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Kinetics of Hydrolysis of *p*-methoxyphenyl Phosphorotriamidate in the pH Region

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Hydrolysis of *p*-methoxyphenyl phosphorotriamidate has been carried out in the pH range 1.24 to 10.0 in 30% acetic acid at 65°C. A higher value of rate coefficients at pH 1.24 is based on the presence of conjugate acid form while the neutral form is active in the entire pH range examined. Three maxima are obtained at pH 4.17, pH 6.43 and pH 10, the first two corresponding to the maxima and minmma observed for the corresponding mono- and di-esters, at which pH both the esters. hydrolyse *via* their monoanion forms. Both the values are probably the mixed rates and are possibly not analysed by the methods used for this purpose. Arrhenius parameters favour bimolecular route of hydrolysis for the neutral form; solvent effect study carried out at pH 1.61 and 4.17 indicates that the rates are elevated (1.61 pH) nearly two and a half times, which is attributed to the lowering of dielectric constant of acetic acid medium which favours the reactions involving protonation. At pH 4.17, when the solvent in increased by nearly one and a half times, the rates are reduced but when the acetic acid is as high as 90% the rates are found to be doubled. Thus most probably here the solvent helps to stabilise the basic leaving group by some sort of salt formation. Comparative kinetic data of some triesters *via* their netural forms has been used to decide the P—N bond cleavage, depending upon the similarity in behaviour in all cases.

INTRODUCTION

Hydrolysis of *p*-methoxyphenyl phosphorotriamidate in the pH region 1.24 to 10.0 has been carried out with a view to finding out whether the operative and contributory forms are similar to those found in the triesters with C—O—P linkage or they are different.

EXPERIMENTAL

p-Methoxyphenyl phosphorotriamidate has been prepared by stirring *p*-anisidine and PCl_5 (3 : 1) in benzene for 18 h. It was recrystallised from dioxane-water mixture.

Kinetics of hydrolysis of *p*-methoxyphenyl phosphorotriamidate has been

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investigated in the pH range 1.24 to 10.0 in 30% acetic acid at 65°C. The progress of the reaction was followed by estimating the rate of appearance of inorganic phospate using Allen's modified method[1].

Buffers required for pH adjustments are employed as cited in different literatures[2, 3]. Concentration of the triester was maintained at 5×10^{-4} mol dm^{-3} throughout the study except when concentration effect was studied.

RESULTS AND DISCUSSION

Kinetic study of hydrolysis of *p*-methoxyphenyl phosphorotriamidate has been pursued in the pH region 1.24 to 10.0 in 30% acetic acid at 65°C. The fist order rate co-efficients have been calculated using the corresponding expression for first order determination and these are summarised in Table-1. Generally the undissociated form is expected to prevail in the entire pH range examined.

TABLE-1
OBSERVED RATE DATA FOR THE HYDROLYSIS OF *p*-METHOXYPHENYL PHOSPHOROTRIAMIDATE IN THE pH REGION 1.24 to 10.0 AT 65°C.

S.No.	pH	10^3 Ke min^{-1}	5 + log K_e
1.	1.24	0.150*	1.17
2.	1.61	0.099	0.99
3.	2.20	0.080	0.90
4.	2.50	0.089	0.95
5.	3.33	0.067	0.83
6.	3.70	0.130	1.11
7.	4.17	0.320	1.50
8.	5.10	0.042	0.62
9.	5.60	0.082	0.91
10.	6.43	0.220	1.34
11.	7.46	0.180	1.25
12.	8.00	0.180	1.25
13.	9.00	0.160	1.20
14.	10.00	0.260	1.41

*K_e calcd 0.17 (from salt effect studies) at 0.1 M.

The first order rate coeficients for this triester are higher at pH 1.24 which decrease slowly up to pH 3.33. After this the rates increase up to pH 4.17. The rates again decrease with another increase at pH 6.43. Beyond pH 7.00 the rates are reduced till pH 9.00 is reached, However, at pH 10.0 another elevation is observed. The first two maxima correspond to the maximum and minimum observed for the corresponding mono- and di-esters, in their pH log rate profiles respectively, where these two esters hydrolyse specifically *via* their monoanion forms. Thus the higher rates at both the values are probably the mixed rates and are possibly not analysed by the methods used for this purpose.

All the Arrhenius parameters[4] (Table-2) suggest the bimolecular route of hydroysis for the neutral fom of the *p*-methoxyphenyl phosphorotriamidate.

TABLE-2
ARRHENIUS PARAMETERS FOR THE HYDROLYSIS OF *p*-METHOXYPHENYL PHOSPHOROTRIAMIDATE AT DIFFERENT pH

pH	Energy of activation ('E')	Frequency factor ('A')	Entropy of activation ($\Delta S^{\neq}$)	Free Energy ($\Delta G^{\neq}$)
1.24	16.88 kcal/mole or 74.04 kJ/mole	1.28×10^{7} sec^{-1}	–31.91 e.u. or +137.2 JK^{-1} mol^{-1}	27.66 kcal/mole or 27.67 kJ/mole
8.0	10.49 k cal/mole or 43.88 kJ/mole	1.60×10^{3} sec^{-1}	–56.09 e.u. or +41.96 JK^{-1} mole^{-1}	29.72 kcal/mole or 29.70 KJ/moe

Solvant effect study was done at pH 1.61 and pH 4.17 (Table-3). At the lower pH the rates are elevated nearly two and half times with increase in the percentage of the polar solvent. This is attributed to a lowering of dielectric constant[5] which favours reactions involving protonation. At pH 4.17 when the solvent is increased by nearly one and a half times the rates are reduced to less than half the normal value, but when percentage of the solvent is as high as 90% the rates are found to be doubled suggesting that the solvent helps to stabilise the basic leaving product by some sort of salt formation. This also suggests the transition state with creation of charges.

TABLE-3
EFFECT OF SOLVENT ON THE HYDROLYSIS OF *p*-METHOXYPHENYL PHOSPHOROTRIAMIDATE IN THE pH REGION AT 65°C

S.No.	pH	Acetic acid (%)	10^{3} Ke min.$^{-1}$
1.	1.61	30	0.099
2.	1.61	60	0.227
3.	4.17	30	0.320
4.	4.17	45	0.190
5.	4.17	90	0.640

TABLE-4
COMPARATIVE KINETIC RATE DATA FOR THE HYDROLYSIS OF SOME TRIESTERS *via* THEIR NEUTRAL SPECIES.

Aniline triester	Temp. °C	10^{5} min.$^{-1}$	E (kcals/mole)	$-\Delta S^{\neq}$ eu	Mole-cularity	Fission	Ref.
o-CH_3	80	a	26.91	11.91	2	P—N	6
m-CH_3	80	12.5	12.79	39.83	2	P—N	7
p-CH_3	80	1.7	5.02	76.40	2	P—N	7
p-NO_2	98	3.8	10.07	62.37	2	P—N	8
m-NO_2	98	1.4	17.11	42.42	2	P—N	9
p-CH_3O	65	8.0	16.88	36.91	2	P—N	This work

Comparative kinetic data (Table-4) *via* the neutral forms of various triesters showing similarity in behaviour suggest P—N bond cleavage for this ester.

On the basis of above discussion the following mechanism has been suggested for the neutral form of the triamidate (Chart 1).

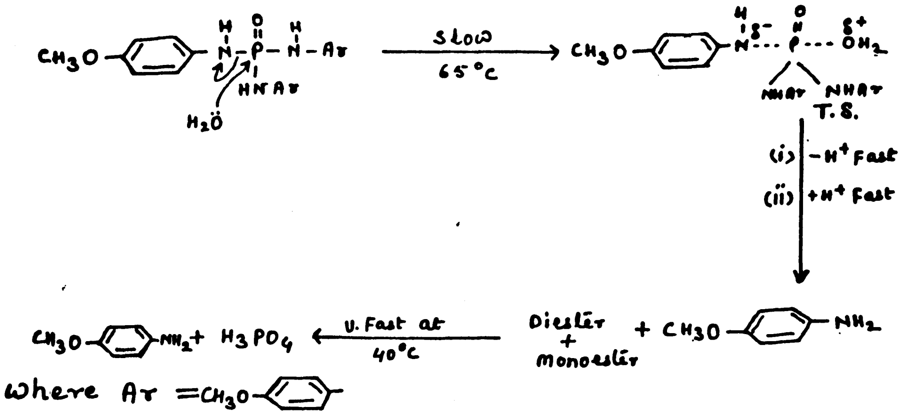

Chart-1. Bimolecular hydrolysis of the neutral form of triester

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