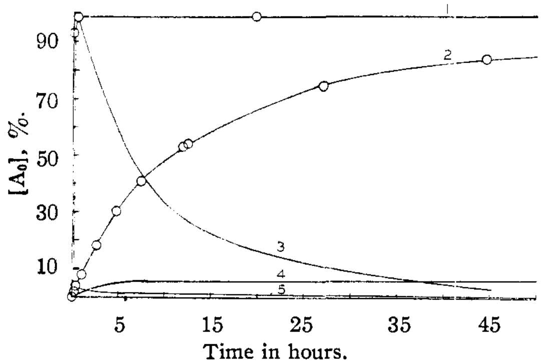


Fig. 3.—Ethyl-bis-β-chloroethylamine in 1:3 acetone-water at 25°, $[A]_0 = 0.1401$: curve 1, chloride ion liberated; curve 2, hydrogen ion liberated; curve 3, [B]; curve 4, (1) − (3) − [B] = 2 × polymer produced; curve 5, [A].

not common, for the decreased dielectric constant of the less aqueous medium to overbalance the diminished concentration of the water, and result in an increased rate of hydrolysis of a positively charged molecular species.

Such a straightforward graphical determination of the separate rate constants could not be carried out with our data on methyl-bis-β-chloroethylamine in 2:1 acetone-water (Part I of this series) because the amount of hydrolysis in that case was too small to permit reliable estimates of the slopes which served as the starting-point in the present case.

Summary

Ethyl-bis-β-chloroethylamine differs from its methyl homolog in undergoing a larger proportion of hydrolysis as compared to dimerization, in part-aqueous solution. Kinetic studies have been made of the reactions of this amine in 2:1 and 1:3 acetone-water solutions and the results are shown to be consistent with the general mechanism involving formation of an ethylene-immonium ion as an intermediate in dimerization, hydrolysis and displacement. The special quantitative relations among the separate rate constants make it possible to evaluate these constants by a graphical method.

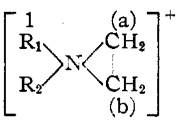
The cyclic dimer of ethyl-bis-β-chloroethylamine, though inert to hydrolysis and displacement in neutral or acid solution, is readily subject to elimination of hydrochloric acid in the presence of sodium hydroxide.

CAMBRIDGE, MASSACHUSETTS RECEIVED MARCH 27, 1947

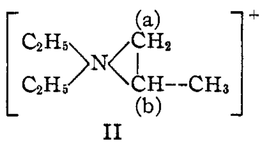
[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Role of Neighboring Nitrogen Atom in the Displacement Reaction; Rearrangement in the Hydrolysis of 1-Diethylamino-2-chloropropane

BY SIDNEY D. ROSS[1]

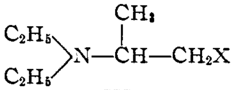


I



II

There is a large body of evidence that a cyclic ethyleneimmonium ion of the type I, where (a) and (b) represent the points of attack, is an intermediate in the dimerization, hydrolysis and displacement reactions of the tertiary β-chloroethylamines.[1a] If an analogous intermediate were formed in the hydrolysis of 1-diethylamino-2-chloropropane it would have structure II. In the case of I (a) and (b) are methylene groups and attack by a reagent, X^-, at either position results in the same product. In the case of II (a) and (b) differ, and the attack of a reagent, X^-, at the two positions should result in two different products. Attack at (a) should give a product, III, having a rearranged carbon skeleton, whereas attack at (b) should restore the original carbon skeleton. Since the attack on II is of the S_N2 type, (a), being least substituted, would be the favored point of attack and the predominant product should be the one having the rearranged carbon skeleton. Moreover, the occurrence of such a rearrangement would constitute evidence for II as an intermediate in the reaction.



$$(C_2H_5)_2N—\overset{CH_3}{\overset{|}{C}H}—CH_2X$$

III

To test this hypothesis we prepared 1-diethylaminopropanol-2 by heating diethylamine with propylene oxide in a sealed tube. 1-Diethylaminopropanol-2, IV, has been previously prepared in this way,[2] and, also, by heating diethylamine with propylene chlorohydrin[3] or propylene bromohydrin.[4] The amino alcohol, IV, gave the

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[1a] Bartlett, Ross and Swain, THIS JOURNAL, **69**, 2971 (1947); Bergmann, Golumbic, Fruton, Stahmann and Stein, *J. Org. Chem.*, **11**, 518-585 (1946), and unpublished war research by Ogston and co-workers in England and Cohen and co-workers in this country. Since submission of this paper a communication by Brode and Hill (THIS JOURNAL, **69**, 724 (1947)) has reported similar results with dimethylaminopropyl chloride.

[2] (a) Cook and Rider, THIS JOURNAL, **58**, 1079 (1936); (b) Krasuskii and Pilyugin, *Urainskii Khem. Zhur.*, **5**, Sci. Pt. 135-138 (1930); *C. A.*, **25**, 2690 (1931).

[3] Ladenburg, *Ber.*, **14**, 2406 (1881).

[4] Fourneau and Puval, *Bull. soc. chim.*, **31**, 429 (1922).

previously reported picrate melting at 89–90°.[2b] On treatment with thionyl chloride in chloroform IV gave the hydrochloride of 1-diethylamino-2-chloropropane, V. The free amine has been previously obtained by Kharasch and Fuchs[5] by addition of hydrogen chloride to diethylallylamine. Its picrate, which Kharasch and Fuchs compared with that from an authentic sample of 1-diethylamino-2-chloropropane, melts at 126–127°. The hydrochloride, V, which we obtained gave, on treatment with picric acid in alcohol, a crude picrate melting at 124–127°. After several crystallizations from ethanol the picrate had a constant melting point of 127°.

Basic hydrolysis of V gave a diethylaminopropanol which had the same neutral equivalent as IV but was not identical with it. Its index of refraction was higher and it gave a picrate melting at 118° whereas the picrate from IV melted at 89–90°. Its physical properties are in good agreement with those reported for 2-diethylaminopropanol-1,[6] previously prepared by the sodium and alcohol reduction of ethyl α-diethylaminopropionate, and this is the only reasonable structure which can be assigned to it. The hydrolysis of 1-diethylamino-2-chloropropane is thus accompanied by rearrangement, and the occurrence of this rearrangement constitutes evidence for II as an intermediate in the reaction.

Experimental

Preparation of 1-Diethylaminopropanol-2, IV.—Freshly distilled diethylamine (19 g., 0.26 mole) and freshly distilled propylene oxide (14.5 g., 0.25 mole) were sealed in a Carius tube and heated for thirty hours at 210°. On distillation 28.5 g. of material boiling at 49–51° at 15 mm. was obtained. Redistillation at atmospheric pressure gave 23.5 g. (72% of the theoretical) of the amino alcohol boiling at 155–157°. Another distillation gave a product boiling at 156–157°; n^{25}_D 1.4244; neutral equivalent: calcd. for $C_7H_{17}ON$ 131, found 133. The amino alcohol gave the known picrate melting at 89–90°.[2b]

Preparation of 1-Diethylamino-2-chloropropane Hydrochloride, V.—Thionyl chloride (14.3 g., 0.12 mole) in 50 cc. of chloroform was added dropwise to 1-diethylaminopropanol-2 (13.1 g., 0.10 mole). The reaction mixture was cooled in an ice-bath during the addition. The mixture was then refluxed for two hours. The solvent was removed *in vacuo* and the crude product was crystallized twice from acetone. The yield was 10.3 g. (55%) of a white, hygroscopic, crystalline solid.

Anal. Calcd. for $C_7H_{17}NCl_2$: ionic chloride 19.0. Found: Cl^-, 18.7.

On treatment with picric acid in ethanol the amine hydrochloride gave a crude picrate melting at 124–127°. After several crystallizations from ethanol the picrate had a constant melting point of 127°.

Hydrolysis of 1-Diethylamino-2-chloropropane Hydrochloride.—1-Diethylamino-2-chloropropane hydrochloride (5 g., 0.027 mole) was treated with sodium hydroxide (4 g., 0.10 mole) in 75 cc. of water and 75 cc. of acetone. The mixture was left standing for forty hours and then extracted continuously with ether for twenty hours. The ether extract consisted of two phases. Concentrated hydrochloric acid (3 cc., 0.036 mole) was added and the solution was taken to dryness. A sirup was obtained and all attempts to obtain the crystalline hydrochloride failed. An aqueous solution of the sirup was made strongly alkaline and extracted with benzene. The benzene extract was dried and distilled, giving 2 g. (56.8%) of 2-diethylaminopropanol-1; b. p. 66° at 25 mm.; n^{25}_D 1.4290; neutral equivalent, calcd. for $C_7H_{17}ON$ 131, found 134. The product gives a deep yellow picrate which melts at 118° and shows a depression to 85° on mix melting with picric acid (m. p. pure, 121.8°).

Anal. Calcd. for $C_{13}H_{20}N_4O_8$: C, 43.33; H, 5.60. Found: C, 43.22; H, 5.56.

Summary

1-Diethylamino-2-chloropropane gives on hydrolysis the rearranged product 2-diethylaminopropanol-1. This constitutes evidence for the occurrence of N,N-diethyl-α-methylethylenimmonium chloride as an intermediate in the reaction.

NORTH ADAMS, MASS. RECEIVED DECEMBER 6, 1946

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[5] Kharasch and Fuchs, *J. Org. Chem.*, **10**, 159 (1945).

[6] V. Braun, Leistner and Münch, *Ber.*, **59**, 1954 (1926); V. Braun, Joster and Wagner, *ibid.*, **61**, 1426 (1928); Grignard, Dupont and Locquin, "Traite de Chimie Organique," Vol. 12, p. 478.

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

Thionol and its Semiquinone Radical

BY S. GRANICK AND L. MICHAELIS

In previous papers from this Laboratory the formation of semiquinone radicals by partial reduction of thiazine dyestuffs has been studied for many representatives of dyes of this class (and also of the class of oxazines and that of selenazines).[1] The various types of representatives may be characterized as follows: they may have no "auxochromic" group at all (phenthiazine itself, unsubstituted); or they may have one auxochromic group, either an amino group[2] (3-aminothiazine), or a hydroxyl group (3-hydroxthiazine); or they may have two auxochromic groups, either two amino groups (3,9-diaminothiazine or thionine, and also methylene blue), or one amino and one hydroxyl group (thionolin) or two hydroxyl groups (3,9-dihydroxythiazine or thionol). Representatives of all these groups were investigated except for the last mentioned one, thionol, which could not be obtained in a sufficiently pure condition. For theoretical reasons to be discussed later, it seemed desirable to fill in this gap.

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[1] (a) L. Michaelis and M. P. Schubert, THIS JOURNAL, **62**, 204 (1940); (b) S. Granick, L. Michaelis and M. P. Schubert, *ibid.*, **62**, 1802 (1940); (c) L. Michaelis, S. Granick and M. P. Schubert, *ibid.*, **63**, 351 (1941); (d) L. Michaelis and S. Granick, *ibid.*, **63**, 1636 (1941); (e) *ibid.*, **64**, 1861 (1942).

[2] As in previous papers, the nomenclature refers to the corresponding leuco dye, instead of the dye itself, for the sake of simplicity.