Kinetics and Mechanism of the Acid-Catalyzed Hydrolysis of α-Phenylvinyl Diethyl Phosphates

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The acid-catalyzed hydrolysis rates of a series of ring-substituted α-phenylvinyl diethyl phosphates in 0.1 *N* HCl–40% aqueous ethanol were measured at four different temperatures. The rate of hydrolysis was accelerated by electropositive substituents, whereas it was lowered by electron-withdrawing groups. From the rate data at different temperatures, the activation energies and activation entropies were calculated. Plots of log k at 85° against Brown's σ^+ substituent constants are linear with slope -1.69. The observed values of the activation parameters are consistent with an A-SE2 mechanism except for the para-nitro compound.

After the discovery of phosphoenolpyruvic acid (PEP) by Meyerhof and Lohmann,[1] vinyl phosphates acquired great importance in biochemistry.

In fact, PEP represents the last phosphorylated three-carbon-atom compound, both in glycolysis and in fermentation, and also seems to play a role in the fixation of carbon dioxide.[2]

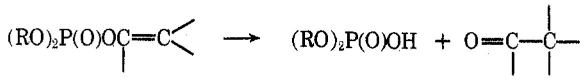
Owing to the difficulties in the preparation of PEP, no other vinyl phosphates had been synthesized until about 1950. However, after work establishing that certain organophosphorus compounds were very potent insecticides,[3] the chemistry of organophosphates developed enormously.

Recently in the acid-catalyzed hydrolysis of vinyl phosphates there has been a good deal of interest, since it has been considered as a model reaction for biological phosphorylations.[4]

It is known that the course of the acid-catalyzed hydrolysis of dialkyl vinyl phosphates is dependent upon the reaction conditions.

With HCl (1:1) at 100° total hydrolysis of all ester groups occurs, forming mainly alkyl chloride, phosphoric acid, and the corresponding ketone.[5,6]

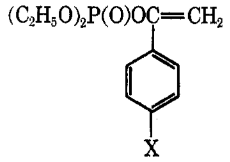
Under milder conditions, however, selective hydrolysis of the vinyl ester group can be effected, yielding the dialkyl phosphate and the corresponding carbonyl compound[7-9] (see Experimental Section).



$$(RO)_2P(O)OC{=}C\langle \;\longrightarrow\; (RO)_2P(O)OH + O{=}C{-}C{-}$$

Recently, Bunton and Robinson[10] have shown that the acid-catalyzed hydrolysis of α-phenylvinyl diethyl phosphate follows an A-SE2 mechanism with slow proton addition to the vinylic double bond.

Although mechanistic studies have been carried out on acid-catalyzed hydrolysis of some vinyl phosphates, in the present paper, following our research work on phosphoric esters,[11] we wish to amplify the study examining the effect of the substituent para to the aromatic ring on the reaction rate of the acid-catalyzed hydrolysis in 0.1 *N* HCl–40% aqueous ethanol of vinyl phosphates previously synthesized[11] (I).



I

X = H, CH_3, CH_3O, Cl, NO_2

We find that the activation parameters are consistent with an A-SE2 mechanism, except for the para-nitro compound.

Results and Discussion

The acid-catalyzed hydrolysis was followed kinetically by titrating of the diethyl phosphate formed with 0.1 *N* NaOH (see Experimental Section).

TABLE I

PSEUDO-FIRST-ORDER RATE CONSTANTS FOR THE ACID HYDROLYSIS OF α-PHENYLVINYL DIETHYL PHOSPHATE IN 0.1 *N* HCl–40% AQUEOUS ETHANOL AT 85°

Run no.	Initial concn, mol/l.	$k_1 \times 10^5$, sec^{-1}
1	0.0213	11.5
2	0.0245	11.2
3	0.0294	11.8
4	0.0315	11.9

TABLE II

ACID HYDROLYSIS OF α-PHENYLVINYL DIETHYL PHOSPHATE[a]

Elapsed time, min	0.1 *N* NaOH, ml	$\log (a/a - x)$
0	0	0
30	1	0.0903
45	1.5	0.1436
60	1.7	0.1670
75	2.2	0.2180
90	2.55	0.2835
120	3	0.3606
150	3.4	0.4430
180	3.8	0.5445

[a] The data refer to the first kinetic run in Table I.

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[11] A. Arcoria and G. Scarlata, *Boll. Sedute Accad. Gioenia Sci. Natur. Catania*, IV, 8 (1), 64 (1964); A. Arcoria, *Ann. Chim. (Rome)*, **56**, 251 (1966); A. Arcoria and S. Fisichella, *ibid.*, **56**, 1504 (1966); **57**, 1128 (1967); *Tetrahedron Lett.*, 3347 (1971).

TABLE III

PSEUDO-FIRST-ORDER RATE CONSTANTS FOR THE ACID HYDROLYSIS OF α-PHENYLVINYL DIETHYL PHOSPHATES IN 40% AQUEOUS ETHANOL

		$k_1 \times 10^5$, sec^{-1}									
No.	Substituent	85°	80°	75°	70°	65°	60°	55°	50°	45°	40°
1	p-H	11.6		5.85		1.90		0.724			
2	p-CH_3	55.4[a]			14.1	9.91	6.64	3.41			
3	p-CH_3O	374[a]						35.5	22.1	14.4	8.82
4	p-Cl	5.91	3.95		1.33	1.05					
5	p-NO_2	0.927	0.653	0.499	0.401						

[a] Extrapolated values from their respective Arrhenius plots (Figure 1).

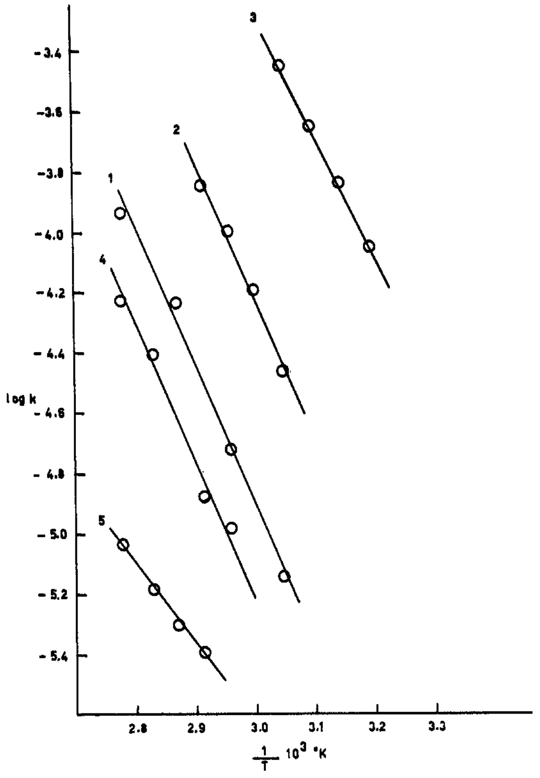

Figure 1.—The Arrhenius activation energy plots. The numbers on the curves refer to the series numbers in Table III.

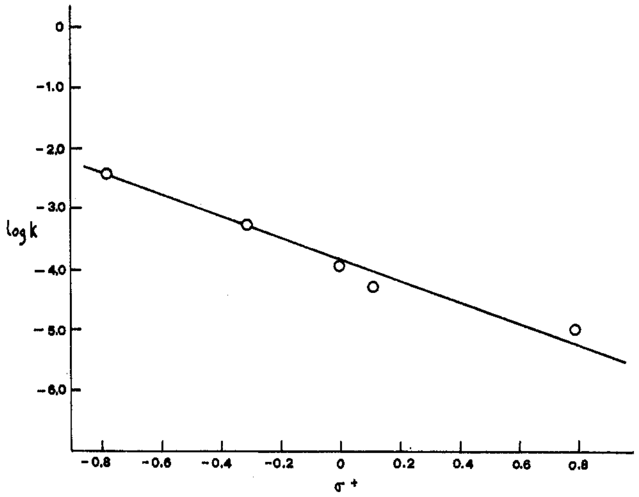

Figure 2.—Substituent effect on rate of hydrolysis.

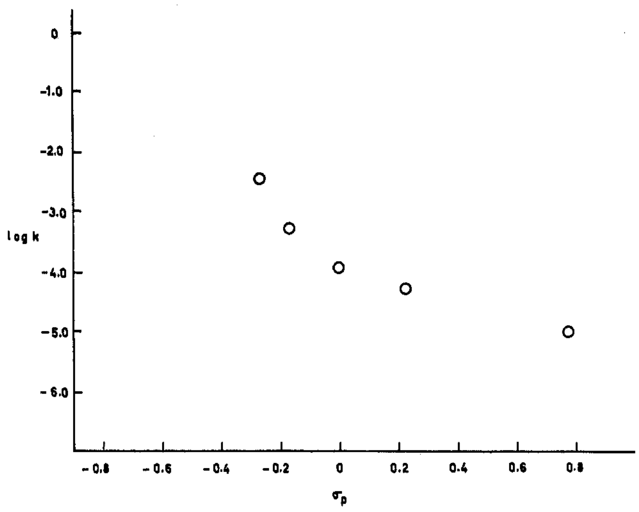

Figure 3.—Substituent effect on rate of hydrolysis.

The rate constants at 85° with varied initial concentrations of α-phenylvinyl diethyl phosphate (X = H), listed in Table I, clearly indicate that the reaction of hydrolysis is pseudo-first-order. A typical kinetic run is shown in Table II.

Considering the rate information at various temperatures, tabulated in Table III, it can be seen that the hydrolysis rate is increased by electropositive substituents, whereas it is decreased by electron-withdrawing groups.

The variation with temperature of the rates of hydrolysis gave the activation energies, activation entropies, and log A presented in Table IV and Figure 1.

These activation parameters are similar for all the compounds, except for the para-nitro compound, and are consistent with an A-SE2 mechanism involving a rate-determining protonation of the carbon–carbon double bond.[12−14]

TABLE IV

ACTIVATION PARAMETERS FOR THE ACID HYDROLYSIS

Substituent	E_A, kcal/mol	ΔS, 85°, cal mol^{-1} °K^{-1}	log A
p-H	22.1	−16.8	9.62
p-CH_3	21.0	−17.1	9.57
p-CH_3O	18.5	−20.3	8.86
p-Cl	21.8	−19.2	9.10
p-NO_2	13.5	−46.1	3.23

Plots of log k at 85° against Brown's σ^+ substituent constants[15] are linear with a slope of −1.69 (Figure 2). The correlation with σ^+ constants is substantially better than with Hammett's σ_p constants[16] (Figure 3), indicating that electron deficiency in the transition state is conjugated with the substituent para to the aromatic ring.

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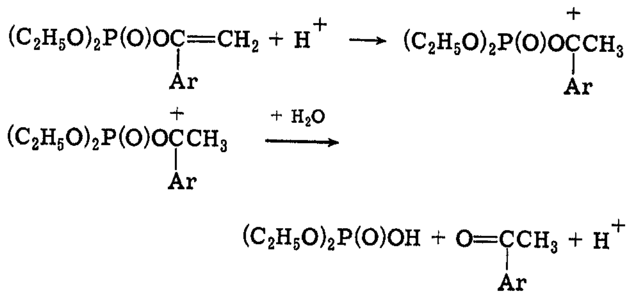
SCHEME I



$$(C_2H_5O)_2P(O)O\underset{Ar}{C}{=}CH_2 + H^+ \longrightarrow (C_2H_5O)_2P(O)O\overset{+}{\underset{Ar}{C}}CH_3$$

$$(C_2H_5O)_2P(O)O\overset{+}{\underset{Ar}{C}}CH_3 \xrightarrow{+\,H_2O} (C_2H_5O)_2P(O)OH + O{=}\underset{Ar}{C}CH_3 + H^+$$

This ρ value is of the same order of magnitude as that found for other similar reactions that follow an A-SE2 mechanism.[12]

The data obtained, then, lead us to postulate that the acid-catalyzed hydrolysis of para-substituted α-phenylvinyl diethyl phosphates in 0.1 *N* HCl–40% aqueous ethanol follows an A-SE2 mechanism with initial protonation of the vinylic double bond followed by the attack by water and collapse to products (Scheme I).

The log *A* and ΔS^* values for the para-nitro compound, however, are considerably dissimilar. The log *A* values, in fact, are in the range expected for an A2 mechanism and the entropies of activation are characteristic of acid hydrolysis in which water molecules are closely bound into the transition state.[17]

However, the values of the activation parameters do not provide conclusive evidence that the para-nitro substituent causes the mechanism to change. Examination of the points of Figure 3 supports this possibility, and indicates that the gradient decreases at the higher values of *T*, and therefore the different values of the activation parameters found for the para-nitro compound may just be due to its slower rate requiring a higher temperature for conveniently measurable rates.

Experimental Section

Materials.—Preparation and purification of the vinyl phosphates have been elsewhere described.[11] Physical constants of the products used are listed in Table V.

Kinetic Procedure.—The reaction was performed with 0.1 *N* HCl–40% ethanol (95%), determining by titrating with 0.1 *N* NaOH the diethyl phosphate formed.

Aliquots of standardized aqueous ethanol, HCl, and vinyl ester (25 ml upon the whole) were mixed in glass-stoppered tubes and placed into a constant-temperature bath (±0.01°). The initial concentration of ester was 0.02 mol l.$^{-1}$.

Tubes were periodically removed from the constant-temperature bath and rapidly cooled in an acetone–solid carbon dioxide mixture, and the contents were poured into a beaker containing 25–30 ml of water. The diethyl phosphate formed was then titrated with standardized 0.1 *N* NaOH using phenolphthalein as indicator.

All rates were run in duplicate to at least 75% completion, with less than 3% deviation between the two rate constants in all cases.

All compounds gave excellent pseudo-first-order kinetics.

Rate constants were calculated by a least squares computer program with an Olivetti Programma 101.

Analysis of the Hydrolysis Products.—The appropriate vinyl phosphate (5 g) was mixed with 100 ml of 0.1 *N* HCl–40% aqueous ethanol in a glass-stoppered tube and maintained at the kinetic temperatures for several hours depending on the rate of the reaction, until complete hydrolysis. An aliquot of the solution was then neutralized to phenolphthalein with barium carbonate and baryta and warmed on the water bath. The barium salt was filtered, washed, and dried and then crystallized from 80% alcohol. The barium content, determined as barium sulfate, proved that the salt was in every case barium diethyl phosphate.[18]

The second aliquot of the solution was buffered with sodium acetate, and the corresponding para-substituted acetophenones were identified as *p*-nitrophenylhydrazones[19] (Table VI).

TABLE V

PHYSICAL CONSTANTS OF α-PHENYLVINYL PHOSPHATES USED IN THE ACID HYDROLYSIS

Substituent	Bp, °C (mm)	$n^{30}\mathrm{D}$
p-H	117 (0.3)	1.4991
p-CH_3	119 (0.15)	1.4995
p-CH_3O	131 (0.15)	1.5114
p-Cl	123 (0.3)	1.5112
p-NO_2[a]		

[a] Mp 25°; recrystallized from anhydrous ether.

TABLE VI

PHYSICAL CONSTANTS OF *p*-NITROPHENYLHYDRAZONES[a]

No.	$p\text{-}\mathrm{XC_6H_4}\overset{\mathrm{CH_3}}{\mathrm{C}}{=}\mathrm{NNHC_6H_4NO_2}\text{-}p$	Mp, °C	Ref
1	X = H	183–184	*b*
2	X = CH_3	196–198	*b*
3	X = CH_3O	193	*b*
4	X = Cl	238–139	*b*
5	X = NO_2	276–278	*c*

[a] All the compounds were crystallized from ethanol, except for the *p*-nitro derivative (compd no. 5), that was crystallized from dioxane. [b] A. Arcoria, *Ann. Chim. (Rome)*, **56**, 251 (1966). [c] A. Arcoria and S. Fisichella, *ibid.*, **57**, 1228 (1967).

The mixture melting point with authentic samples of *p*-nitrophenylhydrazones reveals no depression.

The reaction products from the acid hydrolysis of α-phenylvinyl diethyl phosphates in 0.1 *N* HCl–40% aqueous ethanol are, therefore, diethyl phosphate and the corresponding para-substituted acetophenones.

Registry No.—I (R = H), 1021-45-0; I (R = CH_3), 18276-76-1; I (R = CH_3O), 18275-67-7; I (R = Cl), 18276-77-2; I (R = NO_2), 34804-85-8.

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