

Asymmetric Synthesis of the Polyol Subunit of the Macrolide Antibiotic, Ossamycin: A Unique Approach Utilizing Stereochemical Specificity

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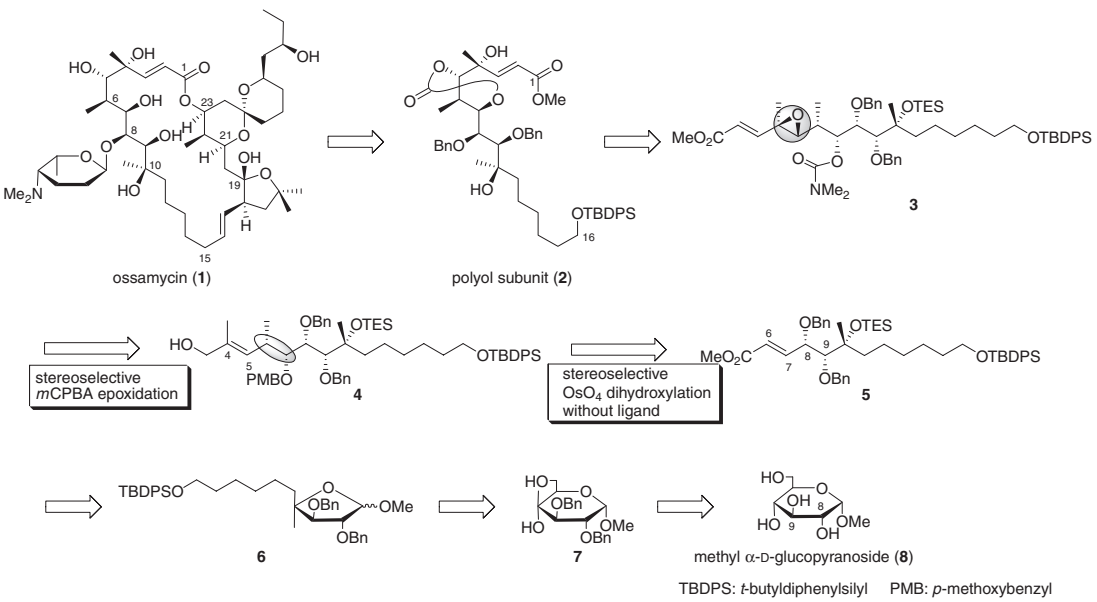
An asymmetric synthesis of the C1–C16 polyol subunit **2** of the macrolide antibiotic ossamycin (**1**) has been achieved through stepwise carbon-chain elongation reaction from D-glucose, based on a chiral pool approach. An outstanding point of this strategy is asymmetric induction by utilizing steric hindrance of neighboring groups. The stereogenic centers at the C4 and C5 positions of **2** were constructed by *m*CPBA epoxidation, and the C6 and C7 positions of **2** were produced by catalytic OsO_4 dihydroxylation under highly stereoselective conditions.

In 1965, ossamycin (**1**) was reported as a second metabolite of *Streptomyces hygroscopicus* var. *ossamyceticus* strain C8158 isolated in South America.[1] Its structure was determined[2] by single crystal X-ray diffraction studies to be a member of such macrolide antibiotics as cytovaricin,[3] oligomycins,[4] A82548A,[5] and rutamycins.[6] The aglycone of **1** possesses a 24-membered macrolide ring system onto which is incorporated both a 6,6-spiroketal and a 5-membered hemiketal ring system. This macrolide series inhibits the mitochondrial H^+-ATPase by interacting with the F_0-sector to block proton translocation, and has potential as a lead for new anticancer drugs from recent biological investigation.[7] A synthesis of **1** was planned to develop an efficient synthetic methodology, which would be useful to elaborate more biologically effective derivatives, and we finally accomplished the asymmetric synthesis of the C1–C16 polyol subunit **2** of **1**.[8] Our synthetic approach is a unique methodology of asymmetric induction by using the steric hindrance of neighboring group. We describe herein our efficient synthetic process of **2**.

Results and Discussion

Our synthetic plan for the polyol subunit **2** of ossamycin (**1**) was based on stepwise carbon-chain elongation reaction by the chiral pool approach employing methyl α-D-glucopyranoside (**8**) as a starting material (Scheme 1). The synthetic strategy to assemble the carbon framework and to build stereogenic centers of **2** employed the Wittig olefination and the following asymmetric dihydroxylation/epoxidation by utilizing steric effects. The combination of chiral pool and flexible diastereoselective reactions affected the efficient synthetic pathway to the target molecule.

Along this line, the known sugar **7**,[9] prepared in seven steps from commercially available **8**, was converted into the iodide **9** via tosylation. Reduction of **9** by zinc powder, followed by



Scheme 1. Retrosynthetic analysis.

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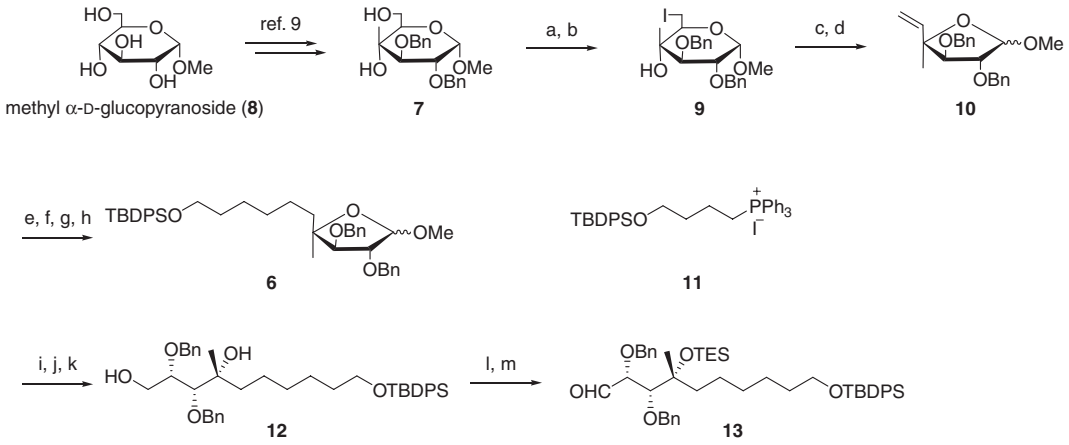
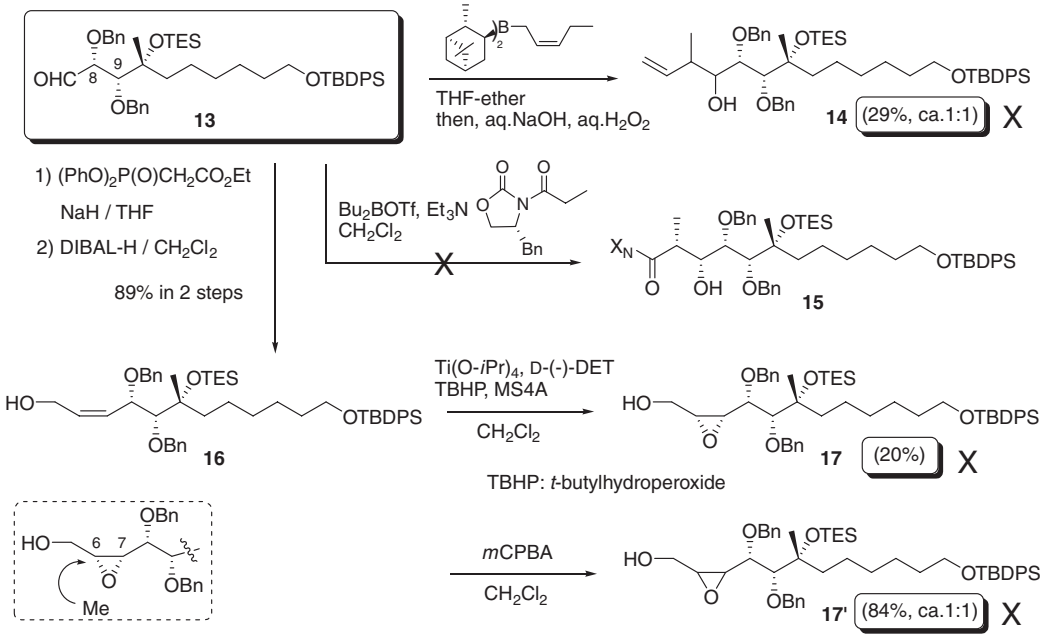


Scheme 2. *Reagents and conditions*: (a) TsCl, pyr (99%). (b) NaI, DMF (92%). (c) Zn powder, EtOH. (d) Amberlyst 15E, MeOH (71% in two steps). (e) 9-BBN, THF, then H_2O_2, NaOH. (f) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2. (g) **11**, *n*BuLi, THF. (h) H_2, 10% Pd–C, EtOH (92% in four steps). (i) $Et_2O{\cdot}BF_3$, Ac_2O. (j) K_2CO_3, MeOH. (k) $NaBH_4$, MeOH (93% in three steps). (l) TESOTf, 2,6-lutidine, CH_2Cl_2 (100%). (m) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2 (95%).

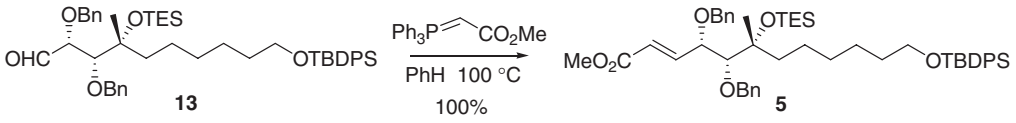


Scheme 3. Attempt to establish the stereogenic centers at the C6–C7 positions.

recyclization[10] and methylation provided the 5-membered sugar **10**. The carbon chain of **10** was extended by successive manipulation involving hydroboration, oxidation of the resulting primary alcohol, the Wittig reaction with the phosphonium salt **11**, and then hydrogenation of the resulting double bond. The furanoside **6** obtained was transformed into the acyclic diol **12** in three steps. Conversion to the di-TES ether (TES: triethylsilyl), followed by the chemoselective Swern oxidation involving a selective deprotection gave the aldehyde **13**,[11] which might be an important synthetic intermediate of **2** (Scheme 2).

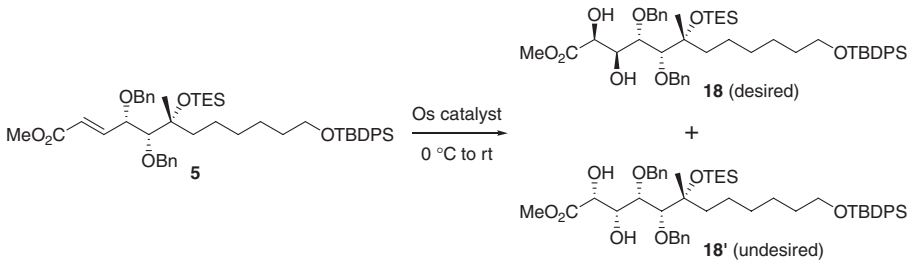
Our first plan for construction of the stereogenic centers at the C6 and C7 positions of **2** was the Brown crotyl-boration[12] or the Evans aldol reaction[13] using the aldehyde **13** as a substrate. However, the former protocol furnished the homoallylic alcohol **14** in poor yield and low selectivity, and the latter provided no reaction. Also, conversion of **13** to the (*Z*)-allyl alcohol **16** in two steps,[14] followed by the Sharpless asymmetric epoxidation[15] or *m*CPBA epoxidation was unsuccessful, because of poor yield or low selectivity. Assembly of the asymmetric carbon centers at the C6–C7 positions was exacerbated by severe steric hindrance of the adjacent benzyl group at the C8 position. The difficulty of reagent control against such bulky substrates prompted us to explore an adverse alternative strategy by utilizing this stereochemical specificity (Scheme 3).

A new approach to produce the stereogenic centers at the C6–C7 positions was an unprecedented pathway that utilizes steric hindrance; thus, the carbon chain of the aldehyde **13** was lengthened by the Wittig reaction to give **5** (Scheme 4). In the next step, asymmetric dihydroxylation of **5** was attempted with catalytic OsO_4 (Table 1). As expected, the approach of



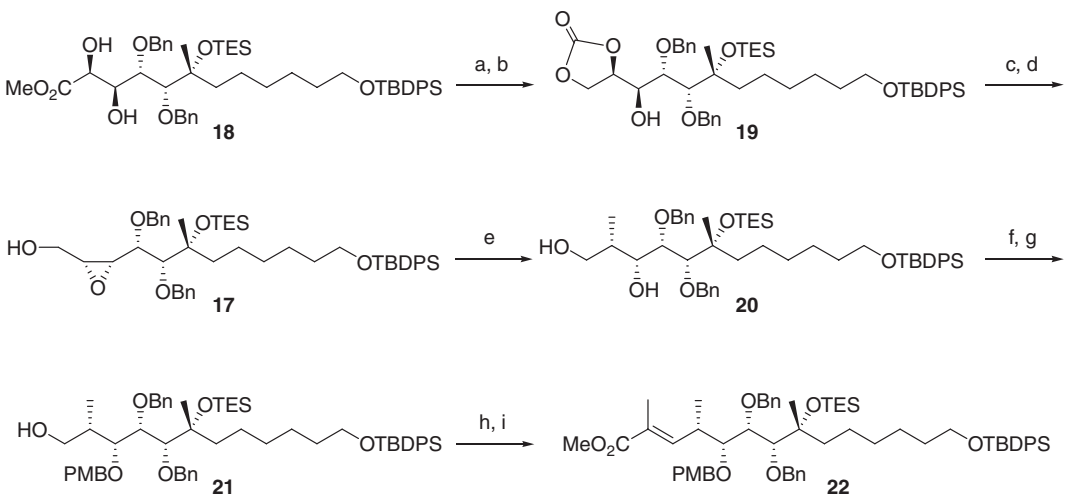
Scheme 4.

Table 1. Asymmetric Dihydroxylation of **5**



Entry	Reagents	Solvent	Yields	Selectivity (desired **18**:undesired **18′**)[a)]
1	OsO_4, NMO	*t*BuOH–H_2O (1/1)	58%	>15:1
2	AD mix α, $MeSO_2NH_2$	*t*BuOH–H_2O (1/1)	57%	1:3
3	AD mix β, $MeSO_2NH_2$	*t*BuOH–H_2O (1/1)	28%	15:1
4	OsO_4, NMO	acetone–H_2O (10/1)	100%	>19:1

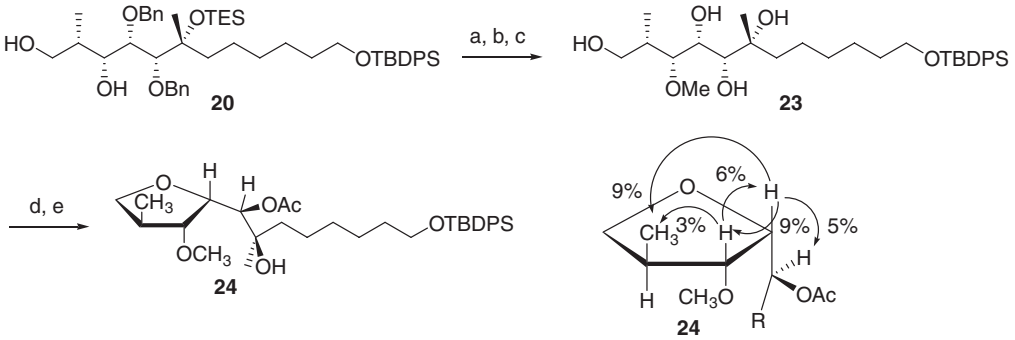
a) Ratio was determined by ^{1}H NMR spectra.



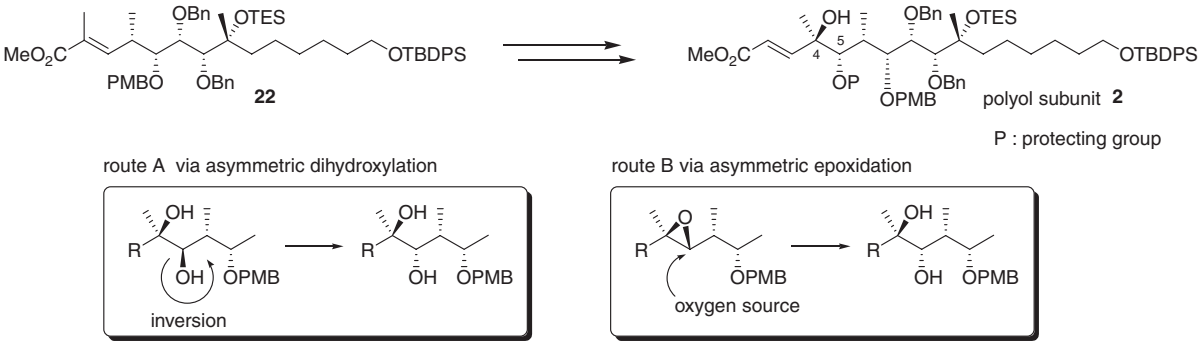
Scheme 5. *Reagents and conditions*: (a) $LiBH_4$, THF (100%). (b) $CO(Im)_2$, PhH (81%). (c) MsCl, DMAP (4-(dimethylamino)pyridine), pyr. (d) NaOMe, MeOH (95% in two steps). (e) $Li_2CuMe_2(CN)$, Et_2O (87%). (f) *p*-Anisaldehyde dimethyl acetal, PPTS (pyridinium *p*-toluenesulfonate), CH_2Cl_2 (100%). (g) DIBAL-H, PhMe (64%). (h) Dess–Martin periodinane, $NaHCO_3$, CH_2Cl_2. (i) $Ph_3P{=}C(Me)CO_2Me$, PhH (94% in two steps).

the oxidant took place from the least hindered side to give **18** as the predominant product (Entries 1–3). The drawback of the yields has dramatically improved through solvent selection: upon using acetone–H_2O (10/1), **18** was obtained in 100% yield (>90% d.e., the minor product could be entirely removed during the following steps. A detailed inspection of **20** indicated that no minor product was observed in the spectroscopic analysis.) (Entry 4).

After $LiBH_4$ reduction, the triol generated was subjected to selective protection to afford **19** (Scheme 5). After mesylation and removal of the cyclic carbonate, the resulting diol was treated under basic conditions to give the epoxy alcohol **17**, the spectroscopic data of which showed the same signal pattern as that of the product of the Sharpless asymmetric epoxidation (Scheme 3). Reaction of **17** with $Li_2CuMe_2(CN)$ effected the predominant introduction of a methyl group to the C2 position, leading to the 1,3-diol **20**.[16] After conversion of **20** to **21** by selective protection of a secondary alcohol, the remaining primary alcohol was subjected to Dess–Martin oxidation, followed by the Wittig reaction to afford **22**. In addition, the stereochemistry of the asymmetric centers at the C6 and C7 positions was unambiguously established by its conversion to the 5-membered **24**. Thus, **20** was transformed to the tetrol **23** by the following three-step sequence: (1) trityl

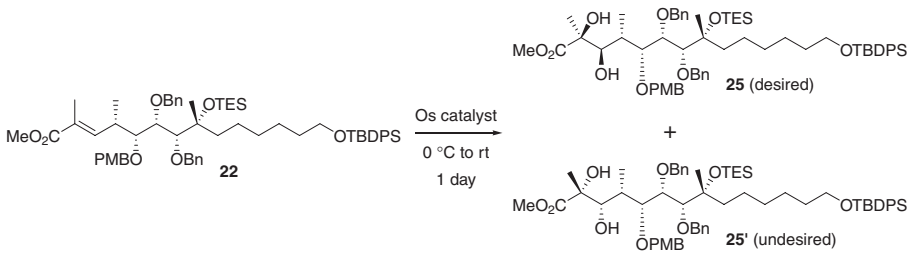


Scheme 6. *Reagents and conditions*: (a) TrCl, pyr, DMAP (86%). (b) MeI, NaH, DMF (74%). (c) H_2, $Pd(OH)_2$–C, MeOH–THF (2/1) (53%). (d) TsCl, pyr. (e) Ac_2O, pyr (67% in two steps).



Scheme 7. Asymmetric induction at the C4–C5 positions.

Table 2. Asymmetric Dihydroxylation of **22**



Entry	Reagents	Solvent	Yields	Selectivity (desired **25**:undesired **25′**)[a)]
1	OsO_4, NMO	acetone–H_2O (10/1)	33%	4:1
2	OsO_4, Me_3NO	acetone–H_2O (10/1)	40%	4:1
3	AD mix β, $MeSO_2NH_2$	*t*BuOH–H_2O (1/1)	No Reaction	
4	AD mix β, DABCO	*t*BuOH–H_2O (1/1)	No Reaction	

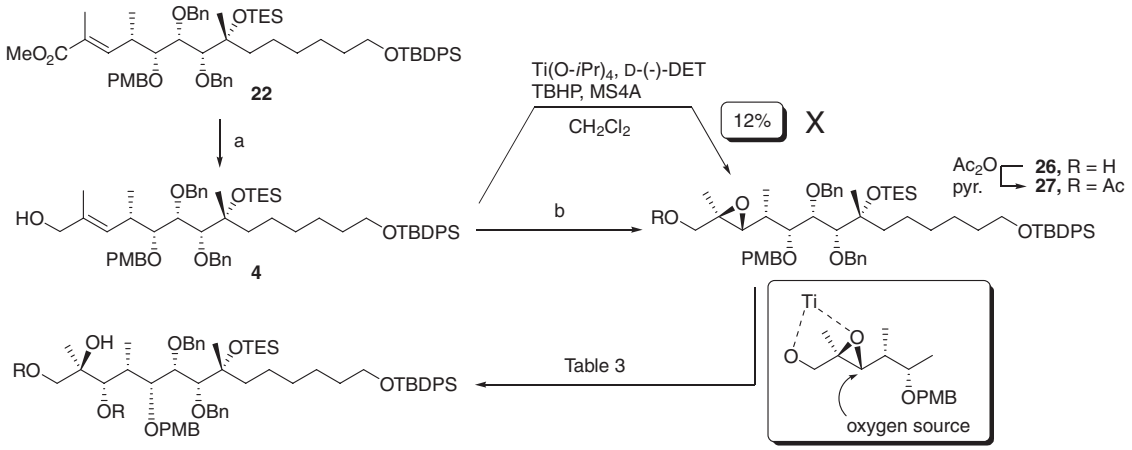
a) Ratio was determined by ^{1}H NMR spectra.

protection of the primary alcohol; (2) methyl protection of the secondary alcohol; and (3) deprotection of trityl, benzyl, and TES groups. After tosylation of the primary alcohol, the resulting triol was treated under basic conditions, followed by acetylation to give the 5-membered **24**, the NOE experiments of which indicated the configuration of the newly introduced stereochemistry as depicted in Scheme 6.

In the next stage, we attempted construction of the stereogenic centers at the C4–C5 positions of **22** coinstantaneously to afford the polyol subunit **2** (Scheme 7). Thus, we considered two possible pathways to transform **22** into the polyol subunit **2**: (1) route A: asymmetric dihydroxylation of **22**, followed by inversion of the secondary alcohol generated and (2) route B: asymmetric epoxidation of **22**, followed by regioselective induction of an oxygen source.

At first, asymmetric dihydroxylation of **22** (Table 2) provided **25** and **25′** with insufficient yields and selectivity (Entry 2). Furthermore, the AD mix (reagent for Sharpless asymmetric dihydroxylation) to improve the selectivity provided no reaction (Entries 3 and 4).

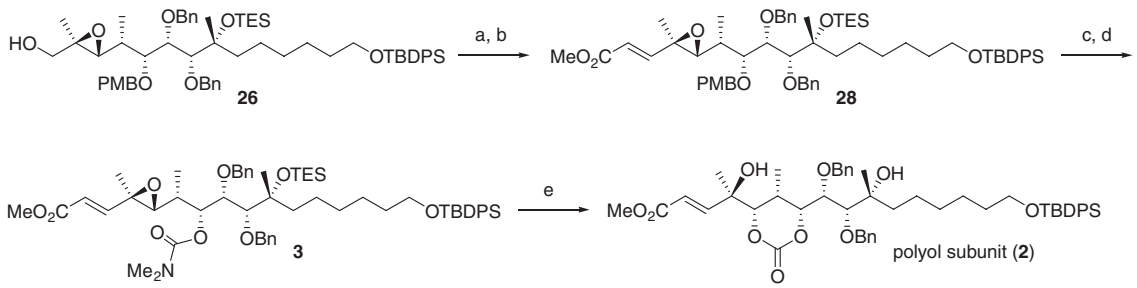
Accordingly, after conversion of **22** to the allyl alcohol **4**, the epoxy alcohol **26** was produced by *m*CPBA (Scheme 8). We disclosed that a *p*-methoxybenzyl group effectively functioned as an anchoring group in the Miyashita epoxidation,



Scheme 8. Asymmetric epoxidation of **4** (route B); *Reagents and conditions*: (a) $LiBH_4$, THF (100%). (b) *m*CPBA, $NaHCO_3$, CH_2Cl_2 (75%).

Table 3. Asymmetric Induction by Oxygen Source

Entry	Substrate	Oxygen source	Additive	Solvent	Conditions	Result
1	**26**	PivOH	Ti(O*i*Pr)$_4$	benzene	rt, 3d.	No Reaction
2	**26**	PivOH	Ti(O*i*Pr)$_4$	benzene	70 °C, 1d.	No Reaction
3	**26**	PivONa	Ti(O*i*Pr)$_4$	DMF	70 °C, 1d.	No Reaction
4	**26**	PivONa	Ti(O*i*Pr)$_4$, 15-crown-5	benzene	reflux, 1d.	No Reaction
5	**26**	Bu_4NOAc	Ti(O*i*Pr)$_4$	benzene	70 °C, 2d.	No Reaction
6	**26**	BzONa	Ti(O*i*Pr)$_4$, 15-crown-5	benzene	70 °C, 2d.	No Reaction
7	**26**	PhCOOH	Ti(O*i*Pr)$_4$	CH_2Cl_2	rt, 1d.	No Reaction
8	**26**	AcOCs	Ti(O*i*Pr)$_4$	CH_2Cl_2	rt, 3d.	No Reaction
9	**27**	PivONa		DMF	115 °C, 3d.	No Reaction
10	**27**	AcONa	15-crown-5	DMF	70 °C, 3d.	No Reaction
11	**27**	BzONa		DMF	100 °C, 1d.	No Reaction
12	**27**	Bu_4NOAc		benzene	reflux, 1d.	No Reaction



Scheme 9. *Reagents and conditions*: (a) TPAP, NMO (*N*-methylmorpholine *N*-oxide), CH_2Cl_2. (b) $Ph_3P{=}CHCO_2Me$, benzene (76% in two steps). (c) DDQ, CH_2Cl_2–H_2O (20/1) (95%). (d) Me_2NCOCl, NaH, DMF (64%). (e) $Et_2O{\cdot}BF_3$, CH_2Cl_2 (36%).

while only that of TES groups was reported.[17] Interestingly, exclusive formation of the diastereomeric epoxide **26** as the sole product was observed from the trisubstituted allylic alcohol **4**, although the Sharpless asymmetric epoxidation provided **26** in poor yield. In addition, as shown in Table 3, we examined introduction of such oxygen sources as *t*BuCOOH, *t*BuCOONa, *n*Bu_4NOAc, NaOBz, BzOH, and CsOAc to **26** by expecting a chelation effect by a titanium ion or **27** under basic conditions. Unfortunately, no desired results were obtained under any of the reaction conditions attempted, because the severe steric hindrance of the neighboring *p*-methoxybenzyl group interfered with the approach of an oxygen function to the reactive site. Consequently, we selected removal of the *p*-methoxybenzyl group and intramolecular reaction pathway. After TPAP (tetrapropylammonium perruthenate) oxidation of the epoxy alcohol **26**, the carbon-chain elongation afforded **28** (Scheme 9). The *p*-methoxybenzyl group of **28** was removed with DDQ, followed by dimethylcarbamation to afford **3**. At the final stage, exposure of the dimethylcarbamyl epoxide **3** to $Et_2O{\cdot}BF_3$ at ambient temperature[18] gave the desired polyol subunit cyclic carbonate **2**, which possessed the same carbon framework (C1–C16) as **1**. The newly intro-

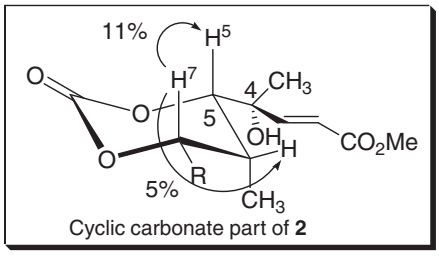


Fig. 1. The NOE correlation of **2**.

duced stereochemistry at the C4–C5 positions of **2** was determined by its reaction process from **3** and the NOE experiments (Fig. 1).

In conclusion, this unique approach of the asymmetric synthesis of polyol subunit **2** was accomplished by utilizing the steric hindrance of neighboring groups. This C1–C16 skeleton could be a useful synthetic intermediate for the total synthesis of ossamycin (**1**).

Experimental

General. IR spectra were recorded on a JASCO Model A-202 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were obtained on JEOL JNM EX-270 and JEOL JNM GX-400 spectrometers in a deuteriochloroform ($CDCl_3$) solution using tetramethylsilane as an internal standard. High-resolution mass spectra were obtained on a Hitachi M-80 B GC-MS spectrometer operating at the ionization energy of 70 eV or on a JEOL JMS-700 (FAB) spectrometer. Optical rotations were recorded at the sodium D line and at ambient temperatures with a JASCO DIP-360 digital polarimeter. Preparative and analytical TLC were carried out on silica-gel plates (Kieselgel 60 F254, E. Merck AG, Germany) using UV light and/or 5% phosphomolybdic acid in ethanol for detection. Kanto Chemical silica 60N (spherical, neutral, 63–210 μm) was used for column chromatography. Silica-gel column chromatography was used for purification of crude products, unless otherwise stated. Work-up procedure: A reaction mixture was partitioned between EtOAc or $CHCl_3$ and H_2O. The organic layer was washed with brine, dried (Na_2SO_4), and then evaporated.

Methyl 2,3-Di-*O*-benzyl-6-iodo-4-*C*-methyl-α-D-glucopyranoside (9). A mixture of **7** (589 mg, 1.5 mmol) and TsCl (640 mg, 3.4 mmol) in pyridine (10 mL) was stirred at ambient temperature for 16 h. After work-up, the residue was chromatographically purified (hexane/EtOAc 3/2) to give a colorless oil (811 mg, 99%): $[\alpha]_D^{22}$ +17.3 (*c* 1.00, $CHCl_3$); IR (film) 3585, 1361, 1176 cm^{-1}; ^{1}H NMR δ 1.07 (3H, s), 1.83 (1H, br), 2.43 (3H, s), 3.33 (3H, s), 3.40 (1H, dd, J = 3.9, 10.3 Hz), 3.68 (1H, d, J = 10.0 Hz), 3.79 (1H, dd, J = 1.5, 8.8 Hz), 4.04 (1H, dd, J = 8.8, 10.7 Hz), 4.28 (1H, dd, J = 1.5, 10.7 Hz), 4.55 (1H, d, J = 3.9 Hz), 4.59–5.02 (4H, complex), 7.23–7.38 (12H, complex), 7.76 (2H, d, J = 8.4 Hz); ^{13}C NMR δ 15.9, 21.7, 55.1, 68.6, 71.0, 72.9, 73.2, 75.6, 78.7, 83.1, 97.6, 127.6, 127.8, 127.9, 128.4, 128.5, 129.7, 132.9, 137.8, 138.6, 144.6; Calcd for $C_{29}H_{34}O_8S$: C, 64.19; H, 6.32; S, 5.91%. Found: C, 64.44; H, 6.40; S, 6.24%.

A mixture of the tosylate (13.8 g, 25.4 mmol) and NaI (38 g) in DMF (150 mL) was stirred at 95 °C for 14 h. After the addition of sat. aq Na_2SO_3 and the following work-up, the crude was chromatographically purified (hexane/EtOAc 3/1) to give **9** (11.7 g, 92%): $[\alpha]_D^{24}$ +9.0 (*c* 1.00, $CHCl_3$); IR (film) 3540 cm^{-1}; ^{1}H NMR δ 1.11 (3H, s), 1.90 (1H, s), 3.07 (1H, t, J = 10.7 Hz), 3.42–3.49 (2H, complex), 3.52 (3H, s), 3.70 (1H, d, J = 9.8 Hz), 3.81 (1H, dd, J = 1.5, 10.7 Hz), 4.59 (1H, d, J = 3.9 Hz), 4.60–5.05 (4H, complex), 7.29–7.40 (10H, complex); ^{13}C NMR δ 2.8, 14.9, 55.9, 73.2, 74.4, 74.5, 75.5, 78.9, 82.8, 98.0, 127.7, 127.8, 127.9, 128.0, 128.4, 128.6, 137.8, 138.7; Calcd for $C_{22}H_{27}IO_5$: C, 53.02; H, 5.46%. Found: C, 53.06; H, 5.53%.

(2*R*,3*S*,4*S*,5*SR*)-3,4-Bis(benzyloxy)tetrahydro-5-methoxy-2-methyl-2-vinylfuran (10). A mixture of **9** (11.7 g, 23.5 mmol) and zinc powder (15 g) in EtOH (400 mL) was refluxed for 15 h, and filtered through a Celite pad. The filtrate was evaporated, and chromatographically purified (hexane/EtOAc 2/1) to give a colorless oil (7.3 g).

A solution of the hemiacetal (7.3 g) in MeOH (110 mL) in the presence of excess amounts of Amberlyst 15E was refluxed for 17 h, and filtered. The filtrate was evaporated, and chromatographically purified (EtOAc) to give **10** (5.9 g, 71% in 2 steps): IR (film) 3064, 923 cm^{-1}; ^{1}H NMR δ 1.37 (5.1H, s), 1.40 (3H, s), 3.40 (3H, s), 3.43 (5.1H, s), 3.81 (1.7H, d, J = 6.4 Hz), 4.00 (2.7H, complex), 4.12 (1H, d, J = 7.3 Hz), 4.51–4.74 (11.8H, complex), 4.89 (1.7H, d, J = 3.4 Hz), 5.16 (2.7H, complex), 5.28 (1H, dd, J = 1.5, 17.1 Hz), 5.42 (1.7H, dd, J = 1.5, 17.1 Hz), 5.98 (1H, dd, J = 10.8, 17.6 Hz), 6.15 (1.7H, dd, J = 10.7, 17.1 Hz), 7.24–7.36 (27H, complex); ^{13}C NMR δ 27.6, 54.8, 72.6, 72.8, 81.0, 83.1, 87.5, 99.5, 113.1, 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.3, 137.8, 138.2, 139.9; Calcd for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39%. Found: C, 74.43; H, 7.23%.

{6-[(2*R*,3*S*,4*S*,5*SR*)-3,4-Bis(benzyloxy)tetrahydro-5-methoxy-2-methylfuran-2-yl]hexyloxy}(*t*-butyl)diphenylsilane (6). A mixture of **10** (3.42 g, 9.7 mmol) and 9-BBN (0.5 M solution in THF, 40 mL, 20.3 mmol) in THF (12 mL) was stirred at ambient temperature for 16 h; the reaction was quenched by the addition of 3 M aq NaOH (10 mL) and 35% aq H_2O_2 (10 mL) at 0 °C. The reaction mixture was stirred at ambient temperature for 5 h. After work-up, the residue was chromatographically purified (hexane/EtOAc 3/1) to give a colorless oil (3.49 g, 97%): IR (film) 3457, 2927, 1496 cm^{-1}; ^{1}H NMR δ 1.36 (3H, s), 1.37 (3H, s), 1.68–2.10 (4H, complex), 2.59 (1H, br), 3.02 (1H, br), 3.37 (3H, s), 3.40 (3H, s), 3.75–4.15 (8H, complex), 4.52–4.87 (10H, complex), 7.32–7.38 (20H, complex); Calcd for $C_{22}H_{28}O_5$: C, 70.94; H, 7.58%. Found: C, 70.65; H, 7.66%.

To a solution of $(COCl)_2$ (0.67 mL, 7.5 mmol) in CH_2Cl_2 (13 mL) was added DMSO (0.67 mL, 9.4 mmol) in CH_2Cl_2 (9 mL) at −78 °C. The mixture was stirred for 5 min, and the alcohol (1.40 g, 3.8 mmol) in CH_2Cl_2 (13 mL) was added slowly. After being stirred at −78 °C for 10 min, Et_3N (2.6 mL, 18.9 mmol) was added and the mixture was allowed to warm to ambient temperature. After work-up, the residue was chromatographically purified (hexane/EtOAc 4/1) to give a colorless oil (1.40 g).

To a suspension of **11** (6.8 g, 9.7 mmol) in THF (20 mL) was added *n*-BuLi (1.58 M solution in hexane, 3.60 mL, 5.7 mmol) at −25 °C for 1.5 h. A solution of the aldehyde (1.4 g, 3.8 mmol) in THF (10 mL) was added at −20 °C. The mixture was stirred at ambient temperature for 13 h, and work-up was performed. The residue was chromatographically purified (hexane/EtOAc 20/1) to give a colorless oil (2.37 g), which was stirred in EtOH (60 mL) in the presence of catalytic 10% Pd–C for 4 h under hydrogen pressure. After filtration through a Celite pad, the solvent was removed. The residue was chromatographically purified (hexane/EtOAc 10/1) to give **6** (2.38 g, 95% in 3 steps): IR (film) 2929, 2360, 2341, 1106 cm^{-1}; ^{1}H NMR δ 1.04 (18H, s), 1.26 (3H, s), 1.26–1.66 (20H, complex), 1.30 (3H, s), 3.36 (6H, s), 3.61–3.66 (4H, complex), 3.75–4.10 (4H, complex), 4.50–4.82 (10H, complex), 7.26–7.41 (32H, complex), 7.66 (8H, complex);

^{13}C NMR δ 19.3, 23.4, 23.7, 24.9, 25.9, 27.0, 28.2, 28.6, 30.1, 30.4, 32.7, 35.6, 37.7, 53.2, 55.4, 55.9, 64.0, 72.3, 72.48, 72.51, 73.0, 77.2, 81.9, 84.0, 84.3, 88.1, 89.3, 89.4, 89.7, 99.4, 99.7, 100.5, 107.2, 111.4, 119.5, 127.4, 127.5, 127.7, 127.9, 128.2, 128.28, 128.33, 129.4, 130.4, 134.1, 135.5, 137.7, 138.2, 142.3, 166.1; Calcd for $C_{42}H_{54}O_5Si$: C, 75.63; H, 8.16%. Found: C, 75.55; H, 8.06%.

(2*S*,3*R*,4*R*)-2,3-Bis(benzyloxy)-10-*t*-butyldiphenylsiloxy-4-methyldecane-1,4-diol (12). To a solution of **6** (2.86 g, 4.3 mmol) in Ac_2O (40 mL) was added $Et_2O\cdot BF_3$ (55 µL, 0.43 mmol) at −25 °C. After being stirred at the same temperature for 30 min and the following work-up, the residue was chromatographically purified (hexane/EtOAc 6/1) to give a crude oil, which was dissolved in MeOH (24 mL), and then K_2CO_3 (62.6 mg, 0.45 mmol) was added. After being stirred at ambient temperature for 3.5 h, the solution was evaporated. The residue was chromatographically purified (hexane/EtOAc 4/1) to give a colorless oil.

A mixture of the hemiacetal and $NaBH_4$ (1.59 g, 42.1 mmol) in MeOH (42 mL) was stirred at ambient temperature for 2 h. After work-up, the residue was chromatographically purified (hexane/EtOAc 3/1) to give **12** (2.61 g, 93% in 3 steps): $[\alpha]_D^{22}$ −6.6 (*c* 1.00, $CHCl_3$); IR (film) 3585, 3397, 3068, 2931 cm^{-1}; ^{1}H NMR δ 1.04 (9H, s), 1.22–1.65 (10H, complex), 1.25 (3H, s), 2.55 (2H, br), 2.69 (1H, br), 3.39 (1H, d, J = 4.9 Hz), 3.64 (2H, t, J = 6.3 Hz), 3.74–3.82 (3H, complex), 4.54 (1H, d, J = 11.2 Hz), 4.66 (2H, s), 4.77 (1H, d, J = 11.2 Hz), 7.23–7.41 (16H, complex), 7.65–7.68 (4H, complex); ^{13}C NMR δ 19.3, 22.9, 23.8, 25.9, 26.9, 30.1, 32.6, 39.5, 62.1, 63.9, 72.7, 74.7, 75.0, 79.2, 82.8, 127.5, 127.7, 127.8, 127.9, 128.0, 134.0, 135.4, 138.0; Calcd for $C_{41}H_{54}O_5Si$: C, 75.19; H, 8.31%. Found: C, 74.87; H, 8.30%.

(2*R*,3*R*,4*R*)-2,3-Bis(benzyloxy)-10-*t*-butyldiphenylsiloxy-4-triethylsiloxy-4-methyldecanal (13). A mixture of **12** (2.61 g, 4.0 mmol) and TESOTf (2.7 mL, 12 mmol) in CH_2Cl_2 (20 mL) in the presence of 2,6-lutidine (4.6 mL, 40 mmol) was stirred at 0 °C for 30 min. After work-up, the residue was chromatographically purified (hexane/EtOAc 5/1) to give a colorless oil (3.52 g, 100%): $[\alpha]_D^{28}$ −1.0 (*c* 1.00, $CHCl_3$); IR (film) 2952, 1456, 1110 cm^{-1}; ^{1}H NMR δ 0.54–0.63 (12H, complex), 0.91–0.97 (18H, complex), 1.05 (9H, s), 1.31 (3H, s), 1.16–1.55 (10H, complex), 3.42 (1H, d, J = 2.9 Hz), 3.62–3.75 (5H, complex), 4.61–4.76 (4H, complex), 7.21–7.41 (16H, complex), 7.66–7.68 (4H, complex); ^{13}C NMR δ 4.5, 6.9, 7.1, 7.4, 18.2, 19.3, 19.6, 23.8, 25.87, 25.90, 25.94, 26.88, 26.92, 30.3, 32.7, 34.5, 39.5, 63.7, 63.9, 64.0, 73.4, 75.4, 76.7, 77.3, 78.67, 78.68, 79.9, 84.3, 122.8, 127.1, 127.3, 127.5, 127.7, 128.02, 128.03, 128.1, 129.4, 134.1, 135.5, 138.9, 139.2, 181.0; Calcd for $C_{53}H_{82}O_5Si_3$: C, 72.05; H, 9.36%. Found: C, 71.70; H, 9.08%.

To a solution of $(COCl)_2$ (0.39 mL, 4.4 mmol) in CH_2Cl_2 (3 mL) was added DMSO (0.63 mL, 8.9 mmol) in CH_2Cl_2 (3 mL) at −78 °C. The mixture was stirred for 15 min, and then the di-TES ether (884 mg, 1.0 mmol) in CH_2Cl_2 (3 mL) was added slowly. After being stirred at −40 °C for 2 h, Et_3N (2.1 mL, 15.1 mmol) was added at −78 °C and the mixture allowed to warm to ambient temperature. After work-up, the residue was chromatographically purified (hexane/EtOAc 5/1) to give **13** (726 mg, 95%): $[\alpha]_D^{26}$ +9.45 (*c* 0.20, $CHCl_3$); IR (film) 3068, 2929, 2856, 1729, 1456, 1427 cm^{-1}; ^{1}H NMR δ 0.56–0.62 (6H, complex), 0.91–0.95 (9H, complex), 0.93–1.55 (9H, complex), 1.05 (9H, s), 1.30 (3H, s), 1.66 (1H, m), 3.58 (1H, d, J = 5.9 Hz), 3.63 (2H, t, J = 6.3 Hz), 4.05 (1H, dd, J = 2.4, 5.9 Hz), 4.49–4.55 (2H, complex), 4.68 (1H, d, J = 11.7 Hz), 4.76 (1H, d, J = 11.2 Hz), 7.26–7.41 (16H, complex), 7.66–7.67 (4H, complex), 9.58 (1H, d, J = 2.8 Hz); ^{13}C NMR δ 6.8, 7.2, 7.5, 19.3, 25.9, 26.9, 32.7, 36.7, 38.9, 64.0, 75.1, 77.2, 84.6, 100.5, 127.5, 127.6, 127.9, 128.1, 128.16, 128.24, 128.3, 129.4, 134.1, 135.5, 202.3; Calcd for $C_{47}H_{66}O_5Si_2\cdot 0.6H_2O$: C, 72.56; H, 8.71%. Found: C, 72.55; H, 9.05%.

(*E*,4*S*,5*R*,6*R*)-Methyl 4,5-Bis(benzyloxy)-12-*t*-butyldiphenylsiloxy-6-triethylsiloxy-6-methyldodec-2-enoate (5). To a stirred solution of **13** (726 mg, 0.95 mmol) in PhH (10 mL) was added $Ph_3P{=}CHCO_2Me$ (949 mg, 2.8 mmol) at 100 °C for 13 h. The reaction mixture was concentrated in vacuo and chromatographically purified (hexane/EtOAc 5/1) to give **5** (779 mg, 100%): $[\alpha]_D^{28}$ +10.5 (*c* 1.00, $CHCl_3$); IR (film) 3068, 3029, 2933, 1725, 1654 cm^{-1}; ^{1}H NMR δ 0.54–0.60 (6H, complex), 0.90–0.94 (9H, complex), 1.05 (9H, s), 1.14–1.55 (10H, complex), 1.31 (3H, s), 3.32 (1H, d, J = 4.9 Hz), 3.63 (2H, complex), 3.75 (3H, s), 4.23 (1H, m), 4.37 (1H, d, J = 11.7 Hz), 4.60 (2H, complex), 4.79 (1H, d, J = 11.7 Hz), 6.02 (1H, dd, J = 1.0, 15.6 Hz), 7.01 (1H, dd, J = 6.3, 15.6 Hz), 7.23–7.43 (16H, complex), 7.66–7.68 (4H, complex); ^{13}C NMR δ 6.7, 6.8, 6.9, 7.3, 19.2, 23.8, 25.7, 25.8, 26.9, 30.1, 32.6, 38.9, 51.4, 63.9, 71.6, 75.7, 77.3, 78.2, 79.0, 87.9, 120.6, 127.2, 127.4, 127.5, 127.7, 127.9, 128.02, 128.1, 128.2, 129.4, 134.0, 135.4, 137.6, 138.5, 147.4, 166.5; Calcd for $C_{50}H_{70}O_6Si_2$: C, 72.95; H, 8.57%. Found: C, 72.89; H, 8.47%.

(2*S*,3*S*,4*S*,5*R*,6*R*)-Methyl 4,5-Bis(benzyloxy)-12-*t*-butyldiphenylsiloxy-6-triethylsiloxy-2,3-dihydroxy-6-methyldodecanoate (18). To a solution of **5** (1.08 g, 1.3 mmol) in acetone (12 mL)–H_2O (1.2 mL) was added OsO_4 (39.3 mM solution in *t*BuOH, 3.3 mL, 0.13 mmol) and *N*-methylmorpholine *N*-oxide (NMO) (461 mg, 3.9 mmol) at 0 °C. The reaction mixture was stirred at the same temperature for 10 h, and then at ambient temperature for 30 h. After the addition of sat. aq Na_2SO_3 and the following work-up, the residue was chromatographically purified (hexane/EtOAc 5/1) to give **18** (1.22 g, 100%): $[\alpha]_D^{25}$ +1.9 (*c* 1.00, $CHCl_3$); IR (film) 3444, 3068, 3029, 2933, 2875 cm^{-1}; ^{1}H NMR δ 0.60–0.66 (6H, complex), 0.92–0.98 (9H, complex), 1.06 (9H, s), 1.06–1.55 (10H, complex), 1.90 (1H, m), 3.09 (1H, d, J = 8.4 Hz), 3.44 (1H, d, J = 4.8 Hz), 3.64 (2H, complex), 3.78 (3H, s), 3.89 (1H, m), 3.96 (1H, m), 4.28 (1H, m), 4.42 (1H, d, J = 11.2 Hz), 4.54 (1H, d, J = 8.4 Hz), 4.69 (2H, m), 4.80 (1H, d, J = 11.6 Hz), 7.22–7.43 (16H, complex), 7.66–7.69 (4H, complex); ^{13}C NMR δ 6.8, 6.9, 7.0, 7.2, 19.3, 24.8, 25.4, 25.9, 26.9, 30.1, 32.6, 40.0, 52.3, 63.9, 71.0, 73.1, 73.8, 73.9, 79.5, 83.8, 127.4, 127.5, 127.56, 127.60, 128.0, 128.16, 128.21, 128.3, 129.4, 134.0, 135.4, 138.2, 138.2, 174.3; Calcd for $C_{50}H_{72}O_8Si_2$: C, 70.05; H, 8.47%. Found: C, 69.88; H, 8.39%.

(*R*)-4-[(1*S*,2*S*,3*R*,4*R*)-2,3-Bis(benzyloxy)-10-*t*-butyldiphenylsiloxy-4-triethylsiloxy-1-hydroxy-4-methyldecyl]-1,3-dioxolan-2-one (19). A mixture of **18** (55.5 mg, 0.065 mmol) and $LiBH_4$ (16.7 mg, 0.77 mmol) in THF (1 mL) was stirred at 0 °C for 2 h, and then work-up was performed. The residue was chromatographically purified (hexane/EtOAc 1/1) to give a colorless oil (58.2 mg, 100%): $[\alpha]_D^{26}$ −4.6 (*c* 1.00, $CHCl_3$); IR (film) 3424, 3068, 3029, 2933, 2875 cm^{-1}; ^{1}H NMR δ 0.60–0.66 (6H, complex), 0.93–0.97 (9H, complex), 0.97–1.55 (9H, complex), 1.05 (9H, s), 1.36 (3H, s), 1.90 (1H, m), 2.73 (1H, d, J = 9.2 Hz), 2.91 (1H, d, J = 8.8 Hz), 3.39 (1H, d, J = 4.8 Hz), 3.64 (2H, complex), 3.75 (1H, m), 3.83 (1H, m), 3.96–4.03 (3H, complex), 4.19 (1H, m), 4.42 (1H, d, J = 11.6 Hz), 4.67 (2H, s), 4.77 (1H, d, J = 11.6 Hz), 7.24–7.43 (16H, complex), 7.66–7.68 (4H, complex); ^{13}C NMR δ 6.8, 7.0, 7.1, 7.3, 19.3, 24.7, 25.0, 25.4, 25.9, 26.9, 30.2, 32.6, 40.2, 63.9, 66.2, 69.5, 73.8, 74.18, 74.21, 77.9, 79.5, 83.5, 126.8, 127.50, 127.54, 127.6, 127.7, 128.0, 128.1, 128.21, 128.24, 128.3, 128.5, 129.4, 130.6, 130.8, 134.0, 135.5,

138.10, 138.15; Calcd for $C_{49}H_{72}O_7Si_2$: C, 70.97; H, 8.75%. Found: C, 70.99; H, 8.69%.

A mixture of the triol (546 mg, 0.66 mmol) and Im_2CO (124 mg, 0.77 mmol) in PhH (7 mL) was stirred at room temperature for 1.5 h. After work-up, the residue was chromatographically purified (hexane/EtOAc 4/1) to give **19** (455 mg, 81%): $[\alpha]_D^{23}$ −35.2 (*c* 1.00, $CHCl_3$); IR (film) 3444, 2935, 1808, 1646 cm^{-1}; ^1H NMR δ 0.60–0.66 (6H, complex), 0.91–0.95 (9H, complex), 1.05 (9H, s), 1.09–1.56 (9H, complex), 1.36 (3H, s), 1.93 (1H, m), 3.43 (1H, d, $J = 3.9$ Hz), 3.65 (2H, complex), 3.94 (2H, complex), 4.19 (1H, m), 4.43 (2H, complex), 4.52 (1H, m), 4.59 (1H, d, $J = 11.2$ Hz), 4.69 (1H, d, $J = 11.2$ Hz), 4.78 (1H, d, $J = 11.2$ Hz), 5.04 (1H, m), 7.25–7.43 (16H, complex), 7.66–7.68 (4H, complex); ^{13}C NMR δ 6.8, 7.0, 19.3, 25.1, 25.4, 26.0, 26.9, 30.2, 32.6, 40.1, 63.9, 65.8, 71.9, 73.9, 74.1, 75.5, 76.7, 77.2, 79.6, 83.2, 127.5, 127.7, 127.8, 127.9, 128.0, 128.3, 128.4, 129.4, 134.0, 135.5, 137.7, 155.3; Calcd for $C_{50}H_{70}O_8Si_2$: C, 70.22; H, 8.25%. Found: C, 70.34; H, 8.20%.

{(2*R*,3*R*)-3-[(1*S*,2*R*,3*R*)-1,2-Bis(benzyloxy)-9-*t*-butyldiphenylsiloxy-3-triethylsiloxy-3-methylnonyl]oxiran-2-yl}methanol (17). A mixture of **19** (455 mg, 0.53 mmol), MsCl (412 µL, 5.3 mmol), and catalytic amounts of DMAP in pyridine (5.3 mL) was stirred at ambient temperature for 12 h. After work-up, the residue was chromatographically purified (PhH/Et_2O 30/1) to give a colorless oil (515 mg).

A mixture of the mesylate (515 mg) and NaOMe (0.5 M solution in MeOH, 0.93 mL, 0.47 mmol) in MeOH (6 mL)–THF (3 mL) was stirred at 0 °C for 4 h and then work-up was performed; the residue was chromatographically purified (hexane/EtOAc 7/1) to give **17** (424 mg, 95% in 2 steps): $[\alpha]_D^{24}$ +19.1 (*c* 1.00, $CHCl_3$); IR (film) 3455, 2935, 2873, 1457, 1106 cm^{-1}; ^1H NMR δ 0.58–0.65 (6H, complex), 0.92–0.96 (9H, complex), 1.02–1.51 (9H, complex), 1.05 (9H, s), 1.37 (3H, s), 1.65 (1H, m), 2.69 (1H, dd, $J = 4.4$, 9.3 Hz), 2.91 (1H, m), 3.34–3.45 (4H, complex), 3.62 (2H, complex), 3.71 (1H, m), 4.49 (2H, complex), 4.59 (1H, d, $J = 11.7$ Hz), 4.83 (1H, d, $J = 12.2$ Hz), 7.25–7.45 (16H, complex), 7.66–7.68 (4H, complex); ^{13}C NMR δ 7.0, 7.2, 19.3, 24.6, 25.7, 25.9, 26.9, 30.1, 32.7, 40.7, 54.6, 58.9, 60.8, 64.0, 72.0, 74.0, 78.8, 83.1, 127.5, 127.6, 128.1, 128.2, 128.4, 129.0, 129.4, 134.0, 135.5, 137.1, 138.0; Calcd for $C_{49}H_{70}O_6Si_2$: C, 72.55; H, 8.70%. Found: C, 72.33; H, 8.64%.

(2*S*,3*R*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-12-*t*-butyldiphenylsiloxy-6-triethylsiloxy-2,6-dimethyldodecane-1,3-diol (20). To a suspension of CuCN (711 mg, 7.9 mmol) in Et_2O (1 mL) was added MeLi (1.02 M solution in Et_2O, 15 mL, 15.3 mmol) at −78 °C. After being stirred at 0 °C for 10 min, **17** (644 mg, 0.79 mmol) in Et_2O (4 mL) was added at −78 °C, and the mixture was stirred at 0 °C for 8 h. After the addition of 35% aq NH_3 and the following work-up, the residue was chromatographically purified (PhH/Et_2O 10/1) to give **20** (570 mg, 87%): $[\alpha]_D^{25}$ −11.3 (*c* 1.00, $CHCl_3$); IR (film) 3446, 3068, 3029, 2933, 2875 cm^{-1}; ^1H NMR δ 0.60–0.65 (6H, complex), 0.94–0.98 (9H, complex), 1.04 (9H, s), 1.04 (3H, m), 1.23–1.59 (9H, complex), 1.26 (3H, s), 2.00 (2H, complex), 2.12 (1H, br), 2.84 (1H, d, $J = 6.8$ Hz), 3.50 (1H, d, $J = 6.4$ Hz), 3.62–3.65 (4H, complex), 3.70 (1H, m), 3.89 (1H, m), 4.48 (1H, d, $J = 10.8$ Hz), 4.53 (1H, d, $J = 11.7$ Hz), 4.82 (1H, d, $J = 11.7$ Hz), 4.94 (1H, d, $J = 10.8$ Hz), 7.25–7.41 (16H, complex), 7.66–7.67 (4H, complex); ^{13}C NMR δ 7.0, 7.3, 12.5, 19.3, 24.8, 25.7, 26.0, 26.9, 30.4, 32.7, 39.1, 39.6, 64.0, 66.8, 73.9, 74.6, 75.4, 78.0, 78.5, 84.0, 127.2, 127.5, 127.6, 128.06, 128.09, 128.3, 129.4, 134.1, 135.5, 138.3, 138.9; Calcd for $C_{50}H_{74}O_6Si_2 \cdot 0.4H_2O$: C, 71.97; H, 9.04%. Found: C, 71.85; H, 8.90%.

(2*S*,3*R*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-12-*t*-butyldiphenylsiloxy-6-triethylsiloxy-3-(4-methoxybenzyloxy)-2,6-dimethyldodecan-1-ol (21). A mixture of **20** (1.7 g, 2.1 mmol) and *p*-anisaldehyde dimethyl acetal (0.35 mL, 2.1 mmol) in CH_2Cl_2 in the presence of catalytic amounts of PPTS was stirred at room temperature for 7 h. After work-up, the residue was chromatographically purified (hexane/EtOAc 2/1) to give a colorless oil (1.4 g, 100%): $[\alpha]_D^{26}$ −20.5 (*c* 1.00, $CHCl_3$); IR (film) 3068, 3029, 2933, 2875, 2858 cm^{-1}; ^1H NMR δ 0.63–0.69 (6H, complex), 1.00 (9H, complex), 1.06 (9H, s), 1.16–1.62 (11H, complex), 1.22 (3H, d, $J = 6.4$ Hz), 1.44 (3H, s), 3.43 (1H, m), 3.65 (2H, complex), 3.77–3.83 (3H, complex), 3.80 (3H, s), 4.29 (1H, d, $J = 8.3$ Hz), 4.56 (1H, d, $J = 10.8$ Hz), 4.63 (1H, d, $J = 12.2$ Hz), 4.92 (2H, complex), 5.44 (1H, s), 6.85 (2H, complex), 7.17–7.44 (18H, complex), 7.67–7.69 (4H, complex); ^{13}C NMR δ 7.1, 7.4, 12.0, 19.3, 24.0, 26.0, 26.3, 26.9, 30.1, 30.3, 32.7, 40.6, 55.3, 63.9, 73.7, 74.2, 75.0, 77.2, 78.0, 80.1, 82.6, 83.1, 101.9, 113.4, 127.1, 127.2, 127.3, 127.5, 127.7, 127.9, 128.19, 128.21, 129.4, 131.4, 134.1, 135.3, 135.5, 138.8, 139.1, 159.6; Calcd for $C_{58}H_{80}O_7Si_2$: C, 73.68; H, 8.53%. Found: C, 73.82; H, 8.42%.

To a solution of the acetal (1.4 g, 1.5 mmol) in PhMe (15 mL) was added DIBAL-H (1.01 M solution in PhMe, 1.8 mL, 1.8 mmol) at 0 °C. After being stirred for 8 h, the reaction was quenched by the addition of sat. aq NH_4Cl, and then work-up was performed. The residue was chromatographically purified (hexane/EtOAc 2/1) to give **21** (0.91 g, 64%): $[\alpha]_D^{26}$ +10.6 (*c* 1.00, $CHCl_3$); IR (film) 3585, 3438, 3068, 3029, 2933, 2875 cm^{-1}; ^1H NMR δ 0.58–0.64 (6H, complex), 0.94–0.99 (9H, complex), 0.94–0.99 (3H, complex), 1.05 (9H, s), 1.09–1.34 (7H, complex), 1.15 (3H, s), 1.49–1.54 (2H, complex), 1.85 (1H, m), 2.14 (1H, m), 2.36 (1H, br), 3.22 (1H, d, $J = 3.9$ Hz), 3.49–3.54 (3H, complex), 3.63 (2H, complex), 3.74 (3H, s), 3.94 (1H, m), 4.50–4.64 (4H, complex), 4.80–4.85 (2H, complex), 6.80 (2H, complex), 7.17–7.27 (12H, complex), 7.36–7.43 (6H, complex), 7.66–7.68 (4H, complex); ^{13}C NMR δ 7.0, 7.3, 12.6, 19.3, 24.7, 25.96, 26.00, 26.9, 30.4, 32.8, 35.9, 40.4, 55.2, 64.0, 65.5, 72.4, 73.9, 74.6, 76.2, 78.7, 81.2, 83.3, 113.7, 126.9, 127.2, 127.46, 127.49, 128.1, 129.4, 130.0, 130.3, 134.1, 135.5, 138.4, 139.6, 159.1; Calcd for $C_{58}H_{82}O_7Si_2$: C, 73.53; H, 8.72%. Found: C, 73.53; H, 8.65%.

(*E*,4*S*,5*R*,6*S*,7*R*,8*R*)-Methyl 6,7-Bis(benzyloxy)-14-*t*-butyldiphenylsiloxy-8-triethylsiloxy-5-(4-methoxybenzyloxy)-2,4,8-trimethyltetradec-2-enoate (22). A mixture of **21** (100 mg, 0.11 mmol) and Dess–Martin periodinane (135 mg, 0.32 mmol) in CH_2Cl_2 (1.1 mL) in the presence of $NaHCO_3$ (89 mg, 1.1 mmol) was added at room temperature for 4 h. After work-up, the residue was chromatographically purified (hexane/EtOAc 3/1) to give a colorless oil (98.1 mg).

A mixture of the aldehyde (98.1 mg) and $Ph_3P{=}C(Me)CO_2Me$ (181 mg, 0.52 mmol) in PhH (4 mL) was stirred at 100 °C for 18 h. The reaction mixture was concentrated in vacuo and chromatographically purified (hexane/EtOAc 10/1) to give **22** (101 mg, 94% in 2 steps): $[\alpha]_D^{25}$ −10.2 (*c* 1.00, $CHCl_3$); IR (film) 3068, 3030, 2933, 2873, 1716, 1612 cm^{-1}; ^1H NMR δ 0.57–0.63 (6H, complex), 0.93–0.97 (9H, complex), 0.97–1.38 (7H, complex), 1.04 (9H, s), 1.15–1.18 (3H, complex), 1.18 (3H, s), 1.50–1.54 (2H, complex), 1.81 (3H, s), 1.90 (1H, m), 3.13 (1H, m), 3.30 (1H, m), 3.37 (1H, m), 3.61–3.64 (2H, complex), 3.70 (3H, s), 3.75 (3H, s), 3.84 (1H, m), 4.36–4.42 (2H, complex), 4.58 (1H, d, $J = 11.2$ Hz), 4.71 (1H, d, $J = 11.2$ Hz), 4.82–4.87 (2H, complex), 6.77 (1H, d, $J = 9.8$ Hz), 6.82 (2H, complex), 7.19–7.26 (12H, complex), 7.35–7.41 (6H, complex), 7.66–7.67 (4H, complex);

^{13}C NMR δ 7.0, 7.3, 12.7, 16.2, 19.3, 24.9, 25.9, 26.1, 26.9, 30.4, 32.8, 35.8, 40.1, 51.7, 55.2, 64.0, 74.2, 74.3, 74.4, 77.3, 78.0, 78.4, 83.3, 84.2, 113.7, 126.76, 126.79, 126.9, 127.2, 127.5, 127.7, 127.85, 127.88, 129.4, 129.8, 130.5, 134.1, 135.5, 139.0, 139.5, 144.7, 159.1, 168.4; Calcd for $C_{62}H_{86}O_8Si_2$: C, 73.33; H, 8.54%. Found: C, 73.38; H, 8.45%.

(2*S*,3*R*,4*R*,5*R*,6*R*)-12-*t*-Butyldiphenylsiloxy-3-methoxy-2,6-dimethyldodecane-1,4,5,6-tetrol (23). A mixture of **20** (329 mg, 0.40 mmol), TrCl (311 mg, 1.1 mmol), and catalytic amounts of DMAP in pyridine (5 mL) was stirred at 75 °C for 18 h. After work-up, the residue was chromatographically purified (hexane/EtOAc 4/1) to give a colorless oil (365 mg, 86%): $[\alpha]_D^{24}$ −14.4 (*c* 1.00, $CHCl_3$); IR (film) 3568, 3066, 3032, 2933, 2873 cm^{-1}; ^{1}H NMR δ 0.55–0.61 (6H, complex), 0.90–0.96 (9H, complex), 1.05 (9H, s), 1.05–1.52 (9H, complex), 1.16 (3H, d, J = 6.8 Hz), 1.19 (3H, s), 1.80 (1H, m), 2.06 (1H, m), 2.46 (1H, d, J = 8.3 Hz), 2.96 (1H, m), 3.27 (1H, m), 3.45 (1H, d, J = 6.4 Hz), 3.61–3.66 (4H, complex), 4.13 (1H, m), 4.47 (1H, d, J = 11.7 Hz), 4.77 (2H, complex), 7.10–7.26 (19H, complex), 7.35–7.44 (12H, complex), 7.66–7.68 (4H, complex); ^{13}C NMR δ 7.0, 7.3, 13.9, 19.3, 24.8, 25.6, 26.0, 26.9, 30.3, 32.7, 37.9, 39.5, 64.0, 66.1, 74.0, 74.3, 74.6, 77.2, 78.4, 78.7, 84.6, 86.5, 126.8, 127.0, 127.2, 127.4, 127.5, 127.6, 127.7, 127.96, 128.04, 128.7, 129.4, 134.1, 135.5, 138.7, 139.0, 144.2; Calcd for $C_{69}H_{88}O_6Si_2$: C, 77.48; H, 8.29%. Found: C, 77.59; H, 8.09%.

A mixture of the trityl compound (365 mg, 0.34 mmol), NaH (60% dispersion in mineral oil, 34 mg, 0.93 mmol), and MeI (0.21 mL, 3.4 mmol) in DMF (5 mL) was stirred at ambient temperature for 16 h. After work-up, the residue was chromatographically purified (hexane/EtOAc 6/1) to give a colorless oil (276 mg, 74%): $[\alpha]_D^{24}$ −12.2 (*c* 1.00, $CHCl_3$); IR (film) 3066, 3031, 2933, 2875 cm^{-1}; ^{1}H NMR δ 0.56–0.62 (6H, complex), 0.92–0.96 (9H, complex), 0.99 (3H, d, J = 6.8 Hz), 1.04 (9H, s), 1.10–1.52 (9H, complex), 1.28 (3H, s), 1.71 (1H, m), 2.17 (1H, m), 3.06 (1H, m), 3.13 (1H, m), 3.30 (3H, s), 3.32 (1H, m), 3.48 (1H, m), 3.61 (2H, complex), 3.72 (1H, m), 4.52 (1H, d, J = 11.2 Hz), 4.64 (2H, complex), 4.85 (1H, d, J = 11.7 Hz), 7.16–7.26 (19H, complex), 7.34–7.41 (12H, complex), 7.65–7.67 (4H, complex); ^{13}C NMR δ 7.1, 7.4, 19.3, 24.5, 25.99, 26.09, 26.9, 30.4, 32.7, 36.0, 40.0, 60.8, 64.0, 65.9, 73.9, 75.0, 77.2, 78.4, 78.7, 83.5, 84.4, 86.5, 126.76, 126.79, 126.82, 127.2, 127.5, 127.56, 127.60, 127.9, 128.7, 129.4, 134.1, 135.5, 139.2, 139.4, 144.2; Calcd for $C_{70}H_{90}O_6Si_2$: C, 77.59; H, 8.37%. Found: C, 77.86; H, 8.29%.

A solution of the methyl ether (193 mg, 0.18 mmol) in MeOH (4 mL)–THF (2 mL) in the presence of catalytic 20% $Pd(OH)_2$–C was stirred for 24 h under hydrogen pressure. After filtration through a Celite pad, the solvent was removed. The residue was chromatographically purified (EtOAc) to give **23** (51.2 mg, 53%): $[\alpha]_D^{24}$ −7.5 (*c* 1.00, $CHCl_3$); IR (film) 3398, 3070, 3049, 2931, 2858 cm^{-1}; ^{1}H NMR δ 0.97 (3H, d, J = 6.8 Hz), 1.05 (9H, s), 1.23 (3H, s), 1.23–1.58 (9H, complex), 1.85 (1H, br), 2.12 (1H, m), 2.98 (1H, br), 3.25 (1H, br), 3.41 (2H, complex), 3.50 (3H, s), 3.54 (1H, m), 3.65 (2H, t, J = 6.3 Hz), 3.76 (1H, m), 3.84 (1H, br), 3.98 (1H, m), 4.10 (1H, m), 7.36–7.42 (6H, complex), 7.65–7.67 (4H, complex); ^{13}C NMR δ 12.1, 19.3, 22.6, 23.9, 25.8, 26.9, 27.4, 30.0, 32.6, 35.8, 39.2, 58.8, 63.2, 63.9, 69.0, 75.0, 75.8, 77.3, 85.5, 127.5, 129.4, 134.0, 135.5; Calcd for $C_{31}H_{50}O_6Si \cdot 1.2H_2O$: C, 65.50; H, 9.30%. Found: C, 65.39; H, 9.58%.

(1*R*,2*R*)-1-Acetoxy-8-*t*-butyldiphenylsiloxy-1-[(2*S*,3*S*,4*R*)-tetrahydro-3-methoxy-4-methylfuran-2-yl]-2-methyloctan-2-ol (24). A mixture of **23** (39 mg, 0.071 mmol) and TsCl (27 mg, 0.14 mmol) in pyridine (1.5 mL) was stirred at room temperature for 13 h. After work-up, the residue was chromatographically purified (hexane/EtOAc 2/1) to give a colorless oil.

A mixture of the product and Ac_2O (0.5 mL, 5.3 mmol) in pyridine (1.5 mL) was stirred at room temperature for 17 h. After work-up, the residue was chromatographically purified (hexane/EtOAc 2/1) to give **24** (27.4 mg, 67% in 2 steps): $[\alpha]_D^{24}$ +9.1 (*c* 1.00, $CHCl_3$); IR (film) 3498, 3070, 2933, 2857, 1741 cm^{-1}; ^{1}H NMR δ 1.03–1.07 (3H, complex), 1.05 (9H, s), 1.21–1.44 (8H, complex), 1.22 (3H, s), 1.54 (2H, complex), 2.09 (3H, s), 2.36 (1H, m), 3.27–3.36 (2H, complex), 3.31 (3H, s), 3.55 (1H, m), 3.63–3.66 (2H, complex), 4.11 (1H, m), 4.33 (1H, m), 5.06 (1H, m), 7.35–7.41 (6H, complex), 7.64–7.68 (4H, complex); ^{13}C NMR δ 16.6, 19.3, 21.4, 23.4, 24.2, 25.9, 26.9, 30.1, 32.6, 38.57, 38.60, 57.9, 64.0, 73.0, 74.1, 74.29, 74.31, 77.8, 88.4, 127.5, 129.4, 134.1, 135.5, 170.3; Calcd for $C_{33}H_{50}O_6Si \cdot 0.1H_2O$: C, 69.21; H, 8.84%. Found: C, 69.02; H, 8.65%.

(*E*,4*S*,5*R*,6*S*,7*R*,8*R*)-6,7-Bis(benzyloxy)-14-*t*-butyldiphenylsiloxy-8-triethylsiloxy-5-(4-methoxybenzyloxy)-2,4,8-trimethyltetradec-2-en-1-ol (4). A mixture of **22** (114 mg, 0.11 mmol) and $LiBH_4$ (25 mg, 1.1 mmol) in THF (1.2 mL) was stirred at room temperature for 3.5 h. After work-up, the residue was chromatographically purified (hexane/EtOAc 3/1) to give **4** (109 mg, 100%): $[\alpha]_D^{27}$ +4.5 (*c* 1.00, $CHCl_3$); IR (film) 3585, 3438, 3030, 2933, 2873, 1612, 1587, 1513 cm^{-1}; ^{1}H NMR δ 0.58–0.64 (6H, complex), 0.93–0.97 (9H, complex), 1.01–1.38 (8H, complex), 1.04 (9H, s), 1.12 (3H, d, J = 6.8 Hz), 1.18 (3H, s), 1.50–1.54 (2H, complex), 1.64 (3H, s), 1.88 (1H, m), 3.01 (1H, m), 3.30 (2H, complex), 3.62 (2H, complex), 3.75 (3H, s), 3.89 (1H, m), 3.93 (2H, complex), 4.41–4.45 (2H, complex), 4.57 (1H, d, J = 11.2 Hz), 4.70 (1H, d, J = 11.2 Hz), 4.81–4.86 (2H, complex), 5.38 (1H, d, J = 9.8 Hz), 6.80–6.82 (2H, complex), 7.17–7.25 (12H, complex), 7.35–7.41 (6H, complex), 7.66–7.68 (4H, complex); ^{13}C NMR δ 7.1, 7.3, 11.2, 14.0, 17.1, 19.3, 24.0, 24.9, 25.9, 26.1, 26.9, 30.4, 32.8, 34.5, 34.6, 40.2, 55.3, 64.0, 68.9, 74.2, 77.3, 78.5, 84.7, 113.6, 126.7, 126.9, 127.2, 127.5, 127.8, 127.85, 127.91, 129.4, 129.8, 130.8, 134.0, 134.1, 135.5, 139.2, 139.7; Calcd for $C_{61}H_{86}O_7Si_2$: C, 74.19; H, 8.78%. Found: C, 73.90; H, 8.84%.

{(2*R*,3*R*)-3-[(2*R*,3*R*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-12-*t*-butyldiphenylsiloxy-6-triethylsiloxy-3-(4-methoxybenzyloxy)-6-methyldodecan-2-yl]-2-methyloxiran-2-yl}methanol (26). A mixture of **4** (109 mg, 0.11 mmol) and *m*CPBA (190 mg, 1.1 mmol) in CH_2Cl_2 (1.1 mL) in the presence of $NaHCO_3$ (185 mg, 2.2 mmol) was stirred at −22 °C for 1 h. After the addition of sat. aq $Na_2S_2O_3$ and the following work-up, the residue was chromatographically purified (hexane/EtOAc 3/1) to give **26** (83 mg, 75%): $[\alpha]_D^{27}$ +4.9 (*c* 0.22, $CHCl_3$); IR (film) 3509, 2931, 1716, 1699, 1605, 1455 cm^{-1}; ^{1}H NMR δ 0.59–0.65 (6H, complex), 0.94–0.98 (9H, complex), 1.02 (9H, s), 1.05–1.59 (10H, complex), 1.06 (3H, d, J = 6.8 Hz), 1.24 (3H, s), 1.29 (3H, s), 1.76–1.87 (2H, complex), 2.98 (1H, d, J = 9.8 Hz), 3.27 (1H, d, J = 3.4 Hz), 3.57–3.67 (4H, complex), 3.76 (3H, s), 3.79 (1H, m), 3.98 (1H, m), 4.57–4.83 (6H, complex), 6.79 (2H, complex), 7.17–7.42 (18H, complex), 7.66–7.68 (4H, complex); ^{13}C NMR δ 7.0, 7.1, 7.3, 7.4, 11.6, 13.4, 14.3, 19.3, 24.6, 25.8, 25.9, 26.0, 30.4, 32.7, 32.8, 35.0, 36.8, 40.0, 55.2, 60.1, 60.9, 61.9, 62.0, 64.0, 65.4, 73.9, 74.0, 74.4, 74.5, 76.3, 77.3, 78.4, 78.5, 78.6, 81.9, 84.7, 113.5, 126.9, 127.1, 127.3, 127.5, 127.8, 127.9, 128.0, 128.06, 128.08, 129.4, 129.7, 130.9, 134.1, 135.5, 139.1, 139.2, 139.5, 158.9; Calcd for $C_{61}H_{86}O_8Si_2 \cdot 1.5H_2O$: C, 71.10; H, 8.71%. Found: C, 71.15; H, 8.90%.

(*E*)-Methyl 3-{(2*R*,3*R*)-3-[(2*R*,3*R*,4*S*,5*R*,6*R*)-4,5-Bis(benzyl-

oxy)-12-*t*-butyldiphenylsiloxy-6-triethylsiloxy-3-(4-methoxybenzyloxy)-6-methyldodecan-2-yl]-2-methyloxiran-2-yl}acrylate (28). To a solution of **26** (313 mg, 0.31 mmol) in CH_2Cl_2 (5 mL) was added catalytic amounts of TPAP and NMO (37 mg, 0.31 mmol) at room temperature. After being stirred for 1.5 h, the reaction mixture was chromatographically purified (hexane/EtOAc 3/1) to give a colorless oil (237 mg).

A mixture of the aldehyde (237 mg, 0.24 mmol) and $Ph_3P{=}CHCO_2Me$ (240 mg, 0.72 mmol) in PhH (3 mL) was stirred at 100 °C for 12 h. The reaction mixture was concentrated in vacuo and chromatographically purified (hexane/EtOAc 5/1) to give **28** (250 mg, 76% in 2 steps): $[\alpha]_D^{28}$ −9.8 (*c* 1.00, $CHCl_3$); IR (film) 2931, 1725, 1654, 1612, 1513, 1247 cm^{-1}; ^1H NMR δ 0.61–0.66 (6H, complex), 0.96–1.00 (9H, complex), 1.02–1.57 (9H, complex), 1.06 (9H, s), 1.10 (3H, d, $J = 6.8$ Hz), 1.29 (3H, s), 1.44 (3H, s), 1.81 (1H, m), 1.89 (1H, m), 2.80 (1H, d, $J = 9.3$ Hz), 3.29 (1H, m), 3.63 (2H, complex), 3.75 (1H, m), 3.77 (3H, s), 3.78 (3H, s), 3.99 (1H, m), 4.57 (1H, d, $J = 11.7$ Hz), 4.66 (2H, complex), 4.76 (2H, complex), 4.83 (1H, d, $J = 11.7$ Hz), 5.99 (1H, d, $J = 15.6$ Hz), 6.77 (1H, d, $J = 16.1$ Hz), 6.81 (2H, complex), 7.19–7.44 (18H, complex), 7.67–7.69 (4H, complex); ^{13}C NMR δ 7.1, 7.4, 11.7, 15.3, 19.3, 24.7, 26.0, 26.9, 32.7, 34.7, 39.9, 55.2, 58.5, 64.0, 68.2, 74.0, 74.5, 75.1, 76.6, 76.7, 77.27, 77.31, 78.4, 78.6, 82.1, 84.6, 113.6, 120.8, 126.9, 127.3, 127.49, 127.51, 127.8, 127.90, 127.95, 129.4, 129.6, 130.8, 134.1, 135.46, 135.48, 139.5, 159.0, 166.5, 182.2; Calcd for $C_{64}H_{88}O_9Si_2$: C, 72.69; H, 8.39%. Found: C, 72.44; H, 8.40%.

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-{(2*R*,3*R*)-3-[(*E*)-2-(Methoxycarbonyl)-vinyl]-3-methyloxiran-2-yl}-4,5-bis(benzyloxy)-12-*t*-butyldiphenylsiloxy-6-triethylsiloxy-6-methyldodecan-3-yl Dimethylcarbamate (3). A mixture of **28** (166 mg, 0.16 mmol) and DDQ (43 mg, 0.19 mmol) in CH_2Cl_2 (1.5 mL)–H_2O (75 µL) was stirred at 0 °C for 50 min. After work-up, the residue was chromatographically purified (benzene and then hexane/EtOAc 5/1) to give a colorless oil (139 mg, 95%): $[\alpha]_D^{26}$ −47.2 (*c* 1.00, $CHCl_3$); IR (film) 3552, 2933, 2874, 1727, 1652, 1454, 1428, 1267 cm^{-1}; ^1H NMR δ 0.60–0.66 (6H, complex), 0.94–0.96 (9H, complex), 1.07 (3H, d, $J = 7.3$ Hz), 1.24–1.55 (9H, complex), 1.28 (3H, s), 1.31 (3H, s), 1.74 (1H, m), 1.87 (1H, m), 2.62 (1H, br), 2.62 (1H, d, $J = 9.8$ Hz), 3.50 (1H, d, $J = 6.8$ Hz), 3.61–3.66 (3H, complex), 3.73 (3H, s), 4.16 (1H, d, $J = 6.8$ Hz), 4.50 (1H, d, $J = 11.7$ Hz), 4.61 (1H, d, $J = 10.3$ Hz), 4.83 (1H, d, $J = 11.2$ Hz), 4.88 (1H, d, $J = 10.3$ Hz), 6.02 (1H, d, $J = 15.6$ Hz), 6.78 (1H, d, $J = 15.6$ Hz), 7.22–7.41 (16H, complex), 7.66–7.69 (4H, complex); ^{13}C NMR δ 7.0, 7.3, 13.3, 15.4, 19.3, 24.7, 25.8, 26.0, 26.9, 30.4, 32.7, 37.3, 39.3, 51.7, 57.9, 64.0, 67.9, 73.9, 74.5, 76.1, 77.2, 78.2, 78.4, 84.1, 120.8, 127.1, 127.3, 127.47, 127.51, 128.0, 128.1, 128.2, 129.4, 134.1, 135.5, 139.0, 150.0, 166.4; Calcd for $C_{56}H_{80}O_8Si_2 \cdot 0.4H_2O$: C, 71.21; H, 8.63%. Found: C, 71.26; H, 8.52%.

To a solution of the epoxy alcohol (49.3 mg, 0.053 mmol) in DMF (1 mL) was added NaH (60% dispersion in mineral oil, 3.6 mg, 0.094 mmol) and Me_2NCOCl (12 µL, 0.13 mmol) at 0 °C. After being stirred for 1 h, the reaction was quenched by the addition of a few drops of a mixture of MeOH in sat. aq NH_4Cl. The resulting mixture was extracted with EtOAc, washed with brine, dried (Na_2SO_4), and then evaporated. The residue was chromatographically purified (hexane/EtOAc 3/1) to give **3** (33.9 mg, 64%): $[\alpha]_D^{24}$ −16.1 (*c* 1.00, $CHCl_3$); IR (film) 3585, 2933, 2875, 2360, 1725, 1704, 1655 cm^{-1}; ^1H NMR δ 0.62–0.68 (6H, complex), 0.95–0.98 (12H, complex), 1.00 (9H, s), 1.20–1.54 (9H, complex), 1.25 (3H, s), 1.42 (3H, s), 2.03 (1H, m), 2.19 (1H, m), 2.77 (1H, d, $J = 9.3$ Hz), 3.00 (6H, d, $J = 16.1$ Hz), 3.27 (1H, d, $J = 5.9$ Hz), 3.62 (2H, t, $J = 6.3$ Hz), 3.75 (3H, s), 4.22 (1H, d, $J = 11.2$ Hz), 4.32 (1H, m), 4.51 (1H, d, $J = 10.7$ Hz), 4.85 (1H, d, $J = 8.8$ Hz), 4.95 (1H, d, $J = 10.7$ Hz), 5.01 (1H, d, $J = 11.2$ Hz), 6.02 (1H, d, $J = 15.6$ Hz), 6.78 (1H, d, $J = 15.6$ Hz), 7.22–7.26 (10H, complex), 7.35–7.41 (6H, complex), 7.66–7.67 (4H, complex); ^{13}C NMR δ 7.0, 7.3, 13.1, 15.4, 19.3, 25.0, 25.7, 25.9, 26.9, 30.4, 32.7, 35.4, 36.0, 36.7, 39.9, 51.7, 57.7, 64.0, 67.4, 73.5, 73.9, 76.5, 77.9, 79.6, 82.7, 120.8, 126.8, 126.9, 127.4, 127.5, 127.8, 127.9, 129.4, 134.1, 135.5, 139.4, 139.8, 150.0, 156.6, 166.5; Calcd for $C_{59}H_{85}NO_9Si_2$: C, 70.27; H, 8.50; N, 1.39%. Found: C, 70.13; H, 8.61; N, 1.46%.

(*R*,*E*)-Methyl 4-{(4*S*,5*R*,6*R*)-6-[(1*S*,2*R*,3*R*)-1,2-Bis(benzyloxy)-9-*t*-butyldiphenylsiloxy-3-hydroxy-3-methylnonyl]-5-methyl-2-oxo-1,3-dioxan-4-yl}-4-hydroxypent-2-enoate (2). To a solution of **3** (17.5 mg, 0.017 mmol) in CH_2Cl_2 (1.7 mL) was added $Et_2O \cdot BF_3$ (2.2 µL, 0.017 mmol) at room temperature. After being stirred for 23 h, the reaction was quenched by the addition of sat. aq $NaHCO_3$. The resulting mixture was extracted with EtOAc, washed with brine, dried (Na_2SO_4), and then evaporated. The residue was chromatographically purified (hexane/EtOAc 3/1) to give **2** (5.4 mg, 36%): $[\alpha]_D^{25}$ −9.5 (*c* 0.20, $CHCl_3$); IR (film) 3585, 2929, 2856, 1806, 1725 cm^{-1}; ^1H NMR δ 1.00 (3H, d, $J = 6.8$ Hz), 1.07 (3H, s), 1.22 (3H, s), 1.22–1.59 (10H, complex), 1.64 (3H, s), 1.90 (1H, m), 2.30 (1H, s), 3.36 (1H, d, $J = 6.8$ Hz), 3.43 (1H, d, $J = 5.4$ Hz), 3.66–3.69 (3H, complex), 3.81 (3H, s), 4.03 (1H, m), 4.40 (1H, d, $J = 10.7$ Hz), 4.50 (1H, d, $J = 11.2$ Hz), 4.54 (1H, d, $J = 11.2$ Hz), 4.73 (1H, d, $J = 11.2$ Hz), 4.82 (1H, d, $J = 10.8$ Hz), 6.23 (1H, d, $J = 15.6$ Hz), 6.93 (1H, d, $J = 15.6$ Hz), 7.28–7.44 (16H, complex), 7.69–7.70 (4H, complex); ^{13}C NMR δ 9.7, 19.3, 22.5, 24.0, 24.8, 25.9, 26.9, 30.1, 32.6, 38.0, 40.1, 52.1, 64.0, 69.9, 73.5, 74.5, 74.8, 77.2, 79.2, 81.8, 84.0, 87.2, 123.3, 127.5, 127.86, 127.92, 128.0, 128.1, 128.4, 129.4, 134.1, 135.5, 137.6, 137.7, 142.1, 152.5, 165.6; HRMS Calcd for $C_{49}H_{64}O_8Si$ ($M^+ + H - COOMe$): 808.4367. Found (FAB): 808.4375.

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