335. *Metal-ion Catalysis and Specific Kinetic Salt Effects in the Alkaline Hydrolysis of Half-esters of Dicarboxylic Acids.*

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The rates of alkaline hydrolysis of potassium ethyl oxalate, malonate, adipate, and sebacate have been studied in the presence of potassium, sodium, lithium, thallous, calcium, barium, and hexamminocobaltic cations. The multivalent ions and the thallous ion catalyse the hydrolysis of the oxalate and malonate esters, and the alkali-metal ions have a marked negative specific salt effect on the rates of reaction of the adipate and sebacate. The catalytic effects are ascribed to the chelation of metal ions with the transition state, and the negative specific salt effects to the separation of the charge of the ester ion from the reaction centre. The catalytic effects are analysed quantitatively.

THERE has recently been considerable interest in the catalysis of reactions by metal ions [1] and in the large specific kinetic salt effects [2] which sometimes occur. It seemed that the rates of alkaline hydrolysis of half-esters of the type $EtO_2C\cdot[CH_2]_n\cdot CO_2^-$ in the presence of various cations might throw further light on both these phenomena, and we now report a study of them.

EXPERIMENTAL

Materials.—Potassium ethyl oxalate and potassium ethyl malonate, prepared from the diethyl esters by Nielsen's method,[3] were recrystallised from absolute ethanol, dried in a vacuum desiccator, and estimated to be 99% pure by complete hydrolysis with excess of potassium hydroxide and back-titration with hydrochloric acid. Further recrystallisation did not improve their purity. Potassium ethyl adipate and potassium ethyl sebacate, prepared from the diethyl esters by Walker's method,[4] were dried in an oven, stored in a vacuum desiccator, and found to be 99·6 and 99·8% pure respectively by potentiometric titration against hydrochloric acid.

Carbonate-free sodium hydroxide solution was prepared by dilution of a concentrated

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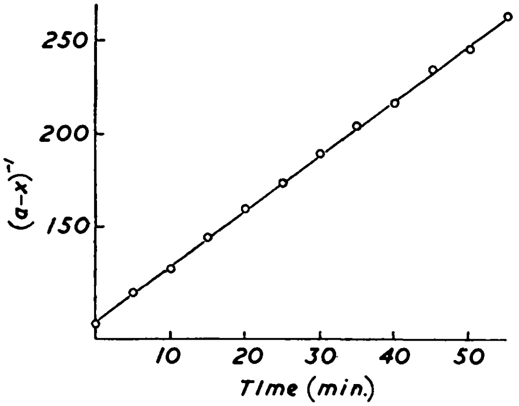
[1] Prue, *J.*, 1952, 2331.
[2] Kilpatrick, *Ann. Rev. Phys. Chem.*, 1951, **2**, 269.
[3] Nielsen, *J. Amer. Chem. Soc.*, 1936, **58**, 206.
[4] Walker, *Proc. Roy. Soc.*, 1906, *A*, **78**, 157.

stock solution, and carbonate-free potassium hydroxide by reaction of potassium iodide with excess of silver oxide. The solutions were stored in Polythene bottles and standardised against "AnalaR" potassium hydrogen phthalate. The potassium, sodium, barium, and calcium chloride used were "AnalaR" samples. Lithium chloride and thallous nitrate were B.D.H. products, the thallous nitrate containing 1% of acidic impurity which was neutralised with potassium hydroxide. Kahlbaum's hexamminocobalt trichloride was used without further purification; a B.D.H. product was purified by Bjerrum's procedure.[5] All solutions were prepared with water of conductivity 10^{-7} ohm^{-1} cm.$^{-1}$ from an ion-exchange column.

Apparatus and Procedure.—We used a sampling technique and followed the decrease in alkali concentration titrimetrically as the reaction proceeded. The usual procedure of withdrawing samples with a pipette from the reaction mixture in a thermostat has several disadvantages, such as the danger of contamination by carbon dioxide and timing errors arising from difficulties of transfer. The reaction vessel was a 100 ml. glass syringe fitted into a glass water-jacket through which water was pumped from a thermostat tank at 25° ± 0·01°. The temperature of solutions in the syringe could be maintained within ±0·01° of this temperature which was checked by a Beckmann thermometer which had been compared with a four-junction thermocouple standardised by the National Physical Laboratory. Water was circulated through the apparatus for ½ hr. before the mixture was introduced into the syringe.

FIG. 1.



The potassium hydroxide solution, after being left in the thermostat for about 20 min., was pipetted into the ester and salt solution in a flask in the thermostat, a stop-watch being started when half the hydroxide had been delivered. (The delivery time for the 50 ml. pipette used was 20 sec.) The solution, protected by an atmosphere of nitrogen, was then rapidly drawn into the syringe through a Polythene tube and the plunger adjusted so that the extended nozzle of the syringe was free from solution. Samples of approximately 10 ml. were delivered (2—3 sec.) at suitable intervals into weighed 100 ml. glass-stoppered flasks containing an excess of potassium hydrogen phthalate solution, and the flasks were then reweighed. The solutions were back-titrated against standard sodium hydroxide solution, an atmosphere of nitrogen being maintained in the titration flask throughout. Separate experiments showed that no hydrolysis of the ester occurred in the phthalate solution.

Results.—All measurements were made with exactly equivalent concentrations a (about 0·01M) of ester and hydroxide, for which the integrated second-order rate equation has the form $(a - x)^{-1} = kt + a^{-1}$, where x is the decrease in concentration after time t and k the rate constant. Values of $(a - x)^{-1}$, equal to the concentration of hydroxyl ions present, were plotted against t, and good second-order plots obtained, in many cases up to 80% reaction. A typical plot is shown in Fig. 1 which relates to the hydrolysis of potassium ethyl adipate in 0·05M-potassium chloride. The rate constants were reproducible within 1—2%, even with times of reaction as short as 5 min. The only deviation from second-order kinetics was observed with potassium ethyl oxalate in the presence of barium ions, when the plots curved because of

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[5] Bjerrum, "Metal ammine formation in aqueous solution," Haase and Son, Copenhagen, 1941, p. 241.

the precipitation of barium oxalate, but as this did not occur until the reaction was about 70% complete it was possible to determine the rate constants from the earlier points. The insolubility of calcium oxalate prevented measurements being made with ethyl oxalate in the presence of calcium.

Measurements were made with a range of metal-ion concentrations up to an ionic strength I of 0·1. The rate constants obtained are collected in Table 1. The stoicheiometric ionic strength at 50% reaction is given by adding 0·025 ± 0·002 to the contribution of the salt.

TABLE 1. *Rate constants (l. mole^{-1} min.$^{-1}$) for hydrolysis of potassium ethyl esters in presence of metal salts (molar concn. ×10^4).*

			Potassium ethyl oxalate					
KCl	—	—	136	271	407	543	679	
k	40·6	40·4	44·5	47·4	49·1	51·6	54·6	
LiCl	232	464	696					
k	48·0	52·9	57·8					
$BaCl_2$	4·3	10·7	21·4	32·1	42·9			
k	49·0	55·3	67·3	78·0	91·7			
$Co(NH_3)_6Cl_3$	130	194	259	324				
k	53·8	60·5	67·8	73·0				
$TlNO_3$	27·9	55·9	112					
k	56·8	75·6	105					
$Ba(NO_3)_2$	23·9							
k	68·0							
			Potassium ethyl malonate					
KCl	—	—	157	313	470	626	783	
k	1·05	1·05	1·15	1·21	1·25	1·30	1·34	
NaCl	234	390	468	624	780			
k	1·14	1·19	1·21	1·26	1·30			
$TlNO_3$	94	188	313	501	595			
k	1·29	1·46	1·68	1·97	2·12			
$CaCl_2$	44	89	133	177	221			
k	2·10	2·83	3·67	4·44	5·00			
$BaCl_2$	42	85	127	170	212			
k	1·36	1·56	1·69	1·81	1·92			
$Co(NH_3)_6Cl_3$	26	51	77	103	128			
k	1·28	1·49	1·63	1·75	1·86			
			Potassium ethyl adipate					
KCl	—	161	192	314	519	544	719	782
k	2·64	2·80	2·74	2·85	2·98	2·97	2·96	3·04
NaCl	83	197	249	374	559	745		
k	2·72	2·68	2·88	2·80	2·90	2·87		
LiCl	151	301	452	603	753			
k	2·73	2·88	2·86	2·87	2·86			
$TlNO_3$	168	336	504					
k	2·92	3·01	3·20					
$CaCl_2$	74	99	148	198	247			
k	2·92	3·05	3·06	3·12	3·30			
$Co(NH_3)_6Cl_3$	26	51	77	102	128			
k	2·91	3·06	3·23	3·29	3·39			
$BaCl_2$	130							
k	3·02							
			Potassium ethyl sebacate					
KCl	—	—	155	310	465	620	775	
k	1·99	1·99	2·06	2·11	2·23	2·22	2·24	
$Co(NH_3)_6Cl_3$	26	26	51	77	102	128		
k	2·19	2·13	2·25	2·38	2·41	2·47		

The reaction is one between two negative ions and the effect of the long-range Debye–Hückel interactions on k was taken into account [6] by plotting $\log k^{0\prime}$, defined by

$$\log k^{0\prime} = \log k - 2AI^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

against I. The value of A, the Debye–Hückel constant, was taken as 0·509 (l. mole^{-1})$^{\frac{1}{2}}$ and the value of I as the mean stoicheiometric value for each run. Fig. 2 shows the results obtained

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[6] Guggenheim and Prue, " Physicochemical Calculations," North-Holland Publishing Co., Amsterdam, 1955, p. 466.

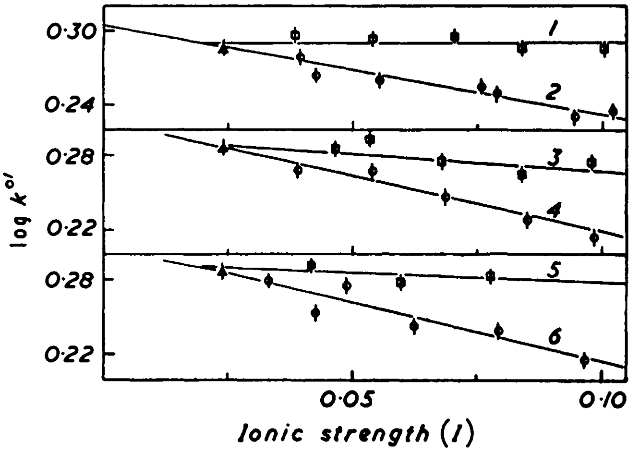


FIG. 2. Δ No added salt; 1, $Co(NH_3)_6Cl_3$; 2, KCl; 3, $CaCl_2$; 4, LiCl; 5, $TlNO_3$; 6, NaCl.

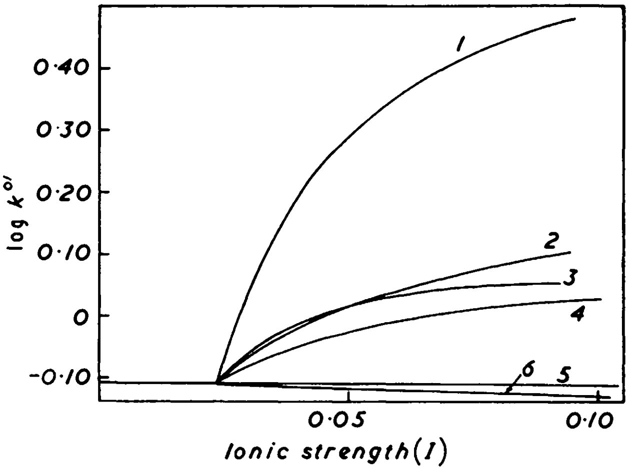


FIG. 3. Potassium ethyl malonate. 1, $CaCl_2$; 2, $TlNO_3$; 3, $BaCl_2$; 4, $Co(NH_3)_6Cl_3$; 5, KCl; 6, NaCl.

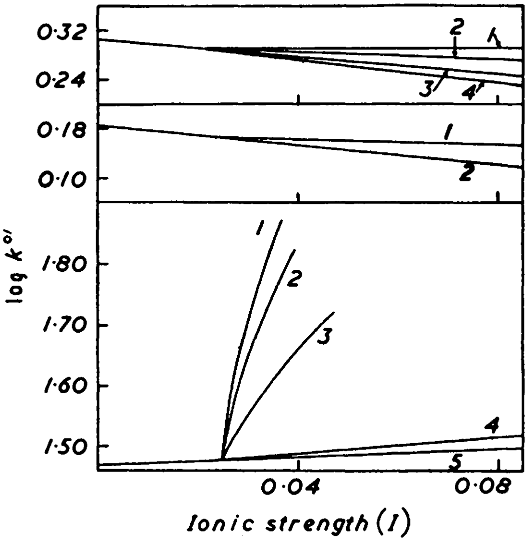


FIG. 4. Top: potassium ethyl adipate. 1, $Co(NH_3)_6Cl_3$; 2, $CaCl_2$; 3, KCl; 4, LiCl.

Middle: potassium ethyl sebacate. 1, $Co(NH_3)_6Cl_3$; 2, KCl.

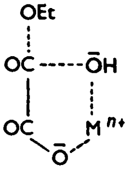
Bottom: potassium ethyl oxalate. 1, $TlNO_3$; 2, $BaCl_2$; 3, $Co(NH_3)_6Cl_3$; 4, LiCl; 5, KCl.

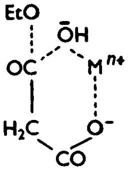
with potassium ethyl adipate, the vertical lines corresponding to 1½% in *k*. These results are typical, and all the results obtained are plotted on the same scale in Figs. 3 and 4 (the experimental points have been omitted for clarity). The effect of changing the anion of the added salt was tested by measuring the hydrolysis of ethyl malonate with barium nitrate instead of the chloride. The results were the same.

A few measurements reported in the literature[3, 7, 8] on the kinetic salt effect in the alkaline hydrolysis of half-esters in the presence of sodium or potassium ions are in general agreement with our own, but a detailed comparison is not profitable because of wide variations of temperature, ionic strength range, and accuracy. Nielsen's assertion[3] that potassium ethyl oxalate, malonate, succinate, and adipate do not show different specific effects in the presence of potassium chloride is based on an inadequate method of analysis by use of the limiting law. His results when analysed by our procedure show effects of the same magnitude as we have observed.

DISCUSSION

The large specific effects of multivalent and thallous cations on the rates of hydrolysis of the oxalate and malonate bear no simple relation to the charge of the ion. We regard them as catalytic effects arising from the formation of chelate complexes between the metal ions and the transition state. The transition state is thereby stabilised and the energy barrier lowered. The chelate complexes may be represented as (*A*) and (*B*) and the greater effect with the oxalate is in line with the greater stability of oxalate chelate complexes (see Table 2). A similar stabilisation of the transition state by chelate formation is probably responsible for the catalysis by heavy-metal ions of the hydrolysis of amino-acid esters[9] and the large effect of calcium ions on the alkaline hydrolysis of acetylcitric and benzoylcitric acids.[10] If our interpretation is correct it follows that there are two alternative reaction paths, for one of which the transition state contains a cation as well as an ester-ion and a hydroxyl ion. We might therefore expect the second-order rate constant *k* to be given by $k = k_1 + k_2[\mathrm{M}^{n+}]$, where $[\mathrm{M}^{n+}]$ is the concentration of the catalysing metal ion and k_1 is the rate constant of the uncatalysed reaction. In fact, plots of *k* against the metal-ion concentration are not linear, because of the incomplete dissociation of the hydroxides and of the metal dicarboxylates formed during the reaction. The measured rate constant is in these circumstances given by


(*A*)


(*B*)

$$k = (k_1[\mathrm{OH}^-] + k_2[\mathrm{M}^{n+}][\mathrm{OH}^-])/[\mathrm{OH}^-]_s \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$= (k_1[\mathrm{OH}^-] + k_3[\mathrm{MOH}^{(n-1)+}])/[\mathrm{OH}^-]_s \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where $[\mathrm{OH}^-]_s$ is the stoicheiometric concentration of hydroxyl ions. The constants k_2 and k_3 are related through the dissociation constant of the hydroxide. Values of k_3 have been calculated from the experimental values of *k* by inserting a k_1 value interpolated from the potassium chloride measurements and concentrations calculated for the mid-point of the run, account being taken of the association equilibrium by successive approximations.

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[7] Westheimer, Jones, and Lad, *J. Chem. Phys.*, 1942, **10**, 478.
[8] Svirbely and Mador, *J. Amer. Chem. Soc.*, 1950, **72**, 5699.
[9] Kroll, *J. Amer. Chem. Soc.*, 1952, **74**, 2036.
[10] Smith, *Z. phys. Chem.*, 1936, **177**, 131.

The values used for the various dissociation constants were taken from those in Table 2. Ionic activity coefficients were calculate from the Güntelberg [11] expression

$$-\log f_i = Az_i^2 I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The calculations were also carried out for ethyl adipate, although the higher-valent cations appear to be more " normal " in their salt effect than potassium. A typical set of results is shown in Table 3 for the hydrolysis of potassium ethyl malonate in the presence of barium ions. The change of k_3 with ionic strength is quantitatively in accord with expectation for a reaction between a negative ion and a positive ion and even if the small specific effect is neglected, the calculated and observed values of k are in agreement within the limits of the estimated experimental accuracy. If the calculations are carried out with use of the Davies [12] standard activity expression, which adds a linear term $0{\cdot}2Az_i^2I$ to the right-hand side of eqn. (4), the differences in the values of k_3 are less than 2%. This method of interpretation gives equally satisfactory results in the other cases. It might be thought that the changes during reaction of the various equilibria involved would cause observable deviations from second-order kinetics. Calculations show that even in the least favourable case, the experiment with the highest concentration of hexamminecobalt trichloride, the theoretical second-order rate constant would only change by 5% during the run. If experimental errors were completely absent the curvature of a second-order plot would be only just detectable, and the best straight line through the points would give a rate constant identical with that for the mid-point of the run.

TABLE 2. *Dissociation constants* (*mole l.*$^{-1}$).

	Oxalate^{2-}	Malonate^{2-}	Adipate^{2-}	OH$^-$	Cl$^-$	NO$_3^-$
Ba^{2+}	0·0047 [a]	0·0196 [b]	0·014 [c]	0·23 [d]	—	—
Ca^{2+}	0·0010 [a]	0·0032 [b]	0·0064 [c]	0·051 [d]	—	—
Co(NH$_3$)$_6^{3+}$	0·0004 [e]	0·00029 [e]	0·00045 [e]	0·014 [f]	0·032 [g]	—
Tl$^+$	—	—	—	0·15 [h]	—	0·52 [i]

[a] Money and Davies, *Trans. Faraday Soc.*, 1932, **28**, 609. [b] Stock and Davies, *J.*, 1949, 1371. [c] Topp and Davies, *J.*, 1940, 87. [d] Bell and Prue, *J.*, 1949, 362. [e] Peacock and James, *J.*, 1951, 2233. [f] Caton and Prue, *J.*, 1956, 671. [g] Jenkins and Monk, *J.*, 1951, 68. [h] Bell and George, *Trans. Faraday Soc.*, 1953, **49**, 619. [i] Davies, *ibid.*, 1927, **23**, 351.

TABLE 3.

10^4[BaCl$_2$]	k (exp.)	10^6[BaOH$^+$]	10^4I	k_1	k_3	k (calc.)
42	1·36	60	348	1·12	30·0	1·33
85	1·56	110	471	1·17	26·0	1·55
127	1·69	155	602	1·22	23·9	1·70
170	1·81	195	730	1·26	22·4	1·83
212	1·92	225	850	1·30	21·5	1·95

Table 4 gives values of k_1^0 and k_3^0, the values of k_1 and k_3 extrapolated to $I = 0$. We observe that k_3^0/k_1^0 varies in the order EtOx$^-$ > EtMal$^-$ > EtAd$^-$ which is the expected order of stability of chelate complexes. The order for the oxalate and malonate of Ca^{2+} $\sim$ Ba^{2+} > Co(NH$_3$)$_6^{3+}$ > Tl$^+$ shows the hexamminocobaltic ion to be less effective than expected by analogy with the dissociation constants in Table 2. It is possible that the ion is too large to satisfy easily the steric requirements of the transition state.

TABLE 4.

Base	Ester: EtOx$^-$	EtMal$^-$	EtAd$^-$
OH$^-$	29·2	0·778	2·01
TlOH	1330	5·65	4·37
BaOH$^+$	9200	38·0	—
CaOH$^+$	—	39·8	7·94
Co(NH$_3$)$_5$OH^{2+}	1740	16·0	17·1

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[11] Güntelberg, *Z. phys. Chem.*, 1926, **123**, 243.

[12] Davies, *J.*, 1938, 2093.

There remains to be explained the rather large but linear specific salt effects of the alkali-metal ions on the hydrolysis of ethyl adipate and sebacate. These effects are 10—20% of the total kinetic salt effect and probably arise as follows: the transition state with a carboxylate ion and a hydroxyl ion at opposite ends of a carbon chain will behave as a conventional doubly-charged ion in sufficiently dilute solution, but when the radius of the Debye–Hückel ionic atmosphere becomes comparable with the separation between the charges, each charge will tend to build up its own ion atmosphere and simulate independent ions. This means that the formation of the transition state from the free ions will be less favoured by increasing ionic strength than would otherwise be the case and a negative specific salt effect will arise. At an ionic strength of 0·1 the radius of the ionic atmosphere is about 10 Å, which is about the distance between the carboxyl groups in adipic acid. A parallel example from equilibrium studies is that the long zwitterion of methyl-orange behaves as a neutral molecule in dilute salt solution and as two separate ions in more concentrated solution.[13] We regard the very small specific effects for the ethyl adipate and sebacate reactions with multivalent cations as being due to an accidental compensation of charge separation and chelate effects.

We thank the British Rayon Research Association for a scholarship (to J. I. H.).

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[13] Bjerrum, *Z. phys. Chem.*, 1923, **104**, 147.