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PII: S0040-4020(16)31327-8

DOI: 10.1016/j.tet.2016.12.041

Reference: TET 28333

To appear in: *Tetrahedron*

Received Date: 23 November 2016

Revised Date: 15 December 2016

Accepted Date: 19 December 2016

Please cite this article as: Sato T, Fujiwara K, Nogoshi K, Goto A, Domon D, Kawamura N, Nomura Y, Sato D, Tanaka H, Murai A, Kondo Y, Akiba U, Katoono R, Kawai H, Suzuki T, Synthesis of the ABCDEF-ring of ciguatoxin 3C, *Tetrahedron* (2017), doi: 10.1016/j.tet.2016.12.041.

Graphical Abstract

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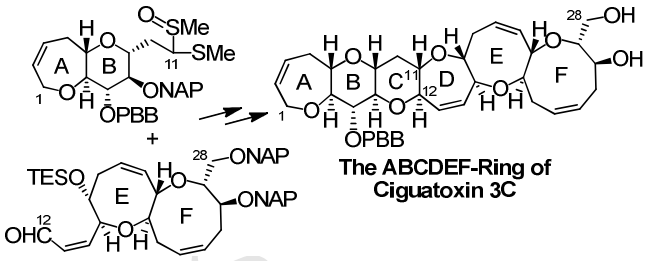

The ABCDEF-Ring of Ciguatoxin 3C

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Natural product synthesis
Fused polycyclic ethers
Ireland-Claisen rearrangement
Ring closing olefin metathesis
Stereoselective Synthesis

ABSTRACT

The synthesis of the ABCDEF-ring of ciguatoxin 3C was achieved via a route that included anion coupling of a dimethyldithioacetal mono-*S*-oxide derivative corresponding to the AB-ring and an aldehyde corresponding to the EF-ring, followed by cyclization using reductive etherification. The AB-ring was synthesized from a known D-glucose derivative based on ring-closing olefin metathesis, and the EF-ring was prepared by a process employing chirality-transferring Ireland-Claisen rearrangement and ring-closing olefin metathesis.

1. Introduction

Ciguatoxin 3C (CTX3C, **1**) is a causative toxin of ciguatera fish poisoning,[1,2] which often breaks out in tropical coral reef regions and affects more than 20,000 patients annually. The symptoms of ciguatera, represented by nausea, emesis, fatigue, arthralgia, and reversal of temperature sensation, are developed when people eat fish poisoned by ciguatera toxins. The toxins are originally produced by dinoflagellates,[3] and are transferred up the food chain to herbivorous fish and then to carnivorous fish. In 1993, Yasumoto and co-workers isolated **1** from cultured dinoflagellates, *Gambierdiscus toxicus*, providing strong evidence that ciguatoxins are produced by the dinoflagellate. They also determined the relative structure of **1** by NMR analysis using only 0.7 mg of the sample, obtained from 1100 L of the culture.[4] The framework of **1** consists of twelve *trans*-fused ether rings with ring sizes ranging from six to nine members, a terminal five-membered spirocyclic acetal, and thirty asymmetric centers. The absolute structure of **1** was determined by the total synthesis achieved by the Hirama group in 2001.[5a]

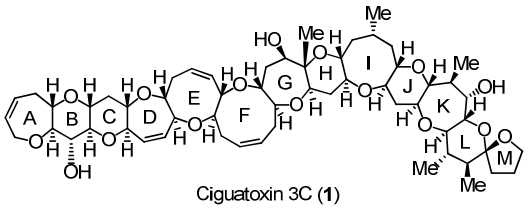

Figure 1. Structure of ciguatoxin 3C (**1**).

The potent toxicity of **1** (MLD = 1.3 μg/kg, ip, in mice) and other ciguatoxin congeners is attributed to strong activation of voltage-gated sodium channels of nerve cells by their firm binding to the channels (**1**: $Ki = 0.81 \times 10^{-4}$ μM).[6] This strong effect on sodium channels has potential for the application of ciguatoxins as biological tools. However, the supply of ciguatoxins from natural sources is insufficient to meet the demand for biological studies. Therefore, a synthetic supply of ciguatoxins is a practical solution.

In the total synthesis of ciguatoxins, the large molecular size and complexity of the structure are challenges that have been tackled by many research groups,[7,8] including our own,[9] since the first publication of the structure of ciguatoxin 1B by Yasumoto. After many years of effort, the Hirama and Isobe groups independently achieved the total synthesis of ciguatoxins with their respective methodologies.[5,8] However, to date, only these two groups have completed the total synthesis of any ciguatoxins. Thus, further studies toward the development of a new synthetic methodology for ciguatoxins have been continued by our and other research groups.

In the course of our program toward the total synthesis of **1**, we established a convergent method for constructing X/6/7/X polycyclic *trans*-fused ethers via a coupling reaction between an acyl anion equivalent and an aldehyde.[10,11] So far, we have synthesized the ABCDE-ring[9a] and the IJKL-ring[9b] of **1** by this method in preliminary studies. Since another convergent method for connecting the F- and the I-ring to afford the FGHI-ring has been developed,[9c] the next challenge is the construction of the

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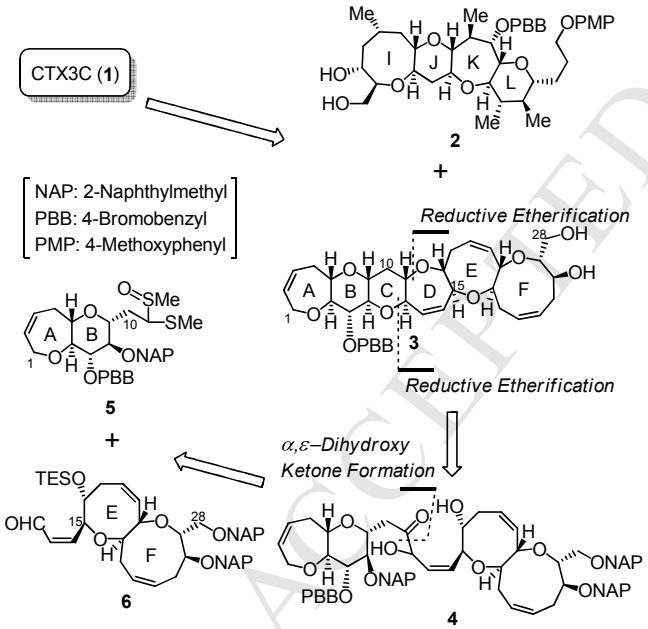
ABCDEF-ring as the counterpart of the IJKL-ring. Although the attachment of the F-ring to the ABCDE-ring failed,[12] the convergent synthesis of the ABCDEF-ring from the AB-ring and the EF-ring was achieved. Here, the details of this achievement are described. The preparation of the AB-ring from a known D-glucose derivative and the construction of the EF-ring by a process including Ireland-Claisen rearrangement and ring-closing olefin metathesis are also described.

2. Synthetic plan for ABCDEF-ring 3

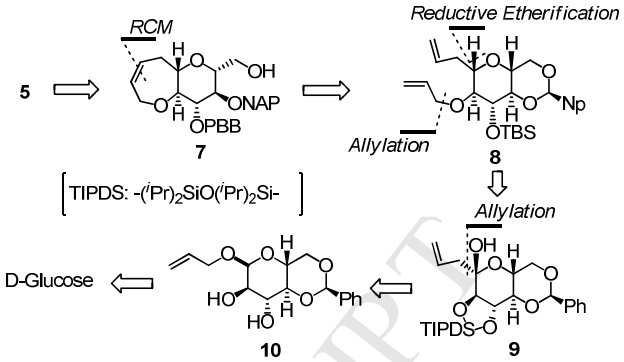
Our final goal is the achievement of the total synthesis of **1** from IJKL-ring **2** and ABCDEF-ring **3** through a process previously developed by our group (Scheme 1). Since the synthetic methodology for **2** was established previously,[9b] the completion of the synthesis of **3** is the subject of this paper. Although the attachment of a ring to the previously synthesized ABCDE-ring segment would have been the ideal access to **3**, the difficulty in manipulating protective groups of the ABCDE-ring prevented the formation of **3**.[12] Therefore, we planned to synthesize **3** from AB-ring **5** and EF-ring **6** in a convergent manner using our previously developed method.[9a] The construction of the C- and D-rings of **3** would employ a stepwise process, including intramolecular reductive etherification reactions,[13] via α,ε-dihydroxy ketone **4**, which would be constructed by a coupling reaction of an acyl anion equivalent, generated from dimethyldithioacetal mono-*S*-oxide **5**, with aldehyde **6** followed by hydrolysis.[10] The convergent route would provide rapid access to **3** from **5** and **6**.



Scheme 1. Retrosynthesis of ciguatoxin 3C (**1**).

3. Synthesis of AB-ring 5

Retrosynthesis of AB-ring **5** is shown in Scheme 2. It was planned to introduce the dimethyldithioacetal mono-*S*-oxide group of **5** to **7** at the final stage of the synthesis. The A-ring of **7** would be formed by Grubbs' ring-closing olefin metathesis (RCM)[14] from diene **8**, which would be prepared from **9** via allyl ether formation and reductive etherification of the hemiacetal. Because of the similarity of **9** to D-glucose in structure and stereochemistry, intermediate **9** would be prepared from known D-glucose derivative **10**.[15]

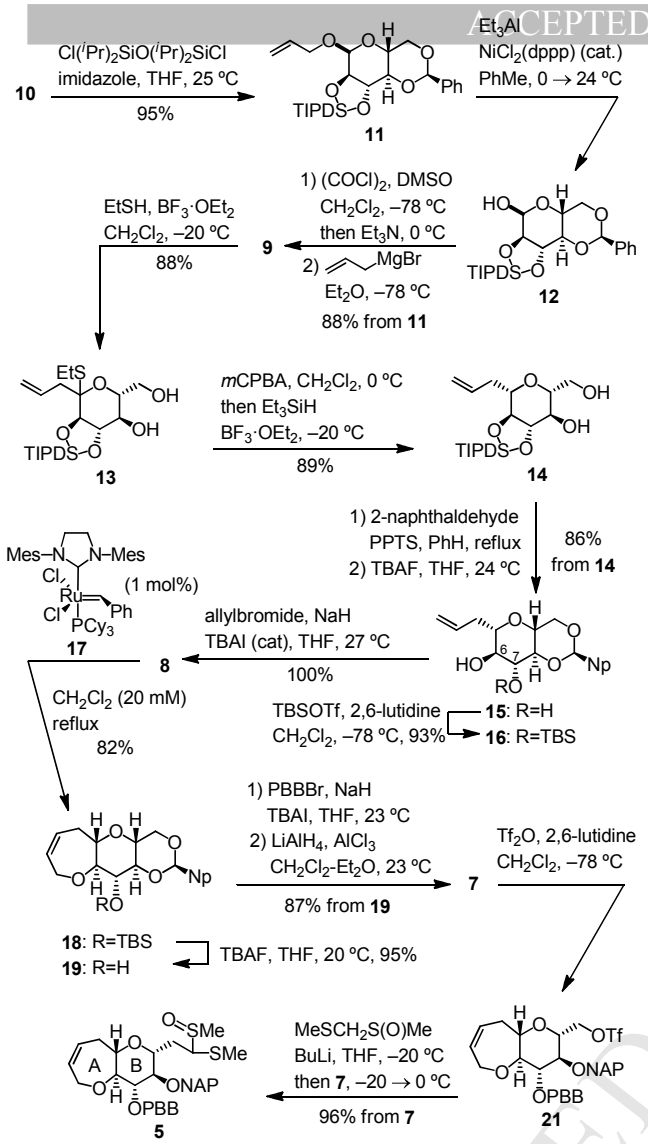


Scheme 2. Retrosynthesis of AB-ring **5**.

Based on the above retrosynthesis, synthesis of **5** began with **10** (Scheme 3). Diol **10** was first transformed to 1,1,3,3-tetraisopropyldisiloxane-1,3-diyl (TIPDS) derivative **11** (95%), which was subjected to the removal of the allyl group with $NiCl_2$(dppp) and Et_3Al to give hemiacetal **12**.[16] After Swern oxidation of **12**,[17] the resulting lactone was converted to **9** with allylmagnesium bromide (88% from **11**). Treatment of **9** with EtSH and $BF_3 \cdot OEt_2$ induced the formation of a thioacetal and the removal of the benzylidene acetal to produce *S*,*O*-acetal **13** (88%). Oxidation of the ethylthio group of **13** followed by reductive etherification with Et_3SiH and $BF_3 \cdot OEt_2$ gave oxane **14** (89%), which was subjected to protection as a 2-naphthylmethylidene acetal. Removal of the TIPDS group afforded 1,2-diol **15** (86% from **14**). Selective protection of the hydroxy group at C7 of **15** with *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) and 2,6-lutidine at –78 ºC produced **16** (93%). Alcohol **16** was reacted with allyl bromide under Williamson conditions to afford diene **8** (100%).

In the RCM reaction of **8**, 10 mol% of the first generation Grubbs catalyst[18] was first used in CH_2Cl_2 under high dilution conditions (5 mM) to give cyclized compound **18** in 80% yield.[9a] However, the conditions were inappropriate for large-scale synthesis. Therefore, after optimizing the amounts of catalyst and solvent, we found that using 1 mol% of the second generation Grubbs catalyst (**17**)[19] in CH_2Cl_2 at a higher concentration (20 mM) gave **18** in 82% yield.

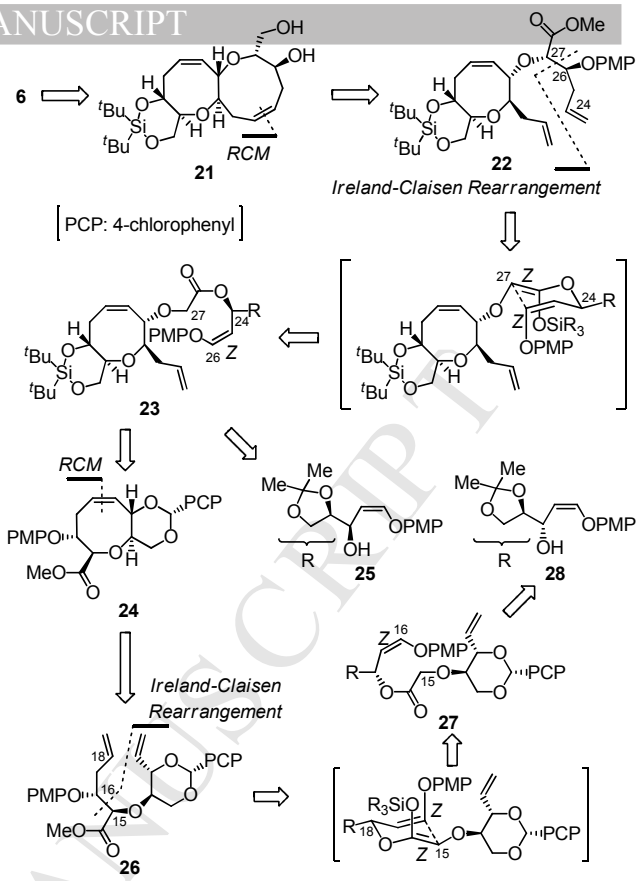
The TBS group of **18** was removed with tetrabutylammonium fluoride (TBAF) to afford alcohol **19** (85%). After the protection of **19** as a 4-bromobenzyl (PBB) ether, the 2-naphthylmethylidene acetal was reductively cleaved to produce alcohol **7** (87% from **19**).[20] Alcohol **7** was then reacted with trifluoromethanesulfonyl anhydride (Tf_2O) to give triflate **21**. In our preliminary study, triflate **21** was purified before use in the next reaction.[9a] However, we found that the instability of **21** during silica gel column chromatography resulted in decreased yield on large scale preparation. Therefore, triflate **21** was used immediately in the next reaction without purification. As a result, the reaction of **21** with deprotonated formaldehyde dimethyl dithioacetal mono-*S*-oxide cleanly afforded AB-ring **5** (96% from **7**). Thus, AB-ring **5** was furnished from D-glucose derivative **10** in 16 steps in 34% overall yield.



Scheme 3. Synthesis of AB-ring **5**.

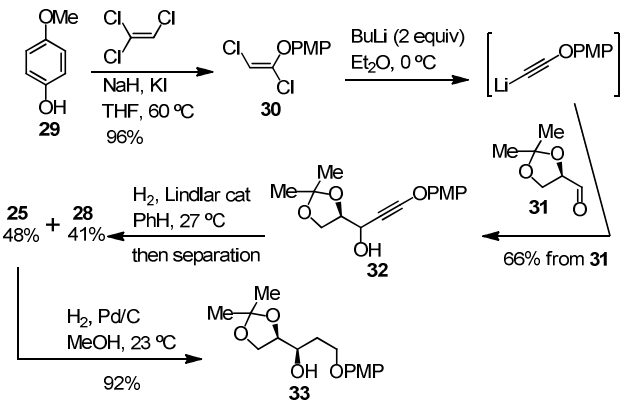
4. Synthesis of EF-ring 6

The retrosynthesis of EF-ring **6** is illustrated in Scheme 4. It was planned to construct the α,β-unsaturated aldehyde moiety of **6** from **21** at the final stage. The F-ring of **21** would be formed by RCM from divinyl compound **22**. Bond formation between asymmetric centers C26 and C27 would be performed by the Ireland-Claisen rearrangement of (*Z*)-3-aryloxyallyl ester **23**.[21,22] The chirality at C24 of **23** was anticipated to be transferred to C27 and C26 of **22** via a chair-form transition state after formation of a (*Z*)-ketene silyl acetal.[22,23] Ester **23** would be prepared from **24** and **25**. It was intended to construct the E-ring of **24** by the same process as the F-ring. Therefore, the eight-membered ring of **24** would be constructed from **26** by RCM, and the C15-C16 bond of **26** would be formed stereoselectively by the Ireland-Claisen rearrangement of (*Z*)-3-aryloxyallyl ester **27**. (*Z*)-3-Aryloxyallyl alcohol **28**, which is a constituent of **27**, is a diastereomer of **25** having the same (4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl group. Both **25** and **28** would be synthesized simultaneously from the known (*R*)-2,3-*O*-isopropylidene glyceraldehyde[24] in a non-stereoselective manner.



Scheme 4. Retrosynthesis of EF-ring **6**.

The preparation of (*Z*)-aryloxyallyl alcohols **25** and **28** is shown in Scheme 5. 4-Methoxyphenol (**29**) was treated with NaH, KI, and trichloroethylene to afford 4-methoxyphenyl (PMP) ether **30** (96%).[25] Exposure of **30** with 2 equivalents of BuLi generated a lithium acetylide,[26] which was reacted with (*R*)-2,3-*O*-isopropylidene glyceraldehyde (**31**)[24] in situ to give alcohol **32** as a 1:1 mixture of diastereomers (66% from **31**). Lindlar hydrogenation of **32** produced a 1:1 mixture of **25** (48% from **31**) and **28** (41% from **31**), which were separated by HPLC. While the (*R*)-2,2-dimethyl-1,3-dioxolan-4-yl group did not influence the stereoselectivity at the addition step, it acted as a "chiral resolving agent" to achieve efficient chromatographic separation of homochiral diastereomers **25** and **28**. The stereochemistry of **25** and **28** was confirmed by X-ray crystallographic analysis of **33** (Figure 2), which was obtained from **25** by Pd/C-catalyzed hydrogenation.



Scheme 5. Synthesis of alcohols **25** and **28**.

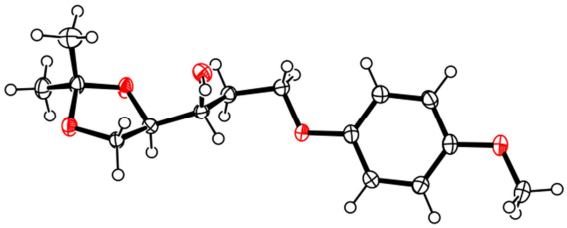
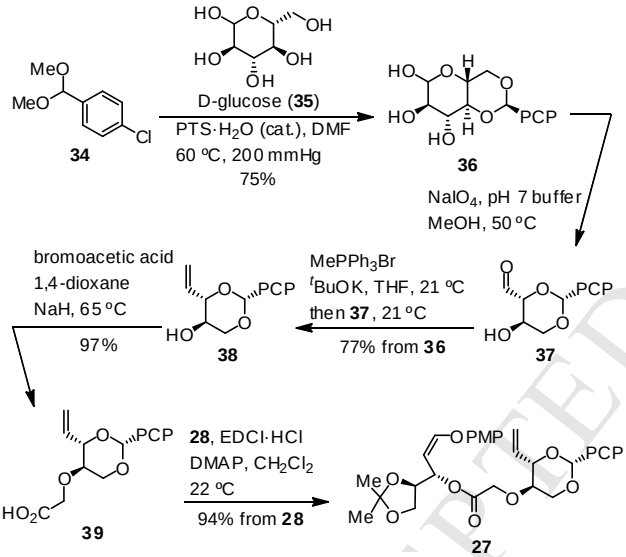


Figure 2. ORTEP diagram of **33**.

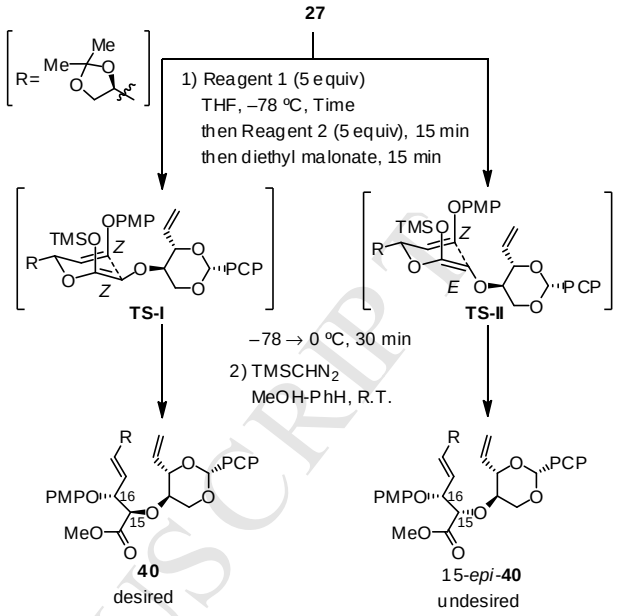
Ester **27** was synthesized from carboxylic acid **39** and alcohol **28** (Scheme 6). Carboxylic acid **39** was prepared from 4-chlorobenzylidene dimethyl acetal (**34**) and D-glucose via a 4-step process similar to the previously reported procedure (55% from **34**).[27] Thus, selective protection of the 1,3-diol at C4 and C6 of D-glucose as a 4-chlorobenzylidene acetal, oxidativecleavage by $NaIO_4$, Wittig methylenation, and formation of a carboxymethyl ether constructed **39**. Carboxylic acid **39** was then condensed with **28** using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI·HCl) and 4-dimethylaminopyridine (DMAP) to afford ester **27**[28] (94% from **28**).



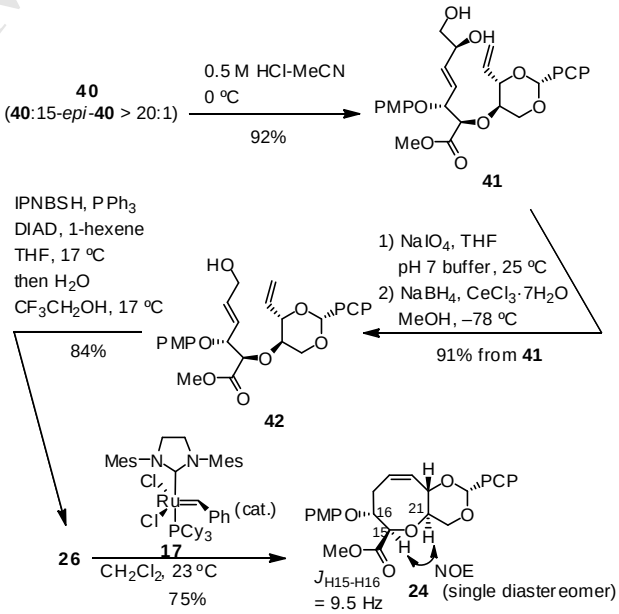
Scheme 6. Synthesis of ester **27**.

Next, we examined the Ireland-Claisen rearrangement of **27** (Table 1). Ester **27** was initially treated with potassium bis(trimethylsilyl)amide (KHMDS) (5 equiv) in tetrahydrofuran (THF) at –78 °C for 2 min, and the resulting enolate was reacted with trimethylsilyl chloride (TMSCl) (5 equiv) for 15 min.[29] After the treatment with diethyl malonate (8 equiv) to scavenge the unreacted base, the resulting ketene silyl acetal was warmed to 0 °C to complete the rearrangement. After methylation with $TMSCHN_2$,[30] 15,16-*anti* diether **40** was obtained exclusively in 65% yield (**40**:15-*epi*-**40** > 20:1) (Entry 1). Because the prolonged exposure of **27** with KHMDS (10 min) resulted in decreased yield due to decomposition of **27** (Entry 2), the time of the deprotonation of **27** was minimized. Thus, we found that the treatment of **27** with KHMDS in the presence of TMSCl improved the yield (96%) with high selectivity (**40**:15-*epi*-**40** > 20:1) (Entry 3). The stereochemistry of **40**, which was confirmed at a later stage of the synthesis, was rationalized by the selective formation of a (*Z*)-ketene silyl acetal intermediate and its rearrangement via a chair-form transition state (TS-I) under the reaction conditions.

Table 1. Ireland-Claisen rearrangement of **27**.



Entry	Reagent 1	Time	Reagent 2	Yield (2 steps)	**40**:15-*epi*-**40**
1	KHMDS	2 min	TMSCl	65%	>20 : 1
2	KHMDS	10 min	TMSCl	32%	>20 : 1
3	TMSCl	3 min	KHMDS	96%	>20 : 1

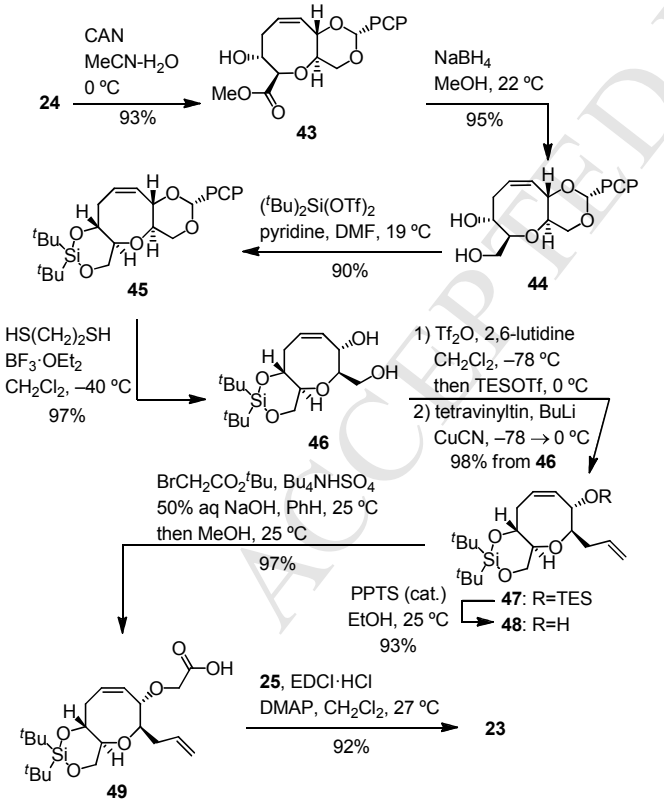


Scheme 7. Synthesis of eight-membered ring ether **24**.

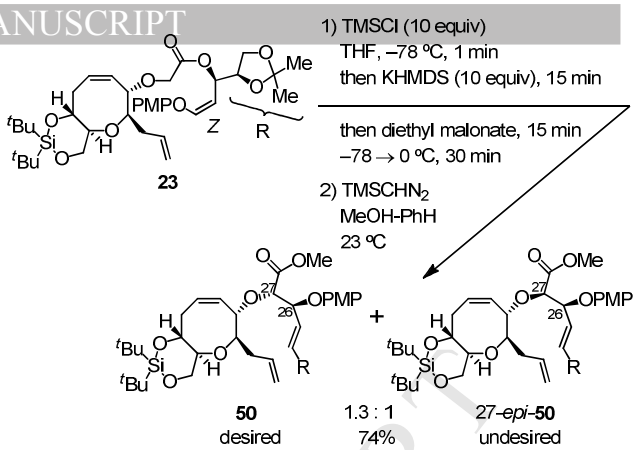
The construction of the E-ring is outlined in Scheme 7. The isopropylidene acetal of **40**, which included a small amount of 15-*epi*-**40** (**40**:15-*epi*-**40** > 20:1), was selectively hydrolyzed upon treatment with 0.5 M aqueous HCl in MeCN without removal of the 4-chlorobenzylidene acetal to afford diol **41** (92%).[31] Oxidative cleavage of diol **41** followed by Luche reduction gave allyl alcohol **42** (91% from **41**).[32] Reductive rearrangement of allyl alcohol **42** was performed with *N*-isopropylidene-*N*'-2-nitrobenzenesulfonyl hydrazine (IPNBSH)

according to Movassaghi's procedure with a slight modification, in which an excess amount of 1-hexene was used as a scavenger of free diimide generated during the reaction, to furnish diene **26** successfully (84%).[33] Diene **26** was then transformed to eight-membered ring ether **24** (75%) by RCM using the second generation Grubbs catalyst (**17**). Although diene **26** included a trace amount of 15-*epi*-**26**, the RCM reaction gave no cyclized product from 15-*epi*-**26**, which was easily separated from **24** by column chromatography. The stereochemistry of **24** was determined by the presence of a nuclear Overhauser effect (NOE) between H15 and H21, a large $J_{H15\text{-}H16}$ value (9.5 Hz), and absence of an NOE between H15 and H16, thereby also confirming the stereochemistry of the major product (**40**) from the Ireland-Claisen rearrangement step.

Toward the F-ring formation, protected cyclic ether **24** was converted to ester **23** (Scheme 8). After removal of the PMP group of **24** with cerium ammonium nitrate (CAN) (93%),[34] the resulting β-hydroxy ester **43** was reduced with $NaBH_4$ to produce 1,3-diol **44** (95%), which was converted to 1,3,2-dioxasilinane **45** (90%). The 4-chlorobenzylidene acetal group of **45** was removed with 1,2-ethanedithiol and $BF_3{\cdot}OEt_2$ to afford diol **46** (97%).[35] One-pot selective triflation/triethylsilyl (TES) protection of **46** followed by vinylation of the triflate ester gave alkene **47** (98% from **46**),[36] which was treated with pyridinium *p*-toluenesulfonate (PPTS) in EtOH to produce alcohol **48** (93%). Etherification of **48** with *tert*-butyl bromoacetate under phase-transfer conditions and subsequent one-pot hydrolysis by simple addition of methanol as a solvent afforded glycolic acid **49** (97%). Condensation of **49** with alcohol **25** afforded (*Z*)-3-aryloxyallyl ester **23** (92%).[28]

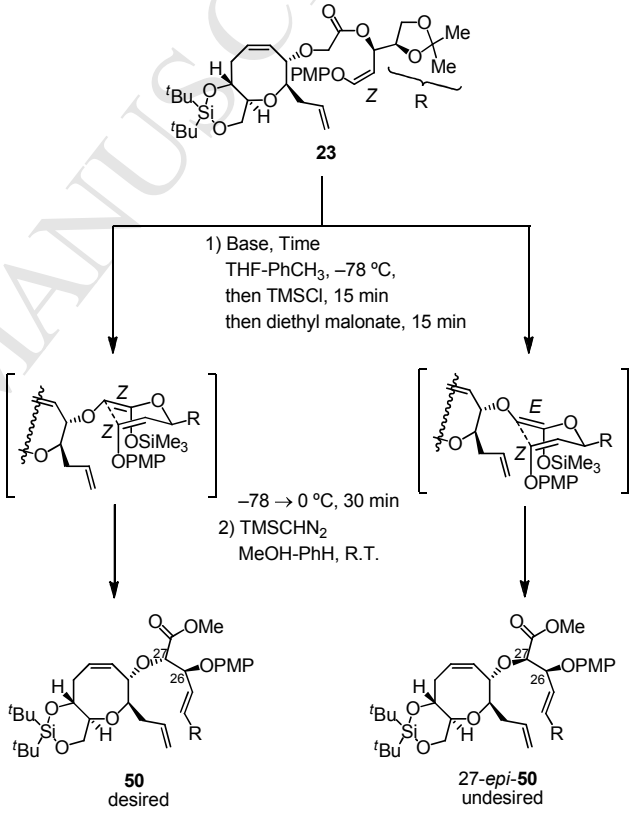


Scheme 8. Synthesis of ester **23**.



Scheme 9. Ireland-Claisen rearrangement of **23** using KHMDS.

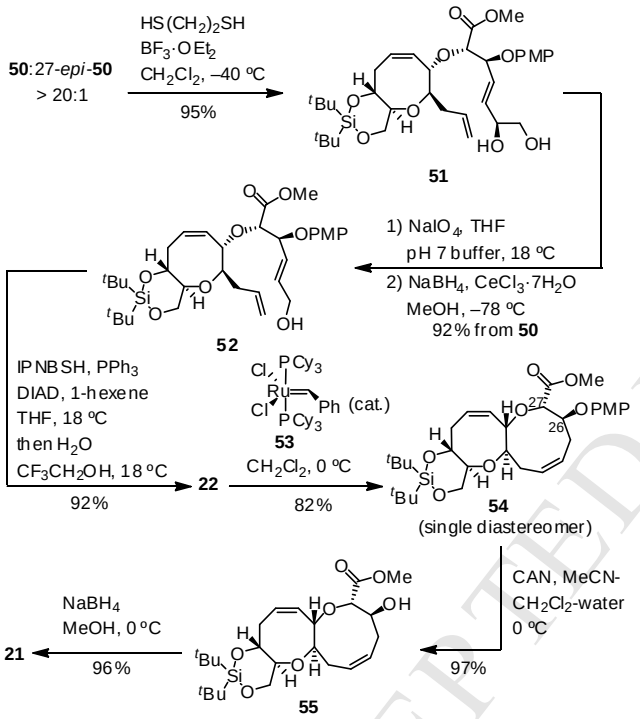
Table 2. Ireland-Claisen rearrangement of **23**.



Entry	Base	Time	Yield (2 steps)	**50**:27-*epi*-**50**
1	LDA	1 min	No Reaction	
2	KHMDS	4 min	28%	2.0:1
3	LDA - KHMDS (1:1)	2 min	93%	1.7:1
4	Et_2NLi - KHMDS (1:1)	1 min	87%	13:1
5	N–Li -KHMDS (1:1)	6.5 min	89%	> 20:1

At the initial stage of the F-ring formation, rearrangement of **23** was first examined under the same conditions as that of **27** (Scheme 9). However, the desired 26,27-*anti* diether from **23** was produced with low stereoselectivity (**50**:27-*epi*-**50** = 1.3:1, 74% combined yield). Upon optimization of the reaction conditions, we found that the selectivity of **50** was improved by modification of the procedure for the enolate formation (Table 2). The enolate

formation from **23** by the treatment with lithium diisopropylamide (LDA) for 1 min and then with TMSCl for 15 min, which was followed by the rearrangement step under the same conditions as above, resulted in recovery of **23** (Entry 1). However, the use of KHMDS instead of LDA produced **50** in low yield with improved stereoselectivity (**50**:27-*epi*-**50** = 2.0:1, 28% combined yield) (Entry 2). Exposure of **23** to the combination of KHMDS (6 equiv) and LDA (6 equiv) as a base in toluene-THF (3.4:1) at –78 °C for 2 min produced **50** somewhat selectively in improved yield (**50**:27-*epi*-**50** = 1.7:1, 93% combined yield) (Entry 3). Interestingly, small lithium amide bases in place of LDA displayed good results: KHMDS-$LiNEt_2$ (6 equiv/6 equiv) showed a ratio of **50**:27-*epi*-**50** = 13:1 (Entry 4) and KHMDS-lithium pyrrolidinide (6 equiv/6 equiv) gave a ratio of **50**:27-*epi*-**50** > 20:1 (Entry 5).[37,38] Thus, we optimized conditions for the stereoselective Ireland-Claisen rearrangement of **23** to **50**, and established the chiral centers at C26 and C27.



Scheme 10. Synthesis of EF-ring diol **21**.

Synthesis of EF-ring diol **21** is outlined in Scheme 10. The second ring was constructed using a procedure similar to that described above. The acetonide group of **50** was removed by $BF_3 \cdot OEt_2$/1,2-ethanedithiol (95%). The oxidative cleavage of 1,2-diol **51** followed by Luche reduction gave allyl alcohol **52** (92% from **51**), which was transformed to **22** by reductive rearrangement (92%). The divinyl compound **22** was cyclized by RCM with the first generation Grubbs catalyst (**53**)[18] at 0 °C to produce bicyclic ether **54** (82%). When the RCM was conducted at higher temperature (> room temperature), significant production of byproducts was observed. The stereochemistry at C26 and C27, generated by the Ireland-Claisen rearrangement, was determined at this stage by X-ray crystallographic analysis (Figure 3). The PMP group of **54** was removed with CAN to afford alcohol **55** (97%),[Error! Bookmark not defined.34] which was reduced with $NaBH_4$ to give EF-ring diol **21** (96%).

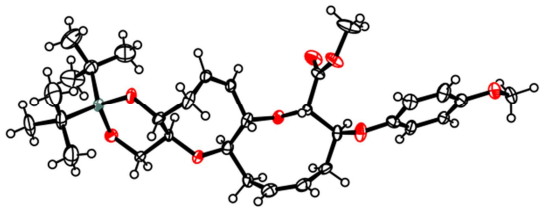
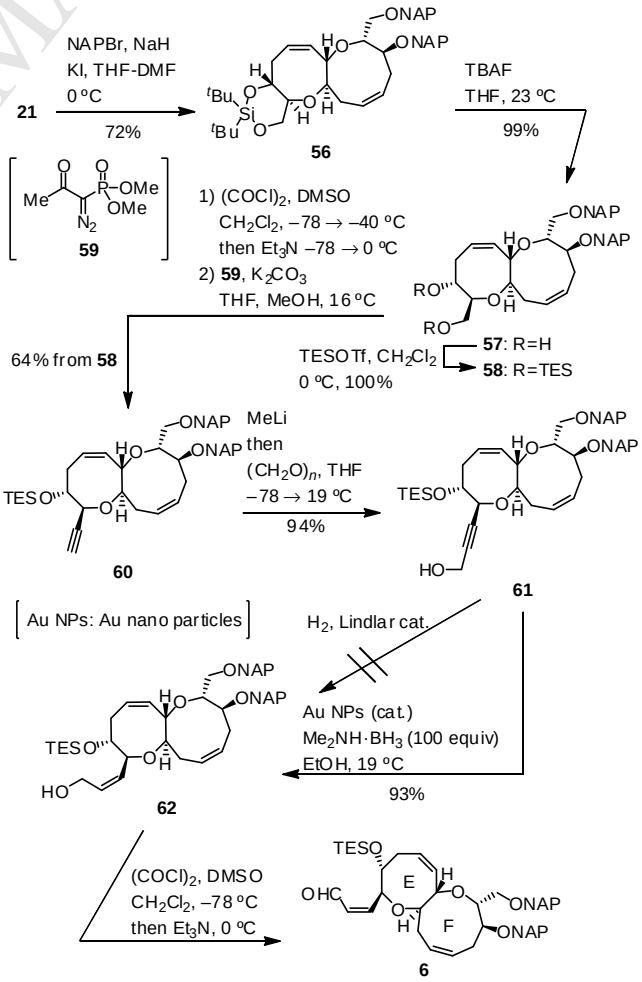


Figure 3. ORTEP diagram of **54**: one of the two crystallographically independent molecules is shown.

EF-ring segment **6**, a key synthetic intermediate for **3**, was prepared from **21** as shown in Scheme 11. After the 1,3-diol group of **21** was protected with 2-naphthylmethyl bromide (NAPBr) (72%), the cyclic silylene group of resulting **56** was removed with TBAF to give diol **57** (99%), which was converted to bis-TES ether **58** upon treatment with TESOTf and 2,6-lutidiene (100%). The regioselective oxidation of **58** under Swern conditions generated an aldehyde,[39] which was alkynylated using Ohira-Bestmann's reagent to afford alkyne **60** (64% from **58**).[40] The treatment of **60** with MeLi generated a lithium acetylide, which was reacted in situ with paraformaldehyde to give alcohol **61** (94%). While partial hydrogenation of **61** with Lindlar catalyst was sluggish and afforded only a trace amount of **62**, Au nanoparticles (AuNPs) catalyzed the hydrogenation of **61** to cleanly provide (*Z*)-alkene **62** in 93% yield.[41] Finally, Swern oxidation of **62** produced aldehyde **6** (100%).[17] Thus, we achieved the synthesis of EF-ring **6** from carboxylic acid **39** over 36 steps by a sequential process including Ireland-Claisen rearrangement and RCM.

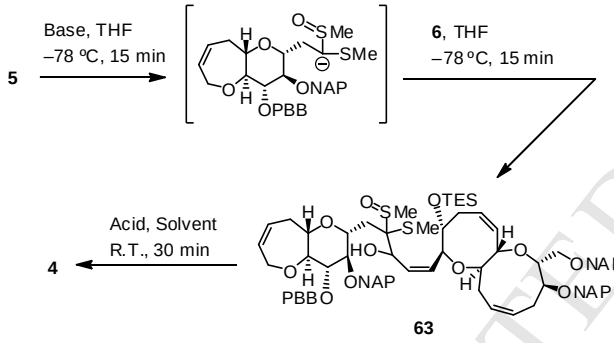


Scheme 11. Synthesis of EF-ring **6**.

5. Synthesis of ABCDEF-ring 3

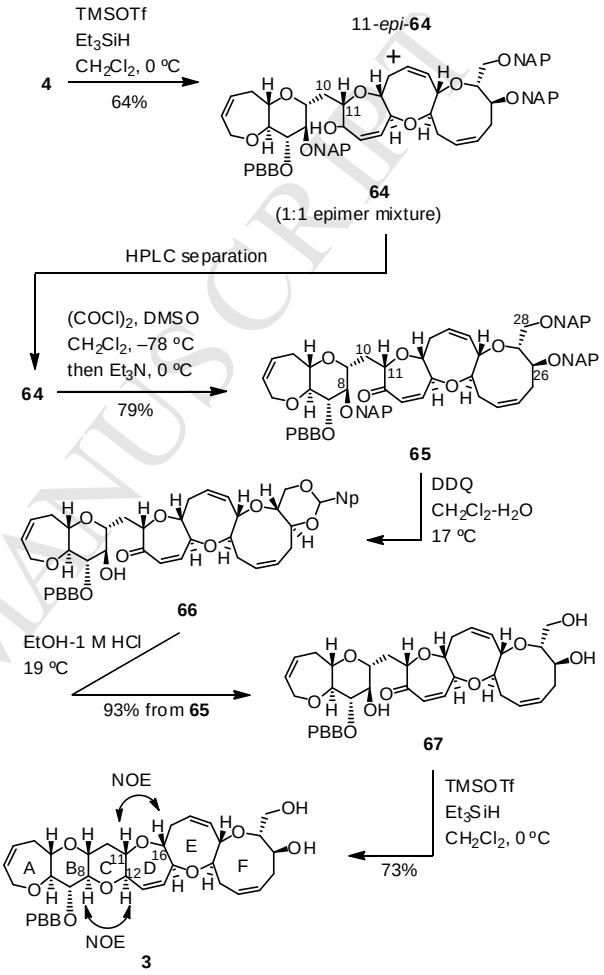
With the AB-ring **5** and EF-ring **6** in hand, we next undertook the completion of the synthesis of ABCDEF-ring **3**. First, we investigated the coupling reaction of **5** with **6** followed by the transformation of resulting adduct **63** into α,ε-dihydroxy ketone **4** (Table 3). Treatment of dimethyldithioacetal mono-*S*-oxide **5** with lithium bis(trimethylsilyl)amide (LiHMDS) in THF at −78 °C for 15 min and then with aldehyde **6** for 15 min only resulted in decomposition of aldehyde **6** with almost complete recovery of **5** (Entry 1). After extensive optimization of the reaction conditions using model compounds, we found that the deprotonation of **5** with sodium bis(trimethylsilyl)amide (NaHMDS) gave the corresponding anion species and that the hydrolysis of the dimethyldithioacetal mono-*S*-oxide group of the adduct proceeded smoothly with *p*-toluenesulfonic acid monohydrate (PTS·H_2O) in CH_2Cl_2-MeOH. Thus, the anion generated from AB-ring **5** and NaHMDS reacted with aldehyde **6** to give **63** cleanly. However, the hydrolysis of **63** with PTS·H_2O in CH_2Cl_2-MeOH gave **4** only in 19% yield from alcohol **62** along with unknown byproducts (Entry 2). After further optimization of the solvent in the hydrolysis, we found that the treatment of **63** with PTS·H_2O in CF_3CH_2OH-H_2O produced α,ε-dihydroxy ketone **4** in an acceptable yield (40% from **62**, Entry 3). Thus, we ensured a sufficient supply of α,ε-dihydroxy ketone **4**.

Table 3. Coupling between AB-ring **5** and EF-ring **6** and hydrolysis of adduct **63**.



Entry	Base	Acid	Solvent	Yield from **62**
1	LiHMDS	TFA	THF-H_2O	decomp
2	NaHMDS	PTS·H_2O	CH_2Cl_2-MeOH	19%
3	NaHMDS	PTS·H_2O	CF_3CH_2OH-H_2O	40%

The completion of the synthesis of ABCDEF-ring **3** from α,ε-dihydroxy ketone **4** is illustrated in Scheme 12. Intramolecular reductive etherification of **4** with Et_3SiH and TMSOTf afforded a 1:1 mixture of **64** and 11-*epi*-**64** (64%), and the desired **64** was separated from 11-*epi*-**64** by HPLC. Swern oxidation of **64** gave ketone **65** (79%).[17] Alcohol 11-*epi*-**64** also oxidized into the corresponding ketone 11-*epi*-**65**, which was isomerized with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in CH_2Cl_2 to produce a 3:1 mixture of **65** and 11-*epi*-**65** in a small scale experiment.[42] Ketone **65** was treated with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) in order to detach the NAP groups at O8, O26, and O28.[43] However, the formation of a 2-naphthylidene acetal between O26 and O28 occurred even though the NAP group at O8 was removed. Therefore, the resulting acetal **66** was then hydrolyzed under acidic conditions to afford trihydroxy ketone **67** (93% from **64**),[44] which was finally subjected to reductive cyclization to produce hexacyclic ether **3** (73%). The stereochemistry of C11 and C12, generated in the reductive etherification steps, was confirmed by the presence of NOEs between H11 and H16, and between H8 and H12. Moreover, after extensive attempts at recrystallization, we obtained a single crystal of **3**, which was subjected to X-ray crystallographic analysis to determine the stereochemistry of **3** as shown in Figure 4. Thus, we achieved the convergent synthesis of ABCDEF-ring **3** in 6.9% yield over 7 steps from EF-ring **6**.



Scheme 12. Synthesis of ABCDEF-ring **3**.

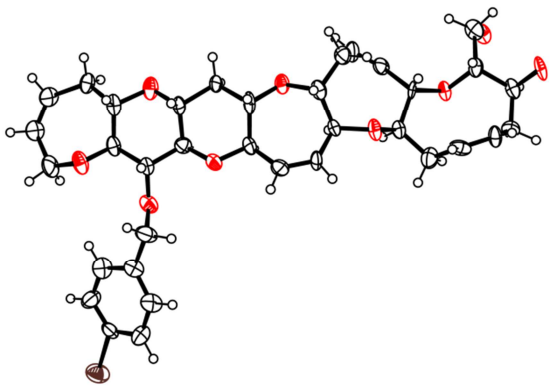


Figure 4. ORTEP diagram of **3**.

6. Conclusion

The synthesis of the ABCDEF-ring (**3**) of ciguatoxin 3C (**1**) was achieved via a route including anion coupling of a dimethyldithioacetal mono-*S*-oxide derivative (**5**) corresponding to the AB-ring and an aldehyde (**6**) corresponding to the EF-ring, followed by cyclization using reductive etherification. AB-ring **5** was synthesized from known D-glucose derivative **10** based on ring-closing olefin metathesis, and EF-ring **6** was prepared by a process employing chirality-transferring Ireland-Claisen rearrangement and ring-closing olefin metathesis. Further studies toward the total synthesis of **1** are currently underway in our laboratory.

7. Experimental

All air sensitive reactions were carried out under argon or nitrogen in oven-dried glassware using standard syringe, cannula and septa techniques. Anhydrous tetrahydrofuran (THF) was prepared by Glass Contour Solvent Dispensing System (Nikko Hansen & Co., Ltd.) or purchased from commercial source. Other dry solvents were purchased from commercial sources. All reactions were monitored by thin-layer chromatography (TLC) with precoated silica gel 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. Column chromatography was performed on YMC Silica Gel 60 (63-40 μm for flash chromatography, 230-63 μm for gravity chromatography) as a stationary phase. High-performance liquid chromatography (HPLC) was performed on a JASCO 880-PU HPLC pump equipped with a pre-packed column (YMC-Pack SIL-06, 5 μm, 150 mm × 4.6 mm ID [for normal-phase chromatography], or YMC-Pack SIL-06, 5 μm, 500 mm × 20 mm ID [for normal-phase chromatography]) and a JASCO UV-975 UV detector (UV 254 nm detection). Optical rotations were recorded on a JASCO P-1020 digital polarimeter at 589 nm. Infrared spectra (IR) were measured on a JEOL JIR-WINSPEC100 infrared spectrometer in noted states and are reported in wave numbers (cm^{-1}). ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JNM-AL300 (^{1}H at 300 MHz, ^{13}C at 75 MHz), a JEOL JNM-α-400 (^{1}H at 400 MHz, ^{13}C at 100 MHz), a JEOL JNM-ECA500 (^{1}H at 500 MHz, ^{13}C at 125 MHz), a Bruker AVANCE III 400 (^{1}H at 400 MHz, ^{13}C at 100 MHz), or a Bruker AMX500 (^{1}H at 500 MHz, ^{13}C at 125 MHz) magnetic resonance spectrometer. Chemical shifts (δ) are reported in ppm based on the resonance of the residual solvent (3.30 ppm in CD_3OD or 7.15 ppm in C_6D_6, ^{13}C NMR: 49.0 ppm in CD_3OD or 128.0 ppm in C_6D_6) as the internal standard. 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, td= triple doublets and ddd= double double doublets; other combination is derived from those listed. Coupling constants (*J*) are reported in Hz. High resolution mass spectra (HRMS) were measured on a JEOL JMS-600H (under electron impact ionization [EI] conditions), a JEOL JMS-SX102A (under field desorption [FD] conditions), a JEOL JMS-700TZ (under field desorption [FD] conditions), or a JEOL JMS-T100GCV (under field desorption [FD] conditions) double focusing magnetic sector mass spectrometer. Several HRMS data were recorded under electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI) conditions on a Thermo Scientific Exactive Fourier transform ion cyclotron resonance mass spectrometer.

7.1.1. (5a*S*,5b*R*,7*R*,9a*R*,11a*R*)-11-(Allyloxy)-2,2,4,4-tetraisopropyl-7-phenylhexahydro[1,3]dioxino[4',5':5,6]pyrano[3,4-*f*][1,3,5,2,4]trioxadisilepine (11).

To a solution of **10** (43.23 g, 0.1402 mol) in DMF (280 ml) were added imidazole (22.91 g, 0.3365 mol) and $ClSi(^iPr)_2O(^iPr)_2SiCl$ (55.0 mL, 0.172 mol) at 25 ºC, and the mixture was stirred for 13 h. Then, the reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc = 50 → 20 → 10) to give **11** (73.12 g, 0.1327 mol, 95%, α-anomer:β-anomer = 2:1) as a colorless oil.

11: colorless oil; IR (film) ν 2944, 2867, 1464, 1382, 1248, 1212, 1176, 1142, 1091, 1048, 990, 923, 886, 847, 746, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.90-1.17 (28H, m), 3.39 (1/3H, dt, *J* = 4.5, 9.5 Hz), 3.49 (2/3H, t, *J* = 9.5 Hz), 3.54 (1/3H, t, *J* = 9.5 Hz), 3.63 (1/3H, t, *J* = 7.8 Hz), 3.73 (2/3H, t, *J* = 10.2 Hz), 3.76-3.83 (1H, m), 3.85-3.93 (1H, m), 4.06 (2/3H, tdd, *J* = 1.5, 5.6, 13.5 Hz), 4.13-4.18 (4/3H, m), 4.21 (1/3H, tdd, *J* = 1.7, 4.9, 13.6 Hz), 4.28 (2/3H, dd, *J* = 4.7, 10.0 Hz), 4.32-4.39 (2/3H, m), 4.45 (1/3H, d, *J* = 7.5 Hz), 4.86 (2/3H, d, *J* = 3.8 Hz), 5.18 (1H, qd, *J* = 1.4, 10.5 Hz), 5.35 (1/3H, qd, *J* = 1.7, 17.3 Hz), 5.36 (2/3H, qd, *J* = 1.7, 17.3 Hz), 5.55 (1H, s), 5.85-5.94 (1H, m), 7.30-7.37 (3H, m), 7.46-7.51 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.3 (CH), 12.46 (CH×2/3), 12.53 (CH×1/3), 12.9 (CH×1/3), 13.0 (CH), 13.2 (CH×2/3), 17.18 (CH_3×2/3), 17.21 (CH_3×1/3), 17.23 (CH_3×1/3), 17.28 (CH_3), 17.33 (CH_3), 17.35 (CH_3×2/3), 17.37 (CH_3×1/3), 17.40 (CH_3×2/3H), 17.42 (CH_3×1/3), 17.45 (CH_3), 17.47 (CH_3×1/3), 17.6 (CH_3×2/3), 17.7 (CH_3×2/3), 62.5 (CH×2/3), 66.3 (CH×1/3), 68.8 (CH_2×2/3), 68.9 (CH_2×1/3), 69.3 (CH_2×2/3), 70.9 (CH_2×1/3), 73.3 (CH×2/3), 76.0 (CH×2/3), 76.8 (CH×1/3), 77.9 (CH×1/3), 80.6 (CH×1/3), 81.7 (CH×2/3), 98.9 (CH×2/3), 101.1 (CH×1/3), 101.2 (CH×2/3), 103.1 (CH×1/3), 117.0 (CH_2×2/3), 117.1 (CH_2×1/3), 126.0 (CH×2), 128.2 (CH×2), 128.78 (CH×2/3), 128.83 (CH×1/3), 134.11 (CH×1/3), 134.13 (CH×2/3), 137.2 (C×1/3), 137.9 (C×2/3); EI-HRMS (m/z) calcd for $C_{25}H_{39}O_7Si_2$ $[M - {}^iPr]^+$: 507.2234, found: 507.2232.

7.1.2. (5a*S*,5b*R*,7*R*,9a*R*,11a*R*)-11-Allyl-2,2,4,4-tetraisopropyl-7-phenylhexahydro[1,3]dioxino[4',5':5,6]pyrano[3,4-*f*][1,3,5,2,4]trioxadisilepin-11-ol (9).

To a solution of **11** (50.90 g, 92.41 mmol) and $NiCl_2$(dppp) (1.008 g, 1.860 mmol) was added Et_3Al (0.92 mol/L in $PhCH_3$, 200 mL, 0.184 mol) at 0 ºC, and the mixture was stirred for 3 h at 28 ºC. Then, the reaction was quenched with saturated aq. potassium sodium tartrate, and the mixture was stirred for 13 h at 28 ºC. The mixture was extracted with Et_2O several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give crude **12**, which was used in the next reaction without purification.

To a solution of $(COCl)_2$ (25.0 mL, 0.291 mol) in CH_2Cl_2 (240 mL) was added a solution of DMSO (33.0 mL, 0.465 mol) in CH_2Cl_2 (240 mL) dropwise at –78 ºC, and the mixture was stirred for 15 min. Then, to the mixture was added a solution of the above crude **12** in CH_2Cl_2 (50 mL) at –78 ºC, and the mixture was stirred for 30 min. To the mixture was added Et_3N (130 mL, 0.925 mol) at –78 ºC, and the mixture was warmed to 0 ºC. After being stirred for 30 min, the reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with Et_2O several times. The combined organic layers were washed with 0.2 mol/L aq. HCl, H_2O, and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude product, which was used in the next reaction without purification.

To a solution of the above crude product in Et_2O (1.9 L) was added dropwise allylmagnesium bromide (1.0 mol/L in Et_2O, 186 mL, 186 mmol) at –78 ºC, and the mixture was stirred for 30 min. Then, the reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 15) to give **9** (44.83 g, 81.39 mmol, 88% from **11**) as a colorless oil.

9: $[\alpha]_D^{30}$ –17.3 (*c* 1.50, $CHCl_3$); IR (neat) ν 3552, 3075, 3036, 2945, 2894, 2867, 1464, 1386, 1247, 1179, 1137, 1092, 991, 919, 886, 861, 817, 749, 698, 653, 520 cm^{-1}; 1H NMR (400 MHz, $CDCl_3$) δ 1.06 (28H, m), 2.43 (1H, dd, *J* = 5.5, 14.2 Hz), 2.56 (1H, dd, *J* = 7.2, 14.2 Hz), 3.12 (1H, s), 3.49 (1H, t, *J* = 9.6 Hz), 3.69 (1H, d, *J* = 8.3 Hz), 3.71 (1H, t, *J* = 10.2 Hz), 3.97-4.02 (1H, m), 4.05 (1H, dd, *J* = 8.3, 9.6 Hz), 4.31 (1H, dd, *J* = 4.9, 10.2 Hz), 5.16 (1H, dd, *J* = 1.7, 17.2 Hz), 5.20 (1H, dd, *J* = 1.7, 10.2 Hz), 5.55 (1H, s), 5.89 (1H, tdd, *J* = 7.2, 10.2, 17.2 Hz), 7.29-7.37 (3H, m), 7.48 (2H, dd, *J* = 2.8, 7.8 Hz); 13C NMR (100 MHz, $CDCl_3$) δ 12.1 (CH), 12.3 (CH), 12.7 (CH), 13.0 (CH), 17.0 (CH_3), 17.1 (CH_3), 17.2 (CH_3), 17.26 (CH_3), 17.34 (CH_3), 17.4 (CH_3), 17.46 (CH_3), 17.51 (CH_3), 43.2 (CH_2), 63.1 (CH), 69.0 (CH_2), 74.2 (CH), 78.2 (CH), 80.7 (CH), 98.5 (C), 101.0 (CH), 119.6 (CH_2), 125.9 (CH×2), 128.0 (CH×2), 128.6 (CH), 131.9 (CH), 137.6 (C); EI-HRMS (m/z) calcd for $C_{25}H_{39}O_7Si_2$ [M – ^{i}Pr]$^+$: 507.2234, found: 507.2281.

7.1.3. (5a*R*,8*R*,9*R*,9a*S*)-6-Allyl-6-(ethylthio)-8-(hydroxylmethyl)-2,2,4,4-tetraisopropyltetrahydro-*6H*-pyrano[3,4-*f*][1,3,5,2,4]trioxadisilepin-9-ol (13). To a solution of **9** (55.61 g, 100.9 mmol) and EtSH (37.4 mL, 505 mmol) in CH_2Cl_2 (500 mL) was added $BF_3{\cdot}OEt_2$ (25.3 mL, 202 mmol) at –20 ºC, and the mixture was stirred for 20 min. Then, the reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 3) to give **13** (45.12 g, 89.02 mmol, 88%) as a colorless solid.

13: mp 69-71 ºC; $[\alpha]_D^{30}$ +56.0 (*c* 0.980, $CHCl_3$); IR (KBr) ν 3576, 3431, 2943, 2886, 1465, 1378, 1250, 1165, 1120, 1086, 1051, 1003, 986, 931, 885, 855, 823, 693, 632, 620, 586 cm^{-1}; 1H NMR (400 MHz, $CDCl_3$) δ 1.06 (30H, m), 1.23 (3H, t, *J* = 7.5 Hz), 1.94 (1H, dd, *J* =5.5, 7.9 Hz), 2.34-2.55 (3H, m), 2.78 (2H, brd, *J* = 6.6 Hz), 3.49 (1H, dt, *J* = 2.2, 9.4 Hz), 3.75-3.92 (4H, m), 4.11 (1H, t, *J* = 8.5 Hz), 5.10 (1H, brs), 5.14 (1H, brdd, *J* = 1.6, 3.4 Hz), 5.82-5.93 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.20 (CH), 12.22 (CH), 12.6 (CH), 12.9 (CH), 14.3 (CH_3), 17.0 (CH_3), 17.1 (CH_3), 17.3 (CH_3), 17.40 (CH_3), 17.41 (CH_3), 17.5 (CH_3), 17.57 (CH_3), 17.59 (CH_3), 19.9 (CH_2), 43.6 (CH_2), 62.8 (CH_2), 71.3 (CH), 72.5 (CH), 76.8 (CH), 77.9 (CH), 91.5 (C), 118.4 (CH_2), 133.0 (CH); EI-HRMS (m/z) calcd for $C_{21}H_{41}O_6Si_2$ [M – SEt]$^+$: 445.2441, found: 445.2446.

7.1.4. (5a*S*,6*S*,8*R*,9*R*,9a*S*)-6-Allyl-8-(hydroxymethyl)-2,2,4,4-tetraisopropyltetrahydro-*6H*-pyrano[3,4-*f*][1,3,5,2,4]trioxa-disilepin-9-ol (14). To a solution of **13** (44.27 g, 87.35 mmol) in CH_2Cl_2 (440 mL) was added *m*CPBA (30.16 g, 174.5 mmol) at 0 ºC, and the mixture was stirred for 1 h. Then, to the mixture were added Et_3SiH (84.0 mL, 526 mmol) and $BF_3{\cdot}OEt_2$ (66.0 mL, 525 mmol) at –20 ºC, and the mixture was stirred for 30 min. Then, the reaction was quenched with 2.0 mol/L aq. NaOH and saturated aq. $Na_2S_2O_3$, and the mixture was filtered through a Celite pad. The filtrate was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5) to give **14** (34.86 g, 78.03 mmol, 89%) as a colorless oil.

14: $[\alpha]_D^{30}$ –21.8 (*c* 1.67, $CHCl_3$); IR (neat) ν 3418, 3076, 2944, 2867, 2758, 2725, 1643, 1464, 1432, 1413, 1387, 1366, 1287, 1248, 1140, 990, 915, 886, 841, 701, 606, 564, 444 cm^{-1}; 1H NMR (400 MHz, $CDCl_3$) δ 1.05 (28H, m), 2.14-2.23 (1H, m), 2.41 (1H, brs), 2.63 (1H, brdd, *J* = 1.4, 6.5 Hz), 3.28-3.38 (2H, m), 3.40 (1H, t, *J* = 9.4 Hz), 3.48 (1H, t, *J* = 9.4 Hz), 3.61 (1H, t, *J* = 8.4 Hz), 3.73 (1H, dd, *J* = 5.4, 11.6 Hz), 3.89 (1H, brdd, *J* = 3.2, 11.6 Hz), 5.08 (2H, dt, *J* = 1.8, 17.2 Hz), 5.88 (1H, tdd, *J* = 6.8, 10.2, 17.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1 (CH), 12.2 (CH), 12.79 (CH), 12.82 (CH), 17.2 (CH_3), 17.25 (CH_3), 17.31 (CH_3), 17.32 (CH_3), 17.36 (CH_3), 17.43 (CH_3×3), 36.1 (CH_2), 63.0 (CH_2), 71.6 (CH), 76.1 (CH), 78.1 (CH), 79.5 (CH), 81.4 (CH), 116.9 (CH_2), 134.8 (CH); EI-HRMS (m/z) calcd for $C_{18}H_{35}O_6Si_2$ [M – ^{i}Pr]$^+$: 403.1972, found: 403.1961.

7.1.5. (2*R*,4a*R*,6*S*,7*R*,8*R*,8a*S*)-6-Allyl-2-(naphthalen-2-yl)hexahydropyrano[3,2-*d*][1,3]dioxine-7,8-diol (15). To a solution of **14** (23.08 g, 51.66 g) in PhH (300 mL) were added 2-naphthaldehyde (16.16 g, 103.4 mmol) and PPTS (1.300 g, 5.173 mmol) at 24 ºC, and the mixture was stirred and heated to reflux with removal of H_2O by a Dean-Stark apparatus. After being stirred for 3 h, the mixture was cooled to 24 ºC, and the reaction was quenched with saturated aq. $NaHCO_3$. Then, the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude product, which was used in the next reaction without purification.

To a solution of the above crude product in THF (260 mL) was added TBAF (1.0 mol/L in THF, 130 mL, 129 mmol) at 0 ºC, and the mixture was stirred for 40 min at 24 ºC. Then, the reaction was quenched with H_2O, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10 → 2 → 1) to give **15** (15.18 g, 44.34 mmol, 86% from **14**) as a colorless solid.

15: mp 144-146 ºC; $[\alpha]_D^{19}$ –27.8 (*c* 0.270, $CHCl_3$); IR (KBr) ν 3447, 3071, 2976, 2867, 1641, 1476, 1435, 1377, 1345, 1328, 1272, 1213, 1179, 1128, 1094, 1078, 1009, 982, 951, 922, 900, 861, 823, 809, 798, 748, 608, 561, 502, 477 cm^{-1}; 1H NMR (400 MHz, $CDCl_3$) δ 2.26 (1H, brtd, *J* = 6.0, 13.5 Hz), 2.57 (1H, brdd, *J* = 6.6, 14.6 Hz), 2.72 (1H, brs), 3.07 (1H, brs), 3.35-3.51 (4H, m), 3.68-3.76 (2H, m), 4.34 (1H, dd, *J* = 5.0, 10.9 Hz), 5.11 (2H, dt, *J* = 1.4, 17.1 Hz), 5.65 (1H, s), 5.87 (1H, tdd, *J* =7.0, 10.2, 17.2 Hz), 7.47-7.52 (2H, m), 7.59 (1H, dd, *J* = 1.5, 8.5 Hz), 7.81-7.87 (3H, m), 7.96 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.0 (CH_2), 68.9 (CH_2), 70.2 (CH), 73.9 (CH), 75.3 (CH), 79.2 (CH), 81.1 (CH), 101.9 (CH), 117.5 (CH_2), 123.7 (CH), 125.8 (CH), 126.3 (CH), 126.5 (CH), 127.7 (CH), 128.29 (CH), 128.33 (CH), 132.9 (C), 133.7 (C), 134.0 (CH), 134.3 (C); EI-HRMS (m/z) calcd for $C_{20}H_{22}O_5$ [M]$^+$: 342.1467, found: 342.1460.

7.1.6. (2*R*,4a*R*,6*S*,7*S*,8*R*,8a*R*)-6-Allyl-8-((*tert*-butyldimethylsilyl)oxy)-2-(naphthalen-2-yl)hexahydropyrano[3,2-*d*][1,3]dioxin-7-ol (16). To a solution of **15** (318.0 mg, 0.9288 mmol) and 2,6-lutidine (0.325 mL, 2.81 mmol) in CH_2Cl_2 (5 mL) was added TBSOTf (0.320 mL, 1.39

mmol) at –78 ºC, and the mixture was stirred for 30 min. The reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10) to give **16** (392.6 mg, 0.8597 mmol, 93%) as a colorless solid.

16: mp 87-88 ºC; $[\alpha]_D^{20}$ –65.9 (*c* 0.210, $CHCl_3$); IR (KBr) ν 3573, 3064, 2951, 2931, 2901, 2855, 1640, 1472, 1388, 1248, 1174, 1128, 1101, 1075, 1020, 911, 857, 778, 670, 473 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.04 (3H, s), 0.11 (3H, s), 0.88 (9H, s), 2.27 (1H, d, *J* = 2.5 Hz), 2.32 (1H, quin, *J* = 7.5 Hz), 2.64 (1H, brd, *J* = 14.2 Hz), 3.35-3.51 (4H, m), 3.71-3.78 (2H, m), 4.36 (1H, dd, *J* = 4.4, 13.2 Hz), 5.11 (1H, dd, *J* = 1.0, 10.2 Hz), 5.16 (1H, dd, *J* = 1.7, 17.3 Hz), 5.65 (1H, s), 5.92 (1H, tdd, *J* = 6.8, 10.2, 17.3 Hz), 7.47-7.52 (2H, m), 7.59 (1H, dd, *J* = 1.6, 8.6 Hz), 7.85 (3H, brd, *J* = 8.6 Hz), 7.97 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.8 (CH_3), –4.0 (CH_3), 18.2 (C), 25.9 (CH_3×3), 36.2 (CH_2), 69.0 (CH_2), 70.7 (CH), 75.0 (CH), 76.7 (CH), 79.2 (CH), 81.5 (CH), 101.7 (CH), 117.3 (CH_2), 123.9 (CH), 125.7 (CH), 126.1 (CH), 126.3 (CH), 127.7 (CH), 128.0 (CH), 128.3 (CH), 132.9 (C), 133.6 (C), 134.2 (CH), 134.7 (C); EI-HRMS (m/z) calcd for $C_{22}H_{27}O_5Si$ $[M - {}^tBu]^+$: 399.1628, found: 399.1637.

7.1.7. (((2*R*,4a*R*,6*S*,7*S*,8*R*,8a*R*)-6-Allyl-7-(allyloxy)-2-(naphthalen-2-yl)hexahydropyrano[3,2-*d*][1,3]dioxin-8-yl)oxy)*tert*-butyldimethylsilane (8). To a solution of **16** (17.77 g, 38.91 mmol), TBAI (1.470 g, 3.979 mmol), and allylbromide (6.7 mL, 78 mmol) in THF (200 mL) was added NaH (60% in mineral oil, 7.7619 g, 194.13 mmol) at 0 ºC, and the mixture was stirred for 10 h. Then, the reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10) to give **8** (19.15 g, 38.55 mmol, 100%) as a colorless solid.

8: mp 65-67 ºC; $[\alpha]_D^{21}$ –65.6 (*c* 0.390, $CHCl_3$); IR (KBr) ν 3075, 2924, 2854, 1644, 1472, 1388, 1256, 1176, 1081, 1031, 856, 776, 671, 473 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.01 (3H, s), 0.08 (3H, s), 0.85 (9H, s), 2.29 (1H, quin, *J* = 7.9 Hz), 2.60 (1H, brd, *J* = 13.9 Hz), 3.12 (1H, t, *J* = 8.5 Hz), 3.38-3.47 (3H, m), 3.72 (1H, t, 9.6 Hz), 3.86 (1H, t, *J* = 8.5 Hz), 4.10 (1H, dd, *J* = 6.0, 11.9 Hz), 4.34 (1H, dd, *J* = 4.6, 10.4 Hz), 4.41 (1H, dd, *J* = 6.0, 11.9 Hz), 5.09-5.20 (3H, m), 5.28 (1H, dd, *J* = 1.5, 17.2 Hz), 5.62 (1H, s), 5.86-5.98 (2H, m), 7.47-7.51 (2H, m), 7.59 (1H, dd, *J* = 1.8, 8.7 Hz), 7.81-7.87 (3H, m), 7.97 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.4 (CH_3), –4.1 (CH_3), 18.2 (C), 25.9 (CH_3×3), 36.0 (CH_2), 69.1 (CH_2), 70.4 (CH), 74.5 (CH_2), 76.3 (CH), 79.3 (CH), 82.2 (CH), 82.4 (CH), 101.9 (CH), 117.2 (CH_2), 117.3 (CH_2), 124.0 (CH), 125.8 (CH), 126.0 (CH), 126.3 (CH), 127.7 (CH), 127.9 (CH), 128.3 (CH), 132.8 (C), 133.6 (C), 134.49 (CH), 134.52 (CH), 134.7 (C); EI-HRMS (m/z) calcd for $C_{25}H_{31}O_5Si$ $[M - {}^tBu]^+$: 439.1941, found: 439.1940.

7.1.8. *tert*-Butyldimethyl(((2*R*,4a*R*,5a*S*,10a*S*,11*R*,11a*R*)-2-(naphthalen-2-yl)-4,4a,5a,6,9,10a,11,11a-octahydro-[1,3]dioxino[4',5':5,6]pyrano[3,2-*b*]oxepin-11-yl)oxy)silane (18). To a solution of **8** (1.006 g, 2.026 mmol) in degassed CH_2Cl_2 (100 mL) was added a solution of the second generation Grubbs catalyst (**17**) (18.3 mg, 0.0216 mmol) in degassed CH_2Cl_2 (1 mL) at 24 ºC, and the mixture was refluxed with stirring. After 2 h from the start of the reaction, the mixture was cooled to 24 ºC and stirred for 1 h under O_2 atmosphere. Then, the mixture was concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel + Florisil®, PhH) to give **18** (767.8 mg, 1.638 mmol, 82%) as a colorless solid.

18: mp 133-136 ºC; $[\alpha]_D^{22}$ –96.9 (*c* 0.0350, $CHCl_3$); IR (neat) ν 3481, 3023, 2927, 2855, 1725, 1510, 1472, 1387, 1247, 1175, 1108, 1011, 970, 855, 770, 740, 669, 623 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.08 (3H, s), 0.11 (3H, s), 0.90 (9H, s), 2.29-2.38 (1H, m), 2.67 (1H, ddd, *J* = 4.4, 8.0, 16.4 Hz), 3.24 (1H, t, *J* = 8.4 Hz), 3.40 (1H, dt, *J* = 4.4, 9.8 Hz), 3.47 (1H, dd, *J* = 5.1, 9.8 Hz), 3.55 (1H, t, *J* = 9.3 Hz), 3.74 (1H, t, *J* = 10.1 Hz), 3.82 (1H, t, *J* = 7.7 Hz), 3.99 (1H, brddd, *J* = 2.7, 5.7, 15.8 Hz), 4.31 (1H, dd, *J* = 5.7, 15.8 Hz), 4.36 (1H, dd, *J* = 5.1, 10.1 Hz), 5.70 (1H, s), 5.73-5.80 (1H, m), 5.85-5.90 (1H, m), 7.47-7.51 (1H, m), 7.60 (1H, dd, *J* = 1.7, 8.7 Hz), 7.82-7.85 (3H, m), 8.01 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.53 (CH_3), –4.46 (CH_3), 18.4 (C), 25.9 (CH_3×3), 34.8 (CH_2), 68.8 (CH_2), 69.0 (CH_2), 69.9 (CH), 74.9 (CH), 77.2 (CH), 82.0 (CH), 88.3 (CH), 101.4 (CH), 123.9 (CH), 125.5 (CH), 126.0 (CH), 126.2 (CH), 126.3 (CH), 127.7 (CH), 127.9 (CH), 128.4 (CH), 131.3 (CH), 132.9 (C), 133.6 (C), 134.9 (C); EI-HRMS (m/z) calcd for $C_{25}H_{31}O_5Si$ $[M]^+$: 411.1628, found: 411.1653.

7.1.9. (2*R*,4a*R*,5a*S*,10a*R*,11*R*,11a*S*)-2-(Naphthalen-2-yl)-4,4a,5a,6,9,10a,11,11a-octahydro-[1,3]dioxino[4',5':5,6]pyrano[3,2-*b*]oxepin-11-ol (19). To a solution of **18** (10.5 g, 22.4 mmol) in THF (120 mL) was added TBAF (1.0 mol/L in THF, 90 mL, 90 mmol) at 20 ºC, and the mixture was stirred for 5 h. Then, the mixture was concentrated under reduced pressure, and the residue was purified by recrystallization (PhH + H_2O) to give **19** (7.50 g, 21.2 mmol, 95%) as a colorless needle.

19: mp 217-219 ºC; $[\alpha]_D^{24}$ –39.7 (*c* 0.0350, $CHCl_3$); IR (KBr) ν 3484, 3054, 3026, 2891, 1436, 1380, 1265, 1103, 1031, 861, 828, 801, 744, 678, 549, 476 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.36-2.45 (1H, m), 2.66 (1H, ddd, *J* = 3.6, 8.3, 15.9 Hz), 2.80 (1H, s), 3.34 (1H, t, *J* = 8.5 Hz), 3.39 (1H, ddd, *J* = 4.0, 9.7, 19.4 Hz), 3.53 (1H, dt, *J* = 5.2, 9.7 Hz), 3.65 (1H, t, *J* = 9.3 Hz), 3.77 (1H, t, *J* = 10.5 Hz), 3.89 (1H, t, *J* = 8.8 Hz), 4.07 (1H, brqd, *J* = 2.9, 15.3 Hz), 4.35-4.40 (2H, m), 5.73 (1H, s), 5.82-5.88 (1H, m), 5.92-5.98 (1H, m), 7.46-7.50 (2H, m), 7.62 (1H, d, *J* = 8.5 Hz), 7.82-7.88 (3H, m), 7.99 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.3 (CH_2), 68.5 (CH_2), 68.9 (CH_2), 69.9 (CH), 73.6 (CH), 76.4 (CH), 80.9 (CH), 87.8 (CH), 101.9 (CH), 123.8 (CH), 125.8 (CH), 126.1 (CH), 126.4 (CH), 127.3 (CH), 127.7 (CH), 128.2 (CH), 128.4 (CH), 131.7 (CH), 132.9 (C), 133.7 (C), 134.4 (C); EI-HRMS (m/z) calcd for $C_{21}H_{22}O_5$ $[M]^+$: 354.1467, found: 354.1464.

7.1.10. ((2*R*,3*R*,4*R*,4a*S*,9a*S*)-4-((4-Bromobenzyl)oxy)-3-(naphthalen-2-ylmethoxy)-3,4,4a,6,9,9a-hexahydro-*2H*-pyrano[3,2-*b*]oxepin-2-yl)methanol (7). To a solution of **19** (11.98 g, 33.80 mmol), PBBBr (14.46 g, 57.84 mmol), and TBAI (1.255 g, 3.398 mmol) in THF (350 mL) was added NaH (60% in mineral oil, 4.995 g, 124.9 mmol) at 0 ºC, and the mixture was stirred for 27 h at 23 ºC. Then, the reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude product, which was used immediately in the next reaction.

To a solution of the above crude product in CH_2Cl_2-Et_2O (240 mL : 240 mL) were added $LiAlH_4$ (7.769 g, 204.7 mmol) and a solution of $AlCl_3$ (9.030 g, 67.72 mmol) in Et_2O (70 mL) at 23

ºC, and the mixture was stirred for 3 h. Then, to the mixture was added saturated aq. potassium sodium tartrate, and the mixture was stirred for 20 h at 23 ºC. Then, the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 2) to give **7** (15.44 g, 29.39 mmol, 87% from **19**) as a colorless solid.

7: mp 101-103 ºC; $[\alpha]_D^{24}$ –32.4 (*c* 1.30, $CHCl_3$); IR (KBr) ν 3587, 3438, 3059, 3020, 2959, 2899, 2861, 2827, 1595, 1484, 1402, 1352, 1237, 1160, 1121, 1071, 1011, 813, 746, 620, 482 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.84 (1H, t, *J* = 6.0 Hz), 2.30-2.41 (1H, m), 2.65 (1H, ddd, *J* = 4.0, 8.0, 16.1 Hz), 3.28 (1H, td, *J* = 4.0, 9.2 Hz), 3.36-3.41 (1H, m), 3.37 (1H, t, *J* = 9.2 Hz), 3.55 (1H, t, *J* = 9.2 Hz), 3.65-3.71 (1H, m), 3.66 (1H, t, *J* = 9.2 Hz), 3.87 (1H, ddd, *J* = 2.8, 6.0, 11.6 Hz), 3.99 (1H, ddd, *J* = 2.4, 6.0, 15.4 Hz), 4.27 (1H, dd, *J* = 6.0, 15.4 Hz), 4.76 (1H, d, *J* = 11.5 Hz), 4.80 (1H, d, *J* = 11.5 Hz), 4.91 (1H, d, *J* = 11.5 Hz), 4.98 (1H, d, *J* = 11.5 Hz), 5.80 (1H, m), 5.90 (1H, m), 7.22 (2H, d, *J* = 8.5 Hz), 7.38 (1H, dd, *J* = 1.6, 8.5 Hz), 7.42 (2H, dt, *J* = 2.4, 8.5 Hz), 7.45-7.50 (2H, m), 7.69 (1H, s), 7.80 (3H, dd, *J* = 7.4, 15.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.5 (CH_2), 62.4 (CH_2), 67.9 (CH_2), 74.7 (CH_2), 75.1 (CH_2), 75.8 (CH), 77.6 (CH), 78.5 (CH), 85.6 (CH), 88.2 (CH), 121.3 (C), 125.9 (CH), 126.0 (CH), 126.2 (CH), 126.7 (CH), 127.1 (CH), 127.7 (CH), 128.0 (CH), 128.3 (CH), 129.5 (CH×2), 131.4 (CH×2), 131.6 (CH), 133.0 (C), 133.3 (C), 135.6 (C), 138.1 (C); FD-HRMS (m/z) calcd for $C_{28}H_{29}O_5{}^{79}Br$ $[M]^+$: 524.1198, found: 524.1206.

7.1.11. (2*R*,3*R*,4*R*,4a*S*,9a*S*)-4-((4-Bromobenzyl)oxy)-2-(2-(methylsulfinyl)-2-(methylthio)ethyl)-3-(naphthalen-2-ylmethoxy)-3,4,4a,6,9,9a-hexahydro-*2H*-pyrano[3,2-*b*]oxepine (5). To a solution of **7** (14.21 g, 27.04 mmol) and 2,6-lutidine (9.40 mL, 81.1 mmol) in CH_2Cl_2 (150 mL) was added Tf_2O (9.20 mL, 54.8 mmol) at –78 ºC, and the mixture was stirred for 30 min. The reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with Et_2O several times. The combined organic layers were washed with 0.5 mol/L aq. HCl, H_2O, and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude **21**, which was used immediately in the next reaction.

To a solution of $MeSCH_2S(O)Me$ (8.80 mL, 86.5 mmol) in THF (170 mL) was added BuLi (1.60 mol/L in hexane, 51.0 mL, 81.6 mmol) at –20 ºC, and the mixture was stirred for 20 min. Then, to the mixture was added a solution of the above crude **21** in THF (100 mL), and the mixture was stirred for 40 min. The reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with $CHCl_3$ several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 1 → 0.5) to give **5** (brown oil, 16.3448 g, 25.88 mmol, 96% from **7**) as an inseparable mixture of 4 diastereomers.

5: IR (neat) ν 3034, 2888, 1593, 1479, 1091, 815, 678 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 1.74-1.78 (2H, m), 1.89 (1H, s), 1.95 (1H, s), 2.13 (2H, s), 2.15-2.29 (2H, m), 2.34-2.52 (2H, m), 3.14-3.38 (4H, m), 3.57-3.67 (2H, m), 3.74-3.82 (1H, m), 3.94 (1H, dd, *J* = 5.1, 14.9 Hz), 4.54 (1/2H, d, *J* = 11.9 Hz), 4.61-4.66 (1H, m), 4.81-4.87 (1H, m), 4.90 (1/4H, d, *J* = 11.8 Hz), 4.93 (1/4H, d, *J* = 11.5 Hz), 5.46-5.59 (2H, m), 6.98-7.06 (2H, m), 7.20-7.35 (5H, m), 7.57-7.68 (4H, m); ^{13}C NMR (100 MHz, C_6D_6) δ 11.7 (CH_3×1/2), 14.1 (CH_3×1/4), 15.1 (CH_3×1/4), 28.8 (CH_2×1/2), 29.2 (CH_2×1/2), 32.9 (CH_3×1/4), 34.5 (CH_2), 35.4 (CH_3×1/4), 36.4 (CH_3×1/2), 61.2 (CH×1/2), 63.2 (CH×1/2), 65.5 (CH_2×1/4), 67.5 (CH_2×3/4), 71.9 (CH×1/4), 74.27 (CH_2×1/2), 74.32 (CH_2×1/2), 74.4 (CH×1/2), 74.9 (CH×1/4), 74.95 (CH_2×1/2), 75.02 (CH_2×1/2), 75.8 (CH), 81.5 (CH×1/2), 81.6 (CH×1/2), 85.69 (CH×1/2), 85.74 (CH×1/2), 88.1 (CH), 121.13 (C×1/2), 121.14 (C×1/2), 125.7 (CH×1/2), 125.83 (CH×1/2), 125.84 (CH×1/2), 125.9 (CH×1/2), 126.1 (CH×1/2), 126.3 (CH×1/2), 126.5 (CH×1/4), 126.56 (CH×1/2), 126.58 (CH×1/4), 127.7 (CH), 127.86 (CH×1/2), 127.89 (CH×1/2), 127.97 (CH×2), 128.04 (CH×1/2), 128.1 (CH×1/2), 129.17 (CH), 129.19 (CH), 131.3 (CH), 131.5 (CH), 133.1 (C×1/2), 133.16 (C×1/4), 133.18 (C×1/4), 133.5 (C), 136.08 (C×1/2), 136.12 (C×1/2), 138.5 (C×1/2), 138.6 (C×1/2); FD-HRMS (m/z) calcd for $C_{31}H_{35}O_5{}^{79}BrS_2Si$ $[M]^+$: 630.1091, found: 630.1100.

7.1.12. (*E*)-1-((1,2-Dichlorovinyl)oxy)-4-methoxybenzene (30). To a stirred solution of 4-methoxyphenol (**29**) (40.06 g, 0.3227 mol) in THF (650 mL) were added NaH (60% in mineral oil, 25.45 g, 0.6361 mol) and KI (2.741 g, 16.51 mmol) at 0 °C. After the effervescence of hydrogen was completed, trichloroethylene (69.6 mL, 773 mmol) was added, and the mixture was heated to 40 °C. After being stirred for 14 h, the reaction was quenched with saturated NH_4Cl aq. at 0 °C and the mixture was filtered through a Celite pad. Then, the filtrate was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 50) to give **30** (67.83 g, 0.3096 mol, 96% from **29**) as a colorless oil.

30: IR (neat) ν 3104, 3003, 2953, 2927, 2852, 2837, 1630, 1596, 1503, 1463, 1442, 1298, 1275, 1248, 1193, 1162, 1103, 1073, 1036, 833, 793, 730, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.80 (3H, s), 5.88 (1H, s), 6.88 (2H, d, *J* = 9.4 Hz), 7.01 (2H, d, *J* = 9.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.7 (CH_3), 102.5 (CH), 114.8 (CH×2), 110.6 (CH×2), 140.8 (C), 147.6 (C), 156.6 (C); FD-HRMS (m/z) calcd for 217.9901, found: 217.9912.

7.1.13 1-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-3-(4-methoxyphenoxy)prop-2-yn-1-ol (32). To a solution of **30** (37.13 g, 0.1695 mmol) in Et_2O (500 mL) was added dropwise BuLi (1.65 mol/L in hexane, 210 mL, 0.347 mmol) over 10 min at 0 ºC, and the mixture was stirred for 1 h 40 min. Then, a solution of **31** (14.68 g, 0.1128 mmol) was added dropwise to the mixture, and the mixture was stirred and allowed to return to ambient temperature (25 ºC) for 15 h. Then, the reaction was quenched with H_2O, and the mixture was extracted with Et_2O several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluent:* hexane/EtOAc = 25: *the eluent contained 10% Et_3N) to give **32** (colorless oil, 20.80 g, 74.74 mmol, 66% from **30**) as a 1:1 mixture of diastereomer.

32 (a 1:1 mixture of diastereomers): $[\alpha]_D^{24}$ +18.3 (c 1.14, $CHCl_3$), IR (neat) ν 3439, 3114, 3076, 2987, 2936, 2903, 2837, 2273, 1501, 1463, 1455, 1443, 1382, 1372, 1297, 1239, 1215, 1173, 1146, 1104, 1069, 1035, 829, 729 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.40 (3H, s), 1.48 (3/2H, s), 1.49 (3/2H, s), 2.25 (1/2H, brd, *J* = 2.4 Hz), 2.41 (1/2H, brd, *J* = 2.4 Hz), 3.79 (3H, s), 3.94 (1/2H, dd, *J* = 5.3, 8.6 Hz), 4.06-4.17 (3/2H, m), 4.23 (1/2H, dt, *J* = 5.3, 6.7 Hz), 4.29 (1/2H, dt, *J* = 4.1, 6.7 Hz), 4.47 (1/2H, brdd, *J* = 4.1, 7.0 Hz), 4.65 (1/2H, brt, *J* = 4.1 Hz), 6.87 (2H, d, *J* = 9.3 Hz), 7.17 (1H, d, *J* = 9.3 Hz), 7.18 (1H, d, *J* = 9.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.1 (CH_3×1/2), 25.20 (CH_3×1/2), 26.3 (CH_3×1/2), 26.8 (CH_3×1/2), 41.36 (C×1/2), 41.45 (C×1/2), 55.7 (CH_3), 62.3 (CH×1/2), 64.1 (CH×1/2), 65.4 (CH_2×1/2), 66.3 (CH_2×1/2), 78.3 (CH×1/2), 79.3 (CH×1/2), 89.1 (C×2), 110.1

(C×1/2), 110.4 (C×1/2), 114.58 (CH×1/2), 114.60 (CH×1/2), 115.77 (CH×1/2), 115.79 (CH×1/2), 149.44 (C×1/2), 149.49 (C×1/2), 156.40 (C×1/2), 156.43 (C×1/2); FD-HRMS (m/z) calcd for $C_{15}H_{18}O_5$ $[M]^+$: 278.1154, found: 278.1155.

7.1.14. (*R*,*Z*)-1-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-3-(4-methoxyphenoxy)prop-2-en-1-ol (25) and (*S*,*Z*)-1-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-(4-methoxyphenoxy)prop-2-en-1-ol (28). To a solution of **32** (12.25 g, 44.02 mmol) in PhH (300 mL) was added Lindlar catalyst (300 mg) at 27 ºC, and the mixture was stirred for 22 h under H_2 atmosphere. Then, the mixture was filtered through a Celite pad, and the filtrate was concentrated under reduced pressure. The residue was purified by HPLC (eluent:* hexane/EtOAc = 1.33: *the eluent contained 5% Et_3N, flow rate: 20 mL/min) to give **25** (brown solid, 5.09 g, 18.16 mmol, 41% from **32**, Rt = 12.8 min) as a less-polar component and **28** (brown oil, 5.93 g, 21.15 mmol, 48% from **30**, Rt = 15.2 min) as a polar component.

25: mp 48-49 ºC; $[\alpha]_D^{23}$ –20.0 (*c* 1.39, $CHCl_3$); IR (neat) ν 3465, 3046, 2986, 2936, 2904, 2836, 1667, 1505, 1466, 1443, 1381, 1371, 1227, 1216, 1182, 1157, 1103, 1065, 1009, 993, 853, 827 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.39 (3H, s), 1.48 (3H, s), 2.55 (1H, s), 3.78 (3H, s), 3.87 (1H, dd, *J* = 6.0, 8.3 Hz), 4.03 (1H, dd, *J* = 6.2, 8.3 Hz), 4.11 (1H, q, *J* = 6.2 Hz), 4.70 (1H, brdt, *J* = 3.1, 7.0 Hz), 4.76 (1H, dd, *J* = 6.0, 8.6 Hz), 6.44 (1H, dd, *J* = 0.8, 6.0 Hz), 6.85 (2H, d, *J* = 9.2 Hz), 6.94 (2H, d, *J* = 9.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.3 (CH_3), 26.8 (CH_3), 55.6 (CH_3), 65.9 (CH_2), 67.3 (CH), 79.2 (CH), 108.7 (CH), 109.8 (C), 114.7 (CH×2), 117.9 (CH×2), 144.6 (CH), 151.0 (C), 155.7 (C); EI-HRMS (m/z) calcd for $C_{15}H_{20}O_5$ $[M]^+$: 280.1311, found: 280.1311.

28: $[\alpha]_D^{24}$ +45.4 (*c* 0.595, $CHCl_3$); IR (neat) ν 3453, 3046, 2986, 2936, 2907, 1667, 1504, 1466, 1456, 1443, 1381, 1371, 1294, 1229, 1182, 1157, 1125, 1104, 1065, 1011, 847, 827 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.38 (3H, s), 1.46 (3H, s), 2.24 (1H, s), 3.78 (3H, s), 3.95 (1H, dd, *J* = 6.6, 8.3 Hz), 4.05 (1H, dd, *J* = 6.6, 8.3 Hz), 4.26 (1H, dt, *J* = 4.4, 6.6 Hz), 4.80 (1H, dd, *J* = 5.8, 8.1 Hz), 4.86 (1H, brdd, *J* = 4.4, 8.1 Hz), 6.45 (1H, d, *J* = 5.8 Hz), 6.85 (2H, d, *J* = 9.1 Hz), 6.93 (2H, d, *J* = 9.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.1 (CH_3), 26.3 (CH_3), 55.5 (CH_3), 65.3 (CH_2), 65.7 (CH), 78.0 (CH), 108.8 (CH), 109.2 (C), 114.6 (CH×2), 117.7 (CH×2), 144.2 (CH), 150.9 (C), 155.6 (C); EI-HRMS (m/z) calcd for $C_{15}H_{20}O_5$ $[M]^+$: 280.1311, found:280.1310.

7.1.15. (*R*)-1-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-3-(4-methoxyphenoxy)propan-1-ol (33). To a solution of **25** (29.6 mg, 0.106 mmol) in methanol (1.2 mL) was added 10% Pd/C catalyst (3.0 mg) at 23 °C, and the mixture was stirred for 2 h under H_2 atmosphere. The mixture was filtered through a Celite pad and concentrated under reduced pressure to give almost pure **33** (27.4 mg, 97 .0 μmol, 92%) as a colorless solid.

33: mp 97-99 °C; $[\alpha]_D^{24}$ +17.8 (*c* 0.120, $CHCl_3$); IR (KBr), ν 3461, 2926, 1512, 1473, 1374, 1231, 1160, 1132, 1055, 1033, 973, 929, 857, 823, 730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 1.38 (3H, s), 1.45 (3H, s), 1.89 (2H, q, *J* = 5.9 Hz), 2.40 (1H, brd, *J* = 3.4 Hz), 3.77 (3H, s), 3.78-3.87 (2H, m), 4.02-4.17 (4H, m), 6.83 (4H, s); ^{13}C NMR (75 MHz, $CDCl_3$), δ 25.2 (CH_3), 26.6 (CH_3), 33.3 (CH_2), 55.7 (CH_3), 65.2 (CH_2), 66.0 (CH_2), 69.7 (CH), 78.9 (CH), 109.5 (C), 114.7 (CH×2), 115.5 (CH×2), 152.8 (C), 153.9 (C); EI-HRMS calcd for $C_{15}H_{22}O_5$ $[M]^+$: 282.1467, found: 282.1475; Crystal Data: Crystals were obtained by recrystallizing from Et_2O/hexane. $C_{15}H_{22}O_5$, *M* = 282.34, colorless platelet, 0.50 × 0.20 × 0.05 mm^3, monoclinic P21 (No. 4), *a* = 8.741(3) Å, *b* = 5.523(2) Å, *c* = 15.366(5) Å, α = 90.000(1)°, β = 103.967(1)°, γ = 90.000(1)°, *V* = 719.9(4) $Å^3$, ρ_{calcd}(*Z* = 2) = 1.302 g cm^{-3}. A total 1799 unique data ($2\theta_{max}$ = 55°) were measured at T = 153 K by Rigaku Mercury CCD apparatus (Mo Kα radiation, λ = 0.71070 Å). Numerical absorption correction was applied (μ = 0.97 cm^{-1}). The structure was solved by the direct method (SIR92) and refined by the full-matrix least-squares method of F^2 with anisotropic temperature factors for non-hydrogen atoms. All the hydrogen atoms were located at the calculated positions. The final *wR* value is 0.0916 (all data) for 1799 reflections and 182 parameters. CCDC 906654.

7.1.16. (2*R*,4a*R*,7*R*,8*R*,8a*S*)-2-(4-Chlorophenyl)hexahydropyrano[3,2-*d*][1,3]dioxine-6,7,8-triol (36). PTS·H_2O (7.90 g, 41.5 mmol) in DMF (1.5 L) is stirred for 70 min at 80 °C in vacuo (200 mmHg) to remove H_2O azeotropically. Then, to the solution were added D-glucose (**35**) (246.0 g, 1.365 mol) and *p*-chlorobenzaldehyde dimethylacetal **34** (127.3 g, 0.6821 mol), and the mixture was stirred at 60 °C for 6 h in vacuo (200 mmHg). After the reaction mixture was cooled and returned to atmospheric pressure, the reaction was quenched with Et_3N, and concentrated under reduced pressure. Then, to the residue was added H_2O, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. After the resulting residue was recrystallized with CH_2Cl_2 several times, all volatiles were removed in vacuo at 80 °C to give **36** (156.0 g, 0.5153 mol, 75% from *p*-chlorobenzaldehyde dimethylacetal **34**, α-anomer:β-anomer = 3:2) as a colorless solid.

36: mp 162-165 °C; $[\alpha]_D^{24}$ +2.34 (*c* 0.820, CH_3OH); IR (KBr), ν 3361, 2926, 2872, 1605, 1496, 1468, 1380, 1303, 1270, 1220, 1083, 1016, 819, 758, 730, 681, 659, 559, 532, 488, 449 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 3.23 (2/5H, t, *J* = 8.0 Hz), 3.37-3.49 (2H, m), 3.61 (2/5H, t, *J* = 8.5 Hz), 3.73 (1H, q, *J* = 9.9 Hz), 3.85 (3/5H, t, *J* = 9.0 Hz), 3.95 (3/5H, dt, *J* = 4.9, 9.9 Hz), 4.16 (3/5H, dd, *J* = 4.9, 9.9 Hz), 4.25 (2/5H, dd, *J* = 4.3, 10.5 Hz), 4.58 (2/5H, d, *J* = 7.7 Hz), 5.12 (3/5H, d, *J* = 3.9 Hz), 5.55 (1H, d, *J* = 3.2 Hz), 7.34 (2H, d, *J* = 8.5 Hz), 7.48 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, CD_3OD) δ 63.5 (CH×3/5), 67.7 (CH×2/5), 69.8 (CH_2×2/5), 70.2 (CH_2×3/5), 71.8 (CH×3/5), 74.4 (CH×3/5), 74.7 (CH×2/5), 77.2 (CH×2/5), 82.4 (CH×2/5), 83.1 (CH×3/5), 94.7 (CH×3/5), 99.0 (CH×2/5), 102.0 (CH×2/5), 102.1 (CH×3/5), 129.16 (CH×2), 129.20 (CH×2), 135.65 (C×3/5), 135.68 (C×2/5), 138.0 (C×2/5), 138.1 (C×3/5); EI-HRMS (m/z) calcd for $C_{13}H_{15}O_6{}^{35}Cl$ $[M]^+$: 302.0557, found: 302.0563.

7.1.17. (2*R*,4*S*,5*R*)-2-(4-Chlorophenyl)-4-vinyl-1,3-dioxan-5-ol (38). To a solution of **36** (30.05 g, 99.26 mmol) in MeOH (500 mL) were added pH 7 phosphate buffer (250 mL) and $NaIO_4$ (44.76 g, 209.3 mmol) at 21 ºC, and the mixture was stirred for 30 min. Then, the mixture was heated to 50 ºC and stirred for 1 h. The mixture was cooled to 21 ºC, and the reaction was quenched with 2.0 mol/L aq. NaOH. Then, the mixture was extracted with EtOAc several times. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give crude **37**, which was used immediately in the next reaction.

To a solution of CH_3PPh_3Br (106.4 g, 297.7 mmol) in THF (300 mL) was added *t*-BuOK (33.36 g, 297.3 mmol) at 21 ºC, and the mixture was stirred for 1 h. Then, the mixture was cooled to 0 ºC, and a solution of the above crude **37** in THF (200 mL) was added dropwise to the mixture. The mixture was wormed to 21 ºC and stirred for 17 h. The reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over

anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 2.5) to give **38** (18.41 g, 76.49 mmol, 77% from **36**) as a colorless solid.

38: mp 78-80 °C; $[\alpha]_D^{23}$ –48.6 (*c* 0.975, $CHCl_3$); IR (KBr), ν 3388, 3091, 3059, 2987, 2926, 2865, 1600, 1496, 1408, 1383, 1270, 1215, 1081, 1015, 981, 967, 930, 814, 730, 636 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.73 (1H, brd, *J* = 3.3 Hz), 3.58-3.70 (2H, m), 4.02 (1H, t, *J* = 8.0 Hz), 4.29-4.41 (1H, m), 5.38 (1H, brdd, *J* = 1.1, 10.4 Hz), 5.49 (1H, dd, *J* = 1.1, 18.0 Hz), 5.52 (1H, s), 5.97 (1H, ddd, *J* = 6.8, 10.4, 18.0 Hz), 7.34 (2H, d, *J* = 8.6 Hz), 7.45 (2H, d, *J* = 8.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 65.1 (CH), 70.7 (CH_2), 83.4 (CH), 100.1 (CH), 119.4 (CH_2), 127.6 (CH × 2), 128.4 (CH×2), 134.4 (CH), 134.8 (C), 136.1 (C); EI-HRMS (m/z) calcd for $C_{12}H_{13}O_3{}^{35}Cl$ $[M]^+$: 240.0553, found: 240.0551.

7.1.18. 2-(((2*R*,4*S*,5*R*)-2-(4-Chlorophenyl)-4-vinyl-1,3-dioxan-5-yl)oxy)acetic acid (39). To a solution of **38** (315.6 mg, 1.311 mmol) in 1,4-dioxane (5 mL) was added NaH (60% in mineral oil, 230.3 mg, 5.760 mmol) at 22 ºC, and heated to 60 ºC. After being stirred for 30 min, bromoacetic acid (220.0 mg, 1.583 mmol) was added, and the mixture was stirred for 11 h. Then, the mixture was cooled to 22 ºC, and the reaction was quenched with H_2O. To the mixture was added Et_2O, and the mixture was extracted with H_2O several times. The combined aqueous layers were acidified to pH 2 with 2.0 mol/L aq. HCl and extracted with Et_2O several times. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give **39** (colorless solid, 378.9 mg, 1.268 mmol, 97%) in an almost pure form.

39: $[\alpha]_D^{24}$ –30.4 (*c* 0.850, $CHCl_3$); IR (KBr) ν 3300-2400 (br), 3044, 2985, 2963, 2927, 2861, 2763, 2668, 2571, 1737, 1709, 1600, 1495, 1420, 1388, 1380, 1360, 1300, 1292, 1270, 1252, 1213, 1142, 1121, 1094, 1080, 1042, 1017, 1003, 992, 983, 965, 938, 930, 885, 878, 817, 808, 692, 644 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (1H, brs), 3.43 (1H, dt, *J* = 5.4, 9.6 Hz), 3.71 (1H, t, *J* = 10.7 Hz), 4.15 (1H, brdd, *J* = 1.2, 8.8 Hz), 4.24 (1H, d, *J* = 2.7 Hz), 4.47 (1H, dd, *J* = 5.4, 10.7 Hz), 5.38 (1H, d, *J* = 10.7 Hz), 5.51 (1H, s), 5.52 (1H, d, *J* = 17.9 Hz), 6.03 (1H, ddd, *J* = 6.8, 10.7, 17.9 Hz), 7.33 (2H, d, *J* = 8.6 Hz), 7.43 (2H, d, *J* = 8.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 67.7 (CH_2), 69.0 (CH_2), 74.6 (CH), 81.3 (CH), 100.1 (CH), 119.1 (CH_2), 127.6 (CH×2), 128.4 (CH×2), 134.4 (CH), 134.9 (C), 135.9 (C), 174.1 (C); EI-HRMS (m/z) calcd for $C_{14}H_{15}O_5{}^{35}Cl$ $[M]^+$: 298.0608, found: 298.0609.

7.1.19. (*S*,*Z*)-1-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-3-(4-methoxyphenoxy)allyl2-(((2*R*,4*S*,5*R*)-2-(4-chlorophenyl)-4-vinyl-1,3-dioxan-5-yl)oxy)acetate (27). To a solution of **39** (33.67 g, 112.7 mmol) in CH_2Cl_2 (600 mL) were added DMAP (1.0670 g, 8.7337 mmol), EDCI·HCl (31.56 g, 165.1 mmol), and a solution of **28** (23.14 g, 82.55 mmol) in CH_2Cl_2 (200 mL) at 22 ºC, and the mixture was stirred for 18 h. The reaction was quenched with 0.2 mol/L aq. HCl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluent:* hexane/EtOAc = 10 → 5: *the eluent contained 5% Et_3N) to give **27** (43.41 g, 77.38 mmol, 94%) as a colorless oil.

27: $[\alpha]_D^{24}$ –0.229 (*c* 1.91, $CHCl_3$); IR (neat) ν 3045, 2987, 2934, 2908, 2837, 1759, 1668, 1603, 1504, 1465, 1457, 1443, 1410, 1382, 1373, 1297, 1214, 1141, 1110, 1090, 1062, 1039, 1016, 977, 942, 827, 758 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.37 (3H, s), 1.45 (3H, s), 3.38 (1H, dt, *J* = 5.1, 13.3 Hz), 3.69 (1H, t, *J* = 10.7 Hz), 3.76-3.84 (2H, m), 3.78 (3H, s), 4.07-4.15 (2H, m), 4.21 (2H, d, *J* = 6.7 Hz), 4.38 (1H, dt, *J* = 3.8, 6.7 Hz), 4.51 (1H, dd, *J* = 5.1, 10.7 Hz), 4.80 (1H, dd, *J* = 6.2, 8.9 Hz), 5.32 (1H, brddd, *J* = 1.0, 1.3, 10.7 Hz), 5.49 (1H, brtd, *J* = 1.3, 17.3 Hz), 5.49 (1H, s), 6.00-6.11 (2H, m), 6.51 (1H, dd, *J* = 0.8, 6.2 Hz), 6.84 (2H, d, *J* = 9.2 Hz), 6.94 (2H, d, *J* = 9.2 Hz), 7.33 (2H, d, *J* = 8.5 Hz), 7.43 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.9 (CH_3), 26.0(CH_3), 55.3 (CH_3), 65.3 (CH_2), 68.0 (CH_2), 68.5 (CH), 69.0 (CH_2), 74.2 (CH), 76.2 (CH), 77.2 (C), 80.8 (CH), 99.5 (CH), 103.4 (CH), 114.4 (CH×2), 117.8 (CH×2), 118.0 (CH_2), 127.5 (CH×2), 128.1 (CH×2), 134.3 (C), 134.4 (CH), 136.0 (C), 145.9 (CH), 150.6 (C), 155.6 (C), 168.9 (C); EI-HRMS (m/z) calcd for $C_{29}H_{33}O_9{}^{35}Cl$ $[M]^+$: 560.1813, found: 560.1817.

7.1.20. Methyl (2*R*,3*R*,*E*)-2-(((2*R*,4*S*,5*R*)-2-(4-chlorophenyl)-4-vinyl-1,3-dioxan-5-yl)oxy)-5-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-(4-methoxyphenoxy)pent-4-enoate (40). To a solution of **27** (41.05 g, 73.17 mmol) in THF (370 mL) was added TMSCl (18.5 mL, 146 mmol) at –78 ºC, and the mixture was stirred for 5 min. Then, KHMDS (0.5 mol/L in $PhCH_3$, 290 mL, 146 mmol) was added dropwise, and the mixture was stirred for 40 min. To the mixture was added diethyl malonate (22.0 mL, 146 mmol) and the mixture was stirred for 15 min. Then, the mixture was warmed to 0 ºC, and stirred for 4 h. The reaction was quenched with 0.5 mol/L aq. HCl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude product, which was used in the next reaction without purification.

To a solution of the above crude product in PhH-MeOH (185 mL:185 mL) was added $TMSCHN_2$ (73.0 mL, 146 mmol) at 21 ºC, and the mixture was stirred for 12 h. Then, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 2) to give **40** (39.93 g, 69.44 mmol, 95% from **27**, containing 15-*epi*-**40** [**40**:15-*epi*-**40** = > 20:1]) as a colorless oil.

40: $[\alpha]_D^{23}$ –42.8 (*c* 1.75, $CHCl_3$); IR (neat) ν 3043, 2987, 2952, 2934, 2905, 2869, 2836, 1750, 1603, 1505, 1463, 1439, 1416, 1381, 1371, 1279, 1226, 1180, 1147, 1109, 1090, 1061, 1038, 1016, 976, 937, 824 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.37 (3H, s), 1.40 (3H, s), 3.40 (1H, ddd, *J* = 5.6, 9.3, 10.0 Hz), 3.53 (1H, t, *J* = 7.7 Hz), 3.67-3.75 (1H, m), 3.75 (3H, s), 3.77 (3H, s), 4.06 (1H, dd, *J* = 6.2, 8.1 Hz), 4.11-4.22 (1H, brdd, 5.6, 8.9 Hz), 4.32 (1H, d, *J* = 4.8 Hz), 4.38 (1H, dd, *J* = 5.0, 10.7 Hz), 4.52 (1H, q, *J* = 6.8 Hz), 4.81 (1H, t, *J* = 5.6 Hz), 5.25 (1H, brd, *J* = 10.6 Hz), 5.44-5.50 (1H, m), 5.49 (1H, s), 5.76 (1H, dd, *J* = 6.2, 15.6 Hz), 5.88 (1H, dd, *J* = 6.2, 15.6 Hz), 6.07 (1H, ddd, *J* = 5.6, 10.7, 17.1 Hz), 6.81 (4H, d, *J* = 2.1 Hz), 7.32 (2H, d, *J* = 8.4 Hz), 7.42 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.8 (CH_3), 26.6 (CH_3), 52.4 (CH_3), 55.7 (CH_3), 69.3 (CH_2), 69.4 (CH_2), 74.7 (CH), 76.0 (CH), 79.5 (CH), 80.9 (CH), 81.3 (CH), 90.9 (CH), 109.5 (C), 114.6 (CH×2), 117.5 (CH×2), 118.4 (CH_2), 127.6 (CH×2), 128.2 (CH), 128.4 (CH×2), 133.0 (CH), 134.5 (CH), 134.8 (C), 136.1 (C), 151.2 (C), 154.6 (C), 170.7 (C); EI-HRMS (m/z) calcd for $C_{30}H_{35}O_9{}^{35}Cl$ $[M]^+$: 574.1969, found: 574.1977.

7.1.21. Methyl (2*R*,3*R*,6*S*,*E*)-2-(((2*R*,4*S*,5*R*)-2-(4-chlorophenyl)-4-vinyl-1,3-dioxan-5-yl)oxy)-6,7-dihydroxy-3-(4-methoxyphenoxy)hept-4-enoate (41). To a solution of **40** (21.68 g, 37.70 mmol) in MeCN (900 mL) was added 0.5 mol/L aq. HCl (150 mL) at 0 ºC, and the mixture was stirred for 47 h.

The reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 3 → 1 → EtOAc) to give **41** (18.57 g, 34.71 mmol, 92%, containing 15-*epi*-**41** [**41**:15-*epi*-**41** = > 20:1]) as a colorless oil.

41: $[\alpha]_D^{22}$ –49.3 (*c* 0.620, $CHCl_3$); IR (neat) ν 3404, 3042, 3002, 2953, 2928, 2865, 2837, 1751, 1646, 1603, 1506, 1465, 1457, 1437, 1419, 1387, 1362, 1297, 1230, 1180, 1109, 939, 877, 823, 761, 733 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.36-3.48 (2H, m), 3.61 (1H, dd, *J* = 3.6, 11.3 Hz), 3.68-3.75 (1H, m), 3.76 (3H, s), 3.78 (3H, s), 4.18 (1H, brdd, *J* = 6.0, 8.9 Hz), 4.27 (1H, brq, *J* = 5.2 Hz), 4.35-4.41 (2H, m), 4.83 (1H, t, *J* = 5.2 Hz), 5.26 (1H, dd, *J* = 1.2, 10.6 Hz), 5.48 (1H, dd, *J* = 1.2, 17.3 Hz), 5.49 (1H, s), 5.72 (1H, dd, *J* = 5.6, 15.9 Hz), 5.90 (1H, dd, *J* = 6.6, 15.9 Hz), 6.09 (1H, ddd, *J* = 5.6, 10.6, 17.3 Hz), 6.78-6.85 (4H, m), 7.32 (2H, d, *J* = 8.4 Hz), 7.42 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.4 (CH_3), 55.5 (CH_3), 65.9 (CH_2), 69.1 (CH_2), 71.9 (CH), 74.8 (CH), 79.5 (CH), 80.6 (CH), 81.2 (CH), 99.7 (CH), 114.5 (CH×2), 117.3 (CH×2), 118.1 (CH_2), 126.8 (CH), 127.6 (CH×2), 128.2 (CH×2), 133.8 (CH), 134.3 (CH), 134.6 (C), 136.0 (C), 151.0 (C), 154.4 (C), 170.8 (C); EI-HRMS (m/z) calcd for $C_{27}H_{31}O_9{}^{35}Cl$ $[M]^+$: 534.1656, found: 534.1657.

7.1.22. Methyl (2*R*,3*R*,*E*)-2-(((2*R*,4*S*,5*R*)-2-(4-chlorophenyl)-4-vinyl-1,3-dioxan-5-yl)oxy)-6-hydroxy-3-(4-methoxyphenoxy) hex-4-enoate (42). To a solution of **41** (464.4 mg, 0.8681 mmol) in THF (4.3 mL) were added pH 7 phosphate buffer (1.0 mL) and $NaIO_4$ (928.4 mg, 4.341 mmol) at 25 ºC, and the mixture was stirred for 1.5 h. Then, the reaction was quenched with saturated aq. $NaHCO_3$ and the mixture was concentrated under reduced pressure to remove organic solvent. The residual aqueous mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude product, which was used immediately in the next reaction.

To a solution of the above crude product in MeOH (18 mL) were added $CeCl_3 \cdot 7H_2O$ (970.7 mg, 2.603 mmol) and $NaBH_4$ (98.5 mg, 2.60 mmol) at –78 ºC, and the mixture was stirred for 20 min. Then, the reaction was quenched with 0.2 mol/L aq. HCl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 2) to give **42** (400.3 mg, 0.7927 mmol, 91% from **41**, containing 15-*epi*-**42** [**42**:15-*epi*-**42** = > 20:1]) as a colorless oil.

42: $[\alpha]_D^{24}$ –54.4 (*c* 1.85, $CHCl_3$); IR (neat) ν 3493, 3043, 2998, 2953, 2930, 2911, 2860, 2836, 1747, 1603, 1509, 1504, 1464, 1455, 1439, 1420, 1416, 1385, 1359, 1280, 1227, 1180, 1109, 1090, 1038, 1016, 980, 941, 825, 733 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.42 (1H, dt, *J* = 4.8, 9.8 Hz), 3.72 (1H, t, *J* = 10.5 Hz), 3.76 (3H, s), 3.78 (3H, s), 4.13-4.21 (3H, m), 4.34 (1H, d, *J* = 4.8 Hz), 4.39 (1H, dd, *J* = 4.8, 11.2 Hz), 4.84 (1H, t, *J* = 5.8 Hz), 5.26 (1H, dd, *J* = 1.1, 10.5 Hz), 5.47 (1H, d, *J* = 16.1 Hz), 5.49 (1H, s), 5.81 (1H, dd, *J* = 6.4, 16.1 Hz), 5.92 (1H, td, *J* = 4.4, 16.1 Hz), 6.09 (1H, ddd, *J* = 5.8, 10.5, 17.2 Hz), 6.78-6.85 (4H, m), 7.32 (2H, d, *J* = 8.4 Hz), 7.42 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.3 (CH_3), 55.5 (CH_3), 62.2 (CH_2), 69.2 (CH_2), 74.6 (CH), 79.4 (CH), 80.6 (CH), 81.3 (CH), 99.7 (CH), 114.5 (CH×2), 117.2 (CH×2), 118.0 (CH_2), 125.4 (CH), 127.5 (CH×2), 128.2 (CH×2), 134.3 (CH), 134.47 (CH), 134.53 (C), 136.0 (C), 151.1 (C), 154.3 (C), 170.7 (C); EI-HRMS (m/z) calcd for $C_{26}H_{29}O_8{}^{35}Cl$ $[M]^+$: 504.1551, found: 504.1552.

7.1.23. Methyl (2*R*,3*R*)-2-(((2*R*,4*S*,5*R*)-2-(4-chlorophenyl)-4-vinyl-1,3-dioxan-5-yl)oxy)-3-(4-methoxyphenoxy)hex-5-enoate (26). To a solution of **42** (27.99 g, 55.43 mmol) in THF-1-hexene (450 mL: 90 mL) were added PPh_3 (29.09 g, 110.9 mmol) and IPNSBH (28.60 g, 111.2 mmol) at 17 ºC, and the mixture was cooled to 0 ºC with stirring. Then, to the mixture was added DIAD (22.0 mL, 112 mmol), and the mixture was warmed to 17 ºC. After being stirred for 10 h, to the mixture were added 2,2,2-trifluoroethanol (200 mL) and H_2O (200 mL), and the mixture was stirred for 19 h. The reaction was quenched with 0.5 mol/L aq. HCl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 20 → 5) to give **26** (22.87 g, 46.77 mmol, 84%, containing 15-*epi*-**26** [**26**:15-*epi*-**26** = > 20:1]) as a colorless oil.

26: $[\alpha]_D^{25}$ –21.7 (*c* 1.14, $CHCl_3$); IR (neat) ν 3078, 3044, 2998, 2953, 2932, 2911, 2858, 2835, 1753, 1642, 1603, 1506, 1464, 1437, 1416, 1385, 1360, 1340, 1280, 1227, 1180, 1146, 1110, 1089, 1038, 1016, 989, 929, 825 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.40-2.61 (2H, m), 3.35 (1H, dt, *J* = 5.2, 10.0 Hz), 3.68-3.73 (1H, m), 3.75 (3H, s), 3.77 (3H, s), 4.16 (1H, brdd, *J* = 5.9, 9.2 Hz), 4.33 (1H, d, *J* = 4.1 Hz), 4.40 (1H, dd, *J* = 5.2, 11.2 Hz), 4.44-4.48 (1H, m), 5.10 (1H, d, *J* = 9.2 Hz), 5.19 (1H, d, *J* = 11.2 Hz), 5.43 (1H, d, *J* = 17.2 Hz), 5.49 (1H, s), 5.82 (1H, tdd, *J* = 7.1, 10.0, 17.2 Hz), 6.01 (1H, ddd, *J* = 5.9, 10.5, 17.2 Hz), 6.80-6.89 (4H, m), 7.32 (2H, d, *J* = 8.4 Hz), 7.42 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.2 (CH_2), 52.2 (CH_3), 55.5 (CH_3), 69.3 (CH_2), 74.5 (CH), 79.0 (CH), 79.5 (CH), 80.9 (CH), 99.7 (CH), 114.6 (CH×2), 117.2 (CH×2), 118.1 (CH_2), 118.4 (CH_2), 127.6 (CH×2), 128.2 (CH×2), 133.3 (CH), 134.3 (CH), 134.6 (C), 136.0 (C), 151.3 (C), 154.3 (C), 171.2 (C); EI-HRMS (m/z) calcd for $C_{26}H_{29}O_7{}^{35}Cl$ $[M]^+$: 488.1601, found: 488.1603.

7.1.24. Methyl (2*R*,4a*R*,6*R*,7*R*,10a*S*,*Z*)-2-(4-chlorophenyl)-7-(4-methoxyphenoxy)-4,4a,6,7,8,10a-hexahydro[1,3]dioxino[5,4-*b*]oxocine-6-carboxylate (24). To a solution of **26** (469.1 mg, 0.9594 mmol) in degassed CH_2Cl_2 (50 mL) was added a solution of the second generation Grubbs catalyst (**17**) (46.8 mg, 0.0551 mmol) in degassed CH_2Cl_2 (2 mL) at 23 ºC, and the mixture was stirred for 14 h. Then, the mixture was stirred under O_2 atmosphere for 2 h. The mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel + Florisil®, hexane/EtOAc = 10 → 5) to give **24** (colorless solid, 329.5 mg, 0.7149 mmol, 75%) as a single diastereomer. Under the reaction conditions, 15-*epi*-**26** was not reactive. Unreacted 15-*epi*-**26** was easily separable from **24** by column chromatography.

24: mp 128-130 ºC; $[\alpha]_D^{25}$ –125 (*c* 1.03, $CHCl_3$); IR (KBr) ν 3017, 2951, 2931, 2868, 2846, 1752, 1509, 1463, 1436, 1381, 1344, 1319, 1292, 1280, 1265, 1251, 1244, 1218, 1196, 1178, 1162, 1119, 1102, 1085, 1055, 1036, 1024, 1010, 978, 837, 818, 767, 662 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 2.32-2.48 (2H, m), 3.28 (3H, s), 3.31 (3H, s), 3.39 (1H, t, *J* = 10.4 Hz), 3.52 (1H, brdt, *J* = 5.0, 9.9 Hz), 4.14 (1H, brt, *J* = 7.2 Hz), 4.22 (1H, dd, *J* = 5.0, 10.4 Hz), 4.26 (1H, d, *J* = 9.6 Hz), 4.91 (1H, td, *J* = 2.7, 9.6 Hz), 5.04 (1H, s), 5.69 (1H, brdq, *J* = 1.6, 9.0 Hz), 5.89 (1H, dd, *J* = 5.0, 10.4 Hz), 6.73 (2H, d, *J* = 8.7 Hz), 6.95 (2H, d, *J* = 8.7 Hz), 7.17 (2H, d, *J* = 8.5 Hz), 7.35 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, C_6D_6) δ 28.1 (CH_2), 51.8 (CH_3), 55.1 (CH_3),

69.3 (CH_2), 77.0 (CH), 79.5 (CH), 80.2 (CH), 80.4 (CH), 100.0 (CH), 115.1 (CH×2), 119.0 (CH×2), 126.4 (CH), 128.2 (CH×2), 128.5 (CH×2), 134.0 (CH), 134.9 (C), 136.8 (C), 151.7 (C), 155.5 (C), 170.6 (C); EI-HRMS (m/z) calcd for $C_{24}H_{25}O_7{}^{35}Cl$ $[M]^+$: 460.1288, found: 460.1289.

7.1.25. Methyl (2*R*,4a*R*,6*R*,7*R*,10a*S*,*Z*)-2-(4-chlorophenyl)-7-hydroxy-4,4a,6,7,8,10a-hexahydro[1,3]dioxino[5,4-*b*]oxocine-6-carboxylate (43). To a solution of **24** (15.43 g, 33.48 mmol) in CH_2Cl_2-DMF (120 mL: 120 mL) was added a solution of CAN (73.41 g, 134.1 mmol) in H_2O (60 mL) dropwise at 0 ºC, and the mixture was stirred for 16 h. Then, the mixture was diluted with H_2O, and extracted with Et_2O several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 3 → 1) to give **43** (11.02 g, 31.06 mmol, 93%) as a colorless solid.

43: mp 95-96 ºC; $[\alpha]_D{}^{23}$ –64.4 (*c* 0.925, $CHCl_3$); IR (KBr) ν 3492, 3034, 2953, 2930, 2902, 2857, 1744, 1603, 1495, 1461, 1440, 1384, 1350, 1293, 1274, 1240, 1203, 1176, 1128, 1110, 1065, 1016, 815, 751, 661 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.40-2.51 (1H, m), 2.63-2.74 (1H, m), 2.93 (1H, brs), 3.54 (1H, dt, *J* = 5.1, 9.6 Hz), 3.66 (1H, brt, *J* = 10.4 Hz), 3.80 (3H, s), 4.00 (1H, d, *J* = 9.6 Hz), 4.15-4.23 (1H, m), 4.37 (1H, dd, *J* = 5.1, 10.4 Hz), 4.67 (1H, brdd, *J* = 2.7, 8.8 Hz), 5.46 (1H, s), 5.83-5.96 (2H, m), 7.34 (2H, d, *J* = 8.6 Hz), 7.43 (2H, d, *J* = 8.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.4 (CH_2), 52.6 (CH_3), 69.1 (CH_2), 72.4 (CH), 76.5 (CH), 79.3 (CH), 80.5 (CH), 100.1 (CH), 126.8 (CH), 127.6 (CH×2), 128.4 (CH×2), 133.2 (CH), 134.9 (C), 135.9 (C), 173.4 (C); ESI-HRMS (m/z) calcd for $C_{17}H_{19}O_6{}^{35}ClNa$ $[M + Na]^+$: 377.0762, found: 377.0765.

7.1.26. (2*R*,4a*R*,6*S*,7*R*,10a*S*,*Z*)-2-(4-Chlorophenyl)-6-(hydroxymethyl)-4,4a,6,7,8,10a-hexahydro[1,3]dioxino[5,4-*b*]oxocin-7-ol (44). To a solution of **43** (11.02 g, 31.06 mmol) in MeOH (160 mL) was added $NaBH_4$ (2.379 g, 62.88 mmol) at 0 ºC, and the mixture was stirred for 1 h at 22 ºC. Then, to the mixture was added extra $NaBH_4$ (1.182 g, 31.23 mmol) at 0 ºC, and the mixture was stirred for 1 h at 22 ºC. The reaction was quenched with $NaHCO_3$ and the mixture was filtered through a Celite pad. The filtrate was evaporated to remove organic solvent, and the aqueous mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 1) to give **44** (9.69 g, 29.6 mmol, 95%) as a colorless solid.

44: mp 54-56 ºC; $[\alpha]_D{}^{26}$ –96.2 (*c* 0.910, $CHCl_3$); IR (KBr) ν 3396, 3033, 2928, 2859, 1603, 1495, 1462, 1442, 1417, 1403, 1383, 1351, 1293, 1276, 1217, 1114, 1091, 1069, 1042, 1015, 875, 816, 760, 735, 660, 617, 521 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.14 (2H, brs), 2.32-2.42 (1H, m), 2.66-2.77 (1H, m), 3.46-3.56 (2H, m), 3.63 (1H, t, *J* = 10.4 Hz), 3.70 (1H, dd, *J* = 5.5, 11.5 Hz), 3.78 (1H, dd, *J* = 5.5, 11.5 Hz), 4.00 (1H, brtd, *J* = 3.1, 9.2 Hz), 4.28 (1H, dd, *J* = 5.0, 10.4 Hz), 4.45 (1H, dd, *J* = 3.1, 8.8 Hz), 5.44 (1H, s), 5.81-5.94 (2H, m), 7.34 (2H, d, *J* = 8.6 Hz), 7.43 (2H, d, *J* = 8.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.7 (CH_2), 64.0 (CH_2), 69.4 (CH_2), 72.6 (CH), 75.7 (CH), 79.7 (CH), 81.8 (CH), 99.9 (CH), 126.4 (CH), 127.6 (CH×2), 128.4 (CH×2), 133.4 (CH), 134.8 (C), 135.9 (C); ESI-HRMS (m/z) calcd for $C_{16}H_{18}O_5{}^{35}Cl$ $[M + H]^+$: 325.0848, found: 325.0856.

7.1.27. (4a*S*,5a*R*,8*R*,9a*S*,12a*R*,*Z*)-2,2-Di-*tert*-butyl-8-(4-chlorophenyl)-4a,5a,6,9a,12,12a-hexahydro-*4H*-[1,3,2]dioxasilino[5,4-*b*][1,3]dioxino[4,5-*g*]oxocine (45). To a solution of **44** (172.7 mg, 0.5285 mmol) and pyridine (0.130 mL, 1.62 mmol) in DMF (2.6 mL) was added $^tBu_2Si(OTf)_2$ (0.260 mL, 0.803 mmol) at 0 ºC, and the mixture was stirred for 3 h at 19 ºC. Then the reaction was quenched with H_2O, and the mixture was extracted with Et_2O several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 20) to give **45** (222.2 mg, 0.4757 mmol, 90%) as a colorless solid.

45: mp 118-120 ºC; $[\alpha]_D{}^{25}$ –93.0 (*c* 0.560, $CHCl_3$); IR (KBr) ν 3036, 2961, 2933, 2889, 2860, 1495, 1474, 1386, 1365, 1295, 1282, 1272, 1213, 1151, 1110, 1091, 1063, 1046, 1016, 987, 972, 951, 933, 902, 826, 795, 765, 653 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (9H, s), 1.02 (9H,s), 2.40-2.51 (1H, m), 2.64-2.74 (1H, m), 3.48 (1H, ddd, *J* = 4.1, 8.4, 10.2 Hz), 3.55 (1H, brt, *J* = 10.2 Hz), 3.66 (1H, ddd, *J* = 4.4, 8.9, 10.7 Hz), 3.74 (1H, dd, *J* = 9.4, 10.7 Hz), 4.03 (1H, dd, *J* = 4.4, 9.4 Hz), 4.13 (1H, ddd, *J* = 2.8, 3.6, 8.9 Hz), 4.22 (1H, dd, *J* = 4.1, 9.9 Hz), 4.42 (1H, brdd, *J* = 2.8, 8.4 Hz), 5.42 (1H, s), 5.82-5.95 (2H, m), 7.33 (2H, d, *J* = 8.5 Hz), 7.42 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1 (C), 22.5 (C), 27.1 (CH_3×3), 27.4 (CH_3×3), 32.7 (CH_2), 67.0 (CH_2), 69.3 (CH_2), 74.7 (CH), 76.6 (CH), 77.7 (CH), 79.8 (CH), 99.9 (CH), 127.1 (CH), 127.6 (CH×2), 128.3 (CH×2), 133.1 (CH), 134.6 (C), 136.1 (C); APCI-HRMS (m/z) calcd for $C_{24}H_{35}O_5{}^{35}Cl_2Si$ $[M + Cl]^-$: 501.1636, found: 501.1642.

7.1.28. (4a*S*,6*R*,7*S*,10a*R*,*Z*)-2,2-Di-*tert*-butyl-6-(hydroxymethyl)-4,4a,6,7,10,10a-hexahydro[1,3,2]dioxasilino[5,4-*b*]oxocin-7-ol (46). To a solution of **45** (222.2 mg, 0.4757 mmol) and 1,2-ethanedithiol (0.164 mL, 1.95 mmol) in CH_2Cl_2 (5.0 mL) was added $BF_3{\cdot}OEt_2$ (0.120 mL, 0.972 mmol) at –40 ºC, and the mixture was stirred for 3 h. Then, the reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 3 → 1) to give **46** (158.8 mg, 0.4609 mmol, 97%) as a colorless oil.

46: $[\alpha]_D{}^{23}$ –56.0 (*c* 0.350, $CHCl_3$); IR (neat) ν 3396, 3025, 2962, 2933, 2860, 1474, 1440, 1387, 1364, 1213, 1200, 1146, 1104, 1075, 1011, 1004, 990, 940, 826, 794, 767, 753, 652 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.96 (9H, s), 1.02 (9H, s), 2.06 (2H, brs), 2.39 (1H, brddd, *J* = 2.4, 6.3, 13.4 Hz), 2.66 (1H, ddd, *J* = 3.9, 8.9, 13.4 Hz), 3.40 (1H, ddd, *J* = 3.9, 5.3, 8.9 Hz), 3.62 (1H, ddd, *J* = 5.0, 9.1, 10.6 Hz), 3.69-3.81 (2H, m), 3.85 (1H, brdd, *J* = 4.1, 11.6 Hz), 4.05 (1H, dd, *J* = 5.0, 9.9 Hz), 4.11 (1H, ddd, *J* = 2.4, 3.9, 9.1 Hz), 4.47 (1H, brdd, *J* = 3.9, 8.9 Hz), 5.74-5.89 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1 (C), 22.5 (C), 27.0 (CH_3×3), 27.4 (CH_3×3), 32.6 (CH_2), 64.0 (CH_2), 67.0 (CH_2), 69.7 (CH), 76.8 (CH), 77.5 (CH), 83.9 (CH), 126.6 (CH), 136.7 (CH); ESI-HRMS (m/z) calcd for $C_{17}H_{32}O_5SiNa$ $[M + Na]^+$: 367.1911, found: 367.1912.

7.1.29. (4a*S*,6*R*,7*S*,10a*R*,*Z*)-6-Allyl-2,2-di-*tert*-butyl-7-((triethylsilyl)oxy)-4,4a,6,7,10,10a-hexahydro[1,3,2]dioxasilino [5,4-*b*]oxocine (47). To a solution of **46** (385.2 mg, 1.118 mmol) and 2,6-lutidine (0.660 mL, 5.70 mmol) in CH_2Cl_2 (10 mL) was added Tf_2O (0.190 mL, 1.13 mmol) at –78 ºC, and the mixture was stirred for 15 min. Then, to the mixture was added TESOTf (0.380 mL, 1.68 mmol) at –78 ºC. Then, the mixture was warmed to 0 ºC, and stirred for 45 min. The reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with 0.5 mol/L aq. HCl

and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 20 → 1 → EtOAc) to give a trifluoromethanesulfonate ester, which was used immediately in the next reaction.

To a solution of tetravinyltin (0.995 mL, 5.48 mmol) in THF (27 mL) was added BuLi (1.60 mol/L in hexane, 13.7 mL, 21.9 mmol) at –78 ºC, and the mixture was stirred for 1 h. To the resulting vinyllithium solution was added a suspension of CuCN (990.5 mg, 11.06 mmol) in THF (27 mL) dropwise at –78 ºC, and the mixture was stirred for 45 min. Then, to the mixture was added a solution of the above trifluoromethanesulfonate ester in THF (10 mL) at –78 ºC. Then, the mixture was warmed to –20 ºC and stirred for 18 h. The reaction quenched with a mixture of saturated aq. NH_4Cl and 25% aq. NH_3 (v/v = 9/1), and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane → hexane/EtOAc = 50) to give **47** (503.5 mg, 1.075 mmol, 98%) as a colorless oil.

47: $[\alpha]_D^{21}$ –30.4 (*c* 1.20, $CHCl_3$); IR (neat) ν 3077, 3027, 2959, 2933, 2876, 2860, 1642, 1474, 1439, 1414, 1386, 1364, 1307, 1241, 1200, 1147, 1102, 1058, 1006, 941, 844, 826, 794, 752, 727, 652, 632 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.60 (6H, q, *J* = 7.9 Hz), 0.94 (9H, s), 0.95 (9H, t, *J* = 7.9 Hz), 1.01 (9H, s), 1.91-2.04 (1H, m), 2.30-2.39 (1H, m), 2.55-2.72 (2H, m), 3.29 (1H, ddd, *J* = 2.5, 8.7, 10.0 Hz), 3.54 (1H, ddd, *J* = 5.0, 9.1, 10.6 Hz), 3.71 (1H, t, *J* = 10.6 Hz), 4.00 (1H, dd, *J* = 5.0, 10.0 Hz), 4.08 (1H, ddd, *J* = 2.5, 4.0, 9.1 Hz), 4.14 (1H, dd, *J* = 3.3, 8.7 Hz), 5.00-5.11 (2H, m), 5.67-5.87 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.9 (CH_2×3), 6.8 (CH_3×3), 20.1 (C), 22.5 (C), 27.1 (CH_3×3), 27.4 (CH_3×3), 32.7 (CH_2), 36.9 (CH_2), 67.1 (CH_2), 72.9 (CH), 76.9 (CH), 77.6 (CH), 85.6 (CH), 116.5 (CH_2), 125.7 (CH), 135.5 (CH), 138.5 (CH); APCI-HRMS (m/z) calcd for $C_{25}H_{49}O_4Si_2$ $[M + H]^+$: 469.3164, found: 469.3167.

7.1.30. (4a*S*,6*R*,7*S*,10a*R*,*Z*)-6-Allyl-2,2-di-*tert*-butyl-4,4a,6,7,10,10a-hexahydro[1,3,2]dioxasilino[5,4-*b*]oxocin-7-ol (48). To a solution of **47** (260.6 mg, 0.5559 mmol) in EtOH (7.0 mmol) was added PPTS (17.6 mg, 0.0700 mmol) at 25 ºC, and the mixture was stirred for 3.5 h. The reaction was quenched with Et_3N, and the mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 50 → 40 → 20) to give **48** (184.2 mg, 0.5195 mmol, 93%) as a colorless oil.

48: $[\alpha]_D^{22}$ –56.7 (*c* 1.33, $CHCl_3$); IR (neat) ν 3455, 3077, 3023, 2961, 2933, 2860, 1642, 1473, 1439, 1393, 1387, 1364, 1306, 1250, 1212, 1199, 1147, 1104, 1072, 1056, 995, 939, 917, 825, 794, 768, 754, 652, 617 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (9H, s), 1.01 (9H, s), 1.79 (1H, brs), 2.11-2.23 (1H, m), 2.36 (1H, ddd, *J* = 2.4, 6.6, 13.5 Hz), 2.53-2.63 (1H, m), 2.68 (1H, ddd, *J* = 4.0, 8.8, 13.5 Hz), 3.32 (1H, dt, *J* = 3.0, 8.9 Hz), 3.55 (1H, ddd, *J* = 5.0, 9.1, 10.6 Hz), 3.74 (1H, t, *J* = 10.6 Hz), 4.01 (1H, dd, *J* = 1H, dd, *J* = 5.0, 10.0 Hz), 4.10 (1H, ddd, *J* = 2.4, 4.0, 9.1 Hz), 4.18-4.26 (1H, m), 5.06 (1H, brd, *J* = 10.0 Hz), 5.11 (1H, brd, *J* = 17.1 Hz), 5.71-5.93 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.2 (C), 22.5 (C), 27.1 (CH_3×3), 27.4 (CH_3×3), 32.8 (CH_2), 37.0 (CH_2), 67.1 (CH_2), 72.2 (CH), 76.9 (CH), 77.5 (CH), 84.5 (CH), 117.1 (CH_2), 127.0 (CH), 135.0 (CH), 136.8 (CH); APCI-HRMS (m/z) calcd for $C_{19}H_{34}O_4{}^{35}ClSi$ $[M + Cl]^-$: 389.1920, found : 389.1929.

7.1.31. 2-(((4a*S*,6*R*,7*S*,10a*R*,*Z*)-6-Allyl-2,2-di-*tert*-butyl-4,4a,6,7,10,10a-hexahydro[1,3,2]dioxasilino[5,4-*b*]oxocin-7-yl)oxy) acetic acid (49). To a solution of **48** (133.6 mg, 0.3768 mmol) in PhH (3.0 mL) were added 50% aq. NaOH (3.0 mL), *tert*-butyl bromoacetate (0.510 mL, 3.77 mmol), and Bu_4NHSO_4 (13.0 mg, 0.0383 mmol), at 25 ºC, and the mixture was stirred for 2 h. Then, the mixture was diluted with H_2O (20 mL) and PhH (10 mL). To the mixture was added MeOH (40 mL) until the solution became homogeneous, and the mixture was stirred for 4 h. After the mixture was evaporated to remove organic solvent, the resulting aqueous mixture was diluted with Et_2O and extracted with H_2O several times. The combined aqueous layers were acidified to pH 4 with 2.0 mol/L aq. HCl and extracted with CH_2Cl_2 several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 3) to give **49** (150.4 mg, 0.3645 mmol, 97%) as a colorless oil.

49: $[\alpha]_D^{21}$ -7.35 (*c* 0.785, $CHCl_3$); IR (neat) ν 3500-2400 (br), 3076, 3022, 2962, 2933, 2860, 2773, 2738, 2710, 2667, 2573, 1764, 1732, 1643, 1474, 1439, 1435, 1393, 1387, 1364, 1307, 1296, 1248, 1213, 1200, 1101, 1074, 1056, 1011, 1000, 970, 938, 919, 825, 794, 755, 652, 634 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (9H, s), 1.01 (9H, s), 2.12-2.25 (1H, m), 2.40 (1H, brddd, *J* = 2.5, 6.8, 13.4 Hz), 2.57-2.71 (2H, m), 3.42 (1H, dt, *J* = 2.8, 8.8 Hz), 3.55 (1H, ddd, *J* = 5.0, 9.1, 10.6 Hz), 3.74 (1H, t, *J* = 10.2 Hz), 3.97-4.05 (2H, m), 4.06 (1H, d, *J* = 16.8 Hz), 4.06-4.13 (1H, m), 4.21 (1H, d, *J* = 16.8 Hz), 5.05 (1H, brd, *J* = 10.2 Hz), 5.08 (1H, brd, *J* = 17.2 Hz), 5.69-5.89 (2H, m), 5.91-6.03 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1 (C), 22.5 (C), 27.0 (CH_3×3), 27.4 (CH_3×3), 32.8 (CH_2), 36.8 (CH_2), 65.6 (CH_2), 66.9 (CH_2), 76.9 (CH), 77.4 (CH), 79.9 (CH), 83.6 (CH), 117.0 (CH_2), 130.1 (CH), 134.0 (CH), 134.9 (CH), 175.2 (C); ESI-HRMS (m/z) calcd for $C_{21}H_{36}O_6SiNa$ $[M + Na]^+$: 435.2173, found: 435.2171.

7.1.32. (*R*,*Z*)-1-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-3-(4-methoxyphenoxy)allyl 2-(((4a*S*,6*R*,7*S*,10a*R*,*Z*)-6-allyl-2,2-di-*tert*-butyl-4,4a,6,7,10,10a-hexahydro[1,3,2]dioxasilino[5,4-*b*]oxocin-7-yl)oxy)acetate (23). To a solution of **25** (3.46 g, 12.3 mmol), DMAP (1.0776 g, 8.8205 mmol), and EDCI·HCl (3.951 g, 20.61 mmol) in CH_2Cl_2 (70 mL) was added a solution of **49** (2.816 g, 6.825 mmol) at 27 ºC, and the mixture was stirred for 15 h. Then, the reaction was quenched with 0.5 mol/L aq. HCl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluent:* hexane → hexane/EtOAc = 5; the eluent contained 5% Et_3N) to give **23** (4.213 g, 6.243 mmol, 92% from **49**) as a colorless oil.

23: $[\alpha]_D^{22}$ +10.1 (*c* 1.85, $CHCl_3$); IR (neat) ν 3075, 2961, 2933, 2860, 1762, 1740, 1669, 1506, 1473, 1442, 1394, 1382, 1371, 1365, 1231, 1214, 1103, 1072, 1044, 1011, 971, 938, 826, 795, 652 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (9H, s), 1.01 (9H, s), 1.36 (3H, s), 1.45 (3H, s), 2.12-2.24 (1H, m), 2.36 (1H, ddd, *J* = 2.7, 6.6, 13.4 Hz), 2.59-2.75 (2H, m), 3.39 (1H, dt, *J* = 2.7, 9.0 Hz), 3.54 (1H, ddd, *J* = 5.0, 9.3, 10.6 Hz), 3.73 (1H, t, *J* = 10.6 Hz), 3.78 (3H, s), 3.85 (1H, dd, *J* = 6.2, 8.7 Hz), 3.97-4.11 (5H, m), 4.21 (1H, d, *J* = 16.3 Hz), 4.28 (1H, q, *J* = 6.6 Hz), 4.70 (1H, dd, *J* = 6.2, 8.7 Hz), 5.02 (1H, brd, *J* = 10.2 Hz), 5.07 (1H, brd, *J* = 17.2 Hz), 5.72-5.99 (4H, m), 6.45 (1H, dd, *J* = 0.9, 6.2 Hz), 6.84 (2H, d, *J* = 9.2 Hz), 6.95 (2H, d, *J* = 9.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1 (C), 22.5 (C), 25.5 (CH_3), 26.4 (CH_3), 27.1 (CH_3×3), 27.4 (CH_3×3), 32.8 (CH_2), 36.9 (CH_2), 55.6 (CH_3), 65.8 (CH_2), 66.3 (CH_2), 67.1 (CH_2), 69.8 (CH), 76.8 (CH), 76.9 (CH), 77.5 (CH), 79.9 (CH), 83.9 (CH), 104.5 (CH), 110.1 (C), 114.7 (CH×2), 116.8 (CH_2), 118.2 (CH×2), 129.7 (CH), 134.6 (CH), 135.3 (CH), 146.0 (CH), 150.9 (C), 155.9 (C), 169.2 C); ESI-

HRMS (m/z) calcd for $C_{36}H_{54}O_{10}SiNa$ [M + Na]$^+$: 697.3379, found: 697.3374.

7.1.33. Methyl (2*S*,3*S*,6*S*,*E*)-2-(((4a*S*,6*R*,7*S*,10a*R*,*Z*)-6-allyl-2,2-di-*tert*-butyl-4,4a,6,7,10,10a-hexahydro[1,3,2]dioxasilino[5,4-*b*]oxocin-7-yl)oxy)-5-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-(4-methoxyphenoxy)pent-4-enoate (50). To a solution of pyrrolidine (0.120 mL, 1.40 mmol) in THF (3.0 mmol) were added KHMDS (0.5 mol/L in $PhCH_3$, 2.80 mL, 1.40 mmol) and BuLi (1.65 mol/L in hexane, 0.848 mL, 1.40 mmol) dropwise at –78 ºC, and the mixture was stirred for 15 min. To the solution was added a solution of **23** (157.8 mg, 0.234 mmol) in $PhCH_3$ (7.5 mL) at –78 ºC. Then, to the solution was added TMSCl (0.354 mL, 2.80 mmol) immediately at –78 ºC, and the mixture was stirred for 15 min. To the mixture was added diethyl malonate (0.425 mL, 2.80 mmol) at –78 ºC, and the mixture was warmed to 0 ºC. After being stirred for 30 min, the reaction was quenched with 0.2 mol/L aq. HCl, and the mixture was extracted with $CHCl_3$ several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude product.

To a solution of the above crude product in PhH-MeOH (1.0 mL: 1.0 mL) was added $TMSCHN_2$ (2.0 mol/L in Et_2O, 0.20 mL, 0.40 mmol) at 24 ºC, and the mixture was stirred for 10 min. Then, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10 → 5) to give **50** (142.9 mg, 0.207 mmol, 89% from **23**, containing a trace of 27-*epi*-**50** [**50**:27-*epi*-**50** = > 20:1]) as a colorless oil.

50: $[\alpha]_D^{24}$ +4.83 (*c* 0.470, $CHCl_3$); IR (neat) ν 3075, 2961, 2934, 2861, 1751, 1643, 1506, 1472, 1465, 1457, 1437, 1380, 1371, 1226, 1180, 1148, 1103, 1071, 1011, 974, 942, 921, 825, 795, 767, 754 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (9H, s), 1.00 (9H, s), 1.36 (3H, s), 1.38 (3H, s), 2.04-2.17 (1H, m), 2.34 (1H, brddd, *J* = 2.4, 6.5, 13.6 Hz), 2.61 (1H, ddd, *J* = 3.9, 9.7, 13.6 Hz), 2.71 (1H, brdd, *J* = 7.2, 15.1 Hz), 3.38-3.47 (1H, m), 3.48 (1H, t, *J* = 7.9 Hz), 3.47-3.57 (1H, m), 3.72 (1H, t, *J* = 10.4 Hz), 3.74 (3H, s), 3.75 (3H, s), 3.96-4.14 (4H, m), 4.20 (1H, d, *J* = 5.0 Hz), 4.51 (1H, q, *J* = 6.5 Hz), 4.87 (1H, t, *J* = 5.8 Hz), 5.04 (1H, brd, *J* = 10.4 Hz), 5.07 (1H, brd, *J* = 17.2 Hz), 5.70-5.96 (5H, m), 6.76-6.85 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1 (C), 22.5 (C), 25.8 (CH_3), 26.6 (CH_3), 27.0 (CH_3×3), 27.4 (CH_3×3), 32.6 (CH_2), 37.0 (CH_2), 52.2 (CH_3), 55.6 (CH_3), 67.0 (CH_2), 69.3 (CH_2), 75.9 (CH), 76.9 (CH), 77.5 (CH), 79.9 (CH), 80.3 (CH), 82.1 (CH), 83.8 (CH), 109.5 (C), 114.6 (CH×2), 117.0 (CH_2), 117.4 (CH×2), 128.4 (CH), 129.2 (CH), 132.9 (CH), 134.3 (CH), 135.1 (CH), 151.2 (C), 154.5 (C), 170.8 (C); ESI-HRMS (m/z) calcd for $C_{37}H_{56}O_{10}SiNa$ [M + Na]$^+$: 711.3535, found: 711.3533.

7.1.34. Methyl (2*S*,3*S*,6*S*,*E*)-2-(((4a*S*,6*R*,7*S*,10a*R*,*Z*)-6-allyl-2,2-di-*tert*-butyl-4,4a,6,7,10,10a-hexahydro[1,3,2]dioxasilino[5,4-*b*]oxocin-7-yl)oxy)-6,7-dihydroxy-3-(4-methoxyphenoxy)hept-4-enoate (51). To a solution of **50** (68.1 mg, 0.0989 mmol) and 1,2-ethanedithiol (0.042 mL, 0.50 mmol) in CH_2Cl_2 (5.0 mL) was added $BF_3\cdot OEt_2$ (0.025 mL, 0.20 mmol) at –40 ºC, and the mixture was stirred for 4 h. Then, the reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with $CHCl_3$ several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 3 → 1 → 0.5) to give **51** (60.7 mg, 0.0935 mmol, 95%, containing 27-*epi*-**51** [**51**:27-*epi*-**51** = > 20:1]) as a colorless oil.

51: $[\alpha]_D^{24}$ –3.33 (*c* 0.535, $CHCl_3$); IR (neat) ν 3440, 3075, 3000, 2958, 2933, 2859, 1747, 1507, 1474, 1440, 1386, 1364, 1286, 1226, 1181, 1103, 1072, 1055, 1041, 1011, 977, 939, 921, 825, 795, 755, 653, 627 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (9H, s), 1.00 (9H, s), 2.00 (1H, brs), 2.06-2.18 (1H, m), 2.23 (1H, brs), 2.34 (1H, brddd, *J* = 2.5, 6.5, 13.4 Hz), 2.61 (1H, ddd, *J* = 3.9, 9.2, 13.4 Hz), 2.72 (1H, brdd, *J* = 6.5, 13.7 Hz), 3.38-3.64 (4H, m), 3.72 (1H, t, *J* = 10.1 Hz), 3.756 (3H, s), 3.760 (3H, s), 4.00 (1H, dd, *J* = 5.0, 10.1 Hz), 4.04-4.15 (2H, m), 4.21-4.30 (1H, m), 4.24 (1H, d, *J* = 4.5 Hz), 4.89 (1H, dd, *J* = 4.5, 6.5 Hz), 5.04 (1H, brd, *J* = 10.2 Hz), 5.07 (1H, brd, *J* = 17.2 Hz), 5.70-5.93 (5H, m), 6.76-6.86 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1 (C), 22.5 (C), 27.0 (CH_3×3), 27.4 (CH_3×3), 32.6 (CH_2), 36.9 (CH_2), 52.3 (CH_3), 55.6 (CH_3), 66.0 (CH_2), 67.0 (CH_2), 72.1 (CH), 76.9 (CH), 77.4 (CH), 79.9 (CH), 80.3 (CH), 82.1 (CH), 83.8 (CH), 114.6 (CH×2), 117.0 (CH_2), 117.4 (CH×2), 127.3 (CH), 129.3 (CH), 134.0 (CH), 134.2 (CH), 135.1 (CH), 151.0 (C), 154.5 (C), 170.9 (C); ESI-HRMS (m/z) calcd for $C_{34}H_{52}O_{10}SiNa$ [M + Na]$^+$: 671.3222, found: 671.3220.

7.1.35. Methyl (2*S*,3*S*,*E*)-2-(((4a*S*,6*R*,7*S*,10a*R*,*Z*)-6-allyl-2,2-di-*tert*-butyl-4,4a,6,7,10,10a-hexahydro[1,3,2]dioxasilino[5,4-*b*]oxocin-7-yl)oxy)-6-hydroxy-3-(4-methoxyphenoxy)hex-4-enoate (52). To a solution of **51** (1.665 g, 2.567 mmol) in THF (20 mL) were added pH 7 phosphate buffer (4.0 mL) and $NaIO_4$ (1.113 g, 5.205 mmol) at 18 ºC, and the mixture was stirred for 1 h. Then, to the mixture was added extra $NaIO_4$ (544.9 mg, 2.548 mmol) at 18 ºC, and the mixture was stirred for 1 h. Then, the mixture was diluted with H_2O and extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude product, which was used immediately in the next reaction.

To a solution of the above crude product in THF-MeOH (12 mL: 12 mL) were added $CeCl_3\cdot 7H_2O$ (4.7850 g, 12.843 mmol) and $NaBH_4$ (484.4 mg, 12.80 mmol) at –78 ºC, and the mixture was stirred for 30 min. Then, the reaction was quenched with saturated aq. NH_4Cl, and the mixture was evaporated to remove organic solvent. The resulting aqueous mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 1) to give **52** (1.463 g, 2.364 mmol, 92% from **52**, containing 27-*epi*-**52** [**52**:27-*epi*-**52** = > 20:1]) as a colorless oil.

52: $[\alpha]_D^{23}$ –6.54 (*c* 1.75, $CHCl_3$); IR (neat) ν 3483, 3075, 3007, 2959, 2934, 2892, 2860, 1748, 1507, 1473, 1440, 1387, 1364, 1285, 1227, 1181, 1146, 1104, 1055, 1040, 1011, 1001, 978, 941, 920, 826, 795, 756, 653, 629 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (9H, s), 1.00 (9H, s), 2.06-2.19 (1H, m), 2.34 (1H, ddd, *J* = 2.4, 6.6, 13.2 Hz), 2.61 (1H, ddd, *J* = 4.0, 9.4, 13.2 Hz), 2.73 (1H, brdd, *J* = 6.6, 14.7 Hz), 3.43 (1H, dt, *J* = 2.7, 9.5 Hz), 3.52 (1H, ddd, *J* = 5.0, 9.3, 10.5 Hz), 3.72 (1H, brt, *J* = 10.3 Hz), 3.75 (3H, s), 3.76 (3H, s), 4.00 (1H, dd, *J* = 5.0, 10.0 Hz), 4.04-4.18 (3H, m), 4.21 (1H, d, *J* = 4.9 Hz), 4.89 (1H, brt, *J* = 5.8 Hz), 5.04 (1H, brd, *J* = 10.2 Hz), 5.07 (1H, brd, *J* = 17.2 Hz), 5.73-5.98 (5H, m), 6.76-6.86 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1 (C), 22.5 (C), 27.0 (CH_3×3), 27.4 (CH_3×3), 32.6 (CH_2), 37.0 (CH_2), 52.2 (CH_3), 55.6 (CH_3), 62.5 (CH_2), 67.0 (CH_2), 76.9 (CH), 77.4 (CH), 79.9 (CH), 80.4 (CH), 82.1 (CH), 83.8 (CH), 114.6 (CH×2), 116.9 (CH_2), 117.4 (CH×2), 126.0 (CH), 129.2 (CH), 134.3 (CH), 134.7 (CH), 135.2 (CH), 151.1 (C), 154.5 (C), 170.9 (C); ESI-HRMS (m/z) calcd for $C_{33}H_{50}O_9SiNa$ [M + Na]$^+$: 641.3116, found: 641.3113.

7.1.36. Methyl (2*S*,3*S*)-2-(((4a*S*,6*R*,7*S*,10a*R*,*Z*)-6-allyl-2,2-di-*tert*-butyl-4,4a,6,7,10,10a-hexahydro-[1,3,2]dioxasilino[5,4-*b*]oxocin-7-yl)oxy)-3-(4-methoxyphenoxy)hex-5-enoate (22) To a solution of **52** (1.357 g, 2.192 mmol), PPh_3 (1.154 g, 4.400 mmol), and IPNBSH (1.129 g, 4.390 mmol) in THF-1-hexene (20 mL: 4.0 mL) was added DIAD (0.860 mL, 4.38 mmol) at 0 ºC, and the mixture was stirred for 6 h at 18 ºC. Then, to the mixture were added CF_3CH_2OH (6.0 mL) and H_2O (6.0 mL) at 18 ºC, and the mixture was stirred for 22 h. The mixture was diluted with brine and extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10) to give **22** (1.218 g, 2.021 mmol, 92%, containing 27-*epi*-**22** [**22**:27-*epi*-**22** = > 20:1]) as a colorless oil.

22: $[\alpha]_D^{25}$ –28.6 (*c* 0.310, $CHCl_3$); IR (neat) ν 3075, 2933, 2859, 1753, 1642, 1507, 1474, 1439, 1227, 1103, 1073, 1055, 1042, 825 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (9H, s), 1.00 (9H, s), 2.06-2.18 (1H, m), 2.26-2.35 (1H, m), 2.41-2.63 (3H, m), 2.74 (1H, brdd, *J* = 6.6, 13.9 Hz), 3.43 (1H, dt, *J* = 2.5, 9.3 Hz), 3.51 (1H, ddd, *J* = 5.0, 9.3, 10.6 Hz), 3.62-3.75 (1H, m), 3.73 (3H, s), 3.76 (3H, s), 3.96-4.09 (3H, m), 4.19 (1H, d, *J* = 4.1 Hz), 4.52 (1H, brtd, *J* = 4.4, 7.0 Hz), 5.02-5.18 (4H, m), 5.74-5.92 (4H, m), 6.77-6.91 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1 (C), 22.5 (C), 27.0 (CH_3×3), 27.4 (CH_3×3), 32.6 (CH_2), 34.2 (CH_2), 36.9 (CH_2), 52.0 (CH_3), 55.6 (CH_3), 67.0 (CH_2), 77.0 (CH), 77.4 (CH), 78.2 (CH), 79.4 (CH), 81.9 (CH), 83.9 (CH), 114.7 (CH×2), 116.9 (CH_2), 117.4 (CH×2), 118.0 (CH_2), 129.0 (CH), 133.5 (CH), 134.2 (CH), 135.1 (CH), 151.3 (C), 154.4 (C), 171.3 (C); ESI-HRMS (m/z) calcd for $C_{33}H_{50}O_8SiNa$ $[M + Na]^+$: 625.3167, found: 625.3174.

7.1.37. Methyl (4a*S*,5a*R*,7*Z*,10*S*,11*S*,12a*S*,13*Z*,15a*R*)-2,2-di-*tert*-butyl-10-(4-methoxyphenoxy)-4,4a,5a,6,9,10,11,12a,15,15a-decahydro[1,3,2]dioxasilino[4',5':7,8]oxocino[3,2-*b*]oxonine-11-carboxylate (54). To a solution of **22** (118.7 mg, 0.1969 mmol) degassed CH_2Cl_2 (37 mL) was added a solution of the first generation Grubbs catalyst (**53**) (32.4 mg, 0.03938 mmol) in degassed CH_2Cl_2 (3.0 mL) at 0 ºC, and the mixture was stirred for 11 h. Then, the mixture was stirred under O_2 atmosphere for 1 h. The mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel + Florisil®, hexane/EtOAc = 20 → 10) to give **54** (colorless platelets, 92.7 mg, 0.161 mmol, 82%) as a single diastereomer.

54: mp 137-139 ºC; $[\alpha]_D^{25}$ –88.5 (*c* 0.750, $CHCl_3$); IR (KBr) ν 3014, 2961, 2932, 2872, 2858, 1742, 1509, 1475, 1466, 1439, 1294, 1253, 1235, 1200, 1181, 1134, 1122, 1109, 1092, 1068, 1047, 1017, 1001, 946, 934, 829, 796, 786, 753, 654 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.08 (9H, s), 1.10 (9H, s), 2.06 (1H, brd, *J* = 12.7 Hz), 2.27-2.38 (2H, m), 2.61 (1H, ddd, *J* = 4.1, 9.8, 13.8 Hz), 2.69 (1H, ddd, *J* = 3.8, 10.3, 14.1 Hz), 2.83 (1H, brt, 11.4 Hz), 3.25-3.36 (1H, m), 3.29 (3H, s), 3.32 (3H, s), 3.51 (1H, ddd, *J* = 5.1, 9.1, 10.5 Hz), 3.82 (1H, t, *J* = 10.5 Hz), 3.99-4.17 (4H, m), 4.89 (1H, brtd, *J* = 3.3, 8.6 Hz), 5.74-5.99 (4H, m), 6.69 (2H, d, *J* = 9.2 Hz), 6.89 (2H, d, *J* = 9.2 Hz); ^{13}C NMR (100 MHz, C_6D_6) δ 20.4 (C), 22.7 (C), 27.4 (CH_3×3), 27.6 (CH_3×3), 27.8 (CH_2), 32.7 (CH_2), 33.0 (CH_2), 51.5 (CH_3), 55.1 (CH_3), 67.7 (CH_2), 78.3 (CH), 78.4 (CH), 79.7 (CH), 84.3 (CH), 84.6 (CH), 85.3 (CH), 115.1 (CH×2), 118.5 (CH×2), 126.6 (CH), 127.7 (CH), 129.1 (CH), 136.5 (CH), 151.9 (C), 155.3 (C), 171.8 (C); ESI-HRMS (m/z) calcd for $C_{31}H_{46}O_8SiNa$ $[M + Na]^+$: 597.2854, found: 597.2853; Crystal data: Crystals were obtained by recrystallizing from Et_2O/hexane. $C_{31}H_{46}O_8Si$, *M* = 574.79, colorless platelet, 0.70 × 0.20 × 0.01 mm^3, triclinic P1 (No. 1), *a* = 8.808(3) Å, *b* = 9.111(3) Å, *c* = 19.458(6) Å, α = 83.231(6)°, β = 89.474(9)°, γ = 89.004(10)°, *V* = 1550.4(8) $Å^3$, ρ_{calcd}(*Z* = 2) = 1.231 g cm^{-1}. A total 6463 unique data ($2\theta_{max}$ = 55°) were measured at T = 150 K by Rigaku Mercury CCD apparatus (Mo Kα radiation, λ = 0.71070 Å). Numerical absorption correction was applied (μ = 1.23 cm^{-1}). The structure was solved by the direct method (SIR92) and refined by the full-matrix least-squares method of F^2 with anisotropic temperature factors for non-hydrogen atoms. All the hydrogen atoms were located at the calculated positions. The final *wR* value is 0.2161 (all data) for 6448 reflections and 718 parameters. CCDC 906653.

7.1.38. Methyl (4a*S*,5a*R*,7*Z*,10*S*,11*S*,12a*S*,13*Z*,15a*R*)-2,2-di-*tert*-butyl-10-hydroxy-4,4a,5a,6,9,10,11,12a,15,15a-decahydro[1,3,2]dioxasilino[4',5':7,8]oxocino[3,2-*b*]oxonine-11-carboxylate (55). To a solution of **54** (647.7 mg, 1.127 mmol) in MeCN-CH_2Cl_2 (10 mL: 5 mL) was added a solution of CAN (3.102 g, 5.658 mmol) in H_2O (10 mL) at 0 ºC, and the mixture was stirred for 30 min. Then, the mixture was diluted with H_2O and extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 3) to give **55** (510.4 mg, 1.089 mmol, 97%) as a colorless oil.

55: $[\alpha]_D^{24}$ –144 (*c* 1.02, $CHCl_3$); IR (neat) ν 3473, 3023, 2959, 2932, 2891, 2859, 1745, 1665, 1474, 1439, 1386, 1364, 1308, 1278, 1249, 1214, 1199, 1173, 1123, 1099, 1048, 1011, 1001, 942, 825, 795, 754, 652 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (9H, s), 1.02 (9H, s), 2.07-2.25 (2H, m), 2.32 (1H, ddd, *J* = 2.2, 6.7, 13.6 Hz), 2.57 (1H, ddd, *J* = 3.9, 9.9, 13.6 Hz), 2.74-2.94 (2H, m), 2.76 (1H, brs), 3.47 (1H, ddd, *J* = 5.0, 9.4, 10.4 Hz), 3.56-3.63 (2H, m), 3.69-3.85 (1H, m), 3.79 (3H, s), 3.89 (1H, brt, *J* = 7.9 Hz), 4.02 (1H, dd, *J* = 5.1, 10.0 Hz), 4.04-4.14 (1H, m), 5.70-5.92 (3H, m), 5.96 (1H, dd, *J* = 6.1, 11.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.2 (C), 22.5 (C), 27.1 (CH_3×3), 27.4 (CH_3×3), 30.9 (CH_2), 32.2 (CH_2), 32.6 (CH_2), 52.3 (CH_3), 67.4 (CH_2), 72.3 (CH), 77.6 (CH), 78.0 (CH), 84.3 (CH), 85.4 (CH), 85.7 (CH), 126.2 (CH), 127.3 (CH), 128.9 (CH), 135.6 (CH), 174.1 (C); ESI-HRMS (m/z) calcd for $C_{24}H_{41}O_7Si$ $[M + H]^+$: 469.2616, found: 469.2612.

7.1.39. (4a*S*,5a*R*,7*Z*,10*S*,11*S*,12a*S*,13*Z*,15a*R*)-2,2-Di-*tert*-butyl-11-(hydroxymethyl)-4,4a,5a,6,9,10,11,12a,15,15a-decahydro[1,3,2]dioxasilino[4',5':7,8]oxocino[3,2-*b*]oxonin-10-ol (21). To a solution of **55** (510.4 mg, 1.089 mmol) in MeOH (10 mL) was added $NaBH_4$ (609.2 mg, 16.10 mmol) at 0 ºC, and the mixture was stirred for 30 min. Then, the reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 2 → 1) to give **21** (459.2 mg, 1.042 mmol, 96%) as a colorless oil.

21: $[\alpha]_D^{25}$ –100 (*c* 1.37, $CHCl_3$); IR (neat) ν 3396, 3020, 2960, 2932, 2893, 2860, 1474, 1463, 1450, 1443, 1386, 1364, 1214, 1199, 1145, 1123, 1099, 1067, 1056, 1011, 941, 825, 795, 777, 755, 652 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (9H, s), 1.02 (9H, s), 2.08-2.22 (3H, m), 2.29-2.42 (2H, m), 2.62 (1H, ddd, *J* = 4.0, 8.2, 13.3 Hz), 2.72-2.90 (2H, m), 3.14 (1H, ddd, *J* = 3.7, 4.9, 8.6 Hz), 3.45 (1H, ddd, *J* = 5.1, 9.2, 10.5 Hz), 3.53 (1H, brtd, *J* = 3.7, 8.7 Hz), 3.64-3.82 (2H, m), 3.76 (1H, t, *J* = 10.5 Hz), 3.90 (1H, dd, *J* = 3.7, 8.7 Hz), 3.98-4.05 (2H, m), 4.09 (1H, ddd, *J* = 2.3, 4.0, 9.2 Hz), 5.71-5.90 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1 (C), 22.5 (C), 27.1 (CH_3×3), 27.4 (CH_3×3), 32.3 (CH_2×2),

32.7 (CH_2), 63.7 (CH_2), 67.4 (CH_2), 71.6 (CH), 77.7 (CH), 78.0 (CH), 84.0 (CH), 84.7 (CH), 86.8 (CH), 126.8 (CH), 127.6 (CH), 128.5 (CH), 136.7 (CH); ESI-HRMS (m/z) calcd for $C_{23}H_{41}O_6Si$ $[M + H]^+$: 441.2667, found: 441.2667.

7.1.40. (4a*S*,5a*R*,7*Z*,10*S*,11*S*,12a*S*,13*Z*,15a*R*)-2,2-Di-*tert*-butyl-10-(naphthalen-2-ylmethoxy)-11-((naphthalen-2-ylmethoxy)methyl)-4,4a,5a,6,9,10,11,12a,15,15a-decahydro-[1,3,2]dioxasilino[4',5':7,8]oxocino[3,2-*b*]oxonine (56). To a solution of **21** (388.1 mg, 0.8807 mmol) in THF-DMF (8.0 mL: 16 mL) were added KI (17.5 mg, 0.105 mmol), NAPBr (589.2 mg, 2.665 mmol), and NaH (60% in mineral oil, 297.9 mg, 7.448 mmol) at 0 ºC, and the mixture was stirred for 75 min. Then, the reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 50 → 20) to give **56** (459.5 mg, 0.6373 mmol, 72%) as a colorless oil.
56: $[\alpha]_D^{21}$ –28.5 (*c* 1.12, $CHCl_3$); IR (neat) ν 3059, 3020, 2971, 2932, 2861, 2806, 1953, 1914, 1853, 1743, 1633, 1605, 1512, 1473, 1445, 1390, 1365, 1351, 1308, 1295, 1274, 1249, 1214, 1196, 1168, 1097, 1014, 947, 902, 855, 821, 796, 750, 655 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.95 (9H, s), 1.00 (9H, s), 2.08 (1H, brd, *J* = 13.0 Hz), 2.26 (1H, ddd, *J* = 2.1, 6.7, 13.5 Hz), 2.34 (1H, brtd, *J* = 3.1, 13.5 Hz), 2.56 (1H, ddd, *J* = 3.8, 10.5, 13.5 Hz), 2.70 (1H, ddd, *J* = 2.9, 10.0, 13.5 Hz), 2.93 (1H, brt, *J* = 10.5 Hz), 3.20 (1H, brd, *J* = 9.1 Hz), 3.45 (1H, dt, *J* = 5.6, 11.3 Hz), 3.53-3.64 (3H, m), 3.75 (1H, t, *J* = 11.3 Hz), 3.84 (1H, brt, *J* = 7.3 Hz), 3.94-4.09 (3H, m), 4.36 (1H, d, *J* = 11.5 Hz), 4.55 (1H, d, *J* = 12.5 Hz), 4.68 (1H, d, *J* = 12.5 Hz), 4.72 (1H, d, *J* = 11.5 Hz), 5.61 (brq, *J* = 10.5 Hz), 5.71-5.84 (2H, m), 5.88 (1H, dd, *J* = 5.9, 10.5 Hz), 7.20 (1H, dd, *J* = 1.8, 8.7 Hz), 7.40-7.48 (5H, m), 7.51 (1H, s), 7.62-7.68 (2H, m), 7.70 (1H, s), 7.73-7.81 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2 (C), 22.5 (C), 27.1 (CH_3×3), 27.4 (CH_3×3), 32.25 (CH_2), 32.27 (CH_2), 32.6 (CH_2), 67.4 (CH_2), 69.1 (CH_2), 71.6 (CH_2), 73.4 (CH_2), 77.7 (CH), 77.8 (CH), 77.9 (CH), 83.8 (CH), 84.7 (CH), 84.9 (CH), 125.6 (CH), 125.8 (CH), 125.85 (CH), 125.86 (CH), 126.0 (CH), 126.1 (CH), 126.2 (CH), 126.4 (CH), 126.9 (CH), 127.6 (CH), 127.7 (CH), 127.8 (CH×2), 128.0 (CH), 128.09 (CH), 128.12 (CH), 128.2 (CH), 132.9 (C), 133.0 (C), 133.2 (C×2), 135.6 (C), 135.8 (C), 137.4 (CH); FD-HRMS (m/z) calcd for $C_{45}H_{56}O_6Si$ $[M]^+$: 720.3846, found: 720.3856.

7.1.41. (2*S*,3*R*,5*Z*,6a*S*,8*R*,9*S*,11*Z*,13a*R*)-2-(Hydroxymethyl)-9-(naphthalen-2-ylmethoxy)-8-((naphthalen-2-ylmethoxy)methyl)-3,4,6a,8,9,10,13,13a-octahydro-*2H*-oxocino[3,2-*b*]oxonin-3-ol (57). To a solution of **56** (459.5 mg, 0.6373 mmol) in THF (6.0 mL) was added TBAF (1.0 mol/L in THF, 1.95 mL, 1.95 mmol) at 23 ºC, and the mixture was stirred for 10 h. Then, the reaction mixture was diluted with H_2O, and extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 1 → EtOAc) to give **57** (364.8 mg, 0.6282 mmol, 99%) as a colorless solid.
57: mp 115 ºC; $[\alpha]_D^{22}$ –41.2 (*c* 0.930, $CHCl_3$); IR (KBr) ν 3296, 3056, 3014, 2975, 2926, 2912, 2891, 2855, 1735, 1601, 1509, 1449, 1365, 1355, 1340, 1306, 1274, 1245, 1127, 1098, 1088, 1060, 1049, 1025, 986, 955, 895, 855, 821, 778, 753, 699, 651, 627, 606, 550, 518, 489, 475 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.92 (1H, brs), 2.01 (1H, brs), 2.08-2.21 (2H, m), 2.36 (1H, brd, *J* = 13.9 Hz), 2.57 (1H, ddd, *J* = 2.6, 10.5, 13.5 Hz), 2.71 (1H, brddd, *J* = 4.0, 10.0, 13.9 Hz), 2.97 (1H, brt, *J* = 9.5 Hz), 3.22 (1H, brd, *J* = 8.8 Hz), 3.31 (1H, td, *J* = 5.0, 10.2 Hz), 3.52-3.70 (4H, m), 3.76 (1H, dd, *J* = 5.0, 11.7 Hz), 3.84-3.92 (2H, m), 3.96 (1H, brtd, *J* = 2.9, 8.8 Hz), 4.36 (1H, d, *J* = 11.5 Hz), 4.55 (1H, d, *J* = 12.3 Hz), 4.67 (1H, d, *J* = 12.3 Hz), 4.73 (1H, d, *J* = 11.5 Hz), 5.60 (1H, brq, *J* = 10.5 Hz), 5.75-5.87 (2H, m), 5.92 (1H, dd, *J* = 5.9, 10.9 Hz), 7.20 (1H, dd, *J* = 1.7, 8.6 Hz), 7.41-7.48 (5H, m), 7.52 (1H, s), 7.62-7.69 (2H, m), 7.70 (1H, s), 7.74-7.81 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.41 (CH_2),27.43 (CH_2), 32.5 (CH_2), 64.5 (CH_2), 69.1 (CH_2), 71.7 (CH_2), 73.3 (CH), 73.4 (CH_2), 77.7 (CH), 83.0 (CH), 83.7 (CH), 85.0 (CH), 86.2 (CH), 124.5 (CH), 125.8 (CH), 125.85 (CH), 125.89 (CH), 126.0 (CH), 126.1 (CH), 126.2 (CH), 126.4 (CH), 127.0 (CH), 127.6 (CH), 127.7 (CH), 127.8 (CH×2), 127.9 (CH), 128.0 (CH), 128.1 (CH), 128.4 (CH), 132.9 (C), 133.0 (C), 133.2 (C×2), 135.6 (C), 135.7 (C), 138.1 (CH); FD-HRMS (m/z) calcd for $C_{37}H_{40}O_6$ $[M]^+$: 580.2825, found: 580.2838.

7.1.42. Triethyl(((2*S*,3*R*,5*Z*,6a*S*,8*R*,9*S*,11*Z*,13a*R*)-9-(naphthalen-2-ylmethoxy)-8((naphthalen-2-ylmethoxy)methyl)-2-(((triethylsilyl)oxy)methyl)-3,4,6a,8,9,10,13,13a-octahydro-*2H*-oxocino[3,2-*b*]oxonin-3-yl)oxy)silane (58). To a solution of **57** (19.6 mg, 0.0338 mmol) and 2,6-lutidine (50.0 μL, 0.432 mmol) was added TESOTf (33.0 μL, 0.146 mmol) at 0 ºC, and the mixture was stirred for 35 min. Then, the reaction was quenched with H_2O, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 20) to give **58** (27.9 mg, 0.0344 mmol, 100%) as a colorless oil.
58: $[\alpha]_D^{22}$ –62.7 (*c* 0.740, $CHCl_3$); IR (neat) ν 3056, 3021, 2953, 2919, 2872, 2802, 2731, 1735, 1636, 1605, 1509, 1457, 1415, 1379, 1355, 1340, 1308, 1291, 1270, 1242, 1210, 1196, 1098, 1060, 1014, 983, 951, 933, 884, 855, 817, 774, 746, 687, 644, 627 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, measured at 50 ºC) δ 0.58 (6H, q, *J* = 8.0 Hz), 0.60 (6H, q, *J* = 8.0 Hz), 0.94 (9H, t, *J* = 8.0 Hz), 0.96 (9H, t, *J* = 8.0 Hz), 2.04 (1H, ddd, *J* = 3.3, 6.6, 13.3 Hz), 2.27-2.39 (2H, m), 2.55 (1H, ddd, *J* = 2.9, 10.4, 13.3 Hz), 2.72 (1H, ddd. *J* = 3.4, 10.9, 14.2 Hz), 2.89 (1H, brddd, *J* = 4.2, 10.9, 14.2 Hz), 3.26-3.31 (2H, m), 3.51 (1H, dd, *J* = 7.2, 10.3 Hz), 3.56-3.64 (3H, m), 3.77-3.81 (2H, m), 3.87 (1H, brt, *J* = 7.6 Hz), 3.92 (1H, brtd, *J* = 3.4, 8.7 Hz), 4.43 (1H, d, *J* = 11.7 Hz), 4.56 (1H, d, *J* = 12.3 Hz), 4.67 (1H, d, *J* = 12.3 Hz), 4.74 (1H, d, *J* = 11.7 Hz), 5.54 (1H, ddd, *J* = 1.6, 6.6, 10.4 Hz), 5.75-5.89 (3H, m), 7.26 (1H, dd, *J* = 1.4, 8.3 Hz), 7.39-7.45 (5H, m), 7.58 (1H, s), 7.64-7.69 (2H, m), 7.71 (1H, s), 7.73-7.79 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$, measured at 50 ºC) δ 4.7 (CH_2×3), 5.1 (CH_2×3), 6.8 (CH_3×6), 27.7 (CH_2), 32.1 (CH_2), 33.1 (CH_2), 65.0 (CH_2), 70.1 (CH_2), 71.8 (CH_2), 72.8 (CH), 73.5 (CH_2), 78.3 (CH), 84.3 (CH), 85.1 (CH), 85.6 (CH), 86.3 (CH), 125.3 (CH), 125.8 (CH×2), 126.0 (CH), 126.06 (CH), 126.09 (CH), 126.2 (CH), 126.5 (CH), 126.9 (CH), 127.7 (CH), 127.78 (CH), 127.82 (CH), 128.0 (CH×2), 128.08 (CH), 128.12 (CH), 129.0 (CH), 133.1 (C), 133.2 (C), 133.5 (C×2), 136.0 (C), 136.1 (C), 137.6 (CH); FD-HRMS (m/z) calcd for $C_{49}H_{68}O_6Si_2$ $[M]^+$: 808.4554, found: 808.4544.

7.1.43. Triethyl(((2*S*,3*R*,5*Z*,6a*S*,8*R*,9*S*,11*Z*,13a*R*)-2-ethynyl-9-(naphthalen-2-ylmethoxy)-8-((naphthalen-2-ylmethoxy)methyl)-3,4,6a,8,9,10,13,13a-octahydro-*2H*-oxocino[3,2-*b*]oxonin-3-yl)oxy)silane (60). To a solution of $(COCl)_2$ (26.0 μL, 0.303 mmol) in CH_2Cl_2 (1.0 mL) was added DMSO (35.0 μL, 0.493 mmol) at -78 ºC, and the mixture was stirred for 10 min. Then, to the mixture was added a solution of **58** (39.2 mg, 0.0484 mmol) in CH_2Cl_2 (1.0 mL) at –78 ºC, and

the mixture was stirred for 5 min. The mixture was warmed to – 40 ºC, and stirred for 30 min. Then, to the solution was added Et_3N (0.140 mL, 1.00 mmol) at –78 ºC, and the mixture was warmed to 0 ºC. After being stirred for 30 min, the reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with 0.5 mol/L aq. HCl and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude product, which was used immediately in the next reaction.

To a solution of the above crude product in THF-MeOH (0.5 mL: 0.5 mL) were added Ohira-Bestmann reagent **59** (19.0 µL, 0.126 mmol) and K_2CO_3 (16.7 mg, 0.121 mmol) at 16 ºC, and the mixture was stirred for 4 h. Then, the reaction was quenched with saturated NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 20 → 10) to give **60** (21.2 mg, 0.0308 mmol, 64% from **57**) as a colorless oil.

60: $[\alpha]_D^{22}$ –59.5 (*c* 0.990, $CHCl_3$); IR (neat) ν 3307, 3058, 3019, 2955, 2917, 2878, 1729, 1634, 1603, 1507, 1454, 1447, 1413, 1362, 1310, 1290, 1273, 1241, 1217, 1199, 1174, 1104, 1083, 1058, 1015, 977, 945, 900, 857, 815, 776, 751, 628 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, measured at 50 ºC) δ 0.62 (6H, q, *J* = 8.0 Hz), 0.96 (9H, t, *J* = 8.0 Hz), 2.08 (1H, ddd, *J* = 2.7, 6.2, 13.3 Hz), 2.25 (1H, brd, *J* = 13.7 Hz), 2.34 (1H, brtd, *J* = 3.9, 13.8 Hz), 2.38 (1H, d, *J* = 2.2 Hz), 2.55 (1H, ddd, *J* = 3.1, 10.6, 13.3 Hz), 2.69 (1H, ddd, *J* = 3.2, 10.2, 13.8 Hz), 2.93 (1H, brddd, *J* = 4.4, 10.2, 13.7 Hz), 3.26 (1H, brtd, *J* = 2.7, 9.2 Hz), 3.54-3.64 (3H, m), 3.84-3.93 (3H, m), 3.97 (1H, td, *J* = 3.1, 9.2 Hz), 4.42 (1H, d, *J* = 11.3 Hz), 4.56 (1H, d, *J* = 12.2 Hz), 4.65 (1H, d, *J* = 12.2 Hz), 4.73 (1H, d, *J* = 11.3 Hz), 5.52 (1H, ddd, *J* = 1.4, 6.2, 10.6 Hz), 5.77-5.89 (3H, m), 7.25 (1H, d, *J* = 8.0 Hz), 7.39-7.45 (5H, m), 7.57 (1H, s), 7.64-7.71 (3H, m), 7.72-7.79 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$, measured at 50 ºC) δ 5.1 (CH_2×3), 6.84 (CH_3×3), 27.6 (CH_2), 32.4 (CH_2), 33.0 (CH_2), 70.0 (CH_2), 71.8 (CH_2), 73.3 (C), 73.5 (CH_2), 74.6 (CH), 75.8 (CH), 78.3 (CH), 83.6 (CH), 84.3 (CH), 85.2 (CH), 85.8 (CH), 124.8 (CH), 125.87 (CH), 125.90 (CH), 125.94 (CH), 126.09 (CH), 126.14 (CH), 126.2 (CH), 126.5 (CH), 126.9 (CH), 127.7 (CH), 127.8 (CH), 128.0 (CH × 2), 128.1 (CH), 128.2 (CH), 128.27 (CH), 128.31 (CH), 133.1 (C), 133.2 (C), 133.4 (C×2), 135.9 (C), 136.1 (C), 137.7 (CH); FD-HRMS (m/z) calcd for $C_{44}H_{52}O_5Si$ $[M]^+$: 688.3584, found: 688.3602.

7.1.44. 3-((2*S*,3*R*,5*Z*,6a*S*,8*R*,9*S*,11*Z*,13a*R*)-9-(Naphthalen-2-ylmethoxy)-8-((naphthalen-2-ylmethoxy)methyl)-3-((triethylsilyl)oxy)-3,4,6a,8,9,10,13,13a-octahydro-*2H*-oxocino[3,2-*b*]oxonin-2-yl)prop-2-yn-1-ol (61). To a solution of **60** (21.2 mg, 0.0308 mmol) in THF (1.0 mL) was added MeLi (1.17 mol/L in Et_2O, 0.260 mL, 0.304 mmol) at –78 ºC, and the mixture was stirred for 15 min. Then, to the solution was added a suspension of $(CH_2O)_n$ (22.2 mg) in THF (0.5 mL) at –78 ºC, and the mixture was rapidly warmed to 19 ºC. After being stirred for 40 min, the reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 3) to give **61** (20.9 mg, 0.0291 mmol, 94%) as a colorless oil.

61: $[\alpha]_D^{23}$ –76.7 (*c* 0.660, $CHCl_3$); IR (neat) ν 3443, 3056, 3020, 2953, 2915, 2875, 2805, 2732, 1949, 1914, 1731, 1635, 1604, 1509, 1456, 1414, 1379, 1354, 1308, 1287, 1273, 1241, 1217, 1199, 1171, 1107, 1051, 1015, 977, 949, 903, 857, 815, 776, 748, 685, 667, 621 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, measured at 50 ºC) δ 0.62 (6H, q, *J* = 7.9 Hz), 0.96 (9H, t, *J* = 7.9 Hz), 1.40 (1H, t, *J* = 6.3 Hz), 2.08 (1H, dd, *J* = 6.4, 12.7 Hz), 2.25 (1H, brd, *J* = 13.1 Hz), 2.34 (1H, brtd, *J* = 4.2, 14.0 Hz), 2.55 (1H, brt, *J* = 12.7 Hz), 2.70 (1H, ddd, *J* = 3.4, 10.2, 14.0 Hz), 2.93 (1H, brddd, *J* = 4.7, 9.7, 13.1 Hz), 3.26 (1H, brtd, *J* = 2.9, 9.0 Hz), 3.54-3.63 (3H, m), 3.86 (1H, brt, *J* = 7.5 Hz), 3.91 (1H, brtd, *J* = 3.3, 9.0 Hz), 3.95 (2H, brs), 4.27 (2H, d, *J* = 6.3 Hz), 4.42 (1H, d, *J* = 11.7 Hz), 4.56 (1H, d, *J* = 12.3 Hz), 4.65 (1H, d, *J* = 12.3 Hz), 4.73 (1H, d, *J* = 11.7 Hz), 5.52 (1H, dddd, *J* = 1.9, 6.4, 8.7, 10.5 Hz), 5.77-5.84 (2H, m), 5.86 (1H, dd, *J* = 6.0, 11.7 Hz), 7.25 (1H, dd, *J* = 1.7, 8.1 Hz), 7.39-7.45 (5H, m), 7.57 (1H, s), 7.65-7.70 (3H, m), 7.73-7.79 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$, measured at 50 ºC) δ 5.1 (CH_3×3), 6.8 (CH_2×3), 27.6 (CH_2), 32.4 (CH_2), 33.1 (CH_2), 51.5 (CH_2), 70.0 (CH_2), 71.8 (CH_2), 73.5 (CH_2), 74.6 (CH), 75.8 (CH), 78.3 (CH), 83.4 (C), 83.6 (CH), 85.2 (CH), 85.6 (CH), 86.3 (C), 124.8 (CH), 125.88 (CH), 125.91 (CH), 125.94 (CH), 126.09 (CH), 126.14 (CH), 126.2 (CH), 126.5 (CH), 126.9 (CH), 127.7 (CH), 127.8 (CH), 128.0 (CH×2), 128.1 (CH), 128.16 (CH), 128.22 (CH), 128.4 (CH), 133.1 (C), 133.2 (C), 133.4 (C×2), 135.9 (C), 136.1 (C), 137.7 (CH); FD-HRMS (m/z) calcd for $C_{45}H_{54}O_6Si$ $[M]^+$: 718.3690, found: 718.3695.

7.1.45. (*Z*)-3-((2*S*,3*R*,5*Z*,6a*S*,8*R*,9*S*,11*Z*,13a*R*)-9-(Naphthalen-2-ylmethoxy)-8-((naphthalen-2-ylmethoxy)methyl)-3-((triethylsilyl)oxy)-3,4,6a,8,9,10,13,13a-octahydro-*2H*-oxocino[3,2-*b*]oxonin-2-yl)prop-2-en-1-ol (62). To a solution of **61** (137.8 mg, 0.1917 mmol) in EtOH (10 mL) were added Au nanoparticles (1% on TiO_2, 214.1 mg) and $Me_2NH{\cdot}BH_3$ (1.148 g, 19.48 mmol) at 19 ºC, and the mixture was stirred for 3 days. The reaction mixture was filtered through a Celite pad, and the mixture was diluted with H_2O. Then, the mixture was evaporated to remove organic solvent, and the residue was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 3) to give **62** (128.1 mg, 0.1777 mmol, 93%) as a colorless oil.

62: $[\alpha]_D^{23}$ –74.2 (*c* 0.690, $CHCl_3$); IR (neat) ν 3454, 3056, 3020, 2953, 2918, 2875, 2802, 1727, 1635, 1604, 1511, 1458, 1416, 1373, 1353, 1307, 1292, 1271, 1243, 1219, 1173, 1127, 1102, 1060, 1017, 947, 898, 859, 817, 778, 750, 687, 669, 627 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, measured at 50 ºC) δ 0.58 (6H, q, *J* = 8.0 Hz), 0.93 (9H, t, *J* = 8.0 Hz), 2.08-2.15 (2H, m), 2.34 (1H, brtd, *J* = 3.4, 13.9 Hz), 2.61 (1H, ddd, *J* = 2.9, 10.5, 13.4 Hz), 2.70 (1H, brddd, *J* = 3.8, 10.0, 13.9 Hz), 2.90 (1H, ddd, *J* = 4.3, 10.1, 13.9 Hz), 3.28 (1H, brtd, *J* = 2.8, 8.9 Hz), 3.52-3.63 (3H, m), 3.72 (1H, td, *J* = 2.9, 9.2 Hz), 3.88-3.94 (2H, m), 4.07-4.17 (3H, m), 4.44 (1H, d, *J* = 11.3 Hz), 4.57 (1H, d, *J* = 12.2 Hz), 4.66 (1H, d, *J* = 12.2 Hz), 4.74 (1H, d, *J* = 11.3 Hz), 5.49-5.58 (2H, m), 5.73-5.84 (3H, m), 5.90 (1H, dd, *J* = 5.9, 11.2 Hz), 7.27 (1H, dd, *J* = 1.6, 8.5 Hz), 7.40-7.45 (5H, m), 7.58 (1H, s), 7.65-7.71 (3H, m), 7.73-7.80 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$, measured at 50 ºC) δ 5.0 (CH_2×3), 6.7 (CH_3×3), 27.6 (CH_2), 32.5 (CH_2), 33.0 (CH_2), 59.5 (CH_2), 70.2 (CH_2), 71.8 (CH_2), 73.6 (CH_2), 75.6 (CH), 78.4 (CH), 79.6 (CH), 83.9 (CH), 84.7 (CH), 65.1 (CH), 124.9 (CH), 125.9 (CH×2), 126.0 (CH), 126.09 (CH), 126.12 (CH), 126.2 (CH), 126.5 (CH), 126.9 (CH), 127.74 (CH), 127.78 (CH), 128.0 (CH×2), 128.1 (CH), 128.2 (CH), 128.3 (CH×2), 130.8 (CH), 132.9 (CH), 133.1 (C), 133.2 (C), 133.4 (C×2), 136.0 (C), 136.1 (C), 137.9 (CH); FD-HRMS (m/z) calcd for $C_{45}H_{56}O_6Si$ $[M]^+$: 720.3846, found: 720.3838.

**7.1.46. (*Z*)-1-((2*R*,3*R*,4*R*,4a*S*,9a*S*)-4-((4-bromobenzyl)oxy)-3-(naphthalen-2-ylmethoxy)-3,4,4a,6,9,9a-hexahydro-*2H*-pyrano[3,2-*b*]oxepin-2-yl)-3-hydroxy-5-

((2*S*,3*R*,5*Z*,6a*S*,8*R*,9*S*,11*Z*,13a*R*)-3-hydroxy-9-(naphthalen-2-ylmethoxy)-8-((naphthalen-2-ylmethoxy)methyl)-3,4,6a,8,9,10,13,13a-octahydro-*2H*-oxocino[3,2-*b*]oxonin-2-yl)pent-4-en-2-one (4). To a solution of $(COCl)_2$ (46.5 µL, 0.542 mmol) in CH_2Cl_2 (2 mL) was added DMSO (64.1 µL, 0.903 mmol) at –78 ºC, and the mixture was stirred for 15 min. Then, to the mixture was added a solution of **62** (130.2 mg, 0.1806 mmol) in CH_2Cl_2 (2 mL) at –78 ºC, and the mixture was stirred for 15 min. Then, to the mixture was added Et_3N (0.252 mL, 1.81 mmol) at –78 ºC, and the mixture was stirred for 30 min at 0 ºC. The reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with 0.5 mol/L aq. HCl and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude **6**, which was used immediately in the next reaction.

To a solution of **5** (356.2 mg, 0.5418 mmol) in THF (2 mL) was added NHMDS (1.10 mol/L in THF, 0.490 mL, 0.539 mmol) at -78 ºC, and the mixture was stirred for 20 min. Then, to the solution was added a solution of the above crude **6** in THF (2 mL) at –78 ºC, and the mixture was stirred for 30 min. The reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 2 → 1) to give **63** (brown oil, diastereomer mixture), which was used immediately in the next reaction.

To a solution of the above **63** in CF_3CH_2OH-H_2O (3.0 mL: 0.3 mL) was added PTS·H_2O (20.5 mg, 0.107 mmol) at 19 ºC, and the suspension was stirred for 1 h. Then, the reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 2 → 1 → 0.5) to give **4** (81.0 mg, 0.0709 mmol, 40% from **62**) as a colorless oil.

4: $[\alpha]_D^{23}$ +7.5 (*c* 1.11, $CHCl_3$); IR (neat) ν 3438, 3052, 3021, 2920, 2889, 2862, 2727, 1953, 1915, 1719, 1655, 1634, 1605, 1511, 1488, 1447, 1396, 1362, 1271, 1244, 1092, 893, 859, 818, 774, 750, 737, 703 cm^{-1}; ^1H NMR (400 MHz, C_6D_6, measured at 50 ºC) δ 2.13 (1H, ddd, *J* = 2.5, 6.5, 13.3 Hz), 2.20-2.34 (3H, m), 2.35-2.43 (1H, m), 2.61-2.78 (3H, m), 2.88 (1H, dd, *J* = 3.2, 14.8 Hz), 3.05-3.13 (2H, m), 3.30 (1H, t, *J* = 9.1 Hz), 3.35 (1H, t, *J* = 9.1 Hz), 3.46-3.54 (2H, m), 3.58 (1H, t, *J* = 9.1 Hz), 3.63-3.71 (3H, m), 3.77 (1H, brtd, *J* = 2.9, 8.6 Hz), 3.85-3.98 (3H, m), 4.14 (1H, brddd, *J* = 1.6, 5.6, 8.6 Hz), 4.30 (1H, t, *J* = 8.7 Hz), 4.39 (1H, d, *J* = 11.9 Hz), 4.45 (1H, d, *J* = 12.3 Hz), 4.52 (1H, d, *J* = 12.3 Hz), 4.59 (1H, d, *J* = 11.9 Hz), 4.62 (1H, d, *J* = 11.9 Hz), 4.70 (1H, d, *J* = 11.9 Hz), 4.81 (1H, d, *J* = 11.9 Hz), 4.89 (1H, dd, *J* = 1.0, 8.6 Hz), 4.97 (1H, d, *J* = 11.9 Hz), 5.39 (1H, ddd, *J* = 0.8, 8.6, 11.1 Hz), 5.43-5.56 (2H, m), 5.63 (1H, brddd, *J* = 1.0, 8.7, 11.1 Hz), 5.89-6.07 (2H, m), 6.10 (1H, dd, *J* = 5.6, 11.2 Hz), 7.02 (2H, d, *J* = 8.1 Hz), 7.22-7.40 (10H, m), 7.57-7.70 (13H, m); ^{13}C NMR (100 MHz, C_6D_6) δ 27.3 (CH_2), 32.0 (CH_2), 32.7 (CH_2), 34.3 (CH_2), 40.9 (CH_2), 67.4 (CH_2), 71.1 (CH_2), 71.3 (CH_2), 73.1 (CH_2), 74.2 (CH_2), 74.59 (CH), 74.61 (CH_2), 75.0 (CH), 75.4 (CH), 75.8 (CH), 78.7 (CH), 79.8 (CH), 81.0 (CH), 83.3 (CH), 84.9 (CH), 85.1 (CH), 85.6 (CH), 88.0 (CH), 121.1 (C), 125.0 (CH), 125.58 (CH×2), 125.64 (CH), 125.72 (CH), 125.74 (CH), 125.8 (CH), 125.9 (CH×2), 126.1 (CH), 126.2 (CH), 126.3 (CH), 126.4 (CH), 126.6 (CH), 127.4 (CH), 127.65 (CH×2), 127.67 (CH), 127.76 (CH), 127.79 (CH×2), 127.9 (CH), 128.08 (CH), 128.14 (CH×2), 128.5 (CH), 129.2 (CH×2), 131.2 (CH×2), 131.3 (CH), 133.2 (C×2), 133.5 (C×2), 133.6 (C), 135.9 (C), 136.2 (C), 136.4 (C), 136.6 (CH), 138.0 (CH), 138.5 (C), 207.4 (C); FD-HRMS (m/z) calcd for $C_{68}H_{69}{}^{79}BrO_{11}$ $[M]^+$: 1140.4023, found: 1140.4029.

7.1.47. (2*S*,5a*S*,6a*R*,8*Z*,11*S*,12*R*,13a*S*,14*Z*,16a*R*)-2-(((2*R*,3*R*,4*R*,4a*S*,9a*S*)-4-((4-Bromobenzyl)oxy)-3-(naphthalene-2-ylmethoxy)-3,4,4a,6,9,9a-hexahydro-*2H*-pyrano[3,2-*b*]oxepin-2-yl)methyl)-11-(naphthalen-2-ylmethoxy)-12-((naphthalen-2-ylmethoxy)methyl)-3,5a,6a,7,10,11,12,13a,16,16a-decahydro-*3H*-oxepino[2',3':7,8]oxocino[3,2-*b*]oxonin-3-ol (64) and (2*R*,5a*S*,6a*R*,8*Z*,11*S*,12*R*,13a*S*,14*Z*,16a*R*)-2-(((2*R*,3*R*,4*R*,4a*S*,9a*S*)-4-((4-Bromobenzyl)oxy)-3-(naphthalen-2-ylmethoxy)-3,4,4a,6,9,9a-hexahydro-*2H*-pyrano[3,2-*b*]oxepin-2-yl)methyl)-11-(naphthalen-2-ylmethoxy)-12-((naphthalene-2-ylmethoxy)methyl)-3,5a,6a,7,10,11,12,13a,16,16a-decahydro-*3H*-oxepino[2',3':7,8]oxocino[3,2-*b*]oxonin-3-ol (11-*epi*-64). To a solution of **4** (11.4 mg, 9.98 µmmol) in CH_2Cl_2-Et_3SiH (0.4 mL: 0.2 mL) was added TMSOTf (4.0 µL, 0.022 mmol) at 0 ºC, and the mixture was stirred for 15 min. Then, the reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 3 → 2) to give a 1:1 diastereomer mixture of **64** and 11-*epi*-**64** (7.2 mg, 64%). The mixture of **64** and 11-*epi*-**64** was separated by HPLC (hexane/EtOAc = 2) to give **64** (colorless oil) as a less-polar component and 11-*epi*-**64** (colorless solid) as a polar component.

64: $[\alpha]_D^{23}$ –30 (*c* 0.41, $CHCl_3$); IR (neat) ν 3464, 3056, 3024, 2956, 2922, 2854, 1727, 1632, 1601, 1512, 1484, 1467, 1449, 1361, 1308, 1290, 1266, 1209, 1171, 1093, 1012, 987, 962, 896, 853, 815, 779, 755, 741, 702, 667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, measured at 50 ºC) δ 1.80 (1H, td, *J* = 6.4, 14.1 Hz), 2.07-2.19 (2H, m), 2.22 (1H, ddd, *J* = 2.1, 6.4, 13.1 Hz), 2.27-2.39 (3H, m), 2.55-2.65 (2H, m), 2.66-2.74 (1H, m), 2.89-2.99 (1H, m), 3.21 (1H, dt, *J* = 4.1, 9.7 Hz), 3.26 (1H, brtd, *J* = 2.6, 9.0 Hz), 3.36 (1H, t, *J* = 8.8 Hz), 3.38 (1H, t, *J* = 8.8 Hz), 3.40-3.46 (1H, m), 3.52-3.66 (5H, m), 3.71-3.78 (2H, m), 3.88 (1H, brt, *J* = 6.6 Hz), 3.93 (1H, brtd, *J* = 3.2, 8.8 Hz), 3.98 (1H, brdd, *J* = 2.3, 15.4 Hz), 4.15 (1H, brd, *J* = 8.1 Hz), 4.25 (1H, dd, *J* = 5.9, 15.4 Hz), 4.43 (1H, d, *J* = 11.7 Hz), 4.56 (1H, d, *J* = 12.4 Hz), 4.66 (1H, d, *J* = 12.4 Hz), 4.726 (1H, d, *J* = 11.5 Hz), 4.732 (1H, d, *J* = 11.7 Hz), 4.83 (1H, d, *J* = 11.3 Hz), 4.88 (1H, d, *J* = 11.3 Hz), 4.97 (1H, d, *J* = 11.5 Hz), 5.61 (1H, brq, *J* = 9.4 Hz), 5.72-5.91 (7H, m), 7.19 (2H, d, *J* = 8.3 Hz), 7.25 (1H, dd, *J* = 1.6, 8.3 Hz), 7.36-7.47 (10H, m), 7.57 (1H, s), 7.64-7.82 (11H, m); ^{13}C NMR (100 MHz, $CDCl_3$, measured at 50 ºC) δ 27.5 (CH_2), 32.58 (CH_2), 32.64 (CH_2), 34.6 (CH_2), 35.4 (CH_2), 67.9 (CH_2), 69.4 (CH), 69.8 (CH_2), 71.6 (CH_2), 73.4 (CH_2), 74.6 (CH_2), 75.1 (CH_2), 75.6 (CH), 75.9 (CH), 78.1 (CH), 80.2 (CH), 81.5 (CH), 81.8 (CH), 83.7 (CH), 85.0 (CH), 85.1 (CH), 85.3 (CH), 85.7 (CH), 88.2 (CH), 121.3 (C), 125.1 (CH), 125.71 (CH), 125.74 (CH), 125.78 (CH), 125.83 (CH×2), 125.9 (CH), 126.00 (CH), 126.02 (CH), 126.04 (CH), 126.3 (CH), 126.5 (CH), 126.7 (CH), 127.0 (CH), 127.58 (CH), 127.63 (CH×2), 127.79 (CH), 127.80 (CH), 127.89 (CH), 127.94 (CH), 128.0 (CH), 128.06 (CH), 128.14 (CH), 128.2 (CH), 129.4 (CH×2), 131.3 (CH×2), 131.4 (CH), 132.97 (C), 133.04 (C), 133.28 (C), 133.34 (C), 135.8 (C), 135.85 (C), 135.94 (C), 137.6 (CH), 138.3 (C), 139.5 (CH); FD-HRMS (m/z) calcd for $C_{68}H_{69}{}^{79}BrO_{10}$ $[M]^+$: 1124.4074, found: 1124.4068.

11-*epi*-**64**: mp 143-144 ºC; $[\alpha]_D^{23}$ –36 (*c* 0.39, $CHCl_3$); IR (neat) ν 3393, 3056, 3027, 2922, 2900, 2875, 1727, 1601, 1510, 1489,

1450, 1394, 1359, 1348, 1309, 1274, 1260, 1218, 1172, 1126, 1109, 1091, 1031, 1013, 996, 950, 932, 907, 890, 858, 816, 770, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, measured at 50 ºC) δ 1.53 (1H, m), 2.08-2.22 (3H, m), 2.27-2.38 (2H, m), 2.52 (1H, ddd, *J* = 3.6, 10.7, 13.8 Hz), 2.60 (1H, ddd, *J* = 4.1, 8.2, 16.4 Hz), 2.70 (1H, brtt, *J* = 3.6, 9.7 Hz), 2.94 (1H, brdd, *J* = 4.0, 9.7, 13.6 Hz), 3.20-3.29 (2H, m), 3.26 (1H, t, *J* = 9.5 Hz), 3.37 (1H, t, *J* = 8.8 Hz), 3.47 (1H, dt, *J* = 1.5, 9.9 Hz), 3.54-3.61 (3H, m), 3.63 (1H, t, *J* = 8.8 Hz), 3.76-3.87 (2H, m), 3.90-4.02 (3H, m), 4.20-4.29 (2H, m), 4.43 (1H, d, *J* = 11.7 Hz), 4.55 (1H, d, *J* = 12.4 Hz), 4.66 (1H, d, *J* = 12.4 Hz), 4.74 (1H, d, *J* = 11.7 Hz), 4.75 (1H, d, *J* = 11.8 Hz), 4.78 (1H, d, *J* = 11.3 Hz), 4.90 (1H, d, *J* = 11.8 Hz), 5.00 (1H, d, *J* = 11.3 Hz), 5.52-5.60 (2H, m), 5.72-5.91 (6H, m), 7.22 (2H, d, *J* = 8.3 Hz), 7.26 (1H, dd, *J* = 1.7, 8.3 Hz), 7.35-7.47 (10H, m), 7.57 (1H, s), 7.64-7.81 (11H, m); ^{13}C NMR (100 MHz, $CDCl_3$, measured at 50 ºC) δ 27.5 (CH_2), 32.4 (CH_2), 32.6 (CH_2), 34.5 (CH_2), 35.1 (CH_2), 67.8 (CH_2), 69.8 (CH_2), 71.7 (CH_2), 71.9 (CH), 73.4 (CH_2), 74.7 (CH_2), 75.2 (CH_2), 75.3 (CH), 75.6 (CH), 75.8 (CH), 76.2 (CH), 78.1 (CH), 79.5 (CH), 81.8 (CH), 83.6 (CH), 85.0 (CH), 85.2 (CH), 85.8 (CH), 88.1 (CH), 131.3 (C), 124.9 (CH), 125.7(CH), 125.76 (CH), 125.77 (CH), 125.92 (CH×2), 125.94 (CH), 125.99 (CH), 126.02 (CH), 126.1 (CH), 126.3 (CH), 126.6 (CH), 126.7 (CH), 127.0 (CH), 127.58 (CH), 127.63 (CH), 127.7 (CH), 127.8 (CH×2), 127.9 (CH), 128.0 (CH), 128.05 (CH), 128.12 (CH), 128.14 (CH), 128.2 (CH), 129.3 (CH), 129.4 (CH×2), 131.37 (CH×2), 131.44 (CH), 132.98 (C), 133.04 (C), 133.1 (C), 133.28 (C×2), 133.33 (C), 135.5 (CH), 135.75 (C), 135.76 (C), 135.9 (C), 137.8 (CH), 138.2 (C); FD-HRMS (m/z) calcd for $C_{68}H_{69}{}^{79}BrO_{10}$ $[M]^+$: 1124.4074, found: 1124.4096.

7.1.48. (2*S*,5a*S*,6a*R*,8*Z*,11*S*,12*R*,13a*S*,14*Z*,16a*R*)-2-(((2*R*,3*R*,4*R*,4a*S*,9a*S*)-4-((4-Bromobenzyl)oxy)-3-(naphthalen-2-ylmethoxy)-3,4,4a,6,9,9a-hexahydro-*2H*-pyrano[3,2-*b*]oxepin-2-yl)methyl)-11-(naphthalen-2-ylmethoxy)-12-((naphthalen-2-ylmethoxy)methyl)-3,5a,6a,7,10,11,12,13a,16,16a-decahydro-*3H*-oxepino[2',3':7,8]oxocino[3,2-*b*]oxonin-3-one (65). To a solution of $(COCl)_2$ (14.0 µL, 0.150 mmol) in CH_2Cl_2 (0.5 mL) was added DMSO (18.0 µL, 0.253 mmol) at –78 ºC, and the mixture was stirred for 15 min. Then, to the mixture was added a solution of **64** (10.3 mg, 9.15 µmol) in CH_2Cl_2 (1.0 mL) at –78 ºC, and the mixture was stirred for 10 min. Then, to the solution was added Et_3N (70.0 µL, 0.502 mmol) at –78 ºC, and the mixture was stirred for 30 min at 0 ºC. The reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with 0.5 mol/L aq. HCl and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 3) to give **65** (8.1 mg, 7.2 µmol, 79%) as a colorless oil.

65: $[\alpha]_D^{26}$ –16 (*c* 0.41, $CHCl_3$); IR (neat) ν 3056, 3024, 2960, 2918, 2847, 2724, 1953, 1914, 1727, 1667, 1632, 1604, 1512, 1488, 1460, 1403, 1389, 1358, 1333, 1277, 1160, 1096, 1012, 959, 896, 857, 811 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, measured at 50 ºC) δ 1.89 (1H, ddd, *J* = 4.6, 8.7, 13.7 Hz), 2.14-2.39 (5H, m), 2.54 (1H, ddd, *J* = 4.2, 7.5, 16.2 Hz), 2.62 (1H, brddd, *J* = 3.7, 10.4, 14.1 Hz), 2.70 (1H, brddd, *J* = 3.3, 10.4, 13.3 Hz), 2.98 (1H, brddd, *J* = 4.2, 10.4, 14.1 Hz), 3.15 (1H, dt, *J* = 4.2, 9.9 Hz), 3.23-3.33 (3H, m), 3.51 (1H, dt, *J* = 3.1, 9.1 Hz), 3.54-3.68 (6H, m), 3.88-3.99 (3H, m), 4.06 (1H, brtd, *J* = 2.3, 9.2 Hz), 4.19-4.31 (2H, m), 4.43 (1H, d, *J* = 11.6 Hz), 4.57 (1H, d, *J* = 12.5 Hz), 4.67 (1H, d, *J* = 12.5 Hz), 4.73 (1H, d, *J* = 11.6 Hz), 4.74 (1H, d, *J* = 11.6 Hz), 4.77 (1H, d, *J* = 11.3 Hz), 4.87 (1H, d, *J* = 11.6 Hz), 4.95 (1H, d, *J* = 11.3 Hz), 5.65 (1H, brq, *J* = 9.5 Hz), 5.69-5.87 (5H, m), 5.94 (1H, dd, *J* = 5.8, 10.8 Hz), 6.42 (1H, dd, *J* = 2.3, 12.8 Hz), 7.19 (2H, d, *J* = 8.3 Hz), 7.25 (1H, dd, *J* = 1.6, 8.3 Hz), 7.35-7.47 (10H, m), 7.57 (1H, s), 7.64-7.82 (11H, m); ^{13}C NMR (100 MHz, $CDCl_3$, measured at 50 ºC) δ 27.6 (CH_2), 31.6 (CH_2), 32.5 (CH_2), 34.4 (CH_2), 36.1 (CH_2), 68.1 (CH_2), 70.0 (CH_2), 71.8 (CH_2), 73.6 (CH_2), 74.3 (CH), 74.6 (CH_2), 75.1 (CH_2), 76.1 (CH), 78.2 (CH), 80.8 (CH), 81.8 (CH), 83.1 (CH), 83.5 (CH), 83.7 (CH), 85.2 (CH), 85.3 (CH), 85.9 (CH), 88.3 (CH), 121.3 (C), 125.2 (CH), 125.85 (CH), 125.86 (CH), 125.89 (CH), 125.92 (CH), 126.0 (CH), 126.06 (CH), 126.10 (CH), 126.14 (CH), 126.2 (CH), 126.4 (CH), 126.6 (CH), 126.8 (CH), 127.0 (CH×2), 127.7 (CH), 127.8 (CH×2), 127.86 (CH), 127.90 (CH×2), 128.0 (CH), 128.1 (CH), 128.15 (CH), 128.18 (CH), 128.5 (CH), 129.5 (CH×2), 131.2 (CH), 131.4 (CH×2), 133.1 (C), 133.2 (C), 133.4 (C×2), 133.5 (C), 135.8 (C), 135.9 (C), 136.0 (C), 138.3 (CH), 138.4 (C), 146.1 (CH), 203.7 (C); FD-HRMS (m/z) calcd for $C_{68}H_{67}{}^{79}BrO_{10}$ $[M]^+$: 1122.3918, found: 1122.3933.

7.1.49. (2*R*,5a*S*,6a*R*,8*Z*,11*S*,12*R*,13a*S*,14*Z*,16a*R*)-2-(((2*R*,3*R*,4*R*,4a*S*,9a*S*)-4-((4-Bromobenzyl)oxy)-3-(naphthalen-2-ylmethoxy)-3,4,4a,6,9,9a-hexahydro-*2H*-pyrano[3,2-*b*]oxepin-2-yl)methyl)-11-(naphthalen-2-ylmethoxy)-12-((naphthalen-2-ylmethoxy)methyl)-3,5a,6a,7,10,11,12,13a,16,16a-decahydro-*3H*-oxepino[2',3':7,8]oxocino[3,2-*b*]oxonin-3-one (11-*epi*-65). To a solution of $(COCl)_2$ (14.0 µL, 0.150 mmol) in CH_2Cl_2 (0.5 mL) was added DMSO (19.0 µL, 0.267 mmol) at –78 ºC, and the mixture was stirred for 10 min. Then, to the mixture was added a solution of 11-*epi*-**64** (10.0 mg, 8.88 µmol) in CH_2Cl_2 (0.5 mL) at –78 ºC, and the mixture was stirred for 10 min. Then, to the solution was added Et_3N (70.0 µL, 0.502 mmol) at –78 ºC, and the mixture was stirred for 30 min at 0 ºC. The reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with 0.5 mol/L aq. HCl and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 3) to give 11-*epi*-**65** (7.4 mg, 6.6 µmol, 74%) as a colorless oil.

11-*epi*-**67**: $[\alpha]_D^{23}$ –34 (*c* 0.37, $CHCl_3$); IR (neat) ν 3059, 3026, 2916, 2899, 2849, 1727, 1666, 1600, 1512, 1490, 1445, 1358, 1281, 1099, 901, 857, 819, 758, 736, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, measured at 50 ºC) δ 2.00 (1H, ddd, *J* = 2.6, 10.5, 15.0 Hz), 2.34 (5H, m), 2.47 (1H, ddd, *J* = 4.1, 10.5, 14.2 Hz), 2.59 (1H, ddd, *J* = 3.8, 7.5, 16.1 Hz), 2.69 (1H, ddd, *J* = 3.4, 10.5, 13.8 Hz), 2.97 (1H, ddd, *J* = 4.1, 11.6, 14.2 Hz), 3.23 (2H, m), 3.29 (1H, t, *J* = 9.2 Hz), 3.39 (1H, t, *J* = 9.0 Hz), 3.53 (3H, m), 3.63 (2H, m), 3.64 (1H, t, *J* = 8.6 Hz), 3.79 (1H, ddd, *J* = 1.6, 6.1, 8.6 Hz), 3.93 (1H, td, *J* = 3.0, 8.6 Hz), 4.01 (1H, ddd, *J* = 2.6, 5.1, 15.0 Hz), 4.16 (1H, t, *J* = 2.6, 9.0 Hz), 4.25 (1H, dd, *J* = 6.1, 15.7 Hz), 4.37 (1H, dd, *J* = 2.5, 11.4 Hz), 4.43 (1H, d, *J* = 11.7 Hz), 4.54 (1H, d, *J* = 12.4 Hz), 4.64 (1H, d, *J* = 12.4 Hz), 4.735 (1H, d, *J* = 11.4 Hz), 4.740 (1H, d, *J* = 11.7 Hz), 4.75 (1H, d, *J* = 11.7 Hz), 4.91 (1H, d, *J* = 11.4 Hz), 5.01 (1H, d, *J* = 11.4 Hz), 5.57 (1H, m), 5.82 (6H, m), 6.53 (1H, dd, *J* = 2.6, 12.4 Hz), 7.21 (2H, d, *J* = 8.6 Hz), 7.29 (1H, ddd, *J* = 1.3, 8.0, 16.0 Hz), 7.41 (9H, m), 7.59 (1H, s), 7.71 (12H, m); ^{13}C NMR (100 MHz, $CDCl_3$, measured at 50 ºC) δ 27.6 (CH_2), 31.7 (CH_2), 32.5 (CH_2), 33.2 (CH_2), 34.6 (CH_2), 68.0 (CH_2), 69.9 (CH_2), 71.8 (CH_2), 73.5 (CH_2), 74.6 (CH), 74.7 (CH_2), 75.4 (CH_2), 75.8 (CH), 78.2 (CH), 79.3 (CH), 80.4 (CH), 80.5 (CH), 82.2 (CH), 83.5 (CH), 85.2 (CH), 85.4 (CH), 86.1 (CH), 88.3 (CH), 121.4 (C), 124.9 (CH), 125.8 (CH), 125.86 (CH × 2), 125.91 (CH), 126.0 (CH), 126.08 (CH), 126.10 (CH), 126.2 (CH), 126.39 (CH), 126.43 (CH), 126.9 (CH), 127.0 (CH), 127.3 (CH), 127.7 (CH), 127.75 (CH),

127.77 (CH), 127.8 (CH), 127.85 (CH), 127.91 (CH × 2), 128.1 (CH), 128.15 (CH), 128.18 (CH), 128.6 (CH), 129.4 (CH × 2), 131.45 (CH), 131.46 (CH × 2), 133.1 (C × 2), 133.2 (C), 133.38 (C), 133.40 (C × 2), 135.8 (C), 135.9 (C), 136.0 (C), 138.35 (CH), 138.37 (C), 148.0 (CH), 202.9 (C); FD-HRMS (m/z) calcd for $C_{68}H_{67}BrO_{10}[M]^+$: 1122.3918, found: 1122.3904.

7.1.50. Isomerization of 11-*epi*-65.
To a solution of 11-*epi*-**65** (3.0 mg, 2.7 µmol) in CH_2Cl_2 (0.5 mL) was added DBU (2 drops) at 24 ºC, and the mixture was stirred for 7 h. Then, the reaction was quenched with 0.5 mol/L aq. HCl, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 5 → 3) to give a 3:1 mixture of **65** and 11-*epi*-**65** (1.6 mg, 1.4 µmol, 53%) as a colorless oil.

7.1.51. (2*S*,5a*S*,6a*R*,8*Z*,11*S*,12*R*,13a*S*,14*Z*,16a*R*)-2-(((2*R*,3*R*,4*S*,4a*S*,9a*S*)-4-((4-Bromobenzyl)oxy)-3-hydroxy-3,4,4a,6,9,9a-hexahydro-*2H*-pyrano[3,2-*b*]oxepin-2-yl)methyl)-11-hydroxy-12-(hydroxymethyl)-3,5a,6a,7,10,11,12,13a,16,16a-decahydro-*3H*-oxepino[2',3':7,8]oxocino[3,2-*b*]oxonin-3-one (67). To a solution of **65** (2.3 mg, 2.1 µmmol) in CH_2Cl_2-H_2O (1.0 mL: 0.5 mL) was added DDQ (6.2 mg, 0.027 mmol) at 17 ºC, and the mixture was stirred for 1 h. Then, the reaction was quenched with saturated aq. $NaHCO_3$ and saturated aq. $Na_2S_2O_3$, and the mixture was extracted with CH_2Cl_2 several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 3 → 2) to give **66**, which was used immediately in the next reaction.
To a solution of the above **66** in EtOH (0.2 mL) was added 1.0 mol/L aq. HCl (0.1 mL) at 17 ºC, and the mixture was stirred for 2 h. Then, the reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 1 → 0.5 → 0.2) to give **67** (1.4 mg, 1.9 µmol, 93% from **65**) as a colorless oil.
67: $[\alpha]_D^{25}$ –23 (*c* 0.12, $CHCl_3$); IR (neat) ν 3429, 3024, 2956, 2918, 2854, 1741, 1724, 1664, 1597, 1486, 1468, 1446, 1405, 1380, 1359, 1331, 1284, 1126, 1088, 1013, 943, 911, 873, 845, 802, 781, 739, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, measured at 50 ºC) δ 1.80-1.86 (1H, m), 1.86-1.94 (1H, m), 2.15 (1H, brd, *J* = 14.2 Hz), 2.21-2.31 (3H, m), 2.40 (1H, brddd, *J* = 2.0, 6.1, 13.8 Hz), 2.53 (1H, ddd, *J* = 4.0, 8.1, 16.2 Hz), 2.69 (1H, ddd, *J* = 4.1, 9.4, 13.8 Hz), 2.81 (1H, brddd, *J* = 3.6, 10.1, 13.8 Hz), 2.91 (1H, brddd, *J* = 4.0, 9.7, 13.8 Hz), 3.11-3.19 (2H, m), 3.26 (1H, t, *J* = 8.5 Hz), 3.31 (1H, t, *J* = 8.5 Hz), 3.33 (1H, t, *J* = 8.5 Hz), 3.41 (1H, dt, *J* = 2.0, 8.5 Hz), 3.61-3.80 (4H, m), 3.89-4.06 (3H, m), 4.11 (1H, td, *J* = 2.9, 8.9 Hz), 4.22 (1H, dd, *J* = 5.7, 15.8 Hz), 4.26-4.32 (1H, m), 4.69 (1H, d, *J* = 12.0 Hz), 4.89 (1H, d, *J* = 12.0 Hz), 5.70-5.89 (7H, m), 6.46 (1H, dd, *J* = 2.9, 13.3 Hz), 7.22 (2H, d, *J* = 8.4 Hz), 7.46 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, measured at 50 ºC) δ 31.5 (CH_2), 32.5 (CH_2), 34.4 (CH_2), 36.2 (CH_2), 63.8 (CH_2), 65.5 (CH_2), 67.9 (CH_2), 71.7 (CH), 73.7 (CH), 74.2 (CH_2), 74.5 (CH), 76.1 (CH), 80.7 (CH), 83.0 (CH), 83.7 (CH), 85.2 (CH), 85.3 (CH), 87.2 (CH), 87.6 (CH), 121.5 (C), 126.3 (CH), 126.97 (CH), 127.03 (CH), 127.9 (CH), 128.2 (CH), 128.8 (CH), 129.3 (CH×2), 130.9 (CH), 131.2 (CH), 131.6 (CH×2), 137.6 (CH), 138.2 (C), 146.1 (CH), 203.5 (C); FD-HRMS (m/z) calcd for $C_{35}H_{43}{}^{79}BrO_{10}[M]^+$: 702.2040, found: 702.2042.

7.1.52. (5a*S*,6a*R*,7a*S*,8a*R*,10*Z*,11a*S*,13*R*,14*S*,16*Z*,18a*R*,19a*S*,21a*R*,22a*R*,23*R*,23a*S*)-23-((4-bromobenzyl)oxy)-13-(hydroxymethyl)-5,5a,6a,7,7a,8a,9,11a,13,14,15,18,18a,19a,21a,22a,23,23a-octadecahydro-*2H*-oxepino[2''',3''':5''',6''']pyrano[2''',3''':5'',6'']pyrano[2'',3'':6',7']oxepino[2',3':7,8]oxocino[3,2-*b*]oxonin-14-ol (3). To a solution of **67** (1.4 mg, 2.0 µmol) in CH_2Cl_2-Et_3SiH (0.2 mL: 0.1 mL) was added TMSOTf (3.0 µL, 0.017 mmol) at 0 ºC, and the mixture was stirred for 15 min. Then, the reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 1 → 0.8 → 0.5) to give **3** (1.0 mg, 1.5 µmol, 73%) as a colorless solid.
3: mp 168-169 ºC; $[\alpha]_D^{24}$ –22 (*c* 0.050, $CHCl_3$); IR (KBr) ν 3418, 3024, 2953, 2925, 2879, 2858, 2823, 1724, 1660, 1632, 1445, 1386, 1294, 1262, 1135, 1086, 1072, 1051, 1015, 804, 769, 687, 670 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.67 (1H, q, *J* = 11.6 Hz), 1.95 (1H, brd, *J* = 13.5 Hz), 2.15 (1H, ddd, *J* = 2.5, 6.3, 13.1 Hz), 2.17-2.27 (2H, m), 2.32 (1H, td, *J* = 4.7, 11.6 Hz), 2.52 (1H, ddd, *J* = 1.0, 2.4, 6.6 Hz), 2.56 (1H, dd, *J* = 3.7, 7.5 Hz), 2.64 (1H, ddd, *J* = 4.3, 10.9, 13.8 Hz), 2.72 (1H, brddd, *J* = 3.2, 9.4, 13.5 Hz), 2.83-2.94 (2H, m), 3.00-3.08 (2H, m), 3.11 (1H, t, *J* = 9.2 Hz), 3.22-3.26 (1H, m), 3.27 (1H, t, *J* = 9.2 Hz), 3.37 (1H, brtd, *J* = 2.8, 8.4 Hz), 3.48-3.57 (3H, m), 3.61-3.69 (1H, m), 3.70-3.75 (2H, m), 3.80 (1H, brd, *J* = 6.9 Hz), 3.91 (1H, brt, *J* = 8.4 Hz), 4.00-4.07 (2H, m), 4.81 (1H, d, *J* = 12.7 Hz), 4.88 (1H, d, *J* = 12.7 Hz), 5.44-5.56 (2H, m), 5.63 (1H, dd, *J* = 5.6, 10.8 Hz), 5.71-5.77 (2H, m), 5.87-6.03 (3H, m), 7.17 (2H, m), 7.36 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, measured at 50 ºC) δ 31.9 (CH_2), 32.5 (CH_2), 32.9 (CH_2), 34.7 (CH_2), 37.0 (CH_2), 63.9 (CH_2), 68.4 (CH_2), 71.8 (CH), 73.3 (CH), 74.2 (CH), 76.9 (CH), 78.1 (CH), 80.7 (CH), 81.0 (CH), 82.3 (CH), 82.4 (CH), 84.0 (CH), 85.0 (CH), 86.1 (CH), 87.4 (CH), 121.2 (C), 126.6 (CH), 126.7 (CH), 127.6 (CH), 128.6 (CH), 129.3 (CH×2), 130.5 (CH), 130.9 (CH), 131.2 (CH), 131.3 (CH×2), 136.2 (CH), 136.5 (CH), 138.5 (C); FD-HRMS (m/z) calcd for $C_{35}H_{43}{}^{79}BrO_9[M]^+$: 686.2090, found: 686.2117; Crystal data: Crystals were obtained by recrystallizing from EtOAc/benzene. $C_{43}H_{53}O_{10}Br$, M = 809.79, colorless needle, 0.50 × 0.02 × 0.01 mm^3, monoclinic $P2_1$ (No. 4), a = 16.716(12) Å, b = 5.985(4) Å, c = 19.98(2) Å, β = 100.006(13)°, V = 1968(3) $Å^3$, ρ_{calcd}(Z = 2) = 1.366 g cm^{-3}. A total 744 unique data ($2\theta_{max}$ = 55°) were measured at T = 150 K by Rigaku Mercury 70 apparatus (Mo Kα radiation, λ = 0.71070 Å). Numerical absorption correction was applied (μ = 11.056 cm^{-1}). The structure was solved by the direct method (SIR2004) and refined by the full-matrix least-squares method of F^2. Some non-hydrogen atoms were refined anisotropically, while the rest were refined isotropically. Hydrogen atoms were included but not refined. The final *wR* value is 0.2301 (all data) for 5928 reflections and 480 parameters. CCDC 1517386.

Acknowledgments

We thank Dr. Eri Fukushi (GC-MS and NMR Laboratory, Faculty of Agriculture, Hokkaido University) for the mesurements of mass and NMR spectra. We are also grateful to Mr. Yusuke Takata, Mr. Kenji Watanabe (GC-MS and NMR Laboratory, Faculty of Agriculture, Hokkaido University), Ms. Seiko Oka, and Ms. Ai Tokumitsu (Equipment Management Center, Creative Research Institution, Hokkaido University) for

the measurements of mass spectra. We thank Mr. Wataru Nojo (Graduate School of Chemical Science and Engineering, Hokkaido University) for assistance in X-ray crystallographic analysis. This work was supported by Grants-in-Aid for Scientific Research from MEXT, Japan.

Supplementary Data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/#####/#####.

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