272. *The Influence of Alkyl Groups upon Reaction Velocities in Solution. Part III. The Alkaline Hydrolysis of Saturated Aliphatic Esters.*

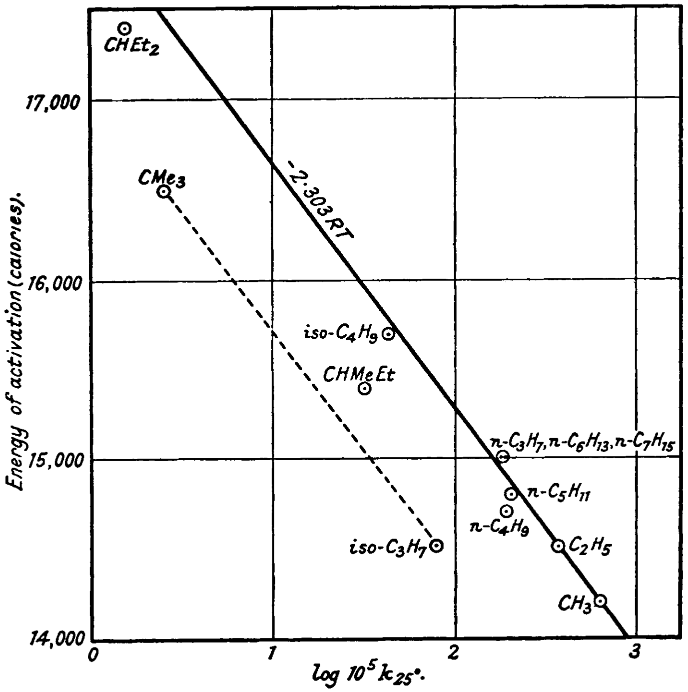
By David P. Evans, James J. Gordon, and H. B. Watson.

A kinetic study is described of the alkaline hydrolysis of twelve esters, R·CO_2Et, where R varies from CH_3 to C_7H_{15}. Analysis of the results on the basis of the equation $k = PZe^{-E/RT}$ shows that the changes in velocity are due almost entirely to changes in the energy of activation except for esters in which the alkyl chain branches at the α-carbon atom. As a rule, E varies in accordance with the inductive effect of R. Certain deviations from these generalisations are discussed, and conclusions are drawn regarding the causes of irregularities in the effects of alkyl groups upon reactivity.

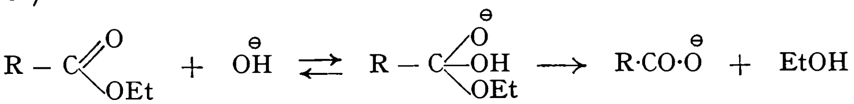
The investigation of the prototropy of phenyl alkyl ketones, described in Parts I and II of this series (Evans, J., 1936, 785; Evans and Gordon, preceding paper), was undertaken in order to obtain further data relating to the effects of alkyl groups upon reactivity. This work has now been extended to include a kinetic study of the alkaline hydrolysis of the ethyl esters of twelve saturated aliphatic acids in 85% alcohol. The results, recorded in the table below, indicate that the velocity coefficients (l. g.-mol.$^{-1}$ sec.$^{-1}$) for the *n*-esters decrease regularly from acetic to *n*-butyric ester and then remain almost constant as the series is further ascended to *n*-octoic ester. Branched chain esters are hydrolysed more slowly than their *normal* isomerides, while ethyl trimethyl- and diethyl-acetates are markedly slow (compare Reicher, *Annalen*, 1885, **228**, 257 and later; Kindler, *ibid.*, 1927, **452**, 90; *Ber.*, 1937, **70**, 2792). The values of the energy of activation are calculated from the plot of log k against $1/T$, which gives a good straight line in each case.

Ethyl ester.	$10^3k_{25°}$.	$10^3k_{35°}$.	$10^3k_{50°}$.	E (cals.).
Acetic	6·21	13·6	38·7	14,200
Propionic	3·63	8·31	24·7	14,500
n-Butyric	1·72	3·94	12·2	15,000
*iso*Butyric	0·801	1·84	5·72	14,500
n-Valeric	1·92	4·42	13·3	14,700
*iso*Valeric	0·427	1·02	3·34	15,700
Methylethylacetic	0·308	0·735	2·36	15,400
Trimethylacetic	0·0254	0·0635	0·241	16,500
n-Hexoic	2·07	4·81	14·5	14,800
Diethylacetic	0·0157	0·0409	0·154	17,400
n-Heptoic	1·79	4·06	12·7	15,000
n-Octoic	1·84	4·30	13·3	15,000

The plot of E against log $k_{25°}$ is shown in the figure, where the straight line has the slope $- 2{\cdot}303\boldsymbol{RT}$; the value of P in the kinetic equation $k = PZe^{-E/\boldsymbol{RT}}$ is the same for those esters which give points on this line. Inspection of the figure reveals the following facts. (*a*) In esters which are not branched at the α-carbon atom, the changes in velocity are due almost entirely to changes in E; (*b*) E increases gradually as the *normal* series is ascended and tends to reach a constant maximum; (*c*) E is much higher for *iso*valeric ester than for its *n*-isomeride, but (*d*) ethyl *iso*butyrate gives a value of E which is smaller than that for ethyl *n*-butyrate and equal to that for ethyl propionate; (*e*) diethylacetic ester gives a very high value of E, much higher than that found for trimethylacetic ester; (*f*) branching at the α-carbon atom leads to a lower value of P; in actual magnitude this fall is not large (*e.g.*, for *iso*butyric and trimethylacetic esters P is about one-sixth of the value for the *n*-esters), but in view of the reproducibility of our results and the constancy of P for the normal esters we feel that this decrease must be considered in any interpretation of the observations.



Any possible complexity of the second stage of the process being disregarded, the mechanism of the hydrolysis of an ester by hydroxyl ion may be written (compare J., 1937, 1431)



In the sequel, the above observations will be discussed on the basis of this mechanism, with introduction of the assumptions that the energy of activation is associated with the production of the transition complex and that the non-exponential factor of the kinetic equation is determined very largely by the proportion of this complex which actually yields the reaction products (as an alternative, of course, to a simple breakdown to give the initial reagents). An attempt will also be made to place the new facts recorded in this series of communications in their appropriate environment with respect to other observations.

EXPERIMENTAL.

Materials.—Ethyl acetate, propionate, *iso*butyrate, *n*-butyrate, *n*-hexoate, *iso*valerate, *n*-heptoate, and *n*-octoate were purchased and purified by repeated fractional distillation; b. p.'s, 77°, 98°, 110°, 120°, 165°, 134·1° under 760 mm., and 114°, 104° under 80 mm. respectively. Ethyl *n*-valerate and ethyl diethylacetate were prepared by esterification of the acids, and purified by redistillation; b. p.'s, 145° and 151° under 760 mm. Trimethylacetic acid was prepared by the Grignard synthesis ("Organic Syntheses," Coll. Vol. I., p. 510) and esterified to give the ethyl ester, b. p. 119°/760 mm. Ethyl methylethylacetate was obtained by esterifying the acid prepared by the method of Conrad and Bischoff (*Annalen*, 1880, **204**, 151); b. p. 132°/760 mm.

Velocity Measurements.—The velocity determinations were carried out in 85% aqueous alcohol (by weight) in the same manner as described by Evans, Gordon, and Watson (J., 1937, 1430). A typical set of results is given below, in which k_2 is the bimolecular velocity coefficient.

Hydrolysis of Ethyl n-*Hexoate at* 50°.

[Ester] = [NaOH] = 0·0478M.

10 Ml. of reaction mixture were pipetted into 10 ml. of 0·06963N-HCl, and the mixture titrated with 0·05158N-NaOH, bromothymol-blue being the indicator.

Time (secs.)	300	600	900	1200	1500	1800	2340	
NaOH titre (ml.)	5·82	6·95	7·81	8·40	8·95	9·40	9·99	
10^3k_2	14·4	14·5	14·6	14·3	14·5	14·7	14·7	Mean 14·5

DISCUSSION.

The results of chemical and physicochemical investigations in diverse fields have led to the conclusion that, relatively to hydrogen, alkyl groups repel electrons by an inductive mechanism. This was pointed out by Lucas and Jameson (*J. Amer. Chem. Soc.*, 1924, **46**, 2475) and by Allan, Oxford, Robinson, and Smith (J., 1926, 405). Since, however, the dipole moments of all saturated aliphatic hydrocarbons are zero, it must be supposed that this $+I$ effect operates only when it is stimulated by other groups (Ingold, *Chem. Reviews*, 1934, **15**, 238). This view of the polar effects of alkyl groups is in harmony with nearly all recorded observations. As Dippy and Page have pointed out, however (this vol., p. 358), certain peculiarities are observed when the group is linked to oxygen; acids having methoxyl as substituent (*e.g.*, $CH_3O{\cdot}CH_2{\cdot}CO_2H$) are actually *stronger* than their analogues containing hydroxyl (*e.g.*, $HO{\cdot}CH_2{\cdot}CO_2H$), and phenol is more susceptible to nuclear substitution by electrophilic reagents than is anisole. Again, the calculations of Groves and Sugden (J., 1937, 1992), equal valency angles being assumed in the two cases, lead to a much larger value for the mesomeric moment in the former (1·12) than in the latter (0·4). Such a line of facts might lead to the conclusion (suggested by Dippy, this vol., p. 1224) that alkyl groups when linked to oxygen are electron-attractive, a possibility foreshadowed by Ingold (*loc. cit.*); on the other hand, the problem may be one of valency angles, a suggestion which would doubtless be accepted (cf. Smyth, *Chem. Reviews*, 1929, **6**, 560) when applied to the dipole moments of water (1·84), methyl alcohol (1·69), and *iso*propyl alcohol (1·63), which fall, whereas those of the corresponding halogen compounds rise.

The electron-repulsive character of alkyl groups in general being accepted, it is a logical deduction that the magnitude of the effect should increase with the length of the group, and also in such series as $CH_3 < CH_2Me < CHMe_2 < CMe_3$, for the higher groups are all derived from the lower by successive replacements of H by CH_3. This order is found in a number of instances, of which the following are representative; (1) dipole moments of the lower alkyl halides (Groves and Sugden, J., 1937, 158); (2) decomposition of mercury dialkyls (Kharasch and Flenner, *J. Amer. Chem. Soc.*, 1932, **54**, 674); (3) directive influences in the nitration of quinol methyl alkyl ethers (Robinson and Smith, J., 1926, 392; 1927, 2647), of phenylalkylsulphones (Baldwin and Robinson, J., 1932, 1445), and of a series of benzoic esters (Zaki, J., 1928, 983; the small deviations here seem to be insignificant); (4) velocity of formation of bisulphite compounds and of oximes from aliphatic ketones (Stewart, J., 1905, **87**, 185, 410); (5) the ratio k_{OH}/k_H for the alkaline hydrolysis of glyceric esters (Ingold *et al.*, J., 1930, 1057). Kinetic studies of the alkaline hydrolysis (Smith and Olsson, *Z. physikal. Chem.*, 1925, **118**, 99, 107) or ammonolysis (French and Wrightsman, *J. Amer. Chem. Soc.*, 1938, **60**, 50) of a series of esters of acetic acid indicate no considerable departure from the order of inductive effects of the alkyl groups except for a low value of the probability factor *P* (for which no explanation at present seems possible) in the cases of *sec.*-butyl and $-CMe_2Pr$.

In the alkaline hydrolyses with which this paper deals, there is a gradual rise in the energy of activation as the *n*-series of esters is ascended (observation *b*, above), and we attribute this to the increasing inductive effect of the group R in $R{\cdot}CO_2Et$. The relatively high value of *E* given by ethyl *iso*valerate (observation *c*) is also in harmony with the anticipated magnitude of the inductive effects (*iso*butyl>*n*-butyl). It has been pointed out in Part II that the energies of activation for the base-catalysed prototropy of a series of phenyl alkyl ketones are also in the order of the inductive effects of the alkyl groups.

The remaining facts which have been revealed by the investigation here described (observations *d*, *e*, and *f*) cannot be interpreted so simply, however. Indeed, a survey of relevant literature shows that the instances where alkyl groups place themselves strictly in their theoretical order are probably outnumbered by those where other influences are evident at some point in the series. Such influences may be manifested only in certain branched alkyl chains, but they frequently make themselves felt in straight chains also. In some of the above examples where the anticipated polar sequence is maintained, a departure from this order might well have been observed, in fact, had the study included a larger number of groups.

In certain cases, apparent peculiarities in the relative effects of alkyl groups are to be ascribed to a change in the reaction mechanism rather than to any feature of the group itself (other than its inductive effect); this has been demonstrated in a convincing manner by Hughes and Ingold (J., 1935, 244, and later papers*). This does not appear to lead to any considerable departure of *n*-alkyl groups from the theoretical sequence, however; primary groups give a reaction of the same mechanistic type (and the same applies to secondary and to tertiary groups). The present work has not revealed further instances which should be placed in this category, but anomalies of three different kinds are illustrated by our observations *d*, *e*, and *f*. These will now be discussed.

Observation (d): *Equality of* E *for Propionic and* iso*Butyric Esters.*—The energies of activation for the hydrolysis of acetic, propionic, *iso*butyric, and trimethylacetic esters (in general $R{\cdot}CO_2Et$) stand in the order Me<Et∼*iso*-Pr⋘*tert.*-Bu, and the same equality in the effects of Et and *iso*-Pr is found in the dissociation constants of the corresponding acids (Dippy, *loc. cit.*) and in the energies of activation for the acid-catalysed prototropy of ketones R·COPh (Part I). Dippy points out that these observations are no doubt related to the anomalous order found by Baker, Dippy, and Page (J., 1937, 1774) in the strengths of the *p*-alkyl-benzoic acids, *viz.*, Me<Et∼*iso*-Pr⋗*tert.*-Bu. It is evident that in

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* Additional strength has been given to the view of Hughes and Ingold in a paper published (this vol., p. 881) since the above was written.

these systems the *total* electron repulsion of the *iso*propyl and the ethyl group must be equal, in spite of the different inductive effects, and such equality indicates the operation of some other factor.

Baker and Nathan (J., 1935, 1844) have suggested an interpretation of peculiarities observed on substitution of the hydrogen atoms of a methyl group linked to a suitable system (the most obvious example, of course, being the predominating substitution at the 2-position in certain *p*-alkyltoluenes; for other instances see Baker and Nathan's paper). On their view, the C–H electron pairs of methyl can come under the control of the adjacent nucleus, giving rise to an effect superimposed upon and of the same sign as the inductive effect; its magnitude will decrease as the hydrogen atoms of CH_3 are replaced. Dippy has suggested (J., 1937, 1777) that the facts might also be explained in terms of an effect opposite in sign to the inductive effect and decreasing in magnitude from *tert.*-Bu to Me. In either case the combination of the inductive effect and the additional effect could lead to a resultant varying in *any* order for the groups referred to above, since the relative magnitudes of the two effects will vary widely in different systems, *e.g.*, in the two series of acids quoted.

In the case of propionic and *iso*butyric esters, now under discussion, the larger inductive effect of the secondary (*iso*-Pr) group appears to be balanced by its smaller electron release by the second effect.* It is implicit in Baker and Nathan's suggestion that their effect should be most pronounced when accession of electrons to the point of reaction is required, and this is illustrated in the acid- and base-catalysed prototropy of phenyl alkyl ketones, where it is observed in the former but not the latter (see Part II). In the present instance the effect appears to operate in a reaction of the opposite type (cf. also Baker, Nathan, and Shoppee, J., 1935, 1847).

Observation (e): *High Value of* E *for Diethylacetic Ester.*—The energy of activation for the alkaline hydrolysis of ethyl diethylacetate is considerably higher than that for ethyl trimethylacetate. The tertiary group certainly has the larger inductive effect, and this appears to be an instance in which ethyl has some effect peculiar to itself. Many comparable examples have been recorded from time to time. Thus, in a study of the directive influences of groups RO upon the nitration of guaiacol ethers of the general formula *o*-$RO{\cdot}C_6H_4{\cdot}OCH_3$, Allan and Robinson (J., 1926, 376; cf. Allan, Oxford, Robinson, and Smith, *ibid.*, p. 406) found a maximum at ethyl, whereas the quinol methyl alkyl ethers, *p*-$RO{\cdot}C_6H_4{\cdot}OCH_3$, show the theoretical order (Robinson and Smith, *loc. cit.*). The unusual basic strengths of dialkylanilines and dialkyltoluidines containing ethyl (Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469) are also significant, and are illustrated by the following figures for p_{K_H}:

Anilines.				*o*-Toluidines.		*p*-Toluidines.	
Me_2	5·06	Et_2	7·09	Me_2	5·86	Me_2	5·50
MeEt	5·98	Pr_2	5·59	Et_2	7·18	Et_2	7·09
MePr	5·64	EtPr	6·34				

It does not seem possible at present to offer any explanation of these phenomena; the environment of the ethyl group is almost certainly an important factor. A further investigation is contemplated.

Observation (f): *Decrease in* P *due to Branching at the α-Carbon Atom.*—In the majority of the esters examined, the P factor does not change (observation *a*), but branching at the α-carbon atom (as, *e.g.*, in *iso*butyric and trimethylacetic esters) leads to a lower P value. This decrease in P for ethyl *iso*butyrate has previously been indicated by the results of Newling and Hinshelwood (J., 1936, 1357) for both acid and alkaline hydrolysis. We suggest that it is due to hydrogen-bond formation between β-carbon and carbonyl oxygen (which will not influence E perceptibly: see J., 1937, 1425), the process occurring

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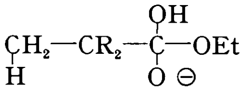
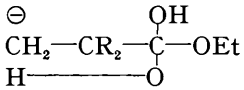
* An alternative explanation of the equality of E in the acid-catalysed prototropy of propio- and *iso*butyro-phenones was considered in Part II and rejected on grounds there given. This explanation was based upon an increased tendency to " chelation " when *two* alkyl groups are suitably placed. It is not applicable in the present case, since E is here not influenced by the hydrogen bond; nor is it capable of explaining the equality of the dissociation constants of propionic and *iso*butyric acids and of *p*-ethyl- and *p*-*iso*propyl-benzoic acids.

simultaneously with the approach of the negative ion. The complex will then be a resonance hybrid including forms (I) and (II). The probability of the formation of a



$$\underset{H}{CH_2}\text{—}CR_2\text{—}\underset{O^{\ominus}}{\overset{OH}{C}}\text{—}OEt$$

(I.)



$$\underset{H\text{————————}}{\overset{\ominus}{CH_2}}\text{—}CR_2\text{—}\underset{O}{\overset{OH}{C}}\text{—}OEt$$

(II.)

hydrogen bond in cases of this kind has been discussed fully in Part II, and only the following additional remarks are necessary here. Branching at the α-carbon appears to be necessary, since there is no fall of P at propionic ester; perhaps this provides the necessary restriction of movement (see Part II). Then, whereas *iso*butyric and trimethylacetic esters give equal P factors (a line joining the points representing these has approximately the theoretical slope $- 2{\cdot}303\boldsymbol{R}T$), in methylethyl- and diethyl-acetic esters there is a distinct increase towards the higher value associated with the normal esters. This may be due to a smaller tendency, in this system, for β-methylene (*e.g.*, in $CHEt_2{\cdot}CO_2Et$) to form a hydrogen bond than for β-methyl (*e.g.*, in $CHMe_2{\cdot}CO_2Et$) to do so.

In the alkaline hydrolysis of aliphatic esters, as also in the prototropy of phenyl alkyl ketones (Parts I and II), the postulated hydrogen bond leads to the completion of a five-membered "chelate ring." On the other hand, in the anion of *o*-toluic acid and the transition complex in the alkaline hydrolysis of ethyl *o*-toluate the results are interpretable on the basis of a six-membered ring (Dippy, Evans, Gordon, Lewis, and Watson, J., 1937, 1421). An enhancement of strength, at *n*-butyric acid, as the aliphatic carboxylic acid series is ascended, also leads to the postulation of a ring of six atoms (Dippy, *loc. cit.*). It should be pointed out, however, that the complexes formed by the catalyst with a ketone or by the hydroxyl ion with a saturated ester contain single bonds only, whereas in the carboxylate anion and the *o*-toluic ester complex the "chelate ring" has either one or two bonds with characters approaching those of a double linkage. This difference will be reflected in the natural valency angles (of which we have no precise knowledge in cases of this type), and the electron-donating oxygen atom will react with the hydrogen which is most favourably placed.

The following is a summary of our general conclusions. Alkyl groups sometimes influence reactivity in accordance with their inductive effects, but there are numerous instances of departure from this sequence. It appears that, in the majority of cases, irregularities may be ascribed to one of three causes, *viz.*, change in reaction mechanism (demonstrated by Hughes and Ingold), an effect of substitution in α-methyl (first pointed out by Baker and Nathan), and an interaction of hydrogen with an electron-donating atom (which, we consider, involves the formation of a hydrogen bond). There are a few instances, however, exemplified by a peculiar effect sometimes shown by the ethyl group, which fall outside this scheme.

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