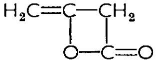
691. *Acylation. Part XVI.** *The Spontaneous and Catalysed Hydrolysis of Diketen* †

By J. M. Briody and D. P. N. Satchell

The kinetics of the spontaneous, the acid-catalysed, and the base-catalysed hydrolysis of diketen in 40 : 60 v/v dioxan–water mixtures have been studied. The general pattern is similar to that for β-lactones, in keeping with the accepted structure of diketen. Acyl–oxygen ring-opening appears to be always involved for diketen, in contrast to saturated β-lactones, and anions do not attack the β-carbon atom. Pyridine leads to nucleophilic catalysis, and acetate, chloroacetate, and acetoacetate ions to a weaker catalysis, which is perhaps of the general base type. Hydrolysis catalysed by hydroxide ion is very rapid, and a previous claim that diketen ionises as an acid of p$K \approx 7$ to yield the anion (IV) is mistaken. The reported apparent stability of diketen towards hydrolysis is superficial, and is due to its insolubility in water.

Much previous work on diketen has been focused on its structure,[1] which now seems solved: various lines of evidence [1,2] suggest the β-lactone formulation (I). Diketen has been shown to be normally an acetoacetylating agent,[1] and it is widely used as such industrially. Few quantitative data exist for a comparison of its reactivity with that of other β-lactones or other acylating agents. However, kinetic studies on the acetoacetylation of substituted anilines in aprotic solvents show the speed of these bimolecular reactions to be related linearly to the basic strength of the aniline.[3] Surprisingly, diketen does not appear to be readily hydrolysed (to produce acetoacetic acid) and may even be distilled in the presence of water with little decomposition.[4] Since (I), as regards reactivity and susceptibility to catalysis,[5] should be similar to β-propio- (II) and β-butyro-lactone (III), we have studied the spontaneous and catalysed hydrolysis of diketen to check this point and to supplement the few available data. Our results cast grave doubt on the proposed [6] ionisation of (I), as an acid of p$K \approx 7$, to give the anion (IV).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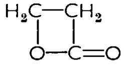
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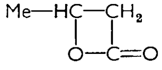
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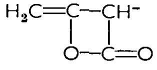
(IV)

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* Part XV, *J.*, 1965, 1057.

† See also *Chem. and Ind.*, 1964, 893.

[1] R. N. Lacey, *Adv. Org. Chem.*, Vol. 2, p. 213.

[2] D. W. Moore, *J. Chem. Phys.*, 1961, **34**, 1470; J. R. Johnson and V. J. Shiner, *J. Amer. Chem. Soc.*, 1953, **75**, 1350.

[3] R. Lyashenko and U. Sokolova, *J. Gen. Chem.* (*U.S.S.R.*), 1947, **17**, 1868.

[4] A. B. Boese, *Ind. Eng. Chem.*, 1940, **32**, 16.

[5] A. R. Olson and R. J. Miller, *J. Amer. Chem. Soc.*, 1938, **60**, 2687; F. A. Long and M. Purchase, *ibid.*, 1950, **72**, 3267.

[6] A. Wassermann, *J.*, 1948, 1323.

EXPERIMENTAL

Materials.—Diketen was prepared by Williams and Krynitsky's method,[7] and purified by three successive fractional distillations, giving a sample with b. p. 69—70°/92 mm., m. p. $-6{\cdot}5°$, which was stable over long periods when stored at $-20°$. (At normal temperatures diketen tends to polymerise.) Dioxan of AnalaR grade was further purified by successive distillations from potassium hydroxide and metallic sodium; it had b. p. 101·5°. Ethyl acetoacetate was purified by Pedersen's method [8] and had b. p. 94°/32 mm. Acetoacetic acid decarboxylates readily, and so standard samples were prepared *in situ* by hydrolysis of the ethyl ester. Acetic and chloroacetic acids were AnalaR samples. Aniline was shaken with stannous chloride, filtered, and distilled from zinc dust. It had b. p. 184°. 2,4- and 2,6-Lutidine, were purified similarly, and shown to be free from other isomers by gas-liquid chromatography (b. p. 157 and 142°, respectively). Pyridinium perchlorate, prepared by neutralisation, was crystallised from water. Inorganic materials were the AnalaR reagents, wherever possible. Stock solutions of perchloric acid in a 40 : 60 v/v dioxan-water mixture were accurately prepared.[9]

Reaction Products and Stoicheiometry.—Diketen and water first yield acetoacetic acid, which, however, decarboxylates to acetone at an appreciable rate, especially in the presence of primary bases.[10] Thus the stoicheiometry cannot be tested by assay of the free acid; decarboxylation must be allowed to go to completion and the amount of acetone determined. The spontaneous and acid-, hydroxide-, chloroacetate-, and amine-catalysed hydrolyses studied gave yields of $>95\%$ of acetone, indicating that under our conditions hydrolysis was essentially complete. Hydrolysis catalysed by acetate and acetoacetate gave decreasing yields of acetone with increasing concentration of catalyst (see below). The acetone was estimated colorimetrically with salicylaldehyde.[11]

Diketen reacts with acetone,[1] and if this reaction occurred during the later stages of the hydrolysis (when some acetone had built up) the kinetic form of the diketen loss would probably have been disturbed. We noted no such disturbance (see below) and therefore this possible side-reaction is probably insignificant under our conditions.

Kinetic Arrangements.—Because diketen is insoluble in pure water, a 40 : 60 v/v dioxan-water solvent was used throughout. The reaction mixtures were contained in 10-ml. volumetric flasks immersed in a thermostat bath. Reaction was initiated by the final addition of *ca.* 0·08 ml. (*ca.* 0·1M) of diketen. At intervals 1-ml. samples were withdrawn and run into dioxan (5 ml.) containing sufficient aniline ($\sim$10%) effectively to quench the hydrolysis by successful competition with the water present for the remaining diketen. Since reaction with even this quantity of aniline is only moderately fast, the quenched solutions were left for 1 hr. at 25° before being made up to 10 ml. with water. After a further hundredfold dilution with dilute hydrochloric acid, the acetoacetanilide content (and hence the diketen content of the original sample) was determined by spectroscopic measurements at 2400 Å against a blank sample containing suitably diluted quenching mixture. Acidification is necessary to convert the excess of aniline into the anilinium ion, and so largely to remove its spectrum from the 2400 Å region. For acid-catalysed hydrolyses the quenching solution contained proportionately more aniline, so that enough remained after the addition of the acidic sample of reaction mixture.

It was shown in independent experiments that diketen is effectively quantitatively converted into acetoacetanilide by the quenching mixture (any free acetoacetic acid is decarboxylated, this reaction being markedly catalysed by aniline).

The observed loss of diketen always proved to be an accurately first-order process (except as noted under acetate catalysis). The rate constants obtained were all reproducible to within $\pm 1\%$.

Determination of pH.—A pH meter (Cambridge Instruments Ltd.), with a glass electrode and a calomel reference electrode, was calibrated with standard aqueous buffers. The apparent pH of the stock dioxan-water medium was 5·8 (the water used was not free of carbon dioxide).

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[7] L. Williams and O. Krynitsky, *Org. Synth.*, Coll. Vol. III, p. 508.

[8] K. J. Pedersen, *J. Phys. Chem.*, 1933, **37**, 751.

[9] C. A. Bunton, J. B. Ley, A. J. Rhind-Tutt, and C. A. Vernon, *J.*, 1957, 2327.

[10] (*a*) K. J. Pedersen (*J. Amer. Chem. Soc.*, 1929, **51**, 2098) states that this has been shown for acetoacetic acid by Ljunggren, Dissertation, Lund, 1925; (*b*) K. J. Pedersen, *Acta Chem. Scand.*, 1961, **15**, 1718.

[11] F. D. Snell and C. T. Snell, "Colorimetric Methods of Analysis," D. Van Nostrand, New York, 1953, p. 292.

The pK values of pyridine and the lutidines in dioxan–water solvent were estimated by measuring the pH at their points of half-neutralisation. Changes of pH during the course of some of the slower reactions were also studied, the readings usually becoming steady after about 2 mins.

Results and Discussion

Spontaneous Hydrolysis.—As noted above, side-reactions were not significant during spontaneous hydrolysis: acetone yields were always >95%. The loss of diketen in the excess of solvent was an accurately first-order process over the whole reaction. The primary product being acetoacetic acid, there is a pH shift during the hydrolysis from *ca.* 5·8 to *ca.* 3·0, depending on the stoicheiometric amount of diketen solvolysed. Since the observed plots were accurately rectilinear, it is clear that the hydrolysis has a pH-independent region. The use of appropriate buffers, and experiments with added perchloric acid, showed this region to extend from *ca.* 8·0 to *ca.* 1·0. Beyond these limits catalysis by both acid and base is detectable, and within them catalysis by certain anions may also supplement the spontaneous rate (see below). Similar effects have been recorded for β-propio- and β-butyro-lactones.[5]

$$\text{CH}_2\text{=C—CH—O—CO} + \text{H}_2\text{O} \longrightarrow \text{CH}_3\text{COCH}_2\text{CO}_2\text{H} \longrightarrow (\text{CH}_3)_2\text{CO} + \text{CO}_2 \qquad (1)$$

The magnitude of the observed first-order rate constant ($k_{\text{H}_2\text{O}}$; Table 2) is approximately two-thirds of the corresponding value for β-propiolactone. The latter, however, refers to pure water and it is probable therefore that diketen is intrinsically somewhat the more easily hydrolysed, though the reactivities of the two compounds must be comparable. The value of the rate constant at 25° is such that if, as reported,[4] diketen and water may be co-distilled with little resulting hydrolysis, then this must be due to their very great mutual insolubility even at 100°.

Table 1

The spontaneous and acid-catalysed hydrolysis of diketen at 24·9°

$[\text{Diketen}]_{\text{initial}} \simeq 0\cdot1\text{M}$ in all Tables; $k_{\text{obs.}}$ = observed first-order rate constant in min.$^{-1}$; $k_{\text{H}_2\text{O}}$ = first-order rate constant for spontaneous hydrolysis; $k_{\text{H}^+} = (k_{\text{obs.}} - k_{\text{H}_2\text{O}})$; H_0 data from ref. 9; square brackets represent molarity.

[HClO$_4$]	$10^3k_{\text{obs.}}$	$10^3k_{\text{H}^+}$	$(3 + \log k_{\text{H}^+})$	H_0
0	2·10	—	—	—
0·49	3·46	1·36	0·134	+1·02
0·98	5·16	3·06	0·486	+0·42
1·47	7·82	5·72	0·757	+0·07
1·96	13·4	11·3	1·052	−0·25
2·45	25·2	23·1	1·363	−0·58
2·93	45·2	43·1	1·635	−0·90
3·42	88·7	86·6	1·938	−1·22
3·91	192	190	2·279	−1·61

Data in Table 2 lead to a value of 12—13 kcal./mole for the activation energy of the spontaneous diketen hydrolysis, considerably less than the 19·4 kcal./mole found for β-propiolactone.[5] It seems that the energy of ring-opening is less for diketen and that the entropy of activation is notably greater than for propiolactone. These facts suggest that acyl–oxygen fission occurs in the spontaneous diketen hydrolysis, rather than the alkyl–oxygen fission found with saturated β-lactones. This suggestion is supported by

Table 2

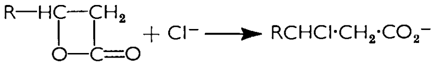
Variation of spontaneous rate with temperature

T_p (°K)	297·9		308·0		322·3
$10^3k_{\text{H}_2\text{O}}$	2·10		4·11		10·7
ΔE (kcal./mole)		11·9		13·2	

facts detailed below. It is also significant that the activation energies for the hydrolysis of compounds (II) and (III) by hydroxide ion—processes known to occur by acyl–oxygen fission—are 11·3 and 13·4, respectively.[5]

The mechanism of the spontaneous hydrolysis is discussed in more detail later.

Effects of neutral salts.—Lactones (II) and (III) react [1,5,12] with a variety of anions to yield products resulting from alkyl–oxygen fission, *i.e.*, from nucleophilic attack on the β-carbon atom as in equation (2).



(2)

The addition of a salt during hydrolysis will therefore often enhance the removal of lactone. Perchlorates and nitrates, however, do not participate in these processes and produce only a normal salt effect. This is quite small. With diketen we find no evidence for attack at the β-carbon atom. Addition of chloride, iodide, or thiocyanate, as well as of perchlorate, does not reduce the acetone yield and produces only small changes in the hydrolysis rate (Table 3). [Iodide and thiocyanate are two of the most potent anions towards compounds (II) and (III).] Thus, as is to be expected, nucleophilic attack at the (unsaturated) β-carbon atom is much less important with diketen than with the saturated lactones, and we consider that all the hydrolyses reported in this Paper involve acyl–oxygen fission.

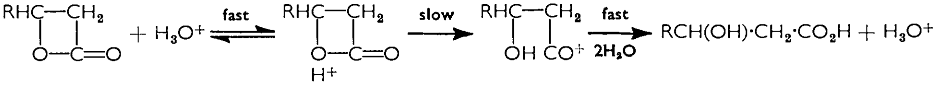
TABLE 3

Effects of added salts at 24·9°

Salt	KCl	KCl	KCl	$NaClO_4$	$HClO_4$	KI	KI	KCNS	KCNS	—
[Salt]	0·0115	0·0470	0·1023	0·0878	0·0978	0·0340	0·0675	0·0623	0·1110	—
$10^3k_{obs.}$	2·16	2·15	2·18	2·11	2·10	1·81	1·62	2·78	3·20	2·10

The presence of a more basic anion—chloroacetate, acetate, or acetoacetate—leads to notably greater acceleration of the loss of diketen. We interpret this as basic catalysis rather than as an electrolyte effect, and discuss it below.

Acidic Catalysis.—When the pH is reduced below *ca.* 1·0, *i.e.*, in acidic solutions >0·1M, acid-catalysed hydrolysis is observed (Table 1). A plot of the logarithm of the first-order catalytic rate constant ($k_{H^+} = k_{obs.} - k_{H_2O}$) against H_0 leads to a straight line of slope 0·91. The acid-catalysed hydrolyses of compounds (II) and (III) are also controlled by H_0, and Long and Purchase have argued (using the Zucker–Hammett hypothesis) that the following mechanism obtains (acyl–oxygen fission is known to be involved for saturated lactones in this case, as for hydroxide ion catalysis [5])



(3)

Although the Zucker–Hammett hypothesis is at present out of favour, we suggest a similar mechanism for the acid-catalysed hydrolysis of diketen. Even if this mechanism proves wrong in detail it seems certain at least that the hydrolysis of (II), (III), and diketen are all very similar under acidic conditions. At a given value of H_0, diketen hydrolyses 20—30 times faster than (II) and about 4—6 times faster than (III).

Catalysis by Hydroxide Ions.—The lactones (II) and (III) react rapidly with hydroxide ions, the reaction first becoming noticeable in comparison with the spontaneous rate at a pH of *ca.* 9. Long and Purchase succeeded in measuring the rate constant for the reaction of compound (II) with hydroxide in water at 0°. We find that diketen in dioxan–water reacts much more rapidly, and we have been unable to establish the corresponding rate constant. The considerable difference in reactivity may reflect a genuine difference between the

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[12] P. D. Bartlett and G. Small, *J. Amer. Chem. Soc.*, 1950, **72**, 4867.

compounds or be a consequence of the difference in medium.[13] The speed of the diketen reaction and the fact that the hydrolysis is effectively quantitative permits the titration of diketen with alkali. This titration is not an acid–base neutralisation as thought by Wassermann:[6]

(I) (IV) (4)

No diketen is recoverable, even on immediate reacidification. Wassermann attempted to establish the pK of (I) as an acid by measuring the pH of aqueous acetone and buffered aqueous acetone solutions at different stoicheiometric concentrations. He considered that his results indicated a p$K \approx 7$. We have obtained somewhat similar pH measurements in dioxan–water. However, their suggestion of an acid with p$K \approx 7$ is entirely fortuitous. When diketen is added to the solvent the latter's pH falls with time owing to the hydrolysis (acetoacetic acid formation), as Wassermann realised. He extrapolated to zero time to obtain the " initial " pH (and thence the supposed acidity constant). However, the first pH reading cannot be taken much sooner than 2 min. after the addition of the diketen and the extrapolation involved is, in fact, quite uncertain because the pH–time curve steepens near the axis. Moreover, a knowledge of the spontaneous rate of hydrolysis (Table 1) and the pK of acetoacetic acid in the solvent (*ca.* 4·8) permits the demonstration that within 2 min. sufficient acetoacetic acid will have formed (very little is needed) to bring the pH, initially at *ca.* 5·8,* to *ca.* 4·7, the value necessary to lead to a p$K \approx 7{\cdot}0$ on the assumption that diketen is an acid. Similar arguments apply to pH measurements on buffered solutions (solutions containing added alkali which reacts with part of the diketen). In these, the general pH level is higher because they, in fact, contain some alkali acetoacetate, a salt whose solutions have pH ≈ 7. In these cases Wassermann interpreted the pH as representing that of the approximately half-*neutralised* diketen, hence again obtaining a pK value of 7 for its supposed acidity constant.

Wassermann was aware that his pH results might be attributable simply to acetoacetic acid formation, but concluded that this implied a pH-dependent equilibrium between diketen and water, an implication he felt able to refute. His reasoning in these contexts is obscure and there is no question that all the observed pH effects are correctly attributable to formation of acetoacetic acid by hydrolysis. The conductances found by Wassermann for diketen in non-hydroxylic media probably arose from enolic condensation products, for diketen polymerises readily.[1]

Other powerful arguments against any ionisation to give the anion (IV) include the deuterium-exchange data of Johnson and Shiner[2] (who found *slow* exchange of the α-hydrogen atoms in neutral solution) and the fact that the spontaneous hydrolysis is pH-indendent over a wide range. This implies that if diketen were to ionise, the reactivities of (I) and (IV) towards hydrolysis would be essentially identical, which is unlikely.

Catalysis by other Bases.—(*a*) *Chloroacetate.* Table 4 contains hydrolysis rates obtained in the presence of chloroacetic acid–chloroacetate buffers, some of constant buffer ratio.†

TABLE 4

Catalysis by chloroacetate at 24·9°

[$ClCH_2{\cdot}CO_2H$]	0·300	0·102	0·203	0·305	0·184	0·126
[$ClCH_2{\cdot}CO_2Na$]	0·0	0·049	0·097	0·148	0·116	0·175
$10^3k_{obs.}$	2·13	3·50	4·30	5·31	4·45	6·70

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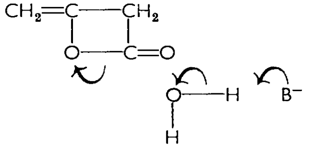
* Curiously, the pH of Wasserman's solvent is given as 4, *i.e.*, it is apparently more acidic before adding the supposedly acidic diketen than it is after this substance has been added (pH $\approx$ 4·5).

† The buffers were produced by partial neutralisation of chloroacetic acid.

[13] Y. Shalitin and S. A. Bernhard, *J. Amer. Chem. Soc.*, 1964, **86**, 2291.

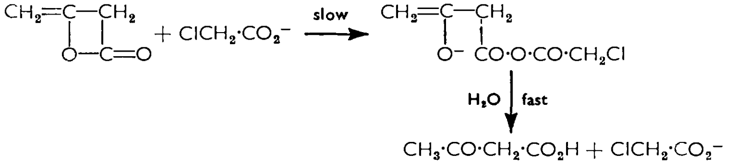
Chloroacetic acid alone does not affect the rate. Chloroacetate was studied in the presence of free acid to keep the pH low and so prevent the conversion of significant amounts of the chloroacetate anion into the free acid by reaction with acetoacetic acid produced during hydrolysis.

Chloroacetate evidently enhances the rate. All the data—even from those experiments without a constant buffer ratio—fall on the same smooth curve. Why the rate is not exactly proportional to salt concentration is not clear, but pH effects are clearly in abeyance (as expected) and, as noted on p. 3781, we attribute the acceleration in rate to catalysis by the chloroacetate ion. The catalysis we favour is that sometimes called base catalysis,[14] where the base renders the substrate (water) more nucleophilic by accepting a proton from it as it attacks the acylating agent,[15] thus:



(5)

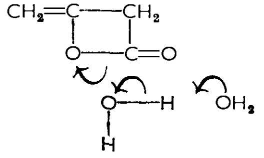
In an alternative mechanism—sometimes called nucleophilic catalysis[14]—the base temporarily takes the place of the substrate by forming a reactive intermediate with the acylating agent. In the present case this would involve the formation of an unsymmetrical anhydride:



(6)

The incursion of nucleophilic catalysis in any given case appears to us[16] a function of both the nucleophilicity of the basic catalyst and the ease of departure of the leaving group from the acylating agent (here involving ring-opening). With good leaving groups the majority of basic catalysts are sufficiently nucleophilic, and this type of catalysis is favoured. Conversely, with poor leaving groups only very powerful nucleophiles (*e.g.*, OH^-, RNH^-) are successful as attacking reagents, and weak bases therefore operate by helping to convert the substrate (*e.g.*, water) into its conjugate anion, which anion then engages in nucleophilic attack, as in (5). There is evidence[17] that chloroacetate provides only this latter kind of catalysis in the hydrolysis of some carboxylic anhydrides (which have even better leaving groups than lactones or esters) and that the more basic acetate ion is also an unsuccessful nucleophile in the hydrolysis of *p*-nitrophenyl esters.[17] It is clear, therefore, that in the present case, chloroacetate is more likely to effect catalysis by route (5), as we have suggested, than by route (6).

Because successful nucleophilic attack requires a strong base, we also consider that a scheme similar to (5) obtains for the spontaneous reaction itself (7). Here other water molecules act as bases and encourage local hydroxide-ion formation.[18]



(7)

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[14] M. L. Bender, *Chem. Rev.*, 1960, **60**, 53.
[15] D. P. N. Satchell, *Quart. Rev.*, 1963, **17**, 160.
[16] J. Hipkin and D. P. N. Satchell, *J.*, 1965, 1057.
[17] A. R. Butler and V. Gold, *J.*, 1962, 1334.
[18] S. L. Johnson, *J. Amer. Chem. Soc.*, 1962, **84**, 1729.

(*b*) *Acetoacetate.* Since the reaction between hydroxide ion and diketen is very fast, solutions of diketen containing sodium acetoacetate were most simply made by adding an excess of diketen to a sodium hydroxide solution of appropriate concentration. Because the hydrolysis product is also acetoacetic acid, it is not necessary to keep the pH low, as it must be in chloroacetate catalysis. Good first-order plots for loss of diketen were obtained. The data are given in Table 5. Acetoacetate produces an acceleration proportional to its concentration. However, this cannot be simply attributed to catalysis of hydrolysis, since the yields of acetone from similar reaction mixtures in which the reaction and subsequent decarboxylation had been taken to completion, fall as the acetoacetate concentration rises (Table 5). Diketen dimerises [1] (to dehydroacetic acid) in the presence of bases like acetate, and we conclude, therefore, that acetoacetate both catalyses the hydrolysis and leads to polymerisation products which do not subsequently yield acetone.

TABLE 5

Effects of acetoacetate at 24·9°

$10^2[CH_3CO{\cdot}CH_2{\cdot}CO_2Na]$	0·00	0·95	1·90	2·85	4·75	6·65	9·49
$10^3k_{obs.}$	2·10	3·21	—	5·56	7·75	10·5	13·7
Acetone yield (%)	96	—	64	—	50	34	25

(*c*) *Acetate.* Work with this anion was difficult because it combined the problems met with chloroacetate and acetoacetate. Acetic acid and acetoacetic acid have similar p*K* values and as hydrolysis proceeds some acetate will be progressively replaced by acetoacetate, unless the solutions are buffered. In the absence of buffering we obtained plots concave to the time axis, indicating that acetate catalysis is more effective than that of acetoacetate. With added acetic acid present initially, moderately rectilinear plots result. These data are in Table 6. Checks of the acetone yield showed, as with acetoacetate, that not all the diketen is hydrolysed, some presumably being converted into polymerisation products (see above). With 0·1M-acetate the acetone (acetoacetic acid) yield is 40%. The fact that, under such conditions, the rate of loss of diketen has increased 25 times, and $\frac{2}{5}$ of the product is still acetoacetic acid, implies that acetate ions are a powerful catalyst of hydrolysis. This is in keeping with the results for chloroacetate. We again suggest a mechanism based on (5) for the catalysed process.

TABLE 6

Effects of acetate at 24·9°

$[CH_3{\cdot}CO_2Na]$	—	—	0·097	0·136	0·175
$[CH_3{\cdot}CO_2H]$	—	0·50	0·40	0·36	0·32
$10^3k_{obs.}$	2·10	2·27	56·5	79·5	113

(*d*) *Pyridine and Lutidines.* Pyridine and substituted pyridines are powerful catalysts for the hydrolysis of carboxylic anhydrides and of some esters.[14] However, 2-substituted pyridines have been found inactive [19] as catalysts in spite of showing fairly comparable activity in proton transfers.[20] Steric factors therefore seem important and pyridine catalysis is consequently considered to be of the nucleophilic variety, *e.g.*, 6, and to involve the intermediate formation of an acyl-pyridinium entity, this being prevented by 2-substituents.

Pyridine catalysis does not appear to have been studied before in lactone hydrolysis. We give below the evidence that the behaviour pattern is, in fact, similar to that for anhydrides. In order to avoid pH changes during hydrolysis the bases were added as their perchlorates, usually with 0·3M-chloroacetic acid to buffer the solution at pH $\approx$ 2·2. This procedure results in only a very small concentration of free base being in solution. The amount present was determined approximately from the pH of the solution and the independently determined p*K* of the base in 40 : 60 v/v dioxan–water. The results are given in Table (7). Pyridine provides a very powerful and approximately linear catalysis.

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[19] A. R. Butler and V. Gold, *J.*, 1961, 4362.

[20] J. A. Feather and V. Gold, *Proc. Chem. Soc.*, 1963, 306.

TABLE 7

Effects of pyridine and lutidines at 24·9°

(*a*) Pyridine (pK = 4·45)						
Reactions conducted in presence of 0·3M-chloroacetic acid						
$10^2[PyH^+ClO_4^-]$	—	0·6	1·8	3·0	4·5	6·0
$10^4[Py]$ (approx.)	—	0·35	1·1	1·8	2·6	3·5
$10^3k_{obs.}$	2·13	3·92	6·86	9·20	12·3	15·2
(*b*) 2,4-Lutidine (pK = 5·90)						
$10^2[2,4\text{-}LuH^+ClO_4^-]$	4·8	4·8	14·4	14·4	24·0	24·0
$[ClCH_2{\cdot}CO_2H]$	0·3	—	0·3	—	0·3	—
$10^4[2,4\text{-}Lu]$ (approx.)	0·1	4·0	0·3	12·0	0·5	20·0
$10^3k_{obs.}$	2·17	2·31	2·18	2·44	2·16	2·47
(*c*) 2,6-Lutidine (pK = 5·94)						
$10^2[2,4\text{-}LuH^+ClO_4^-]$	4·8	4·8				
$[ClCH_2{\cdot}CO_2H]$	0·3	—				
$10^3k_{obs.}$	2·17	2·18				

The catalytic constant $k_{pyr} \approx 40$ l. mole^{-1} min.$^{-1}$. In contrast, 2,4- and 2,6-lutidine have negligible catalytic power. The former produces a small effect, but because of uncertainties about the dependence of salt effects on pH and the generally very low concentration of the free bases, its interpretation is open to question. However, the two lutidines do have different effects. As for anhydrides, nucleophilic catalysis is indicated. However, it is not evident why the hindered lutidines cannot engage in general base catalysis, whether by (5) or some other path. It may be that, in this instance at least, the much greater proton basicity of the lutidines compared with, say, acetate ions, is more than offset by their very much smaller concentration.

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