CLXXVIII.—*The Mechanism of, and Constitutional Factors controlling, the Hydrolysis of Carboxylic Esters. Part III. The Calculation of Molecular Dimensions from Hydrolytic Stability Maxima.*

By Christopher Kelk Ingold.

An important consequence, implicit in the results of modern work on homogeneous catalysis, is the removal, at least for catalysis by acids and bases, of the barrier between the conceptions which formerly were often applied on the one hand to catalysed reactions and on the other to reactions independent of catalysis : since the velocity of a catalysed reaction is affected by the catalyst according to the same laws as those which would apply to an ordinary reactant, it is clearly advantageous to regard the catalyst as occupying the status of an ordinary reactant, for example, in Bronsted's theory of reaction-dynamics (*Z. physikal. Chem.*, 1922, **102**, 169). On this view, a reaction becomes a catalysed reaction when, of the various ways in which the critical complex might decompose, that in which it actually decomposes leads to the formation, as one product, of a substance identical with one of the reactants. Having regard both to modern views on the dynamics of reactions in solution, and to recent work on homogeneously catalysed reactions, the formation of a critical complex between an ester group and a catalyst may, without inevitable commitment to any precise constitutional inference, justifiably be regarded as the initial process in the hydrolysis of a carboxylic ester.

Any general discussion of the factors controlling the speed of hydrolysis of an ester by a catalyst must include consideration of (*a*) statistical requirements, (*b*) polar influences, (*c*) steric factors, and (*d*) effects due to the medium.

(*a*) *Statistical Requirements.*—Count must be taken of statistical requirements when either the ester or the catalyst has alternative seats of reaction, but discussion will here be restricted to cases in which the existence of alternative reactions is due solely to the constitution of the ester.

The formulation of statistical effects on the relative rates of the successive stages in the hydrolysis of a polycarboxylic ester by a single catalyst at constant temperature may be effected by consideration of a compound with s ester groups so situated that the hydrolysis of each proceeds independently of the others. In general, the probability that a catalyst molecule or ion will form a complex with a particular ester group will, for constitutional reasons, be different for each ester group. Let v_q be the catalytic coefficient for the

partial reaction consisting of the hydrolysis of the gth group in the first stage of hydrolysis, and let k_n be the total catalytic coefficient for the nth stage. Then $k_1 = \Sigma v_g$, where the summation extends from 1 to s. In order to calculate k_2, two points must be noted; the first is that, since the fraction of the total quantity of ester which passes on to the second stage of hydrolysis through the gth first-stage product is $v_g/\Sigma v_g$, the contribution to k_2 made by the hydrolysis of the hth ester group in this product is $v_g v_h/\Sigma v_g$; the second is that the s first-stage products yield $s(s - 1)/2$ second-stage products, each of the latter being formed from two of the former. It follows that $k_2 = 2\Sigma v_g v_h/\Sigma v_g$, where the summations extend from 1 to s as before, except that h is excluded from identity with g. Generalising, it is seen that each of the $_sC_n$ products of the nth stage of hydrolysis is formed in n ways, and that $k_n = n\overset{s}{\Sigma}v^{(n)}/\overset{s}{\Sigma}v^{(n-1)}$, where $\overset{s}{\Sigma}v^{(n)}$ is the sum of all the products of n different v's, so that, in particular $\overset{s}{\Sigma}v^{(1)} = \Sigma v_g$ and $\overset{s}{\Sigma}v^{(0)} = 1$. The statistical relation between the velocities of any two stages is therefore

$$\frac{k_m}{k_n} = \frac{m\overset{s}{\Sigma}v^{(m)} \cdot \overset{s}{\Sigma}v^{(n-1)}}{n\overset{s}{\Sigma}v^{(n)} \cdot \overset{s}{\Sigma}v^{(m-1)}} \quad \cdots \cdots \quad (1)$$

In the special case of a dicarboxylic ester, for which $s = 2$, $m = 1$, and $n = 2$, equation (1) becomes

$$k_1/k_2 = (v_1 + v_1)^2/2v_1v_2 \quad \cdots \cdots \quad (2)$$

Furthermore, if the dicarboxylic ester is symmetrically constituted, so that $v_1 = v_2$, this equation reduces to

$$k_1/k_2 = 2 \quad \cdots \cdots \cdots \quad (3)$$

The application of equations (2) and (3) may be illustrated by reference to data by J. Meyer (Z. physikal. Chem., 1909, **66**, 81) for the acid hydrolysis of five dicarboxylic esters (Table I).* In the case of methyl camphorate v_1 and v_2 were independently determined by direct observation on the isomeric methyl hydrogen camphorates.

TABLE I.

Hydrolyte.	Temp.	$v_1 \times 10^3.$	$v_2 \times 10^5.$	$k_1 \times 10^3.$	$k_2 \times 10^5.$	$k_1/k_2.$	$k_1/k_2.$ (calc.).
Methyl succinate	25°	—	—	2·40	121	1·98	2·00
Ethyl succinate	,,	—	—	2·30	121	1·90	2·00
Methyl d-tartrate	,,	—	—	1·24	62	2·00	2·00
Ethyl d-tartrate	,,	—	—	1·40	68	2·06	2·00
Methyl d-camphorate	45	1·54	3·1	1·50	6·1	24·6	25·9

Meyer was the first empirically to observe that the ratios k_1/k_2 for the two-stage acid hydrolysis of symmetrical dicarboxylic esters

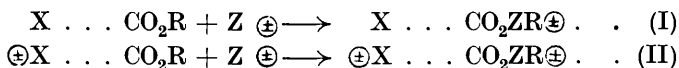* As to units, see footnote in Part I (this vol., p. 1032).

are often closely grouped about the value 2. Wegscheider (*Monatsh.*, 1915, **36**, 471) discussed the dynamical significance of this relation, noting especially that it is a peculiarity of the value 2 that the complete reaction may be represented by an integrated equation of one of the simple forms applicable to a single-stage process. Meyer's result shows clearly that, when carbomethoxyl or carbethoxyl groups are separated by a saturated chain of at least two carbon atoms, the speed of hydrolysis of each group is very nearly independent of the state of hydrolysis of the other; but this approximation would be expected to hold less exactly for malonic and oxalic esters and for completely conjugated unsaturated esters (*e.g.*, fumaric, phthalic) owing to the intramolecular transmission of polar effects; and departures are also to be expected amongst esters of higher alcohols and compounds with endocyclic ester groups (*e.g.*, adipodilactone) owing to spatial influences. Since later workers have usually side-stepped the accurate determination of the coefficients for the consecutive stages by regarding a more or less imperfect conformity with Wegscheider's simplified formulæ as sufficient indication that k_1/k_2 is in the neighbourhood of 2, it is not yet known to what degree of approximation Meyer's result is applicable to the classes of esters mentioned. There are indications (Palomaa, *Ann. Acad. Scient. Fennicæ*, 1917, *A*, **10**, No. 16; Skrabal, *Monatsh.*, 1917, **38**, 29) that it is at least approximately applicable to oxalic and malonic esters as well as to their higher normal homologues.

Meyer noticed (*Z. physikal. Chem.*, 1909, **67**, 257) that equation (3) does not even roughly represent the alkaline hydrolysis of symmetrical dicarboxylic esters, and, indeed, this is apparent from the still earlier work of Knoblauch (*ibid.*, 1898, **26**, 96), whose coefficients for ethyl succinate bear the ratio 9·4, and of Goldschmidt and Scholz (*Ber.*, 1903, **26**, 1333), whose values for ethyl malonate give the ratio 88. Meyer remarked that this notable difference between acid and alkaline hydrolysis is probably connected with the fact that in the latter case the ester which undergoes the second stage of the reaction is an ion.

(b) *Polar Effects.*—Influences arising from the polar characteristics of the ester and catalyst may be propagated to the seat of reaction both externally (through the medium-filled space) or internally (through the linkings), and in both cases an ionic centre, if present, will dominate the situation. In the commonly employed ionic catalysts the pole itself is the reactive centre, but in esters which are also ions the pole is necessarily separated from the seat of reaction, and it is for this case, therefore, that the *propagation* of the effect of the pole requires consideration. Furthermore,

internally propagated polar effects become very small after transmission through more than two single linkings (Gane and Ingold, J., 1929, 1692, and cited references); it is therefore evident that a large class of cases must exist in which the externally propagated polar effect is for practical purposes the sole polar influence.

A basis for the calculation of the externally propagated effect is available in several well-known theoretical investigations—e.g., Langevin's calculations relating to a paramagnetic gas, Debye and Hückel's treatment of the effect of interionic attraction on the activity of strong electrolytes, and especially Bjerrum's investigation of the problem presented by the strengths of polybasic acids—the common feature of all of which is the employment of Boltzmann's law. Consider two esters which are identical in all respects, except that, in some position X, the second ester has a univalent positive or negative charge not possessed by the first ester; and suppose that these esters are being hydrolysed at the same temperature by the same catalyst, which also possesses a univalent positive or negative charge. The catalytic coefficients, k' and k'', of the two reactions may for the present be assumed (see Section d, however) to be proportional to the mass-action rates of formation of the corresponding critical complexes :

$$X \ldots CO_2R + Z \oplus \longrightarrow X \ldots CO_2ZR\oplus \quad . \quad . \quad (I)$$
$$\oplus X \ldots CO_2R + Z \oplus \longrightarrow \oplus X \ldots CO_2ZR\oplus \quad . \quad . \quad (II)$$

The external molecular electric field of the first ester will render the local concentration of $Z\oplus$ in the neighbourhood of the ester group different from its macrochemical concentration, and this will be one of the ways in which the effect exerted by polar influences on the rates of hydrolysis of esters (compare Part I, this vol., p. 1032) enters into the determination of the velocity coefficient. The external electric field of a molecule of the second ester may be regarded as equal to that due to an identically placed molecule of the first ester *plus* the radial field of a unit positive charge situated at X. This being so, Boltzmann's theorem shows that the ratio of the local concentration of $Z\oplus$ in reaction (II) to its local concentration in reaction (I) is $\exp(-WN/JRT)$, where W is the work done *against the radial field alone* when $Z\oplus$ is brought from a great distance to the focus of reaction, N is Avogadro's number, and J is the mechanical equivalent of heat. If r is the distance between the unit charge at X and the focus of reaction, W is equal to $\pm e^2/\varepsilon r$, where e is the charge of an electron, ε is the dielectric constant of the medium, and the upper or lower sign is taken according as the signs of the charges on X and Z are like or unlike. With $e = 4\cdot774 \times 10^{-10}$, $\varepsilon = 80\cdot0$, $N = 6\cdot06 \times 10^{23}$, $J = 4\cdot19 \times 10^7$, $R = 1\cdot985$, and $T =$

298, the exponent has the value $\mp 6.97 \times 10^{-8}/r$; and since the ratio of the local concentrations is also the ratio of the rates of formation of the critical complexes,*

$$k'/k'' = \exp(\pm 6.97 \times 10^{-8}/r) \approx \exp(\pm 7/10^8 r) \quad . \quad . \quad (4)$$

If it is legitimate to assume that in the anion of a partly hydrolysed polycarboxylic ester the external field of each carboxylate ion can, at all distances greater than that of the nearest unhydrolysed ester group, be represented as the vector sum of that of a similarly situated carboxylic ester group and that of a superposed electron, equation (4) may be used to take count of the effect, on each stage after the first in the alkaline hydrolysis of polycarboxylic esters, of externally propagated polar fields : in these reactions the catalyst is a negative ion, and each stage of hydrolysis introduces a new negative charge into the ester molecule.   Introduction of the requisite modification into equation (1) gives the relation

$$\frac{k_m}{k_n} = \frac{m\overset{s}{\Sigma}\{v^{(m)}\rho^{(nC_2)}\} \cdot \overset{s}{\Sigma}\{v^{(n-1)}\rho^{(n-1}C_2)\}}{n\overset{s}{\Sigma}\{v^{(n)}\rho^{(mC_2)}\} \cdot \overset{s}{\Sigma}\{v^{(m-1)}\rho^{(m-1}C_2)\}} \quad . \quad . \quad . \quad (5)$$

where ρ is written for $\exp(-6.97 \times 10^{-8}/r)$, $\rho^{(nC_2)}$ is the product of the $_nC_2$ values of ρ corresponding with the $_nC_2$ distances, r, between n ester groups taken in pairs, and brackets $\{\}$ signify that the product of each group of v's is to be multiplied by the corresponding ρ-product before summation.   The equation for the ratio of the velocities of the stages of hydrolysis of a dicarboxylic ester is obtained from (5) by writing $s = 2$, $m = 1$, and $n = 2$, and remembering that if $n < 2$ then $\rho^{(nC_2)}$, being the product of zero ρ's, is unity :

$$\frac{k_1}{k_2} = \frac{(v_1 + v_2)^2}{2\rho v_1 v_2} = \frac{(v_1 + v_2)^2}{2v_1 v_2} \exp\left(\frac{6.97 \times 10^{-8}}{r}\right) . \quad . \quad (6)$$

For the special case of a symmetrically constituted dicarboxylic ester, $v_1 = v_2$, and equation (6) reduces to

$$k_1/k_2 = 2/\rho = 2 \exp(6.97 \times 10^{-8}/r) \approx 2 \exp(7/10^8 r) . \quad . \quad (7)$$

Table II contains all the recorded *direct* measurements of the coefficients characterising the catalysis by hydroxide ions of the consecutive stages of hydrolysis of esters of dicarboxylic acids (some measurements on hydrolysis in alkaline buffer solutions are also available and these are considered in Section d).   The data here tabulated refer to eleven esters of seven normal dicarboxylic acids. The experimental values of k_1 and k_2 are given in cols. 3 and 4, and all relate to the temperature $25°$ except the two indicated by asterisks for which the temperature is $22.7°$.   Cols. 5 and 6 contain the values

* The activity correction, which is here neglected, is considered in Section (d).

of k_1/k_2, which are seen to be nearly identical for methyl and ethyl esters of the same acid. Col. 7 shows the values of the distance, r, between the carboxyl groups (*i.e.,* between the charge developed on one carboxyl group and the focus of reaction at the other) as calculated from equation (7). It will be seen (*a*) that the distances are of the right order of magnitude (1—20 Å.U.), (*b*) that they place the compounds in the order of the length of the carbon chain, (*c*) that, having regard to the difference of method, they are in fair general agreement with the distances obtained by Gane and Ingold for the corresponding free acids (J., 1928, 1594); these distances are given in the last column for comparison.

TABLE II.

Hydrolyte.		Ref.	k_1.	k_2.	k_1/k_2.	k_1/k_2. (mean).	$r \times 10^8$ (cm.).	$r \times 10^8$ (cm.), G. & I.
Oxalate	methyl	4	ca. 10^6	ca. 10^2	10^4	10^4	1	—
	ethyl	5	ca. $10^{5 \cdot 5}$	ca. $10^{1 \cdot 5}$	10^4			
Malonate	methyl	3	170	1·84	92	91	1·8	1·5
	ethyl	{ 2	112	1·27	88			
		{ 3	136	1·46	93			
Succinate	methyl	{ 3	20·5	2·10	9·8	9·7	4·4	{ 5·0
		{ 6	26·0	2·80	9·4			{ 4·9†
	ethyl	{ 1	13·8*	1·46*	9·4			
		{ 3	16·5	1·59	10·4			
Glutarate	methyl	6	21·6	3·16	6·8	6·4	6·0	9·2
	ethyl	6	10·0	1·63	6·1			
Suberate	methyl	6	1·53	0·49	3·1	3·1	15	14·5
Azelate	methyl	6	1·24	0·42	2·95	2·95	17·5	17
Sebacate	methyl	6	·1·20	0·43	2·8	2·8	20	—

References : (1) Knoblauch, *loc. cit.*; (2) Goldschmidt and Scholz, *loc. cit.*; (3) J. Meyer, *Z. physikal. Chem.*, 1909, **67**, 257; (4) Skrabal, *Monatsh.*, 1917, **38**, 29; (5) Skrabal and Matievic, *ibid.*, 1918, **39**, 765; (6) Skrabal and Singer, *ibid.*, 1920, **41**, 339.

† Calculated by Gane and Ingold from data by Auerbach and Smolczek.

In explanation of the approximate values for the oxalic esters, it should be stated that the only directly determined value is k_2 for the methyl ester; for this the value 92 was found, but the time intervals were so short that the second figure is not significant. The same ester was also hydrolysed in carbonate buffers and from these experiments an apparent value of k_2 can be calculated and compared with the directly observed value. This comparison then affords the means of estimating the true value of k_2 for ethyl oxalate from the apparent values derived from similar measurements in buffers. Of the values of k_1 for methyl and for ethyl oxalate, all that can be said is that they are of the order of a million and that k_1 is about three times as great for the methyl as for the ethyl ester. All the other values of k_1 and k_2 recorded in the table represent direct determinations.

The preceding calculations neglect the internally propagated effect of the carboxylate pole, and this is expected to make the calculated

distances for oxalic and malonic esters too small; a similar error would probably affect completely conjugated unsaturated esters, such as maleic, fumaric, phthalic, and terephthalic esters, although none of these has as yet been investigated by the direct method (compare Section *d*, however); internally propagated effects should be entirely negligible in esters higher than succinic esters (Gane and Ingold, J., 1928, 1691). Furthermore, the catalytic ion has been treated as a point-charge, whereas any actual ion must become dipolarised as it approaches the charged ester molecule; this effect is expected to render the calculated distances too large throughout the series considered, and solvation, including pole–dipole association, is a form of dipolarisation which it would be necessary to envisage in any complete discussion of this disturbance. It should also be pointed out that no account has explicitly been taken of the circumstance that even in alkaline solution the electrically neutral alkyl hydrogen ester must exist as such to a minute extent, and that part of the second stage of alkaline hydrolysis of dicarboxylic esters must proceed through this form. The error due to this cause is very easy to evaluate, but it is entirely negligible in all the cases for which the writer has made the appropriate calculation; there is no point, therefore, in encumbering the equations with terms intended to eliminate this effect.

(c) *Steric Hindrance.*—It is necessary now to give attention to the circumstance that the whole of the space in the neighbourhood of a reacting centre is not *free* space in the sense envisaged by the kinetic theory, on which Boltzmann's theorem depends; in short, the effect of steric hindrance must be considered.

A basis for the discussion of this influence is furnished in Part I of this series (this vol., p. 1032) in which it was shown that velocities of hydrolysis can be represented as a simple function of polarity on the assumption that the effect of steric hindrance on the catalytic coefficients is expressible as the product of two factors C and S respectively dependent on the catalyst alone and the ester alone : if p is a catalytic coefficient (it was called k^p in Part I), which is corrected in such a way as to be independent of the variability of the purely steric influences which affect in different degrees the hydrolysis of each of a series of esters by each of a series of catalysts, then the uncorrected catalytic coefficient k is equal to CSp. Reverting to reactions (I) and (II), and introducing suffixes to indicate the sign of Z, the preceding relation shows that

$$k'_+ = C_+ S' p'_+, \quad k''_+ = C_+ S'' p''_+, \quad k'_- = C_- S' p'_-, \quad k''_- = C_- S'' p''_-,$$

and that, consequently,

$$\frac{k'_- / k'_+}{k''_- / k''_+} = \frac{p'_- / p''_-}{p'_+ / p''_+} \quad . \quad . \quad . \quad . \quad . \quad (8)$$

3 A 2

From the foregoing it will be clear that the k-ratio on the left hand side of equation (4) should really be a p-ratio, wherefore, having regard to equation (8), the equation which takes account of both polar and steric influences may be written

$$\frac{k'_-/k'_+}{k''_-/k''_+} = \exp(\mp 13\cdot94 \times 10^{-8}/r) \approx \exp(\mp 14/10^8 r) \quad . \quad . \quad (9)$$

where the upper or lower sign of the exponent is taken according as the charge on X is positive or negative in reaction (II).

In applying equation (9) to the stage-wise hydrolysis of a polycarboxylic ester, the assumption must be made that the space occupied by a carboxylate ion is equal to that filled by an undissociated carboxyl group, or at least, that it differs therefrom by a much smaller amount than that by which it differs from the space occupied by an esterified carboxyl group. Introduction of the appropriate modification into equation (5) gives the equation

$$\frac{k_{m-}/k_{n-}}{k_{m+}/k_{n+}} = \frac{\Sigma\{v_-^{(m)}\rho^{(_mC_2)}\} \cdot \Sigma\{v_-^{(n-1)}\rho^{(_{n-1}C_2)}\} \cdot \overset{s}{\Sigma}v_+^{(n)} \cdot \overset{s}{\Sigma}v_+^{(m-1)}}{\Sigma\{v_-^{(n)}\rho^{(_nC_2)}\} \cdot \Sigma\{v_-^{(m-1)}\rho^{(_{m-1}C_2)}\} \cdot \overset{s}{\Sigma}v_+^{(m)} \cdot \overset{s}{\Sigma}v_+^{(^{1}-1)}} \quad . \quad . \quad (10)$$

For a dicarboxylic ester equation (10) reduces to the simple form

$$\frac{k_{1-}/k_{2-}}{k_{1+}/k_{2+}} = \frac{v_{1+}v_{2+}(v_{1-} + v_{2-})^2}{\rho v_{1-}v_{2-}(v_{1+} + v_{2+})^2} \cdot \quad . \quad . \quad . \quad (11)$$

The equation for a symmetrically constituted dicarboxylic ester is obtained from (11) by equating v's of like suffix-sign. For hydrolysis by hydrogen and hydroxyl ions the equation is

$$\frac{(k_1)_{OH}/(k_2)_{OH}}{(k_1)_H/(k_2)_H} = \frac{1}{\rho} = \exp(6\cdot97 \times 10^{-8}/r) \approx \exp(7/10^8 r) \quad . \quad (12)$$

This is the equation from which the values of r given in col. 7 of Table II were originally calculated; but since, to the accuracy with which $(k_1)_H/(k_2)_H$ is known for the esters of oxalic acid and its normal homologues, this ratio has the value 2·0 (Palomaa), the figures are identical with those obtained from the simpler, but less theoretically defensible, equation (7).

It is not theoretically necessary that *both* the stages in the hydrolysis of a dicarboxylic ester should be investigated in order that r may be calculated : a suitable study of the second stage of hydrolysis, that is, of the hydrolysis of the acid ester only, would enable equation (9) to be directly applied. The case of acid esters is strictly comparable with that of amino-esters, and, since both forms represent the simplest types of *ionogenic* esters, they may be considered together. It can readily be shown that the curve connecting the velocity of hydrolysis of an acid ester with the hydrion concentration should,

after effects due to any buffers employed have been eliminated (Part II, this vol., p. 1039), correspond to the equation

$$v = \left\{ [H]v'\left(\frac{[H]}{H'} + \frac{H'}{[H]}\right) + K_a v''\left(\frac{[H]}{H''} + \frac{H''}{[H]}\right) \right\} \Big/ 2(K_a + [H]) \quad (13)$$

Similarly the curve for the hydrolysis of a basic ester should be represented by the equation

$$v = \left\{ K_w v'\left(\frac{[H]}{H'} + \frac{H'}{[H]}\right) + K_b [H]v''\left(\frac{[H]}{H''} + \frac{H''}{[H]}\right) \right\} \Big/ 2(K_w + K_b[H]) \quad (14)$$

In these equations K_a and K_b are the so-called affinity constants of the acid and base respectively, and K_w is the ionic product for water. The four quantities, H', H'', v', and v'', are constants which have to be determined from the velocity data themselves, and the significance of the first two of these is that they are the hydrion concentrations at which the neutral and charged species respectively would show a velocity minimum if conversion into the other form could be prevented. Denoting the corresponding p_H's by p_H' and p_H'', and remembering the general relation $\log (k_{OH}/k_H) = -2p_H{}^* - \log K_w$, where $p_H{}^*$ is the p_H of maximal hydrolytic stability, the appropriate application of equation (9) gives

$$p_H' - p_H'' = \pm\, 3\cdot03 \times 10^{-8}/r \approx \pm\, 3/10^8 r . \quad . \quad . \quad (15)$$

where the sign must be chosen to correspond with that of the charge developed on the ionogenic ester.

Suitable data for the evaluation of both p_H' and p_H'' by the application of equations (13) and (14) are not yet available, but in the case of ethyl aminoacetate data leading to an approximate value for p_H'' are on record; the figure thus obtained is not very accurate owing to the absence of data permitting the elimination of buffer effects. The value of p_H' cannot be similarly obtained, but, in accordance with the principles discussed in Part I (*loc. cit.*), it may be interpolated between the values of $p_H{}^*$ for ethyl propionate and ethyl glycollate, both of which are accurately known; the probable uncertainty attending this procedure is unlikely to be much greater than that which relates to the directly measured value of p_H'' in the absence of a correction for buffer effects, and is of the order of $0\cdot1$ p_H unit. There is a small difference in the temperatures to which p_H' and p_H'' apply, but it is negligible in the circumstances. These data are assembled in Table III, and it will be seen that the distance r for $\overset{\oplus}{N}H_3 \cdot CH_2 \cdot CO_2Et$ is practically the same as for $\overset{\ominus}{C}O_2 \cdot CH_2 \cdot CO_2Et$ ($1\cdot8 \times 10^{-8}$ cm.); owing to the structural similarity both values are probably subject to the same disturbances.

TABLE III.

Hydrolyte.	Ref.	Temp.	p_H*.	Δp_H*.	r (cm.).
Ethyl aminoacetate	1	25°	5·3 ⎫		
Ethyl ammonium acetate ...	2	20	3·5 ⎭	1·8	1·7 × 10⁻⁸

References: (1) Bolin, *Z. anorg. Chem.*, 1925, **142**, 201; (2) van Dijken, *Rec. trav. chim.*, 1895, **14**, 106; Findlay and Hickmans, J., 1909, **95**, 1010; Denshel and Dean, *Amer. J. Sci.*, 1912, **34**, 293; 1913, **35**, 486; Dean, *ibid.*, 1913, **35**, 605; 1914, **37**, 331; Taylor, *Medd. K. Vetenskapsakad. Nobel-inst.*, 1913, **2**, No. 34; Palomaa, *Ann. Acad. Scient. Fennicæ*, 1913, A, **4**, No. 2; 1914, A, **5**, No. 4; Lamble and Lewis, J., 1914, **105**, 2330.

(d) *Effects due to the Medium.*—Consideration has not yet been given to possible disturbances due to the medium. The expected disturbances are of two kinds.

(1) The dielectric constant of water containing both electrolytes and non-electrolytes will only be approximately equal to that of pure water even at the considerable dilutions to which the measurements in Table II relate; the non-electrolytic solutes would tend to decrease the constant, whilst the electrolytes might decrease it or increase it according to their concentration (Debye). The consideration of this effect involves no new principle and an appropriate correction could readily be introduced if the requisite data were available.

(2) For solutions of considerable ionic strength, the relation, $v = kC_A C_B$, hitherto used, requires a correction which, according to Brønsted (*loc. cit.*), is represented by $f_A f_B / f_{AB}$ in the equation $v = kC_A C_B f_A f_B / f_{AB}$. This equation shows that, whilst the simpler equation should be valid for the hydrolysis of neutral esters by ions, the velocity of ion-catalysed hydrolysis of ionic esters will increase or decrease with increasing ionic strength (μ) according as the charges on the reactants are like or unlike in sign. In the second stage of the hydrolysis of a dicarboxylic ester the charges are of like sign, and hence the velocity should increase with increasing ionic strength. In order to show that this effect is not negligible, Table IV is appended, the data in which are taken from Skrabal and Singer's published results.

TABLE IV.

Hydrolyte.	Catalyst.	Inert salt.	μ (initial).	k.
NaO₂C·CO₂Me	Na₂CO₃	—	0·40	1·8 ⎫
,,	,,	0·40 N-NaCl	0·80	2·1 ⎭
NaO₂C·(CH₂)₂·CO₂Me	NaOH	—	0·004	2·8 ⎫
,,	,,	—	0·032	3·4 ⎬
,,	,,	—	0·040	3·9 ⎭

Now, assuming for the moment that only univalent anions are under consideration, the formulæ already developed for the ratio, k_{1-}/k_{2-}, obtaining in the two-stage hydrolysis of a dicarboxylic ester,

show that this ratio should be independent of the nature of the catalysing anion, provided that the concentration is so low that the ionic-strength disturbance is negligible. This condition is very approximately fulfilled in the hydrolysis with sodium hydroxide for which the ionic strength is 0·01 or less; but when buffer solutions are employed the ionic strength is usually of the order 0·1—1·0. In the complete hydrolysis of a dicarboxylic ester in alkaline buffers, the first stage escapes the ionic-strength effect, but the second stage is subject to it, and thus the values of k_{1-}/k_{2-} obtained by the use of buffers are rendered too low. Against this must be set the circumstance that some small part of the total hydrolysis will undoubtedly be effected, not by hydroxide ions, but by the buffer anions themselves, and if these are more than univalent—and carbonate–bicarbonate buffers have usually been employed—the higher valency will create an effect tending to make k_{1-}/k_{2-} too large. The general conclusion must, therefore, be that little reliance can be placed on anything but the order of magnitude of this ratio when it is deduced from experiments with buffers; nevertheless, in order to complete the survey of existing relevant data, the values of the ratio, which are deduced from measurements with carbonate–bicarbonate buffers, are given in Table V for those esters which have been studied in this way. The values of r calculated from equation (7) are in the last column. When data become available for the activity coefficients of the electrolytes and the catalytic coefficients of the buffer anions, it should be possible to correct these values; in the meantime it is seen that, where comparison can be made with r-values based on direct determinations of the k-ratio, the agreement is poor to moderate. A clear illustration of the importance of the ionic-strength effect appears in the values for methyl d-tartrate and methyl racemate, for the hydrolysis of which carbonate–bicarbonate buffers of two concentrations have been employed; it will be noticed that when the ionic strength at the commencement of reaction is increased from about 0·05 to about 0·5, the value of k_1/k_2 falls by 30%.

Finally it may be pointed out, first, that since the maleic and fumaric esters were hydrolysed by buffers of similar concentration, the error in r caused by ionic-strength effects is probably similar in both cases, and, secondly, that, although, as explained in Section (b), internally transmitted polar effects will make the r-values too small, the type of conjugation which gives rise to this result is the same for both esters, wherefore the disturbances will probably be nearly the same. Since a little further consideration readily shows that the necessary corrections, which although unknown are presumed to be nearly equal, would be represented by *factors*, and not differences, it follows that the ratio, $r_{\text{fumaric}}/r_{\text{maleic}}$, should be subject, certainly to

TABLE V.

		Measurements in buffers.			From Table II
Hydrolyte.	Ref.	μ (initial).	k_1/k_2.	$r \times 10^8$ (cm.).	$r \times 10^8$ (cm.).
Methyl malonate	1	0·50	73	1·9	1·8
Ethyl malonate	1	0·50	67	2·0	1·8
Methyl succinate	1	0·45	4·7	8·2	4·4
Methyl maleate	3	0·07	67	2·0	—
Methyl fumarate	3	0·05	22	2·9	—
Methyl d-tartrate ......$\left\{\vphantom{\begin{array}{c}a\\b\end{array}}\right.$	2	0·55	14·7	3·5	—
	4	0·06	19·5	3·1	—
Methyl l-tartrate	4	0·06	20	3·0	—
Methyl racemate ......$\left\{\vphantom{\begin{array}{c}a\\b\end{array}}\right.$	4	0·55	14	3·6	—
	4	0·06	20	3·0	—
Methyl mesotartrate ...	4	0·06	28	2·7	—

References : (1) Skrabal and Singer (*loc. cit.*); (2) *idem, Monatsh.*, 1919, **40**, 363; (3) Skrabal and Reith, *ibid.*, 1921, **42**, 245; (4) Skrabal and Hermann, *ibid.*, 1922, **43**, 633.

less error than are the separate r's, and probably to a small error only. It is seen from the table that this ratio is 1·45. Now the same ratio can readily be calculated from the molecular model on the basis of certain assumptions. The assumptions which seem best to conform to existing knowledge of the structures and reactions involved are as follows : (1) The distance between the centres of singly linked carbon atoms is 1·52 Å.U., that is, the value obtaining both for the diamond and for the distance between nuclear and side-chain carbon atoms in hexamethylbenzene. (2) The distance between the centres of doubly linked carbon atoms is 1·35 Å.U., this value being adopted on the ground that the aromatic ortho-distance given by X-ray measurements on graphite and hexamethylbenzene probably approximates to the mean of the distances characteristic of singly and doubly linked atoms. (3) Since the carboxyl group is a symmetrical prototropic system, the charge is symmetrically distributed in the carboxylate ion, and its centre of gravity is therefore at the bisection of the line joining the centres of the oxygen atoms, that is, about 0·7 Å.U. from the carbon centre in line with the carbon–carbon bond. (4) In *alkaline* hydrolysis the attack is at the surface of the carbon atom, the mean focus being about 0·7 Å.U. from the carbon centre in line with the carbon–carbon bond. (5) The angle between the directions of the single linkings of an ethenoid carbon atom is 120° (compare Beesley, Ingold, and Thorpe, J., 1915, **107**, 1080). On the basis of these assumptions, the ratio $r_{\text{fumaric}}/r_{\text{maleic}}$ should be 1·47, and almost any reasonable modification of them leads to values between 1·4 and 1·5.

THE UNIVERSITY, LEEDS. [*Received, April 24th*, 1930.]