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Anomeric Effect in Sulfur Heterocycles Carrying Sulfur Substituents[1]

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Conformational analysis of 1,3,5-trithiane derivatives with sulfur-substituents was carried out with the aid of PMR spectra at various temperatures. 2-Phenylthio-1,3,5-trithiane exhibited the strong anomeric effect whereas 2-phenylthiothiane the moderate. This enhanced anomeric effect in trithiane derivatives was attributed to both the stabilization of the axial form and the destabilization of the equatorial form. *cis*-2,4-Bis(phenylthio)-1,3,5-trithiane was found to possess a diaxial conformation to a fair extent in support of the presence of the strong anomeric effect. Equilibration between *cis* and *trans* forms of 2,4-bis(phenylthio)-1,3,5-trithiane was carried out to show that the *trans* form was more stable than the *cis*. The barrier to inversion of *trans*-2,4-bis(phenylthio)-1,3,5-trithiane was obtained as *ca.* 11 kcal/mol.

Since the discovery of the fact, by Lemieux *et al.*,[2] that pyranose derivatives possessing such substituents as alkoxy, acyloxy, or halogen at 2-position prefer the substituent-axial conformation, the phenomenon has drawn attention of many investigators. This phenomenon is in sharp contrast with the free energy difference in cyclohexane derivatives in which the substituent equatorial conformation predominates. The effect which favors the axial conformation in pyranose and analogous sulfur systems has been recognized as the anomeric effect.

Whereas many reports have been published on this effect in oxane and 1,3-dioxane derivatives,[3] there has been only one report on the anomeric effect in sulfur analogs.[4] Since we have observed strong anomeric effect in benzoyloxy derivatives of thiane and analogs,[5] it must be of interest to see the effect in sulfur-substituted thiane and trithiane.

As to the conformational energy of sulfur-substituents, there are two factors to be considered. These are the bond length and the van der Waals radius. Comparison of these factors with the oxygen compound indicates that a longer C–S distance (1.81 Å) than that of the C–O (1.43 Å) tends to lessen and a larger van der Waals radius of sulfur (1.85 Å) than that of oxygen (1.40 Å) tends to enlarge the 1,3-diaxial interaction. As a consequence, the conformational free energy diference for the SH group (0.9 kcal/mol) is only a little larger than that for the OH (0.7 kcal/mol) in cyclohexane series.[6] There is another factor to be considered in sulfur heterocycles. The larger bond distance of the C–S may lessen the 1,3-diaxial interaction.

This paper reports discovery of strong anomeric effect in trithiane derivatives, compares the effect with another sulfur heterocycle, and discusses equilibria of disubstituted compounds.

Results and Discussion

Monosubstituted 1,3,5-Trithianes. Methylene and methine part of PMR spectra of 2-phenylthio-1,3,5-trithiane (**1**) in $CDCl_3$–CS_2 (1 : 1 v/v) both at room temperature and at −83 °C are shown in Fig. 1. At room temperature, methine and methylene signals are seen at δ 5.35, and 3.73 and 4.80, respectively, whereas at −83 °C, a pair of methine signals at δ 5.46, and 5.10, and a pair of AB signals (δ 3.55 and 5.15, J=14.4 Hz; δ 3.91 and 4.40, J=14.4 Hz) are found. The results must be interpreted on a basis that, while the exchange between two conformations is too fast at room temperature, that at −83 °C is slow enough to detect the respective conformations by means of NMR technique. The integrated intensities of these signals show that the population ratio of these isomers is 8.2±0.2.

The spectral features of the more stable isomer are showing up of the methine signal at lower field than the unstable conformer and larger difference in chemical shifts of the A and B protons. Indeed, the difference in chemical shifts of the AB signals amounts to 1.60 ppm and is much larger than that of 1,3,5-trithiane in $CDCl_3$ at −70 °C (0.75 ppm). In contrast to this feature, the difference in chemical shifts of AB signals of the less stable isomer is only 0.45 ppm which is a little smaller than the corresponding value of trithiane. These spectral features of two conformers should be clues to assign the conformation.

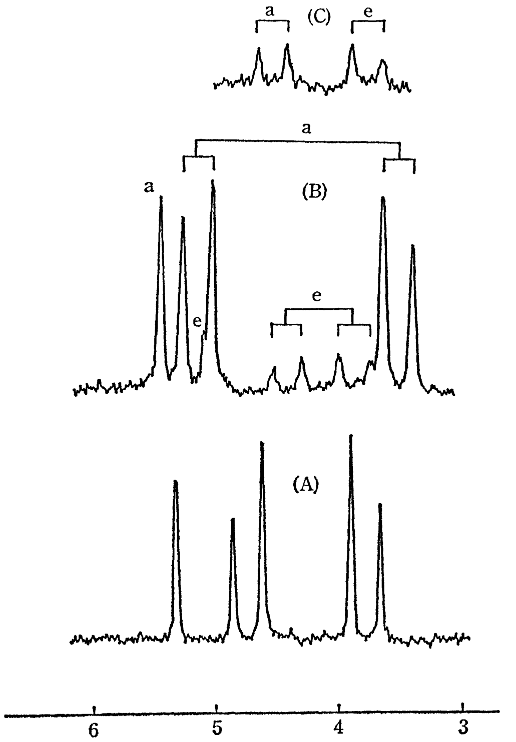
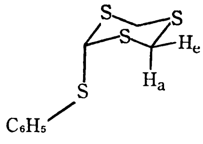
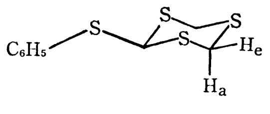


Fig. 1. PMR spectra of 2-phenylthio-1,3,5-trithiane [(A) at 34 °C and (B) at −83 °C] and that of 1,3,5-trithiane [(C) at −70 °C] in $CDCl_3$-CS_2 (1 : 1).

Higher field doublets of the respective AB signals may be assigned to the equatorial proton because equatorial protons are known to give a higher field signal than the axial in trimethyltrithianes.[7] Since 1,3,5-trithiane shows AB signals at δ 3.76 and 4.51 with coupling constant of 14.7 Hz, the equatorial proton of the more populated isomer shows a little up-field shift from the trithiane itself, whereas the axial proton a large low-field shift. As the difference in structure between 1,3,5-trithiane and **1**, the presence of phenylthio group instead of hydrogen can be taken as a major one. Since phenyl is a bulky group, it will not reside above the trithiane ring as one of the possible conformations of phenylthio-axial conformer requests: an assumption that conformations like **1a** only exist becomes a good approximation in the present discussion. Then a major factor which determines the chemical shifts of equatorial and axial protons in the axial isomer is the presence of an axial C–S bond. Likewise, in the phenylthio-equatorial conformer, the C–S bond exerts the major factor for determining the chemical shifts of the axial and equatorial protons. While three conformations are made by the rotation about the C_{ph}–S bond in this case, the phenyl group is located so distantly from the protons in question that its effect may be neglected.



(**1a**)

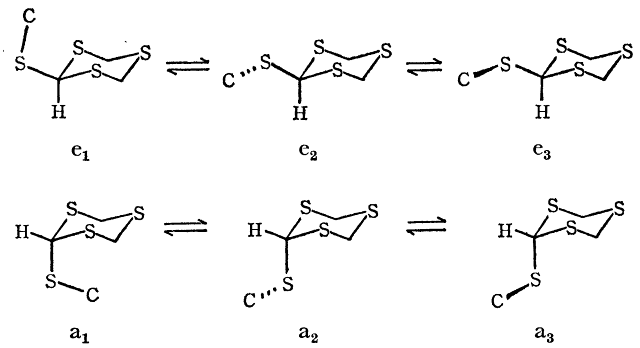


(**1e**)

Consideration of the standard molecular structure, the bond anisotropy of the C–S bond, and McConnell equation[8] reveals that, if there is an axial C–S bond, the axial proton (H_a) at 3-position from the C–S should be strongly deshielded, whereas the equatorial proton (H_e) should be relatively unaffected. Consequently, an increase in chemical shift difference is expected for the methylene protons from that of trithiane. This tendency compares with the observed value of an increase by 0.85 ppm. On the other hand, if there is an equatorial C–S bond, H_e should be unaffected whereas H_a should shift to the higher field slightly. As a consequence, the chemical shift difference should decrease slightly from that of trithiane. This tendency compares with the observed one of a decrease by 0.30 ppm. Thus the more stable isomer must be assigned to phenylthio-axial isomer (**1a**) and the less stable isomer to phenylthio-equatorial isomer (**1e**).

Above assignment is supported by the following fact. When the PMR spectrum of **1** is taken as a CD_3COCD_3 solution at −83 °C, population of the conformer which shows the smaller chemical shift difference increases and the ratio becomes 1.6±0.2 in favor of the isomer which gives larger chemical shift difference. These results indicate that the more polar form is the one which shows less chemical shift difference between protons of the AB type. Since the direction of the dipole in thioethers is known to be that of the lone pairs,[9] compound **1** is considered to be more polar if it takes the phenylthio-equatorial conformation (**1e**).[3] Then a conclusion is drawn that **1a** conformation is more stable and is consistent with that drawn by consideration of the chemical shift difference of the AB protons.

It may be argued that, because of the anisotropy of the C–S bond, the equatorial methine proton at the foot of the phenylthio group should appear at the higher magentic field than the axial, as are the other trithiane protons.[7] The following consideration, however, could give rationale to the apparent reversal of the chemical shifts of axial-equatorial methine protons.



Three stable conformations (e_1, e_2, and e_3) made by the rotation about the S–$C_{trithiane}$ bond of the phenylthio-equatorial conformations may be considered. From the steric grounds, none of these conformations is very unstable and these contribute to a fair extent. On the other hand, the phenylthio-axial form includes other apparently stable conformations (a_1, a_2, and a_3) produced by the rotation about the S–$C_{trithiane}$ bond. As discussed earlier, however, a_1 conformation is considered to be unstable because of the steric effect of the phenyl group and contributes to a very limited extent, if any. Consideration of the dipole moments of the respective conformers reveals that e_1 is the least polar among the phenylthio-equatorial conformations and that there is no appreciable difference in polarity among the phenylthio-axial conformations. Thus, in nonpolar media such as those we are discussing here, the e_1 form is the most populated species among **1e**, whereas the a_1 form will have scarce contribution.[10]

A plausible assumption is again that the chemical shift of the methine proton is mainly determined by the bond anisotropy of the C–S bond. Considered the bond anisotropy of the C–S bond, conformers e_2, e_3, a_2, and a_3 are the ones in which the methine proton suffers from the deshielding, whereas the methine proton in conformation e_1 and a_1 is relatively shielded. Then the phenylthio-equatorial form which exists mainly as e_1 should give the methine proton signal at the relatively high field, compared with the phenylthio-axial form which exists mainly as a_2 and a_3.

One may wonder why the apparently abnormal chemical shift of equatorial protons at the foot of the phenylthio group is not attributed to the effect of the phenyl group. However, that this is not the case is understood when the case of 2-methylthio-1,3,5-trithiane (**2**) is taken into account. This compound in $CDCl_3$–CS_2 showed a single peak for the methine proton

Table 1. Chemical shift differences between two methylene protons of 2-phenylthio-1,3,5-trithiane at various temperatures and equilibrium constants for the equilibrium **1a⇄1e**

in $CDCl_3$-CS_2 (1 : 1 v/v)							
T °C	63	49	33	15	2.5	−15	−35
$\Delta\delta$ ppm	0.84	0.88	0.92	0.99	1.03	1.08	1.19
K	1.8	1.9	2.1	2.4	2.6	3.2	4.1
T °C	−68	−75	−78	−83[a)]			
$\Delta\delta$ ppm	a 1.60 e 0.49	1.60 0.50	1.61 0.48	1.60 0.49			
in CD_3COCD_3							
T °C	49	31	7	−83			
$\Delta\delta$ ppm	0.40	0.42	0.45	a 1.23 e 0.56			
K	1.1_7	1.2_2	1.3_2	1.6[b)]			

a) Equilibrium constant is 8.2, judged from the integrated intensities. b) Obtained by direct integration.

Table 2. Chemical shift differences between two methylene protons of 2-methylthio-1,3,5-trithiane at various temperatures and equilibrium constants for the equilibrium **2a⇄2e**

in $CDCl_3$-CS_2 (1 : 1 v/v)							in CD_3COCD_3					
T °C	61	50	39	26	17.5	−83	T °C	46.5	29	14	−6	−83
$\Delta\delta$ ppm	0.84	0.86	0.88	0.92	0.94	a 1.56 e 0.46	$\Delta\delta$ ppm	0.37	0.37	0.39	0.40	a 1.11 e 0.46
K	1.8	1.9	2.0	2.2	2.3	3.5[a)]	K	1.1	1.1	1.2	1.2	1.2[a)]

a) Otained by direct integration.

at δ 4.95 and a quartet for the methylene protons (δ 4.63 and 3.73, J=14.5 Hz), which split into a pair of singlets (δ 5.05 and 4.95) and a pair of quartets (δ 3.51 and 5.07, J=14.4 Hz; δ 3.99 and 4.45, J=14.4 Hz), respectively, at −83 °C. The ratio of integrated intensities was 3.0±0.2 in favor of the conformer which showed a large chemical shift difference between A and B protons of the AB quartet. The stable isomer may be assigned to the methylthio-axial conformer (**2a**) from the same ground as discussed earlier. This assignment is supported by a fact that the population ratio of these isomers is reduced to 1.1±0.1 when the spectrum is measured with CD_3COCD_3 solution at −83 °C; the less stable form is apparently more polar than the stable.[3)] Taking this assignment into account, the axial proton at the foot of methylthio group is at the higher magnetic field than the equatorial.

(**2e**) (**2a**)

After the establishment of the assignment of conformations, determination of the difference in conformational energies will be worthy of study. The conformational energy may be obtained by applying the following equations and obtaining equilibrium constants (K) at various temperatures.

$$\Delta\delta_{obs} = N_a\Delta\delta_a + N_e\Delta\delta_e \tag{1}$$

$$K = \frac{N_e}{N_a} \tag{2}$$

where $\Delta\delta_{obs}$ is the observed chemical shift difference between A and B protons of the AB type after coalescence, $\Delta\delta_a$ and $\Delta\delta_e$ are those of axial and equatorial conformers, respectively, and N_a and N_e are the mole fractions of axial and equatorial conformers, respectively. A similar treatment would have been possible for the methine protons at 2-position, if the heavy overlap with the strong signal were not present. In order to make Eq. (1) valid, the chemical shift of each isomer should not vary at various temperatures. Measurements at various temperatures after splitting of the signals were thus carried out and the results are listed in Table 1. It will be seen that the chemical shift differences between −68 °C and −85 °C are essentially the same. The same tendency may be extended up to room temperature.* The chemical shift differences after coalescence of the two sets of AB signals are also listed in Table 1.

By the averaging process above the coalescence temperature, an equatorial proton of one conformer is converted to an axial proton of the other. Therefore the sign of $\Delta\delta_a$ and $\Delta\delta_e$ must be different. In the actual calculations $\Delta\delta_a$ was taken as positive and $\Delta\delta_e$ negative. The equilibrium constans thus obtained are shown in Table 1. From these data, ΔH and ΔS for the equilibrium **1a⇄1e** in $CDCl_3$–CS_2 were obtained as 1.3±0.1 kcal/mol and 3.0±0.5 eu, respectively. The conformational energy in acetone-d_6 can be obtained in the same manner: ΔH=0.4±0.1 kcal/mol and ΔS=1.0±0.3 eu. It can be pointed out that

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* This method of determination of thermodynamic parameters can be checked by extrapolating the population ratio to low temperatures. The calculated value is 7.7±0.5 at −83 °C and this compares favorably with the observed ratio of 8.2±0.2

Table 3. Chemical shift difference between two methylene protons of *cis*-2,4-bis(phenylthio)-1,3,5-trithiane at various temperatures and equilibrium constants for the equilibrium **3aa**⇌**3bb** (1 : 1 CDCl$_3$-CS$_2$)

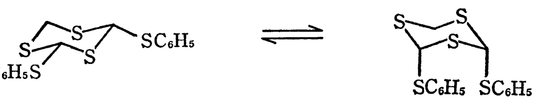
T °C	51	46.5	32	29	14	−6	−83
$\Delta\delta$ ppm	0.21	0.20	0.19	0.17	0.16	0.16	a 1.60 e 0.27
K	0.34	0.33	0.32	0.30	0.29	0.29	0.3[a]

a) Obtained by direct integration.

ΔH is reduced by 0.9 kcal/mol in acetone-d_6, and this change can be attributed largely to the fact that conformer **1e** is stabilized in a high dielectric medium on the electric ground.

Similar treatment was made for 2-methylthio-1,3,5-trithiane. The results are listed in Table 2, which produce ΔH and ΔS, for the equilibrium **2a**⇌**2e** in CDCl$_3$–CS$_2$, of 0.9±0.1 kcal/mol and 1.0±0.5 eu, respectively. These parameters in acetone-d_6 are 0.1±0.1 kcal/mol and 0.2±0.2 eu, respectively. Stabilization, to a large extent, of the polar conformer is observed again.

Disubstituted 1,3,5-Trithianes. Since the anomeric effect in 2-phenylthio-1,3,5-trithiane has been found to be fairly large, it will be interesting to see the effect of substitution by one more phenylthio group in 1,3,5-trithiane system. If 2,4-bis(phenylthio)-1,3,5-trithiane has a *cis* configuration, it will assume either a diequatorial (**3ee**) or a diaxial (**3aa**) conformation. In cyclohexane series, the diequatorial form is overwhelming because of a severe 1,3-*syn*-diaxial interaction, whereas the diequatorial form in 1,3,5-trithiane system is disfavored by the anomeric effect. The PMR spectrum of *cis*-2,4-bis(phenylthio)-1,3,5-trithiane (**3**) in CDCl$_3$–CS$_2$ showed a single peak for methine protons at δ 5.10 and a quartet for methylene protons at δ 3.98 and 4.17, J being 14.4 Hz. On cooling the solution down to −83 °C, however, the spectrum changed to show a pair of singlets at δ 4.92 and 5.38 and two sets of AB quartets (δ 3.88 and 4.15, J=14.4 Hz; δ 3.62 and 5.22, J=14.4 Hz). The results are best interpreted by assuming that the inversion of the ring is fast at room temperature but frozen at −83 °C on the PMR time scale to show the signals of both isomers (**3ee** and **3aa**) separately. The population ratio as determined by the integrated intensity was 3.2±0.3. From an analogy of the discussion given in the part of 2-phenylthio-1,3,5-trithiane, it will be natural to assume that an isomer which has two axial phenylthio groups should give further separation of the chemical shifts of the AB protons, because two C–S bonds are inserted axially. On the contrary, an isomer which has two equatorial phenylthio groups should show smaller separation of the chemical shifts than **1e**. Thus the isomer which gives $\Delta\delta$ of 1.60 ppm is assigned to **3aa** and the other to **3ee**, $\Delta\delta$ for the latter being 0.27 ppm. Then the diequatorial form **3ee** is favored over the diaxial form **3aa**. The chemical shifts and intensities of the methine protons at 2-position are consistent with this assignment: the signal at higher magnetic field is more intense than that at the lower field.



(**3ee**) (**3aa**)

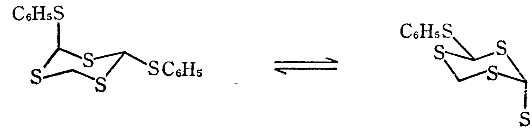
The change in population of **3ee** and **3aa** at various temperatures is tabulated in Table 3. The enthalpy change and entropy change for the equilibrium **3aa**⇌**3ee** are estimated to be −0.2±0.1 kcal/mol and +1.0±0.1 eu, respectively, from these results. Thus composition of **3** at 34 °C is 24.5% **3aa** and 75.5% **3ee**.

It is rather surprising to see that the diaxial form exists to a fair extent in **3**, in view of the results obtained with cyclohexane derivatives. In the cyclohexane series, a substituent of RS type generally shows the free energy difference of *ca.* 0.8 kcal/mol at room temperature, the equatorial form being favored.[6] Existence of 1,3-diaxial conformer **3aa** to a fair extent must then be a reflection of the strong anomeric effect and lessened 1,3-diaxial interaction because of the long distance of C–S bonds in this compound.

Barrier to Inversion of trans-*2,4-Bis(phenylthio)-1,3,5-trithiane.* It may be argued that the ring conformation of 1,3,5-trithiane with a phenylthio axial substituent might be altered from the normal chair as in the case of multisubstituted 1,3-dithiane series.[11] However, this possibility may not be taken as a serious one for the following reason.

Since it is well known that the inversion barrier of the six-membered rings is not largely affected by substituents if the ring structure is not deformed from the normal chair,[12] estimation of the inversion barrier of the system in question must lead help in diagnosing the ring conformation.

trans-2,4-Bis(phenylthio)-1,3,5-trithiane (**4**) was used for the investigation, because this compound should give easier analysis due to the high degree of symmetry. While **4** showed sharp singlets due to methylene (δ 4.37) and methine (δ 5.62) protons at 34 °C, the former split to two singlets (δ 5.52 and 5.69)** and the latter



(**4**) (**4′**)

** The signal at the lower field is assigned to the axial, because the signal at the higher magnetic field is broader probably owing to the long range coupling. This anomaly, compared with other methine protons at the foot of phenylthio group in compounds examined here, may be attributed to the presence of an axial C–S bond at 3-position from the proton.

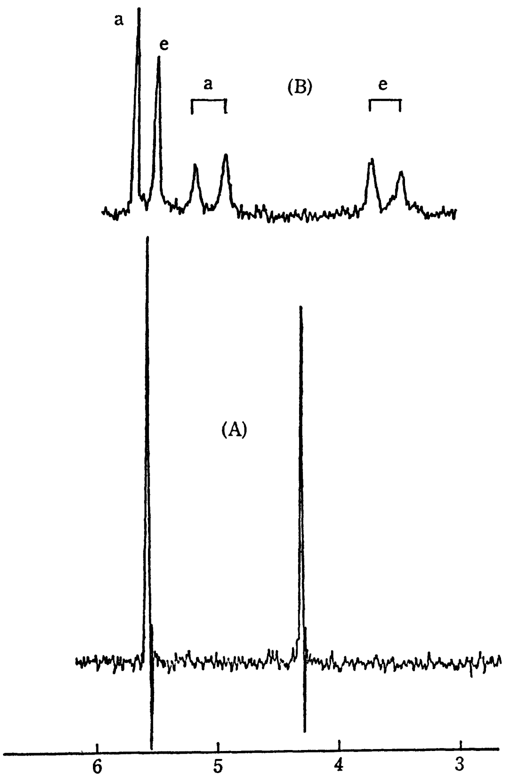


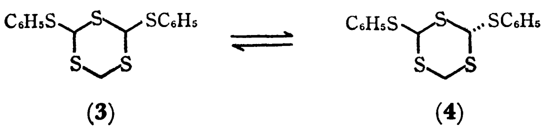
Fig. 2. PMR spectra of *trans*-1,3-bis(phenylthio)-1,3,5-trithiane in $CDCl_3$-CS_2 (1 : 1): (A) at 34 °C and (B) at −80 °C.

changed to an AB quartet (δ 3.70 and 5.09, J=15 Hz) at −80 °C. The methine protons showed coalesence of the signals at −61 °C, whereas the methylene protons at −46 °C. The free energy of activation for inversion was calculated to be 10.4 and 11.1 kcal/mol from methine and methylene protons, respectively, by putting these results into the following equations. Equation (3) was applied for the methine proton and Eq. (4) for the methylene protons. These data are in good agreement with the barrier (11.0 kcal/mol) to inversion of 1,3,5-trithiane.13)

$$\Delta G_C^{\ddagger} = 4.57\,T_C(9.97+\log_{10} T_C/\Delta\nu) \qquad (3)^{14)}$$

$$\Delta G_C^{\ddagger} = 4.57\,T_C(9.97+\log_{10} T_C/\sqrt{\Delta\nu^2+6J_{AB}^2}\,) \qquad (4)^{15)}$$

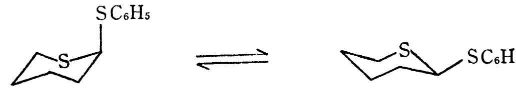
cis-trans *Equilibration of 2,4-Bis(phenylthio)-1,3,5-trithiane.* In view of the fact that 1,3-diaxial form is present to a fair extent in *cis*-2,4-bis(phenylthio)-1,3,5-trithiane (**4**), equilibration between the *cis* and *trans* isomers of **4** will clear another aspect of the conformational energies of the phenylthio group in trithiane. In the *cis* isomer, both phenylthio groups will be either axial or equatorial, whereas one of the phenylthio groups is equatorial and the other axial in the *trans*.



(3) (4)

The equilibration is carried out by heating the *cis*-isomer in $CDCl_3$ at 80 °C in the presence of benzoic acid as a catalyst. Equilibrium constant was obtained as 3.2 in favor of the *trans*. The same ratio of *cis* and *trans* isomers was obtained also by starting from the *trans*-isomer. Since the *trans* form has two degenerate conformations **4** and **4′**, these conformations must contribute to the same degree and the contributions are calculated to be 38% each. On the other hand, the equilibrium constant for **3aa**⇌**3ee** at 80 °C is calculated as 0.37 by using the thermodynamic parameters derived as before. Thus the equilibrium mixture of 2,4-bis(phenylthio)-1,3,5-trithiane at 80 °C must consist of 6% **3aa**, 18% **3ee**, 38% **4** and 38% **4′**. Although detailed discussion on the conformational and configurational equilibrium of *cis* and *trans* compounds is difficult because of the presence of many factors, the preference of the trans compound clearly indicates the presence of strong anomeric effect.

2-Phenylthiothiane. In order to discuss the strength of anomeric effect in 1,3,5-trithiane derivatives, conformational analysis of 2-phenylthiothiane (**5**) will afford the useful information. Thus study on this compound was undertaken. Compound **5** in $CDCl_3$ shows a near double doublet signal (J=7.5 and 3.0 Hz) for the methine proton at 2-position in the PMR spectrum at 34 °C to indicate that the phenylthio equatorial isomer exists to at least some extent. This result is in accordance with those obtained by Zefirov *et al.*4) who reported that 2-phenylthiothiane exists as a mixture of 45% **5a** and 55% **5e** from the shapes of methine proton signals.



(**5a**) (**5e**)

On cooling the solution, the methine proton signal broadened considerably at −80 °C and was split into two peaks at −100 °C: one peak is a near triplet centered at δ 4.26 and the other an apparent double doublet centered at δ 3.89. The assignment is straightforward: the near triplet signal and the double doublet are assigned to **5a** and **5e**, respectively.16) The relative intensity is 1.8±0.2 to 1 in favor of **5a**. From these data ΔH and ΔS are calculated as 0.2±0.1 kcal/mol and 0.4±0.2 eu, respectively. The results indicate that the axial isomer is more stable in terms of enthalpy but, because of unfavorable entropy change probably due to the steric effect in one of the rotational isomers, the equatorial isomer contributes to a fair extent at relatively high temperatures: 44% at 34 °C.

Comparison of the Anomeric Effect in Various Compounds. Three main factors are usually cited for the appearance of the anomeric effect. They are dipole-dipole interactions of the polar bonds,17) repulsive lone-pair-lone-pair interactions of the heteroatoms,18) and the resonance effect which involves overlap between the p-orbitals of the heteroatom and the back lobe of the orbital involved in forming the axial polar bond.19) These three factors operate favorably in axial isomers but not in the equatorial.

It is quite natural to consider that these factors are enhanced when heteroatoms reside on both sides of the axial polar bond and these must cause the enhanced anomeric effect in 1,3,5-trithiane, compared with thiane derivatives. There are reports which contradict this idea: the anomeric effect in 2-methoxy-1,3-dioxane is smaller than that in 2-methoxyoxane.[3] However, the phenomenon was later attributed to the puckering of 1,3-dioxane ring[20] and the short distance in 1,3-*syn*-axial interaction because the C–O bond is shorter than the C–C.[10]

Striking enhancement of the anomeric effect is observed by going from thiane to trithiane. This observation may be attributed to the destabilization of the equatorial form and/or the stabilization of the axial form in trithiane derivatives. In the axial form of 1,3,5-trithiane derivatives, the energy level may not be so high as that of the corresponding thiane derivatives because the 1,3-diaxial interaction is lessened to a considerable extent owing to the longer distance of the C–S bonds and a somewhat flattened conformation of trithiane.[21] In the equatorial form of 2-phenylthiothiane, the repulsive interaction between lone pairs of electrons belonging to two sulfur atoms in the ring and the substituent may be relieved to some extent by increasing the torsion angle about the C_{ring}–C_{subst} bond. However, this mode of relief is not possible for the trithiane derivative: the relief of repulsive interaction with one sulfur atom by increasing the torsion angle necessarily increases the repulsive interaction with another sulfur. Thus both factors seem to enhance the anomeric effect in trithianes.

Experimental

PMR Measurement. The PMR spectra were recorded on a Hitachi R 20B spectrometer equipped with a temperature variation accessory. Temperature was read by the chemical shift difference of methyl and hydroxy protons of methanol at the low temperature and those of ethylene glycol at room temperature or above.

2-Phenylthio-1,3,5-trithiane (1), mp 123.0—123.5 °C, was prepared from 2-benzoyloxy-1,3,5-trithiane and benzenethiol as reported previously.[5]

2-Methylthio-1,3,5-trithiane (2). A solution of 2 g (9 mmol) of 2-benzoyloxy-1,3,5-trithiane[5] and 1.5 g (30 mmol) of methanethiol in 30 ml of chloroform was heated for 5 hr in a reaction vessel equipped with a Dry Ice condenser. Benzoic acid produced during the reaction was removed by passing the solution through a potassium carbonate layer and the solvent was evaporated to give crude products (95 %). Recrystallization from carbon tetrachloride–chloroform (1 : 1 v/v) gave a pure compound, mp 94—95 °C. Found: C, 26.27; H, 4.20%. Calcd for $C_4H_8S_4$: C, 26.06; H, 4.37%. PMR (CDCl$_3$, δ): 2.21 (s, 3H), 3.73 and 4.63 (q, 4H), 4.95 (s, 1H).

2,4-Bis(phenylthio)-1,3,5-trithianes (3 and 4). A solution of 4 g (0.01 mol) of *cis*-2,4-dibenzoyloxy-1,3,5-trithiane[5] and 3 g (0.03 mol) of benzenethiol in 50 ml of benzene was refluxed for 3 hr. Removal of benzoic acid followed by evaporation of the solvent gave an isomeric mixture of bis(phenylthio) derivatives (95%). They were separated by chromatography on neutral alumina.

Elution with hexane-benzene(7 : 3) afforded the trans isomer which was purified by recrystallization from carbon tetrachloride, mp 97—99 °C. Found: C, 51.03; H, 3.82; 45.04%. Calcd for $C_{15}H_{14}S_5$: C, 50.80; H, 3.98; S, 45.21%. PMR (CDCl$_3$, δ): 4.33 (2, 2H), 5.61 (s, 2H), 7.2—7.6 (m, 10H).

Elution with benzene afforded the crude *cis* isomer which was purified by rechromatography. Found: C, 51.07; H, 4.39%. Calcd for $C_{15}H_{14}S_5$: C, 50.80; H, 3.98%. PMR (CDCl$_3$, δ): 4.03 and 4.18 (q, 2H), 5.09 (s, 2H), 7.2—7.6 (m, 10H).

Equilibration of cis- *and* trans-*2,4-bis(phenylthio)-1,3,5-trithianes.* A solution of 60 mg (0.16 mmol) of **3** and 50 mg (0.4 mmol) of benzoic acid in 0.4 ml of deuteriochloroform was heated in a sealed NMR sample tube at 80 °C. The process of equilibration could be monitored by the careful integration of methine proton signals of the respective isomers. It took 10 hr to reach the equilibrium.

The same equilibrium mixture was obtained by starting from the *trans* isomer (**4**). It took 20 hr to reach the equilibrium.

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