

The Structure of the Stereoisomeric Trithianes¹

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When acetaldehyde is treated with hydrogen sulfide and hydrogen chloride, trithioacetaldehyde is formed, and originally (1) three different isomers; α , m.p. 101°; β ; m.p. 125-6°, and γ ; m.p. 81°; were isolated. It was possible to convert α into β by heating with iodine or acetyl chloride. Since the trithiane ring was assumed to be planar, only two isomers, cis-cis (I) and cis-trans (II) should exist. Suyver (2) demonstrated that a eutectic mixture of 60% α and 40% β isomer melts sharply at 75-76° and it was generally conceded that this is the explanation of the γ -isomer. It is still reported in the handbooks, however, and crops up as justification for different structures of the trithiane ring. In 1947, Schonberg and Barakat (3), disturbed by the ready interchange of α to β forms in a cyclic system in which tautomerism is presumably impossible, proposed the following theory:

"The three carbon atoms and the three sulfur atoms in 1, 3, 5-trithiane molecules do not lie in one plane, but may be regarded as 'boat' and 'chair' structures, the interconversion then being readily explained. According to this explanation, the α - and β -forms of trithioacetaldehyde, for example, are either both cis- or both trans-forms; the isomeric change is due to a change of 'boat' into 'chair' structures, or vice versa. This new theory demands a greater number of isomers than have, so far, been isolated, but it is not thereby necessarily invalidated, for some isomers (γ -forms) have occasionally been described, which have been attributed *inter alia* to polymorphism or the occurrence of eutectic mixtures.

"In harmony with the new theory is the fact that the molecule of trithioformaldehyde in benzene solution and in the crystal contains not a planar but a puckered six-membered ring (4)."

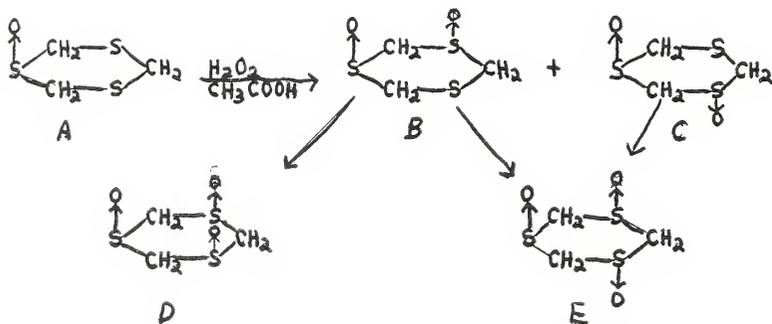
Schonberg attributes the stability of the "boat" and "chair" forms to resonance.

Hinsberg (5) claimed to have isolated two forms of s-trithiane, but Fromm and Soffner (6) repeated the work and claimed that Hinsberg's second compound was actually a cyclic methylene sulfur compound, (CH₂S)_x, where x was greater than 3. In 1929, the planar configuration of the s-trithiane ring was regarded as certain after Bell and Bennett (7) were able to separate all of the isomeric di- and tri-sulfoxides which would theoretically exist for a planar trimethylene trisulfide ring. Oxidation of s-trithiane with hydrogen peroxide in acetone yielded only

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one monoxide, A. Further oxidation with the calculated amount of hydrogen peroxide in acetic acid gave two disulfoxides, B and C, which could be separated by fractional crystallization from water. Since these oxides decompose at high temperatures without melting, their *non-identity* was demonstrated by their crystalline properties and solubility. Compound C, upon further oxidation yielded only one trisulfoxide, E. The



trans-configuration was therefore assigned to C, and *cis-trans* to E. This agrees with their solubilities and stabilities. Compound B upon further oxidation yielded two trisulfoxides, which were separated by fractional crystallization. One of these was identical with E, and the other, D, was assigned the *cis-cis* configuration. This would indicate that B has the *cis*-configuration.

It would seem that Schonberg's principle objection to *cis-cis* and *cis-trans* forms, the ready interconversion of α to β , could be explained by an actual tautomerism:



This is supported by some evidence obtained by Worner (8) and by our group.

Worner (8) studied isomers of the trithiobenzaldehyde series, and carefully developed methods of separating these isomers. In no case did he find more than two isomers formed in thirty different substituted benzaldehydes used. He did find that substituents exerted an influence on the products formed. Thus with certain substituents, both α and β forms could be isolated, while in other cases only one form was obtained. In some cases no trimer could be isolated. Results can be illustrated by a table.

TABLE I. Influence of Substituents on Formation of Thiobenzaldehyde Trimers.

Substituents	No. of Trimers Formed	Substituents	No. of Trimers Formed
none	2	2, 5-di-CH ₃ O—	2
4-CH ₃ O—	2	4-iso-C ₃ H ₇	2
2-CH ₃ O	2	3-CH ₃ —	2
2-iso-C ₄ H ₉ O—	2	4-CH ₃ —	2
3, 4-di-CH ₃ O—	2	2-Br—	2
3, 4-CH ₂ O ₂ =	2	4-Br—	2
3-CH ₃ O—4-OH—	1	2, 4, 6-tri CH ₃ —	1
		(not checked carefully for 2 forms) (9)	
2-HO—	1	3-NO ₂ -4-CH ₃ O	1
3-HO—	1	3-NO ₂ -4-iso-C ₃ H ₇	1
4-HO—	1	3, 5-di NO ₂ -4-CH ₃ O—	1
		2-CH ₃ -4-OH-5-iso-C ₃ H ₇ —	1 (a)
2-C ₆ H ₅ COO—	1	2-NO ₂ —	0
3-C ₆ H ₅ COO—	1	(linear polymer)	
3-CH ₃ O—	1 (?)	3-NO ₂ —	0 (ditto)
4-C ₆ H ₅ COO—	1	4-NO ₂ —	0 (ditto)
4-CH ₃ COO	1 (a)	4-CN	0 (ditto) (a)
3-CH ₃ O—4-C ₆ H ₅ COO—	1	4-COOH	0 (ditto) (a)
2, 5-di-OH—	1	4-COOC ₂ H ₅	0 (ditto) (a)

(a) Prepared in this laboratory.

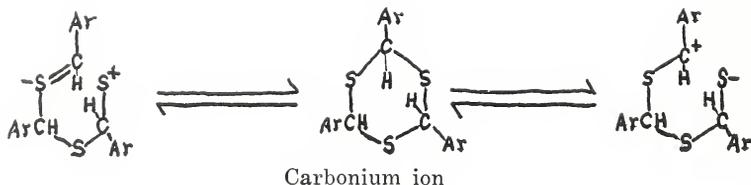
The following related compounds were also prepared:

Compound	No. of Trimers Formed
trithiocinnamaldehyde	2 forms
trithiofurfural	2 forms
trithio-2-thenaldehyde	2 forms
trithio-3-thenaldehyde	2 forms (a)
trithio-2-ethoxy-1-naphthaldehyde	1 form

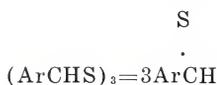
(a) Prepared in this laboratory.

A theory which accounts for most of the cases is as follows:

Just as predicted by the laws of probability, an aryl thioaldehyde may trimerize to give both *cis-cis* and *cis-trans* forms of the puckered "chair" form. (No "boat" forms have been found (4).) In some cases, the resulting trimers are unstable due to the presence of certain labilizing groups on the aromatic ring. One form is always less stable than the other form. The influence of the substituent is due to its electron-attracting or electron-releasing effects.

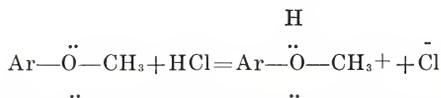


Thus a strong electron-releasing group Ar would allow carbonium ion formation and promote rearrangement of the α to the more stable β form. In the same way a strong electron-attracting Ar group would promote carbanion formation and have a similar effect. Polymer formation would be promoted in either case, and might predominate even over the β -trimer. The above dissociation can just as readily be written:



In this case the same reasoning applies, and dissociation is promoted by either electron-releasing or electron-attracting substituents on the aromatic ring. Thus extremely stable trimers were isolated in two forms, extremely unstable ones dissociate and form polymers, and intermediate stability is represented where only one form was isolated. The dissociation to monomer actually occurs, as shown by the fact that cryoscopic molecular weight determinations of the trimers which are obtained in only one form are usually low (see experimental values).

A glance at Table I shows that all of the aldehydes which yield only one trimer have strong electron-releasing groups, i.e. hydroxy or acyloxy or strong electron-attracting groups, i.e. nitro. Since acyloxy compounds yield only one isomer, it is surprising that methoxy compounds yield two, as methoxy groups are also strongly electron-releasing. It is possible that the hydrogen chloride used as a catalyst coordinates with the ether linkage, forming a weak electron-attracting group, thus permitting both α - and β -forms to be isolated (Note I).



This possibility is substantiated by the observation that when anhydrous zinc chloride is used as a catalyst with anisaldehyde, only the β -isomer of the trithial is obtained, along with linear polymer. A nitro group alone prevents trimerization, but 3-nitro-4-anisaldehyde has two counter-influences in the 3-nitro and 4-methoxy groups, the latter of which does not now coordinate due to lack of basicity (note ortho-nitroaniline).

The lack of a second isomer of *m*-methoxybenzaldehyde can only

Note I. The coordination of hydrogen chloride with ethers is well known; thus anisaldehyde is quite soluble in concentrated HCl, but insoluble in water. Benzaldehyde is insoluble in concentrated HCl.

be explained on the basis of poor technique. It should be present, but may be difficult to isolate.

Compounds which yield two isomers, such as the halogen or alkyl-substituted benzaldehydes, have only weakly electron releasing groups present. It is probable that further work will show that two isomers of trithiomesitaldehyde do exist.

Since the nitro-group was the only strong electron-attracting group which had been incorporated in the molecule, we tried several other such groups with the same results. When p-cyanobenzaldehyde, p-carboxybenzaldehyde, and p-carbethoxybenzaldehyde were treated with hydrogen chloride and hydrogen sulfide in alcohol, only linear polymers of high molecular weight were obtained.

Amino- and substituted amino-groups should represent good examples of electron-releasing and, in acidic solution, electron-attracting groups. p-Aminobenzaldehyde polymerized in acidic solution, but when p-dimethyl- and p-diethylaminobenzaldehyde were treated in the usual manner, crystalline trimers were obtained, only one form being isolated (Table II).

TABLE II. Aminobenzaldehyde products.

Product	M.P.	% Yield	Anal, % S		Mol. Wt.	
			Calcd.	Found	Calcd.	Found
$(p-(\text{CH}_3)_2\text{NC}_6\text{H}_4\text{CHS})_3$	224-5°	81	19.40	20.00	495	467
$(p-(\text{C}_2\text{H}_5)_2\text{NC}_6\text{H}_4\text{CHS})_3$	146-8°	82	16.59	16.48	579	535
$(p-\text{CH}_3\text{CONHC}_6\text{H}_4\text{CHS})_3$	174-6°	70	17.88	17.79		(none)
$(p-\text{C}_6\text{H}_5\text{CONHC}_6\text{H}_4\text{CHS})_3$	264-6°	35	13.29	13.99		(none)

p-Acetaminothiobenzaldehyde was obtained also in what was apparently a trimeric form, but no cryoscopic solvent was found for it. Bromoform was found useful for the dialkylaminothiobenzaldehydes and oxygen-substituted compounds, but could not be used for the acetamino- and benzoylamino-compounds. p-Benzoylaminothiobenzaldehyde apparently formed a polymer, having 16 or 17 units in the chain. When the trithio-p-acetaminobenzaldehyde was hydrolyzed by boiling in aqueous HCl, some hydrogen sulfide was evolved, and a complex polymer was formed! It may be safely stated that the dimethylammonium and diethylammonium groups function as strong electron-attracting groups also, permitting only one trimer to be obtained.

Experimental

Trithio-p-acetoxybenzaldehyde: A solution of 10.1g (0.062mole) of p-acetoxybenzaldehyde in 40 ml. of glacial acetic acid containing 5ml. of propionic acid was cooled to 0° in an ice bath. Hydrogen sulfide and hydrogen chloride were passed into the solution for two hours, after

which the mixture was allowed to stand in the cold for one hour. The slurry of crystals was poured into cold water with stirring, and the solid filtered out and dried. The crude product was recrystallized repeatedly from methanol, yielding glittering white needles which melted at 186-7°. The yield of purified material was 2.8g. or 25%.

Anal: Calcd. for $C_{22}H_{24}O_6S_3$; %S, 17.89; m.w. 540. Found; %S, 18.06; m.w. (Cryoscopically in bromoform) 467.

When the above compound was hydrolyzed by refluxing in a mixture of ethanol and hydrochloric acid for four hours, p-hydroxybenzaldehyde was obtained in 82% yield.

Its identity was further confirmed by conversion to p, p'-diacetoxy-stilbene, as follows: 2.0g of trithio-p-acetoxybenzaldehyde was refluxed in 40 ml. of xylene with 2.0g of copper powder for sixteen hours, and the hot solution filtered. On cooling, a precipitate formed which yielded long white needles, after recrystallization from nitro-methane, which melted at 211-213°. ter Meer (10) reported p,p'-diacetoxy-stilbene to melt at 213°.

Confirmation of the *cis-trans* configuration for trithio-p-acetoxybenzaldehyde was obtained by its preparation from trithio-p-hydroxybenzaldehyde, which had previously been prepared by Kopp (11). A solution of 2.0g of trithio-p-hydroxybenzaldehyde in 15 ml. of acetic anhydride containing 5g of anhydrous potassium acetate was heated on a steam bath for two hours and poured into 50 ml. of cold water. The solid was recrystallized several times from methanol, yielding 75% of the theoretical amount of glittering white needles which melted at 187-188°, and caused no depression in melting point when mixed with the compound prepared from p-acetoxybenzaldehyde.

Trithio-4-thymolaldehyde: 4-thymolaldehyde was prepared by the method of Adams and Montgomery (12). A solution of 3.0g (0.02 mole) of this substance in 40 ml. of ethanol was cooled to -3° in an ice-salt bath, and hydrogen sulfide gas slowly bubbled in the mixture. After 10 minutes hydrogen chloride was also bubbled through the solution, and the temperature was maintained at -5° to +3°. The solution became quite viscous after two hours, and was allowed to stand in the cold for two hours longer, but no precipitate appeared. It was then poured into 200 ml. of cold water with stirring, and the white solid crystallized from hot 50% aqueous ethanol in white needles which weighed 2.8g (76%) and melted at 245-246°.

Anal: Calcd. for $C_{33}H_{42}O_3S_3$; %S, 16.48, m.w., 582. Found; %S, 16.40, m.w. (Cryoscopically in glacial acetic Acid) 483.

α- and β-Trithio-3-thenaldehydes: A solution of 5g (0.045 mole) of 3-thenaldehyde (13) in 30 ml. of a one-third saturated solution of hydrogen chloride in ethanol was cooled to -15° in a Dry Ice-ether bath, and hydrogen sulfide was bubbled into the mixture for one and one-half hours. The solution turns red, and finally forms a slurry of yellow crystals. After standing at -5° for one hour, the solid was removed,

washed with cold ethanol, and dried. It weighed 5.6g (98%). It was extracted by refluxing with three 50ml. portions of boiling benzene, and the residue recrystallized from chloroform to yield small white needles of the β -isomer, melting at 217-218°, and weighing 1.4g (25%).

Anal: Calcd. for $C_{15}H_{12}S_6$; %S, 50.01, m.w. 384. Found; %S, 49.98, m.w. (Cryoscopically in naphthalene) 378.

The benzene extracts of the crude thioaldehyde were evaporated to dryness on a steam bath, and the residue recrystallized twice from nitro-methane, yielding thick white needles of the α -isomer, which melted at 179-180° and weighed 1.7g (30%).

Anal: Calcd. for $C_{15}H_{12}S_6$; %S, 50.01, m.w. 384. Found; %S, 49.88, m.w. 372.

When a small sample of the α -isomer was refluxed in benzene with a crystal of iodine, it was readily converted to the higher melting β -isomer.

Trithio-p-dimethylaminobenzaldehyde: This compound was prepared in a variety of ways, in an effort to isolate a second isomer, but since the same product was obtained in all cases, only the most convenient preparation is described. A solution of 3g (0.02 mole) of p-dimethylaminobenzaldehyde in 45 ml. of 10 N hydrochloric acid was cooled to -5° in an ice-salt bath, and a vigorous stream of hydrogen sulfide was passed through the mixture for one and one-half hours. The solution was then saturated with hydrogen chloride and allowed to stand for one hour. The yellow solution was diluted with 50 ml. of cold water and then made basic with 30% potassium hydroxide solution. The crude yellow precipitate was washed with water and recrystallized from nitromethane in slender yellow needles, which weighed 2.7g (81.4%) and melted at 224-225°.

Anal: Calcd. for $C_{27}H_{33}N_3S_3$; %S, 19.40, m.w. 495. Found; %S, 20.00, m.w. (Cryoscopically in bromoform) 467.

p, p' Di (dimethylamino) stilbene: A mixture of 0.54g of trithio-p-dimethylaminobenzaldehyde and 0.56g of copper powder in 30 ml. of xylene was refluxed for seven hours. The solution exhibited a strong violet fluorescence, and after removing the copper sulfide and cooling, deposited greenish-yellow crystals which weighed 0.22g (50%) and melted at 253-254°.

Anal Calcd. for $C_{15}H_{22}N_2$; %N, 10.53. Found; %N, 10.12.

Trithio-p-diethylaminobenzaldehyde: This compound was prepared by the same procedure as given for the dimethylamine derivative. In a typical experiment, 2.0g of p-diethylaminobenzaldehyde dissolved in 40 ml. of 12 N hydrochloric acid gave 1.8g (82%) of the pure thioaldehyde after recrystallization from nitromethane. The yellow needles melted at 196-198°.

Anal: Calcd. for $C_{33}H_{45}N_3S_3$; %S, 16.59, m.w., 579. Found; %S, 16.48, m.w. (Cryoscopically in bromoform) 535.

Trithio-p-acetaminobenzaldehyde: A solution of 6g (0.037 mole) of p-acetaminobenzaldehyde (14) in 50 ml. of a one-fifth saturated solution of hydrogen chloride in "Cellosolve" was cooled to -25° in a Dry-Ice-ether bath, and a slow stream of hydrogen sulfide introduced for two hours. The viscous yellow mixture was let stand one hour, and then poured into 150 ml. of cold water with vigorous stirring. The oil which precipitated solidified and was crystallized from ethanol, yielding 4.5g (70%) of white crystals which melted at $174-176^{\circ}$.

Anal: Calcd. for $C_{11}H_{12}O_3N_3S_3$; %S, 17.88. Found; %S, 17.79.

When the above experiment was carried out in ethanol solution, a product which melted at $261-262^{\circ}$, and was insoluble in most organic solvents, was produced. Sulfur analysis for this compound was less than the calculated value for a trimer. Its properties suggest a linear polymer.

p-Benzoylaminobenzaldehyde oxime: Pfeiffer (15) reports the melting point of p-benzoylaminobenzaldehyde as $146-147^{\circ}$. When p-aminobenzaldehyde was benzoylated by the Hinsberg method in dioxane, and the product recrystallized from ethanol-water mixture, a 77% yield of a white solid which melted at $149-150^{\circ}$ was obtained. The oxime has not previously been reported. It was prepared by the usual procedure and recrystallized from ethanol, and melted at $192-194^{\circ}$.

Anal: Calcd. for $C_{14}H_{12}O_2N_2$; %N, 11.66. Found; %N, 11.74.

p-Benzoylaminothiobenzaldehyde: A suspension of 24g (0.107 mole) of p-benzoylaminobenzaldehyde in 300 ml. of ethanol was cooled to 0° in an ice-salt bath, and hydrogen sulfide and hydrogen chloride passed into the mixture for three hours. The mixture was allowed to come to room temperature, and the solid collected, washed with water and dried. The 25g of crude product was dissolved in 200 ml. of boiling pyridine, and 100 ml. of chloroform added to the hot solution. On cooling, 9.0g of a white compound melting at $264-266^{\circ}$ was obtained.

Anal: Calcd. for $C_{14}H_{11}ONS$; %S, 13.29. Found; %S, 13.99.

Assuming that the above compound is a linear polymer of the type, $HS(RCHS)_xH$, the approximate value of x may be calculated from the sulfur analysis as follows:

let $p = \% \text{ Sulfur by analysis}$

w—molecular weight of monomeric thial

$$(32 + 32_x) 100$$

$$\text{then } p = \frac{\quad}{\quad}$$

$$34 + xw$$

$$3200 - 34p$$

$$\text{or } x = \frac{\quad}{\quad}$$

$$pw - 3200$$

For the above analysis,

$$3200 - 34 \cdot 14$$

$$x = \frac{\quad}{\quad} = 17$$

$$241 \cdot 14 - 3200$$

Linear Polymers: When p-cyanobenzaldehyde, p-carboxybenzaldehyde, and p-carbethoxybenzaldehyde were treated with hydrogen sulfide and hydrogen chloride in cold solutions, only intractable, evil-smelling substances which were insoluble in most solvents, were obtained. Some of these were plastic in nature, and most of them contained less than the calculated amount of sulfur, indicating that the polymers formed were of the type $\text{HS}(\text{RCHS})_x(\text{RCHO})_y\text{H}$. All efforts to prepare crystalline trimers were fruitless.

Summary

A theory which reconciles the apparently conflicting evidence for puckered and planar configuration of the trithiane ring has been advanced. This assumes that the ring exists in only one puckered "chair" form, and unsymmetrical trithianes may form *cis-cis* and *cis-trans* isomers of this form. Evidence in support of this theory is cited.

A number of new triaryltrithianes and derivatives have been prepared and characterized, including trithio-p-acetoxybenzaldehyde, trithio-4-thymolaldehyde, α and β -trithio-3-thenaldehyde, trithio-p-dimethylaminobenzaldehyde, trithio-p-diethylaminobenzaldehyde, and trithio-p-acetaminobenzaldehyde.

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