Pergamon

Tetrahedron, Vol. 53, No. 37, pp. 12425-12468, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00780-1

The Biomimetic Construction of Fused Cyclic Polyethers

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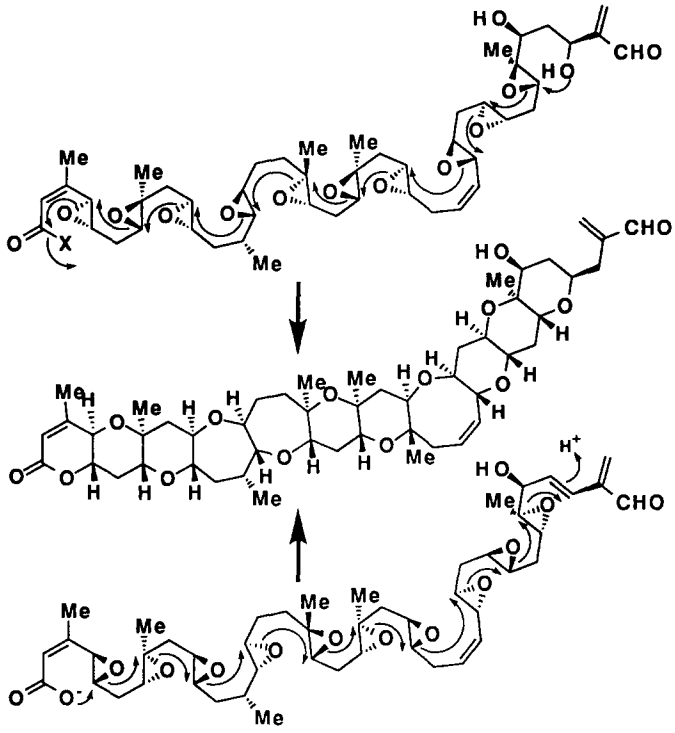
Abstract: The formation of fused cyclic ethers by biomimetic synthesis was demonstrated. The one-pot successive ring-expansion reactions of bromo diepoxides were investigated by regarding the epoxy groups as the nucleophiles for the intramolecular cationic carbons to obtain the fused cyclic ethers.

INTRODUCTION

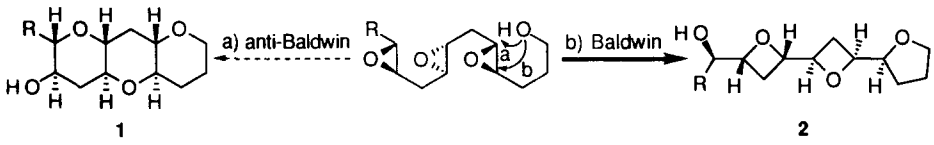
Since brevetoxin B was isolated from the red-tide organism, *Gymnodium breve*, and the structure was determined in 1981,[1] isolation of several marine polyethers has been reported.[2] These compounds are potent neurotoxins, which bind to ion channels and keep sodium channels open to increase sodium ion influx into the cells.[3] These molecular skeletons consist of *trans*-fused cyclic ethers. These unique molecular structures and novel biological activities have attracted a great deal of attention in both chemistry and pharmacology.[4] In the field of synthetic chemistry, the total synthesis of brevetoxin B was accomplished by the Nicolaou group,[5] and hemibrevetoxin B was synthesized by the groups of Nicolaou,[6] Yamamoto,[7] Nakata,[8] and Mori.[9]

However, it seems that the tandem synthetic methods generally require extraordinarily multiple steps. On the other hand, it has been proposed that this class of compounds might be biosynthesized from acyclic polyepoxy compounds (Scheme 1).[10] It has been expected that construction of the polyethers could be efficiently achieved in shorter steps, if this proposal is synthetically realized. The stereochemistries of the *trans*-junctures of the polyethers are assumed to be dependent upon only those of the epoxy groups.

There is a choice of two ways in attempting this cascade reaction; one is the successive ring-closure reaction of a hydroxy polyepoxy compound, the other is the successive ring-expansion reaction of a polyepoxy compound. The epoxy groups play opposite roles in these two methods; in the former case, the epoxy groups work as the electrophile, in the latter case, as the nucleophile. However, from the former method, the assembled cyclic ethers **2** would be obtained according to Baldwin's rules (Scheme 2).[11] If some directing groups are introduced into the substrate,[12] it might be expected that fused cyclic ethers **1** would be obtained by the successive ring-closure method. However, in view of the successive reactions, a difficult problem for

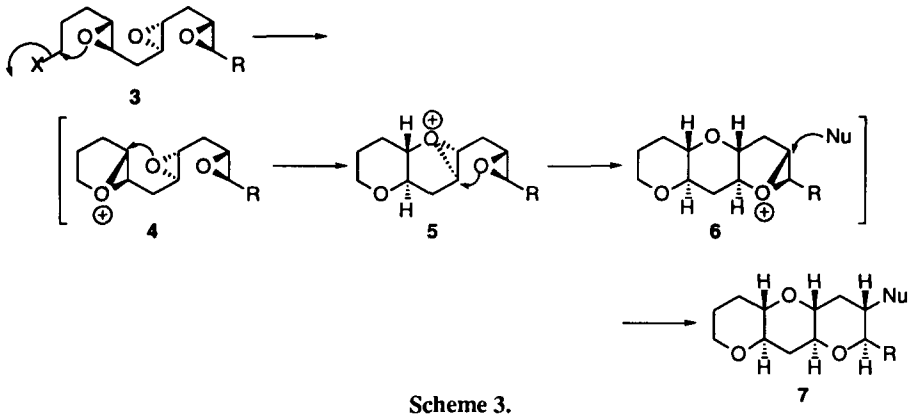


Scheme 1.



Scheme 2.

the removal of those directing groups would remain. On the basis of these expectations, we wanted to realize the biomimetic synthesis in a simple model system without any directing groups by using the property of the molecule itself. Accordingly, the method by the ring-expansion reaction, which would utilize the structural strain in a bridged oxonium ion intermediate, was adopted. The working hypothesis is illustrated in Scheme 3. The first step (the initiation step) is the process in which the first bridged oxonium ion **4** would be formed by the intramolecular nucleophilic attack of the first epoxy group to the cationic site. The next is the propagation step, in which the second epoxy group attacks the first oxonium ion **4** to generate the second oxonium ion **5**. It is assumed that the target molecule **7** could be synthesized, if the same successive reactions of the third, fourth...epoxy groups are followed by trapping of the last oxonium ion by the intermolecular or intramolecular attack of the nucleophile (the termination step).



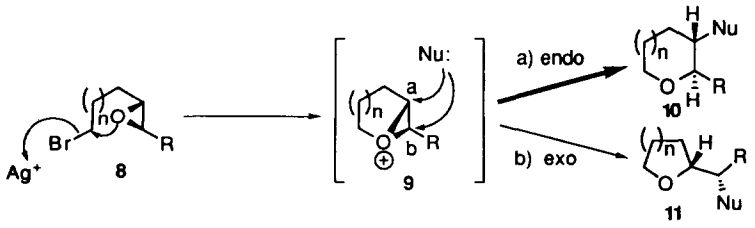
Scheme 3.

Concerning the formation of only a single cyclic ether *via* the bridged oxonium ion, some related approaches have been reported. Martín has demonstrated the intramolecular nucleophilic attack of an epoxy group to the iodonium cation on a carbocyclic framework.[13] However, the problems of low regioselectivity and the participation of the neighboring group still remained. The application to acyclic systems of its reaction described in the proposed biosynthetic process has been unknown. Kishi[14] and Martín[15] have reported the ring expansion of oxolane to oxane *via* the bridged oxonium ions. However, the net difference in the reactivity between the two reactive positions of the bridged oxonium ion is unclear, because of the difference in the chemical environment of the electrophilic site (the difference between the secondary and tertiary carbons of the oxonium ion), or the effects of the neighboring group and the complicated conformational factors.

Therefore, in the investigation of the successive ring expansion of epoxy groups, the problems to be clarified are as follows: 1) the nucleophilic ability of an epoxy group in simple acyclic systems; 2) the directionality of the ring expansion on the systems without any directing groups (endo or exo); 3) the possibility of the successive ring expansion. In this paper, the solutions to the above problems are described.

1. Single Ring Expansion Reactions; the Simplest Initiation and Termination Model.[16,17]

In order to solve the problems of the nucleophilic ability of an epoxy group and the directionality of the ring expansion on an acyclic epoxide without any directing groups, the conversion of 1-bromo epoxide **8** into the cyclic ethers (**10** or **11**) was attempted. This system could be regarded as both the simplest initiation and termination model for the intermolecular attack of a nucleophile in the biomimetic synthesis. The working hypothesis is shown in Scheme 4.



Scheme 4.

Initially, the epoxy group would attack intramolecularly the electrophilic center, which could be generated by the activated bromo group with a silver cation, to form the bridged oxonium ion **9**. The next step is divided into two intermolecular attacks of the external nucleophiles (Nu:) to the oxonium ions **9**; the attack to the site-a would produce **10** (endo-mode), whereas the attack to the site-b, **11**.[18] In order to develop this methodology into the aimed successive reaction, it is desired for this reaction to proceed by an endo-mode.

On the external nucleophile, two possibilities are assumed. One is the case in which an external nucleophile (Nu:) is added into the system. The other is the case in which no external nucleophiles are added into the system. Under the latter condition, the counter anion of the silver cation could act as an external nucleophile. In this chapter, the single ring-expansion reactions are described with respect to both these external nucleophiles.

1.1 AgOTf-Promoted Conversion of *trans*-1-Bromo-4,5-epoxide (18) into Oxane under Aqueous Conditions.

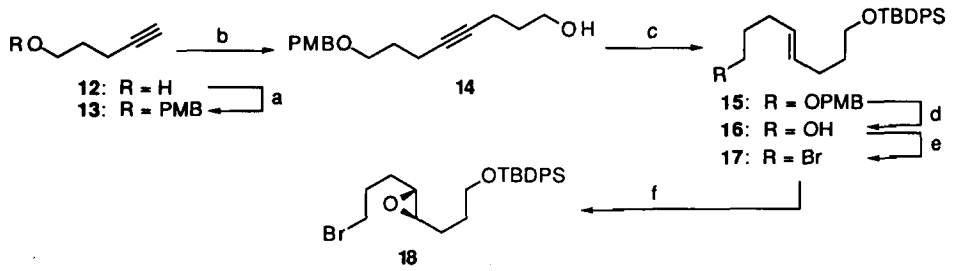
First of all, the conversion of *trans*-1-bromo-4,5-epoxide (n = 1 in Scheme 4) into an oxane was examined under the conditions in which an external nucleophile (Nu:) was added into the system. AgOTf was adopted as a silver cation source, because AgOTf was more soluble in various organic solvents than other silver cation sources. As shown in Scheme 4, if the reaction proceeds in an endo-mode, the oxane derivative would be formed. On the other hand, if in an exo-mode, its oxolane isomer would be produced.

Various chemical species were planned as additive external nucleophiles into the system. Salts were, however, not quite appropriate, because they generally had low solubilities in organic solvents, and caused the counter ion exchange to AgOTf to result in lowering the affinity between silver and bromine. Of neutral molecules, the compounds possessing soft atoms seemed not to be suitable in this reaction, because it was expected that they formed complexes with the silver cation to deactivate it. For these reasons, water as a neutral molecule and not having the soft atoms was chosen as the nucleophile.

The requisite racemic *trans*-bromoepoxide **18** was prepared as outlined in Scheme 5. The acetylenic 4-methoxybenzyl ether **13**, which was prepared from 4-pentyn-1-ol **12** by 4-methoxybenzylation in 95% yield, was converted to the hydroxy compound **14** by the coupling with alkyl bromide **19** followed by hydrolysis of the THP group (94%). The acetylenic part of **14** was reduced with $LiAlH_4$ to afford the *trans*-olefinic compound, whose free hydroxy group was protected as its TBDPS ether in 83% yield. The 4-methoxybenzyl group of compound **15** was removed by treatment with DDQ in aqueous CH_2Cl_2 in 94% yield. The alcohol **16** was converted into **17** by bromination with Ph_3P and CBr_4 in 98% yield, which, on epoxidation with *m*CPBA, gave the *trans*-bromoepoxide **18** in 99% yield.

1.1.1 Results.

The bromoepoxide **18** was treated with AgOTf in various aqueous organic solvents. The results are shown in Table 1. In heterogeneous solvent systems (Et_2O, benzene, and CH_2Cl_2), the reaction proceeded with difficulty, though Et_2O gave the best endo/exo selectivity (17/1) (entries 1, 2, and 3). In the cases of THF/H_2O (5:1), 1,4-dioxane/H_2O (5:1), and acetone/H_2O (5:1), the *trans*-3-hydroxyoxane derivative **21** was obtained as the major product in high stereoselectivities in 72%, 49%, and 55% yields, respectively (entries 4, 5, and 6).



Reagents and conditions: (a) PMBCl, NaH, THF, 25 °C, 14 h, 95%; (b) BuLi, THF, 0 °C, 30 min, then 1-bromo-3-tetrahydropyranyloxypropane **19**, THF/HMPA (2:1), 25 °C, 15 h; 0.5M HCl, THF, 25 °C, 1.5 h, 94%; (c) $LiAlH_4$, diglyme/THF (5:1), 140 °C, 15 h; TBDPSCl, imidazole, DMF, 25 °C, 18 h, 83%; (d) DDQ, CH_2Cl_2/H_2O (10:1), 25 °C, 2 h, 94%; (e) Ph_3P, CBr_4, CH_2Cl_2, 25 °C, 5 min, 98%; (f) *m*CPBA, Na_2HPO_4, CH_2Cl_2, 25 °C, 1 h, 99%.

Scheme 5.

The ratio of **21/22** was determined by ^{1}H-NMR analysis after acetylation of each hydroxy group. The structure of **23**, the acetate of **21**, was determined by NMR analysis (NOE and HMBC experiments, and the H-H coupling constant; $J_{2\text{-}3}$ = 9.4 Hz) as illustrated in Figure 1. The structure of **24**, the acetate of **22**, was determined by comparing the ^{1}H-NMR spectrum with that of **22** prepared in eq 4 in the next section. It seems that the best yield in THF/H_2O was due to the effect of THF as the proton scavenger which prevented cleavage of the TBDPS group. Actually, TBDPSOH was isolated in 18% and 6% yields in dioxane/H_2O and acetone/H_2O, respectively. In DMSO/H_2O or CH_3CN/H_2O, the endo/exo selectivity was lowered (entries 7 and 8). The activity of the silver cation might be lowered in CH_3CN/H_2O, because it might form probably an inert complex with the silver cation.

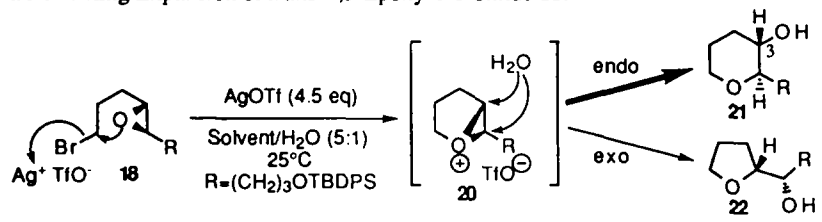
1.1.2 Discussion.

When the ring expansion reactions of *trans*-1-bromo-4,5-epoxide **18** proceeded, the major product was the oxane derivative in every case. The more detailed pathways to the products are described in this section.

It is presumed that the pathways illustrated in Table 1 are not necessarily common under aqueous conditions. Alternative pathways (paths **c**, **e**, **f**, **g**, **h**, **i**, and **j**) are possible as shown in Scheme 6. These pathways mean the following; paths **c** and **e** are the reverse processes of paths **b** and **d**, respectively; path **f** is hydrolysis of the epoxy group of **18** under acidic conditions; paths **g** and **h** are the cyclizations of bromo diol **26** to **21** and **22**, respectively; path **i** is the nucleophilic substitution of Br with H_2O molecule; path **j** is the 5-exo-cyclization of the hydroxy epoxide **25**, to be exact, whose product is the enantiomer of **22**.

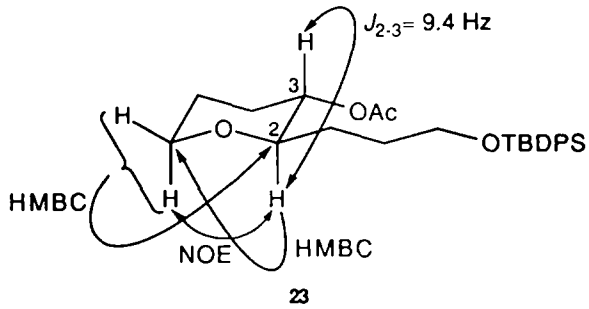
It was investigated whether these possible pathways participated in the generation of **21** and **22**. Firstly, paths **i** and **j** were examined. The olefin bromide **17** was treated with AgOTf (4.5 eq) in THF/H_2O (5:1) at 25 °C for 6.5 h only to recover the starting material **17** in 99% (eq. 1). Accordingly, it was aparent that the terminal bromo group was not displaced by the hydroxy group. Therefore, paths **i** and **j** were excluded. Secondly, in order to investigate path **f**, the epoxide **27** was treated with AgOTf (4.5 eq) in THF/H_2O (5:1) at 25 °C for 6.5 h only to recover the starting material **27** in 92% (eq. 2). However, **27**, on exposure to trifluoromethanesulfonic acid (1.0 eq) in THF/H_2O (5:1) at 25 °C for 6.5 h, afforded the *anti*-diol **28** (5%) in company with the

Table 1. Ring Expansion of *trans*-4,5-Epoxy-1-bromide **18**.



Entry	Solvent	Time/h	Yield/% 21 + 22	Ratio[a] (21/22)	Recovery/% 18
1	CH_2Cl_2	8.0	0	-	92
2	benzene	8.0	3	3.8/1	89
3	Et_2O	8.0	5	17/1	82
4	THF	6.5	91	3.8/1	6
5	1,4-dioxane	8.0	61	4.0/1	6
6	$(CH_3)_2CO$	6.5	70	3.6/1	0
7	CH_3CN	8.0	21	1.5/1	57
8	DMSO	8.0	48	2.4/1	7

a) The ratio of 21/22 was determined by ^{1}H-NMR after acetylation.

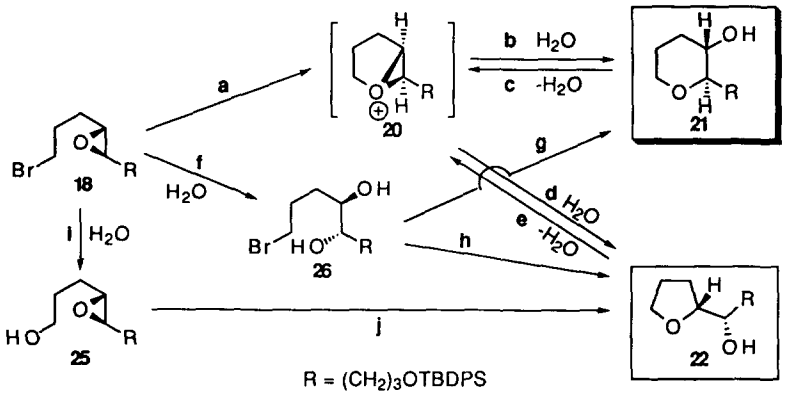


23

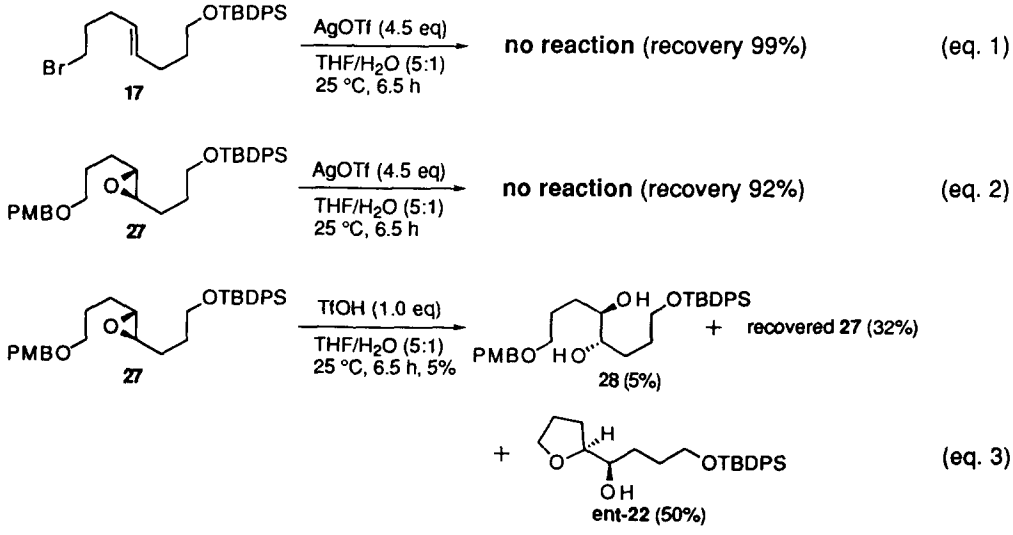
Figure 1. The NOE Interactions, HMBC, and Coupling Constant ($J_{2\text{-}3}$) in the Acetate **23**.

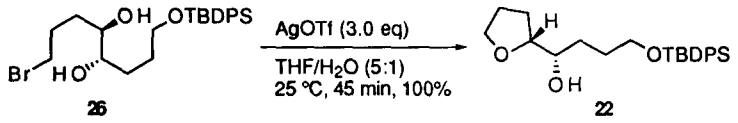
enantiomer of **22** (50%), which was presumably generated by 5-exo-cyclization owing to the stability of the benzyl cation (eq. 3). From this result, it was revealed that the hydrolysis (path **f**) of the epoxy group of **18** might occur, though it was slow. The *anti*-diol **26**, which was prepared as illustrated in Scheme 7, was converted into only the hydroxy oxolane **22** on treatment with AgOTf in THF/H_2O (5:1) (eq. 4). Consequently, it was clarified that path **h** was present, but path **g** was not. Lastly, the rearrangement between **21** and **22** (path **c** → path **d**, and path **e** → path **b**) was examined. The respective compounds **21** and **22** were subjected to AgOTf (4.5 eq) and TfOH (1.0 eq) in THF/H_2O (5:1) at 25 °C for 6.5 h only to recover unchanged **21** and **22**

in 94% and 99%, respectively. Therefore, path **c** and path **e** were ruled out. In conclusion, the following are pointed out. As illustrated in Scheme 8, the hydroxy oxane **21** was produced by only the processes through paths **a** and **b**. On the other hand, two possibilities were present with regard to generation of the hydroxy oxolane **22**. One is the pathway through path **a** and path **d**. The other is through path **f** and path **h**, though it seemed that this pathway did not much participate in the formation of **22** because of the slow process of path **f**. Namely, it is concluded that the hydroxy oxane **21** is the kinetically controlled product in the ring expansion reaction under aqueous conditions, whose net endo-selectivity was estimated to be higher than the results shown in Table 1.

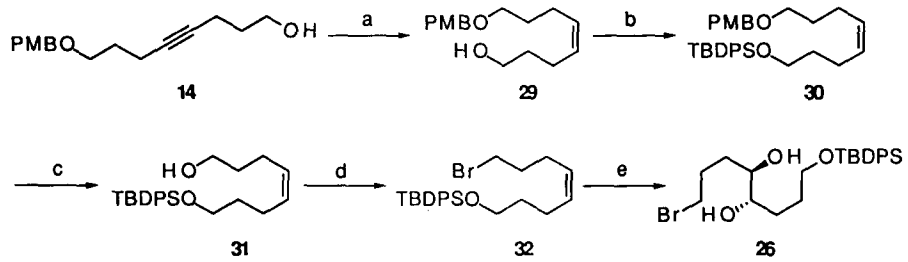


Scheme 6.



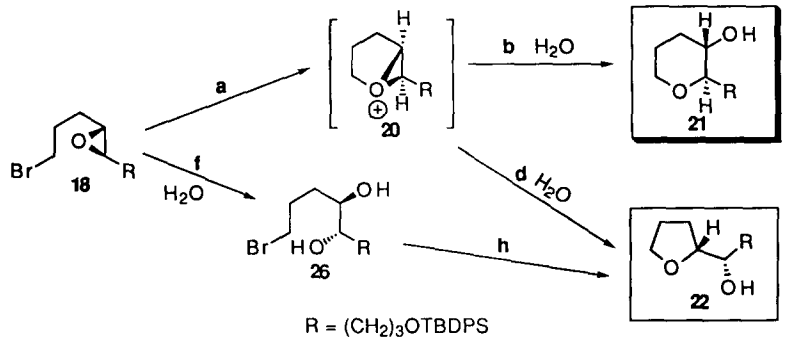


(eq. 4)



Reagents and conditions: (a) H_2, Lindlar cat., quinoline, MeOH, 25 °C, 4 h, 97%; (b) TBDPSCl, imidazole, DMF, 25 °C, 18 h, 100%; (c) DDQ, CH_2Cl_2/H_2O (10:1), 25 °C, 1 h, 88%; (d) Ph_3P, CBr_4, CH_2Cl_2, 25 °C, 5 min, 100%; (e) OsO_4, NMO, 1,4-dioxane/H_2O (10:3), 25 °C, 3 h, 91%.

Scheme 7.

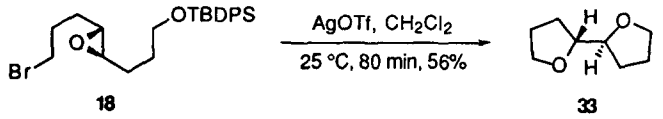


Scheme 8.

1.2 AgOTf-Promoted Conversion of *trans*-1-Bromo-4,5-epoxide (38) into Oxane under Anhydrous Conditions.

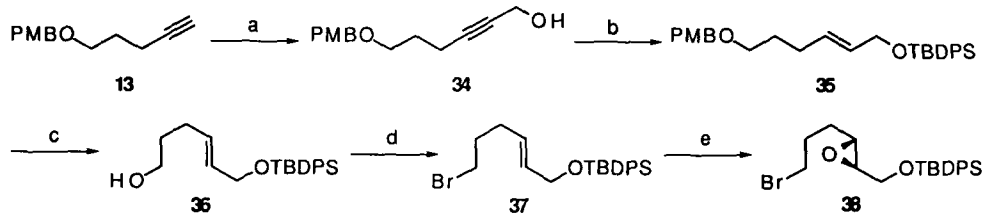
Next, the conversion of *trans*-1-bromo-4,5-epoxide into an oxane was examined under the conditions without any additive external nucleophiles. In these cases, it was anticipated that the counter ion of the silver cation, that is, TfO^-, would act as an external nucleophile.

However, **18** was treated with AgOTf in dry CH_2Cl_2 at 25 °C for 80 min to afford the oxolane rings-assembled bicyclic ether **33** (eq. 5). As this result indicates the participation of the oxygen atom on the side chain to the activated site, it would be necessary to furnish some new substrate in order to investigate the reaction under anhydrous conditions.



18 33 (eq. 5)

The substrate having a shorter side chain was prepared as outlined in Scheme 9. The acetylenic 4-methoxybenzyl ether **13** was converted to the hydroxy methyl compound **34** on reaction with BuLi and paraformaldehyde in quantitative yield. The hydroxy acetylene **34** was reduced with $LiAlH_4$ to afford the *trans*-allylic alcohol, whose free hydroxy group was protected as its TBDPS ether in 92% yield. The 4-methoxybenzyl group of **35** was removed by treatment with DDQ in aqueous CH_2Cl_2 to afford **36** in 74% yield, which was converted into **37** by bromination with Ph_3P and CBr_4 in 98% yield. The *trans*-bromoepoxide **38** was generated from **37** by epoxidation with *m*CPBA in quantitative yield.

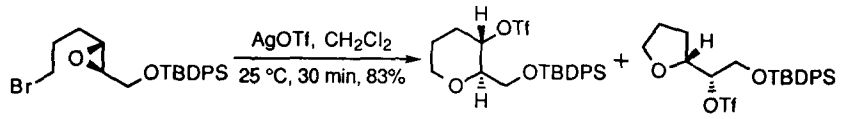


13 34 35 36 37 38

Reagents and conditions: (a) BuLi, $(CH_2O)_n$, THF, 25 °C, 2 h, 100%; (b) $LiAlH_4$, THF, 25 °C, 17 h; TBDPSCl, imidazole, DMF, 25 °C, 17 h, 92%; (c) DDQ, CH_2Cl_2/H_2O (10:1), 25 °C, 1.5 h, 74%; (d) Ph_3P, CBr_4, CH_2Cl_2, 25 °C, 30 min, 98%; (e) *m*CPBA, Na_2HPO_4, CH_2Cl_2, 25 °C, 2 h, 100%.

Scheme 9.

The *trans*-bromoepoxide **38** was treated with AgOTf (1.2 eq) in dry CH_2Cl_2 at 25 °C for 30 min to obtain a 9.8:1 inseparable mixture of the *trans*-3-triflyloxyoxane derivative **39** along with its oxolane isomer **40** in 83% combined yield (eq. 6). The ratio was determined by ^{1}H-NMR. The structure of the triflyloxy oxane **39** was determined by NMR analysis (HMBC experiment and the H-H coupling constant; $J_{2,3}$ = 9.2 Hz) (Figure 2).



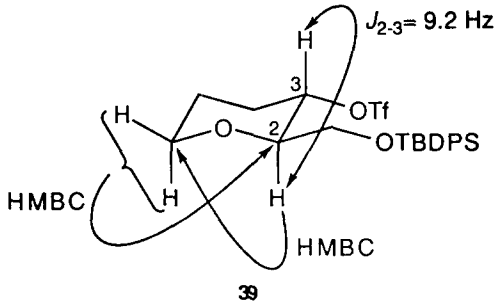
38 39 40 (eq. 6)

(39:40 = 9.8:1)

1.2.1 Discussion.

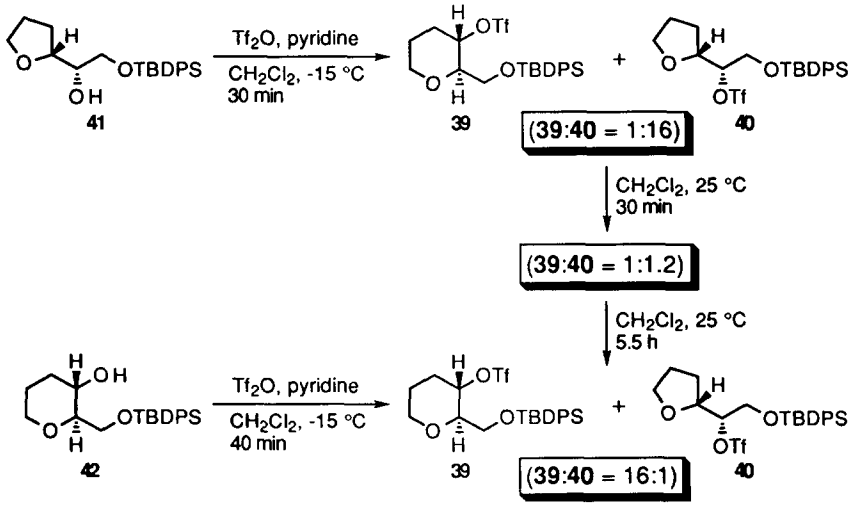
Under anhydrous conditions, the regioselectivity of products was excellent as shown in eq. 6. However, it was clarified from the following experiments that the excellent endo-selectivity did not necessarily reflect the kinetically controlled ratio. The pure hydroxy oxolane **41**, which was prepared by epoxidation and acid-catalyzed cyclization of **36**, was esterified with Tf_2O and pyridine in CH_2Cl_2 to obtain a 1:16 mixture of **39** and **40** (Scheme 10). The ratio was determined by ^{1}H-NMR. In spite of the absence of AgOTf, **40** was converted into **39** in CH_2Cl_2. After 30 min, the ratio of the mixture of **39**:**40** amounted to 1:1.2. After 5.5 h, it was

changed to 16:1.[18] In contrast, when the pure hydroxy oxane **42**, which was prepared by the ring expansion of **38** under aqueous conditions (Scheme 11), was treated under the same conditions as above, a 16:1 mixture of **39**:**40** was obtained. The reversible rearrangement of the skeletons undoubtedly takes place between the oxane **39** and the oxolane **40** as illustrated in Scheme 12.[19] The equilibrium seems to lie in favor of formation of the oxane **39**. Therefore, it is pointed out that the oxane **39** was thermodynamically more stable than its oxolane isomer **40**.



39

Figure 2. The HMBC and Coupling Constant ($J_{2\text{-}3}$) in the Compound (**39**).

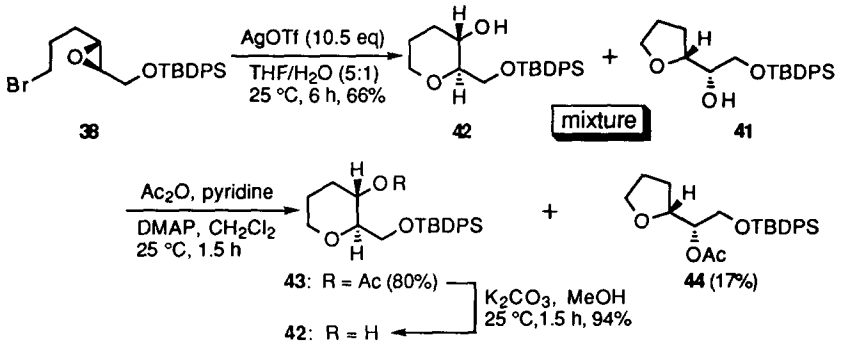


Scheme 10.

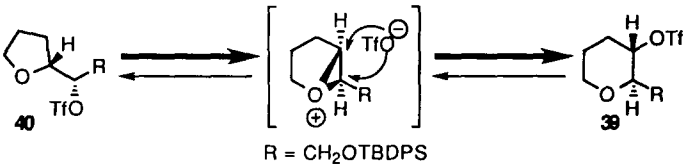
1.2.1 Discussion.

Under anhydrous conditions, the regioselectivity of products was excellent as shown in eq. 6. However, it was clarified from the following experiments that the excellent endo-selectivity did not necessarily reflect the kinetically controlled ratio. The pure hydroxy oxolane **41**, which was prepared by epoxidation and acid-catalized cyclization of **36**, was esterified with Tf_2O and pyridine in CH_2Cl_2 to obtain a 1:16 mixture of **39** and

40 (Scheme 10). The ratio was determined by ^{1}H-NMR. In spite of the absence of AgOTf, **40** was converted into **39** in CH_2Cl_2. After 30 min, the ratio of the mixture of **39**:**40** amounted to 1:1.2. After 5.5 h, it was changed to 16:1.[17] In contrast, when the pure hydroxy oxane **42**, which was prepared by the ring expansion of **38** under aqueous conditions (Scheme 11), was treated under the same conditions as above, a 16:1 mixture of **39**:**40** was obtained. The reversible rearrangement of the skeletons undoubtedly takes place between the oxane **39** and the oxolane **40** as illustrated in Scheme 12.[20] The equilibrium seems to lie in favor of formation of the oxane **39**. Therefore, it is pointed out that the oxane **39** was thermodynamically more stable than its oxolane isomer **40**.



Scheme 11.



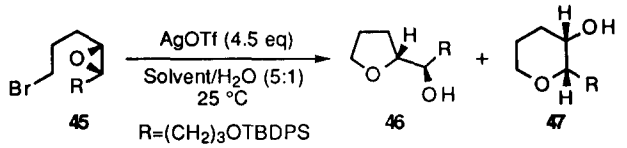
Scheme 12.

1.3 The Ring Expansion of the *cis*-1-Bromo-4,5-epoxide (45).

In order to examine the generality of the reaction, it was attempted to apply this new ring-expansion reaction to *cis*-1-bromo-4,5-epoxide **45**, which was prepared by epoxidation of **32**. The results on the ring expansion reaction of **45** are shown in Table 2. The solvents used for the reaction were aqueous THF, 1,4-dioxane, and acetone, which were the solvents giving the good results in the case of *trans*-epoxide **18**. The reaction of *cis*-epoxide **45** proceeded more slowly than that of its *trans*-isomer **18**. In every case, the hydroxy oxolane **46** was generated as a single product, and no trace amount of **47** was detected. The structure of **46** was determined by the conversion of **46** into the acetate **24** by Mitsunobu reaction.

If the bridged oxonium ion would be formed in the case of *cis*-epoxide **45**, the 1,3-steric interaction shown in Figure 3 could exist between the side chain and the C-H bond. Such an interaction is absent in its *trans*-isomer. However, it is not clear from only these results which pathways illustrated in Scheme 13 caused **47** to produce, though the small reaction rate suggests the difficulty of the intramolecular nucleophilic attack of the epoxy group.

Table 2. The Ring Expansion of *cis*-1-Bromo-4,5-epoxide (**45**).



Entry	Solvent	Time/h	Yield/%[a] 46	47	Recovery/% 45
1	THF	19	54	0	6
2	1,4-dioxane	19	52	0	5
3	$(CH_3)_2CO$	19	49	0	7

a) TBDPSOH was isolated in 9, 27, and 21% yields in entries 1, 2, and 3, respectively.

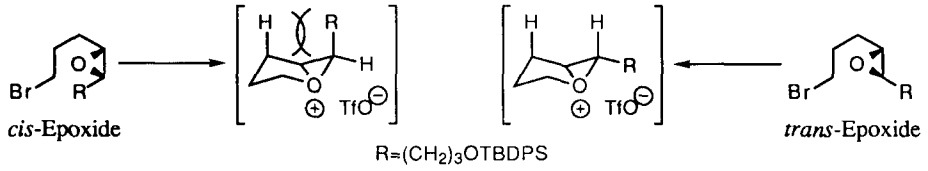
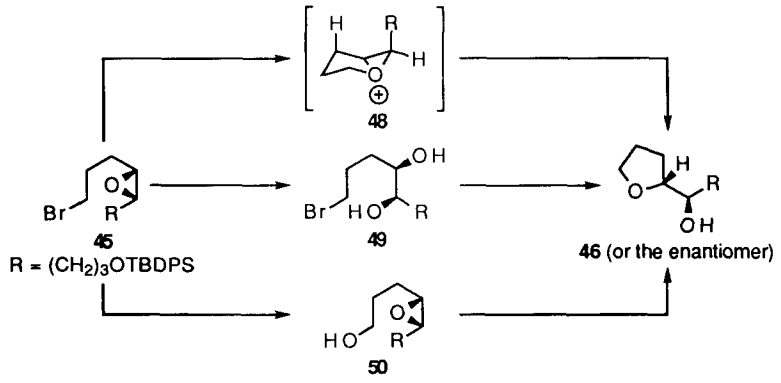


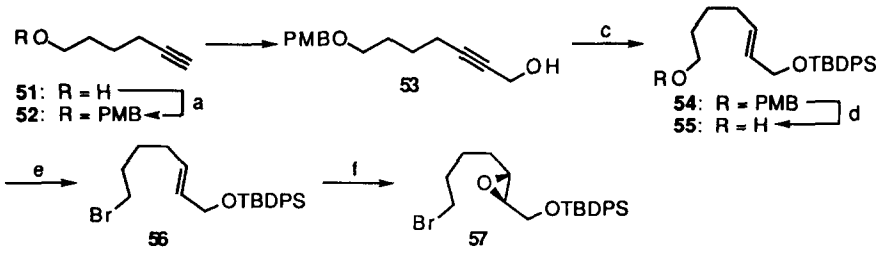
Figure 3.



Scheme 13.

1.4 AgOTf-Promoted Conversion of *trans*-1-Bromo-5,6-epoxide into Oxepane.

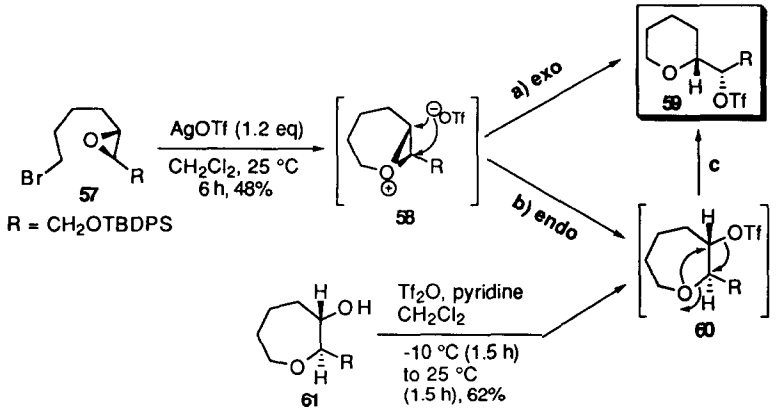
The methodology of this epoxy group's ring-expansion was also applied to *trans*-1-bromo-5,6-epoxide (n = 2 in Scheme 4). The requisite racemic *trans*-1-bromo-5,6-epoxide **57** was prepared by a similar process of the *trans*-1-bromo-4,5-epoxide **38** outlined in Scheme 14.



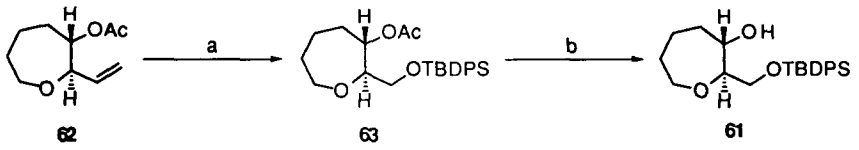
Reagents and conditions: (a) PMBCl, NaH, TBAI, THF, 25 °C, 38 h, 75%; (b) BuLi, $(CH_2O)_n$, THF, 25 °C, 2 h, 90%; (c) $LiAlH_4$, THF, 25 °C, 17 h; TBDPSCl, imidazole, DMF, 25 °C, 14 h, 86%; (d) DDQ, CH_2Cl_2/H_2O (10:1), 25 °C, 1.5 h, 76%; (e) Ph_3P, CBr_4, CH_2Cl_2, 25 °C, 12 min, 94%; (f) *m*CPBA, Na_2HPO_4, CH_2Cl_2, 25 °C, 2 h, 100%.

Scheme 14.

Firstly, the results of the thermodynamic control were examined. The reaction was carried out under conditions without any additives to obtain the triflyloxy oxane **59** (48%) (Scheme 15). The longer reaction time as compared with **38** suggested that the intramolecular nucleophilic attack of the epoxy group was difficult owing to the elongation of the carbon chain. Because the oxepane isomer **60**, the product in an endo-mode, was not detected at all, it was examined whether **60** could be rearranged into **59** (path b → path c illustrated in Scheme 15). The hydroxy group in **61**, which was prepared from the acetoxy oxepane **62** (Scheme 16),[12b] was esterified with Tf_2O and pyridine in CH_2Cl_2 to provide the oxane **59** only (Scheme 15). This result revealed that **60** must be labile and easily rearranged into **59**, which could be, therefore, regarded as a thermodynamically controlled product in the reaction of **57**. The cyclic structure and stereochemistry of **59** were confirmed by NMR analysis (HMBC) on **59**, which was alternatively prepared by the route shown in Scheme 17.

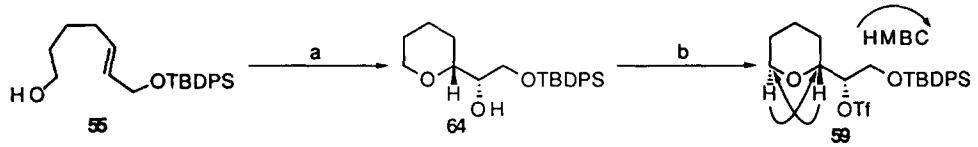


Scheme 15.



Reagents and conditions: (a) OsO_4, $NaIO_4$, Et_2O/H_2O (1:1), 25 °C, 1.5 h; $NaBH_4$, MeOH, 0 °C, 1 h; TBDPSCl, imidazole, 25 °C, 15 h, 64%; (b) K_2CO_3, MeOH, 25 °C, 1.5 h, 78%.

Scheme 16.

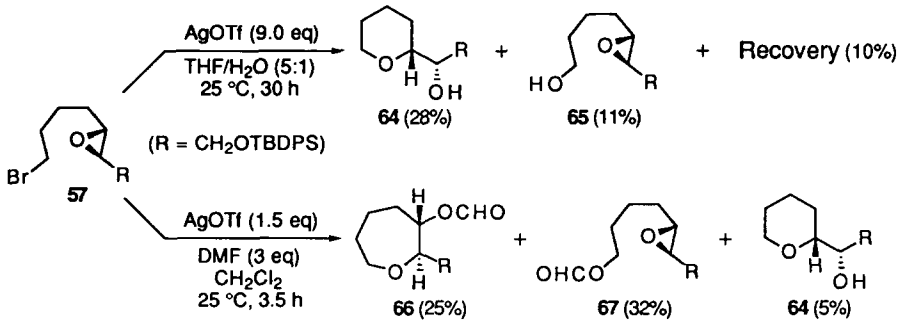


Reagents and conditions: (a) *m*CPBA, CH_2Cl_2, 25 °C, 30 min; PTS·H_2O, CH_2Cl_2, 25 °C, 1 h, 96%; (b) Tf_2O, pyridine, CH_2Cl_2, -10 °C, 30 min, 98%.

Scheme 17.

Next, for examining the results of the kinetic control, the reaction was carried out in the presence of an additive external nucleophile. In aqueous THF (THF/H_2O = 5:1), the products consisted of three components: the hydroxy oxane **64** (28%), the hydroxy epoxide **65** (11%), and a high polar compound, which was assumed to be the coupling product between the activated substrate and THF molecule (Scheme 18). The compound **64** seemed to be formed by the 6-exo-cyclization of **65**. In order to avoid the substitution of the bromo group into the hydroxy group, the additive external nucleophile was exchanged with dimethylformamide (DMF) (Scheme 18). The bromo epoxide **57** was treated with AgOTf in the presence of 3.0 eq of DMF in CH_2Cl_2 to obtain the formyloxy oxepane **66** in 25% yield. However, the reaction was accompanied by a considerable amount of by-products; one was the formyloxy epoxide **67**, another was the hydroxy oxane **64** which was presumably produced by hydrolysis of **59** in the purification with PTLC, and the others were a complex mixture. There still remains a possibility that the compound **66** might be produced by the skeletal rearrangement of **59** which was perhaps formed more rapidly. In order to circumvent this possibility, **59** was treated with DMF (3.0 eq) and AgOTf (1.5 eq) under the same conditions. Nothing was generated with recovery of the starting material **59** in 95%. Namely, the formyloxy oxepane **66** was the kinetically controlled product on the ring-expansion reaction of **57**. The structure of **66** was determined by formylation of **61**.

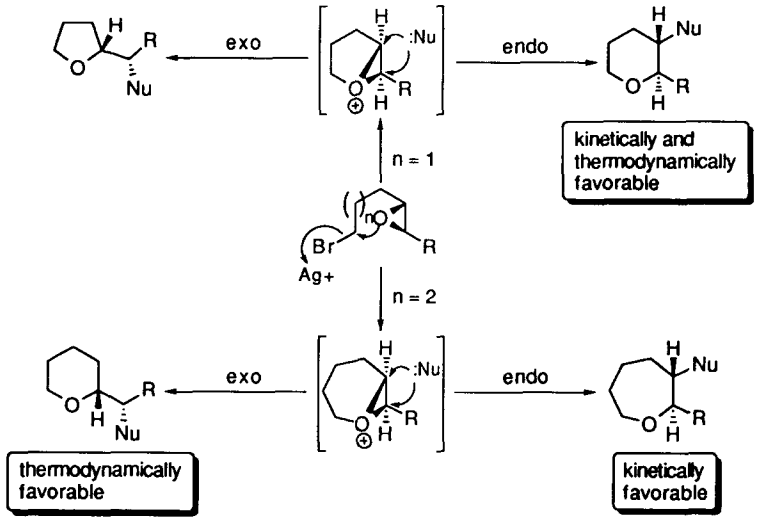
In this section, the following results became apparent on the ring-expansion reaction of the *trans*-1-bromo-5,6-epoxide **57**. Of the two possible ring-expanded compounds, the oxepane and oxane derivatives, the kinetically favorable compound was the former. On the other hand, the thermodynamically more stable compound was the latter. It was very interesting that the kinetically controlled direction of the ring expansion reactions was preferentially in an endo fashion on both *trans*-1-bromo-4,5-epoxide **18** and *trans*-1-bromo-5,6-epoxide **57**.



Scheme 18.

1.5 Conclusion.

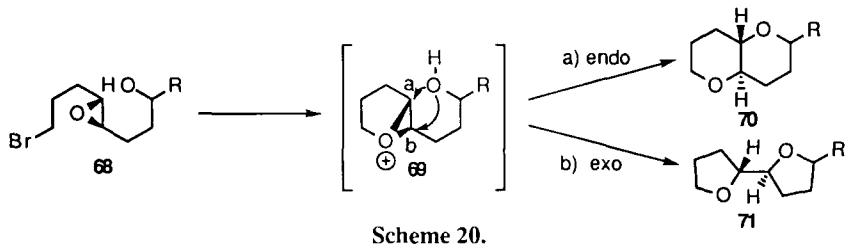
In this chapter, the following facts were clarified as shown in Scheme 19. The *trans*-epoxy groups acted as nucleophiles to attack the intramolecular electrophilic centers. In the systems without any directing groups, the direction of the ring-expansion reaction on the system producing the oxane or the oxolane skeleton could be both kinetically and thermodynamically controlled in an endo-mode. The direction on the system forming the oxepane or the oxane skeleton could be endo-fashion under kinetically controlled conditions, while it could be thermodynamically controlled in an exo-mode.



Scheme 19.

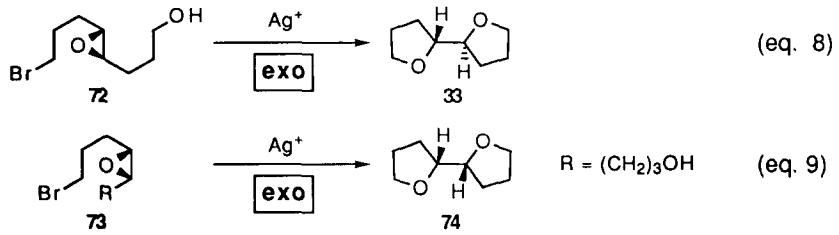
2. Successive Ring Expansion-Cyclization Reactions; the Intramolecular Termination Model.

Successive ring expansion-cyclization reactions by hydroxy epoxides **68** were attempted. The working hypothesis is illustrated in Scheme 20. The first step is the formation of the bridged oxonium ion **69**. The next stage is the intramolecular nucleophilic attack of the hydroxy group. If the attack occurs to the site-a of the oxonium ion **69**, it is expected that the fused bicyclic ether **70** would be obtained. On the other hand, the attack to the site-b of the hydroxy group will result in the generation of the assembled bicyclic ether **71**. In this chapter, the ring expansion-cyclization reactions of primary and secondary hydroxy epoxides are described. From the point of view of successive reactions, these reaction systems could be regarded as the intramolecular termination models.



Scheme 20.

The substrates (*trans*-epoxy alcohol **72** and *cis*-epoxy alcohol **73**) were prepared by desilylation of the corresponding epoxides **18** and **45**, respectively. *trans*-Epoxy alcohol **72** was treated with AgOTf in various organic solvents. However, unfortunately, the endo cyclization of the hydroxy oxonium ion did not occur regardless of the kind of solvent used (eq. 8). Similar results were obtained with the *cis*-epoxy alcohol **73** (eq. 9).



It is a very interesting fact that the side chains on the terminal rings of brevetoxins are present in axial conformations (Figure 4). Even though the generally accepted biosynthetic process is the ring expansion or the cyclization reaction of the polyepoxy compounds, the *cis*-configuration between the epoxy group and the secondary hydroxy group might exert some effect for the endo-attack of the hydroxy group (Scheme 21).

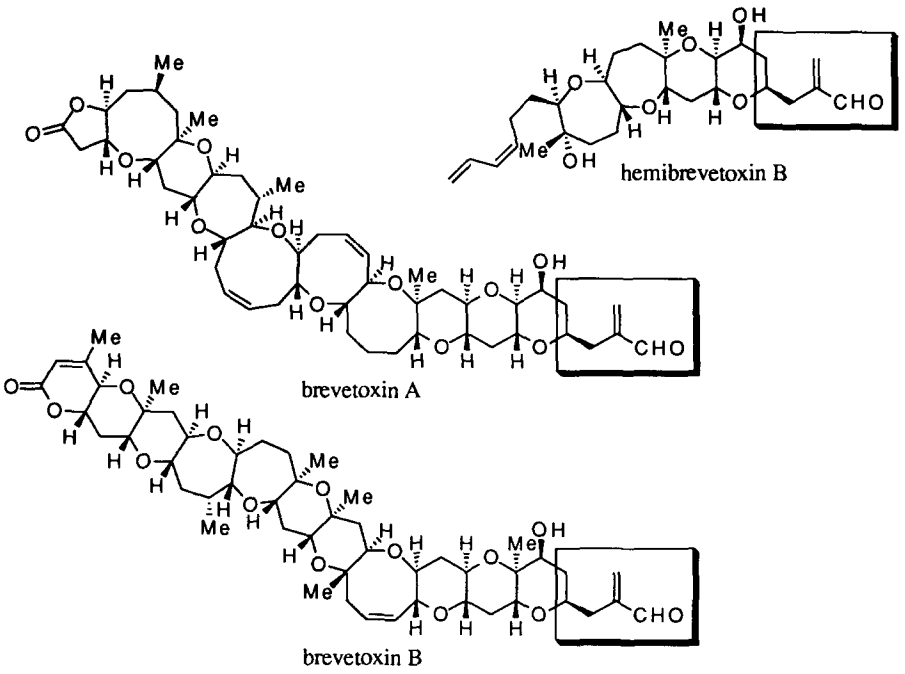
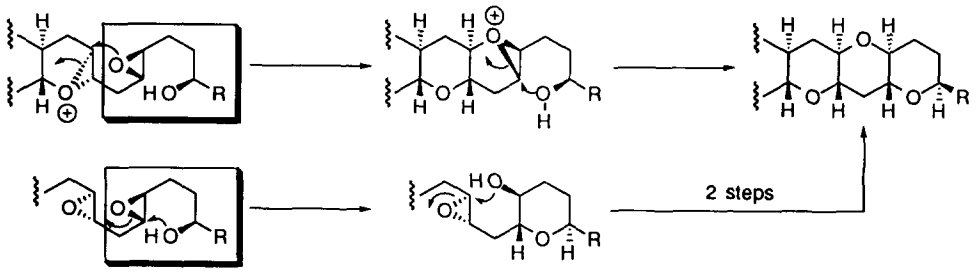
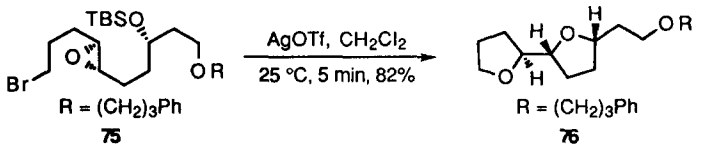


Figure 4.



Scheme 21.

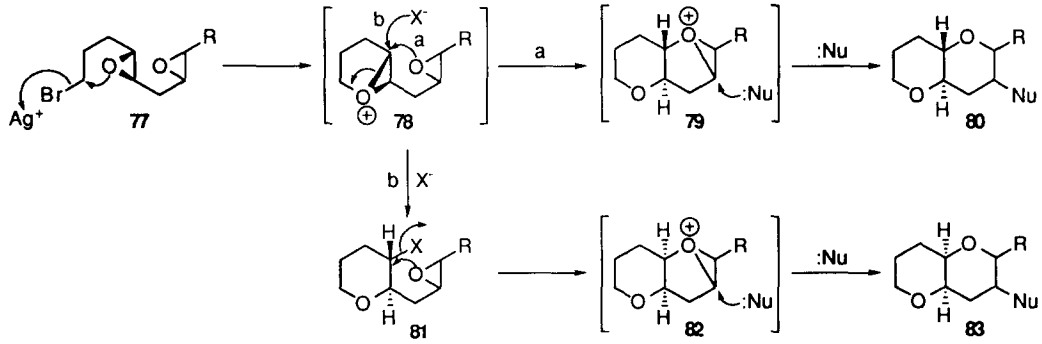
The silyloxy epoxide **75** itself was subjected to the reaction, because, when **75** was treated with TBAF in THF or SiF_4 in CH_3CN in order to obtain the corresponding alcohol, an intramolecular cyclization reaction occurred and the desired hydroxy epoxide corresponding to **75** could not be provided. The compound **75** was treated with AgOTf (1.5 eq) in CH_2Cl_2 under anhydrous conditions. Unexpectedly, the result led to formation of the assembled cyclic ether **76** as the sole product in 82% yield (eq. 10). The reaction aimed at the successive ring expansion-cyclization resulted in formation of the assembled cyclic ethers, even though the hydroxy group was primary or secondary.



(eq. 10)

3. The Successive Ring-Expansion Reaction of Diepoxide; the Simplest Propagation Model.[21]

In this chapter, the successive ring-expansion reactions of the *trans,trans*-diepoxides **77** are described. Various factors were estimated for these reactions. The proposed reaction mode of the successive ring expansion is illustrated in Scheme 22. The first step is the process in which the first bridged oxonium ion **78** would be formed by the intramolecular nucleophilic attack of the first epoxy group to the cationic site. In the next step, if the intramolecular attack of the second epoxy group is a faster process than the intermolecular attack of the external nucleophile (X^-), the reaction would proceed through path **a** to form the second oxonium ion **79**, and the successive ring expansion would be terminated by the intermolecular nucleophilic attack to produce the *trans*-fused bicyclic ether **80**. On the other hand, if the intramolecular attack of the second epoxy group could proceed more slowly than the intermolecular attack of X^-, the reaction would go through path **b** to form the epoxy tetrahydropyran **81**. If the X group is a poor leaving group, the reaction would be completed at this stage. To the contrary, when the X group works as a good leaving group, the second epoxy group would attack further the back side of the X group to provide the *cis*-fused bicyclic ether **83** *via* the second oxonium ion **82**. It was attempted to investigate how the successive ring-expansion reactions of the *syn-trans,trans*-diepoxide **93a** (an unnatural type) and *anti-trans,trans*-diepoxide **93b** (a natural type) could occur. These systems could be regarded as the simplest propagation models in the cascade reaction.



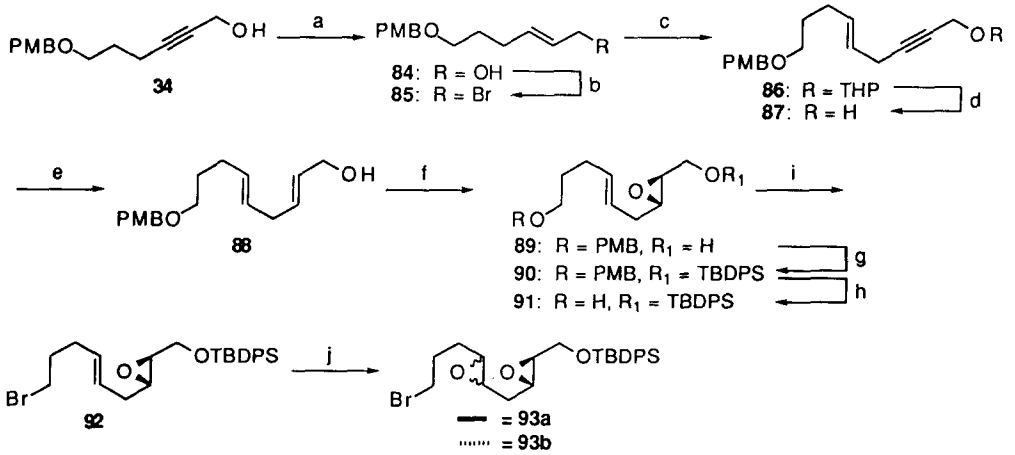
Scheme 22.

The requisite *syn-trans,trans*-diepoxide **93a** and *anti-trans,trans*-epoxide **93b** were prepared as outlined in Scheme 23. The allylic alcohol **84**, which was prepared by reduction of **34** with $LiAlH_4$, was converted into the allylic bromide **85** with Ph_3P and CBr_4 in 90% yield. The compound **85** was coupled with 1-lithio-3-tetrahydropyranyloxypropyne to afford the compound **86** in 52% yield. The recovered allylic bromide **85** (37%) was recycled in the same coupling reaction. Removal of the tetrahydropyranyl group from **86** by

methanolysis afforded the hydroxy compound **87** in quantitative yield. The hydroxy acetylene **87** was reduced with $LiAlH_4$ to obtain the allylic alcohol **88** (94%), which was then subjected to the Sharpless asymmetric epoxidation[22] leading to the hydroxy epoxide **89** in 95% yield. The hydroxy group of **89** was protected as its TBDPS ether **90** in quantitative yield. The 4-methoxybenzyl group of **90** was removed with DDQ in aqueous CH_2Cl_2 to afford alcohol **91** in quantitative yield. The hydroxy compound **91** was converted into the bromide **92** with Ph_3P and CBr_4 in 93% yield. A mixture of *syn*- and *anti-trans-trans*-diepoxides (**93a** and **93b**) was generated from **92** by epoxidation with *m*CPBA in quantitative yield. These diastereomers were separated by HPLC. The relative configuration of the epoxy groups of both of **93a** and **93b** will be identified in the next section.

3.1 Results and Discussion.

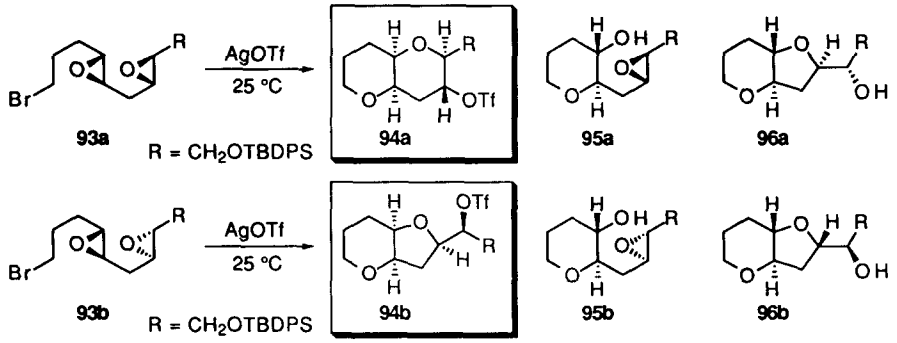
The reactions were initially attempted in the presence of H_2O as the external nucleophile. As shown in Table 3, the *syn*-diepoxide **93a** was treated with AgOTf (10 eq) in THF/H_2O (5:1) at 25 °C for 1 h to give **95a** (31%) and **96a** (11%) along with the corresponding epoxy tetrahydrofuran isomer (1%) (entry 1). From the *anti*-diepoxide **93b**, **95b** (41%) was obtained with the corresponding epoxy tetrahydrofuran isomer (1%) under almost the same conditions (at 25 °C for 1.5 h) (entry 4). The structural formula of **93b** is represented by that of the enantiomer because the discussion is easily understandable. When the reaction time was extended to 4 h and 23 h in the respective cases, the *trans*-fused bicyclic ethers **96a** and **96b** were afforded in 47 and 46% yield, respectively (entries 2 and 5). In these reactions, the respective clear conversions of **95a** and **95b** into **96a** and **96b** were observed by TLC analyses; that is, these results indicate that **96a** and **96b** were produced



Reagents and conditions: (a) $LiAlH_4$, THF, 25 °C, 16 h, 100%; (b) Ph_3P, CBr_4, CH_2Cl_2, 25 °C, 5 min, 90%; (c) 1-lithio-3-tetrahydropyranyloxypropyne, THF, 25 °C, 7 h, 52%; (d) PTS•H_2O, MeOH, 25 °C, 30 min, 100%; (e) $LiAlH_4$, THF, 25 °C, 13 h, 94%; (f) (+)-DET, $Ti(OiPr)_4$, TBHP, MS4A, CH_2Cl_2, -25 °C, 15 h, 95%; (g) TBDPSCl, imidazole, DMF, 25 °C, 14 h, 100%; (h) DDQ, CH_2Cl_2/H_2O (10:1), 25 °C, 1.5 h, 100%; (i) Ph_3P, CBr_4, CH_2Cl_2, 25 °C, 5 min, 93%; (j) *m*CPBA, Na_2HPO_4, CH_2Cl_2, 25 °C, 1 h, 100%.

Scheme 23.

Table 3. Ring Expansion of *syn*- and *anti*-Diepoxides (**93a** and **93b**).



Entry	Substrate	Solvent	AgOTf	Time	Products (%)	Recovery (%)
1	**93a**	THF/H_2O (5/1)	10 eq	1 h	**95a** (31) + **96a** (11)	**93a** (24)
2	**93a**	THF/H_2O (5/1)	10 eq	4 h	**96a** (47)	**93a** (0)
3	**93a**	CH_2Cl_2	1.2 eq	0.5 h	**94a** (39)	**93a** (0)
4	**93b**	THF/H_2O (5/1)	10 eq	1.5 h	**95b** (41)	**93b** (12)
5	**93b**	THF/H_2O (5/1)	10 eq	23 h	**96b** (46)	**93b** (0)
6	**93b**	CH_2Cl_2	1.2 eq	0.5 h	**94b** (29)	**93b** (0)

not by the successive ring expansions of two epoxy groups, but by 5-exo-cyclizations of the hydroxy epoxides (**95a** and **95b**) promoted by the acid in the systems. From these results, it was suggested that the intermolecular nucleophilic attack of H_2O to the first oxonium ion was faster than the intramolecular attack by the second epoxy group.

Next, the reactions were carried out under conditions without any additive, in which a triflate ion (a poor nucleophilic but a very good leaving group) would be expected to act as the external nucleophile. In dry CH_2Cl_2, **93a** was transformed into the *cis*-fused perhydrotriflyloxypyranopyran **94a** (39%) (entry 3), while **93b** was led to the *cis*-fused perhydrotriflyloxypyranofuran **94b** (29%) (entry 6). These rather low yields were attributed to the decomposition of these products in the purification stages. It is to be noted that the sizes of the second ring in the products depend on the stereochemistries of the diepoxides. The other products consisted of a complex mixture in both cases. The respective structures of **94a** and **94b** were determined by NMR analyses (the HMBC, NOE interactions, and H-H coupling constants revealed in Figure 5). Judging from the *cis*-junctures of **94a** and **94b**, it was suggested that the reactions proceeded through path **b** illustrated in Scheme 22. However, the intermediate such as **81** was not isolated, because the conversion of **81** to **82** was presumably the fast process. In order to confirm involvement of the intermediates, the respective triflates **97a** and **97b**, prepared from **95a** and **95b** with Tf_2O and pyridine in CH_2Cl_2, were subjected to the same conditions as the above successive ring-expansion reactions to afford the *cis*-fused bicyclic ethers (**94a** and **94b**), respectively (Scheme 24).

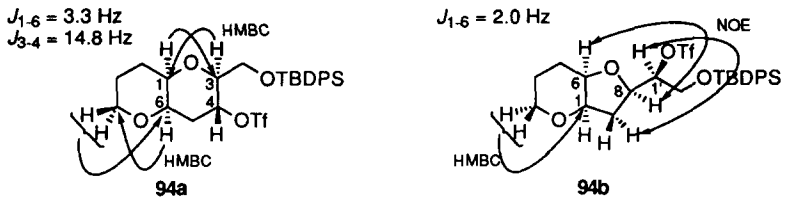
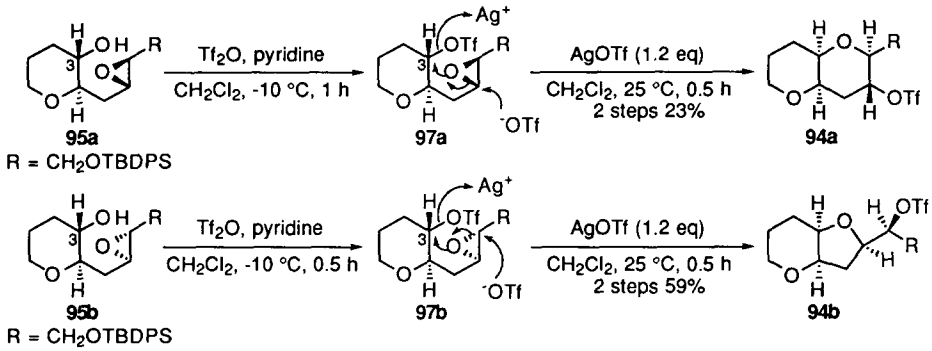


Figure 5. The HMBC, NOE Interactions, and H-H Coupling Constants in the Compounds (**94a** and **94b**).



Scheme 24.

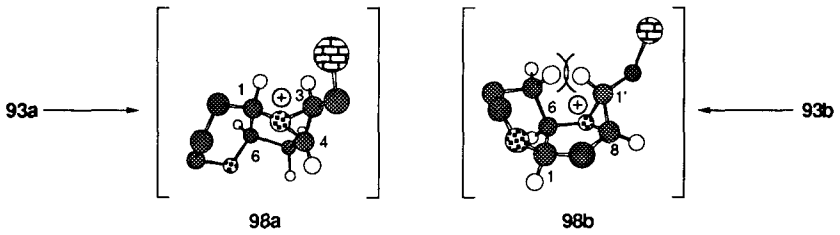


Figure 6. The Assumed Structures of the Second Oxonium Ions (the numberings correspond to those of **94a** and **94b**, respectively.)

From the above results, the following comments can be made. 1) Independently of the stereochemistries of the two epoxy groups, the direct intramolecular nucleophilic attacks of the second epoxy groups to the first activated epoxy groups were slower than the attack of the external nucleophiles such as the triflate ion in these systems. 2) When the triflate ion was used as the external nucleophile, formation of **97a** and **97b** was followed by the intramolecular nucleophilic attacks of the second epoxy groups, respectively, with the activation of the triflyloxy group owing to the silver ion. The *cis*-junctures were eventually formed by the double inversion in the stereochemistries of the C3 in **97a** and **97b**. 3) The direction of the ring expansion of the second epoxy group

depends on the relative configurations of the two epoxy groups. It has not been clarified at the present stage from the experimental results whether the difference in ring sizes between **94a** and **94b** resulted from the kinetic or the thermodynamic control. Because bicyclic systems possess the more rigid conformations, the skeletal rearrangement does not necessarily exist. However, in any event, the reasons why the second epoxy group of **93b** was expanded in exo-mode could be explained as follows. If the reaction was kinetically controlled, the regioselectivity of product depends on the activation energies of the transition states led from the second oxonium ion **98b** shown in Figure 6. If the structures of transition states were reactant-like, it is presumed that the activation energy to the exo-transition state is lower than that to the endo-transition state in the system of **93b**, because of the steric repulsions in **98b**. In the case of the product-like structures of transition states, also, the same result is obtained, because the steric repulsion in **94b** is less than that of its pyranopyran isomer as shown in Figure 7. If the reactions were thermodynamically controlled, the regioselectivity of product depends on the stability of each product. In the case of the system of **93b**, **94b** is expected to be thermodynamically more stable than its pyranopyran isomer, because of the lower steric repulsion as illustrated in Figure 7. It seems that the second epoxy group of **93a** was expanded in the essential direction, that is, endo, because of the absence of the above effects.

The stereochemistries of **93a** and **93b** were identified by the NOE interactions of the respective acetates (**99a** and **99b**) (Figure 8).

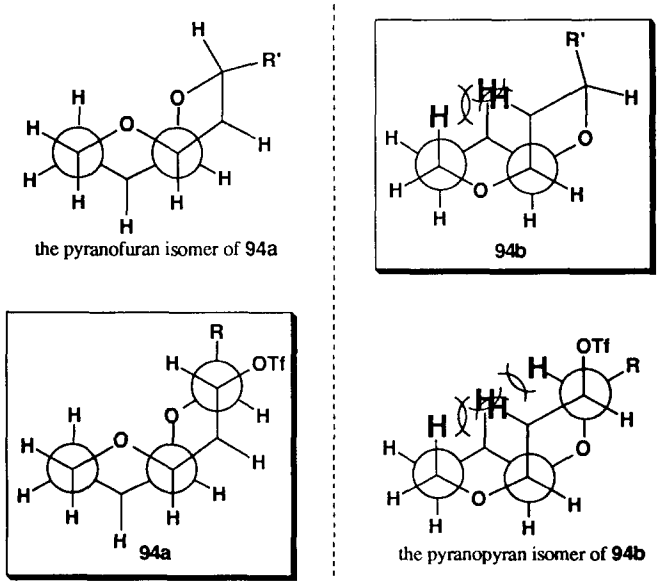


Figure 7.

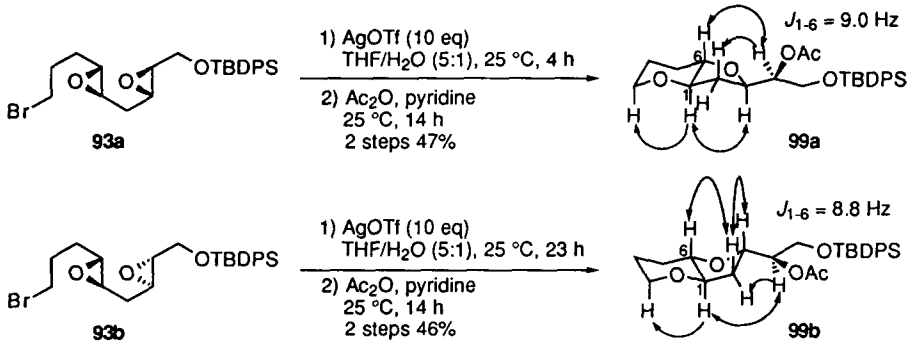
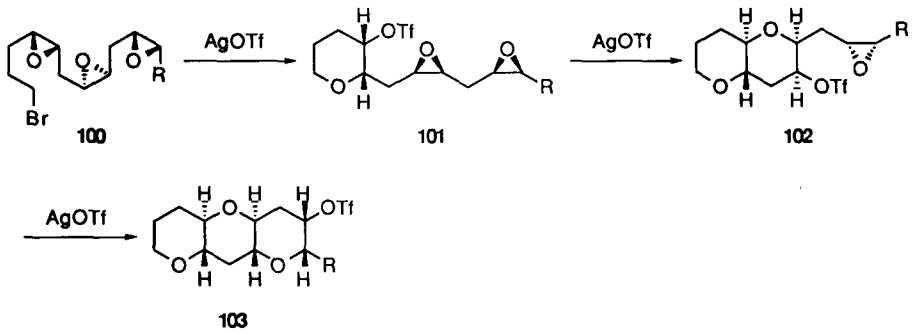


Figure 8. (NOE)

CONCLUSION

The AgOTf-promoted formation of fused cyclic ether systems by the successive ring-expansion reactions of bromo epoxides has been discussed from the three following points: 1) conversion of the oxiranes into the oxane or the oxepane (the initiation and termination model); 2) the successive ring expansion-cyclization reactions of the hydroxy epoxides (the intramolecular termination model); 3) the successive ring-expansion reactions of diepoxides (the propagation model). From these examinations, the following facts were clarified. 1) The *trans*-epoxy groups acted as nucleophiles to attack the intramolecular electrophilic centers. In the systems without any directing groups, the direction of the ring-expansion reaction on the system producing the oxane or the oxolane skeleton could be either kinetically or thermodynamically controlled in an endo-mode. The direction on the system forming the oxepane or the oxane skeleton could be endo-fashion under kinetically-controlled conditions, while it could be thermodynamically controlled in an exo-mode. 2) 5-Exo-cyclization prevails in the intramolecular nucleophilic attack of the hydroxy group to the bridged oxonium ion. 3) In the one-pot successive ring-expansion reaction of the *trans,trans*-diepoxides, the products are the *cis*-fused bicyclic ethers regardless of the relative configurations between both epoxy groups. It is demonstrated that the *cis*-juncture was formed by the double inversion of the stereochemistry on the juncture's carbon atom *via* the alkyl triflate intermediate in each case.

It seems that the last results (3) suggest the higher possibility of ring-expansion reactions. For example, if the reaction starts from the *cis*-epoxide **100**, the desired *trans*-fused cyclic ether **103** could be obtained by the successive double inversion on the juncture's carbon atom *via* the alkyl triflate intermediates (**101** and **102**) as illustrated in Scheme 25. We expect strongly that the formation of the *trans*-fused cyclic ether could be realized by this modified method.



Scheme 25.

EXPERIMENTAL SECTION

Solvents and reagents were dried and distilled before use. Ether, tetrahydrofuran (THF), and 1,4-dioxane were distilled from sodium benzophenone ketyl. Dichloromethane (CH_2Cl_2), benzene, acetonitrile (CH_3CN), and triethylamine (Et_3N) were distilled from calcium hydride (CaH_2). Dimethylsulfoxide (DMSO), dimethylformamide (DMF), and hexamethylphosphoramide (HMPA) were distilled under reduced pressure from CaH_2. Pyridine was distilled from solid potassium hydroxide (KOH). Methanol (MeOH) was distilled from the magnesium alkoxide. Normal reagent-grade solvents were used for flash chromatography, preparative thin layer chromatography (PTLC), and extraction. Special reagent-grade solvents were used for high-performance liquid chromatography (HPLC).

All reactions were monitored by thin-layer chromatography (TLC) with precoated silica gel (SiO_2) plates (Merk, Silica gel 60 F254 Art. 1.05554). Visualization was achieved *via* ultraviolet (UV) light and a 5.6% ethanolic *p*-anisaldehyde solution containing 5.6% of concentrated sulfuric acid (H_2SO_4)-heat. For flash chromatography was utilized SiO_2 (YMC, SIL-60-400/230W). For PTLC were utilized precoated SiO_2 plates (Merk, Silica gel 60 F254 1.05744 or 1.05715). HPLC were run with a JASCO Intelligent HPLC Pump 880-PU, equipped with a JASCO Intelligent UV/VIS Detector 875-UV. For HPLC was utilized SiO_2 column (DEVELOSIL 60-5, NOMURA CHEMICAL).

The NMR spectra were recorded on JEOL model α-400, EX-400 or FX-270 spectrometers in chloroform-d_1 ($CDCl_3$) or benzene-d_6 (C_6D_6). Infrared (IR) spectra were obtained on a Hitachi model 270-30 infrared spectrophotometer in neat state. Chemical shifts (δ) are reported with tetramethylsilane (TMS) (δ = 0.00 ppm) or C_6D_6 (δ = 7.20 ppm) as internal standards. Splitting patterns are designated as "s, d, t, q, qui, and m"; these symbols indicate "singlet, doublet, triplet, quartet, quintet, and multiplet, respectively. Optical rotations were recorded on JASCO model DIP-360 digital polarimeter using $CHCl_3$ or hexane as a solvent. High-resolution mass spectra (HR-MS) were obtained on a JEOL model JMS-HX-110 mass spectrometer under fast atom bombardment (FAB), a JEOL model DX303 mass spectrometer under electron ionization (EI), a JEOL model JMS-AX500 mass spectrometer under electron ionization (EI), a JEOL model JMS-SX102A mass spectrometer under field desorption (FD) condition.

All reactions were carried out under anhydrous conditions and argon atomosphere, unless otherwise noted.

5-(4-Methoxybenzyloxy)-1-pentyne (13). To a suspension of NaH (1.48 g, 36.9 mmol, 60% in oil dispersion) in THF (85 mL) was added a solution of 4-pentyn-1-ol **12** (3.01 g, 35.8 mmol) in THF (9 mL) at 0 °C and the mixture was stirred at 0 °C for 1 h. 4-Methoxybenzyl chloride (5.10 mL, 37.6 mmol) and tetrabutylammonium iodide (1.32 g, 3.58 mmol) were then added and the mixture was stirred at 25 °C for 14 h. Satd aq. ammonium chloride (NH_4Cl) was added to the mixture at 0 °C and the mixture was extracted with EtOAc. The combined organic layers were washed with satd aq. sodium bicarbonate ($NaHCO_3$) and brine, dried over magnesium sulfate ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 100:1) to give **13** (6.92 g, 95%). **13**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.26 (2H, d, *J*=8.6 Hz), 6.88 (2H, d, *J*=8.6 Hz), 4.44 (2H, s), 3.80 (3H, s), 3.54 (2H, t, *J*=6.3 Hz), 2.31 (2H, dt, *J*=2.6, 6.3 Hz), 1.93 (1H, t, *J*=2.6 Hz), and 1.81 (2H, qui, *J*=6.3 Hz); IR (neat), 3592, 3296, 3000, 2952, 2856, 1614, 1588, 1516, 1446, 1366,1302, 1248, 1210, 1174, 1104, 1036, and 820 cm^{-1}; HR-EI-MS, Calcd for $C_{13}H_{16}O_2$ (M^+), 204.1151, found 204.1147.

8-(4-Methoxybenzyloxy)-4-octyn-1-ol (14). To a solution of acetylenic compound **13** (6.62 g, 32.4 mmol) in THF (50 mL) was added BuLi (20.5 mL of a 1.66M solution in hexane, 34.0 mmol) at 0 °C, and then the solution was stirred at 0 °C for 30 min. To this solution was added HMPA (34 mL) at 0 °C, and the mixture was stirred at 0 °C for 20 min. To this solution was added a solution of bromide **19** (7.18 g, 34.0 mmol) in THF (18 mL) at 0 °C. The mixture was allowed to warm to 25 °C, stirred at the same temperature for 15 h, and then diluted with EtOAc (1 L). The organic layer was washed with water (3×100 mL) and brine (2×100 mL), and dried over $MgSO_4$. The solvent was concentrated *in vacuo* to give the crude product, which was dissolved in THF (50 mL). To this solution was added aq. 0.5M HCl (40 mL) at 0 °C and the reaction mixture was stirred at 25 °C for 1.5 h, and brought to about pH 6 by addition of satd aq. $NaHCO_3$. The aq. layer was extracted with EtOAc (4×150 mL). The combined organic layers were washed with satd aq. $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 5:1) to give **14** (3.03 g, 94%). **14**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.26 (2H, d, *J*=8.6 Hz), 6.88 (2H, d, *J*=8.6 Hz), 4.44 (2H, s), 3.81 (3H, s), 3.73 (2H, t, *J*=6.6 Hz), 3.52 (2H, t, *J*=6.6 Hz), 2.26 (4H, t, *J*=6.6 Hz), and 1.67-1.81 (4H, m); IR (neat), 3432, 2944, 2864, 1656, 1614, 1588, 1516, 1464, 1442, 1366, 1302, 1248, 1176, 1102, 1074, 1036, and 818 cm^{-1}; HR-EI-MS, Calcd for $C_{13}H_{22}O_3$ (M^+), 262.1570, found 262.1545.

(4*E*)-1-(*tert*-Butyldiphenylsilyloxy)-8-(4-methoxybenzyloxy)-4-octene (15). To a suspension of $LiAlH_4$ (0.810 g, 21.3 mmol) in diglyme (26 mL) was added a solution of alcohol **14** (3.73 g, 14.2 mmol) in THF (6 mL) dropwise at 0 °C and the mixture was stirred at 140 °C for 15 h. After addition of Et_2O (30 mL) at 0 °C, the reaction was quenched by adding aq. 1M HCl dropwise at 0 °C. The organic layer was washed with aq. 1M HCl, satd aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo*. Column chromatography (SiO_2, hexane-EtOAc, 5:1) gave the mixture of olefinic alcohol and diglyme, which was dissolved in DMF (50 mL). To the solution were added imidazole (2.21 g, 32.5 mmol) and *tert*-butyldiphenylsilyl chloride (3.56 mL, 13.7 mmol) at 0 °C and the mixture was stirred at 25 °C for 18 h, diluted with EtOAc (1 L), washed with water (4×100 mL) and brine (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 100:1) to afford silyl ether **15**

(5.91 g, 83%). **15**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.66 (4H, dd, *J*=2.0, 7.6 Hz), 7.35-7.41 (6H, m), 7.25 (2H, d, *J*=8.6 Hz), 6.87 (2H, d, *J*=8.6 Hz), 5.33-5.40 (2H, m), 4.41 (2H, s), 3.80 (3H, s), 3.65 (2H, t, *J*=6.6 Hz), 3.42 (2H, t, *J*=6.6 Hz), 1.98-2.11 (4H, m), 1.51-1.69 (4H, m), and 1.04 (9H, s); IR (neat), 3072, 3048, 3000, 2936, 2856, 1614, 1516, 1466, 1446, 1430, 1362, 1302, 1248, 1174, 1112, 1038, 970, 824, 756, 740, 702, 688, and 614 cm^{-1}; HR-FAB-MS, Calcd for $C_{32}H_{43}O_3Si$ (M^++H), 503.2983, found 503.2989.

(4*E*)-8-(*tert*-Butyldiphenylsilyloxy)-4-octen-1-ol (16). To a solution of 4-methoxybenzyl ether **15** (573 mg, 1.14 mmol) in CH_2Cl_2 (50 mL) and H_2O (5 mL) was added dichlorodicyanobenzoquinone (388 mg, 1.71 mmol) at 0 °C and the solution was stirred at 25 °C for 2 h, and then satd aq. $NaHCO_3$ was added at 0 °C. The organic layer was separated, diluted with Et_2O (200 mL), washed with water (2×50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 30:1) to give alcohol **16** (410 mg, 94%). **16**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.66 (4H, dd, *J*=2.0, 7.6 Hz), 7.35-7.45 (6H, m), 5.39-5.43 (2H, m), 3.65 (2H, t, *J*=6.3 Hz), 3.62 (2H, t, *J*=6.6 Hz), 2.01-2.12 (4H, m), 1.56-1.66 (4H, m), and 1.04 (9H, s); IR (neat), 3592, 3364, 3072, 2936, 2860, 2316, 1826, 1590, 1474, 1430, 1392, 1362, 1112, 1008, 970, 824, 738, 702, 688, 612, and 434 cm^{-1}; HR-FAB-MS, Calcd for $C_{24}H_{33}O_2Si$ (M^+-H), 381.2251, found 381.2246.

(4*E*)-1-Bromo-8-(*tert*-butyldiphenylsilyloxy)-4-octene (17). To a solution of alcohol **16** (53.0 mg, 0.139 mmol) in CH_2Cl_2 (1.5 mL) were added triphenylphosphine (Ph_3P) (43.8 mg, 0.167 mmol) and carbon tetrabromide (CBr_4) (92.2 mg, 0.278 mmol) at 25 °C. To the mixture stirred at 25 °C for 5 min, was added satd aq. $NaHCO_3$ at 25 °C. The mixture was extracted with Et_2O (40 mL) and the Et_2O layer was washed with water (2×10 mL) and brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 30:1) to give bromide **17** (60.9 mg, 98%). **17**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.66 (4H, dd, *J*=1.7, 7.3 Hz), 7.33-7.44 (6H, m), 5.28-5.49 (2H, m), 3.65 (2H, t, *J*=6.6 Hz), 3.37 (2H, t, *J*=6.6 Hz), 2.10 (4H, m), 1.81-1.92 (2H, m), 1.57-1.66 (2H, m), and 1.05 (9H, s); IR (neat), 3072, 3048, 2936, 2856, 2360, 1844, 1700, 1590, 1474, 1430, 1392, 1246, 1112, 1008, 998, 970, 824, 738, 702, and 688 cm^{-1}; HR-FAB-MS, Calcd for $C_{24}H_{34}O^{79}BrSi$ (M^++H), 445.1563, found 445.1541.

(4*R,5*R**)-1-Bromo-8-(*tert*-butyldiphenylsilyloxy)-4,5-epoxyoctane (18).** To a solution of bromide **17** (23.9 mg, 0.0536 mmol) in CH_2Cl_2 (1.5 mL) cooled to 0 °C were added disodium hydrogen phosphate (Na_2HPO_4) (38.0 mg, 0.0268 mmol) and *m*-chloroperbenzoic acid (33.0 mg, 0.0134 mmol), and the mixture was stirred at 0 °C for 5 min. The solution was warmed to 25 °C, and stirred for 1 h. To the reaction mixture was added satd aq. sodium thiosulfate ($Na_2S_2O_3$) (3 mL) at 0 °C and the mixture was extracted with EtOAc (40 mL). The EtOAc layer was washed with satd aq. $Na_2S_2O_3$ (10 mL), satd aq. $NaHCO_3$ (2×10 mL) and brine (2×10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc 5:1) to give epoxide **18** (24.5 mg, 99%). **18**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.65 (4H, dd, *J*=2.0, 7.6 Hz), 7.35-7.45 (6H, m), 3.64-3.72 (2H, m), 3.38-3.52 (2H, m), 2.64-2.71 (2H, m), 1.92-2.05 (2H, m), 1.48-1.82 (6H, m), and 1.05 (9H, s); IR (neat), 3072, 2936, 2860, 2308, 1590, 1474, 1430, 1392, 1362, 1254, 1206, 1112, 970, 938, 896, 824, 740, 704, and 688 cm^{-1}; HR-FAB-MS, Calcd for $C_{24}H_{34}O_2{}^{79}BrSi$ (M^++H), 461.1512, found 461.1484.

1-Bromo-3-(oxan-2-yl)propane (19). To a solution of 3-bromo-1-propanol (10.2 g, 73.3 mmol) in CH_2Cl_2 (39 mL) cooled to 0 °C were added 2,3-dihydropyran (8.03 mL, 88.0 mmol) and *p*-toluenesulfonic

acid monohydrate (69.8 mg, 0.367 mmol) and the mixture was stirred at 25 °C for 2 h, washed with satd aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by distillation (bp 90-93 °C, 3 mmHg) to give **19** (13.3 g, 82%). **19**: a colorless oil; ^{1}H-NMR (270 MHz, C_6D_6), δ4.50 (1H, t, *J*=3.3 Hz), 3.80 (1H, dt, *J*=15.8, 5.9 Hz), 3.75 (1H, dt, *J*=15.8, 3.3 Hz), 3.35-3.43 (1H, m), 3.30 (1H, dt, *J*=9.9, 5.9 Hz), 3.18-3.26 (2H, m), 1.77-1.86 (2H, m), 1.64-1.73 (1H, m), 1.51-1.57 (2H, m), and 1.20-1.43 (3H, m); IR (neat), 2948, 2872, 1444, 1354, 1324, 1286, 1260, 1202, 1184, 1134, 1120, 1076, 1034, 986, 870, and 814 cm^{-1}; HR-EI-MS, Calcd for $C_8H_{14}O_2{}^{79}Br$ (M^+), 221.0177, found 221.0175.

(2*R,3*S**)-3-Acetoxy-2-[3-(*tert*-butyldiphenylsilyloxy)propyl]oxane (23) and (2*R**,1'*S*'*)-2-[1'-Acetoxy-4'-(*tert*-butyldiphenylsilyloxy)butyl]oxolane (24). General Procedure.** To a solution of epoxide **18** (36.6 mg, 0.0793 mmol) in THF/H_2O (1.2 mL, 5:1) was added silver triflate (AgOTf) (30.6 mg, 0.119 mmol) at three times every 2 h at 25 °C. After stirred for 6.5 h from the first addition of AgOTf, the reaction mixture was poured into satd aq. $NaHCO_3$ (10 mL) at 25 °C and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. PTLC (SiO_2, hexane-EtOAc, 2:1) gave a mixture of oxane derivative **21** and oxolane derivative **22** (29.4 mg). To a solution of the mixture in pyridine (0.50 mL) were added acetic anhydride (Ac_2O) (0.25 mL) at 25 °C and the mixture was allowed to stand for 13 h at 25 °C and the volatiles were removed *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc 4:1) to give acetates **23** (22.4 mg, 69%) and **24** (5.7 mg, 17%). **23**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.66 (4H, dd, *J*=1.5, 7.7 Hz, PhH), 7.35-7.42 (6H, m, PhH), 4.50 (1H, ddd, *J*=4.8, 9.2, 10.6 Hz, C_3H), 3.88 (1H, ddd, *J*=2.6, 4.4, 11.4 Hz, C_6H), 3.61-3.71 (2H, m, C_3·H), 3.30 (1H, dt, *J*=2.9, 11.4 Hz, C_6H), 3.21 (1H, dt, *J*=2.6, 9.2 Hz, C_2H), 2.12-2.18 (1H, m, C_4H), 2.01 (3H, s, CH_3CO), 1.54-1.80 (5H, m, C_5H, C_1·H, C_2·H), 1.35-1.47 (2H, m, C_4H, C_1·H), and 1.04 (9H, s, $C(CH_3)_3$); IR (neat), 3072, 3048, 2956, 2856, 2728, 1738, 1590, 1472, 1466, 1448, 1430, 1374, 1308, 1242, 1188, 1112, 1038, 998, 984, 944, 914, 874, 824, 790, 742, 726, 704, 686, and 614 cm^{-1}; HR-FAB-MS, Calcd for $C_{26}H_{37}O_4Si$ (M^++H), 441.2462, found 441.2441. **24**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.65 (4H, dd, *J*=1.5, 7.7 Hz), 7.37-7.42 (6H, m), 4.94-4.98 (1H, m), 3.89-3.93 (1H, m), 3.82 (1H, dt, *J*=8.1, 6.6 Hz), 3.75 (1H, dt, *J*=8.1, 6.2 Hz), 3.67 (1H, dt, *J*=16.1, 6.2 Hz), 3.65 (1H, dt, *J*=16.1, 5.9 Hz), 1.81-1.97 (3H, m), 1.49-1.79 (5H, m), and 1.04 (9H,s); IR (neat), 3072, 3052, 2960, 2936, 2860, 2368, 1966, 1902, 1742, 1590, 1472, 1464, 1450, 1430, 1372, 1240, 1188, 1110, 1076, 1024, 976, 942, 824, 796, 740, 704, 688, and 612 cm^{-1}; HR-FAB-MS, Calcd for $C_{26}H_{37}O_4Si$ (M^++H), 441.2462, found 441.2432.

(4*R,5*R**)-1-(*tert*-Butyldiphenylsilyloxy)-8-(4-methoxybenzyloxy)-4,5-epoxyoctane (27).** To a solution of olefin **15** (34.4 mg, 0.0684 mmol) in CH_2Cl_2 (1 mL) was added *m*-chloroperbenzoic acid (23.6 mg, 0.137 mmol) at 25 °C and the solution was stirred at 25 °C for 45 min, poured into satd aq. $Na_2S_2O_3$ (10 mL), and extracted with Et_2O (40 mL). The Et_2O layer was washed with aq. 1M KOH (2×10 mL) and brine (2×10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc, 5:1) to give epoxide **27** (32.8 mg, 92%). **27**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.65 (4H, dd, *J*=1.7, 7.3 Hz), 7.33-7.45 (6H, m), 7.25 (2H, d, *J*=8.6 Hz), 6.87 (2H, d, *J*=8.6 Hz), 4.43 (2H, s), 3.79 (3H, s), 3.66-3.70 (2H, m), 3.40-3.53 (2H, m), 2.62-2.68 (2H, m), 1.52-1.78 (8H, m), and 1.04 (9H, s); IR (neat), 3072, 2940, 2860, 1616, 1588, 1516, 1474, 1430, 1392, 1362, 1302, 1250,

1208, 1174, 1112, 1036, 1008, 938, 904, 824, 740, 704, 688, and 612 cm^{-1}; HR-FD-MS, Calcd for $C_{32}H_{42}O_4Si$ (M^+), 518.2854, found 518.2803.

(4*S,5*R**)-1-(*tert*-Butyldiphenylsilyloxy)-8-(4-methoxybenzyloxy)octane-4,5-diol (28).** To a solution of epoxide **27** (14.4 mg, 0.0278 mmol) in THF/H_2O (0.93 mL, 5:1) was added trifluoromethanesulfonic acid (TfOH) (2.5 μL, 0.028 mmol) at 25 °C and the solution was stirred at 25 °C for 6.5 h, poured into satd aq. $NaHCO_3$ (10 mL), and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc, 4:1) to give diol **28** (0.8 mg, 5%). **28**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.65-7.68 (4H, m), 7.35-7.45 (6H, m), 7.25 (2H, d, *J*=8.6 Hz), 6.87 (2H, d, *J*=8.6 Hz), 4.66 (2H, s), 3.80 (3H, s), 3.68-3.72 (2H, m), 3.46-3.62 (4H, m), 1.43-1.80 (8H, m), and 1.05 (9H, s); IR (neat), 3436, 3072, 2936, 2860, 1616, 1590, 1516, 1466, 1430, 1392, 1362, 1304, 1250, 1176, 1114, 1038, 824, 742, and 704 cm^{-1}; HR-FD-MS, Calcd for $C_{32}H_{44}O_5Si$ (M^+), 536.2959, found 536.2909.

(4*Z*)-8-(4-Methoxybenzyloxy)-4-octen-1-ol (29). To a solution of the acetylenic compound **14** (1.48 g, 5.65 mmol) in MeOH (32 mL) were added Pd/$CaCO_3$ (0.15 g) and quinoline (0.21 mL) at 25 °C and the mixture was stirred at 25 °C for 4 h under hydrogen atmosphere and filtered through Celite. The filtrate was concentrated *in vacuo* to give olefin **29** (1.45 g, 97%). **29**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.26 (2H, d, *J*=8.6 Hz), 6.88 (2H, d, *J*=8.6 Hz), 5.39 (2H, t, *J*=4.9 Hz), 4.43 (2H, s), 3.81 (3H, s), 3.63 (2H, t, *J*=6.3 Hz), 3.45 (2H, t, *J*=6.6 Hz), 2.10-2.18 (4H, m), and 1.57-1.72 (4H, m); IR (neat), 3416, 3004, 2936, 2860, 1616, 1516, 1464, 1302, 1248, 1174, 1100, 1074, 1038, and 820 cm^{-1}; HR-EI-MS, Calcd for $C_{16}H_{24}O_3$ (M^+), 264.1726, found 264.1754.

(4*Z*)-1-(*tert*-Butyldiphenylsilyloxy)-8-(4-methoxybenzyloxy)-4-octene (30). To a solution of alcohol **29** (85.2 mg, 0.323 mmol) in DMF (1.3 mL) cooled to 0 °C were added imidazole (55.0 mg, 0.808 mmol) and *tert*-butyldiphenylsilyl chrolide (0.0882 mL, 0.339 mmol) and the mixture was stirred at 25 °C for 18 h, diluted with Et_2O (40 mL), washed with 1M aq. HCl (10 mL), satd aq. $NaHCO_3$ (10 mL) and water (2×10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 100:1) to afford silyl ether **30** (198.4 mg, 100%). **30**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.66 (4H, dd, *J*=1.7, 7.6 Hz), 7.31-7.41 (6H, m), 7.24 (2H, d, *J*=8.6 Hz), 6.86 (2H, d, *J*=8.6 Hz), 5.35 (2H, t, *J*=5.3 Hz), 4.40 (2H, s), 3.79 (3H, s), 3.66 (2H, t, *J*=6.6 Hz), 3.42 (2H, *J*=6.6 Hz), 2.02-2.15 (4H, m), 1.51-1.70 (4H, m), and 1.04 (9H, s); IR (neat), 3072, 3008, 2936, 2860, 1616, 1516, 1466, 1430, 1248, 1174, 1112, 1038, 824, 740, 704, 686, and 614 cm^{-1}; HR-FAB-MS, Calcd for $C_{32}H_{43}O_3Si$ (M^++H), 503.2983, found 503.2992.

(4*Z*)-8-(*tert*-Butyldiphenylsilyloxy)-4-octen-1-ol (31). To a solution of 4-methoxybenzyl ether **30** (72.8 mg, 0.145 mmol) in CH_2Cl_2 (5 mL) and H_2O (0.5 mL) cooled to 0 °C was added dichlorodicyanobenzoquinone (49.5 mg, 0.218 mmol) and the solution was stirred at 25 °C for 1 h, diluted with Et_2O (40 mL), washed with satd aq. $NaHCO_3$ (4×10 mL) and brine (2×10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 30:1) to give alcohol **31** (49.1 mg, 88%). **31**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.66 (4H, dd, *J*=2.3, 7.9 Hz), 7.35-7.42 (6H, m), 5.38 (2H, t, *J*=4.9 Hz), 3.67 (2H, t, *J*=6.3 Hz), 3.62 (2H, t, *J*=6.3 Hz), 2.10 (4H, m), 1.60 (4H, m), and 1.05; IR (neat), 3352, 3072, 3052, 3008, 2936, 1474, 1430, 1392, 1112, 1066, 824, 738, 702, 688, and 614 cm-1; HR-FAB-MS, Calcd for $C_{24}H_{35}O_2Si$ (M^++H), 383.2408, found 383.2416.

(4*Z*)-1-Bromo-8-(*tert*-butyldiphenylsilyloxy)-4-octene (32). To a solution of alcohol **31** (47.6 mg, 0.124 mmol) in CH_2Cl_2 (1.5 mL) were added Ph_3P (39.1 mg, 0.149 mmol) and CBr_4 (61.7 mg, 0.186 mmol) at 25 °C and the mixture was stirred at 25 °C for 5 min, diluted with Et_2O (40 mL), washed with satd aq. $NaHCO_3$ (10 mL) and brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 30:1) to give bromide **32** (55.2 mg, 98%). **32**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.67 (4H, dd, *J*=1.7, 7.3 Hz), 7.33-7.42 (6H, m), 5.25-5.49 (2H, m), 3.67 (2H, t, *J*=6.3 Hz), 3.38 (2H, t, *J*=6.6 Hz), 2.17 (4H, qui, *J*=7.9 Hz), 1.84-1.94 (2H, m), 1.55-1.63 (2H, m), and 1.05 (9H, s); IR (neat), 3072, 3052, 3008, 2936, 2860, 1474, 1430, 1112, 824, 740, 702, 688, and 614 cm^{-1}; HR-FAB-MS, Calcd for $C_{24}H_{34}O^{79}BrSi$ (M^++H), 445.1563, found 445.1552.

(4*R,5*S**)-1-Bromo-8-(*tert*-butyldiphenylsilyloxy)octane-4,5-diol (26).** To a solution of olefin **32** (29.4 mg, 0.0660 mmol) in dioxane/H_2O (1.3 ml, 10:3) were added *N*-methylmorpholine-*N*-oxide (9.7 mg, 0.083 mmol) and osmium tetroxide (OsO_4) (0.34 mL of 19.7mM solution in *tert*-BuOH) at 25 °C and the mixture was stirred at 25 °C for 3 h. Satd aq. $Na_2S_2O_3$ (4 mL) was then added and the mixture was extracted with EtOAc (40 mL). The EtOAc layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc 3:2) to give diol **26** (28.7 mg, 91%). **26**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.67 (4H, dd, *J*=1.6, 7.3 Hz), 7.36-7.46 (6H, m), 3.69-3.74 (2H, m), 3.60-3.67 (2H, m), 3.45-3.51 (2H, m), 2.08 (1H, m), 1.85 (1H, m), 1.50-1.80 (6H, m), and 1.06 (9H, s); IR (neat), 3416, 3072, 3052, 2936, 2896, 2860, 1740, 1474, 1430, 1392, 1362, 1248, 1192, 1112, 1008, 938, 824, 800, 742, 702, 688, and 614 cm^{-1}; HR-FAB-MS, Calcd for $C_{24}H_{36}O_3{}^{79}BrSi$ (M^++H), 479.1618, found 479.1588.

Conversion of 26 into 22. To a solution of **26** (12.1 mg, 0.0252 mmol) in THF/H_2O (1.2 mL, 5:1) was added AgOTf (19.4 mg, 0.0756 mmol) at 25 °C and the solution was stirred at 25 °C for 45 min, and poured into satd aq. $NaHCO_3$ (10 mL) at 25 °C. The mixture was extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc 2:1) to give **22** (10.0 mg, 100%).

Conversion of 18 into 33. To a solution of **18** (29.9 mg, 0.0648 mmol) in CH_2Cl_2 (2.2 mL) was added AgOTf (20.0 mg, 0.0778 mmol) at 25 °C and the solution was stirred at 25 °C for 80 min, and then poured into satd aq. $NaHCO_3$ (10 mL). The mixture was extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc 3:1) to give **33** (5.2 mg, 56%). **33**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ3.84-3.90 (2H, m), 3.81 (2H, ddd, *J*=1.8, 5.1, 7.0 Hz), 3.73-3.78 (2H, m), 1.94-2.03 (2H, m), 1.82-1.93 (4H, m), and 1.68-1.78 (2H, m); IR (neat), 2972, 2868, 1464, 1344, 1288, 1262, 1182, 1068, 968, 910, and 802 cm^{-1}; HR-EI-MS, Calcd for $C_8H_{14}O_2$ (M^+), 142.0994, found 142.1005.

6-(4-Methoxybenzyloxy)-2-hexyn-1-ol (34). To a solution of acetylenic compound **13** (2.55 g, 12.5 mmol) in THF (24 mL) cooled to -78 °C was added dropwise butyllithium (BuLi) (8.17 mL of a 1.69M solution in hexane, 13.8 mmol) and the mixture was stirred at -78 °C for 1 h. Paraformaldehyde [$(CH_2O)_n$] (414 mg, 13.8 mmol) was then added and the solution was stirred at 25 °C for 2 h. After addition of ice chips and satd aq. $NaHCO_3$ (30 mL), the mixture was extracted with EtOAc (4×30 mL). The combined EtOAc layers were washed with brine (2×20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc 4:1) to give hydroxy acetylene compound **34** (2.91 g, 100%). **34**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.26 (2H, d, *J*=8.6 Hz), 6.88 (2H, d, *J*=8.6 Hz), 4.40

(2H, s), 4.22 (2H, t, *J*=2.0 Hz), 3.81 (3H, s), 3.53 (2H, t, *J*=6.9 Hz), 2.33 (2H, tt, *J*=2.0, 6.9 Hz), and 1.79 (2H, qui, *J*=6.9 Hz); IR (neat), 3428, 3004, 2936, 2864, 1614, 1588, 1516, 1466, 1446, 1366, 1302, 1248, 1176, 1136, 1100, 1078, 1034, and 822 cm^{-1}; HR-EI-MS, Calcd for $C_{14}H_{18}O_3$ (M^+), 234.1256, found 234.1227.

(2*E*)-1-(*tert*-Butyldiphenylsilyloxy)-6-(4-methoxybenzyloxy)-2-hexene (35). To a suspension of $LiAlH_4$ (0.318 g, 8.37 mmol) in THF (10 mL) was added dropwise a solution of hydroxy acetylene compound **34** (1.31 g, 5.58 mmol) in THF (6 mL) at 0 °C and the mixture was stirred at 25 °C for 17 h. After the addition of Et_2O (20 mL), the reaction was quenched with aq. 1M HCl (20 mL). The aq. layer was extracted with EtOAc (3×20 mL). The combined organic layers were washed with satd aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. To a solution of the resulting residue in DMF (23 mL) were added imidazole (0.837 mg, 12.3 mmol) and *tert*-butyldiphenylsilyl chloride (1.52 mL, 5.86 mmol) at 0 °C and the mixture was stirred at 25 °C for 17 h, diluted with Et_2O (500 mL), washed with H_2O (4×50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 100:1) to give silyl ether **35** (2.45 g, 92%). **35**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.67 (4H, dd, *J*=1.3, 6.6 Hz), 7.34-7.42 (6H, m), 7.26 (2H, dd, *J*=8.2 Hz), 6.87 (2H, dd, *J*=8.2 Hz), 5.65 (1H, dt, *J*=15.5, 5.9 Hz), 5.54 (1H, dd, *J*=15.5, 4.9 Hz), 4.42 (2H, s), 4.14 (2H, d, *J*=4.9 Hz), 3.79 (3H, s), 3.44 (2H, t, *J*=6.6 Hz), 2.09-2.15 (2H, m), 1.62-1.72 (2H, m), and 1.05 (9H, s); IR (neat), 3072, 3048, 2936, 2856, 1614, 1516, 1466, 1430, 1362, 1302, 1248, 1174, 1112, 1040, 1010, 1000, 972, 822, 740, 704, 690, and 608 cm^{-1}; HR-FD-MS, Calcd for $C_{30}H_{38}O_3Si$ (M^+), 474.2591, found 474.2603.

(4*E*)-6-(*tert*-Butyldiphenylsilyloxy)-4-hexen-1-ol (36). To a solution of 4-methoxybenzyl ether **35** (2.41 g, 5.09 mmol) in CH_2Cl_2/H_2O (182 mL, 10:1) was added dichlorodicyanobenzoquinone (1.73 g, 7.64 mmol) at 0 °C and the solution was stirred at 25 °C for 1.5 h. After the addition of satd aq. $NaHCO_3$ (200 mL) at 0 °C, the aqueous layer was extracted with Et_2O (3×180 mL). The combined organic layers were washed with water (4×100 mL) and brine (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc 10:1) to give alcohol **36** (1.33 g, 100%). **36**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.68 (4H, dd, *J*=1.7, 7.3 Hz), 7.37 -7.45 (6H, m), 5.68 (1H, dt, *J*=15.5, 5.9 Hz), 5.57 (1H, dt, *J*=15.5, 4.6 Hz), 4.16 (2H, d, *J*=4.6 Hz), 3.65 (2H, d, *J*=6.3 Hz), 2.08-2.16 (2H, m), 1.59-1.70 (2H, m), and 1.05 (9H, s); IR (neat), 3340, 3072, 3048, 3020, 2936, 2892, 2856, 2736, 1964, 1890, 1826, 1674, 1590, 1474, 1464, 1450, 1430, 1382, 1362, 1306, 1264, 1188, 1112, 1048, 970, 942, 916, 824, 770, 738, 704, and 612 cm^{-1}; HR-FD-MS, Calcd for $C_{22}H_{31}O_2Si$ (M^++H), 355.2094, found 355.2063.

(2*E*)-6-Bromo-1-(*tert*-butyldiphenylsilyloxy)-2-hexene (37). To a solution of alcohol **36** (736 mg, 2.08 mmol) in CH_2Cl_2 (22 mL) were added Ph_3P (656 mg, 2.50 mmol) and CBr_4 (1.03 g, 3.12 mmol) at 25 °C and the mixture was stirred at 25 °C for 20 min. Satd aq. $NaHCO_3$ (25 mL) was added and the mixture was extracted with hexane (200 mL). The hexane layer was washed with H_2O (3×25 mL) and brine (25 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 100:1) to give bromide **37** (850 mg, 98%). **37**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.67 (4H, dd, *J*=1.7, 6.9 Hz), 7.34 -7.45 (6H, m), 5.57-5.61 (2H, m), 4.16 (2H, broad s), 3.38 (2H, t, *J*=6.9 Hz), 2.14-2.21 (2H, m), 1.86-1.96 (2H, m), and 1.06 (9H, s); IR (neat), 3072, 3048, 3020, 2956,

2936, 2892, 2856, 1590, 1488, 1474, 1464, 1430, 1382, 1362, 1266, 1240, 1188, 1112, 1056, 1008, 1000, 972, 938, 824, 774, 738, 702, and 612 cm^{-1}; HR-FD-MS, Calcd for $C_{22}H_{29}O^{79}BrSi$ (M^+), 416.1172, found 416.1185.

(4*R,5*R**)-1-Bromo-6-(*tert*-butyldiphenylsilyloxy)-4,5-epoxyhexane (38).** To a solution of olefin **37** (830 mg, 1.99 mmol) in CH_2Cl_2 (25 mL) cooled to 0 °C were added Na_2HPO_4 (1.41 g, 9.95 mmol) and *m*-chloroperbezoic acid (859 mg, 4.98 mmol) and the solution was stirred at 25 °C for 2 h, and satd aq. $Na_2S_2O_3$ (30 mL) was added at 0 °C. The mixture was extracted with Et_2O (250 mL) and the Et_2O layer was washed with satd aq. $Na_2S_2O_3$ (50 mL), satd aq. $NaHCO_3$ (2×50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 40:1) to give epoxide **38** (863 mg, 100%). **38**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.67 (4H, dd, *J*=1.7, 5.9 Hz), 7.35 -7.48 (6H, m), 3.76 (2H, d, *J*=4.0 Hz), 3.44 (2H, t, *J*=6.6 Hz), 2.91 (1H, dt, *J*=2.3, 4.0 Hz), 2.79 (1H, ddd, *J*=2.3, 4.9, 6.9 Hz), 1.90-2.02 (2H, m), 1.71-1.83 (1H, m), 1.58-1.68 (1H, m), and 1.05 (9H, s); IR (neat), 3072, 3052, 2960, 2936, 2896, 2860, 1474, 1430, 1392, 1362, 1282, 1252, 1216, 1192, 1114, 1030, 1008, 1000, 940, 888, 824, 800, 740, 704, 690, and 614 cm^{-1}; HR-FD-MS, Calcd for $C_{22}H_{30}O_2{}^{79}BrSi$ (M^++H), 433.1199, found 433.1150.

(2*R,3*S**)-3-Acetoxy-2-[(*tert*-butyldiphenylsilyloxy)methyl]oxane (43) and (2*R**,1'*S**)-2-[1'-Acetoxy-2'-(*tert*-butyldiphenylsilyloxy)ethyl]oxolane (44).** To a solution of bromo epoxide **38** (222 mg, 0.512 mmol) in THF/H_2O (8.7 mL, 5:1) was added AgOTf (197 mg, 0.768 mmol) at 25 °C. After 1, 3.5, 4, 4.5, 5, and 5.5 h, the respective portions of AgOTf (each 197 mg, 0.768 mmol) were added with stirring. After 30 min from the last addition of AgOTf, the reaction mixture was poured into satd aq. $NaHCO_3$ (80 mL), and extracted with Et_2O (220 mL). The Et_2O layer was washed with brine (2×40 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 10:1) to give the mixture of **41** and **42** (125 mg, 66%). To a solution of the mixture in CH_2Cl_2 (5 mL) were added pyridine (0.273 mL, 3.37 mmol), Ac_2O (0.159 mL, 1.69 mmol), and 4-dimethylaminopyridine (4.1 mg, 0.034 mmol) at 25 °C and the solution was stirred at 25 °C for 1.5 h, poured into satd aq. NH_4Cl (20 mL), and extracted with Et_2O (100 mL). The Et_2O layer was washed with satd aq. NH_4Cl (4×20 mL), satd aq. $NaHCO_3$ (2×20 mL) and brine (20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 50:1) and PTLC (SiO_2, hexane-EtOAc, 5:1) to give acetates **43** (111 mg, 52% for 2 steps) and **44** (23.4 mg, 11% for 2 steps). **43**: a colorless oil; ^{1}H-NMR (400 MHz, C_6D_6), δ7.91-7.93 (2H, m, PhH), 7.86-7.89 (2H, m, PhH), 7.23-7.30 (6H, m, PhH), 5.11 (1H, dt, *J*=4.8, 9.5 Hz, C_3H), 3.96 (1H, dd, *J*=2.2, 11.0 Hz, C_1·H), 3.90 (1H, dd, *J*=4.4, 11.0 Hz, C_1·H), 3.72 (1H, ddt, *J*=4.4, 11.7, 1.5 Hz, C_6H), 3.30 (1H, ddd, *J*=2.2, 4.4, 9.5 Hz, C_2H), 3.03 (1H, dt, *J*=2.2, 11.7 Hz, C_6H), 2.15-2.22 (1H, m, C_4H), 1.67 (3H, s, CH_3CO), 1.41-1.53 (1H, m, C_5H), 1.25 (9H, s, $C(CH_3)_3$), 1.20-1.29 (1H, m, C_4H), and 1.09-1.18 (1H, m, C_5H); IR (neat), 3072, 3052, 2936, 2856, 2728, 1746, 1590, 1474, 1466, 1430, 1374, 1336, 1310, 1240, 1192, 1160, 1136, 1112, 1074, 1040, 1000, 958, 938, 896, 864, 824, 784, 742, 704, 666, 648, and 608 cm^{-1}; HR-FD-MS, Calcd for $C_{24}H_{33}O_4Si$ (M^++H), 413.2149, found 413.2106. **44**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.66 (4H, dd, *J*=1.7, 8.1 Hz), 7.35-7.45 (6H, m), 5.05 (1H, q, *J*=5.0 Hz), 4.06 (1H, q, *J*=6.4 Hz), 3.83 (1H, dd, *J*=5.0, 16.3 Hz), 3.80 (1H, dd, *J*=5.0, 16.3 Hz), 3.69-3.79 (2H, m), 2.05 (3H, s), 1.79-1.95 (3H, m), 1.69-1.77 (1H, m), and 1.04 (9H, s); IR (neat), 3072, 3048, 2936, 2860, 1748, 1474, 1466, 1430, 1392, 1372,

1234, 1190, 1114, 1074, 1060, 1030, 944, 824, 794, 740, 704, and 612 cm^{-1}; HR-FD-MS, Calcd for $C_{24}H_{33}O_4Si$ (M^+-*tert*-Bu), 355.1366, found 355.1410.

(2*R,3*S**)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-3-hydroxyoxane (42).** To a solution of acetate **43** (111 mg, 0.268 mmol) in MeOH (5.2 mL) was added K_2CO_3 (63.0 mg, 0.456 mmol) at 25 °C and the mixture was stirred at 25 °C for 1.5 h, poured into brine (10 mL), and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (2×10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 10:1) to give alcohol **42** (93.3 mg, 94%). **42**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.68 (4H, dd, *J*=1.7, 7.6 Hz), 7.36-7.48 (6H, m), 3.89 (1H, dd, *J*=4.6, 10.2 Hz), 3.84 (1H, ddt, *J*=4.0, 11.2, 2.0 Hz), 3.76 (1H, dd, *J*=7.6, 10.2 Hz), 3.66 (1H, dt, *J*=4.6, 9.6 Hz), 3.19-3.35 (2H, m), 2.13-2.18 (1H, m), 1.59-1.70 (2H, m), 1.37-1.52 (1H, m), and 1.07 (9H, s); IR (neat), 3463, 3136, 3072, 3052, 2936, 2856, 2728, 1590, 1474, 1464, 1430, 1392, 1378, 1362, 1328, 1284, 1264, 1214, 1188, 1148, 1112, 1008, 996, 950, 866, 824, 788, 742, 702, 652, and 608 cm^{-1}; HR-FD-MS, Calcd for $C_{22}H_{31}O_3Si$ (M^++H), 371.2043, found 371.2050.

(1*S,2'*R**)-2-(*tert*-Butyldiphenylsilyloxy)-1-(oxolan-2'-yl)ethanol (41).** To a solution of **36** (272 mg, 0.766 mmol) in CH_2Cl_2 (9.5 mL) was added *m*-chloroperbenzoic acid (331 mg, 1.92 mmol) at 25 °C and the mixture was stirred at 25 °C for 30 min. To the solution was added satd aq. $Na_2S_2O_3$ (10 mL) at 25 °C and the mixture was extracted with EtOAc (90 mL). The EtOAc layer was washed with aq. 1M KOH (2×10 mL) and brine (2×10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. To a solution of the residue in CH_2Cl_2 (7.5 mL) was added *p*-toluenesulfonic acid monohydrate (13.0 mg, 0.0683 mmol) at 25 °C and the mixture was stirred at 25 °C for 1 h. Et_3N (47.7 μL, 0.342 mmol) was then added and the mixture was concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 20:1) to give **41** (282 mg, 99%). **41**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.65-7.68 (4H, m), 7.36-7.46 (6H, m), 3.67-3.88 (6H, m), 1.82-1.95 (4H, m), and 1.07 (9H, s); IR (neat), 3440, 3072, 3048, 2936, 2860, 1590, 1568, 1556, 1474, 1430, 1394, 1362, 1310, 1188, 1114, 1066, 936, 824, 740, 702, and 610 cm^{-1}; HR-FD-MS, Calcd for $C_{22}H_{31}O_3Si$ (M^++H), 371.2043, found 371.2082.

(2*R,3*S**)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-3-trifluoromethanesulfonyloxyoxane (39).** To a solution of alcohol **42** (36.7 mg, 0.0990 mmol) in CH_2Cl_2 (2.0 mL) cooled to -10 °C were added pyridine (0.0176 mL, 0.218 mmol) and trifluoromethanesulfonic anhydride (Tf_2O) (0.0333 mL, 0.198 mmol) and the solution was stirred at -10 °C for 30 min, poured into satd aq. $NaHCO_3$ (10 mL) at 0 °C, and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 15:1) to give the mixture of **39** and **40** (38.4 mg, **39**:**40** = 16:1, 77%). **39**: a colorless oil; ^{1}H-NMR (400 MHz, C_6D_6), δ7.87-7.90 (4H, m, PhH), 7.19-7.31 (6H, m, PhH), 5.13 (1H, dt, *J*=5.5, 9.2 Hz, C_3H), 3.81 (1H, dd, *J*=2.4, 11.5 Hz, C_1-H), 3.77 (1H, dd, *J*=2.4, 11.5 Hz, C_1-H), 3.38 (1H, ddt, *J*=4.2, 11.5, 1.8 Hz, C_6H), 2.86 (1H, dt, *J*=9.2, 2.4 Hz, C_2H), 2.65 (1H, dt, *J*=2.4, 11.5 Hz, C_6H), 1.91-2.00 (1H, m, C_4H), 1.21 (9H, s, $C(CH_3)_3$), 1.01-1.20 (1H, m, C_4H, C_5H), and 0.83-0.89 (1H, m, C_5H); IR (neat), 3072, 3052, 3020, 2960, 2936, 2860, 1474, 1466, 1444, 1430, 1414, 1364, 1334, 1314, 1266, 1246, 1212, 1148, 1112, 1072, 1030, 998, 950, 922, 890, 862, 834, 824, 778, 740, 704, 654, and 620 cm^{-1}; HR-FD-MS, Calcd for $C_{19}H_{20}O_5F_3SSi$ (M^+-*tert*-Bu), 445.0753, found 445.0789.

Conversion of 38 into 39 and 40. To a solution of **38** (30.6 mg, 0.0706 mmol) in CH_2Cl_2 (2.4 mL) was added AgOTf (21.8 mg, 0.0847 mmol) at 25 °C and the solution was stirred at 25 °C for 30 min,

poured into satd aq. $NaHCO_3$ (10 mL) at 25 °C. The mixture was extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo* to give the mixture of **39** and **40** (34.6 mg, 83%, **39**:**40** = 9.8:1).

(4*R,5*S**)-1-Bromo-8-(*tert*-butyldiphenylsilyloxy)-4,5-epoxyoctane (45).** To a solution of bromide **32** (944 mg, 2.12 mmol) in CH_2Cl_2 (25 mL) cooled to 0 °C were added Na_2HPO_4 (1.50 g, 10.6 mmol) and *m*-chloroperbenzoic acid (915 mg, 5.30 mmol), and the mixture was stirred at 0 °C for 7 min. The solution was warmed to 25 °C, and stirred for 30 min. To the reaction mixture cooled to 0 °C were added satd aq. $Na_2S_2O_3$ (10 mL) and satd aq. $NaHCO_3$ (10 mL) and the mixture was extracted with Et_2O (180 mL). The Et_2O layer was washed with satd aq. $NaHCO_3$ (3×20 mL) and brine (20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc 60:1) to give epoxide **45** (677 mg, 69%). **45**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.66 (4H, dd, *J*=2.0, 7.6 Hz), 7.35-7.45 (6H, m), 3.68-3.78 (2H, m), 3.39-3.42 (2H, m), 2.89-2.96 (2H, m), 1.92-2.17 (2H, m), 1.55-1.81 (6H, m), and 1.05 (9H, s); IR (neat), 3136, 3072, 3052, 2960, 2860, 2744, 2712, 1964, 1890, 1828, 1590, 1474, 1464, 1430, 1392, 1362, 1304, 1252, 1206, 1192, 1112, 1030, 1008, 1000, 968, 940, 824, 776, 740, 702, 688, and 614 cm^{-1}; HR-FAB-MS, Calcd for $C_{24}H_{34}O_2{}^{79}BrSi$ (M^++H), 461.1512, found 461.1509.

(1*R,2'*R**)-4-(*tert*-Butyldiphenylsilyloxy)-1-(oxolan-2'-yl)butan-1-ol (46).** To a solution of bromo epoxide **45** (15.7 mg, 0.0340 mmol) in THF/H_2O (1.2 mL, 5:1) was AgOTf (13.1 mg, 0.0510 mmol) at 25 °C at three times every 2 h. After stirred for 19 h from the first addition of AgOTf, the reaction mixture was poured into satd aq. $NaHCO_3$ (10 mL) at 25 °C and the mixture was extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc 2:1) to give **46** (28.7 mg, 91%). **46**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.66 (4H, dd, *J*=1.7, 7.3 Hz), 7.33-7.46 (6H, m), 3.67-3.88 (5H, m), 3.37-3.47 (1H, m), 1.37-1.99 (8H, m), and 1.04 (9H, s); IR (neat), 3472, 3072, 3052, 2936, 2860, 1590, 1474, 1450, 1430, 1392, 1362, 1264, 1188, 1112, 1008, 940, 824, 800, 740, 702, 688, and 612 cm^{-1}; HR-FD-MS, Calcd for $C_{24}H_{35}O_3Si$ (M^++H), 399.2357, found 399.2376.

The acetate of 46; (2*R,1'*R**)-2-(1'-Acetoxy-4'-*tert*-butyldiphenylsilyloxybutyl)-oxolane.** To a solution of alcohol **46** (7.3 mg, 0.0184 mmol) in pyridine (0.2 mL) was added Ac_2O (0.1 mL) at 25 °C and the mixture was allowed to stand at 25 °C for 12 h, and then the volatiles were removed *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc 4:1) to give the acetate of **46** (7.5 mg, 92%). The acetate of **46**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.65 (4H, dd, *J*=1.3, 7.5 Hz, PhH), 7.35-7.44 (6H, m, PhH), 4.90 (1H, ddd, *J*=3.9, 5.7, 9.7 Hz, C_1-H), 3.87-3.91 (1H, m, C_2H), 3.81-3.86 (1H, m, C_5H), 3.73-3.78 (1H, m, C_5H), 3.66 (2H, dt, *J*=1.8, 6.8 Hz, C_4-H), 2.07 (3H, s, CH_3CO), 1.80-1.96 (3H, m, C_4H, C_3H), 1.70 (1H, m, C_2-H), 1.51-1.67 (4H, m, C_3H, C_2-H, C_3-H), and 1.04 (9H, s, $C(CH_3)_3$); IR (neat) 3072, 3052, 3020, 2956, 2860, 1740, 1474, 1464, 1448, 1430, 1392, 1372, 1244, 1190, 1112, 1050, 1022, 976, 938, 824, 740, 704, 688, and 614 cm^{-1}; HR-FD-MS, Calcd for $C_{26}H_{37}O_4Si$ (M^++H) 441.2462, found 441.2487.

Conversion of 46 into 24. To a solution of alcohol **46** (5.3 mg, 0.013 mmol) in benzene (1 mL) were added Ph_3P (34.9 mg, 0.133 mmol), diethyl azodicarboxylate (0.017 mL, 0.11 mmol), and AcOH (0.0061 mL, 0.11 mmol) at 25 °C. To the solution stirred at 25 °C for 80 min, were added further Ph_3P (34.9 mg, 0.133 mmol), diethyl azocarboxylate (0.017 mL, 0.11 mmol), and acetic acid (AcOH) (0.0061 mL, 0.11 mmol) at 25 °C, and the mixture was stirred at 25 °C for 30 min, poured into satd aq. $NaHCO_3$ (10 mL), and

extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified by PTLC (SiO_2, hexane-EtOAc 2:1) to give acetate **24** (2.0 mg, 34%).

6-(4-Methoxybenzyloxy)-1-hexyne (52). To a suspension of NaH (1.99 g, 49.7 mmol, 60% in oil dispersion) in THF (105 mL) cooled to 0 °C was added a solution of 5-hexyn-1-ol **51** (4.74 g, 48.3 mmol) in THF (20 mL) at 0 °C and the mixture was stirred at 25 °C for 2 h. 4-Methoxybenzyl chloride (6.87 mL, 50.7 mmol) and tetrabutylammonium iodide (1.78 g, 4.83 mmol) were added, and the mixture was stirred at 25 °C for 38 h. To the mixture were added ice chips and satd aq. NH_4Cl (150 mL) at 0 °C and the mixture was extracted with EtOAc (4×150 mL). The combined organic layers were washed with brine (150 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by distillation (bp 130-132, 1 mmHg) to give ether **52** (7.89 g, 75%). **52**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.26 (2H, d, *J*=8.6 Hz), 6.87 (2H, d, *J*=8.6 Hz), 4.43 (2H, s), 3.80 (3H, s), 3.46 (2H, t, *J*=6.3 Hz), 2.21 (2H, dt, *J*=2.6, 6.9 Hz), 1.94 (1H, t, *J*=2.6 Hz), and 1.56-1.78 (4H, m); IR (neat), 3296, 3000, 2940, 2860, 1614, 1588, 1516, 1466, 1446, 1362, 1302, 1248, 1174, 1100, 1036, 822, and 638 cm^{-1}; HR-EI-MS, Calcd for $C_{14}H_{18}O_2$ (M^+), 218.1307, found 218.1313.

7-(4-Methoxybenzyloxy)-2-heptyn-1-ol (53). To a solution of acetylenic compound **52** (4.99 g, 22.9 mmol) in THF (44 mL) cooled to -78 °C was added dropwise BuLi (15.8 mL of a 1.60M solution in hexane, 25.2 mmol), and the mixture was stirred at -78 °C for 1 h. $(CH_2O)_n$ (757 mg, 25.2 mmol) was then added and the solution was stirred at 25 °C for 2 h. After addition of ice chips and satd aq. $NaHCO_3$ (60 mL), the mixture was extracted with EtOAc (4×60 mL). The combined EtOAc layers were washed with brine (2×30 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc 4:1) to give hydroxy acetylene compound **53** (5.09 g, 90%). **53**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.26 (2H, d, *J*=8.6 Hz), 6.88 (2H, d, *J*=8.6 Hz), 4.43 (2H, s), 4.24 (2H, d, *J*=2.3 Hz), 3.81 (3H, s), 3.46 (2H, t, *J*=6.3 Hz), 2.24 (2H, tt, *J*=2.3, 6.9 Hz), and 1.56-1.76 (4H, m); IR (neat), 3428, 3000, 2940, 2864, 1614, 1588, 1516, 1460, 1364, 1302, 1248, 1176, 1136, 1096, 1032, 822, and 636 cm^{-1}; HR-EI-MS, Calcd for $C_{15}H_{20}O_3$ (M^+), 248.1413, found 248.1403.

(2*E*)-1-(*tert*-Butyldiphenylsilyloxy)-7-(4-methoxybenzyloxy)-2-heptene (54). To a suspension of $LiAlH_4$ (0.448 g, 11.8 mmol) in THF (13 mL) cooled to 0 °C was added dropwise a solution of hydroxy acetylene compound **53** (1.96 g, 7.89 mmol) in THF (10 mL) and the mixture was stirred at 25 °C for 17 h. After the addition of Et_2O (46 mL), the reaction was quenched with aq. 1M HCl (100 mL) at 0 °C. The aq. layer was extracted with EtOAc (4×100 mL). The combined organic layers were washed with satd aq. $NaHCO_3$ (50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. To a solution of the resulting residue in DMF (33 mL) cooled to 0 °C were added imidazole (1.18 g, 17.4 mmol) and *tert*-butyldiphenylsilyl chloride (2.15 mL, 8.28 mmol). The reaction mixture was stirred at 25 °C for 14 h, diluted with Et_2O (500 mL), washed with satd aq. $NaHCO_3$ (50 mL) and H_2O (4×50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 100:1) to give silyl ether **54** (3.31 g, 86%). **54**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.68 (4H, dd, *J*=1.7, 7.3 Hz), 7.34-7.45 (6H, m), 7.26 (2H, d, *J*=8.6 Hz), 6.87 (2H, d, *J*=8.6 Hz), 5.64 (1H, dt, *J*=15.5, 6.3 Hz), 5.52 (1H, dt, *J*=15.5, 4.9 Hz), 4.43 (2H, s), 4.16 (2H, d, *J*=4.9 Hz), 3.80 (3H, s), 3.44 (2H, t, *J*=6.6 Hz), 2.03 (2H, q, *J*=6.3 Hz), 1.53-1.66 (2H, m), 1.38-1.48 (2H, m), and 1.05 (9H, s); IR (neat), 3072, 3048,

2936, 2856, 1616, 1588, 1516, 1464, 1446, 1430, 1380, 1362, 1302, 1248, 1174, 1112, 1040, 1010, 972, 824, 740, 740, 704, 690, and 610 cm^{-1}; HR-FD-MS, Calcd for $C_{31}H_{40}O_3Si$ (M^+), 488.2748, found 488.2760.

(5*E*)-7-(*tert*-Butyldiphenylsilyloxy)-5-hepten-1-ol (55). To a solution of 4-methoxybenzyl ether **54** (1.78 g, 3.64 mmol) in CH_2Cl_2/H_2O (131 mL, 10:1) cooled to 0 °C was added dichlorodicyanobenzoquinone (1.24 g, 5.46 mmol) and the solution was stirred at 25 °C for 1.5 h. After addition of satd aq. $NaHCO_3$ (100 mL) at 0 °C, the aq. layer was extracted with Et_2O (4×100 mL). The combined organic layers were washed with water (3×50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc 10:1) to give alcohol **55** (1.02 g, 76%). **55**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.68 (4H, dd, *J*=2.3, 7.9 Hz), 7.34-7.45 (6H, m), 5.65 (1H, dt, *J*=15.5, 6.3 Hz), 5.55 (1H, dt, *J*=15.5, 4.3 Hz), 4.15 (2H, d, *J*=4.3 Hz), 3.65 (2H, t, *J*=6.3 Hz), 2.06 (2H, q, *J*=6.3 Hz), 1.52-1.62 (2H, m), 1.40-1.49 (2H, m), and 1.05 (9H, s); IR (neat), 3344, 3072, 3052, 3020, 2936, 2896, 2860, 2736, 1592, 1474, 1464, 1430, 1380, 1362, 1336, 1308, 1260, 1188, 1112, 1056, 1010, 1000, 972, 940, 824, 740, 702, 690, and 614 cm^{-1}; HR-FD-MS, Calcd for $C_{23}H_{32}O_2Si$ (M^++H), 369.2251, found 369.2229.

(2*E*)-7-Bromo-1-(*tert*-butyldiphenylsilyloxy)-2-heptene (56). To a solution of alcohol **55** (547 mg, 1.48 mmol) in CH_2Cl_2 (16 mL) cooled to 0 °C were added Ph_3P (467 mg, 1.78 mmol) and CBr_4 (736 mg, 2.22 mmol) and the mixture was stirred at 25 °C for 12 min, and satd aq. $NaHCO_3$ (10 mL) was then added. The mixture was extracted with hexane (40 mL). The hexane layer was washed with H_2O (3×10 mL) and brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 30:1) to give bromide **56** (600 mg, 94%). **56**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.68 (4H, dd, *J*=2.0, 7.6 Hz), 7.34-7.46 (6H, m), 5.63 (1H, dt, *J*=15.2, 5.9 Hz), 5.55 (1H, dt, *J*=15.2, 4.3 Hz), 4.16 (2H, d, *J*=4.3 Hz), 3.40 (2H, t, *J*=6.6 Hz), 2.02-2.09 (2H, m), 1.80-1.90 (2H, m), 1.45-1.56 (2H, m), and 1.05 (9H, s); IR (neat), 3072, 3052, 3020, 2936, 2896, 2856, 1488, 1474, 1464, 1430, 1382, 1362, 1250, 1188, 1112, 1054, 1008, 1000, 972, 942, 824, 738, 702, and 612 cm^{-1}; HR-FD-MS, Calcd for $C_{23}H_{32}O^{79}BrSi$ (M^++H), 431.1407, found 431.1418.

(5*R,6*R**)-1-Bromo-7-(*tert*-butyldiphenylsilyloxy)-5,6-epoxyheptene (57).** To a solution of olefin **56** (593 mg, 1.37 mmol) in CH_2Cl_2 (17 mL) cooled to 0 °C were added Na_2HPO_4 (972 mg, 6.85 mmol) and *m*-chloroperbenzoic acid (592 mg, 3.43 mmol) and the solution was stirred at 25 °C for 2 h, and satd aq. $Na_2S_2O_3$ (20 mL) was then added at 0 °C. The mixture was extracted with Et_2O (250 mL) and the Et_2O layer was washed with satd aq. $Na_2S_2O_3$ (50 mL), satd aq. $NaHCO_3$ (3×50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 40:1) to give epoxide **57** (613 mg, 100%). **57**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.67 (4H, dd, *J*=1.7, 7.6 Hz), 7.35-7.46 (6H, m), 3.76 (2H, d, *J*=4.3 Hz), 3.41 (2H, t, *J*=6.9 Hz), 2.89 (1H, dt, *J*=2.3, 4.3 Hz), 2.75-2.80 (1H, m), 1.84-1.96 (2H, m), 1.53-1.63 (4H, m), and 1.05 (9H, s); IR (neat), 3072, 3052, 2936, 2860, 1590, 1474, 1464, 1430, 1392, 1362, 1286, 1258, 1190, 1112, 1028, 1008, 1000, 940, 898, 866, 824, 792, 740, 704, and 614 cm^{-1}; HR-FD-MS, Calcd for $C_{23}H_{32}O_2{}^{79}BrSi$ (M^++H), 447.1356, found 447.1314.

(2*R,3*S**)-3-Acetoxy-2-[(*tert*-butyldiphenylsilyloxy)methyl]oxepane (63).** To a solution of olefin **62** (259 mg, 1.41 mmol) in Et_2O/H_2O (8.4 mL, 1:1) were added OsO_4 (3.6 mL of 5 mg/mL in *tert*-BuOH, 0.071 mmol) and sodium metaperiodate ($NaIO_4$) (663 mg, 3.10 mmol) at 25 °C and the solution was stirred at 25 °C for 1.5 h, diluted with EtOAc (90 mL), washed with water (10 mL), satd aq. $Na_2S_2O_3$ (2×10

mL), and brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. To a solution of the residue in MeOH (10 mL) cooled to 0 °C was added $NaBH_4$ (53.3 mg, 1.41 mmol) and the mixture was stirred at 0 °C for 1 h. Satd aq. NH_4Cl (10 mL) was then added and the mixture was extracted with EtOAc (90 mL). The EtOAc layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. To a solution of the crude hydroxy acetate in DMF (1.4 mL) were added imidazole (240 mg, 3.53 mmol) and *tert*-butyldiphenylsilyl chloride (0.440 mL, 1.69 mmol) at 25 °C and the solution was stirred at 25 °C for 15 h, diluted with Et_2O (40 mL), washed with water (3×10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 40:1) to give silyl ether **63** (355 mg, 59%). **63**: a colorless oil; ^{1}H-NMR (400 MHz, C_6D_6), δ7.86-7.91 (4H, m), 7.23-7.30 (6H, m), 5.35 (1H, ddd, *J*=3.9, 5.5, 6.6 Hz), 3.97 (1H, ddt, *J*=1.1, 12.3, 4.4 Hz), 3.91 (1H, dd, *J*=5.7, 10.8 Hz), 3.86 (1H, dd, *J*=3.8, 10.8 Hz), 3.64 (1H, ddd, *J*=3.8, 5.7, 6.6 Hz), 3.35 (1H, ddd, *J*=3.3, 9.9, 12.3 Hz), 1.80-1.91 (2H, m), 1.67 (3H, s), 1.20-1.59 (4H, m), and 1.25 (9H, s); IR (neat), 3072, 3052, 3000, 2936, 2860, 1738, 1590, 1464, 1430, 1392, 1372, 1290, 1240, 1196, 1114, 1026, 990, 942, 896, 880, 824, 802, 774, 740, 702, 645, and 610 cm^{-1}; HR-FD-MS, Calcd for $C_{25}H_{35}O_4Si$ (M^++H), 427.2306, found 427.2300.

(2*R,3*S**)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-3-hydroxyoxepane (61).** To a solution of acetate **63** (65.2 mg, 0.153 mmol) in MeOH (3.0 mL) was added K_2CO_3 (35.0 mg, 0.253 mmol) at 25 °C and the mixture was stirred at 25 °C for 1.5 h, poured into brine (10 mL), and extracted with Et_2O (40 mL). The Et_2O layer was washed water (2×10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 10:1) to give alcohol **61** (40.5 mg, 69%). **61**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.68 (4H, dd, *J*=1.7, 7.6 Hz), 7.36-7.48 (6H, m), 3.86-3.98 (2H, m), 3.84 (1H, dd, *J*=5.6, 10.2 Hz), 3.69 (1H, dd, *J*=7.9, 10.2 Hz), 3.49 (1H, ddd, *J*=4.0, 8.2, 12.9 Hz), 3.39 (1H, dt, *J*=5.6, 7.9 Hz), 1.94 (1H, ddd, *J*=4.3, 8.2, 13.2 Hz), 1.59-1.83 (5H, m), and 1.07 (9H, s); IR (neat), 3460, 3072, 3052, 2936, 2860, 1592, 1474, 1430, 1392, 1362, 1334, 1292, 1192, 1146, 1114, 1062, 1012, 984, 940, 914, 886, 840, 824, 802, 776, 740, 702, and 610 cm^{-1}; HR-FD-MS, Calcd for $C_{23}H_{33}O_3Si$ (M^++H), 385.2200, found 385.2151.

Conversion of 61 to 59. To a solution of **61** (15.6 mg, 0.0406 mmol) in CH_2Cl_2 (1 mL) were added pyridine (7.2 μL, 0.089 mmol) and Tf_2O (13.7 μL, 0.081 mmol) at -10 °C, and the solution was stirred at -10 °C for 1.5 h and then at 25 °C for 1.5 h, poured into satd aq. $NaHCO_3$ (10 mL) at 0 °C, and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 20:1) to give **59** (12.9 mg, 62%).

(1*S,2'*R**)-2-(*tert*-Butyldiphenylsilyloxy)-1-(oxan-2'-yl)ethanol (64).** To a solution of olefin **55** (216 mg, 0.586 mmol) in CH_2Cl_2 (7.3 mL) was added *m*-chloroperbenzoic acid (202 mg, 1.17 mmol) at 0 °C and the solution was stirred at 25 °C for 30 min. Satd aq. $Na_2S_2O_3$ (10 mL) was added and the mixture was extracted with EtOAc (90 mL). The EtOAc layer was washed with aq. 1M KOH (2×10 mL) and brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. To a solution of the residue in CH_2Cl_2 (5.7 mL) was added *p*-toluenesulfonic acid monohydrate (5.6 mg, 0.029 mmol) at 25 °C and the mixture was stirred at 25 °C for 1 h. The reaction was quenched with Et_3N (0.023 mL, 0.16 mmol), and the solvent was evaporated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 10:1) to give alcohol **64** (207 mg, 96%). **64**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.66 (4H, dt, *J*=7.6, 2.0 Hz), 7.35-7.47 (6H, m), 3.92 (1H, dt, *J*=11.2, 2.3 Hz), 3.77 (2H, d, *J*=5.0 Hz), 3.62 (1H, q, *J*=5.0 Hz), 3.30-3.42 (2H, m), 1.82-1.90 (1H, m), 1.72-1.80 (1H, m), 1.25-1.58 (4H, m), and 1.06 (9H, s); IR (neat), 3584, 3480, 3072,

3052, 2936, 2856, 1592, 1474, 1466, 1430, 1206, 1114, 1092, 1048, 1002, 894, 822, 792, 740, 702, and 608 cm^{-1}; HR-FD-MS, Calcd for $C_{23}H_{33}O_3Si$ (M^++H), 385.2200, found 385.2179.

(2*R,1'*S*)-2-[2'-(*tert*-Butyldiphenylsilyloxy)-1'-trifluoromethanesulfonyloxyethyl]-oxane (59).** To a solution of alcohol **64** (26.2 mg, 0.0681 mmol) in CH_2Cl_2 (2.0 mL) were added pyridine (0.0276 mL, 0.341 mmol) and Tf_2O (0.0343 mL, 0.204 mmol) at -10 °C. The solution was stirred at -10 °C for 30 min, poured into satd aq. $NaHCO_3$ (10 mL) at 0 °C, and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 20:1) to give triflate **59** (34.4 mg, 98%). **59**: a colorless oil; ^{1}H-NMR (400 MHz, C_6D_6), δ7.91-7.82 (4H, m), 7.25-7.30 (6H, m), 4.95 (1H, ddd, *J*=2.8, 4.8, 6.6 Hz), 4.00 (1H, dd, *J*=6.6, 12.3 Hz), 3.83 (1H, dd, *J*=2.8, 12.3 Hz), 3.62-3.66 (1H, m), 3.35 (1H, ddd, *J*=2.2, 4.8, 11.2 Hz), 2.93 (1H, dt, *J*=2.0, 12.3 Hz), 1.31-1.40 (1H, m), 1.22 (9H, s), 1.02-1.20 (3H, m), and 0.85-0.97 (2H, m); IR (neat), 3144, 3076, 3056, 2940, 2860, 2744, 1732, 1592, 1468, 1444, 1430, 1416, 1364, 1334, 1266, 1246, 1212, 1148, 1114, 1094, 1052, 1020, 998, 960, 920, 872, 824, 806, 788, 760, 740, 704, and 608 cm^{-1}; HR-FD-MS, Calcd for $C_{24}H_{32}O_5F_3SSi$ (M^++H), 517.1693, found 517.1667.

(2*R,3*S**)-[2-(*tert*-Butyldiphenylsilyloxy)methyloxepan-3-yl]formate (66) and (5*R**,6*R**)-[7-(*tert*-Butyldiphenylsilyloxy)-5,6-epoxyheptan-1-yl]formate (67).** To a solution of bromo epoxide **57** (34.8 mg, 0.0778 mmol) and DMF (0.0180 mL, 0.233 mmol) in CH_2Cl_2 (2.6 mL) was added AgOTf (30.1 mg, 0.117 mmol) at 25 °C and the mixture was stirred at 25 °C for 5 h, poured into satd aq. $NaHCO_3$ (10 mL) at 25 °C, and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc, 5:1) to give **66** (8.0 mg, 25%) and **67** (10.3 mg, 32%). **66**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.96 (1H, s), 7.65-7.69 (4H, m), 7.35-7.44 (6H, m), 5.18 (1H, ddd, *J*=0.9, 4.0, 9.5 Hz), 4.09 (1H, dt, *J*=12.5, 4.3 Hz), 3.70 (1H, dd, *J*=6.1, 10.8 Hz), 3.63 (1H, dd, *J*=4.0, 10.8 Hz), 3.57 (1H, dt, *J*=4.0, 6.1 Hz), 3.49-3.54 (1H, m), 1.84-1.93 (2H, m), 1.61-1.73 (4H, m), and 1.05 (9H, s); IR (neat), 3072, 2936, 2860, 1730, 1590, 1466, 1430, 1392, 1362, 1362, 1176, 1114, 984, 940, 904, 878, 824, 802, 740, 704, and 610 cm^{-1}; HR-FD-MS, Calcd for $C_{24}H_{33}O_4Si$ (M^++H), 413.2158, found 413.2149. **67**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ8.06 (1H, s), 7.67 (4H, dt, *J*=7.9, 1.8 Hz), 7.37-7.45 (6H, m), 4.17 (2H, t, *J*=6.4 Hz), 3.77 (1H, dd, *J*=3.9, 11.7 Hz), 3.74 (1H, dd, *J*=4.2, 11.7 Hz), 2.89 (1H, ddd, *J*=2.2, 3.9, 4.2 Hz), 2.78 (1H, dt, *J*=2.2, 5.7 Hz), 1.68-1.75 (2H, m), 1.44-1.61 (4H, m), and 1.05 (9H, s); IR (neat), 3072, 2936, 2860, 1730, 1592, 1474, 1430, 1392, 1364, 1310, 1176, 1114, 1008, 942, 880, 824, 790, 740, 704, and 614 cm^{-1}; HR-FD-MS, Calcd for $C_{24}H_{33}O_4Si$ (M^++H), 413.2158, found 413.2180.

Conversion of 61 to 66. To a solution of alcohol **61** (23.2 mg, 0.0603 mmol) in CH_2Cl_2 (1 mL) were added 4-dimethylaminopyridine (1.5 mg, 0.012 mmol), 1,3-dicyclohexylcarbodiimide (18.7 mg, 0.0905 mmol), and formic acid (2.7 g, 0.072 mmol) at 25 °C. The mixture was stirred at 25 °C for 1 h, poured into satd aq. $NaHCO_3$ (10 mL) at 25 °C, and extracted with Et_2O (40 mL), washed brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc, 5:1) to give formate **66** (12.9 mg, 52%).

(2*E*)-6-(4-Methoxybenzyloxy)-2-hexen-1-ol (84). To a suspension of $LiAlH_4$ (0.622 g, 16.4 mmol) in THF (20 mL) cooled to 0 °C was added dropwise a solution of hydroxy acetylene compound **34** (2.56 g, 10.9 mmol) in THF (10 mL), and the mixture was stirred at 25 °C for 17 h. After addition of Et_2O (30 mL), the reaction was quenched with aq. 1M HCl. The aq. layer was extracted with EtOAc (4×90 mL). The

combined organic layers were washed with satd aq. $NaHCO_3$ (70 mL) and brine (70 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 4:1) to give alcohol **84** (2.59 g, 100%). **84**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.26 (2H, d, *J*=8.6 Hz), 6.88 (2H, *J*=8.6 Hz), 5.58-5.72 (2H, m), 4.43 (2H, s), 4.07 (2H, d, *J*=4.0 Hz), 3.81 (3H, s), 3.45 (2H, t, *J*=6.6 Hz), 2.10-2.17 (2H, m), and 1.69 (2H, qui, *J*=6.6 Hz); IR (neat), 3416, 3004, 2940, 2856, 1672, 1614, 1588, 1516, 1466, 1366, 1302, 1248, 1176, 1098, 1036, 1010, 972, 822, and 756 cm^{-1}; HR-EI-MS, Calcd for $C_{14}H_{20}O_3$ (M^+), 236.1413, found 236.1398.

(2*E*)-1-Bromo-6-(4-methoxybenzyloxy)-2-hexene (85). To a solution of alcohol **84** (1.81 g, 7.67 mmol) in CH_2Cl_2 (79 mL) cooled to 0 °C were added Ph_3P (2.41 g, 9.20 mmol) and CBr_4 (3.81 g, 11.5 mmol), and the mixture was stirred at 25 °C for 5 min. After satd aq. $NaHCO_3$ was added, the mixture was extracted with Et_2O (400 mL). The Et_2O layer was washed with H_2O (3×100 mL) and brine (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 100:1) to give bromide **85** (2.09 g, 90%). **85**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.26 (2H, d, *J*=8.6 Hz), 6.88 (2H, *J*=8.6 Hz), 5.63-5.82 (2H, m), 4.42 (2H, s), 3.93 (2H, d, *J*=6.6 Hz), 3.81 (3H, s), 3.44 (2H, t, *J*=6.6 Hz), 2.12-2.19 (2H, m), and 1.63-1.74 (2H, m); IR (neat), 3004, 2940, 2856, 2324, 1662, 1614, 1588, 1516, 1464, 1444, 1366, 1302, 1248, 1206, 1174, 1102, 1036, 968, and 822 cm^{-1}; HR-EI-MS, Calcd for $C_{14}H_{19}O_2{}^{79}Br$ (M^+), 298.0569, found 298.0593.

(5*E*)-9-(4-Methoxybenzyloxy)-1-(oxan-2-yloxy)-5-nonen-2-yne (86). To a solution of 3-tetrahydropyranyloxypropyne (1.13 g, 8.03 mmol) in THF (24 mL) cooled to -78 °C was added dropwise BuLi (4.8 mL of a 1.66M solution in hexane, 8.03 mmol), and the mixture was stirred at -78 °C for 30 min. A solution of bromide **85** (2.00 g, 6.69 mmol) in THF (5 mL) was then added dropwise at -78 °C. The solution was stirred at 25 °C for 7 h, and satd aq. NH_4Cl was added at 0 °C. The mixture was extracted with EtOAc (450 mL). The EtOAc layer was washed with satd aq. $NaHCO_3$ (50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 20:1) to give acetylenic compound **86** (1.24 g, 54%). **86**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.26 (2H, d, *J*=8.6 Hz), 6.87 (2H, *J*=8.6 Hz), 5.65 (1H, dt, *J*=15.1, 6.3 Hz), 5.40 (1H, dt, *J*=15.1, 5.6 Hz), 4.81 (1H, t, *J*=3.3 Hz), 4.42 (2H, s), 4.32 (1H, dt, *J*=15.2, 2.3 Hz), 4.22 (1H, *J*=15.2, 2.0 Hz), 3.82-3.89 (1H, m), 3.80 (3H, m), 3.48-3.57 (1H, m), 3.44 (2H, t, *J*=6.3 Hz), 2.92-2.96 (2H, m), 2.06-2.14 (2H, m), and 1.51-1.89 (8H, m); IR (neat), 3036, 2940, 2856, 1614, 1516, 1456, 1444, 1390, 1360, 1322, 1302, 1248, 1202, 1182, 1118, 1100, 1080, 1024, 970, 946, 904, 872, and 818 cm^{-1}; HR-FAB-MS, Calcd for $C_{22}H_{29}O_4$ (M^+-H), 357.2067, found 357.2071.

(5*E*)-9-(4-Methoxybenzyloxy)-5-nonen-2-yn-1-ol (87). To a solution of tetrahydropyranyl ether **86** (7.79 g, 21.7 mmol) in MeOH (120 mL) was added *p*-toluenesulfonic acid monohydrate (41.2 mg, 0.217 mmol) at 25 °C. The solution was stirred at 25 °C for 30 min, diluted with EtOAc (900 mL), washed with satd aq. $NaHCO_3$ (2×100 mL) and brine (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 5:1) to give alcohol **87** (5.95 g, 100%). **87**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.26 (2H, d, *J*=8.6 Hz), 6.88 (2H, d, *J*=8.6 Hz), 5.65 (1H, dt, *J*=15.1, 6.6 Hz), 5.39 (1H, dt, *J*=15.1, 4.3 Hz), 4.43 (2H, s), 4.27 (2H, t, *J*=2.0 Hz), 3.80 (3H, s), 3.44 (2H, t, *J*=6.3 Hz), 2.93 (2H, dt, *J*=4.3, 2.0 Hz), 2.04-2.15 (2H, m), and 1.62-1.73 (2H, m); IR (neat), 3416, 3000, 2936, 2860, 1614, 1586, 1516, 1456, 1424, 1364, 1302, 1248, 1176, 1096, 1034, 972, and 822 cm^{-1}; HR-EI-MS, Calcd for $C_{17}H_{22}O_3$ (M^+), 274.1570, found 274.1567.

(2*E*,5*E*)-9-(4-Methoxybenzyloxy)-2,5-nonadien-1-ol (88). A solution of hydroxy acetylene **87** (47.9 mg, 0.185 mmol) in THF (2 mL) was added at 0 °C dropwise *via* cannular to a suspension of $LiAlH_4$ (35.1 mg, 0.925 mmol) in THF (1 mL), and the mixture was stirred at 25 °C for 13 h. Et_2O (3 mL) was then added, and the reaction was quenched with aq. 1M HCl. The mixture was diluted with Et_2O (40 mL), washed with aq. 1M HCl (10 mL), satd aq. $NaHCO_3$ (10 mL) and brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 5:1) to give alcohol **88** (41.9 mg, 94%). **88**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.26 (2H, d, *J*=8.6 Hz), 6.88 (2H, d, *J*=8.6 Hz), 5.58-5.75 (2H, m), 5.35-5.50 (2H, m), 4.43 (2H, s), 4.10 (2H, d, *J*=4.6 Hz), 3.81 (3H, s), 3.44 (2H, t, *J*=6.3 Hz), 2.73 (2H, t, *J*=4.0 Hz), 2.05-2.12 (2H, m), and 1.61-1.72 (2H, m); IR (neat), 3416, 3004, 2936, 2860, 1614, 1588, 1516, 1466, 1444, 1366, 1302, 1248, 1174, 1098, 1036, 998, 972, 820, and 756 cm^{-1}; HR-EI-MS, Calcd for $C_{17}H_{24}O_3$ (M^+), 276.1726, found 276.1714.

(2*S*,3*S*,5*E*)-9-(4-Methoxybenzyloxy)-2,3-epoxy-5-nonen-1-ol (89). $Ti(O^iPr)_4$ (1.18 mL, 3.96 mmol) and (+)-diethyl tartrate (1.02 mL, 5.94 mmol) were added to a suspension of MS4A (10.8 g) in CH_2Cl_2 (200 mL) at -25 °C. After 30 min, *tert*-butyl hydroperoxide (5.52M toluene solution, 7.90 mL) was added, and the solution was maintained at -25 °C for 30 min. A solution of allylic alcohol **88** (5.47 g, 19.8 mmol) in CH_2Cl_2 (50 mL) was added dropwise *via* cannular at -25 °C, and the solution was stirred at the same temperature for 15 h. The reaction was quenched with a solution of tartaric acid (7.13 g) and iron(II) sulfate heptahydrate ($FeSO_4 \cdot 7H_2O$) (13.2 g) in water (100 mL) at 0 °C. After stirred at 0 °C for 1.5 h, the mixture was extracted with Et_2O (3×150 mL). To the combined organic layers was added a 30% NaOH-brine solution (10 mL) and the mixture was stirred vigorously at 0 °C for 1 h. Water (170 mL) was then added and the aq. layer was extracted with Et_2O (3×200 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 2:1) to give epoxy alcohol **89** (5.44 g, 94%). **89**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.26 (2H, d, *J*=8.6 Hz), 6.88 (2H, d, *J*=8.6 Hz), 5.54 (1H, dt, *J*=15.2, 6.3 Hz), 5.40 (1H, dt, *J*=15.2, 6.3 Hz), 4.42 (2H, s), 3.90 (1H, dd, *J*=2.3, 12.5 Hz), 3.80 (3H, s), 3.62 (1H, dd, *J*=4.6, 12.5 Hz), 3.44 (2H, t, *J*=6.3 Hz), 2.99 (1H, dt, *J*=2.3, 7.6 Hz), 2.93 (1H, dt, *J*=4.6, 2.3 Hz), 2.26-2.30 (2H, m), 2.04-2.14 (2H, m), and 1.64-1.72 (2H, m); IR (neat), 3436, 2936, 2856, 1614, 1586, 1516, 1466, 1446, 1366, 1302, 1250, 1176, 1100, 1034, 972, 904, 848, 820, 756, and 636 cm^{-1}; HR-FAB-MS, Calcd for $C_{17}H_{25}O_4$ (M^++H), 293.1754, found 293.1734; $[\alpha]^{22}_D$ -10.2° (c 1.14, $CHCl_3$).

(7*S*,8*S*,4*E*)-9-(*tert*-Butyldiphenylsilyloxy)-1-(4-methoxybenzyloxy)-7,8-epoxy-4-nonene (90). To a solution of alcohol **89** (251 mg, 0.857 mmol) in DMF (3.5 mL) cooled to 0 °C were added imidazole (116 mg, 1.71 mmol) and *tert*-butyldiphenylsilyl chloride (0.245 mL, 0.943 mmol) and the solution was stirred at 25 °C for 14 h, diluted with Et_2O (40 mL), washed with water (4×10 mL) and brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc 25:1) to afford silyl ether **90** (455 mg, 100%). **90**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.65-7.69 (4H, m), 7.37-7.45 (6H, m), 7.25 (2H, d, *J*=8.6 Hz), 6.87 (2H, d, *J*=8.6 Hz), 5.53 (1H, dt, *J*=15.5, 6.3 Hz), 5.39 (1H, dt, *J*=15.5, 6.3 Hz), 4.42 (2H, s), 3.80 (3H, s), 3.79 (1H, dd, *J*=4.6, 11.9 Hz), 3.72 (1H, dd, *J*=4.6, 11.9 Hz), 3.43 (2H, t, *J*=6.6 Hz), 2.91 (1H, dt, *J*=2.0, 4.6 Hz), 2.83 (1H, dt, *J*=2.0, 7.3 Hz), 2.20-2.27 (2H, m), 2.05-2.13 (2H, m), 1.61-1.71 (2H, m), and 1.05 (9H, s); IR (neat), 2936, 2856, 1614, 1516, 1466, 1430, 1248, 1114, 1038, 824, 742, 704, 690, and 614 cm^{-1}; HR-FAB-MS, Calcd for $C_{33}H_{43}O_4Si$ (M^++H), 531.2932, found 531.2943; $[\alpha]^{22}_D$ -3.71° (c 1.62, $CHCl_3$).

(7*S*,8*S*,4*E*)-9-(*tert*-Butyldiphenylsilyloxy)-7,8-epoxy-4-nonen-1-ol (91). To a solution of 4-methoxybenzyl ether **90** (491 mg, 0.925 mmol) in CH_2Cl_2/H_2O (33 mL, 10:1) cooled to 0 °C was added dichlorodicyanobenzoquinone (316 mg, 1.39 mmol) and the solution was stirred at 25 °C for 1.5 h. Satd aq. $NaHCO_3$ (40 mL) was then added at 0 °C and the mixture was extracted with Et_2O (150 mL). The Et_2O layer was washed with water (2×25 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc 20:1) to give alcohol **91** (380 mg, 100%). **91**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.67 (4H, dd, *J*=1.3, 6.3 Hz), 7.35-7.47 (6H, m), 5.56 (1H, dt, *J*=15.2, 6.3 Hz), 5.43 (1H, dt, *J*=15.2, 6.3 Hz), 3.77 (1H, dd, *J*=4.3, 10.5 Hz), 3.76 (1H, dd, *J*=4.3, 10.5 Hz), 3.65 (2H, t, *J*=6.6 Hz), 2.92 (1H, dt, *J*=2.3, 4.3 Hz), 2.84 (1H, dt, *J*=2.3, 5.3 Hz), 2.23-2.29 (2H, m), 2.07-2.15 (2H, m), 1.56-1.69 (2H, m), and 1.05 (9H, s); IR (neat), 3402, 3072, 3048, 2932, 2856, 1474, 1430, 1399, 1114, 1060, 1008, 1000, 972, 824, 740, 704, 690, and 614 cm^{-1}; HR-FAB-MS, Calcd for $C_{25}H_{35}O_3Si$ (M^++H), 411.2357, found 411.2353; $[\alpha]^{22}_D$ -5.65° (c 1.03, $CHCl_3$).

(7*S*,8*S*,4*E*)-1-Bromo-9-(*tert*-butyldiphenylsilyloxy)-7,8-epoxy-4-nonen-1-ol (92). To a solution of alcohol **91** (238 mg, 0.579 mmol) in CH_2Cl_2 (6 mL) were added Ph_3P (182 mg, 0.695 mmol) and CBr_4 (288 mg, 0.869 mmol) at 25 °C and the mixture was stirred at 25 °C for 5 min. Satd aq. $NaHCO_3$ was then added and the mixture was extracted with Et_2O (40 mL). The Et_2O layer was washed with H_2O (3×10 mL) and brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc, 100:1) to give bromide **92** (221 mg, 81%). **92**: a colorless oil; ^{1}H-NMR (270 MHz, $CDCl_3$), δ7.67 (4H, dd, *J*=1.6, 5.9 Hz), 7.35-7.46 (6H, m), 5.40-5.57 (2H, m), 3.77 (1H, dd, *J*=4.3, 11.5 Hz), 3.76 (1H, dd, *J*=4.3, 11.5 Hz), 3.39 (2H, t, *J*=6.6 Hz), 2.91 (1H, dt, *J*=2.3, 4.3 Hz), 2.84 (1H, dt, *J*=2.3, 5.6 Hz), 2.23-2.28 (2H, m), 2.14-2.21 (2H, m), 1.86-1.96 (2H, m), and 1.05 (9H, s); IR (neat), 3072, 3048, 2960, 2936, 2896, 2856, 1474, 1430, 1392, 1362, 1268, 1244, 1190, 1112, 1030, 1008, 1000, 972, 938, 900, 866, 824, 800, 740, 702, 690, and 614 cm^{-1}; HR-FAB-MS, Calcd for $C_{25}H_{34}O_2{}^{79}BrSi$ (M^++H), 473.1512, found 473.1534; $[\alpha]^{22}_D$ -5.33° (c 1.03, $CHCl_3$).

(4*R*,5*R*,7*S*,8*S*)-1-Bromo-9-(*tert*-butyldiphenylsilyloxy)-4,5,7,8-diepoxynonane (93a) and (4*S*,5*S*,7*S*,8*S*)-1-Bromo-9-(*tert*-butyldiphenylsilyloxy)-4,5,7,8-diepoxynonane (93b). To a solution of olefin **92** (117 mg, 0.246 mmol) in CH_2Cl_2 (3.1 mL) cooled to 0 °C were added Na_2HPO_4 (175 mg, 1.23 mmol) and *m*-chloroperbenzoic acid (152 mg, 0.615 mmol) and the solution was stirred at 25 °C for 1 h. Satd aq. $Na_2S_2O_3$ (4 mL) was then added at 0 °C and the mixture was extracted with EtOAc (40 mL). The EtOAc layer was washed with satd aq. $Na_2S_2O_3$ (15 mL), satd aq. $NaHCO_3$ (2×10 mL) and brine (2×10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc 10:1) to give the mixture of epoxides (**93a** and **93b**) (120 mg, 100%). The diastereomeric mixture was separated by HPLC (hexane:EtOAc 7:1). **93a**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.66-7.69 (4H, m), 7.37-7.45 (6H, m), 3.81 (1H, dd, *J*=3.5, 11.7 Hz), 3.74 (1H, dd, *J*=4.4, 11.7 Hz), 3.40-3.50 (2H, m), 3.00 (1H, ddd, *J*=2.2, 3.5, 4.4 Hz), 2.91 (1H, ddd, *J*=2.2, 4.2, 6.2 Hz), 2.81 (1H, dt, *J*=5.3, 2.2 Hz), 2.80 (1H, dt, *J*=6.6, 2.2 Hz), 1.94-2.08 (3H, m), 1.73-1.85 (2H, m), 1.56-1.64 (1H, m), and 1.05 (9H, s); IR (neat), 3072, 3052, 2936, 2860, 2364, 1590, 1474, 1430, 1392, 1362, 1336, 1252, 1190, 1114, 1008, 1000, 962, 938, 908, 886, 824, 790, 740, 704, 690, and 614 cm^{-1}; HR-FAB-MS, Calcd for $C_{25}H_{34}O_3{}^{79}BrSi$ (M^++H), 489.1461, found 489.1431; $[\alpha]^{22}_D$ +2.90° (c 0.965, hexane). **93b**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.66-7.69 (4H, m), 7.37-7.46 (6H, m), 3.81 (1H, dd, *J*=3.7, 11.7 Hz), 3.75 (1H, dd, *J*=4.4, 11.7 Hz), 3.41-3.51 (2H, m), 2.98 (1H, ddd, *J*=2.2, 4.4, 6.8 Hz), 2.93 (1H, ddd,

J=2.2, 3.7, 4.4 Hz), 2.87 (1H, ddd, *J*=2.2, 5.0, 6.6 Hz), 2.75 (1H, ddd, *J*=2.2, 4.8, 6.8 Hz), 1.93-2.10 (2H, m), 1.77-1.86 (2H, m), 1.52-1.73 (2H, m), and 1.05 (9H, s); IR (neat), 3136, 3072, 3052, 2936, 2860, 1590, 1474, 1430, 1392, 1362, 1332, 1304, 1252, 1190, 1112, 1030, 1008, 1000, 962, 938, 886, 824, 798, 740, 702, 690, and 614 cm^{-1}; HR-FAB-MS, Calcd for $C_{25}H_{34}O_3{}^{79}BrSi$ (M^++H), 489.1461, found 489.1484; $[\alpha]^{22}_D$ -21.9° (c 1.00, hexane).

(1*R*,3*S*,4*R*,6*R*)-3-[(*tert*-Butyldiphenylsilyloxy)methyl]-4-trifluoromethanesulfonyloxy-2,7-dioxabicyclo[4.4.0]decane (94a). To a solution of bromo diepoxide **93a** (35.0 mg, 0.0715 mmol) was added AgOTf (22.0 mg, 0.0858 mmol) at 25 °C and the solution was stirred at 25 °C for 30 min, poured into satd aq. $NaHCO_3$ (10 mL) at 0 °C, and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc 10:1) to give **94a** (15.6 mg, 39%). **94a**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.81 (2H, dd, *J*=1.5, 7.9 Hz, PhH), 7.73 (2H, dd, *J*=1.7, 7.9 Hz, PhH), 7.35-7.44 (6H, m, PhH), 5.44 (1H, ddd, *J*=5.1, 9.7, 14.8 Hz, C_4H), 3.96 (1H, dt, *J*=12.5, 2.8 Hz, C_8H), 3.91 (1H, dd, *J*=3.5, 11.7, C_1·H), 3.87 (1H, dd, *J*=2.2, 11.7 Hz, C_1·H), 3.61 (1H, t, *J*=3.3 Hz, C_6H), 3.48 (1H, ddd, *J*=2.2, 3.5, 14.8 Hz, C_3H), 3.47 (1H, t, *J*=3.3 Hz, C_1H), 3.40 (1H, dt, *J*=2.4, 12.5 Hz, C_8H), 2.58 (1H, ddd, *J*=3.3, 5.1, 12.8 Hz, C_5H), 1.89-2.01 (3H, m, C_5H, C_9H, C_{10}H), 1.59-1.69 (1H, m, C_{10}H), 1.26-1.33 (1H, m, C_9H), and 1.07 (9H, s, $C(CH_3)_3$); IR (neat), 2836, 2860, 1430, 1414, 1244, 1210, 1146, 1114, 1006, 932, 898, 702, and 606 cm^{-1}; HR-FD-MS, Calcd for $C_{26}H_{34}O_6FSSi$ (M^++H), 559.1798, found 559.1752; $[\alpha]^{22}_D$-15.0° (c 0.39, hexane).

(1*S*,6*S*,8*S*,1'*R*)-8-[2'-(*tert*-Butyldiphenylsilyloxy)-1'-trifluoromethanesulfonyloxyethyl]-2,7-dioxabicyclo[4.3.0]nonane (94b). To a solution of bromo diepoxide **93b** (45.6 mg, 0.0932 mmol) was added AgOTf (28.8 mg, 0.112 mmol) at 25 °C and the mixture was stirred at 25 °C for 30 min, poured into satd aq. $NaHCO_3$ (10 mL) at 0 °C, and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc 10:1) to give **94b** (14.9 mg, 29%). **94b**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.68-7.73 (4H, m, PhH), 7.37-7.46 (6H, m, PhH), 5.12 (1H, dt, *J*=2.8, 5.7 Hz, C_1·H), 4.30 (1H, ddd, *J*=3.7, 5.7, 9.5 Hz, C_8H), 4.05 (1H, dd, *J*=2.8, 12.6 Hz, C_2·H), 4.00 (1H, dd, *J*=5.7, 12.6 Hz, C_2·H), 3.87 (1H, dd, *J*=2.0, 5.0 Hz, C_1H), 3.68-3.70 (1H, m, C_6H), 3.68 (1H, dt, *J*=13.4, 2.0 Hz, C_3H), 3.23 (1H, dt, *J*=1.8, 13.4 Hz, C_3H), 2.22 (1H, ddd, *J*=5.0, 9.5, 14.5 Hz, C_9H), 1.98-2.06 (1H, m, C_5H), 1.92 (1H, dd, *J*=3.7, 14.5 Hz, C_9H), 1.66 (1H, ddt, *J*=3.5, 4.6, 13.4 Hz, C_5H), 1.53 (1H, tq, *J*=4.2, 13.4 Hz, C_4H), 1.18-1.23 (1H, m, C_4H), and 1.07 (9H, s, $C(CH_3)_3$); IR (neat), 3072, 3052, 2936, 2888, 2860, 1474, 1446, 1430, 1412, 1364, 1332, 1298, 1280, 1244, 1212, 1148, 1112, 1056, 1036, 998, 980, 920, 878, 856, 842, 824, 796, 780, 762, 740, 702, and 614 cm^{-1}; HR-FD-MS, Calcd for $C_{26}H_{34}O_6FSSi$ (M^++H), 559.1798, found 559.1786; $[\alpha]^{22}_D$ -2.53° (c 0.315, hexane).

The acetate of 95a; (2*R*,3*S*,2'*S*,3'*S*)-3-Acetoxy-2-[4'-(*tert*-butyldiphenylsilyloxy)-2',3'-epoxybutyl]oxane. To a solution of bromo diepoxide **93a** (76.2 mg, 0.156 mmol) in THF/H_2O (3.4 mL, 5:1) was added AgOTf (401 mg, 1.56 mmol) at 25 °C and the mixture was stirred at 25 °C for 1 h, poured in satd aq. $NaHCO_3$ (10 mL), and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc 3:1) and PTLC (SiO_2, hexane-EtOAc, 3:2) to give epoxy oxane **95a** (21.1 mg, 32%). To a solution of **95a** (8.2 mg, 0.0192 mmol) in pyridine (0.2 mL) was added Ac_2O (0.1 mL), and the mixture was

allowed to stand at 25 °C for 16 h, and the volatiles were removed *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc, 3:1) to give the acetate of **95a** (6.8 mg, 76%). The acetate of **95a**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.67-7.70 (4H, m), 7.37-7.45 (6H, m), 4.53 (1H, ddd, *J*=4.9, 9.3, 11.0 Hz), 3.91 (1H, ddt, *J*=4.6, 11.7, 1.7 Hz), 3.77 (1H, dd, *J*=4.1, 11.7 Hz), 3.73 (1H, dd, *J*=4.6, 11.7 Hz), 3.34 (1H, ddd, *J*=4.6, 7.8, 9.3 Hz), 3.33 (1H, dt, *J*=2.9, 11.7 Hz), 2.87 (1H, dt, *J*=2.2, 5.4 Hz), 2.94 (1H, ddd, *J*=2.2, 4.1, 4.6 Hz), 2.15-2.23 (1H, m), 2.03 (3H, s), 1.63-1.79 (4H, m), 1.42 (1H, ddt, *J*=4.6, 11.0, 12.7 Hz), and 1.05 (9H, s); IR (neat), 3072, 3052, 2940, 2860, 1746, 1590, 1474, 1432, 1376, 1334, 1310, 1240, 1188, 1110, 1038, 1008, 998, 938, 900, 872, 824, 794, 740, 704, and 612 cm^{-1}; HR-FD-MS, Calcd for $C_{27}H_{37}O_5Si$ (M^++H), 469.2411, found 469.2399; $[\alpha]^{24}_D$ +8.62° (c 0.34, hexane).

The acetate of 95b; (2*S*,3*R*,2'*S*,3'*S*)-3-Acetoxy-2-[4'-(*tert*-butyldiphenylsilyloxy)-2',3'-epoxybutyl]oxane. To a solution of bromo diepoxide **93b** (79.7 mg, 0.163 mmol) in THF/H_2O (3.5 mL, 5:1) was added AgOTf (419 mg, 1.63 mmol) at 25 °C and the mixture was stirred at 25 °C for 1.5 h, poured in satd aq. $NaHCO_3$ (10 mL), and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc 3:1) and PTLC (SiO_2, hexane-EtOAc, 3:2) to give epoxy oxane **95b** (29.3 mg, 42%). To a solution of **95b** (13.3 mg, 0.0312 mmol) in pyridine (0.2 mL) was added Ac_2O (0.1 mL), and the mixture was allowed to stand at 25 °C for 16 h, and the volatiles were removed *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc, 3:1) to give the acetate of **95b** (13.3 mg, 91%). The acetate of **95b**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.73 (4H, dd, *J*=1.7, 7.8 Hz), 7.36-7.45 (6H, m), 4.51 (1H, ddd, *J*=4.6, 9.5, 10.7 Hz), 3.91 (1H, ddt, *J*=4.4, 11.5, 1.7 Hz), 3.82 (1H, dd, *J*=3.4, 11.7 Hz), 3.69 (1H, dd, *J*=5.1, 11.7 Hz), 3.43 (1H, dt, *J*=3.4, 9.5 Hz), 3.38 (1H, dt, *J*=3.2, 11.5 Hz), 3.03 (1H, ddd, *J*=2.2, 4.6, 7.1 Hz), 2.94 (1H, ddd, *J*=2.2, 3.4, 5.1 Hz), 2.14-2.21 (1H, m), 2.03 (3H, s), 1.62-1.80 (4H, m), 1.45 (1H, ddt, *J*=4.6, 10.7, 12.5 Hz), and 1.05 (9H, s); IR (neat), 3072, 3052, 2936, 2860, 1740, 1590, 1474, 1466, 1432, 1376, 1334, 1308, 1238, 1190, 1104, 1036, 1008, 998, 964, 944, 900, 878, 860, 824, 794, 740, 704, 690, and 612 cm^{-1}; HR-FD-MS, Calcd for $C_{27}H_{37}O_5Si$ (M^++H), 469.2411, found 469.2444; $[\alpha]^{24}_D$ -28.8° (c 0.655, hexane).

(1*R*,6*S*,8*R*,1'*S*)-8-[1'-Acetoxy-2'-(*tert*-butyldiphenylsilyloxy)ethyl]-2,7-dioxabicyclo[4.3.0]nonane (99a). To a solution of bromo diepoxide **93a** (21.8 mg, 0.0445 mmol) in THF/H_2O (1.2 mL, 5:1) was added AgOTf (57.3 mg, 0.223 mmol) at 25 °C and the mixture was stirred at 25 °C for 4 h, poured into satd aq. $NaHCO_3$ (10 mL), and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (2×10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by PTLC (SiO_2 , hexane-EtOAc, 2:1) to give alcohol **96a**. To a solution of **96a** in pyridine (0.2 mL) was added Ac_2O (0.1 mL), and the mixture was allowed to stand at 25 °C for 14 h, and the volatiles were evaporated *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc, 3:1) to give acetate **99a** (9.9 mg, 47% for 2 steps). **99a**: a colorless oil; ^{1}H-NMR (400 MHz, C_6D_6), δ7.76-7.78 (4H, m, PhH), 7.18-7.21 (6H, m, PhH), 5.41 (1H, dt, *J*=3.8, 5.7 Hz, C_1-H), 4.27 (1H, dt, *J*=8.8, 5.7 Hz, C_8H), 3.99 (1H, dd, *J*=3.8, 11.2 Hz, C_2-H), 3.93 (1H, dd, *J*=5.7, 11.2 Hz, C_2-H), 3.70 (1H, ddd, *J*=1.1, 4.4, 11.7 Hz, C_3H), 3.15 (1H, ddd, *J*=3.9, 9.0, 11.7 Hz, C_6H), 3.05 (1H, dt, *J*=2.6, 11.7 Hz, C_3H), 2.94 (1H, ddd, *J*=7.0, 9.0, 11.0 Hz, C_1H), 1.96-2.10 (2H, m, C_9H), 1.89-1.93 (1H, m, C_5H), 1.70 (3H, s, CH_3CO), 1.19-1.31 (2H, m, C_4H, C_5H), 1.15 (9H, s, $C(CH_3)_3$), and 1.05-1.11 (1H, m, C_4H); IR (neat), 3072, 3052, 2952, 2856, 1752, 1490, 1466, 1430, 1392, 1372, 1340, 1310, 1278, 1232, 1124, 1068, 968, 942, 918, 896, 880, 852, 824, 790, 742, 702,

and 610 cm^{-1}; HR-FD-MS, Calcd for $C_{27}H_{37}O_5Si$ (M^++H), 469.2411, found 469.2445; $[\alpha]^{24}_D$ +12.7° (c 0.36, hexane).

(1*S*,6*R*,8*R*,1'*S*)-8-[1'-Acetoxy-2'-(*tert*-butyldiphenylsilyloxy)ethyl]-2,7-dioxabicyclo[4.3.0]nonane (99b). To a solution of bromo diepoxide **93b** (20.2 mg, 0.0413 mmol) in THF/H_2O (1.2 mL, 5:1) was added AgOTf (53.1 mg, 0.207 mmol) at 25 °C and the mixture was stirred at 25 °C for 23 h, poured into satd aq. $NaHCO_3$ (10 mL), and extracted with Et_2O (40 mL). The Et_2O layer was washed with brine (2×10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc, 2:1) to give alcohol **96b**. To a solution of **96b** in pyridine (0.2 mL) was added Ac_2O (0.1 mL) and the mixture was allowed to stand at 25 °C for 14 h, and the volatiles were evaporated *in vacuo*. The residue was purified by PTLC (SiO_2, hexane-EtOAc, 3:1) to give acetate **99b** (8.9 mg, 46% for 2 steps). **99b**: a colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$), δ7.65 (4H, dd, *J*=1.5, 7.7 Hz, PhH), 7.36-7.46 (6H, m, PhH), 5.08 (1H, q, *J*=4.6 Hz, C_1·H), 4.33 (1H, ddd, *J*=3.1, 4.6, 10.3 Hz, C_8H), 3.97 (1H, ddd, *J*=1.3, 4.8, 11.7 Hz, C_3H), 3.79 (1H, dd, *J*=4.6, 11.0 Hz, C_2·H), 3.75 (1H, dd, *J*=4.6, 11.0 Hz, C_2·H), 3.42 (1H, dt, *J*=3.9, 11.7 Hz, C_3H), 3.14 (1H, ddd, *J*=3.9, 8.8, 11.5 Hz, C_6H), 3.03 (1H, ddd, *J*=7.7, 8.8, 10.3 Hz, C_1H), 2.19 (1H, dq, *J*=11.5, 3.9 Hz, C_5H), 2.11 (1H, ddd, *J*=3.1, 7.7, 11.9 Hz, C_9H), 2.05 (3H, s, CH_3CO), 1.86 (1H, dt, *J*=11.9, 10.3 Hz, C_9H), 1.60-1.73 (2H, m, C_4H), 1.44 (1H, dq, *J*=5.1, 11.5 Hz, C_5H), and 1.04 (9H, s, $C(CH_3)_3$); IR (neat), 3072, 3052, 2952, 2860, 1748, 1474, 1466, 1430, 1392, 1372, 1340, 1308, 1278, 1236, 1184, 1124, 1076, 1042, 996, 972, 956, 940, 914, 896, 848, 824, 792, 742, 704, 612, and 592 cm^{-1}; HR-FD-MS, Calcd for $C_{27}H_{37}O_5Si$ (M^++H), 469.2411, found 469.2443; $[\alpha]^{24}_D$ +6.66° (c 0.46, hexane).

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19) In order to avoid the skeletal rearrangement as much as possible, the ratios of **39/40** shown in Scheme 10 were determined by ^{1}H-NMR analyses of crude products, which were pure enough to be identified by ^{1}H-NMR. Judging from both the ^{1}H-NMR spectra and the crude weight, the transfomation of **40** into **39** took place very cleanly without decomposition of **40**.
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(*Received in Japan* 16 *May* 1997; *accepted* 7 *July* 1997)