



**Kinetics and Mechanism of L-Histidine by Mn(III)
in Pyrophosphate Medium**

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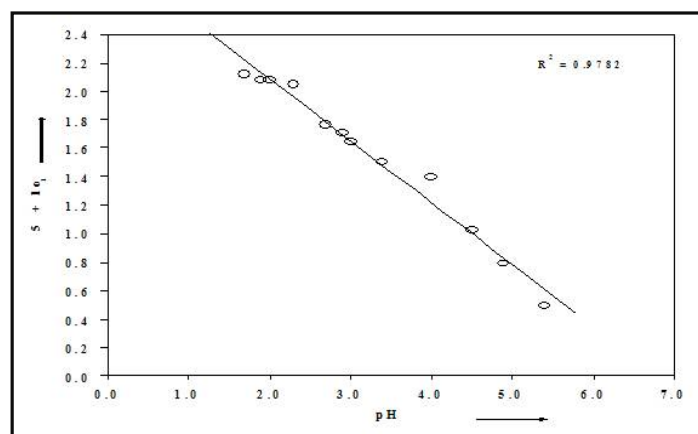
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ABSTRACT

Kinetics of oxidation of L-Histidine by manganese(III)pyrophosphate has been studied in pyrophosphate medium. The reaction shows first order dependence on Mn(III) Py₃, L-Histidine and fractional order with respect to [H⁺]. The rate of oxidation decrease dielectric constant of solvent suggesting ion- dipole interaction. Addition of MnSO₄ and Na₄P₂O₇ shows retarding effect on rate of reaction. Activation parameters have been evaluated. A mechanism consistent with experimental observations has been proposed.

Graphical Abstract



Variation of rate with pH log k₁ v/s pH.

Keywords: Kinetics, Oxidation, L-Histidine, Manganese(III) Pyrophosphate.

INTRODUCTION

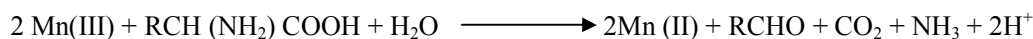
Histidine is used for ulcers, allergic diseases, rheumatoid arthritis, and anemia caused by kidney failure. L-Histidine is mostly contained in protein rich foods and exclusively produced in young plant

tissues and is transferred to animals through the food chain. Histidine regulates the immune defense in the body, allergic reactions and inflammatory processes, so its deficiency causes infection and symptoms of allergies. Stress and injuries increase the daily need of L-Histidine, which can often be fulfilled through the relevant nutritional supplements. Low concentration of Histidine in the blood plasma increases the inflammatory activity of the body and leads to a rise in oxidative stress, so supplementation of L-Histidine is directly associated with a reduced death rate [1, 2].

Few studies were reported on the kinetics of oxidation of L-Histidine in acid medium by using different oxidants like hexachloroplatinate(IV) [3, 4], Thallium (III) [5], Chloramine-T [6], manganese(IV) [7], Manganese(III) [8-10], Manganese(VII) [11-14], tetrachloro aurate(III) [15], Tert. Butylhydroperoxide [16], Hexacyanoferrate [17], N-Bromoacetamide [18] and NaSO₃DPPH and (NaSO₃) DPPH radicals [19]. Manganese is an essential trace mineral in animal as well as in human nutrition. Manganese in oxidation states higher than 2 is involved in redox process at the active site of several Metalloproteins [20-22]. In present paper we have used manganese (III) in pyrophosphate medium to study the kinetics of oxidation of L-Histidine to investigate the mechanism of the reaction and reactive manganese (III) species.

MATERIALS AND METHODS

All the chemicals used were of Analar grade. L-Histidine (Mol. Wt=155.15) used after recrystallization and its purity is checked by M.P. The stock solution of L-Histidine was prepared in minimum amount of H₃PO₄ as it was water insoluble. Mn (III) Pyrophosphate was prepared by the method described by Lingane Karplus [23]. 150 mL of Na₄P₂O₇·10H₂O solution (24 g of Na₄P₂O₇·10H₂O in 300 mL of distilled water), was taken in one liter beaker. About 9 mL of 4N H₂SO₄ was added to the solution to adjust the pH up to 6.75 mL of MnSO₄ (2.2 gm of MnSO₄ in 250 mL of distilled water) solution was gradually added with constant stirring and titrated potentiometrically with KMnO₄ solution (0.158 gm of KMnO₄ in 50 mL of distilled water) to the manganic end point (+ 0.47 ± 0.02V). A cherry red colored complex resulted.

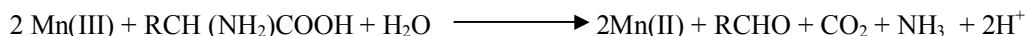


The oxidant was prepared iodometrically by using freshly prepared starch as an indicator. The oxidant immediately decomposes in alkaline solution at pH 6.2, it is quite stable for at least three weeks at room temperature. On acidification the solution becomes bright red violet owing to a change in the degree of ionization of pyrophosphate, since the absorption spectrum of the solution changes but slightly and shows no sign of the characteristic, very strong, absorption band of the MnO₄⁻ anion at 530 nm. After storage of solution at pH 1-2 for some hours a red precipitate was deposited, more rapidly if the solutions are warmed.

Kinetic measurement: The reactions were followed under pseudo first order conditions by keeping the large excess (X 10) of the L-Histidine over Mn (III) Py₃. Decrease in concentration of was followed by taking absorbance at λ_{max} = 485 nm at different time intervals. pH of reaction medium was adjusted by using H₃PO₄. The plot of absorbance versus conc. was linear and passing through origin, hence confirms the validity of Lambert- Beer's law. The rate constant k_{obs} were reproducible within ± 5% error.

Product study and stoichiometry: The qualitative product study was made under kinetic conditions i.e., with an excess of substrate over the oxidant. The solution was kept in dark for 24 h to ensure completion of the reaction, then the solution was treated with excess of saturated solution of 2, 4 DNP in 2M HCl and kept overnight in a refrigerator. The precipitated 2- imidazole aldehyde (2, 4 dinitrophenyl hydrazone) was filtered off, dried, weighed and recrystallized from ethanol and the m.p. of product was found 218°C.

Stoichiometric investigation revealed that 1 mol of amino acid consumed 2 mol of Mn(III)Py₃. Hence the reaction can be represented as:



No polymerization of acrylonitrile was observed in the reaction medium under inert atmosphere (N₂), this suggests that free radicals are not formed in the reaction.

RESULTS AND DISCUSSION

The rate constants were measured by varying concentration of oxidant, substrate, pH, solvent composition, MnSO₄, Na₂P₄O₇, Ionic strength and temperature.

Effect of oxidant: At constant pH with L-Histidine in excess (10 times), plot of log Mn(III) versus time was linear even beyond 70% completion of the reaction indicating a first order in Mn(III). The 1st order rate constants were independent of the initial concentration of [Mn(III) Py₃].

Effect of substrate: The rate of reaction increased with increase in concentration of substrate. Plot of k_{obs} versus [Substrate] gave straight line with slope ≈1. Under pseudo first order conditions, the plot of 1/k_{obs} versus 1/[sub] gave straight line passing through origin suggesting that the reaction does not obey Michaelis-Menten type kinetics. The spectral study gave evidence for the formation of an adduct complex between [L-Histidine] and Mn(III). The study of UV- visible spectra of pure Mn(III)Py₃ and a mixture of Mn(III)Py₃ and a mixture of Mn(III) and L-Histidine shows a change in peak wave length and absorbance, thereby indicating a complex formation between Mn(III) and the substrate (Fig 1).

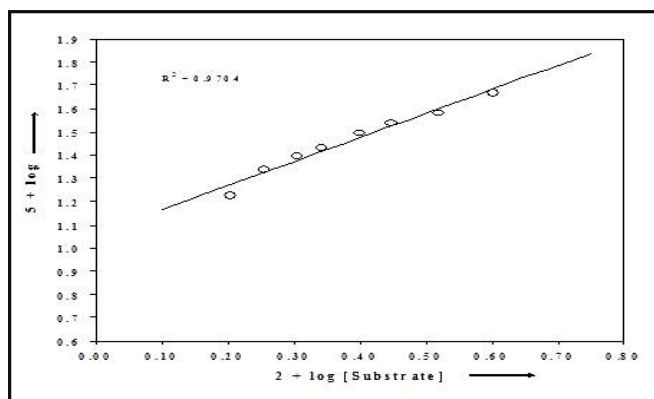


Figure 1. Variation of rate with substrate concentration log k₁ v/s log [Substrate].

Effect of pH: The rate of oxidation was found to increase with decreasing pH. A plot of log k_{obs} versus pH gave straight line with negative slope (slope <1), indicating fractional order dependence on H⁺. Thus, the reaction is acid catalyzed (Fig 2).

Effect of ionic strength: There was no effect of Na₂SO₄ and CH₃COOH concentration on the rate of reaction. This indicates the absence of ion-ion interaction in the rate determining step [24].

Effect of Mn(II) SO₄: The rate of reaction decreased with increase in concentration of Mn(II)SO₄. It may be due to the formation of organomanganous complex with the substrate which reduces the

amount of free substrate for reaction with effect of substrate Mn(III)Py₃. It may be due to formation of inactive Mn(II)-amino acid complex causing decrease in the concentration of free amino-acid:

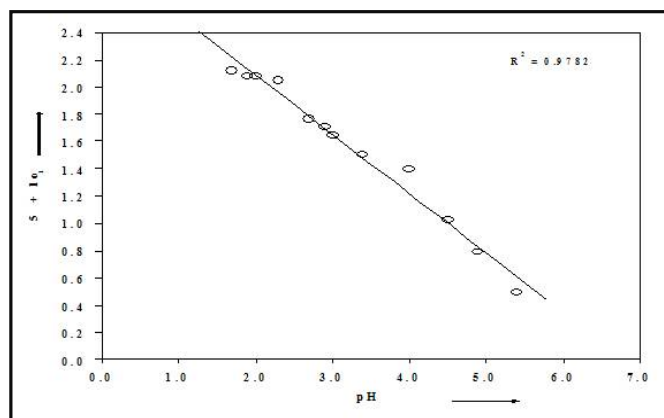
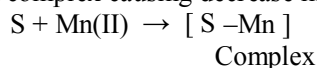


Figure 2. Variation of rate with pH log k_1 v/s pH.

Effect of Na₄P₂O₇: The addition of Na₄P₂O₇ had a retarding effect on the rate of reaction. Addition of Na₄P₂O₇ increases the pH of reaction mixture. Na₄P₂O₇ form stable complex with Mn(III) and Mn(IV) aq which is less reactive compare to Mn(III) aq. and Mn(IV). Therefore the retardation is the result of reduced oxidation potential of Mn(III) and Mn(IV) complexation with sodium pyrophosphate (Table 1).

Table 1. Variation of rate with Mn(II)SO₄, Na₄P₂O₇ and salt concentration.

[Histidine] = 2.0 X 10⁻²M pH = 4.0 [Mn(III)Py₃] = 2.0 X 10⁻³M Temp. = 313K

[Mn(II)SO ₄] X 10 ⁻⁴ M	[Na ₄ P ₂ O ₇] X 10 ⁻² M	[Na ₂ SO ₄] X 10 ⁻² M	[CH ₃ COONa] X 10 ⁻² M	k_1 X 10 ⁻⁵ sec ⁻¹	[Mn(II)SO ₄] X 10 ⁻⁴ M	[Na ₄ P ₂ O ₇] X 10 ⁻² M	[Na ₂ SO ₄] X 10 ⁻² M	[CH ₃ COONa] X 10 ⁻² M	k_1 X 10 ⁻⁵ sec ⁻¹
0.00	0.0	0.0	0.0	24.82	0.0	0.0	0.0	0.0	24.94
0.66	0.0	0.0	0.0	20.72	0.0	0.0	0.5	0.0	24.86
1.33	0.0	0.0	0.0	17.65	0.0	0.0	1.0	0.0	24.10
2.00	0.0	0.0	0.0	15.96	0.0	0.0	1.5	0.0	24.86
2.66	0.0	0.0	0.0	13.81	0.0	0.0	2.0	0.0	24.75
3.33	0.0	0.0	0.0	11.51	0.0	0.0	2.5	0.0	24.84
4.00	0.0	0.0	0.0	10.55	0.0	0.0	3.0	0.0	24.10
0.0	0.0	0.0	0.0	24.14	0.0	0.0	0.0	0.0	24.94
0.0	1.2	0.0	0.0	23.03	0.0	0.0	0.0	0.5	24.10
0.0	2.4	0.0	0.0	20.34	0.0	0.0	0.0	1.0	25.33
0.0	3.6	0.0	0.0	18.42	0.0	0.0	0.0	1.5	24.56
0.0	4.8	0.0	0.0	15.35	0.0	0.0	0.0	2.0	24.10
0.0	6.0	0.0	0.0	13.43	0.0	0.0	0.0	2.5	24.86
0.0	7.2	0.0	0.0	10.55	0.0	0.0	0.0	3.0	25.33

Effect of solvent composition: The rate of oxidation of L-Histidine was affected considerably by changing solvent composition of C₂H₅OH-H₂O mixture. The rate of oxidation decreases with increase in volume % of C₂H₅OH. The rate of oxidation depends on the polarity of the medium. When the polarity of solvent was increased, the rate was decreased. The plot of log k_{obs} versus D-1/D+1 is curvature and the plot of log k_{obs} versus 1/D gives a straight line with negative slope indicating either ion-ion or a dipole-ion interaction between the oxidant and substrate but change ionic strength of the medium has no effect on the rate ruling out the possibility of ion-ion type of interaction between the reactants. Hence it is assumed an ion-dipole interaction (Fig 3).

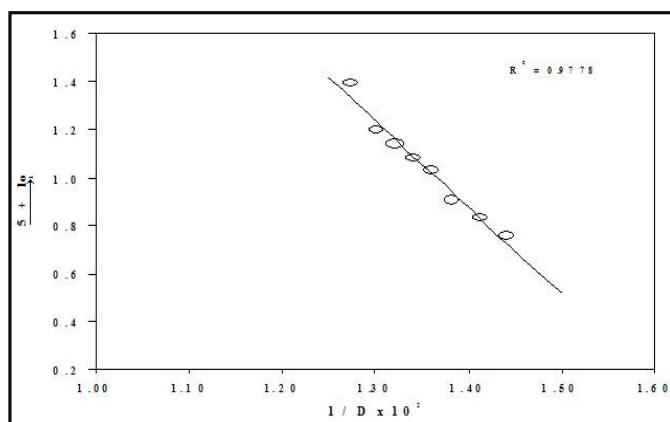


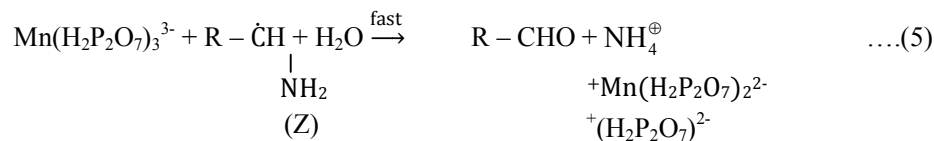
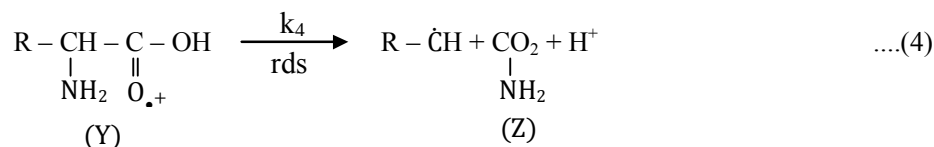
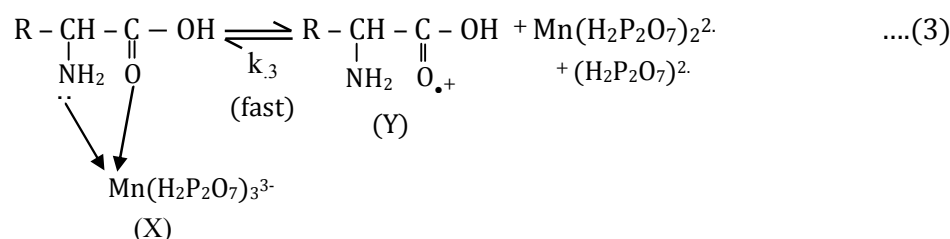
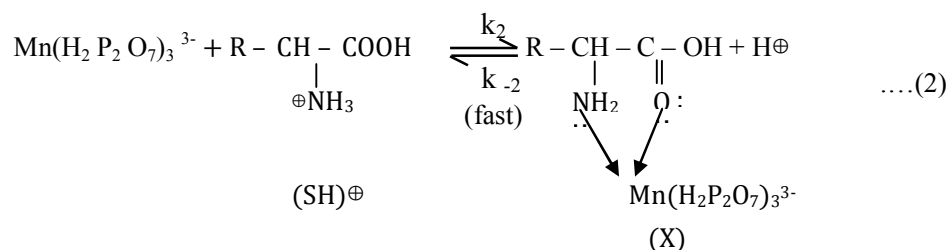
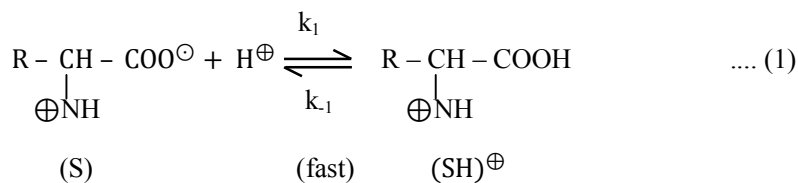
Figure 3. Variation of rate with solvent composition k_1 v/s $1/D$.

Effect of temperature: The rate of oxidation increases with increase in temperature. The plot of $\log k_{\text{obs}}$ versus $1/T$ is a straight line in the temperature range 303-328K. From the Arrhenius plot, activation parameters were calculated and summarized in a table 2. The large and negative value of entropy of activation suggests that the activated complex formed has a more rigid structure the reactant.

Table 2. Variation of rate with Oxidant, Substrate, pH, Temperature and Solvent composition.

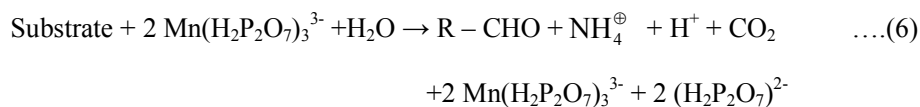
[Mn(II)Py ₃] X 10 ⁻³ M	[Histidine] X 10 ⁻² M	pH	Temp. K	Solvent % V/V	k_1 X 10 ⁻⁵ M	[Mn(II)Py ₃] X 10 ⁻³ M	[Histidine] X 10 ⁻² M	pH	Temp. K	Solvent % V/V	k_1 X 10 ⁻⁵ M
1.00	2.0	4.0	313	0	24.45	2.0	2.0	2.9	313	0	51.04
1.85	2.0	4.0	313	0	25.33	2.0	2.0	3.0	313	0	43.85
1.92	2.0	4.0	313	0	24.56	2.0	2.0	3.4	313	0	31.85
2.00	2.0	4.0	313	0	24.94	2.0	2.0	4.0	313	0	24.94
2.08	2.0	4.0	313	0	25.33	2.0	2.0	4.5	313	0	10.74
2.17	2.0	4.0	313	0	24.94	2.0	2.0	4.9	313	0	6.14
2.27	2.0	4.0	313	0	25.33	2.0	2.0	5.4	313	0	3.07
3.00	2.0	4.0	313	0	24.56	2.0	2.0	4.0	303	0	8.44
2.0	1.53	4.0	313	0	17.92	2.0	2.0	4.0	308	0	19.19
2.0	1.66	4.0	313	0	19.00	2.0	2.0	4.0	313	0	24.94
2.0	1.81	4.0	313	0	21.87	2.0	2.0	4.0	318	0	41.83
2.0	2.00	4.0	313	0	24.94	2.0	2.0	4.0	323	0	61.41
2.0	2.22	4.0	313	0	27.00	2.0	2.0	4.0	328	0	102.09
2.0	2.50	4.0	313	0	31.09	2.0	2.0	4.0	313	0	24.94
2.0	2.85	4.0	313	0	34.54	2.0	2.0	4.0	313	5	18.04
2.0	3.33	4.0	313	0	38.38	2.0	2.0	4.0	313	10	15.99
2.0	4.00	4.0	313	0	46.06	2.0	2.0	4.0	313	15	14.04
2.0	5.00	4.0	313	0	58.13	2.0	2.0	4.0	313	20	12.12
2.0	2.0	1.7	313	0	131.27	2.0	2.0	4.0	313	25	10.74
2.0	2.0	1.9	313	0	121.54	2.0	2.0	4.0	313	30	8.10
2.0	2.0	2.0	313	0	119.94	2.0	2.0	4.0	313	35	6.90
2.0	2.0	2.3	313	0	110.16	2.0	2.0	4.0	313	40	5.75
2.0	2.0	2.7	313	0	57.57						

The moderate value of ΔE_a^\ddagger point out that in the rate determining step the bond breaking and formation were of almost equal magnitude. ΔH^\ddagger is slightly lower than, this is due to decrease in number of moles of products. Before rds large number of equilibria, are formed therefore precise explanation of entropy cannot be given. Glasston [25] has pointed out that if entropy of activation is large and positive, the reaction will be slow. The observed +ve entropy of activation suggests C-C fission in rate determining step.



Scheme 1

Overall reaction is



Thermodynamic parameters.

$\Delta E_a^{\ddagger} \text{kJ mol}^{-1}$	$\Delta H^{\ddagger} \text{kJ mol}^{-1}$	$\Delta S^{\ddagger} \text{Jk}^{-1} \text{mol}^{-1}$	pZ	$\Delta F^{\ddagger} \text{kJk}^{-1} \text{mol}^{-1}$
78.79	76.19	29.56	3.499×10^{14}	66.94

APPLICATION

Chemical Kinetics can be really useful to decide the optimum time for a reaction, which can achieve the maximum obtainable conversion, and also to maintain the most desirable temperature range. Literature can yield values of conversion, and other operating parameters, which can be referred to optimize our reaction, especially in industrial scale.

CONCLUSIONS

This paper presents a detailed kinetics study of the oxidative degradation of L-Histidine by Mn(III) in pyrophosphate medium. Analysis of the kinetics data suggested that the rate-determining involves C-C fission.

The reaction has been found to be first order with respect to Mn (III) Py_3 , L-Histidine and fractional order with respect to $[\text{H}^+]$. A suitable mechanism, consistent with the experimental observations, has been proposed.

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