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Studies on Carbamates

XV. The Carbamates of α-Aminocaproic Acid, ε-Aminocaproic Acid and α,ε-Diaminocaproic Acid

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The velocity constants for the reaction of carbon dioxide with the amino groups giving rise to the formation of carbamate have been determined. The equilibrium between carbamate and carbonate has been studied and equilibrium constants have been determined in the case of α-aminocaproic acid and ε-aminocaproic acid. The velocity of the decomposition of the carbamates of the two last mentioned amino acids has been investigated in basic medium and the experimental results may be interpreted in a way similar to the one used in previous investigations on carbamates.

The equilibrium conditions and the reaction mechanism for the formation and the decomposition of the carbamates formed by the amino acids glycine, α-alanine and β-alanine, in aqueous solution have been studied in previous investigations.[1,2]

The present investigation deals with the corresponding conditions with regard to the carbamates formed by α-aminocaproic acid (norleucine) and ε-aminocaproic acid. The formation of the carbamate and the equilibrium between carbamate and carbonate were also studied for α,ε-diaminocaproic acid (lysine), but in less detail. The experimental method (see below) was the same as has been used previously and the conditions for the formation and the decomposition of the carbamates have been shown to be analogous to those of the carbamates previously investigated. Therefore, we find it is sufficient here to state the experimental data and the calculated constants referring for further informations to the investigations on the alanines.[2]

EXPERIMENTAL

The amino acids used for the experiments were of the best quality commercially available. Their identity and purity were controlled. Lysine was used in the form of the monohydrochloride.

A slightly different modification of the method of analysis employed hitherto was used in the present investigation where the scale was reduced to one tenth. The method also differs from the one used previously in that respect that the amount of carbonate, not that of carbamate, is determined directly. A known volume (about 10 ml) of the solution to be analyzed was placed in a centrifuge tube followed by the addition of barium chloride solution and, in some cases, sodium hydroxide solution. The sample was centrifuged in a hand-driven centrifuge. The barium carbonate was purified by repeated washing and centrifugation. A known volume of 0.1 N hydrochloric acid was then added from a jet syringe. The centrifuge tube was placed in a boiling water bath with a fine stream of air bubbling through the sample in order to expell the carbon dioxide. Back-titration was carried out with 0.1 N sodium hydroxide after cooling (methyl red indicator). Approximately 1 — 4 ml of 0.1 N hydrochloric acid were used in the titrations.

The sum of carbamate and carbonate was determined in a similar way, the carbamate being converted to carbonate by heating the solution with an excess of barium chloride for some hours before the sample was analyzed.

As in previous investigations it was found necessary to carry out blank determinations. All of the data given in the following are calculated from the corrected carbonate determinations. Usually, the correction amounts to about 1—4 % of the carbonate content found directly.

The method of analysis was tested on solutions of sodium carbonate of known strength and the determination of $k(CO_2\text{-Am})$ for an amine which has been investigated previously (butylamine) was repeated using the new technique. In both cases satisfactory results were obtained.

All of the experiments were carried out at 18°C and the velocity constants were calculated by means of Briggs' logarithms, the unit of time being the minute.

The activity coefficient for a monovalent ion was, as in earlier investigations, calculated from the expression of Bjerrum:[3] $-\log f = 0.3\sqrt[3]{c_{ion}}$.

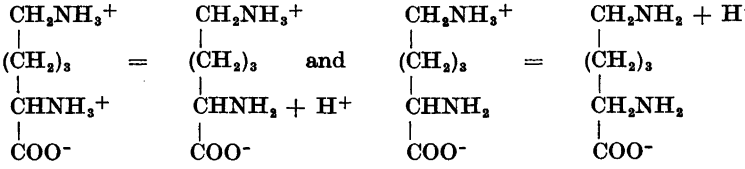
The values $10^{-10.03}$ (Ref.[4]) and $10^{-11.06}$ (Ref.[5]) have been used for the acid dissociation constants, $K(AmH^+)$, of the aminium groups in α-aminocaproic acid and ε-aminocaproic acid, respectively. $K(AmH^+)$ is the dissociation constant for the equilibrium

$$^-OOC\cdot C_5H_{10}NH_3^+ = {}^-OOC\cdot C_5H_{10}NH_2 + H^+$$

or, shorter,

$$AmH^+ = Am + H^+$$

Two sets of acid and corresponding base should be taken into consideration in the case of lysine corresponding to the equilibria



$K(\alpha\text{-AmH}^+)$ and $K(\varepsilon\text{-AmH}^+)$ have the values $10^{-8.95}$ and $10^{-10.53}$ (Ref.[6]), respectively (25°C).

Only recently, our attention has been drawn to a paper by Stadie and O'Brien [7] which in different ways criticizes the investigation on glycine published by one of us in 1925 (Ref.[8]). We find, however, after a close reexamination of the calculations that we cannot acknowledge their criticisms at all.

On the reaction "amine + carbon dioxide = carbamic acid"

The results of the experiments on the absorption of carbon dioxide by solutions containing both an amino acid and sodium hydroxide are given in Table 1.

Table 1. Carbon dioxide in amino caproic acids + NaOH. 18°C.

	Initial solution		Absorbed CO_2 moles/litre	% carbamate	Final solution		Mean		$k(CO_2 \cdot Am)$
	$[OH^-]$	[Am]			$[OH^-]$	[Am]	$[OH^-]$	[Am]	
α	0.099	0.100	0.0187	48.0	0.071	0.091	0.085	0.096	$10^{4.93}$
ε	0.151	0.098	0.0206	53.2	0.121	0.087	0.136	0.092	$10^{5.24}$
α,ε	0.150	0.050*	0.0209	44.7	0.117	0.041	0.134	0.045	$10^{5.40}$

* $(H_2N)_2C_5H_9COO^-$

Table 2. Solutions of carbonate-carbamate in equilibrium. 18°C.

	Initial solution			% carbamate	Equilibrium				K_{Eq}
	$[(AmH)_2CO_3]$	$[AmH^+]$	[Am]		$[AmH^+]$	[Am]	[carbamate]	$[HCO_3^-]$	
α	0.0207	0.0381	0.10	41.3	0.0660	0.105	0.00858	0.0054	$10^{-1.18}$
ε	0.0206	0.093	0.10	38.8	0.124	0.101	0.00802	0.00152	$10^{-1.71}$

Table 3. Solutions of carbonate-carbamate in equilibrium. 18°C.

	pa_H approx.	Gross composition of initial solution			% carbamate
		$[Na_2CO_3]$	[lysine HCl]	[NaOH]	
α,ε	9.0	0.0201	0.184	0.100	75.0
	10.5	0.0189	0.184	0.280	38.2

The table contains also the calculated velocity constants for the addition of carbon dioxide to the amino groups, $k(CO_2 \cdot Am)$.

It will be seen from the table that the addition of carbon dioxide to the α-amino group is comparatively slow. The same is true for the addition of carbon dioxide to the amino group in α-alanine.[2]

$k(CO_2 \cdot Am)$ for lysine, calculated in the usual manner, represents a sum of the velocity constants for the reaction of carbon dioxide with the α-amino group and the ε-amino group. It should be added that the sum of the $k(CO_2 \cdot Am)$-values for the reaction of carbon dioxide with α-$H_2NC_5H_{10}COO^-$ ($10^{4.93}$) and ε-$H_2NC_5H_{10}COO^-$ ($10^{5.24}$) is $10^{5.41}$, *i.e.* practically identical with the $k(CO_2 \cdot Am)$-value ($10^{5.40}$) found for lysine, α,ε-$(H_2N)_2C_5H_9COO^-$.

Table 4. Velocity constants for the process: carbamate → carbonate. pa_H = approx. 13 18°C.

	Initial solution			Min.	% carbamate left	k_{amate}
	[carbamate]	[OH^-]	[Am]			
a	0.018	0.082	0.122	0	100	
				229	77.6	0.000481
				296	72.7	0.000470
				373	67.4	0.000461
				482	59.3	0.000472
				535	56.5	0.000463
				1384	22.7	0.000465
				1539	19.3	0.000466
						Mean: 0.000468
ε	0.018	0.104	0.128	0	100	
				1402	66.4	0.000127
				1643	63.1	0.000122
				2512	50.3	0.000119
				2921	46.0	0.000115
				3967	33.3	0.000121
				4507	28.8	0.000120
						Mean: 0.000121

The equilibrium "carbamate = carbonate"

The experimental data on the equilibrium are listed in Table 2 (*α*-aminocaproic acid and *ε*-aminocaproic acid) and in Table 3 (lysine). The equilibrium constants, K_{Eq}, for the processes

$$^-OOCHNC_5H_{10}COO^- + H_2O = H_2NC_5H_{10}COO^- + HCO_3^-$$

or, shorter,

$$carbamate^- + H_2O = Am + HCO_3^-$$

have been calculated and are also given in Table 2.

It will be seen that the amino acid with the amino group in *α*-position has the greater equilibrium constant. The same was found for the alanines.

Two experiments with lysine are listed in Table 3, one at pa_H = approx. 9.0 and the other at pa_H = approx. 10.5 corresponding to solutions containing approximately equal moles of acid and corresponding base. No equilibrium constants have been calculated since the method of analysis does not permit to distinquish between the three different carbamates, *α*-carbamate, *ε*-carbamate and *α*,*ε*-carbamate.

The velocity of the conversion "carbamate = carbonate"

The experimental data on the decomposition of the carbamates formed by *α*-aminocaproic acid and *ε*-aminocaproic acid are listed in Table 4. The

experiments were carried out in strongly basic solution (p_{a_H} = approx. 13).

The experiments may be interpreted in a way similar to the one used by the carbamates previously examined. The conversion is a two-stage reaction:

carbamate = carbon dioxide + amine
carbon dioxide = carbonate,

and k_{amate} may be calculated in advance from the expression

$$\frac{k(CO_2\cdot Am) \times K_{Eq} \times K(H_2O) \times 1/K(CO_2)}{[OH^-] + \frac{k(CO_2\cdot Am)}{k(CO_2\cdot OH)} \times [Am]}$$

The calculated values are 0.000630 for the carbamate of α-aminocaproic acid and 0.00021 for the carbamate of ε-aminocaproic acid. Considering the nature of the experimental conditions the agreement with the experimental values, 0.000468 and 0.000121, respectively, is regarded as satisfactory.

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