Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron 62 (2006) 7408–7435
Tetrahedron

Convergent synthesis of the common FGHI-ring part of ciguatoxins

Ayumi Takizawa, Kenshu Fujiwara,* Eriko Doi, Akio Murai, Hidetoshi Kawai and Takanori Suzuki

Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo 060-0810, Japan

Received 15 April 2006; revised 28 April 2006; accepted 10 May 2006
Available online 5 June 2006

Abstract—Convergent synthesis of the common FGHI-ring part (**54**) of ciguatoxins was achieved via the following key steps: (i) the Nozaki–Hiyama–Kishi reaction connecting the F-ring part (**6**) with the I-ring part (**7**); (ii) regio- and stereoselective epoxidation; (iii) the 6-*exo*-epoxide opening reaction forming simultaneously the H-ring and the quaternary asymmetric center at C30; (iv) inversion of the C29 stereocenter by a two-step oxidation/reduction process, where the successful inversion depended on proper management of the steric environment of the substrate; and (v) final reductive cyclization constructing the G-ring.

1. Introduction

Ciguatoxins (CTXs, Fig. 1)[1] are the principal toxins responsible for ciguatera,[2] a form of sea food poisoning. More than 25,000 people suffer annually from this poisoning in the Pacific and Indian Oceans as well as the Caribbean Sea.[2b] In 1977, Yasumoto and co-workers identified an epiphytic dinoflagellate, *Gambierdiscus toxicus*, as a causative organism.[3] The dinoflagellate-produced toxins are first transferred to herbivorous fish and accumulated most in carnivorous fish through the marine food chain, thus causing human intoxication. The symptoms of ciguatera are characterized by gastrointestinal and neurological disturbances. Since these disturbances often last for months or years, ciguatera has resulted in serious social problems. Thus, CTXs are now studied by many researchers from a variety of viewpoints in order to prevent and treat ciguatera intoxication.[4]

CTXs have been isolated from both poisonous fish and dinoflagellate *G. toxicus* with great effort over several years and despite the extremely low content of CTXs in these organisms. Ciguatoxin (CTX1B, **1**) was first isolated from the moray eel, *Gymnothorax javanicus*, by Scheuer and co-workers in 1967, and characterized to be a polyether compound in 1980.[5] Determination of the relative structure of **1** was achieved by Yasumoto and co-workers in 1989 with only 0.35 mg of **1** isolated from 4000 kg of *G. javanicus*. The absolute structure of **1** was determined by collaboration of Yasumoto et al. in 1997.[6] CTX3C (**2**) was isolated from cultured *G. toxicus* by Yasumoto and co-workers in 1993.[7]

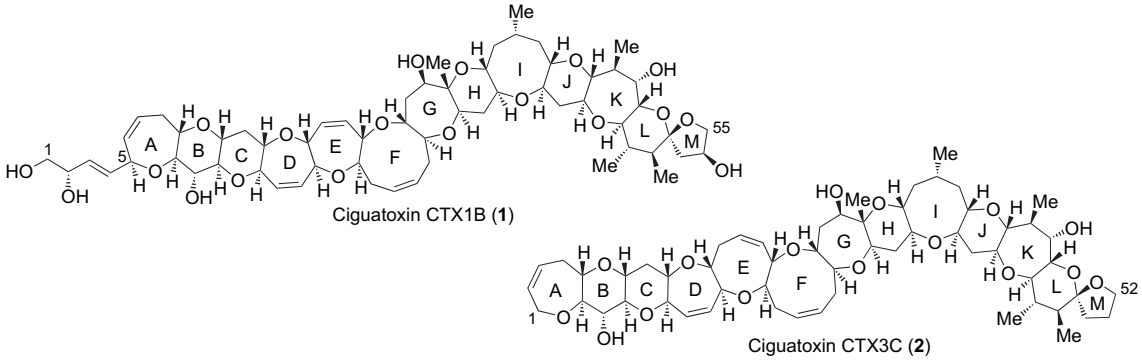


Figure 1. Representative ciguatoxin congeners.

Keywords: Ciguatoxin; *trans*-Fused tetracyclic ether; Reductive etherification; The Nozaki–Hiyama–Kishi reaction; 6-*exo* Hydroxy epoxide opening.
* Corresponding author. Tel.: +81 11 706 2701; fax: +81 11 706 4924; e-mail: fjwkn@sci.hokudai.ac.jp

0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.05.014

They elucidated the structure of **2** with only 0.70 mg of **2** isolated from 1100 l of the culture. So far, more than 20 CTXs have been isolated and structurally identified.

Pharmacological studies have disclosed that the potent neurotoxicity of CTXs arises from the activation of voltage-sensitive sodium channels (VSSCs) in neuron cells by the strong binding to site-5 on the channel, and CTXs share the binding site on VSSC with brevetoxins.[8] However, further progress in these studies has been prevented by the insufficient amounts of CTXs from natural sources. Therefore, synthetic supply of CTXs on a practical scale is desired for the advancement of the above studies as well as the development of therapies for ciguatera and methods for screening of ciguateric fish.

Structural features of CTXs, such as the stereochemical complexity, huge molecular size, and ladder-shaped polyether skeleton possessing five- to nine-membered cyclic ethers, provide remarkable synthetic challenges. Therefore, CTXs have been studied extensively by numerous chemists in the synthetic viewpoint.[9,10] To date, many convergent synthetic strategies[11,12] toward the total synthesis of CTXs have been reported.[9,10]

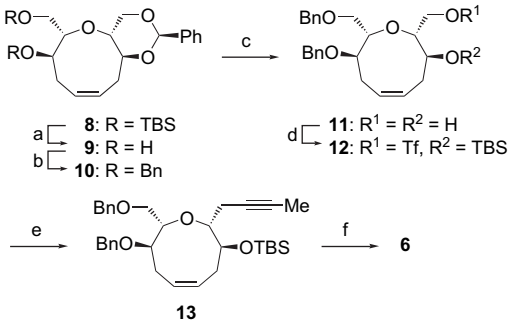
In the course of our program toward the total synthesis of CTXs,[13] we have established a method for the convergent construction of a *trans*-fused X/6/7/X cyclic ether system based on the coupling reaction of an acyl anion equivalent with an aldehyde followed by reductive cyclization reactions.[13g,i,k,14] So far, we reported the synthesis of the ABCDE- and IJKLM-ring parts of **2** by the method[13m,q] as well as by a new procedure for the addition of the F-ring to the E-ring part of **1**, which would also be available for the CTX3C (**2**) synthesis.[13n,o] Accordingly, the remaining issue is development of a synthetic method for the middle (GH-ring) part of **2** from the left (ABCDEF-ring) and the right (IJKLM-ring) segments. Here, a convergent synthesis of the common FGHI-ring part of CTXs from F- and I-ring segments is described.[13r]

2. Synthetic plan for the FGHI-ring part

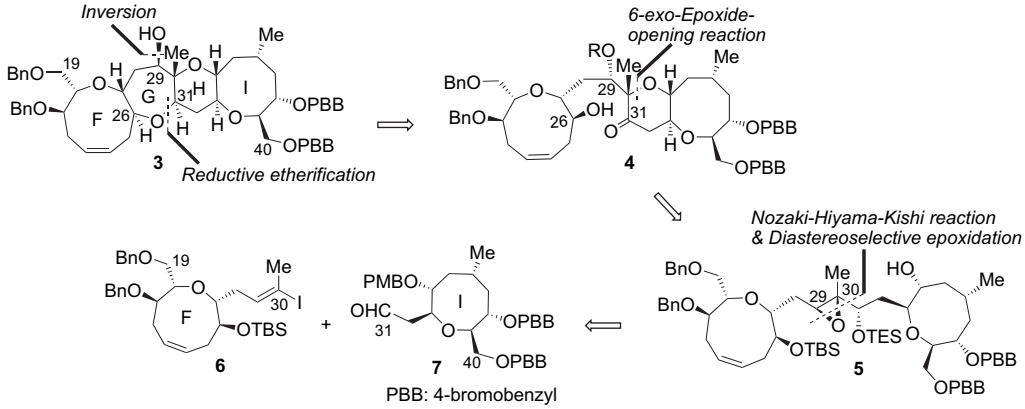
Our synthetic plan for the FGHI-ring part **3** from the F- and I-ring segments (**6** and **7**, respectively) is outlined in Scheme 1. A main issue of the synthesis of **3** was stereocontrolled construction of three contiguous asymmetric centers from C29 to C31 including a quaternary asymmetric center (C30) at the junction between the G- and H-rings.[15] We intended to solve the issue based on the following scheme: (i) The G-ring of **3** was envisioned to be constructed from hydroxy ketone **4** by reductive etherification, which would generate the O26–C31 bond and the C31 stereocenter,[16,17] and inversion of the C29 stereochemistry; (ii) In order to construct the H-ring and the quaternary center at C30 concurrently, the 6-*exo*-epoxide-opening reaction of **5**, whose product was intended to be oxidized to **4**, was planned; (iii) The epoxide **5** would be synthesized from *E*-iodoolefin **6** and aldehyde **7** via the Nozaki–Hiyama–Kishi (NHK) reaction[18] followed by regio- and diastereoselective epoxidation; (iv) Both **6** and **7** would be prepared from our previously reported medium-ring ethers.[10j,p] Although the use of the *cis*-epoxide (C29-*epi*-**5**) corresponding to **5** might be straightforward and excludes the C29-inversion step, the *cis*-epoxide could not be prepared so far because of the difficulty in the synthesis of a *Z*-iodoolefin corresponding to *E*-iodoolefin **6**.[19] Therefore, we decided to adopt the above synthetic plan that employed the NHK reaction with an *E*-iodoolefin at the first stage and C29 inversion at the final stage.

3. Preparation of the F- and I-ring segments

The F-ring segment **6** was synthesized from known **8**[13j] (Scheme 2). Removal of the TBS groups of **8** (98%) followed



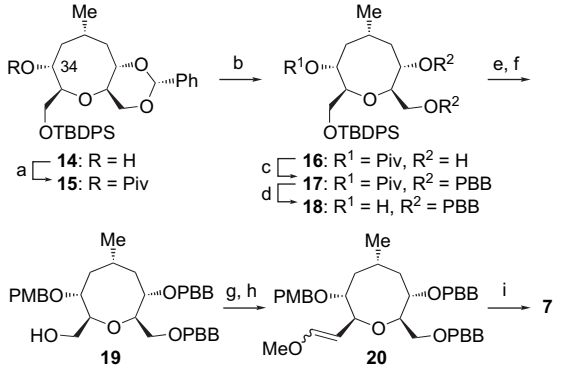
Scheme 2. Reagents and conditions: (a) TBAF, THF, 25 °C, 1 h, 98%; (b) BnBr, NaH, TBAI, THF, 25 °C, 23 h, 98%; (c) THF–3 M HCl (1:1), 21 h, 98%; (d) Tf_2O, 2,6-lutidine, CH_2Cl_2, −78 °C, 15 min, then TBSOTf, 0 °C, 1 h, 95%; (e) propyne, BuLi, THF, −78 °C, 10 min, then **12**, −78→24 °C, 3 h, 99%; (f) Cp_2ZrCl_2, DIBAL, THF, 55 °C, 30 min, then I_2, 0 °C, 15 min, 86%.



Scheme 1. Synthetic plan for the FGHI-ring part (**3**).

by protection with BnBr (98%) provided **10**, which was hydrolyzed to give **11** (98%). The diol **11** was converted to triflate **12** by a one-pot selective triflate formation/TBS-protection process (95%).[20] The subsequent reaction with 1-propynyllithium afforded **13** (99%),[21] which was treated first with a zirconium reagent, prepared from Cp_2ZrCl_2 and DIBAL,[22] and then with I_2 to produce **6** regioselectively (86%).

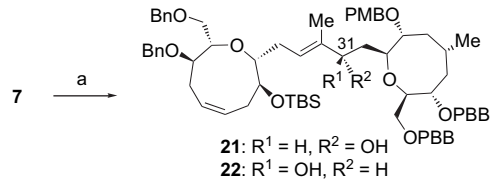
Preparation of the I-ring segment **7** from known **14**[13j,p] is illustrated in Scheme 3. Although direct PMB-protection of the hydroxy group at C34 of **14** was possible, the resulting compound resisted the removal of the benzylidene acetal without detachment of the PMB group. Therefore, the alcohol **14** was first transformed into pivalate **15** (100%), which was converted to PMB ether **19** (overall 83%) by a five-step process [(i) removal of the benzylidene acetal with $Zn(OTf)_2$ and ethanedithiol,[23] (ii) protection of the resulting diol with *p*-bromobenzyl (PBB) bromide, (iii) detachment of the Piv group, (iv) PMB-protection of the resulting alcohol, (v) removal of the TBDPS group]. Oxidation of **19** with Dess–Martin periodinane (DMPI)[24] followed by Wittig reaction afforded **20** (79%), which was hydrolyzed in the presence of $Hg(OAc)_2$ to produce **7** in good yield (99%).[25]



Scheme 3. Reagents and conditions: (a) PivCl, pyridine, 26 °C, 14 h, 100%; (b) $Zn(OTf)_2$, $HS(CH_2)_2SH$, $NaHCO_3$, CH_2Cl_2, 0 °C, 4 h then 25 °C, 1 h, 100%; (c) PBBBr, NaH, TBAI, THF, 25 °C, 14 h, 100%; (d) DIBAL, CH_2Cl_2, −78 °C, 1.5 h, 88%; (e) PMBBr, NaH, TBAI, THF, 26 °C, 21 h; (f) TBAF, THF, 0 °C, 1.5 h, 94% from **18**; (g) DMPI, CH_2Cl_2, 0→23 °C, 50 min; (h) $Ph_3P^+CH_2OMeCl^-$, NHMDS, 0 °C, 30 min, then aldehyde, −78→25 °C, 17 h, 79%; (i) $Hg(OAc)_2$, THF–H_2O (10:1), 23 °C, 1 h, then TBAI, 1.5 h, 99%.

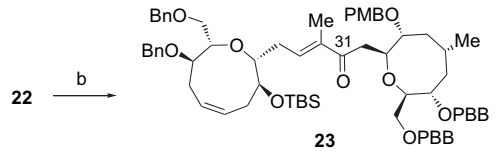
4. Construction of the H-ring

Connection of **6** and **7** is depicted in Scheme 4. According to the Nozaki–Hiyama–Kishi procedure,[18] the segments **6** and **7** were treated with $CrCl_2$ in the presence of $NiCl_2$ (0.5 wt % of $CrCl_2$) in DMSO, and the reaction smoothly proceeded to give **21** (45% from **7**) and its C31-epimer **22** (40% from **7**) in good yield.[26]



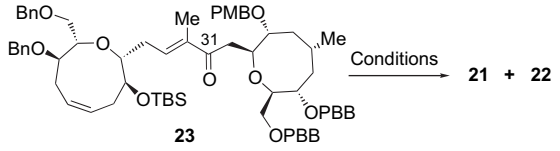
Scheme 4. Reagents and conditions: (a) **6**, $CrCl_2$, $NiCl_2$, DMSO, 25 °C, 25 h, **21**: 45% from **7**, **22**: 40% from **7**.

Since the diastereoselective epoxidation in the next step required *S* configuration at C31 of **21**, inversion of the *R* configuration at C31 of **22** was then examined. Although direct inversion by an S_N2 reaction, such as the Mitsunobu reaction, was unsuccessful, a stepwise oxidation/selective reduction process was found to be effective for the inversion after several examinations (vide infra). Initial oxidation of **22** with DMPI[24] readily afforded α,β-unsaturated ketone **23** in quantitative yield (Scheme 5). Next, stereoselective reduction of **23** was investigated under several conditions (Table 1). Aluminum reducing agents (DIBAL, DIBAL/BuLi,[27] and Red-Al®) exhibited low stereoselectivities (entries 1–3). However, these results suggested that a bulkier reagent would provide better selectivity. Then, boron-reducing agents were examined. In order to avoid conjugate reduction, $NaBH_4$ was first used under the Luche conditions.[28] Although the Luche reduction of **23** at −40 to 0 °C gave low selectivity (**21**:**22**=2:1), the reduction at −78 °C showed enhanced selectivity (4:1) (entries 4 and 5). It was notable that the selectivity of $NaBH_4$ at −78 °C was higher than those of aluminum reductants in spite of the small size of $NaBH_4$. Therefore, bulky L-Selectride® was used instead of $NaBH_4$ under Luche's conditions at −78 °C. As a result, the selectivity increased to 6:1 (entry 6). On the other hand, the reduction with L-Selectride® in the absence of $CeCl_3$ displayed the highest selectivity (>13:1) without side products by conjugate reduction (entry 7). Contrary to the above suggestion, lithium trisiamylborohydride (LS-Selectride®),[29] a bulkier reagent than L-Selectride®, gave only moderate selectivity independently of the presence of $CeCl_3$ (entries 8 and 9).



Scheme 5. Reagents and conditions: (a) DMPI, $NaHCO_3$, CH_2Cl_2, 25 °C, 2.5 h, 100%.

Table 1. Reduction of **23** with several reducing agents

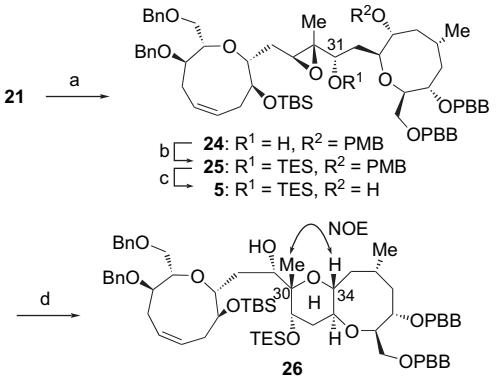


Entry	Conditions	**21**:**22**[a]	Yield (%)[b]
1	DIBAL, CH_2Cl_2, −78 °C, 0.5 h	1:1	~100
2	DIBAL, BuLi, THF, −78 °C, 1 h	2:1	~100
3	Red-Al®, THF, −78→−40 °C, 8 h	3:1	92
4	$CeCl_3\cdot 7H_2O$, $NaBH_4$, MeOH, −40→0 °C, 1.5 h	2:1	75
5	$CeCl_3\cdot 7H_2O$, $NaBH_4$, MeOH, −78 °C, 1.5 h	4:1	35
6	$CeCl_3$, L-Selectride®, THF, −78 °C, 2 h	6:1	~100
7	L-Selectride®, THF, −78 °C, 2 h	>13:1	~100
8	$CeCl_3$, LS-Selectride®, THF, −78→−40 °C, 26 h	6:1	67
9	LS-Selectride®, THF, −40 °C, 18 h	5:1	~100

[a] Determined by ^1H NMR analysis.
[b] Combined yield.

The low reactivity of LS-Selectride® toward **23**, suggested by the fact that LS-Selectride® needed higher temperature to consume the substrate (**23**) than L-Selectride®, was probably due to its excessive bulkiness and might be attributable to the moderate selectivity. Thus, the inversion of the stereochemistry at C31 was efficiently achieved by a two-step Dess–Martin oxidation/L-Selectride® reduction process.

Construction of the H-ring is illustrated in Scheme 6. The $VO(acac)_2$-catalyzed epoxidation of **21** with TBHP exclusively afforded **24** (91%).[30] Protection of the hydroxy group at C31 of **24** by the TES group followed by removal of the PMB group of **25** with DDQ produced **5** in good yield (overall 97%). The hydroxy epoxide **5** was smoothly cyclized with catalytic CSA into **26** (80%). The stereochemistry at C30 of **26** was confirmed by the presence of NOE between H34 and the protons of the methyl group at C30. Thus, the F–HI-ring part **26** was efficiently constructed from **6** and **7** in total seven steps, including the C31-inversion step, in 58% overall yield.

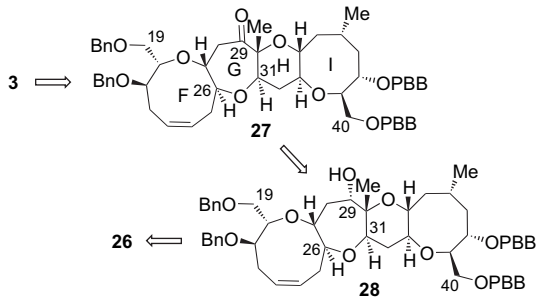


Scheme 6. Reagents and conditions: (a) $VO(acac)_2$, TBHP, toluene, 0 °C, 2 h, 91%; (b) TESOTf, 2,6-lutidine, CH_2Cl_2, 25 °C, 10 min, 100%; (c) DDQ, CH_2Cl_2–pH 7 buffer (10:1), 0 °C, 1 h, 97%; (d) CSA, CH_2Cl_2, 0 °C, 25 min, 80%.

5. Construction of the G-ring

5.1. First-generation approach to the construction of the FGHI-ring part

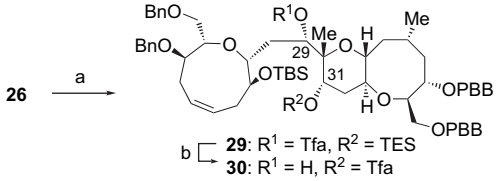
At first, a plan for the construction of the G-ring part including inversion of the stereochemistry at C29 at the final stage, shown in Scheme 7, was examined. The target compound **3** was envisioned to be constructed from ketone **27**, which would be prepared from **28** corresponding to the



Scheme 7. First-generation plan for the construction of the FGHI-ring part (**3**) from **26**.

29-*epi*-FGHI-ring part, by diastereoselective reduction. The reduction of **27** was expected to give **3** with high diastereoselectivity because the methyl group adjacent to the ketone would sterically hinder the approach of a reductant to the ketone from the same side of the methyl group. Accordingly, the construction of the 29-*epi*-FGHI-ring part **28** from **26** was first investigated.

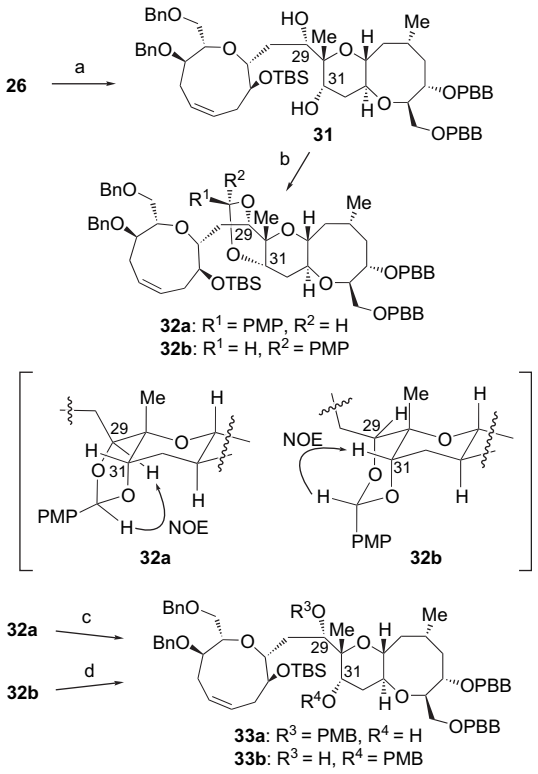
Protection of the hydroxy group at C29 of the F–HI-ring part **26** and the selective deprotection of the TES group at O31 were first examined in order to perform the oxidation at C31 in the later step (Scheme 8). Although the hydroxy group at C29 showed extremely low reactivity to AcCl, Ac_2O, or MsCl, which might be attributable to the steric hindrance of the TES and the C31-methyl groups as well as the F-ring part, the protection with highly reactive trifluoroacetic anhydride successfully afforded Tfa ester **29** in good yield. Then the selective removal of the TES group under mild conditions (THF–H_2O–TFA) was examined. However, the reaction proceeded very slowly with migration of the Tfa group associated with the detachment of the TES group to produce alcohol **30** having a Tfa group at O31 exclusively (63% after three cycles) without the desired O29-protected alcohol.



Scheme 8. Reagents and conditions: (a) $(CF_3CO)_2O$, pyridine, CH_2Cl_2, 0 °C, 1 h, 100%; (b) THF–H_2O–TFA (4:1:0.1), 2 d, 63% after three cycles.

Although selective deprotection of the O31-TES group could not be achieved, this result suggested that the two hydroxy groups at C29 and C31 were in close proximity. Therefore, we next designed a stepwise route for the protection of the C29-hydroxy group via a cyclic acetal, which would be facilely prepared from a 29,31-diol derivative (**31**) of **26** due to close proximity of these two hydroxy groups at C29 and C31 (Scheme 9).

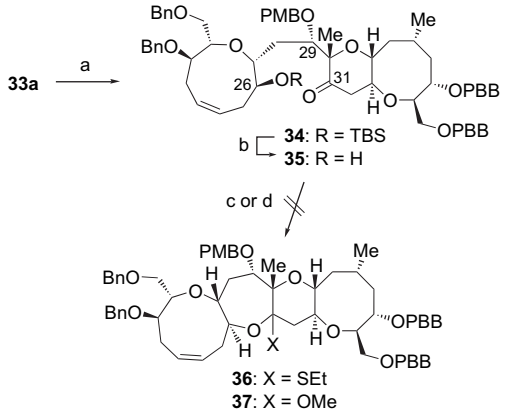
The diol **31** was readily obtained from **26** by selective deprotection of the TES group under mild acidic conditions (Scheme 9).[31] Treatment of **31** with *p*-anisaldehyde under acidic conditions gave a 1:1 mixture of **32a** and **32b** in excellent yield. After the acetals were separated by HPLC, the stereochemistry of **32a** and **32b** was determined from NOE experiments on the basis of *S* configuration at C31 as follows: for **32a**, the presence of NOE between the acetal proton and H29 as well as absence of NOEs between the acetal proton and H31 and between H29 and H31 established the *S* configuration at C29 and *R* at the acetal carbon; for **32b**, the presence of NOE between the acetal proton and H31 as well as the absence of NOEs between the acetal proton and H29 and between H31 and H29 confirmed the *S* configuration at C29 and *S* at the acetal carbon. The reductive cleavage reactions of acetals **32a** and **32b** with DIBAL gave different results. While the cleavage of **32a** showed relatively high selectivity (**33a**:**33b**=5:1), that of **32b** gave opposite but excellent selectivity (**33b**:**33a**>20:1). Although



Scheme 9. Reagents and conditions: (a) PPTS, MeOH–CH_2Cl_2 (4:1), 24 °C, 40 min, 100%; (b) *p*-anisaldehyde, PPTS, benzene, reflux, 3 h, 100% (**32a**:**32b**=1:1); (c) DIBAL, CH_2Cl_2, −30 °C, 1.5 h, 100% (**33a**:**33b**=5:1); (d) DIBAL, CH_2Cl_2, −20 °C, 2 h, 100% (**33b**:**33a**>20:1).

the reason for the regioselectivity of the reductive cleavage with DIBAL cannot be clarified at present, it is suggested that the stereochemistry of the acetal carbon would affect the regioselectivity of the acetal fission. Thus, O29-protected compound **33a** could be obtained though the overall yield from **26** was moderate.

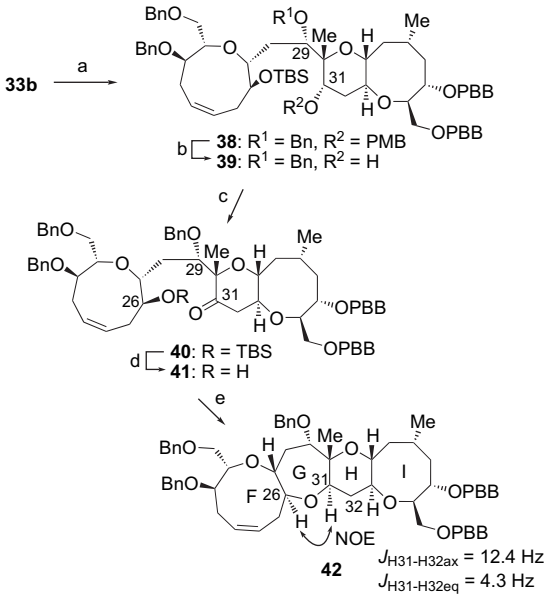
Next, the construction of the G-ring from **33a** via a two-step cyclization/reductive etherification reaction of ketone **35** was examined (Scheme 10). The cyclization precursor **35** was readily synthesized in two steps. Oxidation of **33a** with DMPI[24] followed by deprotection of the TBS group



Scheme 10. Reagents and conditions: (a) DMPI, CH_2Cl_2, 24 °C, 2 h, 70%; (b) HF·Py, THF, 24 °C, 2 d, 63%; (c) $Zn(OTf)_2$, EtSH, $NaHCO_3$, CH_2Cl_2, 25 °C, 1 h; (d) $HC(OMe)_3$, PTS, MeOH, 25 °C, 4 d.

with HF·Py afforded **35** in overall 44% yield. Then, cyclization of **35** into a cyclic *S*,*O*-acetal or a cyclic acetal was attempted. When the ketone **35** was treated with ethanethiol in the presence of $Zn(OTf)_2$,[32] the desired cyclic *S*,*O*-acetal was not produced, and decomposition of **35** due to detachment of the PMB group followed by a retro aldol reaction took place. On the other hand, treatment of **35** with trimethyl orthoformate and catalytic PTS[33] only resulted in recovery of the starting material **35**. These results showed that an acid-labile group, such as PMB, was inappropriate for the protection at O29 during the G-ring formation under acidic conditions. Therefore, an alternative protective group at O29 was then investigated.

Cyclization of the G-ring after protection of O29 as a benzyl ether was performed as shown in Scheme 11. The F–HI-ring part **33b** possessing a PMB group at O31 was used as a starting material. Protection of **33b** with BnBr, which required long reaction time (5 d) for the complete consumption of **33b**, gave **38** in 71% yield. The PMB group of **38** was smoothly deprotected with DDQ to provide **39** (85%). Oxidation of **39** with DMPI[24] followed by deprotection of the TBS group afforded hydroxy ketone **41** in overall 75% yield. The reductive cyclization of **41** with excess Et_3SiH in the presence of TMSOTf furnished the 29-*epi*-FGHI-ring part **42** stereoselectively.[16] The G-ring closure and the desired stereochemistry of C31 in **42** were proved by the presence of NOE between H26 and H31 as well as the large $J_{H31–H32ax}$ (12.4 Hz).



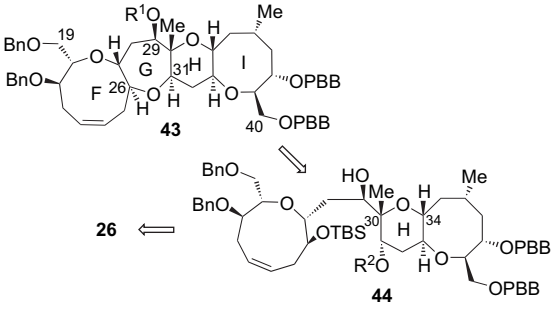
Scheme 11. Reagents and conditions: (a) BnBr, NaH, TBAI, THF, 22 °C, 5 d, 71%; (b) DDQ, CH_2Cl_2–pH 7 buffer (10:1), 0 °C, 35 min, 85%; (c) DMPI, $NaHCO_3$, CH_2Cl_2, 25 °C, 30 min; (d) THF–H_2O–TFA (10:10:1), 25 °C, 2 d, 75% from **39**; (e) TMSOTf, Et_3SiH–CH_2Cl_2 (1:10), 0 °C, 30 min, 70%.

Thus, the 29-*epi*-FGHI-ring part **42** was assembled from **26** in total eight steps in 15% overall yield. Although the synthesis of a key compound (**42**) for the synthesis of the FGHI-ring part **3** succeeded, it is still difficult to supply a reasonable amount of **42** due to some problems, for example, difficulty in the separation of acetals **32a** and **32b**, unusable **33a**, and low reactivity of **33b** in the protection step. On the

other hand, the synthesis of **3** from **42** would require four more steps involving detachment of all Bn groups of **42**, selective protection of the 1,3-diol part, oxidation of the hydroxy group at C29, and reduction of the resulting ketone to **3**. Accordingly, in order to overcome the above difficulties, an alternative synthesis of the FGHI-ring part from **26**, where the C29 configuration was inverted prior to the G-ring cyclization, was designed as described in the next section.

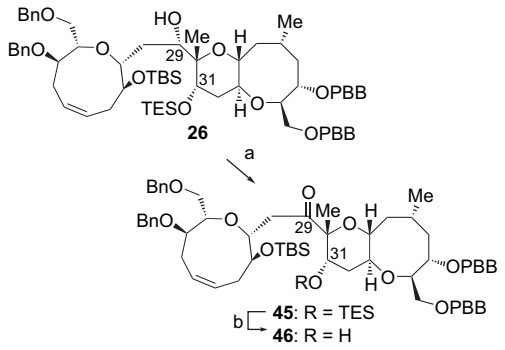
5.2. Second-generation approach to the construction of the FGHI-ring part

Next, a second plan for the synthesis of the FGHI-ring part including inversion of the stereochemistry at C29 in advance of the G-ring formation was investigated. In the plan, outlined in Scheme 12, O29-protected FGHI-ring part **43** was selected as a target compound and envisaged to be synthesized from **26** via the route including (i) inversion of the stereochemistry at C29 providing **44** and (ii) formation of the G ring from **44** through reductive etherification. Success of the plane relied on the C29-inversion step.



Scheme 12. Second-generation plan for the construction of the FGHI-ring part (**43**) from **26**.

At first, inversion of the stereochemistry at C29 of **26** was examined. Since the hydroxy group at C29 of **26** showed seriously low reactivity to electrophiles including several protective groups and MsCl due to steric hindrance around the hydroxy group, as mentioned in the previous section, the inversion at C29 of **26** by an S_N2 reaction was obviously difficult. Therefore, we took an oxidation/reduction process as a reasonable method for inversion of the stereochemistry at C29. Although the alcohol **26** resisted several oxidation reactions (DMPI,[24] SO_3·Py, TPAP, and PCC) owing to the above steric hindrance, Swern oxidation[34] of **26** at higher temperature (−45 °C) for prolonged reaction time (1 h) was able to give the ketone **45** along with recovered **26**. In order to consume the substrate **26**, when the mixture of **45** and **26** was subjected to the Swern oxidation again, the ketone **45** was obtained in 61% yield without recovery of **26** (Scheme 13). However, the reduction of the ketone **45** to C29-*epi*-**26** was not achieved. While treatment of **45** with $NaBH_4$ or $LiAlH_4$ gave only decomposed compounds due to the detachment of the TES and/or TBS groups, DIBAL reduction of **45** regenerated exclusively the original alcohol **26**. Accordingly, we next examined the reduction of **46**, obtained selectively by treatment of **45** with HF·Py (71%), under several conditions as shown in Table 2.

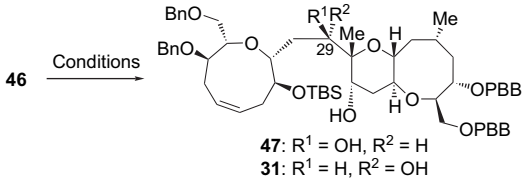


Scheme 13. Reagents and conditions: (a) $(COCl)_2$, DMSO, CH_2Cl_2, −45 °C, 1 h, then Et_3N, 0 °C, 20 min, 61% after two cycles; (b) HF·Py, THF–pyridine (2:1), 25 °C, 6 d, 71%.

Reduction with Red-Al® resulted in exclusive formation of **31** and low yield due to decomposition of the substrate and the product (entry 1, Table 2). Combined use of DIBAL and BuLi at −78 °C also selectively gave **31** along with recovered **46** (entry 2).[27] While reduction with $LiBH_4$ in THF afforded only **31** (entry 3), the reduction in MeOH produced **47** as a mixture with **31** (entry 4). The presence of MeOH in the reaction with $NaBH_4$ and KBH_4 also effectively provided **47** though the selectivity was low (entries 5–8). While use of $Me_4N(AcO)_3BH$[35] afforded only **31** (entry 9), reduction with $NaBH_4$ in the presence of Et_2BOMe[36] gave a similar result as in entries 5–6 (entry 10). Among these experiments, the reduction with $NaBH_4$ in MeOH at 0 °C gave the best result (**47**:**31**=2:1). Although L-Selectride® and Super-Hydride® were also examined, they were not reacted with the ketone in THF at −20 °C. The stereochemistry of the newly generated asymmetric center at C29 in **47** was elucidated at the later stage of the synthesis.

These results suggested that decrease of steric hindrance due to unprotection of C31–OH contributed to increasing reactivity of the ketone. The result from the reaction with $Me_4N(AcO)_3BH$ also suggested that coordination or complexation of the unprotected hydroxyl group at C31 with

Table 2. Reduction of **46** with several reducing agents

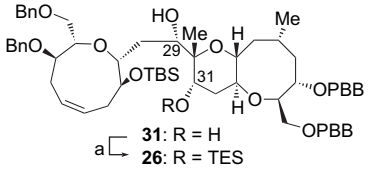


Entry	Conditions	**47**:**31**[a]	Yield (%)[b]
1	Red-Al®, THF, −20 °C, 3 h	0:1	50
2	DIBAL, BuLi, THF, −78 °C, 1.5 h	0:1	ND[c]
3	$LiBH_4$, THF, −20 °C, 40 min	0:1	~100
4	$LiBH_4$, MeOH, −20 °C, 22 h	0.3:1	~100
5	$NaBH_4$, MeOH, −20 °C, 1 h	0.8:1	~100
6	$NaBH_4$, MeOH, 0 °C, 15 min	2:1	~100
7	KBH_4, MeOH, 25 °C, 21 h	1.3:1	ND[c]
8	KBH_4, THF–MeOH (1:1), 0 °C, 22 h	1.5:1	~100
9	$Me_4N(AcO)_3BH$, AcOH, MeCN, 40 °C, 2 d	0:1	~100
10	Et_2BOMe, $NaBH_4$ THF–MeOH (5:1), 0 °C, 15 h	1:1	ND[c]

[a] Determined by ^1H NMR analysis.
[b] Combined yield.
[c] Not determined.

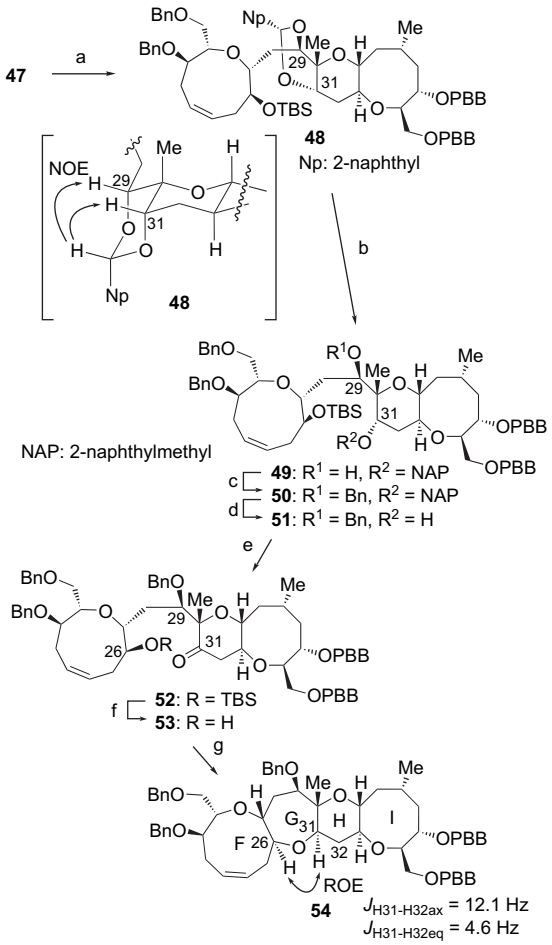
the reducing agent did not participate the production of **47**. Since the reason for the solvent effect of MeOH producing **47** was unclear, we could only speculate the role of MeOH as follows: (i) alteration of the conformation of **46** by hydrogen bonding between the ketone and MeOH, and/or (ii) prohibition of the coordination or complexation of the reducing agent with C31–OH, which would increase external attack of the reagent to the ketone producing **47**.

Thus, the inversion of the stereochemistry at C29 was achieved by the reduction of the β-hydroxy ketone **46** with $NaBH_4$ in MeOH at 0 °C though the selectivity of the reduction was unsatisfactory. Hence, transformation of the undesired diol **31** into the desired **47** was examined. As a result, the hydroxy group at C31 of **31** was simply and selectively protected with TESOTf to provide **26** in excellent yield (Scheme 14), thereby establishing the recycle route from **31** to **47** via **26**.



Scheme 14. Reagents and conditions: (a) TESOTf, 2,6-lutidine, CH_2Cl_2, −40 °C, 1 h, 95%.

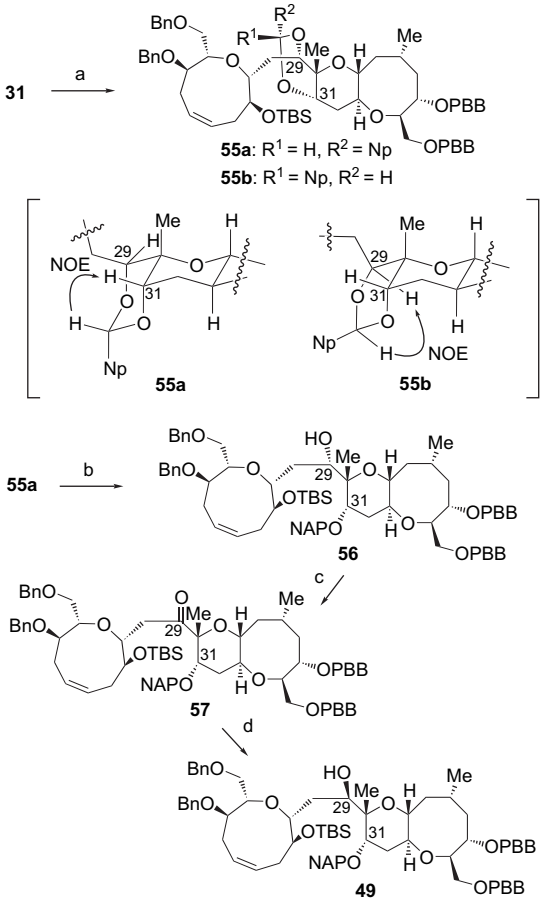
Next, construction of the G-ring from **47** was investigated (Scheme 15). At first, selective protection of the hydroxy group at C29 of the diol **47** via a cyclic acetal was performed. Treatment of **47** with 2-naphthaldehyde dimethyl acetal under acidic conditions gave 2-(2-naphthyl)-1,3-dioxane **48** as the sole product (89%). Stereochemistry of the acetal **48** including the C29-stereocenter, whose formation is described in the above section, was determined by NOE experiment on the basis of *S* configuration at C31. The presence of NOEs between the acetal proton and H31 and between the acetal proton and H29 confirmed the *R* configuration at C29 as well as the *S* configuration at the acetal carbon. Reduction of **48** with DIBAL exclusively afforded **49** possessing the NAP group[35] at O31 in good yield. Protection of the resultant hydroxy group at C29 of **49** with BnBr followed by detachment of the NAP group at O31 provided **51** (overall 91%). Thus, the selective Bn-protection at O29 of **47** was accomplished by the four-step process. Next, G-ring formation via reductive cyclization was executed. The alcohol **51** was oxidized with DMPI,[24] and the resulting **52** was desilylated to give hydroxy ketone **53** quantitatively. The reductive cyclization of **53** with excess Et_3SiH in the presence of TMSOTf at 0 °C produced the FGHI-ring part **54** stereoselectively (78%).[16] The stereochemistry of **54** was confirmed by the presence of ROE between H26 and H31 as well as the large $J_{H31-H32ax}$ (12.1 Hz). Thus, the FGHI-ring part **54** was successfully constructed from the F–HI-ring part **26** in 18% overall yield in 10 steps.



Scheme 15. Reagents and conditions: (a) $NpCH(OMe)_2$, PPTS, benzene, reflux, 1.5 h, 89%; (b) DIBAL, CH_2Cl_2, 10 °C, 3 h, 100%; (c) BnBr, NaH, TBAI, THF, 25 °C, 8 h, 100%; (d) DDQ, CH_2Cl_2–pH 7 buffer (10:1), 0 °C, 20 min, 91%; (e) DMPI, $NaHCO_3$, CH_2Cl_2, 25 °C, 25 min; (f) HF·Py, THF, 25 °C, 2 d, 100% from **51**; (g) TMSOTf, Et_3SiH–CH_2Cl_2 (1:10), 0 °C, 30 min, 78%.

5.2.1. Refinement of the second-generation approach. While construction of the FGHI-ring part was achieved, the yield of β-hydroxy ketone **46** from the F–HI-ring part **26** was low (overall 43%) and the reduction of **46** gave low stereoselectivity (~2:1). Therefore, an improved route for the conversion of the F–HI-ring part **26** to the alcohol **49** was investigated (Scheme 16).

The diol **31** prepared from **26** was treated with 2-naphthaldehyde dimethyl acetal in the presence of PPTS[31] to give a cyclic acetal **55a** as a major product (89%) along with the minor diastereomer **55b** (11%). The stereochemistry of **55a** and **55b** was determined by similar NOE experiments based on the *S* configuration at C31 as described in Section 5.1. The presence of NOE between the acetal proton and H31 as well as the absence of NOEs between the acetal proton and H31 and between H29 and H31 in **55a** confirmed its stereochemistry. The stereochemistry of **55b** was also verified by the presence of NOE between the acetal proton and H29 as well as the absence of NOEs between the acetal proton and H31 and between H29 and H31. The reductive cleavage of the major Np-acetal **55a** with DIBAL selectively provided **56** (93%),[37] where the regioselectivity agreed with the case of **32b** (Section 5.1). Oxidation of **56** with DMPI smoothly afforded the ketone **57** in good yield (90%). Prior to the reduction of **57**, preliminary examinations using ketone **58** (Fig. 2), derived from **33b**, were performed. When the ketone **58** was treated with $NaBH_4$ in MeOH, the starting ketone was only recovered due to



Scheme 16. Reagents and conditions: (a) $NpCH(OMe)_2$, PPTS, benzene, reflux, 2 h, **55a**: 89%, **55b**: 11%; (b) DIBAL, CH_2Cl_2, 0→10 °C, 2 h, 93%; (c) DMPI, $NaHCO_3$, CH_2Cl_2, 25 °C, 8 h, 90%; (d) $NaBH_4$, $CeCl_3\cdot 7H_2O$, THF–H_2O (3:1), 25 °C, 8 d, 96% (**49**:**56**>5:1).

insolubility of the ketone to MeOH. The use of a THF–H_2O (5:1) mixed solvent system in the reduction, where the ketone was soluble, produced alcohols **33b** and 29-*epi*-**33b** as a 1:2 mixture (preliminary data). Therefore, the reduction of **57** with $NaBH_4$ was performed in THF–H_2O (3:1). Although the mixed solvent system gave alcohols **49** and **56**, significant decomposition was observed. After several experiments, the reduction of **57** with $NaBH_4$ in the presence of $CeCl_3\cdot 7H_2O$[28] in THF–H_2O (3:1) was found to proceed cleanly. Although long reaction time (8 d) was required in order to consume the ketone **57**, the reduction showed high yield (96%) and selectivity (**49**:**56**>5:1). Thus, the improved route from the F–HI-ring part **26** to alcohol **49** (overall 59% yield in five steps; previous route: 26% yield in five steps) based on selective protection of O31 and stereoselective reduction of the C29-carbonyl group was developed.

Although it includes preliminary results, we also disclose herein an assessment of the first-generation approach by

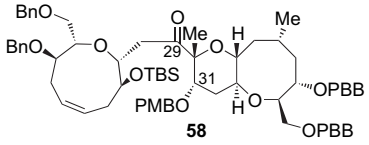
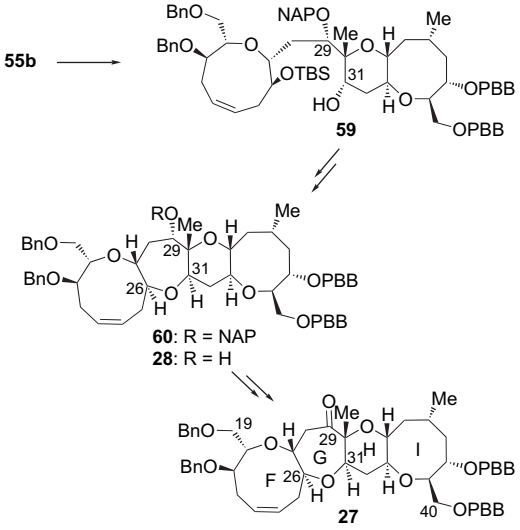


Figure 2.

an alternative method. In the first-generation approach, we expected that the reduction of ketone **27** would produce **3** stereoselectively, but we could not prove the idea (Section 5.1). Since the above-mentioned acetal **55b**, obtained as a minor product, could be converted to 29-*epi*-FGHI-ring part **28** via **59** (Scheme 17), we examined the initial idea with **28**. Reductive cleavage of **55b** with DIBAL exclusively gave **59** possessing an NAP-group at O29, which showed similar stereoselectivity as that of **32b**. Transformation of **59** to a tetracyclic **60**, O29-NAP ether of **28**, was readily performed by the same procedure as that of **33b** to **42**. Deprotection of the NAP-group of **60** with DDQ followed by Dess–Martin oxidation of the resulting hydroxy group afforded the ketone **27**. Contrary to our expectation, reduction of the ketone **27** with $NaBH_4$, $LiAlH_4$, or L-Selectride® provided **28** as a major product. Thus, we found that the first generation-approach was unsuccessful, and the failure suggested that the C29-stereocenter should be constructed at the early stage of the synthesis.



Scheme 17. Synthesis of ketone **27** from **55b**.

6. Conclusion

The aim of this study was the development of an efficient method for the construction of the GH-ring part of ciguatoxins in a convergent manner, which was envisaged to be performed at the final stage of the total synthesis of ciguatoxins. Accordingly, we extensively explored a synthetic route for the common FGHI-ring part (**54**) of ciguatoxins from the F- and I-ring segments. As a result, the convergent synthesis of **54** was achieved via the following key steps: (i) the Nozaki–Hiyama–Kishi reaction connecting the F-ring (**6**) with the I-ring (**7**); (ii) regio- and stereoselective epoxidation; (iii) the 6-*exo*-epoxide opening reaction forming simultaneously the H-ring and the quaternary asymmetric center at C30; (iv) inversion of the C29 stereocenter by a two-step oxidation/reduction process, where the successful inversion depended on proper management of the steric environment of the substrate; and (v) final reductive cyclization constructing the G-ring. Thus, the FGHI-ring part was efficiently synthesized through a novel route in 17 steps in 24% overall yield from **6** and **7**. Further studies toward the

total synthesis of the ciguatoxins are now under way in this laboratory.

7. Experimental

7.1. General methods

All reactions involving air- or moisture-sensitive reagents were carried out under an argon atmosphere in oven-dried glasswares capped with septa, and sensitive liquids and solutions were transferred by using syringe- or cannula-techniques, unless otherwise stated. All commercially available reagents were used without further purification with the following exceptions. Tetrahydrofuran (THF) was distilled from sodium-benzophenone ketyl under argon. Dichloromethane (DCM), dimethylsulfoxide (DMSO), and benzene (PhH) were distilled from CaH_2 prior to use. Normal reagent-grade solvents were used for flash chromatography and extraction. Special reagent-grade solvents were used for high-pressure liquid chromatography (HPLC). All reactions were monitored by thin-layer chromatography (TLC) with precoated silica gel (SiO_2) plates (Merck, silica gel 60 F_{254}). Plates were visualized by ultraviolet light and by treatment with acidic anisaldehyde or phosphomolybdic acid stain followed by heating. SiO_2 (YMC, SIL-60-400/230W) was utilized for flash chromatography. HPLC was run with a JASCO Intelligent HPLC Pump PU-986, equipped with a JASCO Intelligent UV–vis Detector UV-975 and a YMC-Pack SIL-06 (250×10 or 20 mm ID) HPLC column. Melting points were measured on Yanagimoto micro-melting apparatus without calibration. Optical rotations were recorded on a JASCO P-1020 digital polarimeter. Infrared (IR) spectra were measured on a JEOL JIR-WINSPEC100 infrared spectrometer. ^1H and ^{13}C NMR spectra were recorded on JEOL JNM-AL300 (^1H at 300 MHz, ^{13}C at 75 MHz), JNM-α-400 (^1H at 400 MHz, ^{13}C at 100 MHz), JNM-α-500 (^{13}C at 125 MHz) or JNM-ECA600 (^1H at 600 MHz, ^{13}C at 150 MHz) NMR spectrometers. ^1H NMR spectra are reported as chemical shifts (δ) in parts per million (ppm) based on tetramethylsilane (0.00 ppm), C_6HD_5 (7.15 ppm) or $CHD_2C(=O)CD_3$ (2.04 ppm). Splitting patterns were designated as 's, d, t, q, m, and br' indicating 'singlet, doublet, triplet, quartet, multiplet, and broad', respectively. Coupling constants (J) are reported in Hertz (Hz). ^{13}C NMR spectra are reported as chemical shifts (δ) in ppm based on $^{13}CDCl_3$ (77.0 ppm) or $^{13}C^{12}C_5D_6$ (128.0 ppm). High-resolution mass spectra (HRMS) were measured on a JEOL JMS-600H mass spectrometer under electron impact ionization (EI) condition and a JEOL JMS-SX102A mass spectrometer under field desorption ionization (FD) condition.

7.1.1. (1*R*,3*S*,4*R*,6*Z*,9*S*)-3-Hydroxymethyl-11-phenyl-2,10,12-trioxabicyclo[7.4.0]tridecan-6-en-4-ol (9). To a solution of **8** (348 mg, 0.649 mmol) in THF (6.0 ml) was added TBAF (1.95 ml, 1.0 M in THF, 1.95 mmol) at 25 °C and the mixture was stirred for 1 h. After that, saturated aqueous NH_4Cl (6 ml) was added and the aqueous layer was extracted with AcOEt (3×30 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=1 to AcOEt) to give **9** (196 mg, 98%). **9**: a colorless solid; mp 154.0–157.0 °C; $[\alpha]_D^{23}$ +29.3 (*c* 0.10, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$), δ (ppm) 7.49–7.31 (5H, m), 5.88–5.77 (2H, m), 5.43 (1H, s), 4.32 (1H, dd, *J*=3.9, 9.8 Hz), 3.87 (1H, dt, *J*=8.6, 4.4 Hz), 3.73–3.65 (3H, m), 3.63 (1H, dt, *J*=3.9, 9.8 Hz), 3.57 (1H, t, *J*=9.8 Hz), 3.38 (1H, dt, *J*=8.8, 4.4 Hz), 2.71–2.54 (4H, m); IR (KBr), ν (cm^{-1}) 3435, 3091, 2925, 2858, 1455, 1412, 1294, 1219, 1114, 1075, 1015, 963, 948, 916, 883, 759, 700; HR-EIMS, calcd for $C_{17}H_{22}O_5$ $[M]^+$: 306.1467, found: 306.1446.

7.1.2. (1*R*,3*S*,4*R*,6*Z*,9*S*)-4-Benzyloxy-3-benzyloxymethyl-11-phenyl-2,10,12-trioxabicyclo[7.4.0]tridecan-6-ene (10). To a solution of **9** (103 mg, 0.337 mmol) in THF (4.0 ml) were added NaH (33.7 mg, 0.841 mmol) and TBAI (12.4 mg, 0.0337 mmol) at 0 °C and the mixture was stirred for 10 min. Then, benzyl bromide (100 μl, 0.841 mmol) was added at 0 °C, the reaction mixture was warmed to 25 °C, and stirred for 4.5 h. After that, extra NaH (33.7 mg, 0.841 mmol) was added, and the stirring was continued for further 18 h. Saturated aqueous NH_4Cl (4 ml) was added and the aqueous layer was extracted with Et_2O (3×20 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=15 to 5) to give **10** (61.0 mg, 98%). **10**: a colorless solid; mp 110.0–113.0 °C; $[\alpha]_D^{25}$ −12.8 (*c* 0.64, $CHCl_3$); ^1H NMR (300 MHz, C_6D_6), δ (ppm) 7.40–7.00 (10H, m), 5.86–5.70 (2H, m), 5.32 (1H, s), 4.71 (1H, br d, *J*=6.4 Hz), 4.32 (1H, d, *J*=11.7 Hz), 4.31 (1H, d, *J*=12.3 Hz), 4.25 (1H, d, *J*=12.3 Hz), 4.00 (1H, d, *J*=11.7 Hz), 3.57–3.46 (4H, m), 3.48 (1H, br d, *J*=9.7 Hz), 3.31 (1H, dd, *J*=7.5, 9.7 Hz), 3.29–3.21 (1H, m), 2.85–2.78 (1H, m), 2.51–2.44 (2H, m), 2.31–2.25 (1H, m); IR (KBr), ν (cm^{-1}) 3030, 2924, 2856, 1496, 1453, 1393, 1366, 1294, 1213, 1153, 1103, 1027, 976, 747, 697; HR-EIMS, calcd for $C_{31}H_{34}O_5$ $[M]^+$: 486.2406, found: 486.2420.

7.1.3. (2*R*,3*S*,5*Z*,8*R*,9*S*)-8-Benzyloxy-9-benzyloxymethyl-2-hydroxymethyl-2,3,4,7,8,9-hexahydrooxonin-3-ol (11). To a solution of **10** (664 mg, 1.36 mmol) in THF (15.0 ml) was added 3 M HCl (15.0 ml) at 25 °C and the mixture was stirred for 21 h. Then, H_2O (15 ml) was added and the aqueous layer was extracted with AcOEt (4×60 ml). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=5 to AcOEt) to give **11** (529 mg, 98%). **11**: a colorless oil; $[\alpha]_D^{25}$ −68.7 (*c* 1.04, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$), δ (ppm) 7.37–7.20 (10H, m), 5.87–5.73 (2H, m, H5, 6), 4.62 (1H, d, *J*=11.5 Hz), 4.52 (1H, d, *J*=12.1 Hz), 4.46 (1H, d, *J*=12.1 Hz), 4.28 (1H, d, *J*=11.5 Hz), 3.87–3.80 (2H, m, H3, 10), 3.68 (1H, dd, *J*=5.0, 11.3 Hz, H10), 3.60–3.57 (1H, m, H1), 3.51–3.41 (4H, m, H1, 2, 8, OH), 3.25 (1H, ddd, *J*=3.9, 5.0, 8.8 Hz, H9), 2.81 (1H, ddd, *J*=3.7, 9.9, 13.6 Hz, H4), 2.67–2.60 (1H, m, H7), 2.41–2.36 (1H, m, H7), 2.15 (1H, ddd, *J*=3.7, 4.8, 13.6 Hz, H4); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 137.9 (C), 137.2 (C), 128.5 (CH×2), 128.4 (CH×2), 128.1 (CH×3), 127.9 (CH), 127.8 (CH×2), 127.7 (CH), 127.2 (CH), 87.3 (CH), 84.0 (CH), 78.9 (CH), 73.3 (CH_2), 72.0 (CH_2), 71.2 (CH_2),

70.3 (CH), 63.9 (CH_2), 32.3 (CH_2), 26.9 (CH_2); IR (film), ν (cm^{-1}) 3407, 3063, 3027, 2919, 2860, 1496, 1453, 1367, 1310, 1260, 1207, 1098, 772, 698, 695; HR-EIMS, calcd for $C_{24}H_{30}O_5$ $[M]^+$: 398.2093, found: 398.2112.

7.1.4. (2*R*,3*S*,5*Z*,8*R*,9*S*)-[8-Benzyloxy-9-benzyloxymethyl-3-(*tert*-butyldimethylsilyloxy)-2,3,4,7,8,9-hexahydrooxonin-2-yl]methyl trifluoromethanesulfonate (12). To a solution of **11** (11.4 mg, 28.6 μmol) in DCM (0.70 ml) were added 2,6-lutidine (20.0 μl, 172 μmol) and trifluoromethansulfonic anhydride (5.0 μl, 29.7 μmol) at −78 °C and the mixture was stirred for 15 min. Then, TBSOTf (10.0 μl, 43.5 μmol) was added and the reaction mixture was allowed to warm to 0 °C and stirred for 1 h. After that, H_2O (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with 1 M HCl, saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=30) to give **12** (17.5 mg, 95%). **12**: a pale yellow oil; $[\alpha]_D^{19}$ −36.5 (*c* 0.705, $CHCl_3$); ^1H NMR (300 MHz, C_6D_6), δ (ppm) 7.30–7.28 (2H, m), 7.20–7.07 (8H, m), 5.89–5.76 (2H, m), 5.43 (1H, dd, *J*=1.5, 10.1 Hz), 4.54 (1H, d, *J*=12.1 Hz), 4.50 (1H, dd, *J*=1.5, 10.1 Hz), 4.34 (1H, d, *J*=12.1 Hz), 4.30 (1H, d, *J*=12.1 Hz), 4.09 (1H, dt, *J*=3.3, 8.8 Hz), 4.00 (1H, d, *J*=12.1 Hz), 3.64–3.61 (1H, m), 3.50–3.40 (2H, m), 3.27 (1H, dt, *J*=8.4, 3.1 Hz), 3.22 (1H, dt, *J*=8.8, 1.5 Hz), 2.72 (1H, ddd, *J*=3.3, 10.1, 13.8 Hz), 2.56 (1H, ddd, *J*=3.1, 10.1, 13.6 Hz), 2.34 (1H, dt, *J*=13.6, 3.1 Hz), 2.02–1.95 (1H, m), 0.89 (9H, s), 0.03 (3H, s), 0.007 (3H, s); ^{13}C NMR (75 MHz, C_6D_6), δ (ppm) 138.7 (C), 138.5 (C), 128.8 (CH), 128.6 (CH×2), 128.5 (CH×2), 127.4 (CH), 86.4 (CH), 84.5 (CH), 79.0 (CH), 77.1 (CH_2), 73.3 (CH_2), 73.1 (CH_2), 71.3 (CH_2), 69.9 (CH), 32.0 (CH_2), 26.9 (CH_2), 25.8 (CH_3×3), 17.9 (C), −4.3 (CH_3), −5.3 (CH_3) (The signals of seven carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3091, 3035, 2929, 2858, 1496, 1479, 1472, 1454, 1412, 1362, 1336, 1317, 1295, 1245, 1210, 1146, 1102, 1028, 998, 937, 836, 777, 749, 698; HR-EIMS, calcd for $C_{27}H_{34}O_7F_3SiS$ $[M-{}^tBu]^+$: 587.1746, found: 587.1745.

7.1.5. (2*S*,3*R*,5*Z*,8*S*,9*R*)-3-Benzyloxy-2-benzyloxymethyl-8-(*tert*-butyldimethylsilyloxy)-9-(but-2′-ynyl)-2,3,4,7,8,9-hexahydrooxonin (13). To a solution of liquid propyne (excess) in THF (1.0 ml) was added BuLi (0.60 ml, 1.56 M in hexane, 0.936 mmol) at −78 °C and the mixture was stirred for 10 min. Then, a solution of **12** (123 mg, 0.191 mmol) in THF (2.0 ml) was added and the reaction mixture was allowed to warm to 24 °C and stirred for 3 h. After that, H_2O (3 ml) was added and the aqueous layer was extracted with Et_2O (3×15 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=20) to give **13** (101 mg, 99%). **13**: a colorless oil; $[\alpha]_D^{26}$ −78.4 (*c* 1.08, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$), δ (ppm) 7.38–7.23 (10H, m), 5.79 (1H, dt, *J*=4.5, 10.7 Hz), 5.76 (1H, dt, *J*=4.5, 10.7 Hz), 4.62 (1H, d, *J*=11.6 Hz), 4.54 (2H, s), 4.33 (1H, d, *J*=11.6 Hz), 4.07 (1H, dt, *J*=8.6, 3.3 Hz), 3.74 (1H, dt, *J*=8.6, 3.3 Hz), 3.65 (1H, dd, *J*=2.4, 10.3 Hz), 3.51 (1H, dd, *J*=5.0, 10.3 Hz), 3.33 (1H, ddd, *J*=2.4, 5.0, 8.6 Hz), 3.19 (1H, dt, *J*=8.6, 3.3 Hz), 2.83 (1H, ddd, *J*=3.3, 10.7, 13.5 Hz), 2.79–2.66 (2H, m), 2.39 (1H, ddq, *J*=3.3, 16.9, 2.6 Hz), 2.31 (1H, ddd, *J*=3.3, 4.5, 13.6 Hz), 2.05 (1H, ddd, *J*=3.3, 4.5, 13.5 Hz), 1.79 (3H, t, *J*=2.6 Hz), 0.88 (9H, s), 0.11 (3H, s), 0.094 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 138.4 (C), 138.3 (C), 128.24 (CH×2), 128.19 (CH×2), 128.1 (CH), 127.8 (CH×2), 127.7 (CH×2), 127.5 (CH×2), 127.3 (CH), 85.0 (CH), 84.5 (CH), 78.9 (CH), 77.2 (C), 76.2 (C), 73.3 (CH_2), 71.9 (CH), 71.8 (CH_2), 71.3 (CH_2), 32.1 (CH_2), 26.8 (CH_2), 25.7 (CH_3×3), 22.3 (CH_2), 17.8 (C), 3.8 (CH_3), −4.5 (CH_3), −5.0 (CH_3); IR (film), ν (cm^{-1}) 3064, 3026, 2956, 2926, 2855, 1471, 1453, 1360, 1309, 1258, 1196, 1099, 1064, 1027, 836, 809, 776, 735, 697; HR-EIMS, calcd for $C_{33}H_{46}O_4Si$ $[M]^+$: 534.3165, found: 534.3209.

7.1.6. (2*S*,3*R*,5*Z*,8*S*,9*R*,2′*E*)-3-Benzyloxy-2-benzyloxymethyl-8-(*tert*-butyldimethylsilyloxy)-9-(3′-iodo-but-2′-enyl)-2,3,4,7,8,9-hexahydrooxonin (6). To a suspension of Cp_2ZrCl_2 (1.47 g, 4.93 mmol) in degassed THF (4.0 ml) were added DIBAL (5.0 ml, 0.94 M in hexane, 4.70 mmol) and a solution of **13** (548 mg, 1.02 mmol) in degassed THF (5.0 ml) at 25 °C. The mixture was heated to 55 °C and stirred for 30 min in the dark. After the mixture was cooled to 0 °C, I_2 (783 mg, 3.08 mmol) in THF (2.0 ml) was added and the reaction mixture was stirred for 15 min. Then, saturated aqueous Na_2SO_3 (5 ml) and saturated aqueous potassium sodium tartrate (10 ml) was added. The mixture was diluted with Et_2O and stirred at 25 °C for 12 h. The layers were separated and the aqueous layer was extracted with Et_2O (3×50 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=75 to 60) to give **6** (584 mg, 86%). **6**: a colorless oil; $[\alpha]_D^{21}$ −81.2 (*c* 0.46, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$), δ (ppm) 7.33–7.21 (10H, m), 6.30 (1H, tq, *J*=6.6, 1.5 Hz), 5.81–5.70 (1H, m), 4.60 (1H, d, *J*=11.4 Hz), 4.53 (1H, d, *J*=12.0 Hz), 4.43 (1H, d, *J*=12.0 Hz), 4.29 (1H, d, *J*=11.4 Hz), 3.75 (1H, dt, *J*=8.3, 3.4 Hz), 3.71 (1H, dt, *J*=8.6, 3.4 Hz), 3.56 (1H, dd, *J*=2.6, 10.1 Hz), 3.47 (1H, dd, *J*=4.2, 10.1 Hz), 3.32 (1H, ddd, *J*=2.6, 4.2, 8.6 Hz), 3.24 (1H, dt, *J*=8.3, 4.2 Hz), 2.79 (1H, ddd, *J*=3.4, 9.9, 13.4 Hz), 2.66 (1H, ddd, *J*=3.4, 9.9, 13.6 Hz), 2.49 (1H, dddq, *J*=4.2, 6.6, 16.0, 1.7 Hz), 2.36–2.26 (5H, m), 2.05 (1H, dt, *J*=13.4, 3.4 Hz), 0.88 (9H, s), 0.090 (3H, s), 0.023 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 138.3 (C), 138.2 (C), 137.7 (CH), 128.3 (CH×4), 128.0 (CH×3), 127.8 (CH×2), 127.55 (CH), 127.51 (CH), 127.4 (CH), 94.4 (C), 85.4 (CH), 84.0 (CH), 78.3 (CH), 73.4 (CH), 73.3 (CH_2), 71.3 (CH_2), 71.0 (CH_2), 33.5 (CH_2), 32.0 (CH_2), 28.0 (CH_3), 26.9 (CH_2), 25.8 (CH_3×3), 17.9 (C), −4.1 (CH_3), −4.9 (CH_3); IR (film), ν (cm^{-1}) 3063, 3026, 1496, 1471, 1453, 1388, 1360, 1336, 1297, 1256, 1195, 1099, 1027, 939, 923, 835, 811, 775, 734, 697; HR-EIMS, calcd for $C_{33}H_{47}IO_4Si$ $[M]^+$: 662.2288, found: 662.2258.

7.1.7. (1′*R*,3′*S*,4′*R*,6′*R*,8′*S*)-3′-(*tert*-Butyldiphenylsilyloxymethyl)-6′-methyl-10′-phenyl-2′,9′,11′-trioxabicyclo[6.4.0]-dodecan-4′-yl 2,2-dimethylpropanoate (15). To a solution of **14** (48.6 mg, 87.0 μmol) in pyridine (1.0 ml) was added pivaloyl chloride (40.0 μl, 325 μmol) at 0 °C. The reaction

mixture was allowed to warm to 26 °C and stirred for 14 h. Then, saturated aqueous $NaHCO_3$ (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=20 to 15) to give **15** (54.9 mg, ~100%). **15**: a colorless oil; $[\alpha]_D^{26}$ −13.3 (*c* 0.755, $CHCl_3$); ^{1}H NMR (300 MHz, C_6D_6), δ (ppm) 7.81–7.76 (4H, m), 7.70–7.67 (2H, m), 7.28–7.11 (9H, m), 5.37 (1H, s), 4.95 (1H, dt, *J*=2.8, 9.5 Hz), 4.51 (1H, dd, *J*=4.2, 10.6 Hz), 3.68–3.56 (2H, m), 3.51–3.41 (3H, m), 1.94–1.78 (3H, m), 1.73–1.65 (1H, m), 1.55 (1H, ddd, *J*=6.4, 9.5, 14.7 Hz), 1.18 (9H, s), 1.02 (9H, s), 0.91 (3H, d, *J*=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 176.9 (C), 137.9 (C), 135.6 (CH×2), 135.5 (CH×2), 133.25 (C), 133.21 (C), 129.71 (CH), 129.67 (CH), 128.9 (CH), 128.3 (CH×2), 127.7 (CH×4), 126.2 (CH×2), 100.9 (CH), 86.9 (CH), 80.7 (CH), 78.5 (CH), 72.5 (CH), 70.0 (CH_2), 65.3 (CH_2), 44.6 (CH_2), 41.9 (CH_2), 38.5 (C), 27.8 (CH), 27.0 (CH_3), 26.9 (CH_3×3), 26.8 (CH_3×3), 19.1 (C); IR (film), ν (cm^{-1}) 3071, 3047, 2931, 1959, 1889, 1728, 1590, 1456, 1428, 1396, 1276, 1216, 1138, 975, 912, 823, 754, 703, 615; HR-EIMS calcd for $C_{34}H_{41}O_6Si$ [M−^{t}Bu]$^+$: 573.2627, found: 573.2672.

7.1.8. (2′*S*,3′*R*,5′*R*,7′*S*,8′*R*)-2′-(*tert*-Butyldiphenylsilyloxymethyl)-7′-hydroxy-8′-hydroxymethyl-5′-methyl-oxocan-3′-yl 2,2-dimethylpropionate (16). To a suspension of **15** (1.95 g, 3.09 mmol), 1,2-ethanedithiol (2.60 ml, 31.0 mmol), and $NaHCO_3$ (2.65 g, 3.15 mmol) in DCM (30 ml) was added $Zn(OTf)_2$ (1.13 g, 3.11 mmol) at 0 °C and the mixture was stirred for 4 h. After that, the mixture was warmed to 25 °C and stirred for 1 h. Saturated aqueous $NaHCO_3$ (30 ml) was added and the aqueous layer was extracted with Et_2O (2×150 ml) and AcOEt (150 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=10 to 1) to give **16** (1.68 g, ~100%). **16**: a colorless oil; $[\alpha]_D^{26}$ −1.86 (*c* 0.850, $CHCl_3$); ^{1}H NMR (300 MHz, C_6D_6), δ (ppm) 7.80–7.76 (4H, m), 7.25–7.17 (6H, m), 4.66 (1H, dt, *J*=2.8, 9.9 Hz), 4.19 (1H, ddd, *J*=3.3, 9.5, 12.8 Hz), 4.02 (1H, dd, *J*=2.9, 9.5 Hz), 3.94–3.83 (2H, m), 3.76 (1H, dd, *J*=2.8, 10.6 Hz), 3.70 (1H, dd, *J*=8.1, 10.6 Hz), 3.60 (1H, ddd, *J*=3.3, 7.9, 9.0 Hz), 3.46–3.37 (1H, m), 1.85–1.76 (1H, m), 1.70 (1H, dt, *J*=14.3, 2.8 Hz), 1.62–1.55 (1H, m), 1.46 (1H, m), 1.42–1.31 (2H, m), 1.22 (9H, s), 0.93 (9H, s), 0.86 (3H, d, *J*=7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 177.0 (C), 135.6 (CH×2), 135.5 (CH×2), 132.50 (C), 132.47 (C), 129.9 (CH×2), 127.8 (CH×4), 87.5 (CH), 85.9 (CH), 72.7 (CH), 72.0 (CH), 66.7 (CH_2), 65.5 (CH_2), 48.1 (CH_2), 42.5 (CH_2), 38.4 (C), 27.4 (CH), 27.3 (CH_3), 26.8 (CH_3×3), 26.7 (CH_3×3), 19.0 (C); IR (film), ν (cm^{-1}) 3447, 3072, 2932, 2859, 1728, 1473, 1461, 1428, 1395, 1363, 1282, 1154, 1113, 1034, 823, 740, 701; HR-EIMS, calcd for $C_{27}H_{37}O_6Si$ [M−^{t}Bu]$^+$: 485.2359, found: 485.2359.

7.1.9. (2′*S*,3′*R*,5′*R*,7′*S*,8′*R*)-7′-(4-Bromobenzyloxy)-8′-(4-bromobenzyloxymethyl)-2′-(*tert*-butyldiphenylsilyloxymethyl)-5′-methyl-oxocan-3′-yl 2,2-dimethylpropionate (17). To a suspension of **16** (7.0 mg, 12.9 μmol) and TBAI (8.5 mg, 23.0 μmol) in THF (0.50 ml) was added NaH (6.2 mg, 155 μmol) at 0 °C and the mixture was stirred for 10 min. Then, to the mixture was added *p*-bromobenzyl bromide (33.0 mg, 132 μmol) at 0 °C. The reaction mixture was warmed to 25 °C and stirred for 16 h. Saturated aqueous $NaHCO_3$ (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=20 to 15) to give **17** (11.4 mg, ~100%). **17**: a colorless oil; $[\alpha]_D^{25}$ +14.6 (*c* 1.08, $CHCl_3$); ^{1}H NMR (300 MHz, C_6D_6), δ (ppm) 7.87–7.76 (4H, m), 7.31–7.15 (10H, m), 6.88–6.81 (4H, m), 5.25 (1H, dt, *J*=3.2, 9.4 Hz), 4.22 (1H, d, *J*=12.0 Hz), 4.20 (1H, d, *J*=12.1 Hz), 4.10 (1H, d, *J*=12.1 Hz), 3.99 (1H, d, *J*=12.0 Hz), 3.97–3.92 (1H, m), 3.85–3.80 (3H, m), 3.76 (1H, dd, *J*=2.8, 9.7 Hz), 3.59 (1H, dd, *J*=5.5, 9.7 Hz), 3.48 (1H, dt, *J*=3.2, 8.4 Hz), 2.12–2.09 (1H, m), 1.96–1.84 (2H, m), 1.76 (1H, dt, *J*=14.2, 9.4 Hz), 1.59 (1H, dt, *J*=8.4, 14.5 Hz), 1.18 (9H, s), 1.07 (9H, s), 0.94 (3H, d, *J*=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 176.9 (C), 140.2 (C×2), 137.7 (CH×2), 137.5 (CH×2), 133.5 (C), 133.3 (C), 131.4 (CH×2), 131.3 (CH×2), 129.6 (CH×2), 129.4 (CH×2), 129.3 (CH×2), 127.7 (CH×2), 127.6 (CH×2), 121.4 (C), 121.3 (C), 86.0 (CH), 85.6 (CH), 78.3 (CH), 72.6 (CH_2), 72.0 (CH), 71.2 (CH_2), 70.7 (CH_2), 65.9 (CH_2), 41.9 (CH_2), 41.1 (CH_2), 38.5 (C), 27.7 (CH), 26.93 (CH_3), 26.88 (CH_3×3), 26.85 (CH_3×3), 19.2 (C); IR (film), ν (cm^{-1}) 3071, 2930, 2858, 1897, 1726, 1591, 1487, 1461, 1428, 1396, 1361, 1281, 1113, 1012, 823, 804, 739, 702; HR-FDMS, calcd for $C_{45}H_{56}^{79}Br_2O_6Si$ [M+H]$^+$: 879.2286, found: 879.2316.

7.1.10. (2*S*,3*R*,5*S*,7*S*,8*R*)-7-(4-Bromobenzyloxy)-8-(4-bromobenzyloxymethyl)-2-(*tert*-butyldiphenylsilyloxymethyl)-5-methyloxocan-3-ol (18). To a solution of **17** (11.4 mg, 12.9 μmol) in DCM (0.60 ml) was added DIBAL (0.14 ml, 0.95 M in hexane, 133 μmol) at −78 °C and the mixture was stirred for 2 h. After that, MeOH (0.10 ml) and saturated aqueous potassium sodium tartrate (1 ml) were added. The mixture was diluted with Et_2O (5 ml) and stirred at 25 °C for 3 h. The layers were separated and the aqueous layer was extracted with Et_2O (3×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=10 to 3) to give **18** (9.0 mg, 88%). **18**: a colorless oil; $[\alpha]_D^{26}$ +48.1 (*c* 1.26, $CHCl_3$); ^{1}H NMR (300 MHz, C_6D_6), δ (ppm) 7.81–7.74 (4H, m), 7.29–7.16 (10H, m), 6.82 (2H, d, *J*=8.3 Hz), 6.76 (2H, d, *J*=8.4 Hz), 4.18 (1H, d, *J*=11.9 Hz), 4.11 (1H, dd, *J*=5.2, 10.3 Hz), 4.09 (1H, d, *J*=12.4 Hz), 4.02 (1H, dd, *J*=5.9, 10.3 Hz), 3.99 (1H, d, *J*=12.4 Hz), 3.91 (1H, d, *J*=11.9 Hz,), 3.85 (1H, dt, *J*=9.0, 2.6 Hz), 3.68–3.61 (2H, m), 3.58 (1H, dd, *J*=2.6, 9.8 Hz), 3.35 (1H, dd, *J*=6.4, 9.8 Hz), 3.30 (1H, dt, *J*=3.3, 9.1 Hz), 2.69 (1H, d, *J*=2.6 Hz), 1.94–1.73 (4H, m), 1.54 (1H, ddd, *J*=7.9, 9.1, 14.3 Hz), 1.13 (9H, s), 0.98 (3H, d, *J*=7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 137.2 (C), 137.1 (C), 135.52 (CH×2), 135.46 (CH×2), 132.5 (C), 132.4 (C), 131.4 (CH×2), 131.3 (CH×2), 129.93 (CH), 129.91 (CH), 129.2 (CH×2), 129.1 (CH×2), 127.8 (CH×4), 121.4 (C),

121.2 (C), 85.4 (CH), 85.1 (CH), 78.6 (CH), 74.8 (CH), 72.3 (CH_2), 71.5 (CH_2), 70.5 (CH_2), 67.5 (CH_2), 46.3 (CH_2), 42.0 (CH_2), 27.5 (CH), 27.4 (CH_3), 26.7 ($CH_3\times3$), 19.0 (C); IR (film), ν (cm^{-1}) 3481, 3071, 2928, 2858, 1591, 1487, 1471, 1428, 1391, 1361, 1113, 1070, 1012, 823, 802, 740, 701; HR-FDMS, calcd for $C_{40}H_{49}^{79}Br_2O_5Si$ $[M+H]^+$: 795.1711, found: 795.1718.

7.1.11. (2*S*,3*R*,5*S*,7*S*,8*R*)-[7-(4-Bromobenzyloxy)-8-(4-bromobenzyloxymethyl)-3-(4-methoxybenzyloxy)-5-methyloxocan-2-yl]methanol (19). To a suspension of **18** (85.4 mg, 0.107 mmol) and TBAI (17.8 mg, 0.0482 mmol) in THF (0.70 ml) was added NaH (43.4 mg, 1.09 mmol) at 0 °C and the mixture was stirred for 10 min. Then, to the mixture was added a solution of *p*-methoxybenzyl bromide (110 mg, 0.547 mmol) in THF (0.30 ml) at 0 °C. The reaction mixture was warmed to 25 °C and stirred for 21 h. Saturated aqueous $NaHCO_3$ (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with saturated aqueous Na_2SO_3 and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was roughly purified by column chromatography (silica gel, hexane/AcOEt=10) to give a crude product (100 mg), and it was used in the next reaction without further purification. To a solution of the above crude product in THF (1.0 ml) was added TBAF (0.50 ml, 1.0 M in THF, 0.50 mmol) at 25 °C and the mixture was stirred for 2 h. The solvent was removed in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=5 to 1) to give **19** (68.3 mg, 94% from **18**). **19**: a colorless oil; $[\alpha]_D^{26}$ +12.2 (*c* 1.02, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm) 7.49–7.42 (4H, m), 7.21–7.17 (4H, m), 7.05 (2H, d, *J*=8.4 Hz), 6.85 (2H, d, *J*=8.6 Hz), 4.52–4.48 (4H, m), 4.27 (1H, d, *J*=11.0 Hz), 4.21 (1H, d, *J*=11.6 Hz), 4.09–4.03 (1H, m), 3.95–3.88 (1H, m), 3.80 (3H, s), 3.76–3.72 (2H, m), 3.67 (1H, dt, *J*=3.1, 9.0 Hz), 3.43 (1H, dd, *J*=9.0, 11.1 Hz), 3.36 (1H, t, *J*=8.8 Hz), 3.22 (1H, dt, *J*=3.1, 9.5 Hz), 3.14 (1H, dt, *J*=3.3, 10.5 Hz), 2.03–1.98 (1H, m), 1.93–1.88 (1H, m), 1.79–1.55 (3H, m), 1.07 (3H, d, *J*=7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 159.2 (C), 136.9 (C), 136.2 (C), 131.6 (CH×2), 131.5 (CH×2), 130.1 (C), 129.6 (CH×2), 129.4 (CH×2), 129.3 (CH×2), 121.9 (C), 121.6 (C), 113.8 (CH×2), 87.6 (CH), 85.3 (CH), 79.5 (CH), 78.7 (CH), 72.7 (CH_2), 72.6 (CH_2), 71.1 (CH_2), 70.2 (CH_2), 65.6 (CH_2), 55.2 (CH_3), 42.7 (CH_2), 41.8 (CH_2), 27.39 (CH), 27.38 (CH_3); IR (film), ν (cm^{-1}) 3447, 3048, 2927, 1612, 1592, 1513, 1487, 1463, 1428, 1405, 1362, 1302, 1248, 1173, 1070, 1011, 804, 737, 703; HR-FDMS, calcd for $C_{32}H_{38}^{79}Br_2O_6$ $[M]^+$: 676.1035, found: 676.1042.

7.1.12. (2*R*,3*S*,5*S*,7*R*,8*S*,1′*E*)-3-(4-Bromobenzyloxy)-2-(4-bromobenzyloxymethyl)-7-(4-methoxybenzyloxy)-8-(2′-methoxyvinyl)-5-methyloxocane and (2*R*,3*S*,5*S*,7*R*,8*S*,1′*Z*)-3-(4-bromobenzyloxy)-2-(4-bromobenzyloxymethyl)-7-(4-methoxybenzyloxy)-8-(2′-methoxyvinyl)-5-methyloxocane (20). To a solution of **19** (295 mg, 0.435 mmol) in DCM (4.0 ml) was added DMPI (368 mg, 0.868 mmol) at 0 °C. The reaction mixture was warmed to 23 °C and stirred for 1 h. After the mixture was diluted with Et_2O (10 ml), saturated aqueous Na_2SO_3 (2 ml) was added and the aqueous layer was extracted with Et_2O (2×5 ml). The combined organic layers were washed with saturated aqueous Na_2SO_3 and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant crude aldehyde was used in the next reaction without purification. To a solution of $Ph_3P^+CH_2OMeCl^-$ (748 mg, 2.18 mmol) in THF (2.0 ml) was added NHMDS (2.1 ml, 1.0 M in THF, 2.10 mmol) at 0 °C and the mixture was stirred for 30 min at the same temperature before cooling to −78 °C. After that, to the mixture was added a solution of the above crude aldehyde in THF (4.0 ml) at −78 °C and the mixture was stirred for 20 min. The reaction mixture was warmed to 23 °C and stirred for 17 h. Then, brine (6 ml) was added and the aqueous layer was extracted with Et_2O (3×30 ml). The combined organic layers were washed with H_2O, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=15 to 2) to give **20** (241 mg, 79% from **19**, *E*/*Z*=1/1 from ^{1}H NMR). **20**: a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm) 7.44–7.39 (4H, m), 7.26–7.16 (4H, m), 7.08 (2H, d, *J*=8.1 Hz), 6.86–6.82 (2H, m), 6.54 (0.5H, d, *J*=12.7 Hz), 5.98 (0.5H, d, *J*=5.5 Hz), 4.82 (0.5H, dd, *J*=7.3, 12.7 Hz), 4.57–4.35 (6H, m), 4.29–4.24 (1H, m), 3.94–3.83 (1.5H, m), 3.79 (3H), 3.74–3.67 (0.5H, m), 3.64–3.41 (5H, m), 3.36–3.24 (1H, m), 1.96–1.61 (5H, m), 1.05 (1.5H, d, *J*=7.2 Hz), 1.02 (1.5H, d, *J*=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 159.1 (C×0.5), 159.0 (C×0.5), 149.5 (CH×0.5), 148.2 (CH×0.5), 137.8 (C×0.5), 137.5 (C×0.5), 137.4 (C×0.5), 137.3 (C×0.5), 131.41 (CH), 131.36 (CH), 131.3 (CH), 131.2 (CH), 130.8 (C×0.5), 130.5 (C×0.5), 129.5 (CH), 129.31 (CH), 129.25 (CH×4), 121.4 (C×0.5), 121.32 (C×0.5), 121.27 (C×0.5), 121.1 (C×0.5), 113.7 (CH), 113.6 (CH), 107.4 (CH×0.5), 103.4 (CH×0.5), 84.5 (CH×0.5), 83.91 (CH×0.5), 83.86 (CH×0.5), 81.5 (CH×0.5), 80.8 (CH×0.5), 79.0 (CH×0.5), 78.50 (CH×0.5), 78.46 (CH×0.5), 72.5 ($CH_2\times0.5$), 72.4 ($CH_2\times0.5$), 71.6 ($CH_2\times0.5$), 71.3 ($CH_2\times0.5$), 71.1 ($CH_2\times0.5$), 70.9 ($CH_2\times0.5$), 70.6 ($CH_2\times0.5$), 70.5 ($CH_2\times0.5$), 59.7 ($CH_3\times0.5$), 55.8 ($CH_3\times0.5$), 55.27 ($CH_3\times0.5$), 55.25 ($CH_3\times0.5$), 42.1 (CH_2), 41.2 (CH_2), 27.9 (CH×0.5), 27.7 (CH×0.5), 27.3 ($CH_3\times0.5$), 27.2 ($CH_3\times0.5$); IR (film), ν (cm^{-1}) 2926, 2862, 1657, 1612, 1586, 1513, 1487, 1462, 1358, 1302, 1248, 1201, 1172, 1088, 1037, 1011, 803; HR-FDMS, calcd for $C_{34}H_{40}^{79}Br_2O_6$ $[M]^+$: 702.1192, found: 702.1213.

7.1.13. (2*S*,3*R*,5*S*,7*S*,8*R*)-[7-(4-Bromobenzyloxy)-8-(4-bromobenzyloxymethyl)-3-(4-methoxybenzyloxy)-5-methyloxocan-2-yl]ethanal (7). To a solution of **20** (21.9 mg, 31.1 μmol) in THF/H_2O (10/1, v/v, 1.1 ml) was added $Hg(OAc)_2$ (47.3 mg, 148 μmol) at 24 °C and the mixture was stirred for 1 h. Then, TBAI (172 mg, 466 μmol) was added at 24 °C. After the mixture was stirred for 2 h, saturated aqueous NH_4Cl (1 ml) was added and the aqueous layer was extracted with Et_2O (3×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=4 to 3) to give **7** (21.3 mg, 99%). **7**: a colorless oil; $[\alpha]_D^{26}$ +12.7 (*c* 0.803, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm) 9.66 (1H, t, *J*=2.4 Hz), 7.46–7.41 (4H, m), 7.24–7.14 (4H, m), 7.07 (2H, d, *J*=8.3 Hz), 6.86 (2H, d, *J*=8.6 Hz), 4.51 (1H, d, *J*=11.6 Hz), 4.50 (1H, d, *J*=10.9 Hz), 4.44 (1H, d, *J*=12.3 Hz), 4.38 (1H, d, *J*=12.3 Hz), 4.27 (1H, d, *J*=10.9 Hz), 4.24 (1H, d,

J=11.6 Hz), 4.04 (1H, ddd, J=4.7, 7.5, 9.0 Hz), 3.80 (3H, s), 3.78–3.74 (1H, m), 3.59 (1H, dd, J=2.4, 9.7 Hz), 3.39 (1H, dd, J=6.5, 9.7 Hz), 3.38–3.35 (1H, m), 3.23 (1H, dt, J=2.7, 9.0 Hz), 2.77 (1H, ddd, J=2.4, 4.7, 15.8 Hz), 2.54 (1H, ddd, J=2.4, 7.5, 15.8 Hz), 2.01–1.85 (3H, m), 1.77–1.64 (2H, m), 1.09 (3H, d, J=7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 201.2 (CH), 159.3 (C), 137.2 (C×2), 131.44 (CH×2), 131.43 (CH×2), 129.8 (C), 129.7 (CH×2), 129.4 (CH×2), 129.2 (CH×2), 121.5 (C), 121.4 (C), 113.9 (CH×2), 84.6 (CH), 81.5 (CH), 80.8 (CH), 78.6 (CH), 72.6 (CH_2), 71.8 (CH_2), 70.7 (CH_2), 70.6 (CH_2), 55.3 (CH_3), 48.8 (CH_2), 41.0 (CH_2), 40.1 (CH_2), 28.1 (CH), 26.7 (CH_3); IR (film), ν (cm^{-1}) 2923, 2863, 1723, 1612, 1513, 1486, 1456, 1374, 1301, 1248, 1173, 1070, 1011, 804; HR-FDMS, calcd for $C_{33}H_{38}^{79}Br_2O_6$ $[M]^+$: 688.1035, found: 688.1044.

7.1.14. (2*S*,3*E*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*,2″*S*,3″*R*,5″*S*,7″*S*,8″*R*)-5-[8′-Benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-1-[7″-(4-bromobenzyloxy)-8″-(4-bromobenzyloxymethyl)-3″-(4-methoxybenzyloxy)-5″-methyloxocan-2″-yl]-3-methylpent-3-en-2-ol (21) and (2*R*,3*E*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*,2″*S*,3″*R*,5″*S*,7″*S*,8″*R*)-5-[8′-benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-1-[7″-(4-bromobenzyloxy)-8″-(4-bromobenzyloxymethyl)-3″-(4-methoxybenzyloxy)-5″-methyloxocan-2″-yl]-3-methylpent-3-en-2-ol (22). To a suspension of $CrCl_2$ (420 mg, 3.42 mmol) and $NiCl_2$ (2.2 mg, 0.0174 mmol) in degassed DMSO (1.0 ml) was added a solution of **6** (742 mg, 1.12 mmol) and **7** (226 mg, 0.327 mmol) in degassed DMSO (5.0 ml) at 25 °C. The reaction mixture was stirred for 25 h in the dark. Then, saturated aqueous NH_4Cl (6 ml) was added and the aqueous layer was extracted with Et_2O (2×30 ml) and AcOEt (2×30 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, benzene/AcOEt=30 to 10) to give **21** (181 mg, 45%) and **22** (160 mg, 40%). **21**: a colorless oil; $[\alpha]_D^{24}$ −40.4 (c 0.250, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm) 7.43–7.41 (4H, m), 7.31–7.15 (14H, m), 7.04 (2H, d, J=8.1 Hz), 6.84 (2H, d, J=8.6 Hz), 5.78 (1H, dt, J=5.1, 10.1 Hz), 5.74 (1H, dt, J=4.9, 10.1 Hz), 5.62 (1H, t, J=5.7 Hz), 4.60 (1H, d, J=11.5 Hz), 4.50 (2H, d, J=12.9 Hz), 4.49 (1H, d, J=10.7 Hz), 4.46 (1H, d, J=12.9 Hz), 4.42 (1H, d, J=10.9 Hz), 4.39 (1H, d, J=12.9 Hz), 4.33 (1H, d, J=11.7 Hz), 4.30 (1H, d, J=11.7 Hz), 4.20 (1H, d, J=11.5 Hz), 4.41–4.34 (1H, m), 3.91–3.79 (4H, m), 3.77 (3H, s), 3.65–3.58 (3H, m), 3.50 (1H, dd, J=3.3, 10.1 Hz), 3.36–3.26 (5H, m), 2.81–2.76 (1H, m), 2.71–2.65 (1H, m), 2.52–1.48 (1H, m), 2.32–2.28 (2H, m), 2.04–1.93 (3H, m), 1.89–1.71 (4H, m), 1.60 (3H, s), 1.55–1.49 (1H, m), 1.07 (3H, d, J=7.0 Hz), 0.87 (9H, s), 0.06 (3H, s), −0.01 (3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 159.1 (C), 138.6 (C), 138.5 (C), 138.4 (C), 137.2 (C), 136.5 (C), 131.5 (CH×2), 131.4 (CH×2), 130.3 (C), 129.8 (CH×2), 129.23 (CH×2), 129.20 (CH×2), 128.3 (CH), 128.23 (CH×2), 128.21 (CH×2), 127.8 (CH×2), 127.7 (CH×2), 127.44 (CH), 127.36 (CH), 127.2 (CH), 121.7 (C), 121.4 (C), 121.2 (CH), 113.7 (CH×2), 86.1 (CH), 83.7 (CH), 82.7 (CH), 82.5 (CH), 81.4 (CH), 78.8 (CH), 78.2 (CH), 73.4 (CH), 73.1 (CH_2), 72.8 (CH), 72.6 (CH_2), 72.2 (CH_2), 71.3 (CH_2), 71.0 (CH_2), 70.6 (CH_2), 70.3 (CH_2), 55.2 (CH_3), 39.8 (CH_2), 38.9 (CH_2), 38.0 (CH_2), 32.0 (CH_2), 30.4 (CH_2), 28.4 (CH), 27.0 (CH_2), 26.2 (CH_3), 25.8 (CH_3×3), 17.9 (C), 12.3 (CH_3), −4.2 (CH_3), −4.9 (CH_3); IR (film), ν (cm^{-1}) 3482, 2924, 2853, 1611, 1512, 1487, 1452, 1361, 1300, 1248, 1172, 1098, 1011, 775, 697; HR-FDMS, calcd for $C_{66}H_{86}^{79}Br_2O_{10}Si$ $[M]^+$: 1224.4357, found: 1224.4386. **22**: a colorless oil; $[\alpha]_D^{25}$ −29.4 (c 0.190, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm) 7.42–7.39 (4H, m), 7.31–7.16 (14H, m), 7.05 (2H, d, J=8.3 Hz), 6.81 (2H, d, J=8.8 Hz), 5.78 (1H, dt, J=5.3, 10.6 Hz), 5.74 (1H, dt, J=5.0, 10.6 Hz), 5.58 (1H, t, J=6.2 Hz), 4.58 (1H, d, J=11.5 Hz), 4.51 (1H, d, J=11.3 Hz), 4.48 (1H, d, J=11.3 Hz), 4.46 (2H, d, J=11.5 Hz), 4.39 (1H, d, J=11.3 Hz), 4.35 (2H, d, J=11.3 Hz), 4.22 (1H, d, J=11.5 Hz), 4.23–4.21 (1H, m), 4.00–3.97 (1H, m), 3.85 (1H, t, J=11.3 Hz), 3.83 (1H, dt, J=10.1, 3.9 Hz), 3.78–3.74 (2H, m), 3.75 (3H, s), 3.64 (1H, dd, J=2.1, 9.6 Hz), 3.59 (1H, dd, J=2.4, 10.0 Hz), 3.50–3.43 (3H, m), 3.34 (1H, dt, J=8.4, 2.7 Hz), 3.28 (1H, dt, J=8.1, 3.9 Hz), 3.21–3.18 (1H, m), 2.83–2.77 (1H, m), 2.72–2.66 (1H, m), 2.48–2.45 (1H, m), 2.32–2.28 (2H, m), 2.05–2.01 (2H, m), 1.91–1.71 (5H, m), 1.68–1.61 (1H, m), 1.59 (3H, s), 1.06 (3H, d, J=6.8 Hz), 0.87 (9H, s), 0.07 (3H, s), 0.01 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 159.1 (C), 138.5 (C×3), 137.3 (C), 136.9 (C), 131.40 (CH×2), 131.37 (CH×2), 130.2 (C), 129.7 (CH×2), 129.3 (CH×2), 129.2 (CH×2), 128.3 (CH), 128.23 (CH×2), 128.16 (CH×2), 127.8 (CH×2), 127.7 (CH×2), 127.4 (CH), 127.3 (CH), 127.2 (CH), 121.7 (CH), 121.5 (C), 121.4 (C), 113.7 (CH×2), 86.2 (CH), 85.2 (CH), 83.5 (CH), 82.5 (CH), 81.9 (CH), 78.30 (CH), 78.25 (CH), 77.2 (CH), 73.7 (CH), 73.0 (CH_2), 72.6 (CH_2), 71.3 (CH_2), 71.2 (CH_2), 70.9 (CH_2), 70.7 (CH_2), 70.5 (CH_2), 55.2 (CH_3), 40.1 (CH_2), 38.5 (CH_2), 37.6 (CH_2), 31.9 (CH_2), 30.7 (CH_2), 28.3 (CH), 27.0 (CH_2), 26.0 (CH_3), 25.8 (CH_3×3), 17.9 (C), 12.4 (CH_3), −4.2 (CH_3), −4.8 (CH_3); IR (film), ν (cm^{-1}) 3505, 3026, 2926, 2856, 1612, 1513, 1487, 1454, 1381, 1349, 1249, 1172, 1098, 1012, 835, 805, 776, 698; HR-FDMS, calcd for $C_{66}H_{86}^{79}Br_2O_{10}Si$ $[M]^+$: 1224.4357, found: 1224.4386.

7.1.15. (1*R*,1′*R*,2′*E*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*,2‴*S*,3‴*R*,5‴*S*,7‴*S*,8‴*R*)-4′-[8″-Benzyloxy-9″-benzyloxymethyl-3″-(*tert*-butyldimethylsilyloxy)-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl]-1′-[7‴-(4-bromobenzyloxy)-8‴-(4-bromobenzyloxymethyl)-3‴-(4-methoxybenzyloxy)-5‴-methyloxocan-2‴-ylmethyl-2′-methylbut-2′-enyl]-1-methoxy-1-trifluoromethyl-1-phenylacetate {(+)MTPA ester}. To a solution of **22** (2.4 mg, 1.96 μmol) in DCM (0.05 ml) was added triethylamine (16.0 μl, 115 μmol), (+)MTPACl (10.0 μl, 53.4 μmol), and DMAP (3.0 mg, 24.6 μmol) at 0 °C. The reaction mixture was warmed to 25 °C and stirred for 7 h. Then, saturated aqueous $NaHCO_3$ (0.5 ml) was added and the organic layer was extracted with Et_2O (4×3 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, benzene/AcOEt=50 to 10) to give (+)MTPA ester of **22** (2.1 mg, 74%). (+)MTPA ester of **22**: a colorless oil; $[\alpha]_D^{26}$ −13.3 (c 0.110, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm) 7.52–7.49 (2H, m), 7.40–7.34 (7H, m), 7.25–7.16 (14H, m), 7.03 (2H, d, J=8.3 Hz), 6.81

(2H, d, J=8.8 Hz), 5.85 (1H, dd, J=5.9, 9.8 Hz), 5.83 (1H, t, J=6.4 Hz), 5.75 (1H, dt, J=5.1, 10.7 Hz), 5.70 (1H, dt, J=5.1, 10.7 Hz), 4.58 (1H, d, J=11.5 Hz), 4.59 (1H, d, J=11.7 Hz), 4.51 (1H, d, J=11.2 Hz), 4.49 (1H, d, J=12.2 Hz), 4.47 (1H, d, J=11.7 Hz), 4.44 (1H, d, J=11.2 Hz), 4.37 (1H, d, J=11.7 Hz), 4.29 (1H, d, J= 12.2 Hz), 4.23 (1H, d, J=11.2 Hz), 4.22 (1H, d, J=11.7 Hz), 4.16 (1H, d, J=11.2 Hz), 3.79 (1H, dt, J=8.3, 3.4 Hz), 3.75 (3H, s), 3.64 (1H, dt, J=8.1, 3.9 Hz), 3.56–3.53 (2H, m), 3.50 (3H, s), 3.49–3.46 (1H, m), 3.46–3.29 (4H, m), 3.25–3.23 (1H, m), 3.15 (1H, dt, J=2.4, 8.8 Hz), 2.71–2.66 (2H, m), 2.56 (1H, ddd, J=2.9, 10.7, 14.2 Hz), 2.29–2.17 (2H, m), 2.12 (1H, ddd, J=2.9, 9.8, 13.7 Hz), 1.97–1.93 (1H, m), 1.87–1.75 (3H, m), 1.70–1.57 (3H, m), 1.53 (3H, s), 1.05 (3H, d, J=6.8 Hz), 0.84 (9H, s), 0.03 (3H, s), −0.08 (3H, s); IR (film), ν (cm^{-1}) 2925, 2854, 1743, 1612, 1513, 1487, 1453, .1299, 1250, 1169, 1100, 1070, 1012, 836; HR-FDMS, calcd for $C_{76}H_{93}^{79}Br_2F_3O_{12}Si$ $[M]^+$: 1440.4755, found: 1440.4736.

7.1.16. (1*S*,1′*R*,2′*E*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*,2‴*S*,3‴*R*,5‴*S*, 7‴*S*,8‴*R*)-4′-[8″-Benzyloxy-9″-benzyloxymethyl-3″-(*tert*-butyldimethylsilyloxy)-2″,3″,4″,7″,8″,9″-hexahydro-oxonin-2″-yl]-1′-[7‴-(4-bromobenzyloxy)-8‴-(4-bromo-benzyloxymethyl)-3‴-(4-methoxybenzyloxy)-5‴-methyl-oxocan-2‴-ylmethyl-2′-methylbut-2′-enyl]-1-methoxy-1-trifluoromethyl-1-phenylacetate {(−)MTPA ester}. To a solution of **22** (1.2 mg, 0.978 μmol) in DCM (0.05 ml) was added triethylamine (16.0 μl, 115 μmol), (−)MTPACl (10.0 μl, 52.8 μmol), and DMAP (3.0 mg, 24.6 μmol) at 0 °C. The reaction mixture was warmed to 25 °C and stirred for 7 h. Then, saturated aqueous $NaHCO_3$ (0.5 ml) was added and the organic layer was extracted with Et_2O (4×3 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, benzene/AcOEt=50 to 10) to give (−)MTPA ester of **22** (1.1 mg, 78%). (−)MTPA ester of **22**: a colorless oil; $[\alpha]_D^{26}$ −22.6 (c 0.055, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$), δ (ppm) 7.52–7.48 (2H, m), 7.41–7.33 (7H, m), 7.30–7.16 (14H, m), 7.02 (2H, d, J=8.3 Hz), 6.79 (2H, d, J=8.8 Hz), 5.85 (1H, dd, J=5.1, 10.0 Hz), 5.82 (1H, t, J=6.4 Hz), 5.75 (1H, dt, J=4.9, 10.7 Hz), 5.69 (1H, dt, J=4.9, 10.7 Hz), 4.60 (1H, d, J= 12.7 Hz), 4.52–4.46 (4H, m), 4.39–420 (4H, m), 4.15 (1H, d, J=11.7 Hz), 3.82–8.76 (1H, m), 3.73 (3H, s), 3.68 (1H, dd, J=2.0, 9.3 Hz), 3.64–3.60 (2H, m), 3.56 (1H, dd, J= 4.4, 9.3 Hz), 3.51 (3H, s), 3.49–3.29 (6H, m), 3.27–3.23 (2H, m), 2.72–2.65 (2H, m), 2.59–2.52 (1H, m), 2.33–2.18 (3H, m), 1.96–1.87 (4H, m), 1.81–1.64 (3H, m), 1.41 (3H, s), 1.08 (3H, d, J=6.8 Hz), 0.85 (9H, s), 0.04 (3H, s), −0.05 (3H, s); IR (film), ν (cm^{-1}) 2918, 2849, 1744, 1612, 1487, 1462, .1250, 1168, 1100, 836; HR-FDMS, calcd for $C_{76}H_{93}^{79}Br_2F_3O_{12}Si$ $[M]^+$: 1440.4755, found: 1440.4752.

7.1.17. (3*E*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*,2″*S*,3″*R*,5″*S*,7″*S*,8″*R*)-5-[8′-Benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldi-methylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-1-[7″-(4-bromobenzyloxy)-8″-(4-bromobenzyloxy-methyl)-3″-(4-methoxybenzyloxy)-5″-methyloxocan-2″-yl]-3-methylpent-3-en-2-one (23). To a solution of **22** (7.0 mg, 5.70 μmol) in DCM (0.50 ml) were added $NaHCO_3$ (11.1 mg, 132 μmol) and DMPI (9.0 mg, 21.2 μmol) at 0 °C. The reaction mixture was warmed to 25 °C and stirred for 2.5 h. After the mixture was diluted with Et_2O (5 ml), saturated aqueous Na_2SO_3 (1 ml) was added and the aqueous layer was extracted with Et_2O (2×3 ml). The combined organic layers were washed with saturated aqueous Na_2SO_3 and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, benzene/AcOEt=20) to give **23** (7.0 mg, ∼100%). **23**: a colorless oil; $[\alpha]_D^{19}$ −31.4 (c 0.195, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$), δ (ppm) 7.42–7.16 (16H, m), 7.10–7.03 (4H, m), 6.85–6.79 (3H, m), 5.83 (2H, m), 4.60 (1H, d, J=11.4 Hz), 4.50 (1H, d, J=11.0 Hz), 4.47 (1H, d, J=11.9 Hz), 4.43 (2H, d, J=12.5 Hz), 4.34–4.24 (5H, m), 4.17 (1H, dt, J=2.9, 8.5 Hz), 3.83–3.77 (2H, m), 3.75 (3H, s), 3.64 (1H, dt, J=8.2, 3.4 Hz), 3.56 (1H, dd, J=3.8, 10.2 Hz), 3.52–3.40 (3H, m), 3.39–3.34 (2H, m), 3.29 (1H, dt, J=2.6, 8.5 Hz), 3.10 (1H, dd, J=2.9, 16.3 Hz), 2.86 (1H, dd, J=8.5, 16.3 Hz), 2.83–2.76 (1H, m), 2.74–2.69 (1H, m), 2.67–2.61 (1H, m), 2.50 (1H, ddd, J=2.8, 7.8, 17.1 Hz), 2.32 (1H, dt, J=13.8, 3.4 Hz), 2.05 (1H, dt, J=13.2, 3.4 Hz), 1.96–1.86 (3H, m), 1.78–1.72 (2H, m), 1.69 (3H, s), 1.06 (3H, d, J=6.8 Hz), 0.86 (9H, s), 0.054 (3H, s), −0.055 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 199.7 (C), 159.1 (C), 139.4 (CH), 138.6 (C), 138.3 (C), 138.1 (C), 137.58 (C), 137.56 (C), 131.3 (CH×4), 131.2 (CH×2), 130.4 (C), 129.3 (CH×2), 129.2 (CH×2), 129.1 (CH×2), 128.28 (CH×2), 128.26 (CH×2), 127.9 (CH×2), 127.7 (CH×2), 127.55 (CH), 127.53 (CH), 127.50 (CH), 121.18 (C), 121.15 (C), 113.7 (CH×2), 85.2 (CH), 84.20 (CH), 84.15 (CH), 82.0 (CH), 80.8 (CH), 78.5 (CH), 78.1 (CH), 73.3 (CH), 73.1 (CH_2), 72.4 (CH_2), 71.7 (CH_2), 71.3 (CH_2), 70.8 (CH_2), 70.5 (CH_2), 70.4 (CH_2), 55.2 (CH_3), 42.6 (CH_2), 40.9 (CH_2), 40.4 (CH_2), 32.1 (CH_2), 31.8 (CH_2), 28.0 (CH), 26.9 (CH_2), 26.8 (CH_3), 25.7 (CH_3×3), 17.9 (C), 11.9 (CH_3), −4.1 (CH_3), −4.9 (CH_3); IR (film), ν (cm^{-1}) 3026, 2925, 2856, 1665, 1612, 1513, 1487, 1462, 1453, 1361, 1301, 1249, 1207, 1172, 1099, 1012, 836, 805, 776, 698; HR-FDMS, calcd for $C_{66}H_{84}^{79}Br_2O_{10}Si$ $[M]^+$: 1222.4200, found: 1222.4165.

7.1.18. Reduction of 23. To a solution of **23** (2.8 mg, 2.29 μmol) in THF (0.80 ml) was added L-Selectride® (0.10 ml, 1.0 M in THF, 0.10 mmol) at −78 °C and the reaction mixture was stirred for 2 h. After that, 5 M NaOH (1 ml) and 30% aqueous H_2O_2 (1 ml) were added. The mixture was diluted with Et_2O (5 ml) and stirred at 25 °C for 15 h. Then, saturated aqueous $Na_2S_2O_3$ (0.5 ml) was added at 0 °C and the mixture was stirred for 30 min. The layers were separated and the aqueous layer was extracted with Et_2O (2×5 ml) and AcOEt (2×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, benzene/AcOEt=40 to 10) to give a mixture of **21** and **22** (2.8 mg, ∼100%, **21**:**22**≥13:1 from ^1H NMR).

7.1.19. (2*S*,3*S*,4*S*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*,2″*S*,3″*R*,5″*S*, 7″*S*,8″*R*)-5-[8′-Benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethysilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-1-[7″-(4-bromobenzyloxy)-8″-(4-bromobenzyloxy-methyl)-3″-(4-methoxybenzyloxy)-5″-methyloxocan-2″-yl]-3-methyl-3,4-epoxypentan-2-ol (24). To a solution of

21 (287 mg, 0.234 mmol) in toluene (2.0 ml) were added $VO(acac)_2$ (5.6 mg, 0.0211 mmol) and TBHP (0.10 ml, 7.2 M in toluene, 0.720 mmol) at 0 °C. The reaction mixture was stirred for 2.5 h at the same temperature. Then, to the reaction mixture was added dimethylsulfide (0.1 ml) and the mixture was stirred for 0.5 h at 24 °C. After the mixture was diluted with Et_2O (10 ml), saturated aqueous $NaHCO_3$ (2 ml) was added and the aqueous layer was extracted with Et_2O (2×10 ml). The combined organic layers were washed with saturated aqueous Na_2SO_3 and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=5 to 3) to give **24** (263 mg, 91%). **24**: a colorless oil; $[\alpha]_D^{23}$ −72.6 (*c* 0.370, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$), δ (ppm) 7.42–7.40 (4H, m), 7.32–7.21 (12H, m), 7.14 (2H, d, *J*=8.3 Hz), 7.04 (2H, d, *J*=8.3 Hz), 6.82 (2H, d, *J*=8.8 Hz), 5.80 (1H, dt, *J*=4.9, 10.7 Hz), 5.76 (1H, dt, *J*=5.1, 10.7 Hz), 4.61 (1H, d, *J*=11.5 Hz), 4.49 (1H, d, *J*=11.6 Hz), 4.48–4.30 (6H, m), 4.29 (1H, d, *J*=11.5 Hz), 4.21 (1H, d, *J*=11.6 Hz), 4.11–4.08 (1H, m), 3.86–3.81 (2H, m), 3.75 (3H, s), 3.66–3.63 (2H, m), 3.59–3.55 (2H, m), 3.45 (1H, dd, *J*=4.8, 10.1 Hz), 3.41–3.33 (5H, m), 3.29–3.24 (2H, m), 2.83 (1H, ddd, *J*=2.8, 10.7, 13.2 Hz), 2.83 (1H, ddd, *J*=3.2, 10.7, 13.7 Hz), 2.34–2.24 (2H, m), 2.07–2.02 (1H, m), 1.93–1.57 (8H, m), 1.17 (3H, s), 1.06 (3H, d, *J*=6.8 Hz), 0.87 (9H, s), 0.12 (3H, s), 0.079 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 159.0 (C), 138.4 (C), 138.2 (C), 137.3 (C), 136.6 (C), 131.4 (CH×2), 131.3 (CH×2), 130.4 (C), 129.6 (CH×2), 129.3 (CH×2), 129.2 (CH×2), 128.3 (CH), 128.22 (CH×2), 128.19 (CH×2), 127.9 (CH×2), 127.7 (CH×2), 127.5 (CH), 127.4 (CH), 127.1 (CH), 121.6 (C), 121.3 (C), 113.6 (CH×2), 85.1 (CH), 84.0 (CH), 82.9 (CH), 82.1 (CH), 81.3 (CH), 78.6 (CH), 78.5 (CH), 73.3 (CH), 73.0 (CH_2), 72.5 (CH_2), 71.7 (CH_2), 71.6 (CH_2), 71.2 (CH_2), 70.8 (CH), 70.6 (CH_2), 70.3 (CH_2), 60.7 (C), 58.3 (CH), 55.1 (CH_3), 39.8 (CH_2), 39.0 (CH_2), 35.9 (CH_2), 32.1 (CH_2), 30.7 (CH_2), 28.3 (CH), 26.9 (CH_2), 26.3 (CH_3), 25.8 (CH_3×3), 17.9 (C), 12.9 (CH_3), −4.4 (CH_3), −4.5 (CH_3); IR (film), ν (cm^{-1}) 3490, 3028, 2931, 2858, 1612, 1514, 1488, 1454, 1360, 1302, 1251, 1211, 1173, 1011, 939, 836, 777, 698; HR-FDMS, calcd for $C_{66}H_{86}^{79}Br_2O_{11}Si$ $[M]^+$: 1240.4306, found: 1243.4263.

7.1.20. (2*S*,3*R*,5*Z*,8*S*,9*R*,2′*S*,3′*S*,4′*S*,2″*S*,3″*R*,5″*S*,7″*S*,8″*R*)-3-Benzyloxy-2-benzyloxymethyl-9-{5′-[7″-(4-bromobenzyloxy)-8″-(4-bromobenzyloxymethyl)-3″-(4-methoxybenzyloxy)-5″-methyloxocan-2″-yl]-3′-methyl-4′-triethylsilyloxy-2′,3′-epoxypentyl}-8-(*tert*-butyldimethylsilyloxy)-2,3,4,7,8,9-hexahydrooxonin (25). To a solution of **24** (4.5 mg, 3.62 μmol) in DCM (0.50 ml) were added 2,6-lutidine (13.0 μl, 112 μmol) and TESOTf (12.0 μl, 53.1 μmol) at 0 °C. The reaction mixture was warmed to 25 °C and stirred for 10 min. Then, saturated aqueous $NaHCO_3$ (0.5 ml) was added and the aqueous layer was extracted with Et_2O (4×3 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=15 to 10) to give **25** (4.9 mg, ∼100%). **25**: a colorless oil; $[\alpha]_D^{23}$ −102.3 (*c* 1.07, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$), δ (ppm) 7.43–7.37 (4H, m), 7.31–7.15 (14H, m), 7.05 (2H, d, *J*=8.4 Hz), 6.82 (2H, d, *J*=8.8 Hz), 5.79 (1H, dt, *J*=4.9, 10.3 Hz), 5.72 (1H, dt, *J*=4.9, 10.3 Hz), 4.58 (1H, d, *J*=11.5 Hz), 4.53–4.34 (6H, m), 4.33 (1H, d, *J*=11.0 Hz), 4.25 (1H, d, *J*=11.5 Hz), 4.24 (1H, d, *J*=11.7 Hz), 4.12 (1H, dt, *J*=8.4, 3.2 Hz), 3.87–3.82 (2H, m), 3.76 (3H, s), 3.66 (1H, dd, *J*=2.1, 9.3 Hz), 3.60–3.41 (7H, m), 3.38–3.33 (1H, m), 3.25 (1H, dt, *J*=2.9, 6.8 Hz), 3.11 (1H, dd, *J*=1.1, 9.1 Hz), 2.75 (1H, ddd, *J*=3.2, 10.3, 13.2 Hz), 2.63 (1H, ddd, *J*=3.0, 10.3, 13.6 Hz), 2.35–2.24 (2H, m), 2.05–1.98 (2H, m), 1.89–1.60 (6H, m), 1.52 (1H, ddd, *J*=2.4, 9.1, 14.8 Hz), 1.31 (3H, s), 1.06 (3H, d, *J*=6.8 Hz), 0.93 (9H, t, *J*=7.9 Hz), 0.87 (9H, s), 0.58 (6H, q, *J*=7.9 Hz), 0.11 (3H, s), 0.058 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 158.9 (C), 138.4 (C), 138.3 (C), 137.7 (C), 137.6 (C), 131.35 (CH×2), 131.29 (CH×2), 130.9 (C), 129.4 (CH×2), 129.1 (CH×2), 128.8 (CH×2), 128.3 (CH), 128.23 (CH×2), 128.19 (CH×2), 127.6 (CH×4), 127.43 (CH), 127.37 (CH), 127.0 (CH), 121.3 (C), 121.2 (C), 113.6 (CH×2), 85.4 (CH), 84.2 (CH), 82.6 (CH), 82.3 (CH), 80.7 (CH), 78.6 (CH), 78.4 (CH), 73.4 (CH), 73.1 (CH), 72.7 (CH_2), 72.6 (CH_2), 72.4 (CH_2), 71.4 (CH_2), 71.2 (CH_2), 70.23 (CH_2), 70.15 (CH_2), 60.7 (C), 58.2 (CH), 55.2 (CH_3), 39.6 (CH_2), 38.7 (CH_2), 38.3 (CH_2), 32.1 (CH_2), 30.7 (CH_2), 28.3 (CH), 26.8 (CH_2), 26.2 (CH_3), 25.9 (CH_3×3), 17.9 (C), 13.0 (CH_3), 7.1 (CH_3×3), 5.4 (CH_2×3), −4.4 (CH_3), −4.5 (CH_3); IR (film), ν (cm^{-1}) 3063, 2957, 1612, 1586, 1513, 1487, 1454, 1360, 1301, 1249, 1172, 1108, 938, 836, 745, 697; HR-FDMS, calcd for $C_{72}H_{100}^{79}Br_2O_{11}Si_2$ $[M]^+$: 1354.5171, found: 1354.5188.

7.1.21. (2*S*,3*R*,5*S*,7*S*,8*R*,2′*S*,3′*S*,4′*S*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-2-{5′-[8″-Benzyloxy-9″-benzyloxymethyl-3″-(*tert*-butyldimethylsilyloxy)-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl]-3′-methyl-2′-triethylsilyloxy-3′,4′-epoxypentyl}-8-(4-bromobenzyloxy)-9-(4-bromobenzyloxymethyl)-5-methyloxocan-3-ol (5). To a solution of **25** (267 mg, 0.197 mmol) in DCM–pH 7 buffer (10:1, v/v, 2.0 ml) was added DDQ (50.0 mg, 0.220 mmol) at 0 °C and the mixture was stirred for 50 min. Then, to the mixture was added DDQ (20.8 mg, 0.0916 mmol) at 0 °C and the stirring was continued for further 15 min. Saturated aqueous $NaHCO_3$ (2 ml) was added and the aqueous layer was extracted with Et_2O (4×10 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=10 to 4) to give **5** (236 mg, 97%). **5**: a colorless oil; $[\alpha]_D^{24}$ −22.3 (*c* 0.615, $CHCl_3$); ^1H NMR (300 MHz, CD_3COCD_3), δ (ppm) 7.53–7.45 (4H, m), 7.35–7.22 (14H, m), 5.76 (1H, dt, *J*=4.5, 10.7 Hz), 5.72 (1H, dt, *J*=4.5, 10.7 Hz), 4.66 (1H, d, *J*=11.9 Hz), 4.61 (1H, d, *J*=11.9 Hz), 4.59–4.47 (4H, m), 4.36 (2H, d, *J*=11.9 Hz), 4.19 (1H, dt, *J*=8.2, 3.3 Hz), 3.94 (1H, dd, *J*=2.2, 9.5 Hz), 3.79 (1H, ddd, *J*=2.2, 5.9, 8.3 Hz), 3.73 (1H, dt, *J*=2.2, 8.7 Hz), 3.70–3.62 (3H, m), 3.57–3.48 (3H, m), 3.46–3.34 (4H, m), 3.22 (1H, dd, *J*=1.1, 9.4 Hz), 2.73 (1H, ddd, *J*=3.3, 10.7, 13.3 Hz), 2.60 (1H, ddd, *J*=3.1, 10.7, 13.3 Hz), 2.48 (1H, ddd, *J*=1.1, 5.0, 14.7 Hz), 2.33 (1H, dt, *J*=13.3, 4.5 Hz), 2.07–1.71 (5H, m), 1.64 (1H, ddd, *J*=2.2, 8.7, 13.9 Hz), 1.50 (1H, ddd, *J*=2.2, 8.7, 14.7 Hz), 1.13 (3H, s), 1.03 (3H, d, *J*=7.0 Hz), 0.96 (9H, t, *J*=7.9 Hz), 0.89 (9H, s), 0.66 (6H, q, *J*=7.9 Hz), 0.16 (3H, s), 0.12 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 138.31 (C), 138.25 (C), 137.32

(C), 137.29 (C), 131.4 (CH×4), 129.4 (CH×2), 129.2 (CH), 128.2 (CH×4), 128.1 (CH), 127.6 (CH×4), 127.44 (CH), 127.41 (CH), 127.1 (CH), 121.37 (C), 121.35 (C), 85.2 (CH), 85.1 (CH), 84.9 (CH), 84.2 (CH), 78.9 (CH), 78.7 (CH), 75.2 (CH), 74.1 (CH), 73.1 (CH), 72.8 (CH_2), 72.6 (CH_2), 72.4 (CH_2), 72.0 (CH_2), 71.1 (CH_2), 70.4 (CH_2), 60.9 (C), 59.5 (CH), 47.3 (CH_2), 41.2 (CH_2), 41.1 (CH_2), 32.1 (CH_2), 30.5 (CH_2), 28.0 (CH), 27.2 (CH_3), 26.7 (CH_2), 25.8 (CH_3×3), 17.9 (C), 11.9 (CH_3), 6.9 (CH_3×3), 5.0 (CH_2×3), −4.3 (CH_3), −4.5 (CH_3); IR (film), ν (cm^{-1}) 3447, 3063, 3026, 2927, 1593, 1487, 1453, 1360, 1311, 1250, 1210, 1095, 1012, 938, 836, 776, 744, 697; HR-FDMS, calcd for $C_{64}H_{92}^{79}Br_2O_{10}Si_2$ $[M]^+$: 1234.4596, found: 1234.4553.

7.1.22. (1*S*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*,1″*S*,3″*R*,4″*S*,6″*S*,8″*R*,10″*R*,11″*S*)-2-[8′-Benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-1-{4″-(4-bromobenzyloxy)-3″-(4-bromobenzyloxymethyl)-6″,10″-dimethyl-11″-triethylsilyloxy-2″,9″-dioxabicyclo[6.4.0]dodecan-10″-yl}ethanol (26). To a solution of **5** (233 mg, 0.188 mmol) in DCM (3.0 ml) was added CSA (4.3 mg, 0.0185 mmol) at 0 °C and the mixture was stirred for 25 min. Then, Et_3N (0.1 ml) was added at 0 °C and the mixture was warmed to 25 °C and stirred for 30 min. The solvent was removed in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=7 to 2) to give **26** (186 mg, 80%). **26**: a colorless oil; $[\alpha]_D^{23}$ +12.2 (*c* 0.495, $CHCl_3$); ^{1}H NMR (300 MHz, CD_3COCD_3), δ (ppm) 7.52–7.47 (4H, m), 7.37–7.23 (14H, m), 5.70–5.64 (2H, m), 4.65 (1H, d, *J*=11.4 Hz), 4.63 (1H, d, *J*=12.1 Hz), 4.53–4.49 (3H, m), 4.61 (1H, d, *J*=11.4 Hz), 4.38 (1H, d, *J*=11.4 Hz), 4.34 (1H, d, *J*=11.7 Hz), 4.11–4.07 (1H, m), 4.04–4.01 (1H, m), 3.92 (1H, t, *J*=2.9 Hz), 3.86–3.81 (1H, m), 3.78–3.74 (2H, m), 3.70–3.67 (1H, m), 3.64–3.52 (4H, m), 3.44–3.35 (3H, m), 3.28 (1H, d, *J*=4.0 Hz), 2.84–2.63 (2H, m), 2.35 (1H, dt, *J*=12.8, 4.4 Hz), 2.11–2.09 (2H, m), 1.93–1.78 (5H, m), 1.69–1.67 (2H, m), 1.59–1.49 (1H, m), 1.09 (3H, s), 1.03 (3H, d, *J*=7.0 Hz), 0.93 (9H, t, *J*=8.1 Hz), 0.89 (9H, s), 0.60 (6H, q, *J*=8.1 Hz), 0.11 (3H, s), 0.10 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 138.5 (C), 138.3 (C), 137.5 (C), 137.3 (C), 131.4 (CH×2), 131.3 (CH×2), 129.31 (CH×2), 129.30 (CH×2), 129.0 (CH), 128.2 (CH×4), 127.6 (CH×4), 127.4 (CH), 127.3 (CH), 126.2 (CH), 121.4 (C), 121.3 (C), 85.4 (CH), 84.5 (CH), 80.9 (CH), 79.1 (CH), 78.6 (CH), 77.6 (C), 77.1 (CH), 76.6 (CH), 73.4 (CH), 73.1 (CH_2), 72.5 (CH_2), 71.7 (CH_2), 71.6 (CH), 71.2 (CH_2), 70.5 (CH_2), 70.1 (CH), 69.4 (CH_2), 45.4 (CH_2), 40.2 (CH_2), 36.1 (CH_2), 34.6 (CH_2), 29.2 (CH_2), 28.3 (CH), 26.8 (CH_3), 26.3 (CH_2), 25.9 (CH_3×3), 18.0 (C), 14.3 (CH_3), 7.0 (CH_3×3), 5.0 (CH_2×3), −4.6 (CH_3), −4.7 (CH_3); IR (film), ν (cm^{-1}) 3502, 3030, 2926, 1594, 1488, 1456, 1362, 1256, 1206, 1099, 1012, 885, 836, 775, 735, 697; HR-FDMS, calcd for $C_{64}H_{92}^{79}Br_2O_{10}Si_2$ $[M]^+$: 1234.4596, found: 1234.4587.

7.1.23. (1*S*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*,1″*S*,3″*R*,4″*S*,6″*S*,8″*R*,10″*R*,11″*S*)-2-[8′-Benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-1-{4″-(4-bromobenzyloxy)-3″-(4-bromobenzyloxymethyl)-6″,10″-dimethyl-11″-triethylsilyloxy-2″,9″-dioxabicyclo[6.4.0]dodecan-10″-yl}ethyl trifluoroacetate (29). To a solution of **26** (10.8 mg, 8.23 μmol) in pyridine (0.60 ml) was added trifluoroacetic anhydride (20.0 μl, 144 μmol) at 0 °C and the mixture was stirred for 1 h. Then, H_2O (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with 1 M HCl, saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, benzene/AcOEt=100 to 40) to give **29** (11.0 mg, ~100%). **29**: a colorless oil; $[\alpha]_D^{25}$ −2.10 (*c* 0.660, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3/C_6D_6$=1:1), δ (ppm) 7.35–7.31 (6H, m), 7.26–7.11 (8H, m), 7.03 (2H, d, *J*=8.1 Hz), 6.90 (2H, d, *J*=8.1 Hz), 5.84–5.76 (2H, m), 5.67 (1H, t, *J*=6.1 Hz), 4.63 (1H, d, *J*=12.4 Hz), 4.56 (1H, d, *J*=12.4 Hz), 4.47 (1H, d, *J*=11.6 Hz), 4.32 (1H, d, *J*=12.6 Hz), 4.31 (1H, d, *J*=11.5 Hz), 4.29 (1H, d, *J*=12.6 Hz), 4.20 (1H, d, *J*=11.6 Hz), 3.99 (1H, d, *J*=11.5 Hz), 3.93 (1H, q, *J*=6.1 Hz), 3.88 (1H, dd, *J*=1.7, 10.0 Hz), 3.85–3.83 (1H, m), 3.80–3.70 (4H, m), 3.56 (1H, dd, *J*=2.0, 9.5 Hz), 3.54–3.48 (2H, m), 3.45 (1H, dt, *J*=2.6, 9.9 Hz), 3.34 (1H, dd, *J*=6.6, 9.5 Hz), 3.24 (1H, dt, *J*=2.1, 9.4 Hz), 2.84–2.79 (1H, m), 2.74–2.69 (1H, m), 2.33 (1H, dt, *J*=14.9, 6.1 Hz), 2.29–2.24 (1H, m), 2.18 (1H, dt, *J*=13.7, 4.1 Hz), 2.09 (1H, dt, *J*=13.7, 4.5 Hz), 1.86–1.78 (5H, m), 1.64–1.50 (2H, m), 1.16 (3H, s), 0.99 (3H, d, *J*=7.1 Hz), 0.93 (9H, t, *J*=7.9 Hz), 0.92 (9H, s), 0.59 (6H, q, *J*=7.9 Hz), 0.084 (3H, s), 0.080 (3H, s); IR (film), ν (cm^{-1}) 3032, 2927, 1792, 1593, 1487, 1456, 1374, 1336, 1217, 1164, 1098, 1012, 960, 836, 775, 735, 697; HR-FDMS, calcd for $C_{66}H_{91}^{79}Br_2F_3O_{11}Si_2$ $[M]^+$: 1330.4419, found: 1330.4448.

7.1.24. (1*S*,3*R*,4*S*,6*S*,8*R*,10*S*,11*S*,1′*S*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-10-{2′-[8″-Benzyloxy-9″-benzyloxymethyl-3″-(*tert*-butyldimethylsilyloxy)-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl]-1′-hydroxyethyl}-4-(4-bromobenzyloxy)-3-(4-bromobenzyloxymethyl)-6,10-dimethyl-2,9-dioxabicyclo[6.4.0]dodecan-11-yl trifluoroacetate (30). To a solution of **29** (11.0 mg, 8.23 μmol) in THF–H_2O (4:1, v/v, 0.75 ml) was added TFA (15.0 μl) at 22 °C and the mixture was stirred for 2 d. Then, the solvent was removed in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=30 to 7) to give **30** and recovery of **29**. For this recovered starting material, the above procedure was repeated twice to give **30** (6.3 mg, 63%, after three cycles). **30**: a colorless oil; $[\alpha]_D^{19}$ +31.3 (*c* 0.265, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6), δ (ppm) 7.37–7.28 (6H, m), 7.20–7.05 (8H, m), 6.92 (2H, d, *J*=8.3 Hz), 6.82 (2H, d, *J*=8.3 Hz), 5.87 (1H, dt, *J*=6.1, 10.1 Hz), 5.80 (1H, dt, *J*=6.1, 10.1 Hz), 4.52 (1H, d, *J*=11.5 Hz), 4.33 (2H, d, *J*=11.7 Hz), 4.24 (1H, d, *J*=11.5 Hz), 4.20–4.16 (2H, m), 4.13 (1H, d, *J*=12.2 Hz), 4.07 (1H, d, *J*=11.7 Hz), 3.98–3.91 (2H, m), 3.86 (1H, d, *J*=12.2 Hz), 3.82–3.80 (1H, m), 3.75 (1H, dd, *J*=1.8, 10.1 Hz), 3.70–3.66 (1H, m), 3.65 (1H, dd, *J*=3.3, 10.1 Hz), 3.61–3.47 (4H, m), 3.32 (1H, dd, *J*=7.1, 9.8 Hz), 3.26 (1H, dt, *J*=2.9, 8.5 Hz), 2.78–2.69 (2H, m), 2.44 (1H, ddd, *J*=3.0, 4.6, 14.9 Hz), 2.54–2.16 (2H, m), 2.09–2.06 (1H, m), 1.93–1.74 (5H, m), 1.64 (1H, dt, *J*=14.1, 9.8 Hz), 1.55–1.47 (1H, m), 1.04 (3H, s), 1.03 (3H, d, *J*=6.6 Hz), 0.96 (9H, s), 0.036 (3H, s), 0.032 (3H, s); IR (film), ν (cm^{-1}) 3476, 3027, 2931, 1784, 1593, 1488, 1454, 1387, 1167, 1098, 939, 879, 837, 754, 698; HR-FDMS, calcd for $C_{60}H_{77}^{79}Br_2F_3O_{11}Si$ $[M]^+$: 1216.3554, found: 1216.3586.

7.1.25. (1*S*,3*R*,4*S*,6*S*,8*R*,10*R*,11*S*,1′*S*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-10-{2′-[8″-Benzyloxy-9″-benzyloxymethyl-3″-(*tert*-butyldimethylsilyloxy)-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl]-1′-hydroxyethyl}-4-(4-bromobenzyloxy)-3-(4-bromobenzyloxymethyl)-6,10-dimethyl-2,9-dioxabicyclo[6.4.0]dodecan-11-ol (31). To a solution of **26** (60.2 mg, 48.7 μmol) in MeOH–DCM (4:1, v/v, 1.0 ml) was added PPTS (11.3 mg, 45.0 μmol) at 24 °C and the mixture was stirred for 50 min. Then, saturated aqueous $NaHCO_3$ (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml) and AcOEt (5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=7 to 3) to give **31** (54.7 mg, ~100%). **31**: a colorless oil; $[\alpha]_D^{19}$ +14.5 (*c* 0.545, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 7.33–7.26 (5H, m), 7.20–7.05 (9H, m), 7.00 (2H, d, *J*=8.1 Hz), 6.84 (2H, d, *J*=8.3 Hz), 5.96 (1H, dt, *J*=6.0, 10.5 Hz), 5.87 (1H, dt, *J*=5.6, 10.5 Hz), 4.40 (1H, d, *J*=11.8 Hz), 4.35 (1H, d, *J*=11.8 Hz), 4.24 (1H, d, *J*=12.7 Hz), 4.21–4.13 (5H, m), 4.12 (1H, d, *J*=11.8 Hz), 3.97–3.88 (3H, m), 3.87–3.82 (2H, m), 3.69 (1H, dt, *J*=9.0, 3.3 Hz), 3.67–3.65 (1H, m), 3.63–3.56 (3H, m), 3.54 (1H, dd, *J*=2.3, 10.0 Hz), 3.43 (1H, dd, *J*=6.6, 10.0 Hz), 3.34 (1H, dt, *J*=2.7, 8.5 Hz), 3.26–3.20 (1H, m), 2.87–2.75 (2H, m), 2.47 (1H, dt, *J*=13.4, 3.9 Hz), 2.27 (1H, ddd, *J*=3.3, 5.6, 13.8 Hz), 2.19 (1H, dt, *J*=13.2, 6.0 Hz), 2.07–2.03 (1H, m), 2.00–1.79 (5H, m), 1.60 (1H, ddd, *J*=6.1, 8.5, 14.6 Hz), 1.09 (3H, s), 1.05 (3H, d, *J*=7.1 Hz), 0.99 (9H, s), 0.13 (3H, s), 0.086 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 138.4 (C), 137.9 (C), 137.5 (C), 137.3 (C), 131.41 (CH×2), 131.38 (CH×2), 129.3 (CH×4), 129.1 (CH), 128.33 (CH×2), 128.29 (CH×2), 127.8 (CH×2), 127.7 (CH×2), 127.65 (CH), 127.56 (CH), 126.1 (CH), 121.4 (C), 121.3 (C), 85.23 (CH), 85.15 (CH), 80.3 (CH), 79.8 (CH), 78.8 (CH), 77.2 (C), 76.3 (CH), 76.1 (CH), 74.7 (CH), 73.3 (CH), 73.2 (CH_2), 72.5 (CH_2), 71.7 (CH_2), 71.3 (CH_2), 70.5 (CH_2), 70.3 (CH), 68.5 (CH_2), 45.2 (CH_2), 40.3 (CH_2), 34.8 (CH_2), 33.9 (CH_2), 29.5 (CH_2), 28.3 (CH), 26.9 (CH_3), 26.4 (CH_2), 25.8 (CH_3×3), 18.0 (C), 15.8 (CH_3), −4.6 (CH_3), −4.7 (CH_3); IR (film), ν (cm^{-1}) 3474, 3027, 2926, 2854, 1593, 1487, 1453, 1360, 1255, 1205, 1096, 1011, 939, 836, 804, 775, 751, 697; HR-FDMS, calcd for $C_{58}H_{78}^{79}Br_2O_{10}Si$ $[M]^+$: 1120.3731, found: 1120.3763.

7.1.26. (1*R*,3*R*,4*S*,6*R*,8*S*,10*S*,12*R*,13*S*,15*S*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*)-4-[8′-Benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-13-(4-bromobenzyloxy)-12-(4-bromobenzyloxymethyl)-6-(4-methoxyphenyl)-3,15-dimethyl-2,5,7,11-tetraoxatricyclo[8.6.0.0^{3,8}]hexadecane (32a) and (1*R*,3*R*,4*S*,6*S*,8*S*,10*S*,12*R*,13*S*,15*S*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*)-4-[8′-benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-13-(4-bromobenzyloxy)-12-(4-bromobenzyloxymethyl)-6-(4-methoxyphenyl)-3,15-dimethyl-2,5,7,11-tetraoxatricyclo[8.6.0.0^{3,8}]hexadecane (32b). To a solution of **31** (13.2 mg, 11.8 μmol) in benzene (2.0 ml) were added *p*-anisaldehyde (30.0 μl, 247 μmol) and PPTS (3.2 mg, 12.7 μmol). The reaction mixture was heated to 80 °C and stirred for 3 h. Then, saturated aqueous $NaHCO_3$ (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=30 to 7) to give **32** (14.6 mg, ~100%, a 1:1 mixture of **32a** and **32b** from ^1H NMR). This mixture of **32a** and **32b** was separated by HPLC (hexane/AcOEt=7) to give **32a** as less-polar eluate and **32b** as polar eluate. **32a**: a colorless oil; $[\alpha]_D^{24}$ +6.71 (*c* 0.235, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 7.51–7.49 (4H, m), 7.30–7.05 (12H, m), 6.97 (2H, d, *J*=8.3 Hz), 6.90 (2H, d, *J*=8.8 Hz), 6.82 (2H, d, *J*=8.5 Hz), 6.07 (1H, s), 6.04 (1H, dt, *J*=5.1, 10.6 Hz), 5.99 (1H, dt, *J*=5.1, 10.6 Hz), 4.72 (1H, d, *J*=11.8 Hz), 4.54 (1H, dd, *J*=4.1, 8.8 Hz), 4.52 (1H, d, *J*=11.8 Hz), 4.49 (1H, dt, *J*=8.7, 3.2 Hz), 4.45 (1H, d, *J*=11.8 Hz), 4.21 (1H, d, *J*=12.3 Hz), 4.19 (1H, d, *J*=11.8 Hz), 4.18 (1H, d, *J*=11.5 Hz), 4.13 (1H, d, *J*=12.3 Hz), 3.98 (1H, dt, *J*=8.5, 3.2 Hz), 3.93 (1H, t, *J*=4.8 Hz), 3.88 (1H, d, *J*=11.5 Hz), 3.86–3.83 (2H, m), 3.76 (1H, dt, *J*=4.8, 9.0 Hz), 3.64–3.53 (4H, m), 3.43–3.40 (1H, m), 3.38 (1H, dd, *J*=6.6, 9.8 Hz), 3.32 (3H, s), 3.27 (1H, dt, *J*=2.4, 8.7 Hz), 3.07 (1H, ddd, *J*=3.2, 10.6, 13.5 Hz), 2.80 (1H, ddd, *J*=3.2, 10.6, 13.7 Hz), 2.46 (1H, dt, *J*=13.8, 4.8 Hz), 2.31–2.25 (1H, m), 2.17–2.14 (3H, m), 1.98–1.75 (5H, m), 1.56 (1H, ddd, *J*=6.1, 8.7, 14.6 Hz), 1.18 (3H, s), 1.05 (3H, d, *J*=6.6 Hz), 1.04 (9H, s), 0.22 (3H, s), 0.091 (3H, s); ^{13}C NMR (125 MHz, C_6D_6), δ (ppm) 160.4 (C), 139.52 (C), 139.46 (C), 138.2 (C), 138.0 (C), 132.2 (C), 131.6 (CH×4), 129.4 (CH×2), 129.2 (CH×2), 128.6 (CH×2), 128.4 (CH×2), 127.5 (CH×2), 121.6 (C), 121.5 (C), 113.8 (CH×2), 98.6 (CH), 85.1 (CH), 85.0 (CH), 84.9 (CH), 81.0 (CH), 79.8 (CH), 78.7 (CH), 77.4 (CH), 76.1 (C), 74.8 (CH), 73.4 (CH), 73.3 (CH_2), 72.6 (CH_2), 72.4 (CH_2), 72.0 (CH_2), 71.42 (CH), 71.35 (CH_2), 70.3 (CH_2), 54.8 (CH_3), 45.2 (CH_2), 33.0 (CH_2), 32.7 (CH_2), 31.9 (CH_2), 30.2 (CH_2), 28.9 (CH), 27.5 (CH_2), 27.0 (CH_3), 26.2 (CH_3×3), 18.2 (C), 16.3 (CH_3), −3.9 (CH_3), −4.3 (CH_3) (The signals of 10 carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3063, 3026, 2925, 2853, 1614, 1588, 1513, 1487, 1453, 1360, 1301, 1249, 1213, 1170, 1095, 1011, 939, 833, 804, 776, 734, 697; HR-FDMS, calcd for $C_{66}H_{84}^{79}Br_2O_{11}Si$ $[M]^+$: 1238.4150, found: 1238.4125. **32b**: a colorless oil; $[\alpha]_D^{23}$ −8.95 (*c* 0.200, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 7.75 (2H, d, *J*=8.8 Hz), 7.35–7.21 (8H, m), 7.18–7.04 (6H, m), 6.98 (2H, d, *J*=8.5 Hz), 6.87 (2H, d, *J*=8.8 Hz), 6.83 (2H, d, *J*=8.5 Hz), 5.96 (1H, dt, *J*=5.4, 10.2 Hz), 5.90 (1H, s), 5.89 (1H, dt, *J*=5.4, 10.2 Hz), 4.50 (1H, dd, *J*=2.8, 11.3 Hz), 4.47 (1H, d, *J*=11.8 Hz), 4.43 (1H, d, *J*=11.7 Hz), 4.42 (1H, d, *J*=11.8 Hz), 4.22–4.14 (5H, m), 3.92–3.87 (1H, m), 3.86 (1H, d, *J*=12.0 Hz), 3.73–3.58 (6H, m), 3.56–3.50 (3H, m), 3.40 (1H, dd, *J*=6.8, 10.0 Hz), 3.31–3.26 (4H, m), 2.81 (1H, ddd, *J*=2.6, 10.2, 13.6 Hz), 2.71 (1H, ddd, *J*=2.3, 10.2, 12.7 Hz), 2.43 (1H, ddd, *J*=2.8, 4.6, 13.9 Hz), 2.31–2.25 (2H, m), 2.09 (1H, dt, *J*=13.6, 5.4 Hz), 2.02–1.90 (4H, m), 1.88–1.81 (2H, m), 1.57–1.49 (1H, m), 1.04 (3H, s), 1.03 (3H, d, *J*=7.1 Hz), 1.00 (9H, s), 0.15 (3H, s), 0.084 (3H, s); ^{13}C NMR (125 MHz, C_6D_6), δ (ppm) 160.5 (C), 139.3 (C), 139.2 (C), 138.2 (C), 138.1 (C), 132.1 (C), 131.7 (CH×2), 131.6 (CH×2), 129.22 (CH×2), 129.16 (CH×2), 128.54 (CH×2), 128.50 (CH×2), 128.45 (CH×2), 127.5 (CH), 121.5 (C), 121.4 (C), 113.7 (CH×2), 97.0 (CH), 84.8 (CH), 84.1 (CH), 83.8 (CH), 80.3 (CH), 79.7 (CH),

78.8 (CH), 75.3 (CH), 75.0 (CH), 74.8 (CH), 74.3 (C), 74.2 (CH), 73.3 (CH_2), 72.8 (CH_2), 72.7 (CH_2), 72.4 (CH_2), 71.3 (CH_2), 70.2 (CH_2), 54.8 (CH_3), 45.1 (CH_2), 33.9 (CH_2), 32.3 (CH_2), 31.2 (CH_2), 30.2 (CH_2), 28.9 (CH), 27.6 (CH_2), 26.8 (CH_3), 26.2 ($CH_3\times3$), 18.2 (C), 16.5 (CH_3), −4.08 (CH_3), −4.14 (CH_3) (The signals of seven carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3063, 3026, 2927, 2855, 1614, 1589, 1514, 1487, 1453, 1360, 1301, 1249, 1214, 1170, 1098, 1011, 940, 834, 804, 775, 753, 697; HR-FDMS, calcd for $C_{66}H_{84}^{79}Br_2O_{11}Si$ $[M]^+$: 1238.4150, found: 1238.4172.

7.1.27. (1*S*,3*R*,4*S*,6*S*,8*R*,10*R*,11*S*,1′*S*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-10-{2′-[8″-Benzyloxy-9″-benzyloxymethyl-3″-(*tert*-butyldimethylsilyloxy)-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl]-1′-(4-methoxybenzyloxy)ethyl}-4-(4-bromobenzyloxy)-3-(4-bromobenzyloxymethyl)-6,10-dimethyl-2,9-dioxabicyclo[6.4.0]dodecan-11-ol (33a) and (1*S*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*,1″*S*,3″*R*,4″*S*,6″*S*,8″*R*,10″*S*,11″*S*)-2-[8′-benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-1-{4″-(4-bromobenzyloxy)-3″-(4-bromobenzyloxymethy)-11″-(4-methoxybenzyloxy)-6″,10″-dimethyl-2″,9″-dioxabicyclo[6.4.0]dodecan-10″-yl}ethanol (33b).

7.1.27.1. Reaction of 32a. To a solution of **32a** (3.8 mg, 3.06 μmol) in DCM (0.50 ml) was added DIBAL (0.10 ml, 0.94 M in hexane, 94.0 μmol) at −30 °C and the mixture was stirred for 1.5 h. Then, MeOH (0.1 ml) and saturated aqueous potassium sodium tartrate (1 ml) were added. The mixture was diluted with Et_2O (5 ml) and stirred at 25 °C for 2 h. The layers were separated and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=7 to 5) to give **33** (3.8 mg, ∼100%, **33a**:**33b**=5:1 from ^1H NMR).

7.1.27.2. Reaction of 32b. To a solution of **32b** (4.0 mg, 3.22 μmol) in DCM (0.50 ml) was added DIBAL (0.10 ml, 0.94 M in hexane, 94.0 μmol) at −20 °C and the mixture was stirred for 2 h. Then, MeOH (0.1 ml) and saturated aqueous potassium sodium tartrate (1 ml) were added. The mixture was diluted with Et_2O (5 ml) and stirred at 25 °C for 3 h. The layers were separated and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=7 to 4) to give **33** (4.0 mg, ∼100%, **33b**:**33a**>20:1 from ^1H NMR). **33a**: a colorless oil; $[\alpha]_D^{21}$ −3.02 (*c* 0.150, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 7.40 (2H, d, *J*=8.5 Hz), 7.35 (2H, d, *J*=7.1 Hz), 7.29 (2H, d, *J*=8.3 Hz), 7.25–7.05 (8H, m), 6.98 (2H, d, *J*=8.5 Hz), 6.84 (2H, d, *J*=8.3 Hz), 6.81 (2H, d, *J*=8.5 Hz), 6.07 (1H, dt, *J*=5.1, 10.7 Hz), 5.97 (1H, dt, *J*=5.1, 10.7 Hz), 5.20 (1H, d, *J*=10.4 Hz), 4.73 (1H, d, *J*=10.4 Hz), 4.48 (1H, d, *J*=11.7 Hz), 4.46 (1H, d, *J*=11.8 Hz), 4.41 (1H, dt, *J*=7.8, 3.9 Hz), 4.31 (1H, dd, *J*=2.4, 10.2 Hz), 4.30 (1H, d, *J*=11.8 Hz), 4.26–4.16 (4H, m), 4.10–4.04 (1H, m), 3.95–3.92 (1H, m), 3.91 (1H, d, *J*=12.2 Hz), 3.84 (1H, dt, *J*=9.5, 3.4 Hz), 3.73–3.69 (2H, m), 3.65–3.64 (2H, m), 3.57 (1H, dd, *J*=2.4, 10.0 Hz), 3.55–3.49 (2H, m), 3.45 (1H, dd, *J*=6.3, 10.0 Hz), 3.34 (1H, dt, *J*=2.8, 8.8 Hz), 3.27 (3H, s), 2.96–2.89 (1H, m), 2.88–2.81 (1H, m), 2.47 (1H, dt, *J*=13.4, 4.0 Hz), 2.34 (1H, ddd, *J*=3.4, 5.1, 13.8 Hz), 2.14–1.79 (8H, m), 1.67 (1H, ddd, *J*=5.6, 8.9, 14.4 Hz), 1.07–1.05 (6H, m), 1.01 (9H, s), 0.18 (3H, s), 0.038 (3H, s); ^{13}C NMR (125 MHz, C_6D_6), δ (ppm) 159.8 (C), 139.3 (C), 139.1 (C), 138.2 (C), 138.1 (C), 131.7 (CH×2), 131.64 (CH×2), 131.60 (C), 130.1 (CH×2), 129.3 (CH×4), 129.2 (CH), 128.9 (CH), 128.54 (CH×2), 128.50 (CH×2), 121.6 (C), 121.5 (C), 114.1 (CH×2), 85.5 (CH), 85.1 (CH), 84.6 (CH), 80.8 (CH), 79.8 (CH×2), 78.5 (C), 78.1 (CH), 75.3 (CH), 74.3 (CH), 73.2 (CH_2), 72.7 (CH_2), 72.4 ($CH_2\times2$), 71.33 (CH_2), 71.30 (CH_2), 70.9 (CH), 70.3 (CH_2), 54.7 (CH_3), 45.9 (CH_2), 36.1 (CH_2), 32.5 (CH_2), 31.9 (CH_2), 30.4 (CH_3), 30.2 (CH_2), 28.9 (CH), 27.5 (CH_2), 26.9 (CH_3), 26.2 ($CH_3\times3$), 18.2 (C), −4.2 (CH_3), −4.3 (CH_3) (The signals of six carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3420, 3063, 3026, 2926, 2856, 1612, 1586, 1514, 1487, 1453, 1360, 1301, 1249, 1213, 1173, 1097, 1012, 939, 834, 804, 776, 750, 697; HR-FDMS, calcd for $C_{66}H_{86}^{79}Br_2O_{11}Si$ $[M]^+$: 1240.4306, found: 1240.4355. **33b**: a colorless oil; $[\alpha]_D^{20}$ +15.6 (*c* 0.150, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 7.36–7.22 (8H, m), 7.18–7.04 (8H, m), 6.94 (2H, d, *J*=8.5 Hz), 6.83 (2H, d, *J*=8.3 Hz), 6.76 (2H, d, *J*=8.8 Hz), 5.93 (1H, dt, *J*=6.2, 10.4 Hz), 5.85 (1H, dt, *J*=5.7, 10.4 Hz), 4.66–4.63 (1H, m), 4.60 (1H, d, *J*=12.1 Hz), 4.51 (2H, s), 4.38 (1H, d, *J*=11.7 Hz), 4.24 (1H, d, *J*=12.1 Hz), 4.22–4.17 (3H, m), 4.15 (1H, d, *J*=11.7 Hz), 4.06–4.03 (1H, m), 3.95–3.90 (3H, m), 3.87 (1H, d, *J*=11.7 Hz), 3.84–3.79 (2H, m), 3.73–3.68 (3H, m), 3.65 (1H, dt, *J*=2.7, 9.6 Hz), 3.61 (1H, d, *J*=2.7 Hz), 3.59 (1H, dd, *J*=2.3, 9.9 Hz), 3.41 (1H, dd, *J*=7.0, 9.9 Hz), 3.32–3.27 (4H, m, H20), 2.90–2.79 (2H, m), 2.45 (1H, ddd, *J*=3.3, 4.5, 13.8 Hz), 2.26 (1H, ddd, *J*=4.1, 5.7, 13.9 Hz), 2.25–2.17 (2H, m), 2.03–1.74 (6H, m), 1.62 (1H, ddd, *J*=5.5, 8.8, 14.8 Hz), 1.27 (3H, s), 1.08 (3H, d, *J*=6.6 Hz), 0.96 (9H, s), 0.080 (3H, s), 0.054 (3H, s); ^{13}C NMR (125 MHz, C_6D_6), δ (ppm) 159.6 (C), 139.4 (C), 139.1 (C), 138.2 (C), 138.0 (C), 131.73 (C), 131.66 (CH×2), 131.6 (CH×2), 129.3 (CH×2), 129.2 (CH×4), 128.44 (CH×2), 128.37 (CH×2), 127.54 (CH), 127.46 (CH), 126.8 (CH), 121.6 (C), 121.5 (C), 114.1 (CH×2), 86.0 (CH), 85.4 (CH), 81.3 (CH), 80.0 (CH), 79.9 (CH), 78.1 (C), 77.3 (CH), 76.9 (CH), 76.6 (CH), 74.3 (CH), 73.3 (CH_2), 73.0 (CH_2), 72.5 (CH_2), 72.1 (CH), 71.42 (CH_2), 71.37 (CH_2), 70.3 (CH_2), 69.4 (CH_2), 54.7 (CH_3), 45.5 (CH_2), 35.0 (CH_2), 32.0 (CH_2), 30.2 (CH_2), 29.8 (CH_2), 29.0 (CH), 26.9 (CH_2), 26.7 (CH_3), 26.1 ($CH_3\times3$), 18.2 (C), 15.0 (CH_3), −4.5 (CH_3), −4.6 (CH_3) (The signals of five carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3509, 3067, 3032, 2928, 2859, 1616, 1588, 1514, 1488, 1454, 1406, 1361, 1302, 1250, 1207, 1173, 1099, 1012, 940, 836, 805, 775, 735, 698; HR-FDMS, calcd for $C_{66}H_{86}^{79}Br_2O_{11}Si$ $[M]^+$: 1240.4306, found: 1240.4371.

7.1.28. (1*S*,3*R*,4*S*,6*S*,8*R*,10*S*,11*S*,1′*S*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-10-{2′-[8″-Benzyloxy-9″-benzyloxymethyl-3″-(*tert*-butyldimethylsilyloxy)-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl]-1′-(4-methoxybenzyloxy)ethyl}-4-(4-bromobenzyloxy)-3-(4-bromobenzyloxymethyl)-6,10-dimethyl-2,9-dioxabicyclo[6.4.0]dodecan-11-one (34). To a solution

of **33a** (3.0 mg, 2.41 μmol) in DCM (0.80 ml) was added DMPI (9.5 mg, 22.4 μmol) at 24 °C and the reaction mixture was stirred for 2 h. After the mixture was diluted with Et_2O (5 ml), saturated aqueous Na_2SO_3 (1 ml) was added and the aqueous layer was extracted with Et_2O (3×5 ml). The combined organic layers were washed with saturated aqueous Na_2SO_3 and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, benzene/AcOEt=15 to 5) to give **34** (2.1 mg, 70%). **34**: a colorless oil; $[\alpha]_D^{21}$ −14.4 (*c* 0.165, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6), δ (ppm) 7.42–7.28 (8H, m), 7.25–7.09 (8H, m), 6.94 (2H, d, *J*=8.5 Hz), 6.83–6.80 (4H, m), 6.07 (1H, dt, *J*=5.1, 10.6 Hz), 5.97 (1H, dt, *J*=5.1, 10.6 Hz), 4.91 (2H, s), 4.58 (1H, d, *J*=11.7 Hz), 4.49–4.45 (2H, m), 4.35 (1H, d, *J*=11.7 Hz), 4.34 (1H, dd, *J*=2.3, 11.0 Hz), 4.20–4.12 (4H, m), 3.87 (1H, d, *J*=11.7 Hz), 3.85–3.80 (2H, m), 3.68 (1H, dd, *J*=3.2, 10.2 Hz), 3.62 (1H, dd, *J*=2.0, 10.2 Hz), 3.54 (1H, ddd, *J*=2.1, 6.8, 8.8 Hz), 3.52–3.41 (4H, m), 3.33–3.27 (5H, m), 3.21 (1H, dt, *J*=2.1, 8.8 Hz), 2.94–2.87 (1H, m), 2.83–2.76 (1H, m), 2.62 (1H, dd, *J*=6.1, 16.8 Hz), 2.34–2.27 (2H, m), 2.13–2.08 (1H, m), 2.04–2.00 (1H, m), 1.89 (1H, ddd, *J*=2.3, 7.2, 14.5 Hz), 1.82–1.75 (3H, m), 1.61–1.53 (1H, m), 1.28 (3H, s), 1.05 (9H, s), 0.99 (3H, d, *J*=6.6 Hz), 0.25 (3H, s), 0.088 (3H, s); ^{13}C NMR (125 MHz, C_6D_6), δ (ppm) 210.8 (C), 159.6 (C), 139.4 (C), 139.3 (C), 137.9 (C), 137.8 (C), 132.0 (C), 131.73 (CH×2), 131.69 (CH×2), 129.8 (CH×2), 129.4 (CH×4), 128.9 (CH), 128.5 (CH), 121.7 (C), 121.6 (C), 114.0 (CH×2), 88.1 (C), 85.5 (CH), 85.4 (CH), 85.0 (CH), 83.1 (CH), 82.4 (CH), 79.7 (CH), 78.1 (CH), 75.1 (CH_2), 74.7 (CH×2), 73.1 (CH_2), 72.6 (CH_2), 72.2 (CH_2), 71.4 (CH_2), 71.3 (CH_2), 70.4 (CH_2), 54.8 (CH_3), 46.8 (CH_2), 44.6 (CH_2), 39.4 (CH_2), 31.3 (CH_2), 30.2 (CH_2), 28.7 (CH), 27.6 (CH_2), 26.8 (CH_3), 26.2 (CH_3×3), 18.7 (CH_3), 18.2 (C), −4.0 (CH_3), −4.2 (CH_3) (The signals of 10 carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3062, 3026, 2925, 2855, 1593, 1716, 1613, 1586, 1513, 1487, 1454, 1360, 1301, 1249, 1213, 1173, 1071, 1012, 939, 834, 804, 777, 750, 698; HR-FDMS, calcd for $C_{66}H_{84}^{79}Br_2O_{11}Si$ $[M]^+$: 1238.4150, found: 1238.4119.

7.1.29. (1*S*,3*R*,4*S*,6*S*,8*R*,10*R*,11*S*,1′*S*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-10-{2′-[8″-Benzyloxy-9″-benzyloxymethyl-3″-hydroxy-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl]-1′-(4-methoxybenzyloxy)ethyl}-4-(4-bromobenzyloxy)-3-(4-bromobenzyloxymethyl)-6,10-dimethyl-2,9-dioxabicyclo[6.4.0]dodecan-11-one (35). To a solution of **34** (2.1 mg, 1.69 μmol) in THF (0.80 ml) was added HF·Py at 0 °C. The reaction mixture was warmed to 24 °C and stirred for 1 d. After the reaction mixture was diluted with Et_2O and cooling to 0 °C, saturated aqueous $NaHCO_3$ (1 ml) was added and the mixture was stirred for 1 h. The layers were separated and the aqueous layer was extracted with AcOEt (3×5 ml). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=4 to 2) to give **35** (1.2 mg, 63%). **35** was immediately used for the next reaction. **35**: a colorless oil; ^{1}H NMR (400 MHz, C_6D_6), δ (ppm) 7.38–7.33 (4H, m), 7.32–7.27 (4H, m), 7.21–7.15 (6H, m), 7.11–7.07 (2H, m), 6.92 (2H, d, *J*=8.3 Hz), 6.82 (2H, d, *J*=8.5 Hz), 6.79 (2H, d, *J*=8.8 Hz), 5.97 (1H, dt, *J*=5.7, 10.5 Hz), 5.89 (1H, dt, *J*=5.7, 10.5 Hz), 4.86 (1H, d, *J*=11.0 Hz), 4.81 (1H, d, *J*=11.0 Hz), 4.54 (1H, d, *J*=12.2 Hz), 4.41 (1H, d, *J*=11.7 Hz), 4.40 (1H, d, *J*=12.2 Hz), 4.27 (1H, dd, *J*=2.0, 10.2 Hz, H11), 4.20–4.11 (4H, m), 4.02–3.99 (1H, m), 3.87 (1H, d, *J*=11.7 Hz), 3.80 (1H, dt, *J*=9.1, 6.6 Hz), 3.70 (1H, dt, *J*=7.9, 3.3 Hz), 3.63–3.62 (2H, m), 3.56–3.43 (5H, m), 3.30 (1H, dd, *J*=6.8, 10.2 Hz), 3.27 (3H, s), 3.26–3.20 (2H, m), 2.93 (1H, ddd, *J*=3.9, 10.5, 13.4 Hz), 2.72 (1H, ddd, *J*=3.3, 10.5, 13.1 Hz), 2.59 (1H, dd, *J*=6.6, 16.8 Hz), 2.50 (1H, ddd, *J*=1.1, 10.3, 14.6 Hz), 2.30 (1H, ddd, *J*=3.3, 5.7, 13.1 Hz), 2.14–2.08 (1H, m), 2.02 (1H, ddd, *J*=2.0, 7.4, 14.6 Hz), 1.99–1.95 (1H, m), 1.82–1.72 (3H, m), 1.55 (1H, ddd, *J*=5.6, 9.0, 14.4 Hz), 1.30 (3H, s), 0.97 (3H, d, *J*=6.8 Hz).

7.1.30. (1*S*,3*R*,4*S*,6*S*,8*R*,10*R*,11*S*,1′*S*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-10-{1′-Benzyloxy-2′-[8″-benzyloxy-9″-benzyloxymethyl-3″-(*tert*-butyldimethylsilyloxy)-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl]ethyl}-4-(4-bromobenzyloxy)-3-(4-bromobenzyloxymethyl)-11-(4-methoxybenzyloxy)-6,10-dimethyl-2,9-dioxabicyclo[6.4.0]dodecane (38). To a suspension of **33b** (2.5 mg, 2.01 μmol) and TBAI (5.0 mg, 13.5 μmol) in THF (1.0 ml) was added NaH (15.0 mg, 375 μmol) at 0 °C and the mixture was stirred for 10 min. Then, to the mixture was added benzyl bromide (20.0 μmol, 168 μmol) at 0 °C and the reaction mixture was warmed to 25 °C. During 5 d, NaH was added several times to the reaction mixture with stirring until the reaction was complete. After that, H_2O (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=50 to 10) to give **38** (1.9 mg, 71%). **38**: a colorless oil; $[\alpha]_D^{24}$ +8.71 (*c* 0.125, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6), δ (ppm) 7.41–7.03 (17H, m), 6.94 (2H, d, *J*=8.3 Hz), 6.83 (2H, d, *J*=8.5 Hz), 6.72 (2H, d, *J*=8.8 Hz), 6.00 (1H, dt, *J*=5.6, 10.6 Hz), 5.94 (1H, dt, *J*=5.6, 10.6 Hz), 5.03 (1H, d, *J*=12.0 Hz), 4.79 (1H, d, *J*=12.0 Hz), 4.59–4.58 (1H, m), 4.55 (1H, d, *J*=12.8 Hz), 4.48 (1H, d, *J*=12.8 Hz), 4.44 (1H, d, *J*=11.5 Hz), 4.43 (1H, d, *J*=11.3 Hz), 4.24–4.20 (5H, m), 4.17 (1H, d, *J*=11.3 Hz), 3.93 (1H, dt, *J*=8.9, 2.8 Hz), 3.87 (1H, d, *J*=12.0 Hz), 3.86–3.83 (1H, m), 3.82–3.73 (4H, m), 3.72–3.62 (3H, m), 3.61 (1H, dd, *J*=2.2, 9.9 Hz), 3.40 (1H, dd, *J*=7.4, 9.9 Hz), 3.28 (1H, dt, *J*=2.6, 8.7 Hz), 3.26 (3H, s), 2.98–2.84 (2H, m), 2.53 (1H, dt, *J*=14.4, 3.7 Hz), 2.35–2.28 (2H, m), 2.21–2.12 (1H, m), 2.06–1.78 (6H, m), 1.68–1.56 (1H, m), 1.35 (3H, s), 1.08 (3H, d, *J*=6.8 Hz), 1.00 (9H, s), 0.16 (3H, s), 0.048 (3H, s); ^{13}C NMR (125 MHz, C_6D_6), δ (ppm) 159.6 (C), 140.6 (C), 139.9 (C), 139.5 (C), 138.1 (C), 138.0 (C), 131.69 (CH×2), 131.65 (CH×2), 131.2 (C), 129.7 (CH×2), 129.4 (CH×2), 129.3 (CH×2), 128.5 (CH), 127.3 (CH), 127.23 (CH), 127.15 (CH), 121.63 (C), 121.60 (C), 114.1 (CH×2), 85.7 (CH), 84.4 (CH), 82.5 (CH), 81.2 (CH), 79.9 (CH), 78.8 (C), 78.4 (CH), 77.3 (CH), 77.0 (CH), 75.7 (CH), 74.4 (CH), 73.3 (CH_2), 73.1 (CH_2), 72.54 (CH_2), 72.46 (CH_2), 71.5 (CH_2), 71.1 (CH_2), 70.4 (CH_2), 70.3 (CH_2), 54.7 (CH_3), 45.6 (CH_2), 39.4 (CH_2), 33.3 (CH_2), 31.4 (CH_2), 30.9 (CH_2), 29.0 (CH), 27.4 (CH_2), 26.7 (CH_3), 26.2

($CH_3\times3$), 18.2 (C), 15.6 (CH_3), −4.1 (CH_3), −4.4 (CH_3) (The signals of 13 carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3063, 3028, 2926, 2855, 1612, 1586, 1513, 1487, 1454, 1367, 1301, 1249, 1206, 1172, 1097, 1012, 939, 835, 804, 775, 733, 697; HR-FDMS, calcd for $C_{73}H_{92}^{79}Br_2O_{11}Si$ $[M]^+$: 1330.4776, found: 1330.4784.

7.1.31. (1*S*,3*R*,4*S*,6*S*,8*R*,10*R*,11*S*,1′*S*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-10-{1′-Benzyloxy-2′-[8″-benzyloxy-9″-benzyloxymethyl-3″-(*tert*-butyldimethylsilyloxy)-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl]ethyl}-4-(4-bromobenzyloxy)-3-(4-bromobenzyloxymethyl)-6,10-dimethyl-2,9-dioxabicyclo[6.4.0]dodecan-11-ol (39). To a solution of **38** (4.4 mg, 3.30 μmol) in DCM–pH 7 buffer (10:1, v/v, 0.70 ml) was added DDQ (5.0 mg, 22.0 μmol) at 0 °C and the mixture was stirred for 20 min. Then, saturated aqueous $NaHCO_3$ (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=30 to 5) to give **39** (3.4 mg, 85%). **39**: a colorless oil; $[\alpha]_D^{22}$ −2.29 (*c* 0.170, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 7.43 (2H, d, *J*=7.1 Hz), 7.35 (2H, d, *J*=6.8 Hz), 7.31–7.28 (4H, m), 7.24–7.08 (11H, m), 6.98 (2H, d, *J*=8.3 Hz), 6.84 (2H, d, *J*=8.3 Hz), 6.05 (1H, dt, *J*=5.2, 10.9 Hz), 5.95 (1H, dt, *J*=5.2, 10.9 Hz), 5.22 (1H, d, *J*=10.7 Hz), 4.76 (1H, d, *J*=10.7 Hz), 4.47 (1H, d, *J*=11.7 Hz), 4.46 (1H, d, *J*=12.1 Hz), 4.38–4.34 (2H, m), 4.30 (1H, d, *J*=12.1 Hz), 4.25 (1H, d, *J*=12.7 Hz), 4.21 (1H, d, *J*=11.9 Hz), 4.19 (1H, d, *J*=12.7 Hz), 4.17 (1H, d, *J*=11.7 Hz), 4.04–3.98 (1H, m), 3.92–3.89 (2H, m), 3.83 (1H, dt, *J*=9.0, 3.0 Hz), 3.71–3.63 (4H, m), 3.57 (1H, dd, *J*=2.1, 9.9 Hz), 3.54–3.52 (1H, m), 3.50 (1H, dt, *J*=9.0, 3.0 Hz), 3.44 (1H, dd, *J*=6.5, 9.9 Hz), 3.32 (1H, dt, *J*=2.6, 8.9 Hz), 2.88–2.78 (2H, m), 2.43 (1H, dt, *J*=13.4, 4.2 Hz), 2.32 (1H, ddd, *J*=3.0, 5.2, 13.7 Hz), 2.11–1.78 (8H, m), 1.64 (1H, ddd, *J*=6.1, 8.9, 14.6 Hz), 1.06 (3H, s), 1.05 (3H, d, *J*=6.8 Hz), 1.01 (9H, s), 0.17 (3H, s), 0.024 (3H, s); ^{13}C NMR (125 MHz, C_6D_6), δ (ppm) 139.6 (C), 139.3 (C), 139.1 (C), 138.2 (C), 138.1 (C), 131.7 (CH×2), 131.6 (CH×2), 129.33 (CH×2), 129.32 (CH×2), 128.9 (CH), 128.60 (CH×2), 128.55 (CH×2), 128.5 (CH×2), 128.3 (CH×2), 121.6 (C), 121.5 (C), 85.5 (CH), 85.1 (CH), 84.6 (CH), 80.7 (CH), 79.7 (CH×2), 78.5 (C), 78.0 (CH), 75.3 (CH), 74.2 (CH), 73.2 (CH_2), 72.7 (CH_2), 72.4 ($CH_2\times2$), 71.3 (CH_2), 71.2 (CH_2), 70.9 (CH), 70.3 (CH_2), 45.9 (CH_2), 39.9 (CH_2), 36.1 (CH_2), 32.4 (CH_2), 31.8 (CH_2), 30.4 (CH_3), 28.9 (CH), 27.5 (CH_2), 26.9 (CH_3), 26.2 ($CH_3\times3$), 18.2 (C), −4.3 ($CH_3\times2$) (The signals of eight carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3584, 3433, 3063, 3028, 2923, 2857, 1593, 1487, 1454, 1405, 1359, 1298, 1256, 1207, 1096, 1012, 940, 836, 804, 776, 749, 698; HR-FDMS, calcd for $C_{65}H_{84}^{79}Br_2O_{10}Si$ $[M]^+$: 1210.4200, found: 1210.4218.

7.1.32. (1*S*,3*R*,4*S*,6*S*,8*R*,10*S*,11*S*,1′*S*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-10-[1′-Benzyloxy-2′-(8″-benzyloxy-9″-benzyloxymethyl-3″-hydroxy-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl)ethyl]-4-(4-bromobenzyloxy)-3-(4-bromobenzyloxymethyl)-6,10-dimethyl-2,9-dioxabicyclo[6.4.0]dodecan-11-one (41). To a solution of **39** (3.4 mg, 2.80 μmol) in DCM (0.70 ml) were added $NaHCO_3$ (5.0 mg, 59.5 μmol) and DMPI (5.0 mg, 11.8 μmol) at 25 °C and the reaction mixture was stirred for 30 min. After the mixture was diluted with Et_2O (1 ml), saturated aqueous Na_2SO_3 (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with saturated aqueous Na_2SO_3 and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was roughly purified by column chromatography (silica gel, hexane/AcOEt=5 to 4) to give a crude product (3.4 mg), and it was used in the next reaction without further purification. To a solution of the above crude product in THF–H_2O (1:1, v/v, 0.80 ml) was added TFA (40.0 μl) at 0 °C. The reaction mixture was warmed to 25 °C and stirred for 2 d. Then, $NaHCO_3$ (1 ml) was added and the aqueous layer was extracted with AcOEt (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=5 to 2) to give **41** (2.3 mg, 75% from **39**). **41**: a colorless oil; $[\alpha]_D^{21}$ −21.3 (*c* 0.115, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 7.41–7.35 (4H, m), 7.32–7.27 (4H, m), 7.21–7.04 (11H, m), 6.92 (2H, d, *J*=8.3 Hz), 6.82 (2H, d, *J*=8.5 Hz), 5.94 (1H, dt, *J*=5.5, 10.2 Hz), 5.87 (1H, dt, *J*=5.5, 10.2 Hz), 4.90 (1H, d, *J*=11.5 Hz), 4.85 (1H, d, *J*=11.5 Hz), 4.53 (1H, d, *J*=12.1 Hz), 4.40 (1H, d, *J*=12.1 Hz), 4.39 (1H, d, *J*=12.1 Hz), 4.28 (1H, dd, *J*=2.0, 10.4 Hz), 4.18 (1H, d, *J*=11.7 Hz), 4.16 (1H, d, *J*=12.1 Hz), 4.12 (1H, d, *J*=12.1 Hz), 3.98 (1H, dt, *J*=8.8, 3.5 Hz), 3.86 (1H, d, *J*=11.7 Hz), 3.76 (1H, dt, *J*=9.0, 6.6 Hz), 3.69 (1H, dt, *J*=8.7, 3.3 Hz), 3.62 (2H, d, *J*=2.4 Hz), 3.55–3.43 (5H, m), 3.30 (1H, dd, *J*=7.1, 10.2 Hz), 3.23–3.17 (2H, m), 2.87 (1H, ddd, *J*=3.5, 10.2, 13.4 Hz), 2.70 (1H, ddd, *J*=3.3, 10.2, 13.4 Hz), 2.58 (1H, dd, *J*=6.6, 16.8 Hz), 2.50 (1H, ddd, *J*=2.0, 10.4, 14.6 Hz), 2.28 (1H, ddd, *J*=3.3, 5.5, 13.4 Hz), 2.07–1.95 (3H, m), 1.81–1.67 (3H, m), 1.53 (1H, ddd, *J*=6.1, 8.8, 14.9 Hz), 1.28 (3H, s), 0.96 (3H, d, *J*=6.6 Hz); ^{13}C NMR (125 MHz, C_6D_6), δ (ppm) 210.5 (C), 139.5 (C), 139.3 (C), 139.2 (C), 137.9 (C), 137.8 (C), 133.0 (C), 131.74 (CH×2), 131.70 (CH×2), 129.4 (CH×4), 128.6 (CH×2), 128.50 (CH×2), 128.47 (CH×2), 127.6 (CH×2), 121.74 (C), 121.69 (C), 87.8 (C), 85.2 (CH), 84.8 (CH), 84.7 (CH), 82.5 (CH), 82.2 (CH), 79.7 (CH), 78.4 (CH), 75.0 (CH_2), 74.6 (CH), 74.4 (CH), 73.1 (CH_2), 72.6 (CH_2), 72.1 (CH_2), 71.9 (CH_2), 71.3 (CH_2), 70.4 (CH_2), 46.5 (CH_2), 44.4 (CH_2), 39.4 (CH_2), 34.5 (CH_2), 33.1 (CH_2), 28.6 (CH), 27.7 (CH_2), 26.8 (CH_3), 18.5 (CH_3) (The signals of nine carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3465, 3063, 3027, 2924, 2858, 1716, 1592, 1487, 1453, 1405, 1366, 1305, 1256, 1215, 1098, 1027, 1012, 911, 839, 803, 753, 698; HR-FDMS, calcd for $C_{59}H_{68}^{79}Br_2O_{10}$ $[M]^+$: 1094.3179, found: 1094.3176.

7.1.33. (1*R*,3*S*,5*Z*,8*R*,9*S*,11*R*,13*S*,14*S*,16*R*,18*S*,20*S*,21*R*,23*S*)-8,13-Dibenzyloxy-9-benzyloxymethyl-20-(4-bromobenzyloxy)-21-(4-bromobenzyloxymethyl)-14,18-dimethyl-2,10,15,22-tetraoxatetracyclo[12.10.0.0^{3,11}.0^{16,23}]-tetracos-5-ene (42). To a solution of **41** (2.3 mg, 2.10 μmol) in DCM–Et_3SiH (10:1, v/v, 0.70 ml) was added TMSOTf (3.0 μl, 16.6 μmol) at 0 °C and the mixture was stirred for 30 min. Then, saturated aqueous $NaHCO_3$ (1 ml) was added

and the aqueous layer was extracted with Et_2O (5 ml) and AcOEt (3×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=10 to 4) to give **41** (1.6 mg, 70%). **41**: a colorless oil; $[\alpha]_D^{22}$ −60.8 (*c* 0.080, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$), δ (ppm) 7.45–7.41 (4H, m), 7.37–7.18 (17H, m), 7.07 (2H, d, *J*=8.5 Hz), 5.81 (1H, dt, *J*=5.2, 10.7 Hz), 5.71 (1H, dt, *J*=5.2, 10.7 Hz), 4.621 (2H, s), 4.617 (1H, d, *J*=11.3 Hz), 4.525 (1H, d, *J*=12.8 Hz), 4.516 (1H, d, *J*=11.5 Hz), 4.50 (1H, d, *J*=12.1 Hz), 4.465 (1H, d, *J*=12.1 Hz), 4.461 (1H, d, *J*=12.8 Hz), 4.30 (1H, d, *J*=11.3 Hz), 4.23 (1H, d, *J*=11.5 Hz), 4.07–4.03 (1H, m), 3.88 (1H, dd, *J*=4.3, 12.4 Hz), 3.72–3.68 (1H, m), 3.59 (1H, dd, *J*=1.8, 9.8 Hz), 3.56–3.48 (3H, m), 3.45 (1H, dd, *J*=5.7, 9.8 Hz), 3.41–3.29 (4H, m), 3.27–3.21 (2H, m), 2.80–2.73 (1H, m), 2.68–2.61 (1H, m), 2.43 (1H, ddd, *J*=5.5, 9.1, 15.4 Hz), 2.33–2.27 (1H, m), 2.18 (1H, dt, *J*=12.4, 4.3 Hz), 2.12–2.06 (1H, m), 1.98–1.90 (3H, m), 1.80–1.75 (1H, m), 1.71–1.51 (3H, m), 1.06 (3H, d, *J*=7.1 Hz), 1.00 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm) 139.5 (C), 138.4 (C), 138.2 (C), 137.4 (C), 137.3 (C), 131.5 (CH×4), 129.4 (CH×2), 129.3 (CH×2), 128.8 (CH), 128.33 (CH×2), 128.29 (CH×2), 128.1 (CH×4), 127.8 (CH×2), 127.6 (CH×2), 127.5 (CH×2), 127.13 (CH), 127.05 (CH), 121.5 (C), 121.4 (C), 85.8 (CH), 85.2 (CH), 84.8 (CH), 84.2 (CH), 82.5 (CH), 81.6 (CH), 79.7 (C), 79.0 (CH), 77.7 (CH), 73.6 (CH), 73.4 (CH_2), 73.2 (CH_2), 72.7 (CH_2), 72.6 (CH), 71.9 (CH_2), 71.4 (CH_2), 71.1 (CH_2), 70.5 (CH_2), 45.3 (CH_2), 40.6 (CH_2), 37.2 (CH_2), 34.6 (CH_2), 32.1 (CH_2), 28.1 (CH), 27.1 (CH_2, CH_3), 13.7 (CH_3); IR (film), ν (cm^{-1}) 3062, 3027, 2923, 2854, 1593, 1495, 1487, 1454, 1376, 1330, 1315, 1259, 1204, 1096, 1027, 1012, 803, 778, 735, 697; HR-FDMS, calcd for $C_{59}H_{68}^{79}Br_2O_9$ $[M]^+$: 1078.3230, found: 1078.3226.

7.1.34. (2*R*,3*S*,5*Z*,8*R*,9*S*,1′*S*,3′*R*,4′*S*,6′*S*,8′*R*,10′*R*,11′*S*)-[8-Benzyloxy-9-benzyloxymethyl-3-*(tert*-butyldimethylsilyloxy)-2,3,4,7,8,9-hexahydrooxonin-2-yl]methyl 4′-(4-bromobenzyloxy)-3′-(4-bromobenzyloxymethyl)-6′,10′-dimethyl-11′-triethylsilyloxy-2′,9′-dioxabicyclo[6.4.0]dodecan-10′-yl ketone (45). To a solution of oxalyl dichloride (21.0 μl, 241 μmol) in DCM (0.30 ml) was added a solution of DMSO (30.0 μl, 423 μmol) in DCM (0.30 ml) at −78 °C and the mixture was stirred for 10 min. Then, a solution of **26** (32.7 mg, 26.4 μmol) in DCM (0.90 ml) was added at −78 °C and the mixture was warmed to −45 °C and stirred for 1 h. After Et_3N (120 μl, 861 μmol) was added, the reaction mixture was warmed to 0 °C and stirred for 15 min. H_2O (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with 1 M HCl, saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was roughly purified by column chromatography (silica gel, hexane/AcOEt=5) to give a mixture of **26** and **45** (31.6 mg). In order to consume **26** completely, the process was repeated as follows: to a solution of oxalyl dichloride (42.0 μl, 481 μmol) in DCM (0.30 ml) was added a solution of DMSO (60.0 μl, 846 μmol) in DCM (0.40 ml) at −78 °C and the mixture was stirred for 10 min. Then, a solution of the above mixture (31.6 mg) in DCM (0.90 ml) was added at −78 °C and the mixture was warmed to −45 °C and stirred for 1 h. After Et_3N (240 μl, 1.72 mmol) was added, the reaction mixture was warmed to 0 °C and stirred for 20 min. H_2O (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with 1 M HCl, saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=15 to 10) to give **45** (19.8 mg, 61%). **45**: a colorless oil; $[\alpha]_D^{23}$ +27.2 (*c* 0.900, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 7.35–7.23 (8H, m), 7.20–7.06 (6H, m), 6.95 (2H, d, *J*=8.3 Hz), 6.81 (2H, d, *J*=8.3 Hz), 5.96–5.92 (2H, m), 4.51 (1H, d, *J*=12.2 Hz), 4.48 (1H, d, *J*=11.6 Hz), 4.45 (1H, d, *J*=12.2 Hz), 4.39 (1H, ddd, *J*=3.2, 5.4, 8.3 Hz), 4.30 (2H, d, *J*=11.6 Hz), 4.28 (1H, dt, *J*=9.0, 2.6 Hz), 4.21 (1H, d, *J*=11.7 Hz), 4.20 (1H, s), 4.16 (1H, t, *J*=2.9 Hz), 3.98 (1H, dt, *J*=9.0, 3.9 Hz), 3.96 (1H, dt, *J*=2.2, 5.4 Hz), 3.89–3.83 (2H, m), 3.80 (2H, d, *J*=2.6 Hz), 3.72 (1H, ddd, *J*=2.1, 7.1, 9.0 Hz), 3.61 (1H, dd, *J*=2.1, 9.8 Hz), 3.55 (1H, dt, *J*=3.0, 9.4 Hz), 3.38 (1H, dd, *J*=7.1, 9.8 Hz), 3.37 (1H, dd, *J*=8.3, 18.8 Hz), 3.25 (1H, dt, *J*=2.6, 9.0 Hz), 3.03 (1H, dd, *J*=3.2, 18.8 Hz), 2.97–2.90 (1H, m), 2.83 (1H, ddd, *J*=2.9, 9.0, 13.4 Hz), 2.34 (1H, dt, *J*=13.4, 3.9 Hz), 2.25 (1H, dt, *J*=13.4, 5.4 Hz), 2.22 (1H, dt, *J*=13.7, 2.9 Hz), 2.05–2.02 (1H, m), 1.95–1.87 (3H, m), 1.79 (1H, ddd, *J*=2.9, 11.2, 13.7 Hz), 1.65 (1H, ddd, *J*=5.2, 9.0, 14.5 Hz), 1.13 (3H, s), 1.07 (3H, d, *J*=6.3 Hz), 1.004 (9H, t, *J*=7.9 Hz), 0.997 (9H, s), 0.62 (6H, q, *J*=7.9 Hz), 0.19 (3H, s), 0.099 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 212.2 (C), 138.75 (C), 138.68 (C), 137.4 (C), 137.2 (C), 131.5 (CH×2), 131.4 (CH×2), 129.4 (CH×2), 129.3 (CH×2), 128.2 (CH×4), 127.9 (CH×3), 127.8 (CH×3), 127.7 (CH), 127.4 (CH×2), 121.5 (C), 121.4 (C), 85.9 (CH), 83.4 (C), 82.0 (CH), 80.4 (CH), 80.2 (CH), 79.1 (CH), 77.9 (CH), 73.8 (CH), 73.7 (CH), 73.2 (CH_2), 72.5 (CH_2), 72.1 (CH), 72.0 (CH_2), 71.7 (CH_2), 71.4 (CH_2), 70.6 (CH_2), 70.1 (CH_2), 45.6 (CH_2), 44.4 (CH_2), 40.7 (CH_2), 35.7 (CH_2), 32.0 (CH_2), 28.1 (CH), 27.5 (CH_2), 27.0 (CH_3), 26.0 (CH_3×3), 18.20 (CH_3), 18.16 (C), 6.9 (CH_3×3), 4.7 (CH_2×3), −4.5 (CH_3), −4.6 (CH_3); IR (film), ν (cm^{-1}) 3026, 2926, 1719, 1593, 1487, 1453, 1361, 1337, 1257, 1202, 1098, 1070, 1012, 960, 836, 776, 733, 697; HR-FDMS, calcd for $C_{64}H_{90}^{79}Br_2O_{10}Si_2$ $[M]^+$: 1232.4439, found: 1232.4431.

7.1.35. (2*R*,3*S*,5*Z*,8*R*,9*S*,1′*S*,3′*R*,4′*S*,6′*S*,8′*R*,10′*R*,11′*S*)-[8-Benzyloxy-9-benzyloxymethyl-3-*(tert*-butyldimethylsilyloxy)-2,3,4,7,8,9-hexahydrooxonin-2-yl]methyl 4′-(4-bromobenzyloxy)-3′-(4-bromobenzyloxymethyl)-11′-hydroxy-6′,10′-dimethyl-2′,9′-dioxabicyclo[6.4.0]dodecan-10′-yl ketone (46). To a solution of **45** (19.8 mg, 16.0 μmol) in THF–pyridine (2:1, v/v, 1.35 ml) was added HF·Py (excess) at 25 °C. During 6 d, HF·Py was added several times to the reaction mixture with stirring until the reaction was complete. After the reaction mixture was diluted with Et_2O and cooled to 0 °C, saturated aqueous $NaHCO_3$ (1 ml) was added and the mixture was stirred for 1 h. The layers were separated and the aqueous layer was extracted with Et_2O (3×5 ml). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=10 to 3) to give **46**

(13.8 mg, 71%). **46**: a colorless oil; $[\alpha]_D^{23}$ +36.0 (*c* 0.150, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 7.35–7.28 (5H, m), 7.23–7.05 (9H, m), 6.96 (2H, d, *J*=8.3 Hz), 6.82 (2H, d, *J*=8.5 Hz), 5.99 (1H, dt, *J*=4.9, 10.7 Hz), 5.95 (1H, dt, *J*=4.9, 10.7 Hz), 4.48–4.41 (3H, m), 4.24 (1H, dt, *J*=7.6, 3.4 Hz), 4.22–4.14 (4H, m), 4.10 (1H, ddd, *J*=3.4, 5.4, 8.2 Hz), 3.93 (1H, ddd, *J*=2.4, 4.5, 8.3 Hz), 3.88 (1H, d, *J*=12.0 Hz), 3.85–3.73 (3H, m), 3.67 (1H, dd, *J*=4.5, 10.5 Hz), 3.60 (1H, dd, *J*=2.4, 10.5 Hz), 3.58–3.49 (4H, m), 3.38 (1H, dd, *J*=6.6, 10.0 Hz), 3.27 (1H, dt, *J*=2.4, 9.0 Hz), 3.17 (1H, dd, *J*=5.4, 19.5 Hz), 3.04 (1H, ddd, *J*=3.4, 10.7, 13.2 Hz), 2.77 (1H, ddd, *J*=3.0, 10.7, 13.5 Hz), 2.29 (1H, dt, *J*=13.5, 4.9 Hz), 2.23–2.16 (2H, m), 2.00–1.96 (1H, m), 1.92–1.79 (3H, m), 1.70 (1H, ddd, *J*=2.8, 11.0, 13.7 Hz), 1.58 (1H, ddd, *J*=5.4, 9.0, 14.8 Hz), 1.21 (3H, s), 1.04 (3H, d, *J*=6.8 Hz), 0.97 (9H, s), 0.12 (3H, s), 0.075 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 213.3 (C), 138.5 (C), 138.3 (C), 137.4 (C), 137.3 (C), 131.44 (CH×2), 131.41 (CH×2), 129.3 (CH×4), 128.31 (CH×2), 128.26 (CH×2), 127.94 (CH×2), 127.88 (CH), 127.7 (CH×3), 127.6 (CH), 127.5 (CH), 121.5 (C), 121.4 (C), 85.4 (CH), 83.2 (CH), 81.1 (CH), 79.8 (CH), 78.8 (CH), 78.3 (CH), 77.2 (C), 73.7 (CH), 73.1 (CH), 73.0 (CH_2), 72.5 (CH_2), 71.7 (CH_2), 71.2 (CH_2), 70.8 (CH), 70.6 (CH_2), 70.5 (CH_2), 45.3 (CH_2), 41.9 (CH_2), 40.4 (CH_2), 34.5 (CH_2), 32.0 (CH_2), 28.1 (CH), 27.01 (CH_2), 26.96 (CH_3), 25.8 (CH_3×3), 18.2 (CH_3), 17.9 (C), −4.3 (CH_3), −4.8 (CH_3); IR (film), ν (cm^{-1}) 3463, 3026, 2926, 2854, 1715, 1593, 1487, 1453, 1361, 1257, 1204, 1099, 1069, 1011, 836, 803, 776, 735, 697; HR-FDMS, calcd for $C_{58}H_{76}^{79}Br_2O_{10}Si$ $[M]^+$: 1118.3574, found: 1118.3552.

7.1.36. (1*S*,3*R*,4*S*,6*S*,8*R*,10*R*,11*S*,1′*R*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-10-{2′-[8″-Benzyloxy-9″-benzyloxymethyl-3″-(*tert*-butyldimethylsilyloxy)-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl]-1′-hydroxyethyl}-4-(4-bromobenzyloxy)-3-(4-bromobenzyloxymethyl)-6,10-dimethyl-2,9-dioxabicyclo[6.4.0]dodecan-11-ol (47). To a solution of **46** (2.8 mg, 2.31 μmol) in MeOH (0.70 ml) was added $NaBH_4$ (7.3 mg, 193 μmol) at 0 °C and the reaction mixture was stirred for 15 min. Then, H_2O (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=15 to 10) to give a mixture of **47** and **31** (2.8 mg, ~100%, **47**:**31**=2:1 from ^1H NMR). This mixture of **47** and **31** was separated by HPLC (hexane/AcOEt=4) to give **47** (1.6 mg, 61%) as less-polar eluate and **31** (0.7 mg, 27%) as polar eluate. **47**: a colorless oil; $[\alpha]_D^{20}$ +7.67 (*c* 0.225, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 7.40 (2H, d, *J*=7.3 Hz), 7.31−7.05 (12H, m), 7.00 (2H, d, *J*=8.3 Hz), 6.83 (2H, d, *J*=8.3 Hz), 5.93 (1H, dt, *J*=5.5, 10.4 Hz), 5.87 (1H, dt, *J*=5.5, 10.4 Hz), 4.82−4.79 (1H, m), 4.52 (1H, d, *J*=11.6 Hz), 4.40 (1H, d, *J*=11.7 Hz), 4.30 (1H, d, *J*=11.6 Hz), 4.25 (1H, d, *J*=12.3 Hz), 4.24−4.20 (2H, m), 4.19 (1H, d, *J*=12.3 Hz), 4.13 (1H, d, *J*=11.7 Hz), 4.04 (1H, dt, *J*=4.8, 10.4 Hz), 4.02−3.99 (1H, m), 3.96 (1H, dt, *J*=1.8, 5.5 Hz), 3.92−3.89 (2H, m), 3.84−3.82 (1H, m), 3.77−3.72 (3H, m), 3.68 (1H, ddd, *J*=2.2, 6.7, 9.0 Hz), 3.63−3.59 (2H, m), 3.57 (1H, dd, *J*=2.2, 9.8 Hz), 3.45 (1H, dd, *J*=6.6, 9.8 Hz), 3.33 (1H, dt, *J*=2.4, 9.0 Hz), 2.79−2.67 (2H, m), 2.52 (1H, ddd, *J*=2.9, 4.8, 13.3 Hz), 2.29−2.24 (1H, m), 2.15 (1H, dt, *J*=13.5, 5.5 Hz), 2.04−1.77 (7H, m), 1.61 (1H, ddd, *J*=6.1, 9.0, 15.0 Hz), 1.053 (3H, s), 1.050 (3H, d, *J*=6.6 Hz), 0.96 (9H, s), 0.056 (3H, s), 0.030 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm) 138.3 (C), 137.8 (C), 137.5 (C), 137.4 (C), 131.41 (CH×2), 131.39 (CH×2), 129.31 (CH×2), 129.27 (CH×2), 128.4 (CH), 128.3 (CH×3), 128.2 (CH×2), 127.8 (CH×2), 127.7 (CH), 127.6 (CH), 126.9 (CH), 121.4 (C), 121.3 (C), 85.3 (CH), 83.9 (CH), 81.5 (CH), 80.4 (CH), 78.8 (CH), 77.2 (CH), 75.8 (C), 74.5 (CH), 74.0 (CH), 73.6 (CH), 73.2 (CH_2), 72.9 (CH), 72.5 (CH_2), 71.6 (CH_2), 71.4 (CH_2), 70.5 (CH_2), 69.1 (CH_2), 45.6 (CH_2), 40.5 (CH_2), 35.7 (CH_2), 32.5 (CH_2), 29.7 (CH_2), 28.3 (CH), 27.0 (CH_3), 26.8 (CH_2), 25.8 (CH_3×3), 18.0 (C), 17.5 (CH_3), −4.2 (CH_3), −4.6 (CH_3); IR (film), ν (cm^{-1}) 3397, 3026, 2961, 2851, 1593, 1487, 1454, 1405, 1360, 1296, 1256, 1204, 1100, 1028, 1012, 947, 836, 804, 776, 751, 698; HR-FDMS, calcd for $C_{58}H_{78}^{79}Br_2O_{10}Si$ $[M]^+$: 1120.3731, found: 1120.3730.

7.1.37. Conversion of 31 to 26. To a solution of **31** (2.1 mg, 1.87 μmol) in DCM (0.50 ml) were added 2,6-lutidine (20 μl, 172 μmol) and TESOTf (3.0 μl, 13.3 μmol) at −40 °C. After the mixture was stirred for 25 min, TESOTf (2.0 μl, 8.8 μmol) was added to the mixture at −40 °C. The mixture was stirred for 35 min. Then, saturated aqueous $NaHCO_3$ (0.5 ml) was added and the aqueous layer was extracted with Et_2O (4×3 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=7) to give **26** (2.2 mg, 95%).

7.1.38. (1*R*,3*R*,4*R*,6*S*,8*S*,10*S*,12*R*,13*S*,15*S*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*)-4-[8′-Benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-13-(4-bromobenzyloxy)-12-(4-bromobenzyloxymethyl)-3,15-dimethyl-6-(2-naphthyl)-2,5,7,11-tetraoxatricyclo[8.6.0.0^{3,8}]hexadecane (48). To a solution of **47** (4.2 mg, 3.74 μmol) in benzene (1.0 ml) were added 2-naphthaldehyde dimethyl acetal (27.1 mg, 134 μmol) and PPTS (4.3 mg, 17.1 μmol). The reaction mixture was heated to 80 °C and stirred for 1.5 h. Then, saturated aqueous $NaHCO_3$ (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=30 to 4) to give **48** (4.2 mg, 89%,). **48**: a colorless oil; $[\alpha]_D^{22}$ +39.4 (*c* 0.160, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 8.28 (1H, s), 7.93 (1H, dd, *J*=1.5, 8.4 Hz), 7.81–7.76 (2H, m), 7.62 (1H, *J*=1.5, 7.7 Hz), 7.28–7.01 (16H, m), 6.94 (2H, d, *J*=8.3 Hz), 6.78 (2H, d, *J*=8.3 Hz), 5.99 (1H, dt, *J*=6.7, 10.5 Hz), 5.89 (1H, dt, *J*=6.0, 10.5 Hz), 5.75 (1H, s), 4.46 (1H, d, *J*=12.0 Hz), 4.28–4.11 (8H, m), 4.08 (1H, dt, *J*=9.1, 2.2 Hz), 4.02–4.00 (1H, m), 3.96 (1H, dt, *J*=9.1, 2.9 Hz), 3.92–3.86 (2H, m), 3.83 (1H, d, *J*=12.0 Hz), 3.66 (1H, dd, *J*=2.2, 10.1 Hz), 3.58 (1H, t, *J*=2.9 Hz), 3.55 (1H, dt, *J*=2.8, 9.6 Hz), 3.48 (1H, ddd, *J*=2.2, 6.6, 8.8 Hz), 3.46 (1H, dd, *J*=2.2, 10.1 Hz), 3.37 (1H, dd, *J*=6.6, 10.1 Hz), 3.25 (1H, dt, *J*=2.7, 8.8 Hz),

2.98 (1H, ddd, *J*=2.9, 10.5, 13.3 Hz), 2.88–2.82 (1H, m), 2.44 (1H, ddd, *J*=2.9, 4.8, 13.5 Hz), 2.40–2.26 (3H, m), 1.99–1.82 (5H, m), 1.77 (1H, dt, *J*=14.6, 2.7 Hz), 1.46 (1H, ddd, *J*=6.1, 8.8, 14.6 Hz), 1.01 (3H, d, *J*=7.1 Hz), 0.99 (9H, s), 0.97 (3H, s), 0.14 (3H, s), 0.075 (3H, s); ^{13}C NMR (100 MHz, C_6D_6), δ (ppm) 139.40 (C), 139.35 (C), 138.2 (C), 138.1 (C), 137.2 (C), 134.1 (C), 133.6 (C), 131.61 (CH×2), 131.56 (CH×2), 129.7 (CH), 129.2 (CH×4), 128.6 (CH×2), 127.3 (CH×2), 126.4 (CH), 126.3 (CH×2), 125.9 (CH), 124.8 (CH), 121.5 (C), 121.4 (C), 100.5 (CH), 85.0 (CH), 79.9 (CH), 79.80 (CH), 79.77 (CH), 79.6 (CH), 78.3 (CH), 78.23 (CH), 78.20 (CH), 76.1 (CH), 74.8 (CH), 73.2 (CH_2), 72.7 (CH_2), 72.3 (CH_2), 71.3 (CH_2), 70.0 (CH_2), 69.6 (C), 68.7 (CH_2), 45.2 (CH_2), 39.5 (CH_2), 34.9 (CH_2), 34.1 (CH_2), 30.4 (CH_2), 29.0 (CH_2), 28.8 (CH), 26.9 (CH_3), 26.1 (CH_3×3), 18.3 (C), 17.2 (CH_3), −4.4 (CH_3), −4.7 (CH_3) (The signals of seven carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3063, 3025, 2956, 2853, 1593, 1487, 1471, 1453, 1405, 1375, 1359, 1326, 1256, 1214, 1202, 1174, 1098, 1012, 954, 836, 804, 755, 698; HR-FDMS, calcd for $C_{69}H_{84}^{79}Br_2O_{10}Si$ [M]$^+$: 1285.4200, found: 1258.4218.

7.1.39. (1*R*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*,1″*S*,3″*R*,4″*S*,6″*S*,8″*R*,10″*S*,11″*S*)-2-[8′-Benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-1-{4″-(4-bromobenzyloxy)-3″-(4-bromobenzyloxymethy)-6″,10″-dimethyl-11″-(2-naphthylmethyl)-2″,9″-dioxabicyclo[6.4.0]dodecan-10″-yl}ethanol (49). To a solution of **48** (3.2 mg, 2.54 μmol) in DCM (0.70 ml) was added DIBAL (0.15 ml, 0.94 M in hexane, 141 μmol) at 0 °C. The reaction mixture was warmed to 10 °C and stirred for 3 h. Then, MeOH (0.1 ml) and saturated aqueous potassium sodium tartrate (1 ml) were added. The mixture was diluted with Et_2O (5 ml) and stirred at 25 °C for 18 h. The layers were separated and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=4) to give **49** (3.2 mg, ∼100%,). **49**: a colorless oil; $[\alpha]_D^{25}$ +7.40 (*c* 0.160, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6), δ (ppm) 7.84 (1H, s), 7.72–7.62 (3H, m), 7.56 (1H, dd, *J*=1.6, 8.4 Hz), 7.41–7.39 (2H, m), 7.30–7.05 (14H, m), 6.92 (2H, d, *J*=8.5 Hz), 6.82 (2H, d, *J*=8.3 Hz), 5.96 (1H, dt, *J*=6.5, 10.7 Hz), 5.84 (1H, dt, *J*=5.7, 10.7 Hz), 4.65–4.62 (1H, m), 4.58 (1H, d, *J*=12.2 Hz), 4.474 (1H, d, *J*=12.2 Hz), 4.472 (1H, d, *J*=11.7 Hz), 4.284 (1H, d, *J*=11.8 Hz), 4.279 (1H, d, *J*=11.7 Hz), 4.20 (1H, d, *J*=11.8 Hz), 4.17 (2H, s), 4.11 (1H, dt, *J*=9.0, 3.5 Hz), 4.05 (1H, d, *J*=11.8 Hz), 3.96–3.87 (4H, m), 3.86 (1H, d, *J*=11.8 Hz), 3.70 (1H, ddd, *J*=2.1, 7.6, 9.1 Hz), 3.68–3.63 (2H, m), 3.61 (1H, dd, *J*=2.1, 9.9 Hz), 3.53 (1H, dt, *J*=9.0, 3.0 Hz), 3.39 (1H, dd, *J*=7.6, 9.9 Hz), 3.35 (1H, t, *J*=3.3 Hz), 3.25 (1H, dt, *J*=2.4, 9.1 Hz), 3.05 (1H, br s), 2.81 (1H, ddd, *J*=1.3, 10.7, 12.7 Hz), 2.68 (1H, ddd, *J*=3.0, 10.7, 13.4 Hz), 2.50 (1H, dt, *J*=13.9, 3.3 Hz), 2.28–2.22 (1H, m), 2.12 (1H, ddd, *J*=3.0, 5.7, 13.4 Hz), 1.91–1.69 (6H, m), 1.64–1.53 (2H, m), 1.22 (3H, s), 1.01 (3H, d, *J*=7.1 Hz), 0.97 (9H, s), 0.074 (6H, s); ^{13}C NMR (100 MHz, C_6D_6), δ (ppm) 139.6 (C), 139.3 (C), 138.1 (C), 137.9 (C), 136.7 (C), 133.9 (C), 133.4 (C), 131.6 (CH×4), 129.3 (CH×2), 129.2 (CH×2), 129.1 (CH), 128.5 (CH×4), 127.4 (CH), 126.8 (CH), 126.3 (CH×2), 126.2 (CH), 126.0 (CH×2), 121.6 (C), 121.5 (C), 85.7 (CH), 81.8 (CH), 81.2 (CH), 79.9 (CH), 79.5 (CH), 78.8 (C), 77.7 (CH), 77.5 (CH), 77.0 (CH), 74.2 (CH), 73.4 (CH_2), 73.1 (CH_2), 72.4 (CH_2), 71.5 (CH), 71.3 (CH_2), 71.0 (CH_2), 70.2 (CH_2), 70.1 (CH_2), 45.4 (CH_2), 39.7 (CH_2), 36.1 (CH_2), 31.6 (CH_2), 29.8 (CH_2), 28.8 (CH), 27.0 (CH_2), 26.8 (CH_3), 26.1 (CH_3×3), 18.3 (C), 15.6 (CH_3), −4.45 (CH_3), −4.50 (CH_3) (The signals of eight carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3584, 3503, 3061, 3025, 2925, 2854, 1593, 1509, 1487, 1454, 1404, 1375, 1360, 1337, 1298, 1256, 1203, 1100, 1012, 964, 946, 836, 804, 774, 751, 698; HR-FDMS, calcd for $C_{69}H_{87}^{79}Br_2O_{10}Si$ [M+H]$^+$: 1261.4430, found: 1261.4440.

7.1.40. (1*S*,3*R*,4*S*,6*S*,8*R*,10*S*,11*S*,1′*R*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-10-{1′-Benzyloxy-2′-[8″-benzyloxy-9″-benzyloxymethyl-3″-(*tert*-butyldimethylsilyloxy)-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl]ethyl}-4-(4-bromobenzyloxy)-3-(4-bromobenzyloxymethyl)-6,10-dimethyl-11-(2-naphthymethyl)-2,9-dioxabicyclo[6.4.0]dodecane (50). To a suspension of **49** (3.8 mg, 3.01 μmol) and TBAI (3.0 mg, 8.12 μmol) in THF-DMF (5:1, v/v, 1.0 ml) was added NaH (17.4 mg, 435 μmol) at 0 °C and the mixture was stirred for 10 min. Then, benzyl bromide (20.0 μmol, 168 μmol) was added at 0 °C, the reaction mixture was warmed to 25 °C and stirred for 8 h. After that, H_2O (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=50 to 7) to give **50** (4.1 mg, ∼100%). **50**: a colorless oil; $[\alpha]_D^{23}$ −7.61 (*c* 0.205, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6), δ (ppm) 7.95 (1H, s), 7.67–7.51 (6H, m), 7.35–7.03 (14H, m), 6.88 (2H, d, *J*=8.3 Hz), 6.82 (2H, d, *J*=8.3 Hz), 5.88 (1H, dt, *J*=6.8, 10.5 Hz), 5.77 (1H, dt, *J*=5.7, 10.5 Hz), 5.50 (1H, d, *J*=12.2 Hz), 5.06 (1H, d, *J*=12.2 Hz), 4.68 (1H, t, *J*=5.7 Hz), 4.59 (1H, d, *J*=12.6 Hz), 4.48 (1H, d, *J*=12.6 Hz), 4.37–4.31 (2H, m), 4.22–4.16 (3H, m), 4.13 (2H, s), 4.01 (1H, d, *J*=12.0 Hz), 3.94 (1H, br d, *J*=8.7 Hz), 3.93–3.89 (1H, m), 3.86 (1H, d, *J*=12.0 Hz), 3.82 (1H, dd, *J*=1.7, 10.0 Hz), 3.76–3.69 (3H, m), 3.59 (2H, dd, *J*=2.6, 10.0 Hz), 3.40 (1H, dd, *J*=7.4, 10.0 Hz), 3.26 (1H, dt, *J*=2.4, 9.0 Hz), 3.14 (1H, br dd, *J*=10.5, 12.6 Hz), 2.54–2.44 (2H, m), 2.30 (1H, ddd, *J*=6.8, 8.7, 12.6 Hz), 2.01–1.90 (4H, m), 1.82 (1H, ddd, *J*=2.9, 5.7, 13.4 Hz), 1.76 (1H, ddd, *J*=2.6, 11.5, 13.9 Hz), 1.66 (1H, ddd, *J*=5.1, 9.0, 14.3 Hz), 1.41 (1H, t, *J*=5.7 Hz), 1.25 (3H, s), 1.00 (3H, d, *J*=5.9 Hz), 0.95 (9H, s), 0.061 (3H, s), 0.060 (3H, s); ^{13}C NMR (100 MHz, C_6D_6), δ (ppm) 141.5 (C), 139.8 (C), 139.4 (C), 138.1 (C), 137.9 (C), 136.9 (C), 133.9 (C), 133.3 (C), 131.64 (CH×2), 131.60 (CH×2), 129.4 (CH×2), 129.1 (CH×2), 128.5 (CH), 128.4 (CH×4), 127.5 (CH×2), 127.4 (CH), 127.2 (CH×3), 127.0 (CH), 126.8 (CH), 126.2 (CH), 125.8 (CH), 125.5 (CH×2), 121.6 (C), 121.5 (C), 85.8 (CH), 81.3 (CH), 81.0 (C), 80.7 (CH), 79.9 (CH), 79.3 (CH), 78.7 (CH), 78.1 (CH), 77.0 (CH), 76.1 (CH), 75.2 (CH_2), 74.0 (CH), 73.1 (CH_2×2), 72.3 (CH_2), 71.1 (CH_2), 70.8 (CH_2), 70.2 (CH_2), 69.7 (CH_2), 45.7 (CH_2), 39.9 (CH_2), 37.5 (CH_2), 31.4 (CH_2),

28.8 (CH), 27.9 (CH_2), 26.9 (CH_3), 26.2 (CH_2), 26.0 ($CH_3\times3$), 18.3 (C), 14.7 (CH_3), −4.6 (CH_3), −4.8 (CH_3) (The signals of seven carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3062, 3025, 2926, 2855, 1603, 1593, 1509, 1496, 1487, 1453, 1404, 1360, 1338, 1250, 1201, 1096, 1070, 1012, 946, 835, 774, 733, 697; HR-FDMS, calcd for $C_{76}H_{92}^{79}Br_2O_{10}Si$ $[M]^+$: 1350.4826, found: 1350.4854.

7.1.41. (1*S*,3*R*,4*S*,6*S*,8*R*,10*R*,11*S*,1′*R*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-10-{1′-Benzyloxy-2′-[8″-benzyloxy-9″-benzyloxymethyl-3″-(*tert*-butyldimethylsilyloxy)-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl]ethyl}-4-(4-bromobenzyloxy)-3-(4-bromobenzyloxymethyl)-6,10-dimethyl-2,9-dioxabicyclo[6.4.0]dodecan-11-ol (51). To a solution of **50** (10.4 mg, 7.68 μmol) in DCM–pH 7 buffer (10:1, v/v, 0.90 ml) was added DDQ (10.7 mg, 47.1 μmol) at 0 °C and the mixture was stirred for 20 min. Then, saturated aqueous $NaHCO_3$ (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=30 to 5) to give **51** (8.5 mg, 91%). **51**: a colorless oil; $[\alpha]_D^{18}$ +11.8 (*c* 0.425, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 7.48 (1H, d, *J*=7.1 Hz), 7.37–7.21 (9H, m), 7.15–7.01 (10H, m), 6.84 (2H, d, *J*=8.3 Hz), 5.91–5.82 (2H, m), 5.28 (1H, d, *J*=12.0 Hz), 4.88 (1H, d, *J*=12.0 Hz), 4.40 (1H, d, *J*=11.8 Hz), 4.37 (1H, d, *J*=11.7 Hz), 4.30–4.16 (7H, m), 4.13 (1H, d, *J*=11.8 Hz), 4.04 (1H, ddd, *J*=4.5, 9.8, 10.9 Hz), 3.90 (1H, d, *J*=12.0 Hz), 3.82–3.75 (4H, m), 3.72–3.60 (4H, m), 3.47 (1H, dd, *J*=7.0, 10.0 Hz), 3.32 (1H, dt, *J*=2.4, 9.0 Hz), 2.90–2.84 (1H, m), 2.61 (1H, br dd, *J*=8.5, 13.2 Hz), 2.55 (1H, ddd, *J*=3.5, 4.5, 13.3 Hz), 2.38 (1H, ddd, *J*=3.8, 4.5, 13.5 Hz), 2.18 (1H, ddd, *J*=5.6, 8.7, 13.2 Hz), 2.03–1.83 (5H, m), 1.67 (1H, ddd, *J*=5.7, 9.0, 14.8 Hz), 1.45 (2H, dd, *J*=4.1, 6.1 Hz), 1.21 (3H, s), 1.03 (3H, d, *J*=6.8 Hz), 0.94 (9H, s), 0.035 (3H, s), 0.027 (3H, s); ^{13}C NMR (100 MHz, C_6D_6), δ (ppm) 140.9 (C), 139.2 (C), 139.0 (C), 138.3 (C), 138.1 (C), 131.6 (CH×4), 129.4 (CH×2), 129.3 (CH×2), 129.2 (CH), 128.5 (CH×2), 128.4 (CH×2), 127.51 (CH), 127.47 (CH), 127.3 (CH), 126.4 (CH), 121.6 (C), 121.4 (C), 85.6 (CH), 82.1 (CH), 82.0 (CH), 80.5 (CH, C), 79.8 (CH), 77.0 (CH), 76.9 (CH), 76.5 (CH), 75.7 (CH_2), 74.0 (CH), 73.3 (CH_2), 72.9 (CH_2), 72.3 (CH_2), 71.54 (CH_2), 71.48 (CH), 70.3 (CH_2), 69.3 (CH_2), 45.7 (CH_2), 40.1 (CH_2), 38.3 (CH_2), 35.7 (CH_2), 28.8 (CH), 27.6 (CH_2), 27.0 (CH_3), 26.4 (CH_2), 26.0 ($CH_3\times3$), 18.3 (C), 13.8 (CH_3), −4.77 (CH_3), −4.84 (CH_3) (The signals of eight carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3475, 3063, 3027, 2927, 2857, 1593, 1487, 1470, 1453, 1405, 1372, 1360, 1339, 1298, 1250, 1215, 1088, 1028, 1012, 940, 888, 836, 804, 755, 697; HR-FDMS, calcd for $C_{65}H_{84}^{79}Br_2O_{10}Si$ $[M]^+$: 1210.4200, found: 1210.4193.

7.1.42. (1*S*,3*R*,4*S*,6*S*,8*R*,10*S*,11*S*,1′*R*,2″*R*,3″*S*,5″*Z*,8″*R*,9″*S*)-10-[1′-Benzyloxy-2′-(8″-benzyloxy-9″-benzyloxymethyl-3″-hydroxy-2″,3″,4″,7″,8″,9″-hexahydrooxonin-2″-yl)ethyl]-4-(4-bromobenzyloxy)-3-(4-bromobenzyloxymethyl)-6,10-dimethyl-2,9-dioxabicyclo[6.4.0]dodecan-11-one (53). To a solution of **51** (7.5 mg, 6.18 μmol) in DCM (0.80 ml) were added $NaHCO_3$ (21.8 mg, 259 μmol) and DMPI (22.0 mg, 51.9 μmol) at 25 °C and the reaction mixture was stirred for 30 min. After the mixture was diluted with Et_2O (1 ml), saturated aqueous Na_2SO_3 (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with saturated aqueous Na_2SO_3 and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was roughly purified by column chromatography (silica gel, hexane/AcOEt=4) to give a crude product, and it was used in the next reaction without further purification. To a solution of the above crude product in THF (0.80 ml) was added HF·Py at 0 °C. The reaction mixture was warmed to 25 °C and stirred for 2 d. After the reaction mixture was diluted with Et_2O and cooled to 0 °C, saturated aqueous $NaHCO_3$ (1 ml) was added and the mixture was stirred for 1 h. The layers were separated and the aqueous layer was extracted with AcOEt (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=5 to 2) to give **53** (6.8 mg, ~100% from **51**). **53**: a colorless oil; $[\alpha]_D^{22}$ +15.6 (*c* 0.340, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6), δ (ppm) 7.45–7.43 (2H, m), 7.31–7.28 (5H, m), 7.21–7.04 (12H, m), 6.92 (2H, d, *J*=8.3 Hz), 6.81 (2H, d, *J*=8.5 Hz), 5.95 (1H, dt, *J*=5.9, 10.6 Hz), 5.88 (1H, dt, *J*=5.9, 10.6 Hz), 4.79 (1H, d, *J*=10.9 Hz), 4.60 (1H, d, *J*=10.9 Hz), 4.41 (1H, d, *J*=12.3 Hz), 4.39 (1H, d, *J*=11.7 Hz), 4.35 (1H, d, *J*=12.3 Hz), 4.18–4.13 (4H, m), 4.10 (1H, d, *J*=11.7 Hz), 3.85 (1H, d, *J*=12.0 Hz), 3.83–3.80 (2H, m), 3.74 (1H, dt, *J*=6.8, 4.9 Hz), 3.70–3.65 (2H, m), 3.58–3.54 (2H, m), 3.44 (1H, dd, *J*=2.7, 9.8 Hz), 3.40 (1H, dt, *J*=2.7, 6.8 Hz), 3.38 (1H, ddd, *J*=2.0, 6.6, 9.0 Hz), 3.28 (1H, dd, *J*=6.6, 9.8 Hz), 3.16 (1H, dt, *J*=2.4, 9.0 Hz), 3.09 (1H, dd, *J*=7.4, 16.8 Hz), 2.86 (1H, ddd, *J*=2.7, 10.6, 13.4 Hz), 2.75 (1H, ddd, *J*=2.7, 10.6, 13.7 Hz), 2.52 (1H, dd, *J*=6.6, 16.8 Hz), 2.34–2.24 (4H, m), 1.92–1.88 (1H, m), 1.78–1.62 (3H, m), 1.47 (1H, ddd, *J*=5.6, 9.0, 15.6 Hz), 1.22 (3H, s), 0.95 (3H, d, *J*=6.8 Hz); ^{13}C NMR (100 MHz, C_6D_6), δ (ppm) 211.2 (C), 139.1 (C), 139.0 (C), 138.8 (C), 138.0 (C), 137.8 (C), 131.73 (CH×2), 131.67 (CH×2), 129.4 (CH×2), 129.3 (CH×2), 128.64 (CH×2), 128.60 (CH×4), 128.5 (CH×4), 121.69 (C), 121.66 (C), 86.6 (C), 85.1 (CH), 83.0 (CH), 82.7 (CH), 82.6 (CH), 81.7 (CH), 79.6 (CH), 78.7 (CH), 75.6 (CH), 74.8 (CH), 74.7 (CH_2), 73.3 (CH_2), 72.5 (CH_2), 72.0 ($CH_2\times2$), 71.4 (CH_2), 70.3 (CH_2), 46.2 (CH_2), 44.1 (CH_2), 39.6 (CH_2), 36.6 (CH_2), 30.8 (CH_2), 28.6 (CH), 26.9 (CH_3, CH_2), 17.9 (CH_3) (The signals of seven carbons were undetected due to overlapping with solvent signal.); IR (film), ν (cm^{-1}) 3454, 3063, 3027, 2926, 2865, 1717, 1592, 1487, 1453, 1405, 1367, 1321, 1300, 1215, 1099, 1027, 1012, 911, 838, 804, 755, 698; HR-FDMS, calcd for $C_{59}H_{68}^{79}Br_2O_{10}$ $[M]^+$: 1094.3179, found: 1094.3174.

7.1.43. (1*R*,3*S*,5*Z*,8*R*,9*S*,11*R*,13*R*,14*S*,16*R*,18*S*,20*S*,21*R*,23*S*)-8,13-Dibenzyloxy-9-benzyloxymethyl-20-(4-bromobenzyloxy)-21-(4-bromobenzyloxymethyl)-14,18-dimethyl-2,10,15,22-tetraoxatetracyclo[12.10.0.0^{3,11}.0^{16,23}]-tetracos-5-ene (54). To a solution of **53** (6.0 mg, 5.47 μmol) in DCM–Et_3SiH (10:1, v/v, 0.80 ml) was added TMSOTf (3.0 μl, 16.6 μmol) at 0 °C and the mixture was stirred for 30 min. Then, saturated aqueous $NaHCO_3$ (1 ml) was added

and the aqueous layer was extracted with Et_2O (5 ml) and AcOEt (3×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=10 to 4) to give **54** (4.6 mg, 78%). **54**: a colorless oil; $[\alpha]_D^{23}$ −4.96 (*c* 0.025, $CHCl_3$); ^{1}H NMR (600 MHz, C_6D_6), δ (ppm) 7.45 (2H, d, *J*=7.3 Hz), 7.21–7.02 (17H, m), 6.94 (2H, d, *J*=8.1 Hz), 6.83 (2H, d, *J*=8.1 Hz), 5.93 (1H, dt, *J*=6.4, 10.0 Hz), 5.82 (1H, dt, *J*=5.4, 10.0 Hz), 4.85 (1H, d, *J*=12.1 Hz), 4.71 (1H, d, *J*=12.1 Hz), 4.39 (1H, d, *J*=12.3 Hz), 4.37 (2H, s), 4.25 (1H, d, *J*=12.9 Hz), 4.22 (1H, d, *J*=12.9 Hz), 4.21 (1H, d, *J*=11.7 Hz), 4.11 (1H, d, *J*=12.3 Hz), 3.87 (1H, d, *J*=11.7 Hz), 3.70 (1H, t, *J*=6.0 Hz), 3.66–3.53 (6H, m), 3.52–3.50 (1H, m), 3.49–3.47 (1H, m), 3.39 (1H, dd, *J*=7.1, 9.9 Hz), 3.26–3.20 (2H, m), 3.07 (1H, dd, *J*=4.6, 12.1 Hz), 2.94 (1H, ddd, *J*=5.0, 10.0, 13.9 Hz), 2.69–2.63 (2H, m), 2.40 (1H, dt, *J*=12.5, 4.6 Hz), 2.31–2.26 (3H, m), 2.00–1.84 (4H, m), 1.68–1.57 (2H, m), 1.44 (3H, s), 1.00 (3H, d, *J*=7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm) 139.5 (C), 138.3 (C), 138.2 (C), 137.4 (C), 137.2 (C), 131.5 (CH×2), 131.4 (CH×2), 129.4 (CH×4), 128.3 (CH×5), 128.1 (CH×2), 128.0 (CH×2), 127.8 (CH×3), 127.62 (CH), 127.59 (CH), 127.5 (CH×2), 127.1 (CH), 121.5 (C), 121.4 (C), 85.9 (CH), 84.7 (CH), 84.4 (CH), 83.7 (CH), 82.6 (CH×2), 80.4 (C), 79.7 (CH), 79.0 (CH), 78.0 (CH), 73.3 (CH_2), 73.1 (CH_2), 72.7 (CH_2), 72.1 (CH), 71.9 (CH_2), 71.4 (CH_2), 70.54 (CH_2), 70.49 (CH_2), 45.0 (CH_2), 40.6 (CH_2), 38.6 (CH_2), 35.4 (CH_2), 32.5 (CH_2), 27.9 (CH), 27.6 (CH_2), 27.0 (CH_3), 11.5 (CH_3); IR (neat), ν (cm^{-1}) 2954, 2923, 2853, 1594, 1487, 1462, 1376, 1287, 1260, 1204, 1096, 1070, 1027, 1012, 840, 803, 729, 697; HR-FDMS, calcd for $C_{59}H_{68}^{79}Br_2O_9$ $[M]^+$: 1078.3230, found: 1078.3217.

7.1.44. (1*R*,3*R*,4*S*,6*S*,8*S*,10*S*,12*R*,13*S*,15*S*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*)-4-[8′-Benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-13-(4-bromobenzyloxy)-12-(4-bromobenzyloxymethyl)-3,15-dimethyl-6-(2-naphthyl)-2,5,7,11-tetraoxatricyclo[8.6.0.0^{3,8}]hexadecane (55a) and (1*R*,3*R*,4*S*,6*R*,8*S*,10*S*,12*R*,13*S*,15*S*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*)-4-[8′-benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-13-(4-bromobenzyloxy)-12-(4-bromobenzyloxymethyl)-3,15-dimethyl-6-(2-naphthyl)-2,5,7,11-tetraoxatricyclo[8.6.0.0^{3,8}]hexadecane (55b). To a solution of **31** (17.3 mg, 15.4 μmol) in benzene (1.0 ml) were added 2-naphthaldehyde dimethyl acetal (33.3 mg, 165 μmol) and PPTS (6.0 mg, 23.9 μmol). The reaction mixture was heated to 80 °C and stirred for 2 h. Then, saturated aqueous $NaHCO_3$ (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=30 to 4) to give **55a** (17.3 mg, 89%,) and **55b** (2.1 mg, 11%). **55a**: a colorless oil; $[\alpha]_D^{24}$ −27.9 (*c* 0.750, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6), δ (ppm) 8.29 (1H, s), 7.91 (1H, dd, *J*=1.5, 8.5 Hz), 7.75–7.72 (2H, m), 7.62–7.58 (1H, m), 7.34–6.95 (18H, m), 6.81 (2H, d, *J*=8.5 Hz), 6.05 (1H, s), 5.88 (1H, dt, *J*=5.2, 10.4 Hz), 5.83 (1H, dt, *J*=5.2, 10.4 Hz), 4.55 (1H, dd, *J*=2.8, 11.3 Hz), 4.47 (1H, d, *J*=12.0 Hz), 4.41 (1H, d, *J*=12.0 Hz), 4.38 (1H, d, *J*=12.0 Hz), 4.22–4.15 (4H, m), 4.11 (1H, d, *J*=12.0 Hz), 3.93 (1H, dt, *J*=4.8, 9.5 Hz), 3.86 (1H, d, *J*=12.2 Hz), 3.69–3.57 (7H, m), 3.53 (1H, dd, *J*=2.4, 10.0 Hz), 3.43–3.41 (1H, m), 3.40 (1H, dd, *J*=6.7, 10.0 Hz), 3.30 (1H, dt, *J*=2.6, 8.8 Hz), 2.71 (1H, ddd, *J*=2.8, 10.4, 13.2 Hz), 2.52–2.45 (2H, m), 2.30–2.24 (1H, m), 2.17 (1H, dt, *J*=13.2, 5.2 Hz), 2.05–1.82 (7H, m), 1.53 (1H, ddd, *J*=5.4, 8.8, 14.5 Hz), 1.07 (3H, s), 1.03 (3H, d, *J*=6.3 Hz), 0.97 (9H, s), 0.13 (3H, s), 0.063 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 138.6 (C), 138.4 (C), 137.5 (C), 137.4 (C), 136.3 (C), 133.6 (C), 133.0 (C), 131.41 (CH×2), 131.39 (CH×2), 129.2 (CH×4), 128.4 (CH), 128.2 (CH×5), 128.0 (CH×2), 127.8 (CH), 127.7 (CH×2), 127.6 (CH), 127.5 (CH), 127.4 (CH), 127.1 (CH), 125.9 (CH), 125.8 (CH×2), 124.6 (CH), 121.4 (C), 121.3 (C), 95.7 (CH), 84.9 (CH), 83.2 (CH), 82.8 (CH), 80.3 (CH), 79.0 (CH), 78.2 (CH), 77.2 (C), 75.5 (CH), 75.2 (CH), 74.3 (CH), 73.4 (CH), 73.2 (CH_2), 72.5 (CH_2), 72.0 (CH_2), 71.9 (CH_2), 71.2 (CH_2), 70.4 (CH_2), 45.20 (CH_2), 45.18 (CH_2), 40.0 (CH_2), 33.3 (CH_2), 32.2 (CH_2), 28.3 (CH), 27.0 (CH_2), 26.9 (CH_3), 25.9 (CH_3×3), 17.9 (C), 16.4 (CH_3), −4.3 (CH_3), −4.4 (CH_3); IR (film), ν (cm^{-1}) 3062, 3026, 2854, 1593, 1487, 1453, 1370, 1317, 1255, 1213, 1172, 1100, 941, 835, 776, 737, 697; HR-FDMS, calcd for $C_{69}H_{84}^{79}Br_2O_{10}Si$ $[M]^+$: 1258.4200, found: 1258.4202. **55b**: a colorless oil; $[\alpha]_D^{21}$ +12.2 (*c* 0.105, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6), δ (ppm) 8.05 (1H, s), 7.81 (1H, d, *J*=8.1 Hz), 7.75 (1H, d, *J*=8.5 Hz), 7.68–7.65 (2H, m), 7.51 (2H, d, *J*=7.1 Hz), 7.35–6.95 (16H, m), 6.82 (2H, d, *J*=8.3 Hz), 6.20 (1H, s), 6.07 (1H, dt, *J*=5.0, 10.7 Hz), 6.00 (1H, dt, *J*=5.0, 10.7 Hz), 4.74 (1H, d, *J*=11.7 Hz), 4.62 (1H, t, *J*=7.0 Hz), 4.54 (1H, dt, *J*=8.1, 3.3 Hz), 4.52 (1H, d, *J*=11.7 Hz), 4.45 (1H, d, *J*=11.8 Hz), 4.20 (1H, d, *J*=12.3 Hz), 4.190 (1H, d, *J*=11.8 Hz), 4.185 (1H, d, *J*=12.1 Hz), 4.14 (1H, d, *J*=12.3 Hz), 4.00 (1H, dt, *J*=8.4, 3.3 Hz), 3.93 (1H, t, *J*=4.8 Hz), 3.88 (1H, d, *J*=12.1 Hz), 3.86 (2H, d, *J*=2.4 Hz), 3.80 (1H, dt, *J*=4.8, 9.1 Hz), 3.66–3.57 (3H, m), 3.53 (1H, dd, *J*=2.2, 10.0 Hz), 3.43–3.41 (1H, m), 3.39 (1H, dd, *J*=6.7, 10.0 Hz), 3.28 (1H, dt, *J*=2.4, 9.0 Hz), 3.09 (1H, ddd, *J*=3.3, 10.7, 13.1 Hz), 2.81 (1H, ddd, *J*=3.3, 10.7, 14.0 Hz), 2.48 (1H, dt, *J*=13.8, 4.8 Hz), 2.32–2.26 (1H, m), 2.21–2.14 (3H, m), 1.99–1.79 (5H, m), 1.61–1.55 (1H, m), 1.19 (3H, s), 1.06 (3H, d, *J*=7.6 Hz), 1.04 (9H, s), 0.24 (3H, s), 0.083 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm) 138.61 (C), 138.56 (C), 137.4 (C), 137.3 (C), 136.5 (C), 133.4 (C), 132.9 (C), 131.44 (CH×2), 131.41 (CH×2), 129.3 (CH×2), 129.2 (CH×2), 128.3 (CH×3), 128.2 (CH×3), 127.9 (CH×3), 127.8 (CH×2), 127.7 (CH), 127.51 (CH), 127.47 (CH), 127.4 (CH), 126.09 (CH), 126.07 (CH), 125.0 (CH), 124.3 (CH), 121.5 (C), 121.3 (C), 97.9 (CH), 84.9 (CH), 84.5 (CH), 84.3 (CH), 81.0 (CH), 79.1 (CH), 78.3 (CH), 77.2 (CH), 75.4 (C), 74.8 (CH), 73.1 (CH_2), 72.55 (CH_2), 72.52 (CH), 71.8 (CH_2), 71.4 (CH_2), 71.3 (CH), 70.5 (CH_2), 70.3 (CH_2), 45.1 (CH_2), 40.1 (CH_2), 32.6 (CH_2), 32.1 (CH_2), 31.6 (CH_2), 29.7 (CH_2), 28.4 (CH), 26.9 (CH_3), 26.0 (CH_3×3), 18.0 (C), 16.1 (CH_3), −4.2 (CH_3), −4.4 (CH_3); IR (film), ν (cm^{-1}) 3062, 3025, 2924, 2853, 1593, 1507, 1487, 1454, 1371, 1299, 1257, 1214, 1172, 1096, 1012, 940, 836, 803, 776, 752, 697; HR-FDMS, calcd for $C_{69}H_{84}^{79}Br_2O_{10}Si$ $[M]^+$: 1258.4200, found: 1258.4213.

7.1.45. (1*S*,2′*R*,3′*S*,5′*Z*,8′*R*,9′*S*,1″*S*,3″*R*,4″*S*,6″*S*,8″*R*,10″*S*,11″*S*)-2-[8′-Benzyloxy-9′-benzyloxymethyl-3′-(*tert*-butyldimethylsilyloxy)-2′,3′,4′,7′,8′,9′-hexahydrooxonin-2′-yl]-1-{4″-(4-bromobenzyloxy)-3″-(4-bromobenzyloxymethy)-6″,10″-dimethyl-11″-(2-naphthylmethyl)-2″,9″-dioxabicyclo[6.4.0]dodecan-10″-yl}ethanol (56). To a solution of **55a** (26.4 mg, 20.9 μmol) in DCM (0.70 ml) was added DIBAL (0.15 ml, 0.94 M in hexane, 141 μmol) at 0 °C for 5.5 h. Then, MeOH (0.1 ml) and saturated aqueous potassium sodium tartrate (1 ml) were added. The mixture was diluted with Et_2O (5 ml) and stirred at 25 °C for 10 h. The layers were separated and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. Since the resultant residue included **56** and unreacted **55a**, the residue was dissolved in DCM (0.80 ml) and treated again with DIBAL (0.25 ml, 0.94 M in hexane, 235 μmol) at 0 °C for 4.5 h. Then, the reaction was quenched with MeOH (0.1 ml) and saturated aqueous potassium sodium tartrate (1 ml). After the same work-up as described above, the resultant crude mixture was roughly purified by column chromatography (silica gel, hexane/AcOEt=15 to 7) to give **56** (13.6 mg) and a mixture of **55a** and **56** (11.5 mg). The mixture of **55a** and **56** was dissolved in DCM (0.7 ml) and treated with DIBAL (0.20 ml, 0.94 M in hexane, 188 μmol) at 0 °C for 2 h. Then the reaction mixture was warmed to 10 °C and stirred for 2 h. Then, the reaction was quenched with MeOH (0.1 ml) and saturated aqueous potassium sodium tartrate (1 ml). After the same work-up as described above, the resultant crude mixture was purified by column chromatography (silica gel, hexane/AcOEt=15 to 7) to give **56** (11.0 mg). Thus, total 24.6 mg (93%) of **56** was obtained. **56**: a colorless oil; $[\alpha]_D^{23}$ +17.0 (*c* 1.15, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6), δ (ppm) 7.77 (1H, s), 7.66–7.58 (3H, m), 7.47 (1H, dd, *J*=1.6, 8.4 Hz), 7.30–7.00 (16H, m), 6.88 (2H, d, *J*=8.3 Hz), 6.82 (2H, d, *J*=8.3 Hz), 5.92 (1H, dt, *J*=6.2, 10.4 Hz), 5.84 (1H, dt, *J*=5.7, 10.4 Hz), 4.72–4.69 (2H, m), 4.66 (1H, d, *J*=12.4 Hz), 4.49 (1H, d, *J*=12.3 Hz), 4.36 (1H, d, *J*=12.0 Hz), 4.20 (1H, d, *J*=11.8 Hz), 4.17 (1H, d, *J*=12.4 Hz), 4.13 (1H, d, *J*=12.4 Hz), 4.12 (1H, d, *J*=12.0 Hz), 4.09 (1H, d, *J*=12.3 Hz), 4.01–3.91 (4H, m), 3.87 (1H, d, *J*=11.8 Hz), 3.82 (1H, d, *J*=2.4 Hz), 3.80–3.76 (3H, m), 3.71 (1H, ddd, *J*=2.1, 7.1, 8.8 Hz), 3.70–3.66 (1H, m), 3.64 (1H, dd, *J*=2.6, 10.4 Hz), 3.55 (1H, dd, *J*=2.1, 9.9 Hz), 3.38 (1H, dd, *J*=7.1, 9.9 Hz), 3.29 (1H, dt, *J*=2.6, 8.8 Hz), 2.88–2.79 (2H, m), 2.46 (1H, dt, *J*=13.7, 3.9 Hz), 2.29–2.16 (3H, m), 2.04–1.74 (6H, m), 1.63 (1H, ddd, *J*=5.5, 8.8, 14.0 Hz), 1.28 (3H, s), 1.09 (3H, d, *J*=6.3 Hz), 0.94 (9H, s), 0.060 (3H, s), 0.036 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 138.5 (C), 138.2 (C), 137.4 (C), 137.3 (C), 136.8 (C), 133.2 (C), 132.8 (C), 131.4 (CH×2), 131.3 (CH×2), 129.3 (CH×3), 129.1 (CH×2), 128.21 (CH×2), 128.17 (CH×2), 127.9 (CH), 127.8 (CH), 127.7 (CH×2), 127.6 (CH), 127.5 (CH×2), 127.4 (CH), 127.3 (CH), 126.1 (CH), 126.0 (CH), 125.8 (CH×2), 125.7 (CH), 121.5 (C), 121.2 (C), 85.5 (CH×2), 81.3 (CH), 79.0 (CH), 78.4 (CH), 77.6 (C), 77.2 (CH), 76.98 (CH), 75.9 (CH), 73.4 (CH), 72.9 (CH_2), 72.4 (CH_2×2), 72.3 (CH), 71.9 (CH_2), 71.4 (CH_2), 70.5 (CH_2), 67.6 (CH_2), 45.2 (CH_2), 40.3 (CH_2), 35.0 (CH_2), 32.1 (CH_2), 28.8 (CH_2), 28.3 (CH), 26.9 (CH_3), 26.4 (CH_2), 25.9 (CH_3×3), 18.0 (C), 14.6 (CH_3), −4.67 (CH_3), −4.72 (CH_3); IR (film), ν (cm^{-1}) 3584, 3497, 3061, 3026, 2926, 2857, 1593, 1509, 1487, 1453, 1405, 1360, 1337, 1256, 1205, 1099, 1012, 940, 836, 774, 735, 698; HR-FDMS, calcd for $C_{69}H_{86}^{79}Br_2O_{10}Si$ $[M]^+$: 1260.4357, found: 1260.4365.

7.1.46. (2*R*,3*S*,5*Z*,8*R*,9*S*,1′*S*,3′*R*,4′*S*,6′*S*,8′*R*,10′*R*,11′*S*)-[8-Benzyloxy-9-benzyloxymethyl-3-(*tert*-butyldimethylsilyloxy)-2,3,4,7,8,9-hexahydrooxonin-2-yl]methyl 4′-(4-bromobenzyloxy)-3′-(4-bromobenzyloxymethyl)-6′,10′-dimethyl-11′-(2-naphthylmethyl)-2′,9′-dioxabicyclo[6.4.0]dodecan-10′-yl ketone (57). To a solution of **56** (24.6 mg, 19.5 μmol) in DCM (1.0 ml) were added $NaHCO_3$ (24.6 mg, 293 μmol) and DMPI (28.3 mg, 117 μmol) at 0 °C. The reaction mixture was warmed to 25 °C and stirred for 8 h. After the mixture was diluted with Et_2O (5 ml), saturated aqueous Na_2SO_3 (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with saturated aqueous Na_2SO_3 and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, benzene/AcOEt=7 to 5) to give **57** (22.1 mg, 90%). **57**: a colorless oil; $[\alpha]_D^{19}$ +40.3 (*c* 1.11, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6), δ (ppm) 7.75 (1H, d, *J*=8.1 Hz), 7.67 (1H, d, *J*=8.3 Hz), 7.64 (1H, s), 7.59 (1H, d, *J*=8.1 Hz), 7.43 (1H, dd, *J*=1.5, 8.3 Hz), 7.33–7.06 (16H, m), 6.90 (2H, d, *J*=8.3 Hz), 6.83 (2H, d, *J*=8.3 Hz), 5.99–5.91 (2H, m), 4.51 (1H, d, *J*=12.3 Hz), 4.49–4.45 (3H, m), 4.44 (1H, d, *J*=12.3 Hz), 4.36 (1H, dt, *J*=3.9, 6.3 Hz), 4.23 (1H, d, *J*=12.0 Hz), 4.21 (1H, d, *J*=11.3 Hz), 4.18 (1H, dt, *J*=8.7, 3.0 Hz), 4.17 (1H, d, *J*=12.4 Hz), 4.12 (1H, d, *J*=12.4 Hz), 4.04 (1H, ddd, *J*=2.8, 4.9, 6.3 Hz), 3.89 (1H, dt, *J*=8.7, 3.4 Hz), 3.86 (1H, d, *J*=11.3 Hz), 3.84 (1H, dt, *J*=4.4, 11.5 Hz), 3.73 (1H, t, *J*=2.4 Hz), 3.72 (1H, d, *J*=3.0 Hz), 3.71 (1H, ddd, *J*=2.0, 7.1, 9.3 Hz), 3.54 (1H, dd, *J*=2.0, 9.8 Hz), 3.53–3.50 (1H, m), 3.40–3.32 (3H, m), 3.24 (1H, dt, *J*=2.3, 9.3 Hz), 2.98 (1H, ddd, *J*=2.8, 9.4, 13.4 Hz), 2.85 (1H, ddd, *J*=3.4, 9.4, 13.4 Hz), 2.36–2.30 (2H, m), 2.14 (1H, dt, *J*=13.4, 4.9 Hz), 2.03–1.84 (4H, m), 1.63 (1H, ddd, *J*=5.2, 9.3, 14.3 Hz), 1.56 (1H, ddd, *J*=2.4, 11.5, 13.9 Hz), 1.15 (3H, s), 1.06 (3H, d, *J*=6.3 Hz), 0.89 (9H, s), 0.12 (3H, s), 0.019 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm) 212.6 (C), 138.8 (C), 138.6 (C), 137.4 (C), 137.2 (C), 135.8 (C), 133.1 (C), 132.9 (C), 131.5 (CH×2), 131.4 (CH×2), 129.3 (CH×2), 129.2 (CH×2), 128.22 (CH×2), 128.19 (CH×2), 128.1 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH×2), 127.7 (CH×4), 127.3 (CH×2), 126.5 (CH), 126.01 (CH), 125.96 (CH), 125.8 (CH), 121.5 (C), 121.4 (C), 85.7 (CH), 83.0 (C), 82.5 (CH), 80.5 (CH), 80.4 (CH), 79.01 (CH), 78.97 (CH), 78.0 (CH), 73.79 (CH), 73.75 (CH), 73.1 (CH_2), 72.5 (CH_2), 71.9 (CH_2×2), 71.3 (CH_2), 70.5 (CH_2), 70.2 (CH_2), 45.3 (CH_2), 44.3 (CH_2), 40.6 (CH_2), 31.7 (CH_2), 31.1 (CH_2), 28.1 (CH), 27.3 (CH_2), 27.0 (CH_3), 25.8 (CH_3×3), 18.3 (CH_3), 17.9 (C), −4.5 (CH_3), −4.7 (CH_3); IR (film), ν (cm^{-1}) 3061, 3026, 2926, 2857, 1718, 1593, 1509, 1487, 1453, 1361, 1338, 1257, 1214, 1172, 1101, 1012, 948, 836, 775, 735, 697; HR-FDMS, calcd for $C_{69}H_{84}^{79}Br_2O_{10}Si$ $[M]^+$: 1258.4200, found: 1258.4180.

7.1.47. Reduction of 57. To a solution of **57** (13.8 mg, 10.9 μmol) in THF–H_2O (3:1, v/v, 1.2 ml) were added

$CeCl_3 \cdot 7H_2O$ (12.8 mg, 34.4 μmol) and $NaBH_4$ (22.3 mg, 589 μmol) at 25 °C. During 8 d, $NaBH_4$ was added several times to the reaction mixture with stirring until the reaction was complete. After that, saturated aqueous $NaHCO_3$ (1 ml) was added and the aqueous layer was extracted with Et_2O (4×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/AcOEt=4) to give a mixture of **49** and **56** (13.3 mg, 96%, **49**:**56**>5:1 from ^{1}H NMR).

Acknowledgements

We are grateful to Mr. Kenji Watanabe and Dr. Eri Fukushi (GC–MS and NMR Laboratory, Graduate School of Agriculture, Hokkaido University) for the measurements of mass spectra. We also thank Mr. Yasuhiro Kumaki (High Resolution NMR Laboratory, Graduate School of Science, Hokkaido University) for the measurements of NMR spectra. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japanese Government.

References and notes

1. For reviews of ciguatoxins and related marine toxins, see: (a) Yasumoto, T.; Murata, M. *Chem. Rev.* **1993**, *93*, 1897; (b) Scheuer, P. J. *Tetrahedron* **1994**, *50*, 3; (c) Murata, M.; Yasumoto, T. *Nat. Prod. Rep.* **2000**, *17*, 293; (d) Yasumoto, T. *Chem. Rec.* **2001**, *1*, 228.
2. For recent reviews of ciguatera, see: (a) Lehane, L.; Lewis, R. J. *Int. J. Food Microbiol.* **2000**, *61*, 91; (b) Lewis, R. J. *Toxicon* **2001**, *39*, 97.
3. Yasumoto, T.; Nakajima, R.; Bagnis, R.; Adachi, R. *Bull. Jpn. Soc. Sci. Fish.* **1977**, *43*, 1021.
4. Recent reports for immunological detection of CTXs aiming at prevention of ciguatera intoxication: (a) Oguri, H.; Hirama, M.; Tsumuraya, T.; Fujii, I.; Maruyama, M.; Uehara, H.; Nagumo, Y. *J. Am. Chem. Soc.* **2003**, *125*, 7608; (b) Hokama, Y.; Whang, C.; Chun, K. F.; Suma, C.; Higa, N.; Or, B.; Cocchetto, A.; Kansky, G. *J. Toxcol., Toxin Rev.* **2003**, *22*, 547; (c) Nagumo, Y.; Oguri, H.; Shindo, Y.; Sasaki, S.; Oishi, T.; Hirama, M.; Tomioka, Y.; Mizugaki, M.; Tsumuraya, T. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2037; (d) Pauillac, S.; Sasaki, M.; Inoue, M.; Naar, J.; Branaa, P.; Chinain, M.; Tachibana, K.; Legrand, A.-M. *Toxicon* **1999**, *38*, 669; (e) Oguri, H.; Tanaka, S.; Hishiyama, S.; Oishi, T.; Hirama, M.; Tsumuraya, T.; Tomioka, Y.; Mizugaki, M. *Synthesis* **1999**, 1431; (f) Hokama, Y.; Nishimura, K.; Takenaka, W.; Ebesu, J. S. M. *J. Nat. Toxins* **1998**, *7*, 1.
5. (a) Scheuer, P. J.; Takahashi, W.; Tsutsumi, J.; Yoshida, T. *Science* **1967**, *155*, 1267; (b) Tachibana, K. Ph.D. Thesis, University of Hawaii, 1980; (c) Nukina, M.; Koyanagi, L. M.; Scheuer, P. J. *Toxicon* **1984**, *22*, 169; (d) Tachibana, K.; Nukina, M.; Joh, Y. G.; Scheuer, P. J. *Biol. Bull.* **1987**, *172*, 122.
6. Satake, M.; Morohashi, A.; Oguri, H.; Oishi, T.; Hirama, M.; Harada, N.; Yasumoto, T. *J. Am. Chem. Soc.* **1997**, *119*, 11325.
7. Satake, M.; Murata, M.; Yasumoto, T. *Tetrahedron Lett.* **1993**, *34*, 1975.
8. For the bioactivities of ciguatoxins and related compounds, see: (a) Catterall, W. A.; Risk, M. *Mol. Pharmacol.* **1981**, *19*, 345; (b) Bidard, J.-N.; Vijverberg, H. P. M.; Frelin, C.; Chungue, E.; Legrand, A.-M.; Bagnis, R.; Lazdanski, M. *J. Biol. Chem.* **1984**, *259*, 8353; (c) Lombet, A.; Bidard, J.-N.; Lazdanski, M. *FEBS Lett.* **1987**, *219*, 355; (d) Dechraoui, M.-Y.; Naar, J.; Pauillac, S.; Legrand, A.-M. *Toxicon* **1999**, *37*, 125. See also references cited in Ref. 2.
9. For the total synthesis of CTX3C, see: (a) Hirama, M.; Oishi, T.; Uehara, H.; Inoue, M.; Maruyama, M.; Oguri, H.; Satake, M. *Science* **2001**, *294*, 1904; (b) Inoue, M.; Uehara, H.; Maruyama, M.; Hirama, M. *Org. Lett.* **2002**, *4*, 4551; (c) Maruyama, M.; Inoue, M.; Oishi, T.; Oguri, H.; Ogasawara, Y.; Shindo, Y.; Hirama, M. *Tetrahedron* **2002**, *58*, 1835; (d) Uehara, H.; Oishi, T.; Inoue, M.; Shoji, M.; Nagumo, Y.; Kosaka, M.; Brazidec, J.-Y. L.; Hirama, M. *Tetrahedron* **2002**, *58*, 6493; (e) Inoue, M.; Yamashita, S.; Tatami, A.; Miyazaki, K.; Hirama, M. *J. Org. Chem.* **2004**, *69*, 2797; (f) Kobayashi, S.; Takahashi, Y.; Komano, K.; Alizadeh, B. H.; Kawada, Y.; Oishi, T.; Tanaka, S.; Ogasawara, Y.; Sasaki, S.; Hirama, M. *Tetrahedron* **2004**, *60*, 8375; (g) Inoue, M.; Hirama, M. *Synlett* **2004**, 577; (h) Inoue, M.; Hirama, M. *Acc. Chem. Res.* **2004**, *37*, 961; (i) Inoue, M.; Miyazaki, K.; Uehara, H.; Maruyama, M.; Hirama, M. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 12013; (j) Hirama, M. *Chem. Rec.* **2005**, *5*, 240.
10. For recent synthetic studies on ciguatoxins from other groups, see: (a) Takai, S.; Ploypradith, P.; Hamajima, A.; Kira, K.; Isobe, M. *Synlett* **2002**, 588; (b) Takai, S.; Isobe, M. *Org. Lett.* **2002**, *4*, 1183; (c) Kira, K.; Hamajima, A.; Isobe, M. *Tetrahedron* **2002**, *58*, 1875; (d) Sasaki, M.; Ishikawa, M.; Fuwa, H.; Tachibana, K. *Tetrahedron* **2002**, *58*, 1889; (e) Takakura, H.; Sasaki, M.; Honda, S.; Tachibana, K. *Org. Lett.* **2002**, *4*, 2771; (f) Sasaki, M.; Noguchi, T.; Tachibana, K. *J. Org. Chem.* **2002**, *67*, 3301; (g) Candenas, M. L.; Pinto, F. J.; Cintada, C. G.; Morales, E. Q.; Brouard, I.; Díaz, M. T.; Rico, M.; Rodríguez, E.; Rodríguez, R. M.; Pérez, R.; Pérez, R. L.; Martín, J. D. *Tetrahedron* **2002**, *58*, 1921; (h) Bond, S.; Perlmutter, P. *Tetrahedron* **2002**, *58*, 1779; (i) Takai, S.; Sawada, N.; Isobe, M. *J. Org. Chem.* **2003**, *68*, 3225; (j) Baba, T.; Isobe, M. *Synlett* **2003**, 547; (k) Baba, T.; Huang, G.; Isobe, M. *Tetrahedron* **2003**, *59*, 6851; (l) Tatami, A.; Inoue, M.; Uehara, H.; Hirama, M. *Tetrahedron Lett.* **2003**, *44*, 5229; (m) Baba, T.; Takai, S.; Sawada, N.; Isobe, M. *Synlett* **2004**, 603; (n) Fuwa, H.; Fujikawa, S.; Tachibana, K.; Takakura, H.; Sasaki, M. *Tetrahedron Lett.* **2004**, *45*, 4795; (o) Kobayashi, S.; Alizadeh, B. H.; Sasaki, S.-y.; Oguri, H.; Hirama, M. *Org. Lett.* **2004**, *6*, 751; (p) Hamajima, A.; Isobe, M. *Org. Lett.* **2006**, *8*, 1205.
11. For convergent approaches to polycyclic ether systems, see: (a) Alvarez, E.; Díaz, M. T.; Hanxing, L.; Martín, J. D. *J. Am. Chem. Soc.* **1995**, *117*, 1437; (b) Nicolaou, K. C. *Angew. Chem., Int. Ed.* **1996**, *35*, 589; (c) Ravelo, J. L.; Regueiro, A.; Rodríguez, E.; de Vera, J.; Martín, J. D. *Tetrahedron Lett.* **1996**, *37*, 2869; (d) Alvarez, E.; Pérez, R.; Rico, M.; Rodríguez, R. M.; Martín, J. D. *Org. Chem.* **1996**, *61*, 3003; (e) Oishi, T.; Nagumo, Y.; Hirama, M. *Synlett* **1997**, 980; (f) Oishi, T.; Nagumo, Y.; Hirama, M. *Chem. Commun* **1998**, 1041; (g) Sasaki, M.; Inoue, M.; Noguchi, Y.; Takeichi, A.; Tachibana, K. *Tetrahedron Lett.* **1998**, *39*, 2783; (h) Sasaki, M.; Fuwa, H.; Inoue, M.; Tachibana, K. *Tetrahedron Lett.* **1998**, *39*, 9027; (i) Fujiwara, K.; Morishita, H.; Saka, K.; Murai, A. *Tetrahedron Lett.* **2000**, *41*, 503; (j) Matsuo, G.; Hinou, H.; Koshino, H.; Suenaga, T.; Nakata, T. *Tetrahedron Lett.* **2000**, *41*, 903; (k) Mori, Y.; Mitsuoka, S.; Furukawa, H. *Tetrahedron Lett.* **2000**, *41*, 4161; (l) Kadowaki, C.; Chan,

P. W. H.; Kadota, I.; Yamamoto, Y. *Tetrahedron Lett.* **2000**, *41*, 5769; (m) Díaz, M. T.; Pérez, R. L.; Rodríguez, L.; Ravelo, J. L.; Martín, J. D. *Synlett* **2001**, 345; (n) Suzuki, K.; Nakata, T. *Org. Lett.* **2002**, *4*, 2739; (o) Kadota, I.; Ohno, A.; Matsuda, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 3562; (p) Inoue, M.; Wang, G. X.; Wang, J.; Hirama, M. *Org. Lett.* **2002**, *4*, 3439; (q) Oishi, T.; Watanabe, K.; Murata, M. *Tetrahedron Lett.* **2003**, *44*, 7315; (r) Inoue, M.; Wang, J.; Wang, G.-X.; Ogasawara, Y.; Hirama, M. *Tetrahedron* **2003**, *59*, 5645; (s) Sasaki, M.; Fuwa, H. *Synlett* **2004**, 1851; (t) Kadota, I.; Yamamoto, Y. *Acc. Chem. Res.* **2005**, *38*, 423; (u) Inoue, M. *Chem. Rev.* **2005**, *105*, 4379.

12. Recent reviews for the synthesis of polycyclic ethers: (a) Nakata, T. *Chem. Rev.* **2005**, *105*, 4314; (b) Inoue, M. *Chem. Rev.* **2005**, *105*, 4379.
13. For the synthetic studies on ciguatoxins in our laboratory, see: (a) Oka, T.; Murai, A. *Chem. Lett.* **1994**, 1611; (b) Oka, T.; Fujiwara, K.; Murai, A. *Tetrahedron* **1996**, *52*, 12091; (c) Atsuta, H.; Fujiwara, K.; Murai, A. *Synlett* **1997**, 307; (d) Oka, T.; Fujiwara, K.; Murai, A. *Tetrahedron Lett.* **1997**, *38*, 8035; (e) Oka, T.; Murai, A. *Tetrahedron* **1998**, *54*, 1; (f) Oka, T.; Fujiwara, K.; Murai, A. *Tetrahedron* **1998**, *54*, 21; (g) Fujiwara, K.; Saka, K.; Takaoka, D.; Murai, A. *Synlett* **1999**, 1037; (h) Fujiwara, K.; Tanaka, H.; Murai, A. *Chem. Lett.* **2000**, 610; (i) Fujiwara, K.; Takaoka, D.; Kusumi, K.; Kawai, K.; Murai, A. *Synlett* **2001**, 691; (j) Fujiwara, K.; Koyama, Y.; Doi, E.; Shimawaki, K.; Ohtaniuchi, Y.; Takemura, A.; Souma, S.; Murai, A. *Synlett* **2002**, 1496; (k) Fujiwara, K.; Koyama, Y.; Kawai, K.; Tanaka, H.; Murai, A. *Synlett* **2002**, 1835; (l) Tanaka, H.; Kawai, K.; Fujiwara, K.; Murai, A. *Tetrahedron* **2002**, *58*, 10017; (m) Fujiwara, K.; Goto, A.; Sato, D.; Ohtaniuchi, Y.; Tanaka, H.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2004**, *45*, 7011; (n) Takemura, A.; Fujiwara, K.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2004**, *45*, 7567; (o) Takemura, A.; Fujiwara, K.; Shimawaki, K.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron* **2005**, *61*, 7392; (p) Domon, D.; Fujiwara, K.; Ohtaniuchi, Y.; Takezawa, A.; Takeda, S.; Kawasaki, H.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2005**, *46*, 8279; (q) Domon, D.; Fujiwara, K.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2005**, *46*, 8285; (r) Takizawa, A.; Fujiwara, K.; Doi, E.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron Lett.* **2006**, *47*, 747.
14. (a) Ogura, K.; Tsuchihashi, G. *Tetrahedron Lett.* **1972**, *13*, 2681; (b) Herrmann, J. L.; Richman, J. E.; Wepplo, P. J.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, *14*, 4707.
15. The position numbering is according to that of CTX3C.
16. Nicolaou, K. C.; Hwang, C. K.; Nugiel, D. A. *J. Am. Chem. Soc.* **1989**, *111*, 4136.
17. A similar ring closure of the G-ring part by reductive etherification was reported by the Isobe group, where the cyclization of a tricyclic compound corresponding to the EF–H-ring part having 26-keto and 31-hydroxy groups was successfully performed: Takai, S.; Sawada, N.; Isobe, M. *J. Org. Chem.* **2003**, *68*, 3225.
18. (a) Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179; (b) Jin, H.; Uenishi, J.; Christ, W. J.; Kishi, Y. *J. Am. Chem. Soc.* **1986**, *108*, 5644.
19. For successful synthesis of a *Z*-iodoolefin, see: (a) Smith, A. B., III; Beauchamp, T. J.; LaMarche, M. J.; Kaufman, M. D.; Qiu, Y.; Arimoto, H.; Jones, D. R.; Kobayashi, K. *J. Am. Chem. Soc.* **2000**, *122*, 8654; (b) Sawada, D.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 10521; See, also: (c) Tanino, K.; Arakawa, K.; Satoh, M.; Iwata, Y.; Miyashita, M. *Tetrahedron Lett.* **2006**, *47*, 861.
20. Mori, Y.; Yaegashi, K.; Furukawa, H. *J. Am. Chem. Soc.* **1996**, *118*, 8158.
21. (a) Carling, R. W.; Holmes, A. B. *Tetrahedron Lett.* **1986**, *27*, 6133; (b) Kotsuki, H.; Kadota, I.; Ochi, M. *Tetrahedron Lett.* **1990**, *31*, 4609.
22. (a) Negishi, E.; Yoshida, T. *Tetrahedron Lett.* **1980**, *21*, 1501; (b) For the hydrozirconation reaction with the Schwartz reagent (Cp_2ZrHCl), see: Kiyotsuka, Y.; Igarashi, J.; Kobayashi, Y. *Tetrahedron Lett.* **2002**, *43*, 2725 (c) Hart, D. W.; Schwartz, J. *J. Am. Chem. Soc.* **1974**, *96*, 8115; (d) Schwartz, J.; Labinger, J. A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 333.
23. cf. Nocolaou, K. C.; Veale, C. A.; Hwang, C.-K.; Hutchinson, J.; Prasad, C. V. C.; Ogilvie, W. W. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 299.
24. (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155; (b) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.
25. (a) Corey, E. J.; Narasaka, K.; Shibasaki, M. *J. Am. Chem. Soc.* **1976**, *98*, 6417; (b) Crimmins, M. T.; Tabet, E. A. *J. Am. Chem. Soc.* **2000**, *122*, 5473.
26. Since the *R* configuration at C31 of **22** was proved by modified Mosher's method, the C31 configuration of the other diastereomer **21** was determined as S. Preparation and ^{1}H NMR data of MTPA esters of **22** are described in Section 7. Ohtani, I.; Kusumi, T.; Kashuman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092.
27. Kim, S,; Ahn, K. H. *J. Org. Chem.* **1984**, *49*, 1717.
28. Gemal, A. L.; Luche, J. L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.
29. Krishnamurthy, S.; Brown, H. C. *J. Am. Chem. Soc.* **1976**, *98*, 3383.
30. Tanaka, S,; Yamamoto, H.; Nozaki, H.; Sharpless, K. B.; Michaelson, R. C.; Cutting, J. D. *J. Am. Chem. Soc.* **1974**, *96*, 5254.
31. Miyashita, M.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772.
32. Nicolaou, K. C.; Prasad, C. V. C.; Hwang, C.-K.; Duggan, M. E.; Veale, C. A. *J. Am. Chem. Soc.* **1989**, *111*, 5321.
33. Fujiwara, K.; Saka, K.; Takaoka, D.; Murai, A. *Synlett* **1999**, 1037.
34. Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.
35. Evans, D. A.; Gauchet-Prunet, J. A.; Carreira, E. M.; Charette, A. B. *J. Org. Chem.* **1991**, *56*, 741.
36. Chen, K.-M.; Hardtmann, G. E.; Prasad, K.; Repic, O.; Shapiro, M. J. *Tetrahedron Lett.* **1987**, *28*, 155.
37. (a) Gaunt, M. J.; Yu, J.; Spencer, J. B. *J. Org. Chem.* **1998**, *63*, 4172; (b) Xia, J.; Abbas, S. A.; Locke, R. D.; Piskorz, C. F.; Alderfer, J. L.; Matta, K. L. *Tetrahedron Lett.* **2000**, *41*, 169; (c) Wright, J. A.; Yu, J.; Spencer, J. B. *Tetrahedron Lett.* **2001**, *42*, 4033.