446. *The Hydrolysis of Acetic Anhydride. Part VI.* Kinetics in Deuterium Oxide Solution.*

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The velocities of the " spontaneous " and acetate-catalysed hydrolyses of acetic anhydride are reduced (by factors of 2·9 and $\sim$1·7, respectively) on changing from ordinary water to deuterium oxide as solvent. The formate-catalysed reaction is only slightly affected by this change of solvent. A reaction mechanism is put forward which accommodates the isotope effects and, at the same time, provides an explanation of the catalytic effect of acetate ions in this reaction. The rate-controlling step in this mechanism is a proton-transfer from hydrogen ion or acetic acid to the oxygen atom of an anionic intermediate. The general admissibility of a rate-determining step of this kind in a measurably slow reaction is discussed.

THE small but definite catalytic effect of acetate ions on the hydrolysis of acetic anhydride [1] has never been satisfactorily explained. It is possible that it is really the manifestation of a more general catalytic effect of bases. However, with tertiary amines [2] or carboxylate ions [1] (except acetate ions) other catalytic or anti-catalytic phenomena supervene, and these have so far prevented the detection (or proof of the absence) of the suspected general base-catalysis. As a rough rule, the carboxylate ions derived from acids that are stronger than acetic acid appear to be catalysts by virtue of the formation of a more easily hydrolysed unsymmetrical anhydride,[1,3] *e.g.*, acetic formic anhydride, whereas the addition of, for example, propionate ions retards the hydrolysis owing to the formation of the less reactive acetic propionic anhydride.[1,4] No such effect complicates the catalysis of an anhydride by its own carboxylate ions. Since no credible transition state could be formulated by rearrangement of the parts of acetic anhydride and acetate, it was considered that comparative measurements in ordinary and heavy water as solvents might throw some light of the degree of involvement of water in the transition state of the acetate-catalysed and also of the " spontaneous " reaction. In other spontaneous solvolytic hydrolyses, *e.g.*, of alkyl halides and alkyl sulphonates, the formation of the transition state from water and the substrate alone does not give rise to a large kinetic solvent isotope-effect.[5] The

* Part V, *J.*, 1955, 843.

[1] Kilpatrick, *J. Amer. Chem. Soc.*, 1928, **50**, 2891.
[2] Leman, *Bull. Soc. chim. France*, 1945, **12**, 908; 1947, **14**, 514; Bafna and Gold, *J.*, 1953, 1406; Gold and Jefferson, *J.*, 1953, 1409.
[3] Gold and Jefferson, *J.*, 1953, 1416.
[4] Kilpatrick and Kilpatrick, *J. Amer. Chem. Soc.*, 1930, **52**, 1418.
[5] Robertson and Laughton, *Canad. J. Chem.*, 1957, **35**, 1319.

detection of an appreciable solvent isotope-effect in the present case would therefore indicate a substantial difference in transition-state structure from that applying to nucleophilic substitution by water at a saturated carbon atom. These expectations have now been realised by experiment, and the interpretation of the size of the observed isotope effects has led to the formulation of a mechanism for the acetate catalysis.

EXPERIMENTAL

Deuterium oxide was the Norsk Hydro product with a stated deuterium content of $>99\%$, and all the results quoted for heavy water relate to isotopic compositions in the range $99 \cdot 5$—$99 \cdot 8\%$.

Acetic anhydride was purified as described by Gold and Hilton.[6]

Sodium acetate (" AnalaR," anhydrous) and sodium chloride (" AnalaR ") were dried at 110° for several hours and allowed to cool in a vacuum-desiccator. Sodium formate was dried *in vacuo* for several days and its purity was checked by analysis.[7]

Dioxan (" AnalaR ") was refluxed over sodium until the metal surface stayed bright, and then fractionally distilled. Mixtures of dioxan with ordinary and with heavy water were made up by diluting a measured or weighed amount of water to a fixed total volume with dioxan.

Solutions of acetic acid in heavy water were prepared by hydrolysis of acetic anhydride; those of formic acid were made by addition of anhydrous (isotopically normal) acid (" AnalaR "). At an acid concentration of $0 \cdot 03$M, the concentration of protium introduced thereby into the heavy water is insignificant.

In kinetic experiments (at 25°) the concentration of undecomposed acetic anhydride in solution (initial concentration *ca.* 10^{-3}M) was followed as a function of time by a spectrophotometric technique developed from Lees and Saville's colorimetric method.[8] This procedure gave results in agreement with runs followed by Vles's aniline–water method.[9] In order to help rapid dissolution of acetic anhydride, reaction mixtures were prepared by adding *ca.* $0 \cdot 05$ ml. of a stock solution of acetic anhydride in acetone to 10 ml. of water or aqueous buffer solution. The reported rate constants therefore relate to a solvent mixture containing *ca.* $0 \cdot 5\%$ of acetone by volume.

First-order rate constants are expressed in the units sec.$^{-1}$, and second-order constants as l. sec.$^{-1}$ mole^{-1}. In accordance with usual practice, the spontaneous rates are reported as first-order rate constants, k_0 (*i.e.*, without introducing the molarity of water into the calculation). Observed first-order rate constants in the presence of added substances are designated by the symbol k_1. All runs were strictly of first-order. The isotopic nature of the solvent is indicated by the superscripts H and D.

RESULTS

Spontaneous Rate.—The results are given in Tables.

(a) *Spontaneous rate constants in ordinary water* (k_0^{H}).
$2 \cdot 59 \times 10^{-3}$, $2 \cdot 61 \times 10^{-3}$, $2 \cdot 63 \times 10^{-3}$. Mean: $2 \cdot 61 \times 10^{-3}$.

(b) *Spontaneous rate constants in deuterium oxide* (k_0^{D}).
$8 \cdot 94 \times 10^{-4}$, $8 \cdot 97 \times 10^{-4}$, $8 \cdot 97 \times 10^{-4}$. Mean: $8 \cdot 96 \times 10^{-4}$.

Isotope effect: $k_0^{\mathrm{H}}/k_0^{\mathrm{D}} = 2 \cdot 9$.

(c) *Spontaneous rate in dioxan–water mixtures.*

Molarity of water $(\mathrm{H_2O})$	$10^5 k_0^{\mathrm{H}}$	Molarity of water $(\mathrm{H_2O})$	$10^5 k_0^{\mathrm{H}}$	Molarity of water $(\mathrm{D_2O})$	$10^5 k_0^{\mathrm{D}}$	$10^5 k_0^{\mathrm{H}}$ *	$k_0^{\mathrm{H}}/k_0^{\mathrm{D}}$
49·4	172	25·9	13·4	50·1	71	180	2·5
44·1	111	22·0	7·91	42·1	38·4	92	2·4
38·3	59·5	17·6	3·63	34·5	19·5	40	2·1
33·5	41·1	14·2	2·54	25·5	5·22	12·7	2·4
27·7	21·2			23·5	3·84	9·7	2·5
				16·0	1·86	3·3	1·8

* Calc. for the corresponding molarity of ordinary water by interpolation from the experimental rate constants in solvent mixtures with ordinary water.

[6] Gold and Hilton, *J.*, 1955, 838.
[7] Kolthoff and Belcher, " Volumetric Analysis," Interscience Publ. Inc., New York, 1957, Vol. III, p. 567.
[8] Lees and Saville, *J.*, 1958, 2262.
[9] Vles, *Rev. Trav. chim.*, 1933, **52**, 809.

Effect of Added Sodium Chloride.—This effect is also illustrated in Tables.

(a) *Added sodium chloride in ordinary water.*

[NaCl] (M)	—	0·149	0·299	0·397	0·504	0·598
$10^3 k_1$	2·61	2·54	2·45	2·37	2·30	2·25
$10^3 k_1$ (calc.*)	2·61	2·52	2·43	2·37	2·31	2·25

* Calc. from the empirical expression $10^3 k_1 = 2·61 - 0·60$[NaCl].

(b) *Added sodium chloride in heavy water.*

[NaCl] (M)	—	0·443	0·675
$10^4 k_1$	8·96	8·83	8·63
$10^4 k_1$ (calc.*)	8·96	8·78	8·69

* Calc. from expression $10^4 k_1 = 8·96 - 0·40$[NaCl].

Effect of Added Acetic Acid.—This is illustrated by the following results:

[AcOH]	0	0·021	0·031	0·041	0·0875	0·103	0·157	0·205
$10^3 k_1^H$	2·61	2·63	2·54	2·49	2·42	2·36	2·21	2·10

The small increase in rate at low concentrations of acetic acid was observed in a number of independent experiments and is considered to be real.

Acetate Catalysis.—In order to avoid complications from the non-linear effect of added acetic acid (whatever its cause), the acetate catalysis was studied in buffer solutions containing a fairly high concentration (~0·1M) of acetic acid. (This may be done without introducing any significant catalytic effect of hydrogen ions.) The rate increase accompanying the addition of sodium acetate was then found (see Tables) to be proportional to the acetate concentration.

(a) *Added acetic acid and sodium acetate in ordinary water.* [AcOH] = 0·0875M.

[NaOAc] (M)	0	0·031	0·061	0·091	0·120	0·181
$10^3 k_1$	2·42	2·53	2·69	2·78	2·94	3·10
$10^3 k_1$ (calc.*)	2·42	2·54	2·66	2·78	2·90	3·14

* Calc. from expression $10^3 k_1 = 2·42 + 4·0$[NaOAc].

(b) *Added acetic acid and sodium acetate in heavy water.* [AcOH] ~ 0·08M.

[NaOAc] (M)	0	0·103	0·143
$10^3 k_1$	0·88	1·16	1·25
$10^3 k_1$ (calc.*)	0·88	1·15	1·26

* Calc. from expression $10^3 k_1 = 0·88 + 2·6_5$[NaOAc].

Kilpatrick[1] has suggested that the electrolyte effect, which must be presumed to be one of the consequences of the addition of sodium acetate, can be estimated from experiments with sodium chloride[1] so that a corrected catalytic coefficient (k_{OAc}) can be calculated as $k_{OAc} = k_{NaOAc} - k_{NaCl}$, where k_X is the observed coefficient of the concentration of X in the empirical expressions for the variation of k_1 with [X], given as footnotes to the respective Tables above.
On this basis,

$$k^H_{OAc} = (4·0 + 0·60) \times 10^{-3} = 4·6 \times 10^{-3},$$

and

$$k^D_{OAc} = (2·6_5 + 0·04) \times 10^{-3} = 2·7 \times 10^{-3},$$

whence

$$k^H_{OAc}/k^D_{OAc} = 1·7.$$

Without consideration of the electrolyte effect, the solvent isotope-effect for acetate catalysis would be given by:

$$k^H_{NaOAc}/k^D_{NaOAc} = 4·0 \times 10^{-3}/2·6_5 \times 10^{-3}$$
$$= 1·5.$$

The value 1·7 is the more significant ratio, although the relatively great importance of the general electrolyte effect complicates the situation.

Formate Catalysis.—Sodium formate has a much greater effect on the reaction velocity than sodium acetate and, accordingly, the complicating features discussed above for the determination of the catalytic coefficient of the acetate ion are absent. The results are again tabulated.

(a) *Added formate in ordinary water.* [H·CO$_2$H] ~ 0·045M.

100[H·CO$_2$Na] (M)	—	0·96	1·92	2·88	3·66	4·54
10^3k_1	2·79	3·59	4·15	5·03	5·51	6·40
10^3k_1 (calc.*)	2·79	3·53	4·27	5·01	5·61	6·28

* Calc. from expression $10^3 k_1 = 2·79 + 77$[H·CO$_2$Na].

(b) *Added formate in heavy water.* [H·CO$_2$D] $\approx$ 0·035M.

[H·CO$_2$Na] (M)	—	0·0325
10^3k_1	1·06	3·43, 3·38
$k^D_{\text{H·CO}_2\text{Na}}$	—	73, 71

As the electrolyte effect is negligible compared with the catalytic acceleration,

$$k^H_{\text{H·CO}_2\text{Na}}/k^D_{\text{H·CO}_2\text{Na}} = k^H_{\text{H·CO}_2^-}/k^D_{\text{H·CO}_2^-}$$
$$= 77 \times 10^{-3}/72 \times 10^{-3} = 1·0_7.$$

DISCUSSION

The salient results are these: In aqueous solutions at 25°, the velocities of hydrolysis are reduced when the ordinary water of the solvent is replaced by deuterium oxide. The effect is most marked for the spontaneous rate, for which there is a reduction by a factor of 2·9. The corresponding factor for the catalytic coefficient of acetate ions is *ca.* 1·7, and that for formate ions is 1·1. In mixtures of dioxan with ordinary and with heavy water, the solvent isotope-effect of the spontaneous rate falls off gradually, and apparently not quite regularly, with increasing dioxan content of the media.

The small solvent isotope-effect found in the formate catalysis is of the order of magnitude commonly observed for reactions in which O–H bonds of the solvent are not ruptured in the rate-controlling step.[5] This result does not disturb the view[3] that the formation of acetic formic anhydride is the rate-controlling step in formate catalysis.*

The large solvent isotope-effects in the cases of the other two reactions indicate that their mechanism involves a weakening of O–H bonds on formation of the transition state,
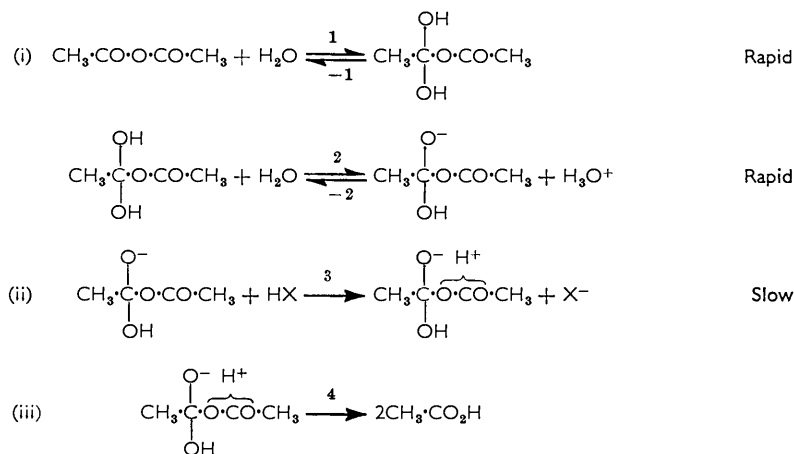
and a mechanism differing appreciably from a simple S_N2 substitution. The following mechanism takes account of Bender's conclusions[10] concerning the importance of hydration of the carbonyl group in the course of ester hydrolysis and also of the detailed information, obtained in the main by R. P. Bell and his school, regarding the thermodynamics and kinetics of the hydration of the carbonyl group in acetaldehyde. The scheme appears to

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* Owing to a misprint, a conclusion that Gold and Jefferson's results were " not incompatible " with the suggestion made by Kilpatrick was erroneously printed in ref. 3 as " not compatible."

[10] Bender, *Chem. Rev..* 1960, **60**, 63.

account for the isotope effects and, at the same time, appears to give an adequate explanation of the occurrence of acetate catalysis.

The mechanism postulates (i) the formation of an anionic species from hydroxide ion and acetic anhydride in a pre-equilibrium, and (ii) the rate-controlling reaction (3) of this anion with an acid. In detail, these steps can be represented as shown. It is assumed that there is no significant accumulation of any of the intermediates. The dissection of the pre-equilibrium (i) into the two steps shown is arbitrary and was done for reasons of thermodynamic convenience which will become obvious; it would have been equally justifiable to represent this reaction as the addition of hydroxide ions to acetic anhydride, the hydroxide ions having been formed by the rapid autoprotolysis of the solvent, or in some other way. Steps following the rate-controlling proton transfer (3) are considered to be kinetically insignificant, *i.e.*, reaction (4) is faster than the reversal of (3). HX represents a general Brønsted acid. Two cases of interest are (*a*) $HX = H_3O^+$ and (*b*) $HX = CH_3 \cdot CO_2H$, and these give rise to the following equations:

$$(a) \quad v = K_1 K_2 k_3^{H_3O^+} [Ac_2O].$$

This corresponds to the " uncatalysed " or " spontaneous " reaction with a first-order rate constant

$$k_0 = K_1 K_2 k_3^{H_3O^+}. \tag{1}$$

$$(b) \quad v = K_1 K_2 k_3^{AcOH} \cdot \frac{[AcOH]}{[H_3O^+]} \cdot [Ac_2O]$$

$$= K_1 K_2 \frac{k_3^{AcOH}}{K_{AcOH}} [OAc^-][Ac_2O],$$

where K_{AcOH} is the acid dissociation constant of acetic acid. This case represents the acetate-catalysed reaction, and the catalytic coefficient is given by

$$k_{OAc^-} = K_1 K_2 k_3^{AcOH} / K_{AcOH}. \tag{2}$$

The rate-controlling step (3) in our scheme is a proton transfer from the conjugate acid of the catalyst to an (unspecified) oxygen atom of the anionic intermediate. The scheme conflicts with a widely accepted principle of solution kinetics. It has, for example, been stated by Bell and Darwent [11] that acid–base reactions involving the transfer of a proton to or from an oxygen atom are known to be very rapid and cannot, therefore, be rate-determining in the reaction mechanism of a catalysed reaction. However, this conclusion is not necessarily correct. While it is true that the *rate constants* of such processes will have large values it does not follow that the processes themselves must be rapid. In our case the reaction velocity will be the product of the rate constant *and of the concentration of the intermediate*. Provided the intermediate is present in very low concentration, a rate-determining step with a very large rate constant may still produce a measurable velocity. This proviso will hold in the present example.

There are, of course, no direct measurements on the postulated pre-equilibrium (i) for acetic anhydride from which the concentration of the intermediate anion could be calculated. The value of the corresponding equilibrium constant (K_i) is, however, known for the addition of hydroxide ion to acetaldehyde in aqueous solution. In this case K_1 lies [12,13] between 1 and 2 and [14] $K_2 = 3 \cdot 3 \times 10^{-14}$ (the concentration of water being set equal to unity), so that $K_i = K_1 K_2 \approx 5 \times 10^{-14}$ (see also ref. 15). The value of this

[11] Bell and Darwent, *Trans. Faraday Soc.*, 1950, **46**, 34.
[12] Bell and Clunie, *Trans. Faraday Soc.*, 1952, **48**, 439; Bell and Rand, *Bull. Soc. chim. France*, 1955, 115.
[13] Rumpf and Bloch, *Compt. rend.*, 1951, **233**, 1364; Lombardi and Sogo, *J. Chem. Phys.*, 1960, **32**, 635.
[14] Bell and McTigue, *J.*, 1960, 2983.
[15] Rumpf, *Bull. Soc. chim. France*, 1946, **13**, 546; 1955, 117.

constant for acetic anhydride may well be somewhat greater, but it is not expected to differ from the acetaldehyde value by many powers of ten. On the basis of considerations put forward by Bell *et al.*,[12] K_1 should be somewhat smaller and (by straightforward analogies) K_2 greater than the values for acetaldehyde. If, for the sake of illustration only, a value of $K_i \approx 10^{-12}$ is taken to apply to acetic anhydride, and we combine this with the experimental rate constant of the spontaneous reaction at 25°, we obtain a value of 2×10^9 for $k_3^{H_3O^+}$. This is clearly a very large rate constant and only about ten times smaller than the value for a diffusion-controlled bimolecular reaction in solution.[16] If K_i were 5×10^{-14}, $k_3^{H_3O^+}$ would roughly equal the rate constant for a diffusion-controlled reaction. The above scheme cannot, therefore, be rejected on the ground that the required rate constant of the rate-controlling step has too *small* a value for a proton-transfer of this type.

The fact that the spontaneous hydration of acetaldehyde is a measurably slow process [11,12] need not conflict with the requirement that the pre-equilibrium (i) must be rapidly established for the hydrolysis of acetic anhydride. It is difficult to predict whether the rate of formation of the dihydroxy-intermediate would be much greater in the case of acetic anhydride, but the problem may not be relevant to the present issue since the anionic intermediate is not necessarily formed *via* the dihydroxy-compound, but could result from the interaction of acetic anhydride and hydroxide ion.

In order to discuss the solvent isotope-effects we must consider how the factors into which k_0 and k_{OAc} can be split [see equations (1) and (2)] would be altered on passing from ordinary to heavy water as solvent. By analogy with the hydration equilibrium for acetaldehyde,[17] K_1^H/K_1^D should have a value not far removed from unity. The ratio K_2^H/K_2^D expresses the solvent isotope-effect on the dissociation constant of an electrically neutral acid, and is expected to lie in the range 2·5—4·5. For acetaldehyde hydrate the corresponding ratio has a value [17] of 4·5. If we consider the general trend of such ratios with acid strength (which holds at least for structurally similar acids [18]), a value between 3 and 3·5 seems reasonable for the hydrate of acetic anhydride. By analogy with other cases,[19] the ratio $(k_3^{H_3O^+})^H/(k_3^{D_3O^+})^D$ will be close to unity. Accordingly, k_0^H/k_0^D should be mainly governed by the value of K_2^H/K_2^D, and the observed value of 2·9 for the rate ratio agrees with this deduction.

For acetate catalysis the effects on K_{AcOH} and k_3^{AcOH} must also be considered. The former is known fairly accurately [20] $(K_{AcOH}^H/K_{AcOD}^D = 3·3)$. We can give no soundly based *a priori* estimate for the latter, but it seems reasonably certain that $(k_3^{AcOH})^H/(k_3^{AcOD})^D$ would be greater than $\sqrt{2}$, on the ground that the attachment of the proton (which is being transferred from one oxygen atom to another) would be loosened during the formation of the transition state. The experimental value of $(k_3^{AcOH})^H/(k_3^{AcOD})^D$ is derived as follows. From equations (1) and (2) we deduce that

$$k_{OAc}/k_0 = k_3^{AcOH}/k_3^{H_3O^+} K_{AcOH},$$ (3)

and hence

$$\frac{(k_3^{AcOH})^H}{(k_3^{AcOD})^D} = \frac{k_0^D}{k_0^H} \cdot \frac{(k_3^{H_3O^+})^H}{(k_3^{D_3O^+})^D} \cdot \frac{k_{OAc}^H}{k_{OAc}^D} \cdot \frac{K_{AcOH}^H}{K_{AcOD}^D}$$

$$= \frac{1}{2·9} \times (\sim 1) \times 1·7 \times 3·3$$

$$\approx 1·9,$$

which is compatible with the above consideration.

[16] Bell, *Quart. Rev.*, 1959, **13**, 169.
[17] Pocker, *Proc. Chem. Soc.*, 1960, 17.
[18] Högfeldt and Bigeleisen, *J. Amer. Chem. Soc.*, 1960, **82**, 15.
[19] Long and Watson, *J.*, 1958, 2019.
[20] Korman and La Mer, *J. Amer. Chem. Soc.*, 1936, **58**, 1396; La Mer and Chittum, *ibid.*, p. 1642.

Equation (3) may also be examined in relation to the Brønsted catalysis law, but the precise conclusion somewhat depends on the convention adopted with regard to the acid strength of the hydrogen ion and the inclusion of the concentration of water in the term for the spontaneous rate. By Bell's usage,[21] equation (3) should in this connection be modified to give

$$55 \cdot 3 k_{\text{OAc}}/k_0 = k_3^{\text{AcOH}}/k_3^{\text{H}_3\text{O}^+} K_{\text{AcOH}}$$

On expressing k_3 as GK^α (the statistical factor for the hydrogen ion being taken as unity [21]) and inserting the experimental values, we obtain

$$55 \cdot 3 \times \frac{4 \cdot 6}{2 \cdot 61} = \left(\frac{1 \cdot 75 \times 10^{-5}}{55 \cdot 3}\right)^\alpha \cdot \frac{1}{1 \cdot 75 \times 10^{-5}}$$

or

$$(55 \cdot 3)^2 \times \frac{4 \cdot 6}{2 \cdot 61} = \left(\frac{1 \cdot 75 \times 10^{-5}}{55 \cdot 3}\right)^{\alpha - 1}$$

whence $\alpha = 0 \cdot 43$. This figure is subject to the uncertainty inherent in the assumptions required, but is probably of some predictive value.

As is well known, the numerical value of the Brønsted exponent decides whether general catalysis is experimentally observable in a given reaction, and the absence of measurable general catalysis does not invalidate a reaction scheme which formally involves general catalysis. The above reaction mechanism may therefore apply to other spontaneous hydrolyses of carbonyl compounds for which large solvent isotope-effects have been observed, even where there is no experimental evidence of catalysis by bases other than water.[22]

Since k_0 is a composite quantity, it follows that the experimental activation energy will be the sum of a number of terms, including the heat of ionisation of the dihydroxy-intermediate. As heats of ionisation are generally temperature-dependent, it is reasonable to suppose that the experimental activation energy should also be markedly temperature-dependent, as was established a number of years ago.[23] The composite nature of the activation energy may also explain its uncommonly small value.[23]

It has previously been remarked [23] that the negative salt effect in this reaction does not seem to be explicable in terms of long-range electrostatic effects. This view is strongly reinforced by our observation that the effect of sodium chloride on the hydrolysis in heavy water is very much less than the effect in ordinary water.

Lest the scope of the above kinetic scheme be misunderstood, we emphasise that our experimental evidence requires solely that the transition state should contain (in a rearranged form) one acetic anhydride, one acetate, and at least one water molecule. The timing of the steps by which these entities come together can be discussed only on the basis of considerations other than those of kinetic orders. The timing implied by the scheme given is preferred to others on the ground of simplicity: it requires no novel mechanistic postulate or steps of molecularity greater than 2 and, as we believe to have shown, it allows us to assign acceptable values to the rate and equilibrium constants involved.
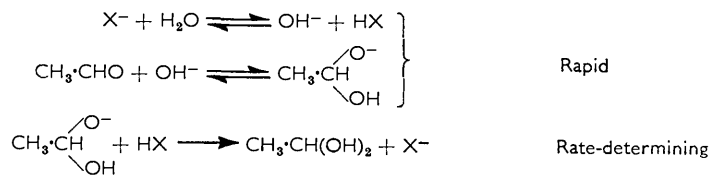
In our discussion we have drawn heavily on analogies with the hydration of acetaldehyde. The analogy also implies that the argument which caused us to admit the possibility of a rate-determining proton transfer to oxygen in the case of acetic anhydride would similarly apply to the mechanisms of the hydration of acetaldehyde. For example, it does not

[21] Bell, " Acid–Base Catalysis," Oxford Univ. Press, 1941, pp. 91, 92.
[22] Butler and Gold, *Chem. and Ind.*, 1960, 1218; cf. Bunton, Fuller, Perry, and Shiner, *Chem. and Ind.*, 1960, 1130.
[23] Gold, *Trans. Faraday Soc.*, 1948, **44**, 506.

seem possible to dismiss a scheme of the following type for the base (X⁻)-catalysed reaction:

$$X^- + H_2O \rightleftharpoons OH^- + HX$$

$$CH_3 \cdot CHO + OH^- \rightleftharpoons CH_3 \cdot CH \underset{\diagdown OH}{\overset{\diagup O^-}{}} \qquad \Bigg\} \qquad \text{Rapid}$$

$$CH_3 \cdot CH \underset{\diagdown OH}{\overset{\diagup O^-}{}} + HX \longrightarrow CH_3 \cdot CH(OH)_2 + X^- \qquad \text{Rate-determining}$$

solely because the rate constant of the final step is expected to have a large value. We are not here concerned with the issue whether such a scheme would be acceptable on other grounds.

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