Synthesis of all Four Stereoisomers of Leucomalure, Components of the Female Sex Pheromone of the Satin Moth, *Leucoma salicis*[‡]

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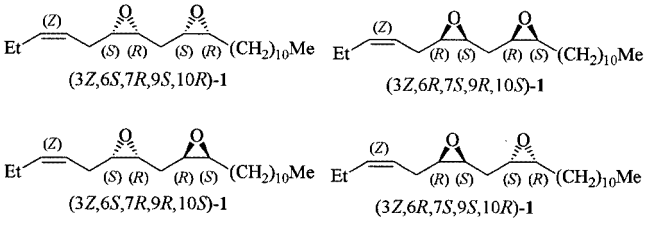
Lipase PS-C(Amano)-catalyzed asymmetric acetylation of (±)-4-(*tert*-butyldiphenylsilyloxy)-*cis*-2,3-epoxy-1-butanol afforded the (2*R*,3*S*)-epoxy alcohol and the (2*S*,3*R*)-epoxyacetate, which were converted into all of the four stereoisomers of leucomalure [(3*Z*)-*cis*-6,7-*cis*-9,10-diepoxy-3-henicosene], the female sex pheromone of the Satin moth, *Leucoma salicis*.

Introduction

In 1997, leucomalure [(3*Z*)-*cis*-6,7-*cis*-9,10-diepoxy-3-henicosene (**1**)] was isolated and identified by Gries et al. as the major component of the female-produced sex pheromone of the Satin moth, *Leucoma salicis*.[1] The authors synthesized a diastereoisomeric mixture of two racemates of **1**, (3*Z*,6*R**,7*S**,9*R**,10*S**)-**1** and (3*Z*,6*R**,7*S**,9*S**,10*R**)-**1** (Scheme 1), and, after their chromatographic separation, found one of them to be identical with the major component of the pheromone as judged by GC-MS and GC-EAD (i.e., electroantennographic detection) analyses on achiral stationary phases, while the other diastereoisomer co-chromatographed with an antennal response to a non-FID-detectable minor component in the pheromone blend. In 1999, Ando and co-workers prepared all of the four stereoisomers of **1**, starting from the enantiomers of (3*Z*,9*Z*)-*cis*-6,7-epoxy-3,9-henicosadiene, by separating the isomers by HPLC employing chiral stationary phases.[2] Furthermore the authors could propose absolute configuration of the stereoisomers by extensive NMR spectroscopic analysis.



Scheme 1. Structures of the stereoisomers of leucomalure

Biological evaluation of these four stereoisomers of **1**, however, has not been reported yet.

On the basis of Ando's stereochemical proposal, we started our endeavor to synthesize all the four stereoisomers of **1** employing conventional MPLC separation on silica gel as the tool for separation of the diastereoisomers. We first attempted the synthesis of two diastereoisomers of (±)-**1**, and published the result in 2001 as a preliminary communication.[3] This paper reports a synthesis of all of the four stereoisomers of **1**.

Results and Discussion

Scheme 2 shows our retrosynthetic analysis of **1**. The target molecule **1** is to be synthesized from 1-butyne (**A**) and diepoxytriflate **B** (R = Tf). Epoxidation of epoxyalkene **C** and subsequent separation of the resulting diastereoisomers would give **B′** (R = TBDPS). Epoxyalkyne **D** serves as the precursor of **C**. The epoxyalkyne **D** is to be obtained by alkylation of 1-tridecyne (**E**) with optically active epoxytriflate **F**. We chose triflates (**B** and **F**) as the alkylating agents for acetylide anions, because triflates are known to be much more reactive than tosylates in substitution reactions.[4]

Our first concern was how to prepare an optically active building block like **G** (Scheme 3) in a manner efficient enough for natural product synthesis. In 1992, we reported a preparative method for **G** starting from *meso*-epoxydiacetate **H**.[5] In principle, asymmetric hydrolysis of *meso*-**H** with an appropriate enzyme can give a quantitative yield of (2*R*,3*S*)-**I**. In practice, however, pig pancreatic lipase (PPL, Sigma) allowed us to obtain **I** (90.8% *ee*) in 71% yield at best. To enhance the enantiomeric purity of the product **I**, a crystalline 3,5-dinitrobenzoate (DNB) of 4-(*tert*-butyldiphenylsilyloxy = TBDPSO)-*cis*-2,3-epoxy-1-butanol (**G**)

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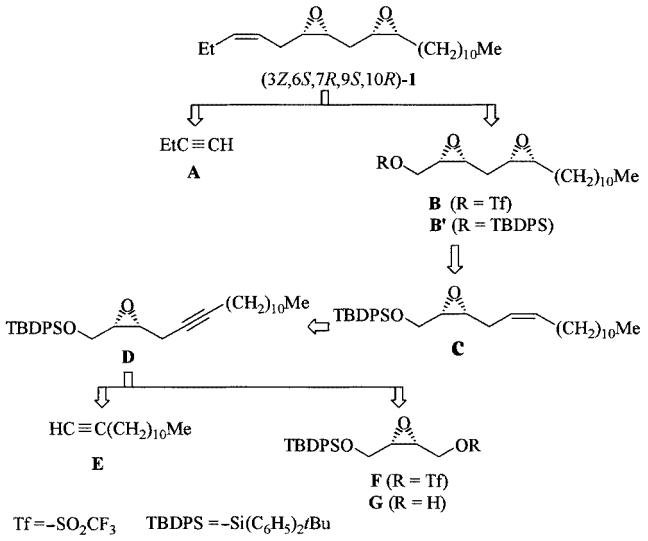
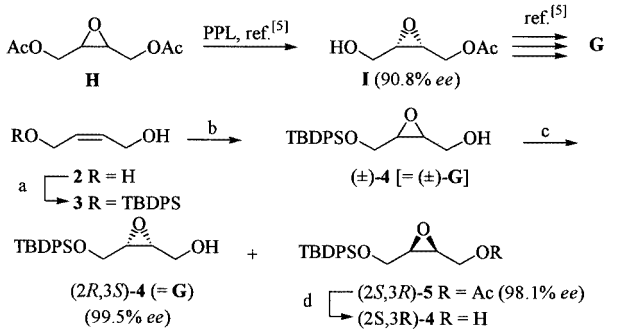


Scheme 2. Retrosynthetic analysis of (3*Z*,6*S*,7*R*,9*S*,10*R*)-leucomalure (**1**)



Scheme 3. Synthesis of the enantiomers of epoxy building block **4**. Reagents: (a) NaH, TBDPSCl, THF (92%); (b) MCPBA, CH_2Cl_2 (94%); (c) Lipase PS-C, CH_2=CHOAc, Et_2O [(2*R*,3*S*)-**4** (49%) and (2*S*,3*R*)-**5** (48%)]; (d) K_2CO_3, MeOH (99%)

was prepared and recrystallized to a purity of ca. 100% *ee*. Removal of the DNB group of that crystalline derivative gave the desired **G** in 36% overall yield (7 steps) based on (*Z*)-2-butene-1,4-diol (**2**). This method, therefore, was cumbersome and inefficient.

Our new method for the preparation of **G** is based on lipase-catalyzed ester exchange of (±)-**G** with vinyl acetate.[6] The substrate (±)-**G** (i.e., **4**) was synthesized in 86% yield by monosilylation of diol **2** to give **3**, followed by subsequent epoxidation of **3** with *m*-chloroperbenzoic acid (MCPBA). Needless to say, enzymatic resolution of (±)-**4** by either asymmetric acetylation of (±)-**4** or asymmetric hydrolysis of the diacetate of (±)-**4** can give the enantiomers of **4**, each in 50% yield at best,[7,8] and in principle is inferior to the so-called "*meso*-trick" which can afford a *single* enantiomer (**H** → **I**) in a better yield. In practice, however, enzymatic hydrolysis of **H**[5] or the corresponding dibutanoate[9−11] never gave a single enantiomer in a quantitative yield [85% yield of **I** (90.8% *ee*),[5] 90% yield of the half butanoate (90% *ee*),[9] 73% yield of the half butanoate (84% *ee*)[11]]. Therefore, if we can shorten the synthetic route by resolving (±)-**4** directly, then we may be able to expect a better overall yield in securing *both* the enantiomers of **4**.

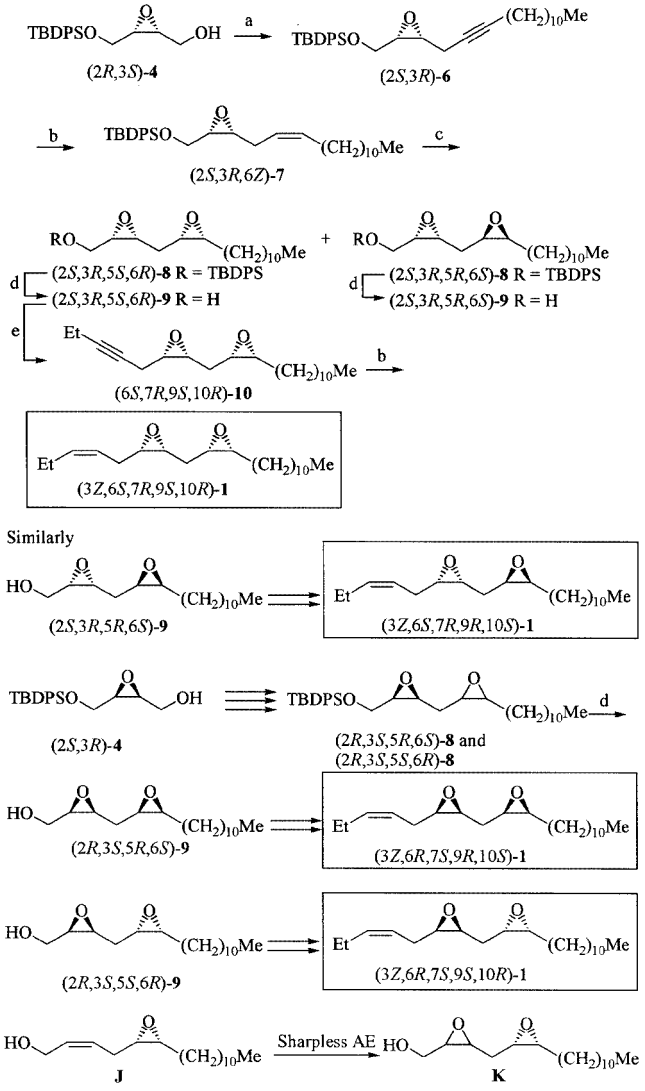
Screening of five Amano enzymes, as shown in Table 1, revealed lipase PS-C as the appropriate enzyme under the acetylation conditions employing vinyl acetate in diethyl ether as the acetyl donor. There was no need to add a phosphate buffer to keep the pH of the reaction mixture constant. Because neither **4** nor **5** was water soluble, while **I** was water soluble, the workup proceeded without problem. In a preparative-scale experiment, (2*R*,3*S*)-**4** (99.5% *ee*) and (2*S*,3*R*)-**5** (98.1% *ee*) were obtained in 49 and 48% yield, respectively. This remarkably high enantioselectivity of the conversion must be due to the presence of a very bulky and hydrophobic TBDPS group in the substrate (±)-**4**, because in the case of the corresponding *tert*-butyldimethylsilyl ether, the enantiomeric purity of the products was ca. 80−84% *ee* (A. Nakanishi, K.Mori, unpublished results). The overall yield of (2*R*,3*S*)-**4** was 42% based on **2** (3 steps) and that of (2*S*,3*R*)-**4** was 41.5% based on **2** (4 steps). The present method, therefore, is simpler and more efficient than the previous one.[5]

Table 1. Screening of enzymes for asymmetric acetylation of (±)-**4**

Entry[a]	Enzyme[b]	Time (h)	(2*R*,3*S*)-**4**		(2*S*,3*R*)-**5**	
			Yield (%)	% *ee*[c]	Yield (%)	% *ee*[d]
1	Lipase AK	7	48	97.5	49	96.6
2	Lipase PS	22	48	98.9	47	97.6
3	Lipase PS-C	5	49	99.5	48	98.1
4	Lipase PS-D	4	49	99.6	49	95.7
5	Pancreatin F	72	no reaction			

[a] All the reactions were executed at room temperature employing vinyl acetate in diethyl ether as the acetyl donor. [b] All the enzymes were kindly supplied to us by Amano Enzyme, Inc. [c] Determined by HPLC analysis (see Exp. Sect.). [d] Determined after methanolysis to give the corresponding alcohol, (2*S*,3*R*)-**4**.

The conversion of the enantiomers of **4** to the stereoisomers of leucomalure (**1**) is summarized in Scheme 4. The synthetic route follows essentially the one developed for the synthesis of (±)-**1** by J. Razkin and K. Mori.[3] For the synthesis of (3*Z*,6*S*,7*R*,9*S*,10*R*)-**1**, the key chiral building block (2*R*,3*S*)-**4** was treated with *n*-butyllithium and trifluoromethanesulfonic anhydride (triflic anhydride, Tf_2O) to give the corresponding triflate, which, without isolation, reacted in situ with 1-tridecynyllithium to furnish (2*S*,3*R*)-**6** in 77% yield. This alkynylation was highly successful with the triflate even in the absence of a cuprous catalyst or boron trifluoride etherate. In our preliminary alkynylation attempts, a similar 2,3-epoxyalkyl iodide did not work at all and the corresponding tosylate gave the alkynylation product in ≤ 22% yield (J. Razkin Lizarraga, K. Mori, unpublished work). Although there are some successful cases of alkylating lithium acetylides with 2,3-epoxyalkyl bromides,[12,13] alkynylation of similar 2,3-epoxyalkyl iodides or tosylates has been reported to be unsuccessful.[14,15] The



Scheme 4. Synthesis of all the four stereoisomers of leucomalure (**1**). Reagents: (a) *n*BuLi, Tf_2O; then $Me(CH_2)_{10}C{\equiv}CLi$, THF, HMPA (77%); (b) H_2, $Pd/CaCO_3-Pb^{2+}$, cyclohexane [98% for (2*S*,3*R*,6*Z*)-**7**; 97% for (3*Z*,6*S*,7*R*,9*S*,10*R*)-**1**]; (c) MCPBA, CH_2Cl_2; then MPLC separation [(2*S*,3*R*,5*S*,6*R*)-**8** (23%) and (2*S*,3*R*,5*R*,6*S*)-**8** (58%)]; (d) TBAF, THF (81%); (e) *n*BuLi, Tf_2O; then $EtC{\equiv}CLi$, THF, HMPA (48%)

usefulness of 2,3-epoxyalkyl triflates in alkynylation was previously noticed by both Wasserman[16] and Hirama.[17] Kotsuki found triflates to be far more reactive than tosylates.[4]

Semi-hydrogenation of the triple bond of (2*S*,3*R*)-**6** over Lindlar's palladium catalyst gave (2*S*,3*R*,6*Z*)-**7**. No signal due to the undesired (*E*)-isomer of **7** could be observed in its ^1H and ^{13}C NMR spectra. Epoxidation of (2*S*,3*R*,6*Z*)-**7** with MCPBA in dichloromethane yielded a diastereoisomeric mixture (40:60) of diepoxides, (2*S*,3*R*,5*S*,6*R*)- and (2*S*,3*R*,5*R*,6*S*)-**8**. This mixture was readily separated by MPLC to afford less-polar (2*S*,3*R*,5*S*,6*R*)-**8** (23%) and more-polar (2*S*,3*R*,5*R*,6*S*)-**8** (57%). Attempts to change the diastereoselectivity of that epoxidation were fruitless. Epoxidation of a double bond with dimethyldioxirane is known to give stereochemical results different from that with MCPBA, as was studied by us in the case of a sphingolipid.[18] Therefore, we examined epoxidation of the olefin (2*S*,3*R*,6*Z*)-**7** with dimethyldioxirane generated from acetone and Oxone®.[18] As shown in Table 2, the degree of diastereoselection [(2*S*,3*R*,5*S*,6*R*)-**8**/(2*S*,3*R*,5*R*,6*S*)-**8** ≈ 40:60 to 36:64] was no different from that (40:60) achieved with MCPBA. Accordingly, epoxidation with dimethyldioxirane could not replace the MCPBA oxidation of **7**. In the earlier phase of the present synthesis, use of Sharpless asymmetric epoxidation to convert **J** to **K** (Scheme 4) was also considered. The asymmetric yield of the Sharpless epoxidation of (*Z*)-double bonds, however, are known to be 80.6% *ee*,[19] 84% *ee*,[20,21] 88% *ee*,[22] 91% *ee*,[19] and 92% *ee*.[23] This means that the resulting diepoxy alcohol **K** would inevitably be a diastereoisomeric mixture, and would need to be purified by chromatography. This drawback made us abandon the **J** → **K** approach.

Table 2. Epoxidation of (2*S*,3*R*,6*Z*)-**7** with dimethyldioxirane

Entry[a]	Solvent	Time	Conversion[b]	Product ratio[b] (2*S*,3*R*,5*S*,6*R*)-**8**/ (2*S*,3*R*,5*R*,6*S*)-**8**
1	CH_2Cl_2	12 h	47%	40:60
2	MeCN	3 h	99%	40:60
3	DME	3 h	96%	36:64
4	DMF	12 h	52%	36:64

[a] Typical procedure: H_2O (1 mL), CH_2Cl_2 (2 mL), $NaHCO_3$ (120 mg) and Oxone® (120 mg) were added to a solution of (2*S*,3*R*)-**7** (20 mg) in acetone (0.5 mL). The mixture was stirred for 12 h at room temperature. The yield and the diastereoisomeric ratio were then assessed by HPLC analysis. [b] Determined by HPLC analysis.

Deprotection of the TBDPS group of the earlier-eluted and minor product, (2*S*,3*R*,5*S*,6*R*)-**8**, by treatment with tetra(*n*-butyl)ammonium fluoride (TBAF) furnished a crystalline alcohol, which was recrystallized to give pure (2*S*,3*R*,5*S*,6*R*)-**9**, m.p. 57.5−58.5 °C, $[\alpha]_D^{24} = -5.35$ (c = 1.05, $CHCl_3$), in 81% yield. Alkylation of 1-butynyllithium with the triflate of (2*S*,3*R*,5*S*,6*R*)-**9** gave diepoxyalkyne (6*R*,7*S*,9*S*,10*R*)-**10** in 48% yield. The observed yield (48%) of (6*R*,7*S*,9*S*,10*R*)-**10** was lower than that (77%) of (2*S*,3*R*)-**6**. This difference might be due to the difference in the solubility of (2*S*,3*R*,5*S*,6*R*)-**9** and (2*R*,3*S*)-**4**. The diepoxy alcohol (2*S*,3*R*,5*S*,6*R*)-**9** easily precipitated out when cooled to −78 °C. Its lithium salt, therefore, had to be prepared at 0 °C in THF, and then triflated with triflic anhydride. In the case of the monoepoxy alcohol (2*S*,3*R*)-**6**, the formation of its lithium salt and its subsequent triflation could be executed at −78 °C, because the alcohol (2*R*,3*S*)-**4** was much more soluble in THF than (2*S*,3*R*,5*S*,6*R*)-**9**. The low temperature must have prevented the possible side reactions such as cleavage of the epoxy ring(s) in the case of preparation of (2*S*,3*R*)-**6**. Finally, Lindlar semi-hydrogenation of (6*R*,7*S*,9*S*,10*R*)-**10** afforded one of the stereoisomers of

leucomalure, (3*Z*,6*S*,7*R*,9*S*,10*R*)-**1**, $[\alpha]_D^{22} = +5.0$ ($c = 0.55$, $CHCl_3$) [ref.[2] $[\alpha]_D = +3.1$ ($c = 0.8$, $CHCl_3$)], which showed ^1H and ^{13}C NMR spectra identical to those reported for (3*Z*,6*S**,7*R**,9*S**,10*R**)-**1**.[3] Its mass spectrum was in good accord with that of the natural leucomalure.[1] The overall yield of (3*Z*,6*S*,7*R*,9*S*,10*R*)-**1** was 2.7% based on **2** (9 steps).

When (2*S*,3*R*,5*R*,6*S*)-**8** was treated with TBAF, a crystalline alcohol (2*S*,3*R*,5*R*,6*S*)-**9**, m.p. 57.5−58.5 °C, $[\alpha]_D^{24} = +0.53$ ($c = 1.1$, $CHCl_3$), was obtained, which eventually yielded (3*Z*,6*S*,7*R*,7*R*,10*S*)-**1**, $[\alpha]_D^{22} = +21.4$ ($c = 0.41$, $CHCl_3$) [ref.[2] $[\alpha]_D = +17.6$ ($c = 1.0$, $CHCl_3$)]. Its ^1H and ^{13}C NMR spectra were identical to those reported for (3*Z*,6*S**,7*R**,9*S**,10*R**)-**1**,[3] and its mass spectrum was indistinguishable from that of (3*Z*,6*S**,7*R**,9*S**,10*R**)-**1**.[1] The overall yield of (3*Z*,6*S*,7*R*,9*R*,10*S*)-**1** was 5.6% based on **2** (9 steps). Similarly, the remaining two isomers of leucomalure, (3*Z*,6*R*,7*S*,9*R*,10*S*)-**1**, $[\alpha]_D^{22} = -4.5$ ($c = 0.55$, $CHCl_3$), and (3*Z*,6*R*,7*S*,9*S*,10*R*)-**1,** $[\alpha]_D^{20} = -21.3$ ($c = 0.50$, $CHCl_3$), were synthesized from (2*S*,3*R*)-**4** via (2*R*,3*S*,5*R*,6*S*)-**8** and (2*R*,3*S*,5*S*,6*R*)-**8** in 2.0 and 7.5% yield, respectively. These four isomers of **1** are thought to be highly enantiomerically pure (98−99% *ee*) because of the high enantiomeric purity of the enantiomers of **4** and purification of the intermediates **9** by recrystallization.

In order to verify Ando's stereochemical assignments, made by NMR spectroscopic analysis, to the stereoisomers of leucomalure,[2] we attempted X-ray analysis of the crystalline diepoxy alcohols, (2*S*,3*R*,5*S*,6*R*)-**9** (m.p. 57.5−58.5 °C) and (2*S*,3*R*,5*R*,6*S*)-**9** (m.p. 88.5−89.5 °C). Unfortunately, however, the prismatic crystals of the former were too small, and the needles of the latter were too fine, to be adequately analyzed. Accordingly, the more-available alcohol (2*S*,3*R*,5*R*,6*S*)-**9** was derivatized to give the corresponding phenylurethane (m.p. 78.5−79.0 °C), *p*-bromobenzoate (m.p. 82.0−83.0 °C), and 3,5-dinitorobenzoate (m.p. 65.0−66.5 °C). All of these compounds were obtained as fine needles. The crystals of the 3,5-dinitorobenzoate were too fine to be analyzed. Dr. M. Bando (Otsuka Pharmaceutical Co.) kindly attempted the X-ray analysis of the phenylurethane and *p*-bromobenzoate. Especially in the case of the latter, the analysis was executed first by using molybdenum and then copper as the X-ray tube target materials. None of the attempts led to the successful solution of the crystal structure. Reflections along the long axis of the crystal could not be separated cleanly, and the crystal seemed to possess pseudo-symmetry. Therefore, we abandoned our X-ray attempts, and relied on Ando's stereochemical assignment by means of NMR spectroscopic analysis.

In conclusion, all of the four stereoisomers of leucomalure (**1**) were synthesized. These synthetic samples will clarify the stereochemistry−bioactivity relationships among the four isomers of **1** through their bioassays. Bioassays will be carried out in Hungary by Drs. M. Tóth and G. Szöcs (Plant Protection Institute, Hungarian Academy of Science) in May and June, 2003.

Experimental Section

General: Melting points: Uncorrected values. IR: Jasco FT/IR-410. ^1H NMR: Jeol JNM-LA 500 (500 MHz), Jeol JNM-LA 400 (400 MHz) (TMS at $\delta = 0.00$ ppm or $CHCl_3$ at $\delta = 7.26$ ppm as an internal standard). ^{13}C NMR: Jeol JNM-LA 500 (126 MHz), Jeol JNM-LA 400 (100 MHz) ($CDCl_3$ at $\delta = 77.0$ ppm as an internal standard). MS: Jeol JMS-SX 102A and Hitachi M-80B. CC: Merck Kieselgel 60 Art 1.07734. TLC: 0.25-mm Merck silica gel plates (60F-254).

4-(*tert*-Butyldiphenylsilyloxy)-2-buten-1-ol (3): Sodium hydride (60% suspension in mineral oil, 912 mg, 23.8 mmol) was slowly added to a solution of (*Z*)-2-butene-1,4-diol (2.00 g, 22.7 mmol) in THF (20 mL) at 0 °C. After stirring for 30 min at room temperature, a solution of TBDPSCl (6.25 g, 22.7 mmol) in THF (8 mL) was added dropwise at 0 °C and then the mixture was warmed to room temperature over 1 h. The mixture was quenched with water and extracted with Et_2O. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 5:1) to give **3** (6.81 g, 92%) as a colorless oil, $n_D^{24} = 1.5151$. IR (film): $\tilde{\nu}_{max} = 3340$ (s, O−H), 2930 (s, C−H), 2860 (s, C−H), 1590 (w, C=C), 1430(s, Si−C), 1110 (s, Si−O). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.05$ (s, 9 H, *t*Bu), 4.01 (m, 2 H, 1-H), 4.26 (d, $J = 5.4$ Hz, 2 H, 4-H), 5.64 (dt, $J = 11.7$, 6.3 Hz, 1 H, 2-H), 5.72 (dt, $J = 11.7$, 5.4 Hz, 1 H, 3-H), 7.38 (m, 6 H, Ar-H), 7.68 (d, $J = 6.3$ Hz, 4 H, Ar-H) ppm. $C_{20}H_{26}O_2Si$ (326.5): calcd. C 73.57, H 8.03; found C 73.46, H 8.21.

(±)-4-(*tert*-Butyldiphenylsilyloxy)-*cis*-2,3-epoxy-1-butanol [(±)-4]: MCPBA (70% purity, 17.0 g, 69.0 mmol) in CH_2Cl_2 (50 mL) was added dropwise to a solution of **3** (15.6 g, 47.6 mmol) in CH_2Cl_2 (200 mL) at 0 °C. The mixture was stirred for 6 h at room temperature, then diluted with saturated aqueous $NaHCO_3$ and extracted with Et_2O. The extract was washed with water, saturated aqueous Na_2SO_3 and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 5:1) to give (±)-**4** (15.3 g, 94%) as a colorless oil, $n_D^{24} = 1.5491$. IR (film): $\tilde{\nu}_{max} = 3420$ (s, O−H), 2930 (s, C−H), 2860 (s, C−H), 1590 (w, C=C), 1430(s, Si−C), 1110 (s, Si−O). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.06$ (s, 9 H, *t*Bu), 1.84 (t, $J = 6.5$ Hz, 1 H, OH), 3.23 (m, 2 H, 2,3-H), 3.67 (m, 2 H, 1-H), 3.74 (dd, $J = 11.7$, 5.1 Hz, 1 H, 4-H_a), 3.91 (dd, $J = 11.7$, 5.5 Hz, 1 H, 4-H_b), 7.41 (m, 6 H, Ar-H), 7.67 (m, 4 H, Ar-H) ppm. $C_{20}H_{26}O_3Si$ (342.5): calcd. C 70.13, H 7.65; found C 70.22, H 7.83.

(2*R*,3*S*)-4-(*tert*-Butyldiphenylsilyloxy)-*cis*-2,3-epoxy-1-butanol [(2*R*,3*S*)-4] and (2*S*,3*R*)-1-Acetoxy-4-(*tert*-butyldiphenylsilyloxy)-*cis*-2,3-epoxybutane (5)

(A) Using Lipase PS-C: Lipase PS-C (50 mg) was added to a solution of (±)-**4** (2.00 g, 5.84 mmol) in Et_2O (20 mL) and vinyl acetate (1.0 mL) at room temperature. After stirring for 5 h at room temperature, the enzyme was filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 5:1) to give more polar (2*R*,3*S*)-**4** (971 mg, 49%) and less polar **5** (1.07 g, 48%) as colorless oils.

(2*R*,3*S*)-**4**: $n_D^{22} = 1.5161$. $[\alpha]_D^{23} = +6.5$ ($c = 1.0$, CH_2Cl_2), {ref.[4] $[\alpha]_D^{22} = +6.4$ ($c = 0.8$, CH_2Cl_2)}. $C_{20}H_{26}O_3Si$ (342.5): calcd. C 70.13, H 7.65; found C 69.94, H 7.67. Its IR and ^1H NMR spectra were identical with those of (±)-**4**.

5: $n_D^{22} = 1.5359$. $[\alpha]_D^{22} = -3.66$ ($c = 1.25$, CH_2Cl_2). IR (film): $\tilde{\nu}_{max} =$ 2930 (s, C−H), 2860 (s, C−H), 1745 (s, C=O), 1590 (w, C=C),

1430(s, Si−C), 1230 (C−O−C), 1110 (s, Si−O). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (s, 9 H, *t*Bu), 2.06 (s, 3 H, Ac), 3.24 (m, 2 H, 2,3-H), 3.78 (dd, *J* = 11.7, 4.6 Hz, 1 H, 1-H_a), 3.82 (dd, *J* = 11.7, 5.3 Hz, 1 H, 1-H_b), 3.95 (dd, *J* = 12.4, 7.1 Hz, 1 H, 4-H_a), 4.24 (dd, *J* = 12.4, 3.4 Hz, 1 H, 4-H_b), 7.40 (m, 6 H, Ar-H), 7.67 (m, 4 H, Ar-H) ppm. $C_{22}H_{28}O_4Si$ (384.5): calcd. C 68.71, H 7.34; found C 68.86, H 7.45.

Determination of the Enantiomeric Purity of (2*R*,3*S*)-4 Obtained with Lipase PS-C: (2*R*,3*S*)-**4** was analyzed by HPLC (Chiralcel OD®, 25 cm × 4.6 mm; eluent: hexane/2-propanol, 9:1; flow rate: 0.5 mL/min): t_R = 14.0 (99.76%), 21.8 (0.24%) min. The enantiomeric purity of (2*R*,3*S*)-**4** was determined to be 99.5% *ee*.

(2*S*,3*R*)-4-(*tert*-Butyldiphenylsilyloxy)-*cis*-2,3-epoxy-1-butanol [(2*S*,3*R*)-4]: K_2CO_3 (4.80 g, 34.7 mmol) was added to a solution of **5** (9.45 g, 24.6 mmol) in MeOH (90 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C, then diluted water, and extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 5:1) to give (2*S*,3*R*)-**4** (4.42 g, 99%) as a colorless oil, n_D^{24} = 1.5515. $[\alpha]_D^{23}$ = −6.3 (*c* = 1.02, CH_2Cl_2). $C_{20}H_{26}O_3Si$ (342.5): calcd. C 70.13, H 7.65; found C 70.20, H 7.90. Its IR and ^{1}H NMR spectra were identical with those of (±)-**4**.

Determination of the Enantiomeric Purity of (2*S*,3*R*)-4 Obtained with Lipase PS-C: (2*S*,3*R*)-**4** was analyzed by HPLC (Chiralcel OD®, 25 cm × 4.6 mm; eluent: hexane/2-propanol, 9:1; flow rate: 0.5 mL/min]: t_R = 14.0 (0.94%), 22.2 (99.06%) min. The enantiomeric purity of (2*S*,3*R*)-**4** was determined to be 98.1% *ee*.

(2*R*,3*S*)-4-(*tert*-Butyldiphenylsilyloxy)-*cis*-2,3-epoxy-1-butanol [(2*R*,3*S*)-4] and (2*S*,3*R*)-1-Acetoxy-4-(*tert*-butyldiphenylsilyloxy)-*cis*-2,3-epoxybutane (5)

(B) Using Lipase PS: Lipase PS (50 mg) was added to a solution of (±)-**4** (2.00 g, 5.84 mmol) in Et_2O (20 mL) and vinyl acetate (1.0 mL) at room temperature. After stirring for 22 h at room temperature, the enzyme was filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 5:1) to give (2*R*,3*S*)-**4** (969 mg, 48%) and **5** (1.06 g, 47%) as colorless oils.

Determination of the Enantiomeric Purity of (2*R*,3*S*)-4 Obtained with Lipase PS: (2*R*,3*S*)-**4** was analyzed by HPLC (Chiralcel OD®, 25 cm × 4.6 mm; eluent: hexane/2-propanol, 9:1; flow rate: 0.5 mL/min): t_R = 12.5 (99.43%), 19.7 (0.57%) min. The enantiomeric purity of (2*R*,3*S*)-**4** was determined to be 98.9% *ee*.

Determination of the Enantiomeric Purity of 5 Obtained with Lipase PS: The corresponding alcohol of **5** was analyzed by HPLC (Chiralcel OD®, 25 cm × 4.6 mm; eluent: hexane/2-propanol, 9:1; flow rate: 0.5 mL/min]: t_R = 14.5 (1.21%), 21.2 (98.79%) min. The enantiomeric purity of (2*S*,3*R*)-**4** was determined to be 97.6% *ee*.

(C) Using Lipase PS-D: Lipase PS-D (50 mg) was added to a solution of (±)-**4** (2.00 g, 5.84 mmol) in Et_2O (20 mL) and vinyl acetate (1.0 mL) at room temperature. After stirring for 4 h at room temperature, the enzyme was filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 5:1) to give (2*R*,3*S*)-**4** (972 mg, 49%) and **5** (1.11 g, 49%) as colorless oils.

Determination of the Enantiomeric Purity of (2*R*,3*S*)-4 Obtained with Lipase PS-D: (2*R*,3*S*)-**4** was analyzed by HPLC (Chiralcel OD®, 25 cm × 4.6 mm; eluent: hexane/2-propanol, 9:1; flow rate: 0.5 mL/min): t_R = 12.4 (99.81%), 19.8 (0.19%) min. The enantiomeric purity of (2*R*,3*S*)-**4** was determined to be 99.6% *ee*.

Determination of the Enantiomeric Purity of 5 Obtained with Lipase PS-D: The corresponding alcohol of **5** was analyzed by HPLC (Chiralcel OD®, 25 cm × 4.6 mm; eluent: hexane/2-propanol, 9:1; flow rate: 0.5 mL/min): t_R = 15.1 (2.13%), 21.8 (97.87%) min. The enantiomeric purity of (2*S*,3*R*)-**4** was determined to be 95.7% *ee*.

(D) Using Lipase AK: Lipase AK (50 mg) was added to a solution of (±)-**4** (2.00 g, 5.84 mmol) in Et_2O (20 mL) and vinyl acetate (1.0 mL) at room temperature. After stirring for 7 h at room temperature, the enzyme was filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 5:1) to give (2*R*,3*S*)-**4** (964 mg, 48%) and **5** (10.9 g, 49%) as colorless oils.

Determination of the Enantiomeric Purity of (2*R*,3*S*)-4 Obtained with Lipase AK: (2*R*,3*S*)-**4** was analyzed by HPLC (Chiralcel OD®, 25 cm × 4.6 mm; eluent: hexane/2-propanol, 9:1; flow rate: 0.5 mL/min): t_R = 12.6 (98.73%), 19.9 (1.27%) min. The enantiomeric purity of (2*R*,3*S*)-**4** was determined to be 96.6% *ee*.

Determination of the Enantiomeric Purity of 5 Obtained with Lipase AK: The corresponding alcohol of **5** was analyzed by HPLC (Chiralcel OD®, 25 cm × 4.6 mm; eluent: hexane/2-propanol, 9:1; flow rate: 0.5 mL/min]: t_R = 13.9 (1.69%), 20.6 (98.31%) min. The enantiomeric purity of (2*S*,3*R*)-**4** was determined to be 96.6% *ee*.

(2*S*,3*R*)-1-(*tert*-Butyldiphenylsilyloxy)-*cis*-2,3-epoxy-5-heptadecyne [(2*S*,3*R*)-6]: A solution of *n*BuLi (1.55 M in hexane; 22.4 mL, 34.7 mmol) was added dropwise to a solution of (2*R*,3*S*)-**4** (10.8 g, 31.6 mmol) in dry THF (100 mL) at −78 °C under argon. After stirring for 30 min at −78 °C, Tf_2O (5.58 mL, 33.2 mmol) was added dropwise. The mixture was stirred for 30 min at −78 °C, and then a solution of freshly prepared 1-tridecynyllithium [1-tridecynyllithium: A solution of *n*BuLi (1.55 M in hexane; 26.5 mL, 41.1 mmol) was added to a solution of 1-tridecyne (6.84 g, 37.9 mmol) and dry HMPA (40 mL) in dry THF (80 mL) at 0 °C under argon, and then the mixture was stirred for 1 h at 0 °C.] was added at −78 °C via cannula. The mixture was stirred for 1.5 h at −78 °C, then quenched with saturated aqueous NH_4Cl, and extracted with Et_2O. The extract was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 100:1) to give (2*S*,3*R*)-**6** (12.3 g, 77%) as a colorless oil, n_D^{23} = 1.5162. $[\alpha]_D^{23}$ = −31.1 (*c* = 1.13, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 2930 (s, C−H), 2855 (s, C−H), 1590 (w, C=C), 1430(s, Si−C), 1110 (s, Si−O). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.0 Hz, 3 H, 17-H), 1.07 (s, 9 H, *t*Bu), 1.20−1.40 (m, 16 H, 9,10,11,12,13,14,15,16-H), 1.46 (m, 2 H, 8-H), 2.10 (tt, *J* = 7.1, 2.4 Hz, 2 H, 7-H), 2.18 (ddt, *J* = 17.0, 6.7, 2.4 Hz, 1 H, 4-H_a), 2.45 (ddt, *J* = 17.0, 5.9, 2.4 Hz, 1 H, 4-H_b), 3.13−3.22 (m, 2 H, 2,3-H), 3.78 (dd, *J* = 11.7, 5.6 Hz, 1 H, 1-H_a), 3.83 (dd, *J* = 11.7, 5.0 Hz, 1 H, 1-H_b), 7.40 (m, 6 H, Ar-H), 7.69 (m, 4 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CHCl_3$): δ = 14.1, 18.7, 18.9, 19.2, 22.7, 26.7, 28.83, 28.87, 29.1, 29.3, 29.5, 29.61, 29.63, 31.9, 55.1, 56.7, 61.9, 74.6, 82.7, 127.7, 129.8, 133.1, 133.3, 135.56, 135.59 ppm. $C_{33}H_{48}O_2Si$ (504.8): calcd. C 78.51, H 9.58; found C 78.57, H 9.29.

(2*R*,3*S*)-1-(*tert*-Butyldiphenylsilyloxy)-*cis*-2,3-epoxy-5-heptadecyne [(2*R*,3*S*)-6]: In the same manner as that described for the preparation of (2*S*,3*R*)-**6**, (2*S*,3*R*)-**4** (5.09 g, 14.9 mmol) gave (2*R*,3*S*)-**6** (5.98 g, 80%) as a colorless oil, n_D^{23} = 1.5167. $[\alpha]_D^{23}$ = +30.8 (*c* = 1.04, $CHCl_3$). $C_{33}H_{48}O_2Si$ (504.8): calcd. C 78.51, H 9.58; found C

78.57, H 9.74. Its IR, ^{1}H NMR and ^{13}C NMR spectra were identical with those of (2*S*,3*R*)-**6**.

(2*S*,3*R*,5*Z*)-1-(*tert*-Butyldiphenylsilyloxy)-*cis*-2,3-epoxy-5-heptadecene [(2*S*,3*R*)-7]: A solution of (2*S*,3*R*)-**6** (10.6 g, 21.0 mmol) in cyclohexane (20 mL) was added to an ice-cooled suspension of Lindlar catalyst (5% Pd-$CaCO_3$−Pb^{2+}; 100 mg) in cyclohexane (100 mL) under H_2. After stirring for 3 h at room temperature, the mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 100:1) to give (2*S*,3*R*)-**7** (10.4 g, 98%) as a colorless oil, n_D^{22} = 1.5165. $[\alpha]_D^{22}$ = −7.87 (*c* = 1.03, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 2925 (s, C−H), 2855 (s, C−H), 1590 (w, C=C), 1430 (m, Si−C), 1110 (m, Si−O). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.9 Hz, 3 H, 17-H), 1.06 (s, 9 H, *t*Bu), 1.23−1.35 (m, 18 H, 8, 9,10,11,12,13,14,15,16-H), 1.94 (dt, *J* = 7.3, 7.3 Hz, 2 H, 7-H), 2.06 (ddd, *J* = 15.1, 7.6, 6.6 Hz, 1 H, 4-H_a), 2.25 (ddd, *J* = 15.1, 7.6, 6.6 Hz, 1 H, 4-H_b), 2.96 (ddd, *J* = 6.6, 6.6, 4.2 Hz, 1 H, 3-H), 3.17 (ddd, *J* = 5.9, 5.1, 4.2 Hz, 1 H, 2-H), 3.78 (dd, *J* = 11.6, 5.1 Hz, 1 H, 1-H_a), 3.81 (dd, *J* = 11.6, 5.9 Hz, 1 H, 1-H_b), 5.37 (dtt, *J* = 10.8, 7.6, 1.4 Hz, 1 H, 5-H), 5.48 (dtt, *J* = 10.8, 7.3, 1.4 Hz, 1 H, 6-H), 7.40 (m, 6 H, Ar-H), 7.69 (m, 4 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CHCl_3$): δ = 14.1, 19.2, 22.7, 26.3, 26.8, 27.4, 29.27, 29.35, 29.5, 29.62, 29.64, 29.66, 31.9, 56.1, 56.7, 62.2, 123.6, 127.7, 129.8, 132.8, 133.2, 135.56, 135.62 ppm. $C_{33}H_{50}O_2Si$ (506.8): calcd. C 78.20, H 9.94; found C 78.18, H 9.75.

(2*R*,3*S*,5*Z*)-1-(*tert*-Butyldiphenylsilyloxy)-*cis*-2,3-epoxy-5-heptadecene [(2*R*,3*S*)-7]: In the same manner as that described for the preparation of (2*S*,3*R*)-**7**, (2*R*,3*S*)-**6** (4.00 g, 7.94 mmol) gave (2*R*,3*S*)-**6** (3.80 g, 95%) as a colorless oil, n_D^{22} = 1.5164. $[\alpha]_D^{22}$ = +7.60 (*c* = 1.14, $CHCl_3$). $C_{33}H_{50}O_2Si$ (506.8): calcd. C 78.20, H 9.94; found C 78.26, H 10.23. Its IR, ^{1}H NMR and ^{13}C NMR spectra were identical with those of (2*S*,3*R*)-**7**.

(2*S*,3*R*,5*S*,6*R*)-1-(*tert*-Butyldiphenylsilyloxy)-*cis*-2,3-*cis*-5,6-diepoxyheptadecane [(2*S*,3*R*,5*S*,6*R*)-8]: A solution of MCPBA (70% purity, 3.58 g, 14.5 mmol) in CH_2Cl_2 (30 mL) was added dropwise to a solution of (2*S*,3*R*)-**7** (6.18 g, 12.3 mmol) in CH_2Cl_2 (50 mL) at 0 °C. The mixture was stirred for 5 h at room temperature, then quenched with saturated aqueous $NaHCO_3$, and extracted with Et_2O. The extract was washed with water, saturated aqueous Na_2SO_3 and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 30:1) to give a diastereomixture (6.26 g). The diastereomeric ratio was determined by HPLC analysis: The mixture of (2*S*,3*R*,5*S*,6*R*)-**8** and (2*S*,3*R*,5*R*,6*S*)-**8** was analyzed by HPLC (Pegasil-Senshu column, 25 cm × 4.6 mm; eluent: hexane/EtOAc, 20:1; flow rate: 1.0 mL/min), t_R of (2*S*,3*R*,5*S*,6*R*)-**8**: 13.7 min (40%), t_R of (2*S*,3*R*,5*R*,6*S*)-**8**: 17.4 (60%) min. The diastereomixture (6.26 g) was repeatedly separated by MPLC (column 50 cm × 7 cm, silica gel SIL-5020−12B 50 ± 20 μm, hexane/Et_2O, 40:1−20:1) using ca. 2 g at a time to yield (2*S*,3*R*,5*S*,6*R*)-**8** (less polar) (1.50 g, 23%) and its diastereoisomer (2*S*,3*R*,5*R*,6*S*)-**8** (more polar) (3.69 g, 57%) as colorless oils.
(2*S*,3*R*,5*S*,6*R*)-8: n_D^{23} = 1.5161. $[\alpha]_D^{23}$ = −0.58 (*c* = 1.2, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 2925 (s, C−H), 2855 (s, C−H), 1590 (w, C=C), 1430 (m, Si−C), 1110 (m, Si−O). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.8 Hz, 3 H, 17-H), 1.04 (s, 9 H, *t*Bu), 1.20−1.50 (m, 20 H, 7,8,9,10,11,12,13,14,15,16-H), 1.61 (ddd, *J* = 14.6, 5.9, 5.9 Hz, 1 H, 4-H_a), 1.64 (ddd, *J* = 14.6, 6.1, 6.1 Hz, 1 H, 4-H_b), 2.89 (m, 1 H, 6-H), 2.99 (ddd, *J* = 7.0, 5.6, 4.4 Hz, 1 H, 5-H), 3.10 (ddd, *J* = 6.2, 6.1, 4.1 Hz, 1 H, 3-H), 3.18 (ddd, *J* = 5.6, 5.4, 4.1 Hz, 1 H, 2-H), 3.71 (dd, *J* = 11.5, 5.6 Hz, 1 H, 1-H_a), 3.84 (dd, *J* = 11.5, 5.4 Hz, 1 H, 1-H_b), 7.39 (m, 6 H, Ar-H), 7.66 (m, 4 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CHCl_3$): δ = 14.1, 19.2, 22.7, 26.5, 26.7, 26.9, 27.8, 29.3, 29.48, 29.54, 29.6, 31.9, 54.0, 54.1, 56.1, 56.6, 61.9, 127.8, 129.8, 132.95, 133.18, 135.52, 135.57 ppm. $C_{33}H_{50}O_3Si$ (522.8): calcd. C 75.81, H 9.64; found C 75.86, H 9.72.
(2*S*,3*R*,5*R*,6*S*)-8: n_D^{23} = 1.5165. $[\alpha]_D^{23}$ = +7.4 (*c* = 1.2, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 2925 (s, C−H), 2855 (s, C−H), 1590 (w, C=C), 1430 (m, Si−C), 1110 (m, Si−O). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.7 Hz, 3 H, 17-H), 1.06 (s, 9 H, *t*Bu), 1.20−1.35 (m, 18 H, 8,9,10,11,12,13,14,15,16-H), 1.41 (m, 2 H, 7-H), 1.54 (ddd, *J* = 15.4, 7.5, 5.4 Hz, 1 H, 4-H_a), 1.61 (ddd, *J*= 15.4, 7.1, 4.6 Hz, 1 H, 4-H_b), 2.93 (m, 2 H, 6-H), 3.06 (dt, *J* = 7.1, 5.4 Hz, 1 H, 5-H), 3.14 (dt, *J* = 7.5, 4.6 Hz, 1 H, 3-H), 3.23 (dt, *J* = 5.4, 4.6 Hz, 1 H, 2-H), 3.76 (dd, *J* = 12.4, 5.4 Hz, 1 H, 1-H_a), 3.79 (dd, *J* = 12.4, 5.4 Hz, 1 H, 1-H_b) ppm. ^{13}C NMR (100 MHz, $CHCl_3$): δ = 14.1, 19.2, 22.7, 26.5, 26.7, 27.3, 27.8, 29.3, 29.48, 29.55, 29.63, 31.9, 53.9, 54.2, 56.5, 57.0, 62.2, 127.7, 129.78, 129.80, 133.06, 133.22, 135.54, 135.59 ppm. $C_{33}H_{50}O_3Si$ (522.8): calcd. C 75.81, H 9.64; found C 75.94, H 9.92.

(2*R*,3*S*,5*R*,6*S*)-1-(*tert*-Butyldiphenylsilyloxy)-*cis*-2,3-*cis*-5,6-diepoxyheptadecane [(2*R*,3*S*,5*R*,6*S*)-8]: In the same manner as that described for the preparation of (2*S*,3*R*,5*S*,6*R*)-**8**, (2*R*,3*S*)-**7** (3.67 g, 7.20 mmol) gave (2*R*,3*S*,5*R*,6*S*)-**8** (721 mg, 19%) and its diastereoisomer (2*R*,3*S*,5*S*,6*R*)-**8** (1.81 g, 48%) as colorless oils.
(2*R*,3*S*,5*R*,6*S*)-8: n_D^{22} = 1.5165. $[\alpha]_D^{24}$ = +0.53 (*c* = 1.1, $CHCl_3$). $C_{33}H_{50}O_3Si$ (522.8): calcd. C 75.81, H 9.64; found C 75.54, H 9.76. Its IR, ^{1}H NMR and ^{13}C NMR spectra were identical with those of (2*S*,3*R*,5*S*,6*R*)-**8**. **(2*R*,3*S*,5*S*,6*R*)-8:** n_D^{23} = 1.5161. $[\alpha]_D^{23}$ = −7.2 (*c* = 1.0, $CHCl_3$). $C_{33}H_{50}O_3Si$ (522.8): calcd. C 75.69, H 9.77; found C 75.54, H 9.76. Its IR, ^{1}H NMR and ^{13}C NMR spectra were identical with those of (2*S*,3*R*,5*R*,6*S*)-**8**.

(2*S*,3*R*,5*S*,6*R*)-*cis*-2,3-*cis*-5,6-Diepoxy-1-heptadecanol [(2*S*,3*R*,5*S*,6*R*)-9]: TBAF (1.0 M in THF; 2.5 mL, 2.5 mmol) was added to a solution of (2*S*,3*R*,5*S*,6*R*)-**8** (1.26 g, 2.41 mmol) in THF (5 mL) at room temperature. After stirring for 1 h at room temperature, the reaction mixture was diluted with water, and extracted with Et_2O. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 5:1) to give crude (2*S*,3*R*,5*S*,6*R*)-**9** (664 mg) as a colorless solid. The solid was recrystallized from hexane/EtOAc to yield (2*S*,3*R*,5*S*,6*R*)-**9** (559 mg, 81%) as colorless plates, m.p. 57.5−58.5 °C. $[\alpha]_D^{24}$ = −5.35 (*c* = 1.05, $CHCl_3$). IR (KBr): $\tilde{\nu}_{max}$ = 3410 (s, O−H), 2915 (s, C−H), 2845 (s, C−H). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.8 Hz, 3 H, 17-H), 1.21−1.45 (m, 18 H, 8,9,10,11,12,13,14,15,16-H), 1.52 (m, 2 H, 7-H), 1.86 (dd, *J* = 7.1, 6.1 Hz, 2 H, 4-H), 1.92 (dd, *J* = 6.8, 5.6 Hz, 1 H, OH), 2.96 (ddd, *J* = 6.6, 6.1, 4.1 Hz, 1 H, 6-H), 3.08 (ddd, *J* = 6.3, 6.1, 4.3 Hz, 1 H, 5-H), 3.20 (m, 2 H, 2,3-H), 3.77 (ddd, *J* = 11.5, 5.6, 1.5 Hz, 1 H, 1-H_a), 3.87 (ddd, *J* = 11.5, 6.8, 4.4 Hz, 1 H, 1-H_b) ppm. ^{13}C NMR (100 MHz, $CHCl_3$): δ = 14.1, 22.7, 26.6, 27.0, 27.8, 29.3, 29.48, 29.52, 29.6, 31.9, 54.1, 54.4, 56.1, 56.8, 60.4, 60.6 ppm. $C_{17}H_{32}O_3$ (284.4): calcd. C 71.79, H 11.34; found C 71.85, H 11.14.

(2*R*,3*S*,5*R*,6*S*)-*cis*-2,3-*cis*-5,6-Diepoxy-1-heptadecanol [(2*R*,3*S*,5*R*,6*S*)-9]: In the same manner as that described for the preparation of (2*S*,3*R*,5*S*,6*R*)-**9**, (2*R*,3*S*)-**8** (718 mg, 1.37 mmol) gave (2*R*,3*S*,5*R*,6*S*)-**9** (277 mg, 70%) as colorless plates, m.p. 57.5−58.5 °C. $[\alpha]_D^{24}$ = +5.52 (*c* = 1.07, $CHCl_3$). $C_{17}H_{32}O_3$ (284.4): calcd. C 71.79, H 11.34; found C 71.82, H 11.53. Its IR, ^{1}H NMR and ^{13}C NMR spectra were identical with those of (2*S*,3*R*,5*S*,6*R*)-**9**.

(2*S*,3*R*,5*R*,6*S*)-*cis*-2,3-*cis*-5,6-Diepoxy-1-heptadecanol [(2*S*,3*R*,5*R*,6*S*)-9]: In the same manner as that described for the preparation

of (2*S*,3*R*,5*S*,6*R*)-**9**, (2*S*,3*R*)-**8** (3.39 g, 6.44 mmol) gave (2*S*,3*R*,5*R*,6*S*)-**9** (1.16 g, 63%) as colorless needles, m.p. 88.5−89.5 °C. $[\alpha]_D^{25}$ = +21.7 (*c* = 1.26, $CHCl_3$). IR (KBr): $\tilde{\nu}_{max}$ = 3275 (s, O−H), 2915 (s, C−H), 2845 (s, C−H). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.8 Hz, 3 H, 17-H), 1.20−1.58 (m, 21 H, 4H$_a$, 5,6,7,8,9,10,11,12,13,14,15,16-H), 2.26 (ddd, *J* = 14.4, 4.9, 3.0 Hz, 1 H, 4-H$_b$), 3.02 (dd, *J* = 9.7, 4.2 Hz, 1 H, O−H), 3.08 (m, 1 H, 6-H), 3.15 (ddd, *J* = 10.0, 4.4, 3.0 Hz, 1 H, 5-H), 3.24 (m, 2 H, 2,3-H), 3.46 (ddd, *J* = 12.2, 7.5, 4.2 Hz, 1 H, 1-H$_a$), 3.88 (ddd, *J* = 12.2, 9.7, 4.8 Hz, 1 H, 1-H$_b$) ppm. ^{13}C NMR (100 MHz, $CHCl_3$): δ = 14.1, 22.7, 26.3, 26.5, 27.8, 29.31, 29.38, 29.48, 29.50, 29.58, 29.60, 31.9, 54.05, 54.09, 55.3, 58.1, 59.9 ppm. $C_{17}H_{32}O_3$ (284.4): calcd. C 71.79, H 11.34; found C 71.88, H 11.61.

(2*R*,3*S*,5*S*,6*R*)-*cis*-2,3-*cis*-5,6-Diepoxy-1-heptadecanol [(2*R*,3*S*,5*S*,6*R*)-9]: In the same manner as that described for the preparation of (2*S*,3*R*,5*S*,6*R*)-**9**, (2*R*,3*S*)-**8** (1.80 g, 3.42 mmol) gave (2*R*,3*S*,5*S*,6*R*)-**9** (574 mg, 57%) as colorless needles, m.p. 88.5−89.5 °C. $[\alpha]_D^{25}$ = −21.7 (*c* = 1.13, $CHCl_3$). $C_{17}H_{32}O_3$ (284.4): calcd. C 71.79, H 11.34; found C 71.86, H 11.62. Its IR, ^{1}H NMR and ^{13}C NMR spectra were identical with those of (2*S*,3*R*,5*R*,6*S*)-**9**.

(6*S*,7*R*,9*S*,10*R*)-*cis*-6,7-*cis*-9,10-Diepoxy-3-henicosyne [(6*S*,7*R*,9*S*,10*R*)-10]: A solution of *n*BuLi (1.58 M in hexane; 0.33 mL, 0.52 mmol) was added dropwise to a solution of (2*S*,3*R*,5*S*,6*R*)-**9** (118 mg, 0.518 mmol) in dry THF (7 mL) at 0 °C under argon. After stirring for 15 min at −78 °C, Tf_2O (87 μL, 0.52 mmol) was added dropwise. The reaction mixture was stirred for 30 min at −78 °C, and then a solution of freshly prepared 1-butynyllithium (2.8 mL, 0.88 mmol) [1-butynyllithium: *n*BuLi (1.58 M in hexane; 6.0 mL, 9.5 mmol) was added to a solution of 1-butyne (1.08 g, 20 mmol) and dry HMPA (7 mL) in dry THF (15 mL) at 0 °C under argon, and the mixture was stirred for 1 h at 0 °C.] was added at −78 °C. The mixture was stirred for 1 h at −78 °C, then quenched with saturated aqueous NH_4Cl, and extracted with Et_2O. The extract was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 30:1) to give (6*S*,7*R*,9*S*,10*R*)-**10** (65 mg, 48%) as a waxy solid, m.p. 31−33 °C. $[\alpha]_D^{22}$ = +44.8 (*c* = 0.95, $CHCl_3$). IR (KBr): $\tilde{\nu}_{max}$ = 2915 (s, C−H), 2850 (s, C−H). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.8 Hz, 3 H, 21-H), 1.11 (t, *J* = 7.6 Hz, 3 H, 1-H), 1.20−1.45 (m, 18 H, 12,13,14,15,16,17,18,19,20-H), 1.53 (m, 2 H, 11-H), 1.78 (ddd, *J* = 14.6, 5.8, 5.8 Hz, 1 H, 8-H$_a$), 1.82 (ddd, *J* = 14.6, 6.6, 6.6 Hz, 1 H, 8-H$_b$), 2.16 (qt, *J* = 7.6, 2.4 Hz, 2 H, 2-H), 2.22 (ddt, *J* = 16.8, 7.6, 2.4 Hz, 1 H, 5-H$_a$), 2.66 (ddt, *J* = 16.8, 5.3, 2.4 Hz, 1 H, 5-H$_b$), 2.97 (ddd, *J* = 7.3, 5.4, 5.3 Hz, 1 H, 10-H), 3.11−3.20 (m, 3 H, 6, 7,9-H) ppm. ^{13}C NMR (100 MHz, $CHCl_3$): δ = 12.4, 14.0, 14.1, 18.8, 22.7, 26.56, 26.68, 27.8, 29.3, 29.50, 29.53, 29.6, 31.9, 54.0, 54.2, 54.9, 56.7, 73.7, 84.2 ppm. HRMS (EI) [M$^+$] ($C_{21}H_{36}O_2$): calcd. 320.2715; found 320.2723.

(6*R*,7*S*,9*R*,10*S*)-*cis*-6,7-*cis*-9,10-Diepoxy-3-henicosyne [(6*R*,7*S*,9*R*,10*S*)-10]: In the same manner as that described for the preparation of (6*S*,7*R*,9*S*,10*R*)-**10**, (2*R*,3*S*,5*R*,6*S*)-**9** (170 mg, 0.599 mmol) gave (6*R*,7*S*,9*R*,10*S*)-**10** (71 mg, 36%) as a waxy solid, m.p. 31−33 °C. $[\alpha]_D^{22}$ = −43.3 (*c* = 1.00, $CHCl_3$). HRMS (EI) [M$^+$] ($C_{21}H_{36}O_2$): calcd. 320.2715; found 320.2698. Its IR, ^{1}H NMR and ^{13}C NMR spectra were identical with those of (6*S*,7*R*,9*S*,10*R*)-**10**.

(6*S*,7*R*,9*R*,10*S*)-*cis*-6,7-*cis*-9,10-Diepoxy-3-henicosyne [(6*S*,7*R*,9*R*,10*S*)-10]: In the same manner as that described for the preparation of (6*S*,7*R*,9*S*,10*R*)-**10**, (2*S*,3*R*,5*R*,6*S*)-**9** (200 mg, 0.704 mmol) gave (6*S*,7*R*,9*R*,10*S*)-**10** (71 mg, 32%) as a waxy solid, m.p. 56.0−57.5 °C. $[\alpha]_D^{20}$ = +45 (*c* = 0.52, $CHCl_3$). IR (KBr): $\tilde{\nu}_{max}$ = 2915 (s, C−H), 2850 (s, C−H). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.8 Hz, 3 H, 21-H), 1.12 (t, *J* = 7.5 Hz, 3 H, 1-H), 1.21−1.57 (m, 20 H, 11,12,13,14,15,16,17,18,19,20-H), 1.73 (ddd, *J* = 14.6, 7.3, 5.3 Hz, 1 H, 8-H$_a$), 1.82 (ddd, *J* = 14.6, 7.3, 4.6 Hz, 1 H, 8-H$_b$), 2.17 (tq, *J* = 7.5, 2.4 Hz, 2 H, 2-H), 2.29 (ddt, *J* = 7.0, 6.7, 2.4 Hz, 1 H, 5-H$_a$), 2.56 (ddt, *J* = 7.0, 5.8, 2.4 Hz, 1 H, 5-H$_b$), 2.99 (m, 1 H, 10-H), 3.12−3.21 (m, 3 H, 6, 7,9-H) ppm. ^{13}C NMR (100 MHz, $CHCl_3$): δ = 12.4, 14.05, 14.11, 18.9, 22.7, 26.5, 27.0, 27.9, 29.3, 29.50, 29.55, 29.61, 29.63, 31.9, 54.16, 54.20, 55.2, 57.1, 73.9, 84.1 ppm. HRMS (EI) [M$^+$] ($C_{21}H_{36}O_2$): calcd. 320.2715; found 320.2720.

(6*R*,7*S*,9*S*,10*R*)-*cis*-6,7-*cis*-9,10-Diepoxy-3-henicosyne [(6*R*,7*S*,9*S*,10*R*)-10]: In the same manner as that described for the preparation of (6*S*,7*R*,9*S*,10*R*)-**10**, (2*R*,3*S*,5*S*,6*R*)-**9** (200 mg, 0.704 mmol) gave (6*R*,7*S*,9*S*,10*R*)-**10** (100 mg, 44%) as a waxy solid, m.p. 56.0−57.5 °C. $[\alpha]_D^{20}$ = −41 (*c* = 0.53, $CHCl_3$). HRMS (EI) [M$^+$] ($C_{21}H_{36}O_2$): calcd. 320.2715; found 320.2712. Its IR, ^{1}H NMR and ^{13}C NMR spectra were identical with those of (6*S*,7*R*,9*R*,10*S*)-**10**.

(3*Z*,6*S*,7*R*,9*S*,10*R*)-*cis*-6,7-*cis*-9,10-Diepoxy-3-henicosene [(3*Z*,6*S*,7*R*,9*S*,10*R*)-1]: A solution of (6*S*,7*R*,9*S*,10*R*)-**10** (30 mg, 0.092 mmol) in cyclohexane(1 mL) was added to an ice-cooled suspension of Lindlar catalyst (5% Pd−$CaCO_3$−Pb^{2+}; 2 mg) in cyclohexane (2 mL) under H_2. After stirring for 2 h at room temperature, the mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography (hexane/EtOAc, 30:1) to give (3*Z*, 6*S*,7*R*,9*S*,10*R*)-**1** (29 mg, 97%) as a colorless oil. n_D^{22} = 1.4639. $[\alpha]_D^{22}$ = +5.0 (*c* = 0.55, $CHCl_3$) {ref.[2] $[\alpha]_D$ = +3.1 (*c* = 0.8, $CHCl_3$)}. IR (film): $\tilde{\nu}_{max}$ = 2925 (s, C−H), 2855 (s, C−H), 1655 (w, C=C), 1460 (s), 1265 (m), 830 (m), 720 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.6 Hz, 3 H, 21-H), 0.98 (t, *J* = 7.5 Hz, 3 H, 1-H), 1.21−1.48 (m, 18 H, 12,13,14,15,16,17,18,19,20-H), 1.58 (m, 2 H, 11-H), 1.76 (ddd, *J* = 14.6, 5.8, 5.8 Hz, 1 H, 8-H$_a$), 1.83 (ddd, *J* = 14.6, 6.7, 6.7 Hz, 1 H, 8-H$_b$), 2.07 (dq, *J* = 7.5, 7.4 Hz, 2 H, 2-H), 2.22 (ddd, *J* = 15.1, 7.3, 6.7 Hz, 1 H, 5-H$_a$), 2.42 (ddd, *J* = 15.1, 7.3, 6.1 Hz, 5-H$_b$), 2.97 (ddd, *J* = 6.2, 6.1, 4.3 Hz, 1 H, 10-H), 3.00 (ddd, *J* = 6.7, 6.1, 4.3 Hz, 1 H, 6-H), 3.09 (m, 2 H, 7,9-H), 5.39 (dt, *J* = 10.7, 7.3 Hz, 1 H, 4-H), 5.45 (dt, *J* = 10.7, 7.4 Hz, 1 H, 3-H) ppm. ^{13}C NMR (126 MHz, $CHCl_3$): δ = 14.10, 14.13, 20.8, 22.7, 26.1, 26.6, 26.9, 27.8, 29.3, 29.51, 29.53, 29.6, 31.9, 54.14, 54.20, 56.1, 56.7, 122.8, 134.6 ppm. EI MS (70 eV): *m*/*z* (%) = 322 (2) [M$^+$], 293 (6), 275 (4), 265 (4), 237 (5), 223 (3), 197 (8), 178 (5), 167 (5), 149 (6), 137 (8), 123 (20), 109 (61), 95 (58), 82 (89), 67 (98), 55 (100), 41 (92), 29 (26). HRMS (EI) [M$^+$] ($C_{21}H_{38}O_2$): calcd. 322.2872; found 322.2869.

(3*Z*,6*R*,7*S*,9*R*,10*S*)-*cis*-6,7-*cis*-9,10-Diepoxy-3-henicosene [(3*Z*,6*R*,7*S*,9*R*,10*S*)-1]: In the same manner as that described for the preparation of (3*Z*,6*S*,7*R*,9*S*,10*R*)-**1**, (6*R*,7*S*,9*R*,10*S*)-**10** (31 mg, 0.095 mmol) gave (3*Z*,6*R*,7*S*,9*R*,10*S*)-**1** (29 mg, 94%) as a colorless oil. n_D^{22} = 1.4639. $[\alpha]_D^{22}$ = −4.5 (*c* = 0.55, $CHCl_3$) {ref.[2] $[\alpha]_D$ = −3.2 (*c* = 0.7, $CHCl_3$)}. HRMS (EI) [M$^+$] ($C_{21}H_{38}O_2$): calcd. 322.2872; found 322.2872. Its IR, ^{1}H NMR and ^{13}C NMR spectra were identical with those of (3*Z*, 6*S*,7*R*,9*S*,10*R*)-**1**.

(3*Z*,6*S*,7*R*,9*R*,10*S*)-*cis*-6,7-*cis*-9,10-Diepoxy-3-henicosene [(3*Z*,6*S*,7*R*,9*R*,10*S*)-1]: In the same manner as that described for the preparation of (3*Z*,6*S*,7*R*,9*S*,10*R*)-**1**, (6*S*,7*R*,9*R*,10*S*)-**10** (42 mg, 0.13 mmol) gave (3*Z*,6*S*,7*R*,9*R*,10*S*)-**1** (41 mg, 97%) as a colorless waxy solid. m.p. 44−45 °C. $[\alpha]_D^{20}$ = +21.4 (*c* = 0.41, $CHCl_3$), {ref.[2] $[\alpha]_D$ = +17.6 (*c* = 1.0, $CHCl_3$)}. IR (KBr): $\tilde{\nu}_{max}$ = 2915 (s, C−H), 2850 (s, C−H), 1470 (s), 830 (m), 720 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.7 Hz, 3 H, 21-H), 0.98 (t, *J* = 7.5 Hz,

3 H, 1-H), 1.20−1.58 (m, 20 H, 11,12,13,14,15,16,17,18,19,20-H), 1.77 (dd, J = 6.3, 6.1 Hz, 2 H, 8-H), 2.07 (dq, J = 7.5, 7.3 Hz, 2 H, 2-H), 2.21 (ddd, J = 14.9, 7.3, 7.0 Hz, 1 H, 5-H_a), 2.38 (ddd, J = 14.9, 7.3, 6.6 Hz, 5-H_b), 2.99 (m, 2 H, 6, 10-H), 3.14 (m, 2 H, 7,9-H), 5.41 (dddt, J = 10.5, 7.3, 7.3, 1.5 Hz, 1 H, 4-H), 5.54 (dtt, J = 10.5, 7.3, 1.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, $CHCl_3$): δ = 14.11, 14.16, 20.8, 22.7, 26.2, 26.5, 27.2, 27.9, 29.3, 29.50, 29.54, 29.61, 29.63, 31.9, 54.30, 54.33, 56.4, 57.0, 122.9, 134.5 ppm. EI MS (70 eV): *m*/*z* (%) = 322 (3) [M^+], 304 (3), 293 (7), 275 (5), 237 (5), 197 (10), 167 (8), 138 (12), 123 (20), 109 (55), 95 (53), 82 (86), 67 (93), 55 (100), 41 (98), 29 (27). HRMS (EI) [M^+] ($C_{21}H_{36}O_2$): calcd. 322.2872; found 322.2855.

(3*Z*,6*R*,7*S*,9*S*,10*R*)-*cis*-6,7-*cis*-9,10-Diepoxy-3-henicosene [(3*Z*,6*R*,7*S*,9*S*,10*R*)-1]: In the same manner as that described for the preparation of (3*Z*,6*S*,7*R*,9*S*,10*R*)-**1**, (6*R*,7*S*,9*S*,10*R*)-**10** (44 mg, 0.14 mmol) gave (3*Z*,6*R*,7*S*,9*S*,10*R*)-**1** (42 mg, 95%) as a colorless waxy solid. m.p. 44−45 °C. $[\alpha]_D^{20}$ = −21.3 (*c* = 0.50, $CHCl_3$) {ref.[2] $[\alpha]_D$ = −19.2 (*c* = 1.0, $CHCl_3$)}. HRMS (EI) [M^+] ($C_{21}H_{36}O_2$): calcd. 322.2872; found 322.2875. Its IR, ^{1}H NMR and ^{13}C NMR spectra were identical with those of (3*Z*,6*S*,7*R*,9*R*,10*S*)-**1**.

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