Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
Tetrahedron 61 (2005) 7392–7419

Synthesis of the EF-ring segment of ciguatoxin CTX1B based on novel regioselective reduction of unsaturated cyanohydrins and ring-closing olefin metathesis

Atsushi Takemura, Kenshu Fujiwara,* Ken Shimawaki, Akio Murai,† Hidetoshi Kawai and Takanori Suzuki

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

Received 22 January 2005; revised 23 May 2005; accepted 24 May 2005

Available online 15 June 2005

Abstract—Aiming at a convergent total synthesis of ciguatoxin CTX1B, its EF-ring segment has been synthesized. During the synthesis, a novel method for the construction of branched ethers, based on regioselective reduction of γ-alkoxy β,γ-unsaturated α-silyloxy nitriles with borontrifluoride etherate and trialkyl silane or tributyltin hydride, has been developed. Combination use of the method and ring-closing olefin metathesis successfully provided medium-sized cyclic ethers. Efficient site-selective reduction of vinyl epoxides into homoallyl alcohols has also been developed.

1. Introduction

Ciguatoxin CTX1B is a causative toxin of ciguatera fish poisoning,[1,2] which afflicts more than 20,000 people in tropical and subtropical areas annually. The toxin is produced originally by the epiphytic dinoflagellate, *Gambierdiscus toxicus*, transferred to herbivorous fish, and accumulated subsequently in carnivorous fish through the food chain, thus causing human intoxication.[3] The symptoms of ciguatera are represented by diarrhea, vomiting, joint pain, prostration and unusual temperature perception disturbance called 'dry-ice sensation'. Generally, patients need several months to recover completely from these symptoms, which has resulted in serious social problems.

CTX1B was first isolated from the moray eel, *Gymnothorax javanicus*, by Scheuer and co-workers in 1967 and characterized as a polycyclic ether compound in 1980.[4] The whole structure of CTX1B, except for the absolute configuration and the relative configuration at C2, was elucidated from a purified sample of only 0.35 mg of CTX1B isolated from 4 t of *G. javanicus* by Yasumoto and co-workers in 1989.[5] They reported that the structure of CTX1B consisted of 12 *trans*-fused cyclic ethers, ranging from six- to nine-membered, and a five-membered spirocyclic ether at one end. Moreover, the absolute configuration of CTX1B was determined in 1997 as shown in Figure 1 by collaboration of Yasumoto, Hirama and Harada.[6]

The potent bioactivity of CTX1B is thought to result from the activation of voltage-sensitive sodium channels (VSSCs) in neuron cells by the strong binding of CTX1B to site 5 on the channel.[7] While it is known that the binding site on VSSC was shared by brevetoxins or another class of structurally related marine toxins,[8] the precise location of the receptor site for these toxins and the binding mode of CTX1B to the channel protein has not yet been elucidated.[9] However, the studies of ciguatoxin in neurology and hygiene have been impeded by the extremely limited availability of CTX1B from natural sources. Therefore, a synthetic supply of CTX1B on a practical scale is essential in order to solve the problem.

From the synthetic viewpoint, its unique *trans*-fused polycyclic ether structure and strong bioactivity have attracted the attention of synthetic chemists. The convergent construction of such large fused polyether structure has been a significant challenge. Intensive efforts by synthetic chemists aiming at the concise construction of the polyether framework as well as completion of the total synthesis of CTX1B and its congeners are ongoing.[10–13] In the course of

Keywords: Ciguatoxin CTX1B; Fused medium-ring ether; Ring-closing olefin metathesis; Branched ether synthesis; Site-selective reduction.
* Corresponding author. Tel.: +81 11 706 2701; fax: +81 11 706 4924; e-mail: fjwkn@sci.hokudai.ac.jp
† Present address: 6-14-44, Asabu-cho, Kita-ku, Sapporo 001-0045, Japan.

0040–4020/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.05.073

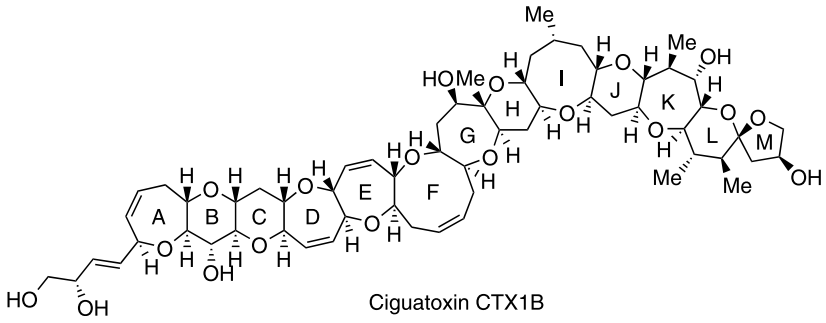
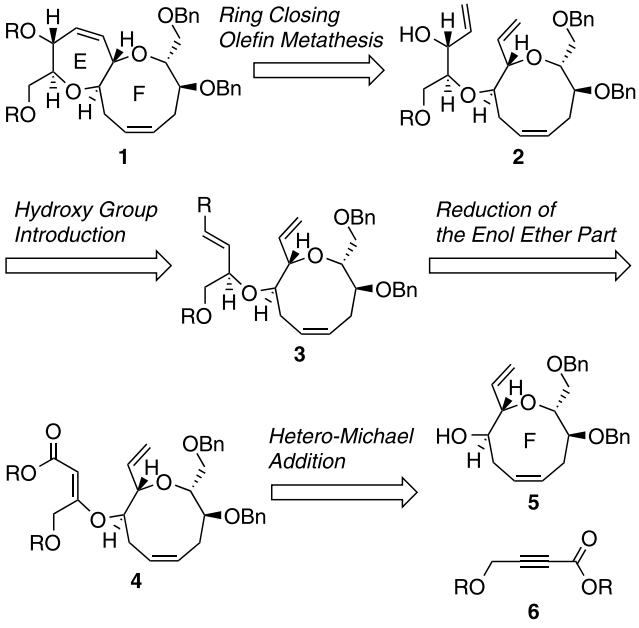


Figure 1.

our synthetic studies on CTX1B and its congeners,[14] we have established a method based on the coupling reaction of an acyl anion equivalent with an aldehyde for the convergent construction of a *trans*-fused 6/6 or 6/7 cyclic ether system in the middle part.[14g,i,k,15] Therefore, we designed the synthetic segments of CTX1B corresponding to the AB-, EF-, I-, and LM-ring parts, and planned to connect them at the CD-,[14i,k] GH-, and JK-ring[14i] parts at the later stage of total synthesis. So far, the AB-,[14l] I-,[14j] and LM-ring[14e] segments have been constructed. Here, synthesis of the remaining EF-ring segment based on a novel branched ether formation using regioselective reduction of unsaturated cyanohydrins and ring-closing olefin metathesis (RCM) is described.[14n] An efficient transformation reaction of a vinyl epoxide into a homoallyl alcohol, developed during the synthesis, is also disclosed.

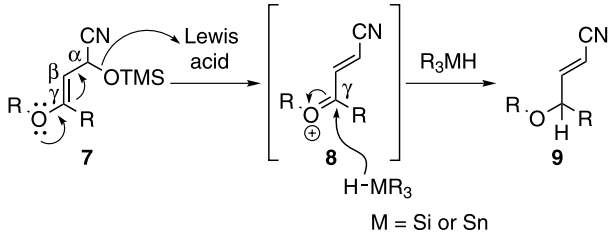
2. First generation synthesis of the EF-ring segment

First, we planned to synthesize the EF-ring segment **1** from the F-ring part **5** (Scheme 1). The synthetic route consisted of the following four processes: (i) construction of the E-ring in **1** from precursor diene **2** by Grubbs' RCM;[16,17] (ii) introduction of a hydroxy group to the β-position of the branched ether part of **3**; (iii) reduction of the 3-alkoxy-2-butenoate part of **4** and (iv) hetero-Michael addition of 2-butynoate ester **6** with the F-ring part **5** according to Paintner's procedure.[18]



Scheme 1. Retrosynthetic analysis for the EF-ring segment **1**.

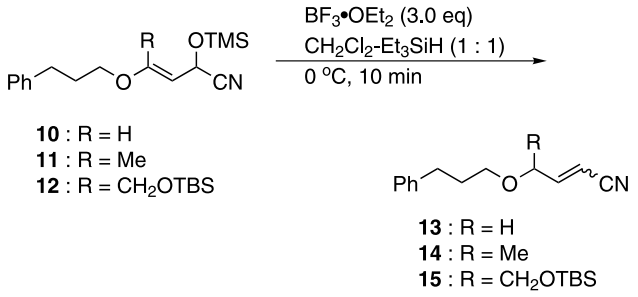
Grubbs' RCM has now become one of the most reliable methods among a number of approaches for the construction of medium-sized cyclic ethers, because it realizes efficient ring-closure under mild catalytic conditions and tolerates a wide variety of functional groups in its substrates.[10,16] Accordingly, we applied Grubbs' RCM to the construction of the E-ring in the process (i). On the other hand, preparation of the precursors for RCM involves a serious difficulty of the stereoselective construction of an acyclic branched ether part in each substrate. Recently, several successful methods based on an alkylation or an aldol reaction of a glycolate ester derivative,[11q,r,19] allyl[11a,f,t,y] or hydride[11e,w] addition to an acetal group, an addition reaction of an α-alkoxy carbon radical to a β-alkoxy propenoate ester,[11h,j,v] or ring cleavage of *C*-glycosides,[14j,20] have been developed to solve the problem. However, the number of methods is insufficient to meet the requirements for the synthesis of a variety of complex natural cyclic ethers. Therefore, a reductive transformation reaction shown in Scheme 2 was newly designed for the process (iii).[14n,21] We expected that γ-alkoxy β,γ-unsaturated α-silyloxy nitrile **7** would be activated by an appropriate Lewis acid to generate oxonium ion **8**, which would be selectively reduced at the γ-position into γ-alkoxy α,β-unsaturated nitrile **9** by a proper reducing agent. The nitrile group of **9** would be available for the synthesis of **2** (process (ii)).



Scheme 2. Lewis-acid-promoted γ-position selective reduction of a γ-alkoxy β,γ-unsaturated α-silyloxy nitrile system.

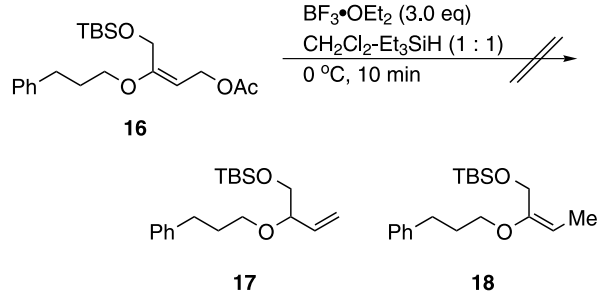
First, γ-position selective reduction of simple acyclic cyanohydrin derivatives **10**, **11**, and **12** was examined. We selected Et_3SiH as a reducing agent because of its efficient reducing ability toward the oxonium ion intermediate. After extensive exploration for effective activators of the cyanohydrins, $BF_3 \cdot OEt_2$ was found to give the best result. Selected successful examples are shown in Table 1. Every

Table 1. $BF_3 \cdot OEt_2$ promoted γ-position selective reduction of model compounds



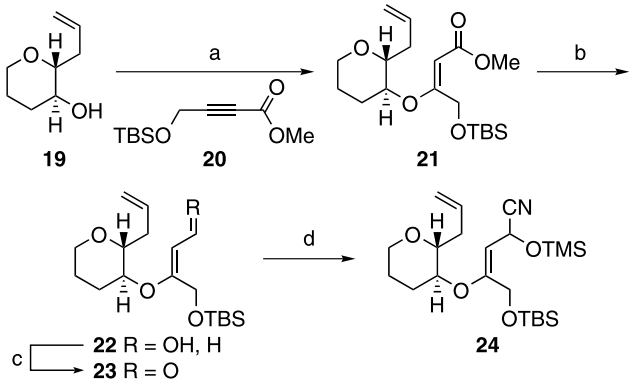
Entry	R	Yield (%)
1	H	64% (*E*:*Z*=6.2:1.0)
2	Me	62% (only *E*)
3	CH_2OTBS	64% (only *E*)

reaction was carried out in a 1:1 (v/v) mixture of Et_3SiH and CH_2Cl_2 in the presence $BF_3 \cdot OEt_2$ (3.0 equiv) at 0 °C and afforded the corresponding γ-alkoxy α,β-unsaturated nitrile (**13**, **14**, or **15**) in good yield. On the other hand, simple and easily available 3-alkoxy-2-propenyl acetate **16** did not produce the corresponding allyl or vinyl ether (**17** or **18**) under the same conditions. It only resulted in decomposition of the substrate. Thus, the γ-alkoxy β,γ-unsaturated α-silyloxy nitrile was found to be a good substrate (Scheme 3).



Scheme 3. An attempt to reduce 3-alkoxy-2-propenyl acetate **16**.

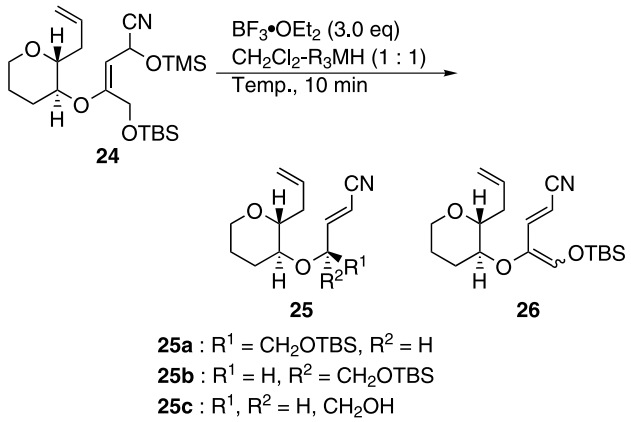
Next, encouraged by the results, we planned to synthesize a *trans*-fused 6/8 cyclic ether model, which has a side chain and a hydroxyl group with proper stereochemistry available for further construction of a *trans*-fused ether ring, from **19**[14g] and **20** according to the above strategy. Reduction precursor **24** was synthesized according to Scheme 4. Hetero-Michael addition of **19** to butynoate **20** in the presence of Me_3P afforded **21** in 95% yield.[22] Reduction of the ester **21** with DIBAH followed by oxidation with TPAP gave the aldehyde **23** in 88% yield. Treatment of **23** with TMSCN (2.5 equiv) in the presence of Me_3Al in benzene at ambient temperature gave **24** as a 1:1 mixture of diastereomers in 74% yield.



Scheme 4. Preparation of reduction precursor **24**. Reagents and conditions: (a) PMe_3 (1.1 equiv), **20** (1.7 equiv), CH_2Cl_2, 0 °C, →24 °C, 1 h, 95% (only *E*); (b) DIBAH (4.0 equiv), CH_2Cl_2, −78 °C, 10 min, ~100%; (c) TPAP (0.1 equiv), NMO (2.0 equiv), MS 4A, CH_2Cl_2, 24 °C, 50 min, 88%; (d) Me_3Al (1.1 equiv), TMSCN (2.5 equiv), benzene, 24 °C, 1 h, 74%.

The regioselective reduction of **24** under the same conditions as the case of acyclic models produced a mixture of **25a**,**b**, and **26** (3.6:6.4:1.0) in 49% yield along with alcohol **25c** in 14% yield (entry 1, Table 2).[23] Although the by-production of **25c** was reduced by lowering reaction temperature to −18 °C, the ratio of diene **26** increased (**25a**:**25b**:**26**=1.9:3.8:1.0, entry 2). In order to suppress the diene, we examined several organometallic hydrides. Trialkyl silanes (Et_3SiH, Et_2MeSiH, $EtMe_2SiH$, and Me_2PhSiH) gave almost the same result, and changing the bulkiness of their alkyl substituents did not affect the diene-formation (entries 2–5). On the other hand, Bu_3SnH provided a good result, where no production of **26** was observed, and the ratio of **25a** to **25b** slightly increased (entry 6). The stereochemistry at the newly formed stereocenters of **25a** and **25b** was determined after transformation of **25b** into bicyclic ether **31** (vide infra). Thus, efficient conditions for the γ-selective reduction of α-silyloxy nitrile **24** were found.

Table 2. $BF_3 \cdot OEt_2$ promoted reduction of **24** with several reducing reagents

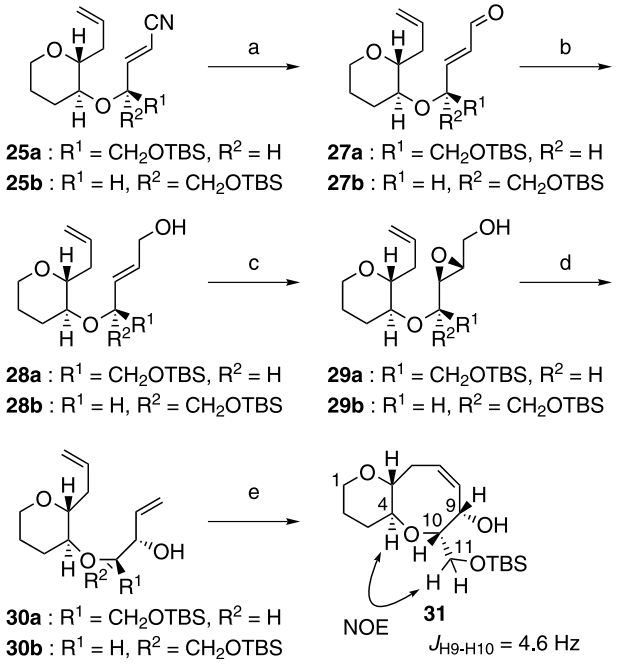


Entry	R_3MH	Temp.	**25a**:**25b**:**26** (Yield) **25c**
1	Et_3SiH	0 °C	3.6:6.4:1.0 (49%) 14%
2[a]	Et_3SiH	−18 °C	1.9:3.8:1.0 (71%)
3	Et_2MeSiH	−18 °C	1.8:3.9:1.0 (65%)
4	$EtMe_2SiH$	−18 °C	1.4:3.5:1.0 (74%)
5	Me_2PhSiH	−18 °C	2.0:4.2:1.0 (61%)
6	Bu_3SnH	−18 °C	1.0:1.3:0 (64%)

[a] Reaction period was 17 min.

Synthesis of a 6/8 bicyclic system from **25a** and **25b** is shown in Scheme 5. A ca. 1:2 mixture of **25a** and **25b** was converted to a mixture of allyl alcohols **28a** and **28b** (68%) by repeated reduction with DIBAH. The Katsuki-Sharpless asymmetric epoxidation[24] of the allyl alcohols using

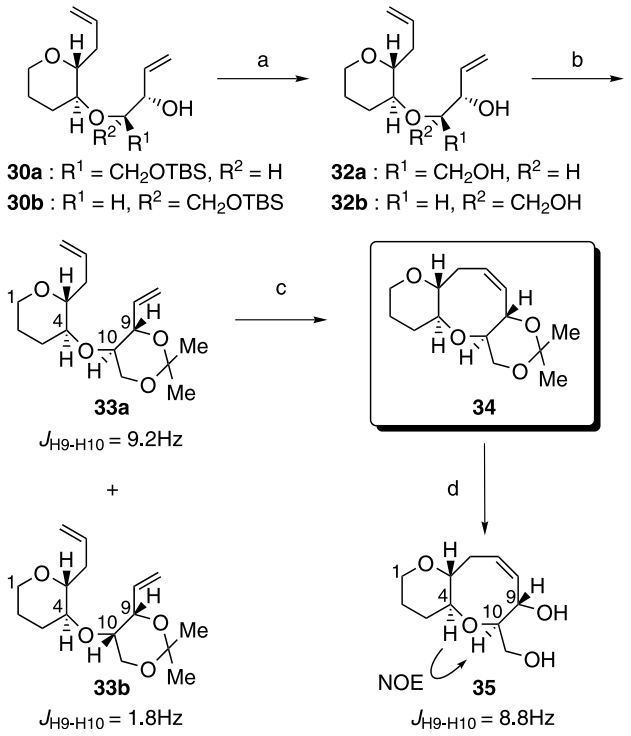
(−)-DET stereoselectively produced a mixture of epoxides **29a** and **29b** (~100%), which was treated with PPh_3 and I_2 in the presence of imidazole at ambient temperature to give allyl alcohols **30a** and **30b** (61%) as a 1:2 mixture.[25,26] Ring closure of dienes **30a** and **30b** in refluxing CH_2Cl_2 by Grubbs' second-generation catalyst[27] gave a mixture of products, in which only **31** was isolated as a bicyclic product (44%), and the desired *trans*-fused 6/8 bicyclic ether was not detected.[28] Stereochemistry of **31** was confirmed by the presence of NOE between H4 and H11 as well as the small *J* value between H9 and H10 (4.6 Hz). From the fact that the 1:2 ratio of the diastereomers was maintained throughout the transformation process from **25** to **30**, and that the yield of **31** (44%) was apparently higher than the ideal yield (33%) of the cyclization product from minor diastereomer **30a**, it was concluded that **31** was produced from **30b** and originated from **25b**.



Scheme 5. Synthesis of bicyclic ether **31**. Reagents and conditions: (a) DIBAH (2.5 equiv), CH_2Cl_2, −78 °C, 10 min, 68%; (b) DIBAH (3.0 equiv), CH_2Cl_2, −78 °C, 8 min, ~100%; (c) D-(−)-DET (0.8 equiv), $Ti(O^iPr)_4$ (0.7 equiv), TBHP (5.0 equiv), MS 4A, CH_2Cl_2, −40 °C, 30 min → −25 °C, 24 h, ~100%; (d) Ph_3P (5.0 equiv), imidazole (5.0 equiv), I_2 (4.0 equiv), THF, 25 °C, 45 min, 61%; (e) $(H_2IMes)(PCy_3)Cl_2Ru$=CHPh (10 mol%), CH_2Cl_2 (5 mM), reflux, 6 h, 44%.

The results from the final RCM step suggested that the vinyl groups of **30a** were apart from each other in the stable conformation of **30a**, and such orientation of the vinyl groups was inappropriate for the cyclization of **30a**. Therefore, we decided to prepare *bicyclic* RCM precursor **33a**, of which the vinyl groups would be placed in close proximity to each other, for successful ring closure in the synthesis of *trans*-fused-bicyclic ether **34** (Scheme 6).

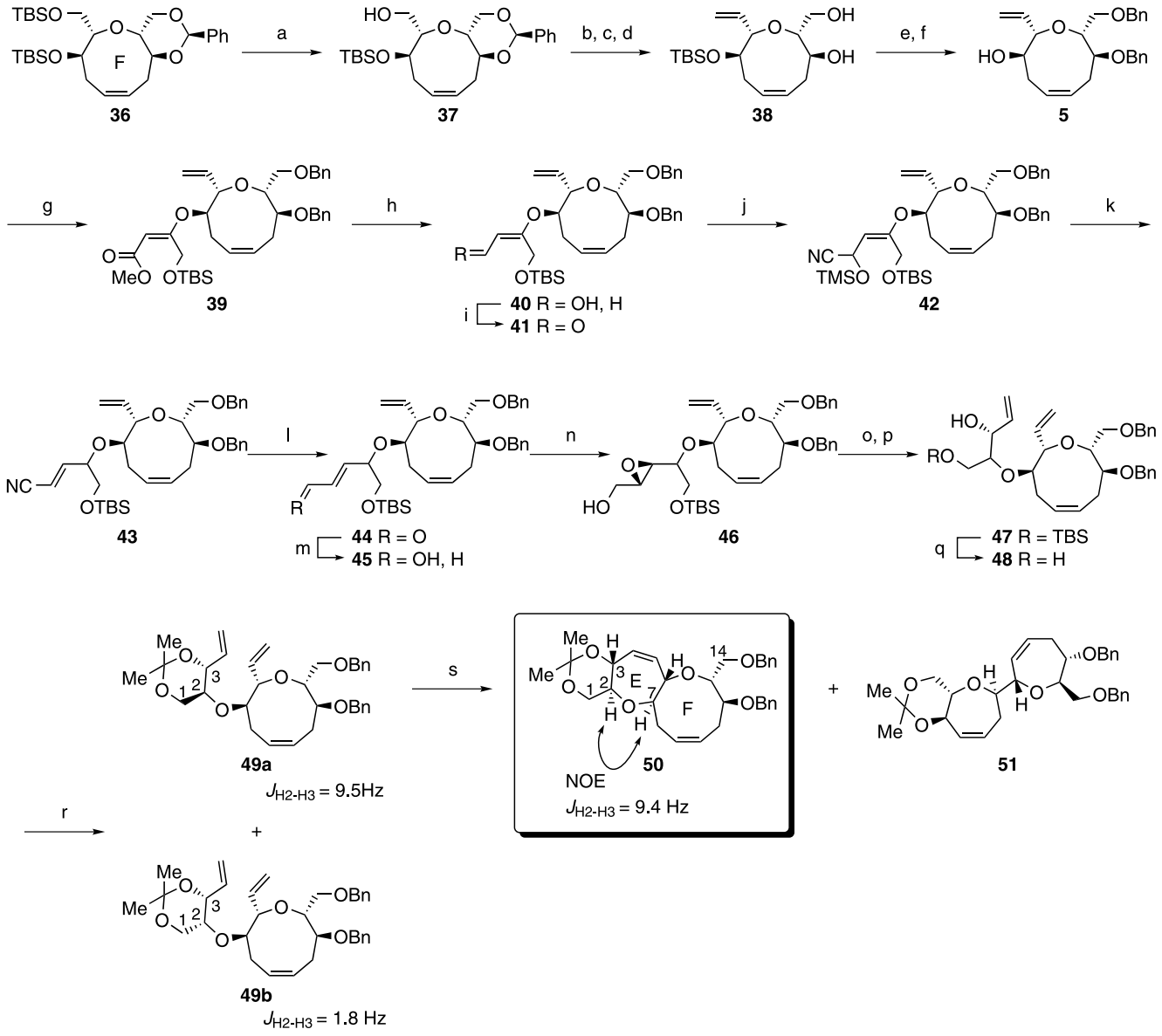
A ca. 1:2 mixture of **30a** and **30b** was converted to a mixture of diols **32a** and **32b** by removal of the TBS group (99%). The acetonide protection of the diols under the standard conditions produced *bicyclic* RCM precursor **33a** (24%) and **33b** (60%), which were easily separated by silica gel column chromatography. The stereochemistry of each



Scheme 6. Synthesis of *trans*-fused bicyclic ether **34**. Reagents and conditions: (a) TBAF (2.0 equiv), THF, 24 °C, 20.5 h, 99%; (b) 2,2-dimethoxypropane (10 equiv), CSA (0.5 equiv), CH_2Cl_2, 24 °C, 7.5 h, **33a**: 24%, **33b**: 60%; (c) $(H_2IMes)(PCy_3)Cl_2Ru$=CHPh (10 mol%), CH_2Cl_2 (4 mM), reflux, 4.5 h, 83%; (d) THF–H_2O–TFA (10:10:1), 23 °C, 11.5 h, 71%.

compound was determined by the *J* value between H9 and H10. RCM[27] of desired **33a** with Grubbs' second-generation catalyst in refluxing CH_2Cl_2 expectedly gave the desired *trans*-fused 6/8 cyclic ether **34** in 83% yield. Since the structure of **34** was difficult to be confirmed, the acetonide **34** was converted to diol **35**. The stereochemistry of **35** was verified by the presence of NOE between H4 and H10 as well as the large *J* value between H9 and H10 (8.8 Hz). Thus, a *bicyclic* precursor was proved to promote efficient ring closure by RCM.

Then, according to the above results, we examined the synthesis of the EF-ring segment **50** from the F-ring part **36**[14j] (Scheme 7). Treatment of **36** with TFA gave primary alcohol **37** selectively in 68% yield along with **36** in 24% recovery. Swern oxidation of the primary alcohol and Wittig reaction followed by removal of benzylidene acetal afforded the diol **38** in 58% yield for three steps. The benzyl (Bn) protection of the diol and removal of the TBS group gave the alcohol **5** in 100% yield. Hetero-Michael addition of the alcohol to 2-butynoate ester **20** produced **39** in good yield (90%),[18] which was converted to α-silyloxy nitrile **42** through reduction, oxidation, and addition of TMSCN. The reduction of **42** with Bu_3SnH in CH_2Cl_2 in the presence of $BF_3{\cdot}OEt_2$ (3.0 equiv) at −18 °C smoothly afforded nitrile **43** as a 1:1 mixture of diastereomers in 55% yield along with **42** in 18% recovery. Conversion of nitrile **43** to allyl alcohol **45** followed by a three-step transformation [(i) Katsuki-Sharpless asymmetric epoxidation[24] using (+)-DET; (ii) iodation of the hydroxy group[25] and (iii) reduction of the resulting epoxy iodide with Zn] gave the corresponding



Scheme 7. Synthesis of the EF-ring segment **50**. Reagents and conditions: (a) THF–H_2O–TFA (10:10:1), 0 °C, 4 h, 68%, 24% recovery of **36**; (b) $(COCl)_2$ (3.0 equiv), DMSO (5.0 equiv), CH_2Cl_2, −78 °C, 15 min then NEt_3 (10 equiv), −20 °C, 10 min; (c) Ph_3PCH_3Br (5.0 equiv), NaHMDS (4.8 equiv), THF, −78 °C, 2.5 h→ 24 °C, 2.5 h; (d) 1,2-ethanedithiol (20 equiv), $NaHCO_3$ (10 equiv), $Zn(OTf)_2$ (1.0 equiv), CH_2Cl_2, 0 °C, 2.5 h, 58% for three steps; (e) NaH (12 equiv), BnBr (6.0 equiv), TBAI (0.1 equiv), THF, 24 °C, 15 h; (f) TBAF (9.0 equiv), THF, 25 °C, 18 h, 100% for two steps; (g) PMe_3 (1.5 equiv), **20** (3.0 equiv), CH_2Cl_2, 0 °C, →24 °C, 1 h, 90% (only *E*); (h) DIBAH (4.0 equiv), CH_2Cl_2, −78 °C, 10 min, 99%; (i) TPAP (0.2 equiv), NMO (2.0 equiv), MS 4A, CH_2Cl_2, 24 °C, 1.5 h, 76%; (j) Me_3Al (1.1 equiv), TMSCN (5.0 equiv), benzene, 24 °C, 1 h, 79%; (k) $BF_3{\cdot}OEt_2$ (3.0 equiv), CH_2Cl_2–Bu_3SnH (1:1), −18 °C, 15 min, 55%, 18% recovery of **42**; (l) DIBAH (2.5 equiv), CH_2Cl_2, −78 °C, 10 min; (m) DIBAH (6.0 equiv), CH_2Cl_2, −78 °C, 20 min, 72% for two steps; (n) L-(+)-DET (1.5 equiv), $Ti(O^iPr)_4$ (1.3 equiv), TBHP (10 equiv), MS 4A, CH_2Cl_2, −40 °C, 30 min→ −25 °C, 26 h; (o) Ph_3P (5.0 equiv), imidazole (5.0 equiv), I_2 (4.0 equiv), THF, 25 °C, 35 min; (p) Zn (7.0 equiv), EtOH-satd. NH_4Claq. (40:1), 25 °C, 2.5 h, 68% for three steps; (q) TBAF (1.5 equiv), THF, 25 °C, 11.5 h, 68%; (r) 2,2-dimethoxypropane (4.0 equiv), CSA (0.5 equiv), CH_2Cl_2, 24 °C, 3 h then acetone (5.0 equiv), 11.5 h, **49a**: 50%, **49b**: 46%; (s) $(Cy_3P)_2Cl_2Ru$=CHPh (25 mol%), CH_2Cl_2 (3 mM), 24 °C, 15 h, **49a**:**50**:**51**=1:1:0.5; $(Cy_3P)_2Cl_2Ru$=CHPh (30 mol%), CH_2Cl_2 (3 mM), 24 °C, 24 h, **50**: 67%, **51**: 24%, after two cycles.

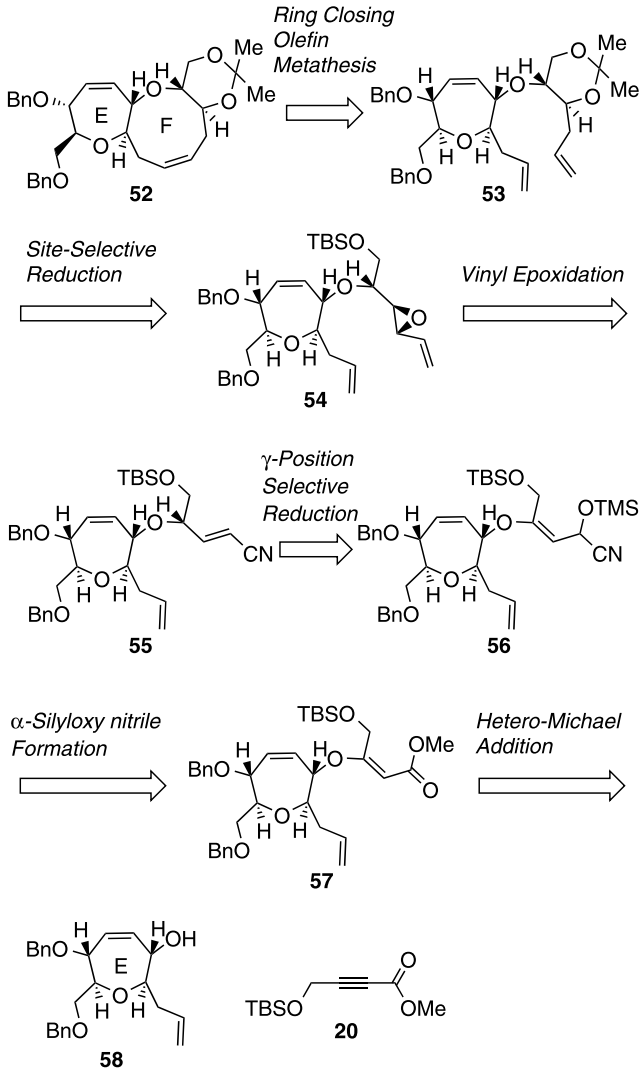
allyl alcohol **47** as a 1:1 mixture of diastereomers in 68% yield. In order to facilitate the closure of the *trans*-fused medium ring by RCM and to confirm the stereochemistry of each diastereomer, acetonides **49a** and **49b** were synthesized from **47** through removal of the TBS group followed by protection of the resulting diol. Diastereomers **49a** and **49b** were easily separated by silica gel column chromatography, and the stereochemistry of each compound was determined by the *J* value between H2 and H3. RCM[16,17] of **49a** with Grubbs' first-generation catalyst in CH_2Cl_2 at ambient temperature successfully produced the desired *trans*-fused EF-ring segment **50** of CTX1B in 67% yield along with **51** in 24% yield. The stereochemistry of **50** was confirmed by the presence of NOE between H2 and H7 as well as the large *J* value between H2 and H3 (9.4 Hz).

Although the synthesis of **50** was thus achieved, two problems arose at the final RCM stage. One was the low reactivity of **49a** under the RCM conditions using Grubbs' first-generation catalyst. The reaction often stopped before completion, and had to be repeated in order to consume **49a** completely. The other problem was a significant

by-production of **51**. It meant that the desired RCM between the terminal vinyl groups making the E-ring was a slow process, and that the metathesis at the olefin part of the F-ring competed with the RCM. These problems would be caused by the severe strain of the E-ring part. In order to solve the problems, we decided to design an alternative improved synthesis of the EF-ring segment.

3. Second generation synthesis of the EF-ring segment

The revised plan for the synthesis of the EF-ring segment of CTX1B is shown in Scheme 8. We intended to cyclize the F-ring by RCM[16,17] at the final stage of the synthesis, and to use the E-ring part as a Michael donor in the initial stage. Therefore, the EF-ring segment **52** was planned to be constructed from the bicyclic diene **53** by RCM.[16,17] The diene would be synthesized via site-selective reduction of vinyl epoxide **54**, which would be prepared from α,β-unsaturated nitrile **55**. According to our established process, the nitrile was designed to be synthesized through hetero-Michael reaction of the E-ring part **58** with **20**,[18] cyanohydrin synthesis from **57**, and regioselective reduction of **56**.[14n]

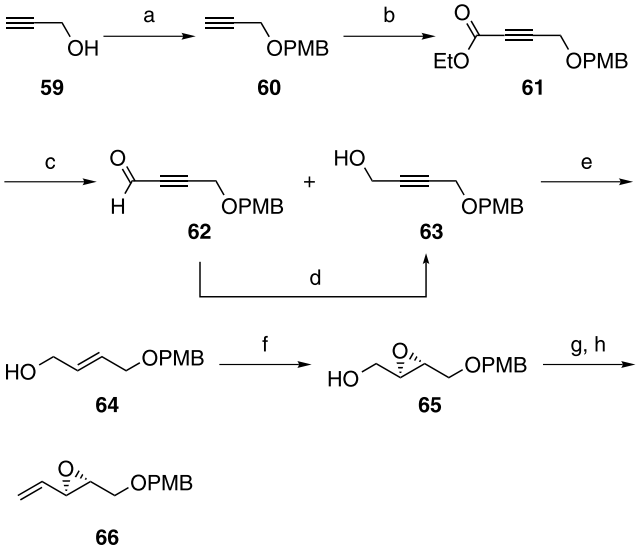


Scheme 8. Retrosynthetic analysis for the EF-ring segment **52**.

In the revised plan, site-selective reduction of vinyl epoxide **54** to the corresponding homoallyl alcohol was a key step. Tsuji and Shimizu reported efficient site-selective hydrogenolysis of epoxides adjacent to an alkene group using a Pd-catalyst and formic acid.[29,30] Therefore, we decided to apply the Pd-catalyzed reduction to our synthesis. Although many trisubstituted epoxides were successfully reduced under the conditions,[29] there were few applications to simple vinyl epoxides.[29a,30] In order to optimize the reduction conditions, epoxide **66** was first examined as a model substrate.

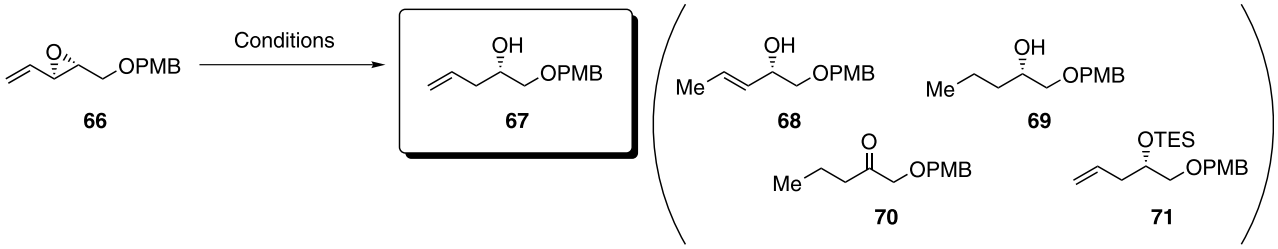
Model compound **66** was synthesized from propargyl alcohol **59**, shown in Scheme 9. Protection of **59** as *p*-methoxy benzyl (PMB) ether (99%) followed by lithiation and addition to ethyl chloroformate produced 2-butynoate ester **61** (79%), which was reduced with DIBAH to give alcohol **63** (26%) and aldehyde **62** (74%). The aldehyde **62** was reduced again with DIBAH to **63** (100%). Reduction of **63** with LAH in THF provided *trans*-allyl alcohol **64**, which was subjected to Katsuki-Sharpless asymmetric epoxidation[24] using (−)-DET to give epoxide **65** (71% yield, 93% ee). Oxidation of **65** followed by Wittig reaction synthesized the desired vinyl epoxide **66** (overall yield 78%).

With the model compound **66** in hand, we examined the site-selective reduction of **66** into homoallyl alcohol **67** in the presence of a Pd-catalyst. First, according to the Tsuji–Shimizu procedure,[29] we attempted the reduction of **66** with formic acid in the presence of triethylamine (entry 1). Although the epoxide **66** was selectively cleaved at the desired site, over-reduced alcohol **69** was mainly produced



Scheme 9. Synthesis of model compound **66**. Reagents and conditions: (a) NaH (1.8 equiv), PMBCl (1.5 equiv), TBAI (0.13 equiv), THF, 24 °C, 16 h, 99%; (b) *n*-BuLi (1.5 equiv), EtOCOCl (1.5 equiv), THF, −78 °C, 1 h→0 °C, 15 min, 79%; (c) DIBAH (2.5 equiv), CH_2Cl_2, −78 °C, 45 min, **62**: 74%, **63**: 26%; (d) DIBAH (2.5 equiv), CH_2Cl_2, −78 °C, 10 min, 100%; (e) LAH (4.0 equiv), THF, −78 °C, 13 min→−20 °C, 26 h, 64%, 24% recovery of **63**; (f) D-(−)-DET (0.20 equiv), $Ti(O^iPr)_4$ (0.15 equiv), TBHP (2.5 equiv), MS 4A, CH_2Cl_2, −40 °C, 30 min→−20 °C, 2.5 d, 71%, 93% ee; (g) SO_3·pyridine (10 equiv), DMSO–NEt_3–CH_2Cl_2 (1:1.4:6), 0 °C→24 °C, 1 h; (h) Ph_3PCH_3Br (5.0 equiv), NaHMDS (4.7 equiv), THF, −78 °C, 2 h→24 °C, 17 h, 78% for two steps.

Table 3. The site-selective reduction of vinyl epoxide **66**



Entry	Conditions	Product
1	$Pd_2(dba)_3\cdot CHCl_3$ (0.1 equiv), n-Bu_3P (0.1 equiv), HCOOH (5.0 equiv), NEt_3 (2.0 equiv), THF, 24 °C, 2.5 h	**69** (83%), **70** (13%)
2	$Pd(PPh_3)_4$ (0.1 equiv), $Me_2NH\cdot BH_3$ (1.1 equiv), AcOH (3.0 equiv), CH_2Cl_2, 23 °C, 1.5 h	**67**:**68**=5.6: 1.0 (97%)
3	$Pd(PPh_3)_4$ (0.1 equiv), Et_3SiH (1.1 equiv), CH_2Cl_2, 24 °C, 1 h	**71** (75%)
4	$Pd(PPh_3)_4$ (0.1 equiv), Bu_3SnH (1.1 equiv), CH_2Cl_2, 24 °C, 20 min	**67** (95%)

along with ketone **70**. Next, as described by Guibé,[31] who reported an improved version of the Tsuji–Shimizu procedure,[29] vinyl epoxide **66** was treated with a catalytic amount of $Pd(PPh_3)_4$ and $Me_2NH\cdot BH_3$ in the presence of acetic acid to give an inseparable 5.6:1.0 mixture of the desired **67** and the isomer **68** (entry 2). On the other hand, when the site-selective reduction was examined with Et_3SiH instead of $Me_2NH\cdot BH_3$ in the absence of acetic acid, not only the desired site selective reduction but also silylation occurred to afford TES ether **71** in 75% yield (entry 3). Eventually, the site-selective reduction with 1.1 equiv of Bu_3SnH gave the best result, where the desired homoallyl alcohol **67** was afforded as the sole product in 95% yield (entry 4). Thus, we found the effective conditions in the site-selective reduction of vinyl epoxide (Table 3).

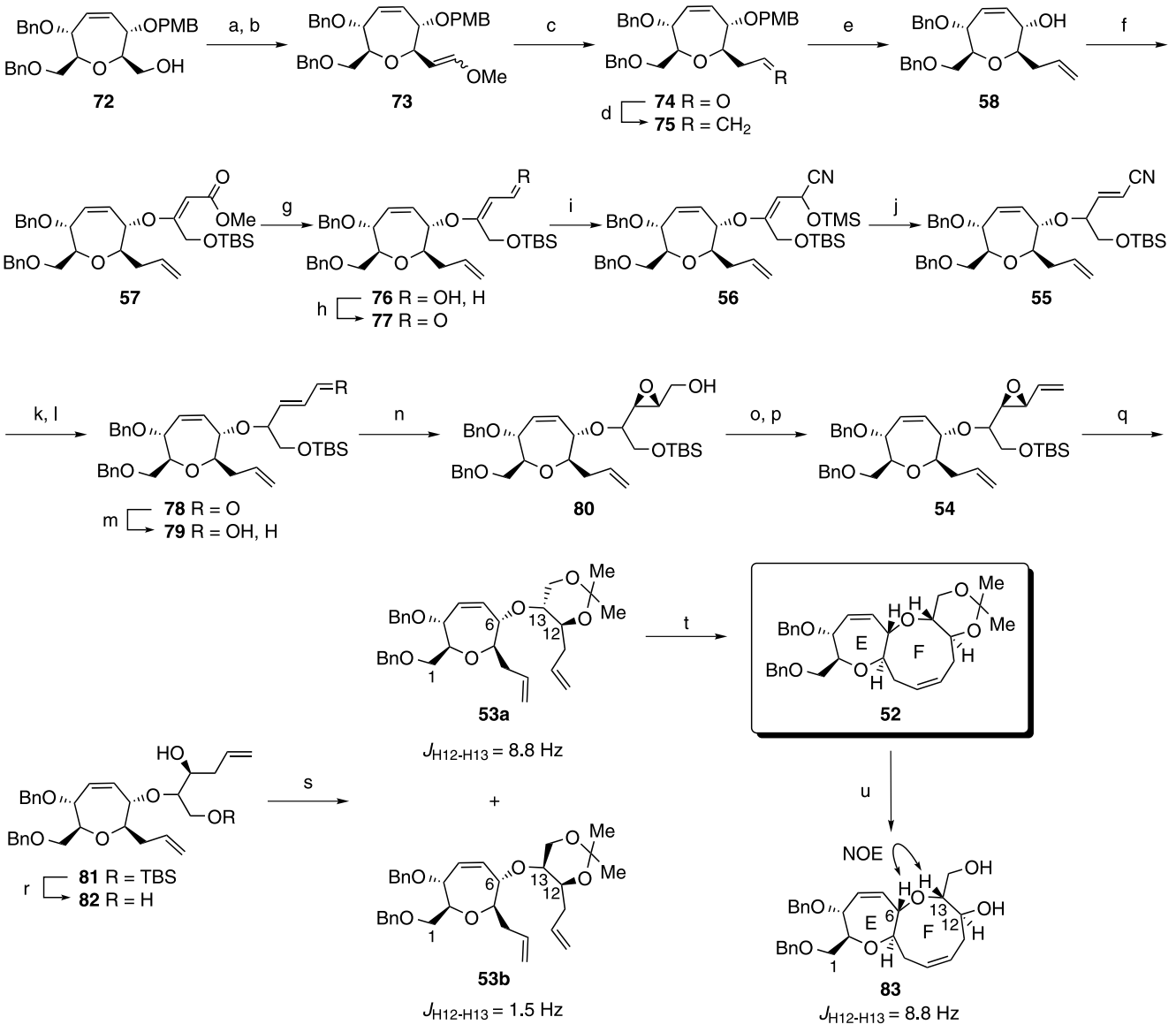
The synthesis of **52** is illustrated in Scheme 10. The Michael donor **58** was prepared from known oxepan alcohol **72**.[32] Swern oxidation of alcohol **72** followed by Wittig reaction gave enol ether **73** (overall yield 70%). Hydrolysis of **73** with $Hg(OAc)_2$ and TBAI in THF–H_2O[33] afforded aldehyde **74** (95%), which was subjected to Wittig reaction and the subsequent removal of the PMB group to provide **58** (overall yield 92%). According to the procedure described in the synthesis of **50**, the alcohol **58** was transformed into α-silyloxy nitrile **56** in four steps ((i) hetero-Michael addition of **58** with **20**;[18] (ii) reduction of ester **57**; (iii) oxidation of the resulting **76** into aldehyde **77**; (iv) addition of TMSCN) (overall yield 57%). The reduction of **56** with Bu_3SnH in CH_2Cl_2 in the presence of $BF_3\cdot OEt_2$ (3.0 equiv) at 0 °C gave nitrile **55** as an inseparable 1:1 mixture of diastereomers in 63% yield with the complete consumption of **56**. The nitrile **55** was reduced to allyl alcohol **79** by a DIBAH reduction–hydrolysis–DIBAH reduction sequence (overall 76%). The allyl alcohol was subjected to Katsuki-Sharpless asymmetric epoxidation[24] using (−)-DET to produce epoxide **80** (76%), which was converted to vinyl epoxide **54** by oxidation with SO_3–pyridine/DMSO[34] and the subsequent Wittig reaction (overall yield 59%). The reduction of vinyl epoxide **54** with $Bu_3SnH/Pd(PPh_3)_4$ under the same conditions described above gave **81** selectively in 88% yield. Removal of the TBS group of **81** followed by protection of the resulting diol afforded acetonides **53a** and **53b**. The diastereomers at C13 were facilely separated by silica gel chromatography at this stage. Stereochemistry of each compound was determined by the J value between H12 and H13. RCM[16,17] of **53a** with Grubbs' first-generation catalyst in CH_2Cl_2 at ambient temperature smoothly produced the desired **52** as the sole product in 97% yield.

Stereochemical confirmation of **52** by ^1H NMR was difficult because the signals of **52** at ambient temperature were extremely broadened due to the slow conformational changes of the F-ring part, as reported for natural CTX1B[5] and other model compounds.[11f,j,o,s,v] Although the spectrum of **52** in pyridine-d_5 at −30 °C exhibited sharp signals of a ca. 1:1 mixture of two conformers, stereochemistry of **52** could not be confirmed due to overlapping signals of both conformers. In order to solve the conformational problem, acetonide **52** was converted to diol **83**. The diol **83** was flexible enough to give a set of sharp and clear signals at ambient temperature. Eventually, the stereochemistry of **52** was proved by the detailed NMR analysis of **83**, which showed the presence of NOE between H6 and H13 as well as the large J value (8.8 Hz) between H12 and H13.

Thus, the F-ring was efficiently cyclized at the final stage whereby the improved synthesis of the EF-ring segment of CTX1B was accomplished.

4. Conclusion

Aiming at the convergent total synthesis of CTX1B, construction of its EF-ring segment has been investigated. During the study, a novel method for the construction of branched ethers based on regioselective reduction of γ-alkoxy β,γ-unsaturated α-silyloxy nitriles with $BF_3\cdot OEt_2$ and R_3SiH or Bu_3SnH has been developed. Combined use of the branched ether synthesis and RCM successfully provided medium-sized cyclic ether **34**, and also contributed to the synthesis of the EF-ring segment **50**. Although a difficulty in the cyclization of the E-ring by RCM arose in the synthesis of **50**, it was solved in a revised synthetic route to the EF-ring part **52**, where the F-ring was cyclized at the final stage. In the course of the synthesis of **52**, efficient site-selective reduction of vinyl epoxides into homoallyl alcohols mediated by Bu_3SnH and $Pd(PPh_3)_4$ was also developed. Thus, a novel route to the EF-ring segment of CTX1B has been established. Further studies toward the



Scheme 10. Synthesis of the EF-ring segment **52**. Reagents and conditions: (a) $(COCl)_2$ (3.0 equiv), DMSO (5.0 equiv), CH_2Cl_2, −78 °C, 15 min then NEt_3 (10 equiv), −18 °C, 10 min; (b) Ph_3PCH_2OMeCl (5.1 equiv), NaHMDS (4.9 equiv), THF, −78 °C, 1.5 h→24 °C, 17.5 h, 70% for two steps; (c) $Hg(OAc)_2$ (3.0 equiv), THF–H_2O (10:1), 24 °C, 1.5 h then TBAI (9.0 equiv), 1 h, 95%; (d) Ph_3PCH_3Br (3.5 equiv), NaHMDS (3.2 equiv), THF, −78 °C, 2 h→22 °C, 18 h, 100%; (e) DDQ (2.5 equiv), CH_2Cl_2—pH 7 buffer (4:1), 0 °C, 3 h, 92%; (f) PMe_3 (1.5 equiv), **20** (3.0 equiv), CH_2Cl_2, 0 °C, →24 °C, 30 min, 98% (only *E*); (g) DIBAH (3.5 equiv), CH_2Cl_2, −78 °C, 1 h, 94%; (h) TPAP (0.2 equiv), NMO (2.0 equiv), MS 4A, CH_2Cl_2, 23 °C, 1.5 h, 84%; (i) Me_3Al (1.1 equiv), TMSCN (2.5 equiv), benzene, 25 °C, 1 h, 74%; (j) $BF_3\cdot OEt_2$ (3.0 equiv), CH_2Cl_2–Bu_3SnH (1:1), 0 °C, 10 min, 63%; (k) DIBAH (4.0 equiv), CH_2Cl_2, −78 °C, 1 h; (l) 0.5 M HCl, CH_2Cl_2, 24 °C, 20 min, 83% for two steps; (m) DIBAH (3.0 equiv), CH_2Cl_2, −78 °C, 30 min, 91%; (n) D-(−)-DET (2.0 equiv), $Ti(O^iPr)_4$ (1.5 equiv), TBHP (20 equiv), MS 4A, CH_2Cl_2, −40 °C, 30 min→−25 °C, 2.5 d, 76%; (o) $SO_3\cdot$pyridine (25 equiv), DMSO–NEt_3–CH_2Cl_2 (1:1.4:3), 0 °C→24 °C, 3 h; (p) Ph_3PCH_3Br (28 equiv), NaHMDS (23 equiv), THF, −78 °C, 2 h→24 °C, 2.5 d, 59% for two steps; (q) $Pd(PPh_3)_4$ (0.1 equiv), Bu_3SnH (1.1 equiv), CH_2Cl_2, 24 °C, 25 min, 88%; (r) TBAF (2.0 equiv), THF, 23 °C, 1.5 h, 100%; (s) 2,2-dimethoxypropane (10 equiv), CSA (0.5 equiv), CH_2Cl_2, 24 °C, 3 h, **53a**: 47%, **53b**: 50%; (t) $(Cy_3P)_2Cl_2Ru{=}CHPh$ (20 mol%), CH_2Cl_2 (3 mM), 23 °C, 4 h, 97%; (u) THF–H_2O–TFA (10:10:1), 23 °C, 3 h, 88%.

total synthesis of CTX1B are currently under way in our laboratory.

5. Experimental

5.1. General methods

All reactions sensitive to air or moisture were carried out under an argon atmosphere in dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. Sensitive liquids and solutions were transferred by syringe-septum and cannula techniques. All commercially available reagents were used without further purification with the following exceptions. THF was distilled from sodium-benzophenone ketyl under argon. CH_2Cl_2, benzene were distilled from CaH_2 prior to use. All reactions were monitored by TLC with precoated 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. Flash chromatography was performed on YMC Silica Gel 60 (230–400 mesh) as a stationary phase. Melting points were measured on YANAGIMOTO micro-melting apparatus without

calibration. Optical rotations were recorded on a JASCO P-1020 digital polarimeter. Infrared spectra (IR) were measured on a JEOL JIR-WINSPEC100 infrared spectrometer in noted states and are reported in wave numbers (cm^{-1}). ^1H NMR and ^{13}C NMR spectra were recorded on a JEOL JNM-AL300 (^1H at 300 MHz, ^{13}C at 75 MHz), JNM-α-400 (^1H at 400 MHz), and/or JNM-α-600 (^{13}C at 150 MHz) magnetic resonance spectrometer. ^1H NMR spectra are reported as chemical shifts (δ) in parts-per-million (ppm) based on tetramethylsilane (0 ppm), C_6HD_5 (7.15 ppm), $CHD_2C(=O)CD_3$ (2.04 ppm) or C_5HD_4N (8.71 ppm). The following abbreviations are used to describe spin multiplicity: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad, dd=double doublets, dt=double triplets, dq=double quartets, and ddd=double double doublets; other combination is derived from those listed. Coupling constants (*J*) are reported in Hertz (Hz). ^{13}C NMR spectra are reported as chemical shifts (δ) in ppm based on $^{13}CDCl_3$ (77.0 ppm) or $^{13}C_6D_6$ (128.0 ppm). Low and high resolution mass spectra were measured on a JEOL JMS-600H mass spectrometer under electron ionization (EI) condition and a JEOL JMS-SX102A mass spectrometer under field desorption (FD) condition.

5.1.1. 4-(3-Phenylpropoxy)but-2-enenitrile (13). To a solution of **10** (50.6 mg, 0.175 mmol) in CH_2Cl_2–Et_3SiH (1:1, v/v, 3.2 ml) was added $BF_3\cdot OEt_2$ (65 μl, 0.524 mmol) at 0 °C and the mixture was stirred for 10 min. Then, saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture 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/EtOAc=10) to give **13** (22.6 mg, 64%) as a inseparable mixture of *E* and *Z*-isomers (*E*/*Z*=6.2:1 from ^1H NMR). **13**: a colorless oil; IR (film), ν_{max} 3063, 3026, 2943, 2861, 2795, 2224, 1693, 1602, 1496, 1477, 1454, 1365, 1264, 1180, 1135, 1047, 1029, 952, 913, 748, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.32–7.15 (5H, m), 6.73 (0.86H, dt, *J*=16.3, 3.7 Hz), 6.57 (0.14H, dt, *J*=11.4, 5.9 Hz), 5.64 (0.86H, dt, *J*=16.3, 2.4 Hz), 5.45 (0.14H, dt, *J*=11.4, 1.8 Hz), 4.29 (0.28H, dd, *J*=5.9, 1.8 Hz), 4.08 (1.72H, dd, *J*=3.7, 2.4 Hz), 3.48 (2H, t, *J*=6.4 Hz), 2.70 (2H, t, *J*=7.7 Hz), 1.98–1.88 (2H, m); LR-EIMS, *m*/*z* 201 (43.5%, $[M]^+$), 118 (bp); HR-EIMS, calcd for $C_{13}H_{15}NO$ $[M]^+$: 201.1154, found: 201.1162.

5.1.2. (2*E*)-4-(3-Phenylpropoxy)pent-2-enenitrile (14). To a solution of **11** (27.3 mg, 0.0900 mmol) in CH_2Cl_2–Et_3SiH (1:1, v/v, 1.8 ml) was added $BF_3\cdot OEt_2$ (33 μl, 0.270 mmol) at 0 °C and the mixture was stirred for 10 min. Then, saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture 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/EtOAc=20→10) to give **14** (12.1 mg, 62%). **14**: a colorless oil; IR (film), ν_{max} 3062, 3026, 2978, 2932, 2856, 2224, 1636, 1602, 1584, 1496, 1476, 1454, 1370, 1340, 1246, 1178, 1150, 1102, 963, 748, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.32–7.16 (5H, m), 6.64 (1H, dd, *J*=16.3, 5.0 Hz), 5.54 (1H, dd, *J*=16.3, 1.7 Hz), 3.96 (1H, qdd, *J*=6.6, 5.0, 1.7 Hz), 3.41 (2H, t, *J*=6.4 Hz), 2.69 (2H, brt, *J*=7.7 Hz), 1.95–1.86 (2H, m), 1.26 (3H, d, *J*=6.6 Hz); LR-EIMS, *m*/*z* 215 (42.5%, $[M]^+$), 91 (bp); HR-EIMS, calcd for $C_{14}H_{17}NO$ $[M]^+$: 215.1310, found: 215.1336.

5.1.3. (2*E*)-5-(*tert*-Butyldimethylsilyloxy)-4-(3-phenylpropoxy)pent-2-enenitrile (15). To a solution of **12** (82.2 mg, 0.190 mmol) in CH_2Cl_2–Et_3SiH (1:1, v/v, 3.0 ml) was added $BF_3\cdot OEt_2$ (70 μl, 0.570 mmol) at 0 °C and the mixture was stirred for 10 min. Then, saturated aqueous $NaHCO_3$ (7 ml) was added and the mixture 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/EtOAc=20→10) to give **15** (41.8 mg, 64%). **15**: a colorless oil; IR (film), ν_{max} 3085, 3063, 3027, 2953, 2929, 2858, 2739, 2225, 1629, 1603, 1497, 1471, 1462, 1455, 1406, 1389, 1361, 1343, 1306, 1254, 1222, 1111, 1006, 965, 939, 837, 814, 779, 747, 700, 670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.31–7.16 (5H, m), 6.72 (1H, dd, *J*=16.4, 4.7 Hz), 5.61 (1H, dd, *J*=16.4, 1.7 Hz), 3.91 (1H, dddd, *J*=6.2, 5.9, 4.7, 1.7 Hz), 3.70 (1H, dd, *J*=10.2, 5.9 Hz), 3.55 (1H, dd, *J*=10.2, 6.2 Hz), 3.49 (2H, t, *J*=6.4 Hz), 2.72–2.67 (2H, m), 1.95–1.86 (2H, m), 0.89 (9H, s), 0.06 (6H, s); LR-EIMS, *m*/*z* 288 (21.9%, $[M-t\text{-Bu}]^+$), 91 (bp); HR-EIMS, calcd for $C_{16}H_{22}NO_2Si$ $[M-t\text{-Bu}]^+$: 288.1420, found: 288.1417.

5.1.4. Methyl (2*E*,2′*R*,3′*S*)-3-{(2′-allyloxan-3′-yl)oxy}-4-(*tert*-butyldimethylsilyloxy)-2-butenoate (21). A solution of butynoate **20** (1.29 g, 5.65 mmol) in CH_2Cl_2 (10 ml) was slowly added dropwise to a solution of **19** (479.0 mg, 3.37 mmol) and PMe_3 (3.7 ml, 1.0 M in THF, 3.71 mmol) in CH_2Cl_2 (24 ml) at 0 °C by means of a syringe. The mixture was warmed to 24 °C and stirred for 1 h. The mixture was cooled to 0 °C and diluted with Et_2O (20 ml) and hexane (20 ml). Then, saturated aqueous NH_4Cl (15 ml) was added and the mixture 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/EtOAc=20) to give **21** (1.19 g, 95%). **21**: a colorless oil; $[\alpha]_D^{26}$ +58.1 (*c* 0.75, $CHCl_3$); IR (film), ν_{max} 3077, 2951, 2856, 1716, 1626, 1472, 1436, 1434, 1389, 1361, 1342, 1310, 1295, 1252, 1189, 1147, 1098, 1051, 1005, 939, 914, 837, 778, 675 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 5.92–5.78 (1H, m), 5.11–5.09 (2H, m), 5.05 (1H, s), 4.90 (1H, d, *J*=13.6 Hz), 4.65 (1H, d, *J*=13.6 Hz), 3.98–3.92 (1H, m), 3.91–3.83 (1H, m), 3.68 (3H, s), 3.45–3.33 (2H, m), 2.59–2.50 (1H, m), 2.34–2.30 (1H, m), 2.25–2.15 (1H, m), 1.75–1.66 (2H, m), 1.52–1.37 (1H, m), 0.90 (9H, s), 0.09 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 170.4 (C), 167.3 (C), 134.2 (CH), 117.1 (CH_2), 91.6 (CH), 79.4 (CH), 74.8 (CH), 67.7 (CH_2), 60.0 (CH_2), 50.8 (CH_3), 36.0 (CH_2), 27.8 (CH_2), 25.7 ($CH_3\times3$), 24.9 (CH_2), 18.2 (C), −5.35 (CH_3), −5.38 (CH_3); LR-EIMS, *m*/*z* 313 (82.4%, $[M-t\text{-Bu}]^+$), 189 (bp); HR-EIMS, calcd for $C_{15}H_{25}O_5Si$ $[M-t\text{-Bu}]^+$: 313.1471, found: 313.1466.

5.1.5. (2*E*,2′*R*,3′*S*)-3-{(2′-Allyloxan-3′-yl)oxy}-4-(*tert*-butyldimethylsilyloxy)-2-butenol (22). To a solution of **21** (115.6 mg, 0.312 mmol) in CH_2Cl_2 (5.0 ml) was added

DIBAH (1.3 ml, 0.95 M in *n*-hexane, 1.25 mmol) at −78 °C and the mixture was stirred for 10 min. Then, saturated aqueous potassium sodium tartrate (5 ml) was added and the mixture was stirred at 24 °C for 3 h. The layers were separated and the aqueous layer was extracted with EtOAc (3×10 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/EtOAc = 5 → 3 → 1) to give **22** (106.6 mg, ~100%). **22**: a colorless oil; $[\alpha]_D^{26}$ +45.1 (*c* 0.65, $CHCl_3$); IR (film), ν_{max} 3417, 3075, 2930, 2857, 2725, 1661, 1472, 1463, 1436, 1389, 1361, 1340, 1306, 1276, 1252, 1184, 1098, 1004, 913, 837, 814, 777, 674 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 5.93–5.79 (1H, m), 5.12–5.04 (2H, m), 4.95 (1H, t, J=7.9 Hz), 4.20–4.15 (4H, m), 3.94 (1H, dtd, J=11.0, 3.3, 1.8 Hz), 3.74 (1H, ddd, J=10.3, 9.0, 4.2 Hz), 3.42–3.29 (2H, m), 2.58–2.49 (1H, m), 2.38–2.29 (1H, m), 2.24–2.13 (1H, m), 1.72–1.63 (2H, m), 1.43–1.21 (1H, m), 0.91 (9H, s), 0.10 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 155.9 (C), 134.6 (CH), 116.5 (CH_2), 100.3 (CH), 79.8 (CH), 73.1 (CH), 67.5 (CH_2), 60.6 (CH_2), 57.6 (CH_2), 36.0 (CH_2), 28.0 (CH_2), 25.5 (CH_3×3), 24.8 (CH_2), 17.9 (C), −5.52 (CH_3), −5.56 (CH_3); LR-EIMS, *m/z* 285 (19.1%, $[M-t\text{-Bu}]^+$), 227 (bp); HR-EIMS, calcd for $C_{14}H_{25}O_4Si$ $[M-t\text{-Bu}]^+$: 285.1522, found: 285.1518.

5.1.6. (2*E*,2′*R*,3′*S*)-3-{(2′-Allyloxan-3′-yl)oxy}-4-(*tert*-butyldimethylsilyloxy)-2-butenal (23). To a mixture of **22** (158.2 mg, 0.462 mmol) and MS 4 Å (158.2 mg, 100 wt%) in CH_2Cl_2 (5.0 ml) was added NMO (108.2 mg, 0.924 mmol) at 24 °C and the mixture was stirred for 10 min. Then, TPAP (16.2 mg, 0.0462 mmol) was added to the reaction mixture at 24 °C and the mixture was stirred for 50 min. The mixture was filtered through Celite and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc = 10 → 5) to give **23** (139.0 mg, 88%). **23**: a colorless oil; $[\alpha]_D^{25}$ +49.0 (*c* 1.01, $CHCl_3$); IR (film), ν_{max} 3075, 2954, 2930, 2857, 2764, 1665, 1615, 1472, 1463, 1438, 1389, 1361, 1323, 1279, 1254, 1209, 1164, 1099, 1041, 1005, 974, 957, 947, 939, 914, 837, 778, 680 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 9.98 (1H, d, J=7.7 Hz), 5.91–5.77 (1H, m), 5.41 (1H, d, J=7.7 Hz), 5.09–5.04 (2H, m), 4.52 (1H, d, J=13.2 Hz), 4.46 (1H, d, J=13.2 Hz), 3.98–3.86 (2H, m), 3.45–3.35 (2H, m), 2.52–2.44 (1H, m), 2.32–2.16 (1H, m), 1.73–1.65 (2H, m), 1.52–1.37 (1H, m), 0.91 (9H, s), 0.11 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 189.9 (CH), 173.7 (C), 133.7 (CH), 117.1 (CH_2), 105.7 (CH), 78.9 (CH), 75.1 (CH), 67.4 (CH_2), 61.1 (CH_2), 35.9 (CH_2), 27.6 (CH_2), 25.5 (CH_3×3), 24.6 (CH_2), 17.9 (C), −5.58 (CH_3×2); LR-EIMS, *m/z* 283 (73.8%, $[M-t\text{-Bu}]^+$), 159 (bp); HR-EIMS, calcd for $C_{14}H_{23}O_4Si$ $[M-t\text{-Bu}]^+$: 283.1365, found: 283.1362.

5.1.7. (3*E*,2′*R*,3′*S*)-4-{(2′-Allyloxan-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2-(trimethylsilyloxy)pent-3-enenitrile (24). To a solution of **23** (43.9 mg, 0.129 mmol) and TMSCN (43 µl, 0.323 mmol) in benzene (1.3 ml) was added Me_3Al (0.14 ml, 1.03 M in *n*-hexane, 0.142 mmol) at 24 °C and the mixture was stirred for 1 h. Then, saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture 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/EtOAc = 30 → 10) to give **24** (42.1 mg, 74%) as an inseparable 1:1 mixture of diastereomers. The nitrile **24** was unstable and immediately used for the next reaction. **24**: a colorless oil; ^1H NMR (300 MHz, $CDCl_3$), δ 5.92–5.78 (1H, m), 5.58 (0.5H, d, J=9.1 Hz), 5.57 (0.5H, d, J=9.1 Hz), 5.12–5.04 (2H, m), 4.75–4.70 (1H, m), 4.20–4.08 (2H, m), 3.97–3.87 (1H, m), 3.79–3.65 (1H, m), 3.42–3.28 (2H, m), 2.54–2.43 (1H, m), 2.37–2.25 (1H, m), 2.23–2.12 (1H, m), 1.74–1.65 (2H, m), 1.41–1.30 (1H, m), 0.92 (9H, s), 0.21 (9H, s), 0.11 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 156.8 (C), 134.5 (CH), 119.9 (C×0.5), 117.2 (C×0.5), 117.0 (CH_2), 98.4 (CH), 79.6 (CH), 74.2 (CH), 67.8 (CH_2), 62.2 (CH_2), 57.6 (CH), 36.3 (CH_2), 28.1 (CH_2), 25.8 (CH_3×3), 25.0 (CH_2), 18.3 (C), −0.10 (CH_3×3), −5.38 (CH_3), −5.53 (CH_3).

5.1.8. (2*E*,4*S*,2′*R*,3′*S*)-4-{(2′-Allyloxan-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)pent-2-enenitrile (25a) and (2*E*,4*R*,2′*R*,3′*S*)-4-{(2′-allyloxan-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)pent-2-enenitrile (25b). *Silane reduction*. The reduction of **24** with organosilanes in entries 1–4 in Table 2 followed the procedure described in the synthesis of model compounds **13**, **14** and **15**.

Stannane reduction. To a solution of **24** (14.7 mg, 0.0334 mmol) in CH_2Cl_2–Bu_3SnH (1:1, v/v, 0.60 ml) was added $BF_3 \cdot OEt_2$ (12 µl, 0.100 mmol) at −18 °C and the mixture was stirred for 10 min. Then, saturated aqueous $NaHCO_3$ (5 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/EtOAc = 30 → 10) to give **25** (7.5 mg, 64%) as an inseparable mixture of two diastereomers (**25a**:**25b** = 1.0:1.3). **25**: a colorless oil; IR (film), ν_{max} 3074, 2954, 2930, 2857, 2225, 2211, 1628, 1472, 1463, 1434, 1389, 1361, 1341, 1255, 1222, 1178, 1099, 1005, 965, 913, 837, 779 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 6.78 (0.57H, dd, J=16.3, 4.6 Hz), 6.69 (0.43H, dd, J=16.3, 5.4 Hz), 5.95–5.80 (1H, m), 5.66 (0.57H, dd, J=16.3, 1.8 Hz), 5.63 (0.43H, dd, J=16.3, 1.6 Hz), 5.13–5.07 (2H, m), 4.11–4.02 (1H, m), 3.92–3.87 (1H, m), 3.72–3.63 (1H, m), 3.54–3.47 (1H, m), 3.39–3.08 (3H, m), 2.67–2.61 (0.57H, m), 2.58–2.50 (0.43H, m), 2.26–2.05 (2H, m), 1.67–1.57 (2H, m), 1.29–1.26 (1H, m), 0.89 (9H, s), 0.06 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) (A 1:2 mixture of **25a** and **25b** was measured), δ 153.6 (CH×0.67), 152.8 (CH×0.33), 135.0 (CH×0.67), 134.7 (CH×0.33), 117.1 (C×0.67), 116.9 (CH_2×0.33), 116.8 (C×0.33), 116.6 (CH_2×0.67), 101.2 (CH×0.33), 100.4 (CH×0.67), 80.2 (CH×0.33), 80.1 (CH×0.67), 77.6 (CH×0.67), 77.4 (CH×0.33), 76.6 (CH×0.33), 76.2 (CH×0.67), 67.6 (CH_2×0.67), 67.5 (CH_2×0.33), 65.3 (CH_2×0.33), 64.6 (CH_2×0.67), 36.41 (CH_2×0.33), 36.37 (CH_2×0.67), 30.2 (CH_2×0.67), 29.7 (CH_2×0.33), 25.8 (CH_3×2), 25.7 (CH_3), 25.23 (CH_2×0.67), 25.19 (CH_2×0.33), 18.14 (C×0.67), 18.09 (C×0.33), −5.45 (CH_3×0.33), −5.53 (CH_3), −5.59 (CH_3×0.67); LR-EIMS, *m/z* 294 (23.7%, $[M-t\text{-Bu}]^+$), 125 (bp);

HR-EIMS, calcd for $C_{15}H_{24}NO_3Si$ $[M-t\text{-}Bu]^+$: 294.1525, found: 294.1523.

5.1.9. (2*E*,4*S*,2′*R*,3′*S*)-4-{(2′-Allyloxan-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2-pentenal (27a) and (2*E*,4*R*,2′*R*,3′*S*)-4-{(2′-allyloxan-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2-pentenal (27b). To a solution of **25** (**25a**:**25b**=1:2, 24.0 mg, 0.0683 mmol) in CH_2Cl_2 (1.0 ml) was added DIBAH (0.18 ml, 0.95 M in *n*-hexane, 0.171 mmol) at −78 °C and the mixture was stirred for 10 min. Then, saturated aqueous potassium sodium tartrate (3 ml) was added and the mixture was stirred at 24 °C for 12 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/EtOAc=10→5) to give **27** (16.5 mg, 68%) as an inseparable mixture of two diastereomers (**27a**:**27b**=1.0:2.0). **27**: a yellow oil; IR (film), ν_{max} 3074, 2953, 2929, 2857, 2723, 1697, 1641, 1472, 1463, 1437, 1389, 1361, 1339, 1279, 1254, 1214, 1186, 1099, 1005, 978, 939, 912, 838, 814, 778, 669 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 9.58 (1H, d, J=7.7 Hz), 6.84 (0.67H, dd, J=15.8, 5.1 Hz), 6.73 (0.33H, dd, J=15.8, 5.9 Hz), 6.38–6.26 (1H, m), 5.97–5.80 (1H, m), 5.15–5.07 (2H, m), 4.28–4.15 (1H, m), 3.92–3.87 (1H, m), 3.78–3.70 (1H, m), 3.62–3.55 (1H, m), 3.36–3.10 (3H, m), 2.72–2.56 (1H, m), 2.27–2.18 (1H, m), 2.12–2.07 (1H, m), 1.68–1.54 (2H, m), 1.44–1.31 (1H, m), 0.89 (9H, s), 0.06 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 193.3 (CH×0.67), 193.1 (CH×0.33), 155.7 (CH×0.67), 154.6 (CH×0.33), 135.2 (CH×0.67), 135.0 (CH×0.33), 133.3 (CH×0.33), 132.5 (CH×0.67), 116.7 (CH_2×0.33), 116.6 (CH_2×0.67), 80.30 (CH×0.33), 80.26 (CH×0.67), 78.1 (CH×0.67), 77.5 (CH×0.67), 77.2 (CH×0.33), 75.9 (CH×0.33), 67.6 (CH_2), 65.6 (CH_2×0.33), 64.9 (CH_2×0.67), 36.44 (CH_2×0.67), 36.40 (CH_2×0.33), 30.4 (CH_2×0.67), 29.6 (CH_2×0.33), 25.77 (CH_3×2), 25.75 (CH_3), 25.29 (CH_2×0.67), 25.25 (CH_2×0.33), 18.2 (C), −5.37 (CH_3×0.33), −5.46 (CH_3), −5.52 (CH_3×0.67); LR-EIMS, *m*/*z* 354 (14.0%, $[M]^+$), 125 (bp); HR-EIMS, calcd for $C_{15}H_{25}O_4Si$ $[M-t\text{-}Bu]^+$: 297.1522, found: 297.1540.

5.1.10. (2*E*,4*S*,2′*R*,3′*S*)-4-{(2′-Allyloxan-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2-pentenol (28a) and (2*E*,4*R*,2′*R*,3′*S*)-4-{(2′-allyloxan-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2-pentenol (28b). To a solution of **27** (**27a**:**27b**=1:2, 16.5 mg, 0.0465 mmol) in CH_2Cl_2 (1.0 ml) was added DIBAH (0.15 ml, 0.95 M in *n*-hexane, 0.140 mmol) at −78 °C and the mixture was stirred for 8 min. Then, saturated aqueous potassium sodium tartrate (3 ml) was added and the mixture was stirred at 24 °C for 12 h. The layers were separated and the aqueous layer was extracted with EtOAc (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/EtOAc=5) to give **28** (16.6 mg, ~100%) as an inseparable mixture of two diastereomers (**28a**:**28b**=1.0:2.0). **28**: a pale yellow oil; IR (film), ν_{max} 3345, 3076, 2931, 2858, 1642, 1472, 1463, 1443, 1378, 1342, 1321, 1279, 1256, 1213, 1098, 1004, 974, 948, 912, 837, 814, 778, 666 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 5.96–5.83 (2H, m), 5.68 (0.67H, dt, J=7.0, 1.5 Hz), 5.62 (0.33H, dt, J=6.6, 1.5 Hz), 5.14–5.05 (2H, m), 4.17 (2H, brs), 3.96–3.86 (2H, m), 3.68–3.59 (1H, m), 3.56–3.49 (1H, m), 3.36–3.10 (3H, m), 2.78–2.69 (0.67H, m), 2.66–2.57 (0.33H, m), 2.22 (1H, dt, J=15.0, 7.7 Hz), 2.14–2.07 (1H, m), 1.64–1.57 (2H, m), 1.43–1.25 (1H, m), 0.89 (9H, s), 0.05 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 135.54 (CH×0.67), 135.45 (CH×0.33), 133.1 (CH×0.33), 131.9 (CH×0.67), 130.2 (CH×0.67), 129.3 (CH×0.33), 116.4 (CH_2), 80.8 (CH×0.67), 80.5 (CH×0.33), 80.4 (CH×0.67), 78.1 (CH×0.33), 76.7 (CH×0.67), 74.2 (CH×0.33), 67.71 (CH_2×0.33), 67.68 (CH_2×0.67), 66.4 (CH_2×0.33), 66.2 (CH_2×0.67), 62.83 (CH_2×0.67), 62.81 (CH_2×0.33), 36.4 (CH_2), 31.0 (CH_2×0.67), 29.3 (CH_2×0.33), 25.85 (CH_3×2), 25.83 (CH_3), 25.5 (CH_2×0.67), 25.3 (CH_2×0.33), 18.29 (C×0.67), 18.27 (C×0.33), −5.21 (CH_3×0.33), −5.33 (CH_3), −5.43 (CH_3×0.67); LR-EIMS, *m*/*z* 299 (2.1%, $[M-t\text{-}Bu]^+$), 125 (bp); HR-EIMS, calcd for $C_{15}H_{27}O_4Si$ $[M-t\text{-}Bu]^+$: 299.1678, found: 299.1674.

5.1.11. (2*R*,3*S*,4*R*,2′*R*,3′*S*)-4-{(2′-Allyloxan-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2,3-epoxypentanol (29a) and (2*R*,3*S*,4*S*,2′*R*,3′*S*)-4-{(2′-allyloxan-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2,3-epoxypentanol (29b). To a mixture of D-(−)-DET (14.4 μl, 0.0840 mmol) and predried MS 4 Å (49.7 mg, 133 wt%) in CH_2Cl_2 (0.5 ml) was added $Ti(O^iPr)_4$ (21.6 μl, 0.0735 mmol) at −40 °C and the mixture was stirred for 30 min. Then, TBHP (0.14 ml, 3.7 M in toluene, 0.525 mmol) was added and the mixture was stirred at −40 °C for 30 min. To the mixture was added dropwise a solution of **28** (**28a**:**28b**=1:2, 37.5 mg, 0.105 mmol) in CH_2Cl_2 (1.5 ml). The reaction mixture was stirred at −40 °C for 30 min. Then, the reaction mixture was warmed to −25 °C and stirred for 24 h. DMS (38.6 μl, 0.525 mmol) was added at −25 °C and the mixture was stirred for 2 h until unreacted TBHP was consumed. To the mixture was added 10% DL-tartaric acid (43.2 μl) and NaF (18.5 mg) at −25 °C. The suspension was warmed to 26 °C and stirred for 24 h. The mixture was filtered through Celite and concentrated in vacuo. To the resultant residue was added Et_2O (3.0 ml) and 30% aqueous NaOH in brine (1.0 ml) at 0 °C 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 brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=5→3) to give **29** (39.2 mg, ~100%) as an inseparable mixture of two diastereomers (**29a**:**29b**=1.0:2.0). **29**: a colorless oil; IR (film), ν_{max} 3468, 3075, 2930, 2857, 1642, 1472, 1463, 1389, 1368, 1257, 1130, 1097, 1027, 939, 910, 837, 815, 778, 669 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 5.96–5.82 (1H, m), 5.15–5.05 (2H, m), 3.96 (1H, brddd, J=12.8, 5.1, 2.2 Hz), 3.92–3.86 (1H, m), 3.73–3.61 (2H, m), 3.60 (1H, dd, J=10.3, 7.3 Hz), 3.36–3.27 (1H, m), 3.24–3.17 (3H, m), 3.12 (1H, dt, J=4.4, 2.2 Hz), 3.03 (1H, dd, J=6.8, 2.2 Hz), 2.67–2.58 (1H, m), 2.33–2.28 (1H, m), 2.25–2.15 (1H, m), 1.71–1.61 (3H, m), 0.90 (3H, s), 0.89 (6H, s), 0.07 (2H, s), 0.06 (4H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 135.33 (CH×0.67), 135.29 (CH×0.33), 116.5 (CH_2×0.33), 116.4 (CH_2×0.67), 80.5 (CH×0.33), 80.4 (CH×0.67), 80.2 (CH), 77.3 (CH×0.67), 76.8 (CH×0.33), 67.7 (CH_2×0.67), 67.6 (CH_2×0.33),

64.3 ($CH_2\times0.33$), 63.0 ($CH_2\times0.67$), 61.4 ($CH_2\times0.33$), 61.2 ($CH_2\times0.67$), 56.9 (CH), 56.3 ($CH\times0.67$), 54.5 ($CH\times0.33$), 36.5 ($CH_2\times0.67$), 36.3 ($CH_2\times0.33$), 30.6 ($CH_2\times0.67$), 29.9 ($CH_2\times0.33$), 25.79 (CH_3), 25.77 ($CH_3\times2$), 25.5 ($CH_2\times0.67$), 25.3 ($CH_2\times0.33$), 18.2 ($C\times0.33$), 18.1 ($C\times0.67$), −5.41 ($CH_3\times0.33$), −5.49 ($CH_3\times0.33$), −5.59 ($CH_3\times1.34$); LR-EIMS, *m/z* 315 (12.4%, $[M-t\text{-Bu}]^+$), 125 (bp); HR-EIMS, calcd for $C_{15}H_{27}O_5Si$ $[M-t\text{-Bu}]^+$: 315.1628, found: 315.1626.

5.1.12. (3*S*,4*R*,2′*R*,3′*S*)-4-{(2′-Allyloxan-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)pent-1-en-3-ol (30a) and (3*S*,4*S*,2′*R*,3′*S*)-4-{(2′-allyloxan-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)pent-1-en-3-ol (30b). To a solution of **29** (**29a**:**29b**=1:2, 23.0 mg, 0.0617 mmol), PPh_3 (80.9 mg, 0.309 mmol), and imidazole (21.0 mg, 0.309 mmol) in THF (1.0 ml) was added I_2 (62.6 mg, 0.247 mmol) at 25 °C and the mixture was stirred for 45 min. Then, saturated aqueous $Na_2S_2O_3$ (5 ml) was added and the mixture 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/EtOAc=30→10→5) to give **30** (13.4 mg, 61%) as an inseparable mixture of two diastereomers (**30a**:**30b**=1.0:2.0). **30**: a colorless oil; IR (film), ν_{max} 3457, 3075, 2929, 2857, 1642, 1472, 1463, 1434, 1389, 1361, 1340, 1279, 1257, 1186, 1098, 1030, 995, 919, 837, 814, 777 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 5.97–5.82 (2H, m), 5.36 (0.67H, dt, J=17.3, 1.5 Hz), 5.35 (0.33H, dt, J=17.3, 1.5 Hz), 5.21 (1H, dt, J=10.3, 1.5 Hz), 5.15–5.06 (2H, m), 4.32–4.17 (1H, m), 3.92–3.87 (1H, m), 3.77–3.69 (1H, m), 3.67–3.61 (1H, m), 3.51–3.41 (1H, m), 3.36–3.26 (1H, m), 3.24–3.13 (2H, m), 2.78–2.65 (2H, m), 2.30–2.13 (2H, m), 1.68–1.53 (2H, m), 1.40–1.23 (1H, m), 0.90 (9H, s), 0.06 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 137.5 ($CH\times0.67$), 136.9 ($CH\times0.33$), 135.4 ($CH\times0.33$), 135.3 ($CH\times0.67$), 116.5 ($CH_2\times0.33$), 116.44 ($CH_2\times0.67$), 116.36 ($CH_2\times0.33$), 116.26 ($CH_2\times0.67$), 80.34 ($CH\times0.33$), 80.31 ($CH\times0.67$), 79.8 ($CH\times0.33$), 78.7 ($CH\times0.67$), 76.7 ($CH\times0.33$), 76.0 ($CH\times0.67$), 73.7 ($CH\times0.33$), 72.3 ($CH\times0.67$), 67.7 ($CH_2\times0.67$), 67.5 ($CH_2\times0.33$), 63.8 ($CH_2\times0.33$), 62.1 ($CH_2\times0.67$), 36.6 (CH_2), 30.2 ($CH_2\times0.33$), 29.8 ($CH_2\times0.67$), 25.8 ($CH_3\times3$), 25.32 ($CH_2\times0.67$), 25.28 ($CH_2\times0.33$), 18.1 (C), −5.47 ($CH_3\times0.33$), −5.57 ($CH_3\times0.33$), −5.62 ($CH_3\times0.67$), −5.64 ($CH_3\times0.67$); LR-EIMS, *m/z* 299 (24.8%, $[M-t\text{-Bu}]^+$), 125 (bp); HR-EIMS, calcd for $C_{15}H_{27}O_4Si$ $[M-t\text{-Bu}]^+$: 299.1678, found: 299.1692.

5.1.13. (1*S*,3*S*,4*S*,5*Z*,8*R*)-3-(*tert*-Butyldimethylsilyloxymethyl)-2,9-dioxabicyclo[6.4.0]dodec-5-en-4-ol (31). To a solution of **30** (**30a**:**30b**=1:2, 13.4 mg, 0.0376 mmol) in CH_2Cl_2 (6.0 ml) was added a solution of $(H_2IMes)(PCy_3)Cl_2Ru$=CHPh (3.2 mg, 3.76 μmol) in CH_2Cl_2 (6.0 ml). The resultant solution was stirred at 45 °C for 6 h. The mixture was cooled to 25 °C and stirred for 24 h under O_2 atmosphere. The reaction mixture was filtered through Celite-Florisil and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=15→7→3) to give **31** (5.4 mg, 44%). **31**: a yellow oil; $[\alpha]_D^{24}$ −14.3 (*c* 0.27, $CHCl_3$); IR (film), ν_{max} 3610, 3428, 3025, 2928, 2856, 1471, 1462, 1439, 1388, 1376, 1361, 1323, 1256, 1217, 1179, 1146, 1089, 1057, 1026, 993, 972, 956, 939, 838, 777, 664 cm^{-1}; ^1H NMR (300 MHz, C_6D_6), δ 5.88–5.73 (2H, m), 4.53–4.52 (1H, m), 4.10 (1H, dt, J=7.9, 4.6 Hz), 4.04 (1H, dd, J=10.8, 4.6 Hz), 3.97 (1H, dd, J=10.8, 7.9 Hz), 3.90–3.80 (1H, m), 3.71–3.65 (1H, m), 3.28 (1H, ddd, J=8.8, 5.1, 2.4 Hz), 3.06–2.97 (1H, m), 2.68 (1H, ddd, J=13.7, 8.4, 5.1 Hz), 2.42–2.34 (1H, m), 2.21–2.04 (1H, m), 1.77–1.75 (1H, m), 1.54–1.42 (2H, m), 1.32–1.16 (1H, m), 0.95 (9H, s), 0.04 (3H, s), 0.03 (3H, s); ^{13}C NMR (75 MHz, C_6D_6), δ 135.8 (CH), 127.8 (CH), 84.8 (CH), 80.3 (CH), 71.1 (CH), 69.2 (CH), 68.1 (CH_2), 60.7 (CH_2), 32.4 (CH_2), 32.0 (CH_2), 26.6 (CH_2), 26.0 ($CH_3\times3$), 18.4 (C), −5.43 (CH_3), −5.46 (CH_3); LR-EIMS, *m/z* 271 (36.4%, $[M-t\text{-Bu}]^+$), 71 (bp); HR-EIMS, calcd for $C_{13}H_{23}O_4Si$ $[M-t\text{-Bu}]^+$: 271.1365, found: 271.1355.

5.1.14. (2*R*,3*S*,2′*R*,3′*S*)-2-{(2′-Allyloxan-3′-yl)oxy}pent-4-en-1,3-diol (32a) and (2*S*,3*S*,2′*R*,3′*S*)-2-{(2′-allyloxan-3′-yl)oxy}pent-4-en-1,3-diol (32b). To a solution of **30** (**30a**:**30b**=1:2, 48.4 mg, 0.136 mmol) in THF (2.0 ml) was added TBAF (0.27 ml, 1.0 M in THF, 0.272 mmol) at 24 °C and the mixture was stirred for 20.5 h. Then, the solvent was removed in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=3→1/2→1/5) to give **32** (32.7 mg, 99%) as an inseparable mixture of two diastereomers (**32a**:**32b**=1.0:2.0). **32**: a pale yellow oil; IR (film), ν_{max} 3423, 3074, 2938, 2855, 1641, 1479, 1463, 1433, 1375, 1340, 1280, 1213, 1099, 995, 918, 869, 856, 681 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 5.99–5.84 (2H, m), 5.42–5.36 (1H, m), 5.25 (1H, dt, J=10.6, 1.5 Hz), 5.16–5.07 (2H, m), 4.36 (0.33H, dd, J=5.5, 4.0 Hz), 4.22 (0.67H, t, J=5.5 Hz), 3.90 (1H, ddd, J=11.4, 4.2, 1.8 Hz), 3.79 (1H, dd, J=11.7, 4.4 Hz), 3.71 (0.33H, dd, J=10.6, 5.5 Hz), 3.66 (0.67H, dd, J=11.7, 4.4 Hz), 3.50 (0.33H, dt, J=5.5, 4.0 Hz), 3.43 (0.67H, dt, J=5.5, 4.4 Hz), 3.34 (1H, td, J=11.4, 2.9 Hz), 3.28–3.21 (2H, m), 2.69–2.57 (1H, m), 2.46 (1H, brs) 2.34–2.21 (2H, m), 1.99 (1H, brs), 1.74–1.53 (2H, m), 1.43–1.26 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$), δ 137.0 ($CH\times0.67$), 136.6 ($CH\times0.33$), 135.24 ($CH\times0.33$), 135.19 ($CH\times0.67$), 117.1 (CH_2), 116.7 ($CH_2\times0.67$), 116.6 ($CH_2\times0.33$), 80.1 ($CH\times0.33$), 79.8 ($CH\times0.67$), 79.2 ($CH\times0.33$), 78.7 ($CH\times0.67$), 76.4 ($CH\times0.33$), 75.7 ($CH\times0.67$), 72.9 ($CH\times0.33$), 72.7 ($CH\times0.67$), 67.6 ($CH_2\times0.33$), 67.5 ($CH_2\times0.67$), 62.0 ($CH_2\times0.33$), 61.4 ($CH_2\times0.67$), 36.7 ($CH_2\times0.33$), 36.5 ($CH_2\times0.67$), 30.1 ($CH_2\times0.33$), 29.6 ($CH_2\times0.67$), 25.3 ($CH_2\times0.33$), 25.2 ($CH_2\times0.67$); LR-EIMS, *m/z* 242 (1.6%, $[M]^+$), 185 (35.3%, $[M-C_3H_5O]^+$), 125 (bp); HR-EIMS, calcd for $C_{10}H_{17}O_3$ $[M-C_3H_5O]^+$: 185.1178, found: 185.1200.

5.1.15. (2*R*,3*S*,4′*S*,5′*R*)-2-Allyl-3-{(2′,2′-dimethyl-4′-vinyl-1′,3′-dioxan-5′-yl)oxy}oxane (33a) and (2*R*,3*S*,4′*S*,5′*S*)-2-allyl-3-{(2′,2′-dimethyl-4′-vinyl-1′,3′-dioxan-5′-yl)oxy}oxane (33b). To a solution of **32** (**32a**:**32b**=1:2, 32.7 mg, 0.135 mmol) and 2,2-dimethoxypropane (83 μl, 0.675 mmol) in CH_2Cl_2 (1.5 ml) was added CSA (15.7 mg, 0.0675 mmol) at 24 °C and the mixture was stirred for 3.5 h. Then, to the mixture was added 2,2-dimethoxypropane (83 μl, 0.675 mmol) and stirred at 24 °C for 4 h. Then, saturated aqueous $NaHCO_3$ (3 ml) was added and the mixture 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/EtOAc = 10 → 5) to give **33a** (9.0 mg, 24%) and **33b** (22.8 mg, 60%). **33a**: a colorless oil; $[\alpha]_D^{23}$ +17.2 (*c* 0.45, $CHCl_3$); IR (film), ν_{max} 3074, 2991, 2939, 2852, 2726, 1641, 1462, 1433, 1409, 1372, 1340, 1261, 1225, 1201, 1167, 1097, 1022, 993, 926, 870, 655 cm^{-1}; ^1H NMR (300 MHz, C_6D_6), δ 6.21–5.99 (2H, m), 5.49 (1H, dd, *J* = 17.3, 1.3 Hz), 5.22 (1H, dd, *J* = 17.3, 1.8 Hz), 5.15 (1H, dd, *J* = 10.6, 1.3 Hz), 5.13–5.09 (1H, m), 4.15 (1H, dd, *J* = 9.2, 5.9 Hz), 3.79 (1H, dd, *J* = 11.4, 5.5 Hz), 3.66–3.64 (1H, m), 3.59 (1H, dd, *J* = 11.4, 9.2 Hz), 3.20 (1H, td, *J* = 9.2, 5.5 Hz), 3.10 (1H, td, *J* = 8.4, 2.9 Hz), 2.98–2.87 (2H, m), 2.82–2.74 (1H, m), 2.36–2.27 (1H, m), 1.64–1.54 (1H, m), 1.49 (3H, s), 1.35–0.89 (3H, m), 1.28 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 135.8 (CH), 135.4 (CH), 118.4 (CH_2), 116.6 (CH_2), 98.5 (C), 80.5 (CH), 77.6 (CH), 74.2 (CH), 73.5 (CH), 67.6 (CH_2), 64.0 (CH_2), 36.5 (CH_2), 31.0 (CH_2), 28.7 (CH_3), 25.2 (CH_2), 19.3 (CH_3); LR-EIMS, *m/z* 267 (17.1%, $[M-CH_3]^+$), 140 (bp); HR-EIMS, calcd for $C_{16}H_{26}O_4$ $[M]^+$: 282.1831, found: 282.1831. **33b**: a colorless oil; $[\alpha]_D^{24}$ +106.4 (*c* 1.14, $CHCl_3$); IR (film), ν_{max} 3076, 2990, 2937, 2854, 2725, 1641, 1453, 1434, 1380, 1371, 1270, 1240, 1199, 1133, 1096, 1049, 1029, 993, 950, 920, 886, 857, 811 cm^{-1}; ^1H NMR (300 MHz, C_6D_6), δ 6.32–6.18 (1H, m), 6.08 (1H, ddd, *J* = 17.3, 10.3, 6.2 Hz), 5.37–5.32 (1H, m), 5.23 (1H, dt, *J* = 17.3, 1.8 Hz), 5.18–5.13 (1H, m), 5.08 (1H, ddd, *J* = 10.3, 1.8, 1.1 Hz), 4.11 (1H, ddt, *J* = 6.2, 1.8, 1.1 Hz), 3.74 (1H, dd, *J* = 12.8, 1.8 Hz), 3.73–3.69 (1H, m), 3.45 (1H, dd, *J* = 12.8, 1.8 Hz), 3.25 (1H, ddd, *J* = 8.8, 7.3, 3.3 Hz), 3.05–2.96 (1H, m), 3.03 (1H, td, *J* = 11.6, 2.5 Hz), 2.87 (1H, ddd, *J* = 10.3, 8.8, 4.4 Hz), 2.64 (1H, q, *J* = 1.8 Hz), 2.56 (1H, dt, *J* = 14.3, 7.3 Hz), 1.75–1.71 (1H, m), 1.50 (3H, s), 1.37–1.01 (3H, m), 1.26 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 135.9 (CH), 135.5 (CH), 117.0 (CH_2), 116.5 (CH_2), 98.6 (C), 80.1 (CH), 74.9 (CH), 73.3 (CH), 70.5 (CH), 67.8 (CH_2), 61.7 (CH_2), 36.4 (CH_2), 29.3 (CH_3), 29.1 (CH_2), 25.4 (CH_2), 19.0 (CH_3); LR-EIMS, *m/z* 282 (1.9%, $[M]^+$), 267 (52.4%, $[M-CH_3]^+$), 125 (bp); HR-EIMS, calcd for $C_{16}H_{26}O_4$ $[M]^+$: 282.1831, found: 282.1824.

5.1.16. (1*S*,3*R*,8*S*,9*Z*,12*R*)-6,6-Dimethyl-2,5,7,13-tetraoxatricyclo[10.4.0.0^{3,8}]hexadeca-9-ene (34). To a solution of **33a** (3.9 mg, 0.0138 mmol) in CH_2Cl_2 (2.5 ml) was added a solution of $(H_2IMes)(PCy_3)Cl_2Ru{=}CHPh$ (1.2 mg, 1.38 μmol) in CH_2Cl_2 (1.0 ml). The resultant solution was stirred at 45 °C for 4.5 h. The mixture was cooled to 24 °C and stirred for 14 h under O_2 atmosphere. The reaction mixture was filtered through Celite-Florisil and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc = 10 → 5) to give **34** (2.9 mg, 83%). **34**: a colorless oil; $[\alpha]_D^{22}$ −79.9 (*c* 0.15, $CHCl_3$); IR (film), ν_{max} 3032, 2991, 2924, 2851, 2722, 1462, 1439, 1372, 1333, 1305, 1298, 1285, 1265, 1223, 1198, 1163, 1147, 1102, 1088, 1050, 1032, 987, 959, 943, 866, 843, 758, 645 cm^{-1}; ^1H NMR (300 MHz, C_6D_6), δ 5.95 (1H, dd, *J* = 10.6, 4.8 Hz), 5.87–5.77 (1H, m), 4.54–4.49 (1H, m), 3.92 (1H, dd, *J* = 11.2, 5.7 Hz), 3.65 (1H, dd, *J* = 11.2, 10.1 Hz), 3.65–3.60 (1H, m), 3.32–3.22 (2H, m), 3.15 (1H, ddd, *J* = 9.2, 4.8, 2.2 Hz), 2.95 (1H, td, *J* = 11.6, 2.6 Hz), 2.72 (1H, ddd, *J* = 13.6, 8.8, 4.8 Hz), 2.33 (1H, ddd, *J* = 13.6, 7.7, 2.2 Hz), 1.67–1.64 (1H, m), 1.49 (3H, s), 1.35–1.11 (3H, m), 1.13 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 134.4 (CH), 126.7 (CH), 98.2 (C), 83.1 (CH), 77.2 (CH), 75.2 (CH), 72.2 (CH), 68.3 (CH_2), 63.0 (CH_2), 31.24 (CH_2), 31.17 (CH_2), 29.0 (CH_3), 26.3 (CH_2), 18.8 (CH_3); LR-EIMS, *m/z* 254 (4.1%, $[M]^+$), 239 (38.5%, $[M-CH_3]^+$), 196 (bp); HR-EIMS, calcd for $C_{13}H_{19}O_4$ $[M-CH_3]^+$: 239.1283, found: 239.1269.

5.1.17. (1*S*,3*R*,4*S*,5*Z*,8*R*)-3-Hydroxymethyl-2,9-dioxabicyclo[6.4.0]dodec-5-en-4-ol (35). To a solution of **34** (2.9 mg, 0.0114 mmol) in THF–H_2O (1:1, v/v, 0.80 ml) was added TFA (40 μl) at 0 °C. The mixture was warmed to 23 °C and stirred for 11.5 h. After the mixture was diluted with Et_2O (3 ml), saturated aqueous $NaHCO_3$ (5 ml) was added. The mixture was extracted with EtOAc (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/EtOAc = 1 → 1/5) to give **35** (1.7 mg, 71%). **35**: a colorless oil; $[\alpha]_D^{23}$ −38.5 (*c* 0.085, $CHCl_3$); IR (film), ν_{max} 3413, 3023, 2932, 2856, 1678, 1439, 1377, 1334, 1308, 1281, 1264, 1205, 1144, 1117, 1085, 1033, 979, 959, 918, 909, 855, 844, 760, 699, 647 cm^{-1}; ^1H NMR (400 MHz, C_5D_5N), δ 6.23 (1H, dd, *J* = 11.0, 5.9 Hz), 5.90–5.82 (1H, m), 4.85 (1H, ddd, *J* = 8.8, 5.9, 2.0 Hz), 4.45 (1H, dd, *J* = 11.5, 3.4 Hz), 4.24 (1H, dd, *J* = 11.5, 5.9 Hz), 3.80–3.77 (1H, m), 3.77 (1H, ddd, *J* = 8.8, 5.9, 3.4 Hz), 3.60 (1H, td, *J* = 9.3, 4.4 Hz), 3.31 (1H, ddd, *J* = 9.3, 4.4, 2.0 Hz), 3.17 (1H, td, *J* = 11.2, 2.9 Hz), 2.91 (1H, ddd, *J* = 13.7, 9.8, 4.4 Hz), 2.34 (1H, ddd, *J* = 13.7, 6.8, 2.0 Hz), 2.06–2.04 (1H, m), 1.50–1.39 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$), δ 136.7 (CH), 127.0 (CH), 83.1 (CH), 82.8 (CH), 77.5 (CH), 70.8 (CH), 68.3 (CH_2), 64.2 (CH_2), 31.0 (CH_2), 29.7 (CH_2), 26.2 (CH_2); LR-EIMS, *m/z* 214 (20.0%, $[M]^+$), 71 (bp); HR-EIMS, calcd for $C_{11}H_{18}O_4$ $[M]^+$: 214.1205, found: 214.1232.

5.1.18. (1*R*,3*S*,4*R*,6*Z*,9*S*,11*R*)-4-(*tert*-Butyldimethylsilyloxy)-3-hydroxymethyl-11-phenyl-2,10,12-trioxabicyclo[7.4.0]tridec-6-ene (37). To a solution of **36** (87.0 mg, 0.160 mmol) in THF–H_2O (1:1, v/v, 2.0 ml) was added TFA (100 μl) at 0 °C and the mixture was stirred for 4 h. After the mixture was diluted with Et_2O (5 ml), saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture was extracted with EtOAc (3×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc = 10 → 3) to give **37** (46.5 mg, 68%) along with recovered **36** (21.2 mg, 24%). **37**: a colorless oil; $[\alpha]_D^{21}$ −2.2 (*c* 0.34, $CHCl_3$); IR (film), ν_{max} 3478, 3018, 2955, 2929, 2857, 1471, 1462, 1455, 1390, 1360, 1340, 1294, 1252, 1213, 1139, 1104, 1074, 1041, 1028, 971, 940, 889, 777, 697, 673 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.37–7.22 (5H, m), 5.73–5.62 (2H, m), 5.31 (1H, s), 4.25 (1H, dd, *J* = 9.3, 3.4 Hz), 3.74–3.70 (1H, m), 3.59–3.52 (3H, m), 3.49–3.42 (2H, m), 3.27–3.22 (1H, m), 2.67–2.61 (1H, m), 2.44–2.40 (3H, m), 0.78 (9H, s), 0.11 (3H, s), 0.08 (3H, s); LR-EIMS, *m/z* 363 (53.8%, $[M-t\text{-Bu}]^+$), 75 (bp); HR-EIMS, calcd for $C_{19}H_{27}O_5Si$ $[M-t\text{-Bu}]^+$: 363.1628, found: 363.1650.

5.1.19. (2*R*,3*S*,5*Z*,8*R*,9*S*)-8-(*tert*-Butyldimethylsilyloxy)-2-hydroxymethyl-9-vinyl-2,3,4,7,8,9-hexahydrooxonin-3-ol (38). To oxalyl chloride (157 μl, 1.80 mmol) in CH_2Cl_2 (2.0 ml) was added DMSO (0.21 ml, 3.00 mmol) in CH_2Cl_2 (1.0 ml) dropwise at −78 °C and the mixture was stirred for 10 min. Then, **37** (259.1 mg, 0.599 mmol) in CH_2Cl_2 (0.9 ml) was added dropwise at −78 °C and the mixture was stirred for 15 min. Et_3N (0.83 ml, 5.99 mmol) was added dropwise at −78 °C. The mixture was warmed to −20 °C and stirred for 10 min. Then, saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture was extracted with Et_2O (3×8 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The resultant crude aldehyde was used immediately in the next reaction without purification. To a stirred suspension of $Ph_3P^+CH_3Br^-$ (1.07 g, 3.00 mmol) in THF (4.0 ml) was added NaHMDS (2.88 ml, 1.0 M in THF, 2.88 mmol) and the mixture was stirred at 24 °C. After 1 h, the resulting yellow suspension was allowed to stand at −78 °C. To the mixture was added dropwise a solution of the above crude aldehyde in THF (4.0 ml) at −78 °C and the mixture was stirred for 2.5 h. Then, the reaction mixture was warmed to 25 °C and stirred for 2.5 h. After the mixture was diluted with hexane (10 ml) and Et_2O (5 ml), saturated aqueous NH_4Cl (10 ml) was added and the mixture was extracted with Et_2O (3×10 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The resultant residue was roughly purified by column chromatography (silica gel, hexane/EtOAc=20) to give a crude olefin compound, and it was used in the next reaction without further purification. To a suspension of the above olefin compound, 1,2-ehtanedithiol (0.79 ml, 9.40 mmol) and $NaHCO_3$ (394.8 mg, 4.70 mmol) in CH_2Cl_2 (7.0 ml) was added $Zn(OTf)_2$ (170.8 mg, 0.470 mmol) at 0 °C and the mixture was stirred for 2.5 h. After the mixture was diluted with Et_2O (5 ml), saturated aqueous $NaHCO_3$ (5 ml) and H_2O (5 ml) were added and the mixture was extracted with Et_2O–EtOAc (1:1, v/v, 3×10 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/EtOAc=3→1) to give **38** (113.5 mg, 58% from **37**). **38**: a colorless oil; $[\alpha]_D^{24}$ −46.9 (*c* 0.21, $CHCl_3$); IR (film), ν_{max} 3584, 3382, 3018, 2955, 2928, 2858, 1472, 1462, 1449, 1256, 1098, 1051, 933, 833, 811, 775, 664 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 5.91–5.78 (3H, m), 5.25 (1H, dt, *J*=17.3, 1.1 Hz), 5.19 (1H, dt, *J*=10.3, 1.1 Hz), 4.02–3.94 (1H, m), 3.74–3.69 (3H, m), 3.52 (1H, brtd, *J*=8.4, 1.1 Hz), 3.23 (1H, dt, *J*=8.8, 4.4 Hz), 2.83–2.73 (2H, m), 2.23–1.99 (4H, m), 0.87 (9H, s), 0.06 (3H, s), 0.01 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 139.5 (CH), 128.6 (CH), 127.2 (CH), 117.2 (CH_2), 89.0 (CH), 86.7 (CH), 74.5 (CH), 71.6 (CH), 63.8 (CH_2), 32.9 (CH_2), 32.5 (CH_2), 25.7 (CH_3×3), 17.9 (C), −4.44 (CH_3), −4.59 (CH_3); LR-EIMS, *m/z* 271 (15.3%, $[M-t\text{-Bu}]^+$), 73 (bp); HR-EIMS, calcd for $C_{13}H_{23}O_4Si$ $[M-t\text{-Bu}]^+$: 271.1365, found: 271.1360.

5.1.20. (2*S*,3*R*,5*Z*,8*S*,9*R*)-8-Benzyloxy-9-benzyloxymethyl-2-vinyl-2,3,4,7,8,9-hexahydrooxonin-3-ol (5). To a solution of **38** (113.5 mg, 0.345 mmol) in THF (4.0 ml) was added NaH (165.7 mg, 60 wt% in oil, 4.14 mmol) at 0 °C and the mixture was stirred for 20 min. Then, to the mixture was added benzyl bromide (0.25 ml, 2.07 mmol) and TBAI (12.7 mg, 0.0345 mmol) at 0 °C. The reaction mixture was warmed to 24 °C and stirred for 15 h. After the mixture was cooled to 0 °C and diluted with Et_2O (5 ml), saturated aqueous NH_4Cl (10 ml) was added and the mixture 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 roughly purified by column chromatography (silica gel, hexane/EtOAc=20) 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 (3.0 ml) was added TBAF (0.69 ml, 1.0 M in THF, 0.690 mmol) at 25 °C and the mixture was stirred for 4 h. Since TLC analysis showed the starting material remained, TBAF (2.41 ml, 1.0 M in THF, 2.41 mmol) was added, and the stirring was continued for further 14 h. The solvent was removed in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=5→3) to give **5** (135.8 mg, 100% from **38**) **5**: a colorless oil; $[\alpha]_D^{27}$ +28.3 (*c* 0.33, $CHCl_3$); IR (film), ν_{max} 3439, 3087, 3063, 3027, 2913, 2864, 1495, 1453, 1364, 1338, 1317, 1274, 1257, 1207, 1097, 1070, 1043, 1027, 928, 773, 736, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.37–7.20 (10H, m), 5.96–5.77 (3H, m), 5.28–5.22 (1H, m), 5.19–5.15 (1H, m), 4.59 (1H, d, *J*=11.4 Hz), 4.54 (1H, d, *J*=12.5 Hz), 4.41 (1H, d, *J*=12.5 Hz), 4.29 (1H, d, *J*=11.4 Hz), 3.93 (1H, dt, *J*=8.4, 3.7 Hz), 3.72 (1H, ddd, *J*=8.8, 4.0, 2.9 Hz), 3.53 (1H, dd, *J*=10.3, 2.9 Hz), 3.49 (1H, dd, *J*=10.3, 2.9 Hz), 3.44 (1H, brt, *J*=8.8 Hz), 3.28 (1H, dt, *J*=8.4, 2.9 Hz), 2.95–2.86 (1H, m), 2.74–2.65 (1H, m), 2.35 (1H, brdt, *J*=13.9, 4.0 Hz), 2.21–2.17 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$), δ 139.0 (CH), 138.4 (C), 138.2 (C), 128.7 (CH), 128.3 (CH×2), 128.2 (CH×2), 128.0 (CH×2), 127.8 (CH×2), 127.5 (CH×2), 127.3 (CH), 117.7 (CH_2), 88.7 (CH), 84.3 (CH), 78.1 (CH), 73.2 (CH_2), 72.7 (CH), 71.6 (CH_2), 69.3 (CH_2), 31.3 (CH_2), 27.4 (CH_2); LR-EIMS, *m/z* 394 (11.4%, $[M]^+$), 92 (bp); HR-EIMS, calcd for $C_{25}H_{30}O_4$ $[M]^+$: 394.2144, found: 394.2145.

5.1.21. Methyl (2*E*,2′*S*,3′*R*,5′*Z*,8′*S*,9′*R*)-3-{(8′-benzyloxy-9′-benzyloxymethyl-2′-vinyl-2′,3′,4′,7′,8′,9′-hexahydro-oxonin-3′-yl)oxy}-4-(*tert*-butyldimethylsilyloxy)-2-butenoate (39). A solution of butynoate **20** (148.0 mg, 0.648 mmol) in CH_2Cl_2 (2.0 ml) was slowly added dropwise to a solution of **5** (85.4 mg, 0.216 mmol) and PMe_3 (0.32 ml, 1.0 M in THF, 0.324 mmol) in CH_2Cl_2 (3.0 ml) at 0 °C by means of a syringe. The mixture was warmed to 24 °C and stirred for 1 h. The mixture was cooled to 0 °C and diluted with hexane (5 ml) and Et_2O (5 ml). Then, saturated aqueous NH_4Cl (5 ml) was added and the mixture was extracted with Et_2O (3×8 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/EtOAc=30→20→10) to give **39** (121.5 mg, 90%). **39**: a colorless oil; $[\alpha]_D^{23}$ +24.8 (*c* 0.91, $CHCl_3$); IR (film), ν_{max} 3027, 2949, 2928, 2857, 1716, 1626, 1471, 1453, 1434, 1389, 1360, 1297, 1253, 1206, 1138, 1096, 1048, 837, 776, 735, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.34–7.19 (10H, m), 5.94–5.80 (2H, m), 5.70 (1H, td, *J*=10.8, 5.5 Hz), 5.32 (1H, dt, *J*=17.2, 1.4 Hz), 5.07 (1H, dt, *J*=10.5,

1.4 Hz), 4.99 (1H, s), 4.80 (1H, d, $J=13.3$ Hz), 4.68 (1H, d, $J=13.3$ Hz), 4.59 (1H, d, $J=11.2$ Hz), 4.54 (1H, d, $J=12.2$ Hz), 4.40 (1H, d, $J=12.2$ Hz), 4.29 (1H, d, $J=11.2$ Hz), 4.23–4.20 (1H, m), 3.98 (1H, dt, $J=8.8$, 3.0 Hz), 3.80–3.76 (1H, m), 3.66 (3H, s), 3.59 (1H, dd, $J=10.1$, 2.4 Hz), 3.53 (1H, dd, $J=10.1$, 2.4 Hz), 3.28 (1H, brdt, $J=8.8$, 2.4 Hz), 2.86–2.76 (1H, m), 2.74–2.65 (1H, m), 2.39–2.30 (2H, m), 0.89 (9H, s), 0.07 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 170.5 (C), 167.4 (C), 138.3 (C), 138.1 (C), 137.8 (CH), 129.1 (CH), 128.3 (CH×2), 128.2 (CH×2), 128.1 (CH×2), 127.8 (CH×2), 127.6 (CH×2), 126.6 (CH), 116.4 (CH_2), 92.6 (CH), 84.9 (CH), 84.7 (CH), 79.6 (CH), 77.5 (CH), 73.3 (CH_2), 71.7 (CH_2), 68.9 (CH_2), 60.1 (CH_2), 50.9 (CH_3), 27.4 (CH_2), 27.0 (CH_2), 25.8 (CH_3×3), 18.3 (C), −5.26 (CH_3), −5.28 (CH_3); LR-EIMS, *m/z* 565 (2.3%, $[M-t\text{-Bu}]^+$), 91 (bp); HR-EIMS, calcd for $C_{32}H_{41}O_7Si$ $[M-t\text{-Bu}]^+$: 565.2621, found: 565.2660.

5.1 .22. (2*E*,2′*S*,3′*R*,5′*Z*,8′*S*,9′*R*)-3-{(8′-Benzyloxy-9′-benzyloxymethyl-2′-vinyl-2′,3′,4′,7′,8′,9′-hexahydrooxonin-3′-yl)oxy}-4-(*tert*-butyldimethylsilyloxy)-2-butenol (40). To a solution of **39** (50.2 mg, 0.0806 mmol) in CH_2Cl_2 (1.5 ml) was added DIBAH (0.34 ml, 0.94 M in *n*-hexane, 0.322 mmol) at −78 °C and the mixture was stirred for 10 min. Then, saturated aqueous potassium sodium tartrate (5 ml) was added and the mixture was stirred at 24 °C for 3 h. The layers were separated and the aqueous layer was extracted with EtOAc (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/EtOAc=10→5→3) to give **40** (47.4 mg, 99%). **40**: a colorless oil; $[\alpha]_D^{22}$ +14.4 (*c* 0.39, $CHCl_3$); IR (film), ν_{max} 3584, 3416, 3087, 3064, 3027, 2952, 2927, 2857, 1660, 1496, 1471, 1462, 1454, 1389, 1360, 1337, 1319, 1295, 1274, 1253, 1203, 1183, 1145, 1096, 1027, 1004, 960, 929, 836, 815, 776, 735, 697, 673 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.33–7.20 (10H, m), 5.94–5.77 (2H, m), 5.69 (1H, td, $J=10.6$, 5.4 Hz), 5.28 (1H, dt, $J=17.3$, 1.7 Hz), 5.05 (1H, ddd, $J=10.5$, 1.7, 1.1 Hz), 4.88 (1H, t, $J=8.1$ Hz), 4.59 (1H, d, $J=11.2$ Hz), 4.54 (1H, d, $J=12.3$ Hz), 4.40 (1H, d, $J=12.3$ Hz), 4.29 (1H, d, $J=11.2$ Hz), 4.19 (1H, d, $J=12.3$ Hz), 4.16–4.09 (2H, m), 4.11 (1H, d, $J=12.3$ Hz), 4.11–4.08 (1H, m), 3.99–3.94 (1H, m), 3.70–3.65 (1H, m), 3.59 (1H, dd, $J=10.1$, 2.8 Hz), 3.53 (1H, dd, $J=10.1$, 2.2 Hz), 3.30–3.26 (1H, m), 2.78–2.66 (1H, m), 2.40–2.31 (2H, m), 0.90 (9H, s), 0.09 (3H, s), 0.08 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 157.4 (C), 138.4 (CH), 138.3 (C), 138.2 (C), 128.5 (CH), 128.3 (CH×2), 128.2 (CH×2), 128.1 (CH×2), 127.8 (CH×2), 127.6 (CH×2), 127.4 (CH), 115.9 (CH_2), 101.0 (CH), 85.5 (CH), 84.5 (CH), 78.0 (CH), 77.6 (CH), 73.3 (CH_2), 71.6 (CH_2), 69.0 (CH_2), 61.5 (CH_2), 58.2 (CH_2), 27.4 (CH_2), 26.8 (CH_2), 25.8 (CH_3×3), 18.2 (C), −5.30 (CH_3), −5.33 (CH_3); LR-EIMS, *m/z* 537 (3.0%, $[M-t\text{-Bu}]^+$), 91 (bp); HR-EIMS, calcd for $C_{31}H_{41}O_6Si$ $[M-t\text{-Bu}]^+$: 537.2672, found: 537.2698.

5.1.23. (2*E*,2′*S*,3′*R*,5′*Z*,8′*S*,9′*R*)-3-{(8′-Benzyloxy-9′-benzyloxymethyl-2′-vinyl-2′,3′,4′,7′,8′,9′-hexahydrooxonin-3′-yl)oxy}-4-(*tert*-butyldimethylsilyloxy)-2-butenal (41). To a mixture of **40** (42.8 mg, 0.0720 mmol) and MS 4 Å (42.8 mg, 100 wt%) in CH_2Cl_2 (1.2 ml) was added NMO (16.7 mg, 0.144 mmol) at 24 °C and the mixture was stirred for 10 min. Then, TPAP (5.1 mg, 0.0144 mmol) was added to the reaction mixture at 24 °C and the mixture was stirred for 1.5 h. The mixture was filtered through Celite and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=10→5) to give **41** (32.5 mg, 76%). **41**: a colorless oil; $[\alpha]_D^{26}$ +33.2 (*c* 0.52, $CHCl_3$); IR (film), ν_{max} 3087, 3064, 3027, 2953, 2928, 2885, 2857, 2766, 1663, 1615, 1496, 1471, 1462, 1389, 1361, 1321, 1295, 1255, 1207, 1144, 1097, 1037, 1006, 921, 837, 777, 736, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$), δ 9.98 (1H, d, $J=7.3$ Hz), 7.35–7.20 (10H, m), 5.91–5.79 (2H, m), 5.66 (1H, td, $J=10.7$, 5.9 Hz), 5.35 (1H, d, $J=7.3$ Hz), 5.28 (1H, dt, $J=17.3$, 1.3 Hz), 5.08 (1H, dt, $J=10.3$, 1.3 Hz), 4.60 (1H, d, $J=11.0$ Hz), 4.53 (1H, d, $J=12.1$ Hz), 4.51 (1H, d, $J=13.2$ Hz), 4.41 (1H, d, $J=12.1$ Hz), 4.39 (1H, d, $J=13.2$ Hz), 4.29 (1H, d, $J=11.0$ Hz), 4.25–4.20 (1H, m), 4.00–3.94 (1H, m), 3.79–3.74 (1H, m), 3.58 (1H, dd, $J=9.9$, 2.8 Hz), 3.52 (1H, dd, $J=9.9$, 2.4 Hz), 3.29 (1H, brdt, $J=8.8$, 2.8 Hz), 2.88–2.79 (1H, m), 2.73–2.63 (1H, m), 2.40–2.26 (2H, m), 0.90 (9H, s), 0.09 (3H, s), 0.08 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 190.5 (CH), 174.2 (C), 138.2 (C), 138.1 (C), 137.5 (CH), 129.6 (CH), 128.32 (CH×2), 128.26 (CH×2), 128.1 (CH×2), 127.8 (CH×2), 127.6 (CH×2), 126.0 (CH), 117.1 (CH_2), 106.6 (CH), 84.8 (CH), 84.6 (CH), 79.9 (CH), 77.6 (CH), 73.3 (CH_2), 71.7 (CH_2), 68.9 (CH_2), 61.6 (CH_2), 27.4 (CH_2), 27.0 (CH_2), 25.7 (CH_3×3), 18.2 (C), −5.33 (CH_3), −5.36 (CH_3); LR-EIMS, *m/z* 535 (29.5%, $[M-t\text{-Bu}]^+$), 50 (bp); HR-EIMS, calcd for $C_{31}H_{39}O_6Si$ $[M-t\text{-Bu}]^+$: 535.2516, found: 535.2514.

5.1.24. (3*E*,2′*S*,3′*R*,5′*Z*,8′*S*,9′*R*)-4-{(8′-Benzyloxy-9′-benzyloxymethyl-2′-vinyl-2′,3′,4′,7′,8′,9′-hexahydrooxonin-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2-(trimethylsilyloxy)pent-3-enenitrile (42). To a solution of **41** (5.2 mg, 8.77 μmol) and TMSCN (5.8 μl, 0.0439 mmol) in benzene (0.40 ml) was added Me_3Al (9.6 μl, 1.01 M in *n*-hexane, 9.65 μmol) at 24 °C and the mixture was stirred for 1 h. Then, saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture 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/EtOAc=20→10) to give **42** (4.8 mg, 79%) as an inseparable 1:1 mixture of diastereomers. The nitrile **42** was unstable and immediately used for the next reaction. **42**: a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.31–7.20 (10H, m), 5.91–5.78 (2H, m), 5.72–5.62 (1H, m), 5.60 (0.5H, d, $J=9.0$ Hz), 5.58 (0.5H, d, $J=9.0$ Hz), 5.29–5.23 (1H, m), 5.10–5.03 (1H, m), 4.68–4.65 (1H, m), 4.60 (1H, d, $J=11.2$ Hz), 4.56–4.52 (1H, m), 4.41 (0.5H, d, $J=12.3$ Hz), 4.40 (0.5H, d, $J=12.3$ Hz), 4.30 (0.5H, d, $J=11.2$ Hz), 4.29 (0.5H, d, $J=11.2$ Hz), 4.19–4.04 (3H, m), 4.00–3.94 (1H, m), 3.68–3.60 (1H, m), 3.57–3.49 (2H, m), 3.29–3.26 (1H, m), 2.82–2.64 (1H, m), 2.39–2.27 (2H, m), 0.91 (4.5H, s), 0.90 (4.5H, s), 0.20 (4.5H, s), 0.18 (4.5H, s), 0.10 (1.5H, s), 0.09 (1.5H, s), 0.08 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 157.3 (C×0.5), 156.9 (C×0.5), 138.3 (C), 138.18 (CH×0.5), 138.16 (C), 138.0 (CH×0.5), 129.0 (CH×0.5), 128.9 (CH×0.5), 128.33 (CH×2), 128.26 (CH×2), 128.1 (CH×2), 127.9 (CH×2), 127.6 (CH×2), 126.9 (CH×0.5), 126.8 (CH×0.5), 120.0 (C×0.5), 119.9

(C×0.5), 116.6 (CH_2×0.5), 116.3 (CH_2×0.5), 99.3 (CH×0.5), 99.1 (CH×0.5), 85.4 (CH×0.5), 85.3 (CH×0.5), 84.6 (CH×0.5), 84.5 (CH×0.5), 78.7 (CH×0.5), 78.5 (CH×0.5), 77.6 (CH), 73.3 (CH_2), 71.6 (CH_2×0.5), 71.3 (CH_2×0.5), 69.0 (CH_2), 62.4 (CH_2×0.5), 62.2 (CH_2×0.5), 57.7 (CH×0.5), 57.6 (CH×0.5), 27.4 (CH_2), 26.9 (CH_2), 25.8 (CH_3×3), 18.3 (C), 0.02 (CH_3×1.5), −0.05 (CH_3×1.5), −5.38 (CH_3×0.5), −5.40 (CH_3×0.5), −5.51 (CH_3×0.5), −5.54 (CH_3×0.5).

5.1.25. (2*E*,2′*S*,3′*R*,5′*Z*,8′*S*,9′*R*)-4-{(8′-Benzyloxy-9′-benzyloxymethyl-2′-vinyl-2′,3′,4′,7′,8′,9′-hexahydrooxonin-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)pent-2-enenitrile (43). To a solution of **42** (58.8 mg, 0.0850 mmol) in CH_2Cl_2–Bu_3SnH (1:1, v/v, 1.0 ml) was added $BF_3\cdot OEt_2$ (31 μl, 0.255 mmol) at −18 °C and the mixture was stirred for 15 min. Then, saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture was extracted with EtOAc (3×5 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=50→10→5) to give **43** (28.3 mg, 55%) as an inseparable 1:1 mixture of diastereomers at C2[35] along with recovered **42** (10.7 mg, 18%). **43**: a colorless oil; IR (film), ν_{max} 3064, 3027, 2954, 2927, 2858, 2225, 1496, 1471, 1462, 1454, 1388, 1361, 1331, 1294, 1254, 1204, 1098, 1027, 1005, 967, 928, 837, 814, 776, 736, 698, 670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.39–7.20 (10H, m), 6.81 (0.5H, dd, J=16.5, 4.4 Hz), 6.62 (0.5H, dd, J=16.5, 4.8 Hz), 5.99–5.70 (3H, m), 5.68 (0.5H, dd, J=16.5, 1.8 Hz), 5.65 (0.5H, dd, J=16.5, 1.5 Hz), 5.32–5.21 (1H, m), 5.12 (0.5H, dd, J=10.3, 1.8 Hz), 5.08 (0.5H, dd, J=10.3, 1.8 Hz), 4.59 (1H, d, J=11.4 Hz), 4.53 (0.5H, d, J=12.1 Hz), 4.52 (0.5H, d, J=12.5 Hz), 4.40 (0.5H, d, J=12.5 Hz), 4.38 (0.5H, d, J=12.1 Hz), 4.28 (1H, d, J=11.4 Hz), 4.08–3.93 (2H, m), 3.69–3.46 (5H, m), 3.38 (1H, dd, J=9.9, 7.3 Hz), 3.24–3.20 (1H, m), 2.82–2.74 (1H, m), 2.67 (1H, ddd, J=13.9, 10.6, 3.3 Hz), 2.36–2.29 (1H, m), 2.21–2.17 (0.5H, m), 2.08–2.02 (0.5H, m), 0.88 (4.5H, s), 0.87 (4.5H, s), 0.05 (1.5H, s), 0.04 (1.5H, s), 0.03 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 153.7 (CH×0.5), 152.7 (CH×0.5), 138.9 (CH×0.5), 138.8 (CH×0.5), 138.4 (C), 138.3 (C), 128.8 (CH×0.5), 128.5 (CH×0.5), 128.32 (CH×2), 128.26 (CH×2), 128.1 (CH×2), 127.8 (CH×2), 127.6 (CH×2), 127.4 (CH×0.5), 127.1 (CH×0.5), 117.4 (CH_2×0.5), 117.2 (C×0.5), 117.1 (C×0.5), 116.1 (CH_2×0.5), 101.1 (CH×0.5), 100.2 (CH×0.5), 86.4 (CH×0.5), 85.9 (CH×0.5), 84.6 (CH×0.5), 84.5 (CH×0.5), 82.7 (CH×0.5), 81.6 (CH×0.5), 78.4 (CH×0.5), 78.2 (CH×0.5), 77.7 (CH×0.5), 77.4 (CH×0.5), 73.3 (CH_2), 71.6 (CH_2), 68.8 (CH_2), 65.2 (CH_2×0.5), 64.2 (CH_2×0.5), 28.9 (CH_2), 28.7 (CH_2), 25.8 (CH_3×3), 18.23 (C×0.5), 18.19 (C×0.5), −5.41 (CH_3×0.5), −5.50 (CH_3×0.5), −5.52 (CH_3×0.5), −5.63 (CH_3×0.5); LR-EIMS, *m/z* 546 (6.0%, $[M-t\text{-Bu}]^+$), 91 (bp); HR-EIMS, calcd for $C_{32}H_{40}NO_5Si$ $[M-t\text{-Bu}]^+$: 546.2675, found: 546.2678.

5.1.26. (2*E*,2′*S*,3′*R*,5′*Z*,8′*S*,9′*R*)-4-{(8′-Benzyloxy-9′-benzyloxymethyl-2′-vinyl-2′,3′,4′,7′,8′,9′-hexahydrooxonin-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2-pentenal (44). To a solution of **43** (39.4 mg, 0.0652 mmol) in CH_2Cl_2 (1.0 ml) was added DIBAH (0.17 ml, 0.94 M in *n*-hexane, 0.163 mmol) at −78 °C and the mixture was stirred for 10 min. Then, saturated aqueous potassium sodium tartrate (5 ml) was added and the mixture was stirred at 24 °C for 10 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/EtOAc=20→10→5) to give **44** (39.6 mg, ~100%) as an inseparable 1:1 mixture of diastereomers at C2.[35] **44**: a colorless oil; IR (film), ν_{max} 3064, 3027, 2953, 2927, 2858, 2736, 1694, 1496, 1471, 1462, 1454, 1377, 1361, 1329, 1294, 1254, 1206, 1099, 1069, 1027, 1005, 981, 928, 837, 814, 776, 736, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 9.58 (0.5H, d, J=8.1 Hz), 9.52 (0.5H, d, J=8.1 Hz), 7.31–7.20 (10H, m), 6.88 (0.5H, dd, J=15.8, 4.8 Hz), 6.66 (0.5H, dd, J=15.8, 5.5 Hz), 6.35 (0.5H, ddd, J=15.8, 8.1, 1.5 Hz), 6.29 (0.5H, ddd, J=15.8, 8.1, 1.5 Hz), 6.03–5.69 (3H, m), 5.33–5.28 (1H, m), 5.11–5.06 (1H, m), 4.58 (1H, d, J=11.4 Hz), 4.53 (0.5H, d, J=12.1 Hz), 4.52 (0.5H, d, J=12.1 Hz), 4.39 (1H, d, J=12.1 Hz), 4.28 (0.5H, d, J=11.4 Hz), 4.27 (0.5H, d, J=11.4 Hz), 4.19–4.18 (1H, m), 3.96 (1H, brdt, J=8.6, 3.1 Hz), 3.76–3.44 (6H, m), 3.24–3.21 (1H, m), 2.82–2.62 (2H, m), 2.36–2.29 (1H, m), 2.25–2.19 (0.5H, m), 2.12–2.10 (0.5H, m), 0.88 (4.5H, s), 0.87 (4.5H, s), 0.06 (1.5H, s), 0.05 (1.5H, s), 0.04 (3H, s); LR-EIMS, *m/z* 606 (12.9%, $[M]^+$), 213 (bp); HR-EIMS, calcd for $C_{32}H_{41}O_6Si$ $[M-t\text{-Bu}]^+$: 549.2672, found: 549.2669.

5.1.27. (2*E*,2′*S*,3′*R*,5′*Z*,8′*S*,9′*R*)-4-{(8′-Benzyloxy-9′-benzyloxymethyl-2′-vinyl-2′,3′,4′,7′,8′,9′-hexahydrooxonin-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2-pentenol (45). To a solution of **44** (39.6 mg, 0.0652 mmol) in CH_2Cl_2 (1.5 ml) was added DIBAH (0.21 ml, 0.94 M in *n*-hexane, 0.196 mmol) at −78 °C and the mixture was stirred for 20 min. Then, saturated aqueous potassium sodium tartrate (5 ml) was added and the mixture was stirred at 24 °C for 2 h. The layers were separated and the aqueous layer was extracted with EtOAc (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/EtOAc=10→3) to give **45** (28.5 mg, 72% from **43**) as an inseparable 1:1 mixture of diastereomers at C2.[35] **45**: a colorless oil; IR (film), ν_{max} 3584, 3443, 3087, 3064, 3027, 2952, 2927, 2857, 1496, 1471, 1454, 1388, 1360, 1336, 1294, 1256, 1206, 1098, 1068, 1027, 1005, 928, 836, 815, 775, 736, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.32–7.19 (10H, m), 6.09–5.76 (4H, m), 5.74–5.66 (0.5H, m), 5.46 (0.5H, ddt, J=15.4, 7.3, 1.5 Hz), 5.36–5.27 (1H, m), 5.05 (1H, ddd, J=10.5, 5.0, 1.7 Hz), 4.58 (1H, d, J=11.0 Hz), 4.54 (0.5H, d, J=12.5 Hz), 4.53 (0.5H, d, J=12.5 Hz), 4.38 (1H, d, J=12.5 Hz), 4.27 (1H, d, J=11.0 Hz), 4.17–4.10 (2H, m), 3.98–3.92 (1H, m), 3.91–3.81 (1H, m), 3.64 (1H, dd, J=13.2, 5.9 Hz), 3.62–3.50 (4H, m), 3.45 (1H, dd, J=10.3, 5.9 Hz), 3.24–3.20 (1H, m), 2.78–2.65 (2H, m), 2.34–2.29 (1H, m), 2.25–2.21 (0.5H, m), 2.17–2.12 (0.5H, m), 0.88 (4.5H, s), 0.87 (4.5H, s), 0.05 (1.5H, s), 0.04 (1.5H, s), 0.03 (3H, s); LR-EIMS, *m/z* 551 (5.0%, $[M-t\text{-Bu}]^+$), 215 (bp); HR-EIMS, calcd for $C_{32}H_{43}O_6Si$ $[M-t\text{-Bu}]^+$: 551.2829, found: 551.2819.

5.1.28. (2*S*,3*R*,2′*S*,3′*R*,5′*Z*,8′*S*,9′*R*)-4-{(8′-Benzyloxy-9′-benzyloxymethyl-2′-vinyl-2′,3′,4′,7′,8′,9′-hexahydrooxonin-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2,3-epoxypentanol (46). To a mixture of L-(+)-DET (12 μl, 0.0702 mmol) and pre-dried MS 4 Å (28.5 mg, 100 wt%) in CH_2Cl_2 (0.5 ml) was added $Ti(O^iPr)_4$ (18 μl, 0.0608 mmol) at −40 °C and the mixture was stirred for 30 min. Then, TBHP (0.13 ml, 3.7 M in toluene, 0.468 mmol) was added and the mixture was stirred at −40 °C for 30 min. To the mixture was added dropwise a solution of **45** (28.5 mg, 0.0468 mmol) in CH_2Cl_2 (1.0 ml). The reaction mixture was stirred at −40 °C for 30 min. Then, the reaction mixture was warmed to −25 °C and stirred for 26 h. DMS (34 μl, 0.463 mmol) was added at −25 °C and the mixture was stirred for 2 h until unreacted TBHP was consumed. To the mixture was added 10% DL-tartaric acid (36 μl) and NaF (15.3 mg) at −25 °C. The suspension was warmed to 24 °C and stirred for 24 h. The mixture was filtered through Celite and concentrated in vacuo. To the resultant residue was added Et_2O (4.0 ml) and 30% aqueous NaOH in brine (2.0 ml) at 0 °C 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 brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=5→3→1) to give **46** (29.2 mg, ~100%) as an inseparable 1:1 mixture of diastereomers at C2.[35] **46**: a colorless oil; IR (film), ν_{max} 3454, 3064, 3027, 2927, 2858, 1496, 1471, 1454, 1389, 1361, 1256, 1096, 1027, 930, 901, 837, 776, 737, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.31–7.19 (10H, m), 6.03–5.89 (1H, m), 5.84–5.74 (2H, m), 5.31–5.26 (1H, m), 5.06 (1H, ddd, *J*=10.3, 4.8, 1.8 Hz), 4.60–4.51 (3H, m), 4.41–4.25 (3H, m), 3.98–3.90 (2H, m), 3.66–3.43 (6H, m), 3.29–3.20 (1H, m), 3.18–3.05 (2H, m), 2.84–2.64 (2H, m), 2.34–2.20 (2H, m), 0.89 (4.5H, s), 0.87 (4.5H, s), 0.06 (3H, s), 0.03 (3H, s); LR-EIMS, *m/z* 624 (14.6%, $[M]^+$), 92 (bp); HR-EIMS, calcd for $C_{36}H_{52}O_7Si$ $[M]^+$: 624.3482, found: 624.3487.

5.1.29. (3*R*,2′*S*,3′*R*,5′*Z*,8′*S*,9′*R*)-4-{(8′-Benzyloxy-9′-benzyloxymethyl-2′-vinyl-2′,3′,4′,7′,8′,9′-hexahydrooxonin-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)pent-1-en-3-ol (47). To a solution of **46** (29.2 mg, 0.0468 mmol), PPh_3 (59.8 mg, 0.228 mmol), and imidazole (15.5 mg, 0.228 mmol) in THF (1.0 ml) was added I_2 (46.3 mg, 0.182 mmol) at 25 °C and the mixture was stirred for 35 min. Then, saturated aqueous $Na_2S_2O_3$ (8 ml) was added and the mixture 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 roughly purified by column chromatography (silica gel, hexane/EtOAc=10→5→3) to give the corresponding crude epoxy iodide, and it was used in the next reaction without further purification. To a solution of the above crude epoxy iodide in EtOH (0.80 ml) was added Zn (17.8 mg, 0.272 mmol) and saturated aqueous NH_4Cl (20 μl) at 25 °C and the mixture was stirred for 2.5 h. The mixture was filtered through Celite-anhydrous $MgSO_4$ and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=20→10→5) to give **47** (19.3 mg, 68% from **45**) as an inseparable 1:1 mixture of diastereomers at C2.[35] **47**: a colorless oil; IR (film), ν_{max} 3488, 3064, 3027, 2953, 2927, 2857, 1496, 1471, 1462, 1454, 1388, 1361, 1337, 1295, 1256, 1206, 1098, 1027, 1004, 925, 837, 814, 776, 735, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.32–7.19 (10H, m), 6.05–5.85 (2H, m), 5.83–5.71 (2H, m), 5.42–5.05 (4H, m), 4.59 (0.5H, d, *J*=11.4 Hz), 4.58 (0.5H, d, *J*=11.4 Hz), 4.53 (0.5H, d, *J*=12.5 Hz), 4.52 (0.5H, *J*=12.5 Hz), 4.40 (0.5H, d, *J*=12.5 Hz), 4.38 (0.5H, d, *J*=12.5 Hz), 4.28 (0.5H, d, *J*=11.4 Hz), 4.27 (0.5H, d, *J*=11.4 Hz), 4.26–4.19 (1H, m), 3.99–3.93 (1H, m), 3.70–3.38 (7H, m), 3.26–3.19 (1H, m), 2.80–2.64 (2H, m), 2.66 (0.5H, d, *J*=7.0 Hz), 2.61 (0.5H, d, *J*=5.5 Hz), 2.35–2.17 (2H, m), 0.88 (9H, s), 0.05 (3H, s), 0.04 (3H, s); LR-FDMS, *m/z* 608 (bp, $[M]^+$); HR-FDMS, calcd for $C_{36}H_{52}O_6Si$ $[M]^+$: 608.3533, found: 608.3512.

5.1.30. (3*R*,2′*S*,3′*R*,5′*Z*,8′*S*,9′*R*)-2-{(8′-Benzyloxy-9′-benzyloxymethyl-2′-vinyl-2′,3′,4′,7′,8′,9′-hexahydrooxonin-3′-yl)oxy}pent-4-en-1,3-diol (48). To a solution of **47** (19.3 mg, 0.0317 mmol) in THF (1.0 ml) was added TBAF (48 μl, 1.0 M in THF, 0.0476 mmol) at 25 °C and the mixture was stirred for 11.5 h. Then, the solvent was removed in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=3→1/2→EtOAc) to give **48** (10.7 mg, 68%) as an inseparable 1:1 mixture of diastereomers at C2.[35] **48**: a colorless oil; IR (film), ν_{max} 3357, 3087, 3063, 3028, 2911, 1498, 1453, 1425, 1422, 1402, 1361, 1337, 1294, 1257, 1207, 1146, 1096, 1070, 1027, 994, 930, 774, 735, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.34–7.20 (10H, m), 6.03–5.87 (1H, m), 5.86–5.69 (3H, m), 5.44–5.17 (4H, m), 4.59 (1H, d, *J*=11.4 Hz), 4.52 (1H, d, *J*=12.5 Hz), 4.41 (0.5H, d, *J*=12.5 Hz), 4.41 (0.5H, *J*=12.5 Hz), 4.33–4.23 (1H, m), 4.28 (1H, d, *J*=11.4 Hz), 3.95 (1H, brdqn, *J*=8.9, 3.0 Hz), 3.73–3.63 (2H, m), 3.60–3.46 (5H, m), 3.28–3.25 (1H, m), 2.85–2.75 (1H, m), 2.73–2.64 (1H, m), 2.54 (0.5H, d, *J*=3.3 Hz), 2.46 (0.5H, d, *J*=2.9 Hz), 2.31–2.22 (2H, m), 1.99–1.90 (1H, m); LR-EIMS, *m/z* 494 (7.7%, $[M]^+$), 91 (bp); HR-EIMS, calcd for $C_{30}H_{38}O_6$ $[M]^+$: 494.2668, found: 494.2666.

5.1.31. (2*R*,3*S*,5*Z*,8*R*,9*S*,4′*R*,5′*S*)-3-Benzyloxy-2-benzyloxymethyl-8-{(2′,2′-dimethyl-4′-vinyl-1′,3′-dioxan-5′-yl)oxy}-9-vinyl-2,3,4,7,8,9-hexahydrooxonin (49a) and (2*R*,3*S*,5*Z*,8*R*,9*S*,4′*R*,5′*R*)-3-benzyloxy-2-benzyloxymethyl-8-{(2′,2′-dimethyl-4′-vinyl-1′,3′-dioxan-5′-yl)-oxy}-9-vinyl-2,3,4,7,8,9-hexahydrooxonin (49b). To a solution of **48** (10.7 mg, 0.0216 mmol) and 2,2-dimethoxypropane (11 μl, 0.0864 mmol) in CH_2Cl_2 (0.5 ml) was added CSA (2.5 mg, 0.0108 mmol) at 24 °C and the mixture was stirred for 3 h. Then, to the mixture was added acetone (7.9 μl, 0.108 mmol) and stirred at 24 °C for 11.5 h. Then, saturated aqueous $NaHCO_3$ (3 ml) was added and the mixture 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/EtOAc=10→5) to give **49a** (5.8 mg, 50%) and **49b** (5.3 mg, 46%). **49a**: a colorless oil; $[\alpha]_D^{19}$ +39.4 (*c* 0.27, $CHCl_3$); IR (film), ν_{max} 3065, 3026, 2992, 2914, 2865, 1453, 1372, 1262, 1201, 1146, 1099, 1027, 696 cm^{-1}; ^1H NMR (300 MHz, C_6D_6), δ 7.29–7.15 (10H, m), 6.14–5.90 (2H, m), 5.89–5.81 (1H, m), 5.79–5.74 (1H, m), 5.52 (1H, dt, *J*=17.3, 1.7 Hz), 5.42 (1H, ddd, *J*=

17.3, 2.0, 1.1 Hz), 5.15 (1H, dt, J=10.6, 1.7 Hz), 5.06 (1H, ddd, J=10.3, 2.6, 1.1 Hz), 4.43 (1H, d, J=11.7 Hz), 4.37 (1H, d, J=11.7 Hz), 4.27 (1H, d, J=11.7 Hz), 4.22 (1H, d, J=11.7 Hz), 4.19–4.16 (1H, m), 3.99 (1H, dt, J=7.7, 3.1 Hz), 3.89 (1H, dd, J=11.2, 5.5 Hz), 3.68–3.63 (1H, m), 3.65 (1H, dd, J=11.2, 9.5 Hz), 3.58 (2H, d, J=2.9 Hz), 3.43–3.36 (2H, m), 3.23 (1H, td, J=9.5, 5.5 Hz), 2.77–2.71 (1H, m), 2.69–2.63 (1H, m), 2.29–2.22 (1H, m), 1.93–1.85 (1H, m), 1.49 (3H, s), 1.27 (3H, s); LR-FDMS, *m/z* 534 (bp, $[M]^+$); HR-FDMS, calcd for $C_{33}H_{42}O_6$ $[M]^+$: 534.2981, found: 534.2957. **49b**: a colorless oil; $[\alpha]_D^{19}$ −15.5 (*c* 0.27, $CHCl_3$); IR (film), ν_{max} 3065, 3012, 2921, 2866, 2803, 1453, 1373, 1365, 1335, 1272, 1241, 1198, 1183, 1152, 1120, 1095, 1063, 1044, 1028, 989, 978, 935, 915, 857, 773, 752, 697 cm^{-1}; ^1H NMR (300 MHz, C_6D_6), δ 7.28–7.15 (10H, m), 6.48 (1H, ddd, J=17.3, 10.6, 4.4 Hz), 6.12 (1H, ddd, J=17.3, 10.6, 6.2 Hz), 6.03–5.97 (2H, m), 5.75 (1H, ddd, J=17.3, 2.2, 1.5 Hz), 5.25 (1H, dt, J=17.3, 1.5 Hz), 5.18 (1H, ddd, J=10.6, 2.2, 1.5 Hz), 5.09 (1H, dt, J=10.6, 1.5 Hz), 4.44 (1H, d, J=11.7 Hz), 4.37 (1H, d, J=11.7 Hz), 4.23 (2H, d, J=11.7 Hz), 4.11–4.05 (2H, m), 3.80–3.76 (1H, m), 3.70 (1H, dd, J=12.8, 1.8 Hz), 3.61 (2H, d, J=2.6 Hz), 3.40 (1H, dd, J=12.8, 1.8 Hz), 3.35 (1H, dt, J=8.4, 2.6 Hz), 3.26 (1H, dt, J=8.8, 2.9 Hz), 2.86–2.70 (2H, m), 2.55 (1H, brqn, J=1.8 Hz), 2.36–2.28 (1H, m), 2.07–2.00 (1H, m), 1.52 (3H, s), 1.24 (3H, s); LR-FDMS, *m/z* 534 (bp, $[M]^+$), 519 (22.0, $[M-Me]^+$); HR-FDMS, calcd for $C_{33}H_{42}O_6$ $[M]^+$: 534.2981, found: 534.2964.

5.1.32. (1*R*,3*S*,8*R*,9*Z*,11*S*,13*R*,14*S*,16*Z*)-14-Benzyloxy-13-benzyloxymethyl-6,6-dimethyl-2,5,7,12-tetraoxatricyclo[9.7.0.0^{3,8}]octadeca-9,16-diene (50) and (1*S*,3*R*,5*Z*,7*R*,2′*S*,3′*Z*,6′*S*,7′*R*)-3-(6′-benzyloxy-7′-benzyloxymethyl-2′,5′,6′,7′-tetrahydrooxepin-2′-yl)-9,9-dimethyl-2,8,10-trioxabicyclo[5.4.0]undec-5-ene (51). To a solution of **49a** (5.8 mg, 0.0108 mmol) in degassed CH_2Cl_2 (3.0 ml) was added a solution of $(Cy_3P)_2Cl_2Ru$=CHPh (0.9 mg, 1.08 μmol) in degassed CH_2Cl_2 (1.0 ml). The resultant solution was stirred at 24 °C for 3 h. Then, extra $(Cy_3P)_2Cl_2Ru$=CHPh (1.3 mg, 1.62 μmol) in degassed CH_2Cl_2 (2.0 ml) was added, and the stirring was continued for further 12 h. After that, the mixture was stirred for 2 h under O_2 atmosphere, and the solvent was removed in vacuo. The resultant residue was purified by column chromatography (silica gel, benzene/EtOAc=40→10) to give the 1:1:0.5 mixture of **49a**, **50** and **51**. In order to consume **49a** completely, the process was repeated as follows. To a solution of the above mixture in degassed CH_2Cl_2 (2.0 ml) was added a solution of $(Cy_3P)_2Cl_2Ru$=CHPh (0.60 ml, 1.64mM in degassed CH_2Cl_2, 0.984 μmol). The resultant solution was stirred at 26 °C for 8 h. Then, extra $(Cy_3P)_2Cl_2Ru$=CHPh (0.80 ml, 1.21 mM in degassed CH_2Cl_2, 0.968 μmol) was added, and the stirring was continued for further 16 h. After that, the mixture was stirred for 2 h under O_2 atmosphere, and the solvent was removed in vacuo. The resultant residue was purified by column chromatography (silica gel, benzene/EtOAc=50→40→10) to give **50** (3.7 mg, 67%, after 2 cycles) and **51** (1.3 mg, 24%, after 2 cycles). **50**: a colorless oil; $[\alpha]_D^{23}$ +13.0 (*c* 0.20, $CHCl_3$); IR (film), ν_{max} 3087, 3063, 3027, 2991, 2922, 2855, 1496, 1454, 1372, 1336, 1311, 1292, 1267, 1221, 1200, 1100, 1027, 988, 945, 893, 866, 779, 767, 735, 697, 680 cm^{-1}; ^1H NMR (300 MHz, C_5D_5N), δ 7.46–7.27 (10H, m), 6.29–6.23 (1H, m), 6.01–5.86 (2H, m), 5.77–5.63 (1H, m), 4.69 (1H, d, J=11.5 Hz), 4.53–4.49 (3H, m), 4.42 (1H, d, J=11.5 Hz), 4.10–4.07 (1H, m), 3.96 (1H, dd, J=11.0, 5.5 Hz), 3.84–3.68 (4H, m), 3.67–3.61 (1H, m), 3.58–3.52 (1H, m), 3.40 (1H, td, J=9.5, 5.5 Hz), 3.00–2.90 (1H, m), 2.76–2.67 (1H, m), 2.44–2.36 (1H, m), 2.19–2.09 (1H, m), 1.47 (3H, s), 1.44 (3H, s); ^1H NMR (300 MHz, $(CD_3)_2C$=O), δ 7.34–7.24 (10H, m), 6.00 (1H, dt, J=12.4, 2.6 Hz), 5.78–5.67 (2H, m), 5.40 (1H, dt, J=12.4, 2.6 Hz), 4.68 (1H, d, J=11.6 Hz), 4.49 (2H, s), 4.41 (1H, d, J=11.6 Hz), 4.30 (1H, brdqn, J=9.4, 2.6 Hz), 3.88–3.83 (1H, m), 3.72 (1H, dd, J=11.3, 5.7 Hz), 3.70–3.61 (3H, m), 3.58–3.50 (1H, m), 3.55 (1H, dd, J=11.3, 9.4 Hz), 3.29 (1H, ddd, J=8.5, 5.7, 2.6 Hz), 3.18 (1H, td, J=9.4, 5.7 Hz), 2.89–2.78 (1H, m), 2.66–2.58 (1H, m), 2.39–2.32 (1H, m), 2.07–1.98 (1H, m), 1.42 (3H, s), 1.28 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$), δ 138.4 (C), 138.1 (C), 136.5 (CH), 131.2 (CH), 128.44 (CH×2), 128.42 (CH×2), 128.3 (CH×2), 128.2 (CH×2), 127.93 (CH), 127.91 (CH), 127.8 (CH), 127.7 (CH), 98.3 (C), 85.8 (CH), 85.5 (CH), 83.3 (CH), 77.7 (CH), 75.0 (CH), 73.4 (CH_2), 73.3 (CH), 71.6 (CH_2), 69.6 (CH_2), 62.9 (CH_2), 31.8 (CH_2), 29.8 (CH_2), 29.0 (CH_3), 18.9 (CH_3); LR-FDMS, *m/z* 506 (22.4%, $[M]^+$), 491 (47.9%, $[M-Me]^+$), 91 (bp); HR-FDMS, calcd for $C_{31}H_{38}O_6$ $[M]^+$: 506.2669, found: 506.2650. **51**: a colorless oil; $[\alpha]_D^{24}$ +3.5 (*c* 0.065, $CHCl_3$); IR (film), ν_{max} 3063, 3029, 2991, 2922, 2854, 1496, 1495, 1454, 1434, 1371, 1301, 1267, 1199, 1161, 1102, 1028, 737, 697 cm^{-1}; ^1H NMR (300 MHz, C_6D_6), δ 7.25–7.05 (10H, m), 5.95 (1H, ddd, J=11.4, 2.8, 1.7 Hz), 5.79–5.74 (1H, m), 5.71–5.61 (2H, m), 4.54–4.47 (2H, m), 4.34 (1H, d, J=11.7 Hz), 4.26 (1H, d, J=11.7 Hz), 4.22 (1H, d, J=12.1 Hz), 4.12–3.99 (4H, m), 3.96 (1H, dd, J=11.4, 5.5 Hz), 3.70 (1H, dd, J=11.4, 9.4 Hz), 3.62–3.51 (3H, m), 2.76–2.67 (1H, m), 2.52–2.41 (3H, m), 1.48 (3H, s), 1.26 (3H, s); LR-FDMS, *m/z* 507 (64.2%, $[M+H]^+$), 506 (bp, $[M]^+$); HR-FDMS, calcd for $C_{31}H_{38}O_6$ $[M]^+$: 506.2669, found: 506.2657.

5.1.33. 1-(4-Methoxybenzyloxy)-2-propyne (60). To a solution of propargyl alcohol **59** (1.50 ml, 25.8 mmol) in THF (70 ml) was added NaH (1.86 g, 60 wt% in oil, 46.4 mmol) at 0 °C and the mixture was stirred for 15 min. Then, *p*-methoxy benzyl chloride (PMBCl) (5.20 ml, 38.7 mmol) and TBAI (1.24 g, 3.35 mmol) was added at 0 °C. The reaction mixture was warmed to 24 °C and stirred for 16 h. After the mixture was cooled to 0 °C and diluted with Et_2O (30 ml), saturated aqueous NH_4Cl (50 ml) was added and the mixture was extracted with Et_2O (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/Et_2O=15→10→5) to give **60** (4.50 g, 99%). **60**: a colorless oil; IR (film), ν_{max} 3289, 3001, 2937, 2907, 2837, 2754, 2115, 1612, 1586, 1513, 1464, 1441, 1422, 1387, 1352, 1302, 1249, 1174, 1078, 1034, 927, 848, 819, 759, 647 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.30–7.26 (2H, m), 6.90–6.87 (2H, m), 4.54 (2H, s), 4.14 (2H, d, J=2.4 Hz), 3.81 (3H, s), 2.45 (1H, t, J=2.4 Hz); LR-EIMS, *m/z* 176 (61.6, $[M]^+$), 121 (bp); HR-EIMS, calcd for $C_{11}H_{12}O_2$ $[M]^+$: 176.0837, found: 176.0822.

5.1.34. Ethyl 4-(4-methoxybenzyloxy)-2-butynoate (61). To a solution of **60** (2.85 g, 16.2 mmol) in THF (40 ml) was

added *n*-BuLi (15.4 ml, 1.58 M in *n*-hexane, 24.3 mmol) at −78 °C and the mixture was stirred for 10 min. Then, ethylchloroformate (2.30 ml, 24.3 mmol) was added at −78 °C and the mixture was stirred for 1 h. The reaction mixture was warmed to 0 °C and stirred for 15 min. After the mixture was diluted with Et_2O (20 ml), H_2O (30 ml) was added and the mixture was extracted with Et_2O (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/Et_2O=20→15→10→5→3) to give **61** (3.18 g, 79%). **61**: a pale yellow oil; IR (film), ν_{max} 2983, 2939, 2907, 2869, 2838, 2235, 1713, 1613, 1586, 1513, 1465, 1443, 1388, 1366, 1302, 1248, 1174, 1091, 1055, 1034, 820, 751, 626 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.29–7.26 (2H, m), 6.90–6.87 (2H, m), 4.54 (2H, s), 4.25 (2H, q, J=7.2 Hz), 4.25 (2H, s), 3.81 (3H, s), 1.32 (3H, t, J=7.2 Hz); LR-EIMS, *m/z* 248 (37.4, $[M]^+$), 121 (bp); HR-EIMS, calcd for $C_{14}H_{16}O_4$ $[M]^+$: 248.1048, found: 248.1051.

5.1.35. 4-(4-Methoxybenzyloxy)-2-butynal (62) and 4-(4-methoxybenzyloxy)-2-butynol (63). To a solution of **61** (2.96 g, 11.9 mmol) in CH_2Cl_2 (35 ml) was added DIBAH (25.6 ml, 0.93 M in *n*-hexane, 23.8 mmol) at −78 °C and the mixture was stirred for 30 min. Then, extra DIBAH (6.40 ml, 0.93 M in *n*-hexane, 5.95 mmol) was added at −78 °C and the mixture was stirred for 45 min. Then, saturated aqueous potassium sodium tartrate (50 ml) was added and the mixture was stirred at 23 °C for 14 h. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (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/EtOAc=3→1→1/2) to give **63** (635.5 mg, 26%) along with **62** (1.80 g, 74%). **62**: a yellow oil; IR (film), ν_{max} 3004, 2973, 2838, 2248, 2182, 1728, 1671, 1612, 1586, 1578, 1513, 1465, 1442, 1428, 1388, 1349, 1302, 1250, 1175, 1160, 1112, 1075, 1032, 817 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 9.25 (1H, d, J=0.55 Hz), 7.29–7.26 (2H, m), 6.92–6.88 (2H, m), 4.56 (2H, s), 4.32 (2H, d, J=0.55 Hz), 3.81 (3H, s); LR-EIMS, *m/z* 204 (75.5%, $[M]^+$), 121 (bp); HR-EIMS, calcd for $C_{12}H_{12}O_3$ $[M]^+$: 204.0786 found: 204.0747. **63**: a yellow oil; IR (film), ν_{max} 3629, 3394, 3000, 2935, 2859, 1612, 1586, 1513, 1464, 1442, 1422, 1386, 1351, 1302, 1248, 1175, 1122, 1072, 1031, 942, 920, 819, 756, 709, 603 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.30–7.26 (2H, m), 6.91–6.87 (2H, m), 4.53 (2H, s), 4.33 (2H, dt, J=6.2, 1.8 Hz), 4.18 (2H, t, J=1.8 Hz), 3.81 (3H, s), 1.62 (1H, t, J=6.2 Hz); LR-EIMS, *m/z* 206 (21.5%, $[M]^+$), 121 (bp); HR-EIMS, calcd for $C_{12}H_{14}O_3$ $[M]^+$: 206.0943 found: 206.0904.

5.1.36. 4-(4-Methoxybenzyloxy)-2-butynol (63). To a solution of **62** (1.80 g, 8.81 mmol) in CH_2Cl_2 (25 ml) was added DIBAH (23.5 ml, 0.93 M in *n*-hexane, 21.9 mmol) at −78 °C and the mixture was stirred for 10 min. Then, saturated aqueous potassium sodium tartrate (50 ml) was added and the mixture was stirred at 24 °C for 10 h. The layers were separated 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/EtOAc=2→1/2) to give **63** (1.83 g, ~100%).

5.1.37. (2*E*)-4-(4-Methoxybenzyloxy)-2-butenol (64). To a mixture of LAH (2.05 g, 43.3 mmol) in THF (25 ml) was added dropwise a solution of **63** (2.23 g, 10.8 mmol) in THF (15 ml) at −78 °C and the mixture was stirred for 13 min. Then, the reaction mixture was warmed to −20 °C and stirred for 26 h. The mixture was warmed to 0 °C and diluted with Et_2O (30 ml). Then, H_2O (2.1 ml), 4N aqueous NaOH (2.1 ml) and H_2O (6.3 ml) were added in turn. The resultant suspension was filtered with Celite-anhydrous $MgSO_4$ and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=3→2→1/2) to give **64** (1.43 g, 64%) along with **63** (0.54 g, 24%). **64**: a colorless oil; IR (film), ν_{max} 3583, 3377, 3003, 2933, 2854, 1612, 1586, 1513, 1463, 1442, 1421, 1404, 1386, 1360, 1302, 1247, 1174, 1093, 1033, 1009, 972, 847, 819, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.28–7.25 (2H, m), 6.89–6.86 (2H, m), 5.96–5.79 (2H, m), 4.46 (2H, s), 4.22–4.16 (2H, m), 4.01 (2H, d, J=5.1 Hz), 3.81 (3H, s); LR-EIMS, *m/z* 208 (21.2%, $[M]^+$), 121 (bp); HR-EIMS, calcd for $C_{12}H_{16}O_3$ $[M]^+$: 208.1099 found: 208.1106.

5.1.38. (2*R*,3*R*)-2,3-Epoxy-4-(4-methoxybenzyloxy)-1-butanol (65). To a mixture of D-(−)-DET (0.22 ml, 1.29 mmol) and pre-dried MS 4 Å (1.35 g, 100 wt%) in CH_2Cl_2 (15 ml) was added $Ti(O^iPr)_4$ (0.29 ml, 0.97 mmol) at −40 °C and the mixture was stirred for 30 min. Then, TBHP (4.6 ml, 3.5 M in toluene, 16.2 mmol) was added and the mixture was stirred at −40 °C for 30 min. To the mixture was added dropwise a solution of **64** (1.35 g, 6.47 mmol) in CH_2Cl_2 (15 ml). The reaction mixture was stirred at −40 °C for 30 min, warmed to −20 °C and stirred for 2.5 d. Then, DMS (1.2 ml, 16.2 mmol) was added at −20 °C and the mixture was stirred for 2 h until unreacted TBHP was consumed. To the mixture was added 10% DL-tartaric acid (0.58 ml) and NaF (244.4 mg) at −25 °C. The suspension was warmed to 23 °C and stirred for 24 h. The mixture was filtered through Celite and concentrated in vacuo. To the resultant residue was added Et_2O (30 ml) and 30% aqueous NaOH in brine (10 ml) at 0 °C and the mixture was stirred for 1 h. The layers were separated 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/EtOAc=3→2→1→1/2→1/4) to give **65** (1.03 g, 71%, 93% ee). **65**: a colorless solid (EtOAc), mp 62.0–63.0 °C; $[\alpha]_D^{25}$ +13.9 (*c* 1.01, $CHCl_3$); IR (KBr), ν_{max} 3442, 3020, 2967, 2937, 2869, 1613, 1585, 1514, 1480, 1459, 1444, 1424, 1369, 1325, 1303, 1250, 1212, 1177, 1145, 1090, 1061, 1030, 1005, 987, 974, 932, 866, 850, 816, 759, 728, 709, 642, 636 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.29–7.24 (2H, m), 6.91–6.86 (2H, m), 4.53 (1H, d, J=11.6 Hz), 4.48 (1H, d, J=11.6 Hz), 3.94 (1H, ddd, J=12.7, 5.3, 2.6 Hz), 3.81 (3H, s), 3.73 (1H, dt, J=11.5, 2.6 Hz), 3.65 (1H, ddd, J=12.7, 7.5, 4.0 Hz), 3.50 (1H, dt, J=11.5, 5.4 Hz), 3.22 (1H, dt, J=5.4, 2.6 Hz), 3.09 (1H, dt, J=4.0, 2.6 Hz), 1.71 (1H, brdd, J=7.5, 5.3 Hz); LR-EIMS, *m/z* 224 (20.6%, $[M]^+$), 121 (bp);

HR-EIMS, calcd for $C_{12}H_{16}O_4$ $[M]^+$: 224.1048, found: 224.1044.

5.1.39. (2*R*,3*R*)-2,3-Epoxy-1-(4-methoxybenzyloxy)-4-pentene (66). To a solution of **65** (78.0 mg, 0.348 mmol) in CH_2Cl_2–NEt_3–DMSO (6:1.4:1, v/v/v, 3.36 ml) was added SO_3·pyridine (553.9 mg, 3.48 mmol) at 0 °C. The mixture was warmed to 24 °C and stirred for 1 h. After the mixture was diluted with Et_2O (5 ml), the mixture was washed with H_2O (2×10 ml). The layers were separated and the aqueous layer was extracted with Et_2O (3×8 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The resultant crude aldehyde was used immediately in the next reaction without purification. To a stirred suspension of $Ph_3P^+CH_3Br^-$ (621.6 mg, 1.74 mmol) in THF (4.0 ml) was added NaHMDS (1.64 ml, 1.0 M in THF, 1.64 mmol) and the mixture was stirred at 24 °C. After 1 h, the resulting yellow suspension was allowed to stand at −78 °C. To the mixture was added dropwise a solution of the above crude aldehyde in THF (2.0 ml) at −78 °C and the mixture was stirred for 2 h. Then, the reaction mixture was warmed to 24 °C and stirred for 17 h. After the mixture was diluted with hexane (10 ml) and Et_2O (5 ml), saturated aqueous NH_4Cl (10 ml) was added and the mixture was extracted with Et_2O (3×10 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/EtOAc=20→10) to give **66** (59.8 mg, 78% from **65**). **66**: a colorless oil; $[\alpha]_D^{24}$ +10.0 (*c* 0.68, $CHCl_3$); IR (film), ν_{max} 3086, 3062, 2995, 2934, 2909, 2855, 2836, 1642, 1612, 1586, 1512, 1464, 1442, 1422, 1405, 1387, 1359, 1302, 1247, 1209, 1173, 1099, 1058, 1033, 987, 928, 877, 849, 820, 757, 681 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.27 (2H, d, J=8.8 Hz), 6.88 (2H, d, J=8.8 Hz), 5.59 (1H, ddd, J=17.3, 9.8, 7.2 Hz), 5.48 (1H, dd, J=17.3, 2.0 Hz), 5.29 (1H, dd, J=9.8, 2.0 Hz), 4.53 (1H, d, J=11.6 Hz), 4.48 (1H, d, J=11.6 Hz), 3.80 (3H, s), 3.72 (1H, dd, J=11.6, 3.3 Hz), 3.49 (1H, dd, J=11.6, 5.3 Hz), 3.26 (1H, dd, J=7.2, 2.2 Hz), 3.09 (1H, ddd, J=5.3, 3.3, 2.2 Hz); LR-EIMS, *m*/*z* 220 (4.2%, $[M]^+$), 121 (bp); HR-EIMS, calcd for $C_{13}H_{16}O_3$ $[M]^+$: 220.1099, found: 220.1082.

5.1.40. (2*S*)-1-(4-Methoxybenzyloxy)pent-4-en-2-ol (67). To a solution of $Pd(PPh_3)_4$ (6.5 mg, 5.63 μmol) in CH_2Cl_2 (0.5 ml) was added Bu_3SnH (16.5 μl, 0.0619 mmol) at 24 °C. To the mixture was added dropwise a solution of **66** (12.4 mg, 0.0563 mmol) in CH_2Cl_2 (1.0 ml) at 24 °C and the mixture was stirred for 20 min. The solvent was removed in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=10→3) to give **67** (11.9 mg, 95%). **67**: a colorless oil; $[\alpha]_D^{26}$ +2.8 (*c* 0.76, $CHCl_3$); IR (film), ν_{max} 3447, 3074, 3001, 2910, 2859, 1641, 1612, 1586, 1513, 1465, 1442, 1419, 1363, 1302, 1249, 1209, 1173, 1101, 1035, 997, 916, 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.26 (2H, d, J=8.7 Hz), 6.88 (2H, d, J=8.7 Hz), 5.82 (1H, ddt, J=17.2, 10.1, 7.1 Hz), 5.15–5.07 (2H, m), 4.49 (2H, s), 3.90–3.82 (1H, m), 3.81 (3H, s), 3.49 (1H, dd, J=9.5, 3.5 Hz), 3.34 (1H, dd, J=9.5, 7.3 Hz), 2.25 (2H, t, J=7.1 Hz); LR-EIMS, *m*/*z* 222 (7.0%, $[M]^+$), 121 (bp); HR-EIMS, calcd for $C_{13}H_{18}O_3$ $[M]^+$: 222.1256, found: 222.1250.

5.1.41. (2*S*,3*R*,4*Z*,6*S*,7*R*,1′*E*)-3-Benzyloxy-2-benzyloxymethyl-6-(4-methoxybenzyloxy)-7-(2′-methoxyvinyl)-2,3,6,7-tetrahydrooxepin and (2*S*,3*R*,4*Z*,6*S*,7*R*,1′*Z*)-3-benzyloxy-2-benzyloxymethyl-6-(4-methoxybenzyloxy)-7-(2′-methoxyvinyl)-2,3,6,7-tetrahydrooxepin (73). To oxalyl chloride (0.19 ml, 2.18 mmol) in CH_2Cl_2 (6.0 ml) was added DMSO (0.28 ml, 3.91 mmol) in CH_2Cl_2 (3.0 ml) dropwise at −78 °C and the mixture was stirred for 10 min. Then, **72** (383.4 mg, 0.782 mmol) in CH_2Cl_2 (6.0 ml) was added dropwise at −78 °C and the mixture was stirred for 15 min. Et_3N (1.10 ml, 7.82 mmol) was added dropwise at −78 °C. The mixture was warmed to −18 °C and stirred for 10 min. Then, saturated aqueous $NaHCO_3$ (10 ml) was added and the mixture was extracted with EtOAc (3×10 ml). The combined organic layers were washed with 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 stirred suspension of $Ph_3P^+CH_2OMeCl^-$ (1.37 g, 3.99 mmol) in THF (8.0 ml) was added NaHMDS (3.8 ml, 1.0 M in THF, 3.83 mmol) and the mixture was stirred at 0 °C. After 30 min, the resulting red solution was allowed to stand at −78 °C. To the mixture was added dropwise a solution of the above crude aldehyde in THF (5.0 ml) at −78 °C and the mixture was stirred for 1.5 h. Then, the reaction mixture was warmed to 24 °C and stirred for 17.5 h. Et_2O (10 ml) and brine (10 ml) were added and the mixture was extracted with Et_2O (3×10 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/EtOAc=15→10→5→3) to give **73** (282.6 mg, 70% from **72**, *E*/*Z*=2:1 from ^1H NMR). **73**: a colorless oil; IR (film), ν_{max} 3062, 3029, 2862, 1657, 1612, 1586, 1513, 1496, 1454, 1365, 1301, 1247, 1210, 1172, 1089, 1029, 938, 820, 736, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.36–7.22 (12H, m), 6.90–6.79 (2H, m), 6.61 (0.67H, d, J=12.8 Hz), 6.04 (0.33H, dd, J=6.2, 0.7 Hz), 5.87 (2H, s), 4.84 (0.67H, dd, J=12.8, 7.3 Hz), 4.71–4.47 (4.33H, m), 4.59 (1H, d, J=11.2 Hz), 4.43 (1H, d, J=11.2 Hz), 4.22–4.17 (1H, m), 4.08–4.03 (1H, m), 3.99–3.91 (1H, m), 3.87 (1H, ddd, J=8.8, 5.1, 3.7 Hz), 3.79 (3H, s), 3.68–3.59 (2H, m), 3.58 (1H, s), 3.53 (2H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 159.3 (C×0.67), 159.1 (C×0.33), 150.3 (CH×0.67), 148.8 (CH×0.33), 138.6 (C×0.33), 138.4 (C×0.67), 138.2 (C×0.33), 138.0 (C×0.67), 132.0 (CH×0.33), 131.9 (CH×0.67), 131.7 (CH×0.33), 131.6 (CH×0.67), 130.5 (C×0.33), 130.1 (C×0.67), 129.6 (CH×0.66), 129.5 (CH×1.34), 128.33 (CH×1.34), 128.29 (CH×0.66), 128.27 (CH×1.34), 128.21 (CH×0.66), 127.82 (CH×0.66), 127.78 (CH×1.34), 127.65 (CH×1.34), 127.55 (CH×0.66), 127.48 (CH×1.34), 127.37 (CH×0.66), 113.8 (CH×1.34), 113.6 (CH×0.66), 106.2 (CH×0.33), 102.5 (CH×0.67), 81.7 (CH×0.67), 81.6 (CH×0.33), 81.4 (CH_3×0.67), 80.3 (CH×0.67), 79.6 (CH×0.33), 77.1 (CH), 76.7 (CH), 76.5 (CH_3×0.33), 73.3 (CH_2×0.67), 73.2 (CH_2×0.33), 71.3 (CH_2), 71.1 (CH_2×0.33), 71.0 (CH_2×0.67), 70.8 (CH_2×0.67), 70.5 (CH_2×0.33), 55.8 (CH_3×0.33), 55.2 (CH_3×0.67); LR-EIMS, *m*/*z* 516 (6.0%, $[M]^+$), 395

(bp); HR-EIMS, calcd for $C_{32}H_{36}O_6$ $[M]^+$: 516.2511, found: 516.2504.

5.1.42. (2*R*,3*S*,4*Z*,6*R*,7*S*)-{6-Benzyloxy-7-benzyloxymethyl-3-(4-methoxybenzyloxy)-2,3,6,7-tetrahydrooxepin-2-yl}ethanal (74). To a solution of **73** (282.6 mg, 0.547 mmol) in THF–H_2O (10:1, v/v, 11.0 ml) was added $Hg(OAc)_2$ (523.0 mg, 1.64 mmol) at 24 °C and the mixture was stirred for 1.5 h. Then, TBAI (1.82 g, 4.92 mmol) was added at 24 °C and the mixture was stirred for 1 h. Then, saturated aqueous NH_4Cl (20 ml) was added and the mixture was extracted with Et_2O (3×10 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/EtOAc=5→3) to give **74** (262.1 mg, 95%). **74**: a colorless oil; $[\alpha]_D^{26}$ +22.5 (*c* 1.35, $CHCl_3$); IR (film), ν_{max} 3063, 3030, 2862, 2735, 1725, 1612, 1586, 1513, 1496, 1454, 1372, 1301, 1248, 1174, 1087, 1029, 821, 737, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 9.73 (1H, t, *J*=2.0 Hz), 7.36–6.85 (14H, m), 5.92 (1H, d, *J*=14.5 Hz), 5.86 (1H, d, *J*=14.5 Hz), 4.63–4.34 (6H, m), 4.21 (1H, d, *J*=8.8 Hz), 4.11 (1H, td, *J*=8.8, 4.0 Hz), 3.92 (1H, d, *J*=8.8 Hz), 3.80 (3H, s), 3.74 (1H, dt, *J*=8.8, 3.5 Hz), 3.61 (2H, d, *J*=3.5 Hz), 2.79 (1H, ddd, *J*=16.5, 4.0, 2.0 Hz), 2.54 (1H, ddd, *J*=16.5, 8.8, 2.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), δ 200.6 (CH), 159.3 (C), 138.0 (C), 137.7 (C), 132.3 (CH), 131.1 (CH), 129.6 (CH×2), 129.2 (C), 128.2 (CH×2), 128.1 (CH×2), 127.6 (CH×2), 127.5 (CH×2), 127.4 (CH×2), 113.7 (CH×2), 82.8 (CH), 79.0 (CH), 78.6 (CH), 76.7 (CH), 73.2 (CH_2), 71.4 (CH_2), 70.7 (CH_2), 70.3 (CH_2), 55.0 (CH_3), 47.4 (CH_2); LR-EIMS, *m*/*z* 502 (6.2%, $[M]^+$), 258 (bp); HR-EIMS, calcd for $C_{31}H_{34}O_6$ $[M]^+$: 502.2355, found: 502.2353.

5.1.43. (2*R*,3*S*,4*Z*,6*R*,7*S*)-2-Allyl-6-benzyloxy-7-benzyloxymethyl-3-(4-methoxybenzyloxy)-2,3,6,7-tetrahydrooxepin (75). To a stirred suspension of $Ph_3P^+CH_3Br^-$ (51.8 mg, 0.145 mmol) in THF (0.5 ml) was added NaHMDS (0.13 ml, 1.0 M in THF, 0.132 mmol) and the mixture was stirred at 20 °C. After 1 h, the resulting yellow suspension was allowed to stand at −78 °C. To the mixture was added dropwise a solution of **74** (20.8 mg, 0.0414 mmol) in THF (1.5 ml) at −78 °C and the mixture was stirred for 2 h. Then, the reaction mixture was warmed to 22 °C and stirred for 18 h. After the mixture was diluted with hexane (5 ml) and Et_2O (3 ml), saturated aqueous NH_4Cl (5 ml) was added. 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/EtOAc=10) to give **75** (20.6 mg, 100%). **75**: a colorless oil; $[\alpha]_D^{25}$ +12.7 (*c* 1.0, $CHCl_3$); IR (film), ν_{max} 3064, 3029, 2864, 1641, 1612, 1586, 1513, 1496, 1454, 1382, 1300, 1248, 1209, 1173, 1074, 1035, 914, 821, 735, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.34–6.85 (14H, m), 5.93 (1H, ddt, *J*=17.1, 10.3, 6.8 Hz), 5.86 (2H, s), 5.07 (1H, d, *J*=17.1 Hz), 5.02 (1H, d, *J*=10.3 Hz), 4.62–4.38 (6H, m), 4.19 (1H, d, *J*=8.8 Hz), 3.91 (1H, d, *J*=8.4 Hz), 3.80 (3H, s), 3.71 (1H, ddd, *J*=8.8, 4.6, 2.0 Hz), 3.64 (2H, m), 3.60 (1H, td, *J*=8.4, 3.1 Hz), 2.54 (1H, ddd, *J*=14.7, 6.8, 3.1 Hz), 2.21 (1H, dt, *J*=14.7, 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), δ 159.2 (C), 138.3 (C), 137.9 (C), 135.2 (CH), 131.6 (CH), 131.5 (CH), 129.9 (C), 129.4 (CH×2), 128.2 (CH×2), 128.1 (CH×2), 127.7 (CH×2), 127.5 (CH×2), 127.3 (CH×2), 116.6 (CH_2), 113.7 (CH×2), 83.1 (CH), 82.3 (CH), 79.4 (CH), 76.9 (CH), 73.2 (CH_2), 71.2 (CH_2), 70.7 (CH_2), 70.5 (CH_2), 55.1 (CH_3), 37.4 (CH_2); LR-EIMS, *m*/*z* 500 (5.0%, $[M]^+$), 122 (bp); HR-EIMS, calcd for $C_{32}H_{36}O_5$ $[M]^+$: 500.2562, found: 500.2572.

5.1.44. (2*R*,3*S*,4*Z*,6*R*,7*S*)-2-Allyl-6-benzyloxy-7-benzyloxymethyl-2,3,6,7-tetrahydrooxepin-3-ol (58). To a solution of **75** (69.6 mg, 0.139 mmol) in CH_2Cl_2—pH 7 buffer (4:1, v/v, 2.0 ml) was added DDQ (47.3 mg, 0.208 mmol) at 0 °C and the mixture was stirred for 2 h. Then, to the mixture was added DDQ (31.6 mg, 0.139 mmol) at 0 °C and the stirring was continued for further 1 h. After the mixture was diluted with Et_2O (3 ml), saturated aqueous $NaHCO_3$ (10 ml) was added. The mixture was extracted with Et_2O (2×5 ml) and EtOAc (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/EtOAc=5) to give **58** (48.5 mg, 92%). **58**: a colorless oil; $[\alpha]_D^{25}$ −33.7 (*c* 0.90, $CHCl_3$); IR (film), ν_{max} 3426, 3065, 3029, 2866, 1818, 1769, 1641, 1496, 1454, 1365, 1208, 1097, 913, 736, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.35–7.24 (10H, m), 5.98 (1H, ddt, *J*=17.1, 10.1, 7.0 Hz), 5.81 (1H, dt, *J*=12.8, 2.2 Hz), 5.74 (1H, dt, *J*=12.8, 2.0 Hz), 5.16–5.09 (1H, m), 5.08–5.04 (1H, m), 4.61 (1H, d, *J*=11.4 Hz), 4.60 (1H, d, *J*=12.3 Hz), 4.55 (1H, d, *J*=12.3 Hz), 4.46 (1H, d, *J*=11.4 Hz), 4.18 (1H, ddd, *J*=8.0, 4.2, 2.0 Hz), 4.15–4.09 (1H, m), 3.74–3.68 (1H, m), 3.62 (2H, d, *J*=3.3 Hz), 3.49 (1H, td, *J*=8.5, 3.5 Hz), 2.60–2.51 (1H, m), 2.37–2.26 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$), δ 138.2 (C), 137.7 (C), 135.1 (CH), 134.1 (CH), 130.0 (CH), 128.3 (CH×2), 128.2 (CH×2), 127.8 (CH×2), 127.6 (CH), 127.5 (CH×2), 127.4 (CH), 116.7 (CH_2), 84.2 (CH), 82.7 (CH), 76.8 (CH), 73.3 (CH), 73.2 (CH_2), 71.4 (CH_2), 70.4 (CH_2), 37.7 (CH_2); LR-FDMS, *m*/*z* 381 (bp, $[M+H]^+$), 380 (21.8%, $[M]^+$); HR-FDMS, calcd for $C_{24}H_{29}O_4$ $[M+H]^+$: 381.2066, found: 381.2081.

5.1.45. Methyl (2*E*,2′*R*,3′*S*,4′*Z*,6′*R*,7′*S*)-3-{(2′-allyl-6′-benzyloxy-7′-benzyloxymethyl-2′,3′,6′,7′-tetrahydrooxepin-3′-yl)oxy}-4-(*tert*-butyldimethylsilyloxy)-2-butenoate (57). A solution of butynoate **20** (462.4 mg, 2.03 mmol) in CH_2Cl_2 (6.0 ml) was slowly added dropwise to a solution of **58** (256.8 mg, 0.675 mmol) and PMe_3 (1.0 ml, 1.0 M in THF, 1.01 mmol) in CH_2Cl_2 (7.0 ml) at 0 °C by means of a syringe. The mixture was warmed to 24 °C and stirred for 30 min. The mixture was cooled to 0 °C and diluted with hexane (10 ml) and Et_2O (10 ml). Then, saturated aqueous NH_4Cl (10 ml) was added and the mixture was extracted with Et_2O (3×10 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/EtOAc=30→20→10) to give **57** (401.6 mg, 98%). **57**: a colorless oil; $[\alpha]_D^{21}$ +17.3 (*c* 0.90, $CHCl_3$); IR (film), ν_{max} 3065, 3030, 2953, 2929, 2885, 2857, 1716, 1629, 1497, 1472, 1462, 1454, 1435, 1389, 1361, 1346, 1313, 1288, 1253, 1207, 1188, 1141, 1051, 1005, 939, 916, 837, 779, 735, 697, 674 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ

7.36–7.23 (10H, m), 5.99–5.85 (1H, m), 5.91 (1H, dt, J= 13.0, 2.4 Hz), 5.59 (1H, dt, J=13.0, 2.4 Hz), 5.11–5.02 (2H, m), 4.97 (1H, d, J=13.6 Hz), 4.95 (1H, s), 4.62 (1H, d, J= 11.2 Hz), 4.61 (1H, d, J=13.6 Hz), 4.60 (1H, d, J= 12.5 Hz), 4.56 (1H, d, J=12.5 Hz), 4.54–4.51 (1H, m), 4.46 (1H, d, J=11.2 Hz), 4.28–4.23 (1H, m), 3.75–3.65 (5H, m), 3.67 (3H, s), 2.58–2.50 (1H, m), 2.28–2.19 (1H, m), 0.90 (9H, s), 0.08 (3H, s), 0.07 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 170.0 (C), 167.1 (C), 138.3 (C), 137.6 (C), 134.1 (CH), 133.6 (CH), 128.9 (CH), 128.3 (CH×2), 128.2 (CH×2), 127.7 (CH×2), 127.6 (CH), 127.5 (CH×2), 127.3 (CH), 117.2 (CH_2), 92.7 (CH), 83.2 (CH), 82.9 (CH), 77.6 (CH), 76.8 (CH), 73.3 (CH_2), 71.6 (CH_2), 70.4 (CH_2), 60.1 (CH_2), 50.9 (CH_3), 36.9 (CH_2), 25.8 (CH_3×3), 18.2 (C), −5.36 (CH_3×2); LR-FDMS, m/z 609 (55.5%, $[M+H]^+$), 608 (34.0%, $[M]^+$), 551 (bp, $[M-t\text{-Bu}]^+$); HR-FDMS, calcd for $C_{35}H_{49}O_7Si$ $[M+H]^+$: 609.3247, found: 609.3228.

5.1.46. (2*E*,2′*R*,3′*S*,4′*Z*,6′*R*,7′*S*)-3-{(2′-Allyl-6′-benzyloxy-7′-benzyloxymethyl-2′,3′,6′,7′-tetrahydrooxepin-3′-yl)oxy}-4-(*tert*-butyldimethylsilyloxy)-2-butenol (76). To a solution of **57** (401.6 mg, 0.660 mmol) in CH_2Cl_2 (7.0 ml) was added DIBAH (2.50 ml, 0.94 M in *n*-hexane, 2.31 mmol) at −78 °C and the mixture was stirred for 1 h. Then, saturated aqueous potassium sodium tartrate (10 ml) was added and the mixture was stirred at 23 °C for 12 h. The layers were separated and the aqueous layer was extracted with EtOAc (3×10 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/EtOAc=10→3→1) to give **76** (361.4 mg, 94%). **76**: a colorless oil; $[\alpha]_D^{25}$ +11.7 (c 0.78, $CHCl_3$); IR (film), ν_{max} 3423, 3065, 3030, 2953, 2928, 2857, 1659, 1497, 1471, 1462, 1454, 1389, 1361, 1294, 1274, 1252, 1187, 1094, 1028, 1004, 914, 837, 778, 735, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.36–7.24 (10H, m), 6.00–5.86 (1H, m), 5.85 (1H, dt, J=13.2, 2.2 Hz), 5.66 (1H, dt, J=13.2, 2.2 Hz), 5.11–5.00 (2H, m), 4.83 (1H, t, J=7.9 Hz), 4.61 (1H, d, J=11.2 Hz), 4.59 (2H, s), 4.45 (1H, d, J=11.2 Hz), 4.42–4.39 (1H, m), 4.26–4.22 (1H, m), 4.20 (2H, s), 4.17–4.15 (2H, m), 3.73–3.60 (4H, m), 2.54–2.46 (1H, m), 2.27–2.17 (1H, m), 1.86–1.84 (1H, m), 0.90 (9H, s), 0.10 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 156.4 (C), 138.3 (C), 137.7 (C), 134.7 (CH), 132.3 (CH), 130.3 (CH), 128.2 (CH×2), 128.1 (CH×2), 127.7 (CH×2), 127.5 (CH), 127.4 (CH), 127.2 (CH×2), 116.7 (CH_2), 101.3 (CH), 83.2 (CH), 83.1 (CH), 76.9 (CH), 76.3 (CH), 73.2 (CH_2), 71.5 (CH_2), 70.4 (CH_2), 61.0 (CH_2), 57.8 (CH_2), 37.1 (CH_2), 25.7 (CH_3×3), 18.1 (C), −5.38 (CH_3), −5.43 (CH_3); LR-FDMS, m/z 581 (44.9%, $[M+H]^+$), 580 (bp, $[M]^+$); HR-FDMS, calcd for $C_{34}H_{48}O_6Si$ $[M]^+$: 580.3220, found: 580.3203.

5.1.47. (2*E*,2′*R*,3′*S*,4′*Z*,6′*R*,7′*S*)-3-{(2′-Allyl-6′-benzyloxy-7′-benzyloxymethyl-2′,3′,6′,7′-tetrahydrooxepin-3′-yl)oxy}-4-(*tert*-butyldimethylsilyloxy)-2-butenal (77). To a mixture of **76** (185.2 mg, 0.319 mmol) and MS 4 Å (185.2 mg, 100 wt%) in CH_2Cl_2 (4.0 ml) was added NMO (74.7 mg, 0.638 mmol) at 23 °C and the mixture was stirred for 10 min. Then, TPAP (22.4 mg, 0.0638 mmol) was added to the reaction mixture at 23 °C and the mixture was stirred for 1.5 h. The mixture was filtered through Celite and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=10→5) to give **77** (155.3 mg, 84%). **77**: a colorless oil; $[\alpha]_D^{20}$ +22.2 (c 0.90, $CHCl_3$); IR (film), ν_{max} 3065, 3030, 2954, 2928, 2885, 2857, 2766, 1666, 1615, 1497, 1471, 1462, 1454, 1389, 1361, 1328, 1292, 1255, 1206, 1100, 1043, 1005, 916, 837, 779, 735, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$), δ 9.98 (1H, d, J=7.7 Hz), 7.36–7.24 (10H, m), 5.98–5.84 (1H, m), 5.92 (1H, dt, J=13.2, 2.6 Hz), 5.55 (1H, dt, J=13.2, 2.6 Hz), 5.32 (1H, d, J=7.7 Hz), 5.10–5.02 (2H, m), 4.63–4.43 (7H, m), 4.22 (1H, dqn, J=8.4, 2.2 Hz), 3.78–3.61 (4H, m), 2.51–2.43 (1H, m), 2.29–2.19 (1H, m), 0.90 (9H, s), 0.10 (3H, s), 0.09 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 189.9 (CH), 173.3 (C), 138.2 (C), 137.5 (C), 134.0 (CH), 133.9 (CH), 128.3 (CH×2), 128.2 (CH×2), 128.1 (CH), 127.8 (CH×2), 127.7 (CH), 127.5 (CH×2), 127.4 (CH), 117.4 (CH_2), 106.7 (CH), 83.1 (CH), 82.3 (CH), 78.0 (CH), 76.7 (CH), 73.3 (CH_2), 71.7 (CH_2), 70.3 (CH_2), 61.2 (CH_2), 37.0 (CH_2), 25.6 (CH_3×3), 18.1 (C), −5.43 (CH_3), −5.46 (CH_3); LR-FDMS, m/z 579 (51.5%, $[M+H]^+$), 578 (47.2, $[M]^+$), 363 (bp); HR-FDMS, calcd for $C_{34}H_{47}O_6Si$ $[M+H]^+$: 579.3142, found: 579.3120.

5.1.48. (3*E*,2′*R*,3′*S*,4′*Z*,6′*R*,7′*S*)-4-{(2′-Allyl-6′-benzyloxy-7′-benzyloxymethyl-2′,3′,6′,7′-tetrahydrooxepin-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2-(trimethylsilyloxy)pent-3-enenitrile (56). To a solution of **77** (155.3 mg, 0.268 mmol) and TMSCN (89 μl, 0.670 mmol) in benzene (5.5 ml) was added Me_3Al (0.29 ml, 1.01 M in *n*-hexane, 0.295 mmol) at 25 °C and the mixture was stirred for 1 h. Then, saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture was extracted with Et_2O (3×8 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/EtOAc=30→10) to give **56** (134.6 mg, 74%) as an inseparable 1:1 mixture of diastereomers. The nitrile **56** was unstable and immediately used for the next reaction. **56**: a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.36–7.24 (10H, m), 5.99–5.84 (2H, m), 5.64 (1H, dt, J=12.8, 2.4 Hz), 5.58 (0.5H, d, J= 8.8 Hz), 5.56 (0.5H, d, J=8.8 Hz), 5.11–5.00 (2H, m), 4.67–4.54 (4H, m), 4.46 (1H, d, J=11.4 Hz), 4.41–4.36 (1H, m), 4.25–4.21 (1H, m), 4.18 (2H, m), 3.72–3.60 (4H, m), 2.48–2.42 (1H, m), 2.28–2.15 (1H, m), 0.92 (4.5H, s), 0.91 (4.5H, s), 0.21 (4.5H, s), 0.20 (4.5H, s), 0.11 (3H, s), 0.10 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 156.6 (C×0.5), 156.4 (C×0.5), 138.4 (C×0.5), 138.3 (C×0.5), 137.75 (C×0.5), 137.70 (C×0.5), 134.4 (CH×0.5), 134.3 (CH×0.5), 133.2 (CH×0.5), 133.1 (CH×0.5), 129.6 (CH×0.5), 129.5 (CH×0.5), 128.31 (CH), 128.30 (CH), 128.2 (CH×2), 127.83 (CH), 127.79 (CH), 127.69 (CH×0.5), 127.60 (CH×0.5), 127.5 (CH×2), 127.4 (CH), 119.8 (C×0.5), 119.6 (C×0.5), 117.2 (CH_2×0.5), 117.0 (CH_2×0.5), 99.55 (CH×0.5), 99.52 (CH×0.5), 83.2 (CH×0.5), 83.1 (CH×0.5), 82.8 (CH), 77.0 (CH×0.5), 76.93 (CH×0.5), 76.92 (CH×0.5), 76.85 (CH×0.5), 73.34 (CH_2×0.5), 73.32 (CH_2×0.5), 71.7 (CH_2), 70.51 (CH_2×0.5), 70.46 (CH_2×0.5), 62.0 (CH_2×0.5), 61.9 (CH_2×0.5), 57.6 (CH×0.5), 57.5 (CH×0.5), 37.23 (CH_2×0.5), 37.15 (CH_2×0.5), 25.8 (CH_3×1.5), 25.7 (CH_3×1.5), 18.2 (C), −0.08 (CH_3×1.5), −0.10 (CH_3×1.5), −5.44 (CH_3×0.5), −5.47 (CH_3×0.5), −5.53 (CH_3×0.5), −5.61 (CH_3×0.5).

5.1.49. (2*E*,2′*R*,3′*S*,4′*Z*,6′*R*,7′*S*)-4-{(2′-Allyl-6′-benzyloxy-7′-benzyloxymethyl-2′,3′,6′,7′-tetrahydrooxepin-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)pent-2-enenitrile (55). To a solution of **56** (220.0 mg, 0.324 mmol) in CH_2Cl_2–Bu_3SnH (1:1, v/v, 3.4 ml) was added $BF_3\cdot OEt_2$ (0.12 ml, 0.972 mmol) at 0 °C and the mixture was stirred for 10 min. Then, saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture 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/EtOAc=50→20→10→5) to give **55** (119.8 mg, 63%) as an inseparable 1:1 mixture of diastereomers at C13.[36] **55**: a colorless oil; IR (film), ν_{max} 3065, 3030, 2954, 2928, 2858, 2225, 1641, 1496, 1471, 1462, 1454, 1388, 1361, 1294, 1253, 1207, 1103, 1028, 1005, 967, 939, 914, 837, 778, 735, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.36–7.24 (10H, m), 6.75 (0.5H, dd, J=16.3, 4.6 Hz), 6.66 (0.5H, dd, J=16.3, 5.7 Hz), 6.00–5.84 (2H, m), 5.75 (0.5H, dt, J=12.8, 2.2 Hz), 5.67–5.59 (1.5H, m), 5.12–5.04 (2H, m), 4.60 (1H, J=11.8 Hz), 4.56 (2H, s), 4.45 (1H, d, J=11.8 Hz), 4.20–4.15 (1H, m), 4.12–4.04 (1H, m), 3.98–3.89 (1H, m), 3.75–3.47 (6H, m), 2.56–2.41 (1H, m), 2.27–2.15 (1H, m), 0.89 (4.5H, s), 0.88 (4.5H, s), 0.05 (3H, s), 0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 152.9 (CH×0.5), 152.3 (CH×0.5), 138.3 (C), 137.9 (C×0.5), 137.8 (C×0.5), 134.9 (CH×0.5), 134.8 (CH×0.5), 132.5 (CH×0.5), 132.2 (CH×0.5), 131.5 (CH×0.5), 130.8 (CH×0.5), 128.4 (CH), 128.3 (CH), 128.2 (CH×2), 127.85 (CH), 127.79 (CH), 127.72 (CH×0.5), 127.69 (CH×0.5), 127.6 (CH×2), 127.4 (CH), 117.03 (C×0.5), 116.96 (C×0.5), 116.8 (CH_2×0.5), 116.7 (CH_2×0.5), 101.7 (CH×0.5), 101.0 (CH×0.5), 82.9 (CH×0.5), 82.5 (CH×0.5), 82.4 (CH×0.5), 82.1 (CH×0.5), 80.3 (CH×0.5), 79.5 (CH×0.5), 78.4 (CH×0.5), 78.2 (CH×0.5), 76.76 (CH×0.5), 76.66 (CH×0.5), 73.4 (CH_2×0.5), 73.3 (CH_2×0.5), 71.59 (CH_2×0.5), 71.57 (CH_2×0.5), 70.4 (CH_2), 64.9 (CH_2×0.5), 64.1 (CH_2×0.5), 37.5 (CH_2×0.5), 37.4 (CH_2×0.5), 25.8 (CH_3×3), 18.2 (C), −5.43 (CH_3×0.5), −5.49 (CH_3×0.5), −5.52 (CH_3×0.5), −5.53 (CH_3×0.5); LR-EIMS, *m*/*z* 589 (5.5%, $[M]^+$), 91 (bp); HR-EIMS, calcd for $C_{31}H_{38}NO_5Si$ $[M-t\text{-Bu}]^+$: 532.2519, found: 532.2510.

5.1.50. (2*E*,2′*R*,3′*S*,4′*Z*,6′*R*,7′*S*)-4-{(2′-Allyl-6′-benzyloxy-7′-benzyloxymethyl-2′,3′,6′,7′-tetrahydrooxepin-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2-pentenal (78). To a solution of **55** (119.8 mg, 0.203 mmol) in CH_2Cl_2 (3.5 ml) was added DIBAH (0.86 ml, 0.94 M in *n*-hexane, 0.812 mmol) at −78 °C and the mixture was stirred for 1 h. Then, saturated aqueous potassium sodium tartrate (5 ml) was added and the mixture was stirred at 24 °C for 10 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. To a mixture of the resultant imine in CH_2Cl_2 (3.0 ml) was added 0.5 M aqueous HCl (1.5 ml) at 24 °C and the mixture was stirred for 20 min. The mixture 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/EtOAc=10→5) to give **78** (100.2 mg, 83% from **55**) as an inseparable 1:1 mixture of diastereomers at C13.[36] **78**: a colorless oil; IR (film), ν_{max} 3066, 3030, 2954, 2928, 2857, 1694, 1641, 1497, 1471, 1462, 1454, 1389, 1361, 1294, 1253, 1207, 1110, 1028, 1005, 979, 939, 913, 837, 778, 735, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 9.57 (0.5H, d, J=7.7 Hz), 9.55 (0.5H, d, J=7.7 Hz), 7.35–7.24 (10H, m), 6.81 (0.5H, dd, J=15.8, 5.5 Hz), 6.71 (0.5H, dd, J=15.8, 6.2 Hz), 6.31 (0.5H, ddd, J=15.8, 7.7, 1.5 Hz), 6.30 (0.5H, ddd, J=15.8, 7.7, 1.3 Hz), 6.01–5.78 (2.5H, m), 5.68 (0.5H, dt, J=12.9, 2.4 Hz), 5.13–5.01 (2H, m), 4.60 (1H, d, J=11.2 Hz), 4.59 (1H, d, J=12.5 Hz), 4.54 (1H, d, J=12.5 Hz), 4.45 (1H, d, J=11.2 Hz), 4.26–4.15 (2H, m), 3.98 (0.5H, brdqn, J=8.4, 2.4 Hz), 3.92 (0.5H, brdqn, J=8.4, 2.4 Hz), 3.80–3.52 (6H, m), 2.62–2.48 (1H, m), 2.27–2.15 (1H, m), 0.89 (4.5H, s), 0.88 (4.5H, s), 0.06 (1.5H, s), 0.05 (1.5H, s), 0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 193.1 (CH×0.5), 192.9 (CH×0.5), 154.8 (CH×0.5), 153.8 (CH×0.5), 138.4 (C), 137.9 (C), 135.1 (CH×0.5), 135.0 (CH×0.5), 133.7 (CH×0.5), 132.9 (CH×0.5), 132.4 (CH×0.5), 132.0 (CH×0.5), 131.7 (CH×0.5), 131.5 (CH×0.5), 128.3 (CH×2), 128.2 (CH×2), 127.80 (CH), 127.78 (CH), 127.6 (CH), 127.58 (CH×2), 127.4 (CH), 116.8 (CH_2×0.5), 116.7 (CH_2×0.5), 83.2 (CH×0.5), 82.9 (CH×0.5), 82.4 (CH×0.5), 82.3 (CH×0.5), 80.3 (CH×0.5), 79.2 (CH×0.5), 78.6 (CH×0.5), 78.4 (CH×0.5), 76.8 (CH×0.5), 76.7 (CH×0.5), 73.3 (CH_2), 71.53 (CH_2×0.5), 71.46 (CH_2×0.5), 70.4 (CH_2), 65.2 (CH_2×0.5), 64.5 (CH_2×0.5), 37.42 (CH_2×0.5), 37.37 (CH_2×0.5), 25.8 (CH_3×3), 18.2 (C), −5.36 (CH_3×0.5), −5.44 (CH_3×0.5), −5.47 (CH_3×0.5), −5.49 (CH_3×0.5); LR-FDMS, *m*/*z* 592 (bp, $[M]^+$), 535 (43.7, $[M-t\text{-Bu}]^+$); HR-FDMS, calcd for $C_{35}H_{48}O_6Si$ $[M-t\text{-Bu}]^+$: 592.3220, found: 592.3230.

5.1.51. (2*E*,2′*R*,3′*S*,4′*Z*,6′*R*,7′*S*)-4-{(2′-Allyl-6′-benzyloxy-7′-benzyloxymethyl-2′,3′,6′,7′-tetrahydrooxepin-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2-pentenol (79). To a solution of **78** (100.2 mg, 0.169 mmol) in CH_2Cl_2 (3.0 ml) was added DIBAH (0.54 ml, 0.94 M in *n*-hexane, 0.507 mmol) at −78 °C and the mixture was stirred for 30 min. Then, saturated aqueous potassium sodium tartrate (5 ml) was added and the mixture was stirred at 24 °C for 15 h. The layers were separated and the aqueous layer was extracted with EtOAc (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/EtOAc=5→3) to give **79** (91.2 mg, 91%) as an inseparable 1:1 mixture of diastereomers at C13.[36] **79**: a colorless oil; IR (film), ν_{max} 3584, 3451, 3065, 3029, 2953, 2927, 2857, 1496, 1471, 1462, 1454, 1388, 1361, 1295, 1252, 1207, 1099, 1028, 1005, 913, 836, 815, 777, 734, 697 cm^{-1}; ^1H NMR (300 MHz, C_6D_6), δ 7.33–7.01 (10H, m), 6.30–6.12 (1H, m), 6.03–5.88 (1.5H, m), 5.78 (0.5H, dt, J=13.0, 2.6 Hz), 5.66–5.47 (2H, m), 5.30–5.09 (2H, m), 4.50–4.35 (3H, m), 4.31 (1H, d, J=11.7 Hz), 4.30–4.23 (1H, m), 4.10–4.05 (1H, m), 4.00–3.94 (1H, m), 3.89–3.83 (2H, m), 3.81–3.63 (5H, m), 3.55 (1H, ddd, J=10.6, 9.0, 4.6 Hz), 2.92–2.74 (1H, m), 2.51–2.34 (1H, m), 1.00 (4.5H, s), 0.98 (4.5H, s), 0.10 (1H, s), 0.08 (2.5H, s), 0.07 (2.5H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 138.4 (C), 138.00 (C×0.5), 137.98 (C×0.5), 135.5 (CH), 133.9 (CH×0.5), 133.2

(CH×0.5), 132.8 (CH×0.5), 132.5 (CH×0.5), 131.5 (CH×0.5), 130.6 (CH×0.5), 129.47 (CH×0.5), 129.46 (CH×0.5), 128.3 (CH×2), 128.2 (CH×2), 127.80 (CH), 127.79 (CH), 127.6 (CH×3), 127.4 (CH), 116.43 (CH_2×0.5), 116.40 (CH_2×0.5), 83.8 (CH×0.5), 83.6 (CH×0.5), 82.7 (CH×0.5), 82.5 (CH×0.5), 81.0 (CH×0.5), 79.7 (CH×0.5), 79.5 (CH×0.5), 77.6 (CH×0.5), 77.0 (CH×0.5), 76.9 (CH×0.5), 73.3 (CH_2), 71.43 (CH_2×0.5), 71.35 (CH_2×0.5), 70.5 (CH_2), 66.1 (CH_2×0.5), 65.9 (CH_2×0.5), 62.8 (CH_2×0.5), 62.7 (CH_2×0.5), 37.31 (CH_2×0.5), 37.26 (CH_2×0.5), 25.86 (CH_3×1.5), 25.84 (CH_3×1.5), 18.29 (C×0.5), 18.27 (C×0.5), −5.19 (CH_3×0.5), −5.32 (CH_3×0.5), −5.36 (CH_3×0.5), −5.41 (CH_3×0.5); LR-FDMS, *m/z* 595 (bp, $[M+H]^+$), 594 (25.1%, $[M]^+$); HR-FDMS, calcd for $C_{35}H_{51}O_6Si$ $[M+H]^+$: 595.3455 found: 595.3467.

5.1.52. (2*R*,3*S*,2′*R*,3′*S*,4′*Z*,6′*R*,7′*S*)-4-{(2′-Allyl-6′-benzyloxy-7′-benzyloxymethyl-2′,3′,6′,7′-tetrahydrooxepin-3′-yl)oxy}-5-(*tert*-butyldimethylsilyloxy)-2,3-epoxypentanol (80). To a mixture of D-(−)-DET (12 μl, 0.0696 mmol) and pre-dried MS 4 Å (20.7 mg, 100 wt%) in CH_2Cl_2 (0.3 ml) was added $Ti(O^iPr)_4$ (15.4 μl, 0.0522 mmol) at −40 °C and the mixture was stirred for 30 min. Then, TBHP (0.14 ml, 4.9 M in toluene, 0.696 mmol) was added and the mixture was stirred at −40 °C for 30 min. To the mixture was added dropwise a solution of **79** (20.7 mg, 0.0348 mmol) in CH_2Cl_2 (1.2 ml). The reaction mixture was stirred at −40 °C for 30 min. Then, the reaction mixture was warmed to −25 °C and stirred for 2.5 d. Then, DMS (52 μl, 0.708 mmol) was added at −25 °C and the mixture was stirred for 2 h until unreacted TBHP was consumed. To the mixture was added 10% DL-tartaric acid (31 μl) and NaF (13.2 mg) at −25 °C. The suspension was warmed to 24 °C and stirred for 24 h. The mixture was filtered through Celite and concentrated in vacuo. To the resultant residue was added Et_2O (1.0 ml) and 30% aqueous NaOH in brine (1.0 ml) at 0 °C 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 brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc=10→7→5→3) to give **80** (16.2 mg, 76%) as an inseparable 1:1 mixture of diastereomers at C13.[36] **80**: a colorless oil; IR (film), ν_{max} 3458, 3065, 3029, 2953, 2927, 2857, 1496, 1471, 1462, 1454, 1388, 1361, 1295, 1253, 1208, 1096, 1028, 1005, 911, 837, 814, 778, 735, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.35–7.24 (10H, m), 6.02–5.78 (3H, m), 5.13–5.01 (2H, m), 4.60 (1H, d, *J*=11.4 Hz), 4.59 (1H, d, *J*=12.5 Hz), 4.54 (1H, d, *J*=12.5 Hz), 4.45 (1H, d, *J*=11.4 Hz), 4.21–4.15 (1H, m), 4.02–3.91 (2H, m), 3.74–3.42 (8H, m), 3.24–3.15 (1H, m), 3.04 (1H, ddd, *J*=10.8, 5.5, 2.2 Hz), 2.60–2.52 (1H, m), 2.27–2.15 (1H, m), 0.90 (4.5H, s), 0.88 (4.5H, s), 0.06 (3H, s), 0.05 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 138.4 (C×0.5), 138.3 (C×0.5), 138.0 (C×0.5), 137.9 (C×0.5), 135.3 (CH×0.5), 135.2 (CH×0.5), 132.5 (CH×0.5), 132.3 (CH×0.5), 131.5 (CH×0.5), 131.1 (CH×0.5), 128.23 (CH×2), 128.16 (CH×2), 127.8 (CH×2), 127.5 (CH×3), 127.34 (CH×0.5), 127.32 (CH×0.5), 116.6 (CH_2×0.5), 116.5 (CH_2×0.5), 83.4 (CH×0.5), 83.2 (CH×0.5), 82.6 (CH×0.5), 82.5 (CH×0.5), 80.8 (CH×0.5), 80.5 (CH×0.5), 80.0 (CH×0.5), 77.9 (CH×0.5), 76.9 (CH), 73.3 (CH_2), 71.4 (CH_2×0.5), 71.3 (CH_2×0.5), 70.5 (CH_2), 63.9 (CH_2×0.5), 62.7 (CH_2×0.5), 61.3 (CH_2×0.5), 61.1 (CH_2×0.5), 56.7 (CH×0.5), 56.6 (CH×0.5), 56.4 (CH×0.5), 53.9 (CH×0.5), 37.3 (CH_2×0.5), 37.2 (CH_2×0.5), 25.8 (CH_3×1.5), 25.7 (CH_3×1.5), 18.2 (C×0.5), 18.1 (C×0.5), −5.43 (CH_3×0.5), −5.54 (CH_3×0.5), −5.61 (CH_3×0.5), −5.63 (CH_3×0.5); LR-FDMS, *m/z* 611 (bp, $[M+H]^+$), 610 (51.7, $[M]^+$); HR-FDMS, calcd for $C_{35}H_{51}O_7Si$ $[M+H]^+$: 611.3404, found: 611.3384.

5.1.53. (2*R*,3*S*,4*Z*,6*R*,7*S*,3′*S*,4′*R*)-2-Allyl-6-benzyloxy-7-benzyloxymethyl-3-{1′-(*tert*-butyldimethylsilyloxy)-3′,4′-epoxyhex-5′-en-2′-yl}oxy-2,3,6,7-tetrahydrooxepin (54). To a solution of **80** (3.4 mg, 5.57 μmol) in CH_2Cl_2–NEt_3–DMSO (3:1.4:1, v/v/v, 0.27 ml) was added SO_3·pyridine (22.2 mg, 0.139 mmol) at 0 °C. The mixture was warmed to 24 °C and stirred for 3 h. After the mixture was diluted with Et_2O (5 ml), the mixture was washed with H_2O (2×5 ml). 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 crude aldehyde was used in the next reaction without purification. To a stirred suspension of $Ph_3P^+CH_3Br^-$ (55.7 mg, 0.156 mmol) in THF (0.90 ml) was added NaHMDS (0.13 ml, 1.0 M in THF, 0.128 mmol) and the mixture was stirred at 24 °C. After 1 h, the resulting yellow suspension was allowed to stand at −78 °C. To the mixture was added dropwise a solution of the above crude aldehyde in THF (0.60 ml) at −78 °C and the mixture was stirred for 2 h. Then, the reaction mixture was warmed to 24 °C and stirred for 2.5 d. After the mixture was diluted with hexane (5 ml) and Et_2O (3 ml), saturated aqueous NH_4Cl (5 ml) was added and the mixture 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/EtOAc=20) to give **54** (2.0 mg, 59% from **80**) as an inseparable 1:1 mixture of diastereomers at C13.[36] **54**: a colorless oil; IR (film), ν_{max} 3065, 2926, 2856, 1473, 1462, 1454, 1361, 1293, 1252, 1097, 1028, 837, 777, 733, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.35–7.21 (10H, m), 6.03–5.81 (3H, m), 5.78–5.42 (2H, m), 5.29 (1H, dt, *J*=9.5, 2.2 Hz), 5.13–5.00 (2H, m), 4.61 (1H, d, *J*=11.2 Hz), 4.60 (1H, d, *J*=13.2 Hz), 4.54 (1H, d, *J*=13.2 Hz), 4.44 (1H, d, *J*=11.2 Hz), 4.23–4.16 (1H, m), 4.03–3.93 (1H, m), 3.75–3.58 (5H, m), 3.50 (1H, ddd, *J*=17.5, 8.9, 2.9 Hz), 3.41–3.34 (0.5H, m), 3.33 (0.5H, dd, *J*=6.8, 1.8 Hz), 3.27 (0.5H, dd, *J*=7.3, 1.8 Hz), 3.21–3.14 (0.5H, m), 2.93 (0.5H, dd, *J*=7.2, 1.8 Hz), 2.88 (0.5H, dd, *J*=5.7, 1.8 Hz), 2.61–2.53 (1H, m), 2.32–2.27 (1H, m), 0.90 (4.5H, s), 0.88 (4.5H, s), 0.06 (3H, s), 0.05 (1.5H, s), 0.04 (1.5H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 138.5 (C×0.5), 138.4 (C×0.5), 138.1 (C×0.5), 138.0 (C×0.5), 135.4 (CH), 134.9 (CH), 132.7 (CH×0.5), 132.3 (CH×0.5), 131.5 (CH×0.5), 131.1 (CH×0.5), 128.33 (CH), 128.31 (CH), 128.2 (CH×2), 127.8 (CH×2), 127.6 (CH×3), 127.41 (CH×0.5), 127.40 (CH×0.5), 119.81 (CH_2×0.5), 119.77 (CH_2×0.5), 116.6 (CH_2), 83.6 (CH×0.5), 83.2 (CH×0.5), 82.7 (CH), 81.2 (CH×0.5), 80.6 (CH×0.5), 80.3 (CH×0.5), 78.6 (CH×0.5), 76.98 (CH×0.5), 76.96 (CH×0.5), 73.4 (CH_2), 71.5 (CH_2×0.5), 71.4 (CH_2×0.5),

70.6 ($CH_2\times0.5$), 70.5 ($CH_2\times0.5$), 64.0 ($CH_2\times0.5$), 62.8 ($CH_2\times0.5$), 61.2 ($CH\times0.5$), 58.5 ($CH\times0.5$), 57.0 ($CH\times0.5$), 56.6 ($CH\times0.5$), 37.42 ($CH_2\times0.5$), 37.38 ($CH_2\times0.5$), 25.9 ($CH_3\times3$), 18.3 ($C\times0.5$), 18.2 ($C\times0.5$), −5.33 ($CH_3\times0.5$), −5.45 ($CH_3\times0.5$), −5.50 ($CH_3\times0.5$), −5.58 ($CH_3\times0.5$); LR-FDMS, *m/z* 606 (bp, $[M]^+$), 549 (29.9, $[M-t\text{-Bu}]^+$); HR-FDMS, calcd for $C_{36}H_{50}O_6Si$ $[M]^+$: 606.3377, found: 606.3369.

5.1.54. (3*S*,2′*R*,3′*S*,4′*Z*,6′*R*,7′*S*)-2-{(2′-Allyl-6′-benzyloxy-7′-benzyloxymethyl-2′,3′,6′,7′-tetrahydrooxepin-3′-yl)oxy}-1-(*tert*-butyldimethylsilyloxy)hex-5-en-3-ol (81). To a solution of $Pd(PPh_3)_4$ (11.8 mg, 0.0102 mmol) in CH_2Cl_2 (0.5 ml) was added Bu_3SnH (30 μl, 0.112 mmol) at 24 °C. To the mixture was added dropwise a solution of **54** (62.2 mg, 0.102 mmol) in CH_2Cl_2 (1.5 ml) at 24 °C and the mixture was stirred for 25 min. The solution was passed through a short silica gel column, and the filtrate was concentrated in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc = 30 → 20 → 10) to give **81** (54.6 mg, 88%) as an inseparable 1:1 mixture of diastereomers at C13.[36] **81**: a colorless oil; IR (film), ν_{max} 3583, 3491, 3067, 3030, 2927, 2856, 1462, 1454, 1257, 1101, 1028, 1005, 914, 837, 776, 734, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.38–7.24 (10H, m), 6.03–5.78 (4H, m), 5.17–5.00 (4H, m), 4.60 (1H, d, *J* = 11.4 Hz), 4.58–4.52 (2H, m), 4.45 (1H, d, *J* = 11.4 Hz), 4.20–4.14 (1H, m), 4.03–3.98 (1H, m), 3.86–3.53 (7H, m), 3.46–3.35 (1H, m), 2.61–2.51 (1H, m), 2.37–2.16 (3H, m), 0.90 (4.5H, s), 0.89 (4.5H, s), 0.07 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 138.44 ($C\times0.5$), 138.41 ($C\times0.5$), 138.0 ($C\times0.5$), 137.9 ($C\times0.5$), 135.31 ($CH\times0.5$), 135.29 ($CH\times0.5$), 135.0 ($CH\times0.5$), 134.8 ($CH\times0.5$), 132.8 ($CH\times0.5$), 132.0 ($CH\times0.5$), 131.4 ($CH\times0.5$), 131.0 ($CH\times0.5$), 128.3 ($CH\times2$), 128.2 ($CH\times2$), 127.9 (CH), 127.8 (CH), 127.7 ($CH\times0.5$), 127.64 ($CH\times2$), 127.61 ($CH\times0.5$), 127.42 ($CH\times0.5$), 127.41 ($CH\times0.5$), 117.7 ($CH_2\times0.5$), 117.1 ($CH_2\times0.5$), 116.64 ($CH_2\times0.5$), 116.59 ($CH_2\times0.5$), 83.4 ($CH\times0.5$), 83.2 ($CH\times0.5$), 82.4 ($CH\times0.5$), 82.1 ($CH\times0.5$), 81.0 ($CH\times0.5$), 79.8 ($CH\times0.5$), 79.0 ($CH\times0.5$), 78.5 ($CH\times0.5$), 76.9 ($CH\times0.5$), 76.7 ($CH\times0.5$), 73.3 (CH_2), 71.6 ($CH_2\times0.5$), 71.54 ($CH\times0.5$), 71.45 ($CH_2\times0.5$), 70.8 ($CH\times0.5$), 70.6 ($CH_2\times0.5$), 70.5 ($CH_2\times0.5$), 62.9 ($CH_2\times0.5$), 61.5 ($CH_2\times0.5$), 37.62 (CH_2), 37.58 (CH_2), 25.83 ($CH_3\times1.5$), 25.80 ($CH_3\times1.5$), 18.2 ($C\times0.5$), 18.1 ($C\times0.5$), −5.43 ($CH_3\times0.5$), −5.56 (CH_3), −5.61 ($CH_3\times0.5$); LR-FDMS, *m/z* 609 (bp, $[M+H]^+$), 608 (36.3%, $[M]^+$), 551 (45.2%, $[M-t\text{-Bu}]^+$); HR-FDMS, calcd for $C_{36}H_{53}O_6Si$ $[M+H]^+$: 609.3611, found: 609.3585.

5.1.55. (3*S*,2′*R*,3′*S*,4′*Z*,6′*R*,7′*S*)-2-{(2′-Allyl-6′-benzyloxy-7′-benzyloxymethyl-2′,3′,6′,7′-tetrahydrooxepin-3′-yl)oxy}hex-5-en-1,3-diol (82). To a solution of **81** (2.5 mg, 4.11 μmol) in THF (0.4 ml) was added TBAF (8.2 μl, 1.0 M in THF, 8.22 μmol) at 23 °C and the mixture was stirred for 1.5 h. The solvent was removed in vacuo. The resultant residue was purified by column chromatography (silica gel, hexane/EtOAc = 1 → 1/2 → EtOAc) to give **82** (2.0 mg, 100%) as an inseparable 1:1 mixture of diastereomers at C13.[36] **82**: a colorless oil; IR (film), ν_{max} 3583, 3420, 3065, 3028, 2924, 2855, 1641, 1454, 1377, 1294, 1207, 1073, 1028, 914, 735, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 7.34–7.24 (10H, m), 6.01–5.75 (4H, m), 5.19–5.01 (4H, m), 4.61 (1H, d, *J* = 11.6 Hz), 4.59 (1H, d, *J* = 12.7 Hz), 4.53 (1H, d, *J* = 12.7 Hz), 4.45 (1H, d, *J* = 11.6 Hz), 4.16–3.98 (2H, m), 3.89–3.79 (2H, m), 3.77–3.60 (4H, m), 3.54 (1H, dd, *J* = 10.5, 4.6 Hz), 3.46–3.42 (1H, m), 2.54–2.14 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$), δ 138.4 (C), 137.8 ($C\times0.5$), 137.7 ($C\times0.5$), 135.1 ($CH\times0.5$), 134.9 ($CH\times0.5$), 134.5 ($CH\times0.5$), 134.3 ($CH\times0.5$), 132.6 ($CH\times0.5$), 132.4 ($CH\times0.5$), 130.65 ($CH\times0.5$), 130.60 ($CH\times0.5$), 128.4 (CH), 128.35 (CH), 128.26 ($CH\times2$), 128.1 (CH), 128.0 (CH), 127.9 ($CH\times0.5$), 127.7 ($CH\times0.5$), 127.67 (CH), 127.65 (CH), 127.5 (CH), 118.2 ($CH_2\times0.5$), 117.6 ($CH_2\times0.5$), 117.0 ($CH_2\times0.5$), 116.8 ($CH_2\times0.5$), 82.6 ($CH\times0.5$), 82.3 ($CH\times0.5$), 81.6 ($CH\times0.5$), 81.1 ($CH\times0.5$), 80.0 ($CH\times0.5$), 79.0 ($CH\times0.5$), 78.6 ($CH\times0.5$), 78.2 ($CH\times0.5$), 76.6 ($CH\times0.5$), 76.2 ($CH\times0.5$), 73.3 (CH_2), 71.9 ($CH_2\times0.5$), 71.7 ($CH_2\times0.5$), 70.9 ($CH\times0.5$), 70.7 ($CH_2\times0.5$), 70.60 ($CH_2\times0.5$), 70.56 ($CH\times0.5$), 61.2 ($CH_2\times0.5$), 61.0 ($CH_2\times0.5$), 37.9 ($CH_2\times0.5$), 37.7 ($CH_2\times0.5$), 37.6 ($CH_2\times0.5$), 37.5 ($CH_2\times0.5$); LR-FDMS, *m/z* 495 (80.0%, $[M+H]^+$), 494 (11.2%, $[M]^+$), 91 (bp); HR-FDMS, calcd for $C_{30}H_{39}O_6$ $[M+H]^+$: 495.2747, found: 495.2754.

5.1.56. (2*R*,3*S*,4*Z*,6*R*,7*S*,4′*S*,5′*R*)-2-Allyl-3-{(4′-allyl-2′,2′-dimethyl-1′,3′-dioxan-5′-yl)oxy}-6-benzyloxy-7-benzyloxymethyl-2,3,6,7-tetrahydrooxepin (53a) and (2*R*,3*S*,4*Z*,6*R*,7*S*,4′*S*,5′*S*)-2-allyl-3-{(4′-allyl-2′,2′-dimethyl-1′,3′-dioxan-5′-yl)oxy}-6-benzyloxy-7-benzyloxymethyl-2,3,6,7-tetrahydrooxepin (53b). To a solution of **82** (44.4 mg, 0.0897 mmol) and 2,2-dimethoxypropane (55 μl, 0.449 mmol) in CH_2Cl_2 (1.5 ml) was added CSA (10.5 mg, 0.0449 mmol) at 24 °C and the mixture was stirred for 2 h. Then, 2,2-dimethoxypropane (55 μl, 0.449 mmol) was added, and the stirring was continued for further 1 h. After that, saturated aqueous $NaHCO_3$ (5 ml) was added and the mixture 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/EtOAc = 15 → 5 → 3) to give **53a** (22.4 mg, 47%) and **53b** (23.7 mg, 50%). **53a**: a colorless oil; $[\alpha]_D^{20}$ −17.1 (*c* 1.12, $CHCl_3$) IR (film), ν_{max} 2924, 2855, 1466, 1461, 1457, 1453, 1446, 1434, 1378, 1372, 1362, 1360, 1261, 1199, 1165, 1092, 697 cm^{-1}; ^1H NMR (300 MHz, C_6D_6), δ 7.41–7.05 (10H, m), 6.16–5.99 (2H, m), 5.77–5.70 (1H, m), 5.59–5.55 (1H, m), 5.19–5.05 (4H, m), 4.46 (1H, d, *J* = 11.4 Hz), 4.44 (1H, d, *J* = 12.3 Hz), 4.38 (1H, d, *J* = 12.3 Hz), 4.30 (1H, d, *J* = 11.4 Hz), 4.18–4.15 (1H, m), 3.99–3.91 (1H, m), 3.92 (1H, dd, *J* = 11.2, 5.1 Hz), 3.84–3.73 (2H, m), 3.70–3.59 (3H, m), 3.63 (1H, dd, *J* = 11.2, 8.8 Hz), 3.31 (1H, td, *J* = 8.8, 5.1 Hz), 2.68–2.53 (2H, m), 2.41–2.24 (2H, m), 1.45 (3H, s), 1.26 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 138.4 (C), 138.0 (C), 135.0 (CH), 134.4 (CH), 131.9 (CH), 131.8 (CH), 128.4 ($CH\times2$), 128.3 ($CH\times2$), 127.9 ($CH\times2$), 127.69 (CH), 127.65 ($CH\times2$), 127.5 (CH), 116.94 (CH_2), 116.92 (CH_2), 98.6 (C), 83.0 (CH), 81.8 (CH), 80.1 (CH), 76.7 (CH), 74.4 (CH), 73.4 (CH_2), 72.4 (CH), 71.5 (CH_2), 70.5 (CH_2), 63.6 (CH_2), 37.6 (CH_2), 36.4 (CH_2), 28.4 (CH_3), 19.5 (CH_3); LR-FDMS, *m/z* 535 (bp, $[M+H]^+$), 534 (50.1, $[M]^+$); HR-FDMS, calcd for $C_{33}H_{43}O_6$ $[M+H]^+$; 535.3059, found: 535.3038. **53b**: a colorless oil; $[\alpha]_D^{22}$ +38.0 (*c* 1.19, $CHCl_3$) IR (film), ν_{max} 3065, 2925, 2855, 1496, 1455, 1419, 1377, 1295, 1278, 1245, 1230, 1198,

1092, 1074, 1028, 995, 984, 912, 733, 697 cm^{-1}; ^1H NMR (300 MHz, $(CD_3)_2C{=}O$), δ 7.38–7.22 (10H, m), 6.12–5.72 (4H, m), 5.11–4.94 (4H, m), 4.66 (1H, d, $J=11.7$ Hz), 4.59 (1H, d, $J=12.5$ Hz), 4.53 (1H, d, $J=12.5$ Hz), 4.49 (1H, d, $J=11.7$ Hz), 4.14–4.09 (1H, m), 4.03–4.00 (1H, m), 4.01 (1H, dd, $J=12.8$, 1.5 Hz), 3.91–3.87 (1H, m), 3.88 (1H, dd, $J=12.8$, 1.5 Hz), 3.75–3.60 (3H, m), 3.57–3.48 (1H, m), 3.29 (1H, brqn, $J=1.5$ Hz), 2.87–2.68 (2H, m), 2.35–2.13 (2H, m), 1.41 (3H, s), 1.28 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 138.5 (C), 138.0 (C), 135.6 (CH), 134.3 (CH), 131.8 (CH), 131.3 (CH), 128.34 (CH×2), 128.26 (CH×2), 127.8 (CH×2), 127.3 (CH×3), 127.4 (CH), 117.3 (CH_2), 116.5 (CH_2), 98.5 (C), 83.8 (CH), 82.9 (CH), 77.2 (CH), 77.0 (CH), 73.4 (CH_2), 71.6 (CH_2), 71.2 (CH), 70.5 (CH_2), 69.0 (CH), 60.8 (CH_2), 37.3 (CH_2), 35.6 (CH_2), 29.3 (CH_3), 18.9 (CH_3); LR-FDMS, *m/z* 535 (bp, $[M+H]^+$), 534 (58.2%, $[M]^+$); HR-FDMS, calcd for $C_{33}H_{43}O_6$ $[M+H]^+$: 535.3059, found: 535.3066.

5.1.57. (1*S*,3*R*,8*S*,10*Z*,13*R*,15*S*,16*R*,17*Z*)-16-Benzyloxy-15-benzyloxymethyl-6,6-dimethyl-2,5,7,14-tetraoxatricyclo[11.5.0.0^{3,8}]octadeca-10,17-diene (52). To a solution of **53a** (22.4 mg, 0.0419 mmol) in degassed CH_2Cl_2 (12 ml) was added a solution of $(Cy_3P)_2Cl_2Ru{=}CHPh$ (6.9 mg, 8.38 μmol) in degassed CH_2Cl_2 (2 ml). The resultant solution was stirred at 23 °C for 4 h. The mixture was stirred for 15.5 h under O_2 atmosphere, and the solvent was removed in vacuo. The resultant residue was purified by column chromatography (silica gel, benzene/EtOAc = 50 → 10) to give **52** (20.5 mg, 97%). **52**: a colorless oil; $[\alpha]_D^{23}$ −22.3 (*c* 0.050, $CHCl_3$); IR (film), ν_{max} 2924, 2854, 1496, 1457, 1454, 1434, 1378, 1267, 1206, 1097, 1028, 732, 697 cm^{-1}; ^1H NMR (400 MHz, C_5D_5N, −30 °C, a 1:1 mixture of conformers), δ 7.52–7.22 (10H, m), 5.99–5.92 (0.5H, m), 5.89–5.63 (2.5H, m), 5.60–5.49 (1H, m) 4.71 (0.5H, d, $J=11.2$ Hz), 4.67 (0.5H, d, $J=11.2$ Hz), 4.61–4.51 (2.5H, m), 4.47 (0.5H, d, $J=11.2$ Hz), 4.36–4.31 (1H, m), 4.28–4.23 (0.5H, m), 3.99–3.92 (1H, m), 3.90–3.81 (2.5H, m), 3.90–3.47 (1H, m), 3.77–3.61 (2.5H, m), 3.56–3.47 (1H, m), 3.34 (0.5H, td, $J=9.6$, 5.9 Hz), 3.01–3.05 (0.5H, m), 2.92–2.78 (1.5H, m), 2.38–2.32 (0.5H, m), 2.19–2.11 (1H, m), 2.04–1.99 (0.5H, m), 1.46 (1.5H, s), 1.39 (1.5H, s), 1.14 (1.5H, s), 1.13 (1.5H, s); ^{13}C NMR data of **52** is not shown because the spectrum of **52** exhibited extremely broadened signals that gave only unclear chemical shifts.; LR-FDMS, *m/z* 507 (64.5%, $[M+H]^+$), 506 (bp, $[M]^+$), 491 (22.9%, $[M-Me]^+$); HR-FDMS, calcd for $C_{31}H_{38}O_6$ $[M]^+$: 506.2668, found: 506.2648.

5.1.58. (1*S*,3*R*,4*S*,6*Z*,9*R*,11*S*,12*R*,13*Z*)-12-Benzyloxy-11-benzyloxymethyl-3-hydroxymethyl-2,10-dioxabicyclo-[7.5.0]tetradeca-6,13-dien-4-ol (83). To a solution of **52** (20.5 mg, 0.0405 mmol) in THF–H_2O (1:1, v/v, 0.80 ml) was added TFA (40 μl) at 0 °C. The mixture was warmed to 23 °C and stirred for 3 h. After the mixture was diluted with Et_2O (3 ml), saturated aqueous $NaHCO_3$ (5 ml) was added. The mixture was extracted with EtOAc (5×5 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/EtOAc = 2 → 1/3) to give **83** (16.6 mg, 88%). **83**: a colorless oil; $[\alpha]_D^{23}$ −34.9 (*c* 0.045, $CHCl_3$); IR (film), ν_{max} 3586, 3411, 2953, 2923, 2853, 1456, 1419, 1377, 1292, 1231, 1214, 1092, 1071, 1027, 934, 730, 695 cm^{-1}; ^1H NMR (400 MHz, C_6D_6), δ 7.36–7.05 (10H, m), 5.99 (1H, td, $J=10.7$, 5.9 Hz), 5.85–5.81 (1H, m), 5.80 (1H, dt, $J=12.7$, 2.4 Hz), 5.70 (1H, dt, $J=12.7$, 2.4 Hz), 4.50 (1H, d, $J=11.7$ Hz), 4.48 (1H, d, $J=11.7$ Hz), 4.45 (1H, d, $J=11.7$ Hz), 4.33 (1H, d, $J=11.7$ Hz), 4.20 (1H, dqn, $J=8.8$, 2.4 Hz), 4.20 (1H, dqn, $J=8.8$, 2.4 Hz), 3.79–3.70 (3H, m), 3.63 (1H, dd, $J=11.0$, 3.7 Hz), 3.59 (1H, ddd, $J=8.8$, 4.4, 2.4 Hz), 3.55–3.51 (1H, m), 3.53 (1H, dd, $J=11.0$, 5.2 Hz), 2.99 (1H, ddd, $J=8.8$, 5.2, 3.7 Hz), 2.78 (1H, brddd, $J=12.8$, 10.7, 3.8 Hz), 2.67–2.59 (1H, m), 2.26–2.21 (1H, m), 1.99 (1H, brddd, $J=13.9$, 5.4, 3.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), δ 138.5 (C), 137.8 (C), 136.2 (CH), 131.8 (CH), 128.8 (CH), 128.4 (CH×2), 128.3 (CH×2), 127.8 (CH×2), 127.7 (CH), 127.6 (CH×2), 127.5 (CH), 127.2 (CH), 87.1 (CH), 85.7 (CH), 84.0 (CH), 82.9 (CH), 77.6 (CH), 73.4 (CH_2), 71.7 (CH_2), 71.3 (CH), 70.9 (CH_2), 63.5 (CH_2), 32.5 (CH_2), 32.3 (CH_2); LR-FDMS, *m/z* 467 (66.6%, $[M+H]^+$), 466 (44.3%, $[M]^+$), 91 (bp); HR-FDMS, calcd for $C_{28}H_{35}O_6$ $[M+H]^+$: 467.2434, found: 467.2455.

Acknowledgements

We thank 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 thank Dr. Yasuhiro Kumaki (High-Resolution NMR Laboratory, Graduate School of Science, Hokkaido University) for the ^{13}C NMR measurement of **50**. 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 ciguatera, see (a) Lehane, L.; Lewis, R. J. *Int. J. Food Microbiol.* **2000**, *61*, 91. (b) Lewis, R. J. *Toxicon* **2001**, *39*, 97.
2. For reviews of ciguatoxins and related marine toxins, see (a) Shimizu, Y. *Chem. Rev.* **1993**, *93*, 1685. (b) Yasumoto, T.; Murata, M. *Chem. Rev.* **1993**, *93*, 1897. (c) Scheuer, P. J. *Tetrahedron* **1994**, *50*, 3. (d) Yasumoto, T.; Murata, M. *Nat. Prod. Rep.* **2000**, *17*, 293. (e) Yasumoto, T. *Chem. Rec.* **2001**, *3*, 228.
3. Yasumoto, T.; Nakajima, R.; Bagnis, R.; Adachi, R. *Bull. Jpn. Soc. Sci. Fish.* **1977**, *43*, 1021.
4. (a) Scheuer, P. J.; Takahashi, W.; Tsutsumi, J.; Yoshida, T. *Science* **1967**, *155*, 1267. (b) Tachibana, K. PhD 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.
5. (a) Murata, M.; Legrand, A.-M.; Ishibashi, Y.; Fukui, M.; Yasumoto, T. *J. Am. Chem. Soc.* **1989**, *111*, 8929. (b) Murata, M.; Legrand, A.-M.; Ishibashi, Y.; Fukui, M.; Yasumoto, T. *J. Am. Chem. Soc.* **1990**, *112*, 4380. (c) Murata, M.; Legrand, A.-M.; Scheuer, P. J.; Yasumoto, T. *Tetrahedron Lett.* **1992**, *33*, 525.

6. Satake, M.; Morohashi, A.; Oguri, H.; Oishi, T.; Hirama, M.; Harada, N.; Yasumoto, T. *J. Am. Chem. Soc.* **1997**, *119*, 11325.
7. For bioactivity of ciguatoxins and related compounds, see (a) Bidard, J.-N.; Vijverberg, H. P. M.; Frelin, C.; Chungue, E.; Legrand, A.-M.; Bagnis, R.; Lazdanski, M. *J. Biol. Chem.* **1984**, *259*, 8353. (b) Lombet, A.; Bidard, J.-N.; Lazdanski, M. *FEBS Lett.* **1987**, *219*, 355. For a review, see (c) Dechraoui, M.-Y.; Naar, J.; Pauillac, S.; Legrand, A.-M. *Toxicon* **1999**, *37*, 125. See also the references cited in Ref. 1.
8. Catterall, W. A.; Risk, M. *Mol. Pharmacol.* **1981**, *19*, 345. See also Ref. 7b.
9. (a) Trainer, V. L.; Thomsen, W. J.; Catterall, W. A.; Baden, D. G. *Mol. Pharmacol.* **1991**, *40*, 988. (b) Trainer, V. L.; Baden, D. G.; Catterall, W. A. *J. Biol. Chem.* **1994**, *269*, 19904.
10. Recent reviews for the synthesis of medium cyclic ethers and polycyclic ethers, see (a) Alvarez, E.; Candenas, M.-L.; Pérez, R.; Ravero, J. L.; Martín, J. D. *Chem. Rev.* **1995**, *95*, 1953. (b) Mori, Y. *Chem. Eur. J.* **1997**, *3*, 849. (c) Hoberg, J. O. *Tetrahedron* **1998**, *54*, 12631. (d) Yet, L. *Chem. Rev.* **2000**, *100*, 2963. (e) Elliot, M. C.; Williams, E. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2303. (f) Elliot, M. C. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2301. (g) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (h) Fujiwara, K.; Murai, A. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 2129.
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. *J. Org. Chem.* **1996**, *61*, 3003. (e) Oishi, T.; Nagumo, Y.; Hirama, M. *Synlett* **1997**, 980. (f) Inoue, M.; Sasaki, M.; Tachibana, K. *Tetrahedron Lett.* **1997**, *38*, 1611. (g) Oishi, T.; Nagumo, Y.; Hirama, M. *Chem. Commun.* **1998**, 1041. (h) Sasaki, M.; Inoue, M.; Noguchi, T.; Takeichi, A.; Tachibana, K. *Tetrahedron Lett.* **1998**, *39*, 2783. (i) Sasaki, M.; Fuwa, H.; Inoue, M.; Tachibana, K. *Tetrahedron Lett.* **1998**, *39*, 9027. (j) Sasaki, M.; Noguchi, T.; Tachibana, K. *Tetrahedron Lett.* **1999**, *40*, 1337. (k) Fujiwara, K.; Morishita, H.; Saka, K.; Murai, A. *Tetrahedron Lett.* **2000**, *41*, 507. (l) Matsuo, G.; Hinou, H.; Koshino, H.; Suenaga, T.; Nakata, T. *Tetrahedron Lett.* **2000**, *41*, 903. (m) Mori, Y.; Mitsuoka, S.; Furukawa, H. *Tetrahedron Lett.* **2000**, *41*, 4161. (n) Kadowaki, C.; Chan, P. W. H.; Kadota, I.; Yamamoto, Y. *Tetrahedron Lett.* **2000**, *41*, 5769. (o) Imai, H.; Uehara, H.; Inoue, M.; Oguri, H.; Oishi, T.; Hirama, M. *Tetrahedron Lett.* **2001**, *42*, 6219. (p) Díaz, M. T.; Pérez, R. L.; Rodríguez, L.; Ravelo, J. L.; Martín, J. D. *Synlett* **2001**, 345. (q) Oishi, T.; Tanaka, S.-i.; Ogasawara, Y.; Maeda, K.; Oguri, H.; Hirama, M. *Synlett* **2001**, 952. (r) Maruyama, M.; Inoue, M.; Oishi, T.; Oguri, H.; Ogasawara, Y.; Shindo, Y.; Hirama, M. *Tetrahedron* **2002**, *58*, 1835. (s) Sasaki, M.; Noguchi, T.; Tachibana, K. *J. Org. Chem.* **2002**, *67*, 3301. (t) Kadota, I.; Ohno, A.; Matsuda, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 3562. (u) Suzuki, K.; Nakata, T. *Org. Lett.* **2002**, *4*, 2739. (v) Inoue, M.; Wang, G. X.; Wang, J.; Hirama, M. *Org. Lett.* **2002**, *4*, 3439. (w) Oishi, T.; Watanabe, K.; Murata, M. *Tetrahedron Lett.* **2003**, *44*, 7315. (x) Sasaki, M.; Fuwa, H. *Synlett* **2004**, 1851. (y) Kadota, I.; Yamamoto, Y. *Acc. Chem. Res.* **2005**, *38*, 423.
12. For recent synthetic studies on ciguatoxins from other groups, see (a) Takai, S.; Sawada, N.; Isobe, M. *J. Org. Chem.* **2003**, *68*, 3225. (b) Baba, T.; Isobe, M. *Synlett* **2003**, 547. (c) Tatami, A.; Inoue, M.; Uehara, H.; Hirama, M. *Tetrahedron Lett.* **2003**, *44*, 5229. (d) Baba, T.; Huang, G.; Isobe, M. *Tetrahedron* **2003**, *59*, 6851. (e) Kobayashi, S.; Alizadeh, B. H.; Sasaki, S.-y.; Oguri, H.; Hirama, M. *Org. Lett.* **2004**, *6*, 751. (f) Baba, T.; Takai, S.; Sawada, N.; Isobe, M. *Synlett* **2004**, 603. (g) Inoue, M.; Yamashita, S.; Tatami, A.; Miyazaki, K.; Hirama, M. *J. Org. Chem.* **2004**, *69*, 2797. (h) Inoue, M.; Yamashita, S.; Hirama, M. *Tetrahedron Lett.* **2004**, *45*, 2053. (i) Inoue, M. *Org. Biomol. Chem.* **2004**, 1811. (j) Fuwa, H.; Fujikawa, S.; Tachibana, K.; Takakura, H.; Sasaki, M. *Tetrahedron Lett.* **2004**, *45*, 4795. (k) Kobayashi, S.; Takahashi, Y.; Komano, K.; Alizadeh, B. H.; Kawada, Y.; Oishi, T.; Tanaka, S.-i.; Ogasawara, Y.; Sasaki, S.-y.; Hirama, M. *Tetrahedron* **2004**, 8375 and references therein.
13. For the total synthesis of ciguatoxin 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) Inoue, M.; Hirama, M. *Synlett* **2004**, 577. (d) Inoue, M.; Hirama, M. *Acc. Chem. Res.* **2004**, *37*, 961.
14. For synthetic studies of 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*, 8053. (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.-i.; 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.
15. (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.
16. *Handbook of Metathesis*; Grubbs, R. H., Ed.; Wiley-VCH: Weinhem, 2003.
17. (a) FuS, G. C.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, 9856. (b) Zuercher, W. J.; Hashimoto, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 6634.
18. (a) Paintner, F. F.; Metz, M.; Bauschke, G. *Synthesis* **2002**, 869. (b) Inanaga, J.; Baba, Y.; Hanamoto, T. *Chem. Lett.* **1993**, 241.
19. Crimmins, M. T.; Choy, A. L. *J. Am. Chem. Soc.* **1999**, *121*, 5653.
20. Fujiwara, K.; Souma, S.-i.; Mishima, H.; Murai, A. *Synlett* **2002**, 1493.
21. Several attempts to reduce selectively the α,β-unsaturated ester part of **21** were unsuccessful.
22. Hetero-Michael addition of **19** to butynoate **20** with a catalytic amount of Me_3P according to Paintner's procedure[18] often stopped before completion. The incomplete reaction was due to the oligomerization of **20**. A stoichiometric amount of Me_3P

and excess **20** (1.7 equiv) were required to accelerate the reaction rate and to improve the yield.
23. When TMSOTf was used instead of $BF_3 \cdot OEt_2$, complex products were obtained. On the other hand, Me_3Al was ineffective in activating the substrate.
24. Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.
25. Classon, B.; Liu, Z.; Samuelsson, B. *J. Org. Chem.* **1988**, *53*, 6126.
26. Under the reaction conditions, epoxides **29a** and **29b** were directly converted to allyl alcohols **30a** and **30b**, respectively. There were several reports for conversion of 2,3-epoxypropanol derivatives to the corresponding 1-propen-3-ol derivatives under Classon–Samuelsson conditions. For examples, (a) Aziz, M.; Rouessac, F. *Tetrahedron* **1988**, *44*, 101. (b) Hayashi, N.; Mine, T.; Fujiwara, K.; Murai, A. *Chem. Lett.* **1994**, 2143. (c) Dorta, R. L.; Rodríguez, M. S.; Salazar, J. A.; Suárez, E. *Tetrahedron Lett.* **1997**, *38*, 4675.
27. Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953.
28. In the RCM reaction, **30a** was not recovered, and an oligomer that would result from **30a** was detected.
29. (a) Tsuji, J.; Shimizu, I.; Minami, I. *Chem. Lett.* **1984**, 1017. (b) Oshima, M.; Yamazaki, H.; Shimizu, I.; Nisar, M.; Tsuji, J. *J. Am. Chem. Soc.* **1989**, *111*, 6280. (c) Nagasawa, K.; Shimizu, I.; Nakata, T. *Tetrahedron Lett.* **1996**, *37*, 6881–6885.
30. See also: Kakei, H.; Nemoto, T.; Ohshima, T.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 317.
31. David, H.; Dupuis, L.; Guillerez, M.-G.; Guibé, F. *Tetrahedron Lett.* **2000**, *41*, 3335.
32. Oxepan alcohol **72** was facilely available from the known E-ring segment.[14j]
33. (a) Crimmins, M. T.; Tabet, E. A. *J. Am. Chem. Soc.* **2000**, *122*, 5473. (b) Sawada, D.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 10521.
34. Parikh, J. R.; Doering, W. v. E. *J. Am. Chem. Soc.* **1967**, *89*, 5505.
35. The position number is corresponding to that of Scheme 7.
36. The position number is corresponding to that of Scheme 10.