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Mechanism of Hydrolysis of Mono-2-chloro Aniline Phosphate *via* Conjugate Acid Species

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The kinetic study of mono-2-chloro aniline phosphate is carried out in acid medium from 0.1 to 7.0 mol dm^{-3} at 50 ºC. The acid log rate profile has a rate maximum at 4.0 mol dm^{-3}. The lowering in rate after 4.0 mol dm^{-3} may be attributed to the lowering in concentration of the water activity or due to positive effect of ionic strength. Ionic strength data exhibit different contribution of neutral species. The observed rates were found in close agreement with the estimated theoretical rates derived from the second empirical term of Debye-Huckel equation. The study of ionic strength, temperature, solvent is provided to identify the reactive species and molecularity. Bimolecular behaviour has been decided by the Arrhenius parameters, Zucker-Hammett hypothesis, Bunnett & Bunnett-Olsen's parameters. The phosphate monoester involves P-N bond fission which is strengthened by comparative kinetic rate data.

Key Words: Hydrolysis, Solvent effect, Mono-2-chloro aniline phosphate.

INTRODUCTION

Phosphate esters of orthophosphoric acid comprise a group of mono, di and tri-esters depending upon the presence of two, one and none hydroxy groups in the phosphate moiety, respectively. Much work has been done about the esters containing C-O-P linkages[1,2] but recently scientists have realized the importance of phosphate esters having C-N-P linkages, known under the name phosphoramides, phosphoramidic acids, phosphoramidates or aminophosphates. Kinetic studies of the phosphate esters show that there are some common reaction paths which are followed both chemically and biochemically processes. Organic phosphates having C-N-P linkages are of great importance. They are used as, fungicides[3], fire retardands[4], antiviral activity[5], radio active tracer techniques[6], pesticides[7], additives for petroleum and corrosion inhibitors[8], smoke generation[9], antitumor agents[10] as well as in the treatment of glucoma[11,12], particularly cyclic amine phosphate in combination with phosphoramidic acid media and sulpha drugs are very important for their pharmaceutical and medicinal value[13] and as cancer chemotherapeutic agents[14].

EXPERIMENTAL

Mono-2-chloro aniline phosphate (Ba-Salt) was prepared by P_2O_5 method by phosphorylation of 2-chloro aniline in the mixture of benzene[15]. The reaction was carried out at 50 ºC employing 5.0 × 10^{-4} mol dm^{-3} solution of the monoester in aqueous medium. The inorganic phosphate obtained during hydrolysis was estimated spectrophotometrically by Allen's modified method[16]. The constant ionic strength were maintained using appropriate mixture of HCl and NaCl. All the chemicals used were of AR grade.

RESULTS AND DISCUSSION

The rate of hydrolysis of mono-2-chloro aniline phosphate was studied in HCl from 0.1 to 7.0 mol dm^{-3} HCl at 50 ºC. The pseudo-first order rate constants are summarized in Table-1. The rate of reaction increases up to 4.0 mol dm^{-3} HCl and there after it decreases. The maximum rate at 4.0 mol dm^{-3} HCl is attributed to complete conversion of the substrate into its conjugate acid species. The decrease in rate after 4.0 mol dm^{-3} HCl is attributed to the lowering of concentration of attacking nucleophile taking part in the reaction, due to variation in water activity. The kinetic runs were made by using adequate mixture of NaCl and HCl at different ionic strength (1, 2, and 3 µ). The plots of rate constants of acid hydrolysis and acid molarity at different ionic strength are linear curves (Fig. 1). The three linear curves which make positive slope with the acid axis show positive salt effect and presence of acid catalyzed hydrolysis. The slope of these curves increase with increase in strength. The corresponding slope values at constant ionic strength 1.0, 2.0 and 3.0 µ are 12.41 × 10^{-3}, 16.95 × 10^{-3} and 19.28 × 10^{-3} mol dm^{-3} min^{-1}, respectively. From the study of ionic strength effect, the total rates contributed by conjugate acid and neutral forms can be calculated by the following second empirical term of Debye-Huckle equation[17].

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

where K_e, $K_H^+.C_H^+$ and K_N are experimental rates, acid catalyzed rates and neutral rates, respectively. Table-1 summarizes both the observed and calculated rates of the hydrolysis in the acid region 0.1 to 4.0 mol dm^{-3} HCl. The lowering in rates in 5.0, 6.0, 7.0 mol dm^{-3} HCl may be attributed to the lowering in concentration and participation of water molecule.

The rates beyond 4.0 mol dm^{-3} HCl were calculated employing Bronsted-Bjerrum equation[18]:

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

where $({}^aH_2O)^n$ is water activity term and n is an integer, which increase with increase in acidity. The revised estimated rates agree well with the experimentally observed rates (Table-1). It is clear from the above result that mono-2-chloro aniline phosphate in acid solution occurs *via* both conjugate acid and neutral species and their rates are subjected to both ionic strength and water activity.

Solvent effect has been studied using different dioxane mixture. Table-2 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

TABLE-1
EXPERIMENTAL AND ESTIMATED RATES FOR THE HYDROLYSIS OF MONO-2-CHLORO ANILINE PHOSPHATE ESTER AT 50 ºC

HCl (mol dm^{-3})	$K_{H^+} \cdot C_{H^+} \times 10^3$ (min^{-1})	$K_N \times 10^3$ (min^{-1})	$K_e \times 10^3$ (min^{-1})	Water activity	$k_e \times 10^3$ (min^{-1}) Est.	$K_e \times 10^3$ (min^{-1}) Exp.
0.1	1.05	5.0	6.05	–	6.05	5.10
0.2	2.14	5.0	7.14	–	7.14	7.20
0.5	5.71	5.0	10.71	–	10.71	10.91
1.0	12.74	5.0	17.74	–	17.74	19.27
1.5	21.33	5.0	26.33	–	26.33	28.40
2.0	31.69	5.0	36.69	–	36.69	33.59
2.5	44.26	5.0	49.26	–	49.26	48.75
3.0	59.16	5.0	64.16	–	64.16	65.18
3.5	77.09	5.0	82.09	–	82.09	82.76
4.0	98.17	5.0	103.17	–	103.17	103.20
5.0	152.76	5.0	157.76	$(0.155)^2$	79.82	78.15
6.0	228.03	5.0	233.03	$(0.211)^3$	58.09	62.08
7.0	331.13	5.0	336.13	$(0.279)^4$	30.35	29.37

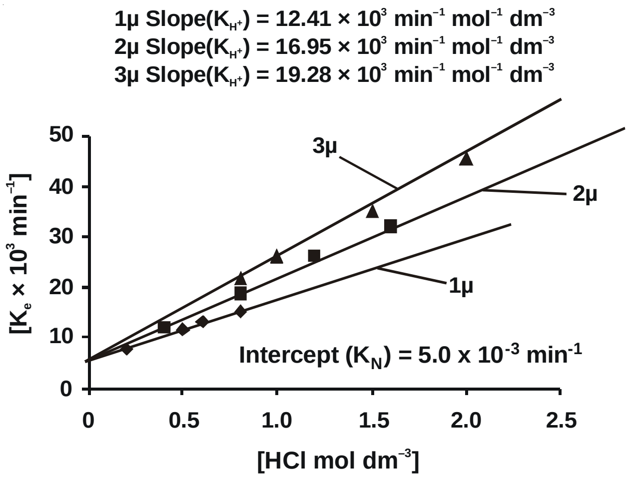


Fig. 1. Acid catalyzed hydrolysis of mono-2-chloro aniline phosphate at constant ionic strength at 50 ºC

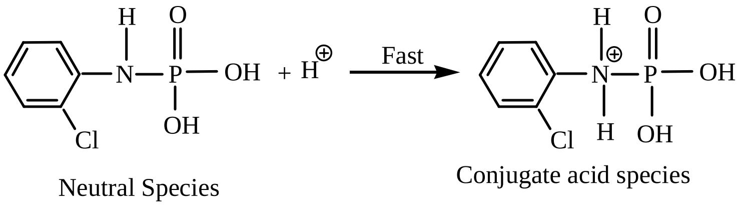
TABLE-2
EFFECT OF SOLVENT ON THE RATE OF HYDROLYSIS OF MONO-2-CHLORO ANILINE PHOSPHATE ESTER AT 50 ºC

HCl (mol dm^{-3})	Percentage of dioxane (v/v)	$K_e \times 10^3$ (min^{-1})
3.0	0.0	65.18
	10.0	75.03
	20.0	79.46
	30.0	85.45

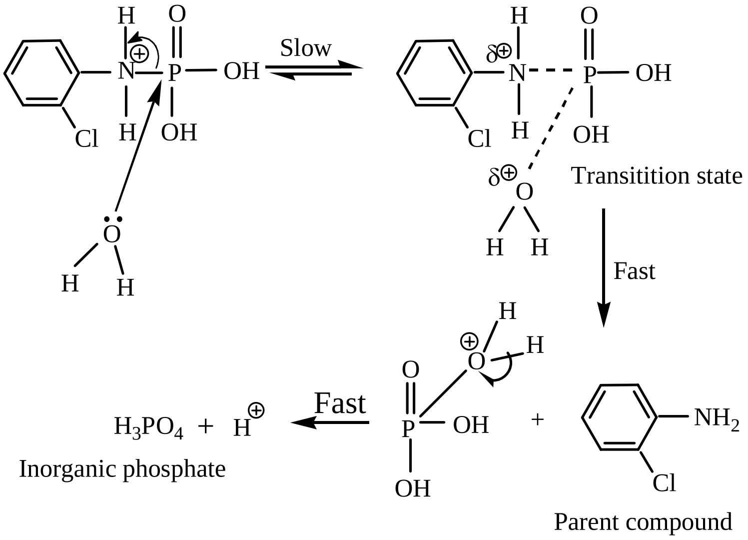
of solvent on the rate of hydrolysis may, therefore, be taken to imply a bimolecular nucleophilic reaction with the formation of a transition state in which the charge is dispersed. This is in accordance with Chanley's observation[19].

Thermodynamic parameters[20] for the reaction at 3.0 mol dm^{-3} HCl were found to be E = 14.63 Kcal/mol, A = $3.14 \times 10^{10}\ s^{-1}$ $\Delta S^{\#}$ = -20.76 e.u. These values are indicative of bimolecular nature of hydrolytic reaction. Bimolecular nature of reaction is further supported by slopes of the plots of Zucker-Hammett[21] = 1.38, Hammett[22] = 0.62, Bunnett[23] w = 7.91, w* = 2.32. Bunnett and Olsen[24] ϕ =1.40 suggested that water is involved as a proton transfer agent in the rate determining step. Bimolecular nature of the hydrolysis of mono ester involving P-N bond fission is further supported by comparative kinetic data (not shown) for the hydrolysis of other esters and isokinetic relationship[25,26]. Thus, acid hydrolysis of mono-2-chloro aniline phosphate involves bimolecular attack of water on phosphorus of conjugate acid species formed by fast pre-equilibrium proton transfer.

(a) Formation of conjugate acid species



(b) Bimolecular nucleophilic attack of water on phosphorous via conjugate acid species $S_N2(P)$



Mechanism of hydrolysis

REFERENCES

1. M.M. Mhala, C.P. Holla, G. Kasturi and K. Gupta, *Indian J. Chem.*, **8**, 51 (1970).
2. C.A. Vernon, Special Publication No. 8. The Chemical Society of London, pp. 17-23 (1957).
3. C.P. Shinde and R. Patil, *Asian J. Chem.*, **5**, 679 (1993).
4. M. Paul, *J. Vinyl Addit. Technol.*, **10**, 187 (2004).
5. D.C. Wright, US Patent, 6,034,073; Appl No. 593651 (1996).
6. G. Gardner and B.A. Kilby, *J. Chem. Soc.*, **3**, 1769 (1950).
7. T.C. Kwong, *The Drug Monit.*, **24**, 144 (2002).
8. L.D. Quin, A Guide to Organ Phosphorus Chemistry, John Wiley and Sons. Inc, New York, pp. 2, 375 (2000).
9. R.A. Moss and H.R. Morales, *J. Am. Chem. Soc.*, **123**, 7457 (2001).
10. H. Arnold, F. Bourseanx and N. Brock, *Arzneim Forsch*, **11**, 143 (1961).
11. G. Schrader and A.G.D.B.P. Farben, *Fabriken Bayer*, **814**, 152 (1948).
12. B. Topley, *Chem. Ind. (London)*, 859 (1950).
13. L.A. Cates and T.E. Johnes, *J. Pharm. Soc.*, **531**, 69 (1964).
14. B. Holmstedt, *Pharmacol. Rev.*, **11**, 567 (1959).
15. J. Cavalier, *Bull. Soc. Chem. (France)*, **13**, 885 (1895).
16. R.J.L. Allen, *Biochem. J.*, **34**, 858 (1940).
17. J.E. Leffer and E. Gurnwald, The Rates and Equilibria of Organic Reactions, John Wiley & Sons, Inc., New York, p. 177, 286 (1889).
18. P.W.C. Barnard, C.A. Bunton, D. D. Kellerman, M.M. Mhala, B. Silver, C.A. Vernon and V.A. Welch, *J. Chem. Soc. B*, 227 (1966).
19. J.D. Chanly and E.J. Feageson, *J. Am. Chem. Soc.*, **80**, 2686 (1958).
20. J.F. Bunnett, *J. Am. Chem. Soc.*, **83**, 4982 (1961).
21. L. Zucker and P. Hammett, *J. Am. Chem. Soc.*, **61**, 2791 (1932).
22. L.P. Hammett, Physical Organic Chemistry, McGraw-Hill, London, p. 335 (1940).
23. J.F. Bunnett, *J. Am. Chem. Soc.*, **83**, 4956 (1961).
24. J.F. Bunnett and F.P. Olsen, *Can. J. Chem.*, **44**, 1917 (1966).
25. R.D. Gilliom, Introduction to Physical Organic Chemistry, Addision Wesley, pp. 167-169 (1970).
26. M.V. Sharma, *Asian J. Chem.*, **5**, 974 (1993).

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