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Transformation of *cis*-Epoxy Compound to *cis*-2,3-Disubstituted Oxane and Investigation on Propagation Step in the Ring-Expansion Reactions of *cis,trans*-Diepoxy Systems

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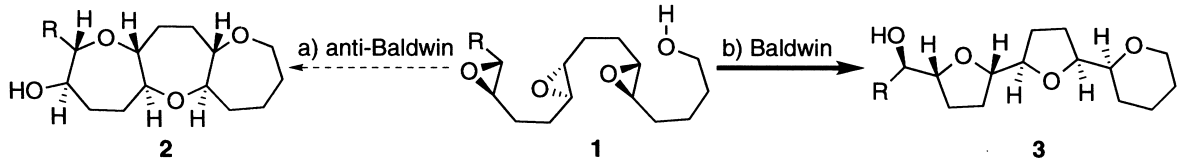
Abstract—Conversion of *cis*-epoxy compounds by successive ring-expansion reaction into *trans*-fused cyclic ethers was examined from both the initiation step and the propagation step. The ring-expansion reaction of *cis*-4,5-epoxy compounds containing a leaving group on C-1 was attempted as a unit process for the successive reaction. When a chloromesyl group was used as a leaving group, the ring expansion proceeded to give an oxane derivative (*endo*-type product) preferentially. On the other hand, investigation of the propagation step was carried out with respect to epoxy oxane derivatives. It was clarified that the ring-expansion reaction of *cis*-2,3-disubstituted oxane derivatives provided spiro acetals as products, not the desired *trans*-fused cyclic ethers, owing to the reaction pathway triggered by 1,2-hydride rearrangement.

Introduction

trans-Fused polycyclic ethers of marine origins, which are represented by brevetoxins,[1] ciguatoxins,[2] maitotoxin[3] and so on, are very interesting compounds owing to the novel molecular structures and biological activities. Especially, the unique ladder structures of these compounds have fascinated many organic synthetic chemists. Some groups have achieved the chemical total syntheses of brevetoxins.[4–6] On the other hand, Nakanishi[7] and Shimizu[8] have proposed that this class of compounds might be biosynthesized from acyclic polyepoxy precursors. If this proposal is synthetically realized, it has been expected that efficient construction of the polyethers could be feasible, because, in this tactic, the stereochemistries of the junctures in the polyethers are supposedly controlled by only those of the epoxy groups. When this cascade reaction is attempted, two ways can be chosen; one is the successive ring-closure reaction of hydroxy polyepoxy compounds, the other is the successive ring-expansion reaction of polyepoxy compounds. The epoxy groups play opposite roles in these two methods; in the former case, the epoxy groups work as an electrophile, in the latter case, as a nucleophile. In the former method, the cyclization of an ordinary hydroxy epoxide such as **1** without any directing groups for opening of the epoxy groups would afford the assembled cyclic polyethers **3** according to Baldwin's rules (Scheme 1).[9] If some directing groups are introduced into the substrate, it might be expected to give a fused cyclic ether by the successive ring-closure method.[10] Actually, Murai's group skillfully succeeded in the construction of a *trans*-fused tricyclic ether from a triepoxy compound.[11] However, as to the systems with some directing groups, the non-removal of them from the products would remain as a difficult problem. Therefore, one of the authors has studied a novel, successive ring-expansion reaction of epoxy compounds in order to investigate whether the direction of the epoxy-opening can be controlled or not with respect to the substrates without any directing groups.[12] The working hypothesis of the first generation is illustrated in Scheme 2.



Scheme 1.

Keywords: cyclic ether; ring-expansion reaction; bridged oxonium ion; spiro acetal.
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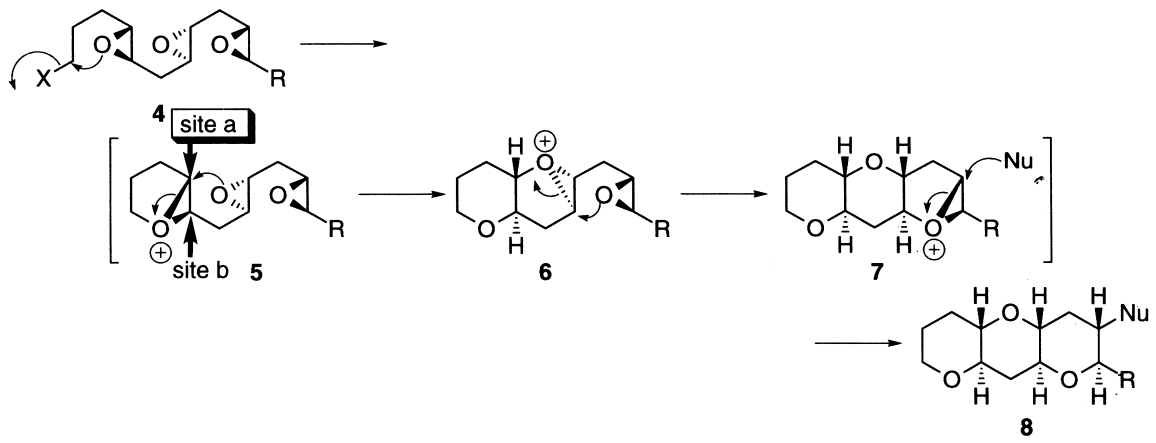
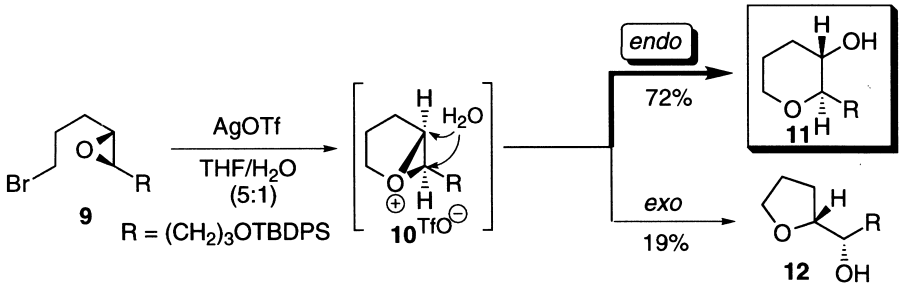


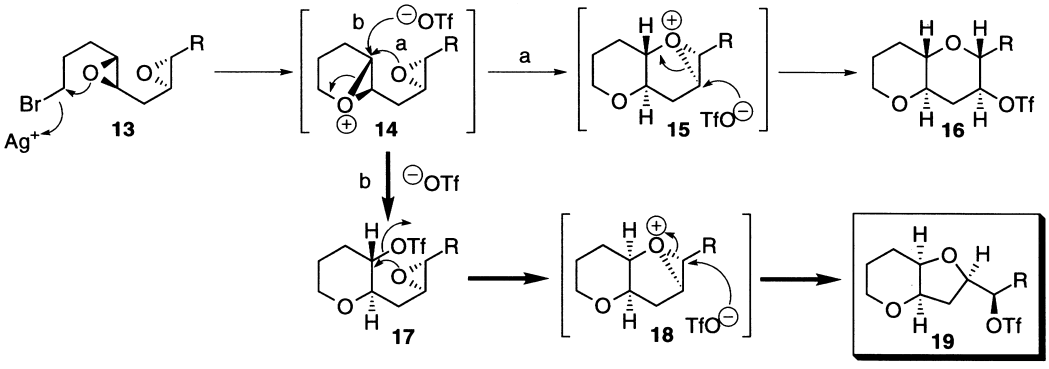
Scheme 2.

The first step (initiation step) is the process in which first bridged oxonium ion **5**[13] would be formed by the intramolecular nucleophilic attack of a first *trans*-epoxy group to a terminal cationic site. The bridged oxonium ion **5** possesses two electrophilic sites (site **a** and site **b**). It was presumed that site **a** might be more electrophilic than site **b** on account of the strain in the bridged system itself in spite of no directing groups on the substrate. Accordingly, in the next propagation step, it was supposed that the second *trans*-epoxy group attacks site **a** on the first oxonium ion **5** to generate second oxonium ion **6**. If the same reaction of the third *trans*-epoxy group is followed by trapping of the last oxonium ion **7** with an external nucleophile (termination step), it was assumed that the target molecule **8** could be synthesized. Previous experiments revealed the following. (1) The ring-expansion reaction of *trans*-1-bromo-4,5-epoxide **9** proceeded in *endo*-mode to give oxane **11** (Scheme 3).[14] (2) The intramolecular nucleophilic attack of the second epoxy group to first oxonium ion **14** (path a in Scheme 4) was a slower process than that of the counter anion of oxonium ions **14** (in this case, triflate anion). Therefore, the one-pot successive ring-expansion reaction of *trans*,*trans*-bromodiepoxide **13** provided *cis*-fused cyclic ether **19** via the double inversion of the juncture's stereochemistry.

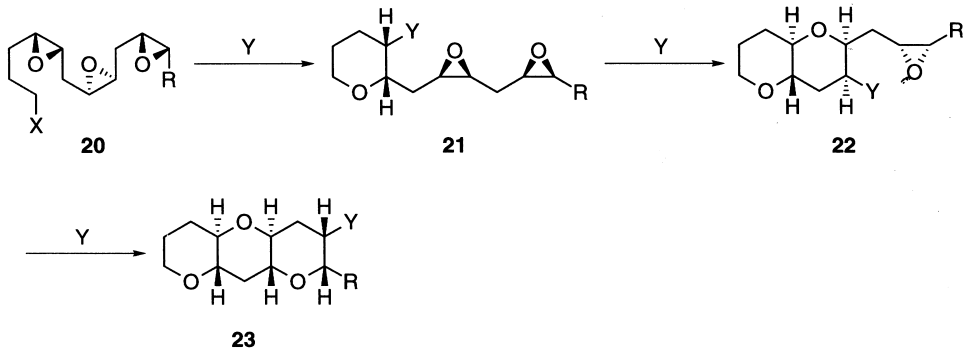
It seemed to us that the formation of the juncture by the double inversion of the stereochemistry might possibly be utilized for the construction of *trans*-fused cyclic ethers. Our new working hypothesis is illustrated in Scheme 5. If the ring-expansion reaction of *cis*-polyepoxy groups on **20** is repeated with the double inversion, it is expected that *trans*-fused cyclic ether **23** can be formed via the intermediates (**21** and **22**). In this report, we describe the results



Scheme 3.



Scheme 4.



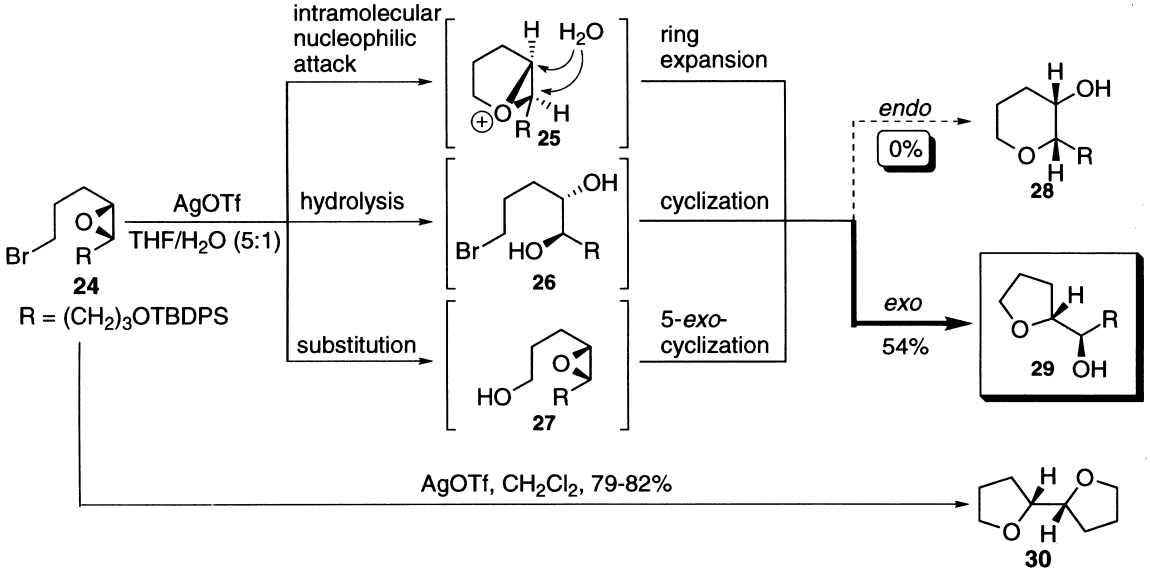
Scheme 5.

with regard to this new strategy from the following two aspects: (1) the single ring-expansion reaction of *cis*-4,5-monoepoxy systems containing a leaving group on C-1 as a unit process for the successive reaction, (2) the propagation step of a *cis*,*trans*-diepoxy system (the simplest propagation model).

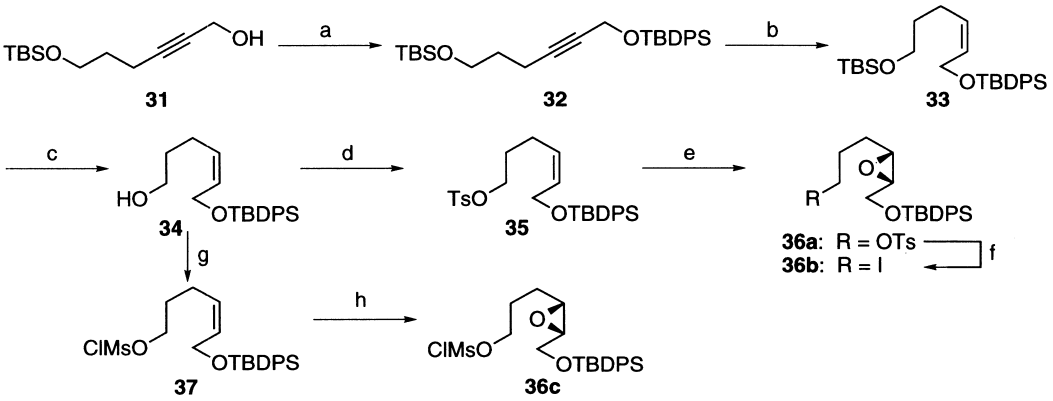
Ring-Expansion Reaction of a *cis*-4,5-Epoxy System Containing a Leaving Group on C-1

In this chapter, the investigation regarding the ring-expansion reaction of *cis*-monoepoxy systems is described. When the ring-expansion reaction of *cis*-bromo epoxide **24** was previously attempted under the conditions of Scheme 3, the only product was oxolane derivative **29** (*exo*-type product).[12d] However, the mechanism generating **29** is unclear (that is to say, it is quite questionable whether **29** is the ring-expanded product or not), because three pathways from **24** to **29** as shown in Scheme 6 were assumed. One is the *exo*-selective ring-expansion reaction via oxonium ion **25**. Another is the cyclization of diol **26** formed by the hydrolysis of the epoxy group on **24**. The third is 5-*exo*-cyclization of hydroxy epoxide **27** produced by the substitution of the bromo group on **24** with water. On the other hand, when the reaction was carried out under anhydrous conditions in order to exclude the above influence of water, unfortunately, assembled bicyclic ether **30** was obtained in good yield by the intramolecular nucleophilic attack of the terminal silyloxy group. Therefore, so as to investigate the ring-expansion reaction of *cis*-epoxy compounds more exactly, the new substrates (**36a**, **36b**, and **36c**) whose side chains cannot participate to the reactive sites were prepared as outlined in Scheme 7. The hydroxy group of alcohol **31**[10a] was protected as the corresponding TBDPS ether **32**. The triple bond in **32** was hydrogenated to afford *cis*-olefin **33**, whose TBS group was selectively removed by treatment with pyridinium *p*-toluenesulfonate in ethanol. Alcohol **34** was converted to sulfonates (**35** and **37**), which were oxidized with *m*CPBA to give *cis*-epoxides **36a** and **36c**, respectively. *cis*-Iodoepoxide **36b** was obtained from **36a** by treatment with TBAI.

With respect to these *cis*-epoxides (**36a**, **36b**, and **36c**), the ring-expansion reactions were examined under the various conditions shown in Table 1. At first, *cis*-iodoepoxide **36b** was treated with AgOTf in aqueous THF to afford only *exo*-product **40b1** similarly to **24** (entry 1). In this reaction, it was observed by TLC analysis that hydroxy epoxide **36d** (X=OH) was temporarily generated and disappeared at the end point of the reaction. The structure of **36d** was identified as the corresponding acetate **36e** (X=OAc),



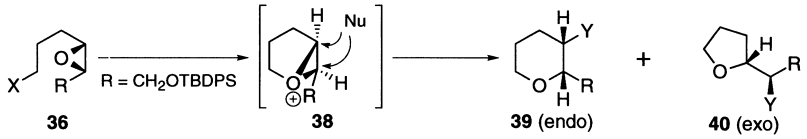
Scheme 6.



Scheme 7. *Reagents and conditions:* (a) TBDPSCl, imidazole, CH_2Cl_2, 25°C, 10 min, 92%; (b) H_2, Lindlar cat., quinoline, MeOH, 25°C, 10 min, 96%; (c) PPTS, EtOH, 25°C, 13 h, 92%; (d) TsCl, Et_3N, DMAP, 25°C, 2.5 h, 92%; (e) *m*CPBA, Na_2HPO_4, 25°C, 2.5 h, 74%; (f) TBAI, THF, 65°C, 3 h, 81%; (g) chloromethanesulfonyl chloride, Et_3N, DMAP, 0°C, 2.5 h, 86%; (h) *m*CPBA, Na_2HPO_4, CH_2Cl_2, 25°C, 3.5 h, 76%.

because **36d** was readily cyclized to **40b1**. Consequently, it was obvious that the reaction using *cis*-4,5-epoxy-1-halides (**24** and **36b**) in aqueous tetrahydrofuran was not a ring-expansion reaction, but 5-*exo*-cyclization reaction of the hydroxy epoxide intermediate **36d**. The above result suggests that the intramolecular nucleophilic attack of the *cis*-epoxy group is a slower process than the intermolecular attack of an external nucleophile such as water. Accordingly, in order to force the *cis*-epoxy group to attack the internal electrophilic site, the external nucleophile for the bridged oxonium ion **38** must not exist at the starting point of the reaction. Therefore, the following reactions were carried out under the conditions without adding an external nucleophile. In the case of treatment of epoxy iodide **36b** with silver triflate in anhydrous dichloromethane (entry 2), it was expected that a triflate anion (the counter anion of oxonium ion **38**) was the scavenger of **38**. However, the products were a complex mixture which consisted of the unknown high-polar products. This result suggested that the anticipated products (**39b2** or **40b2**) were quite unstable because they contain a trifluoromethanesulfonyloxy group or the intramolecular nucleophilic attack of the *cis*-epoxy group could not occur for **36b** itself to decompose because of the low reactivity of the *cis*-epoxy group. In entry 3, the use of silver tosylate as a Lewis acid resulted in the substitution of the iodo group into a tosyloxy group. This result in entry 3 revealed that the nucleophilic ability of the *cis*-epoxy group in this system was lower than that of a weak nucleophile such as a tosylate anion. Therefore, it was considered that any nucleophiles containing the counter anions of Lewis acids should not exist in the reaction system. That is to say, the reaction should depend only on the nucleophilic ability of the *cis*-epoxy group of **36** without adding a Lewis acid in order to form oxonium ion **38**, which should be captured by the X groups eliminated from **36**. On the basis of this concept, **36a** (X=OTs) was heated at reflux in acetonitrile or nitromethane only to recover the starting materials quantitatively (entry 4 and 5). It turned out that the tosyl group did not have enough leaving ability for the nucleophilic attack of the epoxy group of **36a**. Next, the leaving group was changed to a chloromesyloxy group, which was reported by Nakata's group as a better leaving group for the cyclic ether formation.[15] Epoxide **36c** was heated at 83°C in various solvents (1,2-dichloroethane, chlorobenzene, toluene, and benzene) to give two ring-expanded products (**39c** and **40c**) (entry 6 to 9). The *endo*-isomer **39c** was major in all cases. Though the ratio of the *endo*-isomer increased with decreasing the polarity of

Table 1. Ring-expansion reactions of *cis*-epoxy systems **36**



36 **38** **39** (endo) **40** (exo)

Entry	**36**	X	Conditions	Solvent	Nu	Y	**39, 40**	Yield[a] (**39**+**40**) (%)	Ratio[b] (**39**:**40**)	Recovered **36** (%)
1	**b**	I	AgOTf, 25°C, 3 h	THF/H_2O (5:1)	YH	OH	**b1**	75	0.100	0
2	**b**	I	AgOTf, −30°C, 0.5 h	CH_2Cl_2	Y^-	TfO	**b2**	Decomposition		0
3	**b**	I	AgOTs, 83°C, 2 h	CH_3CN	Y^-	TsO	**b3**	–	–	0[c]
4	**a**	TsO	82°C, 2.5 h	CH_3CN	Y^-	TsO	**a**	No reaction		99
5	**a**	TsO	101°C, 2.5 h	CH_3NO_2	Y^-	TsO	**a**	No reaction		99
6	**c**	ClMsO	83°C, 48 h	$Cl(CH_2)_2Cl$	Y^-	ClMsO	**c**	76	2.0:1	17
7	**c**	ClMsO	83°C, 186 h	PhCl	Y^-	ClMsO	**c**	71	1.9:1	6.7
8	**c**	ClMsO	83°C, 168 h	$PhCH_3$	Y^-	ClMsO	**c**	65	2.7:1	43
9	**c**	ClMsO	83°C, 192 h	PhH	Y^-	ClMsO	**c**	37	3.2:1	54
10	**c**	ClMsO	82°C, 7.5 h	CH_3CN	Y^-	ClMsO	**c**	36	1.1:1	0

[a] The yield based on conversion.
[b] The ratios were determined by ^1H NMR analyses.
[c] The 4,5-epoxy-1-tosylate was obtained in 97% yield by substitution reaction.

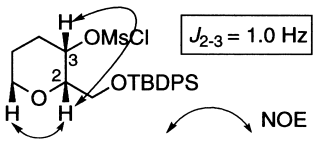


Figure 1.

solvents, the reaction rates tended to diminish. On the other hand, although the reaction rate was greatly accelerated in acetonitrile of a more polar solvent, the marked lowering of both yield and the ratio of the *endo*-isomer was observed (entry 10). The acceleration of reaction rate in the higher polar solvent is attributed to lowering the activation energy to oxonium ion **38** by solvation. The structure of **39c** was determined by ^{1}H NMR analyses (NOE experiment and the H–H coupling constant; J_{2-3}=1.0 Hz) as illustrated in Fig. 1. The structure of **40c** was determined by comparing the ^{1}H NMR spectrum of **40c** with that of the chloromesylate prepared from the hydroxy oxolane **40b1**.

In order to explain the relation between the lowering of the *endo*-selectivity and the polarity of the solvent, the following three facts can be taken into account as possible reasons: (1) the conversion of the kinetic *endo*/*exo*-ratio; (2) the skeletal rearrangement of the *endo*-isomer **39c** into the *exo*-isomer **40c**; (3) the selective decomposition of the *endo*-isomer **39c** (the *endo*-selective decomposition). However, evaluating the net kinetic *endo*/*exo*-ratio is extremely difficult, because these systems possessing a good leaving group such as a sulfonyloxy group always involve the possibilities of the above (2) and (3). Therefore, herein, the relation was discussed except for (1). In order to investigate thermodynamic stability between the *endo*-isomer **39c** and the *exo*-isomer **40c**, the experiments shown in Table 2 were carried out. At first, a 17:1 mixture of **39c** and **40c** was heated at 83°C in 1,2-dichloroethane (entry 1). After 48 h, the ratio changed to 13:1 in 67% recovery. On the other hand, when a 1:15 mixture of **39c** and **40c** was exposed under the same conditions, the *endo*/*exo* ratio changed to 1:23 in 85% recovery (entry 2). The proportion of the *endo*-isomer **39c** was lowered in both experiments. However, this result can not prove that the *exo*-isomer **40c** was thermodynamically more stable than the *endo*-isomer **39c** (in other words, the skeletal rearrangement of **39c** into **40c**), because the low recoveries cannot rule out the possibility of the *endo*-selective decomposition. Similar experiments were also undertaken in acetonitrile (entry 3 and 4) to result in decreasing the proportion of the *endo*-isomer **39c** in a similar tendency as in the above entry 1 and 2. The recoveries in acetonitrile were lower than those in 1,2-dichloroethane, and accompanied with unknown high-polar decomposed products. Although the thermodynamic stability between **39c** and **40c** was unclear from the results shown in Table 2, it was observed that the recoveries from the mixture of *endo*/*exo* (17:1) (entry 1 and 3) were lower than those of the mixture from *endo*/*exo* (1:15) (entry 2 and 4). This result suggests that the *endo*-isomer **39c** decomposed more rapidly than the *exo*-isomer **40c**. Accordingly, concerning the ring expansion reaction of **36c**, the lowering of the *endo*-preference in a high-polar solvent is attributed to the *endo*-selective decomposition. Furthermore, the net *endo*-selectivity can be estimated to be higher than the apparent ratios. In any event, it was revealed that the formation of the *endo*-isomer **39c** was at least kinetically favorable, because the skeletal rearrangement of the *exo*-isomer **40c** into the *endo*-isomer **39c** was not observed under the thermodynamic conditions. The reason for the lability of *endo*-isomer **39c** will be discussed in the next chapter.

Investigation of Propagation Step in the Ring-Expansion Reaction

In this chapter, the propagation steps in the successive ring-expansion reactions of the diepoxy systems **42**, which is illustrated as a process from **43** to **44** in Scheme 8, are discussed. *cis*,*trans*-Diepoxides **42** are the simplest model for obtaining all *trans*-fused cyclic ethers, because, for the relative stereochemistry of the two substituent groups (R and OMsCl) on the final ring in order to be the *trans*-form, the stereochemistry of the last epoxy group must be the *trans*-form.

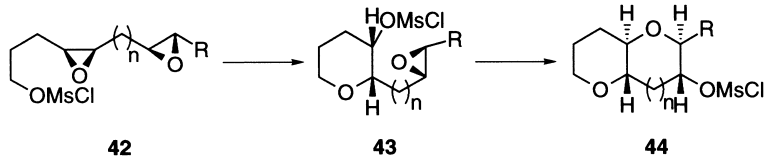
At first, the successive reactions with regard to *cis*,*trans*-diepoxides **55** were investigated. A diastereomeric mixture of *cis*,*trans*-epoxides (**55a** and **55b**) was prepared as outlined in Scheme 9. Allylic alcohol **46**, which was prepared by hydrogenation of propargylic alcohol **45**,[12d] was converted into allylic bromide **47** with Ph_3P and CBr_4 in 85% yield. Allylic bromide **47** was coupled with 1-lithio-3-tetrahydropyranyloxypropyne to afford enyne **48**. Removal of the tetrahydropyranyl group from **48** by methanolysis gave alcohol **49** in 93% yield. The alcohol **49** was reduced with $LiAlH_4$ to obtain allylic alcohol **50** (88%), which was transformed into epoxide **51** with TBHP and $VO(acac)_2$ in 85% yield.[16] Protection of the hydroxy group on **51** was followed by removal of the 4-methoxybenzyl group. Alcohol **53** was converted into sulfonate **54** with chloromethanesulfonylchloride (79%). The sulfonate **54** was oxidized with *m*-chloroperbenzoic acid to give a diastereomeric mixture of diepoxides (**55a** and **55b**).

The mixture of **55a** and **55b** was heated at reflux in 1,2-dichloroethane to afford epoxy oxanes (**56a** and **56b**) in 25%

Table 2. The variations of the ratios between the *endo*-isomer (**39c**) and the *exo*-isomer (**40c**) under thermodynamic conditions

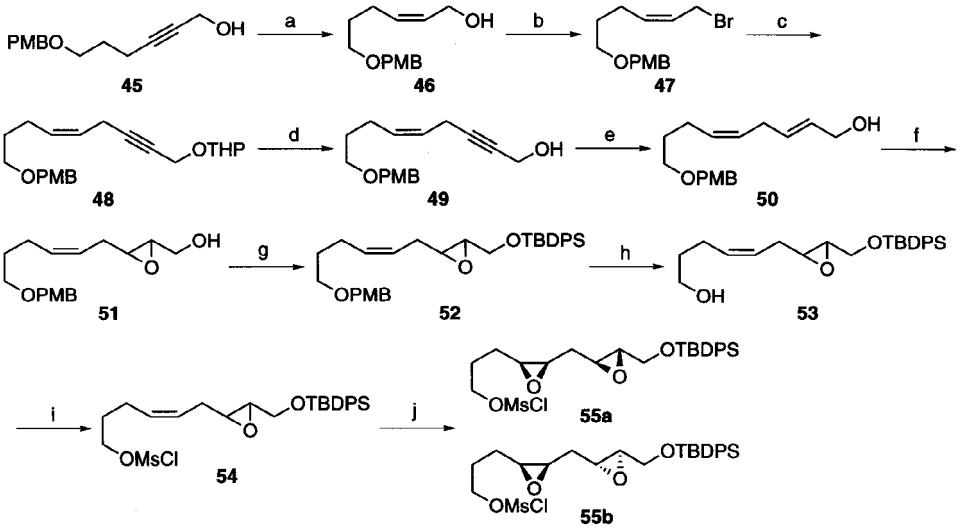
Entry	Initial ratio (**39c**:**40c**)[a]	Conditions	Final ratio (**39c**:**40c**)[a]	Recovery (%)
1	17:1	$ClCH_2CH_2Cl$, reflux, 48 h	13:1	67
2	1:15	$ClCH_2CH_2Cl$, reflux, 48 h	1:23	85
3	17:1	CH_3CN, reflux, 7.5 h	5.2:1	36
4	1:15	CH_3CN, reflux, 7.5 h	1:171	42

[a] The ratios were determined by ^{1}H NMR analyses.

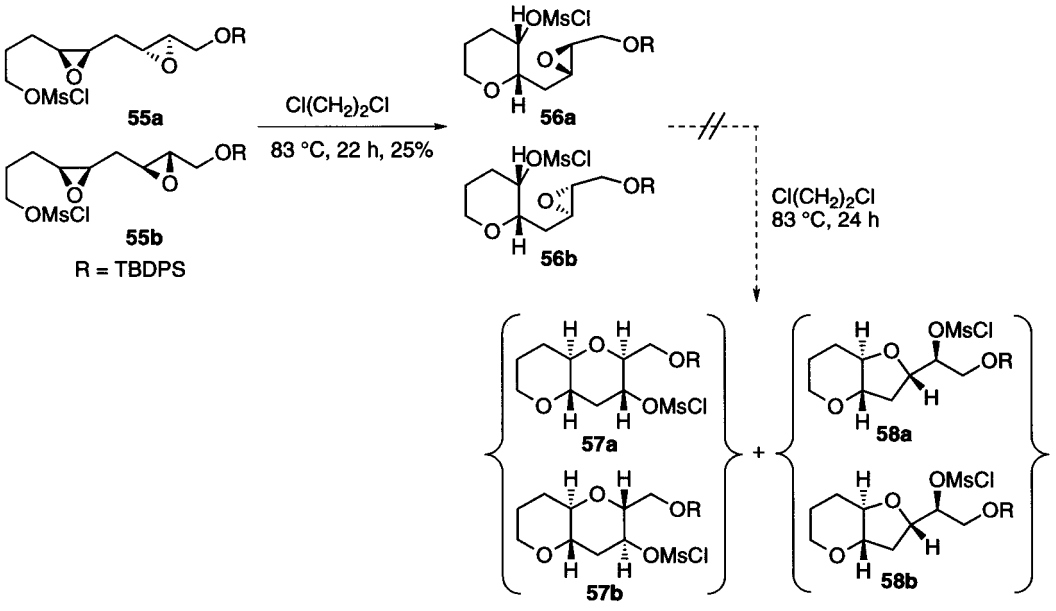


Scheme 8.

yield with epoxy oxolanes (17%) and recovered **55a** and **55b** (25%) (Scheme 10). The other products were unknown high-polar decomposed products. Epoxy oxanes (**56a** and **56b**) were treated under the same conditions to be gradually changed into the high-polar decomposed products, which were not separable. No fused cyclic ethers were detected at all. It seems that the reason why the ring-expansion reaction stopped before the second ring-expansion occurred is owing to the distance of both reactive sites (the epoxy group and the chloromesyloxy group). If the second ring-expansion reaction takes place, the chloromesyloxy group and the side chain containing the epoxy group must orient axial and



Scheme 9. *Reagents and conditions:* (a) H_2, Lindlar cat., quinoline, pyridine, 25°C, 1.5 h, 98%; (b) Ph_3P, CBr_4, CH_2Cl_2, 25°C, 10 min, 85%; (c) LiCC-CH_2OTHP, THF, −78 to 25°C (28 h), 85%; (d) *p*-TsOH, MeOH, 25°C, 3 h, 93%; (e) $LiAlH_4$, THF, 25°C, 14 h, 88%; (f) $VO(acac)_2$, TBHP, benzene, 25°C, 1 h, 85%; (g) TBDPSCl, imidazole, CH_2Cl_2, 25°C, 10 min, >99%; (h) DDQ, CH_2Cl_2/H_2O (10:1), 25°C, 1 h, 98%; (i) $ClCH_2SO_2Cl$, pyridine, CH_2Cl_2, 0°C, 2 h, 79%; (j) *m*CPBA, Na_2HPO_4, CH_2Cl_2, 25°C, 2.5 h, 95%.



Scheme 10.

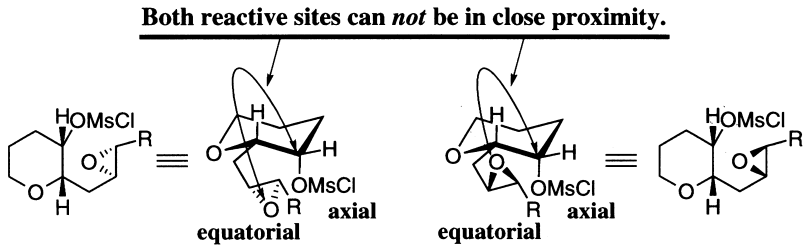
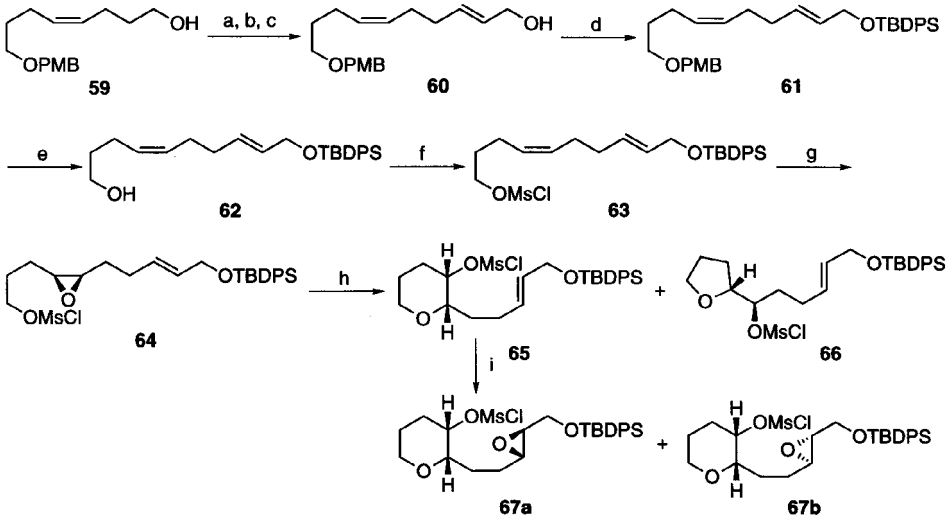


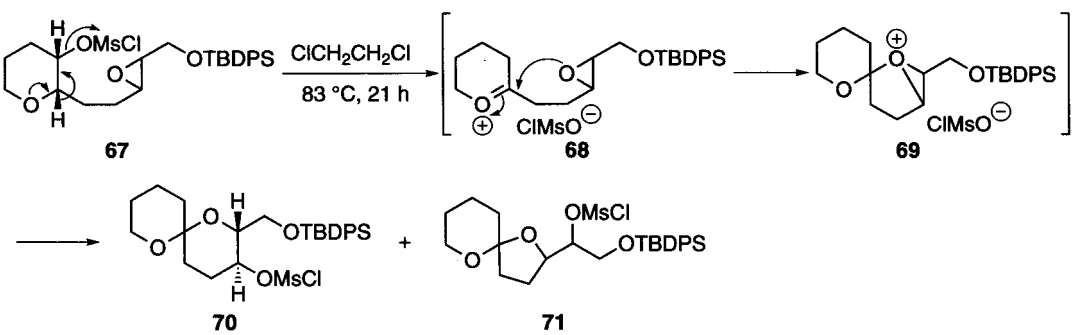
Figure 2.

equatorial, respectively, as illustrated in Fig. 2. Because both reactive sites cannot be in close proximity on account of the strain arisen in the systems, it is presumed that the propagation step of the successive ring expansion could not proceed.

Next, in order to resolve this problem, the propagation step was examined regarding the substrates possessing a longer side chain (that is, a more flexible side chain). New epoxy oxanes (**67a** and **67b**) were prepared as outlined in Scheme 11. PCC-oxidation of alcohol **59**[12d] was followed by Wittig reaction and the reduction with DIBAH to provide allylic alcohol **60** in 67% yield for 3 steps. After protecting the hydroxy group on **60** as a silyl ether, the 4-methoxybenzyl group was removed with DDQ in aqueous dichloromethane. The obtained alcohol **62** was converted into chloromesylate **63**. The compound **63** was treated with one equivalent of *m*-chloroperbenzoic acid to afford monoepoxide **64** in 43% yield with the monoepoxy isomer (13%) and the diepoxides (14%). Though epoxide **64** was transformed into *cis*-oxane **65** (the *endo*-isomer) in 18% yield by ring-expansion reaction, **65** was unfortunately a minor product. Oxolane **66** (the *exo*-isomer) was obtained in 34% yield as a major product with the unknown high-polar decomposed products. As to the ring-expansion reaction of epoxide **64**, the *endo*/*exo*-ratio was contrary to that of the previous experiments.



Scheme 11. *Reagents and conditions:* (a) PCC, MS4A, CH_2Cl_2, 25°C, 1.5 h; (b) $Ph_3P{=}CHCO_2Me$, benzene, 24 h; (c) DIBAH, CH_2Cl_2, −80°C, 1 h, 3 steps for 67%; (d) TBDPSCl, imidazole, CH_2Cl_2, 0°C, 30 min, 97%; (e) DDQ, CH_2Cl_2/H_2O (10:1), 25°C, 2 h, 81%; (f) $ClCH_2SO_2Cl$, pyridine, CH_2Cl_2, 0°C, 1.5 h, 92%; (g) *m*CPBA, Na_2HPO_4, CH_2Cl_2, 25°C, 30 min, 43%; (h) 83°C, 6 h, $ClCH_2CH_2Cl$, **65** (18%), **66** (34%); (i) *m*CPBA, Na_2HPO_4, CH_2Cl_2, 25°C, 2 h, 72%.



Scheme 12.

Figure 3.

This phenomenon will be discussed below. The compound **65** was oxidized with *m*-chloroperbenzoic acid to obtain a diastereomeric mixture of the epoxy oxanes (**67a**:**67b**=1:1) in 76% yield. The mixture of **67a** and **67b** was heated at reflux in 1,2-dichloroethane to carry out the ring-expansion reaction. However, the products were not the desired fused cyclic ethers, but spiro acetals **70** (ca. 31%) and **71** (ca. 9%), unexpectedly.[17] Although the carbon skeleton and the C2–C3's relative stereochemistry of **70** were determined by ^{1}H NMR (H–H coupling constant; J_{2-3}=10.0 Hz), ^{13}C NMR (C-6=95.22 ppm) and H–H COSY, the stereochemistry of the acetal moiety could not be clarified. The structure of **71** could not be established except for only the planar structure determined by ^{1}H NMR and H–H COSY, because of the small amount of **71**. It is assumed that **70** and **71** were generated via non-bridged oxonim ion **68** and bridged oxonium ion **69** as illustrated in Scheme 12. Production of a spiro acetal from a *cis*-disubstituted hydroxy oxepane via a non-bridged oxonium ion is reported by Martin et al.,[18] although the proposed reaction mechanism is different from ours. Whether **70** and **71** were generated from **67a** or **67b** is not important, because at the point of formation of non-bridged oxonium ion **68**, all asymmetric centers on **67**'s ring disappear. It is presumed that this 1,2-hydride rearrangement of the *cis*-2,3-disubstituted oxane system was promoted by the following two stereoelectronic effects shown in Fig. 3: (1) the overlap between the lone pair orbital of an axial position and the antibonding orbital of an adjacent C–H bond, and (2) the overlap between the bonding orbital of a C–H bond and the antibonding orbital of an adjacent C–OMsCl bond. Although the desired fused cyclic ether could not be obtained, this formation of spiro acetal **70** via the 1,2-hydride shift is interesting, because this property of the *cis*-2,3-disubstituted oxane system seems to explain the lability of the oxanes (**39c** and **56**) and the *exo*-preferential ring expansion of the epoxides **64**. Oxolane **40c** (the isomer of **39c**) is much less subject to the above stereoelectronic effects than oxane **39c**, because the **40c**'s flexible conformation prevents the corresponding orbitals from sufficient overlapping. Therefore, **39c** would be converted into the corresponding non-bridged oxonium ion more rapidly than **40c** to decompose faster than **40c** on account of the instability of the non-bridged oxonium ion. It is considered that the formation of the non-bridged oxonium ion is greatly accelerated in a high-polar solvent such as acetonitrile by solvation. This assumption seems quite reasonable, because it can explain why the ratio of the *endo*-isomer decreased with increasing the polarity of the solvents (in other words, why the *endo*-isomer decomposed more rapidly than the *exo*-isomer). It is assumed that the decomposition of **56a** and **56b** in dichloroethane by a prolonged reaction time took place by a similar mechanism. Although there is no obvious experimental evidence at all regarding the *exo*-preferential ring expansion of the epoxides **64**, the participation of the intramolecular olefin to the non-bridged oxonium ion might promote the decomposition of the *endo*-isomer **65**.

Conclusion

In this report, in order to construct the *trans*-fused cyclic ethers, the successive ring-expansion reaction of the diepoxy systems containing the *cis*-epoxy group was investigated from both the unit reaction using the *cis*-monoepoxy system **36** without a directing group and the propagation step in the successive reaction. With respect to the ring-expansion reaction of **36**, when the chloromesyloxy group was used as a leaving group, the ring-expansion reaction proceeded preferentially in *endo*-fashion. It was speculated that the *endo*-product was the kinetically favorable compound as well as in the case of the *trans*-epoxy isomer. The ratio of the *endo*-isomer increased with decreasing the polarity of solvents. As to the propagation step, it was clear that the *cis*-2,3-disubstituted oxane system, which was the ring-expanded product of *cis*-epoxy compound, underwent readily 1,2-hydride rearrangement. Consequently, epoxy oxanes (**67a** and **67b**) were not converted into the desired *trans*-fused cyclic ethers, but into spiro acetal **70** by the ring expansion reaction of the epoxy group. It was assumed that this ring-expansion reaction proceeded via the non-bridged oxonium ion and the bridged oxonium ion. It was suggested that this novel property of the *cis*-2,3-disubstituted oxane system affected greatly also the *endo*/*exo*-ratio of the ring-expansion reaction of **36c**.

Experimental

Solvents and reagents were dried and distilled before use. Dichloromethane, 1,2-dichloroethane, benzene, acetonitrile, nitromethane, and triethylamine were distilled from calcium hydride. Tetrahydrofuran was distilled from sodium benzophenone ketyl. Normal reagent-grade solvents were used for flash chromatography, preparative thin-layer chromatography (PTLC), and extraction.

All reactions were monitored by thin-layer chromatography (TLC) with precoated silica gel (SiO_2) plates (MERCK, Silica gel 60 F254 Art. 1.05554). Visualization was achieved via ultraviolet light and a 5.6% ethanolic *p*-anisaldehyde solution containing 5.6% of concentrated sulfuric acid-heat. For flash chromatography was utilized SiO_2 (MERCK, Silica gel 60 1.09385. 0925). For PTLC were utilized precoated SiO_2 plates (MERCK, Silica gel 60 F254 1.05744 or 1.05715). HPLC were run with a HITACHI HPLC Pump L-7100 equipped with a HITACHI UV detector L-7400. For HPLC was utilized SiO_2 column (Inertsil ODS-3, GL Sciences Inc.).

The NMR spectra were recorded on Varian model VXR200S or VXR500 spectrometers in chloroform-d_1 ($CDCl_3$) or benzene-d_6 (C_6D_6). Infrared (IR) spectra were obtained on a JASCO model FT/IR-5000 infrared spectrophotometer in neat state. Chemical shifts (δ) are reported with tetramethylsilane (TMS) (δ=0.00 ppm) or benzene (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. High-resolution mass spectra (HR-MS) were obtained on a JEOL model JMS600 mass spectrometer under electron ionization (EI) and chemical ionization (CI), a JEOL model JMS-SX102A mass spectrometer under field desorption (FD) condition.

All reactions were carried out under anhydrous conditions and nitrogen atmosphere, unless otherwise noted.

6-(*tert*-Butyldimethylsilyloxy)-1-(*tert*-butyldiphenylsilyloxy)-2-hexyne (32). To a solution of propargylic alcohol **31** (1.54 g, 6.74 mmol) in CH_2Cl_2 (34 mL) were added imidazole (1.14 g, 16.8 mmol) and *tert*-butyldiphenylsilyl chloride (1.93 mL, 7.41 mmol) at 0°C. The mixture was stirred at 25°C for 10 min, diluted with Et_2O (150 mL), and washed with H_2O (50 mL). The organic layer was separated, 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, 100:1) to give silyl ether **32** (2.98 g, 92%) as a colorless oil: R_f=0.71 (hexane–EtOAc, 4:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.75–7.69 (4H, m), 7.48–7.33 (6H, m), 4.30 (2H, t, J=2.2 Hz), 3.66 (2H, t, J=6.0 Hz), 2.25 (2H, tt, J=2.2, 7.2 Hz), 1.72–1.59 (2H, m), 1.07 (9H, s), 0.89 (9H, s), and 0.05 (6H, s); IR (neat) 3076, 3054, 2958, 2934, 1473, 1431, 1390, 1377, 1363, 1257, 1145, 1110, 1073, 1000, 973, 940, 837, 777, 739, and 702 cm^{-1}; HR-CI-MS calcd for $C_{28}H_{43}O_2Si_2$ (M^++H) 467.2802, found 467.2834.

(2*Z*)-6-(*tert*-Butyldimethylsilyloxy)-1-(*tert*-butyldiphenylsilyloxy)-2-hexene (33). To a solution of alkyne **32** (2.88 g, 5.99 mmol) in MeOH (35 mL) were added quinoline (0.22 mL) and Pd/$CaCO_2$ (0.288 g) at 25°C and the mixture was stirred at 25°C for 10 min under hydrogen atmosphere and filtered through Celite. The filtrate was concentrated in vacuo. The residue was purified by flash chromatography (SiO_2, hexane–EtOAc, 100:1) to give alkene **33** (2.76 g, 96%) as a colorless oil: R_f=0.67 (hexane–EtOAc, 8:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70–7.65 (4H, m), 7.43–7.35 (6H, m), 5.64–5.57 (1H, m), 5.44–5.39 (1H, m), 4.26 (2H, dd, J=0.5, 6.0 Hz), 3.52 (2H, t, J=6.5 Hz), 1.92 (2H, q, J=7.5 Hz), 1.48 (2H, quin, J=7.5 Hz), 1.04 (9H, s), 0.85 (9H, s), and 0.00 (6H, s); IR (neat) 3074, 3020, 2958, 2934, 2862, 1473, 1429, 1390, 1363, 1257, 1110, 835, 777, 741, and 702 cm^{-1}; HR-CI-MS calcd for $C_{28}H_{45}O_2Si_2$ (M^++H) 469.2958, found 469.2913.

(4*Z*)-6-(*tert*-Butyldiphenylsilyloxy)-4-hexen-1-ol (34). To a solution of silyl ether **33** (2.72 g, 5.63 mmol) in ethanol (38 mL) was added pyridinium *p*-toluenesulfonate (0.141 g, 0.563 mmol) and the mixture was stirred at 25 °C for 12 h. The solvent was removed in vacuo. The residue was purified by flash chromatography (SiO_2, hexane–EtOAc, 10:1) to give alcohol **34** (1.84 g, 92%) as a colorless oil: R_f=0.11 (hexane–EtOAc, 8:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70–7.66 (4H, m), 7.44–7.36 (6H, m), 5.66–5.61 (1H, m), 5.47–5.42 (1H, m), 4.25 (2H, dd, J=0.5, 6.0 Hz), 3.66 (1H, t, J=6.5 Hz), 3.59–3.54 (2H, m), 2.03–1.98 (2H, m), 1.55 (2H, quin, J=6.5 Hz), and 1.04 (9H, s); IR (neat) 3074, 3020, 2934, 2862, 1475, 1429, 1243, 1112, 1075, and 824 cm^{-1}; HR-FD-MS calcd for $C_{22}H_{31}O_2Si$ (M^++H) 355.2168, found 355.2113.

(2*Z*)-1-(*tert*-Butyldiphenylsilyloxy)-6-(*p*-toluenesulfonyloxy)-2-hexene (35). To a solution of alcohol **34** (0.851 g, 2.40 mmol) in CH_2Cl_2 (24 mL) were added Et_3N (1.00 mL, 7.20 mmol), tosyl chloride (0.549 g, 2.88 mmol), and 4-dimethylaminopyridine (29.3 mg, 0.240 mmol) at 0°C. The mixture was stirred at 25°C for 2.5 h, diluted with diethyl ether (140 mL), and washed with satd aq. NH_4Cl (100 mL). The organic layer was separated, washed with satd aq. $NaHCO_3$ (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, 20:1) to give sulfonate **35** (1.13 g, 92%) as a colorless oil: R_f=0.49 (hexane–EtOAc, 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (2H, d, J=8.0 Hz), 7.68–7.66 (4H, m), 7.44–7.35 (6H, m), 7.29 (2H, d, J=8.0 Hz), 5.63–5.58 (1H, m), 5.30–5.25 (1H, m), 4.18 (2H, dd, J=0.5, 6.5 Hz), 3.93 (2H, t, J=6.0 Hz), 2.42 (3H, s), 1.87 (2H, q, J=7.5 Hz), 1.62–1.57 (2H, m), and 1.04 (9H, s); IR (neat) 3074, 3020, 2934, 2862, 1475, 1429, 1243, 1112, 1075, and 824 cm^{-1}; HR-EI-MS calcd for $C_{25}H_{27}O_4SSi$ (M^+-tBu) 451.1399, found 451.1395.

(2*R,3*R**)-1-(*tert*-Butyldiphenylsilyloxy)-6-(*p*-toluenesulfonyloxy)-2,3-epoxyhexane (36a).** To a solution of olefin **35** (627 mg, 1.23 mmol) in CH_2Cl_2 (25 mL) cooled to 0°C were added Na_2HPO_4 (1.88 g, 6.17 mmol) and *m*-chloroperbenzoic acid (608 mg, 2.47 mmol) and the solution was stirred at 25°C for 3 h, and satd aq. $NaHCO_3$ (5 mL) and satd aq. $Na_2S_2O_3$ (5 mL) was added at 0°C. The mixture was extracted with Et_2O (140 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, 20:1) to give epoxide **36a** (481 mg, 74%) as a colorless oil: R_f=0.40 (hexane–EtOAc, 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (2H, d, J=8.0 Hz), 7.68–7.66 (4H, m), 7.45–7.38 (6H, m), 7.30 (2H, d, J=8.0 Hz), 4.04 (1H, dt, J=10.0, 6.0 Hz), 3.98 (1H, dt, J=10.0, 6.0 Hz), 3.76 (1H, ddd, J=1.5, 5.0, 12.0 Hz), 3.68 (1H, ddd, J=3.0, 5.0, 12.0 Hz), 3.14–3.11 (1H, m) 2.88 (1H, dt, J=8.5, 5.0 Hz), 2.42 (3H, s), 1.83–1.73 (2H, m), 1.53–1.46 (1H, m), 1.33–1.27 (1H, m), and 1.05 (9H, s); IR (neat) 3074, 2962, 2934, 1601, 1473, 1431, 1363, 1178, 1112, 971, 932, 824, 743, 706, 663, and 613 cm^{-1}; HR-EI-MS calcd for $C_{25}H_{27}O_5SSi$ (M^+-tBu) 467.1348, found 451.1351.

(2*R,3*R**)-1-(*tert*-Butyldiphenylsilyloxy)-6-iodo-2,3-epoxyhexane (36b).** To a solution of tosylate **36a** (54.8 mg, 0.104 mmol) in THF (3 mL) was added tetrabutylammonium iodide (46.1 mg, 0.120 mmol) and the solution was stirred at 65°C for 3 h. The solvent was removed in vacuo. The residue was purified by flash chromatography (SiO_2, hexane–EtOAc, 100:1) to give iodide **36b** (40.3 mg, 81%) as a colorless oil; R_f=0.60 (hexane–EtOAc, 4:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.72–7.67 (4H, m), 7.49–7.35 (6H, m), 3.83 (1H, dd, J=5.6, 11.4 Hz), 3.72 (1H, dd, J=5.4, 11.4 Hz), 3.23–3.11 (3H, m), 3.18–3.08 (1H, m), 2.95 (1H, ddd, J=5.4, 5.6, 7.6 Hz), 2.05–1.87 (2H, m), 1.62–1.39 (2H, m), and 1.07 (9H, s); IR (neat) 3074, 2962,

2934, 1473, 1429, 1392, 1363, 1261, 1228, 1112, 824, 741, and 704 cm^{-1}; HR-EI-MS calcd for $C_{18}H_{20}IO_2Si$ (M^+-tBu) 423.0278, found 423.0276.

(2*Z*)-1-(*tert*-Butyldiphenylsilyloxy)-6-chloromethanesulfonyloxy-2-hexene (37). To a solution of alcohol **34** (50.5 mg, 0.140 mmol) in CH_2Cl_2 (1.4 mL) were added Et_3N (60.0 mL, 0.430 mmol), chloromethanesulfonyl chloride (20.0 mL, 0.210 mmol), and 4-(dimethyl)aminopyridine (1.7 mg, 0.014 mmol) at 0°C. The mixture was stirred at 0°C for 2.5 h, diluted with Et_2O (40 mL), and washed with satd aq. NH_4Cl (20 mL). The organic layer was separated, 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 flash chromatography (SiO_2, hexane–EtOAc, 20:1) to give sulfonate **37** (57.6 mg, 86%) as a colorless oil: R_f=0.44 (hexane–EtOAc, 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69–7.66 (4H, m), 7.45–7.37 (6H, m), 5.71–5.66 (1H, m), 5.40–5.35 (1H, m), 4.52 (1H, d, *J*=20.0 Hz), 4.48 (1H, d, *J*=20.0 Hz), 4.30 (2H, t, *J*=7.0 Hz), 4.25 (2H, d, *J*=6.0 Hz), 2.03–1.98 (2H, m), 1.75 (2H, quin, *J*=7.0 Hz), and 1.05 (9H, s); IR (neat) 3071, 3017, 2931, 2857, 1472, 1428, 1371, 1252, 1176, 1112, 938, 880, 824, 742, and 704 cm^{-1}; HR-CI-MS calcd for $C_{23}H_{32}ClO_4SSi$ (M^++H) 467.1479, found 467.1474.

(2*R,3*R**)-1-(*tert*-Butyldiphenylsilyloxy)-6-chloromethanesulfonyloxy-2,3-epoxyhexane (36c).** To a solution of olefin **37** (243 mg, 0.520 mmol) in CH_2Cl_2 (12 mL) cooled to 0°C were added Na_2HPO_4 (437 mg, 3.07 mmol) and *m*-chloroperbezoic acid (379 mg, 1.54 mmol) and the solution was stirred at 25°C for 3.5 h, and satd aq. $NaHCO_3$ (4 mL) and satd aq. $Na_2S_2O_3$ (4 mL) was added at 0°C. The mixture was extracted with Et_2O (80 mL) and the Et_2O layer was washed with satd aq. $Na_2S_2O_3$ (60 mL), satd aq. $NaHCO_3$ (3×60 mL) and brine (60 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography (SiO_2, hexane–EtOAc, 20:1) to give epoxide **36c** (481 mg, 76%) as a colorless oil; R_f=0.40 (hexane–EtOAc, 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69–7.67 (4H, m), 7.46–7.39 (6H, m), 4.57 (1H, d, *J*=12.5 Hz), 4.54 (1H, d, *J*=12.5 Hz), 4.43 (1H, dt, *J*=10.0, 6.5 Hz), 4.38 (1H, dt, *J*=10.0, 6.5 Hz), 3.82 (1H, dd, *J*=6.0, 11.5 Hz), 3.73 (dd, *J*=5.5, 11.5 Hz), 3.19–3.16 (1H, m), 2.97 (1H, dt, *J*=8.5, 4.5 Hz), 1.96–1.90 (2H, m), 1.66–1.59 (1H, m), 1.44–1.37 (1H, m), and 1.06 (9H, s); IR (neat) 3071, 2956, 2858, 1655, 1589, 1560, 1542, 1508, 1472, 1428, 1372, 1253, 1177, 1112, 936, 881, 824, 742, 704, and 612 cm^{-1}; HR-FD-MS calcd for $C_{19}H_{22}ClO_5SSi$ (M^+-tBu) 425.0676, found 425.0624.

(2*R,1′*R**)-2-[2′-(*tert*-Butyldiphenylsilyloxy)-1′-hydroxy]-ethyloxolane (40b).** To a solution of **36b** (27.8 mg, 0.0579 mmol) in THF/H_2O (1.8 mL, 5:1) was added silver triflate (AgOTf) (22.3 mg, 0.0869 mmol) at three times every 1 h at 25°C. After stirred for 3 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, 4:1) gave oxolane **40b** (16.2 mg, 75%) as a colorless oil: R_f=0.29 (hexane–EtOAc, 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68–7.66 (4H, m), 7.45–7.37 (6H, m), 3.94–3.90 (1H, m), 3.87–3.82 (1H, m), 3.79–3.74 (1H, m), 3.70 (2H, d, *J*=5.5 Hz), 3.61–3.58 (1H, m), 1.93–1.84 (3H, m), 1.71–1.66 (1H, m), and 1.06 (9H, s); IR (neat) 3447, 3070, 2930, 2857, 1589, 1427, 1390, 1362, 1113, 938, 823, 741, and 703 cm^{-1}; HR-FD-MS calcd for $C_{22}H_{31}O_3SSi$ (M^++H) 371.2067, found 371.2028.

(2*S,3*S**)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-3-chloromethanesulfonyloxyoxane (39c) and (2*R**,1′*R**)-2-[2′-(*tert*-butyldiphenylsilyloxy)-1′-chloromethanesulfonyloxy]ethyloxolane (40c).** *General Procedure.* A solution of epoxide **36c** (19.4 mg, 0.0402 mmol) in 1,2-dichloroethane (1.3 mL) was heated at reflux for 48 h. The solvent was removed in vacuo. The residue was purified by PTLC (SiO_2, hexane–acetone, 4:1) to give oxane **39c** (8.1 mg, 42%), oxolane **40c** (4.1 mg, 21%), and recovered **36c** (3.3 mg, 17%). **39c:** a colorless oil; R_f=0.50 (developed twice with hexane–acetone, 4:1); ^{1}H NMR (500 MHz, C_6D_6) δ 7.84–7.79 (4H, m, Ph), 7.30–7.20 (6H, m, Ph), 5.01 (1H, broad s, C_3H), 4.04 (1H, dd, *J*=7.5, 10.5 Hz, $C_{1'}$H), 4.00 (1H, dd, *J*=6.0, 10.5 Hz, $C_{1'}$H), 3.83 (1H, d, *J*=12.5 Hz, SO_2CH_2Cl), 3.70 (1H, d, *J*=12.5 Hz, SO_2CH_2Cl), 3.67–3.63 (1H, m, C_6H_α), 3.33 (1H, ddd, *J*=1.0, 6.0, 7.5 Hz, C_2H), 2.93–2.88 (1H, m, C_6H_β), 2.17–2.12 (1H, m, C_4H), 1.87 (1H, tq, *J*=4.5, 13.5 Hz, C_5H), 1.23 (9H, s, *t*Bu), 1.16–1.09 (1H, m, C_4H), and 0.83–0.77 (1H, m, C_5H); ^{13}C NMR (125 MHz, C_6D_6) δ 136.02, 135.96, 133.69, 133.45, 130.16, 130.14, 128.29, 78.39, 77.13, 67.59, 63.23, 53.77, 28.92, 27.08, 20.23, and 19.39;[19] IR (neat) 3076, 3020, 2960, 2862, 1377, 1180, 1094, 905, 824, 795, 741, and 704 cm^{-1}; HR-FD-MS calcd for $C_{19}H_{22}ClO_5SSi$ (M^+-tBu+H) 425.0642, found 425.0648. **40c:** a colorless oil; R_f=0.54 (developed twice with hexane–acetone, 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69–7.65 (4H, m), 7.47–7.39 (6H, m), 4.77 (1H, d, *J*=12.5 Hz), 4.74 (1H, d, *J*=12.5 Hz), 4.68–4.65 (1H, m), 4.14–4.10 (1H, m), 3.91 (1H, dd, *J*=5.5, 12.0 Hz), 3.88–3.76 (3H, m), 2.01–1.84 (2H, m), 1.65–1.57 (2H, m), and 1.07 (9H, s); IR (neat) 2930, 2857, 1472, 1427, 1390, 1362, 1113, 823, 740, and 702 cm^{-1}; HR-CI-MS calcd for $C_{23}H_{32}ClO_5SSi$ (M^++H) 483.1428, found 483.1421.

(2*R,3*R**)-6-Acetoxy-1-(*tert*-butyldiphenylsilyloxy)-2,3-epoxyhexane (36e).** To a solution of iodide **36b** (78.2 mg, 0.163 mmol) in THF/H_2O (5.4 mL, 5:1) was added AgOTf (50.2 mg, 0.195 mmol) at 25°C. After stirring at 25°C for 1 h, AgOTf (50.2 mg, 0.195 mmol) was added again. The solution was stirred at 25°C for 1 h, and poured into Et_2O (30 mL). The mixture was washed with satd aq. $NaHCO_3$ (15 mL) and brine (15 mL). The organic layer was dried over $MgSO_4$, and concentrated in vacuo. To a solution of the residue (79.5 mg) in CH_2Cl_2 (1.6 mL) were added pyridine (0.0527 mL, 0.651 mmol), acetic anhydride (0.0307 mL, 0.326 mmol), and 4-(dimethylamino)pyridine (2.0 mg, 0.016 mmol) at 0°C. The solution was stirred at 25°C for 30 min, and was poured into Et_2O (35 mL). The mixture was washed with satd aq. $NaHCO_3$ (15 mL) and brine (15 mL). The organic layer was dried over $MgSO_4$, and concentrated in vacuo. PTLC (SiO_2, hexane–EtOAc, 3:1) gave acetate **36e** (13.7 mg, 20% for 2 steps) as a colorless oil: R_f=0.29 (hexane–EtOAc=4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69–7.67 (4H, 5m), 7.45–7.37 (6H, m), 4.09–4.01 (2H, m), 3.80 (1H, dd, *J*=6.0, 11.5 Hz), 3.73

(1H, dd, *J*=5.0, 11.5 Hz), 3.17 (1H, dt, *J*=4.5, 5.5 Hz), 3.70 (2H, d, *J*=5.5 Hz), 2.97 (1H, dt, *J*=7.0, 4.5 Hz), 2.00 (3H, s), 1.82–1.69 (2H, m), 1.54–1.38 (2H, m), and 1.06 (9H, s); IR (neat) 3074, 3054, 2962, 2934, 2896, 2862, 1742, 1475, 1431, 1392, 1367, 1243, 1112, 824, 743, and 613 cm^{-1}; HR-EI-MS calcd for $C_{20}H_{23}O_4Si$ (M^+-tBu) 355.1365, found 355.1365.

(2*Z*)-6-(4′-Methoxybenzyloxy)-2-hexen-1-ol (46). To a solution of propargylic alcohol **45** (1.45 g, 6.19 mmol) in pyridine (47 mL) were added quinoline (0.13 mL) and Pd/$CaCO_2$ (0.145 g) at 25°C and the mixture was stirred at 25°C for 1.5 h under hydrogen atmosphere and filtered through Celite. The filtrate was concentrated in vacuo. The residue was purified by flash chromatography (SiO_2, hexane–EtOAc, 3:1) to give allylic alcohol **46** (1.44 g, 98%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (2H, d, *J*=8.5 Hz), 6.88 (2H, d, *J*=8.5 Hz), 5.63–5.69 (1H, m), 5.53 (1H, dt, *J*=10.5, 7.5 Hz), 4.42 (2H, t, *J*=6.0 Hz), 3.81 (3H, s), 3.46 (2H, t, *J*=7.0 Hz), 2.20 (2H, q, *J*=7.0 Hz), 1.68 (2H, qui, *J*=7.0 Hz), and 1.55 (1H, t, *J*=6.0 Hz); IR (neat) 3356, 3014, 2938, 2866, 1613, 1586, 1516, 1464, 1356, 1303, 1249, 1176, 1098, 1036, and 820 cm^{-1}; HR-EI-MS calcd for $C_{14}H_{20}O_3$ (M^+) 236.1412, found 236.1404.

(2*Z*)-1-Bromo-6-(4′-methoxybenzyloxy)-2-hexene (47). To a solution of allylic alcohol **46** (2.81 g, 11.9 mmol) in CH_2Cl_2 (119 mL) were added triphenylphosphine (3.75 g, 14.3 mmol) and carbon tetrabromide (5.94 g, 17.9 mmol) at 0°C and the mixture was stirred at 25°C for 10 min. Satd aq. $NaHCO_3$ (70 mL) was added and the aqueous layer was extracted with Et_2O (3×90 mL). The combined organic layer was washed by 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 **47** (3.01 g, 85%) as a colorless oil: R_f=0.53 (hexane–EtOAc=4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (2H, d, *J*=8.5 Hz), 6.88 (2H, d, *J*=8.5 Hz), 5.75 (1H, dtt, *J*=10.5, 1.5, 8.5 Hz), 5.58 (1H, dt, *J*=10.5, 7.5 Hz), 4.44 (2H, s), 4.00 (2H, d, *J*=8.5 Hz), 3.81 (3H, s), 3.46 (2H, t, *J*=6.0 Hz), 2.24 (2H, dq, *J*=1.5, 7.5 Hz), and 1.68 (2H, qui, *J*=6.0 Hz); IR (neat) 2938, 2860, 1613, 1586, 1516, 1464, 1365, 1303, 1249, 1207, 1174, 1100, 1036, 820, and 754 cm^{-1}; HR-EI-MS calcd for $C_{14}H_{19}O_2Br$ (M^+) 298.0568, found 298.0543.

(5*Z*)-9-(4′-Methoxybenzyloxy)-1-(oxan-2′-yloxy)-5-nonen-2-yne (48). To a solution of 3-tetrahydropyranyloxypropyne (0.655 g, 4.67 mmol) in THF (14 mL) cooled to −78°C was added dropwise *n*-BuLi (3.05 mL of a 1.53 M solution in hexane, 4.67 mmol), and the mixture was stirred at −78°C for 30 min. A solution of bromide **47** (1.16 g, 3.89 mmol) in THF (6 mL) was then added dropwise at −78°C. The solution was stirred at 25°C for 29 h, and satd aq. NH_4Cl was added at 0°C. The mixture was extracted with EtOAc (250 mL). The organic 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 **48** (3.01 g, 85%) as a colorless oil: R_f=0.44 (hexane–EtOAc=4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (2H, d, *J*=8.5 Hz), 6.88 (2H, d, *J*=8.5 Hz), 5.48–5.41 (2H, m), 4.80 (1H, t, *J*=3.5 Hz), 4.43 (2H, s), 4.29 (1H, dt, *J*=15.0, 2.0 Hz), 4.19 (1H, dt), *J*=15.0, 2.0 Hz), 3.86–3.80 (1H, m), 3.81 (3H, s), 3.54–3.50 (1H, m), 3.44 (2H, t, *J*=6.5 Hz), 2.99–2.98 (2H, m), 2.13 (2H, q, *J*=7.0 Hz), 1.87–1.78 (1H, m), and 1.75–1.51 (8H, m); IR (neat) 2944, 2862, 1613, 1586, 1516, 1456, 1363, 1303, 1249, 1203, 1176, 1100, 1025, 973, 946, 903, 872, 818, and 708 cm^{-1}; HR-EI-MS calcd for $C_{22}H_{30}O_4$ (M^+) 358.2144, found 358.2163.

(5*Z*)-9-(4′-Methoxybenzyloxy)-5-nonen-2-yn-1-ol (49). To a solution of tetrahydropyranylether **48** (1.67 g, 4.65 mmol) in MeOH (25 mL) was added *p*-toluenesulfonic acid monohydrate (4.0 mg, 0.023 mmol) at 25°C. The solution was stirred at 25°C for 3 h, and Et_3N (0.65 mL, 4.65 mL) was added. The mixture was concentrated in vacuo. The residue was purified by flash chromatography (SiO_2, hexane–EtOAc, 5:1) to give alcohol **49** (1.19 g, 93%) as a colorless oil: R_f=0.58 (hexane–EtOAc=1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (2H, d, *J*=8.5 Hz), 6.88 (2H, d, *J*=8.5 Hz), 5.49–5.41 (2H, m), 4.43 (2H, s), 4.23 (2H, dt, *J*=6.0, 2.5 Hz), 3.81 (3H, s), 3.45 (2H, t, *J*=6.0 Hz), 2.97–2.96 (2H, m), 2.15 (2H, q, *J*=6.5 Hz), 1.70–164 (2H, m), and 1.64 (1H, t, *J*=6.0 Hz); IR (neat) 3414, 2936, 2866, 1613, 1586, 1516, 1458, 1365, 1303, 1249, 1176, 1098, 1033, 820, and 708 cm^{-1}; HR-EI-MS calcd for $C_{17}H_{22}O_3$ (M^+) 274.1569, found 274.1541.

(2*E*,5*Z*)-9-(4′-Methoxybenzyloxy)-2,5-nonadien-1-ol (50). A solution of propargylic alcohol **49** (0.431 g, 1.57 mmol) in THF (5 mL) was added at 0°C dropwise via cannular to a suspension of $LiAlH_4$ (0.119 mg, 3.14 mmol) in THF (10 mL), and the mixture was stirred at 25°C for 14 h. The reaction was quenched at 0°C with aq. 1 M HCl. The mixture was extracted with EtOAc (150 mL). The organic layer was washed with aq. 1 M HCl (50 mL), satd aq. $NaHCO_3$ (50 mL) and brine (50 mL). The solution was dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography (SiO_2, hexane–EtOAc, 4:1) to give allylic alcohol **50** (0.382 g, 88%) as a colorless oil: R_f=0.47 (hexane–EtOAc=1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (2H, d, *J*=8.5 Hz), 6.88 (2H, d, *J*=8.5 Hz), 5.62–5.49 (2H, m), 5.47–5.38 (2H, m), 4.43 (2H, s), 4.09 (2H, t, *J*=5.0 Hz), 3.81 (3H, s), 3.44 (2H, t, *J*=6.5 Hz), 2.79 (2H, t, *J*=6.0 Hz), 2.13 (2H, q, *J*=7.0 Hz), 1.69–163 (2H, m), and 1.30 (1H, t, *J*=5.0 Hz); IR (neat) 3368, 2938, 2864, 1613, 1586, 1516, 1464, 1365, 1303, 1249, 1176, 1098, 1036, 973, and 820 cm^{-1}; HR-EI-MS calcd for $C_{17}H_{24}O_3$ (M^+) 276.1725, found 276.1723.

(2*S,3*S**,5*Z*)-9-(4′-Methoxybenzyloxy)-2,3-epoxy-5-nonen-1-ol (51).** To a solution of allylic alcohol **50** (0.298 g, 1.08 mmol) in benzene (11 mL) were added $VO(acac)_2$ (28.6 mg, 0.108 mmol) and *t*-butylhydroperoxide (0.95 mL of a 1.37 M solution in toluene, 1.30 mmol) at 25°C. The mixture was stirred at 25°C for 1 h, and diluted with EtOAc (150 mL). The solution was washed with aq. 1 M HCl (50 mL), satd aq. $NaHCO_3$ (50 mL), satd aq. $Na_2S_2O_3$ (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, 2:1) to give epoxide **51** (0.270 g, 85%) as a colorless oil: R_f=0.40 (hexane–EtOAc=1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (2H, d, *J*=8.5 Hz), 6.88 (2H, d, *J*=8.5 Hz), 5.56–5.51 (1H, m),

5.44–5.39 (1H, m), 4.43 (2H, s), 3.89 (1H, ddd, *J*=2.5, 6.5, 12.5 Hz), 3.81 (3H, s), 3.62 (1H, ddd, *J*=4.5, 7.0, 12.5 Hz), 3.44 (2H, t, *J*=6.5 Hz), 2.99 (1H, dt, *J*=2.5, 5.5 Hz), 2.95 (1H, dt, *J*=4.5, 2.5 Hz), 2.40 (1H, dt, *J*=15.0, 5.5 Hz), 2.32 (1H, dt, *J*=15.0, 5.5 Hz), 2.13 (2H, q, *J*=7.0 Hz), 1.69–164 (2H, m), and 1.30 (1H, m); IR (neat) 3408, 2938, 2864, 1613, 1516, 1464, 1365, 1303, 1249, 1176, 1098, 1035, and 820 cm^{-1}; HR-EI-MS calcd for $C_{17}H_{24}O_4$ (M^+) 292.1675, found 292.1642.

(7*S,8*S**,4*Z*)-9-(*tert*-Butyldiphenylsilyloxy)-1-(4′-methoxybenzyloxy)-7,8-epoxy-4-nonene (52).** To a solution of alcohol **51** (0.359 g, 1.23 mmol) in CH_2Cl_2 (7.5 mL) cooled to 0°C were added imidazole (0.201 g, 2.95 mmol) and *tert*-butyldiphenylsilyl chloride (0.385 mL, 1.48 mmol). The solution was stirred at 0°C for 10 min, diluted with Et_2O (70 mL). The mixture was washed with satd aq. NH_4Cl (20 mL), satd aq. $NaHCO_3$ (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, 20:1) to give silyl ether **52** (0.652 g, >99%) as a colorless oil: R_f=0.78 (hexane–EtOAc=1:1); ^1H NMR (500 MHz, $CDCl_3$) δ 7.73–7.66 (4H, m), 7.44–7.36 (6H, m), 7.25 (2H, d, *J*=8.5 Hz), 6.87 (2H, d, *J*=8.5 Hz), 5.54–5.49 (1H, m), 5.42–5.37 (1H, m), 4.42 (2H, s), 3.80 (3H, s), 3.78 (1H, dd, *J*=3.5, 12.0 Hz), 3.72 (1H, dd, *J*=4.5, 12.0 Hz), 3.44 (2H, t, *J*=6.5 Hz), 2.93–2.91 (1H, m), 2.83 (1H, dt, *J*=2.0, 5.5 Hz), 2.37 (1H, dt, *J*=13.5, 5.5 Hz), 2.26 (1H, dt, *J*=13.5, 5.5 Hz), 2.12 (2H, q, *J*=7.0 Hz), 1.69–1.63 (2H, m), and 1.05 (9H, s); IR (neat) 2934, 2860, 1613, 1516, 1464, 1429, 1114, 824, 741, and 702 cm^{-1}; HR-FD-MS calcd for $C_{33}H_{42}O_4Si$ (M^+) 530.2852, found 530.2827.

(7*S,8*S**,4*Z*)-9-(*tert*-Butyldiphenylsilyloxy)-7,8-epoxy-4-nonen-1-ol (53).** To a solution of 4-methoxybenzyl ether **52** (0.652 g, 1.23 mmol) in CH_2Cl_2/H_2O (39.6 mL, 10:1) cooled to 0°C was added dichlorodicyanobenzoquinone (0.420 g, 1.85 mmol) and the solution was stirred at 25°C for 1 h. Satd $NaHCO_3$ was added at 0°C and the mixture was extracted with Et_2O (120 mL). The organic layer was washed with water (3×40 mL), dried over $MgSO_4$, concentrated in vacuo. The residue was purified by flash chromatography (SiO_2, hexane–EtOAc, 20:1 to 2:1) to give alcohol **53** (0.491 g, 98%) as a colorless oil: R_f=0.58 (hexane–EtOAc=1:1); ^1H NMR (500 MHz, $CDCl_3$) δ 7.68–7.66 (4H, m), 7.45–7.37 (6H, m), 5.55–5.49 (1H, m), 5.45–5.40 (1H, m), 3.78 (1H, dd, *J*=4.0, 12.0 Hz), 3.74 (1H, dd, *J*=4.5, 12.0 Hz), 3.63 (2H, q, *J*=5.5 Hz), 2.97–2.95 (1H, m), 2.86 (1H, dt, *J*=2.0, 5.0 Hz), 2.35 (2H, broad t, *J*=6.0 Hz), 2.21–2.08 (2H, m), 1.71 (1H, t, *J*=5.5 Hz), 1.66–1.58 (2H, m), and 1.05 (9H, s); IR (neat) 3352, 2934, 2862, 1473, 1429, 1392, 1363, 1114, 1060, 866, 824, 797, 741, and 704 cm^{-1}; HR-FD-MS calcd for $C_{25}H_{34}O_3Si$ (M^+) 410.2277, found 410.2256.

(7*S,8*S**,4*Z*)-9-(*tert*-Butyldiphenylsilyloxy)-1-chloromethanesulfonyloxy-7,8-epoxy-4-nonene (54).** To a solution of alcohol **53** (0.491 g, 1.20 mmol) in CH_2Cl_2 (12 mL) were added pyridine (0.388 mL, 4.80 mmol), chloromethanesulfonyl chloride (0.214 mL, 2.40 mmol) at 0°C. After stirring at 0°C for 2 h, satd aq. $NaHCO_3$ was added. The mixture was extracted with Et_2O (70 mL). The organic layer was washed with satd aq. NH_4Cl (20 mL), satd aq. $NaHCO_3$ (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, 10:1 to 5:1) to give sulfonate **54** (0.495 g, 79%) as a colorless oil: R_f=0.44 (hexane–EtOAc, 4:1); ^1H NMR (500 MHz, $CDCl_3$) δ 7.69–7.66 (4H, m), 7.45–7.37 (6H, m), 5.52–5.45 (2H, m), 4.59 (2H, s), 4.41 (2H, t, *J*=6.5 Hz), 3.80 (1H, dd, *J*=3.5, 12.0 Hz), 3.73 (1H, dd, *J*=4.5, 12.0 Hz), 2.95–2.93 (1H, m), 2.85 (1H, dt, *J*=2.0, 5.0 Hz), 2.33 (2H, t, *J*=5.0 Hz), 2.21–2.17 (2H, m), 1.71 (1H, t, *J*=5.5 Hz), 1.88–1.83 (2H, m), and 1.05 (9H, s); IR (neat) 2960, 2934, 2862, 1473, 1429, 1373, 1255, 1178, 1114, 938, 882, 824, 795, 743, and 704 cm^{-1}; HR-EI-MS calcd for $C_{22}H_{26}O_5SiSCl$ (M^+-tBu) 465.0959, found 465.0954.

(2*S,8*S**,5*R**,6*S**)-1-(*tert*-Butyldiphenylsilyloxy)-9-chloromethanesulfonyloxy-2,3,5,6-diepoxy-nonane (55a) and (2*R**,8*R**,5*R**,6*S**)-1-(*tert*-butyldiphenylsilyloxy)-9-chloromethanesulfonyloxy-2,3,5,6-diepoxynonane (55b).** To a solution of olefin **54** (76.6 mg, 0.147 mmol) in CH_2Cl_2 (3 mL) cooled to 0°C were added Na_2HPO_4 (0.104 g, 0.735 mmol) and *m*-chloroperbenzoic acid (90.7 mg, 0.368 mmol, purity 70%). The solution was stirred at 25°C for 2.5 h. Satd aq. $NaHCO_3$ (2 mL) and satd aq. $Na_2S_2O_3$ (2 mL) were then added at 0°C. The mixture was extracted with EtOAc (35 mL). The organic layer was washed with satd aq. $Na_2S_2O_3$ (10 mL), 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, 5:1 to 2:1) to give a mixture of diepoxides **55a** and **55b** (75.7 mg, 95%) as a colorless oil: R_f=0.31 (hexane–EtOAc, 2:1); ^1H NMR (500 MHz, $CDCl_3$) δ 7.69–7.67 (4H×2, m), 7.45–7.38 (6H×2, m), 4.64 (1H×2, *J*=13.0 Hz), 4.59 (1H×2, *J*=13.0 Hz), 4.53–4.44 (2H×2, m), 3.84 (1H, dd, *J*=4.0, 12.0 Hz), 3.83 (1H, dd, *J*=4.0, 12.0 Hz), 3.77 (1H, dd, *J*=4.0, 12.0 Hz), 3.76 (1H, dd, *J*=5.0, 12.0 Hz), 3.13–3.10 (1H, m), 3.06–3.02 (1H×2, m), 3.01–2.95 (5H, m), 2.05 (2H×2, m), 1.92–1.87 (2H, m), 1.84–1.73 (2H, m), 1.64–1.51 (2H, m), and 1.06 (9H×2, s); IR (neat) 2960, 2862, 1736, 1591, 1473, 1431, 1375, 1255, 1180, 917, 824, 795, 741, 704, 613, and 547 cm^{-1}; HR-FD-MS calcd for $C_{26}H_{36}O_6SiSCl$ (M^++H) 538.1612, found 539.1682.

Ring expansion reaction of 55a and 55b. A solution of the mixture of diepoxide **55a** and **55b** (30.7 mg, 0.0569 mmol) in 1,2-dichloroethane (1.9 mL) was heated at reflux for 22 h. The solvent was removed in vacuo. The residue was purified by PTLC (SiO_2, hexane–acetone, 3:1) to give a mixture of oxanes **56a** and **56b** (7.7 mg, 25%) as a colorless oil: R_f=(hexane–EtOAc, 2:1); ^1H NMR (500 MHz, $CDCl_3$) δ 7.69–7.67 (4H×2, m), 7.45–7.38 (6H×2, m), 4.84 (1H, broad s), 4.78 (1H, broad s), 4.72 (1H, d, *J*=12.5 Hz), 4.64 (2H, s), 4.61 (1H, d, *J*=12.5 Hz), 3.81 (1H, dd, *J*=3.5, 12.0 Hz), 3.79 (1H, dd, *J*=3.5, 12.0 Hz), 3.73 (1H, dd, *J*=4.0, 12.0 Hz), 3.71 (1H, dd, *J*=5.0, 12.0 Hz), 3.67 (1H, dd, *J*=4.5, 9.0 Hz), 3.57–3.54 (1H, m), 3.53 (1H, dt, *J*=2.5, 11.0 Hz), 3.48 (1H, dt, *J*=2.5, 12.5 Hz), 3.03–2.97 (2H×2, m), 2.41–2.34 (1H×2, broad d, *J*=14.5 Hz), 2.13 (1H, ddd, *J*=3.0, 9.0, 14.5 Hz), 2.09–1.79 (5H, m), 1.53–1.45 (4H, m), 1.051 (9H, s), and 1.048 (9H, s); IR (neat) 3076, 3018, 2960, 2934, 2862, 1473, 1431, 1375, 1255, 1212, 1180, 1112, 1089, 824, 795, 741, 704, 613, and

547 cm^{-1}; HR-FD-MS calcd for $C_{26}H_{35}O_6ClSiS$ (M^++H) 539.1736, found 539.1713.

(2*E*,6*Z*)10-(4′-Methoxybenzyloxy)-2,6-decadien-1-ol (60). To a solution of pyridinium chlorochromate (2.59 g, 12.0 mmol) in CH_2Cl_2 (52 mL) were added molecular sieves 4A powder (2.7 g) and a solution of alcohol **59** (1.58 g, 5.98 mmol) in CH_2Cl_2 (6 mL) at 25°C. After stirring at 25°C for 1.5 h, Et_2O (100 mL) and $MgSO_4$ (24 g) was added. The mixture was stirred at 25°C for 10 min, filtered through Florisil, and concentrated in vacuo. To a solution of the residue in benzene (50 mL) was added methyl (triphenylphosphoranyliden)acetate (2.4 g, 7.18 mmol) at 25°C. After stirring at 25°C for 24 h, the solvent was removed in vacuo. The residue was purified by flash chromatography (SiO_2, hexane–EtOAc, 10:1) to give a mixture of the desired ester and an unknown compound. To a solution of this mixture in CH_2Cl_2 (50 mL) cooled at −78°C was added dropwise diisobutylaluminum hydride (15.8 mL of a 0.95 M in hexane, 15.0 mmol). After stirring at −78°C for 1 h, Et_2O (100 mL), water (1.2 mL), and aq. 4 M NaOH (0.6 mL) were added at 0°C. The mixture was stirred at 25°C until white precipitates were sedimented. After the addition of $MgSO_4$, the mixture was filtered through Celite. The filtrate was concentrated in vacuo. The residue was purified by flash chromatography (SiO_2, hexane–EtOAc, 3:1) to give allylic alcohol **60** (1.17 g, 67% for 3 steps) as a colorless oil: R_f=0.24 (hexane–EtOAc, 3:1); ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (2H, d, *J*=8.5 Hz), 6.88 (2H, d, *J*=8.5 Hz), 5.72–5.61 (2H, m), 5.42–5.33 (2H, m), 4.43 (2H, s), 4.09 (2H, d, *J*=5.5 Hz), 3.81 (3H, s), 3.44 (2H, t, *J*=6.5 Hz), 2.18–2.06 (6H, m), and 1.68–162 (2H, m); IR (neat) 3374, 3008, 2938, 2860, 2364, 1613, 1516, 1458, 1365, 1303, 1249, 1176, 1098, 1036, 1006, 971, and 820 cm^{-1}; HR-EI-MS calcd for $C_{18}H_{26}O_3$ (M^+) 290.1882, found 290.1902.

(2*E*,6*Z*)-1-(*tert*-Butyldiphenylsilyloxy)-10-(4′-methoxybenzyloxy)-2,6-decadiene (61). To a solution of alcohol **60** (0.596 g, 2.05 mmol) in CH_2Cl_2 (20 mL) cooled to 0°C were added imidazole (0.355 g, 4.92 mmol) and *tert*-butyldiphenylsilyl chloride (0.640 mL, 2.46 mmol). The mixture was stirred at 0°C for 30 min, and poured into Et_2O (150 mL). The solution 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, 100:1 to 50:1) to give silyl ether **61** (1.05 g, 97%) as a colorless oil: R_f=0.62 (hexane–EtOAc=3:1); ^1H NMR (500 MHz, $CDCl_3$) δ 7.69–7.67 (4H, m), 7.43–7.35 (6H, m), 7.25 (2H, d, *J*=8.5 Hz), 6.87 (2H, d, *J*=8.5 Hz), 5.66 (1H, dt, *J*=15.0, 5.0 Hz), 5.56 (1H, dt, *J*=15.0, 5.0 Hz), 5.42–5.33 (2H, m), 4.42 (2H, s), 4.15 (2H, d, *J*=5.0 Hz), 3.79 (3H, s), 3.44 (2H, t, *J*=6.5 Hz), 2.13–2.05 (6H, m), 1.65 (2H, qui, *J*=6.5 Hz), and 1.05 (9H, s); IR (neat) 3004, 2934, 2860, 1613, 1589, 1516, 1473, 1464, 1429, 1363, 1303, 1249, 1174, 1112, 1040, 971, 824, 741, 704, and 611 cm^{-1}; HR-FD-MS calcd for $C_{34}H_{44}O_3Si$ (M^+) 528.3060, found 528.3079.

(4*Z*,8*E*)-10-(*tert*-Butyldiphenylsilyloxy)-4,8-decadien-1-ol (62). To a solution of ether **61** (0.520 g, 0.983 mmol) in CH_2Cl_2/H_2O (33 mL, 10:1) cooled to 0°C was added dichlorodicyanobenzoquinone (0.334 g, 1.47 mmol) and the mixture was stirred at 25°C for 2 h. Satd aq. $NaHCO_3$ (30 mL) was added at 0°C and the mixture was extracted with Et_2O (150 mL). The organic layer was 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, 20:1 to 5:1) to give alcohol **62** (0.327 g, 81%) as a colorless oil: R_f=0.33 (hexane–EtOAc=3:1); ^1H NMR (500 MHz, $CDCl_3$) δ 7.70–7.67 (4H, m), 7.43–7.36 (6H, m), 5.66 (1H, dt, *J*=15.0, 5.0 Hz), 5.56 (1H, dt, *J*=15.0, 5.0 Hz), 5.42–5.32 (2H, m), 4.15 (2H, d, *J*=5.0 Hz), 3.65 (2H, t, *J*=6.0 Hz), 2.15–2.06 (6H, m), 1.66–160 (2H, m), and 1.05 (9H, s); IR (neat) 3322, 3074, 3052, 2934, 1591, 1473, 1381, 1189, 1112, 1054, 971, 824, 739, 702, and 613 cm^{-1}; HR-FD-MS calcd for $C_{26}H_{37}O_2Si$ (M^++H) 409.2563, found 409.2584.

(2*E*,6*Z*)-1-(*tert*-Butyldiphenylsilyloxy)-10-chloromethanesulfonyloxy-2,6-decadiene (63). To a solution of alcohol **62** (0.106 mg, 0.260 mmol) in CH_2Cl_2 (2.6 mL) were added pyridine (0.109 mL, 1.35 mmol), chloromethanesulfonyl chloride (0.0603 mL, 0.676 mmol) at 0°C. After stirring at 0°C for 1.5 h, satd aq. $NaHCO_3$ was added and the mixture was extracted with Et_2O (35 mL). The organic layer was washed with satd aq. NH_4Cl (10 mL), 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, 25:1) to give sulfonate **63** (0.124 g, 92%) as a colorless oil: R_f=0.51 (hexane–EtOAc, 3:1); ^1H NMR (500 MHz, $CDCl_3$) δ 7.70–7.67 (4H, m), 7.44–7.36 (6H, m), 5.69–5.64 (1H, m), 5.57 (1H, dt, *J*=15.0, 4.0 Hz), 5.48–5.43 (1H, m), 5.37–5.32 (1H, m), 4.57 (2H,s), 4.40 (2H, t, *J*=6.5 Hz), 4.16 (2H, d, *J*=5.0 Hz), 2.18 (2H, q, *J*=8.0 Hz), 2.12–2.08 (4H, m), 1.84 (2H, qui, *J*=6.5 Hz), and 1.05 (9H, s); IR (neat) 3018, 2934, 2860, 1473, 1431, 1375, 1178, 1112, 1052, 1000, 967, 938, 880, 824, 741, 704, and 611 cm^{-1}; HR-FD-MS calcd for $C_{23}H_{28}O_4ClSiS$ (M^+-tBu) 463.1166, found 463.1172.

(2*E*,6*R,7*S**)-1-(*tert*-Butyldiphenylsilyloxy)-10-chloromethanesulfonyloxy-6,7-epoxy-2-decene (64).** To a solution of olefin **63** (0.124 g, 0.238 mmol) in CH_2Cl_2 (2 mL) cooled to 0°C were added Na_2HPO_4 (67.6 mg, 0.476 mmol) and *m*-chloroperbenzoic acid (28.8 mg, 0.238 mmol, purity 70%). The solution was stirred at 25°C for 30 min. Satd aq. $NaHCO_3$ (2 mL) and satd aq. $Na_2S_2O_3$ (2 mL) were then added at 0°C. The mixture was extracted with EtOAc (38 mL). The organic layer was washed with satd aq. $Na_2S_2O_3$ (10 mL), 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, 25:1 to 6:1) to give epoxide **64** (54.9 mg, 43%) as a colorless oil: R_f=0.37 (hexane–EtOAc, 3:1); ^1H NMR (500 MHz, $CDCl_3$) δ 7.69–7.67 (4H, m), 7.44–7.36 (6H, m), 5.69 (1H, ddt, *J*=1.5, 16.0, 6.0 Hz), 5.60 (1H, dt, *J*=16.0, 5.0 Hz), 4.63 (1H, d, *J*=13.0 Hz), 4.53 (1H, d, *J*=13.0 Hz), 4.51 (1H, dt, *J*=10.0, 6.0 Hz), 4.46 (1H, dt, *J*=10.0, 6.5 Hz), 4.17 (2H, dd, *J*=1.5, 5.0 Hz), 2.97–2.93 (2H, m), 2.28–2.14 (2H, m), 2.03–1.97 (2H, m), 1.81–1.75 (2H, m), 1.62–1.52 (2H, m), and 1.06 (9H, s); IR (neat) 2960, 2934, 1473, 1429, 1375, 1255, 1180, 1114,

1052, 936, 882, 824, 743, 704, and 611 cm^{-1}; HR-FD-MS calcd for $C_{27}H_{38}O_5ClSiS$ (M^++H) 537.1898, found 537.1905.

(2*S,3*S**,3′*E*)-3-Chloromethanesulfonyloxy-2-[5′-(*tert*-butyldiphenylsilyloxy)-3′-pentenyl]-oxane (65) and (2*R**,1′*R**,4*E*)-2-[1′-chloromethanesulfonyloxy-6′-(*tert*-butyldiphenylsilyloxy)-4′-hexenyl]oxolane (66).** A solution of epoxide **64** (73.7 mg, 0.137 mmol) in 1,2-dichloroethane (5 mL) was heated at reflux for 6 h. The solvent was removed in vacuo. The residue was purified by PTLC (SiO_2, hexane–EtOAc, 3:1) to give epoxide **65** (12.9 mg, 18%) and **66** (25.0 mg, 34%). 65: a colorless oil; R_f=0.47 (hexane–EtOAc, 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68–7.66 (4H, m), 7.44–7.36 (6H, m), 5.63 (1H, dt, *J*=15.0, 6.0 Hz), 5.58 (1H, dt, *J*=15.0, 4.5 Hz), 4.79 (1H, broad s), 4.64 (1H, d, *J*=13.0 Hz), 4.61 (1H, d, *J*=13.0 Hz), 4.05–4.01 (1H, m), 3.55 (1H, dt, *J*=2.0, 12.0 Hz), 3.39 (1H, dd, *J*=5.0, 9.0 Hz), 2.38–2.32 (1H, m), 2.22–2.08 (2H, m), 2.02 (1H, tq, *J*=4.5, 13.5 Hz), 1.83–1.75 (2H, m), 1.60–1.52 (1H, m), 1.51–1.46 (1H, m), and 1.05 (9H, s); IR (neat) 3074, 3050, 2958, 2860, 1715, 1591, 1473, 1464, 1431, 1361, 1255, 1178, 1112, 1050, 919, 824, 741, and 704 cm^{-1}; HR-FD-MS calcd for $C_{27}H_{38}O_5ClSiS$ (M^++H) 537.1898, found 537.1879. **66:** a colorless oil; R_f=0.53 (hexane–EtOAc, 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69–7.66 (4H, m), 7.44–7.36 (6H, m), 5.66 (1H, dt, *J*=15.5, 5.5 Hz), 5.62 (1H, dt, *J*=15.5, 4.0 Hz), 4.90 (1H, d, *J*=12.0 Hz), 4.62 (1H, d, *J*=12.0 Hz), 4.62 (1H, dt, *J*=4.0, 9.0 Hz), 4.17–4.16 (2H, m), 3.99 (1H, q, *J*=8.0 Hz), 3.88–3.81 (2H, m), 2.32–2.24 (1H, m), 2.22–2.16 (1H, m), 2.04–1.89 (3H, m), 1.78–1.72 (1H, m), 1.71–1.64 (1H, m), 1.59–1.51 (1H, m), and 1.05 (9H, s); IR (neat) 3074, 3030, 2960, 2934, 2862, 1473, 1462, 1429, 1365, 1180, 1112, 1069, 919, 824, 741, and 704 cm^{-1}; HR-FD-MS calcd for $C_{23}H_{28}O_5ClSiS$ (M^+−*t*Bu) 479.1116, found 479.1127.

(2*S,3*S**,3′*R**,4′*R**)-3-Chloromethanesulfonyloxy-2-[5′-(*tert*-butyldiphenylsilyloxy)-3′,4′-epoxy-pentenyl]oxane (67a) and (2*S**,3*S**,3′*S**,4′*S**)-3-chloromethanesulfonyl-oxy-2-[5′-(*tert*-butyl-diphenylsilyloxy)-3′,4′-epoxypentenyl]oxane (67b).** To a solution of olefin **65** (11.5 mg, 0.0221 mmol) in CH_2Cl_2 (1.5 mL) cooled to 0°C were added Na_2HPO_4 (15.6 mg, 0.0111 mmol) and *m*-chloroperbenzoic acid (13.6 mg, 0.0553 mmol, purity 70%). The solution was stirred at 25°C for 2 h. Satd aq. $NaHCO_3$ (2 mL) and satd aq. $Na_2S_2O_3$ (2 mL) were then added at 0°C. The mixture was extracted with EtOAc (38 mL). The organic layer was washed with satd aq. $Na_2S_2O_3$ (10 mL), satd aq. $NaHCO_3$ (10 mL) and 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 a diastereomeric mixture of epoxides **67a** and **67b** (8.8 mg, 72%) as a colorless oil; R_f=0.23 (hexane–EtOAc, 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68–7.66 (4H×2, m), 7.45–7.37 (6H×2, m), 4.87–4.74 (1H×2, m), 4.63 (2H, s), 4.62 (2H, s), 4.03–3.99 (2H, m), 3.77 (1H, dd, *J*=3.5, 12.0 Hz), 3.75 (2H, d, *J*=4.0 Hz), 3.71 (1H, dd, *J*=5.0, 12.0 Hz), 3.50–3.44 (2H×2, m), 2.93–2.89 (1H×2, m), 2.83–2.79 (1H×2, m), 2.38–2.31 (1H×2, m), 2.06–1.96 (1H×2, m), 1.86–1.74 (6H, m), 1.72–1.61 (4H, m), 1.48 (2H×2, broad d, *J*=9.5 Hz), and 1.05 (9H×2, s); IR (neat) 2958, 2862, 1473, 1431, 1375, 1178, 1114, 1091, 919, 824, 797, 741, and 704 cm^{-1}; HR-FD-MS calcd for $C_{27}H_{38}O_6ClSiS$ (M^++H) 553.1846, found 553.1833.

Spiro acetal (70). A solution of **67** (8.4 mg, 0.0152 mmol) in 1,2-dichloroethane (3 mL) was heated at reflux for 21 h. The solvent was removed in vacuo. The residue was purified by PTLC (SiO_2, hexane–EtOAc, 3:1) to give the mixture of **70** and **71** (3.5 mg, **70**:**71**=3.4:1, 42%). The pure **70** (2.4 mg) was obtained by preparative HPLC (hexane, flow rate 0.5 mL/min, retention time 10.5 min) as a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76–7.12 (4H, m), 7.45–7.36 (6H, m), 4.94 (1H, dt, *J*=5.5, 10.0 Hz), 4.61 (1H, d, *J*=12.5 Hz), 4.48 (1H, d, *J*=12.5 Hz), 3.97 (1H, dd, *J*=3.5, 11.5 Hz), 3.90 (1H, dd, *J*=1.5, 11.5 Hz), 3.72 (1H, ddd, *J*=1.5, 3.5, 10.0 Hz), 3.62–3.58 (1H, m), 3.56 (1H, dt, *J*=2.5, 11.0 Hz), 2.28–2.18 (2H, m), 1.86 (1H, dt, *J*=13.0, 4.0 Hz), 1.82 (1H, dt, *J*=13.5, 3.0 Hz), 1.67–1.48 (6H, m), and 1.09 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.94, 135.55, 133.55, 133.01, 129.72, 129.67, 127.69, 127.55, 95.22, 77.85, 70.69, 62.73, 60.74, 53.72, 34.91, 34.25, 26.01, 24.93, 19.35, and 18.60; IR (neat) 3076, 3052, 3018, 2936, 2860, 1464, 1431, 1379, 1274, 1230, 1181, 1114, 1046, 1021, 982, 965, 849, 822, 797, 737, 704, 634, and 605 cm^{-1}; HR-FD-MS calcd for $C_{27}H_{38}O_6ClSiS$ (M^++H) 553.1846, found 553.1845.

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