

293. *The Kinetics of the Acid and the Alkaline Hydrolysis of Esters.*

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ESTERIFICATION of a carboxylic acid by an alcohol requires a catalyst, which may be either an alcoholated hydrion or a molecule of an undissociated acid. For the former, the value of P in the usual expression for the reaction velocity, $PZe^{-E/RT}$, is several powers of ten greater than for the latter (Hinshelwood and Legard, J., 1935, 587). The question arises how far the difference between the catalysts is purely a function of the ionic charge. In the reaction between acetone and iodine, P varies widely with change of catalyst, and the values seem to fall into two well-defined groups, being high for the hydrion, and for the anions of acetic and propionic acids, but small for undissociated acids. Smith (J., 1934, 1744) considers that there is, within the group of undissociated acids, a functional relation between P and the acid strength, but this is less striking than the contrast between the charged and the uncharged groups.

Ester hydrolysis offers the opportunity of investigating the matter further by comparing the behaviour of hydrogen ions and hydroxyl ions in catalysing the same reaction. This, together with the accumulation of further information about the nature of the factor P , was the principal object of the following experiments.

EXPERIMENTAL.

The solvent chosen was aqueous acetone containing 40 c.c. of water in each 100 c.c. This contains enough acetone to dissolve aromatic esters up to $N/10$, and so much water that we may assume (i) that $[H_2O]$ is constant during the course of the hydrolysis, and (ii) that sodium hydroxide and hydrochloric acid are completely ionised in $N/20$ -solution. Although, in principle, this solvent is unstable to alkali, no changes occurred to a freshly prepared solution which affected the velocity constants even in the slowest experiments.

The rates of hydrolysis were measured by the ordinary titration methods, with a special device for the more rapid reactions. In general, the initial concentrations of ester and alkali or hydrogen chloride were $0.05N$. For $25-80^\circ$ electrically controlled thermostats were used, for 0° a Dewar vessel containing ice and water, and for temperatures above 80° special boilers containing water, perchloroethylene, or xylene. Temperatures were measured with N.P.L. thermometers.

For the alkaline hydrolysis, satisfactory constants were always obtained with the usual bimolecular formula. For the acid hydrolysis, various methods of treating the results were employed according to the circumstances. Where it was practicable to measure the equilibrium constant, the integrated form of the equation

$$dx/dt = k_1[HCl](a - x) - k_2[HCl]x^2$$

was used to determine k_1 , and gave satisfactory constants. In some cases the hydrolysis was so nearly complete that the second term was negligible and the unimolecular formula was applicable. The catalytic action of the acid products of hydrolysis was negligible in presence of hydrogen chloride except in the case of dichloroacetic acid, where, however, it was easy to allow for it, the initial constants being taken. In the slowest reactions the equilibrium constant could not be measured, since, in the long times necessary for the attainment of equilibrium, secondary reactions of hydrogen chloride with the alcoholic product occurred. The velocity constants were therefore calculated from the initial rates, which were found by drawing tangents to reaction-time curves. The admissibility of this procedure was verified by determining the constants in this way also for those reactions where the integrated formula involving the equilibrium constant could be used: there was satisfactory agreement—*e.g.*, 0.00360 and 0.00351 for methyl acetate at 80.2° .

Constants were determined in all cases at four, and sometimes at five, temperatures. The Arrhenius equation was obeyed within the limits of experimental error. All constants were corrected for the thermal expansion of the solvent (the correction represents about 200 cal. in the activation energy).

TABLE I.

Ethyl m-nitrobenzoate and sodium hydroxide, 0.05N.

(1) Reaction at 15.2° , started by breaking bulb containing 5 c.c. $N/10$ -alkali in tube with 5 c.c. $N/10$ -ester, the whole previously brought to 15.2° . Stopped by pouring into excess standard acid, the rate of the acid hydrolysis being negligible. Timing by stop-watch. t is the time, x the percentage change, and k_1 the bimolecular constant.

t	120	180	240	330	530	600
x	32.95	41.75	48.8	58.05	69.0	70.35
k_1	0.0819	0.0796	0.0794	0.0839	0.0840	0.0792

(2) Temperature coefficient.

Temperature	0.1°	15.2°	24.9°	39.9°
$100k_1$ (obs.)	2.31	8.15	17.15	48.8
$100k_1$ (calc., Arrhenius)	2.35	8.22	17.1	48.5

Ethyl m-nitrobenzoate and hydrogen chloride, 0.05N.

Velocity constants obtained by initial tangent method.

Temperature	60.0°	80.0°	99.7°	119.8°	136.8°	139.0°
$k_1 \times 10^6$ (obs.)	3.63	19.6	88.1	328	933	1045
$k_1 \times 10^6$ (calc., Arrhenius)	3.63	19.5	86.3	335	955	1086

Esters were distilled to constant b. p., except that the *m*-nitrobenzoate was recrystallised from ligroin, the *p*-nitrobenzoate was crystallised successively from ligroin, aqueous acetone, and aqueous alcohol, and the anisate was frozen out several times.

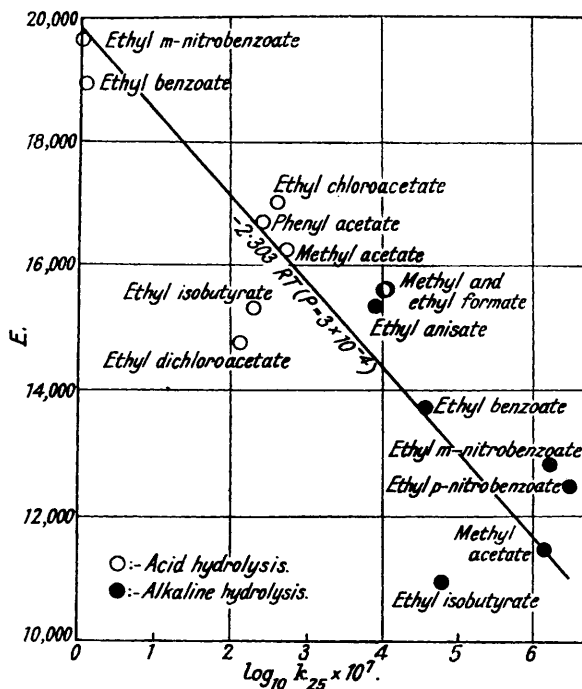
The results are given in the tables. The units are seconds and g.-mol./litre. Table I gives typical results for ethyl *m*-nitrobenzoate, and Table II summarises the values found for all the esters.

TABLE II.

Acid hydrolysis.			Alkaline hydrolysis.		
Ester.	$k_{25^\circ} \times 10^7$.	E , cal.		$k_{25^\circ} \times 10^4$.	E , cal.
Ethyl <i>m</i> -nitrobenzoate ...	1.10	19,600	Ethyl anisate	7.9	15,350
Ethyl benzoate	1.29	18,900	Ethyl benzoate	38.0	13,750
Ethyl dichloroacetate	136	14,750	Ethyl isobutyrate	62.4	11,000
Ethyl isobutyrate.....	210	15,300	Methyl acetate.....	1375	11,500
Phenyl acetate	267	16,700	Ethyl <i>m</i> -nitrobenzoate ...	1715	12,850
Ethyl chloroacetate	382	17,000	Ethyl <i>p</i> -nitrobenzoate ...	3055	12,500
Methyl acetate	549	16,250			
Ethyl formate	10,700	15,600			
Methyl formate.....	10,100	15,600			

DISCUSSION.

Comparison of P for Catalysis by Hydrion and by Hydroxyl Ion.—In the figure, $\log k$ is plotted against E . If the difference between the acid and the alkaline hydrolysis of a given

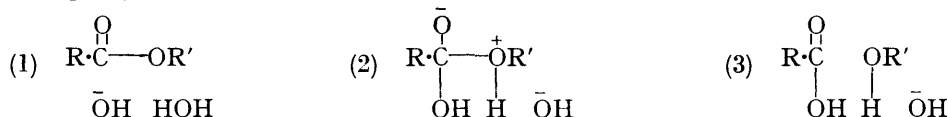


ester is due solely to change in E , the slope of the line joining the points representing the two reactions will have the standard slope $-2.303RT$. From the diagram it appears that the changes in E do, in fact, account in the majority of cases for nearly all the difference, and that, on the average, P is nearly the same for both types. This contrasts with the large difference, in esterification, between the values of P for reactions catalysed severally by hydrion and by an un-ionised acid. This result lends support to the belief that the actual ionic charge is an important factor in determining P .

The common mean value of P for the alkaline and the acid hydrolysis further suggests that the two modes of reaction have an analogous mechanism. Acid hydrolysis must

involve a molecule of water as well as the ester and the acid catalyst, but alkaline hydrolysis might conceivably be formulated as a simple bimolecular interaction of a hydroxyl ion with the ester without the intervention of water. For the latter mechanism we should expect a value of P more nearly equal to unity, as in the reactions of negative ions with halides. The observed value suggests that the intervention of the water molecule is just as necessary in alkaline as in acid hydrolysis.

Polar Effects and the Mechanism of Hydrolysis.—Polar substituents in a benzoic ester greatly influence the rate of alkaline hydrolysis. In agreement with Ingold and Nathan (this vol., p. 222), who used alcoholic solutions, we find that electron sources increase and electron sinks lower the activation energy. An electron sink makes the carbonyl carbon atom more positive and readier to attach a negative hydroxyl ion. The effect of the polar substituents suggests therefore that the stage leading to the addition of the hydroxyl to the carbonyl oxygen is the rate-determining one in which most of the activation energy is required. The results of the last section suggest that the co-operation of a water molecule is also necessary. The water gives a proton to the alkoxy group of the ester and simultaneously liberates a hydroxyl ion, forming a structure which immediately breaks down into alcohol and acid by a simple electronic rearrangement. We thus arrive at the scheme of hydrolysis formulated by Lowry (see Waters, "Physical Aspects of Organic Chemistry," 1935, Chap. 12) :



The next point to consider is the difference between alkaline and acid hydrolysis. According to Lowry's mechanism, the first stage in acid hydrolysis will be the addition of a proton from the acid to the alkoxy oxygen. The formation of such an oxonium ion will probably require little activation energy, and, in contrast with the primary attachment of hydroxyl to carbonyl carbon in alkaline hydrolysis, will not be the rate-determining process, as is shown by the fact that variations in the nature of the alcohol group have little effect on the rate (compare acetate and benzoate, on the one hand, and methyl and phenyl acetates, on the other; Table II). The rate must thus be determined as in alkaline hydrolysis by the addition of hydroxyl to the carbonyl carbon, but, whereas in alkaline hydrolysis free hydroxyl ions are available in high concentration, in acid hydrolysis they must be torn from water molecules. This latter fact probably explains why the activation energy is several thousand calories greater for the acid hydrolysis.

More difficult problems arise in considering the influence of substitution in acid hydrolysis. For example, both the dichloroacetate and the dimethylacetate (*isobutyrate*) show abnormally small values of P , and the activation energies are both smaller than for the acetate. The relatively low value of P might be explained geometrically, and it is understandable that the strongly negative chlorine should lower the activation energy, but it is surprising that the methyl groups should exert their effect in the same direction as chlorine. Steric hindrance cannot explain this, since it would lead to an increase and not a decrease of the activation energy. Analogous difficulties arise in comparing the behaviour of trichloro- and trimethyl-acetic acids in esterification (J., 1935, 1588; cf. also Evans, this vol., p. 785). It may be mentioned that we have also made experiments on the acid hydrolysis of ethyl *p*-nitrobenzoate and ethyl anisate. The rate of reaction of each ester differed from that of the benzoate by a small factor only, but the activation energies appeared to be abnormally low. The anomaly may be specially connected with the influence of para-substitution. The reactions showed no obvious abnormality, but in view of the high temperatures which had to be used (80—140°), we prefer to withhold the data until the absence of disturbing reactions has been more conclusively proved, and the whole question of para-substituents more thoroughly investigated.

Influence of the Solvent.—Comparison of the present results for the alkaline hydrolysis of benzoic esters with those of Ingold and Nathan shows that on passing from 56% acetone to 85% alcohol the activation energy increases by 3000—5000 cal. At the same time P

increases by nearly two powers of ten. Where comparison is possible, the results for both k and E in aqueous acetone appear to correspond more nearly to the values for aqueous solutions.

Correlation of P with Entropy Changes.—Various authors have discussed possible relations between reaction velocity and entropy change. According to Soper (J., 1935, 1393), the value of P might be expected in certain cases to be given by the expression $e^{\Delta S/R}/(1 + e^{\Delta S/R})$, where ΔS is the increase in entropy accompanying the reaction. It is interesting to see how nearly true this is for a given type of reaction.

With methyl acetate, the equilibrium in aqueous acetone was reached at 90% hydrolysis, when the initial concentration was 0.05. It was independent of temperature. This gives $K = 0.405/[H_2O]$. The actual value of $[H_2O]$ in the solvent is 22.2 g.-mols./l. Thus the equilibrium constant is 0.405 or 0.0182, according as the water is regarded as solvent or as reactant. The entropy increase, which is $R \ln K$ since ΔH is negligible, is in the former case -1.79 and in the latter -7.93 . The corresponding values of P from Soper's equation are 0.29 and 0.018 respectively. In deriving the former, the entropy is calculated by taking as the standard state of water, not unit concentration, but its actual concentration in the solvent. Kinetically this would appear to be equivalent to the assumption that water is always available whenever a suitable collision occurs between ester and catalyst, and naturally leads to a value of P greater than that found when water is assumed to be competing on equal terms with the other reactants. The greater value is the one which should correspond to our present experimental conditions. On the assumption that water is always present when hydrion and ester meet, Z of the formula $PZe^{-E/RT}$ is simply the number of collisions between ester and hydrion. By using the ordinary collision formula, and taking σ to be 3.5×10^{-8} cm., the value of P is found to be 3×10^{-4} , which is markedly smaller than that predicted by the formula. A difference of nearly the same magnitude is found with ethyl isobutyrate. But acid hydrolysis of esters involving proton transfers are obviously not the best cases for testing a theory of this sort.

SUMMARY.

The values of P in the equation for the reaction rate, $PZe^{-E/RT}$, have been compared for the acid and for the alkaline hydrolysis of a series of esters in aqueous acetone, the bearing of the results on the theory of hydrolysis being discussed. The mean value of P appears to be approximately the same whether the catalyst is the hydrion or the hydroxyl ion.

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