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Preparation, Structure, and Optical Properties of Chiral Sulfoxides and Disulfoxide with a Trithiole Ring

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ABSTRACT: *Optically active 4,9-diethyl[1,4]-dithiino[5,6-f]benzo[1,2,3]trithiole 5-oxide (**3**) and 4,9-diethyl[1,4]dithiino[5,6-f]benzo[1,2,3]trithiole 5, 8-dioxide (**4**) were obtained by the asymmetric oxidation of 6,11-diethyl[1,4]dithiino[5,6-h]benzo-[1,2,3,4,5]pentathiepin (**1**). The reaction was accompanied by desulfurization and ring-contraction reactions of the pentathiepin ring. Similarly, optically active 4,8-diethyl[1,3]dithiolo[4,5-f]benzo-[1,2,3]trithiole 5-oxide (**7**) was produced by the analogous asymmetric oxidation of 6,10-diethyl-[1,3]dithiolo[4,5-h]benzo[1,2,3,4,5]pentathiepin (**2**). The specific rotations of **3**, **4**, and **7** were measured in chloroform, and their optical purity was verified by ^1H NMR with a shift reagent [Eu(hfc)$_3$]. The structures of **4** and **7** were determined by X-ray crystallography using Cu Kα radiation, and the absolute configuration of the sulfinyl group was examined based on the Flack parameter, which revealed that **4** has an RR configuration, while **7** has an S configuration. The circular dichroism spectra of **3**, **4**, and **7** were measured in chloroform.* © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:88–94, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10104

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INTRODUCTION

Varacin and *Lissoclinotoxin A*, the first benzo-[1,2,3,4,5]pentathiepins obtained from marine ascidian, are known for their antitumor and antifungal activities (Fig. 1) [1,2]. Since the conformational change of the 1,2,3,4,5-pentathiepin ring is relatively slow at room temperature [3–5], these asymmetrically substituted benzopentathiepins are chiral molecules that bear a plane of chirality that arises from the conformation of the pentathiepin ring. We recently reported the preparation, structure, conformational analysis, and optical properties of 6,10-diethyl[1,2,3]trithiolo[4,5-*h*]benzo[1,2,3,4,5]pentathiepin 7-oxides as asymmetrically substituted chiral benzopentathiepins (Fig. 1). It appeared that the specific rotation and the Cotton effect observed in circular dichroism spectroscopy of these molecules were strongly affected by the conformation

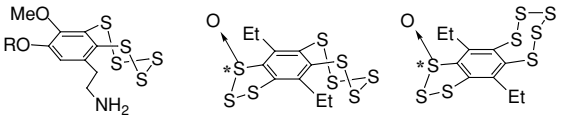


FIGURE 1 Chiral benzopentathiepins.

of the pentathiepin ring [5]. To prepare chiral cyclic oligosulfides by asymmetric oxidation, 6,11-diethyl[1,4]dithiino[5,6-*h*]benzopentathiepin (**1**) and 6,10-diethyl[1,3]dithiolo[4,5-*h*]benzopentathiepin (**2**) were oxidized by using a Sharpless reagent [6]. Unexpectedly, however, desulfurization and the ring-contraction reactions of the pentathiepin ring proceeded under these reaction conditions, with **1** giving 4,9-diethyl[1,4]dithiino[5,6-*f*]benzo[1,2,3]-trithiole 5-oxide (**3**) and 4,9-diethyl[1,4]dithiino[5,6-*f*]benzo[1,2,3]trithiole 5,8-dioxide (**4**), and **2** giving 4,8-diethyl[1,3]dithiolo[4,5-*f*]benzo[1,2,3]trithiole 5-oxide (**7**). This article reports the preparation, structural determination, and optical properties of chiral benzotrithioles **3**, **4**, and **7** obtained by the asymmetric oxidation of **1** and **2**.

RESULTS AND DISCUSSION

As a preliminary experiment, **1** was treated with an equivalent amount of *m*CPBA in dichloromethane at room temperature. Unexpectedly, a 91% yield of 4,9-diethyl[1,4]dithiino[5,6-*f*]benzotrithiole 5-oxide (**3**) was obtained (a 1:1 mixture of enantiomers), instead of 6,11-diethyl-[1,4]dithiino[5,6-*h*] benzopentathiepin 7-oxides (**5**) and (**6**) (Fig. 2). The formation of 4,9-diethyl[1,4]dithiino[5,6-*f*] benzotrithiole 1-oxide (**10**) and 2-oxide (**11**) was not observed in this oxidation reaction, although these compounds are produced as by-products of the oxidation of 4,9-diethyl [1,4]dithiino[5,6-*f*]benzotrithiole with *m*CPBA [7]. Thus, the oxidation reaction of **1** predominantly proceeded on the dithiin ring, not on the pentathiepin ring, which brought about the selective production of **3** after desulfurization and the ring-contraction reactions of the pentathiepin ring. We suppose that **5** and **6** were unstable because of the steric repulsion between the sulfinyl group and the ethyl group, and between the ethyl group and the pentathiepin ring, and that the compounds, therefore decomposed immediately to produce **3** while generating S_2O or S_2 [8].

Subsequently, **1** was oxidized by a Sharpless reagent [Ti(O-*i*-Pr)$_4$/*R,R*-DET/*t*-BuOOH] in dichloromethane at −10°C in an argon atmosphere for 24 h (Scheme 1) [5,6]. After the usual work up and separation of the Ti complex and *R,R*-DET (*R,R*-diethyl tartrate) by filtration, the products were purified by means of column chromatography. This reaction produced a 54% yield of desulfurized **3** and a 29% yield of ring-contracted **4**. Products **5**, **6**, **10**, and **11** were not produced by this oxidation reaction.

In the ^{1}H NMR spectrum of **3**, double quartet, quartet, and two triplet signals were observed for two ethyl groups, while four ddd signals were recorded for the methylene protons of the dithiin ring, suggesting that a steric repulsion between the sulfinyl group and the neighboring ethyl group restricts the free rotation of this ethyl group. In the IR spectrum, the sulfinyl group was determined to be 1020 cm^{-1}. The structure of **3** was further assigned by mass spectrometry and elemental analysis. On the other hand, triplet and double quartet signals for the ethyl group, and one pair of multiplet signals for the dithiin ring were found in the ^{1}H NMR spectrum of **4**, while six signals were observed in the ^{13}C NMR spectrum, implying that **4** has a symmetrical structure. The IR signal of the sulfinyl groups of **4** was observed at 1023 cm^{-1}. Based on these results, mass spectrometry, and elemental analysis, the structure of **4** was determined to be 4,9-diethyl[1,4]dithiino[5,6-*f*]benzotrithiole 5,8-dioxide, which was ultimately proven by X-ray crystallographic analysis (vide infra).

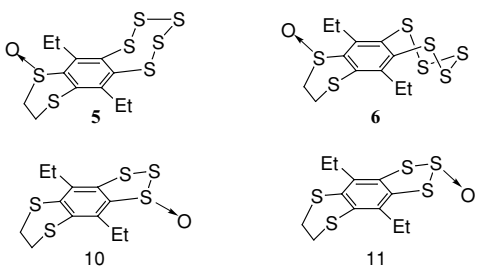
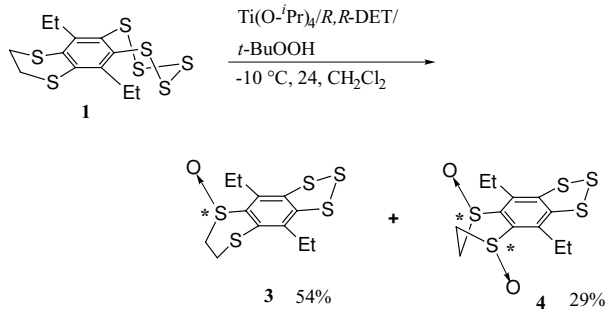


FIGURE 2

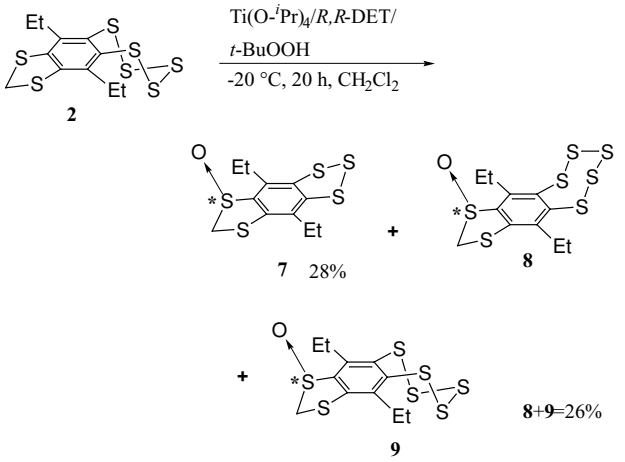


SCHEME 1

The specific rotation $[\alpha]_D$ was measured by irradiation with a sodium lamp in chloroform, after column chromatography of the products. Measurement of the spectra produced the following results: $[\alpha]^{20}{}_D = -80^\circ$ ($c = 0.21$) for **3**, and $[\alpha]^{20}{}_D = -522^\circ$ ($c = 0.48$) for **4**. Subsequently, ^{1}H NMR of **3** and **4** was measured using a shift reagent, Eu(hfc)$_3$, (Europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate]) to determine the optical purity; however, the spectra showed that **3** and **4** each contained their enantiomer with a reversed configuration of the sulfinyl group. The enantiomeric excess (ee) of **3** was determined to be 63%, while for **4** the value was determined to be 76%. Therefore, to purify **3** and **4**, they were recrystallized from hexane/dichloromethane (1:1) to produce compounds of optically pure yellow crystals. Then, by measuring $[\alpha]_D$ in chloroform it appeared that for **3** $[\alpha]^{20}{}_D = -126^\circ$ ($c = 0.085$), while for **4** $[\alpha]^{20}{}_D = -685^\circ$ ($c = 0.231$). The optical purity of these compounds was determined by measuring ^{1}H NMR with Eu(hfc)$_3$. No signal for the enantiomer of **3** was observed in the spectrum. So, the ee of **3** was determined to be >99%. Using a similar spectroscopic procedure, the ee of **4** was verified to be >99%.

Subsequently, compound **2** with a five-membered dithiole ring instead of a six-membered dithiin ring was oxidized using a procedure similar to that described above. In a previous paper, we reported that the *m*CPBA oxidation of **2** gave 4,8-diethyl[1,3]dithiolo[4,5-*f*]benzotrithiole 5-oxide (**7**) and 6,10-diethyl[1,3]dithiolo[4,5-*h*]benzopentathiepin 7-oxides **8** and **9** [5b]. Although the pentathiepin rings of **8** and **9** were expected to be stable relative to those of **5** and **6**, a steric repulsion similar to that described above may cause desulfurization and ring-contraction reactions to produce **7**. Compound **2** was then treated with Ti(O-*i*-Pr)$_4$/*R*,*R*-DET/*t*-BuOOH to produce a 28% yield of **7** together with a 26% yield of a mixture of **8** and **9**, after purification by column chromatography (Scheme 2). $[\alpha]^{21}{}_D$ of **7** was then determined to be -564° ($c = 0.161$, $CHCl_3$). Since **7** contains its enantiomer as a minor product (the ee of **7** is 90%), it was recrystallized from hexane/dichloromethane (1:1) to give optically pure yellow crystals. The specific rotation of **7** was then determined to be $[\alpha]^{21}{}_D = -627^\circ$ ($c = 0.223$), and the ee was verified by ^{1}H NMR to be >99%. On the other hand, the recrystallization failed to produce optically pure crystals of **8** and **9**.

The purified crystals of **4** and **7** were found to be suitable for X-ray crystallography. To determine the structure and the absolute configuration with respect to the sulfinyl group, an X-ray crystallographic analysis of **4** and **7** was carried out by using Cu Kα



SCHEME 2

radiation. The crystal data, bond lengths, and bond angles are shown in Tables 1–3 [9]. As shown in Fig. 3, the ORTEP drawings of **4** and **7** exhibit *RR* and *S* configurations on the sulfinyl groups, respectively. To determine the correct configuration of the sulfinyl groups, the *RR* configuration for **4** and the *S* configuration for **7** were examined by the Flack parameter *x* [10]. The process showed that **4** is $x = 0.054(5)$ for the *RR* configuration, while **7** is $x = 0.14(4)$ for the *S* configuration and $x = 0.99(5)$ for the *R* configuration. Furthermore, the structures of **4** and **7** were calculated using the anomalous dispersion factor. The results are summarized in Table 4 [11]. Thus, the *RR* configuration for **4**, and the *S* configuration for **7** are the correct structures.

Meanwhile, it was reported that ring inversion of the trithiolane ring of epitrithioacenaphtho

TABLE 1 Crystallographic Data of Compounds **4** and **7**

	4	**7**
Cryst syst	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	$P2_1$
Cryst color	Orange	Orange
a (Å)	8.936 (2)	4.811 (5)
b (Å)	32.872 (2)	8.521 (3)
c (Å)	5.076 (3)	16.490 (2)
β (deg)		90.37 (3)
V (Å^3)	1491.1 (9)	676.0 (5)
Z	4	2
D_{calc} (g cm^{-3})	1.561	1.575
μ (Cu $K\alpha$) (cm^{-1})	71.17	77.33
Total refl	3463	2557
Unique refl	3407	2555
$I > 1.50\sigma(I)$	2747	2037
Obs/param	15.97	12.57
R	0.078	0.069
R_w	0.115	0.105
GOF	1.03	1.23

TABLE 2 Bond Lengths (Å) of Compounds **4** and **7**

	4	**7**
C1—C2	1.40 (1)	1.42 (1)
C1—S1	1.782 (6)	1.784 (8)
C2—S3	1.795 (7)	1.772 (7)
S1—S2	2.050 (5)	–
S1—S2a	–	1.989 (4)
S1—S2b	–	2.118 (9)
S2—S3	2.008 (4)	–
S2a—S3	–	2.053 (5)
S2b—S3	–	1.82 (1)
C2—C3	1.383 (9)	1.39 (1)
C3—C4	1.412 (9)	1.415 (10)
C4—C5	1.371 (9)	1.41 (1)
C4—S4	1.824 (6)	1.742 (7)
C5—S5	1.809 (6)	1.776 (6)
C5—C6	1.412 (9)	1.41 (1)
C1—C6	1.40 (1)	1.36 (1)
S4—C7	1.777 (9)	1.797 (9)
S5—C8	1.779 (7)	–
C7—C8	1.53 (1)	–
S5—O1	–	1.488 (6)
S4—O1	1.499 (5)	–
S5—O2	1.505 (5)	–
S5—C7	–	1.804 (9)
S5—O1	–	1.488 (6)
C3—C11	1.509 (10)	1.49 (2)
C11—C12	1.50 (1)	1.46 (2)
C6—C13	1.51 (1)	1.53 (1)
C13—C14	1.52 (1)	1.52 (2)

TABLE 3 Bond Angles (deg) of Compounds **4** and **7**

	4	**7**
S1—C1—C2	116.3 (6)	116.3 (5)
S2—S1—C1	95.2 (3)	–
S1—S2—S3	96.2 (2)	–
S2—S3—C2	95.5 (3)	–
S2a—S1—C1	–	96.6 (3)
S2a—S3—C2	–	97.6 (2)
S2a—S3—C2	–	94.8 (3)
S2b—S1—C1	–	95.1 (4)
S2b—S3—C2	–	100.9 (3)
S2b—S3—C2	–	101.1 (4)
S1—C1—C6	122.1 (6)	120.5 (7)
S3—C2—C1	117.7 (5)	118.1 (6)
S3—C2—C3	120.0 (6)	120.1 (6)
S4—C4—C5	125.9 (5)	115.5 (5)
C4—S4—C7	99.6 (3)	94.1 (4)
S5—C5—C4	126.6 (4)	117.6 (5)
C4—S4—O1	105.6 (3)	–
C7—S4—O1	106.4 (4)	–
S4—C7—C8	110.5 (5)	–
C5—S5—O2	108.1 (3)	–
C8—S5—O2	106.1 (3)	–
S5—C8—C7	110.2 (4)	–
C5—S5—C8	101.9 (3)	–
C5—S5—O1	–	110.8 (4)
C7—S5—O1	–	110.5 (4)
C5—S5—C7	–	91.3 (4)
S4—C7—S5	–	112.1 (4)
S4—C4—C3	111.9 (5)	122.1 (6)
S5—C5—C6	111.7 (5)	121.9 (6)
C1—C6—C5	116.2 (6)	117.0 (7)
C2—C3—C4	116.3 (6)	115.5 (7)
C2—C3—C11	118.5 (6)	123.6 (7)
C4—C3—C11	125.0 (6)	120.6 (7)
C1—C6—C13	118.9 (6)	123.1 (7)
C5—C6—C13	124.8 (6)	119.8 (6)
C3—C11—C12	113.4 (7)	114.9 (8)
C6—C13—C14	110.8 (6)	112.8 (8)

[1,2-*a*]acenaphthylene proceeds readily in solution at room temperature, while the inversion can be frozen at low temperature and in the crystalline state [12]. As shown in Fig. 3, the central sulfur atom of the trithiole ring of **7** is distributed to two positions in the structure, namely S2a and S2b, and the occupancy ratio of the S2a and S2b atoms was determined to be 0.68:0.32. Thus, the conformational isomers with respect to the trithiole ring were observed by X-ray crystallography in the benzotrithiole derivatives, although the two isomers could not be distinguished by other spectroscopic procedures [13].

The circular dichroism spectra of chiral benzotrithioles **3**, **4**, and **7** were measured in chloroform. As shown in Fig. 4A , the UV spectra were measured in chloroform in the following concentrations, **3**: 5.4×10^{-5} mol l^{-1}, **4**: 4.3×10^{-5} mol l^{-1}, and **7**: 5.3×10^{-5} mol l^{-1}. In the spectra, the absorption of **3** and **4** was found in the region from 240 to about 510 nm, while the absorption region of **7** is elongated to about 550 nm, unlike that of **3** and **4**. On the other hand, the circular dichroism spectrum of **4** shows a positive first Cotton effect at 502 nm (4.31×10^{-5} mol l^{-1}), while that of **3** shows a positive first Cotton effect at 477 nm (5.38×10^{-5} mol l^{-1}), as shown in Fig. 4B. Furthermore, a positive first Cotton effect was observed at 504 nm for **7** (5.49×10^{-5} mol l^{-1}). Since the configuration of **4** was determined as the *RR* configuration of two sulfinyl groups, and the circular dichroism spectrum of **3** is correlated to that of **4**, the configuration of the sulfinyl group of **3** is expected to be the *R* configuration.

CONCLUSION

Compounds **1** and **2** were oxidized by a Sharpless reagent to produce **3**, **4**, and **7**, by way of desulfurization and ring-contraction reactions. The structures of **4** and **7** were determined by X-ray crystallographic analysis, with their absolute configurations being determined with respect to their sulfinyl groups. The specific rotation and the circular dichroism spectra of **3**, **4**, and **7** were measured in chloroform. The correlations between the absolute configurations of **3**, **4**, and **7** and their CD spectra were determined.

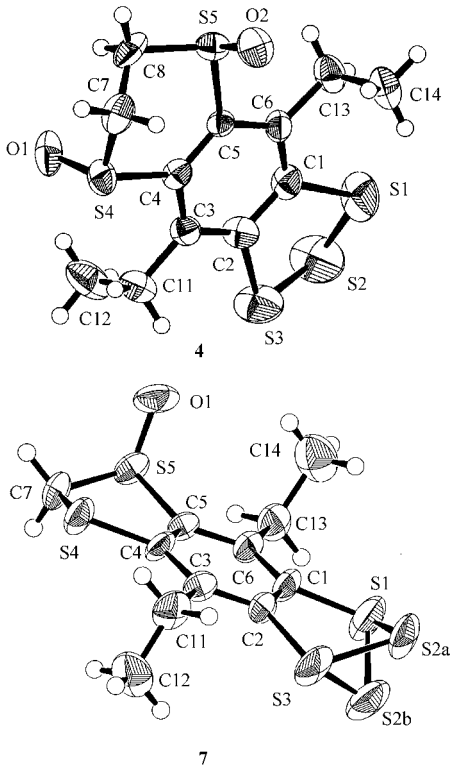


FIGURE 3 ORTEP drawings of **4** and **7**.

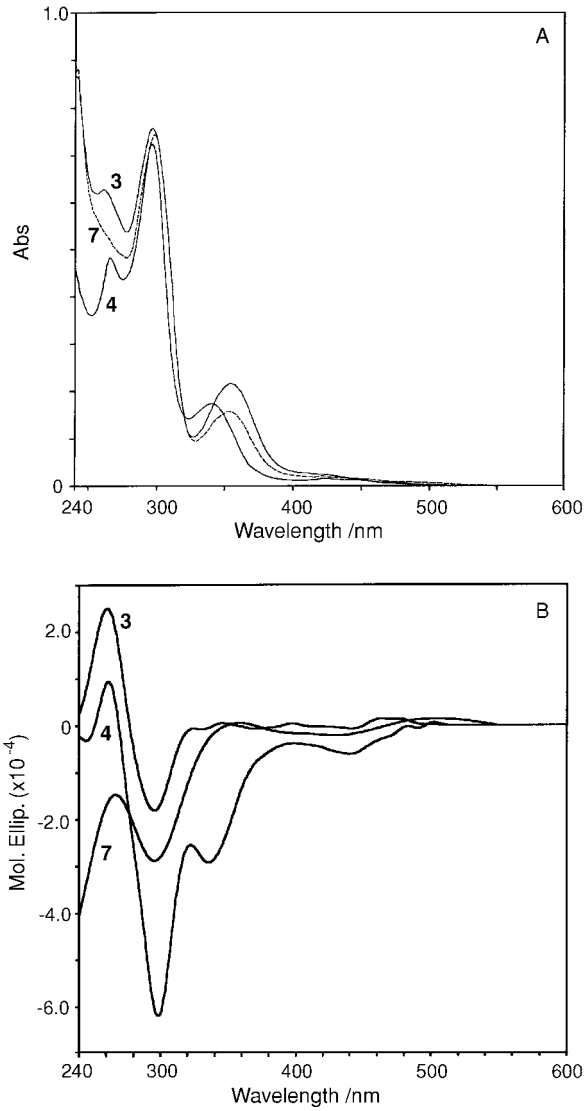


FIGURE 4 UV and CD spectra of **3, 4**, and **5** measured in $CHCl_3$. (A) UV: **3** (5.4×10^{-5} mol l^{-1}), **4** (4.3×10^{-5} mol l^{-1}), and **7** (5.3×10^{-5} mol l^{-1}); (B) CD: **3** (5.38×10^{-5} mol l^{-1}), **4** (4.31×10^{-5} mol l^{-1}), and **7** (5.49×10^{-5} mol l^{-1}).

EXPERIMENTAL

General

For the asymmetric oxidation, *t*-butyl hydroperoxide (a solution in di-*t*-butyl peroxide; assay $\cong$ 80%; Merck) was used. The IR spectra were recorded using a JASCO FT-7300 spectrometer, and the NMR spectra were measured with $CDCl_3$ on a Bruker AC-400 spectrometer. The mass spectra were obtained using a Hitachi M-2000 mass spectrometer, while the UV spectra were measured using a JASCO Ubest-30 spectrometer. The elemental analyses were performed using a Yanako MT5 analyzer. X-ray data collection was performed using a Rigaku AFC7R diffractometer, while all the structure solution calculations were performed using the teXsan crystallographic software package. The CD spectra were measured using a JASCO J-720 spectrometer equipped with a Xenon lamp.

TABLE 4 Anomalous Dispersion Factor

	4			**7**		
	No	*Yes (SS)*	*Yes (RR)*	*No*	*Yes (S)*	*Yes (R)*
R	0.0796	0.0829	0.0782	0.0708	0.0694	0.0736
R_w	0.1189	0.1219	0.1152	0.1072	0.1052	0.1120
GOF	1.066	1.093	1.032	1.248	1.226	1.305

*Preparation of 6,11-Diethyl[1,4]dithiino[5,6-h]-benzopentathiepin (**1**).* $NaBH_4$ (88 mg, 2.34 mmol) was gradually added to a solution of 6,10-diethyl-[1,2,3]trithiolo[4,5-*h*]benzopentathiepin (452 mg, 1.17 mmol) in THF (40 ml) and ethanol (15 ml), and the solution was stirred for 30 min. Dibromoethane (2.0 ml, 23.4 mmol) was added to this solution, after which the mixture was stirred for 17 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. The residue was then treated with $NaBH_4$ (57 mg, 1.5 mmol) in THF (40 ml) and ethanol (15 ml) for 30 min. Elemental sulfur (480 mg, 15 mmol) was added to this solution 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 a 70% yield of **1**; mp 162.5–164.0°C; ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 1.17$ (t, $J = 7.4$ Hz, 6H), 3.10–3.33 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) $\delta = 14.5$, 27.7, 30.1, 136.5, 140.8, 145.6; MS (*m/z*) 382 (M^+); Anal Found: C, 37.98; H, 3.57%. Calcd for $C_{12}H_{14}S_7$: C, 37.66; H, 3.69%.

*Preparation of 6,10-Diethyl[1,3]dithiolo[4,5-h]benzopentathiepin (**2**).* Compound **2** was prepared by using the method we reported in an earlier study [5].

Oxidation of **1** *with mCPBA.* First, *m*CPBA (68 mg, 0.37 mmol, assay ≥95%) in CH_2Cl_2 (50 ml) was added to a solution of **1** (143 mg, 0.37 mmol) in CH_2Cl_2 (50 ml), and the solution was stirred for 24 h. The solution was treated with a $NaHCO_3$ solution and then extracted with CH_2Cl_2. Then, the solution was dried with $MgSO_4$ and the solvent was evaporated. After purification by column chromatography (silica gel; CH_2Cl_2, followed by CH_2Cl_2/ethyl acetate (1:1)), a 91% yield of compound **3** was obtained (114 mg) together with a trace amount of **4**. **3**: mp 158.0–159.0°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (t, $J = 7.5$ Hz, 3H), 1.30 (t, $J = 7.5$ Hz, 3H), 2.65 (ddd, $J = 13.8$, 13.8, 2.7 Hz, 1H), 2.68 (q, $J = 7.5$ Hz, 2H), 3.05 (ddd, $J = 13.8$, 4.7, 2.7 Hz, 1H), 3.14 (dq, $J = 15.0$, 7.5 Hz, 1H), 3.21 (dq, $J = 15.0$, 7.5 Hz, 1H), 3.64 (ddd, $J = 13.8$, 4.7, 2.7 Hz, 1H), 3.89 (ddd, $J = 13.8$, 13.8, 2.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 11.9, 14.4, 15.1, 28.0, 28.7, 41.9, 131.3, 131.6, 135.5, 137.3, 140.6, 146.2; IR (KBr) 1020 cm^{-1} (SO); MS (*m/z*) 334 (M^+); Anal Found: C, 42.71; H, 4.44%. Calcd for $C_{12}H_{14}OS_5$: C, 43.08; H, 4.22%. **4**: mp 175.0–176.0°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, $J = 7.5$ Hz, 6H), 3.13 (dq, $J = 15.0$, 7.5 Hz, 2H), 3.31 (dq, $J = 15.0$, 7.5 Hz, 2H), 3.39–3.47 (m, 2H), 3.92–4.03 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.6, 27.9, 33.8, 131.9, 141.1, 148.3; IR (KBr) 1023 cm^{-1}(SO); MS (*m/z*) 350 (M^+); Anal Found: C, 41.03; H, 4.34%. Calcd for $C_{12}H_{14}O_2S_5$: C, 41.11; H, 4.02%.

Asymmetric Oxidation of **1**. First, *t*-BuOOH (0.07 ml, 0.56 mmol) at −10°C was added to a solution of Ti(O-*i*-Pr)$_4$ (0.15 ml, 0.5 mmol), then *R,R*-DET (0.34 ml, 2.0 mmol) in CH_2Cl_2 (50 ml) was added in an Ar atmosphere, and the solution was stirred for 30 min. Then, **1** (191 mg, 0.5 mmol) in CH_2Cl_2 (35 ml) was added slowly, and the solution was stirred for 12 h. The solution was poured into a $NaHCO_3$ solution, and then filtered under reduced pressure. The solution was extracted with CH_2Cl_2, and the extract dried with $MgSO_4$. The solvent was evaporated and the products were purified by column chromatography (silica gel; CH_2Cl_2 and then CH_2Cl_2/ethyl acetate (1:1)) to produce a 54% yield of **3** and a 29% yield of **4.** Compounds **3** and **4** were purified by recrystallization from hexane/$CHCl_3$ (1:1).

Asymmetric Oxidation of **2**. First, *t*-BuOOH (0.05 ml, 0.4 mmol) at −20°C was added to a solution of Ti(O-*i*-Pr)$_4$ (0.2 ml, 0.67 mmol) and *R, R*-DET (0.4 ml, 2.4 mmol) in CH_2Cl_2 (50 ml) in an Ar atmosphere, and the solution was stirred for 30 min. Then, **2** (184 mg, 0.5 mmol) in CH_2Cl_2 (40 ml) was slowly added to this solution, which was then stirred for 24 h. Then, sodium sulfite (1.26 g) and brine (50 ml) were added to the solution, after which the solution was stirred vigorously for 1 h. After the usual work up and separation of the Ti complex and *R,R*-DET by filtration, compound **7** and a mixture of a 28% yield of **8** and a 26% yield of **9** were obtained by column chromatography (silica gel, hexane/$CHCl_3$ (1:1)). Compounds **8** and **9** were further purified by column chromatography (silica gel, hexane/$CHCl_3$ (1:1)); **8**: $[\alpha]^{19}{}_D = -185°$ ($c = 0.080$, $CHCl_3$), ee = 53%; **9**: $[\alpha]^{21}{}_D = -654°$ ($c = 0.133$, $CHCl_3$), ee = 55%.

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