

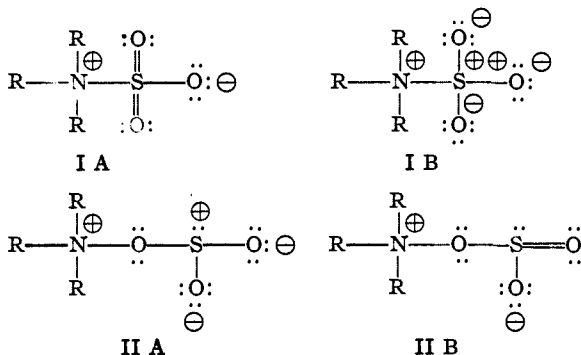
[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, CALCO CHEMICAL DIVISION, AMERICAN CYANAMID COMPANY]

Compounds of Trialkylamine Oxides with Sulfur Dioxide and Trioxide

BY H. Z. LECHER AND W. B. HARDY

Compounds of tertiary amines with sulfur trioxide, which had been known for a long time,¹ attained considerable practical interest in the twenties for the conversion of reduced vat dyes into the sulfuric esters of the leuco compounds which are being used extensively in the arts of textile dyeing and printing. Until recently it has been an unsolved problem to carry out this esterification in an aqueous medium. It has been found in our Research Department² that, contrary to the previously used sulfur trioxide compounds of weak tertiary bases such as pyridine and dimethylaniline, the sulfur trioxide compounds of stronger basic tertiary amines, such as trialkylamines, are sufficiently stable to water and still sufficiently reactive to allow this desired aqueous esterification of reduced vat dyes.³ The practical results of our investigation have been⁴ or will be published in patents, but some observations of predominantly theoretical interest shall be presented to THIS JOURNAL.

While investigating the above-mentioned esterification reaction, we became interested in the structure of the trialkylamine-sulfur trioxide compounds. The most obvious formulas of isomers are



A. B. Burg⁵ has already pointed out that formula IB infringes Pauling's "adjacent charge rule"⁶ which states that structures involving the juxtaposition of atoms with charges of the same sign are unstable and that, therefore, the octet rule might not hold for such compounds as, for in-

(1) F. Beilstein and E. Wiegand, *Ber.*, **16**, 1267 (1883), prepared the compound from triethylamine and sulfur trioxide.

(2) H. Z. Lecher, M. Scalera and C. T. Lester, U. S. Patent 2,403,226 (1946).

(3) This aqueous process is being used by the Calco Chemical Division in the manufacture of sulfuric esters of leuco vat dyes.

(4) Cf. also H. Z. Lecher, M. Scalera, E. M. Hardy, U. S. Patent 2,402,647 (1946) and H. Z. Lecher, M. Scalera, E. M. Hardy, U. S. Patent 2,396,582 (1946).

(5) Burg, *THIS JOURNAL*, **65**, 1629 (1943).

(6) L. Pauling and L. O. Brockway, *ibid.*, **59**, 13, 17 (1937); cf. also L. Pauling, *Proc. Natl. Acad. Sci. U. S. A.*, **18**, 498 (1932); and L. O. Brockway and L. Pauling, *ibid.*, **19**, 860 (1933).

stance, dithionic acid. It seems, therefore, that formula IA is more probable than formula IB.

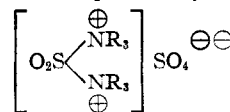
It generally has been assumed that the compounds obtained from tertiary amines and sulfur trioxide correspond to formula I. The formation of a compound corresponding to type II from trimethylamine oxide and sulfur dioxide was observed by Burg⁵ but the compound was not isolated. It seemed desirable to prepare a trialkylamine oxide-sulfur dioxide compound of the type II in pure state, and to determine how its behavior differs from that of type I.⁷

M. Délépine and R. Demars⁸ stated that trimethylamine-sulfur trioxide (type I) is formed from trimethylamine oxide and sulfur dioxide without, however, giving the yield. Also, R. Wolfenstein⁹ stated that the reaction of amine oxides derived from various tertiary amines with sulfur dioxide gave him compounds of the type I, but did not give yields.

We have found that the main product of this reaction is the isomer of the type II. When sulfur dioxide is passed over a suspension of anhydrous trimethylamine oxide in benzene the crude reaction product is obtained in 90% yield and contains only about 5% of the isomeric compound of type I as was shown by the extraction of the crude product with cold water in which the compound of type I is stable and only slightly soluble, while the compound of type II is extremely soluble, probably with decomposition. On the other hand, the compound of type II is quite stable in hot absolute ethanol, while trimethylamine-sulfur trioxide reacts with this solvent to give the trimethylamine salt of ethyl sulfuric acid¹⁰ which remains in solution. As a result, when the crude product was extracted with hot ethanol, the pure compound of type II, trimethylamine oxide-sulfur dioxide, was obtained melting at 164° with decomposition.

Trimethylamine oxide-sulfur dioxide was also prepared by reaction of sulfur dioxide with trimethylamine oxide dissolved in ethylene chloride, ethanol, or acetic acid. Under these conditions, a little more of the isomeric trimethylamine-sulfur

(7) A third possible form represented by the formula:



and corresponding to the formula which K. Wickert and G. Jander, *Ber.*, **70B**, 251 (1937), assigned to the addition product of triethylamine with sulfur dioxide is ruled out by the fact that the trialkylamine-sulfur trioxide compounds in aqueous solution do not give a precipitate with barium chloride.

(8) Délépine and Demars, *Bull. sci. pharmacol.*, **30**, 577 (1923).

(9) M. Auerbach and R. Wolfenstein, *Ber.*, **32**, 2507 (1899); L. Mamlock and R. Wolfenstein, *ibid.*, **34**, 2499 (1901).

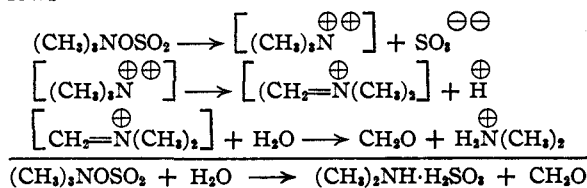
(10) W. Traube, H. Zander and H. Gaffron, *ibid.*, **87**, 1045 (1924).

trioxide, about 20% of the total product, was formed.¹¹

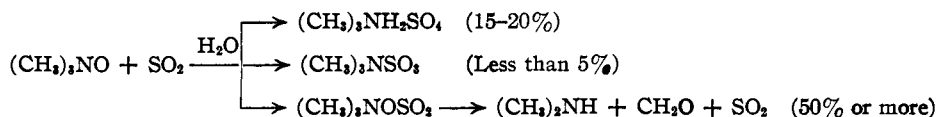
Before the reaction of trimethylamine oxide with sulfur dioxide in water will be discussed, it is necessary to consider the behavior of the compounds of type II in hydrolytic reactions. The type I regenerates the tertiary amine on hydrolysis. In contrast thereto, trimethylamine oxide-sulfur dioxide (II) in acid solution undergoes complete decomposition into dimethylamine, formaldehyde and sulfur dioxide. Dimethylamine and sulfur dioxide were also formed in essentially quantitative yields by alkaline hydrolysis, but in this case formaldehyde was not identified, presumably due to its dismutation under the conditions of hydrolysis. This decomposition, at least on the alkaline side, occurs under very mild conditions. Thus, when trimethylamine oxide-sulfur dioxide was added to cold barium hydroxide a precipitate of barium sulfite formed immediately.

Since, as shown by an independent experiment, trimethylamine oxide does not react at any appreciable rate with sodium sulfite in alkaline solution to give dimethylamine, the first stage of the hydrolysis reaction cannot be the formation of amine oxide and sulfurous acid or sulfite.

The mechanism of the hydrolysis of trimethylamine oxide-sulfur dioxide is believed to be as follows¹²



In view of the easy breakdown of the compound $(\text{CH}_3)_3\text{NOSO}_2$ in water, it appeared possible that this product might be formed momentarily when the components were brought together in aqueous medium with subsequent degradation of the amine oxide. When aqueous trimethylamine oxide was treated with sulfur dioxide at 10°, a small amount of trimethylamine-sulfur trioxide, large quantities (50% or more) of dimethylamine and formaldehyde, and some sulfuric acid were formed. Presumably an equimolar amount of trimethylamine was formed concomitantly with the sulfuric acid. These reactions may be summarized as



Triethylamine oxide was found to decompose in a similar manner when treated with sulfur dioxide in aqueous solution.

(11) As efforts to produce the isomerization of trimethylamine oxide-sulfur dioxide to trimethylamine-sulfur trioxide were unsuccessful it is concluded that the two compounds are formed in independent reactions.

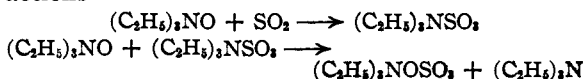
(12) J. Meisenheimer, *Ber.*, **46**, 1148 (1913), postulated a similar mechanism for degradation of tertiary amines by means of chlorine.

It was beyond the scope of the present investigation to examine the general applicability of this reaction or to determine the maximum yields obtainable. However, this method of degradation of a tertiary to a secondary amine appears to be novel and should offer advantages.

It is, therefore, well established that the compounds obtained from tertiary amines and sulfur trioxide (or chlorosulfonic acid) represent type I and are distinctly different from the addition products of sulfur dioxide on amine oxides which represent type II. D. McLachlan, Jr., and R. C. Gore in the Stamford Research Laboratories of our Company have carried out X-ray and infrared work which furnished physical proof of the structure of trimethylamine- and triethylamine-sulfur trioxide, as corresponding to Type I.

The reaction of anhydrous triethylamine oxide with sulfur dioxide in benzene gave an unexpected result. Whereas the normal addition compound $(\text{C}_2\text{H}_5)_3\text{NOSO}_2$ analogous to that obtained from trimethylamine oxide would be expected, the product was shown to be $(\text{C}_2\text{H}_5)_3\text{NOSO}_3$ by analysis and by its hydrolysis reactions. This compound is stable in cold water but decomposes on warming in dilute acid to give triethylamine oxide and sulfuric acid. Its hydrolysis in alkaline solution parallels the behavior of trimethylamine oxide-sulfur dioxide in that diethylamine, sodium sulfate and (presumably) acetaldehyde are formed. It is of interest to note that the compound $(\text{C}_2\text{H}_5)_3\text{NOSO}_3$ hydrolyzes at the O-S bond in acid solution, whereas in alkaline solution the O-S bond is stable so that the SO_4^{\ominus} ion is eliminated while the electron deficiency of the remaining nitrogen radical results in its decomposition. The mechanism appears to be similar to that postulated for the hydrolysis of trimethylamine oxide-sulfur dioxide.

The formation of the compound $(\text{C}_2\text{H}_5)_3\text{NOSO}_3$ in the reaction of sulfur dioxide with triethylamine oxide probably occurs through the following reactions



This implies that triethylamine oxide, which is a very weak base in water,^{13,14} is able to take sulfur trioxide from the strongly basic triethylamine.

That this is actually the case was demonstrated by adding an ethylene chloride solution of triethylamine-sulfur trioxide to anhydrous triethylamine oxide in benzene. Immediate precipitation of the

(13) T. D. Stewart and S. Maeser, *THIS JOURNAL*, **46**, 2583 (1924), found the ionization constant of trimethylamine oxide hydrate to be 4×10^{-10} .

(14) Taylor and Baker, "Sidgwick's Organic Chemistry of Nitrogen," Oxford University Press, 1937, p. 168.

compound $(C_2H_5)_3NOSO_3$ occurred with evolution of heat, illustrating again the powerful electron-donor character of amine oxides.¹⁵

An addition compound of pyridine N-oxide and sulfur trioxide was described by P. Baumgarten and H. Erbe.¹⁶

Experimental

Trimethylamine Oxide-Sulfur Dioxide

Preparation.—Trimethylamine oxide was prepared in aqueous solution by oxidation of trimethylamine with 3% hydrogen peroxide.¹⁷ Concentration of the aqueous solution gave the solid dihydrate. Anhydrous trimethylamine oxide was prepared by dehydration and sublimation under reduced pressure.¹⁸

Six grams (0.08 mole) of powdered trimethylamine oxide was placed in 75 cc. of dry benzene. While the suspension was rapidly stirred and the temperature maintained at 20°, dry sulfur dioxide was passed over its surface. Moist air was thoroughly excluded. The reaction was strongly exothermic at first so that it was necessary to control the gas flow carefully during the first half hour. The mixture was saturated with sulfur dioxide in one hour. It was stirred for three hours longer in order to insure more complete reaction.

The white precipitate was filtered off at 10° and washed with 10 cc. of dry benzene. The yield of crude vacuum dried product was 10.3 g., or 92% of the theoretical value. It sintered at 114° and melted at 125–133° with decomposition. The crude product contained about 5% of a solid which was slightly soluble in water and which was shown to be trimethylamine-sulfur trioxide. Two grams of the crude product was recrystallized from 135 cc. of absolute ethanol, whereby 0.8 g. of pure product was recovered. It sintered at 158° and melted at 162–164° (dec.). The crude product was also satisfactorily purified by stirring with 12 parts boiling ethanol and filtering at 10° to give an over-all yield of 46%.

Anal. Calcd. for $C_3H_9O_2NS$: C, 25.9; H, 6.46; N, 10.1; S, 23.0. Found: C, 25.7; H, 6.83; N, 10.3; S, 23.0.

Trimethylamine oxide-sulfur dioxide is very slightly soluble in ethylene chloride, *t*-butanol, acetone, benzene, sulfuryl chloride or thionyl chloride. It is moderately soluble in morpholine, aniline or acetic acid and very soluble in liquid sulfur dioxide.⁵

Trimethylamine oxide is readily soluble in ethylene dichloride, ethanol, and acetic acid. It reacts with sulfur dioxide in these solvents to give the addition compound but the crude product contained about 15–25% of the isomeric trimethylamine-sulfur trioxide.

Alkaline Hydrolysis.—A solution of 5.0 g. (0.036 mole) of trimethylamine oxide-sulfur dioxide in 20 cc. of 5 *N* sodium hydroxide was boiled gently for half an hour and the evolved gas was absorbed by 1 *N* hydrochloric acid. Titration of an aliquot showed that 0.036 mole of an amine had been neutralized. This amine was identified as dimethylamine by conversion into its *p*-toluenesulfonyl derivative which was isolated in 76% yield (based on trimethylamine oxide-sulfur dioxide). There was no indication of the formation of methylamine, since the crude sulfonamide did not contain an alkali soluble component. The residual alkaline solution obtained in the hydrolysis experiment contained sulfite, but only a little sulfate (0.356 g. barium sulfate, corresponding to about 4% of the sulfur in the starting material).

Acid Hydrolysis.—A solution of 5.0 g. (0.036 mole) of trimethylamine oxide-sulfur dioxide in 25 cc. of 5 *N* hydrochloric acid was heated at the boil for half an hour. The vapors smelled strongly of formaldehyde, and gave a strong positive test with Schiff aldehyde reagent. The

evolved gases were collected in 100 cc. of 2.5 *N* sodium hydroxide. Oxidation of the alkaline solution with sodium hypochlorite followed by treatment with excess barium chloride gave 8.8 g. of barium sulfate which proves that the theoretical amount of sulfur dioxide was obtained from the trimethylamine oxide-sulfur dioxide.

One-fifth of the acid solution (obtained in this hydrolysis experiment) was used to identify the formaldehyde as the 2,4-dinitrophenylhydrazone, m. p. 162–163°. The remaining four-fifths of the acid solution was evaporated on the steam-bath to give 2.4 g. of solid. A 1-g. sample was converted into the *p*-toluenesulfonyl derivative of dimethylamine (m. p. and mixed m. p. of the purified product 81–82°). The yield was 1.8 g., or 73.4% of the theoretical amount.

When a 10% aqueous solution (slightly acid) of trimethylamine oxide-sulfur dioxide was treated with picric acid no picrate was obtained which proves that no trimethylamine oxide was present.

Attempted Conversion to $(CH_3)_3NSO_3$: A. In Ethylene Chloride.—Three grams of trimethylamine oxide-sulfur dioxide was stirred in 30 cc. of ethylene chloride in a dry atmosphere for three hours at 35°. After filtering at 15° and drying over phosphorus pentoxide *in vacuo*, 2.8 g. (93%) of unchanged starting material (m. p. 161–163°) was recovered. A 0.5-g. sample gave a clear solution in 2 cc. of water indicating the absence of more than traces of trimethylamine-sulfur trioxide.

B. In Acetic Acid.—Two grams of the addition compound was dissolved in a mixture of 9.5 cc. of acetic acid and 0.5 cc. of acetic anhydride at 85°. The hot solution was treated with 10 cc. of carbon tetrachloride. The solid which precipitated weighed 2.0 g., m. p. 163–165°. It was completely soluble in a small volume of water.

Trimethylamine Oxide and Sulfur Dioxide in Water

A solution of 4.0 g. (0.036 mole) of trimethylamine oxide dihydrate in 25 cc. of water was saturated with sulfur dioxide gas at 10°; 0.05 g. of crude trimethylamine-sulfur trioxide (m. p. 210–220°) separated. The filtrate was treated with 25 cc. of 5 *N* sodium hydroxide and the gases evolved on heating were collected in 100 cc. of 1 *N* hydrochloric acid. Titration of one-tenth of the acid solution showed that 94.3% of the theoretical amount of amine had been taken up by the acid. The remaining nine-tenths of the acid solution was evaporated to dryness to give 2.2 g. of amine hydrochloride. It was converted into the *p*-toluenesulfonyl derivative of dimethylamine; however, the yield of this derivative was lower than that obtained from the alkaline hydrolysis of trimethylamine oxide-sulfur dioxide, because trimethylamine was also formed. The residual alkaline solution obtained in the hydrolysis experiment gave with barium chloride and hydrochloric acid 1.36 g. of barium sulfate. Thus, approximately 16% of the amine oxide was reduced to trimethylamine, assuming that part of the amine oxide was reduced by sulfur dioxide to give trimethylamine and sulfuric acid.

As a control experiment 0.036 mole of trimethylamine oxide was heated with 0.036 mole of sodium sulfite in 20 cc. of 5 *N* sodium hydroxide for half an hour at the boil with the vapors being passed into standard acid as before. Since a maximum of 0.00133 mole (2.8%) of base was absorbed, it is clear that the decomposition products noted were due solely to reaction of the amine oxide with sulfur dioxide and not due to the alkaline distillation.

In order to demonstrate the nature of the product formed concomitantly with dimethylamine in the hydrolysis, a second reaction was carried out between aqueous trimethylamine oxide and sulfur dioxide as described above. Upon completion of the reaction the mixture was heated under gentle reflux for half an hour. The vapors gave a strong test with Schiff aldehyde reagent and a 45% yield of the 2,4-dinitrophenylhydrazone of formaldehyde (m. p. 161–163°) was obtained from the reaction mixture.

Triethylamine Oxide and Sulfur Dioxide

Reaction in Aqueous Solution.—A 15.0% aqueous solution of triethylamine oxide was prepared following the pro-

(15) A. B. Burg, *THIS JOURNAL*, **67**, 2261 (1945).

(16) Baumgarten and Erbe, *Ber.*, **71**, 2603 (1938).

(17) W. R. Dunstan and E. Goulding, *J. Chem. Soc.*, **75**, 1005 (1899).

(18) J. Meisenheimer and K. Bratring, *Ann.*, **397**, 286 (1913).

cedure outlined by Dunstan and Goulding.¹⁷ This oxidation required seventy-two hours at 25–30° and a 20% excess of hydrogen peroxide to proceed to completion. The excess peroxide was added as a 30% solution in portions during the reaction. Analysis of the amine oxide solution by precipitation of the picrate (m. p. 163–164°) showed that a 90% yield was obtained.

Thirty-seven grams (0.045 mole real) of the above triethylamine oxide solution was saturated with sulfur dioxide at 10°. A small amount (0.1 g.) of triethylamine-sulfur trioxide (m. p. 85–92°) was filtered off. The filtrate was treated with 20 cc. of 40% sodium hydroxide and diluted and the volatile amine was distilled into 100 cc. of 1 *N* hydrochloric acid. Titration of one-tenth of this acid solution showed that 76% of the amine oxide had decomposed to yield a volatile base. The remaining nine-tenths of the acid solution was evaporated to dryness on the steam-bath to give 3.6 g. (80%) of amine hydrochloride. When treated with *p*-toluenesulfonyl chloride it gave the diethylamine derivative melting at 60–62°.

As a control experiment 20 cc. (0.03 mole real) of an aqueous triethylamine oxide solution was mixed with 20 cc. of 5 *N* sodium hydroxide and 0.03 mole of sodium sulfite. The solution was heated at the boil for half an hour with the vapors passing into standard hydrochloric acid. No base was absorbed in the acid solution.

When the solution obtained by action of sulfur dioxide on aqueous triethylamine oxide was boiled with hydrochloric acid, a strong aldehyde odor was noted and the vapors gave a positive test on filter paper wet with Schiff aldehyde reagent. This solution gave an impure 2,4-dinitrophenylhydrazone melting from 149 to 175° after recrystallization from ethanol. It was shown that triethylamine oxide does not decompose into an aldehyde when boiled with dilute hydrochloric acid.

Reaction under Anhydrous Conditions.—Since ordinary methods of dehydration such as azeotropic removal of water with benzene or drying *in vacuo* over powerful desiccants resulted in decomposition of the amine oxide, recourse was had to the following procedure. A 15% aqueous triethylamine oxide solution made as above was evaporated under 25 mm. pressure at 50–55° to a viscous liquid containing about 75% of the amine oxide. Five grams (0.03 mole real) of this concentrated solution was placed in 75 cc. of benzene and 10 g. of freshly crushed barium oxide was added. This mixture was stirred for five hours at 30° in a flask protected from atmospheric moisture. The mixture was filtered and the insoluble material was washed with 20 cc. of dry benzene. The slightly yellow filtrate was then stirred with 6 g. of freshly powdered calcium hydride for eight hours at 25–30°. At the end of this period there was essentially no gas (hydrogen) being evolved. A small portion of this dry solution was evaporated to give a viscous oil. Treatment of this oil with saturated aqueous picric acid gave a picrate melting at 167–172°. The remainder of the dry amine oxide solution was treated with sulfur dioxide gas as described under preparation of triethylamine oxide-sulfur dioxide. After saturation with sulfur dioxide was obtained the solution was concentrated at 20° under reduced pressure to one-third of the initial volume. The resulting solid was removed by filtration and washed with 5 cc. of dry benzene. The precipitate (containing some benzene) weighed 4.1 g. A 1.0-g. sample was slurried in 2.5 cc. of cold absolute ethanol and washed with 2 cc. of cold ethanol. This purification was repeated and the product was dried *in vacuo* over phosphorus pentoxide to give 0.4 g. of white solid sintering at 116° and melting at 119–120°. This product was moderately soluble in cold water and gave no precipitate with barium chloride in the cold but precipitated barium sulfate

on heating. An alkaline solution of the product darkened on heating and an amine was liberated. As shown in the following section, this product is (C₂H₅)₃NOSO₃.

Anal. Calcd. for C₆H₁₅O₄NS: C, 36.5; H, 7.6; N, 7.1; S, 16.2. Found: C, 37.3; H, 8.2; N, 7.0; S, 16.0.

Triethylamine Oxide-Sulfur Trioxide

Preparation.—Eighteen grams (0.11 mole real) of a 75% solution of triethylamine oxide was added to 170 cc. of benzene and the solution was dehydrated with barium oxide and calcium hydride as described above. While stirring the clear filtrate at 15–17° (moist air being excluded), 20 g. (0.11 mole) of triethylamine-sulfur trioxide dissolved in 50 cc. of ethylene chloride was added during fifteen minutes. A white solid precipitated quickly and the temperature tended to rise. After stirring for a few minutes longer, the solid was filtered off, slurried with 35 cc. of absolute ethanol at 20°, filtered cold and washed with 10 cc. of cold ethanol. The filter cake from the ethanol was then stirred with 50 cc. of ethylene dichloride at 25° to remove unreacted triethylamine-sulfur trioxide. The insoluble product was again purified from ethanol and dried *in vacuo* over calcium chloride to give 12.7 g. (58%) of white solid, m. p. 124–125°.

Hydrolysis.—A 0.4-g. sample of pure triethylamine oxide-sulfur trioxide was dissolved in 3 cc. of water and acidified with hydrochloric acid. After boiling for five minutes a strong test for sulfate was obtained. The hydrolyzed solution was treated with aqueous picric acid. The picrate obtained was recrystallized from water to give 0.15 g. of product sintering at 154° and melting at 158–162°.

In order to determine the products of alkaline hydrolysis, a 0.9 g. (0.0045 mole) portion of the pure compound was placed in 15 cc. of 10% sodium carbonate solution. The solution was heated at the boil for ten minutes and the distillate which came off during this time was collected in 4 cc. of water. The residue was dark yellow in color and an oily layer had formed at the surface. It gave a positive test for sulfate ion. The distillate was treated with *p*-toluenesulfonyl chloride. After recrystallization from 50% aqueous ethanol, the product sintered at 54° and melted at 58–61° (m. p. of *p*-toluenesulfonyldiethylamine 62°). The yield was 50% of theoretical.

Summary

Trimethylamine oxide-sulfur dioxide was prepared and shown to be distinctly different from triethylamine-sulfur trioxide in its structure and reactions. The latter hydrolyzes to trimethylamine and sulfuric acid, while the former gives dimethylamine, formaldehyde and sulfurous acid on hydrolysis. The reaction of sulfur dioxide on triethylamine oxide in water yields essentially the same products, and indicates a new method for the degradation of tertiary to secondary aliphatic amines.

The reaction of triethylamine oxide with triethylamine-sulfur trioxide gives triethylamine oxide-sulfur trioxide which hydrolyzes in acidic medium to the amine oxide and sulfuric acid, in alkaline medium to diethylamine, acetaldehyde and sulfuric acid.

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