α-Sulfenyl-Directed Ring-Opening Reactions of Epoxides. 1. Highly Regio- and Stereoselective Reaction with Organo-Aluminum Reagents and Application to the Synthesis of an Aggregation Pheromone

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The reaction of 1-phenylthio-2,3-epoxyalkanes with trialkylaluminum showed definite C-2 selectivity for nucleophilic ring-opening and gave C-2 alkylated products exclusively with the complete retention of the configuration at the C-2. In contrast, upon reacting with alkenyl(dialkyl)aluminum, dialkyl(alkynyl)aluminum, or DIBAL, the nucleophilic attack occurred at the C-1 with concomitant rearrangement of the sulfenyl group to the C-2 with the complete inversion of the configuration at the C-2. The reactions of these epoxides were considered to proceed via an episulfonium ion intermediate. Upon applying the present reaction, an aggregation pheromone of African Palm Weevil was stereoselectively synthesized in short steps.

The nucleophilic ring-opening reaction of epoxides by organometallic reagents has long been exploited for the stereospecific transformation of the epoxides to β-substituted alcohols. The special value of this general type of reaction in synthetic organic chemistry makes epoxides very useful synthetic intermediates. Diverse arrays can be afforded by the combination of many stereoselective alkene-forming methods and a number of diastereospecific and, more recently, highly enantioselective epoxidation methods that are available.[1] Thus, depending upon the initial choice of the substitution pattern of an epoxide, the reaction of a nucleophilic organometallic reagent with the three-membered ring of the epoxide affords the corresponding β-substituted alcohol with the inversion of the configuration at the β-position and with a considerable structural latitude. The ring-opening reactions of monosubstituted, geminally disubstituted, and trisubstituted epoxides generally proceed with a decided preference for a nucleophilic attack at the least substituted or the most substituted ring carbon upon being activated by a base or an acid, respectively. However, the ring-opening reactions of vicinally disubstituted epoxides, especially those with negligible steric and/or electronic bias to the three-membered ring, exhibits poor regioselectivity.[2] Hence, many efforts have been devoted to the regioselective, nucleophilic ring-opening reactions of vicinally disubstituted epoxides. Up to now, most of the regioselective ring-opening reactions of vicinally disubstituted epoxides are oxygen-directed reactions; there are a number of reports concerning the hydride reductions of cyclohexene oxide derivatives having an oxygenated function at the α-position, where the substituent appears to play a major role in the determination of the direction of oxirane-opening.[3] An example is found in the work of Fales and Wildman[4] on an alkaloid, crimamidine, and its *O*-tetrahydropyranyl derivative; the materials exhibit different regioselectivity for a hydride attack. Subsequently, it has been demonstrated that monocyclic vicinally disubstituted epoxides are versatile candidates for oxygen-directed ring-opening reactions. For example, the reaction of monocyclic β-alkoxy epoxides with organocuprate reagents shows a clear preference for alkylation distal to the alkoxy group.[5] The reaction of α-hydroxy epoxides with suitable organometallic reagents provides distal or proximal ring-opened products regioselectively.[6] Chong and Sharpless reported that 2,3-epoxy acids are regioselectively opened at the C-3 by nucleophiles in the presence of $Ti(O\text{-}i\text{-}Pr)_4$.[7] Most of the oxygen-directed nucleophilic ring-opening reactions of epoxides are based on the chelation control of a metallic reagent with the epoxide oxygen and with a suitably positioned, oxygenated substituent. Thus, the oxygen-directed, regioselective ring-opening reactions of epoxides have been intensively investigated.

Recently, there have been some reports on the sulfur-directed ring-opening reactions of epoxides.[8] For example, Rayner and co-workers reported the Lewis acid-promoted regio- and stereoselective ring-opening reaction of α-sulfenyl epoxides with nitrogen nucleophiles via episulfonium ions generated in situ. However, compared with the many investigations on the oxygen-directed ring-opening reactions of epoxides, the number of studies concerning the sulfur-directed ones has been relatively limited.

Over the past several years, we have been applying the neighboring group participation of a sulfenyl group to synthetic organic chemistry, and reported regio- and/or stereoselective reactions using an episulfonium or a related cationic intermediate.[9] In the course of our studies, we were interested in the ring-opening reactions of α-sulfenyl epoxides.

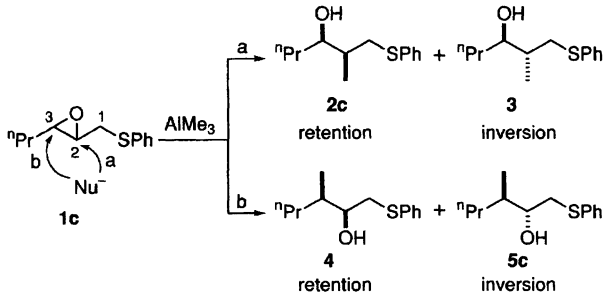
In our investigation, we carried out the reaction of α-sulfenyl epoxides with organo-aluminum reagents, which are known to act both as a Lewis acid and as a nucleophile, to develop a new method for the regio- and stereoselective construction of a C–C bond. We considered that a Lewis acid-activated ring-opening reaction of α-sulfenyl epoxides will proceed via an episulfonium ion.

In this paper, we report on the reaction of α-sulfenyl epoxides with organo-aluminum reagents in detail and discuss the mechanistic aspects. We also report on a short-step synthesis of an aggregation pheromone of African Palm Weevil by using this reaction.

Results and Discussion

At first, in order to prepare a model substrate, we introduced a sulfenyl group at the α-position of an oxirane ring by the reaction of *trans*-2,3-epoxy-1-hexanol with diphenyl disulfide and tributylphosphine in pyridine,[10] giving *trans*-2,3-epoxy-1-phenylthiohexane (**1c**) in 88% yield. The reaction of **1c** with trimethylaluminum in hexane at 0 °C exclusively gave C-2 methylated product **2c** with the retention of the configuration at the C-2 in 27% yield, and no diastereo- nor regioisomer, such as **3**, **4**, and **5c**, was detected (Scheme 1). The major by-products were the dimers and the rearranged products, and 28% of starting material **1c** was recovered. Prompted by this finding, we optimized the reaction conditions by using **1c** and trimethylaluminum. The results are listed in Table 1.

First, we examined the effect of the amount of trimethylaluminum for the reaction carried out in hexane at 0 °C. The results listed in Table 1 show that the yield of **2c** dramatically increased with increasing the amount of trimethylaluminum (Entries 1—4). Although the yield of **2c** reached 77%, when 1.5 equimolar amount of trimethylaluminum was used, there was still 8% of **1c** recovered. When 2 equimolar amounts of trimethylaluminum was used, starting material **1c** was completely consumed and the yield of **2c** reached 93% (Entry 4); in order to achieve high conversion, an additional equimolar amount of trimethylaluminum was required, presumably due to the coordination of trimethylaluminum with the formed alkoxy(dimethyl)aluminum.[11] Next, the reaction was performed in various solvents (Entries 4—8). When the reaction was conducted in diethyl ether, no C-2 methylated product **2c** was obtained and 95% of starting material **1c** was recovered (Entry 7). In acetonitrile, only 4% of **2c** was obtained and 81% of starting material **1c** was recovered. The negligible reactivity of trimethylaluminum in such Lewis-basic solvents is likely due to the strong solvation of trimethylaluminum to diminish its coordination toward the epoxide oxygen in **1c**. Although the reactions in dichloromethane (Entry 5) and benzene (Entry 6) also gave **2c** in good yields, the reaction in hexane gave **2c** in the best yield (Entry 4).



Scheme 1.

Table 1. The Reactions of **1c** with Trimethylaluminum under Various Conditions[a]

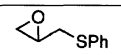
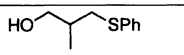
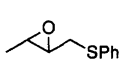
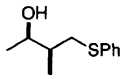
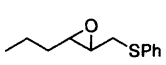
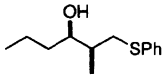
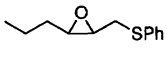
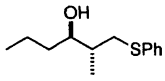
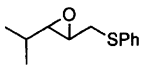
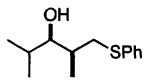
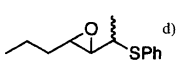
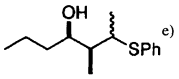
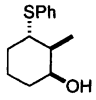
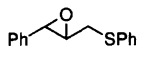
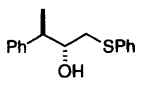
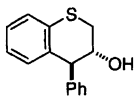
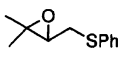
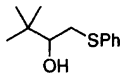
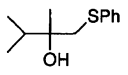
Entry	$AlMe_3$ (molar amount)	Solvent	Yield of **2c**/%[b]
1	1.0	Hexane	27
2	1.2	Hexane	44
3	1.5	Hexane	77
4	2.0	Hexane	92
5	2.0	CH_2Cl_2	79
6	2.0	Benzene	84
7	2.0	Et_2O	0
8	2.0	MeCN	4

a) The reaction was carried out at 0 °C for 1 h. b) Isolated yield.

In the next stage, we investigated the effects of the stereochemistry and substituents of an epoxide on the regioselectivity of the methylation reaction; epoxides **1a—i** (see Table 2) were used in our investigation, and the reactions were carried out at 0 °C in hexane. The results are listed in Table 2.

For mono-substituted epoxide **1a**, the ring-opening reaction proceeded exclusively at the C-2 to give the methylated product **2a** in fair yield (Entry 1). Moreover, 1,2-disubstituted epoxides **1b—g** showed an exclusive preference for C-2 methylation (Entries 2—7). It is noteworthy that the stereochemistry of the epoxides did not affect the regioselectivity of the reaction to give the C-2 methylated products with the retention of the configuration at the C-2 (Entries 3 and 4). It is also worthy to note that an alkyl group at the α-position of the 1,2-disubstituted epoxides showed no effect on the regio- and stereoselectives of the reaction (Entries 5—7). Chini and co-workers[12] reported that the regioselectivity of the reaction of 1-alkoxy-2,3-epoxyalkane with nucleophiles in the presence of a metal ion is affected by the steric hindrance of the substituent adjacent to the oxirane ring; this reaction is considered to be controlled by a bidentate chelation. In contrast, our finding indicates that the regioselectivity of the present reaction is controlled by a factor different from such a bidentate control (vide infra). The reaction of 1,2-disubstituted epoxide **1h**, however, showed quite different regio- and stereoselectivities (Entry 8). C-3 methylated product **5h** and cyclized product **6** were obtained in 77 and 12% isolated yields, respectively, with the complete inversion of the configuration at the C-3. This reverse selectivity would be due to the overwhelming directing-effect of the phenyl group on the ring-opening reaction of the epoxide.[6a] In the case of trisubstituted epoxide **1i**, the reaction proceeded sluggishly with 2 equimolar amounts of trimethylaluminum at 0 °C in hexane. After the reaction was performed for 24 h at room temperature, C-3 methylated product **5i** and rearranged product **7** were obtained in 54 and 18% yields, respectively, and

Table 2. The Reactions of Various Epoxides with Trimethylaluminum[a)]

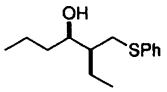
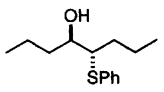
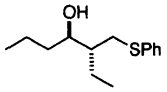
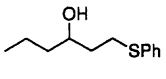
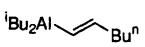
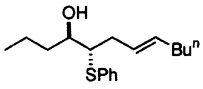
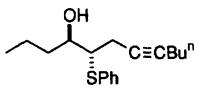
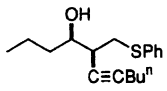
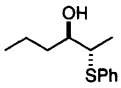
Entry	Epoxide	Reaction time/h	Product (Yield / %)[b)]	
1		0.5		(72)
	1a		**2a**	
2		1		(89)
	1b		**2b**	
3		1		(92)
	1c		**2c**	
4		1		(92)
	1d		**2d**	
5		0.5		(96)[c)]
	1e		**2e**	
6		0.6		(91)
	1f		**2f**	
7		0.6		(74)
	1g		**2g**	
8		0.6		
	1h		**5h** (72)	**6** (12)
9[f)]		24		
	1i		**5i** (54)[c)]	**7** (18)[c)]

a) The reaction was carried out at 0 °C in hexane. b) Isolated yield of the corresponding acetate otherwise stated. c) Isolated yield of the alcohol. d) Diastereomer ratio: 26 : 74, determined by GC. e) Diastereomer ratio; 27 : 73, determined by ^{1}H NMR. f) The reaction was carried out at room temperature.

no C-2 methylated product was detected (Entry 9); **7** would be produced by the ring-opening at the C-3 to give a tertiary cation, followed by the hydride shift from the C-2 to the C-3 and methylation of the resulting ketone.

Next we examined the reaction of epoxides **1c** and **1d** with various organo-aluminum reagents (Table 3). All of the reactions were performed at 0 °C in hexane, and 2 equimolar amounts of the organo-aluminum reagents were used. The reaction of **1c** with triethylaluminum gave C-2 ethylated product **8c** almost exclusively accompanied with only a small amount of sulfenyl-shifted, C-1 ethylated product **9** (Entry 3). The reaction of **1d** with triethylaluminum also gave C-2 ethylated product **8d** and ring-opened product **10**, formed by a hydride attack at the C-2, in 43% and 40% yields, respectively. Although the reaction gave two products, the regio- and stereoselectivities were maintained; the

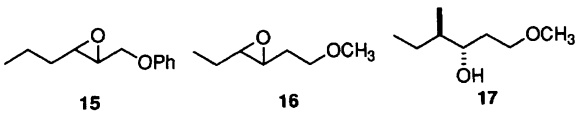
Table 3. The Reactions of Epoxides **1c** and **1d** with Various Aluminum Reagents[a)]

Entry	Aluminum regent	Epoxide	Reaction time/h	Product (Yield / %)[b)]
1	Me_3Al	**1c**	1	**2c** (92)
2	Me_3Al	**1d**	1	**2d** (92)
3	Et_3Al	**1c**	2	  (86)[c)] **8c** >96:<4 **9**
4	Et_3Al	**1d**	2	  **8d** (43) **10** (40)
5	$^iBu_2Al$ 	**1c**	2	 **10** (13) **11** (58)
6	$Et_2AlC{\equiv}CBu^n$	**1c**	2	  (78)[c)] **12** 90:10 **13c**
7	DIBAL	**1c**	1	 (86)[d)] **10**(5)[d)] **14**

a) The reaction was carried out at 0 °C in hexane. b) Isolated yield of the corresponding acetate otherwise stated.
c) Yield of mixture and the ratio was determined by GC. d) Yield of the alcohol.

ring-opening reaction exclusively occurred at the C-2 (Entry 4). To our surprise, the reactions of **1c** with the other organoaluminum reagents showed quite different regioselectivity. The reaction of **1c** with 1-hexenyl(diisobutyl)aluminum gave sulfenyl-shifted, C-1 ring-opened product **11** as a major product, accompanied with 13% yield of C-2 ring-opened product **10** (Entry 5). The reactions of **1c** with diethyl(1-hexynyl)-aluminum and diisobutylaluminum hydride (DIBAL) also gave mainly sulfenyl-shifted, C-1 ring-opened products **12** and **14**, along with a small amount of C-2 ring-opened products **13c** and **10**, respectively (Entries 6 and 7). Sulfenyl-shifted, C-1 ring-opened products **11**, **12**, and **14** were obtained with the complete inversion of the configuration at the C-2. Ring-opened product **10** in Entries 4 and 5 was considered to be produced by the nucleophilic attack of the β-hydrogen of the organo-aluminum reagent. The facts that sulfenyl-shifted products were obtained in Entries 3—7 strongly suggest that the neighboring sulfenyl group participated in the ring-opening reaction.

To elucidate the effect of the sulfenyl group, a control experiment was carried out by using **15** (Chart 1) and trimethylaluminum. Epoxide **15** showed no reactivity toward trimethylaluminum at 0 °C in hexane for 3 h, and over 90% of



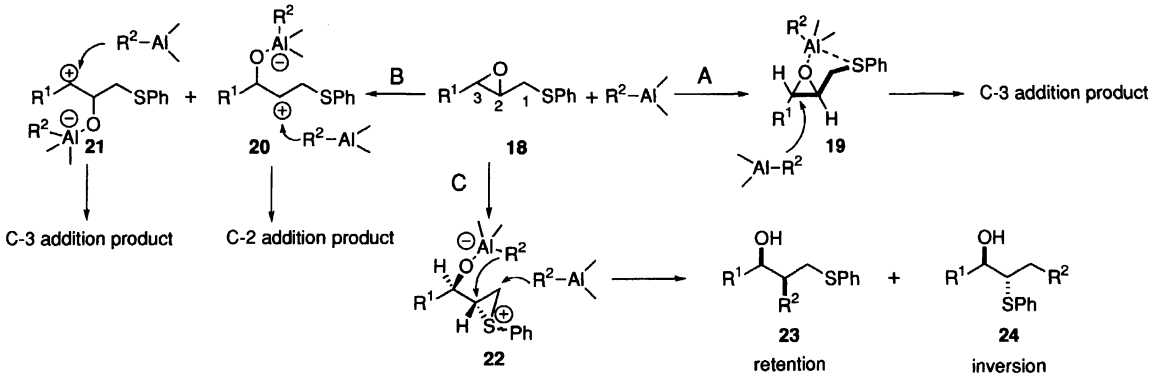
15 **16** **17**

Chart 1.

the epoxide was recovered after the usual work-up. Flippin and co-workers[5a)] reported that epoxide **16** reacted very sluggishly with 2 equimolar amounts of trimethylaluminum (hexane, 0 °C, 16 h) to give a 1 : 1 mixture of the starting material and single β-methyl alcohol **17**, accompanied with a small amount of an unidentified substance. These facts strongly suggest that the sulfenyl group in the epoxides is effective for acceleration as well as for controlling the regioselectivity and stereospecificity of the ring-opening reaction.

For the present reaction, three paths are considered to be possible, as depicted in Scheme 2.

Path A is similar to that proposed for the ring-opening reaction of 1-alkoxy-2,3-epoxyalkane catalyzed by a Lewis acid.[5b,11)] The reaction, which proceeds through Path A via chelating intermediate **19**, would predominantly give the C-3 ring-opened product,[7,11)] and the regioselectivity may be affected by the steric hindrance of the substituent adjacent



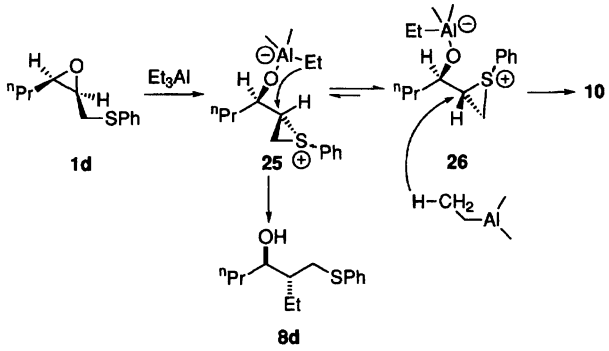
Scheme 2.

to the oxirane ring. However, our reactions gave C-2 ring-opened products or sulfenyl-shifted, C-1 ring-opened products, and the steric hindrance of the substituent adjacent to the oxirane ring had no effect on the regioselectivity. Moreover, epoxide **15** showed no reactivity toward trimethylaluminum under our reaction conditions. On the basis of these facts, the possibility of Path A should be excluded.

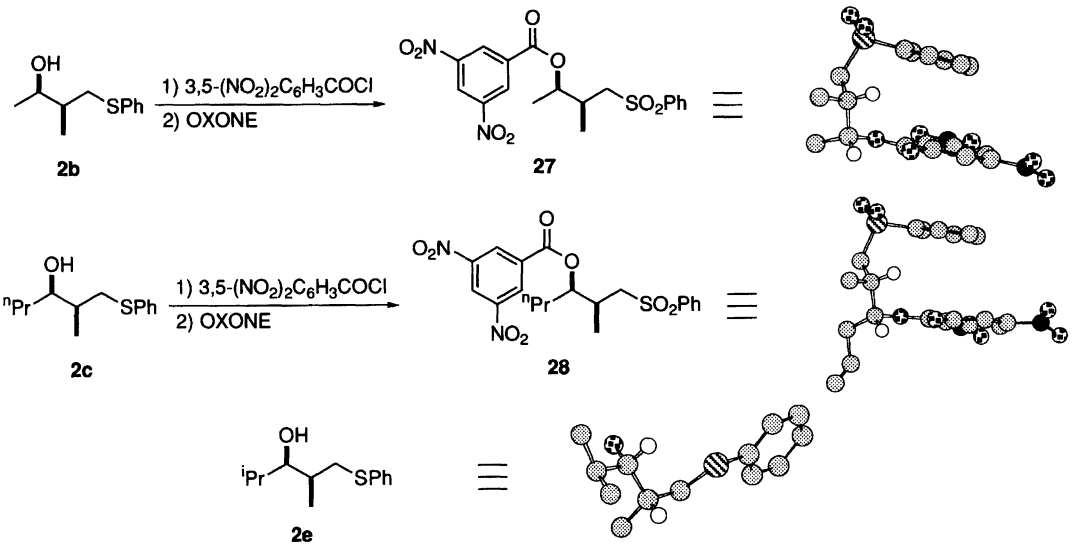
In Path B, the cationic species would be formed by the coordination of the organo-aluminum reagent to the epoxide oxygen. Namy and Boireau[11] proposed a similar mechanism for the reaction of 1,2-epoxy-3-phenylpropane with trimethylaluminum, in which the carbocation was stabilized by the phenyl group. The reaction of **1i** with trimethylaluminum would proceed though this path, since the C-3 carbocation is a relatively stable tertiary carbocation; a nucleophilic attack at the C-3 carbocation and a hydride transfer from the C-2 to the C-3, followed by a nucleophilic attack at the C-2, may explain the formation of compounds **5i** and **7**, respectively. However, it would be very difficult to form such a cationic species, when the carbocation is not efficiently stabilized. This explanation is supported by the fact that epoxide **15** did not react with trimethylaluminum under our conditions. Moreover, when the R^1 group is an alkyl group, it is hard to produce **20** or **21** exclusively, since both **20** and **21** are secondary carbocations with similar stability if the difference in electron-inducing effect between the R^1 group and phenylthiomethyl group is negligible. Hence, this reaction should show poor regioselectivity; only when the R^1 group was a pheyl group (**1h**), which may efficiently stabilize carbocation **21**, did this reaction proceed through this path with high C-3 regioselectivity (Table 2, Entry 8). An S_N2-type reaction via a tight ion pair may explain the observed inversion of the configuration at the C-3.

In Path C, the organo-aluminum reagent coordinates to the epoxide oxygen, and the sulfur atom attacks at the C-2 from the back-side of the C–O bond with the scission of the C–O bond, forming fairly stable episulfonium ion **22**. Then, the nucleophilic attack of the R^2 group at the C-2 or C-1 of episulfonium ion **22** gives C-2 ring-opened product **23** with the retention of the configuration or sulfenyl-shifted, C-1 ring-opened product **24**. When trimethylaluminum was used, an intramolecular nucleophilic attack would occur due to an entropic advantage to give C-2 methylated product **23** exclusively. The formation of minor C-1 ethylated product **9** in the case of the reaction of **1c** with triethylaluminum (Table 3, Entry 3) may be explained by the terms that an intermolecular nucleophilic attack occurs at the C-1, where steric hindrance is small. Conformational preference for the intermediate episulfonium ion as well as low reactivity of the organo-aluminum reagent can be considered in order to explain the low yield of ethylated product **8d** (Table 3, Entry 4). A study by using molecular models revealed that, between conformers **25** and **26** derived from *cis* epoxide **1d**, **26** is apparently more stable than **25** (Scheme 3). Conformer **25** is necessary for an intramolecular nucleophilic attack at the C-2, whereas conformer **26** is favorable for an intermolecular nucleophilic attack by the β-hydrogen of triethylaluminum. Thus, the intramolecular ethylation and intermolecular hydride attack competitively occur to give **8d** and **10** in 43 and 40% yields, respectively. The fact that sulfenyl-shifted, C-1 ring-opened products became the major products in the reactions of **1c** with 1-hexenyl(diisobutyl)aluminum, diethyl(1-hexynyl)aluminum, and DIBAL (Table 3, Entries 5—7) supports this mechanism through an episulfonium ion. The phenomenon can be explained consistently as follows: An intermolecular nucleophilic attack becomes possible, since the reactivity of alkenyl- or alkynylaluminum or aluminum hydride is higher than that of alkylalulminum and/or since a nucleophilic attack at the C-2 has to overcome steric disadvantage, which is more serious than that at the C-1.[8a]

Thus, the observed high regioselectivity and stereospecificity of the present reaction can be explained by Path C.



Scheme 3.



Scheme 4.

In conclusion, the ring-opening reactions of 1-phenylthio-2,3-epoxyalkanes showed definite C-2 regioselectivity with the complete retention of the configuration at the C-2 upon reacting with trialkylaluminum, while they showed C-1 regioselectivity upon reacting with alkenyl(dialkyl)aluminum, dialkyl(alkynyl)aluminum, or DIBAL. As intermediates of these reactions, episulfonium ions should be formed by the neighboring participation of the sulfenyl group.

Determination of the Stereochemistry. X-Ray crystallographic analyses were performed in order to establish the structures of the following compounds: **2e**, **6**, sulfone **27** derived from **2b**, and sulfone **28** obtained from **2c** (Scheme 4). The stereochemistry of **2d** was confirmed on the basis of careful comparison of the ^{1}H NMR and MS spectra with those of **2c**. The stereochemistry of **5h** was confirmed by the fact that the coupling constant between H_{C-2} and H_{C-3} ($J = 7.6$ Hz) is much larger than the corresponding coupling constant of a similar compound, (2*R**, 3*S**)-1,2-diacetoxy-3-phenylbutane ($J = 2.0$ Hz).[6e] The stereochemistry of **14** was confirmed by comparison of the coupling constant between H_{C-2} and H_{C-3} with that of *β*-sulfenyl alcohols reported by Shimagaki and co-workers.[13] The stereochemistry of **2g** was determined on the basis of its ^{1}H NMR spectrum.

The stereochemistry of some other compounds were confirmed on the basis of a correlation of the ^{1}H NMR chemical shift of a selected peak (PhSC*H*).

Synthesis of an Aggregation Pheromone of African Palm Weevil. The structure R^1–CHMeCH(OH)–R^2 is often found in natural products, for example, an aggregation pheromone of African Palm Weevil (**29**),[14] a pheromone of Rhynchophorus vulneratus (**30**),[15] and a pheromone of the Smaller European Elm Bark Beetle (**31**)[16] (Chart 2). In the synthesis of such compounds, the construction of the two chiral centers would be the most important step. Since *α*-sulfenyl epoxides were easily synthesized from *α*-hydroxy epoxides, and since high regioselectivity and complete retention of the configuration were achieved, the present reaction would be applicable to the synthesis of such natural compounds, coupled with the Sharpless asymmetric epoxidation. Thus, we tried to synthesize an aggregation pheromone of African Palm Weevil (**29**). As shown in Scheme 5, optically active epoxy alcohol **33**[17] was prepared by the Sharpless asymmetric epoxidation of allyl alcohol **32** by using *t*-butyl hydroperoxide (TBHP) and L-(+)-diisopropyl tartrate (L-(+)-DIPT)[18] in 80% yield (based on TBHP; ca 1.7 equimolar amounts of racemic allylic alcohol **32** were used) with a 95 : 5 diastereomer ratio. Optically active alcohol **33** was allowed to react with tributylphosphine/*N*-(phenylthio)succinimide in benzene[19] to give phenylthio epoxide **34** in 73% yield. The nucleophilic ring-opening reaction of epoxide **34** with trimethylaluminum gave methylated **35** in 92% yield. Desulfurization of **35** with Raney Ni W-2[20] afforded diastereomerically pure pheromone **29** in 85% yield with an optical purity of 94%. Thus, our method for the preparation of pheromone **29** is much more effective and simple than that described in the literature.[14]

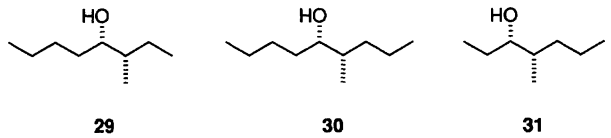
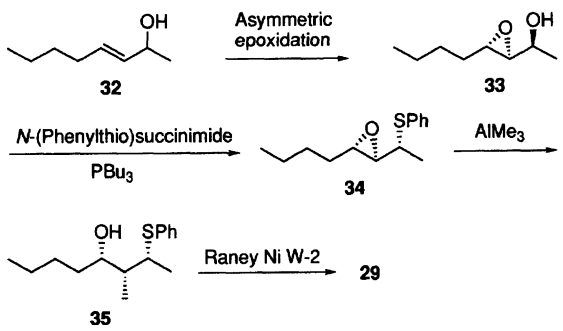


Chart 2.



Scheme 5.

Experimental

General. The starting materials and reagents, purchased from commercial suppliers, were used without further purification. All of the solvents were dried and distilled before use, and were stored over sodium wire or molecular sieves.

The melting points were measured using a metal-block apparatus and an open capillary tube, and are uncorrected. Infrared spectra were determined with a JASCO IR-810 spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured on a JEOL JNM-EX 270 instrument with tetramethylsilane as an internal standard. Gas chromatography was performed on a Shimadzu GC-14A. Mass spectra were obtained with a Shimadzu QP-2000 or a JEOL JMS AX-505H instrument. Column chromatography was carried out with Merck Kiesegel 60 (70—230 mesh). Wakogel B-5F was used for preparative TLC.

Diethyl(1- hexenyl)aluminum[21] and 1- hexynyl(diisobutyl)-aluminum[22] were prepared according to procedures described in references. Raney Ni W-2 was prepared by a known procedure.[23] Epoxy alcohols were prepared by epoxidation of the corresponding allyl alcohols with TBHP/VO(acac)$_2$.[24] 2,3-Epoxy-1-phenylthiopropane (**1a**) was prepared according to a method described in the literature: 95% yield; bp 110 °C (1 mmHg, Kugel rohr oven temperature, 1 mmHg = 133.322 Pa). The ^{1}H NMR spectrum was identical with that in the literature.[25]

X-Ray Measurement. Intensity data were measured on MAC-Science four-circle diffractometer (MXC-18) with graphite-monochromated Cu $K\alpha$ radiation. Accurate cell dimensions were obtained by a least-squared refinement of 20 reflections in the range of $50° < 2\theta < 60°$. Data were collected with three check reflections. The observed reflections with $|F_o| > 3\sigma(|F_o|)$ were used in the solutions and refinements; no absorption correction was made. The structures were solved and refined by applying the Crystal-GM package.[26] Tables of the coordinates, thermal parameters, bond lengths, and angles have been deposited as Document No. 69042 at the Office of the Editor of Bull. Chem. Soc. Jpn.

***trans*-2,3-Epoxy-1-phenylthiobutane (1b).** To a solution of *trans*-2,3-epoxy-1-butanol (1.2 g, 13.6 mmol) in dry pyridine (17 ml) were added triphenylphosphine (6.9 g, 34 mmol) and diphenyl disulfide (7.4 g, 34 mmol). After being stirred for 1.5 h at room temperature, the reaction mixture was poured into a mixture of cracked ice (30 g) and concentrated hydrochloric acid (5 ml). The resulting mixture was extracted with ethyl acetate (3×20 ml), and the combined organic layers were washed with saturated $NaHCO_3$ solution (20 ml), dried over anhydrous Na_2SO_4, and concentrated with a rotary evaporator. The residue was purified by column chromatography (eluent: hexane/AcOEt = 10/1), followed by distillation, to give the title compound in 70% yield (1.72 g); Colorless oil; bp 128 °C (2.8 mmHg, Kugel rohr oven temperature); ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 1.22 (d, 3H, J = 5.0 Hz, CHC*H*$_3$), 2.71 (dq, 1H, J = 1.8 and 5.1 Hz, CH$_3$C*H*), 2.84—2.95 (m, 2H), 3.15 (dd, 1H, J = 6.9 and 15.8 Hz, PhSCH*H*), and 7.15—7.5 (m, 5H); IR (neat) 1585, 1480, 1440, 1090, 1025, 940, 740, and 695 cm^{-1}; MS *m/z* (rel intensity) 180 (M$^+$; 31), 137 (31), 110 (34), 71 (43), and 43 (100). Found: C, 66.58; H, 6.72%. Calcd for $C_{10}H_{12}OS$: C, 66.63; H, 6.71%.

***trans*-2,3-Epoxy-1-phenylthiohexane (1c).** Prepared from *trans*-2,3-epoxy-1-hexanol in 88% yield: Colorless oil; 131 °C (0.9 mmHg, Kugel rohr oven temperature); ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.90 (t, 3H, J = 7.3 Hz, CH$_2$C*H*$_3$), 1.27—2.55 (m, 4H), 2.69 (dt, 1H, J = 2.0 and 5.5 Hz, CH$_2$C*H*CH), 2.85—2.98 (m, 2H), 3.18 (dd, 1H, J = 6.9 and 16.2 Hz, PhSC*H*H), and 7.15—7.5 (m, 5H); IR (neat) 1587, 1485, 1443, 1027, 923, 743, and 695 cm^{-1}; MS *m/z* (rel intensity) 208 (M$^+$; 29), 165 (20), 135 (9), 123 (31), and 110 (36). Found: C, 68.99; H, 7.58%. Calcd for $C_{12}H_{16}OS$: C, 69.17; H, 7.74%.

***cis*-2,3-Epoxy-1-phenylthiohexane (1d).** Prepared from *cis*-2,3-epoxy-1-hexanol in 80% yield: Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.96 (t, 3H, J = 7.1 Hz, CH$_2$C*H*$_3$), 1.35—1.55 (m, 4H), 2.88—3.03 (m, 2H), 3.10—3.22 (m, 2H), 7.15—7.36 (m, 3H), and 7.36—7.50 (m, 2H); IR (neat) 1585, 1483, 1440, 1026, 740, and 695 cm^{-1}; MS *m/z* (rel intensity) 208 (M$^+$; 48), 165 (8), 137 (28), 123 (25), and 110 (37). Found: C, 68.90; H, 7.57%. Calcd for $C_{12}H_{16}OS$: C, 69.17; H, 7.74%.

***trans*-2,3-Epoxy-4-methyl-1-phenylthiopentane (1e).** Prepared from *trans*-2,3-epoxy-4-methyl-1-pentanol in 79% yield: Colorless oil; 138 °C (1.6 mmHg, Kugel rohr oven temperature); ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.83 (d, 3H, J = 6.9 Hz), 0.94 (d, 3H, J = 6.9 Hz), 1.45 (octet, 1H, J = 6.9 Hz), 2.51 (dd, 1H, J = 2.0 and 6.9 Hz, Me$_2$CHC*H*), 2.86—3.0 (m, 2H), 3.11—3.26 (m, 1H), and 7.12—7.46 (m, 5H); IR (neat) 1582, 1480, 1438, 1025, 915, 740, and 690 cm^{-1}; MS *m/z* (rel intensity) 165 (M$^+$−43; 11), 137 (3), 123 (14), 110 (18), 81 (15), 73 (13), 65 (10), 55 (57), and 43 (100). Found: C, 68.92; H, 7.58%. Calcd for $C_{12}H_{16}OS$: C, 69.17; H, 7.74%.

***trans*-3,4-Epoxy-2-phenylthioheptane (1f).** Prepared from *trans*-3,4-epoxy-2-heptanol in 61% yield: Colorless oil; 145 °C (13 mmHg, Kugel rohr oven temperature); ^{1}H NMR ($CDCl_3$, 270 Hz) δ = 0.84 (t, 0.26×3H, J = 7.1 Hz, CH$_2$C*H*$_3$), 0.94 (t, 0.74×3H, J = 7.1 Hz, CH$_2$C*H*$_3$), 1.27 (d, 0.74×3H, J = 6.9 Hz, CHC*H*$_3$), 1.40 (d, 0.26×3H, J = 6.9 Hz, CHC*H*$_3$), 1.1—1.6 (m, 4H), 2.43 (dt, 0.26×1H, J = 2.3 and 5.7 Hz, CH$_2$C*H*CH), 2.69 (dd, 0.26×1H, J = 2.3 and 8.3 Hz, CHC*H*CH), 2.80 (dt, 0.74×1H, J = 2.3 and 5.7 Hz, CH$_2$C*H*CH), 2.85 (dd, 0.74×1H, J = 2.3 and 6.3 Hz, CHC*H*CH), 2.86 (dq, 0.26×1H, J = 6.9 and 8.3 Hz, PhSC*H*), 3.15 (dq, 0.74×1H, J = 6.3 and 6.9 Hz, PhSC*H*), 7.2—7.35 (m, 3H), and 7.4—7.53 (m, 2H); IR (neat) 1583, 1480, 1440, 1376, 905, 750, and 693 cm^{-1}; MS *m/z* (rel intensity) for minor isomer 222 (M$^+$; 25), 165 (18), 123 (26), and 110 (37); for major isomer 222 (M$^+$; 20), 165 (17), 137 (7), 123 (16), and 110 (17). Found C, 70.11; H, 8.11%. Calcd for $C_{13}H_{18}OS$: C, 70.22; H, 8.16%.

(1*R, 2*R**, 3*R**)-2,3-Epoxy-1-phenylthiocyclohexane (1g).** To a stirred solution of tributylphosphine (1.94 g, 9.6 mmol) in benzene (25 ml) at room temperature was added solid *N*-(phenylthio)succinimide[27] (1.99 g, 9.6 mmol) in one portion. After being stirred for 5 min at room temperature, (1*R**, 2*S**, 3*S**)-2,3-epoxy-1-cyclohexanol[24b] (1.0 g, 8.8 mmol) was added all at once. Stirring was continued for 1 h at room temperature. The solvent was evaporated, and the residue was treated with hexane (20 ml). The precipitate was collected by filtration and washed with hexane (2×10 ml), and the combined hexane solutions were washed with brine (20 ml), dried over anhydrous Na_2SO_4, and concentrated with a rotary evaporator. The residue was purified by column chromatography (eluent: hexane/AcOEt = 10/1) to give the title compound in 47% yield (0.86 g): Colorless oil; ^{1}H NMR ($CDCl_3$, 270 Hz) δ = 1.2—1.6 (m, 3H), 1.67—1.86 (m, 1H), 1.88—2.12 (m, 2H), 3.17—3.27 (m, 2H), 3.58 (dd, 1H, J = 5.6 and 8.6 Hz), and 7.15—7.5 (m, 5H); IR (neat) 1585, 1485, 1442, 1269, 1028, 965, 760, 740, and 695 cm^{-1}; MS *m/z* (rel intensity) 149 (M$^+$−57; 6), 110 (80), 97 (24), 79 (29), 67 (31), 55 (22), and 43 (100). Found C, 69.73; H, 6.71; S, 15.88%. Calcd for $C_{12}H_{14}OS$: C, 69.86; H, 6.84; S, 15.54%.

***trans*-2,3-Epoxy-3-phenyl-1-phenylthiopropane (1h).** Prepared from *trans*-2,3-epoxy-3-phenyl-1-propanol in 81% yield: Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 3.09 (dd, 1H, J = 5.1

and 13.1 Hz, PhSC*H*H), 3.16—3.32 (m, 2H), 3.58 (d, 1H, $J=1.6$ Hz, PhC*H*), 7.02—7.15 (m, 2H), 7.15—7.40 (m, 6H), and 7.40—7.50 (m, 2H); IR (neat) 1585, 1485, 1443, 1027, 740, and 695 cm^{-1}; MS *m/z* (rel intensity) 242 (M^+; 16), 133 (100), 123 (58), and 110 (52). Found: C, 74.17; H, 5.92%. Calcd for $C_{15}H_{14}OS$: C, 74.34; H, 5.82%.

2,3-Epoxy-3-methyl-1-phenylthiobutane (1i). Prepared from 2,3-epoxy-3-methyl-1-butanol in 91% yield: Colorless oil; ^1H NMR ($CDCl_3$, 270 Hz) $\delta=1.08$ (s, 3H), 1.27 (s, 3H), 2.86—3.06 (m, 2H), 3.13 (dd, 1H, $J=4.1$ and 12.7 Hz), 7.17—7.35 (m, 3H), and 7.37—7.5 (m, 2H); IR (neat) 1585, 1485, 1442, 1383, 1130, 1028, 900, 742, and 695 cm^{-1}; MS *m/z* (rel intensity) 194 (M^+; 11), 123 (24), 110 (12), 71 (31), and 43 (100). Found: C, 67.74; H, 7.18%. Calcd for $C_{11}H_{14}OS$: C, 68.00; H, 7.26%.

***trans*-2,3-Epoxy-1-phenoxyhexane (15).** Prepared by the epoxidation of *trans*-2-hexenyl phenyl ether with *m*-chloroperbenzoic acid in dichloromethane in 83% yield: Colorless oil; ^1H NMR ($CDCl_3$, 270 Hz) $\delta=0.97$ (t, 3H, $J=7.1$ Hz), 1.40—1.50 (m, 4H), 2.90—2.99 (m, 1H), 3.05—3.13 (m, 1H), 3.98 (dd, 1H, $J=5.4$ and 10.9 Hz), 4.14 (dd, 1H, $J=3.6$ and 10.9 Hz), 6.84—7.05 (m, 3H), and 7.22—7.38 (m, 2H); IR (neat) 1600, 1590, 1500, 1246, 905, 755, and 693 cm^{-1}; MS *m/z* (rel intensity) 192 (M^+; 23), 149 (8), 107 (13), and 94 (36). Found: C, 74.87; H, 8.48%. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39%.

General Procedure for the Reaction of 2,3-Epoxy-1-phenylthioalkanes with Organo-aluminum Reagents. To a stirred solution of the organo-aluminum reagent (1 mmol) in hexane (1 ml) was added the 2,3-epoxy-1-phenylthioalkane (0.5 mmol) in hexane (1 ml) at 0 °C. Stirring was continued until the reaction was complete. The reaction mixture was diluted with ethyl acetate (5 ml), treated successively with NaF (1 g, 24 mmol) and water (0.13 ml, 7 mmol). Vigorous stirring of the resulting suspension was continued at room temperature for 0.5 h. The mixture was filtered through a pad of anhydrous Na_2SO_4, and the remaining solid was washed with ethyl acetate (3×5 ml). The combined filtrate and washings were concentrated with a rotary evaporator, giving the crude ring-opening product. Purification by the preparative TLC (eluent: AcOEt/hexane=1/3) gave the pure alcohol; or acetylation of the above alcohol with Ac_2O/*p*-dimethylaminopyridine (DMAP) in pyridine, followed by purification by the preparative TLC (eluent: AcOEt/hexane=1/10) gave the corresponding acetate.

Acetate of 2-Methyl-3-phenylthio-1-propanol (2a). Colorless oil; ^1H NMR ($CDCl_3$, 270 MHz) $\delta=1.07$ (d, 3H, $J=6.9$ Hz, CHC*H*$_3$), 2.04 (s, 3H, acetyl), 1.98—2.17 (m, 1H, CH$_3$C*H*), 2.80 (dd, 1H, $J=7.3$ and 13.2 Hz, PhSC*H*H), 3.03 (dd, 1H, $J=5.9$ and 13.2 Hz, PhSCH*H*), 4.05 (d, 2H, $J=5.9$ Hz, OC*H*$_2$), and 7.1—7.42 (m, 5H); IR (neat) 1740, 1582, 1480, 1438, 1375, 1240, 1035, 740, and 690 cm^{-1}; MS *m/z* (rel intensity) 164 (M^+-60; 5), 123 (18), 110 (24), and 43 (100). Found: *m/z* 224.0855. Calcd for $C_{12}H_{16}O_2S$: M, 224.0871.

Acetate of (2*R,3*S**)-3-Methyl-4-phenylthio-2-butanol (2b).** Colorless oil; ^1H NMR ($CDCl_3$, 270 MHz) $\delta=1.06$ (d, 3H, $J=6.6$ Hz, CHC*H*$_3$), 1.20 (d, 3H, $J=6.3$ Hz, CHC*H*$_3$), 1.80—1.95 (m, 1H, CH$_2$C*H*CH), 2.03 (s, 3H, acetyl), 2.70 (dd, 1H, $J=8.6$ and 13.0 Hz, PhSC*H*H), 3.06 (dd, 1H, $J=5.3$ and 13.0 Hz, PhSCH*H*), 5.02 (dq, 1H, $J=6.6$ and 4.0 Hz, CH$_3$C*H*CH), and 7.10—7.40 (m, 5H); IR (neat) 1740, 1587, 1485, 1378, 1250, 1027, 743, and 698 cm^{-1}; MS *m/z* (rel intensity) 238 (M^+; 28), 178 (19), 163 (15), 129 (23), 123 (38), and 110 (66). Found: *m/z* 238.1018. Calcd for $C_{13}H_{18}O_2S$: M, 238.1027.

Acetate of (2*R,3*S**)-2-Methyl-1-phenylthio-3-hexanol (2c).** Colorless oil; ^1H NMR ($CDCl_3$, 270 MHz) $\delta=0.90$ (t, 3H, $J=7.3$ Hz, CH$_2$C*H*$_3$), 1.05 (d, 3H, $J=6.9$ Hz, CHC*H*$_3$), 1.15—1.66 (m, 4H), 1.82—1.99 (m, 1H, CH$_3$C*H*), 2.04 (s, 3H, acetyl), 2.66 (dd, 1H, $J=7.9$ and 12.9 Hz, PhSC*H*H), 3.03 (dd, 1H, $J=4.9$ and 12.9 Hz, PhSCH*H*), 4.96—5.07 (m, 1H, OC*H*), and 7.12—7.38 (m, 5H); IR (neat) 1735, 1582, 1375, 1240, 1022, 965, 738, and 690 cm^{-1}; MS *m/z* (rel intensity) 266 (M^+; 9), 206 (7), 163 (12), 135 (6), 123 (15), 110 (19), 97 (29), 55 (51), and 43 (100). Found: *m/z* 266.1333. Calcd for $C_{15}H_{22}O_2S$: M, 266.1340.

Acetate of (2*R,3*R**)-2-Methyl-1-phenylthio-3-hexanol (2d).** Colorless oil; ^1H NMR ($CDCl_3$, 270 MHz) $\delta=0.90$ (t, 3H, $J=7.1$ Hz, CH$_2$C*H*$_3$), 1.04 (d, 3H, $J=6.6$ Hz, CHC*H*$_3$), 1.15—1.40 (m, 2H), 1.40—1.63 (m, 2H), 1.90—2.05 (m, 1H, CH$_3$C*H*), 2.06 (s, 3H, acetyl), 2.63 (dd, 1H, $J=9.2$ and 12.9 Hz, PhSC*H*H), 3.11 (dd, 1H, $J=4.3$ and 12.9 Hz, PhSCH*H*), 4.87—4.97 (m, 1H, OC*H*), and 7.12—7.40 (m, 5H); IR (neat) 1735, 1582, 1372, 1240, 1022, 965, 740, and 692 cm^{-1}; MS *m/z* (rel intensity) 266 (M^+; 9), 206 (8), 163 (14), 135 (6), 123 (16), 110 (22), 97 (30), 55 (56), and 43 (100). Found: *m/z* 266.1331. Calcd for $C_{15}H_{22}O_2S$: M, 266.1340.

(2*R,3*S**)-2,4-Dimethyl-1-phenylthio-3-pentanol (2e).** Colorless crystals; mp 69—70.5 °C (from hexane–dichloromethane); ^1H NMR ($CDCl_3$, 270 MHz) $\delta=0.81$ (d, 3H, $J=6.9$ Hz), 0.98 (d, 6H, $J=6.9$ Hz), 1.51 (broad s, 1H, O*H*), 1.6—1.79 (m, 1H, Me$_2$C*H*), 1.93 (d sextet, 1H, $J=3.0$ and 6.9 Hz, MeC*H*), 2.89 (dd, 1H, $J=6.9$ and 12.7 Hz, PhSC*H*H), and 3.05 (dd, 1H, $J=7.5$ and 12.7 Hz, PhSCH*H*), 3.32—3.43 (m, 1H, O*H*), and 7.10—7.25 (m, 5H); IR (KBr) 3320 (w), 1583, 990, 738, and 695 cm^{-1}; MS *m/z* (rel intensity) 224 (M^+; 21), 151 (6.6), 123 (63), 110 (69), and 71 (100). Found: C, 69.68; H, 9.08%. Calcd for $C_{13}H_{20}OS$: C, 69.59; H, 8.98%.

Acetate of (3*R,4*S**)-3-Methyl-2-phenylthio-4-heptanol (2f).** Colorless oil; ^1H NMR ($CDCl_3$, 270 MHz) $\delta=0.89$ (t, 3H, $J=7.3$ Hz, CH$_2$C*H*$_3$), 1.00 (d, 0.27×3H, $J=6.9$ Hz), 1.09 (d, 0.73×3H, $J=6.9$ Hz), 1.23 (d, 0.27×3H, $J=6.9$ Hz), 1.28 (d, 0.73×3H, $J=6.9$ Hz), 1.18—1.34 (m, 2H), 1.41—1.67 (m, 2H), 1.74—1.93 (m, 1H), 2.03 (s, 0.23×3H, acetyl), 2.05 (s, 0.73×3H, acetyl), 3.20 (dq, 0.73×1H, $J=5.3$, and 6.9 Hz, PhSC*H*), 3.30 (dq, 0.27×1H, $J=5.0$, and 6.9 Hz, PhSC*H*), 5.05—5.14 (m, 0.27×1H, OC*H*), 5.15—5.25 (m, 0.73×1H, OC*H*), 7.15—7.34 (m, 3H), and 7.36—7.45 (m, 2H); IR (neat) 1738, 1583, 1375, 1242, 1020, 750, and 695 cm^{-1}; MS *m/z* (rel intensity) for minor isomer 280 (M^+; 11), 171 (19), 137 (41), and 110 (36); for major isomer 280 (M^+; 10), 171 (22), 137 (41), and 110 (30). Found: C, 68.43; H, 8.53; S, 11.76%. Calcd for $C_{16}H_{24}O_2S$: C, 68.53; H, 8.63; S, 11.43%.

Acetate of (1*R, 2*R**, 3*R**)-2-Methyl-3-phenylthiocyclohexanol (2g).** Colorless oil; ^1H NMR ($CDCl_3$, 270 MHz) $\delta=1.13$ (d, 3H, $J=6.9$ Hz, CHC*H*$_3$), 1.3—1.9 (m, 6H), 1.95—2.15 (m, 1H, CH$_3$C*H*), 2.09 (s, 3H, acetyl), 3.10 (dt, 1H, $J=4.0$ and 10.4 Hz, PhSC*H*), 5.05—5.15 (m, 1H, OC*H*), 7.15—7.37 (m, 3H), and 7.38—7.48 (m, 2H); IR (neat) 1740, 1583, 1375, 1240, 740, and 695 cm^{-1}; MS *m/z* (rel intensity) 264 (M^+; 10), 155 (34), and 110 (31). Found: C, 68.05; H, 7.55; S, 12.57%. Calcd for $C_{15}H_{20}O_2S$: C, 68.14; H, 7.62; S, 12.13%.

Acetate of (2*R,3*R**)-3-Phenyl-1-phenylthio-2-butanol (5h).** Colorless oil; ^1H NMR ($CDCl_3$, 270 MHz) $\delta=1.26$ (d, 3H, $J=6.9$ Hz, CHC*H*$_3$), 1.93 (s, 3H, acetyl), 2.83 (dd, 1H, $J=7.3$ and 14.2 Hz, PhSC*H*H), 3.05 (dd, 1H, $J=4.0$ and 14.2 Hz, PhSCH*H*), 3.13 (dq, 1H, $J=6.9$ and 7.6 Hz, CH$_3$C*H*), 5.13—5.24 (m, 1H, OC*H*), and 7.12—7.34 (m, 10H); IR (neat) 1740, 1585, 1375, 1240, 1022, 768, 705, and 695 cm^{-1}; MS *m/z* (rel intensity) 300 (M^+; 2), 240 (12), 131 (45), 105 (14), 109 (4), and 43 (100). Found: *m/z* 300.1186. Calcd for $C_{18}H_{20}O_2S$: M, 300.1184.

Acetate of *trans*-3-Hydroxy-4-phenylthiachroman (6). Col-

orless crystals; mp 127.5—128.5 °C (from EtOH); ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 2.01 (s, 3H, acetyl), 2.99 (ddd, 1H, J = 1.0, 5.3, and 13.2 Hz, SC*H*H), 3.12 (dd, 1H, J = 2.6 and 13.2 Hz, SCH*H*), 4.32 (d, 1H, J = 5.3 Hz), 5.41 (dt, 1H, J = 5.3 and 2.6 Hz, OC*H*), and 6.85—7.35 (m, 9H); IR (KBr) 1730, 1495, 1428, 1375, 1250, 1232, 1025, 770, 755, and 705 cm^{-1}; MS *m/z* (rel intensity) 284 (M^+; 7), 224 (91), 197 (27), 165 (15), 147 (100), 91 (31), and 43 (53). Found: C, 71.99; H, 5.69%. Calcd for $C_{17}H_{16}O_2S$: C, 71.80; H, 5.67%.

3,3-Dimethyl-1-phenylthio-2-butanol (5i). Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.94 (s, 9H, C(CH_3)$_3$), 2.53 (d, 1H, J = 2.6 Hz, O*H*), 2.74 (dd, 1H, J = 11.1 and 13.7 Hz, PhSC*H*H), 3.23—3.34 (m, 2H), and 7.15—7.42 (m, 5H); IR (neat) 3480 (w), 1582, 1480, 1440, 1363, 1070, 1008, 738, and 690 cm^{-1}; MS *m/z* (rel intensity) 153 (M^+−57; 7), 124 (100), 109 (15), and 57 (22). Found: *m/z* 210.1082. Calcd for $C_{12}H_{18}OS$: M, 210.1078.

2,3-Dimethyl-1-phenylthio-2-butanol (7). Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.91 (d, 3H, J = 6.9 Hz, CHCH_3), 0.98 (d, 3H, J = 6.9 Hz, CHCH_3), 1.17 (s, 3H, CCH_3), 1.87 (septet, 1H, J = 6.9 Hz, (CH_3)$_2$C*H*), 2.14 (s, 1H, O*H*), 3.12 (d, 1H, J = 13.2 Hz, PhSC*H*H), 3.19 (d, 1H, J = 13.2 Hz, PhSCH*H*), and 7.1—7.45 (m, 5H); IR (neat) 3470 (w), 1580, 1478, 1438, 1085, 1020, 930, 735, and 688 cm^{-1}; MS *m/z* (rel intensity) 192 (M^+−18; 3), 167 (7), 149 (9), 124 (100), 109 (11), 87 (50), and 69 (33). Found: *m/z* 210.1070. Calcd for $C_{12}H_{18}OS$: M, 210.1078.

Acetates of (3*R,4*S**)-3-Phenylthiomethyl-4-heptanol (8c) and (4*R**,5*S**)-5-Phenylthio-4-octanol (9).** Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) for **8c** δ = 0.90 (t, 3H, J = 6.9 Hz, CH_2CH_3), 0.95 (t, 3H, J = 7.4 Hz, CH_2CH_3), 1.15—1.65 (m, 6H), 1.67—1.80 (m, 1H), 2.02 (s, 3H, acetyl), 2.81 (dd, 1H, J = 12.9 and 6.9 Hz, PhSC*H*H), 3.00 (dd, 1H, J = 12.9 and 5.6 Hz, PhSCH*H*), 5.06—5.18 (m, 1H, OC*H*), and 7.10—7.4 (m, 5H); for **9** (only the characteristic peaks were recorded) δ = 2.05 (s, 3H, acetyl), 3.22—3.32 (m, 1H, PhSC*H*), 4.95—5.05 (m, 1H, OC*H*); IR (neat) 1735, 1582, 1240, 1020, 738, and 690 cm^{-1}; MS *m/z* (rel intensity) for **8c** 280 (M^+; 18), 220 (48), 123 (18), 110 (58), and 69 (100); for **9** 220 (M^+−60; 24), 165 (16), 123 (34), 110 (38), and 69 (100). Found: *m/z* 280.1490. Calcd for $C_{16}H_{24}O_2S$: M, 280.1496.

Acetate of (3*R,4*R**)-3-Phenylthiomethyl-4-heptanol (8d).** Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.89 (t, 3H, J = 7.3 Hz, CH_2CH_3), 0.91 (t, 3H, J = 7.3 Hz, CH_2CH_3), 1.15—1.8 (m, 7H), 2.04 (s, 3H, acetyl), 2.80 (dd, 1H, J = 7.9 and 12.9 Hz, PhSC*H*H), 3.07 (dd, 1H, J = 12.9 and 5.0 Hz, PhSCH*H*), 5.02—5.15 (m, 1H, OC*H*), and 7.1—7.4 (m, 5H); IR (neat) 1735, 1583, 1240, 1020, 738, and 690 cm^{-1}; MS *m/z* (rel intensity) 280 (M^+; 7), 220 (8), 123 (18), 110 (27), 69 (53), and 43 (100). Found: *m/z* 280.1487. Calcd for $C_{16}H_{24}O_2S$: M, 280.1496.

Acetate of 1-Phenylthio-3-hexanol (10). Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.90 (t, 3H, J = 7.3 Hz, CH_2CH_3), 1.2—1.4 (m, 2H), 1.45—1.65 (m, 2H), 1.8—1.95 (m, 2H), 2.05 (s, 3H, acetyl), 2.8—3.0 (m, 2H, PhSCH_2), 4.9—5.1 (m, 1H, OC*H*); IR (neat) 1732, 1582, 1480, 1438, 1372, 1240, 1022, 738, and 690 cm^{-1}; MS *m/z* (rel intensity) 252 (M^+; 34), 149 (45), 123 (36), 110 (87), 83 (79), and 55 (100). Found: *m/z* 252.1177. Calcd for $C_{14}H_{20}O_2S$: M, 252.1184.

Acetate of (4*R,5*S**,7*E**)-5-Phenylthio-7-dodecen-4-ol (11).** Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.88 (t, 3H, J = 6.9 Hz, CH_2CH_3), 0.89 (t, 3H, J = 6.9 Hz, CH_2CH_3), 1.18—1.45 (m, 6H), 1.5—1.65 (m, 1H), 1.7—1.85 (m, 1H), 1.87 (s, 3H, acetyl), 1.95—2.1 (m, 2H), 2.2—2.45 (m, 2H), 3.25—3.4 (m, 1H, PhSC*H*), 4.95—5.1 (m, 1H, OC*H*), 5.43—5.6 (m, 2H), 7.1—7.35 (m, 3H) and 7.35—7.5 (m, 2H); IR (neat) 1735, 1580, 1371, 1238, 1022, 745, and 692 cm^{-1}; MS *m/z* (rel intensity) 334 (M^+; 1), 274 (2), 195 (13), 177 (9), 123 (13), 109 (22), 67 (41), and 43 (100). Found: *m/z* 334.1947. Calcd for $C_{20}H_{30}O_2S$: M, 334.1966.

Acetates of (4*R,5*S**)-5-Phenylthio-7-dodecyn-4-ol (12) and (4*R**,5*S**)-5-Phenylthiomethyl-6-undecyn-4-ol (13c).** Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) for **12** δ = 0.90 (t, 6H, J = 7.2 Hz, CH_2CH_3) 1.2—1.55 (m, 6H), 1.55—1.85 (m, 2H), 1.93 (s, 3H, acetyl), 2.12—2.22 (m, 2H), 2.47—2.54 (m, 2H), 3.41 (dt, 1H, J = 4.9 and 6.9 Hz, PhSC*H*), 5.14—5.24 (m, 1H, OC*H*), and 7.13—7.53 (m, 5H); for **13c** (only the characteristic peaks were recorded) δ = 2.06 (s, 3H, acetyl), 2.72—2.82 (m, 1H), 3.02 (d, 2H, J = 7.2 Hz, PhSCH_2), and 5.02—5.12 (m, 1H); IR (neat) 1740, 1580, 1370, 1235, 1020, 745, and 690 cm^{-1}; MS *m/z* (rel intensity) for **12** 290 (M^+−42; 2), 273 (7), 195 (11), 177 (5), 135 (8), 123 (6), 110 (8), 91 (12), 79 (15), and 43 (100); for **13c** 273 (M^+−59; 4), 255 (8), 195 (10), 123 (14), 110 (18), 91 (9), 79 (9), and 43 (100). Found: *m/z* 332.1815. Calcd for $C_{20}H_{28}O_2S$: M, 332.1810.

(2*R,3*S**)-2-Phenylthio-3-hexanol (14).** Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.89 (t, 3H, J = 6.9 Hz, CH_2CH_3), 1.27 (d, 3H, J = 6.9 Hz, CHCH_3), 1.25—1.62 (m, 4H), 2.29 (broad s, 1H, O*H*), 3.34 (dq, 1H, J = 2.6 and 6.9 Hz, CH_3C*H*), 3.55—3.7 (m, 1H, OC*H*); IR (neat) 3425 (w), 1585, 1482, 1442, 1027, 748, and 695 cm^{-1}; MS *m/z* (rel intensity) 210 (M^+; 26), 138 (100), 137 (73), and 110 (69). Found: *m/z* 210.1093. Calcd for $C_{12}H_{18}OS$: M, 210.1078.

(1*R,2*S**)-1,2-Dimethyl-3-(phenylsulfonyl)propyl 3,5-Dinitrobenzoate (27).** A benzene (2 ml) solution of 3,5-dinitrobenzoyl chloride (92 mg, 0.4 mmol) was added to a solution of **2b** (64.8 mg, 0.33 mmol) and pyridine (46.8 mg, 0.6 mmol) in benzene (2 ml) at 0 °C. The reaction mixture was allowed to warm to room temperature and was then stirred overnight. After aqueous work-up, the organic layer was dried and concentrated to give an oil (126.1 mg), which was essentially pure (1*R**,2*S**)-1,2-dimethyl-3-(phenylthio)propyl 3,5-dinitrobenzoate judging from its ^{1}H NMR. The obtained oil was in turn dissolved in benzene (4 ml). To the solution were added $VO(acac)_2$ (0.11 g, 0.4 mmol) and TBHP (4.3 mol dm^{-3} solution in isooctane, 0.15 ml, 0.66 mmol), and then the mixture was stirred for 3 h at room temperature. Usual aqueous work-up, followed by recrystallization from EtOH, gave 90.1 mg (80% overall yield from **2b**) of the title compound: Colorless crystals; mp 156.5—158.0 °C (from EtOH); ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 1.25 (d, 3H, J = 6.9 Hz, CH_3CH), 1.36 (d, 3H, J = 6.6 Hz, CH_3CHO), 2.57—2.75 (m, 1H, CH_3C*H*), 3.00 (dd, 1H, J = 8.1 and 14.1 Hz, PhSC*H*H), 3.34 (dd, 1H, J = 3.8 and 14.1 Hz, PhSCH*H*), 5.31 (dq, 1H, J = 3.8 and 6.6 Hz, CH_3C*H*O), 7.48—7.7 (m, 3H), 7.86—8.0 (m, 2H), 9.08 (d, 2H, J = 2.2 Hz), and 9.23 (t, 1H, J = 2.2 Hz); IR (KBr) 1720, 1630, 1550, 1347, 1147, 1085, 605, and 535 cm^{-1}. Found: C, 51.32; H, 4.25; N, 6.45%. Calcd for $C_{18}H_{18}N_2O_8S$: C, 51.18; H, 4.30; N, 6.63%.

(*R)-1-[(*S**)-1-Methyl-2-(phenylsulfonyl)ethyl]butyl 3,5-Dinitrobenzoate (28).** Prepared by a similar procedure for the preparation of **27** in 86% overall yield from **2c**: Colorless crystals; mp 181.0—182.0 °C (from EtOH); ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.94 (t, 3H, J = 7.3 Hz, CH_2CH_3), 1.24 (d, 3H, J = 6.9 Hz, CHCH_3), 1.2—1.5 (m, 2H), 1.5—1.8 (m, 2H), 2.55—2.75 (m, 1H, CH_3C*H*), 2.97 (dd, 1H, J = 7.9 and 14.2 Hz, PhSC*H*H), 3.31 (dd, 1H, J = 3.6 and 14.2 Hz, PhSCH*H*), 5.25 (ddd, 1H, J = 4.3, 4.3, and 7.2, OC*H*), 7.45—7.68 (m, 3H), 7.85—7.95 (m, 2H), 9.08 (d, 2H, J = 2.0 Hz), and 9.23 (t, 1H, J = 2.0 Hz); IR (KBr) 1725, 1628, 1550, 1350, 1147, 1085, 610, and 535 cm^{-1}; Found: C, 53.41; H, 5.10; N, 6.15%. Calcd for $C_{20}H_{22}N_2O_8S$: C, 53.33; H, 4.92; N, 6.22%.

(2*S*,3*S*,4*S*)-3,4-Epoxy-2-octanol (33). To a stirred solution of

Ti(O-*i*-Pr)$_4$ (8.53 g, 30 mmol), L-(+)-DIPT (8.43 g, 36 mmol), and racemic *trans*-3-octen-2-ol (3.84 g, 30 mmol) in dichloromethane (300 ml) was added TBHP (1.49 g, 16.5 mmol) in dichloromethane (10 ml). The reaction mixture was maintained at −20 °C for 15 h. After work-up as described by Martin et al.,[18] **33** was obtained in 80% yield (2.11 g, based on TBHP) as a 95 : 5 diastereomeric mixture: Colorless oil; bp 65—68 °C (4 mmHg); ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.92 (t, 3H, J = 6.9 Hz, CH_2CH_3), 1.25 (d, 3H, J = 6.6 Hz, $CHCH_3$), 1.2—1.75 (m, 6H), 1.84 (broad s, 0.05×1H, O*H*), 2.10 (broad s, 0.95×1H, O*H*), 2.72 (dd, 0.05×1H, J = 2.3 and 5.3 Hz), 2.76 (dd, 0.95×1H, J = 2.3 and 3.3 Hz), 2.90 (dt, 0.05×1H, J = 2.3 and 5.3 Hz), 2.99 (dt, 0.95×1H, J = 2.3 and 5.6 Hz), 3.56—3.7 (m, 0.05×1H), and 3.9—4.02 (m, 0.95×1H); IR (neat) 3450, 1470, 1105, 1070, 950, 905, and 875 cm^{-1}; MS *m/z* (rel intensity) 87 (M^+−57; 2), 69 (42), 58 (100), and 57 (52). The ^{1}H NMR data were essentially identical with those reported in the literature.[17]

(2*R*,3*S*,4*S*)-3,4-Epoxy-2-phenylthiooctane (34). The reaction of **33** with tributylphosphine and *N*-(phenylthio)succinimide in benzene at room temperature as described for the preparation of **1g** gave **34** in 73% yield as a 97 : 3 diastereomeric mixture: Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.83 (t, 0.03×3H, J = 6.9 Hz, CH_2CH_3), 0.89 (t, 0.97×3H, J = 6.9 Hz, CH_2CH_3), 1.27 (d, 3H, J = 6.9 Hz, $CHCH_3$), 1.25—1.65 (m, 6H), 2.42 (dt, 0.03×1H, J = 2.1 and 5.4 Hz, CH_2CHCH), 2.69 (dd, 0.03×1H, J = 2.1 and 8.6 Hz, $CHCHCH$), 2.76—2.93 (m, 0.03×1H, PhSC*H*), 2.79 (dt, 0.97×1H, J = 2.1 and 5.6 Hz, CH_2CHCH), 2.84 (dd, 0.97×1H, J = 2.1 and 6.2 Hz, $CHCHCH$), 3.15 (dq, 0.97×1H, J = 6.2 and 6.9 Hz, PhSC*H*), 7.2—7.35 (m, 3H), and 7.42—7.5 (m, 2H); IR (neat) 1585, 1480, 1440, 1380, 1090, 1025, 898, 750, and 693 cm^{-1}; MS *m/z* (rel intensity) for major diastereomer 236 (M^+; 12), 179 (13), 137 (10), 127 (13), 110 (29), and 69 (100); for minor diastereomer 236 (M^+; 10), 150 (10), 127 (10), 110 (34), and 69 (100). Found: *m/z* 236.1251. Calcd for $C_{14}H_{20}OS$: M, 236.1235.

(2*R*,3*R*,4*S*)-3-Methyl-2-phenylthio-4-octanol (35). The methylation of **34** with trimethylaluminum was carried out in a similar manner to the general procedure described above to give the title compound in 93% yield as a 97 : 3 diastereomeric mixture (epimers at C-2): Colorless oil; ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.90 (t, 3H, J = 7.1 Hz, CH_2CH_3), 1.00 (d, 0.03×3H, J = 6.9 Hz), 1.07 (d, 0.97×3H, J = 6.9 Hz), 1.36 (d, 3H, J = 6.6 Hz), 1.2—1.6 (m, 6H), 1.6—1.75 (m, 1H), 2.06 (d, 1H, J = 4.3 Hz), 3.30 (dq, 1H, J = 4.7 and 6.9 Hz, PhSC*H*), 3.83—3.97 (m, 1H), and 7.15—7.5 (m, 5H); IR (neat) 3425 (w), 1580, 1478, 1438, 1378, 1022, 1005, 745, and 690 cm^{-1}; MS *m/z* (rel intensity) 252 (M^+; 14), 165 (5), 137 (48), 110 (100), and 85 (41). Found: *m/z* 252.1556. Calcd for $C_{15}H_{24}OS$: M, 252.1548.

(3*S*,4*S*)-3-Methyl-4-octanol (29). To a stirred solution of **35** (327.6 mg, 1.3 mmol) in a mixed solvent of acetone/ethanol (9/1, 14 ml) was added Raney Ni W-2 (about 2 g) at room temperature. The reaction mixture was stirred at room temperature for 1 h, and was carefully filtered through a celite pad, and the remaining mass was washed with dichloromethane (3×20 ml). The combined filtrate and washings were concentrated, and the residue was purified by column chromatography (CH_2Cl_2/Et_2O: 10/1), followed by distillation, to give the title compound in 85% yield (160 mg): Bp 110 °C (20 mmHg, Kugel rohr oven temperature); $[\alpha]_D^{16.8}$ −19.6° (*c* 0.918, diethyl ether) [lit,[15] $[\alpha]_D^{20}$ −20.7° (*c* 1.01, diethyl ether)]; ^{1}H NMR ($CDCl_3$, 270 MHz) δ = 0.87 (d, 3H, J = 6.8 Hz), 0.91 (t, 6H, J = 7.2 Hz), 1.13—1.55 (m, 10H), and 3.45—3.56 (m, 1H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ = 11.8, 13.1, 14.0, 22.8, 26.0, 28.4, 34.1, 39.9, and 74.8; IR (neat) 3370 and 1000 cm^{-1}; MS *m/z* (rel intensity) 87 (M^+−57; 17) and 69 (100). The IR and NMR data were identical with those reported in the literature.[15]

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