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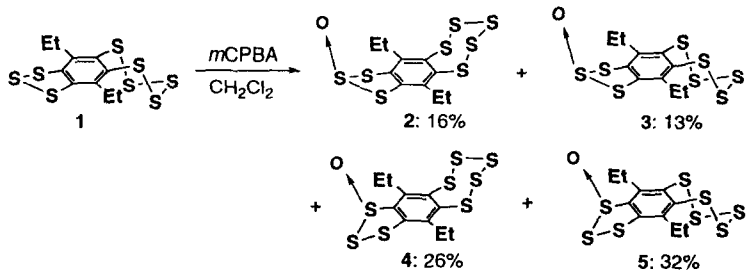
Preparation and Conformational Analysis of 6,10-Disubstituted [1,2,3]Trithiolo[*h*]benzopentathiepin Monooxides

Takeshi Kimura,[†] Masayuki Hanzawa,[†] Ernst Horn,[‡] Yasushi Kawai,[††] Satoshi Ogawa,[†] and Ryu Sato[†*]

[†]Department of Applied Chemistry and Molecular Science, Faculty of Engineering, Iwate University, Morioka, Iwate 020, Japan
[‡]Tsukuba Advanced Research Alliance Center, University of Tsukuba, Tsukuba, Ibaraki 305, Japan
[††]Institute for Chemical Research, Kyoto University, Uji, Kyoto 611, Japan

Abstract: 6,10-Diethyl[1,2,3]trithiolo[*h*]benzopentathiepin was oxidized with *m*CPBA (1 eq.) to produce four monooxides, 6,10-diethyl[1,2,3]trithiolo[*h*]benzopentathiepin 8-oxides and 6,10-diethyl[1,2,3]trithiolo[*h*]benzopentathiepin 7-oxides. The structure of the four monooxides obtained was determined by X-ray crystallography. The activation parameters, $\Delta G^{\neq}$, $\Delta H^{\neq}$, and $\Delta S^{\neq}$ of these compounds with respect to the inversion of their pentathiepin rings were determined by the results of ^{1}H-NMR spectroscopy.

The chemistry of the cyclic polysulfides (C_mS_n: m+n≥5, n≥3) has become of great interest to organosulfur chemists in view of their structure and biological activities. Therefore, there have been many reports with respect to the synthesis, structure, reactivities and electrochemical properties of the cyclic polysulfides.[1-3] Recently, we have reported that 6,10-diethyl[1,2,3]trithiolo[*h*]benzopentathiepin (**1**) and its analogs were first synthesized as a new type of compounds bearing two polysulfide rings.[4] In order to verify the reactivity of the cyclic polysulfides, the oxidation of **1** was performed by using *m*-chloroperbenzoic acid (*m*CPBA) to give the corresponding sulfoxides. This paper reports that 6,10-diethyl[1,2,3]trithiolo[*h*]-benzopentahiepin 8-oxides (**2**) and (**3**), and 6,10-diethyl[1,2,3]trithiolo[*h*]benzopentathiepin 7-oxides (**4**) and (**5**) were obtained by treatment of **1** with *m*CPBA, and the structure of **2**, **3**, **4**, and **5** was determined by X-ray crystallographic analysis. Furthermore, we also describe that the trithiole 2-oxides **2** and **3**, and the trithiole 1-oxides **4** and **5** were found to isomerize to each other in a $CHCl_3$ solution by inversion of their pentathiepin rings, respectively, and their activation parameters, $\Delta G^{\neq}$, $\Delta H^{\neq}$, and $\Delta S^{\neq}$ were calculated by the results of ^{1}H-NMR spectroscopy.



Scheme 1

The compound **1** (773 mg, 2.0 mmol) was oxidized by *m*CPBA (assay>95%, 363 mg, 2.0 mmol) in CH_2Cl_2 at room temperature for 6 h. Then the solvent was evaporated off and the residue was separated by column chromatography to produce one mixture of **2** and **3** (231 mg) and the other mixture of **4** and **5** (468 mg). The yields were calculated on the basis of the integral ratios determined by ^{1}H-NMR: **2**: 16%; **3**: 13%; **4**: 26%; **5**: 32% (Scheme 1). These four monooxides were isolated by recrystallization as yellow crystals, after separation by silica gel column chromatography.

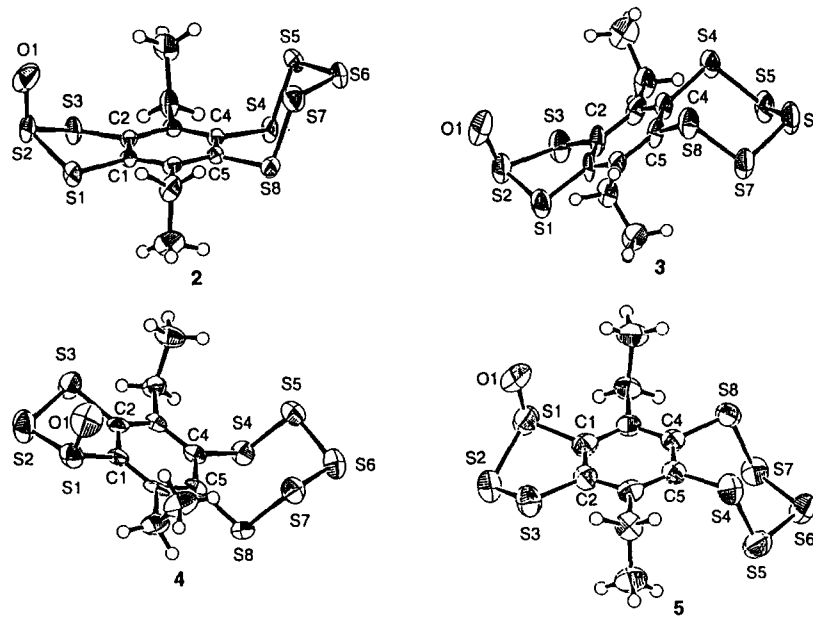


Figure 1. The ORTEP Drawings of Compounds **2**, **3**, **4**, and **5**.

Since the position of the oxidized sulfur atoms of **2**, **3**, **4**, and **5** could not be established exactly by the spectral data, the structure of the four monooxides was determined by X-ray crystallography.[5,6] The results of the crystallographic analysis of these monooxides reveal that these four monooxides have the oxygen atom on the trithiole ring, not on the pentathiepin ring; **2** and **3** are benzotrithiole 2-oxides, and **4** and **5** are benzotrithiole 1-oxides (Figure 1). In the structure, the oxygen atoms coordinated to the sulfur atom of **2**, **3**, **4** and **5** are located on the axial position of the trithiole ring. Furthermore, the oxygen atoms of **2** and **4** exist on the *syn* side to the pentathiepin ring, and those of **3** and **5** orient to the *anti* side to the pentathiepin ring.

As shown in Figure 1, while the trithiole 2-oxides **2** and **3** are the conformational isomers with respect to the pentathiepin ring, the trithiole 1-oxides **4** and **5** are the diastereomers with respect to the conformation of the pentathiepin ring and the configuration of the sulfinyl sulfur atom. Interestingly, though the trithiole 2-oxides **2** and **3** and the trithiole 1-oxides **4** and **5** were stable in the crystalline forms, they were found to isomerize to each other slowly in a $CHCl_3$ solution at room temperature. For example, each purified **2** and **3** isomerized to an about 1:1 mixture of **2** and **3**. Similar isomerization was observed in the case of **4** and **5**. When the equilibrium ratios of these compounds were determined by the homo-spin-decoupled ^{1}H-NMR spectroscopy in $CDCl_3$, the equilibrium ratio of **2** and **3** was 55:45, and that of **4** and **5** was 45:55. The pyramidal inversion of

the sulfinyl group has been known not to proceed at room temperature.[7] Therefore, these isomerization reactions of **2**, **3**, **4** and **5** should proceed via the inversion of their pentathiepin rings.

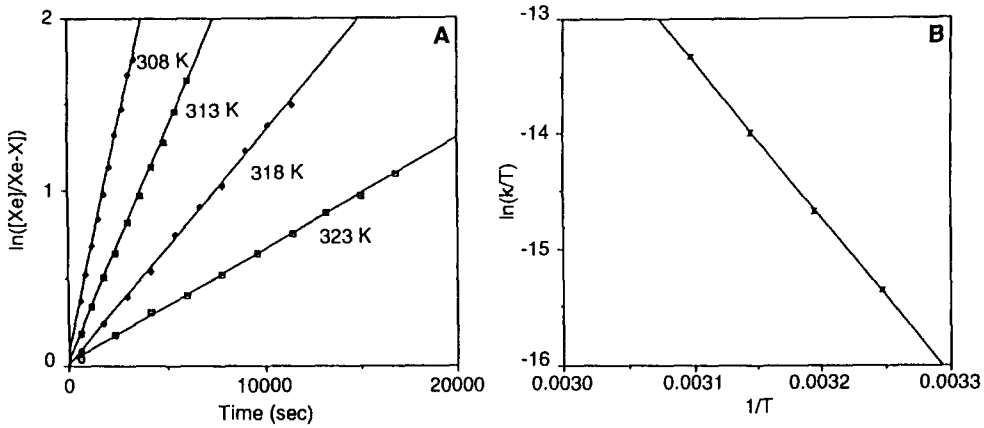


Figure 2. A: The Representative Kinetic Data for the Inversion of the Pentathiepin Ring of the Compound **5**; [Xe]: Equilibrium Concentration; [Xe-X]: Concentration as a Function of Time; B: Eyring Treatment with Standard Deviation for the Inversion of the Pentathiepin Ring of the Compound **5**.

Table 1 Kinetic and Thermodynamic Parameters.

	2	**3**	**4**	**5**
^{303}k (sec^{-1})	$(4.71\pm1.17)\times10^{-5}$	$(3.89\pm0.18)\times10^{-5}$	-	-
^{308}k (sec^{-1})	$(7.79\pm0.95)\times10^{-5}$	$(8.53\pm0.31)\times10^{-5}$	$(6.38\pm0.35)\times10^{-5}$	$(6.42\pm0.13)\times10^{-5}$
^{313}k (sec^{-1})	$(1.62\pm0.24)\times10^{-4}$	$(1.84\pm0.36)\times10^{-4}$	$(1.24\pm0.06)\times10^{-4}$	$(1.32\pm0.03)\times10^{-4}$
^{318}k (sec^{-1})	$(3.15\pm0.54)\times10^{-4}$	$(3.81\pm0.50)\times10^{-4}$	$(2.33\pm0.05)\times10^{-4}$	$(2.65\pm0.09)\times10^{-4}$
^{323}k (sec^{-1})	$(6.09\pm0.23)\times10^{-4}$	$(6.41\pm0.94)\times10^{-4}$	$(4.64\pm0.20)\times10^{-4}$	$(5.23\pm0.10)\times10^{-4}$
$^{298}\Delta G^{\neq}$ (kcal/mol)	23.8±0.1	23.9±0.1	24.0±0.1	24.1±0.0
$\Delta H^{\neq}$ (kcal/mol)	25.1±1.0	27.0±1.8	25.4±0.7	27.1±0.1
$\Delta S^{\neq}$ (eu)	4.4±3.1	10.3±5.9	4.7±2.2	9.9±0.3

On the other hand, it was reported that unsymmetrically substituted benzopentathiepin derivatives were isolated as asymmetric molecules because of their high energy barrier to the inversion of the pentathiepin ring.[2e,f] The inversion energy of pentathiepin rings has not been determined by the experimental procedure. Therefore, in order to verify the inversion energy of the pentathiepin ring of **2**, **3**, **4** and **5** experimentally and to accumulate data on the activation parameters, their isomerization was monitored by ^{1}H-NMR spectroscopy at 303 K, 308 K, 313 K, 318 K, and 323 K. The isomerization reactions of these compounds were 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 ^{1}H-NMR spectra. Calculated kinetic parameters of these compounds are shown in Figure 2-A and Table 1. Furthermore, as shown in Figure 2-B, the Eyring treatment of the rate constants obtained at those temperatures enabled us to calculate the activation parameters of the isomerization of these compounds. All the activation parameters, $\Delta G^{\neq}$, $\Delta H^{\neq}$, and $\Delta S^{\neq}$ of **2**, **3**, **4** and **5** are listed in Table 1. The values of $^{298}\Delta G^{\neq}$ are about 24.0 kcal/mol, suggesting that the inversion of the pentathiepin rings of these compounds proceeds very slowly at room temperature. Furthermore, the values of $\Delta S^{\neq}$ support the finding that the isomerization reaction of **2**, **3**, **4** and **5** is the conformation change of the pentathiepin rings.

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5. **2**: mp 125.0-127.5 °C (decomp); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 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. Calcd for $C_{10}H_{10}OS_8$: C, 29.82; H, 2.50. Found: C, 29.85; H, 2.48; the crystal data: monoclinic, $P2_1$, a=7.192(1) Å, b=6.119(1) Å, c=18.233(1) Å, β=99.89(1)°, V=790.5(2) Å^3, Z=2, ρ=1.692 g/cm^3, μ(CuKα)=103.59 cm^{-1}, R=0.037 (Rw=0.051); **3**: mp 134.0-135.5 °C (decomp); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 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. Calcd for $C_{10}H_{10}OS_8$: C, 29.82; H, 2.50. Found: C, 30.21; H, 2.60; the crystal data: monoclinic, $P2_1/n$, a=18.077(3) Å, b=36.560(5) Å, c=4.717(7) Å, β=91.17(4)°, V=3116(4) Å^3, Z=8, ρ=1.716 g/cm^3, μ(CuKα)=105.10 cm^{-1}, R=0.067 (Rw=0.075); **4**: mp 107.5-109.5 °C (decomp); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 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. Calcd for $C_{10}H_{10}OS_8$: C, 29.82; H, 2.50. Found: C, 29.90; H, 2.15; the crystal data: monoclinic, $P2_1/n$, a=11.260(5) Å, b=8.090(8) Å, c=17.241(5) Å, β=96.94(3)°, V=1559(1) Å^3, Z=4, ρ=1.715 g/cm^3, μ(CuKα)=105.05 cm^{-1}, R=0.046 (Rw=0.052); **5**: mp 133.0-134.5 °C (decomp); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 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. Calcd for $C_{10}H_{10}OS_8$: C, 29.82; H, 2.50. Found: C, 29.87; H, 2.45; the crystal data: orthorhombic, Pbca, a=18.827(4) Å, b=18.504(5) Å, c=8.984(4) Å, V=3129(1) Å^3, Z=8, ρ=1.709 g/cm^3, μ(MoKα)=11.27 cm^{-1}, R=0.032 (Rw=0.032).

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