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of J. TH. G. OVERBEEK

THE HYDROLYSIS AND AMINOLYSIS OF ETHYL THIOACETATE

III. RATE CONSTANTS AT 25° C, ACTIVATION ENERGIES AND
 PROBABILITY FACTORS

BY

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1. *Introduction*

The measurements of the alkaline hydrolysis and of the simultaneous hydrolysis and aminolysis of ethyl thioacetate (E.T.A.) [1, 2, 3] were continued at 25° C. From the experimental data the kinetic constants were determined for the hydrolysis and aminolysis by glycine of E.T.A. at 25° C. Furthermore, activation energies and approximate probability factors were calculated from these constants, and those obtained at 37° C [2, 3].

2. *Experimental methods and calculation of concentrations*

The rate of disappearance of E.T.A. in the reaction mixtures and the pH were determined according to the methods described before [1, 2].

OH⁻ ion concentrations in borate buffer solutions were calculated approximately [2] according to

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

Glycinate (R-NH₂) concentrations were calculated [3] from total glycine (RNH₃⁺ + RNH₂) concentrations with an empirical titration constant K_{NH₃}, which was calculated from pH determinations in some pure glycine buffers according to:

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

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

trations in borate buffer solutions were also calculated according to eq. (2). Concentrations are indicated by symbols between square brackets.

TABLE 1
Determined pH and calculated pK_{NH_3} of pure glycine buffers at 25° C

$\frac{[RNH_2]}{[RNH_2] + [RNH_3^+]}$	Total glycine (mol l ⁻¹)	pH	pK_{NH_3} calc.
0.036	1	8.33	9.76
0.715	1	8.63	9.74
0.143	1	8.90	9.68
0.143	0.5	8.92	9.70
0.143	0.1	8.91	9.69

3. Experimental results

As all reactions investigated are first order with respect to [E.T.A.], the results can be expressed by means of K_{obs} , defined by

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

The experimental data are listed in table 2 (for the alkaline hydrolysis), table 3 (for the simultaneous hydrolysis and aminolysis at low pH) and table 4 (hydrolysis and aminolysis at high pH).

TABLE 2

Alkaline hydrolysis of E.T.A. solutions at 25° C. In exp. 131, 132 and 133 the pH was measured with the aid of a hydrogen electrode. In exp. 124, 125, 123 and 120 [OH] was calculated from the composition of the reaction mixtures. In exp. 124, 125 and 123 [E.T.A.] was equal to [OH], in the other experiments [E.T.A.] was 0.0025 molar

Exp. No.	pH	[OH] × 10 ⁹ (mol ml ⁻¹)	$K_{obs} \times 10^6$ (sec ⁻¹)	{ $K_{obs}/[OH]$ } × 10 ⁻² (ml mol ⁻¹ sec ⁻¹)
131	9.34	28	13	4.76
132	9.66	58	21	3.71
133	10.06	147	36	2.45
124	—	625	— *)	1.20 *)
125	—	1250	— *)	1.10 *)
123	—	5000	— *)	0.81 *)
120	—	49400	4120	0.83

*) The cases where [E.T.A.] = [OH] have been calculated according to a second order rate equation in stead of with eq. (3). The second order rate constant is equal to $K_{obs}/[OH]$.

TABLE 3

Simultaneous hydrolysis and aminolysis by glycine at 25° C of 0.0025 m E.T.A. solutions in borate buffers of various pH. In exp. 100, 101, 102 and 105 the measurements were carried out in pure glycine buffers; no activity correction was used for the calculation of [OH] from pH in these experiments

Exp. No.	pH	[OH] × 10 ⁹ (mol ml ⁻¹)	[total glycine] × 10 ⁴ (mol ml ⁻¹)	[RNH ₂] × 10 ⁶ (mol ml ⁻¹)	K _{obs} × 10 ⁶ (sec ⁻¹)	{K _{obs} /[OH]} × 10 ⁻³ (ml mol ⁻¹ sec ⁻¹)
128	8.24	2.1	2	5.8	11	5.6
126	8.47	3.7	2	9.8	19	5.2
130	8.10	1.6	5	10.4	18	11.4
104	8.42	3.3	5	21.7	35	10.7
103	8.59	5.0	5	32.0	61	12.3
105	8.92	8.3	5	71.4	127	15.3
102	8.33	2.1	10	35.7	73	35
101	8.63	4.3	10	71.0	184	43
100	8.90	8.0	10	143	460	58

TABLE 4

Simultaneous hydrolysis and aminolysis by glycine of 0.0025 m E.T.A. solutions at 25° C and high pH. [OH] concentrations were calculated from the composition of the reaction mixtures

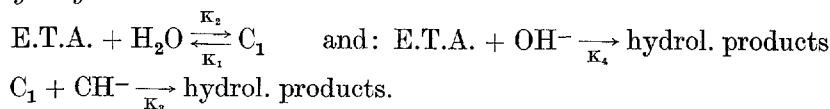
Exp. No.	[OH] × 10 ⁹ (mol ml ⁻¹)	[total glycine] = = [RNH ₂] × 10 ⁶ (mol ml ⁻¹)	K _{obs} × 10 ⁶ (sec ⁻¹)	{K _{obs} /[OH]} × 10 ⁻³ (ml mol ⁻¹ sec ⁻¹)
110	40000	10	3610	0.90
111	20000	10	1750	0.88
112 *)	10000	10	930	0.93
113	40000	20	3840	0.96
114	20000	20	1920	0.96
115	10000	20	960	0.95
116	40000	40	4530	1.13
117	20000	40	2330	1.17
118	10000	40	1190	1.19

*) In exp. 112 the reaction velocity began to decrease slightly when about 30 % of the E.T.A. had disappeared. The apparent change of the first order rate constant was attributed to the fact that the excess of [OH] and [RNH₂] over [E.T.A.] was rather small. In all other cases mentioned in this table the excesses of [OH] and [RNH₂] were large enough to mask any deviation from a first order rate law.

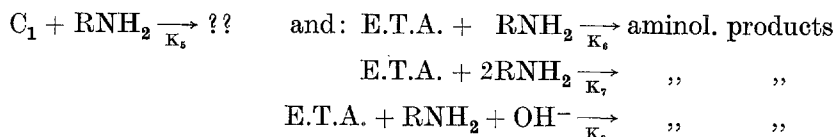
4. Kinetic analysis of the experimental data

The following reaction scheme has been proposed [3] for the simultaneous hydrolysis and aminolysis of E.T.A.:

Hydrolysis:



Aminolysis:



where: $\text{RNH}_2 = -\text{OOC}-\text{CH}_2\text{NH}_2$.

A reaction kinetic analysis of this scheme yields the following equation for K_{obs} (eq. 3) in the hydrolysis experiments [2]:

$$(4) \quad K_{\text{obs}} = K_{\text{H. obs}} = K'_1 \frac{K_3}{K_2} [\text{OH}] \frac{1}{1 + \frac{K_3}{K_2} [\text{OH}]} + K_4 [\text{OH}]$$

with $K'_1 = K_1 [\text{H}_2\text{O}]$,

whereas K_{obs} for the simultaneous hydrolysis and aminolysis experiments was found to be [3]:

$$(5) \quad \left\{ \begin{aligned} K_{\text{obs}} &= K_{\text{H. obs}} + K_{\text{A. obs}} = \\ &= K'_1 \frac{K_3 [\text{OH}] + K_5 [\text{RNH}_2]}{K_2 + K_3 [\text{OH}] + K_5 [\text{RNH}_2]} + K_4 [\text{OH}] + K_6 [\text{RNH}_2] + \\ &\quad + K_7 [\text{RNH}_2]^2 + K_8 [\text{RNH}_2] [\text{OH}]. \end{aligned} \right.$$

The determination and calculations of the kinetic constants were completely analogous to those at 37° C [2, 3]; the results obtained are listed in table 5.

TABLE 5

List of constants for the alkaline hydrolysis and aminolysis by glycine of E.T.A. at 25° C

K'_1	$= 3 \times 10^{-5} \text{ sec}^{-1}$
K_3/K_2	$= 1.5 \times 10^7 \text{ ml mol}^{-1}$
K_4	$= 80 \text{ ml mol}^{-1} \text{ sec}^{-1}$
K_5/K_2	$= 2 \times 10^4 \text{ ml mol}^{-1}$
K_6	$= 1.0 \text{ ml mol}^{-1} \text{ sec}^{-1}$
K_7	$= 1.5 \times 10^4 \text{ ml}^2 \text{ mol}^{-2} \text{ sec}^{-1}$
K_8	$= 7.5 \times 10^3 \text{ ml}^2 \text{ mol}^{-2} \text{ sec}^{-1}$

Finally, experimental and calculated values of K_{obs} for the simultaneous hydrolysis and aminolysis experiments are compared in table 6.

TABLE 6

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

Exp. No.	$[\text{OH}] \times 10^9$ (mol ml ⁻¹)	$[\text{RNH}_2] \times 10^6$ (mol ml ⁻¹)	$K_{\text{obs}} \times 10^6$ experimental (sec ⁻¹)	$K_{\text{obs}} \times 10^6$ calculated (sec ⁻¹)
110	40000	10	3610	3542
111	20000	10	1750	1792
112	10000	10	930	917
113	40000	20	3840	3856
114	20000	20	1920	1956
115	10000	20	960	1006
116	40000	40	4530	4510
117	20000	40	2330	2310
118	10000	40	1190	1210
128	2.1	5.8	11	10.4
126	3.7	9.8	19	17
130	1.6	10.4	18	17.5
104	3.3	21.7	35	39
103	5.0	32.0	61	60
105	8.3	71.4	127(?)	170
102	2.1	35.7	73	66
101	4.3	71.0	184	167
100	8.0	143	460	473

5. Activation energies and probability factors

The rate constants at 25° C and at 37° C [2, 3] were used to calculate the energy of activation and the empirical constant A from the ARRHENIUS equation:

$$(6) \quad K = Ae^{-E_A/RT}$$

The constant A can be regarded as the product of a collision frequency Z and a "probability" or "steric" factor, P, so:

$$(7) \quad A = PZ$$

or:

$$(8) \quad K = PZe^{-E/RT} \quad (1).$$

As the collision frequency Z in solutions is of the same order of magnitude as that in the gas phase [4a] it may be taken as [5]:

$$Z \approx 10^{13} - 10^{14} \text{ sec}^{-1} \quad \text{for a monomolecular reaction}$$

$$Z \approx 10^{11} - 10^{12} \text{ l mol}^{-1} \text{ sec}^{-1} \quad \text{for a bimolecular reaction}$$

$$Z \approx 10^9 - 10^{10} \text{ l}^2 \text{ mol}^{-2} \text{ sec}^{-1} \quad \text{for a termolecular reaction.}$$

¹) The true critical energy increment E involved in eq. (8) is related to E_A by:

$$E = E_A - \frac{1}{2} RT$$

Consequently, the difference between E and E_A is only noticeable when T is high or E_A very low.

TABLE 7

Approximate activation energies and probability factors of the alkaline hydrolysis and aminolysis by glycine of E.T.A. as calculated from eq. (6) and eq. (7). The collision frequency Z was taken as 10^{11} l mol⁻¹ sec⁻¹ for bimolecular reactions and as 10^{918} mol⁻³ sec⁻¹ for termolecular reactions.

Reaction	25° C	37° C	E (cal/mol)	A = PZ	P
1. E.T.A. + H ₂ O → C ₁ K ₁ =(K ₁ '/[H ₂ O]) (l mol ⁻¹ sec ⁻¹)	5.4 × 10 ⁻⁷	11 × 10 ⁻⁷	10500	18 (l mol ⁻¹ sec ⁻¹)	10 ⁻¹⁰
2. E.T.A. + H ₂ O + OH ⁻ → hydrol. products K ₁ (K ₃ /K ₂) (l ² mol ⁻² sec ⁻¹)	8 × 10 ⁻³	21 × 10 ⁻³	14500	2 × 10 ⁸ (l ² mol ⁻² sec ⁻¹)	10 ⁻¹
3. E.T.A. + OH ⁻ → hydrol. products K ₄ (l mol ⁻¹ sec ⁻¹)	8 × 10 ⁻²	15 × 10 ⁻²	9700	7 × 10 ⁵ (l mol ⁻¹ sec ⁻¹)	10 ⁻⁵
4. E.T.A. + H ₂ O + RNH ₂ →?? K ₁ (K ₅ /K ₂) (l ² mol ⁻² sec ⁻¹)	1.1 × 10 ⁻⁵	2.2 × 10 ⁻⁵	10500	36 × 10 ² (l ² mol ⁻² sec ⁻¹)	10 ⁻⁷
5. E.T.A. + RNH ₂ → aminol. products K ₆ (l mol ⁻¹ sec ⁻¹)	10 ⁻³	1.5 × 10 ⁻³	6100	23.5 (l mol ⁻¹ sec ⁻¹)	10 ⁻¹⁰
6. E.T.A. + 2RNH ₂ → aminol. products K ₇ (l ² mol ⁻² sec ⁻¹)	1.5 × 10 ⁻²	3 × 10 ⁻²	10500	5 × 10 ⁵ (l ² mol ⁻² sec ⁻¹)	10 ⁻⁴
7. E.T.A. + RNH ₂ + OH ⁻ → aminol. products K ₈ (l ² mol ⁻² sec ⁻¹)	7.5 × 10 ⁻¹	3	21000	7.5 × 10 ⁴ (l ² mol ⁻² sec ⁻¹)	10 ⁴

If the factor P is of the order of unity the reaction is called normal, for "slow" reactions P varies between 10⁻⁵—10⁻¹⁰ and for "fast" reactions between 10² and 10¹⁰. The energies of activation and the orders of the P-factors of the hydrolysis and aminolysis by glycine of E.T.A. are listed in table 7.

With respect to the data listed in table 7 the following remarks may be made:

1. All activation energies and P-factors lie within the known range, but most of them are rather small. As both the hydrolysis and aminolysis of E.T.A. are probably highly exothermic, it should be mentioned, that quite often highly exothermic reactions are "slow" [4b].
2. The complex formation of E.T.A. with water (reaction 1 of table 7) and the uncatalysed aminolysis of E.T.A. by glycine (reaction 5) are undisputably "slow" reactions: their velocities are about 10¹⁰ × too low with respect to their small energy of activation. It should be noted,

- however, that the P-factors involved lie still within the range which GLASSTONE, LAIDLER and EYRING [6] have calculated for a bimolecular reaction between two polyatomic molecules ($P = 10^{-5} - 10^{-10}$).
3. Any conclusion from the data referring to the termolecular reactions 2, 4, 6 and 7 should be drawn very cautiously. We have assumed an intermediate bimolecular E.T.A.—H₂O complex (C₁) because its formation proved to be rate determining in certain conditions. Consequently, reaction 2 and 4, which might be regarded as a normal and as a slow termolecular reaction respectively, certainly follow a more complicated stepwise mechanism. Reactions 6 and 7 might be taken as a slow and as a fast reaction respectively. However, in these cases also an intermediate bimolecular E.T.A.—RNH₂ complex formation may be involved.
 4. We have compared our data on the OH⁻ion catalysed hydrolysis of E.T.A. (reaction 3) with the data on the alkaline hydrolysis in aqueous solutions of a number of alifatic acetates [4c]. A fair conformity in the E_A values was found: E_A = 10500 cal/mol for the hydrolysis of E.T.A. and E_A = 11000—11500 cal/mol for the hydrolysis of 7 acetates. The values of the empirical constant A differed somewhat more, A being equal to 7×10^5 for the hydrolysis of E.T.A. and about $1 - 3 \times 10^7$ for the hydrolysis of the acetates. As the P-factor for the alkaline hydrolysis of both categories of esters may be valued roughly at $10^{-6} - 10^{-4}$, we may conclude that rather "slow" reactions are involved.

In a next paper a tentative reaction scheme for these kinetic data will be proposed.

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6. Summary

The kinetics of the alkaline hydrolysis and aminolysis by glycine of ethyl thioacetate were investigated at 25° C. Furthermore, activation energies and probability factors were calculated from the data on the rate constants, obtained at 25° C and at 37° C. Generally, low activation energies and slow reactions proved to be involved in both processes.

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