A STUDY OF THE REACTIONS OF AROMATIC AMINE-SULFUR DIOXIDE PRODUCTS WITH VARIOUS ORGANIC SUBSTANCES

By

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CONTENTS

STATEMENT OF PROBLEM

This dissertation is concerned with the reactions of primary, secondary and tertiary amine-sulfur dioxide addition products with various other organic substances. There is much confusion in the literature on the structures of the products formed from the reactions of primary amine-sulfur addition products with aldehydes and ketones. Since there is no agreement between any of the previous authors on the structures of these products, a portion of this dissertation is devoted to the evaluation and correlation of the previous work and to the assigning of correct structures to these products. In some instances it was considered necessary to duplicate the previous work in order to establish the validity of certain facts.

It will be shown that there are actually three types of compounds formed from the reactions of primary aromatic amine-sulfur dioxide addition products with aldehydes. In the analogous reactions with ketones it will be shown that only one structure is formed.

Since many of the products formed by these reactions were unstable, a method for the proof of structures of the different types of compounds had to be developed.

It will be further shown that primary amines are not analogous to secondary and tertiary amines in their reactions with aldehydes and ketones since only primary amines are capable of forming Schiff bases. This fact was evidently overlooked by Adams and Garber and, therefore, they assumed that primary amine-sulfur dioxide addition products reacted similarly to tertiary amine-sulfur dioxide addition products to give only amine bisulfite derivatives of aldehydes and ketones.

Since no work was previously reported on reactions of secondary amine-sulfur dioxide products with aldehydes, this work will be presented for the first time. Also brought out for the first time is the fact that the reactions of amine-sulfur dioxide addition products are not limited only to reactions with aldehydes and ketones.

It will be shown that quaternary ammonium salts do not form bisulfite type compounds with sulfurous acid and aldehydes; however, a compound analogous to a quaternary ammonium salt is formed by the reaction of phenyltrimethylammonium iodide with the sodium bisulfite derivative of the Schiff base formed from the reaction of aniline and m-nitrobenzaldehyde.

Logical mechanisms will be presented for the reactions of amine-sulfur dioxide addition products with aldehydes and ketones. This will include those reactions found in the literature and the new reactions given in this dissertation.

CHAPTER I

INTRODUCTION

This dissertation is an outgrowth of work done previously at this university on reactions of the aniline-sulfur dioxide addition product in air.[1] During this study an interest in the reactions of amine-sulfur dioxide addition products with various organic substances was developed. The most notable reactions were the ones in which the amine-sulfur dioxide addition products were reacted with aldehydes and ketones.

A survey of the literature on the reactions of amines and sulfur dioxide with aldehydes and ketones showed vast disagreement between the various authors. This fact effected a greater interest in this study, and, therefore, one aim of this dissertation is to evaluate this previous work using electronic concepts of organic chemistry as well as experimental evidence to ascertain the structures of the products formed by the reactions of amine-sulfur dioxide addition products with aldehydes and ketones.

During this study, new processes were also developed since no previous authors had reported any reactions of secondary amine-sulfur dioxide addition products with aldehydes and ketones. It was also found that amine-sulfur dioxide products would react with compounds other than aldehydes and ketones.

The first report on reactions of amine-sulfur dioxide products with

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[1] Harold D. Lyons, "A Study of the Reaction Mechanisms of the Aniline-Sulfur Dioxide Addition Product in Air," Master's Thesis, University of Alabama, 1941.

aldehydes was that of Schiff.[2] This report was followed a short time later by that of Boessneck[3] in which reactions of ketones with amine-sulfur dioxide addition products were discussed. Michaelis[4] stated that he had obtained in reactions with benzaldehyde a product identical to the one reported by Schiff, however, his reactants were not identical with those of Schiff. Eibner[5] studied reactions of amines and sulfurous acid with aldehydes. More recent work on reactions of ketones with amines and sulfur dioxide has been reported by Feigl and Feigl.[6]

The most recent work on the reactions of aldehydes and ketones with sulfur dioxide and amines was reported in 1949. Adams and Lipscomb[7] reported reactions of aldehydes and ketones with tertiary amines and sulfur dioxide while Adams and Garber[8] reported reactions of aldehydes and ketones with primary amines and sulfur dioxide.

Since there is no agreement among the above authors as to the structures of the products obtained in the reactions of aldehydes and ketones with amines and sulfur dioxide, the work reported by them will be combined with the experimental work and theories of this author, and these will be correlated in order to arrive at a solution to the problem of assigning

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2. Schiff, Ann., 210, 123 (1881).
3. Boessneck, Ber., 21, 1906 (1888).
4. A. Michaelis, Ber., 24, 749 (1891).
5. Alexander Eibner, Ann., 316, 89 (1901).
6. Von F. Feigl and E. Feigl, Z. Anorg. Allgem. Chem., 203, 57 (1931).
7. Roger Adams and R. D. Lipscomb, J. Am. Chem. Soc., 71, 519 (1949).
8. Roger Adams and John D. Garber, J. Am. Chem. Soc., 71, 522 (1949).

correct structures to these products.

CHAPTER II

HISTORICAL

There is a vast amount of previous work which relates either directly or indirectly to the structures and reactions of aldehydes and ketones with amines and sulfur dioxide; however, some material that is well known to organic chemists will be excluded. Only material which has a direct bearing on this work or which is needed to substantiate certain theories of this author will be presented.

Reactions of Amine-Sulfur Dioxide Products with Aldehydes and Ketones

Included in this section will be the previous work that has been reported on the reactions of aldehydes and ketones with amines and sulfur dioxide. The material will be presented in chronological order beginning with the work of Schiff in 1881 and ending with the work of Adams and Garber in 1949.

The first reported work on the reactions of primary amines and sulfur dioxide with aldehydes was that of Schiff.[1] He concluded that the reaction usually produced a product consisting of one mole each of the amine, aldehyde and sulfurous acid when carried out in aqueous solution. He noted, however, an exception in the reaction of aniline, sulfur dioxide and benzaldehyde. He stated that this product contained one mole of sulfur dioxide and two moles each of benzaldehyde and aniline.

The first work on reactions of ketones with amines and sulfur dioxide

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1. Schiff, Ann., 210, 123 (1881).

was that of Boessneck.[2] He reacted primary, secondary and tertiary amines with various ketones. He stated that the products consisted of one mole of each of the reactants; he made no distinction between the products formed by primary, secondary and tertiary amines.

Michaelis[3] stated that he obtained the same compound from the reaction of thionyl aniline, aniline and benzaldehyde as Schiff had obtained from sulfurous acid, aniline and benzaldehyde since they had similar melting points. Michaelis stated that Schiff's ratio was incorrect, and he gave the ratio, according to his analyses, as two moles of aniline to one of benzaldehyde and sulfur dioxide.

In his study of the reactions of aldehydes, Eibner[4] did a great deal of work on the reactions of amine sulfites with aldehydes. He reacted each of several different aldehydes with aniline and sulfurous acid; he also studied the reactions of sodium bisulfite addition compounds of aldehydes with aniline.

Eibner stated that four different types of compounds were formed from the reactions of aniline and sulfur dioxide with aldehydes. He divided them into two main classes. They are as follows:

I. Addition products of sulfurous acid with the Schiff base.

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2. P. Boessneck, Ber., 21, 1906 (1881).

3. A. Michaelis, Ber., 24, 749 (1891).

4. Alexander Eibner, Ann., 316, 89 (1901).

$RCH{=}NC_6H_5SO_3H_2$ $(RCH{=}N{-}C_6H_5)_2\ SO_3H_2$ $RCH{=}(NHC_6H_5)_2\ SO_3H_2$

I II III

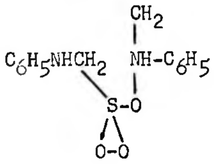
II. Addition products of sulfur dioxide and the diphenylamine compound.

$$RCH{=}(NHC_6H_5)_2\ SO_2$$

IV

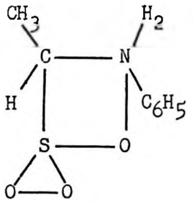
Eibner divided the aldehydes not into the aliphatic and aromatic, but into water soluble aldehydes and water insoluble aldehydes. He stated that formaldehyde, acetaldehyde, propionaldehyde and chloral, the water soluble aldehydes, belonged to the compounds of class I, while the aldehydes, isobutyraldehyde, isovaleraldehyde, and benzaldehyde belonged to class II. Meta-nitrobenzaldehyde formed two products when reacted with aniline sulfite, one of which Eibner assigned to class I while the other he assigned to class II. From salicyaldehyde he obtained a compound of the type shown as I.

Eibner stated that the reaction of formaldehyde with aniline and sulfurous acid was different from the reaction of other water soluble aldehydes. This reaction gave a compound of the type shown as II. He presented for the structural formula the one shown here as V.



V

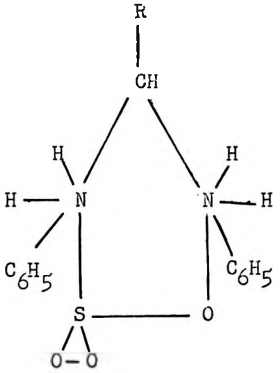
The reaction of acetaldehyde with aniline and sulfur dioxide was studied quite extensively by Eibner. A white solid melting at 94° was formed from this reaction; Eibner also found this same compound could be formed by reaction of the sodium bisulfite derivative of acetaldehyde with aniline followed by acidification. When sulfurous acid was reacted with the Schiff base from aniline and acetaldehyde, the white solid melting at 94° was again obtained. Reaction of this Schiff base with sodium bisulfite formed the same product as was formed when aniline was reacted with the sodium bisulfite derivative of acetaldehyde. When the compound formed from the reaction of acetaldehyde with aniline and sulfurous acid was reacted with sodium bicarbonate in neutral solution, the same compound as was formed from the reaction of aniline with the sodium bisulfite derivative of acetaldehyde was again formed. Eibner presents as the structural formula for the compound formed from the reaction of acetaldehyde with aniline and sulfurous acid the structure shown as VI.



VI

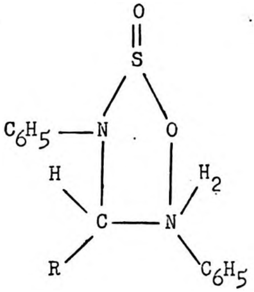
Eibner stated that this structure is not unique to the compound formed from reactions of acetaldehyde with aniline and sulfurous acid but is applicable to any aldehyde that forms a compound of the type shown as I. He stated that the reactions of compounds of type I took place as if the compound contained a bond between the carbon and sulfur atoms, and he further stated that these compounds might actually be alpha-aminosulfonic acids.

Eibner stated that propionaldehyde and chloral formed two types of products; the general formulas for these were shown previously as I and III. The structural formula for I has been given; the structural formula proposed by Eibner for products of type III is shown here as VII.



VII

M-nitrobenzaldehyde also formed two products when reacted with aniline and sulfur dioxide, however, Eibner assigned to them the formulas shown as I and IV. The structure for formula IV which Eibner believed to be most plausible is shown here as VIII.



VIII

According to Eibner, the water insoluble or slightly water soluble aldehydes form compounds of class II whose general formula was represented previously as IV. He stated that the following aldehydes form compounds of this type: isobutryaldehyde, isovalderaldehyde, benzaldehyde and m-nitrolgenzaldehyde. These compounds were produced by passing sulfur dioxide into an ether solution of aniline and the aldehyde. Eibner did not explain the fact that salicyaldehyde formed a compound of the type shown as I. From his work he made the general conclusion that the water soluble aldehydes usually formed compounds of the type shown as I when reacted with aniline and sulfurous acid, while the aromatic and water insoluble aldehydes formed either compounds of type III or IV in their reactions.

Mayer[6] stated that he obtained two compounds from the reaction of aniline and benzaldehyde with sulfurous acid; one melted at 125° and the other at 145°. He represented the compound melting at 125° as having the formula shown as IX and the compound melting at 145° as having the formula shown as X.

$C_6H_5NH{=}CHC_6H_5SO_3H \cdot C_6H_5NH_2$

IX

$C_6H_5CH{=}NC_6H_5 \cdot H_2SO_3$

X

Mayer assigned these formulas by use of picrate derivatives. He stated that IX gave the picrate of both aniline and benzalaniline while X gave only the picrate of benzalaniline.

Feigl and Feigl[7] prepared what they termed ternary compounds from

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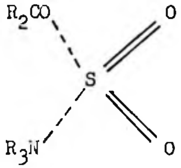
[6] Mario Mayer, <u>Gass. Chim. Ital.</u>, <u>42</u>, <u>I</u>, 50 (1912) Ref. cit., <u>6</u>, 1138 (1912)

[7] Von F. Feigl and E. Feigl, <u>Z. Anorg. Allgem. Chem.</u>, <u>203</u>, 57 (1931).

the reaction of sulfur dioxide, ketones and amines. They stated that these crystalline compounds contained one mole each of the amine, sulfur dioxide and the ketone. They detected no difference in the reactivity of primary, secondary or tertiary amines with ketones. By using sulfur analyses they gave XI as the probable structure of these compounds.



XI

Adams and Lipscomb[8] have successfully prepared amine bisulfite addition products of aldehydes and ketones. They prepared several addition products of tertiary amine bisulfites with aldehydes and ketones. These were prepared by passing sulfur dioxide into the tertiary amine mixed with sufficient water (mole per mole) until a white solid, which they postulated was the amine sulfite, was separated. The bisulfites of trimethylamine.triethylamine, N-butylpiperdine, N-n-butylmorpholine, N-benzylpiperdine, N-methylpiperdine, N-dodecylpiperdine, N-hexadecylpiperdine and pyridine were studied. They stated that several amines gave unstable, colored liquids or other amorphous type compounds.

The ketones used were cyclohexanone, cyclopentanone, acetone and methyl n-propyl ketone. The aldehydes used were benzaldehyde and 2-ethylhexanal.

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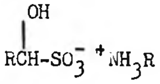
[8] Roger Adams and R. D. Lipscomb, J. Am. Chem. Soc., 71, 519 (1949).

They stated that the structure of the compounds formed from the reaction of tertiary amine bisulfites with aldehydes and ketones was analogous to that formed from the reaction of alkali metal bisulfites with aldehydes and ketones which is shown as XII.



$\mathrm{R\overset{\overset{OH}{|}}{C}H{-}SO_3^{-}\ {}^{+}NH_3R}$

XII

These products formed well-defined crystalline structures with sharp melting points. In two cases analyses indicated that the compounds contained one molecule of water of crystallization which was not removed by recrystallization or by drying in air at 50-60°. These products resembled the analogous sodium bisulfite derivatives of aldehydes and ketones in that they were decomposed into their components upon addition of dilute mineral acid or dilute alkali.

Further work done at the University of Illinois by Adams and Garber[9] made use of the primary amine sulfur dioxide products resolving agents for aldehydes and ketones. They stated that steroisomers of certain of the adducts were possible, but that only one form predominated and was isolated in good yield.

Adams and Garber stated that when sulfur dioxide was allowed to bubble through an equimolar mixture of the amine and water with the addition of ether or ethanol, a white solid was usually formed. They postulated that this white solid was chiefly the amine sulfite; however, it

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[9] Roger Adams and John D. Carber, *J. Am. Chem. Soc.*, *71*, 522 (1949).

was not isolated. Sulfur dioxide was bubbled into the mixture until a homogenous, yellow, viscous liquid was produced which they stated was due to formation of a complex of the type $(RNH_2)_x:(SO_2)_y$ in which "y" is greater than "x".

Adams and Garber devised a method of analyses in which they added an excess of standard iodine solution to a slightly acid solution of the adduct and back-titrated with sodium thiosulfate. They stated that this procedure gave excellent results, although poor results were obtained in some cases due to the fact that a pure analytical sample could not be obtained. They assumed the same structure for their compounds from reactions of primary amines as Adams and Lipscomb had shown for the compounds of aldehydes and ketones with tertiary amine bisulfites.

Some Reactions of Aldehyde and Ketone Bisulfite

Some of the preparations and reactions of alkali metal bisulfites will be presented here since comparisons of the reactions of alkali metal bisulfites to those of amine bisulfites will be made in a later chapter.

Aldehydes, aliphatic methyl ketones, and alicyclic ketones up to cyclooctanone yield sodium bisulfite compounds.[10] Some less reactive ketones react slowly or not at all with bisulfites.[11] Aliphatic methyl ketones become less reactive as the size and complexity of the second alkyl radical are increased. Compounds like diethyl ketone, methyl isopropyl ketone and methyl iso-butyl ketone react very slowly with bisulfite. When there

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[10] Reynold C. Fuson, "Advanced Organic Chemistry," p. 377.

[11] A. W. Stewart, J. Chem. Soc., 87, 185 (1905).

groups larger than ethyl on each side of the carbonyl group, no noticeable reaction is obtained.

Keto esters, such as ethyl pyruvate, ethyl acetoacetate, and ethyl levulinate are known to form bisulfite addition compounds.[12] A number of aliphatic diketones will react with bisulfite; the ketone in this case reacts with two moles of the bisulfite.

The aromatic ketones, including acetophenone, do not form bisulfite compounds.[13]

Olefins apparently do not react with bisulfites in the absence of oxygen.[14] In the presence of oxygen, addition occurs in a manner opposite to that predicted by Markownikoff's rule.

Bisulfites add to olefinic linkages that are conjugated with carbonyl groups, cyano groups, or other such withdrawal groups. They will not add to unconjugated olefinic linkages unless an oxidizing agent is present.[15] Propylene, allyl alcohol, cyclohexene, and similar compounds take up bisulfite in the presence of oxygen.

Lepetit[16] found that when sodium bisulfite and formaldehyde were reacted with aromatic amines, a crystalline substance was formed. For

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12. J. B. Ekely and A. A. O'Kelly, _J. Am. Chem. Soc._, 50, 2731 (1928).

13. Fuson, _Op. cit._, p. 378.

14. M. S. Kharasch, E.M.May and F.R. Mayo, _Chem. and Ind._ _16_, 744 (1938); M.S. Kharasch, E.M. May and F.R. Mayo, _J. Org. Chem._ _3_, 175, (1938); Kolker and A. Lapworth, _J. Chem. Soc._, _127_, 307 (1925); F.R. Mayo and Cheves Walling, _Chem. Rev._, _27_, 394 (1940).

15. M.S. Kharasch, R.T.E. Schenck, and F.R. Mayo, _J. Am. Chem. Soc._ _61_, 3092, (1939).

16. Fuson, _Op. cit._, p. 474.

example, when sodium bisulfite was reacted with a mixture of formaldehyde and p-phenetidine, crystals were formed which proved to be sodium p-ethoxyphenylaminomethanesulfonate. The sodium aminomethanesulfonate derivatives of aniline, o-toluidine, xylidine, o-anisidine, alpha and beta naphthylamine and o-chloroaniline were prepared. All were found to contain one mole of water of crystallization.

Peterson[17] stated that the reaction of sodium bisulfite with isocyanates formed products of the type represented by $RNHCOSO_3Na$. He stated that acetone and acetaldehyde bisulfites also react with isocyanates, but he gave no structures for these compounds.

The reaction of bisulfites presents a large field for the study of reactions of amine bisulfites since this dissertation will show that the reactions of the two classes of bisulfites are analogous in many cases.

Some Reactions of Schiff Bases

Some reactions of Schiff bases are presented since in the reactions of primary amine-sulfur dioxide products with aldehydes and ketones, it is likely that the first reaction is the formation of a Schiff base; therefore, the reactions of Schiff bases become of interest.

Schiff bases react very much in the same way as do carbonyl compounds. In their addition reactions they behave more like carbonyl compounds than ethylenic compounds; for example, they are known to add Grignard reagents

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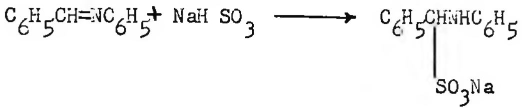
[17] Seigfried Peterson, *Ann.*, *562*, 205 (1949).

and sodium bisulfite as do carbonyl compounds.[18]

Gilman does not agree with the ether structure as assigned to the addition products of sodium bisulfite and Schiff bases.[19] He stated that the reaction is analogous to the reaction of bisulfite with carbonyl compounds which he represents as follows:



$$C_6H_5CH{=}NC_6H_5 + NaH\,SO_3 \longrightarrow C_6H_5\underset{SO_3Na}{\underset{|}{CH}}NHC_6H_5$$

Schiff bases have a tendency to polymerize; in fact, no monomolecular compounds have been obtained with formaldehyde and amines.[20] Only one Schiff base has been isolated using ammonia, this being the derivative of ammonia and alpha-alpha diphenyl acetaldehyde, and in this case is was isolated as the hydrochloride salt which was also very unstable.[21] In reactions of Schiff bases with bisulfites, the fact that a polymerization could take place as the first reaction must be kept in mind.

Structure and Reactions of Alpha-Aminosulfonic Acids

The structure and reactions of alpha-aminosulfonic acids will be taken up since it is probable that reactions of amines and sulfur dioxide with aldehydes and ketones form products of this type. There is much controversy in the literature on the structure of alpha-aminosulfonic acids. The structures which were proposed by different investigators are

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[18] Henry Gilman and R. H. Kirby, *J. Am. Chem. Soc.*, *55*, 1265 (1933).

[19] Gilman, *op. cit.*

[20] *Ibid.*

[21] E. P. Kohler and N. L. Drake, *J. Am. Chem. Soc.*, *45*, 1281 (1923).

given below as I and II.

$NH_2CH_2OSO_2H$ I

$NH_2CH_2SO_3H$ II

Schroeter[22] and Knoevenagel[23] claimed that they had evidence to show that structure I was correct. Backer and Mulder[24] believed that structure II was the correct one. They studied the reaction of ammonia and formaldehyde bisulfite quite extensively and stated that by chemical reactions and the preparation of many derivatives they had proved that structure II was the correct one.

Bucherer and Schwalbe[25] obtained arylaminomethanesulfonic acids by reaction of sodium hydroxymethanesulfonate with aromatic amines.

Abelin and Perelstein[26] stated that the formation of compounds of the type $RNHCHR'OSO_2H$ (where R is alkyl; R' is H, alkyl or aryl) was possible by condensation of amines with the bisulfite compounds of aldehydes and ketones. It was found that in some cases sodium ethoxide accelerated the reaction. The free acids obtained from this method contained one mole of water of crystallization. They stated that the aldehydes chloral and valeraldehyde did not give the expected products; however,

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[22] G. Schroeter, Ber., 66B, 1038 (1933); Ref. cit., C. A., 27, 5054 (1933).

[23] E. Knovenagel, Ber., 37, 4087 (1904).

[24] H. J. Backer and H. Mulder, Rec. trav. Chim., 53, 1120 (1934); ibid., 52, 454 (1933).

[25] H. Bucherer and A. Schwalbe, Ber., 39, 2796 (1906).

[26] I. J. Abelin and M. Perelstein, Ann., 411, 216 (1916).

they did not suggest any structures for these products.

McIlwain[27] prepared alpha-aminosulfonic acids from acetaldehyde, isobutyraldehyde, isovaleraldehyde, benzaldehyde and substituted benzaldehydes, by acidifying the products obtained from the reactions of amines with aldehyde-bisulfite compounds. All of these products were assumed to be analogous to those obtained from the reaction of ammonia on the bisulfite derivative of formaldehyde as obtained by Backer and Mulder and, therefore, are considered to be true alpha-aminosulfonic acids.

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[27] Henry McIlwain, J. Chem. Soc., 75, (1941).

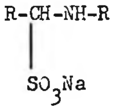
CHAPTER III

EXPERIMENTAL PROCEDURES AND RESULTS

Preliminary experiments showed that the aniline-sulfur dioxide addition product appeared to react with a great many different types of organic compounds. In some cases the sulfur dioxide was lost during the reaction, and the same product was obtained as would have been obtained if only aniline had been used. It was found in the preliminary experiments that the reactions of amines and sulfur dioxide with aldehydes and ketones took place more readily and gave in most cases crystalline products; therefore, a great part of the experimental work described herein will be concerned with these reactions.

The general procedure used for the preparation of derivatives of amine-sulfur dioxide products and various organic substances was as follows: Sulfur dioxide was bubbled into water at 0° in order to obtain a solution containing around 5-6% sulfurous acid, and the amine was added to this solution followed by the addition of the organic material; however, different procedures were used from time to time for comparison of results.

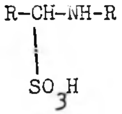
In order to indicate the structure of the derivative formed from the reaction of amines and sulfur dioxide with aldehydes and ketones, the Schiff base from the aldehyde and the amine was formed and reacted with sodium bisulfite to form the following type compound ( ):



$$\underset{\displaystyle SO_3Na}{\underset{|}{R\text{-}CH}}\text{-}NH\text{-}R$$

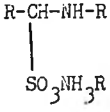
I

The solution of the compound (I) was divided into two portions one of which was reacted with sulfurous acid while the other was reacted with aniline hydrochloride. If the compound formed from the reaction of this product with sulfurous acid had the same melting point as the product formed from the reaction of the amine sulfur dioxide product with the aldehyde, then this compound was assigned the structure shown below as II (an amino sulfonic acid), whereas, if the reaction with aniline hydrochloride with this product produced a compound with an identical melting point, then this compound was assigned the structure of an amine bisulfite derivative of the Schiff base formed from the reaction of the amine and aldehyde shown below as III. Carbon and hydrogen analyses were used together with theories and mechanisms by this author to assign the structure of a sulfonanilide derivative of the Schiff base formed from the aldehyde and amine used; this is shown below as IV. Mixed melting points of the products prepared by different methods were taken.



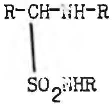
$$\begin{array}{l} \mathrm{R{-}CH{-}NH{-}R} \\ \quad | \\ \quad \mathrm{SO_3H} \end{array}$$

II



$$\begin{array}{l} \mathrm{R{-}CH{-}NH{-}R} \\ \quad | \\ \quad \mathrm{SO_3NH_3R} \end{array}$$

III



$$\begin{array}{l} \mathrm{R{-}CH{-}NH{-}R} \\ \quad | \\ \quad \mathrm{SO_2NHR} \end{array}$$

IV

It was found that compounds such as aldol, cinnamylaldehyde, formaldehyde, furfural, glyoxal and heptaldehyde formed only gummy or tarry substances; therefore, no further work was attempted on these products.

The aniline used in the following experiments was Eimer and Amend, C. P. Bakers Analyzed, C. P. sodium bisulfite, aniline hydrochloride and Mathesons anhydrous sulfur dioxide was used. All other organic substances were Eastman Kodak white label chemicals unless otherwise indicated.

Reactions of the Aniline-Sulfur Dioxide Addition product with Various Aldehydes

The section which now follows deals with the reactions of the aniline-sulfur dioxide addition product with various aldehydes. It will also include reactions which show proof of the structure of the compounds formed in these cases.

Reaction with Acetaldehyde

When aniline was added to a saturated solution of sulfur dioxide followed by the addition of a few drops of acetaldehyde, there was formed a white crystalline product which melted at 92-93°. This product was unstable on heating and was decomposed on standing in air.

The above product with a melting point of 92-93° was prepared by addition of acid to the sodium bisulfite derivative of the Schiff base from aniline and acetaldehyde. The two products were mixed in varying proportions and the melting points of these mixtures were taken; no lowering of the melting points was noticed.

Reaction with Anisaldehyde

To a saturated solution of sulfur dioxide was added 15g. (0.16 moles) of aniline followed by the addition of 22 g. (0.16 moles) of anisaldehyde. There was an immediate reaction with the formation of a solid mass of light yellow crystals. The crystals became white when washed with ether. After recrystallization from 95% ethanol the crystals were found to melt at 115-116°. These crystals were unstable upon exposure to air.

The above product with a melting point of 115-116° was prepared by addition of sulfurous acid to the sodium bisulfite derivative of the

Schiff base from aniline and anisaldehyde. This indicates that the product is an aminosulfonic acid as shown in type II. No lowering of the melting points was noted when the products obtained from the above procedures were mixed in varying proportions.

Reaction with Benzaldehyde

To 9.3 g. (0.1 mole) of aniline was added 200 ml. of 6% sulfurous acid (Mallinkrodt). To this mixture was added 10.6 g. (0.1 mole) of benzaldehyde. On addition of benzaldehyde the mixture turned to a dark orange color and upon standing for thirty minutes formed a mass of white crystals. Upon recrystallization from water there was obtained a white crystalline product which melted at 127-127.5°. It was dried over phosphorus pentoxide and sent to the Clark Microanalytical Laboratories, Urbana, Illinois, for analyses. Their results along with the theoretical calculated for a type IV compound are given below:

Clark's Results	Theoretical for IV
C- 65.62% 65.58%	C- 65.70%
H- 5.60% 5.56%	H- 5.22%

To 9.3 g. (0.1 mole) of aniline was added 10.6 g. (0.1 mole) of benzaldehyde to form the Schiff base melting at 59-60°. This solid was placed in ether solution and into this solution was passed sulfur dioxide. A white solid melting at 127° separated from the solution. There was also separated an oil which has the characteristic odor of benzaldhyde. The solid was recrystallized from water and was analyzed by Mr. Vergil M. Benson, a graduate student in the department of analytical chemistry at the Univer-

sity of Alabama. He reported 8.99% sulfur; the theoretical for the type IV compound is 9.23% sulfur.

To 18.6 g. (0.2 mole) of aniline was added 21.2 g. (0.2 mole) of benzaldehyde in a solution of 95% ethanol. To this solution was added 20.8 g. (0.2 mole) of sodium bisulfite dissolved in a small amount of water. This solution was divided into two equal portions, and to one portion was added 20 ml. of dilute hydrochloric acid; crystals melting at 127° appeared after standing for a short time.

To the second portion of this solution was added 13 g. (0.1 mole) of aniline hydrochloride dissolved in a small amount of water. On addition of the aniline hydrochloride solution there appeared crystals which upon recrystallization from water melted at 132-133°. These crystals were dried in a vacumn oven and sent to Clark Microanalytical Laboratory for analyses. Their results together with the theoretical for a type III compound are shown below.

Clark's Results	Theoretical for type III
C- 65.05%	C- 64.14%
H- 5.91%	H- 5.63%

If a type III compound was formed in this case, it evidentally was transformed to a type IV compound. A mixture of the compound melting at 127° with the one melting at 133° was made. This mixture appeared to melt in the range of 127-133°; no sharp melting was observed.

An attempt was made to prepare a type IV compound by reaction of benzal chloride with sodium sulfite followed by reaction with aniline, however, under these conditions the benzal chloride hydrolyzed to benzaldehyde.

Reaction with o-Chlorobenzaldehyde

To 100 ml. of a saturated solution of sulfurous acid at 0° was added 9.3 g. (0.1 mole) of aniline followed by the addition of 14 g. (0.1 mole) of o-chlorobenzaldehyde. There was an immediate reaction with the formation of white crystals. Upon recrystallization from isopropyl alcohol the crystals melted at 120-121°. These crystals were too unstable for analyses.

The above product with a melting point of 120-121° was prepared by addition of sulfurous acid to the sodium bisulfite derivative of the Schiff base from aniline and o-chlorobenzaldehyde. This indicates that the product is an aminosulfonic acid as shown in type II. No lowering of the melting points was noted when the two products obtained from the above procedures were mixed in varying proportions.

Reaction with 2,4-Dichlorobenzaldehyde

To a saturated solution of sulfurous acid at 0° was added 9.3 g. (0.1 mole) of aniline followed by the addition of 9.0 g. (0.05 mole) of 2,4-dichlorobenzaldehyde dissolved in 150 ml. of ether. A white crystalline product was formed immediately, and it was recrystallized from isopropyl alcohol to a constant melting point of 115-116°. These crystals were too unstable for analyses.

The above product with a melting point of 115-116° was prepared by addition of sulfurous acid to the sodium bisulfite derivative of the Schiff base from aniline and 2,4-dichlorobenzaldehyde. This indicates that the product is an aminosulfonic acid as shown in type II. No lowering of the melting points was noted when the two products obtained from the above procedures were mixed in varying proportions.

Reaction with m-Nitrobenzaldehyde

Into 9.3 g. (0.1 mole) of aniline was bubbled sulfur dioxide to form the yellow solid addition product. This was added to 15.2 g. (0.1 mole) of m-nitrobenzaldehyde dissolved in 200 ml. of ethanol. A yellow crystalline product was formed immediately. This product could be recrystallized from either water or ethanol. After two recrystallizations from ethanol, it melted at 126-126.5°. This compound was dried over phosphorus pentoxide and sent to Clark Microanalytical Laboratory for analyses. Their results together with the theoretical for a compound of type III are shown below.

Clark's Results	Theoretical for III
C- 56.60% 56.50%	C- 56.85%
H- 4.96% 4.77%	H- 4.78%

If the above substances are reacted at a temperature of 60-70°, there is obtained a white product which melts at 175-176°. If the yellow product melting at 126-126.5° is heated with sulfurous acid and ethanol, a product melting at 175-176° is obtained. This product melting at 175-176° is an aminosufonic acid as will be shown later. This was a duplication of the work of Eibner.

A solution of the sodium bisulfite derivative of the Schiff base from m-nitrobenzaldehyde and aniline was divided into two portions, and to the first portion was added dilute hydrochloric acid; upon evaporation of the solution to dryness, there was obtained the aminosulfonic acid shown as II. This compound melted at 175-176°. To the second portion was added a water solution of aniline hydrochloride. There was an immediate precipitation of yellow crystals melting at 126°. No lowering of the melting points was noted when the products having the same melting points, but obtained by different procedures, were mixed in varying proportions.

Reaction of Aniline and Salicyaldehyde with Sodium Bisulfite

To 6.2 g. (0.05 mole) of salicyaldehyde was added 4.7 g. (0.05 mole) of aniline, and to a solution of this in alcohol was added 5.2 g. (0.05 mole) of sodium bisulfite dissolved in water. This solution was divided into two equal portions, and to the first was added a solution of sulfurous acid, which gave a precipitate on standing overnight. This compound melted at 126-128°. This indicates that it has the aminosulfonic acid structure as shown by II. This compound was prepared previously by Eibner.

Reaction with Vanillin

To 100 ml. of a saturated solution of sulfurous acid at 0° was added 9.3 g. (0.1 mole) of aniline followed by the addition of 15.4 g. (0.1 mole) of vanillin dissolved in 150 ml. of ethanol. The temperature of the reaction mixture was kept at 0°, and the formation of yellow-orange crystals occurred in a very few minutes. The product was recrystallized from chloroform until a constant melting point of 93-94° was obtained. The crystals were too unstable for analyses.

The above product with a melting point of 93-94° was prepared by addition of sulfurous acid to the sodium bisulfite derivative of the Schiff base from aniline and vanillin. This indicated that the product is an aminosulfonic acid as shown in type II. No lowering of the melting points was noted when the two products obtained from the above procedures were mixed in varying proportions.

TABLE I

Crystalline Products from Reactions of the Aniline -Sulfur Dioxide Addition Product with Various Aldehydes

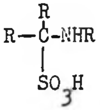
Aldehyde	M. P.	Structure indicated by chemical methods	Theoretical Analyses	Found Analyses
*Acetaldehyde	92-93°	II	Too unstable	
Anisaldehyde	115-116°	II	Too unstable	
*Benzaldehyde	127-127.5°	IV	C-65.70% H- 5.22%	C-65.60% H- 5.58%
o-Chlorobenzaldehyde	120-121°	II	Too unstable	
2,4-Dichlorobenzaldehyde	115-116°	II	Too unstable	
*m-Nitrobenzaldehyde	126-126.5°	III	C-56.85% H- 4.78%	C-56.55% H- 4.87%
**m-Nitrobenzaldehyde	175-176°	II		
**Salicyaldehyde	126-128°	II		
Vanillin	93-94°	II	Too unstable	

*This reaction has been noted previously by other investigators.

**This compound has been analyzed by other investigators.

Reactions of the Aniline-Sulfur Dioxide Product with Various Ketones

The following section deals with the reactions of the aniline-sulfur dioxide addition products with ketones, including reactions of sulfurous acid and aniline hydrochloride with the sodium bisulfite derivative of the Schiff base from the amine and ketone, as has been described before. The aminosulfonic acids formed from ketones appear to have the following structure:



$$R-\overset{R}{\underset{SO_3H}{C}}-NHR$$

V

The aliphatic ketones containing one methyl group reacted with the aniline-sulfur dioxide product; however, di-isopropyl ketone would not react. Mixed melting points were used as a criteria to acertain the correct structures. These aminosulfonic acids were prepared by using Schiff bases as described earlier in this chapter.

Reactions with Acetone

To 9.3 g. (0.1 mole) of aniline dried over sodium hydroxide was added 100 ml. of benzene which had been dried over calcium hydride. Into this solution was bubbled sulfur dioxide until a yellow precipitate separated, and to this was added 4.6 g. (0.1 mole) of acetone which had been dried with calcium chloride. No noticeable reaction was obtained in this case.

When sulfur dioxide was bubbled into a mixture of 5 ml. of aniline and 7.5 ml. of water, and an excess of acetone was added to this mixture, there was formed crystals which melted at 88-90°.

A compound melting at 88-90° was obtained from the reaction of the sodium bisulfite derivative of the Schiff base of aniline and acetone by addition of sulfurous acid. No reaction was obtained when aniline hydrochloride was used in place of sulfurous acid. This indicates that the compound is an aminosulfonic acid as shown in V. The two products were mixed in varying proportions and the melting points of these mixtures taken. No lowering of the melting points was noticed.

Reaction with Acetophenone

To a saturated solution of sulfurous acid at 0° was added 18.6 g. (0.2 mole) of aniline followed by the addition of 48 g. (0.4 mole) of acetophenone. Crystals formed upon standing for a few minutes. The crystals were found to be insoluble in all solvents tried; therefore, they were washed with hot acetone followed by washing with hot benzene. White crystals with a faint yellow tint were obtained. They were found to melt at 136-137°. They were dried over phosphorus pentoxide in an evacuated tube and sent to Clark Microanalytical Laboratory for analyses. Their result along with the theoretical for the aminosulfonic acid are shown below:

Clark's Results	Theoretical for V + H_2O
C- 57.72%	C-56.97%
H- 5.89%	H- 5.77%

A compound melting at 136-137° was obtained from the reaction of the sodium bisulfite derivative of the Schiff base of aniline and acetophenone by addition of sulfurous acid. This indicates that this compound is an aminosulfonic acid as shown in V. The two products melting at 136-137° were mixed in varying proportions and the melting points of these mixtures taken; no lowering of the melting points was noticed.

Reaction of Methyl Ethyl Ketone

To 9.3 g. (0.1 mole) of aniline was added 2 ml. of water, and this mixture was saturated with sulfur dioxide at 0° until there was obtained a solid mass of yellow-white crystals. To this product was added 7.2 g. (0.1 mole) of methyl ethyl ketone, and on stirring the solution is solidified into a solid mass of white crystals which melted at 68-69°. It was unstable in air, and, therefore, no analyses were made.

The above product with a melting point of 67-68° was prepared by addition of acid to the sodium bisulfite derivative of the Schiff base from aniline and methyl ethyl ketone. The two products were mixed in varying proportions and the melting points of these mixtures taken; no lowering of the melting points was noticed.

Reaction with Methyl Isopropyl Ketone

To 9.3 g. (0.1 mole) of aniline was added 2 ml. of water, and this mixture was saturated with sulfur dioxide until the yellow-white product was obtained. To this was added 8.6 g. (0.1 mole) of methyl isopropyl ketone. On stirring there were formed white crystals which melted at 70-71°. This product was found to be unstable and, therefore, was not analyzed.

The above product with a melting point of 70-71° was prepared by addition of acid to the sodium bisulfite derivative of the Schiff base from aniline and methyl isopropyl ketone. The two products were mixed in varying proportions and the melting points of these mixtures taken; no lowering of the melting points was noticed.

TABLE II

Reactions of the Aniline-Sulfur Dioxide Product with Various Ketones

Ketone	M.P.	Structure indicated by Chemical Reaction	Analyses Theoretical	 Found
* Acetone	88-90°	V	Too unstable	
* Acetophenone	136-137°	V	C-56.97% H- 5.77%	C-57.72% H- 5.89%
Methyl Ethyl Ketone	68-69°	V	Too unstable	
Methyl Isopropyl Ketone	70-71°	V	Too unstable	

* This reaction has been noted previously by other investigators.

Reactions of the Aniline-Sulfur dioxide product with Compounds other than Aldehydes and Ketones

This section deals with the reactions of the aniline-sulfur dioxide product with compounds other than aldehydes and ketones. In some instances the same product was obtained as would have been obtained if only aniline had been used in the reaction. Reactions were tried with different types of compounds in order to find which types of compounds would react with the aniline sulfur dioxide product.

No reactions were obtained with the following compounds: Allyl alcohol, ethyl acetoacetate, methyl salicylate and styrene.

Reaction with Acrylonitrile

To 93.0 g. (1 mole) of aniline was added 18 g. (1 mole) of water, and this mixture was saturated with sulfur dioxide until white crystals appeared. To this mixture was added 106 g. (2 moles) of acrylonitrile.

A product melting at 198-199° was obtained. It was recrystallized from water and washed with isopropyl alcohol. This compound was sent to Clark Microanalytical Laboratory for analyses, and their results along with the theoretical percentage calculated for the aniline bisulfite derivative of acrylonitrile will be presented below:

Clark's Results	Theoretical for $C_9H_{12}N_2SO_3$
C-47.59%	C-47.37%
H- 5.19%	H- 5.26%

Reaction with Benzoyl Chloride

Into 9.3 g. (0.1 mole) of aniline was bubbled sulfur dioxide to form the yellow addition product. To this was added 34.0 g. (0.2 mole) of benzoyl chloride (Coleman and Bell, C.P.) After standing at room temperature for one hour crystals were formed. Water was added to this mixture, and it was allowed to stand overnight. The white mass of crystals were recrystallized once from isopropyl alcohol and three times from chloroform, followed by two recrystallizations from ethyl alcohol until a constant melting point of 163-163.5° was attained. This compound appeared to be benzanilide since there was no lowering of the melting point when this product was mixed in various proportions with known benzanilide.

Reaction with Alpha-Naphthyl Isocyanate

To 9.3 g. (0.1 mole) of aniline in benzene which had been saturated with sulfur dioxide was added 14.0 g. (0.5 mole) of alpha-naphthyl isocyanate, and there was an immediate formation of white crystals which melted at 233-235°. They appeared to be alpha-naphthylphenyl urea, since there was no lowering of the melting point when they were added to various proportions of known alpha-naphthylphenyl urea.

Reaction with Salicyaldoxime

To a saturated solution of 50 ml. of sulfurous acid at 0° was added 1.9 g. (0.2 mole) of aniline followed by the addition of 2.8 g. (0.02 mole) of salicyaldoxime. Upon addition of the salicyaldoxime an oil was formed in the reaction flask, which upon standing overnight formed light brown crystals which melted at 90-95°. They were very impure, and no solvent was found from which they could be recrystallized, therefore, no analyses were made.

Reactions of the N-Methyl Aniline-Sulfur Dioxide Product with Aldehydes and Ketones

Since there was no report in the literature on the reactions of secondary amine-sulfur dioxide products with aldehydes, the following reactions will be given in this section. Some reactions with ketones will also be shown for use in proof of structure of these compounds.

Reactions with Acetone

To 21.4 g. (0.2 mole) of N-methyl aniline was added 4 ml. of water, and the mixture was saturated with sulfur dioxide. The mixture turned a deep red, then became very viscous and upon stirring crystallized. An excess of acetone was added, and the crystalline product which formed was washed in acetone. A white crystalline product melting at 82-83° was obtained. This product was too unstable to be recrystallized, and therefore, was useless for analyses.

Reaction with Acetophenone

To a saturated solution of 200 ml. of sulfurous acid at 0° was added 53.5 g. (0.5 mole) of N-methyl aniline followed by the addition of 60 g.

(0.5 mole) of acetophenone; there was no immediate reaction. After the mixture had been standing for twelve hours, it was stirred mechanically for a few minutes, and an orange-yellow product which melted at 78-78.5° was obtained. This compound was so unstable that it decomposed upon standing in a stoppered bottle at room temperature.

Reaction with Benzaldehyde

To 21.4 g. (0.2 mole) of N-methyl aniline was added 5 ml. of water, and the mixture was saturated with sulfur dioxide until a crystalline mass as stated above was formed. To this crystalline mixture was added 21.3 g. (0.2 mole) of benzaldehyde. This produced a pasty mass which was washed in chloroform; white crystals melting at 93-94° were obtained. These crystals were fairly stable in air, but they were very sensitive to heat and had to be dried at room temperature. After drying over phosphorus pentoxide they were sent to Clark Microanalytical Laboratory for analyses and their results along with the theoretical calculated for the N-methyl aniline bisulfite derivative of benzaldehyde is as follows:

Clark's Results	Theoretical for $C_{14}H_{17}NSO_3 + H_2O$
C- 57.08%	C-56.56%
H- 5.87%	H- 6.40%

Reaction with m-Nitrobenzaldehyde

To 21.4 g. (0.2 mole) of N-methyl aniline was added 4 ml. of water, and this mixture was saturated with sulfur dioxide. The mixture behaved as has been described in the previous reactions. To this mixture was added 15.1 g. (0.1 mole) of m-nitrobenzaldehyde dissolved in ethanol. Upon addition of the m-nitrobenzaldehyde a crystalline compound was obtained which upon recrystallization from 95° ethanol was found to melt at 124-

124.5°. This compound is fairly stable in air; therefore, it was dried over phosphorus pentoxide at room temperature and sent to Clark Microanalytical Laboratory for analyses; their analyses together with the theoretical calculated for the N-methyl aniline bisulfite derivative of m-nitrobenzaldehyde is as follows:

Clark's Analyses	Theoretical for $C_{14}H_{16}N_2SO_5{+}H_2O$
C- 49.56%	C-49.12%
H- 4.75%	H- 5.27%

It should be noted that the analyses of the products from some reactions show a high carbon content and a low hydrogen content. This is apparently due to the fact that some of the water of crystallization was lost during the drying procedure. If the compound had been more stable, perhaps all the water of crystallization could have been removed at a higher temperature.

TABLE III

Reactions of the N-methyl Aniline-Sulfur Dioxide Product with Aldehyde and Ketones

Compound	M.P.	Analyses Theoretical	 Found
*Acetone	82-83°	Too unstable	
*Acetophenone	78-78.5°	Too unstable	
Benzaldehyde	93-94°	C- 56.56% H- 6.40%	C-57.08% H- 5.87%
m-Nitrobenzaldehyde	124.5°	C-49.12% H- 5.27%	C-49.56% H- 4.75%

*This reaction has been previously noted by other investigators.

Miscellaneous Reactions of Amines, Sulfur Dioxide and Various Organic Substances

In some cases the work of other authors was duplicated, and also certain reactions were studied in order to clear up certain situations in which it was suspected that the previous work was incorrect. The puspose of these reactions will be discussed in the chapter which follows:

Reaction of the Benzylamine-Sulfur Dioxide Product with Benzaldehyde

To 200 ml. of a saturated solution of sulfurous acid at 0° was added 18.2 g. (0.15 moles) of benzylamine followed by the addition of 31.8 g. (0.30 moles) of benzaldehyde. The mixture crystallized to a solid mass in a very few minutes. After two recrystallizations from 95% ethanol, silvery white crystals melting at 113-114° were obtained. This material was dried in an evacuated tube over phosphorus pentoxide and sent to the Clerk Microanalytical Laboratory for analyses. Their results along with the theoretical for an aminosulfonic acid will be shown below:

Clark's Analyses	Theoretical for $C_{14}H_{15}NSO_3 + 1/2\ H_2O$
C-58.16%	C-58.72%
H- 6.01%	H- 5.25%

Reaction of Benzylamine and Benzaldehyde with Sodium Bisulfite

To 10.7 g. (0.1 mole) of benzylamine was added 10.6 g. (0.1 mole) of benzaldehyde. There was an immediate reaction with the formation of a white solid. To this solid was added a solution of 10.4 g. (0.1 mole) of sodium bisulfite. The solution was divided into two equal portions, and to the first portion was added sulfurous acid causing precipitation of crystals which melted at 115-116°. This compound appears to be an aminosulfonic acid. To the second portion was added 6.5 g. (0.5 mole) of aniline hydrochloride dissolved in water. There was an immediate precipitation, and crystals melting at 145-146° were obtained. This is probably the aniline bisulfite derivative of the Schiff base of benzylamine and benzaldehyde.

Reaction of Benzylamine and Acetone with Sodium Bisulfite

To 10.7 g. (0.1 mole) of benzylamine was added 5.8 g. of acetone. There was an immediate precipitation of the Schiff base. To this mixture was added 10.4 g. (0.1 mole) of sodium bisulfite, and the mixture was heated to boiling and divided into two equal portions. To the first was added sulfurous acid, and there was obtained a crystalline compound melting at 91-92° which is probably an aminosulfonic acid. No reaction was obtained when the second portion was reacted with aniline hydrochloride.

Preparation of Phenyltrimethylammonium Iodide

To 12.1 g. (0.1 mole) of dimethylaniline was added 14.2 g. (0.1 mole) of methyl iodide (Eimer and Amend, C.P.) There was an immediate formation of yellow-white crystals. This quaternary ammonium salt was recrystallized from 95% ethanol and upon recrystallization was found to melt at 231-232°.

Reaction of Phenyltrimethylammonium Iodide with Sulfur Dioxide and Acetaldehyde

To 1.9 g. (0.02 mole) of aniline was added an alcohol solution of 3.0 g. of m-nitrobenzaldehyde followed by the addition of 2.0 g. (0.02 mole) of sodium bisulfite. To this mixture was added a water solution of phenyltrimethylammonium iodide, and there was an immediate precipitation of a white crystalline compound. This compound was washed with ether and was found to be stable even when heated to 300°.

Reaction of Phenylsulfimic acid with Benzalaniline

Sulfur dioxide was bubbled into 9.3 g. of aniline until formation of the light yellow phenylsulfimic acid was attained. This was added to a freshly prepared solution of benzalaniline in ether. The phenylsulfimic acid caused an immediate precipitation on its addition. The crystals that formed melted at 127-127.5° on crystallization from water; benzaldehyde was found in the mother liquor.

CHAPTER IV

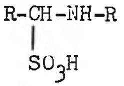
DISCUSSION OF RESULTS

Since a study of the literature showed that there was a great deal of confusion among the various authors as to just what types of products were formed from the reactions of amines and sulfur dioxide with aldehydes and ketones, an attempt will be made to prove the structures of these products. The first portion of this discussion will be concerned with proof of the structures of the products formed from the reactions of amine-sulfur dioxide addition products with aldehydes and ketones.

Reactions of Amine Sulfurdioxide Addition Products with Aldehydes and Ketones

The work of this author will be discussed before that of previous authors so that a basis for a critical discussion of the previous work will be obtained. The experimental work of this author will be used to point out some of the erroneous conclusions of other authors.

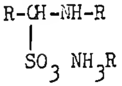
It appears that the reaction of primary amines, sulfur dioxide and aldehydes produces not one but three different products. These products are represented below is I, II and III.



$R-\underset{\displaystyle |\atop \displaystyle SO_3H}{CH}-NH-R$

Amino Sulfonic acid

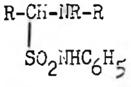
I



$R-\underset{\displaystyle |\atop \displaystyle SO_3\ NH_3R}{CH}-NH-R$

Amine bisulfite derivative of a Schiff base

II



$R-\underset{\displaystyle |\atop \displaystyle SO_2NHC_6H_5}{CH}-NH-R$

Sulfonanilide derivative of a Schiff base

III

A method for the proof of the structures of I and II has been developed. When the sodium derivative of a Schiff base is acidified, the product formed is an aminosulfonic acid (I) as shown by the following equation:

$$\underset{\displaystyle SO_3Na}{\text{R-CH-NH-R}} \xrightarrow{H^+} \underset{\displaystyle SO_3H}{\text{R-CH-NH-R}}$$

Mixed melting points were used as the criterion to show that the compounds were identical. In the cases in which aminosulfonic acids are formed their structure can be ascertained from the above reaction by using the Schiff base formed by the aldehyde and amine in question.

Amine bisulfite derivatives of Schiff bases (II) are also formed in some cases by reactions of amine-sulfur dioxide addition products with aldehydes, and their structures are ascertained by a method analogous to this described above. The sodium bisulfite derivative of a Schiff base is reacted with aniline hydrochloride, and this forms a compound of the type shown as II. This reaction is represented by the following equation:

$$\underset{\displaystyle SO_3Na}{\text{R-CH-NH-R}} + C_6H_5NH_3Cl \longrightarrow \underset{\displaystyle SO_3NH_3C_6H_5}{\text{R-CH-NH-R}} + NaCl$$

As in the above case mixed melting points were used as the criterion to show that the compounds were identical.

The compound shown as III has not been prepared by other methods as were I and II. Since the type of compounds represented by III is more stable than the types shown as I and II, it can be determined fairly well by ultimate analyses, however, the fact that some of the compounds contain water of crystallization must be taken into account.

Only one compound of this type was prepared by this author; this was obtained from the reaction of the aniline-sulfur dioxide addition product with benzaldehyde. An attempt was made to prepare a compound of type II by reacting the sodium bisulfite addition product of benzalaniline with aniline hydrochloride; this produced a product melting at 133°. The product formed by the reaction of aniline and sulfur dioxide with benzaldehyde melts at 127°. Analyses of this compound melting at 133° did not indicate a compound of type II, but it appeared to indicate a compound with a structure between those shown as II and III. The analyses of the Clark Microanalytical Laboratory along with the theoretical for structures II and III will be shown below:

Analyses of Clark Microanalytical Laboratory	Theoretical for Structure II	Theoretical for Structure III
C-65.05% H- 5.91%	C-64.14% H- 5.63%	C-65.70% H- 5.22%

It is possible that a compound of type II was formed, but was unstable and was transformed to the stable compound represented by III.

An attempt was made to prepare the compound shown as III by reacting benzal chloride with sodium sulfite followed by reaction with aniline, however, the benzal chloride hydrolyzed under these conditions.

The analyses of the compound melting at 127° indicates that it has a structure of that shown as III. It appears to contain one-half mole of water of crystallization.

Analyses by Clark Microanalytical Laboratory	Theoretical for $C_{19}H_{18}N_2SO_2 + 1/2\ H_2O$
C-65.62% 65.58%	C-65.70%
H- 5.60% 5.56%	H- 5.22%

This compound melting at 127° was also obtained by reaction of the aniline-sulfur dioxide addition product with benzalaniline. This is another indication that III is the correct structure. This mechanism will be presented later with the other theories and mechanisms of the author.

New compounds not previously reported from the reactions of aldehydes with the primary amine-sulfur dioxide addition product were those with anisaldehyde, o-chlorobenzaldehyde, 2,4-dichlorobenzaldehyde and vanillin. A method for the proof of the structures of these compounds was developed; it is as follows: The Schiff base is prepared and reacted with sodium bisulfite, and the solution is divided into two portions, one of which is reacted with sulfurous acid, while the other portion is reacted with aniline hydrochloride. If the portion that is acidified has the same melting point as the compound formed from the reaction of the amine sulfur dioxide product with the aldehyde, then the product formed from the reaction is assigned the structure shown as I. If the product formed when the aniline hydrochloride is reacted with the solution of the bisulfite compound of the Schiff base has the same melting point as the compound formed from the reaction of the amine-sulfur dioxide product with the aldehyde, then this product is assigned the structure shown as II. It can apparently be used quite successfully with substituted aromatic aldehydes which yield products that are too unstable for analyses.

In quite a few cases there is apparently only one stable product formed from the reaction of the amine sulfur dioxide product with the aldehyde. In this case there is obtained only a clear solution, and no crystals form when the above described method is used.

The compounds acetaldehyde, anisaldehyde, o-chlorobenzaldehyde, 2,4-dichlorobenzaldehyde, salicyaldehyde and vanillin were treated according to the above procedure. From the reactions it appeared that all these compounds had the type structure shown as I. Mixed melting points gave a further indication that this was the correct structure for these compounds.

M-Nitrobenzaldehyde was different from the other aldehydes in that two products were obtained from this compound when reacted with aniline and sulfur dioxide. A compound with a melting point of 126-126.5° and also one melting at 175-176° was obtained from the reaction of aniline and sulfur dioxide with m-nitrobenzaldehyde. The structures of these products were assigned by the reactions of the sodium bisulfite derivatives of the Schiff base of m-nitrobenzaldehyde and aniline as described above. Reaction of the sodium bisulfite derivative of the Schiff base of aniline and m-nitrobenzaldehyde with hydrochloric acid gave a compound melting at 175-176° which indicated structure I for this compound, while reaction with aniline hydrochloride gave a compound melting at 126° indicating structure II for this compound. Since there was some question on the previous analyses of the compound melting at 126°, this compound was sent to Clark Microanalytical Laboratories for analyses. Their results will be shown with the theoretical for a compound with structure II.

Reported by Clark Microanalytical Laboratory	Theoretical for Structure II
C-56.60% 56.50%	C-56.85%
H- 4.96% 4.77%	H- 4.78%

This analysis bears out the theory of this author. Since this was a very stable compound, a good analysis was obtained.

The reaction of benzylamine and sulfur dioxide with benzaldehyde was studied since this is one of the compounds reported by a previous author to have the structure of a benzylamine bisulfite derivative of benzaldehyde. The work of this author indicated that this compound was actually an aminosulfonic acid and, therefore, has the structure shown as I.

The report of this analysis and the theoretical for a structure I compound containing one-half mole of water is given below:

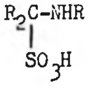
Report by Clark Microanalytical Laboratory	Structure I Compound + 1/2 Mole water
C-58.16%	C-58.72%
H- 6.01%	H- 5.25%

The fact that the carbon analyses are low and the hydrogen analyses are high is probably due to the fact that the compound was somewhat unstable and could not be dried except at low temperatures. Also it was analyzed as received at Clark Microanalytical Laboratory due to this instability.

The Schiff base from benzylamine and benzaldehyde was formed, and this was reacted with sodium bisulfite followed by reaction with both sulfurous acid and aniline hydrochloride. The reaction of the sodium bisulfite derivative of the Schiff base of benzylamine and benzaldehyde with sulfurous acid gives a compound melting at 115-116° which corresponds to that of the compound from benzylamine, sulfur dioxide and benzaldehyde prepared by Adams and Garber. The reaction of the compound with aniline hydrochloride produces crystals which melted at 145° and which should have the structure shown as II. This is also another proof that the compound formed by the reaction of benzylamine and sulfur dioxide and benzaldehyde has the structure shown as I. This would appear to be a better proof of structure in this case than use of analyses since this compound was fairly unstable making it hard to remove the water without decomposition of the compound.

Thus it would appear that the compounds prepared by Adams and Garber from primary amines, sulfur dioxide, and aldehydes are not really amine bisulfite derivatives of aldehydes but are in reality alpha-aminosulfonic acids.

Ketones appear to react with primary amines and sulfur dioxide somewhat differently from aldehydes in that only one type of product has been isolated. The product is an aminosulfonic acid and has the general formula shown as IV.



$$\begin{array}{l} R_2C\text{-}NHR \\ \;\;| \\ \;SO_3H \end{array}$$

IV

The aniline-sulfur dioxide addition product was reacted with acetone, methyl ethyl ketone, methyl isopropyl ketone, and acetophenone. The reaction with di-isopropyl ketone was unsuccessful.

In the cases where a reaction occurred, the same product could be obtained by reaction of the sodium bisulfite derivative of the Schiff base from the ketone and amine with sulfurous acid. When aniline hydrochloride was used in place of sulfurous acid, only a clear solution was obtained. This would indicate that all the ketones formed products of the type shown as IV. The products of the aliphatic ketones were all of low melting point and extremely unstable; therefore, no analyses of these products were attempted. The product from the reaction of acetophenone with aniline and sulfur dioxide was the most stable of any of the products formed from ketones. Even though a faint odor of sulfur dioxide could be detected which showed that the compound was somewhat unstable, it was sent to the Clark Microanalytical Laboratory for analyses. Their report along with the theoretical for a compound of structure IV is given below:

Report by Clark Microanalytical Laboratory	Theoretical for a compound of Structure IV
C-57.72%	C-56.96%
H- 5.89%	H- 5.77%

The reason for the high carbon analysis is probably due to the fact that this compound lost sulfur dioxide. It is also probable that the compound was not completely dry since the hydrogen was not as low as would be expected if sulfur dioxide was lost; this would also account for the very low carbon analysis. The preparation of this compound by another method indicates that IV is the correct structure.

Another point which would indicate that the amine bisulfite derivative was not formed by the reaction of aniline and sulfur dioxide with acetophenone is the fact that acetophenone and other aromatic ketones will not form sodium bisulfite addition products.

Thus it would appear that ketones form only one type of compound with primary amine sulfur dioxide products, these compounds being alpha-amino-sulfonic acids.

Reactions of Secondary and Tertiary Aromatic Amine-Sulfur Dioxide Products with Aldehydes and Ketones

Since there have been no reports of any work with secondary aromatic amine sulfur dioxide addition products with aldehydes, reactions of this type will be presented. It is also a conclusion of the author that the structure of compounds presented by previous authors for the reactions of secondary aromatic amine-sulfur dioxide addition products is incorrect; therefore, reactions with ketones will also be included. Since secondary amines do not form Schiff bases with aldehydes and ketones, it was assumed that they would react like tertiary amines, thereby forming amine bisulfite addition products of aldehydes and ketones. The N-methyl aniline sulfur dioxide product was reacted with acetone, acetophenone, benzaldehyde and m-nitrobenzaldehyde. The compounds formed from the reactions with acetone and acetophenone were very unstable, and, therefore, were not sent for analyses.

The products from the reactions of the N-methyl aniline-sulfur dioxide addition product with benzaldehyde and also with m-nitrobenzaldehyde were sent to Clark Microanalytical Laboratory; they reported the following results for the benzaldehyde derivatives:

Report by Clark Microanalytical Laboratory	Theoretical for the amine bisulfite, $C_{14}H_{17}NSO_3 + H_2O$
C-57.08%	C-56.56%
H- 5.78%	H- 5.67%

For the m-nitrobenzaldehyde derivative they reported:

Report by Clark Microanalytical Laboratory	Theoretical for the amine bisulfite, $C_{14}H_{16}N_2SO_5+H_2O$
C-49.56%	C-49.12%
H- 4.75%	H- 5.27%

The analyses show that the carbon is high and that the hydrogen is low. This is probably due to loss of water of crystallization during drying. The analyses indicate that the secondary amines are probably analogous in their reactions to the tertiary amine bisulfites.

The products from the reactions of the secondary aromatic amine sulfur dioxide products with aldehydes and ketones are much more unstable than those compounds formed from the primary aromatic amine sulfur dioxide products. In fact, the compounds from the reactions of N-methyl aniline-sulfur dioxide with benzaldehyde and m-nitrobenzaldehyde were so unstable that they had to be dried at room temperature. The analogous reactions with the primary amines produced the most stable compounds of any that were prepared. It appears that many amine bisulfites are unstable compounds. The compounds from ketones appeared to be more unstable than the aldehydes.

No reactions with tertiary amines were studied since it is the conclusion of the author that the work previously reported on these reactions is correct. Some studies were made, however, on reactions of a quaternary ammonium salt. It was found that no reaction occurred when phenyltrimethylammonium iodide was reacted with sulfur dioxide and acetaldehyde.

Discussion of Previous Work on Reactions of Amines, Sulfur Dioxide, Aldehydes and Ketones

A critical discussion of the previous work on the reactions of amines and sulfur dioxide with aldehydes and ketones will be made. An attempt will be made to correct the erroneous conclusions of certain authors as well as to point out the valid conclusions of certain authors.

A survey of Schiff's[1] work shows that he obtained two types of compounds from the reactions of primary amines with sulfur dioxide and aldehydes. He reported that in one case he obtained a product consisting of one mole each of the amine, aldehyde and sulfurous acid. It would appear that he obtained aminosulfonic acids in these cases. He also noticed that a different ratio of reacting substances was obtained in the product when benzaldehyde was used as the aldehyde in the reaction; however, his analyses in this case were evidentally not too accurate since he stated that the product contained two moles each of benzaldehyde and aniline to one of sulfur dioxide. The structure presented by this author has only one mole each of benzaldehyde and sulfur dioxide to two moles of aniline and one-half mole of water.

The work of Michaelis[2] followed that of Schiff. He stated that Schiff's analyses of the compound from benzaldehyde was incorrect. He

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1. Schiff, Ann., 210, 123 (1881).

2. A. Michaelis, Ber., 24, 749 (1891).

formulated the same structure as presented by this author for this compound with one exception; he did not indicate that there was water of crystallization in the product. He further stated that he obtained a compound with this same ratio from the reaction of thionyl aniline with aniline and benzaldehyde. He also stated that his product was identical with that of Schiff since both of them have the same melting point.

Mayer[3] also discussed the compound formed from the reaction of aniline, sulfur dioxide and benzaldehyde. He stated that this compound contained one mole of benzaldehyde, two moles of aniline and one mole of sulfurous acid. He assigned this ratio by use of picrate derivatives and he stated that this reaction gave the picrate of aniline and benzalaniline; therefore, he assigned to it the above ratio of two moles of aniline to one of benzaldehyde and one of sulfurous acid. He further stated that he had obtained the aniline bisulfite derivative of benzaldehyde. This compound has not been reported by any other author, and all the experimental evidence obtained by this author indicates that this compound is unstable. Mayer assigned the structure of the aniline bisulfite derivative since he obtained only the picrate derivative of benzalaniline with it.

Eibner[4] did quite a bit of work with primary amines and their reactions with sulfurous acid and aldehydes. He stated that the reactions produced four different types of products. His structural formulas for these pro-

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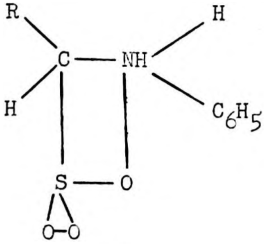
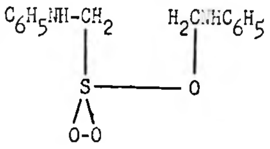
[3] Mario Mayer, Gazz. Chim. ital., 42, I, 50(1912); Ref. cit., C. A., 6, 1138 (1912).

[4] Alexander Eibner, Ann., 316, 89 (1901).

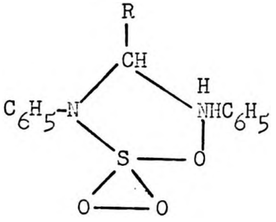
ducts. His structural formulas for these products are shown as V, VI, VII and VIII.



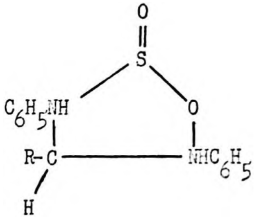
V



VI



VII



VIII

Eibner assigned structural formulas to all his products. He depicted formaldehyde as forming a compound with a structure shown as VI. He showed a formula with the oxygen joined to the nitrogen atom leaving only three bonds on the carbon of the second formaldehyde atom; however, this must have been a misprint. This also gave four bonds to the nitrogen, a structure not found in any of his other formulas; therefore, it is probable that the oxygen should be attached to the carbon atom instead of the nitrogen atom. Aniline and formaldehyde apparently do not form a monomolecular Schiff base. Therefore, the product that Eibner obtained was a polymerized product. Using Eibner's analyses this compound appears to be a dimer of formaldehyde with a molecule of sulfurous acid.

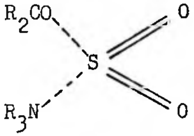
This author agrees with the ratio as given by Eibner, however, the structure of an aminosulfonic acid containing two moles each of formaldehyde and aniline is presented by this author. The reason for the presentation of this formula will be shown later in the section on theory and mechanisms.

Eibner showed acetaldehyde as having the structure shown as V. He also stated that salicyaldehyde formed a compound of this type: the aldehydes, chloral and propionaldehyde, each formed two products, one of which was shown as having a formula of type V, while the other was shown having a formula of type VII. Eibner stated that m-nitrobenzaldehyde also formed two products. He represented one product as having a structural formula of type V and the other as having a structural formula of type VIII. He represented isobutryaldehyde, isovaleraldehyde and benzaldehyde as having the structural formula shown as VIII.

Eibner stated that the compounds shown as having structure V might actually be aminosulfonic acids. This is also the conclusion of this author. Eibner's analyses appear to be correct, however, this author presents different structural formulas for the products from those of Eibner. The formulas presented by this author have the same theoretical analyses as the ones presented by Eibner. One exception was with the product from m-nitrobenzaldehyde which Eibner presented as VIII. From the analyses and chemical reactions of this author it appears that this product really is an amine bisulfite derivative of the Schiff base from m-nitrobenzaldehyde and aniline as shown earlier in this chapter.

Boessneck[5] was one of the first to study the reactions of ketones with amines and sulfur dioxide. He stated that ternary compounds were formed containing one mole each of the amine, sulfur dioxide and the ketone. He did not report any difference in the reactions of primary, secondary, or tertiary amines with ketones.

In 1932, Feigl and Feigl[6] stated that they had prepared additional compounds to those prepared by Boessneck, and they assigned to these compounds the structure shown as IX.



IX

They were of the same opinion as Boessneck that there was no difference in the type of compounds formed from the reactions of primary, secondary and tertiary amines.

Feigl and Feigl used only a sulfur analysis to determine the structure of their compounds; their analyses did not agree very well with the theoretical. In one case, for example, there was a difference of twelve percent, while in a number of others, the analyses varied one to three percent from the theoretical calculated values.

According to the experimental evidence, it appears that the primary amine sulfur dioxide products react differently with ketones than do the

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[5] P. Boessneck, Ber., 21, 1906 (1888).

[6] Von F. Feigl and E. Feigl, Z. Anorg. Allgem. Chem., 203, 57 (1931).

secondary and tertiary amines. This is readily explained by the experimental fact that primary amines form Schiff bases with ketones, which react differently with sulfurous acid than do the secondary amine sulfur dioxide products with ketones, since the secondary and tertiary amines cannot form Schiff bases.

It is the author's opinion that Boessneck and Feigl and Feigl actually obtained aminosulfonic acids from reactions of primary amines and sulfur dioxide with ketones, and that they obtained amine bisulfite derivatives of the ketones when secondary and tertiary amines were used in the reactions.

The more recent work reported on the reactions of amines and sulfur dioxide with aldehydes and ketones was that reported by Adams and Garber[7] and Adams and Lipscomb[8]. Adams and Lipscomb stated that amine bisulfite addition products similar to those obtained from reactions of alkali metal bisulfite with aldehydes and ketones were obtained from the reactions of tertiary amines and sulfur dioxide with aldehydes and ketones. Adams and Garber later used primary amines in place of tertiary amines, and they claimed that the same type of structure was formed. The latter authors did not take into account the fact that Schiff bases would be obtained when the primary amines came into contact with aldehydes and ketones. They assigned the structures by use of a method for sulfur analyses which they devised especially for this work. The method appears to be sound from a chemical point of view; however, their results deviated

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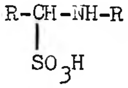
7. Roger Adams and John D. Garber, _J. Am. Chem. Soc._, _71_, 522 (1949).

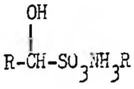
8. Roger Adams and R. D. Lipscomb, _J. Am. Chem. Soc._, _71_, 519 (1949).

from the theoretical calculated percentages in a number of cases. It is the author's opinion that sulfur analyses alone are not sufficient to establish the structure for the compounds discussed here since the structure of an amine bisulfite derivative of an aldehyde or ketone is different from the analogous aminosulfonic acid by only a molecule of water. There is also the additional handicap that many of the compounds contain water of crystallization. The two structures are represented as shown below, X being the structure proposed by this author and XI the structure assumed by Adams and Garber.



$R-\underset{SO_3H}{\underset{|}{CH}}-NH-R$

X .



$R-\overset{OH}{\overset{|}{CH}}-SO_3NH_3R$

XI

By using the results shown in their analyses the theoretical percentage which would be required for both structures shown as X and XI are shown.

Results obtained by Adams and Garber	Theory: Benzylamine-benzaldehyde derivative	
	X	XI
S- 10.8%	S- 11.50%	S-11.00%
	C- 60.64%	C-56.96%
	Benzylamine-isovalderaldehyde derivative	
S- 11.6%	S- 12.40%	S-10.6%
	C- 56.03%	C-52.36%

The results of the carbon and hydrogen analyses of the compound formed from the reaction of benzylamine with benzaldehyde have been discussed previously in this chapter, and it was shown that the carbon analyses do not agree very closely with the theoretical due to the instability of this compound.

Thus it appears that even with carbon analyses, it is hard to assign valid structures to these compounds. A look at the benzaldehyde-benzylamine sulfur dioxide reaction product shows that although the sulfur analyses agreed within 0.2% of their calculated value for structure XI, there was only a 0.5% difference in their results and the theoretical percentage of sulfur calculated for structure X. If we assumed that this compound is an aminosulfonic acid containing one-half mole of water, then the theoretical sulfur content of this compound would be 11.19%, which differs from the theoretical percentage calculated for structure XI by only 0.19%. It would be virtually an impossibility to perfect an analyses to distinguish between two compounds that differed by this small amount. The carbon analyses of an aminosulfonic acid with one-half mole of water and the structure shown as XI differ by 1.76%, which is great enough difference to assign a structure with some assurance even to a compound which is slightly unstable. Although the actual analyses of this author as shown previously differ by 0.5% from the theoretical calculated value for an aminosulfonic acid with one-half mole of water, the structure can be assigned with some assurance, but if the sulfur analyses were off by 0.1%, the analyses would be of no value.

The difference between the calculated value and the found value of Adams and Garber's sulfur analyses of the compound from benzylamine and isovaleraldehyde was 1.0%. From their sulfur analyses the structure shown as X would be indicated, however, Adams and Garber postulated the incorrect structure shown as XI. Thus we can see from these examples that the analyses of Adams and Garber were not valid enough to assign structures, especially since water of crystallization is found in many of the compounds.

Adams and Garber stated that they obtained no compound from aniline, sulfur dioxide and benzaldehyde. This appears very unusual since this compound has been reported by a number of investigators and is very easily obtainable no matter what proportions of the reacting materials were used.

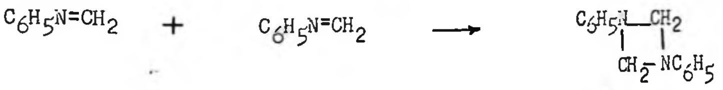
Since it has been shown previously in this chapter that the chemical method of analyses of this author indicated that an aminosulfonic acid is the correct structure for the compounds obtained by Adams and Garber, it is the author's opinion from this portion of the work that the chemical method of analyses is a more reliable criterion for use in assigning the structures of these compounds.

Mechanisms and Theories Presented for some Reactions of Amines and Sulfur Dioxide with Aldehydes and Ketones

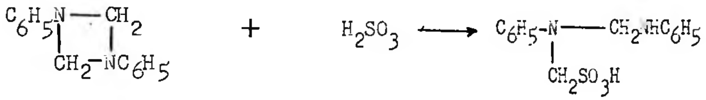
In the course of this work the author developed certain theories and mechanisms to account for some of the facts obtained and also to show how some of the reactions might take place.

Since the reaction of formaldehyde and sulfur dioxide with aniline produced a product unlike that obtained from any other aldehyde, a mechanism is presented by this author to account for this reaction. It is as follows:

$$C_6H_5NH_2 + CH_2O \longrightarrow C_6H_5N{=}CH_2 + H_2O$$

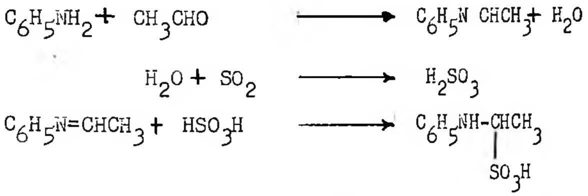


(unstable intermediate)



The first step would be the formation of a monomolecular Schiff base which would then dimerize, and this compound would immediately react with sulfurous acid since the four membered ring would be fairly unstable. In the reaction of sulfurous acid with the dimer, no matter how the ring opens the same product will be obtained.

The mechanism given by this author for the reaction of aldehydes and ketones and sulfur dioxide with primary amines to produce aminosulfonic acids is presented as follows using acetaldehyde as an example.



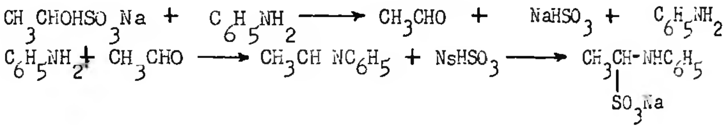
$$C_6H_5NH_2 + CH_3CHO \longrightarrow C_6H_5N\ CHCH_3 + H_2O$$

$$H_2O + SO_2 \longrightarrow H_2SO_3$$

$$C_6H_5N{=}CHCH_3 + HSO_3H \longrightarrow C_6H_5NH\text{-}\underset{\displaystyle SO_3H}{\underset{|}{C}}HCH_3$$

The first step would be the formation of the Schiff base followed by the addition of sulfurous acid to the unsaturated system in the same manner that sodium bisulfite as added to an aldehyde.

The reaction of acetaldehyde sodium bisulfite with aniline probably goes by a mechanism analogous to that shown above. Since aniline is a base and aldehyde sodium bisulfite products are decomposed by acids and bases, a decomposition would take place when a base such as aniline is added, regenerating the aldehyde and the sodium bisulfite. The acetaldehyde would then react with aniline to form the Schiff base, which would then react with the freed sodium bisulfite. When this mixture is acidified, the free aminosulfonic acid would be formed. The mechanism for this reaction is pictured as follows:



$$CH_3CHOHSO_3Na + C_6H_5NH_2 \longrightarrow CH_3CHO + NaHSO_3 + C_6H_5NH_2$$

$$C_6H_5NH_2 + CH_3CHO \longrightarrow CH_3CH\ NC_6H_5 + NsHSO_3 \longrightarrow \underset{\displaystyle SO_3Na}{\underset{|}{CH_3CH}}\text{-}NHC_6H_5$$

The fact that Abelin and Perelstein stated that sodium ethoxide accelerated the reaction[9] gives a further indication that the above mechanisms are correct since the presence of a base would accelerate the decomposition of the aldehyde-sodium bisulfite derivative.

The sulfonic acid structure has been shown by many investigators to be the correct one for the product formed when a primary amine is condensed with the sodium bisulfite derivative of an aldehyde. Backer and Mulder[10] prepared the aminomethanesulfonic acid by condensation of ammonia with the sodium bisulfite addition product of formaldehyde. They performed a great number of experiments in order to prove this structure. One of the most conclusive bits of evidence was the preparation of the potassium salt of chloromethane sulfonic acid by a known method and also by reaction of the product obtained from the condensation of ammonia with formaldehyde bisulfite. Backer and Mulder also prepared a large number of derivatives of the aminomethanesulfonic acid to prove its structure. Bucherer and Schwalbe[11] also claimed that an aryl-aminomethanesulfonic acid was obtained by the reaction of aromatic amines with sodium hydroxymethanesulfonates. Abelin

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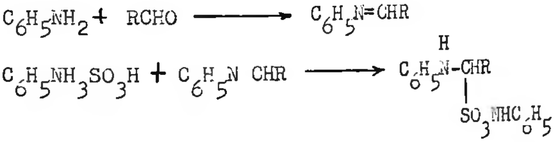
[9] I.J. Abelin and M. Perelstein, Ann., 411, 216 (1916).

[10] H.J. Backer and H. Mulder, Rec. trav. chem., 52, 454 (1933).

[11] H. Bucherer and A. Schwalbe, Ber., 39, 2796 (1906).

and Perelstein also showed this reaction to be feasible for preparation of many alpha-aminosulfonic acids[12]. They were of the opinion, however, that the ether structure shown as II in Chapter II was correct. This was later proven to be incorrect. McIlwain[13] also stated that alpha-aminosulfonic acids were formed from the reaction of amines with sodium bisulfite compounds of aldehydes.

The mechanism for formation of an amine bisulfite derivative of the Schiff base is given as follows:



$$C_6H_5NH_2 + RCHO \longrightarrow C_6H_5N{=}CHR$$

$$C_6H_5NH_3SO_3H + C_6H_5N\ CHR \longrightarrow C_6H_5\overset{H}{N}\text{-}\underset{\displaystyle SO_3NHC_6H_5}{CHR}$$

The Schiff base was probably formed first and this reacted with the aniline bisulfite to form the amine bisulfite derivative of the Schiff base. This compound usually is more unstable than the aminosulfonic acid and formation would probably be more likely with an excess of the amine bisulfite. In all cases in which this type of compound was formed, the aminosulfonic acid was also formed and in all cases except when m-nitrobenzaldehyde was used, the aminosulfonic acid appeared to be the most stable compound. Chloral and propionaldehyde each formed two compounds, and the aminosulfonic acid structure was the most stable compound in these cases.

An attempt was made to prepare a compound with the structure of a sulfonanilide derivative of the Schiff base in a manner similar to that

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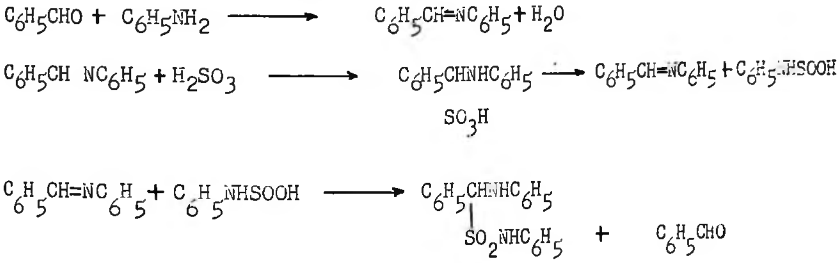
[12] Abelin and Perelstein, *loc. cit.*

[13] Henry McIlwain, *J. Chem. Soc.*, *75* (1951).

of Backer and Mulder in which they reacted methylene chloride with sodium sulfite and obtained the chlorosulfonic acid. Using benzal chloride in place of methylene chloride was unsatisfactory since the benzal chloride is hydrolyzed to benzaldehyde under these conditions.

This author presents as the third type of compound formed from the reaction of aniline, sulfur dioxide and aldehydes a sulfonanilide derivative of a Schiff base shown as III in this chapter. This type of compound was obtained when benzaldehyde was used as the aldehyde. The mechanisms for the formation of this structure are shown as follows:



$$C_6H_5CHO + C_6H_5NH_2 \longrightarrow C_6H_5CH{=}NC_6H_5 + H_2O$$

$$C_6H_5CH\ NC_6H_5 + H_2SO_3 \longrightarrow \underset{SO_3H}{C_6H_5CHNHC_6H_5} \longrightarrow C_6H_5CH{=}NC_6H_5 + C_6H_5NHSOOH$$

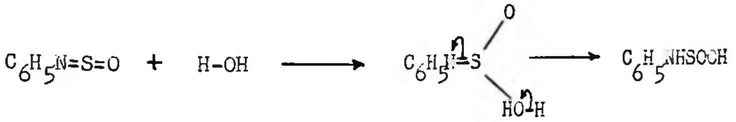
$$C_6H_5CH{=}NC_6H_5 + C_6H_5NHSOOH \longrightarrow \underset{SO_2NHC_6H_5}{C_6H_5CHNHC_6H_5} + C_6H_5CHO$$

The first step would be the formation of the Schiff base which would add sulfurous acid. This compound could break down to form the Schiff base, phenylsulfimic acid and benzaldehyde. The Schiff base then could combine with the phenylsulfimic acid, leaving the benzaldehyde in the free form.

This mechanism, described above, is indicated by the fact that when phenylsulfimic acid is added to an ether solution of freshly prepared benzalaniline, there is formed the sulfonanilide derivative of benzalaniline having the melting point of 127°, as does the compound formed when the aniline sulfur dioxide addition product is added to benzaldehyde.

Bucherer and Schwalbe[14] have shown that the compound formed from the condensation of the bisulfite compound of benzaldehyde with aniline produces the compound melting at 127° on acidification. Their analyses show it to have the same empirical formula as has been shown. This gives another proof that the mechanism shown above is correct since the structure of the compounds formed from condensation of amines with aldehyde bisulfite derivatives are definitely known to be alpha-amino sulfonic acids. This indicates that the aminosulfonic acid is unstable in this case.

Another proof of this mechanism is taken from the work of Michaelis[15], in which he obtained a product with a melting point of 124-125° by reaction of thionyl aniline, aniline and benzaldehyde. The formation of the Schiff base between aniline and benzaldehyde furnishes water which can react with the thionyl aniline to produce the phenylsulfimic acid, and, therefore, the identical mechanism is indicated when the formation of these compounds is shown. The formation of phenylsulfimic acid from thionyl aniline and water is as follows:



This is analogous to the formation of a phenyl carbamic acid when water is added to phenylisocyanate; however, in this case the acid is unstable and decomposes to give aniline. This reaction is shown as follows:

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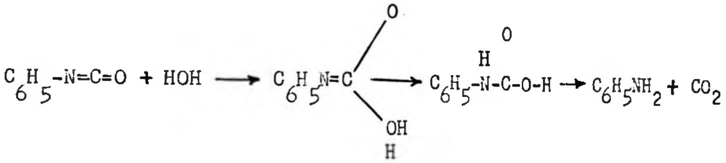
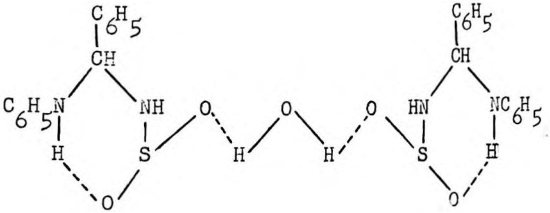
[14] Bucherer and Schwalbe, loc, cit.

[15] Michaelis, loc. cit.



Many structures have been assigned to the compound obtained by the reaction of aniline, sulfur dioxide and benzaldehyde. The analyses of many investigators show that the compound contains one-half mole of water. The following structure has the same empirical formula and would also account for the presence of the one-half mole of water.



XII

This structure shows that a possible chelate could be formed, and in this case the chelate would be a pseudo-six membered ring. This structure accounts for the stability of this type of compound, in contrast to the instability of many of the compounds formed from the reactions of amine-sulfur dioxide addition compounds with aldehydes.

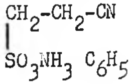
Miscellaneous Reactions of Amine-Sulfur Dioxide Addition Products

It was found that the amine-sulfur dioxide addition product would react with a number of different organic compounds; however, in many cases the same product was obtained as would have been obtained if only aniline was used.

Aniline and sulfurous acid were reacted with acrylonitrile and a very stable compound was obtained; it was sent to Clark Microanalytical Laboratory for analyses. They reported the following results.

Report by Clark Microanalytical Laboratory	Theoretical for the aniline bisulfite compound, $C_9H_{12}N_2SO_3$
C- 47.57%	C- 47.37%
H- 5.19%	H- 5.26%

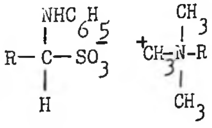
Thus it appears that primary amines can form still another type of compound, that is the primary amine bisulfite of compounds with which they are not capable of forming Schiff bases. This primary amine bisulfite compound is shown as XIII, and is analogous to the compounds formed by reaction of sodium bisulfite with unsaturated compounds.



$$\begin{array}{l} CH_2-CH_2-CN \\ | \\ SO_3NH_3\ C_6H_5 \end{array}$$

XIII

An interesting compound was obtained from reaction of phenyltrimethylammonium iodide with a sodium bisulfite derivative of a Schiff base. The structure of this product is presented below as XIV. This compound appears to be analogous to a quaternary ammonium salt.



$$R-\underset{H}{\overset{NHC_6H_5}{C}}-SO_3^{-}\quad {}^{+}CH_3-\underset{CH_3}{\overset{CH_3}{N}}-R$$

XIV

Since the reaction of a primary amine and sulfurous acid gave an amine bisulfite derivative, some reactions with this type of compound were studied; it is assumed that secondary and tertiary amine-bisulfite will react similarly. Reaction of primary amine bisulfites were tried with compounds such as allyl alcohol and styrene in the presence of hydrogen peroxide in an attempt to get an amine bisulfite derivative since sodium bisulfite forms an addition product under these conditions; however, these reactions were unsuccessful.

Reactions of primary amines and sulfurous acid with various esters were unsuccessful; it would appear that reactions of amine bisulfites are not completely analogous with those of alkali metal bisulfites, however, as has been shown they are analogous in some cases.

CHAPTER V

SUMMARY AND CONCLUSIONS

1. The work done previously on the reactions of aromatic amine sulfur dioxide addition products with aldehydes and ketones has been correlated and summarized.

2. It appears that there are three main structures which may be assigned to the substances formed from the reactions of primary aromatic amine sulfur dioxide addition products with aldehydes, which are alpha-aminosulfonic acids, amine bisulfite and sulfonanilide derivatives of Schiff bases.

3. It has been shown that all the ketones that were reacted with primary aromatic amine sulfur dioxide products gave only one type of product, namely alpha-aminosulfonic acids.

4. Reactions of secondary aromatic amine sulfur dioxide addition substances with aldehydes to form amine bisulfite derivatives are reported for the first time.

5. The secondary and tertiary aromatic amine sulfur dioxide addition products are analogous in their reactions with aldehydes and ketones, since both products formed amine bisulfite derivatives.

6. The reactions of aromatic amine sulfur dioxide addition products with ketones do not produce ternary compounds, as reported in the literature, but give amine bisulfites. This is shown by the fact that no reaction takes place between amines, sulfur dioxide and ketones in the absence of water.

7. It has been shown that sulfur analyses alone, as was reported in the literature, are not sufficient for proof of structures of all the compounds described in this dissertation. Chemical means for proof of these structures are described.

8. It has been shown for the first time that the aniline sulfur dioxide addition product will react with compounds other than aldehydes and ketones.

9. Adams and Garber gave incorrect structures for the reactions of primary amine sulfur dioxide addition products with aldehydes and ketones although the earlier work of Adams and Lipscomb, in which tertiary amines were used, is correct.

10. Eibner's analyses of the amine sulfur dioxide aldehyde products were found to be correct, but new formulas were given to replace many of those he had incorrectly proposed.

11. Reactions of aniline bisulfite with unsaturated, unconjugated systems such as styrene and allyl alcohol in the presence of peroxides were unsuccessful since the amine bisulfites were too easily oxidized.

12. A reaction of aniline bisulfite with acrylonitrile to form an aniline bisulfite derivative has been discovered.

13. A compound analogous to a quaternary ammonium salt has been prepared for the first time from the sodium bisulfite addition compounds of Schiff bases by reaction with a quaternary ammonium salt.

14. Mechanisms have been given to show the formation of compounds from the reactions of aromatic sulfur dioxide addition products with aldehydes and ketones.

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