$$k_{H^+} = k_{31}\frac{k_{22}k_{34}K_3 + k_{32}k_{35}K_3 + k_{-22}k_{33}K_3' + (k_{33}k_{34} + k_{33}k_{35})(H^+)}{k_{-22}k_{-31}K_3' + k_{-22}k_{33}K_3' + k_{22}k_{34}K_3 + k_{22}k_{35}K_3 + (k_{-31}k_{34} + k_{-31}k_{35} + k_{33}k_{34} + k_{33}k_{35})(H^+)} \quad (23)$$

and

$$f = \frac{k_{22}k_{35}K_3}{k_{22}k_{34}K_3 + k_{22}k_{35}K_3 + k_{-22}k_{33}K_3' + (k_{33}k_{34} + k_{33}k_{35})(H^+)} \quad (24)$$

These equations are of the form already given as eq 12 and 7.

Neutral Region. The kinetic equations and the equation for the fraction of exocyclic cleavage in the region from pH 4 to 11 are complicated and cannot easily be reduced to a simple form. The rate can be expressed by the equation

$$k_{obsd} = Q[k_{31}(H^+) + k_{21} + k_{11}(OH^-)] \quad (25)$$

where

$$Q = \frac{\vartheta + \kappa(H^+) + \lambda(H^+)^2}{1 + \mu(H^+) + \nu(H^+)^2} \quad (26)$$

and the fraction of exocyclic cleavage by the equation

$$= \frac{\xi(H^+) + \pi(H^+)^2}{1 + \varphi(H^+) + \chi(H^+)^2} \quad (27)$$

Here ϑ, κ, λ, μ, ν, ξ, π, φ, and χ are functions of the various constants of eq 15. The way in which Q depends on pH is obscure, but it could easily be relatively insensitive to the concentration of hydrogen ion, so that the dependence of the rate on acidity would be controlled by the expression in square brackets in eq 25. Even if Q varied somewhat with acidity, this variation might not be easy to detect in a complicated pH–rate profile such as that represented by eq 4. The fraction, f, of exocyclic cleavage, as shown in eq 27, decreases to zero in regions of low acidity.

Strong Alkali. In strong alkali eq 22 reduces to an equation of the form of eq 14. Then f can be proportional to the hydroxide ion concentration, or, in very strong alkali, be independent of the hydroxide ion concentration. The data so far obtained correspond only to the region where f is proportional to (OH^-).

The Mechanism and Micellar Catalysis of the Acid Cleavage of α-Phenylvinyl Diethyl Phosphate[1]

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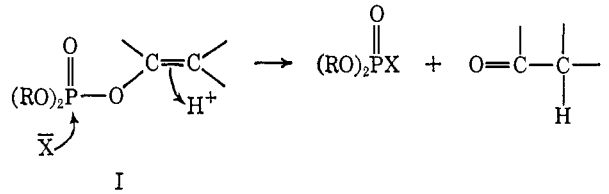
Abstract: The acid cleavage of α-phenylvinyl diethyl phosphate follows an A-Se2 mechanism. Plots of log k_ψ against $-H_0'$ are linear with slopes 1.07–1.4 for hydrochloric, perchloric, and sulfuric acids, with $-\phi = 0.2$–0.6. In moderately concentrated acid the Arrhenius parameters depend on both acidity and temperature, but in dilute acid $\Delta S^* = -8.8$ eu, $k_{H_2O}/k_{D_2O} = 2.5$, and the positive salt effect of $LiClO_4$ is greater than that of LiCl, although $LiClO_4$ "salts in" and LiCl "salts out" the substrate. At concentrations above the cmc, sodium lauryl sulfate is an effective catalyst of the acid cleavage and $k_{H_2O}/k_{D_2O} \approx 2.2$. The catalysis is inhibited by cations with the rate sequence no salt > Li^+ > Na^+ > $(CH_3)_4N^+$.

The acid-catalyzed cleavage of enol phosphates has been considered as a model reaction for biological phosphorylations by phosphoenolpyruvic acid, and a general discussion of these reactions has been given by Bruice and Benkovic.[2] The postulated mechanism for acid-catalyzed phosphorylation by an enol phosphate involves attack of the proton and the nucleophile as shown in I.[2,3]



I

Enol phosphates are more reactive than the corresponding trialkyl phosphates, whose hydrolysis is not strongly dependent upon acidity and involves carbon–rather than phosphorus–oxygen fission.[4]

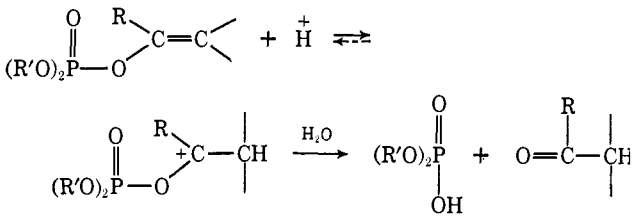
The various bond-making and -breaking steps may be stepwise, rather than concerted, and the addition of the proton could be fast and be followed by a rate-limiting attack of water and breaking of the phosphorus–oxygen bond. The available evidence suggests, however, that the transition state has little carbonium ion character, because the rate sequence with substituents, R, in the 1 position is $CH_3 > C_6H_5 > CO_2C_2H_5 > H$.[2]

(1) Support of this work by the National Institute of Arthritis and Metabolic Diseases, U. S. Public Health Service, is gratefully acknowledged.

(2) T. C. Bruice and S. Benkovic, "Bio-Organic Mechanisms," Vol. II, W. A. Benjamin, Inc., New York, N. Y., 1966, Chapter V; S. J. Benkovic and K. J. Schray, *Biochemistry*, 7, 4090 (1968).

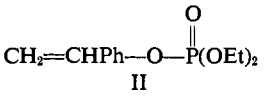
(3) F. W. Lichtenthaler and F. Cramer, *Ber.*, 95, 1971 (1962).

(4) P. W. C. Barnard, C. A. Bunton, D. R. Llewellyn, C. A. Vernon, and V. A. Welch, *J. Chem. Soc.*, 1636 (1961); J. R. Cox and O. B. Ramsay, *Chem. Rev.*, 64, 343 (1964).



We have applied some of the usual mechanistic tests for acid hydrolysis, *e.g.*, variation of reaction rate with acidity,[5] the value of the entropy of activation,[6] and the magnitude of the deuterium solvent isotope effect.[7] In addition we were concerned about the micellar catalysis of these reactions as an extension of our other investigations of micellar effects upon reactions of phosphate esters.[8,9]

We found that the acid cleavage of phosphoenolpyruvic acid was not catalyzed by detergents, and therefore did most of the work using α-phenylvinyl diethyl phosphate (II). This compound also avoided complications



II

which could arise from ionization of phosphoenolpyruvic acid.

Experimental Section

Materials. α-Phenylvinyl diethyl phosphate was prepared by heating α-chloroacetophenone (Aldrich) and triethyl phosphite at 120° in the absence of solvent,[10,11] and purified by short-path distillation, 85–88° (10^{-2} mm), with the collector cooled in liquid N_2 (lit. 106–107° (0.1 mm)[11] and 110–118° (0.15 mm).[10] The nmr spectrum was identical with that reported,[10] and showed that the product contained no ketophosphonate; however, distillation at 3 mm gave a product of bp 130–140° which contained some ketophosphonate, showing that these enol phosphate esters can be distilled only at low pressures. The preparation and purification of NaLS and the acids and salts have been described.[8,12]

Sodium cetylsulfonate was shaken with Dowex 50W-X8 resin in the acid form to give the sulfonic acid.[13] The solubility of this material is so low that its catalysis was not studied in detail.

Phosphoenolpyruvic acid (Nutritional Biochemicals) was obtained as the monocyclohexylammonium salt.

Kinetics. The reaction was followed spectrophotometrically at 2150 Å using a Gilford spectrophotometer with a water-jacketed cell compartment. The faster reactions were carried out in the cell compartment, and the slower ones in stoppered cells. The absorbance corresponding to complete reaction was generally determined experimentally, but it was calculated for some of the slower reactions. The first-order rate constants, k_ψ, are in sec^{-1}, and the concentration of α-phenylvinyl phosphate was 10^{-5} *M*. Good first-order rate plots were obtained for up to 2 half-lives for the slower reactions, and for up to 3 half-lives for the faster ones. Micellization of long chain alkyl sulfates speeds their hydrolysis,[14] and this hydrolysis of sodium lauryl sulfate sets a limit on the length of time for which the slower runs could be followed.

The cleavage of phosphoenolpyruvic acid was followed spectrophotometrically at 2200 Å. The acid and salt solutions were all made up at 25°, and the concentrations refer to this temperature.

Determination of Activity Coefficient of the Substrate. The effect of LiCl and $LiClO_4$ upon the activity coefficient of α-phenylvinyl diethyl phosphate was determined by extracting 5 ml of a hexane (spectroquality) solution of the ester with 50 ml of water or aqueous salt solutions, and determining the concentration of the ester in the hexane layer spectrophotometrically.[15]

Results

Reaction in the Absence of Detergents. The variation of k_ψ with acid concentration is shown in Table I. The rate in the absence of acid is very low, and the second-order rate constants, k_ψ/C_{H^+}, are constant in dilute acid, and then increase steadily with increasing acid concentration. For acid concentrations greater than 1 *M*, the values of k_ψ follow the sequence $HClO_4 > H_2SO_4 > HCl$. Plots of log k_ψ against Hammett's acidity function,[5a,16,17] $-H_0'$, are linear with slopes 1.4 for HCl, 1.15 for $HClO_4$, and 1.07 for H_2SO_4 at 25.0°. At 35.9° the slopes are 1.19 for HCl and 1.20 for $HClO_4$, based only on two points, and 0.97 for H_2SO_4, based on three points. At 45.0° they are 1.05 for HCl and $HClO_4$, based on three points, and 0.87 for H_2SO_4, based on four points. These slopes were calculated using the values of H_0' at 25°. The values of Bunnett's and Olsen's ϕ parameters[5c] were −0.6 for HCl, and *ca.* −0.2 for $HClO_4$ and H_2SO_4, at 25.0°. However there was slight curvature in these plots for H_2SO_4 and marked curvature for $HClO_4$. These relations between k_ψ and acidity suggest that water molecules are not involved as nucleophiles in the rate-limiting step.[5]

The values of the deterium solvent isotope effect, $k_{H_2O}/k_{D_2O} = 2.62$ at 45.0° in 0.01 *M* $HClO_4$ (Table I) and 2.51 at 25.0° in 2.43 *M* H_2SO_4, are consistent with a slow proton transfer being involved in the rate-limiting step.

Added salts increase the protonating power of acids, as measured by Hammett's acidity function,[16] and they increase the rate of acid cleavage of α-phenylvinyl phosphate (Table II).

The Arrhenius parameters depend both upon acidity and temperature and the values of *E* and log *A* are given over the various temperature ranges in Table III. Because of the breakdown of the Arrhenius equation for reactions in moderately concentrated acid we have not tabulated values of the enthalpy and entropy of activation, but for reaction in 0.1 *M* perchloric acid, where the Arrhenius equation is obeyed (Table III), $\Delta S^* = -8.8$ eu (calcd for 1 *M* acid).

Added lithium chloride and perchlorate exert strong positive salt effects upon the acid cleavage of α-phenylvinyl diethyl phosphate (Table II). Plots of log k_ψ against C_s are approximately linear, and their slopes are not markedly sensitive to temperature, in contrast to the results in moderately concentrated acid. The relation between the rate constants and salt concentration is

$$\log k^s = \log k^0 + ac_s$$

(5) (a) F. A. Long and M. A. Paul, *Chem. Rev.*, **57**, 935 (1957); (b) J. F. Bunnett, *J. Amer. Chem. Soc.*, **83**, 4956 (1961), and accompanying papers; (c) J. F. Bunnett and F. R. Olsen, *Can. J. Chem.*, **44**, 1899, 1917 (1967).

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Table I. Acid Hydrolysis of α-Phenylvinyl Diethyl Phosphate[a]

Temp, °C	C_{H^+}, M	HCl		$HClO_4$		H_2SO_4	
		10^5k_ψ	$10^5k_\psi/C_{H^+}$	10^5k_ψ	$10^5k_\psi/C_{H^+}$	10^5k_ψ	$10^5k_\psi/C_{H^+}$
25.0	1.50	4.42	2.95	5.78	3.85	5.17	3.45
25.0	2.00	8.37	4.19	11.8	5.90	10.1	5.05
25.0	2.43					18.6[b]	7.66
25.0	2.43					7.42[c]	3.05[c]
25.0	2.50					20.3	8.12
25.0	3.00	27.8	9.27	39.0	13.0	40.7	13.6
25.0	3.50			69.2	19.7	72.5	20.7
25.0	4.00	85.3	21.3	134	33.4	141	35.3
25.0	4.50			219	48.7		
35.9	1.50	16.0	10.7	19.7	13.2	18.7	12.5
35.9	2.00	29.2	14.6	39.3	19.7	35.0	17.5
35.9	2.50					66.5	26.6
45.0	0.01			0.121	12.1		
45.0	0.01			0.046[d]	4.7[d]		
45.0	0.10			1.23	12.3		
45.0	1.00	18.7	18.7	22.8	22.8	20.0	20.0
45.0	1.50	36.8	24.5	47.8	31.9	38.8	25.8
45.0	2.00	60.1	30.1	85.6	42.8	68.2	34.1
45.0	2.50					120	48.0

[a] In the absence of detergent. [b] Interpolated value. [c] D_2SO_4 in D_2O. [d] In D_2O.

Table II. Salt Effects upon the Acid Cleavage of α-Phenylvinyl Diethyl Phosphate[a]

Salt	Temp, °C		
	25.0	45.0	63.5
	1.15	12.3	79.3
1 M LiCl	2.61	26.5	155
2 M LiCl	5.17	52.3	292
4 M LiCl	23.9	223	
1 M $LiClO_4$	3.17	31.3	183
2 M $LiClO_4$	7.58	67.0	337
4 M $LiClO_4$	49.0	323	

[a] Values of 10^5k_ψ sec^{-1} in 0.1 M $HClO_4$.

Table III. Arrhenius Parameters for the Acid-Catalyzed Hydrolysis[a]

Reagent	25.0–35.9°		35.9–45.0°	
	E	Log A	E	Log A
1.5 M HCl	21.7	11.5	18.0	8.9
2.0 M HCl	21.1	11.3	15.6	7.4
1.5 M $HClO_4$	20.7	10.9	19.1	9.7
2.0 M $HClO_4$	20.3	10.9	16.8	8.4
1.5 M H_2SO_4	21.7	11.5	15.7	7.3
2.0 M H_2SO_4	21.0	11.3	14.4	6.7
2.5 M H_2SO_4	20.0	10.9	12.7	5.8

[a] In the absence of detergent. In 0.1 M $HClO_4$, E = 22.2 kcal mol^{-1} and log A = 10.3 in the temperature range 25.0–45.0°, and E = 21.6 kcal mol^{-1} and log A = 10.0 in the temperature range 45.0–63.5°. The Arrhenius parameters were calculated using the first-order rate constants.

Table IV. Salt Effects upon the Activation Energy for the Acid Cleavage[a]

Salt	E, kcal mol^{-1}	
	22.2[b]	21.6[c]
1 M LiCl	21.9[b]	20.5[c]
2 M LiCl	21.9[b]	19.9[c]
4 M LiCl	21.1[b]	
1 M $LiClO_4$	21.6[b]	20.4[c]
2 M $LiClO_4$	20.6[b]	18.7[c]
4 M $LiClO_4$	17.8[b]	

[a] In 0.1 M $HClO_4$. [b] Temperature range 25.0–45.0°. [c] 45.0–63.5°.

Table V. Salt Effects upon Activity Coefficient of the Substrate and the Transition State[a]

Salt	C_s, M	f_s	$a_{H^+}/f_{X^\pm}$[b]
LiCl	1.0	1.27	1.8
LiCl	2.0	1.77	2.5
LiCl	3.0	3.0	3.7[b]
$LiClO_4$	1.0	0.90	3.1
$LiClO_4$	2.0	0.80	8.2
$LiClO_4$	4.0	0.58	73

[a] At 25° in aqueous solutions. [b] Relative to aqueous 0.1 M perchloric acid. [c] Calculated using the interpolated value of k_ψ = 12.6 × 10^{-6} sec^{-1}.

With LiCl, a = 0.33 at 25.0°; 0.32 at 45.0°; and 0.28 at 63.5°. With $LiClO_4$, a = 0.41 at 25.0°; 0.36 at 45.0°; and 0.34 at 63.5°. The activation energy depends slightly upon the temperature and electrolyte (Table IV), but the effect is much less marked than with moderately concentrated acids.

Salt Effects upon the Activity Coefficients of the Substrate. Lithium chloride salts out α-phenylvinyl diethyl phosphate, and lithium perchlorate salts it in (Table V), as is often found for polar nonelectrolytes.[15,18] Plots of the logarithms of the activity coefficients (f_s) against salt concentration are close to linear for lithium perchlorate, with slope ≈ −0.05, and for up to 2 M lithium chloride, with slope ≈0.12. The plots are curved at concentrations above 2 M especially for lithium chloride. The activity coefficients of the substrate could not be determined in the acid solutions because of the ease of acid cleavage.

Micellar-Catalyzed Cleavage. The variations of k_ψ with concentration of NaLS are shown for 0.01 and 0.1 M in Figure 1, and k_ψ increases sharply at detergent concentrations above the cmc which is 6.4 × 10^{-3} M in water.[19] Cetylsulfonic acid is a better catalyst than NaLS; with 0.00051 M cetylsulfonic acid in 0.01 M $HClO_4$, k_ψ = 2.94 × 10^{-6} sec^{-1} at 45.0°, as compared with k_ψ = 1.21 × 10^{-6} sec^{-1} at 45.0° with 0.01 M $HClO_4$ in the absence of detergent. This over twofold rate enhancement by 0.00051 M cetylsulfonic acid should be compared with the enhancement of k_ψ from

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1.21×10^{-6} sec^{-1} to 3.75×10^{-6} sec^{-1} with 0.005 M NaLS (Figure 1). The effectiveness of cetylsulfonic acid as a micellar catalyst may be related to its low cmc (4.2×10^{-4} M as determined by surface tension, or 2.8×10^{-4} M as determined by the dye method).[13] Unfortunately the solubility of cetylsulfonic acid and its sodium salt was not sufficiently high for the micellar catalysis to be studied extensively with this detergent.

Added salts inhibit the micellar catalysis of the acid cleavage of α-phenylvinyl diethyl phosphate by NaLS (Table VI), and the micellar-catalyzed reaction is slower in D_2O than in H_2O (Table VII). The values of k_{H_2O}/k_{D_2O} increase to a maximum with increasing detergent concentration.

Table VI. Salt Inhibition of the Micellar-Catalyzed Hydrolysis[a]

Salt	C_{salt}, M	$10^5 k_\psi$, sec^{-1}
		1.05
		1.07[b]
LiCl	0.01	0.87
LiCl	0.03	0.65
NaCl	0.01	0.86
NaCl	0.03	0.61
$(CH_3)_4NCl$	0.01	0.50[b]
$(CH_3)_4NCl$	0.03	0.24[b]

[a] At 45.0° with 0.01 M NaLS and 0.01 M $HClO_4$ unless specified. [b] 0.01 M HCl.

Table VII. Deuterium Solvent Isotope Effect on the Micellar-Catalyzed Hydrolysis[a]

C_{NaLS}, M	H_2O	D_2O[b]	k_{H_2O}/k_{D_2O}
0.0050	3.75	2.86	1.31
0.0075	9.22	5.00	1.84
0.0100	10.5	5.11	2.15
0.0200	9.89	4.50	2.18
0.0300	7.68[c]	3.61	2.14

[a] Values of $10^5 k_\psi$, sec^{-1} at 45.0° with 0.01 M $HClO_4$ and NaLS. [b] 99.8% deuterium. [c] Interpolated value.

We made a few preliminary runs with phosphoenolpyruvic acid (as the monocyclohexylammonium salt), and the values of k_ψ are given in Table VIII. At 100°

Table VIII. Hydrolysis of Phosphoenolpyruvic Acid[a]

C_{H^+}	$10^4 k_\psi$, sec^{-1}
0.10[b]	1.80
1.00[b]	1.95
0.10[b]	0.97[c]
0.10[b]	0.97[c]
0.10[d]	0.98[c]
0.10[a]	0.95[e]

[a] At 73.0° in aqueous solutions. [b] HCl. [c] 0.01 M NaLS. [d] $HClO_4$. [e] 0.01 M CTACl.

with aqueous 1 M HCl $t_{1/2}$ = 8.6 min for the cleavage of phosphoenolpyruvic acid,[2] corresponding to $k_\psi' \approx 1.4 \times 10^{-3}$ sec^{-1}. In the absence of detergent we found similar values of k_ψ at 0.1 and 1.0 M HCl, showing that we are not dealing with a simple acid-catalyzed cleavage, and ionization of the substrate may be a complicating factor. In addition we found that both NaLS and cetyltrimethylammonium chloride (CTACl) slightly retarded the reaction. The detergent inhibition could be caused by several factors, *e.g.*, the detergent may affect the dissociation constants of the substrate, and the substrate may not be incorporated extensively into the micelles. Because of these complications we did not examine this substrate further.

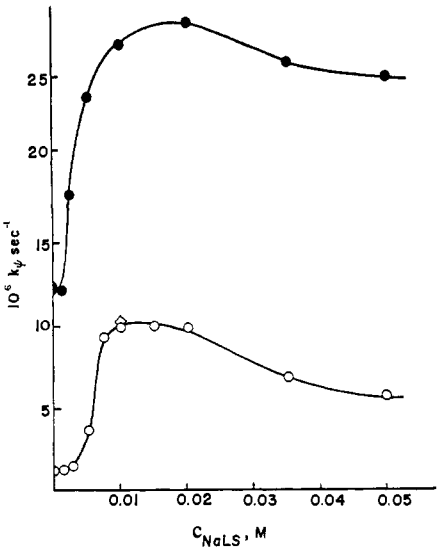

Figure 1. Micellar catalysis of the acid cleavage of α-phenylvinyl diethyl phosphate at 45.0°: ○, 0.01 M $HClO_4$; ◇, 0.01 M HCl; ●, 0.1 M $HClO_4$.

Discussion

Before we can discuss the nature of the micellar catalysis it is necessary to understand the acid-catalyzed cleavage.

Hydrolysis in Aqueous Acids. Plots of log k_ψ against $-H_0'$ are linear and have slopes in the range 1.1–1.4, suggesting that the reaction has either an A1 mechanism in which a preequilibrium proton transfer is followed by a slow step not involving water, or an A-SE2 mechanism in which the proton transfer is rate limiting as in addition to an olefinic double bond.[5a] The values of Bunnett's and Olsen's ϕ parameter are in the range associated with A1 and A-SE2[5c] reactions.

The relation between log k_ψ and $-H_0'$ may not be particularly informative of itself, because H_0' may not be the appropriate acidity scale for protonation of an olefinic double bond, and the relation between the H_0', H_0'', and H_R scales depends upon the nature of the acid,[20] as does the relation between reaction rate and acidity function.[12,21,22]

However, there are a number of examples of well-authenticated examples of rate-limiting proton transfers to olefinic double bonds for which plots of log k_ψ against $-H_0'$ are linear with slopes 1.1–1.3,[23–25] suggesting that the relation between rate constant and H_0' which we observe supports an A-SE2 mechanism.

Noyce and Pollack have shown that at 1 M acid the hydrolysis of α-acetoxy-*p*-nitrostyrene, like other simple

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(22) C. A. Bunton and E. Humeres, *J. Org. Chem.*, **34**, 572 (1969).
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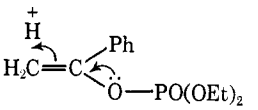
(24) W. M. Schubert, B. Lamm, and J. R. Keeffe, *ibid.*, **86**, 4724 (1964).
(25) D. S. Noyce, D. R. Hartter, and F. B. Miles, *ibid.*, **90**, 4633 (1968).

esters, follows an $A_{Ac}2$ mechanism, but that at higher acidities the dominant mechanism becomes an A-SE2 proton addition,[26] showing that although quantitative relations between rate and acidity cannot always be established, qualitative relations are valuable, and that A-SE2 mechanisms show a high rate dependence upon acidity.

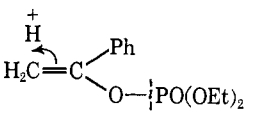
Other kinetic evidence supports an A-SE2 mechanism. The activation parameters depend upon acidity, excepting in dilute acid, but the log A values are smaller (*i.e.*, the ΔS^* values more negative), especially in the more concentrated acid, than those generally found for A1 hydrolyses of esters and related compounds, including phosphate esters,[6,22] and for cleavage in 0.1 M acid the value of $\Delta S^* = -8.8$ eu (calculated for 1 M $HClO_4$) is similar to those found for A-SE2 reactions. Matesich has surveyed the literature on these slow proton additions and found an approximate correlation between substrate reactivity and ΔS^*, with values of ΔS^* varying from -30 eu to 0 with substrate reactivity,[27] but for proton addition to ethyl vinyl ether $\Delta S^* = -11$ eu,[28] and for the cleavage of allyl mercuric iodide by hydronium ion $\Delta S^* = -12$ eu,[29] and for the hydration of isobutylene $\Delta S^* = -3$.[30]

The use of activation parameters as mechanistic tests in the cleavage of α-phenylvinyl diethyl phosphate is complicated by their marked dependence on acidity and temperature when moderately concentrated acids are used. These variations of the activation parameters are often observed when two reactions run simultaneously, but then the activation energy increases with temperature, because the contribution of the reaction with the higher activation energy increases with temperature. This situation is not observed here, and we believe that the failure of the Arrhenius equation arises from temperature effects upon acidity of the various strong acids. This problem has not been investigated widely, although H_0' is temperature dependent.[5a,16] Relations between rate and acidity have usually been examined at whatever temperature happened to be convenient to the experimentalist, and Bunnett has noted that temperature effects could cause complications, and the present results support his note of caution.[5b] The failure of the Arrhenius equation to apply to cleavage in moderately concentrated acid could mean simply that the dependence of pK_a upon temperature is quite different for a Hammett indicator and the transition state for protonation of an enol phosphate. In this context it is important to note that the Arrhenius equation is obeyed reasonably well for reaction in aqueous salt solutions, and the activation energy decreases only slightly with increasing salt concentration, with lithium perchlorate having a larger effect than lithium chloride (Table II).

Therefore, although the values of the activation parameters do not provide conclusive evidence for the mechanism of the cleavage of α-phenylvinyl diethyl phosphate, they are consistent with slow proton addition. Protonation may require a particular conformation of the substrate which would allow formation of a new carbon–oxygen double bond with or without cleavage of the phosphorus–oxygen bond (IIIa or IIIb), so that either an oxonium ion or the ketone and a phosphoryl cation are generated, but all the kinetic evidence suggests that water is not involved as a nucleophile in the transition state.



IIIa



IIIb

Comparison between the isotope effects on the acid cleavage of 1-phenylvinyl diethyl phosphate and enol ethers and related compounds and the hydrolysis of α-acetoxy-p-nitrostyrene is informative. The mechanism of hydrolysis of α-acetoxy-p-nitrostyrene changes with increasing acidity, and at low acid concentrations where an $A_{Ac}2$ mechanism is followed $k_{H_2O}/k_{D_2O} = 0.75$ (*cf.* ref 7), but in more concentrated acid where proton addition is rate limiting $k_{H_2O}/k_{D_2O} = 3.25$.[26] The deuterium solvent isotope effect for acid cleavage of the vinyl phosphate is similar, but slightly smaller than those found for the hydrolyses of enol ethers and esters.

The kinetic solvent isotope effect $k_{H_2O}/k_{D_2O} \approx 2.5$ (Table I) therefore fits the expected A-SE2 mechanism. For other SE2 proton additions to olefinic double bonds the kinetic isotope effects are generally smaller than those expected for complete loss of the zero point of energy of the stretching vibration of the hydronium ion, in part because the primary hydrogen isotope depends upon the extent of the proton transfer, but also because of secondary solvent isotope effects which oppose the primary effect.[28,29,31–35] In addition there is evidence that changes in bending vibrations, and possibly tunneling, may be important in determining the primary isotope effect in some proton transfers.[36–38]

Kinetic Salt Effects in the Absence of Detergent. Added electrolytes assist the acid-catalyzed cleavage of α-phenylvinyl diethyl phosphate, and lithium perchlorate is a better catalyst than lithium chloride, even though it is less effective at increasing the protonating power of an acid, as measured by H_0'.[16] The salt order is therefore the same as that found for A1, rather than A2, hydrolyses of carboxylic esters.[12] For ester hydrolysis it appears that a transition state which has considerable carbonium ion character is stabilized by a low charge density anion, such as perchlorate, whereas the opposite is true for the transition state of an A2 reaction which has the ability to hydrogen bond strongly with the solvent. To this extent it would appear that water molecules are not strongly involved as nucleophiles in the acid cleavage of α-phenylvinyl diethyl phosphate, as indicated by other evidence.

For proton addition to the substrate S

$$H^+ + S \rightleftharpoons [X^{\ddagger}] \longrightarrow \text{product}$$

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the Bronsted–Bjerrum rate equation gives

$$k_\psi = k_0 a_{H^+} f_s / f_{X^\pm}$$

or

$$a_{H^+}/f_{X^\pm} = k_\psi / k_0 f_s$$

The values of $a_{H^+}/f_{X^\pm}$ (relative to salt-free 0.1 M perchloric acid) are given in Table V. Lithium chloride destabilizes the substrate and this effect of itself should lead to a positive kinetic salt effect, whereas lithium perchlorate has the opposite effect (Table V). However, the salts also affect the hydrogen ion activity and the activity coefficient of the transition state. We cannot separate these two factors, but there is no reason to believe that lithium perchlorate increases hydrogen ion activity more than does lithium chloride. Indeed the opposite may be true, because chlorides increase Hammett's acidity function H_0', but not H_R,[12,39] more than do perchlorates, but because salt effects upon acidity functions depend upon changes in both hydrogen ion activity and activity coefficients of the indicator and its conjugate acid, we cannot put too much weight upon this behavior. However, it has often been suggested that hydrogen ion activity is markedly increased by a decrease in the water activity,[39a,40] and to this extent lithium chloride should enhance hydrogen ion activity more than the perchlorate. The water activity is lower in lithium chloride than in lithium perchlorate.[41]

Therefore it seems that the larger values of $a_{H^+}/f_{X^\pm}$ in lithium perchlorate over chloride (Table V) are caused by the greater ability of perchlorates over chlorides to stabilize the bulky cationic transition state for an Al ester hydrolysis,[12] or an A-SE2 cleavage of a vinyl phosphate. Similarly anions of low charge density stabilize a bulky triarylmethylcarbonium ion more than do anions of high charge density, relative to their effects on anilinium ions, suggesting that these salt effects upon rates and equilibria in water depend upon the charge densities of the cationic transition or final states and of the anion of the electrolyte.[12]

Micellar-Catalyzed Hydrolysis. The kinetic form of the micellar catalysis is simple. The rate enhancement (relative to reaction in the absence of detergent) is considerably greater in 0.01 M than in 0.1 M acid, approximately tenfold as opposed to twofold (Figure 1). Such a result is to be expected, because too much strong acid will simply saturate the available micelles, and therefore be ineffective as a catalyst. The dependence of rate upon detergent concentration is different at the two acidities. The cmc for NaLS in water is 6.4×10^{-3} M,[19] and on the simple theory for micellar catalysis or retardation there should be no kinetic effect at detergent concentrations below the cmc.[42] This simple treatment is never wholly correct,[43–45] but its failure in our present work is more evident at the higher acidity, possibly because of electrolyte effects upon the cmc; however, at detergent concentrations well above the cmc the rates are the same with hydrochloric and perchloric acids.

With 0.01 M acid there is a rate maximum at *ca.* 0.01 M detergent, and the decrease at higher detergent concentrations appears to be general for detergent-catalyzed anion–molecule reactions, and can be explained in terms of either a negative salt effect of the counterion of the anionic detergent,[46] or a deactivation of the ionic reagent,[45] in this case the hydrogen ion, by the anionic detergent. In some nucleophilic substitutions catalyzed by a cationic micelle it was found that the rate maximum disappeared if the concentration of the counteranion was maintained.[46]

Added salts effectively inhibit the micellar catalysis (Table VI). The salt order upon the reaction is no salt > LiCl > NaCl > $(CH_3)_4NCl$, as expected in terms of an interaction between cations and the anionic micelle which depends upon the charge density of the cation. In general counterions of an ionic micelle decrease its catalytic efficiency by making it more difficult for an ionic reagent to be incorporated preferentially into the Stern layer around the micelle.[8,9,14,45–47] The importance of charge density in determining the extent of salt inhibition suggests that both hydrophobic[48,49] and electrostatic interactions are important, and that an ion of low charge density does not have a large amount of hydration energy to lose in going from water into the Stern layer of an ionic micelle.

Deuterium Solvent Isotope Effect on the Micellar-Catalyzed Reaction. The kinetic isotope effect depends on the detergent concentration (Table VII), and at all detergent concentrations is smaller than those found in the absence of detergent. With detergent concentrations above 0.01 M all the substrate should be in the micellar phase, and the value of k_{H_2O}/k_{D_2O} should be that for reaction in this phase. The over-all value of k_{H_2O}/k_{D_2O} is the product of a primary effect, with $k_{H_2O}/k_{D_2O} > 1$, and an opposing, but generally smaller, secondary effect.[29,35] Both these effects could be different in the micellar as compared with the aqueous phase.

For detergent concentrations <0.01 M the substrate is distributed between the two phases, and the over-all isotope effect will depend upon the kinetic isotope effects in the two phases and the isotope effect upon the properties of the micelle and the relative solubility of the substrate in the two phases. Robertson and his coworkers have interpreted the deuterium solvent isotope effect for alkyl halide and sulfonate solvolyses in terms of changes in the structure of the solvation shell in going from the initial to transition state for protium and deuterium oxide.[50] These structural differences between the two solvents should be important in certain aspects of micellar catalysis.

However, the solvent isotope effect for the micellar-catalyzed reaction suggests that an A-SE2 mechanism is followed in the micellar as in the aqueous phase.

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