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REARRANGEMENT REACTIONS OF SOME
AROMATIC SULFUR COMPOUNDS

by

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INTRODUCTION

By reason of their location in the same group of the periodic table, many similarities in the chemical and physical properties of aromatic oxygen compounds to those of analogous aromatic sulfur compounds have been demonstrated. In the observation of the chemical properties of the two classes of compounds, these obvious analogies are not necessarily confined to the typical reactions of aromatic compounds, but may be extended to include the abnormal reactions of these compounds, such as rearrangement reactions.

A new type of rearrangement reaction, a rearrangement amination, has recently been developed (1) in these laboratories. This rearrangement amination has been shown to take place in the reaction of sodamide in liquid ammonia with o-halogen aryl alkyl ethers; the amino group replaces the halogen group but in so doing assumes the meta position to the alkoxy rather than the ortho position. It shall be one of the purposes of this thesis to demonstrate further the similarity between aromatic oxygen and sulfur compounds, i.e., ethers and thioethers, especially in the new rearrangement amination. Since the analogies between aromatic oxygen and sulfur compounds must be restricted to the sulfur compounds containing divalent

1. Gilman and Avakian, J. Am. Chem. Soc., 67, 349 (1945).

sulfur, we shall be deviating from a real comparison of oxygen and sulfur compounds if the investigation of the rearrangement amination should be carried to compounds containing sulfur in a higher valence state. However, it will be within the purpose of this thesis to investigate the newly observed rearrangement amination in aromatic sulfur compounds in which the sulfur is oxidized beyond the divalent state.

HISTORICAL

One of the earliest recognized and established rearrangements of an aromatic sulfur compound was that involved in the preparation of sulfanilic acid. This acid is prepared on a technical scale by mixing equal molecular quantities of aniline and sulfuric acid and baking the resultant acid sulfate at 180° until aniline can no longer be liberated from test portions. Actually two rearrangements are involved. Bamberger (2) in 1897 established that the initial reaction in the preparation is the loss of water from the sulfate with the formation of phenylsulfamic acid. He further demonstrated that when phenylsulfamic acid was heated cautiously, the sulfonic acid group first migrated to the ortho position, giving orthanilic acid, which rearranged at 180° to give sulfanilic acid.

There have been many other observations of rearrangement reactions involving aromatic sulfur compounds. In our treatment of the subject, we plan to discuss rearrangements involving migration of the sulfur containing groups, as well as those in which the re-orientation of the sulfur atom is not concerned.

It is interesting at this time to note that many of these rearrangements are of the type which are not ordinarily associated with sulfur compounds. For example, allyl aryl sulfides

2. Bamberger and Hindermann, *Ber.*, 30, 654 (1897); Bamberger and Kunz, *ibid.*, 30, 2274 (1897).

have been shown to undergo the Claisen rearrangement (3). Benzenesulfonyl esters of ketoximes and related compounds, e.g., ethyl-syn-benzhydroxamic acid, have shown typical Beckmann rearrangement (4). Again, certain sulfonic acid esters undergo the well-known Fries rearrangement (5). On the other hand, the Jacobsen rearrangement of polyalkylated aromatic sulfonic acids (6) is one rearrangement commonly associated with sulfur compounds.

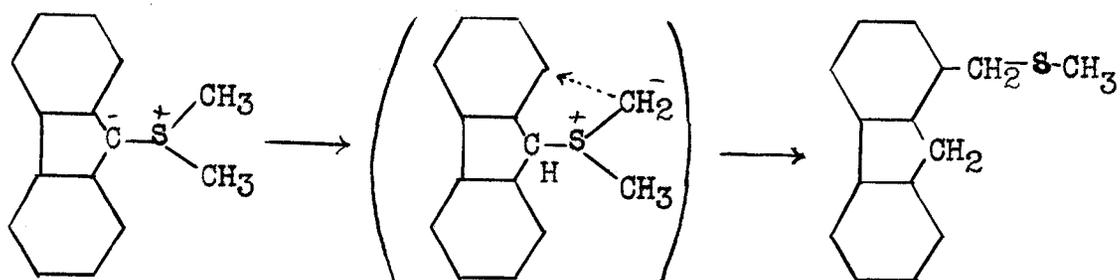
Numerous rearrangements of aromatic sulfides have also been reported in the literature. Hurd and Greengard (3) have reported a rearrangement of aryl allyl sulfides by pyrolysis, analogous to that sustained by a similar pyrolysis of allyl aryl ethers. The yields of the resultant thiophenols were not nearly as remarkable as the yield of o-allylphenol (80%) by the pyrolysis of allyl phenyl ether. Both allyl phenyl sulfide and allyl p-tolyl sulfide were studied in the rearrangement. The products, o-allylthiophenol and 2-allyl-4-methylthiophenol, were clearly identified as the lead salts and as the oxidation products, the sulfonic acids.

Taylor (7), in a study of the reaction between aromatic mercaptals and formaldehyde, observed products which suggested

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3. Hurd and Greengard, J. Am. Chem. Soc., 52, 3356 (1930).
 4. Komatsu, "Mitsuru Kuhara's on the Beckmann Rearrangement", Kyoto, 1926, pp. 38, 47, 52, 72, 73.
 5. Simons, Archer, and Randall, J. Am. Chem. Soc., 62, 485. (1940).
 6. Jacobsen, Ber., 19, 1209 (1886); ibid., 20, 2837 (1887).
 7. Taylor, J. Am. Chem. Soc., 58, 2649 (1936); ibid., 57, 1065 (1935).

a rearrangement of formaldehyde diaryl mercaptals which involved the migration of the $-CH_2$ group from the sulfur to the benzene nucleus, with a regeneration of the $-SH$ groups. To substantiate his ideas on the rearrangement, one which would be essentially a rearrangement of alkyl aryl thioethers, the author investigated the possibilities of such a rearrangement under his working conditions. It was subsequently observed, then, that allyl *p*-tolyl sulfide, *s*-butyl phenyl sulfide, and *s*-butyl *p*-tolyl sulfide all rearranged at temperatures as low as $135-150^\circ$ under the influence of a zinc chloride-acetic acid reagent. The products were alkyl substituted thiophenols; some cleavage of the alkyl group was also observed. The oxygen analogues have shown the same type of rearrangement (8).

Hilbert and Pinck (9) have observed that fluorylidene dimethyl sulfide rearranges in alkaline medium, such as alcoholic sodium hydroxide or liquid ammonia, to fluorene-1-dimethyl sulfide. The rearrangement is shown as follows:



-
8. Sprung and Wallis, *ibid.*, 56, 1715 (1934).
 9. Hilbert and Pinck, *ibid.*, 60, 494 (1938).

The structure of the rearrangement product was elucidated by mild oxidation of the compound to the sulfone, and by strong oxidation to the fluorenone-1-carboxylic acid.

A rearrangement of phenacylbenzylmethylsulfonium bromide to 1,1-benzylbenzoylmethyl methyl sulfide by the action of alkali was noted by Thomson and Stevens (10). Previously the rearrangement had been observed in similar ammonium salts, e.g., phenacylbenzyltrimethylammonium bromide (11). An attempt to rearrange phenacyl benzyl sulfone in the same fashion to the expected sulfinic acid was unsuccessful.

Other rearrangements of sulfonium compounds have been reported. Ray and Farmer (12), in the preparation of methyldibenzylsulfonium methyl sulfate from dibenzyl sulfide and methyl sulfate, noticed that rearrangement took place to give, in addition, some benzyldimethylsulfonium methyl sulfate. Dibenzyl sulfide also gives a rearranged product with methyl hydrogen sulfate; some tribenzylsulfonium methyl sulfate is formed in addition to the expected dibenzylmethylsulfonium sulfate.

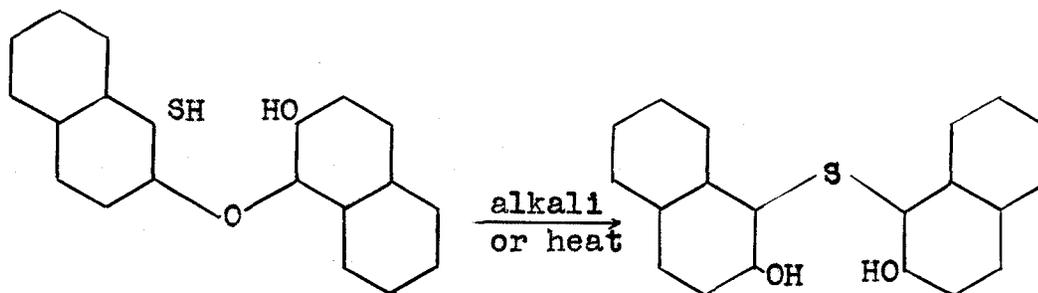
An exchange of radicals in sulfonium compounds had been observed earlier by Auwers and Arndt (13). In an attempt to purify by distillation the oily product obtained from the interaction of *p*-tolyl ethyl sulfide and dimethyl sulfate, they obtained *p*-tolyl methyl sulfide rather than the pure *p*-tolyl-

-
10. Thomson and Stevens, J. Chem. Soc., 69 (1932).
 11. Stevens, ibid., 2107 (1930); Stevens, Snedden, Stillier, and Thomson, ibid., 2119 (1930).
 12. Ray and Farmer, J. Org. Chem., 8, 391 (1943).
 13. Auwers and Arndt, Ber., 42, 2713 (1909).

ethylmethylsulfonium methyl sulfate.

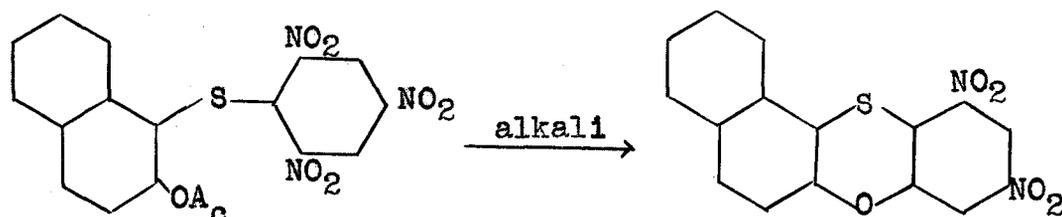
Warren and Smiles (14) proposed a structure for the controversial iso- β -naphthol sulfide and showed its actual existence. The so-called iso- β -naphthol sulfide (15) was formed in two steps from 2,2'-dihydroxy-1,1'-dinaphthyl sulfide, the so-called 2-naphthol 1-sulfide. The 2-naphthol 1-sulfide was oxidized first to remove two hydrogen atoms and then the dehydro-2-naphthol sulfide was reduced to the iso- β -naphthol sulfide by the absorption of two hydrogen atoms. The iso- β -naphthol sulfide should be renamed for clarity, 2-hydroxy-1'-mercapto-1,2'-dinaphthyl ether and is, of course, an isomeride of the 2-naphthol 1-sulfide. The overall conversion of 2-naphthol-1 sulfide to iso- β -naphthol sulfide was not considered a rearrangement, for the intermediate product was actually isolated during the conversion so that the process was not continuous. However, Warren and Smiles (16) have shown that the reconversion of the iso- β -naphthol sulfide to 2-naphthol 1-sulfide is a rearrangement reaction. This rearrangement was easily effected by heat, either with or without suitable solvents, and by alkali. The rearrangement is presented as follows:

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14. Warren and Smiles, J. Chem. Soc., 956 (1931).
 15. Henriques, Ber., 27, 3000 (1894); Hinsberg, J. prakt. Chem., 90, 345 (1914).
 16. Warren and Smiles, J. Chem. Soc., 914 (1931).

(iso- β -naphthol sulfide)

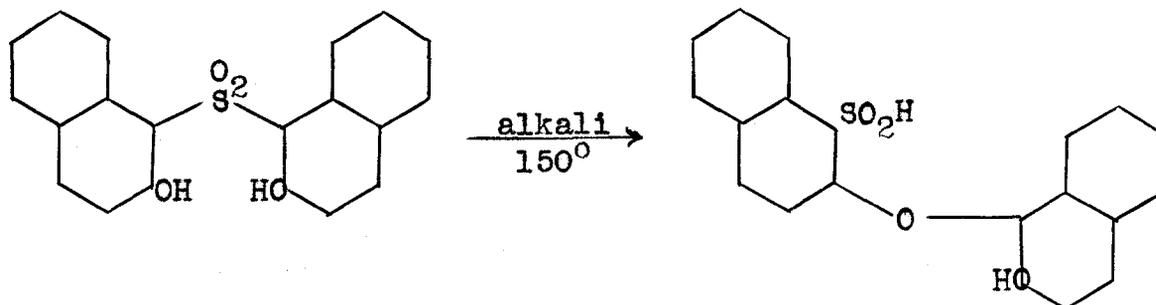
(2-naphthol 1-sulfide)

The authors regarded the rearrangement as a direct displacement of the hydroxynaphthyl group from the α -carbon atom by a more highly negative thiol group. This displacement was evidently due, primarily, to the positive character of the α -carbon atom, and was facilitated by an increase in this positive character by the tautomeric capacity of the system due to the β -hydroxyl group. The possibility that cleavage of iso- β -naphthol sulfide might yield 1-mercapto-2-naphthol or its ion and the quinoid radical which would reunite to give 2-naphthol 1-sulfide was discarded. If cleavage did occur with alkali the S-picryl derivative should yield the characteristic dinitrothioxin as does the picryl derivative of 1-mercapto-2-acetoxynaphthalene with alkali. This reaction, however, was not observed.



(a dinitrothioxin)

The 2-naphthol 1-sulfone was prepared by the oxidation of the 2-naphthol 1-sulfide. In view of the above described rearrangement, it was predicted that the 2-naphthol 1-sulfone should also rearrange, to 1-sulfino-2'-hydroxy-2,1'-dinaphthyl ether, so-called iso- β -naphthol sulfone.



(2-naphthol 1-sulfone)

(iso- β -naphthol sulfone)

In this case the relative polarities of the hydroxyl oxygen and sulfur were reversed in comparison with the same atoms in the 2-naphthol 1-sulfide. The sulfur by having been converted to a sulfone assumed a positive character. According to the interpretation given to the conversion of iso- β -naphthol sulfide to 2-naphthol 1-sulfide, 2-naphthol 1-sulfone should

rearrange to iso- β -naphthol sulfone. Warren and Smiles (17) found this to be true. The iso- β -naphthol sulfone itself could not be isolated under the conditions used for the rearrangement, but the decomposition product, 2-hydroxy-1,2'-dinaphthyl ether, was isolated.

In an effort to find a more general application of the type of rearrangement shown by 2-naphthol 1-sulfone to a sulfinic acid, Levy, Rains, and Smiles (18) investigated the rearrangement with other hydroxy-sulfones. The rearrangement worked smoothly on both 2-nitrophenyl 4-hydroxy-m-tolyl sulfone, and 2-nitrophenyl 2-hydroxy-1-naphthyl sulfone. The rearrangements ran smoothly at low temperatures in alkaline solutions so that the sulfinic acids could be isolated unaffected. Here again the electronic conditions for such rearrangements, drawn up by Warren and Smiles (17), were fulfilled. The sulfonyl group was attached to a strongly positive carbon atom in virtue of the nitro group ortho to it; thus the more positive sulfonyl group was easily displaced by the negative phenolic group.

Warren and Smiles (19) also observed that the rearrangement occurred even in hydroxy sulfones as 2-hydroxy-1-naphthyl 4-methanesulfonylphenyl sulfone, 2-hydroxy-1-naphthyl phenyl-4-sulfonanilide sulfone, and 2-hydroxy-1-naphthyl phenyl-4'-sulfonmethylanilide sulfone. As was expected, these sulfone

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17. Warren and Smiles, J. Chem. Soc., 2207 (1931).
 18. Levy, Rains, and Smiles, ibid., 3264 (1931).
 19. Warren and Smiles, ibid., 1040 (1932).

groups in the 4-position of the phenyl ring did not activate the p-nuclear carbon atom to the extent that the o-nitro groups did (18). Probably, as a result, the rearrangements were not effected by the previously mild conditions but had to be carried out at temperatures around 150°. A methylthiol group in the 4-position, as in 2-hydroxy-1-naphthyl 4-methylthiolphenyl sulfone, in place of the sulfonyl group allows no rearrangement under similar reaction conditions.

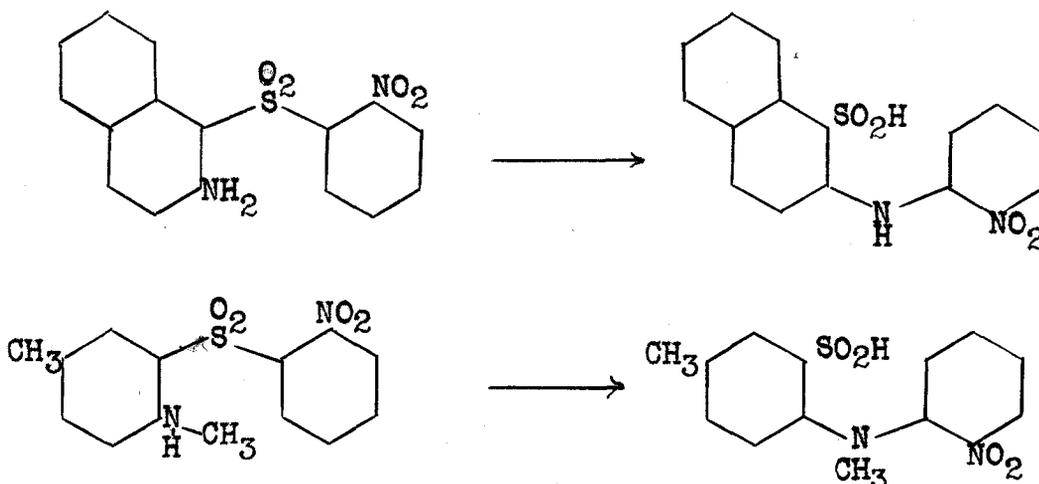
Levi and Smiles (20) investigated the rearrangement of certain hydroxy sulfones further. They found that, if the hydroxy group were in the para position rather than the ortho position in compounds which ordinarily underwent rearrangement, the ability of these compounds to rearrange was lost. If, however, the activating nitro group were moved from the ortho position, in those sulfones that ordinarily rearranged to sulfinic acids (18), the rearrangement ability was not lost but was definitely altered. The rearrangement with the nitro group in the para position proceeds more slowly and less smoothly.

Certain ortho-amino-sulfones (21) also have undergone the same type rearrangement that has been observed in hydroxy sulfones (18, 19, 20). Apparently here again the activating o-nitro group was an important factor in the success of the rearrangement. 2-Amino-1-naphthyl o-nitrophenyl sulfone rearranged more easily to its sulfinic acid than did o-nitrophenyl 3-methyl-

20. Levi and Smiles, J. Chem. Soc., 1488 (1932).

21. Warren and Smiles, ibid., 2774 (1932).

amino-2-tolyl sulfone.



2-Acetamino-1-naphthyl *o*-nitrophenyl sulfoxide was also observed to undergo a similar rearrangement (21) to a sulfenic acid. This acid, of course, underwent immediate decomposition in the alkaline medium to give a disulfide. Two other cases of rearrangement of *o*-acetaminosulfoxides are cited by Levi, Warren, and Smiles (22), who felt that this occurrence could be generalized provided a suitably positive group were attached to the thionyl group. Both 2-nitro-2'-acetaminodiphenyl sulfoxide and 4-chloro-2-nitro-2'-acetaminodiphenyl sulfoxide rearranged in the presence of 1N sodium hydroxide.

Kent and Smiles (23), in addition to showing further examples of rearrangements of *o*-hydroxy sulfones where both radicals attached to the sulfonyl group are aryl, widened the application of this rearrangement. They found that if the

22. Levi, Warren, and Smiles, *J. Chem. Soc.*, 1490 (1933).

23. Kent and Smiles, *ibid.*, 422 (1934).

group containing the hydroxy group were aliphatic, e.g., the ethyl group, the rearrangement went extremely rapidly. The β -hydroxyethyl aryl sulfoxides rearranged rapidly in the alkaline medium also; however, the β -hydroxyethyl aryl sulfides did not undergo rearrangement.



Undoubtedly the increased rapidity of rearrangement, in the cases of the β -hydroxyethyl sulfones and sulfoxides, was associated with the increased activity of the hydroxyl group as compared to the aromatic hydroxy compounds.

Evans and Smiles (24) continued the investigation of rearrangements of *o*-acetamino sulfones as well as *o*-acetamino sulfides. 2-Acetamino-2'-nitro-4'-chloro-diphenyl sulfone and 2-acetamino-2'-nitrodiphenyl sulfone rearranged easily to give the substituted phenylaminobenzenesulfinic acids. The authors found it more advantageous to isolate the sulfinic acids as derivatives by their treatment with mercuric chloride to give the organomercury halide. The mercury could be cleaved from the molecule then by treatment with hydrochloric acid. Several substituted amino sulfides were shown to undergo the rearrangement if the substituent on the amino group were the

24. Evans and Smiles, J. Chem. Soc., 181 (1935).

acyl group of weak acids, e.g., acetyl or o-nitrobenzoyl. Substituents of strong acids, as the benzenesulfonyl group, did not allow rearrangement in the sulfide.

Thus far from the efforts of Smiles and his co-workers (16, 17, 18, 19, 20, 21, 22, 23), the following generalizations of the rearrangement, first observed in iso- β -naphthol sulfide (16), might be cited (24):



The character of the compound to undergo rearrangement must fulfill the following requirements. C must be of highly positive character in virtue of a highly negative substituent ortho or para to C. The activating groups that have been shown to give C a positive character are the o- and p- nitro groups, the 5,6-benzo group and the p-methanesulfonyl group. YH must have a tendency to lose a proton in the medium (alkali) employed. In addition to this, Y must have the capacity to meet the electron demand at C. Actually the character of X was also involved in the tendency toward rearrangement, inasmuch as a decrease in the negative character of X favored rearrangement, whereas an increase of negativity retarded it. In other words, a rearrangement might take place if Y satisfies the electron demand at C better than X. It was shown that only one

substituent on X needed to be aromatic. In the rearrangements investigated up to this time by Smiles and co-workers (16, 17, 18, 19, 20, 21, 22, 23, 24), it was shown that, if YH was the acetamino group, the rearrangement occurred when X was the sulfone, sulfoxide or sulfide group. If YH was the aromatic amino group, it did not occur in the sulfide but only in the sulfone group. If YH was the aromatic hydroxy group, X had to be a sulfone group for rearrangement, the sulfoxide and sulfide groups were not suitable. If, however, the hydroxy group at YH were aliphatic, rearrangement occurred when X was either sulfone or sulfoxide. When YH was the mercapto group, rearrangement occurred, only if X were an ether group. As was stated previously, the acetamino group in the YH position apparently could be replaced by other acyl-amino groups, provided the acyl groups were derived from weak acids, such as nitrobenzoic acid. Wight and Smiles (25) extended the YH groups to include the formamino and the benzamino groups in compounds where the X group is a sulfide.

Galbraith and Smiles (26) have shown later that the 1-carbon atom of the 1-anthraquinonyl group has sufficient positive character to allow rearrangement of its 2-hydroxyphenyl and 2-hydroxy-1-naphthyl sulfones. The rearrangement did not go as easily as many of the other sulfones. 1-Anthraquinonyl β -hydroxyethyl sulfone was found to rearrange extremely rapidly

26. Wight and Smiles, J. Chem. Soc., 1234 (1935).

in alkali to the sulfinic acid. However, 2-carboxyphenyl β -hydroxyethyl sulfone was observed not to rearrange probably because the o-carboxy group did not impart sufficiently positive character to the ortho carbon atom.

Evans and Smiles made an interesting observation in that, just as 2'-nitro-2-acetaminodiphenyl sulfone was rearranged to N-acetyl-2-sulfino-2'-nitrodiphenylamine (4), β -(2-nitro-1-benzenesulfonyl)-acetanilide rearranged to give N-(β -sulfinoacetyl)-2-nitrodiphenylamine (27). Of course, under the conditions of the reaction, the sulfino group was hydrolyzed away. Similarly the m-nitroanilide of 2-nitrophenylsulfonylacetic acid rearranged. However, with the anilide of 2-nitrophenylsulfonylpropionic acid, no evidence of rearrangement could be obtained. A similar result was observed with the corresponding sulfide. On the other hand, the anilide of 2-nitrophenylthiolacetic acid was observed to rearrange. In the cases where rearrangement did not occur, the reason might be attributed to the less favorable steric relations between the positive carbon of the nitrophenyl nucleus and the amido-nitrogen. Instead the products were obtained from the tendency of a β -thiopropionic acid to suffer cleavage at the sulfur group (28). 2-Carbanido-2'-nitrodiphenyl sulfide as well as N-phenyl-2-(o-nitrophenyl)-sulfinobenzamide and the similarly substituted thiol benzamide

27. Evans and Smiles, J. Chem. Soc., 329 (1936).

28. Nicolet, J. Am. Chem. Soc., 53, 3066 (1931).

were noticed to have suffered rearrangement in the presence of alkali.

2-Nitro-5'-chloro-2'-hydroxydiphenyl sulfone was shown to be retarded in its rearrangement (23) by the presence of the chloro group in the 5-position. However, the following sulfone, 2-nitro-2'-hydroxy-5'-chloro-4',6'-dimethyldiphenyl sulfone, was shown by McClement and Smiles (29) to undergo rearrangement. Further investigation confirmed the conclusion that the 6-methyl group allowed the rearrangement in spite of the 5-chloro group.

As a climax to the work of Smiles and co-workers (16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 29), Coats and Gibson (30) observed that the rearrangements, of seven of the nine *o*-hydroxy sulfones investigated by both groups of researchers, were reversible. The sulfinic acids, which were the products of the initial rearrangement, i.e., by Smiles et al, were found to rearrange back again to the original *o*-hydroxy sulfones. These reverse rearrangements were carried out at 50°. The optimum pH for this reversal was not the same with each sulfinic acid; some of the acids reverted best in sodium acetate solution, others in sodium formate and still others merely on recrystallization from aqueous acetone.

29. McClement and Smiles, *J. Chem. Soc.*, 1016 (1937).

30. Coats and Gibson, *ibid.*, 442 (1940).

Analogous work on the rearrangement of amino and acetaminodiphenyl ethers has been investigated by Roberts and collaborators (31). The rearrangements, however, in this case, were run in solvents such as ethanol and pyridine, and water solutions of pyridine and ethanol. Apparently these rearrangements were governed by the same constitutional factors that were concerned in the rearrangement of the sulfones, sulfides, and sulfoxides.

Tozer and Smiles (32) observed rearrangements in the o-carbonyl diphenyl ethers analogous to those shown by o-carbonyl sulfides and sulfones (27).

The rearrangements of the sulfones, sulfides, and sulfoxides, studied by Smiles, were reviewed in two articles (33).

Perhaps the most widely observed rearrangements of aromatic sulfur compounds have occurred in the aromatic sulfonic acids. Furthermore, the most extensively studied sulfonic acids that undergo rearrangement are probably the naphthalenesulfonic acids. This may be due to the fact that the water-solubilizing sulfonic acid group is so very important in the naphthalene dye industry, which in itself is very extensive.

A very interesting and complete discussion of naphthalene-sulfonic acids is given by Suter (34).

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31. Roberts and de Worms, ibid., 727 (1934); 1309 (1935); Roberts, de Worms, and Clark, ibid., 196 (1935).
 32. Tozer and Smiles, ibid., 2052 (1938).
 33. Watson, Ann. Reports Chem. Soc., 30, 188 (1933); 36, 197 (1939).
 34. Suter, "The Organic Chemistry of Sulfur", John Wiley and Sons, Inc., New York (1944). pp. 268.

Armstrong and Wynne (35), in the course of their extensive investigations in the sulfonation of naphthalene, came to the conclusion that, regardless of the experimental conditions, there were certain limitations on the position which a sulfo-group would assume when one or more other such groups were already present. No sulfonic acid could be prepared by direct methods in which two sulfo groups were ortho, para or peri to one another. Of the seventy-five theoretically possible naphthalenesulfonic acids, only twelve have been obtained by sulfonation reactions. There are only two possible monosulfonic acids of naphthalene, ten di, fourteen tri, and twenty-two tetrasulfonic acids.

The simplest rearrangement observed in the naphthalenesulfonic acids is the rearrangement of the 1-sulfonic acid to the 2-naphthalenesulfonic acid. Heating the 1-sulfonic acid at 129° with an equimolecular amount of sulfuric acid for seven hours converted 47% of it into the 2-isomer. In all monosulfonations of naphthalene, both the 1- and 2- sulfonic acid have been observed in the products. The relative amount of each isomer apparently depended on the temperature at which the reaction was carried out. If the sulfonation was carried out at 0°, only about 2% of the 2-sulfonic acid was formed (36). At 40°, the yield of the 2-isomer was 4% (37), whereas, at 129°

35. Armstrong and Wynne, Ber., 24, 718 (1891).

36. Fierz and Weissenback, Helv. Chim. Acta., 3, 316 (1920).

37. Fierz-David, J. Soc. Chem. Ind., 42, 421 (1923).

the percentage of 2-naphthalenesulfonic acid was 48.4. Obviously an equilibrium between the two isomers existed.

The 2-naphthalenesulfonic acid on further sulfonation was converted totally into the 1,6-(80%) and the 1,7-(20%) disulfonic acids (38). The 1,5-disulfonic acid was rearranged at 130° almost entirely into the 1,6- and the 2,7-compounds (39). Heating the 2,7-disulfonic acid with 95% sulfuric acid at 160° transformed 42% of the diacid into the 2,6-isomer (40).

Treatment of 2,6-naphthalenedisulfonic acid with oleum at 100° yielded the 1,3,7-trisulfonic acid (41). The 2,6-dimethyl-8-naphthalenesulfonic acid, when heated with 78% sulfuric acid at 135-40°, rearranged to give the 7-sulfonic acid (42).

A very interesting point in connection with the sulfonation of the halonaphthalenes concerns the directive influence exhibited by chlorine, bromine, and iodine in the 2-position of the naphthalene ring. Chlorine and bromine directed the entering sulfo group to the 6- and 8-positions; iodine directed the sulfo group to the 5- and the 8-positions. Armstrong and Wynne

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38. Ewer and Pick, German pat., 45,229; Chuksanova and Bilik, Anilinokrasochnaya Prom., 4, 488 (1934) /C.A., 29, 1085 (1935)/.
39. Baum, German pat., 61,730.
40. Heid, J. Am. Chem. Soc., 49, 844 (1927).
41. Cassella and Co., German pat., 75,432.
42. Weissgerber and Kurber, Ber., 52, 346 (1919); Ges. fur Teerverwertung, German pat., 301,079.

(43) suggested that for all three halides the 5- and 8- compounds were formed at first, then the 5-acid rearranged immediately to the 6-isomer where the halogen was chlorine or bromine. All three 8-isomers rearranged under the influence of heat to the 6-sulfonic acid (43, 44).

If 2-naphthol was sulfonated at 10° for one hour, the 1-sulfonic acid was the major product. When the reaction times were lengthened, the 1-isomer seemed only transitory and the 6-, 7-, and 8- acids were observed in the products (45). The 1,6- and 1,5- disulfonyl chlorides of β -naphthol, upon further treatment with chlorosulfonic acid, rearranged to give the 3,6,8- trisulfonyl chloride (46).

2-Naphthyl methyl ether with chlorosulfonic acid in carbon disulfide yielded a mixture of the 6- and 8- sulfonic acids. However, the corresponding ethyl ether and chlorosulfonic acid in chloroform gave first the 1- sulfonic acid which upon standing rearranged to a mixture of the 6- and 8- sulfonic acids (47).

The sodium salt of 1- naphthylaminosulfonic acid rearranged when heated in a stream of carbon dioxide at $185-90^{\circ}$ to the 1-amino-2-naphthalenesulfonic acid (48). This reaction

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43. Armstrong and Wynne, Chem. News., 60, 58 (1889).
 44. Armstrong, ibid., 58, 295 (1888).
 45. Armstrong, Ber., 15, 202 (1882).
 46. Pollak and Blumenstock-Halward, Monatsh., 49, 203 (1928).
 47. Lapworth, Chem. News, 71, 206 (1895).
 48. Tobias, German pat., 79,132.

is similar to the reaction mentioned earlier (2) for the preparation of sulfanilic acid. Sodium naphthionate (salt of 1-amino-4-naphthalenesulfonic acid) likewise rearranged in carbon dioxide at 200° - 250° (49) or by heating the compound in boiling naphthalene (50) to give 80% of the 1-amino-2-naphthalenesulfonic acid. When 2-amino-8-naphthalenesulfonic acid was heated to 80 - 120° with 10-96% sulfuric acid, it was transformed into the 5-sulfonic acid (51).

1-Amino-8-naphthalenesulfonic acid was converted into its isomer, naphthionic acid, when it was heated for a long time at 90° with sulfuric acid (52).

When either the 5- or 8- sulfonic acid of 2-naphthylamine was heated at 160° with sulfuric acid, it rearranged into a mixture of the 6- and 7- isomers (53). By heating the 1,5,7,-trisulfonic acid of 2-naphthylamine with oleum at 140 - 60° , a rearrangement of the compound to the 3,5,7-trisulfonic acid was obtained (54).

The literature was reviewed on the sulfonation of naphthalene, naphthol, and naphthylamine by Hodgson (55). A discussion of the conditions influencing the migration of the sulfonic acid group in the naphthalene series was also included.

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49. Landshoff and Meyer, German pat., 56,563; Cleve, Ber., 24, 3472 (1891); Erdmann, Ann., 275, 226 (1893).
 50. Bayer and Co., German pat., 72,833.
 51. Green and Vakil, J. Chem. Soc., 113, 40 (1918).
 52. Wahl and Vermeylen, Bull. soc. chim., 41, 514 (1927).
 53. Bayer and Co., German pats., 42,272 and 42,273; Weinberg, Ber., 20, 3354 (1887).
 54. Bayer and Co., German pat., 90,489.
 55. Hodgson, Z. Farben-Ind., 20, 124 (1928).

Martinet (56) discussed the migration of the sulfonic acid group in aromatic molecules and pointed out that there are three important causes that influence such a migration. These causes were cited to be, (1) the nature of the groups present and the structure of the molecule, (2) the temperature, (3) the effect of the solvent, particularly with reference to ionization. He suggested that when a group was introduced into a molecule it took the most mobile position, which incidentally was also the least stable. Under the conditions of higher temperature and in a dissociating medium, the entering group passed into more stable positions and finally remained where the attachments were the strongest.

The rearrangements undergone by naphthalenesulfonic acids were also reviewed very satisfactorily by Fierz-David and Blangey (57).

Shagova (58) rearranged 4-methyl-3-nitrobenzenesulfonic acid in 10% sodium hydroxide at 93-96° to 4-sulfoanthranilic acid. The rearrangement of the sulfonic acid group occurred in addition to the intramolecular oxidation-reduction exchange.

Tozer and Smiles (59) observed that appropriate phenyl-*o*-hydroxybenzenesulfonates rearranged to give sulfodiphenyl ethers.

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56. Martinet, Rev. gen. mat. color., 25, 49 (1921).
 57. Fierz-David and Blangey, "Grundlegende Operationen der Farbenchemie", J. Springer, Vienna (1938).
 58. Shagova, Anilinokrasochanya Prom., 4, 264 (1934) /C.A., 28, 7254 (1934).
 59. Tozer and Smiles, J. Chem. Soc., 1897 (1938).

Accordingly 2-nitrophenyl 4-hydroxytoluene-3-sulfonate rearranged in the presence of alkali to the 2-sulfo-4-methyl-2'-nitrodiphenyl ether. This rearrangement was predicted after the workers observed that certain aryl salicylates rearranged to carboxydiphenyl ethers (59).

A rearrangement, analogous to the Fries rearrangement of esters of aromatic carboxylic acids, was observed by Simons, Archer, and Randall (60) in *p*-cresyl benzenesulfonate. The catalyst for the rearrangement was hydrogen fluoride rather than aluminum chloride. The rearrangement occurred at 100° in the presence of the catalyst but gave only a 10% yield of 2-hydroxy-4-methyldiphenyl sulfone.

The 2,4-disulfonic acid of *m*-xylene transformed readily into the chloride of the 4,6-disulfonic acid on an attempt to make the 2,4-disulfonyl chloride (61).

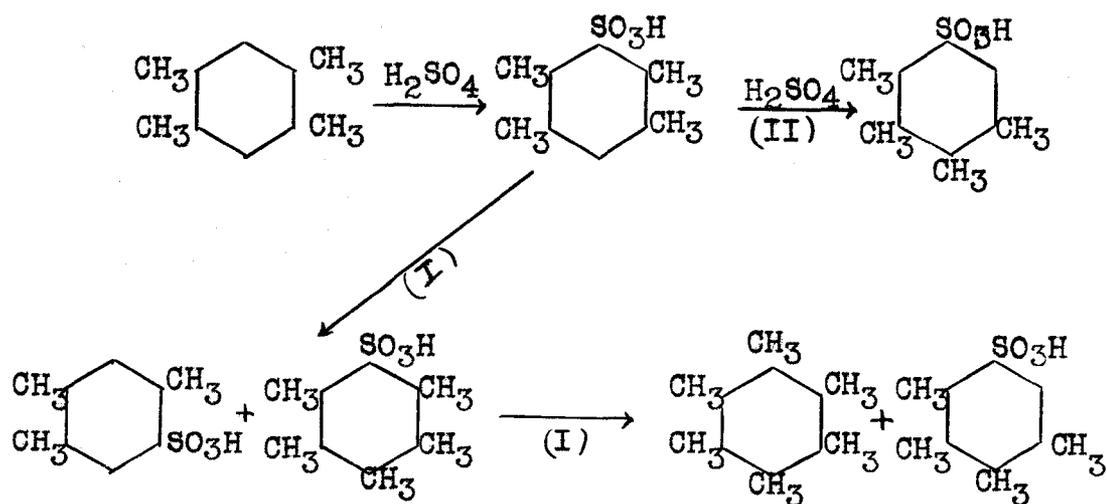
Few sulfonic acids of heterocycles have been observed to undergo rearrangements; however, both the 5- (62) and the 8-quinolinesulfonic acids (63) have been shown to rearrange to the 6-isomer when they were heated to 300° in the presence of concentrated sulfuric acid.

The migration of an alkyl group or a halogen atom in a sulfonic acid derived from a polyalkylbenzene, a halogenated

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60. Simons, Archer, and Randall, J. Am. Chem. Soc., 62, 485 (1940).
 61. Pollak and Meissner, Monatsh., 50, 237 (1928).
 62. Lellmann and Reusch, Ber., 22, 1391 (1889).
 63. von Georgievics, Monatsh., 8, 639 (1886).

polyalkylbenzene, or a polyhalogenated benzene is known as the Jacobsen reaction. The reaction is nearly always effected by treating the hydrocarbon or halogenated hydrocarbon with concentrated sulfuric acid and allowing the resulting sulfonic acid to remain in contact with the sulfuric acid. The first observation of a rearrangement of this kind was made by Herzig (64) who recorded the rearrangement of a polyhalogenated benzenesulfonic acid. However, the reactions have taken the name of Jacobsen (65), who discovered the rearrangement of polyalkylbenzenesulfonic acids.

The migrations of the Jacobsen reaction were noticed to be of two types, intermolecular (I) and intramolecular (II). Generally, however, both types of migrations were noticed simultaneously.

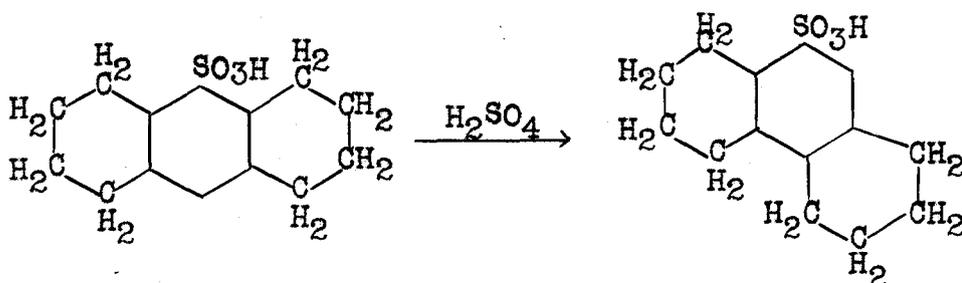


64. Herzig, *Ber.*, 14, 1205 (1881).

65. Jacobsen, *ibid.*, 19, 1209 (1886).

Smith and Cass (66) have shown that the rearrangements involved the sulfonic acids and not the hydrocarbons. Durene-sulfonic acid underwent rearrangement in contact with phosphorus pentoxide, whereas durene itself was unaffected. Also penta-methylbenzenesulfonic acid rearranged when left in a desiccator over sulfuric acid; the hydrocarbon was unchanged under the same conditions.

It is interesting to observe that octahydroanthracene-sulfonic acid rearranged in a manner exactly analogous to the sulfonic acid of 1,2,4,5-tetramethylbenzene (durene). The sulfonic acid on standing with sulfuric acid rearranged (67) to the sulfonic acid of octahydrophenanthrene.



A very comprehensive discussion of the Jacobsen reaction is given by Smith (68).

Barnett and Smiles (69a) observed that in the presence of acids 3,9-dinitrophenothiazine-1-oxide rearranged to give the 3,9-dinitrophenazothionium hydroxide. The rearrangement also

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66. Smith and Cass, *J. Am. Chem. Soc.*, **54**, 1614 (1932).
 67. Schroeter, *Ber.*, **57**, 2009 (1924); Schroeter and Gotzky, *Ber.*, **60**, 2035 (1927).
 68. Adams, "Organic Reactions", Vol. I, John Wiley and Sons, Inc., New York (1942), p. 370.
 69a. Barnett and Smiles, *J. Chem. Soc.* **95**, 1253 (1909).

occurred very readily in phenothiazine-1-oxide itself. Later (69b) these same authors showed that N-methyl phenothiazine-1-oxide formed a phenazothionium hydroxide so that the hydrogen atom in the hydroxide group did not migrate from the nitrogen atom. Page and Smiles (70) however found that the phenazothionium chloride that was easily prepared from the hydroxide rearranged on heating the acid solution to give chlorophenothiazine. By heating phenazothionium chloride in a large excess of hydrogen chloride, even the tetrachlorophenothiazine was obtained.

Hilditch and Smiles (71) obtained thioxanthanol from thioxanthonium chloride. In an effort to obtain an analogous compound, the oximino derivative of phenothiazine, Hilditch and Smiles (71a) found that the result was a rearrangement of the phenazothionium hydroxide to the hydroxyphenothiazine.

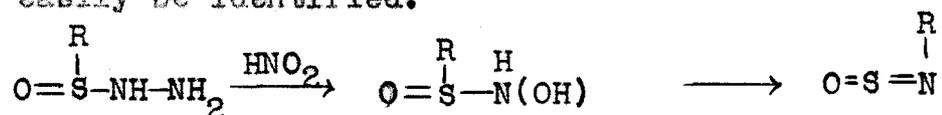
Christopher and Smiles (72) were unable to obtain the thioxonium chloride from naphthathioxin but obtained only the rearrangement product, chloronaphthathioxin. Nolan and Smiles (73) were able to obtain the thioxonium bromide of naphthathioxin; however, it also rearranged to give the bromonaphthathioxin.

Kenyon and Phillips (74) found that the optically active

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- 69b. Barnett and Smiles, ibid., 97, 186 (1910).
 70. Page and Smiles, ibid., 97, 1112 (1910).
 71. Hilditch and Smiles, ibid., 99, 145 (1911).
 71a. Hilditch and Smiles, ibid., 101, 2294 (1912).
 72. Christopher and Smiles, ibid., 101, 710 (1912).
 73. Nolan and Smiles, Proc. Chem. Soc., 28, 276 (1912).
 74. Kenyon and Phillips, J. Chem. Soc., 1676 (1930).

1-phenylmethylcarbonyl *p*-toluenesulfinate was rearranged spontaneously to optically inactive *p*-tolyl α -phenylethyl sulfone. Here and later (75) evidence was presented which indicated strongly that an intramolecular rearrangement was occurring by way of ionization of the active radicals involved in the transformation. The net result was a racemized product which no longer showed optical activity.

Several attempts have been made to involve organic sulfur acid derivatives in rearrangements that are common to carboxylic acid derivatives. Whalen and Jones (76) attempted to prepare the hydroxamic acids of benzenesulfinic acids hoping to observe a rearrangement similar to that which occurs in the Curtius reaction. The thionylamines which would result in the rearrangement step of the reaction were known compounds and could easily be identified.



However, all attempts at the preparation of the sulfinhydroxamic acid failed.

Hoogewerff and van Dorp (77) were unable to find evidence of rearrangement in an attempted Hofmann reaction on halogen derivatives of benzenesulfonamide. Curtius and Hass (78) were also unsuccessful in their effort to run a Curtius reaction on

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75. Arcus, Balfe, and Kenyon, *ibid.*, 486 (1938).
 76. Whalen and Jones, *J. Am. Chem. Soc.*, **47**, 1353 (1925).
 77. Hoogewerff and van Dorp, *Rec. trav. chim.*, **6**, 373 (1888).
 78. Curtius and Hass, *J. prakt. Chem.*, **102**, 87 (1921).

benzenesulfonylazides. Piloty (79) in the study of benzenesulfonylhydroxamic acid found that unlike other monohydroxamic acids, this acid did not undergo rearrangement.

Witt and Uermenyl (80) observed that heating certain substituted arylsulfonamides with concentrated sulfuric acid caused rearrangements. Thus N-methyl-N-phenyl-p-toluenesulfonamide and the corresponding N-ethyl compound, both rearranged under the above conditions to give small amounts of the 2-alkylaminophenyl-p-tolylsulfone. N-ethyl-N-o-tolyl-p-toluenesulfonamide rearranged to give a small amount of 3-methyl-4-ethylaminophenyl p-tolyl sulfone; 80% of the 5-methyl-2-ethylaminophenyl p-tolyl sulfone was obtained by rearrangement of N-ethyl-N-p-tolyl-p-toluenesulfonamide.

In continuing the investigation of the rearrangements of arylsulfonamides, Witt and Truttwin (81) observed that N-methyl-N-(m-nitrophenyl)-p-toluenesulfonamide rearranged in 83% yield to the 2-methylamino-5-methyl-3'-nitrodiphenyl sulfone, merely by heating the starting material on a water bath with concentrated sulfuric acid. s-(N-Dimethyl-N-di-p-tolyl)-diphenyl-o-disulfonamide cleaved as well as rearranged in 66% sulfuric acid to give a methylamino-p-tolyl o-diphenyl sulfone.

79. Piloty, Ber., 29, 1560, 2324 (1896).

80. Witt and Uermenyl, ibid., 46, 296 (1913).

81. Witt and Truttwin, ibid., 47, 2786 (1914).

Halberkann (82) ran similar rearrangements and found that *N*-methyl-*N*-(*p*-anisyl)-*p*-toluenesulfonamide rearranged to yield 2-methylamino-5-methoxyphenyl *p*-tolyl sulfone. He also found that the non-alkylated sulfamide, *N*-(*p*-anisyl)-*p*-toluenesulfonamide, gave 2-hydroxy-5-aminobenzenesulfonic acid by treatment with sulfuric acid.

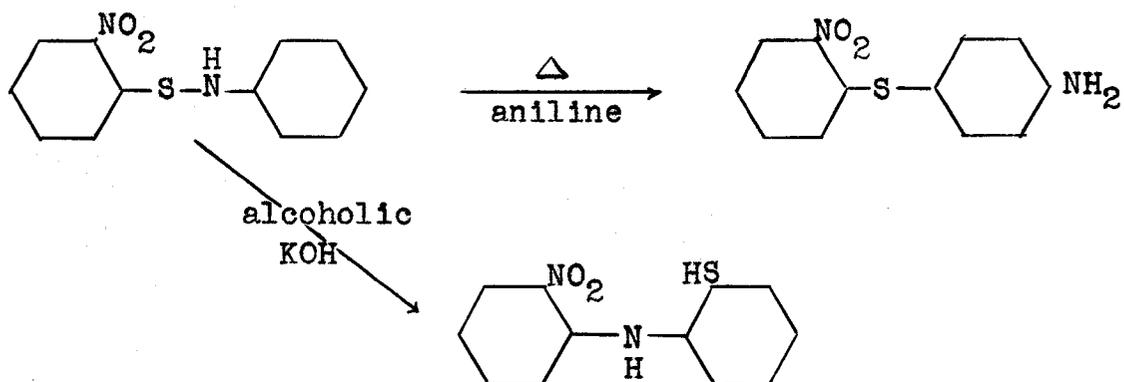
Truttwin (83) has described in some detail several rearrangement reactions of the arylamides of *m*-nitrobenzenesulfonic acid.

Two molecules of *p*-hydroxylaminobenzenesulfonamide and one molecule of *p*-aminobenzenesulfonamide form a stable complex which melts at 161.5° (84). This complex was treated with sulfuric acid; by treatment of the products with benzyl chloride and potassium hydroxide there was obtained (85) some *p*-benzylaminophenylbenzyl ether, which was probably a result of the rearrangement of the *p*-hydroxylaminobenzenesulfonamide.

In a series of articles, Moore and Johnson (86, 87) discussed some interesting rearrangements that were shown by substituted sulfenamidides. Two general types of transformations

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82. Halberkann, *ibid.*, 54, 1665-75 (1921).
 83. Truttwin, "Ueber Umlagerungs-Reaktionen bei Arylamiden der *m*-nitrobenzolsulfonsaure", G. Stalling's Verlag, Oldenburg (1919).
 84. Sevag, *J. Am. Chem. Soc.*, 65, 110 (1943).
 85. Burton and Walker, *J. Chem. Soc.*, 656 (1943).
 86. Moore and Johnson, *J. Am. Chem. Soc.*, 57, 1517 (1935); *ibid.*, 57, 2234 (1935); *ibid.*, 58, 1091 (1936); *ibid.*, 58, 1960 (1936).
 87. Johnson and Moore, *Science*, 81, 643 (1935).

have been observed in their work. First, substituted *o*-nitro-sulfenilides rearranged, on heating alone or on heating with the respective amine, to the isomeric 2-nitro-4'-aminodiphenyl disulfide. In some cases also the amino group was observed to have rearranged to the 2'-position rather than the 4'-position. Secondly, these sulfenilides, when warmed in alcohol in the presence of sodium hydroxide, underwent a different type of rearrangement and were converted smoothly into 2-mercapto-2'-nitrodiphenylamines. Smiles (24) studied rearrangements of this type with the acetyl and the benzoyl derivatives of *o*-aminodiphenyl sulfides. He also found that the *o*-aminodiphenyl sulfides were not rearranged by sodium hydroxide.



Quilico (88) showed that the acids described by Paal and Janicke (89) as sulfamic acids were actually sulfonic acids derived from the intermediate sulfamic acids by rearrangement. The acids included those derived from Δ -naphthylamine, aniline,

88. Quilico, Gazz. chim. ital., 56, 620 (1926).

89. Paal and Janicke, Ber., 28, 3160 (1895).

and *o*-toluidine. *m*-Toluidine when heated with sulfamic acid gave a stable salt. This salt when heated at 100° was converted to the ammonium *m*-toluensulfamate; when heated to 180°, however, the product was the rearranged 2-methyl-4-aminobenzenesulfonic acid.

Bergmann (90) observed the rearrangement of cinnamyl thiocyanate to the isothiocyanate merely by heating the compound.

Ruggli and Dahn (91) observed that, even at -10°, 3-nitro-5-sulfobenzoyl chloride was rearranged by pyridine to the nitrosulfobenzoyl chloride-pyridine complex.

Very recently a new type of rearrangement amination on 4-iododibenzothiophene has been observed by Gilman and Nobis (92). 4-Iododibenzothiophene upon treatment with sodamide in liquid ammonia yielded 3-aminodibenzothiophene. This type of rearrangement amination was first observed (1) in the dibenzofuran series by the formation of 3-aminodibenzofuran from the 4-iododibenzofuran. *o*-Chloroanisole, *o*-bromo- and *o*-iodoanisole were also found to undergo the same rearrangement of the amino group to the meta position when aminated in liquid ammonia with sodamide (1).

90. Bergmann, J. Chem. Soc., 1361 (1935).

91. Ruggli and Dahn, Helv. Chim. Acta, 27, 867 (1944).

92. Gilman and Nobis, J. Am. Chem. Soc., 67, 000 (1945).

EXPERIMENTAL

A. Rearrangement Reactions in Liquid Ammonia

Potassium ethylxanthate.

This compound was prepared in essential accordance with the method of Sacc (93). In a three-necked flask of convenient size, equipped with a reflux condenser, stirrer, and dropping funnel, there was prepared a solution of 140 g. (2.5 moles) of potassium hydroxide in 600 cc. of warm absolute ethanol. The system was protected from moisture and carbon dioxide by a soda-lime tube. To the prepared solution, stirred rapidly, was added in a slow stream, 190 g. (2.5 moles) of carbon disulfide. The potassium salt soon began to separate in long needles. The mixture was stirred for one-half hour after the addition of the carbon disulfide was complete. The mixture was then cooled in an ice bath and the potassium ethylxanthate was filtered. The residue was washed well with dry ether. The salt was freed of residual solvent in a vacuum desiccator over sulfuric acid. The yield of the potassium ethylxanthate, a pale yellow solid, was 250 g. (63%).

93. Sacc, Ann., 51, 346 (1884).

o-Bromothiophenol.

The o-bromothiophenol was prepared by a modification of the method described by Schwarzenback and Egli (94).

In a 1-l. three-necked flask a solution of 69 g. (0.4 mole) of o-bromoaniline in 67 cc. (0.8 mole) of concentrated hydrochloric acid, diluted by 180 cc. of water, was prepared by heating the mixture. Prior to diazotization the hot solution was cooled to -5° while being stirred very rapidly. The stirring was continued and a solution of 28.3 g. (0.41 mole) of 95% sodium nitrite in 50 cc. of water was added dropwise to the mixture. The temperature was maintained at -5° during the whole addition. When an excess of nitrous acid had been observed in the diazotization mixture, the solution of the diazonium chloride was transferred portionwise to a separatory funnel, whence it was added in a thin stream to a stirred solution of 172 g. (1 mole) of potassium ethylxanthate in 600 cc. of water, maintained at 80° . The mixture was then allowed to stand overnight. The red oil that had formed was extracted with a minimum amount of benzene and the extract was washed with water. The extract was now added slowly to a refluxing stirred solution of 112 g. (2 moles) of potassium hydroxide in 200 cc. of ethanol and 100 cc. of water. The mixture was refluxed and stirred for three hours. At this

94. Schwarzenback and Egli, Helv. Chim. Acta, 17, 1176 (1934).

time the solution was concentrated until the benzene had been eliminated from the solution. The remaining solution was then poured into one liter of water; a small amount of red oil, that separated, was removed by extraction with ether. The basic solution was then cooled and acidified with concentrated sulfuric acid. The oil that separated on acidification was extracted with ether, and the extract was dried for a short time over sodium sulfate. Upon distillation of the ether and subsequent distillation of the residue under reduced pressure there was obtained 45.5 g. (60.5%) of o-bromothiophenol distilling at 58-60° at 0.5 mm.

o-Chlorothiophenol.

This compound was prepared (95) by the same procedure used for the preparation o-bromothiophenol. From 95.5 g. (0.75 mole) of o-chloroaniline there was obtained 55.4 g. (51%) of o-chlorothiophenol distilling at 87-88° at 12 mm.

o-Bromophenyl methyl sulfide.

Forty-three grams (0.228 mole) of o-bromothiophenol was dissolved with stirring in 60 cc. (0.30 mole) of a 20% sodium hydroxide solution. The solution was refluxed and stirred while it was treated dropwise with 38 g. (0.30 mole) of practical dimethyl sulfate. After the addition of this

95. Daccamo, Arch. Chem. Farm., 14, 1 (1891) [Chem. Zentr., 62, II, 656 (1891)]

amount of dimethyl sulfate, the reaction mixture was still not acidic so additional reagent was added until the solution became acidic. Now another 5 cc. of 20% sodium hydroxide solution was added to make the solution again alkaline. A further quantity of dimethyl sulfate was added to the hot stirred solution until the reaction mixture again tested acid.

This method of making the reaction mixture basic again after initial methylation, and re-treating with dimethyl sulfate was intended to insure complete methylation of a valuable thiophenol. The acidic mixture was then refluxed and stirred for three hours. After the mixture was cooled, the oily layer and the water layer were separated; and the water layer was extracted with a small amount of ether. The layer of oil and the ether extract were combined and dried over potassium carbonate. The drying agent was removed from the ether solution by filtration, and the ether was removed from the filtrate. The residue was distilled under reduced pressure through a fractionating column; 42 g. (90.5%) of pure *o*-bromophenyl methyl sulfide was collected, distilling at 81-83° at 0.3 mm. An index of refraction was taken on the product, n_D^{20} 1.6348.

The boiling point for *o*-bromethioanisole reported by van Hove (96) was 253.5° at 760 mm. and 152-153° at 35 mm.

96. van Hove, Bull. classe sci. Acad. roy. Belg., 5 12, 929 (1926).

o-Chlorophenyl methyl sulfide.

The o-chlorothioanisole was prepared in 92.5% yield from 55.4 g. (0.383 mole) of o-chlorothiophenol according to the procedure described for the preparation of o-bromophenyl methyl sulfide. The product distilled at 116.5-117^o at 15 mm. n_{D}^{20} 1.6067; d_{4}^{20} 1.2377.

Anal. Calcd. for C₇ H₇ Cl S: M. R., 44.4; S, 20.19.

Found: M. R., 44.2; S, 20.11.

Rearrangement amination of o-bromophenyl methyl sulfide with sodamide in liquid ammonia.

A solution of sodamide (0.24 mole) in liquid ammonia was prepared by the addition of 5.66 g. (0.24 g. atom) of sodium, cut in small pieces, to 300 cc. of liquid ammonia to which 0.3 g. of ferric nitrate had already been added. Ferric nitrate catalyzed the conversion of sodium (dissolved) to sodamide. When the blue color of the sodium solution in liquid ammonia was replaced by a steel-gray color, the conversion was complete. Twenty-five grams (0.123 mole) of o-bromophenyl methyl sulfide was then added to the sodamide solution over a period of about ten minutes. The last traces of the sulfide were washed into the reaction mixture with a small amount of dry ether. The reaction was allowed to stir for twenty minutes, after which time 13.3 g. (0.246 mole) of powdered ammonium chloride was added to the reaction mixture to decompose any

unused sodamide. The mixture was thereafter stirred until all of the ammonia had evaporated. Up until the time when the unused sodamide was destroyed by the addition of ammonium chloride, the system was protected against moisture and carbon dioxide by a soda-lime tube.

After all the ammonia had evaporated, the residue was treated with water to dissolve the inorganic materials. The oil that separated was immediately extracted with ether and the ether solution was dried over sodium sulfate. The ether solution was later filtered and then saturated with dry hydrogen chloride gas. The amine hydrochloride that separated was filtered off and washed well with ether. The solid hydrochloride was then dissolved and suspended in 500 cc. of water and treated with concentrated ammonium hydroxide until the solution was basic. The oil that separated was extracted with three 75 cc. portions of ether. Again the extracts were combined and dried over magnesium sulfate. The ether was removed from the solution and the residue was distilled under reduced pressure. The aminophenyl methyl sulfide distilled at $101.5-102.5^{\circ}$ at 0.3 mm. and amounted to 7.8 g. (45.5%).

The acetamino derivative was prepared from the amine in 20% sodium hydroxide solution by the addition of acetic anhydride. One recrystallization of the crude acetamino compound from dilute ethanol gave a pure sample melting at $78-78.5^{\circ}$ (corr.). The melting point (97) for m-acetaminophenyl 97. Zincke and Muller, Ber., 46, 776 (1913).

methyl sulfide was 75° . The boiling point recorded by the same investigator for the m-aminophenyl methyl sulfide was $163-165^{\circ}$ at 16 mm.

By evaporation of the ether solution from which the amine hydrochloride had been precipitated, and distillation of the residue, there was recovered 5.2 g. (21%) of o-bromophenyl methyl sulfide. The boiling point again was $82-83^{\circ}$ at 0.3 mm.

The yield of m-aminophenyl methyl sulfide, based on the amount of o-bromophenyl methyl sulfide actually utilized in the reaction, was 57.5%.

Rearrangement amination of o-chlorophenyl methyl sulfide with potassium amide in liquid ammonia.

The reaction was run in a similar fashion to the rearrangement amination of o-bromophenyl methyl sulfide. A solution of potassium amide in liquid ammonia was prepared from 9.85 g. (0.252 g. atom) of potassium. Each piece of metallic potassium was carefully covered with dry mineral oil until it was ready to be added to the reaction mixture. Potassium is easily oxidized, heat being given off; the potassium melts under the influence of the increased temperature and is handled with great difficulty and danger in this molten state. To the solution of potassium amide was added 20 g. (0.126 mole) of o-chlorophenyl methyl sulfide. The reaction was allowed to progress for twenty minutes before the unused potassium amide was destroyed by the addition of ammonium chloride. Six and two-tenths grams (35.4%) of m-aminophenyl methyl sulfide were

obtained by the rearrangement amination. The product distilled at 144-146° at 11 mm. The index of refraction was taken as n_D^{20} 1.6427.

The acetamino derivative was prepared; the m-acetaminophenyl methyl sulfide melted at 77.5-78.5 (corr.). A mixed melting point between this sample and that obtained from the rearrangement amination of o-bromophenyl methyl sulfide gave no depression.

There was recovered from the reaction 6.7 g. (33.5%) of unused o-chlorophenyl methyl sulfide, boiling at 117.5-118° at 15 mm., whose index of refraction was n_D^{20} 1.6062 (compare with starting material, p. 37).

The yield of the m-aminophenyl methyl sulfide, calculated on the amount of o-chlorophenyl methyl sulfide that actually entered into reaction, was 53%.

o-Bromophenyl methyl sulfone.

To a solution of 10 g. (0.0493 mole) of o-bromophenyl methyl sulfide in 70 cc. of warm glacial acetic acid, was added slowly through the top of the reflux condenser a solution of 11.2 g. (0.0986 mole) of 30% hydrogen peroxide in 10 cc. of glacial acetic acid. The ensuing reaction was observed to be exothermic. After the initial reaction had subsided, another 5 g. of 30% hydrogen peroxide was added to the solution which was then refluxed for three hours over a

free flame. After this time the solution was cooled but no crystals were deposited. The solution, therefore, was poured into 500 cc. of water whereupon a crystalline solid separated. The solid was filtered and washed well with water. After being air-dried the product amounted to 10.9 g. (94%) and melted at 108-108.5°. This product was analyzed.

Anal. Calcd. for $C_7H_7O_2BrS$: Br, 34.0. Found: Br, 33.6.

Rearrangement amination of o-bromophenyl methyl sulfone with sodamide in liquid ammonia.

A solution of sodamide (0.106 mole) in 30 cc. of liquid ammonia was prepared by the addition of 4.6 g. (0.2 g. atom) of metallic sodium, cut in small pieces, to the liquid ammonia already containing in solution 0.3 g. of ferric nitrate. To this solution was added, over a period of ten minutes, 23.5 g. (0.1 mole) of o-bromophenyl methyl sulfone. The liquid ammonia solution assumed a blood red color. At this time liquid ammonia was added to the reaction mixture to replace that lost by evaporation. The mixture was then stirred for twenty minutes, after which time the unused sodamide was destroyed by the addition of 15.7 g. (0.29 mole) of ammonium chloride. The red color of the liquid ammonia solution was retained even after the addition of the ammonium chloride. The solution was then stirred until the ammonia had evaporated completely. The solid that remained was extracted with 250 cc. of anhydrous

benzene. The benzene solution was treated with dry hydrogen chloride gas until the amino compound was completely precipitated as the hydrochloride. The hydrochloride, after being filtered and washed well with ether, weighed 8.3 g.

By evaporation of the solvent in the filtrate there was recovered 11.5 g. (49.5%) of crude *o*-bromophenyl methyl sulfone. By recrystallization of the crude material from Skelly D (petroleum ether, boiling range 77-115^o), 8 g. (34%) of pure *o*-bromophenyl methyl sulfone was separated from an insoluble tarry material. The sulfone melted at 106-108^o and a mixed melting point with the starting material was not depressed.

The 8.3 g. of amine hydrochloride was decomposed with 5% sodium hydroxide solution; the free amine was then extracted with chloroform. The chloroform solution was dried over sodium sulfate. After evaporation of the solvent, the remaining residue was distilled under reduced pressure. The material that distilled at 165-170^o at 0.3 mm. amounted to 1.7 g. (10%) and was almost entirely crystalline. The undistilled residue was dissolved in dry benzene and treated with acetic anhydride but no acetamino derivative could be isolated. Difficulty was encountered in the attempt to recrystallize the distillate because of its solubility in organic solvents. Therefore, the amino sulfone was dissolved in 7 cc. of dry chloroform and treated with 1.0 cc. of acetic anhydride. After the solution had stood for two hours a crystalline product had separated. It was filtered off and the filtrate was treated with Skelly B

(petroleum ether, boiling range 68-75°) whereupon an additional amount of crystals separated. The total yield of acetamino compound from the 1.7 g. of amino sulfone was 1.3 g. (62% from the amino compound or 6.2% from the bromo sulfone) melting at 134-138°. After one recrystallization from a chloroform-Skelly B mixture, the acetamino compound melted at 137.5-139°. The melting point reported by Zincke and Muller (97) for the m-acetaminophenyl methyl sulfone was 137°. That reported for the o-acetaminophenyl methyl sulfone was 139-140° (98). A mixed melting point between the above acetamino sulfone and that obtained by oxidation of the m-acetaminophenyl methyl sulfide, obtained in the rearrangement amination of o-bromophenyl methyl sulfide, was not depressed. Therefore, the compound obtained was the m-acetaminophenyl methyl sulfone and not the ortho derivative. There was no question as to the identity of the m-acetaminophenyl methyl sulfide, obtained in the rearrangement amination of o-bromophenyl methyl sulfide, because of the great difference between its melting point, and those of the other two isomers.

The yield of m-aminophenyl methyl sulfone, calculated from the bromo compound that was actually used in the reaction, was 15%. On this same basis the overall yield of the m-acetaminophenyl methyl sulfone was 9.3%.

The yield of distilled m-aminophenyl methyl sulfone in

98. Zincke and Siebert, Ber., 48, 1246 (1915).

another run, in which the conditions were duplicated exactly, was 12% or, based on the o-bromophenyl methyl sulfone used in the reaction, 16.5%. In the above described run the yield was 10%, or 15% after taking into account the recovered o-bromophenyl methyl sulfone. When the reaction time was increased from twenty minutes to one hour, the yield of amino sulfone was almost halved as determined by the yield of pure m-acetaminophenyl methyl sulfone (3.7% overall yield as compared to a previous 6.2% overall yield). However, if the yields are calculated from the o-bromophenyl methyl sulfone actually used in the reaction, they compare favorably, 10% and 9.3%, respectively. When the reaction was run in liquid ammonia at room temperature, i.e., under pressure, for twenty-one hours, no amino sulfone or derivative could be isolated from the reaction mixture. In each case the longer reaction time improved the yield of recovered o-bromophenyl methyl sulfone, from 34% to 62% to 72%.

Failure to recover more than 34% of the starting material in this rearrangement amination with o-bromophenyl methyl sulfone when the reaction time was only twenty minutes, led us to examine the solid residue which remained after benzene extraction for possible cleavage products. The most probable cleavage product was expected to be a sulfinic acid occurring as its sodium salt. The addition products of sulfinic acids and benzalacetophenone were shown (p.46) to be excellent derivatives for most sulfinic acids. However, neither

benzalacetophenone nor benzyl chloride proved capable of derivatizing the suspected sulfinic acid, probably because it was not present.

m-Acetaminophenyl methyl sulfone (97).

One gram (0.0047 mole) of m-acetaminophenyl methyl sulfide, obtained by the rearrangement amination of o-bromophenyl methyl sulfide, was dissolved in 5 cc. of glacial acetic acid and treated with 2 cc. (0.017 mole) of 35% hydrogen peroxide. The solution was then heated on a water bath at 70° for two hours. Higher temperatures than this carried the oxidation beyond the sulfone stage to give oily and resinous products. At the end of the heating period, the acetic acid was removed under reduced pressure at a temperature below 70°. The oily residue was treated with a small amount of warm benzene and then the solution was cooled. A crystalline solid separated which was recrystallized from benzene. The pure product amounted to 0.95 g. (80%) and melted at 136.8-137.5°. A mixed melting point with the m-acetaminophenyl methyl sulfone obtained from the rearrangement amination of o-bromophenyl methyl sulfone was not depressed.

o-Chlorophenyl methyl sulfone.

This compound was prepared by Todd and Shriner (99) from sodium o-chlorobenzenesulfinate and methyl iodide. They reported a melting point of 90° for the sulfone.

A solution of 17 g. (0.107 mole) of o-chlorophenyl methyl sulfide in 75 cc. of warm glacial acetic acid was treated with 35 g. (0.308 mole) of 30% hydrogen peroxide solution. The resulting solution was refluxed for three hours; it was then cooled and added to ice cold water. The crystalline solid that separated was washed well with cold water; it amounted to 18.0 g. (88.5%) and melted at 93.5-94.2°.

Derivatives of sulfinic acids. ω -Phenyl- ω -benzenesulfonyl-propiophenone.

One gram (0.0061 mole) of sodium benzenesulfinate was added to 20 cc. of absolute ethanol and treated with 0.5 cc. (0.006 mole) of concentrated hydrochloric acid. The mixture was shaken well for about five minutes, then filtered free of the sodium chloride that formed. The filtrate containing the free sulfinic acid was immediately treated with 1 g. (0.0048 mole) of benzalacetophenone in which the reagent dissolved on shaking. The solution was allowed to stand until the crystal formation was complete. Crystals usually began to

99. Todd and Shriner, J. Am. Chem. Soc., 56, 1382 (1934).

separate about ten minutes after the solution was completed. The long white needles that separated were filtered off and amounted to 1.65 g. (98%). After one recrystallization from 95% ethanol the product amounted to 1.5 g. (89%) and melted at 153.5-154.5°.

Anal. Calcd. for $C_{21}H_{18}O_3S$: S, 9.15. Found: S, 9.30.

ω -Phenyl- ω -(p-toluenesulfonyl)-propiophenone.

One gram (0.0056 mole) of sodium p-toluenesulfinate and 1 g. (0.0048 mole) of benzalacetophenone were added to 20 cc. of absolute ethanol to which 0.5 cc. (0.0087 mole) of glacial acetic acid had been added. In about ten minutes crystals of the sulfone began to separate, so the mixture was warmed and shaken to insure complete conversion of the sodium sulfinate to the free acid. The mixture was then allowed to cool before the crystalline mass was filtered off. It amounted to 1 g. (58.5%) and melted at 168.5-169.5°. By concentration of the filtrate additional crude product was obtained. By recrystallization of the total amount of crude material from 95% ethanol, there was obtained 1.45 g. (85%) of pure product melting at 169-169.5°. This corresponds to the melting point given by Kohler and Reimer (100) for this compound. They prepared their compound in ethanol from the free sulfinic acid and benzalacetophenone.

100. Kohler and Reimer, Am. Chem. J., 31, 176 (1904).

ω -Phenyl- ω -(2-chloro-5-nitrobenzenesulfonyl)-propiofenone.

One gram (0.0041 mole) of sodium 2-chloro-5-nitrobenzenesulfinate and 1 g. (0.0048 mole) of benzalacetophenone were added to 20 cc. of absolute ethanol and shaken until solution was complete. To this solution then was added 0.35 cc. (0.0042 mole) of concentrated hydrochloric acid. The mixture was shaken until the yellow color had disappeared from the solution which indicated that all of the sodium sulfinate had reacted to give the free sulfinic acid. The sodium chloride was filtered off and the solution was allowed to stand. No crystals separated in twenty-four hours, so the alcohol was evaporated until the solution was half of the original volume. Still no crystals separated after this concentration so water was added to the alcoholic solution. An oil separated which crystallized after standing in an ice bath for a short time. The crude material amounted to 1.6 g. (91%). After several recrystallizations from 95% ethanol 1.0 g. (57%) of pure product was obtained melting at 135.6-136.4° (dec.).

Anal. Calcd. for $C_{21}H_{16}O_5ClNS$: N, 3.26; S, 7.46.

Found: N, 3.28; S, 7.63.

ω-Phenyl-*ω*-(2-thiophenoxy-4-nitrobenzenesulfonyl)-propiophenone.

One gram (0.0034 mole) of 4-nitro-2-sulfinodiphenyl sulfide and 1 g. (0.0048 mole) of benzalacetophenone were dissolved in 20 cc. of absolute ethanol. The solution was allowed to stand until crystal formation was complete. After twenty-four hours the mixture was filtered. One and seven-tenths grams (99%) of yellow needles had separated. This product was recrystallized from 95% ethanol to give 1.1 g. (65%) of pure product melting at 134.5-136° (dec.).

Anal. Calcd. for $C_{27}H_{21}O_5NS_2$: N, 2.79; S, 12.7. Found:
N, 2.90; S, 12.9.

Magnesium methylsulfinate.

This material was prepared according to the method described by Rosenheim and Singer (101) for the preparation of magnesium ethylsulfinate. To 3 g. (0.12 g. atom) of magnesium turnings in 25 cc. of dry ether was added dropwise a solution of 17 g. (0.12 mole) of methyl iodide in 35 cc. of ether. The mixture was stirred and refluxed in a nitrogen atmosphere until the preparation of methylmagnesium iodide had been complete. An additional 100 cc. of ether was added to the solution and dry sulfur dioxide was bubbled through the stirred mixture until the formation of a white solid prevented

101. Rosenheim and Singer, Ber., 37, 2152 (1904).

both agitation of the mixture and introduction of sulfur dioxide. The reaction was stopped at this point and the solid was washed several times with dry ether by decantation. The solid was then filtered from the remaining solution on a "Buchner funnel and washed well with ether. The solid became somewhat discolored on the filtration in air. The crude magnesium methylsulfinatate was then stored in a vacuum desiccator over sulfuric acid.

ω -Phenyl- ω -methanesulfonylpropionophenone.

One gram (0.055 mole) of the crude magnesium methylsulfinatate and 1 g. (0.0048 mole) of benzalacetophenone were completely dissolved in 10 cc. of absolute ethanol. To the solution was then added 0.30 cc. (0.0048 mole) of glacial acetic acid; in about three minutes the sulfone began to separate. The crude product was filtered off and amounted to 1.2 g. (87%); it melted at 146.8-148°. After one recrystallization from 95% ethanol the product melted at 149°.

Anal. Calcd. for $C_{16}H_{16}O_3S$: S, 11.1. Found: S, 10.7.

It has been found in the study of sulfinic acid derivatives that in some cases acetic acid could be used as the solvent to replace ethanol. Also it could be used rather generally to liberate the sulfinic acid from its salt, provided it was done in the presence of the benzalacetophenone which immediately combined with the free acid.

2-Bromo-4-methylbenzenesulfonic acid.

The halogen sulfonic acid was prepared from the amino acid by diazotization and treatment of the diazonium compound with a freshly prepared hydrobromic acid-cuprous bromide solution.

A mixture of 12.5 g. (0.05 mole) of cupric sulfate pentahydrate, 4.0 g. (0.06 g. atom) of copper turnings, 20.8 g. (0.202 mole) of sodium bromide, 6.0 g. (0.056 mole) of concentrated sulfuric acid, and 200 cc. of water were refluxed for about four hours when the green solution finally turned yellow.

When the hydrobromic acid-cuprous bromide solution was ready for use, the diazonium solution was prepared. A suspension of 37.4 g. (0.2 mole) of 2-amino-4-methylbenzenesulfonic acid in a mixture of 100 g. of ice, 100 cc. of water, and 41 g. (0.4 mole) of concentrated sulfuric acid was prepared. The mixture was cooled by means of an ice-salt bath to 0° , at which time the diazotization was begun. While the reaction mixture was maintained between $0-5^{\circ}$, a solution of 14.5 g. (0.2 mole) of 95% sodium nitrite in 40 cc. of water was added dropwise. A flask of at least one liter capacity had to be used since considerable foaming accompanied the diazotization. Rapid stirring of the mixture was maintained throughout. The mixture was allowed to stir for one hour

after all the sodium nitrite solution had been added. The diazonium salt was not soluble in the reaction medium so a suspension was carried through the whole reaction.

The suspension of the diazonium compound was then added portionwise to the rapidly stirred, boiling hydrobromic acid-cuprous bromide solution prepared earlier. After all the suspension had been added the resulting solution was dark green. It was refluxed and stirred for another one-half hour after the addition of the diazonium complex was complete. The solution was then cooled to about 50° and treated with hydrogen sulfide gas until the solution was completely saturated. A voluminous precipitate of copper sulfide was observed. The mixture was then heated and treated with Norite to facilitate the filtration of the copper sulfide. After the filtration, the filtrate was no longer green in color but was now red-brown. The filtrate was evaporated to about one-third of its volume (about 125-150 cc.) and allowed to cool. The crystalline solid that separated was filtered and washed with a small amount of cold water. The nearly white sodium sulfonate amounted to 20 g. Another 22 g. of sodium salt was obtained by concentrating the filtrate further to about 30 cc. under reduced pressure. This solution had to be filtered immediately on cooling as it was very hygroscopic. The total yield of sodium 2-bromo-4-methylbenzenesulfonate was 42 g. (77%).

p-Toluidine salt of 2-bromo-4-methylbenzenesulfonic acid.

This salt was prepared as a suitable derivative for 2-bromo-4-methylbenzenesulfonic acid according to the method described by Shriner and Fuson (102). There was obtained from 0.5 g. of the sodium sulfonate and 0.5 g. p-toluidine, 0.5 g. (80%) of crude p-toluidine salt melting at 213-217°. After recrystallization from water the derivative melted at 216-218°.

Anal. Calcd. for $C_{14}H_{16}O_3BrNS$: S, 8.95. Found: S, 8.76.

2-Bromo-4-methylbenzenesulfonyl chloride.

An intimate mixture of 5 g. (0.0183 mole) of powdered sodium 2-bromo-4-methylbenzenesulfonate and 15 g. (0.072 mole) of finely divided phosphorus pentachloride was prepared. The mixture was heated in a moisture-free system under reflux for one hour at a temperature of 160°. The initial reaction began at about 130-140°. After the heating was completed, the melt was poured slowly onto 150 g. of ice. The mixture was stirred well during the addition of the sulfonyl chloride melt to the ice to insure gradual hydrolysis of the acidic components. The sulfonyl chloride fell to the bottom of the hydrolysis mixture as an oil. By cooling, and by stirring, and working the oil, it soon solidified. The solid was then filtered from

102. Shriner and Fuson, "The Systematic Identification of Organic Compounds", John Wiley and Sons, Inc., New York (1940), page 177.

the liquid and washed well with cold water. The crude sulfonyl chloride was then immediately placed in a vacuum desiccator over sulfuric acid for drying. The crude dry 2-bromo-4-methylbenzenesulfonyl chloride amounted to 4.05 g. (82%) and melted at 56-62°. After one recrystallization of the crude product from Skelly A (petroleum ether, boiling range 28-35°), a pure sample for analysis was obtained melting at 64-65°.

Anal. Calcd. for $C_7H_6O_2BrClS$: S, 11.9. Found: S, 12.15.

Methyl 2-bromo-4-methylbenzenesulfonate.

Five-tenths gram (0.00185 mole) of the crude 2-bromo-4-methylbenzenesulfonyl chloride was dissolved in 2 cc. of absolute methanol by warming the mixture slightly. Now four drops of dry pyridine were added to the solution; an exothermic reaction occurred which caused the methanol solution to boil. The solution was then cooled and diluted with water. The crystalline ester which separated amounted to 0.37 g. (75%) and melted at 62-63°.

Anal. Calcd. for $C_8H_9O_3BrS$: S, 12.07. Found: S, 12.0.

Ethyl 2-bromo-4-methylbenzenesulfonate.

The ethyl ester was prepared from 0.5 g. of crude sulfonyl chloride in the same manner that the methyl ester was prepared. The yield of crude ester was 0.47 g. (90.5%). After one recrystallization from dilute ethanol the pure ethyl ester melted at 70-71°.

Anal. Calcd. for $C_9H_{11}O_3BrS$: S, 11.45. Found: S, 11.80.

2-Bromo-4-methylbenzenesulfonamide.

To 5.3 g. (0.0197 mole) of crude finely powdered 2-bromo-4-methylbenzenesulfonyl chloride in an appropriate container was added 40 cc. of concentrated ammonium hydroxide. The mixture was stirred rapidly and warmed with a free flame until the sulfonyl chloride became molten. The reaction between the base and the sulfonyl chloride set in at this time and soon the melt was replaced with a fine white solid. The mixture was cooled and filtered. The sulfonamide that was collected was washed well with water and air-dried. It amounted to 3.4 g. (70%) and melted $150-152.5^{\circ}$. One recrystallization from dilute ethanol gave a product melting at $153.5-154.5^{\circ}$.

Anal. Calcd. for $C_7H_8O_2BrNS$: Br, 31.99. Found: Br, 31.72.

Yields up to 86% were observed on smaller runs.

2-Iodo-4-methylbenzenesulfonic acid.

The diazotization of the 0.2 mole of the amino sulfonic acid used in this preparation, was carried out in the manner described for the preparation of 2-bromo-4-methylbenzenesulfonic acid. (p. 51). After the suspension of the diazonium compound had stirred one hour subsequent to the addition of the sodium nitrite solution, any excess nitrous acid that was

present in the mixture was destroyed by the cautious addition of urea. Now a solution of 40 g. (0.24 mole) of potassium iodide in 40 cc. of water was added to the cold suspension of the diazonium compound. The mixture was allowed to warm to room temperature whereupon the suspension of the diazonium compound slowly disappeared to give a clear solution. The solution was allowed to stir overnight; after this time a crystalline solid had separated. The potassium salt of the sulfonic acid was filtered off and washed with a small amount of cold water. It amounted to 38.5 g. By evaporating the filtrate to about one-third (125-150 cc.) of its volume, another 20 g. of the potassium salt was obtained. This batch was more crude than the first and seemed to be very discolored with free iodine. By evaporation of the filtrate further to 30-40 cc. still another 5 g. of crude potassium 2-iodo-4-methylbenzenesulfonate was obtained. The total crude yield of potassium salt was 63.5 g. (94%).

p-Toluidine salt of 2-iodo-4-methylbenzenesulfonic acid.

The p-toluidine salt was prepared according to the method of Shriner and Fuson (99). It melted at 227.5-230° after recrystallization from water.

Anal. Calcd. for $C_{14}H_{16}O_3INS$: S, 7.90. Found: S, 8.00.

2-Iodo-4-methylbenzenesulfonyl chloride.

An intimate mixture of 5 g. (0.0149 mole) of potassium 2-iodo-4-methylbenzenesulfonate and 15 g. (0.072 mole) of phosphorus pentachloride was heated in the absence of moisture under reflux at 165° for one hour. The temperature had to be raised to 180° to initiate the reaction. The melt obtained after one hour's heating was poured cautiously onto ice. The mixture was stirred thoroughly during the addition to insure gradual hydrolysis. The oily sulfonyl chloride that separated initially, solidified upon cooling and working the oil. The tan solid was filtered and washed well with cold water. It was dried immediately in a vacuum desiccator over sulfuric acid. The crude sulfonyl chloride amounted to 3.9 g. (83%) and melted at 53-61°. After two recrystallizations from Skelly A (petroleum ether, boiling range 28-35°), the pure sample for analysis melted at 66-67°.

Anal. Calcd. for $C_7H_6O_2ClIS$: S, 10.10. Found: S, 9.85.

2-Iodo-4-methylbenzenesulfonamide.

To 7.5 g. (0.0238 mole) of powdered crude 2-iodo-4-methylbenzenesulfonyl chloride in an appropriate container was added 50 cc. of concentrated ammonium hydroxide. The mixture was stirred rapidly and warmed gently until the sulfonyl chloride melted. The sulfonyl chloride was soon converted into the sulfonamide, which separated as a finely divided white solid.

It was filtered off and washed well with water. The air-dried material amounted to 7.4 g. After one recrystallization from 95% ethanol there was obtained 5.5 g. (58.5%) of pure sulfonamide melting at 165-166°. By dilution of the filtrate from which the pure sulfonamide had been separated there was obtained another 1 g. (10.6%) of 2-iodo-4-methylbenzenesulfonamide melting at 162-164°.

Anal. Calcd. for $C_7H_8O_2IN_2$: I, 42.9. Found: I, 43.2.

An attempted rearrangement amination of 2-iodo-4-methylbenzenesulfonamide with sodamide in liquid ammonia.

A solution of sodamide (0.068 mole) in 200 cc. of liquid ammonia was prepared from 1.56 g. (0.068 g. atom) of sodium, cut in small pieces. The preparation of the sodamide was catalyzed by 0.3 g. of ferric nitrate dissolved in the ammonia before the sodium was added. To the sodamide solution was then added, in a period of about 3-4 minutes, 5.05 g. (0.017 mole) of 2-iodo-4-methylbenzenesulfonamide. The reaction mixture was stirred for forty minutes; then it was treated with 5.5 g. (0.07 mole) of ammonium nitrate to destroy the unused sodamide. The ammonia was evaporated completely from the mixture. The residue was thereafter treated with water to dissolve the inorganic material. The water-insoluble portion was filtered off, washed well with water, and air-dried. The water solution gave a positive test for the iodide ion. The

air-dried residue amounted to 4.65 g. and melted at 158-160.5°. It was completely dissolved in 20 cc. of warm nitrobenzene; a small amount of ferric oxide that was suspended in the solution was filtered off. The nitrobenzene solution, now cooled to room temperature, was treated with dry hydrogen chloride gas until it was saturated. Only an insignificant amount of amine hydrochloride separated. The nitrobenzene solution was filtered and diluted with Skelly B (petroleum ether, boiling range 68-75°). This dilution precipitated 3.7 g. (74% recovered) of 2-iodo-4-methylbenzenesulfonamide which melted at 158-160.5°. A mixed melting point with the starting material was not depressed.

An attempted rearrangement amination of 2-bromo-4-methylbenzenesulfonamide with sodamide in liquid ammonia.

A solution of sodamide (0.048 mole), prepared from 1.1 g. (0.048 g. atom) of sodium and 200 cc. of liquid ammonia, was treated in 3-4 minutes with 3.0 g. (0.012 mole) of 2-bromo-4-methylbenzenesulfonamide. The mixture was allowed to stir for forty minutes before 4.0 g. (0.05 mole) of ammonium nitrate was added to decompose the unused sodamide. The residue, after complete evaporation of the ammonia, was treated with water to dissolve the inorganic salts. A positive test for bromide ion was given by the water solution. The water-insoluble portion amounted to 2.65 g. and melted at 145-150° after softening at around 130°. This portion was dissolved in 12 cc. of

warm nitrobenzene and the solution filtered free of a small amount of suspended ferric oxide. Upon treatment of the nitrobenzene solution with dry hydrogen chloride gas, an amine hydrochloride separated which was filtered off. The residue on the filter paper was washed first with warm nitrobenzene, then with dry ether until all the nitrobenzene was removed. The solid amounted to 0.2 g. and was completely soluble in a small amount of water and the solution gave no precipitate on neutralization with ammonium hydroxide. Upon dilution of the nitrobenzene solution with Skelly B (petroleum ether, boiling range 68-75°), 1.75 g. (58.5% recovered) of 2-bromo-4-methylbenzenesulfonamide separated which melted at 150-152.5°. A mixed melting point with starting material gave no depression.

2-Acetamino-4-methylbenzenesulfonic acid.

A solution of 20 g. (0.107 mole) of 2-amino-4-methylbenzenesulfonic acid in a sodium hydroxide solution, containing 4.8 g. (0.12 mole) of sodium hydroxide and 48.0 g. of water, was prepared by warming the mixture. To the stirred solution, 20 cc. of acetic anhydride was added dropwise; the solution became very hot with the introduction of the acetic anhydride and refluxed slowly. After the addition was complete, the solution was stirred for one-half hour and then evaporated until a coating of crystals first appeared on top of the solution. A mass of white needles separated when the solution was cooled. These were filtered off and washed with a minimum amount of cold

water; the yield of sodium 2-acetamino-4-methylbenzenesulfonate was 17.5 g. (65%). By further evaporation of the filtrate until a coat of crystals was again noticed in the solution, another 2.5 g. of the sodium salt separated. The total yield was 20.0 g. (74.5%).

p-Toluidine salt of 2-acetamino-4-methylbenzenesulfonic acid.

The salt prepared from 1 g. (0.004 mole) of the sodium 2-acetamino-4-methylbenzenesulfonate and 0.5 g. (0.0047 mole) of p-toluidine amounted to 1.05 g. (80%) and melted at 214-217°. After recrystallization from hot water the product melted at 218-219.5°.

Anal. Calcd. for $C_{16}H_{20}O_4N_2S$: S, 9.54. Found: S, 9.74.

B. Cleavage Reactions With Sodamide

It was believed that perhaps *o*-bromophenyl methyl sulfone also underwent cleavage during its rearrangement amination with sodamide in liquid ammonia (p. 41). Pursuant to the rearrangement amination studies of *o*-halogenated sulfones and sulfoxides, we deemed it advisable to investigate the possible cleavage reactions of sodamide on non-halogenated sulfones and sulfoxides.

Attempted cleavage of diphenyl sulfone with sodamide in liquid ammonia.

To a solution of sodamide (0.2 mole) in 300 cc. of liquid ammonia, prepared from 4.6 g. (0.2 g. atom) of sodium metal, was added over a period of 10-15 minutes, 21.8 g. (0.1 mole) of diphenyl sulfone. The conversion of the sodium to sodamide in liquid ammonia was catalyzed by 0.3 g. of ferric nitrate. The liquid ammonia solution, containing sodamide and diphenyl sulfone, was greenish-yellow in color. This mixture was stirred for thirty minutes before 10.7 g. (0.2 mole) of ammonium chloride was added to destroy the unused sodamide. The color of the liquid ammonia reaction mixture was retained until the last bit of ammonium chloride was added. Very probably the color was in some way connected with the existence of sodamide in the reaction mixture. The ammonia was now allowed to

evaporate completely. The solid material that remained after evaporation of the ammonia was extracted with 250 cc. of dry benzene. Upon saturation of the benzene extract with dry hydrogen chloride gas, no amine hydrochloride separated. An amine and a sodium sulfinate were expected as the most probable cleavage products. By evaporation of the benzene there was recovered 21.5 g. (98.5%) of the diphenyl sulfone melting at 125-127°. A mixed melting point with the starting material (m.p., 125.5-127°) was not depressed.

Attempted cleavage of diphenyl sulfoxide with sodamide in liquid ammonia.

To a solution of 0.2 mole of sodamide in 300 cc. of liquid ammonia was added, over a period of 10-15 minutes, 20.2 g. (0.1 mole) of diphenyl sulfoxide. The liquid ammonia mixture was colored deep brown after the addition. The reaction mixture was stirred for thirty minutes, then treated with 10.7 g. (0.2 mole) of ammonium chloride. The brown color of the mixture disappeared after it was treated with ammonium chloride. The ammonia was now completely evaporated from the reaction flask. The residue was extracted with 250 cc. of dry benzene. Again saturation of the benzene extract with hydrogen chloride gas gave no precipitate of an amine hydrochloride. Thereafter, evaporation of the benzene from the solution yielded 19.8 g. of recovered crude diphenyl sulfoxide melting at 61-70°. After one recrystallization from Skelly D

(petroleum ether, boiling range 77-115°), the diphenyl sulfoxide melted at 70-71.5° and amounted to 18.4 g. (91% recovered). A mixed melting point with starting material (m.p., 71-72°) was not depressed.

Phenyl methyl sulfide.

Obermeyer (103) prepared this compound from lead thiophenolate and methyl iodide. Later (104) it was prepared in absolute ethanol at 100° from sodium thiophenolate and methyl iodide. We found that thiophenol was easily methylated with dimethyl sulfate to give phenyl methyl sulfide.

Fifty grams (0.454 mole) of thiophenol were dissolved in 110 cc. (0.46 mole) of a 20% sodium hydroxide solution. This solution was heated nearly to boiling and stirred rapidly, while 57.5 g. of dimethyl sulfate was added dropwise to the solution. The mixture at this point still tested alkaline so additional dimethyl sulfate was added until it became acidic. Now another 15 cc. of 20% sodium hydroxide was added to the mixture; dimethyl sulfate was again added to the hot stirred reaction mixture until it tested acid. The mixture was then stirred and refluxed for an additional two hours. After the mixture was cooled, the oily layer was separated and the water layer was extracted with ether. The oil and the ether extract were combined and dried over potassium carbonate.

103. Obermeyer, Ber., 20, 2926 (1887).

104. Bourgeois and Abraham, Rec. trav. chim., 30, 413 (1911).

After the ether was evaporated, the product was distilled under reduced pressure. It distilled at 42-44° at 0.3 mm.

and amounted to 49 g. (87%). n_{29}^{28} 1.5818; n_{28}^{27} 1.5822;
 n_{27}^{26} 1.5828; n_{26}^{25} 1.5831; n_{20}^{19} 1.5870.
 D D D

The boiling point for this compound at atmospheric pressure was reported (103) to be 187-188°. According to the literature (105) $n_{26.5}^{26}$ was 1.5826.
 D

Phenyl methyl sulfone.

Michael and Palmer (106) prepared this sulfone from benzenesulfinic acid, sodium ethoxide, and methyl iodide in absolute ethanol. No reference has been made in the literature to its preparation by the oxidation of phenyl methyl sulfide by hydrogen peroxide.

A solution of 18 g. (0.145 mole) of phenyl methyl sulfide in 80 cc. of glacial acetic acid was treated portion-wise with 40 cc. (0.35 mole) of 30% hydrogen peroxide. This solution was then heated under a reflux condenser at 100° for two hours. Another 15 cc. (0.132 mole) of 30% hydrogen peroxide was added to the solution and the heating was continued for another hour. The solution was then concentrated to about 30 cc. and treated with water. The crystalline solid that separated was filtered and air-dried. It amounted to 21.75 g. (96%) and melted at 88-88.2°. This melting point

105. Taboury, Ann. chim. phys., [8] 15, 60 (1909).

106. Michael and Palmer, Am. Chem. J., 6, 254 (1884-5).

corresponded to the melting point reported in the literature (106).

Attempted cleavage of phenyl methyl sulfone with sodamide in liquid ammonia.

To a solution of 0.2 mole of sodamide in 300 cc. of liquid ammonia was added 15.6 g. (0.1 mole) of phenyl methyl sulfone. No color change accompanied the addition of the sulfone to the liquid ammonia. The mixture was stirred for thirty minutes before the unused sodamide was destroyed by the addition of 10.7 g. (0.2 mole) of ammonium chloride. The ammonia was evaporated completely from the mixture, and the solid residue was then extracted with 250 cc. of dry benzene. The benzene solution was treated with dry hydrogen chloride gas, but no amine hydrochloride separated. By evaporation of the benzene there was recovered 15.0 g. (96.5%) of the phenyl methyl sulfone which melted at 88-88.5°. A mixed melting point with the starting material was not depressed.

Dibenzothiophene-5-dioxide.

A solution of 25 g. (0.136 mole) of dibenzothiophene in 150 cc. of acetic acid was prepared, and this solution was heated to 80°. Then 35 cc. (0.31 mole) of 30% hydrogen peroxide solution was added and the resultant solution was heated at 80-90° for one hour. After this time the solution was refluxed for twenty minutes whereupon the dioxide began

to separate. Another 10 cc. (0.089 mole) of 30% hydrogen peroxide was added to the mixture and the refluxing was continued for another hour. The mixture was allowed to cool, and the crystalline solid was filtered off and washed with water. The yield of product, melting at 233-234^o, was 29 g. (98.5%).

Attempted cleavage of dibenzothiophene-5-dioxide with sodamide in liquid ammonia.

To a solution of 0.16 mole of sodamide in liquid ammonia was added 17.0 g. (0.0788 mole) of dibenzothiophene-5-dioxide. The liquid ammonia solution was colored blood-red after the addition of the dioxide. The mixture was stirred for thirty minutes, and then 13.0 g. (0.162 mole) of ammonium nitrate was added to the mixture to destroy the unused sodamide. The red color of the liquid ammonia solution disappeared after the ammonium nitrate had been added. The ammonia was evaporated completely from the reaction mixture. The residue amounted to 31 g.

A 5 g. portion of the residue was treated with water and the water-insoluble material was filtered off. It amounted to 2.15 g. Based on the 31 g. of residue, after the evaporation of the ammonia, this corresponded to a total recovery of 13.3 g. (78.5%) of dibenzothiophene-5-dioxide. After one recrystallization from ethanol a sample of the recovered dibenzothiophene-5-dioxide melted at 232.5-233.5^o. A mixed

melting point with the starting material was not depressed. By acidification of the water solution, from which 2.15 g. of starting material had been filtered, with sulfuric acid, a gummy material separated which could not be solidified or characterized. It could not be redissolved in base.

It was believed that this gummy material might be a spontaneous decomposition product of a sulfinic acid due to the acidic medium. Therefore, an effort was made to derivatize this possible sulfinic acid under milder conditions. The addition product of a sulfinic acid to benzalacetophenone (p. 46) was chosen as a suitable derivative.

Two grams of the residue (containing recovered dibenzothiophene-5-dioxide, inorganic salts, and possibly an aromatic sodium sulfinate) were treated in 10 cc. of absolute ethanol with 0.5 cc. (0.0083 mole) of glacial acetic acid and 0.25 g. (0.0012 mole) of benzalacetophenone. The mixture was heated for a short time, and then cooled to room temperature. No additional crystal formation was noticed so the insoluble material was filtered off. The filtrate was allowed to stand eight hours but no crystalline derivative separated, even on concentration of the solution. Dilution of the ethanol solution with water allowed the recovery of 0.25 g. of benzalacetophenone melting at 56-58°. A mixed melting point with an authentic specimen of benzalacetophenone was not depressed.

In another attempt to derivatize the sulfinic acid, 2 g. of the residue, after evaporation of the ammonia, was treated

in 10 cc. absolute ethanol with 0.5 cc. (0.0083 mole) of acetic acid. The mixture was warmed at first, then cooled to room temperature. The mixture was filtered on the assumption that the free sulfinic acid would be in the filtrate. However, after treatment of the filtrate with 0.3 g. of benzalacetophenone and allowing the solution to stand for eight hours, the benzalacetophenone was recovered quantitatively from the reaction.

A sulfinic acid was not isolated from the indicated cleavage of dibenzothiophene-5-dioxide.

Cleavage of thianthrene-9,10-tetroxide.

The preparation of thianthrene and thianthrene-9,10-tetroxide are given later (pp. 73 and 74).

A solution of sodamide (0.2 mole) in 300 cc. of liquid ammonia was treated over a period of ten minutes with 14.0 g. (0.05 mole) of thianthrene-9,10-tetroxide. In the liquid ammonia solution a color change accompanied the addition of the tetroxide. The color of the solution turned from violet to green to brown. After the reaction mixture was stirred for thirty minutes, it was treated with 10.7 g. (0.2 mole) of ammonium chloride to decompose the unused sodamide. The solution even after this treatment retained its dark brown color. The ammonia was evaporated completely. The residue remained very sticky until the occluded ammonia was removed. The re-

removal of the occluded ammonia was facilitated by removing the sticky residue from the reaction flask to a container having a larger area exposed to the air. A crystalline solid resulted from this treatment. Upon treatment of this solid with water, it was observed that all but 1.05 g. was soluble. This 1.05 g. (7.5%) represented crude thianthrene-9,10-tetroxide; therefore, 92.5% cleavage was observed. A small portion of this material was recrystallized from benzene to give a product that melted at 319-21^o. A mixed melting point with thianthrene-9,10-tetroxide was not depressed. Evaporation of the water solution to dryness gave a sticky solid that was no longer completely soluble in water. This might have been due to the fact that at the temperature of the evaporation the sodium sulfinate hydrolyzed to the free acid which underwent spontaneous decomposition.

A portion of the residue remaining after the evaporation of the water was extracted with benzene to remove the water-insoluble material. The 1 g. that remained was warmed in 20 cc. of glacial acetic acid with 1 g. of benzalacetophenone. The only material that separated on cooling was inorganic and was filtered off. No other product separated even after standing twenty-four hours. By concentration of the solution and subsequent dilution with water there was recovered 0.6 g. of benzalacetophenone.

In another run, in which 14 g. (0.05 mole) of the tetroxide

was added to a liquid ammonia solution of only 0.1 mole of sodamide, the recovered crude thianthrene-9,10-tetroxide amounted to 1.82 g. or 13%. Cleavage, therefore, amounted to only 87%.

An effort was made to salt out the sodium sulfinic acid from a portion of the water solution by the addition of sufficient sodium chloride to saturate the solution. However, no sodium sulfinic acid separated. By concentration of the solution by a slow evaporation of the water, only sodium chloride crystallized.

By acidification of another portion of the water solution with concentrated hydrochloric acid a white solid separated. Ether was added to the solution to extract the white solid after the addition of each drop of acid. When the precipitation was complete, the ether layer was separated and placed in a vacuum desiccator over sulfuric acid. A white solid remained when the ether had evaporated, and it was easily soluble in base. The melting point of the solid was not very exact since it softened over a range, 100-129^o, then finally melted 129-130.5^o.

A solution of 0.5 g. of this solid (perhaps the sulfinic acid resulting from cleavage; see discussion, p.110) in 5 cc. of absolute ethanol was treated with 0.67 g. (0.0032 mole) of benzalacetophenone. No crystalline derivative separated, even after the solution had stood for twenty-four hours. Dilution of the solution with water resulted only in recovery of 0.4 g.

(60%) of benzalacetophenone that melted at 56-57^o. A mixed melting point with an authentic specimen was not depressed.

In a subsequent run, in which one molecular equivalent was reacted with four equivalents of sodamide, the residue that remained after complete evaporation of the ammonia was utilized as such without separation from the uncleaved tetroxide.

By warming a portion of this residue with absolute methanol, it was possible to effect a separation of the thianthrene-9,10-tetroxide and the inorganic salts from the methanol-soluble sodium sulfinate. However, after evaporation of the methanol, it was observed that the residue was no longer completely water-soluble. A product separated that melted over the range of 107-114^o. Probably an alcoholysis of the salt had taken place by heating the sodium sulfinate with methanol.

A mixture of 1 g. of the residue remaining after evaporation of the ammonia, and 1 g. (0.0048 mole) of benzalacetophenone in 20 cc. of absolute ethanol containing 0.5 cc. (0.0083 mole) of glacial acetic acid, was heated nearly to boiling and allowed to cool slowly. The small amount of insoluble material (recovered thianthrene-9,10-tetroxide) was filtered off. Even after the filtrate had stood for twenty-four hours, no derivative had separated. Dilution of the solution with water yielded only recovered benzalacetophenone.

The suspected cleavage products of thianthrene-9,10-tetroxide (see discussion, p.110) were not able to be derivatized.

C. Thianthrene Compounds

Thianthrene.

The preparation of thianthrene from benzene and sulfur monochloride has been reported by Fleischer and Stemmer (107). More recently this preparation from the same starting materials has been reported in a Russian publication (108). Dougherty and Hammond (109) reported good yields of thianthrene from benzene and sulfur. These methods all used aluminum chloride as the condensing agent. Our method employs benzene, sulfur dichloride, and aluminum chloride.

A mixture of 531 g. (6.8 moles) of dry benzene and 202 g. (1.5 moles) of anhydrous aluminum chloride was heated to 50-60°. The mixture was maintained at this temperature and 352 g. (3.41 moles) of sulfur dichloride was added to the mixture at such a rate that hydrogen chloride gas was evolved in a steady stream. In about three hours the addition of the sulfur dichloride was complete. The mixture was then heated at 70° for one hour. After this the reaction mixture was stirred thoroughly and any lumps that were present were broken up. The gummy solid that resulted from the hydrolysis was filtered off. The benzene layer that was found in the filtrate

107. Fleischer and Stemmer, Ann., 423, 465 (1921).

108. Kozlov, Fruktova, Shemyakina, J. Gen. Chem. (U.S.S.R.), 10, 1077 (1940) [C.A., 4028 (1941)].

109. Dougherty and Hammond, J. Am. Chem. Soc., 57, 117 (1935).

was evaporated to recover any dissolved thianthrene. The gummy solid was extracted under reflux with 1100 cc. of benzene. Most of the solid dissolved but a layer of water and a residue of oil remained after the extract was removed by decantation. The residual oil was again extracted with a 700 cc. portion, then a 200 cc. portion of hot benzene. All the benzene extracts were combined and cooled in an ice bath. The crystalline material that separated was filtered off and recrystallized once from acetic acid to give a pure product melting at 155.5-157°. The benzene filtrate from which the nearly pure thianthrene had been filtered was freed entirely of its solvent. The semi-solid residue (152 g.) was then distilled under reduced pressure. The thianthrene distilled at 165-175° at 0.5 mm. and was light tan in color. One recrystallization of the distillate from acetic acid gave a product melting at 153-157°. The total yield of pure product amounted to 220 g. (60%).

For some reason the yields of thianthrene by this method of preparation have ranged from 35% to 60%. One explanation might rest in the difference in quality of the sulfur dichloride used.

Thianthrene-9,10-tetroxide.

No record has been made in the literature of the use of hydrogen peroxide to oxidize thianthrene to its tetroxide.

Kozlov, Fruktova, and Shemyakina (108) reported a 92% yield of the tetroxide by oxidation of thianthrene with chromic acid.

A solution of 10 g. (0.0463 mole) of thianthrene in 100 cc. of hot glacial acetic acid was treated at 80° with a solution of 22.1 g. (0.194 mole) of 30% hydrogen peroxide in 100 cc. of acetic acid. No tetroxide separated even after the addition of hydrogen peroxide was complete, so another 22.1 g. (0.194 mole) of 30% hydrogen peroxide was added, and the solution was refluxed for one hour. Soon after the solution began to reflux the crystalline tetroxide began to separate. The mixture was cooled and the thianthrene-9,10-tetroxide was filtered off. After the acetic acid had evaporated from the product, it weighed 12.5 g. (97%) and melted at 321-322°. The reported melting point is 321° (108).

Thianthrene-9,10-tetroxide was also prepared according to the method of the Russian authors (108) in 99.2% yield. A solution of 17 g. (0.0787 mole) of thianthrene and 29 g. (0.29 mole) of chromic acid in 300 cc. of glacial acetic acid was refluxed for one hour. The mixture was cooled and poured into one liter of water. The solid that separated was filtered and washed well with water. The product amounted to 21.8 g. (99.2%) and melted at 318-321°.

Preparation of 2-aminothianthrene. -- 2-Chloro-5-nitrobenzene-sulfonic acid.

The method of preparation of this acid was that of Ullmann

and Jungel (110) but the method of isolation was modified.

A solution of 157.5 g. (1 mole) of p-chloronitrobenzene in 200 cc. of 20% fuming sulfuric acid was heated and stirred at 160° for six hours. After this time the solution was cooled to room temperature and then poured onto ice. When all the ice had melted, sufficient water was added to the mixture to dissolve the precipitated sulfonic acid. The solution was filtered free of a small amount of carbonaceous material and the filtrate was heated to 90°. The solution was then treated portionwise with stirring with about 80% of the sodium chloride calculated to saturate that volume of solution. The sodium chloride was finely powdered and the solution was well agitated to insure solution of the sodium chloride. The sodium sulfonate separated from the hot solution in brown platelets. When the mixture was cooled, a nearly quantitative (90-100%) yield of sodium 2-chloro-5-nitrobenzenesulfonate was obtained. If the calculated amount of sodium chloride required to saturate that volume were added to the solution of the sulfonic acid, invariably the yield would be in excess of the theoretical and the product would be contaminated with sodium chloride.

2-Chloro-5-nitrobenzenesulfonyl chloride.

This compound was prepared in 87% crude yield by the

110. Ullmann and Jungel, Ber., 42, 1077 (1909).

method of Fischer (111) by heating 40 g. (0.154 mole) of sodium 2-chloro-5-nitrobenzenesulfonate and 50 g. (0.24 mole) of phosphorus pentachloride at 150° under reflux for one hour.

2-Chloro-5-nitrobenzenesulfinic acid.

Much difficulty was encountered in attempting to duplicate the efforts of Krishna (112) in this preparation, particularly with regard to the melting point of the acid. By following exactly Krishna's procedure for the preparation of the acid by the reduction of the sulfonyl chloride with sodium sulfite, we invariably obtained 50-55% of an acid that melted at 118° and then resolidified to decompose slowly up to 170°. A neutral equivalent on the compound indicated that it was the 2-chloro-5-nitrobenzenesulfinic acid.

Anal. Calcd. for $C_6H_4ClNO_2S$: neut. equiv., 221.5.

Found: neut. equiv., 221.

The same results were observed when the sulfinic acid was prepared according to the method of Claasz (113) by reduction of the sulfonyl chloride in absolute ethanol with stannous chloride.

It was found later, however, that if the freshly precipitated sulfinic acid were dried immediately in a vacuum desiccator over sodium hydroxide pellets, the product melted at 136-140° regardless of the method of reduction.

111. Fischer, Ber., 24, 3194 (1891).

112. Krishna, J. Chem. Soc., 123, 156 (1923).

113. Claasz, Ann., 380, 315 (1911).

Anal. Calcd. for $C_6H_4O_4ClNS$: neut. equiv., 221.5.

Found: neut. equiv., 224, 223.

The sodium 2-chloro-5-nitrobenzenesulfinate was isolated in 88.5% yield by saturating the water solution of the sodium sulfinate, obtained according to Krishna's method (112), with sodium chloride. The crude product was sometimes contaminated with sodium chloride. The crude product was sometimes contaminated with sodium chloride but this material was eliminated by the solution of the sodium sulfinate in ethanol and filtration. The evaporation of the ethanol left pure sodium 2-chloro-5-nitrobenzenesulfinate.

4-Nitro-2-sulfinodiphenyl sulfide.

This compound was reported to have a melting point of 135° (112). In several preparations of the compound exactly according to the procedure described, we found the melting point of the sulfinic acid to be $117-118^{\circ}$. A neutral equivalent on the compound indicated that it was 4-nitro-2-sulfinodiphenyl sulfide.

Anal. Calcd. for $C_{12}H_9O_4NS_2$: neut. equiv., 295.

Found: neut. equiv., 291, 291.

2-Nitrothianthrene.

We were unable to obtain this compound as easily as the method of Krishna (112) suggested. In fact the only way that 2-nitrothianthrene could be obtained pure was to distill it from the crude reaction mixture.

A solution of 1 g. (0.0034 mole) of 4-nitro-2-sulfinodiphenyl sulfide in 10 cc. of concentrated sulfuric acid was allowed to stand twenty-five minutes before it was poured into 100 cc. of water. The crude solid that separated was filtered off and washed well with hot water. The crude material melted during the washing with hot water. It could not be recrystallized from formic acid or any other solvent. The 0.9 g. (96%) of crude material that was obtained, was placed in a distilling flask and heated under reduced pressure until no more distillate could be collected. The crude distillate amounted to 0.48 g. (51%) and melted 121-131°. After two recrystallizations from 85% formic acid the product melted 134-135.5°. Krishna reported a melting point of 128° (112).

Anal. Calcd. for $C_{12}H_7O_2NS_2$: N, 5.36. Found: N, 5.12.

The distillation procedure for the procurement of pure 2-nitrothianthrene was not adaptable to larger amounts, for the high temperature required to distill the product from increased quantities of crude material caused very extensive decomposition.

2-Aminothianthrene.

This compound was obtained by the reduction of the crude 2-nitrothianthrene with zinc dust in acetic acid.

Five grams (0.019 mole) of crude 2-nitrothianthrene were powdered and suspended in 33 cc. of 90% acetic acid. This

mixture was treated portionwise with 10 g. (0.153 g. atom) of zinc dust. When all the zinc had been added the mixture was refluxed and stirred for five hours. During the reduction the color of the solution turned from dark brown to nearly colorless. The solution was filtered hot to eliminate the unused zinc. The filtrate was poured into water and the white solid that separated was filtered. It was warmed with concentrated ammonium hydroxide to insure the decomposition of the thianthrene ammonium acetate. This treatment caused the product to darken. It amounted to 4.3 g. and melted at 147-161^o. This crude product was extracted with acetone in a Soxhlet extractor over a period of thirty-six hours. By concentration of the acetone solution to 50 cc. and the addition of the acetone solution to 400 cc. of water, there was obtained 1.1 g. (25.5%) of platelets melting at 179-183^o. The reported melting point was 185^o.

1-Iodothianthrene.

Fifty-four grams (0.25 mole) of pure thianthrene was treated with 700 cc. (0.41 mole) of a 0.585 N solution of n-butyllithium in dry ether. The mixture was stirred and refluxed for twenty-four hours. At this time no n-butyllithium remained according to Color Test II (114). To the reaction mixture, cooled in an ice bath, was added 63 g. (0.25 mole)

114. Gilman and Swiss, J. Am. Chem. Soc., 62, 1847 (1940).

of powdered iodine in small portions. After all the iodine had been added, Color Test I (115) was still positive so additional powdered iodine was added to the reaction mixture until the test was negative. The mixture was treated cautiously with water and the ether and water layers were separated. The ether layer was treated with sodium bisulfite solution to remove any excess iodine. The ether solution was dried over calcium chloride. The residue after evaporation of the ether was a very viscous oil. Ten grams of the residue was removed for attempted isolation of the 2-iodothianthrene by the selectivity of various solvents. An attempt was made to distill the remainder of the residue under reduced pressure. Extensive decomposition accompanied the distillation even under the reduced pressure supplied by a mercury vapor pump in series with a "Cenco Megavac" pump. Free iodine colored the small amount of distillate. The distillate could not be induced to crystallize under any circumstance. The portion that was set aside before distillation was treated and warmed with acetone. On cooling, the solution deposited a solid which, when filtered and washed with acetone, melted at 163-179°. It amounted to 4.0 g. (4.7%). After a recrystallization of the crude product from acetone and then from Skelly D (petroleum ether, boiling range 77-115°) there was obtained 2 g. (2.4%) of product melting at 182-186°. A sample for analysis was

115. Gilman and Schulze, J. Am. Chem. Soc., 47, 2002 (1925).

obtained after two more recrystallizations of the product from Skelly B (petroleum ether, boiling range 68-75^o); it melted at 187.5-188.5^o.

Anal. Calcd. for C₁₂H₇IS₂: I, 37.15. Found: I, 37.5.

D. Dibenzofuran Compounds

3-Aminodibenzofuran.

This compound was originally prepared by the reduction of 3-nitrodibenzofuran with tin and hydrochloric acid (116). More recently modifications of this method have been discussed (117, 118, 119, 120). We have found that pure 3-nitrodibenzofuran can be reduced easily with hydrogen in the presence of Raney nickel catalyst.

To a suspension of 10 g. (0.047 mole) of pure 3-nitrodibenzofuran in 100 cc. of absolute ethanol was added 3 g. of Raney nickel catalyst. The hydrogenation was run at 45 lbs. pressure in a steam-jacketed hydrogenation bottle. In ten minutes the hydrogenation was complete and a colorless alcohol solution was observed, free of suspended nitro compound. The hot ethanol solution was carefully filtered free of the Raney nickel and concentrated to about 20 cc. in an atmosphere of nitrogen. When the solution was cooled, the amine crystallized

116. Borsche and Bothe, Ber., 41, 1940 (1908).

117. Cullinane, J. Chem. Soc., 2365 (1932).

118. Oatfield, Doctoral Dissertation, Iowa State College (1933).

119. Kirkpatrick, Doctoral Dissertation, Iowa State College (1935).

120. Bradley, Doctoral Dissertation, Iowa State College (1937).

and was filtered off. It amounted to 8.5 g. (89%) and melted at 97-98°.

3-Fluorodibenzofuran.

A mixture of 23.4 g. (0.128 mole) of 3-aminodibenzofuran and 26.9 cc. (0.32 mole) of concentrated hydrochloric acid in 30 cc. of water was stirred at 75° for one hour. The mixture was then cooled to -5° and diazotized with a solution of 9.3 g. (0.128 mole) of 95% sodium nitrite in 13 cc. of water. The mixture was stirred at 0° for one-half hour after a test for nitrous acid in the reaction mixture was positive. A cold solution of fluoboric acid was added slowly from a copper beaker to the reaction mixture. The fluoboric acid solution was prepared by dissolving 8.75 g. (0.14 mole) of boric acid in 21.4 g. (0.513 mole) of a cold 48% hydrofluoric acid solution. The mixture was stirred at 0° for one hour before being filtered. The residue was immediately washed with 250 cc. of cold water, then 50 cc. of cold methanol and finally 50 cc. of cold ether. The solid was quickly transferred to a vacuum desiccator and dried over sulfuric acid. The crude diazonium fluoborate amounted to 40 g. and decomposed at 155-157°. The total amount of crude diazonium fluoborate was placed in a distilling flask. Spontaneous decomposition of the complex was initiated by heating the solid along the upper edge. The decomposition automatically progressed through the whole mass with little

external heating. When the spontaneous decomposition had subsided the mass was heated further until no more nitrogen was evolved. The melt was then distilled under reduced pressure; the material distilling at 125-140° at 0.5 mm. was collected. This crude product amounted to 23.9 g. By one recrystallization from 95% ethanol there was obtained 17 g. (80% based on the amino compound) of pure product melting at 88.5°. A mixed melting point determination with pure dibenzofuran (m.p., 82.5-83°) gave a melting point of 80°.

Anal. Calcd. for $C_{12}H_7OF$: F, 10.21. Found: F, 10.01, 10.02.

2-Fluorodibenzofuran.

In the same way that has been described for the diazotization of 3-aminodibenzofuran, 11.3 g. (0.0618 mole) of the 2-amino compound was diazotized. The suspension of the diazonium complex was treated at 0° with a solution of fluoboric acid, prepared by the solution of 5.7 g. (0.0925 mole) of boric acid in 10.3 g. (0.247 mole) of cold 48% hydrofluoric acid. The mixture was stirred for one-half hour after the addition of the fluoboric acid was complete. The diazonium fluoborate was filtered and washed successively with cold water, methanol, and ether. The crude product was then dried in a vacuum desiccator over sulfuric acid. It amounted to only 10 g.; this low yield was attributed to the increased solubility of this diazonium fluoborate in the wash solvents.

Decomposition of the diazonium complex by heat and distillation of the melt gave only 5.0 g. (44% based on the amino compound) of crude 2-fluorodibenzofuran. Recrystallization of the crude material from 95% ethanol gave 4.4 g. (38.5%) of pure material melting at 88.5-88.8°. A mixed melting point determination with 3-fluorodibenzofuran gave a melting point of 80-81°.

Anal. Calcd. for $C_{12}H_7OF$: F, 10.21. Found: F, 10.12.

2,3-Diaminodibenzofuran.

A suspension of 0.27 g. (0.0018 mole) of 2-nitro-3-aminodibenzofuran in 30 cc. of absolute ethanol was treated with 1 g. of Raney nickel. The compound was hydrogenated in a steam-jacketed hydrogenation bottle under 40 lbs. pressure of hydrogen. In about one-half hour the hydrogenation was complete and no suspended 2-nitro-3-aminodibenzofuran remained. The alcohol solution was filtered and the ethanol was evaporated from the filtrate in a nitrogen atmosphere. The white solid that remained amounted to 0.22 g. (93.5%) and melted at 164-165°. This melting point corresponded to that reported in the literature (121, 122). The quinoxaline compound was prepared by heating 0.19 g. of the diamino compound with 0.19 g. of benzil in 3 cc. of absolute ethanol for three minutes. The solution was cooled and the crystals that separated were

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121. Gilman, Brown, Bywater, and Kirkpatrick, J. Am. Chem. Soc., 56, 2473 (1934).
122. Borsche and Schacke, Ber., 56, 2498 (1923).

recrystallized from acetic acid. The product melted at 175.5-176°. The melting point reported (121) was 178.5-179.5°.

E. Quinoline Compounds.

4-Styrylquinoline.

This compound was prepared with a slight modification of the method of Ainley and King (123).

A mixture of 171.6 g. (1.2 moles) of lepidine, 600 cc. (7.0 moles) of benzaldehyde, and 72 g. (0.51 mole) of anhydrous zinc chloride was refluxed for five hours. It was then treated with one liter of hot benzene to dissolve the excess benzaldehyde. This mixture was in turn treated with 1800 cc. of 5 N sulfuric acid. The 4-styrylquinoline sulfate separated as an oil that solidified on cooling. The sulfate was filtered off and washed well with benzene; thereafter, it was allowed to air-dry. The 4-styrylquinoline sulfate was almost completely dissolved in six liters of water. The yellow solution was treated with a 30% sodium hydroxide solution until the mixture was basic. The mixture was stirred well while the alkali was being added; the free 4-styrylquinoline separated immediately as an oil which soon solidified. The crude product melted at 77-89° and was not purified further. The yield of crude product was 248 g. (89.5%).

123. Ainley and King, Proc. Roy. Soc. London, B 125, 72 (1938).

Quinoline-4-carboxylic acid.

This acid was prepared in 68% yield by the method of Ainley and King (123) by oxidation of the crude 4-styrylquinoline obtained above. The acid was obtained in a very pure state and melted invariably at 253.5-255.5° with decomposition.

8-Sulfoquinoline-4-carboxylic acid.

The preparation of this acid was reported by Fuson (124) by the sulfonation of cinchoninic acid in a sealed tube at 200°. We have found that sulfonation occurred satisfactorily in an open vessel. A solution of 10 g. (0.0579 mole) of pure cinchoninic acid in 20 g. of 20% fuming sulfuric acid was treated with 10 g. of phosphorous pentoxide. The mixture was heated under an air condenser at 200° for two hours. After the heating was completed the mixture was cooled to room temperature and then treated with 300 cc. of water. The mixture that resulted was allowed to stand at least for four hours in order to assure complete precipitation of the sulfonic acid. The 8-sulfocinchoninic acid was filtered and washed well with water. The dry product amounted to 13.55 g. (93%) and melted above 400°.

8-Hydroxyquinoline-4-carboxylic acid.

The 8-sulfocinchoninic acid obtained above by the open vessel method was characterized by its conversion to the
124. Fuson, J. Am. Chem. Soc., 47, 2018 (1925).

8-hydroxycinchoninic acid according to the potassium hydroxide fusion method described by Fuson (124). From 5 g. (0.0197 mole) of the sulfonic acid there was obtained 3.0 g. (60%) of hydroxy acid, melting at 258-261^o with decomposition. The decomposition point reported by Fuson (124) was 258-259^o. A mixed melting point with 8-hydroxycinchoninic acid obtained by fusion of the sulfo acid prepared by the sealed tube method (124) was not depressed.

Methyl 8-hydroxyquinoline-4-carboxylate.

It was felt a more accurate characterization of the 8-sulfocinchoninic acid could be obtained from the methyl ester of the 8-hydroxycinchoninic acid. This ester was first prepared by Mr. Leo Tolman (125) from the 8-hydroxycinchoninic acid derived from 8-sulfocinchoninic acid prepared by the sealed tube method (124). His ester was analyzed and melted at 94-95^o.

One gram (0.0053 mole) of the 8-hydroxycinchoninic acid was added to 25 cc. of absolute methanol. The mixture was saturated with hydrogen chloride gas whereupon the acid dissolved. The solution was allowed to stand for four hours, then it was poured into water. This mixture was treated with solid sodium bicarbonate until it was neutral. The ester was filtered off and washed well with water. The crude product

125. Tolman, Unpublished studies.

was recrystallized from Skelly B (petroleum ether, boiling range 68-75°) to give 0.8 g. (74%) of pure ester melting at 95-96°. A mixed melting point of our ester with that prepared by Tolman (125) was not depressed.

We have shown that 8-sulfocinchoninic acid can be prepared by the method of Fuson (124) without using a sealed tube reaction.

4-Chlorocarbonyl-8-quinolinesulfonyl chloride.

An intimate mixture of 15 g. (0.0593 mole) of 8-sulfocinchoninic acid and 39 g. (0.187 mole) of phosphorus pentachloride was heated under reflux at 160-165° for one hour. The melt was then poured cautiously onto ice in order to effect a gradual hydrolysis of the mixture. The sulfonyl chloride separated as an oil at first but finally solidified. The crude 4-chlorocarbonyl-8-quinolinesulfonyl chloride was filtered off and washed well with cold water. The product was immediately placed in a vacuum desiccator over sulfuric acid to dry. It amounted to 15.8 g. (92.5%) and melted at 118-123°. Recrystallization of a sample for analysis from a dry benzene-dry Skelly A (petroleum ether, boiling range 28-35°) mixture raised the melting point to 120.5-126°. Further recrystallization did not improve the melting point.

Anal. Calcd. for $C_{10}H_5O_3Cl_2NS$: Cl, 24.45. Found:
Cl, 23.90.

Quinoline-4-carboxamide-8-sulfonamide.

Five-tenths gram (0.00172 mole) of 4-chlorocarbonyl-8-quinolinesulfonyl chloride was treated dropwise with 5 cc. of concentrated ammonium hydroxide. After the initial reaction had subsided the mixture was boiled for a few minutes, then cooled, and filtered. The crude product amounted to 0.3 g. (70%) and melted at 269-277^o with decomposition. After treatment of the product with hot chloroform and filtering off the hot liquid, it melted at 273-277^o with decomposition.

Anal. Calcd. for C₁₀H₉O₃N₃S: S, 12.75. Found: S, 12.40.

Methyl 4-carbomethoxy-8-quinolinesulfonate.

Five-tenths gram (0.00172 mole) of 4-chlorocarbonyl-8-quinolinesulfonyl chloride was treated with 2 cc. of absolute methanol and refluxed gently for two minutes. The mixture was cooled and diluted with water. The crystalline product that separated was filtered off and air-dried. It amounted to 0.45 g. (92.5%) and melted at 143.5-146.5^o. After recrystallization from a dry benzene-dry Skelly A (petroleum ether, boiling range 28-35^o) mixture, the product melted at 144-147^o.

Anal. Calcd. for C₁₂H₁₁O₅NS: S, 11.39. Found: S, 11.14.

The methyl ester could not be recrystallized from methanol because the action alcoholized the sulfonic acid ester to give a sulfonic acid and probably dimethyl ether. The product was soluble in bicarbonate after refluxing for a short time with methanol.

The stannic chloride complex of 8-mercaptoquinoline-4-carboxylic acid.

A solution of 5 g. (0.0172 mole) of 4-chlorocarbonyl-8-quinolinesulfonyl chloride in 100 cc. of cold concentrated hydrochloric acid was added to a solution of 15.75 g. (0.0707 mole) of stannous chloride dihydrate in 42 cc. of concentrated hydrochloric acid. The reaction mixture was maintained between 0° and 5° during the addition. Soon after the addition had begun the yellow complex began to separate. The mixture was stirred in the cooling bath for one-half hour after all the sulfonyl chloride had been added. The reaction mixture was removed from the cooling bath and allowed to stir at room temperature for two hours. It stood for an additional 10-12 hours before being filtered to improve the crystal formation and to allow for complete precipitation. The product was dried in an oven at 60°; it amounted to 6.2 g. The exact composition of this complex was not known.

No direct means for obtaining 8-mercaptoquinolinic acid from this complex were available. The complex was refluxed with strong base in an inert atmosphere. Invariably, after filtration of the reaction mixture, the product that was obtained, by acidification of the filtrate, contained tin salts.

The complex was soluble in 5% base and could be benzoylated in the mercapto group by treatment of this basic solution with benzoyl chloride. The benzoylated product still contained tin

salts, that could not be eliminated by saponification of the compound with strong base. The S-benzoylated 8-mercaptocinchoninic acid was esterified in methanol with hydrogen chloride gas. Neither could this ester be freed of tin salts. Saponification of the S-benzoylated ester with strong base also yielded the 8-mercaptocinchoninic acid contaminated with tin salts.

8-Methylmercaptoquinoline-4-carboxylic acid.

Two grams of the stannic chloride complex of 8-mercaptocinchoninic acid were dissolved in 3 cc. (0.0151 mole) of a 20% sodium hydroxide solution. The solution was refluxed and treated dropwise with 0.8 g. (0.00635 mole) of dimethyl sulfate. A solid separated initially but redissolved on further heating and stirring. Another 1 cc. of 20% sodium hydroxide solution was added to the hot solution, then another 0.25 g. of dimethyl sulfate. No more solid separated so the mixture was poured into 50 cc. of water. The solution was warmed with Norite to facilitate the filtration of a flocculent precipitate that had separated. The mixture was filtered and the filtrate was acidified. The yellow solid that separated was redissolved by the addition of a small amount of solid sodium bicarbonate. Another small amount of flocculent precipitate was observed so the solution was again treated with Norite and filtered. The filtrate upon acidification yielded 0.85 g.

(70% based on the 4-chlorocarbonyl-8-quinolinesulfonyl chloride) of 8-methylmercaptoquinoline-4-carboxylic acid, melting at 210-213°. A sample of the acid for analysis was recrystallized from hot water and then melted at 215-215.5°.

Anal. Calcd. for $C_{11}H_9O_2NS$: neut. equiv., 219. Found: neut. equiv., 215.5, 219.

These values were determined by a potentiometric titration of the acid with standard base. The following ionization constant was also observed. $K_a = 2.6 \times 10^{-4}$.

Methyl 8-methylmercaptoquinoline-4-carboxylate.

Five-tenths gram (0.00226 mole) of the 8-methylmercapto-cinchoninic acid was added to 25 cc. of absolute methanol. The mixture was saturated with hydrogen chloride gas and allowed to stand four hours. The solution was then poured into water. This mixture was treated with solid sodium bicarbonate until it was neutral. The yellow solid that had separated was filtered off and washed with water. After one recrystallization from a benzene-Skelly B (petroleum ether, boiling range 68-75°) mixture the ester melted at 140-141°. It amounted to 0.5 g. (94%).

Anal. Calcd. for $C_{12}H_{11}O_2NS$: S, 13.65. Found: S, 13.99.

Bis-(4-carboxy-8-quinolyl)disulfide.

A solution of 60 g. (1.5 moles) of sodium hydroxide and 10 g. (0.0394 mole) of powdered iodine in 500 cc. of water was cooled to 5°. To this solution was added 10 g. of the finely powdered stannic chloride complex of 8-mercaptocinchoninic acid. The mixture was stirred for one and one-half hours in an ice bath; it was then neutralized and made fairly acidic by the addition of concentrated hydrochloric acid. The mixture was treated with sodium bicarbonate until the solution was again neutral. Solid sodium bisulfite was added to discharge the iodine color. At this time the mixture was filtered from a white sludge. The red filtrate was made strongly acid and the solution was evaporated until the red color was discharged. Precipitation of a yellow solid accompanied this treatment. The solution was cooled to room temperature and filtered. The yellow solid amounted to 4.9 g. (92% based on 4-chlorocarbonyl-8-quinolinesulfonyl chloride) and melted at 282-284.5° with decomposition. This acid still was not pure; the pure acid was obtained by saponification of the dimethyl ester. It melted at 289.5-290.5°. The analysis indicated it was a tetrahydrate.

Anal. Calcd. for $C_{20}H_{12}O_4N_2S_2$: S, 15.65; N, 6.87.
 Calcd. for $C_{20}H_{12}O_4N_2S_2 \cdot 4H_2O$: S, 13.35; N, 5.84. Found:
 S, 13.45; N, 5.87.

Bis-(4-carbomethoxy-8-quinolyl)disulfide.

Five grams (0.0122 mole) of the crude diacid disulfide, prepared as described above, were finely powdered and suspended in 75 cc. of absolute methanol. The mixture was treated with dry hydrogen chloride gas until the crude acid had completely dissolved. The solution was allowed to stand overnight. After this time it was poured into 200 cc. of water and the whole mixture was neutralized with solid sodium bicarbonate. The solid that had separated was filtered off, washed well with water, and air-dried. The crude material amounted to 4.95 g. It was extracted with hot toluene until the extracts were no longer colored. The extracts were combined and treated with Norite. The mixture was filtered and the filtrate was concentrated to about 50 cc. The toluene solution was then cooled and treated with petroleum ether until the precipitation of the dimethyl ester was complete. The crystalline product was filtered off; it amounted to 3.40 g. (63% calculated from the crude acid, or 59% calculated from the 4-chlorocarbonyl-8-quinolinesulfonyl chloride), and melted at 190.5-191.5°.

Anal. Calcd. for $C_{22}H_{16}O_4N_2S_2$: S, 14.65. Found: S, 14.62.

Five-tenths gram (0.00115 mole) of the dimethyl ester was saponified by heating under reflux with 20 cc. of a 15% sodium hydroxide solution for forty-five minutes. The solution after this time was cooled and diluted with 50 cc. of water; the resultant solution was made strongly acid and heated until

the red color was discharged. A yellow solid precipitated upon such treatment and was filtered off after the solution was cooled somewhat. It amounted to 0.52 g. (94.5%) and melted at 289.5-290.5°.

6-Methoxy-2-phenylquinoline-4-carboxylic acid.

This compound was prepared by the method of F. Marshall (126) who modified somewhat the procedure described by John (127).

To a solution of 881 g. (4.18 moles) of benzal-p-anisidine in 1200 cc. of refluxing absolute ethanol was added dropwise, over a period of seven hours, 372 g. (4.23 moles) of pyruvic acid. The mixture was stirred efficiently during the whole reaction. The mixture was also stirred and refluxed for three hours after the addition was complete. The mixture was then cooled to room temperature and filtered. The yellow crystalline product was washed with about two liters of absolute ethanol and then was air-dried. It amounted to 375 g. (32%) and melted at 240-241.5° with decomposition.

6-Methoxy-2-phenylquinoline.

Tolman's (125) modification of Halberkann's (128) method was used in this preparation.

To a distilling flask of appropriate size was added

126. Marshall, Unpublished studies.

127. John, J. prakt. Chem., 2 130, 314 (1931).

128. Halberkann, Ber., 54, 3100 (1921).

77.5 g. (0.277 mole) of 6-methoxy-2-phenylquinoline-4-carboxylic acid. The whole mass was heated until it melted, and then the heating was continued until the gas evolution had ceased. The system was evacuated and the liquid was distilled as rapidly as possible under this reduced pressure. The distillate amounted to 59 g. (91%) and melted at 125-132°. After two recrystallizations from 95% ethanol the product melted at 129.5-133°. It now amounted to only 46 g. (71%).

Nitration of 6-methoxy-2-phenylquinoline. Preparation of dinitro-6-methoxy-2-phenylquinoline and mononitro-6-methoxy-2-phenylquinoline.

The compound was nitrated according to the method of LeFevre and Mathur (129) who nitrated 2-phenylquinoline.

Five grams (0.0213 mole) of 6-methoxy-2-phenylquinoline were added to 40 cc. of fuming nitric acid ($d = 1.5$) with cooling, at such a rate that the temperature did not rise above 15°. The temperature of the solution was then allowed to rise slowly to room temperature where it was stirred for one hour. The reaction mixture was then poured onto ice, and neutralized by the addition of 30% sodium hydroxide solution. The yellow solid was filtered off and washed well with water. After it was air-dried it amounted to 7.85 g. The solid was placed in a Soxhlet extractor and extracted for twenty hours with Skelly B (petroleum ether, boiling range 68-75°). The

129. LeFevre and Mathur, J. Chem. Soc., 2238 (1930).

extract yielded only 0.65 g. of material melting at 151-187°. The residue weighed 6.75 g. and melted at 173-203°. This residue was then placed in a Soxhlet extractor and extracted with dioxane until the extracts were colorless. About 0.6 g. of material, inorganic in nature, were not extracted. The dioxane was removed completely from the extract; 6.15 g. of solid remained. This amount of material was dissolved in 50 cc. of hot dioxane; when the solution cooled, yellow crystals separated which were filtered off. The filtrate was retained. The crystalline solid amounted to 2.5 g. (36%) and melted over a range of 204-211°. A recrystallization of this product from dioxane gave 2.4 g. (35%) melting at 210.5-214°. A sample for analysis was recrystallized from dioxane until it gave a maximum melting point of 214.5-215°.

Anal. Calcd. for $C_{16}H_{11}O_5N_3$: N, 12.91. Found: N, 12.59, 12.59.

This compound is a dinitro-6-methoxy-2-phenylquinoline compound.

By slow evaporation of the filtrate from which the dinitro compound was separated, large yellow monoclinic crystals separated. They were filtered from the small amount of mother liquor and washed with cold acetone. The crystalline material amounted to 1 g. (17%) and melted at 153-156°. After one recrystallization from acetone, a sample for analysis melted at 156-156.5°. Analysis indicated that this was one of the possible mononitro isomers.

Anal. Calcd. for $C_{16}H_{12}O_3N_2$: N, 10.00. Found: N, 10.19.

The nitration, in the cases of both the mononitro and dinitro compounds, probably occurred in the quinoline nucleus since the introduction of a nitro group in the 2-phenyl ring did not seem to increase the melting point of the parent compound. Miller and Kinkelin (130) reported the melting point of 6-methoxy-2-(m-nitrophenyl)quinoline to be 130°. Mathur and Robinson (131) reported the melting point of 6-methoxy-2-(o-nitro-phenyl)quinoline as 133-134°. The compound containing the nitro group in the para position in the 2-phenyl ring has not been reported.

6-Methoxy-2-(m-nitrophenyl)quinoline-4-carboxylic acid.

This compound was prepared according to the method of Mathur and Robinson (131) from 0.3 mole of m-nitrobenzal-p-anisidine and 0.308 mole of pyruvic acid. The product was filtered from the hot ethanol solution and washed with 100 cc. of hot ethanol. The product amounted to 30 g. (31%) and melted at 264.5-269° with decomposition. The melting point reported by the original investigators (131) was 268-269° with decomposition.

Decarboxylation of 6-methoxy-2-(m-nitrophenyl)quinoline-4-carboxylic acid.

Mathur and Robinson (131) were unable to decarboxylate

130. Miller and Kinkelin, Ber., 20, 1919 (1887).

131. Mathur and Robinson, J. Chem. Soc., 1520 (1934).

this acid to obtain 6-methoxy-2-(m-nitrophenyl)quinoline.

An intimate mixture of 2 g. (0.00617 mole) of the acid with 4 g. of copper bronze was heated under an air condenser at 230-235° for three hours. After this time the solid reaction mixture was powdered and extracted with 25 cc. of hot benzene. The benzene was evaporated and a residue of 0.06 g. (3.5%) remained. After one recrystallization from ethanol, the solid melted at 129-131°. Miller and Kinkelin (130) reported a melting point of 130° for 6-methoxy-2-(m-nitrophenyl)quinoline. A mixed melting point of the material obtained by decarboxylation, with authentic 6-methoxy-2-phenylquinoline (m.p., 129-131°) began to melt at 95°.

Nitration of 6-methoxy-2-phenylquinoline-4-carboxylic acid.

Preparation of nitro-6-methoxy-2-phenylquinoline-4-carboxylic acid and dinitro-6-methoxy-2-phenylquinoline-4-carboxylic acid.

The nitration of this acid was carried out precisely according to the procedure described by Halberkann (132).

Five grams (0.0179 mole) of the acid were dissolved in 30 cc. of concentrated sulfuric acid, and the solution was cooled below 10°. To the solution was then added 1.8 g. (0.0179 mole) of sodium nitrate. The mixture was allowed to warm to room temperature where it was stirred for one hour before it was poured onto ice. The solid that separated was filtered and washed well with water. It amounted to 5.5 g. and melted at 132. Halberkann, Ber., 54, 3092 (1921).

229-235°. The crude acid was dissolved in 6% sodium carbonate solution by heating the mixture. After the solution was cooled, some of the sodium salt separated. This was filtered and washed with cold water. The filtrate was retained. The sodium salt that was collected was recrystallized from hot water. The salt was once more dissolved in hot water and the solution was treated with acetic acid to precipitate the nitrated 6-methoxy-2-phenylquinoline-4-carboxylic acid. It was filtered off and amounted to 0.65 g. (9.9%, assuming that it is a dinitro compound); it melted at 269-270.5° with decomposition. Halberkann (132) reported a melting point of 262° for the acid he assumed to be the 5-nitro-6-methoxy-2-phenylquinoline-4-carboxylic acid. This acid after two recrystallizations from acetic acid melted at 273-275° with decomposition. It was shown to be a dinitro acid by analysis.

Anal. Calcd. for $C_{17}H_{11}O_7N_3$: N, 11.38. Found: N, 11.68.

A mixed melting point of this acid and an authentic specimen of 6-methoxy-2-(m-nitrophenyl)quinoline-4-carboxylic acid was depressed.

Three-tenths gram (0.000815 mole) of the dinitro acid was placed in a distilling flask and decarboxylated by heating it just above its melting point. The system was placed under reduced pressure when the gas evolution had almost ceased, and the liquid was distilled as rapidly as possible. The distillate was extracted with hot dioxane and the dioxane was removed under

reduced pressure. The residue amounted to 0.13 g.; after one recrystallization from dioxane it amounted to 0.1 g. (38%) and melted at 209-213^o. A mixed melting point of this compound with the dinitro compound (p. 98) prepared by the direct nitration of 6-methoxy-2-phenylquinoline was not depressed. Therefore, 6-methoxy-2-phenylquinoline-4-carboxylic acid dinitrated in the same positions that 6-methoxy-2-phenylquinoline did.

By treatment of the filtrate, from which the sodium salt of the dinitro acid was filtered, with acetic acid, there separated 3.5 g. (60%) of an acid melting at 247-250^o with decomposition. Recrystallization of a sample for analysis from acetic acid gave a melting point of 250-251^o with decomposition.

Anal. Calcd. for $C_{17}H_{12}O_5N_2$: N, 8.65. Found: N, 8.99.

2-Nitro-4-aminoanisole.

The only reference to the preparation of this compound was given in a German patent (133). We found that *p*-anisidine could be readily nitrated to give about 60% of the 2-nitro-4-aminoanisole.

A solution of 12.3 g. (0.1 mole) of practical *p*-anisidine in 50 cc. of concentrated sulfuric acid was cooled to 0^o and treated with a solution of 12 g. (0.105 mole) of 55% nitric acid in 25 cc. of sulfuric acid. The mixture was maintained at 0^o during the addition and was stirred at 2-5^o for forty-five

133. Lucius and Bruning, German pat., 101778 [Chem. Zentr., I 1175 (1899)]7.

minutes after the addition was complete. The reaction mixture was poured into 200 cc. of water and the amine sulfate that separated was filtered off. The filtrate was retained. The amine sulfate was dissolved in hot water and filtered free of a small amount of tarry material. The hot solution was then cooled to 45° and treated with solid sodium carbonate until the mixture was alkaline. The oil that separated solidified on standing. This material was filtered off and dried. It was then extracted with ether to rid it of a small amount of insoluble material. The ether was evaporated slowly from the solution in a large crystallizing dish to give 5.6 g. (33%) of beautiful red crystals that melted at 42-46°. The compound was reported to melt at 50° (133).

By neutralizing the filtrate from which the amine sulfate had originally been separated there was obtained an additional 4.5 g. (27%) of red crystals melting at 39-47°. The total crude yield was 10.1 g. (60%).

Benzal-3-nitro-4-methoxyaniline.

To a refluxing solution of 2.65 g. (0.025 mole) of benzaldehyde in 15 cc. of absolute ethanol was added a solution of 4.2 g. (0.025 mole) of 2-nitro-4-aminoanisole in 35 cc. of absolute ethanol. The resulting solution was stirred and refluxed for two hours. When the solution was cooled in an ice bath a light yellow solid separated. This was filtered off and amounted to 5.25 g. (82%). It melted at 92-94°; after recrystallization of

a sample for analysis from 95% ethanol it gave a maximum melting point of 93.5-94°.

Anal. Calcd. for $C_{14}H_{12}O_3N_2$: 10.92. Found: N, 11.28.

Attempted preparation of nitro-6-methoxy-2-phenylquinoline-4-carboxylic acid from benzal-3-nitro-4-methoxyaniline. Preparation of α -phenyl-N-(3-nitro-4-methoxyphenyl)- α',β' -diketopyrrolidine- β' -(3-nitro-4-methoxyphenyl)anil.

To a solution of 5.5 g. (0.0215 mole) of benzal-3-nitro-4-methoxyaniline in 25 cc. of hot ethanol was added dropwise 1.95 g. (0.0221 mole) of pyruvic acid. The mixture was refluxed and stirred for one hour although a yellow solid had begun to separate after thirty minutes' refluxing. The mixture was cooled and the product was filtered; it amounted to 3.35 g. and melted at 209-210°. After recrystallization from 95% ethanol and finally from acetic acid, there was obtained 1.7 g. (33%) of pure material melting at 231-232°.

Anal. Calcd. for $C_{24}H_{20}O_7N_4$: N, 11.75. Found: N, 11.52.

Obviously instead of obtaining the desired quinoline acid, we obtained the substituted pyrrolidine. This was in agreement with Borsche's (134) findings in the reaction of a mixture of m-nitroaniline, benzaldehyde, and pyruvic acid.

134. Borsche, Ber., 41, 3668, 3693 (1908).

DISCUSSION

A. Rearrangement Reactions

The experiments in this work have clearly shown that the ordinary analogies that exist between aromatic sulfur and aromatic oxygen compounds with respect to their chemical and physical properties can be extended to include rearrangement aminations. 4-Iododibenzofuran was shown (1) to undergo amination and rearrangement when treated with sodamide in liquid ammonia. Later (92) it was shown that the sulfur analogue, 4-iododibenzothiophene, underwent the same type of reaction with sodamide in liquid ammonia.

o-Chloro and o-bromoanisole were both treated with sodamide in liquid ammonia (1) to give an aminated and rearranged anisole. The work in this thesis has demonstrated the same rearrangement amination in o-chloro and o-bromothioanisole.

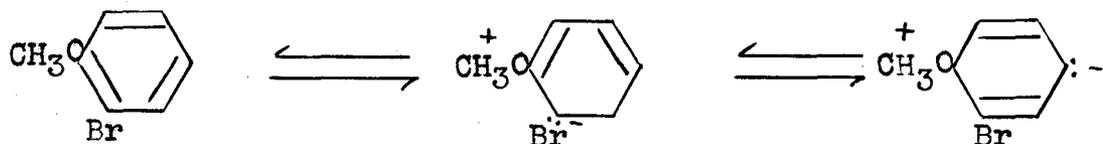
The fact that o-bromophenyl methyl sulfone underwent this rearrangement amination with sodamide to a more limited extent than the corresponding sulfides, indicates that the increased electronegativity of the sulfur group in a more highly oxidized state exerts considerable influence on the reaction. When it is noticed that the o-halogenated sulfonamides did not undergo the rearrangement amination at all, it becomes even more obvious that this highly electronegative group in the sulfur series is

certainly concerned with the outcome of such a reaction.

If we should propose that the group ortho to the halogen is the factor determining the extent of the rearrangement amination, we should probably have struck the vital spot of the explanation. It seems that we might draw the same generalizations for the conditions of rearrangement amination that Meerwein et al.(135) made in their study of the "wandering of aromatic halogens". Though an incomplete study has as yet been made, results seem to suggest that the groups, ortho to halogen atoms, of greater tendency toward electron donation, i.e., more electropositive groups, would allow rearrangement amination to a greater extent than the more electronegative groups. Thus we see that groups like $-\text{NH}_2$, $-\text{OCH}_3$, $-\text{SCH}_3$, and $-\text{OH}$ should favor rearrangement aminations whereas less electropositive groups such as the sulfone group should permit this reaction to a lesser extent. This sulfone group, on the other hand, should be distinguished from the $-\text{SO}_3\text{H}$ group or its derivatives which should be classed as a highly electronegative group along with the $-\text{NO}_2$, and the $-\text{COOH}$ groups. Meerwein et al.(135) suggested that these ortho electropositive groups effected a negativity of the carbon atom to which the halogen was attached, which increased the tendency of the halogen atom to migrate. Of course the carbon atom in the para position would also show the same

135. Meerwein, Hoffman, and Schill, J. prakt. Chem., 154, 266 (1940).

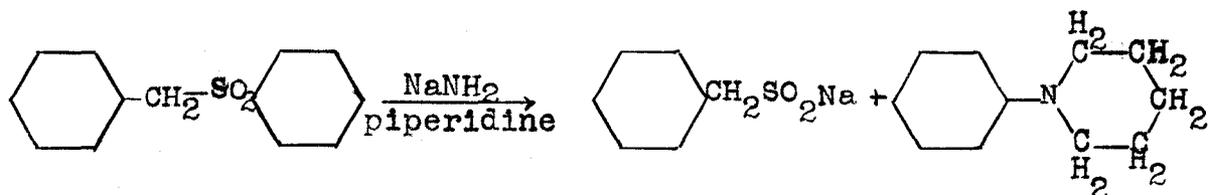
negativity according to the following diagram:



It is interesting to note that the electronic character of the meta position does not change. This may be the reason that the amination, in the newly observed rearrangement amination (1, 92), occurs in the meta position.

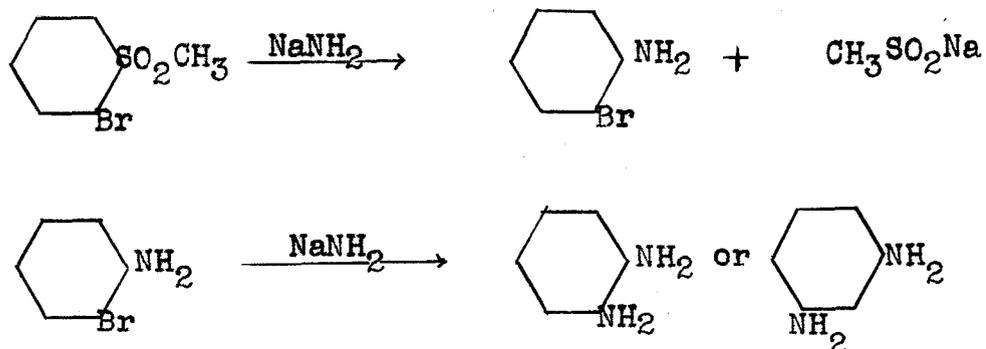
B. Cleavage Reactions

Since only a small amount of amination was observed in the rearrangement amination of o-bromophenyl methyl sulfone, it was believed that perhaps cleavage of the sulfone was occurring. Bradley (136) observed that sulfones, among them phenyl methyl sulfone, were cleaved by sodamide in boiling piperidine to give N-substituted piperidines and sulfinic acids. In cases where aliphatic radicals occurred in the sulfones with aromatic radicals, the sulfinic acid group were found attached to the aliphatic radical in the cleavage products.



136. Bradley, J. Chem. Soc., 458 (1938).

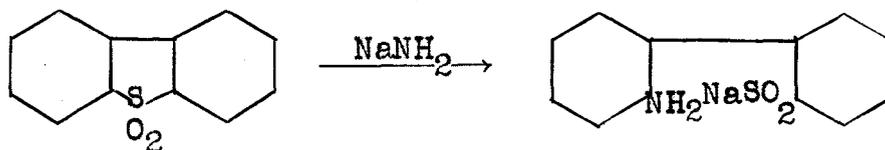
Theoretically *o*-bromophenyl methyl sulfone would be cleaved in liquid ammonia by sodamide as follows:



However, no evidence to support such conjecture was observed in our experiments.

Diphenyl sulfoxide was reported (137) to react with sodamide in boiling toluene to give dibenzothiophene, diphenyl sulfide, diphenyl disulfide, and aniline. Sodamide was not observed to react with diphenyl sulfoxide in liquid ammonia.

If dibenzothiophene-5-dioxide were cleaved by sodamide in liquid ammonia the products would probably be similar to those observed by Bradley (136).

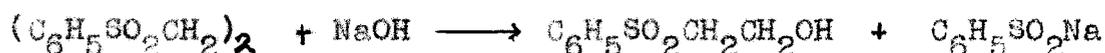


Steric effects might make it difficult to form the addition product of the free sulfinic acid with benzalacetophenone.

Stuffer (138) has drawn a sharp differentiation between

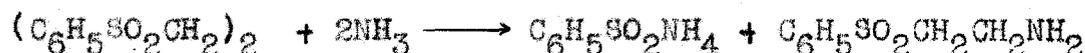
137. Schönberg, *Ber.*, 56, 2275 (1923); Chaix and Kelner, *Compt. rend.*, 194, 1837 (1932).
 138. Stuffer, *Ber.*, 23, 1412, 3232 (1890).

γ -disulfones and all other disulfones in virtue of their easy cleavage into an alcohol and a sulfinate by alkali. Numerous such cleavages have been recorded but invariably they have been observed in the aliphatic series. The cleavage of α, β -bis-(phenylsulfonyl)ethane with dilute alkali required eight days at 100° (139).

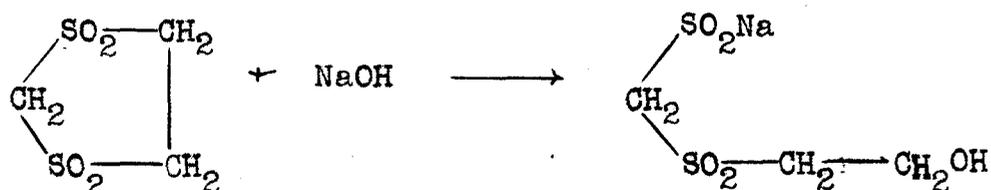


Ethylene bis-(sulfonylacetic acid) cleaved somewhat more rapidly (140).

Cleavage of μ -disulfones was also effected by ammonia or ethylamine but not by aniline (141).

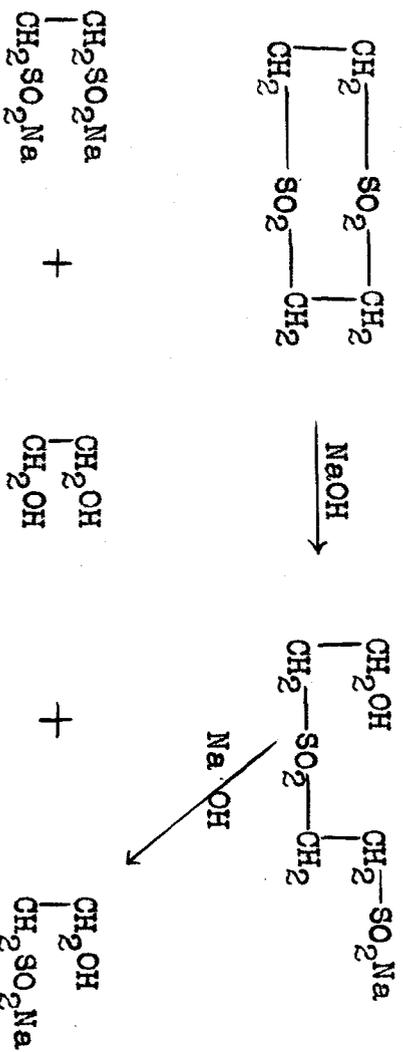


μ -Disulfones, in which the sulfur atoms form part of an aliphatic ring system, have been found to undergo cleavage with alkali as do the straight-chained compounds. Thus the following cleavage has been observed (142).



The free sulfinic acid loses sulfur dioxide readily. 1,4-Dithiane tetroxide was likewise cleaved in alkaline solution (139, 142, 143) but the cleavage occurred at both sulfone groups.

139. Otto, J. prakt. Chem., 2/36, 437 (1887).
 140. Reuterskiöld, ibid., 2/127, 269 (1930).
 141. Otto and Damkohler, ibid., 2/30, 171, 321 (1884).
 142. Baumann and Walter, Ber., 26, 1124 (1893).
 143. Crafts, Ann., 125, 123 (1863).

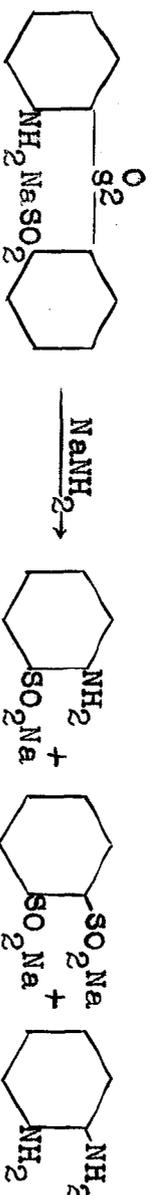


Though the analogy between the cleavage of thienthrene-2,10-tetroxide and that of those reviewed γ -disulfones is not exact, it nevertheless, is closely related. The fact remains that the thienthrene-2,10-tetroxide cleaves in about 80% yield in alkaline medium. The following series of reactions might be pictured:



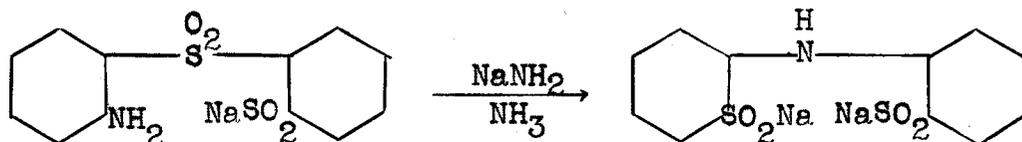
It is easily seen why this cleaved product might not lend itself to derivatization with benzalacetophenone because of steric effects. The cleavage probably does not proceed further or *o*-phenylenediamine should have been detected in the products.

Thus:



It might be possible that ammonia itself could effect such a cleavage (141).

It is still possible to conceive a type of rearrangement, observed by Smiles (21) (see p. 11) in o-amino-sulfones in alkaline medium.



However, for this type of rearrangement to occur it would be necessary, first, that the sulfone group be sufficiently electronegative, and second, that sodamide in liquid ammonia be the proper alkaline medium. Smiles (21) made no study of these rearrangements in liquid ammonia using sodamide.

C. Thianthrene Compounds

In an effort to make 2-aminothianthrene for further substitution in the amino group in connection with certain physiological studies, we came upon many difficulties and inconsistencies in the preparation that were not cited by Krishna (112). The results of our findings have been written as a guide for future workers in this series.

D. Dibenzofuran Compounds

2- and 3-Fluorodibenzofuran were prepared in connection with certain pharmaceutical studies. The findings cannot at this time be divulged because the tests were made under the auspices of the United States Government and the information is restricted.

E. Quinoline Compounds

All efforts to obtain 8-mercaptocinchoninic acid free of its complex with tin salts formed by the reduction of the sulfonyl chloride with stannous chloride have thus far failed. It has been observed that the tin salt complex of 8-mercaptoquinoline could be destroyed by benzylation of the mercapto group in alkaline solution and then hydrolysis of the S-benzoylated product with hydrochloric acid (144). No doubt, however, the matter is complicated in this case by the presence of a carboxyl group in the molecule.

The tin salt complex of the 8-mercaptocinchoninic acid was destroyed readily enough, however, in the methylation of the mercapto group to give 8-methylmercaptocinchoninic acid. Also it was destroyed by oxidation of the mercapto group to the disulfide in the preparation of bis-(4-carboxy-8-quinolyl)disulfide.

The proof of structure of the mononitro and dinitro 6-methoxy-2-phenylquinoline and 6-methoxy-2-phenylquinoline-4-carboxylic acid compounds that have been prepared, has been complicated by the inability to prepare 6-methoxy-2-phenylquinoline-4-carboxylic acids in which the nitro group occurs in the benzo ring. The unsuccessful attempt to prepare the nitro-6-methoxy-

144. Edinger, Ber., 41, 938 (1908).

2-phenylquinoline-4-carboxylic acid was through a modification of the Doebner-Miller (145) synthesis of quinoline compounds using 3-nitro-4-methoxyaniline, benzaldehyde, and pyruvic acid. Borsche (135) reported no success in the preparation of a nitroquinoline-4-carboxylic acid from the nitroanilines, benzaldehyde and pyruvic acid. In our attempt, however, we first isolated the benzal-3-nitro-4-methoxyaniline; then reacted this compound with pyruvic acid. Apparently the isolation of the anil before the addition of pyruvic acid had no effect on the final result, for a diketopyrrolidine was still the product of the reaction. Borsche (135, 146) has done considerable work on the condensation products of a number of arylamines, pyruvic acids, and aldehydes. Baeyer (147) also failed to obtain quinoline compounds from the nitroanilines. Roberts and Turner (148) have presented an excellent discussion of the effect of substituents upon ring closure in the Doebner-Miller (145) and related syntheses.

At best, oxidation of the nitro molecules for proof of structure would give a difficulty resolved mixture. Proof of the identity of the resolution product would add another real problem of synthesis.

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145. Doebner and Miller, Ber., 14, 2812 (1881).
146. Borsche, Ber., 42, 4072 (1909).
147. Baeyer, ibid., 12, 1320 (1876).
148. Roberts and Turner, J. Chem. Soc., 1835 (1927).

SUMMARY

An historical survey of the rearrangement reactions undergone by aromatic sulfur compounds has been given.

A recently described (1, 92) rearrangement amination with sodamide in liquid ammonia has been shown to be effected in *o*-halogen phenyl methyl sulfides and *o*-halogen phenyl methyl sulfones. No rearrangement was observed in two *o*-halogen benzene-sulfonamides.

The extensive cleavage of thianthrene-9,10-tetroxide by sodamide in liquid ammonia has been demonstrated and discussed.

A number of corrections and additions to the preparation of 2-aminothianthrene according to the method of Krishna (112) has been made. The preparation and properties of 1-iodothianthrene have been included.

The syntheses of several new compounds derived from 8-sulfoquinoline-4-carboxylic acid have been described.

A mononitro and a dinitro product from the nitration of 3-methoxy-2-phenylquinoline have been isolated. Likewise a mononitro and a dinitro product from the nitration of 6-methoxy-2-phenylquinoline-4-carboxylic acid have been separated and identified.

2- and 3-Fluorodibenzofuran have been prepared and the properties given.