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Synthesis, Structure, and Oxidation of 3,4-Dihydro-1,2,5-benzotrithiepins

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ABSTRACT

*Stable benzene-fused polysulfide compounds, 3,4-dihydro-1,2,5-benzotrithiepins (**1a–c**), have been prepared, and the structure of **1a** has been determined by X-ray crystallographic analysis. While the electrophilic oxidation of compounds **1** with m-chloroperbenzoic acid gave the corresponding 3,4-dihydro-1,2,5-benzotrithiepin 5-oxides (**2**) in moderate yields, the oxidation of **1** with N-bromosuccinimide afforded a mixture of 5-oxides **2**, unexpected, inseparable 3,4-dihydro-1,2,5-benzotrithiepin 2,2-dioxides (**3**), and 3,4-dihydro-1,2,5-benzotrithiepin 1,1-dioxides (**4**). Semiempirical PM3 calculations were carried out, and the computed HOMO of **1a** suggested a significant favoring of electrophilic reactions at the sulfur atom at the 5-position. The treatment of 5-oxides **2** with acetyl bromide or oxalyl dibromide as halogenating reagents gave 2,2-dioxides **3** and 1,1-dioxides **4**, suggesting that an intramolecular halogen transfer from the 5-position (sulfide moiety) to the 1- and 2-positions (disulfide moiety) took place in the reactions.*

INTRODUCTION

Recently, organic polysulfides have attracted attention in organic chemistry for their biological activities [1] and unique chemical properties [2]. We have studied the chemistry of cyclic benzopolysulfides and developed some new routes for the synthesis of novel benzene-fused heterocycles containing multi-sulfur linkages [2b,3]. In the course of our investigation on structures, reactivities, and synthetic utility of cyclic benzopolysulfides, we have succeeded in the synthesis of new heterocyclic compounds, 3,4-dihydro-1,2,5-benzotrithiepins (**1a–c**), containing both sulfide and disulfide moieties in the ring. In spite of their characteristic structures, there have been only a few reports on the synthesis and reactions of 1,2,5-trithiepanes and 1,2,5-trithiepins [4]. We wish to report here the synthesis, structural characterization, and oxidation of 3,4-dihydro-1,2,5-benzotrithiepins (**1a–c**) with m-chloroperbenzoic acid (mCPBA) and N-bromosuccinimide (NBS), and to propose a mechanism of the halogen transfer reaction from the sulfide to the disulfide moiety via a bromosulfonium ion on the basis of the results of the halogenation of the corresponding 5-oxides (**2a–c**) and a related cross-over experiment.

RESULTS AND DISCUSSION

Preparation of 3,4-Dihydro-1,2,5-benzotrithiepins

3,4-Dihydro-1,2,5-benzotrithiepin (**1a**) was synthesized by the reaction of 1,2-benzenedithiol with ethylene sulfide in the presence of 0.3 equiv of triethylamine in *N,N*-dimethylformamide (DMF) at room temperature [3a]. 2,3,3a,10a-Tetrahydro-

Dedicated to Prof. Shigeru Oae on the occasion of his seventy-fifth birthday.

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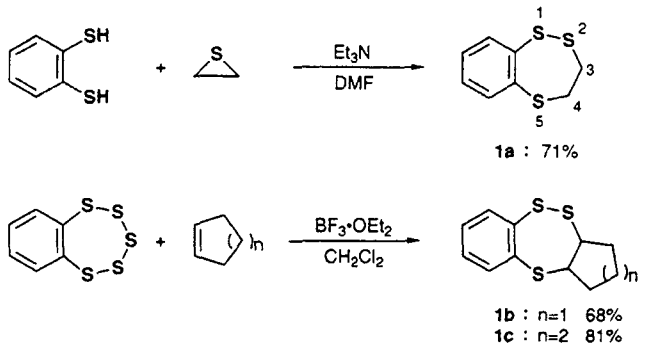


SCHEME 1

1*H*-cyclopenta[*c*][1,2,5]benzotrithiepin (**1b**) and 1,2,3,4,4a,11a-hexahydrodibenzo[*c,f*][1,2,5]trithiepin (**1c**) were prepared by the reactions of 1,2,3,4,5-benzopentathiepin with the corresponding cyclic olefins in the presence of boron trifluoride etherate in refluxing dichloromethane (CH_2Cl_2) (Scheme 1) [3e].

X-Ray Crystallographic Analysis of 3,4-Dihydro-1,2,5-benzotrithiepin (**1a**)

There are several problems inherent in the identification of the cyclic structure of polysulfides. These compounds are often formed as a mixture of oligomeric forms. Therefore, final proof of the structure of 3,4-dihydro-1,2,5-benzotrithiepin (**1a**) was obtained by an X-ray crystallographic analysis. The geometric parameters and ORTEP drawing of **1a** are depicted in Table 1 and Figure 1, respectively. The conformation of the seven-membered trithiepin ring, C_4S_3, is the chair form as well as those of the 1,2,3,4,5-benzopentathiepin ring, C_2S_5 [5], and the 3-hydro-1,2,4,5-benzotetrathiepin ring, C_3S_4 [6]. The sulfur–sulfur, sulfur–carbon (sp^3), and sulfur-carbon (sp^2) bond lengths and bond angles are similar to those in 1,2,3,4,5-benzopentathiepin and 3-hydro-1,2,4,5-benzotetrathiepin. The CSSC torsion angles are marginally smaller than that of 3-hydro-1,2,4,5-benzotetrathiepin.

Oxidation of 3,4-Dihydro-1,2,5-benzotrithiepins (**1a–c**)

Oxidation of compounds **1a–c** with 1.2 equiv of mCPBA in CH_2Cl_2 at 25°C gave the corresponding sulfoxides, 3,4-dihydro-1,2,5-benzotrithiepin 5-oxide (**2a**), 2,3,3a,10a-tetrahydro-1*H*-cyclopenta[*c*]-[1,2,5]benzotrithiepin 5-oxide (**2b**), and 1,2,3,4,4a,11a-hexahydrodibenzo[*c,f*][1,2,5]trithiepin 5-oxide (**2c**), in 71, 55, and 50% yields, respectively. The structures of compounds **2a–c** were determined by the spectral data and elemental analyses. These results indicate that the oxidation occurred only on the sulfur atom at the 5-position (sulfide moiety). However, oxidation of compounds **1a–c** with 1.2 equiv of NBS in aqueous 1,4-dioxane at room temperature gave a mixture of three oxidized products, 5-oxides **2a–c**, 2,2-dioxides **3a–c**, and 1,1-dioxides **4b, c** (Scheme 2, Table 2). Compounds **3a–c** and **4b, c** were not obtained in the oxidation using mCPBA. The structures of compounds **3a** and those of the inseparable mixtures of **3b**, **4b**, and **3c**, **4c** were determined by the spectral data and elemental analyses. The ratios of **3/4** were determined by 500 MHz ^{1}H NMR spec-

TABLE 1 Selected Bond Lengths, Bond Angles, and Torsion Angles for **1a**

Bond Lengths (Å)		Bond Angles (*deg*)		*Torsion Angles (deg)*	
S(1)–S(2)	2.036(1)	S(2)–S(1)–C(8)	103.1(1)	S(1)–S(2)–C(1)–C(2)	69.6(3)
S(2)–C(1)	1.804(4)	C(2)–S(3)–C(7)	104.1(2)	S(1)–C(8)–C(7)–S(3)	0.6(4)
S(3)–C(7)	1.775(4)	C(3)–C(4)–C(5)	120.2(4)	S(2)–S(1)–C(8)–C(6)	−109.7(3)
C(3)–C(4)	1.385(7)	C(5)–C(6)–C(8)	120.6(4)	S(2)–C(1)–C(2)–S(3)	−74.8(4)
S(1)–C(8)	1.770(4)	S(3)–C(7)–C(8)	122.4(3)	S(3)–C(7)–C(8)–C(6)	−176.9(3)
S(3)–C(2)	1.817(4)	S(1)–C(8)–C(6)	118.5(3)	C(1)–C(2)–S(3)–C(7)	87.4(3)
C(1)–C(2)	1.504(6)	C(6)–C(8)–C(7)	119.8(4)	C(2)–S(3)–C(7)–C(8)	−71.6(3)
C(3)–C(7)	1.384(5)	S(1)–S(2)–C(1)	130.7(1)	C(3)–C(7)–C(8)–C(6)	−1.3(5)
C(4)–C(5)	1.365(8)	S(2)–C(1)–C(2)	115.3(3)	C(4)–C(5)–C(6)–C(8)	0.2(6)
C(5)–C(6)	1.375(7)	S(3)–C(2)–C(1)	115.4(3)	C(5)–C(6)–C(8)–C(7)	1.1(6)
C(6)–C(8)	1.378(5)	C(4)–C(3)–C(7)	120.4(5)	S(1)–C(8)–C(6)–C(5)	−176.4(3)
C(7)–C(8)	1.399(5)	C(4)–C(5)–C(6)	120.1(4)	S(1)–C(8)–C(7)–C(3)	176.1(3)
		S(3)–C(7)–C(3)	118.6(3)	S(2)–S(1)–C(8)–C(7)	72.8(3)
		C(3)–C(7)–C(8)	118.9(4)	S(3)–C(7)–C(3)–C(4)	176.0(3)
		S(1)–C(8)–C(7)	121.6(3)	C(1)–S(2)–S(1)–C(8)	−83.6(2)
				C(2)–S(3)–C(7)–C(3)	112.9(3)
				C(3)–C(4)–C(5)–C(6)	−1.3(7)
				C(4)–C(3)–C(7)–C(8)	0.3(5)
				C(5)–C(4)–C(3)–C(7)	1.0(6)

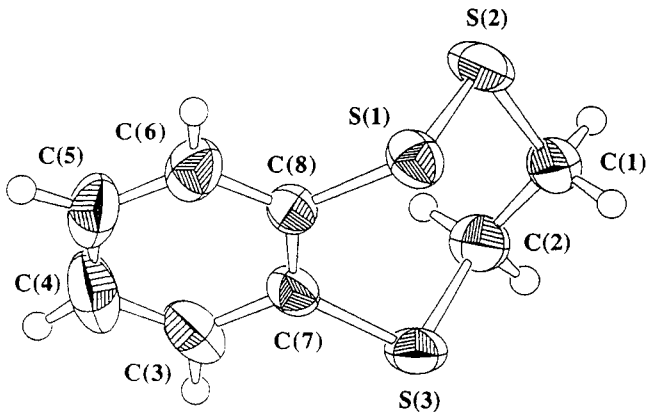
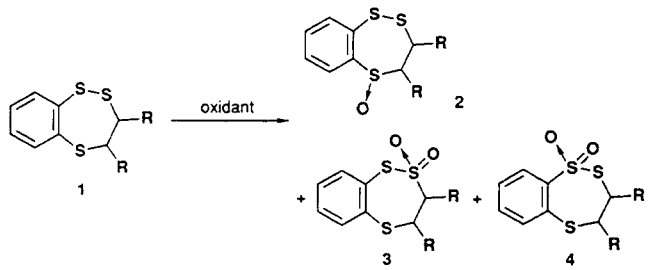


FIGURE 1 ORTEP drawing of **1a**.

troscopy. Interestingly, different regioselective reactions were observed in the oxidation of each with mCPBA and NBS, respectively. Furthermore, the product distribution of NBS oxidation was affected by the reaction temperature. Thus, the oxidation of **1c** at low temperature preferentially gave the 5-oxide **2c**, whereas at high temperature, it gave the 2,2-dioxide **3c** and the 1,1-dioxide **4c** preferentially.

It has been known that oxygen transfer reactions do not occur in these types of oxidation processes [7]. The present results suggest that an equilibrium which is controlled thermodynamically among 1-, 2-, and 5-bromosulfonium ions exists in the oxidation process, accompanying a halogen transfer from the sulfide to the disulfide moiety. To gain insight as to the initial site for electrophilic reactions, we have carried out semiempirical molecular orbital calculations on the compound **1a** using the recently developed PM3 parametrization [8]. The density gradient of the virtual HOMO of the polysulfide ring suggests a significant favoring of the electrophilic attack on the sulfur atom at the 5-position (Figure 2). Therefore, electrophilic oxidation will presumably proceed initially on the sulfur atom at the 5-position.



SCHEME 2

The Halogen Transfer Reaction

Intermolecular halogen transfer reactions from a halosulfonium ion to a sulfide have been reported [9,10], but there have been no reports that the halogen cation in a halosulfonium ion can be transferred from a sulfide to a disulfide moiety. To examine possible halogen transfer reactions from the 5-position to the 1- and 2-positions, 5-bromo-3,4-dihydro-1,2,5-trithiepinium ions were generated by the reactions of 3,4-dihydro-1,2,5-benzotrithiepin 5-oxides with halogenating reagents, such as acetyl bromide (AcBr) [11] or oxalyl dibromide ($(COBr)_2$) [12]. The treatment of 3,4-dihydro-1,2,5-benzotrithiepin 5-oxides **2a–c** with AcBr or $(COBr)_2$ in 1,4-dioxane at 20°C, followed by quenching of the reactions with saturated aqueous sodium hydrogencarbonate solution, afforded in each case a mixture of recovered **2a–c**, 3,4-dihydro-1,2,5-benzotrithiepins **1a–c** as reduced products, 3,4-dihydro-1,2,5-benzotrithiepin 2,2-dioxides **3a–c**, and 3,4-dihydro-1,2,5-benzotrithiepin 1,1-dioxides **4b, c** (Scheme 3, Table 3). 3,4-Dihydro-1,2,5-benzotri-

TABLE 2 Oxidation of **1a–c** with mCPBA and NBS

Substrate	*Oxidant*	*Solvent*	*Temperature (°C)*	*Yield (%)*			
				2	**3**	**4**	*Recov.* **1**
1a	mCPBA	CH_2Cl_2	25	71	0	0	trace
1b	mCPBA	CH_2Cl_2	25	55	0	0	15
1c	mCPBA	CH_2Cl_2	25	50	0	0	15
1a	NBS	aq 1,4-dioxane	25	trace	40	0	46
1b	NBS	aq 1,4-dioxane	25	trace	20[a]		62
1c	NBS	aq 1,4-dioxane	0	16	14		61
1c	NBS	aq 1,4-dioxane	25	12	20[b]		67
1c	NBS	aq 1,4-dioxane	50	11	22		54
1c	NBS	aq 1,4-dioxane	75	10	24		53

All reactions were carried out with 1.2 equiv of oxidant for 1 hours.
[a]**3b/4b** = 55/45 (by 500 MHz ^{1}H NMR).
[b]**3c/4c** = 64/36 (by 500 MHz ^{1}H NMR).

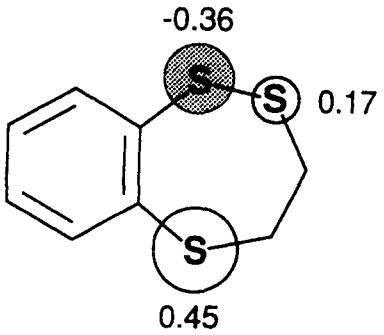


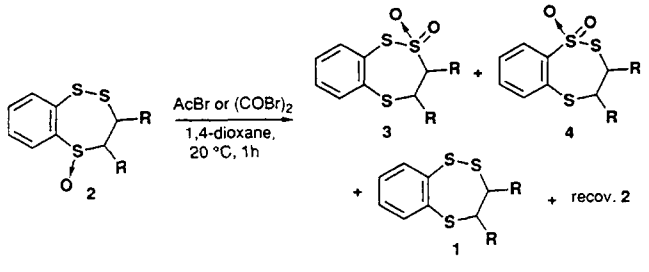
FIGURE 2 Computed HOMO of **1a**.

thiepins **1a–c** were not halogenated with AcBr or $(COBr)_2$ under the same conditions.

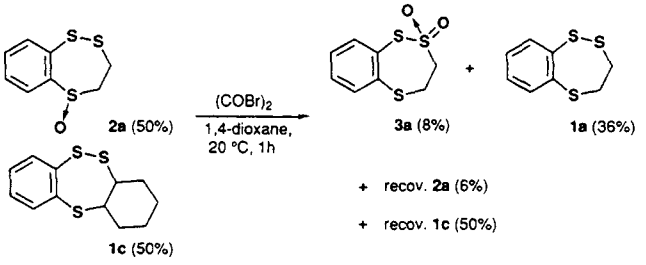
It is well known that an oxidation of a sulfide with a halogenating reagent in an aqueous medium gives the corresponding sulfoxide via rapidly hydrolysis of a halosulfonium ion [13]. Therefore, the formation of 2,2-dioxides **3** indicates that 1- and 2-bromosulfonium ions were generated in the present reactions. However, acetyl bromide or oxalyl dibromide reacted with 5-oxides **2** only at the sulfinyl moiety (5-position). These results suggest that the bromonium cation from 5-bromosulfonium ions, which were generated by the treatment of 5-oxides with halogenating agents in situ, were transferred to the 1- and 2-positions. In order to confirm whether the halogen transfer reactions take place intra- or intermolecularly, crossover experiments between **2a** and **1c** were carried out under the same conditions. When an equimolar mixture of 3,5-dihydro-1,2,5-benzotrithiepin 5-oxide (**2a**) and 1,2,3,4,4a,11a-hexahydrodibenzo-[*c,f*][1,2,5]trithiepin (**1c**) was treated with 0.5 equiv of $(COBr)_2$, 3,5-dihydro-1,2,5-benzotrithiepin 2,2-dioxide **3a** derived from **2a** was obtained solely, without 1,2,3,4,4a,11a-hexahydrodibenzo[*c,f*][1,2,5]trithiepin 1,1- and 1,2-dioxides (**3c**, **4c**) being formed (Scheme 4). These results suggest that the bromonium cation generated from the bromosulfonium salt transferred from the 5-position to the 1- and 2-positions intramolecularly.

Based on these results, the proposed mechanism of the halogen transfer reaction is illustrated in Scheme 5. A 3,4-dihydro-1,2,5-trithiepin **1** reacts with NBS to give the 5-bromosulfonium ion **5**. The 5-bromosulfonium ion **5** transfers a bromonium cation from the 5-position to the 1- and 2-positions intramolecularly. Then, the bromosulfonium ions **5**, **6**, and **7** are hydrolyzed with water to give the corresponding 5-oxide **2**, 2-oxide **8**, and 1-oxide **9**, which, except for **2**, were further oxidized in situ to give the 2,2-dioxides **3** and 1,1-dioxides **4**. Indeed, 2-oxide **8c** was readily oxidized under the same conditions to give **3c** in 71% yield without disproportionation [14].

In conclusion, the first structural characterization of 1,2,5-trithiepin **1a** was performed by X-ray crystallographic analysis and interesting regioselective reactions were observed in the oxidations of **1a–c** with electrophilic oxidants such as mCPBA and NBS, and unique intramolecular halogen transfer reactions from the sulfide to the disulfide moiety were found in the oxidation processes of **1a–c** with NBS.



SCHEME 3



SCHEME 4

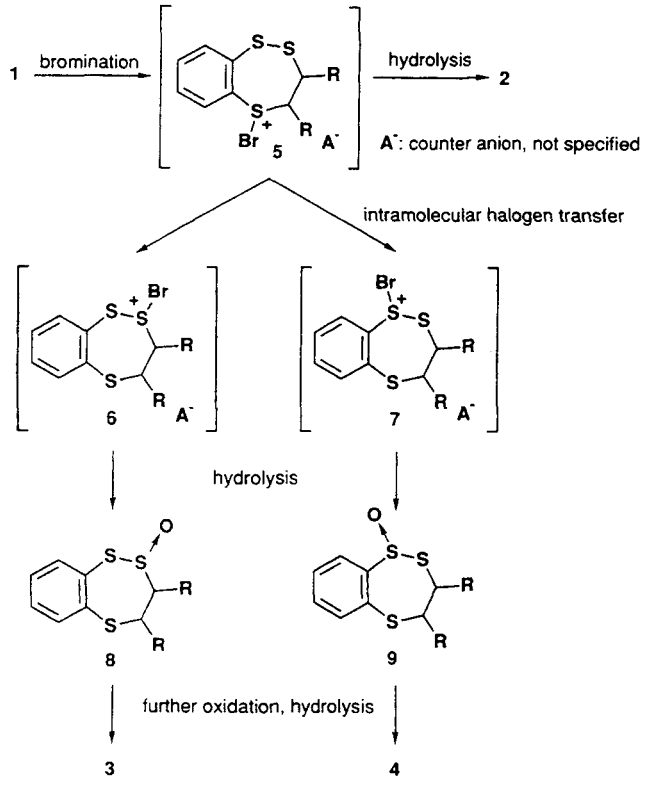
EXPERIMENTAL

Melting points are uncorrected. NMR spectra were recorded on a Hitachi R-22, a Varian XL-GEM 200, a Bruker AC-400, or a Bruker AM-500 spectrometer. IR spectra were recorded on a Hitachi 295 or a JASCO FT IR-7300 spectrometer. Mass spectra

TABLE 3 Reactions of **2a–c** with AcBr or $(COBr)_2$

		Yield (%)[a]			
Substrate	*Reagent*	**3**	**4**	**1**	*Recov.* **2**
2a	AcBr	28	0	70	0
2a	$(COBr)_2$	21	0	65	14
2b	AcBr	19		72	0
2b	$(COBr)_2$	20		66	14
2c	AcBr	4		70	10
2c	$(COBr)_2$	6		62	32

All reactions were carried out with 1.2 equiv of reagent at 20°C.
[a]Yields were determined by HPLC.



SCHEME 5

were taken with a Hitachi M-2000 mass spectrometer. Elemental analyses were performed on a Yanagimoto MT-3 analyzer. Analytical HPLC was performed on a JASCO 880-PU instrument with a YMC ODS-AM (4.6 mm, 15 cm) column using a UV detector (JASCO 875-UV). Acetyl bromide was used as 1.0 mol dm^{-3} in CH_2Cl_2 solution. Oxalyl dibromide was used as 2.0 mol dm^{-3} in CH_2Cl_2 solution. The reaction solvents were further purified by general methods.

Synthesis of 3,4-Dihydro-1,2,5-benzotrithiepin (**1a**)

To a stirred solution of 1,2-benzenedithiol (1.42 g, 10 mmol) in DMF (100 mL) containing triethylamine (0.42 mL, 3 mmol) was slowly added ethylene sulfide (0.60 mL, 10 mmol). The mixture was stirred for 6 hours at room temperature. After treatment with a saturated aqueous solution of ammonium chloride (100 mL), the mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was washed with water (3 × 200 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel; eluent, CCl_4) to give **1a** in 71% yield. Colorless crystals; mp (hexane) 48–49°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.22 (brs, 4H, CH_2), 7.19–7.30 (m, 2H, ArH), 7.69–7.81 (m, 2H, ArH); IR (KBr) 3046, 2962, 2909, 1636, 1441, 1395, 1285, and 1127 cm^{-1}; MS *m/z* 200 (M^+); Anal. found: C, 47.90, H, 4.04%. Calcd. for $C_8H_8S_3$: C, 48.00; H, 4.02%.

Synthesis of 3,5-Dihydro-1,2,5-benzotrithiepins (**1b,c**)

A typical procedure is as follows. To a stirred solution of benzopentathiepin (2.36 g, 10 mmol) in CH_2Cl_2 (100 mL) was added cyclopentene (1.9 mL, 22 mmol) and boron trifluoride etherate (1.5 mL, 12 mmol). The mixture was refluxed for 120 hours under an N_2 atmosphere and then treated with ice water (100 mL). The resulting organic layer was washed with brine (100 mL) and dried over anhydrous sodium sulfate. After the solvent had been removed, the residue was purified by column chromatography (silica gel; eluent, CCl_4) to give **1b** in 68% yield.

2,3,3a,10a-Tetrahydro-1H-cyclopenta[c][1,2,5]-benzotrithiepin (**1b**). Yield 68%; colorless crystals; mp (hexane) 59–60°C (Ref. [3e] 60°C); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.29–1.86 (4H, m, c-pentyl), 2.08–2.33 (2H, m, c-pentyl), 2.69–2.83 (1H, m, SS–CH–CH–S), 3.40 (1H, ddd, J = 11.8, 10.0, 7.8 Hz, SS–CH–CH–S), 7.21–7.34 (2H, m, ArH), 7.71–7.86 (2H, m, ArH).

1,2,3,4,4a,11a-hexahydrodibenzo[c,f][1,2,5]trithiepin (**1c**). Yield 81%; colorless crystals; mp (hexane) 59–60°C (Ref. [3e] 59°C); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.05–1.60 (4H, m, c-hexyl), 1.73–1.93 (2H, m, c-hexyl), 1.93–2.12 (1H, m, c-hexyl), 2.12–2.30 (1H, m, c-hexyl), 2.90–3.18 (2H, m, SS–CH–CH–S), 7.13–7.35 (2H, m, ArH), 7.56–7.85 (2H, m, ArH).

X-Ray Crystal and Experimental Data for **1a**

A colorless prismatic crystal of $C_8H_8S_3$, recrystallized from n-hexane, FW = 200.33, crystal size 0.22 × 0.18 × 0.35 mm, monoclinic space group $P2_1/c$, a = 9.446(2) Å, b = 8.633(1) Å, c = 11.1723(9) Å, β = 92.150(9)°, V = 910.5(2) Å^3, Z = 4, D_c = 1.461 g/cm^3, μ (Cu K_α = 68.64 cm^{-1} was used. The intensity data ($2\theta_{max}$ = 120.1°) were collected on a Rigaku AFC7R diffractometer at 20°C with ω-2θ scan technique, scan speed = 8.0°/min (in ω), scan width = (1.47 + 0.30 tanθ)°, and Cu K_α radiation (λ = 1.54178 Å). The structure was solved by heavy-atom Patterson methods (PATTY) and expanded using Fourier techniques (DIRDIF92). All calculations were performed using the TEXSAN crystallo-

TABLE 4 Atomic Coordinates of Nonhydrogen Atoms in **1a** and Equivalent Isotropic Temperature Factors, B_{eq}, with Estimated Standard Deviations in Parentheses

Atom	x	y	z	B_{eq} [a]
S(1)	0.34595(9)	0.3025(1)	0.50411(8)	4.16(2)
S(2)	0.1408(1)	0.3752(1)	0.49924(9)	4.91(3)
S(3)	0.2206(1)	0.0365(1)	0.31935(8)	4.42(2)
C(1)	0.0739(4)	0.3155(4)	0.3531(3)	4.15(8)
C(2)	0.0570(4)	0.1435(5)	0.3363(4)	4.28(9)
C(3)	0.2790(4)	−0.1603(5)	0.5052(4)	4.85(10)
C(4)	0.3316(5)	−0.2005(7)	0.6184(6)	6.3(1)
C(5)	0.3815(5)	−0.0888(7)	0.6955(5)	5.8(1)
C(6)	0.3824(4)	0.0638(6)	0.6603(3)	4.70(9)
C(7)	0.2786(4)	−0.0072(4)	0.4685(3)	3.51(7)
C(8)	0.3327(3)	0.1059(4)	0.5474(3)	3.31(7)

[a] $B_{eq} = (8/3)\pi^2(U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}aa^*bb^* \cos\gamma + 2U_{13}aa^*cc^* \cos\beta + 2U_{23}bb^*cc^* \cos\alpha)$.

graphic software package. The value of the goodness of fit indicator was 2.52. The final cycle of full-matrix least-squares refinement was based on 1177 observed reflections ($I > 4.00\sigma(I)$) and 133 variable parameters with R (R_w) = 0.043 (0.056).

Oxidation of **1a–c** *with mCPBA*

A typical run is as follows. To a stirred solution of **1a** (100 mg, 0.5 mmol) in CH_2Cl_2 (5.0 mL) at 0°C was slowly added mCPBA (assay 96%, 108 mg, 0.6 mmol) in CH_2Cl_2 (5.0 mL). The mixture was warmed to 25°C and stirred for 1 hour. The reaction mixture was poured into 10% aqueous sodium hydrogensulfite (10 mL), and the resulting organic layer was washed with saturated aqueous sodium hydrogencarbonate (20 mL) and brine (20 mL). After the organic layer had been dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel; eluent, CCl_4/AcOEt = 3/1) to give **2a** in 71% yield.

3,4-Dihydro-1,2,5-benzotrithiepin 5-Oxides (**2a**)

Yield 71%; colorless crystals; mp (hexane) 123–124°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.25 (1H, ddd, J = 15.2, 4.9, 2.4 Hz, SS–C<u>H</u>$_2$–CH$_2$–SO), 3.45 (1H, ddd, J = 12.9, 4.9, 2.4 Hz, SS–C<u>H</u>$_2$–CH$_2$–SO), 3.53 (1H, td, J = 12.9, 2.4 Hz, SS–CH$_2$–C<u>H</u>$_2$–SO), 4.04 (1H, ddd, J = 15.2, 12.9, 2.4 Hz, SS–CH$_2$–C<u>H</u>$_2$–SO), 7.42 (1H, td, J = 7.7, 1.4 Hz, ArH), 7.654 (1H, dd, J = 7.7, 1.4 Hz, ArH), 7.655 (1H, td, J = 7.7, 1.4 Hz, ArH), 7.96 (1H, dd, J = 7.7, 1.4 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.8, 57.3, 126.0, 130.5, 130.7, 133.7, 134.4, 151.4; IR (KBr) 2952, 2911, 1423, 1050 (SO), and 1020 cm^{-1}; MS m/z 216 (M^+). Anal. found: C, 44.25; H, 3.69%. Calcd. for $C_8H_8OS_3$: C, 44.41; H, 3.73%.

2,3,3a,10a-Tetrahydro-1H-cyclopenta[c][1,2,5]-trithiepin 5-Oxide (**2b**). Yield 55%; colorless crystals; mp (hexane) 90–91°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45–1.56 (1H, m, c-pentyl), 1.72–1.83 (1H, m, c-pentyl), 1.88–1.98 (1H, m, c-pentyl), 2.12–2.24 (1H, m, c-pentyl), 2.25–2.34 (1H, m, c-pentyl), 2.35–2.45 (1H, m, c-pentyl), 3.25 (1H, td, J = 11.1, 8.0 Hz, S–C<u>H</u>–CH–SO), 4.02 (1H, td, J = 11.1, 8.0 Hz, S–CH–C<u>H</u>–SO), 7.44 (1H, td, J = 7.6, 1.3 Hz, ArH), 7.66 (1H, td, J = 7.6, 1.3 Hz, ArH), 7.68 (1H, dd, J = 7.6, 1.3 Hz, ArH), 8.03 (1H, dd, J = 7.6, 1.3 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 28.0, 31.7, 55.9, 69.0, 125.8, 130.6, 130.8, 134.1, 135.2, 150.8; IR (KBr) 3074, 2979, 2970, 1442, 1050 (SO), and 1025 cm^{-1}; MS m/z 256 (M^+). Anal. found: C, 51.53; H, 4.70%. Calcd. for $C_{11}H_{12}OS_3$: C, 51.53; H, 4.72%.

1,2,3,4,4a,11a-Hexahydrodibenzo[c,f][1,2,5]trithiepin 5-Oxide (**2c**). Yield 50%; colorless crystals; mp (hexane) 114–115°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.08–2.06 (8H, m, c-hexyl), 3.07 (1H, td, J = 12.4, 4.0 Hz, S–C<u>H</u>–CH–SO), 3.76 (1H, td, J = 12.4, 4.0 Hz, S–CH–C<u>H</u>–SO), 7.39 (1H, t, J = 7.5 Hz, ArH), 7.62 (1H, d, J = 7.5 Hz, ArH), 7.63 (1H, t, J = 7.5 Hz, ArH), 7.99 (1H, d, J = 7.5 Hz, ArH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 25.4, 26.1, 27.1, 32.4, 53.0, 68.5, 126.6, 130.5, 130.7, 133.4, 136.6, 151.1; IR (KBr) 2923, 2852, 1443, 1056 (SO), and 1027 cm^{-1}; MS m/z 270 (M^+). Anal. found: C, 53.42; H, 5.13%. Calcd. for $C_{12}H_{14}OS_3$: C, 53.30; H, 5.22%.

Oxidation of **1a–c** *with NBS*

In a typical run, to a stirred solution of **1a** (100 mg, 0.5 mmol) in 70% aqueous 1,4-dioxane (5.0 mL) was added NBS (107 mg, 0.6 mmol) in 1,4-dioxane (3.5 mL). The mixture was stirred for 1 hour at 25°C. The reaction mixture was poured into water (10 mL) and extracted with $CHCl_3$ (3 × 10 mL). The combined organic layer was washed with brine (20 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel; eluent, CCl_4/AcOEt = 3/1) to give **2a**, **3a**, and recovered **1a** in trace amount, 40, and 46% yields, respectively.

3,4-Dihydro-1,2,5-benzotrithiepin 2,2-Dioxide (**3a**). Colorless crystals; mp (CCl_4) 154°C (decomp.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.40 (2H, brs, S–C<u>H</u>$_2$–CH$_2$–SO$_2$–S), 3.89 (2H, brs, S–CH$_2$–C<u>H</u>$_2$–SO$_2$–S), 7.42–7.46 (2H, m, ArH), 7.75–7.81 (2H, m, ArH); IR (KBr) 3000, 1440, 1330 (SO_2), and 1110 (SO_2) cm^{-1}; MS m/z 232 (M^+). Anal. found: C, 41.05; H, 3.44%. Calcd. for $C_8H_8O_2S_3$: C, 41.35; H, 3.47%.

A Mixture of 2,3,3a,10a-Tetrahydro-1H-cyclopenta [c][1,2,5]benzotrithiepin 2,2-Dioxide (**3b**) *and 1,1-Dioxide* (**4b**). Colorless crystals; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.57–2.41 (6H, m, c-pentyl), 3.01–

3.07 and 3.34–3.40 (1H, m, S–CH–CH–SO_2–S, isomer ratio = 45/55), 3.99–4.05 and 3.89–3.95 (1H, m, S–CH–CH–SO_2–S, isomer ratio = 45/55), 7.40–8.11 (m, 4H, ArH); IR (KBr) 2958, 1332 (SO_2), and 1146 (SO_2) cm^{-1}; MS *m/z* 272 (M^+).

A Mixture of 1,2,3,4,4a,11a-Hexahydrodibenzo[c,f][1,2,5]trithiepin 2,2-Dioxide (**3c**) *and 1,1-Dioxide* (**4c**). Colorless crystals; ^1H NMR (500 MHz, $CDCl_3$) δ 1.30–2.54 (8H, m, c-hexyl), 3.14–3.20 and 3.31–3.38 (1H, m, S–CH–CH–SO_2–S, isomer ratio = 36/64), 3.73–3.78 and 3.95–4.01 (1H, m, S–CH–CH–SO_2, isomer ratio = 36/64), 7.38–8.04 (4H, m, ArH); IR (KBr) 2920, 1440, 1310 (SO_2), and 1130 (SO_2) cm^{-1}; MS *m/z* 286 (M^+).

Reactions of **2a–c** *with AcBr or $(COBr)_2$*

A typical run is as follows. To a stirred solution of **2a** (22 mg, 0.1 mmol) in 1,4-dioxane (1.0 mL) was added 2.0 mol dm^{-3} $(COBr)_2$ (0.06 mL, 0.12 mmol) or 1.0 mol dm^{-3} AcBr (0.12 mL, 0.12 mmol). After having been stirred for 1 hour at 20°C under an N_2 atmosphere, the mixture was mixed with saturated aqueous sodium hydrogencarbonate (1.0 mL). The reaction mixture was extracted with $CHCl_3$ (2 mL). The organic layer was washed with brine and dried over anhydrous sodium sulfate. The resulting mixture was analyzed by HPLC.

Crossover Experiment

To a stirred solution of a mixture of **2a** (22 mg, 0.1 mmol) and **1c** (25 mg, 0.1 mmol) in 1,4-dioxane (1.0 mL) was added 2.0 mol dm^{-3} oxalyl dibromide (0.06 mL, 0.12 mmol). After having been stirred for 1 hour at 20°C under an N_2 atmosphere, the solution was treated with saturated aqueous sodium hydrogencarbonate (1.0 mL). The mixture was extracted with $CHCl_3$ (2 mL). The organic layer was washed with brine and dried over anhydrous sodium sulfate. The resulting mixture was analyzed by HPLC. Compounds **1a**, **2a**, and **3a** were obtained in 36, 6, and 8% yields, respectively, and **1c** was recovered quantitatively.

Further Oxidation of 1,2,3,4,4a,11a-Hexahydrodibenzo[c,f][1,2,5]trithiepin 2-Oxide (**3c**) *with NBS.* To a stirred solution of **8c** (12 mg, 0.044 mmol) in 70% aqueous 1,4-dioxane (0.5 mL) was added NBS (9.2 mg, 0.052 mmol) in 1,4-dioxane (0.35 mL). The mixture was stirred for 30 minutes at 25°C. The reaction mixture was poured into water (1 mL) and extracted with $CHCl_3$ (3 × 3 mL). The combined organic layer was washed with brine (10 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel; eluent, CCl_4/AcOEt = 3/1) to give **3c** in 71% yield.

1, 2, 3, 4, 4a,11a-Hexahydrodibenzo[c,f][1,2,5]trithiepin 2-Oxide (**8c**). Colorless crystals; mp ($CHCl_3$/hexane) 121–123°C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.34–1.41 (2H, m, c-hex), 1.47–1.58 (1H, m, c-hex), 1.65–1.75 (1H, m, c-hex), 1.78–1.83 (1H, m, c-hex), 1.85–1.90 (1H, m, c-hex), 2.10–2.15 (1H, m, c-hex), 2.32–2.36 (1H, m, c-hex), 2.98–3.03 (1H, m, SSO–CH–CH–S), 3.14 (1H, ddd, *J* = 12.7, 10.5, 4.4 Hz, SSO–CH–CH–S), 7.34–7.36 (2H, m, ArH), 7.62–7.64 (1H, m, ArH), 7.80–7.82 (1H, m, ArH); IR (KBr) 2932, 1443, 1081, 1071 (SO), and 765 cm^{-1}; MS *m/z* 270 (M^+). Anal. found: C, 52.90; H, 5.16%. Calcd. for $C_{12}H_{14}OS_3$: C, 53.30; H, 5.22%.

1, 2, 3, 4, 4a,11a-Hexahydrodibenzo[c,f][1,2,5]trithiepin 2,2-Dioxide (**3c**). Colorless crystals; mp (hexane) 165°C (decomp.); ^1H NMR (400 MHz, $CDCl_3$) δ 1.28–1.45 (2H, m, c-hex), 1.48–1.69 (2H, m, c-hex), 1.81–1.85 (1H, m, c-hex), 1.90–1.94 (1H, m, c-hex), 2.25–2.30 (1H, m, c-hex), 2.50–2.55 (1H, m, c-hex), 3.34 (1H, ddd, *J* = 12.7, 10.6, 4.3 Hz, SSO_2–CH–CH–S), 3.76 (1H, ddd, *J* = 12.7, 10.6, 3.7 Hz, SSO_2–CH–CH–S), 7.39–7.42 (2H, m, ArH), 7.74–7.79 (2H, m, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 25.5, 25.9, 33.9, 49.9, 80.4, 130.4, 131.6, 135.2, 136.4, 136.7, 141.1; IR (KBr) 2941, 1448, 1307 (SO_2), 1127 (SO_2), and 764 cm^{-1}; MS *m/z* 286 (M^+). Anal. found: C, 50.02; H, 4.97%. Calcd. for $C_{12}H_{14}O_2S_3$: C, 50.32; H, 4.93%.

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