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ACID CATALYZED HYDROLYSIS OF MONO-2,3-DICHLOROANILINE PHOSPHATE

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The present investigation belongs to study of kinetic behaviour of acid catalyzed hydrolysis of mono-2,3-dichloroaniline phosphate in 0.1-7.0 mol dm^{-3} HCl at $60^{o}C$ in aqueous medium. The log rate profile shows that the rate of reaction increases up to 4.0 mol dm^{-3} HCl. The results show that mono-2,3-dichloroaniline phosphate is reactive mainly via conjugated acid species. Positive salt effect has been exhibited through ionic strength data. Behaviour of molecularity and order of reaction have been estimated by the use of different concepts and hypothesis, such as Hammett acidity function, Zucker-Hammett hypothesis, Bunnett, Bunett-Olsen and Arrhenius parameters. Isokinetic relationship has been applied to propose probable reaction mechanism. Experimental rate coefficients have been found to agree well with theoretical rates in the entire acid range.

KEYWORDS : Hydrolysis, mono-2, 3-dichloroaniline phosphate, molecularity, bond-fission.

INTRODUCTION

Phosphate-containing molecules are essential constituents of all living cells. Phosphate is chemically versatile and can form mono-, di- and tri-esters with alkyl and aryl hydroxyl groups, as well as acid anhydrides. In addition, phosphorus can form P–N (phosphoramidate), P–S (phosphorothioate) and P–C (phosphonate) linkages [1]. Phosphate esters are used as insecticides, fire-resistant hydraulic fluids, fire retardant plasticizers, and in many other applications in agriculture and industry; therefore, they are found throughout the environment and in close contact with humans [2-4]. Phosphate esters have been shown great importance due to their potential bioactivity and significant biological interest [5]. These are used as chemotherapeutic agents as antibacterial, antifungal and antioxidants [6]. Hydrolysis of phosphate esters plays significant role in various biological processes such as biological detoxification, energy and signal transduction, the replication of the genetic material, etc. [7-14]. In the natural environment, hydrolysis is the most common nucleophilic reaction. Depending on the substituents of the molecule and local environmental conditions, these compounds may undergo acid, base, or neutral (general base) hydrolysis [15]. In present investigation the hydrolysis of mono-2, 3-dichloroaniline phosphate has been studied in acidic medium.

EXPERIMENTAL

Mono-2, 3-dichloroaniline phosphate has been synthesized by literature method [16], which involves the reaction of 2, 3-dichloroaniline with phosphorylating agent phosphorus pentaoxide (P_2O_5) in 1 : 1 mole ratio. Hydrolytic reactions of mono-2, 3-dichloroaniline phosphate has been carried out at 60 ± 0.5°C and concentration of ester was kept constant at 5.0×10^{-4} mol dm^{-3}. The progress of kinetics of hydrolysis has been studied by Allen's modified method [17]. The constant ionic strengths have been maintained by using the mixture of HCl and NaCl. First-order rate coefficients have been determined from the first-order rate equation. All the chemicals used were of A. R. grade. HCl was standardized by N/10 sodium tetra borate (Borax) solution. Triple distilled water has been used in all experiments.

RESULTS AND DISCUSSIONS:

Hydrolysis via conjugate acid species

In order to understand the behaviour of mono-2, 3-dichloroaniline phosphate during the hydrolysis *i.e.* involvement of its reactive forms as well as their modes of hydrolysis, kinetic runs were performed in 0.1 to 7.0 mol dm^{-3} HCl at 60°C. The first order rate coefficients obtained are shown in Table 2 and illustrated in Figure 1. From the result it is observed that in acid region rate of hydrolytic reaction increases with increase in acid molarity up to 4.0 mol dm^{-3} HCl and after that decreases. The initial rise in rate in acid media may either be due to complete conversion of substrate in to its conjugate acid species (acid catalyzed reaction). Decrease in rate was attributed to lowering of the concentration of attacking nucleophile in the reaction *i.e.* due to variation in water activity.

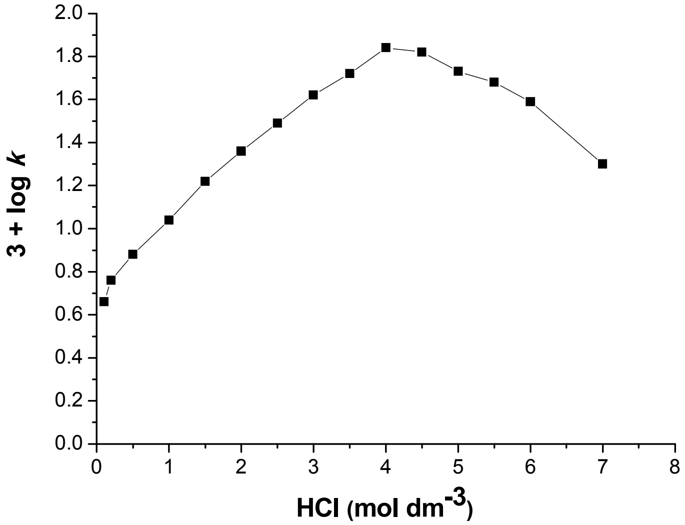


Fig. 1. The plot of 3+log *k* versus HCl mol dm^{-3} for acid catalyzed hydrolysis of mono-2, 3-dichloroaniline phosphate

Kinetic Salt Effect

In order to understand the salt effect kinetic runs were performed at different constant ionic strength using appropriate molarities of hydrochloric acid (HCl) and sodium chloride (NaCl). Plot of rate coefficients of acid hydrolysis and acid molarities is illustrated in Figure 2. Hydrolysis at each ionic strengths (μ) is denoted by six straight lines that make a positive slope with acid axis, hydrolysis is subjected to acid-catalysis. The slope of straight lines increases with increase in ionic strength. Thus acid catalyzed hydrolysis is attributed to positive salt effect. Straight lines meet at different points on rate axis indicate that there is involvement of other species in addition to conjugate acid species. The possibility of neutral species can not be ignored due to the fact that mononegative species can not be reactive at higher concentration more than 1.0 mol dm^{-3}. Linear curves are intercepting the rate axis at different points which show that the contribution of neutral species at different acidities is varying. Specific acid catalyzed rate with their logarithmic values at that ionic strength are summarized in Table 1 and illustrated in Figure 3.

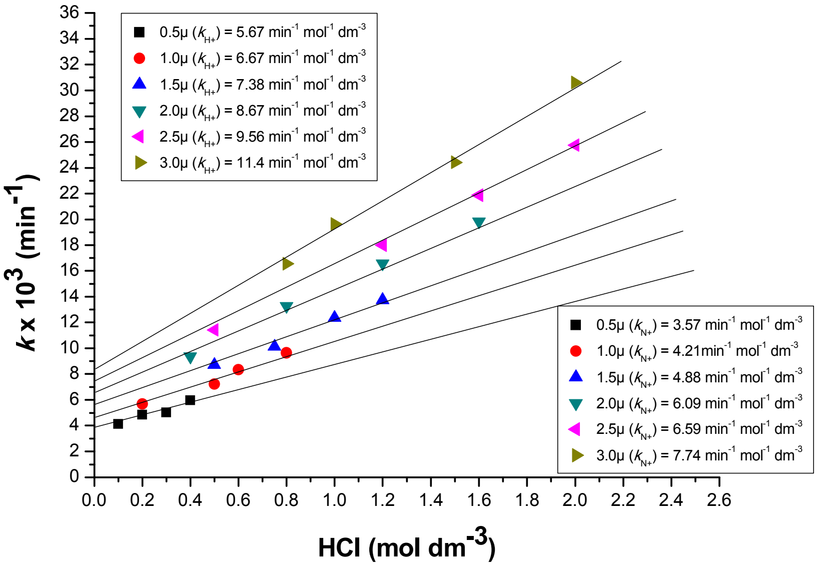


Fig. 2. Acid catalyzed hydrolysis of mono-2,3-dicloroaniline phosphate at constant ionic strength

Table 1. Specific acid catalyzed rates for the hydrolysis of mono-2,3-dichloroaniline phosphate via its conjugate acid and neutral species

Ionic strength (μ)	**$k \times 10^3$ (k_{H^+})**	**3 + log k**	**$k_N \times 10^3$**	**3 + log k**
0.5	5.67	0.55	3.57	0.75
1.0	6.67	0.62	4.21	0.82
1.5	7.38	0.68	4.88	0.86
2.0	8.67	0.78	6.09	0.93
2.5	9.56	0.81	6.59	0.98
3.0	11.3	0.88	7.74	1.05

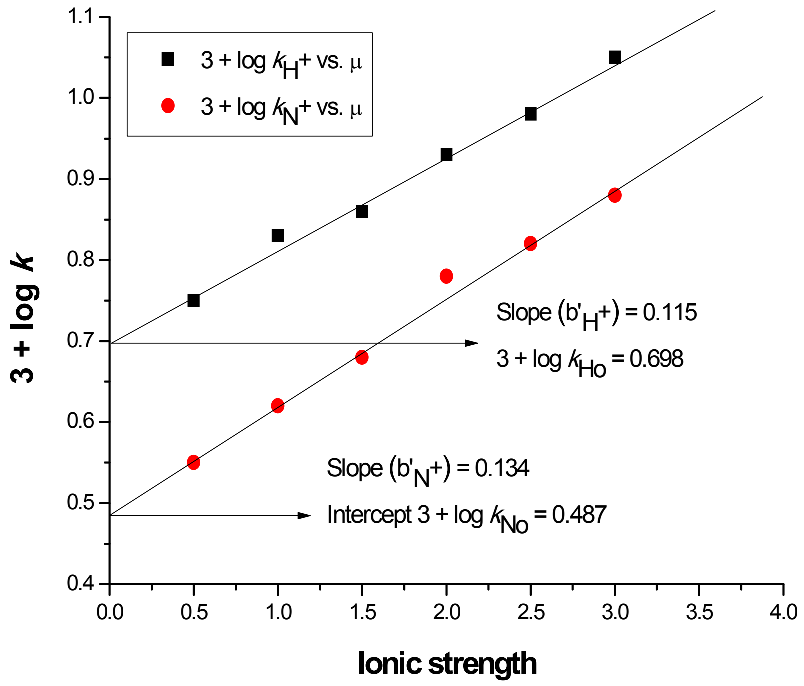


Fig. 3. Plot of 3 + log *k* versus ionic strength (μ) for acid catalyzed hydrolysis of mono-2, 3-dichloroaniline phosphate

The slope of lines represents a constant, b'_{H^+} which is equal to $b'_{H^+}/2.303$ and intercepts on rate axis represent the specific acid catalyzed rate (k_{H^+}). From the study of ionic strength effect, the total rates contributed by conjugate acid and neutral species can be calculated by the following second empirical term of Debye-Huckle equation [18].

$$k = k_{H^+}.C_{H^+} + k_N \qquad \text{... (1)}$$

where k, $k_{H^+}.C_{H^+}$, k_N are observed rate coefficient, specific acid catalyzed rate and specific neutral rate at that ionic strength respectively.

Specific acid catalyzed rate and neutral rate can be represented by following equation:

$$k_{H^+}.C_{H^+} = k_{H_o^+} . \exp . b'_{H^+} . \mu \qquad \text{... (2)}$$

$$k_N = k_{N_0} . \exp . b'_N . \mu \qquad \text{... (3)}$$

Equation 1 was used to determine the calculated rates. Table 2 summarizes both the estimated and experimental rate of the hydrolysis in acid region from 0.1 to 7.0 mol dm^{-3} HCl. The lowering in rate after 4.0 mol dm^{-3} may be due to the lowering in the concentration of water molecules. The rate beyond 4.0 mol dm^{-3} HCl was calculated employing the Bronsted Bjerrum Equation [19].

$$k = k_{H^+}.C_{H^+} (a_{H_2O})^n + k_N . (a_{H_2O})^n \qquad \text{... (4)}$$

Table 2. Estimated and experimental rate data for acid catalyzed hydrolysis of mono-2, 3-dichloroaniline phosphate ester

HCl (mol dm^{-3})	**$k_{H^+}.C_{H^+} \times 10^3$**	**$k_N \times 10^3$**	**$k \times 10^3$**	**$-\log a_{H_2O}$**	**$k \times 10^3$ (Estd.)**	**$k \times 10^3$ (Exp.)**	**3+log*k* (Estd.)**	**3+log*k* (Exp.)**
0.1	0.51	3.14	3.65	-	3.65	4.58	0.56	0.66
0.2	1.05	3.26	4.31	-	4.31	5.73	0.63	0.76
0.5	2.85	3.58	6.43	-	6.43	7.60	0.81	0.88
1.0	6.51	4.18	40.69	-	10.69	11.10	1.02	1.04
1.5	11.15	4.88	16.03	-	16.03	16.81	1.20	1.22
2.0	16.98	5.69	22.67	-	22.67	23.06	1.35	1.36
2.5	24.24	6.65	30.89	-	30.89	31.62	1.49	1.49
3.0	33.22	7.76	40.98	-	40.98	41.52	1.61	1.62
3.5	44.26	9.06	53.32	-	53.32	52.98	1.73	1.72
4.0	57.78	10.5	68.28	-	68.28	69.30	1.83	1.84
4.5	74.07	12.3	86.37	(0.130)	64.18	65.68	1.81	1.82
5.0	94.21	14.4	108.21	$(0.155)^2$	53.19	54.21	1.72	1.73
5.5	118.36	16.81	135.17	$(0.181)^{2.5}$	47.69	48.11	1.68	1.68
6.0	147.47	19.62	167.09	$(0.211)^3$	38.90	39.01	1.59	1.59
7.0	224.44	26.73	251.17	$(0.279)^4$	19.23	20.16	1.28	1.30

where n is an integer and a_{H_2O} is water activity. The estimated rates agree well with the experimentally observed rates. It is clear from the results that hydrolysis of mono-2, 3-dichloroaniline phosphate in acid occurs via both conjugated acid species and neutral species, and their rates are subjected to positive ionic strength or water activity.

Molecularity of the Hydrolytic Reaction:

Zucker-Hammett Hypothesis [20] is made up of two parts, in the first part Hammett postulated [21] that the reactions which give linear plot of log rate constants against acidity function (–Ho) did not involve water molecule in rate determining step (*i.e.* unimolecular hydrolysis). The slope value 0.67 (± 0.02) of the plot (figure not shown) is far from unity, indicating the absence of unimolecular hydrolytic reaction of phosphate ester.

Second part of hypothesis deals with a plot between the log rate constant and log acid molarities. A unit or approximately unit slope of plot was used as a criterion to predict the probable mechanism to be bimolecular, *i.e.* reaction involves the participation of water molecule in the transition state (Scheme 1). The slope value 1.32 (±0.10) clearly shows the bimolecular nature of the reaction (figure not shown).

Bunnett [22] suggested two parameters ω, ω*. The former is the slope of plot between log rate constant + Ho vs. $-\log a_{H_2O}$. The slope value ω = 7.81, ω* = 2.20, and ϕ = 1.38 for Bunnett and Bunnett-Olsen parameters [23] (figure not shown) for mono-2,3-dihloroaniline phosphate also indicate a slow proton transfer with a nucleophilic attack of the water molecule.

Further evidences regarding molecularity and rigidity of transition state with probable mechanism of hydrolysis may be obtained by Arrhenius parameters [24]. Arrhenius parameters were determined for the hydrolysis of mono-2, 3-dichloroaniline phosphate at 3.5 mol dm^{-3} HCl and presented in Table 3. The results favour the bimolecular nature of hydrolytic reaction.

Table 3. Arrhenius plot data for the hydrolysis of mono-2, 3-dichloroaniline phosphate

HCl (mol dm^{-3})	**Parameters**			
	Slope	**E$_a$ kcal mol^{-1}**	**A (s^{-1})**	**-ΔS$^{\neq}$ (e.u.)**
3.5	– 0.031	14.18	1.07×10^8	24.01

Effect of Solvent:

Chemical reactions may be affected by the solvent through several kinds of interactions. Table 4 shows significant rise in rates with increase in percentage of 1,4-dioxane. 1,4-dioxane is regarded as a polar aprotic solvent and being a better proton donor than water. It increases the concentration of conjugated species resulting in the increase in rate. Effect of solvent on rate of the hydrolysis indicates the transition state in which charge is dispersed. This is in accordance with Chanley's observation [25].

Table 4. Solvent effect rate data for acidic hydrolysis of mono-2, 3-dichloroaniline phosphate

HCl (mol dm^{-3})	**% of 1,4-dioxane (v/v)**	**$k \times 10^3$ (min^{-1})**
3.0	20	52.26
	30	59.50
	40	66.63
	50	72.07

Bond Fission:

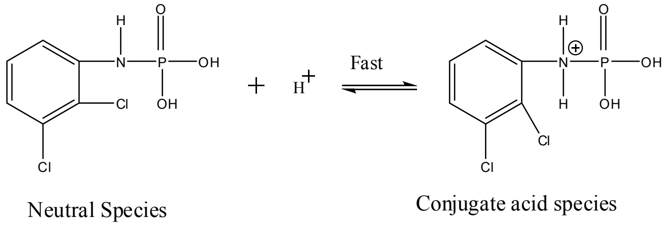
A comparative kinetic rate data for hydrolysis of some phosphate monoesters also support the bimolecular nature of hydrolysis of mono-2,3-dichloroaniline phosphate involving cleavage of P-N bond by attack of water molecule on phosphorus of the monoester is mentioned in Table 5.

Table 5. Comparative kinetic rate data for acidic hydrolysis of some mono-phosphate via conjugate acid species

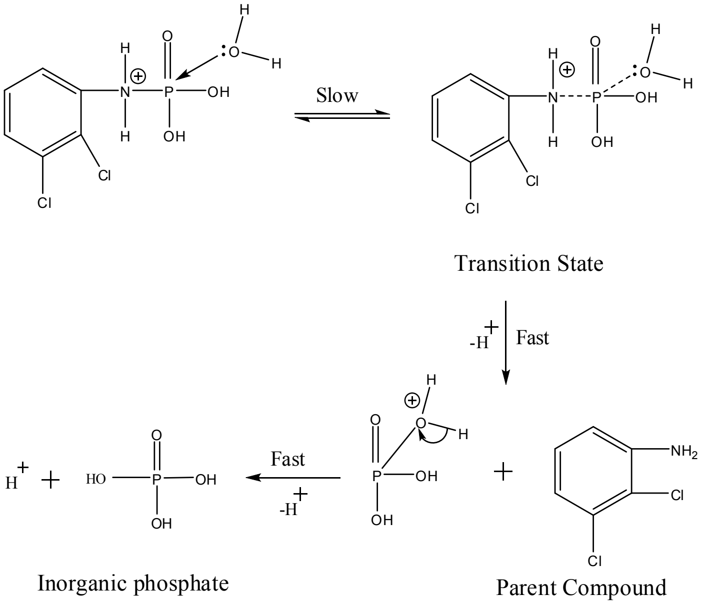
Phosphate monoesters	**T (°C)**	**HCl (mol dm^{-3})**	**E$_a$ (kcal mol^{-1})**	**-ΔS$^{\neq}$ (e.u.)**	**Molecularity**	**Bond fission**
2-chloroaniline	50	3.0	14.60	20.8	2	P–N
2-chloro-5-nitroaniline	60	4.0	13.54	32.6	2	P–N
2-nitro-4-methoxy aniline	60	4.0	6.610	54.8	2	P–N
2,5-dichloro aniline	80	3.0	7.320	53.7	2	P–N
1-nitroso-2-naphthyl	60	3.0	11.39	40.2	2	P–N
N-ethyl-o-toluidine	50	3.0	13.73	23.6	2	P–N
2,3-dichloroaniline	60	3.5	14.18	24.01	2*	Present Work*

Mechanism of hydrolysis:

Scheme 1: Formation of conjugate acid species by fast pre-equilibrium proton transfer



Scheme 2: Bimolecular nucleophilic attack of water on phosphorous atom of conjugate acid species



CONCLUSIONS

Acid catalyzed hydrolysis of mono-2,3-dichloroaniline phosphate in 0.1-7.0 mol dm^{-3} was found to proceed via neutral and conjugate acid species. The acid catalyzed hydrolysis is subjected to the positive salt effect of ionic strength. Bimolecular nature of hydrolysis was supported by different concepts and hypothesis such as Hammett, Zucker Hammatt, and Bunnett, Bunnett Olsen. Arrhenius parameters also supported the bimolecular nature of reaction. Isokinetic relationship plot supported the P-N bond fission. S_N^2 (P) mechanism was suggested for the hydrolysis via conjugate acid species.

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