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Kinetic Study of the Hydrolysis of *p*-Anisidine Phosphoric Triamide (C—N—P) in Acid Medium

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Hydrolytic fragmentation of tri-*p*-anisidine orthophosphate has been pursued in the acid range 1.0 to 8.0 M-HCl in 20% acetic acid (v/v) at 65°C (± 0.5°C). Neutral electrolyte effect study reveals the contribution of conjugate acid form with the absence of any participation of the neutral form in the entire acid region examined. First order rate law best fits the results in the entire acid range, leading to overall pseudo-first order rate coefficients in the medium used. Solvent and solvent-isotope effect studies support the existence and contribution of monoprotonated species formed by a specific acid catalysed reaction for this triester bimolecular mode of hydrolysis is derived by the application of Arrhenius equation and various correlations given by Bunnett and others. The P—N bond cleavage is confirmed by comparison of kinetic and thermodynamic parameters of the closely related triamidates.

INTRODUCTION

The hydrolysis of this triester with C—N—P linkage was carried out in order to see whether the operative and contributory forms are the same as in the triester with C—O—P linkage or they are different.

EXPERIMENTAL

p-Methoxy phenyl phosphorotriamidate was prepared by stirring *p*-anisidine and PCl_5 (3 : 1) in benzene for about 18 h. It was recrystallised from dioxane and water mixture, m.p. 182°C (found: C 60.8; H 7.8; N 5.2; P 7.5%; calculated for $C_{21}H_{24}N_3PO_4$: C 61.0, H 5.8, N 10.1, P 7.5%).

All chemicals used were either of AnalaR or GR (SM) quality. Deuterium oxide was procured from Bhabha Atomic Research Centre, Trombay and its isotopic purity as reported was > 99.4%.

Kinetics of hydrolysis of *p*-methoxyphenyl phosphorotriamidate has been investigated in the acid range 1.0 to 8.0 M HCl in 20% (v/v) acetic acid at 65°C (± 0.5°C). The progress of the reaction was followed by estimating the rate of appearance of inorganic phosphate.[1] The concentration of the triester was maintained at 5×10^{-4} mol dm^{-3} throughout the study, except when its concentration effect was determined.

RESULTS AND DISCUSSION

The first order rate constants for the hydrolysis of tri-*p*-anisidine phosphate consistently increase with the increase in acid molarity up to 4.0 M, where the

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maximum appears. After this, the rates decrease gradually. This decrease in rates, after the maximum, is attributed either to the negative electrolyte effect or decrease in water activity or both.

In order to find and distinguish between the operative and reactive forms, ionic strength studies[2] have been carried out using appropriate proportions of sodium chloride and HCl. The fist order rate constants are summarised in Table-1. The addition of the electrolyte made the triester sparingly soluble in even acetic acid, so that a higher composition of acetic acid (24%) was required. The triester does behave like other triesters and gives three linear curves (Fig.1). All the curves

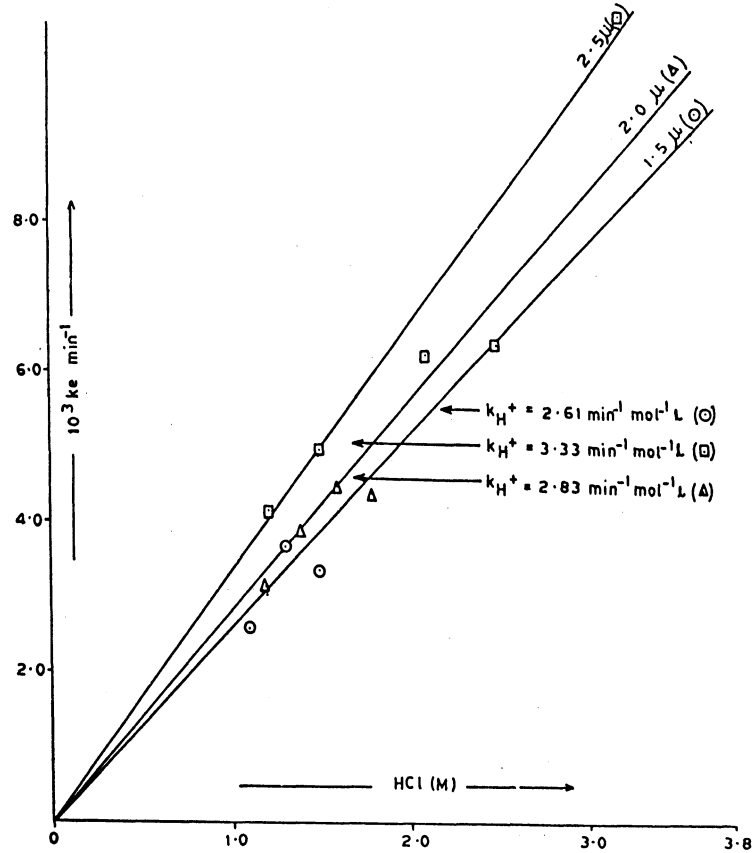


Fig. 1. Hydrolysis of tri-*p*-anisidne phosphate at constant ionic strengths at 65°c.

meet at the origin indicating the absence of the neutral form. it is noticed that these values when further modified give a linear curve (Fig.2). In order to analyse the observed rates for the sole reactive form, the conjugate acid species, of this triester, 2nd empirical term of the Debye-Hückel equation[3] has been used as below:

$$ke = k_{H^+} \cdot C_{H^+} \quad (i)$$

$$= k_{H^+} \cdot C_{H^+} \exp b_{H^+} \cdot \mu \quad (ii)$$

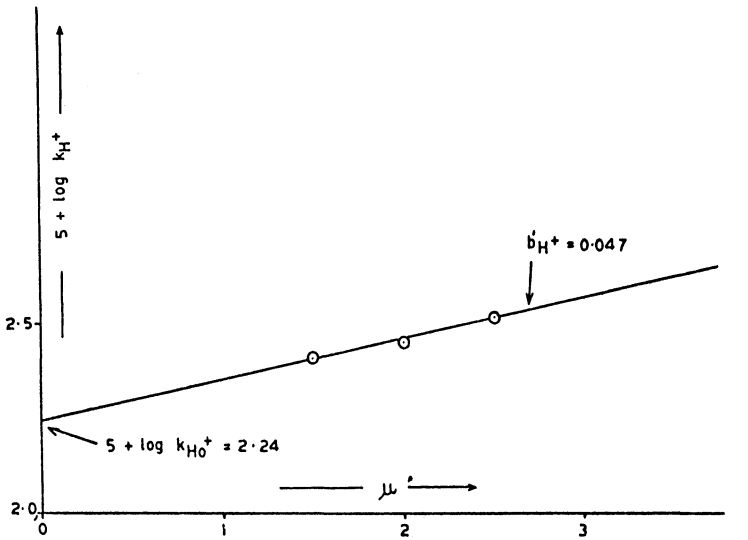


Fig .2. Plot of log acid-rates *vs.* ionic strengths for the hydrolysis of tri-*p*-anisidine phosphate at 65°C.

Thus the equation (ii) may be further modified for the conjugate acid form as:

$$5 + \log k_{H^+} C_{H^+} = 5 + \log k_{H_0^+} + \log C_{H^+} + b'_{H^+} \cdot \mu \qquad \text{(iii)}$$

The calculated rates thus obtained on the basis of equation (iii) agree closely with the observed rate (Table-1) especially in the low acid molarity (1.0 to 2.5 M-HCl). Beyond this the calculated rates are found to differ largely and these rates are due to the protonated form all alone. Thus only the conjugate acid form is present and is contributory.

TABLE-1
OBSERVED AND CALCULATED RATE DATA FOR THE HYDROLYSIS OF TRI-*p*-ANISIDINE PHOSPHATE AT 65°C

S. No.	Acid	log C_{H^+}	$10^3 k_{H^+} C_{H^+}$	10^3 ke (calcd.) min^{-1}	10^3 ke (obsd.) min^{-1}	4 + log ke (obsd.)
1.	1.0	0.00	1.94	1.94	2.68	1.43
2.	2.0	0.30	4.31	4.31	4.49	1.65
3.	2.5	0.40	5.69	5.69	6.05	1.78
4.	3.0	0.48	7.21	7.21	10.25	2.11
5.	4.0	0.60	10.72	10.72	19.12	2.28
6.	5.0	0.70	14.93	14.93	16.41	2.21
7.	6.0	0.78	19.96	12.28[a]	12.95	2.11
8.	7.0	0.84	25.95	9.99[b]	11.11	2.04
9.	8.0	0.90	33.05	9.59[b]	8.99	1.95

a – n = 1, b – n = 1.5 in $(aH_2O)_n$ in equation.

The lowering in rates after the maximum *i. e.* 4.0 M, is attributed to a decrease in water activity. At 5.0 M, the calculated rates resemble the observed rates, and do not require any explanation in terms of water activity. This factor becomes operative at 6.0 M and onwards when the number of water molecules vary from 1.0 to 1.5 and this has been determined by applying the modified form of Brönsted Bjerrum equation.[4]

$$\log ke = \log k_{H_0^+} + \log C_{H^+} + b'_{H^+} \cdot \mu + \log (a\, H_2O)_n \qquad \text{(iv)}$$

where n is the number of water molecules involved. Concepts of Hammett[5] and Zücker-Hammett[6] giving the value of slopes as 0.54 and 1.33 favour the bimolecular route of hydrolysis. Bunnett parameters[7] (w = 6.69 w* = – 0.86) are favourable for the participation of water molecule in the rate determining step. Value of ϕ (1.32) based on Bunnett and Olsen[8] plot postulates further that water acts as a proton-transfer agent. Arrhenius parameters[9] Table-2 account for the bimolecular route of hydrolysis. Both E (energy of activation) and E-based $\Delta S^{\neq}$ (entropy of activation) favour the presence and contribution of water molecule in the formation of a transition state. However all the Arrhenius parameters postulate a bimolecular mechanism.

TABLE-2
ARRHENIUS PARAMETERS AT DIFFERENT ACID MOLARITIES

HCl (M)	Energy of activation E	Frequency factor 'A' sec^{-1}	Entropy of activation $\Delta S^{\neq}$	Free energy $\Delta G^{\neq}$
3.0	18.69 kcal/mole or 78.20 kJ/mol	3.56×10^{11}	$-22.70\ e \cdot \mu$ or $153.3\ J\ K^{-1}\ mol^{-1}$	26.36 kcal/mole or 26.38 kJ/mole
5.0	13.68 kcal/mole or 57.23 kJ/mole	6.95×10^{9}	$-35.5\ e \cdot \mu$ or $+92.21\ J\ K^{-1}\ mol^{-1}$	26.04 kcal/mole or 26.07 kJ/mole

The solvent effect study was carried out to see the involvement of monoprotonated form in the present triester. At 2.0 M rates increase one and half times when the percentage of acetic acid was doubled and nearly about ten times with a large percentage of acetic acid (82%). This favours formation of an extremely large proportion of conjugate acid form of the triamidate. Similar study was carried out at 5.0 M which gaves similar results.

In order to find the nature of proton transfer in the pre-equilibrium step solvent-istope[10] effect study was done. The change over from an aqueous medium to 76% D_2O at 1.0 M leads to an increase in rates (nearly double) suggesting a fast pre-equilibrium proton transfer. The increase in rates in D_2O suggests a specific acid-catalysed reaction too which is also decided by ionic strength studies.

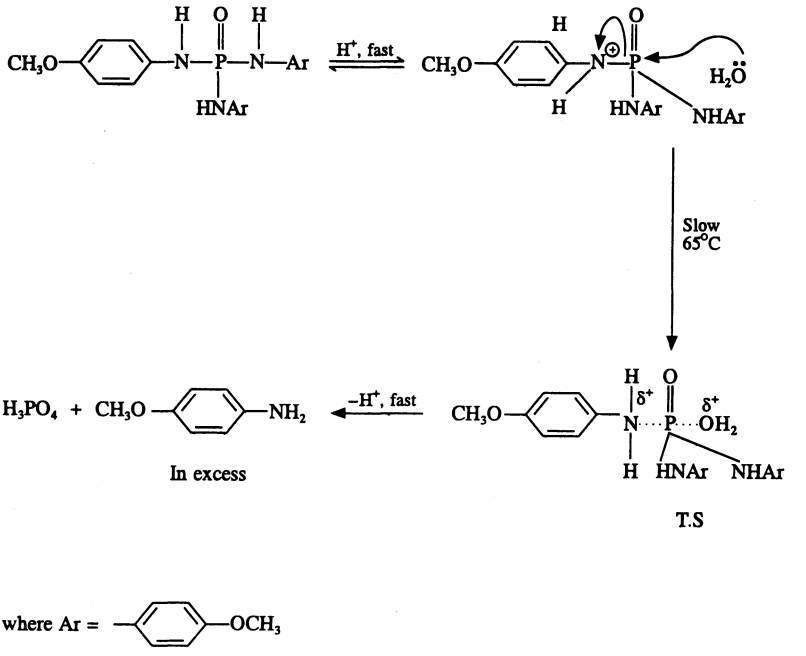
Common-ion effect study was performed using acetates of sodium and potassium. Here the rates at 1.0 M were examined in 24% acetic acid due to solubility reasons. Sodium acetate slightly increases the rates (2.68 to $2.89 \times 10^{-3}\ min^{-1}$) which may be due to the excess of the solvent present. On the

other hand potassium acetate loweres the rate of hydrolysis (2.68 to 1.47×10^{-3} $min.^{-1}$). The crystal radii of H and Na are nearly the same whereas that of K is different. This size difference is propably applicable here too, accounting for the difference in behaviour of the two reagents used for the bulky triester.

The concentration effect study was carried out at 2.0 and 4.0 M. The rates are found to be insensitive to concentration changes. Thus the reaction is proved to be of the first order type. The second reaction partner water, in this bimolecular reaction is always present in excess, so that the rates are better called as pseudo-first order rates.

Existence of the isokinetic relationship[11] ($\beta = 350.1°$) and comparative kinetic data Table-3 showing similarity in behaviour suggests P—N bond cleavage for this triester. This P—N bond fission is supported by the formation of a very stable free *p*-anisidine molecule. The magnitude of rates is the highest for this triester in the list of triesters included (Table-3) since the reaction occurs even at 65°C. As compared to similar triesters with *p*-substituents only, the lowest negative entropy value decreases rigidity of the transition state leading to its facile hydrolysis. The present triester behaves similarly undergoing bimolecular hydrolysis.

On the basis of above discussion the following solitary suitable mechanism may be suggested for the reactive conjugate acid form of the triester.



Mechanism of hydrolysis for the reactive conjugate acid form of the triester.

TABLE-3
COMPARATIVE KINETIC DATA AND ISOKINETIC RELATIONSHIP PLOT DATA FOR THE HYDROLYSIS OF SOME TRIESTERS*via* THEIR CONJUGATE ACID SPECIES

S. No.	Aniline triesters	Temp. °C	Maxima	10^3 ke min^{-1}	E kcals/mole	ΔS^* e · μ	Molecularity	Fission	Ref.
1.	*p*-CH_3	80	5.0 M	14.34	15.08	–25.85	2	P—N	12
2.	*m*-CH_3	80	3.5 M	14.78	14.62	–32.92	2	P—N	12
3.	*o*-CH_3	80	a	a	26.00	– 4.57	2	P—N	13
4.	*p*-Cl^-	90	4.0 M	14.4	11.44	–47.68	2	P—N	14
5.	2,4-dichloro	80	5.0 M	4.01	30.56	+ 6.27	1	P—N	15
6.	*p*-NO_2	98	2.0 M	0.77	15.25	–42.71	2	P—N	16
7.	*m*-NO_2	98	4.0 M	5.10	16.83	–34.53	2	P—N	17
8.	*p*-OC_2H_5	98	3.0 M	20.56	7.59	–52.20	2	P—N	18
9.	*p*-OCH_3^-	65	4.0 M	19.12	18.67	–22.70	2	P—N	This work

[a]Data not available.

REFERENCES

1. R.J.L. Allen, *Biochem. J.*, **34**, 858 (1940).
2. K.J. Laidler, Reaction Kinetics, Pergamon, London, Vol. II, pp. 63, 225 (1963).
3. F.A. Long and W.F. Me Devit, *Chem. Rev.*, **51**, 119 (1952).
4. P.W.C. Barnard, C.A. Bunton, D. Kellerman, M.M. Mhala, B. Silver, C.A. Vernon and V.A. Welch, *J. Chem. Soc.* p. 227 (1966).
5. L.P. Hammett, Physical Organic Chemistry, McGraw-Hill, New York (1940).
6. L. Zücker and L.P. Hammett, *J. Am. Chem. Soc.*, **61**, 2791 (1936).
7. J.F. Bunnett, *J. Am. Chem. Soc.*, **83**, 4956 (1961).
8. J.F. Bunnett and Olsen, *Can. J. Chem.*, **44**, 1899, 1917 (1966).
9. S. Arrhenius *Z Phys. Chem.*, **4**, 226 (1889).
10. R.D. Gilliom, Introduction to Physical Organic Chemistry, Addison Wesley, p. 200 (1970).
11. N.B. Chapman and J. Shorter, Advances in Linear Free Energy Relationship, Plenum Press, London, pp. 204, 309 (1972).
12. A.K. Bhoite, Ph.D. Thesis, Jiwaji University, Gwalior (1977).
13. A.N. Sagne, Ph.D. Thesis, Jiwaji University, Gwalior (1972).
14. (Miss) N. Agarwal, Ph.D. Thesis, Jiwaji University, Gwalior (1983).
15. (Miss) R. Shrivastav, Ph.D. Thesis, Jiwaji University, Gwalior (1972).
16. P. Jain, Ph.D. Thesis, Jiwaji University, Gwalior (1982).
17. (Miss) K. Kulshrestha, Ph.D. Thesis, Jiwaji University, Gwalior (1982).
18. A.K. Bhadoria, Ph.D. Thesis, Jiwaji University, Gwalior (1982)

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