Yamafuji⁵ on this point cannot be regarded as conclusive evidence. The question is thus still open. The other possibility that the oximes formed are hydrolyzed, and that the free hydroxylamine is then reduced to ammonia also lacks experimental evidence.

At the moment it seems very likely that the physiological function of the formation of "bound hydroxylamine" is the "trapping" of hydroxylamine in case it is not reduced to ammonia quickly enough. On the other hand, it is still unsettled if the formation of oximes at the same time constitutes a special pathway for amino acid synthesis. The significance of acetylhydroxamic acid is also obscure.

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Activation Energies in the Alkaline Hydrolysis of Saturated Aliphatic Esters

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The volatility and low solubility of saturated aliphatic esters in water may lead to appreciable errors in the determination of the rates of hydrolysis.

In the present study, the air volume above the solution was kept small by using two ampoules, one of about 6 ml capacity and the other of about 10.5 ml, which were connected by a short length of rubber tubing. 5 ml of an 0.02 M aqueous solution of the ester was

measured into the larger ampoule and 5 ml of 0.02 M aqueous sodium hydroxide into the other. After the rubber tubing was closed with a screw fastener, the ampoules were placed alongside each other in the thermostat; in this way evaporation of the ester into the alkali solution was avoided. After both ampoules had attained the thermostat temperature, the tubing was opened, the alkali was transferred into the ester solution with vigorous shaking, and the tubing was closed again. The ampoules were taken from the thermostat after suitable intervals, the tubing was removed, and the reaction mixture poured rapidly into an ice-cold hydrochloric acid solution. The excess of hydrogen chloride was titrated with baryta solution using phenolphthalein as indicator. The rate constants were calculated from the second-order rate equation. The values of the rate constants obtained are given in Table 1 (the values for ethyl formate from a publication of Tommila and Maltamo¹ have been included for comparison).

The rate constants for all the esters studied are in good agreement with the values reported by Salmi and Leimu², and those for ethyl acetate with the values published by Tommila and coworkers^{3,4}. From the calculated activation energy and frequency factor values given in the table it is seen that for the last three esters the decrease in the rate is mainly due to a decrease in the frequency factor, and that the activation energy increases from ethyl formate to ethyl acetate and then decreases slowly in the series ethyl acetate, ethyl propionate and ethyl isobutyrate. On the other hand, the activation energies for ethyl propionate and ethyl *n*-butyrate do not differ from each other. The rate falls greatly from ethyl formate to ethyl acetate and the difference between the rates of ethyl propionate and ethyl butyrate is abnormally large (cf. Ref.⁴). The rate decreases only slightly from ethyl acetate to ethyl propionate in the temperature range studied (as calculated from the Arrhenius plot, ethyl propionate hydrolyses more rapidly than ethyl acetate at temperatures below -3° C).

The differences in the rates of hydrolysis can be explained by assuming that the activation energy differences are mainly determined by hyperconjugation and that the differences in the inductive and steric effects appear mainly in the frequency factors. In a previous study⁵, it was concluded that the conjugation between the

Table 1. Alkaline hydrolysis of esters in water.

Ester	k l mol. ⁻¹ sec. ⁻¹				E cal	log A
	0.00°	20.00°	25.00°*	40.00°		
H—CO ₂ Et	5.07	—	—	—	9.680	8.46
CH ₃ —CO ₂ Et	0.0177	0.0764	0.109	0.284	11.790	7.68
CH ₃ —CH ₂ —CO ₂ Et	0.0170	0.0657	0.0880	0.206	10.590	6.71
CH ₃ —CH ₂ —CH ₂ —CO ₂ Et	0.00906	0.0361	0.0477	0.111	10.660	6.49
$\begin{array}{c} \text{CH}_3 \\ \diagup \\ \text{CH} \end{array} \text{—CO}_2\text{Et}$	0.00621	0.0226	0.0300	0.0678	10.170	5.93

* Computed from the Arrhenius equation.

carboxyl carbonyl group and the α,β -unsaturated bond is an important factor determining the activation energy in alkaline ester hydrolysis. As compared with ethyl formate, ethyl acetate contains a methyl group which enters into conjugation with the carboxyl carbonyl group and also possesses weak inductive and steric effects. The ethyl group in the acid part of ethyl propionate possesses stronger inductive and steric effects, but a weaker hyperconjugative effect, than the methyl group in ethyl acetate. The decreased hyperconjugation lowers the activation energy and hence increases the hydrolysis rate, which is in accordance with the fact that the ethyl propionate hydrolyses more rapidly than ethyl acetate at low temperatures. This increase in the hydrolysis rate is opposed by the strengthened inductive and steric effects. In ethyl isobutyrate the inductive and steric effects are even larger, but there is no hyperconjugation. If the hyperconjugation alone determined the differences in the activation energies, the activation energy should be the same for both ethyl isobutyrate and ethyl formate. Since the observed difference is 490 cal, it must be concluded that also the inductive and steric effects increase the activation energy in some degree.

The hyperconjugation is the same in both ethyl propionate and ethyl *n*-butyrate, and so also are the activation energies. The change in the inductive effect is slight, and hence the observed abnormal

fall in the rate is due to a marked steric effect in ethyl *n*-butyrate. The steric effect may evidently be considered to involve geometrical hindrance, since there is no difference in the activation energies. Quantitatively this steric effect is comparable with the difference in the rates of hydrolysis of the methyl and ethyl esters of acids in general. The mean ratios of the rates of both pairs are both approximately 1.8 (see Table 1 and the data of Leimu and Salmi²). The decisive influence of the steric effect is also apparent from the observation that the ratio of the rates of hydrolysis of the methyl and ethyl esters increases rapidly as the degree of branching increases in the acid component of the ester².

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