

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]  
**IDENTIFICATION OF AMINES. IV. METHANESULFONAMIDES**

BY C. S. MARVEL, M. D. HELFRICK AND J. P. BELSLEY

RECEIVED NOVEMBER 21, 1928

PUBLISHED APRIL 5, 1929

The arylsulfonyl derivatives of primary and secondary amines have been carefully investigated and are very useful in the separation and identification of amines. However, very little work has been done on the alkylsulfonyl derivatives of this type. The work of Johnson and Ambler<sup>1</sup> shows that benzylsulfonamides are more easily hydrolyzed than are arylsulfonamides. It was thought that the simple alkylsulfonamides might hydrolyze even more readily than the benzyl derivatives and since ease of hydrolysis is a desirable property in sulfonamides if they are to be of value in the separation of amines, some of the methanesulfonamides were prepared and characterized.

Methanesulfonyl chloride has been prepared by the action of phosphorus pentachloride on methanesulfonic acid.<sup>2</sup> In this work the mixture of sodium methanesulfonate and sodium methyl sulfate obtained by the action of dimethyl sulfate on sodium sulfite was dried and treated directly with phosphorus pentachloride.

The methanesulfonamides could be prepared by the usual procedure using the sulfonyl chloride, the amine and aqueous alkalis. However, methanesulfonyl chloride is fairly easily hydrolyzed by water and the best yields of sulfonamides were obtained by working in benzene solutions. The methanesulfonamides were readily hydrolyzed by boiling them with 60% sulfuric acid for six hours.

Methanesulfonyl chloride has certain disadvantages as a reagent for the separation of amines. When an unknown mixture of primary, secondary and tertiary amines was treated with an excess of the reagent in the presence of cold aqueous alkalis, the primary amine was converted quite largely to the disulfonyl compound, which precipitated with the derivative of the secondary amine. Unless an excess of the reagent was used the tertiary amine was always contaminated with unchanged primary and secondary amine. When a known mixture of amines was treated with a known excess of the reagent, the amines were separated satisfactorily and the primary and secondary amines were recovered by hydrolysis of the derivatives.

### Experimental Part

**Methanesulfonyl Chloride.**—In a 5-liter three-necked flask fitted with a reflux condenser, mechanical stirrer and a separatory funnel, were placed 1 kg. of anhydrous sodium sulfite and 2 liters of hot water (80–90°). The mixture was stirred and heated

<sup>1</sup> Johnson and Ambler, *THIS JOURNAL*, **36**, 385 (1914).

<sup>2</sup> Carius, *Ann.*, **114**, 142 (1860).

on the steam cone for about ten minutes to get as much in solution as was possible. The heating was discontinued and then 1 kg. of dimethyl sulfate was added at such a rate that the solution boiled gently. When all of the dimethyl sulfate had been added, the condenser was set for distillation and the water was distilled off under reduced pressure until a pasty mass just fluid enough to pour remained in the flask. This mixture was transferred to a large porcelain dish and dried in an oven at 120° until the mass was solid. This mass was then ground in a mortar and dried again for about six hours at 120°. The powdered mixture of sodium methanesulfonate and sodium methyl sulfate was transferred to a 5-liter flask and mixed thoroughly with 1.4 kg. of phosphorus pentachloride. About 2 liters of dry benzene was added to give better contact between the two reacting substances. This mixture was heated to gentle boiling under a reflux condenser for ten to twelve hours. The reaction mixture was cooled and filtered with suction. The salt cake was washed with 500 cc. of dry benzene. The benzene solution was then carefully fractionated using a good column. The yield of methanesulfonyl chloride boiling at 158–162° was 200–250 g. (21–27% of the theoretical amount based on the sodium sulfite).

**Methanesulfonamides.**—For the preparation of the pure amide it was found that the best results were obtained by treating a benzene solution of two molecular proportions of the amine with a benzene solution of one molecular proportion of methanesulfonyl chloride. The amine hydrochloride was filtered off, the benzene evaporated and the sulfonamide recrystallized from dilute alcohol until it had a constant melting point. The results of these experiments are given in Table I.

TABLE I  
METHANESULFONAMIDES

Amine	M. p. of amide, °C.	Amine	M. p. of amide, °C.
Aniline <sup>a</sup>	100.5	2,5-Dichloro-aniline	174
<i>o</i> -Toluidine	103	$\alpha$ -Naphthylamine	125.5
<i>p</i> -Toluidine	102.5	$\beta$ -Naphthylamine	153.5
<i>o</i> -Anisidine	115.5	$\delta$ -Phenoxybutylamine	79.5
<i>p</i> -Anisidine	116	Methylaniline	76.5
<i>p</i> -Phenetidine	125	Ethylaniline	59
<i>o</i> -Chloro-aniline	90.5	<i>n</i> -Propylaniline	76
<i>p</i> -Chloro-aniline	148	<i>n</i> -Butylaniline	73
<i>p</i> -Bromo-aniline	136	Benzylaniline	122

<sup>a</sup> McGowan, *J. prakt. Chem.*, [2] 30, 282 (1884), prepared this amide but does not list its properties; Duguet, *Chem. Zentr.*, [1] 854 (1902), gives 99° as the melting point of this compound.

The derivatives of *N*-ethyl-*p*-toluidine, *N*-ethyl-*o*-toluidine, *l*-menthylamine, *sec.* butylaniline, diethylamine, di-*n*-butylamine and di-*n*-propylamine were oils. Satisfactory nitrogen analyses were obtained on the solid compounds. The derivatives of the primary amines were soluble in 10% aqueous sodium hydroxide.

**Hydrolysis of Methanesulfonamides.**—A suspension of 9.3 g. of methanesulfone-*N*-methylanilide in a solution of 30 cc. of concentrated sulfuric acid (sp. gr. 1.84) in 30 cc. of water was boiled under a reflux condenser for about six hours. The solution was made alkaline and distilled with steam. The distillate was extracted with ether and the ether evaporated. The residual oil weighed 3.8 g. (about 71% of the theoretical amount) and was shown to be methylaniline.

The oily methanesulfonyl derivative prepared from 17 g. of di-*n*-butylamine was hydrolyzed by boiling under reflux for six hours with a solution of 30 cc. of concentrated

sulfuric acid in 30 cc. of water. The solution was then made alkaline and extracted with ether. The ether was extracted with aqueous hydrochloric acid. This solution was then evaporated to dryness. The yield of di-*n*-butylamine hydrochloride was 7.8 g.

**Separation of Amine Mixtures.**—A mixture of 10 g. of aniline, 10 g. of methylaniline, and 10 g. of dimethylaniline was suspended in a 10% excess of cold 10% aqueous sodium hydroxide. To the cold suspension 27 g. (about 20% excess) of methanesulfonyl chloride was added during about ten minutes. The temperature was never above 25° and was usually about 10–15°. When the methanesulfonyl chloride had reacted, the solution was extracted with ether. The ether was evaporated and this residue was again treated with methanesulfonyl chloride and aqueous alkali as before.

After the second treatment the derivative of the primary amine was obtained by acidifying the combined alkaline solutions. The yield was 10.2 g. (55% of the theoretical amount). The unchanged tertiary amine was extracted from the ether solution with hydrochloric acid and the ether was then evaporated. The residue weighed 10.5 g. (60% of the theoretical amount) and was the pure secondary amine derivative. The tertiary amine was recovered to the extent of about 95% from the acid solution.

When the composition of the amine mixture was not known the results were never as satisfactory as those described above. Prolonged action of the sulfonyl chloride converted the primary amines to alkali-insoluble derivatives. These are undoubtedly the disulfonyl derivatives although they were not isolated and characterized.

### Summary

Several methanesulfonamides have been prepared and characterized. They make suitable derivatives for many amines and they are more readily hydrolyzed than most sulfonamides. Some difficulties are encountered when methanesulfonyl chloride is used as a reagent for the separation of unknown amine mixtures.

URBANA, ILLINOIS

---

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

## RESEARCHES ON PYRIMIDINES. CVI. LEUCO BASES OF A NEW CLASS OF DYESTUFFS CONTAINING PYRIMIDINE RINGS

BY TREAT B. JOHNSON

RECEIVED NOVEMBER 23, 1928

PUBLISHED APRIL 5, 1929

Certain representatives of the aniline dyes hold a place of great importance in the chemotherapy of bacterial diseases, and their practical use for the disinfection of tissues has received increased attention during recent years.<sup>1</sup> Some of these combinations, especially members of the triphenylmethane series, are highly bactericidal. Gentian violet and magenta, for example, have been shown to be able to inhibit growth of staphylococci and streptococci in culture media in dilutions as high as 1:100,000 to 1:1,000,000. It is important also to note that several of these dyestuffs

<sup>1</sup> J. W. Churchman, *J. Am. Med. Assoc.*, **79**, 1657 (1922); *Chim. industrie*, **10**, 212 (1923); *Stain Tech.*, **1**, 27, 103 (1926); *Ind. Eng. Chem.*, **18**, 1322 (1926).