Bull. Chem. Soc. Jpn. Vol. 80, No. 6, 1173–1186 (2007) 1173

Synthesis and Relative Stereochemistry of the A- and F-Rings of Goniodomin A

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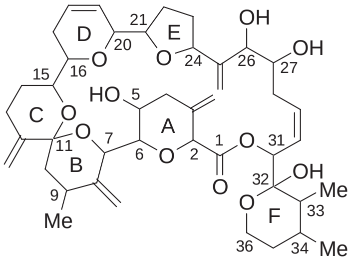
The synthesis of the A- and F-rings of goniodomin A (**1**), which is a stereochemically unidentified antifungal agent isolated from dinoflagellate *Alexandrium hiranoi*, was performed to determine of the relative stereochemistry of these parts. The relative stereochemistry of the A- and F-rings was first deduced from Murakami's NMR data, and model compounds corresponding to these parts were then synthesized. The synthetic A-ring model, of which the structure was established by X-ray crystallographic analysis, showed good agreement with the natural A-ring on the basis of *J* and NOE behavior in the ^{1}H NMR spectroscopy. The chemical shifts in ^{1}H and ^{13}C NMR specta and $J_{32\text{-OH–H33}}$ of the synthetic F-ring model having a 33*S*,34*R* configuration also agreed with those of the F-ring of **1**. Thus, the relative stereochemistry of the A- and F-rings of **1** was elucidated.

Goniodomin A (**1**, Fig. 1) was first isolated from dinoflagellate *Alexandrium hiranoi* as an antifungal agent by Murakami et al. in 1988.[1] It has been found to have diverse bioactivity, such as modulation of actomyosin ATPase activities,[2] increasing the filamentous actin content of human astronoma cells,[3] and antiangiogenic activity via inhibition of actin reorganization in endothelial cells.[4] Very recently, Moeller and co-workers have also isolated **1** as a cytotoxin from *Alexandrium monilatium*.[5] Although the unique planar structure of **1** featured by a 32-membered macrolactone including 5- and 6-membered cyclic ethers (the A-, D-, and E-rings), a spirocyclic acetal (the BC-ring part), and a 6-membered cyclic hemiacetal (the F-ring part) has been reported, the stereochemistry of **1** has not been determined. Since the complex structure and the remarkable bioactivities of **1** attracted our interest, we started the total synthesis in order to determine the absolute stereochemistry of **1**. Here, stereochemical prediction, synthesis, and determination of the relative stereochemistry of the A- and F-rings of **1** are reported as a part of our program.

Results and Discussion

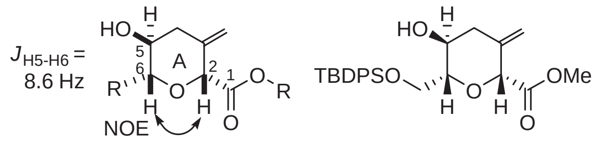
Synthesis and Relative Stereochemistry of the A-Ring Part of 1. Since Murakami performed extensive NMR analysis of **1** and reported large $J_{\text{H5–H6}}$ (8.6 Hz) and NOE between H2 and H6 in its A-ring, the relative stereochemistry of the A-ring has been deduced as **2** in Fig. 2, where the relationship of the substituents at C2 and C6 is *cis* and that of the substituents at C5 and C6 is *trans*. In order to confirm the deduced stereostructure, we undertook comparison of the NMR data of **1** with that of synthetic A-ring model **3** possessing the same relative stereochemistry as **2**. The synthetic strategy for A-ring model **3** is shown in Scheme 1. In order to avoid undesired migration of the double bond from the β-position of the ester group to the α-position, it was planned to prepare ester **3** from **4** by oxidative diol fission at the last stage of the synthesis, and tetrahydropyran **4** should be made from **5** through 6-*exo* epoxide ring-opening.



Goniodomin A (**1**)

Fig. 1.

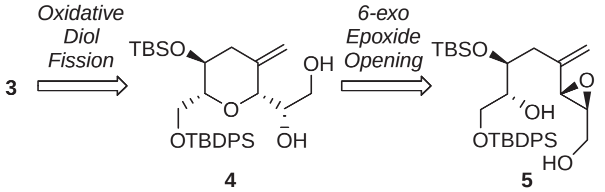
The synthesis of **3**, starting from known epoxide **6** (87%ee),[6] is illustrated in Scheme 2. Epoxide **6** was treated with 4-methoxybenzyl alcohol and Ti(O^{i}Pr)$_4$ to give **7** (60%),[7] which was transformed into epoxide **8** through tosylation of



2
(A-Ring of **1**)

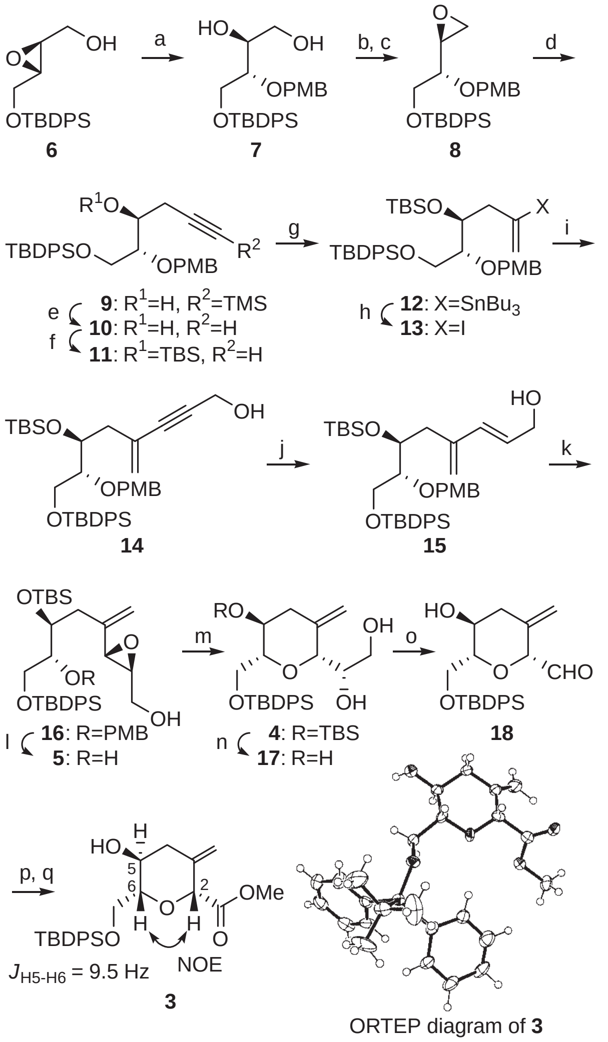
Synthetic
A-Ring Model **3**

Fig. 2.

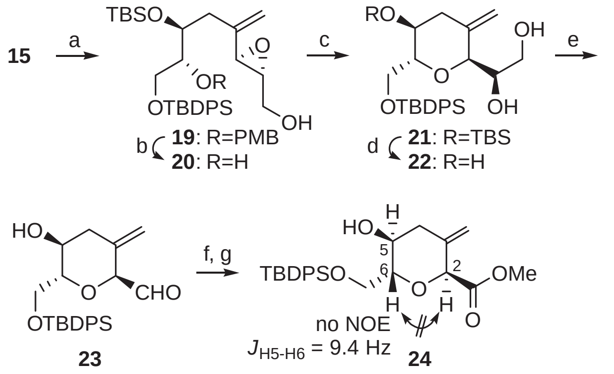


Scheme 1.

Published on the web June 13, 2007; doi:10.1246/bcsj.80.1173



Scheme 2. Reagents and conditions: (a) PMBOH, $Ti(O\text{-}i\text{-}Pr)_4$, toluene, reflux, 1.5 h, 60%; (b) TsCl, pyridine, CH_2Cl_2, 0 °C, 11 h; (c) K_2CO_3, MeOH, 25 °C, 1 h, 64% from **7**; (d) ethynyltrimethylsilane, BuLi, $Et_2O\cdot BF_3$, THF, −78 °C, 35 min, ≈100%; (e) K_2CO_3, MeOH, 25 °C, 1 h, 88%; (f) TBSOTf, 2,6-lutidine, CH_2Cl_2, 25 °C, 30 min, 86%; (g) LDA, Bu_3SnH, THF, −40 °C, 30 min, then CuCN, **11**, −78 °C, 55 min, then MeOH, $-78 \rightarrow 0$ °C, 20 min; (h) I_2, Et_2O, 25 °C, 15 min, 62% from **11**; (i) 2-propynyl alcohol, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, $BuNH_2$, benzene, 25 °C, 2 h, 96%; (j) Red-Al®, Et_2O, −25 °C, 1 h, 83% from **13**; (k) TBHP, (+)-DET, $Ti(O\text{-}i\text{-}Pr)_4$, MS4A, CH_2Cl_2, −25 °C, 27 h, 94%; (l) DDQ, CH_2Cl_2–H_2O (20:1), 0 °C, 50 min, 94%; (m) CSA, CH_2Cl_2, 0 °C, 10 min, 60%; (n) pyridine•HF, MeCN, 0 °C, 1.5 h, 42%; (o) $NaIO_4$, MeOH–H_2O (2:1), 25 °C, 15 min; (p) $NaClO_2$, $NaH_2PO_4\cdot 2H_2O$, 2-methyl-2-butene, t-BuOH–H_2O (3.5:1), 25 °C, 30 min; (q) CH_2N_2, THF, 0 °C, 10 min, 71% from **17**.



Scheme 3. (a) TBHP, (−)-DET, $Ti(Oi\text{-}Pr)_4$, MS4A, CH_2Cl_2, −25 °C, 33 h, 98%; (b) DDQ, CH_2Cl_2–H_2O (10:1), 0 °C, 1 h, 82%; (c) CSA, CH_2Cl_2, −20 °C, 30 min, 90%; (d) pyridine•HF, MeCN, 0 °C, 1.5 h, 61%; (e) $NaIO_4$, MeOH–H_2O (2:1), 25 °C, 15 min; (f) $NaClO_2$, $NaH_2PO_4\cdot 2H_2O$, 2-methyl-2-butene, t-BuOH–H_2O (3.5:1), 25 °C, 40 min; (g) CH_2N_2, THF, 0 °C, 15 min, 64% for 3 steps.

the primary alcohol followed by basic treatment (64%). Substitution with ethynyltrimethylsilane[8] and the subsequent removal of the TMS (Me_3Si) group afforded **10** (88%). After protection of alcohol **10** as a TBS (t-$BuMe_2Si$) ether (86%), the resulting acetylene **11** was converted with a higher order tin cuprate reagent to vinyltin **12**,[9] which reacted with I_2 to produce **13** (62%). Iodide **13** was coupled with 2-propynyl alcohol by Sonogashira reaction[10] to give **14**, which was reduced with Red-Al® to (*E*)-allyl alcohol **15** (80%). Katsuki–Sharpless asymmetric epoxidation of **15** using (+)-DET (diethyl tartrate) stereoselectively yielded almost optically pure **16** (94%),[11] which was transformed into diol **5** with DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) (93%). Treatment of **5** with CSA (camphor-10-sulfonic acid) successfully gave 6-*endo* cyclized product **4** (60%). Removal of TBS (42%) followed by oxidative cleavage of the diol part afforded aldehyde **18**, which was converted to methyl ester **3** (colorless needles, mp 118.0–118.3 °C) through oxidation with $NaClO_2$ and methylation with CH_2N_2 (71% for 3 steps).[12] Stereochemistry of **3** was established by X-ray crystallographic analysis, and a large $J_{H5\text{–}H6}$ value (9.5 Hz) was observed. In addition, the presence of NOE between H2 and H6 was similar to that observed in natural **1**.

The C2 epimer (**24**) of **3** was also synthesized from **15** through a 7-step process including Katsuki–Sharpless asymmetric epoxidation with (−)-DET (Scheme 3). Although epimer **24** had a large $J_{H5\text{–}H6}$ value (9.4 Hz), no NOE was present between H2 and H6, which was different from **1**.

Thus, two A-ring models **3** and **24** were stereoselectively synthesized, and the stereochemistry of **3** was unambiguously confirmed by X-ray crystallographic analysis. Although the deviations in the NMR chemical shifts and coupling constants from the reported values of **1** (Table 1) were similar for both compounds, the relative stereochemistry of the A-ring part of **1** was judged to be identical with that of **3** on the basis of the presence of NOE between H2 and H6 in both **1** and **3** as well as the absence of NOE between H2 and H6 in **24**.

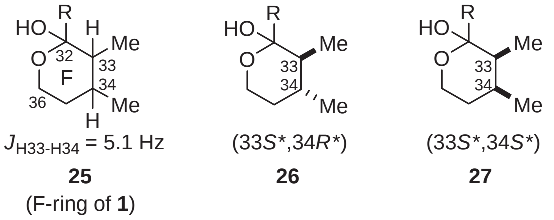
Synthesis and Relative Stereochemistry of the F-Ring Part of 1. The presence of two methyl groups at C33 and C34 in the F-ring (**25**) of **1** has been reported by Murakami et al. (Fig. 3).[1a,b] However, it has been unclear whether the stereochemical relationship of the groups is *trans* (**26**) or *cis* (**27**). The stereochemistry of C32 has not been determined, and we could only speculate that the hydroxy group at C32 has an axial position in the chair conformation of the F-ring on the basis of the anomeric effect. Therefore, we undertook the

Table 1. Comparison of Selected NMR Data of **1**, **3**, and **24**

Position	^{1}H NMR (C_6D_6)			^{13}C NMR ($CDCl_3$)		
	δ(**1**) /ppm[a)]	δ(**3**) /ppm	δ(**24**) /ppm	δ(**1**) /ppm[a)]	δ(**3**) /ppm	δ(**24**) /ppm
1				168.1	169.2	170.8
2	4.309	4.34	4.58	76.2	78.7	75.0
3				139.7	139.2	139.0
3=CHa	4.779	4.74	4.78	112.1	111.9	115.5
3=CHb	5.002	4.80	4.79			
4a	2.331	2.03	2.38	40.7	40.3	37.8
4b	2.820	2.57	2.56			
5	4.133	3.70	3.78	70.2	71.2	70.8
5-OH	4.455	2.17	2.47			
6	3.683	3.27	4.28	80.2	78.7	77.2
7	5.133	3.95/3.98	4.00/4.12	73.1	66.7	66.5

	J(**1**) /Hz[a)]	J(**3**) /Hz	J(**24**) /Hz
J_{H4a-H5}	10.5	9.5	11.4
J_{H4b-H5}	5.3	5.5	5.1
$J_{H4a-H4b}$	13.3	13.0	13.0
J_{H5-H6}	8.6	9.5	19.4

a) Data from Ref. 1a.

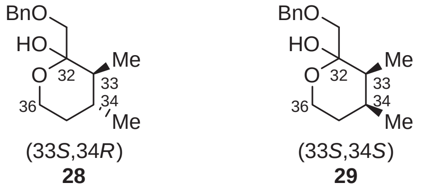


$J_{H33-H34}$ = 5.1 Hz **25** (F-ring of **1**)

(33*S**,34*R**) **26**

(33*S**,34*S**) **27**

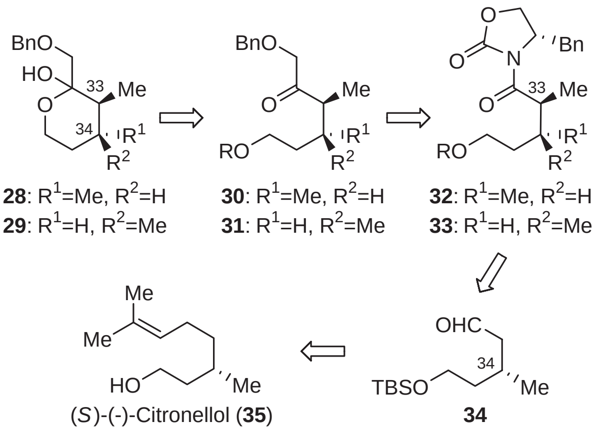
Fig. 3.



(33*S*,34*R*) **28**

(33*S*,34*S*) **29**

Fig. 4.



28: R^1=Me, R^2=H
29: R^1=H, R^2=Me

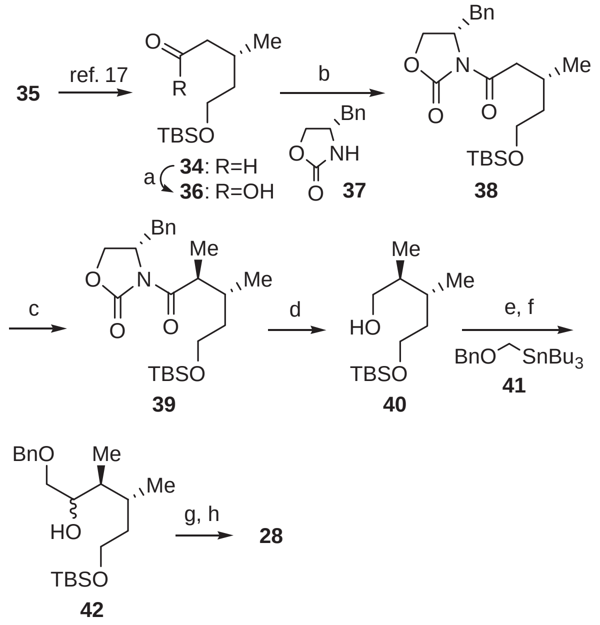
30: R^1=Me, R^2=H
31: R^1=H, R^2=Me

32: R^1=Me, R^2=H
33: R^1=H, R^2=Me

(*S*)-(-)-Citronellol (**35**)

34

Scheme 4.

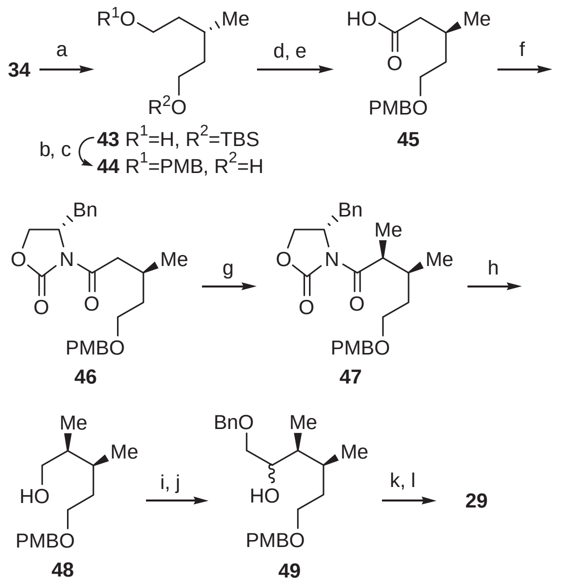


Scheme 5. Reagents and conditions: (a) $NaClO_2$, $NaH_2PO_4 \cdot 2H_2O$, 2-methyl-2-butene, *t*-BuOH–H_2O (3.5:1), 25 °C, 30 min, 93%; (b) PivCl, Et_3N, CH_2Cl_2, 0 °C, 30 min, then **37**, LiCl, THF–CH_2Cl_2 (1:1), 25 °C, 9 h, 76%; (c) NHMDS, THF, −78 °C, 30 min, then MeI, −78 °C, 33 h, 88%; (d) $LiAlH_4$, THF, 0 °C, 10 min, 67%; (e) TPAP (cat.), NMO, MS4A, CH_2Cl_2, 25 °C, 20 min; (f) **41**, BuLi, THF, −78 °C, 30 min, then aldehyde, −78 °C, 30 min, 66% from **40**; (g) DMPI, CH_2Cl_2, 25 °C, 6 h; (h) Bu_4NF, THF, 25 °C, 40 min, 81% from **42**.

synthesis of F-ring models **28** and **29** having *trans* (33*S*,34*R*) and *cis* (33*S*,34*S*) relationships, respectively, in order to determine the relative configuration of the F-ring of **1** by comparison of the NMR data of **1** and that of the models (Fig. 4).

As shown in Scheme 4, it was planned to synthesize the cyclic hemiacetals **28** and **29** from the corresponding keto alcohols **30** and **31** at the last stage of the synthesis. In both cyclization reactions, the anomeric effect was expected to manage the hydroxy group at C32 to have an axial position as speculated above. Ketones **30** and **31** can be prepared from the corresponding **32** and **33**, of which the methyl group at C33 can be introduced by using the Evans method.[13] In order to establish the stereochemistry at C34, we envisioned the use of **34**, preparable from (*S*)-(−)-citronellol (**35**) by the Lee procedure,[14] as a common intermediate for **32** and **33**. Because of the potential symmetry of **34**, its 34*R* configuration should be inverted facilely to 34*S* configuration by a four-step reduction/protection/deprotection/oxidation process.

The synthesis of **28** is depicted in Scheme 5. According to the Lee procedure,[14] (*S*)-(−)-citronellol (**35**) was first converted to **34**. Aldehyde **34** was oxidized with $NaClO_2$[15] to afford **36** (93%), which was condensed with (*S*)-4-benzyl-2-oxazolidinone **37** by the Ho method to provide **38** (76%).[16] Treatment of **38** with NHMDS (sodium hexamethyldisilazanide) followed by the reaction with MeI selectively produced **39** in good yield (88%). The chiral auxiliary of **39** was reductively removed



Scheme 6. Reagents and conditions: (a) $LiAlH_4$, THF, 25 °C, 30 min; (b) NaH, PMBCl, Bu_4NI, DMF, 25 °C, 18 h; (c) Bu_4NF, THF, 25 °C, 30 min, 100% from **34**; (d) TPAP (cat.), NMO, MS4A, CH_2Cl_2, 25 °C, 20 min; (e) $NaClO_2$, $NaH_2PO_4{\cdot}2H_2O$, 2-methyl-2-butene, *t*-BuOH–H_2O (3.5:1), 25 °C, 30 min, 79% from **44**; (f) PivCl, Et_3N, CH_2Cl_2, 0 °C, 30 min, then **37**, LiCl, THF–CH_2Cl_2 (1:1), 25 °C, 3 h, 68%; (g) NHMDS, THF, −78 °C, 30 min, then MeI, −78 °C, 33 h, 53%; (h) $LiAlH_4$, THF, 0 °C, 30 min, 80%; (i) TPAP (cat.), NMO, MS4A, CH_2Cl_2, 25 °C, 20 min; (j) **41**, BuLi, THF, −78 °C, 30 min, then aldehyde, −78 °C, 30 min, 48% from **48**; (k) DMPI, CH_2Cl_2, 25 °C, 2 h; (l) DDQ, CH_2Cl_2–H_2O (20:1), 25 °C, 1.5 h, 82% from **49**.

(67%) to yield **40**, which was transformed into **42** (66% for two steps) through TPAP (tetrapropylammonium perruthenate) oxidation[17] and the subsequent reaction with benzyloxymethyllithium derived from **41**. The Dess–Martin oxidation[18] of **42**, followed by desilylation, afforded **28** as a single product (81% for two steps).

Next, another F-ring model **29** was synthesized from **34** (Scheme 6). The stereochemistry at C34 was successfully inverted as follows. Reduction of **34** with $LiAlH_4$ followed by a conventional PMB-protection/desilylation process (PMB: 4-methoxybenzyl) gave **44** (100% for three steps), which was oxidized to **45** on treatment with TPAP[17] followed by $NaClO_2$[15] (79% for two steps). Then, the carboxylic acid **45** was condensed with **37** to afford **46** (68%). Stereoselective methylation of **46** in accordance with the Evans procedure (53%),[13] and its subsequent reduction afforded **48** (80%). After alcohol **48** was oxidized to the corresponding aldehyde, it was reacted with benzyloxymethyllithium, prepared from **41**, to give **49** (48% for two steps), which was then oxidized, followed by removal of PMB, to produce **29** stereoselectively (82% for two steps).

The stereochemistry of the two F-ring models **28** and **29** was confirmed by ^{1}H NMR analysis in C_6D_6 (Fig. 5). Model **28** showed NOEs between one of the protons at C36 (H36a) and the proton of the hydroxy group at C32 (C32-OH) and between H36a and H34, which suggested that all of C32-OH, H34, and H36ax had axial positions at the same side of the chair-shaped oxane ring. The large (10.6 Hz) coupling constant between H33 and H34 ($J_{H33\text{–}H34}$) in **28** indicated an *anti*-diaxial relationship between H33 and H34. Accordingly, it was confirmed that F-ring model **28** had two equatorial methyl groups at C33 and C34, an equatorial benzyloxymethyl group at C32, and an axial hydroxy group at C32. On the other hand, model **29** displayed NOEs between H36a and H34 and between H34 and the proton of C32-OH, which explained the chair conformation of the oxane ring of **29** having axial C32-OH, H34, and H36a. Since the value of $J_{H33\text{–}H34}$ was small (4.0 Hz), it was suggested that H33 had an equatorial position. Thus, the presence of an axial methyl group at C33, an equatorial methyl group at C34, an equatorial benzyloxymethyl group at C32, and an axial hydroxy group at C32 in **29** was confirmed. It is notable that both hydroxy groups of **28** and **29** had axial positions as expected.

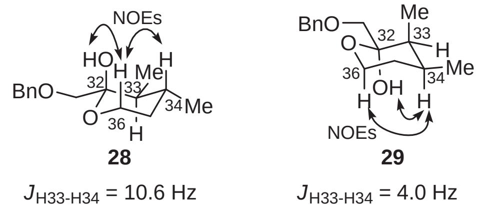


Fig. 5.

Next, the NMR data of **28** and **29** were compared with the reported data of **1** (Table 2).[1a,b] The ^{1}H and ^{13}C chemical shifts of **1** were in agreement with those of *trans*-dimethyl model **28**. The deviation of the chemical shifts of **28** and **29** from those of **1** is shown in Fig. 6, and the similarity in the stereostructures of **28** and the F-ring of **1** is clearly seen.[19] On the other hand, the reported $J_{H33\text{–}H34}$ of **1** (5.1 Hz) agreed with that of **29** (4.0 Hz) rather than that of **28** (10.6 Hz). However, other reported *J* values of **1** were almost identical with those of **28**. Especially, the long-range coupling between H33 and the proton of C32-OH ($^4J_{32\text{-OH–H33}}$) was observed (1.0 Hz) in both **1** and **28**, but not in **29**. ^4J coupling is typically observed when four successive bonds lie in the same plane and form a W-shaped conformation. Although in both **28** and **29**, the four successive bonds H–O–C32–C33–H33 are in the same plane, only in **28** can they be arranged in a W-shaped conformation. Accordingly, the presence of clear $^4J_{32\text{-OH–H33}}$ in both **1** and **28** strongly suggested the same relative stereochemistry at C32 and C33 of **1** as that of **28**. Thus, it was concluded that the relative stereochemistry of the F-ring of **1**, including the anomeric C32 position, was identical to that of **28**.

In conclusion, the synthesis of the A- and F-ring parts of goniodomin A (**1**), a stereochemically unidentified antifungal agent isolated from dinoflagellate *Alexandrium hiranoi*,[1a,b] was performed to determine of the relative stereochemistry of these parts. The relative stereochemistry of the A- and F-rings was first deduced from Murakami's NMR data,[1a,b] and model compounds corresponding to these rings were then synthesized. A-ring model **3**, of which the structure was determined by X-ray crystallographic analysis, showed good agreement with the natural A-ring on the basis of its *J* values and the NOE behavior in ^{1}H NMR spectroscopy. The chemical shifts

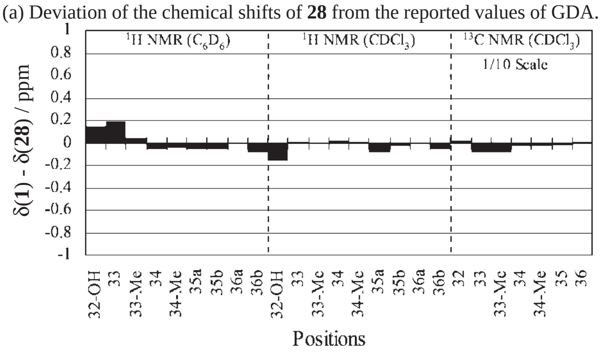
Table 2. Comparison of Selected NMR Data of **1**, **28**, and **29**

Position	^{1}H NMR (C_6D_6)			Position	^{1}H NMR ($CDCl_3$)		
	δ(**1**)/ppm[a)]	δ(**28**)/ppm	δ(**29**)/ppm		δ(**1**)/ppm[b)]	δ(**28**)/ppm	δ(**29**)/ppm
31	5.962	3.34/3.41	3.27/3.45	31	5.714	3.40/3.52	3.31/3.53
32-OH	2.979	2.83	3.47	32-OH	2.773	2.93	3.50
33	1.329	1.14	1.63	33	1.240	1.23	1.64
33-Me	0.984	0.94	0.66	33-Me	0.920	0.92	0.76
34	1.664	1.72	2.48	34	1.720	1.70	2.36
34-Me	0.740	0.79	0.75	34-Me	0.910	0.90	0.87
35a	1.170	1.23	0.96	35a	1.280	1.36	1.22
35b			1.33	35b	1.490	1.52	1.46
36a	3.560	3.57	3.60	36a	3.650	3.66	3.66
36b	3.902	3.98	4.03	36b	3.910	3.97	3.97

Position	^{1}H NMR (C_6D_6)			Position	^{13}C NMR ($CDCl_3$)		
	J(**1**)/Hz[a)]	J(**28**)/Hz	J(**29**)/Hz		δ(**1**)/ppm[a)]	δ(**28**)/ppm	δ(**29**)/ppm
32-OH–H33	1.0	1.0	0.0	31	73.5	73.9	74.9
H33–33Me	6.5	6.6	7.1	32	97.5	97.3	97.1
H33–H34	5.1	10.6	4.0	33	40.9	41.7	38.9
H34–34Me	6.5	6.6	7.0	33-Me	12.7	13.5	6.8
H36a–H36b	11.0	11.0	11.0	34	30.8	31.1	27.1
				34-Me	20.0	20.3	19.0
				35	34.2	34.4	27.7
				36	60.6	60.5	61.1

a) Data from Ref. 1a. b) Data from Ref. 1b.

(a) Deviation of the chemical shifts of **28** from the reported values of GDA.



(b) Deviation of the chemical shifts of **29** from the reported values of GDA.

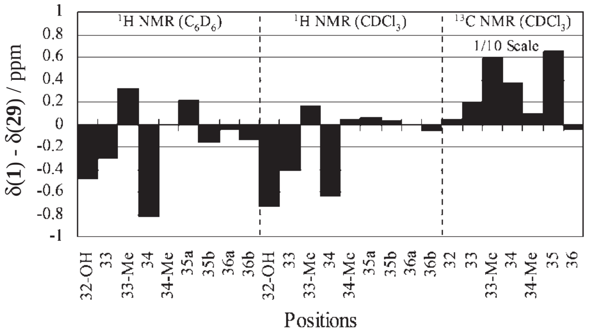
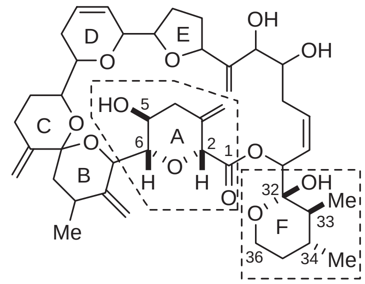


Fig. 6.

in ^{1}H and ^{13}C NMR and $J_{32\text{-OH–H33}}$ of F-ring model **28**, having a 33*S*,34*R* configuration, also coincided with those of the F-ring of **1**. Thus, the relative stereochemistry of the A- and F-rings of **1** was elucidated as shown in Fig. 7. Further studies toward the total synthesis of **1** are currently under way in this laboratory.



Goniodomin A (**1**)

Fig. 7.

Experimental

General Methods. All reactions involving air- or moisture-sensitive reagents were carried out in an anhydrous solvent system under an argon atmosphere in oven-dried glassware capped with septa, and sensitive liquids and solutions were transferred by using syringe- or cannula-techniques, unless otherwise noted. All commercially available reagents including anhydrous solvents, such as dichloromethane, ether, and *N*,*N*-dimethylformamide (DMF), were used without further purification with the following exceptions: tetrahydrofuran (THF) was distilled from sodium diphenylketyl under argon and benzene was distilled from CaH_2 prior to use. Normal reagent-grade solvents were used for flash chromatography and extraction. Special reagent-grade solvents were used for high-pressure liquid chromatography (HPLC). All reactions were monitored by thin-layer chromatography (TLC) with precoated silica gel (SiO_2) plates (Merck, silica gel 60 F_{254}). Plates were visualized by ultraviolet light and by treatment with acidic anisaldehyde or phosphomolybdic acid stain, followed by heating. For flash chromatography was utilized SiO_2 (YMC, SIL-60-400/230W). HPLC was run with a JASCO Intelligent HPLC Pump

PU-986, equipped with a JASCO Intelligent UV/VIS Detector UV-975 and a YMC-Pack SIL-06 (250×10 or 20 mm I.D.) HPLC column. Melting points were measured on Yanagimoto micro-melting apparatus without calibration. Optical rotations were recorded on a JASCO P-1020 digital polarimeter. Infrared (IR) spectra were measured on a JEOL JIR-WINSPEC100 infrared spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-AL300 spectrometer (^{1}H at 300 MHz, ^{13}C at 75 MHz). ^{1}H NMR spectra are reported as chemical shifts (δ) in parts-per-million (ppm) referenced to tetramethylsilane (0.00 ppm) in $CDCl_3$ or C_6HD_5 (7.15 ppm) in C_6D_6. Splitting patterns were designated as "s, d, t, q, m, and br" indicating "singlet, doublet, triplet, quartet, multiplet, and broad," respectively. *J* values are reported in Hertz (Hz). ^{13}C NMR spectra are reported as chemical shifts (δ) in ppm referenced to $^{13}CDCl_3$ (77.0 ppm) in $CDCl_3$ or $^{13}C^{12}C_5D_6$ (128.0 ppm) in C_6D_6. High-resolution mass spectra (HR-MS) were measured on a JEOL JMS-600H mass spectrometer under electron impact ionization (EI) condition, a JEOL AX500 mass spectrometer under EI condition, and a JEOL JMS-SX102A mass spectrometer under field desorption ionization (FD) condition.

X-ray Measurement. Crystal data of **3**: $C_{25}H_{32}O_5Si$, $M_r = 440.61$, colorless block, $0.20 \times 10.00 \times 0.05\,\text{mm}^3$, monoclinic $P2_1$ (No. 4), $a = 9.350(4)$ Å, $b = 9.597(4)$ Å, $c = 14.130(7)$ Å, $\beta = 108.039(2)°$, $V = 1205.6(10)$ Å^3, D_{calcd} $(Z = 2) = 1.214$ g cm^{-3}. A total of 2850 unique data ($2\theta_{\max} = 54.9°$) were measured at $T = 153$ K by a Rigaku/MSC Mercury CCD apparatus (Mo Kα radiation, $\lambda = 0.71069$ Å). Numerical absorption correction was applied ($\mu = 1.29\,\text{cm}^{-1}$). The structure was solved by direct methods and refined by using the full-matrix least-squares method of *F* with anisotropic temperature factors for non-hydrogen atoms. Hydrogen atoms were included but not refined. The final *R* and *Rw* values were 0.069 and 0.107, respectively, for 2808 reflections with $I > 3\sigma I$ and 280 parameters. Crystallographic data of **3** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication numbers CCDC 632022. Copies of the data can be obtained, free of charge, via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Center, 12, Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk).

(2*S*,3*R*)-4-(*t*-Butyldiphenylsilyloxy)-3-(4-methoxybenzyloxy)-butane-1,2-diol (7). A mixture of 4-methoxybenzyl alcohol (120 mL, 962 mmol) and Ti(O*i*-Pr)$_4$ (52 mL, 175 mL) was heated at 100 °C under reduced pressure for 100 min and then was cooled to 25 °C. To the resulting Ti(OPMB)$_4$ (PMB: 4-methoxybenzyl) was added a solution of **6** (29.3 g, 85.6 mmol) in toluene (90 mL), and the mixture was stirred and refluxed for 90 min. After the mixture was cooled to ambient temperature, 10% aqueous DL-tartaric acid (80 mL) was added, and the mixture was stirred for 35 min. Then, EtOAc (500 mL) and NaF (43.8 g) were added, and the resulting mixture was stirred for 30 min. The mixture was filtered through a celite pad, and the pad was washed with EtOAc several times. The combined filtrates were condensed under reduced pressure, and the residue was purified by silica-gel chromatography (600 g, hexane/EtOAc = 3) to give **7** (24.7 g, 60%).

7: a colorless oil; $[\alpha]_D^{17} = -14.8$ (*c* 0.950, $CHCl_3$); IR (neat) $\nu_{\max}$ 3423, 3071, 3050, 3000, 2950, 2930, 2890, 2857, 1612, 1588, 1514, 1470, 1463, 1428, 1302, 1248, 1173, 1112, 1040, 823, 743, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (9H, s), 2.22 (1H, t, $J = 6.3$ Hz), 2.96 (1H, d, $J = 5.5$ Hz), 3.59 (1H, q, $J = 5.5$ Hz), 3.63–3.90 (5H, m), 3.79 (3H, s), 4.36 (1H, d, $J = 11.3$ Hz), 4.50 (1H, d, $J = 11.3$ Hz), 6.83 (2H, d, $J = 8.6$ Hz), 7.15 (2H, d, $J = 8.6$ Hz), 7.35–7.49 (6H, m), 7.64–7.70 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.9 (C), 26.6 ($CH_3 \times 3$), 55.0 (CH_3), 63.3 (CH_2), 63.6 (CH_2), 72.0 (CH), 72.2 (CH), 79.4 (CH), 113.6 (CH $\times$ 2), 127.6 (CH $\times$ 4), 129.3 (CH $\times$ 2), 129.7 (CH $\times$ 2), 130.0 (C), 132.7 (C), 132.8 (C), 135.4 (CH $\times$ 4), 159.1 (C); LR-FDMS, *m/z* 481 (63.5%, $[M + H]^+$), 121 (bp, $[C_8H_9O]^+$); HR-FDMS, calcd for $C_{28}H_{37}O_5Si$ $[M + H]^+$: 481.2411, found: 481.2428.

(2*S*,3*R*)-4-(*t*-Butyldiphenylsilyloxy)-1,2-epoxy-3-(4-methoxy-benzyloxy)butane (8). To a solution of **7** (11.21 g, 23.32 mmol) in CH_2Cl_2 (200 mL) were added pyridine (21 mL, 260 mmol) and TsCl (Ts: 4-toluenesulfonyl) (4.891 g, 25.7 mmol) at 0 °C, and the mixture was stirred for 3 h. Then, TsCl (4.891 g, 25.7 mmol) was added, and the mixture was stirred for 11 h. Then, TsCl (1.70 g, 8.91 mmol) was added. After the mixture was stirred for 2 h, the reaction was quenched with H_2O. The mixture was extracted with ether ($\times$3), and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was dissolved in MeOH (250 mL), and K_2CO_3 (9.259 g, 70.0 mmol) was added to the solution at 0 °C. Then, the mixture was warmed to 25 °C and stirred for 1 h. The reaction was quenched with H_2O, and the mixture was extracted with ether ($\times$3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (150 g, hexane/EtOAc = 10) to give **8** (6.939 g, 64% from **7**).

8: a colorless oil; $[\alpha]_D^{17} = -10.0$ (*c* 0.855, $CHCl_3$); IR (neat) $\nu_{\max}$ 3074, 3052, 3000, 2960, 2934, 2900, 2861, 2838, 1614, 1590, 1516, 1473, 1460, 1429, 1303, 1250, 1173, 1114, 1038, 824, 743, 703 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (9H, s), 2.72 (1H, dd, $J = 2.9$, 5.4 Hz), 2.74 (1H, dd, $J = 3.9$, 5.4 Hz), 3.12 (1H, ddd, $J = 2.9$, 3.9, 4.5 Hz), 3.46 (1H, brq, $J = 5.0$ Hz), 3.76–3.84 (2H, m), 3.80 (3H, s), 4.51 (1H, d, $J = 11.5$ Hz), 4.54 (1H, d, $J = 11.5$ Hz), 6.84 (2H, d, $J = 8.7$ Hz), 7.22 (2H, d, $J = 8.7$ Hz), 7.32–7.46 (6H, m), 7.65–7.71 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1 (C), 26.7 ($CH_3 \times 3$), 44.8 (CH_2), 51.3 (CH), 55.0 (CH_3), 64.4 (CH_2), 72.1 (CH_2), 77.9 (CH), 113.6 (CH $\times$ 2), 127.6 (CH $\times$ 4), 129.1 (CH $\times$ 2), 129.6 (CH $\times$ 2), 130.4 (C), 133.2 (C $\times$ 2), 135.5 (CH $\times$ 4), 159.0 (C); LR-EIMS, *m/z* 405 (0.4%, $[M - t\text{-Bu}]^+$), 121 (bp, $[C_8H_9O]^+$); HR-EIMS, calcd for $C_{24}H_{25}O_4Si$ $[M - t\text{-Bu}]^+$: 405.1522, found: 405.1517.

(2*S*,3*R*)-1-(*t*-Butyldiphenylsilyloxy)-2-(4-methoxybenzyloxy)-hex-5-yn-3-ol (10). To a solution of ethynyltrimethylsilane (8.5 mL, 60.1 mmol) in THF (150 mL) was added BuLi (38 mL, 1.58 M in hexane, 60.0 mmol) at −78 °C, and the mixture was stirred for 15 min. Then, $Et_2O \cdot BF_3$ (7.6 mL, 60.0 mmol) was added at −78 °C, and the mixture was stirred for 30 min. A solution of **8** (6.935 g, 14.99 mmol) in THF (20 mL) was then added, and the mixture was stirred for 35 min. The reaction was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with ether ($\times$3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was roughly purified by silica-gel chromatography (80 g, hexane/EtOAc = 5). The resulting impure (2*S*,3*R*)-1-(*t*-butyldiphenylsilyloxy)-2-(4-methoxybenzyloxy)-6-trimethylsilyl-hex-5-yn-3-ol (**9**) was dissolved in MeOH (150 mL), and K_2CO_3 (6.125 g, 45.0 mmol) was added to the solution at 25 °C. After the mixture was stirred for 1 h, the reaction was quenched with H_2O. The mixture was extracted with ether ($\times$3), and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (60 g, hexane/EtOAc = 5) to give **10** (6.417 g, 88% from **8**).

10: a colorless oil; $[\alpha]_D^{17} = -23.69$ (c 0.640, $CHCl_3$); IR (neat) ν_{max} 3485, 3312, 3075, 3050, 3010, 3000, 2950, 2931, 2890, 2850, 2120, 1614, 1589, 1514, 1472, 1460, 1429, 1391, 1362, 1303, 1248, 1173, 1112, 1075, 1040, 1010, 930, 823, 742, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.06 (9H, s), 2.03 (1H, t, $J = 2.6$ Hz), 2.50 (1H, ddd, $J = 2.6$, 6.4, 16.5 Hz), 2.55 (1H, ddd, $J = 2.6$, 5.0, 16.5 Hz), 2.78 (1H, d, $J = 5.0$ Hz), 3.56 (1H, td, $J = 5.0$, 6.4 Hz), 3.80 (3H, s), 3.86 (2H, d, $J = 5.0$ Hz), 3.97 (1H, tt, $J =$ 5.0, 6.4 Hz), 4.42 (1H, d, $J = 11.1$ Hz), 4.55 (1H, d, $J = 11.1$ Hz), 6.84 (2H, d, $J = 8.7$ Hz), 7.19 (2H, d, $J = 8.7$ Hz), 7.34–7.48 (6H, m), 7.66–7.71 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1 (C), 23.2 (CH_2), 26.8 ($CH_3 \times 3$), 55.2 (CH_3), 63.7 (CH_2), 70.4 (CH), 70.6 (CH), 72.4 (CH_2), 80.0 (CH), 81.0 (C), 113.7 (CH × 2), 127.7 (CH × 4), 129.4 (CH × 4), 129.8 (CH × 2), 130.2 (C), 132.8 (C), 132.9 (C), 135.6 (CH × 4), 159.2 (C); LR-EIMS, m/z 431 (0.11%, $[M - t\text{-Bu}]^+$), 121 (bp, $[C_8H_9O]^+$); HR-EIMS, calcd for $C_{26}H_{27}O_4Si$ $[M - t\text{-Bu}]^+$: 431.1679, found: 431.1641.

(2*S*,3*R*)-3-(*t*-Butyldimethylsilyloxy)-1-(*t*-butyldiphenylsilyloxy)-2-(4-methoxybenzyloxy)-5-hexyne (11). To a stirred solution of **10** (1.00 g, 2.046 mmol) and 2,6-lutidine (1.0 mL, 8.6 mmol) in CH_2Cl_2 (20 mL) was added TBSOTf (TBS: t-BuMe_2Si, Tf: CF_3SO_2) (0.9 mL, 3.9 mmol) at 0 °C. The mixture was warmed to 25 °C and stirred for 30 min. The reaction was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (50 g, hexane/EtOAc = 20) to give **11** (1.066 g, 86% from **8**).

11: a colorless oil; $[\alpha]_D^{17} = -8.73$ (c 1.005, $CHCl_3$); IR (neat) ν_{max} 3310, 3072, 3049, 2999, 2950, 2929, 2890, 2857, 2120, 1613, 1588, 1514, 1472, 1460, 1428, 1390, 1361, 1302, 1248, 1173, 1113, 1038, 1006, 928, 824, 778, 740, 701, 620, 615 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ −0.04 (3H, s), 0.07 (3H, s), 0.83 (9H, s), 1.06 (9H, s), 1.96 (1H, t, $J = 2.6$ Hz), 2.40 (1H, ddd, $J = 2.6$, 4.9, 17.1 Hz), 2.54 (1H, ddd, $J = 2.6$, 5.5, 17.1 Hz), 3.67–3.78 (2H, m), 3.80 (3H, s), 3.80–3.88 (1H, m), 3.95 (1H, brq, $J = 5.0$ Hz), 4.59 (1H, d, $J = 11.0$ Hz), 4.67 (1H, d, $J = 11.0$ Hz), 6.84 (2H, d, $J = 8.6$ Hz), 7.24 (2H, d, $J = 8.6$ Hz), 7.30–7.45 (6H, m), 7.65–7.70 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.7 (CH_3), −4.6 (CH_3), 18.0 (C), 19.2 (C), 23.6 (CH_2), 25.8 ($CH_3 \times 3$), 26.9 ($CH_3 \times 3$), 55.2 (CH_3), 64.3 (CH_2), 70.0 (CH), 71.0 (CH), 73.2 (CH_2), 81.8 (CH), 81.9 (C), 113.7 (CH × 2), 127.7 (CH × 4), 129.4 (CH × 2), 129.6 (CH × 2), 131.1 (C), 133.4 (C), 133.5 (C), 135.6 (CH × 2), 135.7 (CH × 2), 159.1 (C); LR-EIMS, m/z 602 (0.06%, $[M]^+$), 121 (bp, $[C_8H_9O]^+$); HR-EIMS, calcd for $C_{36}H_{50}O_4Si_2$ $[M]^+$: 602.3248, found: 602.3248.

(4*S*,5*R*)-4-(*t*-Butyldimethylsilyloxy)-6-(*t*-butyldiphenylsilyloxy)-2-iodo-5-(4-methoxybenzyloxy)-1-hexene (13). To a solution of i-Pr_2NH (1.9 mL, 13.46 mmol) in THF (20 mL) was added BuLi (8.2 mL, 1.58 M in hexane, 12.96 mmol) at 0 °C, and the solution was stirred for 20 min. After the solution was cooled to −40 °C, Bu_3SnH (3.4 mL, 12.83 mmol) was added, and the mixture was stirred for 30 min. Then, the mixture was cooled to −78 °C, CuCN (594 mg, 6.632 mmol) was added. After the mixture was stirred for 15 min, a solution of **11** (1.0 g, 1.659 mmol) in THF (8 mL) was added, and the mixture was stirred for 40 min. Then, MeOH (5.4 mL, 133 mmol) was added, and the mixture was allowed to warm to 0 °C for 20 min. The reaction was quenched with an aqueous solution of NH_4Cl/NH_4OH (saturated aqueous NH_4Cl/conc. NH_4OH = 9), and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was roughly purified by silica-gel chromatography (150 g, hexane/benzene = 4). The resulting impure (4*S*,5*R*)-4-(*t*-butyldimethylsilyloxy)-6-(*t*-butyldiphenylsilyloxy)-5-(4-methoxybenzyloxy)-2-(tributylstannyl)-1-hexene (**12**) was dissolved in ether (20 mL), and iodine was added portionwise to the stirred solution at 25 °C until the solution turned yellow. After the mixture was stirred for 15 min, the reaction was quenched with saturated aqueous Na_2SO_3, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (50 g, hexane/benzene = 2.5) to give **13** (752 mg, 62% from **11**).

13: a colorless oil; $[\alpha]_D^{19} = 0.46$ (c 0.385, $CHCl_3$); IR (neat) ν_{max} 3070, 3049, 3030, 2950, 2928, 2890, 2855, 1610, 1585, 1513, 1470, 1460, 1430, 1390, 1360, 1300, 1249, 1170, 1140, 1112, 1040, 1005, 940, 845, 825, 810, 780, 740, 701, 678 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (3H, s), 0.11 (3H, s), 0.85 (9H, s), 1.06 (9H, s), 2.51–2.67 (2H, m), 3.57–3.70 (3H, m), 3.79 (3H, s), 4.22 (1H, ddd, $J = 2.0$, 4.6, 7.0 Hz), 4.54 (1H, d, $J = 11.4$ Hz), 4.64 (1H, d, $J = 11.4$ Hz), 5.72 (1H, d, $J = 1.0$ Hz), 6.04 (1H, d, $J = 1.0$ Hz), 6.83 (2H, d, $J = 8.7$ Hz), 7.22 (2H, d, $J =$ 8.7 Hz), 7.30–7.45 (6H, m), 7.63–7.70 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.1 ($CH_3 \times 2$), 18.1 (C), 19.1 (C), 26.0 ($CH_3 \times 3$), 26.8 ($CH_3 \times 3$), 48.8 (CH_2), 55.2 (CH_3), 63.5 (CH_2), 71.6 (CH), 72.7 (CH_2), 82.5 (CH), 109.3 (C), 113.6 (CH × 2), 127.7 (CH × 4), 128.4 (CH_2), 129.2 (CH × 2), 129.6 (CH), 129.7 (CH), 130.9 (C), 133.3 (C × 2), 135.6 (CH × 2), 135.7 (CH × 2), 159.0 (C); LR-EIMS, m/z 673 (0.5%, $[M - t\text{-Bu}]^+$), 121 (bp, $[C_8H_9O]^+$); HR-EIMS, calcd for $C_{32}H_{42}O_4Si_2I$ $[M - t\text{-Bu}]^+$: 673.1666, found: 673.1677.

(6*S*,7*R*)-6-(*t*-Butyldimethylsilyloxy)-8-(*t*-butyldiphenylsilyloxy)-7-(4-methoxybenzyloxy)-4-methyleneoct-2-yn-1-ol (14). To a stirred solution of $[PdCl_2(PPh_3)_2]$ (730.7 mg, 1.041 mmol), CuI (317.2 mg, 1.666 mmol), and PPh_3 (546.1 mg, 2.082 mmol) in benzene (50 mL) were added a solution of 2-propynyl alcohol (2.4 mL, 41.6 mmol) and **13** (7.3578 g, 10.411 mmol) in benzene (50 mL) and $BuNH_2$ (4.1 mL, 41.6 mmol) at 25 °C, and the resulting solution was stirred for 2 h. The reaction was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was roughly purified by silica-gel chromatography (500 g, hexane/benzene = 2) to give **14** (6.590 g, 96%).

14: a colorless oil; $[\alpha]_D^{16} = 11.9$ (c 0.545, $CHCl_3$); IR (neat) ν_{max} 3418, 3090, 3072, 3050, 3000, 2950, 2930, 2890, 2857, 1612, 1585, 1514, 1472, 1460, 1428, 1390, 1360, 1300, 1249, 1170, 1112, 1040, 1005, 940, 905, 827, 780, 740, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.02 (3H, s), 0.05 (3H, s), 0.84 (9H, s), 1.06 (9H, s), 1.43 (1H, brt, $J = 6.2$ Hz), 2.35 (2H, d, $J = 6.1$ Hz), 3.61–3.75 (3H, m), 3.80 (3H, s), 4.23 (1H, dt, $J = 2.3$, 6.1 Hz), 4.28 (2H, d, $J = 6.2$ Hz), 4.58 (1H, d, $J = 11.3$ Hz), 4.67 (1H, d, $J =$ 11.3 Hz), 5.28 (1H, brs), 5.39 (1H, brd, $J = 1.9$ Hz), 6.84 (2H, d, $J = 8.8$ Hz), 7.24 (2H, d, $J = 8.8$ Hz), 7.32–7.45 (6H, m), 7.64–7.69 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6 (CH_3), −4.3 (CH_3), 18.1 (C), 19.1 (C), 25.9 ($CH_3 \times 3$), 26.8 ($CH_3 \times 3$), 40.6 (CH_2), 51.5 (CH_2), 55.2 (CH_3), 63.9 (CH_2), 71.3 (CH), 72.8 (CH_2), 82.9 (CH), 86.3 (C), 87.4 (C), 113.6 (CH × 2), 124.7

(CH_2), 127.7 (CH × 4), 128.1 (C), 129.2 (CH × 2), 129.7 (CH × 2), 131.1 (C), 133.3 (C), 133.5 (C), 135.6 (CH × 4), 159.0 (C); LR-EIMS, *m/z* 601 (0.61%, $[M - t\text{-Bu}]^+$), 121 (bp, $[C_8H_9O]^+$); HR-EIMS, calcd for $C_{35}H_{45}O_5Si_2$ $[M - t\text{-Bu}]^+$: 601.2806, found: 601.2801.

(2*E*,6*S*,7*R*)-6-(*t*-Butyldimethylsilyloxy)-8-(*t*-butyldiphenylsilyloxy)-7-(4-methoxybenzyloxy)-4-methyleneoct-2-en-1-ol (15). To a solution of **14** (6.590 g, 10.00 mmol) in ether (100 mL) was added Red-Al® (7.0 mL, 65% solution in toluene, 23.3 mmol) at −25 °C. After the mixture was stirred for 1 h, the reaction was quenched with EtOAc (7 mL) and 2 M aqueous NaOH (7 mL). The mixture was stirred for 30 min at ambient temperature, filtered through a celite pad, and condensed under reduced pressure. The residue was purified by silica-gel chromatography (300 g, hexane/EtOAc = 5) to give **15** (5.455 g, 83%).

15: a colorless oil; $[\alpha]_D^{17} = 3.32$ (*c* 1.50, $CHCl_3$); IR (neat) ν_{max} 3421, 3071, 3050, 3030, 3010, 2998, 2950, 2926, 2890, 2855, 1611, 1588, 1513, 1472, 1462, 1428, 1389, 1360, 1302, 1248, 1173, 1112, 1037, 1006, 971, 937, 895, 826, 776, 741, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ −0.07 (3H, s), −0.06 (3H, s), 0.82 (9H, s), 1.06 (9H, s), 1.23 (1H, brt, $J = 5.8$ Hz), 2.36 (1H, dd, $J = 8.4, 14.1$ Hz), 2.45 (1H, dd, $J = 3.7, 14.1$ Hz), 3.60 (1H, dt, $J = 2.4, 6.0$ Hz), 3.70–3.86 (2H, m), 3.80 (3H, s), 4.03–4.12 (1H, m), 4.13 (2H, brt, $J = 5.6$ Hz), 4.60 (1H, d, $J = 11.4$ Hz), 4.65 (1H, d, $J = 11.4$ Hz), 5.02 (1H, brs), 5.07 (1H, brs), 5.77 (1H, td, $J = 5.6, 16.0$ Hz), 6.22 (1H, d, $J = 16.0$ Hz), 6.84 (2H, d, $J = 8.5$ Hz), 7.24 (2H, d, $J = 8.5$ Hz), 7.32–7.45 (6H, m), 7.63–7.69 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5 (CH_3), −4.3 (CH_3), 18.0 (C), 19.1 (C), 25.9 (CH_3 × 3), 26.8 (CH_3 × 3), 35.9 (CH_2), 55.2 (CH_3), 63.5 (CH_2), 64.1 (CH_2), 71.7 (CH), 72.9 (CH_2), 83.0 (CH), 113.6 (CH × 2), 119.0 (CH_2), 127.7 (CH × 4), 128.0 (CH), 129.3 (CH × 2), 129.6 (CH × 2), 131.1 (C), 133.3 (C + CH), 133.5 (C), 135.6 (CH × 4), 142.1 (C), 158.9 (C); LR-EIMS, *m/z* 603 (0.69%, $[M - t\text{-Bu}]^+$), 121 (bp, $[C_8H_9O]^+$); HR-EIMS, calcd for $C_{35}H_{47}O_5Si_2$ $[M - t\text{-Bu}]^+$: 603.2962, found: 603.2952.

(2*S*,3*S*,6*S*,7*R*)-6-(*t*-Butyldimethylsilyloxy)-8-(*t*-butyldiphenylsilyloxy)-2,3-epoxy-7-(4-methoxybenzyloxy)-4-methyleneoctan-1-ol (16). To a suspension of MS4A (powder, 5.0 g) in CH_2Cl_2 (100 mL) were added (+)-DET (diethyl tartrate) (0.21 mL, 1.24 mmol) and Ti(O*i*-Pr)$_4$ (0.24 mL, 0.83 mmol) at −40 °C, and the mixture was stirred for 30 min. TBHP (*t*-butyl hydroperoxide) (3.2 mL, 5.29 M in toluene, 16.5 mmol) was then added at the same temperature. After the mixture was stirred for 30 min, a solution of **15** (5.4546 g, 8.2516 mmol) in CH_2Cl_2 (10 mL) was added dropwise to the mixture at −40 °C. Then, the mixture was warmed to −25 °C and stirred for 27 h. Dimethyl sulfide (2.7 mL) was added to the mixture, and the mixture was stirred for 30 min. Then, 10% aqueous DL-tartaric acid (0.5 mL) was added at ambient temperature. After the mixture was stirred for 30 min, NaF (250 mg) was added, and the mixture was further stirred for 1 h. The reaction mixture was filtered through a celite pad and condensed under the reduced pressure. The residue was purified by silica-gel chromatography (20 g, hexane/EtOAc = 10) to give **16** (5.253 g, 94%).

16: a colorless oil; $[\alpha]_D^{18} = -5.87$ (*c* 0.490, $CHCl_3$); IR (neat) ν_{max} 3447, 3070, 3047, 3000, 2950, 2926, 2890, 2854, 1611, 1585, 1512, 1472, 1460, 1427, 1249, 1170, 1112, 1085, 1040, 1005, 970, 940, 905, 825, 775, 745, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ −0.02 (3H, s), 0.00 (3H, s), 0.82 (9H, s), 1.06 (9H, s), 1.62 (1H, dd, $J = 5.3, 7.8$ Hz), 2.13 (1H, dd, $J = 3.5, 14.2$ Hz), 2.21 (1H, dd, $J = 8.1, 14.2$ Hz), 3.02 (1H, brtd, $J = 2.4, 3.9$ Hz), 3.37 (1H, d, $J = 2.1$ Hz), 3.55–3.67 (2H, m), 3.71 (2H, d, $J = 6.2$ Hz), 3.80 (3H, s), 3.85 (1H, brddd, $J = 2.8, 5.3, 12.5$ Hz), 4.02–4.08 (1H, m), 4.62 (2H, s), 5.03 (1H, s), 5.22 (1H, s), 6.84 (2H, d, $J = 8.5$ Hz), 7.23 (2H, d, $J = 8.5$ Hz), 7.32–7.45 (6H, m), 7.64–7.69 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.41 (CH_3), −4.36 (CH_3), 18.0 (C), 19.1 (C), 25.9 (CH_3 × 3), 26.8 (CH_3 × 3), 34.9 (CH_2), 55.2 (CH_3), 57.5 (CH), 59.0 (CH), 61.4 (CH_2), 64.3 (CH_2), 72.8 (CH), 72.9 (CH_2), 83.0 (CH), 113.6 (CH × 2), 115.7 (CH_2), 127.7 (CH × 4), 129.2 (CH × 2), 129.6 (CH), 129.7 (CH), 131.0 (C), 133.3 (C × 2), 135.6 (CH × 4), 141.9 (C), 159.0 (C); LR-EIMS, *m/z* 645 (0.26%, $[M - CH_3O]^+$), 121 (bp, $[C_8H_9O]^+$); HR-EIMS, calcd for $C_{38}H_{53}O_5Si_2$ $[M - CH_3O]^+$: 645.3432, found: 645.3433.

(2*S*,3*S*,6*S*,7*R*)-6-(*t*-Butyldimethylsilyloxy)-8-(*t*-butyldiphenylsilyloxy)-2,3-epoxy-4-methyleneoctane-1,7-diol (5). To a solution of **16** (4.212 g, 6.221 mmol) in CH_2Cl_2–H_2O (20:1, 63 mL) was added DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) (2.824 g, 12.442 mmol) at 0 °C, and the mixture was stirred for 50 min. The reaction was quenched with saturated aqueous $NaHCO_3$, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (5 g, hexane/EtOAc = 15) to give **5** (3.259 g, 94%).

5: a colorless oil; $[\alpha]_D^{18} = -0.19$ (*c* 0.460, $CHCl_3$); IR (neat) ν_{max} 3445, 3071, 3049, 3013, 2954, 2928, 2885, 2856, 1472, 1462, 1428, 1390, 1361, 1253, 1112, 1085, 1006, 937, 904, 836, 776, 740, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ −0.03 (3H, s), 0.02 (3H, s), 0.80 (9H, s), 1.07 (9H, s), 1.58–1.65 (1H, m), 2.17 (2H, d, $J = 5.7$ Hz), 2.49 (1H, d, $J = 2.0$ Hz), 3.06 (1H, td, $J = 2.5, 4.0$ Hz), 3.41 (1H, brd, $J = 2.1$ Hz), 3.60–3.78 (4H, m), 3.85–3.97 (2H, m), 5.05 (1H, brs), 5.24 (1H, brs), 7.34–7.44 (6H, m), 7.62–7.68 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.7 (CH_3), −4.2 (CH_3), 18.0 (C), 19.2 (C), 25.8 (CH_3 × 3), 26.8 (CH_3 × 3), 34.5 (CH_2), 57.5 (CH), 59.0 (CH), 61.4 (CH_2), 64.7 (CH_2), 72.7 (CH), 74.3 (CH), 116.1 (CH_2), 127.8 (CH × 4), 129.8 (CH × 2), 133.1 (C × 2), 135.5 (CH × 4), 141.3 (C); LR-FDMS, *m/z* 557 (bp, $[M + H]^+$), 499 (bp, $[M - t\text{-Bu}]^+$); HR-FDMS, calcd for $C_{31}H_{49}O_5Si_2$ $[M + H]^+$: 557.3119, found: 557.3133.

(1*S*)-1-[(2*R*,5*S*,6*R*)-5-(*t*-Butyldimethylsilyloxy)-6-(*t*-butyldiphenylsilyloxymethyl)-3-methyleneoxan-2-yl]-1,2-ethanediol (4). To a solution of **5** (120 mg, 0.215 mmol) in CH_2Cl_2 (2.2 mL) was added CSA (*dl*-camphor-10-sulfonic acid) (5 mg, 0.022 mmol) at 0 °C, and the mixture was stirred for 10 min. The reaction was quenched with saturated aqueous $NaHCO_3$, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (10 g, hexane/EtOAc = 6) to give **4** (72 mg, 60%).

4: a colorless oil; $[\alpha]_D^{15} = 0.73$ (*c* 0.545, $CHCl_3$); IR (neat) ν_{max} 3398, 3070, 3040, 3013, 2955, 2925, 2855, 1470, 1460, 1425, 1380, 1355, 1340, 1245, 1180, 1105, 1005, 905, 850, 830, 775, 740, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ −0.09 (3H, s), 0.02 (3H, s), 0.79 (9H, s), 1.05 (9H, s), 2.22 (1H, brdd, $J = 8.6, 13.3$ Hz), 2.34 (1H, brdd, $J = 4.5, 8.0$ Hz), 2.39 (1H, d, $J = 7.5$ Hz), 2.60 (1H, dd, $J = 5.2, 13.3$ Hz), 3.33 (1H, ddd, $J = 2.3, 6.1, 8.3$ Hz), 3.63–3.94 (6H, m), 4.02 (1H, d, $J = 5.3$ Hz), 4.92 (1H, brs), 4.97 (1H, brs), 7.33–7.45 (6H, m), 7.63–7.69 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.0 (CH_3), −4.2 (CH_3), 17.8 (C), 19.2 (C), 25.6 (CH_3 × 3), 26.8 (CH_3 × 3), 42.1 (CH_2), 63.8 (CH_2), 63.9 (CH_2), 68.1 (CH), 71.2 (CH), 80.5 (CH), 83.0 (CH), 110.4 (CH_2), 127.7 (CH × 4), 129.6 (CH × 2), 133.4 (C), 133.5 (C), 135.6 (CH × 4), 141.7 (C); LR-EIMS, *m/z* 499 (14.8%, $[\mathrm{M}-t\text{-Bu}]^+$), 73 (bp, $[\mathrm{C_3H_5O_2}]^+$); HR-EIMS, calcd for $\mathrm{C_{27}H_{39}O_5Si_2}$ $[\mathrm{M}-t\text{-Bu}]^+$: 499.2336, found: 499.2349.

(1*S*)-1-[(2*R*,5*S*,6*R*)-6-(*t*-Butyldiphenylsilyloxymethyl)-5-hydroxy-3-methyleneoxan-2-yl]-1,2-ethanediol (17). To a mixture of **4** (59.3 mg, 0.106 mmol) in acetonitrile (1.5 mL) was added 29 drops of pyridine•HF complex (70% in pyridine) at 0 °C, and the mixture was stirred for 1.5 h. The reaction was quenched with saturated aqueous $\mathrm{NaHCO_3}$, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $\mathrm{MgSO_4}$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (10 g, hexane/EtOAc = 1/3) to give **17** (19.5 mg, 42%).

17: a colorless oil; $[\alpha]_{\mathrm{D}}^{23} = -24.0$ (*c* 0.980, $\mathrm{CHCl_3}$); IR (neat) $\nu_{\max}$ 3411, 3070, 3050, 2960, 2927, 2855, 1470, 1460, 1425, 1390, 1355, 1250, 1190, 1110, 1060, 1000, 905, 820, 740, 700 cm^{-1}; ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$) δ 1.06 (9H, s), 2.19 (1H, brs), 2.26 (1H, dd, $J = 8.4$, 13.5 Hz), 2.50 (1H, brs), 2.65 (1H, brs), 2.72 (1H, dd, $J = 5.6$, 13.5 Hz), 3.35 (1H, ddd, $J = 5.1$, 5.6, 8.4 Hz), 3.60–3.95 (6H, m), 4.03 (1H, d, $J = 4.6$ Hz), 4.93 (1H, brs), 5.05 (1H, brs), 7.36–7.50 (6H, m), 7.63–7.69 (4H, m); ^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$) δ 19.1 (C), 26.8 ($\mathrm{CH_3}$ × 3), 40.4 ($\mathrm{CH_2}$), 63.4 ($\mathrm{CH_2}$), 65.4 ($\mathrm{CH_2}$), 69.8 (CH), 70.8 (CH), 80.1 (CH), 80.7 (CH), 111.4 ($\mathrm{CH_2}$), 127.9 (CH × 4), 130.0 (CH × 2), 132.5 (C × 2), 135.5 (CH × 4), 141.1 (C); LR-EIMS, *m/z* 385 (2.6%, $[\mathrm{M}-t\text{-Bu}]^+$), 199 (bp, $[\mathrm{C_{12}H_{11}OSi}]^+$); HR-EIMS, calcd for $\mathrm{C_{21}H_{25}O_5Si}$ $[\mathrm{M}-t\text{-Bu}]^+$: 385.1472, found: 385.1502.

Methyl (2*R*,5*S*,6*R*)-6-(*t*-Butyldiphenylsilyloxymethyl)-5-hydroxy-3-methyleneoxane-2-carboxylate (3). To a solution of **17** (19.5 mg, 0.044 mmol) in methanol (1.0 mL) was added a solution of $\mathrm{NaIO_4}$ (14.0 mg, 0.065 mmol) in water (0.5 mL) dropwise at 0 °C, and the mixture was then stirred for 15 min at 25 °C. The mixture was diluted with water and extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $\mathrm{MgSO_4}$, filtered, and concentrated under reduced pressure. The resulting crude (2*R*,5*S*,6*R*)-6-(*t*-butyldiphenylsilyloxymethyl)-5-hydroxy-3-methyleneoxane-2-carbaldehyde (**18**) was dissolved in *t*-BuOH–$\mathrm{H_2O}$ (3.5:1, 4.5 mL). To the solution were added 2-methyl-2-butene (0.37 mL, 4.4 mmol) and $\mathrm{NaH_2PO_4 \cdot 2H_2O}$ (69 mg, 0.44 mmol) at 25 °C, and the mixture was stirred for 1 h. Then, $\mathrm{NaClO_2}$ (20 mg, 0.22 mmol) was added, and the mixture was stirred for 30 min. The reaction was quenched with saturated aqueous $\mathrm{NaHSO_3}$, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $\mathrm{MgSO_4}$, filtered, and concentrated under reduced pressure. The resulting crude carboxylic acid was dissolved in THF (2.0 mL), and a solution of diazomethane in ether, prepared from *N*-nitro-*N*-nitrosomethylguanidine, was added dropwise to the solution at 0 °C until the solution turned yellow. After the mixture was stirred for 10 min, it was concentrated under the reduced pressure. The residue was purified by silica-gel chromatography (1 g, hexane/EtOAc = 6) to give **3** (13.7 mg, 71% from **17**).

3: colorless needles; mp 118.0–118.3 °C; $[\alpha]_{\mathrm{D}}^{22}$ $-9.07°$ (*c* 0.710, $\mathrm{CHCl_3}$); IR (KBr) $\nu_{\max}$ 3508, 3077, 3069, 3010, 2997, 2960, 2928, 2855, 1748, 1475, 1465, 1440, 1430, 1305, 1278, 1270, 1113, 1069, 1048, 1005, 902, 880, 825, 800, 745, 706, 690, 620 cm^{-1}; ^{1}H NMR (300 MHz, $\mathrm{C_6D_6}$) δ 1.13 (9H, s), 2.03 (1H, brdd, $J = 9.5$, 13.0 Hz), 2.17 (1H, brs), 2.57 (1H, dd, $J = 5.5$, 13.0 Hz), 3.30–3.23 (1H, brtd, $J = 5.1$, 9.5 Hz), 3.32 (3H, s), 3.70 (1H, brdt, $J = 5.5$, 9.5 Hz), 3.95 (1H, dd, $J = 5.1$, 10.6 Hz), 3.98 (1H, dd, $J = 5.1$, 10.6 Hz), 4.34 (1H, s), 4.74 (1H, s), 4.80 (1H, s), 7.20–7.28 (6H, m), 7.78–7.84 (4H, m); ^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$) δ 19.1 (C), 26.8 ($\mathrm{CH_3}$ × 3), 40.3 ($\mathrm{CH_2}$), 52.1 ($\mathrm{CH_3}$), 66.7 ($\mathrm{CH_2}$), 71.2 (CH), 78.7 (CH × 2), 111.9 ($\mathrm{CH_2}$), 127.9 (CH × 4), 130.0 (CH × 2), 132.2 (C), 135.5 (CH × 4), 139.2 (C × 2), 169.2 (C); LR-FDMS, *m/z* 441 (9.5%, $[\mathrm{M}+\mathrm{H}]^+$), 383 (bp, $[\mathrm{M}-t\text{-Bu}]^+$); HR-FDMS, calcd for $\mathrm{C_{25}H_{33}O_5Si}$ $[\mathrm{M}+\mathrm{H}]^+$: 441.2097, found: 441.2099.

(2*R*,3*R*,6*S*,7*R*)-6-(*t*-Butyldimethylsilyloxy)-8-(*t*-butyldiphenylsilyloxy)-2,3-epoxy-7-(4-methoxybenzyloxy)-4-methyleneoctan-1-ol (19). To a suspension of MS4A (powder, 15 g) in $\mathrm{CH_2Cl_2}$ (120 mL) were added (−)-DET (0.41 mL, 2.39 mmol) and Ti(O-*i*-Pr)$_4$ (0.47 mL, 1.58 mmol) at −40 °C, and the mixture was stirred for 30 min. TBHP (7.2 mL, 4.92 M in toluene, 35.4 mmol) was then added at the same temperature. After the mixture was stirred for 30 min, a solution of **15** (10.6 g, 16.0 mmol) in $\mathrm{CH_2Cl_2}$ (40 mL) was added dropwise to the mixture at −40 °C. Then, the mixture was warmed to −25 °C and stirred for 33 h. Dimethyl sulfide (5.4 mL) was added to the mixture, and the mixture was stirred for 30 min. Then, 10% aqueous DL-tartaric acid (0.94 mL) was added at ambient temperature. After the mixture was stirred for 30 min, NaF (403 mg) was added, and the mixture was further stirred for 5 h. The reaction mixture was filtered through a celite pad and concentrated under the reduced pressure. The residue was purified by silica-gel chromatography (200 g, hexane/EtOAc = 6) to give **19** (10.62 g, 98%).

19: a colorless oil; $[\alpha]_{\mathrm{D}}^{19} = 0.34$ (*c* 1.055, $\mathrm{CHCl_3}$); IR (neat) $\nu_{\max}$ 3450, 3073, 3050, 2999, 2950, 2930, 2895, 2858, 1610, 1585, 1514, 1472, 1460, 1429, 1390, 1360, 1300, 1249, 1170, 1113, 1085, 1036, 1005, 940, 905, 836, 776, 745, 701 cm^{-1}; ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$) δ −0.03 (3H, s), 0.00 (3H, s), 0.82 (9H, s), 1.06 (9H, s), 2.15–2.30 (2H, m), 2.98 (1H, brtd, $J = 2.3$, 3.6 Hz), 3.36 (1H, brd, $J = 1.9$ Hz), 3.54–3.65 (2H, m), 3.69–3.88 (3H, m), 3.80 (3H, s), 4.03 (1H, dt, $J = 3.3$, 6.2 Hz), 4.61 (2H, s), 5.03 (1H, s), 5.21 (1H, s), 6.84 (2H, d, $J = 8.7$ Hz), 7.23 (2H, d, $J = 8.7$ Hz), 7.32–7.45 (6H, m), 7.63–7.69 (4H, m); ^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$) δ −4.5 ($\mathrm{CH_3}$ × 2), 18.0 (C), 19.2 (C), 25.9 ($\mathrm{CH_3}$ × 3), 26.9 ($\mathrm{CH_3}$ × 3), 35.4 ($\mathrm{CH_2}$), 55.3 ($\mathrm{CH_3}$), 56.8 (CH), 59.2 (CH), 61.3 ($\mathrm{CH_2}$), 64.3 ($\mathrm{CH_2}$), 71.7 (CH), 72.7 ($\mathrm{CH_2}$), 82.2 (CH), 113.6 (CH × 2), 116.1 ($\mathrm{CH_2}$), 127.7 (CH × 4), 129.2 (CH × 2), 129.6 (CH), 129.7 (CH), 131.1 (C), 133.3 (C), 133.4 (C), 135.6 (CH × 4), 141.0 (C), 159.0 (C); LR-FDMS, *m/z* 676 (46.0%, $[\mathrm{M}]^+$), 121 (bp, $[\mathrm{C_8H_9O}]^+$); HR-FDMS, calcd for $\mathrm{C_{39}H_{56}O_6Si_2}$ $[\mathrm{M}]^+$: 676.3616, found: 676.3624.

(2*R*,3*R*,6*S*,7*R*)-6-(*t*-Butyldimethylsilyloxy)-8-(*t*-butyldiphenylsilyloxy)-2,3-epoxy-4-methyleneoctan-1,7-diol (20). To a solution of **16** (10.62 g, 15.69 mmol) in $\mathrm{CH_2Cl_2}$–$\mathrm{H_2O}$ (10:1, 176 mL) was added DDQ (7.123 g, 31.38 mmol) at 0 °C, and the mixture was stirred for 40 min. The reaction was quenched with saturated aqueous $\mathrm{NaHCO_3}$, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $\mathrm{MgSO_4}$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (200 g, hexane/EtOAc = 5) to give **20** (7.17 g, 82%).

20: a colorless oil; $[\alpha]_{\mathrm{D}}^{17} = 2.78$ (*c* 1.04, $\mathrm{CHCl_3}$); IR (neat) $\nu_{\max}$ 3447, 3071, 3049, 2955, 2930, 2890, 2857, 1472, 1460, 1428, 1390, 1361, 1253, 1113, 1085, 1006, 940, 907, 836, 776, 740, 701 cm^{-1}; ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$) δ −0.05 (3H, s), 0.02 (3H, s), 0.79 (9H, s), 1.07 (9H, s), 1.74 (1H, brt, $J = 7.0$ Hz), 2.22 (1H, dd, $J = 5.1$, 14.4 Hz), 2.28 (1H, dd, $J = 5.8$, 14.4 Hz), 2.59 (1H, d, $J = 2.9$ Hz), 2.98–3.02 (1H, m), 3.39 (1H, brd, $J = 2.1$ Hz), 3.63–3.93 (6H, m), 5.02 (1H, brs), 5.22 (1H, brs), 7.34–7.47

(6H, m), 7.62–7.67 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.8 (CH_3), −4.2 (CH_3), 18.0 (C), 19.2 (C), 25.8 ($CH_3 \times 3$), 26.9 ($CH_3 \times 3$), 55.4 (CH_2), 57.2 (CH), 59.7 (CH), 61.5 (CH_2), 64.7 (CH_2), 71.5 (CH), 73.7 (CH), 115.7 (CH_2), 127.8 (CH × 4), 129.8 (CH × 2), 133.1 (C × 2), 135.5 (CH × 4), 140.5 (C); LR-EIMS, *m/z* 499 (6.2%, $[M - t\text{-Bu}]^+$), 73 (bp, $[C_3H_5O_2]^+$); HR-EIMS, calcd for $C_{27}H_{39}O_5Si_2$ $[M - t\text{-Bu}]^+$: 499.2336, found: 499.2330.

(1*R*)-1-[(2*S*,5*S*,6*R*)-5-(*t*-Butyldimethylsilyloxy)-6-(*t*-butyldiphenylsilyloxymethyl)-3-methyleneoxan-2-yl]-1,2-ethanediol (21). To a solution of **20** (7.17 g, 12.88 mmol) in CH_2Cl_2 (150 mL) was added CSA (300 mg, 1.291 mmol) at −20 °C, and the mixture was stirred for 30 min. The reaction was quenched with saturated aqueous $NaHCO_3$, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (200 g, hexane/EtOAc = 3) to give **21** (6.45 g, 90%).

21: a colorless oil; $[\alpha]_D^{17} = 20.3$ (*c* 0.745, $CHCl_3$); IR (neat) ν_{max} 3399, 3089, 3071, 3034, 2955, 2926, 2890, 2854, 1472, 1462, 1427, 1389, 1361, 1340, 1251, 1180, 1106, 1006, 905, 888, 855, 836, 776, 740, 701, 676 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.17 (3H, s), −0.01 (3H, s), 0.76 (9H, s), 1.06 (9H, s), 1.70 (1H, t, $J = 3.4$ Hz), 2.35 (1H, brdd, $J = 10.6$, 13.3 Hz), 2.54 (1H, brdd, $J = 5.0$, 13.3 Hz), 3.43 (1H, ddd, $J = 5.0$, 9.1, 10.6 Hz), 3.53 (1H, dd, $J = 7.4$, 10.5 Hz), 3.65 (1H, ddd, $J = 1.5$, 7.4, 9.1 Hz), 3.78–4.10 (5H, m), 5.00 (1H, brs), 5.02 (1H, brs), 7.30–7.45 (6H, m), 7.64–7.71 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.2 (CH_3), −4.2 (CH_3), 17.7 (C), 19.1 (C), 25.6 ($CH_3 \times 3$), 26.7 ($CH_3 \times 3$), 39.2 (CH_2), 64.6 (CH_2), 64.8 (CH_2), 67.7 (CH), 68.5 (CH), 78.2 (CH), 79.7 (CH), 114.1 (CH_2), 127.6 (CH × 4), 129.6 (CH × 2), 133.1 (C), 133.4 (C), 135.6 (CH × 4), 141.1 (C); LR-EIMS, *m/z* 499 (7.8%, $[M - t\text{-Bu}]^+$), 57 (bp, $[C_4H_9]^+$); HR-EIMS, calcd for $C_{27}H_{39}O_5Si_2$ $[M - t\text{-Bu}]^+$: 499.2336, found: 499.2321.

(1*R*)-1-[(2*S*,5*S*,6*R*)-6-(*t*-Butyldiphenylsilyloxymethyl)-5-hydroxy-3-methyleneoxan-2-yl]-1,2-ethanediol (22). To a mixture of **21** (78.7 mg, 0.141 mmol) in acetonitrile (1.5 mL) was added 29 drops of HF•pyridine complex (70% in pyridine) at 0 °C, and the mixture was stirred for 1.5 h. The reaction was quenched with saturated aqueous $NaHCO_3$, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (10 g, hexane/EtOAc = 1/3) to give **22** (38.2 mg, 61%).

22: a colorless oil; $[\alpha]_D^{18} = 13.1$ (*c* 1.69, $CHCl_3$); IR (neat) ν_{max} 3436, 3072, 3051, 2955, 2929, 2894, 2857, 1470, 1463, 1428, 1390, 1360, 1253, 1113, 1085, 1006, 938, 910, 836, 776, 740, 701 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (9H, s), 1.97 (1H, brs), 2.22 (1H, brs), 2.34 (1H, brdd, $J = 10.9$, 13.4 Hz), 2.68 (1H, dd, $J = 4.9$, 13.4 Hz), 3.16 (1H, brs), 3.50–4.05 (8H, m), 5.00 (1H, brs), 5.07 (1H, brs), 7.36–7.49 (6H, m), 7.63–7.70 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.0 (C), 26.8 ($CH_3 \times 3$), 37.4 (CH_2), 63.7 (CH_2), 66.4 (CH_2), 67.8 (CH), 70.6 (CH), 74.4 (CH), 78.1 (CH), 114.6 (CH_2), 127.8 (CH × 4), 130.0 (CH × 2), 132.4 (C × 2), 135.5 (CH × 4), 140.5 (C); LR-EIMS, *m/z* 385 (1.3%, $[M - t\text{-Bu}]^+$), 199 (bp, $[C_{12}H_{11}OSi]^+$); HR-EIMS, calcd for $C_{21}H_{25}O_5Si$ $[M - t\text{-Bu}]^+$: 385.1471, found: 385.1442.

Methyl (2*S*,5*S*,6*R*)-6-(*t*-Butyldiphenylsilyloxymethyl)-5-hydroxy-3-methyleneoxane-2-carboxylate (24). To a solution of **22** (38.2 mg, 0.086 mmol) in methanol (2.0 mL) was added a solution of $NaIO_4$ (28.0 mg, 0.13 mmol) in water (1.0 mL) dropwise at 0 °C, and the mixture was then stirred for 15 min at 25 °C. The mixture was diluted with water and extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude (2*S*,5*S*,6*R*)-6-(*t*-butyldiphenylsilyloxymethyl)-5-hydroxy-3-methyleneoxane-2-carbaldehyde (**23**) was dissolved in *t*-BuOH–H_2O (3.5:1, 4.5 mL). To the solution were added 2-methyl-2-butene (0.72 mL, 8.6 mmol) and $NaH_2PO_4 \cdot 2H_2O$ (134 mg, 0.859 mmol) at 25 °C, and the mixture was stirred for 1 h. Then, $NaClO_2$ (39 mg, 0.430 mmol) was added, and the mixture was stirred for 40 min. The reaction was quenched with saturated aqueous $NaHSO_3$, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude carboxylic acid was dissolved in THF (2.0 mL), and a solution of diazomethane in ether, prepared from *N*-nitro-*N*-nitrosomethylguanidine, was added dropwise to the solution at 0 °C until the solution turned yellow. After the mixture was stirred for 15 min, it was concentrated under the reduced pressure. The residue was purified by silica-gel chromatography (1 g, hexane/EtOAc = 6) to give **24** (24.4 mg, 64% from **22**).

24: a colorless oil; $[\alpha]_D^{25}$ +68.75 (*c* 1.095, $CHCl_3$); IR (film) ν_{max} 3511, 3074, 3051, 2955, 2934, 2859, 1748, 1473, 1463, 1429, 1391, 1362, 1341, 1327, 1264, 1210, 1113, 1010, 998, 913, 823, 789 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 1.14 (9H, s), 2.38 (1H, tdd, $J = 1.8$, 11.4, 13.0 Hz), 2.43–2.50 (1H, brs), 2.56 (1H, dd, $J = 5.1$, 13.0 Hz), 3.22 (3H, s), 3.73–3.83 (1H, m), 4.00 (1H, dd, $J = 5.5$, 10.6 Hz), 4.12 (1H, dd, $J = 4.4$, 10.4 Hz), 4.28 (1H, brtd, $J = 4.4$, 9.4 Hz), 4.58 (1H, s), 4.78–4.80 (2H, m), 7.15–7.24 (6H, m), 7.74–7.81 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1 (C), 26.8 ($CH_3 \times 3$), 37.8 (CH_2), 52.2 (CH_3), 66.5 (CH_2), 70.8 (CH), 75.0 (CH), 77.2 (CH), 115.5 (CH_2), 127.9 (CH × 4), 130.0 (CH × 2), 132.5 (C), 135.6 (CH × 4), 139.0 (C × 2), 170.8 (C); LR-FDMS, *m/z* 441 (10%, $[M + H]^+$), 383 (bp, $[M - t\text{-Bu}]^+$); HR-FDMS, calcd for $C_{25}H_{33}O_5Si$ $[M + H]^+$: 441.2097, found: 441.2076.

(3*R*)-5-(*t*-Butyldimethylsilyloxy)-3-methylpentanoic Acid (36). To a solution of **34** (290.7 mg, 1.262 mmol) in *t*-BuOH–H_2O (3.5:1, 11.7 mL) were added 2-methyl-2-butene (10.6 mL, 126 mmol) and $NaH_2PO_4 \cdot 2H_2O$ (1.969 g, 12.62 mmol) at 25 °C, and the mixture was stirred for 1 h. Then, $NaClO_2$ (570 mg, 6.302 mmol) was added, and the mixture was stirred for 30 min. The reaction was quenched with saturated aqueous $NaHSO_3$, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (20 g, hexane/EtOAc = 15) to give **36** (290 mg, 93%).

36: a colorless oil; $[\alpha]_D^{18} = -0.92$ (*c* 0.495, $CHCl_3$); IR (neat) ν_{max} 3600–2500 (br), 2960, 2930, 2855, 1709, 1472, 1463, 1381, 1256, 1174, 1097, 836, 776 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.89 (9H, s), 1.00 (3H, d, $J = 6.5$ Hz), 1.41–1.66 (2H, m), 2.04–2.26 (2H, m), 2.41 (1H, dd, $J = 5.6$, 14.5 Hz), 3.61–3.75 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.4 ($CH_3 \times 2$), 18.3 (C), 19.8 (CH_3), 25.9 ($CH_3 \times 3$), 27.3 (CH), 39.1 (CH_2), 41.4 (CH_2), 61.1 (CH_2), 178.8 (C); LR-EIMS, *m/z* 189 (39.8%, $[M - t\text{-Bu}]^+$), 75 (bp, $[M + H]^+$); HR-EIMS, calcd for $C_8H_{17}O_3Si$ $[M - t\text{-Bu}]^+$: 189.0947, found: 189.0948.

(4*S*)-4-Benzyl-3-[(3*R*)-5-(*t*-butyldimethylsilyloxy)-3-methylpentanoyl]oxazolidin-2-one (38). To a solution of **36** (84.9 mg, 0.345 mmol) in CH_2Cl_2 (1.5 mL) were added Et_3N (0.14 mL, 1.003 mmol) and trimethylacetyl chloride (0.051 mL, 0.414 mmol) at 0 °C, and the mixture was stirred for 30 min. Then, THF (1.5 mL), LiCl (29 mg, 0.684 mmol), and (*S*)-(−)-4-benzyl-2-oxazolidinone (**37**) (79 mg, 0.446 mmol) were added, and the mixture was warmed to 25 °C and stirred for 9 h. The reaction was quenched with 0.5 M aqueous NaOH, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (10 g, hexane/EtOAc = 7) to give **38** (105.9 mg, 76%).

38: a colorless oil; $[\alpha]_D^{23} = 32.1$ (*c* 0.965, $CHCl_3$); IR (neat) ν_{max} 3090, 3060, 3028, 2955, 2926, 2880, 2854, 1780, 1696, 1495, 1475, 1460, 1450, 1385, 1349, 1250, 1210, 1193, 1094, 1045, 1005, 835, 775, 760, 745, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (6H, s), 0.89 (9H, s), 1.02 (3H, d, $J = 6.7$ Hz), 1.40–1.54 (1H, m), 1.59–1.71 (1H, m), 2.16–2.33 (1H, m), 2.75 (1H, dd, $J = 9.8$, 13.3 Hz), 2.82–2.97 (2H, m), 3.32 (1H, dd, $J = 3.3$, 13.3 Hz), 3.62–3.75 (2H, m), 4.12–4.22 (2H, m), 4.68 (1H, tdd, $J = 3.3$, 6.8, 9.8 Hz), 7.19–7.37 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.3 ($CH_3 \times 2$), 18.3 (C), 19.8 (CH_3), 25.9 ($CH_3 \times 3$), 26.7 (CH), 38.0 (CH_2), 39.4 (CH_2), 42.4 (CH_2), 55.2 (CH), 61.1 (CH_2), 66.0 (CH_2), 127.3 (CH), 128.9 (CH × 2), 129.4 (CH × 2), 135.3 (C), 153.4 (C), 172.6 (C); LR-EIMS, *m/z* 405 (3.6%, $[M]^+$), 348 (bp, $[M - t\text{-Bu}]^+$); HR-EIMS, calcd for $C_{18}H_{26}NO_4Si$ $[M - t\text{-Bu}]^+$: 348.1631, found: 348.1628.

(4*S*)-4-Benzyl-3-[(2*S*,3*R*)-5-(*t*-butyldimethylsilyloxy)-2,3-dimethylpentanoyl]oxazolidin-2-one (39). To a solution of **38** (105.9 mg, 0.261 mmol) in THF (2.6 mL) was added NHMDS (sodium hexamethyldisilazanide) (0.3 mL, 1.0 M solution in THF, 0.3 mmol) at −78 °C, and the mixture was stirred for 30 min. Then, MeI (0.08 mL, 1.285 mmol) was added, and the mixture was stirred for 33 h. The reaction was quenched with saturated aqueous NH_4Cl. After the mixture was warmed to ambient temperature, saturated aqueous $Na_2S_2O_3$ was added, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (10 g, hexane/EtOAc = 20) to give **39** (96.1 mg, 88%).

39: a colorless oil; $[\alpha]_D^{18} = 62.8$ (*c* 0.630, $CHCl_3$); IR (neat) ν_{max} 3090, 3060, 3030, 2950, 2929, 2880, 2857, 1783, 1698, 1498, 1472, 1460, 1455, 1384, 1349, 1289, 1239, 1208, 1195, 1100, 1051, 1030, 1015, 990, 975, 903, 836, 812, 776, 763, 747, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (6H, s), 0.89 (9H, s), 0.91 (3H, d, $J = 6.8$ Hz), 1.16 (3H, d, $J = 6.7$ Hz), 1.34–1.47 (1H, m), 1.58–1.70 (1H, m), 1.89–2.05 (1H, m), 2.76 (1H, dd, $J = 9.7$, 13.3 Hz), 3.29 (1H, dd, $J = 3.2$, 13.3 Hz), 3.57–3.77 (3H, m), 4.10–4.21 (2H, m), 4.65 (1H, brtdd, $J = 3.5$, 6.2, 9.7 Hz), 7.19–7.37 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.37 (CH_3), −5.32 (CH_3), 12.7 (CH_3), 15.4 (CH_3), 18.3 (C), 25.9 ($CH_3 \times 3$), 32.1 (CH), 37.8 (CH_2), 38.1 (CH_2), 42.2 (CH), 55.5 (CH), 61.5 (CH_2), 65.9 (CH_2), 127.3 (CH), 128.9 (CH × 2), 129.4 (CH × 2), 135.4 (C), 153.0 (C), 176.7 (C); LR-EIMS, *m/z* 419 (3.8%, $[M]^+$), 362 (bp, $[M - t\text{-Bu}]^+$); HR-EIMS, calcd for $C_{19}H_{28}NO_4Si$ $[M - t\text{-Bu}]^+$: 362.1788, found: 362.1783.

(2*S*,3*R*)-5-(*t*-Butyldimethylsilyloxy)-2,3-dimethylpentanol (40). To a solution of $LiAlH_4$ (113 mg, 2.978 mmol) in THF (10 mL) was added a solution of **39** (416 mg, 0.991 mmol) in THF (3.0 mL) at 0 °C, and the mixture was stirred for 10 min. The reaction was quenched with saturated aqueous potassium sodium tartrate, and the mixture was stirred at ambient temperature until the solution became clear. The mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (10 g, hexane/EtOAc = 6) to give **40** (164.8 mg, 67%).

40: a colorless oil; $[\alpha]_D^{16} = 4.0$ (*c* 0.725, $CHCl_3$); IR (neat) ν_{max} 3357, 2955, 2927, 2880, 2857, 1472, 1465, 1385, 1360, 1256, 1095, 1030, 1005, 940, 895, 835, 805, 774 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (6H, s), 0.81 (3H, d, $J = 7.0$ Hz), 0.84 (3H, d, $J = 7.0$ Hz), 0.90 (9H, s), 1.32–1.45 (1H, m), 1.53–1.82 (3H, m), 3.43–3.75 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.3 ($CH_3 \times 2$), 11.8 (CH_3), 14.7 (CH_3), 18.3 (C), 26.0 ($CH_3 \times 3$), 30.1 (CH), 37.8 (CH_2), 39.8 (CH), 61.7 (CH_2), 66.7 (CH_2); LR-FDMS, *m/z* 247 (1.7%, $[M + H]^+$), 189 (bp, $[M - t\text{-Bu}]^+$); HR-FDMS, calcd for $C_9H_{21}O_2Si$ $[M - t\text{-Bu}]^+$: 189.1311, found: 189.1313.

(2*R*,3*S*,4*R*)- and (2*S*,3*S*,4*R*)-1-(Benzyloxy)-6-(*t*-butyldimethylsilyloxy)-3,4-dimethylhexan-2-ol (42). To a solution of **40** (137.0 mg, 0.556 mmol) in CH_2Cl_2 (6.0 mL) were added MS4A (powder, 150 mg), NMO (4-methylmorpholine *N*-oxide) (130 mg, 1.11 mmol), and TPAP (20 mg, 0.057 mmol) at 25 °C, and the mixture was stirred for 20 min. Then, the mixture was immediately filtered through a Florisil pad, and the filtrate was condensed under reduced pressure. The resulting aldehyde was dissolved in THF (2 mL), and the solution was added dropwise at −78 °C to a solution of benzyloxymethyllithium, generated in situ from (benzyloxymethyl)tributylstannane (**41**) (1.011 g, 2.459 mmol) and BuLi (1.5 mL, 1.58 M in hexane, 2.37 mmol) in THF (5.0 mL) at −78 °C for 30 min. After the mixture was stirred for 30 min, the reaction was quenched with MeOH. The mixture was condensed under reduced pressure, and the residue was diluted with ether and saturated aqueous $NaHCO_3$. The mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (15 g, hexane/EtOAc = 10) to give **42** (108.0 mg, 66% from **40**) as a 5:1 mixture of diastereomers.

42: a colorless oil; IR (neat) ν_{max} 3484, 3092, 3067, 3034, 2963, 2932, 2900, 2861, 1500, 1473, 1463, 1454, 1390, 1360, 1257, 1099, 1025, 1005, 940, 900, 836, 810, 776, 740, 698, 668 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.037 (6H × 5/6, s), 0.041 (6H × 1/6, s), 0.80 (3H × 1/6, d, $J = 6.9$ Hz), 0.81 (3H × 5/6, d, $J = 6.7$ Hz), 0.87–0.90 (3H × 1/6, m), 0.88 (9H × 5/6, s), 0.89 (9H × 1/6, s), 0.90 (3H × 5/6, d, $J = 7.0$ Hz), 1.32–1.73 (4H, m), 2.28 (1H × 1/6, d, $J = 3.4$ Hz), 2.32 (1H × 5/6, d, $J = 3.3$ Hz), 3.39 (1H × 5/6, t, $J = 8.8$ Hz), 3.43 (1H × 1/6, t, $J = 8.8$ Hz), 3.51–3.70 (3H, m), 3.70–3.80 (1H, m), 4.56 (2H, s), 7.25–7.40 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) (major isomer) δ −5.3 ($CH_3 \times 2$), 9.7 (CH_3), 14.9 (CH_3), 18.3 (C), 26.0 ($CH_3 \times 3$), 30.6 (CH), 38.2 (CH_2), 39.4 (CH), 61.4 (CH_2), 72.5 (CH), 73.34 (CH_2), 73.39 (CH_2), 127.7 (CH × 2), 127.8 (CH), 128.4 (CH × 2), 138.0 (C); LR-EIMS, *m/z* 366 (0.5%, $[M]^+$), 309 (1.4%, $[M - t\text{-Bu}]^+$), 91 (bp, $[C_7H_7]^+$); HR-EIMS, calcd for $C_{17}H_{29}O_3Si$ $[M - t\text{-Bu}]^+$: 309.1886, found: 309.1884.

(2*S*,3*S*,4*R*)-2-Benzyloxymethyl-3,4-dimethyloxan-2-ol (28). To a solution of **42** (10.3 mg, 0.028 mmol) in CH_2Cl_2 (1.0 mL) was added DMPI (Dess–Martin periodinane) (24 mg, 0.056 mmol) at 25 °C, and the mixture was stirred for 6 h. Then, saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$ were added, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was passed through a short silica-gel column (1 g) with hexane–EtOAc (30:1), and the eluate was condensed under reduced pressure. The resulting crude ketone was dissolved in THF (0.8 mL), and Bu_4NF (0.057 mL, 1.0 M in THF, 0.057 mmol) was added to the solution at 25 °C. After the mixture was stirred for 40 min, water was added to the mixture. The resulting mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (1 g, hexane/EtOAc = 7) to give **28** (5.9 mg, 81% from **42**).

28: a colorless oil; $[\alpha]_D^{24} = -50.9$ (*c* 1.70, $CHCl_3$); IR (neat) ν_{max} 3434, 3090, 3070, 3030, 2975, 2950, 2931, 2877, 1495, 1455, 1375, 1260, 1205, 1155, 1092, 1060, 995, 975, 950, 910, 880, 840, 740, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (3H, d, $J = 6.6$ Hz), 0.92 (3H, d, $J = 6.6$ Hz), 1.23 (1H, dqd, $J = 1.7$, 6.6, 11.0 Hz), 1.36 (1H, brdq, $J = 4.8$, 12.8 Hz), 1.52 (1H, dddd, $J = 1.5$, 2.6, 4.0, 13.2 Hz), 1.70 (1H, dqdd, $J = 4.0$, 6.6, 11.0, 12.8 Hz), 2.93 (1H, d, $J = 1.7$ Hz), 3.40 (1H, d, $J = 9.5$ Hz), 3.52 (1H, d, $J = 9.5$ Hz), 3.66 (1H, ddd, $J = 1.5$, 4.8, 11.2 Hz), 3.97 (1H, ddd, $J = 2.6$, 11.2, 12.8 Hz), 4.62 (1H, d, $J = 12.2$ Hz), 4.66 (1H, d, $J = 12.2$ Hz), 7.24–7.39 (5H, m); ^1H NMR (300 MHz, C_6D_6) δ 0.79 (3H, d, $J = 6.6$ Hz), 0.94 (3H, d, $J = 6.6$ Hz), 1.14 (1H, dqd, $J = 1.0$, 6.6, 10.6 Hz), 1.23 (2H, m), 1.72 (1H, qndd, $J = 6.6$, 9.2, 10.6 Hz), 2.83 (1H, d, $J = 1.0$ Hz), 3.34 (1H, d, $J = 9.9$ Hz), 3.41 (1H, d, $J = 9.9$ Hz), 3.57 (1H, ddd, $J = 2.9$, 4.4, 11.0 Hz), 3.98 (1H, m), 4.43 (1H, d, $J = 12.1$ Hz), 4.47 (1H, d, $J = 12.1$ Hz), 7.03–7.19 (3H, m), 7.23–7.28 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.5 (CH_3), 20.3 (CH_3), 31.1 (CH), 34.4 (CH_2), 41.7 (CH), 60.5 (CH_2), 73.89 (CH_2), 73.94 (CH_2), 97.3 (C), 127.7 (CH), 127.8 (CH × 2), 128.4 (CH × 2), 137.8 (C); LR-FDMS, *m/z* 250 (11.5%, $[M]^+$), 129 (bp, $[M - BnOCH_2]^+$); HR-FDMS, calcd for $C_{15}H_{22}O_3$ $[M]^+$: 250.1568, found: 250.1548.

(3*R*)-5-(4-Methoxybenzyloxy)-3-methylpentan-1-ol (44). To a solution of $LiAlH_4$ (164 mg, 4.32 mmol) in THF (20 mL) was added a solution of **34** (684 mg, 2.97 mmol) in THF (5.0 mL) at 25 °C, and the mixture was stirred for 30 min. Then, water (0.7 mL), 15% aqueous NaOH (0.7 mL), and water (2.1 mL) were added dropwise in turn to the stirred reaction mixture. The mixture was filtered through a celite pad, and the pad was washed with EtOAc several times. The combined filtrate and washings were condensed under reduced pressure. The crude alcohol **43** was dissolved in DMF (30 mL), and NaH (724 mg, 60% oil suspension, 18.1 mmol) was added to the mixture at 0 °C. After the mixture was vigorously stirred for 15 min, 4-methoxybenzyl chloride (0.82 mL, 6.05 mmol) and Bu_4NI (111 mg, 0.301 mmol) were added. Then, the mixture was warmed to 25 °C and stirred for 18 h. The reaction was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was dissolved in THF (30 mL), and Bu_4NF (6.0 mL, 1.0 M in THF, 6.0 mmol) was added to the solution at 25 °C. After the mixture was stirred for 30 min, water was added to the mixture. The resulting mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (20 g, hexane/EtOAc = 7) to give **44** (710 mg, 100% from **34**).

44: a colorless oil; $[\alpha]_D^{24} = -3.01$ (*c* 0.760, $CHCl_3$); IR (neat) ν_{max} 3399, 3070, 3030, 3000, 2955, 2931, 2871, 1614, 1587, 1514, 1465, 1366, 1302, 1249, 1173, 1095, 1036, 821 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.91 (3H, d, $J = 6.6$ Hz), 1.38–1.51 (2H, m), 1.52–1.81 (3H, m), 3.42–3.57 (2H, m), 3.58–3.76 (2H, m), 3.80 (3H, s), 4.43 (2H, s), 6.87 (2H, d, $J = 8.8$ Hz), 7.25 (2H, d, $J = 8.8$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8 (CH_3), 26.7 (CH), 36.5 (CH_2), 39.8 (CH_2), 55.2 (CH_3), 60.7 (CH_2), 68.1 (CH_2), 72.6 (CH_2), 113.7 (CH × 2), 129.2 (CH × 2), 130.5 (C), 159.1 (C); LR-EIMS, *m/z* 238 (6.1%, $[M]^+$), 121 (bp, $[C_8H_9O]^+$); HR-EIMS, calcd for $C_{14}H_{22}O_3$ $[M]^+$: 238.1569, found: 238.1570.

(3*S*)-5-(4-Methoxybenzyloxy)-3-methylpentanoic Acid (45). To a solution of **44** (640.0 mg, 2.685 mmol) in CH_2Cl_2 (25.0 mL) were added MS4A (powder, 600 mg), NMO (799 mg, 6.82 mmol), and TPAP (96 mg, 0.273 mmol) at 25 °C, and the mixture was stirred for 20 min. Then, the mixture was immediately filtered through a Florisil pad, and the filtrate was condensed under reduced pressure. The resulting aldehyde was dissolved in *t*-BuOH–H_2O (3.5:1, 18 mL), and 2-methyl-2-butene (22 mL, 262 mmol) and $NaH_2PO_4 \cdot 2H_2O$ (4.2 g, 26.9 mmol) were added to the mixture at 25 °C. After the mixture was stirred for 10 min, $NaClO_2$ (1.214 g, 13.42 mmol) was added, and the mixture was stirred for 30 min. The reaction was quenched with saturated aqueous $NaHSO_3$, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (20 g, hexane/EtOAc = 2) to give **45** (534 mg, 79% from **44**).

45: a colorless oil; $[\alpha]_D^{18} = -0.81$ (*c* 0.520, $CHCl_3$); IR (neat) ν_{max} 3600–2400 (br), 2959, 2930, 2870, 1709, 1611, 1586, 1514, 1463, 1443, 1421, 1410, 1380, 1366, 1303, 1249, 1173, 1096, 1035, 947, 850, 822, 665, 636 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.99 (3H, d, $J = 6.5$ Hz), 1.55 (1H, brqd, $J = 6.6$, 13.9 Hz), 1.69 (1H, brqd, $J = 6.4$, 13.9 Hz), 2.07–2.25 (2H, m), 2.39 (1H, dd, $J = 5.5$, 14.5 Hz), 3.44–3.56 (2H, m), 3.80 (3H, s), 4.43 (2H, s), 6.87 (2H, d, $J = 8.6$ Hz), 7.25 (2H, d, $J = 8.6$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8 (CH_3), 27.6 (CH), 36.1 (CH_2), 41.3 (CH_2), 55.2 (CH_3), 67.8 (CH_2), 72.6 (CH_2), 113.8 (CH × 2), 129.3 (CH × 2), 130.4 (C), 159.2 (C), 178.7 (C); LR-EIMS, *m/z* 252 (9.0%, $[M]^+$), 137 (bp, $[C_8H_9O2]^+$); HR-EIMS, calcd for $C_{14}H_{20}O_4$ $[M]^+$: 252.1362, found: 252.1362.

(4*S*)-4-Benzyl-3-[(3*S*)-5-(4-methoxybenzyloxy)-3-methylpentanoyl]oxazolidin-2-one (46). To a solution of **45** (69.6 mg, 0.276 mmol) in CH_2Cl_2 (1.5 mL) were added Et_3N (0.11 mL, 0.794 mmol) and trimethylacetyl chloride (0.041 mL, 0.333 mmol) at 0 °C, and the mixture was stirred for 30 min. Then, THF (1.5 mL), LiCl (23 mg, 0.543 mmol), and (*S*)-(−)-4-benzyl-2-oxazolidinone (**37**) (63 mg, 0.356 mmol) were added, and the mixture was warmed to 25 °C and stirred for 3 h. The reaction was quenched with 0.5 M aqueous NaOH, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (2 g, hexane/EtOAc = 8) to give **46** (76.6 mg, 68%).

46: a colorless oil; $[\alpha]_D^{16} = 30.7$ (*c* 0.545, $CHCl_3$); IR (neat) ν_{max} 3090, 3060, 3030, 2955, 2927, 2850, 1780, 1696, 1610, 1585, 1510, 1455, 1380, 1350, 1300, 1245, 1095, 1030, 820, 760, 745, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.00 (3H, d, $J = 6.7$ Hz), 1.51–1.64 (1H, m), 1.69–1.81 (1H, m), 2.19–2.36 (1H, m), 2.66 (1H, dd, $J = 9.8$, 13.3 Hz), 2.77 (1H, dd, $J = 7.9$, 16.4 Hz), 3.00 (1H, dd, $J = 5.8$, 16.4 Hz), 3.30 (1H, dd, $J = 3.3$, 13.3 Hz), 3.53 (2H, brt, $J = 6.7$ Hz), 3.79 (3H, s), 4.07–4.19 (2H, m), 4.42 (1H, d, $J = 11.5$ Hz), 4.45 (1H, d, $J = 11.5$ Hz), 4.65 (1H, tdd, $J = 3.3$, 6.9, 9.8 Hz), 6.87 (2H, d, $J = 8.7$ Hz), 7.17–7.36 (7H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.9 (CH_3), 26.9 (CH), 36.2 (CH_2), 37.9 (CH_2), 42.4 (CH_2), 55.1 (CH), 55.2 (CH_3), 66.0 (CH_2), 67.9 (CH_2), 72.5 (CH_2), 113.7 (CH × 2), 127.2 (CH), 128.9 (CH × 2), 129.2 (CH × 2), 129.3 (CH × 2), 130.6 (C), 135.3 (C), 153.4 (C), 159.0 (C), 172.4 (C); LR-EIMS, *m/z* 411 (6.8%, $[M]^+$), 121 (bp, $[C_8H_9O]^+$); HR-EIMS, calcd for $C_{24}H_{29}NO_5$ $[M]^+$: 411.2046, found: 411.2047.

(4*S*)-4-Benzyl-3-[(2*S*,3*S*)-2,3-dimethyl-5-(4-methoxybenzyloxy)pentanoyl]oxazolidin-2-one (47). To a solution of **46** (84.9 mg, 0.206 mmol) in THF (2 mL) was added NHMDS (0.23 mL, 1.0 M solution in THF, 0.23 mmol) at −78 °C, and the mixture was stirred for 30 min. Then, MeI (0.063 mL, 1.012 mmol) was added, and the mixture was stirred for 33 h. The reaction was quenched with saturated aqueous NH_4Cl. After the mixture was warmed to ambient temperature, saturated aqueous $Na_2S_2O_3$ was added, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (5 g, hexane/EtOAc = 9) to give **47** (46.1 mg, 53%) and unreacted **46** (20.5 mg, 24% recovery).

47: a colorless oil; $[\alpha]_D^{18} = 44.1$ (*c* 0.760, $CHCl_3$); IR (neat) ν_{max} 3091, 3071, 3035, 2965, 2937, 2876, 1780, 1699, 1613, 1586, 1514, 1499, 1480, 1455, 1384, 1350, 1303, 1247, 1209, 1100, 1035, 972, 920, 823, 762, 749, 731, 703, 682 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (3H, d, $J = 6.7$ Hz), 1.17 (3H, d, $J = 6.9$ Hz), 1.30–1.43 (1H, m), 1.73–1.87 (1H, m), 1.96–2.07 (1H, m), 2.74 (1H, dd, $J = 9.6$, 13.3 Hz), 3.28 (1H, dd, $J = 3.2$, 13.3 Hz), 3.39–3.57 (2H, m), 3.71 (1H, qn, $J = 6.9$ Hz), 3.77 (3H, s), 3.97 (1H, brdd, $J = 7.7$, 8.9 Hz), 4.07 (1H, dd, $J = 2.4$, 8.9 Hz), 4.38 (1H, d, $J = 11.4$ Hz), 4.41 (1H, d, $J = 11.4$ Hz), 4.57 (1H, dddd, $J = 2.4$, 3.2, 7.7, 9.6 Hz), 6.84 (2H, d, $J = 8.7$ Hz), 7.18–7.36 (7H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.0 (CH_3), 18.0 (CH_3), 32.0 (CH_2), 32.6 (CH), 37.8 (CH_2), 42.5 (CH), 55.2 (CH_3), 55.6 (CH), 65.9 (CH_2), 68.1 (CH_2), 72.6 (CH_2), 113.7 (CH × 2), 127.3 (CH), 128.9 (CH × 2), 129.2 (CH × 2), 129.4 (CH × 2), 130.7 (C), 135.4 (C), 153.2 (C), 159.1 (C), 176.7 (C); LR-EIMS, *m/z* 425 (7.4%, $[M]^+$), 121 (bp, $[C_8H_9O]^+$); HR-EIMS, calcd for $C_{25}H_{31}NO_5$ $[M]^+$: 425.2202, found: 425.2202.

(2*S*,3*S*)-2,3-Dimethyl-5-(4-methoxybenzyloxy)pentan-1-ol (48). To a solution of $LiAlH_4$ (96 mg, 2.53 mmol) in THF (6.0 mL) was added a solution of **39** (270 mg, 0.635 mmol) in THF (6.0 mL) at 0 °C, and the mixture was stirred for 30 min. The reaction was quenched with saturated aqueous potassium sodium tartrate, and the mixture was stirred at ambient temperature until the solution became clear. The mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (2 g, hexane/EtOAc = 2) to give **48** (128.7 mg, 80%).

48: a colorless oil; $[\alpha]_D^{19} = -10.2$ (*c* 0.530, $CHCl_3$); IR (neat) ν_{max} 3416, 2959, 2930, 2875, 1613, 1590, 1514, 1465, 1380, 1370, 1303, 1249, 1173, 1093, 1037, 820 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84 (3H, d, $J = 7.0$ Hz), 0.90 (3H, d, $J = 6.9$ Hz), 1.23–1.36 (1H, m), 1.57–1.85 (3H, m), 3.39–3.59 (4H, m), 3.80 (3H, s), 4.42 (1H, d, $J = 11.5$ Hz), 4.44 (1H, d, $J = 11.5$ Hz), 6.87 (2H, d, $J = 8.6$ Hz), 7.25 (2H, d, $J = 8.6$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.7 (CH_3), 17.5 (CH_3), 30.9 (CH_2), 32.0 (CH), 40.3 (CH), 55.3 (CH_3), 65.9 (CH_2), 68.9 (CH_2), 72.7 (CH_2), 113.8 (CH × 2), 129.3 (CH × 2), 130.4 (C), 159.1 (C); LR-EIMS, *m/z* 252 (11.9%, $[M]^+$), 121 (bp, $[C_8H_9O]^+$); HR-EIMS, calcd for $C_{15}H_{23}O_3$ $[M]^+$: 252.1725, found: 252.1722.

(2*R*,3*S*,4*S*)- and (2*S*,3*S*,4*S*)-1-(Benzyloxy)-3,4-dimethyl-6-(4-methoxybenzyloxy)hexan-2-ol (49). To a solution of **48** (128.7 mg, 0.510 mmol) in CH_2Cl_2 (5.0 mL) were added MS4A (powder, 130 mg), NMO (150 mg, 1.28 mmol), and TPAP (18 mg, 0.051 mmol) at 25 °C, and the mixture was stirred for 20 min. Then, the mixture was immediately filtered through a Florisil pad, and the filtrate was condensed under reduced pressure. The resulting aldehyde was dissolved in THF (2 mL), and the solution was added dropwise at −78 °C to a solution of benzyloxymethyllithium, generated in situ from (benzyloxymethyl)tributylstannane (**41**) (1.049 g, 2.551 mmol) and BuLi (1.55 mL, 1.58 M in hexane, 2.45 mmol) in THF (5.0 mL) at −78 °C for 30 min. After the mixture was stirred for 30 min, the reaction was quenched with MeOH. The mixture was condensed under reduced pressure, and the residue was diluted with ether and saturated aqueous $NaHCO_3$. The mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (15 g, hexane/EtOAc = 10) to give **49** (92.5 mg, 48% from **48**) as a 3:2 mixture of diastereomers.

49: a colorless oil; IR (neat) ν_{max} 3447, 3080, 3060, 3028, 2957, 2929, 2861, 1612, 1512, 1495, 1453, 1380, 1360, 1300, 1247, 1175, 1095, 1035, 820, 740, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82 (3H × 2/5, d, $J = 6.8$ Hz), 0.89 (3H × 2/5, d, $J = 7.0$ Hz), 0.91 (3H × 3/5, d, $J = 7.0$ Hz), 0.92 (3H × 3/5, d, $J = 6.8$ Hz), 1.20–1.81 (4H, m), 2.25 (1H × 3/5, d, $J = 3.4$ Hz), 2.32 (1H × 2/5, d, $J = 3.4$ Hz), 3.33–3.60 (4H, m), 3.72–3.90 (1H, m), 3.79 (3H, s), 4.34–4.48 (2H, m), 4.49–4.58 (2H, m), 6.86 (2H, d, $J = 8.6$ Hz), 7.18–7.38 (7H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.6 (CH_3 × 2/5), 10.4 (CH_3 × 3/5), 15.0 (CH_3 × 2/5), 18.0 (CH_3 × 3/5), 31.0 (CH × 2/5), 32.0 (CH × 3/5), 32.4 (CH_2 × 3/5), 35.0 (CH_2 × 2/5), 39.3 (CH × 2/5), 40.5 (CH × 3/5), 55.2 (CH_3), 68.3 (CH_2 × 2/5), 68.7 (CH_2 × 3/5), 71.8 (CH × 3/5), 72.5 (CH × 2/5), 72.6 (CH_2), 73.3 (CH_2), 73.4 (CH_2 × 2/5), 73.6 (CH_2 × 3/5), 113.7 (CH × 2), 127.7 (CH × 2), 128.3 (CH), 128.4 (CH × 2), 129.2 (CH × 2), 130.7 (C), 138.0 (C), 159.1 (C); LR-EIMS, *m/z* 372 (0.5%, $[M]^+$), 121 (bp, $[C_8H_9O]^+$); HR-EIMS, calcd for $C_{23}H_{32}O_4$ $[M]^+$: 372.2301, found: 372.2300.

(2*R*,3*S*,4*S*)-2-Benzyloxymethyl-3,4-dimethyloxan-2-ol (29). To a solution of **49** (12.9 mg, 0.034 mmol) in CH_2Cl_2 (1.0 mL) was added DMPI (29 mg, 0.068 mmol) at 25 °C, and the mixture was stirred for 2 h. Then, saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$ were added, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was passed through a short silica-gel column (1 g) with hexane–EtOAc (10:1), and the eluate was condensed under reduced pressure. The resulting crude ketone was dissolved in CH_2Cl_2 (1.0 mL), and water (0.05 mL) and DDQ (10 mg, 0.044 mmol) was added to the solution at 0 °C. After the mixture was stirred for 1 h, DDQ (10 mg, 0.044 mmol) was added. The reaction mixture was warmed to 25 °C and stirred for 30 min. Then, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with ether (×3). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (2 g, hexane/EtOAc = 15) to give **29** (7.0 mg, 82% from **49**).

29: a colorless oil; $[\alpha]_D^{23} = 39.9$ (*c* 1.085, $CHCl_3$); IR (neat) ν_{max} 3444, 3090, 3070, 3030, 2960, 2934, 2876, 1500, 1454, 1440, 1410, 1380, 1340, 1310, 1290, 1270, 1210, 1200, 1180, 1094, 1064, 1029, 990, 945, 920, 910, 875, 736, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.76 (3H, d, $J = 7.0$ Hz), 0.87 (3H, d, $J = 7.0$ Hz), 1.23 (1H, brtddd, $J = 1.1$, 3.1, 4.0, 13.4 Hz), 1.46 (1H, brdq, $J = 5.3$, 13.0 Hz), 1.64 (1H, brdq, $J = 4.0$, 7.0 Hz), 2.36 (1H, tqd, $J = 4.0$, 7.0, 13.0 Hz), 3.31 (1H, d, $J = 9.5$ Hz), 3.50 (1H, s), 3.53 (1H, d, $J = 9.5$ Hz), 3.66 (1H, brddd, $J = 1.1$, 5.3, 11.2 Hz), 3.97 (1H, brddd, $J = 3.1$, 11.2, 13.0 Hz), 4.56 (1H, d, $J = 11.9$ Hz), 4.72 (1H, d, $J = 11.9$ Hz), 7.25–7.39 (5H, m); ^{1}H NMR (300 MHz, C_6D_6) δ 0.66 (3H, d, $J = 7.0$ Hz), 0.75 (3H, d, $J = 7.0$ Hz), 0.96 (1H, brddd, $J = 2.9$, 4.0, 13.2 Hz), 1.33 (1H, brdq, $J = 5.5$, 13.0 Hz), 1.63 (1H, dq, $J = 4.0$, 7.0 Hz), 2.48 (1H, tqd, $J = 4.0$, 7.0, 12.5 Hz), 3.27 (1H, d, $J = 9.9$ Hz), 3.45 (1H, d, $J = 9.9$ Hz), 3.47 (1H, brs), 3.60 (1H, brdd, $J = 5.5$, 11.0 Hz), 4.03 (1H, ddd, $J = 2.9$, 11.0, 12.8 Hz), 4.32 (1H, d, $J = 12.1$ Hz), 4.47 (1H, d, $J = 12.1$ Hz), 7.04–7.25 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 6.8 (CH_3), 19.0 (CH_3), 27.1 (CH), 27.7 (CH_2), 38.9 (CH), 61.1 (CH_2), 73.9 (CH_2), 74.9 (CH_2), 97.1 (C), 127.8 ($CH \times 2 + CH$), 128.4 ($CH \times 2$), 137.7 (C); LR-FDMS, m/z 250 (6.0%, $[M]^+$), 232 (bp, $[M - H_2O]^+$); HR-FDMS, calcd for $C_{15}H_{22}O_3$ $[M]^+$: 250.1568, found: 250.1568.

We thank Mr. Kenji Watanabe and Dr. Eri Fukushi (GC-MS & NMR Laboratory, Graduate School of Agriculture, Hokkaido University) for the measurements of mass spectra. We are also grateful to Prof. Makoto Sasaki and Prof. Masato Oikawa (Graduate School of Life Sciences, Tohoku University) for helpful discussions. This work was supported in part by Grant-in-Aid (Nos. 18510179 and 18032001) from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

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