CCCCXXIX.—*The Saponification of Di-esters.*

By MOWBRAY RITCHIE.

CATALYTIC hydrolysis by hydrochloric acid of dialkyl esters such as ethyl succinate or tartrate is a two-stage process, in which the velocity coefficient for the first stage is almost exactly double that for the second stage. By reason of this integral relationship, the reaction is pseudo-unimolecular, and can be represented by the ordinary unimolecular reaction formula, where the characteristic constant so obtained can be shown mathematically to be a function of the velocity coefficients of both reaction stages (Meyer, *Z. physikal. Chem.*, 1909, **66**, 81, 98).

For the saponification by alkali of such substances as glycol diacetate or glycerol triacetate, the rate of removal of alkali as sodium salt can be similarly explained on the assumption that for the former ester the velocity coefficient for the first stage is double that for the second. Similarly, the ratios of the corresponding velocity coefficients for the glycerol compounds under such conditions are 3 : 2 : 1 (Meyer, *ibid.*, 1909, **67**, 272).

These simple relationships do not apply, however, to the saponification by alkali of the dialkyl esters of dibasic acids. With ethyl succinate, for example, the first reaction involves the negatively charged hydroxyl ion and the neutral ester, whereas the second reaction now involves the same ion and the negatively charged anion of the sodium ethyl succinate. The ratio of the first velocity coefficient to the second will in all probability be greater than 2, owing to the mutual repulsion of the negative ions in the second stage, and will indeed be dependent on the structure and polar nature of the acid anion (compare Gane and Ingold, J., 1928, 10).

Although indications of the relative values of these velocity coefficients can be obtained from a study of the methods employed in the preparation of the mono-esters (compare Walker, J., 1892, **61**, 708), yet apparently no complete mathematical formula has been developed by which the first coefficient k_1 can be accurately determined in a way analogous to the application of the ordinary bimolecular formula to the second reaction. In certain suitable cases, the second reaction can be neglected in the initial stages, and the primary reaction neglected in the final stages, by which approximate values can be obtained. Knoblauch (*Z. physikal. Chem.*, 1898, **26**, 96) calculated on this basis the composition at the intermediate stages in the saponification of various di-esters; the agreement was such that the general principles of two-stage hydrolysis were regarded as experimentally verified. Meyer (*Z. physikal.*

Chem., 1909, **67**, 257; compare von Peskoff and Meyer, *ibid.*, 1913, **82**, 129) attempted a complete mathematical analysis of the problem, but no general method for the determination of k_1 was obtained except for the very limited number of cases where k_1 is a simple integral multiple of k_2. The importance of an accurate knowledge of the k_1/k_2 ratio under such conditions has recently been emphasised by Ingold (this vol., p. 2170) by its application to the determination of the distance between a point in the charged carboxylate group and a point in the neutral carboxylate group of the ester anion. The method of measurement again involves successive approximations. In the present communication a general method is developed in which such approximation is not required. The equations have been applied in two ways in the case of ethyl succinate in aqueous solution, alcoholic solution, and solutions containing alcohol and water in the molecular proportion 1 : 1. The temperatures concerned were 25°, 15°, and 0°. Similar determinations have been carried out on the unsubstituted ethyl malonate, and on ethyl methylmalonate, dimethylmalonate, and diethylmalonate, to explain as far as possible the different methods necessary for the production of the half-ester in each case, with special reference to the three-carbon system of the malonic esters.

Derivation of Formulæ.

The following considerations are based on the applicability of the mass-action law, the active mass being regarded as the concentration of the reacting substance (the conditions under which this may be considered to apply are considered later).

The reactions are

$$(\alpha)\ R(CO_2Et)_2 + NaOH = R(CO_2Na)(CO_2Et) + EtOH,$$
$$(\beta)\ R(CO_2Na)(CO_2Et) + NaOH = R(CO_2Na)_2 + EtOH.$$

Let the velocity coefficient of the reaction (α) be k_1 and that for the second reaction k_2. At the beginning of the reaction, at time $t = 0$, let the concentration of di-ester be A, and that of the alkali, [NaOH], be B. At any other time t, let the concentrations be represented as follows:

$$[R(CO_2Et)_2] = A - x \qquad [R(CO_2Na)(CO_2Et)] = y$$
$$[NaOH] = B - w\ . \qquad [R(CO_2Na)_2] = z$$

By consideration of the amount of alkali (w) used in production of the mono-ester (y) and disodium salt (z), it follows that $x = y + z$, and $w = y + 2z$, whence

$$y = 2x - w \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The differential equations are then

$$d(A - x)/dt = - dx/dt = - k_1(A - x)(B - w) \quad . \quad . \quad (2)$$

and

$$dy/dt = dx/dt - k_2y(B - w) \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The problem is to eliminate x and y, in order to obtain a relationship between A, B, k_1, k_2, w, and t.

From equation (3), $d(x - y)/dt = k_2(B - w)y$, and by applying equation (2), $d(x - y)/dx = k_2y/k_1(A - x)$, or $1 - dy/dx = k_2y/k_1(A - x)$. Substituting $v = y/(A - x)$, we have

$$k_1 . dv/[k_1 + (k_1 - k_2)v] = dx/(A - x),$$

whence, on integration and employment of the initial conditions, $x = y = 0$ when $t = 0$,

$$\frac{k_1}{(k_1 - k_2)} . \log [k_1 + (k_1 - k_2)v] = \log \frac{A}{(A - x)} + \frac{k_1}{(k_1 - k_2)} . \log k_1.$$

Since $v = y/(A - x)$, it follows that

$$\frac{k_1}{(k_1 - k_2)} . \log \left[1 + \frac{(k_1 - k_2)}{k_1} . \frac{y}{(A - x)}\right] = \log \frac{A}{(A - x)},$$

or, on putting $(k_1 - k_2)/k_1 = m$,

$$\log [1 + my/(A - x)] = m \log A/(A - x) \quad . \quad . \quad (4)$$

Since $y = 2x - w$,

$$\log [1 + m(2x - w)/(A - x)] = \log A^m/(A - x)^m$$

and hence

$$mw = A + x(2m - 1) - A^m(A - x)^{1-m} \quad . \quad . \quad (5)$$

Differentiating this equation with respect to w, it follows that

$$\frac{A^m}{(A - x)^m} = \frac{m}{(1 - m)} . \frac{dw}{dx} - \frac{(2m - 1)}{(1 - m)},$$

and by substitution in (5),

$$w(1 - m) = (A - x) - (A - x) . \frac{dw}{dx} + 2x - 2mx \quad . \quad . \quad (6)$$

From equation (2), $(A - x) . dw/dx = (dw/dt)/k_1(B - w)$. Hence, from equation (6),

$$x(1 - 2m) = w(1 - m) - A + (dw/dt)/k_1(B - w) \quad . \quad . \quad (7)$$

x can now be eliminated from equation (5); and by simplication and application of the identity $m = 1 - k_2/k_1$, the equation finally obtained is

$$2A - w - \frac{dw(1 - m)}{dt.k_2(B - w)} = A^m\left[\frac{1 - m}{2m - 1}\right]^{1-m}\left[\frac{dw}{dt} . \frac{1}{k_2(B - w)} - (2A - w)\right]^{1-m} \quad . \quad . \quad (8)$$

which is a relation between the unknown k_1 as given by $m = 1 - k_2/k_1$ in terms of A, B, w, k_2, and dw/dt.

The two equations which have been applied to the determination of m or k_1 are (4) and (8). The first of these is of limited application, since evaluation of m depends on the accurate determination of y and $(a - x)$, *i.e.*, the quantities of mono- and di-ester present; it does not involve t. The second has not been found integrable, but completely satisfactory values of m can be obtained as follows. By plotting experimental values of w against t, dw/dt can be obtained for any value of t or w. For a given value of w and the corresponding value of dw/dt, the left-hand side of equation (8) can then be plotted as a straight line for different values of m; the right-hand side is represented by a curve. The intersection gives the required values of m and k_1.

Constant values for k_1 and k_2 can only be obtained if (1) the active masses of the reactants can be truly represented by their concentrations, in a reaction which is not affected by varying proportions of other catalysts, and (2) the effect of the reverse or esterifying reaction is negligible. The concentrations in the actual experiments were usually between 0·01 and 0·02*N*, and seldom exceeded 0·03*N*. No salt was present except that produced during the reaction. It appears probable that active mass can be here replaced without much error by concentration; and even if a certain catalytic activity must be ascribed to the other ions and molecules present in the solution, their effect on the reaction must be very small in comparison with that of the hydroxyl ion (compare Dawson and co-workers, J., 1913, **103**, 2135, and later papers).

For aqueous-alcoholic solutions, it has been shown by Wegscheider (*Monatsh.*, 1918, **39**, 201) and by Caudri (*Rec. trav. chim.*, 1929, **48**, 422, 589) for the saponification of esters such as ethyl acetate, that a bimolecular formula can still be applied and constancy of k obtained if allowance is made for the partial conversion of sodium hydroxide into ethoxide. The chief postulates in the mathematical considerations are a rapid attainment of equilibrium between hydroxide and ethoxide and the application of the mass-action law in the given solution. For dilute solutions, the constant found will be practically independent of the initial concentration. Such predictions have received further experimental confirmation by McCombie, Scarborough, and co-workers (J., 1921—1926) for the saponification of various esters of the ethyl acetate type.

EXPERIMENTAL.

Preparation and Purification of Esters.—Ethyl succinate was prepared by direct esterification of succinic acid by absolute alcohol in the presence of concentrated sulphuric acid, and the ethyl hydrogen ester by the action of sodium ethoxide on succinic anhydride in absolute alcohol (compare Blaise, *Bull. Soc. chim.*, 1899, **21**, 643). Ethyl methylmalonate, dimethylmalonate, and diethylmalonate were obtained from ethyl malonate by the sodium iodide method (Conrad, *Annalen*, 1880, **204**, 129; Perkin, J., 1884, **45**, 570). The mono-esters were in these cases prepared by the method of half-saponification (Freund, *Ber.*, 1884, **17**, 780; Walker, J., 1892, **61**, 708).

Satisfactory purification of the succinic esters was accomplished by distillation. The di-ester was distilled both at atmospheric and at reduced (10 mm.) pressure. The mono-ester was distilled several times under about 4 mm. by the aid of a Hyvac oil-pump. Tests for purity included titration by standard alkali of the mono-ester, together with complete saponification of both mono- and di-esters: the amount of alkali required was in good agreement with the theoretical values (99·8—100·5%).

It was more difficult to purify the substituted esters sufficiently for the purpose in view. About one-quarter of the alkali necessary for complete saponification was, therefore, added to the crude ester in alcoholic solution, any ethyl malonate present being thus removed owing to its preferential saponification (see k_1, p. 3120), the amount remaining being shown to be very small by determinations of velocity coefficients carried out after redistillation. A similar difficulty occurs to a less degree in the preparation of the hydrogen esters from the di-esters by half-saponification. In the case of the substituted esters whose velocity coefficients are very small, further purification by complete hydrolysis, recrystallisation of the resulting dibasic acids, and re-esterification would appear to be desirable (compare Gane and Ingold, J., 1926, 10). Distillation of the mono-ester in the malonic series is rendered less effective by the tendency of such esters to decompose into alcohol and dibasic acid even at 4 mm. pressure. In titrations for purity, the amount of alkali used was about 0·5% greater than that theoretically required, and a correction was accordingly applied in the calculation of the velocity coefficient.

All esters were obtained as perfectly clear, colourless liquids.

Procedure.—The velocity coefficient of the second reaction, *i.e.*, the saponification of the hydrogen ester, was calculated by the ordinary bimolecular formula

$$k_2 = 2{\cdot}303t/(a - b) \,.\, \log_{10} b(a - x)/a(b - x) \quad . \quad . \quad (9)$$

where a and b are the initial concentrations (in g.-mols. per litre) of the reacting substances, and x is the number of g.-mols. per litre transformed in t minutes. Examination of the formula shows that a small error in a has a comparatively small effect on the calculated value of k. The value of x, however, must be determined accurately, especially in the initial stages of the reaction, where x and $b(a - x)/a(b - x)$ are small. If x is large, the reverse reaction must be considered.

Experimentally, x was determined by the fall in alkali concentration as based on titration with dilute hydrochloric acid (approx. $N/100$), standardised against sodium hydroxide, which, in turn, had been standardised by means of pure succinic acid. Phenolphthalein was the indicator employed. In such titrations every precaution was taken to exclude carbon dioxide, in view of the dilution of the solutions involved. All aqueous solutions were made up from distilled water which had been boiled and cooled in an atmosphere free from carbon dioxide. The reaction and titration vessels were always well washed out with carbon dioxide-free air. During the withdrawal of solution by pipette from the reaction mixture, a current of such air was passed into the reaction vessel, the measured volume transferred to a conical flask (free from carbon dioxide and also immersed in the thermostat), phenolphthalein added, the flask removed, and titration performed as rapidly as possible at a noted time. The complete disappearance of the pink colour was taken as the end-point.

When the reaction investigated was a rapid one, alkali of accurately known normality (approx. $N/10$) was placed in a thin glass bulb which was inserted into the reaction vessel containing the ester solution. The closed vessel was immersed in the thermostat until temperature equilibrium was judged to have been attained; then, at a noted time, the glass bulb was broken, and mixing rapidly accomplished. Another method involved the addition of alkali from a flask containing a known volume, the remaining alkali being determined at once by titration. No difference could be detected in the velocity coefficients obtained for a given ester by the two methods.

A complete series of control experiments without ester was undertaken, to determine any loss of alkali which might be occasioned by the procedure involved in withdrawal of solution by pipette, etc. For all solutions, alcoholic as well as aqueous, the alkali recovered was in good agreement with that initially added. Results showed a slight tendency to be low, the discrepancy being equivalent to not more than 0·1 c.c. of the $N/100$-hydrochloric acid used in the titration. If the reaction is strictly bimolecular, this error would result in high values of k in the initial stages of the reaction, where x is small, and the effect of such an error is relatively large.

Determination of k_1.—Calculation of m from equation (4) involves the accurate determinations of y and $(A - x)$; and w must satisfy the relation $y = 2x - w$.

The case of ethyl succinate was here examined in detail. If at any time the reaction is stopped by titration with hydrochloric acid, the resultant solution contains sodium chloride, ethyl succinate, sodium ethyl succinate, and sodium succinate. Extraction of the di-ester by ether, followed by determination of its amount by complete saponification, did not give satisfactory results. It was then found that 10 minutes' steam distillation at atmospheric pressure completely removed the di-ester from mixtures with sodium ethyl succinate, which remained unaffected, and this procedure was checked by complete saponification of the two esters thus separated from artificial mixtures. With the actual experimental solutions of the reaction mixture, however, this method did not give accurate results, as judged by application of the equation $y = 2x - w$. This was found to be due to the presence of sodium succinate, a solution of which, when steam-distilled, becomes alkaline owing to the removal of succinic acid. The free alkali thus produced reacted with the esters present and caused inaccurate values to be recorded. Satisfactory results were finally obtained by adding about 0·5 c.c. of N/100-hydrochloric acid before distillation, practically the only acid then present being succinic acid, which would have a very small hydrolytic effect, even at 100°. Any succinic acid (or anhydride) which collected with the di-ester was neutralised by alkali before determination of the amount of ester by saponification was begun. Such saponification involved the addition of at least twice the required amount of sodium hydroxide, the solution being allowed to stand for 2—3 days, and the reaction finally completed by several hours' warming. The unused alkali was determined by titration with acid as before. Control experiments with alkali were here also carried out.

Preparation of Ester Solutions.—All solutions of di-esters were made up by dissolving the weighed amount in the required solvent in a standard flask.

Sodium ethyl ester solutions were prepared by neutralisation of a weighed amount of ethyl hydrogen ester by addition of the calculated volume of standard sodium hydroxide solution, precautions being taken to prevent saponification. The solution was then made up to the mark in a standard flask with the required solvent. No indicator was employed; any excess alkali required was determined in a separate portion and deducted from the amount added in an actual velocity-coefficient determination. The amount of mono-ester present was calculated from the weight taken, on the assumption that the corresponding free dibasic acid was the only impurity which could raise the alkali required for neutralisation above the theoretically calculated value. The correction was always small, being seldom greater than 0·5%, and it affects the calculated velocity coefficient to a very slight extent.

Sodium Hydroxide Solutions.—In each case, the required solution was made by dissolving stick alkali in the necessary solvent, the outer surface of the stick having previously been removed by washing. Every precaution was taken to prevent access of carbon dioxide in any operation.

Specimen Calculations.—(1) *Determination of* k$_2$. The following figures refer to the saponification of sodium ethyl succinate in aqueous solution at 15°; k_2 is calculated by equation (9).

$a = 0{\cdot}02105$; $b = 0{\cdot}00933$.

t (mins.).	HCl (c.c.).	$(b - x) \times 10^5$.	$x \times 10^5$.	$(a - x) \times 10^5$.	k_2.
4·0	15·10	855	78	2027	(1·07)
10·75	13·32	753	180	1925	0·981
16·0	12·08	684	249	1856	0·987
23·0	10·77	610	323	1782	0·960
28·5	9·74	551	382	1723	0·975
34·75	8·75	495	438	1667	0·982
39·0	8·19	464	469	1636	0·979
				Mean	0·977

(2) *Determination of* k$_1$. Ethyl succinate in aqueous solution at 15°.

$A = 0{\cdot}00891$; $B = 0{\cdot}00838$.

		(*a*) Time-titration method.		(*b*) Separation method.		
t (mins.).	HCl (c.c.).	$(B - w) \times 10^5$.	$w \times 10^5$.	$y \times 10^5$.	$x \times 10^5$.	$(A - x) \times 10^5$.
0	—	838	0	—	—	—
3·75	10·00	691	147	—	—	—
8·25	8·19	566	272	256	264	627
13·5	6·76	467	371	336	353	538
19·0	5·62	389	449	395	422	469
23·0	4·99	346	492	—	—	—

In method (*a*), by plotting t against w, the following values were obtained :

$w \times 10^5$	267	384
$dw/dt \times 10^7$	2415	1592

Employing then the general formula (8), with $k_2 = 0{\cdot}974$ (average value), we obtain, by graphical intersection of the curves representing the value of each side of the equation for various values of m, the values $m_1 = 0{\cdot}856$ and $m_2 = 0{\cdot}850$; hence $m = 0{\cdot}853$, and $k_1 = k_2/(1 - m) = 6{\cdot}63$.

In method (*b*), which gave y directly, the values of x were calculated from the equation $2x = w + y$. Other experimental values of $(A - x)$ are tabulated below, together with the means; and the corresponding values of m calculated by the aid of equation (4) are shown : they are in good agreement with the values 0·850 and 0·856 obtained by method (*a*).

Results.

$(A - x) \times 10^5$	624	530	458
,, ,, , mean	626	534	464
$x \times 10^5$, mean	265	357	427
$y \times 10^5 = (2x - w) \times 10^5$	258	343	405
m	0·84	0·85	0·85

Ethyl ester.	Temp.	k_2.	m.	m'.	k_1.	k_1/k_2.
	1. *Aqueous solution.*					
Succinate	25°	1·93	0·843	0·82	12·3	6·37
	15	0·974	0·849	0·83	6·38	6·55
	0	0·330	0·853	0·81	2·24	6·79
Malonate	25	1·08	0·9915		127	118
	15	0·56	0·9927		76·7	137
	0	0·190	0·9935		29·2	154
Methylmalonate	25	0·40	0·9886		35·1	87·8
	15	0·195	0·990		19·5	100
	2. *Aqueous-alcoholic solution* (50% *by mols.*).					
Succinate	25	0·325	0·826	0·81	1·87	5·75
	15	0·136	0·831	0·83	0·80	5·88
	0	0·038	0·820	0·81	0·211	5·55
Malonate	25	0·217	0·9872		16·9	77·9
	15	0·088	0·9855		6·11	68·9
	0	—	—		1·72	
Methylmalonate	25	0·0838	0·965		2·40	28·7
	15	0·041	0·963		1·11	27·1
Dimethylmalonate	25	0·0042	0·926		0·057	13·6
Diethylmalonate	25	0·00024	0·784		0·0011	4·57
	3. *Alcoholic solution.*					
Succinate	25	0·0195			0·024	
Malonate	25	0·006			0·220	
	15				0·090	

k_2 = average value of the second-stage velocity coefficient,
m = average value derived from method (*a*),
m' = average value derived from method (*b*),
k_1 = average value of the first-stage velocity coefficient calculated from $k_1 = k_2/(1 - m)$.

In view of the very limited solubility of the disubstituted di-esters in water, such determinations were not attempted. Even in 50% alcoholic solution, the second-stage reactions are so slow that the bimolecular formula can be applied without much error directly to the primary reaction.

General Conclusions.—1. The various equations based on the mass-action law, and dependent on the equivalence of " active mass " and " concentration," hold for all aqueous and aqueous-alcoholic solutions under the conditions of dilution, etc., obtaining in the experiments.

2. Increase of temperature produces increased velocity of reaction in all cases, the coefficients in both reaction stages ranging from 1·7 to 2·7 per 10°. Increase of alcoholic content in the solution decreases very considerably the rate of reaction, the decrease being proportionately greater for a rapid reaction in aqueous solution. In such a case, the alcohol actually produced during the saponification may cause decreasing velocity coefficients to be obtained in a given experiment. In purely alcoholic solutions, the velocity of reaction tends to zero. Owing to the method of preparation adopted for the necessary solutions of sodium ethyl esters, such solutions always contained the small amounts of water produced in the neutralisation of the ethyl hydrogen ester and the sodium hydroxide. Velocity coefficients are therefore not strictly comparable in "alcoholic" solution. In 50% alcoholic solutions, the effect of such water will be negligible, and in any case will tend to be counteracted by the alcohol produced during the reaction.

3. The ratio of the velocity coefficients for the first and second stages $[k_1/k_2 = 1/(1 - m)]$ varies definitely with alteration of temperature and solvent. With aqueous solutions the ratio increases with fall in temperature. Increasing proportions of alcohol decrease the ratio for a given temperature. For a given series of alcoholic concentrations, the effect of temperature appears to be less as the proportion of alcohol increases.

Discussion.

The velocity coefficient k_1 expresses the rate of the reaction involving essentially the neutral symmetrical ester and the negative hydroxyl ion. Assuming that reaction means the presence, momentary or otherwise, of electric charges at the points of attack, then obviously ethyl malonate itself, with its relatively very large value for k_1, is the example in which such effects show themselves at a maximum. This is, of course, in agreement with those other well-known phenomena, the peculiarity or essence of which lies in the presence of the groups CO, CN, etc., or duplications of these. If the double-bonded carbonyl group be taken here as the chief origin of disturbance, the ethoxy-group as well as the central methylene group must be regarded as similarly affected. In ethyl malonate, the ready reactivity of the hydrogen atoms of the central carbon atom is due to the two carbonyl groups acting in the same sense, as is exemplified by their easy replacement by sodium atoms under suitable conditions. If one replaceable hydrogen atom is replaced by an alkyl group, the reactivity of the remaining atom is not destroyed.

In the same way, the high k_1 for ethyl malonate must indicate that a similar effect is produced on the ethoxy-group, the ethyl group being easily replaced by a sodium atom under proper conditions. The velocity coefficient can thus be taken as expressing the state of activation of the ethoxy-group, this activation being dependent mainly on the presence of the double-bonded carbonyl group adjacent. It does not follow that the saturated ether linkage is necessarily the first point of attack by the reagent. Comparison between the different esters cannot be undertaken, however, without a knowledge of all conditions that are likely to affect the molecules. The electronic nature and the size of a replacing group in the malonic series must be considered, the first with relation to the distribution of reactivity throughout the molecule, and the second with regard to the spatial alterations which undoubtedly are involved (compare, *inter alia*, Gane and Ingold, *loc. cit.*). Many factors, *e.g.*, the ease of anhydride formation in the substituted dibasic acids, show that, for the lower members of the series, at least, the distance between the terminal carboxy-groups decreases on substitution. In the esters, substitution will radically alter the rate of saponification, not only from the steric-hindrance point of view, but also from the polar point of view, involving the space effect of the poles on the distribution of reactivity. Finally, such changes will undoubtedly affect the arrangement of the solvent dipoles round the reactive centres of the molecules; and it would seem that the presence of such "screens" of dipoles would be of the greatest importance in the attack by a saponifying agent.

Increase of alcoholic content in the solvent is accompanied by a rapid fall in velocity coefficient. It appears extremely probable that in 100% alcohol k is zero; in other words, sodium ethoxide has no effect on the saponification. Addition of alcohol to an aqueous solution will reduce the effective concentration of sodium hydroxide by reason of the equilibrium $NaOH + C_2H_5OH \rightleftharpoons C_2H_5ONa + H_2O$. This would apply to any ester solution; but in the case of ethyl malonate, where the fall in velocity coefficient is very large (127 in aqueous solution to 16·9 in 50% aqueous-alcoholic solution) the effective sodium hydroxide concentration may be further reduced by replacement of the hydrogen atom, since it is under these conditions, *viz.*, in alcoholic alkali solution, that such replacement is experimentally carried out. A rapid fall in velocity coefficient is thus to be expected as the solution increases in alcoholic content. In any given experiment with ethyl malonate in aqueous-alcoholic solution, a fall in velocity coefficient in the initial stages of saponification was experienced, and thought to be due to a slight progressive reduction in the effective hydroxide concentration (in addition to that due to saponification). Under these conditions, the true meaning of the "velocity coefficient" would appear to require consideration; the actual figures obtained would be misleading for purposes of comparison, in the sense that the true value of the alkali concentration is not accurately known but is less than that determined by analysis. The ratios of the velocity coefficients for the first and second reaction stages ought, however, to remain unaffected. According to Caudri (*loc. cit.*) and McCombie, Scarborough, and co-workers (*e.g.*, J., 1921, **119**, 970), the variation of velocity coefficient with alcohol percentage for an ester of the ethyl acetate type follows an irregular curve; the effective alkali concentration may be again altered, due either to solvent complexes or to selective adsorption or attraction of solvent dipoles (compare Kolthoff, *Rec. trav. chim.*, 1929, **48**, 220; Burrows, J., 1921, **119**, 1798).

In the cases investigated, the temperature coefficient per 10° increases with increasing content of alcohol, increase being greatest for ethyl malonate. Below are given for three esters the temperature coefficients for the range 15—25° in (i) aqueous solution and (ii) 50% aqueous-alcoholic solution :

	(i.)	(ii.)
Ethyl succinate	1·93	2·34
,, malonate	1·66	2·76
,, methylmalonate	1·80	2·20

Rise in temperature may mean the partial removal of "screening" dipoles, thus affording a relatively greater chance of attack by the reagent. It is to be expected that alcohol molecules would be more loosely held than water molecules, and in consequence a rise in temperature would involve a higher temperature coefficient.

The dissociation constants for the corresponding dibasic acids are of interest in this connexion, in that the primary constant expresses the tendency of the acid molecule to part with one hydrogen atom in the form of the proton, whereas k_1 expresses the tendency for the ester molecule to lose its corresponding ethyl group. It must be remembered that the saponification represents a bimolecular process subject to steric effects which are not so evident in the unimolecular dissociation. Col. 1 below gives the ester involved, col. 2 the first-stage velocity coefficient in 50% alcohol solution, and col. 3 the dissociation constant for the corresponding dibasic acid as obtained by Vogel (J., 1929, 1486) for aqueous solution.

Ester.	k_1.	$K . 10^4$.
Ethyl malonate	16·9	14·10
,, methylmalonate	2·4	7·99
,, dimethylmalonate	0·057	6·57
,, diethylmalonate	0·0011	63·9

Obviously, other factors are involved.

When the first ethyl group of the di-ester has been removed by saponification, the molecule is no longer symmetrical, the negatively charged ion being involved in the reaction. According to Meyer, the effect of the negative charge is the repulsion of the hydroxyl ion which is essentially responsible for the removal of the ethyl group. The further away the remaining carbethoxy-group from the negative charge of the ester kation, the less will be the effect, and the more nearly will the ratio k_1/k_2 approach the value 2. The ratio for the succinic esters is nearer to 2 than is that for the malonic esters. The figures given by Ingold (this vol., p. 2176) for the series show that such a decrease is actually obtained, the ratio at 20·3° for methyl azelate being, however, 3·61. As indicated also by conductivity measurements on the dibasic acids of this homologous series (Gane and Ingold, J., 1928, 1594), the distance between the terminal groups increases steadily with, though not proportionately to, the total number of carbon atoms. The increase in the k_1/k_2 ratio with fall in temperature, observed in aqueous solution, presumably corresponds in part to the normal contraction of the molecule.

In the malonic ester series, substitution by methyl or ethyl groups of the replaceable hydrogen atoms is also accompanied by fall in the k_1/k_2 ratio, a fall which may be explained by an increase in valency angle (of the central carbon atom) on ionisation due to the attraction of the negative charge for the substituting positive group. The sequence for k_1/k_2 in 50% alcoholic solution at 25° is : unsubstituted ester 77·9, monomethyl derivative 28·6, dimethyl derivative 13·5, diethyl derivative 4·57. The large value for ethyl malonate as compared with ethyl succinate (5·75) is probably to be attributed to the fact that the charge produced by ionisation is directly transferable in part to the carbon atom of the carboxy-group (compare Ingold, *Rec. trav. chim.*, 1929, **48**, 804), and acts in opposition to the carbonyl group, the final retarding effect on the k_2 reaction being at its greatest in the short-chain unsubstituted ester.

The ratio k_1/k_2 seems definitely to decrease as the proportion of alcohol increases in the solution. This holds for the succinic as well as for the malonic esters, and consequently the ratio seems to be a function of the general mechanism of the saponification rather than of any peculiarity of the ester itself. It represents a relatively greater retardation of the k_1 reaction, and may be explained as due to the " blanketing " effect of the larger ethyl alcohol polar molecules attached to, or surrounding, the reactive centres; the greater the number of such molecules, the less will be the reactivity of the molecule as a whole.

Summary.

A general method has been developed for the determination of the velocity coefficient of the first reaction in the saponification of dialkyl esters by alkali. The equations have been tested in two ways in the case of ethyl succinate. The temperatures concerned were 25°, 15°, and 0°, the solvents being water, ethyl alcohol, and an equimolecular aqueous-alcohol mixture. The effect of alteration of such conditions on the velocity coefficients and on the ratio of this function for the first- and second-stage reactions has been investigated and discussed for ethyl succinate, malonate, methylmalonate, dimethylmalonate, and diethylmalonate.

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THE UNIVERSITY, EDINBURGH. [*Received, October 20th*, 1931.]