

Studies on Carbamates

V. The Carbamates of α -Alanine and β -Alanine

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1. In previous investigations has been studied the equilibrium conditions and reaction mechanism of the formation and decomposition in aqueous medium of ammonium carbamate^{1, 2}, and of the carbamates formed by dimethylamine², ethylamine and diethylamine³, and hydrazine⁴.

The present investigation deals with the corresponding conditions with regard to the carbamates formed by α -alanine and β -alanine. The conditions have been shown to be analogous to those of the carbamates previously investigated, only differing somewhat quantitatively.

On the following pages α -alanine, $\text{CH}_3 \cdot \text{CHNH}_3^+ \cdot \text{COO}^-$, as well as β -alanine, $\text{CH}_2\text{NH}_3^+ \cdot \text{CH}_2 \cdot \text{COO}^-$, both of which should be regarded as ammonium ions, will frequently be referred to as "AmH⁺". Accordingly the corresponding bases $\text{CH}_3 \cdot \text{CHNH}_2 \cdot \text{COO}^-$ and $\text{CH}_2\text{NH}_2 \cdot \text{CH}_2 \cdot \text{COO}^-$ will be referred to as "Am". "carbamates" signify the carbamates of the alanines, *i. e.* $\text{CH}_3 \cdot \text{CHNHCOO}^- \cdot \text{COO}^-$ and $\text{CH}_2\text{NHCOO}^- \cdot \text{CH}_2 \cdot \text{COO}^-$.

2. The following substances have been used in the present experiments:

dl- α -Alanine, L. Light & Co. Ltd., consisting of small needle-shaped crystals, the melting point of which was found to be 260 to 262° C, and the molecular weight, determined by means of the Kjeldahl method, was 89.25 (theoretically 89.09). β -Alanine was specially prepared and furnished us through the generosity of Løvens kemiske Fabrik (Leo Pharmaceutical Products), Copenhagen. The analysis was stated to yield the following results: melting point 198° C, 99.5 % of alanine by formol titration, 98.3 % of alanine by the Kjeldahl method, less than 0.1 % loss by drying, less than 0.1 % of ash, and a slight trace of halogen. We found the melting point to be 196—199° C, and 98.4 % of alanine by the Kjeldahl method.

3. No attempt has been made to isolate the carbamates and carbonates as substances. Solutions of carbamate were prepared by neutralizing the ammonium ion with the equivalent amount of sodium hydroxide, *e.g.* in the case of α -alanine " $\text{CH}_3 \cdot \text{CHNH}_3^+ \cdot \text{COO}^- + \text{Na}^+ + \text{OH}^- = \text{CH}_3 \cdot \text{CHNH}_2 \cdot \text{COO}^- + \text{Na}^+ + \text{H}_2\text{O}$ ", whereupon a deficient amount of carbon dioxide was added to the solution; practically all of the carbon dioxide is thus converted to carbamate " $\text{CH}_3 \cdot \text{CHNH}_2 \cdot \text{COO}^- + \text{CO}_2 = \text{CH}_3 \cdot \text{CHNHCOO}^- \cdot \text{COO}^- + \text{H}^+$ ", the latter of course being neutralized by excess amine. Solutions of carbonate were made from equivalent amounts of ammonium ion and sodium carbonate, " $2\text{CH}_3 \cdot \text{CHNH}_3^+ \cdot \text{COO}^- + 2\text{Na}^+ + \text{CO}_3^{--} = (\text{CH}_3 \cdot \text{CHNH}_3 \cdot \text{COO}^-)_2\text{CO}_3 + 2\text{Na}^+$ ". Solutions of carbamate as well as solutions of carbonate thus contain sodium ions; this, however, is of no importance in the present investigation.

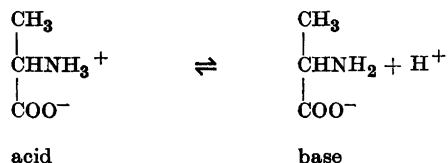
4. The method of analysis was, as in previous investigations, precipitation with barium chloride, *i.e.* barium chloride is added to 100 ml of the solution, if necessary previously made alkaline by the addition of sodium hydroxide. In this way the carbonate is precipitated, whilst the carbamate remains dissolved. By centrifugation the precipitate and the supernate are separated as quickly as possible. If the supernate is left standing or is heated, the carbamate decomposes forming a precipitate of barium carbonate, the amount of which can be determined by titration with 0.1 *N* hydrochloric acid.

Since solutions containing only carbonate, and no carbamate, upon precipitation with barium chloride yield a supernate precipitating a small amount of barium carbonate, it was found necessary to carry out blank experiments. The value of the blanks amounts to about 3 units of the percentage. All of the experimental results in the later tables are corrected with regard to the value of the blank experiments.

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

As in earlier investigations the activity coefficient *f* of monovalent ions was calculated from the expression of Bjerrum⁵: $-\log f = 0.3 \sqrt[3]{c_{\text{ion}}}$.

6. The calculation of certain experiments was carried out on the basis of the acidic dissociation constant, K'_{AmH^+} , for



and the corresponding value of β -alanine. These constants were calculated by us (Table 1) on the basis of determinations of the hydrogen ion activity in solutions containing equal moles of corresponding acid and base, prepared by the mixing of alanine with half the number of moles of sodium hydroxide. The determinations were carried out by means of a hydrogen electrode against a 0.1 *N* calomel electrode, and were calculated from the expression $p\alpha_{\text{H}} = -\log a_{\text{H}^+} = (E - E_0) \frac{F \log e}{R T}$, E_0 being fixed at 0.3360⁶. No corrections were made for the diffusion potentials, these being insignificant as in the glycine measurements in the investigation just cited.

Table 1. Determination of the acidic dissociation constants of the alanines.

c_{acid}	c_{base}	$p\alpha_{\text{H}}$	
		α	β
0.1	0.1	10.00	10.42
0.05	0.05	10.01	10.42
0.02	0.02	10.02	10.41
0.01	0.01	9.99	10.40

i.e. pK' : 10.00 10.41

accordingly the expression

$$\frac{a_{\text{H}^+} \cdot c_{\text{CH}_3 \cdot \text{CHNH}_2 \cdot \text{COO}^-}}{c_{\text{CH}_3 \cdot \text{CHNH}_3^+ \cdot \text{COO}^-}} = K'_{\text{AmH}^+}$$

and the corresponding one for β -alanine has a practically constant value independant of the ion concentration. From this it may be further concluded that the activity coefficients of the divalent amphi-ion $\text{CH}_3 \cdot \text{CHNH}_3^+ \cdot \text{COO}^-$ ($\text{CH}_2\text{NH}_3^+ \cdot \text{CH}_2 \cdot \text{COO}^-$, respectively) are of practically the same magnitude as are those of the monovalent ion $\text{CH}_3 \cdot \text{CHNH}_2 \cdot \text{COO}^-$ ($\text{CH}_2\text{NH}_2 \cdot \text{CH}_2 \cdot \text{COO}^-$, respectively). This fact is used later on.

On the reaction "amine + carbon dioxide \rightleftharpoons carbamic acid"

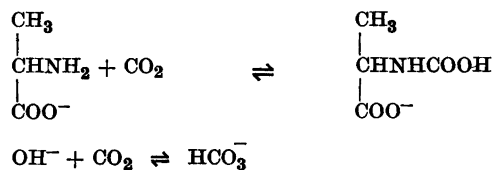
1. *The reaction from left to right.* 500 ml of an aqueous solution of alanine, containing excess sodium hydroxide, were placed in a 2 liter flask; if, for instance, 250 ml of 0.2 *M* alanine are added to 250 ml of 0.4 *M* NaOH, the

resulting solution will have $c_{\text{NaOH}} = 0.10$ and $c_{\text{Am}} = 0.10$. In the gas phase above this solution approximately 250 ml of carbon dioxide were substituted for an equal amount of atmospheric air, and the flask was shaken vigorously for about 2 minutes to obtain absorption of the carbon dioxide. In 100 ml of the reaction mixture the carbamate content was determined immediately, and in another 100 ml of the reaction mixture carbamate + carbonate were determined. Per cent carbamate in table 2 indicates how many per cent of the carbon dioxide absorbed have been converted to carbamate.

Table 2. Carbon dioxide in alanine + NaOH. 18°.

	Initial solution		Absorbed CO ₂ Mol./liter	% carba- mate	Final solution		Mean		$k_{\text{CO}_2 \cdot \text{Am}}$	
	c_{NaOH}	c_{Am}			c_{NaOH}	c_{Am}	c_{NaOH}	c_{Am}		Mean
α	0.10	0.10	0.0193	41	0.07	0.09	0.09	0.10	10 ^{4.81}	10 ^{4.82}
	0.10	0.15	0.0188	55	0.07	0.14	0.09	0.15	10 ^{4.87}	
	0.06	0.09	0.0116	49	0.04	0.08	0.05	0.09	10 ^{4.77}	
β	0.10	0.10	0.0175	54	0.07	0.09	0.09	0.10	10 ^{5.05}	10 ^{5.04}
	0.20	0.10	0.0154	34	0.17	0.10	0.19	0.10	10 ^{5.02}	
	0.20	0.20	0.0129	53	0.18	0.19	0.19	0.20	10 ^{5.05}	

The results of the experiments can be interpreted in that carbon dioxide is reacting partly with the amine, partly with the hydroxyl ion:



according to the following equation:

$$\frac{dc_{\text{CO}_2}}{dt} = - (k_{\text{CO}_2 \cdot \text{Am}} \cdot c_{\text{Am}} + k_{\text{CO}_2 \cdot \text{OH}^-} \cdot c_{\text{OH}^-}) c_{\text{CO}_2}$$

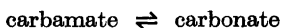
For the interrelation between the percentages of carbamate formed and carbonate formed we have the expression

$$\frac{k_{\text{CO}_2 \cdot \text{Am}} \cdot c_{\text{Am}}}{k_{\text{CO}_2 \cdot \text{OH}^-} \cdot c_{\text{OH}^-}} = \frac{\text{per cent carbamate}}{\text{per cent carbonate}}$$

Upon introduction into this expression of the mean values of the concentrations at the beginning and at the end of the experiment for c_{OH^-} and c_{Am} , and of the value $10^{5.02}$ for $k_{\text{CO}_2 \cdot \text{OH}^-}$, the values $10^{4.82}$ and $10^{5.04}$ are obtained for $k_{\text{CO}_2 \cdot \text{Am}}$ for α -alanine and β -alanine, respectively, *i.e.* carbon dioxide reacts with α -alanine approximately 1.5 times slower than it does with β -alanine.

2. *The reaction from right to left.* Previously it has been shown that ordinary carbamate, NH_2COO^- , by acidification is extremely quickly and completely decomposed into carbon dioxide and ammonia, or rather ammonium ion. The decomposition of the alanine carbamates in acid solution has not been investigated directly. As shown in a previous investigation it is possible, however, by means of the velocity constant, $k_{\text{CO}_2 \cdot \text{Am}}$, to estimate that these carbamates, too, are decomposed practically instantaneously and completely in acid solution.

3. *The equilibrium "carbamate \rightleftharpoons carbonate".* In acid and in strongly basic solutions the carbamates are practically completely decomposed into carbon dioxide and carbonate, respectively, but in a weakly basic solution an equilibrium, which can be easily determined, is established,



For the determination of the equilibrium value 0.02 *M* solutions of $(\text{AmH})_2\text{CO}_3$ containing Am and AmH^+ as well, were prepared, see Table 3. Accordingly the initial composition of the solution in *e.g.* the experiment "0.02 *M* $(\text{AmH})_2\text{CO}_3$, 0.05 *M* AmH^+ , 0.05 *M* Am" was 0.14 *M* alanine, 0.05 *M* NaOH and 0.02 *M* Na_2CO_3 . The solutions were left until an equilibrium was established. In the table "% carbamate" indicates the percentage of carbonate converted to carbamate. The constitution of the equilibrium solutions was calculated. $\text{p}K$ of the carbamic acids supposedly being approximately 5 the amount of free carbamic acid present in these solutions is insignificant, *i.e.* $c_{\text{carbamate ion}}$ can be fixed at that of the carbamate found analytically. The concentrations of AmH^+ , Am and HCO_3^- were calculated from the following expressions:

$$\frac{c_{\text{Am}} \cdot c_{\text{HCO}_3^-}}{c_{\text{AmH}^+} \cdot c_{\text{CO}_3^{--}} \cdot f} = \frac{K'_{\text{AmH}^+}}{K_{\text{HCO}_3^-}} = \frac{K'_{\text{AmH}^+}}{10^{-10.3}}$$

$$c_{\text{carbamate}} + c_{\text{HCO}_3^-} + c_{\text{CO}_3^{--}} = \text{total concentration of CO}_2$$

$$c_{\text{carbamate}} + c_{\text{AmH}^+} + c_{\text{Am}} = \text{total concentration of alanine,}$$

$$c_{\text{Am}} = c_{\text{Am}} \text{ (column 4 in the table) } + c_{\text{HCO}_3^-},$$

where $c_{\text{AmH}^+} = c_{\text{CH}_2 \cdot \text{CHNH}_2 \cdot \text{COO}^-}$ ($c_{\text{CH}_2 \cdot \text{NH}_2 \cdot \text{CH}_2 \cdot \text{COO}^-}$, respectively), and $c_{\text{Am}} = c_{\text{CH}_2 \cdot \text{CHNH}_2 \cdot \text{COO}^-}$ ($c_{\text{CH}_2 \cdot \text{NH}_2 \cdot \text{CH}_2 \cdot \text{COO}^-}$, respectively).

Table 3. The solutions of carbonate-carbamate in equilibrium. 18°.

	Initial solution			% carba- mate	Equilibrium				K_{Eq}	
	$c_{(AmH)_2CO_3}$	c_{AmH^+}	c_{Am}		c_{AmH^+}	c_{Am}	$c_{carba-mate}$	$c_{HCO_3^-}$		Mean
α	0.02	0.05	0.05	26 ¹	0.075	0.060	0.0052	0.0097	10 ^{-0.96}	10 ^{-0.97}
	0.02	0.10	0.10	39 ²	0.125	0.108	0.0078	0.0075	10 ^{-0.99}	
β	0.02	0.05	0.05	44 ³	0.076	0.055	0.0089	0.0049	10 ^{-1.52}	10 ^{-1.51}
	0.02	0.10	0.10	59 ⁴	0.125	0.104	0.0117	0.0035	10 ^{-1.51}	

¹ Mean of 4 determinations: 25.3, 27.4, 25.4, 25.7.

² » » 4 » 39.1, 39.1, 39.1, 38.5.

³ » » 4 » 44.8, 45.0, 44.1, 44.0.

⁴ » » 3 » 57.5, 60.3, 58.1.

Further the equilibrium constants of the reactions "carbamate ion + H₂O = HCO₃⁻ + Am", *i. e.*

$$\frac{a_{Am} \cdot a_{HCO_3^-}}{a_{carbamate\ ion}} = \frac{c_{CH_3 \cdot CHNH_2 \cdot COO^-} \cdot f \cdot c_{HCO_3^-} \cdot f}{c_{CH_3 \cdot CHNHCOO^-} \cdot COO^- \cdot f^2} = K_{Eq}$$

and the analogous one for β -alanine, in both of which the activity coefficients neutralize each other, were calculated. The constants are listed in the last column of Table 3.

The velocity of the conversion "carbamate \rightleftharpoons carbonate"

In Table 4 are listed data on the velocity when equilibrium is ensuing in buffer solutions of $pa_H =$ about 10. All experiments are from the carbonate side.

In addition to the experimental data are listed in Table 4 in the column $k_{amate} + k_{onate}$ the values of $\frac{1}{t} \log \frac{K \cdot a}{K \cdot a - (1 + K)x}$, the expression for a process which is monomolecular from both sides and which does not run to completion. The constant K signifies the relation between the equilibrium values of the concentrations of carbamate and carbonate. The sum " $k_{amate} + k_{onate}$ " is approximately constant within each experiment. k_{amate} is the

Table 4. Velocity constants for the process: carbamate \rightleftharpoons carbonate; $p_{aH} = ca. 10$. 18° .

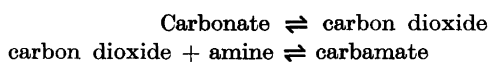
	Initial solution			Min.	% carbamate	$k_{amate} + k_{onate}$
		c_{AmH^+}	c_{Am}			
α	0.02 M (AmH) ₂ CO ₃	0.05	0.05	40	9.7	0.00506
				160	22.1	0.00515
				1494	25.3	Mean: 0.0051
				4202	25.4	k_{amate} : 0.0038
						k_{onate} : 0.0013
	0.02 M (AmH) ₂ CO ₃	0.10	0.10	40	10.5	0.00340
				80	17.7	0.00330
				120	22.4	0.00309
				155	26.3	0.00316
				1080	39.1	Mean: 0.0033
2520	39.1	k_{amate} : 0.0020				
		k_{onate} : 0.0013				
β	0.02 M (AmH) ₂ CO ₃	0.05	0.05	43	7.8	0.00193
				81	13.6	0.00196
				161	22.5	0.00190
				241	28.9	0.00189
				1320	44.8	Mean: 0.00192
	2910	44.1	k_{amate} : 0.00107			
			k_{onate} : 0.00085			
	0.02 M (AmH) ₂ CO ₃	0.10	0.10	40	6.3	0.00123
				80	11.7	0.00121
				155	19.9	0.00116
240				27.7	0.00116	
1269				56.1	0.00107	
2655	57.5	Mean: 0.00117				
4486	58.1	k_{amate} : 0.00048				
		k_{onate} : 0.00069				

velocity constant for the conversion of carbamate to carbonate, and k_{onate} the one for the reversed reaction.

By means of $\frac{k_{onate}}{k_{amate}} = \frac{\text{equilibrium value of } c_{\text{carbamate}}}{\text{equilibrium value of } c_{\text{carbonate}}} = K$, the values of k_{amate} and k_{onate} are obtained.

In Table 5 are presented data on the decomposition of the carbamates in strong basic solution, $p\alpha_{\text{H}} =$ about 13. The solutions of the carbamates were prepared by dissolving carbon dioxide in a mixture of practically equal moles alanine and sodium hydroxide and subsequently add the desired excess sodium hydroxide. The initial composition of *e. g.* the solution "0.018 *M* carbamate, 0.18 *M* OH^- and 0.08 *M* Am" was accordingly 0.10 *M* alanine, 0.30 *M* NaOH, and 0.018 *M* CO_2 . k_{amate} is the value of $k = \frac{1}{t} \log \frac{a}{a-x}$.

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



and it is possible to calculate in advance the velocity constants.

The conversion "carbon dioxide \rightleftharpoons carbonate" is known to take place through two reactions: " $\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3$ " and " $\text{CO}_2 + \text{OH}^- \rightleftharpoons \text{HCO}_3^-$ "; as the $p\alpha_{\text{H}}$ of the solution is about 10 or more, only the latter reaction need, as previously shown, to be taken into consideration.

k_{amate} is calculated from the expression previously deduced³

$$k_{\text{amate}} = \frac{k_{\text{CO}_2 \cdot \text{Am}} \cdot K_{\text{Eq}} \cdot K_{\text{H}_2\text{O}} \cdot 1/K_{\text{CO}_2}}{c_{\text{OH}^-} + \frac{k_{\text{CO}_2 \cdot \text{Am}}}{k_{\text{CO}_2 \cdot \text{OH}^-}} \cdot c_{\text{Am}}}$$

i. e. in order to calculate the velocity at which a carbamate, following the above mentioned sequence of reactions, is decomposed, only two experiments need to be carried out, *viz.* 1) a determination of the distribution of carbon dioxide on carbamate and carbonate upon introducing the gas into a solution of amine and sodium hydroxide, thus attaining the value of $k_{\text{CO}_2 \cdot \text{Am}}$, and 2) a determination of the carbamate-carbonate equilibrium value *i. e.* K_{Eq} .

From the expression for k_{amate} it is seen that for a weakly basic solution the c_{OH^-} of the denominator is but slight compared to the other term of the denominator, *i. e.* in such solutions the velocity of the decomposition of carbamate is inversely proportional to the concentration of amine.

k_{onate} is calculated from the expression previously deduced²

$$k_{\text{onate}} = \frac{k_{\text{HCO}_3^-}}{1 + \frac{a_{\text{H}^+}}{K_{\text{H}_2\text{CO}_3}} \cdot f + \frac{K_{\text{HCO}_3^-}}{a_{\text{H}^+}} \cdot \frac{1}{f}}$$

The middle term of the denominator being so slight that it is discarded.

Table 5. Velocity constants for the process: carbamate \rightarrow carbonate; $p_{aH} = ca. 13$. 18° .

	Initial solution			Min.	% carbamate left	k_{amate}
	$c_{carbamate}$	c_{NaOH}	c_{Am}			
α	0.018	0.18	0.08	0	100	
				384	70.3	0.000398
				1049	36.0	0.000423
				1568	21.7	0.000424
				2538	8.2	0.000428
				2988	5.0	0.000437
				3921	1.8	0.000443
				ca. 1 month	0	Mean: 0.00043
β	0.019	0.18	0.08	0	100	
				362	89.2	0.000137
				1382	60.8	0.000156
				1744	53.3	0.000157
				2906	37.2	0.000148
				3381	30.2	0.000154
				4210	22.3	0.000155
				ca. 2 months	0	Mean: 0.00015
	0.020	0.18	0.18	0	100	
				402	90.8	0.000104
				1350	70.4	0.000113
				1855	62.7	0.000109
				2715	50.4	0.000110
				3182	44.6	0.000110
ca. 1 month	0	Mean: 0.00011				

In calculating the values of k_{amate} and k_{onate} were used $K_{H_2O} = 10^{-14.22}$, $K_{CO_2} = 10^{-6.52}$, $K_{HCO_3^-} = 10^{-10.3}$, $k_{HCO_3^-} = 10^{-2.74}$, $k_{CO_3^{2-}OH^-} = 10^{-5.02}$ and for K_{Eq} the values obtained in the preceding paragraph, these being $10^{-0.97}$ for α -alanine and $10^{-1.51}$ for β -alanine.

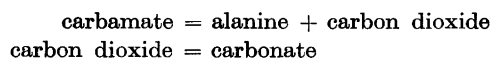
Table 6 contains a survey of the experimental and calculated values of k_{amate} and k_{onate} . Considering the nature of the conditions the agreement may be described as satisfactory.

Table 6. Velocity constants, experimental and calculated.

Initial solution						k_{amate}		k_{onate}	
	$c_{(\text{AmH})_2\text{CO}_3}$	$c_{\text{carbamate}}$	c_{AmH^+}	c_{Am}	c_{NaOH}	exp.	calc.	exp.	calc.
α	0.02		0.05	0.05		0.0038	0.0041	0.0013	0.0013
	0.02		0.10	0.10		0.0020	0.0021	0.0013	0.0012
		0.018		0.08	0.18	0.00043	0.00062		
β	0.02		0.05	0.05		0.0011	0.0012	0.00085	0.00087
	0.02		0.10	0.10		0.00048	0.00063	0.00069	0.00074
		0.019		0.08	0.18	0.00015	0.00025		
		0.020		0.18	0.18	0.00011	0.00018		

SUMMARY

The velocity constant of the reaction " $\text{CH}_3 \cdot \text{CHNH}_2 \cdot \text{COO}^- + \text{CO}_2 = \text{CH}_3 \cdot \text{CHNHCOOH} \cdot \text{COO}^-$ " and the equilibrium constant for the reaction " $\text{CH}_3 \cdot \text{CHNHCOO}^- \cdot \text{COO}^- + \text{H}_2\text{O} = \text{HCO}_3^- + \text{CH}_3 \cdot \text{CHNH}_2 \cdot \text{COO}^-$ " have been determined. The velocity of the decomposition of $\text{CH}_3 \cdot \text{CHNHCOO}^- \cdot \text{COO}^-$ in basic medium was investigated and may be explained in assuming that the decomposition is a two-stage reaction, *viz.*



The carbamate of β -alanine was studied in a similar way.

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