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THE ANOMERIC EFFECT IN 1,3,5-TRITHIANE DERIVATIVES

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Strong anomeric effect is observed in 1,3,5-trithiane derivatives. Phenylthio-axial conformation is found to be more stable than the equatorial in 2-phenylthio-1,3,5-trithiane in contrast to the fact that the anomeric effect is very small in 2-alkylthiothiane. 2-Benzoyloxy-1,3,5-trithane exists solely as the benzoyloxy-axial conformer.

During the course of other study, it became necessary to know the preferred conformation of 1,3,5-trithiane derivatives. This paper concerns with the results of examination of NMR spectra at various temperatures which revealed that, in trithiane derivatives, the anomeric effect with the sulfur-containing substituent is greater than the case of oxane and thiane derivatives.$^{1,2)}$

Although the NMR spectrum of 2-phenylthio-1,3,5-trithiane (1) shows a single peak for the methine proton at 5.35 ppm and a quartet (3.73 and 4.80 ppm and J = 14.5 Hz) for methylene protons in $CDCl_3$ at room temperature, both signals split into a pair of singlets and a pair of quartets respectively at -83°C. The ratio of integrated intensities is 11 and the stable conformer shows the signal of the methine proton at a lower field and that of AB quartet which has a larger chemical shift.

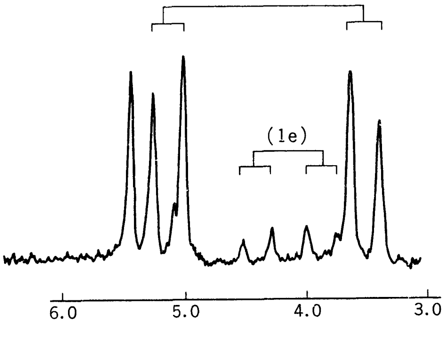
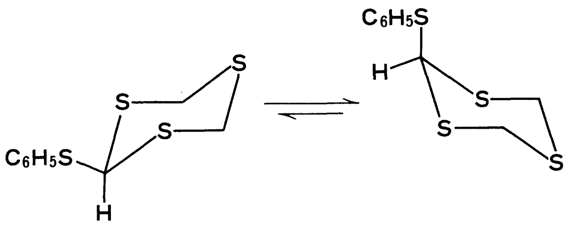


Fig. 1 The NMR spectrum of 2-phenylthio-1,3,5-trithiane at -83°C in CS_2-$CDCl_3$.

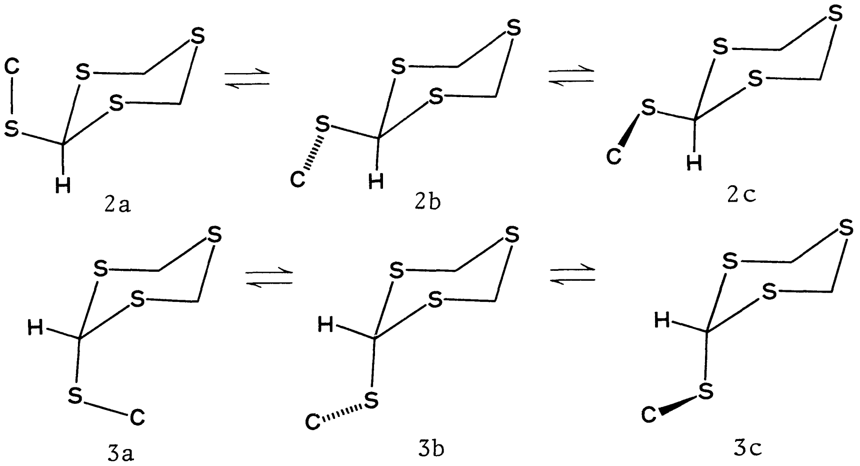
The assignment of the conformations of stable and less stable isomers can be performed in the following way. The NMR spectrum of 1,3,5-trithiane in $CDCl_3$ at -70°C shows a quartet (3.76 and 4.51 ppm and J = 14.7 Hz). The protons at the higher magnetic field are assigned to the equatorial ones[3)] by considering the C-S bond anisotropy.[4)] Since another C-S bond is added to 1,3,5-trithiane in compound 1, the effect of the bond must be estimated. Consideration of the C-S bond anisotropy and the McConnell's equation[5)] reveals that the axial proton of the methylene groups must be further deshielded if the C-S bond is in axial orientation, whereas it is rather shielded if the C-S bond is equatorial. The equatorial protons of the methylene groups at 4 and 6 positions are rather unaffected by introduction of the equatorial C-S bond at 2-position, compared with the axial. Consequently the difference in chemical shifts of the methylene protons is expected to increase as the axial C-S bond is inserted whereas it is relatively unaffected when the C-S bond is equatorial. Then, it is natural to assign the more stable isomer to the phenylthio-axial conformation (1a).



1e 1a

This assignment is supported by the following fact. When the NMR spectrum of 1 is taken as an CD_3COCD_3-$CDCl_3$ solution at -80°C, the population of the conformer which shows the smaller chemical shift difference increases and the ratio becomes 2.3 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. Since the direction of the dipole in thioethers is known to be that of the lone pairs,[6)] the compound 1 is considered to be more polar when it takes the phenylthio equatorial conformation (1e). Thus the conclusion is drawn that 1a conformation is more stable.

It may be argued that, because of the anisotropy of the C-S bond, the equatorial proton should appear at the higher magnetic field than the axial[4)] and that thus the assignment should be reversed. However, the reasons mentioned above are so convincing that the chemical shift of the methine proton only will not be good enough to reverse the assignment. Rather, we believe the following consideration could rationalize the apparent reversal of the chemical shifts of axial-equatorial protons.



Three stable conformations (2a, 2b, and 2c) made by the rotation about the S-$C_{trithiane}$ bond of the phenylthio-equatorial conformation may be considered. On the other hand, of three stable conformations (3a, 3b, and 3c) of the phenylthio-axial form 3a must be very unstable, because this is the phenyl-inside conformation and the severe steric interaction is expected. The difference between the phenylthio-axial and the phenylthio-equatorial conformations is the scarce contribution of 3a to the former. Considered the anisotropy of the C-S bond, conformers b and c are the ones in which the methine proton suffers from the deshielding, whereas the methine proton in conformations 2a and 3a is relatively shielded. Thus near absence of 3a will shift the methine proton signal to lower field relative to the shift of the axial methine proton of the phenylthio-equatorial conformation.$^{7)}$

The conformational energy of the phenylthio group in 1,3,5-trithiane may be estimated by applying the following equation, if the chemical shifts do not drift at various temperatures.

$$\delta_{obs} = N_A\delta_A + N_B\delta_B$$

The assumption may be valid since no significant deviation of chemical shifts was observed between -68°C and -85°C with the $CDCl_3$-CS_2 solution. Thus the chemical shifts after coalescence at various temperatures were observed and equilibrium constants calculated. ΔH and ΔS for the equilibrium 3a $\rightleftarrows$ 3e were thus obtained as 1.4 kcal/mole and 3.1 eu, respectively.

Since even the sulfur atom is favored at the axial orientation, the preference of the oxygen-axial conformation of the oxygen substituent must be still larger. The results with 2-benzoyloxy-1,3,5-trithiane are in conformity with this expectation. The spectrum of this compound shows a quartet (3.72 and 4.96 ppm, J = 15.0 Hz) due to methylene protons. The proton at the higher magnetic field, which is assigned to the equatorial, shows some fine structures to indicate that the molecule is fairly rigid. The spectrum was not affected, although the temperature was lowered to -80°C. These results may best be interpreted as indicating that this compound exists as benzoyloxy-axial conformer only.

The cause for the enhanced anomeric effect in 1,3,5-trithiane may be the presence of lonw pairs of electrons at both sides of the substituent. Possibly the repulsive interaction between the lone pair electrons of the ring-heteroatom and the substituent is relieved by changing the torsion angle about the substituent-ring-carbon bond, in the case of oxanes and thianes. However, in the case of 1,3,5-trithiane, this mode of relief is not possible: increase in torsion angles may decrease the interaction with one sulfur atom on one hand, but on the other, it increases the interaction with another sulfur atom.

References

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