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Kinetics & Mechanism of Oxidation of Sulphanilamide by Peroxomonophosphoric Acid

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Oxidation of sulphanilamide by peroxomonophosphoric acid (PMPA) in the *p*H range 0-7 is first order both in [PMPA] and [sulphanilamide]. Dependence in $[H^+]$ is complex and rate-*p*H profile shows rate maximum around *p*H 1.1. The observed data have been rationalised in terms of an electrophilic attack by neutral PMPA species namely H_3PO_5 on the amino group of sulphanilamide.

The title investigation forms a part of a broad programme from our laboratory on peroxomonophosphoric acid oxidation of aminobenzoic acids[1], aminopyridine[2], aniline[3], sulphanilic acid[4] etc.

Materials and Methods

All the chemicals were of AR grade. All solutions were prepared in conductivity water. PMPA was prepared by acid hydrolysis of $K_4P_2O_8$ (ref. 5) and its concentration checked frequently by iodometry. The self decomposition was found negligible in the *p*H region examined. The acidity was adjusted by adding appropriate amounts of perchloric acid or standard buffers[6]. Sulphanilamide (EGA-CHEMIE, W. Germany) was used after checking its purity.

The kinetics was followed upto three half-lives under pseudo-first order conditions in the temperature range 35-50°C by measuring the rate of disappearance of PMPA iodometrically, in acetic acid-acetate buffer medium (*p*H 4-5) containing a drop of ammonium molybdate solution[7]. The rate constants were computed by the usual method and were found to be reproducible within ±7-10%. Dissociation constant (K_h) for the conjugate acid was measured by *p*H-metric titration of hydrochloride of sulphanilamide. *p*H values were reproducible within ±0.05 *p*H units.

Results

Good agreement (within 10%) was noticed in the first order rate constant values calculated upto three half-lives for each run and those obtained from the slopes of the linear plots of log[PMPA] versus time. No change in the values of first order rate constants was noticed even in repeating experiments with varying [PMPA] but constant [sulphanilamide] and *p*H (Table 1). At fixed [PMPA] and [acid] with [sulphanilamide] varying, the k_1 values (Table 1) increased with increase in [sulphanilamide] and k_2 ($= k_1/$[sulphanilamide]) was constant indicating order in sulphanilamide to be one.

Table 1—Rate Constants for the Oxidation of Sulphanilamide in Aqueous Medium by Peroxomonophosphoric Acid (PMPA)

Temp. °C	*p*H (±0.02)	10^3 [Sulphanilamide] (mol dm^{-3})	10^4 [PMPA] (mol dm^{-3})	$10^4\,k_1$ (s^{-1})	$10^2\,k_2$ (dm^3 mol s^{-1})
35	0.85	2.903	2.573	2.04	
	0.85	2.903	5.1	1.99	
	0.85	2.903	6.3	1.85	
	0.85	2.903	7.6	1.95	
	1.12	1.742	4.105	1.24	7.16
	1.12	2.915	4.105	2.24	7.69
	1.12	5.772	4.105	3.92	6.79
	1.12	5.8	4.105	4.09	7.04
	1.12	8.7	4.105	6.51	7.4
	1.12	11.6	4.105	9.25	7.9
40	1.12	2.903	4.105	2.52	8.68
45	1.12	2.903	4.105	4.42	15.22
50	1.12	2.903	4.105	4.91	16.90

Since the rates were not influenced by added salts, no attempt was made to maintain the ionic strength constant during the rate measurement. The plot of k_{obs} versus *p*H (varied from 0 to 7) at 45 and 50°C, showed rate maximum around *p*H 1.1 indicating participation of different species of PMPA resulting from dissociation as well as involvement of protonation equilibria of sulphanilamide.

Addition of acrylamide did not affect the kinetic results or produce any turbidity indicating that no radical intermediate is involved in the oxidation of sulphanilamide by PMPA.

Under the condition [sulphanilamide] ≫ [PMPA], one mol of PMPA was found to consume one mol of sulphanilamide. However, the product of oxidation could not be isolated. It may be concluded that sulphonamide derivative of hydroxylamine is formed since the NH_2 group is converted into NHOH when heterolytic oxidation occurs. Further the reaction mixtures were almost colourless. Formation of condensation products like azo or azoxy derivatives would have resulted in coloured mixtures. This is at variance with the observations of Srivastava *et al.*[8] who identified the corresponding azoxy derivative in the oxidation of sulphanilamide with peroxodisulphate ion.

Plots of log k_2 (*p*H = 1.1 ± 0.02) versus 1/T (T varied in the range 308 to 323 K) were linear. The energy of activation E_a and entropy of activation $\Delta S^{\ddagger}$ were calculated from the linear plots and the values were found to be 34.1 kJ mol^{-1} and −213 J K^{-1} mol^{-1} respectively in the *p*H range 2.0 to 5.0.

Discussion

Based on the kinetic results, the rate law can be expressed by Eq. (1) at constant acidity

$$\text{Rate} = k' [\text{Sulphanilamide}]_T [\text{PMPA}] \quad \ldots (1)$$

where k' is the second order rate constant and the subscript T denotes total concentration. The rate maximum at *p*H 1.1 may arise from contribution of proton dissociation equilibria for both the oxidant and substrate. The PMPA is known to undergo dissociation as shown by Eqs (2-4) (ref. 9).

$$H_3PO_5 \rightleftarrows H_2PO_5^- + H^+ \ (K_1 = 8 \times 10^{-2} \text{ at } 25°C) \quad \ldots (2)$$

$$H_2PO_5^- \rightleftarrows HPO_5^{2-} + H^+ \ (K_2 = 4.2 \times 10^{-6}) \quad \ldots (3)$$

$$HPO_5^{2-} \rightleftarrows PO_5^{3-} + H^+ \ (K_3 = 1.6 \times 10^{-13}) \quad \ldots (4)$$

The proton dissociation constants[9] suggest that in the *p*H region 0-2 PMPA exists as H_3PO_5 and $H_2PO_5^-$, former being present in significant concentration over the latter. It is reasonable to expect that in the *p*H range 0-1, it is H_3PO_5 species which is most important and hence any reaction in this region is due to neutral H_3PO_5. This is consistent with the idea put forth by Secco and Venturini[10] who demonstrated higher reactivity of H_3PO_5 over $H_2PO_5^-$ in terms of greater leaving group ability of H_3PO_4 over $H_2PO_4^-$. Equilibrium given by Eq. (4) is of little significance.

Sulphanilamide is also likely to be protonated in this *p*H region and equilibrium (5) may be important.

$$BH^+ \overset{K_h}{\rightleftarrows} B + H^+ \quad \ldots (5)$$

where $B = (p)H_2NC_6H_4SO_2NH_2$

However, the value of K_h is not available and hence it has been measured by *p*H-metric titration of sulphanilamide hydrochloride. The K_h value comes out to be $\sim 1 \times 10^{-3}$. This suggests substantial protonation of sulphanilamide below *p*H 3. As has been established in our earlier work[1-4] oxidations by PMPA are basically polar in nature and nucleophiles are oxidised with ease. In the present case the amino group gets protonated (Eq. 5) and it is the unprotonated sulphanilamide molecule which undergoes oxidation with PMPA. However, the protonated species is not capable of reacting with PMPA presumably due to reduced nucleophilicity as indicated by very slow reactivity at high $[H^+]$ (*p*H < 1). The observed rate maximum at *p*H 1.1 can be rationalised as follows:

As *p*H increases, the equilibrium concentration of neutral sulphanilamide increases and it is this species which undergoes oxidation. Similarly with increase in *p*H, H_3PO_5 concentration decreases from a high value and $H_2PO_5^-$ slowly accumulates and in significant amount after *p*H 2. Therefore, initial increase in rate with increase in *p*H from 0 to 1.1 is due to increase in neutral sulphanilamide concentration and this species is oxidised by H_3PO_5 only because of its higher nucleophilicity. As no $H_2PO_5^-$ species is available in significant amount at *p*H 1.1, one cannot expect any reaction between sulphanilamide and $H_2PO_5^-$ below *p*H 1.1. As *p*H increases beyond 1.1, $H_2PO_5^-$ slowly starts accumulating and hence one can expect oxidation of sulphanilamide by both H_3PO_5 and $H_2PO_5^-$.

In view of the experimental results obtained, the reaction steps involving oxidation of sulphanilamide may be visualised as shown in Scheme 1.

$$BH^+ \overset{K_h}{\rightleftarrows} B + H^+$$

$$H_3PO_5 \overset{K_1}{\rightleftarrows} H_2PO_5^- + H^+$$

$$B + H_3PO_5 \xrightarrow{k_1} \text{Product} + H_3PO_4$$

$$B + H_2PO_5^- \xrightarrow{k_2} \text{Product} + H_2PO_4^-$$

Scheme 1

These steps lead to rate law (6)

$$-\frac{d[\text{PMPA}]_T}{dt} = k_1[B][H_3PO_5] + k_2[B][H_2PO_5^-] \quad \ldots (6)$$

Equilibrium concentration can be expressed by the following relationships in terms of their total concentrations, since whole of PMPA in the *p*H range studied would be present as H_3PO_5 and $H_2PO_5^-$ only.
From Eq. (5), we get,

$$[B] = \frac{K_h[B]_T}{K_h + [H^+]} \quad \ldots (7)$$

From Eqs 2 and 3,

$$[H_3PO_5] = \frac{[H^+]}{K_1 + [H^+]}[\text{PMPA}]_T \quad \ldots (8)$$

and

$$[H_2PO_5^-] = \frac{K_1}{K_1 + [H^+]}[\text{PMPA}]_T \quad \ldots (9)$$

Substituting Eqs 7-9, in the rate expression (6) we get Eq. (10)

$$-\frac{d[\text{PMPA}]_T}{dt} = \frac{k_1 K_h[H^+] + k_2 K_h K_1}{(K_h + [H^+])(K_1 + [H^+])}[B]_T[\text{PMPA}]_T \quad \ldots (10)$$

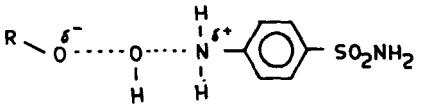
Equation (10) is similar to Eq. (1) where

$$k' = \frac{k_1 K_h[H^+] + k_2 K_h K_1}{(K_h + [H^+])(K_1 + [H^+])}$$

Validity of the rate expression (Eq. 10) consequently of the oxidation steps represented by Eq. (5) and the last two steps in Scheme 1 would require that plot of $k'(K_h + [H^+])(K_1 + [H^+])$ versus $[H^+]$ should be linear with a positive slope and positive intercept. To test this, K_1 reported by Battaglia and Edwards[9] and K_h values determined by us were used to evaluate the left hand side term. In fact such a plot was linear with a positive slope but almost negligible intercept. As the rate expression (Eq. 10) suggests the slope and intercept should be a measure of k_1 (oxidation brought by H_3PO_5) and k_2 (oxidation by $H_2PO_5^-$) respectively. However, zero intercept signifies that the second term in Eq. (10) i.e. $k_2 K_1 K_h$ is equal to zero. Since K_1 and K_h are finite, it implies k_2 shall be either zero or negligibly small. Hence the contribution to the rate of oxidation by $H_2PO_5^-$ species is not very significant. It can therefore be concluded that oxidation of sulphanilamide is only affected by H_3PO_5 but not by any of the charged PMPA species. In the same way it can be concluded that protonated sulphanilamide, is also inert towards the oxidant species. Consequently the reaction step which should rightfully represent the oxidation process is

$$B + H_3PO_5 \xrightarrow{k_1} \text{Product} + H_3PO_4 \text{ (see Scheme 1)}$$

This mechanism of the reaction in essence would be a polar one involving electrophilic attack on the lone pair of nucleophilic amino group in the rate-limiting step forming a bimolecular S_N2 transition state (A).



(A)

where R = H_2PO_3 or HPO_3^-

This is supported by the observed kinetic data and large negative entropy of activation which indicates a large structured unit with much decreased rotational and vibrational degrees of freedom[11].

The mechanism postulated here is different from that of the oxidation of sulphanilamide by $S_2O_8^{2-}$ proposed by Srivastava and others[8] which essentially involved a radical process. These workers observed that the rate increased upto a *p*H of 5.34 only beyond which the rate remained constant and no sharp maximum was reported.

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