Hydrolysis of Mono-*p*-Toluidine Phosphate in Buffer Media

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Kinetic study of hydrolysis of mono-*p*-toluidine phosphate has been investigated in the pH range 0.00 to 7.46 at 50 ºC. The pH log rate profile has a rate maximum at pH 4.17. Hydrolysis of monoester carried out in buffer shows that only mononegative, mononegative and neutral species are reactive at pH 2.00-7.46 and pH 0.00 to 2.00, respectively. Their di-negative species have been found to be inert. The theoretical rate determined from specific rate and fractions of the neutral species agree closely with the experimental rates. The nature of molecularity of hydrolytic reaction has been decided on the basis of temperature and solvent effect. The monoester involves P-N bond fission, which is strengthened by comparative kinetic rate data.

Key Words: Hydrolysis, Mono-*p*-toluidine phosphate.

INTRODUCTION

The importance of phosphoric acid derivatives and role of phosphate linkages in biochemistry are well understood. The kinetics of reaction of simple organic phosphates provides an insight into more complicated reactions during their metabolism. The determination of mechanism of hydrolysis of organic phosphate is expected to reveal the possible correlations between the reaction path of chemical and enzymatic hydrolysis of biologically important phosphate esters[1]. Organic phosphate having C-N-P linkages are of great importance. They are used as insecticides[2], pesticides[3], cancer chemotherapeutic agent[4], plasticizers[5], smoke generation[6], additives for fire-retardant[7], petroleum and corrosion inhibitors[8]. Hydrolytic reaction of phosphate ester is now a subject of kinetic study due to its application in engineering, agriculture chemistry, medicinal chemistry and pharmaceutical chemistry. Keeping this in view, the hydrolytic bond cleavages of mono-*p*-toluidine phosphate has been investigated. Mono-*p*-toluidine phosphate is reactive *via* different species depending upon the nature of ester and hydrogen ion concentration of the reaction mixture.

EXPERIMENTAL

Mono-*p*-toluidine phosphate (Barium salt) has been prepared from *p*-toluidine and phosphorus pentaoxide by the method described earlier[9]. All the reactions have been carried out at the 50 ± 0.05 ºC employing 5×10^{-4} M solution of the monoester in aqueous medium. Buffer solutions for kinetic experiments were used for which

pH values have been given at 20 ºC and 150 ºC by Stene[10]. The interploted values of these buffer solutions at 98-100 ºC were used. Allen's modified method[11] was used for spectrophotometric determination of inorganic phosphate. All the chemicals used during work were of AR grade.

RESULTS AND DISCUSSION

Hydrolysis of mono-*p*-toluidine phosphate has been studied in the pH range 0.00 to 7.46 at 50 ºC in aqueous medium. Fig. 1 shows the pH log rate profile in which theoretical rates closely agreed with those observed rates.
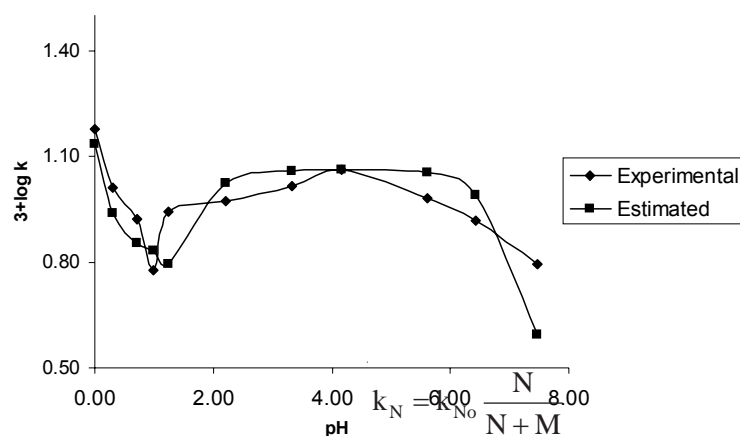

$$k_N = k_{No} \frac{N}{N+M}$$

Fig. 1. pH log rate profile for the hydrolysis of mono-*p*-toluidine phosphate at 50 ºC

As in other mono aryl phosphate the rate first rises with the rise in pH till it attains maximum at pH 4.17 and then decreases due to the inertness of the dinegative species. The maximum value at pH 4.17 is due to hydrolysis *via* mononegative species and dissociation of neutral species into mononegative species is almost complete at this pH. A slight deviation of the experimental rate in pH range 0.00 to 2.00 has been found due to the incursion of the neutral species. Similar nature of hydrolysis observed in the case of *o*- and *p*-methoxy phenyl dihydrogen phosphate[12], *p*-ethoxy phenyl dihydrogen phosphate[12], 2,3-dimethoxy phenyl dihydrogen phosphate monoester[13]. Neutral and mononegative rates can be represented as:

$$ (1) $$

$$k_M = k_{Mo} \frac{M}{M+N} \tag{2}$$

where k_{No} is specific neutral rate, k_{Mo} (specific mononegative rate) is experimental rate at pH 4.17 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:

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

where k is experimental rate. There is good agreement between values of specific neutral rate k_{No} determined by eqn. 3 is 4.19×10^{-3} min^{-1} at different pH from pH 0.00 to 1.00 and from ionic strength data is 3.63×10^{-3} min^{-1}.

It is clear from Table-1 that in the pH range 0.00 to 1.00, the hydrolysis governs by neutral, conjugate and mononegative species. In the pH range 1.00 to 1.24, the reactions are *via* neutral and mono negative species. In the pH range 1.24 to 7.46, only mononegative species are reactive.

TABLE-1
ESTIMATED AND EXPERIMENTAL RATES OF THE HYDROLYSIS OF MONO-*p*-
TOLUIDINE PHOSPHATE (Ba Salt) *via* NEUTRAL AND MONONEGATIVE
SPECIES AT DIFFERENT pH VALUES AT 50 ºC

pH	M/M+N	N/N+M	$k_M 10^3$ (min^{-1})	$K_N 10^3$ (min^{-1})	$k_H^+ \cdot C_H^+$ 10^3 (min^{-1})	k 10^3 (min^{-1}) Estd.	k 10^3 (min^{-1}) Expt.	3 + log k (Estd.)	3 + log k (Expt.)
0.00	0.063	0.937	0.73	3.401	9.54	13.67	14.98	1.136	1.176
0.30	0.119	0.881	1.37	3.198	4.11	8.68	10.24	0.938	1.010
0.70	0.253	0.747	2.91	2.711	1.51	7.13	8.34	0.853	0.921
1.00	0.403	0.597	4.64	2.167	0.73	6.81	6.00	0.833	0.778
1.24	0.540	0.450	6.22	1.634	–	6.22	8.74	0.793	0.942
							9.18*		
							10.87†		
							12.95‡		
2.20	0.915	0.085	10.54	0.308	–	10.54	9.42	1.023	0.974
3.33	0.993	0.007	11.44	0.025	–	11.44	10.39	1.058	1.017
4.17	0.999	0.001	11.51	0.003	–	11.51	11.52	1.061	1.061
							12.33*		
							14.25†		
							16.91‡		
5.60	0.980	–	11.29	–	–	11.29	9.56	1.053	0.980
6.43	0.850	–	9.79	–	–	9.79	8.31	0.991	0.919
7.46	0.340	–	3.92	–	–	3.92	6.25	0.593	0.795

*10 % dioxane, †20 % dioxane, ‡30 % dioxane.

Kinetic rate laws for the hydrolysis of mono-*p*-toluidine phosphate may be represented as:

In the pH range 0.00 to 1.00

$$k = k_H^+ \cdot C_H^+ + 11.52 \times 10^{-3}\frac{M}{M+N} + 3.63 \times 10^{-3}\frac{N}{N+M}$$

In the pH range 1.00 to 1.24

$$k = 11.52 \times 10^{-3}\frac{M}{M+N} + 3.63 \times 10^{-3}\frac{N}{N+M}$$

In the pH range 1.24 to 7.46

$$k = 11.52 \times 10^{-3} \frac{M}{M+N}$$

A change over from water to aqueous dioxane increases the rate showing dispersion of charges in the transition state[14] as shown in Table-1. Arrhenius parameter for hydrolysis *via* neutral and mononegative species summarize in Table-2 are in favour of a bimolecular reaction.

TABLE-2
ARRHENIUS PARAMETER FOR THE HYDROLYSIS OF MONO-*p*-TOLUIDINE
PHOSPHATE (Ba Salt) *via* NEUTRAL & MONONEGATIVE SPECIES AT 50 ºC

pH	E (Kcal/mol)	A (s⁻¹)	-ΔS$^{\neq}$ (e.u.)
1.24	10.94	1.31×10^7	36.19
4.17	12.26	1.37×10^8	31.56

A comparative kinetic rate data for the hydrolysis of some phosphate monoesters *via* neutral and mono-negative species as shown in Tables 3 and 4 also supports the bimolecular nature of hydrolysis involving P-N bond fission.

TABLE-3
COMPARATIVE KINETIC RATE DATA FOR THE HYDROLYSIS OF SOME
PHOSPHATE MONOESTERS *via* NEUTRAL SPECIES

| Phosphate monoesters	Medium pH	E (Kcal/mol)	-ΔS$^{\neq}$ (e.u.)	Molecularity	Bond fission
p-Nitro aniline	1.20	11.44	48.52	2	P-N
Dinitro diphenyl amine	1.24	7.59	57.40	2	P-N
p-Toluidine	1.24	10.94	36.19	2	Present work
2,5-Dichloro aniline	1.24	5.03	64.77	2	P-N
p-Butyl aniline	1.24	9.15	55.70	2	P-N
Di-isopropyl amine	1.24	6.86	60.33	2	P-N

TABLE-4
COMPARATIVE KINETIC RATE DATA FOR THE HYDROLYSIS OF SOME
PHOSPHATE MONOESTERS *via* MONONEGATIVE SPECIES

Phosphate monoesters	Medium pH	E (Kcal/mol)	-ΔS$^{\neq}$ (e.u.)	Molecularity	Bond fission
2,4-Dinitro aniline	4.17	13.30	44.40	2	P-N
p-Methoxy aniline	4.17	9.57	37.96	2	P-N
o-Toluidine	5.20	10.05	40.52	2	P-N
p-Toluidine	4.17	12.26	31.56	2	Present work
2,4-Dinitro aniline	5.20	15.05	40.42	2	P-N

The probable reaction mechanism for the hydrolysis of mononegative species and neutral species of mono-*p*-toluidine phosphate may, therefore, be suggested as shown below:

Mechanism via mononegative species

(A) Formation of mononegative species
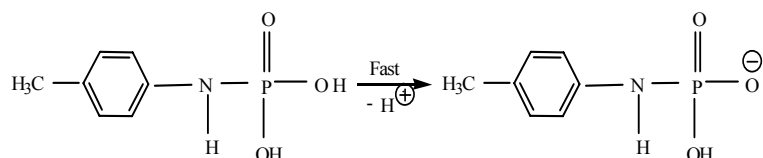
(B) Bimolecular nucleophilic attack of water on phosphorus via mononegative species SN^2 (P)

Transition state

(C)

Parent compound
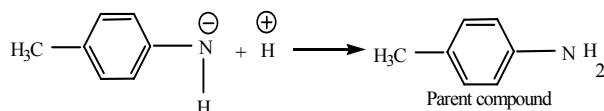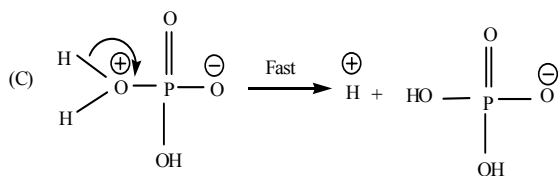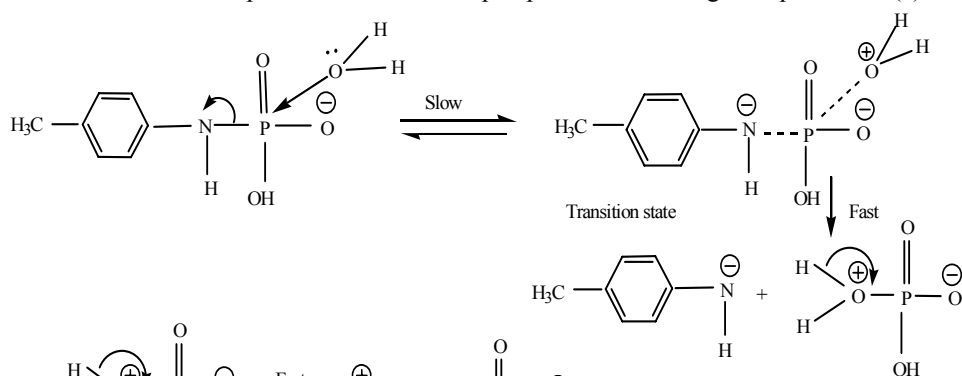
Mechanism via neutral species

Bimolecular attack of water on phosphorus atom of the neutral species SN^2 (P)

Transition state

Parent compound
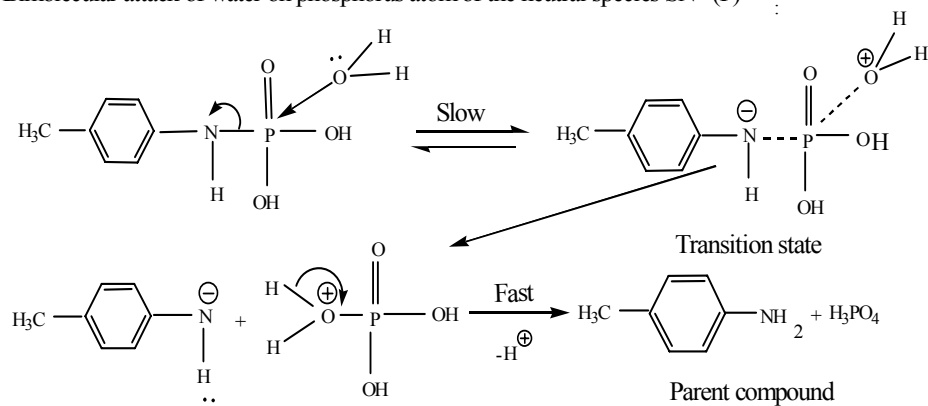
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