

638. *The Separation of Polar and Steric Effects. Part IV.¹ The Kinetics of the Alkaline Hydrolysis of Methyl Arylaliphatic Carboxylates, and the Ionization of Arylaliphatic Carboxylic Acids.*

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Rate coefficients have been measured for the alkaline hydrolysis in 80% v/v methanol-water at several temperatures of methyl esters of the following acids: acetic, phenylacetic, diphenylacetic, 2,2-diphenylpropionic, 2,2-diphenylbutyric, triphenylacetic, 9-X-fluorene-9-carboxylic (X = H, Me, Et, Prⁱ, Bu^t, or Ph), and 9,10-dihydroanthracene-9-carboxylic acid. Arrhenius parameters and the related quantities of the transition-state theory have been evaluated. The changes in the entropy of activation are discussed mainly in terms of a balance between steric hindrance to motions and steric inhibition of solvation. The changes in the enthalpy of activation are examined in terms of a balance between polar and steric effects. A linear relation between the entropy and enthalpy terms has been observed and its implications are considered.

We also discuss the alkaline hydrolysis results in the way developed by Taft, by using the E_s values previously determined (Part III). The polar substituent constants, σ^* , thereby derived do not agree with the σ^* values determined previously (Part III) from rate coefficients for the reactions of the acids with diazodiphenylmethane, and the series of values contains many internal inconsistencies. A modified analysis in which the rate coefficients for alkaline hydrolysis are correlated with E_s values, and with σ^* values based on the diazodiphenylmethane reaction, is more successful.

The p*K* values of the above acids in 50% v/v 2-n-butoxyethanol-water in the presence of 0.05M-lithium chloride have been measured potentiometrically. The acid-strengthening polar effects of the substituents are moderated by an acid-weakening steric effect. Changes in p*K* are correlated with the Taft polar and steric parameters, σ^* and E_s .

IN Part III¹ we dealt with the evaluation of polar effects (Taft σ^* values) in arylaliphatic compounds by studying the reactions between a series of arylaliphatic carboxylic acids and diazodiphenylmethane in 2-n-butoxyethanol and in toluene. The steric effects (Taft E_s values) in the compounds were evaluated from rate coefficients for the acid-catalysed esterification of the acids in methanol. The present Paper deals with the kinetics of alkaline hydrolysis of the methyl esters of the same acids in 80% v/v methanol-water, and the ionization constants of the acids in 50% v/v 2-n-butoxyethanol-water, which was 0.05M in lithium chloride. Our purpose was first to separate polar and steric effects in the alkaline hydrolysis in the way developed by Taft,² and secondly to examine the applicability to the two reaction systems of the polar and steric parameters previously¹ evaluated.

The kinetics of alkaline hydrolysis of the ethyl esters of some of the simpler arylaliphatic carboxylic acids were previously studied,³ but not of the methyl esters. The ionization constants of certain of the simpler arylaliphatic acids in aqueous solution have also been measured.^{4,5}

EXPERIMENTAL

Materials.—Methyl esters of the arylaliphatic carboxylic acids (themselves prepared as described in Part III¹) were usually prepared [method (a)] by esterification of the free acid with

¹ Part III, Bowden, Chapman, and Shorter, *J.*, 1963, 5239.

² Taft, "Steric Effects in Organic Chemistry," ed. Newman, ch. 13, Wiley, New York, 1956.

³ (a) Levenson and Smith, *J. Amer. Chem. Soc.*, 1940, **62**, 2324; (b) Evans, Gordon, and Watson, *J.*, 1938, 1439.

⁴ (a) Dippy, Hughes, and Rozanski, *J.*, 1959, 1441; (b) Hammond and Hogle, *J. Amer. Chem. Soc.*, 1955, **77**, 338.

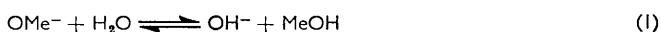
⁵ Kilpatrick and Fackenthal, *J. Electrochem. Soc.*, 1953, **100**, 185.

diazomethane or methanolic hydrogen chloride. Methyl 9-alkylfluorene-9-carboxylates were prepared, however, by alkylation of methyl fluorene-9-carboxylate¹ [method (b)]. They were either fractionally distilled, or recrystallised (from methanol) to constant m. p. (see Table I). The purity of the esters was determined by gas chromatography as described in Part III.¹ No significant impurity was found in any sample of an ester subsequently used for measurements. Methanol and 2-n-butoxyethanol were purified as described in Part III.¹

Kinetic Procedure for Alkaline Hydrolysis.—Rate coefficients were usually measured as described in Part II.⁶ Equal concentrations of ester and alkali ($\sim 0.0200N$ -sodium hydroxide in 80% v/v methanol-water) were generally used. Reactive esters were studied by the "H-bulb" method and less reactive esters by the reaction-tube method, the latter being used for reactions above 60°. Stainless steel tubes were used instead of glass tubes for slow reactions above 95°.

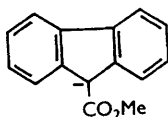
The rate coefficient k ($\text{l. mole}^{-1} \text{sec.}^{-1}$) was calculated from the second-order expression when the reactants are present in equal initial concentrations, *viz.*, $k = x/at(a - x)$, where t is the time in seconds, a the initial concentration of the reactants, and $(a - x)$ their concentration (mole l.^{-1}) at time t . Values of k from reaction-tube experiments were corrected for solvent expansion. Because of their low solubility, methyl triphenylacetate and 9-phenylfluorene-9-carboxylate were studied at concentrations of $\sim 0.003M$ and $0.005M$, respectively.

Since the position of the equilibrium,

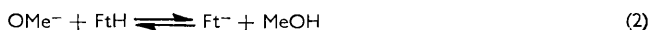


with $K = [\text{OH}^-]/[\text{OMe}^-]$, lies significantly to the left even in moderately aqueous solutions, measurements of the rates of alkaline hydrolysis of the methyl esters in 80% v/v methanol-water give apparent rate-coefficients (see Part II).⁶ However, for comparison of the hydrolyses of a series of esters, apparent rate-coefficients, k_a , are satisfactory since they are related to true rate coefficients, k_t , by the equation $k_t\alpha = k_a$, where $\alpha = K/(1 + K)$. It was also shown in Part II that for activation energies, $E_t = E_a - \Delta H(1 - \alpha)$, and for the Arrhenius pre-exponential factors, $\ln A_t = \ln A_a - [\ln \alpha - \Delta H(1 - \alpha)/RT]$. ΔH is the enthalpy change for the forward reaction in the reversible process (1), above. Although Arrhenius parameters determined for the reactions in aqueous methanol are not absolute values, they are suitable for comparison with each other.

The alkaline hydrolysis of methyl fluorene-9-carboxylate (FtH) is complicated by the presence of the anion, (Ft⁻ I) which is revealed by its fluorescence. The observed second-order rate coefficient (k_b) increases as the reaction proceeds. The initial rate-coefficient can be found graphically, and the final rate-coefficient can be found, by extrapolation, from a plot of instantaneous rate-coefficient against the reciprocal of time. The initial rate-coefficient varied with concentration, and therefore all the measurements were made with the concentration of ester and base $0.0200M$. The observed rate-coefficient at infinite time will be equal to the apparent rate-coefficient normally measured, for a consideration of the equilibrium (1) and the equilibrium



(I)



with $K' = [\text{Ft}^-]/[\text{FtH}][\text{OMe}^-]$, shows that

$$K^2 k_t = k_b(1 + K + K'[\text{FtH}])(K + K'[\text{OH}^-]).$$

For infinite time the relation becomes $k_t\alpha = k_b$, and then k_b corresponds to k_a as usually observed (full details in ref. 7). After hydrolysis with an excess of alkali, the ester gave no ether-soluble products that could be detected by gas chromatography. The saponification equivalent was 220 (theor. 224).

Measurement of pK Values of the Carboxylic Acids.—These were determined at 25° by potentiometric titration of the acids in 50% v/v 2-n-butoxyethanol-water ($0.05M$ in LiCl) with $0.0500N$ -aqueous sodium hydroxide, by using a direct-reading pH-meter (Electronic Instruments

⁶ Part II, Chapman, Shorter, and Utley, *J.*, 1963, 1291.

⁷ Bowden, Ph.D. thesis, University of Hull, 1962.

Limited, model 23A) and glass and calomel electrodes. The acid (0.000250 mole) was dissolved in pure 2-n-butoxyethanol (50.0 ml.) and aqueous 0.1M-lithium chloride (50.0 ml.) was added. 2-n-Butoxyethanol was added during the titration to maintain a constant solvent composition. The pH was read after the addition of sodium hydroxide equivalent to 0.2, 0.3, and so on to 0.8 of the molarity of the acid. Great care was taken to exclude carbon dioxide at all stages; carbon-dioxide-free reagents were used, solutions were protected by soda-lime tubes, and a stream of nitrogen was played on to the solution in the titration vessel.

Values of pK were calculated from the equation:

$$pK = pH + \log \frac{([HA] - c_{H^+})}{([A] + c_{H^+})}$$

in which K is the dissociation constant (at a given ionic strength)⁸ based on "concentration" terms for anion and undissociated acid and an "activity" term for hydron, $[HA]$ is the concentration of residual organic acid, $[A]$ is the concentration of the salt formed, and c_{H^+} is the concentration of hydron. Above pH 5.3, c_{H^+} may be neglected in comparison with $[HA]$ and $[A]$. Below this pH, c_{H^+} was taken to be $-\text{antilog pH}$. (c_{H^+} was always fairly small relative to $[HA]$ and $[A]$, so the distinction between the activity and the concentration of the hydron was not important.)

TABLE I.
Physical constants of esters.

Methyl esters	M. p. or b. p.	Lit. m. p. or b. p.	Ref.	Synthetic method (see text)
Acetate	57—58°/760 mm.	57°/760 mm.	<i>a</i>	*
Phenylacetate.....	98—100/15 mm.	94—95/11 mm.	<i>b</i>	(<i>a</i>)
Diphenylacetate.....	59—60	58.5—60	<i>b</i>	(<i>a</i>)
2,2-Diphenylpropionate	160—162/5 mm.	149—152/3 mm.	<i>c</i>	(<i>a</i>)
2,2-Diphenylbutyrate †	164—165/5 mm.	—	—	(<i>a</i>)
Triphenylacetate	184—185	184—185	<i>b</i>	(<i>a</i>)
Fluorene-9-carboxylate.....	64—65	64—65	<i>d</i>	(<i>a</i>)
9-Methylfluorene-9-carboxylate	107—108	108—109	<i>d</i>	(<i>b</i>)
9-Ethylfluorene-9-carboxylate.....	81.5—82.5	81.5—82	<i>d</i>	(<i>b</i>)
9-Isopropylfluorene-9-carboxylate	79—80	79—80	<i>d</i>	(<i>b</i>)
9- <i>t</i> -Butylfluorene-9-carboxylate	112—113	112—113	<i>d</i>	(<i>b</i>)
9-Phenylfluorene-9-carboxylate ‡	165—166	—	—	(<i>a</i>)
9,10-Dihydroanthracene-9-carboxylate ...	96—97	94—96	<i>e</i>	(<i>a</i>)

* Commercially available. † Found: C, 80.3; H, 7.1. $C_{17}H_{18}O_2$ requires C, 80.3; H, 7.0%.
‡ Found: C, 84.2; H, 5.6. $C_{21}H_{18}O_2$ requires C, 84.0; H, 5.4%.

a, Timmermans, "Physico-Chemical Constants of Pure Organic Compounds," Elsevier, Amsterdam, 1950. *b*, Pitha, Hefmánek, and Vít, *Coll. Czech. Chem. Comm.*, 1960, **25**, 736. *c*, Bateman and Marvel, *J. Amer. Chem. Soc.*, 1927, **49**, 2914. *d*, Bavin, *Analyt. Chem.*, 1960, **32**, 554. *e*, Schlenk and Bergmann, *Annalen*, 1928, **463**, 147.

DISCUSSION

Alkaline Hydrolysis of Esters. Substituent Effects on the Entropy (ΔS^\ddagger) and Enthalpy of Activation (ΔH^\ddagger).—Rate coefficients are summarised in Table 2, and Arrhenius parameters and the related quantities of transition-state theory in Table 3. Earlier workers³ studying the alkaline hydrolysis of ethyl esters of substituted acetic acids established that only "bulky" substituents cause a decrease in the $\log A$ term of the Arrhenius equation; for smaller substituents $\log A$ is constant. They also found that electron-withdrawing groups decreased the activation energy, whilst "bulky" and electron-releasing groups increased it. The kinetics of alkaline hydrolysis, in 85% v/v ethanol-water, of ethyl acetate, phenylacetate, and diphenylacetate were studied by Levenson and Smith.^{3a} In Table 4 their results are compared with those obtained in the present study of the methyl esters in 80% v/v methanol-water. The values of $\Delta\Delta S^\ddagger$ and $\Delta\Delta H^\ddagger$ for each series do not correspond with one another at all. It is noteworthy that Gore and his co-workers,⁹ investigating the entropy and enthalpy of activation for alkaline hydrolysis in a common solvent of

⁸ Wooten and Hammett, *J. Amer. Chem. Soc.*, 1935, **57**, 2289.

⁹ Gore, Vignes, and Feinstein, *Chem. and Ind.*, 1958, 1514.

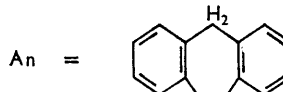
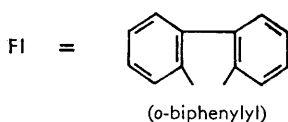
[1964] *The Separation of Polar and Steric Effects. Part IV.* 3373

the methyl and ethyl esters of a series of acids, found that the reactions of the methyl and ethyl esters exhibit different changes in ΔS^\ddagger and ΔH^\ddagger relative to the standard ester for each series; the relative rates were similar, however, at the experimental temperatures.

TABLE 2.

Rate coefficients for the alkaline hydrolysis of methyl esters (RCO_2Me) in 80% v/v methanol-water.

R	10^4k (l. mole ⁻¹ sec. ⁻¹); temperature (°c) in parentheses							
1 Me	17.3	(16.1)	40.0	(24.95)	102.7	(35.5)	215	(44.9)
2 PhCH ₂	27.5	(16.15)	61.5	(24.95)	155.7	(35.5)	332	(44.9)
3 Ph ₂ CH	8.67	(25.1)	19.7	(34.6)	55.5	(47.3)	101.8	(55.25)
4 Ph ₂ CMe	6.25	(75.8)	12.7	(84.9)	29.7	(95.15)	160.2	(118.55)
5 Ph ₂ CEt	7.85	(96.0)	16.8	(105.2)	38.7	(115.8)	72.7	(124.2)
6 Ph ₃ C	0.593	(60.0)	—	—	—	—	—	—
7 FICH (initial)	17.8	(26.4)	38.2	(35.2)	71.5	(44.4)	135.5	(53.4)
FICH (final)	29.7	"	57.7	"	111.5	"	207	"
8 FICMe	10.3	(44.8)	23.8	(54.65)	53.3	(65.15)	115.2	(75.25)
9 FICEt	5.05	(45.25)	9.27	(52.85)	27.2	(66.0)	54.0	(75.0)
10 FICPr ⁱ	2.72	(74.75)	5.95	(85.4)	33.8	(105.2)	76.2	(115.8)
11 FICBu ^t	5.92	(135.4)	15.4	(145.6)	32.3	(154.4)	73.2	(164.8)
12 FICPh	3.88	(60.0)	7.68	(69.5)	16.3	(81.0)	37.5	(89.8)
13 AnCH	43.3	(44.6)	91.2	(54.8)	177	(64.85)	347	(75.0)



Individual rate coefficients are usually accurate to $\pm 2\%$ except for reactions of esters 6, 7, and 12, for which they are accurate to $\pm 5\%$.

TABLE 3.

Alkaline hydrolysis of methyl esters (RCO_2Me) in 80% v/v methanol-water at 60°.

R	E (kcal. mole ⁻¹)	ΔH^\ddagger	$\log A$ (sec. units)	ΔS^\ddagger (cal. mole ⁻¹ deg. ⁻¹)	10^4k (60°) (l. mole ⁻¹ sec. ⁻¹)	ΔF^\ddagger (kcal. mole ⁻¹)
1 Me	16.0	15.4	9.35	-18.0	692	21.4
2 PhCH ₂	15.9	15.2	9.41	-17.7	933	21.1
3 Ph ₂ CH	15.9	15.3	8.60	-21.4	144 ₅	22.4
4 Ph ₂ CMe	20.7	20.1	9.75	-16.1	1.48	25.5
5 Ph ₂ CEt	23.0	22.3	10.51	-12.7	0.263	26.6
6 Ph ₃ C	—	—	—	—	0.589	26.0
7 FICH (initial)	14.5	13.8	7.82	-25.0	199	22.1
FICH (final)	14.0	13.3	7.66	-25.7	295	21.9
8 FICMe	17.4	16.8	8.98	-19.7	36.3	23.4
9 FICEt	17.6	17.0	8.79	-20.5	17.0	23.8
10 FICPr ⁱ	22.2	21.5	10.32	-13.5	0.550	26.0
11 FICBu ^t	30.4	29.7	13.04	-1.1	0.00120	30.1
12 FICPh	17.9	17.2	8.31	-22.7	3.72	24.8
13 AnCH	15.0	14.3	7.95	-24.2	129	22.4

For key to Fl, An, see Table 2. Values of E and ΔH^\ddagger are generally accurate to ± 300 cal., of $\log A$ to ± 0.2 unit, and of ΔS^\ddagger to ± 1.0 e.u.; for reactions of esters 7 and 12 the parameters are accurate to ± 600 cal., ± 0.4 unit, and ± 2.0 e.u., respectively.

The nature of the important transition state in alkaline hydrolysis was discussed in Part II.⁶

The entropy of activation (ΔS^\ddagger). For alkaline hydrolysis, bulky substituents near to the reaction site will reduce the number of accessible energy levels available to the transition state relative to the initial state.⁶ This "bulk" (steric hindrance to motions) effect will decrease ΔS^\ddagger . The methoxycarbonyl group and the hydroxide ion are strongly solvated.

Despite the apparent dispersion of charge resulting from the formation of the transition state in the first stage of alkaline hydrolysis, the reaction responds to a change in solvating power of the medium as if the transition state were more polar than the initial state.¹⁰ Bulky substituents near to the reaction site will inhibit the solvation of this site in both the initial and the transition states. Because of the congestion accompanying the formation of the transition state, solvation will be more strongly inhibited in this state. Entropy, being a measure of the disorder of the system, will be increased, and this results in an increase in ΔS^\ddagger .

The variations in ΔS^\ddagger for these reactions of the esters are shown in Table 3. The opposing influences of the "bulk" effect and steric inhibition of solvation are evident. Groups of moderate size (esters 3, 7, 8, 9, and 13) give rise to decreases in ΔS^\ddagger (relative to ester 1) because hindrance to motions predominates. Very large substituents (esters 4, 5, 10, and 11) cause inhibition of solvation in the transition state, which overcomes the "bulk" effect and increases ΔS^\ddagger . This steric inhibition of solvation is particularly marked with ester 11. It is interesting that it is also observed in the alkaline hydrolysis of methyl *o*-*t*-butylbenzoate.⁶ For methyl 9-phenylfluorene-9-carboxylate (12), the effective size of the group attached to the ester function (as measured by its E_s value,¹ see Table 5) is about the same as for the 9-isopropyl ester (10), but the ΔS^\ddagger values for alkaline hydrolysis are very different. Although the rate measurements for the 9-phenyl ester (12) are somewhat less accurate than those for the other compounds, they can be regarded as showing a polar effect which reduces ΔS^\ddagger (by comparison with the reaction of the isopropyl ester), for the relatively electron-withdrawing 9-phenyl-9-fluorenyl group (see σ^* values in Table 5).¹ The effect may be analogous to the polar facilitation of solvation postulated for the alkaline hydrolysis of methyl *o*-halogenobenzoates.⁶ The reduced ΔS^\ddagger values for the reactions of esters 7 and 13 compared with that for ester 3 suggest that the interannular link facilitates solvation by reducing congestion in the transition state.

The enthalpy of activation (ΔH^\ddagger). Electron-withdrawing substituents will decrease ΔH^\ddagger , and conversely for electron-releasing substituents. Steric effects on ΔH^\ddagger will be of two kinds. First, the increase in non-bonded interactions caused by the formation of the tetrahedral transition state when bulky substituents are present will cause repulsive forces, and so ΔH^\ddagger will be increased. Secondly, the steric inhibition of solvation will reduce the

TABLE 4.
Alkaline hydrolysis of $\text{RCO}_2\text{R}'$ at 60°.

System	Transition-state parameters (relative to those for reactions of $\text{MeCO}_2\text{R}'$)	
	R = PhCH_2	Ph_2CH
85% v/v Ethanol-water ^{3a}		
R' = Et	$\Delta\Delta S^\ddagger$ (cal. mole ⁻¹ deg. ⁻¹)	-1.3
	$\Delta\Delta H^\ddagger$ (cal. mole ⁻¹)	-600
80% v/v Methanol-water (present work)		
R' = Me	$\Delta\Delta S^\ddagger$ (cal. mole ⁻¹ deg. ⁻¹)	+0.3
	$\Delta\Delta H^\ddagger$ (cal. mole ⁻¹)	-100

stability of the transition state relative to the initial state and will also increase ΔH^\ddagger . The effects described can be used to explain the results shown in Table 3. (Another effect, which will probably be of minor importance, is the loss, when the transition state is formed, of resonance energy derived from the hyperconjugation of α -hydrogen atoms.)

Highly electron-withdrawing substituents of moderate steric requirements (esters 7 and 13) decrease ΔH^\ddagger (relative to ester 1). The significantly lower value of ΔH^\ddagger for the reaction of ester 13 compared with that of ester 3 is no doubt due to the smaller steric

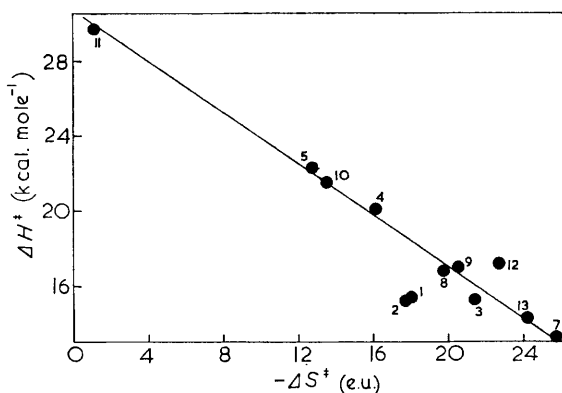
¹⁰ (a) Laidler and Eyring, *Ann. New York Acad. Sci.*, 1940, **39**, 303; (b) Fairclough and Hinshelwood, *J.*, 1937, 538.

effect with ester 13 (see E_s values in Table 5).¹ The steric effect in the hydrolysis of ester 7 will be slightly smaller than in that of ester 13, and the relatively electron-attracting character of the 9-fluorenyl group will also contribute to the reduction in ΔH^\ddagger . However, with more bulky substituents (esters 4, 5, 8, 9, 10, and 11) of lower electron-withdrawing powers (see σ^* values in Table 5), steric strain and steric inhibition of solvation predominate and cause large increases in ΔH^\ddagger . The reaction of ester 12 has a smaller ΔH^\ddagger value than that of ester 10, even though the substituents are of similar size (see E_s values in Table 5). This is in accord with the electronic character of the groups. Only for esters 2 and 3 do the two effects, polar and steric, appear to be approximately equal, so that the value of ΔH^\ddagger is close to that for ester 1.

Relation between enthalpy of activation and entropy of activation. A linear relationship between the entropy of activation and enthalpy of activation has been found for the alkaline hydrolysis of this series of esters (Fig. 1). In the equation $\Delta H^\ddagger = \Delta H_0^\ddagger + \beta \Delta S^\ddagger$, ΔH_0^\ddagger has the value 30.7 kcal. mole⁻¹ and β the value 687°K, for all esters except 1, 2, 6, and

FIG. 1. Relationship between enthalpy and entropy of activation for alkaline hydrolysis of methyl arylaliphatic carboxylates.

Key to numbering in Table 3.



12. (In the least-squares calculation, ΔH^\ddagger was regarded as the independent variable. The correlation coefficient is 0.992.) The constant β is termed the isokinetic temperature, and at this temperature all the reactions would have the same rate coefficient, if the relation were perfectly obeyed.¹¹ The temperature is not within the range of the present experimental measurements, so that it has no importance for this work. The continuous relationship shown by the majority of esters probably signifies a mechanism constant in its main details. The divergence for esters 1 and 2 is probably significant (approximately 4 e.u.). These two esters contain groups of comparatively small steric requirements. In these cases the formation of the intermediate may be appreciably reversible,¹² whilst for esters with bulky substituents it is likely that each individual formation of the intermediate results in hydrolysis. Methyl 9-phenylfluorene-9-carboxylate (12) also diverges from the regression line (about 3 e.u.), but the ΔH^\ddagger and ΔS^\ddagger values are much less certain than those for the other compounds.

There appears to be no deep understanding of the existence of linear entropy-enthalpy relations. Laidler and Eyring^{10a} point out that the relation $T\Delta S = \alpha\Delta H + \beta$ has been found empirically to hold for heats and entropies of solution, and will be applicable to the initial state, to any intermediates, and to the transition states in solution. The observed linear relation between ΔH^\ddagger and ΔS^\ddagger implies that the other (structural) factors which determine ΔH^\ddagger and ΔS^\ddagger give rise, in sum, to linearly related contributions to them.

Taft Analysis of Alkaline Hydrolysis of Esters.—The Taft-Ingold equation² can be used to analyse directly the results obtained for the alkaline hydrolysis of esters. This equation

¹¹ Leffler, *J. Org. Chem.*, 1955, **20**, 1202.

¹² Bender, *J. Amer. Chem. Soc.*, 1951, **73**, 1626.

has been used, in the form suggested by Taft,² to calculate the polar substituent constants, σ^* , *i.e.*,

$$\sigma^* = [\log (k/k_0)_B - E_s]/2.48 \quad (3)$$

In Table 5 are shown the values of $\log k_B$ for alkaline hydrolysis at 60°, E_s values obtained from acid-catalysed esterification rates¹ at 60°, the σ^* values obtained from equation (3), and those obtained from rate coefficients for the diazodiphenylmethane reaction.¹

TABLE 5.

Taft analysis of alkaline hydrolysis; pK values of acids.

Ester RCO ₂ Me or acid RCO ₂ H	R	$\log k_B$ at 60° (l. mole ⁻¹ sec. ⁻¹)	E_s at 60°	σ^* Taft-Ingold eqn.	σ^* Diazodiphenyl- methane reaction	pK †
1	Me	-1.16	0.0	0.0	0.0	6.05
2	PhCH ₂	-1.03	-0.37	+0.200	+0.215	5.55
3	Ph ₂ CH	-1.84	-1.43	+0.305	+0.405	5.33
4	Ph ₂ CMe	-3.83	-3.55	+0.355	+0.270	6.24
5	Ph ₂ CEt	-4.58	-4.34	+0.370	+0.210	6.57
6	Ph ₂ C	-4.23	-4.68	+0.650	+0.560	5.74
7	FICH	-1.53	-1.10	+0.295	+0.500	5.01
8	FICMe	-2.44	-1.73	+0.180	+0.320	5.63
9	FICEt	-2.77	-1.97	+0.145	+0.255	5.86
10	FICPr ⁱ	-4.26	-3.30	+0.080	+0.195	6.35
11	FICBu ^t	-6.92	-4.12	-0.660	+0.150	6.69
12	FICPh	-3.43	-3.03	+0.325	+0.585	5.24
13	AnCH	-1.89	-1.29	+0.225	+0.400	5.30

For key to Fl, An, see Table 2. Values of E_s are accurate to ± 0.02 unit, values of σ^* (Taft-Ingold equation) in general to 0.03 unit, and values of σ^* (diazodiphenylmethane reaction) to ± 0.01 unit. The least accurate value of $\log k_B$ is that for 11, involving a 75° extrapolation; this is estimated as accurate to about ± 0.04 unit; the other values should be accurate to 0.02 unit or better. † Mean of at least two determinations, accurate to ± 0.01 unit.

Apart from the value of σ^* obtained from results for methyl phenylacetate, the polar substituent constants obtained from the analysis of the alkaline hydrolysis results agree poorly with those derived from the rates of esterification of the acids with diazodiphenylmethane. The agreement would not be improved appreciably by replacing the factor 2.48 by some other value. Further, numerous inconsistencies are apparent within the set of values from alkaline hydrolysis; *e.g.*, the substituent group Ph₂CH (3) appears more electron-releasing than Ph₂CEt (5). The modified Taft equation² (4) was therefore applied to the results in Table 5 by using the polar and steric constants obtained in Part III¹ (cf. Table 5).

$$\log k_B = \sigma^* \rho^* + \delta E_s + \log k_0, \quad (4)$$

where ρ^* is the polar reaction constant and δ is the steric reaction constant. Ester 11 is excluded from these considerations because of the extreme discrepancy between the values of σ^* in Table 5, and this is discussed further later. Equation (4) may be further modified by using a corrected steric substituent constant E_s^c and a hyperconjugative parameter, h_B , thus:

$$\log k_B = \sigma^* \rho^* + \delta E_s^c + h_B(n - 3) + \log k_0, \quad (5)$$

where h_B is a reaction constant for α -bound hydrogen in alkaline hydrolysis and n is the number of α -hydrogen atoms. Hancock, Meyers, and Yager¹³ elaborated and applied this equation, but the correlation they obtained with it was little better than that obtained

¹³ Hancock, Meyers, and Yager, *J. Amer. Chem. Soc.*, 1961, **83**, 4211.

by using equation (4), so the introduction of further disposable constants does not appear to be justified. The application¹⁴ of the modified Taft equation (4) to the complete series of results gives a poor correlation, as shown in Table 6. However, separation of the results into two series, the "linked" and "unlinked," gives good correlations, as shown in Table 6 and in Figs. 2 and 3.

TABLE 6.
Taft analysis of alkaline hydrolysis.

Esters considered	ρ^*	Parameters obtained			
		δ	$\log k_0$	r	s
All esters except 11	1.30	0.86 ₅	-1.23 ₅	0.985	0.246
Ester 1 and esters with an interannular link (7, 8, 9, 10, 12, 13).....	1.51	1.02 ₅	-1.16	1.000	v. small
Ester 1 and esters without an interannular link (2, 3, 4, 5, 6)	1.63 ₅	0.86 ₅	-1.16	0.999	0.095

r = Correlation coefficient. s = Standard deviation from regression line.

The ρ^* values obtained for the "linked" and "unlinked" series are effectively the same. The significant difference in the susceptibility of the two systems to structural changes is indicated by the ratio of their steric reaction constants, *viz.*, 1.18. The explanation of the susceptibility of the "linked" series to steric effects being greater than that of the "unlinked" series probably resides in differences in the rigidity of the substituents.

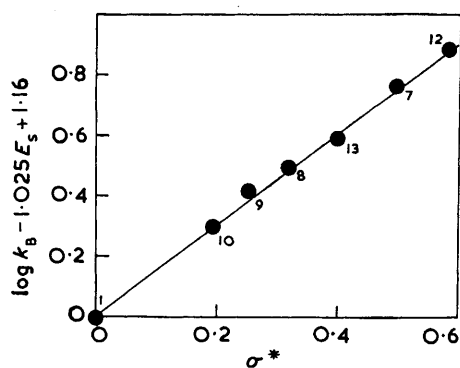


FIG. 2. Polar and steric effects in the alkaline hydrolysis of methyl arylaliphatic carboxylates: "linked" series.

Key to numbering in Table 5.

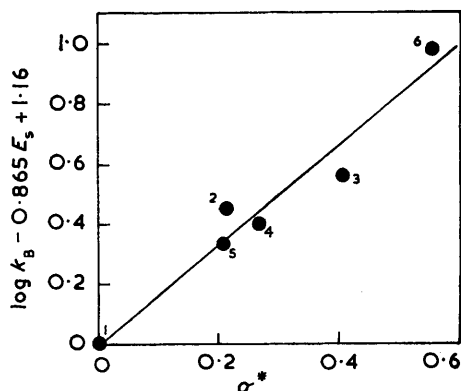


FIG. 3. Polar and steric effects in the alkaline hydrolysis of methyl arylaliphatic carboxylates: "unlinked" series.

Key to numbering in Table 5.

The "unlinked" substituents are able to accommodate the interactions set up by adjusting their conformation to minimise the steric effect. The "linked" substituents are rigid and unable to do so.

The absolute values of the reaction constants for steric effects have less significance than their ratio, because of the limitations of our experimental methods, *i.e.*, the solvent for esterification was methanol, whereas for alkaline hydrolysis it was 80% v/v methanol-water. E_s values obtained from results for acid-catalysed hydrolysis in 80% v/v methanol-water⁶ of methyl *o*-toluate and *o*-ethylbenzoate are larger than those from results for the acid-catalysed esterification of the corresponding acids (results obtained in this laboratory¹⁵).

¹⁴ Pavelich and Taft, *J. Amer. Chem. Soc.*, 1957, **79**, 4940.

¹⁵ Rodgers, unpublished results.

For the reactions of arylaliphatic acids, E_s values proper to 80% v/v methanol-water (if these could be measured¹) might well, therefore, be larger than those based on esterification in methanol. The use of the former set of values of E_s in equation (4) would then give values of δ lower than those in Table 6, and all would be <1 . For the compounds being considered, it thus seems likely that susceptibility to steric effects is greater in acid-catalysed ester reactions than in alkaline hydrolysis in the same solvent. If the susceptibilities of the two kinds of reaction were the same, δ would be unity.

This effect can be produced only by a difference in the solvent steric interactions as between acid-catalysed and alkaline ester reactions.[†] The solvation pattern of the transition states for acid-catalysed esterification and alkaline hydrolysis may well be different. The transition state for acid-catalysed reactions has a positive charge, and Swain and Eddy¹⁶ suggested that solvent molecules solvate a positive site with the "negative" part of the molecule. The transition state for alkaline hydrolysis will, however, be solvated by the "positive" part. For the compounds studied in the present work, it appears that the solvent interactions caused by the formation of the acid-catalysed transition state are the greater. On the other hand, the rates of alkaline hydrolysis of methyl *cis*- and *trans*-4-*t*-butylcyclohexanecarboxylate indicate that the steric interactions are more important in alkaline than in acidic hydrolysis.¹⁷ However, in the present work we have substituent groups of much greater steric requirements than in the work with cyclohexanecarboxylic esters. Evidence that E_s values are not a quantitative measure of the steric effects in the basic hydrolysis of *o*-halogeno- or *o*-alkyl-substituted methyl benzoates has already been presented (Part II⁶).

A low ρ^* value (about 1.6) has been found for alkaline hydrolysis of the di- and tri-substituted esters, compared with the value originally used by Taft (2.48) and which appears to be suitable for the hydrolysis of the esters (mostly mono-substituted) in his study. Taft assumed the value of 2.48, which was the mean Hammett ρ value for the basic hydrolysis of *meta*- and *para*-substituted benzoates. It is clear, however, from a consideration of the reaction series presented by Jaffé¹⁸ and Taft,² that the susceptibilities to polar effects are quite different in the aromatic (ρ) and aliphatic (ρ^*) systems; *e.g.*, for acid dissociation in water at 25°, ρ is 1.00 whilst ρ^* is 1.72.

Methyl 9-*t*-butylfluorene-9-carboxylate (11) has not been included in these considerations. The rate coefficient for alkaline hydrolysis is very much lower than that predicted by use of the Taft equation. An explanation of this might be that this ester has a different mechanism from the others at the high temperatures which had to be used. However, this ester obeys the enthalpy-entropy relationship which is usually considered to be excellent evidence of a constant mechanism. It seems reasonable to suppose, therefore, that this very low rate is caused by extreme steric inhibition of solvation and steric compression at the reaction site.

Criticism of Taft Analysis.—We now reconsider, in the light of the present results, the assumptions involved in the Taft analysis (cf. Part II⁶). Taft assumed that steric and resonance effects in acid-catalysed esterification and alkaline hydrolysis are the same; resonance effects apparently are the same. However, the several steric effects depend on the changes in compressive interactions caused by the formation of the transition states. As the corresponding solvation patterns apparently differ, these interactions will also differ and the steric parameter obtained from results for esterification will not be directly applicable to alkaline hydrolysis. It seems likely that the polar substituent constants, σ^* ,

[†] R. M. Noyes (*J. Amer. Chem. Soc.*, 1964, **86**, 971), whom we thank for a personal communication on this point, estimated the electrostriction around aqueous hydrogen ion at ~ 1.3 ml. mole⁻¹, and around hydroxide ion at ~ 22.0 ml. mole⁻¹. He concludes that, "if the hydration of positive and negative ions differs as much as the present paper suggests, Taft's treatment may not have separated steric effects as clearly as was hoped."

¹⁶ Swain and Eddy, *J. Amer. Chem. Soc.*, 1948, **70**, 2989.

¹⁷ Chapman, Shorter, and Toyne, *J.*, 1961, 2543.

¹⁸ Jaffé, *Chem. Rev.*, 1953, **53**, 191.

obtained by use of the Taft "polar free energy" relations are meaningful, and also that the Taft steric substituent constants, E_s , are a measure of the steric interactions involved in ester reactions, but their applicability depends on the type of substituent and the system to which they are applied.

Ionization of Arylaliphatic Carboxylic Acids.—In Table 5 the effect of substitution on the ionization constants of the arylaliphatic carboxylic acids in 50% v/v 2-n-butoxyethanol-water is shown in terms of pK values. The principal factor governing the ionization of an acid should be the polar effect of the substituent. There is, however, no linear relation between pK and the polar substituent constants, σ^* (Part III¹). The occurrence of a steric effect is conceivable, but there is no linear relationship between pK and the steric substituent constants, E_s (Part III¹). The application, however, of the modified Taft relation:

$$pK_0 - pK = \sigma^* \rho^* + \delta E_s \quad (6)$$

gives an excellent correlation. Multiple-regression treatment of the results¹⁴ gives the reaction constant for polar effects, ρ^* , as 2.66₅, and the reaction constant for steric effects, δ , as 0.25, with pK_0 6.04₅. The correlation coefficient is 1.000, and the mean deviation from the regression line 0.052. This correlation is shown graphically in Fig. 4. The

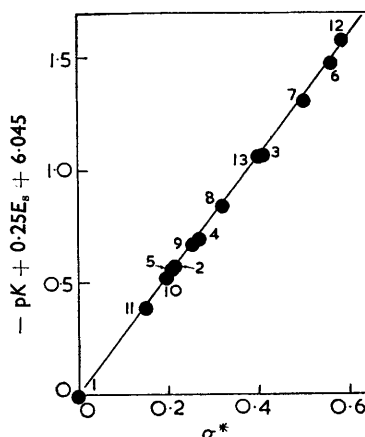


FIG. 4. Polar and steric effects in the ionisation of arylaliphatic carboxylic acids.

Key to numbering in Table 5.

steric effect is thus acid-weakening. The ratio, ρ^*/δ , of the reaction constants for alkaline hydrolysis is ~ 1.7 , whilst for ionization in 50% 2-n-butoxyethanol-water it is ~ 10 .

The explanation of the acid-weakening steric effect must lie in the inhibition of solvation by the bulky groups, which will preferentially reduce the stability of the anion RCO_2^- with respect to that of the acid RCO_2H since the anion is more highly solvated than the undissociated acid.^{4,5} The success of the above correlation suggests that the factors responsible for the retardation of esterification are similar to those opposing solvation in acid dissociation. The initial states in the two processes are similar. The increase in steric interactions in attaining the transition state in esterification is evidently proportional to the increase in steric interactions in going to the final state in acid dissociation. This study emphasises the danger of attempting to investigate polar effects of substituents solely by studying the dissociation constants of carboxylic acids, when steric requirements may vary.

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