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Kinetics and Mechanism of the Hydrolysis of 4-Bromo-2,6-Dimethylphenyl Phosphate Monoester

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Hydrolysis of 4-bromo-2,6-dimethylphenyl phosphate monoester has been carried out in acid (HCl) solution at 97 ± 0.5°C and the inorganic phosphate obtained during hydrolysis has been estimated colorimetrically. Pseudo first order rate coefficients have been calculated. Neutral and conjugate acid species have been found to be reactive and contribute to the overall hydrolysis in the acid region. The calculated rate coefficients are in good agreement with the experimentally observed ones. 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—O bond.

Key Words: Kinetics, Hydrolysis, Phosphate Monoester.

INTRODUCTION

Bunton *et al.*[1] found that acid catalyzed hydrolysis occuurs only when an electron attracting substituent is present in the aryl moiety, as in nitrophenyl phosphate monoester. 4-Chlorophenyl phosphate monoester[2] and 2,6-dimethylphenyl phosphate monoester[3], showed only feeble acid catalysis, while 4-bromo-2,6-dimethylphenyl phosphate monoester showed acid catalysis. The title investigation has been undertaken to provide support to our contention.

RESULTS AND DISCUSSION

Hydrolysis of mono-4-bromo-2,6-dimethylphenyl phosphate was kinetically studied in 0.1 to 6.0 mol dm^{-3} HCl at 97 ± 0.5°C. Pseudo first order rate coefficients have been summarized in Table-1.

A plot of log rate constants *vs.* pH (figure not shown) shows that the rate of hydrolysis increases with increase in acid molarity. The rate maxima is at 4.0 mol dm^{-3} HCl and it gradually falls with further increase in acid molarity. The rate maxima or bend of pH log-rate profile in acid region have also been found in some other cases[4, 5].

In organic amides system[4, 6, 7], similar rate maxima was observed and was supposed due to full conversion into their conjugate acid species[1], the rate decrease is attributed to the lowering of concentration of attacking nucleophile

taking part in the reaction. Although, it appears that there is no similarity in rate maxima with amides as it is not possible due to complete protonation because there is a small variation in temperature coefficient before and after rate maxima and it may be taken as an indication for the absence of maximum protonation. The rate maxima in mono-4-bromo-2,6-dimethylphenyl phosphate may be due to either ionic strength effect or acid catalyzed hydrolysis or due to both.

TABLE-1
pH-Log RATE PROFILE OF MONO-4-BROMO-2,6-DIMETHYLPHENYL PHOSPHATE AT 97 ± 0.5°C

HCl (mol dm^{-3})	pH	$10^5 K_e$ (mol dm^{-3} min^{-1}) (Obsd.)	$5 + \log K_e$
6.0	–0.778	40.80	1.61
5.0	–0.699	76.25	1.88
4.0	–0.602	143.71	2.15
3.5	–0.544	136.22	2.13
3.0	–0.477	130.71	2.11
2.5	–0.397	119.11	2.07
2.0	–0.300	114.08	2.05
1.5	–0.176	104.52	2.01
1.0	0.000	92.88	1.96
0.5	0.301	90.52	1.95
0.4	0.400	73.48	1.86
0.3	0.520	69.26	1.84
0.2	0.700	79.23	1.89
0.1	1.000	89.12	1.94
Composition of buffers	1.240	93.30	1.96
	2.200	120.32	2.08
	3.330	128.27	2.10
	4.170	135.17	2.13
	5.600	131.82	2.12
	6.430	128.82	2.11
	7.460	125.89	2.09

The initial decrease in rate of hydrolysis may be attributed to a decrease in the concentration of more reactive mononegative species. Increase in rate in the region 1.0 to 4.0 mol dm^{-3} HCl may be due to either acid catalyzed hydrolysis or increase in the reactivity of neutral species by ionic strength effect. Therefore, effect of ionic strength[8] was studied by carrying out kinetic runs at different ionic strengths maintained constant by adding appropriate mixtures of KCl and HCl. The plots of the rate constants of acid hydrolysis *vs.* acid molarity at different ionic strengths are given in Table-2 and Fig. 1.

TABLE-2
HYDROLYSIS OF MONO-4-BROMO, 2,6-DIMETHYLPHENYL PHOSPHATE AT CONSTANT IONIC STRENGTH AT 97 ± 0.5°C

Ionic strength (μ) (mol dm^{-3})	Composition		$10^5 K_e$ (mol dm^3 min^{-1}) (Obsd.)
	HCl (mol dm^{-3})	KCl (mol dm^{-3})	
1.0	0.2	0.8	60.96
1.0	0.4	0.6	69.56
1.0	0.6	0.4	72.56
1.0	0.8	0.2	78.29
1.0	1.0	0.0	92.88
2.0	0.2	1.8	56.39
2.0	0.5	1.5	65.37
2.0	1.0	1.0	78.60
2.0	1.5	0.5	89.70
2.0	1.8	0.2	96.32
2.0	2.0	0.0	114.08
3.0	0.5	2.5	59.55
3.0	1.0	2.0	66.89
3.0	1.5	1.5	78.83
3.0	2.0	1.0	92.14
3.0	2.5	0.5	106.32
3.0	3.0	0.0	130.71

Three linear plots show the acid catalyzed hydrolysis of mono-4-bromo, 2,6-dimethylphenyl phosphate at three different ionic strengths (1.0 μ, 2.0 μ and 3.0 μ).

The intercepts on the rate axis are the neutral rates (K_N) which decrease with the increase in ionic strength, showing ionic acceleration effect on the hydrolysis of the monoester *via* its neutral species. Therefore, the calculated rates were obtained by eqn. (1).

$$K_e = K_H \cdot C_H + K_N \quad (1)$$

where K_e, $K_H \cdot C_H$ and K_N are experimental rates, acid catalyzed rates and neutral rates respectively.

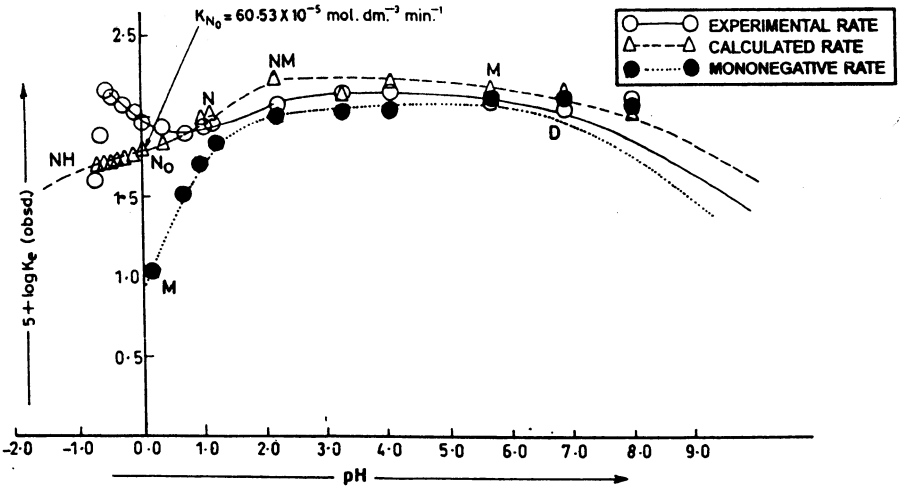


Fig. 1. pH-log Rate profile of mono-4-bromo, 2,6-dimethylphenyl phosphate at 97 ± 0.5°C

The plot of mono-4-bromo-2,6-dimethylphenyl phosphate shows that three plots are intersecting the rate axis at different points (Fig. 2), hence, this indicates in addition to conjugate acid species, the presence of some other species.

Since it is an established fact that mononegative species cannot be reactive at higher acidities, *i.e.*, >1.0 mol. dm.$^{-3}$ HCl, so the neutral species participation may be expected together with conjugate acid species, as it is evident that straight

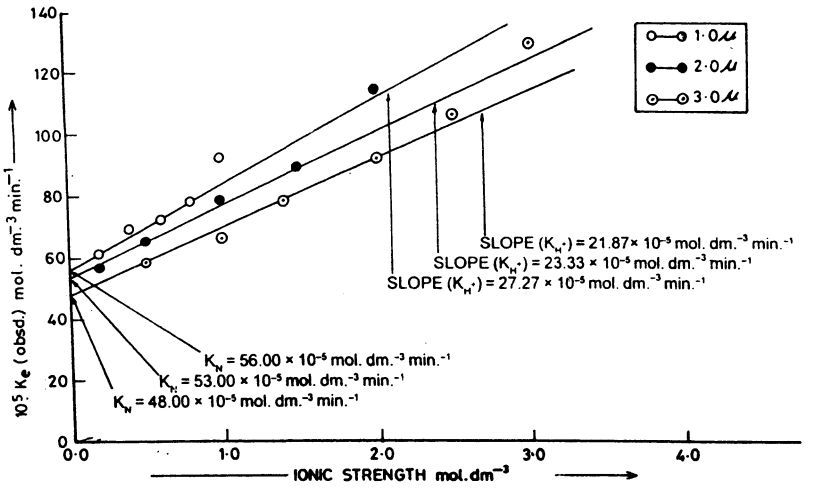


Fig. 2. Hydrolysis of mono-4-bromo, 2,6-dimethylphenyl phosphate at constant ionic strength at 97 ± 0.5°C

lines are intersecting the rate axis at different points, which shows the contribution of neutral species at different acid concentration is varying definitely.

K_{H^+} is a slope of linear curves and its value decreases with the increase in ionic strength. It is an ionic retarding effect, which indicates that mono-4-bromo-2,6-dimethylphenyl phosphate undergoes acid catalyzed hydrolysis with negative effect of ionic strength. The slope of these curves represents the specific acid catalysed rates at that ionic strength, which also decreases with the increase in ionic strength. Thus, both specific neutral rates and specific acid catalyzsed rates are subjected to negative effect of ionic strength. The neutral rates may be calculated using second empirical term of Debye-Huckel equation[1, 9, 10] and modifying it logarithmically.

$$\log K_N = \log K_{N_0} + b_N \cdot \mu \tag{2}$$

and its logarithmic form can be represented as

$$5 + \log K_N = 5 + \log K_{N_0} + b_n \cdot \mu \tag{3}$$

where $b_N = \dfrac{b_N}{2.303}$.

In equation (2), K_N, K_{N_0}, b_N and μ respectively are specific neutral rates at that ionic strength, specific neutral rates at zero ionic strength and the slope of the linear curve, and ionic strength (figure not shown).

The intercept on the rate axis of such a plot, *i.e.*, $\log K_N$ is found to be different. Thus, the increase in specific neutral rate is due to ($b_N \cdot \mu$) factor, supporting ionic acceleration effect. The specific neutral rates calculated by eqn. (2) are almost different from the experimental rates up to 4.0 mol dm^{-3} HCl and shown in Table-1. The rates above 4.0 mol. $dm.^{-3}$ HCl, however, deviate probably due to decrease in the reactivity of the neutral form as a result of decrease in water activity. Therefore, the rates beyond 4.0 mol dm^{-3} HCl were calculated employing the Bronsted-Bjerrum equation[1, 11, 12].

$$K_e = K_{H^+} \cdot C_{H^+} \exp b'_{H^+} \cdot \mu(a_{H_2O})^n + K_{N_0} \cdot \exp b'_N \cdot \mu(a_{H_2O})^n \tag{4}$$

and its logarithmic form can be represented as:

$$5 + \log K_e + 5 + \log K_{H^+} + \log C_{H^+} + b'_{H^+} \cdot \mu + n \log (a_{H_2O}) + 5 + \log K_{N_0} + b'_N \cdot \mu + n \log a_{H_2O} \tag{5}$$

where, $(a_{H_2O})^n$ represents the water activity parameter[13].

The values of $n = 2$, 3 were calculated for 5.0 and 6.0 mol dm^{-3} HCl respectively. The experimental rates thus calculated are in good agreement with the theoretical rates. The thermodynamic parameters[14] for the reaction at 3.0 and 5.0 mol dm^{-3} HCl were found to be $\Delta E = 21.96$ and 22.42 kcal. mol^{-1}; frequency factor (A) = 2.05×10^8 and 2.22×10^8 sec^{-1} and $\Delta S = -22.93$ and -22.76 e.u. These values indicatte the bimolecular nature of hydrolytic reaction.

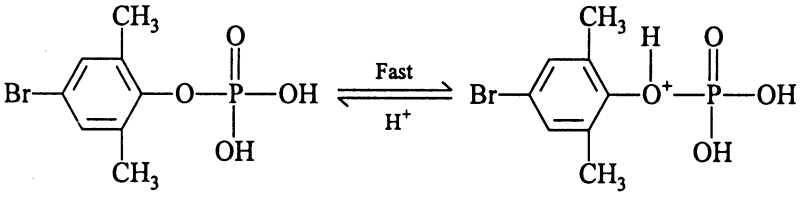
Solvent effects[15, 16] have been studied using different water-dioxan mixtures. The results show that there is significant decrease in rate as a result of change over from pure water to 30% aqueous dioxan. Due to bimolecular nucleophilic

attack of solvent water molecule, the unit positive charge is created, dispersed in the transition state. Consequently, the rates are higher in more polar medium (pure water) than in aqueous dioxan. Since the rate coefficients are rarely similar and are independent of initial concentration of the monoester, the reaction may be taken as kinetically of first order.[17] The hydrolysis of monoester, which occurs by the cleavage of P—O bond, follows the isokinetic relationship[18, 19] (figure not shown).

The acid hydrolysis of monester, therefore, involves bimolecular attack of water on phosphorus of the neutral species and conjugate acid species[1] as shown in **Schemes I** and **II**.

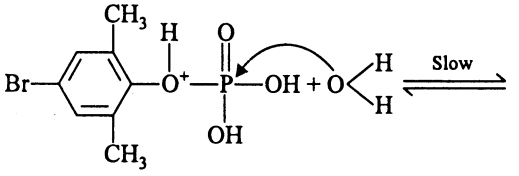
Scheme I

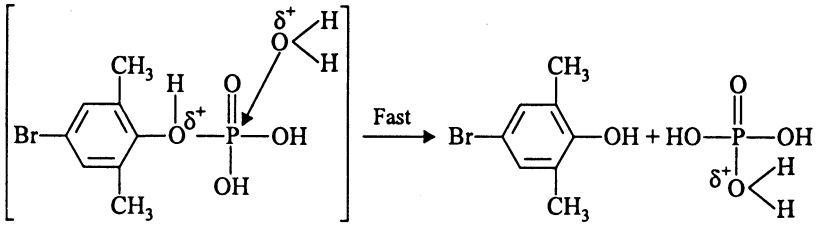
(a) Formation of Conjugate Acid Species



(Neutral species) (Conjugate species)

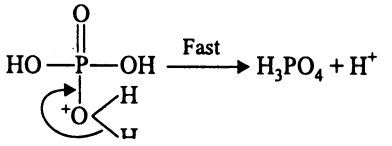
(b) Bimolecular Nucleophilic Attack of Water on Phosphorus Via Conjugate Acid Species {S_N^2(P)}





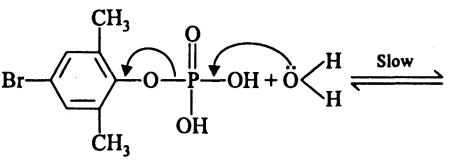
(Transition state) (Parent compound)

(c)

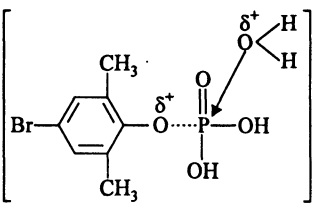


Scheme II

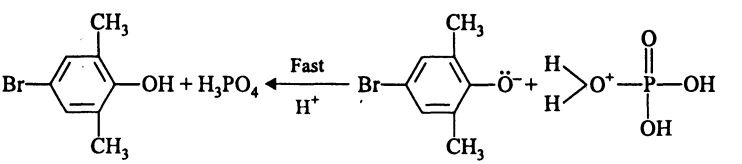
Bimolecular Nucleophilic Attack of Water Molecule on Phosphorus of the Monoester [Neutral Molecule {S_N^2(P)}]



(Neutral species)



(Transition state)



(Parent compound)

EXPERIMENTAL

Preparation of Mono-4-bromo-2,6-dimethylphenyl phosphate

4-bromo-2,6-dimethylphenyl phosphate mono-ester has been prepared by Rudert Method[2, 20, 21] by treating the excess of phosphorylating agent phosphorus oxy-trichloride ($POCl_3$) in dry benzene.

Took 19.3 g of 4-bromo-2-6-dimethyl phenol in a round-bottom flask with 150 mL of dry benzene; 9.0 mL of phosphorus oxy-trichloride ($POCl_3$) was added drop by drop with constant stirring to the ice-cooled solution with the help of separating funnel at about 1/2 h. After the addition, it was refluxed for about 40 h on a soxhlet heater at constant temperature 55°C, in order to ensure complete reaction and then distilled at reduced pressure. The first fraction of benzene and unreacted $POCl_3$ was removed by distillation at b.p. 48°C. The second fraction of a pungent smelling liquid which was supposed to be 4-bromo-2-6-dimethylphenyl phosphate dichloridate, distilled at b.p. 100–120°C. It was dissolved in 100 mL of ice-cooled water and kept at low temperature overnight. The 4-bromo-2,6-dimethylphenyl phosphate dichloridate converted into 4-bromo-2-6-dimethylphenyl dihydrogen phosphate, which was extracted with solvent

ether. After removing the solvent ether a light brown coloured crystalline solid was obtained, which on recrystallisation with absolute ethyl alcohol gave a white crystalline solid and it was identified to be mono-4-bromo-2,6-dimethylphenyl phosphate and confirmed the following physical characteristics:

m.p. (observed) = 112°C. Theoretical percentage of 'P' = 11.03%. Observed percentage of 'P' = 11.20%. The infrared spectrum of monoester showed the appearance of absorption bands characteristic of C—H stretching = 2957–2941 cm^{-1}, ν(—C=C—) = 1640–1580 cm^{-1}, $—CH_3$ stretching = 1440–1395 cm^{-1}, ν(—P—O) = 1300–1280 cm^{-1} ν—P(=O)—OH = 1200–1180 cm^{-1} ν(—P—OH) = 1040–910 cm^{-1}, substitution aromatic ring = 800–710 cm^{-1} C—Br = 700–600 cm^{-1}.

Above characteristics confirm the structure of mono-4-bromo-2,6-dimethylphenyl phosphate.

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