[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

THE FORMATION OF PYRROLIDINE DERIVATIVES FROM DIETHYL α,α'-DIBROMO-ADIPATE AND CERTAIN SECONDARY AMINES

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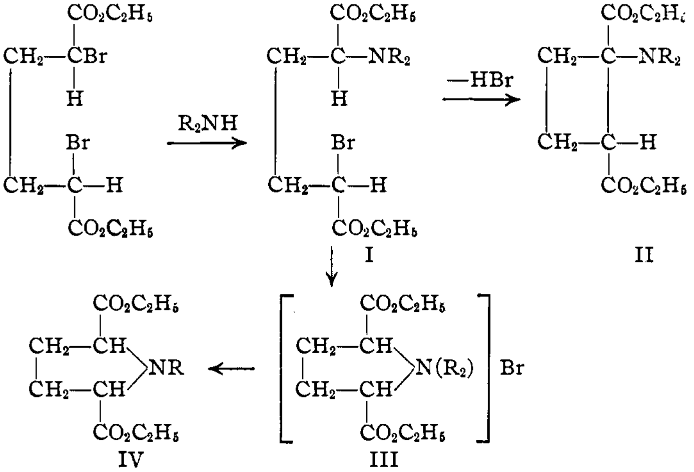
It has been shown by von Braun and his collaborators[1] that the cleavage of diethyl α,α'-dibromo-adipate by secondary amines is general for a wide variety of aliphatic amines. Of the amines whose action was studied only piperidine and dimethylamine failed to produce the cleavage. The mechanism proposed by Fuson[2] for the cleavage involves the intermediate formation of an unstable cyclobutane derivative (II) from the α-bromo-α'-dialkylamino-adipic ester (I) postulated as the initial reaction product.



This theory has been supported by evidence presented by Fuson and Kao[3] and by von Braun, Jostes and Wagner.[1] On the basis of this mechanism, there seemed to be no reason for the abnormal behavior of piperidine and dimethylamine. The action of these amines has, therefore, been reinvestigated. Work by Fuson and Bradley[4] and by von Braun[5] has subsequently shown that under favorable conditions piperidine also gives a good yield of the cleavage products.

The present paper is a report of a study of the dimethylamine case. Although it has not been possible to obtain cleavage products from α,α'-

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[1] Von Braun, Leistner and Münch, *Ber.*, **59B**, 1950 (1926); von Braun, Jostes and Wagner, *ibid.*, **61B**, 1423 (1928).

[2] Fuson, THIS JOURNAL, **50**, 1444 (1928).

[3] Fuson and Kao, *ibid.*, **51**, 1536 (1929).

[4] Fuson and Bradley, *ibid.*, **51**, 599 (1929).

[5] Von Braun, *Ber.*, **62B**, 1694 (1929).

dibromo-adipic esters by the action of this amine, evidence has been obtained which seems to clear up the difficulty.

In studying the reaction of dimethylamine with diethyl α,α'-dibromo-adipate, the authors noted a large loss of material when the reaction mixture was worked up with dilute hydrochloric acid and ether. The aqueous solution was extracted with ether, made alkaline and again extracted with ether. The ether-soluble product so obtained amounted to less than a fourth of the starting materials. The explanation which at once suggested itself was the formation of a cyclic quaternary ammonium bromide (III, $R = CH_3$).

In order to test this hypothesis, the following experiments have been carried out. The reaction mixture after treatment with dilute hydrochloric acid was thoroughly extracted with benzene. The aqueous layer was then made alkaline and was again extracted repeatedly with benzene. The aqueous solution was then distilled under diminished pressure. After the water had been distilled the residue was heated until decomposition took place. In this way, there was obtained a water-insoluble base which has been shown to be diethyl 1-methyl-pyrrolidine-2,5-dicarboxylate.

The identity of the diethyl 1-methyl-pyrrolidine-2,5-dicarboxylate was established by a comparison of its chloroplatinate with that of an authentic specimen made by the method of von Braun and Seemann.[6] The melting point of a mixture of the two chloroplatinates showed no depression.

Results very similar to these have been reported by Le Sueur and Haas[7] who obtained dialkyl 1-phenylpyrrolidine-2,5-dicarboxylates by treating α,α'-dibromo-adipic esters with mono- and diethylaniline. It would appear from the present work that, in these cases, also, a cyclic quaternary ammonium bromide (III) is formed as an intermediate product which yields the pyrrolidine derivative (IV) when decomposed by heat.

Experimental Part

Meso-diethyl α,α'-Dibromo-adipate and Dimethylamine.—To 108 g. of a 25% solution of dimethylamine in absolute alcohol (0.6 mole of dimethylamine) was added 36 g. (0.1 mole) of meso-diethyl α,α'-dibromo-adipate. The mixture was heated gently to bring the ester into solution, and after a few minutes reaction was evidenced by the evolution of heat which soon caused the solution to boil. After two hours' refluxing on the steam-bath, the clear slightly yellow solution was placed in a Claisen flask and the alcohol and excess amine distilled under diminished pressure (water pump).

The residue, which consisted of a mixture of crystals and a viscous liquid, was filtered, the crystals were washed thoroughly with dry benzene and the latter was then used to extract any benzene-soluble material from the filtrate. The benzene solution was dried over sodium sulfate and distilled. It yielded 3 g. of an oil boiling at 140–145° (8 mm.), 150–160° (20 mm.). This corresponds to the diethyl α,α'-tetra-ethyl-diamino-adipate $(CH_2CHN(CH_3)_2CO_2C_2H_5)_2$ described by von Braun and Münch and represents a yield of 20% of the theoretical.

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[6] Von Braun and Seemann, *Ber.*, **56B**, 1841 (1923).

[7] Le Sueur and Haas. *J. Chem. Soc.*, **97**, 173 (1910).

The water-soluble, benzene-insoluble portion of the residue after being, as indicated above, repeatedly washed with benzene, was placed in a Claisen flask and heated under diminished pressure. The temperature of the bath was gradually raised to about 250°. An oily distillate was obtained, part of which crystallized at once and proved to be dimethylamine hydrobromide. The oil was washed with water, dried over potassium carbonate and distilled. There was obtained 2 g. of a slightly yellow oil boiling at 112–113° (3 mm.). The chloroplatinate formed in deep yellow crystals melting at 180–180.5° (corr.).

The chloroplatinate of the base was prepared by dissolving 0.2 g. in 2 cc. of 95% alcohol and 1 cc. of dilute hydrochloric acid, and adding to this solution 4.5 g. of a 10% solution of chloroplatinic acid. The solution was concentrated on a steam-bath and allowed to stand overnight at 0°. Deep yellow crystals were obtained which after repeated recrystallization from alcohol melted at 180–180.5° (corr.). It was found that the precipitation of the chloroplatinate from the reaction mixture could be induced by the addition of a little ether. A mixture of the chloroplatinate with that of diethyl 1-methylpyrrolidine-2,5-dicarboxylate, prepared as described below, melted at 179–180° (corr.).

The Chloroplatinate of Diethyl 1-Methylpyrrolidine-2,5-dicarboxylate.—This salt was prepared by the method of von Braun and Seeman. From 36 g. of diethyl α,α'-dibromo-adipate and 310 g. of a 30% solution of methylamine in absolute alcohol (corresponding to 0.3 mole of methylamine) 2 g. or 10% of the theoretically possible yield, of diethyl 1-methylpyrrolidine-2,5-dicarboxylate was obtained. The chloroplatinate melted at 179–180° (corr.).

Summary

The failure of dimethylamine to bring about the dibromo-adipic ester cleavage is accounted for by the fact that the chief reaction in this case is one leading to the formation of a water-soluble, benzene-insoluble product which is believed to be the cyclic quaternary ammonium bromide. This explanation is supported by the fact that the material when dry distilled yields diethyl 1-methyl-pyrrolidine-2,5-dicarboxylate.

The formation of dialkyl 1-phenylpyrrolidine-2,5-dicarboxylates when mono- or diethylaniline is used is explained by a similar mechanism.

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