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S_N2 Mechanism of Cationic Micelles on the Hydrolysis of Bis-*p*-Methoxyphenyl Phosphate Ester

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Abstract. Hydrolysis of bis-*p*-methoxyphenyl phosphate ester (bis-*p*-MPPE) was studied in micellar solutions of cityltrimethylammoniumbromide n-$C_{16}H_{33}N^+(CH_3)_3Br^-$ (CTABr) at pH-9.0. The hydrolysis followed first order kinetics with respect to bis-*p*-MPPE concentration. At the concentration of critical micelle concentration (CMC) the rate of hydrolysis increased with increasing CTABr concentration. Surfactant with cationic or polar head group form micelles in water with hydrocarbon like interior or polar groups at the surface and bind cationic solute. The binding constant of micelle for bis-*p*-MPPE and the rate constant in micellar pseudo phase were determined from kinetic data using the pseudophase model.

Keywords: micelle, bis-*p*-methoxyphenyl phosphate ester, reaction mechanism, binding constant, critical micelle concentration, surfactant

Introduction

Phosphate esters are very important biologically and most naturally occurring phosphorous compounds containing a terminal unsubstituted –PO $(OH)_2$ group. Introduction of this group into molecule is known as phosphorylation. If the protected group is not used, then polymers containing the P-O-P linkage are obtained. Many of the essential chemicals in life processes are phosphate esters. These include the genetic substances DNA and RNA as well as cyclic AMP (adenosine monophosphate). In addition, the transfer of phosphate groups between ATP and ADP is of fundamental importance in the biological systems. All the biological reactions involving formation and hydrolysis of these phosphate esters and polyphosphates are affected by enzyme catalysis. Due to importance of such substance the hydrolysis of phosphate esters has received much fundamental study. The strongly acidic bis-esters are entirely in the anionic form at normal and physiological at pH-8.0. They are thus, relatively resistant to nucleophilic attack by either OH^- or H_2O.

Most work has involved organic reactions, generally in water, mediated by organic micelles which absorb reactants, providing a reaction region distinct from the bulk solvent. Hydrolysis of bis-ester depends upon the experimental conditions (Ghosh *et al*., 2008). In the most kinetic studies of micellar catalysed reactions in the case of substrate into the micellar phase brings pull to the micelle by the electrostatic force (Domingos *et al*., 2003) or it gets chemically bonded in it (Brinchi *et al*., 2000). Interaction between ester is very important in finding the conditions in which micelles would enhance the hydrolysis of di- substituted phenyl phosphate esters. Bis-*p*-MPPE was the preferred substrates because with bis-*p*-MPPE the neutral species is the most reactive species (Behme *et al*., 1965). At pH-9.0 bis-*p*-MPPE also reacts with hydroxide ion (Bruice *et al*., 1968) and therefore by appropriate choice of a substrate it is possible to examine the micellar effects upon the mechanism of bis-*p*-methoxyphenyl phosphate ester hydrolysis (Scheme 1).

In earlier work on acid-base reactions of charge-charge interactions between micelles and ions in solution, with anionic micelles attracting cations and repelling anions cationic micelles having opposite behaviour with the cationic micelles of CTABr there was catalysis of the hydrolysis of bis-*p*-MPPE mono anion (Cox *et al*., 1964).

Materials and Methods

The details of preparation of the phosphate esters of -*p*-methoxy phenol involves with direct reaction of phosphorus oxytrichloride ($POCl_3$). Mono, bis- and tri-phosphate esters of the above mentioned phenol have been prepared by the standard method (Bunton *et al*., 1967). 12.4 g of *p*-methoxy phenol dissolved in benzene (100 mL) and 9.05 mL of phosphorus oxytri-chloride was added slowly during 20 min with constant stirring. The reaction mixture was refluxed for 18 h and distilled at reduced pressure. The first fraction of benzene and

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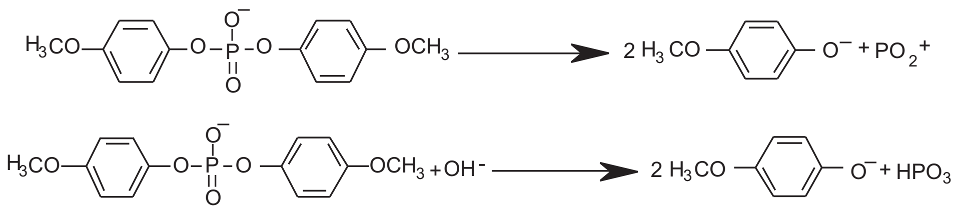


Scheme 1. Hydrolysis of bis-*p*-methoxy phenyl phosphate ester.

unreacted phosphorus oxytrichloride was removed by distillation at b$_{72}$ 60-80 °C. It was dissolved in 100 mL of ice cold distilled water and kept at low temperature overnight. Mono-*p*-methoxy phenyl phosphorodichloridate was converted into mono-*p*-methoxy phenyl dihydrogen phosphate and extracted with solvent ether.

The residue left after removing mono-*p*-methoxy phosphate at b$_{72}$ 60-80 °C was washed several times with boiling distilled water and 0.2N NaOH solution, to remove mono-*p*-methoxy phosphate ester, unreacted phosphorus oxytrichloride and the phenol and finally digested in hot 0.5N NaOH solution. It was filtered and the filtrate was acidified with dilute HCl using phenolphthalein as an indicator. A white precipitate was obtained that was separated by filtration and made free from hydroxyl ions with repeated washings with boiling water. It was then dried at room temperature and recrystallised with absolute ethyl alcohol to give a white crystalline solid which was identified bis-*p*-methoxy phenyl phosphate.

Kinetics and reaction mechanism. Investigation of micellar catalysis in mechanism of bis-*p*-MPPE with hydroxide ion has been carried out at temperature (40±0.2 °C). Kinetics runs were performed by using double distilled water. Reactions were followed by spectrophotometrically at using the wavelength (λ) 660 nm by the rate of development of inorganic phosphate.

Results and Discussion

The absorbed bands in the I.R. spectrum showed characteristics bands of bis-*p*-MPPE is γ -C-H [Aromatic ring] = 2882.5 cm^{-1}, γ –OH = 3449.3 cm^{-1}, γ- P=O = 1745.9 cm^{-1}, γ -C=C-C=C- = 1518.7 cm^{-1}, γ -P-O = 1386.1 cm^{-1}, γ -C-O = 1149.1 cm^{-1}, γ -C-H [out of plane bending] = 1040-936 cm^{-1}, characterised the structure of bis-*p*-methoxyphenyl phosphate.

In previous work on chemical reaction, base equilibrium was examined by using visual indicators and apparent base dissociation continuous was sensitive to cationic micelles (Bunton *et al*., 1984). The reactions of phosphate bis-ester were strappingly catalysed at different concentrations of CTABr at which pseudo first order rate constants were obtained. Investigation of micelles catalysed hydrolysis (Bunton, 2011; Reale *et al*., 2010; Silva *et al*., 2009) of bis-*p*-MPPE with hydroxide ion has been carried out at temperature (40±0.2 °C) in presence or absence of detergent (10^{-3} to 10^{-4} mol/dm) at pH-8.0 to 10.0 using borate buffers. Effect of cationic (CTABr) detergent on the rate of hydrolysis of bis-*p*-MPPE in presence of hydroxide ion has been measured spectrophotometrically by the rate of appearance of inorganic phosphate (Kumar and singh, 2011) (Table 1) and rate increases sharply at CTABr concentration greater than the critical micelle concentration (CMC) for CTABr at pH-9.0 in 2.5×10^{-3} mol/dm^3 borate buffer CMC = 80×10^{-3} M determined by dye method (Jaks *et al*., 2010; Duynstee and Grunward, 1959). The pseudo first order rate constant for bis-*p*-MPPE has been carried out in presence of detergent. It has been observed that, with the increasing detergent concentration, the rate increases to a maximum value of $K_\Psi = 75.18\times10^{-5}$/sec at 1.6×10^{-3}

Table 1. Reaction of (5×10^{-4}) mol/dm^3 bis-*p*-methoxyphenyl phosphate with constant (OH^-) in presence of different 10^3 (CTABr) at pH-9.0 and temperature (40±0.2 °C)

S.no.	10^3 (CTABr) mol/dm^3	10^5K_Ψ/s
1	0.2	13.07
2	0.4	21.86
3	0.6	24.27
4	0.8	38.16
5	1.0	44.49
6	1.2	58.04
7	1.4	66.53
8	1.6	75.18
9	1.8	70.52
10	2.0	64.49

mol/dm^3 CTABr, respectively. This maximum rate has been shown in rate constant against detergent concentration (Table 1). Investigation of the relation between the observed pseudo rate constant K_Ψ and the surfactant concentration for a spontaneous dephosphorylation of bis-*p*-MPPE is presented in Fig. 1.

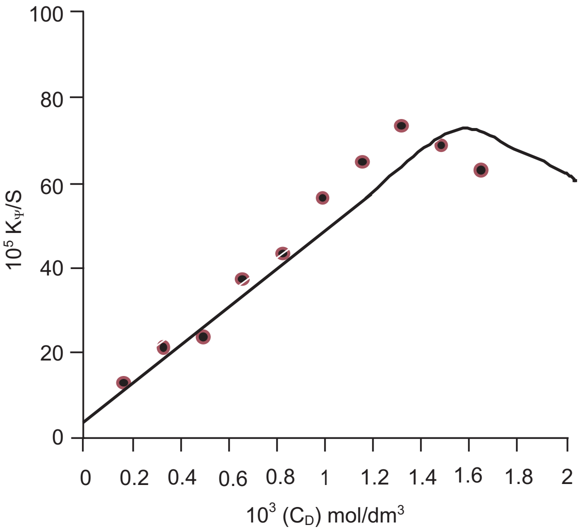
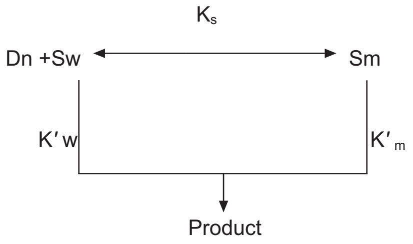


Fig. 1. A plot of rate constants against detergent concentrations (CTABr) 20.8×10^{-3} mol/dm^3 (OH^-) with (5×10^{-4}) mol/dm^3 bis-*p*-methoxyphenyl phosphate at pH-9.0 and temperature (40±0.2 °C).

Presuming protonation of the neutral ester or neutral species of the bis-*p*-MPPE, the bend obtained by rates constants against detergent concentration was through due to the result of the maximum protonation which is common in amide system (Bunton and Moffatt, 1986). Unless the energy of protonation is small, the difference in activation energies should result at point before and after the bend. With this view, kinetic runs were made at maximum where substrate is completely micellar bound at 1.6×10^{-3}/mol/dm^3 CTABr where maximum rates K_Ψ =75.18×10^{-5}/s for the hydrolysis of bis-*p*-MPPE with micelles of CTABr in buffer solutions. The hydrolysis was studied in absence and in presence of surfactant. Investigations of Arrhenius parameters for the hydrolysis of bis-*p*-MPPE are shown in Table 2. The rate of enhance arise approximately complete from a lowering of activation energy in absence of CTABr -ΔE =19.09 K. Cals/mole and entropy of -ΔS ≠ 56.24 (e.u.) and in presence of CTABr -ΔE =20.02 K. Cals/mole and entropy of -ΔS ≠51.99 (e.u.).

Table 2. Arrhenius parameters for the hydrolysis of bis-*p*-MPPE

Ester	ΔE K.Cals./mole	-ΔS ≠ / (e.u.)
Bis-*p*-MPPE without (CTABr)	19.09	56.24
Bis-*p*-MPPE with (CTABr)	20.02	51.99



(1)

Scheme 2.

Where:

Sw and Sm are substrates in aqueous and micellar pseudo phase respectable;
K′w and K′m are the related first order rate constants and
Ks is the binding constant (Domingos *et al*., 2003).

Reaction in the water make minor contribution to the observed rate constant. The first order rate constant for K_Ψ OH ion is given by the following equation:

$$K_\Psi = \frac{K'w + K'm\, Ks\,(Dn)}{1 + Ks\,(Dn)} \quad \text{......................} \ (2)$$

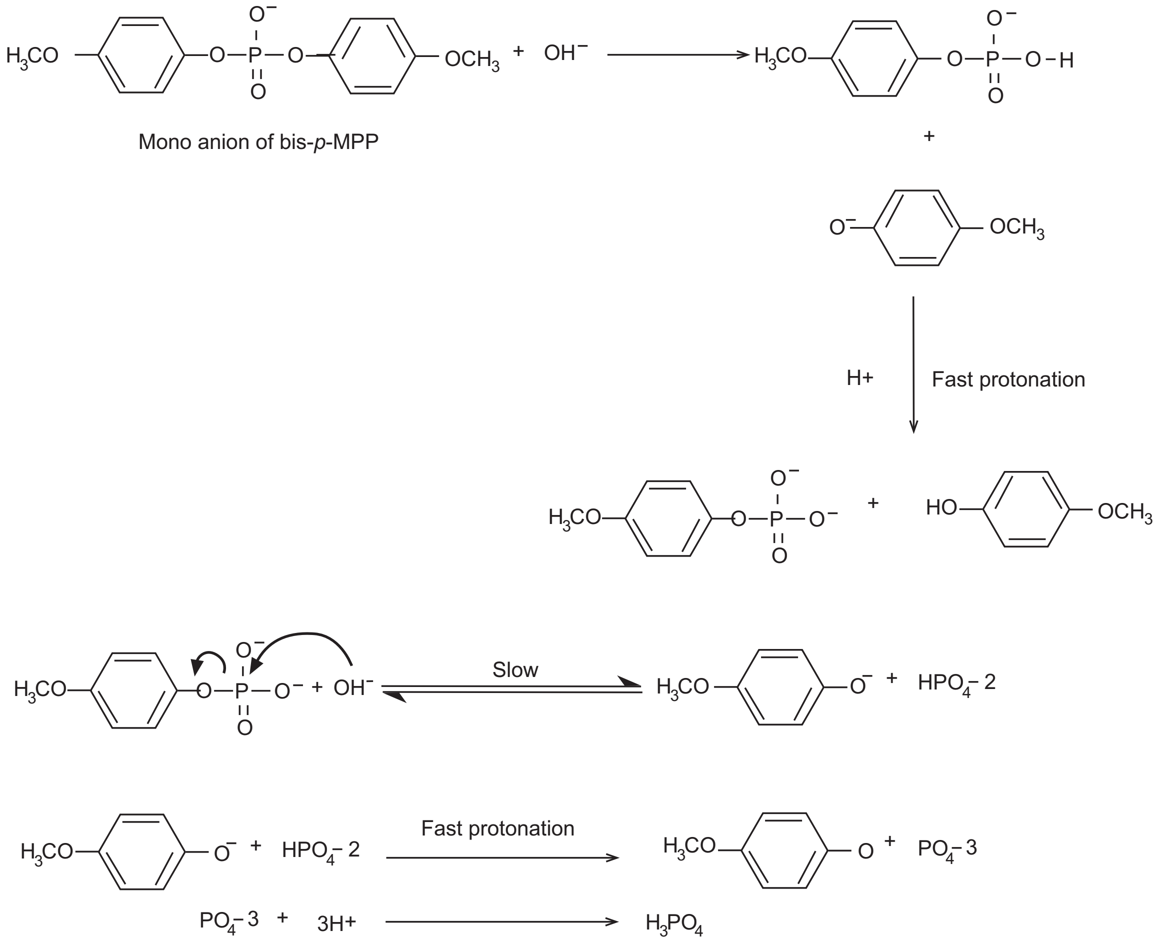
The value of K′ m can be obtained by analysis of the variations of Ks with Dn or by choosing conditions such that substrate is essentially fully micellar bound (Bunton *et al*., 1979).

The main feature of the mechanism of the micellar catalysed hydrolysis of bis-*p*-methoxyphenyl phosphate in presence of hydroxide ion on the basis of the above kinetic results may be formulated as under:

1. The study of substrate concentration shows insignificant increase in rates hence, reaction is taken kinetically of first order. Where water molecule is one of the reaction partner along with [OH^-] ion, attack bimolecular. Forming a transition state hence reaction is considered kinetically bimolecular.

2. The comparative values of $K^2_m = 16.06\times10^{-4}$/s mol/dm^3 at pH-9.0, $K'_w = 6.60\times10^{-5}$/s $K'_m = 114.70\times10^{-5}$/s along with the values of $\beta = 0.75$ for bis-*p*-MPPE resembles that of literature values are enough indicative for correctness of the model of ion exchange application, from which we draw the conclusion that the local concentration [OH^-] bound to micelle is = 3.58×10^{-4} mol/dm^3 in borate buffer at pH-9.0 and that in water shows smaller volume of [OH^-] ion and monoanion of bis-*p*-MPPE is present in aqueous micelle pseudo phase. This reasonably accounts for intramolecular proton transfer by concerted mechanism.
3. Charge densities are important for the inhibition by salts the order is Cl > Br.
4. Observation of stable suspension formed with low concentration of bis-*p*-MPPE in presence of slight excess of monomer (CTABr) due to interaction between mono anionic substrate and cationic surfactant. The turbidity decreases with increasing CTABr concentration and above cmc, a clear solution is obtained. Formation of strongly soluble ion pairs between the detergent cations and bis-*p*-MPPE mono anions or other sub micelle aggregates have been postulated because of turbidity.
5. The isokinetic data and ranges of Arrhenius parameters i.e. energy of activation and entropy of the reaction support bimolecular nucleophilic attack of [OH^-] ion on the phosphorus atom of bis-*p*-MPPE passing through a transition state involving ‘P-O’ bond fission.

The mechanism of the reaction may be suggested as shown in Scheme 3.



Scheme 3. Bimolecular nucleophilic substitution of hydroxide ion with ‘P-O’ bond fission.

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