

## CHEMISTRY

# THE HYDROLYSIS AND AMINOLYSIS OF ETHYL THIOACETATE. II. KINETICS OF THE SIMULTANEOUS HYDROLYSIS AND AMINOLYSIS

BY

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### 1. Introduction

In a preceding paper [1] we presented the results of a kinetic analysis of the alkaline hydrolysis of ethyl-thioacetate (E.T.A.). The aminolysis in aqueous media is always accompanied by some hydrolysis. By determining the rate of disappearance of E.T.A. in aqueous glycine solutions we obtained overall reaction rates, from which the kinetic constants for the aminolysis could be calculated.

### 2. Experimental methods and calculation of concentrations

The measurements were carried out at 37° C. The rate of disappearance of E.T.A. in the reaction mixtures and the pH were determined according to the methods described before [1].

OH-ion concentrations in borate buffer solutions were calculated approximately [1] according to:

$$(1) \quad [\text{OH}] = \frac{2.4 \times 10^{-14}}{\text{antilog}(-\text{pH})} \cdot \frac{1}{\sqrt{\frac{\gamma_{\text{H}^+} \gamma_{\text{OH}^-}}{a_{\text{H}_2\text{O}}}}}$$

Concentrations are indicated by symbols between square brackets.

For the interpretation of our measurements accurate estimates of the glycinate ( $\text{R}-\text{NH}_2$ ) concentrations are essential. At high pH practically all the glycine was present in the glycinate form. At lower pH the ratio of glycine ( $\text{RNH}_3^+$ ) to glycinate ( $\text{RNH}_2$ ) has to be evaluated from the pH. As little is known about the activity coefficients of amino acids in solution glycinate concentrations were determined empirically. Glycine buffers of various concentrations with a well known ratio of glycine to glycinate were prepared. The pH of these buffers was determined at 37° C. An empirical titration constant  $K_{\text{NH}_3}$  was calculated from the measurements according to

$$(2) \quad \text{p}K_{\text{NH}_3} = \text{pH} + \log \frac{[\text{RNH}_3^+]}{[\text{RNH}_2]}$$

Table 1 shows that the pK so defined varies only very slightly with glycine concentration and somewhat more with pH.

Unknown glycinate concentrations were calculated from total glycine ( $[\text{RNH}_3^+] + [\text{RNH}_2]$ ) and pH using the appropriate  $\text{pK}_{\text{NH}_3}$  as interpolated from the data in table 1.

TABLE 1  
Determined pH and calculated  $\text{pK}_{\text{NH}_3}$  of various glycine buffers at 37° C

$\frac{[\text{RNH}_2]}{[\text{RNH}_2] - [\text{RNH}_3^+]}$	Total glycine (mol l <sup>-1</sup> )	pH	$\text{pK}_{\text{NH}_3}$ calc.
0.250	1	8.92	9.40
0.250	0.1	8.93	9.41
0.143	1	8.67	9.45
0.143	0.1	8.68	9.46
0.100	1	8.51	9.46
0.100	0.5	8.52	9.47
0.100	0.1	8.53	9.48
0.05	1	8.21	9.49
0.033	1	8.03	9.49

### 3. Simultaneous hydrolysis and aminolysis

All reactions investigated are first order with respect to [E.T.A.]. The results can therefore be expressed by means of  $K_{\text{obs}}$ , defined by

$$(3) \quad -\frac{d[\text{E.T.A.}]}{dt} = K_{\text{obs}} [\text{E.T.A.}]$$

Tables 2 (low pH) and 3 (high pH) show the results obtained.

TABLE 2  
Simultaneous hydrolysis and aminolysis by glycine at 37° C of 0.0025 m E.T.A. solutions in borate buffers of various pH. In exp. 86 the measurement was carried out in a pure glycine buffer; no activity correction was used for the calculation of [OH] in this experiment

Exp. No.	pH	$[\text{OH}] \times 10^9$ (mol ml <sup>-1</sup> )	$[\text{glycine}]^{\text{total}} \times 10^4$ (mol ml <sup>-1</sup> )	$K_{\text{obs}} \times 10^6$ (sec <sup>-1</sup> )	$\{K_{\text{obs}}/[\text{OH}]\} \times 10^{-3}$ (ml mol <sup>-1</sup> sec <sup>-1</sup> )
8	7.87	2.2	1	8	3.6
12	8.10	3.6	1	13	3.6
88	8.62	12.5	1	42	3.4
70	8.25	5.3	2	33	6.2
71	8.61	12.8	2	64	5.0
87	8.94	21	2	119	5.7
67	8.05	3.4	5	56	16
66	8.22	5.0	5	91	18
32	8.28	5.7	5	107	18
33	8.43	8.2	5	144	18
22	8.45	8.6	5	146	17
51	8.99	30	5	730	24
57	8.16	4.5	10	190	42
86	8.67	11.3	10	806	71
60	8.64	13	10	880	68
56	8.88	23	10	2020	88

TABLE 3

Simultaneous hydrolysis and aminolysis by glycine of E.T.A. solutions at 37° C and high pH. [OH] concentrations were calculated from the composition of the reaction mixtures

Exp. No.	[OH] × 10 <sup>9</sup> (mol ml <sup>-1</sup> )	$\frac{[\text{total glycine}] \times 10^4 = [\text{RNH}_2] \times 10^4}{(\text{mol ml}^{-1})}$	C <sub>1</sub> <sup>*</sup> × 10 <sup>5</sup> (sec <sup>-1</sup> )	K <sub>obs</sub> × 10 <sup>6</sup> (sec <sup>-1</sup> )	{K <sub>obs</sub> /[OH]} × 10 <sup>-2</sup> (ml mol <sup>-1</sup> sec <sup>-1</sup> )
73	2250	0.1	7.7	480	2.1
72	14500	0.1	7.7	2600	1.8
81	5000	0.2	10.1	1270	2.5
77	10000	0.2	10.1	2150	2.2
84	5000	0.4	16.9	1650	3.3
83	10000	0.4	16.9	2760	2.8

\*) For the meaning and calculation of C<sub>1</sub> see the end of section 4.

Evidently, K<sub>obs</sub> contains contributions from hydrolysis and from aminolysis. A provisional separation may be based upon the assumption that hydrolysis and aminolysis proceed completely independently and thus:

$$(4) \quad K_{\text{obs}} = K_{\text{H, obs}} + K_{\text{A, obs}}$$

where K<sub>H, obs</sub> is the rate constant of hydrolysis, determined in the previous paper [1].

An analysis of the data of tables 2 and 3 then leads in the first place to the following conclusions:

1. Extrapolation of the data at low pH (<9) to [OH]=0 (see fig. 1 A and 1 B) shows that the limiting rate constant of aminolysis is

$$(5) \quad (K_{\text{obs}})_{[\text{OH}] \rightarrow 0} = (K_{\text{H, obs}})_{[\text{OH}] \rightarrow 0} + K [\text{RNH}_3^+] [\text{OH}^-]$$

where  $\text{RNH}_3^+ = \text{H}_3\text{N}^+ - \text{CH}_2 - \text{COO}^-$ .

The value for  $(K_{\text{H, obs}})_{[\text{OH}] \rightarrow 0} = 1300 \times [\text{OH}] \text{ sec}^{-1}$  follows from paper [1] of this series.

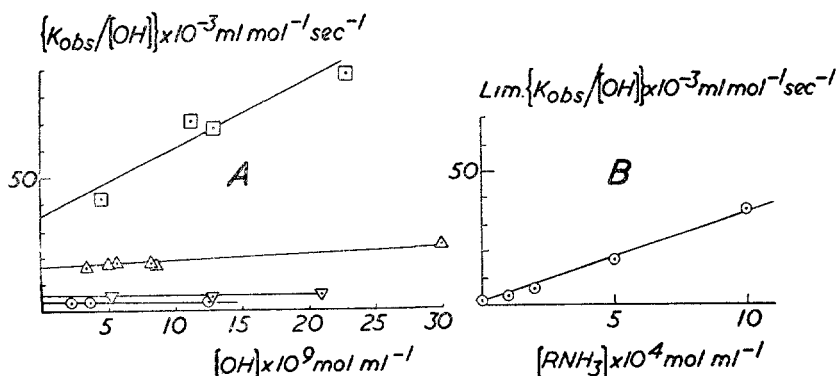


Fig. 1. Simultaneous hydrolysis and aminolysis by glycine at 37° C of 0.0025 m E.T.A. solutions under the experimental conditions described in table 2. The four curves represent the data with 0.1, 0.2, 0.5 and 1.0 m glycine

A:  $K_{\text{obs}}/[\text{OH}]$  plotted against [OH]

B:  $\lim_{[\text{OH}] \rightarrow 0} K_{\text{obs}}/[\text{OH}]$  plotted against [total glycine] =  $[\text{RNH}_3]$

2. By extrapolation of the data for high pH ( $>10.5$ ) it appears (see fig. 2 A and 2 B), that the rate constant approaches:

$$(6) \quad (K_{\text{obs}})_{[\text{OH}] \rightarrow \infty} = (K_{\text{H, obs}})_{[\text{OH}] \rightarrow \infty} + K'' [\text{RNH}_2] [\text{OH}] + f(\text{RNH}_2)$$

where  $f(\text{RNH}_2)$  depends upon the concentration of glycinate but not upon the pH.

According to our previous paper [1]  $(K_{\text{H, obs}})_{[\text{OH}] \rightarrow \infty} = 150 [\text{OH}] \text{ sec}^{-1}$ .

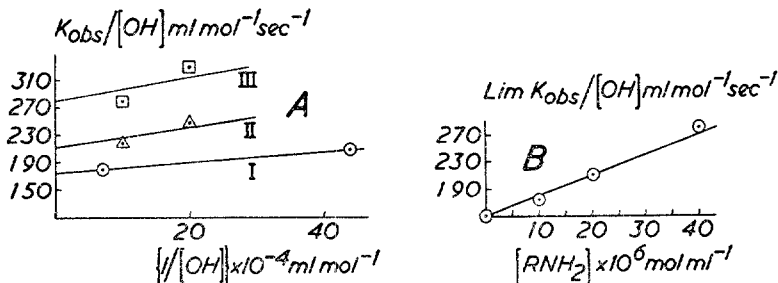


Fig. 2. Simultaneous hydrolysis and aminolysis by glycine at 37°C of E.T.A. solutions at high pH: the experimental conditions are summarized in table 3

A:  $K_{\text{obs}}/[\text{OH}]$  plotted against  $1/[\text{OH}]$  for:

I aminolysis by 0.01 m glycine

II " " 0.02 " "

III " " 0.04 " "

B:  $\text{lim}_{[\text{OH}] \rightarrow \infty} K_{\text{obs}}/[\text{OH}]$  plotted against  $[\text{RNH}_2] = [\text{glycine}]$

According to the dissociation equation

$$(7) \quad \frac{[\text{RNH}_3^+] [\text{OH}^-]}{[\text{RNH}_2]} = K_{\text{base}}$$

the rate of aminolysis at low pH (eq. (5)) can be considered to be proportional to the glycinate concentration

$$(8) \quad (K_{\text{A, obs}})_{[\text{OH}] \rightarrow 0} = K' [\text{RNH}_2].$$

Similar findings have been reported by other investigators [2, 3, 4, 5] and a reaction scheme in good harmony with the data has been proposed [4].

The data at high pH, as represented in eq. (6) are in good agreement with data published by TARBELL and HAWKINS [6]. At low pH ( $<9$ ) the contribution of this reaction is not measurable because of the relatively low value of  $K''$ .

It follows from fig. 1 A and more clearly from a plot of  $K_{\text{A, obs}}/[\text{RNH}_2]$  against  $[\text{OH}]$  (see table 4 and fig. 3) that eq. (5) is insufficient to describe the aminolysis at low pH.

This equation would give one straight horizontal line for all concentrations of glycine when plotted in the same way as in fig. 3. The fact that the reduced aminolysis constant  $K_{\text{A, obs}}/[\text{RNH}_2]$  for small concentrations of glycine decreases with increasing  $[\text{OH}]$  points to a certain competition between hydrolysis and aminolysis. The fanning out of the

TABLE 4

Aminolysis by glycine at 37°C of 0.0025 m E.T.A. solutions in borate buffers of various pH.  $K_{H, \text{obs}}$  was calculated from the data on the spontaneous hydrolysis of E.T.A. [1]

Exp. No.	$[\text{OH}] \times 10^9$ (mol ml <sup>-1</sup> )	[Glycine] $\times 10^4$ (mol ml <sup>-1</sup> )	$[\text{RNH}_2] \times 10^6$ (mol ml <sup>-1</sup> )	$K_{H, \text{obs}} \times 10^6$ (sec <sup>-1</sup> )	$K_{A, \text{obs}} \times 10^6$ (sec <sup>-1</sup> )	$K_{A, \text{obs}}/[\text{RNH}_2]$ (ml mol <sup>-1</sup> sec <sup>-1</sup> )
8	2.2	1	2.2	2.8	5.2	2.4
12	3.6	1	3.8	4.6	8.4	2.2
88	12.5	1	12.5	14	28	2.2
70	5.3	2	10.8	7	26	2.5
71	12.8	2	24.4	15	49	2.0
67	3.4	5	17	4.4	52	3.0
66	5.0	5	25.5	6.4	85	3.3
32	5.7	5	29	7.2	100	3.5
33	8.2	5	41	10	134	3.3
22	8.6	5	43	10.4	136	3.2
51	30	5	138	29	701	5.1
57	4.5	10	44	5.8	184	4.2
86	11.3	10	143	14	792	5.5
60	13	10	132	15	865	6.6
56	23	10	230	24	1196	8.7

curves with increasing amounts of glycine indicates a measurable contribution of a reaction proportional to the square of the glycinate concentration.

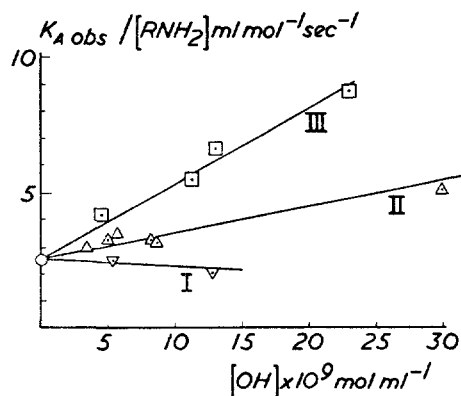


Fig. 3. Fan-shaped bundle of curves for the values of  $\frac{K_{A, \text{obs}}}{[\text{RNH}_2]}$  obtained for different glycine concentrations under the experimental conditions summarized in table 4.

- I Total glycine concentration = 0.2 mol l<sup>-1</sup>.  
 II " " " = 0.5 " "  
 III " " " = 1.0 " "

#### 4. Discussion of a complete reaction scheme

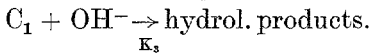
The phenomena described above can be explained by assuming the following reactions:

- a) The complex  $C_1$  (see: [1]) reacts with both  $\text{OH}^-$  ions and  $\text{RNH}_2$

molecules. It is not certain whether acetyl glycine or hydrolysis products are formed during this reaction.

b) A reactive complex is formed by E.T.A. and glycine ( $\text{RNH}_2$ ) which decomposes spontaneously but more rapidly in the presence of  $\text{OH}^-$  ions and  $\text{RNH}_2$  molecules (base-catalysis). These reactions may yield the aminolysis product, acetyl glycine, which has been isolated [7]. Consequently, the most simple reaction scheme for the simultaneous hydrolysis and aminolysis of E.T.A. would be:

*Hydrolysis:* (see: [1])



*Aminolysis:*

1.  $\text{C}_1 + \text{RNH}_2 \xrightarrow[\text{K}_5]{} ??$  and:
2.  $\text{E.T.A.} + \text{RNH}_2 \xrightarrow[\text{K}_6]{} \text{aminol. products.}$
3.  $\text{E.T.A.} + 2\text{RNH}_2 \xrightarrow[\text{K}_7]{} \text{aminol. products.}$
4.  $\text{E.T.A.} + \text{RNH}_2 + \text{OH}^- \xrightarrow[\text{K}_8]{} \text{aminol. products.}$

A reaction kinetic analysis of this scheme gives the following equation for the disappearance of E.T.A. with the time of incubation<sup>1)</sup>:

$$(9) \quad \left\{ \begin{aligned} -\frac{d[\text{E.T.A.}]}{dt} &= [\text{E.T.A.}] \left\{ \text{K}'_1 \frac{\text{K}_3[\text{OH}] + \text{K}_5[\text{RNH}_2]}{\text{K}_2 + \text{K}_3[\text{OH}] + \text{K}_5[\text{RNH}_2]} + \right. \\ &\quad \left. + \text{K}_4[\text{OH}] + \text{K}_6[\text{RNH}_2] + \text{K}_7[\text{RNH}_2]^2 + \text{K}_8[\text{RNH}_2][\text{OH}] \right\} \end{aligned} \right\}$$

with  $\text{K}'_1 = \text{K}_1[\text{H}_2\text{O}]$ .

It follows from eq. (9) that  $\text{K}_{\text{obs}}$  should be a pseudo first order rate constant if the reaction velocity measurements are carried out in buffered solutions and in the presence of an excess of glycine (and—at high pH—of  $\text{OH}^-$  ions) for:

$$(10) \quad \left\{ \begin{aligned} \text{K}_{\text{obs}} &= \text{K}'_1 \frac{\text{K}_3[\text{OH}] + \text{K}_5[\text{RNH}_2]}{\text{K}_2 + \text{K}_3[\text{OH}] + \text{K}_5[\text{RNH}_2]} + \text{K}_4[\text{OH}] + \text{K}_6[\text{RNH}_2] + \\ &\quad + \text{K}_7[\text{RNH}_2]^2 + \text{K}_8[\text{RNH}_2][\text{OH}] = \text{constant.} \end{aligned} \right\}$$

After substitution of  $\frac{[\text{RNH}_3][\text{OH}]}{\text{K}_b}$  for  $[\text{RNH}_2]$  and expansion for small values of  $[\text{OH}]$  eq. (10) can be written as:

$$(11) \quad (\text{K}_{\text{obs}})_{[\text{OH}] \rightarrow 0} = [\text{OH}] \left\{ \text{K}'_1 \frac{\text{K}_3}{\text{K}_2} + \text{K}_4 + \frac{[\text{RNH}_3]}{\text{K}_b} \left( \text{K}'_1 \frac{\text{K}_5}{\text{K}_2} + \text{K}_6 \right) \right\}$$

In fig. 1 B the extrapolated value of  $\text{K}_{\text{obs}}/[\text{OH}]$  is plotted against the

<sup>1)</sup> For the derivation of this equation: see appendix.

total glycine concentration which for  $[\text{OH}] \rightarrow 0$  is equal to  $[\text{RNH}_3^+]$ . The total slope of the line leads to the value:

$$\frac{1}{K_{\text{base}}} \left( K_1' \frac{K_5}{K_2} + K_6 \right) = 3.3 \pm 0.5 \text{ ml}^2 \text{ mol}^{-2} \text{ sec}^{-1}$$

$K_{\text{base}}$  according to the data of table 1 and extrapolated to low pH ( $\text{p}K_{\text{NH}_3} = 9.51$ ) would be

$$K_{\text{base}} = \frac{K_{\text{water}}}{\text{antilog } \text{p}K_{\text{NH}_3}} \times 10^{-3} = \frac{2.4 \times 10^{-14} \times 10^{-3}}{3.09 \times 10^{-10}} = 7.7 \times 10^{-8} \text{ mol ml}^{-1}$$

which is in reasonable agreement with the value  $K_{\text{base}} = 7.16 \times 10^{-8} \text{ mol ml}^{-1}$  interpolated from OWEN's [8] data. Consequently we obtain:

$$(12) \quad K_1' \frac{K_5}{K_2} + K_6 = 2.5 \text{ ml mol}^{-1} \text{ sec}^{-1}$$

in perfect harmony with the extrapolation to  $[\text{OH}] = 0$  of the fanshaped bundle of fig. 3.

No simple and direct way has been found to determine the constants  $K_5$ ,  $K_6$  and  $K_7$  separately. This is caused partly by the rather complicated way in which  $K_5$  occurs in the rate equation (9), partly by the relatively strong influence of errors in experiments and calculations on the results. The constant  $K_8$  can be determined separately from experiments at high pH. Its value is small and only of minor influence in the calculation of  $K_5$ ,  $K_6$  and  $K_7$ .

We determined the best set of values for  $K_5$ ,  $K_6$  and  $K_7$  by using successive approximations. To start with  $K_5$  was given the largest value compatible with eq. (12) i.e.

$$K_1' \frac{K_5}{K_2} = 2.5 \text{ ml mol}^{-1} \text{ sec}^{-1} \text{ or, with } K_1' = 6 \times 10^{-5} \text{ sec}^{-1} \text{ (see [1])}$$

$$\frac{K_5}{K_2} = 4 \times 10^4 \text{ ml mol}^{-1}.$$

Rearranging eq. (10) to

$$(13) \quad \left\{ \frac{K_{\text{obs}} - K_1' \frac{(K_3/K_2)[\text{OH}] + (K_5/K_2)[\text{RNH}_2]}{1 + (K_3/K_2)[\text{OH}] + (K_5/K_2)[\text{RNH}_2]} + K_4[\text{OH}] + K_8[\text{RNH}_2][\text{OH}]}{[\text{RNH}_2]} = \frac{K_6'}{[\text{RNH}_2]} = K_6 + K_7[\text{RNH}_2] \right.$$

and using  $(K_3/K_2) = 1.9 \times 10^7 \text{ ml mol}^{-1}$ ,  $K_4 = 150 \text{ ml mol}^{-1} \text{ sec}^{-1}$  (see [1]) and  $K_8 = 3 \times 10^6 \text{ ml}^2 \text{ mol}^{-2} \text{ sec}^{-1}$  (see at the end of this section), the left hand side of eq. (13) can be plotted against  $[\text{RNH}_2]$ . The triangles in fig. 4 represent these points.

It is evident that a straight line through these points would not extrapolate to the origin. Consequently  $K_6$  is at least  $1-1.5 \text{ ml mol}^{-1} \text{ sec}^{-1}$  and

$K_5/K_2$  has to be decreased correspondingly. The circles in fig. 4 are calculated for  $(K_5/K_2) = 2 \times 10^4 \text{ ml mol}^{-1}$  and  $K_6 = 1.4 \text{ ml mol}^{-1} \text{ sec}^{-1}$ . From the slope of the line through the circles the value  $3.2 \times 10^4 \text{ ml}^2 \text{ mol}^{-2} \text{ sec}^{-1}$  for  $K_7$  is found.

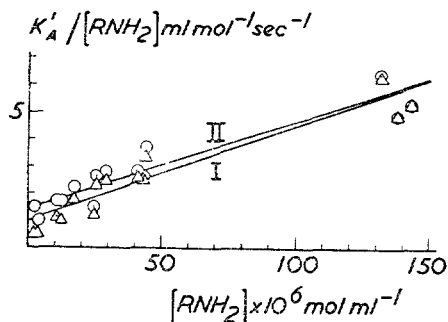


Fig. 4. Provisional and final values of  $K'_A/[RNH_2]$  plotted against  $[RNH_2]$ :  
 I Provisional values calculated with  $(K_5/K_2) = 4 \times 10^4 \text{ ml mol}^{-1}$   
 II Final values calculated with  $(K_5/K_2) = 2 \times 10^4 \text{ ml mol}^{-1}$

The value of  $K_8$  can only be determined from experiments at high pH. These data (table 2) are relatively inaccurate on account of the high reaction velocities.

For very high  $[OH]$  eq. (10) may be written as:

$$(14) \quad \begin{cases} K_{\text{obs}} = K_1 + K_4[OH] + K_6[RNH_2] + K_7[RNH_2]^2 + K_8[RNH_2][OH] = \\ = C_1 + C_2[OH] \end{cases}$$

with

$$(14a) \quad C_1 = K_1 + K_6[RNH_2] + K_7[RNH_2]^2$$

$$(14b) \quad C_2 = K_4 + K_8[RNH_2]$$

or

$$(15) \quad \lim_{[OH] \rightarrow \infty} \frac{K_{\text{obs}}}{[OH]} = C_1 \frac{1}{[OH]} + C_2.$$

The slopes  $C_1$  have been calculated with the values of  $K_6$  and  $K_7$  as found above, and have been included in table 3.

In fig. 2 A straight lines corresponding to eq. (15) have been drawn and in fig. 2 B the intercepts of fig. 2 A have been plotted against  $[RNH_2]$ . From the slope of this line the value of

$$(16) \quad K_8 = 3 \times 10^6 \text{ ml}^2 \text{ mol}^{-2} \text{ sec}^{-1}$$

has been found.

Finally we have calculated the values of  $K_{\text{obs}}$  from the theoretical equation (10) and compared these values in table 6 to the experimental ones.

Some trial and error showed that the best fit to all the data was obtained with the values of the constants listed in table 5. The accuracy of the



TABLE 5

List of constants of hydrolysis and aminolysis by glycine of E.T.A. at 37° C

$K_1'$	$= 6 \times 10^{-5} \text{ sec}^{-1}$
$K_3/K_2$	$= 1.9 \times 10^7 \text{ ml mol}^{-1}$
$K_4$	$= 150 \text{ ml mol}^{-1} \text{ sec}^{-1}$
$K_5/K_2$	$= 2 \times 10^4 \text{ ml mol}^{-1}$
$K_6$	$= 1.5 \text{ ml mol}^{-1} \text{ sec}^{-1}$
$K_7$	$= 3 \times 10^4 \text{ ml}^2 \text{ mol}^{-2} \text{ sec}^{-1}$
$K_8$	$= 3 \times 10^6 \text{ ml}^2 \text{ mol}^{-2} \text{ sec}^{-1}$

constants is not very large, but it seems a fair estimate that the actual values lie within 20 % of the ones given in the table.

TABLE 6

Values of  $K_{\text{obs}}$  as calculated with the constants of table 5 from eq. (10) and as determined experimentally

Exp. No.	[OH] $\times 10^9$ (mol ml $^{-1}$ )	[RNH $_2$ ] $\times 10^6$ (mol ml $^{-1}$ )	$K_{\text{obs}} \times 10^6$ experimental (sec $^{-1}$ )	$K_{\text{obs}} \times 10^6$ calculated (sec $^{-1}$ )
73	2250	10	480	483
72	14500	10	2600	2688
81	5000	20	1270	1152
77	10000	20	2150	2202
84	5000	40	1650	1518
83	10000	40	2760	2868
8	2.2	2.2	8	8.4
12	3.6	3.8	13	13.8
88	12.5	12.5	42	45
70	5.3	10.8	33	35
71	12.8	24.4	64	82
67	3.4	17.0	56	52
66	5.0	25.5	91	81
32	5.7	29	107	95
33	8.2	41	144	144
22	8.6	43	146	153
51	30	138	730	840
57	4.5	44	190	155
86	11.3	143	806	879
60	13	132	880	772
56	23	230	2020	2001

### 5. Reaction products

The isolation of acetyl glycine from the reaction mixture was described in a previous paper [7]. The experimental conditions of that reaction (pH = 8.4, total glycine concentration 1 molar) were such, that the main reaction paths were the spontaneous and the glycinate catalysed aminolysis ( $K_6$  and  $K_7$ ). In order to show definitely whether reactions  $K_8$  and  $K_5$  lead to aminolysis or hydrolysis new experiments under suitable reaction conditions are planned.

6. *Kinetics at 25° C*

Meanwhile the kinetic experiments have been continued at 25° C. The overall picture of the two reactions is the same as that at 37° C. The energies of activation as deduced from preliminary experiments are all low (5—15 k cal).

A discussion of the mechanism of the reaction will be postponed until the data at the lower temperature are completed.

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7. *Appendix*

Derivation of equation (9) for the velocity of simultaneous hydrolysis and aminolysis by glycine of E.T.A.:

According to the proposed reaction scheme the reaction velocity can be written as:

$$(9a) \quad \left\{ \begin{aligned} -\frac{d[\text{E.T.A.}]}{dt} &= K_1[\text{E.T.A.}][\text{H}_2\text{O}] - K_2[\text{C}_1] + K_4[\text{E.T.A.}][\text{OH}] + \\ &+ K_6[\text{E.T.A.}][\text{RNH}_2] + K_7[\text{E.T.A.}][\text{RNH}_2]^2 + K_8[\text{E.T.A.}][\text{RNH}_2][\text{OH}]. \end{aligned} \right.$$

Assuming the existence of a stationary state with respect to  $\text{C}_1$ , we may write:

$$\frac{d[\text{C}_1]}{dt} = K_1[\text{E.T.A.}][\text{H}_2\text{O}] - K_2[\text{C}_1] - K_3[\text{C}_1][\text{OH}] - K_5[\text{C}_1][\text{RNH}_2] = 0$$

or:

$$(9b) \quad [\text{C}_1] = \frac{K_1[\text{E.T.A.}][\text{H}_2\text{O}]}{K_2 + K_3[\text{OH}] + K_5[\text{RNH}_2]}.$$

After substitution of  $\text{C}_1$  eq. (9a) is written as:

$$\begin{aligned} -\frac{d[\text{E.T.A.}]}{dt} &= K_1[\text{E.T.A.}][\text{H}_2\text{O}] - K_2 \frac{K_1[\text{E.T.A.}][\text{H}_2\text{O}]}{K_2 + K_3[\text{OH}] + K_5[\text{RNH}_2]} + K_4[\text{E.T.A.}][\text{OH}] + \\ &+ K_6[\text{E.T.A.}][\text{RNH}_2] + K_7[\text{E.T.A.}][\text{RNH}_2]^2 + K_8[\text{E.T.A.}][\text{RNH}_2][\text{OH}] \\ &= K_1[\text{ETA}][\text{H}_2\text{O}] \frac{K_3[\text{OH}] + K_5[\text{RNH}_2]}{K_2 + K_3[\text{OH}] + K_5[\text{RNH}_2]} + K_4[\text{E.T.A.}][\text{OH}] + \\ &+ K_6[\text{E.T.A.}][\text{RNH}_2] + K_7[\text{E.T.A.}][\text{RNH}_2]^2 + K_8[\text{E.T.A.}][\text{RNH}_2][\text{OH}]. \end{aligned}$$

By substituting  $K'_1 = K_1[\text{H}_2\text{O}]$  and rearranging we obtain:

$$(9) \quad \left\{ \begin{aligned} -\frac{d[\text{E.T.A.}]}{dt} &= [\text{E.T.A.}] \left\{ K'_1 \frac{K_3[\text{OH}] + K_5[\text{RNH}_2]}{K_2 + K_3[\text{OH}] + K_5[\text{RNH}_2]} + \right. \\ &\left. + K_4[\text{OH}] + K_6[\text{RNH}_2] + K_7[\text{RNH}_2]^2 + K_8[\text{RNH}_2][\text{OH}] \right\}. \end{aligned} \right.$$

### 8. *Summary*

The kinetics of the aminolysis of ethyl thioacetate (E.T.A.) by glycine at 37° were investigated between pH=8 and pH=12. The reaction is of the first order in E.T.A. The dependence on the pH and the concentration of glycine is complicated. Three reactions run parallel, one first order with respect to glycinate ( $\text{H}_2\text{NCH}_2\text{COO}^-$ ), one second order with respect to glycinate and at high pH one that is first order in glycinate and in the  $\text{OH}^-$ -ion concentration. A fourth reaction in which the glycinate is involved was found at low pH. This reaction is competitive with one of the hydrolysis reactions.

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