SULFAMIC ACID, SULFAMIDE, AND RELATED AQUO-AMMONOSULFURIC ACIDS[1]

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Received August 3, 1939

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[1] Presented at the Symposium on the Chemistry of Liquid Ammonia Solutions, held at Milwaukee, Wisconsin, September, 1938, under the auspices of the Division of Physical and Inorganic Chemistry and the Division of Organic Chemistry of the American Chemical Society.

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I. INTRODUCTION

Prior to the general acceptance of Franklin's work, no successful attempt to systematize the chemistry of nitrogen had ever been made. Recorded investigations, despite their number, lacked a fundamental and unifying basis. It is not surprising, therefore, that the chemical relationships of a large number of nitrogen–sulfur compounds had remained obscure. The recent announcement that sulfamic acid is now being produced on a commercial scale (43, 66) has aroused and stimulated new interest in this group of compounds. In his notable monograph on *The Nitrogen System of Compounds* (59) Franklin calls attention to the fact that a large number of compounds may be regarded as derivatives of a relatively small number of so-called aquo-ammonosulfuric acids. These are depicted diagrammatically in chart I.

Successive replacement of the hydroxyl groups in sulfuric acid by the isosteric NH_2 group leads to sulfamic acid (1) and sulfamide (2), both of which are formally mixed aquo-ammonosulfuric acids. Imidodisulfonic (3) and nitrilosulfonic (4) acids are to be considered deammonation products of sulfamic acid. Imidodisulfamide (5), as well as sulfimide (6) and trisulfimide (7), are in a like manner related to sulfamide. The arrangement depicted in chart I is reminiscent of the relationships which obtain among the aquo-ammonocarbonic acids, such as carbamic acid, urea, cyanic acid, and cyanuric acid. This similarity is apparent not only from a comparison of the respective compounds as listed in table 1, but becomes increasingly more evident in the discussion of the properties and reactions of the various aquo-ammonosulfuric acids which follows.

It is, of course, a relatively simple matter to set up formal relationships among compounds of this sort, as has been done above, and even to extend this limited list of known aquo-ammonosulfuric acids to many other hypothetical ones, but such a procedure deserves no consideration unless (*1*) it represents a definite contribution to the organization of existing knowledge, and (*2*) it is so designed as to be of value in the further investigation of this field. It is, therefore, the purpose of the authors to present in this paper a concise outline of the chemistry of the compounds listed in table 1. An especial attempt is made in the treatment of the subject to demonstrate (*1*) that the aquo-ammonosulfuric acids are prepared (*a*) either by sol-

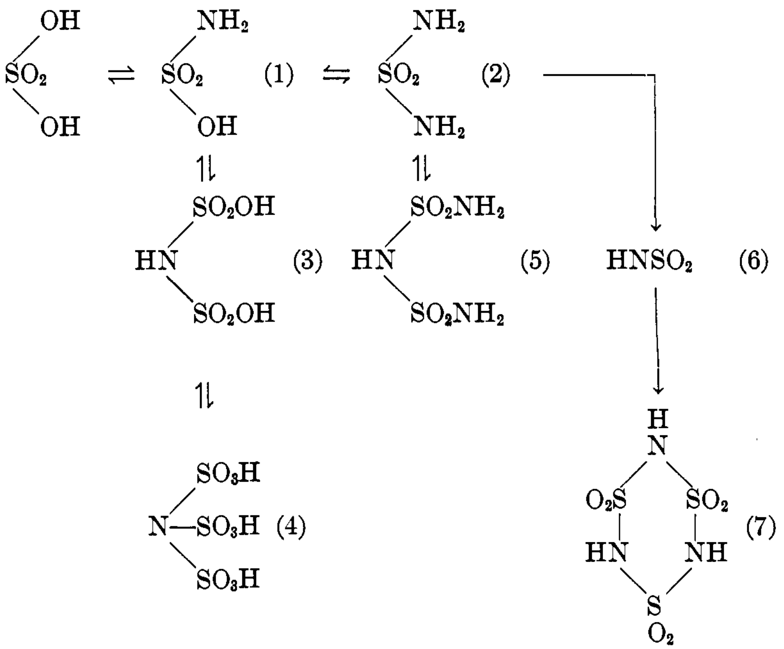


CHART I. The aquo-ammonosulfuric acids. Only known compounds are listed, but it is obvious that the above outline could be extended by processes of ammonation, deammonation and ammonolysis, to include innumerable hypothetical aquo-ammonosulfuric acids and ammonosulfuric acids.

TABLE 1

Mixed aquo-ammono acids related to sulfuric acid and to carbonic acid

RELATED TO $SO_2(OH)_2$		RELATED TO $CO(OH)_2$	
Formula	Name	Formula	Name
H_2NSO_2OH	Sulfamic acid (amidosulfonic, amidosulfuric)	H_2NCOOH	Carbamic acid
$H_2NSO_2NH_2$	Sulfamide (diamide of sulfuric acid, diamidosulfuric acid)	H_2NCONH_2	Urea
$HN(SO_2NH_2)_2$	Imidodisulfamide	$HN(CONH_2)_2$	Biuret
$HN(SO_2OH)_2$	Imidodisulfonic acid	$HN(COOH)_2$	Imidodicarbonic acid
$HNSO_2$	Sulfimide	$HNCO$	Cyanic acid
$(HNSO_2)_3$	Trisulfimide	$(HNCO)_3$	Cyanuric acid

volysis (ammonolysis or aminolysis) of sulfuric acid and its derivatives, or (*b*) in some instances by the nitridation of sulfurous acid; (*2*) that experimental evidence shows that the various aquo-ammonosulfuric acids are actually interconvertible by processes of solvation and desolvation (specifically in the case of the compounds listed in table 1, by the addition or removal of ammonia); (*3*) that hydrolysis leads to sulfuric acid and ammonia (or amines) as end products; and (*4*) that these substances actually do behave as acids in liquid ammonia, warranting their designation as aquo-ammonosulfuric acids.

II. Sulfamic Acid, NH_2SO_3H

A. PREPARATION

Sulfamic acid was first isolated by Berglund (31) in 1878, but it was not until 1887, when Raschig (102) discovered a comparatively simple method for its preparation, that the substance became interesting to chemists. It is referred to as amidosulfonic acid in the older literature, but is now generally known as sulfamic acid because its structure is not unlike that of carbamic acid, NH_2COOH.

Four general methods may be used in the preparation of sulfamic acid. All are based upon certain fundamental reactions which serve to emphasize the chemical character of sulfamic acid as an aquo-ammonosulfuric acid. These are summarized briefly.

1. Ammonolysis of sulfuric acid and related compounds

Such procedures as those which involve the action of aqueous or liquid ammonia upon fluoro- and chloro-sulfonates (132), upon nitrosylsulfuric acid (118), and upon sulfur trioxide addition compounds, *viz.*, with pyridine (9), tertiary amines (11), and dioxane (121), are ammonolytic in character and involve conversion of an aquo derivative of sulfuric acid into an aquo-ammonosulfuric acid.

2. The nitridation of sulfur dioxide, sulfurous acid, sulfites, and hydrosulfites

In some instances sulfamic acid is obtained directly; in other instances related aquo-ammonosulfuric acids are formed which undergo hydrolysis to sulfamic acid. Thus, the Raschig method (102), involving the reaction of sulfur dioxide with hydroxylamine salts in aqueous solution or in the presence of pyridine, may be interpreted as representing the nitridation of tetravalent sulfur to the hexavalent state with the corresponding reduction of the nitrogen to the ammonia state.

$$NH_2OH + SO_2 \rightarrow NH_2SO_2OH$$

Hydroxylamine salts and bisulfites react in a similar fashion to give sulfamates (102, 103, 104).

Acetoxime reacts with sulfurous acid, probably with the intermediate formation of an unstable addition compound, to give sulfamic acid (56a).

$$(CH_3)_2C{=}NOH + SO_2 \rightarrow (CH_3)_2C{=}NSO_3H \xrightarrow{HOH} (CH_3)_2C{=}O + NH_2SO_2OH$$

Chloramine (ammonohypochlorous acid) reacts with sulfites to give sulfamic acid (60).

The interaction of nitrous acid with bisulfite, as depicted in chart II, is a specific case where the reduction of nitrous acid can be shown to proceed through a number of intermediate stages leading, under proper conditions (high temperature and excess bisulfite), to a nitrilosulfonate, a salt of an aquo-ammonosulfuric acid (see page 72). This compound undergoes hydrolysis to the sulfamate.

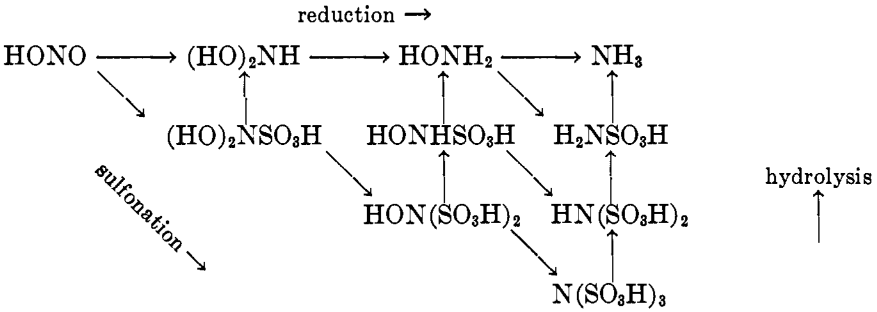


CHART II. Interaction of sulfurous acid with nitrous acid. The reduction of nitrous acid in its simplest aspect is depicted horizontally, leading to ammonia as the end product. Actual, as well as hypothetical, sulfonation reactions are represented diagonally. At low temperature nitrites and bisulfites react to give hydroxylaminodisulfonates, while at higher temperature with excess bisulfite the nitrilosulfonates are obtained. The reactions upward represent hydrolytic processes.

3. *Hydrolysis of aquo-ammonosulfuric acids*

Attention has already been called to the fact that the hydrolysis of nitrilosulfonates and imidodisulfonates leads to sulfamic acid (47, 113).

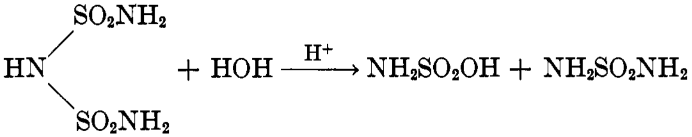
$$N(SO_3K)_3 + 2HOH \rightarrow NH_2SO_2OK + 2KHSO_4$$

$$NH(SO_3K)_2 + HOH \rightarrow NH_2SO_2OK + KHSO_4$$

Hydrolysis of sulfamide in alkaline solution (128) proceeds in accordance with the equation:

$$NH_2SO_2NH_2 + NaOH \rightarrow NH_2SO_2ONa + NH_3$$

Acid hydrolysis of imidodisulfamide (70) presumably yields both sulfamic acid and sulfamide.

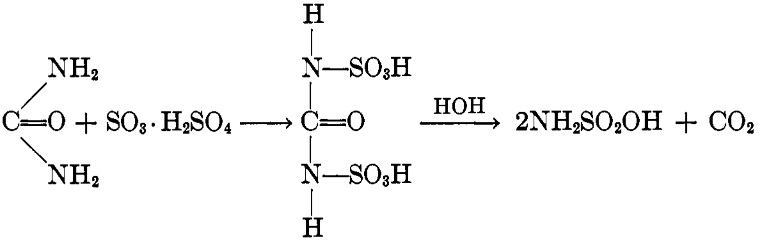


$$HN(SO_2NH_2)_2 + HOH \xrightarrow{H^+} NH_2SO_2OH + NH_2SO_2NH_2$$

All these reactions represent cases of partial hydrolysis of aquo-ammonosulfuric acids stopping at the sulfamic acid stage.

4. Hydrolysis of N-acyl sulfamic acids

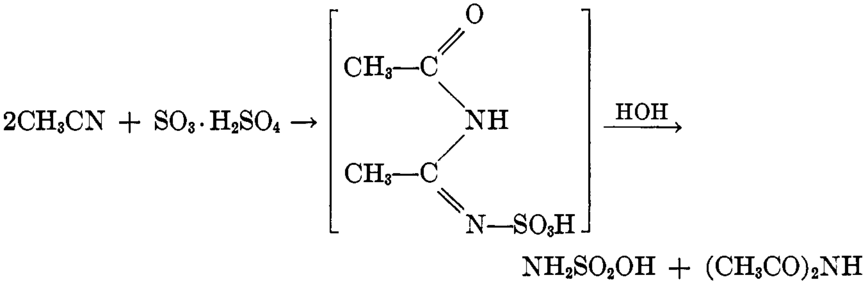
Many of these substances are known; some of them are quite resistant to hydrolysis. The present commercial method for the production of sulfamic acid, involving the action of fuming sulfuric acid upon urea (13, 18), presumably goes through the following steps:



$$(NH_2)_2C{=}O + SO_3 \cdot H_2SO_4 \longrightarrow (HSO_3NH)_2C{=}O \xrightarrow{HOH} 2NH_2SO_2OH + CO_2$$

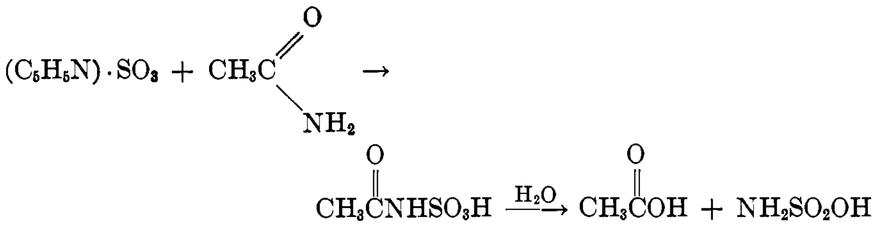
The intermediate is not very stable and under proper conditions undergoes hydrolysis and decarboxylation.

The action of fuming sulfuric acid on acetonitrile (51) likewise leads to an unstable intermediate, which hydrolyzes in accordance with the following equation:



$$2CH_3CN + SO_3 \cdot H_2SO_4 \rightarrow \left[CH_3C(=O)\text{—}NH\text{—}C(CH_3){=}N\text{—}SO_3H\right] \xrightarrow{HOH} NH_2SO_2OH + (CH_3CO)_2NH$$

Trisubstituted sulfamic acids, such as pyridine–sulfur trioxide, react with acid amides (22, 23) to give *N*-sulfonated products, which hydrolyze to give sulfamic acid.



$$(C_5H_5N)\cdot SO_3 + CH_3C\begin{matrix}\diagup O \\ \diagdown NH_2\end{matrix} \rightarrow CH_3\overset{\overset{O}{\|}}{C}NHSO_3H \xrightarrow{H_2O} CH_3\overset{\overset{O}{\|}}{C}OH + NH_2SO_2OH$$

Chlorosulfonic acid (42, 144) and urea also react to form an unstable *N*-acylsulfamic acid, which likewise breaks down to form sulfamic acid as the principal product.

Cyanic acid (85) and sulfuric acid react in ethereal solution to give sulfamic acid.

B. PHYSICAL PROPERTIES OF SULFAMIC ACID

Sulfamic acid is a crystalline, non-hygroscopic solid, melting with decomposition at 205°C. It is obtained from aqueous solution in the form of rhombic crystals. The solubility in 100 g. of water (43, 66) varies from 14.689 g. at 0°C. to 47.08 g. at 80°C. This solubility in water is decreased markedly by sulfuric acid, so that sulfamic acid is practically insoluble in 70–80 per cent sulfuric acid (43). Its solubility in organic oxygen-containing solvents is only slight or negligible (43). In nitrogenous solvents such as liquid ammonia (37) and formamide (43) sulfamic acid, as might be predicted, is very soluble.

C. CHEMICAL PROPERTIES OF SULFAMIC ACID

Sulfamic acid is highly ionized in aqueous solution. Conductometric (112) and pH measurements (43) place it in the same range of acid strength as hydrochloric, nitric, and sulfuric acids. In view of its strength as an acid, together with its desirable physical properties, sulfamic acid has been recommended for use as a primary standard in acidimetry (38, 71, 72, 92). It has actually been found to be superior to such standards as benzoic acid, succinic acid, potassium biiodate, and potassium acid phthalate. It can be titrated using indicators whose transition points lie within a pH range of 4.5 to 9.

Thus far standard solutions have not been used, because of the fact that sulfamic acid undergoes hydrolysis (that is, conversion from an ammonosulfuric acid into an aquosulfuric acid) in accordance with the equation:

$$NH_2SO_3H + HOH \rightarrow HOSO_3H + NH_3 \text{ (or } NH_4HSO_4)$$

This reaction is barely discernible at ordinary temperatures (no appreciable concentration of sulfate ion can be detected until after several weeks), but becomes quite rapid at higher temperatures. According to Cupery (43) a 10 per cent solution of sulfamic acid hydrolyzes to the extent of 40 per cent in 6 hr. at 80°C.

In the cold, chlorine, bromine, and chlorates oxidize sulfamic acid to sulfuric acid. Potassium permanganate, chromic acid, and ferric chloride exert no oxidizing action (47).

At low temperatures hypochlorous acid is said to form an unstable *N*-chloro derivative (135).

$$NH_2SO_2OH + HOCl \rightarrow ClNHSO_3H + HOH$$

The free *N*-chlorosulfamic acid is not sufficiently stable to be isolated. Some of its salts, however, were found to be more stable and were obtained in crystalline form.

Ephraim and Gurewitsch (53) allowed thionyl chloride to react with sulfamic acid at 150°C. in the hope of obtaining sulfamyl chloride. Curiously, other investigators confused the purpose with the results of these experiments, asserting that the work of Ephraim and Gurewitsch could not be substantiated. Actually, these subsequent investigators verified the results obtained by Ephraim and Gurewitsch to the effect that the reaction does not proceed in accordance with the equation (45)

$$NH_2SO_2OH + SOCl_2 \rightarrow NH_2SO_2Cl + HCl + SO_2$$

Denivelle also hoped to prepare sulfamyl chloride by the action of ammonia upon phenyl chlorosulfonate. While it is possible that sulfamyl chloride does form as an intermediate, Denivelle believes that it is decomposed rapidly with the formation of trisulfimide.

$$C_6H_5OSO_2Cl + NH_3 \rightarrow C_6H_5OH + NH_2SO_2Cl$$

$$3NH_2SO_2Cl \rightarrow (NHSO_2)_3 + 3HCl$$

Phosphorus pentachloride was allowed to react with sulfamic acid in another attempt to prepare sulfamyl chloride. A complex addition compound was isolated, corresponding to the formula $PCl_3 \cdot ClSO_2NH_2$ (53). Thus far, all attempts to isolate sulfamyl chloride have failed.

Solutions of sulfamic acid or acid solutions of its salts are rapidly and completely decomposed by the addition of nitrite (32, 66).

$$NH_2SO_2OH + KNO_2 \xrightarrow{H^+} KHSO_4 + N_2 + H_2O$$

This reaction takes place quantitatively and is, therefore, useful in the qualitative and quantitative determination of either sulfamic acid or nitrite, especially in the presence of nitrate (21). This reaction has also been adapted to the separation of lanthanum earths from the rare-earth metals included in the yttrium group. Sodium nitrite is added to a slightly acid solution of the sulfamates of the rare-earth metals. Reaction takes place, resulting in the precipitation of the double sodium rare-earth sulfates of the lanthanum earths which are practically insoluble, while the corresponding compounds of yttrium and rare earths of higher atomic weight stay in solution (82).

Sulfamic acid reacts with concentrated nitric acid to form nitrous oxide (14).

$$NH_2SO_2OH + HNO_3 \rightarrow H_2SO_4 + H_2O + N_2O$$

This reaction can readily serve as a convenient method for preparing pure nitrous oxide.

D. SALTS OF SULFAMIC ACID (43, 66)

A further proof of the strength of sulfamic acid is furnished by the fact that it reacts readily with basic oxides, hydroxides, and carbonates to yield the corresponding sulfamates. These are, with but few exceptions, soluble in water. The sulfamates of lead, magnesium, and sodium are more soluble in water than the corresponding sulfates, nitrates, chlorides, and acetates. Not only have simple salts of sulfamic acid been isolated, but a number of basic silver and mercury salts as well as a whole series of cobalt (52) and platinum (81, 101) complexes have been characterized.

Ammonium sulfamate is readily obtainable by solution of the free acid in liquid ammonia (37). Solutions of ammonium sulfamate in liquid ammonia are definitely acidic in character. Because of the highly basic nature of ammonia as a solvent, not only is the hydroxylic hydrogen of the acid dissociated, but an amidic hydrogen as well, with the result that sulfamic acid behaves as a dibasic acid forming a disodium (37, 66) and a dipotassium (34) salt.

As might be expected, sulfamic acid enters into combination with compounds containing a basic amino group to give both alkyl- (37, 66) and aryl-substituted ammonium salts.

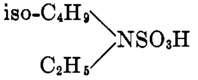
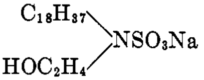
III. NITROGEN-SUBSTITUTED DERIVATIVES OF SULFAMIC ACID

The large number of *N*-substituted sulfamic acids may readily and easily be placed in certain distinct classes depending upon the nature of the substituent attached to the nitrogen atom. The following classification is recommended. Typical examples are given under each group for illustration.

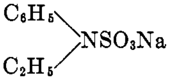
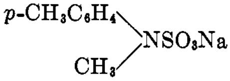
I. *N*-monosubstituted sulfamic acids, $RNHSO_3H$, where R = alkyl, aryl, acyl, or arylsulfonyl:
  (a) CH_3NHSO_3H (131); $C_{15}H_{31}NHSO_3Na$ (67)
  (b) $C_6H_5NHSO_3K$ (17); α-$C_{10}H_7NHSO_3NH_4$ (99)

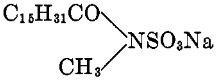
(c) $CH_3CONHSO_3K$ (23); $C_{15}H_{31}CONHSO_3Na$ (68)
(d) $C_6H_5SO_2NHSO_3K$ (23)

II. *N*-disubstituted sulfamic acids, $RR'NSO_3H$, where $R(R')$ = alkyl, aryl, or acyl:

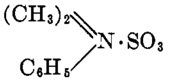
(a)

$\begin{matrix}\text{iso-}C_4H_9 \\ C_2H_5\end{matrix}\!>\!NSO_3H$ (86);

$\begin{matrix}C_{18}H_{37} \\ HOC_2H_4\end{matrix}\!>\!NSO_3Na$ (67)

(b) $(C_6H_5)_2NSO_3Na$ (76)

(c)

$\begin{matrix}C_6H_5 \\ C_2H_5\end{matrix}\!>\!NSO_3Na$ (130);

$\begin{matrix}p\text{-}CH_3C_6H_4 \\ CH_3\end{matrix}\!>\!NSO_3Na$ (139)

(d)

$\begin{matrix}C_{15}H_{31}CO \\ CH_3\end{matrix}\!>\!NSO_3Na$ (68)

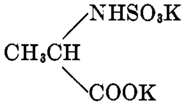
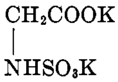
III. *N*-trisubstituted sulfamic acids (tertiary amine–sulfur trioxide addition compounds), $R(R')(R'')\overset{+}{N}SO_3^-$ (betaine form of $R'R''NSO_3R$):

$(C_2H_5)_3N\cdot SO_3$ (28); $C_5H_5N\cdot SO_3$ (8, 23)

$\begin{matrix}(CH_3)_2 \\ C_6H_5\end{matrix}\!>\!N\cdot SO_3$ (141)

IV. *N*-alkylidenesulfamic acids, $RCH{=}NSO_3H$ and $R_2C{=}NSO_3H$:

$C_6H_5CH{=}NSO_3H$ (83); $CH_3CH{=}NSO_3K$ (117)
$(CH_3)_2C{=}NSO_3H$ (83)

V. *N*-sulfonated amino acids:


$CH_3CH\begin{matrix}NHSO_3K \\ COOK\end{matrix}$ (24);

$\begin{matrix}CH_2COOK \\ | \\ NHSO_3K\end{matrix}$ (24)

Such compounds as CH_3ONHSO_3K (133) might be included as *N*-alkoxysulfamic acids, although they are more properly to be classed as hydroxylamine derivatives. In like manner the compound $C_6H_5NHNHSO_3K$ (56a) might be classed as an *N*-amino derivative, although it is actually an *N*-sulfonated hydrazine.

A. PREPARATION

The general methods for preparing organic derivatives of sulfamic acid lend themselves to two types of classification. The classification which will be employed here in the discussion of the general methods is based on the type of chemical reaction which occurs during the process. It should be pointed out that there is no essential difference between the methods used in preparing sulfamic acid and those employed in the preparation of the *N*-substituted compounds. Where ammonolytic processes were used, we may now substitute an amine to effect "aminolysis."

A second classification is based on the type of organic compounds used as the starting material and would be employed if it were desired to list and index all known organic derivatives of sulfamic acid. Such a tabulation has been made (124a), but because of its scope cannot be included in this paper.

1. *Aminolytic reactions*

The most useful types of general reactions for the preparation of *N*-substituted sulfamic acids involve the utilization of some form of hexavalent sulfur for either of the following two fundamental processes: (*a*) the interposition of a bivalent —SO_3— group between the nitrogen and a hydrogen in primary amines, secondary amines, or amides of the types $RCONH_2$ and RSO_2NH_2; and (*b*) the addition of sulfur trioxide through a coördinate link to the nitrogen in a tertiary amine.

TABLE 2

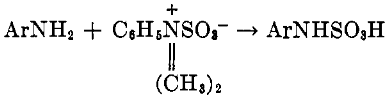
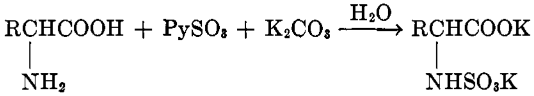
Aminolysis of some derivatives of aquosulfuric acid

NO.	REACTION	REFERENCE
1	$ArNH_2 + K_2S_2O_7 \rightarrow ArNHSO_3K$	(12)
2	$R_3N + K_2S_2O_7 \rightarrow R_3\overset{+}{N}SO_3^-$	(12)
3	$RR'NH + SO_3 \rightarrow RR'NSO_3H$	(28)
4	$RNH_2 + FSO_3K(Na) \rightarrow RNHSO_3K(Na)$	(67)
5	$RNH_2 + NH_4SO_3F \rightarrow RNHSO_3H$	(131)
6	$ArNH_2 + C_2H_5SO_3Cl \rightarrow Ar\underset{C_2H_5}{\underset{\vert}{N}}SO_3H$	(130)
7	$R_2NH + R'SO_3Cl \rightarrow R_2NSO_3R'$	(44)
8	$RR'NH + ClSO_3H \rightarrow RR'NSO_3H$	(95)
9	$R_3N + ClSO_3H \rightarrow R_3\overset{+}{N}SO_3^-$	(141)
10	$R_3N + SO_3 \rightarrow R_3\overset{+}{N}SO_3^-$	(86)
11	$R_3N + C_2H_5SO_3Cl \rightarrow R_3\overset{+}{N}SO_3^-$	(8)
12	$RR'NH + ClSO_3H \xrightarrow{R''_3N} RR'NSO_3H$	(105)
13	$ArNH_2$ + dioxane (1 or 2)$SO_3 \rightarrow ArNHSO_3^-$	(121)
14	$R_2NH + NaSO_3Cl \cdot SO_3 \rightarrow R_2NSO_3Na$	(129)
15	$Ar_3N + SO_2Cl_2 \rightarrow$ addition compound $\xrightarrow{ROH} Ar_3\overset{+}{N}SO_3^-$	(10)
16	$R_2NH + SO_3 \xrightarrow{C_6H_5N(CH_3)_2} R_2NSO_3H$	(76)
17	$RSO_4H + ArNH_2 \rightarrow ArNHSO_3H$	(100)
18	$ArCONH_2 + H_2SO_4 \xrightarrow{(CH_3CO)_2O} ArCONHSO_3H$	(36)
19	$RCONH_2 + ClSO_3H \xrightarrow{C_6H_5N(CH_3)_2} RCONHSO_3H$	(68)

It is evident, therefore, that either free sulfur trioxide or a derivative which would readily donate this molecule would be logical sources of the hexavalent sulfur required for these processes. Indeed, free sulfur trioxide can be used. However, two types of derivatives are usually employed, *viz.*, aquosulfuric acids and ammonosulfuric acids. The use of sulfur trioxide and aquosulfuric acid derivatives is shown in the list of equations in table 2, while the equations involving the use of ammonosulfuric acids are listed in table 3. All of the reactions under these two classifications are aminolytic in character, that is, either sulfur trioxide or one of its derivatives is treated with an amine or an amide. In the equations listed in table 2 both types of fundamental processes mentioned above are in evidence, while in table 3 the methods of preparation depend solely on the fundamental process designated above under (*a*).

TABLE 3

*Aminolysis of some aquo-ammonosulfuric acids**

NO.	REACTION	REFERENCE
20	$RNH_2 + NH_2SO_3H \rightarrow RNHSO_3H \cdot NH_2R$	(96)
21	$ArNH_2 + NH_2SO_3H \rightarrow ArNHSO_3NH_4$	(94)
22	 $ArNH_2 + C_6H_5\underset{\underset{(CH_3)_2}{\Vert}}{\overset{+}{N}}SO_3^- \rightarrow ArNHSO_3H$	(141)
23	$ArNH_2 + (CH_3)_3\overset{+}{N}SO_3^- \rightarrow ArNHSO_3H$	(9)
24	$R_2NH + PySO_3 \rightarrow R_2NSO_3H$	(138)
25	$ArCONH_2 + NH_2SO_3H \xrightarrow{pyridine} ArCONHSO_3H$	(88)
26	$RCONH_2 + PySO_3 \rightarrow RCONHSO_3H$	(23)
27	$ArSO_2NH_2 + PySO_3 \rightarrow ArSO_2NHSO_3H$	(23)
28	$ArCONHSO_3H \cdot NH_2Ar \xrightarrow{excess\ ArNH_2} ArNHSO_3NH_4$	(36)
29	 $\underset{NH_2}{\underset{\vert}{R}CHCOOH} + PySO_3 + K_2CO_3 \xrightarrow{H_2O} \underset{NHSO_3K}{\underset{\vert}{R}CHCOOK}$	(15, 24)

* All of the aquo-ammonosulfuric acids here are sulfamic acids.

Closer scrutiny of the ammonosulfuric acids used as reactants in the equations in table 3 shows that they are all sulfamic acids themselves. With the exception of the carboxyacylsulfamic acid employed in method 28, these reacting sulfamic acids are of two types: *viz.*, free sulfamic acid itself and trisubstituted sulfamic acids of the general formula $RR'R''NSO_3$. To show the interrelationship of the preparative methods listed in these two tables, all of the sulfamic acids noted as reactants in table 3 are obtained as products of particular reactions in table 2, that is, some sulfamic acids formed by the aminolysis of aquosulfuric acids can themselves be further aminolyzed to yield other sulfamic acids. Even free sulfamic acid is, of course, obtainable directly or indirectly by the ammonolysis of an aquosulfuric acid derivative.

Occasionally it is difficult to decide whether the reaction occurring involves the aminolysis of a derivative of aquosulfuric acid or the aminolysis of a derivative of ammonosulfuric acid. One of these instances is illustrated in the following equations:

From table 2: $R_3N + ClSO_3H \rightarrow R_3NSO_3$ (equation 9)

$RR'NH + ClSO_3H \rightarrow RR'NSO_3H$ (equation 10)

From table 3: $R_2NH + PySO_3 \rightarrow R_2NSO_3H$ (equation 24)

In reaction 9 a tertiary amine, such as pyridine, is treated with chlorosulfonic acid to give a trisubstituted sulfamic acid, while in reaction 24 a secondary amine is treated with this trisubstituted sulfamic acid to form an *N*,*N*-disubstituted sulfamic acid. In reaction 10 a secondary amine is treated with a mixture of chlorosulfonic acid and a tertiary amine, such as pyridine, and an *N*,*N*-disubstituted sulfamic acid is also the product. Obviously, then, in reaction 10 it is difficult to decide whether the secondary amine reacts with the chlorosulfonic acid, a derivative of aquosulfuric acid, or with the pyridine–sulfur trioxide addition compound, which may form as an intermediate.

The question is clarified somewhat by determining which types of amines yield mono- or di-substituted sulfamic acids by direct aminolysis of chlorosulfonic acid, and which fail to undergo this reaction. An elaboration of equation 8

$$3RR'NH + ClSO_3H \rightarrow RR'NSO_3H \cdot HNRR' + RR'NH \cdot HCl$$

shows that the amine used must be sufficiently basic to form not only the amine salt of the desired sulfamic acid, but also the hydrochloride which is formed as a by-product of the reaction. In general, amines possessing basic properties lower than those of aniline will not yield sulfamic acids when treated directly with chlorosulfonic acid. This failure of certain amines to react with chlorosulfonic acid undoubtedly lies in the inherent instability of the free sulfamic acids formed from amines of low basicity. Therefore, if the amine is not sufficiently basic to stabilize the sulfamic acid by salt formation, aminolysis is not effected. In fact, since hydrogen chloride is more acidic than any of the organic acids under discussion, it can be said that amines which do not form hydrochlorides readily, will not aminolyze chlorosulfonic acid. Thus diphenylamine neither forms a hydrochloride nor aminolyzes chlorosulfonic acid.

However, if a tertiary amine like pyridine or dimethylaniline is added to a reaction mixture consisting of diphenylamine and chlorosulfonic acid, subsequent treatment with aqueous sodium hydroxide leads to the isolation of the desired sodium diphenylsulfamate. A plausible explanation of the function of the tertiary amine is that the latter forms a salt of the diphenylsulfamic acid when once aminolysis does occur, whereas diphenylamine is not sufficiently basic to stabilize the acid formed.

Several considerations permit a possible conjecture as to whether a trisubstituted sulfamic acid is first formed in this reaction. When a chloroform solution of pyridine is treated with chlorosulfonic acid, the pyridine–sulfur trioxide addition compound precipitates immediately. On the other hand, according to the patent literature, the composite reaction mixture consisting of diphenylamine, pyridine, and chlorosulfonic acid must be heated for some hours on the steam bath before the desired reaction occurs. From these qualitative statements of the reaction rates involved, it is fairly certain that the reaction which finally yields the disubstituted sulfamate is the aminolysis of the trisubstituted sulfamic acid formed as an intermediate.

There is less certainty as to the mechanism of the reaction when the amine used forms a sulfamate from chlorosulfonic acid with or without the addition of a tertiary amine. Methylaniline is an example of this type of amine. Qualitative reaction rates are of no value here, since the reaction times are so nearly alike. Furthermore, the necessary data are not available.

The reactions in which free sulfamic acid is aminolyzed by primary aliphatic or aromatic amines require comment, because the type of sulfamic acid derivative produced appears to depend on the basicity of the amine. This is evident from an examination of equations 20 and 21 in table 3.

$$\mathrm{RNH_2 + NH_2SO_3H \rightarrow RNHSO_3H \cdot H_2NR} \quad \text{(equation 20)}$$

$$\mathrm{ArNH_2 + NH_2SO_3H \rightarrow ArNHSO_3NH_4} \quad \text{(equation 21)}$$

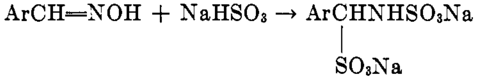
In equation 20, R is an aliphatic group such as isoamyl, whereas in equation 21, Ar refers to a strictly aromatic group such as phenyl. If an amine containing either type of organic residue is treated with free sulfamic acid, the product first formed is the corresponding amine sulfamate. When this salt is heated with an excess of the corresponding amine, an *N*-substituted sulfamic acid is formed, undoubtedly with the elimination of a molecule of ammonia. Here, however, the similarity of the reactions is terminated, and the differentiation appears to be a function of the basicity of the amine. Isoamylamine has a basicity comparable to that of ammonia. Therefore, a severalfold excess of the former leads to the formation of the amine salt of the *N*-substituted sulfamic acid, rather than to the ammonium isoamylsulfamate. On the other hand, the low basicity of aniline permits the preferential formation of ammonium phenylsulfamate.

2. Nitridation reactions

Although the most useful reactions for the preparation of *N*-substituted sulfamic acids are aminolytic in nature, methods exist in which nitridation of some form of sulfur not in the hexavalent state is involved. From an examination of the equations listed in table 4 it is easily discernible that the usual nitridizing agents are aromatic nitro compounds and hydroxylamine derivatives. Mono-, di-, and tri-substituted sulfamic acids are formed when hydroxylamines are employed, while only monosubstituted sulfamic acids result from aryl nitro compounds.

TABLE 4

Nitridation of some form of sulfur which is not in hexavalent state

NO.	REACTION	REFERENCE
30	$ArNH_2 + SO_2 \xrightarrow[\text{and heat}]{\text{sealed tube}} ArNHSO_3H$	(80)
31	$ArNO_2 + NaHSO_3 \rightarrow ArNHSO_3Na$	(139)
32	$ArNO_2 + Na_2S_2O_4 \rightarrow ArNHSO_3Na$	(119)
33	$ArNO_2 + (NH_4)_2SO_3 \rightarrow ArNHSO_3H$	(99)
34	$RR'R''N{\rightarrow}O + SO_2 \rightarrow RR'R''\overset{+}{N}SO_3^-$	(86)
35	$RR'C{=}NOH + (NH_4)_2SO_3 \rightarrow RR'CHNHSO_3H$	(1)
36	 $ArCH{=}NOH + NaHSO_3 \rightarrow Ar\underset{\displaystyle SO_3Na}{\underset{\vert}{C}}HNHSO_3Na$	(97)
37	$ArCH_2NHOH{\cdot}HCl + SO_2 \rightarrow ArCH_2NHSO_3H$	(115)
38	$(ArCH_2)_2NOH + NaHSO_3 \xrightarrow{\text{then add HCl}} (ArCH_2)_2NSO_3H$	(115)
39	$RR'NOH + SO_2 \rightarrow RR'NSO_3H$	(86)
40	$ArNHOH + ArN{=}SO \rightarrow ArNHSO_3H$	(91)
41	$ArN{=}NAr + NH_4HSO_3 \rightarrow NH_2Ar{-}ArNHSO_3NH_4$	(123)
42	$ArN{=}NAr + NaHSO_3 \rightarrow NH_2Ar{-}ArNHSO_3Na$ (small yield)	(35)

When the reactions by which certain types of sulfamic acids can be prepared from free hydroxylamine and ammonia are summed up, as in chart III, certain similarities and differences appear in the types of chemical reactions involved. For instance, alkylation of either parent substance leads to exactly analogous compounds, if the uniformly higher state of oxidation of the hydroxylamines is borne in mind. This difference in oxidation level is important, for on it depends the subsequent choice of the types of sulfur compounds which lead to the production of identical types of sulfamic acids from the corresponding substituted hydroxylamines and amines.

To determine logically what types of sulfur compounds, when treated with a member of either series of nitrogen compounds, would produce sulfamic acids, the characteristic functional group, $>NSO_3H$, must also be envisioned. It is obvious that when amines are employed the sulfur compound must furnish all three of the oxygen atoms required to produce this group. On the other hand, hydroxylamines, since they already contain an atom of oxygen, would require treatment with a sulfur compound which need furnish only two atoms of oxygen. Therefore, as has been mentioned under the discussion of the equations in table 2 and table 3, hexavalent sulfur in the form of free sulfur trioxide, or one of its derivatives, is the logical compound of sulfur with which amines can be treated to produce sulfamic acids. Equally logical is the choice of tetravalent sulfur in the form of sulfur dioxide, or one of its derivatives, for the production of sulfamic acids from hydroxylamines. Since sulfamic acids contain

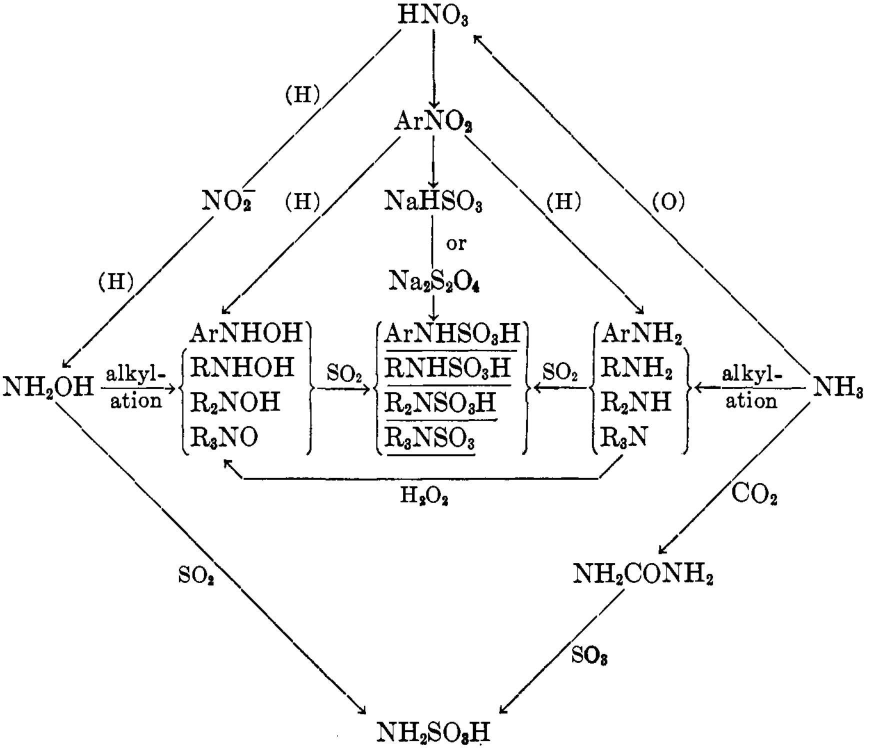


CHART III

hexavalent sulfur, the overall reaction, by which these compounds are produced from hydroxylamines and a reagent in which sulfur is originally in the tetravalent condition, is one involving nitridation of sulfur.

The interrelation of these methods is evident from the alternative procedures by which the identical sulfamic acids can be prepared from a tertiary amine. The latter can either be treated directly with a derivative of sulfur *trioxide*; or the amine can first be converted to an amine oxide, which can then be treated with sulfur *dioxide*. Both procedures lead to the identical trisubstituted sulfamic acid. Thus, trimethyl- and tripropylsulfamic acids are produced either by the reaction of the corresponding amines with sulfur trioxide, or by the reaction between the amine oxides and sulfur dioxide.

While the production of sulfamic acids from hydroxylamines probably involves only one nitridation process, the formation of sulfamic acids from aromatic nitro compounds probably involves two. When alkali sulfites or hyposulfites are nitridized in aqueous solution by aromatic nitro compounds, the nitrogen in the latter is undoubtedly reduced first to some lower valence state. The resulting aromatic nitrogen compound then reacts with some form of sulfur present in the solution to produce the monosubstituted sulfamic acid. At first glance it is difficult to determine whether the reduction proceeds to the amine stage, with the subsequent aminolysis of the sulfur trioxide derivative formed by the nitridation process, or whether the reduction ceases at the hydroxylamine stage, the sulfamic acid then being formed by another nitridation process involving the excess of the sulfur dioxide derivative present. As is evident from chart III, either process might conceivably occur, since, for example, both aniline and phenylhydroxylamine, when treated with sulfur trioxide and sulfur dioxide, respectively, are converted into phenylsulfamic acid. However, aqueous alkali sulfates, the sulfur trioxide derivatives formed by the first nitridation reaction, do not react with amines, whereas either aqueous sulfur dioxide or an alkali bisulfite does react with phenylhydroxylamine to produce phenylsulfamic acid. Therefore aromatic nitro compounds, when treated with aqueous alkali bisulfites or hyposulfites, are first reduced to the corresponding hydroxylamine, the latter then nitridizing the excess of sulfur dioxide present in order to produce the monoarylsulfamic acid.

3. Hydrolysis of organic derivatives of other aquo-ammonosulfuric acids

The equations listed in table 5 are of interest because Nos. 43, 45, and 46 represent the only known methods for the preparation of polymethylenedisulfamic acids, alkoxysulfamic acids,[5] and polymethylenedioxydisulfamic acids,[5] respectively. Only one example of each of these various types of

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[5] These compounds could be considered as derivatives of hydroxylaminomonosulfonic acid.

sulfamic acids is known, the substituent groups being ethylene, methoxy, and ethylenedioxy. It should be noted that the first step in the production of sulfamic acids by the reactions listed in table 5 is the formation of *N*-substituted imidodisulfonic acids. The desired sulfamic acids are then obtained by the removal of one sulfonic acid group through acidic hydrolysis.

4. Miscellaneous methods

Two general methods by which sulfamic acids are produced from ammonosulfuric acids have already been discussed. In the reactions listed in table 3, ammonosulfuric acids which are also sulfamic acids are aminolyzed to produce other sulfamic acids. In those listed in table 5, which have just been discussed, ammonosulfuric acids other than sulfamic acids are first alkylated to produce imidodisulfonic acid derivatives, which upon hydrolysis yield the desired sulfamic acids.

TABLE 5

Hydrolysis of other aquo-ammonosulfuric acids

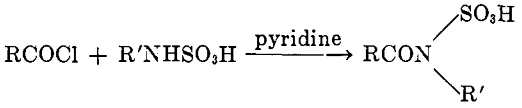
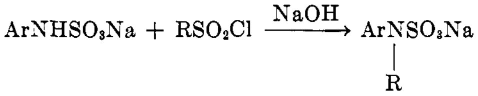
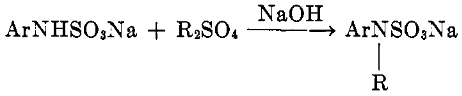
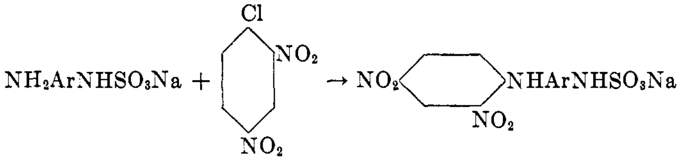
NO.	REACTION	REFERENCE
43	$Br(CH_2)_nBr + KN(SO_3K)_2 \rightarrow (KSO_3)_2N(CH_2)_nN(SO_3K)_2$ $\downarrow H^+$ $KSO_3NH(CH_2)_nNHSO_3K$	(136)
44	$R_2SO_4 + KN(SO_3K)_2 \rightarrow RN(SO_3K)_2 \xrightarrow{H^+} RNHSO_3K$	(136)
45	$R_2SO_4 + KON(SO_3K)_2 \rightarrow RON(SO_3K)_2 \xrightarrow{H^+} RONHSO_3K$	(133)
46	$Br(CH_2)_nBr + KON(SO_3K)_2 \rightarrow (KSO_3)_2NO(CH_2)_nON(SO_3K)_2$ $\downarrow H^+$ $KSO_3NH{-}O{-}(CH_2)_n{-}O{-}NHSO_3K$	(133)

In the equations listed in table 6, a number of sulfamic acid derivatives are treated with various reagents in order to produce other derivatives of sulfamic acid. The reactions involved in these transformations are not aminolytic. Furthermore, the ammonosulfuric acids used as starting materials are in themselves sulfamic acids. All other preparative methods are, therefore, grouped together in table 6. Some semblance of classification according to the type of chemical reaction involved is attained by distributing the equations under the five subdivisions.

Several equations in this miscellaneous class are of distinct interest. For instance, equations 48 and 64 illustrate two methods of producing an arylsulfamic acid containing a free amino group in the ring. In addition,

TABLE 6

*Miscellaneous methods for preparation of N-substituted sulfamic acids**

NO.	REACTION	REFERENCE
	a. Hydrolysis	
47	$R_2NSO_2Cl + H_2O \rightarrow R_2NSO_3H$	(26)
48	$RCONHArNHSO_3Na \xrightarrow{NaOH} NH_2ArNHSO_3Na$	(140)
49	$Ar_3\overset{+}{N}SO_3^- \xrightarrow{NaOH}$ decomposition products	(8)
	b. Alcoholysis	
50	$RR'NSO_2Cl + NaOR'' \rightarrow RR'NSO_3R''$	(137)
	c. *N*-acylation	
51	 $RCOCl + R'NHSO_3H \xrightarrow{pyridine} RCON\genfrac{}{}{0pt}{}{SO_3H}{R'}$	(68)
	d. *N*-alkylation or *N*-arylation	
52	$ArCHCl_2 + NH_2SO_3H \rightarrow ArCH{=}NSO_3H$	(83)
53	$ArCH_2Cl + AgSO_3NH_2 \rightarrow ArCH_2NHSO_3CH_2Ar$	(137)
54	$RI + AgSO_3NH_2 \rightarrow R_2NSO_3R$	(137)
55	$CH_3I + \begin{Bmatrix} NH_2SO_3Ag \\ CH_3NHSO_3Ag \\ (CH_3)_2NSO_3Ag \end{Bmatrix} \rightarrow (CH_3)_3\overset{+}{N}SO_3^-$	(137)
56	$RCHN_2 + NH_2SO_3H \rightarrow (RCH_2)_3\overset{+}{N}SO_3^-$	(137)
57	Aldehyde patents; reaction is probably as follows: $RCHO + NH_2SO_3(metal) \rightarrow RCH{=}NSO_3(metal)$	(117)
58	 $ArNHSO_3Na + RSO_2Cl \xrightarrow{NaOH} \underset{\textstyle R}{\underset{\vert}{ArNSO_3Na}}$	(130)
59	 $ArNHSO_3Na + R_2SO_4 \xrightarrow{NaOH} \underset{\textstyle R}{\underset{\vert}{ArNSO_3Na}}$	(139)
60		(140)
	e. Reactions involving introduction of substituents on an aryl ring	
61	$(ArNHSO_3)_2Ba + Br_2 \rightarrow$ ring-brominated product	(123)
62	$Ar(NHSO_3H)_2 + HONO \rightarrow XN_2ArNHSO_3H$	(114)
63	$NH_2ArNHSO_3H + HONO \rightarrow XN_2ArNHSO_3H$	(78)
64	$NO_2ArNHSO_3H \xrightarrow{reduction} NH_2ArNHSO_3H$	(78)

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* These reactions involve treatment of a sulfamic acid derivative with various agents to effect conversion into other types of organic derivatives.

the first of these two equations focuses attention on the stability of sulfamates towards alkaline solutions, and the second is important in the dye industry. In fact, equations 64, 62, and 63 represent processes which are the basis for several patents in this field. All involve the production of dyes which are prepared by two successive diazotizations. In equation 62 an aromatic diamine which has been converted to the disulfamic acid derivative is treated with sufficient nitrous acid to diazotize only one sulfamic acid group. With one amino group protected as a sulfamate, coupling occurs only on the diazotized portion of the molecule. After this first coupling reaction is complete, the other sulfamic acid group is diazotized by an excess of nitrous acid, and another group is introduced, again by coupling.

B. PHYSICAL PROPERTIES

All metallic and amine salts of *N*-substituted sulfamic acids are solids. The free acids, where they are known, are also solids, including the trisubstituted derivatives which exist in the betaine-like form, $RR'R''NSO_3$. Trisubstituted sulfamic acids in the ester form, $RR'NSO_3R''$, are oils, but on rearrangement to the betaine-like structure, of course, become solids.

C. REACTIONS

1. *With alkalies*

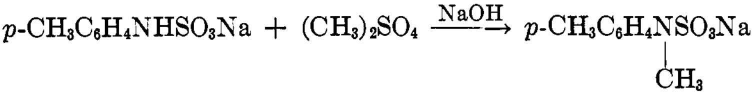
As a rule, salts of sulfamic acids of the types $RR'NSO_3H$, $ArNHSO_3H$, $RNHSO_3H$, and $ArRNSO_3H$ are fairly stable towards alkaline solutions, whereas compounds of the type $RCH{=}NSO_3M$ (M = metal) are not.

Some monoaryl derivatives like sodium phenylsulfamate and sodium *p*-tolylsulfamate are said to be stable towards fused sodium hydroxide up to 250°C., but decomposition occurs at 280°C. These two sulfamates are also stable towards a tenfold quantity of 50 per cent potassium hydroxide for 1 hr. under reflux. On the other hand, sodium *p*-ethoxyphenylsulfamate undergoes decomposition under the same conditions to the free amine in a short time (139).

This stability towards alkaline solutions is utilized in the preparation of arylsulfamic acids containing a free amino group (140).

$$p\text{-}CH_3CONHC_6H_4NHSO_3Na \xrightarrow{NaOH} p\text{-}NH_2C_6H_4NHSO_3Na$$

N-alkylation, which requires a basic reaction medium, is also possible (139).



$$p\text{-}CH_3C_6H_4NHSO_3Na + (CH_3)_2SO_4 \xrightarrow{NaOH} p\text{-}CH_3C_6H_4\underset{\displaystyle CH_3}{\underset{|}{N}}SO_3Na$$

Trisubstituted sulfamic acids are not stable toward alkaline solutions. Decomposition products have been isolated from the pyridine–sulfur trioxide (16, 8) and the isoquinoline–sulfur trioxide addition compounds (25). In both instances ring fission occurs.

2. With water

As a rule, salts of sulfamic acids which are stable toward alkalies are stable in neutral solution. However, sulfamic acids as a class are more stable toward basic solutions than toward acidic solutions. If hydrolysis proceeds to any extent, hydrogen ion is liberated.

$$RNHSO_3Na + H_2O \rightarrow RNH_2 + NaHSO_4$$

The slight amount of hydrogen ion liberated may catalyze further hydrolysis, and, whereas that slight acidity would be neutralized immediately in alkaline solution, this would not be true in a neutral solution. For this reason, if incipient hydrolysis occurs in a neutral solution, the remaining sulfamate may undergo rapid decomposition.

3. With acids

As mentioned in the preceding section, sulfamic acids as a class are not as stable in acidic solution as they are in basic solution. However, the behavior of alkyl- and aryl-sulfamic acids toward acids is sharply differentiated. No *N*-substituted sulfamic acid in which the nitrogen of the functional group is directly attached to a carbon in an aryl ring is stable for more than a few seconds toward a boiling dilute mineral acid solution. In fact, this instability is employed as a test to differentiate *N*-arylsulfamic acids from the isomeric aminoarylsulfonic acids. A solution containing the suspected *N*-arylsulfamate and some barium chloride is merely acidified with a drop of hydrochloric acid. If on boiling this solution, barium sulfate precipitates, a positive test for an *N*-arylsulfamate is in evidence. The isomeric aminoarylsulfonic acids, of course, do not undergo decomposition under these conditions. Since *N*-arylsulfamic acids are so labile toward acidic solutions, it is a foregone conclusion that very few of them are known in the free state.

On the other hand, both mono- and di-alkylsulfamic acids are much more stable toward acidic solutions, and many of these are known in the free state.

The alkylidenesulfamic acids, that is, compounds of the type $RCH{=}NSO_3$metal, are not stable toward acids (117).

4. With nitrous acid and nitrites

Free acids of the type $RNHSO_3H$, where R is either an alkyl or an aryl group, dissolve in a cold concentrated solution of alkali nitrite. On standing, salts of the type $RN(NO)SO_3M$ precipitate from solution. These *N*-nitroso derivatives as a class are extremely reactive and sometimes explode when heated (95, 96, 131).

The use of arylsulfamic acids in the dye industry has been discussed under the general methods listed in table 6.

5. Rearrangements

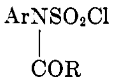
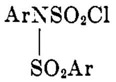
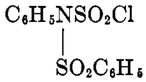
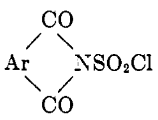
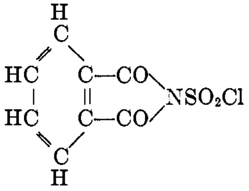
There is a more or less general rule in organic chemistry that almost any functional group on an amino nitrogen directly attached to a carbon in an aryl ring can be rearranged into the aryl ring. The familiar rearrangement of aniline sulfate to sulfanilic acid, and of *N*-nitrosomethylaniline to *p*-nitrosomethylaniline are examples of this rule. The rearrangements of *N*-arylsulfamic acids to the isomeric *p*- and *o*-sulfanilic acids are further examples of the generality of this statement. Thus, potassium phenylsulfamate in a solution containing 20 drops of concentrated sulfuric acid in 25 cc. of ice water yields potassium *o*-sulfanilate after 80 hr., and the latter compound in 25 g. of concentrated sulfuric acid at 180–190°C. yields potassium *p*-sulfanilate after 7 hr. (3). This would lead one to generalize that at a low temperature phenylsulfamic acid rearranges to *o*-sulfanilic acid, and at a high temperature to *p*-sulfanilic acid. The barium salt of phenylsulfamic acid on heating at 180°C. is rearranged to barium *p*-sulfanilate (2, 125). Ammonium salts of *N*-arylsulfamic acids rearrange on heating to form ammonium salts of the isomeric aminoarylsulfonic acids.

Various workers have postulated that in the Piria reaction, that is, the action of an alkali bisulfite on an aromatic nitro compound, the aminoarylsulfonic acid formed as a by-product is formed from the sulfamic acid by rearrangement. However, some recent work has shown that treatment of the sodium salts of various arylsulfamic acids with hydrochloric acid in concentrations from 0.47 to 5.35 *N* at 47–50°C. permits the quantitative precipitation of the sulfur as barium sulfate. This, of course, precludes any possibility of rearrangement (73). This work is not conclusive, since some investigators carry out the Piria reaction under reflux (139). Obviously, then, checking the rearrangement at 47–50°C. and then stating that in the Piria reaction the aminoarylsulfonic acids are not formed through the *N*-arylsulfamic acids as intermediates, is an error. The only logical conclusion from these studies (73) is that if the Piria reaction is carried out at 47–50°C. rearrangement does not occur.

The esters of *N*-dialkylsulfamic acids are very labile oils. If the three groups are small, as in $(CH_3)_2NSO_3C_2H_5$ and $(CH_3)_2NSO_3CH_3$, the esters rearrange very easily on heating to the betaine-like structure $RR'R''\overset{+}{N}SO_3^-$. Compounds having the latter structure are solids. The compound $(C_2H_5)_2NSO_3C_2H_5$ does not undergo this rearrangement (137, 141). However, the betaine-like form can be prepared from $(C_2H_5)_3N$ and SO_3 (28). Only one ester of an *N*-monosubstituted sulfamic acid, $C_6H_5CH_2NHSO_3CH_2C_6H_5$, is recorded in the literature. This does not rearrange on heating (137).

IV. Nitrogen-substituted Sulfamyl Halides

It is perhaps significant that *N*-substituted sulfamyl halides are quite stable and readily prepared, whereas the parent substance, H_2NSO_2Cl, has not yet been prepared or identified. Four distinct types of sulfamyl chlorides are listed in the literature. The generic name adopted for this survey, the type formula, and a specific example of each follow:

GENERIC NAME	TYPE FORMULA	EXAMPLE	REFERENCE
1. Dialkyl	$RR'NSO_2Cl$	$(CH_3)_2NSO_2Cl$	(45)
2. Aryl-acyl	 $\underset{\substack{\mid \\ COR}}{ArNSO_2Cl}$	 $\underset{\substack{\mid \\ COCH_3}}{C_6H_5NSO_2Cl}$	(90)
3. (Aryl)-arylsulfonyl	 $\underset{\substack{\mid \\ SO_2Ar}}{ArNSO_2Cl}$	 $\underset{\substack{\mid \\ SO_2C_6H_5}}{C_6H_5NSO_2Cl}$	(6)
4. Diacyl			(4)

In addition to the various classes of sulfamyl chlorides given above, a number of dialkylsulfamyl fluorides are described in the patent literature (75). Since the information concerning these is very indefinite, little can be said about their properties.

Although the $>NSO_2Cl$ group is common to all four classes of sulfamyl chlorides, the various types of organic residues in the molecule cause a profound difference in many of the reactions of each class toward a particular reagent or set of conditions. Therefore, wherever these peculiarities are in evidence, the reactions of each class will be considered separately.

A. PREPARATION

All sulfamyl chlorides have been prepared by the action of sulfuryl chloride on the appropriate amine or amine hydrochloride, or on a metallic salt of the appropriate amide. In addition, diethylsulfamyl chloride has been prepared by the action of excess phenyl chlorosulfonate on diethylamine.

1. Preparation of dialkylsulfamyl chlorides

Diethyl- and dimethyl-sulfamyl chlorides are prepared by heating the corresponding amine hydrochloride with an excess of sulfuryl chloride on the steam bath for several hours. After washing the crude product with sodium carbonate solution, the pure compound is obtained by vacuum distillation.

The dialkylsulfamyl chlorides containing larger carbon residues are obtained by treating the free amine with sulfuryl chloride in an indifferent diluent.

An alternative procedure for the preparation of the diethyl derivative depends on the use of excess phenyl chlorosulfonate on the free amine (45).

2. Preparation of sulfamyl chlorides containing either acylsulfonyl or arylsulfonyl residues

The ring-chlorinating action which sulfuryl chloride exerts on free aryl amides is suppressed by utilizing the corresponding alkali salts. Since benzoylphenylsulfamyl chloride is obtained in low yield by this method, a nitrogen-Grignard derivative has been employed with greater success for the preparation of this compound (6).

The procedure requiring either type of metallic derivative presents no technical difficulties, save that of rigorously excluding moisture. The anhydrous alkali salts of the amides are obtained by treating a solution of the amide in toluene either with the finely divided alkali metal or with the alkali ethoxide. For the preparation of the Grignard derivative of benzanilide, the latter must be treated with propylmagnesium chloride, since ethylmagnesium bromide does not give satisfactory results. Either type of metallic derivative is then treated with sulfuryl chloride, and the pure sulfamyl chloride is obtained by recrystallization from an appropriate solvent.

B. PHYSICAL PROPERTIES

The dialkylsulfamyl chlorides are oily liquids, whereas those having at least one acylsulfonyl, or arylsulfonyl, group attached to the nitrogen are solids, regardless of what the other substituent on the nitrogen may be. Without exception, all of the sulfamyl chlorides are practically insoluble in cold water. Boiling water reacts to give decomposition products, presumably hydrolytic in character. Data are available for the solubilities in alcohol of all types of sulfamyl chlorides, with the exception of the diacyl derivatives. Alcohol is the best crystallizing solvent for the (aryl)-arylsulfonyl derivatives. Aryl-acyl derivatives undergo reaction with the solvent, while the dialkylsulfamyl chlorides probably merely dissolve. Ether and benzene are used as reaction media for the preparation of most sulfamyl halides, and appear, therefore, to be without action.

C. REACTIONS

Since the various classes of sulfamyl chlorides have been studied by investigators for widely differing purposes, they have not all been subjected to the same set of conditions or reagents. Therefore, no mention of a particular class of sulfamyl chlorides will be made in the subdivisions below unless that class has been subjected to the conditions under discussion.

1. Action of heat

Gentle warming has no effect on any of the sulfamyl chlorides. Since the dialkyl derivatives are liquids at room temperature, they are best purified by distillation under reduced pressure. Heating the (aryl)-arylsulfonylsulfamyl chlorides on an oil bath results in the liberation of hydrogen chloride and sulfur dioxide, and the formation of unidentified colored products. When the (aryl)-acylsulfamyl chlorides are heated above their melting points, decomposition also occurs with the formation of hydrogen chloride, sulfur dioxide, and the chloride of the acyl residue in the original molecule. Thus, acetylphenylsulfamyl chloride liberates acetyl chloride as one of the products.

2. Action of hydrolyzing agents

(*a*) *Boiling water.* Dialkylsulfamyl chlorides are rapidly split by boiling water with the formation mainly of the corresponding dialkylsulfamic acid. The hydrochloric acid liberated in this reaction presumably catalyzes to a slight degree the secondary hydrolysis of the sulfamic acid to the corresponding amine and sulfuric acid.

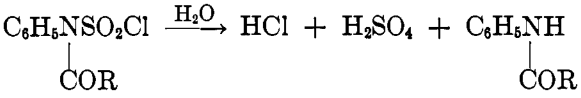
$$\mathrm{RR'NSO_2Cl + H_2O \longrightarrow RR'NSO_3H + HCl}$$

$$\mathrm{RR'NSO_3H + H_2O \xrightarrow{HCl} RR'NH\cdot H_2SO_4}$$

The first equation above represents one of the general methods of preparing free dialkylsulfamic acids (26).

For a given aryl group in (aryl)-acylsulfamyl chlorides, the reactivity of this class of compounds toward boiling water depends on the acyl group present. Thus, (*1*) phenylformylsulfamyl chloride, (*2*) phenylacetylsulfamyl chloride, and (*3*) phenylbenzoylsulfamyl chloride undergo complete solution in boiling water in 10, 60, and 480 min., respectively.

Titration with standard alkali shows—assuming that hydrochloric acid and sulfuric acid are formed as two of the products—that (*1*) yields formanilide, which is then partially split to aniline and formic acid, (*2*) yields aniline and acetic acid, and (*3*) yields benzanilide (90).

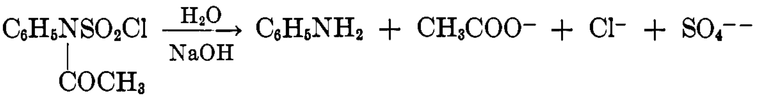


$$\underset{\displaystyle \mathrm{COR}}{\mathrm{C_6H_5NSO_2Cl}} \xrightarrow{\mathrm{H_2O}} \mathrm{HCl} + \mathrm{H_2SO_4} + \underset{\displaystyle \mathrm{COR}}{\mathrm{C_6H_5NH}}$$

(The anilide may undergo further hydrolysis to give aniline and a carboxylic acid.)

(Aryl)-arylsulfonylsulfamyl chlorides are only slowly hydrolyzed by boiling water.

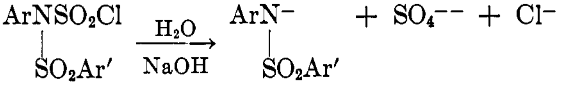
(*b*) *Alkalies.* The reactivity of the (aryl)-acylsulfamyl chlorides toward alkalies again depends on the acyl group present. Thus dilute sodium hydroxide splits phenylformylsulfamyl chloride even in the cold with the formation of benzonitrile, the latter being recognized by its odor (90). Warm alkali must be employed to cause hydrolysis of phenylacetylsulfamyl chloride according to the following equation:



$$\underset{\displaystyle \mathrm{COCH_3}}{\mathrm{C_6H_5NSO_2Cl}} \xrightarrow[\mathrm{NaOH}]{\mathrm{H_2O}} \mathrm{C_6H_5NH_2} + \mathrm{CH_3COO^-} + \mathrm{Cl^-} + \mathrm{SO_4^{--}}$$

Warm alkali splits phenylbenzoylsulfamyl chloride still more slowly, the hydrolysis being arrested at the benzanilide stage.

(Aryl)-arylsulfonylsulfamyl chlorides are split to the corresponding sulfonamides only after a 1-hr. treatment with boiling alkali.



$$\underset{\displaystyle \mathrm{SO_2Ar'}}{\mathrm{ArNSO_2Cl}} \xrightarrow[\mathrm{NaOH}]{\mathrm{H_2O}} \underset{\displaystyle \mathrm{SO_2Ar'}}{\mathrm{ArN^-}} + \mathrm{SO_4^{--}} + \mathrm{Cl^-}$$

(*c*) *Acids.* The action of mineral acids on both acyl and arylsulfonyl derivatives is identical with that of alkalies, but is much less rapid.

3. Action of sodium ethoxide or sodium phenoxide

The reaction between sodium alcoholates and dialkylsulfamyl chlorides is one of the general methods for preparing trisubstituted sulfamic acids (137).

$$\mathrm{RR'NSO_2Cl} + \mathrm{NaOR''} \rightarrow \mathrm{RR'NSO_3R''} + \mathrm{NaCl}$$

The first product is the true ester of an *N*,*N*-disubstituted sulfamic acid, but it may rearrange to form the betaine-like salt, $RR'R''NSO_3$.

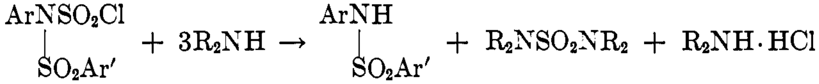
4. Action of ammonia and amines

Treatment of dialkylsulfamyl chlorides with ammonia, alkyl amines, or aryl amines yields the corresponding substituted sulfamides (26, 27). The equation for the reaction with ammonia is

$$\mathrm{RR'NSO_2Cl} + 2\mathrm{NH_3} \rightarrow \mathrm{RR'NSO_2NH_2} + \mathrm{NH_4Cl}$$

The sulfamides resulting from amines are formed in an analogous manner.

The (aryl)-arylsulfonylsulfamyl chlorides, in their overall reaction with ammonia or with primary or secondary amines, appear to act primarily as intermediates for introducing a sulfonyl group between two nitrogen atoms. In this reaction, the original sulfamyl chloride is degraded to the sulfonamide from which it was prepared.

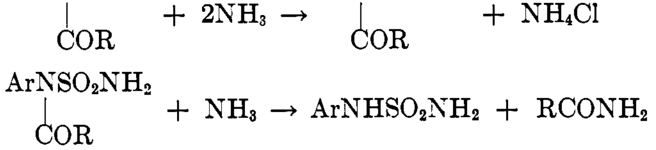


$$\begin{array}{l}\mathrm{ArNSO_2Cl}\\ |\\ \mathrm{SO_2Ar'}\end{array} + 3\mathrm{R_2NH} \rightarrow \begin{array}{l}\mathrm{ArNH}\\ |\\ \mathrm{SO_2Ar'}\end{array} + \mathrm{R_2NSO_2NR_2} + \mathrm{R_2NH\cdot HCl}$$

When R_2NH in the above equation represents a primary or secondary aliphatic amine, the reaction constitutes a general method for the production of *N*,*N'*-dialkylsulfamides or *N*,*N*,*N'*,*N'*-tetraalkylsulfamides (45). On the other hand, when both R groups represent hydrogen, that is, when ammonia itself is used, the reaction produces what is presumably a mixture of sulfamide and trisulfimide.

On aromatic amines, the action of (aryl)-arylsulfonylsulfamyl chlorides is primarily one of oxidation. Thus, with aniline sulfur dioxide is evolved, while the residue consists of aniline hydrochloride, oxidation products of aniline, and the arylsulfonamide from which the original sulfamyl chloride was made (90).

The substitution of an acyl group for the arylsulfonyl group in an organic sulfamyl chloride causes a profound difference in the reaction of the resulting molecule toward ammonia and amines. Undoubtedly, the first action of ammonia and amines on (aryl)-acylsulfamyl chlorides is the replacement of the chlorine. This is followed by ammonolysis or aminolysis of the resulting molecule.



$$\begin{array}{l}\mathrm{ArNSO_2Cl}\\ |\\ \mathrm{COR}\end{array} + 2\mathrm{NH_3} \rightarrow \begin{array}{l}\mathrm{ArNSO_2NH_2}\\ |\\ \mathrm{COR}\end{array} + \mathrm{NH_4Cl}$$

$$\begin{array}{l}\mathrm{ArNSO_2NH_2}\\ |\\ \mathrm{COR}\end{array} + \mathrm{NH_3} \rightarrow \mathrm{ArNHSO_2NH_2} + \mathrm{RCONH_2}$$

Although acetamide, which should be a product of the reaction when phenylacetylsulfamyl chloride is treated with ammonia, has not been isolated, the corresponding *N*,*N*-dimethylacetamide has been identified when dimethylamine was employed. The reaction between this class of sulfamyl chlorides and ammonia or amines is an important general method for the preparation of organic sulfamides (4, 7, 90).

The action of ammonia on the only diacylsulfamyl chloride known, *viz.*, the phthalyl derivative, constitutes a method for the preparation of sulfamide. On the other hand, phthalylsulfamyl chloride and amines form stable organic sulfamides of the type $C_6H_4(CO)_2NSO_2NRR'$ (4).

5. *Action of metallic fluorides*

When a dialkylsulfamyl chloride is heated in an indifferent diluent with potassium, sodium, or zinc fluorides, a reaction occurs which merely results in the replacement of the chlorine by a fluorine atom. The substituted sulfamyl fluorides thus prepared are patented for use as insecticides (75).

V. SULFAMIDE

A. PREPARATION

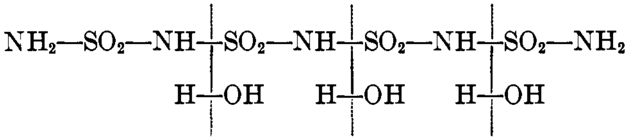
Sulfamide, $NH_2SO_2NH_2$, the diamide of sulfuric acid, was first isolated and characterized by Regnault (106). However, even at the present time, despite a great amount of research, it is difficult to prepare in any considerable quantity. Practically all the methods which have been investigated depend upon the ammonolysis of either sulfuryl chloride or sulfuryl fluoride or of chlorosulfonyl imides. Theoretically the following equation represents a possible reaction between sulfuryl chloride and ammonia:

$$SO_2Cl_2 + 4NH_3 \rightarrow SO_2(NH_2)_2 + 2NH_4Cl$$

Unfortunately, there is no indication that the ammonolysis of sulfuryl chloride gives very much sulfamide as a primary product.

The earlier investigators allowed gaseous ammonia to react with an excess of sulfuryl chloride dissolved in an inert solvent such as chloroform, petroleum ether, or carbon tetrachloride. The reaction product was obtained as a gelatinous mass containing large quantities of ammonium chloride (106, 127, 128). For the most part the chloride was tediously removed by precipitation with silver or lead oxides. None of the early workers obtained pure sulfamide, as the melting points reported by them varied between 75°C. and 81°C.

Ruff (111) was the first one to reverse the procedure by keeping ammonia in excess. He removed sulfamide from the reaction mixture by extraction with ethyl acetate and obtained pure sulfamide (m. p. 93°C.). A careful study of the reaction product obtained when ammonia is kept in excess was carried out by Ephraim and Michel (55). They concluded that long-chain compounds of the type $NH_2(SO_2NH)_nSO_2NH_2$ were formed by the action of sulfuryl chloride upon ammonia in excess and that chains containing four —SO_2— groups were the most common. They pointed out that the very small yield of sulfamide could be ascribed to the only way in which such chain compounds would probably hydrolyze.



$$\begin{array}{ccccccc} NH_2\text{—}SO_2\text{—}NH & | & SO_2\text{—}NH & | & SO_2\text{—}NH & | & SO_2\text{—}NH_2 \\ & H\,|\,OH & & H\,|\,OH & & H\,|\,OH & \end{array}$$

Each one of these chains would be able to furnish only one molecule of sulfamide to three molecules of sulfamic acid.

The method for preparing sulfamide from sulfuryl chloride and liquid ammonia was developed by Ephraim and Gurewitsch (53). This method is used today in preference to any other (143). One of the main products of the reaction is thought to be imidodisulfamide, $HN(SO_2NH_2)_2$. The entire liquid ammonia reaction product is dissolved in a weak nitric acid solution and allowed to hydrolyze overnight.

$$HN(SO_2NH_2)_2 + HOH \rightarrow NH_2SO_2NH_2 + NH_2SO_2OH$$

The solution is then evaporated to dryness under reduced pressure and the residue extracted with ethyl acetate. Sulfamide, melting at 93°C., is recovered from the ethyl acetate.

The reaction between sulfuryl fluoride and ammonia is apparently much simpler, leading directly to sulfamide (134). Curiously enough, aqueous ammonia may be used. While sulfuryl fluoride appears to be quite resistant to hydrolysis it does undergo ammonolysis readily. Schlesinger and Shroyer (120) found this procedure to be the most satisfactory one. Wood (143), however, stated that this method could not be recommended, because of the difficulty in handling gaseous sulfuryl fluoride and preparing it in the pure state.

Ammonolysis of aryl chlorosulfonates and *N*-(chlorosulfonyl)acylamides leads to sulfamide, presumably through the intermediate formation of monomolecular and trimolecular sulfimide (4, 5).

A patent (93) has recently been issued describing the preparation of sulfamide directly from sulfur trioxide and ammonia.

$$SO_3 + 2NH_3 \rightarrow SO_2(NH_2)_2 + HOH$$

According to the disclosure and claims the success of this process depends mainly upon two factors: (*1*) Pure dry ammonia must be used and must always be present in large excess, and (*2*) the water which is formed must be removed immediately from the reaction zone. The patent, further, claims that sulfamide may be extracted from the mixture containing ammonium imidodisulfonate, sulfamic acid, and ammonium sulfate by means of acetone.

B. PHYSICAL AND CHEMICAL PROPERTIES

Sulfamide is a white crystalline solid, which melts sharply at 93°C. (53, 111). It is very stable in air. Although sulfamide is quite soluble in water, its solutions are practically non-conducting. Sulfamide, however, is capable of acting as a dibasic acid, for it forms insoluble salts with the heavy metals, e.g., $SO_2(NHAg)_2$, and soluble salts of similar structure with the alkali metals.

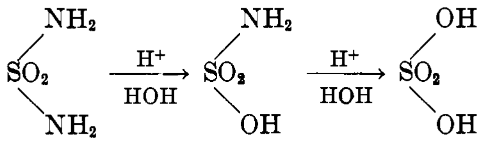
There is a very striking similarity between the structures of sulfamide and urea. An interesting parallelism existing between the formal deammonation products of these compounds is depicted in chart IV. These possible deammonation steps have not all been realized experimentally. It is a well-known fact, however, that biuret is formed when urea is heated; at higher temperatures cyanuric acid is obtained. It has also been demonstrated that triuret is readily deammonated to cyanuric acid (58). Imidodisulfamide and trisulfimide are among the products formed when sulfamide is fused (55, 128). Trisulfimide could also probably be formed by the loss of ammonia from the open-chain trisulfamide (58).

$$NH_2SO_2NHSO_2NHSO_2NH_2 \rightarrow (SO_2NH)_3 + NH_3$$

Sulfamide is stable in neutral, dilute acidic, and dilute alkaline solutions. It readily loses one molecule of ammonia when boiled with strong alkali, to yield the corresponding sulfamate.

$$NH_2SO_2NH_2 + NaOH \rightarrow NH_2SO_2ONa + NH_3$$

When boiled for a long time with hydrochloric acid complete hydrolysis is effected. The stepwise reaction may be represented as follows:



$$SO_2(NH_2)_2 \xrightarrow[HOH]{H^+} SO_2(NH_2)(OH) \xrightarrow[HOH]{H^+} SO_2(OH)_2$$

Sulfamide is ammono deliquescent (53, 62, 120) and is very soluble in liquid ammonia. The resulting solution has marked electrical conductivity (61, 62). This is in sharp contrast with its non-electrolytic character in aqueous solution, but again emphasizes its similarity to urea which also acts as an acid in liquid ammonia. Its behavior as an acid in liquid ammonia is in line with its characterization as an aquo-ammonosulfuric acid, just as urea is an aquo-ammonocarbonic acid.

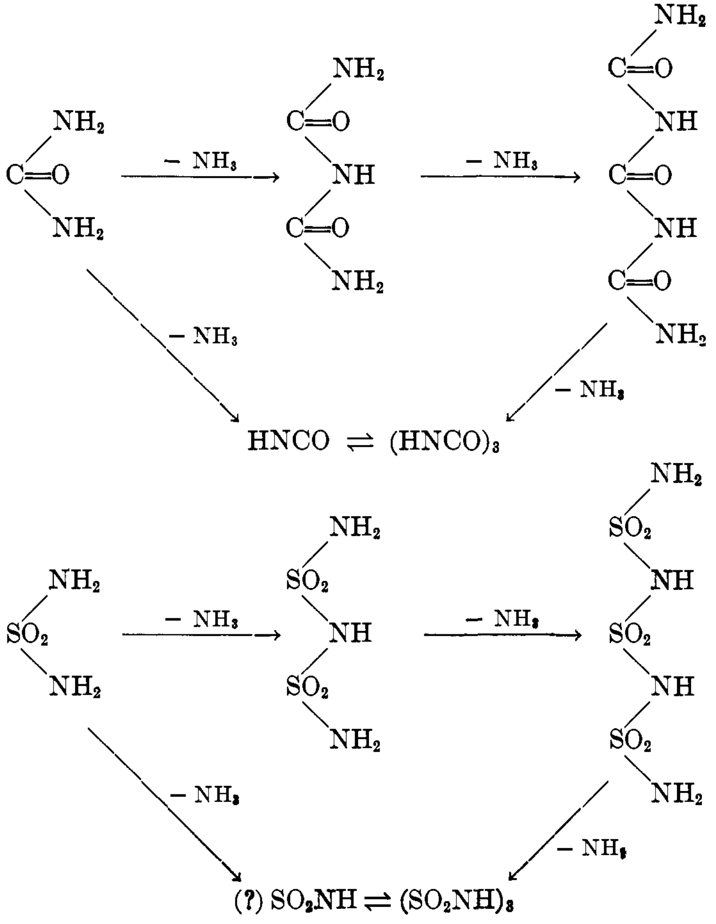


Chart IV. Parallelism existing between formal deammonation products of urea and sulfamide.

C. CHEMICAL REACTIONS OF SULFAMIDE

Although sulfamide dissolves readily in concentrated nitric acid, nitration does not occur unless concentrated sulfuric acid is present, in which case nitrosulfamide precipitates immediately (54).

$$NH_2SO_2NH_2 + HNO_3 \xrightarrow{H_2SO_4} NH_2SO_2NHNO_2 + HOH$$

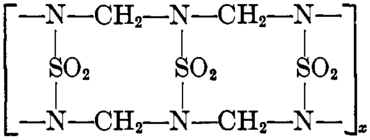
Monochlorosulfamide is formed when an aqueous solution of hypochlorous acid is allowed to react with a concentrated solution of sulfamide (54).

$$NH_2SO_2NH_2 + HOCl \rightarrow NH_2SO_2NHCl + HOH$$

This compound can be obtained in crystalline form (m.p. 66°C.). It is soluble in water, ethanol, ether, and chloroform. In the presence of alkali or ammonia it decomposes and nitrogen is evolved.

$$2NH_2SO_2NHCl + 2NaOH \rightarrow 2NH_2SO_2ONa + 2NaCl + N_2$$

The reaction between sulfamide and formaldehyde has also been studied. This investigation was undoubtedly inspired by the striking similarity between sulfamide and urea. Wood and Battye (143) found that sulfamide and formaldehyde reacted to give a hard water-clear resin. This resin was found to be insoluble in such organic solvents as ethanol, ethyl acetate, toluene, ligroin, and xylene, but slightly soluble in acetone. It softens when placed in warm water and is entirely soluble in boiling water. These authors postulate that the structure of the polymer is similar to that given for the urea–formaldehyde resin, the —CO— group being replaced by the —SO_2— group.



$$\left[\begin{array}{ccccc} —N— & CH_2 & —N— & CH_2 & —N— \\ | & & | & & | \\ SO_2 & & SO_2 & & SO_2 \\ | & & | & & | \\ —N— & CH_2 & —N— & CH_2 & —N— \end{array}\right]_x$$

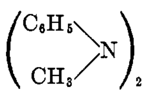
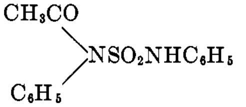
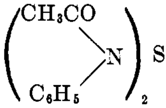
D. METALLIC DERIVATIVES OF SULFAMIDE

Attention has already been called to the marked solubility of sulfamide in liquid ammonia. Both the mono- and di- sodium and potassium salts (63) have been prepared by interaction with the corresponding amides in liquid ammonia. Sulfamide appears to be much more capable of acting as a proton donor, even in aqueous solution, than urea. Insoluble lead (127), mercuric (127), and silver (50, 53, 69, 113, 127) sulfamides, as well as the alkali and alkaline-earth salts (134) and a number of rhodium complexes (87), have been prepared.

VI. THE NITROGEN-SUBSTITUTED SULFAMIDES

A classification of known organic derivatives of sulfamide based upon the number and nature of the nitrogen substituents is proposed here in order to emphasize their diversity. An example of each class is given for illustration.

1. *N*,*N'*-dialkylsulfamides, $CH_3NHSO_2NHCH_3$ (26, 57)
2. *N*,*N*-dialkylsulfamides, $(CH_3)_2NSO_2NH_2$ (26, 27)
3. *N*,*N*,*N'*,*N'*-tetraalkylsulfamides, $(C_2H_5)_2NSO_2N(C_2H_5)_2$ (45)
4. *N*-monoarylsulfamides, $C_6H_5NHSO_2NH_2$ (7, 90)
5. *N*,*N'*-diarylsulfamides, $C_6H_5NHSO_2NHC_6H_5$ (90, 126, 142)

6. *N*,*N'*-dialkyl-*N*,*N'*-diarylsulfamides,  $\left(\begin{matrix}C_6H_5\\CH_3\end{matrix}>N\right)_2SO_2$ (142)
7. *N*,*N*-dialkyl-*N'*-arylsulfamides, $(CH_3)_2NSO_2NHC_6H_5$ (7, 90)
8. *N*-monoalkylidene sulfamides, $C_6H_5CH{=}NSO_2NH_2$ (134)
9. *N*-acyl-*N*,*N'*-diarylsulfamides,  $\begin{matrix}CH_3CO\\C_6H_5\end{matrix}>NSO_2NHC_6H_5$ (142)
10. *N*,*N'*-diacyl-*N*,*N'*-diarylsulfamides,  $\left(\begin{matrix}CH_3CO\\C_6H_5\end{matrix}>N\right)_2SO_2$ (142)

A. PREPARATION

Sulfamides are not produced in the reactions between sulfuryl chloride, or dialkylsulfamyl chlorides, and amines unless the basicity of the amines is above a certain rather definite minimum. Thus, aniline treated with sulfuryl chloride yields *N*,*N'*-diphenylsulfamide without any difficulty, whereas nitroaniline, acetanilide, and phenylammonium chloride treated with the same inorganic reagent undergo ring-chlorination. On the other hand, methylaniline, which is certainly more basic than aniline, is oxidized by sulfuryl chloride to a dark green mass.

However, the sulfamides which should theoretically result from the reaction of sulfuryl chloride with nitroaniline, acetanilide, or methylaniline can be prepared indirectly. Thus, *N*,*N'*-diphenylsulfamide can be acetylated or methylated to give two of the desired derivatives, and the acetylated product can be nitrated to give the third.

Sulfuryl chloride may be used either directly on amines, or it may be in the form of a derivative before being introduced into the reaction mixture which finally produces the organic sulfamide. The derivatives of sulfuryl chloride which may be employed are phenyl chlorosulfonate, dialkylsulfamyl chlorides, (aryl)-arylsulfonylsulfamyl chlorides, (aryl)-acylsulfamyl chlorides, phthalylsulfamyl chloride, or sulfamide. It should be emphasized that the synthesis of all of these intermediates, save possibly that of sulfamide, requires sulfuryl chloride as an essential reagent.

Since the reaction between the various types of sulfamyl chlorides and ammonia or amines to produce organic sulfamides has already been discussed (page 75), only the methods utilizing phenyl chlorosulfonate, sulfamide, or sulfuryl chloride will be included here.

1. Action of sulfuryl chloride on amines

It has already been emphasized that all types of amines will not react with sulfuryl chloride to produce symmetrically substituted sulfamides.

Apparently it makes little difference which strictly aliphatic amine is employed, be it either primary or secondary in character, for amines with such widely differing organic substituents as methyl, benzyl, dimethyl, and cyclopentamethylene form the corresponding sulfamides. On the other hand, of the aromatic amines, only aniline and *p*-toluidine are known to react smoothly with sulfuryl chloride to give symmetrically substituted sulfamides.

2. Action of phenyl chlorosulfonate on amines

Phenyl chlorosulfonate, $C_6H_5SO_3Cl$, when treated with either mono- or di-alkylamines, first donates the chlorosulfonyl group to the amine with the formation of a sulfamyl chloride, which then immediately reacts with another molecule of the amine to produce the sulfamide. Phenol and hydrogen chloride are by-products of the reaction (45). The equation for the overall reaction is

$$C_6H_5SO_3Cl + 3R_2NH \rightarrow C_6H_5OH + R_2NSO_2NR_2 + R_2NH \cdot HCl$$

The most obvious mechanism would postulate the formation of an ester, a phenyl sulfamate, which would then be aminolyzed to produce the sulfamide. However, Denivelle (45) has shown that phenyl cyclopentamethylenesulfamate, $(CH_2)_5NSO_3C_6H_5$, which is formed from sodium phenoxide and cyclopentamethylenesulfamyl chloride, undergoes no change when refluxed with piperidine. On the other hand, cyclopentamethylenesulfamyl chloride reacts immediately with piperidine to yield dicyclopentamethylenesulfamide.

3. Action of sulfamide on various reagents

The direct replacement of the hydrogens on free sulfamide has not been studied extensively, probably because of the relative difficulty encountered in the preparation of the starting compound. Only three organic sulfamides have been prepared in this manner, *viz.*, benzal (134), tetramethylol (143), and dixanthyl (145). The first two were prepared by the action of benzaldehyde and formaldehyde, respectively, on sulfamide, while the third was isolated from the reaction mixture obtained when sulfamide was treated with xanthydrol.

Arylsulfamides in which the aromatic residue does not contain highly negative substituents like nitro groups behave as acids toward aqueous sodium hydroxide but not toward aqueous sodium bicarbonate, provided the nitrogen carrying the simple aryl radical carries a free hydrogen as well. In other words, this type of sulfamide behaves like an acid toward phenolphthalein. (Should nitro groups be attached to the ring, the resulting sulfamide is easily split by hydrolysis.) Obviously, then, a sulfamide which dissolves in sodium hydroxide merely because of salt formation can be recovered unchanged by passing carbon dioxide into the solution.

As mentioned previously in this discussion, certain amines will not react directly with sulfuryl chloride to produce sulfamides. However, a number of sulfamides which cannot be made directly can be prepared indirectly. The reactions which lead to these difficultly accessible compounds will now be discussed.

Although methylaniline is certainly more basic than aniline, the former does not yield the corresponding sulfamide derivative when treated with sulfuryl chloride at a low temperature. This rather unexpected failure to produce a sulfamide may be caused by the sensitivity of the ring to oxidation, so that the molecule is disrupted before the amino hydrogen can react, with the simple elimination of hydrogen chloride between the amine and sulfuryl chloride. It is well known that the para hydrogen in methylaniline is quite labile, since, for example, the nitroso group in *N*-nitrosomethylaniline is readily rearranged into the ring. Whatever the explanation may be, *N*,*N′*-dimethyl-*N*,*N′*-diphenylsulfamide can not be prepared directly. However, when *N*,*N′*-diphenylsulfamide is treated with metallic sodium and methyl iodide in methyl alcohol, methylation occurs readily to produce the desired product (142).

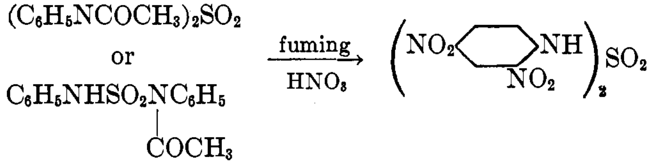
$$(C_6H_5NH)_2SO_2 + 2CH_3I + 2Na \xrightarrow{CH_3OH} (C_6H_5NCH_3)_2SO_2 + 2NaI + H_2$$

It has already been noted under the discussion of sulfamyl halides (page 72) that sulfuryl chloride exhibits a ring-chlorinating action on acetanilide, and that in order to produce acetylphenylsulfamyl chloride the chlorinating action must be inhibited by employing *N*-sodiumacetanilide. Obviously, then, *N*,*N′*-diphenyl-*N*,*N′*-diacetylsulfamide cannot be prepared directly. If, however, *N*,*N′*-diphenylsulfamide is treated for several hours with acetic anhydride containing a drop of sulfuric acid, the diacetylated product is obtained (142).

$$(C_6H_5NH)_2SO_2 + (CH_3CO)_2O \rightarrow (C_6H_5NCOCH_3)_2SO_2 + H_2O$$

Also under sulfamyl halides (page 75) it was shown that acetylphenylsulfamyl chloride produces *N*,*N′*-diphenylsulfamide when treated with aniline, and not *N*-acetyl-*N*,*N′*-diphenylsulfamide. The latter compound can be prepared merely by decreasing the time during which the acetylating mixture described above is permitted to act on *N*,*N′*-diphenylsulfamide.

Difficulty is again encountered in the reaction between nitroanilines and sulfuryl chloride, and, furthermore, the desired sulfamide cannot be prepared by the most obvious alternative reaction, *viz.*, direct nitration of N,N'-diphenylsulfamide. If the latter compound is treated directly with fuming nitric acid in concentrated sulfuric acid, a mixture of 3-nitro-4-amino- and 2-nitro-5-amino-benzenesulfonic acids is obtained. These are undoubtedly formed by the rearrangement of the intermediate sulfamic acids. On the other hand, when either the monoacetylated or the diacetylated N,N'-diphenylsulfamide is treated with fuming nitric acid, N,N'-2,4,2',4'-tetranitrodiphenylsulfamide is obtained smoothly (142).



Mention should also be made of the fact that N,N'-dimethylsulfamide, when treated with nitric acid, yields an N,N'-dinitro derivative (142); and that N,N'-diphenylsulfamide forms an N,N'-dinitroso derivative when treated with nitrogen trioxide in ether (57). No other examples of either type of compound have been reported.

VII. IMIDODISULFONATES

A. PREPARATION

Derivatives of the aquo-ammonosulfuric acid, $HN(SO_3H)_2$, were first prepared in 1834 by Heinrich Rose (107, 108, 109, 110) by the interaction of gaseous ammonia and solid sulfur trioxide. All the methods for preparing imidodisulfonates are in agreement with their designation as aquo-ammonosulfates. Recorded procedures are either ammonolytic or hydrolytic in character, or involve deammonation reactions.

1. *Ammonolytic reactions*

Depending upon the relative quantities of the reactants, di- and triammonium imidodisulfonates are obtained when gaseous (113), aqueous (19, 20), or liquid (56) ammonia is allowed to react with solid (56) or gaseous (19, 20, 77, 113) sulfur trioxide.

$$4NH_3 + 2SO_3 \rightarrow NH_4N(SO_3NH_4)_2$$

$$3NH_3 + 2SO_3 \rightarrow HN(SO_3NH_4)_2$$

Triammonium imidodisulfonate is obtained by the action of ammonia on chlorosulfonic acid (30, 33). Diammonium imidodisulfonate is obtained when ammonium carbamate is added to pyrosulfuryl chloride, sulfuryl chloride, or chlorosulfonic (89) acid. When molecular amounts of 100 per cent sulfuric acid and urea are mixed at 140°C., the reaction mixture solidifies to a mass containing diammonium imidodisulfonate and ammonium sulfate. When excess of sulfuric acid or oleum is used, sulfamic acid is obtained (13).

2. Hydrolytic reactions

Imidodisulfonates are produced by careful hydrolysis of nitrilosulfonates (41, 49, 65, 102, 103). If potassium nitrilosulfonate is heated in neutral solution, potassium imidodisulfonate is formed according to the equation:

$$N(SO_3K)_3 + H_2O \rightarrow HN(SO_3K)_2 + KHSO_4$$

This reaction takes place more rapidly in an acid solution.

3. Deammonation reactions

The sulfamates of ammonium, potassium, and lithium (31, 33, 46) have been found to undergo deammonation in accordance with the equation:

$$2NH_2SO_3M \rightarrow NH_3 + HN(SO_3M)_2$$

In the case of the ammonium salt a temperature of 160°C. (31) is required, while for the potassium salt, Divers and Haga (46) give 350°C. as the most suitable temperature.

The fusion of molar quantities of ammonium sulfamate and sulfamic acid leads directly to diammonium imidodisulfonate (13).

$$NH_2SO_3H + NH_2SO_3NH_4 \rightarrow HN(SO_3NH_4)_2$$

B. CHEMICAL PROPERTIES

Free imidodisulfonic acid is apparently not stable in the pure state. An aqueous solution of the free acid was first prepared by Jacquelain (79), who treated the lead salt with hydrogen sulfide. It was also prepared in this way by Berglund (30) and by Divers and Haga (46).

The imidodisulfonate ion may be distinguished from the sulfamate ion by the fact that the former gives a precipitate with barium hydroxide solution or with a solution of barium chloride containing ammonia. This precipitate can be distinguished from barium sulfate, as it is completely soluble in dilute acids.

The imidodisulfonate ion is more stable toward hydrolysis (102, 121) than the nitrilosulfonate ion. However, it does undergo hydrolysis (102, 121) in acid solution to the sulfamate in accordance with the equation:

$$HN(SO_3)_2^{--} + H_2O \rightarrow H_2NSO_3^- + HSO_4^-$$

Although the imido hydrogen is much less acidic than the hydrogen atoms on the sulfonic groups, it is, nevertheless, replaceable by metal ions. Hence, imidodisulfonic acid forms two series of salts: *viz.*, (*1*) the *basic salts,* those in which all three hydrogen atoms are replaced and (*2*) the *neutral salts,* in which only two hydrogen atoms are replaced. These are represented, respectively, by the type formulae:

$$(1)\ MN(SO_3M)_2 \qquad (2)\ HN(SO_3M)_2$$

With the exception of the dipotassium salt, most of the neutral imidodisulfonates are easily soluble. The basic salts are usually more stable and less soluble in water than the neutral salts (29, 30). The basic salts are readily converted into the corresponding neutral salts by treatment with even weak acids. Conversely, the neutral salts are converted to the basic salts by excess base.

The so-called mercuri-salts form a very interesting group of imidodisulfonates. They are derivatives of an acid with the formula $(HO_3S)_2NHgN(SO_3H)_2$. The parent acid appears to be very strong, but is not very stable. It may be obtained by treating the barium salt with sulfuric acid (30).

C. ALKYL DERIVATIVES OF IMIDODISULFONIC ACID

Traube and Wolfe (136) found that an aqueous solution of tripotassium imidodisulfonate reacts with alkyl halides or dialkyl sulfates to give *N*-alkyl derivatives of dipotassium imidodisulfonate.

$$KN(SO_3K)_2 + RI \rightarrow RN(SO_3K)_2 + KI$$

$$KN(SO_3K)_2 + R_2SO_4 \rightarrow RN(SO_3K)_2 + RSO_4K$$

These reactions give good yields in the case of the methyl and ethyl compounds. However, with other alkyl halides, e.g., propyl or benzyl iodides, the reaction takes place much more slowly and the yields of the alkylated products are smaller. Traube and Wolfe explain these low yields by assuming that the composition of a solution containing one mole of potassium hydroxide and one mole of dipotassium imidodisulfonate is represented by the following equilibrium:

$$HN(SO_3K)_2 + KOH \rightleftarrows KN(SO_3)_2 + H_2O$$

Two possible reactions can, therefore, take place when the alkylating agent is added to this system: (*1*) formation of the *N*-alkylimidodisulfonate from the tripotassium salt and (*2*) reaction of the alkylating agent with potassium hydroxide to give either the alcohol or the olefin.

The alkylimidodisulfonates are stable well-crystallized salts. They are stable in alkaline or neutral solutions, but in acid solution undergo hydrolysis to yield the *N*-alkylsulfamic acids.

$$RN(SO_3K)_2 + H_2O \rightarrow RNHSO_3K + KHSO_4$$

These alkylsulfamic acids can, in turn, be hydrolyzed by prolonged action of mineral acids to the corresponding amine salts.

$$RNHSO_3K + H_2O + H^+ \rightarrow RNH_3^+ + KHSO_4$$

It is interesting to note that this series of reactions provides a method for preparing amines which is analogous to the Gabriel phthalimide synthesis, the former utilizing the potassium derivative of an inorganic imido compound, $KN(SO_3K)_2$, and the latter utilizing the potassium derivative of an organic imide, phthalimide.

VIII. NITRILOSULFONATES

The nitrilosulfonates, derivatives of the aquo-ammonosulfuric acid, $N(SO_3H)_3$, are of interest mainly because they hydrolyze to imidodisulfonates which, in turn, yield sulfamates. The nitrilosulfonates were undoubtedly first prepared by Fremy (64, 65), along with a number of other sulfur–nitrogen compounds. Although he had no idea concerning the structure or nature of these substances, most of his experimental observations were later substantiated. Claus and Koch (39, 40, 41) also investigated the nitrilosulfonates, but considered them to be derivatives of pentavalent nitrogen rather than of ammonia. Despite the fact that much of this early work was later proved to be faulty, these investigators were correct in assuming that the sulfur atoms in the nitrilosulfonates are attached directly to the nitrogen atom. Berglund (33) gave them their name, nitrilosulfonates. Raschig (102, 103) systematized the chemistry of the sulfur–nitrogen compounds, rendering the structure of the nitrilosulfonates still clearer. Divers and Haga (48, 49) devised new methods for preparing some of these compounds and carried out extensive studies on the nature of the nitrite–bisulfite reaction.

A. PREPARATION

The only general method for preparing nitrilosulfonate salts involves the sulfonation of nitrous acid. Raschig (102, 103) represented this stepwise nitridation reaction, as well as the products of the hydrolysis of the intermediate compounds, by the scheme given in chart I (see page 51).

The amount and nature of the products of the nitrite–bisulfite reaction are dependent on the ratio of the reactants. A large excess of bisulfite favors the formation of the nitrilosulfonate, although it has been observed that some nitrilosulfonate is always formed whenever nitrite and bisulfite react, regardless of conditions. Sisler and Audreith (122) studied this reaction and found that the best yields of nitrilosulfonate are obtained (*1*) when the mole ratio of the bisulfite to the nitrite is 4:1 or more and

(*2*) when the bisulfite and nitrite solutions are heated to boiling before mixing.

$$KNO_2 + 4KHSO_3 \rightarrow N(SO_3K)_3 + K_2SO_3 + 2H_2O$$

B. PROPERTIES OF NITRILOSULFONIC ACID

Free nitrilosulfonic acid is not known, since nitrilosulfonates hydrolyze immediately in acid solution. Hydrolysis takes place when a solution of a salt is acidified, or when the neutral solution is heated or allowed to stand for a short time. The initial step in hydrolysis is represented by the following equation (102, 103):

$$N(SO_3)_3^{---} + H_2O \rightarrow HN(SO_3)^{--} + HSO_4^-$$

Imidodisulfonates hydrolyze further to the sulfamate stage, and hence the nitrilosulfonates may be used to prepare sulfamates and sulfamic acid. The hydrolysis of this series of aquo-ammonosulfuric acids is repressed by alkali.

Potassium nitrilosulfonate, $N(SO_3K)_3 \cdot 2H_2O$, is the best characterized derivative of nitrilosulfonic acid (49, 102, 103, 122). It is the most insoluble of the nitrilosulfonates and is indeed more insoluble than potassium perchlorate (49). It loses two molecules of water of crystallization at 100–110°C. and at higher temperatures is decomposed completely. Hydrolysis gradually takes place when the substance stands in air at room temperature, although carefully prepared samples will last about a month before decomposition becomes appreciable. A number of other nitrilosulfonates, both simple (49, 65, 102) and complex (52), have been prepared.

IX. IMIDODISULFAMIDE

A. PREPARATION

A survey of the literature leads to the conclusion that the existence of imidodisulfamide has not yet been demonstrated beyond a question of doubt. Mente (89) claims to have obtained the compound by interaction of chlorosulfonic anhydride and ammonium carbamate. His work has never been substantiated.

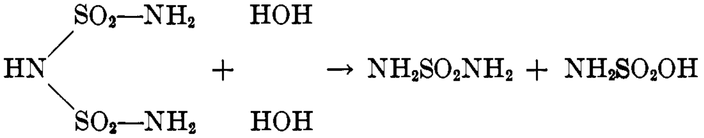
Hantzsch and his coworkers (69, 70) claim to have prepared imidodisulfamide starting with the reaction product obtained by passing gaseous ammonia into a solution of sulfuryl chloride in ligroin. After removal of chloride ion from an aqueous solution of this product, the residual material was treated with silver nitrate to precipitate a mixture of the silver salts of various nitrogen–sulfur acids. Silver sulfamide, obtained from this mixture, was decomposed by heating to give the silver salt of trisulfimide, $(AgNSO_2)_3$, which on treatment with hydrochloric acid and hydrolysis presumably yielded imidodisulfamide, although Hantzsch first thought a hydrate of trisulfimide had been isolated.

Ephraim and Gurewitsch (53) state that imidodisulfamide is the principal product when sulfuryl chloride is allowed to react with liquid ammonia in excess at low temperatures. At higher temperatures (55), using a solution of ammonia in ligroin, this same reaction presumably causes chain formation to take place with production of compounds of the type $H_2N(SO_2NH)_nSO_2NH_2$.

Most plausible among recorded procedures is the statement that thermal decomposition of sulfamide results in deammonation with formation of some imidodisulfamide (55, 128).

B. PHYSICAL AND CHEMICAL PROPERTIES OF IMIDODISULFAMIDE

Imidodisulfamide is said to be a white crystalline solid melting at 166°C. (70). It is said to be unstable in aqueous solutions, hydrolyzing to form sulfamide and sulfamic acid.



Hantzsch and Stuer (70) present excellent data to show that imidodisulfamide is cleaved instantly by water, even at 0°C. According to them aqueous solutions of imidodisulfamide are strongly acidic because of the sulfamic acid formed by hydrolysis. Ephraim and Gurewitsch (53), however, could not substantiate these findings. Their investigation led them to state that imidodisulfamide is stable for some time, even in acid solution.

In the presence of excess alkali, solutions of imidodisulfamide are apparently stabilized, presumably because of the formation of the corresponding imidodisulfamides. However, these salts have not been isolated. Only the ammonium and silver salts appear to have been characterized. The ammonium salt is formed when pure dry ammonia is passed over the dry imidodisulfamide; its formula is believed to be $NH_3 \cdot HN(SO_2NH_2)_2$. The silver salt, $AgN(SO_2NH_2)_2 \cdot 1.5H_2O$, is slightly soluble in cold but readily soluble in boiling water. It can be recrystallized from hot water without undergoing hydrolysis (70). That the silver is attached to nitrogen seems probable, for treatment with alkali causes no precipitate of silver oxide.

The chemistry of imidodisulfamide needs further investigation in order to clarify the contradictory statements now recorded in the literature.

X. SULFIMIDE AND TRISULFIMIDE

A. METHODS OF PREPARATION

Traube (127) isolated a number of salts from the product he had obtained by the reaction of sulfuryl chloride with ammonia. The analyses of these salts led him to believe that they were derived from the imide of sulfuric acid, $SO_2{=}NH$. He called the salts sulfimides. After many unsuccessful attempts to isolate the free imide he concluded that it could not exist in the solid state.

Later it was established by Hantzsch and Holl (69) that sulfimide did not exist in the simple $SO_2{=}NH$ form in the solution, but that it was present in a trimolecular form, $(SO_2{=}NH)_3$. A ring structure was assigned to this compound, based on its resemblance to cyanuric acid. Hantzsch and Holl (69) even claimed to have isolated "trisulfimide" as a white crystalline substance, melting at 161°C. Four years later, however, Hantzsch and Stuer (70) repeated and extended this investigation and came to the conclusion that the substance reported as free trisulfimide in the earlier work was in reality impure imidodisulfamide. Using extreme precaution to exclude every trace of moisture from their reaction mixture, they isolated a white compound melting at 166°C., which they identified as imidodisulfamide.

All attempts thus far to obtain trisulfimide in the solid state have been unsuccessful. Ammonium acid sulfate is the only product obtained when solutions which should lead to the imide are evaporated. When sulfamide is heated above its melting point and held at a temperature of 170°C. for some time, ammonia is given off. A mixture of trisulfimide and imidodisulfamide is presumably formed.

$$3SO_2(NH_2)_2 \rightarrow (SO_2{=}NH)_3 + 3NH_3$$

$$2SO_2(NH_2)_2 \rightarrow NH(SO_2NH_2)_2 + NH_3$$

It has been suggested recently that trisulfimide is formed as a result of the decomposition of sulfamyl chloride, which is thought to be an intermediate in the reaction between aryl chlorosulfonates and ammonia (45).

$$\begin{array}{l} C_6H_5OSO_2Cl + NH_3 \rightarrow NH_2SO_2Cl + C_6H_5OH \\ \qquad\qquad\qquad\qquad\qquad\quad \downarrow \\ \qquad\qquad\qquad\qquad\quad (SO_2NH)_3 + 3HCl \end{array}$$

During the investigation of the reaction between phosgene and sodium amide by Perret and Perrot, it was noted that derivatives of melanuric acid were present in the reaction products. Because of the structural similarities existing between trisulfimide and melanuric acid, it occurred to the investigators that trisulfimide might be obtainable by the reaction of sulfuryl chloride with sodium amide (98). By a process of fractional precipitation of their reaction product with silver nitrate appreciable quantities of silver trisulfimide, $(SO_2NAg)_3$, were obtained. It was also demonstrated that no sulfamide is formed in this reaction.

B. DERIVATIVES OF TRISULFIMIDE

It is highly probable that the salts of sulfimide prepared by Traube (127) in 1892 are actually derivatives of trisulfimide. The preparation of the silver salt is given in detail. Large quantities can be prepared by treating the aqueous solution of the product obtained from the reaction between sulfuryl chloride and ammonia with just sufficient silver nitrate to precipitate the chlorine. The precipitated silver chloride is collected and the filtrate, which is acidic, is made ammoniacal. Further addition of silver nitrate causes precipitation of silver trisulfimide, which is only slightly soluble in cold water but fairly soluble in hot water. Its solutions are very stable; the addition of barium nitrate causes no precipitation of sulfate. It is only when the solution, strongly acidified with nitric acid, is boiled that the salt is decomposed and barium sulfate precipitates. The potassium, sodium, and barium salts are also described by Traube (127).

Trimethyltrisulfimide was prepared by Hantzsch and Holl (69) from methyl iodide and silver trisulfimide.

$$3CH_3I + (SO_2{=}NAg)_3 \rightarrow (SO_2NCH_3)_3 + 3AgI$$

It is described as a colorless, odorless, tasteless solid, melting at 121°C. and subliming without decomposition when the temperature is raised above the melting point. The compound is soluble in boiling water and in such organic solvents as ether, chloroform, benzene, and alcohol. Hantzsch and Holl also prepared tribenzoylsulfimide, $(SO_2{=}NCOC_6H_5)_3$, a colorless crystalline compound melting at 112°C.

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