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Formation, Structure, and Thionation of 1,2,4,5-Tetrathianes [*cis*- and *trans*-3,6-Bis(1,1,3,3-tetramethyl-4-oxo-4-phenylbutyl)-1,2,4,5-tetrathianes]

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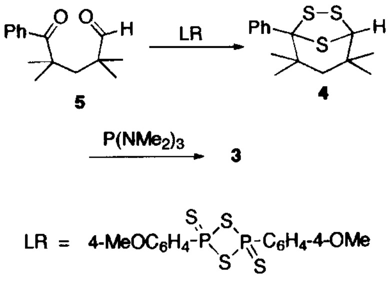
2,2,4,4-Tetramethyl-1-phenyl-6,7-dithiabicyclo[3.1.1]heptane was treated with $2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$ to yield *cis*- and *trans*-3,6-bis(1,1,3,3-tetramethyl-4-oxo-4-phenylbutyl)-1,2,4,5-tetrathianes. The formation mechanism of the tetrathianes is discussed. X-Ray crystallography disclosed that the *cis*- and *trans*-isomers take twist and chair conformations, respectively, in the solid state. Variable-temperature ^1H NMR spectroscopy in solution showed that the *cis*-isomer takes a twist conformation exclusively in the temperature range, whereas the *trans*-isomer exists as an equilibrium mixture of chair and twist conformers. The *cis*-tetrathiane reacted with Lawesson's reagent at 50 °C to give the corresponding di-2-thianyl disulfide.

The chemistry of 1, 2, 4, 5- tetrathianes has been drawing much attention from the viewpoints of their stereochemistry[1—5] and, more recently, their formation mechanism.[5—9] In the course of our study on the reactivities of bicyclic 1,3-dithietanes,[10] we observed the formation of *cis*- and *trans*-3,6-disubstituted 1,2,4,5-tetrathianes, **1** and **2**, by the reaction of the 6,7-dithiabicyclo[3.1.1]heptane **3** with $2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$ (OXONE®). Here, we report on the formation mechanism of **1** and **2**, their structures both in the solid state and in solution, and thionation of the side-chain carbonyl groups. An abbreviation R* for $CMe_2CH_2CMe_2COPh$ is used throughout this paper for convenience (Chart 1).

Results and Discussion

The 6,7-dithiabicyclo[3.1.1]heptane **3** was prepared by desulfurization of the 6,7,8-trithiabicyclo[3.2.1]octane **4** with $P(NMe_2)_3$. Compound **4** was obtained by a reaction of the keto aldehyde **5** with Lawesson's reagent (LR)[11] (Scheme 1).[12]



Scheme 1.

The 1,3-dithietane **3** was treated with $2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$ in dichloromethane–water with the expectation of the formation of the corresponding dithiirane **6** (Chart 2);[10a,10b,10f] the product was not **6**, but a 1 : 1 mixture of 1,2,4,5-tetrathianes **1** and **2** (at 0 °C for 4 d in 72% combined yield; at r.t. for 1 d in 69% combined yield) (Eq. 1). These stereoisomers were separable by HPLC. Tetrathianes **1** and **2** were thermally stable, and neither decomposed nor isomerized to each other upon heating in refluxing toluene.

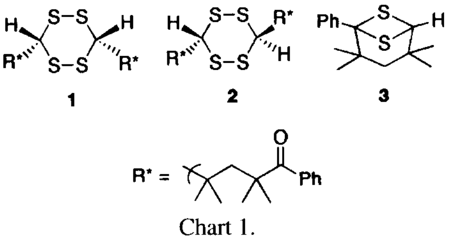


Chart 1.

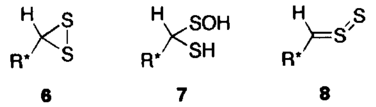
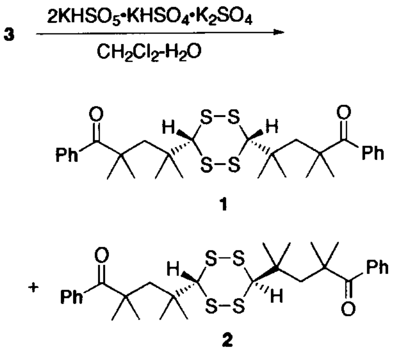


Chart 2.



(1)

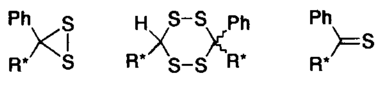
Formation Mechanism for 1,2,4,5-Tetrathianes 1 and 2. As for the formation of 1,2,4,5-tetrathianes, a mechanism involving the dimerization of thioketone *S*-sulfides (thiosulfines) or dithiiranes was previously proposed,[6—9] while Huisgen and Rapp claimed that such reactions might not be possible.[5] As working hypotheses concerning the mechanism of the formation of **1** and **2**, dimerizations of the α-mercapto sulfenic acid **7**, the dithiirane **6**, and an isomer of **6**, the thiosulfine **8**, were considered (Chart 2). Some attempts to trap these hypothetical intermediates were then carried out (Table 1).

First, PhC≡CH or $PhCH_2SH$ was added to a two-phase mixture of **3** and $2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$ in dichloromethane–water to trap the sulfenic acid **7**. Although no expected trapping products were obtained, these reagents led to a retardation (Run 3; 13% recovery of **3**) or interruption (Run 4) of the reaction. In the latter case, ca. 20% of the 1,3-dithietane **3** was lost without the formation of the tetrathianes **1** and **2** (Run 4).

Next, an isolable dithiirane **9**[10a,10f] was added to the reaction mixture with the expectation that it may react with the intermediate dithiirane **6** to yield the mixed 1,2,4,5-tetrathiane **10** (Chart 3). In this experiment, the combined yield of **1** and **2** was reduced to 5% with the recovery of **3** (67%) (Run 5); also, **9**, itself, decomposed to the thioketone **11**.[13] Because dithiirane **9** was stable under the reaction conditions, the presence of an intermediate that induces the decomposition of **9** to **11** and sulfur is implied. We have often observed the decomposition of **9** by nucleophiles;[10a,10f] also, the nucleophilicity of sulfenic acids toward some sulfenyl derivatives is well known.[14] Therefore, sulfenic acid **7** might be a possible intermediate. In addition, the recovery of a substantial amount of **3**, as well as in Run 4, indicates that the reaction proceeds through the reaction of **7** with the unchanged **3**, and not the dimerization of **7**.

Table 1. Reactions of **3** with $2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$ in the Absence or Presence of an Additive

Run	Additives	Temp	Equiv	Time/d	Results/%	
					1 and **2**	**3**
1	None	0 °C	—	4	72	0
2	None	r.t.	—	1	69	0
3	PhC≡CH	r.t.	3	1	69	13
4	$PhCH_2SH$	r.t.	3	1	0	81
5	Dithiirane **9**	0 °C	1.1	4	5	67
6	$MeO_2CC{\equiv}CCO_2Me$	r.t.	3	1	69	0



9 **10** **11**

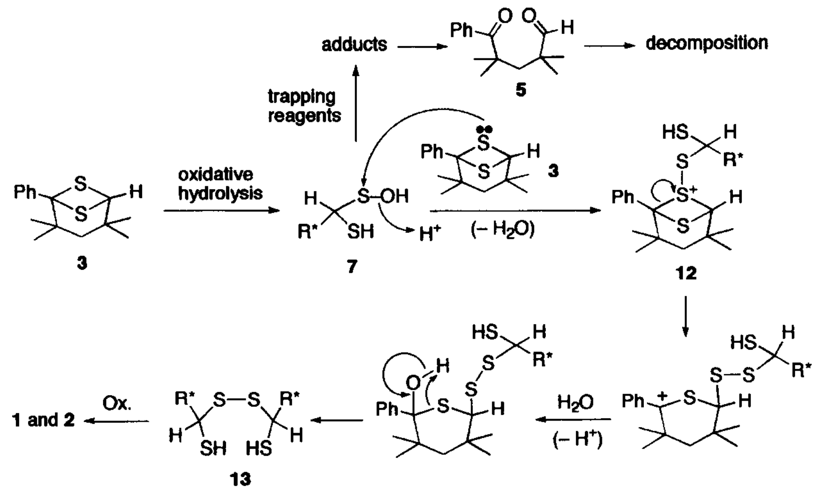
Chart 3.

The addition of DMAD as a trapping reagent of thiosulfine **8**[5,15] did not influence either the rate of the reaction or the combined yield of **1** and **2** (Table 1, Run 6). Therefore, the intervention of **8** is unlikely.

The results of the trapping experiments provide a plausible mechanism, shown in Scheme 2. Thus, the oxidative hydrolysis of the 1,3-dithietane **3** leads to sulfenic acid **7**, which reacts with **3** to give an intermediate **12**. The hydrolysis of **12** gives dithiol **13**, which would be oxidized to give **1** and **2**. The intermediate sulfenic acid **7** can be trapped by some reagents, but the trapping products seem to be hydrolyzed under the reaction conditions to give the keto aldehyde **5**. In fact, a small amount of **5** was isolated or detected by TLC in some cases, and a control experiment showed that **5** was unstable under the reaction conditions to decompose to unidentifiable products.

Structures of 1 and 2 in the Solid State and in Solution. The structures of **1** and **2** in the solid state were confirmed by X-ray crystallography to disclose that **1** and **2** take twist and chair conformations, respectively (Figs. 1 and 2). The S–S bonds in the chair-**2** [2.039(2) Å] are longer than those in the twist **1** [2.024(2) and 2.023(2) Å] by ca. 0.015 Å. A similar tendency was observed in 3,3,6,6-tetrasubstituted 1,2,4,5-tetrathianes **14**[4c,16] and **15**,[17] and was explained in terms of the larger deviation of the C–S–S–C dihedral angle from 90° in the chair form than that in the twist form (Chart 4).[17]

Extensive studies have been carried out so far on the conformation of the parent[2] and 3,3,6,6-tetrasubstituted[3,4b,4c,5] 1,



Scheme 2.

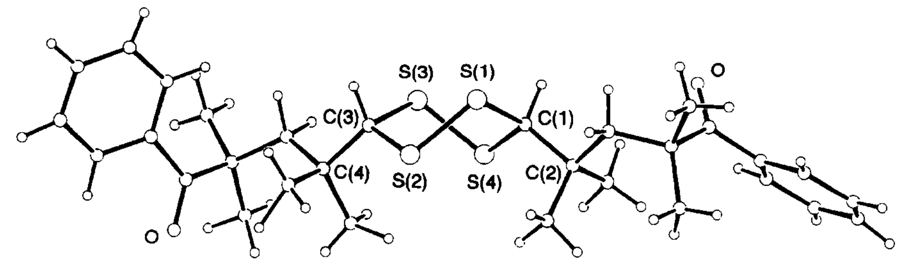


Fig. 1. Molecular structure of the *cis*-isomer **1**. Relevant bond lengths (Å), bond angles (deg), and torsion angles (deg): S(1)–S(2), 2.024(2); S(3)–S(4), 2.023(2); S(1)–C(1), 1.849(4); S(2)–C(3), 1.851(4); S(4)–C(1), 1.828(4); C(1)–C(2), 1.553(5); C(3)–C(4), 1.548(6); S(2)–S(1)–C(1), 104.2(2); S(1)–S(2)–C(3), 102.9(2); S(4)–S(3)–C(3), 104.4(2); S(3)–S(4)–C(1), 103.2(2); S(1)–C(1)–S(4), 110.2(2); S(1)–C(1)–C(2), 114.9(3); S(4)–C(1)–C(2), 111.7(3); S(2)–C(3)–S(3), 110.1(2); S(2)–C(3)–C(4), 110.0(3); S(3)–C(3)–C(4), 115.6(3); S(2)–S(1)–C(1)–S(4), 31.3(2); S(2)–S(1)–C(1)–C(2), 95.9(3); C(1)–S(1)–S(2)–C(3), 79.1(2); S(1)–S(2)–C(3)–S(3), 39.2(2); S(1)–S(2)–C(3)–C(4), 167.8(3); S(4)–S(3)–C(3)–S(2), 31.7(2); C(3)–S(3)–S(4)–C(1), 80.1(2); S(4)–S(3)–C(3)–C(4), 93.8(3); S(3)–S(4)–C(1)–S(1), 39.8(2); S(3)–S(4)–C(1)–C(2), 168.8(3).

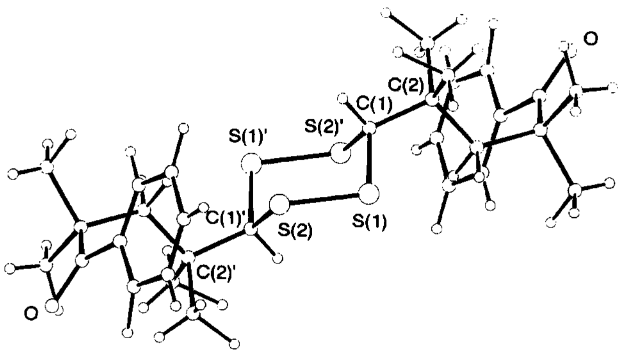
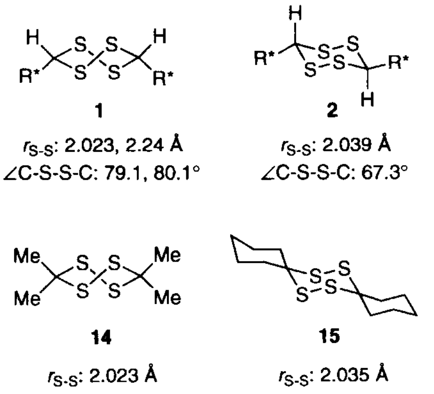


Fig. 2. Molecular structure of the *trans*-isomer **2**. Relevant bond lengths (Å), bond angles (deg), and torsion angles (deg): S(1)–S(2), 2.039(2); S(1)–C(1), 1.836(4); S(2)–C(1), 1.836(3); S(2)–S(1)–C(1), 102.2(2); S(1)–S(2)–C(1), 102.5(1); S(1)–C(1)–S(2), 108.8(2); S(1)–C(1)–C(2), 111.9(3); S(2)–C(1)–C(2), 112.4(2); C(1)–S(1)–S(2)–C(1)′, 67.3(2); S(1)–S(2)–C(1)–C(2), 163.2(3); S(1)–C(1)–S(2)–S(1)′, 72.3(2).



1
$r_{S\text{-}S}$: 2.023, 2.24 Å
∠C-S-S-C: 79.1, 80.1°

2
$r_{S\text{-}S}$: 2.039 Å
∠C-S-S-C: 67.3°

14
$r_{S\text{-}S}$: 2.023 Å
∠C-S-S-C: 81.1°

15
$r_{S\text{-}S}$: 2.035 Å
∠C-S-S-C: 66.5°

Chart 4.

2,4,5-tetrathianes in solution by a dynamic NMR technique. It was reported that the parent tetrathiane takes a chair form more preferentially than a twist form,[2] whereas the geminal methyl substituents in 3,3,6,6-tetramethyl-1,2,4,5-tetrathiane (**14**) reverses the preference.[3] On the other hand, 3,3 : 6,6-bis(pentamethylene)-1,2,4,5-tetrathiane (**15**) takes a chair form in the solid state, but prefers a twist form in solution.[4c] There appeared no report on a dynamic NMR study on 3,6-disubstituted 1,2,4,5-tetrathianes, like **1** and **2**, as far as we know.

In the present case, two forms of **1** and three forms of **2** are to be considered (Chart 5). It should be safe to place boat forms **16** and **17** (Chart 6) out of consideration because they correspond to an energy maximum or a point on the side of the potential well, respectively.[18] In the five forms of **1** and **2**, only the chair-**1** leads to nonequivalency of the methine (CH) protons in ^{1}H NMR spectroscopy. In twist-**1** and twist-**2** the geminal methyls nearer to the tetrathiane ring, Me_A [Chart 7(a)], are magnetically nonequivalent [Chart 7(b)], as are other tetrathianes,[4b,4c,5] thus making the methylene (CH_2) protons diastereotopic.

In case of the *trans*-isomer **2**, upon lowering the temperature (in $CDCl_3$), the singlet at $\delta = 4.34$ (CH) [Fig. 3(a)] gradually broadened and split into two singlets at $\delta = 4.36$ and 4.22 at 233 K with an integral ratio of 2.44 : 1 [Fig. 3(c)],

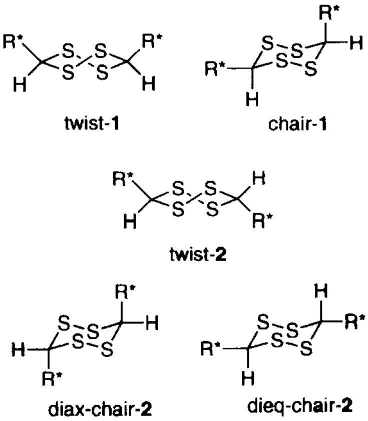


Chart 5.

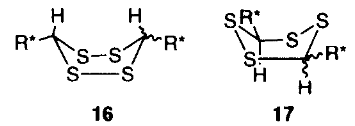


Chart 6.

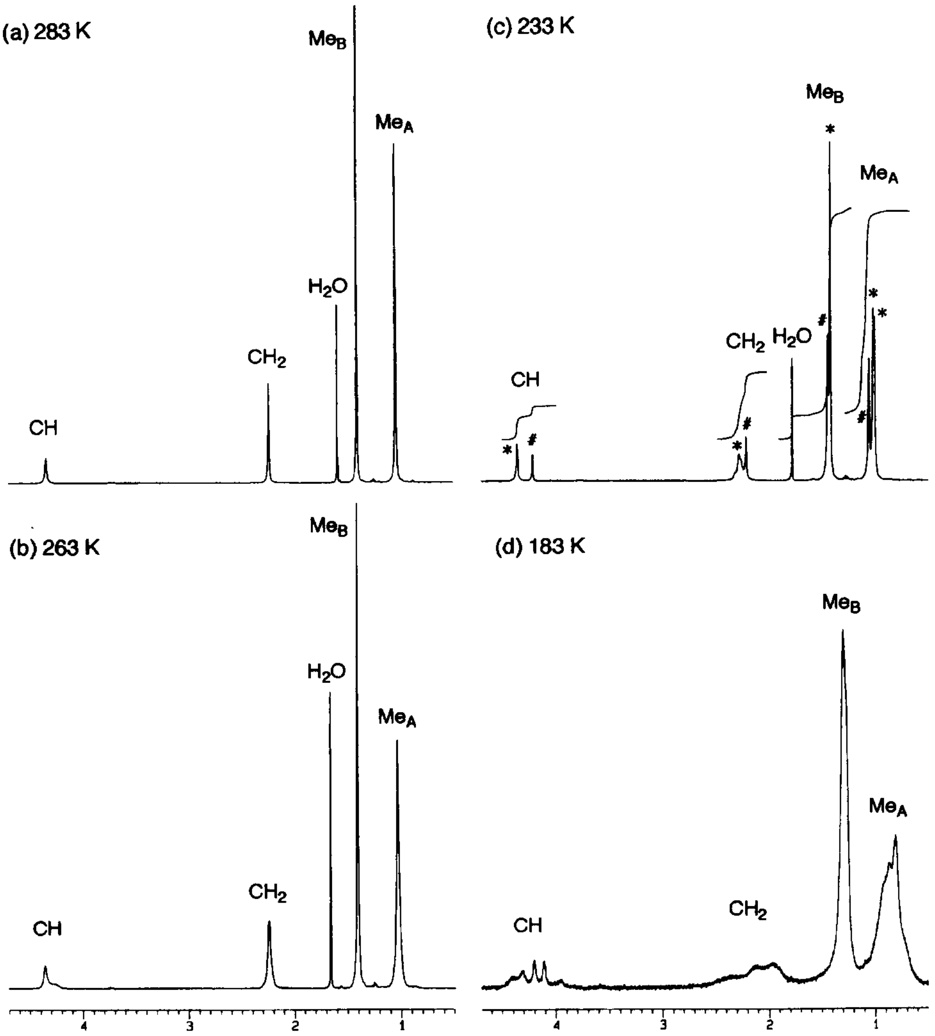


Fig. 3. ^{1}H NMR spectra of **2** at (a) 283 K (in $CDCl_3$), (b) 263 K (in $CDCl_3$), (c) 233 K (in $CDCl_3$), and (d) 183 K (in CD_2Cl_2).

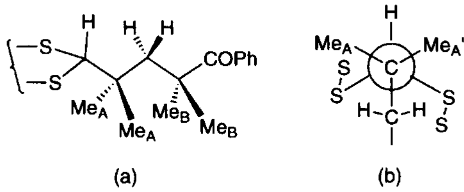


Chart 7.

indicating the existence of two conformers. During this course, the signal due to the CH_2 protons changed from a singlet to a collapsed AB quartet and another singlet, while the signals due to the *gem*-Me_A and the *gem*-Me_B split into three and two singlets, respectively [Fig. 3(c)]. Based on the integral ratio of the CH protons (2.44 : 1), signals due to the major conformer (checked by *) are picked up as $\delta = 1.00$ (s, 3H, Me_A), 1.01 (s, 3H, Me_A), 1.42 (s, 6H, $2Me_B$), 2.28 (ABq, 2H, CH_2), 4.36 (s, 1H, CH), and aromatic protons, while those due to the minor one (checked by #) as $\delta = 1.06$ (s, 6H, $2Me_A$), 1.44 (s, 6H, $2Me_B$), 2.21 (s, 2H, CH_2), 4.21 (s, 1H, CH), and aromatic protons [the aromatic region is omitted in Fig. 3].

The major conformer is assigned to the twist-**2** on the basis of the nonequivalency of the Me_A and the CH_2 protons, and the minor conformer to one of the chair forms, diax-chair-**2** or dieq-chair-**2**. To obtain information about the free-energy differences (ΔG°) among the three forms of **2**, PM3 calculations[19] were performed on a model compound, *trans*-3,6-di-*t*-butyl-1,2,4,5-tetrathiane (**18**) (Chart 8). The results show that the diax-chair-**18** is less stable than the other two forms over 1.5 kcal mol^{-1} (1 cal = 4.184 J), indicating the diax-chair-**18** is unimportant in the equilibrium. Thus, the

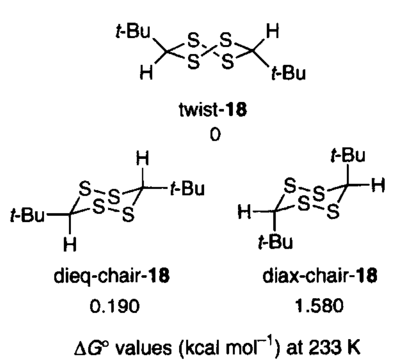


Chart 8.

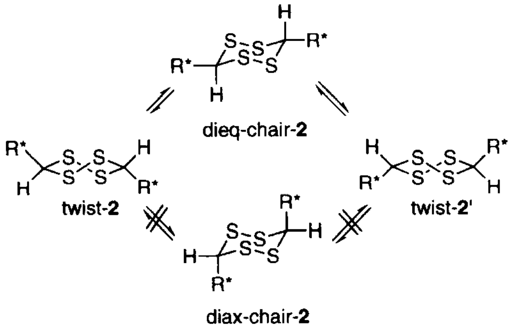
minor conformer of **2** at 233 K should be assigned to the dieq-chair-**2**. The interconversion between the twist-**2** and the chair-**2** is therefore depicted as shown in Scheme 3.[3a,3b,3d,4c,18]

The free energy of activation ($\Delta G^{\ddagger}$) was estimated from the coalescence temperature (T_c) (263 K), the relative ratio (2.44 : 1), and the peak separation (57.88 Hz) of the CH protons by using an approximate equation.[20,21] Thus, the estimated $\Delta G^{\ddagger}$ values are 13.3 kcal mol^{-1} for conversion of the twist-**2** to the chair-**2** and 12.8 kcal mol^{-1} for the reverse process.

The $\Delta G^{\ddagger}$ value for the twist-chair interconversion in **2** was substantially small, compared with those in the parent (14.5 kcal mol^{-1})[2] and 3,3,6,6-tetrasubstituted 1,2,4,5-tetrathianes (around 16 kcal mol^{-1}).[3—5] Because of the relatively small $\Delta G^{\ddagger}$ value for **2**, when its crystals, in which **2** takes a twist conformation, were dissolved, even at −78 °C, only a twist-chair equilibrium mixture was observed in the ^{1}H NMR spectrum, unlike the case of the tetramethyltetrathiane **14**, where the conformation in the crystalline state was maintained in a solution for a long time at appropriate low temperatures when the crystals were dissolved in a solvent at low temperatures.[3b,3d,22]

Upon further lowering the temperature (in CD_2Cl_2), the CH protons in **2** broadened further, and at 183 K they consisted of at least five broad peaks [Fig. 3(d)]. This behavior can not be explained by a simple twist-chair equilibration, and seems to be due to a slow down of C–C bond rotation in the side chains. Meanwhile, the first decoalescence below 263 K in **2** is not due to the slow C–C bond rotation because the dithiirane **9** (Chart 9), which has the same side chain as **2**, exhibited no substantial change in the ^{1}H NMR spectra at temperatures down to 233 K.

In the case of the *cis*-isomer **1**, the CH and the Me_A protons appeared as the sole singlet (δ = 4.22 and 1.04, respectively) at 282 K in $CDCl_3$ along with the CH_2 protons as an AB quartet (δ = 2.24) and the *gem*-Me_B protons as two close singlets (δ = 1.406 and 1.416) [Fig. 4(a)]. Upon further lowering the temperature (in CD_2Cl_2), the singlet at δ = 4.22 broadened [Fig. 4(b)] and split into two peaks at δ = 4.20 and 3.93 at 193 K (T_c = 217 K) [Fig. 4(c)]. At this temperature, the signals due to the CH_2 and the geminal methyls comprised several overlapping broad peaks.



Scheme 3.

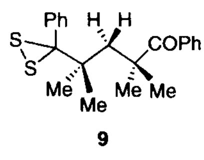


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Chart 9.

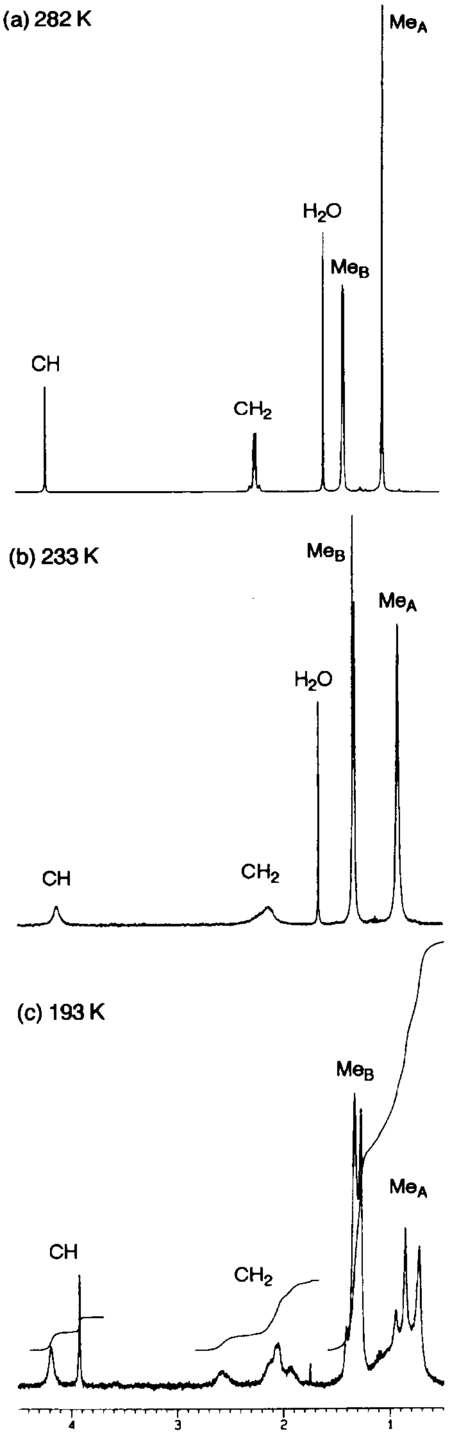


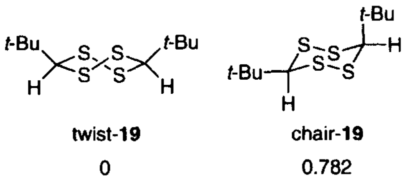
Fig. 4. ^{1}H NMR spectra of **1** at (a) 282 K (in $CDCl_3$), (b) 233 K (in CD_2Cl_2), and (c) 193 K (in CD_2Cl_2).

The integral ratio of two peaks at δ = 4.20 and 3.93 at 193 K was 1.18 : 1 (downfield vs. upfield), indicating that they can not be assigned to the CH protons of the chair-**1**, which requires the appearance of two singlets of equal intensity.

The assumption that the downfield singlet is made up of two overlapping peaks of the one CH proton in the chair-**1** and the two equivalent CH protons in the twist-**1** leads to a twist-**1**/chair-**1** ratio of $(1.18-1.00)/(1.00\times2) = 1/11.1$, meaning that the chair form is more stable than the twist form in **1**. However, this is not in harmony with the results of PM3 calculations on a model compound, *cis*-3,6-di-*t*-butyl-1,2,4,5-tetrathiane (**19**) (Chart 10). The calculations showed that the chair-**19** is less stable than the twist-**19** by a ΔG° value of 0.782 kcal mol^{-1} at 193 K, which corresponds to 7.7/1 of the twist/chair ratio. We therefore conclude that twist-**1** exists exclusively in solution, and that interconversion between twist-**1** and chair-**1** does not take place.

Because the signals due to the CH_2 protons and the geminal methyls in **1** [Fig. 4(c)] are similarly complex in the ^{1}H NMR spectrum of **2** at 183 K [Fig. 3(d)], the decoalescence observed in **1** would also be ascribed to slow C–C bond rotation in the side chains. Since, reportedly, no peak separation has been observed in the *t*-butyl group of 2-*t*-butyl-1,3-dithiane at low temperatures,[23] the CMe_{A2}–CH_2 and/or CH_2–CMe_{B2}, not the CH–CMe_{A2}, seem to cause the slow C–C bond rotation. The $\Delta G^\ddagger$ was estimated to be 10.2 kcal mol^{-1} from the coalescence temperature (217 K), the relative ratio (1.18 : 1.00), and the peak separation (106.5 Hz at 203 K) of the CH protons.[20,21]

Reaction of 1 and 2 with Lawesson's Reagent. The thionation of side-chain carbonyl groups in the *cis*-isomer **1** was examined with the expectation of the formation of the bis(thiocarbonyl) compound **20** followed by the intramolecular cyclization to give a cyclophane-type compound **21** (Chart 11). The *cis*-isomer **1** reacted with LR at 50 °C in benzene for 72 h to give the disulfide **22** (57%) and **4** (26%) (Eq. 2) without the expected **20** and **21**. Compound **4** is a secondary product derived from **22**: The treatment of isolated **22** with LR in benzene at 50 °C gave **4**. The structure of **22** was determined by X-ray crystallography (Fig. 5). In the thiane rings, the sulfur substituents on the 2 and 6 positions are *trans* to each other.

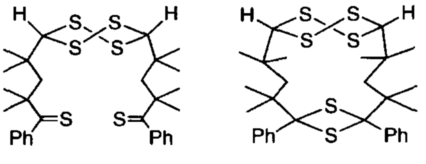


twist-**19** chair-**19**

0 0.782

ΔG° values (kcal mol^{-1}) at 193 K

Chart 10.



20 **21**

Chart 11.

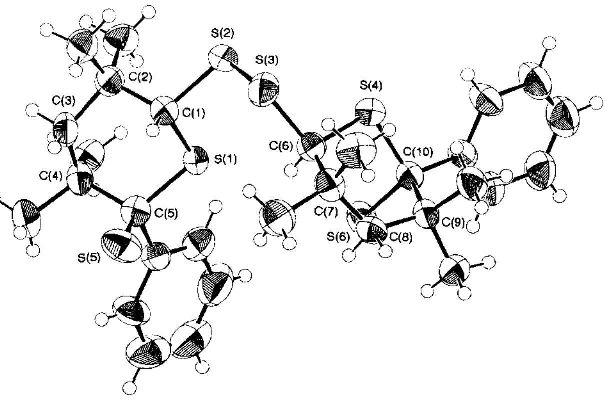
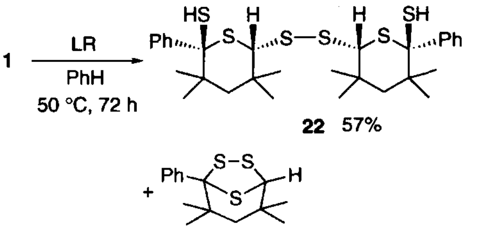


Fig. 5. ORTEP drawing of the disulfide **22** (50% ellipsoids). Relevant bond lengths (Å), bond angles (deg), and a torsion angle (deg): S(2)–S(3), 2.021(2); S(2)–C(1), 1.857(3); C(1)–C(2), 1.522(4); C(2)–C(3), 1.550(4); C(3)–C(4), 1.552(5); C(4)–C(5), 1.569(4); C(5)–S(1), 1.835(3); S(1)–C(1), 1.771(3); S(5)–C(5), 1.902(4); S(3)–C(6), 1.848(3); C(6)–C(7), 1.528(4); C(7)–C(8), 1.535(4); C(8)–C(9), 1.555(4); C(9)–C(10), 1.566(4); C(10)–S(4), 1.854(3); S(4)–C(6), 1.781(3); S(6)–C(10), 1.832(3); S(3)–S(2)–C(1), 105.3(1); S(2)–C(1)–C(2), 112.9(2); C(1)–C(2)–C(3), 107.7(2); C(2)–C(3)–C(4), 122.6(3); C(3)–C(4)–C(5), 110.6(3); C(4)–C(5)–S(1), 110.7(2); C(5)–S(1)–C(1), 101.7(2); S(1)–C(1)–C(2), 115.2(2); S(1)–C(1)–S(2), 104.3(2); S(1)–C(5)–S(5), 105.9(2); S(5)–C(5)–C(4), 109.1(2); S(2)–S(3)–C(6), 104.1(2); S(3)–C(6)–C(7), 108.7(2); C(6)–C(7)–C(8), 107.9(3); C(7)–C(8)–C(9), 122.3(3); C(8)–C(9)–C(10), 111.2(2); C(9)–C(10)–S(4), 108.2(2); C(10)–S(4)–C(6), 100.2(2); S(4)–C(6)–C(7), 114.0(2); S(4)–C(6)–S(3), 107.6(2); S(4)–C(10)–S(6), 109.1(2); S(6)–C(10)–C(9), 107.6(2); C(1)–S(2)–S(3)–C(6), 80.5(2).



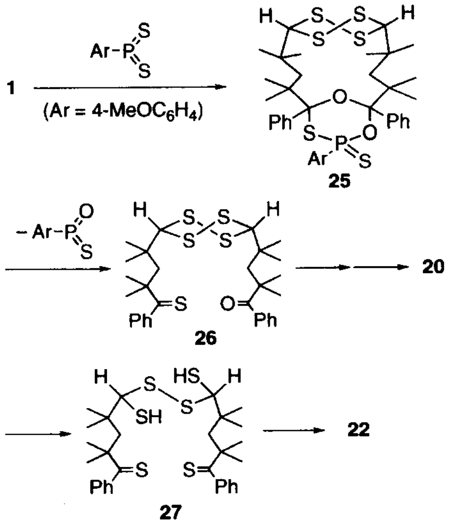
22 57%

4 26%

(2)

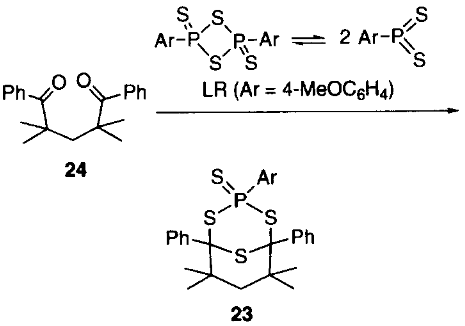
$$\mathbf{2} \xrightarrow[\text{PhCH}_3,\ \text{reflux, 48 h}]{\text{LR}} \underset{67\%}{\mathbf{2}} + \underset{29\%}{\mathbf{4}} \qquad (3)$$

It is noteworthy that the reaction of the *trans*-isomer **2** with LR was considerably sluggish compared with that of **1** and LR; heating **2** with LR in refluxing toluene for 48 h resulted in a 67% yield recovery of **2** with the formation of **4** in 29% yield (Eq. 3). Thus, the higher reactivity of the *cis*-isomer **1** to LR would be ascribed to the *cis* configuration of the two substituents (R*), which enables the two C=O groups to interact with each other intramolecularly. We have observed the formation of the trithiaphosphorinane *P*-sulfide **23** in the reaction of the dicarbonyl compound **24** with LR;[10i] the compound **23** corresponds to a [2+2+2] cycloaddition product among two thiocarbonyls and one P=S of



Scheme 4.

4-MeOC$_6$H$_4$PS$_2$ generated from LR[24] (Eq. 4).



(4)

In an analogous way, the thionation of C=O groups of the *cis*-isomer **1** might proceed by repeating the first half of the process in Scheme 4; the formation of the intermediate **25** followed by the elimination of 4-MeOC$_6$H$_4$P(O)S gives the thiocarbonyl compound **26**. Formally, the reductive cleavage of the S–S bond of the tetrathiane ring in **20** gives the dithiol **27**, and the addition of the SH groups to the respective C=S groups furnishes the disulfide **22**. Although, we do not have any further data to determine the true mechanism of the S–S bond cleavage, it is likely that strained cyclophane-type intermediates undergo cleavage by interaction with LR or contaminated hydrogen sulfide.

Experimental

General. The melting points were determined on a Mel-Temp capillary tube apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were determined on Bruker AM400 or ARX400 (400 and 100.6 MHz, respectively), AC300P (300 MHz for ^{1}H), or AC200 (200 and 50 MHz, respectively) spectrometers using CDCl$_3$ as the solvent, unless otherwise noted. IR spectra were taken on a Hitachi 270-50 spectrometer. UV-vis spectra were measured using a JASCO V-560 spectrophotometer. Mass spectra were determined on a JEOL JMS-DX303 spectrometer operating at 70 eV in the EI mode. Elemental analysis was performed by the Chemical Analysis Center of Saitama University.

2KHSO$_5$·KHSO$_4$·K$_2$SO$_4$ (OXONE®) was used as purchased from Aldrich. Lawesson's reagent (LR) was prepared from anisol and P$_2$S$_5$ by a reported method.[11]

Throughout this work, the organic layer of the reaction mixture was dried over anhydrous magnesium sulfate. Column chromatography was performed with silica gel; the eluent is shown in parentheses.

2,2,4,4-Tetramethyl-6,7,8-trithiabicyclo[3.2.1]octane (4). A mixture of 2,2,4,4-tetramethyl-5-oxo-5-phenylpentanal (5)[12] (1.07 g, 4.62 mmol) and Lawesson's reagent (3.74 g, 9.24 mmol) in xylene (50 ml) was heated under reflux for 49 h. The mixture was cooled to room temperature, washed with aqueous NaHCO$_3$ and water, dried, and evaporated to dryness under reduced pressure. The residue was subjected to chromatography (CCl$_4$) to give the crude **4**. The crude product was recrystallized from hexane to give pure **4** as yellow needles (477 mg, 35%): Mp 145.3—145.7 °C (hexane); ^{1}H NMR (400 MHz) δ = 1.06 (s, 3H), 1.15 (d/d, J = 14.6/1.5 Hz, 1H), 1.14 (s, 3H), 1.16 (s, 3H), 1.41 (s, 3H), 1.89 (d, J = 14.6 Hz, 1H), 4.95 (d, J = 1.3 Hz, 1H), 7.28—7.32 (m, 3H), 7.46—7.51 (m, 2H); ^{13}C NMR (100.6 MHz) δ = 26.5 (CH$_3$), 27.9 (CH$_3$), 29.7 (CH$_3$), 32.1 (CH$_3$), 39.2 (C), 43.8 (C), 48.2 (CH$_2$), 72.5 (CH), 90.0 (C), 127.3 (CH), 127.9 (CH), 129.7 (CH), 138.2 (C); MS m/z 296 (M$^+$; 72), 232 (83), 217 (35), 199 (18), 176 (100), 143 (71), 121 (54). Found: C, 60.96; H, 6.82%. Calcd for C$_{15}$H$_{20}$S$_3$: C, 60.76; H, 6.80%.

2,2,4,4-Tetramethyl-1-phenyl-6,7-dithiabicyclo[3.1.1]heptane (3). To a solution of the trithiolane **4** (987 mg, 3.33 mmol) in benzene (100 ml) under argon was added P(NMe$_2$)$_3$ (1.82 ml, 10 mmol). The mixture was heated under reflux for 14 h and then evaporated to dryness. The residue was subjected to column chromatography (hexane–Et$_2$O 1 : 1) to give **3** (798 mg, 91%): Colorless needles, mp 123.2—123.6 °C (MeOH); ^{1}H NMR (300 MHz) δ = 1.16 (s, 6H), 1.35 (s, 6H), 2.15 (s, 2H), 3.36 (s, 1H), 6.85—6.88 (m, 2H), 7.18—7.29 (m, 3H); ^{13}C NMR (50 MHz) δ = 27.1 (CH$_3$), 28.8 (CH$_3$), 36.9 (C), 40.5 (C), 52.7 (CH$_2$), 53.4 (CH), 67.8 (C), 125.0 (CH), 126.7 (CH), 127.2 (CH), 141.9 (C); MS m/z 264 (M$^+$; 51), 207 (8), 193 (14), 175 (11), 143 (72), 121 (100). Found: C, 68.29; H,7.74%. Calcd for C$_{15}$H$_{20}$S$_2$: C, 68.13; H, 7.62%.

Reaction of the 1,3-Dithietane 3 with 2KHSO$_5$·KHSO$_4$·K$_2$SO$_4$ (OXONE®). To a solution of **3** (77 mg, 0.29 mmol) in CH$_2$Cl$_2$ (12.5 ml) was added aqueous OXONE® (2.22 g, 3.61 mmol, 20 ml). The pH of the aqueous layer was adjusted to 4 by adding 1 M KOH (1 M = 1 mol dm^{-3}). The mixture was stirred vigorously on an ice-water bath for 96 h. The organic layer was separated, washed with water, dried, and evaporated to dryness. The residue was subjected to column chromatography (CH$_2$Cl$_2$–CCl$_4$ 1 : 1) to give a 1 : 1 mixture of the *cis*- and *trans*-tetrathianes **1** and **2** (59 mg, 72%). The mixture was separated by HPLC (CH$_2$Cl$_2$–hexane 2 : 1) to give **1** (26.5 mg) and **2** (28 mg). When the reaction was conducted in a half scale of the above at room temperature, it took 24 h for consumption of the starting material to give a 1 : 1 mixture of **1** and **2** (69%).

***cis*-3,6-Bis(1,1,3,3-tetramethyl-4-oxo-4-phenylbutyl)-1,2,4,5-tetrathiane (1):** Colorless crystals, mp 108 °C (MeOH); ^{1}H NMR (400 MHz) δ = 1.05 (s, 12H), 1.40 (s, 12H), 2.24 (pseudo d, J = 2.8 Hz, 4H), 4.23 (s, 2H), 7.40 (t, J = 7.5 Hz, 4H), 7.47 (t, J = 7.2 Hz, 2H), 7.75 (d, J = 7.3 Hz, 4H); ^{13}C NMR (100.6 MHz) δ = 25.3 (CH$_3$), 29.1 (CH$_3$), 41.8 (C), 48.1 (C), 48.2 (CH$_2$), 67.7 (CH), 128.2 (CH), 128.5 (CH), 131.2 (CH), 138.5 (C), 208.5 (C=O). Found: C, 64.23; H, 7.25%. Calcd for C$_{30}$H$_{40}$O$_2$S$_4$: C, 64.24; H, 7.19.

X-Ray Crystal Structure Determination of 1. C$_{30}$H$_{40}$O$_2$S$_4$, M_w 560.88. Colorless cube, 0.12×0.10×0.04 mm^3, triclinic, space group $P\bar{1}$, a = 9.462(1), b = 12.417(2), c = 13.311(2) Å, α = 81.74(1), β = 99.83(2), γ = 74.19(1)°, V = 1484.5(4) Å^3, D_c = 1.254 g cm^{-3}, Z = 2, μ(Cu $K\alpha$) = 17.5 mm^{-1}. Mac Science

MXC3KHF diffractometer with graphite-monochromated Cu $K\alpha$ radiation (λ = 1.54178 Å), $\theta/2\theta$ scans method in the range $3° < 2\theta < 120°$ ($0 < h < 10$, $-13 < k < 13$, $-14 < l < 14$), 4854 reflections measured, 3932 unique reflections. The structure was solved by direct methods using SIR92[25] in the CRYSTAN GM program system and refined by a full-matrix least-squares method using 3447 reflections [$I \geq 1\sigma(I)$] for 476 parameters. An absorption correction was made by the psi-scan method. The non-hydrogen atoms were refined anisotropically. The final R (R_w) = 0.0581 (0.0482) and GOF = 1.441; max/min residual electron density = 0.29/−0.29 e Å^{-3}.

***trans*-3,6-Bis(1,1,3,3-tetramethyl-4-oxo-4-phenylbutyl)-1,2,4,5-tetrathiane (2):** Colorless crystals, mp 114 °C (MeOH); ^{1}H NMR (400 MHz) δ = 1.05 (s, 12H), 1.40 (s, 12H), 2.23 (s, 4H), 4.34 (s, 2H), 7.41 (t, J = 7.4 Hz, 4H), 7.48 (t, J = 7.3 Hz, 2H), 7.74 (d, J = 7.2 Hz, 4H); ^{13}C NMR (100.6 MHz, 323 K) δ = 25.8 (CH$_3$), 29.1 (CH$_3$), 41.8 (C), 48.2 (C), 48.5 (CH$_2$), 66.5 (CH), 128.1 (CH), 128.5 (CH), 131.1 (CH), 138.8 (C), 208.3 (C=O). Found: C, 64.33; H, 7.20%. Calcd for $C_{30}H_{40}O_2S_4$: C, 64.24; H, 7.19%.

X-Ray Crystal Structure Determination of 2. $C_{30}H_{40}O_2S_4$, M_w 560.88. Colorless plates, 0.25×0.10×0.04 mm^3, monoclinic, space group $P2_1/n$, a = 10.920(2), b = 21.330(5), c = 6.473(2) Å, β = 99.83(2)°, V = 1485.5(6) Å^3, D_c = 1.254 g cm^{-3}, Z = 2, μ(Cu $K\alpha$) = 30.755 mm^{-1}. Mac Science MXC3KHF diffractometer with graphite-monochromated Cu $K\alpha$ radiation (λ = 1.54178 Å), $\theta/2\theta$ scans method in the range $3° < 2\theta < 140°$ ($-13 < h < 13$, $0 < k < 26$, $0 < l < 7$), 3264 reflections measured, 2503 unique reflections. The structure was solved by direct methods using SIR92[25] in the CRYSTAN GM program system and refined by a full-matrix least-squares method using 1920 reflections [$I \geq 2\sigma(I)$] for 243 parameters. An absorption correction was performed by the psi-scan method. The non-hydrogen atoms were refined anisotropically. The final R (R_w) = 0.0561 (0.0556) and GOF = 1.683; max/min residual electron density = 0.50/−0.33 e Å^{-3}.

Reaction of the *cis*-Tetrathiane 1 with Lawesson's Reagent (LR). A mixture of **1** (39 mg, 0.07 mmol) and LR (88 mg, 0.22 mmol) in benzene (20 ml) was heated at 50 °C for 72 h under argon. The mixture was cooled on an ice-water bath and precipitates of unreacted LR were removed by filtration. The filtrate was washed with aq NaHCO$_3$ and water, dried, and evaporated to dryness. The residue was subjected to column chromatography (hexane–CH$_2$Cl$_2$ 3 : 1) and then HPLC [INERTSIL PREP-SIL (GLScience Inc.), hexane–CH$_2$Cl$_2$ 5 : 1] to give the disulfide **22** (24 mg, 57%) and the trithiolane **4** (11 mg, 26%).

3,3′,3′,5,5,5′,5′-Octamethyl-6,6′-diphenyl-*t*-6,*t*-6′-disulfanyl-*r*-2,*r*-2′-dithiodi(thiane) (22): Colorless prisms, mp 164—165 °C (hexane); ^{1}H NMR (400 MHz) δ = 0.90 (s, 6H), 0.96 (s, 6H), 1.24 (s, 6H), 1.29 (d, J = 14.6 Hz, 2H), 1.29 (s, 6H), 2.10 (d, J = 14.6 Hz, 2H), 2.47 (s, 2H, SH×2), 5.07 (s, 2H, CH×2), 7.25 (t, J = 7.0 Hz, 4H), 7.30 (t, J = 7.3 Hz, 4H), 7.94 (d, J = 7.6 Hz, 4H); ^{13}C NMR (100.6 MHz) δ = 23.0 (CH$_3$), 26.2 (CH$_3$), 28.6 (CH$_3$), 30.9 (CH$_3$), 38.1 (C), 41.3 (C), 53.8 (CH$_2$), 68.5 (CH), 71.8 (C), 127.1 (CH), 127.3 (CH), 129.3 (C), 142.6 (C). Found: C, 60.40; H, 7.14%. Calcd for $C_{30}H_{42}S_6$: C, 60.55; H, 7.11.

X-Ray Crystal Structure Determination of 22. $C_{30}H_{42}S_6$, M_w 595.00. Colorless prism, 0.30×0.20×0.10 mm^3, monoclinic, space group $P2_1$, a = 14.227(5), b = 12.790(4), c = 8.657(8) Å, β = 98.37(5)°, V = 1558.6(16) Å^3, D_c = 1.267 g cm^{-3}, Z = 2, μ(Cu $K\alpha$) = 41.193 mm^{-1}. Mac Science MXC3KHF diffractometer with graphite-monochromated Cu $K\alpha$ radiation (λ = 1.54178 Å), $\theta/2\theta$ scans method in the range $3° < 2\theta < 140°$ ($-17 < h < 17$, $-15 < k < 0$, $0 < l < 10$), 3424 reflections measured, 3079 unique reflections. The structure was solved by direct methods using SIR92[25] in the CRYSTAN GM program system and refined by a full-matrix least-squares method using 2977 reflections [$I \geq 2\sigma(I)$] for 326 parameters. An absorption correction was made by the psi-scan method. The non-hydrogen atoms were refined anisotropically. The final R (R_w) = 0.066 (0.077) and GOF = 4.218; max/min residual electron density = 0.48/−0.62 e Å^{-3}.

Reaction of the *trans*-Tetrathiane 2 with LR. A mixture of **2** (30 mg, 0.053 mmol) and LR (67 mg, 0.165 mmol) in xylene (5 ml) was heated under argon at 50 °C for 72 h and then at 100 °C for 72 h. Because the reaction did not proceed, the mixture was heated under reflux for 48 h. After cooling over an ice-water bath, precipitates of unreacted LR was removed by filtration. The filtrate was washed with aq NaHCO$_3$ and water, dried, and evaporated to dryness. Column chromatography (hexane–CH$_2$Cl$_2$, 1 : 1) of the residue gave the trithiolane **4** (9 mg, 29%) and **2** (20 mg, 67%).

Structure determination summaries and tables of X-ray structure data for **1**, **2**, and **22** have been deposited as Document No. 73017 at the Office of the Editor of Bull. Chem. Soc. Jpn. 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 CCDC 138169-138171.

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