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Synthesis of the AB-ring segment for the convergent construction of the left half in ciguatoxin

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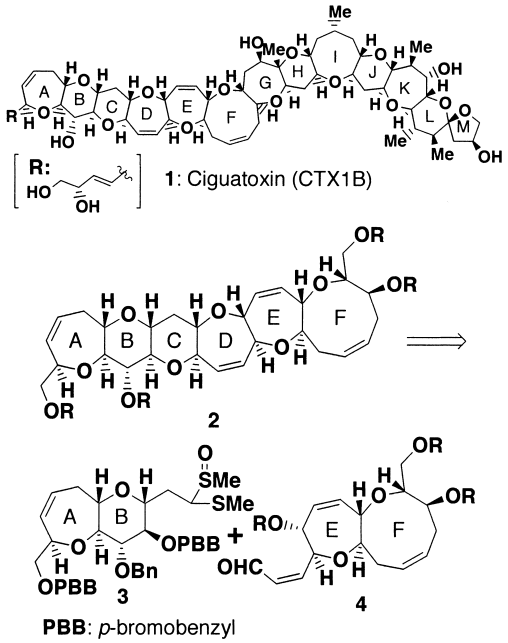
Abstract—The synthesis of the AB-ring segment aiming at the convergent construction of the left half in ciguatoxin (CTX1B) has been achieved by a strategy based on ring-closing metathesis (RCM) and diastereocontrolled hydroboration to cyclic vinyl ethers.

1. Introduction

Ciguatera[1] is a food poisoning caused by ingestion of coral reef fishes that have become toxic through a food chain process. It is estimated that more than 20,000 people suffer annually from this poisoning. The symptoms of ciguatera are represented by diarrhea, vomiting, joint pain, and prostration as well as neurologic disturbance characterized by reversal of thermal sensation called 'dry-ice sensation'. Generally, patients need several months to recover completely from these symptoms, which has resulted in serious social problems.

Ciguatoxin was first isolated as one of the causative toxins of ciguatera from the moray eel, *Gymnothorax javanicus*, by Scheuer's group.[2] Later, it was clarified that the toxin is produced originally by the epiphytic dinoflagellate, *Gambierdiscus toxicus*, transferred to herbivorous fish, and accumulated subsequently in carnivorous fish through the food chain.[3] Although the structure of ciguatoxin was characterized as a polycyclic ether compound in 1980,[2] further characterization of the toxin made slow progress because of difficulty in providing the toxin from ciguatera fish, which contained an extremely small quantity of the toxin. In 1989, Yasumoto and co-workers isolated only 0.35 mg of ciguatoxin (CTX1B, **1**) again from 4 t of *G. javanicus*, from which they determined the relative structure of **1** through detailed ^{1}H NMR analysis.[4,5] They reported that the molecular formula of **1** is $C_{60}H_{86}O_{19}$ and that the structure of **1** consists of 12 *trans*-fused cyclic ethers and a spirocyclic ether at one end. Finally, the absolute configuration of **1** was determined in 1997 as shown in Scheme 1 by collaboration of Yasumoto, Hirama and Harada.[6]

One bioactivity of **1** has been reported to be strong activation of voltage-sensitive sodium channels (VSSC).[7] While its binding site on VSSC was shared by brevetoxins, another class of structurally related marine toxins,[8] the precise location of receptor site of these toxins has not been fully identified.[9] In order to understand the toxic action of **1** from a neurologic standpoint, these further mechanistic



Scheme 1. Structure of ciguatoxin (CTX1B, **1**) and synthetic plan for the ABCDEF-ring segment of **1**.

Keywords: ciguatoxin; hydroboration; polyethers; ring-closing metathesis; vinyl ether.

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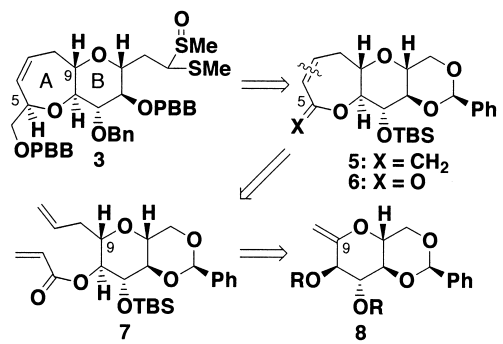
studies are necessitated. On the other hand, the development of highly specific assays for detection of minute amounts of **1** in marine food sources has been required urgently in view of preventive hygiene. However, the extremely limited availability of **1** from natural sources has impeded further advance in these studies. Therefore, a synthetic supply of **1** on a practical scale is essential in order to solve the problem.

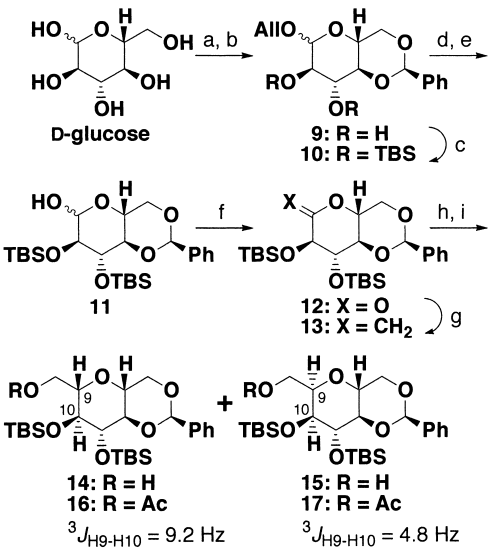
From the synthetic viewpoint, the large molecular size and the complex ladder-shaped polycyclic ether framework as well as the irregularity in the arrangement of the cyclic ether components of **1** are regarded as significant challenges. Synthetic chemists have continued intensive efforts aiming at concise construction of the polyether frameworks as well as completion of the total syntheses of **1** and the congeners.[10–13] In the course of our studies toward total synthesis of **1**,[14] we have established a method based on the coupling reaction of a dithioacetal mono-*S*-oxide derivative with an aldehyde for the convergent construction of a *trans*-fused polyether framework involving a 6/6 or 6/7-fused ring system in the middle part.[14g,i,k,15] Therefore, we planned to connect the synthetic segments of **1** at the CD-, GH-, and JK-ring parts in the later stage of the total synthesis. In fact, the convergent assembling of the CD and JK-ring parts has been successfully accomplished in model systems.[14i,k] To date, the preparation of the E, F, and I-ring parts[14j] as well as the LM-ring part[14e] of **1** has been also established. Thus, we now plan to synthesize the ABCDEF-ring system **2** in **1** commencing from the AB-ring segment **3** with the dithioacetal mono-*S*-oxide part[15] and the EF-ring segments **4** with the aldehyde part by the above methods (Scheme 1). Here, the synthesis of **3** starting from D-glucose, based on ring-closing olefin metathesis (RCM) and diastereo-controlled hydroboration to cyclic vinyl ethers, is described.

2. Results and discussion

The synthetic plan for the AB-ring segment **3** is shown in Scheme 2. Formation of the asymmetric centers at C5[16] and C9[16] in **3** was considered to be the main subject in this Scheme. The C5-stereocenter would be constructed by the hydroboration reaction of conjugated exocyclic vinyl ether **5** followed by oxidation reaction. Although the stereoselective hydroboration of the exocyclic vinyl ether part in the seven-membered cyclic ether system having an alkoxy group adjacent to the vinyl ether part has been reported by Sasaki and Tachibana, the stereoselectivity in the seven-membered system without the neighboring alkoxy group is



Scheme 2. Synthetic plan for the AB-ring segment of **1**.

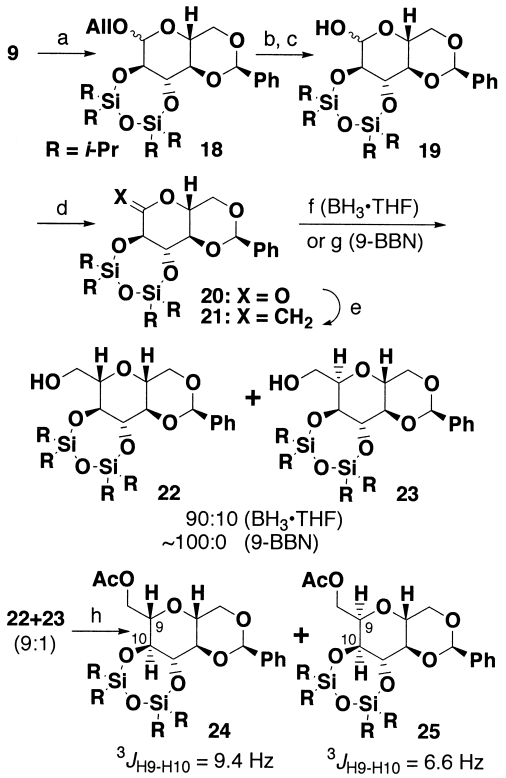


Scheme 3. *Reagents and conditions*: (a) allyl alcohol (13 equiv.), TfOH (0.02 equiv.), 0→80°C, 72 h; (b) $PhCH(OMe)_2$ (2.0 equiv.), $PTS{\cdot}H_2O$ (0.01 equiv.), DMF, 80°C, 2.5 h, 65% for two steps; (c) TBSOTf (2.5 equiv.), 2,6-lutidine (5.0 equiv.), CH_2Cl_2, 0→24°C, 12.5 h, ~100%; (d) $RhCl(PPh_3)_3$ (1.2 mol%), *i*-Pr_2NEt (1.5 equiv.), EtOH, reflux, 1 h; (e) $HgCl_2$ (2.0 equiv.), HgO (2.5 equiv.), acetone/H_2O (9:1), 24°C, 1.5 h, ~100% for two steps; (f) $(COCl)_2$ (3.0 equiv.), DMSO (4.8 equiv.), CH_2Cl_2, −78°C, 15 min, then Et_3N (10 equiv.), −78→0°C, 25 min, 92%; (g) Tebbe's reagent (1.9 equiv.), toluene/THF (1:33), 0→24°C, 40 min, ~100%; (h) $BH_3{\cdot}THF$ (3.2 equiv.), THF, 0°C, 4.5 h, then 5 M NaOH (9.8 equiv.), 30% H_2O_2 (9.6 equiv.), 0→24°C, 12.5 h, 80%; (i) Ac_2O/Py (1:2), 25°C, 22 h, **16**: 35%, **17**: 65%.

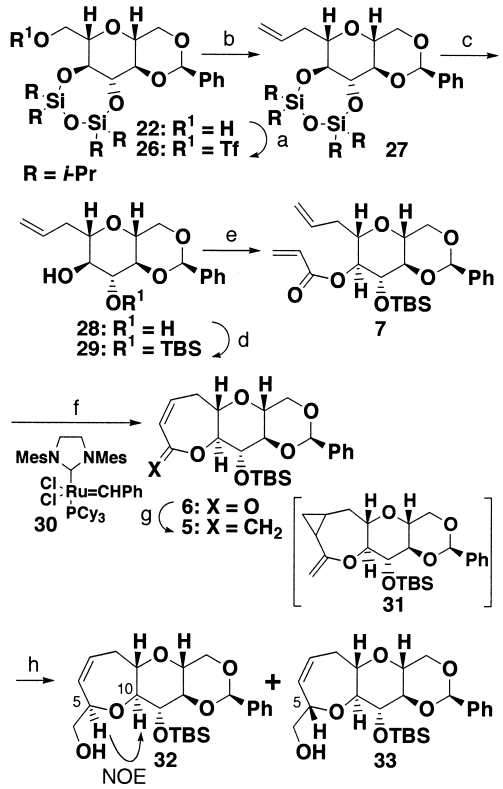
still unclear.[17a] The vinyl ether **5** would be prepared from seven-membered α,β-unsaturated lactone **6**, which would be constructed by the RCM reaction using the second-generation Grubbs catalyst.[19,20] In order to arrange the stereocenter of C9 in **7**, we adopt RajanBabu's method to the stereoselective hydroboration of the 1-methylene-D-glucose derivative **8** which would be easily prepared from D-glucose.[17b]

First, the B-ring part was synthesized from D-glucose (Scheme 3). *O*-Allyl glycosilation of D-glucose and the subsequent selective protection as a benzylidene acetal afforded diol **9**,[21] which was protected as a TBS ether in 65% yield for three steps. After isomerization of the allyl group of **10** with Wilkinson's catalyst,[22] hydroxymercuration followed by hydrolysis[23] provided lactol **11** in a quantitative yield. Swern oxidation[24] of **11** produced lactone **12** in 92% yield, which was smoothly converted to vinyl ether **13** by treatment with Tebbe's reagent.[18] Compound **13** was subjected to hydroboration with $BH_3{\cdot}THF$ followed by oxidation to give the desired alcohol **14** and the epimer at C9 **15** as an inseparable mixture in 80% yield, which afforded the respective acetates **16** and **17** in 35 and 65% yields. Stereochemistries at C9 in **16** and **17** were assigned by their $^3J_{H9-H10}$ values (**16**: 9.2 Hz, **17**: 4.8 Hz). An attempt to improve the stereoselectivity using bulky 9-BBN[17] was unsuccessful because the reaction rate of the hydroboration was too slow to give a practical amount of the products.

Next, we examined vinyl ether **21** protected as a cyclic silyl ether (Scheme 4). Protection of diol **9** gave a 1,3-(1,1,3,3-tetraisopropyldisiloxanylidene) (TIPDS) derivative **18** in



Scheme 4. *Reagents and conditions*: (a) 1,3-dichlorotetraisopropyldisiloxane (1.2 equiv.), imidazole (2.4 equiv.), DMF, 0→24°C, 11.5 h, 95%; (b) $RhCl(PPh_3)_3$ (1.2 mol%), *i*-Pr_2NEt (1.5 equiv.), EtOH, reflux, 1 h; (c) $HgCl_2$ (2.0 equiv.), HgO (2.6 equiv.), acetone/H_2O (9:1), 25°C, 1 h, 97% for two steps; (d) $(COCl)_2$ (1.5 equiv.), DMSO (2.4 equiv.), CH_2Cl_2, −78°C, 20 min, then Et_3N (5.0 equiv.), −78→0°C, 30 min; (e) Tebbe's reagent (1.5 equiv.), toluene/THF (1:6), 0→23°C, 0.5 h, 73% for two steps; (f) BH_3·THF (1.6 equiv.), THF, 0°C, 0.5 h, then 5 M NaOH (4.8 equiv.), 30% H_2O_2 (4.8 equiv.), 0→26°C, 23.5 h, 83%; (g) 9-BBN (2.5 equiv.), THF, 23°C, 2 h, then 3 M NaOH (7.6 equiv.), TBHP (7.6 equiv.), 0→23°C, 11 h, 85%; (h) Ac_2O/Py (1:2), 25°C, 11 h, **24**: 81%, **25**: 10%.



Scheme 5. *Reagents and conditions*: (a) Tf_2O (1.5 equiv.), 2,6-lutidine (3.0 equiv.), CH_2Cl_2, −78°C, 0.5 h, 98%; (b) CH_2=$CHSnBu_3$ (5.0 equiv.), BuLi (5.0 equiv.), THF, −78°C, 1 h, then CuCN (2.5 equiv.), −78→0°C, 25 min, then **26**, −78→0°C, 1.5 h, 93%; (c) TBAF (4.0 equiv.), THF, 25°C, 0.5 h, 99%; (d) TBSOTf (1.5 equiv.), 2,6-lutidine (3.0 equiv.), CH_2Cl_2, 0°C, 0.5 h, 89%; (e) acryloyl chloride (3.0 equiv.), *i*-Pr_2NEt (6.0 equiv.), CH_2Cl_2, 0→25°C, 3.5 h, 99%; (f) Grubbs' catalyst **30** (5.0 mol%), $(CH_2Cl)_2$ (2 mM of **7**), reflux, 12 h, 85%; (g) Tebbe's reagent (2.0 equiv.), toluene/THF (1:5), −40°C, 0.5 h, 82%; (h) 9-BBN (2.0 equiv.), THF, 25°C, 2 h, then 3 M NaOH (6.0 equiv.), TBHP (6.0 equiv.), 0→24°C, 12 h, **32**: 59%, **33**: 5%.

95% yield. After removal of the allyl group of **18** and the subsequent oxidation of **19**, the resultant lactone **20** was easily converted to vinyl ether **21** by olefination with Tebbe's reagent[18] in 71% yield for four steps. When **21** was subjected to hydroboration with BH_3·THF followed by oxidation, the desired alcohol **22** and the epimer at C9 **23** were produced as an inseparable mixture (**22**/**23**=9:1) in 83% yield. Stereochemical assignments at C9 in **22** and **23** were confirmed by the coupling constants ($^3J_{H9-H10}$) of the corresponding acetates **24** and **25**. Production of the desired **22** was improved by treatment of **21** with 9-BBN[17] and the subsequent oxidation providing **22** as a single diastereomer in 85% yield.

It is speculated that the difference between the stereoselectivities in the hydroboration reactions of **13** and **21** might be attributed to the difference between their

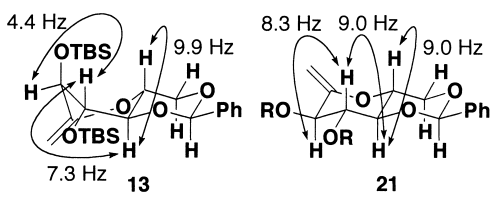
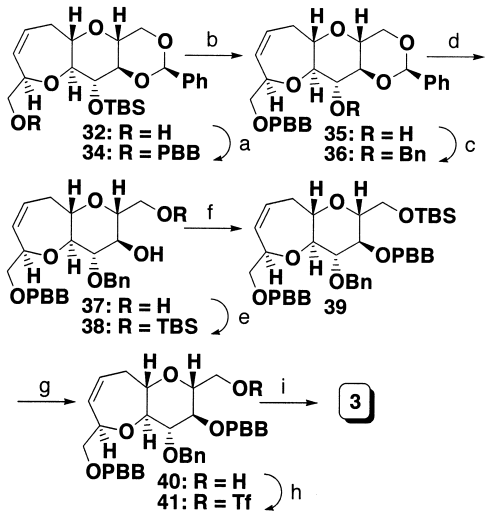


Figure 1. NMR analyses on the coupling constants of **13** and **21**.

conformations. In fact, detailed NMR analyses on the coupling constants of **13** and **21** elucidated the boat conformation of **13** and the chair conformation of **21** (Fig. 1). The boat conformation of **13** would arise from large gauche repulsion between two TBSO groups at C10 and C11.[25] The low selectivity in **13** could be explained by the steric hindrance of the pseudoaxial TBSO group at C10, which would obstruct the approach of a borane reagent to C9 from its axial side.

Then, the A-ring part was constructed from alcohol **22** (Scheme 5). Triflate **26** derived from **22** was reacted with salt-free cyanocuprate[26] to produce **27** in 93% yield. After deprotection of the TIPDS group in **27**, the resultant diol **28** was protected regioselectively with TBSOTf affording alcohol **29** in 88% yield for two steps, which provided **7** with acryloyl chloride in 99% yield. Compound **7** was subjected to the RCM reaction with the second-generation Grubbs catalyst **30**[19] (5 mol%) in 1,2-dichloroethane under diluted conditions (2 mM of **7**). The reaction proceeded smoothly to give lactone **6** in 85% yield. When CH_2Cl_2 was used as a solvent, the reaction rate became slow. In order to consume **7** completely, an increased amount (10–20 mol%) of the catalyst was required, but the yield of **6** was moderate (50–68%). Tebbe olefination[18] of **6** with careful



Scheme 6. *Reagents and conditions*: (a) PBBBr (2.0 equiv.), NaH (3.1 equiv.), TBAI (0.5 equiv.), THF, 0→25°C, 14 h; (b) TBAF (2.0 equiv.), THF, 25°C, 16 h, 99% for two steps; (c) BnBr (2.0 equiv.), NaH (3.3 equiv.), TBAI (0.5 equiv.), THF, 0→25°C, 5 h, 99%; (d) 3 M HCl/THF (1:1), 25°C, 12 h, 99%; (e) TBSCl (3.0 equiv.), Et_3N (3.0 equiv.), DMAP (0.2 equiv.), CH_2Cl_2, 25°C, 9.5 h, ~100%; (f) PBBBr (2.0 equiv.), NaH (3.5 equiv.), TBAI (0.5 equiv.), THF, 0→24°C, 12 h; (g) TBAF (1.5 equiv.), THF, 25°C, 15 h, 99% for two steps; (h) Tf_2O (2.0 equiv.), 2,6-lutidine (4.0 equiv.), CH_2Cl_2, −78°C, 0.5 h, 95%; (i) $MeSCH_2S(O)Me$ (3.1 equiv.), BuLi (3.1 equiv.), THF, −20°C, 1 h, 93%.

temperature-control (−40°C) produced the desired vinyl ether **5** cleanly in 82% yield. When the reaction was performed at 0°C, cyclopropanation occurred to give **31** in 90% yield.[27] Next, vinyl ether **5** was subjected to hydroboration with 9-BBN followed by oxidation to afford the desired alcohol **32** regio- and stereoselectively in 59% yield together with the epimer at C5 **33** in 5% yield. The stereochemistry at C5 in **32** was verified from the existence of NOE (H5/H10). Although the mechanistic details of the stereoselectivity are unclear at this time, we were able to obtain the desired stereoisomer.

Finally, alcohol **32** was transformed into a dithioacetal mono-*S*-oxide derivative (Scheme 6). Protection of **32** as a *p*-bromobenzyl (PBB) ether[28] and the subsequent removal of the TBS group in **34** afforded monoalcohol **35**, which was benzylated to **36** in 98% yield for three steps. After the benzylidene acetal of **36** was removed, the resultant diol **37** was treated with TBSCl in the presence of Et_3N and DMAP to provide alcohol **38** selectively in 99% yield for two steps. Compound **38** was protected as a PBB ether followed by removal of the TBS group of **39** affording alcohol **40** in 99% yield for two steps. When triflate **41** derived from **40** was treated with the anion of methyl methylsulfinylmethyl sulfide, the AB-ring segment **3** was produced in 93% yield. Thus, we achieved the synthesis of the desired **3**.

3. Conclusion

We have synthesized the AB-ring segment **3** as a dithioacetal mono-*S*-oxide derivative starting from D-glucose for the convergent construction of the ABCDEF-ring system in **1**. The asymmetric centers of C5 and C9 were efficiently introduced by diastereocontrolled hydroboration reactions of the corresponding cyclic vinyl ethers **5** and **21** derived from lactones **6** and **20**, respectively. Further studies toward the total synthesis of **1** as well as the left half are currently under way in our laboratory.

4. Experimental

The following general procedures were used in all reactions unless otherwise noted. Oxygen- and moisture-sensitive reactions were carried out in oven-dried (>130°C) glassware sealed under a positive pressure of dry argon from a manifold or balloon. Sensitive liquids and solutions were transferred by syringe or cannula through rubber septa. Reactions were run at the noted temperature and stirred with a Teflon-covered magnetic stirring bar. All commercially available reagents were used without further purification with the following exceptions. THF was distilled from sodium-benzophenone ketyl under argon. Allyl alcohol, 1,2-dichloroethane, CH_2Cl_2, *N*-ethyldiisopropylamine (*i*-Pr_2NEt), 2,6-lutidine, and Et_3N were distilled from CaH_2 under argon prior to use. Analytical TLC was performed with 0.25 mm Silica Gel 60 plates with a 254-nm fluorescent indicator from Merck. Plates were developed in a covered chamber and visualized by ultraviolet light and by treatment with acidic anisaldehyde or phosphomolybdic acid stain followed by heating. Flash chromatography was performed on YMC Silica Gel 60 (230–400 mesh) as a stationary phase. Preparative TLC was performed with 0.25 mm Silica Gel 60 plates with a 254-nm fluorescent indicator from Merck. Preparative liquid chromatography was achieved on a JASCO PU-986 instrument equipped with a JASCO UV-975 detector and a packed column (YMC-Pack SIL-06, 250×10 mm or 250×20 mm) with hexane/EtOAc as a liquid phase. Melting points were obtained using a YANAGIMOTO micro-melting point apparatus without calibration. Optical rotations were recorded on a JASCO P-1020 digital polarimeter in appropriate solvents. IR spectra were measured on a JEOL JIR-WINSPEC100 infrared spectrometer in noted states and are reported in wave numbers (cm^{-1}). NMR spectra were measured on a JEOL JNM-AL300 (^1H at 300 MHz, ^{13}C at 75 MHz) magnetic resonance spectrometer. ^1H NMR spectra are reported as chemical shifts in parts-per-million (ppm) based on tetramethylsilane (0 ppm) or one of the signals of the solvents (noted in each case). The following abbreviations are used to describe spin multiplicity: s= singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad, dd=double doublets, dt=double triplets, dq= double quartets, and ddd=double double doublets; other combination is derived from those listed. Coupling constants (*J*) are reported in Hertz (Hz). ^{13}C NMR spectra are reported as chemical shifts in ppm based on one of the signals of the solvent (noted in each case) and recorded with complete hetero-decoupling. Low and high resolution mass spectra were measured on a JEOL JMS-600H mass spectrometer under electron ionization (EI) condition and a JEOL JMS-SX102A mass spectrometer under field desorption (FD) condition.

4.1. Synthesis of the AB-ring segment

4.1.1. Allyl 4,6-*O*-benzylidene-D-glucopyranoside (9). To

a suspension of D-glucose (10.08 g, 55.9 mmol) in allyl alcohol (50 ml, 735 mmol) was added trifluoromethanesulfonic acid (0.10 ml, 1.13 mmol) at 0°C and the mixture was stirred for 15 min. The mixture was warmed to 25°C and stirred for 45 min. Then, the mixture was heated to 80°C and stirred for 71 h. After the mixture was cooled to 25°C, Et_3N (0.16 ml, 1.15 mmol) was added. The mixture was concentrated under reduced pressure. The resultant residue was purified by flash chromatography (silica gel, CH_2Cl_2/MeOH=5) to provide a mixture of allyl D-glucopyranoside and unidentified by-products. The mixture was used in the next reaction without further purification. To the above mixture including allyl D-glucopyranoside and benzaldehyde dimethylacetal (16.6 ml, 112 mmol) in DMF (100 ml) was added PTS·H_2O (106.3 mg, 0.559 mmol) at 28°C and the mixture was stirred for 5 min. Then, the mixture was heated to 80°C and stirred for 2.5 h. After the mixture was cooled to 28°C, an excess amount of Na_2CO_3 was added. The mixture was concentrated under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 (100 ml) and the mixture was washed with H_2O (100 ml). The aqueous layer was extracted with CH_2Cl_2 (3×100 ml). The combined organic layers were washed with brine (50 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=3→1) provided **9** (11.16 g, 65% from D-glucose) as a mixture of α and β-anomers (α/β=3:2 from ^{1}H NMR). The mixture of α and β-anomers was used in the next reaction without separation. Pure α and β-anomers of **9** were obtained partly by careful flash chromatography and used for spectrometric analyses. *α-Anomer of* ***9***: white needles (EtOAc), mp 135–137°C; $[\alpha]_D^{23}$=+109.3° (*c* 1.01, $CHCl_3$); IR (KBr), ν_{max} 3389, 2910, 2866, 1452, 1372, 1210, 1149, 1127, 1076, 1042, 1014, 997, 969, 935, 749, 699, 658 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.53–7.47 (2H, m), 7.41–7.33 (3H, m), 5.93 (1H, dddd, *J*=17.3, 10.3, 6.4, 5.3 Hz), 5.54 (1H, s), 5.33 (1H, dq, *J*=17.3, 1.5 Hz), 5.26 (1H, dq, *J*=10.3, 1.5 Hz), 4.96 (1H, d, *J*=4.0 Hz), 4.29 (1H, dd, *J*=10.1, 4.6 Hz), 4.26 (1H, ddt, *J*=12.8, 5.3, 1.5 Hz), 4.07 (1H, ddt, *J*=12.8, 6.4, 1.5 Hz), 3.97 (1H, brtd, *J*=9.2, 1.8 Hz), 3.86 (1H, brddd, *J*=10.1, 9.2, 4.6 Hz), 3.74 (1H, t, *J*=10.1 Hz), 3.64 (1H, brddd, *J*=9.9, 9.2, 4.0 Hz), 3.51 (1H, t, *J*= 9.2 Hz), 2.68 (1H, brd, *J*=1.8 Hz), 2.21 (1H, d, *J*=9.9 Hz); LR-EIMS, *m/z* 308 (16.7%, $[M]^+$), 107 (bp); HR-EIMS, calcd for $C_{16}H_{20}O_6$ $[M]^+$: 308.1260, found: 308.1254. *β-Anomer of* ***9***: white needles (EtOAc), mp 146–148°C; $[\alpha]_D^{23}$=−57.6° (*c* 1.02, $CHCl_3$); IR (KBr), ν_{max} 3512, 3230, 2924, 2863, 1452, 1423, 1373, 1350, 1266, 1219, 1207, 1170, 1087, 1043, 1004, 931, 749, 699, 655, 610, 593, 556 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.52–7.46 (2H, m), 7.41–7.33 (3H, m), 5.95 (1H, dddd, *J*=17.3, 10.5, 6.4, 5.3 Hz), 5.54 (1H, s), 5.34 (1H, dq, *J*=17.3, 1.5 Hz), 5.25 (1H, dq, *J*=10.5, 1.5 Hz), 4.46 (1H, d, *J*=7.7 Hz), 4.39 (1H, ddt, *J*=12.5, 5.3, 1.5 Hz), 4.35 (1H, dd, *J*=10.5, 5.0 Hz), 4.15 (1H, ddt, *J*=12.5, 6.4, 1.5 Hz), 3.83 (1H, td, *J*=9.0, 2.2 Hz), 3.80 (1H, t, *J*=10.5 Hz), 3.57 (1H, t, *J*=9.0 Hz), 3.54 (1H, ddd, *J*=9.0, 7.7, 2.4 Hz), 3.46 (1H, brddd, *J*=10.5, 9.0, 5.0 Hz), 2.73 (1H, d, *J*=2.2 Hz), 2.58 (1H, d, *J*=2.4 Hz); LR-EIMS, *m/z* 308 (9.7%, $[M]^+$), 107 (bp); HR-EIMS, calcd for $C_{16}H_{20}O_6$ $[M]^+$: 308.1260, found: 308.1256.

4.1.2. Allyl 4,6-*O*-benzylidene-2,3-bis-*O*-(*tert*-butyldimethylsilyl)-D-glucopyranoside (10). To a mixture of **9** (75.9 mg, 0.180 mmol) and 2,6-lutidine (105 μl, 0.901 mmol) in CH_2Cl_2 (1.8 ml) was added TBSOTf (105 μl, 0.457 mmol) at 0°C. The mixture was warmed to 24°C and stirred for 12.5 h. Saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture was extracted with CH_2Cl_2 (3×5 ml). The combined organic layers were dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=50) provided **10** (96.5 mg, ~100%). The mixture of α and β-anomers was used in the next reaction without separation. The following spectral data were obtained from the pure α and β-anomers of **10** prepared alternatively from the corresponding pure α and β-anomers of **9** under the same conditions as the above. *α-Anomer of* ***10***: a colorless oil; $[\alpha]_D^{26}$=+48.4° (*c* 1.02, $CHCl_3$); IR (film), ν_{max} 2953, 2928, 2885, 2857, 1472, 1462, 1410, 1385, 1361, 1251, 1211, 1172, 1145, 1112, 1089, 1048, 1003, 968, 931, 860, 837, 779, 760, 697, 667 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.50–7.43 (2H, m), 7.39–7.31 (3H, m), 5.95 (1H, dddd, *J*=17.3, 10.3, 6.6, 5.5 Hz), 5.44 (1H, s), 5.32 (1H, dq, *J*=17.3, 1.4 Hz), 5.23 (1H, brdq, *J*=10.3, 1.4 Hz), 4.81 (1H, d, *J*=3.7 Hz), 4.23 (1H, dd, *J*=10.1, 4.8 Hz), 4.20 (1H, ddt, *J*=12.7, 5.5, 1.4 Hz), 4.02 (1H, brdd, *J*=9.4, 8.8 Hz), 4.00 (1H, ddt, *J*=12.7, 6.6, 1.4 Hz), 3.86 (1H, brddd, *J*=10.1, 9.4, 4.8 Hz), 3.68 (1H, t, *J*=10.1 Hz), 3.64 (1H, dd, *J*=8.8, 3.7 Hz), 3.38 (1H, t, *J*=9.4 Hz), 0.92 (9H, s), 0.80 (9H, s), 0.11 (3H, s), 0.09 (3H, s), 0.04 (3H, s), −0.01 (3H, s); LR-EIMS, *m/z* 479 (49.0%, $[M-t\text{-Bu}]^+$), 73 (bp); HR-EIMS, calcd for $C_{24}H_{39}O_6Si_2$ $[M-t\text{-Bu}]^+$: 479.2285, found: 479.2281. *β-Anomer of* ***10***: a colorless oil; $[\alpha]_D^{25}$=−41.5° (*c* 1.03, $CHCl_3$); IR (film), ν_{max} 2954, 2929, 2885, 2857, 1472, 1462, 1388, 1361, 1250, 1172, 1089, 1032, 998, 929, 837, 781, 760, 697, 674 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.48–7.42 (2H, m), 7.40–7.33 (3H, m), 5.95 (1H, dddd, *J*=17.3, 10.3, 6.6, 5.7 Hz), 5.41 (1H, s), 5.29 (1H, dq, *J*=17.3, 1.3 Hz), 5.20 (1H, brdq, *J*=10.3, 1.3 Hz), 4.38–4.27 (2H, m), 4.35 (1H, d, *J*= 7.3 Hz), 4.06 (1H, ddt, *J*=11.9, 6.6, 1.3 Hz), 3.79–3.69 (2H, m), 3.50 (1H, brdd, *J*=7.7, 7.3 Hz), 3.47–3.39 (2H, m), 0.91 (9H, s), 0.79 (9H, s), 0.12 (3H, s), 0.10 (3H, s), 0.01 (3H, s), −0.04 (3H, s); LR-EIMS, *m/z* 479 (41.8%, $[M-t\text{-Bu}]^+$), 73 (bp); HR-EIMS, calcd for $C_{24}H_{39}O_6Si_2$ $[M-t\text{-Bu}]^+$: 479.2285, found: 479.2288.

4.1.3. 4,6-*O*-Benzylidene-2,3-bis-*O*-(*tert*-butyldimethylsilyl)-D-glucopyranose (11). To a mixture of **10** (113.6 mg, 0.212 mmol) and *i*-Pr_2NEt (56.0 μl, 0.321 mmol) in EtOH (2.1 ml) was added $RhCl(PPh_3)_3$ (2.3 mg, 0.00249 mmol) at 23°C and the mixture was stirred for 5 min. Then, the mixture was heated to 100°C and stirred for 1 h. The mixture was cooled to 23°C and concentrated under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 (5 ml) and the mixture was washed with brine (5 ml). The aqueous layer was extracted with CH_2Cl_2 (3×5 ml). The combined organic layers were dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. The solution of the crude vinyl ether in acetone/H_2O (9:1, 3 ml) was added to a suspension of $HgCl_2$ (114.1 mg, 0.420 mmol) and HgO (red, 113.8 mg, 0.525 mmol) in acetone/H_2O (9:1, 1 ml) at 24°C and the mixture was stirred for 1.5 h. The mixture was

filtered through Celite and concentrated under reduced pressure. The resulting residue was dissolved in ether (5 ml) and the mixture was washed with saturated aqueous KI (5 ml). The aqueous layer was extracted with ether (3×5 ml). The combined organic layers were washed with brine (3 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=10) provided **11** (105.3 mg, ~100% from **10**) as an inseparable mixture of α and β-anomers (α/β=4:1 from ^{1}H NMR). **11**: a colorless syrup; $[\alpha]_D^{25}$=+0.2° (*c* 1.09, $CHCl_3$); IR (film), ν_{max} 3442, 2953, 2929, 2885, 2857, 1472, 1462, 1388, 1361, 1255, 1169, 1144, 1089, 1051, 1028, 996, 858, 838, 780, 759, 697, 667 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.49–7.42 (2H, m), 7.36–7.32 (3H, m), 5.44 (1H, s), 5.14 (4/5H, dd, *J*=3.5, 1.5 Hz), 4.69 (1/5H, brdd, *J*=7.2, 6.2 Hz), 4.31 (1/5H, dd, *J*=10.3, 4.6 Hz), 4.29 (4/5H, dd, *J*=10.3, 5.0 Hz), 4.06 (4/5H, brddd, *J*=10.3, 9.4, 5.0 Hz), 3.94 (4/5H, brdd, *J*=9.4, 8.4 Hz), 3.78 (1/5H, brdd, *J*=9.7, 7.2 Hz), 3.71 (1/5H, t, *J*=10.3 Hz), 3.67 (4/5H, t, *J*=10.3 Hz), 3.66 (4/5H, dd, *J*=8.4, 3.5 Hz), 3.55 (1/5H, brddd, *J*=10.3, 9.7, 4.6 Hz), 3.48 (1/5H, t, *J*=9.7 Hz), 3.48 (1/5H, t, *J*=7.2 Hz), 3.39 (4/5H, t, *J*=9.4 Hz), 3.12 (4/5H, d, *J*=1.5 Hz), 3.00 (1/5H, d, *J*=6.2 Hz), 0.94 (36/5H, s), 0.92 (9/5H, s), 0.80 (9H, s), 0.15 (3H, s), 0.13 (12/5H, s), 0.12 (3/5H, s), 0.03 (3H, s), −0.02 (3/5H, s), −0.03 (12/5H, s); LR-EIMS, *m/z* 479 (31.5%, $[M\text{-}OH]^+$), 439 (28.4%, $[M-t\text{-}Bu]^+$), 73 (bp); HR-EIMS, calcd for $C_{25}H_{43}O_5Si_2$ $[M-OH]^+$: 479.2649, found: 479.2652.

4.1.4. 4,6-*O*-Benzylidene-2,3-bis-*O*-(*tert*-butyldimethylsilyl)-D-glucono-1,5-lactone (12). To oxalyl chloride (10.3 μl, 0.118 mmol) in CH_2Cl_2 (1 ml) was added DMSO (13.4 μl, 0.189 mmol) in CH_2Cl_2 (1 ml) dropwise at −78°C and the mixture was stirred for 10 min. Then, **11** (19.4 mg, 0.0391 mmol) in CH_2Cl_2 (2 ml) was added dropwise at −78°C and the mixture was stirred for 15 min. Et_3N (54.5 μl, 0.391 mmol) was added dropwise at −78°C and the mixture was stirred for 5 min. The mixture was warmed to 0°C and stirred for 20 min. H_2O (4 ml) was added and the mixture was extracted with hexane/CH_2Cl_2 (1:1, 8 ml). The organic layer was washed with 0.5 M aqueous HCl (2×4 ml), H_2O (4 ml), saturated aqueous $NaHCO_3$ (4 ml), and brine (4 ml). The organic layer was dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=10) provided **12** (17.8 mg, 92%). **12**: a colorless oil; $[\alpha]_D^{21}$=+32.5° (*c* 1.03, $CHCl_3$); IR (film), ν_{max} 2954, 2930, 2885, 2858, 1770, 1472, 1463, 1406, 1376, 1362, 1310, 1259, 1202, 1087, 1039, 1005, 938, 889, 837, 781, 751, 697, 672, 652 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.51–7.46 (2H, m), 7.42–7.36 (3H, m), 5.55 (1H, s), 4.67 (1H, brddd, *J*=10.5, 10.1, 5.3 Hz), 4.51 (1H, dd, *J*=10.5, 5.3 Hz), 4.15 (1H, d, *J*=1.7 Hz), 4.02 (1H, dd, *J*=6.2, 1.7 Hz), 3.78 (1H, t, *J*=10.5 Hz), 3.70 (1H, dd, *J*=10.1, 6.2 Hz), 0.91 (9H, s), 0.88 (9H, s), 0.17 (3H, s), 0.14 (3H, s), 0.11 (3H, s), 0.09 (3H, s); LR-EIMS, *m/z* 437 (75.7%, $[M-t\text{-}Bu]^+$), 73 (bp); HR-EIMS, calcd for $C_{21}H_{33}O_6Si_2$ $[M-t\text{-}Bu]^+$: 437.1815, found: 437.1816.

4.1.5. General procedure of an in situ preparation of Tebbe's reagent.[18d] To titanocene dichloride (881.9 mg, 3.54 mmol) was added $AlMe_3$ (4.00 ml, 15% in toluene, 7.08 mmol) dropwise in the dark at 23°C and the mixture was stirred for 72 h. The resulting mixture was used as a 0.885 M toluene solution of Tebbe's reagent without purification.

4.1.6. (1*R*,3*R*,6*R*,9*R*,10*S*)-9,10-Bis(*tert*-butyldimethylsilyloxy)-8-methylene-3-phenyl-2,4,7-trioxabicyclo[4.4.0]decane (13). To Tebbe's reagent (0.060 ml, 0.885 M in toluene, 0.0531 mmol) was added **12** (14.0 mg, 0.0283 mmol) in THF (2 ml) dropwise in the dark at 0°C and the mixture was stirred for 10 min. The mixture was warmed to 24°C and stirred for 30 min. After the mixture was diluted with ether (2 ml), 2 M aqueous NaOH (ca. 1 ml) was added dropwise until evolution of CH_4 was ceased. Then, anhydrous $MgSO_4$ was added. The mixture was filtered through Celite and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=50 containing 1% v/v Et_3N) provided **13** (13.9 mg, ~100%). **13** was unstable and immediately used for the next reaction. **13**: a pale yellow oil; ^{1}H NMR (300 MHz, C_6D_6, C_6HD_5 as 7.15 ppm), δ 7.57–7.53 (2H, m), 7.19–7.05 (3H, m), 5.21 (1H, s), 4.70 (1H, s), 4.55 (1H, s), 4.26 (1H, dd, *J*=10.3, 5.1 Hz), 4.12 (1H, d, *J*=4.4 Hz), 4.07 (1H, brddd, *J*=10.3, 9.9, 5.1 Hz), 4.00 (1H, dd, *J*=7.3, 4.4 Hz), 3.51 (1H, dd, *J*=9.9, 7.3 Hz), 3.47 (1H, t, *J*=10.3 Hz), 0.99 (9H, s), 0.98 (9H, s), 0.17 (3H, s), 0.16 (3H, s), 0.13 (6H, s).

4.1.7. {(1*R*,3*R*,6*R*,8*S*,9*S*,10*S*)-9,10-Bis(*tert*-butyldimethylsilyloxy)-3-phenyl-2,4,7-trioxabicyclo[4.4.0]dec-8-yl}methanol (14) and {(1*R*,3*R*,6*R*,8*R*,9*S*,10*S*)-9,10-bis(*tert*-butyldimethylsilyloxy)-3-phenyl-2,4,7-trioxabicyclo[4.4.0]dec-8-yl}methanol (15). To **13** (13.9 mg, 0.0282 mmol) in THF (0.3 ml) was added BH_3·THF (0.045 ml, 1.0 M in THF, 0.045 mmol) at 0°C and the mixture was stirred for 2.5 h. Then, additional BH_3·THF (0.045 ml, 1.0 M in THF, 0.045 mmol) was added at 0°C and the mixture was stirred for 2 h. 5 M aqueous NaOH (55.0 μl, 0.275 mmol) and 30% aqueous H_2O_2 (28.0 μl, 0.272 mmol) were added at 0°C. The mixture was warmed to 24°C and stirred for 12.5 h. Saturated aqueous Na_2SO_3 (5 ml) was added and the mixture was extracted with ether (3×5 ml). The combined organic layers were dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=5) provided an inseparable mixture (11.5 mg, 80%) of **14** and the epimer at C9 **15** (**14**/**15**=3:5 from ^{1}H NMR).

4.1.8. {(1*R*,3*R*,6*R*,8*S*,9*S*,10*S*)-9,10-Bis(*tert*-butyldimethylsilyloxy)-3-phenyl-2,4,7-trioxabicyclo[4.4.0]dec-8-yl}methyl acetate (16) and {(1*R*,3*R*,6*R*,8*R*,9*S*,10*S*)-9,10-bis(*tert*-butyldimethylsilyloxy)-3-phenyl-2,4,7-trioxabicyclo[4.4.0]dec-8-yl}methyl acetate (17). To the above mixture (11.5 mg, 0.0225 mmol) of **14** and **15** in pyridine (0.4 ml, 4.95 mmol) was added acetic anhydride (0.2 ml, 2.12 mmol) at 25°C and the mixture was stirred for 22 h. The mixture was concentrated under reduced pressure. Purification of the resultant residue by flash chromatography

(silica gel, hexane/EtOAc=20) provided **16** (4.3 mg, 35%) and **17** (8.1 mg, 65%). **16**: a colorless oil; $[\alpha]_D^{26}=-40.6°$ (*c* 0.36, $CHCl_3$); IR (film), ν_{max} 2955, 2929, 2894, 2857, 1745, 1472, 1462, 1388, 1368, 1251, 1237, 1171, 1152, 1106, 1074, 1027, 1005, 970, 936, 915, 837, 779, 760, 698, 672 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, C_6HD_5 as 7.15 ppm), δ 7.52–7.49 (2H, m), 7.19–7.06 (3H, m), 5.16 (1H, s), 4.64 (1H, dd, *J*=11.9, 2.2 Hz), 4.18–4.11 (2H, m), 3.76 (1H, brdd, *J*=9.0, 7.7 Hz), 3.59 (1H, brdd, *J*=9.2, 7.7 Hz), 3.44 (1H, t, *J*=10.3 Hz), 3.38 (1H, ddd, *J*=9.2, 6.1, 2.2 Hz), 3.26 (1H, brddd, *J*=10.3, 9.0, 4.8 Hz), 3.17 (1H, t, *J*=9.0 Hz), 1.70 (3H, s), 1.01 (9H, s), 0.95 (9H, s), 0.23 (3H, s), 0.13 (3H, s), 0.12 (6H, s); LR-EIMS, *m/z* 495 (bp, $[M-t\text{-Bu}]^+$); HR-EIMS, calcd for $C_{24}H_{39}O_7Si_2$ $[M-t\text{-Bu}]^+$: 495.2234, found: 495.2234. **17**: a colorless oil; $[\alpha]_D^{25}=+17.6°$ (*c* 0.68, $CHCl_3$); IR (film), ν_{max} 2954, 2929, 2895, 2857, 1746, 1472, 1462, 1368, 1252, 1236, 1172, 1151, 1100, 1038, 1004, 856, 838, 779, 760, 698 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, C_6HD_5 as 7.15 ppm), δ 7.60–7.56 (2H, m), 7.21–7.07 (3H, m), 5.27 (1H, s), 4.65 (1H, dd, *J*=12.2, 9.2 Hz), 4.42 (1H, dd, *J*=12.2, 3.5 Hz), 4.33 (1H, brddd, *J*=9.2, 4.8, 3.5 Hz), 4.27 (1H, dd, *J*=10.1, 5.0 Hz), 4.01 (1H, brddd, *J*=10.1, 9.7, 5.0 Hz), 3.92–3.83 (2H, m), 3.48 (1H, t, *J*=10.1 Hz), 3.32 (1H, dd, *J*=9.7, 7.9 Hz), 1.68 (3H, s), 0.98 (9H, s), 0.94 (9H, s), 0.14 (6H, s), 0.13 (3H, s), 0.05 (3H, s); LR-EIMS, *m/z* 495 (70.9%, $[M-t\text{-Bu}]^+$), 117 (bp); HR-EIMS, calcd for $C_{24}H_{39}O_7Si_2$ $[M-t\text{-Bu}]^+$: 495.2234, found: 495.2234.

4.1.9. Allyl 4,6-*O*-benzylidene-2,3-*O*-(3,5-diisopropyl-2,6-dimethyl-4-oxa-3,5-disilaheptane-3,5-diyl)-D-glucopyranoside (18). To a mixture of **9** (3.44 g, 11.1 mmol) and imidazole (1.82 g, 26.7 mmol) in DMF (22 ml) was added 1,3-dichlorotetraisopropyldisiloxane (4.30 ml, 13.4 mmol) at 0°C. The mixture was warmed to 24°C and stirred for 11.5 h. After the mixture was diluted with ether (50 ml), saturated aqueous $NaHCO_3$ (50 ml) was added. The mixture was extracted with ether (3×50 ml). The combined organic layers were washed with brine (25 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=50) provided **18** (5.79 g, 95%). The mixture of α and β-anomers was used in the next reaction without separation. The following spectral data were obtained from the pure α and β-anomers of **18** prepared alternatively from the corresponding pure α and β-anomers of **9** under the same conditions as the above. *α-Anomer of 18*: a colorless oil; $[\alpha]_D^{27}=+24.9°$ (*c* 1.00, $CHCl_3$); IR (film), ν_{max} 2944, 2867, 1464, 1382, 1248, 1212, 1176, 1142, 1091, 1048, 990, 923, 886, 847, 746, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.52–7.45 (2H, m), 7.38–7.29 (3H, m), 5.89 (1H, dddd, *J*=17.3, 10.5, 5.5, 4.8 Hz), 5.55 (1H, s), 5.36 (1H, dq, *J*=17.3, 1.7 Hz), 5.18 (1H, dq, *J*=10.5, 1.7 Hz), 4.85 (1H, d, *J*=3.9 Hz), 4.28 (1H, dd, *J*=10.1, 4.8 Hz), 4.21 (1H, ddt, *J*=13.6, 4.8, 1.7 Hz), 4.16 (1H, brdd, *J*=9.2, 8.6 Hz), 4.06 (1H, ddt, *J*=13.6, 5.5, 1.7 Hz), 3.90 (1H, brddd, *J*=10.1, 9.2, 4.8 Hz), 3.80 (1H, dd, *J*=8.6, 3.9 Hz), 3.73 (1H, t, *J*=10.1 Hz), 3.49 (1H, t, *J*=9.2 Hz), 1.13–0.93 (28H, m); LR-EIMS, *m/z* 507 (bp, $[M-i\text{-Pr}]^+$); HR-EIMS, calcd for $C_{25}H_{39}O_7Si_2$ $[M-i\text{-Pr}]^+$: 507.2234, found: 507.2232. *β-Anomer of 18*: colorless needles (hexane), mp 111–113°C; $[\alpha]_D^{27}=-66.5°$ (*c* 1.01, $CHCl_3$); IR (KBr), ν_{max} 2944, 2867, 1463, 1451, 1378, 1179, 1092, 1033, 1007, 985, 923, 886, 840, 745, 696, 651, 614, 591 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.50–7.45 (2H, m), 7.38–7.29 (3H, m), 5.90 (1H, dddd, *J*=17.3, 10.5, 5.7, 5.1 Hz), 5.55 (1H, s), 5.34 (1H, dq, *J*=17.3, 1.7 Hz), 5.18 (1H, dq, *J*=10.5, 1.7 Hz), 4.44 (1H, d, *J*=7.3 Hz), 4.37 (1H, ddt, *J*=13.2, 5.1, 1.7 Hz), 4.34 (1H, dd, *J*=10.3, 5.0 Hz), 4.16 (1H, ddt, *J*=13.2, 5.7, 1.7 Hz), 3.87 (1H, dd, *J*=9.2, 7.9 Hz), 3.79 (1H, t, *J*=10.3 Hz), 3.62 (1H, brdd, *J*=7.9, 7.3 Hz), 3.54 (1H, t, *J*=9.2 Hz), 3.39 (1H, brddd, *J*=10.3, 9.2, 5.0 Hz), 1.13–0.93 (28H, m); LR-EIMS, *m/z* 507 (bp, $[M-i\text{-Pr}]^+$); HR-EIMS, calcd for $C_{25}H_{39}O_7Si_2$ $[M-i\text{-Pr}]^+$: 507.2234, found: 507.2235.

4.1.10. 4,6-*O*-Benzylidene-2,3-*O*-(3,5-diisopropyl-2,6-dimethyl-4-oxa-3,5-disilaheptane-3,5-diyl)-D-glucopyranose (19). To a mixture of **18** (3.96 g, 7.18 mmol) and *i*-Pr_2NEt (1.90 ml, 10.9 mmol) in EtOH (36 ml) was added $RhCl(PPh_3)_3$ (80.6 mg, 0.0871 mmol) at 25°C and the mixture was stirred for 10 min. Then, the mixture was heated to 100°C and stirred for 1 h. The mixture was cooled to 25°C and concentrated under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 (35 ml) and the mixture was washed with brine (35 ml). The aqueous layer was extracted with CH_2Cl_2 (3×35 ml). The combined organic layers were dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. The solution of the crude vinyl ether in acetone/H_2O (9:1, 36 ml) was added to a suspension of $HgCl_2$ (3.96 g, 14.6 mmol) and HgO (red, 3.96 g, 18.3 mmol) in acetone/H_2O (9:1, 36 ml) at 25°C and the mixture was stirred for 1 h. The mixture was filtered through Celite and concentrated under reduced pressure. The resulting residue was dissolved in ether (35 ml) and the mixture was washed with saturated aqueous KI (35 ml). The aqueous layer was extracted with ether (3×35 ml). The combined organic layers were washed with brine (20 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=10→5) provided **19** (3.57 g, 97% from **18**) as an inseparable mixture of α and β-anomers (α/β=1:1 from ^1H NMR). **19**: white needles (hexane/ether), mp 165–167°C; $[\alpha]_D^{25}=-37.4°$ (*c* 1.05, $CHCl_3$); IR (KBr), ν_{max} 3449, 2943, 2866, 1463, 1451, 1378, 1248, 1180, 1128, 1095, 1031, 1006, 983, 884, 848, 833, 745, 698, 653, 574 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.49–7.46 (2H, m), 7.38–7.33 (3H, m), 5.564 (1/2H, s), 5.558 (1/2H, s), 5.21 (1/2H, d, *J*=3.7 Hz), 4.73 (1/2H, dd, *J*=7.3, 5.0 Hz), 4.36 (1/2H, dd, *J*=10.3, 5.3 Hz), 4.34 (1/2H, dd, *J*=10.3, 5.3 Hz), 4.11–4.03 (2/2H, m), 3.89 (1/2H, brdd, *J*=9.4, 7.7 Hz), 3.82 (1/2H, dd, *J*=8.1, 3.7 Hz), 3.79 (1/2H, t, *J*=10.3 Hz), 3.73 (1/2H, t, *J*=10.3 Hz), 3.57 (1/2H, t, *J*=9.4 Hz), 3.55 (1/2H, brdd, *J*=7.7, 7.3 Hz), 3.51 (1/2H, t, *J*=9.4 Hz), 3.47 (1/2H, brddd, *J*=10.3, 9.4, 5.3 Hz), 3.23 (1/2H, brs), 3.02 (1/2H, d, *J*=5.0 Hz), 1.15–0.98 (28H, m); LR-EIMS, *m/z* 467 (63.9%, $[M-i\text{-Pr}]^+$), 235 (bp); HR-EIMS, calcd for $C_{22}H_{35}O_7Si_2$ $[M-i\text{-Pr}]^+$: 467.1921, found: 467.1922.

4.1.11. 4,6-*O*-Benzylidene-2,3-*O*-(3,5-diisopropyl-2,6-dimethyl-4-oxa-3,5-disilaheptane-3,5-diyl)-D-glucono-1,5-lactone (20). To oxalyl chloride (265 μl, 3.04 mmol) in CH_2Cl_2 (6.1 ml) was added DMSO (345 μl, 4.86 mmol) in

CH_2Cl_2 (9.7 ml) dropwise at −78°C and the mixture was stirred for 20 min. Then, **19** (1.03 g, 2.01 mmol) in CH_2Cl_2 (5.5 ml) was added dropwise at −78°C and the mixture was stirred for 20 min. Et_3N (1.40 ml, 10.0 mmol) was added dropwise at −78°C and the mixture was stirred for 10 min. The mixture was warmed to 0°C and stirred for 20 min. H_2O (10 ml) was added and the mixture was extracted with CH_2Cl_2 (30 ml). The organic layer was washed with 0.1 M aqueous HCl (2×10 ml), H_2O (10 ml), saturated aqueous $NaHCO_3$ (10 ml), and brine (10 ml). The organic layer was dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. The resultant crude **20** (991.9 mg, ~97%) was almost pure (checked by ^1H NMR) and used in the next reaction without further purification. **20**: colorless needles (hexane/CH_2Cl_2), mp 207–209°C; $[\alpha]_D^{26}=-17.8°$ (*c* 0.88, $CHCl_3$); IR (KBr), ν_{max} 2945, 2894, 2867, 1774, 1463, 1450, 1380, 1239, 1219, 1188, 1139, 1094, 1080, 1065, 1041, 1008, 986, 916, 885, 842, 829, 746, 698, 656, 619, 604 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.50–7.45 (2H, m), 7.41–7.34 (3H, m), 5.63 (1H, s), 4.46 (1H, dd, *J*=10.5, 5.0 Hz), 4.34 (1H, d, *J*=7.9 Hz), 4.21 (1H, dd, *J*=9.5, 7.9 Hz), 4.13 (1H, brddd, *J*=10.5, 9.5, 5.0 Hz), 3.85 (1H, t, *J*=9.5 Hz), 3.84 (1H, t, *J*=10.5 Hz), 1.13–1.03 (28H, m); LR-EIMS, *m/z* 465 (93.9%, $[M-i\text{-}Pr]^+$), 149 (bp); HR-EIMS, calcd for $C_{22}H_{33}O_7Si_2$ $[M-i\text{-}Pr]^+$: 465.1765, found: 465.1765.

4.1.12. (1*S*,2*R*,4*R*,7*R*,10*R*)-12,12,14,14-Tetraisopropyl-9-methylene-4-phenyl-3,5,8,11,13,15-hexaoxa-12,14-disilatricyclo[8.5.0.0^{2,7}]pentadecane (21). To the above crude **20** (991.9 mg, 1.95 mmol) in THF (20 ml) was added Tebbe's reagent (3.50 ml, 0.870 M in toluene, 3.05 mmol) dropwise in the dark at 0°C and the mixture was stirred for 10 min. The mixture was warmed to 23°C and stirred for 20 min. After the mixture was diluted with THF (20 ml), 0.1 M aqueous NaOH (ca. 20 ml) was added dropwise until evolution of CH_4 was ceased. The mixture was filtered through Celite and extracted with ether (3×20 ml). The combined organic layers were washed with brine (10 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=10 containing 1% v/v Et_3N) provided **21** (742.4 mg, 73% from **19**). **21** was unstable and immediately used for the next reaction. **21**: a pale yellow oil; ^1H NMR (300 MHz, C_6D_6, C_6HD_5 as 7.15 ppm), δ 7.64–7.61 (2H, m), 7.22–7.06 (3H, m), 5.30 (1H, s), 5.06 (1H, d, *J*=2.1 Hz), 4.87 (1H, d, *J*=2.1 Hz), 4.31 (1H, dt, *J*=8.3, 2.1 Hz), 4.20 (1H, m), 3.96 (1H, brdd, *J*=9.0, 8.3 Hz), 3.52 (1H, t, *J*=9.0 Hz), 3.50–3.36 (2H, m), 1.21–0.99 (28H, m).

4.1.13. {(1*S*,2*R*,4*R*,7*R*,9*S*,10*S*)-12,12,14,14-Tetraisopropyl-4-phenyl-3,5,8,11,13,15-hexaoxa-12,14-disilatricyclo-[8.5.0.0^{2,7}]pentadec-9-yl}methanol (22) and {(1*S*,2*R*,4*R*,7*R*,9*R*,10*S*)-12,12,14,14-tetraisopropyl-4-phenyl-3,5,8,11,13,15-hexaoxa-12,14-disilatricyclo[8.5.0.0^{2,7}]pentadec-9-yl}methanol (23). To **21** (14.2 mg, 0.0280 mmol) in THF (0.3 ml) was added BH_3·THF (0.045 ml, 1.0 M in THF, 0.0450 mmol) at 0°C and the mixture was stirred for 1.5 h. 5 M aqueous NaOH (27.0 μl, 0.135 mmol) and 30% aqueous H_2O_2 (14.0 μl, 0.136 mmol) were added at 0°C. The mixture was warmed to 26°C and stirred for 11.5 h. Saturated aqueous Na_2SO_3 (5 ml) was added and the mixture was extracted with ether (3×5 ml). The combined organic layers were washed with brine (3 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=5) provided an inseparable mixture (12.2 mg, 83%) of **22** and the epimer at C9 **23** (**22/23**=9:1 from ^1H NMR).

4.1.14. {(1*S*,2*R*,4*R*,7*R*,9*S*,10*S*)-12,12,14,14-Tetraisopropyl-4-phenyl-3,5,8,11,13,15-hexaoxa-12,14-disilatricyclo-[8.5.0.0^{2,7}]pentadec-9-yl}methyl actate (24) and {(1*S*,2*R*,4*R*,7*R*,9*R*,10*S*)-12,12,14,14-tetraisopropyl-4-phenyl-3,5,8,11,13,15-hexaoxa-12,14-disilatricyclo[8.5.0.0^{2,7}]pentadec-9-yl}methyl acetate (25). To the above mixture (12.2 mg, 0.0232 mmol) of **22** and **23** in pyridine (0.4 ml, 4.95 mmol) was added acetic anhydride (0.2 ml, 2.12 mmol) at 25°C and the mixture was stirred for 11 h. After the mixture was diluted with ether (5 ml), saturated aqueous $CuSO_4$ (5 ml) was added. The mixture was extracted with ether (3×5 ml). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (3 ml) and brine (3 ml). The organic layers were dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=5) provided a mixture (12.1 mg) of **24** and **25**. **24** and **25** were separated by TLC (silica gel, hexane/ether=3) to give **24** (10.7 mg, 81%) and **25** (1.3 mg, 10%). **24**: colorless needles (hexane), mp 112–113°C; $[\alpha]_D^{25}=-62.8°$ (*c* 0.89, $CHCl_3$); IR (KBr), ν_{max} 2964, 2942, 2867, 1749, 1462, 1378, 1366, 1240, 1178, 1117, 1102, 1081, 1036, 1010, 998, 989, 887, 835, 744, 695, 567 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.50–7.46 (2H, m), 7.38–7.33 (3H, m), 5.56 (1H, s), 4.43 (1H, dd, *J*=11.9, 2.0 Hz), 4.36 (1H, dd, *J*=10.3, 4.8 Hz), 4.18 (1H, dd, *J*=11.9, 5.3 Hz), 3.88 (1H, brdd, *J*=8.8, 7.9 Hz), 3.76 (1H, brdd, *J*=9.4, 7.9 Hz), 3.74 (1H, t, *J*=10.3 Hz), 3.56 (1H, ddd, *J*=9.4, 5.3, 2.0Hz), 3.54 (1H, t, *J*=8.8 Hz), 3.43 (1H, brddd, *J*=10.3, 8.8, 4.8 Hz), 2.10 (3H, s), 1.10–0.93 (28H, m); LR-EIMS, *m/z* 523 (85.5%, $[M-i\text{-}Pr]^+$), 277 (bp); HR-EIMS, calcd for $C_{25}H_{39}O_8Si_2$ $[M-i\text{-}Pr]^+$: 523.2183, found: 523.2186. **25**: a colorless oil; $[\alpha]_D^{25}=-8.2°$ (*c* 0.11, $CHCl_3$); IR (film), ν_{max} 2925, 2866, 1735, 1461, 1368, 1249, 1181, 1104, 1078, 1032, 1006, 982, 884, 840, 748, 708, 651 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.49–7.46 (2H, m), 7.38–7.33 (3H, m), 5.55 (1H, s), 4.66 (1H, dd, *J*=12.6, 9.3 Hz), 4.34–4.25 (3H, m), 4.06 (1H, brdd, *J*=8.8, 6.6 Hz), 3.98 (1H, t, *J*=8.8 Hz), 3.76 (1H, brddd, *J*=9.9, 8.8, 4.2 Hz), 3.67 (1H, t, *J*=9.9 Hz), 3.49 (1H, t, *J*=8.8 Hz), 2.10 (3H, s), 1.09–0.96 (28H, m); LR-EIMS, *m/z* 523 (79.9%, $[M-i\text{-}Pr]^+$), 277 (bp); HR-EIMS, calcd for $C_{25}H_{39}O_8Si_2$ $[M-i\text{-}Pr]^+$: 523.2183, found: 523.2183.

4.1.15. {(1*S*,2*R*,4*R*,7*R*,9*S*,10*S*)-12,12,14,14-Tetraisopropyl-4-phenyl-3,5,8,11,13,15-hexaoxa-12,14-disilatricyclo-[8.5.0.0^{2,7}]pentadec-9-yl}methanol (22). To **21** (742.4 mg, 1.46 mmol) in THF (15 ml) was added 9-BBN (4.40 ml, 0.5 M in THF, 2.20 mmol) at 23°C and the mixture was stirred for 1 h. Then, additional 9-BBN (2.90 ml, 0.5 M in THF, 1.45 mmol) was added at 23°C and the mixture was stirred for 1 h. After the mixture was cooled to 0°C, 3 M

aqueous NaOH (3.70 ml, 11.1 mmol) and TBHP (3.20 ml, 3.46 M in toluene, 11.1 mmol) were added. The mixture was warmed to 23°C and stirred for 11 h. Saturated aqueous Na_2SO_3 (15 ml) was added and the mixture was extracted with ether (3×15 ml). The combined organic layers were washed with brine (8 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=10⟶5) provided **22** (647.8 mg, 85%) as a single diastereomer. **22**: colorless needles (hexane/ether), mp 157–159°C; $[\alpha]_D^{26}=-62.5°$ (*c* 1.18, $CHCl_3$); IR (KBr), ν_{max} 3589, 3575, 2943, 2893, 2866, 1463, 1452, 1384, 1181, 1150, 1123, 1103, 1031, 1009, 986, 886, 838, 748, 699, 651, 612, 566 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.52–7.45 (2H, m), 7.38–7.29 (3H, m), 5.56 (1H, s), 4.37–4.32 (1H, m), 3.92 (1H, ddd, *J*=11.6, 6.1, 2.6 Hz), 3.89 (1H, t, *J*=8.3 Hz), 3.77–3.68 (3H, m), 3.53–3.42 (3H, m), 1.89 (1H, t, *J*=6.1 Hz), 1.10–0.93 (28H, m); LR-EIMS, *m/z* 523 (24.2%, $[M-H]^+$), 481 (75.8%, $[M-i\text{-}Pr]^+$), 235 (bp); HR-EIMS, calcd for $C_{23}H_{37}O_7Si_2$ $[M-i\text{-}Pr]^+$: 481.2078, found: 481.2080.

4.1.16. {(1*S*,2*R*,4*R*,7*R*,9*S*,10*S*)-12,12,14,14-Tetraisopropyl-4-phenyl-3,5,8,11,13,15-hexaoxa-12,14-disilatricyclo-[8.5.0.0^{2,7}]pentadec-9-yl}methyl trifluoromethanesulfonate (26). To a mixture of **22** (1.00 g, 1.91 mmol) and 2,6-lutidine (670 μl, 5.75 mmol) in CH_2Cl_2 (38 ml) was added trifluoromethanesulfonic anhydride (485 μl, 2.88 mmol) at −78°C and the mixture was stirred for 30 min. Saturated aqueous $NaHCO_3$ (40 ml) was added and the mixture was extracted with CH_2Cl_2 (3×40 ml). The combined organic layers were dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=20) provided **26** (1.22 g, 98%). **26** was unstable and immediately used for the next reaction. **26**: a white solid; ^1H NMR (300 MHz, C_6D_6, C_6HD_5 as 7.15 ppm), δ 7.63–7.61 (2H, m), 7.23–7.18 (2H, m), 7.13–7.07 (1H, m), 5.23 (1H, s), 4.52 (1H, dd, *J*=10.8, 1.8 Hz), 4.32 (1H, dd, *J*=10.8, 4.6 Hz), 4.07 (1H, dd, *J*=10.3, 5.0 Hz), 3.73 (1H, brdd, *J*=8.8, 7.9 Hz), 3.63 (1H, brdd, *J*=9.4, 7.9 Hz), 3.33 (1H, t, *J*=10.3 Hz), 3.24 (1H, brdd, *J*=9.4, 8.8 Hz), 3.09–3.00 (2H, m), 1.20–0.87 (28H, m).

4.1.17. (1*S*,2*R*,4*R*,7*R*,9*S*,10*S*)-9-Allyl-12,12,14,14-tetraisopropyl-4-phenyl-3,5,8,11,13,15-hexaoxa-12,14-disilatricyclo[8.5.0.0^{2,7}]pentadecane (27). To tributylvinyltin (665 μl, 2.28 mmol) in THF (5.7 ml) was added BuLi (1.43 ml, 1.6 M in hexane, 2.29 mmol) at −78°C and the mixture was stirred for 1 h.[29] The vinyllithium was added to a suspension of CuCN (113.6 mg, ~90%, 1.14 mmol) in THF (2.0 ml) at −78°C and the mixture was stirred for 20 min. The mixture was warmed to 0°C and stirred for 5 min. After the resultant mixture was cooled to −78°C, **26** (298.8 mg, 0.455 mmol) in THF (1.9 ml) was added dropwise. Then, the mixture was stirred for 10 min. The mixture was warmed to 0°C and stirred for 80 min. 1 M aqueous NH_3 (10 ml) was added and the mixture was extracted with ether (3×10 ml). The combined organic layers were washed with brine (5 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/benzene=3 then hexane/EtOAc=50) provided **27** (226.7 mg, 93%). **27**: colorless needles (hexane), mp 113–115°C; $[\alpha]_D^{22}=-60.2°$ (*c* 1.01, $CHCl_3$); IR (KBr), ν_{max} 2964, 2944, 2895, 2867, 1463, 1379, 1179, 1147, 1114, 1087, 1029, 1009, 985, 914, 883, 837, 745, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.51–7.46 (2H, m), 7.38–7.31 (3H, m), 5.90 (1H, ddt, *J*=17.1, 10.3, 6.8 Hz), 5.55 (1H, s), 5.15–5.06 (2H, m), 4.33 (1H, dd, *J*=10.3, 4.8 Hz), 3.84 (1H, dd, *J*=8.8, 7.9 Hz), 3.70 (1H, t, *J*=10.3 Hz), 3.52 (1H, dd, *J*=9.4, 7.9 Hz), 3.49 (1H, brdd, *J*=9.4, 8.8 Hz), 3.42–3.34 (2H, m), 2.65 (1H, dddt, *J*=14.9, 6.8, 2.8, 1.5 Hz), 2.27–2.17 (1H, m), 1.10–0.92 (28H, m); LR-EIMS, *m/z* 491 (42.5%, $[M-i\text{-}Pr]^+$), 235 (bp); HR-EIMS, calcd for $C_{25}H_{39}O_6Si_2$ $[M-i\text{-}Pr]^+$: 491.2285, found: 491.2291.

4.1.18. (1*S*,3*R*,6*R*,8*S*,9*R*,10*R*)-8-Allyl-3-phenyl-2,4,7-trioxabicyclo[4.4.0]decane-9,10-diol (28). To **27** (717.9 mg, 1.34 mmol) in THF (13.5 ml) was added TBAF (5.35 ml, 1.0 M in THF, 5.35 mmol) at 25°C and the mixture was stirred for 30 min. The mixture was concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=1) provided **28** (388.4 mg, 99%). **28**: a colorless syrup; $[\alpha]_D^{24}=-29.2°$ (*c* 1.07, $CHCl_3$); IR (film), ν_{max} 3415, 2872, 1456, 1384, 1215, 1100, 1009, 916, 761, 699, 652, 603 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.52–7.46 (2H, m), 7.42–7.33 (3H, m), 5.89 (1H, ddt, *J*=17.3, 10.1, 6.8 Hz), 5.52 (1H, s), 5.19–5.08 (2H, m), 4.35–4.30 (1H, m), 3.76–3.63 (2H, m), 3.49–3.38 (4H, m), 2.79 (1H, brs), 2.61 (1H, brdddt, *J*=14.7, 6.8, 2.9, 1.5 Hz), 2.51 (1H, brs), 2.36–2.25 (1H, m); LR-EIMS, *m/z* 292 (bp, $[M]^+$); HR-EIMS calcd for $C_{16}H_{20}O_5$ $[M]^+$: 292.1311, found: 292.1304.

4.1.19. (1*R*,3*R*,6*R*,8*S*,9*S*,10*R*)-8-Allyl-10-(*tert*-butyldimethylsilyloxy)-3-phenyl-2,4,7-trioxabicyclo[4.4.0]decan-9-ol (29) and (1*S*,3*R*,6*R*,8*S*,9*R*,10*S*)-8-allyl-9-(*tert*-butyldimethylsilyloxy)-3-phenyl-2,4,7-trioxabicyclo[4.4.0]-decan-10-ol (29′). To a mixture of **28** (388.4 mg, 1.33 mmol) and 2,6-lutidine (465 μl, 3.99 mmol) in CH_2Cl_2 (13.5 ml) was added TBSOTf (455 μl, 2.00 mmol) at 0°C and the mixture was stirred for 30 min. Saturated aqueous $NaHCO_3$ (15 ml) was added and the mixture was extracted with CH_2Cl_2 (3×15 ml). The combined organic layers were washed with brine (8 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=1) provided a mixture (525.3 mg) of **29** and the regioisomer **29′**. **29** and **29′** were separated by HPLC (YMC-Pack SIL-06, 250×20 mm, hexane/EtOAc=20) to give **29** (479.6 mg, 89%) and **29′** (43.1 mg, 8%). **29**: a colorless oil; $\alpha]_D^{21}=-36.5°$ (*c* 1.00, $CHCl_3$); IR (film), ν_{max} 3600, 3509, 2953, 2926, 2890, 2857, 1472, 1462, 1386, 1249, 1172, 1103, 1068, 1020, 915, 837, 781, 760, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.51–7.45 (2H, m), 7.39–7.33 (3H, m), 5.90 (1H, ddt, *J*=17.3, 10.3, 6.8 Hz), 5.48 (1H, s), 5.18–5.07 (2H, m), 4.33–4.28 (1H, m), 3.75–3.63 (2H, m), 3.47–3.32 (4H, m), 2.62 (1H, dddt, *J*=14.9, 6.8, 3.3, 1.7 Hz), 2.36–2.25 (1H, m), 2.24 (1H, d, *J*=2.6 Hz), 0.87

(9H, s), 0.09 (3H, s), 0.02 (3H, s); LR-EIMS, *m/z* 405 (0.5%, $[M-H]^+$), 349 (92.2%, $[M-t\text{-Bu}]^+$), 75 (bp); HR-EIMS, calcd for $C_{18}H_{25}O_5Si$ $[M-t\text{-Bu}]^+$: 349.1471, found: 349.1471. **29′**: a colorless oil; $[\alpha]_D^{23}=-30.9°$ (*c* 0.33, $CHCl_3$); IR (film), ν_{max} 3488, 2955, 2927, 2856, 1471, 1462, 1387, 1250, 1108, 1028, 1004, 987, 915, 854, 836, 779, 760, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.50–7.45 (2H, m), 7.41–7.34 (3H, m), 5.88 (1H, ddt, *J*=17.1, 10.3, 6.9 Hz), 5.51 (1H, s), 5.15–5.06 (2H, m), 4.36–4.31 (1H, m), 3.72–3.62 (2H, m), 3.46–3.33 (4H, m), 2.65–2.56 (1H, m), 2.44 (1H, d, *J*=2.6 Hz), 2.26–2.16 (1H, m), 0.91 (9H, s), 0.15 (3H, s), 0.13 (3H, s); LR-EIMS, *m/z* 405 (0.8%, $[M-H]^+$), 349 (0.6%, $[M-t\text{-Bu}]^+$), 157 (bp); HR-EIMS, calcd for $C_{18}H_{25}O_5Si$ $[M-t\text{-Bu}]^+$: 349.1471, found: 349.1481.

4.1.20. (1*R*,3*R*,6*R*,8*S*,9*S*,10*S*)-8-Allyl-10-(*tert*-butyldimethylsilyloxy)-3-phenyl-2,4,7-trioxabicyclo[4.4.0]dec-9-yl acrylate (7). To a mixture of **29** (421.8 mg, 1.04 mmol) and *i*-Pr_2NEt (1.09 ml, 6.26 mmol) in CH_2Cl_2 (11 ml) was added acryloyl chloride (255 μl, 3.14 mmol) at 0°C. The mixture was warmed to 25°C and stirred for 3.5 h. Saturated aqueous $NaHCO_3$ (10 ml) was added and the mixture was extracted with CH_2Cl_2 (3×10 ml). The combined organic layers were dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=20) provided **7** (472.2 mg, 99%). **7**: a colorless oil; $[\alpha]_D^{28}=-49.8°$ (*c* 1.02, $CHCl_3$); IR (film), ν_{max} 2954, 2929, 2884, 2858, 1735, 1472, 1462, 1404, 1387, 1294, 1259, 1189, 1168, 1105, 1064, 1005, 916, 837, 779, 761, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.51–7.45 (2H, m), 7.39–7.30 (3H, m), 6.44 (1H, dd, *J*=17.3, 1.5 Hz), 6.13 (1H, dd, *J*=17.3, 10.3 Hz), 5.87 (1H, dd, *J*=10.3, 1.5 Hz), 5.82 (1H, m), 5.51 (1H, s), 5.09–5.02 (2H, m), 4.96 (1H, dd, *J*=9.7, 8.8 Hz), 4.32 (1H, dd, *J*=10.3, 5.0 Hz), 3.89 (1H, t, *J*=8.8 Hz), 3.71 (1H, t, *J*=10.3 Hz), 3.52 (1H, dd, *J*=9.2, 8.8 Hz), 3.51 (1H, ddd, *J*=9.7, 7.2, 4.2 Hz), 3.42 (1H, brddd, *J*=10.3, 9.2, 5.0 Hz), 2.33–2.16 (2H, m), 0.77 (9H, s), −0.03 (6H, s); LR-EIMS, *m/z* 403 (76.1%, $[M-t\text{-Bu}]^+$), 129 (bp); HR-EIMS, calcd for $C_{21}H_{27}O_6Si$ $[M-t\text{-Bu}]^+$: 403.1577, found: 403.1583.

4.1.21. (1*S*,2*S*,3*R*,5*R*,8*R*,10*S*,12*Z*)-2-(*tert*-Butyldimethylsilyloxy)-5-phenyl-4,6,9,15-tetraoxatricyclo[8.5.0.0^{3,8}]-pentadec-12-en-14-one (6). To tricyclohexylphosphine-[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-yl-idene][benzylidene]ruthenium (IV) dichloride **30** (96.9 mg, 0.114 mmol) in 1,2-dichloroethane (1.1 L) was added **7** (1.04 g, 2.27 mmol) in 1,2-dichloroethane (40 ml) at 25°C. Then, the mixture was heated to 120°C and stirred for 12 h. After the mixture was cooled to 25°C, DMSO (405 μl, 5.71 mmol) was added.[30] Then, the mixture was stirred for 16.5 h. The mixture was concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=5→3) provided **6** (838.7 mg, 85%). **6**: a colorless oil; $[\alpha]_D^{22}=+32.3°$ (*c* 1.01, $CHCl_3$); IR (film), ν_{max} 2954, 2928, 2885, 2857, 1725, 1472, 1462, 1388, 1311, 1272, 1250, 1213, 1174, 1141, 1118, 1098, 1069, 1030, 1005, 915, 838, 781, 752, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.52–7.46 (2H, m), 7.40–7.31 (3H, m), 6.33 (1H, ddd, *J*=12.3, 6.1, 3.9 Hz), 6.00 (1H, brddd, *J*=12.3, 2.2, 1.7 Hz), 5.53 (1H, s), 4.34–4.29 (1H, m), 4.18 (1H, dd, *J*=9.2, 7.7 Hz), 4.08–4.02 (1H, m), 3.94 (1H, ddd, *J*=9.2, 7.3, 6.6 Hz), 3.70–3.63 (1H, m), 3.53–3.42 (2H, m), 2.97 (1H, dddd, *J*=19.8, 7.3, 3.9, 2.2 Hz), 2.48 (1H, brddd, *J*=19.8, 6.6, 6.1, 1.7 Hz), 0.86 (9H, s), 0.15 (3H, s), 0.08 (3H, s); LR-EIMS, *m/z* 375 (bp, $[M-t\text{-Bu}]^+$); HR-EIMS, calcd for $C_{19}H_{23}O_6Si$ $[M-t\text{-Bu}]^+$: 375.1264, found: 375.1264.

4.1.22. (1*S*,2*R*,3*R*,5*R*,8*R*,10*S*,12*Z*)-2-(*tert*-Butyldimethylsilyloxy)-14-methylene-5-phenyl-4,6,9,15-tetraoxatricyclo[8.5.0.0^{3,8}]pentadec-12-ene (5). To **6** (73.1 mg, 0.169 mmol) in THF (1.7 ml) was added Tebbe's reagent (0.34 ml, 1.00 M in toluene, 0.340 mmol) dropwise in the dark at −40°C and the mixture was stirred for 30 min. After the mixture was diluted with ether (2 ml), 1 M aqueous NaOH (ca. 1 ml) was added dropwise until evolution of CH_4 was ceased. The mixture was extracted with ether (3×5 ml). The combined organic layers were dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered through Celite and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=10 containing 1% v/v Et_3N) provided **5** (59.8 mg, 82%). **5** was unstable and immediately used for the next reaction. **5**: a pale yellow oil; ^1H NMR (300 MHz, C_6D_6, C_6HD_5 as 7.15 ppm), δ 7.65–7.58 (2H, m), 7.23–7.08 (3H, m), 5.74 (1H, dt, *J*=12.7, 2.1 Hz), 5.23 (1H, s), 5.07 (1H, brdt, *J*=12.7, 5.0 Hz), 4.86 (1H, brd, *J*=0.9 Hz), 4.26 (1H, s), 4.10 (1H, dd, *J*=10.1, 5.0 Hz), 3.95 (1H, dd, *J*=9.0, 7.7 Hz), 3.72 (1H, dd, *J*=9.0, 7.7 Hz), 3.46 (1H, brddd, *J*=9.0, 8.6, 6.4 Hz), 3.37 (1H, t, *J*=10.1 Hz), 3.24 (1H, brdd, *J*=9.2, 9.0 Hz), 3.15 (1H, brddd, *J*=10.1, 9.2, 5.0 Hz), 2.63–2.52 (1H, m), 2.17–2.05 (1H, m), 1.05 (9H, s), 0.29 (3H, s), 0.21 (3H, s).

4.1.23. {(1*S*,2*R*,3*R*,5*R*,8*R*,10*S*,12*Z*,14*R*)-2-(*tert*-Butyldimethylsilyloxy)-5-phenyl-4,6,9,15-tetraoxatricyclo-[8.5.0.0^{3,8}]pentadec-12-en-14-yl}methanol (32) and {(1*S*,2*R*,3*R*,5*R*,8*R*,10*S*,12*Z*,14*S*)-2-(*tert*-butyldimethylsilyloxy)-5-phenyl-4,6,9,15-tetraoxatricyclo[8.5.0.0^{3,8}]pentadec-12-en-14-yl}methanol (33). To **5** (59.8 mg, 0.139 mmol) in THF (1.4 ml) was added 9-BBN (0.42 ml, 0.5 M in THF, 0.210 mmol) at 25°C and the mixture was stirred for 70 min. Then, additional 9-BBN (0.14 ml, 0.5 M in THF, 0.070 mmol) was added at 25°C and the mixture was stirred for 50 min. After the mixture was cooled to 0°C, 3 M aqueous NaOH (280 μl, 0.840 mmol) and TBHP (243 μl, 3.46 M in toluene, 0.841 mmol) were added. The mixture was warmed to 24°C and stirred for 12 h. Saturated aqueous Na_2SO_3 (5 ml) was added and the mixture was extracted with ether (3×5 ml). The combined organic layers were washed with brine (3 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=5) provided a mixture (40.2 mg) of **32** and the epimer at C5 **33**. **32** and **33** were separated by HPLC (YMC-Pack SIL-06, 250×10 mm, hexane/EtOAc=5) to give **32** (36.9 mg, 59%) and **33** (3.3 mg, 5%). **32**: a colorless oil; $[\alpha]_D^{22}=-18.7°$ (*c* 1.00, $CHCl_3$); IR (film), ν_{max} 3475, 2952, 2928, 2885, 2857, 1472, 1462, 1387, 1314, 1272, 1248, 1214, 1174, 1105, 1075, 1029, 1004, 969, 913, 837, 780, 761, 698, 670 cm^{-1}; ^1H NMR (300 MHz, C_6D_6, C_6HD_5 as 7.15 ppm), δ 7.62–7.58 (2H, m), 7.23–7.08 (3H,

m), 5.57–5.47 (2H, m), 5.25 (1H, s), 4.16 (1H, dd, J=10.1, 4.8 Hz), 3.86–3.82 (1H, m), 3.78 (1H, brdd, J=8.8, 8.3 Hz), 3.57–3.53 (2H, m), 3.43 (1H, t, J=10.1 Hz), 3.30 (1H, brdd, J=9.2, 8.8 Hz), 3.27 (1H, brdd, J=9.4, 8.3 Hz), 3.20 (1H, brddd, J=10.1, 9.2, 4.8 Hz), 3.07 (1H, brddd, J=9.9, 9.4, 3.9 Hz), 2.45–2.36 (1H, m), 2.27–2.17 (1H, m), 1.84 (1H, brt, J=6.3 Hz), 1.03 (9H, s), 0.19 (3H, s), 0.15 (3H, s); LR-EIMS, m/z 391 (bp, $[M-t\text{-Bu}]^+$); HR-EIMS, calcd for $C_{20}H_{27}O_6Si$ $[M-t\text{-Bu}]^+$: 391.1577, found: 391.1580. **33**: a colorless oil; $[\alpha]_D^{21}=-44.9°$ (c 0.30, $CHCl_3$); IR (film), ν_{max} 3511, 2928, 2857, 1471, 1463, 1387, 1313, 1273, 1253, 1213, 1174, 1110, 1039, 1004, 969, 914, 882, 837, 782, 762, 698, 673 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.50–7.44 (2H, m), 7.40–7.33 (3H, m), 5.73 (1H, brddd, J=11.9, 7.0, 2.8 Hz), 5.64 (1H, ddd, J=11.9, 4.4, 2.4 Hz), 5.46 (1H, s), 4.48 (1H, brddd, J=9.4, 4.4, 4.2 Hz), 4.31–4.27 (1H, m), 3.91–3.85 (1H, m), 3.76 (1H, ddd, J=12.5, 9.4, 2.8 Hz), 3.70–3.40 (6H, m), 2.88 (1H, dd, J=10.6, 2.8 Hz), 2.67 (1H, brdddd, J=16.9, 7.0, 4.8, 0.9 Hz), 2.36–2.25 (1H, m), 0.84 (9H, s), 0.10 (3H, s), 0.04 (3H, s); LR-EIMS, m/z 391 (bp, $[M-t\text{-Bu}]^+$); HR-EIMS, calcd for $C_{20}H_{27}O_6Si$ $[M-t\text{-Bu}]^+$: 391.1577, found: 391.1580.

4.1.24. (1*S*,2*R*,3*R*,5*R*,8*R*,10*R*,12*Z*,14*R*)-14-(4-Bromobenzyloxymethyl)-2-(*tert*-butyldimethylsilyloxy)-5-phenyl-4,6,9,15-tetraoxatricyclo[8.5.0.0^{3,8}]pentadec-12-ene (34). To a mixture of **32** (35.1 mg, 0.0782 mmol), *p*-bromobenzyl bromide (39.4 mg, 0.158 mmol), and TBAI (14.6 mg, 0.0395 mmol) in THF (0.8 ml) was added NaH (9.8 mg, 60wt% in oil, 0.245 mmol) at 0°C. The mixture was warmed to 25°C and stirred for 14 h. Saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture was extracted with ether (3×5 ml). The combined organic layers were washed with brine (3 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=20→10) provided a mixture (51.7 mg) of **34** and unidentified by-products. The mixture was used in the next reaction without further purification. Pure **34**, used for spectrometric analyses, was obtained alternatively by preparative HPLC. **34**: a colorless oil; $[\alpha]_D^{19}=-7.1°$ (c 1.03, $CHCl_3$); IR (film), ν_{max} 2951, 2927, 2885, 2856, 1487, 1471, 1461, 1386, 1247, 1175, 1106, 1010, 837, 780, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.50–7.44 (4H, m), 7.39–7.30 (3H, m), 7.21 (2H, brdt, J=8.8, 2.2 Hz), 5.92 (1H, dt, J=11.4, 2.9 Hz), 5.82 (1H, dddd, J=11.4, 7.9, 3.5, 2.2 Hz), 5.49 (1H, s), 4.54 (1H, d, J=12.4 Hz), 4.46 (1H, d, J=12.4 Hz), 4.31–4.26 (1H, m), 4.19–4.13 (1H, m), 3.82–3.76 (1H, m), 3.65 (1H, t, J= 10.1 Hz), 3.61 (1H, dd, J=9.5, 4.4 Hz), 3.53 (1H, dd, J=9.5, 5.9 Hz), 3.48–3.33 (4H, m), 2.64 (1H, brddd, J= 16.0, 7.9, 3.3 Hz), 2.41–2.30 (1H, m), 0.83 (9H, s), 0.04 (3H, s), 0.00 (3H, s); LR-EIMS, m/z 561 (32.7%, $[(M+2)-t\text{-Bu}]^+$), 559 (31.8%, $[M-t\text{-Bu}]^+$), 91 (bp); HR-EIMS, calcd for $C_{27}H_{32}BrO_6Si$ $[M-t\text{-Bu}]^+$: 559.1151, found: 559.1151.

4.1.25. (1*R*,2*R*,3*S*,5*R*,8*R*,10*S*,12*Z*,14*R*)-14-(4-Bromobenzyloxymethyl)-5-phenyl-4,6,9,15-tetraoxatricyclo[8.5.0.0^{3,8}]-pentadec-12-en-2-ol (35). To the above mixture including **34** (51.7 mg) in THF (0.8 ml) was added TBAF (155 μl, 1.0 M in THF, 0.155 mmol) at 25°C and the mixture was stirred for 16 h. Saturated aqueous NH_4Cl (5 ml) was added and the mixture was extracted with ether (3×5 ml). The combined organic layers were washed with brine (3 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=2→1) provided **35** (38.8 mg, 99% from **32**). **35**: colorless plates (ether), mp 121–123°C; $[\alpha]_D^{21}=-11.2°$ (c 1.02, $CHCl_3$); IR (KBr), ν_{max} 3481, 2863, 1488, 1450, 1382, 1328, 1272, 1212, 1102, 1073, 1053, 1030, 1013, 989, 802, 752, 699, 547 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.53–7.44 (4H, m), 7.39–7.30 (3H, m), 7.21 (2H, brdt, J=8.6, 2.0 Hz), 5.88 (1H, dddd, J=11.2, 8.3, 3.3, 2.2 Hz), 5.78 (1H, brdt, J=11.2, 3.2 Hz), 5.55 (1H, s), 4.54 (2H, s), 4.31 (1H, dd, J=10.3, 5.0 Hz), 4.26–4.20 (1H, m), 3.90–3.85 (1H, m), 3.70 (1H, t, J=10.3 Hz), 3.61 (1H, dd, J=10.2, 7.2 Hz), 3.60 (1H, t, J=9.2 Hz), 3.55 (1H, dd, J=10.2, 4.6 Hz), 3.47 (1H, brddd, J=10.3, 9.2, 5.0 Hz), 3.42–3.30 (2H, m), 2.85 (1H, brs), 2.67–2.58 (1H, m), 2.45–2.34 (1H, m); LR-EIMS, m/z 504 (35.3%, $[M+2]^+$), 502 (36.3%, $[M]^+$), 303 (bp); HR-EIMS, calcd for $C_{25}H_{27}BrO_6$ $[M]^+$: 502.0990, found: 502.0991.

4.1.26. (1*R*,2*R*,3*S*,5*R*,8*R*,10*S*,12*Z*,14*R*)-2-Benzyloxy-14-(4-bromobenzyloxymethyl)-5-phenyl-4,6,9,15-tetraoxatricyclo[8.5.0.0^{3,8}]pentadec-12-ene (36). To a mixture of **35** (34.7 mg, 0.0689 mmol), benzyl bromide (16.5 μl, 0.139 mmol), and TBAI (12.6 mg, 0.0341 mmol) in THF (0.7 ml) was added NaH (9.1 mg, 60wt% in oil, 0.228 mmol) at 0°C. The mixture was warmed to 25°C and stirred for 5 h. Saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture was extracted with ether (3×5 ml). The combined organic layers were washed with brine (3 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=10→5) provided **36** (40.4 mg, 99%). **36**: white needles (hexane/CH_2Cl_2), mp 102–104°C; $[\alpha]_D^{19}=-25.1°$ (c 1.02, $CHCl_3$); IR (KBr), ν_{max} 2875, 1487, 1452, 1367, 1213, 1147, 1114, 1085, 1070, 1013, 999, 836, 801, 744, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.51–7.17 (14H, m), 5.89–5.78 (2H, m), 5.57 (1H, s), 4.89 (1H, d, J=11.7 Hz), 4.85 (1H, d, J=11.7 Hz), 4.53 (2H, s), 4.31 (1H, dd, J=10.3, 5.0 Hz), 4.29–4.25 (1H, m), 3.73 (1H, dd, J=9.2, 8.3 Hz), 3.68 (1H, t, J=10.3 Hz), 3.63 (1H, t, J=9.2 Hz), 3.62 (1H, dd, J=9.9, 6.2 Hz), 3.53 (1H, brdd, J=9.0, 8.3 Hz), 3.53 (1H, dd, J=9.9, 5.0 Hz), 3.47–3.36 (2H, m), 2.70–2.60 (1H, m), 2.42–2.32 (1H, m); LR-EIMS, m/z 594 (6.5%, $[M+2]^+$), 592 (6.5%, $[M]^+$), 91 (bp); HR-EIMS, calcd for $C_{32}H_{33}BrO_6$ $[M]^+$: 592.1460, found: 592.1460.

4.1.27. (1*S*,3*Z*,5*R*,7*R*,8*S*,9*S*,10*R*)-8-Benzyloxy-5-(4-bromobenzyloxymethyl)-10-hydroxymethyl-6,11-dioxabicyclo[5.4.0]undec-3-en-9-ol (37). To **36** (40.4 mg, 0.0681 mmol) in THF (0.7 ml) was added 3 M aqueous HCl (0.7 ml) at 25°C and the mixture was added for 12 h. After the mixture was neutralized with 3 M aqueous NaOH (0.7 ml), saturated aqueous $NaHCO_3$ (5 ml) was added. The mixture was extracted with EtOAc (3×5 ml). The combined organic layers were washed with brine (3 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=1/3) provided **37** (34.1 mg, 99%). **37**: white

needles (hexane/CH_2Cl_2), mp 115–116°C; $[\alpha]_D^{20}$= −10.6° (*c* 1.03, $CHCl_3$); IR (KBr), ν_{max} 3431, 2862, 1486, 1454, 1402, 1384, 1361, 1098, 1072, 1053, 1011, 800, 737, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.39 (2H, brdt, *J*=8.4, 2.1 Hz), 7.35–7.25 (5H, m), 7.16 (2H, brdt, *J*=8.4, 2.1 Hz), 5.87 (1H, dddd, *J*=11.4, 7.9, 3.3, 2.2 Hz), 5.82–5.76 (1H, m), 5.09 (1H, d, *J*=11.6 Hz), 4.65 (1H, d, *J*=11.6 Hz), 4.49 (2H, s), 4.30–4.24 (1H, m), 3.85 (1H, ddd, *J*=11.7, 6.2, 3.5 Hz), 3.69 (1H, brddd, *J*=11.7, 6.2, 5.5 Hz), 3.60 (1H, dd, *J*=9.9, 6.8 Hz), 3.54–3.44 (4H, m), 3.37–3.26 (2H, m), 2.64 (1H, brddd, *J*=15.8, 7.9, 3.9 Hz), 2.45–2.34 (1H, m), 2.35 (1H, brd, *J*=1.3 Hz), 2.00 (1H, t, *J*=6.2 Hz); LR-EIMS, *m/z* 506 (1.4%, $[M+2]^+$), 504 (1.5%, $[M]^+$), 415 (17.6%, $[(M+2)-Bn]^+$), 413 (18.6%, $[M-Bn]^+$), 91 (bp); HR-EIMS, calcd for $C_{18}H_{22}BrO_6$ $[M-Bn]^+$: 413.0599, found: 413.0597.

4.1.28. (1*S*,3*Z*,5*R*,7*R*,8*S*,9*S*,10*R*)-8-Benzyloxy-5-(4-bromobenzyloxymethyl)-10-(*tert*-butyldimethylsilyloxymethyl)-6,11-dioxabicyclo[5.4.0]undec-3-en-9-ol (38). To a mixture of **37** (27.3 mg, 0.0540 mmol), Et_3N (22.5 μl, 0.161 mmol), and DMAP (1.4 mg, 0.0115 mmol) in CH_2Cl_2 (0.6 ml) was added TBSCl (24.4 mg, 0.162 mmol) at 25°C and the mixture was stirred for 9.5 h. Saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture was extracted with CH_2Cl_2 (3×5 ml). The combined organic layers were washed with brine (3 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=10→5) provided **38** (33.4 mg, ~100%). **38**: a colorless oil; $[\alpha]_D^{19}$=−0.9° (*c* 1.02, $CHCl_3$); IR (film), ν_{max} 3482, 2951, 2927, 2882, 2856, 1487, 1471, 1462, 1360, 1252, 1143, 1099, 1071, 1012, 836, 779, 734, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.39 (2H, brdt, *J*=8.4, 2.1 Hz), 7.31–7.26 (5H, m), 7.16 (2H, brdt, *J*=8.4, 2.1 Hz), 5.91–5.77 (2H, m), 5.04 (1H, d, *J*=11.4 Hz), 4.72 (1H, d, *J*=11.4 Hz), 4.49 (2H, s), 4.28–4.23 (1H, m), 3.81 (2H, d, *J*=4.6 Hz), 3.62–3.55 (2H, m), 3.53–3.44 (3H, m), 3.29 (1H, dt, *J*=9.4, 4.6 Hz), 3.29–3.21 (1H, m), 2.80 (1H, d, *J*=1.7 Hz), 2.62 (1H, brddd, *J*=16.0, 7.9, 3.9 Hz), 2.43–2.32 (1H, m), 0.89 (9H, s), 0.07 (6H, s); LR-EIMS, *m/z* 620 (0.7%, $[M+2]^+$), 618 (0.5%, $[M]^+$), 563 (2.6%, $[(M+2)-t\text{-}Bu]^+$), 561 (2.3%, $[M-t\text{-}Bu]^+$), 91 (bp); HR-EIMS, calcd for $C_{27}H_{34}BrO_6Si$ $[M-t\text{-}Bu]^+$: 561.1307, found: 561.1310.

4.1.29. (1*S*,3*Z*,5*R*,7*R*,8*S*,9*S*,10*R*)-8-Benzyloxy-9-(4-bromobenzyloxy)-5-(4-bromobenzyloxymethyl)-10-(*tert*-butyldimethylsilyloxymethyl)-6,11-dioxabicyclo[5.4.0]-undec-3-ene (39). To a mixture of **38** (36.3 mg, 0.0586 mmol), *p*-bromobenzyl bromide (29.5 mg, 0.118 mmol), and TBAI (10.9 mg, 0.0295 mmol) in THF (0.6 ml) was added NaH (8.1 mg, 60wt% in oil, 0.203 mmol) at 0°C. The mixture was warmed to 24°C and stirred for 12 h. Saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture was extracted with ether (3×5 ml). The combined organic layers were washed with brine (3 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=20→10) provided a mixture (46.7 mg) of **39** and unidentified by-products. The mixture was used in the next reaction without further purification. Pure **39**, used for spectrometric analyses, was obtained alternatively by preparative HPLC. **39**: a colorless oil; $[\alpha]_D^{19}$=+0.2° (*c* 1.00, $CHCl_3$); IR (film), ν_{max} 2951, 2926, 2856, 1487, 1471, 1461, 1360, 1251, 1154, 1102, 1070, 1012, 836, 803, 778, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.43–7.36 (4H, m), 7.28–7.24 (5H, m), 7.17–7.10 (4H, m), 5.90–5.77 (2H, m), 5.03 (1H, d, *J*=10.9 Hz), 4.78 (1H, d, *J*=11.3 Hz), 4.69 (1H, d, *J*=10.9 Hz), 4.58 (1H, d, *J*=11.3 Hz), 4.49 (2H, s), 4.29–4.24 (1H, m), 3.82 (1H, dd, *J*=11.7, 2.2 Hz), 3.78 (1H, dd, *J*=11.7, 3.3 Hz), 3.63 (1H, t, *J*=8.8 Hz), 3.59 (1H, dd, *J*=9.9, 6.6 Hz), 3.56 (1H, brdd, *J*=9.9, 8.8 Hz), 3.50 (1H, dd, *J*=9.9, 4.8 Hz), 3.46 (1H, t, *J*=8.8 Hz), 3.26–3.18 (2H, m), 2.63 (1H, brddd, *J*=16.0, 8.3, 3.9 Hz), 2.42–2.31 (1H, m), 0.88 (9H, s), 0.042 (3H, s), 0.038 (3H, s); LR-EIMS, *m/z* 733 (2.3%, $[(M+4)-t\text{-}Bu]^+$), 731 (3.9%, $[(M+2)-t\text{-}Bu]^+$), 729 (2.0%, $[M-t\text{-}Bu]^+$), 699 (25.5%, $[(M+4)-Bn]^+$), 697 (42.9%, $[(M+2)-Bn]^+$), 695 (20.3%, $[M-Bn]^+$), 91 (bp); HR-EIMS, calcd for $C_{31}H_{41}Br_2O_6Si$ $[M-Bn]^+$: 695.1038, found: 695.1038.

4.1.30. {(1*S*,3*Z*,5*R*,7*R*,8*S*,9*S*,10*R*)-8-Benzyloxy-9-(4-bromobenzyloxy)-5-(4-bromobenzyloxymethyl)-6,11-dioxabicyclo[5.4.0]undec-3-en-10-yl}methanol (40). To the above mixture including **39** (46.7 mg) in THF (0.6 ml) was added TBAF (88.0 μl, 1.0 M in THF, 0.088 mmol) at 25°C and the mixture was stirred for 15 h. Saturated aqueous NH_4Cl (5 ml) was added and the mixture was extracted with ether (3×5 ml). The combined organic layers were washed with brine (3 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=3→1) provided **40** (39.0 mg, 99% from **38**). **40**: white needles (hexane/ether), mp 127–128°C; $[\alpha]_D^{20}$=−3.9° (*c* 1.00, $CHCl_3$); IR (KBr), ν_{max} 3422, 2863, 1488, 1453, 1399, 1384, 1362, 1098, 1070, 1012, 803, 749, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.42 (2H, brdt, *J*=8.4, 2.1 Hz), 7.38 (2H, brdt, *J*=8.4, 2.1 Hz), 7.28–7.22 (5H, m), 7.14 (2H, brdt, *J*=8.4, 2.1 Hz), 7.10 (2H, brdt, *J*=8.4, 2.1 Hz), 5.90–5.78 (2H, m), 5.06 (1H, d, *J*=11.0 Hz), 4.79 (1H, d, *J*=11.3 Hz), 4.69 (1H, d, *J*=11.0 Hz), 4.55 (1H, d, *J*=11.3 Hz), 4.48 (2H, s), 4.44–4.24 (1H, m), 3.83 (1H, ddd, *J*=11.7, 5.9, 2.8 Hz), 3.67 (1H, t, *J*=8.8 Hz), 3.67–3.59 (1H, m), 3.58 (1H, dd, *J*=9.9, 6.6 Hz), 3.50 (1H, t, *J*=8.8 Hz), 3.50 (1H, dd, *J*=9.9, 4.4 Hz), 3.47 (1H, brdd, *J*=9.7, 8.8 Hz), 3.34 (1H, ddd, *J*=9.7, 4.8, 2.8 Hz), 3.28 (1H, brddd, *J*=10.3, 8.8, 3.9 Hz), 2.68–2.59 (1H, m), 2.43–2.32 (1H, m), 1.84 (1H, brdd, *J*=7.0, 5.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$, $^{13}CDCl_3$ as 77.0 ppm), δ 138.8, 137.2, 136.9, 133.0, 131.5, 129.6, 129.4, 128.3, 128.0, 127.8, 127.5, 121.6, 121.5, 88.1, 85.1, 78.4, 77.5, 77.1, 75.5, 75.2, 74.1, 72.7, 72.6, 62.3, 34.2; LR-FDMS, *m/z* 676 (36.2%, $[M+4]^+$), 674 (58.3%, $[M+2]^+$), 672 (30.0%, $[M]^+$), 585 (56.4%, $[(M+4)-Bn]^+$), 583 (bp, $[(M+2)-Bn]^+$), 581 (53.2%, $[M-Bn]^+$); HR-FDMS, calcd for $C_{32}H_{34}Br_2O_6$ $[M]^+$: 672.0722, found: 672.0724.

4.1.31. {(1*S*,3*Z*,5*R*,7*R*,8*S*,9*S*,10*R*)-8-Benzyloxy-9-(4-bromobenzyloxy)-5-(4-bromobenzyloxymethyl)-6,11-dioxabicyclo[5.4.0]undec-3-en-10-yl}methyl trifluoromethanesulfonate (41). To a mixture of **40** (32.9 mg, 0.0488 mmol) and 2,6-lutidine (23.0 μl, 0.197 mmol) in CH_2Cl_2 (0.5 ml) was added trifluoromethanesulfonic anhydride (16.5 μl,

0.0981 mmol) at −78°C and the mixture was stirred for 30 min. Saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture was extracted with CH_2Cl_2 (3×5 ml). The combined organic layers were dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=5) provided **41** (37.3 mg, 95%). **41** was unstable and immediately used for the next reaction. **41**: a colorless oil; ^{1}H NMR (300 MHz, C_6D_6, C_6HD_5 as 7.15 ppm), δ 7.30–7.08 (9H, m), 6.83–6.76 (4H, m), 5.58–5.46 (2H, m), 5.20 (1H, d, J=11.2 Hz), 4.63 (1H, d, J=11.2 Hz), 4.63 (1H, d, J=11.7 Hz), 4.28 (1H, brdd, J=10.8, 2.0 Hz), 4.20 (1H, d, J=11.7 Hz), 4.14 (1H, dd, J=10.8, 4.8 Hz), 4.03 (2H, s), 4.03–4.00 (1H, m), 3.50 (1H, t, J=8.8 Hz), 3.37 (1H, dd, J=10.1, 7.5 Hz), 3.28 (1H, t, J=8.8 Hz), 3.23 (1H, dd, J=9.9, 8.8 Hz), 3.14 (1H, dd, J=10.1, 4.4 Hz), 3.00 (1H, ddd, J=9.9, 4.8, 2.0 Hz), 2.95 (1H, brddd, J=9.9, 8.8, 3.9 Hz), 2.45–2.35 (1H, m), 2.22–2.12 (1H, m).

4.1.32. (1*S*,3*Z*,5*R*,7*R*,8*S*,9*S*,10*R*)-8-Benzyloxy-9-(4-bromobenzyloxy)-5-(4-bromobenzyloxymethyl)-10-[2-(methylsulfinyl)-2-(methylthio)ethyl]-6,11-dioxabicyclo[5.4.0]undec-3-ene (3). To methyl methylsulfinylmethyl sulfide (15.0 μl, 0.144 mmol) in THF (0.2 ml) was added BuLi (0.09 ml, 1.59 M in hexane, 0.143 mmol) at −20°C and the mixture was stirred for 15 min. To the resultant mixture was added **41** (37.3 mg, 0.0463 mmol) in THF (0.5 ml) dropwise at −20°C. Then, the mixture was stirred for 1 h. Saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture was extracted with EtOAc (3×5 ml). The combined organic layers were washed with brine (3 ml) and dried over anhydrous $MgSO_4$. The crude reaction mixture was filtered and concentrated under reduced pressure. Purification of the resultant residue by flash chromatography (silica gel, hexane/EtOAc=1→1/3 containing 1% v/v Et_3N) provided **3** (33.7 mg, 93%) as an inseparable mixture of diastereomers. **3**: a white solid; $[\alpha]_D^{25}$=+15.2° (c 1.01, $CHCl_3$) (This value was obtained from the mixture of diastereomers produced under the above conditions.); IR (KBr), ν_{max} 2893, 2862, 1487, 1361, 1092, 1069, 1051, 1011, 841, 803, 737, 699 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6, C_6HD_5 as 7.15 ppm), δ 7.35–7.07 (9H, m), 7.03 (2/10H, brd, J=8.4 Hz), 6.97 (2/10H, brd, J=8.4 Hz), 6.88–6.80 (36/10H, m), 5.67–5.53 (2H, m), 5.26–5.20 (1H, m), 4.81 (1/10H, d, J=11.2 Hz), 4.79 (1/10H, d, J=11.2 Hz), 4.74–4.68 (18/10H, m), 4.52 (1/10H, d, J=11.2 Hz), 4.43 (1/10H, d, J=11.2 Hz), 4.30 (4/10H, d, J=11.6 Hz), 4.19 (4/10H, d, J=11.6 Hz), 4.17–4.10 (1H, m), 4.07 (2H, s), 3.79–3.59 (3H, m), 3.51–3.40 (2H, m), 3.24–3.14 (3H, m), 2.56–2.03 (4H, m), 2.18 (12/10H, s), 2.15 (3/10H, s), 2.07 (3/10H, s), 2.05 (12/10H, s), 1.89 (12/10H, s), 1.81 (3/10H, s), 1.79 (3/10H, s), 1.74 (12/10H, s); LR-FDMS, m/z 783 (4.6%, $[(M+4)+H]^+$), 781 (7.1%, $[(M+2)+H]^+$), 779 (4.5%, $[M+H]^+$), 719 (57.5%, $[(M+4)-MeSO]^+$), 717 (bp, $[(M+2)-MeSO]^+$), 715 (49.6%, $[M-MeSO]^+$); HR-FDMS, calcd for $C_{35}H_{41}Br_2O_6S_2$ $[M+H]^+$: 779.0711, found: 779.0681.

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