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Nuclear Magnetic Resonance Spectra of 1,3,5-Trithiane and 2,4,6-Substituted 1,3,5-Trithianes[1]

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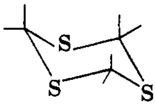
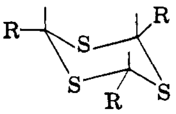
The proton magnetic resonance spectrum of 1,3,5-trithiane indicates a rapidly oscillating chair structure, in which the axial and equatorial hydrogens are indistinguishable. Reconciliation of this evidence with the existing evidence that trithiane is a rigid molecule is based on the ability of NMR to detect interchange rates which are slower than those detectable by optical methods but faster than those detectable by chemical methods. The presence of axial and equatorial hydrogen in a ratio of 2:1 in α-trithioacetaldehyde clearly prove this to be the *cis, trans*-2,4,6-trimethyl-1,3,5-trithiane. Analysis of the NMR spectrum of γ-trithioacetaldehyde confirms its earlier assignment as an eutectic mixture of α- and β-isomers. Likewise the presence of both axial and equatorial hydrogens in α-trithiobenzaldehyde shows it to be the *cis, trans*-2,4,6-triphenyl-1,3,5-trithiane, while the presence of a single trithiane ring hydrogen type in β-trithiobenzaldehyde confirms that it is the all-*cis* isomer. Possible explanations for differences in the relative chemical shifts of the axial and equatorial hydrogens in these particular compounds are offered in terms of the diamagnetic anisotropies of the various groups involved. An unexpectedly large shift in β-trithiobenzaldehyde might be due to an unusual resonance between the benzene and trithiane rings.

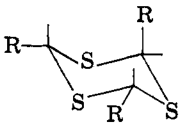
Since the first preparation of 1,3,5-trithiane by Hofmann in 1868,[4] the structure of this substance and its, 2,4,6-trialkyl and 2,4,6-triaryl derivatives have been the subject of controversy. The state of the structural arguments in 1945 were reviewed,[5] with the conclusion that chemically trithiane behaved as a planar or labile puckered symmetrical molecule. This was based chiefly on the isolation of the correct theoretical number of di- and trisulfoxides by Bell and Bennett.[6] X-ray diffraction studies,[7] and more recently electron diffraction[8] and dipole moment studies,[9] all show that the *sym*-trithiane molecule exists solely in the puckered chair form I in the crystal state or in solution.



I



II



III

2,4,6-Trimethyl-1,3,5-trithiane, or trithioacetaldehyde, was originally isolated by Klinger[10] as two isomers, α-, m.p. 101°, and β-, m.p. 126°. Assuming a planar ring, and analogy to maleic and fumaric acids, Baumann and Fromm[11] incorrectly assigned the *cis-trans* configuration III ($R = CH_3$) to the higher melting, less soluble, β-isomer. Chattaway and Kellett,[12] on the basis of isolation of the theoretical number of monosulfones (two from α, one from β), suggested that the higher melting β-form was actually all *cis*. This was confirmed by Hassell and Viervoll,[8] who identified β-trithioacetaldehyde as the symmetrical *cis,cis*-2,4,6-trimethyl-1,3,5-trithiane, a chair structure with all equatorial methyl groups (II, $R = CH_3$) and α-trithioacetaldehyde as the corresponding *cis, trans* isomer having one axial methyl group (III, $R = CH_3$).

A third isomer, γ-trithioacetaldehyde, m.p. 76°, which was described and discussed at some length for a time[13,14] was shown to be a difficulty separable eutectic mixture of 60% α- and 40% β-isomers.[14,15] Even so, the existence of a γ-isomer has been claimed as support for other structural theories.[16]

The history of the elucidation of the structure of the isomeric 2,4,6-triaryl-1,3,5-trithianes (trithiobenzaldehydes) parallels that of the trithioacetaldehydes. Baumann and Fromm[17a] isolated α-, m.p. 166–167°, and β-, m.p. 225–226°, trithiobenzaldehyde and later[17b] showed by molecular weight determinations that a compound reported by Klinger[17c] as α-trithiobenzaldehyde (m.p. 83–85°)

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[4] A. W. Hofmann, *Ann.*, **145,** 360 (1868).

[5] E. Campaigne, *Chem. Revs.*, **39,** 42–46 (1946).

[6] E. V. Bell and G. M. Bennett, *J. Chem. Soc.*, 15 (1929).

[7] N. F. Moerman and E. H. Wibenga, *Z. Krist.*, **97,** 323 (1937).

[8] O. Hassell and H. Viervoll, *Acta Chim. Scand.* **1,** 149 (1947).

[9] K. E. Calderbank and R. J. W. Le Fevre, *J. Chem. Soc.*, 199 (1949).

[10] H. Klinger, *Ber.*, **10,** 1023 (1878).

[11] E. Baumann and E. Fromm, *Ber.*, **24,** 1428 (1891). *Cf.* also K. V. Auwers and B. Ottens, *Ber.*, **57,** 439 (1924). The proper analogy, to the hexahydroisophthalic acids, would have led to the correct conclusion.

[12] F. D. Chattaway and E. G. Kellett, *J. Chem. Soc.*, 1359 (1930).

[13] W. Marckwald, *Ber.*, **19,** 1826 (1886).

[14] E. V. Bell, G. M. Bennett, and F. G. Mann, *J. Chem. Soc.*, 1462 (1929).

[15] J. F. Suyver, *Rec. trav. chim.*, **24,** 377 (1905).

[16] *Cf.* A. Schonberg and M. Z. Barakat, *J. Chem. Soc.*, 693 (1947).

[17] (a) E. Baumann and E. Fromm, *Ber.*, **22,** 2600 (1889). (b) E. Baumann and E. Fromm, *Ber.*, **24,** 1431 (1891). (c) Klinger, *Ber.*, **9,** 1893 (1876).

was actually $(C_6H_5CHS)_9$. Some forty or more different aromatic aldehydes have been converted to trithianes,[18,19] but never more than two isomers have been obtained, and for some only one trithiane could be prepared. It is generally assumed that the all-*cis* equatorial isomer is the compound isolated when only one trithiane can be found, but there is no proof of this. The only direct evidence for the structure of the trithiobenzaldehydes so far separated was obtained by Hayasaki,[20] who reported a difference in the dipole moments of the α- and β-isomers of trithio-*p*-bromo- and thithio-*p*-chlorobenzaldehydes. These values were in agreement with calculated values for a chair trithiane ring having all-equatorial *p*-halophenyl groups in the β-isomer (II, R = *p*-XC_6H_4) and one axial *p*-halophenyl (III, R = *p*-XC_6H_4) in the α-isomer. Similar calculated values for planar or boat forms did not agree with the experimental values.

It would be of interest to have further unambiguous proof of the structure of the isomeric substituted trithianes, particularly in the benzaldehyde series, where melting points are sometimes very close. NMR appears to offer a rapid and convenient tool for differentiating between the all *cis* and *cis,trans* forms. It has been shown[21] that axial and equatorial hydrogen atoms in a six-membered ring resonate at different field strengths. Trithiane rings having all-*cis* equatorial substituents should therefore exhibit only one ring hydrogen peak, while the *cis, trans* isomer should have two peaks for ring hydrogens, in a ratio of 2:1. Such NMR studies should also supply useful information pertaining to the identification of axial and equatorial groups on six-membered rings in general.

EXPERIMENTAL

sym-Trithiane. The crude product, prepared by the method of Bost and Constable[22] in 70% yield, melted at 243–245° after drying in air overnight. Recrystallizing from benzene produced small hexagonal blocks which sintered at 215°, and melted from 219–220° (corr.).

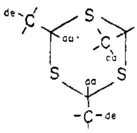
α-Trithioacetaldehyde. Following the method of Suyver,[15] treatment of freshly distilled acetaldehyde with hydrogen sulfide in 2*N* hydrochloric acid at 15° produced a white solid which was recrystallized several times from ethanol as white needles melting sharply at 100.5–101°.

γ- and β-Trithioacetaldehydes.[15] Treatment of freshly distilled acetaldehyde in concd. hydrochloric acid with hydrogen sulfide and hydrogen chloride at ambient temperature produced a white solid melting at 77–80°. Three recrystallizations from acetone gave material melting from 82–85°, which was taken as γ-trithioacetaldehyde. Recrystallization from *n*-hexane produced fine needles of β-trithioacetaldehyde, m.p. 126–127°. The mother liquors of these recrystallizations deposited warty aggregates of the α-isomer, melting at 100–101° after further recrystallization from alcohol.

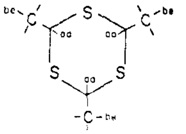
α- and β-Trithiobenzaldehyde. Treatment of 50 g. of benzaldehyde with hydrogen sulfide and dry hydrogen chloride in ethanol at −5° to 0°[15] produced a mixture of white crystals and red resinous polymer. Extraction with nitromethane removed the white product, and addition of benzene to the nitromethane solution caused precipitation of 25 g. of β-trithiobenzaldehyde, melting at 229–230° after further recrystallization from benzene. Addition of ethanol to the nitromethane-benzene mother liquor caused the α-isomer (1 g.) to crystallize. It melted at 166–167° after further recrystallization from ethanol.

NMR spectra were produced with a modified Varian V-4300 B spectrometer operating at 40 mc. The magnetic field was stabilized to an extremely high degree by proton-resonance control in addition to the Varian Super Stabilizer. The peak separations were precise to ±2 c.p.s. (0.5 p.p. 10 m.). Operating variables were as indicated in the figures.[23] The cross-hatched portions of Figs. 1 and 2 are resonances

α-Isomer (2,*trans* 4, *trans* 6), m.p. 100.5–101°



β-Isomer (2, *cis* 4, *cis* 6), m.p. 126–127°



γ-Isomer, m.p. 82°–85°

Mixture of 56% α-isomer and 44% β-isomer

Note: In the structure diagrams the first small letter denotes hydrogen type while the second denotes axial or equatorial position.

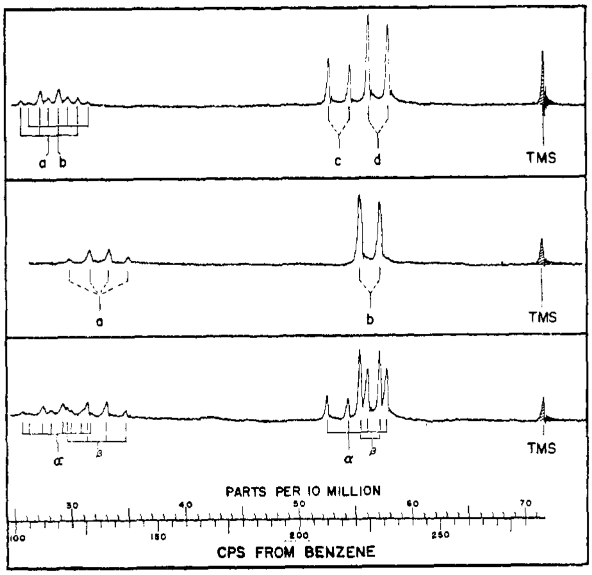


Fig. 1. 2,4,6-Trimethyl-1,3,5-trithiacyclohexanes (trithioacetaldehydes)

Purity: Recrystallized; see m.p. data. Concentration and solvent: 10 wt. % in carbon tetrachloride. Int. Std.: Tetramethylsilane (<1%). Freq.: 40 mc. Isotope: H^1. H_1: 0.04 milligauss. Scan rate: 1 c.p.s./sec. Sample temp.: Approx. 30°. Date run: Nov. 21, 1958.

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[18] E. Campaigne and W. Budde, *Proc. Indiana Acad. Sci.*, **58**, 111 (1948).

[19] J. A. Stanfield and L. B. Reynolds, Jr., *J. Am. Chem. Soc.*, **74**, 2878 (1952).

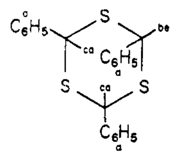
[20] K. Hayasaki, *J. Chem. Soc. Japan, Pure Chem. Sect.*, **74**, 386 (1953); *Chem. Abstr.*, **48**, 11e (1954), *J. Chem. Soc. Japan, Pure Chem. Sect.*, **76**, 284 (1955); *Chem. Abstr.*, **50**, 11749b (1956).

[21] R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Am. Chem. Soc.*, **80**, 6098 (1958).

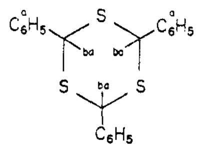
[22] R. W. Bost and E. W. Constable, *Org. Syntheses*, **Coll. Vol. II**, 610 (1943).

[23] The authors are indebted to R. K. Saunders and T. J. Denson of Humble for production of the NMR spectra.

α-Isomer (2, *trans* 4, *trans* 6), m.p. 168–170°



β-Isomer (2, *cis* 4, *cis* 6), m.p. 229–230°



Note: In the structure diagrams the first small letter denotes hydrogen type while the second denotes axial or equatorial position in the most probable conformation.

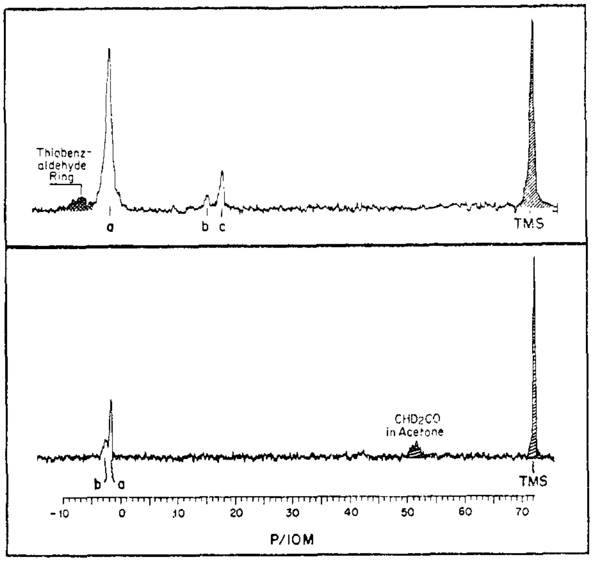


Fig. 2. 2,4,6-Triphenyl-1,3,5-trithiacyclohexanes (trithiobenzaldehydes)

Purity: See m.p. data. Solvents: $CDCl_3$ for α-isomer; CD_3COCD_3 for β-isomer. Concentration: Saturated solutions at 30°. Int. ref.: Tetramethyl silane. Isotope: H^1. Freq.: 40 mc. Scan rate: 2 c.p.s./sec. H_1: 0.04 milligauss. Sample temp.: 30°. Date: Feb. 16, 1959 and Mar. 17, 1959.

not produced by the compound of interest. They are produced by the internal reference compound or by impurities in the sample or solvent and are identified separately on each spectrum.

RESULTS AND DISCUSSION

The NMR spectrum of 1,3,5-trithiane in carbon disulfide consists of a single sharp peak with a chemical shift of 30.2 p.p. 10 m. from benzene (τ 5.82). Because of the low solubility of the compound in acceptable solvents and the resulting low signal to noise ratio, it was not possible to determine whether impurities were present in significant amounts. The chemical shift of the trithiane resonance was determined by use of cyclohexane as an internal reference. The chemical shift is in reasonable agreement with the value predicted from available charts.[24] The spectrum is explained in terms of a rapid interchange of each hydrogen atom of the trithiane ring back and forth between axial and equatorial positions. When a single hydrogen can occupy two different environmental positions in a molecule, the spectrum produced by this hydrogen depends on the length of time it dwells in each environment and the frequency separation between the positions of the resonances corresponding to the two environments. If the frequency of interchange is slow compared to the frequency separation, two sharp peaks corresponding to the two resonance positions will be observed. If the frequency of interchange is much faster than the frequency separation, only one sharp peak will be observed, its position depending on the relative length of time the hydrogen dwells in each environment.[25,26] Since the frequency separation between axial and equatorial positions of the trithiane ring hydrogens appears to be of the order of 4 to 20 c.p.s. (Fig. 1), an interchange rate of only 10 to 50 $sec.^{-1}$ would produce the observed sharp resonance.

No evidence for the existence of a boat form of 1,3,5-trithiane has been reported or seen in the NMR spectrum. Since trithiane was shown to exist only in the chair form in crystals or in solution,[5,7–9] and ultraviolet spectra show interaction of sulfur atoms in trithiane,[27] it might be assumed that the three sulfur atoms of trithiane are held rather rigidly. This assumption is supported by the high melting point and extreme stability of trithiane compared to trioxane. However, since the Franck-Condon principle requires that there be no appreciable motion of atomic nuclei during an electronic transition, the apparent contradiction of the rapidly inverting trithiane molecule as seen by the NMR experiment is merely a graphic illustration of a very important use of NMR, namely, the observation of processes too slow for optical detection and too fast for chemical detection (*e.g.*, changes in molecular conformation and fast exchange reactions).

The spectra of the α-, β-, and γ-trithioacetaldehydes are shown in Fig. 1. The spectrum of the α-isomer exhibits a definite chemical shift between axial (c) and equatorial (d) methyl groups and between axial (a) and equatorial (b) ring hydrogens. The resonances of the axial groups are at lower field positions than the resonances of the corresponding equatorial groups (assuming the most probable conformation is as shown in the structure diagram of Fig. 1). No corresponding axial-equatorial shifts occur in the spectrum of the β-isomer, although the corresponding spin-spin multiplets appear. This is

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[24] Chamberlain, N. F., *Anal. Chem.*, **31**, 56 (1959) reports the shift for CH_2 alpha to an ether oxygen in 5-membered rings averages 36 p.p. 10 m. from benzene, while the shift for CH_2 alpha to a sulfide sulfur in 5-membered rings averages 45 p.p. 10 m. Thus the $—S—CH_2—$ group exhibits a 9 p.p. 10 m. greater chemical shift than the $—O—CH_2$ group in such cyclic structures. The chemical shift of trioxane is 19.6 p.p. 10 m. The predicted shift of trithiane is therefore 19.6 + 9 = 28.6 p.p. 10 m. with a precision of about ±2 p.p. 10 m., as compared to the measured value of 30.2.

[25] *Cf.* H. S. Gutowsky, in *Physical Methods of Chemical Analysis*, Vol. III, W. G. Berl, Ed., Academic Press, New York, 1956, pp. 303–381.

[26] L. H. Piette, *NMR and EPR Spectroscopy*, Pergamon Press, New York, 1960, pp. 140–146.

[27] E. Fehnel and M. Carmack, *J. Am. Chem. Soc.*, **71**, 84 (1949).

completely in accord with the symmetrical structure assigned to this isomer. The γ-isomer is clearly a mixture of the α- and β-isomers, and quantitative measurements indicate it to be 56% α- and 44% β-isomer, in reasonably good agreement with Suyver.[15]

The relative shift between axial and equatorial hydrogens is a function of the diamagnetic anisotropy of nearby bonds or rings and the inductive effects of neighboring atoms or groups. In the asymmetrical α-trithioacetaldehyde, the principal effect is expected to be due to the anisotropy of the carbon-sulfur bonds in the ring. Jackman[28] has shown that the anisotropy of the carbon-carbon single bond is directed so that the resonance of an axial hydrogen is forced to a higher field than that of an equatorial hydrogen. Since the axial hydrogens in α-trithioacetaldehyde resonate at *lower* field than the equatorial hydrogen, it is suggested that the anisotropy of the carbon-sulfur single bond is opposite in sense to that of the carbon-carbon single bond.[29]

The spectra of the trithiobenzaldehydes are shown in Fig. 2. The spectrum of the α-isomer exhibits two resonances (b and c) in a ratio of 2:1 in the region expected[24] for the resonances of the trithiane ring hydrogens of these compounds. The phenyl hydrogen resonance band (a) appears to be somewhat broadened, indicating some nonequivalence among the phenyl hydrogens. Both factors show that the molecule is asymmetric. The spectrum of the β-isomer, on the other hand, exhibits a single trithiane ring hydrogen resonance (b) and a single sharp phenyl hydrogen resonance (a), indicating that this molecule is symmetric. The α-isomer is, therefore, the asymmetric isomer and is presumed to have one equatorial and two axial hydrogens in the most probable conformation. Intensities of the two trithiane ring hydrogen resonances show that the axial hydrogens resonate at higher field than the equatorial hydrogen, just the opposite of the corresponding resonances of the trithioacetaldehydes. This is attributed to the anisotropy (π-electron currents) of the axial benzene ring, which is in a position to produce additional shielding at the axial hydrogens. Calculation of the effect of the benzene ring currents on the relative shifts of the trithiane ring hydrogens by the method of Johnson and Bovey[30] proved inconclusive, however.

The resonances of the trithiane ring hydrogens of the β-isomer are at an unexpectedly low field position. It was necessary to change from deuterochloroform to deuteroacetone solvent to make this resonance visible apart from that of the phenyl hydrogens.[31] A calculation of the effect of the benzene ring currents in β-trithiobenzaldehyde accounts for only about half of the additional downfield shift of the trithiane ring hydrogen resonance. The remaining shift may possibly be the result of resonance interaction between the benzene rings and some of the sulfur-carbon resonance structures discussed by Fehnel and Carmack.[27] In particular, structures which lead to positive charges on the hydrogens could produce the necessary additional downfield shift. Since the α-isomer does not exhibit a corresponding shift, it is necessary to assume that the resonance interactions are much stronger in the β-isomer. This effect is not a solvent shift, since the trithiane ring proton resonance in the symmetrical isomer is shifted less than one p.p. 10 m. on changing solvents from deuterochloroform to deuteroacetone.

The above discussion has been confined to qualitative and semiquantitative statements only because some of the necessary data for reliable quantitative calculations are not available to the authors. NMR studies carried out at a range of temperatures, including those low enough to "freeze" trithiane in one conformation, should lead to more precise values for the rates of interconversion and the diamagnetic anisotropies of the bonds in the trithiane ring. Better insight into the nature of the resonance structures which have been postulated may be obtained from the NMR spectra of p-substituted triphenyltrithianes.

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[28] L. M. Jackman, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, Pergamon Press, New York, 1959, pp. 115-119.

[29] After this paper was completed, A. S. Matlack, J. C. W. Chien, and D. S. Breslow, *J. Org. Chem.*, **26**, 1455 (1961), reported the preparation and NMR spectra of α- and β-trithiochloroacetaldehyde. They assigned structures on the basis of the NMR spectra and noted the anomalous (with respect to the work of Lemieux, *et al.*[21]) upfield shift of the equatorial proton in the α-isomer. They sought to explain this shift by the assumption that the α-isomer exists in a boat form, in which there would be two kinds of axial protons, in the ratio 2:1. This explanation, though tempting does not seem reasonable in the light of the results reported here. The axial-equatorial shift in α-trithioacetaldehyde is also upfield, and this molecule has been shown by Hassell and Viervoll[8] to exist in the chair form.

[30] C. E. Johnson and F. A. Bovey, *J. Chem. Phys.*, **29**, 1012-1014 (1958).

[31] Mass spectra of the two triphenyltrithiane samples are very similar, indicating that they are indeed isomers of the same basic structure. Although no parent mass peaks were detected, the presence of large peaks corresponding to the $C_6H_5-\overset{+}{C}=S$ and $C_6H_5-\overset{\overset{H^+}{|}}{C}=S$ ions shows that the thiobenzaldehyde group comprises at least a major portion of both molecules. This is additional evidence that these samples are the two isomers of trithiobenzaldehyde, and that the unexpected chemical shift is not the result of unexpected molecular structure. The authors are indebted to T. Aczel and H. E. Lumpkin of Humble for determining and interpreting the mass spectra.