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

THE CLEAVAGE OF DIETHYL α,α'-DIBROMO-ADIPATE BY DIETHYLAMINE

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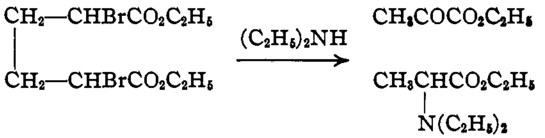
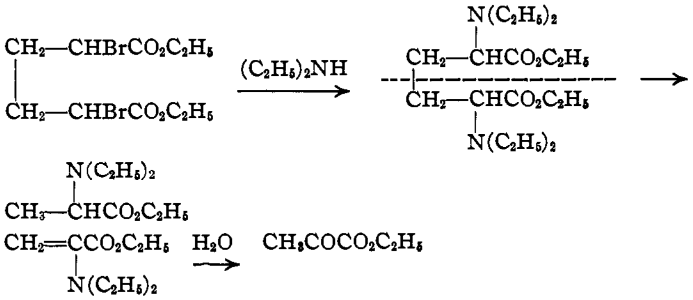
In a recent article von Braun, Leistner and Münch[1] described a remarkable and apparently novel type of rupture of an aliphatic carbon chain. Diethyl α,α'-dibromo-adipate on treatment with certain secondary amines does not yield the expected diamino-adipic esters but is severed into two three-carbon chains. Thus, in the case of diethylamine the products are ethyl pyruvate and an amino ester which was identified by von Braun and his co-workers as ethyl α-diethylaminopropionate.



$$\begin{array}{l} \mathrm{CH_2{—}CHBrCO_2C_2H_5} \\ | \\ \mathrm{CH_2{—}CHBrCO_2C_2H_5} \end{array} \xrightarrow{\mathrm{(C_2H_5)_2NH}} \begin{array}{l} \mathrm{CH_3COCO_2C_2H_5} \\ \\ \mathrm{CH_3\underset{\displaystyle N(C_2H_5)_2}{\underset{|}{C}}HCO_2C_2H_5} \end{array}$$

It has further been shown that this type of reaction is peculiar to adipic esters. It does not take place when the corresponding dibromo esters of glutaric, pimelic and suberic acids are used.

The authors explain the chain decomposition by assuming replacement of the bromine atoms by amino groups and subsequent breaking down of the resulting diamino ester. Thus, when diethylamine is used it is assumed that diethyl α,α'-tetraethyldiamino-adipate is formed in the normal manner and that it then breaks down to form ethyl α-diethylaminopropionate and ethyl α-diethylamino-acrylate, the latter being hydrolyzed to ethyl pyruvate



$$\begin{array}{l} \mathrm{CH_2{—}CHBrCO_2C_2H_5} \\ | \\ \mathrm{CH_2{—}CHBrCO_2C_2H_5} \end{array} \xrightarrow{\mathrm{(C_2H_5)_2NH}} \begin{array}{l} \mathrm{CH_2{—}\overset{\displaystyle N(C_2H_5)_2}{\overset{|}{C}}HCO_2C_2H_5} \\ \text{-- -|- - - - - - - - - - - - -} \\ \mathrm{CH_2{—}\underset{\displaystyle N(C_2H_5)_2}{\underset{|}{C}}HCO_2C_2H_5} \end{array} \longrightarrow$$

$$\begin{array}{l} \mathrm{CH_3{—}\overset{\displaystyle N(C_2H_5)_2}{\overset{|}{C}}HCO_2C_2H_5} \\ \mathrm{CH_2{=}\underset{\displaystyle N(C_2H_5)_2}{\underset{|}{C}}CO_2C_2H_5} \xrightarrow{\mathrm{H_2O}} \mathrm{CH_3COCO_2C_2H_5} \end{array}$$

To account for the breaking of the carbon chain an explanation based on space considerations is advanced. It is assumed that the adipic ester molecule is bent about as in I so that the two bromine atoms are held very close together in space.

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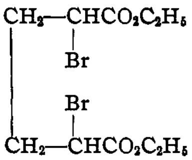
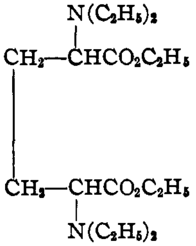
[1] Von Braun, Leistner and Münch, *Ber.*, 59B, 1950 (1926).



I

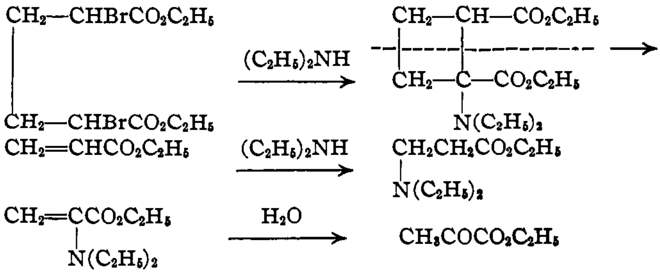


II

The exigency of space at this point in the molecule is assumed to be such that when the diethylamino groups are introduced they serve as a wedge, prying the ends of the molecule apart and rupturing the chain.

This mechanism is objectionable for several reasons. In the first place, diethyl α,α'-tetraethyldiamino-adipate when once formed is quite stable—a fact which cannot be explained on this theory. Furthermore, it seems unlikely that the bromine atoms or the diethylamino groups which replace them must necessarily lie near together as in I; they should be free to rotate and to occupy, for instance, the positions indicated in II if space factors demand it. It is hard to understand why substituents on the α-carbon atoms would prevent the free rotation of these atoms especially if the "preferred" position involves such internal stress in the molecule as would bring about its decomposition.

It is the object of the present article to show that the facts outlined above may be explained in another way—a way not only more completely in harmony with these facts but which identifies the apparently novel chain fission with a known type of reaction. It is postulated that a four-membered ring is formed as an intermediate and that this, in accordance with the well-known tendency of cyclobutane derivatives, dissociates into two molecules of ethylenic character.[2] Thus, again taking the diethylamine case as an example, the first step is the elimination of hydrobromic acid and the replacement of the second bromine atom by a diethylamino group to give diethyl 1-diethylamino-1,2-cyclobutanedicarboxylate. This compound then dissociates into ethyl acrylate and ethyl α-diethylamino-acrylate



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[2] Staudinger, *Ber.*, **44**, 526 (1911).

Ethyl α-diethylamino-acrylate like other amines of this general type should be easily hydrolyzed[3] and under the conditions of the experiment should appear as ethyl pyruvate, its hydrolysis product. This ester is actually obtained.

Ethyl acrylate, however, would not be expected to yield ethyl α-diethylaminopropionate—the other product reported by von Braun, Leistner and Münch. Flürscheim[4] has shown that in the presence of diethylamine and at a temperature of approximately 100°, ethyl acrylate is transformed quantitatively into ethyl β-diethylaminopropionate. Under the conditions of the experiment, therefore, ethyl β-diethylaminopropionate should appear among the reaction products instead of the corresponding α-compound reported by von Braun and his collaborators.

An examination of the experimental work, however, reveals the fact that, although the amino ester in question was characterized by analysis and by the preparation of two derivatives, there is no evidence to show that it is the α- rather than the β-ester. The work has, accordingly, been repeated and it has been shown that the amino ester obtained is really the β-isomer[5]—a result in accord with the reaction mechanism advanced in the present paper.

The identity of the amino ester was established by comparing it with authentic specimens of ethyl α-diethylaminopropionate and ethyl β-diethylaminopropionate. Both of these compounds are known, the former having been prepared by Flürscheim[4,6] and the latter by Adams and Dreger.[7] The following table gives the boiling points, densities, refractive indices and the melting points of the methyl iodide derivatives of the two known esters and of the unknown one.

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[3] Examples of this type of behavior are ethyl β-aminocrotonate [Geuther, *Z. Chem.*, **7**, 247 (1871)], ethyl α-methyl-β-aminocrotonate [Conrad and Epstein, *Ber.*, **20**, 3056 (1887)] and ethyl β-diethylaminocrotonate [Kuckert, *Ber.*, **18**, 619 (1885)], all of which are more or less easily hydrolyzed to amines (or ammonia) and the corresponding esters.

β-Piperidinobenzalacetophenone [$C_6H_5COCH{=}C(NC_5H_{10})C_6H_5$] [André, *Ann. chim. phys.*, [8] **29**, 577 (1913)] and α-piperidinobenzalacetophenone [$C_6H_5COC(NC_5H_{10}){=}CHC_6H_5$] [Watson, *J. Chem. Soc.*, **85**, 1322 (1904)] are hydrolyzed at room temperature to give piperidine and the corresponding diketone [Dufraisse and Moureu, *Bull. soc. chim.*, [4] **41**, 547 (1927)].

[4] Flürscheim, *J. prakt. Chem.*, [2] **68**, 347 (1903).

[5] It should be noted also that the alcohol obtained from this ester by reduction must be γ-diethylamino-*n*-propyl alcohol, $CH_2[N(C_2H_5)_2]CH_2CH_2OH$, and not β-diethylamino-*n*-propyl alcohol as reported by von Braun, Leistner and Münch.

Also, the compounds reported as ethyl α-di-*n*-propylaminopropionate, ethyl α-di-*iso*-amylaminopropionate, ethyl α-kopellidinopropionate and ethyl α-diethylamino-*n*-butyrate are presumably really the corresponding β-compounds. A report covering this point is in preparation.

[6] See also Gault, *Bull. soc. chim.*, [4] **3**, 376 (1908).

[7] Adams and Dreger, unpublished work.

Table I

Data on Ester Derivatives

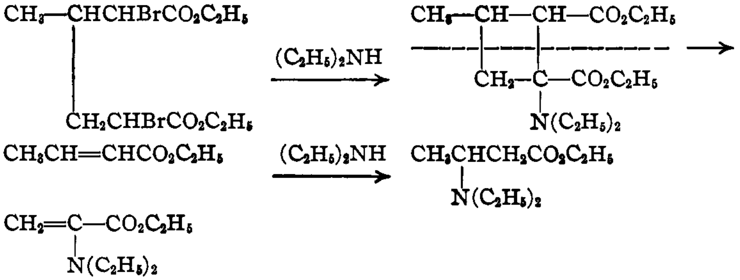
	α-Ester	β-Ester	Unknown
Boiling point	50–52°/3–4 mm.	63–65°/4 mm.	59–63°/3–4 mm.
Density at 20°	0.9077	0.9095	0.9097
n_D^{22}	1.4229	1.4266	1.4268
M. p. of CH_3I deriv.	....	80–81°	80–81°

The melting point of a mixture of the methyl iodide derivative of the β-ester and that of the unknown ester was 80–81°.

In order to determine whether ethyl α-diethylamino-acrylate was actually formed or not the decomposition was carried out in the normal way and the products were isolated without being allowed to come in contact with water or hydrochloric acid. In this way no ethyl pyruvate was obtained. The sole product was a liquid boiling at 76–82° (5–6 mm.) which is approximately the boiling point of pure ethyl β-diethylaminopropionate. It was suspected that this liquid was a mixture of ethyl β-diethylaminopropionate and ethyl α-diethylaminoacrylate. The high refractive index pointed to this conclusion.

Since it was not possible to separate the mixture by fractional distillation the whole was treated with dilute hydrochloric acid. From this reaction mixture were obtained not only pure ethyl β-diethylaminopropionate but ethyl pyruvate as well. This confirms the presence of ethyl α-diethylamino-acrylate as an intermediate.

The results obtained by von Braun and his associates with diethyl β-methyl-α,α'-dibromo-adipate serve to confirm the mechanism proposed here to explain the formation of the β-ester. In this case the reaction would be expected to take the following course, yielding ethyl crotonate in place of the ethyl acrylate postulated as an intermediate in the simpler case.



$$\begin{array}{l} CH_3-CHCHBrCO_2C_2H_5 \\ \quad\;\; | \\ \quad\;\; CH_2CHBrCO_2C_2H_5 \end{array} \xrightarrow{(C_2H_5)_2NH} \begin{array}{l} CH_3-CH-CH-CO_2C_2H_5 \\ \qquad\;\; CH_2-\underset{N(C_2H_5)_2}{C}-CO_2C_2H_5 \end{array} \longrightarrow$$

$$CH_3CH{=}CHCO_2C_2H_5 \xrightarrow{(C_2H_5)_2NH} CH_3\underset{N(C_2H_5)_2}{CH}CH_2CO_2C_2H_5$$

$$CH_2{=}\underset{N(C_2H_5)_2}{C}-CO_2C_2H_5$$

Here, however, the presence of the methyl group would be expected to retard the addition of diethylamine to the conjugated system. The isolation by the above-mentioned authors of *both* ethyl crotonate and ethyl β-diethylamino-n-butyrate is consistent with the above mechanism.

As a further confirmation of the mechanism given in this paper the stability of diethyl 1-diethylamino-1,2-cyclobutanedicarboxylate and similar cyclobutane derivatives is being studied.

Experimental Part

Meso-Diethyl α,α′-Dibromo-adipate and Diethylamine.—The procedure of von Braun, Leistner and Münch[8] was followed minutely; meso-diethyl α,α′-dibromo-adipate (m. p. 67°) was treated with three times the theoretical amount of diethylamine and the reaction products were worked up by treatment with ether and an excess of dilute hydrochloric acid. The neutral ester boiled at 155° at atmospheric pressure and formed a phenylhydrazone melting at 117–117.5°. The semicarbazone melted at 205°. A mixed melting point with the semicarbazone of an authentic specimen of ethyl pyruvate gave no depression.

The amino ester boiled at 59–63° (3–4 mm.); d^{20}, 0.9097; n_D^{22}, 1.4268. When heated at 100° with methyl iodide it gave a thick, brown sirup; this soon set to a mass of crystals which on recrystallization from ethyl acetate melted at 80–81°. A mixed melting point with the methyl iodide derivative of an authentic specimen (see below) of ethyl β-diethylaminopropionate gave no depression.

The Preparation of Ethyl β-Diethylpropionate

This ester was prepared from ethyl β-bromopropionate according to the procedure of Flürscheim.[4] The ethyl β-bromopropionate, which was made from ethylene cyanohydrin,[9] was treated with diethylamine in the following way.

Seventy-three grams (1.0 mole) of diethylamine was added slowly to 90 g. (0.5 mole) of ethyl β-bromopropionate. The reaction was vigorous at the beginning but slowed down at the end of about thirty minutes. The mixture was then made up largely of crystals of diethylamine hydrobromide and was heated for an hour on the steam-bath. After being allowed to cool it was taken up in ether and an excess of dilute hydrochloric acid. The ether layer was removed and the aqueous layer was made alkaline with potassium hydroxide. The amino ester which separated as an oil was removed by extraction with ether. The ether solution was dried over anhydrous potassium carbonate and distilled. The ester came over at 63–65° (4 mm.); d^{20}, 0.9095; n_D^{22}, 1.4266.

Contrary to the experience of Flürscheim, ethyl β-diethylaminopropionate cannot be distilled undecomposed at atmospheric pressure. At its boiling point (190–195°) it decomposes slowly to give diethylamine and ethyl acrylate.

The Preparation of Ethyl α-Diethylaminopropionate

The procedure of Adams and Dreger[7] was used. Twenty-three grams of ethyl α-bromopropionate was treated with 92 g. of diethylamine and the amino ester was isolated in the manner described above for the corresponding β-compound. It boiled at 178–183° (1 atm.); 50–52° (3–4 mm.); d^{20}, 0.9077; n_D^{22}, 1.4228. Attempts to prepare a methyl iodide derivative yielded an oil which did not crystallize.

Meso-Diethyl α,α′-Dibromo-adipate and Diethylamine (Second Procedure)

Thirty grams of meso-diethyl α,α′-dibromo-adipate (m. p. 67°) was treated with 37 g. of diethylamine in the manner described by von Braun, Leistner and Münch.[10]

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[8] Ref. 1, p. 1953.

[9] Kendall and MacKenzie, "Organic Syntheses," John Wiley and Sons, Inc., New York, **3**, 25 (1923).

[10] Ref. 1, p. 1953.

When the reaction was complete, the white crystalline solid, diethylamine hydrobromide, was filtered off, dried and weighed. The yield was practically theoretical.

The liquid product (filtrate) was distilled with a column. After the diethylamine was distilled off the product passed over at 90–100° (21 mm.). A considerable dark-colored residue remained in the flask. On redistillation the liquid boiled at 76–82° (5–6 mm.); n^{24}_{D}, 1.4385. There was again a dark-colored residue.

This redistilled product was shaken with dilute hydrochloric acid and the mixture, after being allowed to stand for an hour, was extracted with ether. The ether extract when dried and distilled yielded a liquid boiling at 155° which formed a phenylhydrazone melting at 117–117.5°. A mixed melting point with the phenylhydrazone of ethyl pyruvate gave no depression.

The aqueous layer was made alkaline and extracted with ether. The dried ether extract was found on distillation to contain a liquid boiling at 63–65° (4 mm.) which formed a methyl iodide derivative melting at 80–81°. By the method of mixed melting points this compound was identified as the methyl iodide derivative of ethyl β-diethylaminopropionate.

Summary

When diethyl α,α'-dibromo-adipate is treated with an excess of diethylamine the products are ethyl pyruvate and ethyl β-diethylaminopropionate.

It has been shown that ethyl α-diethylamino-acrylate is probably an intermediate in the formation of the pyruvic ester.

A mechanism involving the intermediate formation of a cyclobutane ring is suggested to explain these results.

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[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

THE CATALYTIC OXIDATION WITH AIR OF ETHYL, ISOPROPYL AND *n*-BUTYL ALCOHOLS

BY ROBERT M. SIMINGTON[1] AND HOMER ADKINS

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In seeking information as to the role played by the catalyst in the oxidation of alcohols by air an extended experimental study has been made as to the relative amounts of reaction products obtained by the oxidation of ethyl, *iso*propyl and *n*-butyl alcohols over some 30 catalysts. The products of oxidation are carbon dioxide, carbon monoxide, saturated and unsaturated hydrocarbons, hydrogen, an aldehyde or ketone and an acid and its ester. The relative amounts of these products are determined by the nature of the alcohol, the alcohol–air ratio, and the chemical and physical properties of the catalyst.[2]

[1] The authors are indebted to the E. I. DuPont de Nemours Co. for the support of a fellowship enjoyed by Dr. Simington during the academic year 1926–27.

[2] Orloff, *J. Russ. Phys.-Chem. Soc.*, 40, 203 (1908), *C. A.*, 2, 3346 (1908); also a footnote by Gibbs on p. 93 of Sabatier-Reid, "Catalysis in Organic Chemistry," D. Van Nostrand Co., New York, 1922.