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RESEARCH ARTICLE

MECHANISTICALLY CATIONIC MICELLAR CATALYSIS ON THE HYDROLYSIS OF MONO 2,5-DI METHOXY PHENYL PHOSPHORAMIDE.

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Abstract

Hydrolysis of mono- 2,5-dimethoxy phenyl phosphoramidate (mono-2,5-DMPP) was studied in micellar solutions of cetyltrimethylammonium bromide (CTABr) at pH-9.0. The hydrolysis followed first order kinetics with respect to mono-2,5DMPP concentration. At the concentration of critical micelle concentration (CMC) the rate of hydrolysis increased with increasing CTABr concentration. The binding constant of micelle for mono-2,5-DMPP and the rate constant in micellar pseudo phase were determined from kinetic data using the pseudo phase model.

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Introduction:-

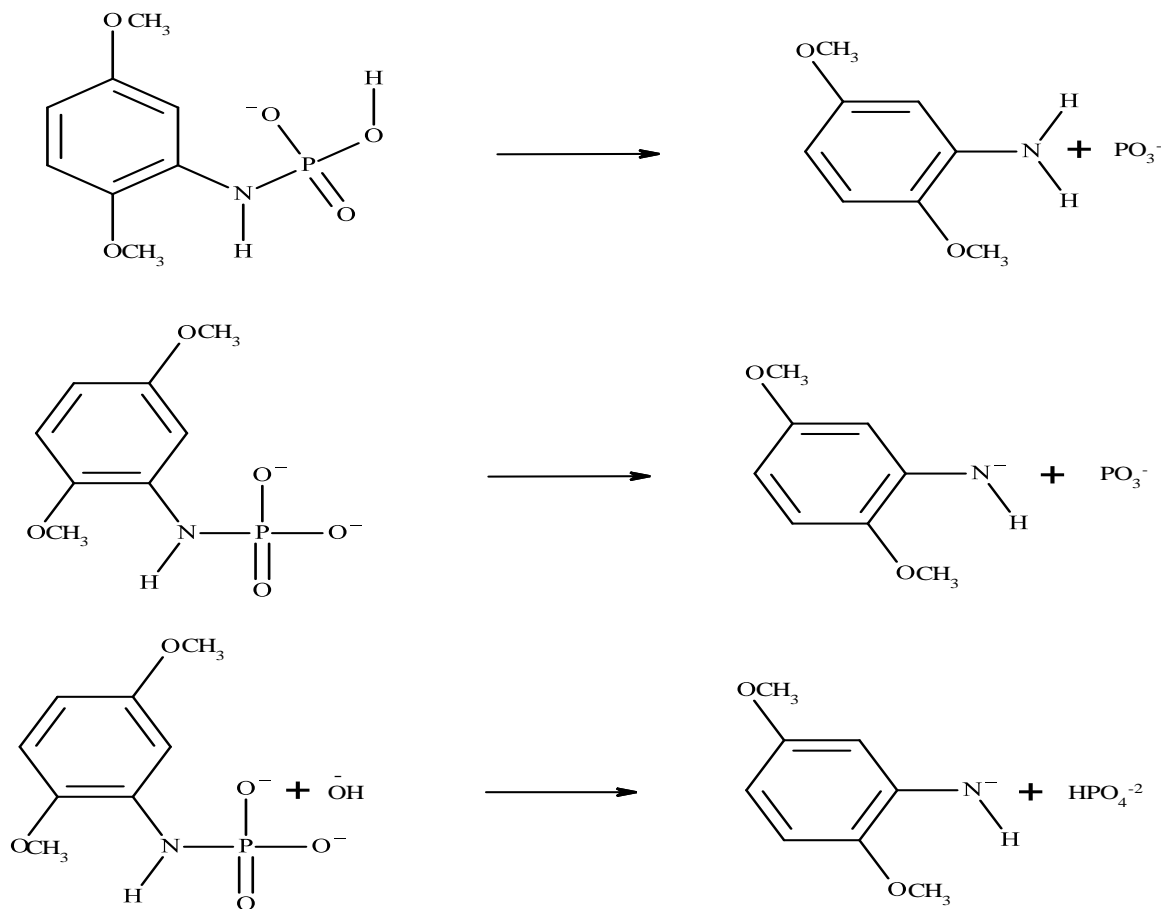
Quite a lot of the imperative chemicals in living processes are phosphate esters. These including the inherited substances DNA and RNA in addition to cyclic AMP, the moving of phosphate groups among ATP and ADP of indispensable substance in the living systems (Cuccovia, I.M. et al., 1978). Bioactivatable protecting groups represent an enormously powerful tool to increase bioavailability or to generally help deliver drugs to cells. This approach is particularly valuable in the case of biologically active phosphate because of the high intrinsic hydrophilicity and the multitude of biological functions phosphate esters exhibit inside cells. Here, the most prominent masking groups used so far are introduced (Bunton, C.A. et al., 1981).

Aminophosphonates are analogues of amino acids in which a carboxylic moiety is replaced by phosphonic acid or related groups. Acting as antagonists of amino acids, they inhibit enzymes involved in amino acids metabolism and thus affect the physiological activity of cell. These effects may be exerted as antibacterial, plant growth regulatory or neuromodulatory (Cox, J.R. et al., 1964). All part of the heritable reactions involving configuration and hydrolysis of these phosphate esters and polyphosphates are inflated by enzyme catalysis. Suitable to significance such substance the hydrolysis of phosphate esters has reputable seriously original study. Phosphate esters are tremendously very important biologically and most occurring phosphorous compounds contain a terminal unsubstituted $-PO(OH)_2$ groups. Introduction of these groups into molecule is known as phosphorylation (Jacks, P. et al., 2010). Requirement the protected group is not used. Then polymers containing the P-O-P linkage are obtained. In no small determine because of the magnitude of such substances and process as these immediately mention, the hydrolysis of phosphoramidate has accepted much critical study (Yunes, S. et al., 2005). The largest part work has implicated macrobiotic reactions, commonly in water, mediated by organic micelles which attract reactants, on condition that a reaction region dissimilar from the bulk solvent (Kumar, A. et al., 2011).

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Orthophosphoric acid being a tribasic acid will form a series of esters with phenols, alcohols, aryl amines and their derivatives. Orthophosphoric acid interacts with 2,5-dimethoxy aniline to form mono-, di- and tri-phosphoramides or phosphate esters (Bunton, C.A. 1979). Hydrolysis of mono phosphoramide depends upon the experimental conditions. In the most kinetic studies of micellar catalyzed reactions, in the case of substrate into the micellar phase brings pull to the micelle by the electrostatic force (Bunton, C.A. 2011). Or it gets chemically bonded in it (Bruce, T.C., et al., 1968). Interaction between phosphoramide in finding the conditions in which micelles would the hydrolysis of mono substituted phenyl phosphoramide. Mono-2,5-DMPP was the preferred substrates because with mono-2,5-DMPP the mono anion is the most reactive species (H.A. Al-Loedan, 1995). At pH-9.0 mono-2,5-DMPP reacts also with hydroxide ion (Brinchi, L., et al., 2000) and therefore by appropriate choice of a substrate. It is possible to examine the micellar effects upon three mechanism of mono- 2,5-DMPP hydrolysis (Singh, A.P. et al., 2013).



With the cationic micelles of cetyltrimethylammonium bromide (CTABr) there was catalysis of the hydrolysis of mono-2,5-DMPP mono anion (Ingold, C.K. 1953).

Experimental:-

Materials:-

Preparation of phosphate mono ester has been described by standard method (Duynstee, E.F. et al., 1959) and was purified by recrystallization from ethyl alcohol.

Kinetics:-

Investigation of micellar catalysis in reaction of mono- 2,5-DMPP with hydroxide ion has been carried out at 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 formation of inorganic phosphate (J.R.Cox et al., 1964).

Result and Discussion:-

The reactions of phosphate mono ester were strongly catalyzed at different concentration of (CTABr) at which pseudo first order rate constants were obtained. Investigation of micellar catalyzed hydrolysis (Bunton, C.A. et al., 1967) of mono-2,5-DMPP with hydroxide ion have been carried out at $40 \pm 0.2^\circ\text{C}$ in presence or absence of detergent [10^{-3} to 10^{-4} mol $^{-1}$ dm $^{-3}$] at pH 8.0 to 10.0 using borate buffers. Effect of cationic cetyltrimethylammonium bromide [CTABr] detergent on rate of hydrolysis of mono-2,5-DMPP in presence of hydroxide ion has been measured spectrophotometrically by the rate of appearance of inorganic phosphate (Al-Shamary, M.N. et al., 2012) [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. borate buffer CMC = 80×10^{-3} M determined by dye method (Kumar, A. 2015). The pseudo first order rate constant for mono-2,5-DMPP has been carried out in presence of detergent. It has been observed that whether the increasing detergent concentration the rate increases to a maximum value of 30.14×10^{-5} sec $^{-1}$ at 1.6×10^{-3} 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 mono-2,5-DMPP may be shown in [Fig.-1].

Presuming protonation of the neutral phosphoramidate or neutral species of the mono-2,5-DMPP the bend in the obtained by rates constants against detergent concentration was through due to the result of the maximum protonation which is common in amide system (Bunton, C.A. et al., 1984), unless the heat of protonation is small, the difference in activation energies should result at points before and after the bend, with this view kinetic runs were made at maximum where substrate is fully micellar bound at 1.6×10^{-3} mol. dm $^{-3}$ CTABr where maximum rates $K_\psi = 30.14 \times 10^{-5}$ s $^{-1}$ for the hydrolysis of mono-2,5-DMPP with micelles of CTABr in buffer solutions. The hydrolysis was studied in absence and presence of surfactant. Investigations of Arrhenius parameters for the hydrolysis of mono-2,5-DMPP are shown [Table-2]. The rate of enhancement arises almost completely from a lowering of activation energy in absence of CTABr $-\Delta E = 17.41$ K. Cals / mole and entropy of $-\Delta S \neq 57.32$ (e.u.) and in presence of CTABr $-\Delta E = 25.20$ K. Cals / mole and entropy of $-\Delta S \neq 53.88$ (e.u.).

S.No.	CTABr 10^{-3} Mol. dm $^{-3}$	$K_\psi 10^5$ S $^{-1}$
1	0.2	5.08
2	0.4	7.02
3	0.6	8.18
4	0.8	11.32
5	1.0	13.97
6	1.2	18.52
7	1.4	23.04
8	1.6	30.14
9	1.8	26.34
10	2.0	22.92

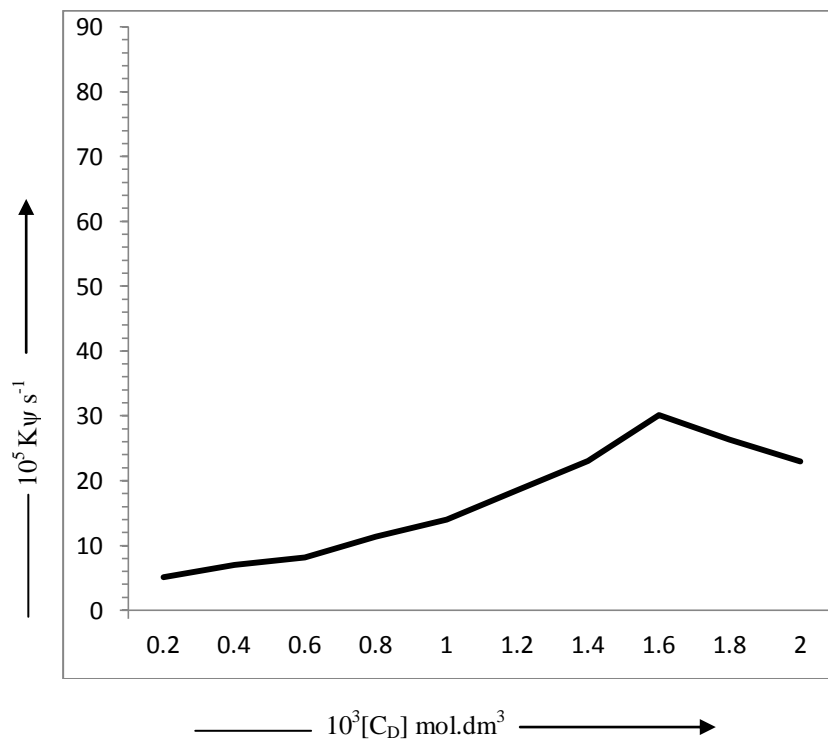


Table-1:-Reaction of mono-2,5-DMPP in presence of cationic surfactant.

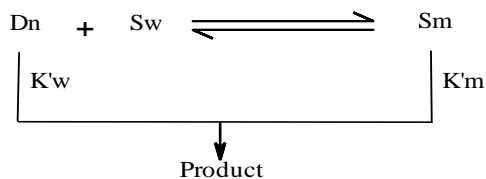
Fig.-1:-Reaction for the micellar catalyzed of mono-2,5-DMPP with (20.8×10^{-3}) NaOH at PH-9.0 and Temp.($40 \pm 0.2^\circ\text{C}$) in 10^{-3} mol.dm $^{-3}$ [CTABr].

ESTER	$-\Delta E$ KCal	$-\Delta S^\ddagger$ (e.u)
Mono-2,5-DMPP Without CTABr	17.41	57.32
Mono-2,5-DMPP With CTABr	25.20	53.88

Table-II:-Arrhenius parameters for the hydrolysis of mono-2,5-dimethoxy phenyl phosphoramidate.

Where S_w and S_m are substrates in aqueous and micellar pseudo phase respectively. K'_w and K'_m are the related first order rate constants and K_s are the binding constant (Al-Lohedan, H. et al., 1981).

Scheme-1



Reaction in the water makes minor contribution to the observed rate constant (Ghosh, K.K. et al., 2008). The first order rate constant for OH⁻ ion is given by the following equation.

$$K_\psi = \frac{K'_w + K'_m K_s [D_n]}{1 + K_s [D_n]} \quad \dots\dots\dots(1)$$

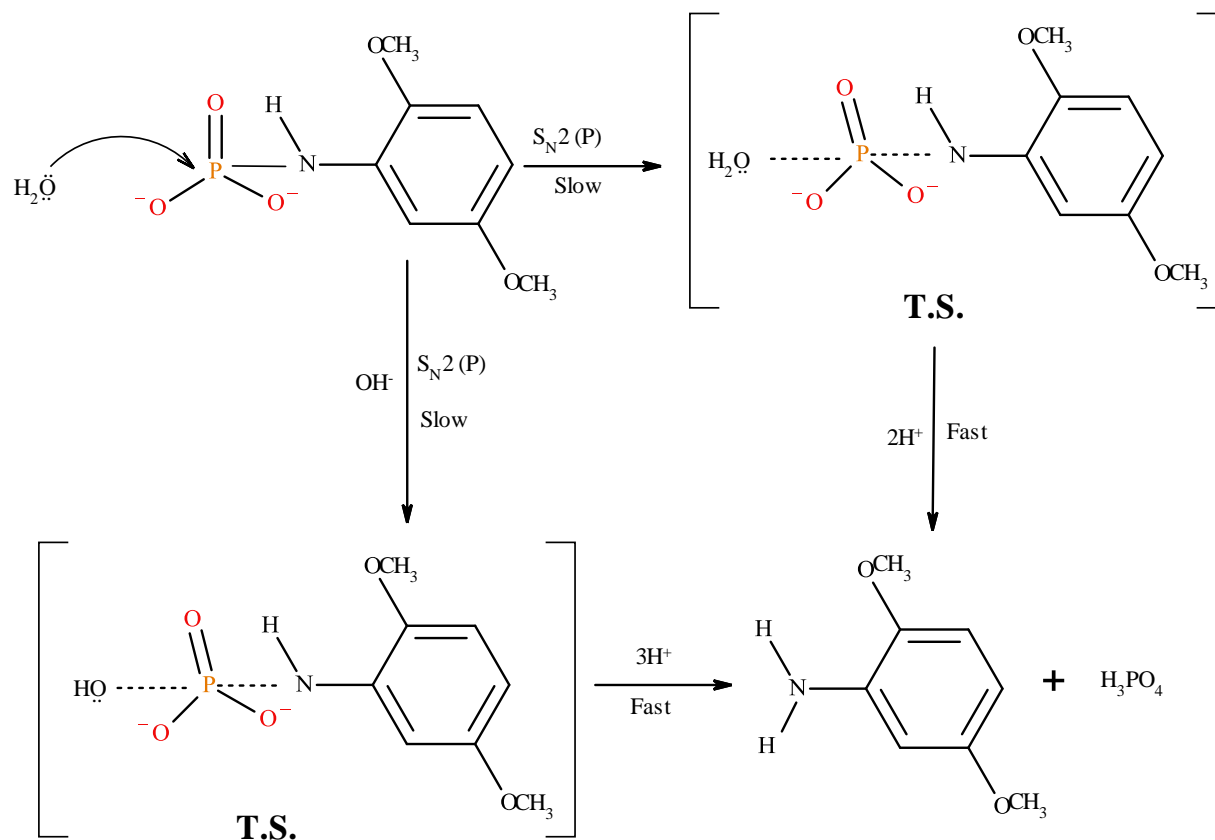
The value of K'_m can be obtained by analysis of the variations of K_s with D_n or by choosing conditions such that substrate is essentially fully micellar bound (Behme, M.T.A. et al., 1965).

The main features of mechanism of micellar catalyzed hydrolysis of with the hydroxide ion in presence of [CTABr] detergent (Kumar, A. 2016) may be concluded point wise under.

1. The study of substrate concentration effect found in significant increases in rates. Hence the reaction may be considered kinetically of first order.
2. The higher rate of mono-2,5-DMPP are in consistent in our observations, suggesting the intra molecular transfer of a protonation to the leaving group by concerted mechanism S_N^2 .
3. Since the only reactive species of mono-2,5-DMPP in the pH region 8.0 to 10.0 appears to favour nucleophilic attack by the hydroxide ion on the phosphorus atom of the group of phosphoramidate. However K_ψ the pseudo first order rate coefficient does not increase linearly with the increase of CTABr. Suggesting that the dianion of phenyl phosphoramidate intramolecularly involved in proton transfer to the leaving group in the transition state forming a metaphosphoramidate ion in bimolecular hydrolysis, which is more probable due to high negative value of entropy and energy of activation.
4. The nucleophile (OH⁻) anions bind strongly to the micelles in which dianion of mono-2,5-DMPP is buried in the interior of the micelles and suitably exposed to the nucleophilic attack of (OH⁻).

Above mentioned factors at least following reaction paths of dianion mono-2,5-DMPP are possible.

A comparative bimolecular nucleophilic attack of $[\text{OH}^-]$ and $[\text{H}_2\text{O}]$ at the phosphorus atom of dianion of mono- 2,5-DMPP.



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