

The Influence of the Solvent on Reaction Velocity

IV.* Alkaline Hydrolysis of Ethyl Propionate and Ethyl Butyrate in Ethanol-Water Mixtures

EERO TOMMILA and SIRKKU HIETALA

Institute of Chemistry, University of Helsinki, Helsinki, Finland

Comparison of results concerning the alkaline hydrolysis of ethyl acetate¹, ethyl benzoate², and benzyl acetate² in various mixed solvents reveals that the solvent effects show the same general picture irrespective of the different acid or alcoholic components in the esters. This being found, it seemed desirable, in order to get more detailed information in the matter, to study the reaction with the ethyl esters of the other simple fatty acids, the reaction rate being more sensitive to substitution of a CH₂ group in the acid than in the alcohol radical^{3,4}. The present paper contributes certain data concerning ethyl propionate and ethyl butyrate, a series of mixtures of ethyl alcohol and water being used as solvent.

EXPERIMENTAL

Chemicals. The esters were prepared from the acids and ethyl alcohol⁵. The acids were commercial products of high purity. The esters, purified by repeated fractional distillation, had the following boiling points: ethyl propionate 99.4–99.7° (777 mm), ethyl butyrate 121.1–121.5°C.

The ethanol used in the kinetic experiments was commercial absolute ethanol, but purified by Walden's⁶ method. The water was always freshly distilled.

Method. The alcohol-water mixtures and the solutions of ester and NaOH were prepared in the way described previously¹. The concentration of the ester was always checked by total hydrolysis and then adjusted to the exact value. Both ester and sodium hydroxide were used in equal concentrations. For ethyl propionate 0.1 *M*, for ethyl butyrate, owing to its poorer solubility, 0.05 *M* solutions were used, so that, after mixing equal amounts (5 ml), the initial concentrations of each were 0.05 or 0.025 *M*. The fact that the experiments were carried out with different initial concentrations is not significant since the initial concentration has practically no influence upon the rate constants⁷. The reactions were carried out in vessels designed for volatile reagents and described previously⁸. The reaction was stopped by an excess of 0.02 or 0.01 *N* HCl, and the acid titrated with 0.02 or 0.01 *N* baryta solution, cresol red being used as indicator.

Since the object of the experiments was to measure the activation energies as accurately as possible, the preparation of the solvent and all other operations were carefully standardised. All the measurements were made by one of the authors (S.H.) in order to eliminate personal factors as fully as possible. Each solvent was prepared in a quantity

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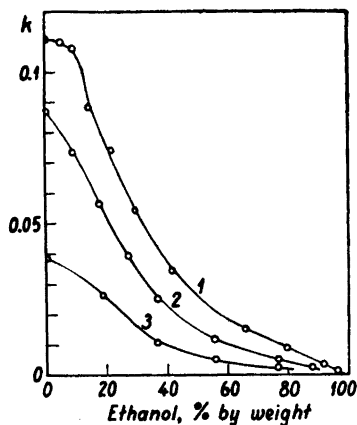


Fig. 1. Variation of the rate constant with the percentage of ethanol in the solvent at 25°. 1. Ethyl acetate, 2. Ethyl propionate, 3. Ethyl butyrate.

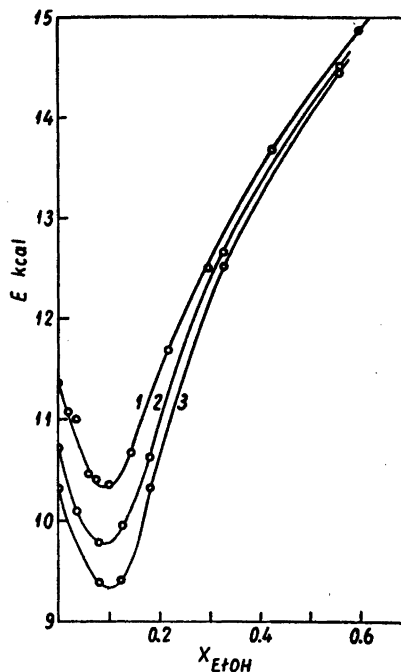


Fig. 2. Graphs to show the correlation between E and the mole fraction of ethanol in the solvent. 1. Ethyl acetate, 2. Ethyl propionate, 3. Ethyl butyrate.

sufficient for all experiments with this solvent composition. This is very important since the kinetic constants are very sensitive to the composition of the solvent. The number of observations in each run was at least seven, in most cases, however, much larger. The present results are used in direct comparison with those previously obtained for ethyl acetate in ethanol-water.

Second order kinetics were observed in all cases. The values of the rate constants obtained by the usual formula $dx/dt = k(a-x)^2$ were averaged and corrected for change of concentration due to thermal expansion of the solvent.

Table 1. Alkaline hydrolysis of ethyl propionate.

H ₂ O vol. %	EtOH wt. %	x_{H_2O}	10% liter mole ⁻¹ sec. ⁻¹							E cal.	log A	ΔS^* E.U.
			0.00°	15.00°	20.00°	25.00°	35.00°	40.00°	50.00°			
100	0	1.000	15.4	46.4	66.9	87.0	133	191		10 720	6.780	-29.5
90	8.7	0.964	14.6	40.9		73.9		157		10 090	6.252	-31.9
80	17.8	0.922	12.2	32.5		56.7		122		9 770	5.912	-33.5
70	27.0	0.874	8.15	22.8		39.5		84.8		9 940	5.876	-33.6
60	36.3	0.818	4.76	13.5		25.0		57.9		10 620	6.177	-32.3
40	55.7	0.670	1.55	5.50		11.6		29.3		12 650	7.317	-27.0
20	76.5	0.440	0.538	2.27		5.29		16.3	30.2	14 500	8.339	-22.4
10	87.9	0.260	0.231	1.10		2.74		9.23	19.8	15 230	8.596	-21.2

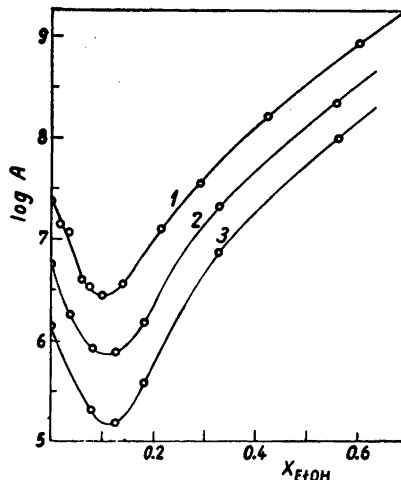


Fig. 3. Graphs to show the correlation between $\log A$ and the mole fraction of ethanol in the solvent. 1. Ethyl acetate, 2. Ethyl propionate, 3. Ethyl butyrate.

Activation energies, E , and frequency factors, A , were obtained from the variation of $\log k$ with $1/T$, the method of least squares being used in all cases. The entropy of activation, ΔS^* , was calculated from the frequency factor A by means of the equation ⁹.

$$A = e \frac{kT}{h} e^{\Delta S^*/R}.$$

RESULTS AND DISCUSSION

General. The values of k , E , $\log A$, and ΔS^* are given in Tables 1 and 2. ΔS^* is calculated for 25° C. Figures 1, 2, and 3 show the plots of k , E , and $\log A$ against the alcohol content of the solvent. The values for ethyl acetate are taken from the previous investigation. We see that the curves of Figs. 2 and 3 are very similar for all three esters. The depth of the minimum in the activation energy, with regard to the value of E in pure water, is about 1 000 calories in all three cases.

The behaviour of k , E and A in alcohol-rich mixtures after the minimum is partly due to the equilibrium

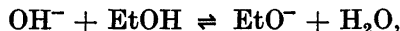


Table 2. Alkaline hydrolysis of ethyl butyrate.

H ₂ O vol. %	EtOH wt. %	$x_{\text{H}_2\text{O}}$	10 ³ k liter mole ⁻¹ sec. ⁻¹					E cal.	$\log A$	ΔS^* E.U.	
			0.00°	5.00°	15.00°	25.00°	40.00°				50.00°
100	0	1.000	7.69		20.6	38.3	86.8		10 320	6.142	-32.4
80	17.8	0.922		8.68	15.7	26.6	58.3		9 390	5.316	-36.2
70	27.0	0.874		6.13	11.6	19.8	41.3		9 400	5.184	-36.8
60	36.3	0.818		2.90	5.83	10.5	23.6		10 320	5.583	-35.0
40	55.6	0.671		1.13	2.46	5.17	14.0		12 500	6.879	-29.1
20	76.6	0.438			1.08	2.55	8.17	16.5	14 440	7.984	-24.0

which lies surprisingly far to the right¹⁰. In the whole domain from pure water upward, on changing from one solvent mixture to another, a very important part is played by changes in the solvation of the reactants and the transition state^{1,9}. Undoubtedly, the changes in the internal structure of the solvent are of importance. Many physical properties of alcohol-water mixtures, such as the partial molar volumes of the components, molar polarisation, compressibility, and viscosity, show pronounced maxima or minima in the region of 10 mole per cent of ethanol. Furthermore, many observations indicate that ethanol, when its concentration is small, is molecularly dispersed in water, greatly disturbing the structure of the water, whereas when a small amount of water is added to alcohol, single water molecules can easily enter into the chains of alcohol molecules, without any marked disturbance of the one-dimensional association and the structure of the liquid¹¹. All this must be borne in mind in the interpretation of solvent effects on reaction rates.

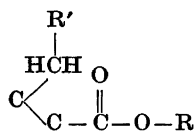
The rate constants. It has been known for a long time that the bimolecular rate constants for the alkaline hydrolysis of the esters of *n*-fatty acids decrease with increasing length of the carbon chain. There is a significant drop in the rate of hydrolysis in passing from ethyl propionate to ethyl butyrate, the change in passing from ethyl acetate to ethyl propionate being less. After butyric acid a further lengthening of the chain has only a very weak effect on the rate constants^{12,13}. For the hydrolysis in pure water, the values of *k* at 25°C are, according to our results, 0.111, 0.087, and 0.0383 l. mole⁻¹ sec.⁻¹ for ethyl acetate, ethyl propionate, and ethyl butyrate, respectively. The ratio of the rate constants of ethyl propionate and ethyl acetate decreases with the increasing alcohol content of the solvent, but that of ethyl butyrate and ethyl propionate is, as a first approximation, independent of the solvent composition:

Alcohol % by weight	0	17.8	27.0	36.3	55.6	76.6
k_{Pr}/k_{Ac}	0.78	0.71	0.65	0.59	0.55	0.53
k_{Bu}/k_{Pr}	0.44	0.47	0.50	0.42	0.45	0.48

The order of the activation energies and frequency factors is, as seen from Figs. 2 and 3, ethyl acetate > ethyl propionate > ethyl butyrate. Thus the differences in the rate constants are wholly accounted for by the differences in frequency factors, *i. e.* in the differences in activation entropies. These are more than sufficient to offset the effect on the reaction rates of the changes in the activation energies. This was rather surprising and contrary to the results of Evans, Gordon and Watson¹³, but in better agreement with those of Smith and Levenson¹⁴. Evans, Gordon, and Watson thought that in the alkaline hydrolysis of aliphatic carboxylic esters the activation energy increases with the chain length of the acid component: "as a rule, *E* varies in accordance with the inductive effect of R", which increases in magnitude from Me to Bu. Smith and Levenson found that the energy of activation was practically constant within the precision of the measurements for this series of esters and that the changes in the velocity had to be attributed to a large extent to changes in the frequency factor. Both of these investigations were made in 85 % aqueous ethanol (by weight), where the differences in *E* between the three esters are very small (Fig. 2). The only data concerning the temperature dependence

of the reaction in water reported in the literature are those given by Salmi and Leimu¹⁵, for the esters of *n*-fatty acids, but their measurements were carried out at three temperatures only and thus do not give *E* values accurate enough for a critical study of the problem. In the same manner as in the alkaline hydrolysis of the esters of *n*-fatty acids, *k* behaves in their acid hydrolysis¹⁶ and in the acid-catalysed esterification¹⁷. In the alkaline hydrolysis of benzyl esters of *n*-fatty acids in 56 % aqueous acetone (by weight) the differences in the values of *k* are also occasioned principally by changes in *A*, with *E* remaining constant within experimental error from benzyl acetate onward¹⁸.

As stated above, the effect of lengthening of the carbon chain in the acid part of the ester on the rate constant is certainly not explained in terms of inductive effect. The sequence of the activation energies, ethyl acetate > ethyl propionate > ethyl butyrate, is the direct opposite of that predicted by the inductive effect. The differences are especially distinct in the region from pure water to about 40 % acetone (Figs. 2 and 3). Since it appeared unlikely that the structural changes involved could have any significant effect on the carbonyl group through altered inductive or hyperconjugative effects, Smith and McReynolds¹⁹, who thought that for each of the above sets of reactions the activation energy is practically constant, concluded that in butyric acid and higher homologs a coiled structure, in which the hydrogens on the third methylene group come close to the oxygen of the carboxyl group, is possible and is probably responsible for the rate decrease:



In the orientation assumed, approach of the hydroxyl ion (alkaline hydrolysis), water molecule (acid hydrolysis), or alcohol molecule (esterification, R = H) is sterically hindered in one direction and accordingly the frequency factor is reduced. The idea has been further developed by Newman²⁰. A direct interaction between the methyl group and carbonyl oxygen was supposed also by Evans, Gordon, and Watson¹³, who believed that this involves the formation of a hydrogen bond. Similar suggestions have been proposed by other investigators, too. Bennett and Mosses²¹ compared the dissociation constants of propionic, butyric, and heptonic acids (1.33, 1.50, and 1.3×10^{-5} , respectively) and attributed the high value in the case of butyric acid to the fact that the terminal methyl, being free to move, occasionally comes into close proximity to the carbonyl group and facilitates ionisation, exerting a direct polar effect of opposite sign to its inductive effect. Dippy²² considered that this is due to an attraction between the C—CH₃ and C = O dipoles (hydrogen-bonding), particularly in the anion. Magee, Ri, and Eyring²³, discussing the enhanced *K* for *n*-butyric acid, also give ring closure as the probable reason for this large value. The same view was expressed by Ayling²⁴ as the explanation of a number of phenomena. Independent evidence favouring this suggestion has been supplied by McReynolds and Witmeyer²⁵ in a study of the stabilities to race-

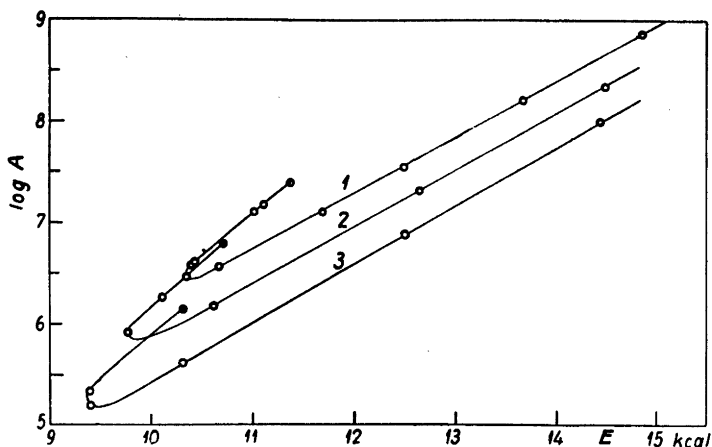


Fig. 4. Plot of $\log A$ against E . 1. Ethyl acetate, 2. Ethyl propionate, 3. Ethyl butyrate.

misation of certain salts containing aliphatic acid radicals. Anomalies were found and a hydrogen bond linking the β -carbon with the carbonyl oxygen was postulated in acid-catalysed prototropy of phenyl alkyl ketones also²⁶. The *ortho*-effect in the alkaline hydrolysis of the ethyl ester of *o*-methylbenzoic acid has led to the conclusion that a direct interaction of the methyl group with the carbonyl oxygen is operative²⁷.

These ideas are in good agreement with our experimental results. Whatever its detailed mechanism, there is every reason to suppose that in *n*-paraffinic esters $R\cdot COOEt$ an additional effect opposed to the chain-transmitted (inductive) effect is operative. This additional effect tends to lower the energy of activation, and since in the alkaline hydrolysis the chief resistance to the reaction is represented by the energy required for bringing the hydroxyl ion up to the carbonyl carbon²⁸, it obviously tends to make the carbonyl carbon more positive. A hydrogen-bonding between the terminal methyl group of the coiled R and the oxygen atom of the carbonyl group would explain the direction of this additional effect, and there seem to be no serious objections to such a supposition²⁹.

The values of the activation energies show that, in contrast to the older views, the additional effect is already operative and more powerful than the inductive effect even in the case of ethyl propionate, and is obviously at maximum with ethyl butyrate, after which a further lengthening of the chain, according to all previous workers, has very little influence on the reaction rate. From molecular models it can be seen that a hydrogen bonding in propionate is geometrically not impossible, although its strength, of course, is weaker than in the case of butyrate. It is noteworthy that the difference in E is larger between ethyl acetate and ethyl propionate than between ethyl propionate and ethyl butyrate. The decrease of the frequency factor in passing from ethyl acetate to ethyl butyrate is, as concluded by Smith and Reynolds, explained in terms of increasing steric hindrance^{cf.30}. In this connection it is of special

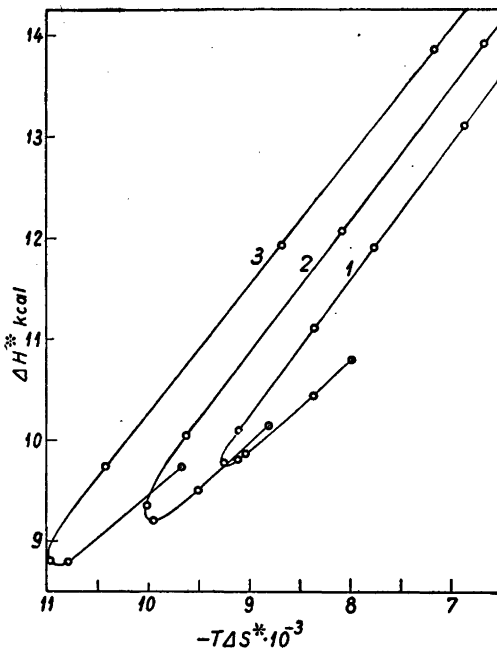


Fig. 5. Plot of ΔH^{\ddagger} against $-T\Delta S^{\ddagger}$. 1. Ethyl acetate, 2. Ethyl propionate, 3. Ethyl butyrate.

interest that behaviour of k , E , and A closely similar to that observed in the hydrolysis of carboxylic esters has been found in the alkaline and acid hydrolysis of aliphatic amides³¹. With regard to hydrolysis, there is a marked analogy between the amides and esters³².

Figs. 2 and 3 show that the solvent effect is very similar in magnitude in all three cases. The differences between the values of $\log A$ are practically independent of the composition of the solvent. The differences between the values of E , however, become smaller as the alcohol content is increased from the mole fraction 0.1, which indicates a weak special solvent effect for each reaction. This is probably connected with differences in the changes of the solubility of the esters. With an increasing alcohol content, the solubility of the esters of the series increases the greater the length of the carbon chain, from which it directly follows that the differences between the activation energies must become smaller, since an increase in the solvation of the reactants rises the energy of activation¹, and the effect increases with the solvation. It is reasonable to assume that the transition complex, which is very polar, is, if the solvent is the same, solvated to practically the same extent in the three cases.

The relation between A and E . In the previous investigations^{1,2} it was found that the plot of $\log A$ versus E is linear on either side of the minima of E and A . From Fig. 4 we see that this is also the case for the hydrolysis of

ethyl propionate and ethyl butyrate and, furthermore, that the slopes of the lines are almost identical. Between pure water and the minimum $\Delta \log A/\Delta E$ is about 0.80 (E expressed in kilocalories), in solutions containing more than 20 % by weight of ethanol $\Delta \log A/\Delta E$ is 0.56 (for ethyl acetate 0.55, ethyl propionate 0.56, ethyl butyrate 0.57). The corresponding values for the alkaline hydrolysis of ethyl benzoate in ethanol-water and in acetone-water, and benzyl acetate in acetone-water are of the same order of magnitude.³

The linear relationship between $\log A$ and E is equivalent to a linear relationship between the heat of activation, $\Delta H^* = E - RT$, and $T\Delta S^*$, as expressed by the equation^{33,1}

$$T\Delta S^* = \alpha\Delta H^* + \beta.$$

From Fig. 5, where the plots are given, we obtain for all three esters, in the region from pure water to about 18 wt. % ethanol roughly $\alpha = 1$. In the ethanol-richer region the values for α are: ethyl acetate 0.75, ethyl propionate 0.77, ethyl butyrate 0.80.

SUMMARY

The alkaline hydrolysis of ethyl propionate and ethyl butyrate in pure water and various ethanol-water mixtures was kinetically investigated. The results are compared with previous results for ethyl acetate, and discussed.

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