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Synthetic Studies on Ciguatoxin [2]; Synthesis of the A,B,C-ring System

Takahiro Oka, Kenshu Fujiwara, and Akio Murai*

Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo 060, Japan

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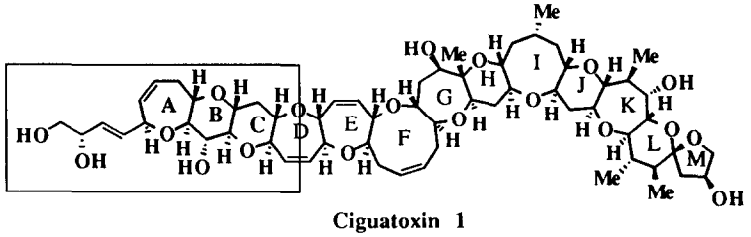
Abstract The synthesis of the A,B,C-ring system having all the natural substituents of ciguatoxin was achieved from D-glucose.

INTRODUCTION

As a course of the synthetic studies on ciguatoxin **1** isolated from moray eel *Gymnothorax javanicus* and determined structurally by Yasumoto *et al.*,[1] we have reported the first substrate-controlled and stereoselective synthesis of the natural enantiomer of the A,B,C-ring system of **1** including the completely constructed C-ring part from commercially available D-glucose as a communication.[2] The syntheses of the model compounds corresponding to the A,B,C-ring system of **1** have been recently accomplished by the Isobe and Hirama groups.[3] Continuing the previous paper,[4] we describe herein the detailed results of our A,B,C-ring system construction of **1**.

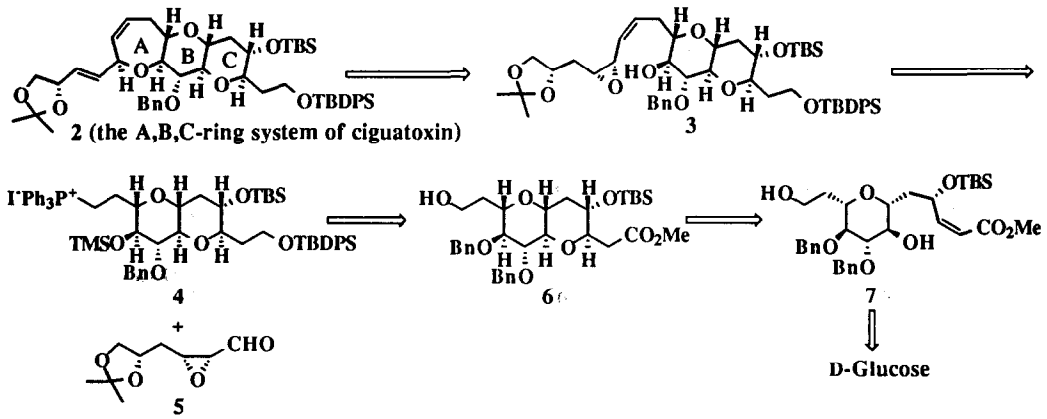


Ciguatoxin 1

0040-4020/98/$19.00
PII: S0040-4020(97)10254-X

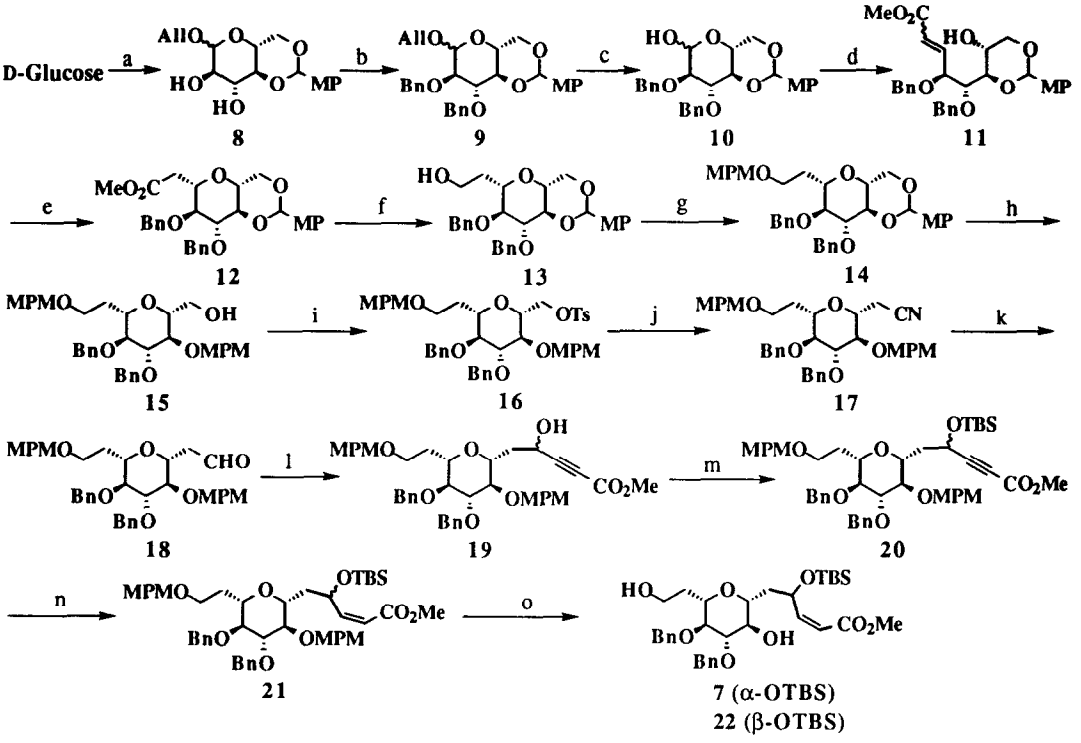
RESULTS AND DISCUSSION

The synthetic aim in this paper is to construct stereoselectively the natural enantiomer of the A,B,C-ring system in **1**. We planned to synthesize the compound **2** as a target of the A,B,C-ring system as shown in Scheme 1. The formation of the A-ring part would be expected to be derived from the epoxy alcohol **3**, as a crucial stage, which could be made from the phosphonium salt **4** and the aldehyde **5** by the Wittig reaction. Compound **4** could be produced from compound **6** using a standard manipulation, which would be constructed from the hydroxy α,β-unsaturated ester **7** by intramolecular cyclization reaction. We started our synthesis using the commercially available D-glucose for the preparation of **7**.



Scheme 1.

D-Glucose was converted *via* an allyl acetal, to the *p*-methoxybenzylidene acetal **8**,[5] which was transformed into the benzyl ether **9** (Scheme 2). Compound **9** provided the hemiacetal **10** using $(PPh_3)_3RhCl$ and then $HgCl_2$ and HgO[6] in a good yield. The Wittig reaction with $Ph_3P{=}CHCO_2Me$ of **10** led to an *E*:*Z*=2:1 mixture of the ester **11**, and the intramolecular cyclization reaction of **11** with NaH produced the tetrahydropyran **12** in a good yield and high stereoselectivity. Compound **12** was reduced with $LiAlH_4$ to the corresponding primary alcohol **13** which was protected to an MPM ether **14**. The highly selective cleavage of the *p*-methoxybenzylidene acetal part in **14** gave rise to the primary alcohol **15**. After tosylation of the hydroxy group of **15**, the tosyl group of **16** was substituted to the cyano group with KCN to obtain **17** which was reduced with DIBAL to the corresponding aldehyde **18**. The coupling reaction of **18** with lithiated methyl propiolate proceeded smoothly to yield an α:β=2:5 mixture of acetylene alcohols **19**. Although the yield of the α-OH product was low, the β-OH product could also be converted into the α-OH at an later stage. A mixture of **19** was silylated with TBSOTf to afford **20** which was hydrogenated with Lindlar catalyst to the *Z*-olefins **21**. MPM deprotection with DDQ allowed the separation of **7** and **22** in 22% and 58% yields, respectively.

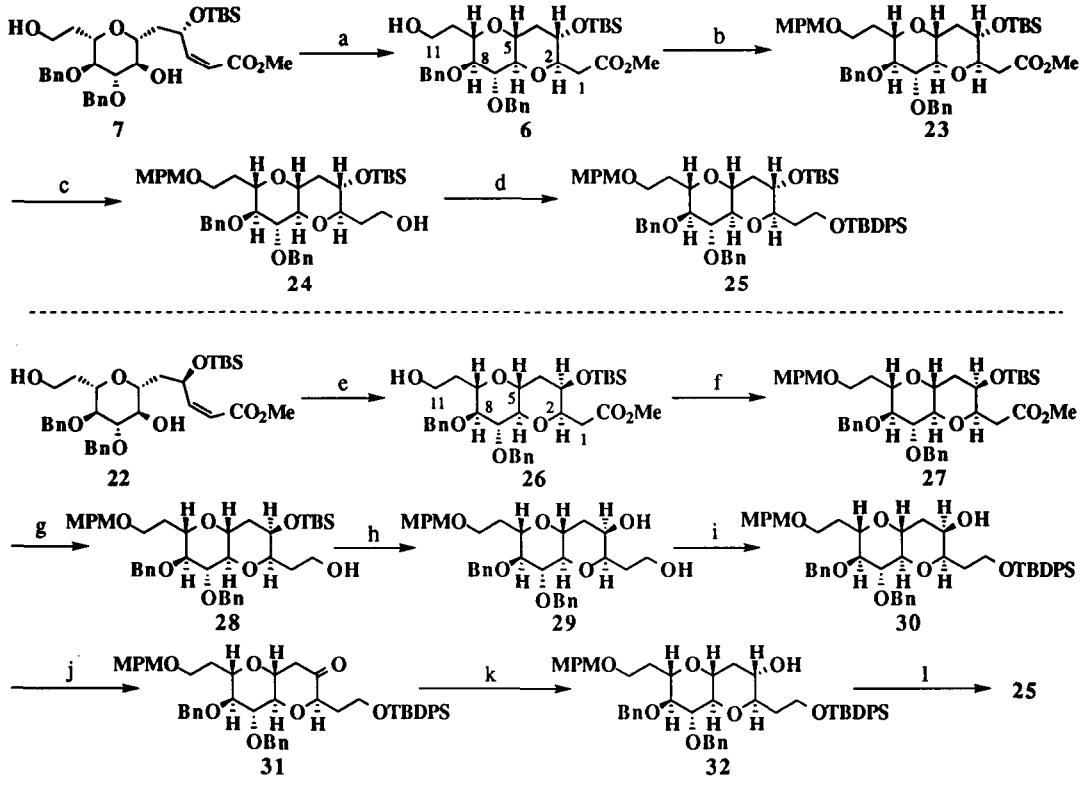


Reagents and Conditions: a) allyl alcohol, TfOH, 80 °C, 2 d; 4-MeO-PhCH(OMe)$_2$, PTS·H$_2$O, DMF, *in vacuo*, 50 °C, 4 h (67% for 2 steps); b) BnBr, NaH, THF-DMF (1:1), r.t., 5 h (62%); c) (Ph$_3$P)$_3$RhCl, *i*-Pr$_2$NEt, EtOH, reflux, 4 h; HgCl$_2$, HgO, acetone-H$_2$O (9:1), r.t., 1 h (92% for 2 steps); d) Ph$_3$P=CHCO$_2$Me, PhH, reflux, 24 h (99%, *E*:*Z*=4:1); e) NaH, THF, r.t., 16 h (94%); f) LiAlH$_4$, ether-THF (4:1), 0 °C, 30 min (98%); g) MPMCl, KH, TBAI, THF, r.t., 3 h (quant.); h) DIBAL, CH$_2$Cl$_2$, 0 °C, 1 h (95%); i) TsCl, NEt$_3$, DMAP, CH$_2$Cl$_2$, r.t., 6 h (quant.); j) KCN, DMSO, 50 °C, 7 h (99%); k) DIBAL, CH$_2$Cl$_2$, -78 °C, 30 min (95%); l) methyl propiolate, LDA, THF, -78 °C, 1 h (98%, α:β=2:5); m) TBSOTf, 2,6-lutidine, CH$_2$Cl$_2$, r.t., 15 min (97%); n) H$_2$, Lindlar cat., MeOH-PhH (6:1), r.t., 7 d (99%); o) DDQ, CH$_2$Cl$_2$-H$_2$O (10:1), r.t., 30 min (**7**, 22%; **22**, 58%).

Scheme 2.

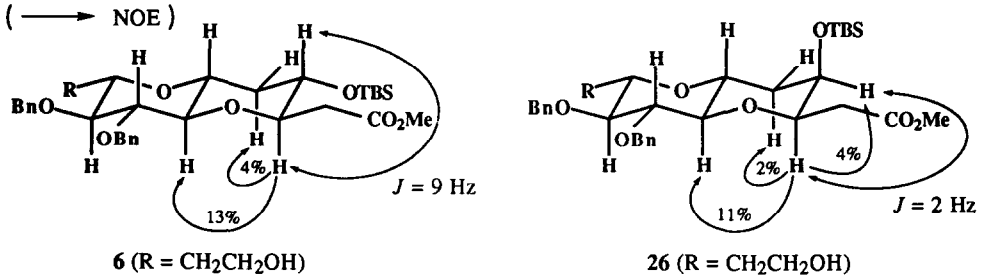
The cyclization reaction of **7** (α-OTBS) with NaH in THF produced a mixture of the cyclic product **6** and its dimer. Further treatment of the crude products with *t*-BuOK in MeOH[7] converted successfully compound **6** as a single product in a 91% total yield from **7** (Scheme 3). The stereochemistry at the C-2 position in **6** was determined by NOE experiments of the ^{1}H-NMR spectrum (Figure 1). Protection of the primary hydroxy group of **6** with *p*-methoxybenzyl-2,2,2-trichloroacetimidate and TfOH[8] afforded compound **23**. The ester group of **23** was reduced with LiAlH$_4$ to alcohol **24**. Compound **24** was protected with TBDPSCl to obtain compound **25** that corresponds to the B,C-ring part of ciguatoxin **1**. On the other hand, conversion of **22** (β-OTBS) involving the cyclization reaction with NaH in THF and treatment with *t*-BuOK in MeOH gave compound **26** stereoselectively in 99% yield. The stereochemistry of the C-2 position in **26** was deduced from the NOE experiments of the ^{1}H-NMR spectrum (Figure 1). The hydroxy group of **26** was protected as MPM ether to yield compound **27**. LiAlH$_4$ reduction of **27** produced alcohol **28**, which afforded diol **29** using TBAF. Selective silylation of the primary alcohol in **29** after treatment with TBDPSCl gave the compound **30**, which was oxidized under Swern conditions to the ketone **31**. The highly selective reduction

of **31** with $LiAlH_4$ provided compound **32** with an α-OH group as the sole product, which led to compound **25** with TBSOTf in an excellent total yield.



Reagents and Conditions: a) NaH, THF, -40 °C → r.t., 2 h; *t*-BuOK, MeOH, r.t., 18 h (91% for 2 steps); b) MPMOC(=NH)CCl_3, TfOH, ether, r.t., 10 min (75%); c) $LiAlH_4$, ether, -10 °C, 30 min (quant.); d) TBDPSCl, NEt_3, DMAP, CH_2Cl_2, r.t., 9 h (95%); e) NaH, THF, -40 °C → r.t., 4.5 h; *t*-BuOK, MeOH, r.t., 14 h (99% for 2 steps); f) MPMOC(=NH)CCl_3, TfOH, ether, r.t., 10 min (86%); g) $LiAlH_4$, ether, -10 °C, 30 min (99%); h) TBAF, THF, r.t., 1 h (quant.); i) TBDPSCl, NEt_3, DMAP, CH_2Cl_2, r.t., 12 h (quant.); j) Swern oxid. (quant.); k) $LiAlH_4$, ether, -20 °C, 15 min (99%); l) TBSOTf, 2,6-lutidine, CH_2Cl_2, r.t., 1 h (97%).

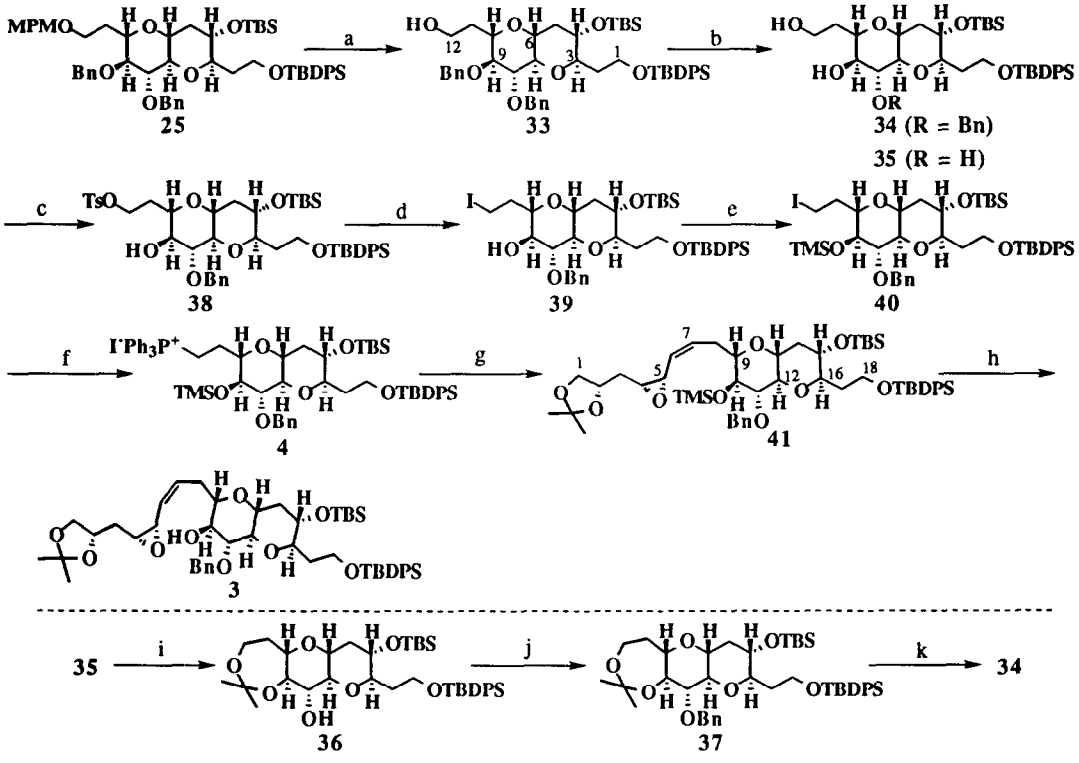
Scheme 3.



6 (R = CH_2CH_2OH) **26** (R = CH_2CH_2OH)

Figure 1.

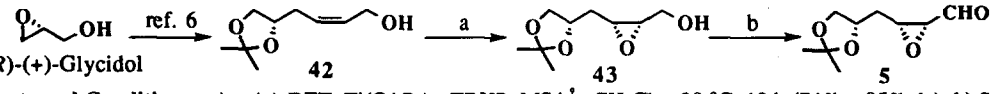
The MPM ether of **25** was detached with DDQ to afford alcohol **33**. The Bn ether of **33** was hydrogenated with $Pd(OH)_2/C$ to give a 1:1 mixture of diol **34** and triol **35** (Scheme 4). Compound **35** was converted into the desired diol **34** as follows. Treatment with acetone and PTS produced dimethyldioxepane **36** as a sole product. Reaction of **36** with BnBr provided compound **37**, which was hydrolyzed to the diol **34** in a good total yield. After selective mono-tosylation of the diol **34** to **38**, displacement of the primary tosyl group with NaI produced the iodide **39**. Protection of the secondary hydroxy group in **39** as a TMS ether afforded **40** which, on further treatment with PPh_3, was derivated to the phosphonium salt **4** in an excellent total yield. Generation of the ylide from **4** with NaHMDS followed by addition of the aldehyde **5** (Scheme 5) produced the *Z*-olefin **41** exclusively which was desilylated to the alcohol **3** in a moderate yield (38% based on **4**). The attempted use of various conditions in the Wittig reaction led all to the same yield as mentioned above [for example, solvents (THF, ether, PhH, DMSO, and HMPA), temperature, bases (BuLi or NaHMDS), equivalence of the reagents, and use of other phosphonium salts]. The results might be due to enolization of the aldehyde under basic conditions (estimated to be max. 10% which was observed by ^{1}H-NMR spectrum of the recovered aldehyde).



Reagents and Conditions: a) DDQ, CH_2Cl_2-H_2O (10:1), r.t., 40 min (quant.); b) H_2, $Pd(OH)_2/C$, EtOH-EtOAc (4:1), r.t., 7 d (**34**, 44%; **35**, 44%; recovery 5%); c) TsCl, NEt_3, DMAP, CH_2Cl_2, r.t., 20 h (90%); d) NaI, acetone, 50 °C, 8 h (86%); e) TMSOTf, NEt_3, CH_2Cl_2, -10 °C, 10 min (98%); f) PPh_3, CH_3CN, 60 °C, 27 h (98%); g) NaHMDS (1.5 eq), THF, r.t., 30 min, then **5** (2.0 eq), r.t., 30 min (38%, based on **4**); h) K_2CO_3, MeOH, 0 °C, 1.5 h (96%); i) PTS·H_2O, acetone, r.t., 30 min (4 cycles, total 95%); j) BnBr, NaH, TBAI, THF, r.t., 31 h (99%); k) PTS·H_2O, MeOH, r.t., 30 min (94%).

Scheme 4.

Preparation of the aldehyde **5** commenced with the known allylic alcohol **42** which was prepared in 6 steps from the commercially available (*R*)-(+)-glycidol (Scheme 5).[7] Epoxidation of **42** under Sharpless conditions produced epoxy alcohol **43** in a good diastereoselectively (>95% de). Compound **43** afforded under Swern conditions the aldehyde **5** which was not isomerized on silica gel column chromatography.

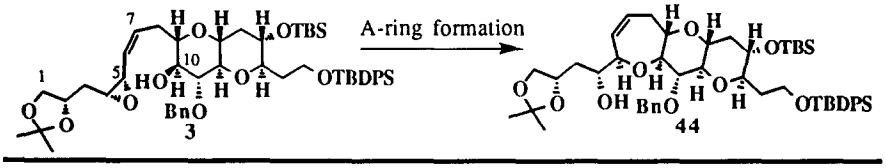


Reagents and Conditions: a) L-(+)-DET, Ti(O*i*-Pr)$_4$, TBHP, MS4Å, CH_2Cl_2, -20 °C, 18 h (74%, >95% de); b) Swern oxid. (93%).

Scheme 5.

Construction of **44** was examined under various conditions, and the results are given in Table 1. It was supposed that the A-ring was rather difficult to form because the C-10 hydroxy group would be nearer to the C-7 olefinic carbon than to the C-5 epoxide carbon on the basis of molecular mechanics calculations for the ground state of **3**. Basic treatments of **3** (entries 1 and 2) provided decomposed products. Reaction with CSA as protonic acid produced the compound **45** *via* SN2' reaction in 72% yield (entry 3). Use of $Zn(OTf)_2$ provided **45** and **46** in 39% and 30% respective yields (entry 4). Reaction with $La(OTf)_2$ or $Eu(dpm)_3$ did not proceed (entries 5 and 7). Treatment with $VO(acac)_2$ gave a complex mixture (entry 6). The desired ring-closure reaction was achieved only under the conditions using $Eu(fod)_3$ in toluene to afford **44** in 38% yield along with **46** in 32% yield (entry 8). These results reveal that there might be some dependence of acidity strengths of the Lewis acids as well as that of the bond lengths of chelation with O-functions of the epoxy alcohol. Eventually, the C-10 hydroxy group in **3** could be near the C-5 epoxide carbon only in the case of $Eu(fod)_3$. We applied the ring-closure reaction using $(Bu_3Sn)_2O$ and Lewis acids recently reported by Suzuki[9] and obtained the same results as in the case of entry 8 (entry 9). The C-10 hydroxy group could not be activated by $(Bu_3Sn)_2O$ because of the steric hindrance around this group. The stereochemistry at the C-5 position in **44** was determined from the NOE experiments of the ^{1}H-NMR spectrum of the acetate **47** (Figure 2).

Table 1.



entry	reagents and conditions	results		
		44	**45**	**46**
1	$NaCH_2SOCH_3$, THF 0 °C, 1 h		decompose	
2	NaH, THF, r.t., 18 h		decompose	
3	CSA, CH_2Cl_2, -40 °C → 8 °C, 3 h	0%	72%	0%
4	$Zn(OTf)_2$, PhH, r.t., 5 h	0%	39%	30%
5	$La(OTf)_2$, CH_2Cl_2, r.t., 24 h		no reaction	
6	$VO(acac)_2$, toluene, 70 °C, 9 h		complex mixture	
7	$Eu(dpm)_3$, toluene, reflux, 13 h		no reaction	
8	$Eu(fod)_3$, toluene, 80 °C, 15 h	38%	trace	32%
9	$(Bu_3Sn)_2O$, toluene, reflux, 3 h, then $Eu(fod)_3$, 90 °C, 19 h	36%	trace	25%

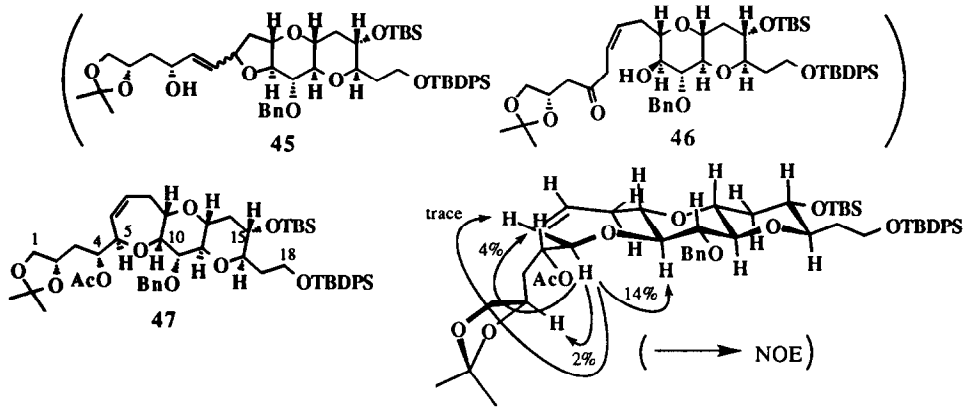
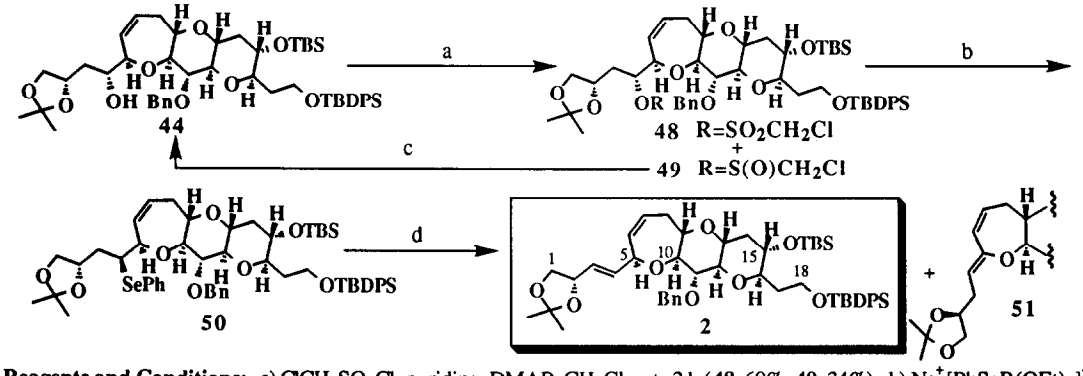


Figure 2.

Finally, transformation of the compound **44** into the A,B,C-ring system **2** was achieved (Scheme 6). The secondary hydroxy group in **44** was converted on treatment with $ClCH_2SO_2Cl$[10] into the chloromethanesulfonate **48** and sulfinate **49** [HR-FD/FI-MASS, calcd. for $C_{51}H_{74}O_{10}ClSi_2S$ (M^++H) 969.4232, found *m/z* 969.4257] in 60% and 34% yields, respectively. However, the compound **49** could smoothly be transformed back to **44** with DBU. Phenylselenation[11] of **48** proceeded smoothly *via* SN2 reaction to afford the selenide **50**, of which the *syn* elimination with H_2O_2 led to the A,B,C-ring system **2** in 59% yield along with the conjugated diene **51** in 39% yield. Compound **48** led only to **51** in 70% yield by *anti* elimination with DBU. These results are supposed as follows: In the reaction of **50** using H_2O_2 under an approximately neutral conditions, the major elimination occurred at the less hindered position (C-3 proton), while, on treatment of **48** with DBU as a strong base, the reaction proceeded at the more acidic position (C-5 proton) to be attacked. The configuration of the newly formed 4,5-double bond is tentatively deduced as *Z* from mechanistic grounds.

In conclusion, our synthetic route is characterized by the following three points; i) use of the readily available D-glucose as the starting material; ii) construction of the substituted A-ring by the novel ring-closure reaction of the vinylic epoxy alcohol; iii) introduction of the necessary substituents in the C-ring aiming to the linear construction of the D-ring. Further studies aiming at the total synthesis of **1** are now in progress in our laboratory.



Reagents and Conditions: a) $ClCH_2SO_2Cl$, pyridine, DMAP, CH_2Cl_2, r.t., 2 h (**48**, 60%; **49**, 34%); b) $Na^+[PhSeB(OEt)_3]^-$, EtOH, reflux, 3 h (62%); c) DBU, toluene, reflux, 1 h (88%); d) H_2O_2, pyridine, CH_2Cl_2, 0 °C → r.t., 1 h (**2**, 59%; **51**, 39%).

Scheme 6.

EXPERIMENTAL

General: All reactions involving air- or moisture-sensitive reagents were conducted under argon atmosphere, and solvents and reagents were dried and distilled before use. Ether and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl. Dichloromethane (CH_2Cl_2), acetonitrile (CH_3CN), benzene (PhH), and toluene were distilled from calcium hydride (CaH_2). Methanol (MeOH) and ethanol (EtOH) were distilled from magnesium turnings. Molecular sieves 4Å (MS4Å) were finely powdered and activated at 220 °C for 3 h *in vacuo*. All reactions were monitored by thin-layer chromatography with pre-coated silica gel (SiO_2) plates (E. Merck, Silica gel 60 F_{254} Art. 5554). Flash chromatography utilized silica gel (SiO_2) (YMC, YMCGEL SIL-60-400/230W). Infrared (IR) spectra were obtained on a Hitachi 270-30 infrared spectrophotometer. ^1H NMR spectra were recorded on JEOL JNM-FX-270 (270 MHz), JNM-AL-270 (270 MHz), JNM-AL-300 (300 MHz), and JNM-α-400 (400 MHz) NMR spectrometers. Splitting patterns are designated as "s, d, t, q, m, and br," indicating "singlet, doublet, triplet, quartet, multiplet, and broad," respectively. Tetramethylsilane (δ 0.00) was used as an internal reference for spectra measured in $CDCl_3$, and residual PhH (δ 7.20) in C_6D_6. High-resolution mass spectra (HR-MS) were obtained on a JEOL JMS-AX500 or a JMS-SX102A mass spectrometer. Optical rotations were recorded on JASCO DIP-360 digital polarimeter. Melting points were measured on YANAGIMOTO micro-melting point apparatus without correction.

Allyl 4,6-O-*p*-methoxybenzylidene-D-glucopyranoside (8).

To a suspension of D-glucose (100 g, 555 mmol) in allyl alcohol (250 ml) was added triflic acid (TfOH) (1.00 ml, 11.3 mmol) at 0 °C. The mixture was warmed up to 80 °C, and stirred at the same temperature for 2 days. The reaction were terminated by addition of triethylamine (NEt_3) (1.60 ml, 11.5 mmol) and the mixture was concentrated *in vacuo*. The crude allyl glucopyranoside (130 g, α-:β-anomers=2.6:1) was obtained, and used for the next reaction without further purification.

A solution of the crude allyl glucopyranoside (66.0 g), 4-methoxybenzaldehyde dimethyl acetal [4-MeO-PhCH$(OMe)_2$] (62.0 ml, 367 mmol), and *p*-toluenesulfonic acid monohydrate (PTS·H_2O) (0.94 g, 4.65 mmol) in dimethylformamide (DMF) (200 ml) was stirred *in vacuo* by aspirator at 50-55 °C for 4 h. The solution was warmed to 70 °C *in vacuo* by aspirator, and DMF was removed. The mixture was partitioned between ethyl acetate (EtOAc) and satd. aq. sodium bicarbonate ($NaHCO_3$). The water layer was extracted repeatedly with EtOAc. The combined organic layers were washed with brine, dried over magnesium sulfate ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 1:1 → 1:3) to afford **8** (63.9 g, 67% yield for 2 steps) as white crystals.

Data of pure samples.

α-anomer: m.p. 128-130 °C; $[\alpha]_D^{22}$ +85.3° (*c* 1.27, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.42 (2H, d, *J* = 9 Hz), 6.89 (2H, d, *J* = 9 Hz), 5.93 (1H, dddd, *J* = 6, 7, 10, 17 Hz), 5.49 (1H, s), 5.23 (1H, br dd, *J* = 2, 17 Hz), 5.25 (1H, br dd, *J* = 2, 10 Hz), 4.94 (1H, d, *J* = 4 Hz), 4.26 (1H, dd, *J* = 4, 9 Hz), 4.28-4.21 (1H, m), 4.05 (1H, br dd, *J* = 6, 13 Hz), 3.94 (1H, br t, *J* = 9 Hz), 3.83 (1H, br dt, *J* = 5, 9 Hz), 3.80 (3H, s), 3.71 (1H, t, *J* = 9 Hz), 3.62 (1H, dt, *J* = 4, 9 Hz), 3.47 (1H, t, *J* = 9 Hz), 2.87 (1H, br s), and 2.34 (1H, br d, *J* = 10 Hz); IR (KBr), ν_{max} 3464, 3084, 2920, 2864, 1616, 1520, 1374, 1248, 1150, 1078, 1030, 930, and 818 cm^{-1}; HR-EI-MS, calcd. for $C_{17}H_{22}O_7$ (M^+) 338.1366, found *m/z* 338.1360.

β-anomer: m.p. 151-153 °C; $[\alpha]_D^{22}$ -31.1° (*c* 1.07, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.41 (2H, d, *J* = 9 Hz), 6.89 (2H, d, *J* = 9 Hz), 5.95 (1H, dddd, *J* = 6, 7, 11, 17 Hz), 5.50 (1H, s), 5.34 (1H, br dd, *J* = 2, 17 Hz), 5.25 (1H, br dd, *J* = 2, 11 Hz), 4.46 (1H, d, *J* = 8 Hz), 4.39 (1H, br dd, *J* = 6, 13 Hz), 4.33 (1H, dd, *J* = 5, 10 Hz), 4.15 (1H, dd, *J* = 7, 13 Hz), 3.87-3.80 (1H, m), 3.80 (3H, s), 3.78 (1H, t, *J* = 10 Hz), 3.58-3.51 (1H, m), 3.55 (1H, t, *J* = 9 Hz), 3.45 (1H, br dt, *J* = 5, 9 Hz), 2.75 (1H, br s), and 2.60 (1H, br s); IR (KBr), ν_{max} 3524, 3224, 2932, 2864, 1618, 1520, 1378, 1252, 1172, 1084, 1042, 1002, and 824 cm^{-1}; HR-EI-MS, calcd. for $C_{17}H_{22}O_7$ (M^+) 338.1366, found *m/z* 338.1366.

Allyl 2,3-O-dibenzyl-4,6-O-*p*-methoxybenzylidene-D-glucopyranoside (9).

Benzyl bromide (BnBr) (54.0 ml, 453 mmol) was added dropwise to a stirred suspension of **8** (63.9 g, 189 mmol) and sodium hydride (NaH) (22.7 g, 954 mmol) in a 1:1 mixture of THF-DMF (1 l) at 0 °C. After 6 h at room temperature, the reaction was completed and MeOH (100 ml) was added to the mixture at 0 °C. The mixture was diluted with EtOAc and then with water. The water layer was extracted repeatedly with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 5:1) to afford **9** (60.1 g, 61% yield) as white crystals.

Data of pure samples.

α-anomer: m.p. 77-79 °C; $[\alpha]_D^{22}$ -11.0° (*c* 0.94, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$), δ 7.43-7.25 (12H, m), 6.90 (2H, d, *J* = 9 Hz), 5.94 (1H, dddd, *J* = 5, 7, 10, 17 Hz), 5.51 (1H, s), 5.33 (1H, br dd, *J* = 1, 17 Hz), 5.24 (1H, br d, *J* = 10 Hz), 4.91 (1H, d, *J* = 11 Hz), 4.83 (2H, br d, *J* = 12 Hz), 4.79 (1H, d, *J* = 4 Hz), 4.68 (1H, d, *J* = 12 Hz), 4.23 (1H, dd, *J* = 5, 10 Hz), 4.18 (1H, br dd, *J* = 5, 13 Hz), 4.07 (1H, br t, *J* = 9 Hz), 4.03 (1H, br d, *J* = 7, 13 Hz), 3.88 (1H, dt, *J* = 5, 10 Hz), 3.81 (3H, s), 3.68 (1H, t, *J* = 10 Hz), 3.59 (1H, t, *J* = 9 Hz), and 3.56 (1H, dd, *J* = 4, 9 Hz); IR (KBr), ν_{max} 3064, 3036, 3012, 2920, 2868, 1616, 1518, 1456, 1370, 1252, 1172, 1090, 1030, 932, 824, 734, and 698 cm^{-1}; HR-EI-MS, calcd. for $C_{31}H_{34}O_7$ (M^+) 518.2305, found *m/z* 518.2264.

β-anomer: m.p. 122-123 °C; $[\alpha]_D^{22}$ -36.3° (*c* 0.90, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$), δ 7.42-7.25 (12H, m), 6.90 (2H, d, *J* = 9 Hz), 5.95 (1H, br ddd, *J* = 7, 10, 17 Hz), 5.53 (1H, s), 5.35 (1H, br dd, *J* = 2, 17 Hz), 5.22 (1H, br dd, *J* = 2, 10 Hz), 4.91 (1H, d, *J* = 11 Hz), 4.90 (1H, d, *J* = 11 Hz), 4.79 (1H, d, *J* = 11 Hz), 4.77 (1H, d, *J* = 11 Hz), 4.56 (1H, d, *J* = 8 Hz), 4.40 (1H, br dd, *J* = 5, 12 Hz), 4.33 (1H, dd, *J* = 5, 9 Hz), 4.16 (1H, br dd, *J* = 6, 12 Hz), 3.81 (3H, s), 3.78 (1H, t, *J* = 9 Hz), 3.74 (1H, t, *J* = 8 Hz), 3.67 (1H, br t, *J* = 9 Hz), 3.49 (1H, t, *J* = 9 Hz), and 3.39 (1H, br dt, *J* = 5, 9 Hz); IR (KBr), ν_{max} 3032, 2900, 2876, 1616, 1518, 1368, 1248, 1088, 1030, 828, 732, and 696 cm^{-1}; HR-EI-MS, calcd. for $C_{31}H_{34}O_7$ (M^+) 518.2305, found *m/z* 518.2316.

2,3-O-Dibenzyl-4,6-O-*p*-methoxybenzylidene-D-glucopyranose (10).

A mixture of **9** (100 mg, 193 μmol) and tris(triphenylphosphine)rhodium(I) chloride [$(Ph_3P)_3RhCl$] (2.0 mg) in EtOH (2.5 ml) containing diisopropylethylamine (*i*-Pr_2NEt) (60 μl, 344 μmol) was heated under reflux for 2 h, cooled, and evaporated *in vacuo* to give a brown residue which was dissolved in CH_2Cl_2. The solution was washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. To a suspension of mercuric oxide (HgO) (100 mg) and mercuric chloride ($HgCl_2$) (100 mg) in a 9:1 mixture of acetone-water (1 ml) was added a solution of the brown syrup in 9:1 acetone-water (6 ml). The reaction mixture was stirred at room temperature for 1 h. The solvent was evaporated *in vacuo* and the residue was dissolved in ether, and the solution was washed with satd. aq. potassium iodide (KI) and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on SiO_2 (PhH:EtOAc, 2:1) to afford **10** (84.7 mg, α-:β-anomers=8:5, 92% yield for 2 steps) as white crystals: m.p. 171-172 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.43-7.27 (12H, m), 6.90 (2H, d, *J* = 9 Hz), 5.53 and 5.52 (totally 1H, each s), 5.19 (8/13H, dd, *J* = 2, 4 Hz), 4.94 and 4.93 (totally 1H, each d, *J* = 11 Hz), 4.87 and 4.84 (totally 1H, each d, *J* = 11 Hz), 4.84 and 4.80 (totally 1H, each d, *J* = 11 Hz), 4.79 and 4.72 (totally 1H, each d, *J* = 11 Hz), 4.81 (5/13H, dd, *J* = 5, 8 Hz), 4.32 and 4.27 (totally 1H, each dd, *J* = 5, 10 Hz), 4.06 (8/13H, br dt, *J* = 5, 10 Hz), 4.00 (8/13H, t, *J* = 9 Hz), 3.82 (3H, s), 3.78 (5/13H, t, *J* = 9 Hz), 3.77 (5/13H, t, *J* = 10 Hz), 3.69 (5/13H, t, *J* = 9 Hz), 3.68 (8/13H, t, *J* = 10 Hz), 3.62 (8/13H, t, *J* = 9 Hz), 3.59 (8/13H, dd, *J* = 4, 9 Hz), 3.45 (5/13H, br dt, *J* = 5, 10 Hz), 3.41 (5/13H, dd, *J* = 8, 9 Hz), 3.21 (5/13H, br d, *J* = 5 Hz), and 3.09 (8/13H, d, *J* = 2 Hz); IR (KBr), ν_{max} 3440, 3064, 3032, 2912, 2876, 1620, 1520, 1426, 1370, 1252, 1172, 1096, 1036, 827, 744, and 696 cm^{-1}; HR-EI-MS, calcd. for $C_{28}H_{30}O_7$ (M^+) 478.1992, found *m/z* 478.2025.

Methyl (4*S*,5*R*,6*S*,7*R*)-6,8-*p*-methoxybenzylidenedioxy-4,5-dibenzyloxy-7-hydroxy-2-octenoate (11).

A solution of **10** (4.84 g, 10.1 mmol) and methyl (triphenylphosphoranylidene)acetate (Ph_3P=$CHCO_2Me$) (6.75 g, 20.2 mmol) in PhH (60 ml) was heated under reflux for 24 h. The solvent was evaporated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 2:1 → 3:2) to afford **11** (5.32 g, *E*:*Z*=4:1, 99% yield) as a pale yellow oil: ^{1}H NMR (270 MHz, $CDCl_3$), δ 7.40-7.26 (12H, m), 6.98 (4/5H, dd, *J* = 7, 16 Hz), 6.87 (2H, d, *J* = 9 Hz), 6.30 (1/5H, dd, *J* = 9, 12 Hz), 6.13 (4/5H, dd, *J* = 1, 16 Hz), 5.94 (1/5H, *J* = 12 Hz), 5.60 (1/5H, br dd, *J* = 5, 9 Hz), 5.34 and 5.32 (totally 1H, each s), 4.84 (4/5H, d, *J* = 12 Hz), 4.78 (1/5H, d, *J* = 12 Hz), 4.73 (4/5H, d, *J* = 12 Hz), 4.71 (1/5H, d, *J* = 12 Hz), 4.62 (1H, d, *J* = 12 Hz), 4.55 (1/5H, d, *J* = 11 Hz), 4.49 (4/5H, d, *J* = 11 Hz), 4.40 (4/5H, dt, *J* = 1, 7 Hz), 4.20 and 4.19 (totally 1H, each dd, *J* = 5, 10 Hz), 3.91-3.67 (2H, m), 3.803 and 3.797 (totally 3H, each s), 3.75 and 3.50 (totally 3H, each s), 3.56 (1H, dd, *J* = 4, 9 Hz), 3.48 (1H, t, *J* = 10 Hz), and 2.25 and 1.69 (totally 1H, each d, *J* = 5 Hz); IR (film), ν_{max} 3480, 3064, 2952, 2864, 1726, 1660, 1616, 1520, 1252, 1086, 1032, 830, 736, and 700 cm^{-1}; HR-EI-MS, calcd. for $C_{31}H_{34}O_8$ (M^+) 534.2254, found *m/z* 534.2226.

Methyl {(1*R*,6*R*,8*S*,9*S*,10*R*)-9,10-dibenzyloxy-3-*p*-methoxyphenyl-2,4,7-trioxabicyclo[4.4.0]decan-8-yl}acetate (12).

To a solution of **11** (6.19 g, 11.6 mmol) in THF (65 ml) was added NaH (0.42 g, 17.4 mmol) and the mixture was stirred at room temperature for 16 h. To the reaction mixture were added ether and satd. aq. ammonium chloride (NH_4Cl) at 0 °C. The water layer was extracted repeatedly with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on SiO_2 (hexane:EtOAc, 2:1) to afford **12** (6.17 g, 100% yield) as white crystals: m.p. 93-95 °C; $[\alpha]_D^{22}$ -41.0° (*c* 1.07, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6), δ 7.56 (2H, d, *J* = 9 Hz), 7.41 (2H, br d, *J* = 7 Hz), 7.30 (2H, br d, *J* = 7 Hz), 7.22-7.10 (6H, m), 6.85 (2H, d, *J* = 9 Hz), 5.35 (1H, s), 5.10 (1H, d, *J* = 11 Hz), 5.04 (1H, d, *J* = 11 Hz), 4.78 (1H, d, *J* = 11 Hz), 4.59 (1H, d, *J* = 11 Hz), 4.20 (1H, dd, *J* = 5, 10 Hz, H-7-eq), 3.98 (1H, ddd, *J* = 4, 8, 9 Hz, H-2), 3.80 (1H, br t, *J* = 9 Hz, H-4), 3.57 (1H, t, *J* = 9 Hz, H-5), 3.49 (1H, t, *J* = 10 Hz, H-7-ax), 3.42 (1H, dd, *J* = 8, 9 Hz, H-3), 3.36-3.30 (1H, m, H-6), 3.34 (3H, s), 3.30 (3H, s), 2.79 (1H, dd, *J* = 8, 15 Hz, H-1), and 2.49 (1H, dd, *J* = 8, 15 Hz, H-1); IR (film), ν_{max} 3064, 3032, 2952, 2872, 1742, 1616, 1520, 1456, 1252, 1174, 1102, 1030, 828, 738, and 700 cm^{-1}; HR-EI-MS, calcd. for $C_{31}H_{34}O_8$ (M^+) 534.2254, found *m/z* 534.2260.

2-{(1*R*,6*R*,8*S*,9*S*,10*R*)-9,10-Dibenzyloxy-3-*p*-methoxyphenyl-2,4,7-trioxabicyclo[4.4.0]decan-8-yl}-ethanol (13).

To a suspension of lithium aluminum hydride ($LiAlH_4$) (77.0 mg, 20.3 mmol) in ether (10 ml) was added dropwise a solution of **12** (452 mg, 846 μmol) in a 2:1 mixture of ether-THF (6 ml) at 0 °C, and the mixture was stirred at the same temperature for 30 min. Water (0.1 ml) was added to the mixture, and the mixture was stirred vigorously at room temperature until a white gel was generated. To the mixture were added 4 M aq. sodium hydroxide (NaOH) (0.1 ml) and water (0.2 ml), and the mixture was stirred vigorously at room temperature until a white solid was generated. The mixture was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on SiO_2 (hexane:EtOAc, 1:1) to afford **13** (420 mg, 98% yield) as white crystals: m.p. 111-113 °C; $[\alpha]_D^{21}$ -46.2° (*c* 1.02, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$), δ 7.44-7.25 (12H, m), 6.90 (2H, d, *J* = 9 Hz), 5.53 (1H, s), 4.99 (1H, d, *J* = 11 Hz), 4.96 (1H, d, *J* = 11 Hz), 4.78 (1H, d, *J* = 11 Hz), 4.63 (1H, d, *J* = 11 Hz), 4.30 (1H, dd, *J* = 5, 10 Hz), 3.86-3.56 (6H, m), 3.81 (3H, s), 3.44 (1H, br dt, *J* = 5, 10 Hz), 3.35 (1H, dd, *J* = 9, 10 Hz), 2.15-2.04 (2H, m), and 1.78-1.64 (1H, m); IR (film), ν_{max} 3320, 3068, 3036, 2936, 2876, 1618, 1520, 1456, 1254, 1096, 1034, 826, 746, and 696 cm^{-1}; HR-EI-MS, calcd. for $C_{30}H_{34}O_7$ (M^+) 506.2305, found *m/z* 506.2330.

(1*R*,6*R*,8*S*,9*S*,10*R*)-9,10-Dibenzyloxy-8-(2-*p*-methoxybenzyloxyethyl)-3-*p*-methoxyphenyl-2,4,7-trioxabicyclo[4.4.0]decane (14).

To a suspension of potassium hydride (KH) [3.93 g (35% in oil), 34.3 mmol] in THF (80 ml) was

added dropwise a solution of **13** (4.95 g, 9.77 mmol) in THF (20 ml) at 0 °C, and the mixture was stirred at room temperature for 30 min. *p*-Methoxybenzyl chloride (MPMCl) (2.00 ml, 14.7 mmol) was added dropwise to the mixture, and the mixture was stirred at room temperature for 3 h. After cooling to 0 °C, the mixture was diluted with ether and treated with water. The water layer was extracted repeatedly with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 5:1) to afford **14** (6.11 g, 100% yield) as white crystals: m.p. 91-93 °C; $[\alpha]_D^{23}$ -34.4° (*c* 1.05, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.43-7.22 (14H, m), 6.90 (2H, d, *J* = 9 Hz), 6.86 (2H, d, *J* = 9 Hz), 5.52 (1H, s), 4.97 (1H, d, *J* = 11 Hz), 4.93 (1H, d, *J* = 11 Hz), 4.77 (1H, d, *J* = 11 Hz), 4.63 (1H, d, *J* = 11 Hz), 4.45 (1H, d, *J* = 11 Hz), 4.37 (1H, d, *J* = 11 Hz), 4.25 (1H, dd, *J* = 5, 10 Hz), 3.85-3.77 (1H, m), 3.81 (3H, s), 3.80 (3H, s), 3.68-3.47 (5H, m), 3.41-3.26 (2H, m), 2.26-2.13 (1H, m), and 1.75-1.60 (1H, m); IR (KBr), ν_{max} 3036, 2968, 2900, 2872, 1616, 1516, 1254, 1102, 1034, 826, 752, and 702 cm^{-1}; HR-EI-MS, calcd. for $C_{38}H_{42}O_8$ (M^+) 626.2881, found *m/z* 626.2875.

{[(2*R*,3*R*,4*R*,5*S*,6*S*)-4,5-Dibenzyloxy-3-*p*-methoxybenzyloxy-6-(2-*p*-methoxybenzyloxyethyl)}oxan-2-yl]methanol (15).

To a solution of **14** (680 mg, 1.08 mmol) in CH_2Cl_2 (10 ml) was added dropwise diisobutylaluminum hydride (DIBAL) (0.95 M solution in hexane, 3.42 ml, 3.25 mmol) at -78 °C. The mixture was warmed to 0 °C and stirred at the same temperature for 40 min. Water (0.15 ml) was added to the mixture, and the mixture was stirred vigorously at room temperature until a white gel was generated. To the mixture were added 4 M aq. NaOH (0.15 ml) and water (0.30 ml), and the mixture was stirred vigorously at room temperature until a white solid was generated. The mixture was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 3:2) to afford **15** (649 mg, 95% yield) as white crystals: m.p. 97-98 °C; $[\alpha]_D^{22}$ -6.70° (*c* 1.05, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.35-7.19 (14H, m), 6.86 (2H, d, *J* = 9 Hz), 4.93 (1H, d, *J* = 11 Hz), 4.88 (1H, d, *J* = 11 Hz), 4.86 (1H, d, *J* = 11 Hz), 4.78 (1H, d, *J* = 11 Hz), 4.64 (1H, d, *J* = 11 Hz), 4.58 (1H, d, *J* = 11 Hz), 4.44 (1H, d, *J* = 12 Hz), 4.37 (1H, d, *J* = 12 Hz), 3.85-3.72 (2H, m), 3.792 (3H, s), 3.789 (3H, s), 3.69 (1H, t, *J* = 9 Hz), 3.65-3.48 (1H, m), 3.55 (1H, dd, *J* = 6, 7 Hz), 3.50 (1H, t, *J* = 9 Hz), 3.43 (1H, dt, *J* = 3, 9 Hz), 3.29-3.22 (1H, m), 3.25 (1H, t, *J* = 9 Hz), 2.25-2.10 (1H, m), 1.79 (1H, br t, *J* = 7 Hz), and 1.72-1.60 (1H, m); IR (KBr), ν_{max} 3428, 3068, 3036, 2960, 2908, 2864, 1616, 1516, 1458, 1358, 1302, 1252, 1104, 1072, 1038, 990, 822, 808, and 742 cm^{-1}; HR-EI-MS, calcd. for $C_{38}H_{43}O_8$ (M^++H) 627.2959, found *m/z* 627.2966.

[(2*R*,3*R*,4*R*,5*S*,6*S*)-4,5-Dibenzyloxy-3-*p*-methoxybenzyloxy-6-(2-*p*-methoxybenzyloxyethyl)-2-*p*-toluenesulfonyloxymethyl]oxane (16).

To a solution of **15** (645 mg, 1.02 mmol), NEt_3 (0.54 ml, 3.88 mmol), and 4-dimethylaminopyridine (DMAP) (a cat. amount) in CH_2Cl_2 was added *p*-toluenesulfonyl chloride (TsCl) (370 mg, 1.94 mmol), and the mixture was stirred at room temperature for 6 h. The reaction was quenched with satd. aq. $NaHCO_3$. The water layer was extracted repeatedly with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 4:1 → 3:1) to afford **16** (798 mg, 100% yield) as a pale yellow oil: $[\alpha]_D^{21}$ +2.11° (*c* 1.63, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.75 (2H, d *J* = 7 Hz), 7.37-7.18 (14H, m), 7.10 (2H, d, *J* = 9 Hz), 6.86 (2H, d, *J* = 9 Hz), 6.82 (2H, d, *J* = 9 Hz), 4.88 (2H, s), 4.82 (1H, d, *J* = 11 Hz), 4.74 (1H, d, *J* = 11 Hz), 4.61 (1H, d, *J* = 11 Hz), 4.44 (1H, d, *J* = 11 Hz), 4.42 (1H, d, *J* = 12 Hz), 4.33 (1H, d, *J* = 12 Hz), 4.14-4.08 (2H, m), 3.797 (3H, s), 3.794 (3H, s), 3.61 (1H, t, *J* = 9 Hz), 3.50-3.38 (3H, m), 3.37-3.25 (2H, m), 3.19 (1H, t, *J* = 9 Hz), 2.41 (3H, s), 2.19-2.02 (1H, m), and 1.60-1.45 (1H, m); IR (film), ν_{max} 3068, 3036, 2916, 2868, 1616, 1516, 1456, 1362, 1250, 1178, 1096, 978, 820, and 700 cm^{-1}; HR-EI-MS, calcd. for $C_{45}H_{49}O_{10}S$ (M^+-H) 781.3048, found *m/z* 781.3029.

{[(2*R*,3*R*,4*S*,5*S*,6*S*)-4,5-Dibenzyloxy-3-*p*-methoxybenzyloxy-6-(2-*p*-methoxybenzyloxyethyl)]oxan-2-yl}acetonitrile (17).

To a solution of **16** (226 mg, 289 μmol) in dimethylsulfoxide (DMSO) (2 ml) was added potassium cyanide (KCN) (56 mg, 866 μmol), and the mixture was stirred at 50 °C for 7 h. After cooling to room temperature, the reaction mixture was diluted with ether, and treated with half satd. aq. $NaHCO_3$. The water layer was extracted repeatedly with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on SiO_2 (hexane:EtOAc, 3:1) to afford **17** (183 mg, 99% yield) as a colorless oil: $[\alpha]_D^{22}$ +9.35° (*c* 1.05, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.36-7.16 (14H, m), 6.87 (2H, d, *J* = 9 Hz), 6.86 (2H, d, *J* = 9 Hz), 4.93 (1H, d, *J* = 11 Hz), 4.88 (1H, d, *J* = 11 Hz), 4.85 (1H, d, *J* = 11 Hz), 4.84 (1H, d, *J* = 11 Hz), 4.66 (1H, d, *J* = 11 Hz), 4.57 (1H, d, *J* = 11 Hz), 4.44 (1H, d, *J* = 11 Hz), 4.38 (1H, d, *J* = 11 Hz), 3.80 (3H, s), 3.79 (3H, s), 3.70-3.61 (1H, m), 3.57 (2H, br dd, *J* = 6, 8 Hz), 3.44 (1H, br dt, *J* = 3, 9 Hz), 3.38-3.35 (2H, m), 3.30 (1H, t, *J* = 9 Hz), 2.57 (1H, br dd, *J* = 3, 17 Hz), 2.40 (1H, br dd, *J* = 7, 17 Hz), 2.24-2.08 (1H, m), and 1.74-1.60 (1H, m); IR (film), ν_{max} 3064, 3036, 3008, 2908, 2868, 2256, 1614, 1516, 1250, 1096, 822, 738, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{39}H_{43}O_7N$ (M^+) 637.3041, found *m/z* 637.3015.

{[(2*R*,3*R*,4*R*,5*S*,6*S*)-4,5-Dibenzyloxy-3-*p*-methoxybenzyloxy-6-(2-*p*-methoxybenzyloxyethyl)]oxan-2-yl}acetaldehyde (18).

To a solution of **17** (184 mg, 289 μmol) in CH_2Cl_2 (4 ml) was added dropwise DIBAL (0.95 M solution in hexane, 344 μl, 317 μmol) at -78 °C, and the mixture was stirred at the same temperature for 30 min. To the reaction mixture was added a half satd. solution of Rochele salt at -78 °C, and the mixture was stirred vigorously at room temperature for 1 h. The water layer was extracted repeatedly with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 2:1) to afford **18** (176 mg, 95% yield) as white crystals: m.p. 97-98 °C; $[\alpha]_D^{21}$ -3.07° (*c* 1.18, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 9.58 (1H, br t, *J* = 2 Hz), 7.35-7.16 (14H, m), 6.87 (2H, d, *J* = 9 Hz), 6.84 (2H, d, *J* = 9 Hz), 4.91 (2H, s), 4.85 (1H, d, *J* = 11 Hz), 4.80 (1H, d, *J* = 11 Hz), 4.64 (1H, d, *J* = 11 Hz), 4.51 (1H, d, *J* = 11 Hz), 4.43 (1H, d, *J* = 12 Hz), 4.34 (1H, d, *J* = 12 Hz), 3.79 (6H, s), 3.71 (1H, br dt, *J* = 5, 9 Hz), 3.69 (1H, t, *J* = 9Hz), 3.50 (2H, br dd, *J* = 6, 8 Hz), 3.43 (1H, br dt, *J* = 3, 9 Hz), 3.26 (2H, t, *J* = 9 Hz), 2.64 (1H, ddd, *J* = 2, 5, 17 Hz), 2.38 (1H, ddd, *J* = 2, 9, 17 Hz), 2.24-2.08 (1H, m), and 1.68-1.54 (1H, m); IR (KBr), ν_{max} 3068, 3036, 3004, 2936, 2860, 2740, 1722, 1616, 1516, 1250, 1094, 822, 740, and 696 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{43}H_{48}O_{10}$ (M^+) 640.3037, found *m/z* 640.3018.

Methyl 4-hydroxy-5-{[(2'*R*,3'*R*,4'*R*,5'*S*,6'*S*)-4',5'-dibenzyloxy-3'-*p*-methoxybenzyloxy-6'-(2-*p*-methoxybenzyloxyethyl)]oxan-2'-yl}-2-pentynoate (19).

To a solution of diisopropylamine (121 μl, 864 μmol) in THF (5 ml) was added dropwise butyllithium (BuLi) (1.63 M solution in hexane, 494 μl, 806 μmol) at -78 °C, and the mixture was warmed to 0°C, and stirred at the same temperature for 30 min. After cooling to -78 °C, methyl propiolate (76.9 μl, 864 μmol) was added to the mixture and the mixture was stirred at the same temperature for 30 min. To the mixture was added dropwise a solution of **18** (369 mg, 576 μmol) in THF (3 ml) at -78 °C, and the mixture was stirred at the same temperature for 1 h. The reaction mixture was diluted with ether and treated with satd. aq. NH_4Cl at -78 °C, and warmed to room temperature. The water layer was extracted repeatedly with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 3:1 → 2:1) to afford **19** (413 mg, an α-OH:β-OH=1:2 mixture, 98% yield) as a pale yellow oil: ^1H NMR (270 MHz, $CDCl_3$), δ 7.35-7.17 (14H, m), 6.90-6.82 (4H, m), 4.93-4.75 (4H, m), 4.67-4.32 (14/3H, m), 4.10 (1/3H, d, *J* = 10 Hz), 3.80 (6H, br s), 3.77 and 3.76 (totally 3H, each s), 3.75-3.19 (7H, m), 2.25-2.11 (2H, m), 1.90-1.74 (1H, m), and 1.74-1.58

(1H, m); IR (film), ν_{max} 3428, 3064, 3032, 2908, 2872, 2240, 1718, 1616, 1516, 1254, 1094, 822, 752, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{43}H_{48}O_{10}$ (M^+) 724.3248, found *m/z* 724.3216.

Methyl 4-*tert*-butyldimethylsilyloxy-5-{[(2'*R*,3'*R*,4'*R*,5'*S*,6'*S*)-4',5'-dibenzyloxy-3'-*p*-methoxybenzyloxy-6'-(2-*p*-methoxybenzyloxyethyl)]oxan-2'-yl}-2-pentynoate (20).

To a solution of **19** (3.19 g, 4.40 mmol) and 2,6-lutidine (1.53 ml, 13.2 mmol) in CH_2Cl_2 (20 ml) was added dropwise *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (1.52 ml, 6.60 mmol) at 0 °C, and the mixture was stirred at room temperature for 15 min. The reaction was quenched with brine, and the water layer was extracted repeatedly with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 9:2) to afford **20** (3.57 g, an α-OTBS:β-OTBS=1:2 mixture, 97% yield) as a pale yellow oil: ^1H NMR (270 MHz, $CDCl_3$), δ 7.38-7.18 (14H, m), 6.86 (2H, d, *J* = 9 Hz), 6.85 (2H, d, *J* = 9 Hz), 4.92-4.51 (7H, m), 4.41 (2H, br s), 3.79 (6H, s), 3.78 and 3.72 (totally 3H, each s), 3.69-3.11 (7H, m), 2.32-2.08 (2H, m), 1.85-1.56 (2H, m), 0.90 and 0.87 (totally 9H, each s), 0.14 and 0.13 (totally 3H, each s), and 0.10 and 0.06 (totally 3H, each s); IR (film), ν_{max} 3068, 3036, 2936, 2860, 2240, 1722, 1616, 1516, 1252, 1096, and 838 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{49}H_{62}O_{10}Si$ (M^+) 838.4114, found *m/z* 838.4091.

Methyl (2*Z*)-4-*tert*-butyldimethylsilyloxy-5-{[(2'*R*,3'*R*,4'*R*,5'*S*,6'*S*)-4',5'-dibenzyloxy-3'-*p*-methoxybenzyloxy-6'-(2-*p*-methoxybenzyloxyethyl)]oxan-2'-yl}-2-pentenoate (21).

A suspension of **20** (3.57 g, 4.25 mmol) and Lindlar cat. (0.71 g) in a 6:1 mixture of MeOH-PhH (31 ml) was stirred under H_2 atmosphere (ca. 1 atm) at room temperature for 7 days. The reaction mixture was filtered over Celite, and concentrated *in vacuo*. The crude product was purified by column chromatography on SiO_2 (hexane:EtOAc, 10:1 → 8:1) to afford **21** (3.57 g, an α-OTBS:β-OTBS=1:2 mixture, 99% yield) as pale yellow oils.

Data of pure samples.

α-OTBS: $[\alpha]_D^{21}$ -11.9° (*c* 0.98, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$), δ 7.32-7.25 (12H, m), 7.19 (2H, d, *J* = 9 Hz), 6.86 (2H, d, *J* = 9 Hz), 6.84 (2H, d, *J* = 9 Hz), 6.13 (1H, dd, *J* = 8, 11 Hz), 5.61 (1H, br d, *J* = 11 Hz), 5.54 (1H, br t, *J* = 8 Hz), 4.89 (1H, d, *J* = 11 Hz), 4.85 (1H, d, *J* = 11 Hz), 4.84 (1H, d, *J* = 11 Hz), 4.77 (1H, d, *J* = 11 Hz), 4.63 (1H, d, *J* = 11 Hz), 4.57 (1H, d, *J* = 11 Hz), 4.46 (1H, d, *J* = 11 Hz), 4.42 (1H, d, *J* = 11 Hz), 3.793 (3H, s), 3.789 (3H, s), 3.69-3.58 (3H, m), 3.65 (3H, s), 3.33 (1H, br t, *J* = 9 Hz), 3.31 (1H, dt, *J* = 2, 9 Hz), 3.24 (1H, t, *J* = 9 Hz), 3.19 (1H, t, *J* = 9 Hz), 2.22-2.14 (1H, m), 2.10 (1H, br dd, *J* = 9, 13 Hz), 1.78-1.64 (2H, m), 0.87 (9H, s), 0.03 (3H, s), and 0.01 (3H, s); IR (film), ν_{max} 3068, 3036, 2956, 2860, 1726, 1650, 1616, 1516, 1250, 1094, 836, 778, and 698 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{49}H_{64}O_{10}Si$ (M^+) 840.4270, found *m/z* 840.4304.

β-OTBS: $[\alpha]_D^{21}$ +6.47° (*c* 1.11, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$), δ 7.33-7.25 (12H, m), 7.21 (2H, d, *J* = 9 Hz), 6.85 (2H, d, *J* = 9 Hz), 6.83 (2H, d, *J* = 9 Hz), 6.13 (1H, dd, *J* = 9, 12 Hz), 5.61 (1H, dd, *J* = 1, 12 Hz), 5.52 (1H, br t, *J* = 9 Hz), 4.90 (1H, d, *J* = 11 Hz), 4.87 (1H, d, *J* = 11 Hz), 4.86 (1H, d, *J* = 11 Hz), 4.77 (1H, d, *J* = 11 Hz), 4.64 (1H, d, *J* = 11 Hz), 4.56 (1H, d, *J* = 11 Hz), 4.46 (2H, s), 3.79 (6H, s), 3.75 (1H, dt, *J* = 5, 9 Hz), 3.70-3.57 (2H, m), 3.69 (3H, s), 3.43 (1H, br t, *J* = 10 Hz), 3.32 (1H, dt, *J* = 2, 9 Hz), 3.31 (1H, t, *J* = 9 Hz), 3.18 (1H, t, *J* = 9 Hz), 2.24-2.16 (1H, m), 1.96 (1H, br dd, *J* = 10, 12 Hz), 1.89-1.65 (1H, m), 1.38 (1H, ddd, *J* = 2, 10, 12 Hz), 0.86 (9H, s), 0.01 (3H, s), and -0.01 (3H, s); IR (film), ν_{max} 3066, 3034, 2958, 2858, 1727, 1653, 1615, 1517, 1251, 1095, 825, 735, and 699 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{49}H_{64}O_{10}Si$ (M^+) 840.4270, found *m/z* 840.4300.

Methyl (2*Z*,4*S*)-4-*tert*-butyldimethylsilyloxy-5-{[(2'*R*,3'*R*,4'*R*,5'*S*,6'*S*)-4',5'-dibenzyloxy-3'-hydroxy-6'-(2-hydroxyethyl)]oxan-2'-yl}-2-pentenoate (7) and (4*R*)-diastereoisomer (22)

To a solution of **21** (3.54 g, 4.21 mmol) in CH_2Cl_2 (40 ml) and water (4 ml) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (2.87 g, 12.6 mmol) at room temperature, and the mixture was stirred

at room temperature for 30 min. The mixture was quenched with satd. aq. $NaHCO_3$ and extracted repeatedly with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 4:1→3:1) to afford **7** (0.57 g, 22% yield) and **22** (1.47 g, 58% yield) as colorless oils.

Data of pure samples.

7: $[\alpha]_D^{22}$ -1.05° (*c* 1.10, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$), δ 7.38-7.24 (10H, m), 6.18 (1H, dd, *J* = 9, 12 Hz), 5.80 (1H, dd, *J* = 1, 12 Hz), 5.57 (1H, br dt, *J* = 4, 8 Hz), 4.92 (1H, d, *J* = 12 Hz), 4.87 (1H, d, *J* = 11 Hz), 4.81 (1H, d, *J* = 12 Hz), 4.65 (1H, d, *J* = 11 Hz), 3.93 (1H, br t, *J* = 11 Hz), 3.75-3.63 (1H, m), 3.71 (3H, s), 3.46 (1H, t, *J* = 9 Hz), 3.45 (1H, dt, *J* = 3, 10 Hz), 3.35 (1H, br t, *J* = 9 Hz), 3.26 (1H, br t, *J* = 9 Hz), 3.45 (1H, br dt, *J* = 4, 9 Hz), 2.81-2.68 (1H, br s), 2.22-2.07 (1H, m), 2.01 (1H, ddd, *J* = 3, 8, 14 Hz), 1.80 (1H, ddd, *J* = 4, 8, 14 Hz), 1.65-1.46 (2H, m), 0.88 (9H, s), 0.07 (3H, s), and 0.03 (3H, s); IR (film), ν_{max} 3504, 3068, 3036, 2956, 2860, 1716, 1652, 1408, 1094, 836, 780, and 698 cm^{-1}; HR-EI-MS, calcd. for $C_{33}H_{48}O_8Si$ (M^+) 600.3119, found *m/z* 600.3134.

22: $[\alpha]_D^{22}$ -14.1° (*c* 1.00, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$), δ 7.39-7.27 (10H, m), 6.20 (1H, dd, *J* = 8, 12 Hz), 5.69 (1H, dd, *J* = 1, 12 Hz), 5.47 (1H, br t, *J* = 8 Hz), 4.97 (1H, d, *J* = 11 Hz), 4.89 (1H, d, *J* = 11 Hz), 4.80 (1H, d, *J* = 11 Hz), 4.64 (1H, d, *J* = 11 Hz), 3.82-3.75 (2H, br, m), 3.71 (3H, s), 3.50 (1H, dt, *J* = 2, 9 Hz), 3.49 (1H, t, *J* = 9 Hz), 3.43 (1H, dt, *J* = 1, 9 Hz), 3.35 (1H, t, *J* = 9 Hz), 3.31 (1H, t, *J* = 9 Hz), 2.18-2.45 (2H, m), 1.87-1.71 (1H, m), 1.53 (1H, ddd, *J* = 2, 9, 14 Hz), 0.88 (9H, s), 0.07 (3H, s), and 0.01 (3H, s); IR (film), ν_{max} 3432, 3068, 3036, 2956, 2860, 1724, 1650, 1404, 1198, 1082, 836, 778, and 698 cm^{-1}; HR-EI-MS, calcd. for $C_{33}H_{48}O_8Si$ (M^+) 600.3119, found *m/z* 600.3132.

Methyl {(1*R*,3*R*,4*S*,6*R*,8*S*,9*S*,10*R*)-9,10-dibenzyloxy-4-*tert*-butyldimethylsilyloxy-8-(2-hydroxyethyl)-2,7-dioxabicyclo[4.4.0]decan-3-yl}acetate (6).

To a solution of **7** (56.3 mg, 93.7 μmol) in THF (5 ml) was added NaH (15.5 mg, 646 μmol) at -40 °C, and the mixture was stirred at room temperature for 2 h. After cooling to 0 °C, the reaction was quenched with satd. aq. NH_4Cl and extracted repeatedly with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give the crude products. To a solution of the crude products in MeOH (5 ml) was added potassium *tert*-butoxide (*t*-BuOK) (31.6 mg, 282 μmol), and the mixture was stirred at room temperature for 18 h. The reaction mixture was diluted with ether, and treated with satd. aq. NH_4Cl. The water layer was extracted repeatedly with ether, and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on SiO_2 (hexane:EtOAc, 3:1) to afford **6** (51.5 mg, 91% yield for 2 steps) as white crystals: m.p. 155-156 °C; $[\alpha]_D^{20}$ +24.3° (*c* 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.38-7.23 (10H, m), 4.93 (1H, d, *J* = 11 Hz), 4.90 (1H, d, *J* = 11 Hz), 4.65 (1H, d, *J* = 11 Hz), 4.58 (1H, d, *J* = 11 Hz), 3.74 (2H, br t, *J* = 5 Hz, H-11), 3.67 (1H, br dt, *J* = 3, 10 Hz, H-2), 3.60 (3H, s), 3.56 (1H, t, *J* = 9 Hz, H-7), 3.50 (1H, dt, *J* = 3, 9 Hz, H-9), 3.42 (1H, ddd, *J* = 5, 9, 11 Hz, H-3), 3.27 (1H, br t, *J* = 9 Hz, H-8), 3.23 (1H, t, *J* = 9 Hz, H-6), 3.13 (1H, ddd, *J* = 4, 9, 11 Hz, H-5), 2.86 (1H, dd, *J* = 3, 15 Hz, H-1), 2.36 (1H, dd, *J* = 10, 15 Hz, H-1), 2.30 (1H, br dt, *J* = 12, 5 Hz, H-4-eq), 2.06 (1H, br ddt, *J* = 3, 15, 5 Hz, H-10), 1.68 (1H, br ddt, *J* = 9, 15, 6 Hz, H-10), 1.54 (1H, q, *J* = 11 Hz, H-4-ax), 0.88 (9H, s), 0.08 (3H, s), and 0.07 (3H, s); IR (KBr), ν_{max} 3496, 3068, 3032, 2956, 2860, 1738, 1458, 1260, 1084, 856, 776, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{33}H_{49}O_8Si$ (M^++H) 601.3198, found *m/z* 601.3201.

Methyl {(1*R*,3*R*,4*S*,6*R*,8*S*,9*S*,10*R*)-9,10-dibenzyloxy-4-*tert*-butyldimethylsilyloxy-8-(2-*p*-methoxybenzyloxyethyl)-2,7-dioxabicyclo[4.4.0]decan-3-yl}acetate (23).

To a solution of **6** (58.2 mg, 96.9 μmol) and *p*-methoxybenzyl-2,2,2-trichloroacetimidate [MPMOC(=NH)CCl_3] (30.2 μl, 145 μmol) in ether (3 ml) was added dropwise a 11.3 mM solution of TfOH in ether (17.2 μl, 0.194 μmol) and the mixture was stirred at room temperature for 10 min. The reaction was quenched with satd. aq. $NaHCO_3$ and extracted repeatedly with ether. The combined organic layers were

washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 15:1, and PhH:EtOAc, 50:1) to afford **23** (52.7 mg, 75% yield) as white crystals: m.p. 101-103 °C, $[\alpha]_D^{20}$ +21.4° (*c* 0.87, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.38-7.20 (12H, m), 6.85 (2H, d, *J* = 9 Hz), 4.91 (1H, d, *J* = 11 Hz), 4.89 (1H, d, *J* = 11 Hz), 4.64 (1H, d, *J* = 11 Hz), 4.59 (1H, d, *J* = 11 Hz), 4.44 (1H, d, *J* = 12 Hz), 4.37 (1H, d, *J* = 12 Hz), 3.79 (3H, s), 3.65 (1H, dt, *J* = 2, 9 Hz), 3.61-3.52 (3H, m), 3.60 (3H, s), 3.47-3.35 (2H, m), 3.23 (1H, t, *J* = 9 Hz), 3.20 (1H, t, *J* = 9 Hz), 3.06 (1H, dt, *J* = 5, 9 Hz), 2.86 (1H, dd, *J* = 3, 15 Hz), 2.35 (1H, dd, *J* = 10, 15 Hz), 2.33-2.11 (2H, m), 1.74-1.55 (1H, m), 1.52 (1H, br q, *J* = 11 Hz), 0.88 (9H, s), 0.09 (3H, s), and 0.07 (3H, s); IR (film), ν_{max} 3068, 3036, 2956, 2936, 2864, 1746, 1616, 1516, 1252, 1090, 1040, 838, 736, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{41}H_{56}O_9Si$ (M^+) 720.3695, found *m/z* 720.3717.

2-{(1*R*,3*R*,4*S*,6*R*,8*S*,9*S*,10*R*)-9,10-Dibenzyloxy-4-*tert*-butyldimethylsilyloxy-8-(2-*p*-methoxybenzyloxyethyl)-2,7-dioxabicyclo[4.4.0]decan-3-yl}ethanol (24).

To a solution of **23** (371 mg, 515 μmol) in ether (15 ml) was added $LiAlH_4$ (63.0 mg, 1.86 mmol) at -5 °C, and the mixture was stirred at the same temperature for 30 min. Water (70 μl) was added to the mixture, and the mixture was stirred vigorously at room temperature until a white gel was generated. To the mixture were added 4 M aq. NaOH (70 μl) and water (140 μl), and the mixture was stirred vigorously at room temperature until a white solid was generated. The mixture was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 3:1) to afford **24** (356 mg, 100% yield) as a colorless oil: $[\alpha]_D^{20}$ +17.6° (*c* 0.80, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.39-7.20 (12H, m), 6.86 (2H, d, *J* = 9 Hz), 4.90 (1H, d, *J* = 11 Hz), 4.86 (1H, d, *J* = 11 Hz), 4.75 (1H, d, *J* = 11 Hz), 4.62 (1H, d, *J* = 11 Hz), 4.45 (1H, d, *J* = 12 Hz), 4.38 (1H, d, *J* = 12 Hz), 3.79 (3H, s), 3.58 (2H, br t, *J* = 6 Hz), 3.57 (1H, t, *J* = 9 Hz), 3.49-3.38 (2H, m), 3.32 (1H, dt, *J* = 2, 9 Hz), 3.26 (1H, t, *J* = 9 Hz), 3.15 (1H, t, *J* = 9 Hz), 3.07 (1H, dt, *J* = 2, 9 Hz), 2.28 (1H, dt, *J* = 11, 4 Hz), 2.21-2.02 (2H, m), 2.02-1.83 (1H, br s), 1.75-1.57 (2H, m), 1.49 (1H, br q, *J* = 11 Hz), 0.88 (9 H, s), 0.09 (3H, s), and 0.08 (3H, s); IR (film), ν_{max} 3484, 3068, 3036, 2956, 2936, 2860, 1614, 1516, 1458, 1362, 1250, 1088, 856, 838, 776, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{40}H_{56}O_8Si$ (M^+) 692.3746, found *m/z* 692.3708.

(1*R*,3*S*,4*S*,5*R*,6*R*,8*R*,9*S*)-4,5-Dibenzyloxy-9-*tert*-butyldimethylsilyloxy-8-(2-*tert*-butyldiphenylsilyloxyethyl)-3-(2-*p*-methoxybenzyloxyethyl)-2,7-dioxabicyclo[4.4.0]decane (25).

From **24:**

To a solution of **24** (356 mg, 514 μmol), NEt_3 (172 μl, 1.23 mmol), and DMAP (a cat. amount) was added dropwise *tert*-butyldiphenylsilyl chloride (TBDPSCl) (160 μl, 617 μmol), and the mixture was stirred at room temperature for 9 h. The reaction was quenched with brine, and the water layer was extracted repeatedly with ether. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 12:1) to afford **25** (454 mg, 95% yield) as a colorless oil:

From **32:**

To a solution of **32** (97.8 mg, 120 μmol) and 2,6-lutidine (55.5 μl, 480 μmol) in CH_2Cl_2 (3 ml) was added dropwise TBSOTf (55.1 μl, 240 μmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. The mixture was treated with brine, and the water layer was extracted repeatedly with ether. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 12:1) to afford **25** (108 mg, 97% yield) as a colorless oil: $[\alpha]_D^{23}$ +15.5° (*c* 1.17, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.68-7.60 (4H, m), 7.42-7.15 (18H, m), 6.85 (2H, d, *J* = 9 Hz), 4.99 (1H, d, *J* = 11 Hz), 4.81 (1H, d, *J* = 11 Hz), 4.57 (2H, d, *J* = 11 Hz), 4.44 (1H, d, *J* = 12 Hz), 4.37 (1H, d, *J* = 12 Hz), 3.87 (2H, br t, *J* = 7 Hz), 3.79 (3H, s), 3.56 (2H, br t, *J* = 7 Hz), 3.52 (1H, t, *J* = 9 Hz), 3.45-3.26 (3H, m), 3.22 (1H, t, *J* = 9 Hz), 3.09 (1H, t, *J* = 9 Hz), 3.02 (1H, dt, *J* = 4, 9 Hz), 2.20-2.10 (3H, m), 1.74-1.50 (2H, m), 1.47 (1H, br q, *J* = 11 Hz), and 1.03 (9H, s); IR (film), ν_{max} 3072, 3036, 2960,

2936, 2860, 1616, 1516, 1250, 1092, 838, 736, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{56}H_{74}O_8Si_2$ (M^+) 930.4924, found *m/z* 930.4869.

Methyl {(1*R*,3*R*,4*R*,6*R*,8*S*,9*S*,10R)-9,10-dibenzyloxy-4-*tert*-butyldimethylsilyloxy-8-(2-hydroxyethyl)-2,7-dioxabicyclo[4.4.0]decan-3-yl}acetate (26).

To a solution of **22** (37.8 mg, 62.9 μmol) in THF (5 ml) was added NaH (10.0 mg, 417 μmol) at -40 °C, and the mixture was stirred at room temperature for 4.5 h. After cooling at 0 °C, the reaction was quenched with satd. aq. NH_4Cl and extracted repeatedly with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give crude products. To a solution of the products in MeOH (5 ml) was added *t*-BuOK (21.2 mg, 189 μmol), and the mixture was stirred at room temperature for 14 h. The reaction mixture was diluted with ether, and treated with satd. aq. NH_4Cl. The water layer was extracted repeatedly with ether, and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 2:1) to afford **26** (37.5 mg, 99% yield for 2 steps) as a colorless oil: $[\alpha]_D^{20}$ -9.44° (*c* 1.34, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$), δ 7.38-7.23 (10H, m), 4.94 (1H, d, *J* = 11 Hz), 4.93 (1H, d, *J* = 11 Hz), 4.70 (1H, d, *J* = 11 Hz), 4.59 (1H, d, *J* = 11 Hz), 3.94 (1H, br s, H-3), 3.88 (1H, ddd, *J* = 2, 5, 8 Hz, H-2), 3.74 (2H, br t, *J* = 5 Hz, H-11), 3.68 (1H, t, *J* = 9 Hz, H-7), 3.61 (3H, s), 3.52 (1H, dt, *J* = 3, 9 Hz, H-9), 3.46 (1H, ddd, *J* = 4, 9, 12 Hz, H-5), 3.28 (1H, br t, *J* = 9 Hz, H-8), 3.22 (1H, t, *J* = 9 Hz, H-6), 2.67 (1H, dd, *J* = 8, 16 Hz, H-1), 2.46 (1H, dd, *J* = 5, 16 Hz, H-1), 2.15-2.03 (2H, m, H-4-eq and H-10), 1.75-1.61 (2H, m, H-10 and H-4-ax), 0.92 (9H, s), 0.08 (3H, s), and 0.04 (3H, s); IR (film), ν_{max} 3480, 3068, 3032, 2956, 2860, 1742, 1258, 1076, 838, 748, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{33}H_{49}O_8Si$ (M^+) 601.3198, found *m/z* 601.3209.

Methyl {(1*R*,3*R*,4*R*,6*R*,8*S*,9*S*,10*R*)-9,10-dibenzyloxy-4-*tert*-butyldimethylsilyloxy-8-(2-*p*-methoxybenzyloxyethyl)-2,7-dioxabicyclo[4.4.0]decan-3-yl}acetate (27).

To a solution of **26** (140 mg, 233 μmol) and MPMOC(=NH)CCl_3 (72.6 μl, 350 μmol) in ether (4 ml) was added dropwise a 11.3 mM solution of TfOH in ether (20.7 μl, 0.233 μmol) and the mixture was stirred at room temperature for 10 min. The mixture was treated with satd. aq. $NaHCO_3$ and extracted repeatedly with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 5:1) to afford **27** (144 mg, 86% yield) as a colorless oil: $[\alpha]_D^{20}$ -3.61° (*c* 1.16, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.37-7.21 (12H, m), 6.85 (2H, d, *J* = 9 Hz), 4.93 (1H, d, *J* = 11 Hz), 4.91 (1H, d, *J* = 11 Hz), 4.69 (1H, d, *J* = 11 Hz), 4.60 (1H, d, *J* = 11 Hz), 4.40 (2H, s), 3.94 (1H, br s), 3.88 (1H, br dd, *J* = 5, 8 Hz), 3.79 (3H, s), 3.66 (1H, t, *J* = 9 Hz), 3.61 (3H, s), 3.56 (2H, dd, *J* = 6, 7 Hz), 3.47-3.37 (2H, m), 3.25 (1H, br t, *J* = 9 Hz), 3.20 (1H, t, *J* = 9 Hz), 2.67 (1H, dd, *J* = 8, 16 Hz), 2.46 (1H, dd, *J* = 5, 16 Hz), 2.26-2.05 (2H, m), 1.75-1.55 (2H, m), 0.92 (9H, s), 0.08 (3H, s), and 0.04 (3H, s); IR (film), ν_{max} 3068, 3032, 2956, 2860, 1742, 1616, 1516, 1458, 1364, 1296, 1250, 1100, 838, 776, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{41}H_{56}O_9Si$ (M^+) 720.3694, found *m/z* 720.3696.

2-{(1*R*,3*R*,4*R*,6*R*,8*S*,9*S*,10*R*)-9,10-Dibenzyloxy-4-*tert*-butyldimethylsilyloxy-8-(2-*p*-methoxybenzyloxyethyl)-2,7-dioxabicyclo[4.4.0]decan-3-yl}ethanol (28).

To a solution of **27** (831 mg, 1.15 mmol) in ether (20 ml) was added $LiAlH_4$ (145 mg, 3.84 mmol) at -5 °C, and the mixture was stirred at the same temperature for 20 min. Water (150 μl) was added to the mixture, and the mixture was stirred vigorously at room temperature until a white gel was generated. To the mixture were added 4 M aq. NaOH (150 μl) and water (300 μl), and the mixture was stirred vigorously at room temperature until a white solid was generated. The mixture was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 3:2) to

afford **28** (789 mg, 99% yield) as a colorless oil: $[\alpha]_D^{22}$ +1.97° (*c* 1.03, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.39-7.20 (12H, m), 6.85 (2H, d, *J* = 9 Hz), 4.91 (2H, br d, *J* = 11 Hz), 4.78 (1H, d, *J* = 11 Hz), 4.63 (1H, d, *J* = 11 Hz), 4.41 (2H, br s), 3.83-3.74 (4H, m), 3.79 (3H, s), 3.69 (1H, t, *J* = 9 Hz), 3.57 (2H, br t, *J* = 6 Hz), 3.52-3.36 (2H, m), 3.27 (1H, t, *J* = 9 Hz), 3.16 (1H, t, *J* = 9 Hz), 2.26-1.92 (3H, m), 1.75-1.46 (3H, m), 0.92 (9H, s), 0.09 (3H, s), and 0.07 (3H, s); IR (film), ν_{max} 3486, 3068, 3032, 2956, 2860, 1616, 1516, 1250, 1088, 838, 776, and 700 cm^{-1}; HR-EI-MS, calcd. for $C_{40}H_{55}O_8Si$ (M^+-H) 691.3668, found *m/z* 691.3651.

(1*R*,3*R*,4*R*,6*R*,7*R*,8*S*,9*S*)-7,8-Dibenzyloxy-4-(2-hydroxyethyl)-9-(2-*p*-methoxybenzyloxyethyl)-5,10-dioxabicyclo[4.4.0]decan-3-ol (29).

To a solution of **28** (6.0 mg, 8.66 μmol) in THF (0.5 ml) was added dropwise tetrabutylammonium fluoride (TBAF) (1.0 M solution in THF, 17.3 μl, 17.3 μmol), and the mixture was stirred at room temperature for 30 min. The reaction mixture was diluted with EtOAc, and water was added. The water layer was extracted repeatedly with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 1:10 → 0:1) to afford **29** (5.0 mg, 100% yield) as white crystals: m.p. 97-98 °C; $[\alpha]_D^{26}$ -1.20° (*c* 0.93, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.38-7.20 (12H, m), 6.87 (2H, d, *J* = 9 Hz), 4.92 (1H, d, *J* = 11 Hz), 4.90 (1H, d, *J* = 11 Hz), 4.77 (1H, d, *J* = 11 Hz), 4.62 (1H, d, *J* = 11 Hz), 4.46 (1H, d, *J* = 12 Hz), 4.35 (1H, d, *J* = 12 Hz), 3.89 (1H, br s), 3.85-3.72 (2H, m), 3.81 (3H, s), 3.68 (1H, t, *J* = 9 Hz), 3.64 (1H, br dd, *J* = 6, 8 Hz), 3.54 (2H, dd, *J* = 5, 8 Hz), 3.49-3.33 (2H, m), 3.23 (1H, br t, *J* = 9 Hz), 3.19 (1H, t, *J* = 9 Hz), 2.24-2.10 (2H, m), 2.05-1.91 (1H, m), 1.86-1.69 (1H, m), and 1.68-1.52 (2H, m); IR (film), ν_{max} 3444, 3036, 2872, 1614, 1516, 1456, 1362, 1250, 1096, 822, and 700 cm^{-1}; HR-EI-MS, calcd. for $C_{34}H_{41}O_8$ (M^+-H) 577.2802, found *m/z* 577.2805.

(1*R*,3*R*,4*R*,6*R*,7*R*,8*S*,9*S*)-7,8-Dibenzyloxy-4-(2-*tert*-butyldiphenylsilyloxyethyl)-9-(2-*p*-methoxybenzyloxyethyl)-5,10-dioxabicyclo[4.4.0]decan-3-ol (30).

To a solution of **29** (89.8 mg, 155 μmol), NEt_3 (86.7 μl, 621 μmol), and DMAP (a cat. amount) was added dropwise TBDPSCl (80.8 μl, 310 μmol), and the mixture was stirred at room temperature for 15 h. The reaction was quenched with brine, and the water layer was extracted repeatedly with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 4:1 → 3:1) to afford **30** (127 mg, 100% yield) as a colorless oil: $[\alpha]_D^{25}$ -0.89° (*c* 1.06, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.68-7.61 (4H, m), 7.45-7.20 (18H, m), 6.87 (2H, d, *J* = 9 Hz), 4.90 (1H, d, *J* = 11 Hz), 4.89 (1H, d, *J* = 11 Hz), 4.68 (1H, d, *J* = 11 Hz), 4.60 (1H, d, *J* = 11 Hz), 4.45 (1H, d, *J* = 12 Hz), 4.36 (1H, d, *J* = 12 Hz), 3.91 (1H, br s), 3.90-3.71 (2H, m), 3.80 (3H, s), 3.68 (1H, t, *J* = 9 Hz), 3.62 (1H, br t, *J* = 8 Hz), 3.54 (2H, br t, *J* = 7 Hz), 3.48-3.35 (2H, m), 3.22 (1H, br t, *J* = 9 Hz), 3.17 (1H, t, *J* = 9 Hz), 2.77 (1H, br s), 2.28-2.11 (2H, m), 1.99-1.81 (2H, m), 1.70-1.50 (4H, m), and 1.05 (9H, s); IR (film), ν_{max} 3464, 3072, 3032, 2932, 2860, 1614, 1250, 1100, 822, 738, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{50}H_{60}O_8Si$ (M^+) 816.4059, found *m/z* 816.4036.

(1*R*,4*R*,6*R*,7*R*,8*S*,9*S*)-7,8-Dibenzyloxy-4-(2-*tert*-butyldiphenylsilyloxyethyl)-9-(2-*p*-methoxybenzyloxyethyl)-5,10-dioxabicyclo[4.4.0]decan-3-one (31).

To a solution of oxalyl chloride (270 μl, 3.09 mmol) in CH_2Cl_2 (15 ml) was added DMSO (292 μl, 4.12 mmol) in CH_2Cl_2 (2 ml) at -78 °C and the mixture was stirred at -78 °C for 30 min. A solution of **30** (841 mg, 1.03 mmol) in CH_2Cl_2 (3 ml) was added and the mixture was stirred at -78 °C for 3 h. NEt_3 (1.15 ml, 8.24 mmol) was added at -78 °C and the mixture was stirred at 0 °C for 10 min. The reaction mixture was diluted with ether, and treated with water. The water layer was extracted repeatedly with ether, and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 4:1 → 3:1) to afford **31** (838 mg, 100% yield) as a pale yellow oil: $[\alpha]_D^{23}$ -6.67° (*c* 0.91, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.65-7.60

(4H, m), 7.42-7.20 (18H, m), 6.85 (2H, d, J = 9 Hz), 4.91 (1H, d, J = 11 Hz), 4.85 (1H, d, J = 11 Hz), 4.66 (1H, d, J = 11 Hz), 4.61 (1H, d, J = 11 Hz), 4.44 (1H, d, J = 12 Hz), 4.36 (1H, d, J = 12 Hz), 4.02 (1H, dd, J = 4, 8 Hz), 3.84 (2H, br t, J = 7 Hz), 3.79 (3H, s), 3.63 (1H, t, J = 9 Hz), 3.54 (2H, br dd, J = 6, 7 Hz), 3.46 (1H, br t, J = 9 Hz), 3.49-3.41 (1H, m), 3.43-3.33 (1H, m), 3.30 (1H, br t, J = 9 Hz), 2.86 (1H, dd, J = 5, 16 Hz), 2.41 (1H, dd, J = 11, 16 Hz), 2.30-2.11 (2H, m), 1.89-1.73 (1H, m), 1.73-1.58 (1H, m), and 1.03 (9H, s); IR (film), ν_{max} 3072, 3036, 2936, 2860, 1730, 1616, 1516, 1250, 1106, 822, 738, and 702 cm^{-1}; HR-FD/FI-MS calcd. for $C_{50}H_{58}O_8Si$ (M^+) 814.3902, found *m/z* 814.3863.

(1*R*,3*S*,4*R*,6*R*,7*R*,8*S*,9*S*)-7,8-Dibenzyloxy-4-(2-*tert*-butyldiphenylsilyloxyethyl)-9-(2-*p*-methoxybenzyloxyethyl)-5,10-dioxabicyclo[4.4.0]decan-3-ol (32).

To a solution of **31** (86.5 mg, 106 μmol) in ether (4 ml) was added $LiAlH_4$ (16.0 mg, 472 μmol) at -20 °C, and the mixture was stirred at the same temperature for 15 min. The reaction was quenched with 1 M aq. HCl, and the water layer was extracted repeatedly with ether. The combined organic layers were washed with satd. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 2:1) to afford **32** (85.8 mg, 99% yield) as a colorless oil: $[\alpha]_D^{16}$ +2.11° (*c* 1.00, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.69-7.62 (4H, m), 7.48-7.20 (18H, m), 6.86 (2H, d, J = 9 Hz), 4.89 (1H, d, J = 11 Hz), 4.83 (1H, d, J = 11 Hz), 4.65 (1H, d, J = 11 Hz), 4.60 (1H, d, J = 11 Hz), 4.45 (1H, d, J = 12 Hz), 4.37 (1H, d, J = 12 Hz), 3.89-3.81 (2H, m), 3.80 (3H, s), 3.60-3.34 (6H, m), 3.28-3.17 (2H, m), 3.14-3.00 (2H, m), 2.37 (1H, br dt, J = 11, 4 Hz), 2.25-2.11 (1H, m), 2.06-1.93 (1H, m), 1.93-1.79 (1H, m), 1.74-1.58 (1H, m), 1.45 (1H, br q, J = 11 Hz), and 1.05 (9H, s); IR (film), ν_{max} 3448, 3072, 3036, 2936, 2860, 1614, 1516, 1250, 1104, 1038, 824, 738, and 702 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{50}H_{61}O_8Si$ (M^++H) 817.4137, found *m/z* 817.4094.

2-[(1*R*,3*S*,4*S*,5*R*,6*R*,8*R*,9*S*)-4,5-Dibenzyloxy-9-*tert*-butyldimethylsilyloxy-8-(2-*tert*-butyldiphenylsilyloxyethyl)-2,7-dioxabicyclo[4.4.0]decan-3-yl]ethanol (33).

To a solution of **25** (106 mg, 113 μmol) in CH_2Cl_2 (4 ml) and water (0.4 ml) was added DDQ (38.7 mg, 170 μmol) at room temperature, and the mixture was stirred at room temperature for 40 min. The mixture was treated with satd. aq. $NaHCO_3$ and extracted repeatedly with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 7:1 → 4:1) to afford **33** (92.0 mg, 100% yield) as a colorless oil: $[\alpha]_D^{22}$ +18.7° (*c* 1.17, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$), δ 7.65-7.62 (4H, m), 7.39-7.19 (16H, m), 4.91 (1H, d, J = 11 Hz), 4.82 (1H, d, J = 11 Hz), 4.58 (1H, d, J = 11 Hz), 4.57 (1H, d, J = 11 Hz), 3.87 (2H, br dd, J = 6, 8 Hz, H-1), 3.74 (2H, br t, J = 6 Hz, H-12), 3.54 (1H, t, J = 9 Hz, H-8), 3.49 (1H, dt, J = 3, 9 Hz, H-10), 3.36 (1H, br dt, J = 4, 10 Hz, H-4), 3.30 (1H, br dt, J = 2, 10 Hz, H-3), 3.26 (1H, t, J = 9 Hz, H-9), 3.13 (1H, t, J = 9 Hz, H-7), 3.10 (1H, br dt, J = 4, 10 Hz, H-6), 2.52-2.30 (1H, br s, OH), 2.27 (1H, br dt, J = 11, 4 Hz, H-5-eq), 2.25-2.16 (1H, m, H-2), 2.10-2.01 (1H, m, H-11), 1.73-1.63 (1H, m, H-11), 1.61-1.49 (1H, m, H-2), 1.50 (1H, br q, J = 11 Hz, H-5-ax), 1.04 (9H, s), 0.90 (9H, s), and 0.08 (6H, s); IR (film), ν_{max} 3464, 3072, 3036, 2960, 2936, 2860, 1474, 1430, 1362, 1254, 1088, 858, 838, 776, 736, 700, and 614 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{48}H_{67}O_7Si_2$ (M^++H) 811.4427, found *m/z* 811.4394.

(1*R*,2*R*,3*S*,4*S*,6*R*,8*S*,9*R*)-8-*tert*-Butyldimethylsilyloxy-9-(2-*tert*-butyldiphenylsilyloxyethyl)-4-(2-hydroxyethyl)-5,10-dioxabicyclo[4.4.0]decane-2,3-diol (35).

A suspension of **33** (355 mg, 438 μmol) and 10% palladium hydroxide on carbon [$Pd(OH)_2$/C] (70 mg) in a 4:1 mixture of EtOH-EtOAc (5 ml) was stirred under H_2 atmosphere (ca. 1 atm) at room temperature for 7 days. The reaction mixture was filtered over Celite, and concentrated *in vacuo*. The crude product was purified by column chromatography on SiO_2 (hexane:EtOAc, 3:1 → 1:1 → 1:9) to afford **35** (258 mg, 44% yield), **34** (293 mg, 44% yield), and the starting material (34.6 mg, 5% yield) as colorless oils, respectively:

35: $[\alpha]_D^{23}$ +20.7° (*c* 0.51, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$), δ 7.68-7.63 (4H, m), 7.45-7.27 (6H, m),

3.87-3.72 (4H, m), 3.51-3.28 (4H, m), 3.27 (1H, dt, J = 2, 9 Hz), 3.10 (1H, dt, J = 4, 9 Hz), 3.09 (1H, dt, J = 4, 9 Hz), 3.02-2.88 (1H, br s), 2.88 (1H, t, J = 9 Hz), 2.61-2.47 (1H, br s), 2.47-2.39 (1H, br s), 2.32-2.14 (2H, m), 2.13-2.00 (1H, m), 1.89-1.75 (1H, m), 1.57-1.41 (2H, m), 1.04 (9H, s), 0.89 (9H, s), and 0.07 (6H, s); IR (film), ν_{max} 3392, 3072, 2956, 2932, 2860, 1430, 1256, 1110, 1082, 1028, 836, 776, 758, 702, and 614 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{34}H_{55}O_7Si_2$ (M^++H) 631.3488, found *m/z* 631.3483.

(1*S*,2*R*,3*R*,5*R*,6*S*,8*R*,10*R*)-6-*tert*-Butyldimethylsilyloxy-5-(2-*tert*-butyldiphenylsilyloxyethyl)-14,14-dimethyl-4,9,13,15-tetraoxatricyclo[8.5.0.0^{3,8}]pentadecan-2-ol (36).

To a solution of **35** (20.4 mg, 32.3 μmol) in acetone (2 ml) was added dropwise a solution of PTS·H_2O (0.61 mg, 3.23 μmol) in acetone (0.1 ml), and the mixture was stirred at room temperature for 30 min. The reaction mixture was neutralized with $NaHCO_3$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 5:1 → 0:1) to afford **36** and the starting material. The recovered starting material was treated under the same conditions for 3 cycles to afford **36** (total 20.9 mg, total 96%) as a colorless oil: $[\alpha]_D^{20}$ +31.3° (*c* 0.98, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$), δ 7.67-7.63 (4H, m), 7.43-7.34 (6H, m), 3.84-3.69 (3H, m), 3.60-3.27 (7H, m), 3.07 (1H, ddd, J = 5, 9, 12 Hz), 2.90 (1H, t, J = 9 Hz), 2.28 (1H, dt, J = 12, 4 Hz), 2.24-2.13 (2H, m), 1.99-1.88 (1H, m), 1.77-1.61 (1H, m), 1.50 (1H, br q, J = 12 Hz), 1.41 (3H, s), 1.36 (3H, s), 1.04 (9H, s), 0.89 (9H, s), and 0.06 (6H, s); IR (film), ν_{max} 3528, 3072, 2932, 2856, 1430, 1386, 1252, 1220, 1100, 1086, 838, 702, and 614 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{37}H_{59}O_7Si_2$ (M^++H) 671.3801, found *m/z* 671.3822.

(1*S*,3*R*,5*S*,6*R*,8*R*,9*R*,10*S*)-8-Benzyloxy-5-*tert*-butyldimethylsilyloxy-6-(2-*tert*-butyldiphenylsilyloxyethyl)-12,12-dimethyl-2,7,11,13-tetraoxatricyclo[8.5.0.0^{3,8}]pentadecane (37).

To a solution of **36** (278 mg, 414 μmol) in THF (10 ml) was added NaH (400 mg, 16.6 mmol) at 0 °C. After warming to room temperature, BnBr (98.5 μl, 828 μmol) and tetrabutylammonium iodide (TBAI) (15.2 mg, 41.4 μmol) were added to the mixture, and the mixture was stirred at the same temperature for 31 h. After cooling at 0 °C, the reaction mixture was diluted with ether, and treated with satd. aq. NH_4Cl. The water layer was extracted repeatedly with ether, and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 12:1) to afford **37** (313 mg, 99% yield) as a colorless oil: $[\alpha]_D^{20}$ +38.1° (*c* 0.49, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.66-7.60 (4H, m), 7.40-7.20 (11H, m), 4.69 (1H, d, J = 12 Hz), 4.56 (1H, d, J = 12 Hz), 3.95-3.81 (2H, m), 3.72 (1H, br t, J = 12 Hz), 3.61-3.52 (2H, m), 3.41-3.20 (4H, m), 3.12-3.00 (2H, m), 2.33-2.14 (2H, m), 1.97-1.87 (1H, m), 1.73-1.47 (2H, m), 1.49 (1H, q, J = 11 Hz), 1.49 (3H, s), 1.34 (3H, s), 1.04 (9H, s), 0.90 (9H, s), 0.08 (3H, s), and 0.07 (3H, s); IR (film), ν_{max} 3072, 2932, 2856, 1474, 1430, 1362, 1252, 1220, 1108, 1088, 1042, 838, 776, 736, 700, and 612 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{44}H_{65}O_7Si_2$ (M^++H) 761.4271, found *m/z* 761.4250.

(1*R*,2*R*,3*S*,4*S*,6*R*,8*S*,9*R*)-2-Benzyloxy-8-*tert*-butyldimethylsilyloxy-9-(2-*tert*-butyldiphenylsilyloxyethyl)-4-(2-hydroxyethyl)-5,10-dioxabicyclo[4.4.0]decan-3-ol (34).

To a solution of **37** (9.2 mg, 12.1 μmol) in MeOH (1 ml) was added dropwise PTS·H_2O (0.23 mg, 1.21 μmol), and the mixture was stirred at room temperature for 50 min. The reaction mixture was neutralized with $NaHCO_3$, and filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 3:2 → 1:1) to afford **34** (8.2 mg, 94% yield) as a colorless oil: $[\alpha]_D^{20}$ +38.1° (*c* 0.49, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.65-7.39 (4H, m), 7.39-7.24 (9H, m), 7.20-7.16 (2H, m), 4.82 (1H, d, J = 11 Hz), 4.46 (1H, d, J = 11 Hz), 3.85 (2H, dd, J = 5, 8 Hz), 3.78 (2H, br t, J = 5 Hz), 3.48-3.26 (5H, m), 3.18-3.07 (2H, m), 2.53 (2H, br s), 2.32-2.17 (2H, m), 2.10-1.98 (1H, m), 1.84-1.72 (1H, m), 1.60-1.46 (2H, m), 1.03 (9H, s), 0.91 (9H, s), and 0.08 (6H, s); IR (film), ν_{max} 3392, 3072, 2932, 2856, 1430, 1254, 1108, 1086, 858, 838, 776, 738, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{41}H_{61}O_7Si_2$ (M^++H)

721.3957, found *m/z* 721.3951.

(1*R*,2*R*,3*S*,4*S*,6*R*,8*S*,9*R*)-2-Benzyloxy-8-*tert*-butyldimethylsilyloxy-9-(2-*tert*-butyldiphenylsilyloxyethyl)-4-(2-*p*-toluenesulfonyloxyethyl)-5,10-dioxabicyclo[4.4.0]decan-3-ol (38).

To a solution of **34** (104 mg, 144 μmol), NEt_3 (52.2 μl, 374 μmol), and DMAP (a cat. amount) in CH_2Cl_2 was added TsCl (35.7 mg, 187 μmol), and the mixture was stirred at room temperature for 3 h. The reaction was quenched with satd. aq. $NaHCO_3$. The water layer was extracted repeatedly with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 5:1 → 2:1) to afford **38** (104 mg, 83% yield) as a pale yellow oil: $[\alpha]_D^{20}$ +30.8° (*c* 1.11, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.78 (2H, d, *J* = 8 Hz), 7.65-7.61 (4H, m), 7.39-7.25 (11H, m), 7.21-7.14 (2H, m), 4.80 (1H, d, *J* = 12 Hz), 4.44 (1H, d, *J* = 12 Hz), 4.24-4.11 (2H, m), 3.84 (2H, dd, *J* = 5, 8 Hz), 3.40-3.14 (5H, m), 3.04 (1H, t, *J* = 9 Hz), 2.98 (1H, dt, *J* = 4, 9 Hz), 2.43 (3H, s), 2.28-2.13 (4H, m), 1.76-1.63 (1H, m), 1.43 (1H, br q, *J* = 11 Hz), 1.03 (9H, s), 0.92 (9H, s), 0.101 (3H, s), and 0.098 (3H, s); IR (film), ν_{max} 3556, 3068, 2932, 2856, 1598, 1430, 1362, 1252, 1178, 1090, 838, 776, 702, 664, 614, and 554 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{48}H_{67}O_9Si_2S$ (M^++H) 875.4046, found *m/z* 875.3999.

(1*R*,2*S*,3*S*,4*S*,6*R*,8*S*,9*R*)-2-Benzyloxy-8-*tert*-butyldimethylsilyloxy-9-(2-*tert*-butyldiphenylsilyloxyethyl)-4-(2-iodoethyl)-5,10-dioxabicyclo[4.4.0]decan-3-ol (39).

To a solution of **38** (26.6 mg, 30.4 μmol) in acetone (2 ml) was added sodium iodide (NaI) (22.8 mg, 152 μmol), and the mixture was stirred at 50 °C for 8 h. The reaction mixture was diluted with ether, and treated with 10% aq. sodium thiosulfate ($Na_2S_2O_3$). The water layer was extracted repeatedly with ether, and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 15:1) to afford **39** (21.8 mg, 86% yield) as a pale yellow oil: $[\alpha]_D^{20}$ +23.2° (*c* 1.09, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.65-7.61 (4H, m), 7.39-7.24 (9H, m), 7.19-7.15 (2H, m), 4.81 (1H, d, *J* = 11 Hz), 4.45 (1H, d, *J* = 11 Hz), 3.85 (2H, dd, *J* = 5, 8 Hz), 3.43-3.17 (7H, m), 3.15-3.03 (2H, m), 2.43-2.16 (3H, m), 2.31 (1H, br s), 1.98-1.80 (1H, m), 1.61-1.43 (2H, m), 1.03 (9H, s), 0.91 (9H, s), 0.097 (3H, s), and 0.093 (3H, s); IR (film), ν_{max} 3483, 3068, 2932, 2856, 1430, 1254, 1110, 1088, 836, 702, and 614 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{41}H_{60}O_6Si_2I$ (M^++H) 831.2975, found *m/z* 831.2967.

(1*R*,3*S*,4*S*,5*S*,6*R*,8*R*,9*S*)-5-Benzyloxy-9-*tert*-butyldimethylsilyloxy-8-(2-*tert*-butyldiphenylsilyloxyethyl)-3-(2-iodoethyl)-4-trimethylsilyloxy-2,7-dioxabicyclo[4.4.0]decane (40).

To a solution of **39** (68.4 mg, 82.3 μmol) and NEt_3 (45.9 μl, 329 μmol) in CH_2Cl_2 was added dropwise trimethylsilyl trifluoromethanesulfonate (TMSOTf) (31.8 μl, 165 μmol) at -10 °C, and the mixture was stirred at the same temperature for 10 min. The reaction was quenched with satd. aq. $NaHCO_3$, and the water layer was extracted repeatedly with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 15:1) to afford **40** (72.8 mg, 98% yield) as a pale yellow oil: $[\alpha]_D^{22}$ -2.04° (*c* 1.04, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.60-7.54 (4H, m), 7.38-7.22 (11H, m), 4.86 (1H, d, *J* = 11 Hz), 4.48 (1H, d, *J* = 11 Hz), 3.78 (2H, br t, *J* = 6 Hz), 3.41-3.17 (7H, m), 3.14-3.02 (2H, m), 2.33-2.10 (3H, m), 1.90-1.77 (1H, m), 1.59-1.39 (2H, m), 1.00 (9H, s), 0.90 (9H, s), 0.09 (3H, s), 0.08 (3H, s), and 0.05 (9H, s); IR (film), ν_{max} 3068, 2956, 2856, 1430, 1252, 1088, 840, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{44}H_{68}O_6Si_3I$ (M^++H) 903.3370, found *m/z* 903.3348.

{2-[(1*R*,3*S*,4*S*,5*S*,6*R*,8*R*,9*S*)-5-Benzyloxy-9-*tert*-butyldimethylsilyloxy-8-(2-*tert*-butyldiphenylsilyloxyethyl)-4-trimethylsilyloxy-2,7-dioxabicyclo[4.4.0]decan-3-yl]-ethyl}triphenylphosphonium iodide (4).

To a solution of **40** (72.8 mg, 80.6 μmol) in CH_3CN (4 ml) was added triphenylphosphine (PPh_3) (63.5 mg, 242 μmol), and the mixture was stirred at 60 °C for 27 h. After the solvent was removed, a syrup was washed repeatedly with hexane to remove triphenylphosphine to afford **4** (92.4 mg, 98% yield) as a pale yellow amorphous material: $[\alpha]_D^{22}$ +17.6° (*c* 0.97, CH_2Cl_2); ^{1}H NMR (300 MHz, C_6D_6), δ 7.86-7.77 (4H, m), 7.74-7.65 (6H, m), 7.47-6.92 (20H, m), 5.56-5.39 (1H, m), 5.19 (1H, d, *J* = 11 Hz), 4.62 (1H, d, *J* = 11 Hz), 4.45 (1H, br, t, *J* = 10 Hz), 4.07-3.93 (4H, m), 3.69-3.51 (3H, m), 3.36 (1H, t, *J* = 9 Hz), 3.35 (1H, t, *J* = 9 Hz), 3.28-3.20 (1H, m), 2.52-2.40 (1H, m), 2.30-2.16 (1H, m), 1.82-1.66 (2H, m), 1.44-1.32 (1H, m), 1.21 (9H, s), 1.05 (9H, s), 0.30 (3H, s), 0.23 (3H, s), and 0.01 (9H, s); IR (film), ν_{max} 3048, 2956, 2932, 1588, 1440, 1252, 1088, 838, 778, 736, 698, and 614 cm^{-1}; HR-FAB-MS, calcd. for $C_{62}H_{82}O_6Si_3P$ (M^+-I) 1037.5160, found *m/z* 1037.5173.

(2*S*,3*R*,5*S*)-2,3-Epoxy-5,6-(dimethylmethylenedioxy)-1-hexanol (43).

To a cold (-30 °C) suspension of titanium tetraisopropoxide [Ti(O*i*-Pr)$_4$] (830 μl, 2.79 mmol) and MS4Å (320 mg) in CH_2Cl_2 (10 ml) was added diethyl L-(+)-tartrate [L-(+)-DET] (526 μl, 3.07 mmol) and the mixture was stirred at -30 °C for 30 min. To the mixture was added *tert*-butyl hydroperoxide (TBHP) (3.70 M solution in toluene, 1.66 ml, 6.14 mmol) at -30 °C for 30 min. To the mixture was added dropwise a solution of **42** (481 mg, 2.79 mmol) in CH_2Cl_2 (3 ml) at -30 °C, and the mixture was stirred at -20 °C for 18 h. The solution was poured into a solution of tartaric acid (5.58 g) and iron(II) sulfate heptahydrate ($FeSO_4 \cdot 7H_2O$) (1.11 g) in water (56 ml) at 0 °C, and the mixture was stirred at the same temperature for 10 min. The water layer was extracted repeatedly with ether and EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was dissolved in ether (200ml), and cooled at 0 °C. To the solution was added 30% NaOH brine solution (6.1 ml), and the mixture was stirred vigorously at 0 °C for 1 h. To the reaction mixture was added brine, and the water layer was extracted repeatedly with ether and EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 3:2 → 1:4) to afford **43** (377 mg, 72% yield) as a colorless oil: $[\alpha]_D^{19}$ -2.06° (*c* 1.26, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$), δ 4.38-4.27 (1H, m), 4.10 (1H, dd, *J* = 6, 8 Hz), 3.88-3.66 (2H, m), 3.77 (1H, dd, *J* = 7, 8 Hz), 3.23-3.11 (2H, m), 2.23 (1H, dd, *J* = 6, 8 Hz), 2.00 (1H, br dt, *J* = 16, 6 Hz), 1.88 (1H, ddd, *J* = 5, 7, 16 Hz), 1.45 (3H, s), and 1.38 (3H, s); IR (film), ν_{max} 3463, 2987, 2935, 2883, 1457, 1373, 1217, 1161, 1045, 837, and 789 cm^{-1}; HR-EI-MS, calcd. for $C_8H_{13}O_4$ (M^+-Me) 173.0814, found *m/z* 173.0810.

(2*R*,3*R*,5*S*)-2,3-Epoxy-5,6-(dimethylmethylenedioxy)hexanal (5).

To a solution of oxalyl chloride (76.2 μl, 875 μmol) in CH_2Cl_2 (4 ml) was added DMSO (70.6 μl, 992 μmol) in CH_2Cl_2 (1 ml) at -78 °C and the mixture was stirred at -78 °C for 30 min. A solution of **43** (110 mg, 583 μmol) in CH_2Cl_2 (2 ml) was added and the mixture was stirred at -78 °C for 1 h. NEt_3 (243 μl, 1.75 mmol) was added at -78 °C and the mixture was stirred at 0 °C for 10 min. The reaction mixture was diluted with ether, and treated with brine. The water layer was extracted repeatedly with ether, and the combined organic layers were, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 2:1 → 1:1) to afford **5** (101 mg, 93% yield) as a colorless oil: $[\alpha]_D^{23}$ +75.9° (*c* 1.37, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), δ 9.48 (1H, d, *J* = 5 Hz), 4.30-4.21 (1H, m), 4.09 (1H, dd, *J* = 6, 8 Hz), 3.71 (1H, dd, *J* = 7, 8 Hz), 3.47 (1H, br t, *J* = 5 Hz), 3.41 (1H, br t, *J* = 5 Hz), 2.05 (1H, br dt, *J* = 14, 6 Hz), 1.95 (1H, br dt, *J* = 14, 5 Hz), 1.44 (3H, s), and 1.36 (3H, s); IR (film), ν_{max} 2988, 2940, 2880, 1726, 1428, 1378, 1218, 1158, 1062, and 836 cm^{-1}; HR-EI-MS, calcd. for $C_8H_{11}O_4$ (M^+-Me) 171.0657, found *m/z* 171.0673.

(1*R*,3*S*,4*S*,5*R*,6*R*,8*R*,9*S*,2'*Z*,4'*S*,5'*R*,7'*S*)-5-Benzyloxy-9-*tert*-butyldimethylsilyloxy-8-(2-*tert*-butyldiphenylsilyloxyethyl)-4-trimethylsilyloxy-3-[7',8'-(dimethylmethylenedioxy)-4',5'-epoxy-2'-octenyl]-2,7-dioxabicyclo[4.4.0]decane (41).

To a solution of **4** (19.8 mg, 17.0 μmol) in THF (0.5 ml) was added sodium bis(trimethylsilyl)amide (NaHMDS) (1.0 M solution in THF, 25.0 μl, 25.0 μmol) at -10 °C, and the mixture was stirred at room temperature for 1 h. To the mixture was added dropwise **5** (10.1 mg, 54.0 μmol) in THF (0.5 ml), and the mixture was stirred at room temperature for 30 min. The reaction mixture was diluted with ether and treated with satd. aq. NH_4Cl. The water layer was extracted repeatedly with ether, and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 10:1) to afford **41** (6.1 mg, 38% yield) as a colorless oil: $[\alpha]_D^{23}$ +26.1° (*c* 0.30, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.60-7.52 (4H, m), 7.38-7.32 (2H, m), 7.30-7.23 (5H, m), 7.19 (4H, br, s), 5.90 (1H, dt, *J* = 7, 11 Hz, H-7), 5.30 (1H, br dd, *J* = 8, 11 Hz, H-6), 4.89 (1H, d, *J* = 11 Hz), 4.47 (1H, d, *J* = 11 Hz), 4.24 (1H, m, H-2), 4.07 (1H, dd, *J* = 6, 7 Hz, H-1), 3.77 (2H, br dd, *J* = 6, 8 Hz, H-18), 3.68 (1H, br t, *J* = 7 Hz, H-1), 3.63 (1H, br dd, *J* = 4, 8, H-5), 3.39-3.20 (6H, m, H-9, 10, 11, 15, 16, and 4), 3.13-3.04 (2H, m, H-12 and 13), 2.66 (1H, br ddt, *J* = 7, 15, 2 Hz, H-8), 2.34-2.24 (2H, br m, H-14-eq and 8), 2.21-2.12 (1H, m, H-17), 1.89 (1H, dt, *J* = 15, 7 Hz, H-3), 1.78 (1H, dt, *J* = 15, 6 Hz, H-3), 1.56-1.46 (2H, m, H-14-ax and 17), 1.43 (3H, s), 1.37 (3H, s), 1.00 (9H, s), 0.90 (9H, s), 0.08 (3H, s), 0.07 (3H, s), and 0.06 (9H, s); IR (film), ν_{max} 3068, 2956, 2856, 1736, 1430, 1252, 1214, 1090, 878, 840, 776, 738, 700, and 614 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{53}H_{81}O_9Si_3$ (M^++H) 945.5190, found *m/z* 945.5169.

(1*R*,2*R*,3*S*,4*S*,6*R*,8*S*,9*R*,2'*Z*,4'*S*,5'*R*,7'*S*)-2-Benzyloxy-8-*tert*-butyldimethylsilyloxy-9-(2-*tert*-butyldiphenylsilyloxyethyl)-4-[7',8'-(dimethylmethylenedioxy)-4',5'-epoxy-2'-octenyl]-5,10-dioxabicyclo[4.4.0]decan-3-ol (3).

To a solution of **41** (5.2 mg, 5.50 μmol) in MeOH (1 ml) was added potassium carbonate (K_2CO_3) (an excess amount) at 0 °C, and the mixture was stirred at same temperature for 1.5 h. The reaction mixture was diluted with ether, and water was added. The water layer was extracted repeatedly with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 3:1) to afford **3** (4.6 mg, 96% yield) as a colorless oil: $[\alpha]_D^{24}$ +57.4° (*c* 0.23, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.65-7.60 (4H, m), 7.39-7.24 (9H, m), 7.21-7.16 (2H, m), 5.87 (1H, br, dt, *J* = 11, 7 Hz), 5.32 (1H, br, dd, *J* = 8, 11 Hz), 4.81 (1H, d, *J* = 11 Hz), 4.47 (1H, d, *J* = 11 Hz), 4.27-4.18 (1H, m), 4.06 (1H, dd, *J* = 6, 8 Hz), 3.85 (2H, br dd, *J* = 6, 8 Hz), 3.68 (1H, br dd, *J* = 4, 8 Hz), 3.66 (1H, br t, *J* = 8 Hz), 3.42-3.25 (5H, m), 3.20 (1H, br dt, *J* = 4, 6 Hz), 3.15-3.04 (2H, m), 2.66-2.45 (2H, m), 2.49 (1H, br s), 2.35-2.18 (2H, m), 1.87 (1H, dt, *J* = 14, 7 Hz), 1.76 (1H, dt, *J* = 14, 6 Hz), 1.64-1.46 (2H, m),1.42 (3H, s), 1.35 (3H, s), 1.03 (9H, s), 0.91 (9H, s), and 0.08 (6H, s); IR (film), ν_{max} 3460, 3072, 2932, 2856, 1732, 1430, 1254, 1218, 1088, 838, and 702 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{50}H_{73}O_9Si_2$ (M^++H) 873.4795, found *m/z* 873.4772.

(1*R*,3*S*)-3,4-(Dimethylmethylenedioxy)-1-{(1'*S*,3'*R*,5'*S*,6'*R*,8'*R*,9'*R*,10'*S*,12'*R*,13'*Z*)-9'-benzyloxy-5'-*tert*-butyldimethylsilyloxy-6'-(2-*tert*-butyldiphenylsilyloxyethyl)-2',7,'11'-trioxatricyclo[8.5.0.0$^{3',8'}$]-pentadec-13'-en-12'-yl}-1-butanol (44).

A solution of **3** (8.6 mg, 9.85 μmol) and tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium [Eu(fod)$_3$] (30.6 mg, 29.5 μmol) in toluene (6 ml) was stirred at 80 °C for 21 h. After cooling to room temperature, the mixture was quenched with brine, and the water layer was extracted repeatedly with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 9:2) to afford **44** (3.3 mg, 38% yield) as a colorless oil: $[\alpha]_D^{25}$ +25.2° (*c* 0.13, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.67-7.60 (4H, m), 7.38-7.19 (11H, m), 5.94-5.82 (2H, br m), 4.78 (1H, d, *J* = 11 Hz), 4.54 (1H, d, *J* = 11 Hz), 4.28-4.14 (1H, m), 3.94 (1H, dd, *J* = 6, 8 Hz), 3.92-3.88 (1H, br m), 3.85 (2H, br dd, *J* = 6, 8 Hz), 3.78-3.70 (1H, br m),

3.47-3.15 (6H, m), 3.14-3.04 (2H, m), 3.03 (1H, d, J = 2 Hz), 2.65-2.54 (1H, m), 2.43-2.13 (3H, m), 1.83-1.66 (2H, m), 1.62-1.41 (2H, m), 1.39 (3H, s), 1.34 (3H, s), 1.02 (9H, s), 0.90 (9H, s), and 0.08 (6H, s); IR (film), ν_{max} 3552, 3036, 2932, 2856, 1734, 1430, 1254, 1090, 838, and 702 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{50}H_{73}O_9Si_2$ (M^++H) 873.4795, found *m/z* 873.4800.

^{1}H NMR of **47**: (400 MHz, $CDCl_3$), δ 7.63-7.58 (4H, m), 7.38-7.19 (11H, m), 5.87-5.80 (1H, m, H-7), 5.76 (1H, br dt, J = 11, 3 Hz, H-6), 4.80 (1H, d, J = 11 Hz), 4.54 (1H, d, J = 11 Hz), 4.19-4.14 (1H, br m, H-5), 4.02 (1H, br dt, J = 13, 6 Hz, H-2), 3.83 (2H, br dd, J = 5, 7 Hz, H-18), 3.56 (1H, dd, J = 6, 8 Hz, H-1), 3.49 (1H, br t, J = 9 Hz, H-11), 3.36 (1H, br dt, J = 4, 10 Hz, H-15), 3.35 (1H, t, J = 9 Hz, H-10), 3.34-3.27 (2H, m, H-16 and 9), 3.15 (1H, dd, J = 7, 8 Hz, H-1), 3.14-3.07 (2H, m, H-13 and 12), 2.63 (1H, br ddd, J = 4, 7, 16 Hz, H-8), 2.38-2.26 (2H, m, H-8 and 14-eq), 2.24-2.18 (1H, m, H-17), 2.06 (3H, s), 1.85 (2H, br t, J = 7 Hz, H-3), 1.61-1.46 (2H, m, H-17 and 14-ax), 1.36 (3H, s), 1.26 (3H, s), 1.02 (9H, s), 0.90 (9H, s), and 0.06 (6H, s).

(1*S*,3*R*,5*S*,6*R*,8*R*,9*R*,10*S*,12*R*,13*Z*,1'*R*,3'*S*)-9-Benzyloxy-5-*tert*-butyldimethylsilyloxy-6-(2-*tert*-butyldiphenylsilyloxyethyl)-12-[3',4'-(dimethylmethylenedioxy)-1'-chloromethanesulfonyloxybutyl]-2,7,11-trioxatricyclo[8.5.0.0^{3,8}]pentadec-13-ene (48).

To a solution of **44** (4.0 mg, 4.58 μmol) and DMAP (a cat. amount) in a 5:1 mixture of CH_2Cl_2-pyridine (0.6 ml) was added chloromethylsulfonyl chloride ($ClCH_2SO_2Cl$) (10.0 μl, 58.9 μmol), and the mixture was stirred at room temperature for 20 min. The reaction mixture was quenched with satd. aq. $NaHCO_3$, and the water layer was extracted repeatedly with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 6:1) to afford **48** (2.7 mg, 60% yield) and **49** (1.5 mg, 34% yield) as pale yellow oils, respectively.

48: $[\alpha]_D^{24}$ +17.3° (*c* 0.12, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.62-7.57 (4H, m), 7.38-7.17 (11H, m), 6.01-5.84 (2H. m), 4.95 (1H, br ddd, J = 3, 6, 8 Hz), 4.82 (1H, d, J = 11 Hz), 4.66 (1H, d, J = 12 Hz), 4.60 (1H, d, J = 12 Hz), 4.45 (1H, d, J = 11 Hz), 4.32-4.26 (1H, br m), 4.06-3.96 (1H, m), 3.87-3.77 (2H, m), 3.51-3.26 (6H, m), 3.18-3.08 (2H, m), 3.03 (1H, dd, J = 6, 8 Hz), 2.72-2.61 (1H, m), 2.40-2.07 (5H, m), 1.97-1.86 (1H, m), 1.57-1.47 (1H, m), 1.36 (3H, s), 1.24 (3H, s), 1.02 (9H, s), 0.90 (9H, s), and 0.08 (6H, s); IR (film), ν_{max} 3068, 2956, 2856, 1732, 1712, 1430, 1252, 1088, 840, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{51}H_{74}O_{11}ClSi_2S$ (M^++H) 985.4181, found *m/z* 985.4166.

49 was converted to **44** as follows: To a solution of **49** (1.5 mg, 1.55 μmol) in toluene (0.5 ml) was added 1,8-diazabicyclo[4.3.0]undec-7-ene (DBU) (5.0 μl, 33.5 μmol), and the mixture was stirred at reflux temperature for 2 h. After cooling, the reaction mixture was purified by column chromatography on SiO_2 (hexane:EtOAc, 6:1 → 2:1) to afford **44** (1.1 mg, 81% yield).

(1*S*,3*R*,5*S*,6*R*,8*R*,9*R*,10*S*,12*R*,13*Z*,1'*E*,3'*S*)-9-Benzyloxy-5-*tert*-butyldimethylsilyloxy-6-(2-*tert*-butyldiphenylsilyloxyethyl)-12-[3',4'-(dimethylmethylenedioxy)-1'-butenyl]-2,7,11-trioxatricyclo[8.5.0.0^{3,8}]pentadec-13-ene (2) (the A,B,C-ring system of ciguatoxin).

A solution of sodium phenylseleno(triethyl)borate {$Na^+[PhSeB(OEt)_3]^-$} (0.20 M solution in EtOH) was prepared as follows: To a ice cooled solution of diphenyldiselenide (156 mg, 0.50 mmol) in EtOH (5 ml) was added sodium borohydride ($NaBH_4$) (77 mg, 1.01 mmol) (the reaction was exothermic and vigorous hydrogen evolution occurred), and the mixture was stirred at the same temperature for 5 min, and was then allowed to warm to room temperature over 30 min. After the color of the reaction solution had changed from brown to pale yellow, $Na^+[PhSeB(OEt)_3]^-$ (0.20 M solution in EtOH) was formed.

To a solution of **48** (3.0 mg, 3.04 μmol) in EtOH (0.5 ml) was added $Na^+[PhSeB(OEt)_3]^-$ (0.20 M solution in EtOH, 200 μl, 40.0 μmol), and the mixture was stirred at reflux temperature for 50 min. After cooling, the reaction solution was diluted with EtOAc and treated with half satd. aq. sodium chloride (NaCl), and the water layer was extracted repeatedly with EtOAc. The combined organic layers were washed with

brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 12:1) to afford **50** (1.8 mg, 60% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.63-7.55 (4H, m), 7.54-7.52 (2H, m), 7.39-7.14 (14H, m), 5.88 (1H, br d, *J* = 11 Hz), 5.81 (1H, br dd, *J* = 8, 11 Hz), 4.72 (1H, d, *J* = 11 Hz), 4.65 (1H, d, *J* = 11 Hz), 4.50-4.40 (1H, m), 4.21-4.27 (1H, m), 3.95 (1H, dd, *J* = 6, 8 Hz), 3.85 (2H, br t, *J* = 7 Hz), 3.47-3.12 (6H, m), 3.12-3.03 (2H, m), 2.58 (1H, br ddd, *J* = 4, 8, 16 Hz), 2.37-1.96 (6H, m), 1.75-1.50 (2H, m), 1.38 (3H, s), 1.28 (3H, s), 1.01 (9H, s), 0.89 (9H, s), and 0.07 (6H, s).

To an ice cooled solution of **50** (1.2 mg, 1.19 μmol) and pyridine (3.0 μl, 37.1 μmol) in CH_2Cl_2 (0.5 ml) was added 30% aq. hydrogen peroxide (H_2O_2) (3 drops *via* pipet), and the mixture was stirred at the same temperature for 5 min, and was then allowed to warm to room temperature over 1 h. After cooling to 0 °C, the reaction was quenched with satd. aq. $NaHCO_3$ and satd. aq. $Na_2S_2O_3$, and the water layer was extracted repeatedly with ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (hexane:EtOAc, 11:1 → 8:1) to afford **2** (0.6 mg, 59% yield) and **51** (0.4 mg, 39% yield) as colorless oils, respectively.

2: $[\alpha]_D^{26}$ +30.2° (*c* 0.04, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.65 (4H, br d, *J* = 7 Hz), 7.40-7.19 (11H, m), 5.89 (1H, br dd, *J* = 5, 16 Hz, H-4), 5.78 (1H, br ddd, *J* = 1, 7, 16 Hz, H-3), 5.79-5.75 (2H, m, H-6 and 7), 4.71(1H, d, *J* = 11 Hz), 4.64 (1H, d, *J* = 11 Hz), 4.59-4.56 (1H, br m, H-5), 4.52 (1H, br q, *J* = 7 Hz, H-2), 4.06 (1H, dd, *J* = 6, 8 Hz, H-1), 3.89 (2H, br t, *J* = 7 Hz, H-18), 3.53 (1H, t, *J* = 8 Hz, H-1), 3.46-3.38 (2H, m, H-11 and 10), 3.37 (1H, br dt, J = 5, 9 Hz, H-15), 3.32-3.25 (2H, m, H-16 and 9), 3.12-3.07 (2H, m, H-12 and 13), 2.64 (1H, br ddd, *J* = 4, 8, 16 Hz, H-8), 2.39-2.29 (1H, m, H-8), 2.32-2.25 (1H, m, H-14-eq), 2.25-2.16 (1H, m, H-17), 1.67-1.50 (2H, m, H-17 and 14-ax), 1.42 (3H, s), 1.40 (3H, s), 1.04 (9H, s), 0.90 (9H, s), and 0.08 (6H, s); IR (film), ν_{max} 2924, 2852, 1734, 1714, 1466, 1380, 1252, 1088, 856, 828, 776, and 700 cm^{-1}; HR-FD/FI-MS, calcd. for $C_{50}H_{70}O_8Si_2$ (M^+) 854.4611, found *m/z* 854.4634.

^{1}H NMR of **51**: (300 MHz, $CDCl_3$), δ 7.61-7.56 (4H, m), 7.36-7.20 (11H, m), 5.84 (1H, br d, *J* = 12 Hz), 5.33 (1H, br dt, *J* = 12, 5 Hz), 4.90 (1H, d, *J* = 11 Hz), 4.76 (1H, t, *J* = 7 Hz), 4.60 (1H, d, *J* = 11 Hz), 4.03-3.93 (1H, m), 3.82 (2H, dd, *J* = 5, 8 Hz), 3.70-3.62 (3H, m), 3.62-3.54 (1H, m), 3.45-3.26 (3H, m), 3.19-3.11 (2H, m), 2.89-2.76 (1H, br d, *J* = 16 Hz), 2.47-2.13 (5H, m), 1.62-1.43 (2H, m), 1.36 (3H, s), 1.30 (3H, s), 1.01 (9H, s), 0.90 (9H, s), and 0.08 (6H, s).

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