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# Preparation and Conformational Analysis of 6,10-Diethyl[1,2,3]trithiolo-[4,5-*h*]benzopentathiepin Monoxides: Isolation and Optical Properties of Chiral Benzopentathiepin Derivatives

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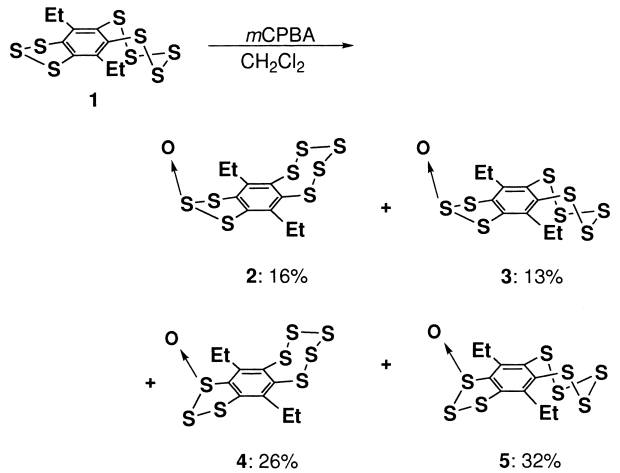
6,10-Diethyl[1,2,3]trithiolo[4,5-*h*]benzopentathiepin (**1**) was oxidized by *m*CPBA in dichloromethane to produce the corresponding four monoxides. The structures of the monoxides **2**, **3**, **4**, and **5** were determined by X-ray crystallography to be 6,10-diethyl[1,2,3]trithiolo[4,5-*h*]benzopentathiepin 8-oxides (1,2,3-trithiole 2-oxides) for **2** and **3**, and 6,10-diethyl[1,2,3]trithiolo[4,5-*h*]benzopentathiepin 7-oxides (1,2,3-trithiole 1-oxides) for **4** and **5**, respectively. Compounds **2** and **3** are isomers with respect to the conformation of the 1,2,3,4,5-pentathiepin ring, and **4** and **5** are also the conformational isomers. These compound pair members, **2** and **3**, and **4** and **5**, were found to isomerize each other by inversion of the pentathiepin ring. The activation parameters of the isomerization, $\Delta G_{298}^{\neq}$, $\Delta H^{\neq}$, and $\Delta S^{\neq}$, were determined by $^1$H NMR spectroscopy. Because of the slow inversion of the pentathiepin ring, isolation of unsymmetrically substituted benzopentathiepin as a chiral molecule is possible. Asymmetric oxidation of **1** was performed by a Sharpless reagent [**1**/Ti(O$^i$Pr)$_4$/*R*,*R*-DET/*t*-BuOOH = 1:2:4:4] to produce optically active monoxides **4a** and **5a**. The configuration of **4a** and **5a** was confirmed as *R* configuration on the sulfinyl sulfur atom, respectively. The specific rotation and the circular dichroism spectra of **4a** and **5a** were measured in chloroform; such data are apparently affected by the conformation of the pentathiepin ring.

Benzopentathiepins and analog compounds are interesting molecules for their structure, reactivity, electrochemical property, metabolism, and biological activities.[1–5] For instance, *Varacin* and *Lissoclinotoxin A*, which have antitumor and antifungal activities, were isolated from marine ascidian.[1] Such unsymmetrically substituted benzopentathiepins constitute a chiral molecule, if the inversion of the pentathiepin ring proceeds very slowly. Recently, we and Nakayama reported the first experimental determination of the inversion energy of the pentathiepin and pentathiepane rings, respectively, which reveal that the ring inversion of these seven-membered rings is very slow at room temperature.[6,7] On the other hand, when 6,10-diethyl[1,2,3]trithiolo[4,5-*h*]benzopentathiepin (**1**) was oxidized by *m*-chloroperbenzoic acid (*m*CPBA), the corresponding four monoxides were obtained in moderate yields.[8a] These four monoxides consisted of two pairs of isomers with respect to the orientation of the 1,2,3,4,5-pentathiepin ring and the position of the sulfinyl group. Furthermore, two of the monoxides were chiral molecules since they contain a plane of chirality. This article reports the preparation and structure determination of these four monoxides, the conformational analysis of the pentathiepin ring, and the isolation and optical properties of the chiral benzopentathiepin derivatives.

## Results and Discussion

**Preparation and Structure of Monoxides 2, 3, 4, and 5.** In order to examine the reactivity between the 1,2,3,4,5-pentathiepin and 1,2,3-trithiole rings, **1** was oxidized with equimolar amount of *m*CPBA in dichloromethane at room temperature. After the usual work-up, four oxidized compounds **2**, **3**, **4**, and **5** were obtained as the major products. The following yields of these compounds were determined by the integral ratio of $^1$H NMR spectra: **2**, 16%; **3**, 13%; **4**, 26%; **5**, 32% (Scheme 1). These four oxidized compounds were purified by repeated recrystallization, after separation by silica-gel column chromatography, the process gave pure yellow crystals.

In the $^1$H NMR spectra, the methylene protons of two ethyl groups were recorded as one double quartet signal for **2** ($\delta$ = 3.12, 3.21; dq, $J$ = 15.1, 7.6 Hz) and **3** ($\delta$ = 3.09, 3.18; dq, $J$ = 14.9, 7.6 Hz), while two double quartet signals of the methylene protons were observed for **4** ($\delta$ = 3.18, 3.25; dq, $J$ = 14.7,




Scheme 1.

7.5 Hz. $\delta$ = 3.44, 3.46; $J$ = 9.6, 7.5 Hz) and **5** ($\delta$ = 3.19, 3.25; dq, $J$ = 13.9, 7.5 Hz. $\delta$ = 3.36, 3.53; dq, $J$ = 9.6, 7.5 Hz). These spectra show that **2** and **3** have a symmetric structure, while **4** and **5** have an unsymmetric structure. In the IR spectra, the sulfinyl group of these compounds is observed at 1119 $cm^{-1}$ for **2**, 1118 $cm^{-1}$ for **3**, 1098 $cm^{-1}$ for **4**, and 1088 $cm^{-1}$ for **5**, as the wave number of the absorption. The structure of these compounds was determined by spectroscopical examination and elemental analysis to be $C_{10}H_{10}OS_8$. To our knowledge, there is no report with respect to the preparation and isolation of benzopentathiepin monoxide. Therefore, we predicted that **2**, **3**, **4**, and **5** are diethyl[1,2,3]trithiolo[4,5-*h*]benzopentathiepin monoxides bearing one oxygen atom on the 1,2,3-trithiole ring. However, it is impossible to establish the exact position of the oxidized sulfur atom, the exact configuration of the sulfinyl group, and the exact conformation of the pentathiepin ring of **2**, **3**, **4**, and **5** by the analytical data described above. So the structure of the four monoxides was determined by X-ray crystallographic analysis, revealing that they have the oxygen atom on the trithiole ring, not on the pentathiepin ring; **2** and **3** are benzotrithiole 2-oxides, while **4** and **5** are benzotrithiole 1-oxides. The ORTEP drawings of **2** and **3** are shown in Fig. 1. Meanwhile, instead of compounds **4** and **5**, the ORTEP drawings of **4a** and **5a** which were obtained by asymmetric oxidation of **1**, are shown in Fig. 3 (vide infra). In these molecules, the oxygen atoms coordinated to the sulfur atoms of **2** and **3** orient to the *end* side of the trithiole ring, and the oxygen atoms of **4** and **5** are located to the *exo* side of the trithiole ring. Meanwhile, the oxygen atoms of **2** and **4** exist on the syn side to the pentathiepin ring (syn isomers), and the oxygen atoms of **3** and **5** orient to the anti side to the pentathiepin ring (anti isomers). The structural data with respect to the crystal data, partial bond lengths, and bond angles are summarized in Tables 1, 2 and 3.

Consequently, benzopentathiepin monoxide was not obtained at all by the *m*CPBA oxidation of **1**. However, as minor products, benzobistrithiole 1-oxide and 2-oxide were obtained in low yields, instead of the corresponding benzopentathiepin monoxide.[8b] Furthermore, in our preliminary experiment, when 6,9-diethylbenzopentathiepin (**6**) was oxidized by *m*CPBA, a ring contraction reaction of the pentathiepin ring proceeded under the reaction conditions to produce not 6,9-diethylbenzopentathiepin monoxide (**7**) but 4,7-diethylbenzotrithiole monoxides (**8**) and (**9**) in low yields (Scheme 2). These results suggest that **7** is unstable under the *m*CPBA oxidation condition, and decomposes immediately to produce **8** and **9** together with generation of $S_2O$ or $S_2$.[9] However, we could not trap these species, in spite of the addition of 2,3-dimethyl-1,3-butadiene to the solution; hence the concentration of $S_2O$ or $S_2$ is predicted to be very low under the reaction conditions.

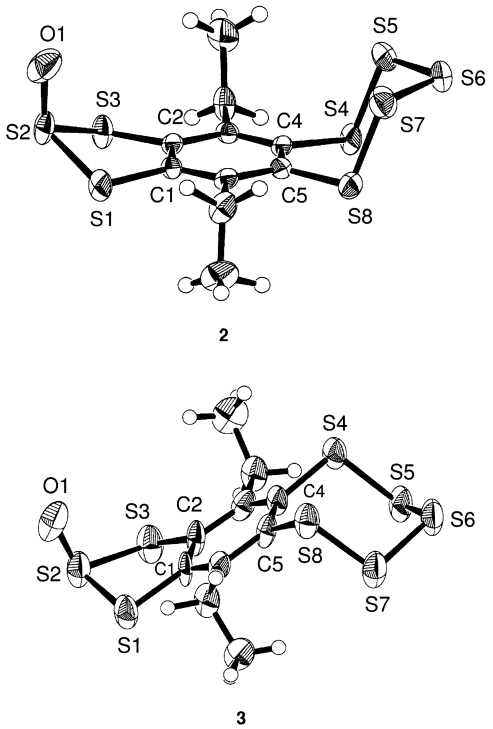



Fig. 1. The ORTEP Drawings of **2** and **3**.

**Conformational Analysis of 2, 3, 4, and 5.** As shown in Fig. 1, compounds **2** and **3** are the conformational isomer with respect to the pentathiepin ring. On the other hand, since unsymmetrically substituted benzopentathiepin is a chiral molecule, **4** and **5** are diastereomers with respect to the conformation of the pentathiepin ring and the configuration of the sulfinyl sulfur atom, respectively. Interestingly, **2** and **3**, and **4** and **5** were found to isomerize into each other in the chloroform solution, although those compounds were stable in the crystalline forms (Scheme 3). For example, purified **2** and **3** each isomerized slowly in chloroform at room temperature to produce about 1:1 mixtures of **2** and **3** under the equilibrium state. Similar isomerization was observed in the case of **4** and **5** at room temperature. The equilibrium ratio of these compounds was determined by $^1H$ NMR spectroscopy in deuterated chloroform: the ratio of **2** and **3** was 55:45, while that of **4** and **5** was 45:55. Under the equilibrium state, the syn isomer **2** is predominant compared with the anti isomer **3** in the case of trithiole 2-oxides, while for trithiole 1-oxide the anti isomer **5** is dominant compared with the syn isomer **4**. It is well known that the pyramidal inversion of the sulfinyl group does not proceed at room temperature.[10] These results suggest that the isomerization of **2**, **3**, **4**, and **5** should proceed by way of the in-

Table 1. Crystallographic Data of Compounds **2**, **3**, **4**, **5**, **4a**, and **5a**

| | **2** | **3** | **4** | **5** | **4a** | **5a** |
|---|---|---|---|---|---|---|
| Cryst syst | monoclinic | monoclinic | monoclinic | orthorhombic | monoclinic | orthorhombic |
| Space group | $P2_1$ | $P2_1/c$ | $P2_1/n$ | *Pbca* | $P2_1$ | $P2_12_12_1$ |
| Cryst color | yellow | yellow | yellow | yellow | yellow | yellow |
| $a$/Å | 7.192(1) | 18.077(3) | 11.260(5) | 18.827(4) | 8.832(2) | 18.793(2) |
| $b$/Å | 6.119(1) | 36.560(5) | 8.090(8) | 18.504(5) | 7.727(2) | 20.675(2) |
| $c$/Å | 18.233(1) | 4.717(7) | 17.241(5) | 8.984(4) | 11.685(2) | 8.091(2) |
| $\beta$/deg | 99.89(1) | 91.17(4) | 96.94(3) | 90.00 | 99.40(1) | 90.00 |
| $V$/Å$^3$ | 790.5(2) | 3116(4) | 1559(1) | 3129(1) | 786.7(3) | 3143.8(7) |
| $Z$ | 2 | 8 | 4 | 8 | 2 | 8 |
| $D_{calc}$/g cm$^{-3}$ | 1.692 | 1.716 | 1.715 | 1.709 | 1.700 | 1.701 |
| $\mu$/cm$^{-1}$ | 103.59[a)] | 105.10[a)] | 105.05[a)] | 11.27[b)] | 104.09[a)] | 104.19[a)] |
| obs/param ratio | 11.73 | 6.92 | 6.34 | 6.83 | 15.67 | 16.52 |
| $R$ | 0.037 | 0.067 | 0.046 | 0.032 | 0.065 | 0.051 |
| $R_w$ | 0.051 | 0.075 | 0.052 | 0.032 | 0.085 | 0.069 |
| GOF | 1.66 | 1.41 | 1.24 | 2.06 | 1.18 | 1.21 |

a) Cu$K\alpha$, b) Mo$K\alpha$.

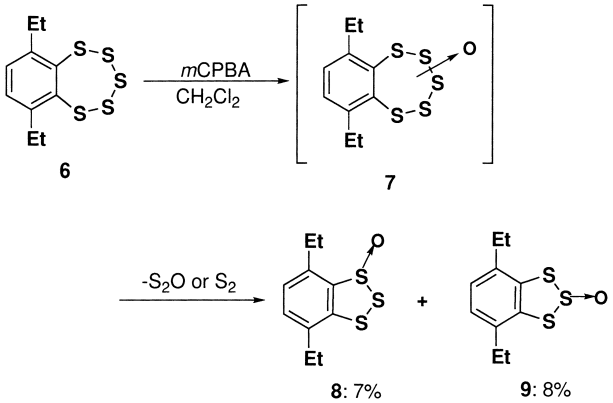
Table 2. Partial Bond Lengths/Å of Compounds **2**, **3**, **4**, and **5**

| | **2** | **3** | **4** | **5** |
|---|---|---|---|---|
| C1–C2 | 1.392(6) | 1.40(2) | 1.37(1) | 1.393(7) |
| C1–S1 | 1.765(4) | 1.75(1) | 1.810(9) | 1.797(5) |
| C2–S3 | 1.759(4) | 1.76(1) | 1.74(1) | 1.756(5) |
| S1–S2 | 2.104(2) | 2.115(5) | 2.103(4) | 2.105(2) |
| S2–S3 | 2.108(2) | 2.104(5) | 2.051(4) | 2.057(2) |
| C4–C5 | 1.407(6) | 1.42(2) | 1.40(1) | 1.409(7) |
| C4–S4 | 1.781(4) | 1.79(1) | 1.783(9) | 1.783(5) |
| C5–S8 | 1.785(4) | 1.77(1) | 1.780(10) | 1.791(5) |
| S4–S5 | 2.040(2) | 2.043(5) | 2.032(4) | 2.035(2) |
| S5–S6 | 2.056(2) | 2.051(6) | 2.056(4) | 2.058(2) |
| S6–S7 | 2.052(2) | 2.049(5) | 2.036(4) | 2.051(2) |
| S7–S8 | 2.045(2) | 2.035(5) | 2.043(4) | 2.040(2) |
| S1–O1 | — | — | 1.456(8) | 1.483(5) |
| S2–O1 | 1.472(4) | 1.47(1) | — | — |

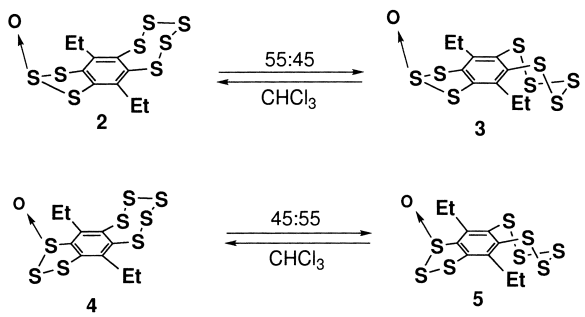
Table 3. Partial Bond Angles/deg of Compounds **2**, **3**, **4**, and **5**

| | **2** | **3** | **4** | **5** |
|---|---|---|---|---|
| S1–C1–C2 | 117.5(3) | 118(1) | 119.8(8) | 118.7(4) |
| S2–S1–C1 | 100.3(1) | 99.0(5) | 91.7(3) | 92.3(2) |
| S1–S2–S3 | 92.36(6) | 92.8(2) | 98.5(2) | 96.59(9) |
| S2–S3–C2 | 100.3(1) | 98.9(4) | 95.4(3) | 96.2(2) |
| S3–C2–C1 | 118.3(3) | 118.2(9) | 119.9(8) | 118.6(4) |
| S4–C4–C5 | 121.1(3) | 120.3(10) | 121.5(8) | 122.1(4) |
| S5–S4–C4 | 104.3(1) | 104.3(4) | 102.8(3) | 104.0(2) |
| S4–S5–S6 | 103.91(7) | 104.1(2) | 104.9(2) | 103.8(1) |
| S5–S6–S7 | 103.66(7) | 103.2(2) | 104.0(2) | 103.08(10) |
| S6–S7–S8 | 105.46(8) | 104.1(2) | 105.2(2) | 104.64(9) |
| S7–S8–C5 | 103.8(3) | 104.5(5) | 102.7(3) | 102.8(2) |
| S8–C5–C4 | 120.2(3) | 121.0(9) | 121.1(7) | 120.0(4) |
| O1–S1–C1 | — | — | 106.9(4) | 104.4(3) |
| S2–S1–O1 | — | — | 112.6(4) | 113.2(2) |
| S1–S2–O1 | 110.4(2) | 106.7(5) | — | — |
| S3–S2–O1 | 110.1(2) | 109.5(5) | — | — |

version of their pentathiepin rings. Therefore, in order to verify the inversion energy of the pentathiepin ring experimentally, and to accumulate data on the activation parameters of the




Scheme 2.




Scheme 3.

molecules, the isomerizations of **2**, **3**, **4**, and **5** were monitored by $^1$H NMR spectroscopy at 303 K, 308 K, 313 K, 318 K, and 323 K.[11] Typically, the results of the isomerization of **5** are shown in Fig. 2-A. The kinetic parameters of all compounds calculated are shown in Table 4. The isomerization of these compounds was the first order with respect to the increase and decrease of the integral ratio of the methyl protons of **2** and **3**, and the methylene protons of **4** and **5**, in their $^1$H NMR spectra. Furthermore, as shown in Fig. 2-B, the Eyring treatment of the rate constants of **5**, obtained at those temperatures, enabled us

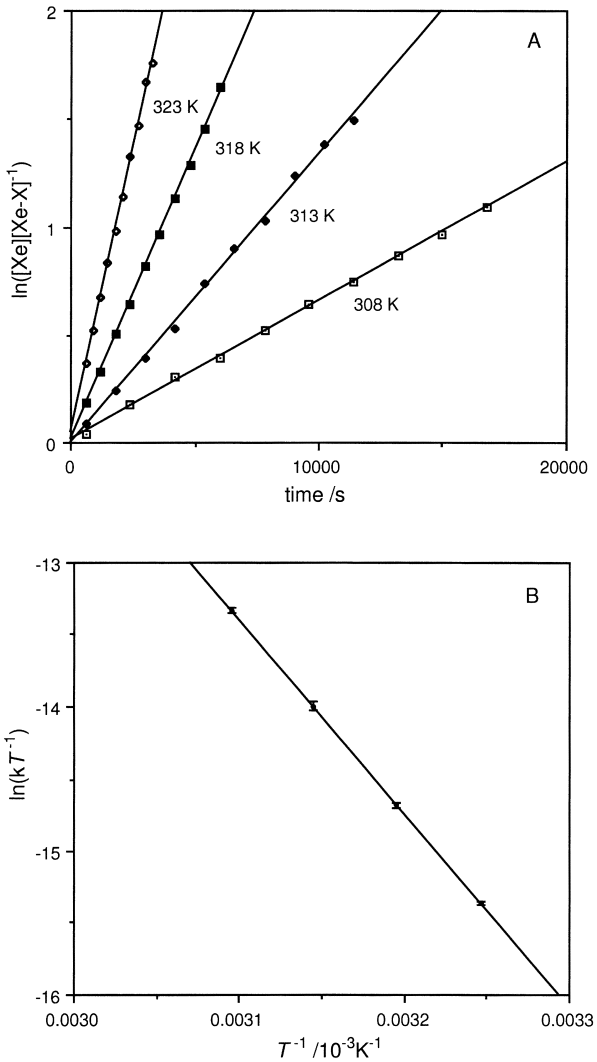



Fig. 2. A: The Representative Kinetic Data for Inversion of the Pentathiepin Ring of **5**; [Xe]: Equilibrium Concentration; [Xe-X]: Concentration as a Function of Time; B: Eyring Treatment with Standard Deviation for the Inversion of the Pentathiepin Ring of **5**.

to calculate the activation parameters of this molecule. The activation parameters $\Delta G_{298}^{\neq}$, $\Delta H^{\neq}$, and $\Delta S^{\neq}$ of **2**, **3**, **4**, and **5** are listed in Table 4. The values of $\Delta G_{298}^{\neq}$ of these compounds are about 100.4 kJ/mol, suggesting that the inversion of the pentathiepin ring of these compounds proceeds very slowly at room temperature. Furthermore, the values of $\Delta S^{\neq}$ support the finding that the isomerization of **2**, **3**, **4**, and **5** is the conformation change of the pentathiepin ring, not the pyramidal inversion of the sulfinyl group.[7]

**Preparation and Oxidation of [1,3]Dithiolo[4,5-*h*]benzopentathiepin.** It was reported that the racemization of chiral dithiiran oxides proceeded via homolytic S–S bond cleavage.[12] To demonstrate that the isomerization of **2**, **3**, **4**, and **5** did not proceed by way of the cleavage of the trithiole S–S bonds, 6,10-diethyl[1,3]dithiolo[4,5-*h*]benzopentathiepin monoxides (**11**) and (**12**) were prepared by the oxidation of 6,10-diethyl[1,3]dithiolo[4,5-*h*]benzopentathiepin (**10**), and the isomerization was examined similarly (Scheme 4). The treatment of **10** with *m*CPBA in dichloromethane gave **11** and **12** together with 4,8-diethyl[1,3]dithiolo[4,5-*f*]benzotrithiole monoxide (**13**), which was produced by way of a desulfurization reaction from the pentathiepin ring. In the $^1$H NMR spectra of **11**, two double quartet signals of the methylene proton were observed at $\delta$ = 3.18 and 3.25 ($J$ = 14.7, 7.5 Hz) and at $\delta$ = 3.44 and 3.46 ($J$ = 9.6, 7.5 Hz). Meanwhile, the methylene protons of **12** were observed as one quartet signal ($\delta$ = 3.18; $J$ = 7.5 Hz) and one double quartet signal ($\delta$ = 3.18, 3.25; dq, $J$ = 14.7, 7.5 Hz). These spectra show that **11** and **12** are an unsymmetric structure. In the IR spectra, the sulfinyl group of these compounds is observed at 1034 cm$^{-1}$ for **11** and at 1032 cm$^{-1}$ for **12**, as the wave number of the absorption. The structure of these compounds was determined by the spectroscopic and elemental analysis as $C_{11}H_{12}OS_7$. As we expected, each purified dithiole monoxide **11** and **12** was also found to isomerize in the chloroform solution at room temperature to produce about 1:1 mixtures of **11** and **12**. These results support the conclusion that the isomerizations of **2**, **3**, **4**, and **5** proceed by the inversion of their pentathiepin rings, not by S–S bond cleavage of the trithiole ring.

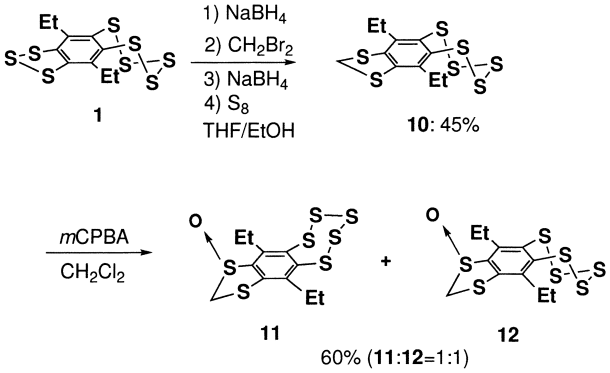
**Asymmetric Oxidation of Compound 1.** Unsymmetrically substituted benzopentathiepins, *Varacin* and *Lissoclinotoxin A*, are chiral molecules because of the slow inversion of the pentathiepin ring. There are two diastereomers of benzopentathiepin prepared by treatment of *Varacin* with chiral auxiliaries. In these molecules, however, only one compound was isolated and detected by $^1$H NMR spectroscopy, and hence there is no report with respect to the optical properties of benzopentathiepins such as specific rotation and circular dichroism.[1] In order to prepare a chiral molecule from benzopentathiepin derivatives and to examine the optical properties arising from the conformation of the pentathiepin ring, asymmetric oxidation of **1** was performed by a Sharpless reagent.[13]

The compound **1** was oxidized by a reagent which consisted of Ti(O$^i$Pr)$_4$/*R*,*R*-DET/*t*-BuOOH in dichloromethane at −20 °C under an argon atmosphere for 24 h (Scheme 5). The reactants, **1**/Ti(O$^i$Pr)$_4$/*R*,*R*-DET/*t*-BuOOH were in the ratio of 1:2:4:4, which gave the best result in the asymmetric oxidation. In spite of a large amount of an oxidizing reagent, the corresponding bissulfoxide and sulfone were not detected at all; the oxidation reaction of **1** appears to proceed very slowly under the reaction conditions. After the usual work-up and separation of the Ti complex and *R*,*R*-DET by filtration, the products were purified by column chromatography. By this reaction, four monoxides **2**, **3**, **4a**, and **5a** were obtained, similarly to the case of the *m*CPBA oxidation. In these monooxides, **2** and **3** are not chiral, while **4a** and **5a** are optically active molecules with respect to the conformation of the pentathiepin ring and the configuration of the sulfinyl sulfur atom. Compounds **4a** and **5a** could be separated easily by column chromatography in 18% and 23% yields, respectively. Meanwhile, **2** and **3** were obtained as a mixture in 29% yield.

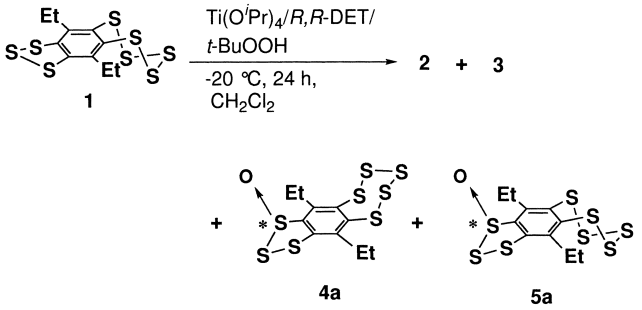
After column chromatography, the specific rotation $[\alpha]_D$ of **4a** and **5a** was measured by radiation with a sodium lamp in chloroform: $[\alpha]_D^{19} = -613°$ ($c$ = 0.130) for **4a** and $[\alpha]_D^{20} = -971°$ ($c$ = 0.282) for **5a**. However, compound **4a** and **5a** each contained its enantiomer **4b** and **5b** bearing a reversed configuration of the sulfinyl group. The compounds **4b** and **5b**

Table 4. Kinetic and Thermodynamic Parameters

| | 2 | 3 | 4 | 5 |
|---|---|---|---|---|
| $k_{303}/s^{-1}$ | $(4.71 \pm 1.17)\times10^{-5}$ | $(3.89 \pm 0.18)\times10^{-5}$ | — | — |
| $k_{308}/s^{-1}$ | $(7.79 \pm 0.95)\times10^{-5}$ | $(8.53 \pm 0.31)\times10^{-5}$ | $(6.38 \pm 0.35)\times10^{-5}$ | $(6.42 \pm 0.13)\times10^{-5}$ |
| $k_{313}/s^{-1}$ | $(1.62 \pm 0.24)\times10^{-4}$ | $(1.84 \pm 0.36)\times10^{-4}$ | $(1.24 \pm 0.06)\times10^{-4}$ | $(1.32 \pm 0.03)\times10^{-4}$ |
| $k_{318}/s^{-1}$ | $(3.15 \pm 0.54)\times10^{-4}$ | $(3.81 \pm 0.50)\times10^{-4}$ | $(2.33 \pm 0.05)\times10^{-4}$ | $(2.65 \pm 0.09)\times10^{-4}$ |
| $k_{323}/s^{-1}$ | $(6.09 \pm 0.23)\times10^{-4}$ | $(6.41 \pm 0.94)\times10^{-4}$ | $(4.64 \pm 0.20)\times10^{-4}$ | $(5.23 \pm 0.10)\times10^{-4}$ |
| $\Delta G_{298}^{\neq}$/kJ mol$^{-1}$ | 99.6 ± 0.4 | 100.0 ± 0.4 | 100.4 ± 0.4 | 100.8 ± 0.0 |
| $\Delta H^{\neq}$/kJ mol$^{-1}$ | 105.0 ± 4.2 | 113.0 ± 7.5 | 106.3 ± 2.9 | 113.4 ± 0.4 |
| $\Delta S^{\neq}$/eu | 18.4 ± 13.0 | 43.1 ± 24.7 | 19.7 ± 9.2 | 41.4 ± 1.3 |




Scheme 4.




Scheme 5.

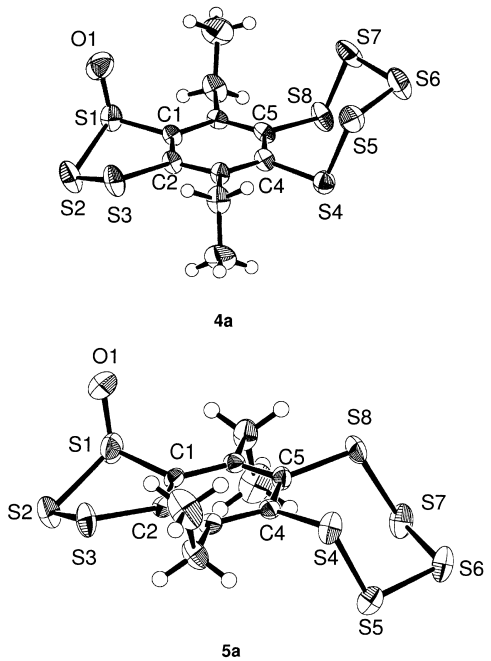



Fig. 3. The ORTEP Drawings of **4a** and **5a**.

could be observed as enantiomers of **4a** and **5a**, respectively, in the $^1$H NMR spectra measured by using [Eu(hfc)$_3$]. In order to purify **4a** and **5a**, these compounds were recrystallized from hexane:dichloromethane = 1:1 at −20 °C. By the repeated recrystallization, **4a** and **5a** were obtained as optically pure yellow crystals, respectively. Then the specific rotation $[\alpha]_D$ of **4a** and **5a** was measured in chloroform and established as $[\alpha]_D^{20} = -775°$ ($c = 0.204$) for **4a** and $[\alpha]_D^{19} = -1364°$ ($c = 0.161$) for **5a**. On the other hand, the diastereomeric excess of these compounds was determined by measurement of $^1$H NMR using [Eu(hfc)$_3$] as de = 100% for **4a** and de = 98% for **5a**.

In order to determine the absolute configuration of the chiral sulfinyl groups of **4a** and **5a**, X-ray crystallographic analysis of optically pure **4a** and **5a** was carried out by using Cu$K\alpha$ radiation. As shown in Fig. 3, the ORTEP drawings of **4a** and **5a** are *R* configuration on the sulfinyl sulfur atoms, respectively. In order to determine the correct configuration of the sulfinyl sulfur atoms, the *R* configuration is examined by the value of the parameter *x* which was defined by Flack for determination of the absolute configuration of the chiral molecules; **4a** has the value $x = 0.03(1)$ for the *R* configuration, while **5a** has the value $x = -0.009(1)$ for the *R* configuration.[14] These results reveal clearly that both **4a** and **5a** are *R* configuration on the sulfinyl sulfur atoms.

The compounds **4a** and **5a** were stable in the chloroform solution at −20 °C, and no isomerization was observed at this temperature. Meanwhile, the ring inversion of the pentathiepin ring was found to proceed slowly in the solution at room temperature; however, there is no epimerization of the sulfinyl group on the trithiole ring under the isomerization condition.

**Circular Dichroism Spectra of 4a and 5a.** Since there is no report with respect to the optical property of the chiral benzopentathiepin derivatives, the circular dichroism spectra of **4a** and **5a** were measured in chloroform (concentration: $6.46\times10^{-5}$ mol/L). The UV spectra of **4a** and **5a** show similar absorption curves; the absorption wavelength ($\lambda$max) and molar absorptivity ($\varepsilon$) of **4a** are $\lambda_{max} = 385$ nm and $\varepsilon = 4960$, while those of **5a** are $\lambda_{max} = 380$ nm and $\varepsilon = 5700$. Furthermore, the absorption wavelength of **1** was observed at $\lambda_{max} =$

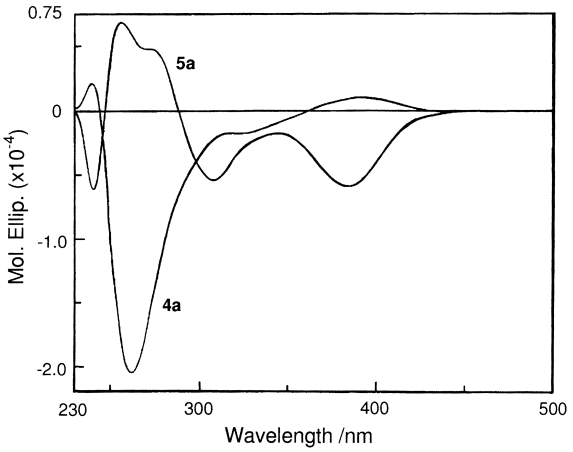



Fig. 4. The Circular Dichroism Spectra of **4a** and **5a** (Concentration; $6.46\times10^{-5}$/mol L$^{-1}$).

362 nm ($\varepsilon = 2820$). On the other hand, as shown in Fig. 4, the circular dichroism spectrum of **4a** shows a positive first Cotton effect at 391 nm, while that of **5a** shows a negative first Cotton effect at 384 nm. Since the configuration of the sulfinyl sulfur atoms of **4a** and **5a** are both *R* configuration as described above, and the absorption curve of **1** is similar to that of **4a** and **5a**, the different sign of this first Cotton effect should arise from the conformation of the pentathiepin ring. These results reveal that the conformation of the pentathiepin ring strongly affects the circular dichroism spectra, which is the first example of the optical property with respect to the conformation of the chiral benzopentathiepin derivatives.

## Conclusion

Compound **1** was oxidized by *m*CPBA and a Sharpless reagent to produce four monoxides **2**, **3**, **4**, and **5**. Their structure was determined by X-ray crystallographic analysis, and their activation parameters $\Delta G_{298}^{\neq}$, $\Delta H^{\neq}$, and $\Delta S^{\neq}$ were determined by measurement of $^1$H NMR spectroscopy. The isomerization of these monoxides was demonstrated to proceed by the inversion of the pentathiepin ring, not by the pyramidal inversion of the sulfinyl group and the S–S bond cleavage of the trithiole ring. Unsymmetrically substituted benzopentathiepins **4a** and **5a** have a plane of chirality, because of the slow inversion of the pentathiepin ring. The specific rotation and the circular dichroism spectra of **4a** and **5a** are strongly affected by the conformation of the pentathiepin ring.

## Experimental

**General.** For the asymmetric oxidation, *t*-butyl hydroperoxide (an 80% solution in di-*t*-butyl peroxide; Merck) was used. IR spectra were recorded on a JASCO FT-7300 spectrometer. NMR spectra were measured with $CDCl_3$ on a Bruker AC-400 spectrometer. Mass spectra were obtained with a Hitachi M-2000 mass spectrometer. UV spectra were measured with a JASCO Ubest-30 spectrometer. Elemental analyses were performed on a Yanako MT5 analyzer. The X-ray data collection were made on a Rigaku AFC7R diffractometer Cu$K\alpha$ radiation and a 12 kW rotating anode generator, and on a Enraf-Nonius CAD4 computer-controlled kappa axis diffractometer. All calculations for structure solution were performed using teXsan crystallographic software package.[15] CD spectra were measured by JASCO J-720 spectrometer equipped with Xenon lamp.

Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition numbers 179646–179651). The complete data are deposited as Document No. 75015 at the Office of the Editor of Bull. Chem. Soc. Jpn

**Oxidation of 6,10-Diethyl[1,2,3]trithiolo[4,5-*h*]benzopentathiepin (1).** To a solution of **1** (773 mg, 2.0 mmol, in 100 mL of $CH_2Cl_2$) was added *m*CPBA (assay > 95%, 363 mg, 2.0 mmol, in 100 mL of $CH_2Cl_2$) and the mixture was stirred at room temperature for 6 h. Then the solvent was evaporated off and the residue was purified by column chromatography (silica gel, $CHCl_3$:hexane = 1:1 and 1:2) to produce one mixture of **2** and **3** (231 mg) and the other mixture of **4** and **5** (468 mg), respectively. The ratios of compounds **2** and **3**, and **4** and **5** were determined by the integral ratio of $^1$H NMR as follows: **2**:**3** = 55 :45; **4**:**5** = 45:55, and the yields were calculated on the basis of these ratios: **2**, 16%; **3**, 13%; **4**, 26%; **5**, 32%. These four compounds were purified by repeated recrystallization (hexane:$CH_2Cl_2$ = 1:1); **2**:mp 125.0–127.5 °C (decomp); $^1$H NMR (400 MHz) $\delta$ 1.25 (t, $J$ = 7.6 Hz, 6H, $CH_3$), 3.12 (dq, $J$ = 15.1, 7.6 Hz, 2H, $CH_2$), 3.21 (dq, $J$ = 15.1, 7.6 Hz, 2H, $CH_2$); IR (KBr) 1119 cm$^{-1}$ (SO); MS *m/z* 402 (M$^+$); Anal. Found: C, 29.85; H, 2.48%. Calcd for $C_{10}H_{10}OS_8$: C, 29.82; H, 2.50%; **3**: mp 134.0–135.5 °C (decomp); $^1$H NMR (400 MHz) $\delta$ 1.27 (t, $J$ = 7.6 Hz, 6H, $CH_3$), 3.09 (dq, $J$ = 14.9, 7.6 Hz, 2H, $CH_2$), 3.18 (dq, $J$ = 14.9, 7.6 Hz, 2H. $CH_2$); IR (KBr) 1118 cm$^{-1}$ (SO); MS *m/z* 402 (M$^+$); Anal. Found: C, 30.21; H, 2.60%. Calcd for $C_{10}H_{10}OS_8$: C, 29.82; H, 2.50%; **4**: mp 107.5–109.5 °C (decomp); $^1$H NMR (400 MHz) $\delta$ 1.34 (t, $J$ = 7.5 Hz, 3H, $CH_3$), 1.37 (t, $J$ = 7.5 Hz, 3H, $CH_3$), 3.18 (dq, $J$ = 14.7, 7.5 Hz, 1H, $CH_2$), 3.25 (dq, $J$ = 14.7, 7.5 Hz, 1H, $CH_2$), 3.44 (dq, $J$ = 9.6, 7.5 Hz, 1H, $CH_2$), 3.46 (dq, $J$ = 9.6, 7.5 Hz, 1H, $CH_2$); IR (KBr) 1098 cm$^{-1}$ (SO); MS *m/z* 402 (M$^+$); Anal. Found: C, 29.90; H, 2.15%. Calcd for $C_{10}H_{10}OS_8$: C, 29.82; H, 2.50%; **5**:mp 133.0–134.5 °C (decomp); $^1$H NMR (400 MHz) $\delta$ 1.32 (t, $J$ = 7.5 Hz, 3H, $CH_3$), 1.36 (t, $J$ = 7.5 Hz, 3H, $CH_3$), 3.19 (dq, $J$ = 13.9, 7.5 Hz, 1H, $CH_2$), 3.25 (dq, $J$ = 13.9, 7.5 Hz, 1H, $CH_2$), 3.36 (dq, $J$ = 9.6, 7.5 Hz, 1H, $CH_2$), 3.53 (dq, $J$ = 9.6, 7.5 Hz, 1H, $CH_2$); IR (KBr) 1088 cm$^{-1}$ (SO); MS *m/z* 402 (M$^+$); Anal. Found: C, 29.87; H, 2.45%. Calcd for $C_{10}H_{10}OS_8$: C, 29.82; H, 2.50%.

**Preparation of 6,9-Diethylbenzopentathiepin (6).** Compound **6** was prepared from 4,7-diethyl-2,2-dimethylbenzo[*d*]-[1,3,2]dithiastannole in 60% yield by the method previously reported;[3] **6**: mp 38.0–39.0 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.21 (t, $J$ = 7.5 Hz, 6H), 2.88 (dq, $J$ = 13.8, 7.5 Hz, 2H), 2.98 (dq, $J$ = 13.7, 7.5 Hz, 2H), 7.19 (s, 2H); MS *m/z* 292 (M$^+$); Anal. Found: C, 41.21; H, 4.47%. Calcd for $C_{10}H_{12}S_5$: C, 41.06; H, 4.13%.

**Oxidation of 6,9-Diethylbenzopentathiepin (6).** To a solution of **6** (138 mg, 0.47 mmol, in 80 mL of $CH_2Cl_2$) was added *m*CPBA (assay > 90%, 90.5 mg, 0.58 mmol, in 80 mL of $CH_2Cl_2$) and the mixture was stirred for 12 h. Then the solvent was evaporated off and the residue was purified by column chromatography (silica gel, hexane:$CHCl_3$ = 1:2), and **8** and **9** were obtained in 7 % and 8% yields, respectively; **8**: yellow oil; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.34 (t, $J$ = 7.5 Hz, 3H), 1.37 (t, $J$ = 7.5 Hz, 3H), 2.80 (dq, $J$ = 15.2, 7.6 Hz, 1H), 2.87 (dq, $J$ = 15.2, 7.6 Hz,.1H), 3.07 (dq, $J$ = 15.0, 7.5 Hz,.1H), 3.15 (dq, $J$ = 15.0, 7.5 Hz,.1H), 7.18 (ABq, $J$ = 7.6 Hz, 1H), 7.28 (ABq, $J$ = 7.6 Hz, 1H); MS *m/z* 244 (M$^+$); Anal. Found: C, 49.47; H, 5.22%. Calcd for $C_{10}H_{12}OS_3$: C,

49.15; H, 4.95%; **9**: mp 47.0–48.0 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.28 (t, $J$ = 7.5 Hz, 3H), 2.73 (dq, $J$ = 14.8, 7.5 Hz, 1H), 2.81 (dq, $J$ = 14.8, 7.5 Hz, 1H), 7.18 (S, 2H); MS $m/z$ 244 ($M^+$); Anal. Found: C, 48.93; H, 4.96%. Calcd for $C_{10}H_{12}OS_3$: C, 49.15; H, 4.95%.

**Preparation of 6,10-Diethyl[1,3]dithiolo[4,5-*h*]benzopentathiepin (10).** Compound **1** (386 mg, 1 mmol) was treated with $NaBH_4$ (46 mg, 1.2 mmol) in THF (60 mL) and ethanol (20 mL) for 30 min. To this solution, dibromomethane (1.04 mL, 12.5 mmol) was added slowly and the mixture was stirred for 16 h. After treatment with water, the solvent was evaporated and the aqueous solution was extracted with $CH_2Cl_2$ (3×30 mL). The extract was dried with $MgSO_4$ and the solvent was evaporated. Then the residue was treated with $NaBH_4$ (38 mg, 1 mmol) in THF (40 mL) and ethanol (15 mL) for 30 min. To this solution, elemental sulfur (320 mg, 10 mmol) was added and the mixture was stirred for 24 h. After treatment with water, the solvent was evaporated and the aqueous solution was extracted with $CH_2Cl_2$ (3×30 mL). The extract was dried with $MgSO_4$ and the solvent was evaporated. Then the product was purified by column chromatography (silica gel, hexane) to give **10** in 45% yield; mp 151.5–152.5 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.18 (t, $J$ = 7.5 Hz, 6H), 2.88 (dq, $J$ = 15.0, 7.5 Hz, 2H), 2.95 (dq, $J$ = 15.0, 7.5 Hz, 2H), 4.46 (ABq, $J$ = 9.5 Hz, 1H), 4.52 (ABq, $J$ = 9.5 Hz, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 13.9, 31.3, 34.4, 140.6, 141.8, 142.2; MS $m/z$ 368 ($M^+$); Anal. Found: C, 35.88; H, 3.38%. Calcd for $C_{11}H_{12}S_7$: C, 35.83; H, 3.28%.

**Oxidation of 6,10-Diethyl[1,3]dithiolo[4,5-*h*]benzopentathiepin (10).** Compound **10** (92 mg, 0.25 mmol, in 25 mL of $CH_2Cl_2$) was oxidized by *m*CPBA (assay > 95%, 46 mg, 0.25 mmol, in 25 mL of $CH_2Cl_2$) at room temperature for 13 h. Then the solvent was evaporated off and the residue was purified by column chromatography (silica gel, AcOEt:$CHCl_3$ = 1:10) to produce a mixture of **11** and **12** in 60% yield (**11**:**12** = 1:1) together with 4,8-diethyl[1,3]dithiolo[4,5-*f*]benzotrithiole 5-oxide (**13**) in 10% yield. The compounds **11** and **12** were purified by recrystallization, respectively (hexane:$CH_2Cl_2$ = 1:1); **11**: mp 147.0–148.0 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.26 (t, $J$ = 7.5 Hz, 3H), 1.35 (t, $J$ = 7.5 Hz, 3H), 2.98 (dq, $J$ = 15.0, 7.5 Hz,1H), 3.12 (dq, $J$ = 15.0, 7.5 Hz, 1H), 3.28 (dq, $J$ = 15.0, 7.5 Hz, 1H), 3.32 (dq, $J$ = 15.0, 7.5 Hz, 1H), 4.15 (ABq, $J$ = 13.7 Hz, 1H), 4.35 (ABq, $J$ = 13.7 Hz, 1H); IR (KBr) 1036 cm$^{-1}$ (SO); Anal. Found: C, 34.21; H, 3.11%. Calcd for $C_{11}H_{12}OS_7$: C, 34.34; H, 3.14%; **12**: mp 141.5–143.0 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.24 (t, $J$ = 7.5 Hz, 3H), 1.33 (t, $J$ = 7.5 Hz, 3H), 3.06 (q, $J$ = 7.5 Hz, 2H), 3.28 (dq, $J$ = 15.0, 7.5 Hz, 1H), 3.41 (dq, $J$ = 15.0, 7.5 Hz, 1H), 4.19 (ABq, $J$ = 13.6 Hz, 1H), 4.32 (ABq, $J$ = 13.6 Hz, 1H); IR (KBr) 1034 cm$^{-1}$ (SO); Anal. Found: C, 34.28; H, 3.20%. Calcd for $C_{11}H_{12}OS_7$: C, 34.34; H, 3.14%; **13**: mp 181.0–182.0 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.24 (t, $J$ = 7.5 Hz, 3H), 1.31 (t, $J$ = 7.5 Hz, 3H), 2.78 (q, $J$ = 7.5 Hz, 2H), 3.04 (dq, $J$ = 9.9, 7.5 Hz, 1H), 3.41 (dq, $J$ = 9.9, 7.5 Hz, 1H), 4.19 (ABq, $J$ = 13.3 Hz, 1H), 4.32 (ABq, $J$ = 13.3 Hz, 1H); IR (KBr) 1033 cm$^{-1}$ (SO); Anal. Found: C, 40.89; H, 3.53%. Calcd for $C_{11}H_{12}OS_5$: C, 41.21; H, 3.77%.

**Asymmetric Oxidation of 1.** Compound **1** (580 mg, 1.5 mmol) was oxidized by a reagent which consisted of Ti(O$^i$Pr)$_4$/*R*,*R*-DET/*t*-BuOOH in $CH_2Cl_2$ (120 mL) at −20 °C under Ar for 24 h (**1**/Ti(O$^i$Pr)$_4$/*R*,*R*-DET/*t*-BuOOH = 1:2:4:4). Then, sodium sulfite (1.26 g) and brine (50 mL) were added to the solution, and the solution was stirred vigorously for 1 h. After usual work-up and separation of the Ti complex and *R*,*R*-DET by filtration, the products were purified by column chromatography (Wako-gel C-400, hexane:$CHCl_3$ = 1:1). Compounds **4a** and **5a** could be separated easily by column chromatography in 18% (108 mg) and 23% (141 mg) yields, respectively; **4a**: mp 105–106 °C; **5a**: mp 128–129 °C.

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