867. *The Hydrolysis of Carboxylic Anhydrides. Part II.* The Effects of Salts of Strong Acids on the Hydrolysis of Acetic Anhydride.*

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Uni-univalent salts of strong acids decrease the rate of hydrolysis of acetic anhydride in water at 0°, the effect increasing with increasing size of the anion or cation. Lithium and magnesium sulphate increase the rate. From solubility measurements on acetic anhydride it is shown that this is partly due to salt effects on the activity coefficient of the initial state, but that salts of the strong acids destabilise the transition state (increase f_*).

SALTS affect the rates of hydrolysis of carboxylic anhydrides in water.[1] The effect of salts of the strong acids appears to depend on the charge density of the ions, because the uni-univalent salts decrease the rate and some bivalent salts increase it. Salts of the weak acids increase the rate, sometimes very markedly. They may convert the anhydride

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* The paper, *J.*, 1960, 3070, is regarded as Part I.

[1] (*a*) Gold, *Trans. Faraday Soc.*, 1948, **44**, 506; (*b*) Koskikallio, *Ann. Acad. Sci. Fennicae*, 1954, AII, **57**, 1; and references cited therein.

into a reactive intermediate—this is the probable role of formate[2] or nitrite[3] ions—or they may act as general bases rather than as nucleophiles,[4] as does acetate ion.

The Brönsted–Bjerrum rate equation expresses the first-order rate constant, k_1, for the hydrolysis of acetic anhydride as $k_1 = k_0 f_{Ac_2O}/f_*$, where f_{Ac_2O} and f_* are the activity coefficients of the initial and the transition state, respectively. We have not explicitly included the activity of water in this rate equation, and all the interactions between the water molecules and the initial and the transition state are included in f_{Ac_2O} and f_*. This is purely a convention; we could instead have included the activity of water, raised to some power, in the rate equation, to allow for these interactions (cf. ref. 5). In our reactions the activity of water is close to unity.[6]

For reactions done in the usual way, *i.e.*, in homogeneous solution, the salt effect depends upon the ratio $f_{Ac_2O} : f_*$, and for its understanding it is necessary to separate the effects upon f_{Ac_2O} and f_*. We have attempted to do this by studying the partitioning of acetic anhydride between carbon tetrachloride and the aqueous solutions.

Rate Measurements in Homogeneous Media.—Our rate measurements for various salt

TABLE 1.

First-order constants for hydrolysis of acetic anhydride at 0° (aqueous salt solutions, unless specified).

Salt (M)	—	Li₂SO₄	CaCl₂	SrCl₂	BaCl₂	MgCl₂	LiBr	NaNO₃	NaBr	
10⁴k_1 (sec.⁻¹)	4·70	7·40	4·26	3·84	3·52	3·39	3·59	3·44	3·42	4·06 ᵇ

Salt (M)	KBr	RbBr	CsBr	Et₄NBr	NaI	KI		NaC₇H₇SO₃	
10⁴k_1 (sec.⁻¹)	3·00	3·02	2·98	2·82	2·88	2·65	4·26 ᵃ	0·9 ᶜ	3·14 ᵇ

ᵃ 0·3M. ᵇ 0·6M. ᶜ 3M. ᵈ 25·0°.

Variation of concentration.

[Salt] (M)	0·1	0·5	1·0	1·50	2·00	3·00	4·00
NaCl	4·61	4·30	3·65	3·07	2·65	2·02	—
NaClO₄	4·72	3·52	2·75	—	1·56	0·885	0·48
MgSO₄	—	5·95	7·05	7·80	—	—	—

Salt order in water (for 1 equiv. per l.): Li₂SO₄ > MgSO₄ > no salt > CaCl₂ > SrCl₂ > BaCl₂ > MgCl₂ > NaCl > LiBr > NaNO₃, NaBr > KBr, RbBr, CsBr > NaI > Et₄NBr > NaClO₄ > KI > NaC₇H₇SO₃.

60 : 40 v/v *Dioxan–water.*

Salt	—	0·4M-NaClO₄	0·4M-Et₄NBr	—	2·0M-LiClO₄
10⁶k_1 (sec.⁻¹)	66·0 ᵈ	85·6 ᵈ	66·9 ᵈ	12·1	9·35

40 : 60 v/v *Dioxan–water.*

Salt	—	0·4M-NaClO₄	2·0M-LiClO₄
10⁶k_1 (sec.⁻¹)	58·2	60·0	36·4

solutions are shown in Table 1 and the Figure. The points fit reasonably on linear plots of log k_1 against salt concentration. Small amounts of sodium perchlorate (<0·1M) do not depress the rate, but larger concentrations have a striking effect. The plot for log k_1 against the concentration of magnesium sulphate, in particular, curves down slightly, perhaps because this salt is not a strong electrolyte.[7] We can exclude an ionic strength effect, involving purely coulombic interactions, as a major factor, and we must consider the specific effects of the ions. These effects may be upon the initial or the transition state, directly or through changes in the water–solute interactions. No single effect can

² Kilpatrick and Kilpatrick, *J. Amer. Chem. Soc.*, 1930, **52**, 1418; Gold and Jefferson, *J.*, 1953, 1416.
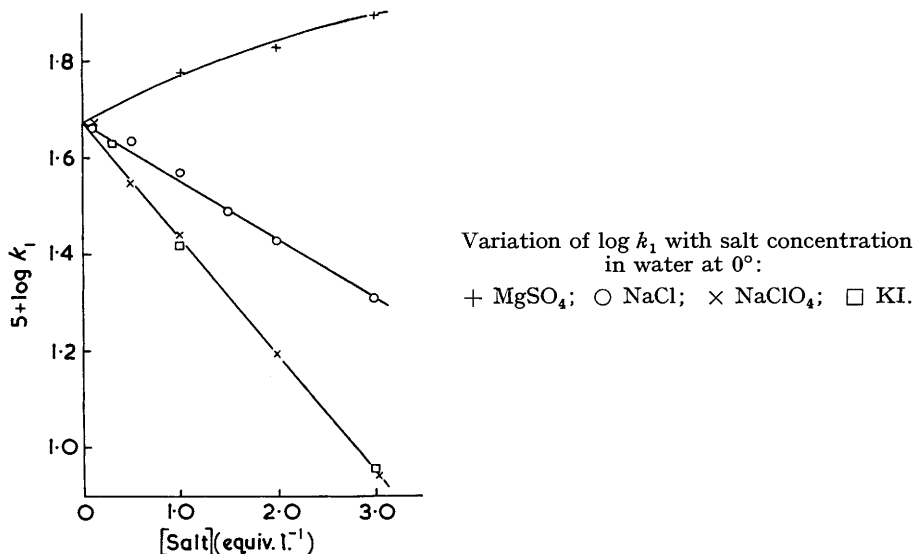³ Lees and Saville, *J.*, 1958, 2262.
⁴ Butler and Gold, *J.*, 1961, 2305.
⁵ Bunnett, *J. Amer. Chem. Soc.*, 1961, **83**, 4956, and accompanying papers.
⁶ R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," Butterworths Scientific Publns., London, 1959, Appendix 8.
⁷ C. W. Davies in "The Structure of Electrolytic Solutions," ed. W. J. Hamer, Wiley, New York, 1959, p. 19; Nancollas, *Quart. Rev.*, 1960, **14**, 402.

explain all the facts; *e.g.*, we might suppose that salts retard the reaction by binding the water molecules about themselves, but it is the large, lightly solvated ions, *e.g.*, R_4N^+ and $R \cdot SO_3^-$, which decrease the rate most, and the small, heavily solvated ions which increase it. Alternatively, magnesium salts might act as electrophilic catalysts and co-ordinate with the oxygen atom of the anhydride (cf. ref. 8), but then we have to explain the retarding effect of magnesium chloride and the accelerating effect of lithium sulphate.

Variation of log k_1 with salt concentration in water at $0°$:

$+$ $MgSO_4$; $\bigcirc$ NaCl; $\times$ $NaClO_4$; $\square$ KI.

If we consider only uni-univalent electrolytes the important factor seems to be the ionic size. This can be seen by comparing a series of salts in which either the anion or cation is unchanged. For a series of bromides the rate decreases in the sequence:

	No salt	>	Li$^+$	>	Na$^+$	>	K$^+$	$\approx$	Rb$^+$	$\approx$	Cs$^+$	>	Et$_4$N$^+$
k_s/k_0	1		0·77		0·73		0·64		0·64		0·64		0·60
Crystal radius (Å) [9]	—		0·60		0·95		1·33		1·48		1·69		—

(k_s/k_0 is in this context the rate with 1M-salt relative to that in water.)

For a series of sodium salts we have the sequence:

	No salt	>	Cl$^-$	>	NO$_3^-$		Br$^-$	>	I$^-$	>	ClO$_4^-$	>	C$_7$H$_7 \cdot$SO$_3^-$
k_s/k_0	1		0·78		0·73		0·73		0·61		0·58		0·56
Crystal radius (Å) [9]	—		1·81		—		1·95		2·16		—		—

(Fluoride ion is not included in this sequence because it has a powerful catalytic effect which we believe may be due to its action as either a general base or a general nucleophile.[10])

There is a similar sequence for the alkaline-earth chlorides (excepting magnesium chloride):

	No salt	>	Ca^{2+}	>	Sr^{2+}	>	Ba^{2+}	>	Mg^{2+}	(>2Na$^+$)
k_s/k_0	1		0·91		0·82		0·75		0·72	
Crystal radius (Å) [9]	—		0·99		1·13		1·35		0·65	

The anomalous position of magnesium may be related to its strong solvation by water.

These results, and the others given in Table 1 and ref. 1, suggest that some of the salt effect is upon the initial state.

[8] Stiles, *Ann. N.Y. Acad. Science*, 1960, **88**, 323.
[9] L. Pauling, " Nature of the Chemical Bond," Oxford University Press, London, 1940, Chap. X.
[10] Fuller, unpublished results.

It is well established that large ions " salt-in " some non-electrolytes (decrease their activity coefficients) in water, whereas small ions have the opposite effect.[11] Our rate measurements fit this pattern, and the linear relation between the logarithm of the first-order rate constant and the salt concentration is similar to the relation between activity coefficient of a non-polar solute and salt concentration.[11] (However, such relations exist also between the activity of water and salt concentration.[12])

We also measured some salt effects upon the rate of hydrolysis of acetic anhydride in dioxan–water (60 : 40 v/v and 40 : 60 v/v) (Table 1). These systems were not studied systematically, in part because the solubilities of some of the salts were limited, but largely because there is a difficulty in interpretation due to the second component of the solvent. The salt order appears to be:

$$NaClO_4 > No \; salt \approx Et_4NBr > LiClO_4$$
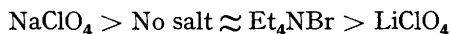
We could not do distribution experiments with acetic anhydride in these mixed solvents, and the difference in the behaviour of lithium and sodium salts in water and aqueous dioxan may be caused by salt effects upon the interactions between the components of the solvent, as well as upon those between solute and solvent. However, for camphoric anhydride in dioxan–water (12·5 : 87·5 v/v), at 25°, we found that in highly aqueous solvent the solubility was increased by sodium perchlorate, almost unaffected by tetraethylammonium bromide and decreased by magnesium sulphate.[13] This solubility effect was paralleled by the rates of hydrolysis at 101° which were decreased markedly by sodium perchlorate, decreased slightly by tetraethylammonium bromide, and increased by magnesium sulphate. These experiments will be described elsewhere.

Partitioning of Acetic Anhydride between Water and Carbon Tetrachloride.—We measured the distribution of acetic anhydride between water and carbon tetrachloride at 0° in the presence and absence of salt (Table 2). We had little choice of temperature. Above 0°

TABLE 2.

Mean values of distribution coefficients of acetic anhydride between water and carbon tetrachloride at 0°.

Salt		NaCl			NaClO$_4$		KBr	KI		MgSO$_4$	Li$_2$SO$_4$
Molarity ...		0·5	1·0	3·0	1·0	3·0	1·0	1·0	3·0	1·0	1·0
γ	0·93	0·97	1·05	1·14	0·73	0·52	0·82	0·73	0·59	3·3	3·3
$f^*_{Ac_2O}/f^\circ_{Ac_2O}$	—	1·0$_4$	1·1$_3$	1·2$_3$	0·7$_8$	0·5$_6$	0·8$_8$	0·7$_9$	0·6	3·6	3·6
f^*_*/f°_*	—	1·1	1·5	2·9	1·3	3·0	1·4	1·4	3	2·4	2·3

the reaction becomes too fast for experiment and because these salt effects probably depend upon the modification of the water structure by ions it was desirable to work at the lowest possible temperature (where water will be most ordered). The values of the distribution coefficients are much less precise than those of the rate constants, simply because the acetic anhydride is reacting during the measurements (the half-life in water at 0° is *ca.* 25 min.). We used various methods of sampling in order to show that our results are meaningful, and as evidence that equilibrium is maintained between the two layers we showed that the instantaneous rate constants in the aqueous layer $(-d[Ac_2O]/A[Ac_2O])/dt$ were in reasonable agreement with those measured conventionally (see p. 4485). The values of the empirical Setschenow constants [11] K_s are given below; because of the imprecision of the distribution measurements moderately high salt concentrations (1—3M) were used.

K_s: Li$_2$SO$_4$, MgSO$_4$, 0·27; NaCl, 0·03; KBr, −0·06; KI, NaClO$_4$, −0·1.

[11] Long and McDevit, *Chem. Rev.*, 1952, **51**, 119.
[12] Ref. 6, Chap. 2.
[13] Perry, Thesis, London, 1958.

If we assume that the activity coefficient of acetic anhydride in carbon tetrachloride is constant we can relate its activity coefficients in water and the salt solutions in terms of the distribution coefficient, r $(= [Ac_2O]$ in $CCl_4/[Ac_2O]$ in $H_2O)$, and $f^o{}_{Ac_2O}/f^s{}_{Ac_2O} = r^o/r^s$ (the superscript " o " relates to water, and " s " to salt solutions).

The Brönsted–Bjerrum rate equation then gives: $k_o r^s/k_s r^o = f_*{}^s/f_*{}^o$.

The results (Table 2) show that the salt affects the activity coefficient of both the initial and the transition state.

The effect upon the initial state is similar to those that have been found for other polar oxygen-containing non-electrolytes.[11,14] The anhydride is " salted out " strongly by lithium and magnesium sulphate, and weakly by sodium chloride, but is " salted in " by salts with larger ions. The solubilities of carboxylic esters and lactones and of sulphite esters are similarly affected, and the values of the constant K_s are in the same general range. Whereas large ions stabilise the initial state, and small ions destabilise it, they all destabilise the transition state.* This observation may be fortuitous; we studied six salts only, an insufficient number to establish a complete picture of the system. Calculations of K_s are based upon the salt concentration in equiv. per l.; some of the electrolytes are not fully dissociated in water,[7] and the values of K_s may depend upon this factor to some extent.

Nature of the Salt Effect.—Our experimental evidence suggests that salts affect the stabilities of both the initial and the transition state, but we still have to explain the source of these effects.

Electrolytes are known to affect the activity coefficients of non-electrolytes in water, and the salt order is little dependent upon the nature of the solutes, which are generally " salted out " most by the small ions (with occasional exceptions for lithium). Hydrocarbons, alkyl halides, and inorganic gases are " salted-out " of water by nearly all electrolytes, but oxygen compounds are " salted in " by some of the larger ions.[11,14] An electrolyte might affect solubility by interacting directly with the solute, or indirectly by modifying the structure of the water. Grunwald and his co-workers [16] have shown that the vapour pressure of dioxan in water is decreased by many electrolytes, and they suggest that the larger cations, especially the quaternary 'onium ions, may be specifically solvated by dioxan, even in the presence of water. However it seems difficult to be certain that this lowering of the vapour pressure of dioxan is not in some cases an indirect effect due to water–salt interactions.

We could postulate direct interactions between the anhydride and a cation (I) or an anion (II) (cf. ref. 14a). Interaction with cations to give a species (I) should increase the
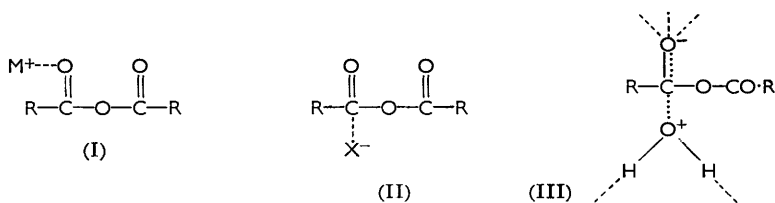
electrophilicity of the anhydride, and so assist hydrolysis. There is no evidence that it occurs in anhydride hydrolysis, except for the proton, but such action is important in Friedel–Crafts reactions of anhydrides. Interaction with anions (as in II) might be

* This is true only for the salts of the strong acids; sodium acetate stabilises the transition state and destabilises the initial state.[15]

[14] (a) Waind, *J.*, 1954, 2879; (b) Altshuller and Everson, *J. Amer. Chem. Soc.*, 1953, **75**, 4823; (c) Davies and Tillett, *J.*, 1958, 4766.

[15] Pitman, unpublished results.

[16] E. Grunwald, " Solvation of Electrolytes in Dioxan–Water Mixtures," in " Electrolytes," ed. B. Pesce, Pergamon Press, Oxford, 1962, p. 62.

important; with some nucleophilic anions it leads to chemical reactions,[2,3] and an anion which did not react chemically might block approach of a water molecule.

All the salts which we have studied deactivate the transition state (except sodium acetate [15]), and classical ionic-strength effects due to coulombic interactions seem to be comparatively unimportant, although the reaction rate is very sensitive to the water content of the solvent.   (In solvolysis of many alkyl halide parallels can be drawn between salt and solvent effects, because charge formation, as in an $S_N 1$ reaction of an uncharged reactant, will be favoured both by a high ionic strength and by a high dielectric constant of the solvent.[17])   But the important factor in anhydride hydrolysis is, not the dielectric constant, but the hydrogen-bonding power of the solvent.   It is probable that the transition state for anhydride hydrolysis derives considerable stability from hydrogen-bonding between water and the anhydride, and the nucleophilic water molecule which we formally include in it; *e.g.*, the transition state can be written crudely as (III) (the broken lines represent hydrogen-bonding interactions which will spread the positive and negative charges over the neighbouring water molecules).   Thus the transition state should be stabilised by solvation by many water molecules, and this results in anhydride hydrolyses having negative entropies of activation [1] and being much slower in deuterium oxide than in water.[18]   The ions of a salt will compete with this transition state for the water molecules and therefore destabilise it, and because the charges upon the polar transition state are diffused by hydrogen bonding the ionic atmosphere of the salts will not stabilise it.   We did not include the activity of water in the Brönsted–Bjerrum equation, and some of the increase in f_* may be caused simply by a decrease in the activity of water.

To account for the effect of electrolytes on the structure of water Frank and others [19] have suggested that ions are surrounded by a tightly held layer of water molecules which is itself surrounded by a layer of disordered water molecules, that the size of these layers depends upon the charge density of the ions, and that the solvated ions are therefore in a region in which the regular structure of the water is broken down.   This disordering of the structure of water should affect its properties as a solvent, and we might also expect to find some differences between salts in respect to their interactions with the transition state.   Our present evidence is too limited to show such differences, and we plan to extend it by studying other salts, and in particular by studying other less reactive anhydrides in order to determine more accurate values of f_*.

However, we believe that these salt effects can be interpreted only in terms of the effects upon water, and that it is interesting to note that such varied properties as rates of hydrolysis,[1] changes in nuclear magnetic resonance shifts, and dielectric constant due to ions,[20] and such bulk properties as solubilities [11] and viscosity,[19] all show similar dependences upon the charge densities of the ions.   It has been suggested that the salt effects upon the hydrolysis of anhydrides are related to two factors, one electrostatic and the other due to solvation,[16] and correlations have been made of reaction rate with viscosity [21] and ionic hydration.[22]

It is interesting to compare the salt effects on the hydrolysis of acetic anhydride with those on other reactions.   Taft and his co-workers [23] have studied the hydrolysis of t-butyl chloride in water in great detail, and have shown that the salt effects on the activity coefficients of the initial and the transition state are highly specific, but that for many salts specific (non-coulombic) interactions cancel in the initial and the transition state.   The net

[17] C. K. Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, pp. 347, 362.
[18] Bunton and Shiner, *J. Amer. Chem. Soc.*, 1961, **83**, 3207.
[19] Frank and Wen-Yang Wen, *Discuss. Faraday Soc.*, 1957, **24**, 133; Samoilov, *ibid.*, p. 141; Kaminsky, *ibid.*, p. 171; Swain and Bader, *Tetrahedron*, 1960, **10**, 182.
[20] See ref. 6, Chap. 1, for summary.
[21] Szabo, *Z. phys. Chem.*, 1926, **122**, 405; cf. E. A. Moelwyn-Hughes, " Kinetics of Reactions in Solution," Oxford University Press, London, 1947, p. 216.
[22] Connolly, *Carnegie Inst. Publ.*, 1918, **260**, 131; *Chem. Abs.*, 1919, **13**, 3053.
[23] Clarke and Taft, *J. Amer. Chem. Soc.*, 1962, **84**, 2295.

kinetic salt effect for hydrolysis in homogeneous solution is then that due to the ionic-strength effect.[24] Salt effects on the acid hydrolyses of γ-butyrolactone and methylal can be assigned in part to effects on the initial state,[25] although such simple explanations do not apply to salt effects upon the acid hydrolysis of sulphite esters.[14c, 26] The hydrolysis of methyl and phenyl trifluoroacetate in aqueous dioxan is retarded by added salts, probably for the same reasons that apply to the hydrolysis of acetic anhydride.[27]

EXPERIMENTAL

All experiments were at 0°.

Homogeneous Solution.—The general procedure was that described in Part I. Reaction was followed by adding portions of the solution to an excess of aniline and titrating the acetic acid with standard sodium hydroxide.[28]

Partitioning Experiments.—Partitioning between water and an organic solvent seemed to be the most direct method for determination of the activity coefficients of acetic anhydride in aqueous salt solution. Water and carbon tetrachloride are almost completely immiscible, and neither acetic acid nor the salts are extracted into carbon tetrachloride. These solvents separate quickly and cleanly after shaking; this simplifies the removal of samples; however, sometimes, and particularly with the more concentrated salt solutions, we found that globules of carbon tetrachloride were slow to settle; some attempted experiments were spoilt for this reason.

Calculation of the distribution of acetic anhydride between water and carbon tetrachloride requires knowledge of the concentrations in both layers. That in the water layer was determined by withdrawing samples, with a pipette, and adding them to either water (samples A) or aniline (samples B). These samples were then titrated with standard alkali (for samples A it was most convenient to add an excess of standard alkali, and then to back-titrate with standard acid). If the molar concentration of acetic acid in the water layer is a, and that of acetic anhydride is b, then the titre of standard alkali for sample A is proportional to $(a + 2b)$, and that for sample B is proportional to $(a + b)$. Thus we determined the concentrations in the water layer. To determine them in the carbon tetrachloride layer we either removed some of this layer and estimated the anhydride in it directly (the " direct method "), or we calculated it from the amount of acetic anhydride added initially and the amounts of acetic anhydride and acetic acid present in the water layer (this we call the " mass-balance method "). We also showed that under our conditions acetic acid was not measurably extracted into carbon tetrachloride. A difficulty is that, because acetic anhydride was being hydrolysed and we could not determine a and b at the same time, it was necessary to interpolate the titration values, which are proportional to $(a + b)$ and $(a + 2b)$, to the same times. In most of the experiments we took the samples as quickly as possible (*ca.* one per min.) in order to reduce these uncertainties, and we took samples which were small ($<3\%$) compared with the total volume. The " mass-balance method " of calculation could then be applied to several points of the run provided that we allowed for the material removed from the water layer for titration and did not accidentally remove any of the carbon tetrachloride layer. In some of our early experiments we also removed some of the carbon tetrachloride layer by pipette, and we estimated the concentration of acetic anhydride in it by titration; this was not very successful, and in later experiments we removed this layer through a capillary tube at the bottom of the flask. The values of the distribution coefficients, and the methods of determining them, are given in Table 3.

It was necessary to show that the equilibrium between the phases was rapid in comparison with the hydrolysis. The half-life of the reaction is *ca.* 25 min. and therefore the composition of the phases was not changing very rapidly but we also used two different types of apparatus. In one a large bladed stirrer was used to agitate the interface, in the other the stoppered flask was shaken vigorously between the removal of samples. As further evidence that our

[24] Bateman, Church, Hughes, Ingold, and Taher, *J.*, 1940, 979.
[25] Long, McDevit, and Dunkle, *J. Phys. Chem.*, 1951, **55**, 829; Paul, *J. Amer. Chem. Soc.*, 1954, **76**, 3236; Long and McIntyre, *ibid.*, pp. 3240, 3243.
[26] Bunton, de la Mare, and Tillett, *J.*, 1958, 4754; 1959, 1766.
[27] Bunton and Hadwick, *J.*, 1958, 3248; 1961, 943.
[28] Vlés, *Rec. Trav. chim.*, 1933, **52**, 809; Kappelmeir and Van Goor, *Analyt. Chim. Acta*, 1948, **2**, 146.

TABLE 3.

Distribution coefficients of acetic anhydride between water and carbon
tetrachloride at 0°.

No Salt.

$H_2O : CCl_4$	50 : 200		200 : 300	
r	0·84 [d], 0·88(3) [a]		0·95 [d], 1·03(3) [a]; 0·85 [d], 0·95(3) [e]	
$H_2O : CCl_4$	50 : 50		60 : 20	300 : 100
r	0·97 [d], 1·1(2) [c]; 0·92(2) [c]	0·97 [d], 0·92 [c]; 1·1 [d], 1·03(3) [c]		0·93(2) [bd]

Added salt	0·5M-NaCl	1·0M-NaCl	3·0M-NaCl	1·0M-NaClO₄	3·0M-NaClO₄
$H_2O : CCl_4$	150 : 50	300 : 100	60 : 20	50 : 50	50 : 50
r	0·97 [b]	1·05(3) [b]	1·14 [d], 1·14(3) [c]	0·67 [d], 0·76(3) [c]	0·48 [d], 0·53(3) [c]

Added salt	1·0M-KBr	1·0M-KI	3·0M-KI	1·0M-MgSO₄	1·0M-Li₂SO₄
$H_2O : CCl_4$	200 : 50	60 : 20	50 : 50	300 : 100	300 : 100
r	0·82(5) [a]	0·71 [d], 0·75 [c]	0·59(3) [c]	3·5 [d], 3·2(3) [a]	3·3(3) [a]

Figures in parentheses are the number of values calculated. [a] 500 c.c. flask with stirrer and exit tube. [b] 500 c.c. flask with stirrer. [c] 100 c.c. stoppered cylinder with exit tube, shaken by hand. [d] Value determined directly; other values were obtained by the mass-balance calculation.

distribution experiments are meaningful we sometimes calculated the specific rates of hydrolysis in the aqueous layer, $(-d[Ac_2O]/[Ac_2O])/dt$, and found that they were in fair agreement with those determined conventionally. This meant that the transfer of anhydride across the phase boundary was either much faster or much slower than hydrolysis. The second possibility is highly improbable. In these experiments we did not take the samples quickly, but spread them out over a longer period of time (*e.g.*, there was a gap of 2—3 min. between each pair of readings).

All experiments were made with ice–water cooling, the apparatus and reagents were precooled to 0°, and samples were withdrawn with a cooled pipette. The ratio of water : carbon tetrachloride was varied between 3 : 1 and 1 : 4, the concentration of acetic anhydride in the water layer between 0·04M and 0·2M, and the volume of water between 50 and 300 c.c.

TABLE 4.

Time (sec.)	$a + b$	$a + 2b$	Time (sec.)	$a + b$ (Interpolated)	$a + 2b$ (Interpolated)	Time (sec.)	$a + b$	$a + 2b$
56		46·93	90	26·2	47·2	384	29·71	
94	26·28		300	28·8	48·9	522		49·83
220		48·55	400	29·8	49·4	560	31·00	
350		49·19	500	30·6	49·8			

Table 4 gives experimental results with CCl_4 50 c.c., M-NaClO₄ 50 c.c., and Ac_2O 20·3 mmoles. *a* and *b* are expressed as c.c. of 0·0205N-NaOH per 2 c.c. samples. At 470 sec. a portion of the carbon tetrachloride layer was equivalent to 31·9 c.c. of 0·0205N-sodium hydroxide per 5 c.c.; $r = 0·76$ (mass balance, mean of 3 values), and 0·67 (direct measurement). Some values of the instantaneous rate constants $10^4 k$(sec.$^{-1}$) taken at 200 sec. intervals are:

H_2O	4·5,	4·7,	4·7,	4·8,	4·6
,,	5·1,	5·1,	5·0,	5·0	
M-KBr	3·0,	2·6,	2·7,	2·7,	2·8
M-Li₂SO₄	6·6,	6·7,	7·0,	7·0,	7·3, 7·3

The mean values of other instantaneous rate constants were: 0·5M-NaCl 4·2; M-NaCl 4·0, 3·9; M-MgSO₄ 6·5. Iodine was liberated towards the end of the experiments with 3M-potassium iodide.