SIGNIFICANT STUDIES IN THE ORGANIC CHEMISTRY OF SULFUR

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It is proposed in this article to indicate how some of the results recently reached in investigating sulfur compounds have important repercussions on general chemical theory. It is not so much an exhaustive review of sulfur work as an attempt to indicate how chemistry as a whole might benefit by a more general knowledge of the results of those who concern themselves specially with sulfur. A very instructive example of the need for this will be found in some recent work on orientation in the benzene nucleus (124).

The line of treatment has permitted the exclusion of certain topics such as the sulfite wood pulp process (1, 2, 3, 3a), the commercial aspects of mercaptans (4), the nature of sulfur dyes (5, 6, 7), and the stereochemistry of sulfoxides (8, 58), all of which have, for other reasons, recently been much to the fore. Of the elements commonly occurring in organic compounds, sulfur can exhibit the greatest variety of valency forms in comparatively stable compounds. This is one reason for the diversity of problems on which some light may be thrown by the behavior of an appropriate sulfur derivative. No attempt has been made to fuse this paper into a continuous narrative, for it is felt that that would only serve to create the false impression that many of the topics had been satisfactorily correlated with the main body of chemical theory; whereas their real significance is that they are very imperfectly explained inclusions in the alloy which modern research is producing.

The aldehyde bisulfite compounds are probably the most generally familiar of the subjects discussed. The sum of evidence here compels us to exclude all ordinary chemical formulas, and it may well be that one of the new types of formulation suggested will find wider application.

Nine years ago glutathione had been isolated and "synthesized." Today its constitution is far from decided, and it seems that the purer it is obtained, the less does it behave in vitro as its biological significance would make us expect.

The direction of addition of unsymmetrical addenda to ethylenic linkages has been viewed from numerous angles and speculations have been as numerous. In sharp contrast to all these theories is the valuable work of Kharasch (9), marking peroxide impurity as a major source of confusion and incidentally substantiating the highly significant but rather inadequate experiments of Posner (10) on the addition of mercaptans to unsaturated compounds.

Many lines of work have combined to demonstrate that the coördination bond is as real as an electrovalent or covalent bond. One of the most convincing of these is to be found in Mann's resolution of β,β-diaminodiethyl sulfide platinichloride (12). Mann has also to his credit the resolution of a sulfamide complex which has the distinction of being the second compound containing no carbon whatever to be resolved. In developing his idea of covalency maxima Sidgwick stressed the fact that it was in their compounds with fluorine that elements were most likely to attain this maximum. It seems probable that this may be the underlying reason why sulfonyl fluorides behave quite differently from sulfonyl chlorides with Grignard reagents (11).

The very close similarity between thiophene and benzene prompted Hinsberg (13) to adopt a model of the sulfur atom in which the valencies of sulfur proceeded from *two* centers. The five-membered thiophene was in his view virtually a hexagon. His idea never gained much acceptance, and, with the advent of the Bohr atom, it was abandoned. (Nevertheless, it served its purpose in attracting attention to several cases of isomerism which have received quite interesting explanations.) Still there is no escaping the extraordinary parallelisms between benzene and thiophene, and Erlenmeyer and Leo (14) are to be complimented on introducing fresh life into the old problem by regarding one —CH = CH— as pseudo sulfur, and hence benzene as a pseudo pentagon.

Methylene groups can be activated by adjacent SO_2 as well as by CO, but the former present simpler conditions, as the work of Shriner (17) and of Arndt (18) shows that nothing parallel to keto-enol tautomerism takes place. Sulfonylmethanes are weakly acidic; trisulfonylmethanes comparable with chloroacetic acid. Attempts to realize an optically active *ion* of this type were unsuccessful (19), and the problem remains unsolved, although Kipping (20) has succeeded in resolving a compound in which the central C—H linkage is not an electrovalency.

The question of transmission of the effects of an atom through space, rather than along the intervening chain of atoms, is being exhaustively studied by Bennett (21). Frequent reference is made to inter- and intramolecular rearrangements which, so far as our present knowledge goes, are peculiar to sulfur chemistry, though they are probably only special cases of more general types.

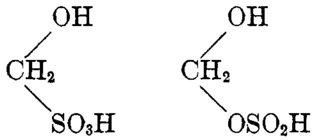
The thioketones developed by Schönberg's school demonstrate remarkable similarities to the compounds of trivalent carbon, and probably represent the high water mark of technique in this field, culminating in the recent demonstration of the monovalency of sulfur (22).

The writer hopes that in the following pages sufficient detail of these important advances is given so that it will be evident how little is definitely settled—how much remains to be done.

FORMALDEHYDE BISULFITE

The formula of the formaldehyde bisulfite compound has been attracting fresh interest. Naturally, it includes by implication the bisulfite compounds of all aldehydes (23, 23a).

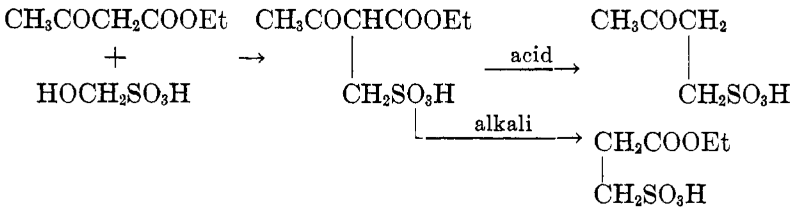
Of the alternatives which have been seriously considered formula I has, until recently, been preferred to II,



II I

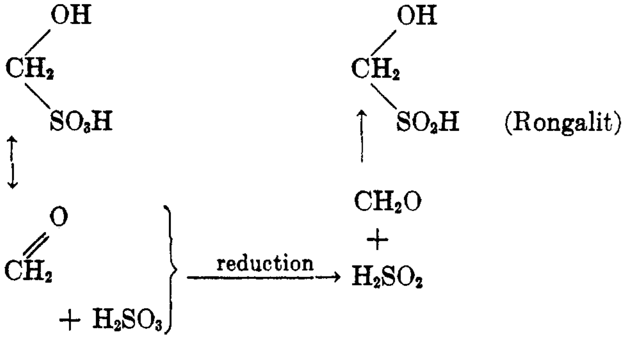
as formula II was claimed for the product obtained by sulfurating methyl alcohol (23b). Moreover, sulfonic acids are in general resistant to reduction, so that the well-known formation of sodium formaldehydesulfoxylate (Rongalit) by reduction of the bisulfite compound would seem to support formula I.

The whole question has been reëxamined by Raschig (24), who has shown that the sulfonation of methyl alcohol really produces sodium methyl sulfate. Formula II is thus once more free for formaldehyde sodium bisulfite. Raschig supports his contention by showing that formaldehyde sodium bisulfite readily reacts with ethyl acetoacetate, incidentally affording a convenient route to some rather inaccessible compounds:—



$$CH_3COCH_2COOEt + HOCH_2SO_3H \rightarrow CH_3COCH(CH_2SO_3H)COOEt \xrightarrow{acid} CH_3COCH_2CH_2SO_3H; \quad \xrightarrow{alkali} CH_2(COOEt)CH_2SO_3H$$

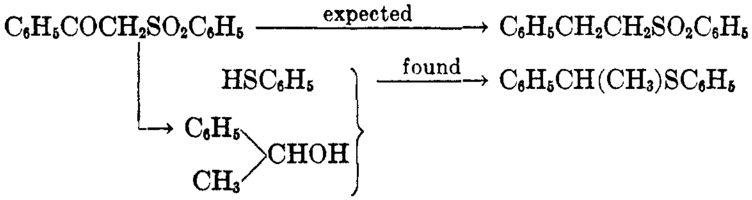
Further, Bazlen (25) in support of Raschig has shown that the hydroxyl group greatly reduces the strength of the C—S bond so that reduction actually occurs.



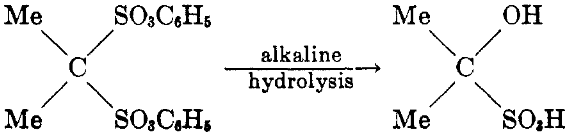
Holmberg (26, 26a) has noted a similar lability in the C—S linkage. Formaldehyde can displace many other (aromatic) aldehydes from their mercaptals. If we postulate that this change is dependent on the reversible formation of mercaptals,

$$C_6H_5CH(SCH_2COOH)_2 \leftrightarrow C_6H_5CHO + 2HSCH_2COOH + CH_2O \leftrightarrow CH_2(SCH_2COOH)_2$$

v. Braun and Weissbach (27) offer a very probable explanation of the formation of α-phenylethyl phenyl sulfide by reduction of phenacyl phenyl sulfone (28).



Further, Raschig and Prahl (29) quote Stelling's book "Über den Zusammenhang zwischen chemischen Konstitution und Röntgen Absorptionspectra," in which it is said that the only formula consistent with Röntgen data is II; moreover Raschig considers that any application of Hinsberg's ideas on the dipolar character of the sulfur atom would lead "zu uferlosen Folgerungen." With all these arguments against formula I Schroeter is in complete agreement, but in his notable work on methionic acid (30) he encountered an hydroxyisopropylsulfonic acid:



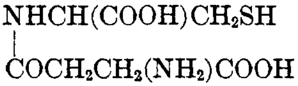
From the nature of its preparation, this substance could not possibly be identical with acetone sodium bisulfite; consequently formula II was also rejected. Raschig, however, in what was unfortunately his final contribution (123), pointed out that Schroeter's analyses (30a) were by no means convincing for a compound of such importance. Consequently the whole subject was reinvestigated by Schroeter (31), and now there is no longer any doubt that neither I nor II adequately represents the bisulfite compounds. We are accordingly compelled to consider formulas of types less familiar in organic chemistry. Of these, a coördination formula has been rather sketchily mooted by Binz (32). Schroeter himself is inclined to regard the bisulfite compounds as polymolecules (33), the constituents R_2CO, SO_2, and H_2O being held together by electron sharing, not between atoms, but between molecules.

CYSTEINE–GLUTATHIONE

There is much evidence for the idea that the oxidation-reduction processes in living tissue are dependent on an equilibrium.

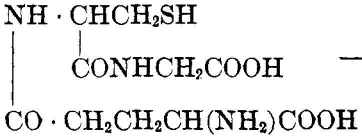
$$2HS\ldots.NH_2\ldots.COOH \leftrightarrow (\text{—}S\ldots.NH_2\ldots.COOH)_2$$

In 1921, Hopkins (34) isolated glutathione from tissue, and its synthesis by Stewart and Tunnicliffe (35) confirmed the view that it is a dipeptide.



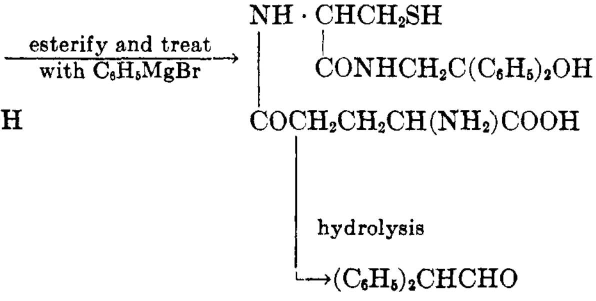
$$\begin{array}{l}NHCH(COOH)CH_2SH\\ |\\ COCH_2CH_2(NH_2)COOH\end{array}$$

In more recent work, Hunter and Eagles (36) indicated the presence of another amino acid in the extract. Further work by Hopkins (37) and Kendall, Mason, and McKenzie (38) has resulted in regarding glutathione as γ-glutamylcysteinylglycine (I) or glycylcysteine (II),

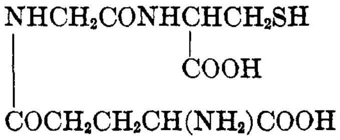


$$\begin{array}{l}NH\cdot CHCH_2SH\\ |\qquad |\\ |\quad CONHCH_2COOH\\ |\\ CO\cdot CH_2CH_2CH(NH_2)COOH\end{array}$$

I



$$\xrightarrow[\text{with } C_6H_5MgBr]{\text{esterify and treat}} \begin{array}{l}NH\cdot CHCH_2SH\\ |\qquad |\\ |\quad CONHCH_2C(C_6H_5)_2OH\\ |\\ COCH_2CH_2CH(NH_2)COOH\\ \quad |\\ \quad |\ \text{hydrolysis}\\ \quad \llcorner\!\!\rightarrow (C_6H_5)_2CHCHO\end{array}$$



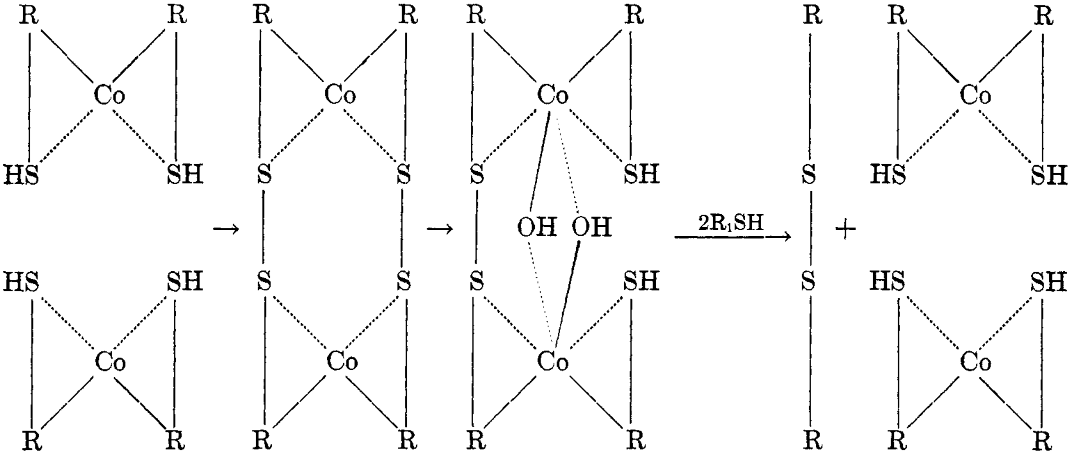
$$\begin{array}{l}NHCH_2CONHCHCH_2SH\\ |\qquad\qquad\quad |\\ |\qquad\qquad\ COOH\\ |\\ COCH_2CH_2CH(NH_2)COOH\end{array}$$

II

of which the former is preferred as more readily explaining the production of diphenylacetaldehyde from glutathione ethyl ester hydrochloride by the action of phenylmagnesium bromide.

Curiously, this fuller chemical knowledge has resulted in an increasing doubt as to the true physiological function of glutathione, for while the earlier preparations indicated that it could function as a catalyst in the oxidation of the fats and proteins by oxygen, the pure glutathione has now been found to possess this activity only with fats, and even then at an acidity not found in vivo (39).

There seems to be some hydrolysis product of glutathione containing a thiol group which, acting in conjunction with iron, brings about the oxidations formerly attributed to glutathione. Further, in the course of an interesting polarographic study on the activation of hydrogen in the sulfhydryl group in cysteine and glutathione, Brdicka (40) points out that some oxidizing agents, which easily oxidize cobaltous salts and cysteine if they are in common solution, remain without influence on either if they act on them separately. Thus, following Schubert (41), he writes:



R———SH = Cysteine

In this connection, the investigations of Nicolet (42), Schoberl (43), and McClelland (44) may be particularly mentioned as illustrating the conditions under which simpler disulfides of perfectly definite composition undergo decomposition.

Other cognate nitrogen–sulfur derivatives occur in protein (I) (45) and in wallflower seeds (II) (46).

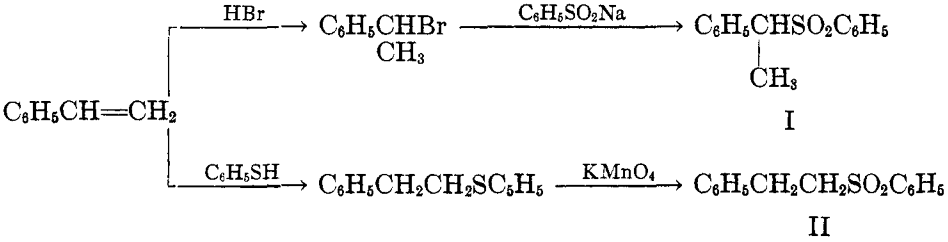
$CH_3SCH_2CH_2CH(NH_2)COOH$ I

$CH_3SO_2CH_2CH_2CH_2NCS$ II

Mention may also be made here of the mustard oil glucosides which are giving rise to the rapidly developing subject of the sulfur sugars (47, 48).

Addition of sulfur compounds to unsaturated linkages

A striking exception to Markownikoff's rule was discovered by Posner (10). He allowed various unsymmetrical unsaturated compounds to react with thiophenol and oxidized the resulting sulfides to sulfones; in each case the product was different from the sulfone obtained by the action of sodium benzenesulfinate on the hydrobromide formed from the unsaturated hydrocarbon.



$$C_6H_5CH{=}CH_2 \xrightarrow{HBr} C_6H_5\underset{CH_3}{CH}Br \xrightarrow{C_6H_5SO_2Na} C_6H_5\underset{CH_3}{CH}SO_2C_6H_5 \quad \text{I}$$

$$C_6H_5CH{=}CH_2 \xrightarrow{C_6H_5SH} C_6H_5CH_2CH_2SC_5H_5 \xrightarrow{KMnO_4} C_6H_5CH_2CH_2SO_2C_6H_5 \quad \text{II}$$

It will be noticed that the course of mercaptan addition is implied by non-identity with I rather than by comparison with an otherwise authenticated specimen of II, and while Posner's conclusions as regard styrene have been confirmed and amplified by Ashworth and Burkhardt, other examples which he gave have been shown to correspond neither to type I nor to type II (49), but these discrepancies are probably due to Posner's having handled mixtures of I and II, so that the general accuracy of his scheme is not in doubt.

On the contrary, it receives very important confirmation from the work of Kharasch (9), who shows that the direction of addition of hydrogen bromide to an unsaturated system is controlled by the presence or absence of contaminating peroxide in the unsaturated compound. Thus while pure propylene yields isopropyl bromide, the addition of a trace of benzoyl peroxide results in the formation of propyl bromide.

It seems possible therefore that with those unsaturated compounds which are especially easily contaminated with peroxides arising from their own oxidation, mercaptans first purify the compound and then add on in the "normal" way; whereas with hydrobromic acid the direction of addition is controlled by the contaminating peroxide.

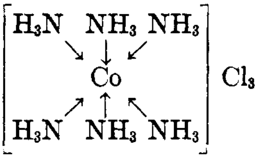
A most ingenious application of the additivity of the thiol group was made by Holmberg (50), who allowed thioglycolic acid to act on rubber and so converted it to an alkali-soluble product.

The work of Mulder (51), Backer (52), and Eigenberger (53) may be consulted on the addition of sulfur dioxide or sulfites to unsaturated compounds.

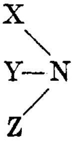
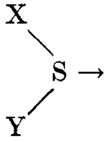
COÖRDINATION COMPOUNDS

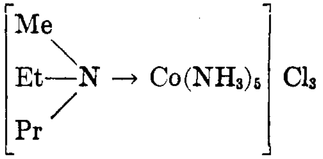
Of the many recent investigations of coördination compounds containing sulfur (125) mention must be made of four which have an important bearing on general chemical theory.

For instance, it is tacitly assumed, although difficult of experimental verification, that the ammonia groups in cobalt hexammine trichloride



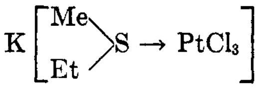
$[Co(NH_3)_6]Cl_3$

are bound to the central atom by coördination bonds. Now since aminoöxides  $XYZN \rightarrow O$ and sulfoxides  $XYS \rightarrow O$ have been resolved[1] (54, 55, 56),



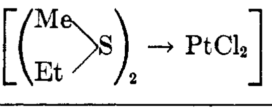
$[MeEtPrN \rightarrow Co(NH_3)_5]Cl_3$

should be resolvable. Difficulties with the nitrogen compounds led Mann (12) into the sulfur series. Here again was disappointment, for instead of



$K[MeEtS \rightarrow PtCl_3]$

he always obtained



$[(MeEtS)_2 \rightarrow PtCl_2]$

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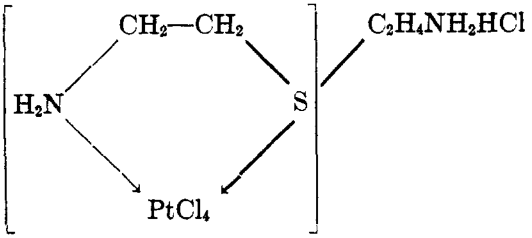
[1] Bergmann does not accept the usual explanation.

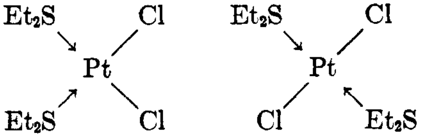
but this was surmounted in the end by preparing



which he resolved with camphor-β-sulfonic acid (the bonds concerned in asymmetry being in heavy type).

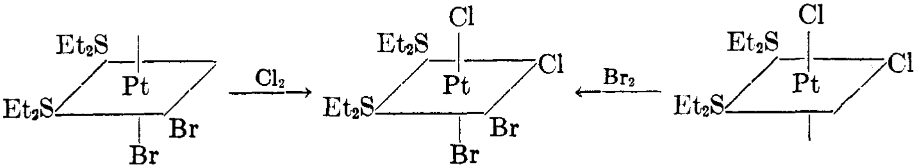
It has long been known that salts of the platino series $(Et_2S)_2PtCl_2$ exist in two modifications, and various explanations of the isomerism have been proposed (57).

The most important feature of the accepted view is the postulate that the four valencies of platinum lie in one plane



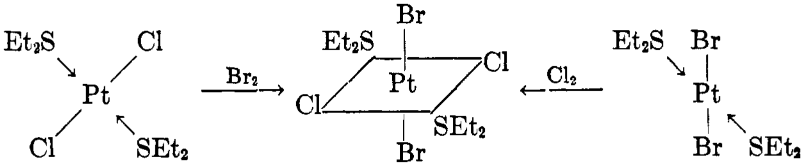
α (Werner) β (Werner)

The dihalides are readily converted to tetrahalides in which, as is well-known, the groups have octahedral configuration. Angell, Drew, and Wardlaw (58) found that the α-dichloride reacts also with bromine, and the α-dibromide with chlorine, to yield one and the same dibromodichloride. They interpreted this as indicating a tetrahedral structure for the α-dihalides:—

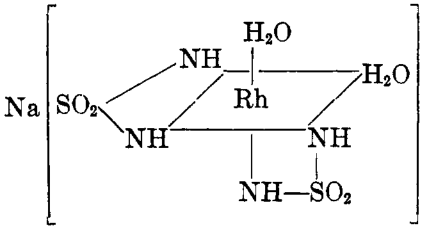


It is obvious that Werner's α-sulfine dichloride should yield a dichlorodibromide *different* from the dichlorodibromide arising from Werner's α-sulfine dibromide.

Without going into the question of the β-series it may be said that severe criticism of their conclusions (59) has impelled Drew and Wyatt to further work (60), in which they revert to the planar configuration for the α-disulfine by ascribing to it the formula Werner used for the β-disulfine.



One of the final steps in Werner's classic work was the preparation of an optically active cobaltammine containing no carbon atom whatever (61). A second and much simpler example has just been recently reported by Mann (62).

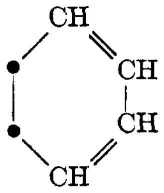


A most interesting dilemma is presented by Manchot and Gall's (63) work on the valence of iron. By the action of nitric oxide on solutions of ferrous sulfate and a mercaptan, they obtained a product A,$Fe(NO)_2(SR)_2$, which breaks down with formation of a thionitrite R·SNO and B,$Fe(NO)_2(SR)$. Apparently iron is tetravalent in A and trivalent in B, or divalent in A and monovalent in B: "Man kommt also nicht darum herum entweder ......oder......, eine ungewöhnliche Wertigkeit des Eisens anzunehmen."

An even more critical case of abnormal valency concerns beryllium. In keeping with its covalency maximum 4, many of its salts crystallize with four molecules of water of crystallization. The benzenesulfonates and naphthalenesulfonates are, however, exceptional in having six molecules of water of crystallization (15). Other work of Pfeiffer (16) makes it improbable that this surplus is associated with the negative ion. There is thus the interesting possibility that in these compounds beryllium actually exceeds its covalency maximum.

ISOMERISM AMONG SULFUR COMPOUNDS

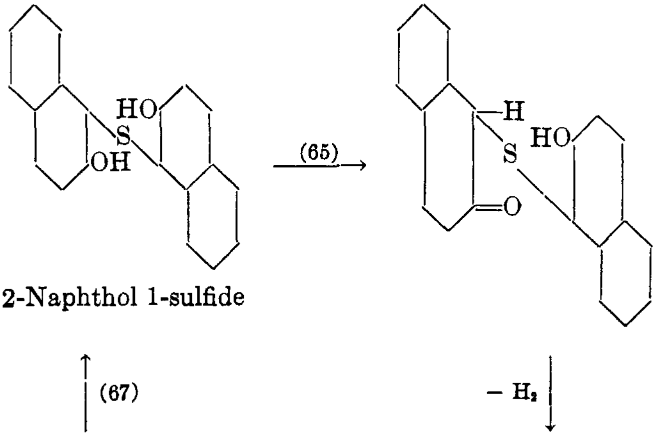
The very striking similarity between benzene and thiophene and their derivatives led Hinsberg to suggest (13) that their ring systems must closely resemble each other—that the sulfur atom had two centers from which valency bonds could radiate (88).

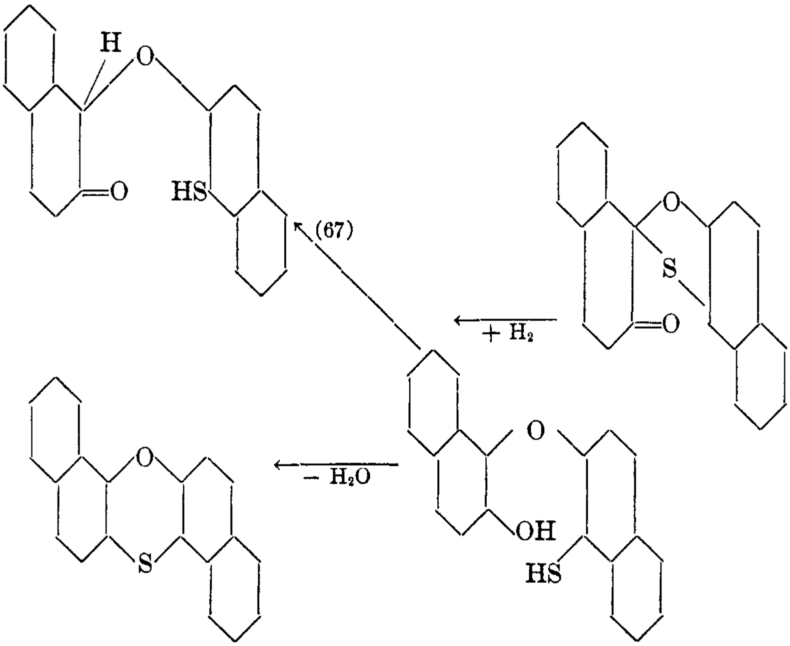


Such a view postulated a suspiciously large number of isomers throughout the compounds of sulfur, and after performing the useful service of directing attention to a variety of actual isomers, it has naturally fallen into discredit with modern views of the atom. In this connection it is interesting to note what remarkably divergent values have recently been proposed for the valence angle of sulfur—the figures ranging from 62° to 146°. Bennett and Glasstone (65) consider that the non-planar configuration of thianthrene indicates that the valence bonds of sulfur adopt an angle of less than 120°. The actual isomers to which Hinsberg's theory directed attention have received other and no less interesting explanation.

The problem of the existence of two "sulfides" of naphthol, also cited by Hinsberg, has quite a different cause which has required many years to elucidate.

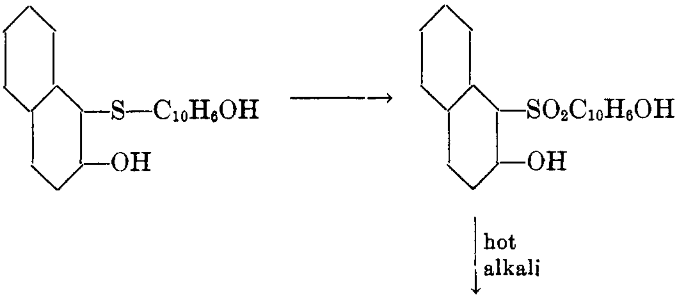
When 2-naphthol 1-sulfide is oxidized, a dehydrosulfide is formed (66), which on reduction yields iso-2-naphthol sulfide, which yields $\alpha,\beta,\beta',\alpha$-dinaphthathioxin (67) on dehydration, and regenerates 2-naphthol 1-sulfide on treatment with alkali (68). These changes can be formulated:

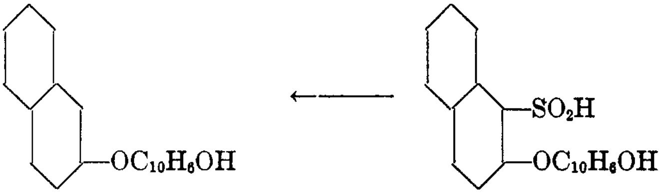

2-Naphthol 1-sulfide



Naphthathioxin (66)   Isosulfide

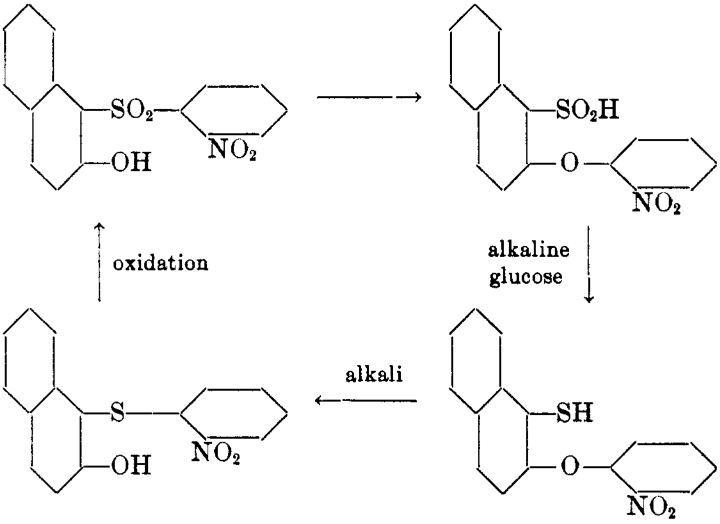
Smiles regards the reconversion of "iso" to β-naphthol sulfide as replacement of the hydroxynaphthyl group from the alpha carbon atom by the more negative thiol group, and he confirms this by showing that when β-naphthol sulfide is oxidized to sulfone with peroxide, the opposite change occurs, for the sulfur atom has assumed a positive character (68). The rearrangement of 2-naphthol 1-sulfone with alkali is unfortunately accompanied by elimination of sulfur dioxide.





(not isolated,
loses SO_2 immediately)

Were it not so, the sulfinic acid (isosulfone) initially produced could no doubt be reduced to "isosulfide" and so a complete cycle realized, as indeed has since been achieved with 2-nitrophenyl-2-hydroxy-1-naphthyl sulfone (69, 70) in which the 2-nitrophenyl nucleus was transferred from sulfur to oxygen and vice versa.



(not isolated)

It has long been known that sulfonic esters act as alkylating agents; recently Peacock and Tha (71) have applied them to alkylating malonic esters. Gilman and Beaber (72) have gone one step further and shown that they can, under suitable conditions, even yield hydrocarbons:—

$$RSO_2O\cdot Alk + Alk\cdot MgBr \longrightarrow Alk\cdot Alk$$

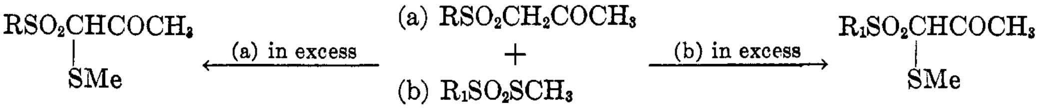
$$RSO_2O\cdot Aryl + Alk\cdot MgBr \longrightarrow RSO_2Alk + Aryl\cdot OH$$

The thiosulfonic esters (formerly called disulfoxides) (73) behave differently for, as Brooker and Smiles showed (74), one can use them to introduce the —SR group into the reactive methylene group.

$$\mathrm{RSO_2SR + CH_2(COR)_2 \rightarrow 2RSO_2H + (RS)_2C(COR)_2}$$

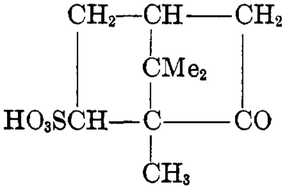
When the methylene group is activated by two sulfonyl groups (bis(sulfonyl)methane) or by one carbonyl and one sulfonyl group (sulfonylacetone) only one hydrogen atom is replaced (75).

During this substitution the sulfonylacetones are, moreover, subject to an exchange of radicals in a rather unusual way:

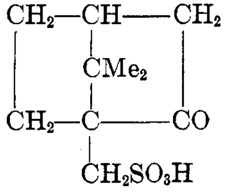


$$\begin{array}{c}\mathrm{RSO_2CHCOCH_3}\\ |\\ \mathrm{SMe}\end{array} \xleftarrow{\text{(a) in excess}} \begin{array}{c}\text{(a) }\mathrm{RSO_2CH_2COCH_3}\\ +\\ \text{(b) }\mathrm{R_1SO_2SCH_3}\end{array} \xrightarrow{\text{(b) in excess}} \begin{array}{c}\mathrm{R_1SO_2CHCOCH_3}\\ |\\ \mathrm{SMe}\end{array}$$

A further peculiarity of this exchange is that it occurs only when an alkyl thio group is the entering substitutent (76). From what has just been said, it might seem that in migration of the sulfonyl group the work of Armstrong and Lowry (77) could be reconciled with that of Wedekind, Schenk, and Stusser (78). The former assigned the structure I to Reychler's acid, the latter structure II.

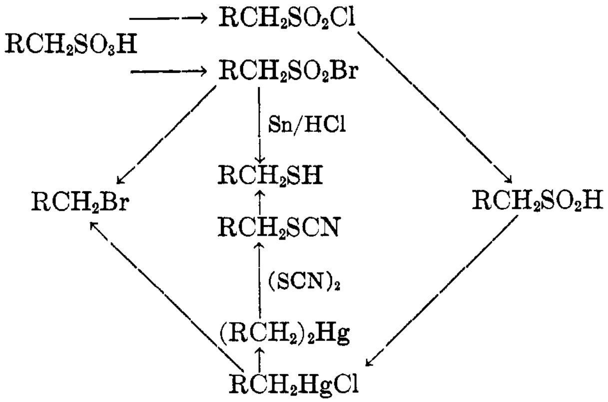


I

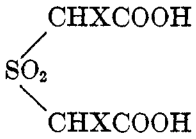


II

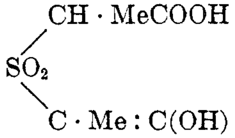
Such, however, is not the case, for Loudon (79), by completing the following cycle under the mildest conditions, was able to show that the substituent remained, as Wedekind, Schenk, and Stusser indicated, in the 10′-position



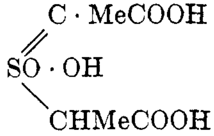
In Sweden the sulfo-fatty acids have received close attention. Ahlberg (80) for instance, has examined the optical activity of acids of the type



He found that where X = Me the acid is so readily racemized as to be incapable of isolation in the active condition, but with X = Et or isopropyl, the active acid is readily obtained. He considered that the racemization was due to the tautomeric changes represented by either A or B:



A



B

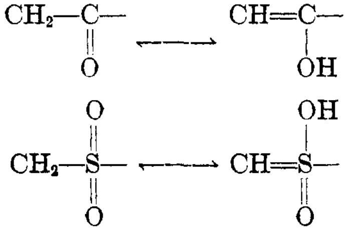
He preferred B and suggested that the efficacy of the higher alkyl groups was to be explained on the basis of a steric hindrance effect in the 1,5-position (ethyl). Now, because compounds containing the groupings

$—SO_2CH_2CO$

$—SO_2 \cdot CH_2—SO_2$

$SO_2—CH_2 \cdot CN$

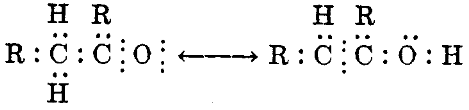
dissolve in alkali, are readily methylated, and give compounds with diazobenzene chloride, Hinsberg and others (81, 81a, 81b) extended the idea of enolization to the sulfone group.



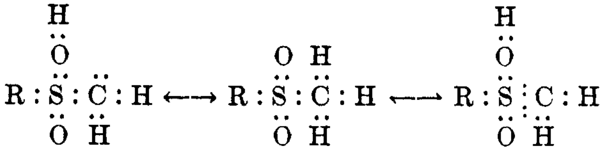
$$CH_2—\underset{\underset{O}{\|}}{C}— \rightleftarrows CH{=}\underset{\underset{OH}{|}}{C}—$$

$$CH_2—\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}— \rightleftarrows CH{=}\underset{\underset{O}{\|}}{\overset{\overset{OH}{|}}{S}}—$$

Expressed in that way, it did no obvious violence to the existing ideas of valence; but on the modern electronic conception it is evident that the sulfonyl group has quite another character from the carbonyl.



$$R:\underset{H}{\overset{H}{C}}:\overset{R}{C}:O: \longleftrightarrow R:\overset{H}{C}:\overset{R}{C}:\ddot{O}:H$$



$$R:\underset{O}{\overset{\overset{H}{O}}{S}}:\underset{H}{C}:H \longleftrightarrow R:\underset{O}{\overset{O}{S}}:\underset{H}{\overset{H}{C}}:H \longleftrightarrow R:\underset{O}{\overset{\overset{H}{O}}{S}}:\underset{H}{C}:H$$

A B

The "enolization" of the sulfone group leads either to the establishment of a lone pair of electrons on the carbon atom (formula A), or to the sulfur atom being surrounded by ten electrons (formula B) (18).

The former alternative would not involve any movement of electrons, but it would lack driving force, for the proton would be leaving an atom to which it is firmly attached (carbon) to take up its position on one to which its attachment is much looser (oxygen) as, e.g., the strength of sulfuric acid indicates.

Since in methylene disulfones, where only one electronic arrangement is possible, the electron system of the anion must be identical with the free hydrogen compound, these salts are C-salts in this sense that the anionic charge corresponds to a lone pair of electrons on the carbon atom. That means there is no binding between metal and carbon comparable to that in an organometallic compound. Unlike the aliphatic diazo compounds which also have a lone pair of electrons on carbon, these polysulfonyl salts are colorless, because the lone pair is so firmly bound.

Another point of interest is the behavior of methylene disulfones on bromination in aqueous solution. As is well-known, acids promote the bromination of such compounds as acetylacetone. The effect with the sulfur derivatives is quite the reverse; this leads Arndt and Martius to postulate their bromination occurring by either (or possibly both),

$$Br_2 + H_2O \rightarrow HBr + HBrO; \qquad HBrO + \rangle CH \rightarrow H_2O + CBr$$

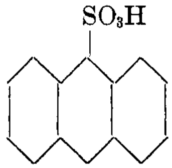
$$Br_2 \longleftrightarrow Br^+ + Br^-; \quad \rangle CH \longleftrightarrow \rangle C^- + H^+; \quad \rangle C^- + Br^+ \rightarrow CBr$$

for, evidently, both processes would be retarded by acid.

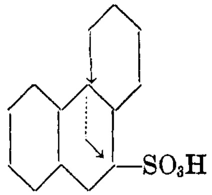
This real difference between carbonyl and sulfonyl accounts for the resistance of methanesulfonyl chloride to chlorination (82) and is also perhaps the reason why chloroiodomethanesulfonic acid (83) can be obtained optically stable while chloroiodoacetic acid has not been resolved (126).

We are thus obliged to reject Ahlberg's explanation (B) of the optical instability of sulfodipropionic acid, and the fact that sulfopropionic acid has been resolved (84) rather speaks against his alternative formula (A) as he himself admits.

Another rearrangement recently described by Schroeter and Gotzsky (85) resembles these involving the migration of a sulfonyl group.

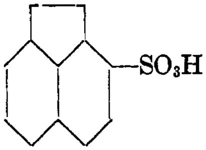


Octhracenesulfonic acid

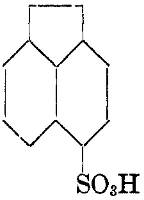


Octanthrenesulfonic acid

Likewise, the sulfonation of acenaphthene may yield either X or Y.

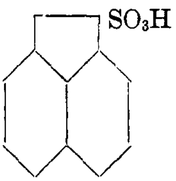


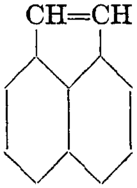
X



Y

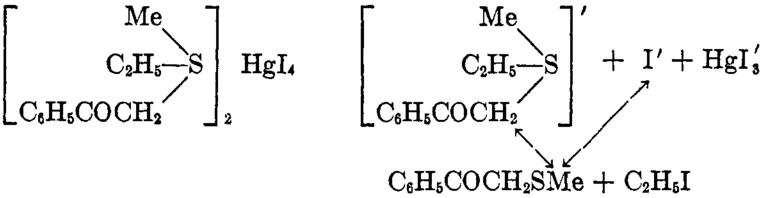
Each of these undergoes rearrangement on fusion with alkali, the final product being acenaphthylene.



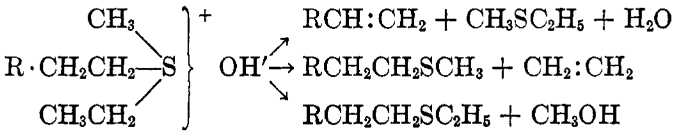


Sulfonium salts

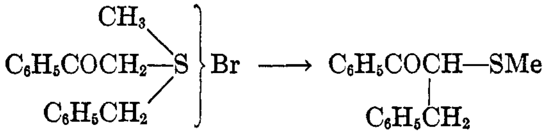
These are in many ways similar to quaternary ammonium salts. Thirty years ago representatives of each class were resolved, and problems which arose then (92) are still attracting interest (93). The ready racemization of sulfonium mercuriiodides has, for instance, recently been shown to depend on a reversible decomposition of the ions:—



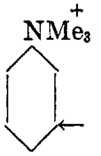
The thermal decomposition of sulfonium hydroxides has been found by Ingold, Jessop, Kuriyan, and Mandour (87) to be quite parallel to that observed with ammonium hydroxides.



Even more interesting is Stevens' discovery that with phenacylbenzylmethylsulfonium bromide a transformation of a type first observed by himself (96) in the ammonium series can be realized (97).



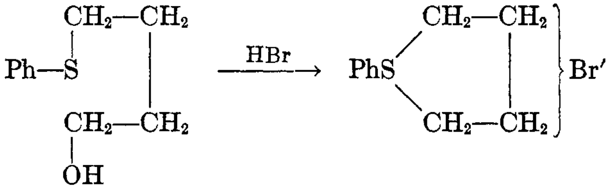
The similarity between ammonium and sulfonium salts extends to aromatic substitution, both groups being powerfully meta directing (89, 90, 91).



On the other hand, it is by no means obvious that the suppression of basic characteristics in pyrrole and thiophene has as yet been satisfactorily explained (122); although it may be true that in pyrrole the lone pair of nitrogen electrons is absorbed in an aromatic sextet, since the sulfur atom in thiophene has *two* lone pairs, one of these, on the above theory should remain and so give rise to a methiodide or a sulfoxide, which, as a matter of fact, has never been observed. A valuable paper by Richardson and Soper (98; also 99) indicates that the combination of a bromide and a sulfide to form sulfonium bromide should be greatly facilitated by use of a solvent of high cohesion, e.g., nitromethane.[2] Application of this important solvent enabled Ingold and Jessop (100) to isolate fluorenyl-9-dimethylsulfonium bromide, but it is by no means certain that their interpretation of the subsequent degradation of this compound is fully established.

It is well-known that many substances which show no other basic characteristics will form salts with perchloric acid. Following this up Hinsberg has recently subjected diphenyl sulfide, dibenzyl sulfide, and di-*n*-butyl sulfide to the action of hot perchloric acid, and in each case claims to have isolated an isomeric sulfide. It is unfortunate that these seem rather ill-defined unstable bodies (94, 95).

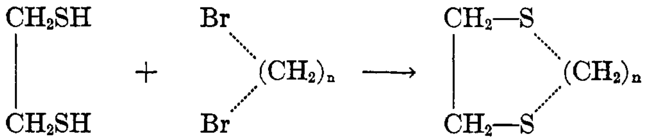
An interesting example of the transmission of the influence of a sulfur atom directly through space rather than along the intervening chain of atoms is provided by Bennett and Mosses' (21) discovery that phenyl δ-hydroxybutyl sulfide is convertible to the cyclic sulfonium bromide under conditions that scarcely affect the γ-hydroxypropyl or ε-hydroxyamyl sulfides:—



Phenyl δ-butyl sulfide

NEW CYCLIC TYPES

It has long been known that in the preparation of cyclic sulfides, such as dithiane, more or less of the material is converted to high molecular polymers (101). These, which have usually been removed and considered as loss, have now been investigated by Tucker and Reid (102).



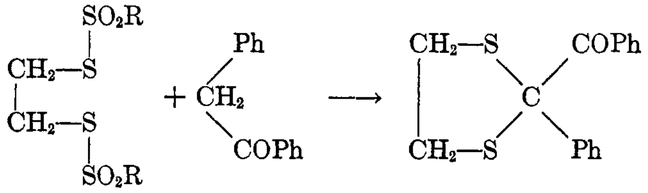
where n is 1, 2, 3, 4, 5, or 6. They find that in every case the polymers

---

[2] Attempts to prepare thiophenesulfonium derivatives in nitromethane were, however, unsuccessful, and yet this cannot be attributed to inherent instability, for Backer and Strating (127) have quite recently isolated the sulfones of methylated thiophenes by combining butadienes with sulfur dioxide.

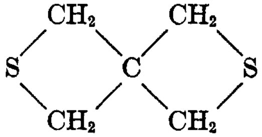
can be degraded to dithiane by heating with ethylene bromide or, in some cases, with hydrogen chloride.

Similar ring systems have also been prepared by Chivers and Smiles (103),

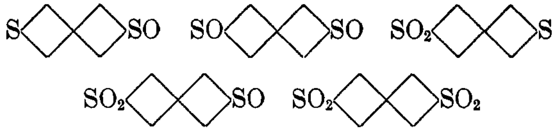


and Gibson (104) has found evidence that the unsubstituted 1,3-dithiolane can give rise to a ψ base.

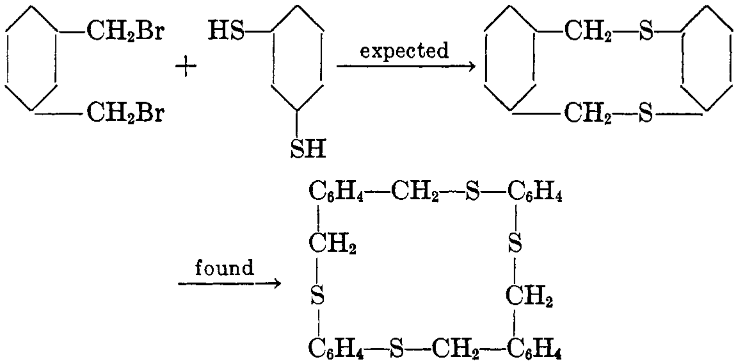
A most interesting spiro cyclic type has just been isolated by Backer and Kenning (105). They find that pentaerythritol tetrabromide reacts very easily with potassium sulfide to give



which is stable enough to allow of the isolation of the five expected oxides

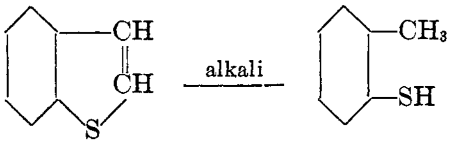


and of being brominated without rupture of the spirane system. On the other hand Reindel and Schuberth (106), attempting to make ten-membered rings from meta-substituted benzenes, obtained only polymeric products.



In investigating a number of cases where ring closure may take place to form either a nitrogen or a sulfur ring compound, Arndt and Bielich (107) find that in neutral or acid media the heterocyclic member is sulfur; in alkaline media it is nitrogen.

The reverse process, the rupture of a sulfur ring compound, has been developed by Weissberger and Seidler (108) as a valuable method for removing thionaphthene from naphthalene.

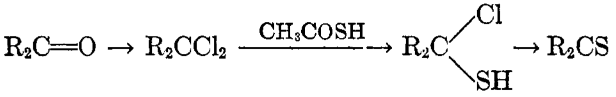


SACCHARIN

Although it is nearly fifty years since saccharin was discovered, the secret of its sweetness is still unexplained. Various attempts on the lines of "glucophores" and "auxoglucs" have met with little success. The fact that very concentrated solutions are relatively less sweet than the more dilute led Magidson and Gorbatschow (109) to suggest that as saccharin is an acid, its sweetness bears a direct relationship to its degree of dissociation. They attribute a bitter taste to the undissociated molecule, but although they bring forward some evidence in support of their contention, Taufel and Wagner consider it inconclusive.

THIOKETONES

During the last few years Schönberg has made an exhaustive study of thioaldehydes and thioketones. He finds (110) that those constitutional changes which favor or inhibit the existence of free "triarylmethyl" groups also favor or inhibit the tendency of thioketones to polymerize; and likewise that those changes which favor or inhibit the dissociation of hexaaryl ethanes also favor or inhibit the dissociation of polymerized thioketones. Thus while thioformaldehyde and thiobenzaldehyde are known only trimeric, thiobenzophenone exists only monomeric. The existing routes to thioketones being of rather restricted applicability, it is of interest to mention that a more general route has now been devised (111).

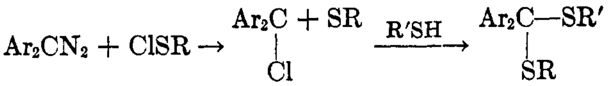


$$R_2C{=}O \rightarrow R_2CCl_2 \xrightarrow{CH_3COSH} R_2C\left\langle\begin{matrix}Cl\\ SH\end{matrix}\right. \rightarrow R_2CS$$

The corresponding mercaptides are accessible from diaryldiazomethanes,

$$Ar_2CN_2 + RSSR \rightarrow Ar_2C(SR)_2 + N_2$$

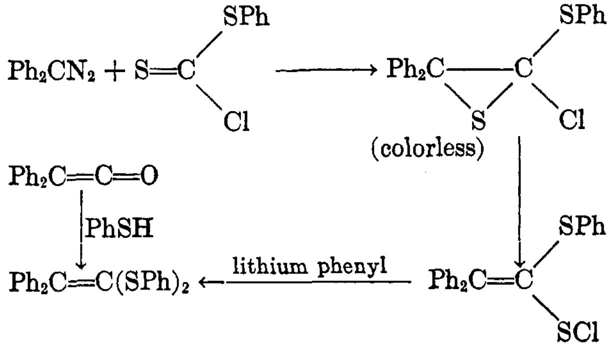
and also the unsymmetrical mercaptides by using aryl sulfur chlorides (112).



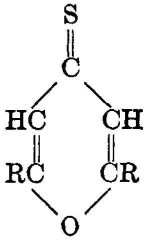
$$Ar_2CN_2 + ClSR \rightarrow \underset{\displaystyle Cl}{\underset{|}{Ar_2C}} + SR \xrightarrow{R'SH} \underset{\displaystyle SR}{\underset{|}{Ar_2C}}{-}SR'$$

The necessary aryl sulfur chloride is readily obtained, according to Lecher and Holzschneider (113), by adding the mercaptan to a solution of chlorine (not vice versa).

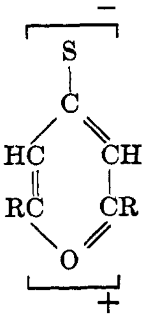
Substituted diazomethanes also react with chlorothiocarbonic esters; in examination of such a reaction Schönberg and Vargha (114) detected a most unusual rearrangement and most ably substantiated their explanation.



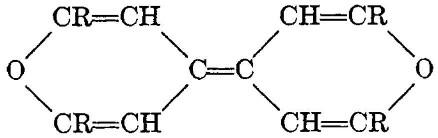
Arndt, Scholz, and Nachtwey (115) find that thioketones of the type,



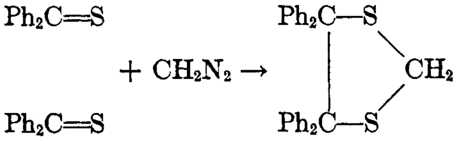
can also exist in the form



Where R is an acidifying substituent (C_6H_5 or COOEt), the true thioketone form is favored, as is shown by the readiness with which it decomposes to give sulfur and

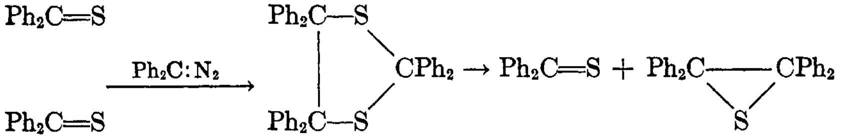


These substances are not only thermolabile, but extraordinarily sensitive to what one might consider slight changes in constitution. Thus while thiobenzophenone reacts with diazomethane to give a relatively stable 1,3-disulfide,



I

the corresponding product from diphenyldiazomethane is easily decomposed with regeneration of half of the thiobenzophenone.



II III

The regenerated thiobenzophenone undergoes reaction afresh with diazodiphenylmethane, and so on until all is converted to tetraphenylethylene sulfide. Even more sensitive are the products from diphenyl trithiocarbonate (V),

$$(C_6H_5S)_2C:S$$

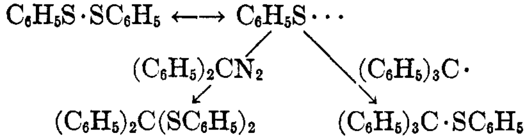
V

for with diazomethane it gives a 1,3-disulfide analogous to II, while with diazoethane it breaks down as II → III (116, 117).

Monovalent sulfur

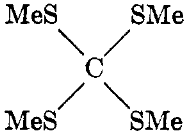
The question whether disulfides are capable of dissociating into free radicals with monovalent sulfur was examined by Lecher, who came to the conclusion that they were not (118). Schönberg, Rupp, and Gumlich

(119) now show that his experimental technique was not sensitive enough, and that with suitable reagents diphenyl disulfide shows all the characteristics of dissociation.



Admittedly, solutions of diphenyl disulfide are stable to oxygen, and the extent of dissociation is too small to be detected by molecular weight measurement, but Beer's law is not obeyed, and some more complicated disulfides decolorize metal–ketyl solutions practically instantaneously (22).

In direct contrast to such supra-activity there is tetramethylthiomethane



which has been isolated, after many failures, in the Groningen laboratory. It is quite remarkable for an inertness reminiscent of sulfur hexafluoride (121).

Modern microcombustion methods greatly simplify the analysis of sulfur compounds. For compounds containing carbon, hydrogen, and sulfur only, Pregl's combustion method over platinum followed by titration is so simple and speedy that it leaves little to be desired. For compounds which contain nitrogen and for halogen as well, Friedrich (120) has devised a satisfactory modification.

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