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# Kinetics of oxidation of pyridoxine by manganese (III) in pyrophosphate medium

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Manganese(III) has been stabilised in weakly acidic solution by means of pyrophosphate and the nature of the complex formed elucidated spectrophotometrically. Stoichiometry of manganese(III) oxidation of pyridoxine hydrochloride (PRX) in pyrophosphate medium has been established in the *p*H range below 1 to 5 by iodometric, gravimetric and spectrophotometic methods. Kinetics of the reaction has been studied over the *p*H range 2.5 to 3.5. The oxidation follows second order kinetics with Mn(III), as evident from the linearity of $1/[Mn(III)]$ versus time plot. The effect of varying [Mn(III)], [PRX], added [Mn(II)], dissociated $[H^+]$, total $[P_2O_7^{4-}]$ and added $ClO_4^-$, $Cl^-$ and $SO_4^{2-}$ ions have also been studied. The order in [PRX] is unity and increase in $[H^+]$ increases the rate. With increase in [Mn(II)] and $[P_2O_7^{4-}]$ a retardation effect is noticed. Oxidation products have been identified. Dependence of reaction rate on temperature has been studied, actication parameters computed from the Arrhenius and Eyring plots. A mechanism consistant with kinetic results has been proposed.

Pyridoxine (5-hydroxy 6-methyl 3,4-pyridinedimethanol, PRX) or vitamin $B_6$ is a weak base, obtained from rice bran and yeast. In the biological systems it is converted into pyridoxal phosphate which is the co-enzyme for amino acid decarboxylase and for transaminase. PRX has been oxidised to pyridoxal by acidic $MnO_2^1$, alkaline $KMnO_4$ solutions[2] and aromatic halosulphonamides[3]. But there seems to be no report in literature on the kinetics of oxidation of pyridoxine with Mn(III). Such oxidation studies may throw some light on the mechanism of conversions of the compounds in biological systems. Hence as a part of our work on mechanistic studies on Mn(III) oxidations of organic and inorganic substrates in general and medicinal compounds in particular[4-7], we have investigated the stoichiometry and mechanism of oxidations of pyridoxine by Mn(II) in pyrophosphate medium.

## Materials and Methods

Manganese(III) pyrophosphate was prepared by the literature method, and was standardised by iodometric method and it was further checked by titrating against standard Fe(II) using diphenyl sulphonate as an internal indicator.

A Simadz model UV-visible spectrophotometer with 1 cm quartz cell was used for the absorption measurements. Under the experimental conditions, absorption maximum for the prepared manganese(III) species in a solution of *p*H 2.7 occurred at 500 nm, which slightly varied as a function of *p*H. Pyridoxine hydrochloride (Sisco Chem, India) was used without further purification and aqueous solutions of the compound was prepared in doubly distilled water and used as a stock solution. All other reagents used were of analytical grade.

### *Kinetic measurements*

Known amount of Mn(III) pyrophosphate was thermally equilibrated at 313K. It was added to a mixture of PRX, Mn(II), $P_2O_7^{4-}$ (for ionic strength), orthophosphoric acid (for maintaining *p*H) and water (to keep the total volume constant) taken in another glass stoppered bottle also maintained at the same temperature. The progress of the reaction was monitored by the iodometric estimation of unreacted Mn(III) pyrophosphate present in known aliquots of the mixture withdrawn at regular intervals of time. The course of the reaction was studied over 75% of the reaction. The rate constants calculated were reproducible within ± 5% error. Identical results were obtained when the reaction was monitored by spectrophotometric method[7].

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## Results

*Stoichiometry and product analysis*

To investigate the stoichiometry under excess [oxidant] condition, a known amount of pyridoxine solution ($3.0 \times 10^{-3}$ mol $dm^{-3}$) was allowed to react completely with a six fold excess of Mn(III) at 50°C in the presence of proportionate amount of orthophosphoric acid to maintain *p*H. The excess Mn(III) was estimated by iodometric method.

Stoichiometry of the reaction between manganese(III) pyrophosphate and PRX was found to be *p*H dependent. Below *p*H = 1 the stoichiometry approached 12:1, at *p*H = 1.25, 2.0, 2.5 and 3, the stoichiometries were 10:1, 6.5:1, 5:1 and 4:1 respectively and above *p*H = 4 it was nearrer to 2:1. Below *p*H = 1 the reaction was instantaneous. Above *p*H = 2.5 the reaction became gradually slow and this condition was used for the kinetic measurements.

The stoichiometry was also established under kinetic conditions. The reaction was allowed to proceed to completion by heating at about 40° to 50°C for about half an hour and the oxidation product pyridoxal was extracted with ether. Then ether was distilled off and the substance was dissolved in alcohol to which was added a solution of semicarbazide. A crystalline product obtained was identified[8] as semicarbazone (melting point 509K) and weighed. The observed stoichiometry of oxidant to substrate was conformed to 2:1 as represented by Eq. (1).

$$2Mn^{III}(H_2P_2O_7)_3^{3-} + \underset{\text{(Pyridoxine)}}{C_8H_{11}NO_3} \rightarrow \underset{\text{(Pyridoxal)}}{C_8H_9NO_3} + 2Mn^{II}(H_2P_2O_7)_2^{2-} + H_2P_2O_7^{2-} + 2H^+ \quad \ldots (1)$$

Above *p*H 4 the iodometric method for the determination of stoichiometry fails since at this *p*H, Mn(III) does not oxidise iodide to liberate iodine. Therefore spectrophotometric method was employed.

*Dependence of rate on [Mn(III)] and [PRX]*

Second order dependence with Mn(III) was indicated by the linearity of $1/V_t$ or 1/[Mn(III)] versus time plot even beyond 75% of the reaction (Fig. 1).

At constant [Mn(III)], *p*H, $[P_2O_7^{4-}]$ the rate constants increased with increase in [PRX] (Table 1) and log*k* versus log[PRX] showed that order in [PRX] was one.

*Dependence of rate on p*H

*p*H of the reaction was varied between 2.5 to 3.25 by varying [orthophosphoric acid] at fixed [Mn(II)], $[P_2O_7^{4-}]$ and [Mn(III)]. The reaction rate increased with increase in $[H^+]$ (Table 1). The order in $[H^+]$ was found to be ~ 0.5.

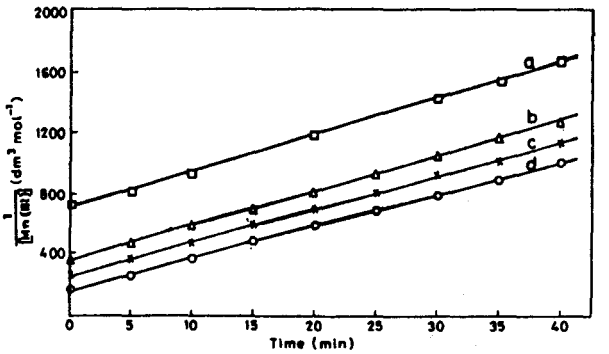



Fig. 1—Plot of 1/[Mn(III)] versus time $10^2$[PRX] (mol $dm^{-3}$) = 4.0, $10^3$[Mn(II)] (mol $dm^{-3}$) = 4.0, $10^2[P_2O_7^{4-}]$ (mol $dm^{-3}$) = 5.79, *p*H = 2.95, temp = 313K, $10^3[Mn(III)]_0$ (mol $dm^{-3}$) = 1.42(a), 2.84(b), 3.98(c), 5.68(d)

Table 1—Second order rate constants ($k_{obs}$) for the oxidation of PRX by manganese(III) pyrophosphate at 313K. $[Mn(II)] = 4.0 \times 10^{-3}$ mol $dm^{-3}$, $[P_2O_7^{4-}] = 5.79 \times 10^{-2}$ mol $dm^{-3}$

| $[Mn(III)]10^3$ (mol $dm^{-3}$) | $[PRX]10^2$ (mol $dm^{-3}$) | *p*H | $k_{obs}$ ($dm^3 mol^{-1} s^{-1}$) |
|---|---|---|---|
| 1.42 | 4.0 | 2.95 | 0.43 |
| 2.84 | 4.0 | 2.95 | 0.43 |
| 3.98 | 4.0 | 2.95 | 0.42 |
| 5.68 | 4.0 | 2.95 | 0.42 |
| 2.84 | 2.0 | 2.95 | 0.21 |
| 2.84 | 6.0 | 2.95 | 0.60 |
| 2.84 | 8.0 | 2.95 | 0.81 |
| 2.84 | 4.0 | 2.75 | 0.52 |
| 2.84 | 4.0 | 3.10 | 0.36 |
| 2.84 | 4.0 | 3.30 | 0.30 |

*Effect of ionic strength and added Mn(II)*

Increase in ionic strength by varying [sodium pyrophosphate] decreased the rate of reaction with inverse dependence. Mn(II) is the reduced product of the oxidant. As initial concentration of added Mn(II) was increased the rate progressively decreased (Table 2). The order in Mn(II) was also found to be − 1.0.

*Effect of added salts*

Added anions like $ClO_4^-$ and $Cl^-$ had negligible effect on the reaction rate. The retardation effect by the added $SO_4^{2-}$ could be due to the presence of additional equilibrium.

$$SO_4^{2-} + H^+ \rightleftharpoons HSO_4^- \quad \ldots (2)$$

This brings down the effective $[H^+]$ in the reaction mixture as indicated by the change in measured *p*H values thereby decreasing the rate of the reaction (Table 3).

Table 2—Effect of variation of [Mn(II)], $[P_2O_7^{4-}]$ and temperature on the reaction rate

$[Mn(III)] = 2.84 \times 10^{-3}$ mol dm$^{-3}$, $[PRX] = 4.0 \times 10^{-2}$ mol dm$^{-3}$, *p*H = 2.95

| $[Mn(II)]10^3$ (mol dm$^{-3}$) | $[P_2O_7^{4-}]10^2$ (mol dm$^{-3}$) | Temp K | $k_{obs}$ (dm$^3$mol$^{-1}$s$^{-1}$) |
|---|---|---|---|
| 4.0 | 5.79 | 313 | 0.43 |
| 6.0 | 5.79 | 313 | 0.26 |
| 8.0 | 5.79 | 313 | 0.19 |
| 12.0 | 5.79 | 313 | 0.11 |
| 4.0 | 3.79 | 313 | 0.75 |
| 4.0 | 5.79 | 313 | 0.43 |
| 4.0 | 7.79 | 313 | 0.30 |
| 4.0 | 9.79 | 313 | 0.24 |
| 4.0 | 5.79 | 303 | 0.13 |
| 4.0 | 5.79 | 308 | 0.25 |
| 4.0 | 5.79 | 313 | 0.43 |
| 4.0 | 5.79 | 318 | 0.85 |

Table 3—Effect of variation of $[SO_4^{2-}]$ and solvent compositions on the reaction rate

$[Mn(III)] = 2.84 \times 10^{-3}$, $[PRX] = 4.0 \times 10^{-2}$ mol dm$^{-3}$, $[Mn(II)] = 4.0 \times 10^{-3}$ mol dm$^{-3}$, temp. = 313K, $[P_2O_7^{4-}] = 5.79 \times 10^{-2}$ mol dm$^{-3}$

| $[SO_4^{2-}] \times 10^2$ (mol dm$^{-3}$) | $k_{obs}$ (dm$^3$mol$^{-1}$ s$^{-1}$) | Percentage of absolute alcohol | Dielectric constant | $k_{obs}$ (dm$^3$mol$^{-1}$ s$^{-1}$) |
|---|---|---|---|---|
| 0.0(2.95) | 0.43 | 0.0 | — | 0.43 |
| 5.0(3.05) | 0.38 | 3.0 | 76.7 | 0.34 |
| 10.0(3.29) | 0.30 | 5.0 | 75.6 | 0.32 |
| 15.0(3.52) | 0.22 | 10.0 | 72.9 | 0.26 |

Values in the parentheses are the measured *p*H of the reaction mixture.

*Effect of dielectric constant of the reaction mixture*

The observed decrease in rate with decrease in dielectric constant of the medium (Table 3) is in conformity with equation for ion-ion interactions[9].

$$\ln k = \ln k_\infty - \frac{e^2}{2D\,k_B\,T}\left[\frac{(Z_A+Z_B)^2}{r_\neq} - \frac{Z_A^2}{r_A} - \frac{Z_B^2}{r_B}\right] \quad \ldots (3)$$

where $k_\infty$ is the rate constant in a medium of infinite dielectric constant, $Z_A$ and $Z_B$ are the charge on the ion A and B of radii $r_A$ and $r_B$, D the dielectric constant of the medium, $k_B$ = Boltzman constant, and $r_\neq$ is the radius of the transition state.

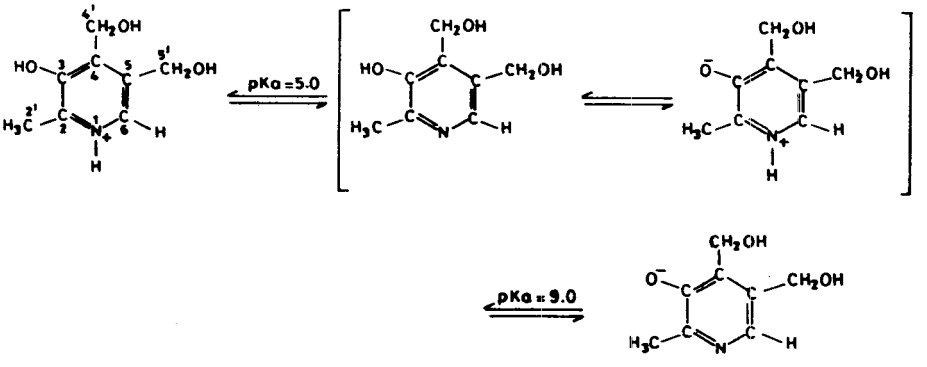
*Effect of temperature*

The reaction was carried out at 303, 308, 313 and 318 K at fixed [Mn(III)], ionic strength, *p*H and [Mn(II)]. Arrhenius and Eyring plots, log *k* versus 1/T and log (k/T) versus 1/T, were linear. From the slopes and intercepts, energy of activation ($E_a$) and frequency factor (log A), entropy of activation ($\Delta S^\ddagger$) enthalpy of activation ($\Delta H^\ddagger$) and free energy of activation ($\Delta G^\ddagger$) for the overall reaction were calculated to be: $E_a = 98.86$ kJ mol$^{-1}$, log A = 16.3 s$^{-1}$, $\Delta H^\ddagger = 97.20$ kJ mol$^{-1}$, $\Delta S^\ddagger = 58.04$ JK$^{-1}$mol$^{-1}$ and $\Delta G^\ddagger = 79.03$ kJ mol$^{-1}$.

## Discussion

The substrate pyridoxine exhibits several equilibria depending on the *p*H of the solution[10] (Scheme 1). In other words the concentration of $SH^+$ under the reaction condition is governed by the $pK_a$ value of $SH^+$.

In acidic conditions employed in the present investigation, the substrate(s) exists in the protonated form ($SH^+$). Further crystallographic study of the complex Cd(pyridoxine)$Cl_2$ has shown[11] that




Scheme - 1

pyridoxine molecule acts as a bidentate ligand towards cadmium atom through oxygen atoms O(4′) and O(3). On the same lines it can be assumed that, in solution, electron transfer to Mn(III) involves the formation of a pyridoxine-Mn(III) intermediate (X) through the same two oxygen atoms. The intermediate then disproportionates to give a radical ion (γ) and as one more Mn(III) interacts oxidatively, it yields the reaction products.

The most likely reaction mechanism which can satisfactorily explain the observed rate is as shown in Scheme 2.

$$S + H^+ \underset{\text{fast}}{\overset{K_1}{\rightleftharpoons}} SH^+ \quad \ldots (4)$$

$$Mn^{III}L_3 + SH^+ \underset{\text{fast}}{\overset{K_2}{\rightleftharpoons}} X + H^+ \quad \ldots (5)$$

$$X \underset{\text{fast}}{\overset{K_3}{\rightleftharpoons}} Y + Mn^{II}L_2 + L \quad \ldots (6)$$

$$Mn^{III}L_3 + Y \xrightarrow[\text{slow}]{k_4} \text{Products} \quad \ldots (7)$$

(slow and rate determining step)

Scheme 2

The rate of oxidation is given by

$$-\frac{d[Mn^{III}L_3]}{dt} = k_4[Mn^{III}L_3][Y]$$

$L = H_2P_2O_7^{2-}$, X is the $Mn^{III}$-pyridoxine complex having the charge and Y is the radical cation. Applying steady state approximation to the intermediates Y and X, one gets Eq. (8)

$$-\frac{d[Mn^{III}L_3]}{dt} = \frac{k_2k_3k_4[Mn^{III}L_3]^2[SH^+]}{\{k_{-3}[Mn^{II}L_2][L] + k_4[Mn^{III}L_3]\} \times \{k_2[H^+] + k_3\}}$$

or

$$-\frac{1}{[Mn^{III}L_3]^2}\frac{d[Mn^{III}L_3]}{dt} = \frac{k_2k_3k_4[SH^+]}{\{k_{-3}[Mn^{II}L_2][L] + k_4[Mn^{III}L_3]\}\{k_2[H^+] + k_3\}}$$

$$k_{obs} = \frac{k_2k_3k_4[SH^+]}{\{k_{-3}[Mn^{II}L_2][L] + k_4[Mn^{III}L_3]\}\{k_2[H^+] + k_3\}} \quad \ldots (8)$$

$k_4$ is negligible compared to $k_{-3}$, $k_2$, $k_3$ and $[Mn^{III}L_3]$ is small compared to $[Mn^{II}L_2]$, [L] or $[H^+]$. Hence neglecting the term $k_4[Mn^{III}L_3]$ in denominator,

$$k_{obs} = \frac{k_2k_3k_4[SH^+]}{\{k_{-3}[Mn^{II}L_2][L]\}\{k_2[H^+] + k_3\}} \quad \ldots (9)$$

or

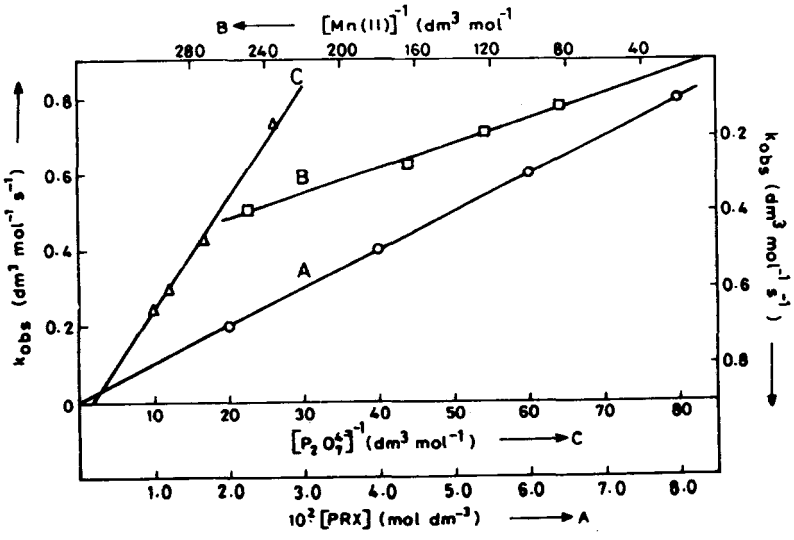
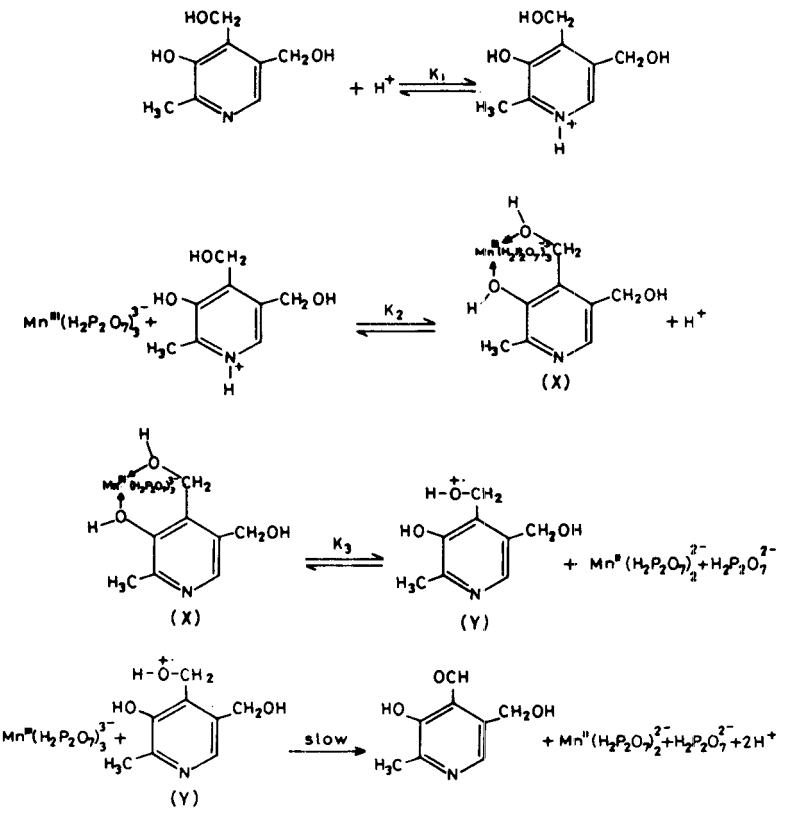



Fig. 2—Plot of $k_{obs}$ versus [PRX] (A), $[Mn(II)]^{-1}$ (B) and $[P_2O_7^{4-}]^{-1}$ (C), $10^3$[Mn(III)] (mol dm$^{-3}$) = 2.84, pH = 2.95, temp = 313K



Scheme - 3

$$k_{obs} = \frac{K_1 k_2 K_3 k_4 [S][H^+]}{\{[Mn^{II}L_2][L]\}\{k_2[H^+] + k_3\}} \quad \ldots (10)$$

Plot of $k_{obs}$ versus [PRX] was linear passing through the origin (Fig. 2) showing order in [PRX] as one. Plots of $k_{obs}$ versus $1/[Mn(II)]$ and $1/[P_2O_7^{4-}]$ are also linear passing through the origin in accordance with the equation $y = mx + c$, where $c \sim 0$ with m values of $0.1 \times 10^2$ $dm^6 mol^{-1} s^{-1}$, $1.714 \times 10^{-3} s^{-1}$ and $3.0 \times 10^{-2} s^{-1}$ respectively. The correlation coefficient was 0.997 in all three cases (Fig. 2).

The proposed mechanism is also supported by the observed thermodynamic parameters. As shown in the detailed mechanism (Scheme 3), a bulkier metal substrate complex breaks down to simpler intermediates and ion during the stages activation. This accounts for the positive entropy of activation.

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