771. *A Kinetic Study of the Alkaline Hydrolysis of Some Aliphatic Esters.*

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Velocities and Arrhenius activation energies have been determined for the alkaline hydrolysis of the ethyl esters of ten olefinic acids in 85% alcohol. The results can be understood in the light of the inductive effects of alkyl groups, mesomeric effects in cases where a double bond is conjugated with the ethoxycarbonyl group, and hyperconjugation in suitable structures. Earlier results, some of which have been redetermined, for the alkaline hydrolysis of saturated aliphatic esters are also discussed.

EVANS, GORDON, and WATSON,[1] and Smith and Levenson,[2] determined bimolecular velocity coefficients and Arrhenius activation energies for the alkaline hydrolysis of the ethyl esters of a series of saturated aliphatic acids in 85% alcohol. No similar investigation of the hydrolysis of unsaturated esters has hitherto been conducted, however. We now further consider the kinetics of alkaline hydrolysis of the saturated esters, and describe an extension of the work to ten unsaturated esters. The results are analysed on the basis of the kinetic equation $k = PZe^{-E/RT}$, the new experimental results being summarised in Table 1.

TABLE 1. *Alkaline hydrolysis of esters in 85% alcohol.*

Ester	10^3k_{25}	10^3k_{40}	10^3k_{55}	10^3k_{65}	E (cal./mole)	$\log_{10} PZ$
Acetic [a]	6·98	23·0	—	—	14,700 [b]	8·6
Propionic	3·65	11·7	33·9	—	14,500 [c]	8·2
Trimethylacetic	—	0·107	0·248	0·814	17,100 [d]	8·0
Acrylic	4·67	16·3	49·7	—	15,400	8·9
But-3-enoic [e]	3·63	11·6	33·8	—	14,500	8·2
Pent-4-enoic	3·62	11·8	34·0	—	14,500	8·2
Crotonic	0·625	2·34	7·95	—	16,500	8·9
β-Methylcrotonic [f]	—	0·322	1·19	2·71	18,000	9·0
Non-2-enoic	0·660	2·36	7·64	—	15,900	8·5
Penta-2 : 4-dienoic	1·42	5·50	18·8	—	16,800	9·5
Sorbic	0·473	1·96	7·11	—	17,600	9·6
α-Methylacrylic	0·933	3·30	10·9	—	16,000	8·7
Tiglic	—	0·563	1·96	4·29	17,100	8·7

[a] A determination at 20° gave $10^3k = 4.54$. [b] Confirms Smith and Levenson.[2] [c] Confirms Evans, Gordon, and Watson.[1] [d] Confirms Evans, Gordon, and Watson (recalc.). [e] Values for first 10% of reaction; see p. 3963. [f] A determination at 70° gave $10^3k = 4.04$.

Discussion.—Alkaline hydrolysis of saturated esters. The rather weak electron-repelling character of alkyl groups ($+I$ effect) renders the attack of the negative ion progressively more difficult, leading to an increasing value of the energy of activation, both as the chain of the ester becomes longer, and in series such as $CH_3 \cdot CO_2Et < CH_2R \cdot CO_2Et < CHR_2 \cdot CO_2Et < CR_3 \cdot CO_2Et$ (compare instances cited by Evans, Gordon, and Watson [1]). The magnitude of this inductive effect falls off very rapidly as the substituent alkyl group is moved further from ethoxycarbonyl, and accordingly Evans, Gordon, and Watson [1] found that the energy of activation for alkaline hydrolysis rose from acetic to butyric ester, beyond

[1] Evans, Gordon, and Watson, *J.*, 1938, 1439.
[2] Smith and Levenson, *J. Amer. Chem. Soc.*, 1939, **61**, 1172.

which only minor and irregular variations occurred in the *n*-acid esters. The value of E rose quite sharply with substitution of methyl groups in the α-position, however, and this was interpreted as a manifestation of the inductive effects of the methyl groups. In Table 2 values of E recorded by Evans, Gordon, and Watson, and by Smith and Levenson, certain of them confirmed or modified in the present work, are classified in accordance with the number of alkyl groups which are substituted at the α- and β-positions, the effect of substitution beyond the β-position being negligible.

Table 2 shows that, in the main, the energies of activation are determined by the number of alkyl groups present at the α- and β-positions, but three peculiarities call for comment. (1) An appreciable rise in E would be expected in passing from acetic to propionic ester

TABLE 2. *Energies of activation for alkaline hydrolysis of saturated esters in 85% alcohol.*

Number of α- and β-substitutions	Position	Ester	E (cal./mole)	Ref.
0	—	$CH_3 \cdot CO_2Et$	14,700	2 [a]
1	α	$CH_2Me \cdot CO_2Et$	14,500	1 [a]
2	2α	$CHMe_2 \cdot CO_2Et$	15,000	1 [b]
	1α, 1β	$CH_2Me \cdot CH_2 \cdot CO_2Et$ and higher *n*-esters	15,000	1
3	1α, 2β	$CHMe_2 \cdot CH_2 \cdot CO_2Et$	15,700	1
	1α, 2β	$CHMeEt \cdot CH_2 \cdot CO_2Et$	15,700	3
	2α, 1β	$CH_2Me \cdot CHMe \cdot CO_2Et$	15,600	1 [c]
	3α	$CMe_3 \cdot CO_2Et$	17,100	1 [d]
4	2α, 2β	$CHEt_2 \cdot CO_2Et$	17,300	1; 3
	2α, 2β	$CHPr_2 \cdot CO_2Et$	17,200	3
	2α, 2β	$CHBu_2 \cdot CO_2Et$	17,700	3

[a] Confirmed in present work. [b] Recalc. by Davies and Evans, *J.*, 1940, 339. [c] Recalc. in present work. [d] Recalc. and confirmed experimentally in present work.

(one α-substitution), but such is not found. (2) Substitutions at the α- and β-positions have similar effects, *viz.*, a rise of 500 to 700 cal. for each substitution, in spite of the weakening of the inductive effect by interposition of a saturated carbon atom. (3) The effect of substituting a *third* methyl group at the α-position is much greater than that produced by the first two substitutions, the value of E for ethyl trimethylacetate being 2000 cal. higher than for ethyl *iso*butyrate and 1500 cal. higher than for ethyl α-methylbutyrate where the third substitution is in the β-position. The esters of the last group (two α- and two β-substitutions) also show unusually high energies of activation.

The first two of the peculiarities noted above may be understood in the light of hyperconjugation, which will be exhibited by any ester having one or more α-hydrogen atoms, and will oppose the attack of the nucleophilic reagent. In ethyl acetate there are three hydrogen atoms available for this process and an appreciable increase in the energy of activation must result. In ethyl propionate, however, with only two α-hydrogen atoms, there will be less hyperconjugation, and the decrease in this effect may well balance the inductive effect of the α-methyl group, leaving the value of E not very different from that for ethyl acetate. In the other esters, also, α-substitution involves the loss of one hydrogen atom capable of participating in hyperconjugation, and hence the *total* effect of α-substitution becomes no greater than that of β-substitution where the inductive effect of the β-alkyl group is reduced by passage through a saturated carbon atom.

The structure of trimethylacetic ester may be compared with that of the *neo*pentyl halides, $CMe_3 \cdot CH_2X$, as pointed out by Dostrovsky, Hughes, and Ingold,[4] who showed that the very low rates of bimolecular (S_N2) substitution in these halides were to be ascribed to steric retardation. It is reasonable to conclude that the same phenomenon is responsible for the unusually high energy of activation observed in the hydrolysis of ethyl trimethylacetate, although, as Dostrovsky, Hughes, and Ingold have explained, the retardation of ester hydrolysis will not be so powerful as that found in the *neo*pentyl compounds because

³ Levenson and Smith, *J. Amer. Chem. Soc.*, 1940, **62**, 1556.
⁴ Dostrovsky, Hughes, and Ingold, *J.*, 1946, 173.

the unsaturation of the ethoxycarbonyl group allows a transition state with only four groups attached to the seat of substitution. It appears very probable, however, that the same factor operates in the two cases and also, perhaps, in the alkaline hydrolysis of diethyl-, dipropyl-, and dibutyl-acetic ester which also show high energies of activation. Suggestions on these lines have been made previously; thus, Smith [5] recognised the possibility of steric retardation in some cases of esterification and hydrolysis, and still earlier Hinshelwood and Legard [6] expressed doubt as to whether the slow rate of esterification of trimethylacetic acid could be interpreted on the basis of polar effects alone.

Alkaline hydrolysis of unsaturated esters. The olefinic linkage has electron-attractive characters, usually denoted by $-I$, and this is illustrated by the enhanced strengths of acrylic, but-3-enoic, and pent-4-enoic acid as compared with the corresponding saturated acids.[7] Relatively to the $\beta\gamma$- and $\gamma\delta$-double linkages, however, the $\alpha\beta$-double bond in acrylic acid has an effect which is smaller than would be expected, and Dippy [7] has suggested that there is an opposing mesomeric effect in cases where the double bond is conjugated with the carboxyl group. The values of the energies of activation for the alkaline hydrolysis of acrylic, but-3-enoic, and pent-4-enoic ester have now given a very clear demonstration of the existence of an effect opposite in sign to the inductive effect of the olefinic linkage. In ethyl acrylate, the value (15,400 cal./mole) is nearly a thousand calories *higher* than that for ethyl propionate (14,500 cal./mole), whereas the inductive effect of the unsaturated grouping would cause a decrease. On the other hand, the energies of activation for the hydrolysis of the $\beta\gamma$- and $\gamma\delta$-unsaturated esters are somewhat *lower* than those for the corresponding saturated esters (14,500 cal./mole, which, for ethyl but-3-enoate is a maximum value, see p. 3963, against 15,000 for the saturated esters), in accordance with the $-I$ effect of the double linkage. Similar phenomena were observed by Levenson and Smith [8] in their comparison of the alkaline hydrolysis of α-, β-, γ-, and δ-phenyl-substituted esters with that of ethyl benzoate.

β-Methyl substitution in ethyl acrylate. The inductive effect of the olefinic linkage and the conjugation of the double bond with ethoxycarbonyl are also present in crotonic and β-methylcrotonic ester, but these have in addition one and two methyl groups respectively, substituted at the β-position. By analogy with the saturated esters considered above, the presence of these methyl groups would be expected to lead to increments of about 600 and 1200 cal./mole, respectively, in the energy of activation for alkaline hydrolysis. The observed increases are much greater, however, *viz.*, 1100 and 2600 cal./mole. The relevant figures, with those of the corresponding saturated esters, are as follows :

Acrylic	15,400	Crotonic	16,500	β-Methylcrotonic	18,000
Propionic	14,500	Butyric	15,000	*iso*Valeric	15,700

The additional factor responsible for these larger energies of activation is probably hyperconjugation, for which the β-methyl group in crotonic ester and the *two* methyl groups in β-methylcrotonic ester are suitably placed. The same effect may account for the fall in the dissociation constants of the acids,[7] the values of 10^5K being as follows : acrylic, 5·56; crotonic, 2·03; β-methylcrotonic, 0·76.

For an ester with a lengthened chain, *viz.*, ethyl non-2-enoate, the energy of activation (15,900 cal./mole) lies between the values for acrylic and crotonic ester, and a contributory factor is probably the reduction of hyperconjugation by replacement of the $-CH_3$ of crotonic ester by $-CH_2-$, but the longer chain may introduce other factors also. For ethyl penta-2 : 4-dienoate (16,800 cal./mole) and ethyl sorbate (17,600) the energies of activation are considerably higher than for ethyl acrylate, and it would appear that the extended conjugation brings out the mesomeric effect more powerfully, while in sorbic ester hyperconjugation may be considerable.

α-Methyl substitution in ethyl acrylate. For the alkaline hydrolysis of α-methylacrylic

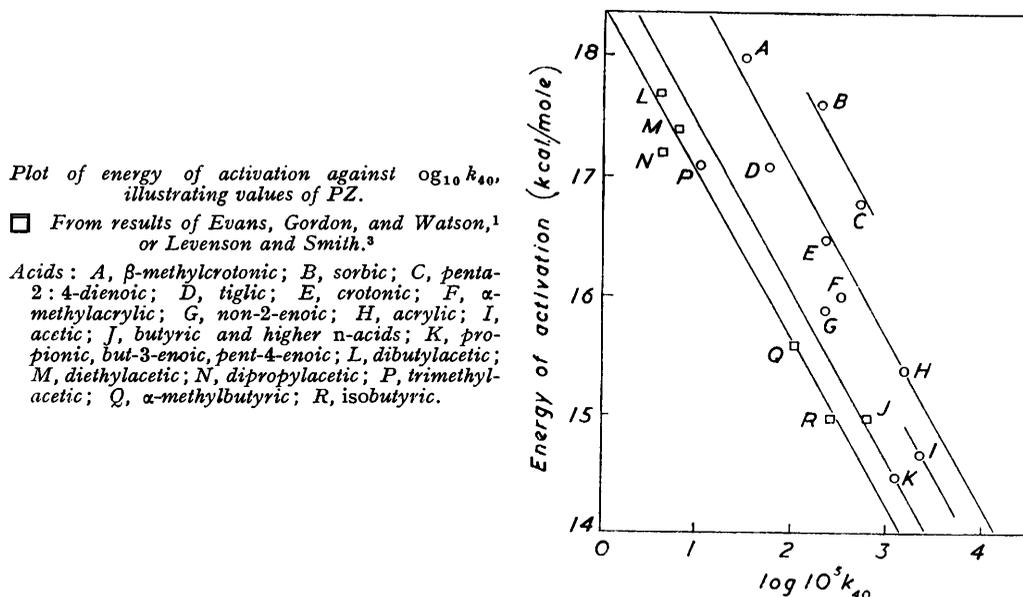[5] Smith, *J. Amer. Chem. Soc.*, 1940, **62**, 1139.
[6] Hinshelwood and Legard, *J.*, 1935, 1588.
[7] Dippy, *Chem. Rev.*, 1939, **25**, 180.
[8] Levenson and Smith, *J. Amer. Chem. Soc.*, 1940, **62**, 2324.

and tiglic ester, the energies of activation (16,000 and 17,100 cal./mole, respectively) are 600 cal./mole higher than for ethyl acrylate and crotonate, and this is the increment produced by substitution of one methyl group in the α- or β-position of a saturated ester and ascribed above to the inductive effect of methyl. Comparison of the values for ethyl α-methylacrylate and ethyl tiglate shows a difference of 1100 cal./mole, identical with that found for acrylic and crotonic ester, and doubtless to be ascribed to the same factors. Thus, no new or unexpected influences are revealed in the α-substituted esters.

Variations in the non-exponential term of the kinetic equation. The above discussion of the effects of structural changes in R upon the alkaline hydrolysis of esters $R \cdot CO_2Et$ has been based upon the values of the energy of activation. The changes in E are in some cases accompanied by variations in the PZ term of the kinetic equation. These differences are not large, however, and it would be unwise to draw detailed conclusions from them; but the general tendency is in harmony with that which would be expected on the basis of mesomeric and hyperconjugative effects. The variations in PZ are illustrated in the

Plot of energy of activation against $og_{10} k_{40}$, illustrating values of PZ.

☐ From results of Evans, Gordon, and Watson,[1] or Levenson and Smith.[3]

Acids : A, β-methylcrotonic; B, sorbic; C, penta-2 : 4-dienoic; D, tiglic; E, crotonic; F, α-methylacrylic; G, non-2-enoic; H, acrylic; I, acetic; J, butyric and higher n-acids; K, propionic, but-3-enoic, pent-4-enoic; L, dibutylacetic; M, diethylacetic; N, dipropylacetic; P, trimethylacetic; Q, α-methylbutyric; R, isobutyric.

Figure, where values of E are plotted against $\log_{10} k_{40}$, and the straight lines have the theoretical slope $-2 \cdot 303RT$: that is, points lying on the same straight line indicate equal values of PZ.

The relevant observations are as follows. (a) Evans, Gordon, and Watson found that lengthening of the chain in the n-acid esters beyond ethyl propionate led to no change in PZ, and we have now observed that a double bond at the βγ- or γδ-position does not change this factor. In these cases, neither mesomeric nor hyperconjugative effects are involved. (b) Branching at the α-carbon atom leads to a small decrease in PZ, as shown by the following values of $\log_{10} PZ$: acetate, 8·6; propionate and higher n-acid esters (calculated from the results of Evans, Gordon, and Watson), 8·2—8·3; isobutyrate, α-methylbutyrate, diethyl-, dipropyl-, and dibutyl-acetate (calc. from results of Evans, Gordon, and Watson and of Smith and Levenson), and trimethylacetate, 7·8—8·0. The differences are small, but may be due to the successive removal of α-hydrogen atoms, leading to less hyperconjugation. (c) An αβ-double bond raises $\log PZ$ to an appreciable extent; e.g., for acrylic, crotonic, and β-methylcrotonic ester it has a value of 8·9—9·0, and it is difficult to resist the conclusion that the mesomeric effect is responsible in these cases where the double bond is conjugated with the ethoxycarbonyl group. Moreover, in penta-2 : 4-dienoic and sorbic ester, where the energy of activation has already indicated that this effect is more

powerful in the extended conjugated system, the *PZ* factor is increased further (log *PZ* = 9·5). In α-methylacrylic and tiglic ester, with branching at the α-carbon, there is an indication of a falling *PZ* (log *PZ* = 8·7), and a rather larger fall in non-2-enoic ester (log *PZ* = 8·5) may be connected with the influences already referred to.

In view of the relatively small differences concerned, these comments upon the values of the non-exponential factor are merely tentative; the effect of an αβ-double bond on the value of *PZ* is doubtless a real one, however.

Results recently reported by Humphreys and Hammett [9] for the alkaline hydrolysis of ethyl formate place this ester in a unique position, as would be expected from other known facts such as the relatively high dissociation constant of formic acid.

Experimental

Materials.—But-3-enoic acid, prepared by hydrolysis of allyl cyanide with concentrated hydrochloric acid,[10] was esterified by the Fischer–Speier method and after fractional distillation the ester had b. p. 124·5°/768 mm. (Falaise and Frognier [11] give b. p. 124·2—124·4°/761·5 mm.). Ethyl non-2-enoate was obtained by esterification of the acid got by condensation of *n*-heptaldehyde with malonic acid in presence of pyridine,[12] and had b. p. 118°/12 mm. Penta-2 : 4-dienoic acid, prepared by Muskat's method,[13] was esterified by the Fischer–Speier method in presence of 0·3% of quinol as stabiliser, and had b. p. 57—57·5°/13 mm. The remaining esters were either purchased or prepared by Fischer–Speier esterification of the appropriate acids, and purified by fractional distillation, 0·3% and 0·1% of quinol being added to ethyl acrylate and ethyl α-methylacrylate respectively before distillation. The b. p.s agreed well with those found in the literature and were as follows : ethyl acetate, 76·9—77·2°/760 mm.; propionate, 99°/755 mm.; acrylate, 99·5°/758 mm.; crotonate, 137°/756 mm.; α-methylacrylate, 117·5°/752 mm.; pent-4-enoate, 144°/767 mm.; β-methylcrotonate, 61·5°/30 mm.; sorbate, 85°/20 mm.; tiglate, 156°/758 mm.; trimethylacetate, 118·5°/758 mm.

Medium.—The hydrolyses were carried out in 84·7% ethyl alcohol, of d_4^{20} 0·8316. This was prepared by keeping ethyl alcohol, previously shaken with silver oxide, over freshly baked lime, distilling, and diluting the distillate with distilled water which had been passed four times through an ion-exchange column (" Bio-deminrolit FF ").

Velocity Measurements.—25 ml. of 0·2N-alcoholic sodium hydroxide, prepared from the above 84·7% alcohol and " AnalaR " sodium hydroxide pellets, and 10 ml. of a 0·5M-solution of the ester in the 84·7% alcohol, were measured into separate 150 ml. conical flasks fitted with waxed corks. Sufficient 84·7% alcohol was then added to the flasks to bring the combined volume on mixing, at the temperature of the reaction, to 100 ml. The initial concentrations of both ester and alkali were thus 0·05M. Zero time was taken as the half-point of mixing the contents of the flasks. At suitable intervals 10 ml. of the mixture were withdrawn and added to 10 ml. of N/15-hydrochloric acid, and the excess of acid titrated with N/20-sodium hydroxide to bromothymol-blue. Each end-point was matched against a freshly prepared solution of 15 ml. of M/30-sodium benzoate in 15 ml. of 50% aqueous alcohol containing the same amount of indicator as in the titration. Bimolecular velocity coefficients were calculated from the equation $k_2 = (1/t)x/a(a - x)$. A typical run is tabulated.

Hydrolysis of ethyl α-methylacrylate at 40°. [Ester] = [NaOH] = 0·0508M.

(10 Ml. of the reaction mixture were pipetted into 10 ml. of 0·0668N-HCl, and the titration carried out with 0·0511N-sodium hydroxide.)

Time (sec.)	600	1500	2400	3600	4800	6600
NaOH titre (ml.)	4·03	5·11	5·98	6·86	7·57	8·36
$10^3 k_2$	3·26	3·26	3·30	3·28	3·31	3·31

Mean value of $10^3 k_2$ = 3·29.

The plot of log *k* against $1/T$ gave a good straight line in each case, and hence the energies of activation were calculated.

[9] Humphreys and Hammett, *J. Amer. Chem. Soc.*, 1956, **78**, 521.
[10] Mannich, *Arch. Pharm.*, 1935, **273**, 415.
[11] Falaise and Frognier, *Bull, Soc. chim. Belg.*, 1933, **42**, 427.
[12] Knoevenagel, D.-R.P. 156,560; *Chem. Zentr.*, 1905, I, 56.
[13] Muskat, *J. Amer. Chem. Soc.*, 1930, **52**, 326.

The bimolecular velocity coefficient for ethyl but-3-enoate showed a rapid decrease as the reaction progressed, as illustrated below for 40°. The figures in the last column are calculated

Time (sec.)	Titre (ml.)	10^3k	$10^3k'$	Time (sec.)	Titre (ml.)	10^3k	$10^3k'$	Time (sec.)	Titre (ml.)	10^3k	$10^3k'$
180	4·07	11·43	—	3000	6·13	2·84	2·33	9000	8·44	2·50	2·32
600	4·41	4·85	—	5400	7·26	2·58	2·31				

on the basis of 600 sec. as zero time, and they are identical with the bimolecular coefficient found for ethyl crotonate (Table 1). The ethyl but-3-enoate clearly isomerises during the reaction (cf. Goldberg and Linstead [14]). The values of k recorded for ethyl but-3-enoate in Table 1 are those for approximately the first 10% of the reaction. They are, of course, not as accurate as the remaining velocity coefficients, since, once the isomerisation has begun, the measured velocity is partly that of the hydrolysis of ethyl crotonate. The value of E for this hydrolysis is considerably higher than that for ethyl but-3-enoate, and the figure of 14,500 cal./mole for the latter should therefore be regarded as a maximum value: the true value is probably lower.

[14] Goldberg and Linstead, *J.*, 1928, 2343.