

Kinetic Study of Hydrolysis of Mono-2-methyl- 5-Nitroaniline phosphate

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Abstract: Kinetic study of the acid-catalyzed hydrolysis of mono-2-methyl-5-nitroaniline phosphate has been studied in 0.1-7.0 mol dm⁻³ hydrochloric acid at 50°C in aqueous medium. In the presence of acid, the rate constant increased with increasing acidity up to 4 mol dm⁻³. Neutral and conjugate acid species have been found to be reactive and contribute to the overall hydrolysis in the acid region. Ionic strength data show the positive salt effect. The effects of temperature, solvent and substrate concentration on the rate of hydrolysis have been studied. The results suggest that the hydrolysis of monoester occurs by the cleavage of P-N bond.

Keywords: kinetics; ionic strength; solvent; bond fission.

INTRODUCTION

Organic phosphates are very important, due to their wide range of applications in various branches of chemistry. Organophosphorous compounds play a key role in life processes¹, in living organism for growth, development and maintenance of all plants² and animals³. Phosphate monoesters are intermediates in a variety of metabolic pathways⁴. Phosphate tri-esters are more reactive than the corresponding mono- and di-esters and do not participate in living organism as metabolites⁵. Organophosphorous compounds are widely used as pesticides⁶, insecticides⁷, chemical warfare agents⁸, fire retardants⁹, smoke generation¹⁰, additives for petroleum and corrosion inhibitors¹¹, selective extractants for metal salts from ores¹¹. Cyclic amine phosphate in combination with phosphoramidic acid and sulfa drugs are very important for their pharmaceutical and medicinal value¹² and as cancer chemotherapeutic agents¹³.

EXPERIMENTAL

Mono-2-methyl-5-nitroaniline phosphate has been synthesized by the literature method in our laboratory¹⁴. The method involves the reaction of 2-

methyl-5-nitroaniline and phosphorous pentoxide in 1:1 mol ratio. The solid mass obtained was separated and water soluble part was precipitate out using Ba(OH)₂ solution. Thus the Barium salt of monoester obtained as white solid was washed several times with distilled water with few drops of acetic acid to remove inorganic phosphate. All the chemicals used were of A.R. grade and all solutions have been prepared in triply distilled water. The confirmation of compound was done by comparing theoretical and observed percentage of elements and by recording IR spectrum as shown below:

a) Elemental analysis

C, Theoretical = 22.86 %

Observed = 21.72 %

H, Theoretical = 1.91 %

Observed = 2.21 %

N, Theoretical = 7.62 %

Observed = 7.12 %

b) IR absorption spectra

The spectrum of mono-2-methyl-5-nitroaniline phosphate was recorded by FTIR Model 136 Shimadzu.

ν (KBr) cm^{-1} : 3325(O-H); 3195(N-H); 2875(C=C); 1131(P=O); 724(P-N)

Hydrolysis of mono-2-methyl-5-nitroaniline phosphate has been carried out at 50°C employing 5.0×10^{-4} mol

dm^{-3} solution in aqueous medium. The progress of the kinetic study has been carried out by Allen's modified method¹⁵, using spectrophotometer at 735 nm. The constant ionic strength has been maintained by using mixtures of HCl and NaCl. Pseudo-first-order rate constants have been derived from the first-order rate equation.

Table – 1: Estimated & experimental rates of hydrolysis of Mono-2-methyl-5-nitroaniline phosphate at 50°C

HCl (mol dm^{-3})	$k_{\text{H}^+} \cdot \text{C}_{\text{H}^+} 10^3$ (min^{-1})	$k_{\text{N}} 10^3$ (min^{-1})	$k 10^3$ (min^{-1})	$-\log (a_{\text{H}_2\text{O}})^n$	$k 10^3$ (min^{-1}) Estd.	$k 10^3$ (min^{-1}) Expt.	4+log k Estd.	4+log k Expt.
0.1	1.09	1.30	2.39	-	2.39	5.12	1.38	1.71
0.2	2.24	1.37	3.61		3.61	5.87	1.56	1.77
0.5	6.59	1.62	8.21		8.21	9.33	1.91	1.97
1.0	13.2	2.14	15.3		15.3	16.6	2.19	2.22
2.0	33.1	3.72	36.8		36.8	36.2	2.57	2.56
3.0	60.3	6.76	66.7		66.7	66.3	2.82	2.82
4.0	98.2	11.2	109.4		109.4	109.7 112.3 ^a 115.5 ^a 118.0 ^c	3.04	3.04
5.0	151.0	19.5	170.5	$(0.155)^2$	83.5	94.7	2.92	2.98
6.0	222.9	33.9	256.8	$(0.211)^3$	59.8	62.5	2.78	2.80
7.0	319.9	58.9	378.8	$(0.279)^4$	29.0	32.9	2.46	2.51

Note -: a = 10 % dioxane, b = 20 % dioxane, c = 30% dioxane

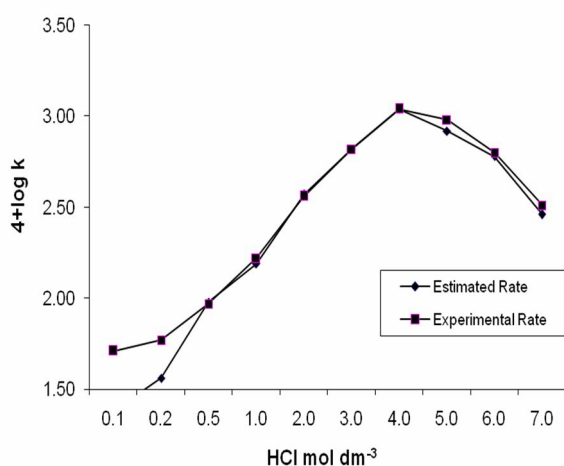
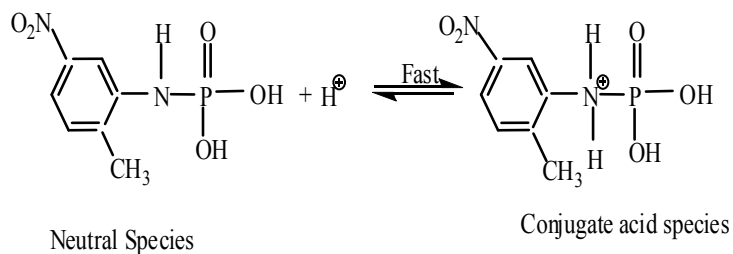
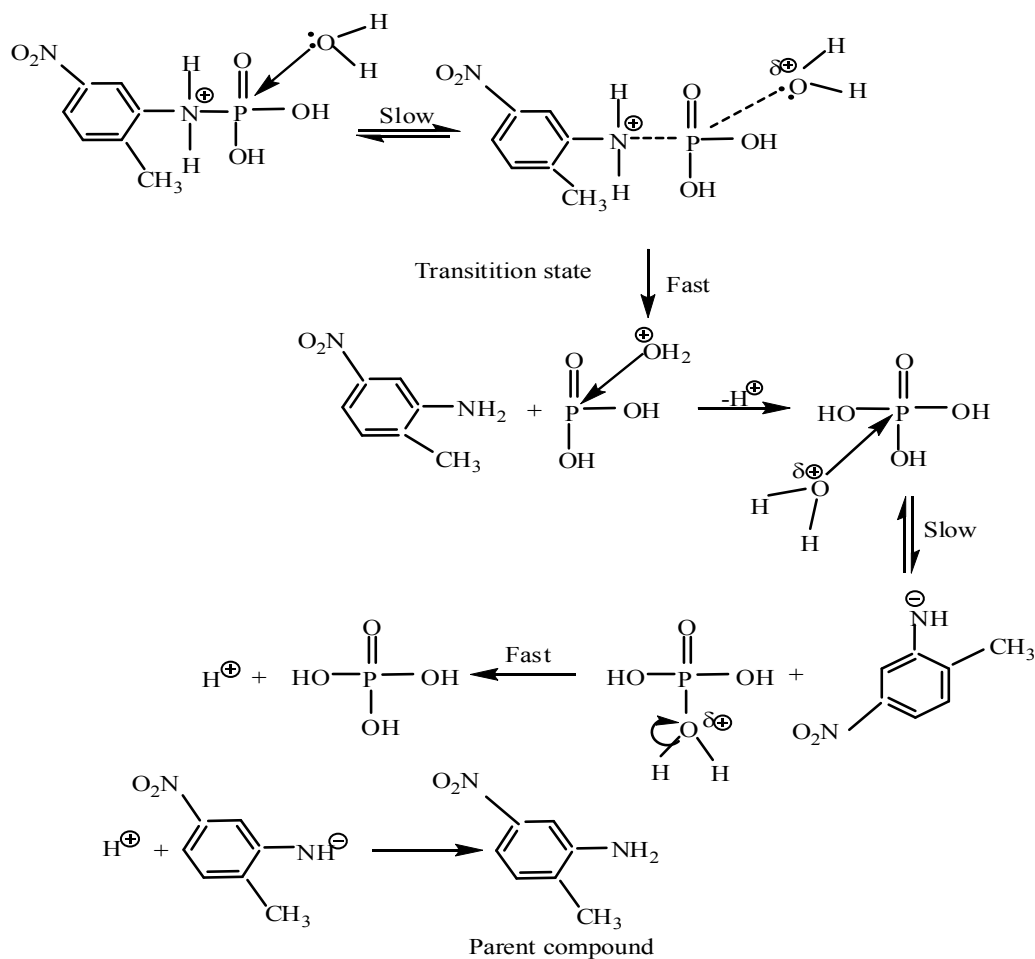


Fig 1: Acid log rate profile for the hydrolysis of Mono-2-methyl-5-nitroaniline phosphate at 50°C

Chart – 1- Mechanism of hydrolysis-**(a) Formation of conjugate acid species by fast pre-equilibrium proton transfer****Scheme I****(b) Bimolecular nucleophilic attack of water on phosphorous via conjugate acid species S_N^2** **Scheme II**

RESULTS AND DISCUSSION

The kinetics of the hydrolysis of mono-2-methyl-5-nitroaniline phosphate has been studied in 0.1-7.0 mol dm⁻³ hydrochloric acid at 50°C. Pseudo-first-order-rate constant have been obtained at several hydrochloric acid concentrations which are summarized in Table-1 and illustrated in **Figure-1**. From the results, it may be seen that the rate of hydrolysis increases with the increase in acid molarity up to 4.0 mol dm⁻³ hydrochloric acid. The maximum rate at 4.0 mol dm⁻³ hydrochloric acid has been attributed to complete conversion of the substrate into its conjugate acid species as described in **Scheme I**.

After complete conversion of the protonated species, rate should remain constant but it further decreases with the increase in acid molarity. The decrease in the rate is attributed to the lowering of concentration of attacking nucleophile taking part in the reaction, i.e., due to variations in water activity. Therefore rate maxima may be due to maximum protonation or due to effect of ionic acceleration or due to water activity.

Kinetic salt effect has been studied at different ionic strengths 1.0, 2.0 and 3.0μ, using appropriate mixtures of NaCl and HCl. Figure-2 describes a plot between rate coefficients and acid molarity. Three linear plots are obtained and each represents the kinetics at that ionic strength. Since each linear curve makes the positive slope with the acid axis, hydrolysis is subjected to acid catalysis at each ionic strength. The slopes of straight lines increased with the increase in ionic strength. Hence, acid catalysis is subjected to the positive salt effect. These lines meet at different points on rate axis indicating the participation of neutral species as described in **Scheme I**. The constant values of intercepts show the constant contribution of neutral species. Neutral and conjugate acid-catalyzed rates have been shown to be related with the ionic strength by second empirical term of Debye-Huckel equation¹⁶.

$$k_{H^+} = k_{H_0^+} \cdot \exp. b'_{H^+} \cdot \mu \quad \dots \dots (1)$$

Where, k_{H^+} , $k_{H_0^+}$, b'_{H^+} and μ are specific acid catalysed rates at that ionic strength, specific acid catalysed rate at zero ionic strength, a constant and ionic strength respectively.

Specific acid catalysed rates can be converted into acid catalysed rates.

$$k_{H^+} \cdot C_{H^+} = k_{H_0^+} \cdot C_{H^+} \cdot \exp. b'_{H^+} \cdot \mu \dots \dots (2)$$

$$\log k_{H^+} \cdot C_{H^+} = \log k_{H_0^+} + \log C_{H^+} + b'_{H^+} \cdot \mu \dots \dots (3)$$

Where, for HCl, μ and C_{H^+} are of same value.

Figure-3 shows the specific acid catalysed rates with their logarithmic values at that ionic strength. The slope value of linear curve is b'_{H^+} which is equal to $b'_{H^+}/2.303$ and intercepts on the log rate axis represents $3 + \log k_{H_0^+}$. Its value in mono-2-methyl-5-nitroaniline phosphate is as:

$$3 + \log k_{H_0^+} = 1.03$$

The neutral rate may be represented by the following equation:

$$k_N = k_{N_0} \cdot \exp. b'_N \cdot \mu \dots \dots (4)$$

$$\log k_N = \log k_{N_0} + b'_N \cdot \mu \dots \dots (5)$$

Where, b'_N is equal to $b'_N/2.303$ and the intercept on log neutral rate axis is equal to $3 + \log k_{N_0}$. Its value in mono-2-methyl-5-nitroaniline phosphate is as:

$$3 + \log k_{N_0} = 0.09$$

The overall hydrolysis has been represented by the equation:

$$k = k_{H^+} \cdot C_{H^+} + k_N \dots \dots (6)$$

The equation (6) can be used to estimate theoretical rates which are then compared with the experimental rates.

It is seen that there is good agreement between the estimated and experimental rates up to 4.0 mol HCl. However, there is disagreement in rates of 5.0, 6.0 and 7.0 mol HCl, which has been found to be owing to the incursion of water activities and can be represented by following equation:

$$k_{H^+} \cdot C_{H^+} = k_{H_0^+} \cdot C_{H^+} \cdot \exp. b'_{H^+} \cdot \mu (a_{H_2O})^n C \dots \dots (7)$$

$$\log k_{H^+} \cdot C_{H^+} = \log k_{H_0^+} + \log C_{H^+} + b'_{H^+} \cdot \mu + n \log a_{H_2O} \dots \dots (8)$$

And neutral rate at higher concentration is as follows:

$$k_N = k_{N_0} \cdot \exp. b'_N \cdot \mu (a_{H_2O})^n C \dots \dots (9)$$

$$\log k_N = \log k_{N_0} + b'_N \cdot \mu + n \log a_{H_2O} \dots \dots (10)$$

Where water activity and n is an integer which increases with increase in acidity. Hence, complete rate of hydrolysis can be represented at higher acidity by following equation:

$$k = k_{H_0^+} \cdot C_{H^+} \cdot \exp. b'_{H^+} \cdot \mu (a_{H_2O})^n + k_{N_0} \cdot \exp. b'_N \cdot \mu (a_{H_2O})^n \dots \dots (11)$$

Where n is an integer and $a_{\text{H}_2\text{O}}$ is water activity. The revised estimated rates agree well with the experimentally observed rates (**Table-1**). It has been clear from the above results that hydrolysis of mono-2-methyl-5-nitroaniline phosphate ester in acid solution occurs via both conjugate acid and neutral species and their rates are subjected to ionic strength or 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 rates. Effect on the rate of hydrolysis may, therefore, be taken to indicate the formation of transition state in which charge is dispersed; this is accordance with Chanley's observation¹⁸.

Table- 2: Arrhenius parameters for hydrolysis of Mono-2-methyl-5-nitroaniline phosphate

HCl (mol dm ⁻³)	E (Kcal/mole)	A (sec ⁻¹)	- ΔS^\ddagger (e.u.)
3.00	14.64	8.95 X 10 ⁶	20.76
5.00	13.73	3.10 X 10 ⁶	22.87

Table-3: Comparative kinetic rate data for the hydrolysis of some phosphate monoester via their conjugate acid species

S.No.	Phosphate Monoester	HCl (mol dm ⁻³)	E (Kcal mol ⁻¹)	- ΔS^\ddagger (e.u.)	Bond fission	Molecularity
1	2-chloro-5-nitro aniline	4.0	13.54	32.65	P-N	2
2	1-nitroso-2-naphthyl	3.0	11.39	40.25	P-N	2
3	2-methyl-5-nitroaniline	3.0	14.64	20.76	P-N	Present work
4	2-methyl-5-nitroaniline	4.0	13.73	22.87	P-N	Present work
5	Diethyl amine	4.0	6.61	60.65	P-N	2
6	p-nitro aniline	3.0	15.25	9.5	P-N	2

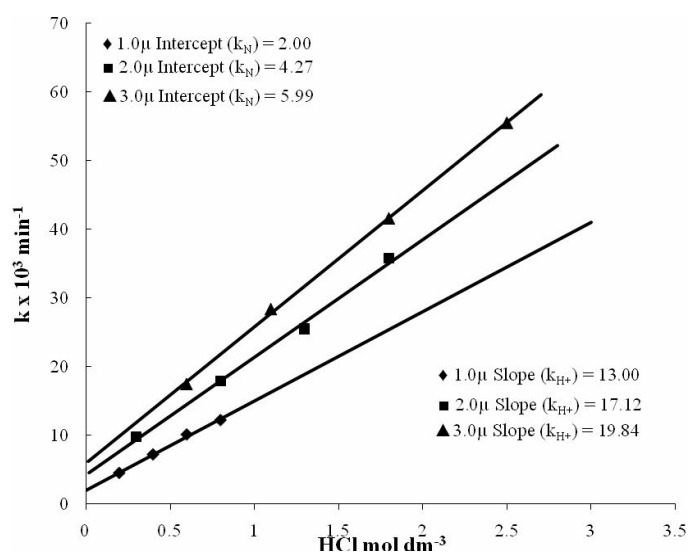


Fig 2: Acid catalyzed hydrolysis of Mono-2-methyl-5-nitroaniline phosphate at constant ionic strength at 50°C

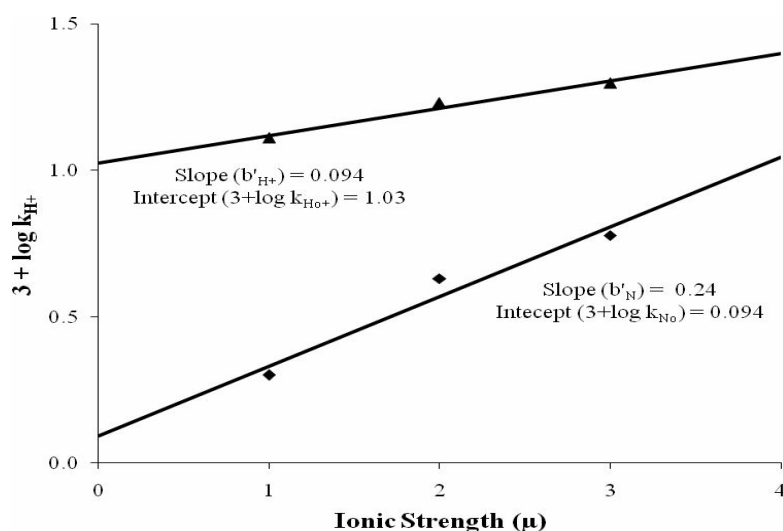


Fig 3: Acid catalyzed hydrolysis of Mono-2-methyl-5-nitroaniline phosphate at constant ionic strength at 50°C (Log specific rate Vs Ionic strength)

Arrhenius parameters are determined for the hydrolysis at 3.0 and 5.0 mol dm⁻³ HCl (**Table-2**).

The magnitude of the Arrhenius parameters falls in the range of bimolecular reaction¹⁹. Bimolecular nature of reaction is further supported by plots of Hammett²⁰ (0.69), Zucker-Hammett²¹ (1.35) & Bunnett²² ($w = 7.68$, $w^* = 2.09$). Bunnett-olsen²³ parameter ($\phi = 1.27$ which is greater than 0.58) (plots not shown) suggested that water involved as a proton transfer agent in the rate determining step.

The effect of concentration of monoester on the rate of hydrolysis also confirms the order of reaction²⁴ to be one with respect to the monoester by reducing half ($k = 109.12 \times 10^{-3} \text{ min}^{-1}$) or double ($k = 110.28 \times 10^{-3}$

min^{-1}) the normal concentration ($k = 109.74 \times 10^{-3} \text{ min}^{-1}$) at 4.0 mol dm⁻³ HCl.

Mono-2-methyl-5-nitroaniline phosphate may undergo hydrolysis either by P-N or C-N bond fission. Table-3 summarizes comparative rate data for the hydrolysis of other monoesters studied kinetically shows isokinetic relationship²⁵. The point of mono-2-methyl-5-nitroaniline phosphate lies on the linear curve of those monoesters which are known to undergo hydrolysis via P-N bond fission (Fig. not shown). Thus P-N rather than C-N bond fission appears to be more probable. The bimolecular hydrolysis with P-N bond fission of the conjugate acid species has been proposed as shown in chart -1.

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