Kinetics & Mechanism of Oxidation of Aralkyl Amines by Peroxomonophosphoric Acid

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Peroxomonophosphoric acid oxidises N-methylaniline and N-ethylaniline smoothly, in the pH range 0-10, beyond which no reaction is observed. p-Aminophenol is found to be the major reaction product. A rate law consistent with the results has been proposed. This takes into account the different oxidant species involved in the oxidation process.

PEROXOMONOPHOSPHORIC acid (PMPA) oxidations differ significantly from other peracid oxidations in respect of the number of reactive species involved which in turn depend upon the medium and the nature of the substrate employed. This is well reflected in the oxidation of aromatic aldehydes[1], dialkyl sulphides[2], dimethyl sulphoxide[3], thiophenoxyacetic acids[4], aromatic amines[5] and hypophosphite[6]. Oxidation of primary aromatic amines by PMPA[7] follows a pH-rate profile which is characteristic of the substrate and shows a marked difference from that of tertiary amine[5] oxidations. The products of oxidation of aniline[7] by PMPA are p-aminophenol, azobenzene, azoxybenzene and p-benzoquinone in aqueous medium. Interestingly, however, phosphate ester[8] has also been isolated as one of the products in the presence of acetone. In view of the divergent results obtained under different conditions in the oxidation of amines, it was considered desirable to study the hitherto unreported oxidation of aromatic secondary amines by PMPA.

Materials and Methods

N-Methylaniline (NMA) and N-ethylaniline (NEA), both BDH products, were distilled before use. Acetonitrile was distilled over P_2O_5 b.p. 81-82°C. Carbonate free NaOH was prepared and standardised against succinic acid with phenolphthalein as indicator. $HClO_4$, potassium hydrogen phthalate, KH_2PO_4, Na_2HPO_4 and NaOH were used to maintain pH. PMPA was prepared afresh by acid hydrolysis of $K_4P_2O_8$ which is a two stage consecutive reaction[9].

$$H_4P_2O_8 + H_2O \rightarrow H_3PO_5 + H_3PO_4$$
$$H_3PO_5 + H_2O \rightarrow H_2O_2 + H_3PO_4$$
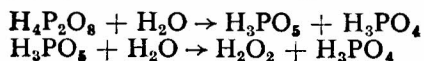
The rate of PMPA hydrolysis to H_2O_2 is at least two orders of magnitude slower than the rate of hydrolysis of PDP to PMPA[10] and is negligible at $[H^+] < 1M$.

Kinetic run — In a typical procedure, a known quantity of $K_4P_2O_8$ was dissolved in conductivity water (10 ml) and to this was added a calculated amount of standard $HClO_4$ to get an acid strength of 0.5 M in 50 ml. The solution was made up to 50 ml and thermostated at 35°C for 3.5 hr till hydrolysis was complete (> 98 %). For runs which necess-, sitated the use of buffers, the acid after hydrolysis was completely neutralised by adding standard NaOH and calculated amount of buffers were weighed into the flask to get the desired pH. The pH of the solution was measured at the end of each run with the help of a Systronics digital pH-meter 335. The progress of the reaction was monitored by estimating the residual PMPA by iodometry at pH 4-5 (acetic acid-sodium acetate buffer) with a drop of 1% ammonium molybdate solution[1]. In each case kinetics were followed up to 70% completion of the reaction with respect to PMPA. All the reported rate constants computed by the usual method are reproducible within ± 5%. Least squares analysis of the rate laws were done with the help of a DCM Microsystem 1121.

Stoichiometry and product analysis — The stoichiometric runs conducted at pH values 0.5 and 4.8 indicate 1 : 1 stoichiometry for the oxidation of secondary amines giving p-aminophenol (m.p. 185°C) which was isolated and fully characterised.

Results and Discussion

Oxidation of both NMA and NEA is smooth in aqueous acetonitrile (10% v/v) at ambient temperatures in the pH range 0-10.0. The rate data at constant acidity affords the rate law,

$$\text{Rate} = k_2'[\text{Amine}]_T \, [\text{PMPA}]_T$$

where k_2' is the observed second order rate constant, and the subscript T refers to total analytical concentration. The rate constants at various initial concentrations of substrate and oxidant are listed in Table 1. The kinetic experiments, when repeated in the presence of varying concentrations of salts like $NaClO_4$ or KNO_3 keeping all other conditions constant, do not lead to any change in rate data. Similarly, varying [sodium acetate] or [potassium hydrogen phthalate] at constant pH also does not affect the rate constants. These observations conclusively

TABLE 1 — SECOND ORDER RATE CONSTANTS AT VARIOUS INITIAL CONCENTRATIONS OF THE AMINE-PMPA REACTION IN AQUEOUS ACETONITRILE;10% v/v) AT 35°C AND $\mu = 0.25M$

[PMPA] × 10⁴ (M)	[Amine] × 10³ M	k'_{2obs} (litre mol⁻¹ min⁻¹)
	N-METHYLANILINE; $pH = 1.25$	
2.44	3.93	1.57
4.45	3.93	1.58
7.75	3.93	1.60
4.45	7.84	1.59
4.24	9.35	1.61
4.24	12.87	1.58
4.49	8.61	1.57ᵃ
4.49	8.61	1.60ᵇ
	N-ETHYLANILINE; $pH = 0.94$	
2.52	3.47	0.47
4.03	3.47	0.46
6.04	3.47	0.47
3.94	6.94	0.47
4.32	8.52	0.46
4.32	10.33	0.47

(a) [acrylamide] = 1×10^{-3} M
(b) $\mu = 0.5M$

demonstrate that the main reaction is either between a dipole and a dipole or an ion and a dipole[11].

The rate increases in the pH range 0–5 and thereafter it decreases with further increase in pH of the medium and becomes negligible beyond pH 8. Although the kinetics could not be followed in the pH range 4–6 due to high relative rate of the reaction, existence of a maximum rate in the pH range is discernible, or in other words a single bell shaped pH profile exists for the reaction in the entire pH range unlike the aminobenzoic acid oxidations[12]. However,
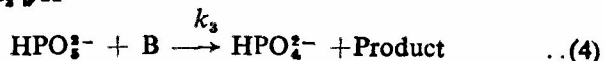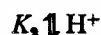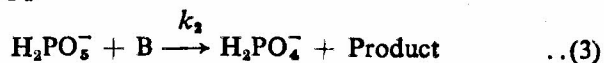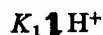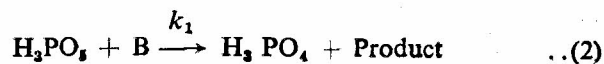
a rough estimate from k'_2 versus pH plots suggests that the maximum in the pH-rate profile occurs at a pH 5.0 ± 0.4 for both NMA and NEA, which also corresponds to pK_a values of the amines.

Activation parameters have been evaluated (Table 2) from the linear Arrhenius plots of log k'_2 versus T^{-1} by measuring the rate of oxidation at four temperatures in the range 303–323 K.

The bell shaped log k'_2 versus pH profile strongly suggests that various species of the oxidant differing in degrees of protonation, oxidise the substrate molecule simultaneously, which is also involved in a protonation equilibrium (1),

$$C_6H_5 - \overset{+}{N}H_2R \overset{K_a}{\rightleftharpoons} C_6H_5 - NHR + H^+ \quad ..(1)$$
$$(BH^+) \qquad\qquad\qquad (B)$$
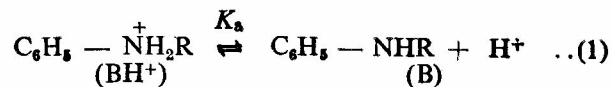
where R = —CH₃ or — C₂H₅, BH⁺ and B are the protonated and unprotonated amines respectively. Considering this the various steps involved in the oxidation of NMA and NEA by PMPA are represented by Eqs (2) to (4),

$$H_3PO_5 + B \overset{k_1}{\longrightarrow} H_3PO_4 + Product \quad ..(2)$$

$$K_1 \updownarrow H^+$$

$$H_2PO_5^- + B \overset{k_2}{\longrightarrow} H_2PO_4^- + Product \quad ..(3)$$

$$K_2 \updownarrow H^+$$

$$HPO_5^{2-} + B \overset{k_3}{\longrightarrow} HPO_4^{2-} + Product \quad ..(4)$$

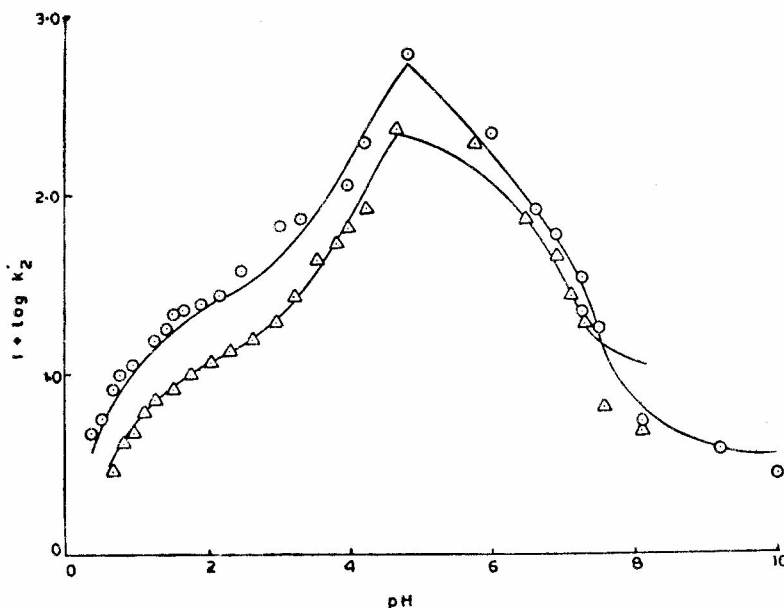where $K_1 = 0.08$ and $K_2 = 4.2 \times 10^{-6}$ mol litre⁻¹.

Fig. 1 — Plots of second order rate constants versus pH for N-methylaniline (O) and N-ethylaniline (△) [Points represent k_{2obs} values and the line has been drawn using k_{2calc}. values]

TABLE 2 — ENTHALPY AND ENTROPY OF ACTIVATION FOR THE AMINE-PMPA REACTION IN AQUEOUS ACETONITRILE

[Solvent : aq. acetonitrile (10% v/v); $pH = 1.2$; temp. 308K]

Substrate	$\Delta H\ddagger$ (kJmol^{-1})	$\Delta S\ddagger$(JK^{-1} mol^{-1})
NMA	84.6 ± 0.05	+ 2.2 ± 0.2
NEA	73.7 ± 0.05	—38.1 ± 0.2

TABLE 3 — SECOND ORDER RATE CONSTATS (litre mol^{-1} min^{-1}) OF DIFFERENT PMPA SPECIES

Substrate	k_1	k_2	k_3	S.D.
NMA	13500	144	0.38	12%
NEA	13140	97	0.84	10%

TABLE 4 — pH DEPENDENCE OF THE AMINE-PMPA REACTION IN AQUEOUS ACETONITRILE (10% v/v) AT 35°C

pH	k_2' (litre mol^{-1} min^{-1})		pH	k_2'(litre mol^{-1} min^{-1})	
	Obs	Calc		Obs	Calc
	N-METHYLANILINE			N-ETHYLANILINE	
0.35	0.48	0.36	0.64	0.31	0.33
0.48	0.58	0.46	0.80	0.43	0.43
0.65	0.82	0.63	0.94	0.47	0.53
0.95	1.17	1.01	1.25	0.72	0.75
1.26	1.60	1.42	1.49	0.85	0.92
1.39	1.87	1.61	1.75	1.05	1.71
1.51	2.23	1.75	2.05	1.20	1.22
1.67	2.32	1.93	2.32	1.41	1.35
1.94	2.45	2.23	2.58	1.58	1.51
2.14	2.80	2.43	2.67	1.60	1.58
2.45	3.78	2.80	2.95	1.98	1.91
2.99	6.86	4.23	3.20	2.83	2.41
3.33	7.64	6.42	3.50	4.37	3.52
3.88	11.00	15.00	3.58	4.59	3.96
4.22	20.00	27.00	3.81	5.66	5.70
4.83	62.00	55.00	3.95	6.77	7.22
5.97	22.00	28.00	4.22	8.24	11.00
6.60	8.32	8.33	4.67	24.00	22.00
6.87	5.95	4.80	5.78	22.00	22.00
7.26	3.35	2.22	6.48	7.80	7.54
7.53	1.81	1.37	6.88	4.92	3.70
8.10	0.56	0.64	7.11	2.84	2.56
9.21	0.39	0.39	7.30	2.07	1.96
10.00	0.28	0.37	7.56	0.68	1.46
			8.12	0.51	1.02

The reasons for not considering oxidation by PO_4^{3-} species resulting from dissociation of HPO_4^{2-} are evident from the following discussion.

The first, second and third dissociation constants of PMPA are 0.08, 4.2×10^{-6} and 1.6×10^{-13} mol litre^{-1} respectively[13] at 25°C. Therefore the abundance of different PMPA species, viz. H_3PO_5, $H_2PO_5^-$, HPO_5^{2-} and PO_5^{3-} at different pH values as reported by Battaglia and Edwards[10] are: H_3PO_5 and $H_2PO_5^-$ (pH 0-2); $H_2PO_5^-$ and HPO_5^{2-} (pH 4-7); HPO_5^{2-} and PO_5^{3-} (pH 7-11); and PO_5^{3-} (above pH 11.0). In the present study above pH 8 the rate for NMA is very small and no reactivity is observed for NEA. All these facts eliminate the possibility of oxidation by PO_5^{3-} species. This is not surprising in view of greater nucleophilicity and negligible electrophilicity of PO_5^{3-}. Hence the third dissociation is not considered significant for the oxidation of secondary amines.

In the [H$^+$] range employed, the total [PMPA] can be broadly expressed as,

$$[PMPA]_T = [H_3PO_5] + [H_2PO_5^-] + [HPO_5^{2-}] \quad ..(5)$$

and that of amine by the expression,

$$[Amine]_T = [BH^+] + [B] \quad ..(6)$$

We do not envisage oxidation steps to include protonated amine molecules for the well known reasons, that the protonated amine nitrogen is devoid of any nucleophilicity and hence not likely to be attacked by the peracid[5]. Earlier findings in this laboratory[2,12] and elsewhere[5] have already established that peracid oxidations are facile when substrates involve nucleophilic centers.

Therefore the rate law can be visualised as,

$$-d[PMPA]/dt = k_1[H_2PO_5][B] + k_2[H_2PO_5^-][B] + k_3[HPO_5^{2-}][B] \quad ..(7)$$

In the pH range under examination the rate law (7) can be rearranged to,

$$-\frac{d[PMPA]}{dt} = \frac{k_1[H^+]^2 + k_2K_1[H^+] + k_3K_1K_2)}{([H^+]^2+K_1[H^+]+K_1K_2)(1+[H^+]/K_a)}[PMPA]_T[Amine]_T \quad ..(8)$$

where

$$k_2'_{obs} = \frac{k_1[H^+]^2 + k_2K_1[H^+] + k_3K_1K_2}{([H^+]^2+K_1[H^+]+K_1K_2)(1+[H^+]/K_a)} \quad ..(9)$$

The second order rate constants k_1, k_2 and k_3 (Table 3) were evaluated by the least esquares analysis applied to the data in Table 4. For the solution of
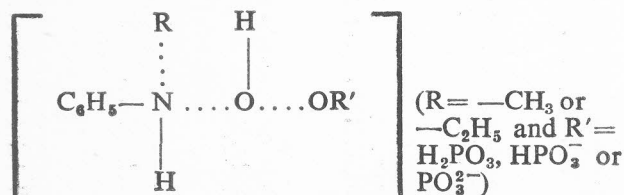
Eq. (9) the dissociation constants K_1 and K_2 of PMPA as given by Battaglia and Edwards[12] were used, The K_a (1.4×10^{-5} mol litre^{-1} for NMA and 7.8×10^{-6} mol litre^{-1} for NEA) values computed from pK_a of bases reported in the literature[14] were employed. The hydrogen ion concentrations were evaluated from experimentally measured pH values of the reaction system. k_1, k_2 and k_3 were used to calculate the over all $k_2'_{calc}$ from the rate expression at different pH values. Comparison of $k_2'_{obs}$ values with $k_2'_{calc}$ values in Table 4 shows a fair agreement and validity of the rate expression derived (Eq. 9) is thus established. Slight deviations of calculated data from experimental results in certain pH regions might be due to contributions from less abundant species, which are difficult to estimate.

Close scrutiny of the k_1, k_2 and k_3 values for both the amines shows the order as $k_1 > k_2 > k_3$. Since these are rate constants associated with different oxidant species, the relative order of reactivities among them shall therefore be $H_3PO_5 > H_2PO_5^- > HPO_5^{2-}$, which also parallels the order of decreasing electrophilicity of the oxidant species[5].

Between NMA and NEA, the former reacts faster than the latter, although nucleophilicity of the former is less than that of the latter. This reversal in reacti-

vity can be attributed to steric factors[15] in NEA, which has a destabilising influence on the transition state.

Mechanism — The results indicate a polar mechanism involving a bimolecular transition state in which both the reactant species are participating. The low positive or low negative entropy of activation (Table 2) indicates that the bond cleavage is much faster than the bond formation between the reactant molecules. That the N-alkyl bond is cleaved rather than the N-H bond is supported by the low positive or low negative entropy. N-H bond cleavage will result in appreciable entropy difference. The cleavage of N-alkyl bond has also been postulated in H_2O_2 and Caro's acid oxidations of secondary amines earlier[16]. Hence the transition state can be picturised as,

$$\left[\begin{array}{c} R \qquad\quad H \\ \vdots \qquad\quad | \\ C_6H_5-N \ldots O \ldots OR' \\ | \\ H \end{array} \right] \quad \begin{array}{l}(R=-CH_3 \text{ or} \\ -C_2H_5 \text{ and } R'= \\ H_2PO_3, HPO_3^- \text{ or} \\ PO_3^{2-}) \end{array}$$

from which phenylhydroxylamine can be expected to result.

Once the phenylhydroxylamine is formed either it can undergo, in a fast step, further oxidation to nitroso derivative followed by condensation with un-reacted substrate or rearrangement[17] in the presence of acid to yield *p*-aminophenol. Since in our present study we could only isolate *p*-aminophenol, it is presumed that mostly rearrangement step has occurred. Incidentally *p*-aminophenol is found to be stable towards PMPA under the experimental conditions. This finds support from the observed stoichiometry and is also in agreement with observations of Boyland and Manson[8].

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