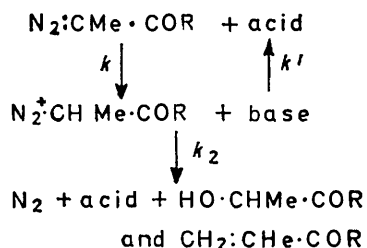# Kinetic Isotope Effects and Aliphatic Diazo-compounds. Part II.[1] Experiments at High Buffer Concentrations

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The general acid-catalysed decomposition of 3-diazobutan-2-one and ethyl diazopropionate exhibits a decrease in the expected rate as the buffer concentration is increased. This decrease is attributed to the second step in the reaction, the loss of nitrogen, becoming partially rate-determining. The free-energy difference between the transition states has been determined for both compounds. For 3-diazobutan-2-one the solvent isotope effect in the second transition state confirms the analysis. An alternative explanation of the decrease in rate in terms of the dimerisation and association of the buffer species is considered but it is shown that all the data for the hydrolysis of cyanoketen dimethyl acetal can be fitted to the second transition state hypothesis with only one extra parameter. The solvent isotope effect indicates that in this case, the second transition state involves a proton transfer which is similar to the rate-determining step in the hydrolysis of ethyl orthocarbonate.

THIS paper describes experiments in high buffer concentrations (up to 0·50M) of acetic acid on the acid-catalysed

$$N_2{:}CMe{\cdot}COR \quad + acid$$

$$k\downarrow \qquad\qquad \uparrow k'$$

$$N_2^+{:}CH\,Me{\cdot}COR \quad + base$$

$$\downarrow k_2$$

$$N_2 + acid + HO{\cdot}CHMe{\cdot}COR$$

$$and \ CH_2{:}CHe{\cdot}COR$$

SCHEME 1

decomposition of 3-diazobutan-2-one and ethyl diazopropionate. As in the case of diazoacetate ion[2] the

higher concentration of base causes the second step in the reaction to become partially rate-determining (Scheme 1).

EXPERIMENTAL

The chemicals and techniques have been described.[1] D_2O was supplied by Norsk Hydro Electrisk.

RESULTS AND DISCUSSION

The full expression for the observed first-order rate constant for the reaction taking place in a buffer solution

$$k_{obs} = \frac{k_{H^+}[H^+] + k_{HA}[HA] + k_{H_2O}}{1 + (k'_{H_2O} + k'_{A^-}[A^-] + k'_{OH^-}[OH^-])/k_2} \quad (1)$$

of HA and A^- is (1) where k_x are forward rate constants

[1] Part I, W. J. Albery, A. N. Campbell-Crawford, and K. S. Hobbs, preceding paper.

[2] M. M. Kreevoy and D. E. Konasewich, *J. Phys. Chem.*, 1970, **74**, 4464.

for the protonation step, k'_x are backward rate constants for this step, and k_2 is the forward rate constant for the destruction of the intermediate; k_2 may describe the sum of two different processes leading to two different products but this is immaterial to the argument. Now k_{H_2O} is much smaller [1,3] than k_{obs}, hence we can ignore the terms k_{H_2O} and $k'_{OH^-}[OH^-]$, giving equation (2). For the

$$k_{obs} = \frac{k_{H^+}[H^+] + k_{HA}[HA]}{1 + (k'_{H_2O} + k'_{A^-}[A^-])/k_2} \quad (2)$$

remaining rate constants we also have the thermodynamic relationship (3).

$$k_{HA}k'_{H_2O}/k_{H^+}k'_{A^-} = K = [H^+] \times [A^-]/[HA] \quad (3)$$

The experiments with ethyl diazopropionate and 3-diazobutan-2-one were carried out in slightly different ways. Those for the ester were as described,[1] while those for the ketone were done in the more conventional manner, the buffer ratio being kept constant at unity. If there was no interference from the second term in the

For 3-diazobutan-2-one we plot the left-hand side against $[HA]^{-1}$ since $[H^+] = K$ and is constant. These plots for both H_2O and D_2O are shown in Figure 1; reasonable straight lines are obtained. For ethyl diazopropionate we multiply equation (6) by $[H^+]$ and then

$$\frac{1}{k_{obs} - k''_{H^+}[H^+]} = \frac{1}{[HA]} \cdot \frac{(1 + k'_{H_2O}/k_2)^2}{k_{HA}} + \frac{1}{[H^+]} \cdot \frac{k'_{H_2O}}{k''_{H^+}k_2} \quad (6)$$

plot the left-hand side against $[H^+]/[HA]$; this is shown in Figure 2. Table 1 contains values of rate constants derived from these plots together with Kreevoy and Konasewich's data [2] for diazoacetate anion.

It is satisfactory that the rate constants k_{HA} determined from the gradients are in good agreement with those determined at lower buffer concentrations;[1] the small difference for the diazo-ketone may be due to the higher ionic strength used in this work. For the diazo-ester the ionic strength was the same as before ($\mu = 0.05M$)

<div align="center">TABLE 1</div>

<div align="center">Kinetic parameters for diazo-compounds in acetic acid buffers (all errors are standard)</div>

	3-Diazobutan-2-one		Ethyl diazopropionate	N_2:CHCO$_2^-$ (ref. 2)
	H_2O	D_2O		
$10^3 k_{LA}/s^{-1}$ [a]	5.5 ± 0.2	1.33 ± 0.04	151 ± 2	
$10^3 k_{HA}/s^{-1}$ [b]	5.0 ± 0.2		147 ± 7	
Intercepts in Figures 1 and 2	0.42 ± 0.05ks	0.6 ± 0.1ks	0.48 ± 0.06 mol l^{-1} ms	
$k'_{L_2O}/k_{2,L}$	$(9 \pm 1) \times 10^{-3}$ [c]	$(1.6 \pm 0.4) \times 10^{-3}$ [d]	$(10 \pm 1) \times 10^{-3}$ [e]	5×10^{-3}
$(\Delta G^{\ddagger}_1 - \Delta G^{\ddagger}_2)/kJ$ mol^{-1}	12	16	11	13
$(k_{DA}/k_{HA})_1$		0.24 ± 0.01	0.25 ± 0.01 [f]	0.18 [g]
$(k_{DA}/k_{HA})_2$		0.71 ± 0.15		
$\Pi(\phi^{\ddagger})_2$		0.76 ± 0.16		1.2 [h]

[a] This work. [b] Ref. 1. [c] Calculated with $K = 3.0 \times 10^{-5}$ mol l^{-1} (ref. 4) and $k_{H^+} = 0.74$ l mol^{-1} s^{-1} (ref. 1). [d] Calculated with $K = 9.2 \times 10^{-6}$ mol l^{-1} (refs. 4 and 6) and $k_{D^+} = 0.24$ l mol^{-1} s^{-1} (ref. 18). [e] Calculated with $K = 2.6 \times 10^{-5}$ mol l^{-1} (ref. 1) and $k_{H^+} = 20.4$ l mol^{-1} s^{-1} (ref. 1). [f] Ref. 3. [g] Calculated from T product analysis (ref. 2), on the assumption of the Swain–Schaad relationship, and that other fractionation factors are unity. [h] Calculated from $(k_{H^+}k_{2,H}k'_{D_2O})/(k_{D^+}k_{2,D}k'_{H_2O}) = 0.28$ and $l^3 = 0.33$.

denominator then the data for the ketone and the ester plotted according to equations (4) and (5) respectively should give straight lines. In either case as $[HA]/[H^+]$

$$k_{obs} = k_{H^+}[H^+] + k_{HA}[HA] \quad (4)$$

$$\frac{k_{obs}}{[H^+]} = k_{H^+} - k_{HA} + k_{HA}([H^+] + [HA])/[H^+] \quad (5)$$

for ethyl diazopropionate or $[HA]$ at constant buffer ratio for 3-diazobutan-2-one increases the $[A^-]$ increases and may cause $\partial^2y/\partial x^2$ to be negative. Such curvature has been found for both compounds in acetic acid–acetate buffers. At the higher base concentrations the contribution from $k_{H^+}[H^+]$ is less important so we rearrange equation (2) and use equation (3) to give equation (6), where $k''_{H^+} = k_{H^+}/(1 + k'_{H_2O}/k_2)$ and is the observed rate constant in solutions of mineral acid.

and we used [1] $K = 2.56 \times 10^{-5}$ mol l^{-1} in the calculations. For the diazo-ketone μ was kept constant at $0.10M$ except for the two points at highest concentration. Fortunately K is not very sensitive to μ at these ionic strengths since it passes through a maximum at $\mu = ca.$ $0.5M$.[4] In calculating k_{H_2O}/k_2 from the intercept we have used $K = 3 \times 10^{-5}$ mol l^{-1}; the data do not warrant more sophisticated corrections. In Table 1 the errors are standard and it is clear that the intercepts are significantly different from zero. From them we can calculate the ratio k'_{L_2O}/k_2 which describes the relative rates for the loss of proton to the solvent compared with the loss of nitrogen from the protonated intermediate. While it is not surprising that the ratios for our diazo-compounds are almost identical it is either significant or else a curious coincidence that the ratio for diazoacetate anion is so

[3] W. J. Albery, A. N. Campbell-Crawford, and R. W. Stevenson, *J.C.S. Perkin II*, 1972, 2198.

[4] H. S. Harned and B. B. Owen, 'The Physical Chemistry of Electrolyte Solutions,' Reinhold, New York, 1958, p. 676.

similar. This point will be discussed in Part VI.[5] The isotope effect $(k_{DA}/k_{HA})_1$ is the ratio of rates for the protonation of the diazo-compound by acetic acid. The

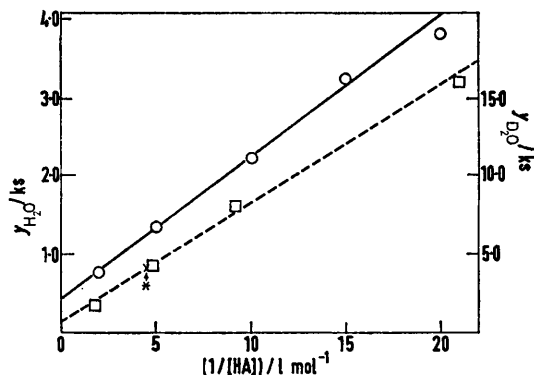FIGURE 1 Plot of equation (6) for 3-diazobutan-2-one and acetic acid in H_2O (solid line) and D_2O (broken line); $y = (k_{obs} - k''_{H+}[H^+])^{-1}$. The point * is plotted as $y/10$ and $x/10$; if $y = a + bx$, then $(y/10) + 9a/10 = a + b(x/10)$ and the shift of $9a/10$ gives the point X

fractionation factor ϕ_{HA} for the reactant acetic acid is almost unity [6] and hence we obtain equation (7),

$$(k_{DA}/k_{HA})_1 \simeq \phi^{\ddagger} \qquad (7)$$

where $\phi^{\ddagger}$ is the fractionation factor for the proton in flight in the transition state. The values in Table 1 are very reasonable for such a proton.
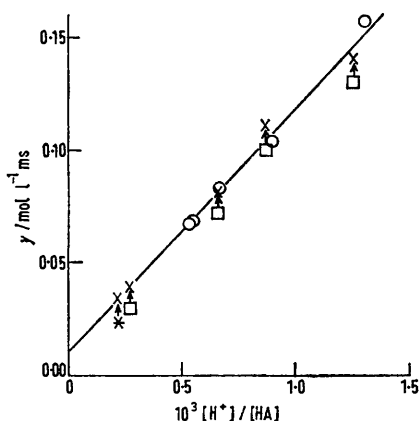

FIGURE 2 Plot of equation (6) multiplied by $[H^+]$, for ethyl diazopropionate and acetic acid in H_2O; $y = (k_{obs}/[H^+] - k''_{H+})^{-1}$. The points $\bigcirc$ are plotted with scales as shown while $\square$ are points at large values of y and x, plotted as $y/10$ and $x/10$, and * is a point plotted as $y/100$ and $x/100$. If $y = a + bx$ then $(y/10) + 9a/10 = a + b(x/10)$; the shifts of $9a/10$ (a for *) give the points X

The isotope effect $(k_{DA}/k_{HA})_2$ describes the free-energy differences between the reactants and the second transition state(s) for the reaction(s) losing nitrogen

[5] W. J. Albery, A. N. Campbell-Crawford, and J. S. Curran, *J.C.S. Perkin II*, 1972, 2206.
[6] V. Gold and B. M. Lowe, *J. Chem. Soc. (A)*, 1968, 1923.

[reaction (8)]. It is calculated directly from the ratio of

$$LA + S \rightleftharpoons A^- + LS^+ \longrightarrow$$
$$A^- + [LS^+]^{\ddagger} \longrightarrow products \qquad (8)$$
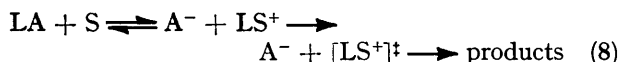
the intercepts; at 'infinite' base concentration, a pre-equilibrium would be established between S and LS$^+$ and the second step would indeed be rate-determining. Since the intercepts are small the error on the ratio $(k_{DA}/k_{HA})_2$ is inevitably rather large.

This ratio includes some fractionation factors for LA and A$^-$. To separate the fractionation factors for the second transition state, $\Pi(\phi^{\ddagger})_2$, we make use of the experimental values for the dissociation of acetic acid in H_2O and D_2O by use of equations (9) and (10), which lead to equation (11). Values of $\Pi(\phi^{\ddagger})_2$ are in Table 1.

$$K_D/K_H = l^3 \Pi \phi_{A^-}/\phi_{HA} \qquad (9)$$

$$(k_{DA}/k_{HA})_2 = (\Pi \phi_{A^-})\Pi(\phi^{\ddagger})_2/\phi_{HA} \qquad (10)$$
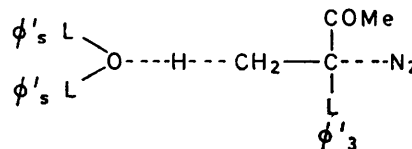
$$\Pi(\phi^{\ddagger})_2 = (k_{DA}/k_{HA})_2 l^3 (K_H/K_D) \qquad (11)$$

If, as for ethyl diazoacetate, the mechanism is A-2, fractionation in the transition state leading to the major product can be written as in Scheme 2. For ethyl di-
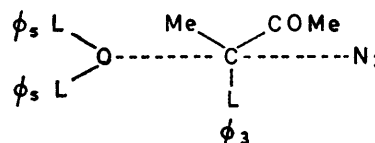
SCHEME 2

azoacetate [7] $\phi_3 = 1.00$, $\phi_s = 0.95$, and hence $\Pi(\phi^{\ddagger})_2 = 0.90$. For the minor product we can write a similar transition state (Scheme 3). We have found the ratio of

SCHEME 3

the two products to be the same within experimental error in H_2O and D_2O (acetoin : olefin $= 3.0 \pm 0.5$) so $\phi'_s{}^2\phi'_3 \simeq \phi^2_s\phi_3$ and we would expect equations (12).

$$\Pi(\phi^{\ddagger})_2 \simeq 0.75\phi_3\phi_s{}^2 + 0.25\phi'_3(\phi'_s)^2 \simeq 0.90 \qquad (12)$$

This is the expression for an A-2 mechanism. For an A-1 mechanism we would have simply equations (13).
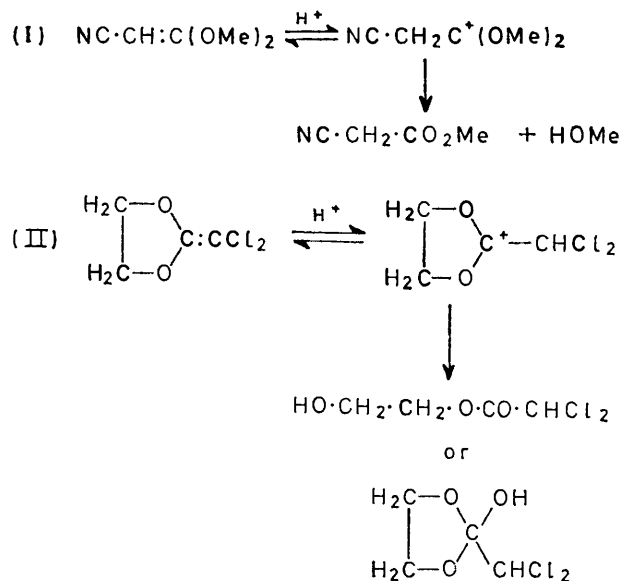
$$\Pi(\phi^{\ddagger})_2 = \phi_3 \simeq 1.0 \qquad (13)$$

The value in Table 1 may be smaller than unity owing to ϕ_s and/or ϕ'_s being less than unity; the large error does not allow us to be certain about this; the odds are 4 : 1 in favour of some solvent contribution. However, there is no doubt that $\Pi(\phi^{\ddagger})_2$ does have a value which is close

[7] W. J. Albery and M. H. Davies, *Trans. Faraday Soc.*, 1965, 65, 1066.

enough to 0·90 or unity to lend support to this analysis and to the argument that the curvature at high buffer concentrations is caused by the second transition state(s).

An alternative explanation of this type of curvature advanced by Gold and Waterman [8] is that the buffer species become dimerised and associated at the higher concentrations. On the other hand, Kreevoy [2,9] has suggested that a second transition state might also be responsible for the curvature in Gold and Waterman's reactions,[8,10] as shown in Scheme 4. To test this

$$(I) \quad NC \cdot CH:C(OMe)_2 \underset{\overset{H^+}{\rightleftharpoons}}{} NC \cdot CH_2 C^+(OMe)_2$$

$$\downarrow$$

$$NC \cdot CH_2 \cdot CO_2Me \quad + \quad HOMe$$

SCHEME 4

hypothesis we have plotted Gold and Waterman's data according to equation (6). Reasonable straight lines are found with small but significant positive intercepts. A more critical test is that the value of k'_{L_2O}/k_2 calculated from the intercepts should be independent of the buffer species and buffer ratios. The results are in Table 2. To fit the curvature all the data for the cyanoketen dimethyl acetal in H_2O require only one extra parameter, k'_{H_2O}/k_2, on the second transition state hypothesis rather than two parameters K_d and K_{ass} for each acid on the dimerisation hypothesis. Further, the dimerisation hypothesis predicts that for any one acid at the same buffer ratio the curve should be independent of substrate. If we regard the straight-line plots in Figures 1 and 2 as merely functional plots to describe the data then the parameters k'_{L_2O}/k_2 just describe the amount of curvature. Table 3 compares results for acetic acid at a buffer ratio of unity.

The results in H_2O are close enough to fit the dimeris-

ation hypothesis but those in D_2O make it seem rather unlikely; the odds against a common value of 3 are ca. 10^7 to 1. Also, one would not expect the change of solvent from H_2O to D_2O to produce such large changes in K_{dis} and K_{ass} as to cause a five-fold difference in the

TABLE 2

Values of kinetic parameters

Reaction	Solvent	Acid	$\dfrac{[A^-]}{[LA]}$	$\dfrac{10^2 k_{LA}}{l\ mol^{-1}\ s^{-1}}$	$\dfrac{10^3 k'_{L_2O}}{k_2}$
(I)	H_2O	3-Chloro-propionic	1·00	45 ± 2	6·0 ± 1·6
		3-Chloro-propionic	2·63	59 ± 2	7·0 ± 0·7
		Isobutyric	0·985	18·6 ± 0·1	7·8 ± 0·1
		Pivalic	0·279	16·8 ± 0·3	6·6 ± 1·8
		Pivalic	0·773	17·9 ± 0·2	8·4 ± 0·6
		Acetic	0·20	13·7 ± 0·4	8·5 ± 0·4
		Acetic	1·00	15·2 ± 0·2	7·2 ± 0·5
		Acetic	2·00	15·3 ± 0·3	7·0 ± 0·7
				Mean	7·3 ± 0·3
(I)	D_2O	Acetic	1·00	2·84 ± 0·03	4·8 ± 0·5
		Glycollic	1·00	11·7 ± 0·2	4·2 ± 0·7
(II)	H_2O	Acetic	2·00	267 ± 16	3 ± 1

TABLE 3

Comparison of k'_{L_2O}/k_2 in acetic acid buffers with ratio of unity

	$10^3(k'_{H_2O}/k_2)$	$10^3(k'_{D_2O}/k_2)$
3-Diazobutan-2-one	9 ± 1	1·6 ± 0·4
Cyanoketen dimethyl acetal	7·2 ± 0·5	4·8 ± 0·5

curvature parameter for 3-diazobutan-2-one. Thus, although the results for cyanoketen dimethyl acetal could be plausibly fitted [10] by the dimerisation hypothesis our new results for 3-diazobutan-2-one in D_2O make it seem less likely than the second transition-state hypothesis.

In addition other reactions, for instance the base-catalysed ketone to enol transformation [11,12] and the ionisation of nitro-compounds,[13] do not show any detectable curvature in acetic acid acetate buffers of concentrations ca. 0·1M. If dimersiation and association were taking place one would expect curvature in these reactions as well. It is much more likely that in these reactions there is only one rate-determining transition state giving a well behaved system.*

If our analysis is correct we can then derive the isotope effects for Gold's reaction (I). We obtain much the same value [equation (14)] as Gold and Waterman for the isotope effect on the first proton transfer. For the

$$(k_{DA}/k_{HA})_1 = 0·193 \pm 0·006 \quad (cf.\ 0·186) \quad (14)$$

isotope effect from acetic acid plus cyanoketen dimethyl acetal to the second transition state we obtain equations

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* We are grateful to Professor Bell for conversation on this point.

[8] V. Gold and D. C. A. Waterman, J. Chem. Soc. (B), 1968, 839.

[9] M. M. Kreevoy, Public Communication at the Chemical Society Conference on Chemical Kinetics, Canterbury, 1970.

[10] V. Gold and D. C. A. Waterman, J. Chem. Soc. (B), 1968, 849.

[11] R. P. Bell and O. M. Lidwell, Proc. Roy. Soc. (A), 1940, 176, 88.

[12] R. P. Bell and P. De Maria, Trans. Faraday Soc., 1960, 66, 930.

[13] R. P. Bell and D. M. Goodall, Proc. Roy. Soc., 1966, A, 294, 273.

(15) and (16). These values suggest that, unlike our

$$(k_{DA}/k_{HA})_2 = 0.28 \pm 0.03 \qquad (15)$$

$$\Pi(\phi^{\ddagger})_2 = 0.30 \pm 0.03 \qquad (16)$$

diazo-system, a proton is being transferred in the second transition state. After the first protonation the reaction could proceed in a number of ways (Scheme 5). Transition states 1, 2, 4, and 5 lead either to or from

SCHEME 5
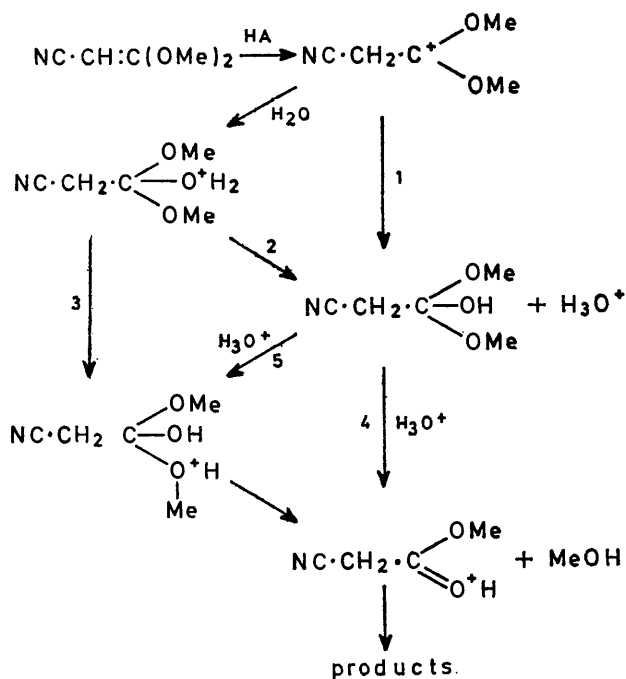
$NC \cdot CH_2 \cdot C(OH)(OMe)_2 + H_3O^+$. They are similar to the transition state that arises in the hydrolysis of an ortho-ester. Kresge and Preto [14] have established that the mechanism for many orthoesters is $A-S_E2$ with rate-determining proton transfer. They speculate as to whether the proton transfer is simultaneous with the C–O bond breaking (as in our transition states 1 or 4) or

stepwise (our transition states 2 or 5). Reactions 4 and 5 would be subject to general acid catalysis; no general acid catalysis can be detected in the data in Table 2. However, from the size [15] of $\Pi\phi^{\ddagger}$, $\alpha = ca.$ 0.80, and this value is large enough for the general acid term to remain undetected. So transition states 4 and 5 cannot be ruled out. The value of $\Pi\phi^{\ddagger}$ of 0.30 might seem rather large for a proton transfer; values are more typically $ca.$ 0.10—0.15. However from Kresge and Preto's data for ethyl orthocarbonate [14] we obtain equations (17).

$$\Pi\phi^{\ddagger} = l^3/0.70 = 0.45 \qquad (17)$$

These large values indicate asymmetric transition states, reactant-like for 1 and 2, product-like for 4 and 5. Compared with ortho-esters, transition states 1, 2, and 4 have an extra proton which would contribute a ϕ less than unity. The intermediate considered here has an OH instead of one of the alkoxy-groups of an ortho-ester. Comparing the hydrolysis of an acetal [16] with the dehydration of a gem-diol [17] we find that the substitution of OH for an alkoxy-group shifts the mechanism from rate-determining CO cleavage to rate-determining proton transfer. Hence the intermediate in this reaction of cyanoketen dimethyl acetal is more likely to have rate-determining proton transfer than the equivalent ortho-ester. Indeed, for the transition state in the hydration of acetaldehyde or 1,3-dichloroacetone [17] we have equation (18). It is satisfactory that our value of 0.30 lies

$$\Pi\phi^{\ddagger} \sim 0.78l^3 = 0.26 \qquad (18)$$

between the values of these two analogous reactions.

For completeness we have also included transition state 3 which is an intramolecular proton transfer although, as in the dehydration reaction,[17] it could proceed through a cyclic chain including other solvent molecules. It is impossible to choose between these different transition states but we believe that the plausible value of $\Pi\phi^{\ddagger} = 0.30$ further supports our analysis.

[14] A. J. Kresge and R. S. Preto, J. Amer. Chem. Soc., 1965, 87, 4593.
[15] R. A. More O'Ferrall, G. W. Koeppl, and A. J. Kresge, J. Amer. Chem. Soc., 1971, 93, 9.
[16] M. M. Kreevoy and R. W. Taft, J. Amer. Chem. Soc., 1955, 77, 3146.
[17] R. P. Bell and J. E. Critchlow, to be published.
[18] W. J. Albery and A. N. Cambell-Crawford, J.C.S. Perkin II, 1972, following paper.