.4 ml) and 15% NaOH (1.2 ml) were added, and the mixture was vigorously stirred at room temperature for 1.5 h. After removal of insoluble materials by filtration, the filtrate was evaporated *in vacuo* and the residue was chromatographed on a short silica gel column (EtOAc–hexane, 4:1) to give a triol as a colorless oil (3.09 g, 100%). MS *m/z* (relative intensity): 229 (M^+-17, 0.3), 221 (0.5), 195 (0.5), 182 (0.6), 169 (10), 143 (11.5), 125 (10), 115 (8), 108 (13), 103 (26), 97 (20), 85 (45), 57 (55), 43 (100). Exact MS *m/z* Calcd for $C_{13}H_{25}O_3$ (M^+-17): 229.1805. Found: 229.1808.

A solution of the above triol (3.06 g, 12.4 mmol), 2,2-dimethoxypropane (50 ml), and CSA (300 mg) in CH_2Cl_2 (20 ml) was stirred at room temperature for 3 h, then neutralized with Et_3N, and evaporated *in vacuo*. The residue was chromatographed on a short silica gel column (EtOAc–hexane, 2:1) to give the mono-2-methoxypropyl ether (3.29 g, 83%).

A solution of the above ether (3.29 g, 10.3 mmol) in THF (25 ml) was added dropwise to a stirred suspension of NaH (1.64 g, 68.2 mmol) in DMSO (18 ml) under argon. After evolution of H_2 had ceased, the solution was treated with MPM chloride (6.2 g, 41.3 mmol) as described for **7** to give the di-MPM compound as a colorless oil, which was treated with 1 N HCl (20 ml) in MeOH (80 ml) at room temperature for 20 min. The reaction mixture was neutralized with $NaHCO_3$ and evaporated *in vacuo*. Et_2O (250 ml) and H_2O (100 ml) were added to the residue, and the aqueous layer was extracted with Et_2O. The combined extracts were dried ($MgSO_4$), and evaporated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 2:3) to give **21** as a colorless oil (4.48 g, 89%). $[\alpha]_D^{25}$ $+26°$ ($c=2.6$). ^{1}H-NMR δ: 0.88 (3H, t, $J=7.0$ Hz), 1.25 (3H, d, $J=7.0$ Hz), 1.26 (3H, s), 1.40—2.05 (11H, m), 3.58—3.69 (3H, m), 3.78 (6H, s), 4.10 (1H, q, $J=7.0$ Hz), 4.25 (1H, d, $J=9.0$ Hz), 4.34 (1H, d, $J=10.0$ Hz), 4.36 (1H, d, $J=9.0$ Hz), 4.54 (1H, d, $J=10.0$ Hz), 6.82 (2H, d, $J=8.0$ Hz), 6.83 (2H, d, $J=9.0$ Hz), 7.21 (2H, d, $J=9.0$ Hz), 7.30 (2H, d, $J=8.0$ Hz). MS *m/z* (relative intensity): 365 (M^+-121, 0.2), 305 (0.4), 229 (1), 211 (4), 121 (100), 111 (11), 85 (22). Exact MS *m/z* Calcd for $C_{21}H_{33}O_5$ (M^+-121): 365.2330. Found: 365.2308.

(2*E*,6*S*)-[(2*R*,5*R*,6*S*)-5-Ethyl-5-(4-methoxybenzyloxy)-6-methyltetrahydropyran-2-yl]-6-(4-methoxybenzyloxy)hept-2-en-1-ol (22) Compound **21** (2.0 g, 4.11 mmol) was oxidized with $(COCl)_2$ (1.3 ml, 14.8 mmol), DMSO (3.2 ml, 44.4 mmol), and Et_3N (4.2 ml, 30.0 mmol) as described for **8** to give the aldehyde as a colorless oil (1.80 g, 90%). IR ν_{max} cm^{-1}: 2700, 1720, 1610, 1585. ^{1}H-NMR δ: 0.88 (3H, t, $J=7.5$ Hz), 1.25 (3H, s), 1.26 (3H, d, $J=7.0$ Hz), 1.32—1.51 (4H, m), 1.81—2.17 (4H, m), 2.50—2.57 (2H, m), 3.60 (1H, dd, $J=11.5$, 2.0 Hz), 3.78 (3H, s), 3.79 (3H, s), 4.13 (1H, q, $J=7.0$ Hz), 4.23 (1H, d, $J=10.0$ Hz), 4.30 (1H, d, $J=11.0$ Hz), 4.36 (1H, d, $J=11.0$ Hz), 4.46 (1H, d, $J=10.0$ Hz), 6.83 (2H, d, $J=9.0$ Hz), 6.84 (2H, d, $J=9.0$ Hz), 7.18 (2H, d, $J=9.0$ Hz), 7.30 (2H, d, $J=9.0$ Hz), 9.76 (1H, t, $J=2.0$ Hz). MS *m/z* (relative intensity): 363 (M^+-121, 0.3), 227 (4), 209 (5), 121 (100). Exact MS *m/z* Calcd for $C_{21}H_{31}O_5$ (M^+-121): 363.2173. Found: 363.2163.

A solution of the above aldehyde (1.80 g, 3.70 mmol) and ethoxycarbonylmethylenetriphenylphosphorane (2.60 g, 7.46 mmol) in $(CH_2Cl)_2$ (45 ml) was stirred at 70 °C for 2.5 h under argon. The reaction mixture was evaporated *in vacuo* and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1:4) to give the α,β-unsaturated ester as a colorless oil (1.96 g, 95%). IR ν_{max} cm^{-1}: 1720, 1660, 1620, 1590. ^{1}H-NMR δ: 0.88 (3H, t, $J=7.5$ Hz), 1.24 (3H, s), 1.24 (3H, d, $J=7.0$ Hz), 1.28 (3H, t, $J=7.5$ Hz), 1.35—2.00 (8H, m), 2.15—2.31 (2H, m), 3.65 (1H, dd, $J=11.5$, 1.5 Hz), 3.79 (6H, s), 4.11 (1H, q, $J=7.0$ Hz), 4.18 (2H, d, $J=7.5$ Hz), 4.22 (1H, d, $J=10.5$ Hz), 4.31 (1H, d, $J=8.5$ Hz), 4.36 (1H, d, $J=8.5$ Hz), 4.44 (1H, d, $J=10.5$ Hz), 5.82 (1H, dt, $J=15.5$, 1.0 Hz), 6.84 (4H, d, $J=8.0$ Hz), 7.02 (1H, dt, $J=15.5$, 7.0 Hz), 7.20 (2H, d, $J=8.0$ Hz), 7.30 (2H, d, $J=8.0$ Hz). MS *m/z* (relative intensity): 433 (M^+-121, 0.4), 373 (0.2), 297 (6.5), 279 (2), 251 (1), 137 (3), 121 (100). Exact MS *m/z* Calcd for $C_{25}H_{37}O_6$ (M^+-121): 433.2592. Found: 433.2599.

A solution of the above ester (1.90 g, 3.43 mmol) in CH_2Cl_2 (60 ml) was treated with a 1.0 M DIBAH solution (14.1 ml, 14.1 mmol) in hexane at -78 °C for 40 min under argon. The reaction mixture was quenched with MeOH, diluted with CH_2Cl_2 (30 ml), and washed with 2 N HCl, H_2O, 10% $NaHCO_3$ and brine. The aqueous layer was extracted with Et_2O. Combined extracts were dried ($MgSO_4$), and evaporated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOA–hexane, 2:3) to give **22** as a colorless oil (1.68 g, 96%). ^{1}H-NMR δ: 0.88 (3H, t, $J=7.5$ Hz), 1.23 (3H, s), 1.25 (3H, d, $J=7.0$ Hz), 1.29—1.94 (9H, m), 2.11—2.19 (2H, m), 3.63 (1H, dd, $J=11.0$, 2.0 Hz), 3.79 (6H, s), 4.06—4.09 (2H, m), 4.10 (1H, q, $J=7.0$ Hz), 4.24 (1H, d, $J=12.5$ Hz), 4.33 (1H, d, $J=10.5$ Hz), 4.36 (1H, d, $J=12.5$ Hz), 4.44 (1H, d, $J=10.5$ Hz), 5.63 (1H, dt, $J=15.5$, 5.0 Hz), 5.75 (1H, dt, $J=15.5$, 6.0 Hz), 6.84 (4H, d, $J=9.0$ Hz), 7.21 (2H, d, $J=9.0$ Hz), 7.31 (2H, d, $J=9.0$ Hz). MS *m/z* (relative intensity): 391 (M^+-121, 0.1), 278 (0.1), 255 (2), 237 (0.9), 151 (1), 121 (100), 57 (11), 43 (13). Exact MS *m/z* Calcd for $C_{23}H_{35}O_5$ (M^+-121): 391.2487. Found: 391.2509.

(*S*)-1-[(2*R*,5*S*)-5-[(2*R*,5*R*,6*S*)-5-Ethyl-5-(4-methoxybenzyloxy)-6-methyltetrahydropyran-2-yl]-5-methyltetrahydrofuran-2-yl]ethane-1,2-diol (23) A solution of diethyl (+)-L-tartrate (87 μl, 0.507 mmol) in CH_2Cl_2 (0.4 ml) was added *via* a syringe to a stirred solution of titanium (IV) isopropoxide (0.151 ml, 0.507 mmol) in CH_2Cl_2 (4 ml) at -23 °C under argon. After 7 min, a solution of **22** (200 mg, 0.309 mmol) in CH_2Cl_2 (1.0 ml) and a 4.2 M *tert*-butylhydroperoxide solution (0.241 ml, 1.01 mmol) in toluene were added. The solution was stirred at -20 °C for 2 d, and then 10% tartaric acid (1.5 ml) was added. After 30 min, the solution was allowed to warm to room temperature, and the stirring was continued for 1 h. The organic layer was diluted with CH_2Cl_2, washed with brine, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was taken up in Et_2O (10 ml) and stirred with 1 N NaOH (1.5 ml) at 0 °C for 30 min. The organic layer was diluted with Et_2O, washed with brine, dried ($MgSO_4$), and evaporated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 2:3) to give recovered **22** (42 mg, 21%) and **23** as a colorless oil (52 mg, 33%). ^{1}H-NMR δ: 0.87 (3H, t, $J=7.5$ Hz), 1.14 (3H, s), 1.27 (3H, d, J=7.0 Hz), 1.35—1.63 (6H, m), 1.65—2.02 (5H, m), 2.23—2.37 (1H, m), 3.60 (2H, d, J=5.0 Hz), 3.65 (1H, dd, J=9.5, 2.5 Hz), 3.80 (3H, s), 3.80—3.86 (1H, m), 4.12—4.19 (2H, m), 4.22 (1H, d, J=10.0 Hz), 4.36 (1H, d, J=10.0 Hz), 6.87 (2H, d, J=9.0 Hz), 7.30 (2H, d, J=9.0 Hz), Diacetate: ^{1}H-NMR δ: 0.87 (3H, t, J=7.5 Hz), 1.15 (3H, s), 1.24 (3H, d, J=7.0 Hz), 1.37—2.17 (10H, m), 2.05 (3H, s), 2.07 (3H, s), 3.41 (1H, dd, J=11.5, 2.5 Hz), 3.79 (3H, s), 4.10 (2H, q, J=7.0 Hz), 4.12 (1H, dd, J=12.0, 7.0 Hz), 4.23 (1H, d, J=10.5 Hz), 4.37 (1H, d, J=10.5 Hz), 4.49 (1H, dd, J=12.0, 3.0 Hz), 5.05 (1H, dt, J=3.0, 7.0 Hz), 6.86 (2H, d, J=9.0 Hz), 7.31 (2H, d, J=9.0 Hz). MS m/z (relative intensity): 356 (M^+−136, 2), 338 (2), 327 (13), 255 (9), 229 (49), 207 (6.5), 169 (5), 121 (100), 113 (14), 67 (21), 57 (30), 43 (65). Exact MS m/z Calcd for $C_{19}H_{32}O_6$ (M^+−136): 356.2201. Found: 356.2221.

Ethyl (2*E*,6*S*)-6-[(2*R*,5*R*,6*S*)-5-Ethyl-5-hydroxy-6-methyltetrahydropyran-2-yl]-9-hydroxyhept-2-enoate (24) A solution of **20** (135 mg, 0.553 mmol) and ethoxycarbonylmethylenetriphenylphosphorane (289 mg, 0.829 mmol) in CH_2Cl_2 (8 ml) was stirred at 60 °C for 6 h, then evaporated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 2 : 1) to give **24** as a colorless oil (148 mg, 90%). $[\alpha]_D^{17.5}$ −15° (c=0.84). IR ν_{max} cm^{-1}: 3450, 1720, 1650. ^{1}H-NMR δ: 0.88 (3H, t, J=7.5 Hz), 1.15 (3H, s), 1.24 (3H, d, J=7.0 Hz), 1.28 (3H, t, J=7.0 Hz), 1.34—1.81 (8H, m), 2.34—2.44 (2H, m), 2.27 (1H, s), 2.40 (1H, s), 3.42 (1H, d, J=10.5 Hz), 3.83 (1H, q, J=7.0 Hz), 4.18 (2H, q, J=7.0 Hz), 5.84 (1H, dt, J=15.5, 1.5 Hz), 7.00 (1H, dt, J=15.5, 7.0 Hz). MS m/z (relative intensity): 314 (M^+, 0.2), 296 (4.0), 281 (1.4), 269 (2.4), 250 (9), 171 (48), 143 (58), 125 (100). Exact MS m/z Calcd for $C_{17}H_{30}O_5$ (M^+): 314.2095. Found: 314.2094.

(2*E*,6*S*)-6-Acetoxy-6-[(2*R*,5*R*,6*S*)-5-acetoxy-5-ethyl-6-methyltetrahydropyran-2-yl]hept-2-en-1-ol (25) A 1 M DIBAH solution (2.3 ml) in hexane was added dropwise to a stirred solution of **24** (144 mg, 0.458 mmol) in CH_2Cl_2 (5 ml) at −78 °C under argon. After 45 min, MeOH was added and the reaction mixture was allowed to warm to room temperature. H_2O (1 ml) was added and after 20 min, 1 N HCl was added until the turbid solution became clear. The solution was extracted with CH_2Cl_2. The extract was washed with 10% $NaHCO_3$ and brine, dried (Na_2SO_4), and evaporated *in vacuo* to leave a triol as a colorless oil (114 mg, 91%), which was subjected to the next reaction without further purification.

Imidazole (53 mg, 0.77 mmol) and TBDMS chloride (70 mg, 0.463 mmol) were added to a stirred solution of the above triol (105 mg, 0.386 mmol) in CH_2Cl_2 (3 ml) at room temperature. After 1 h, the reaction mixture was diluted with CH_2Cl_2 (20 ml), washed with brine, dried (Na_2SO_4), and evaporated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 3) to give the silyl ether as a colorless oil (117 mg, 79%). ^{1}H-NMR δ: 0.07 (6H, s), 0.91 (9H, s), 0.92 (3H, t, J=7.5 Hz), 1.14 (3H, s), 1.23 (3H, d, J=7.0 Hz), 1.34—1.70 (8H, m), 2.05—2.21 (2H, m), 2.21 (1H, s), 2.48 (1H, s), 3.41 (1H, d, J=10.0 Hz), 3.82 (1H, q, J=7.0 Hz), 4.12 (2H, d, J=4.5 Hz), 5.61 (2H. m).

A solution of the above silyl ether (114 mg, 0.295 mmol), Et_3N (298 mg, 2.95 mmol), 4-dimethylaminopyridine (50 mg), and Ac_2O (150 mg, 1.47 mmol) in toluene (4.5 ml) was heated at 70 °C for 36 h, and then cooled to room temperature. After addition of MeOH (1 ml), the reaction mixture was evaporated *in vacuo* and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 5) to give the diacetate as a colorless oil (117 mg, 84%). $[\alpha]_D^{16}$ −17° (c=1.72). IR ν_{max} cm^{-1}: 1730. ^{1}H-NMR δ: 0.06 (6H, s), 0.80 (3H, t, J=7.5 Hz), 0.90 (9H, s), 1.20 (3H, d, J=7.0 Hz), 1.40 (3H, s), 1.24—1.92 (8H, m), 1.98 (3H, s), 2.04 (3H, s), 2.32—2.44 (2H, m), 4.10 (2H, d, J=4.0 Hz), 4.14 (1H, br d, J=10.5 Hz), 4.40 (1H, q, J=7.0 Hz), 5.58 (2H, m). MS m/z (relative intensity): 413 (M^+−57, 3.3), 410 (1.6), 395 (1.0), 353 (3.9), 293 (10), 43 (100). Exact MS m/z Calcd for $C_{21}H_{37}O_6Si$ (M^+−57): 413.2361. Found: 413.2345.

A 1.0 M tetra-n-butylammonium fluoride solution (0.26 ml, 0.26 mmol) in THF was added to a stirred solution of the above diacetate (114 mg, 0.242 mmol) in THF (3 ml) at room temperature. After 1.5 h, the reaction mixture was evaporated *in vacuo* and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 1) to give **25** as a colorless oil (82 mg, 90%), $[\alpha]_D^{24}$ −21° (c=1.08). IR ν_{max} cm^{-1}: 3450, 1750. ^{1}H-NMR δ: 0.81 (3H, t, J=7.5 Hz), 1.21 (3H, d, J=7.0 Hz), 1.40 (3H, s), 1.45—2.49 (11H, m), 1.99 (3H, s), 2.05 (3H, s), 4.06—4.15 (3H, m), 4.42 (1H, q, J=7.0 Hz), 5.56—5.67 (2H, m). MS m/z (relative intensity): 296 (M^+−60, 1.7), 281 (1.7), 278 (1.9), 236 (5.7), 225 (26), 212 (7.8), 185 (18), 165 (34), 125 (64), 43 (100). Exact MS m/z Calcd for $C_{19}H_{32}O_6$ (M^+−60): 296.2009. Found: 296.2008.

(2*S*,3*S*,6*S*)-6-Acetoxy-6-[(2*R*,5*R*,6*S*)-5-acetoxy-5-ethyl-6-methyltetrahydropyran-2-yl]-2,3-epoxyheptan-1-ol (26) A solution of diethyl (+)-L-tartrate (393 mg, 1.91 mmol) in CH_2Cl_2 (2.0 ml) was added dropwise to a stirred solution of titanium (IV) isopropoxide (391 mg, 1.37 mmol) in CH_2Cl_2 (2 ml) at −25 °C under argon. After 7 min, a solution of **25** (136 mg, 0.382 mmol) in CH_2Cl_2 (1.1 ml) and a 3.3 M *tert*-butylhydroperoxide solution (0.347 ml) in toluene were added and the solution was stirred at −20 °C overnight. A 10% tartaric acid solution (2 ml) was added at −23 °C, and after 30 min, the solution was allowed to warm to room temperature. After 1 h, the reaction mixture was filtered through celite. The filtrate was washed with 10% $NaHCO_3$ and brine, dried (Na_2SO_4), and evaporated. The residue was dissolved in ether (30 ml), and this solution was washed with H_2O and brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 1) to give **26** as a colorless oil (123 mg, 87%). $[\alpha]_D^{23.5}$ −28° (c=1.00). IR ν_{max} cm^{-1}: 3450, 1750. MS m/z (relative intensity): 312 (M^+−60, 5.1), 251 (2.8), 237 (2.9), 225 (10), 185 (25), 43 (100). Exact MS m/z Calcd for $C_{17}H_{28}O_5$ (M^+−60): 312.1938. Found: 312.1924.

tert-Butyldimethylsilyl Ether: ^{1}H-NMR δ: 0.06 (3H, s), 0.07 (3H, s), 0.81 (3H, t, J=7.5 Hz), 0.90 (9H, s), 1.20 (3H, d, J=7.0 Hz), 1.40 (3H, s), 1.45—2.30 (10H, m), 1.98 (3H, s), 2.05 (3H, s), 2.82 (2H, t, J=4.5 Hz), 3.64 (1H, dd, J=12.0, 4.0 Hz), 3.80 (1H, dd, J=12.0, 3.0 Hz), 4.10 (1H, d, J=8.0 Hz), 4.25 (1H, q, J=7.0 Hz).

(1*S*,4*S*)-4-Acetoxy-4-[(2*R*,5*R*,6*S*)-5-acetoxy-5-ethyl-6-methyltetrahydropyran-2-yl]-1-[(*R*)-2-oxo-1,3-dioxolan-4-yl]pentan-1-ol (27) A solution of **26** (120 mg, 0.322 mmol), Et_3N (90 mg, 0.889 mmol), and PhNCO (46 mg, 0.387 mmol) in CH_2Cl_2 (1.5 ml) was stirred at room temperature for 40 min, and then concentrated *in vacuo*. The residue was dissolved in acetone (10 ml) and H_2O (2 ml) and the solution was stirred for 40 min. The reaction mixture was evaporated *in vacuo*, and the residue was extracted with ether. The extract was dried, and evaporated again. The residue was dissolved in MeCN (11 ml). This solution was mixed with 5% $HClO_4$ (3 ml) and stirred at room temperature for 2.5 h. The reaction mixture was concentrated *in vacuo*, and extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 1) to give **27** as a colorless oil (105 mg, 78%). $[\alpha]_D^{20}$ −22° (c=2.28). IR ν_{max} cm^{-1}: 3450, 1790, 1720. ^{1}H-NMR δ: 0.81 (3H, t, J=7.5 Hz), 1.21 (3H, d, J=7.0 Hz), 1.40 (3H, s), 1.46—2.45 (10H, m), 2.00 (3H, s), 2.06 (3H, s), 2.55 (1H, br s), 3.83—3.96 (1H, m), 4.04 (1H, d, J=11.0 Hz), 4.40 (1H, q, J=7.0 Hz), 4.41—4.59 (3H, m). MS m/z (relative intensity): 356 (M^+−60, 8.5), 296 (11), 269 (11), 209 (10), 185 (18), 125 (49), 43 (100). Exact MS m/z Calcd for $C_{18}H_{28}O_7$ (M^+−60): 356.1837. Found: 356.1834.

(2*S*,5*S*,6*R*)-6,7-Diacetoxy-2-[(2*R*,5*R*,6*S*)-5-ethyl-5-hydroxy-6-methyltetrahydropyran-2-yl]-5-methoxymethoxyheptan-2-ol (28) Diisopropylethylamine (65 mg, 0.50 mmol) and methoxymethyl chloride (26 mg, 0.327 mmol) were added to a stirred solution of **27** (68 mg, 0.163 mmol) in CH_2Cl_2 (0.6 ml) at room temperature under argon. After 36 h, the reaction mixture was evaporated *in vacuo* and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 1) to give the MOM ether as a colorless oil (71 mg, 94%). $[\alpha]_D^{19}$ −3.5° (c=0.68). ^{1}H-NMR δ: 0.80 (3H, t, J=7.5 Hz), 1.20 (3H, d, J=7.0 Hz), 1.38 (3H, s), 1.49—2.06 (9H, m), 1.98 (3H, s), 2.04 (3H, s), 2.35—2.52 (1H, m), 3.37 (3H, s), 3.80—4.10 (2H, m), 4.39—4.47 (2H, m), 4.59—4.88 (2H, m), 5.29 (2H, s). MS m/z (relative intensity): 400 (M^+−60, 13), 340 (7), 295 (10), 185 (37), 125 (69), 57 (57), 43 (100). Exact MS m/z Calcd for $C_{20}H_{32}O_8$ (M^+−60): 400.2099. Found: 400.2102.

A solution of the above MOM ether (100 mg, 0.217 mmol) in THF was reduced with $LiAlH_4$ in the usual way to give the tetraol, which was acetylated with Ac_2O, Et_3N, and 4-dimethylaminopyridine in CH_2Cl_2 as usual to give **28** as a colorless oil (92 mg, 98%). $[\alpha]_D^{21}$ −81° (c=1.00). IR ν_{max} cm^{-1}: 3450, 1740. ^{1}H-NMR δ: 0.92 (3H, t, J=7.0 Hz), 1.13 (3H, s), 1.23 (3H, d, J=7.0 Hz), 1.43—2.50 (12H, m), 2.06 (3H, s), 2.09 (3H, s), 3.39 (3H, s), 3.42 (1H, d, J=8.5 Hz), 3.82 (1H, q, J=7.0 Hz), 3.70—3.79 (1H, m), 4.14 (1H, dd, J=12.0, 7.5 Hz), 4.43 (1H, dd, J=12.0, 3.0 Hz), 4.61 (1H, d, J=6.5 Hz), 4.70 (1H, d, J=6.5 Hz), 5.15 (1H, quintet, J=4.0 Hz). MS m/z (relative intensity): 416 (M^+−18, 0.6), 373 (1.3), 355 (2.3), 259 (25), 229 (100), 43 (100). Exact MS m/z Calcd for $C_{21}H_{36}O_8$ (M^+−18): 416.2412. Found: 416.2392.

(2*R*,3*S*,6*S*)-1-*tert*-Butyldiphenylsilyloxy-6-[(2*R*,5*R*,6*S*)-5-ethyl-5-methoxymethoxy-6-methyltetrahydropyran-2-yl]-3,6-bismethoxymethoxyheptan-2-ol (29) The MOM ether (colorless oil, 101 mg, 93%) was prepared from **28** (90 mg, 0.207 mmol) as described for **28**. IR ν_{max} cm^{-1}: 1740. ^{1}H-NMR δ: 0.84 (3H, t, J=7.5 Hz), 1.22 (3H, d, J=7.0 Hz), 1.22 (3H, s), 1.35—1.98 (10H, m), 2.05 (3H, s), 2.08 (3H, s), 3.36 (3H, s), 3.38 (3H, s), 3.46 (3H, s), 3.58 (1H, d, J=10.0 Hz), 3.78—3.83 (1H, m), 4.10 (1H, q, J=7.0 Hz), 4.15 (1H, dd, J=12.0, 7.5 Hz), 4.40 (1H, dd, J=12.0, 3.5 Hz), 4.59—4.80 (6H, m), 4.76 (1H, quintet, $J=4.0$ Hz). MS m/z (relative intensity): 461 (M^+-61, 0.3), 429 (0.4), 399 (0.5), 355 (2.8), 327 (3.0), 259 (32), 229 (35), 45 (100). Exact MS m/z Calcd for $C_{23}H_{41}O_9$ (M^+-61): 461.2753. Found: 461.2746.

K_2CO_3 (105 mg, 0.758 mmol) was added to a stirred solution of the above MOM ether (99 mg, 0.189 mmol) in MeOH (1 ml) at room temperature. After 40 min, the reaction mixture was evaporated and the residue was chromatographed on a silica gel column (MeOH–CH_2Cl_2, 1 : 10) to give the diol as a colorless oil (83 mg, 100%). $[\alpha]_D^{18.5}$ +19° ($c=0.64$). ^{1}H-NMR δ: 0.84 (3H, t, $J=7.5$ Hz), 1.20 (3H, s), 1.22 (3H, d, $J=7.0$ Hz), 1.35—1.82 (10H, m), 2.30 (1H, t, $J=6.0$ Hz), 3.37 (3H, s), 3.41 (3H, s), 3.46 (3H, s), 3.40—3.72 (6H, m), 4.08 (1H, q, $J=7.0$ Hz), 4.61—4.80 (6H, m). FD-MS m/z (relative intensity): 439 (M^++1, 17), 407 (18), 376 (41), 187 (100).

A solution of the above diol (80 mg, 0.182 mmol), imidazole (94 mg, 1.38 mmol), and *tert*-butyldiphenylsilyl chloride (94 μl, 0.361 mmol) in CH_2Cl_2 (1 ml) was stirred at 0 °C for 3 h and at room temperature for 13 h. After addition of CH_2Cl_2 (20 ml), the reaction mixture was washed with brine, dried (Na_2SO_4), and evaporated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 2 : 3) to give **29** as a colorless oil (116 mg, 94%). $[\alpha]_D^{18}$ +2.0° ($c=0.84$). ^{1}H-NMR δ: 0.83 (3H, t, $J=7.5$ Hz), 1.07 (9H, s), 1.18 (3H, d, $J=6.5$ Hz), 1.19 (3H, s), 1.34—1.82 (10H, m), 2.83 (1H, d, $J=2.0$ Hz), 3.25 (3H, s), 3.22 (3H, s), 3.46 (3H, s), 3.46—3.81 (5H, m), 4.12 (1H, q, $J=6.5$ Hz), 4.56 (1H, d, $J=7.0$ Hz), 4.62 (1H, d, $J=7.0$ Hz), 4.68 (1H, d, $J=7.5$ Hz), 4.69 (1H, d, $J=4.0$ Hz), 4.72 (1H, d, $J=4.0$ Hz), 4.78 (1H, d, $J=7.5$ Hz), 7.37—7.41 (4H, m), 7.64—7.78 (6H, m). MS m/z (relative intensity): 677 (M^++1, 31), 645 (100), 633 (22), 614 (96), 601 (35), 587 (34), 557 (45), 543 (21), 513 (35), 427 (76), 241 (56).

(2*R*,3*S*,6*S*)-6-[(2*R*,5*R*,6*S*)-5-Ethyl-5-methoxymethoxy-6-methyltetrahydropyran-2-yl]-3,6-bismethoxymethoxy-2-(tetrahydropyran-2-yloxy)heptanal (30) A solution of **29** (42 mg, 0.06 mmol), pyridinium *p*-toluenesulfonate (6 mg), and dihydropyran (0.1 ml) in CH_2Cl_2 (1 ml) was stirred at room temperature for 3 h. The reaction mixture was evaporated *in vacuo* and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 3) to give the THP ether as a colorless oil (48 mg, 100%). ^{1}H-NMR δ: 0.83 (3H, t, $J=7.5$ Hz), 1.04 (4.5H, s), 1.05 (4.5H, s), 1.15 (1.5H, d, $J=7.0$ Hz), 1.17 (1.5H, d, $J=7.0$ Hz), 1.18 (1.5H, s), 1.20 (1.5H, s), 1.23—1.81 (16H, m), 3.29 (1.5H, s), 3.31 (1.5H, s), 3.33 (1.5H, s), 3.35 (1.5H, s), 3.45 (1.5H, s), 3.46 (1.5H, s), 3.44—3.54 (1H, m), 3.75—4.15 (7H, m), 4.54—4.87 (7H, m), 7.31—7.39 (5H, m), 7.63—7.73 (5H, m).

A 1.0 M tetra-*n*-butylammonium fluoride solution (0.138 ml, 0.138 mmol) in THF was added to a stirred solution of the above THP ether (48 mg, 0.06 mmol) at room temperature. After 6 h, the reaction mixture was evaporated *in vacuo* and the residue was chromatographed on a silica gel column (EtOAc–hexane, 2 : 1) to give the alcohol as a colorless oil (28 mg, 86%), which was subjected to Swern oxidation as described for **8** to give **30** as a colorless oil (28 mg, 100%). IR ν_{max} cm^{-1}: 3400, 1720. ^{1}H-NMR δ: 0.84 (3H, t, $J=7.5$ Hz), 1.19—1.26 (6H, m), 1.27—2.25 (17H, m), 3.35—3.47 (11H, m), 3.70—4.14 (5H, m), 4.60—4.84 (7H, m), 9.67 (0.5H, d, $J=2.5$ Hz), 9.72 (0.5H, d, $J=1.5$ Hz).

(3*R*,4*S*,7*S*)-7-[(2*R*,5*R*,6*S*)-5-Ethyl-5-methoxymethoxy-6-methyltetrahydropyran-2-yl]-4,7-bismethoxymethoxy-3-(tetrahydropyran-2-yloxy)oct-1-yne (3) Triphenylphosphine (280 mg, 1.65 mmol) and CBr_4 (350 mg, 1.06 mmol) were added to a stirred suspension of Zn dust (70 mg, 1.07 matom) in CH_2Cl_2 (8 ml) at room temperature under argon. After 18 h, the above solution (4 ml) was added to a stirred solution of **30** (28 mg, 0.054 mmol) in CH_2Cl_2 (1 ml) at room temperature. After 3 h, the reaction mixture was evaporated *in vacuo*. The residue was extracted with Et_2O, and the extract was dried, and evaporated. The residue was chromatographed on a silica gel column (EtOAc–hexane, 2 : 3) to give (3*R*,4*S*,7*S*)-1,1-dibromo-7-[(2*R*,5*R*,6*S*)-5-ethyl-5-methoxymethoxy-6-methyltetrahydropyran-2-yl]-4,7-bismethoxymethoxy-3-(tetrahydropyran-2-yloxy)oct-1-ene as a colorless oil (37 mg, 100%). ^{1}H-NMR δ: 0.84 (3H, t, $J=7.5$ Hz), 1.22 (3H, s), 1.24 (3H, d, $J=6.5$ Hz), 1.29—1.98 (16H, m), 3.37 (3H, s), 3.39 (1.5H, s), 3.40 (1.5H, s), 3.46 (3H, s), 3.37—3.39 (1H, m), 3.59 (1H, d, $J=10.5$ Hz), 3.72—3.95 (2H, m), 4.12 (1H, q, $J=6.5$ Hz), 4.27 (0.5H, dd, $J=9.0$, 3.0 Hz), 4.59 (0.5H, dd, $J=9.5$, 3.0 Hz), 4.62—4.88 (7H, m), 6.55 (0.5H, d, $J=9.5$ Hz), 6.64 (0.5H, d, $J=9.0$Hz). MS m/z (relative intensity): 615 (M^+-59, 0.1), 613 (0.1), 149 (100). CI-MS (NH_4^+) m/z (relative intensity): 696 (M^++22, 64), 694 (100), 692 (61).

A 1.6 M *n*-BuLi solution (0.118 ml) in hexane was added to a stirred solutin of the above olefin (32 mg, 0.047 mmol) in THF (3 ml) at −78 °C under argon. The reaction mixture was gradually warmed to 0 °C during 3 h, then poured into cold aqueous NH_4Cl, and extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 2 : 3) to give **3** as a colorless oil (16 mg, 67%). IR ν_{max} cm^{-1}: 3250, 2300, 2250. ^{1}H-NMR δ: 0.84 (3H, t, $J=3.5$ Hz), 1.23 (3H, s), 1.23 (3H, d, $J=6.5$ Hz), 1.25—1.89 (16H, s), 2.41 (0.5H, d, $J=2.0$ Hz), 2.45 (0.5H, d, $J=2.0$ Hz), 3.37 (3H, s), 3.40 (1.5H, s), 3.42 (1.5H, s), 3.46 (3H, s), 3.54 (1H, d, $J=9.5$ Hz), 3.70—4.07 (4H, m), 4.40—4.42 (0.5H, m), 4.42—4.44 (0.5H, m), 4.45—4.99 (7H, m). FD-MS m/z (relative intensity): 517 (M^++1, 13), 485 (29), 454 (15), 187 (100).

1,2-*O*-Isopropylidene-3-*O*-(4-methoxybenzyl)-α-D-glucofuranose (34) Diacetoneglucose (**33**) (1.0 g, 3.58 mmol) was treated with NaH (110 mg, 4.62 mmol) in DMSO (15 ml), and then MPM chloride (723 mg, 4.62 mmol) and Et_2NH (1 ml) as described for **7** to afford 1,2:5,6-di-*O*-isopropylidene-3-*O*-(4-methoxybenzyl)-α-D-glucofuranose as a colorless oil (1.47 g, 100%). ^{1}H-NMR δ: 1.31 (3H, s), 1.38 (3H, s), 1.42 (3H, s), 1.49 (3H, s), 3.80 (3H, s), 3.96—4.54 (6H, m), 4.58 (2H, s), 5.88 (1H, d, $J=4$ Hz), 6.87 (2H, d, $J=9$ Hz), 7.27 (2H, d, $J=9$ Hz). MS m/z (relative intensity): 380 (M^+, 0.4), 365 (0.5), 322 (2.4), 264 (3.9), 135 (12), 121 (100). Exact MS m/z Calcd for $C_{20}H_{28}O_7$ (M^+): 380.1837. Found: 380.1828.

The above MPM ether (32.81 g, 86.3 mmol) in MeOH (250 ml) and 2% H_2SO_4 (50 ml) was stirred for 54 h at room temperature. After neutralization with $NaHCO_3$, the mixture was evaporated, and the residue was chromatographed on a silica gel column (EtOAc–benzene, 1 : 2) to afford **34** as a colorless oil (27.53 g, 94%). ^{1}H-NMR δ: 1.33 (3H, s), 1.48 (3H, s), 1.95 (1H, t, $J=5$ Hz), 2.44 (1H, d, $J=6$ Hz), 3.60—3.79 (2H, m), 3.81 (3H, s), 3.86—4.28 (3H, m), 4.50 (1H, d, $J=12$ Hz), 4.62 (1H, d, $J=4$ Hz), 4.69 (1H, d, $J=12$ Hz), 5.94 (1H, d, $J=4$ Hz), 6.90 (2H, d, $J=9$ Hz), 7.28 (2H, d, $J=9$ Hz). MS m/z (relative intensity): 340 (M^+, 0.2), 282 (1.1), 265 (2.8), 150 (12), 121 (100). Exact MS m/z Calcd for $C_{17}H_{24}O_7$ (M^+): 340.1524. Found: 340.1524.

5-*O*-Benzyl-1,2-*O*-isopropylidene-3-*O*-(4-methoxybenzyl)-α-D-xylofuranose (35) A solution of $NaIO_4$ (19.06 g, 89.1 mmol) in water (150 ml) was added to a stirred MeOH solution (150 ml) of **34** (27.53 g, 81 mmol) at 0 °C. After 1 h, $NaBH_4$ (3.06 g, 81 mmol) was added slowly and the mixture stirred for 1 h. After removal of insoluble materials by filtration, the filtrate was evaporated, and the residue was extracted with CH_2Cl_2. The extract was washed with brine, dried (Na_2SO_4), and evaporated to leave 1,2-*O*-isopropylidene-3-*O*-(4-methoxybenzyl)-α-D-xylofuranose as a colorless oil (24.22 g, 96%). ^{1}H-NMR δ: 1.33 (3H, s), 1.48 (3H, s), 2.06 (1H, dd, $J=5$, 3 Hz), 3.81 (3H, s), 3.83—3.92 (2H, m), 4.00 (1H. d. $J=4$ Hz), 4.20—4.28 (1H, m), 4.40 (1H, d, $J=12$ Hz), 4.62 (1H, d, $J=4$ Hz), 4.66 (1H, d, $J=12$ Hz), 5.98 (1H, d, $J=4$ Hz), 6.89 (2H, d, $J=9$ Hz), 7.25 (2H, d, $J=9$ Hz). MS m/z (relative intensity): 310 (M^+, 0.6), 295 (0.7), 252 (3.7), 235 (6.7), 150 (7), 121 (100). Exact MS m/z Calcd for $C_{16}H_{22}O_6$ (M^+): 310.1418. Found: 310.1436.

The above alcohol (19.81 g, 64.1 mmol) was treated with NaH (2.31 g, 96.2 mmol) in DMSO (140 ml), and then Bn chloride (9.74 g, 76 mmol) as described for **13** to afford **35** as a colorless solid (20.86 g, 82%), mp 69—70 °C (EtOH–hexane). ^{1}H-NMR δ: 1.31 (3H, s), 1.48 (3H, s), 3.73 (2H, d, $J=6$ Hz), 3.79 (3H, s), 3.95 (1H, d, $J=3$ Hz), 4.35—4.44 (1H, m), 4.47—4.66 (5H, m), 5.92 (1H, d, $J=4$ Hz), 6.84 (2H, d, $J=9$ Hz), 7.20 (2H, d, $J=9$ Hz), 7.29 (5H, br s). MS m/z (relative intensity): 385 (M^+-15, 0.2), 342 (1.4), 309 (4.8), 250 (4.8), 236 (6.0), 121 (100), 91 (56). *Anal.* Calcd for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 68.96; H, 7.00.

3-*O*-(4-Methoxybenzyl)-5-*O*-benzyl-α-D-xylofuranose (36) A solution of **35** (23.07 g, 57.7 mmol) in THF (200 ml) was treated with 4 N HCl (70 ml) at 55 °C for 3.5 h as described for **17** to give the recovered **35** (2.21 g) and **36** as a colorless solid (13.22 g, 64%, net 70%), mp 98.5—100 °C (EtOH–hexane). ^{1}H-NMR δ: 1.59 (1H, br s), 1.84—2.08 (0.5H, m), 2.72 (0.5H, d, $J=6$ Hz), 3.50—3.78 (2H, m), 3.80 (3H, s), 3.88—4.30 (2H, m), 4.31—4.74 (5H, m), 5.09 (0.5H, d, $J=12$ Hz), 5.49 (0.5H, t, $J=5$ Hz), 6.85 (2H, d, $J=9$ Hz), 7.21 (2H, d, $J=9$ Hz), 7.33 (5H, br s). MS m/z (relative intensity): 269 (M^+-91, 2.1), 251 (2.2), 236 (1.4), 175 (2.0), 137 (36), 121 (100), 91 (79). *Anal.* Calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.65; H, 6.83.

(2*S*,3*R*)-4-Benzyloxy-2-(4-methoxybenzyloxy)butane-1,3-diol (37) A solution of **36** (13.22 g, 36.7 mmol) in THF (60 ml) and MeOH (60 ml) was treated with $NaIO_4$ (15.69 g, 73.4 mmol) in H_2O (120 ml) at 0 °C for 30 min as described for **35** to afford (2*S*,3*R*)-4-benzyloxy-3-formyloxy-2-(4-methoxybenzyloxy)butanal as an oil (13.54 g, 100%). IR ν_{max} cm^{-1}: 1720. ^{1}H-NMR δ: 3.66—3.78 (2H, m), 3.79 (3H, s), 4.05 (1H, d, $J=4$ Hz), 4.48 (2H, s), 4.52 (1H, d, $J=12$ Hz), 4.70 (1H, d, $J=12$ Hz), 5.39 (1H, q, $J=6$ Hz), 6.64 (2H, d, $J=9$ Hz), 7.21 (2H, d, $J=9$ Hz), 7.28 (5H, br s), 8.00 (1H, s), 9.58 (1H, d, $J=2$ Hz).

A solution of the above aldehyde (13.54 g, 37.8 mmol) in THF (100 ml) was reduced with $\mathrm{LiAlH_4}$ (4.30 g, 113.4 mmol) in the usual way to give **37** as a colorless oil (9.27 g, 74%). ^{1}H-NMR δ: 2.22 (1H, t, J=7 Hz), 2.58 (1H, d, J=5 Hz), 3.48—3.79 (5H, m), 3.80 (3H, s), 3.84—4.08 (1H, m), 4.50 (1H, d, J=12 Hz), 4.54 (2H, s), 4.61 (1H, d, J=12 Hz), 6.87 (2H, d, J=9 Hz), 7.23 (2H, d, J=9 Hz), 7.33 (5H, br s). MS *m/z* (relative intensity): 332 (M$^+$, 0.3), 241 (5.0), 211 (2.5), 178 (1.6), 160 (2.4), 137 (53), 121 (100). Exact MS *m/z* Calcd for $\mathrm{C_{19}H_{24}O_5}$ (M$^+$): 332.1625. Found: 332.1618.

(2*R*,3*R*)-2,4-Isopropylidenedioxy-3-(4-methoxybenzyloxy)butanal (31) A solution of **37** (4.37 g, 13.2 mmol) in acetone (30 ml) was stirred with 2,2-dimethoxypropane (10 ml) and CSA (100 mg) for 30 min. After neutralization with $\mathrm{Et_3N}$, the mixture was evaporated and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 5) to afford (2*R*,3*R*)-1-benzyloxy-2,4-isopropylidenedioxy-3-(4-methoxybenzyloxy)butane as a colorless oil (4.74 g, 96%). ^{1}H-NMR δ: 1.45 (6H, s), 3.29 (1H, q, J=2 Hz), 3.57 (1H, dd, J=9.5, 6 Hz), 3.67 (1H, dd, J=9.5, 6 Hz), 3.77 (3H, s), 3.88 (1H, dd, J=13, 2 Hz), 3.96 (1H, dd, J=13, 2 Hz), 4.11 (1H, dt, J=6, 2 Hz), 4.43 (1H, d, J=12 Hz), 4.46 (1H, d, J=12 Hz), 4.55 (1H, d, J=12 Hz), 4.63 (1H, d, J=12 Hz), 6.82 (2H, d, J=9 Hz), 7.23 (2H, d, J=9 Hz), 7.30 (5H, br s). MS *m/z* (relative intensity): 372 (M$^+$, 3.8), 357 (1.1), 281 (0.6), 251 (0.5), 227 (1.3), 223 (6.9), 137 (22). 121 (100), 91 (45). Exact MS *m/z* Calcd for $\mathrm{C_{22}H_{28}O_5}$ (M$^+$): 372.1938. Found 372.1937.

A solution of the above acetonide (4.39 g, 11.8 mmol) in EtOH (20 ml) was hydrogenated with a suspension of Raney Ni (W-2) in EtOH (20 ml) at ordinary temperature and pressure for 7 h. After removal of the catalyst, the filtrate was evaporated *in vacuo* and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 5→1 : 1) to afford (2*R*,3*R*)-2,4-isopropylidenedioxy-3-(4-methoxybenzyloxy)butanol as a colorless oil (2.91 g, 87%). ^{1}H-NMR δ: 1.46 (6H, s), 1.93 (1H, dd, J=8.5, 4 Hz), 3.30 (1H, q, J=2 Hz), 3.56 (1H, dd, J=11, 5 Hz), 3.65 (1H, dd, J=11, 4 Hz), 3.80 (3H, s), 3.84—4.12 (3H, m), 4.36 (1H, d, J=12 Hz), 4.71 (1H, d, J=12 Hz), 6.88 (2H, d, J=9 Hz), 7.27 (2H, d, J=9 Hz). MS *m/z* (relative intensity): 282 (M$^+$, 3.1), 224 (2.2), 136 (27), 121 (100). Exact MS *m/z* Calcd for $\mathrm{C_{15}H_{22}O_5}$ (M$^+$): 282.1469. Found: 282.1479.

The above alcohol (36.5 mg, 0.13 mmol) was oxidized with $\mathrm{(COCl)_2}$ (50 μl, 0.59 mmol), DMSO (0.1 ml, 1.41 mmol), and then $\mathrm{Et_3N}$ (0.2 ml, 1.44 mmol) in $\mathrm{CH_2Cl_2}$ as described for **8** to afford **31** as a colorless oil (36.8 mg, 100%). IR ν_{max} cm^{-1}: 1735. ^{1}H-NMR δ: 1.45 (3H, s), 1.56 (3H, s), 3.67 (1H, q, J=2 Hz), 3.80 (3H, s), 3.90—4.00 (2H, m), 4.29 (1H, dd, J=3, 0.5 Hz), 4.39 (1H, d, J=12 Hz), 4.59 (1H, d, J=12 Hz), 6.86 (2H, d, J=9 Hz), 7.21 (2H, d, J=9 Hz), 9.56 (1H, s).

(2*S*,6*S*)-2-Benzyloxymethoxy-6,7-isopropylidenedioxyheptan-3-one (39) Compounds **38** (9.38 g, 72 mmol) and **10** (22.7 g, 72 mmol) were condensed with NaH (1.56 g, 65 mmol) in DMSO and THF as described for **11** to afford (2*S*,3*E*,6*S*)-2-benzyloxymethoxy-6,7-isopropylidenedioxyhept-4-en-3-one as a colorless oil (17.12 g, 83%). $[\alpha]_D^{15}$ $-18.8°$ (c=0.68). IR ν_{max} cm^{-1}: 1695, 1630. ^{1}H-NMR δ: 1.36 (3H, d, J=7 Hz), 1.39 (3H, s), 1.41 (3H, s), 3.61 (1H, dd, J=8, 7 Hz), 4.00—4.22 (1H, m), 4.35 (1H, q, J=7 Hz), 4.60 (1H, d, J=5 Hz), 4.63 (1H, d, J=5 Hz), 4.76 (1H, d, J=7 Hz), 4.83 (1H, d, J=7 Hz), 6.66 (1H, dd, J=16, 1 Hz), 6.87 (1H, dd, J=16, 5 Hz), 7.32 (5H, s). MS *m/z* (relative intensity): 305 (M$^+$ $-$15, 0.4), 155 (7.8), 91 (100). Exact MS *m/z* Calcd for $\mathrm{C_{17}H_{21}O_5}$ (M$^+$ $-$15): 305.1390. Found: 305.1384.

The enone (2.17 g, 6.78 mmol) in EtOAc (30 ml) was hydrogenated with 10% Pd–C (0.5 g) for 1 h to give **39** as a colorless oil (2.14 g, 98%). $[\alpha]_D^{15}$ $-22.2°$ (c=0.45). IR ν_{max} cm^{-1}: 1720. ^{1}H-NMR δ: 1.28 (3H, d, J=7 Hz), 1.31 (3H, s), 1.32 (3H, s), 1.60—1.95 (2H, m), 2.39—2.93 (2H, m), 3.35—3.56 (1H, m), 3.88—4.14 (2H, m), 4.21 (1H, q, J=7 Hz), 4.63 (2H, s), 4.76 (1H, d, J=7 Hz), 4.83 (1H, d, J=7 Hz), 7.33 (5H, s). MS *m/z* (relative intensity): 307 (M$^+$ $-$15, 0.1), 277 (2.0), 186 (3.1), 172 (3.7), 157 (9.5), 99 (34), 91 (100). Exact MS *m/z* Calcd for $\mathrm{C_{17}H_{23}O_5}$ (M$^+$ $-$15): 307.1547. Found: 307.1572.

(2*S*,3*R*,6*S*)-2-Benzyloxymethoxy-3-ethyl-6,7-isopropylidenedioxyheptan-3-ol (40) A THF solution (25 ml) of **39** (1.47 g, 4.57 mmol) was added dropwise to a stirred Grignard reagent solution prepared from Mg (729 mg, 30 matom) and EtBr (2.74 ml, 36.5 mmol) in THF (25 ml) at -93 °C under argon. After 2 h, the reaction mixture was allowed to warm to 0 °C, poured into cold saturated $\mathrm{NH_4Cl}$, and extracted with ether. The extract was washed with brine, dried ($\mathrm{MgSO_4}$), and evaporated, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 5) to afford **40** as a colorless oil (1.61 g, 100%). ^{1}H-NMR δ: 0.89 (3H, t, J=7 Hz), 1.19 (3H, d, J=7 Hz), 1.35 (3H, s), 1.41 (3H, s), 1.42—1.74 (6H, m), 2.42 (1H, br s), 3.49—3.56 (1H, m), 3.72 (1H, q, J=7 Hz), 4.00—4.10 (2H, m), 4.61 (1H, d, J=12 Hz), 4.66 (1H, d, J=12 Hz), 4.80 (1H, d, J=7 Hz), 4.86 (1H, d, J=7 Hz), 7.34 (5H, s). MS *m/z* (relative intensity): 305 (M$^+$ $-$47, 0.2), 265 (0.4), 235 (1.6), 229 (9.5), 187 (18), 129 (95), 91 (100).

(2*S*,3*R*,6*S*)-3-Benzyloxy-3-ethyl-7-toluenesulfonyloxyheptane-2,6-diol (41) Compound **40** (24.11 g, 68.5 mmol) was benzylated with NaH (5.04 g, 210 mmol) and BnBr (20.2 ml, 170 mmol) in DMF (200 ml) at room temperature overnight as described for **13** to afford (2*S*,3*R*,6*S*)-3-benzyloxy-2-benzyloxymethoxy-3-ethyl-6,7-isopropylidenedioxyheptane as a colorless oil (30.37 g, 100%). ^{1}H-NMR δ: 0.93 (3H, t, J=7 Hz), 1.28 (3H, d, J=6 Hz), 1.34 (3H, s), 1.39 (3H, s), 1.60—2.00 (6H, m), 3.38—3.64 (1H, m), 3.85 (1H, q, J=4 Hz), 3.92—4.20 (2H, m), 4.48 (1H, d, J=11.5 Hz), 4.60 (1H, d, J=11.5 Hz), 4.63 (2H, s), 4.76 (1H, d, J=7 Hz), 4.85 (1H, d, J=7 Hz), 7.30—7.35 (5H, m), 7.33 (5H, s). MS *m/z* (relative intensity): 277 (M$^+$ $-$165, 0.5), 229 (1.3), 219 (13), 149 (9.5), 91 (100).

The above Bn ether (1.58 g, 3.58 mmol) in THF (20 ml) was treated with 4 N HCl (10 ml) at 50 °C for 2 h as described for **36** to afford (2*S*,5*R*,6*S*)-5-benzyloxy-5-ethylheptane-1,2,6-triol as a colorless oil (0.86 g, 85%). ^{1}H-NMR δ: 0.94 (3H, t, J=8 Hz), 1.21 (3H, d, J=7 Hz), 1.40—2.00 (6H, m), 2.20—2.80 (3H, m), 3.28—3.80 (3H, m), 3.98 (1H, q, J=7 Hz), 4.48 (2H, s), 7.34 (5H, s). MS *m/z* (relative intensity): 233 (M$^+$ $-$49, 0.1), 219 (4.5), 158 (1.4), 143 (1.7), 91 (100).

A pyridine solution (10 ml) of the triol (444 mg, 1.58 mmol) and TsCl (330 mg, 1.73 mmol) was stirred at room temperature for 8.5 h. The reaction mixture was poured into ice-water and extracted with ether. The extract was washed successively with 10% HCl, brine, saturated $\mathrm{NaHCO_3}$ and brine, dried ($\mathrm{MgSO_4}$), and evaporated, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 1) to give **41** as a colorless oil (409 mg, 59%). ^{1}H-NMR δ: 0.91 (3H, t, J=8 Hz), 1.16 (3H, d, J=7 Hz), 1.30—2.00 (6H, m), 2.00—2.36 (2H, m), 2.44 (3H, br s), 3.60—4.20 (4H, m), 4.43 (2H, s), 7.20—7.40 (7H, m), 7.78 (2H, d, J=8 Hz). MS *m/z* (relative intensity): 310 (M$^+$ $-$126, 12), 283 (20), 155 (35), 91 (100).

[(2*R*,5*R*,6*S*)-5-Benzyloxy-5-ethyl-6-methyltetrahydropyran]-2-methanol (42) A solution of **41** (33.9 mg, 0.078 mmol) in THF (5 ml) was added to a stirred suspension of NaH (93.3 mg, 3.89 mmol) in DMSO (5 ml) at room temperature under argon. After 1.75 h, the reaction mixture was poured into saturated $\mathrm{NH_4Cl}$, and extracted with $\mathrm{CH_2Cl_2}$. The extract was washed with brine, dried ($\mathrm{Na_2SO_4}$), and evaporated, and the residue was subjected to silica gel TLC (EtOAc–hexane, 1 : 1) to afford **42** as a colorless oil (14.0 mg, 68%). $[\alpha]_D^{15}$ $+16.0°$ (c=2.65). ^{1}H-NMR δ: 0.88 (3H, t, J=7.5 Hz), 1.28 (3H, d, J=7 Hz), 1.35—2.05 (6H, m), 2.05—2.30 (1H, m), 3.44—3.90 (3H, m), 4.11 (1H, q, J=7 Hz), 4.30 (1H, d, J=10.5 Hz), 4.43 (1H, d, J=10.5 Hz), 7.18—7.48 (5H, m). MS *m/z* (relative intensity): 264 (M$^+$, 0.1), 233 (0.9), 175 (2.3), 158 (21), 129 (17), 91 (100), 57 (58). Exact MS *m/z* Calcd for $\mathrm{C_{16}H_{24}O_3}$ (M$^+$): 264.1727. Found: 264.1742.

Methyl [(2*R*,5*R*,6*S*)-5-Benzyloxy-5-ethyl-6-methyltetrahydropyran]-2-carboxylate (43) An acetone solution (3 ml) of **42** (97.6 mg, 0.37 mmol) was stirred with 2.67 M Jones reagent (0.3 ml, 0.80 mmol) at 0 °C for 1 h. The reaction mixture was quenched with iso-PrOH, poured into water, and extracted with ether. The extract was washed with brine, dried ($\mathrm{MgSO_4}$), and evaporated to leave an oil, which was treated with excess diazomethane in ether. The solution was evaporated and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 2) to give **43** as a colorless oil (75.7 mg, 70%). $[\alpha]_D^{15}$ $-0.6°$ (c=1.58). ^{1}H-NMR δ: 0.91 (3H, t, J=7 Hz), 1.26 (3H, d, J=7 Hz), 1.40—2.20 (6H, m), 3.77 (3H, s), 3.98—4.40 (2H, m), 4.35 (1H, d, J=11 Hz), 4.51 (1H, d, J=11 Hz), 7.16—7.44 (5H, m). MS *m/z* (relative intensity): 292 (M$^+$, 0.1), 235 (1.2), 201 (1.3), 186 (6.7), 175 (4.8), 157 (23), 129 (9.0), 97 (27), 91 (100). Exact MS *m/z* Calcd for $\mathrm{C_{17}H_{24}O_4}$ (M$^+$): 292.1676. Found: 292.1690.

[(2*R*,5*R*,6*S*)-5-Benzyloxy-5-ethyl-6-methyltetrahydropyran-2-yl]-2-dimethoxyphosphonoethan-1-one (32) A 1.6 M hexane solution of *n*-BuLi (0.3 ml, 0.48 mmol) was added to a stirred THF solution (0.3 ml) of $\mathrm{MePO(OMe)_2}$ (0.1 ml, 0.92 mmol) at -93 °C under argon. After 30 min, a THF solution (0.8 ml) of **43** (15.6 mg, 53.4 μmol) was added dropwise, then the reaction mixture was allowed to warm gradually to room temperature, poured into saturated $\mathrm{NH_4Cl}$, and extracted with $\mathrm{CH_2Cl_2}$. The extract was washed with brine, dried ($\mathrm{Na_2SO_4}$), and evaporated, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 2 : 1) to afford **32** as a colorless oil (18.7 mg, 91%). $[\alpha]_D^{15}$ $+34.8°$ (c=1.62). ^{1}H-NMR δ: 0.91 (3H, t, J=7.5 Hz), 1.28 (3H, d, J=7 Hz), 1.35—2.00 (6H, m), 3.15 (1H, dd, J=21.5, 14.5 Hz), 3.55 (1H, dd, J=21.5, 14.5 Hz), 3.73 (3H, d, J=7.5 Hz), 3.77 (3H, d, J=7.5 Hz), 4.09 (1H, q, J=6.5 Hz), 4.14 (1H, dd, J=9, 4 Hz), 4.32 (1H, d, J=9 Hz), 4.42 (1H, d, J=9 Hz), 7.20—7.40 (5H, m). MS *m/z* (relative intensity): 384 (M$^+$, 0.1), 340 (0.6), 338 (0.6), 278 (1.6), 269 (1.6), 249 (17), 231 (12), 193 (10), 151 (16), 91 (100). Exact MS *m/z* Calcd for $\mathrm{C_{19}H_{29}O_6P}$ (M$^+$): 384.1704. Found: 384.1678.

(4*R*,5*R*)-1-[(2*R*,5*R*,6*S*)-5-Benzyloxy-5-ethyl-6-methyltetrahydropyran-2-yl]-4,6-isopropylidenedioxy-5-(4-methoxybenzyloxy)hexan-1-one (45)

Compounds **31** (32.3 mg, 0.12 mmol) and **32** (38.6 mg, 0.10 mmol) were condensed with NaH (1.9 mg, 0.08 mmol) in DMSO and THF as described for **11** to afford an *E*:*Z* (5:1) mixture of enones as a colorless oil (45.2 mg, 100%). *E*-From: IR ν_{max} cm^{-1}: 1690. ^{1}H-NMR δ: 0.92 (3H, t, $J=7.5$ Hz), 1.26 (3H, d, $J=6.5$ Hz), 1.43 (3H, s), 1.47 (3H, s), 1.50—2.05 (6H, m), 3.20 (1H, q, $J=2$ Hz), 3.77 (3H, s), 3.85—3.99 (2H, m), 4.13 (1H, q, $J=6.5$ Hz), 4.26 (1H, dd, $J=10$, 4 Hz), 4.30 (1H, d, $J=11$ Hz), 4.42 (1H, d, $J=12.5$ Hz), 4.46 (1H, d, $J=11$ Hz), 4.49 (1H, dd, $J=3$, 2.5 Hz), 4.56 (1H, d, $J=12.5$ Hz), 6.73 (1H, dd, $J=16$, 2 Hz), 6.83 (2H, d, $J=9$ Hz), 7.02 (1H, dd, $J=16$, 4 Hz), 7.24 (2H, d, $J=9$ Hz), 7.26—7.40 (5H, m). MS *m*/*z* (relative intensity): 447 (M$^{+}-91$, 0.2), 438 (0.2), 121 (100), 101 (25), 91 (70).

Z-Form: IR ν_{max} cm^{-1}: 1690. ^{1}H-NMR δ: 0.92 (3H, t, $J=7.5$ Hz), 1.27 (3H, d, $J=7$ Hz), 1.45 (6H, s), 1.50—2.05 (6H, m), 3.63 (1H, q, $J=2$ Hz), 3.71 (3H, s), 3.74—4.24 (4H, m), 4.25—4.65 (4H, m), 5.33 (1H, dd, $J=8$, 4 Hz), 6.37 (1H, dd, $J=12$, 6 Hz), 6.63 (1H, dd, $J=12$, 1 Hz), 6.74 (2H, d, $J=8.5$ Hz), 7.14 (2H, d, $J=8.5$ Hz), 7.23—7.45 (5H, m). MS *m*/*z* (relative intensity): 438 (M$^{+}-100$, 0.2), 400 (0.3), 207 (4.3), 121 (100), 101 (26), 91 (72).

The mixture of enones (20.5 mg, 38.1 μmol) in EtOAc (1.5 ml) was hydrogenated with 10% Pd–C (17.5 mg) for 10 min to give **45** as a colorless oil (20.2 mg, 98%). $[\alpha]_D^{15}$ $-6.4°$ ($c=0.73$). IR ν_{max} cm^{-1}: 1705. ^{1}H-NMR δ: 0.90 (3H, t, $J=7.5$ Hz), 1.24 (3H, d, $J=7$ Hz), 1.36 (3H, s), 1.40 (3H, s), 1.42—2.08 (8H, m), 2.45—2.74 (2H, m), 3.09 (1H, q, $J=2$ Hz), 3.78 (3H, s), 3.84 (1H, dd, $J=7.5$, 2 Hz), 3.96 (1H, dd, $J=10$, 2 Hz), 4.03 (1H, dd, $J=9.5$, 3.5 Hz), 4.07 (1H, q, $J=7$ Hz), 4.32 (1H, q, $J=6$ Hz), 4.41 (1H, d, $J=12$ Hz), 4.44 (1H, d, $J=9$ Hz), 4.62 (1H, q, $J=6$ Hz), 4.65 (1H, d, $J=12$ Hz), 6.85 (2H, d, $J=8.5$ Hz), 7.26 (2H, d, $J=8.5$ Hz), 7.30—7.40 (5H, m). MS *m*/*z* (relative intensity): 540 (M^{+}, 2.8), 522 (0.3), 255 (1.6), 233 (3.4), 211 (4.3), 141 (6.9), 121 (100), 91 (57). Exact MS *m*/*z* Calcd for $C_{32}H_{44}O_7$ (M^{+}): 540.3090. Found: 540.3085.

(2*S*,5*R*,6*R*)-2-[(2*R*,5*R*,6*S*)-5-Benzyloxy-5-ethyl-6-melthyltetrahydropyran-2-yl]-5,7-isopropylidenedioxy-6-(4-methoxybenzyloxy)heptan-2-ol (46) An ether solution (1.5 ml) of **45** (18.2 mg, 0.034 mmol) was added dropwise to a stirred 1.4 M ether solution of MeLi (0.5 ml, 0.70 mmol) diluted with ether (1 ml) at, −93 °C under argon. After 2 h, the reaction mixture was allowed to warm to room temperature, poured into saturated NH_4Cl, and extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated, and the residue was subjected to silica gel TLC (EtOAc–hexane, 1:1) to give **46** as a colorless oil (16.3 mg, 87%). $[\alpha]_D^{15}$ $-18.8°$ ($c=0.54$). IR ν_{max} cm^{-1}: 3450. ^{1}H-NMR δ: 0.88 (3H, t, $J=7.5$ Hz), 1.13 (3H, s), 1.24 (3H, d, $J=7$ Hz), 1.39 (3H, s), 1.42 (3H, s), 1.43—2.00 (10H, m), 2.55 (1H, br s), 3.07, (1H, q, $J=2$ Hz), 3.42 (1H, dd, $J=8$, 2 Hz), 3.74 (1H, dd, $J=4$, 2 Hz), 3.78 (3H, s), 3.83 (1H, dd, $J=11$, 2 Hz), 3.95 (1H, dd, $J=9$, 2 Hz), 4.11 (1H, q, $J=7$ Hz), 4.31 (1H, d, $J=11$ Hz), 4.37 (1H, d, $J=11$ Hz), 4.42 (1H, d, $J=12$ Hz), 4.64 (1H, d, $J=12$ Hz), 6.84 (2H, d, $J=9$ Hz), 7.27 (2H, d, $J=9$ Hz), 7.20—7.42 (5H, m). MS *m*/*z* (relative intensity): 556 (M^{+}, 1.1), 432 (0.1), 305 (1.1), 209 (1.9), 185 (2.1), 121 (100), 91 (27). Exact MS *m*/*z* Calcd for $C_{33}H_{48}O_7$ (M^{+}): 556.3403. Found: 556.3391.

(2*S*,5*R*,6*R*)-2-[(2*R*,5*R*,6*S*)-5-Benzyloxy-5-ethyl-6-methyltetrahydropyran-2-yl]-7-*tert*-butyldimethylsilyloxy-6-(4-methoxybenzyloxy)heptane-2,5-diol (47) A solution of **46** (26 mg, 47 μmol) in THF (2 ml) and 1 N HCl (1 ml) was stirred at room temperature for 30 min. Work-up and chromatography on a silica gel column (EtOAc→MeOH–CH_2Cl_2, 1:10) gave the triol as a colorless oil (23.1 mg, 96%). $[\alpha]_D^{15}$ $-8.3°$ ($c=0.44$). IR ν_{max} cm^{-1}: 3400. ^{1}H-NMR δ: 0.88 (3H, t, $J=7.5$ Hz), 1.13 (3H, s), 1.24 (3H, d, $J=7$ Hz), 1.30—2.05 (8H, m), 2.10—2.25 (1H, m), 2.50—3.00 (2H, m), 3.33 (1H, q, $J=5$ Hz), 3.42 (1H, dd, $J=11.5$, 2.5 Hz), 3.64 (1H, dd, $J=11.5$, 4 Hz), 3.69 (1H, dd, $J=9$, 5 Hz), 3.75—3.85 (1H, m), 3.78 (3H, s), 4.11 (1H, q, $J=7$ Hz), 4.31 (1H, d, $J=10.5$ Hz), 4.38 (1H, d, $J=10.5$ Hz), 4.53 (1H, d, $J=11$ Hz), 4.63 (1H, d, $J=11$ Hz), 6.88 (2H, d, $J=8.5$ Hz), 7.27 (2H, d, $J=8.5$ Hz), 7.20—7.42 (5H, m). MS *m*/*z* (relative intensity): 408 (M$^{+}-108$, 0.2), 368 (0.2), 317 (2), 277 (1), 271 (1.5), 209 (4), 169 (2.5), 137 (3), 121 (100), 91 (39), 57 (9), 43 (9). Exact MS *m*/*z* Calcd for $C_{23}H_{36}O_6$ (M$^{+}-108$): 408.2514. Found: 408.2529. *Anal.* Calcd for $C_{30}H_{44}O_7$: C, 69.74; H, 8.58. Found: C, 69.55; H, 8.67.

Imidazole (11.4 mg, 0.168 mmol) and TBDMS chloride (12.4 mg, 82 μmol) were added to a stirred solution of the above triol (9.4 mg, 18.2 mol) in CH_2Cl_2 (0.4 ml) at room temperature. After 30 min, the reaction mixture was diluted with CH_2Cl_2, washed with brine, dried (Na_2SO_4), and evaporated *in vacuo*, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 3:1→2:1) to give **47** as a colorless oil (11.6 mg, 100%). $[\alpha]_D^{15}$ $-13.6°$ ($c=0.46$). ^{1}H-NMR δ: 0.07 (6H, s), 0.88 (3H, t, $J=8.0$ Hz), 0.90 (9H, s), 1.13 (3H, s), 1.24 (3H, d, $J=7.0$ Hz), 1.30—1.65 (7H, m), 1.79 (1H, dt, $J=12.0$, 4.0 Hz), 1.94 (1H, d, $J=14.0$ Hz), 2.50—2.80 (2H, m), 3.35 (1H, q, $J=4.0$ Hz), 3.42 (1H, dd, $J=12.0$, 2.0 Hz), 3.55—3.66 (1H, m), 3.62 (1H, dd, $J=10.0$, 5.5 Hz), 3.80 (1H, dd, $J=11.0$, 5.5 Hz), 3.80 (3H, s), 4.11 (1H, q, $J=7.0$ Hz), 4.32 (1H, d, $J=11.0$ Hz), 4.38 (1H, d, $J=11.0$ Hz), 4.50 (1H, d, $J=11.5$ Hz), 4.68 (2H, d, $J=11.5$ Hz), 6.87 (2H, d, $J=9.0$ Hz), 7.25 (2H, d, $J=9.0$ Hz), 7.20—7.43 (5H, m). MS *m*/*z* (relative intensity): 435 (M$^{+}-195$, 0.2), 385 (0.6), 379 (0.9), 327 (0.2), 317 (0.6), 277 (0.4), 259 (0.9), 209 (1), 121 (100), 91 (22), 75 (4), 57 (7), 43 (5). Exact MS *m*/*z* Calcd for $C_{24}H_{39}O_5Si$ (M$^{+}-195$): 435.2569. Found: 435.2569.

(*R*)-2-[(2*RS*,5*S*)-5-[(2*R*,5*R*,6*S*)-5-Benzyloxy-5-ethyl-6-methyltetrahydropyran-2-yl]-2-methoxy-5-methyltetrahydrofuran-2-yl]-2-(4-methoxybenzyloxy)ethanol (48) A solution of **47** (11.4 mg, 18.1 μmol) was oxidized with $(COCl)_2$ (25 μl, 0.30 mmol), DMSO (50 μl, 0.70 mmol), and then Et_3N (0.1 ml, 0.73 mmol) in CH_2Cl_2 (0.7 ml) as described for **8** to give the hemiacetal as a colorless oil (10.9 mg, 96%). ^{1}H-NMR δ: 0.06 (6H, s), 0.88 (3H, t, $J=7.5$ Hz), 0.90 (9H, s), 1.14 (3H, s), 1.30 (3H, d, $J=7.0$ Hz), 1.34—2.45 (11H, m), 3.53 (1H, dd, $J=7.0$, 3.0 Hz), 3.56—3.64 (1H, m), 3.71 (1H, dd, $J=10.0$, 7.0 Hz), 3.80 (3H, s), 3.92 (1H, dd, $J=10.0$, 3.0 Hz), 4.21 (1H, q, $J=7.0$ Hz), 4.31 (1H, d, $J=10.5$ Hz), 4.43 (1H, d, $J=10.5$ Hz), 4.71 (2H, s), 6.85 (2H, d, $J=9.0$ Hz), 7.27 (2H, d, $J=9.0$ Hz), 7.20—7.42 (5H, m). MS *m*/*z* (relative intensity): 433 (M$^{+}-195$, 0.3), 417 (1), 409 (0.2), 383 (0.3), 368 (0.7), 311 (6), 213 (10), 121 (100), 91 (44), 75 (10), 57 (7). Exact MS *m*/*z* Calcd for $C_{24}H_{37}O_5Si$ (M$^{+}-195$): 433.2412. Found: 433.2406. *Anal.* Calcd for $C_{36}H_{56}O_4Si$: C, 68.75; H, 8.98. Found: C, 68.69; H, 9.14.

CSA (20.0 mg, 86 μmol) was added to a stirred solution of the above hemiacetal (12.7 mg, 20.2 μmol) in MeOH (1.5 ml) at room temperature. After 5 min, the solution was neutralized with Et_3N, and evaporated *in vacuo*, and the residue was subjected to silica gel column chromatography (EtOAc–hexane, 1:1→2:1) and TLC (EtOAc–hexane, 1:2) to give **48a** (5.4 mg, 51%) and **48b** (5.1 mg, 48%) as colorless oils.

48a: $[\alpha]_D^{15}$ $+6.1°$ ($c=0.36$). ^{1}H-NMR δ: 0.87 (3H, t, $J=7.0$ Hz), 1.22 (3H, d, $J=7.0$ Hz), 1.26 (3H, s), 1.27—2.80 (11H, m), 3.18 (3H, s), 3.60 (1H, dd, $J=12.0$, 3.0 Hz), 3.70 (2H, dd, $J=12.0$, 5.5 Hz), 3.80 (3H, s), 3.83 (1H, q, $J=7.0$ Hz), 4.17 (1H, q, $J=7.0$ Hz), 4.28 (1H, d, $J=11.0$ Hz), 4.41 (1H, d, $J=11.0$ Hz), 4.57 (1H, d, $J=7.0$ Hz), 4.64 (1H, d, $J=7.0$ Hz), 6.86 (2H, d, $J=9.0$ Hz), 7.29 (2H, d, $J=9.0$ Hz), 7.21—7.41 (5H, m). MS *m*/*z* (relative intensity): 497 (M$^{+}-31$, 0.2), 466 (0.6), 437 (10), 347 (12), 233 (8), 121 (100), 91 (67), 57 (7). Exact MS *m*/*z* Calcd for $C_{24}H_{37}O_7$ (M$^{+}-91$): 437. 2541. Found: 437.2540.

48b: $[\alpha]_D^{15}$ $-18.2°$ ($c=0.37$). ^{1}H-NMR δ: 0.89 (3H, t, $J=7.5$ Hz), 1.22 (3H, s), 1.27 (3H, d, $J=7.0$ Hz), 1.30—2.40 (11H, m), 3.25 (3H, s), 3.48 (1H, dd, $J=5.0$, 2.5 Hz), 3.52 (1H, dd, $J=5.5$, 3.0 Hz), 3.63 (1H, dd, $J=8.0$, 4.5 Hz), 3.72 (1H, dd, $J=8.0$, 5.0 Hz), 3.81 (3H, s), 4.13 (1H, q, $J=7.0$ Hz), 4.33 (1H, d, $J=11.0$ Hz), 4.45 (1H, d, $J=11.0$ Hz), 4.49 (1H, d, $J=11.0$ Hz), 4.79 (1H, d, $J=11.0$ Hz), 6.88 (2H, d, $J=9.0$ Hz), 7.27 (2H, d, $J=9.0$ Hz), 7.20—7.45 (5H, m). MS *m*/*z* (relative intensity): 497 (M$^{+}-31$, 0.3), 466 (0.5), 437 (8), 347 (22), 233 (7), 121 (100), 91 (65), 57 (7). Exact MS *m*/*z* Calcd for $C_{24}H_{37}O_7$ (M$^{+}-91$): 437.2541. Found: 437.2569.

(*R*)-3-[(2*RS*,5*S*)-5-[(2*R*,5*R*,6*S*)-5-Benzyloxy-5-ethyl-6-methyltetrahydropyran-2-yl]-2-methoxy-5-methyltetrahydrofuran-2-yl]-3-(4-methoxybenzyloxy)prop-1-yne (4) A solution of **48a** (78.0 mg, 0.147 mmol) was oxidized with $(COCl)_2$ (32 μl, 0.368 mmol), DMSO (37 μl, 0.515 mmol), and then Et_3N (0.104 ml, 0.75 mmol) in CH_2Cl_2 (4 ml) as described for **8** to give the aldehyde-a as a colorless oil (70.2 mg, 91%). ^{1}H-NMR δ: 0.86 (3H, t, $J=7.0$ Hz), 1.14 (3H, d, $J=7.0$ Hz), 1.25 (3H, s), 1.26—2.30 (10H, m), 3.14 (3H, s), 3.30—3.50 (1H, m), 3.80 (3H, s), 3.90—4.16 (2H, m), 4.26 (1H, d, $J=12.0$ Hz), 4.38 (1H, d, $J=12.0$ Hz), 4.44 (1H, d, $J=12.0$ Hz), 4.68 (1H, d, $J=12.0$ Hz), 6.84 (2H, d, $J=9.0$ Hz), 7.16—7.40 (7H, m), 9.68 (1H, d, $J=1.5$ Hz).

Similarly, **48b** (30.0 mg, 56.7 μmol) gave the aldehyde-b as a colorless oil (29.0 mg, 97%). ^{1}H-NMR δ: 0.88 (3H, t, $J=7.0$ Hz), 1.19 (3H, s), 1.26 (3H, d, $J=7.0$ Hz), 1.27—2.40 (10H, m), 3.29 (3H, s), 3.40—3.60 (1H, m), 3.80 (3H, s), 3.95 (1H, d, $J=2.0$ Hz), 4.10 (1H, q, $J=7.0$ Hz), 4.30 (1H, d, $J=11.0$ Hz), 4.42 (1H, d, $J=11.0$ Hz), 4.59 (2H, s), 6.89 (2H, d, $J=11.0$ Hz), 7.16—7.46 (7H, m), 9.61 (1H, d, $J=2.0$ Hz).

A solution of the above aldehyde-a (70.2 mg, 0.133 mmol), Ph_3P (70 mg, 0.266 mmol), and $PhHgCBrCl_2$ (117 mg, 0.266 mmol) in benzene (3 ml) was refluxed under argon for 30 min. The solution was evaporated *in vacuo*, and the residue was dissolved in EtOAc–hexane (1:3). This solution was passed through a short silica gel column to remove the excess reagents. The eluate was evaporated *in vacuo* and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1:7) to give the dichloroolefin-a as a colorless oil (78.3 mg, 99%).

Similarly, the above aldehyde-b (colorless oil, 90 mg, 0.151 mmol) gave the dichloroolefin-b as a colorless oil (90 mg, 89%).

A 1.6 M n-BuLi solution (0.21 ml, 0.336 mmol) in hexane was added to a stirred solution of the above dichloroolefin-a (78.3 mg, 0.132 mmol) in THF (2 ml) at $-78\,^{\circ}$C under argon. After 40 min, the reaction mixture was allowed to warm to room temperature, then poured into cold saturated NH_4Cl, and extracted with ether. The extract was washed with brine, dried (Na_2SO_4), and evaporated, and the residue was chromatographed on a silica gel column (EtOAc–hexane, 1:5) to give **4a** as a colorless oil (59.0 mg, 85%). IR ν_{max} cm^{-1}: 3250, 2120, 1610, 1585. ^{1}H-NMR δ: 0.87 (3H, t, $J=7.0$ Hz), 1.18 (3H, d, $J=7.0$ Hz), 1.27 (3H, s), 1.28—2.38 (10H, m), 2.44 (1H, d, $J=2.0$ Hz), 3.06 (3H, s), 3.40—3.60 (1H, m), 3.80 (3H, s), 4.07 (1H, q, $J=7.0$ Hz), 4.24 (1H, d, $J=2.0$ Hz), 4.32 (1H, d, $J=11.0$ Hz), 4.40 (1H, d, $J=11.0$ Hz), 4.55 (1H, d, $J=11.0$ Hz), 4.79 (1H, d, $J=11.0$ Hz), 6.98 (2H, d, $J=9.0$ Hz), 7.16—7.48 (7H, m). MS m/z (relative intensity): 491 (M^+-31, 0.1), 361 (0.5), 347 (7), 289 (5), 239 (8), 143 (6), 121 (100), 91 (68), 57 (13), 43 (7). Exact MS m/z Calcd for $C_{31}H_{39}O_5$ (M^+-31): 491.2800. Found: 491.2781.

Similarly, the dichloroolefin-b (90 mg, 0.151 mmol) gave **4b** as a colorless oil (74.0 mg, 94%). IR ν_{max} cm^{-1}: 3250, 2120, 1610, 1585. ^{1}H-NMR δ: 0.87 (3H, t, $J=7.0$ Hz), 1.18 (3H, s), 2.04 (3H, d, $J=7.0$ Hz), 2.09—2.36 (10H, m), 2.41 (1H, d, $J=2.0$ Hz), 3.28 (3H, s), 3.40—3.60 (1H, m), 3.79 (3H, s), 4.09 (1H, q, $J=7.0$ Hz), 4.21 (1H, d, $J=2.0$ Hz), 4.30 (1H, d, $J=11.0$ Hz), 4.40 (1H, d, $J=11.0$ Hz), 4.52 (1H, d, $J=11.0$ Hz), 4.72 (1H, d, $J=11.0$ Hz), 6.84 (2H, d, $J=9.0$ Hz), 7.16—7.44 (7H, m). MS m/z (relative intensity): 491 (M^+-31, 0.1), 361 (0.5), 347 (7), 289 (5), 239 (8.5), 143 (6), 121 (100), 91 (70), 57 (14), 43 (9).

References and Notes

1) Chiral Synthesis of Polyketide-Derived Natural Products. XXIV. For part XXIII, see: K. Horita, Y. Oikawa and O. Yonemitsu, *Chem. Pharm. Bull.*, **37**, 1698 (1989).

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16) In the absence of Zn dust the starting material (**30**) decomposed.

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20) Undesirable side reactions occurred concomitantly in the usual procedure, *i.e.*, conversion of **41** into **44** with potassium carbonate in methanol and acid-catalyzed recyclization of **44** with CSA in dichloromethane gave mainly (S)-1-[(2R,5R)-2-ethyl-5-hydroxymethyltetrahydrofuran-2-yl]ethanol. For an example of the base-catalyzed recyclization of epoxy-alcohols see: L. A. Leed, III, Y. Ito, S. Masamune and K. B. Sharpless, *J. Am. Chem. Soc.*, **104**, 6468 (1982).

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