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Intramolecular Ring Opening of a 2,3-Epoxy Alcohol by a Xanthate Anionic Center; Stereospecific Preparation of 2-Mercapto-1,3-diol Units

Jun'ichi Uenishi,* Mitsuhiro Motoyama, Yoshitaka Nishiyama, Yuichi Hirota, and Yuki Kubo

Department of Chemistry, Okayama University of Science, Ridaicho, Okayama 700, Japan

Haruo Akashi

Analytical Center, Okayama University of Science, Ridaicho, Okayama 700, Japan

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ABSTRACT

Stereospecific ring openings of optically active 2,3-epoxy alcohols were performed by the reaction of ***1****,* ***3****,* ***5****, and* ***7*** *with carbon disulfide and sodium hydride to give the five-membered xanthates* ***2****,* ***4****,* ***6****, and* ***8****. Both enantiomers of 2-mercapto-1,3-diol triacetates,* ***11*** *and* ***14****, were derived from* ***4*** *and* ***6****, respectively. The ring opening reaction proceeded at −78°C to −30°C, and the yields were around 80%. However, at a higher temperature between 0°C to room temperature, a complicated reaction took place and led to the formation of two isomers of the cyclic thiol carbonates* ***15*** *and* ***16*** *from* ***1*** *or* ***5****. These processes were also stereospecific, and mechanisms have been proposed. In the case of the 3,4-epoxy alcohol* ***20****, the epoxide ring opening gave the six-membered xanthate* ***21*** *stereospecifically.*

INTRODUCTION

Since Sharpless first reported the asymmetric epoxidation of allylic alcohol [1], enormous numbers of synthetic applications and developments have been made [2]. Utilizations of epoxy alcohols having high enantiomeric purities at the two asymmetric carbon centers have been revealed as useful synthetic tools for asymmetric syntheses of a variety of organic compounds. During these synthetic studies, regio and stereospecific reactions of 2,3-epoxy alcohols were well investigated by Sharpless [3] and others [4]. In particular, ring opening reactions of 2,3-epoxy alcohols by heteroatom nucleophiles were found to be very important. Introduction of sulfide functions to the C_2 or C_3 position of 2,3-epoxy alcohols [3,5a,5b] and their analogues [5c] was reported by Sharpless who used thiophenol [5a], tert-butyl mercaptan [3], or benzyl mercaptan [5b] as the sulfur nucleophiles, and the regioselectivities were found to be in a range of 1~20:1. However, generation of thiols from the resulting sulfides was not examined. Related to our biological interest in 4'-thionucleosides [6], we required a general synthetic method for the generation of the 2-mercapto-1,3-diol unit in a highly optically pure form. In this article, we report the facile preparation of 2-mercapto-1,3-diol units from 2,3-epoxy alcohols via 1,3-oxathiolane-2-thione (five-membered cyclic xanthate) intermediates in which an intramolecular ring opening reaction by the S-xanthate anion takes place as a key reaction.

Intramolecular ring opening reactions of 2,3-epoxy alcohols by carbonates and urethanes were reported by Kishi et al. and Roush et al. [8], as

*To whom correspondence should be addressed.

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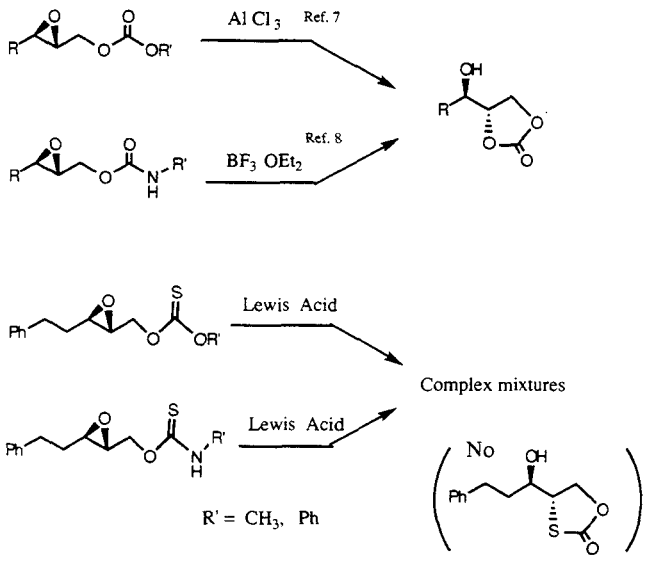


SCHEME 1

shown in Scheme 1. The reactions were mediated by Lewis acids to form a cyclic carbonate in both cases. These reactions were effective for the stereospecific preparation of consecutive 1,2,3-triols and were used for polyol syntheses, particularly of sugars [7,8]. We attempted similar reactions in order to obtain a cyclic thiol carbonate from the corresponding acyclic thiocarbonate or thiourethane. We prepared the starting thiocarbonate and thiourethane by standard methods and tested the ring formation reaction in the presence of various kinds of Lewis acids and solvents. However, the reactions all failed to give the desired 1,3-oxathiolan-2-one ring but instead gave complex mixtures. Therefore, we decided to find our own method and developed an intramolecular ring opening of a 2,3-epoxy alcohol via the xanthate anion in a 5-exo-tetragonal fashion.

Intramolecular Stereospecific Ring Opening of a 2,3-Epoxy Alcohol by a Sulfur Nucleophile

The optically active (2R,3S)-2,3-epoxy alcohol (**1**) was obtained from 5-phenyl-2-penten-1-ol [9] in 94% enatiomeric excess by the Sharpless asymmetric epoxidation using (+)-diethyl tartrate [1]. It was treated with NaH in a mixture of carbon disulfide and THF (1:1–3) at −78°C, and then the mixture was warmed gradually to −30°C to give [4R,(1'S)]-4-[1-hydroxy-3-phenylpropyl]-1,3-oxathiolane-2-thione (**2**) in 83% yield. The product was a single stereoisomer, and the other diastereoisomer was not detected in the reaction mixture. The proposed reaction mechanism is shown in Scheme 2.

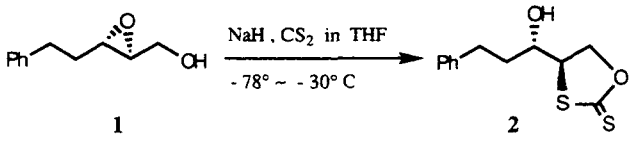
Initially, the epoxy alcohol reacts with NaH at −78°C to form the corresponding sodium alkoxide, which may react with carbon disulfide present in a large excess to produce the sodium S-xanthate. This sulfur nucleophilic center attacks the adjacent epoxide carbon center from the backside in a 5-exo-tetragonal fashion to open the ring and afford the hydroxy cyclic xanthate (**2**). Regio and stereospecificities of this reaction gave no other isomers in the crude reaction mixture. This distinctive selectivity was also observed in the similar types of reactions reported in Refs. [7] and [8]. In the same manner, reactions with the cis epoxy alcohol (**3**) and the epoxy alcohols (**5**) and (**7**) gave the corresponding hydroxy cyclic xanthates **4**, **6**, and **8** in 80, 81, and 77% yields, respectively, as shown in Scheme 3. The optical purities of **2**, **4**, **6**, and **8** were assumed to be 94, 92, 85, and 87% on the basis of ee values of the starting epoxy alcohols which were determined by the Mosher's method [10].

Preparation of 2-Mercapto-1,3-diol Triacetates

Transformation of the hydroxy cyclic xanthates to 2-mercapto-1,3-diol triacetates was performed in five steps, which are depicted in Scheme 4. Optically pure xanthate **4** was silylated with tert-butyldimethylsilyl trifluoromethanesulfonate in the presence of 2,6-lutidine to give **9** in 90% yield. Then the xanthate was subjected to reduction by $LiAlH_4$ to give the mercapto alcohol, which was acetylated with acetic anhydride in pyridine to afford **10** in 41% yield. The silyl group was converted to an acetate in two steps: (1) desilylation of **10** by hydrofluoric acid in ethanol and (2) acetylation of the resulting alcohol with acetic anhydride in pyridine. Triacetate **11** was obtained in 72% yield and showed the optical rotation $[\alpha]_D^{24}$ + 6.1° (c 1.0, chloroform). The transformation of the xanthate **6** to the triacetate **14** was carried out by the same five reaction steps described for the preparation of compound **11**. Silylation of **6** by tert-butyldimethylsilyl trifluoromethanesulfonate gave **12** in 88% yield, and reduction by $LiAlH_4$ followed by acetylation provided **13** in 35% yield. Finally, the silyl group was replaced and the molecule was transformed to the triacetate **14** in 74% yield. The spectroscopic data of **14** were exactly the same as those of compound **11** except for the polarity of the optical rotation, which showed $[\alpha]_D^{24}$ −6.0° (c 1.0, chloroform). These results clearly showed that the compounds **11** and **14** are enantiomers.

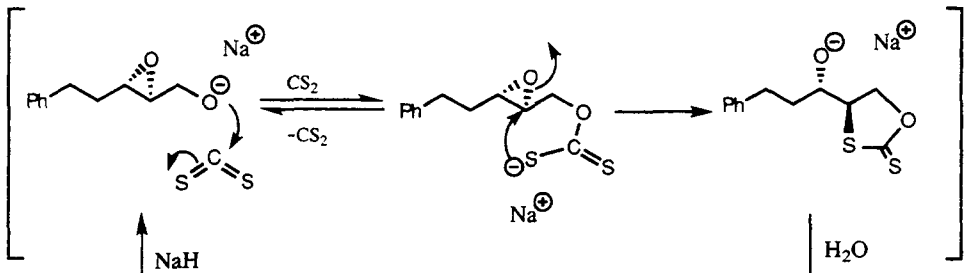
Reactions at Higher Temperature

It was found that the reaction temperature was very important for the reaction. When the temperature of reaction of **1** was maintained from −78°C to 0°C during 3 hours, compound **2** was obtained in only 35% yield, and considerable amounts of the side products **15** and **16** were produced, as shown in Scheme 5. When the reaction of **1** was conducted at room temperature, the xanthate **2** was not ob-



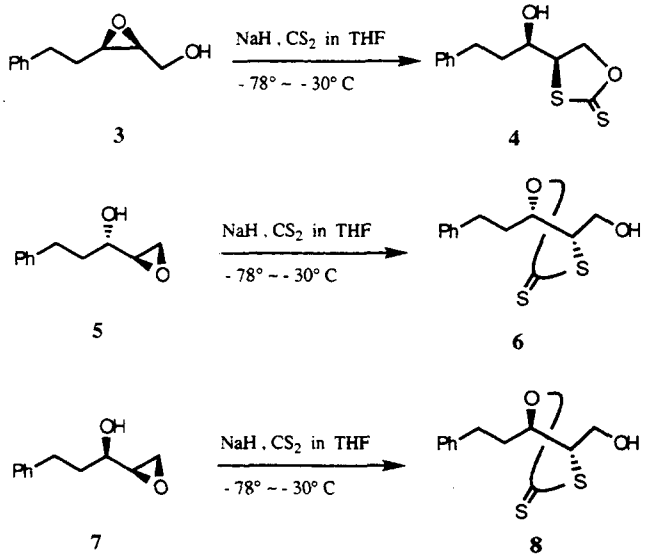
1 2

Mechanism of Stereospecific Ring Opening Reaction of 2,3-Epoxy Alcohol by Carbon Disulfide under Basic Condition



1 2

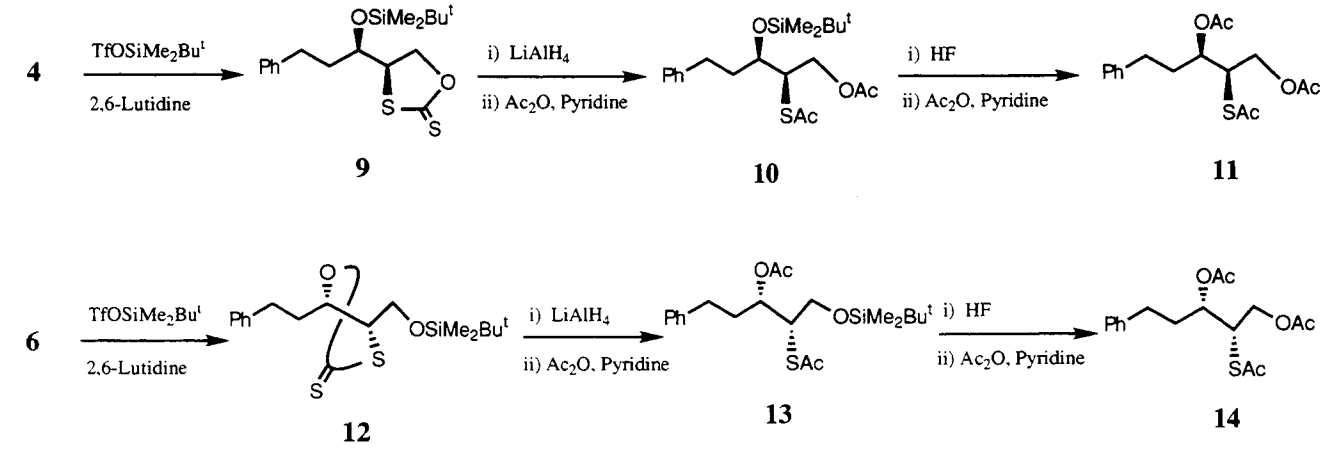
SCHEME 2



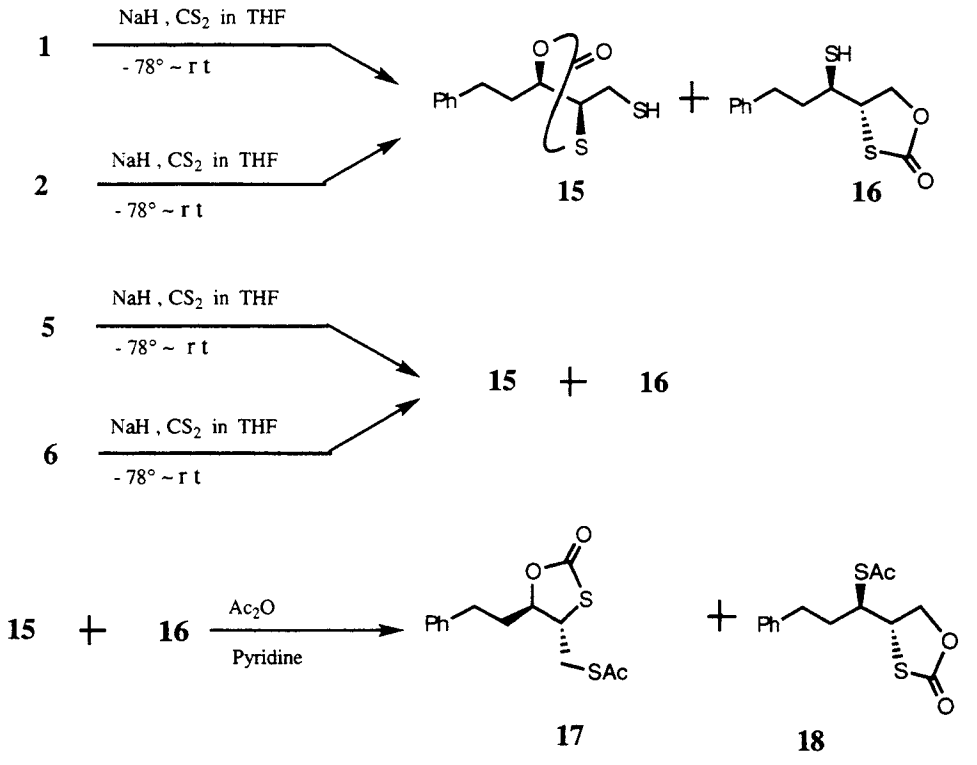
3 4 5 6 7 8

SCHEME 3

tained but instead a mixture of **15** and **16**. This proved to be an inseparable mixture, but the acetates, **17** and **18**, could be isolated. The acetylated compounds were identified as five-membered 1,3-oxathiolan-2-ones. Both compounds **17** and **18** showed the same molecular ion peaks at *m/e* 296 by low resolution mass spectroscopy. High resolution mass spectroscopy and elemental analyses revealed their compositions to be $C_{14}H_{16}O_3S_2$. Their IR spectra implied the presence of esters, but no thione adsorption was observed around 1200 cm^{-1}. The proton nmr spectrum of **17** showed a peak at δ = 4.40 as a doublet of triplets due to the methine proton at the 4-position of the 1,3-oxathiolan-2-one ring, while the corresponding peak could not be found in the spectrum of **18**. The nmr spectrum of **18** indicates the presence of methylene protons at the 5-position in the same ring at δ = 4.47 as a doublet of doublets and at δ = 4.25 as a doublet of doublets [11]. Both spectra have the S-acetyl protons at δ = 2.36 in **17** and at δ = 2.42 in **18**. Based on these spectroscopic data, we confirmed the structures of **15**, **16**, **17** and **18** as shown in Scheme 5. Even more decisively, the structure of **17** was determined by a single crystal X-ray diffraction analysis, the ortep view of which is shown in Figure 1. The compounds **15** and **16** were also produced when **2** was treated with NaH and carbon disulfide in THF at −30°C to room temperature. This observation means that the compounds are formed through the same sodium alkoxide of **2**. More interestingly, they were also formed by the reaction starting either from the compound **5** or **6**, as summarized in Scheme 5. When the temperature was raised from −78°C to room temperature, the reaction gave the two isomers of the 2,3-dimercapto alcohols. Four remarkable changes took place in these reaction processes from **1**, **2**, **5**, or **6** to **15** and **16**; (1) inversion of the carbon center of the secondary alcohol in **2** and of the carbon center of the O-xanthate in **6**; (2) substitution of the O-



SCHEME 4



SCHEME 5

xanthate by mercaptan; (3) positional changes of 1,3-oxathiolan rings; and (4) substitution of the thione by a ketone group. These are complicated phenomena, and it is difficult to fully explain their formation mechanistically. However, we currently speculate the reaction mechanisms to be as shown in Scheme 6.

The alkoxide (**I**) derived from **1** or **2** reacts with carbon disulfide to form the S-xanthate anion (**II**), which may attack the carbon centers of the O-xanthate (path **A**) or of the S-xanthate (path **B**) above −30°C. Consideration of path A indicates that it may afford the six-membered xanthate (**III**), and a reversible equilibrium reaction may give back the five-membered xanthate (**II**). However, by path **D**, the O-xanthate (**III**) anionic center may attack the carbon of the O-xanthate to invert the stereocenter of the cyclic xanthate ester to give **IV** which eventually goes to **15**. On the other hand, when the path **B** is operative in **II**, the isomeric cyclic xanthate (**VI**) would be formed. **VI** is also the same intermediate that can be derived from **5** or **6**, and it is in equilibrium with **II**. If **VI** cyclizes to give the six-membered xanthate **VII** by path **C** and the re-

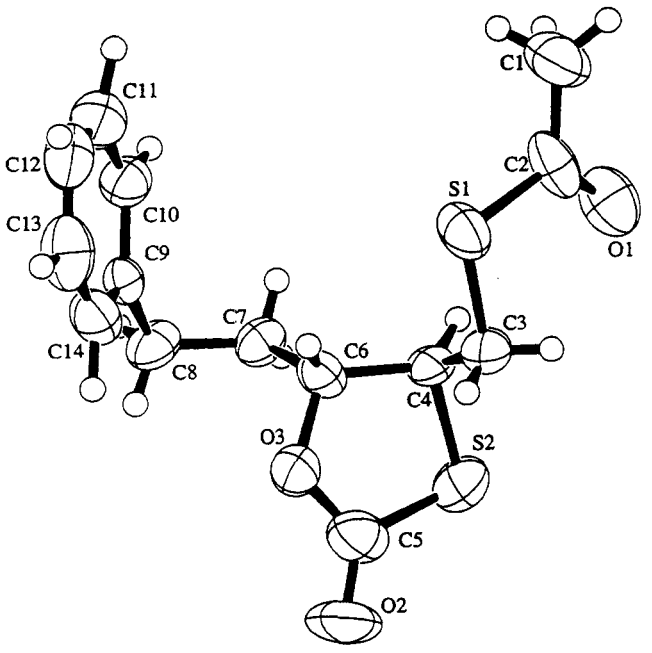


FIGURE 1 ORTEP view of **17**.

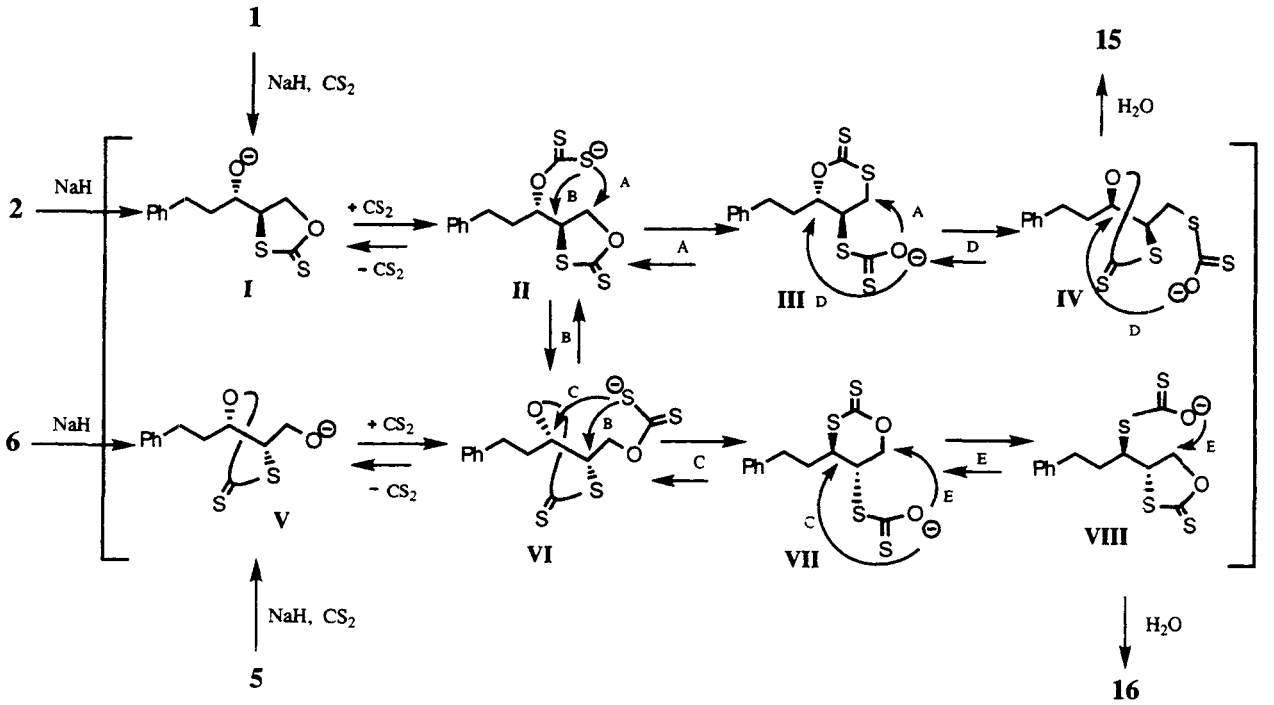
action further proceeds by an attack of O-xanthate anionic center on the terminal carbon of **VII**, **16** can eventually be formed via **VIII**. Although it is not clear at which stage the cyclic xanthate (1,3-oxathiolane-2-thione ring) has been transformed to the cyclic thiol carbonate (1,3-oxathiolan-2-one ring), a substitution of thiocarbonyl for carbonyl for related systems has often been observed under basic conditions.

Ring Opening Reaction of the 3,4-Epoxy Alcohol

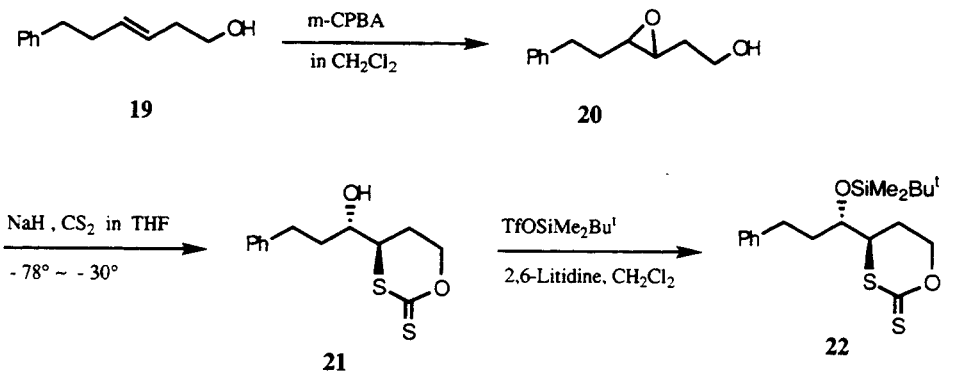
We next became interested in the reaction of a 3,4-epoxy alcohol under identical conditions. In this case, formation of a six-membered cyclic xanthate or a seven-membered cyclic xanthate could be anticipated by the occurrence of 6-exo-tetragonal or 7-endo-tetragonal ring openings, which are both allowed by Baldwin and Kruse's rule [12]. Epoxidation of the homoallylic alcohol **19** by mCPBA gave the 3,4-epoxy alcohol **20** in 81% yield. This epoxy alcohol was treated with NaH or KH and carbon disulfide to give the hydroxy xanthate **21** in 44% yield, the starting material being recovered in 34% yield. The structure of **21** was fully identified by nmr spectroscopy, including its decoupling experiment. In the proton nmr spectrum of the crude reaction mixture, none of the seven-membered xanthate could be detected. Finally, the hydroxy group of **21** was silylated with TBSOTf to afford **22** in 80% yield.

CONCLUSIONS

We have described a new method for introduction of a sulfur function to acyclic carbon chains by a stereospecific ring opening of an epoxy alcohol with



SCHEME 6



SCHEME 7

use of carbon disulfide. Low-temperature control of the reactions gave stereospecifically five- or six-membered cyclic xanthates, and the methodology was found to be useful for the preparation of 2-mercapto-1,3-diol units.

EXPERIMENTAL

Melting points were taken on a Yanako micro-melting apparatus and were uncorrected. ^1H and ^{13}C NMR spectra were recorded on a JEOL GXS and Varian Gemini 300 for ^1H (400 MHz or 300 MHz) and for ^{13}C (100 MHz or 75 MHz). The chemical shifts were shown as δ values using tetramethylsilane (0 ppm) for proton spectra and $CHCl_3$ (77 ppm) for carbon spectra as internal standards. Infrared (IR) spectra were recorded by use of a JASCO IRA-1 spectrometer and were taken as liquid films on NaCl plates or as tablets. Low and high resolution mass spectra (LRMS and HRMS) were obtained on a JEOL JMS 303HF spectrometer at the Analytical Center of the Okayama University of Science by the electron impact (EI) method at 70 eV unless otherwise stated. Only significant peaks are described here for IR and MS spectra. Silica gel (Merck 7734, 70–300 mesh) was used for gravity column chromatography and silica gel (Merck 9385, 230–400 mesh) for flash column chromatography. Precoated silica gel plates (Merck 5715, 60F254) were used for thin layer chromatography. All air sensitive reactions were conducted in flame dried glassware under an Ar atmosphere. THF and ether used as solvents for reactions were dried over sodium benzophenone ketyl, and methylene chloride and carbon disulfide were dried over phosphorus pentoxide. These solvents and reagents were freshly distilled just before use.

Materials

Optically active epoxy alcohols **1** and **3** were prepared from the corresponding allylic alcohols by the Sharpless asymmetric epoxidation procedure using (+)-diethyl tartrate [1] and **5** was prepared by the Sharpless kinetic resolution procedure using (+)-diethyl tartrate [13]. Optical purities were determined by Mosher's method [10]. The physical data are as follows.

1: Oil, $[\alpha]_D^{24}$ + 45.7° (c 1.0, chloroform), ee 94%. ^1H NMR ($CDCl_3$) δ 7.38–7.15 (5H, m), 3.88 (1H, m), 3.55 (1H, m), 3.00 (1H, m), 2.88–2.68 (3H, m), 1.98–1.80 (2H, m); IR (film) 3400 cm^{-1}. MS *m/z* (rel. intensity, %) 178 (M^+, 91), 135 (13), 107 (19). HRMS Anal. calcd for $C_{11}H_{14}O_2$: 178.0994. Found: 178.0985.

3: Oil, $[\alpha]_D^{24}$ − 7.3° (c 1.0, chloroform), ee 93%. ^1H NMR ($CDCl_3$) δ 7.33–7.20 (5H, m), 3.57 (2H, d, J = 5.1 Hz), 3.10 (1H, td, J = 5.1 and 4.4 Hz), 3.07 (1H, td, J = 6.2 and 4.4 Hz), 2.88 (1H, ddd, J = 13.9, 8.1, and 5.9 Hz), 2.73 (1H, dt, J = 13.9 and 8.1 Hz), 1.98 (1H, dddd, J = 14.1, 8.1, 6.2, and 5.9 Hz), 1.80 (1H, dtd, J = 14.1, 8.1, and 6.2 Hz). IR (film) 3400 cm^{-1}. MS (relative intensity) *m/z* 178 (M^+, 14), 160 (71), 61 (base). HRMS Anal. calcd for $C_{11}H_{14}O_2$: 178.0994. Found: 178.1016.

5: Oil, $[\alpha]_D^{24}$ + 8.3° (c 1.0, chloroform), ee 85%. ^1H NMR ($CDCl_3$) δ 7.31–7.12 (5H, m), 3.83 (1H, dt, J = 7.7 and 3.8 Hz), 2.99 (1H, ddd, J = 4.0, 3.8 and 2.9 Hz), 2.85 (1H, m), 2.81 (1H, dd, J = 5.1 and 2.9 Hz), 2.75 (1H, m), 2.71 (1H, dd, J = 5.1 and 4.0 Hz), 1.94–1.76 (2H, m). IR (film) 3400 cm^{-1}. MS (relative intensity) *m/z* 178 (M^+, 33), 133 (28), 119 (base). HRMS Anal. calcd for $C_{11}H_{14}O_2$: 178.0994. Found 178.1002.

After the kinetic resolution of **5** [13], the remaining allylic alcohol was obtained in 41% yield, as an oil. $[\alpha]_D^{24}$ + 5.3° (c 1.0, chloroform). ^1H NMR (CDCl3) δ 7.32–7.15 (5H, m), 5.90 (1H, ddd, J = 16.5, 10.3, and 6.2 Hz), 5.24 (1H, ddd, J = 16.5, 1.5, and 1.1 Hz), 5.13 (1H, ddd, J = 10.3, 1.5, and 1.1 Hz), 4.14 (1H, m), 2.76–2.69 (2H, m) 1.88–1.83 (2H, m), 1.59 (1H, bs). MS (relative intensity) *m/z* 162 (M^+, 12), 144(6), 129(11). HRMS Anal. calcd for $C_{11}H_{14}O$: 162.1045. Found 162.1029. This allylic alcohol was subjected to standard epoxidation by mCPBA to give two diastereoisomeric epoxides. Separation by sil-

ica gel chromatography gave **7** in 41% yield and its diastereoisomer in 40% yield.

7: Oil, $[\alpha]_D^{24}$ + 5.1° (c 1.0, chloroform), ee 87%. ^{1}H NMR ($CDCl_3$) δ 7.34–7.11 (5H, m), 3.48 (1H, dt, J = 8.4 and 3.3 Hz), 3.03 (1H, m), 2.85 (1H, m), 2.75 (1H, m), 2.00–1.80 (2H, m), 1.32–1.20 (2H, m). IR (film) 3400 cm^{-1}. MS (relative intensity) m/z 178 (M^+, 25), 133 (20), 119 (base). HRMS Anal. calcd for $C_{11}H_{12}O_2$: 178.0994. Found: 178.0971.

Typical Xanthate Formation Reaction

Into a suspension of NaH (9 mmol, 360 mg in mineral oil) or KH (9 mmol) in a mixture of anhydrous THF (15 mL) and carbon disulfide (15 mL) was dropped the epoxy alcohol (890 mg, 5 mmol) in THF (3 mL) at −78°C. The reaction mixture was allowed to warm to −30°C. When a trace of less polar material was detected by tlc (Rf = 0.83, 0.86, 0.85, and 0.75 in the cases of the compounds, **2**, **4**, **6**, and **8**, respectively, developed by methylene chloride), the reaction was stopped by addition of saturated ammonium chloride (5 mL), and the mixture was extracted with ether (80 mL). The extract was washed with water and dried over $MgSO_4$. The solvent was evaporated and the residual oil was purified by silica gel chromatography to give the cyclic xanthates in 77–83% yields and some starting materials in 10–15% yields.

2: 83% yield. Colorless crystals, mp 65–67°C recrystallized from benzene:hexane (2:1), Rf = 0.46 (methylene chloride) $[\alpha]_D^{24}$ −82.8° (c 1.0, chloroform). ^{1}H NMR ($CDCl_3$) δ 7.34–7.19 (5H, m), 5.07 (1H, dd, J = 9.9 and 7.0 Hz), 4.84 (1H, dd, J = 9.9 and 3.7 Hz), 3.94 (1H, dt, J = 7.0 and 3.7 Hz), 3.80 (1H, ddd, J = 9.5, 7.0 and 2.6 Hz), 2.87 (1H, m), 2.74 (1H, m), 1.91 (1H, m), 1.80 (1H, m). IR (film) 3420, 1220 cm^{-1}. MS (relative intensity) m/z 254 (M^+, 20), 221 (44), 194 (39), 91 (base). HRMS Anal. calcd for $C_{12}H_{14}O_2S_2$: 254.0435. Found: 254.0443. Anal. calcd for $C_{12}H_{14}O_2S_2$: C, 56.66; H, 5.55. Found: 56.81; H, 5.61.

4: 80% yield. Colorless crystals, mp 109–111°C recrystallized from benzene:hexane (2:1), Rf = 0.24 (methylene chloride), $[\alpha]_D^{24}$ −48.9° (c 1.0, chloroform). ^{1}H NMR ($CDCl_3$) δ 7.37–7.18 (5H, m), 4.87 (2H, d, J = 5.9 Hz), 4.09 (1H, dt, J = 11.0 and 5.9 Hz), 3.81 (1H, br), 2.86 (1H, ddd, 13.9, 7.7, and 6.2 Hz), 2.72 (1H, ddd, 13.9, 8.1, and 7.7 Hz), 1.83–1.77 (2H, m). IR (film) 3400, 1230 cm^{-1}. MS (relative intensity) m/z 254 (M^+, 91), 221 (10), 160 (49), 143 (base). HRMS Anal. calcd for $C_{12}H_{14}O_2S_2$: 254.0435. Found: 254.0405. Anal. calcd for $C_{12}H_{14}O_2S_2$: C, 56.66; H, 5.55. Found: C, 56.81; H, 5.63.

6: 81% yield. Oil, Rf = 0.38 (methylene chloride), $[\alpha]_D^{24}$ −88.2° (c 1.0, chloroform). ^{1}H NMR ($CDCl_3$) δ 7.42–7.15 (5H, m), 5.07 (1H, ddd, J = 8.4, 4.8, and 3.7 Hz), 4.70–3.87 (3H, m), 2.92 (1H, ddd, J = 14.3, 9.2, and 5.5 Hz), 2.81 (1H, ddd, J = 14.3, 8.8, and 7.0 Hz), 2.12 (1H, dddd, J = 17.6, 8.8, 8.4, and 5.5 Hz), 2.07 (1H, dddd, J = 17.6, 9.2, 7.0, and 4.8 Hz). IR (film) 3400, 1200 cm^{-1}. MS (relative intensity) m/z 254 (M^+, 82), 163 (26), 143 (80), 129 (90), 123 (base), 117 (92). HRMS Anal. calcd for $C_{12}H_{14}O_2S_2$: 254.0435. Found: 254.0423.

8: 77% yield. Oil, Rf = 0.32 (methylene chloride), $[\alpha]_D^{24}$ + 14.8° (c 1.0, chloroform). ^{1}H NMR ($CDCl_3$) δ 7.38–7.19 (5H, m), 5.03 (1H, ddd, J = 9.5, 5.5, and 4.0 Hz), 3.94–3.84 (3H, m), 3.00 (1H, ddd, J = 14.3, 8.8, and 5.5 Hz), 2.83 (1H, ddd, J = 14.3, 8.8, and 7.3 Hz), 2.41 (1H, ddt, 14.9, 8.8, and 5.5 Hz), 2.10 (1H, dddd, J = 14.9, 8.8, 7.3, and 4.0 Hz). IR (film) 3400, 1200 cm^{-1}. MS (relative intensity) m/z 254 (M^+, 1), 143 (16), 117 (37), 104 (39), 91 (base). HRMS Anal. calcd for $C_{12}H_{14}O_2S_2$: 254.0435. Found: 254.0423.

Optically Pure Triacetates of 2-Mercapto-1,3-diols

Silylation of **2**. To a stirred methylene chloride solution (25 mL) of the hydroxy xanthate **2** (500 mg, 2.16 mmol) and 2,6-lutidine (1 mL, 8.6 mmol) was added TBSOTf (0.7 mL, 3.05 mmol) at room temperature. The mixture was further stirred for 25 minutes. The reaction mixture was washed with water (2 mL X2) and brine (2 mL). The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by column chromatography on silica gel and eluted with 10% ethyl acetate in hexane to give 696 mg of **9** in 90% yield. Oil, $[\alpha]_D^{24}$ −51.2° (c 1.0, chloroform). ^{1}H NMR ($CDCl_3$) δ 7.38–7.16 (5H, m), 4.83 (1H, dd, J = 9.9 and 4.7 Hz), 4.77 (1H, dd, J = 9.9 and 7.0 Hz), 4.15 (1H, ddd, J = 7.0, 5.5, and 4.7 Hz), 3.91 (1H, dt, J = 5.9 and 5.5 Hz), 2.70 (1H, ddd, J = 13.9, 6.6, and 3.5 Hz), 2.62 (1H, ddd, J = 13.9, 9.9, and 4.0 Hz), 1.96 (1H, dddd, J = 14.3, 5.9, 4.0, and 3.5 Hz), 1.81 (1H, dddd, J = 14.3, 9.9, 6.6, and 5.9 Hz), 0.92 (9H, s), 0.11 (3H, s), 0.10 (3H, s). IR (film) 1210 cm^{-1}. MS (relative intensity) m/z 311 (M − 57, 13), 251 (21), 235 (base), 217 (52). MS (FAB) m/z 369 (M + 1). HRMS (FAB) Anal. calcd for $C_{18}H_{29}O_2S_2Si$: 369.1378. Found: 369.1365.

Preparation of Diacetate **10**. To a suspension of $LiAlH_4$ (400 mg, 10 mmol) in ether (40 mL) was added an ethereal solution (10 mL) of the cyclic xanthate **9** (620 mg, 1.68 mmol) at 0°C during 5 minutes. The mixture was stirred for 10 minutes at the same temperature. Usual work up and extraction with ether (80 mL) gave the crude mercapto alcohol as an oil. ^{1}H NMR ($CDCl_3$) δ 7.37–7.18 (5H, m), 3.94 (1H, td, J = 6.5 and 2.2 Hz), 3.74 (1H, dd, J = 11.0 and 6.6 Hz), 3.62 (1H, dd, J = 11.0 and 7.3 Hz), 2.99 (1H, ddd, J = 7.3, 6.6, and 2.2 Hz), 2.60 (2H, t, J = 8.4 Hz), 2.17 (1H, m), 1.79 (1H, m), 0.91 (9H, s), 0.08 (3H, s), 0.06 (3H, s); MS (rel. intensity) 269 (M − 57), 236 (80), 222 (48), 221 (base). This alcohol was directly acetylated with

Ac_2O (1 mL) in pyridine (3 mL) in the presence of DMAP (50 mg) in an ice bath. The reaction took 30 minutes. The mixture was extracted with ether (80 mL), and the extract was washed with dilute HCl (5%, 3 mL X3), water (3 mL X2), and brine (3 mL). The ethereal extract was dried over $MgSO_4$, and the solvent was evaporated. The residual oil was purified by column chromatography on silica gel and eluted with 20% ethyl acetate in hexane to give diacetate **10**, 283 mg in 41% yield. Oil, $[\alpha]D^{24}$ −5.1° (c 1.0, chloroform). ^1H NMR ($CDCl_3$) δ 7.37–7.13 (5H, m), 4.23 (1H, dd, J = 11.1 and 8.1 Hz), 4.12 (1H, dd, J = 11.1 and 6.6 Hz), 4.00–3.95 (2H, m), 2.58 (2H, t, J = 8.4 Hz), 2.37 (3H, s), 2.03 (3H, s), 1.96 (1H, m), 1.78 (1H, m), 0.88 (9H, s), 0.36 (3H, s), 0.01 (3H, s). IR (film) 1750, 1690 cm^{-1}. MS (relative intensity) m/z 410 (M^+, 2), 385 (66), 353 (base); MS (FAB) m/z 411 (M + 1). HRMS (FAB) Anal. calcd for $C_{21}H_{35}O_4SSi$: 411.2028. Found: 411.2000.

Preparation of Triacetate **11.** Silyl ether **10** (242 mg, 0.59 mmol) in ethanol (5 mL) was cooled in an ice bath and treated with hydrofluoric acid (47% in water, 2 mL). The mixture was stirred for 3 hours at room temperature. It was neutralized with saturated sodium bicarbonate (60 mL) and extracted with chloroform (20 mL X3). The organic layer was washed with water (4 mL X2) and dried over $MgSO_4$, and the solvent was evaporated to give crude product. This was acetylated with acetic anhydride (1 mL) and DMAP (50 mg) in pyridine (2 mL) at room temperature. The reaction was completed in 10 minutes. The reaction mixture was extracted with ethyl acetate (30 mL) and washed with water (3 mL X5) and brine (5 mL). Evaporation of the solvent from extract and purification of the residue by column chromatography on silica gel and elution with 10% ethyl acetate in hexane gave triacetate **11**, 143 mg in 72% yield. Oil, $[\alpha]D^{24}$ + 6.1° (c 1.0, chloroform). ^1H NMR ($CDCl_3$) δ 7.30–7.15 (5H, m), 5.32 (1H, ddd, J = 10.3, 5.5, and 2.2 Hz), 4.20 (1H, m), 4.05–4.00 (2H, m), 2.67–2.55 (2H, m), 2.38 (3H, s), 2.05 (1H, m), 2.04 (3H, s), 2.03 (3H, s), 1.86 (1H, ddd, J = 14.3, 7.0, 5.5, and 2.9 Hz). IR (film) 1750, 1745, 1690 cm^{-1}. MS (relative intensity) m/z 338 (M^+, 14), 293 (76), 255 (28), 160 (base). MS (FAB) m/z 339 (M + 1). HRMS (FAB) Anal. calcd for $C_{17}H_{23}O_5S$: 339.1266. Found: 339.1283.

Preparation of **12.** The silyl ether **12** was synthesized in the same manner as described for the compound **9**. 88% yield. Oil, $[\alpha]D^{24}$ − 73.0° (c 1.0, chloroform). ^1H NMR ($CDCl_3$) δ 7.23–7.10 (5H, m), 4.94 (1H, dt, J = 8.4 and 4.4 Hz), 3.70 (1H, ddd, J = 6.6, 5.5, and 4.4 Hz), 3.66–3.59 (2H, m), 2.80 (1H, ddd, J = 14.3, 9.2, and 5.5 Hz), 2.69 (1H, dt, J = 14.3 and 8.4 Hz), 2.20 (1H, dtd, J = 13.9, 8.4, and 5.5 Hz), 1.96 (1H, ddt, J = 13.9, 9.2, and 8.4 Hz), 0.76 (9H, s), −0.05 (3H, s), −0.06 (3H, s). IR (film) 1210 cm^{-1}. MS (relative intensity) m/z 369 (M^+, 11), 311 (base), 277 (11), 253 (64), 252 (75), 219 (59), 218 (81). MS (FAB) m/z 369 (M + 1). HRMS (FAB) Anal. calcd for $C_{18}H_{29}O_2S_2Si$: 369.1378. Found: 369.1378.

Preparation of Diacetate **13.** The same synthetic procedure for the compound **10** was used for the synthesis of **13**. 35% yield. Colorless crystals, mp 48–51°C, $[\alpha]D^{24}$ + 4.8° (c 1.0, chloroform). ^1H NMR ($CDCl_3$) δ 7.28–7.13 (5H, m), 5.41 (1H, ddd, J = 7.3, 5.9, and 2.9 Hz), 3.87 (1H, ddd, J = 8.1, 5.5, and 2.9 Hz), 3.66 (1H, dd, J = 10.3 and 8.1 Hz), 3.58 (1H, dd, J = 10.3 and 5.5 Hz), 2.61 (2H, ddd, J = 9.5, 7.0, and 2.6 Hz), 2.36 (3H, s), 2.04 (3H, s), 2.03 (1H, m), 1.96 (1H, dddd, J = 13.2, 8.8, 7.0, and 2.9 Hz), 0.87 (9H, s), 0.04 (3H, s), 0.03 (3H, s). IR (film) 1750, 1700 cm^{-1}. MS (relative intensity) m/z 410 (M^+, 6), 293 (54), 279 (21), 251 (21), 217 (34), 149 (base). MS (FAB) m/z 411 (M + 1); HRMS (FAB) Anal. calcd for $C_{21}H_{35}O_4SSi$: 411.2028. Found: 411.2041. Anal. calcd for $C_{21}H_{34}O_4SSi$: C, 61.42; H, 8.35. Found C, 61.71; H, 8.40.

Preparation of Triacetate **14.** Triacetate **14** was prepared in 74% yield by the same procedure used for **11** which is an enantiomer of **14**. All spectroscopic data were exactly the same as those described for **11**. $[\alpha]D^{24}$ − 6.0° (c 1.0, chloroform).

Synthesis of **15** *and* **16** *from* **1**, **2**, **5**, *or* **6.** The reaction was employed exactly in the same way as described in the typical xanthate formation reaction, except that the temperature was raised to room temperature. A mixture of **15** and **16** was purified by column chromatography on silica gel and eluted with 40% ethyl acetate in hexane, but they were not separable. Yields were in 65 to 90%. Rf = 0.70 (CH_2Cl_2). ^1H NMR ($CDCl_3$) δ 7.35–7.15 (5H, m), 4.58 (1/2H, dd, J = 10.3 and 7.0 Hz), 4.55 (1/2H, m), 4.47 (1/2H, dd, J = 10.3 and 5.1 Hz), 3.95 (1/2H, ddd, J = 9.2, 7.0, and 5.1 Hz), 3.70 (1/2H, td, J = 3.0 and 7.0 Hz), 2.99 (1/2H, ddd, J = 9.2, 8.8, and 4.9 Hz), 2.91–2.71 (3H, m), 2.25–2.10 (1H, m), 2.03 (1/2H, m), 1.75 (1/2H, m). IR (film) 1730 cm^{-1}. MS (relative intensity) m/z 254 (M+, 41), 210 (2), 143 (17), 117 (45), 91 (base).

Preparation of **17** *and* **18.** To a mixture of **15** and **16** (110 mg, 0.41 mmol) in pyridine (600 μL) was added an excess of acetic anhydride (300 μL), and the mixture was stirred for 9 hours at room temperature. Standard workup and purification by column chromatography on silica gel (eluted with 30% ethyl acetate in hexane) gave the less polar **17** in 47% yield and the polar **18** in 44% yield. **17**: Colorless crystals, mp 55–56°C recrystallized from benzene:hexane (1:2), Rf = 0.25 (30% ethyl acetate in hexane), $[\alpha]D^{24}$ −60.4° (c 1.0, chloroform). ^1H NMR ($CDCl_3$) δ 7.34–7.20 (5H, m), 4.40 (1H, dt, J = 8.5 and 4.0 Hz), 3.80 (1H, dt, J = 7.0 and 3.7 Hz), 3.23 (1H, dd, J = 14.1 and 7.0 Hz), 3.14 (1H,

dd, J = 14.1 and 7.0 Hz), 2.90–2.69 (2H, m), 2.36 (3H, s), 2.17 (1H, m), 2.01 (1H, m). ^{13}C NMR ($CDCl_3$) δ 194.3, 171.1, 139.8, 128.6, 128.4, 126.4, 83.2, 52.3, 35.3, 33.5, 31.3, 30.5. IR (chloroform) 1735, 1685 cm^{-1}. MS (relative intensity) m/z 296 (M+, 59), 254 (74), 222 (base), 210 (94), 174 (70), 161 (75), 142 (76). MS (FAB) m/z 297 (M + 1). HRMS (FAB) Anal. calcd for $C_{14}H_{17}O_3S_2$: 297.0619. Found: 297.0599. Anal. calcd for $C_{14}H_{16}O_3S_2$: C, 56.73; H, 5.44. Found C, 56.94; H, 5.48. **18**: Colorless crystals, mp 53–55°C recrystallized from benzene:hexane (1:2), Rf = 0.19 (30% ethyl acetate in hexane), $[\alpha]D^{24}$ + 65.0° (c 1.0, chloroform). ^{1}H NMR ($CDCl_3$) δ 7.32–7.13 (5H, m), 4.47 (1H, dd, J = 9.9 and 6.8 Hz), 4.25 (1H, dd, J = 9.9 and 4.6 Hz) 4.16 (1H, ddd, J = 11.6, 6.8, and 4.6 Hz), 3.74 (1H, ddd, J = 11.6, 7.8, and 3.9 Hz), 2.84 (1H, ddd, J = 13.8, 8.9, and 5.3 Hz), 2.63 (1H, ddd, J = 13.8, 7.1, and 2.0 Hz), 2.42 (3H, s), 2.06–1.95 (2H, m). ^{13}C NMR ($CDCl_3$) δ 194.2, 171.9, 140.1, 128.5, 128.3, 126.3, 71.2, 52.9, 46.8, 33.2, 32.6, 30.8. IR (chloroform) 1735, 1690 cm^{-1}. MS (relative intensity) m/z 296 (M$^+$, 37), 254 (9), 220 (base), 176 (27), 143 (34), 117 (24). MS (FAB) m/z 297 (M + 1); HRMS (FAB) Anal. calcd for $C_{14}H_{17}O_3S_2$: 297.0619. Found: 297.0648. Anal. calcd for $C_{14}H_{16}O_3S_2$: C, 56.73; H, 5.44. Found C, 56.92; H, 5.48.

Parameters of X-Ray Crystallographic Analysis for **17.** A suitable single crystal of **17** was obtained as described above. Initial lattice parameters were obtained from least-squares fits to 41 reflections, $30 < 2\theta < 36$, accurately centered on a MAC Science MXC18 automated diffractometer. **17**: $C_{14}H_{16}S_3O_2$, Mr = 312.46, orthorhombic, space group $P2_12_12_1$, a = 11.304(4) Å, b = 21.790(10) Å, c = 6.000(2) Å, U = 1477.9(9) Å^3, Dc = 1.404 g cm^{-3}, Z = 4, λ (Mo K_α) = 0.71069 Å, μ = 4.96 cm^{-1}. Total of 2009 reflections were collected at 25°C, using the ω scan mode over the range $3.0° < 2\theta < 55°$. The data were corrected for Lorentz and polarization effects. No absorption correction was applied. The crystal structure was solved by a direct method and refined by a full-matrix least-squares technique. The programs in the Rigaku supplied TEXAN package were employed. The final residuals were R = 0.074 and Rw = 0.078 for 1397 reflections ($I > 3\sigma(I)$).

trans-3,4-Epoxy Alcohol **20.** mCPBA (651 mg, 80% purity, 3.02 mmole) was added to a methylene chloride solution (11 mL) of (E)-6-phenyl-3-hexen-1-ol (438 mg, 2.52 mmole) at room temperature. After having been stirred for 50 minutes, the mixture was diluted with methylene chloride (40 mL) and washed with saturated $Na_2S_2O_3$ solution (6 mL), $NaHCO_3$ (3 mL), and brine (3 mL). The organic layer was dried over $MgSO_4$ and the solvent evaporated. Purification of the crude residual oil by silica gel chromatography (eluted with 40% ethyl acetate in hexane) gave the pure epoxy alcohol **20**, 391 mg in 81% yield. Oil. ^{1}H NMR ($CDCl_3$) δ 7.31–7.26 (2H, m), 7.21–7.18 (3H, m), 3.70 (2H, t, J = 5.9 Hz), 2.84–2.67 (3H, m), 2.24 (1H, bs), 1.92–1.80 (3H, m), 1.69–1.60 (1H, m). ^{13}C NMR ($CDCl_3$) δ 141.11, 128.40, 128.32, 126.02, 58.85, 57.60, 57.08, 34.16, 32.63, 32.11. IR (film) 3440 cm^{-1}. MS (relative intensity) m/z 192 (M$^+$, 19), 175 (62), 147 (56), 146 (65), 127 (75). HRMS Anal. calcd for $C_{12}H_{16}O_2$: 192.1150. Found: 192.1143.

Six-Membered Cyclic Xanthate Formation. The ring opening reaction of **20** was carried out under the same reaction conditions used for five-membered cyclic xanthate formation, except for the temperature. In this case, the temperature was allowed to rise 0°C, and it was kept there for 2 hours. Subsequent workup and purification by column chromatography on silica gel (eluted with 50% ethyl acetate in hexane) gave **21** in 44% yield and recovery of the starting epoxide in 34% yield. **21** Oil. ^{1}H NMR ($CDCl_3$) δ 7.37–7.18 (5H, m), 4.75 (1H, ddd, J = 11.7, 5.1, and 2.9 Hz), 4.39 (1H, ddd, J = 11.7, 10.3, and 1.8 Hz), 3.73 (1H, bt, J = 5.7 Hz), 3.43 (1H, dt, J = 9.9 and 5.5 Hz), 2.85 (1H, m), 2.72 (1H, ddd, J = 15.4, 13.9, and 7.7 Hz), 2.34 (1H, dddd, J = 12.8, 5.5, 5.1, and 1.8 Hz), 2.17 (1H, dddd, J = 12.8, 10.3, 5.5, and 2.9 Hz), 1.87 (1H, m), 1.67 (1H, ddd, J = 14.3, 11.4, and 5.9 Hz). ^{13}C NMR ($CDCl_3$) δ 200.51, 140.74, 128.75, 128.33, 126.22, 72.04, 71.82, 51.14, 35.25, 31.85, 22.55. IR (film) 3400, 1220 cm^{-1}. MS (rel. intensity) m/z 268 (M$^+$, base), 208 (27), 174 (21). HRMS Anal. calcd for $C_{13}H_{16}O_2S_2$: 268.0592. Found: 268.0566.

Silyl Ether **22.** To a mixture of **21** (100 mg, 0.37 mmol) and 2,6-lutidine (87 μL, 0.75 mmol) in methylene chloride (1 mL) was added TBSOTf (111 μL, 0.48 mmole) at room temperature. The mixture was stirred for 10 minutes and diluted with ethyl acetate (30 mL). It was washed with water (2 mL X3) and brine (3 mL) and dried over $MgSO_4$, and the solvent was evaporated. The crude product obtained was purified by column chromatography on silica gel (eluted with 10% ethyl acetate in hexane) to give **22**, 114 mg in 80% yield. Colorless crystals, mp 76–78°C recrystallized from hexane. ^{1}H NMR ($CDCl_3$) δ 7.36–7.19 (5H, m), 4.76 (1H, ddd, J = 11.5, 5.1, and 2.9 Hz), 4.38 (1H, ddd, J = 11.5, 10.3, and 1.8 Hz), 3.79 (1H, q, J = 5.5 Hz), 3.56 (1H, dt, J = 10.3 and 5.5 Hz), 2.70–2.57 (2H, m), 2.33 (1H, ddt, J = 10.3, 5.1 and 1.8 Hz), 2.09–1.77 (3H, m), 0.93 (9H, s), 0.11 (6H, s). IR (film) 1225 cm^{-1}. MS (rel. intensity) m/z 382 (M$^+$, 22), 325 (base), 307 (65), 265 (91). HRMS Anal. calcd for $C_{19}H_{30}O_2S_2Si$: 382.1457. Found: 382.1492. Anal. calcd for $C_{19}H_{30}O_2S_2Si$: C, 59.64; H, 7.79. Found: C, 59.37; H, 7.91.

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