

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

A NEW METHOD FOR THE PREPARATION OF O,N-DIALKYLHYDROXYLAMINES

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The present methods used in the preparation of O,N-dialkylhydroxylamines¹ were found to be inadequate and too expensive to produce the relatively large amounts of these compounds required in the recent work in this Laboratory.

Hydroxyurethan prepared by Jones' modification of Hantzsch's method² was alkylated with a little more than two moles of dialkyl sulfate in alkaline solution. A small amount of O-alkylhydroxyurethan was separated by extraction with alkali from the O,N-dialkylhydroxyurethan which was formed during the reaction. These O,N-dialkylhydroxyurethans were hydrolyzed by refluxing them with a 50% solution of potassium hydroxide in alcohol. The free O,N-dialkylhydroxylamine was distilled into hydrochloric acid and recovered in the usual manner. O,N-dimethyl- and O,N-diethylhydroxylamines were prepared by this method.

A study of the boiling points of mixtures of O,N-dialkylhydroxylamines with water revealed a constant boiling mixture of O,N-diethylhydroxylamine and water at 74°. No corresponding mixture could be detected in the case of O,N-dimethylhydroxylamine and water.

Experimental Part

Preparation of O,N-Dimethylhydroxyurethan, $\text{CH}_3\text{ONCH}_2\text{COOC}_2\text{H}_5$.—Two moles of hydroxyurethan was dissolved in 1200 cc. of a 20% solution of potassium hydroxide and to this was added, in small portions, with vigorous shaking, 4.25 moles of dimethyl sulfate. During this operation the temperature was kept below 25°. An oily layer soon appeared above the aqueous solution. The mixture was stirred vigorously for one hour after the addition of the dimethyl sulfate had been completed. The mixture was then made acid to congo red with sulfuric acid and extracted with ether; the ether solution was then extracted with 400 cc. of a 20% solution of sodium hydroxide in 100cc. portions. The ether layer was dried with anhydrous sodium sulfate, the ether removed by distillation and the oil which remained distilled *in vacuo*. The portion boiling below 80° under 25 mm. was collected. O,N-dimethylhydroxyurethan was then separated by fractionation at atmospheric pressure. The portion boiling between 150 and 155°³ was collected; yield, 80 g. The fraction which was left, after the O,N-dimethylhydroxyurethan had been distilled, decomposed when an attempt was made to distil it. A copious quantity of formaldehyde was present among the products of decomposition.

¹ (a) Lossen, *Ann.*, **252**, 230 (1889); (b) Jones, *Am. Chem. J.*, **20**, 40 (1898); (c) **38**, 253 (1907); (d) Hecker, *ibid.*, **50**, 444 (1913); (e) Jones and Neuffer, *THIS JOURNAL*, **36**, 2202 (1914); (f) Neuffer and Hoffman, *ibid.*, **47**, 1685 (1925).

² Hantzsch, *Ber.*, **27**, 1254 (1894); ref. 1b, p. 39.

³ Jones, ref. 1b, p. 42, gives 150–155° as the b. p.

The sodium hydroxide extract, from the above procedure, was made acid to congo red, extracted with ether and the ether solution dried with calcium chloride. Eleven g. of O-methylhydroxyurethan was obtained; b. p. 186–188°.⁴

Preparation of O,N-Diethylhydroxyurethan, $C_2H_5ONC_2H_5COOC_2H_5$.—To a solution of 2 moles of hydroxyurethan and 4.25 moles of diethyl sulfate was added, in small portions accompanied by vigorous shaking, 1200 cc. of a 20% solution of potassium hydroxide. Heat rapidly developed in the mixture. The temperature was allowed to rise to 65° and was maintained between 60 and 65° throughout the course of the reaction. More alkali was not added in any case until the rise in temperature produced by the previous addition had ceased. An oily layer appeared above the aqueous solution. After all of the potassium hydroxide had been added the mixture was vigorously stirred for an hour, cooled, made acid to congo red with sulfuric acid and extracted with ether. This ether solution was then extracted with 400 cc. of a 20% solution of sodium hydroxide in 100cc. portions. The ether solution was dried with anhydrous sodium sulfate, the ether distilled and the resulting oil fractionated *in vacuo*. The fraction boiling between 107 and 112° under 70 mm.⁵ was recovered; yield, 162 g.

The sodium hydroxide extract from the above procedure was made acid to congo red, extracted with ether and the ether solution dried with calcium chloride. Eighteen g. of O-ethylhydroxyurethan was recovered; b. p. 195–196°.⁶

Preparation of O,N-Dialkylhydroxylamines, RONRH.—One mole of O,N-dialkylhydroxyurethan was added to a cold solution of 3 moles of potassium hydroxide dissolved in 350 cc. of 50% alcohol. Hydrolysis, accompanied by considerable heat, at once commenced. The solution was refluxed for one hour. The O,N-dialkylhydroxylamine was then distilled into ice-cooled dilute hydrochloric acid. The hydrochloric acid solution was concentrated on the water-bath and then placed in a vacuum desiccator containing concentrated sulfuric acid and solid potassium hydroxide. O,N-dimethylhydroxylammonium chloride separated in the form of white crystals. It was recrystallized from absolute alcohol by addition of dry ether; m. p. 115–116°. The O,N-diethylhydroxylammonium chloride remained as an oil.

To prepare O,N-dialkylhydroxylamine the hydrochloride was distilled with an excess of concentrated potassium hydroxide solution and the vapors passed over solid pieces of potassium hydroxide heated to 95° before they were condensed. O,N-dimethylhydroxylamine distilled at 42–43° and corresponded in every respect to this compound as described by Jones.⁷ O,N-diethylhydroxylamine distilled at 83° and had the same properties as those ascribed to it by Lossen.⁸

The Effect of Water upon the Boiling Point of O,N-Diethylhydroxylamine.—A solution of molecular equivalents of O,N-diethylhydroxylamine and water distilled at 74°. When a second molecular equivalent of water was added, two layers appeared. The upper layer distilled at 74° and then the temperature of the vapors rapidly rose to that of boiling water. The fraction distilling at 74° was dried over solid potassium hydroxide and redistilled; b. p. 83°.

The authors wish to express their appreciation to Professor Lauder W. Jones for many helpful suggestions and criticisms.

⁴ Jones, ref. 1b, p. 41, gives 186–188° as the b. p.

⁵ Hecker, ref. 1d, p. 449, gives 107–112° (70 mm.) as the b. p.

⁶ Jones, ref. 1b, p. 45, gives 195–196° as the b. p.

⁷ Jones, ref. 1b, p. 44, gives 42.2–42.6° as the b. p.

⁸ Lossen, ref. 1a, p. 234, gives 83° as the b. p.

Summary

1. O,N-dialkylhydroxyurethans have been prepared by the action of alkyl sulfates on hydroxyurethan.
2. O,N-dialkylhydroxylamines have been obtained by hydrolysis of O,N-dialkylhydroxyurethans with alcoholic potassium hydroxide.
3. The addition of water has been shown to lower the boiling point of O,N-diethylhydroxylamine but not that of O,N-dimethylhydroxylamine.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BARNARD COLLEGE]

5-BROMO-2,4-DIMETHOXYBENZOYLACRYLIC ACID AND ITS ESTERS. II

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In a study¹ of bromodimethoxybenzoylacrylic acid it has been found that the esters of this unsaturated γ -ketonic acid readily form addition products with alcohols in the presence of a trace of potassium hydroxide. This reaction suggested an investigation of the behavior of the dibromo addition products of the acid and its esters on treatment with alkaline reagents under conditions which would favor the formation of acetylenic compounds as intermediate products.

On treatment with bromine, bromodimethoxybenzoylacrylic acid gives one dibromo acid, but under the same conditions the methyl and ethyl esters give mixtures of racemic compounds which were separated only after tedious fractional crystallization; the pairs of isomers have practically the same solubilities in the common organic solvents and the two racemic methyl esters have melting points within one degree of each other.² The mixture of racemic dibromomethyl esters was shown to give the same products with sodium methylate as the higher melting one of the isomers; in subsequent work therefore the mixtures of both dibromo esters were used.

The products obtained are alkoxy and hydroxy compounds which can be explained as addition products of bromodimethoxybenzoylpropionic ester, formed by loss of two molecules of hydrogen bromide from the dibromo esters. No attempt has been made to isolate the acetylenic compounds, which would be expected to show the same ease of addition as the corresponding ethylenic esters.¹ Pairs of ethylenic bromo isomers, however, have been prepared from the dibromo methyl and ethyl esters and one of these ethylenic bromo methyl esters has been shown to give the same products as the saturated dibromo ester on treatment with a methyl alcohol solution of potash. That a second molecule of hydrogen bromide

¹ Rice, *THIS JOURNAL*, 50, 229 (1928).

² Lutz, *ibid.*, 48, 2905 (1926).