Oxidation of L-Valine by Manganese(III) in Pyrophosphate Medium: Kinetics and Mechanism

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Abstract Kinetics of oxidation of L-valine (Val) by manganese(III) pyrophosphate has been studied as a function of pH (0.94-1.90) at 313 K. The reaction shows a first-order dependence of rate each on [Mn(III)] and [Val], a fractional-order on [H^+], and an inverse fractional-order each on [$Na_4P_2O_7$] and [Mn(II)]. Effects on the rate of anions, such as [F^-], [Cl^-] and [ClO_4^-], and the dielectric constant of the solvent medium have been studied. Solvent isotope studies have been performed in D_2O medium. Activation parameters have been determined from Arrhenius and Eyring plots. A mechanism consistent with the observed kinetics is proposed and discussed.

Keywords Kinetics, manganese(III), valine, oxidation, reduction, mechanism, rate law

1. Introduction

Studies of oxidation of organic substrates such as amino acids by transition metal ions of higher oxidation states in solution have received considerable attention. of these, manganese(III) oxidations are of special importance because of their biological relevance[1]. Manganese-porphyrins have been studied as possible models for closely related and biologically significant systems[2]. Several studies have been reported on the kinetics oxidations of substrates by manganese(III) in perchlorate, sulfate, and acetate media[3]. As a part of our investigations on the redox reactions of transition metal compounds [4-10], we report herein the kinetics of oxidation of L-valine by manganese(III) pyrophosphate.

2. Experimental

Materials

Stock solutions of manganese(III) pyrophosphate (0.05 M at pH 5.0) were prepared by the standard method of Belcher and West[11]. The pH of the solution was varied by adding the required amount of phosphoric acid or sodium pyrophosphate. Chromatographically pure sample of L-valine (Sisco Research Laboratories, India) was further assayed by standard methods[12]. Aqueous stock solution of Val (0.400 M) was freshly prepared and used, whenever needed. All other chemicals used were of analytical grade. Triply distilled

water was employed for preparing all aqueous solutions.

2.1. Kinetic Procedure

The kinetic studies were made in glass-stoppered Pyrex tubes under pseudo-first order conditions of [substrate] >> [Mn(III)]. Each reaction mixture consisted of solutions of Val, the acid (phosphoric acid to maintain acid concentration), the salt (sodium pyrophosphate to maintain constant ionic strength), manganese(II). Water was added to keep the total volume constant and the mixture was thermally equilibrated at constant temperature (e.g., 313 K). A known amount of the standard manganese(III) pyrophosphate stock solution maintained at the same temperature was added and mixed thoroughly to initiate the reaction. The progress of the reaction was monitored for at least two half-lives by iodometric determination of the unreacted Mn(III) at regular intervals of time. The pseudo-first order rate constants (k′ or k_{obs}) obtained by a graphical method of plotting log (Mn(III) titer value) *vs.* time were found to be reproducible within ± 5% error.

2.2. Preliminary Studies

The maximum absorption wavelength of manganese(III) pyrophosphate solution at pH 5.0 occurs at 500 nm which on variation of pH shifts significantly along with a change in molar absorptivity (Fig. 1). The formal redox potential (E_o^1) of the Mn(III)-Mn(II) couple was measured by the usual method of mixing different proportions of air-free oxidized and reduced forms of manganese ion solutions containing an overall 0.50 M pyrophosphate in the pH range 0.70-3.0. The values of $E_{(V vs SCE)}$ are 1.090, 1.218, 1.231, 1.259, 1.289 and 1.307 V at pH values of 2.9, 1.65, 1.53, 1.33. 1.01 and 0.70,

respectively, which are consistent with the literature data [6-10].
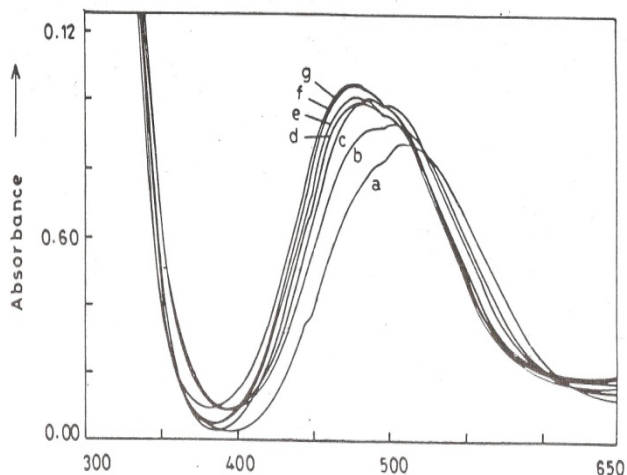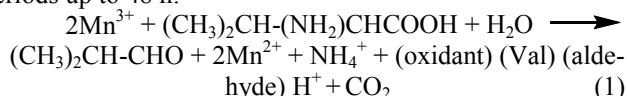

Figure 1. Absorption spectra of 1.00×10^{-3} M Mn(III) in pyrophosphate solutions. pH=0.31(a); 1.85(b); 2.9(c); 3.9(d); 5.20(e); 6.26(f); and 8.09 (g)

2.3. Reaction Stoichiometry and Product Analysis

The following 2:1 stochiometry was observed, with reaction mixtures of [Mn(III)] > [Val] studied for various time periods up to 48 h:

$$2Mn^{3+} + (CH_3)_2CH\text{-}(NH_2)CHCOOH + H_2O \longrightarrow$$
$$(CH_3)_2CH\text{-}CHO + 2Mn^{2+} + NH_4^+ + \text{(oxidant) (Val) (alde-}$$
$$\text{hyde) } H^+ + CO_2 \qquad (1)$$

The oxidation product of Val, isobutyraldehyde, was quantified through its 2,4-dinitrophenyl hydrazone derivative[12]. The IR spectral data of the hydrazone derivative supported the characterization of the product. Ammonia and CO_2 were determined by conventional tests[12-14].

2.4. Test Free Radicals

The reaction mixtures of Val and Mn(III) were tested for the presence of free radicals using monomers, acrylonitrile and methyl methacrylate (10% solution)[14-17]. The addition of the monomer to the reaction mixture, after it was purged with nitrogen, in the dark resulted in the precipitation of a polymer product. This positive response indicated the *in situ* generation of free radicals in the reaction mixture. Control experiments with the solutions of Mn(III), Mn(II), and Val were also performed under the same experimental conditions, which did not show any precipitation.

3. Results

3.1. Dependence of the Rate on [Mn(III)] and [Val]

In the Mn(III) oxidation of valine, the effect on the reaction rate was investigated by varying either [Mn(III)]$_o$ or [Val]$_o$ at constant pH and temperature. The linearity of the pseudo-first order plots of log [Mn(III)] or titer value) *vs.* time showed the first–order dependence of the reaction rate on [Mn(III)], which was monitored in the reaction (Table 1, Fig. 2). The increase in the [Val]$_o$ increased the rate constant

at constant pH and other conditions (Table 1). A linear plot of log k′ or *vs.* log [Val]$_o$ with a unit slope showed the first–order dependence of the rate on [Val].

Table 1. Rate constants for the l-valine oxidation by manganese(III) Temp. = 313 K; pH = 1.3

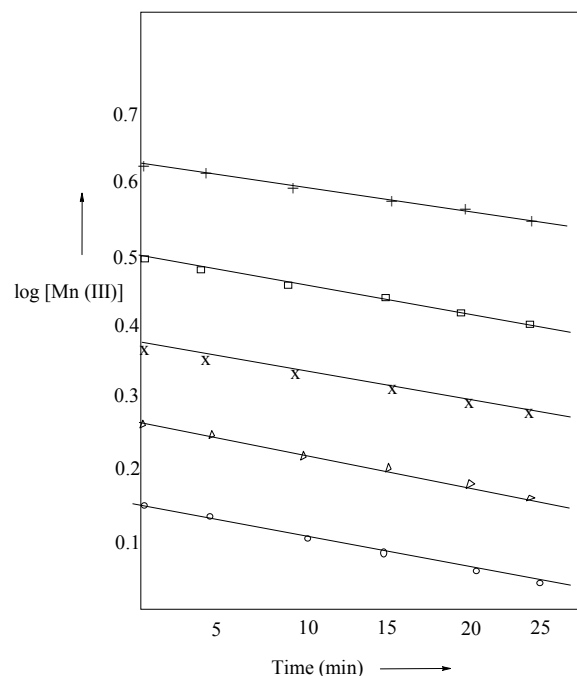| 10^3 [Mn(III)]$_o$ (M)	10^2 [Val]$_o$ (M)	10^2 [Mn(II)] (M)	10^2 [Na$_4$P$_2$O$_7$] (M)	10^4 k′ (s^{-1})
0.5	4.0	1.0	1.0	1.03
1.0	4.0	1.0	1.0	1.04
2.0	4.0	1.0	1.0	1.02
3.0	4.0	1.0	1.0	1.05
4.0	4.0	1.0	1.0	1.04
1.0	1.0	1.0	1.0	0.88
1.0	2.0	1.0	1.0	1.02
1.0	3.0	1.0	1.0	1.12
1.0	4.0	1.0	1.0	1.04
1.0	5.0	1.0	1.0	1.12
1.0	4.0	0.5	1.0	2.16
1.0	4.0	1.0	1.0	1.04
1.0	4.0	2.0	1.0	0.58
1.0	4.0	3.0	1.0	0.35
1.0	4.0	4.0	1.0	0.21
1.0	4.0	1.0	0.5	1.97
1.0	4.0	1.0	1.0	1.04
1.0	4.0	1.0	2.0	0.53
1.0	4.0	1.0	3.0	0.45
1.0	4.0	1.0	4.0	0.34

Figure 2. Pseudo first-order plots of log [Mn(III)] *vs.* time Temp = 313 K; [Val]$_o$ = 4.00×10^{-2} M; [Mn(II)] = 1.00×10^{-2} M; [Na$_4$P$_2$O$_7$] = 1.00×10^{-2} M; [Mn(III)]$_o$ (10^{-3} M) = 0.500(a), 1.00(b), 2.00(c), 3.00(d), and 4.00 (e)

3.2. Dependence of the Rate on pH

The reaction rate increased with a decrease in pH and a plot of log k′ *vs.* pH was linear (Fig. 3) with a negative slope of -0.53, indicating a positive fractional-order dependence of the rate on [H$^+$].
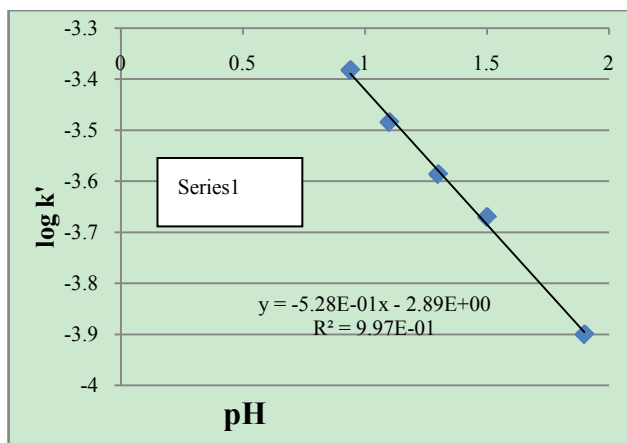
Figure 3. Plot of log k' vs. −log [H+]. [Mn(III)]$_o$ = 1.00 X 10^{-3} M; [Val]$_o$ = 4.00 X 10^{-2} M; [Mn(II)] = 1.00 x10^{-2} M; [Na$_4$P$_2$O$_7$]=1.00 X10^{-2}M; T=313 K

3.3. Dependence of the Rate on Ionic Strength

The rate decreased with an increase in the [Na$_4$P$_2$O$_7$] leading to a linear plot of log k' vs. log [Na$_4$P$_2$O$_7$] with a negative slope, showing an inverse fractional-order dependence of the rate on [Na$_4$P$_2$O$_7$].

3.4. Dependence of Rate on [Mn(II)] and Salts

An increase in the concentration of the reduction product, Mn(II), decreased the rate (Table 1) and a log-log plot gave a negative fractional-order in [Mn(II)]. Also, the effects of added sodium salts containing anions such as F−, Cl− and ClO$_4$− on the rate of reaction were investigated (Table 3). Increase in [Cl−] and [ClO$_4$−] increased the rate, while increase in [F−] decreased the rate. This effect is attributable to the replacement of the pyrophosphate ligand in the complex with other anions leading to the establishment of a new Mn(III)-Mn(II) redox couple involving ligands, F−, Cl− and ClO$_4$−.

Table 3. Effects of salts on the rate of L-valine oxidation by manganese(III) in pyrophosphate medium [Mn(III)]$_o$ = 4.00 X 10^{-3} M; [Val]$_o$ = 6.00 X 10^{-2} M; [Mn(II)] = 1.00 x10^{-2} M; [Na$_4$P$_2$O$_7$]=1.00 X10^{-2}M; T = 313 K; pH = 1.3

10^2 [Cl−] (M)	10^4 k' (s^{-1})	10^2 [F−] (M)	10^4 k' (s^{-1})	10^2 [ClO$_4$−] (M)	10^4 k' (s^{-1})
0.0	1.04	0.0	1.04	0.0	1.04
0.05	1.34	0.5	0.41	0.05	1.46
0.10	1.70	0.10	0.37	0.10	1.61
0.15	1.72	0.15	0.30	0.15	2.01

Table 4. Effect of ethanol variation on the rate of L-valine oxidation by manganese(III) [Mn(III)]$_o$ = 4.00 X 10^{-3} M; [Val]$_o$ = 6.00 X10^{-2} M; [Mn(II)] = 1.00 X 10^{-3} M; [Na$_4$P$_2$O$_7$] = 1.00 X10^{-2}M; T = 313 K; pH = 1.3

% Ethanol (v/v)	10^4 k' (s^{-1})
0	1.04
5	0.90
10	0.83
15	0.62

3.5. Effect of Solvent Composition or Dielectric Constant on the Reaction Rate

The dependence of the reaction rate on dielectric constant (D) of the reaction medium was verified by studying the

reaction at various percentages of EtOH in water. It was found that the rate decreased with an increase in the percentage of EtOH. In other words, the observed rate constant decreased with a decrease in D (Table 4). A plot of ln k' vs. ln 1/D had a slope, which is consistent with the Amis concept for dipole-dipole or ion–dipole interactions[7].

3.6. Dependence of the Rate on Temperature

The effect of temperature on the rate constant was determined by performing the reaction in the range, 308 K-328 K, at constant [Mn(III)], [Val], [Mn (II)], [P$_2$O$_7^{4-}$] and pH (Table 5). Arrhenius and Eyring[13] plots of log k' vs. 1/T and log (k'/T) vs. 1/T (Fig. 4), respectively, gave good straight lines. From the slopes and intercepts, the activation parameters were calculated as summarized in Table 5.

Table 5. Temperature effect and activation parameters for the L-valine oxidation by manganese(III)[a] [a]Reaction conditions are as stated in Table 4; [b]$\Delta G^{\neq}$ value at 308 K

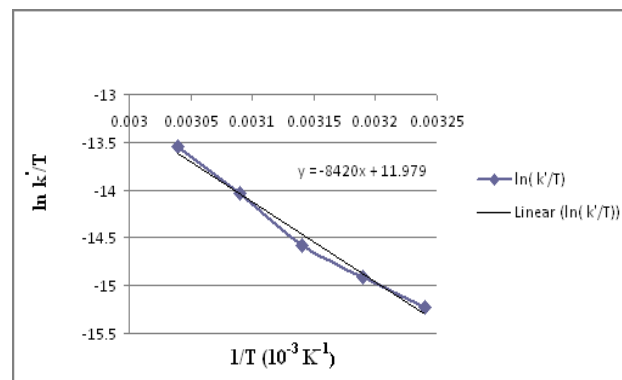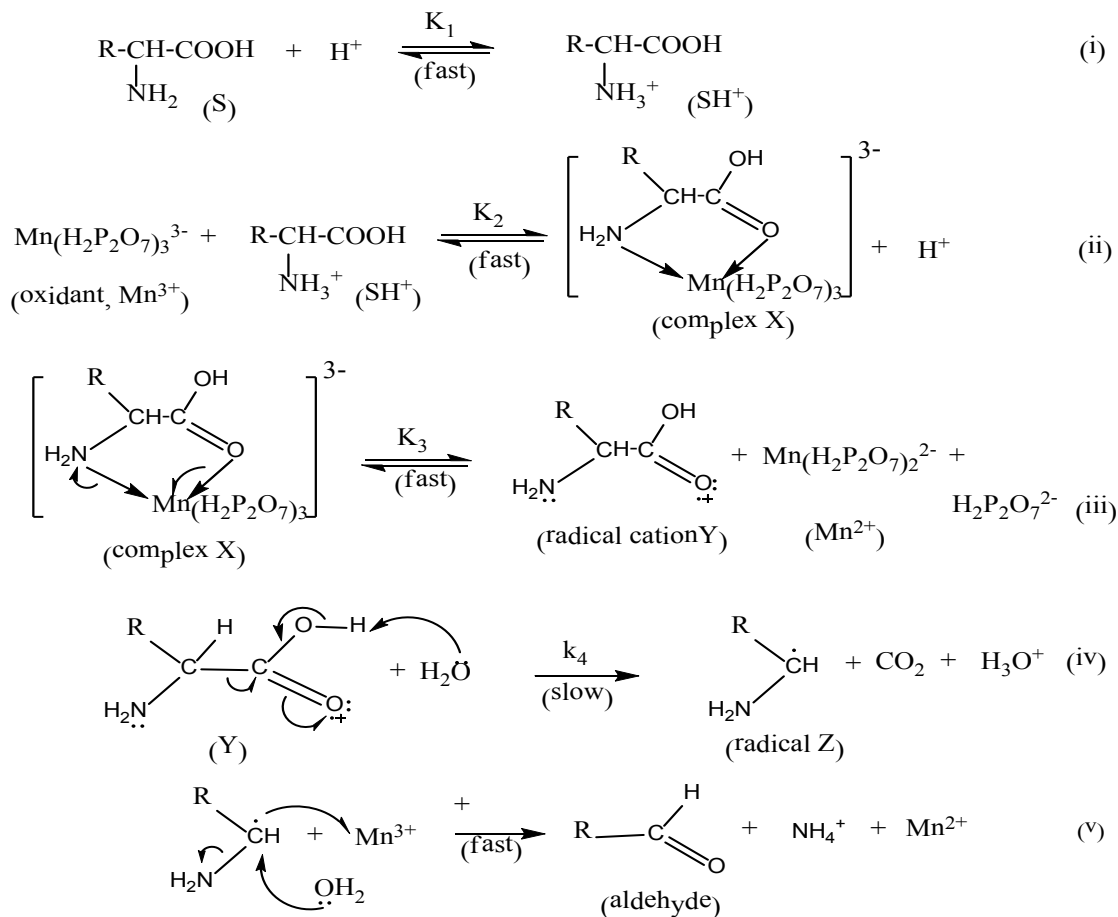| Temp. (K)	10^4 k' (s^{-1})		
308	0.75	Ln A	18.9
313	1.04	E_a	73.1 kJ mol^{-1}
318	1.47	$\Delta H^{\neq}$	70.0 kJ mol^{-1}
323	2.58	$\Delta S^{\neq}$	-98.0 JK^{-1}mol^{-1}
328	4.28	$\Delta G^{\neq b}$	100 kJ mol^{-1}

Figure 4. Eyring plot

3.7. Solvent Isotope Studies

The reaction was studied in D$_2$O medium (60%). Rate constants in H$_2$O and D$_2$O were found to be 1.04 x 10^{-4} s^{-1} and 2.1 x 10^{-4} s^{-1}, respectively. These values lead to the solvent isotope effect[17], k$_{(H2O)}$/ (k$_{D2O}$), of 0.51.

4. Discussion

4.1. Mechanism

In acidic pH, chelating pyrophosphate ligand coordinates to manganese(II and III) to form chelates containing complex anions, Mn(H$_2$P$_2$O$_7$)$_3^{4-}$ and Mn(H$_2$P$_2$O$_7$)$_3^{3-}$. Therefore, the oxidant Mn(III) is a complex species. The observed kinetic results of first-order each in [Mn(H$_2$P$_2$O$_7$)$_3^{-3}$] and [Val], a fractional-order in [H+] and an inverse fractional-order in [Mn(H$_2$P$_2$O$_7$)$_3^{-4}$] and [H$_2$P$_2$O$_7^{-2}$] can be supported by Scheme I below.

$$R-CH-COOH \;+\; H^+ \;\underset{(fast)}{\overset{K_1}{\rightleftharpoons}}\; R-CH-COOH \qquad\qquad (i)$$

with NH$_2$ (S) on the left and NH$_3^+$ (SH$^+$) on the right.

$$Mn(H_2P_2O_7)_3^{3-} \;+\; R-CH-COOH \;\underset{(fast)}{\overset{K_2}{\rightleftharpoons}}\; [complex\ X]^{3-} \;+\; H^+ \qquad (ii)$$

(oxidant, Mn^{3+})   NH$_3^+$ (SH$^+$)

complex X $\underset{(fast)}{\overset{K_3}{\rightleftharpoons}}$ (radical cation Y) $+\ Mn(H_2P_2O_7)_2^{2-} + $ (Mn^{2+}) $+ H_2P_2O_7^{2-}$ (iii)

$$(Y) \;+\; H_2O \;\underset{(slow)}{\overset{k_4}{\longrightarrow}}\; (radical\ Z) \;+\; CO_2 \;+\; H_3O^+ \qquad (iv)$$

(radical Z) $+\ Mn^{3+} \xrightarrow{(fast)} R-C(H)=O$ (aldehyde) $+\ NH_4^+ + Mn^{2+}$ (v)

Scheme I.   Mechanism of valine oxidation by Mn(III) in acid solutions

Here X is the substrate-manganese(III) pyrophosphate complex, Y is a radical cation and Z is a free radical. The existence of the transient intermediate free radicals was indicated by the induced polymerization of the olefinic monomers added to the reaction mixture. The evidence for similar discrete formation of metal-substrate complexes is available in the literature [8,9,13-15].

4.2. Rate law Derivation

The rate of oxidation is given by the slow step in Scheme I as,

$$-d[Mn^{3+}]/dt = rate = k_4[Y] \qquad (2)$$

The total concentration of Mn^{3+} species is given by,

$$[Mn^{3+}]_{tot} = [Mn^{3+}] + [X] + [Y] \qquad (3)$$

Solving for [Y] with substitutions for [Mn^{3+}] and [X] from equilibria (ii) and (iii) of Scheme I into eq. (3) leads to,

$$[Y] = K_2K_3[Mn^{3+}][SH^+]/\{[H^+][Mn^{2+}][H_2P_2O_7^{2-}] + K_2[SH^+][Mn^{2+}][H_2P_2O_7^{2-}] + K_2K_3[SH^+] \qquad (4)$$

The substitution for [SH$^+$] from equilibrium (i) gives eq. (5),

$$[Y] = K_1K_2K_3[Mn^{3+}][S][H^+] / \{[H^+][Mn^{2+}][H_2P_2O_7^{2-}] + K_1K_2[S][H^+][Mn^{2+}][H_2P_2O_7^{2-}] + K_1K_2K_3[S][H^+]\} \qquad (5)$$

Since K$_1$K$_2$K$_3$ represent fast equilibria, the first term in the denominator containing low concentrations of species can be assumed to be relatively small and negligible.

$$[Y]=K_1K_2K_3[Mn^{3+}][S][H^+]/\{ K_1K_2[S][H^+][Mn^{2+}][H_2P_2O_7^{2-}] + K_1K_2K_3[S][H^+]\} \qquad (6)$$

The substitution for [Y] from eq. (6) in eq. (2) results in the rate law, eq. (7).

$$rate = K_1K_2K_3k_4[Mn^{3+}][S][H^+] / \{K_1K_2[S][H^+][Mn^{2+}][H_2P_2O_7^{2-}] + K_1K_2K_3[S][H^+]\} \qquad (7)$$

Since under pseudo first-order conditions, rate = k$'$ [Mn^{3+}], rearrangements of eq. (7) give eq. (8).

$$k' = K_1K_2K_3k_4[S][H^+] /\{ K_1K_2[S][H^+][Mn^{2+}][H_2P_2O_7^{2-}] + K_1K_2K_3[S][H^+]\} \text{ OR } 1/k' = K_3k_4 / [Mn^{2+}][H_2P_2O_7^{2-}] + k_4 \qquad (8)$$

The observed dependencies of the rate, first-order each on [Mn(III)] and [Val], fractional-order on [H+], and negative fractional-order each on Mn(II)] and [H2P2O72-], support the rate law (eq.(7)) derived based on the proposed mechanism in Scheme I.

The proposed reaction mechanism and the derived rate law are also supported by the following experimental facts:

A negative dielectric constant (D) effect, determined by varying the EtOH content in the solvent medium, provides

support for the proposed mechanism (Scheme I). Bronsted and Bjerrum[16,21] have explained the primary salt effect on the reaction rates through the relation,

$$\log k' = \log k_o + 1.02\ Z_A Z_B\ \mu^{1/2} \qquad (9)$$

where μ is the ionic strength of the medium, A and B are the reacting ions, Z_A and Z_B are charges on the respective species, k' and k_o are rate constants in the presence and absence of the added electrolyte, respectively. According to eq. (9), a plot of $\log k'$ vs. $\mu^{1/2}$ should be linear with a slope of $1.02\ Z_A Z_B$ and intercept of $\log k_o$. As the slope of the line depends on $Z_A Z_B$, the reaction rate may increase, decrease or remain unaffected with the ionic strength of the medium. In the present case, the negative effect of ionic strength on the rate signifies ion-molecule interactions as shown in slow step (iv) of Scheme I. Hence, the observed ionic strength effect is consistent with the Bronsted-Bjerrum concept [16,21] for the proposed scheme. Solvent isotope studies have shown that the rate of reaction is higher in D_2O medium for acid or base catalyzed reactions [16,21,22]. For a reaction involving a fast pre-equilibrium with H_3O^+ or OH^- ion transfer, the rate increases in D_2O medium since D_3O^+ and OD^- are stronger acid and stronger base, respectively, than H_3O^+ and OH^- ions. In the present case, where the reaction has negative fractional order in $[H^+]$, the observed solvent isotope effect of $k'(H_2O)/k'(D_2O) > 1$ is due to the greater acid effect of D^+ ion as compared to H^+ ion. The magnitude of the effect in D_2O is consistent with the expected value of 2 to 3 times greater, which is supporting the negative fractional-order dependence of the rate on $[H^+]$. The moderate values of energy of activation and other activation parameters are supportive of the proposed mechanism. The fairly positive values of free energy of activation and enthalpy of activation indicate that the transition state is highly solvated while the negative entropy of activation suggests an associative, rigid transition state with reduced degrees of freedom. Also, the negative value of $\Delta S^{\neq}$ suggests that the Mn(III)-Val reaction is controlled by entropy instead of enthalpy.

5. Conclusions

The redox reaction of Val with Mn(III) pyrophosphate has been investigated in acid solutions. The reaction stoichiometry, involving the oxidation of Val to isobutyraldehyde and reduction of Mn(III) to Mn(II), has been found to be 1 mol Val : 2 mol Mn(III).

The reaction shows the following experimental rate law: rate = k' [Mn(III)] [Val] $[H^+]^x/[Mn(II)]^y$ $[Na_4P_2O_7]^z$, where x, y, and z represent fractional orders. A free radical mechanism (Scheme I) proposed is consistent with the experimental rate law. The activation parameters, E_a, $\Delta H^{\neq}$, $\Delta G^{\neq}$, and $\Delta S^{\neq}$, have been determined to understand whether the reaction is controlled by entropy or enthalpy. The negative $\Delta S^{\neq}$ indicates the rigid transition state formation with a loss of degrees of freedom and the entropy-controlled reaction.

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