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Kinetics and Mechanism of Hydrolysis of Di-p-Phenatidin Phosphate via Conjugate Acid Species

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Kinetic study of di-p-phenatidin-phosphate has been made in acid region (0.1 to 7.0 mol dm^{-3}) at 98°C in 20% aqueous dioxane mixture (v/v). Ionic strength data exhibits different contribution of neutral species and presence of acid catalysis. Theoretical rates, estimated from 2nd empirical term of Debye-Huckel equation, have been found in close agreement with experimental rates. Arrhenius parameters and comparative kinetic rate data have been used to propose the tentative mechanism.

INTRODUCTION

Phosphate having C–N–P linkages are of great importance. They are used as pesticides, insecticides[1], fire retardants[2], plasticizers[3], synthetic lubricants[4] etc. The undertaken compound *i.e.* di-p-phenatidine phosphate was chosen for the kinetic study as this compound is reactive via different species depending upon the experimental conditions.

EXPERIMENTAL

Di-p-phenatidin phosphate was prepared by $POCl_3$ method[5,6]. It was recrystallised from absolute alcohol, m.pt. 198°. (Found: C, 56.05; H, 6.58; N, 7.84; P, 9.90%: Calcd.: C, 57.14; H, 6.25; N, 8.30; P. 9.22%).

The progress of the reaction was followed by estimating the rate of appearance of inorganic phosphate using Allen's method[7]. Concentration of the Diester was maintained at 5×10^{-4} mol. dm^{-3} throughout the study.

RESULTS AND DISCUSSION

The rate of hydrolysis of di-p-phenatidin phosphate increases first slowly in lower acid region and then rises rapidly, maximum occurs at 4.0 M HCl. Further rise in acidity decreases the rate uniformly upto 7.0 M HCl (Table I).

In order to determine whether or not there is effect of ionic strength or the presence of acid catalysis, kinetic runs were made at three different ionic strengths (1, 2 & 3μ) which were maintained by adequate mixture of NaCl & HCl.

Hydrolysis at each ionic strength is represented by a linear curve (Fig. not shown) that makes a −ve slope with the acid axis indicating the presence of acid catalysis. Since the slope decreases with increase in ionic strength acid catalysis is subjected to −ve effect of ionic strength. These curves make intercepts on the rate axis, indicating the presence of side reaction of the neutral species. Since with the increase in ionic strength neutral species is also subjected to a —ve effect of ionic strength.

TABLE 1

RATE OF HYDROLYSIS OF di-p-PHENATIDIN PHOSPHATE AT 98°C

HCl (mol dm^{-3})	$10^2K_{H^+}C_{H^+}$ (min^{-1})	$10^2.K_N$ (min^{-1})	$10^2K_{calc.}$ (min^{-1}) from eqn. (1)	$(-\log aH_2O)^n$	$10^2K_{calc.}$ (min^{-1}) from eqn. (2)	$10^2K_{obs.}$ (min^{-1})
0.1	0.714	8.810	9.524	—	—	7.526
0.2	1.409	8.540	9.920	—	—	8.710
0.5	3.380	7.674	11.054	—	—	9.852
1.0	6.310	6.457	12.767	—	—	11.642
1.5	8.832	5.433	14.265	—	—	13.687
2.0	10.990	4.571	15.560	—	—	15.447
2.5	12.822	3.846	16.668	—	—	15.665
3.0	15.634	2.723	18.357	—	—	18.545, 22.94[a], 28.50[b]
4.0	16.676	2.291	18.867	—	—	18.568
4.5	17.505	1.928	19.433	$(0.130)^1$	6.750	4.969
5.0	18.115	1.622	19.77	$(0.154)^1$	3.250	3.247, 4.20[a], 5.44[b]
6.0	18.972	1.148	20.12	$(0.211)^5$	0.185	0.183
7.0	19.278	0.812	20.09	$(0.279)^5$	0.082	0.159

Note : a–30% dioxane b–40% dioxane

From the study of ionic strength effect, the total rates contributed by conjugate acid neutral forms can be calculated by the following 2nd empirical term of Debye-Huckel[8] equation.

$$K_e = K_{H^+}C_{H^+} + K_N \qquad (1)$$

In the above eqn. the terms K_e, $K_H +$ & K_N are the observed rate constants, the specific acid catalysed and specific neutral rate at that ionic strength respectively.

The sum of neutral and acid rates agrees well with the experimentally observed rates (Table 1) up to 4.0 mol dm^{-3} HCl. The lowering in rates in 4.5, 5.0, 6.0 & 7.0 mol dm^{-3} HCl can be explained by considering water activity[8–10] as an additional parameter. The hydrolysis at these acidities may be represented as

$$K_e = K_{H^+} C_{H^+}(aH_2O)^n + K_N(aH_2O)^n \qquad (2)$$

where aH_2O is water activity and n is an integer. The revised estimated rates now agree well with the experimentally observed rates (Table 1). It is clear from the above results that di-p-phenatidin phosphate in acid solutions occurs via both conjugate acid and neutral species and their rates are subjected to both ionic strength and water activity.

Solvent effect (Table 1) shows a significant rise in rates, dioxane being a better proton donor than water increases the concentration of conjugate acid species resulting in the increase in rates. Effect of solvent on the rate of hydrolysis may therefore be taken to indicate the formation of transition state in which charge is dispersed.

Arrhenius parameters[11] determined for the hydrolysis at 3.0 & 5.0 mol dm^{-1} HCl (Table 2). The magnitude of Arrhenius parameters fall in the range of bi-molecular reaction. Bi-molecular nature of reaction is further supported by Zucker-Hammett[12] (0.96), Hammett[13] (0.309) and Bunnett[14] ($W = 12.0$, $W^* = 5.55$) plots (not shown).

TABLE 2

CALCULATED ARRHENIUS PARAMETERS

HCl mol dm^{-3}	Temp. t°C.	$K_e \times 10^2$ obsd. (min^{-1})	E (K. cal: $mole^{-1}$)	A (sec^{-1})	$-\Delta S^{\neq}$ e.u.
3.0	80	7.99			
3.0	90	10.08	5.72	8.341×10^4	+ 70.55
3.0	98	13.56			
5.0	80	2.37			
5.0	90	2.50	4.57	8.434×10^5	+ 73.11
5.0	98	2.85			

Bunnett-Olson[15] parameter ($\phi = 2.20$, which is greater than 0.58) suggests that water is involved as a proton transfer agent in the rate determining step.

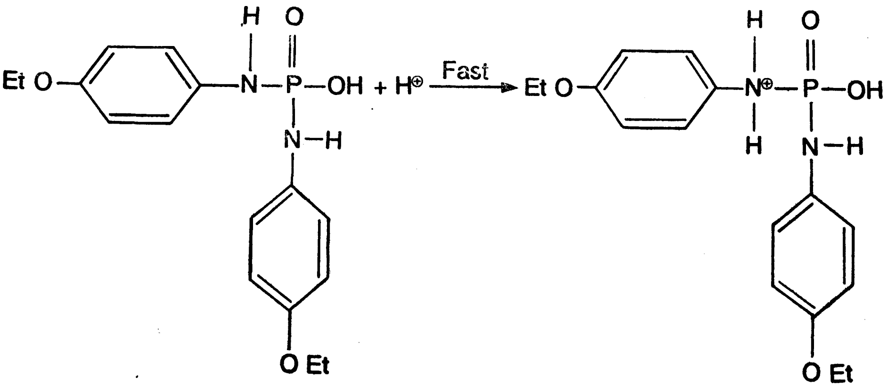
The effect of concentration of diester on the rate of hydrolysis also confirms the order of reaction to be one with respect to the diester by reducing either half

$$(K_e = 13.39 \times 10^{-2}\ min^{-1}) \text{ or double } (K_e = 13.52 \times 10^{-2}\ min^{-1})$$

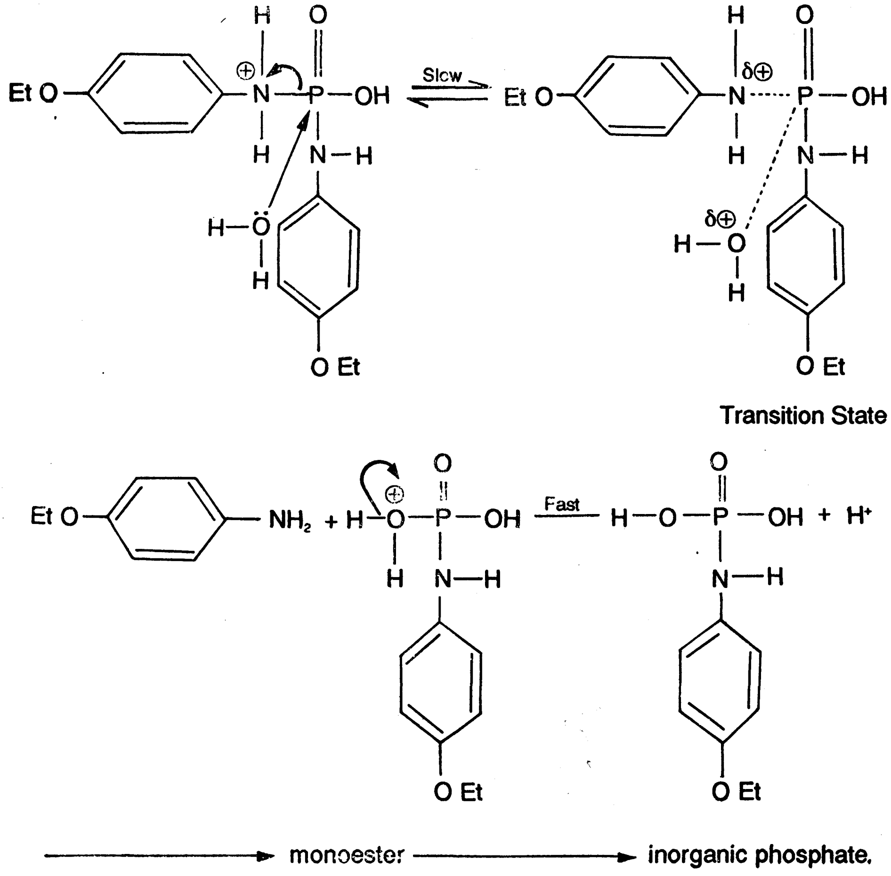
the normal concentration ($K_e = 13.56 \times 16^{-2}\ min^{-1}$) at 3.0 mol dm^{-3} HCl. Comparative kinetic data[16] (not shown) also support the bi-molecular nature of the hydrolysis involving attack of water on phosphorus of the diester.

On the basis of above evidences and discussions, the most tentative mechanistic routes may be formulated as

(1) Formation of conjugate acid species by a fast pre-equilibrium proton transfer.



(2) Bimolecular heterolysis of the conjugate acid species S_N2 (P).



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