

## THIONES AND THIALS

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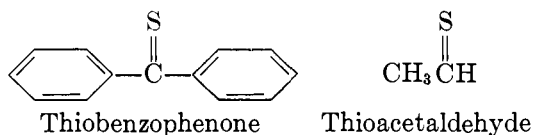
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I. INTRODUCTION

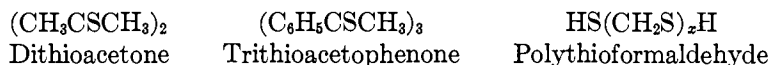
The thiones and thials are compounds of the structure,  $\overset{\text{S}}{\parallel}\text{RCR}'$ , where R and R' may be hydrogen, or alkyl or aryl groups. However, the tendency of the thiocarbonyl group to trimerize or polymerize is so great that it is necessary to include those compounds which can be illustrated by the formula  $(\text{RCSR}')_n$ , where  $n$  is 1, 2, or 3, or by the formula  $\text{HS}(\text{RCSR}')_x\text{H}$ , where  $x$  is any number, usually greater than 3.

II. NOMENCLATURE

Compounds of this type have been given a variety of names in the early literature. Thiobenzaldehyde has been called "sulfurbenzene" (43, 64) and dithioacetone was referred to as "duplosulfacetone" (223). The Geneva System requires the use of the suffixes "thial" and "thione" to indicate the thioaldehydes and thioketones (151). For example, thioacetone is "propane-thione" and thioacetaldehyde is "ethanethial". No provision is made for the naming of the aromatic derivatives. The most common system of nomenclature, and that used here, is to name the compound as the thio derivative of its oxygen analog.



The trimers of thials and thiones are sometimes named as derivatives of the trimethylene trisulfide ring (88, 92, 119). In *The Ring Index* (152) preference is given to *s*-trithiane. However, the relation of the monomers, dimers, trimers, and polymers is more clearly indicated by the most commonly used system of naming them as multiples of the parent thiocarbonyl compound. For example:



The general class of compounds usually referred to as thioketones has been indexed since 1938 by *Chemical Abstracts* under the name "thiones", as suggested by the Definitive Report of the Commission on the Reform of the Nomenclature of Organic Chemistry (152). Since this same report suggests "thials" for thioaldehydes, this term has been used here, although *Chemical Abstracts* uses "aldehydes, thio" for indexing.

These compounds have been briefly discussed by Connor, in his chapter on "Organic Sulfur Compounds," in Gilman's *Organic Chemistry* (50). The monomeric diaryl and heterocyclic thiones have been reviewed by Schönberg (174).

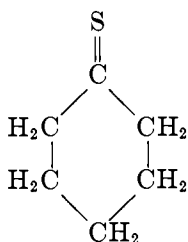
### III. CLASSIFICATION

The thials may be divided into two main groups:

- A. The alkyl thials, RCHS, and
- B. The aryl thials, ArCHS.

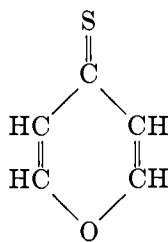
The thiones may be divided into five principal types:

- C. Dialkyl thiones, RCSR',
- D. Alkyl aryl thiones, ArCSR,
- E. Diaryl thiones, ArCSAr',
- F. Homocyclic thiones, like thiocyclohexanone (I), and
- G. Heterocyclic thiones, like  $\gamma$ -thiopyrone (II) and thioacridone (III).

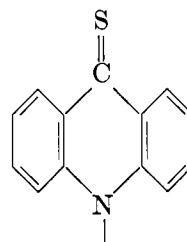


I

Thiocyclohexanone



II

 $\gamma$ -Thiopyrone

III

Thioacridone

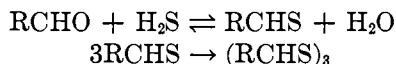
### IV. PREPARATION OF THIALS AND THIONES

#### A. ALKYL THIALS

##### 1. Effect of hydrogen sulfide on aldehydes

Thioformaldehyde has never been prepared in the monomeric form, and in fact it is highly questionable whether any monomeric alkyl thials have ever been

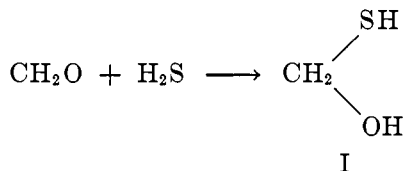
prepared. Methods designed for their synthesis usually lead to the formation of trithials. The most useful and most widely applied method for the preparation of trithials is the treatment of an acid solution of the aldehyde with hydrogen sulfide.



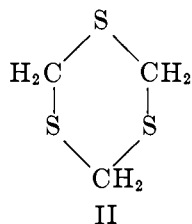
This reaction was first applied to the preparation of thioformaldehyde in 1868 by Hofmann (93), who obtained a compound which melted at 218°C. and for which he suggested the formula  $(\text{CH}_2\text{S})_n$ , which was later (95, 158) changed to  $(\text{CH}_2\text{S})_3$ . Bost and Constable (38) report yields of 92–94 per cent of trithioformaldehyde when hydrogen sulfide is passed for 12 to 24 hr. into a tall cylinder containing a solution of formaldehyde in concentrated hydrochloric acid.

In addition to trithioformaldehyde, a variety of other products have been isolated from this reaction. Baumann (11) isolated a compound which corresponded to the formula  $(\text{CH}_2\text{S})_3\text{CH}_2\text{O}$ . No structure was assigned to this substance, although it was also obtained by Drugman and Stockings (54) when hydrogen sulfide was passed into a neutral solution of formaldehyde. A highly insoluble amorphous white powder, called thiometaformaldehyde, was produced by treating a solution of hexamethylenetetramine with hydrogen sulfide and ammonia (Wohl (224)). Baumann and Fromm (20) also isolated this product, melting at 175–176°C., and assigned to it the polymeric formula  $(\text{CH}_2\text{S})_x$ . Fromm and Soffner (71) describe a dimercaptan melting at 216°C. to which the structure  $\text{HS}(\text{CH}_2\text{S})_x\text{H}$  has been assigned.

Baumann (11) proposed a mechanism for the reaction between hydrogen sulfide and aldehydes which accounted for the formation of these compounds. In the first step, hydrogen sulfide adds to formaldehyde.

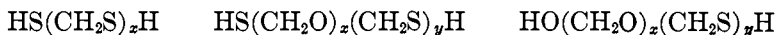


Three molecules of I may then react to give the trimer (II) and water, or they

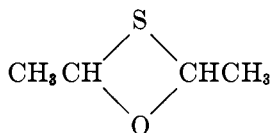


may polymerize to give  $\text{HSCH}_2\text{SCH}_2\text{SCH}_2\text{OH}$  or larger molecules (20). A high concentration of hydrogen ion seems to catalyze the trimerization. At the present time, it would seem that any confusion in the properties of compounds

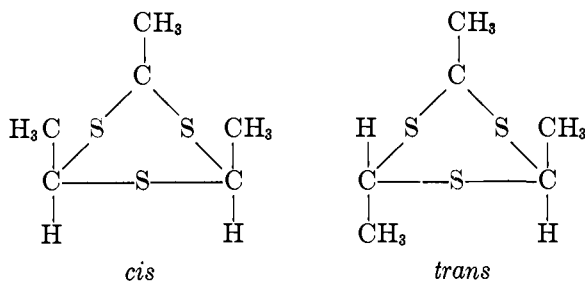
formed in the treatment of formaldehyde with hydrogen sulfide is due to the existence of polymers of the formulas:



The preparation of thioacetaldehyde has also been studied extensively. In 1848, Weidenbusch (221) described a water-insoluble oil produced by treating an aqueous solution of acetaldehyde with hydrogen sulfide. Treatment of this oil with acid gave white crystals which sublimed at 45°C. and had the composition  $\text{C}_4\text{H}_4\text{S}_2$ . Pinner (155) also obtained a low-melting oil by treating acetaldehyde with hydrogen sulfide in aqueous solution; this oil may have been a complex of thioacetaldehyde and acetaldehyde with the structure:



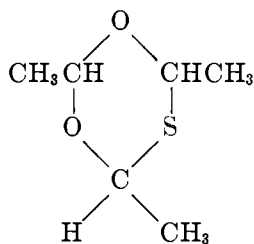
When this oil was treated with concentrated hydrochloric acid, thioacetaldehyde, of indefinite melting point, was obtained. Klinger (105, 107) reinvestigated these products more carefully and isolated an insoluble oil, to which the formula  $(\text{C}_2\text{H}_4\text{S})_3 \cdot \text{H}_2\text{S}$  was assigned. Treatment of this oil with strong acids, or acidification of the original aldehyde solution before addition of the hydrogen sulfide, gave a white crystalline mass which could be separated by recrystallization into two compounds: one melting at 101°C. and designated  $\alpha$ -trithioacetaldehyde; the other melting at 125–126°C. and called  $\beta$ -trithioacetaldehyde. Since molecular-weight determinations showed them both to have the formula  $(\text{CH}_3\text{CHS})_3$ , Klinger pointed out that they may be *cis-trans* isomers. By controlling the conditions, Baumann and Fromm (15) found it possible to prepare either the  $\alpha$ - or the  $\beta$ -form. If acetaldehyde was dissolved in ethyl alcohol



and this solution saturated with dry hydrogen chloride and hydrogen sulfide at 0°C., the  $\beta$ -form, m.p. 125–126°C., was obtained. If the reaction was run at room temperature in hydrochloric acid solution, the  $\alpha$ -form, m.p. 101°C., was obtained. On the other hand, Suyver (215) found that when acetaldehyde was dissolved in 2 *N* hydrochloric acid and hydrogen sulfide added at -15°C.,  $\alpha$ -trithioacetaldehyde was formed. If concentrated hydrochloric acid was used as a solvent and the reaction run at room temperature, the  $\beta$ -isomer was formed. The  $\alpha$ -form may be converted to the  $\beta$ -form by the use of catalysts such as io-

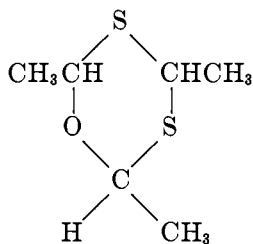
dine, sulfur trioxide, or hydrogen chloride. Drugman and Stockings (54) isolated the  $\alpha$ - and  $\beta$ -forms from an acid solution of acetaldehyde, and also reported a  $\gamma$ -form, m.p. 76°C. The existence of a  $\gamma$ -form is doubtful, however. The question of the absolute configurations of these isomers and of other unsymmetrical thiocarbonyl trimers will be discussed later (Section V, A).

Muller and Schiller (146) attempted to prepare thioacetaldehyde directly from acetylene. A mixture of acetylene and hydrogen sulfide was passed into 63 per cent sulfuric acid containing mercuric sulfate at 30–40°C. The product crystallized in white needles, melting at 78–80°C., and had the composition  $(\text{CH}_3\text{CHS})_3$ . Acetaldehyde was undoubtedly an intermediate in this reaction, however, since monothioparaldehyde (III), melting at 55°C., was also isolated. This compound and dithioparaldehyde (IV), m.p. 70–72°C., had previously been isolated (107, 115, 127). Either of them may be converted to trithioacetaldehyde and acetaldehyde by treatment with strong acids.



III

Monothioparaldehyde



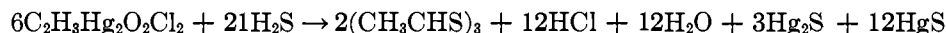
IV

Dithioparaldehyde

Little effort has been made to prepare any alkyl thials of higher molecular weight, either by the use of hydrogen sulfide or by other methods. By the reaction between *n*-valeraldehyde and aqueous hydrogen sulfide Schroder (194) had isolated a compound of very unpleasant odor and melting at 69°C., to which was assigned the monomeric formula  $\text{C}_5\text{H}_{10}\text{S}$ . The color of the compound was not mentioned. About the same time, Pfeiffer (154) treated isobutyraldehyde with hydrogen sulfide and obtained an oil which could be steam distilled, but was not further purified. It had an unpleasant onion-like odor.

Drugman and Stockings (54) discuss the effect of hydrogen sulfide on propionaldehyde and isobutyraldehyde, but did not isolate any pure products.

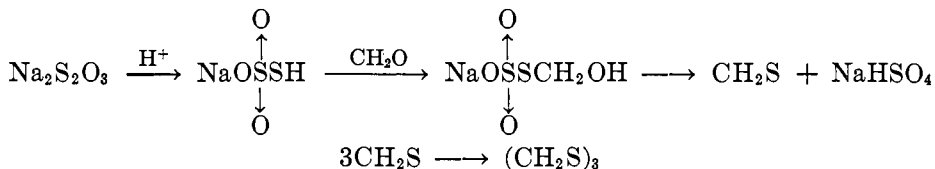
A recent German patent (147) deals with the preparation of unsaturated aliphatic thioaldehydes by treating the unsaturated aldehyde with hydrogen sulfide in a neutral medium, but no specific examples are given. Poleck and Thrummel (158) claim to have isolated the  $\gamma$ -trithioacetaldehyde, m.p. 75–76°C., by treating vinylmercuryoxychloride,  $\text{CH}_2=\text{CHO}_2\text{Hg}_2\text{Cl}_2$ , with hydrogen sulfide. They give the following equation for the reaction:



### 2. Action of sodium thiosulfate on aldehydes

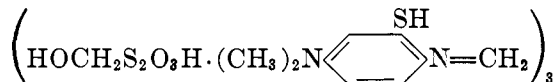
Although the use of hydrogen sulfide has been most widely studied, aliphatic thioaldehydes have been obtained by a number of different methods. Vanino (217, 218) found that addition of hydrochloric acid to a solution of sodium

thiosulfate in formalin produced a mixture of sulfur and trithioformaldehyde. The yield was not reported, but the following mechanism for the reaction was proposed:



When paraldehyde was used in this reaction a compound was obtained which analyzed for  $(\text{CH}_3\text{CHS})_3$ , but it could not be purified.

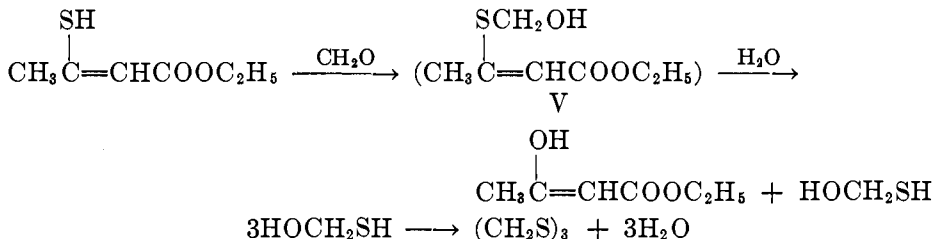
This reaction was also investigated by Schmidt (169, 170), who was able to isolate a salt of the intermediate acid,  $\text{HOCH}_2\text{SSO}_3\text{H}$ , postulated by Vanino. When a solution containing 2-amino-5-dimethylaminothiophenol dissolved in ammonium hydroxide was mixed with sodium thiosulfate and formalin, and acidified with hydrochloric acid, white plate-like crystals were deposited. This compound melted at  $122^\circ\text{C}$ ., analyzed for  $\text{C}_{30}\text{H}_{48}\text{N}_6\text{S}_9\text{O}_{12}$ , and upon treatment with sodium hydroxide produced formaldehyde, sodium thiosulfate, and a polymeric anhydroformaldehyde-2-amino-5-dimethylaminothiophenol. Schmidt therefore proposed the following structure for the salt:



Although both Vanino and Schmidt report that this reaction works with water-soluble aldehydes other than formaldehyde, no compounds except trithioformaldehyde have been reported.

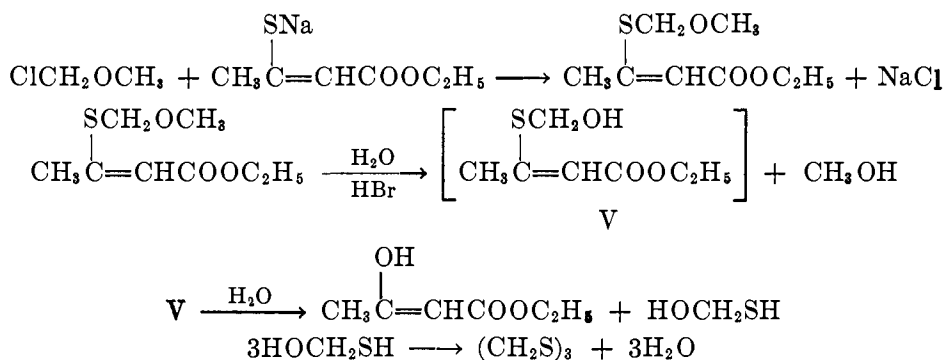
### 3. Reaction of thioacetoacetic esters with aldehydes

S. K. Mitra investigated the  $\beta$ -thioketonic esters (136, 143) extensively, and found that these compounds condensed with aldehydes in the presence of acids and a trace of moisture to form the trithioaldehydes and the ketonic esters. Mitra utilized this reaction to prepare a number of aryl thials, but only one alkyl thial, trithioformaldehyde (142). Trithioformaldehyde, m.p.  $218^\circ\text{C}$ ., was obtained when an alcohol solution of ethyl thioacetoacetate which had been saturated with dry hydrogen chloride at  $0^\circ\text{C}$ . was treated with a 40 per cent solution of formaldehyde, heated on a steam bath, and let stand overnight. Mitra suggests, as a mechanism, addition of the thiol phase of the ester to the aldehyde, and subsequent hydrolysis of the hydroxymethylthioether formed.





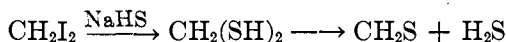
This is similar to the mechanism proposed by Baumann (11) for the reaction of hydrogen sulfide with aldehydes. As evidence in support of this mechanism, Mitra found that the reaction required a trace of moisture, and he was also able to prepare the methyl ether of the hypothetical ethyl  $\beta$ -hydroxymethylmercaptocrotonate (V) (142). A mixture of chloromethyl ether and ethyl sodiothioacetoacetate was refluxed in benzene for 6 hr., to give the ethyl  $\beta$ -methoxymethylmercaptocrotonate,  $C_8H_{11}SO_3$ ,  $b_{12}$  120°C. Hydrolysis of this oil with concentrated hydrobromic acid at room temperature gave trithioformaldehyde.



The same reaction occurred when ethyl  $\alpha$ -isobutylthioacetoacetate was used in place of ethyl thioacetoacetate.

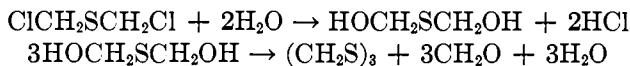
#### 4. Reaction of sulfides with alkyl halides

A well-known method of preparing mercaptans is to treat an alkyl halide with a metal sulfide or bisulfide. Husemann (98) attempted to apply this reaction to the preparation of thioformaldehyde.

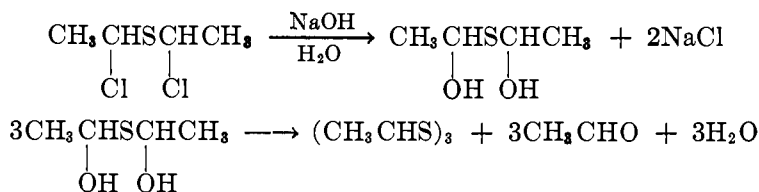


When methylene iodide was refluxed with sodium bisulfide in alcohol, a white powder was obtained which sublimed at 150°C. The compound had many of the reactions of trithioformaldehyde, forming addition products with metal salts and oxidizing to a sulfoxide. Husemann called it dimethylenesulfur and assumed it to be  $(\text{CH}_2\text{S})_2$ . It behaved like a compound prepared by Girard with the empirical formula  $\text{CH}_2\text{S}$  (76).

The trithioaldehydes are obtained when  $\alpha, \alpha'$ -dichlorodialkyl sulfides are hydrolyzed. Block and Hohn (36) obtained trithioformaldehyde when dichlorodimethyl sulfide was treated with water.



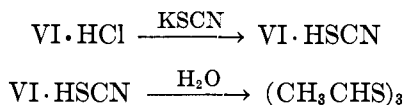
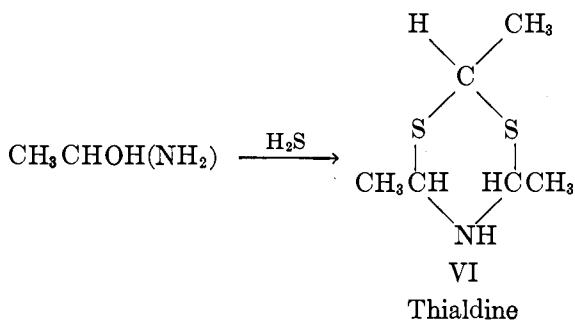
Mann and Pope (125) obtained the  $\gamma$ -trithioacetaldehyde, m.p. 81°C., when  $\alpha, \alpha'$ -dichlorodiethyl sulfide was treated with silver sulfide, hydrogen sulfide, silver oxide, or sodium hydroxide. These reactions are probably similar to the hydrolysis of the dichlorodimethyl sulfide.



These same authors (126) noted that  $\beta$ -trithioacetaldehyde was obtained when diethylidene trisulfide,  $(\text{CH}_3\text{CH})_2\text{S}_3$ , was treated with methyl iodide. None of these methods are useful preparative methods, since the  $\alpha, \alpha'$ -dichlorodialkyl sulfides and diethylidene trisulfide are prepared from the trithioaldehydes originally.

### 5. Special preparations

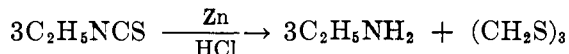
(a) *Thialdine thiocyanate*: Marckwald investigated the decomposition of thialdine thiocyanate (127). Thialdine (VI) was prepared by passing hydrogen sulfide into a solution of aldehyde ammonia. The thiocyanate was made from it by treating a solution of thialdine hydrochloride with excess potassium thiocyanate.



Boiling this salt with water caused it to decompose, and crystals<sup>2</sup> of the  $\gamma$ -trithioacetaldehyde, m.p.  $76^\circ\text{C}$ ., were obtained. The  $\gamma$ -isomer was also obtained from methylthialdine thiocyanate (128). Marckwald noted (127, 129) that the  $\gamma$ -isomer could be converted to  $\beta$ -trithioacetaldehyde by treatment with concentrated sulfuric acid or ethyl iodide.

(b) *Reduction of carbon disulfide*: In 1856, Girard (76) isolated a white crystalline compound, which sublimed at  $150^\circ\text{C}$ . and decomposed at  $200^\circ\text{C}$ ., by reducing carbon disulfide with zinc and hydrochloric acid. This compound was soluble in organic solvents, insoluble in water, and gave addition complexes with silver, gold, mercury, and platinum salts. The analysis corresponded closely to that calculated for  $\text{CH}_2\text{S}$ . Husemann (98) later prepared the same compound by a different method, as already noted. It is probably a thioformaldehyde polymer.

(c) *Reduction of ethyl isothiocyanate*: Hofmann (94) obtained trithioformaldehyde by reduction of ethyl isothiocyanate with zinc and hydrochloric acid.



(d) *Pyrolysis of mercaptals*: Schönberg and Schutz (187) were unable to prepare thioformaldehyde compounds by heating the dibenzylmercaptal of formaldehyde, although aryl thials and thiones could be obtained by heating the corresponding aryl mercaptals or thioketals.

(e) *Heating glycerol with sulfur*: Delson (52) has patented a process for making thioacrolein by heating sulfur with glycerol at 175–200°C. for 1–1½ hr. in a steel retort under pressure. The patent does not describe the characteristics of  $\text{CH}_2=\text{CHCHS}$ , but notes that the compound is germicidal and non-poisonous.

#### B. ARYL THIALS

The aryl thials have been investigated rather thoroughly. In particular, Worner (228) has studied the substituted trithiobenzaldehydes and prepared a large number of new compounds. He was particularly interested in obtaining both the  $\alpha$ -, or *cis*, and  $\beta$ -, or *cis-trans*, isomers of each compound. Frequently, only one isomer can be obtained. This is regarded as the  $\beta$ - or *cis-trans* isomer, because the  $\beta$ -isomer is always the most stable and least soluble of the two isomers when both are known, and in preparations in which both isomers are formed, the  $\beta$ -form usually is heavily predominant.

In addition to the trithials, a number of arylpolythials have been obtained. The molecular weights of some of the polythiobenzaldehydes have been found, but in the other cases the compounds have been too insoluble for molecular-weight determinations. No pure monomeric aryl thials have been described.

##### 1. Action of hydrogen sulfide on aldehydes

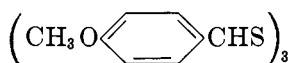
This method has been most extensively applied in this series of thiocarbonyl compounds. The earliest report is probably that of Bertagnini (34), who noted in 1851 that when hydrogen sulfide was passed into "nitrated benzaldehyde" in alcohol solution, an amorphous, highly insoluble white powder was obtained. This was undoubtedly the same polymeric *m*-nitrothiobenzaldehyde prepared much later by Mitra in another way (137). Klinger (105) was the first to prepare  $\beta$ -trithiobenzaldehyde, by passing dry hydrogen chloride and hydrogen sulfide into a solution of benzaldehyde in absolute alcohol. The product, to which the formula  $(\text{C}_6\text{H}_5\text{CHS})_n$  was assigned, melted at 225–226°C.

Baumann and Fromm (15, 18) studied the compounds obtained when an alcohol solution of benzaldehyde was treated with hydrogen sulfide and various concentrations of hydrogen chloride. It was noted that the amount of  $\beta$ -isomer was greatly increased as the temperature of the reaction and the concentration of hydrogen chloride increased. Among the products obtained were the two trimers,  $\alpha$ -trithiobenzaldehyde, m.p. 167°C., and  $\beta$ -trithiobenzaldehyde, m.p. 225°C. Another product, previously called  $\alpha$ -trithiobenzaldehyde, which melted at 83–85°C., was shown to be the same as Laurent's thioaldehyde (114) which

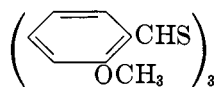
melted at 80–90°C. Baumann and Fromm (18) determined the molecular weights of this compound and of another low-melting polymer first prepared by Klinger, and found them to correspond to  $(C_6H_5CHS)_{10}$  and  $(C_6H_5CHS)_9$ , respectively. Suyver (215) also made a careful study of the two isomers, determining the solubilities and extent of conversion of the  $\alpha$ - into the  $\beta$ -form by treatment with catalysts. The  $\alpha$ -form could be prepared in high yield by diluting an alcohol solution of benzaldehyde with one-fourth its volume of alcohol saturated with hydrogen chloride, cooling this mixture to  $-15^\circ C.$ , and saturating with hydrogen sulfide. The  $\beta$ -form was obtained by saturating an alcohol solution of benzaldehyde with hydrogen chloride and hydrogen sulfide at  $0^\circ C.$  If the  $\alpha$ -trithiobenzaldehyde was heated alone, only a small amount of the  $\beta$ -isomer was formed, but if it was heated with an acid catalyst, such as acetyl chloride, hydrogen chloride, sulfur trioxide, or iodine, it was largely converted to the more stable  $\beta$ -isomer. The  $\alpha$ -isomer is 55 times as soluble in chloroform and 435 times as soluble in benzene at  $25^\circ C.$  as the  $\beta$ -isomer.

More recently Wood and Bost (226) have studied the formation of thiobenzaldehyde from benzaldehyde and hydrogen sulfide in alcohol. These authors noted that when the alcohol was saturated with hydrogen chloride, the  $\beta$ -trimer was formed exclusively, but if the concentration of the hydrogen chloride was decreased, gummy linear polymers of thiobenzaldehyde were obtained. If the reaction was run in basic alcohol solution (potassium or sodium hydroxide), a mixture of sulfur compounds, including the salts of benzyl mercaptan and dithiobenzoic acid, as well as thiobenzaldehyde, was obtained. Wood and Bost attempted to prepare monomeric thiobenzaldehyde from the  $\beta$ -trimer by distillation. With a drop of sulfuric acid added, the compound decomposed to give an impure red oil which may have been chiefly monothiobenzaldehyde.

Numerous substituted benzaldehydes have been prepared by the hydrogen sulfide reaction. In addition to the polymeric nitrothiobenzaldehyde of Bertagnini (34), Jackson and White (99) obtained reddish white gummy compounds when *p*-chloro-, *p*-bromo-, or *p*-iodo-benzaldehyde was treated with hydrogen sulfide in alcohol solution without additional acid. These compounds were not further investigated. Baumann and Fromm (19) prepared several alkoxy-substituted trithiobenzaldehydes by treating acidic alcohol solutions of the aldehyde with hydrogen sulfide. Both the  $\alpha$ - and the  $\beta$ -forms of trithioanisaldehyde (I), trithiomethylsalicylaldehyde (II), trithioisobutylsalicylaldehyde (III), and trithiocinnamaldehyde (IV) were obtained.



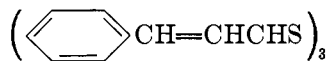
I



II



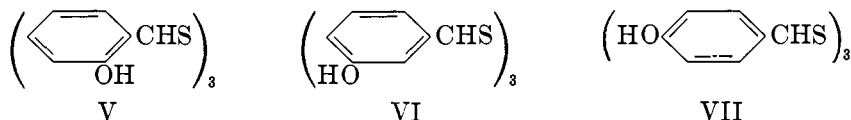
III



IV

The  $\alpha$ -form of I was obtained from an alcohol solution of the aldehyde to which one-tenth of its volume of concentrated hydrochloric acid had been added before saturating with hydrogen sulfide gas.

Kopp (111) prepared the trithials of salicylaldehyde (V), *m*-hydroxybenzaldehyde (VI), and *p*-hydroxybenzaldehyde (VII), and their benzoyl esters, but was



unable to obtain the  $\alpha$ -modification of any of these compounds. Lowering the acid concentration of the reaction gave linear polymers, in the case of the *o*- and *p*-benzoyloxybenzaldehydes, which could be converted to the  $\beta$ -trimer by treatment with acid or iodine. Kopp also attempted to prepare both forms of *m*-methoxybenzaldehyde, but was only able to obtain the  $\beta$ -form, m.p. 147°C., and a linear polymer, m.p. 95–97°C.

Worner (228) carried on Baumann's original idea in attempting the isolation of the *cis*- and *trans*-isomers of numerous substituted benzaldehydes by the method of lowering the acid concentration and the temperature of the reaction in order to promote the formation of the  $\alpha$ -isomer. This gave mixtures of the two isomers, which could then be separated by fractional crystallization. Worner was able to make several generalizations based on the data obtained. Like Kopp, he was unable to obtain the  $\alpha$ -forms of trithiosalicylaldehyde, trithio-*m*-hydroxybenzaldehyde, trithio-*p*-hydroxybenzaldehyde, trithiovanillin, and trithiogentisaldehyde. Also, only the  $\beta$ -forms of the benzoyl derivatives of the first four were obtained. (No attempt was made to prepare the dibenzoyl derivative of thiogentisaldehyde.) The nitrobenzaldehydes gave linear polymers, while *m*-nitroanisaldehyde, 3,5-dinitroanisaldehyde, and *m*-nitrocuminaldehyde yielded only the  $\beta$ -trithio derivatives.

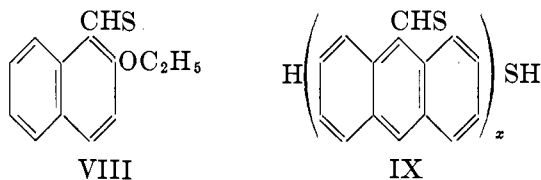
However, when alkyl groups or halogen groups were substituted in benzaldehyde, both the  $\alpha$ - and the  $\beta$ -trithio isomers were readily isolated. Also, if the hydrogens of the hydroxyl groups in the hydroxybenzaldehydes were replaced by alkyl groups, as in methylsalicylaldehyde, isobutylsalicylaldehyde, anisaldehyde, *p*-benzyloxybenzaldehyde, methylvanillin, piperonal, or dimethylgentisin-aldehyde, both isomers were obtained, except in the case of *m*-methoxybenzaldehyde.

Worner made the following generalizations: (1) Substituted aromatic aldehydes give two isomeric trithials only when the substituent is positive or neutral. When it is negative, the lower-melting  $\alpha$ -form is not obtained. When the acidity of the phenol group is masked by methyl or benzyl, both isomers are obtained, but benzoylation gives only the  $\beta$ -isomer. (2) The phenolic aldehydes give only the  $\beta$ - or *cis-trans* trithials. (3) Trithials are generally easier to prepare when positive substituents are present. When negative substituents are present, the tendency is to form high polymers.

The absence of the  $\alpha$ -trithio-*m*-methoxybenzaldehyde has not been explained.

Several obvious tests of Worner's hypotheses should be made. The substitution of a benzoyl group for hydrogen in the hydroxyaldehydes may have a volume effect which would prevent the formation of the *cis*-isomer. This is contraindicated by the existence of only one *p*-benzyloxybenztrithial, but both *p*-benzyloxy isomers. However, more light would be shed on the situation by the preparation of the *o*- and *m*-benzyloxy isomers, and the preparation of the various acetyl derivatives. It would be interesting to test the value of positive substituents by reacting the three aminobenzaldehyde hydrochlorides with hydrogen sulfide in alcohol. The strongly positive ammonium substituent should greatly influence the reaction.

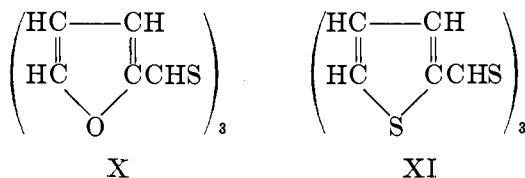
Wood and Bost (227) attempted to prepare monomeric aryl thials by increasing the size of the aryl group, and obtained a red solution of 2-ethoxy-1-naphthial (VIII) which slowly trimerized to the  $\beta$ -form, m.p. 283°C. The 9-anthracene-aldehyde, on treatment with hydrogen sulfide or hydrogen sulfide and hydrogen



chloride, gave only intractable linear polymers (IX) of indefinite melting point. The authors attribute this to the volume effect of the anthracene nucleus. Later, Wood and coworkers (225) described the preparation of linear polymers of  $\alpha$ -naphthial,  $\beta$ -naphthial, 3-phenanthrylthial, and 2-methoxy-1-phenanthrylthial, using hydrogen sulfide and hydrogen chloride with alcohol, or mixtures of alcohol and benzene or ethyl acetate and benzene, as solvents. The trimers could not be isolated in these preparations.

Trithiomesitaldehyde, m.p. 186–187°C., was prepared by Fuson and Best (73) from the aldehyde in cold absolute alcohol, saturated with hydrogen sulfide and hydrogen chloride. Only one isomer was obtained, which was probably the  $\beta$ - or *trans* form.

Both isomers of trithiofurfuraldehyde (X) and trithio-2-thiophenaldehyde (XI) have been prepared by the hydrogen sulfide reaction with the aldehyde. The first was isolated by Baumann and Fromm (21), who reported the  $\beta$ -trithiofurfuraldehyde to precipitate as black needles from chloroform, while the  $\alpha$ -isomer was colorless. Steinkopf and Jakob (213) prepared the thiophene compounds, and separated the isomers by fractional crystallization from benzene.

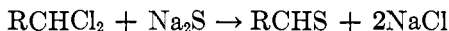


### 2. Action of thioacetoacetic esters on aldehydes

Mitra used the method of reacting aldehydes and thioacetoacetic esters both in alkaline medium (137) and in the presence of acids (142). Ethyl thioacetoacetate and benzaldehyde condense in piperidine to an oil which solidifies on standing. This solid reacts with various aldehyde reagents to give the benzyldene compounds, and on treatment with hydrogen chloride it is converted to  $\beta$ -trithiobenzaldehyde. Molecular-weight determinations and analyses indicated that this compound is a polymer,  $(C_6H_5CHS)_7$ . Treatment of anisaldehyde in the same way gave a solid, melting at 73–75°C., which proved to be  $(CH_3OC_6H_4CHS)_{11}$ . Benzaldehyde and ethyl thioacetoacetate in alcohol, treated with hydrogen chloride, gave  $\beta$ -trithiobenzaldehyde almost quantitatively. Other  $\beta$ -thioketobutyric esters, such as  $\alpha$ -methyl- and  $\alpha$ -isobutylthioacetoacetic esters, could be used in this reaction, as could diethyl thioacetonedicarboxylate,  $CS(CH_2COOC_2H_5)_2$ , and thioacetomalonic ester,  $CH_3CSCH(COOC_2H_5)_2$ . Anisaldehyde and vanillin similarly yielded the  $\beta$ -trithials with these reagents. *o*-Nitrobenzaldehyde yielded a polymeric thial of unknown molecular weight, melting at 168–172°C., which is probably the same as that obtained by Wood and coworkers (225) using the hydrogen sulfide reaction. *m*-Nitrobenzaldehyde gave a similar polythial, melting at 185–190°C. Mitra noted that these various polythials were depolymerized in basic medium, since they gave phenylhydrazones with phenylhydrazine alone or in pyridine.

### 3. Reaction of benzal halides with metal sulfides

The reaction of benzal halides with metal sulfides should represent a possible



method of synthesizing the aromatic thials. Cahours (43) treated benzal chloride with potassium bisulfide, and obtained a crystalline compound in white needles, melting at 64°C., to which was assigned the formula  $C_{14}H_6S_2$  (*sic*) and the name "sulfobenzol." Fleischer (64) performed the same reaction in boiling alcohol and obtained a crystalline solid, melting at 68–70°C. The analysis corresponded to  $C_7H_6S$ . These compounds were undoubtedly thiobenzaldehyde polymers. Klinger (108) repeated the reaction, using a slight excess of potassium bisulfide, and isolated benzyl disulfide and dithiobenzoic acid. He suggested that thiobenzaldehyde was an intermediate in this reaction, since



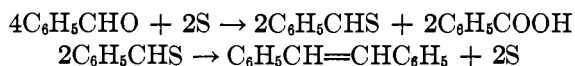
treatment of polythiobenzaldehyde with potassium bisulfide yielded the same products. Since potassium bisulfide provides an alkaline medium, a Cannizzaro reaction may be involved in the formation of these substances.

### 4. Special preparations

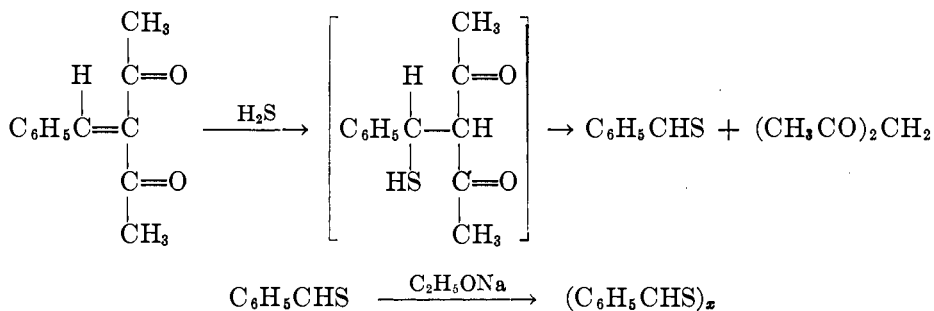
(a) *Reaction of benzaldehyde with ammonium sulfide*: Laurent (114) studied the products of the reaction of ammonium sulfide or ammonium bisulfide with

benzaldehyde, and isolated eight different compounds, most of which contained nitrogen. One of these compounds was a white crystalline solid, melting at 90–95°C., which analyzed correctly for the formula  $(C_7H_5S)_n$ . Laurent called it hydrosulfobenzoyl, and assumed it to be the dimer. The yield was evidently very low.

(b) *Reaction of benzaldehyde with sulfur*: Barbaglia and Marquardt (10) heated benzaldehyde with an equimolar quantity of sulfur at 180°C., and isolated benzoic acid and stilbene from the reaction mixture, along with a small amount of a sulfur-containing compound melting at 164–167°C., which may have been  $\alpha$ -trithiobenzaldehyde. These authors suggested that thiobenzaldehyde was an intermediate in the reaction.



(c) *Action of hydrogen sulfide on benzylideneacetylacetone*: Ruhemann (166) obtained a white crystalline sulfur compound, melting at 75–85°C., when benzylideneacetylacetone was treated with hydrogen sulfide in a warm alcoholic solution containing a small amount of sodium ethoxide. The compound was undoubtedly the polythiobenzaldehyde usually obtained in alkaline solutions. Thiobenzaldehyde is probably first formed by addition of hydrogen sulfide to the double bond, followed by decomposition, and is then polymerized under the influence of the alkali.



(d) *Pyrolysis of mercaptals*: As previously noted, Schönberg and Schutz (187) heated a number of alkyl and aryl mercaptals and thioketals to form the thiocarbonyl compounds. The dibenzyl mercaptal of benzaldehyde is reported to be very heat stable, but no figures are given as to temperature or yield in this reaction.

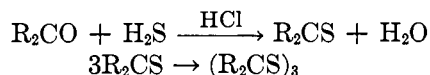
### C. DIALKYL THIONES AND SUBSTITUTED DIALKYL THIONES

#### 1. Action of hydrogen sulfide on ketones

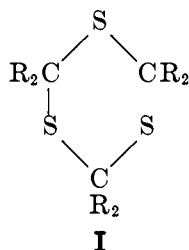
The simple ketones, acetone (14) and ethyl methyl ketone (119), have been shown to react with hydrogen sulfide in the presence of hydrogen chloride to



produce thiones which immediately trimerize. In the case of acetone a second compound,  $C_{15}H_{23}S_4$ , was also isolated by Baumann and Fromm (14) as well as

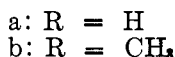
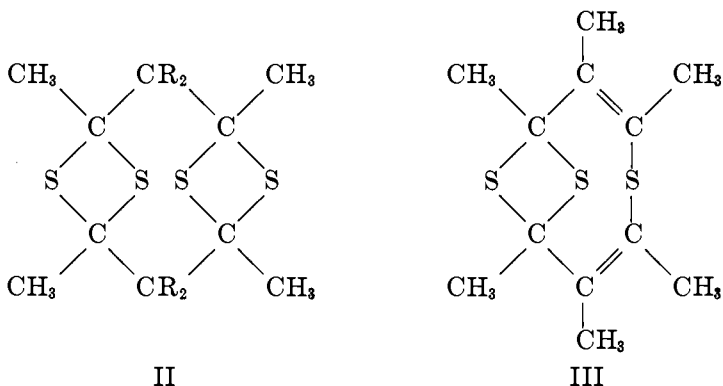


the trimer,  $(CH_3CSCH_3)_3$ . Presumably these trimers possess the cyclic structure I, analogous to the trithials.



An unsaturated ketone, such as dibenzalacetone, has been found to produce a compound,  $C_{20}H_{23}NS_2$ , upon treatment with ammonia and hydrogen sulfide (68, 69). Its structure has not been established.

Diketones, such as acetylacetone, also react with hydrogen sulfide in the presence of hydrogen chloride to form very stable dimers to which the cyclic structure IIa has been assigned (72). Dimethylacetylacetone gave an analogous compound of formula IIb, but monomethylacetylacetone, hydrogen sulfide,

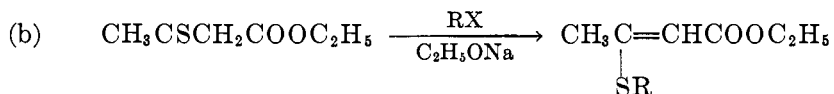
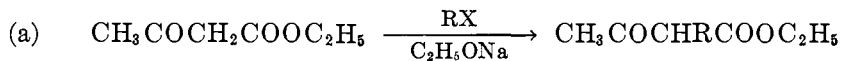


and hydrogen chloride led to the formation of a more reactive compound, to which structure III was assigned (72).

$\beta$ -Thioketo esters are formed in 85 per cent yields when a cold alcoholic solution of  $\beta$ -keto ester is treated with hydrogen sulfide and hydrogen chloride (138). Ethyl thioacetoacetate is an orange liquid with a pleasant odor, and boils at 75–80°C. at 12 mm. pressure. It can be purified by precipitation of a

lead salt, which is easily decomposed by hydrogen sulfide. Ethyl thioacetone-dicarboxylate was obtained from the corresponding ketone in 75 per cent yield by this method. It is also a pleasant-smelling, rose-red liquid. Similarly, the  $\alpha$ -methyl-,  $\alpha$ -ethyl-, and  $\alpha$ -isobutyl-acetoacetic esters yielded the corresponding thio derivatives in good yield, as did acetylmalonic ester.

Mitra attempted to use these compounds in acetoacetic ester condensations,

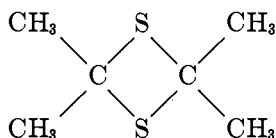


(a), but found in every case that the vinyl thioether was obtained, indicating that the reaction proceeded as in (b).

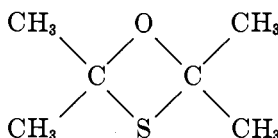
The compounds are probably entirely converted to the thiol form in an alkaline medium.

## 2. Action of phosphorus sulfides on ketones

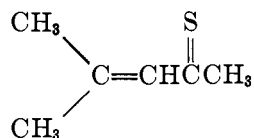
This method has been used frequently in synthesizing the thiones. As early as 1869, Wislicenus (223) obtained dithioacetone (IV),  $\text{C}_6\text{H}_{12}\text{S}_2$ , by treating acetone with phosphorus pentasulfide. Baumann and Fromm (14) later prepared this same compound and found it to be different from their trimeric thioacetone, which could be converted into the dimer by heating to  $200^\circ\text{C}$ . Spring (204) reinvestigated the action of phosphorus pentasulfide on acetone, and isolated methyl mercaptan, isopropyl mercaptan, oxythioacetone (V), and perhaps mesityl sulfide (VI) from the reaction, in addition to dithioacetone (IV). The compound called mesityl sulfide had the formula  $\text{C}_6\text{H}_{10}\text{S}$ , but was not clearly characterized, and did not behave toward chemical reagents, such as sodium



IV  
Dithioacetone

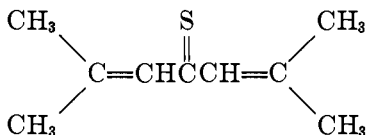


V  
Oxythioacetone



VI  
Mesityl sulfide

amalgam, as would a compound of structure VI. In addition, Spring found some evidence that thiophorone (VII) may have been formed in the reaction.



VII  
Thiophorone

This assumption was based on the isolation, upon the oxidation of crude residues with nitric acid, of a nitrososulfonic acid of unidentified structure and the formula  $C_6H_{10}SO_3H \cdot (NO)_2$ .

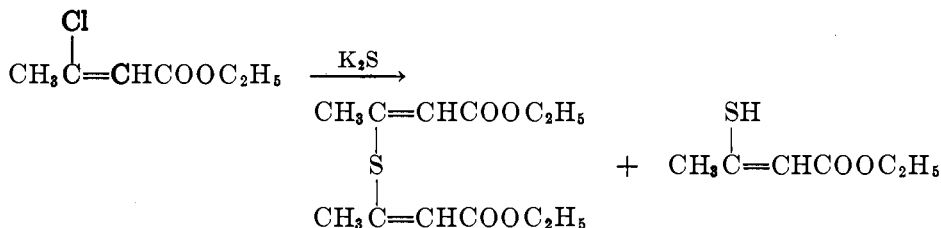
Phosphorus trisulfide was used by Autenrieth (6), who isolated dithioacetone from the reaction of the trisulfide with acetone in a sealed tube. Kretov and Komissarov (113) refluxed powdered phosphorus pentasulfide with various ketones in toluene, and isolated and purified the thiones or dithiones by distillation. These authors note that, in all cases, small yields of impure products were obtained. The ketones used were acetone, ethyl methyl ketone, diethyl ketone, di-*n*-propyl ketone, and di-*tert*-butyl ketone. Analyses of the red oils obtained indicated that acetone, ethyl methyl ketone, and diethyl ketone gave dimeric thiones, while di-*tert*-butyl ketone yielded the monomeric di-*tert*-butyl thione. The product of the reaction of phosphorus pentasulfide and di-*n*-propyl ketone was apparently a mixture of monomeric and dimeric thiones.

Bohme, Pfeifer, and Schneider (37) were unable to prepare dithioacetone by the use of either phosphorus trisulfide or phosphorus pentasulfide, and found that heating trithioacetone gave isopropyl mercaptan, rather than the dimeric compound, as reported by Baumann and Fromm (14).

The treatment of 1,4-diketones with phosphorus trisulfide or phosphorus pentasulfide does not result in the formation of the corresponding 1,4-dithiones. The thiones may be intermediates in the reaction, but the final product is the 2,5-disubstituted thiophenes, which are obtained in good yield (150).

### 3. Reaction of vinyl halides with metal sulfides

This reaction has been investigated in connection with the synthesis of thioacetoacetic ester. Scheibler and Bube (167) treated ethyl  $\beta$ -chlorocrotonate with potassium sulfide in alcohol, and obtained a mixture of the sulfide and the vinyl mercaptan. The yield of the  $\beta$ -mercaptocrotonic ester (or thioacetoacetate) was greatly increased by the use of excess potassium bisulfide. Later

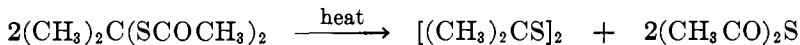
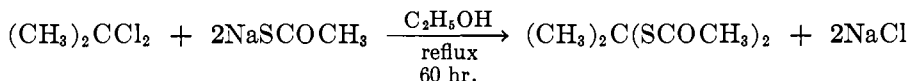


Scheibler, Tapouzada, and Schulze (168) studied the  $\beta$ -mercaptocrotonic ester, and found it to be a mixture of the *cis* and *trans* isomers, which could be separated by repeated fractionation. These authors found no evidence of a ketone form. The compound was a red oil boiling at 77°C. at 18 mm. pressure, and thus corresponds very closely to the product obtained from ethyl acetoacetate and hydrogen sulfide (137). Mitra also prepared the ethyl thioacetoacetate by the reaction of potassium bisulfide with  $\beta$ -chlorocrotonic ester (136), but the yield in this case (30 per cent) was much lower than that by the hydrogen sul-

fide-hydrogen chloride method. Mitra found that the compound reacted with phenylhydrazine to give phenylmethylpyrazolone, and evolved hydrogen sulfide when reacted with hydroxylamine. These reactions indicate the presence of some keto form. Methyl  $\alpha$ -benzyl- $\beta$ -mercaptocrotonate was prepared by Scheibler and coworkers (168) from the methyl  $\alpha$ -benzyl- $\beta$ -chlorocrotonate and sodium bisulfide. The pure compound obtained by this method was red-orange in chloroform solution, but was not well characterized.

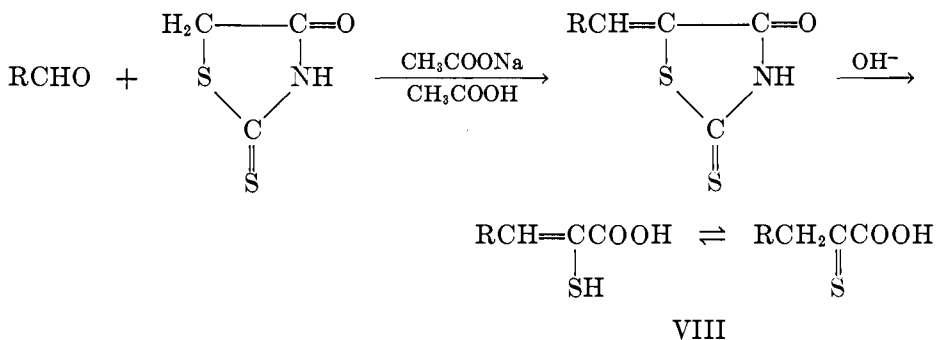
A recent British patent (109) reports the preparation of thiones by treating vinyl halides with sulfides or thiosulfates in alcohol solution, but no details of the compounds prepared are given.

2,2-Dichloropropane has been used to synthesize dithioacetone by Spring (203). The dichloride was treated with sodium thioacetate in alcohol, and the dithioacetate isolated and heated to give the dithioacetone, b.p. 180–185°C. The yield was less than 2 per cent.



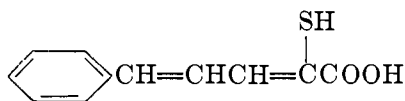
#### 4. $\alpha$ -Thionic acids from aldehydes and rhodanine

An aldehyde condenses with rhodanine in acetic acid-sodium acetate mixture to give the substituted rhodanine, which on alkaline hydrolysis yields the  $\alpha$ -thionic acid (VIII).

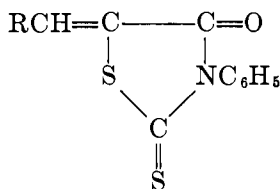


Zipser (230) treated cinnamylidenerhodanine with barium hydroxide, and obtained  $\alpha$ -sulfhydrylcinnamylacrylic acid (IX), which was assumed to occur only in the enol form, since the compound reacted with sodium hydroxide and benzyl chloride to give the benzyl thioether.

Andreasc (1) prepared a number of  $\alpha$ -thionic acids by hydrolysis of the corresponding substituted phenylrhodanine compounds (X) with sodium pentoxide.



IV

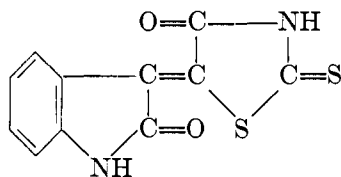


X

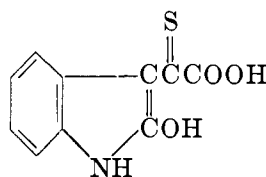
The aldehydes used in the rhodanine condensation which gave stable  $\alpha$ -thionic acids were piperonal, vanillin, furfural, *p*-hydroxybenzaldehyde, and *p*-dimethylaminobenzaldehyde. No  $\alpha$ -thionic acids could be isolated by alkaline hydrolysis of the rhodanine condensation product formed from *p*-aminobenzaldehyde or *o*-nitrobenzaldehyde.

Granacher (79) studied the properties of phenylthiopyruvic acid (VIII, R = C<sub>6</sub>H<sub>5</sub>) and found that it gave the same oxime and phenylhydrazone as phenylpyruvic acid, thus indicating the presence of the thione form. Undoubtedly both tautomers exist. Granacher, Gero, Ofner, Klopfenstein, and Schlatter (80) attempted to prepare the aliphatic  $\alpha$ -thionic acids from the rhodanine condensation products of acetaldehyde, crotonaldehyde, and isovaleraldehyde, but obtained only intractable oils. These authors obtained a 96 per cent yield of *p*-methoxyphenylpyruvic acid (VIII, R = *p*-CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub>) from anisylidenerhodanine, however. *p*-Isopropylbenzylidenerhodanine yielded an amorphous, intractable solid (VIII, R = *p*-(CH<sub>3</sub>)<sub>2</sub>CHC<sub>6</sub>H<sub>4</sub>), which reacted with hydroxylamine to give an oxime and hydrogen sulfide.

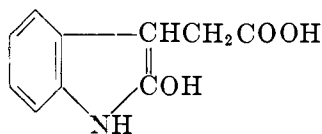
Granacher and Mahal (81) prepared rhodanal- $\beta$ -oxindole (XI) from isatin and rhodanine. Boiling pyridine converted it readily to the  $\beta$ -oxindolythionacetic acid (XII), a dark red crystalline solid which on heating gradually softened to a wax-like mass. Compound XII is remarkable for the number of tautomeric forms which are possible. The structure of XII was indicated by conversion to the oxime and reduction to the known  $\beta$ -oxindoleacetic acid (XIII).



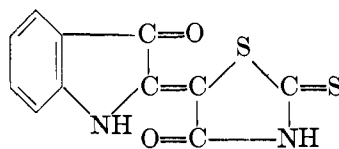
XI



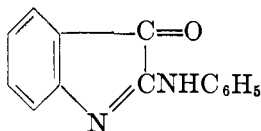
XII



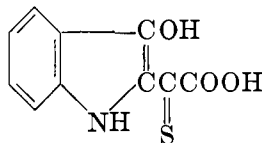
XIII



XIV



XV



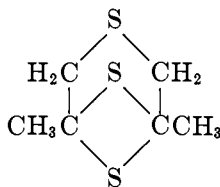
XVI

Rhodanine-2-indolyindigo (XIV) was prepared by condensing isatinanilide (XV) with rhodanine in acetic anhydride. Sodium hydroxide readily converted XIV to  $\alpha$ -indoxylthionacetic acid (XVI), an amorphous red powder, which begins to decompose at 148°C.

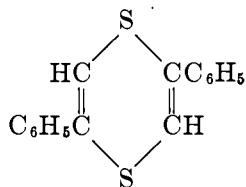
Julian and Sturgis (100) condensed rhodanine with veratraldehyde, and upon alkaline hydrolysis of the product obtained 3,4-dimethoxyphenyl-2-thioketopropionic acid (VIII, R = 3,4-(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>). Recently Plucker and Amstutz (157) resynthesized 3- $\alpha$ -furyl-2-thioketopropionic acid (VIII, R = C<sub>4</sub>H<sub>4</sub>O) by this method and obtained a better yield of higher-melting product than did Andreasch (1).

### 5. Special methods

(a) *Reaction of ketones with carbon disulfide:* Although Bohme, Pfeifer, and Schneider (37) were unable to obtain the simple dimeric thiones by previously reported methods (see above), they were able to prepare a compound containing the four-membered carbon-sulfur ring present in the dimers. Chloroacetone, when treated with carbon disulfide and dry hydrogen chloride, yielded 2,6-dimethyl-2,6-endothio-1,4-dithian (XVII). Acetone reacted with carbon disulfide and anhydrous zinc chloride to give the trithioacetone rather than the dimer. The product of the reaction with  $\alpha$ -chloroacetophenone and carbon disulfide was not the expected endothio compound, but 2,5-diphenyl-1,4-dithiane (XVIII). Compound XVIII may be derived from the endothio-dithiane by loss of hydrogen sulfide.



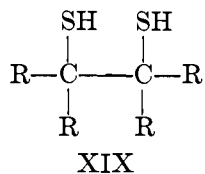
XVII



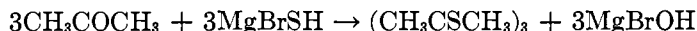
XVIII

(b) *Action of ammonium sulfide on ketones:* Thiones have not been obtained by the reaction of metal or ammonium sulfides on the ketones. Reduction products are usually obtained from this reaction. Willgerodt (222) treated acetone with ammonium sulfide and obtained a compound which melted at 98°C. and boiled at 243°C., and which was thought to be dithioacetone, but the constants differ from those of either dithioacetone (b.p. 183–185°C.) or trithioacetone (m.p. 24°C.). Manchot and Krische (124) attempted to prepare the dibenzylthione and di- $\beta$ -phenylethylthione by treating the respective ketones

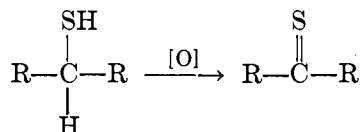
with ammonium sulfide or ammonium bisulfide. The product obtained in each case was the thiopinacol (XIX), in which  $R = C_6H_5CH_2$  or  $C_6H_5CH_2CH_2$ .



(c) *Treatment of ketone with magnesium bromobisulfide*: Mingoia (135) succeeded in synthesizing trithioacetone by treating anhydrous acetone with magnesium bromobisulfide in absolute ether. The yield was low, however.

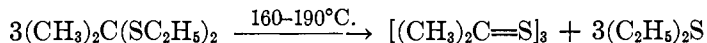


(d) *Oxidation of mercaptans*: By analogy with the oxygen series, it should be possible to convert the secondary mercaptans to thiones by oxidation, but only one attempt to complete this reaction has been made with the dialkyl thiones.



Claus (48) oxidized isopropyl mercaptan with chromium trioxide, and obtained a sulfur-containing compound which boiled at 165–170°C. and seemed to be an impure form of Wislicenus' "dithioacetone" (b.p. 183–185°C.).

(e) *Pyrolysis of thioketals*: Baumann and Fromm (16) attempted the synthesis of thioacetone from acetone diethylmercaptal by heating, but reported the method not feasible, since there are many side reactions. Similarly, Schön-



berg and Schutz (187) report acetone dibenzylmercaptal as relatively heat stable.

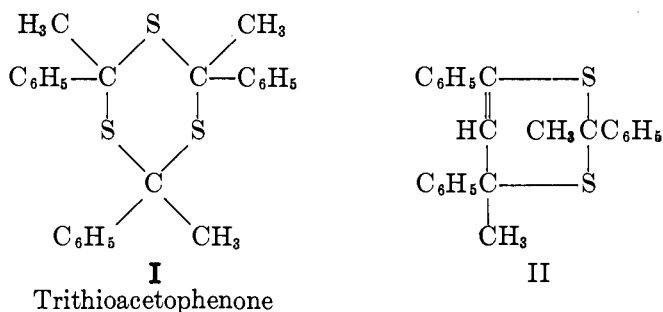
#### D. ALKYL ARYL THIONES

Very few thiones of this type have been prepared. Trithioacetophenone, which is well characterized, should be a valuable compound in studying the reactions of the thiocarbonyl group. It is a stable trimer below its melting point, but dissociates to the monomer at about 140°C. Thus both forms are readily obtained.

##### 1. Action of hydrogen sulfide on ketones

This method is the only one which has received much attention in the preparation of the alkyl aryl thiones. Baumann and Fromm (22) investigated the reaction of acetophenone with hydrogen sulfide and obtained four products. Hydrogen sulfide and dry hydrogen chloride gas were passed into an alcohol

solution of acetophenone which was maintained at 0°C. The solution became intense blue-violet in color. The blue monomeric thioacetophenone could not be isolated at this time, however, since it was unstable. After about 24 hr. the reaction mixture had faded in color, and white crystals of trithioacetophenone (I) were deposited. This compound was odorless, and was stable in boiling potassium hydroxide solution or in chloroform containing a trace of iodine. The mother liquors from this preparation were allowed to stand for several days



at room temperature, and the crystals which deposited were collected and analyzed. This compound melted at 107–108°C. after recrystallization from alcohol or acetone, and had the formula  $\text{C}_{24}\text{H}_{22}\text{S}_2$ . Baumann and Fromm proposed the structure II for this compound, and called it anhydrotriacetophenone disulfide. A green resin was also isolated when the reaction was run at slightly higher temperatures, but this substance was not identified.

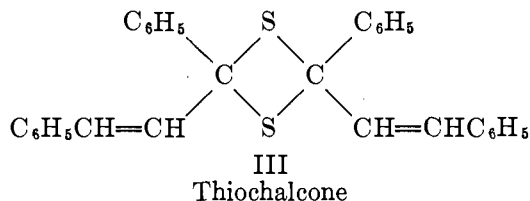
Theoretically, two isomers of trithioacetophenone would be expected, the *cis* and the *cis-trans* forms. Only one form was found, which Baumann and Fromm believed to be the more stable *cis-trans* form. The “anhydrotriacetophenone disulfide” (II) may have been formed by loss of hydrogen sulfide from the *cis*-trithioacetophenone. Recently it has been found (44) that if an alcohol solution of acetophenone was first treated with hydrogen chloride, followed by a mixture of hydrogen sulfide and hydrogen chloride, very little trithioacetophenone was formed, but the “anhydrotriacetophenone disulfide” was obtained in good yield. This suggests that dypnone, which is formed when an alcohol solution of acetophenone is treated with dry hydrogen chloride, may be an intermediate substance in the formation of II.

Monomeric thioacetophenone was obtained by Baumann and Fromm (22) on heating trithioacetophenone above its melting point in a vacuum. The compound first melts to a blue oil, which distills as a violet vapor. It was never completely purified, since it decomposed to styrene and hydrogen sulfide when hot, and was partially reconverted to the trimer when cold.

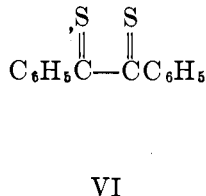
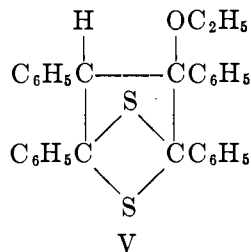
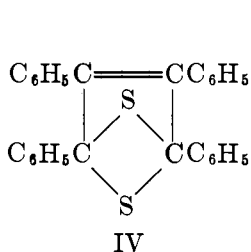
Steinkopf and Jakob (213) treated 2-acetylthiophene with hydrogen sulfide and hydrogen chloride in cold alcohol. They obtained a violet oil which was probably the monomeric 2-thienylmethylthione, but it was not further purified. Fromm (65) treated chalcone with hydrogen sulfide and dry hydrogen chloride in cold alcohol, and obtained a small yield of an unstable crystalline material,



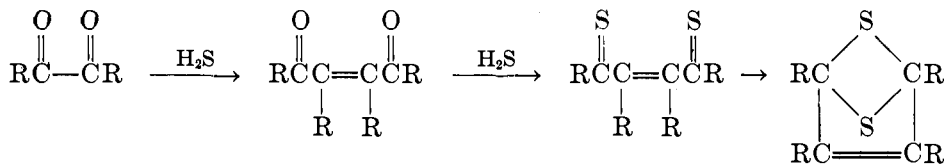
which melted at 191°C. and had a molecular weight of 456. It was thought to be the dimeric thiochalcone (III), but the structure was not proven.



When benzoin was treated with hydrogen chloride and hydrogen sulfide in cold alcohol, a mixture of three compounds was obtained (Mitra (141)). These compounds were separated by crystallization, and their structures proved. They were tetraphenyl-2,5-endothiothiophene (IV), tetraphenyl-3-ethoxy-4-hydro-2,5-endothiothiophene (V), and dithiobenzoin (VI). VI was obtained



in small yield. Mitra investigated the mechanism of the reaction, and concluded that treatment of diketones with hydrogen sulfide first caused condensation to  $\gamma$ -diketones, which are then converted to the dithiones and rearranged to the endothiothiophene derivatives.



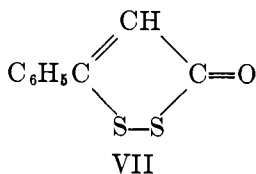
## 2. Special methods

(a) *Use of thioacetoacetic esters:* Mitra (137) treated acetophenone with ethyl thioacetoacetate and obtained a deep blue oil, boiling at 110°C. at 20 mm. This was undoubtedly monomeric thioacetophenone.

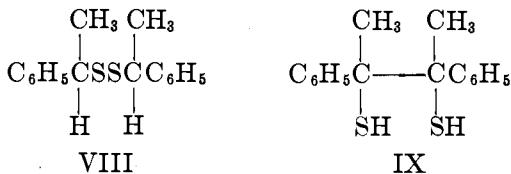
(b) *Use of magnesium bromobisulfide:* Mingoia (135) used the reaction of magnesium bromobisulfide with ketones (see above) to prepare trithioacetone. However, when acetophenone was used, the monomeric blue-violet oil was obtained. Distillation caused decomposition, and the compound was not further purified.

(c) *Reaction of sulfur with ethyl cinnamate:* Baumann and Fromm (24) treated ethyl cinnamate with sulfur and obtained the disulfide of thiobenzoyl-

thioacetic acid (VII) in yellow needles, melting at 117°C. Distillation of this compound in vacuum yielded a mixture of monomeric thioacetophenone, 2,4-diphenylthiophene, and hydrogen sulfide.



(d) *Reaction of ammonium bisulfide on ketones:* Willgerodt (222) had obtained a sulfur-containing compound when acetone was treated with ammonium sulfide, but no sulfur compounds were obtained when aryl ketones like  $\alpha$ -naphthylmethyl ketone, acetophenone, or 2,4-dimethylacetophenone were used. Engler (58) treated acetophenone with alcoholic ammonium bisulfide for six weeks, and isolated a solid which crystallized in white needles, melting at 119.5°C. On the basis of analysis, Engler suggested that it was thioacetophenone or a polymer of thioacetophenone. This reaction was checked by Baumann and Fromm (23), who obtained  $\alpha$ -phenylethyl disulfide (VIII), melting at 57–58°C., by treating acetophenone with a 65 per cent saturated solution of ammonium bisulfide in alcohol for 8 days. Using various conditions, these authors were unable to obtain any thioketones. Manchot and Krische (124) were able to obtain a compound melting at 118–119°C.,  $\text{C}_{16}\text{H}_{18}\text{S}_2$ , which resembled Engler's preparation from acetophenone and ammonium sulfide in alcohol. This compound was



shown to be the thiopinacol (IX). It is therefore highly improbable that any alkyl aryl thiones have been prepared by the action of ammonium sulfide or bisulfide on the ketones.

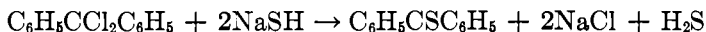
#### E. DIARYL THIONES

The preparation and properties of the diaryl thiones have been extensively investigated, because they exist in the monomeric form only and therefore may be more readily compared to the oxygen analogues. Studies in this series have shown that the thiones behave differently from the ketones in many reactions. A characteristic of the monomeric thiones is that they are all highly colored compounds. Schönberg (190) has reviewed useful methods which have been developed for the preparation and isolation of diaryl thiones.

##### 1. Preparation from diaryl keto chlorides

(a) *Action of diaryl keto chlorides with metal sulfides:* The preparation of thio-benzophenone has been carried out by Gattermann and Schulz (75), who treated

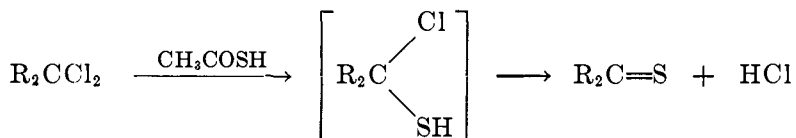
benzophenone dichloride with potassium sulfide in alcohol. A refinement of this method has been described by Staudinger and Freudenberg (209). Benzophenone dichloride was treated with an alcoholic solution of sodium bisulfide



in an atmosphere of carbon dioxide, causing a vigorous reaction, and the mixture became deep blue in color. The mixture was diluted with water, the thio-benzophenone extracted with ether, and distilled at reduced pressure in an atmosphere of carbon dioxide. The blue oil produced in this way formed beautiful blue crystals, m.p. 53–54°C., on cooling and recrystallizing from the petroleum ether. Thiobenzophenone must be preserved in a sealed glass tube in an atmosphere of carbon dioxide, as it is unstable in the air.

It is interesting to note that Behr (26) reported in 1872 that treatment of benzophenone dichloride with potassium bisulfide in alcohol solution gave a reddish yellow solid which on recrystallization from glacial acetic acid gave snow-white crystals melting at 152–153°C.! This compound analyzed correctly for the formula  $\text{C}_{13}\text{H}_{10}\text{S}$ , but no molecular weight was determined. However, when it was heated above its melting point, an intense blue color developed, and oxidation gave benzophenone. The preparation of this compound has never been duplicated, and its identity is unknown. It behaved like the trimeric thioketones of higher molecular weight, however.

(b) *Action of diaryl keto chlorides with thioacetic acid:* Schönberg, Schutz, and Nickel (190) described a number of aromatic thiones which were prepared by treating the diaryl keto chloride with thioacetic acid. Most of the thiones could be crystallized directly from the reaction mixture, but thiobenzophenone was purified by distillation in an inert atmosphere. The compounds prepared



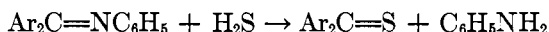
were the *p,p'*-diphenyl-, *p,p'*-dimethoxy-, *o,o'*-dimethoxy-, and *p*-methoxy-*p'*-ethoxy-thiobenzophenones. Kitamura (104) used this method to prepare *p,p'*-diethoxythiobenzophenone.

## 2. Preparation by the action of hydrogen sulfide on ketones and ketone derivatives

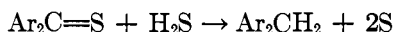
Thiobenzophenone was originally prepared by Staudinger and Freudenberg from benzophenone and hydrogen sulfide (207). Passing hydrogen sulfide and hydrogen chloride into a mixture of benzophenone and alcohol in an ice-salt bath for 2–3 hr., followed by hydrogen sulfide for 20 hr., produced deep blue needles of thiobenzophenone in 68 per cent yield, which melted at 51–52°C. after one recrystallization from ligroin. The compound was unstable in air, and was filtered in an atmosphere of carbon dioxide. Steinkopf and Jakob (213) attempted to prepare phenyl-2-thienylthione by passing hydrogen sulfide and hydrogen chloride into a cold alcoholic solution of the ketone. The solution turned violet in color, and after 14 days this color changed to deep green.

Distillation yielded a green oil which was not further identified. Several unsymmetrical thiones were prepared by Bost and Cosby (39), using this method. They found that diphenylphenylthione, phenyl- $\alpha$ -naphthylthione, and phenyl-*p*-tolylthione were all stable monomers which could be produced by this method. However, when a nitro group was substituted in the aromatic ring of the aryl ketones, no thiones were obtained.

Reddelien and Daniloff (162) prepared several diaryl thiones by treating the diaryl ketone anil or anil hydrochloride with hydrogen sulfide. The reaction was complicated by reduction of the thione to the corresponding diarylmethane



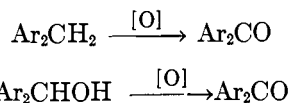
by hydrogen sulfide in the reaction mixture. They noted that when a negative substituent, such as the dimethylamino group, was present in the anil, the reaction proceeded much more readily. Thiobenzophenone was obtained in 55 per



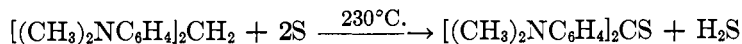
cent yield from benzophenone anil hydrochloride treated with hydrogen sulfide in benzene solution for 6 days, but *p*-dimethylaminobenzophenone anil hydrochloride yielded the corresponding thione in 28 per cent yield on treatment with hydrogen sulfide for 3 hr. in boiling benzene. Fehrmann (59) had previously investigated the reaction of hydrogen sulfide on the imine and anil of Michler's ketone and reported yields of 94 per cent and 86 per cent, respectively, but the melting point of the thione was given as 164–166°C., which is about 40°C. lower than that given for *p, p'*-tetramethyldiaminothiobenzophenone by other workers. The compound was not well characterized in other ways by Fehrmann.

### 3. Oxidation reactions

(a) *Diarylmethanes with sulfur*: Diaryl ketones may be prepared by the careful oxidation of the corresponding diarylmethane or substituted diarylmethane. Several instances of analogous reactions in the sulfur series have been reported.



Wallach (220) reported the preparation of Michler's thioketone from *p, p'*-tetramethyldiaminodiphenylmethane by heating the compound with sulfur

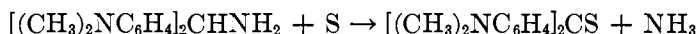


at 230°C. No yield was given for this reaction. Much later, Tschitschibabin and Knunjanz (216) prepared 2,2'-tetramethyldiamino-4,4'-dipyridylthione in 25 per cent yield by heating the corresponding disubstituted methane with sulfur at 190°C. for 5 hr.

(b) *Diarylmethanes with polysulfides*: Willgerodt investigated the reaction of polysulfides with various ketones (222) but was unable to prepare thiones by

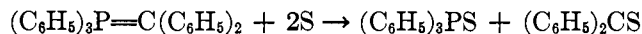
this method. It was noted that in some cases the polysulfides reduced the ketones to methanes. In contrast to this, Badische (7) has patented a method for the production of *N*-alkylated 4,4'-diaminodiaryl thiones by treating the corresponding diaminodiarylmethanes with polysulfides. 4,4'-Tetramethyldiaminothiobenzophenone, 4,4'-dimethyldiamino-3,3'-dimethylthiobenzophenone, and 4,4'-tetraethyldiaminothiobenzophenone were listed as having been prepared by this method, but no constants for the compounds were given.

(c) *Leukauramine with sulfur*: Mohlau, Heinz, and Zimmermann (144) have reported that leukauramine, *p,p'*-tetramethyldiaminodiphenylmethylamine, was



oxidized to Michler's thioketone in 60 per cent yield on heating with sulfur. Although the yield is good, and the product apparently pure (m.p. 202°C.), there seems to have been no attempt to prepare other diaryl thiones by this method, or by oxidation of the diarylcarbinols by sulfur.

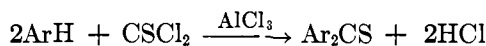
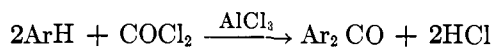
(d) *Triphenylphosphinediphenylmethylene with sulfur*: Staudinger and Meyer (211) reported that when triphenylphosphinediphenylmethylene was heated with sulfur it gave triphenylphosphine sulfide and thiobenzophenone. The



thiobenzophenone was not isolated, however, but merely identified by color and the preparation of the benzophenone phenylhydrazone.

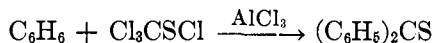
#### 4. The Friedel-Crafts reaction

(a) *With thiophosgene*: The preparation of diaryl ketones from phosgene and aromatic compounds by the Friedel-Crafts reaction is common practice. The



analogous reaction in the sulfur series has been well investigated, but is complicated by the difficulty of obtaining pure thiophosgene. Bergreen (33) treated thiophosgene ( $\text{CSCl}_2$ ) with aluminum chloride in benzene solution, and obtained an impure red oil, which yielded benzophenone oxime on treatment with hydroxylamine, and benzophenone phenylhydrazone with phenylhydrazine. Gattermann (74) investigated this reaction extensively, using a variety of phenolic ethers, such as anisole or phenetole, as the aromatic reactant, and was able to isolate the corresponding thiones and determine their properties. The yields in these reactions were rather poor.

(b) *With trichloromethylsulfur chloride*: Vorlander and Mittag (219) attempted to prepare triphenylmethylsulfur compounds by treating trichloromethylsulfur chloride with benzene and aluminum chloride. Instead of the expected products, thiobenzophenone was obtained in 34 per cent yield.



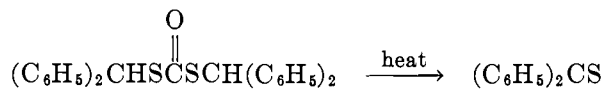
### 5. Pyrolysis of mercaptals and thioethers

Schönberg and Schutz (184) noted that the mercaptals of aromatic ketones decompose to give highly colored compounds when heated. A later study (187) compared the heat-stability of a large number of aromatic mercaptals, but no attempt was made to purify the resulting thiones, or determine the yields on the various reactions.

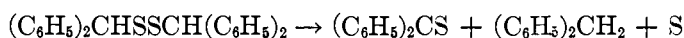
Schönberg, Schutz, Bruckner, and Peters (188) noted that certain high-molecular-weight thioethers were thermolabile, decomposing to the thione and methane derivatives. The thioethers therefore differ in their behavior toward heat from the ethers. Thus, tetraphenyldimethyl ether (I) could be distilled at 267°C., but when tetraphenyldimethyl sulfide (II) was heated to this temperature, the color changed and diphenylmethane and thiobenzophenone were obtained. Again the yields on this reaction were too low to be useful preparative methods.



Biilman (35) noted that the characteristic color of thiobenzophenone was obtained when diphenylmethyldithiol carbonate was heated. Wuyts (229)



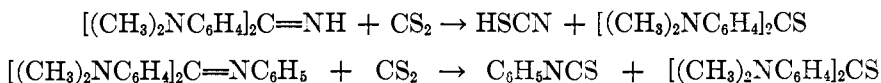
obtained thiobenzophenone, diphenylmethane, and sulfur on distillation of



tetraphenyldimethyl disulfide.

### 6. Special methods

(a) *Action of carbon disulfide on imines and anils:*



Fehrmann (59) reported that Michler's thioketone could be formed by warming the corresponding anil or imine with carbon disulfide. Phenyl isothiocyanate or thiocyanic acid was obtained as the other product.

(b) *Action of phosphorus pentasulfide on ketones:* Treatment of diaryl ketones with phosphorus pentasulfide has not been generally successful. Gattermann and Schulze (75) pointed out that thiobenzophenone could not be prepared by this method, and made the general statement that it was a poor method of preparing diaryl thiones. However, the preparation of *p,p'*-tetramethyldiaminodiphenyl thione by treating Michler's ketone with phosphorus pentasulfide has been patented (German patent 39,074; see Schönberg *et al.* (190)).

(c) *Action of thioacetoacetic ester on benzophenone:* Mitra (137) reported the

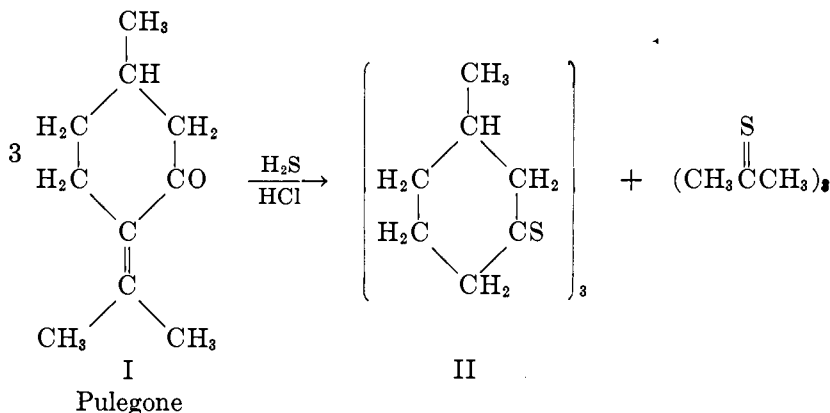
preparation of a blue oil, boiling at 175°C. at 10 mm. pressure, by treating benzophenone with ethyl thioacetoacetate and dry hydrogen chloride. This compound was not crystallized, but it analyzed correctly for  $C_{13}H_{10}S$  and the molecular weight was 198. The yield in this reaction was 27 per cent of the redistilled oil.

#### F. HOMOCYCLIC THIONES

A few of the simple homocyclic thiones have been prepared, and some of the thiones of the terpene series (thiocamphor, etc.) have been investigated. Two authors, Ray (160) and Sen (195), prepared thiocamphor by the hydrogen sulfide-hydrogen chloride method, and obtained a red crystalline compound which analyzed correctly for  $C_{10}H_{16}S$ , gave the oxime, phenylhydrazone, and semicarbazone of camphor, and melted at 145°C. In the earlier literature, however, three other reports, by Houben and Doscher (96), Rimini (164), and Wuyts (229), describe the preparation of a red crystalline compound which also analyzed correctly for thiocamphor, gave camphor derivatives, and melted at 119°C. These authors prepared the compounds by pyrolysis of the disulfides, a reaction which involves rearrangement. It is difficult to choose the correct constants for thiocamphor from the available data.

##### 1. Action of hydrogen sulfide on ketones

This method has been used to prepare most of the known homocyclic thiones. Fromm (66) noted that cyclopentanone, cyclohexanone, and *p*-methylcyclohexanone all give well-crystallized trithiones in good yield upon treatment with hydrogen sulfide and hydrogen chloride in cold alcohol. However, when pulegone (I) was treated in a similar manner, a compound,  $C_{21}H_{48}S_3$ , which is probably trithio-*m*-methylcyclohexanone (II), was obtained. Trithioacetone was



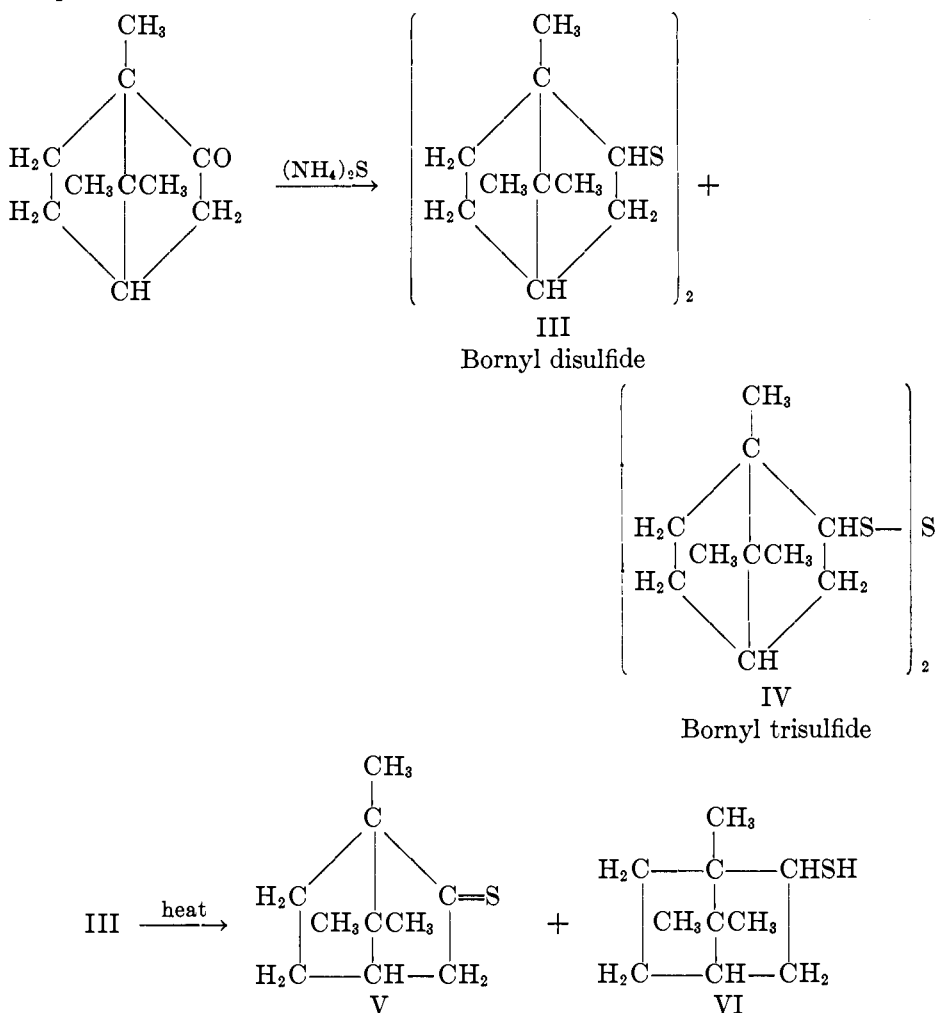
not isolated, but was identified by its characteristic odor.

Sen (196) prepared the monomeric thiocyclopentanone and thiocyclohexanone by passing hydrogen sulfide and hydrogen chloride into a cold alcohol solution of the respective ketone for 1½ hr. At this point deep red solutions were obtained, which were distilled in vacuum. The resulting red oils gave the ex-

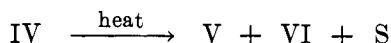
pected semicarbazones and phenylhydrazones. If these oils were further treated with hydrogen chloride in cold alcohol, they could be converted to the trithiones, which were identical with those prepared by Fromm. Molecular-weight determinations of the monomers in benzene indicated partial association. Ray (160) also reported the preparation of monomeric and trimeric thiocyclohexanone from cyclohexanone and hydrogen sulfide in cold alcoholic hydrogen chloride solution. Sen (195) reported a yield of 47 per cent of the purified thio-camphor by this method, and also prepared thiofenchone from fenchone (197) similarly.

### 2. Pyrolysis of disulfides and mercaptals

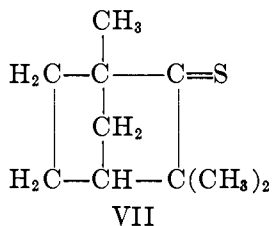
This method has been used to prepare thiocamphor and thiofenchone. Wuyts (229) obtained bornyl disulfide (III) and bornyl trisulfide (IV) when he treated camphor with ammonium sulfide.







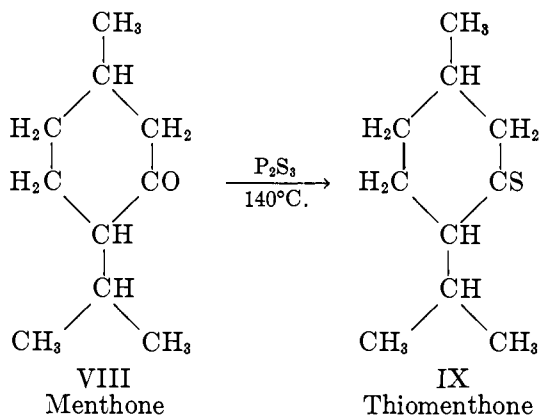
III gave thiocamphor (V) and thioborneol (VI) on heating, while IV gave V, VI, and sulfur on heating. Houben and Doscher (96) prepared bornyl disulfide (III) by oxidizing thioborneol (VI) with chromium trioxide. Pyrolysis of III gave V and VI. Rimini (164) prepared both thiocamphor and thiofenchone (VII) by pyrolysis of the disulfides.



Schönberg and Schutz (184, 187) heated the dibenzylmercaptol of fluorenone, and obtained a highly colored compound, presumably thiofluorenone, but did not record the properties of this thione.

### 3. Action of phosphorus trisulfide on ketones

Speranski (202) has investigated the effect of phosphorus trisulfide on various homocyclic ketones. When menthone (VIII) was heated with phosphorus trisulfide, thiomenthone (IX) was obtained as a high-boiling red oil. The

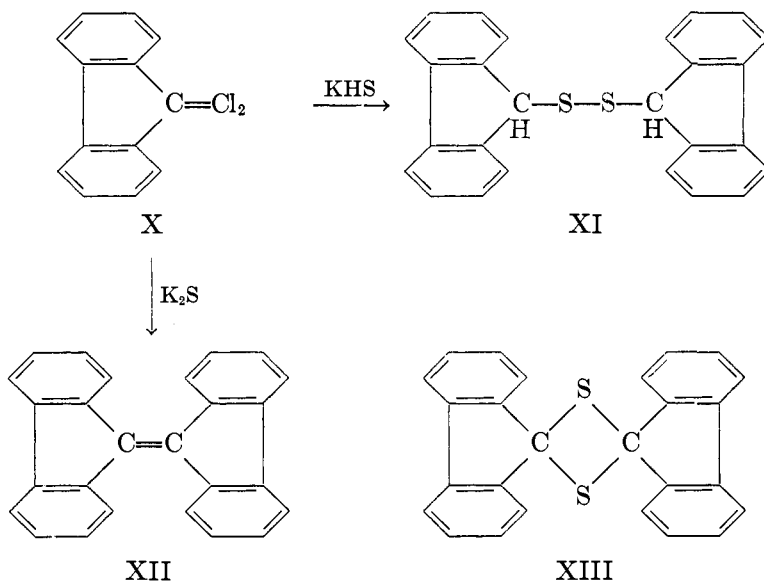


molecular weight of this compound indicates that it is the monomer. Camphor and methylcyclohexanone also reacted with phosphorus trisulfide to yield the corresponding thiones.

### 4. Special methods: reaction of halides with metal sulfides

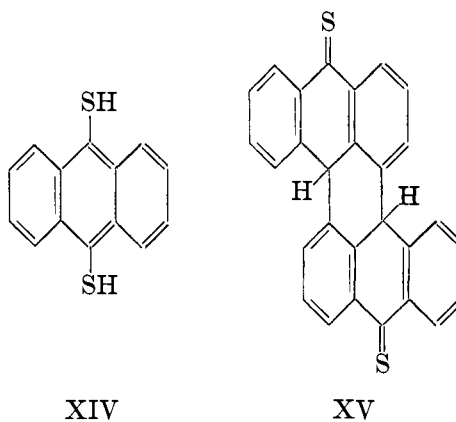
Smedley (201a) attempted to prepare thiofluorenone by treating 9,9-dichlorofluorene (X) with alcoholic potassium bisulfide or potassium sulfide. The reaction with potassium bisulfide yielded a white crystalline compound, melting at 167°C., which was thought to be the dimeric thiofluorenone, but was later

shown by Bergmann and Hervey (30) to be the disulfide (XI). Treatment of X with potassium sulfide gave bis-diphenyleneethylene (XII), red plates, m.p.



187–188°C. Bergmann and Hervey (30) were able to prepare the dimer XIII, m. p. 232°C., by treating fluorenone with hydrogen sulfide and hydrogen chloride in cold alcohol. No monomeric thiofluorenone was obtained in either of the above reactions, or by treatment of the ketone with phosphorus pentasulfide.

Heilbron and Heaton (86) attempted to prepare anthracene-9,10-dithiol (XIV) by treating 9,10-dibromoanthracene with sodium bisulfide in amyl alcohol. Instead they obtained a bright yellow, highly insoluble compound, melting at 320°C., to which they assigned structure XV and the name "dithioheptacylene." In a later paper, Cooke, Heilbron, and Walker (51) noted that

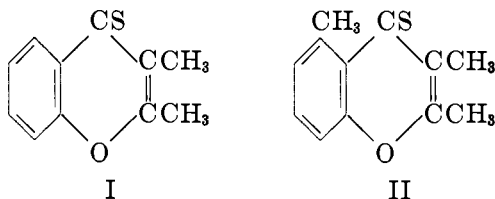


9,10-dibromoanthracene was completely converted to XV by treatment with excess sodium sulfide for 2 hr. in an autoclave at 150°C. The structure XV has not been proven.

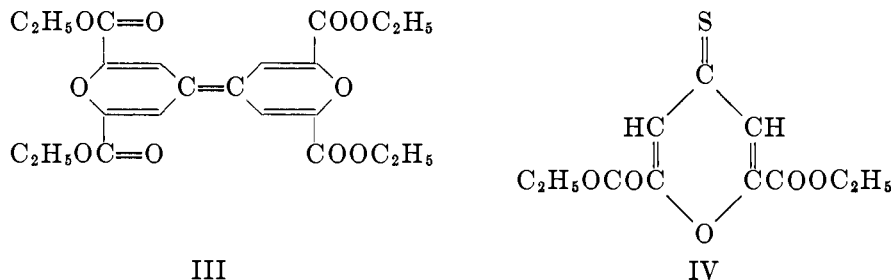
### G. HETEROCYCLIC THIONES

#### 1. Effect of phosphorus pentasulfide on ketones

The heterocyclic thiones are relatively stable, high-melting compounds, which are easily prepared by several methods. By far the largest number of heterocyclic thiones have been prepared by fusing phosphorus pentasulfide with the required ketone, and extracting the cooled, pulverized mass with a solvent, such as benzene or acetone. The solvent is then removed and the residue recrystallized from an appropriate solvent, such as alcohol. The yields on this reaction are generally good. Thus, Simonis and Rosenberg (201) obtained 2,3-dimethylthiochromone (I) in 70 per cent yield, and 2,3,5-trimethylthiochromone (II) in 100 per cent yield. The reaction is sometimes complicated by the conversion of the thione to an ethylene derivative by loss of sulfur.

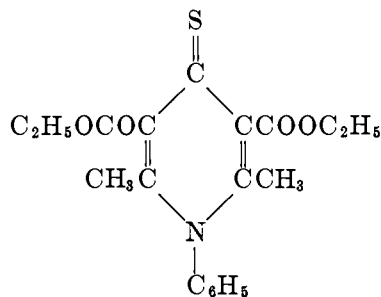
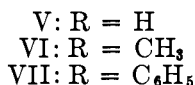
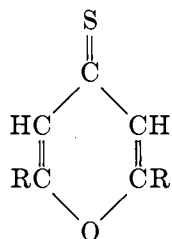


Arndt and Nachtwey (3) boiled phosphorus pentasulfide with diethyl chelidonate in benzene, and obtained the tetracarbethoxydipyrylene (III) instead of the expected diethyl 4-thiochelidonate (IV). They were able to obtain the desired compound by running the reaction in the presence of mercuric chloride, which precipitated as an insoluble complex with the thione.



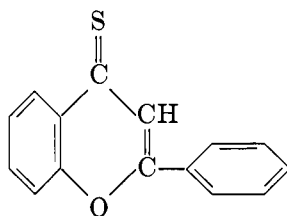
However, most of the heterocyclic thiones are sufficiently stable to be prepared by fusing with phosphorus pentasulfide. Arndt, Scholz, and Nachtwey (5) prepared 4-thiopyrone (V), 2,6-dimethyl-4-thiopyrone (VI), and 2,6-diphenyl-4-thiopyrone (VII) by fusing the ketone with twice the calculated quantity of phosphorus pentasulfide for  $\frac{1}{2}$  to 1 hr., followed by extraction with

benzene and recrystallization of the product from petroleum ether. This method has received its largest application with those heterocyclic ketones containing



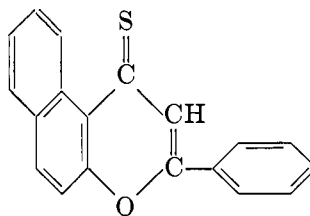
VIII

oxygen or sulfur in the ring. In this way, Schönberg and Nickel (181) synthesized 4-thioflavone (IX) and  $\alpha$  naphtho-4-thioflavone (X); Simonis and Elias (199) prepared 2,3-dimethyl-1,4-dithiochromone (XI); and Arndt, Nachtwey, and Pusch (4) obtained 1,4-dithioflavone (XII).

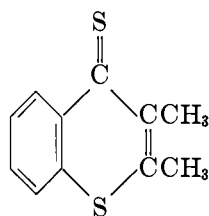


IX

4-Thioflavone

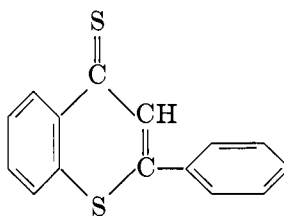


X

 $\alpha$ -Naphtho-4-thioflavone

XI

2,3-Dimethyldithiochromone

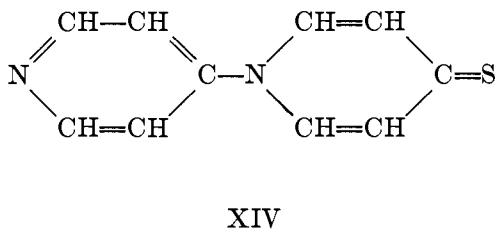
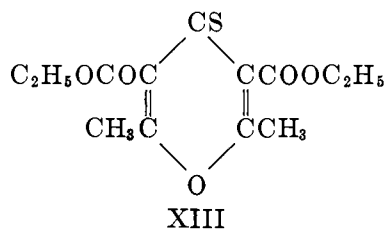


XII

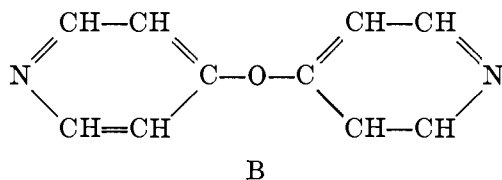
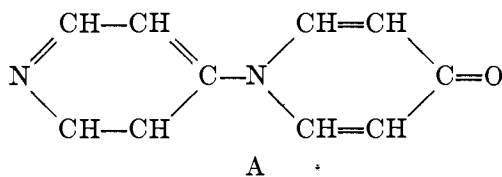
1,4-Dithioflavone

This method can be used with the nitrogen heterocycles, but apparently other methods are more efficient. Guthzeit and Epstein (83) prepared diethyl *N*-phenyl-2,6-dimethyl-4-thiopyridone-3,5-dicarboxylate (VIII) by fusing the ketone with phosphorus pentasulfide, and also by heating diethyl 2,6-dimethyl-

4-thiopyrone-3,5-dicarboxylate (XIII) with aniline in acetic acid. Arndt (2) prepared *N*-4-pyridyl-4-thiopyridone (XIV) by fusing the anhydride of 4-

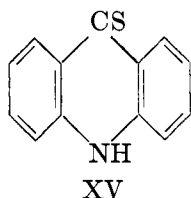


hydroxypyridine with phosphorus pentasulfide, and offers this compound as evidence for the keto form (A) of the 4-hydroxypyridine anhydride, rather than the ether form (B).

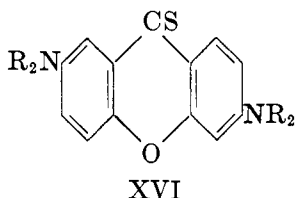


### 2. Oxidation of methylene and ethylene derivatives with sulfur

Several basic methylene derivatives have been converted to the thiones by simply heating the compound with sulfur. Edinger and Arnold (56, 101) obtained thioacridone (XV) by heating acridine with sulfur at 190–195°C. for 4 hr., and recrystallizing the product from alcohol. Rodd and Stocks (165) patented a process for the preparation of 3,7-tetraalkyldiaminoxanthenes, which depends on the formation of the xanthenes (XVI) by heating the 3,7-



Thioacridone

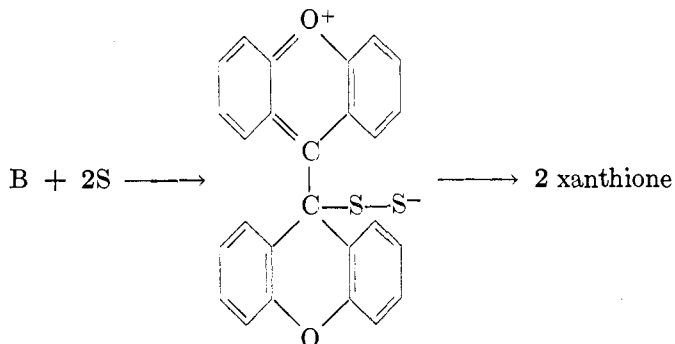


tetraalkyldiaminoxanthenes with sulfur in boiling xylene for 24 hr. The xanthenes may be converted to the xanthenes by boiling with hydrochloric acid.

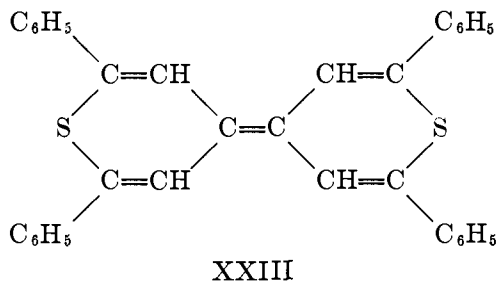
Schönberg (172) originally noted that dixanthylene (XVII) was converted to



Schönberg and Askar therefore conclude that the reaction is due to the heterocyclic structure, and may be explained on the basis of resonance hybrids. For instance, xanthylene may exist in five different resonance structures A, B, B', C, and C', in which the prime letters indicate quinoid structure in the alternate aromatic ring. Sulfur may then add to the unshared electrons on the negative carbon and the resulting disulfide could dissociate to two molecules of xanthione. The failure of 2,6,2',6'-tetraphenyldithiopyrylene (XXIII) to form the thio-



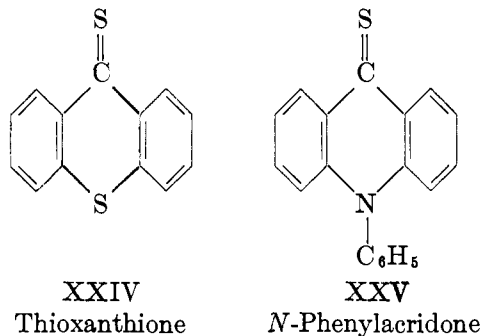
pyrylene when heated with sulfur is attributed to the fact that the reverse reaction



(conversion of the thiopyrylene to the dithiopyrylene) takes place at low temperature.

3. Action of thioacetic acid on keto chlorides

The reaction of thioacetic acid with the keto chlorides of diaryl ketones has been mentioned previously (page 27). Schönberg, Schutz, and Nickel (190)

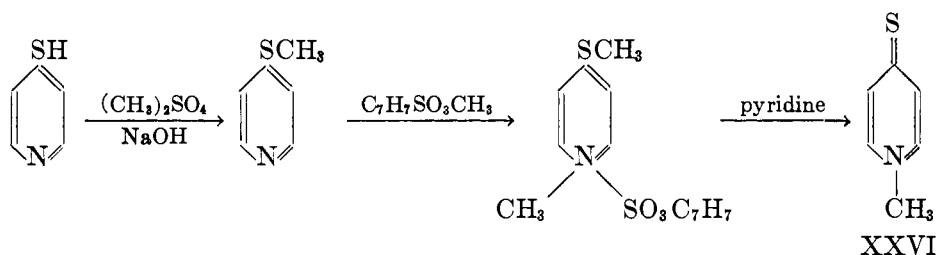


found this reaction to be equally valuable in the heterocyclic series, and in this manner were able to prepare xanthione (XVIII), thioxanthione (XXIV), and *N*-phenylthioacridone (XXV). The properties of thioxanthione prepared in this way differ from those of the thioxanthione prepared by fusion of the ketone with phosphorus pentasulfide, however. Meyer and Szaneci (132) prepared both xanthione and thioxanthione by fusion of the ketones with phosphorus pentasulfide. The properties of xanthione are the same when it is prepared by either method (red needles, m.p. 155–156°C.), but Schönberg and coworkers report thioxanthione to be greenish black plates, melting at 168°C. This compound is also obtained from dithioxanthylene and sulfur. Meyer and Szaneci report the compound to be olive-green, and to melt at 215°C. The properties of thioxanthione (XXIV) are therefore indefinite.

#### 4. Special methods

##### (a) From thioethers of heterocyclic nitrogen bases

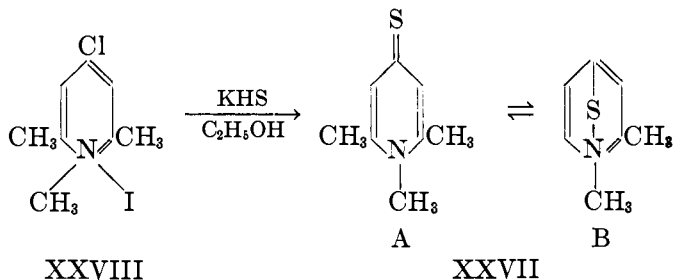
Kendall (103) has patented a method for the synthesis of *N*-alkylated heterocyclic thiones from the mercaptans, which involves heating the quaternary salt of the thioether in a weak organic base, such as pyridine. In this manner *N*-methyl-4-thiopyridone (XXVI) was synthesized by treating 4-mercaptopyridine with methyl sulfate and alkali, and converting the resulting thioether to the



quaternary methyl tosylate with methyl toluenesulfonate. Boiling this salt in pyridine resulted in the formation of *N*-methyl-4-thiopyridone.

##### (b) Action of halogenated nitrogen heterocycles with metal bisulfides or thiosulfates

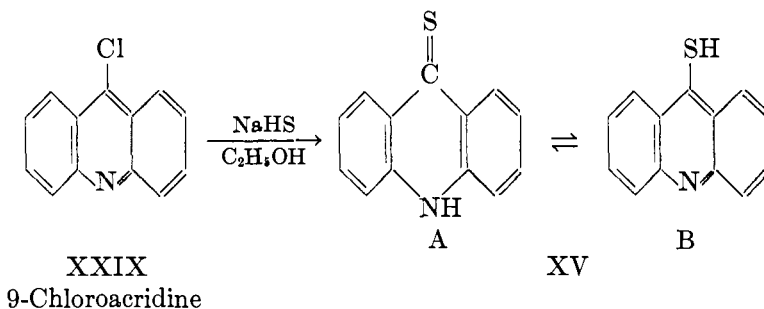
The  $\gamma$ -halogenated pyridines and acridines have been found to react with metal bisulfides to give the thiopyridones and thioacridones. By this means





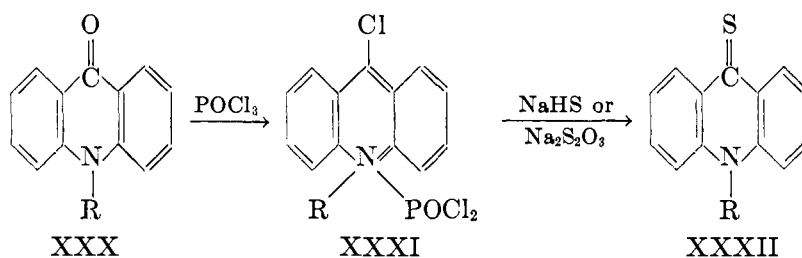
Michaelis and Holken (134) were able to prepare *N*-methyl-4-thiolutidone (XXVII) by treating 4-chlorolutidine methiodide (XXVIII) with potassium bisulfide. It was suggested that this compound exists in the tautomeric thione (A) and thiol salt (B) forms because, although it gave several thione reactions, treatment with methyl iodide gave the thiomethyl ether methiodide.

A series of thioacridones has been prepared by Cherntsov (47) by treating 9-chloroacridine (XXIX) or its derivatives with sodium bisulfide in alcohol, and



yields of over 90 per cent in all cases were reported. The compounds prepared were chloro, methyl, and methoxy derivatives of thioacridone (XV). These compounds also exist in the thione-thiol (A-B) tautomeric forms.

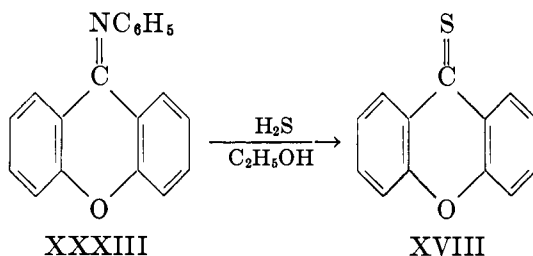
Gleu and Schaarschmidt (77) used a variation of this method to synthesize several *N*-substituted thioacridones, after trying several alternate methods. These authors found that alkylation of thioacridones gave exclusively the *S*-alkyl derivatives, which did not isomerize to the desired *N*-alkyl compounds on heating. Heating the appropriate *N,N'*-disubstituted acridylenes with sulfur gave the desired compounds, but the most efficient preparation utilized the 9-chloroacridinium dichlorophosphates as intermediates. When *N*-substituted



acridones (XXX) are treated with phosphorus oxychloride, the quaternary 9-chloroacridinium dichlorophosphates (XXXI) result. When these salts are reacted with sodium bisulfide or sodium thiosulfate, the desired thiones (XXXII) are produced in good yield. Gleu and Schaarschmidt reported that the reaction with sodium thiosulfate was almost quantitative even in excess mineral acid, indicating that it was faster than the decomposition of thiosulfuric acid. Sodium thiosulfate does not react readily with the non-quaternary salts of 9-chloroacridine, however. This method was used to prepare the *N*-methyl-, *N*-ethyl-, and *N*-phenyl-thioacridones.

## (c) Action of hydrogen sulfide on ketone derivatives

When the anil of xanthone (XXXIII), prepared by heating *o,o'*-dihydroxybenzophenone with aniline, was dissolved in alcohol, and the hot solution saturated with hydrogen sulfide for 24 hr., xanthione (XVIII) was obtained (Graebe



and Roder (78)). No yield was reported for this reaction.

## (d) Pyrolysis of mercaptals and thioethers

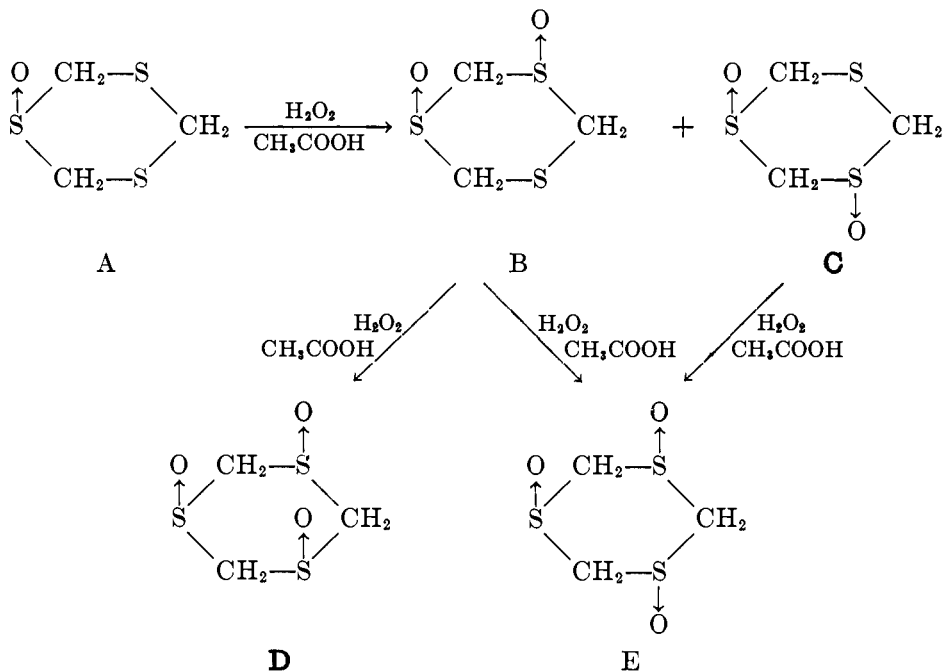
Schönberg and Schutz (184, 187) found that the mercaptals of xanthone and thioxanthone were most easily converted to the thiones by heat. Schönberg, Schutz, Bruckner, and Peters (188) found that dixanthyl thioether was converted at 185°C. to xanthene and xanthione. The yield in this reaction is not high.

## V. PHYSICAL PROPERTIES AND MOLECULAR STRUCTURE

## A. ISOMERS OF THE TRIMETHYLENE TRISULFIDE RING

The problem of *cis* and *trans* isomers has been difficult to resolve in the case of the trimethylene trisulfide ring, owing to the occurrence of polymorphism, eutectic mixtures, and trithioformaldehyde polymers. For a time, it was assumed that there were two isomers of *s*-trithiane itself. As previously noted (page 5), Baumann and Fromm (20) had separated a variety of compounds from a crude preparation of *s*-trithiane, which included polymers and complex oxygen- and sulfur-containing compounds. Hinsberg (87, 88) reduced trimethylene trisulfoxide with concentrated hydrogen iodide, and obtained a compound melting at 247°C. which he claimed to be a  $\beta$ -form of *s*-trithiane. (The  $\alpha$ -form melts at 216°C.) It was possible to reconvert this compound to the  $\alpha$ -form by recrystallization. Hinsberg attributed the existence of a second isomer of *s*-trithiane to the spacial characteristics of the sulfur atom (90). Fromm and Soffner (71) investigated this problem, and concluded that Hinsberg's  $\beta$ -form was actually a cyclic methylene sulfur compound,  $(\text{CH}_2)_x$ , in which  $x$  was greater than 3. Hinsberg, however (92), claimed that his compound gave the same trisulfone,  $(\text{CH}_2\text{SO}_2)_3$ , upon complete oxidation with potassium permanganate, as did *s*-trithiane, and that therefore it must retain the same ring structure as *s*-trithiane. This is not very conclusive, since trithiane trisulfone decomposes without melting at about 320°C., making its identity with other sulfones difficult to prove.

Fromm and Soffner's criticism was beautifully confirmed by Bell and Bennett (27), who were able to separate all of the sulfoxides which would theoretically exist for a planar trimethylene trisulfide ring. Oxidation of *s*-trithiane with hydrogen peroxide in acetone yielded only 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 also decompose at high temperatures without melting, their non-identity was demonstrated by their crystalline properties and solubility. Compound C, upon further oxidation with hydrogen peroxide in acetic acid



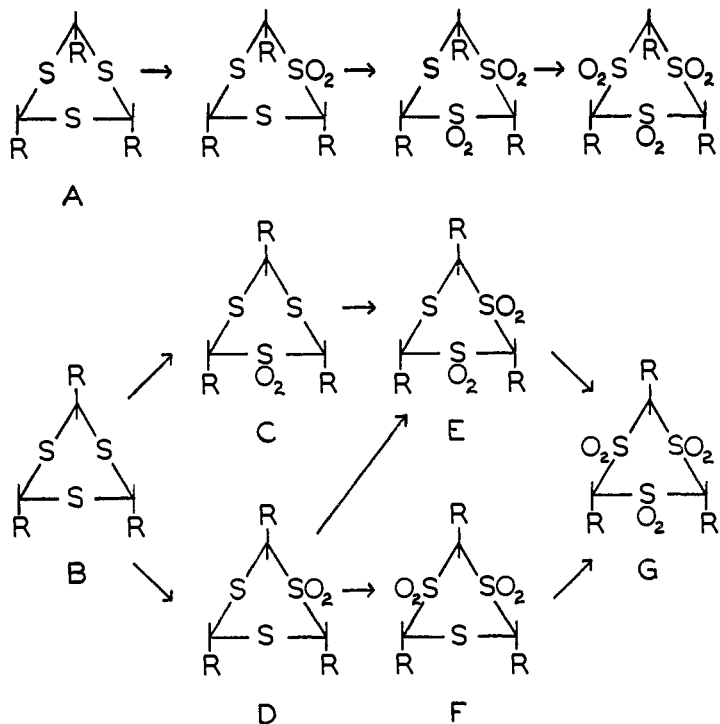
acid, yielded only one trisulfoxide, E. The *trans* configuration was therefore assigned to C, and the *cis-trans* configuration to E. This agrees with their solubilities and stabilities. Compound B, upon further oxidation, yielded two trisulfoxides, which were separated by fractional crystallization. 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. The existence of these various *cis*- and *trans*-sulfoxides proves that *s*-trithiane exists in a simple planar ring structure.

### 1. Trithioacetaldehyde

Trithioacetaldehyde is the only 2,4,6-trialkyltrithiane which has been investigated in regard to *cis* and *trans* forms. Klinger (107) originally proposed the cyclic structure for trithioacetaldehyde, and separated the two isomers,  $\alpha$ -trithioacetaldehyde, m.p.  $101^\circ\text{C}$ ., and  $\beta$ -trithioacetaldehyde, m.p.  $125$ – $126^\circ\text{C}$ .

Baumann and Fromm (15) carried out an extensive investigation of the *cis* and *trans* isomers of both trithioacetaldehyde and trithiobenzaldehyde. By treating acetaldehyde with hydrogen sulfide and hydrogen chloride in cold alcohol, they were able to isolate the  $\alpha$ - and  $\beta$ -forms, and a  $\gamma$ -form, m.p. 85–95°C., which they later (17) showed to be a mixture of the two isomers. Suyver (215) explored the eutectic mixtures of  $\alpha$ - and  $\beta$ -trithioacetaldehydes, and found that a mixture of 60 per cent  $\alpha$ -form and 40 per cent  $\beta$ -form melts rather sharply at 75–76°C. This is undoubtedly the  $\gamma$ -form, which Mann and Pope (125) claimed was formed when  $\alpha, \alpha'$ -dichlorodiethyl sulfide was treated with silver sulfide, hydrogen sulfide, silver oxide, or sodium hydroxide (page 9). Fromm and Engler (67) prepared the trisulfoxides of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -trithioacetaldehydes by oxidation with 30 per cent hydrogen peroxide in glacial acetic acid, and obtained an  $\alpha$ -trisulfoxide melting at 184°C. and a  $\beta$ -trisulfoxide melting at 153°C. The trisulfoxide from the  $\gamma$ -form was identical with that from the  $\alpha$ -form. This work is not conclusive, however, since there should theoretically be two trisulfoxides for each form.

Baumann and Fromm (15) had concluded that the more stable, higher-melting  $\beta$ -forms of trithioacetaldehyde and trithiobenzaldehyde were the *trans* isomers, by analogy with the *trans*-hexahydrophthalic acid. These authors realized that the sulfoxides would give too many isomers to be useful for positively proving which of the two forms was *cis*, and which *trans*, and therefore proposed to use the mono-, di-, and tri-sulfones (17). Thus the *cis* form of a 2,4,6-trisubstituted trithiane (A) would theoretically yield only one mono-



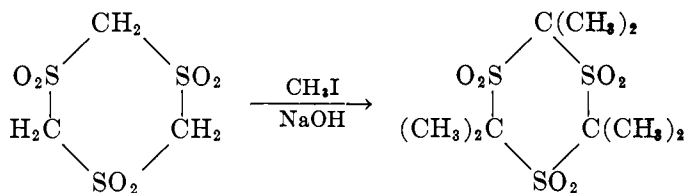
sulfone, one disulfone, and one trisulfone, while the *cis-trans* form (B) would yield two monosulfones, depending on whether the sulfur atom between the two *cis* substituents was oxidized (C) or whether either of the other two sulfur atoms were attacked (D). The monosulfone C would then yield only one disulfone (E), while the monosulfone D would yield two disulfones (E and F), and both E and F would yield the same trisulfone (G). Baumann and Fromm were unable to carry out all of these reactions, but found that direct oxidation of  $\alpha$ - and  $\beta$ -trithioacetaldehydes to the trisulfones with potassium permanganate in sulfuric acid yielded products melting above 300°C. which were apparently the same! This was later proved to be the case by Lomnitz (122), who prepared derivatives of both trisulfones which were identical with one another. Baumann (12) was able to prepare the disulfones by permanganate oxidation of the  $\alpha$ - and  $\beta$ -trithioacetaldehydes, and again found only one disulfone, melting at 283–284°C., instead of three, as called for by the theory. It was therefore assumed that rearrangement had occurred on oxidation.

Chattaway and Kellett (46) investigated the monosulfoxides and monosulfones of  $\alpha$ - and  $\beta$ -trithioacetaldehydes, and found that oxidation of  $\beta$ -trithioacetaldehyde (m.p. 126°C.) with hydrogen peroxide gave one monosulfoxide, which on oxidation with potassium permanganate in dilute magnesium sulfate solution gave one monosulfone, m.p. 190°C. This sulfone could not be reduced to the original  $\beta$ -trithioacetaldehyde, but the sulfoxide was so reduced by zinc and hydrochloric acid. Oxidation of the  $\alpha$ -isomer (m.p. 101°C.) in a similar manner yielded two monosulfones, one melting at 157°C., and the other at 115–116°C. Mixed melting points proved these three monosulfones to be different. Since the  $\alpha$ -isomer yielded two monosulfones, and the  $\beta$ -isomer only one, it was concluded that the lower-melting, more soluble  $\alpha$ -compound had the *cis-trans* configuration (B, R = CH<sub>3</sub>) and that the higher-melting, less soluble  $\beta$ -compound was the *cis* compound (A, R = CH<sub>3</sub>). This is contrary to the usual behavior of *cis* and *trans* isomers. The conversion of Chattaway and Kellett's monosulfones to the corresponding disulfones has not been reported. Of the trithioacetaldehyde isomers, the  $\gamma$ -form has fairly definitely been proved to be a mixture of the  $\alpha$ - and  $\beta$ -forms, but which of the two pure forms is *cis-trans* and which *cis-cis* may still be open to question.

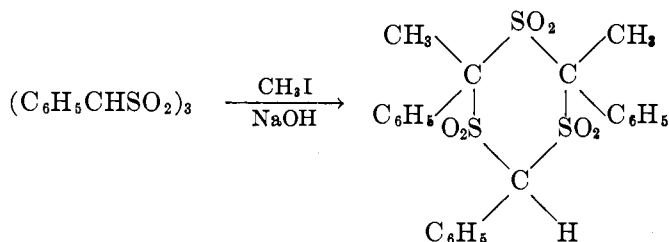
## 2. Trithiobenzaldehyde and derivatives

The problem of the isomeric *cis-cis* and *cis-trans* trithiobenzaldehydes parallels very closely the same question in the thioacetaldehyde group. Baumann and Fromm (15) originally separated three compounds,  $\alpha$ -trithiobenzaldehyde, m.p. 166–167°C.,  $\beta$ -trithiobenzaldehyde, m.p. 225–226°C., and  $\gamma$ -trithiobenzaldehyde, m.p. 83–85°C. By analogy with the trithioacetaldehydes, they concluded that the  $\gamma$ -form was a mixture of the  $\alpha$ - and  $\beta$ -forms. Suyver (215) later confirmed this conclusion, and studied the solubilities of the  $\alpha$ - and  $\beta$ -forms. It was found that the  $\alpha$ -trithiobenzaldehyde was much more soluble than the  $\beta$ -isomer, e.g., fifty times more soluble in chloroform, and sixty times more soluble in benzene.

Baumann and Fromm prepared a series of substituted trithiobenzaldehydes (18, 19, 21) and found two isomers for each of the compounds they prepared. Kopp (111) and Worner (228) also prepared substituted trithiobenzaldehydes, and although they were sometimes only able to prepare one of the two possible isomers, in no case were more than two isomers found. Hinsberg (89, 91) claimed to have prepared a third modification of trithiobenzaldehyde by oxidation of the  $\beta$ -isomer to the tetroxide, and reduction of this oxide with hydrogen iodide, but Fromm and Schultis (70) were able to refute this claim by demonstrating that rearrangement occurs very readily on oxidation of the 2,4,6-triphenyltrithiane isomers. Thus the same trisulfoxide was obtained when either  $\alpha$ - or  $\beta$ -trithiobenzaldehyde was oxidized with hydrogen peroxide in acetic acid. Reduction of this trisulfoxide yielded only  $\beta$ -trithiobenzaldehyde, the more stable form. Fromm and Schultis believed this to be the *cis-trans* form, because of its stability, high melting point, and low solubility, and because it exhibited hindrance when the trisulfone was treated with methyl iodide in sodium hydroxide solution. Ordinarily, when a trimethylene trisulfone is treated in this manner, all of the hydrogens on the methylene groups are replaced by methyl groups. In this way, Baumann and Camps (13) obtained the trisulfone of trithioacetone by treating trimethylene trisulfone with methyl iodide in sodium hydroxide. However, if the trisulfone of trithiobenzaldehyde is treated in this manner, only two methyl groups are added. Fromm and



Schultis explain this on the assumption that one of the methylene hydrogens is less reactive because it is between two phenyl groups, thus indicating the *cis-trans* structure for the trisulfone and trisulfoxides of trithiobenzaldehyde, and



consequently, the same structure for the  $\beta$ -trithiobenzaldehyde itself.

#### B. COLOR OF MONOMERIC THIOCARBONYL COMPOUNDS

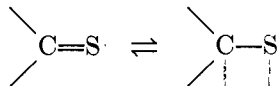
With few exceptions, all of the monomeric thiones are colored compounds. This property is useful in determining the point at which the trimers dissociate.

For instance, trithioacetophenone gives a blue solution in boiling xylene; the color gradually fades as the solution is cooled and association takes place. In the monomeric thiones, the color varies with the temperature. Cherntsov (47) noted an increase in the color intensity of thioacridones when they were heated above 110–120°C. Schönberg (174) mentioned the fact that some of the substituted diaryl thiones and heterocyclic thiones changed color on cooling to very low temperatures. Di-*p*-anisylthione changes from blue to violet on cooling in an acetone and dry ice mixture. Straus and Zeime (214) noted the influence of auxochrome groups on the thiones. Tetramethyldiaminothiobenzophenone is orange-red, while thiobenzophenone itself is deep blue in color. Staudinger and Siegvart (212) also commented on this variation of color, but showed that it did not influence the reactivity of the thione group. Violet thiobenzophenone, blue *p,p'*-dimethoxythiobenzophenone, and red *p,p'*-tetramethyldiaminothiobenzophenone all react with equal speed with diphenyldiazomethane.

### 1. Absorption spectra

The absorption curves of various thiones have been measured. Bost and Cosby (39) found absorption bands at about 5900 Å. for phenyldiphenylthione, phenyl-*p*-tolylthione, and phenyl- $\alpha$ -naphthylthione. Sen (197) found a band at 4950 Å. for thiofenchone. Burawoy (41, 42) compared the absorption spectra of the chromophoric C=NH, C=O, and C=S groups, and found that extinction increased in that order, and also noted that the absorption bands were shifted toward the red in the same order. On the basis of the optical properties of the thiones, Burawoy proposed that they may exist in a free-radical form to a small extent. Donle and Volkert (53) also found a significant difference in the ultraviolet-absorption curves of compounds containing the carbonyl and thiocarbonyl groups, a result which showed a difference in the structure of the two groups.

The color characteristics associated with the thiocarbonyl group are comparable to the color properties of free radicals. Bergman, Magat, and Wagenberg (31) noted the similarity in the color change when the methoxy or dimethylamino groups were introduced into diaryl ketones or into hexarylethanes, and suggested that the monomeric thione group may be represented as a tautomeric thione-free-radical arrangement. This is borne out by other observations. In

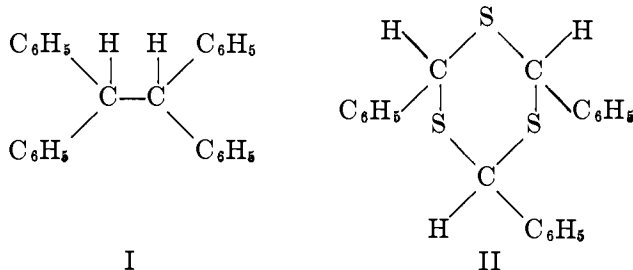


many chemical reactions, diaryl thiones behave like triarylmethyls. For example, both triphenylmethyl and thiobenzophenone take up oxygen in the air to form unstable peroxides.

### 2. Tendency to polymerize

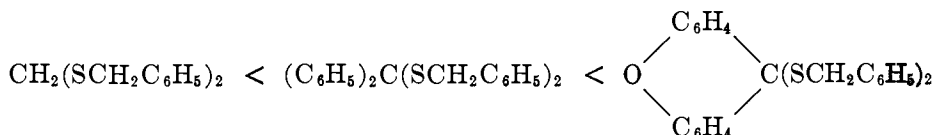
The suggestion that the monomeric thiones may exist as free radicals caused Schönberg (173) to compare the dissociation tendencies of the polymeric thiones

with the dissociation tendencies of corresponding members of the ethane series. Tetraphenylethane (I) and 2,4,6-triphenyltrithiane (II) are stable, but if the hydrogens are replaced by phenyl groups, then the tendency to dissociate is

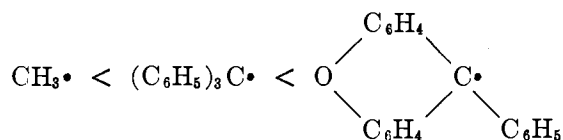


greatly increased. Schönberg made the generalized statement that the same substituents which increase the stability of free radicals will increase the stability of the thione monomers.

Parallel observations were made by Schönberg and Schutz (184, 187) on the pyrolysis of mercaptals. In the dibenzylmercaptal series, the tendency to decompose on heating increases with the size of the methylene substituents, and this tendency parallels the dissociation of substituted ethanes. The ease of pyrolysis may be represented by the following series:

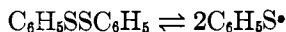


in which the xanthone derivative decomposes most readily. The stability of the free radicals may be represented by the series:



in which phenylxanthyl is the most stable.

Schönberg, Rupp, and Gumlick (183) found evidence for the existence of free sulfur radicals in compounds other than the thiones, and they suggest the name "thiyl" for the free radicals of this type. It was found that diphenyl disulfide did not obey Beer's law in solution, and that it reacted with diazomethane and other reagents like a free radical.



### C. OTHER PHYSICAL EVIDENCE OF MOLECULAR STRUCTURE

#### 1. Dipole moment

Sidgwick (198) has reviewed the work on the dipole moment of the C=S group. The results of several groups of workers indicate that the moment of



the C=S group is about  $0.5 \times 10^{-18}$  greater than that of the C=O group. Sidgwick assigned to them the values  $3.0 \times 10^{-18}$  and  $2.5 \times 10^{-18}$ , respectively. Donle and Volkert (53) measured the moments of dianisyl ketone and dianisyl thioketone, and obtained  $3.8 \times 10^{-18}$  for the former and  $4.44 \times 10^{-18}$  for the latter, a difference of  $0.6 \times 10^{-18}$ . These authors believed that this indicates a significant structural difference in the C=O and C=S groups, since a smaller moment would be expected for the C=S group. Hunter and Partington (97) corroborated these findings with the value of  $2.95 \times 10^{-18}$  for benzophenone and  $3.4 \times 10^{-18}$  for thiobenzophenone, an increase of  $0.45 \times 10^{-18}$  for the latter.

### 2. Bond energies and interatomic distance

The bond energy for the C=O group is 152 kg.-cal., and that for the C=S group is 103 kg.-cal. (reference 117, page 1800; after Pauling). This rather large difference, indicating a much weaker bond, is not contradictory to the concept of the existence of a free-radical type of structure in the C=S group.

The interatomic distance is also in agreement with this concept. Use of the interatomic radii of Pauling and Huggins (117, page 1772) gives the value 1.61 Å. for the carbon-to-sulfur distance in C=S, and 1.26 Å. for the carbon-to-oxygen distance in C=O. These figures have been determined from measurements on carbon disulfide, thiourea, etc., and not on thiones.

Sufficient data are not available for any conclusions to be drawn about refractive indices or parachors for the thiones or thials.

### 3. Phosphorescence

Recently, Lewis and Kasha (120, 121) have made some interesting calculations based on phosphorescence and absorption of compounds in the triplet or biradical state. A typical example of this biradical state would be the free radical of thiobenzophenone ( $\phi = \text{C}_6\text{H}_5$ ):



Thiobenzophenone was used by these authors to demonstrate the identity of the phosphorescent and the triplet states. Thus they were able to calculate the triplet-state energy ( $E_t = \text{kg.-cal.}$ ) for thiobenzophenone from both phosphorescence and absorption-spectrum data. It was shown that the abnormal colors of the monomeric thiones are due to absorption from the singlet to the triplet state.

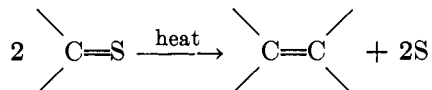
Lewis and Kasha (121) have also discussed the tendency of thiones to dimerize or trimerize, and have pointed out that, if  $E_{\text{Dim}}$  is written for the energy of association, then the dimer is thermodynamically stable when  $E_{\text{Dim}} > 2E_t$ , where  $E_t$  stands for the triplet-state energy. Therefore, in all cases where  $E_t$  is small, dimerization might be expected, except where  $E_{\text{Dim}}$  is small, owing to steric hindrance or other effects, as in the case of di-*tert*-butyl thione. Similar conditions apply to the case of trimerization also.

## VI. REACTIONS OF THIALS AND THIONES

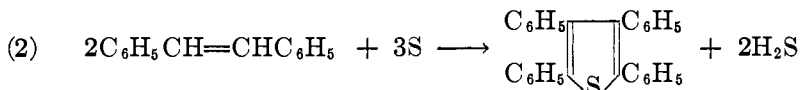
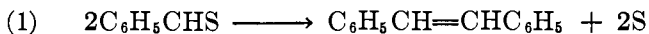
There is considerable physical evidence which indicates that the monomeric thiones exist partially in the biradical state, which frequently causes the C=S group to behave in chemical reactions in a different manner from the C=O group. In other reactions, however, it may behave as an analog of the carbonyl group.

## A. EFFECT OF HEAT ON THIONES AND THIALS

The thiones and thials tend to lose sulfur under the influence of heat, to form ethylene derivatives. Although this reaction does not occur with all thiocar-

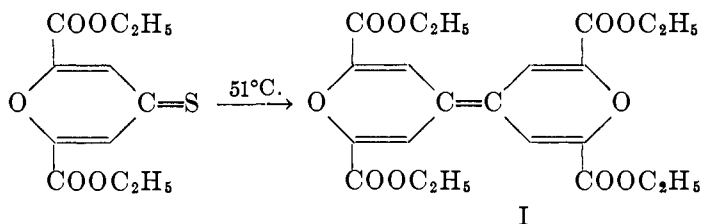


bonyl compounds, it seems to occur with both the monomers and trimers of those compounds which do react. The reaction has long been known. Fleischer reported the formation of stilbene and thionessal from the dry distillation of thiobenzaldehyde in 1866 (64). The thionessal was formed by the reaction of sulfur and stilbene at high temperatures. Barbaglia and Marquardt (10) obtained stilbene when benzaldehyde and sulfur were heated to 180°C. for 36



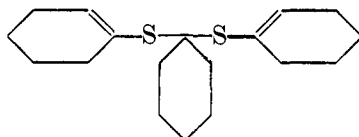
hr., and undoubtedly thiobenzaldehyde was an intermediate in this reaction. Kopp (110, 111) investigated the effect of heat on a series of aromatic thial trimers and found that the trimers of *o*-, *m*-, and *p*-hydroxythiobenzaldehydes were converted to the respective stilbene derivatives when they were heated above their melting points. *o*-Methoxythiobenzaldehyde was converted directly to the tetra-*o*-methoxyphenylthiophene on heating to 145°C., and no stilbene could be isolated from this reaction mixture. Wood and Bost (226) repeated Fleischer's work on the formation of thionessal by distillation of tri-thiobenzaldehyde. Later, these same authors (227) found that the ethylene derivative was obtained in 70 per cent yield when  $\beta$ -ethoxy- $\alpha$ -thionaphthaldehyde was heated to 300°C.

The conversion of heterocyclic thiones to the corresponding ethylene derivatives by heat has been investigated by Arndt and coworkers (3, 4, 5) and re-



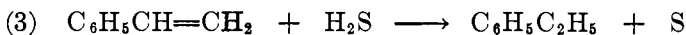
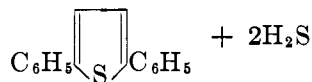
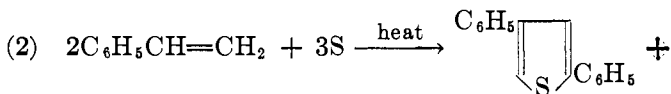
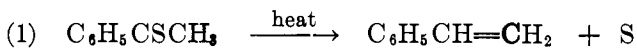
viewed by Schönberg and Askar (176). Arndt and Nachtwey (3) observed that diethyl 4-thiochelidonate was converted at its melting point (51°C.) to the dipyrlylene derivative (I). The remarkable ease of this conversion led Arndt, Scholz, and Nachtwey (5) to test thiopyrone, 2,6-dimethylthiopyrone, 2,6-diphenylthiopyrone, and xanthione in the same way. These authors found that the 2,6-diphenylthiopyrone was converted to the dipyrlylene derivative above its melting point (173°C.), but that the others were not affected. Later Arndt, Nachtwey, and Pusch (4) found that 2,6-diphenyl-1,4-dithiopyrone was converted to the dithiopyrlylene derivative at 145°C., but that 1,4-dithioflavone did not decompose on heating. It was therefore concluded that acidic groups, such as carboxy or phenyl, in the 2- and 6-positions were necessary for the conversion.

Behr (26) obtained some tetraphenylethylene upon heating thiobenzophenone, but the yield was very low. Fromm and Ziersch (72) found that thioacetylthioacetone dimer did not decompose on distillation. Fromm (66) found that when trithiocyclohexanone was heated above its melting point, hydrogen sulfide was evolved, and a compound, C<sub>13</sub>H<sub>23</sub>S<sub>2</sub>, was obtained to which the following structure (II) was assigned.

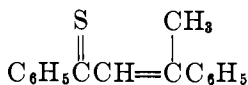


II

When trithioacetophenone was heated, several products were obtained (22). The trimer first dissociated to the monomer at about 145°C., and upon distillation this gave hydrogen sulfide, ethylbenzene, styrene, and both 2,4- and 2,5-diphenylthiophenes. No  $\alpha,\alpha'$ -dimethylstilbene was found. The various compounds are probably formed according to the following equations:



Baumann and Fromm (22) also noted that heating "anhydroacetophenone disulfide" converted it to 2,4-diphenylthiophene. Probably thiodypnone (III)



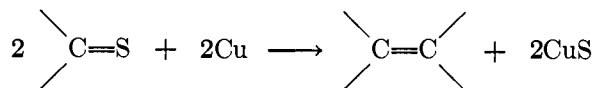
III

Thiodypnone

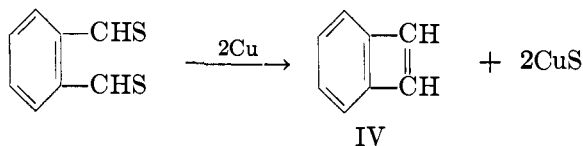
was an intermediate in this reaction, being converted to 2,4'-diphenylthiophene by loss of hydrogen. The reaction is facilitated by the use of copper chromite, a dehydrogenating catalyst (44).

#### B. REACTION WITH METALS

The thiocarbonyl compounds are converted to ethylene derivatives with great ease when a metal which reacts with sulfur is present. The most commonly



used metal is copper or some form of activated copper, but iron, zinc, and nickel have been found effective also. Wislicenus (223) reported that heating thioacetone with copper powder gave copper sulfide, but the organic product was not identified. Later Klinger (105, 106) found that trithiobenzaldehyde was readily converted to stilbene when heated with copper powder, and suggested that this reaction might be used to prepare benzocyclobutadiene (IV). This synthesis has not been confirmed. Kopp (110) found that many of the substituted

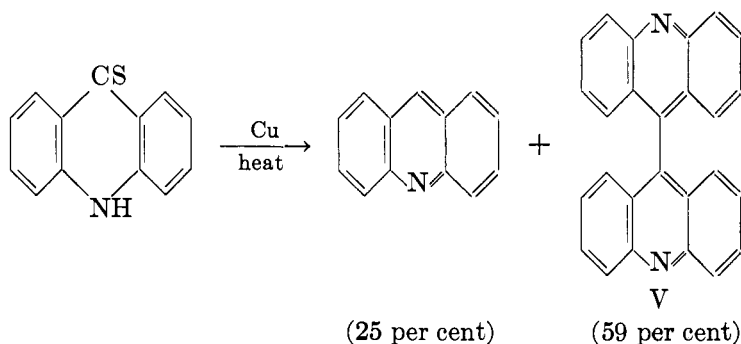


thiobenzaldehydes were converted directly to the tetraarylthiophenes by heat, but if the compounds were heated with iron powder or zinc dust, the stilbene derivative was the chief product. Richtzentrain and von Hofe (163) converted trithiovanillin and trithioveratraldehyde to the corresponding ethylene derivatives by distillation with copper and iron powder, respectively. Even the hindered trithiomesitaldehyde was converted to hexamethylstilbene in 42 per cent yield by heating to 220–230°C. with copper bronze (73). The conditions for synthesizing symmetrical diarylethylenes in this manner were studied by Wood, Bacon, Meibohm, Throckmorton, and Turner (225). In these experiments, the appropriate substituted trithiobenzaldehyde was heated for  $\frac{1}{2}$  hour at 10–15°C. above its melting point with three to four times the calculated quantity of freshly reduced copper powder, and the substituted ethylene was isolated. The reaction was found to be applicable to unsubstituted, or alkoxy-substituted aryl thials. Trithiobenzaldehyde gave a 45 per cent yield of stilbene, and trithioveratraldehyde gave 25 per cent of the 3,4,3',4'-tetramethoxystilbene, but hydroxy derivatives gave only traces of product and nitro derivatives did not react. Dithienylethylene was prepared by Steinkopf and Jakob (213) by heating trithiothienyl aldehyde with copper powder.

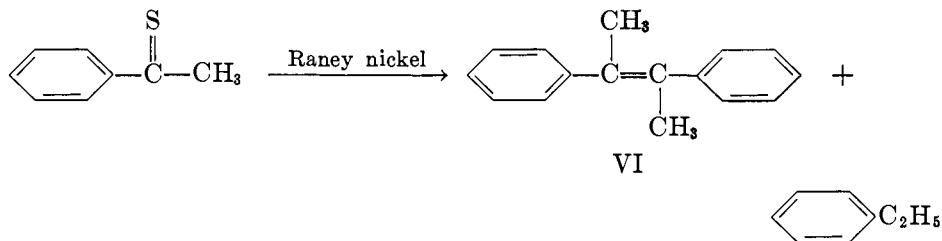
The reaction of copper powder with diaryl thiones to give the tetraarylethylenes has been found to take place with ease in most cases. Gattermann found the reaction to proceed with all of the alkoxy and halogenated diaryl thiones prepared by him (74). The reaction has been used as a means of identifying

thiones (75, 219). Schönberg, Schutz, and Nickel (190) found that the reaction proceeded smoothly in boiling xylene. When thiobenzophenone was treated in this manner with copper bronze powder until the blue color of the solution disappeared—about 45 min.—tetraphenylethylene was obtained in 76 per cent yield. The alkoxy-substituted thiobenzophenones reacted somewhat less readily, and tetramethyldiaminothiobenzophenone gave very poor yields of the ethylene derivative.

The reaction is not very useful in the heterocyclic series. Those heterocyclic thiones which are not converted to ethylene derivatives by heat are resistant to the reaction with copper (176). Schönberg (171) synthesized dixanthylene by heating xanthione with copper bronze, but when thioacridone was heated with copper powder, Lehmstedt and Hundertmark (118) obtained a mixture of reduction products containing 25 per cent of acridine and 59 per cent of 9,9'-diacridyl (V).



Interest in stilbenes as synthetic sex hormones led Cline, Campaigne, and Spies (49) to investigate the conversion of thioacetophenone to  $\alpha, \alpha'$ -dimethylstilbene (VI). Copper powder did not react, either when fused with the dry



compound, or when refluxed in boiling xylene, but an 18 per cent yield of VI was obtained when excess Raney nickel was refluxed with trithioacetophenone in boiling xylene. Since no thione was recovered from the reaction, the main product was probably ethylbenzene. The reduction of thiones to hydrocarbons by Raney nickel alone has not been demonstrated, but Bougault, Cattelain, and Chabier (40) found that phenylthiopyruvic acid was converted to  $\beta$ -phenylpropionic acid by Raney nickel in cold aqueous or alcoholic solution.

The reaction of alkali metals on thiocarbonyl compounds has not been ade-

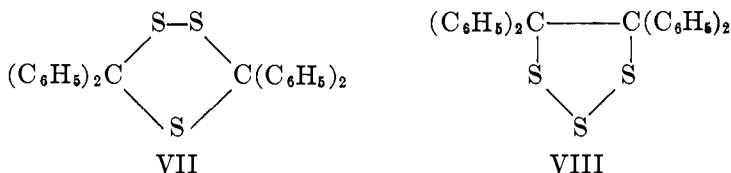
quately described. Schönberg (172) noted that alkali metals reacted with xanthione to give colored products which were unstable in air, and may have been the metal ketyls. Bergmann (28) pointed out that thiones react with sodium differently from ketones. No experimental details were given in either of these papers. In those cases where enolization may occur, such as in thioacetoacetic esters (140), alkali metals react to evolve hydrogen and form the metal mercaptides.

### C. OXIDATION

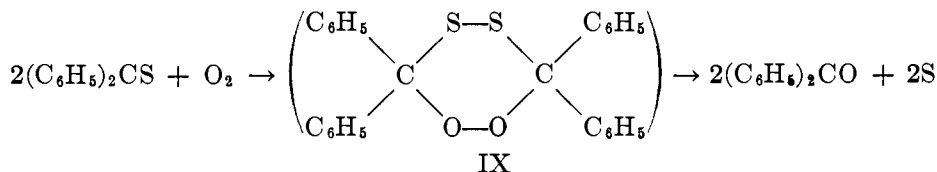
Thiones and thials have been treated with a variety of oxidizing agents. In general, the trimeric thiones and thials behave like sulfides, being converted to the sulfoxides and sulfones. The monomeric thiones usually yield the ketone and sulfur dioxide on oxidation, with intermediate peroxides sometimes formed. The monomeric thiocarbonyl compounds are much less stable toward oxidizing agents than the trimers.

#### 1. Oxidation by air or gaseous oxygen

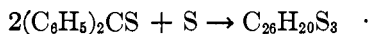
Thiobenzophenone is unstable in air and must be isolated and stored in an inert atmosphere. Schönberg, Schutz, and Nickel (191) investigated the products formed when thiobenzophenone was exposed to dry air for four weeks, and isolated benzophenone and an unidentified compound,  $C_{26}H_{20}S_3$ , which is most probably represented by VII or VIII.



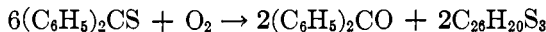
The effect of oxygen on thiobenzophenone has been studied by several workers. Staudinger and Freudenberger (208) found that, contrary to expectation, very little sulfur dioxide was formed when thiobenzophenone was exposed to dry oxygen, but instead benzophenone and a tetraphenyldimethylene trisulfide were formed. This trisulfide is apparently the same as that formed by the action of air on thiobenzophenone. These authors therefore assumed that the first step was unusual, in that oxidation took place on the carbon atom to give the unstable peroxide (IX), which decomposed to benzophenone and nascent sulfur. The nascent sulfur could then combine with two molecules of thio-



benzophenone to form the trisulfide.

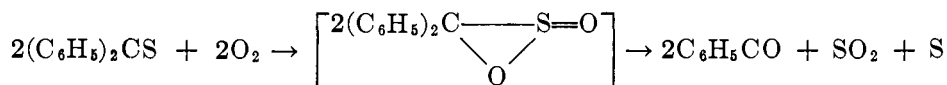


Quantitative estimates of the amount of oxygen used up corresponded very closely to the over-all equation:



The similarity between triphenylmethyl and thiobenzophenone in taking up two atoms of oxygen to form an unstable peroxide has been noted by Bergmann *et al.* (31).

Schönberg and Mostafa (180) found that passing oxygen through a benzene solution of thiobenzophenone for 5 hr. produced benzophenone, sulfur, and sulfur dioxide. The reaction was light-catalyzed, since *p,p'*-dimethoxythiobenzophenone, *p,p'*-tetramethyldiaminothiobenzophenone, xanthione, and thioxanthione were almost completely stable to oxygen in the dark, but were readily oxidized to the ketones, sulfur, and sulfur dioxide in bright sunlight. *N*-Phenylthioacridone, 4-thioflavone, and 2,6-diphenyldithiopyrone were almost completely stable even in sunlight. The reaction with oxygen in benzene solution apparently proceeds in the normal manner, oxidation first occurring on the sulfur atom.



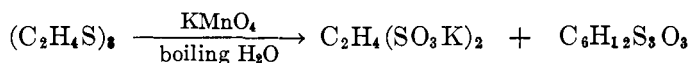
### 2. Oxidation by hydrogen peroxide

The effect of hydrogen peroxide on the trimethylene trisulfide ring has been described by Hinsberg (87, 88, 89), Fromm and Schultis (70), and Bell and Bennett (27). These authors were interested in preparing the stereoisomeric trimethylene trisulfoxides to prove the structure of the original trisulfides. Bell and Bennett (27) give the most exact conditions for the oxidation of trimethylene trisulfide. Treatment with 27 per cent hydrogen peroxide in acetone at 40°C. for 6 hr. yields the monosulfoxide. The monosulfoxide was converted to a mixture of the disulfoxides by 27 per cent hydrogen peroxide in glacial acetic acid at room temperature for 6 hr. Prolonged oxidation in the glacial acetic acid solution caused the formation of the trisulfoxides.

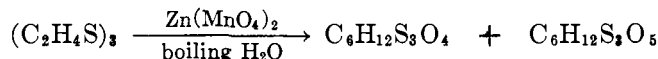
Kitamura (104) found that diaryl thiones were converted to ketones and sulfur dioxide by hydrogen peroxide in potassium hydroxide solution.

### 3. Oxidation by potassium permanganate

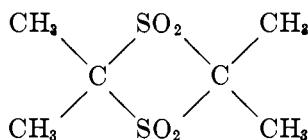
Guareschi (82) and Autenrieth (6) investigated the action of neutral permanganate solutions on trimethylene trisulfides. Guareschi treated trithioacetaldehyde with boiling neutral potassium permanganate solution, and obtained a mixture of the potassium salt of ethane-1,1-disulfonic acid, and a trioxide of the trisulfide compound. Zinc permanganate gave a tetroxide and a pentoxide on similar treatment.



Autenrieth (6) treated dithioacetone with boiling 5 per cent neutral potassium permanganate, and obtained a compound,  $\text{C}_6\text{H}_{12}\text{S}_2\text{O}_4$ , which he believed to be



tetramethyldimethylene disulfone (X).



X

Baumann and coworkers (12, 13, 14, 15, 16) studied the products of the oxidation of trimethylene trisulfides with acidic permanganate solutions, and found that treatment with potassium permanganate in dilute sulfuric acid at steam bath temperature produced a mixture of trisulfones and disulfone-sulfides. When trithioacetone was thus oxidized (16) a pentoxide,  $\text{C}_9\text{H}_{18}\text{S}_3\text{O}_5$ , was apparently obtained, but it was shown to be a eutectic mixture, since it could be separated into a hexoxide,  $\text{C}_9\text{H}_{18}\text{S}_3\text{O}_6$ , and a tetroxide,  $\text{C}_9\text{H}_{18}\text{S}_3\text{O}_4$ . Camps (45) was able to separate effectively the trisulfone from the disulfone-sulfide of trithioformaldehyde, and noted that the reaction was more efficient at  $0^\circ\text{C}$ . than at higher temperatures. Thus, when 5 per cent potassium permanganate in 5 per cent sulfuric acid in an ice bath was used, a 51 per cent yield of the trisulfone and a 33 per cent yield of the disulfone-sulfide was obtained, while at  $60\text{--}80^\circ\text{C}$ ., with the same concentration of reactants, only 35 per cent of the trisulfone and 10 per cent of the disulfone-sulfide were found. Lomnitz (122) prepared the di- and tri-sulfones of trithioacetaldehyde by similar reactions. Chattaway and Kellett (46) were able to prepare the monosulfone-disulfide of trithioacetaldehyde by first preparing the monosulfoxide with hydrogen peroxide, and then oxidizing it to the monosulfone with potassium permanganate in glacial acetic acid.

Fromm (66) oxidized several cyclic thiones with potassium permanganate in dilute sulfuric acid. Trithiocyclopentanone gave a trisulfone, but trithiocyclohexanone and trithio-*p*-methylcyclohexanone gave mixtures from which only the disulfone-sulfides were isolated with difficulty. It may be concluded that some steric hindrance is involved in the oxidation of *s*-trithianes to the trisulfones, since while the trisulfones of trithioformaldehyde, trithioacetaldehyde, and trithiocyclopentanone were readily obtained, the trisulfones of trithioacetone, trithiobenzaldehyde, and trithiocyclohexanone were obtained only with difficulty, or not at all.

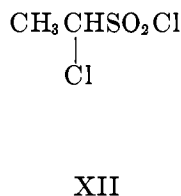
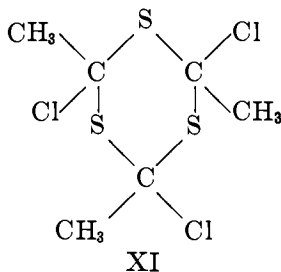


## 4. Oxidation by nitric acid

Nitric acid generally reacts too violently with thiones and thials to be of much interest. Husemann (98) claimed to have obtained an oxide of thioformaldehyde on treatment with nitric acid. Fleischer (64) treated a polymer of thiobenzaldehyde with nitric acid, and obtained sulfuric acid and benzoic acid, along with some benzaldehyde and an unidentified compound,  $C_7H_6SO$ . Baumann and Fromm (16) obtained an explosive reaction when trithioacetone was treated with concentrated nitric acid but isolated sulfuric acid as one of the products.

## 5. Oxidation by halogens

Direct chlorination of trithioacetaldehyde in glacial acetic acid replaces the methylene hydrogens, yielding 2,4,6-trimethyl-2,4,6-trichlorotrimethylene 1,3,5-trisulfide (XI) (63). If water is present, however, the chief product is  $\alpha$ -chloroethanesulfonyl chloride (XII). Muller and Schiller (146) obtained the  $\alpha$ -chlorosulfonyl chloride when a water suspension of trithioacetaldehyde was treated with chlorine. Kostsova (112) obtained chloromethanesulfonyl chloride, or bromomethanesulfonyl bromide, when aqueous suspensions of tri-



thioformaldehyde were treated with chlorine or bromine with cooling. The yield of chloromethanesulfonyl chloride was 51 per cent. Lee and Dougherty (116) carried out the oxidation with chlorine and water in glacial acetic acid, and obtained formaldehyde as one of the products. The equation for the reaction is:



Baither (8) treated tetramethyldiaminothiobenzophenone with bromine in glacial acetic acid, and obtained an impure unidentified compound which contained 60 per cent of bromine and no sulfur.

## D. REDUCTION

The trimethylene trisulfide ring is apparently quite stable toward reducing agents, since compounds of this type have been made by reducing carbon disulfide or phenyl isothiocyanate. Fromm and Ziersch (72) reported that thioacetylthioacetone dimer was quite stable toward zinc and hydrochloric acid. The monomeric thiones behave in general like the analogous ketones toward reducing agents.

### 1. Clemmensen reduction

Using zinc and hydrochloric acid, Granacher (79) converted phenylthiopyruvic acid to  $\beta$ -phenylpropionic acid. Sen (195), however, obtained the thiol, thioborneol, when thiocamphor was treated with zinc and hydrochloric acid. Schönberg (172) obtained 9,9'-dixanthyl when xanthione was reduced with zinc in glacial acetic acid. The diaryl thiones are probably converted to the methylene derivatives by zinc and acid. Baither (8) obtained *p,p'*-tetramethyldiaminodiphenylmethane when Michler's thioketone was treated with zinc dust and steam.

### 2. Reduction by sodium amalgam

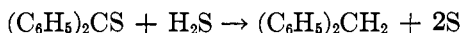
Granacher (79) found that phenylthiopyruvic acid was easily converted to  $\beta$ -phenyl- $\alpha$ -thiolpropionic acid by treatment with sodium amalgam. Spring (204) reported that treatment of dithioacetone with sodium amalgam for two weeks gave isopropyl mercaptan. This reaction has not been confirmed in recent literature, however.

### 3. Reduction by hydrogen on Raney nickel

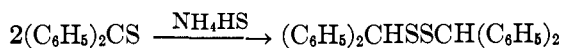
Bougault, Cattelain, and Chabrier (40) found that when phenylthiopyruvic acid was treated with Raney nickel in cold aqueous or alcoholic solution,  $\beta$ -phenylpropionic acid was formed.

### 4. Reduction by sulfides

Hydrogen sulfide or ammonium sulfide will reduce monomeric thiones. Reddelien and Danilof (162) obtained diphenylmethane when excess hydrogen sulfide was used in preparing thiobenzophenone from benzophenone anil.



Bergmann, Magat, and Wagenberg (31) noted that thiobenzophenone behaved differently from benzophenone on reduction, since, as with oxidation, the carbon rather than the sulfur is first attacked. Thus benzophenone is first reduced to the pinacol, but thiobenzophenone, on treatment with ammonium bisulfide, yields the disulfide.



### 5. Enzymatic reduction

Neuberg and Nord (148) demonstrated that the thiocarbonyl group may behave like the carbonyl group toward enzyme systems. In their experiments thialdine was used as a source of thioacetaldehyde, since trithioacetaldehyde was insoluble in water solutions. An alcoholic solution of thialdine was added to a fermenting mixture of sugar and water, and within 5 min. ethyl mercaptan was detected in the evolving gases. Yeast killed by boiling was not effective in reducing thioacetaldehyde to ethyl mercaptan.

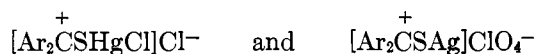
## E. REACTION WITH SALTS OF METALS

One of the earliest reactions noted in the thione-thial series was the formation of complex addition compounds with the salts of heavy metals. In 1863, Husemann (98) reported that his "dimethylene sulfur", from methylene iodide and sodium bisulfide, formed salts with mercuric chloride, platinum chloride, and gold chloride. The formation of these complexes was used as a means of confirming the identification of thiones and thials by numerous investigators (14, 127, 203, 224). Hofmann (95) analyzed the silver nitrate and platinum chloride addition compounds of thioformaldehyde and showed them to have the formulas  $C_3H_6S_3 \cdot AgNO_3$  and  $C_3H_6S_3 \cdot PtCl_4$ , thus showing 3 moles of  $CH_2S$  per mole of salt, and indicating the trimeric structure for thioformaldehyde. Klinger (107) used the silver nitrate and platinum chloride addition complexes to show the trimeric structure of thioacetaldehyde.

The mercuric chloride addition complex was used by Arndt and Nathwey (3) to isolate the unstable diethyl thiochelidonate. By preparing the thione in the presence of mercuric chloride, the stable complex was obtained. When an ether suspension of this compound was treated with concentrated potassium iodide solution, mercuric iodide was precipitated, and the free thione was obtained.

The nature of these colored complex addition products has been studied by Simonis and Elias (200) and Schönberg (172, 192). The former authors investigated a large series of addition complexes of 2,3-dimethyl-4-thiochromone, and found that the molar ratio of the monomeric thione to metal salt varied with the nature of the solvent as well as with the nature of the salt. When the reaction was run in fuming hydrochloric acid, 2 moles of thione were precipitated with 1 mole of mercuric chloride, but if ether or absolute alcohol was the solvent, the molar ratio was one to one. When fuming hydrochloric acid was used as the solvent, the ratio of thione to metal salt in the complex was 2:1 for platinum chloride, 1:2 for bismuth iodide, and 3:1 for gold chloride. In addition to those already mentioned, complexes with cuprous chloride, cupric chloride, uranium oxychloride, ferric chloride, cadmium iodide, mercuric iodide, silver nitrate, zinc chloride, stannic chloride, and antimony chloride were prepared.

Schönberg (172) noted that when these molecular compounds were formed, a distinct color shift occurred which was probably associated with a structural change. Later, Schönberg and Stolpp (192) investigated the structure of metal salt complexes of diaryl thiones, and found that these compounds behaved like carbonium ions, in which the metal is associated with the sulfur atom. Thus the diaryl thione complexes with mercuric chloride and silver chlorate may be represented as:

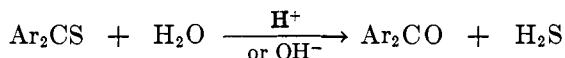


This concept does not account for the varying molar ratios of thione to salt found by Simonis and Elias.

## F. EFFECTS OF ACIDS AND BASES

Baumann and Fromm (15) noted that treatment of the less stable  $\alpha$ -trithioaldehydes with acid solutions caused partial inversion to the  $\beta$ -forms, and treatment of the polymeric thioaldehydes with alcoholic hydrogen chloride solution converted the polymers to a mixture of trimers. This reaction was carefully investigated by Suyver (215), who noted that acid catalysts give equilibrium mixtures of  $\alpha$ - and  $\beta$ -trithioaldehydes which are the same, whether the pure  $\alpha$ - or the pure  $\beta$ -form is used as starting material. The  $\beta$ -form usually predominates in these mixtures. Thus, treatment of  $\alpha$ - or  $\beta$ -trithioacetaldehyde with alcoholic hydrogen chloride gives a mixture containing 89 per cent  $\beta$ -trithioacetaldehyde. Hydrogen iodide was used to effect a similar conversion by Fromm and Soffner (71).

When monomeric thiones are boiled in aqueous acid or base, hydrolysis occurs. Baither (8) boiled *p,p'*-tetramethyldiaminothiobenzophenone in hydrochloric



acid, and obtained Michler's ketone and hydrogen sulfide. Wallach (220) obtained the same result with dilute sulfuric acid. Both Gattermann and Schulze (75) and Vorlander and Mittag (219) obtained benzophenone and potassium sulfide when thiobenzophenone was boiled in alcoholic potassium hydroxide. Thioacridone was converted to acridone by boiling sulfuric acid (Edinger and Arnold (57)). Granacher (79) found that phenylthiopyruvic acid was hydrolyzed to phenylpyruvic acid by boiling ammonium hydroxide solution. Mitra investigated the acidic and basic hydrolysis of thioacetoacetic esters (136, 139), and found that hydrolysis of the thiocarbonyl group occurred along with normal ketonic decomposition of the acids. Thus, when ethyl thioacetoacetate was boiled with 10 per cent sulfuric acid or 10 per cent aqueous potassium hydroxide, the products were acetone, hydrogen sulfide, and carbon dioxide. Ethyl ethylthioacetoacetate yielded hydrogen sulfide, carbon dioxide, and methyl propyl ketone.

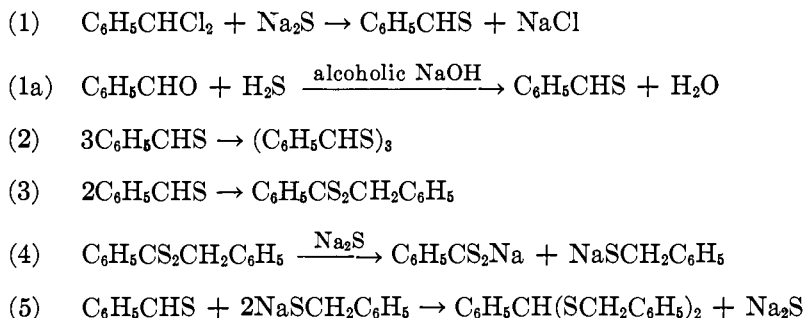
Edinger (55, 56) pointed out that thioacridone was soluble in aqueous alkali and behaved in alkaline solution like the tautomeric 9-mercaptoacridine.

The aromatic trithials are quite stable in alkaline solutions. When the monomeric aromatic thials are treated with alkali, however, the Cannizzaro reaction can occur. This condition is obtained when aromatic thials are prepared in alkaline solution. The reaction was first observed by Klinger (108), who attempted to prepare thiobenzaldehyde by treating benzal chloride with excess potassium bisulfide. The products obtained were benzyl disulfide (XIII) and potassium dithiobenzoate (XIV). These same products were obtained when a



polymeric thiobenzaldehyde (m.p. 80–90°C.) was treated with alcoholic potassium bisulfide, but  $\beta$ -trithiobenzaldehyde did not react. Wood and Bost (226) investigated the conditions of the Cannizzaro reaction with thiobenzalde-

hyde rather carefully, and found that when thiobenzaldehyde was prepared in alkaline solutions the monomer was first formed, but reacted immediately in several ways. Some trimerized to  $\beta$ -trithiobenzaldehyde, but dismutation occurred with the greater part to form benzyl dithiobenzoate, and a small portion was converted to the benzylmercaptal of thiobenzaldehyde. The reactions occurring when benzal chloride is treated with sodium sulfide in alcoholic solution (1), or when benzaldehyde is treated with hydrogen sulfide in alcoholic sodium or potassium hydroxide solution (1a), are as follows:



That thiobenzaldehyde actually dismutates to benzyl dithiobenzoate was demonstrated by distilling  $\beta$ -trithiobenzaldehyde under reduced pressure in the presence of one drop of concentrated sulfuric acid (226). Under these conditions the trimer dissociated to the monomer, part of which reassociated to the trimer, and part of which dismutated to the dithio ester. Treatment of the ester with sodium sulfide caused the hydrolysis to the dithio acid salt and sodium mercaptide.

#### G. KETO-ENOL ISOMERISM

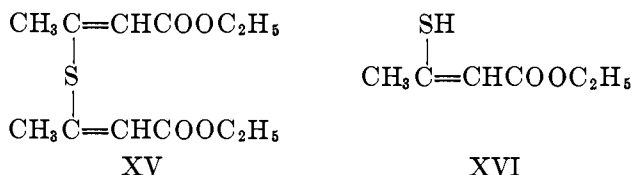
In those cases in which there is a hydrogen atom alpha to a thiocarbonyl group, one would expect keto and enol forms to exist. These forms could not exist if the thione or thial is in the trimeric form, and are therefore unknown among the simple alkyl thiones and thials.

##### 1. The $\alpha$ - and $\beta$ -thioketo acids

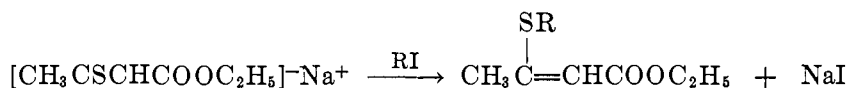
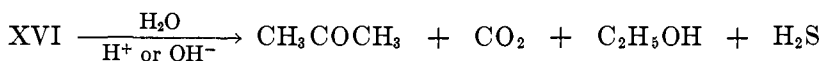
The  $\alpha$ -thioketo acids undoubtedly exist in both forms. Although they react readily with ketone reagents, such as phenylhydrazine and hydroxylamine (79, 100, 157), they also react in alkaline solution as thiols. Zipser (230) found that  $\alpha$ -sulfhydrylcinnamylacrylic acid readily yielded  $\alpha$ -thiobenzylcinnamylacrylic acid when treated with benzyl chloride in alkaline solution.

The thione-thiol isomers have been rather extensively investigated in the  $\beta$ -thioketo acids, particularly in the case of ethyl thioacetoacetate. Scheibler and Bube (167) prepared this compound by treatment of ethyl  $\beta$ -chlorocrotonate with potassium sulfide in alcohol, and obtained a mixture of ethyl di- $\beta$ -crotonyl sulfide (XV) and ethyl  $\beta$ -mercaptocrotonate (XVI). Later Scheibler, Topouzada, and Schulze (168) found that XVI existed in *cis* and *trans* forms which

could be separated with difficulty by repeated fractionation. These authors noted that treatment of the sodium salt of XVI with methyl iodide, benzyl



chloride, or ethyl chloroacetate gave only the thioethers and no alkylation of the  $\alpha$ -carbon, and therefore concluded that the compound did not exist in the keto form. Mitra undertook the investigation of thioacetoacetic esters, and reported the results in a series of papers (136-143). It was found that these compounds gave reactions of both thione and thiol types. Thus, they reacted with hydroxylamine to evolve hydrogen sulfide, gave pyrazolones with phenylhydrazine, and were hydrolyzed by acidic or basic solutions to give ketones. However, the sodium derivatives always gave the thioethers with alkyl halides,



indicating complete conversion to the thiol phase. The per cent of thiol in the equilibrium at various temperatures was estimated by Mitra (143) for thioacetoacetic ester and several  $\alpha$ -substituted thioacetoacetic esters. The proce-

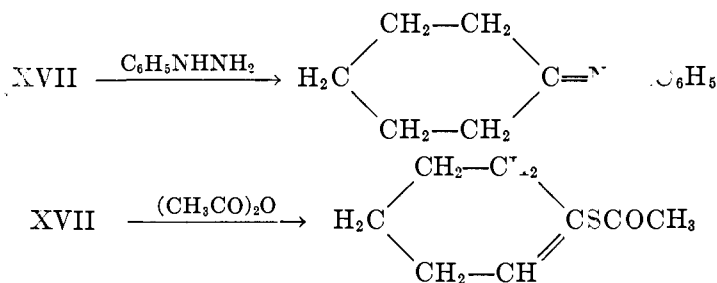
TABLE 1

CH <sub>3</sub> CSCHRCOOC <sub>2</sub> H <sub>5</sub>	PER CENT THIOL IN EQUILIBRIUM AT GIVEN TEMPERATURE		
	30°C.	40°C.	60°C.
1. R = H	41.0		38.7
2. R = CH <sub>3</sub>	62.8	61.9	60.0
3. R = CH <sub>2</sub> CH(CH <sub>3</sub> ) <sub>2</sub>			64.4
4. R = CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	61.1		58.5

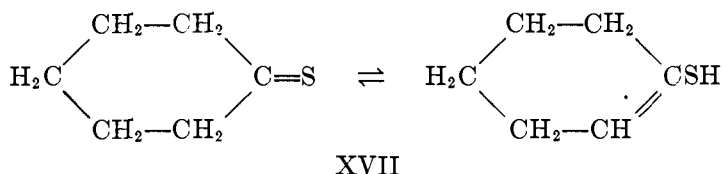
cedure was to maintain the compound in alcohol in a thermostat at the required temperature for 6 hr., then quickly transfer it to an iodine solution in alcohol at  $-7^\circ\text{C}$ ., and titrate the excess iodine with sodium thiosulfate. The iodine oxidizes the thiol to the disulfide without affecting the thione. Mitra's results are summarized in table 1, from which it is evident that there is a shift toward the thione phase as the temperature is increased, and that substitution on the  $\alpha$ -carbon increases the thiol phase.

## 2. The cyclic thiones

Sen (196) found that monomeric cyclohexanone gave both ketone derivatives, such as the carbazone and phenylhydrazone, and mercaptan derivatives, such as the thiomethyl derivative with methyl sulfate, and the acetyl derivative with

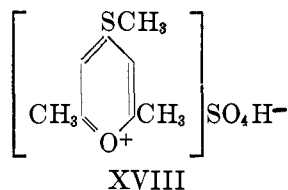


acetic anhydride. These reactions indicated the existence of the thione-thiol equilibrium:

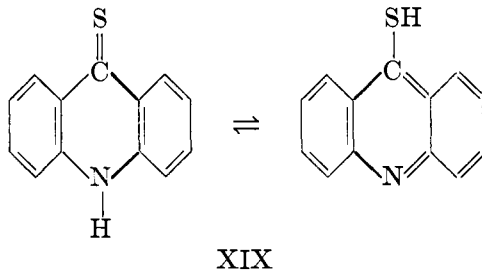


Using the iodine oxidation method, Sen found that there was 38 per cent thiol in freshly distilled thiocyclohexanone, and 70 per cent thiol in a preparation 1 hr. old, a result which would indicate that the thiol tautomer is more stable.

Reactions in the heterocyclic thione series indicate that these compounds probably exist in both thione and thiol forms. Hantzsch (85) noted that treatment of 2,6-dimethylthiopyrone with methyl sulfate gave a thiomethyl oxonium salt (XVIII).



Edinger and Arnold (56, 57) noted that thioacridone gave acridone in boiling sulfuric acid, but yielded 9-thiobenzylacridine with benzyl chloride in alkaline solution. The existence of the thione-thiol isomers in thioacridone (XIX)



was also confirmed by Gleu and Schaarschmidt (77) and by Chernstov (47). Gleu and Schaarschmidt found that alkylation of thioacridone gave the *S*-

alkyl derivatives exclusively, and these could not be rearranged to the *N*-alkyl derivatives by heat. The equilibrium has not been estimated quantitatively.

#### H. CARBONYL REAGENTS

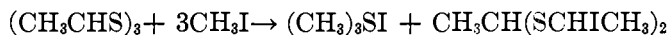
The dimeric and trimeric thiones and thials do not react with carbonyl reagents, unless dissociated in some manner. However, the monomeric thiones readily form derivatives with the usual carbonyl reagents, such as hydroxylamine, phenylhydrazine, etc., reacting to split out hydrogen sulfide instead of water. This is good evidence that the  $\alpha$ - and  $\beta$ -thio keto acids are monomers, since they react with these reagents (79, 136, 157). As previously noted, thioacetoacetic esters react like acetoacetic esters with phenylhydrazine to give the pyrazolones.

The diaryl thiones react readily with carbonyl reagents. Baither (8, 9) investigated the reactions of *p,p'*-tetramethyldiaminothiobenzophenone and found that it gave the oxime and phenylhydrazone of Michler's ketone. The thione also reacted with aniline to give the anil. Bergreen (33) and Gattermann and Schulze (75) prepared the oxime and phenylhydrazone of thiobenzophenone, and found them to be identical with those prepared from benzophenone itself.

The monomeric cyclic thiones also give carbonyl derivatives. Sen (195) prepared the camphor oxime, phenylhydrazone, and semicarbazone from thio-camphor, and also prepared the semicarbazones and phenylhydrazones from thiocyclohexanone and thiocyclopentanone (196). Graebe and Roder (78) obtained xanthone oxime and xanthone phenylhydrazone from xanthione. Simonis and Rosenberg (201) found the thiocarbonyl group in various thiochromones to react readily with hydroxylamine and phenylhydrazine.

#### I. ALKYL HALIDES

Alkyl halides react with thials and thiones in several ways. Early investigators (Marckwald (129); Baumann and Fromm (15)) noted that when  $\alpha$ -trithioacetaldehyde or polymeric thioacetaldehyde was treated with methyl or ethyl iodide, it was converted to the more stable  $\beta$ -isomer. Mann and Pope (125) reported that their  $\gamma$ -trithioacetaldehyde was converted to the  $\beta$ -compound by methyl iodide. Alkyl halides have also been found to react with trithials and trithiones to produce halogenated sulfur compounds. Klinger (106) gives the following equation:



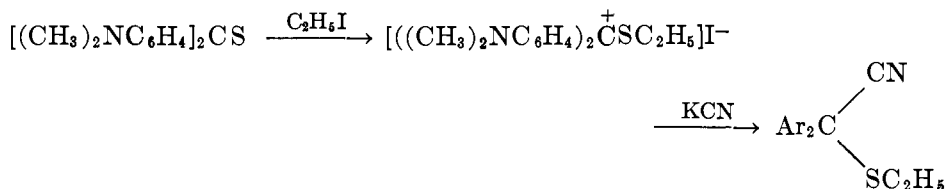
Platonov and Anisimov (156) found that trialkylsulfur iodides were obtained in every case where a trithial was treated with an alkyl iodide at 100–110°C. for 20 hr. Alkyl bromides were not very reactive.

The alkylation of ethyl thioacetoacetate has been investigated by Ray, Mitra, and Ghosh (161). The thioethers were obtained in every case when the

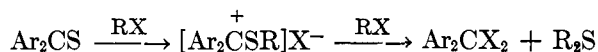


sodium derivative of ethyl thioacetoacetate was treated with an alkyl halide, such as ethyl iodide, propyl iodide, amyl bromide, benzyl chloride, or phenacyl bromide. This is therefore a reaction of the mercaptan group, rather than a thione reaction.

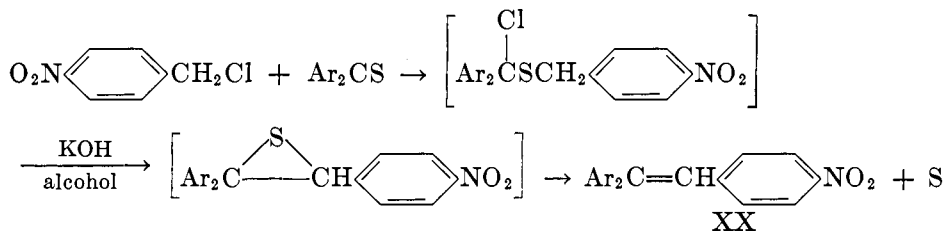
Several reactions of diaryl thiones with alkyl halides have been reported. Baither (9) found that when *p,p'*-tetramethyldiaminothiobenzophenone was treated with benzyl chloride in carbon disulfide solution, dibenzyl sulfide and *p,p'*-tetramethyldiaminobenzophenone dichloride were formed. Madelung (123) obtained a highly colored cyanide by treating *p,p'*-tetramethyldiaminothiobenzophenone with ethyl iodide and potassium cyanide. Since the cyanide could be prepared in another way, the structure of the carbonium ion formed by



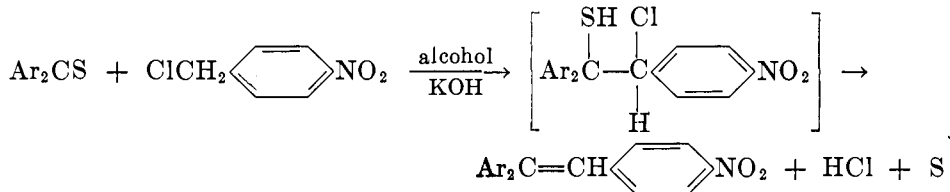
addition of the alkyl halide is probably correct. Alkyl halides probably react with diaryl thiones in two steps:



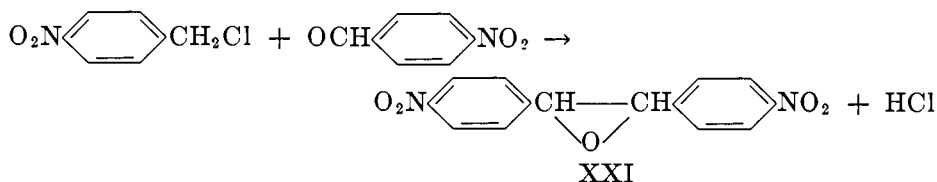
A similar mechanism is postulated for the reaction of *p*-nitrobenzyl chloride with diaryl thiones by Bergmann and Hervey (30). When Michler's thioketone was treated with *p*-nitrobenzyl chloride in alcoholic potassium hydroxide, the triarylethylene (XX) and sulfur were obtained. The reaction may be pictured as follows:



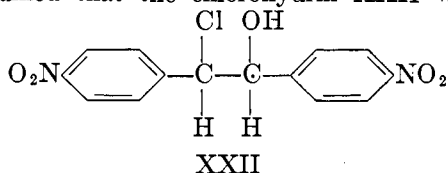
Hahn (84) believed that the reaction was of an aldol type and represented it thus:



The evidence for this mechanism was based on the reaction of *p*-nitrobenzyl chloride with *p*-nitrobenzaldehyde to give an ethylene oxide derivative (XXI).

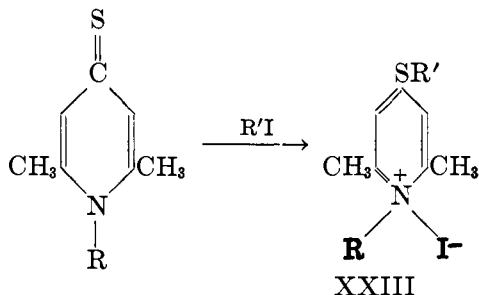


Hahn therefore assumed that the chlorohydrin XXII was an intermediate.



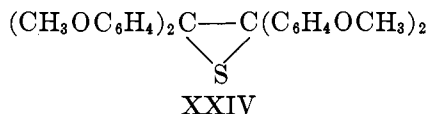
The analogy with thiocarbonyls is not conclusive however, since these compounds do not necessarily behave like carbonyls.

The effect of alkyl iodides on *N*-alkylthiopyridones was investigated by Michaelis and Holken (134), who observed that the thiones were readily converted to the thioalkylpyridinium iodides (XXIII) at ordinary temperatures.

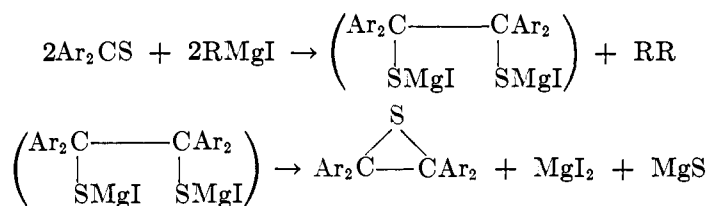


#### J. GRIGNARD REAGENTS

The Grignard reagent reacts differently with thiones than with ketones. The reaction has been investigated by Schönberg and coworkers, who found that when di-*p*-anisyl thione was treated with phenylmagnesium bromide or  $\alpha$ -naphthylmagnesium bromide, the ethylene sulfide XXIV was formed (172). Schönberg, Schutz, and Marschner (189) treated thiobenzophenone with magnesium subiodide and obtained tetraphenylethylene sulfide. Since the same



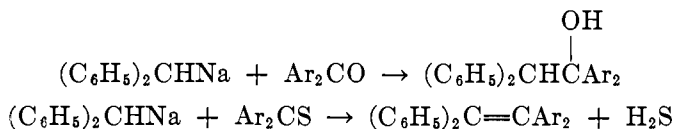
product is obtained with Grignard reagents, the mechanism of the Grignard reaction was postulated as follows:



A variety of alkyl and aryl Grignard reagents were used by Schönberg, Rosenbach, and Schutz (182), and the ethylene sulfide was obtained in every case. Phenylmagnesium bromide gave the highest yield (about 70 per cent) of the ethylene sulfide, while ethylmagnesium bromide gave low yields. In some cases, such as xanthione, the ethylene sulfide was unstable, decomposing spontaneously to the ethylene derivative and sulfur.

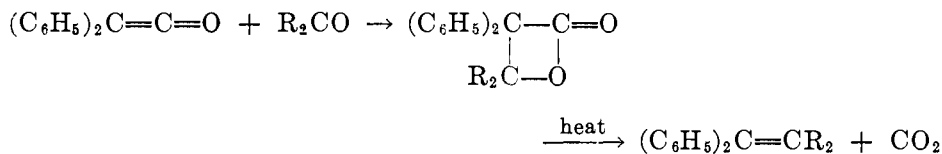
#### K. METAL ALKYLs

Bergmann and Wagenberg (32) investigated the reaction of diphenylmethylsodium on aromatic ketones and thiones, and found that the reactions follow the same course, but that the mercaptans lose hydrogen sulfide more readily than the alcohols lose water, so that the ethylene derivative is usually isolated as the product of the thione reaction. The thiones used were thiobenzophenone, di-*p*-anisyl thione, and *p,p'*-tetramethyldiaminothiobenzophenone.

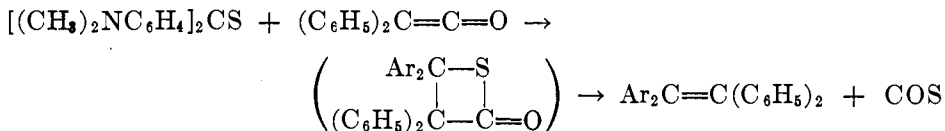


#### L. DIPHENYLKETENE

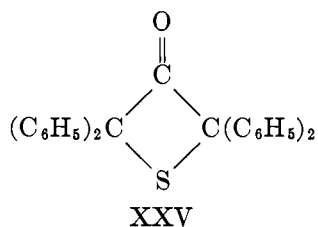
Diphenylketene reacts with ketones to give a lactone which decomposes on heating to carbon dioxide and the ethylene derivative (Staudinger and Kon (210)). Staudinger (205) found that diaryl thiones behave in two ways toward diphenylketene. The negatively substituted *p,p'*-tetramethyldiaminothiobenzophenone



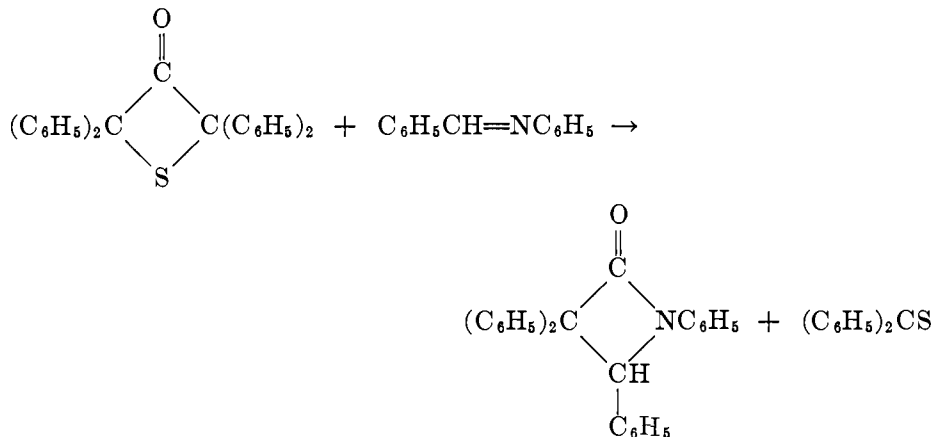
benzophenone reacted like ordinary ketones, to give an unstable intermediate which decomposed to the ethylene derivative and carbon oxysulfide. With



thiobenzophenone or di-*p*-anisyl thione, however, a different product was obtained. When thiobenzophenone was treated with diphenylketene, a stable crystalline sulfur compound,  $C_{27}H_{20}OS$ , melting at  $180-181^{\circ}C.$ , was obtained. On melting, it dissociated to thiobenzophenone and diphenylketene, but recombined on cooling. This compound was assigned structure XXV by Staudinger. A similar reaction was obtained with di-*p*-anisyl thione. This compound

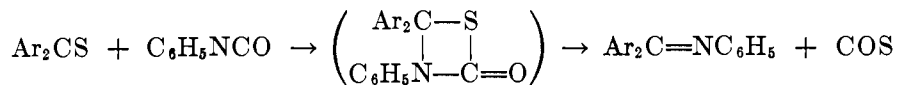


(XXV) was later used by Staudinger and Freudenberger (207) to purify thiobenzophenone. Impure thiobenzophenone was reacted with diphenylketene, and compound XXV was isolated and heated with benzaldehyde anil at reduced pressure until pure thiobenzophenone distilled.



#### M. PHENYL ISOCYANATE

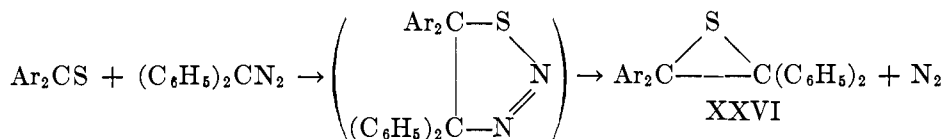
Staudinger and Endle (206) point out that phenyl isocyanate reacts like ketene at elevated temperatures. With *p, p'*-tetramethyldiaminothiobenzophenone, the products are the ketone anil and carbon oxysulfide, which may be derived through the cyclic four-membered ring.



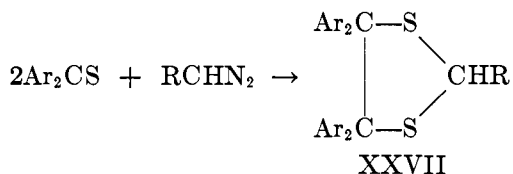
#### N. ALIPHATIC DIAZO COMPOUNDS

Diazomethane reacts differently with thiones than with ketones because the thiocarbonyl group is more highly polarized, according to Meerwein, Bersin,

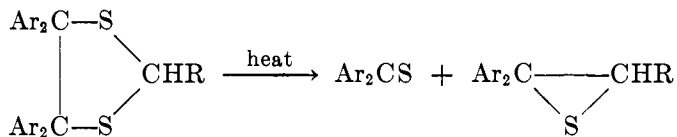
and Burneleit (130). Staudinger and Siegwart (212) caused several diaryl thiones to react with diphenyldiazomethane, and obtained the corresponding tetraarylethylene sulfide (XXVI) and nitrogen. These authors assumed that an unstable nitrogen compound was first formed. Bergmann, Magat, and



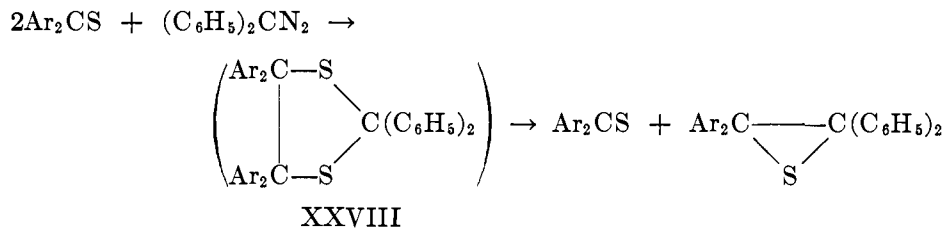
Wagenberg (31) reacted diazomethane with diaryl thiones, and obtained a stable compound containing a trimethylene disulfide ring (XXVII). This



work was repeated by Schönberg, Cernik, and Urban (177), who used diazoethane and ethyl diazoacetate, as well as diazomethane in these reactions. In each case, the trimethylene disulfide compound (XXVII), in which R equals —H, —CH<sub>3</sub>, or —COOC<sub>2</sub>H<sub>5</sub>, was obtained. These authors found that when compound XXVII was subjected to heat, it decomposed to give the thione and ethylene sulfide, and also noted that when R was CH<sub>3</sub> or COOC<sub>2</sub>H<sub>5</sub>, decomposition occurred more readily. It was therefore assumed that the reaction with



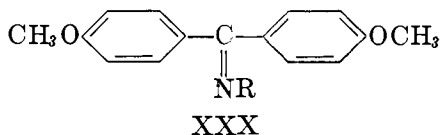
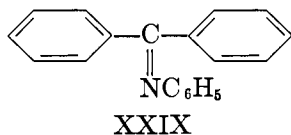
diphenyldiazomethane actually followed the same course as other substituted diazomethanes, but that the intermediate hexaaryltrimethylene disulfide (XXVIII) was unstable. Schönberg and Nickel (181) found that xanthione,



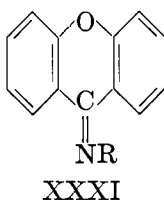
thiochromone, and several of the thioflavones reacted with aliphatic diazo compounds in the same way, yielding ethylene sulfides with diphenyldiazomethane, and trimethylene disulfides with diazomethane.

## O. PHENYL AZIDE

Schönberg and Urban (193) found that although azides do not react with ketones, they react quite readily with thiones to form Schiff's bases. The following Schiff's bases were obtained by reacting the azide with the thione:



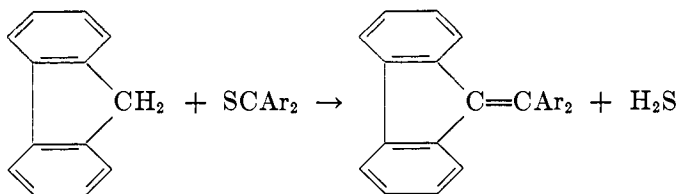
- a: R = C<sub>6</sub>H<sub>5</sub>  
 b: R = α-C<sub>10</sub>H<sub>7</sub>  
 c: R = CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>



- a: R = C<sub>6</sub>H<sub>5</sub>  
 b: R = SO<sub>2</sub>C<sub>6</sub>H<sub>5</sub>

## P. DIARYLMETHANES

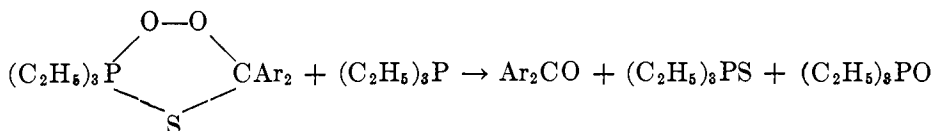
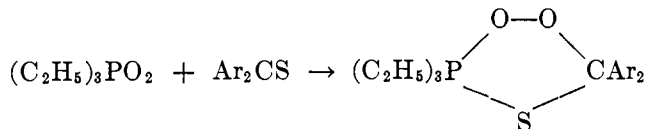
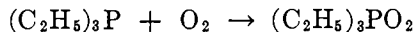
Schönberg (172) reported that when fluorene was fused with diaryl thiones, hydrogen sulfide was evolved, and the biphenylenediarylethylenes were formed.



A similar reaction was observed between xanthene and xanthione (188).

## Q. TRIETHYLPHOSPHINE

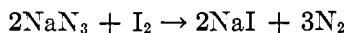
Triethylphosphine does not react with thiones in the absence of air, even at the boiling point. Schönberg and Krukll (179) found that in boiling toluene,



however, in the presence of dry air, the diaryl ketone, triethylphosphine sulfide, and triethylphosphine oxide are formed, and proposed that triethylphosphine peroxide was the active agent. It was found that the alkoxy-substituted diaryl thiones and xanthione reacted with triethylphosphine peroxide, but that *p,p'*-tetramethyldiaminothiobenzophenone did not.

#### VII. DETECTION OF THIALS AND THIONES

The presence of monomeric thiones may be detected by their intense colors. Feigl and Bondi (61) found that a reaction occurred between silver saccharide and monomeric thiones to precipitate silver sulfide, and suggested the usefulness of this reaction in the identification of thiones. Later Feigl (60) and Feigl and Dacorso (62) found that the reaction of iodine with sodium azide was greatly enhanced by the catalytic effects of divalent sulfur compounds, and



suggested the use of this reaction to detect very small quantities of thiones.

#### VIII. USES OF THIALS AND THIONES

No significant uses have yet been reported for thials and thiones. However, several patents suggest uses to which these compounds might be put. Möller (145) discussed the use of trithioformaldehyde in tanning, since it had been found that this material could replace sulfur in the tanning process. Delson (52) reports that thioacrolein is germicidal and non-poisonous, and therefore suitable for skin ointments and internal administration. Kodak, Ltd. (109) has patented a process for the production of thiones, and their use as sensitizers for photographic emulsions.

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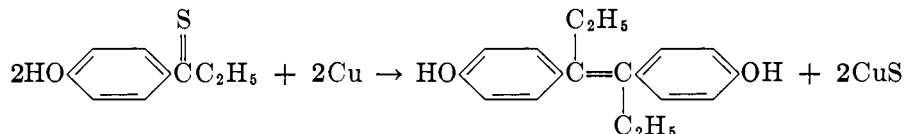
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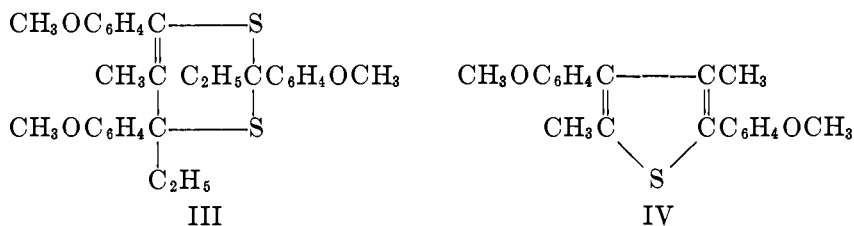
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## X. ADDENDUM

Since this review was submitted for publication, the following information has been obtained. Linnell and Sharma (235) proposed to synthesize  $\alpha, \alpha'$ -diethylstilbestrol by condensing *p*-hydroxythiopropiophenone or *p*-methoxythiopropiophenone with copper powder, according to the reaction:



However, attempts to synthesize the required thiones were unsuccessful. *p*-Hydroxypropiophenone yielded an unidentified, red, sulfur-containing compound when treated with hydrogen sulfide and hydrogen chloride in alcohol solution. *p*-Methoxypropiophenone when treated with these reagents yielded a white crystalline compound (I) which, on being heated with copper bronze, yielded a stable sulfur-containing compound (II). Linnell and Sharma believed that compound I was 2,4,5-tri-*p*-anisyl-2,4,5-triethyltrimethylene-1,3-disulfide, and that compound II was 2,3,5,6-tetra-*p*-anisyl-2,3,5,6-tetraethyl-1,4-dithiane. However, a comparison of the physical properties and analyses indicates that these two compounds are identical with the compounds prepared from *p*-methoxypropiophenone by Campaigne (232), which were shown to be "anhydrotri-*p*-methoxypropiophenone disulfide" (III) and 2,4-di-*p*-anisyl-3,5-dimethylthiophene (IV), respectively.



Linnell and Shaikmahamud (234) treated 2-ethyl-4-methoxybenzaldehyde with hydrogen sulfide in cold alcohol containing a trace of piperidine, and obtained what was undoubtedly a polymeric thial, although the molecular weight was not determined. This compound was converted to 2,2'-diethyl-4,4'-dimethoxystilbene, an isomer of  $\alpha,\alpha'$ -diethylstilbestrol, by heating with copper powder.

Bergmann and Israelashwili (231) studied the conversion of the trimeric 9-phenanthrenethial to the corresponding ethylene derivative by heating with copper or nickel. Copper was found to give a mixture of the ethylene derivative and the disulfide, but nickel yielded the pure ethylene derivative in 20 per cent yield.

Another use of thiones is suggested by a recent British patent (233) for therapeutic ointments which contain either monomeric or polymeric thiocyclohexanone, ethyl methyl thione, or diethyl thione.

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