HYDROLYSIS OF DI-3-CHLORO-2-METHYLANILINE PHOSPHATE IN BUFFER MEDIUM

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Kinetic study of the hydrolysis of di-3-chloro-2-methylaniline phosphate has been investigated in the range of pH 0.00 to 7.60 at 80 ± 0.5^{o}C in 40% (v/v) dioxane-water medium. The pH log rate profile has a rate maximum at pH 4.11. Hydrolysis of diester carried out in buffer solution shows that neutral and mononegative species are reactive in the range of pH 0.00 to 2.23 and only mononegative species in the range of pH 2.23 to 7.60 respectively. The theoretical rate determined from specific rates and fractions of the neutral and mononegative species agree closely with the experimental rates. Bimolecular nature of hydrolytic reaction has been supported on the basis of temperature and solvent effect study. Di-3-chloro-2-methylanline phosphate involves P-N bond fission, which is strengthened by isokinetic relationship. Probable reaction mechanism has been proposed for the hydrolysis of di-ester *via* its neutral and mononegative species.

KEYWORDS : Hydrolysis, Di-3-chloro-2-methyl aniline phosphate, P-N bond fission Neutral and Mononegative species.

INTRODUCTION

Phosphorus is one of the most abundant elements on earth. Phosphorus has a broad role in living systems, and so the reactions of phosphate esters in solution and in enzyme are of the great importance [1]. Most of the phosphorus in living system exists in the form of phosphate. It is part of many essential biological components such as lipids, bones, genetic materials, energy rich molecules (*e.g.* – ATP) and signaling molecules (*e.g.* – GTP) [2]. Phosphate esters are very essential in life processes [3], in living organism for growth, development and maintenance of plants and animals. Phosphate esters have wide range of applications in the areas of industrial, agricultural and medicinal chemistry owing to their biological and physical properties, as well as their utility as synthetic intermediates [4]. These esters are important surfactants, which are widely used in many fields, such as chemical fibers, daily chemical products, plastic and paper-making [5]. These are also used as additives in the textile and clothing dyeing industry. The extreme toxicity, broad-spectrum activity and low cost of organophosphorus compounds have made them popular as pesticides, insecticides, bactericides and antibiotics [6, 7]. The hydrolysis of phosphate esters is one of the most fundamental chemical and biochemical reactions. The mechanisms of hydrolysis of phosphate diesters are of great interest because phosphate diester linkage is highly stable toward

solvolytic cleavage and is widely utilized throughout the nature [8]. Hydrolysis of phosphate ester is ubiquitous in biology, being involved in protein synthesis, energy transduction, and the replication of genetic material [9]. Therefore, phosphate esters have been the subject of extensive experimental [10] and theoretical [11] studies.

EXPERIMENTAL

Di-3-chloro-2-methyl aniline phosphate was synthesized by the method of Rudert [12] in our laboratory, which involves the reaction of 3-chloro-2-methyl aniline with phosphorylating agent phosphorus oxychloride in 2 : 1 mol ratio in solvent benzene. All reactions were carried out at 80^0C employing 5.0×10^{-4} mol dm^{-3} concentration of the di-ester in 40% (v/v) dioxane-water medium. Buffer solutions were prepared using appropriate mixture of KCl, $COOH.C_6H_4.COOK$, NaOH and H_3BO_3 [13]. The progress of the hydrolysis of di-3-chloro-2-methyl aniline phosphate was followed by estimation of inorganic phosphate, using Allen's modified method [14] spectrophotometrically. All the chemicals used were of A.R. grade. All the solutions were prepared in triple distilled water.

RESULT AND DISCUSSION

Hydrolysis via neutral and mononegative species : The kinetics of the hydrolysis of di-3-chloro-2-methylaniline phosphate was studied in the range of pH 0.00 to 7.60 in 40% (v/v) dioxane-water medium at 80^oC. Figure.1 shows the pH log rate profile in which theoretical rates closely agreed with those experimental rates.
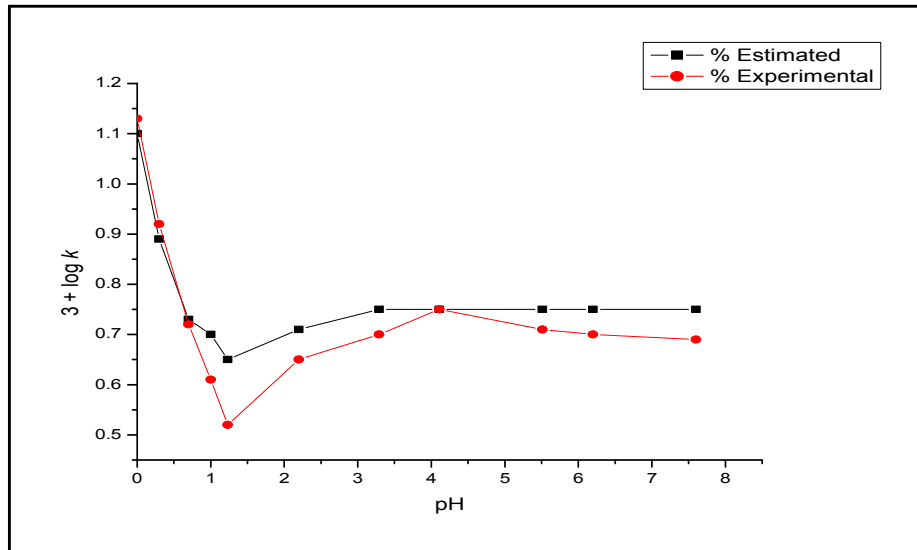

Fig. 1. pH log rate profile for the hydrolysis of di-3-chloro-2-methylaniline phosphate

In this pH range the hydrolysis of di-3-chloro-2-methyl aniline phosphate has been found to be governed by two reactive species namely neutral and mononegative species. Both species are participating in hydrolysis but the reactive nature of neutral species decreases due to its conversion into mononegative species. The appearance of mononegative species starts at pH 0.00 and attains maximum value at pH 4.11. The hydrolysis at the latter pH range has been

found to be exclusively governed by mononegative species. The rise in higher pH range (more than 1.00 pH) is due to the incursion of more reactive mononegative species while the rise in rate in low pH range (less than 1.00 pH) is attributed to incursion of neutral and conjugate species. Similar nature of hydrolysis has been observed in the case of di-2-methoxy-4-nitroaniline phosphate [15]. Neutral and mononegative rates may be represented as:

$$k_N = k_{No} \frac{N}{N+M} \qquad \qquad \text{... (1)}$$

$$k_M = k_{Mo} \frac{M}{M+N} \qquad \qquad \text{... (2)}$$

where k_{No} is specific neutral rate, k_{Mo} (specific mononegative rate) is experimental rate at pH 4.11 and $N/N + M$ and $M/M + N$ are the fraction of neutral and mononegative species respectively. The value of specific neutral rate i.e. k_{No} were determined from the reaction:

$$k = k_{Mo} \frac{M}{M+N} + k_{No} \frac{N}{N+M} + k_H^+ . C_H^+ \qquad \qquad \text{... (3)}$$

where, k is experimental rate. There is good agreement between values of specific neutral rate k_{No} determined by equation (3) is 3.26×10^{-3} min^{-1} at different pH 0.00 to 1.00 & from ionic strength data is 2.80×10^{-3} min^{-1}.

Hydrolysis via mononegative species : Mono and diester are known to dissociate almost complete at pH 4.11, thus in the range of pH 4.11 to 7.60 mononegative species of diesters are reactive. Since they are not further converted into dinegative species as mononegative species of the monoester do, their concentration remains constant. As the mononegative rates are directly proportional to the concentration of their ions, the experimental rate of hydrolysis in this range is expected to be constant. The experimental rates (pH log rate profile Figure 1) also show consistency of rate of hydrolysis of di ester. A slight elevation in rate at pH 5.51 may be attributed to incursion of more nucleophilic hydroxide ion than water molecules. Similar observation has also been made for the hydrolysis of di-phenyl phosphate and di-p-chloro phenyl phosphate [16]. It is clear from table-1 that in the range of pH 0.00 to 1.00 hydrolysis governs by neutral, conjugate and mononegative species. In the range of pH 1.00 to 1.23, the reactions are via neutral and mononegative species. In the range of pH 1.23 to 7.60, only mononegative species are reactive.

Kinetic rate laws for the hydrolysis of di-3-chloro-2-methylaniline phosphate may be represented as:

In the range of pH 0.00 to 1.00

$$k = k_H^+ . C_H^+ + 5.62 \times 10^{-3} \frac{M}{M+N} + 3.26 \times 10^{-3} \frac{N}{N+M} \qquad \qquad \text{... (4)}$$

In the range of pH 1.00 to 1.23

$$k = 5.62 \times 10^{-3} \frac{M}{M+N} + 3.26 \times 10^{-3} \frac{N}{N+M} \qquad \qquad \text{... (5)}$$

In the range of pH 1.23 to 7.60

$$k_N = 5.62 \times 10^{-3} \frac{M}{M+N} \qquad \qquad \text{... (6)}$$

**Table 1- Estimated and experimental rates for the hydrolysis of di-3-chloro-2
methylaniline phosphate via neutral and mononegative species**

pH	$M/(M+N)$	$N/(N+M)$	$k_M \times 10^3$ (min⁻¹)	$k_N \times 10^3$ (min⁻¹)	$k_H^+C_H^+ \times 10^3$ (min⁻¹)	$K \times 10^3$ (min⁻¹) Estd.	$K \times 10^3$ (min⁻¹) Expt.	$3 + \log k$ Estd.	$3 + \log k$ Expt.
0.00	0.06	0.94	0.34	3.06	9.20	12.60	13.35	1.10	1.13
0.30	0.12	0.88	0.67	2.87	4.14	7.68	8.41	0.89	0.92
0.70	0.25	0.75	1.41	2.45	1.56	5.42	5.28	0.73	0.72
1.00	0.40	0.60	2.25	1.96	0.76	4.97	4.12	0.70	0.61
1.23	0.54	0.45	3.03	1.47	-	4.50	3.34	0.65	0.52
2.20	0.92	0.09	5.17	0.29	-	5.17	4.51	0.71	0.65
3.29	0.99	0.01	5.56	0.03	-	5.56	5.02	0.75	0.70
4.11	1.00	0.00	5.62	-	-	5.62	5.62	0.75	0.75
5.51	1.00	-	5.62	-	-	5.62	5.12	0.75	0.71
6.20	1.00	-	5.62	-	-	5.62	5.05	0.75	0.70
7.60	1.00	-	5.62	-	-	5.62	4.91	0.75	0.69

Solvent effect : Most chemical reactions are carried out in solution. Solvent play an important role in determining chemical reactivity. The rate of an elementary chemical reaction may change by order of magnitude when the solvent is changed. Kinetic solvent effects on chemical reactions in different media are usually correlated in terms of "solvent polarity", which sums up all the specific and non-specific interactions of the media with initial and transition state [17-19]. According to Chanley's observation [20], effect 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. Table-2 shows a significant rise in rates with increase in dioxane percentage.

Table 2. Rate of the hydrolysis of di-3-chloro-2-methylaniline phosphate *via* neutral and mononegative species.

pH	Dioxane (%) V/V	$k \times 10^3$ (min⁻¹)	pH	Dioxane (%) V/V	$k \times 10^3$ (min⁻¹)
1.23	40	3.34	4.11	40	5.62
	45	3.97		45	6.12
	50	4.45		50	6.96
	55	5.06		55	7.64
	60	5.89		60	8.22

Temperature effect : The effect of temperature gives valuable information about the energy requirements of reaction. In order to determine the Arrhenius parameters, kinetic runs were carried out at different temperature in pH 1.23 and pH 4.11. Prediction of the molecularity of the reaction may be made by determining Arrhenius parameters. Figure-2 describes the Arrhenius plot between log rate coefficients and reciprocal of the absolute temperature. Linearity of the plot shows the validity of Arrhenius equation for the temperature range used. Arrhenius parameters for hydrolysis *via* neutral and mononegative species summarized in Table-3 are in favour of a bimolecular reaction [21].
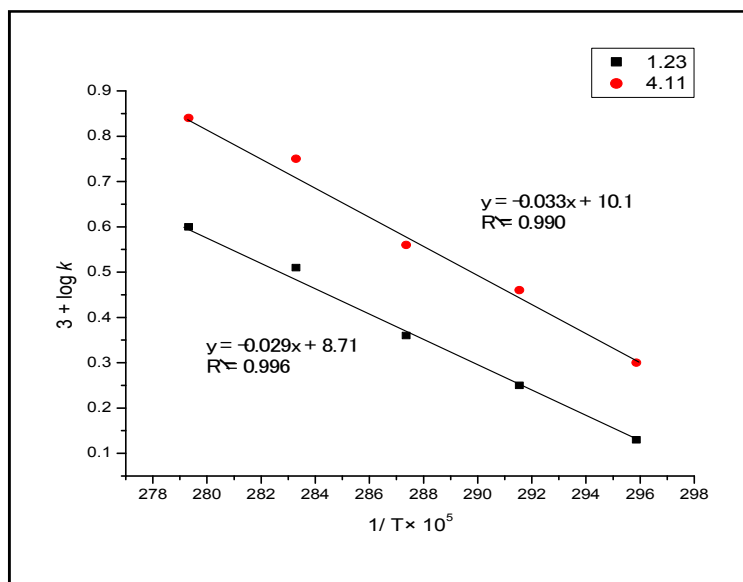
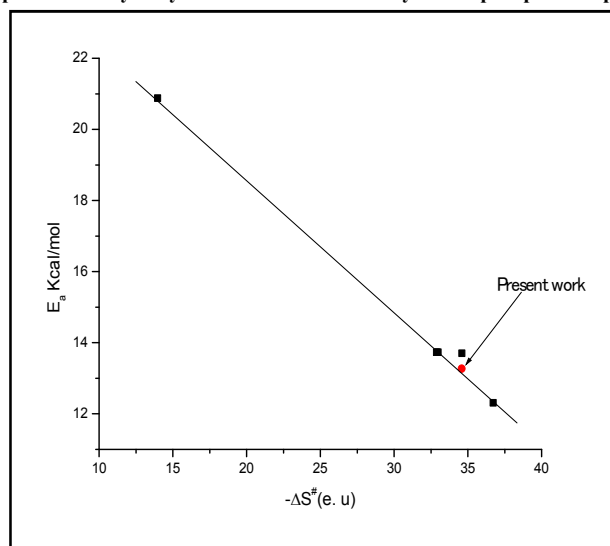**Fig. 2. Arrhenius plot for the hydrolysis of di-3-chloro-2-methyaniline phosphate at pH 1.23 and pH 4.11**

Fig. 3. Isokinetic relationship plot for the hydrolysis of some phosphate diesters *via* their neutral species

Table 3. Arrhenius parameters for the hydrolysis of di-3chloro-2-methylaniline phosphate *via* neutral & mononegative species

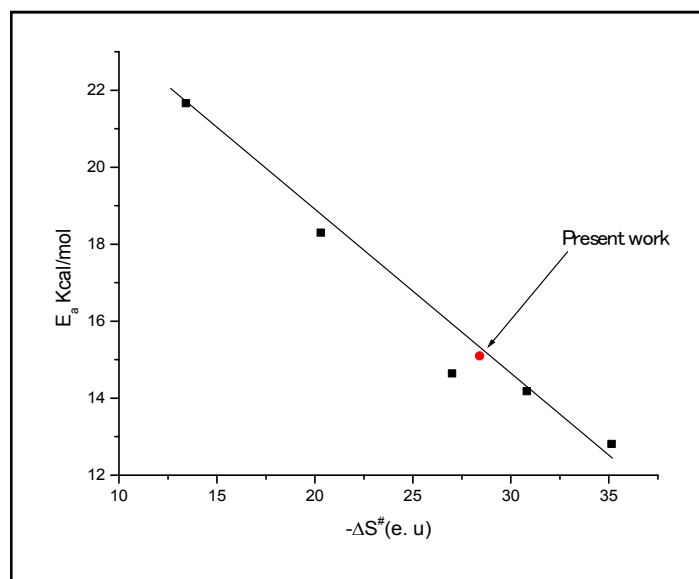| pH	Slope	Parameters		
		E (kcal mol^{-1})	A (sec^{-1})	$-\Delta S^{\neq}$ (e.u.)
1.23	-0.029	13.27	5.58×10^5	34.59
4.11	-0.033	15.10	1.25×10^7	28.40

Fig. 4. Isokinetic relationship plot for the hydrolysis of some phosphate via their neutral species

Di-3-chloro-2-methylaniline phosphate may undergo hydrolysis either by P-N or C-N bond fission Table-4 and 5 summarizes comparative kinetic rate data [22-26] for the hydrolysis of other diesters. The point of di-3-chloro-2-methylaniline phosphate lies on the linear curve of those diesters which are known to undergo hydrolysis *via* P-N bond fission (figure 3 & figure 4). Thus P-N rather than C-N bond fission appears to be more probable. The probable reaction mechanism for the hydrolysis of mononegative and neutral species of di-3-chloro-2-methylaniline phosphate may be suggested as shown in chart-1 & chart-2.

Table 4. Comparative kinetic rate data for the hydrolysis of some phosphate diester *via* their neutral species

Diesters	pH	E (Kcal/mol)	$-\Delta S^{\neq}$ (e.u.)	Molecularity	Bond fission
o-toluidine	1.24	12.31	36.72	2	P-N
m-toluidine	1.24	13.73	32.88	2	P-N
2-methyl-5-nitroaniline	1.24	13.73	32.99	2	P-N
Naphthyl amine	1.24	20.88	13.97	2	P-N
2-chloroaniline	1.24	13.70	34.60	2	P-N
3-chloro-2-methylaniline	1.23	13.27	34.59	2*	Present Work

Table 5. Comparative kinetic rate data for the hydrolysis of some phosphate diester *via* their mononegative species

Diesters	pH	E (Kcal/mol)	$-\Delta S^{\neq}$ (e.u.)	Molecularity	Bond fission
Naphthylamine	4.17	21.66	13.42	2	P-N
m-toluidine	4.17	14.18	30.81	2	P-N

2-methoxy-4-nitroaniline	4.17	14.64	27.00	2	P-N
2-chloroaniline	4.17	18.30	20.30	2	P-N
2-methyl-5-nitroaniline	4.17	12.81	35.14	2	P-N
3-chloro-2-methylaniline	4.11	15.10	28.41	2*	Present Work

Chart-1: The mechanism of hydrolysis via neutral species: Bimolecular attack of water on phosphorur of the neutral species S_N^2
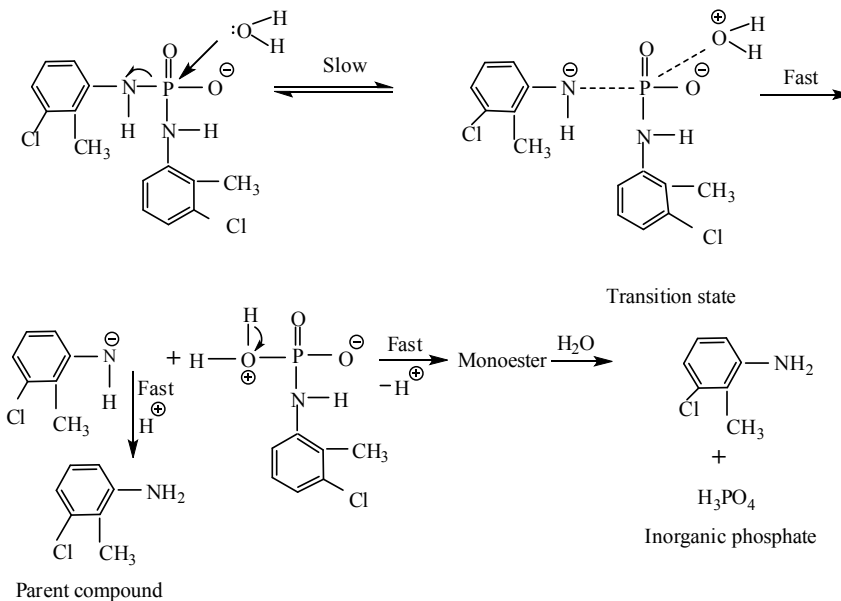

Transition state

Parent compound
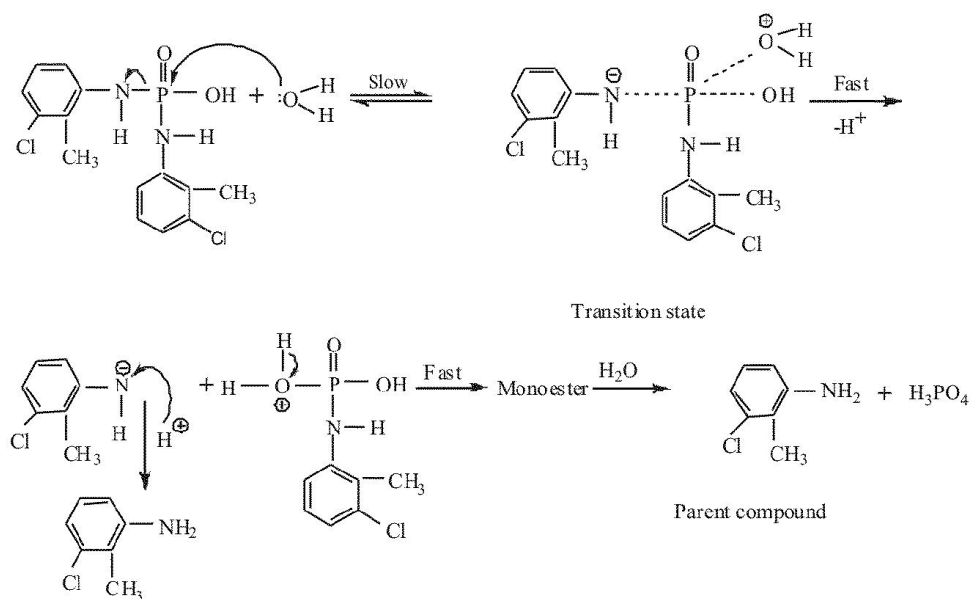
Chart-2: The mechanism of hydrolysis via mononegative species:

(a) Formation of mononegative species

Neutral species

Mononegative species
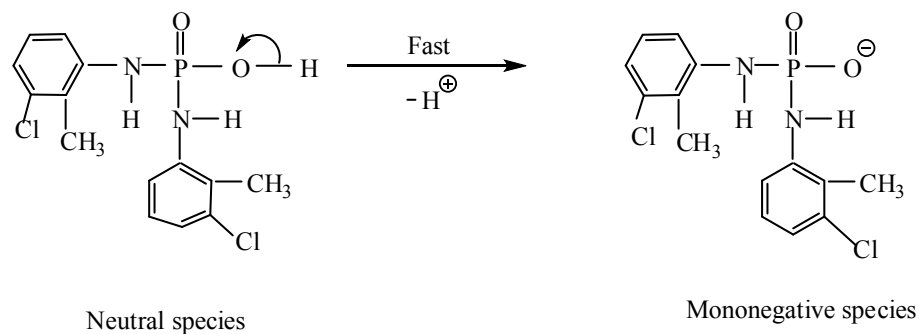
(b) Bimolecular nucleophilic attack of water on phosphorous of mononegative species S_N^2 (P)

Transition state

Parent compound

Monoester

Inorganic phosphate

CONCLUSION

Di-3-chloro-2-methylaniline phosphate in range of pH 1.00 to 8.04 was found to hydrolyze *via* neutral and mononegative species. The maximum value at pH 4.11 is due to hydrolysis *via* mononegative and neutral species. The pH log rate profile shows that the estimated rates closely agreed well with those experimental rates. Bimolecular nature of hydrolytic reactions has been supported by Arrhenius parameters. The diester involves P-N bond fission, which is strengthened by comparative kinetic rate data.

ACKNOWLEDGMENT

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