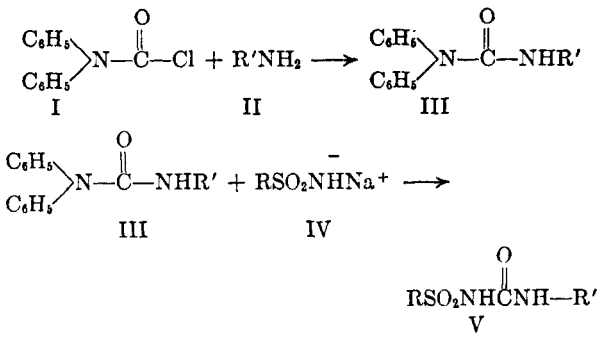
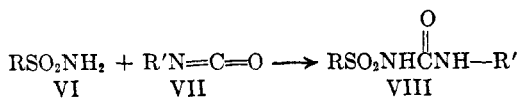
The sulfonylureas were prepared by either of two following routes, and are described in Table I.

Method A



Method B



EXPERIMENTAL[9]

Method A. Preparation of the triarylureas (III). To 300 ml. of absolute ethanol there was added 1 mole of the amine and 2.3 moles of diphenylcarbamyl chloride. This mixture was heated to reflux for 16 hr., concentrated *in vacuo*, and the residue extracted with chloroform and water. The chloroform layer was separated, washed with *N* hydrochloric acid and water, and dried over sodium sulfate. Chloroform was removed *in vacuo* and the resulting product crystallized from 95% ethanol.

All the triarylureas (III) were prepared by this procedure with the exception of those having a basic function, in which case the acid wash was omitted.

Preparation of the sulfonylureas (V). A mixture of 0.034 mole of the triarylurea (III) and 0.034 mole of the sodium salt of the sulfonamide (IV) was heated in 50 ml. of dimethylformamide at 100° for 16 hr. After cooling, the dimethylformamide mixture was diluted with 100 ml. of 2% sodium carbonate solution and extracted twice with ether. The aqueous layer was cooled and acidified with *N* hydrochloric acid. The white crystalline product that separated was collected by suction filtration and dried.[10]

All of the method A preparations essentially followed this procedure, except that in the preparation of compounds containing a basic function the alkaline aqueous layer was carefully acidified in the cold to *p*H 4, and the product that separated was collected and dried.

Method B. Preparation of the sulfonylureas (VIII). To a mixture of 30 ml. of triethylamine and 15 ml. of dimethylformamide was added 0.064 mole of the sulfonamide (VI) and 0.064 mole of the isocyanate (VII). After being stirred overnight, the mixture was diluted with 100 ml. of water and extracted twice with ether. The aqueous layer was collected and acidified in the cold with *N* hydrochloric acid. The product was collected by suction filtration and dried.

(9) All melting points are uncorrected.

(10) Method A gives in most cases high yields of the desired product; low yields in a few cases can be attributed to the fact that no effort was made to purify the commercially available amines. In two cases, the sodium salt of the sulfonylurea was insoluble in water, both these compounds were analyzed and tested as such.

Acknowledgment. The author wishes to thank Mrs. Joyce Abrams and Mr. Robert Sacco for assistance in the preparation of these compounds.

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The Preparation and Attempted Chlorosulfonation of *N,N*-Dimethylbenzylamine Sulfur Trioxide

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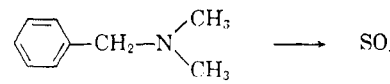
Some aminomethylbenzenesulfonyl chlorides were desired for studies on the preparation of aminomethylthiophenols. The chlorosulfonation of *N,N*-dimethylbenzylamine in chloroform solution and in the absence of a solvent gave us, unexpectedly, *N,N*-dimethylbenzylamine sulfur trioxide (also called the anhydro sulfate salt of *N,N*-dimethylbenzylamine) to which we have assigned the structure:



The following amine sulfur trioxide salts have previously been reported in the literature: the salt of pyridine, *N,N*-dimethylaniline, and trimethylamine.[1,2]

An attempt to rearrange dimethylbenzylamine sulfur trioxide to a dimethylaminomethylbenzenesulfonic acid by heating in a chloroform solution at reflux for five hours was unsuccessful.

Treatment of *N,N*-dimethylbenzylamine sulfur trioxide with an excess of chlorosulfonic acid produced a homogeneous pale-yellow solid which showed properties characteristic of both a sulfonyl chloride and of an amine sulfur trioxide salt. However, the chlorosulfonation reaction was accompanied by the evolution of sulfur dioxide indicating that there was an extensive oxidation of the amine sulfur trioxide salt. Various conditions, such as variation of reaction temperature, length of reaction time, amount of chlorosulfonic acid used and inverse addition, were employed in an unsuccessful attempt to prevent the oxidation reaction. The only analogy to this oxidation reaction that has been reported in the literature is the treatment of *N,N*-dimethylaniline with the phenyl ester of chlorosulfonic acid in the cold in which the salt of structure

(1) H. H. Sisler and L. F. Audrieth, *Inorganic Syntheses*, Vol. II, W. C. Fernelius, ed., McGraw-Hill, New York, 1946, pp. 173–175.

(2) O. W. Willcox, *Am. Chem. J.*, **32**, 446 (1904).

$C_6H_5N(CH_3)_2 \cdot C_6H_5OSO_2Cl$

forms. At higher temperature oxidation occurs and sulfur dioxide is liberated.[3] Attempts to reduce the chlorosulfonated sulfur trioxide salt using zinc and hydrochloric acid gave no identifiable organic product.

The reaction of ammonia on the product which resulted from the action of excess chlorosulfonic acid on the amine sulfur trioxide apparently yields a mixture of amides which could not be separated into individual compounds.

A study of chlorosulfonation in the benzylamine series has been done mainly by Momose.[4] who reports the preparation of the sulfonyl chlorides of *N*-benzylacetamide and *N*-methyl-*N*-benzylacetamide. Momose found a *para* to *meta* ratio in these products of 5:1; there apparently was no detectable *ortho* isomer due to steric hindrance.

EXPERIMENTAL[5]

N,N-Dimethylbenzylamine sulfur trioxide. *N,N*-Dimethylbenzylamine (91.5 g., 0.68 mole) and chloroform (350 ml.) were placed in a 1-l. three neck flask which was cooled in an ice salt bath. After cooling to 0° and while stirring, 79.7 g. (0.68 mole) of chlorosulfonic acid was added dropwise at such a rate as to keep the temperature between 0 and 10°. After addition of the chlorosulfonic acid the reaction mixture was cautiously and slowly poured over a rapidly stirred ice water mixture to decompose any excess chlorosulfonic acid. The resulting material was then transferred to a separatory funnel and the water layer was removed. The chloroform layer was then washed with several portions of cold water until the washings were free of sulfate and chloride ions as indicated by the addition of barium chloride and silver nitrate to separate portions of the washings. The solvent was then removed by evaporation under reduced pressure. The solid relatively pure *N,N*-dimethylbenzylamine sulfur trioxide was dried by allowing it to stand overnight exposed to the air. The yield was 60 g., 83%. The material was purified by recrystallization from a chloroform-ether solution and melted at 217° dec.

Anal. Calcd. for $C_9H_{13}NO_3S$: S, 14.8; N, 6.50. Found: S, 14.8; N, 6.43.

N,N-Dimethylbenzylamine sulfur trioxide is insoluble in a variety of organic solvents. It is but slightly soluble in chloroform and is hydrolyzed very slowly to sulfate ions by boiling water.

In the absence of solvent the yield of the dimethylbenzylamine sulfur trioxide was only 18%.

The reaction of chlorosulfonic acid with N,N-dimethylbenzylamine sulfur trioxide. To 30 g. (0.139 mole) of *N,N*-dimethylbenzylamine sulfur trioxide was added 155.8 g. (1.34 moles) of chlorosulfonic acid (with stirring) at such a rate that the temperature of the reaction mixture did not rise above room temperature. During the addition there was an immediate liberation of a gas which consisted in part of sulfur dioxide and the formation of a greenish solution. After all the chlorosulfonic acid was added, stirring was continued for 24 hr. during which time no more gas evolution was observed. The reaction mixture was then poured over a rapidly stirred ice water mixture. The fine granular pale yellow crystals were separated and washed with several portions of cold water. The melting point of the crude product was 112–120°. This material contained 20.4% sulfur, 4.47% nitrogen, and 11.3% chlorine. It could not be purified by recrystallization because of its insolubility in all common organic solvents. It must consist of a mixture of substances as its reaction with ammonia produces amides melting in the range 104–260°. Based upon differences in solubility in ethanol, sodium hydroxide, and hydrochloric acid, these latter were separated into three fractions which still were mixtures that could not be separated further into individual pure compounds.

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(3) L. Denivelle, *Bull. Soc. Chem.*, (5), **3**, 2143 (1936).

(4) T. Momose, *Nippon Saikingaku Zasshi* (*Japanese Journal of Bacteriology*), **5**, 119 (1950); also private communication.

(5) Elemental analyses were performed by Drs. Weiler and Strauss, 164 Banbury Lane, Oxford, England.

Transthiazolination: The Rearrangement of 2-(2′-Aminoethylthio)-2-thiazoline

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S-(2-Aminoethyl)isothiourea has been shown by Doherty *et al.*,[1] to undergo rearrangement to 2 mercaptoethylguanidine in neutral aqueous solution, and a cyclic intermediate has been postulated for the reaction. The rearrangement of a number of aminoalkylisothioureas to mercaptoalkylguanidines by this transguanylation reaction has been studied by ion exchange analysis.[2,3] In addition, it was demonstrated by ion exchange analysis that 2-(2′-aminoethylthio)-2-imidazoline underwent transimidazolination to 2-(2′-mercaptoethylamino)-2-imidazoline rapidly at *p*H 7.0; the properties of the compounds involved were not described.

We have found that 2-(2′-aminoethylthio)-2-thiazoline (I) undergoes a similar type of rearrangement, for which a symmetrical bicyclic intermediate can be postulated. The dihydrobromide of I was prepared by the reaction of 2-thiazolidinethione and 2-bromoethylamine hydrobromide in refluxing isopropyl alcohol. When an aqueous solution of I dihydrobromide was neutralized or made weakly alkaline, rearrangement to 2-(2′-mercaptoethylamino)-2-thiazoline (III) occurred. The latter compound readily underwent oxidation in air to the disulfide IV. Color tests on IV, its analytical data, and its infrared spectrum were consistent with its formulation as bis[2-(2′-thiazolinyl-2′-amino)ethyl] disulfide. Proof of this structure was obtained by alternate synthesis.

2-Methylthio-2-thiazoline and 2-mercaptoethylamine hydrochloride in refluxing methanol[4] af-

(1) D. G. Doherty, R. Shapira, and W. T. Burnett, Jr., *J. Am. Chem. Soc.*, **79**, 5667 (1957).

(2) J. X. Khym, R. Shapira, and D. G. Doherty, *J. Am. Chem. Soc.*, **79**, 5663 (1957).

(3) J. X. Khym, D. G. Doherty, and R. Shapira, *J. Am. Chem. Soc.*, **80**, 3342 (1958).