168. *The Activation Energy of Organic Reactions. Part III. The Kinetics of Acid Hydrolysis of Esters.*

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The parameters of the Arrhenius equation have been determined for the acid hydrolysis of a series of esters in alcohol–water and acetone–water solvents, and these values are compared with those for the alkaline hydrolysis. Both reactions are facilitated by recession of electrons from the seat of reaction. E is higher in acid hydrolysis and the effect of substituents is smaller; also, PZ increases with E in contrast with the constant value in alkaline hydrolysis. The effect of solvent is apparently opposite in the two cases.

The alkaline hydrolysis of substituted benzoic esters in 85% aqueous alcohol has been studied by Ingold and Nathan (J., 1936, 222) and by Evans, Gordon, and Watson (J., 1937, 1430). Data for four of the corresponding esters, hydrolysed by alkali in 56% aqueous acetone, are given by Newling and Hinshelwood (J., 1936, 1357). These investigations showed that in alkaline hydrolysis the reaction is facilitated by recession of electrons from the seat of reaction, and hence, in the terminology of Ingold, is a Class B reaction. Furthermore, in the *m*- and *p*-substituted series of ethyl benzoates, the PZ factor in the Arrhenius equation (when written $k = PZe^{-E/RT}$) is constant, changes in reaction velocity being entirely due to changes in E. Newling and Hinshelwood (*loc. cit.*) concluded that the mean value of PZ was very nearly the same for acid as for alkaline hydrolysis, but from the data then available, chiefly on aliphatic esters, it was impossible to say whether the reaction belonged to Class A or to Class B. The proximity of the substituent and reacting group in these aliphatic esters complicated the picture because of steric effects. It therefore seemed desirable to study the acid hydrolysis of substituted benzoic esters with a view to determining the effect of substituents on the trend of activation energies, and also whether altered reactivity is due to changes in E alone, or to changes in both in E and PZ. The chloroacetic esters were also studied, since a wider range of E was expected in view of the wider range in the dissociation constants of the corresponding acids.

The reactions included in this investigation are the acid hydrolysis of ethyl acetate and the three chloroacetates in ethyl alcohol–water, of nine ethyl benzoates in ethyl alcohol–water and acetone–water, and of three methyl benzoates in methyl alcohol–water.

The ordinary titration methods were used to measure the rates of hydrolysis. In general, 5 c.c. of N/10-ester and 5 c.c. of N/10-catalyst were mixed in approximately 11 c.c. reaction bulbs which were then sealed off and placed in the thermostats. After reaction had proceeded for the desired length of time, the tubes were rapidly cooled and the contents titrated with N/50-baryta or ammonia (in the case of the chloroacetates), bromocresol-purple being used as indicator. In the presence of the phenolic *p*-hydroxy-group this indicator does not give a sharp end-point. By using B.D.H. universal indicator the two-stage titration curve was obtained, from which the titre measuring the quantity of carboxylic acid could be determined.

At these concentrations benzoic esters do not hydrolyse at measurable speed below 60°. To obtain a wide enough temperature range for accurate determinations of E it was necessary to work at temperatures up to 155°. Ordinary soda-glass is very appreciably affected at these temperatures when in contact with aqueous solutions; therefore it was necessary to use Pyrex glass for the reaction tubes.

It was desired to study the hydrolysis in both acetone–water and alcohol–water. Since hydrogen chloride esterifies ethyl or methyl alcohol rapidly at these temperatures it is unsuitable as a catalyst, for in any case it esterifies the alcohol formed as a product of the reaction, and when alcohol is also present as solvent the rapid removal of the catalyst cannot be coped with. To solve these difficulties, benzenesulphonic acid was used, since it possesses the desirable properties both of being practically completely dissociated at these concentrations and of not esterifying alcohols under the conditions used.

The solvents were prepared by diluting 400 c.c. of water to 1 l. with acetone, ethyl alcohol, or methyl alcohol respectively. Distilled water was freed from dissolved carbon dioxide by boiling. Commercial acetone was purified by drying for several days over potassium carbonate and then by fractionation through a 5′ column. Absolute ethyl alcohol was used, the 0·2% of water present being allowed for in making up the solvent. The methyl alcohol was purified by the method of Hartley and Raikes (J., 1925, **127**, 524) using aluminium amalgam.

According to the physical properties, purification of the esters used was carried out in an all-glass still at atmospheric pressure, by reduced pressure distillation, by recrystallisation from ligroin or absolute alcohol, or in the case of ethyl anisate by recrystallisation from the melt. All esters existing in the liquid state at room temperature were first dried over calcium chloride. The purity was checked by complete alkaline hydrolysis, except with the chloroacetates and ethyl *p*-hydroxybenzoate. The purity of the latter was checked by titration of the phenolic group. Table I gives the determined physical properties of the esters, together with those recorded in Beilstein.

At and below 80°, electrically-controlled thermostats were used. At higher temperatures special boilers containing water, perchloroethylene, xylene, or anisole were used. Temperatures were standardised with N.P.L. thermometers. Glassware was standardised. Velocity constants were measured at four or five temperatures, over a range of 55—80°, and were corrected for change of concentration due to thermal expansion of the solvent. The Arrhenius equation was obeyed within the limits of experimental error.

Since the hydrolysis is a reversible reaction, treatment of the results depended upon whether or not it was possible to determine the equilibrium concentration accurately. In the hydrolysis of ethyl acetate in alcohol–water the equilibrium concentration was determined over a 60° temperature range and found to be independent of temperature (zero heat of reaction). It was then possible to use the integrated form of the equation

$$\mathrm{d}x/\mathrm{d}t = k_1[\mathrm{H}^+](a - x) - k_2[\mathrm{H}^+]x \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

namely,

$$k_1 = (2{\cdot}303\xi/[\mathrm{H}^+]at) \log_{10} \xi/(\xi - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where ξ is the amount changed at equilibrium, to determine k_1 accurately. The concentration of water and alcohol does not change detectably during the reaction and is therefore not included in the equation. All velocity constants are expressed in l. g.-mol.$^{-1}$ sec.$^{-1}$. It is not possible, in general, to determine the equilibrium concentrations accurately because of the long time required for equilibrium to be reached, during which time side reactions may become appreciable; it is necessary in these cases to use the equation

$$dx/dt = k[H^+](a - x) \qquad (3)$$

in the integrated form

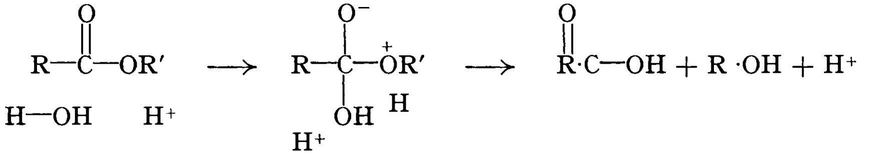
$$k = (2{\cdot}303/[H^+]t) \log_{10} a/(a - x) \qquad (4)$$

In alcohol–water, values of k calculated by (4) will fall as the reaction proceeds. It is then necessary to plot k against percentage of products formed and extrapolate to zero percentage change; k calculated from the initial slope of the percentage change–time curve serves as a check on this method. This fall in k is largely due to esterification of the solvent alcohol molecules by the acid formed from hydrolysis. In acetone–water, hydrolysis will proceed much further, since only the products tend to reverse the reaction. Over the first 30% of reaction this fall is inappreciable and values of k can be averaged. Table II shows values of k_1 for the hydrolysis of ethyl acetate at 80·10°, calculated by formula (2), and Table III shows k_1 and k for each temperature [calculated by formulæ (2) and (4) and corrected for solvent expansion], and the corresponding values of E calculated by the method of least squares. Values of k calculated from the rate equation, $\log_{10}k_1 = 7{\cdot}525 - 16{,}200/\boldsymbol{R}T$, are included for comparison. Table IV gives the constants and the corresponding temperature for the other esters. In Table V the values of E, $\log_{10}PZ$, and $\log_{10}(k_{100^\circ} \times 10^6)$ are collected.

DISCUSSION.

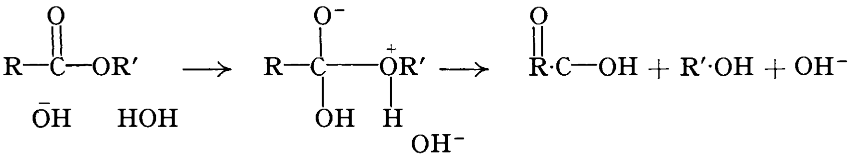
The Effect of Substituents on E.—In acid hydrolysis the activation energy is lowered by substituents which attract electrons (electron sinks) and raised by electron sources; *i.e.*, acid hydrolysis is a Class B reaction. The order of the *p*-substituents in their effect on E is that generally found, *viz.*, OCH_3, CH_3, (H), Halogen, NO_2. The *m*-nitro-group falls between the *p*-nitro-group and the unsubstituted ester, also in agreement with expectations. The fact that acid and alkaline hydrolysis are both Class B reactions is clearly set forth in Fig. 1, where the activation energies for the acid hydrolysis of *p*-substituted esters are plotted as abscissæ and the activation energies for the alkaline hydrolysis of the corresponding esters are plotted as ordinates. This grouping about a line indicates behaviour approximating to the relationship $\Delta E_{\text{acid}} = \alpha\Delta E_{\text{alkaline}}$ (Hinshelwood, J., 1937, 635). In Part I the smaller effects of substituents and the higher activation energies in acid hydrolysis are explained by considering the relative repulsions on the proton and water molecule in acid hydrolysis, and on the hydroxyl ion and water molecule in alkaline hydrolysis. The Lowry mechanism is as follows:

Acid hydrolysis.



$$\underset{\text{H—OH}\quad \text{H}^+}{\text{R—}\overset{\overset{\text{O}}{\|}}{\text{C}}\text{—OR}'} \longrightarrow \underset{\text{H}^+}{\underset{\text{OH}\ \ \text{H}}{\text{R—}\overset{\overset{\text{O}^-}{|}}{\underset{|}{\text{C}}}\text{—}\overset{+}{\text{O}}\text{R}'}} \longrightarrow \text{R}{\cdot}\overset{\overset{\text{O}}{\|}}{\text{C}}\text{—OH} + \text{R}{\cdot}\text{OH} + \text{H}^+$$

Alkaline hydrolysis.

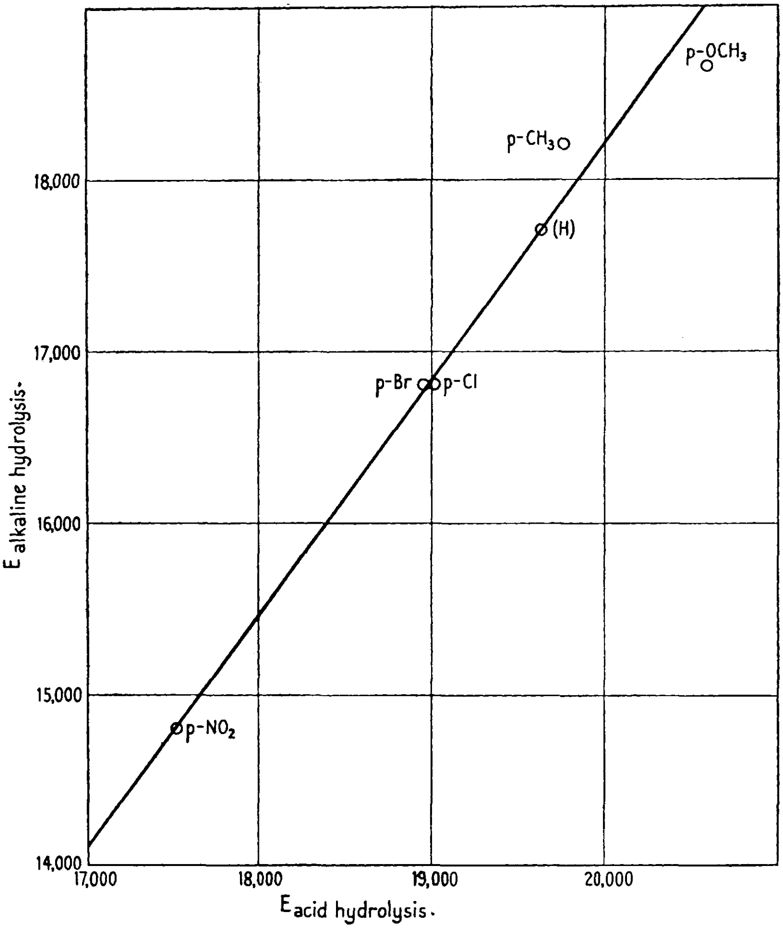


$$\underset{\bar{\text{O}}\text{H}\quad \text{HOH}}{\text{R—}\overset{\overset{\text{O}}{\|}}{\text{C}}\text{—OR}'} \longrightarrow \underset{\text{OH}^-}{\underset{\text{OH}\quad \text{H}}{\text{R—}\overset{\overset{\text{O}^-}{|}}{\underset{|}{\text{C}}}\text{——}\underset{|}{\overset{+}{\text{O}}}\text{R}'}} \longrightarrow \text{R}{\cdot}\overset{\overset{\text{O}}{\|}}{\text{C}}\text{—OH} + \text{R}'{\cdot}\text{OH} + \text{OH}^-$$

It was shown that in acid hydrolysis the most important step involves the overcoming of the repulsion of an approaching water molecule from which a hydroxyl group must be obtained, whereas in alkaline hydrolysis the corresponding process involves the free hydroxyl ion.

Relation of PZ *and* E.—In Fig. 2, $\log_{10}k$ is plotted against E both for the acid and for the alkaline hydrolysis of *m*- and *p*-substituted benzoic esters in alcohol–water. The results for alkaline hydrolysis are those of Ingold and Nathan (*loc. cit.*) and Evans, Morgan, and Watson (*loc. cit.*). As previously stated, in the alkaline hydrolysis changes in k are due to changes in E alone, shown by the fact that the points lie on the line of slope $-2{\cdot}303/\boldsymbol{R}T$ which corresponds to constant PZ. In contrast, in the acid hydrolysis the points are grouped about a line considerably steeper than the line of standard slope: this corresponds to an increase of PZ with E. Fig. 3 shows how $\log_{10}PZ$ is related to $1/\sqrt{E}$. A functional relation of this type may be explained on statistical grounds (Fairclough and Hinshelwood, J., 1937, 538) by assuming that the average time required for reaction is large compared with the average duration of the collision, this relative time condition varying with the mechanism of reaction so that the increase of PZ with E sometimes does and sometimes does not occur on substitution (see Part I). Considering the wide range over which PZ may vary in general, we may say that here it is substantially the same for acid and for alkaline hydrolysis so long as the solvent remains the same (cf. Newling and Hinshelwood, *loc. cit.*, and present results for acetone–water solvent). This is evidence in favour of the Lowry mechanism, which postulates a similar plan for the two reactions.

FIG. 1.



The change of PZ with E counteracts the effect of E to a certain extent, but with the benzoic esters, except the *o*-nitrobenzoate, the velocity constants at 100° follow the trend of E. The *o*-nitrobenzoate has both a high value of E and a low value of PZ. It appears that here the proximity of the nitro-group reduces k both by decreasing PZ and by raising E, although from its electronic nature we would expect E to be lowered. In the chloroacetic esters the PZ factor increases markedly with E, so that the effects of changes in E and PZ are practically counterbalanced, as shown in the close grouping of the values for $k_{100°}$. Steric factors apparently work in conjunction with the general factors operating in the *m*- and *p*-substituted benzoic esters in bringing about this large increase of PZ with E. This series shows the advantage of comparing activation energies rather than velocity constants at a given temperature. At 100°, k varies only slightly and in a random manner, while the activation energy decreases as successive chlorine atoms are introduced into the acetyl group, in accordance with expectations based upon the application of the electronic theory.

FIG. 2.

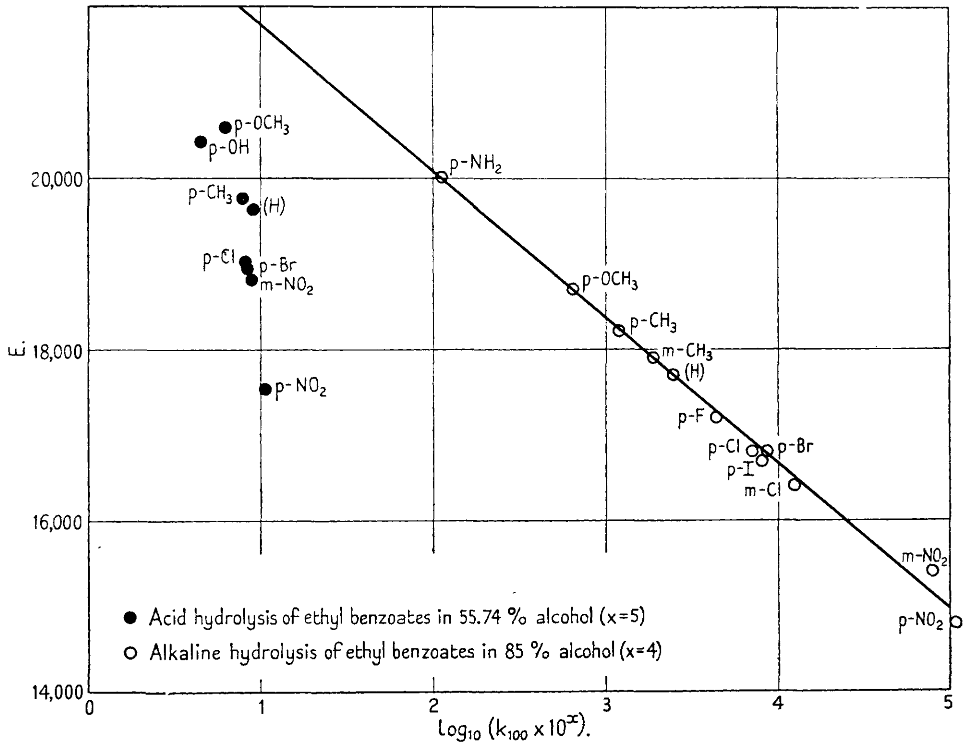
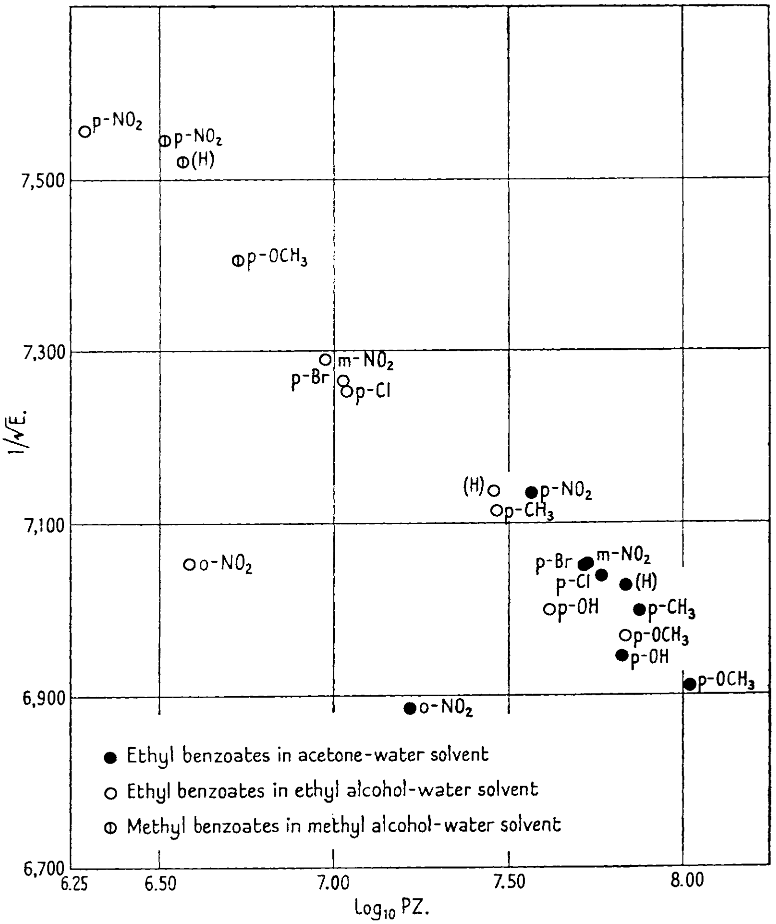


TABLE I.

	Values determined.		Values given in Beilstein.	
	M. p.	B. p.	M. p.	B. p.
Ethyl anisate	6·8°	—	7·0°	—
Ethyl *p*-hydroxybenzoate	113·5	—	112·5—115	—
Ethyl *p*-toluate	—	111°/13 mm.	—	235·5°/760 mm.
Ethyl benzoate	—	213	—	211—212
Ethyl *p*-chlorobenzoate	—	122/15 mm.	—	238
Ethyl *p*-bromobenzoate	(100% hydrolysis only)			
Ethyl *p*-nitrobenzoate	56·5	—	57	—
Ethyl *m*-nitrobenzoate	46·7	—	47	—
Ethyl *o*-nitrobenzoate	30·0	149/10 mm.	30	149/10 mm.
Methyl anisate	47·7	—	47	—
Methyl benzoate	—	197—198	—	198—199
Methyl *p*-nitrobenzoate	96·2	—	96	—
Ethyl acetate	—	76·9—77·1	—	77·1
Ethyl chloroacetate	—	143·8—144·2	—	144
Ethyl dichloroacetate	—	157·3—158·0	—	158
Ethyl trichloroacetate	—	167·5	—	167·8

FIG. 3.



Solvent Effects.—In acid hydrolysis the activation energy of a given ester increases as we go from alcohol–water to acetone–water solvent, whereas in alkaline hydrolysis this trend is reversed. Another fact also emerges, *viz.*, that the effect of substituents is greater in alcohol–water. These effects must be related to the manner in which the potential field due to the solvent molecules affects the repulsion energies between and the bond energies of the reactants. Until our knowledge of the liquid state is greater, it is difficult to say more by way of explaining these differences.

TABLE II.

Acid hydrolysis of ethyl acetate.

Values of k_1 from formula (2) at 80·10°; t is the time in seconds, x and ξ the concentrations of products at time t and at equilibrium respectively, and k_1 the bimolecular constant. $100 \times \xi/a = 40{\cdot}2$.

t	645	900	1140	1440	1740	2040	2280	2640	3240	3840	4440	5040	5670	6660	7440
$100x/\xi$	20·13	28·61	33·00	41·05	47·08	52·80	58·25	61·50	69·85	75·80	80·30	83·70	87·35	90·10	93·25
$k_1 \times 10^6$	2815	3026	2840	2965	2956	2975	3095	2920	2990	2986	2958	2906	2946	2806	2927

$k_1 \times 10^6$ (average) = 2941 (uncorrected for expansion).

TABLE III.

Temperature coefficient in acid hydrolysis of ethyl acetate.

Temp.	24·86°	39·80°	60·09°	80·10°
$k_1 \times 10^6$ [average from (2)]	42·6	167·9	788	3119
$k \times 10^6$ [extrapolated from (4)]	43·3	173·7	780	3158
$k \times 10^6$ (calc., Arrhenius)	43·8	161·4	785	3163

E (from k_1) = 16,200; E (from k) = 16,130.

TABLE IV.

Acid Hydrolysis of Esters.

(a) *Ethyl esters in ethyl alcohol–water solvent.*

Temp.	$k \times 10^6$.	Temp.	$k \times 10^6$.	Temp.	$k \times 10^6$.
Chloroacetate.		Dichloroacetate.		Trichloroacetate.	
24·86°	39·48	24·86°	21·26	24·84°	82·6
39·79	134·8	39·79	65·9	39·97	238·6
60·04	619	60·04	270·4	60·34	761
80·10	2259	80·10	925	80·15	2166
Anisate.		*p*-Hydroxybenzoate.		*p*-Toluate.	
60·00	2·05	80·20	9·92	60·05	3·24
80·20	14·10	99·50	41·6	80·25	16·5
99·40	56·5	120·0	191·0	99·90	81·9
119·9	257	138·5	570	120·3	301
138·1	800			139·7	978
Benzoate.		*p*-Chlorobenzoate.		*p*-Bromobenzoate.	
60·00	3·92	80·30	18·65	80·20	20·0
80·20	20·5	100·00	81·2	100·00	86·2
99·60	84·5	120·6	312	120·2	302
120·2	335	139·3	861	139·4	955
138·6	1140				
p-Nitrobenzoate.		*m*-Nitrobenzoate.		*o*-Nitrobenzoate.	
80·20	28·6	80·20	20·9	80·30	1·495
98·90	103·8	99·45	88·5	100·00	5·91
119·3	332	119·9	332	120·6	26·2
138·0	952	138·3	900	138·9	85·6

(b) *Ethyl esters in acetone–water solvent.*

Anisate.		*p*-Hydroxybenzoate.		*p*-Toluate.	
60·00	1·98	80·20	9·82	80·30	16·79
80·20	13·38	99·80	46·9	100·05	83·1
99·20	58·3	120·2	196	120·5	349
119·9	256	138·9	668	138·9	1051
138·5	875				
Benzoate.		*p*-Chlorobenzoate.		*p*-Bromobenzoate.	
80·30	20·9	80·30	18·49	60·05	3·40
100·20	94·4	99·85	87·5	80·20	18·5
120·9	396	120·2	355	100·15	86·4
139·3	1293	139·4	1177	120·2	346
				139·2	1115
p-Nitrobenzoate.		*m*-Nitrobenzoate.		*o*-Nitrobenzoate.	
60·00	4·38	60·00	3·48	80·30	1·46
80·20	27·1	80·20	19·3	99·85	7·04
99·40	108·6	99·90	86·4	120·7	32·2
120·0	420	120·4	368	139·2	107·6
138·5	1382	139·0	1150		

(c) *Methyl esters in methyl alcohol–water solvent.*

Anisate.		Benzoate.		*p*-Nitrobenzoate.	
99·85	108·8	100·20	168	100·12	165
120·45	392	121·20	556	120·75	574
138·5	1006	139·2	1564	138·4	1538
153·9	2592	153·9	3207	153·0	3175

Table V.

Acid Hydrolysis.

Ester.	$\log_{10} k_{100°} \times 10^6$.	$\log_{10} PZ$.	E (cals.).
(a) *In ethyl alcohol–water solvent.*			
Ethyl acetate	4·03	7·53	16,200
Ethyl chloroacetate	3·86	6·86	15,350
Ethyl dichloroacetate	3·44	5·82	14,300
Ethyl trichloroacetate	3·74	4·94	12,280
Ethyl anisate	1·79	7·84	20,590
Ethyl *p*-hydroxybenzoate	1·65	7·62	20,420
Ethyl *p*-toluate	1·89	7·47	19,760
Ethyl benzoate	1·955	7·46	19,630
Ethyl *p*-chlorobenzoate	1·90	7·04	19,010
Ethyl *p*-bromobenzoate	1·92	7·03	18,950
Ethyl *p*-nitrobenzoate	2·025	6·29	17,520
Ethyl *m*-nitrobenzoate	1·945	6·98	18,820
Ethyl *o*-nitrobenzoate	0·71	6·59	20,100
(b) *In acetone–water solvent.*			
Ethyl anisate	1·79	8·07	20,950
Ethyl *p*-hydroxybenzoate	1·67	7·83	20,730
Ethyl *p*-toluate	1·91	7·88	20,420
Ethyl benzoate	1·97	7·84	20,250
Ethyl *p*-chlorobenzoate	1·95	7·77	20,190
Ethyl *p*-bromobenzoate	1·93	7·72	20,120
Ethyl *p*-nitrobenzoate	2·06	7·57	19,650
Ethyl *m*-nitrobenzoate	1·95	7·73	20,110
Ethyl *o*-nitrobenzoate	0·85	7·22	21,100
(c) *In methyl alcohol–water solvent.*			
Methyl anisate	2·038	6·73	18,240
Methyl benzoate	2·206	6·57	17,690
Methyl *p*-nitrobenzoate	2·220	6·52	17,570

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