Kinetics and Mechanism of Oxidation of L-Histidine by Permanganate Ions in Sulfuric Acid Medium

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ABSTRACT: The reaction kinetics for the oxidation of L-histidine by permanganate ions have been investigated spectrophotometrically in sulfuric acid medium at constant ionic strength and temperature. The order with respect to permanganate ions was found to be unity and second in acid concentration, whereas a fractional order is observed with respect to histidine. The reaction was observed to proceed through formation of a 1:1 intermediate complex between oxidant and substrate. The effect of the acid concentration suggests that the reaction is acid catalyzed. Increasing the ionic strength has no significant effect on the rate. The influence of temperature on the rate of reaction was studied. The presence of metal ion catalysts was found to accelerate the oxidation rate, and the order of effectiveness of the ions was $Cu^{2+} > Ni^{2+} > Zn^{2+}$. The final oxidation products were identified as aldehyde (2-imidazole acetaldehyde), ammonium ion, manganese(II), and carbon dioxide. Based on the kinetic results, a plausible reaction mechanism is proposed. The activation parameters were determined and discussed with respect to a slow reaction step. © 2014 Wiley Periodicals, Inc. Int J Chem Kinet 46: 370–381, 2014

INTRODUCTION

Kinetic investigations on the oxidation of amino acids are important because of their biological significance and a precise understanding of the mechanism of such biological redox reactions. Hence, a kinetic and mechanistic study of their oxidation using various oxidants has received considerable attention. L-Histidine (His) is an essential component of almost all the proteins, found abundantly in hemoglobin, and has been used in the treatment of rheumatoid arthritis, allergic diseases, ulcers, and anemia. Its deficiency can cause poor hearing. The importance of the amino acid, histidine, lies in the fact that the body uses it to manufacture histamine, which is responsible for a wide range of physiological processes. It also provides metal-binding sites in many enzymes. Owing to the high reactivity of its imidazole group, histidine residue is often found at the active site

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of enzymes and involved directly in catalysis. It controls the transmission of metals in biological bases [1]. The formation and structure of histidine complexes with some transition metal ions have been studied in aqueous medium [2,3].

On the other hand, permanganate is a unique oxidizing agent in neutral, alkaline, and acidic media. In acidic media, the permanganate ion (MnO_4^-) can exist in several different forms: $HMnO_4$, $H_2MnO_4^+$, and Mn_2O_7, depending on the nature of the reductant; the oxidant has been assigned with innersphere and outer-sphere mechanism pathways in their redox reactions [4,5]. In general, the reduction of the permanganate ion in acid medium goes to either Mn^{IV} or Mn^{II}, where the reduction potential of the Mn^{VII}/Mn^{IV} couple is 1.695 V and of the Mn^{VII}/Mn^{II} couple is 1.51 V [6].

The permanganate oxidation of amino acids in strong acid medium [7–13] and weak acid medium [14,15] has been investigated. The occurrence of an autocatalysis effect in a weak acid medium, neutral aqueous solution, and weak basic medium has been extensively reported [14–18], whereas no rigorous evidence of such an effect has been reported in a strong acid medium. There have been just two reports [10,11] of a "double-stage" process vaguely attributed to possible autocatalysis.

A literature survey reveals that there are no reports on the oxidation of L-histidine by the permanganate ion in acidic media. This prompted us to study the title reaction to shed some light on its oxidation mechanism.

EXPERIMENTAL

Materials and Methods

Materials. All the reagents were obtained from Sigma-Aldrich (St. Louis, MO, USA). Stock solutions of L-histidine, potassium permanganate, and other reagents were prepared by dissolving the appropriate amount of the samples in the required volume of double-distilled water. The stock solution of potassium permanganate was standardized against As_2O_3. The permanganate ion concentration was then determined [19] spectrophotometrically prior to each run at $\lambda = 525$ nm, its absorption maximum. The ionic strength was maintained constant (4.0 mol dm^{-3}) using a Na_2SO_4 electrolyte.

Kinetic Procedure. Kinetic runs were performed under pseudo–first-order conditions, where L-histidine (His) was present in a large excess with respect to the permanganate concentration at a constant ionic strength of 4.0 mol dm^{-3}.

The absorbance measurements were made in a thermostated cell compartment at the desired temperature on a Shimadzu UV-1800 PC automatic scanning double-beam spectrophotometer fitted with a program controller using cells of path length 1 cm. The course of reactions was followed up to not less than two half-lives of the reaction completion by recording the decrease in the absorbance of the permanganate ion at $\lambda = 525$ nm as a function of time. It was verified that there is no interference from other reagents at these wavelengths. The reaction temperature was controlled within $\pm 0.1^\circ$C.

RESULTS

Stoichiometry and Product Analysis

Reaction mixtures containing different initial concentrations of the reactants at $[H^+] = 3.0$ and $I = 4.0$ mol dm^{-3} were equilibrated away from light. The residual $[MnO_4^-]$ was estimated periodically using both titrimetric and spectrophotometric techniques. A stoichiometric ratio of $([His]_0/[MnO_4^-]_{consumed})$ was found to be 2.5 ± 0.1 mol. This result confirms the following stoichiometric equation:

$$5C_6H_9O_2N_3 + 2MnO_4^- + 11H^+ \rightarrow 5C_5H_6ON_2 + 2Mn^{2+} + 5NH_4^+ + 5CO_2 + 3H_2O \quad (1)$$

where $C_6H_9O_2N_3$ and $C_5H_6ON_2$ are histidine and its corresponding aldehyde (2-imidazole acetaldehyde), respectively. The above stoichiometric equation is consistent with the results of product analysis. The product, aldehyde was estimated quantitatively as its 2,4-DNP derivative [20]. Mn^{2+} was qualitatively identified by a reaction with indole [21,22]. Other products were identified as discussed earlier [23,24]. Similar reaction products were observed during the oxidation of amino acids by the permanganate ion [25] or by other oxidants [26].

Spectral Changes

Figure 1 illustrates the permanganate absorption curves versus wavelength at 3 min intervals as the reaction proceeds, which indicate a gradual disappearance of MnO_4^- bands at $\lambda = 525$ nm, its absorption maximum. Regarding the previous studies [16–18], manganese(IV) ions absorb in the region 400–650 nm. Figure 1 shows no features in this wavelength area, meaning that MnO_2 is not a reaction product.

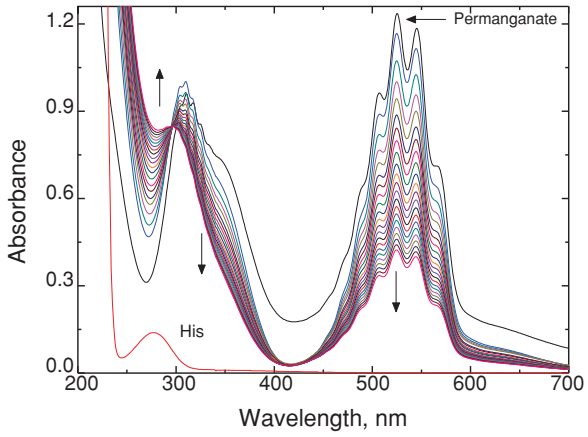


Figure 1 Spectral changes during the oxidation of histidine by acidic permanganate. [His] = 8×10^{-3}, [MnO_4^-] = 4×10^{-4}, [H^+] = 3.0 and I = 4.0 mol dm^{-3} at 25°C. Scanning time intervals = 3 min.

Furthermore, since no rise and fall in absorption is observed at 418 nm, it is concluded that Mn^{IV} ions do not intervene as a possible oxidizing agent.

Order of Reaction

The reaction orders were determined from the slopes of log k_{obs} (observed a first-order rate constant) versus log (concentration) by varying the concentrations of substrate and acid in turn, while keeping the others constants. The initial concentration of permanganate ions, [MnO_4^-]$_0$, was varied in the range of 2×10^{-4} to 6×10^{-4} mol dm^{-3} at constant concentrations of both substrate and acid, ionic strength, and temperature. Plots of ln (absorbance) versus time were linear as shown in Fig. 2. The linearity indicated a reaction order in [MnO_4^-] as unity. This was also supported by the independence of k_{obs} on different initial [MnO_4^-] as listed in Table I.

The substrate concentration was varied keeping all other reactants concentrations and conditions constant. The experimental results indicate that the rate of oxidation increased appreciably with an increase in the substrate concentration (Table I). A plot of k_{obs} versus

Table I Influence of [MnO_4^-], [Histidine], and [H^+] on the First-Order Rate Constant Values in the Oxidation of Histidine by Acidic Permanganate at 25°C

10^4 [MnO_4^-] (mol dm^{-3})	10^3 [Histidine] (mol dm^{-3})	[H^+] (mol dm^{-3})	10^5 k_{obs} (s^{-1})
2.0	8.0	3.0	44
3.0	8.0	3.0	43
4.0	8.0	3.0	43
5.0	8.0	3.0	42
6.0	8.0	3.0	42
4.0	6.0	3.0	33
4.0	8.0	3.0	43
4.0	10.0	3.0	50
4.0	12.0	3.0	56
4.0	8.0	2.5	32
4.0	8.0	3.0	43
4.0	8.0	3.5	66
4.0	8.0	4.0	80

The experimental error is equal to 3–4%.

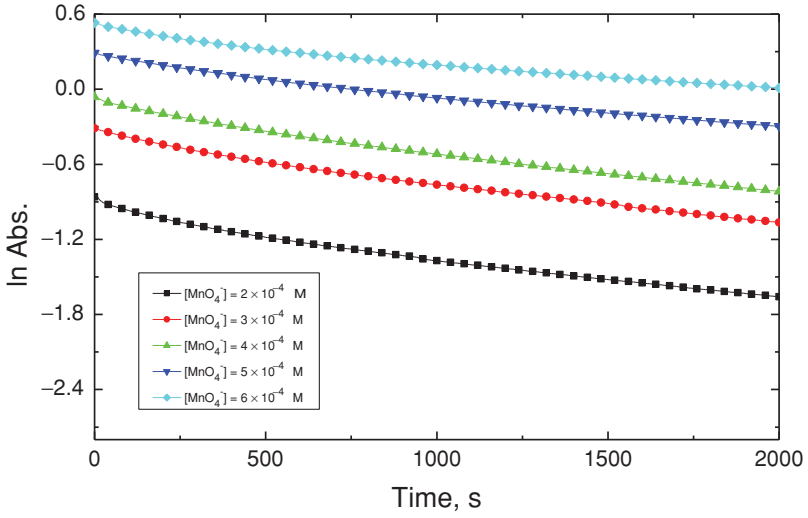


Figure 2 Influence of [MnO_4^-] on the first-order rate constant plots in the oxidation of histidine by acidic permanganate. [His] = 8×10^{-3}, [H^+] = 3.0, and I = 4.0 mol dm^{-3} at 25°C.

[His] was linear with a nonzero intercept (figure not shown), thus indicating the reaction order with respect to amino acid to be fractional first.

The reaction order with respect to the acid concentration was studied by using different concentrations of sulfuric acid and constant substrate and oxidant concentrations, ionic strength, and temperature. An increase in the acid concentration was found to accelerate the reaction rate (Table I). A plot of k_{obs} versus $[H^+]^2$ gave a good straight line with a negligible intercept (see Fig. 4 later in this article), indicating a fractional second-order dependence with respect to $[H^+]$, and this is supported by the linear plot of log k_{obs} – log $[H^+]$ with a slope 2.1 (figures not shown).

Dependence of the Reaction Rate on the Ionic Strength

The effect of the ionic strength (I) on the reaction rate has been investigated by means of a series of experiments carried out at a constant concentration of permanganate, histidine, and the acid as the concentration of Na_2SO_4 was increased in the reaction medium. The experimental results indicate that increasing the ionic strength has no significant effect on the rate constant.

Dependence of the Reaction Rate on Added Salts

Since Mn^{2+} is one of the oxidation products of permanganate ions in acid medium, its effect on the reaction rate should be examined. It is well known [27] that acidified permanganate is reduced by addition of Mn^{2+} to give Mn^{3+} and Mn^{4+} according to the following equation:

$$MnO_4^- + 3Mn^{2+} + 8H^+ \rightarrow 3Mn^{3+} + Mn^{4+} + 4H_2O \quad (2)$$

where Mn^{3+} and Mn^{4+} can be removed by fluoride ions through complex formation [27]. If MnO_4^- ions are primarily responsible for oxidation, a reduction in the initial rate should be observed in the presence of Mn^{2+} ions, which reduce the concentration of permanganate ions [28]. If the intermediates Mn^{3+} and/or Mn^{4+} are the reactive oxidizing species, the addition of Mn^{2+} should accelerate the reaction rate. Similarly, the addition of F^- ions should retard the rate of reaction if the intermediate manganese(III) and/or manganese(IV) ions are the mainly responsible for the oxidation and cause no significant change if MnO_4^- ions are the principle oxidizing entities [29,30]. On the other hand, the catalytic effect of Mn^{2+} may be attributed to the formation of a complex with the substrate that is then oxidized by $HMnO_4$.

The influence added Mn^{2+} and F^- ions was examined by the addition of each salt to the reaction medium of histidine with permanganate ions at $[MnO_4^-] = 4 \times 10^{-4}$, $[His] = 8 \times 10^{-3}$, $[H^+] = 3.0$, $I = 4.0$ mol dm^{-3}, and $T = 25°C$. The experimental observations indicated that the reaction rate was progressively increased with increasing $[Mn^{2+}]$, whereas a decrease in the reaction rate was observed upon the addition of F^- ions as shown in Fig. 3.

Effect of Metal Ion Catalysts

If the reactive molecular species or activated complex formed are either charged or dipolar in nature, a

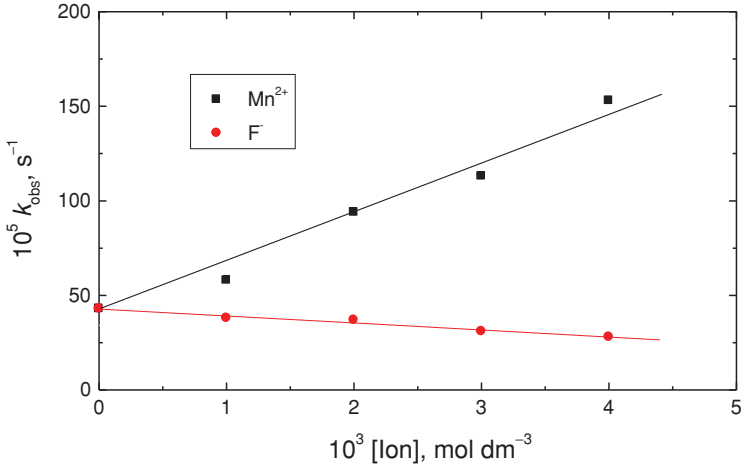


Figure 3 Influence of $[Mn^{2+}]$ and $[F^-]$ on the first-order rate constant in the oxidation of histidine by acidic permanganate. $[His] = 8 \times 10^{-3}$, $[MnO_4^-] = 4 \times 10^{-4}$, $[H^+] = 3.0$, and $I = 4.0$ mol dm^{-3} at 25°C.

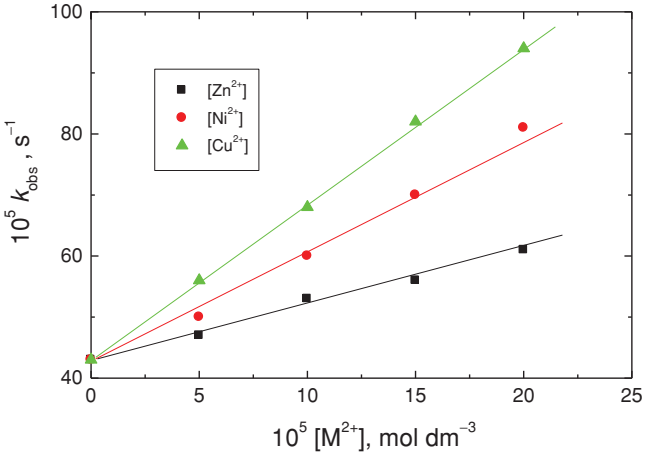


Figure 4 Influence of some metal ions on the first-order rate constant in the oxidation of histidine by acidic permanganate. [His] = 8×10^{-3}, [MnO_4^-] = 4×10^{-4}, [H^+] = 3.0, and I = 4.0 mol dm^{-3} at 25°C.

specific influence of added metal ions on the reaction velocity may be expected, depending on their charge, size, complexing tendency, and general nature. Therefore, sulfates of some selected divalent transition metal ions such as Cu^{2+}, Ni^{2+}, and Zn^{2+} were added to the reaction medium at identical concentrations. The experimental observations show that the presence of such ions accelerates the reaction rate. The order of effectiveness of the ions was $Cu^{2+} > Ni^{2+} > Zn^{2+}$. A plot of k_{obs} versus the electrolyte concentration exhibits a nonzero rate at the zero electrolyte concentration as shown in Fig. 4.

Effect of Temperature

To determine the activation parameters, the reaction was studied at four temperatures, namely 25, 30, 35, and 40°C, and at constants of pH and ionic strength. The experimental results indicated that the rate of oxidation speeds up by increasing the temperature. The temperature dependence was found to fit Arrhenius and Erying equations.

Polymerization Test

The possibility of formation of free radicals was examined by adding 10% (v/v) acrylonitrile to the partially oxidized reaction mixture. After a lapse of 20 min mixing (on warming), an appreciable white precipitate was observed indicating that the oxidation reaction probably proceeds via the generation of free radicals. No detectable polymerization was shown in both experiments in which either of the reactants was absent.

DISCUSSION

The enhancement of the reaction rate with increasing acid concentration (experimentally) and the chemistry of potassium permanganate (as reported in Ref. [31]) suggest the formation of a more powerful oxidant, namely permanganic acid, by the following equilibrium:

$$MnO_4^- + H^+ \overset{K_1}{\rightleftarrows} HMnO_4 \qquad (3)$$

where K_1 is the protonation constant of permanganate ion ($K_1 = 2.99 \times 10^{-3}$ dm^3 mol^{-1} at 25°C [32]). The protonation of the permanganate ion shifts the Mn^{VII}/Mn^{VI} couple to a more positive value (+1.3 V), which makes $HMnO_4$ a stronger oxidizing agent than MnO_4^- [32,33].

Also, it is reported [34] that in acid solutions, amino acids exist in zwitterions and predominantly tend to protonate at higher acid concentrations according to the following equilibria:

$$R - CH(NH_2)COOH \rightleftarrows R - CH(^+NH_3)COO^- \qquad (4)$$

(zwitterion)

$$\underset{\text{(His)}}{R{-}CH(NH_3)^+COO^-} + H^+ \overset{K_2}{\rightleftarrows} \underset{(His^+)}{R{-}CH(NH_3)^+COOH} \qquad (5)$$

where R-$CH(NH_2)COOH$ and R-$CH(^+NH_3)COOH$ denote the histidine substrate (His) and its protonated form (His^+), respectively, and K_2 is the protonation constant of histidine.

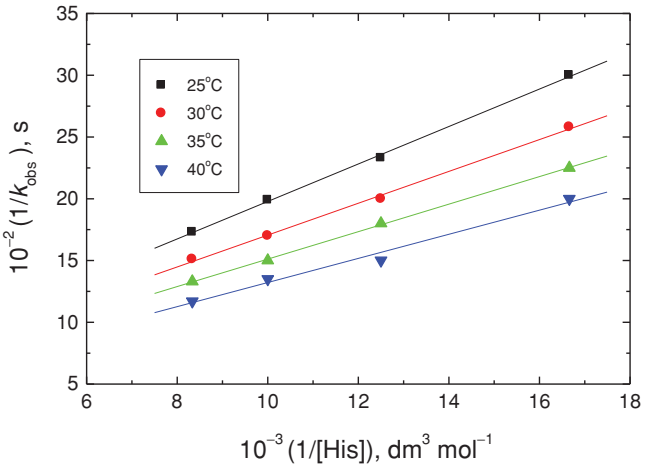


Figure 5 Plots of $1/k_{obs}$ versus 1/[His] in the oxidation of histidine by acidic permanganate. $[MnO_4^-] = 4 \times 10^{-4}$, $[H^+] = 3.0$, and $I = 4.0$ mol dm^{-3}

The second-order dependence of the reaction in $[H^+]$ suggests that both amino acid substrate and oxidant are subjected to protonation, i.e., the protonated forms of both reactants will be considered as the reactive species in the rate-determining step as defined by the above-mentioned equilibria, (3) and (5).

Again, the linearity of the plots of $1/k_{obs}$ versus 1/[His] (Fig. 5) is considered as a kinetic evidence in favor of possible formation of an intermediate complex between the oxidant and substrate, similar to the well-known Michaelis–Menten [35] mechanism for enzyme–substrate reactions. The formation of an intermediate complex is also confirmed by the increase in the initial absorbance observed in the UV region on mixing the solutions of the substrate and permanganate ion especially at lower temperatures. The failure of the spectrophotometric detection of such an intermediate complex may be interpreted by either a lower concentration of the reactants used and, hence, the expected lower absorbitivity of the formed complex and/or the fast subsequent decomposition of the intermediate in comparison with its formation. Furthermore, the negligible effect of the ionic strength on the rate indicates that the reaction is between an ion and a neutral molecule [36].

In view of the above arguments, the following reaction mechanism may be suggested, which involves the attack of the powerful oxidant, acid permanganate, on the protonated histidine leading to the formation a complex (C) in a prior equilibrium step:

$$His^+ + HMnO_4 \overset{K_3}{\rightleftarrows} [His - HMnO_4]^+ (C) \qquad (6)$$

where K_3 is the formation constant of the complex between the oxidant and the substrate.

The cleavage of such a complex leads to the formation of a free radical intermediate of histidine and manganate(VI)

$$[His - HMnO_4]^+ (C) \underset{(slow)}{\overset{k_1}{\longrightarrow}} His^{\cdot} + HMnO_4^- + H^+ \qquad (7)$$

followed by decarboxylation of histidine free radical, forming a new radical intermediate ($X^{\cdot}$)

$$His^{\cdot} \overset{fast}{\rightarrow} X^{\cdot} + CO_2 \qquad (8)$$

This intermediate ($X^{\cdot}$) is rapidly attacked by the manganate(VI) ion of the oxidant to yield the final oxidation products

$$X^{\cdot} + HMnO_4^- \overset{fast}{\rightarrow} Aldehyde + NH_4^+ + HMnO_4^{2-} \qquad (9)$$

Knowing the fact that the species Mn^V is very unstable in strong acidic media, it will be converted into Mn^{II} and Mn^{VII} by means of a rapid disproportionation as follows:

$$5HMnO_4^{2-} + 11H^+ \rightarrow 3MnO_4^- + 2Mn^{2+} + 8H_2O \qquad (10)$$

Multiplying equations from (3) to (9) by a factor of five and then summing them with Eq. (10) results in the overall reaction with the stoichiometry satisfied.

According to the rate-determining step (reaction (7)), in the above-mentioned mechanism, the rate of disappearance of the permanganate ion or the formation of the intermediate complex can be expressed by the following rate law:

$$\text{Rate} = \frac{-\mathrm{d}\left[\mathrm{MnO_4^-}\right]}{\mathrm{d}t} = \frac{+\mathrm{d}\left[\mathrm{His-HMnO_4}\right]^+}{\mathrm{d}t} = k_1\left[\mathrm{His-HMnO_4}\right]^+ \quad (11)$$

The change in the rate of complex formation with the change in the substrate, hydrogen ion, and oxidant concentrations can be deduced (see the Appendix) to give the following equation:

$$\text{Rate} = \frac{k_1K_1K_2K_3[\mathrm{MnO_4^-}][\mathrm{His}][\mathrm{H^+}]^2}{1+K_1[\mathrm{H^+}]+K_1K_2K_3[\mathrm{His}][\mathrm{H^+}]^2} \quad (12)$$

Under the pseudo–first-order condition in the presence of a large excess of substrate over that of $[\mathrm{MnO_4^-}]$, the rate law can be expressed by Eq. (13):

$$\text{Rate} = \frac{-\mathrm{d}\left[\mathrm{MnO_4^-}\right]}{\mathrm{d}t} = k_{\mathrm{obs}}\left[\mathrm{MnO_4^-}\right] \quad (13)$$

Comparing Eqs. (12) and (13) and rearrangement, the following relationship is obtained:

$$\frac{1}{k_{\mathrm{obs}}} = \left(\frac{1+K_1[\mathrm{H^+}]}{k_1K_1K_2K_3[\mathrm{H^+}]^2}\right)\frac{1}{[\mathrm{His}]} + \frac{1}{k_1} \quad (14)$$

According to Eq. (14), plots of $1/k_{\mathrm{obs}}$ against $1/[\mathrm{His}]$ at a constant $[\mathrm{H^+}]$ should be straight lines with positive intercepts on $1/k_{\mathrm{obs}}$ axis as is observed experimentally at four temperatures (Fig. 5). From the intercepts of such plots, the rate constant values of the rate-determining step, k_1, at various temperatures were determined as 2.16×10^{-3}, 2.41×10^{-3}, 2.62×10^{-3}, and 2.89×10^{-3} $\mathrm{s^{-1}}$ at 25, 30, 35, and 40°C, respectively. Again, a plot of $1/k_{\mathrm{obs}}$ against $1/[\mathrm{H^+}]^2$ at a constant [His] also should give a straight line with a positive intercept on the $1/k_{\mathrm{obs}}$ axis as was experimentally observed in Fig. 6.

The small intercepts observed in Fig. 5 may lead us to simplify Eq. (14) to Eq. (15), which is considered to be the suitable rate law expression

$$\frac{[\mathrm{His}][\mathrm{H^+}]}{k_{\mathrm{obs}}} = \frac{1}{k'}\frac{1}{[\mathrm{H^+}]} + \frac{1}{k''} \quad (15)$$

where k' and k'' are the apparent rate constants and are equal to $k_1K_1K_2K_3$ and $k_1K_2K_3$, respectively.

According to the above equation, when a plot was made between $[\mathrm{His}][\mathrm{H^+}]/k_{\mathrm{obs}}$ and $1/[\mathrm{H^+}]$ a good straight line would be observed in favor of the suggested mechanism and the rate law (Fig. 7), from its slope and intercept, the apparent rate constants, k' and k'', are calculated as 62.21×10^{-5} $\mathrm{dm^9\ mol^{-3}\ s^{-1}}$ and 21.01×10^{-2} $\mathrm{dm^6\ mol^{-2}\ s^{-1}}$, respectively. Again, the protonation constant of the permanganate ion can be evaluated by dividing k' on k'' ($K_1 = k'/k''$). This value was found to be equal to 2.96×10^{-3} $\mathrm{dm^3\ mol^{-1}}$ at 25°C in good agreement with that reported elsewhere [32] (2.99×10^{-3} $\mathrm{dm^3\ mol^{-1}}$), indicating the validity of the proposed mechanism. Unfortunately, the value of the formation constant of the intermediate

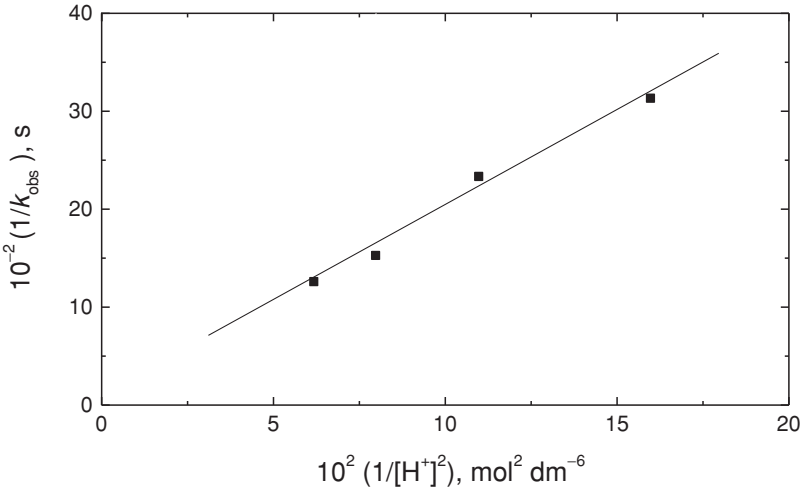


Figure 6 Plot of $1/k_{\mathrm{obs}}$ versus $1/[\mathrm{H^+}]^2$ in the oxidation of histidine by acidic permanganate. $[\mathrm{His}] = 8 \times 10^{-3}$, $[\mathrm{MnO_4^-}] = 4 \times 10^{-4}$, and $I = 4.0$ mol $\mathrm{dm^{-3}}$ at 25°C.

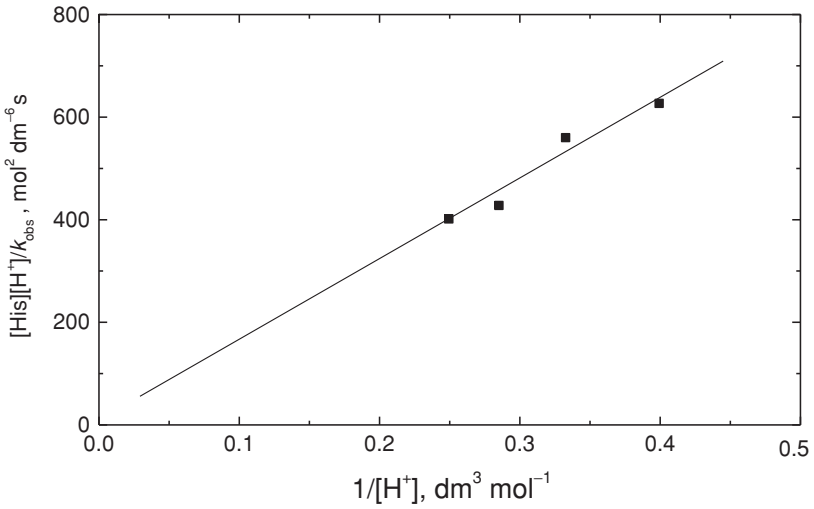


Figure 7 Plot of $[His][H^+]/k_{obs}$ versus $1/[H^+]$ in the oxidation of histidine by acidic permanganate. $[MnO_4^-] = 4 \times 10^{-4}$ and $I = 4.0$ mol dm^{-3} at 25°C.

complex, K_3, could not be calculated because of the nonavailability of the protonation constants of histidine (K_2) at the same conditions.

The activation parameters of the rate constants (k_1 and k_{obs}) are calculated using Eyring and Arrhenius plots as are given in Table II. The observed large negative values of $\Delta S^{\neq}$ confirms the compactness of the intermediate complex formed, and such an activated complex is more ordered than the reactants due to loss of degree of freedom. This is also supported by very small values of the frequency factor A [37]. Again, the positive values of both $\Delta H^{\neq}$ and $\Delta G^{\neq}$ indicate the endothermic formation of the intermediate and its nonspontaneity, respectively. This evidence accords with the suggested transition states, which may confirm the formation of the intermediate complex via the inner sphere electron transfer mechanism. This mechanism is supported by the proposition made by Stewart and co-workers [37,38] for ionic transition states in the oxidation of many organic substrates by the permanganate ion. They reported that the entropy of activation tends to be more positive for reactions of outer sphere mechanisms, whereas it is more negative for reactions of inner sphere type. Therefore, such agreement may be considered as evidence to support the formation of an intermediate complex of inner sphere nature for the electron transfer mechanism with respect to the present redox reaction. On the other hand, values of thermodynamic parameters with those obtained for a slow step of the reaction shows that these values mainly refer to the rate-limiting step, supporting the fact that the reaction before the rate-determining step is fairly slow and involves high activation energy [39].

The activation parameters for oxidation reactions of some amino acids with acidic permanganate having negative entropies of activation are summarized in Table III. Leffler and Grunwald [40] have pointed out that many reactions show an isokinetic relationship, $\Delta H^{\neq} = \alpha + \beta \Delta S^{\neq}$, where β is called the isokinetic temperature. As shown in Fig. 8, a plot of $\Delta H^{\neq}$ versus $\Delta S^{\neq}$ for some reactions of amino acids with acidic permanganate is fairly linear with $\alpha = 80$ kJ mol^{-1} and $\beta = 271$ K. The value of the isokinetic temperature (271 K) is smaller than the experimental temperature (298 K). This indicates that the rate is governed by the enthalpy of activation [41]. The linearity and the slope

Table II Activation Parameters of the Rate Constants: k_1 and k_{obs} in the Oxidation of Histidine by Acidic Permanganate. $[MnO_4^-] = 4 \times 10^{-4}$, $[H^+] = 3.0$, and $I = 4.0$ mol dm^{-3}

	Parameter				
Rate Constant	$\Delta S^{\neq}$ (J mol^{-1}K^{-1})	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta G^{\neq}$ (kJ mol^{-1})	$E_a^{\neq}$ (kJ mol^{-1})	A (mol^{-1} s^{-1})
k_1	−254.65	12.28	88.17	14.80	0.86
k_{obs}	−244.26	19.37	92.16	21.86	3.01

Table III Activation Parameters for the Oxidation of Some Amino Acids by Acidic Permanganate

Amino Acid	$\Delta S^{\neq}$ (J mol^{-1}K^{-1})	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta G^{\neq}_{25^{\circ}C}$ (kJ mol^{-1})	Reference
DL-Alanine	− 53	70	86	[4]
DL-Valine	− 105	51	82	[4]
L-Arginine	− 127	50	88	[9]
Phenylalanine	− 160	34	82	[11]
L-Histidine	− 244.26	19.37	92.16	This work

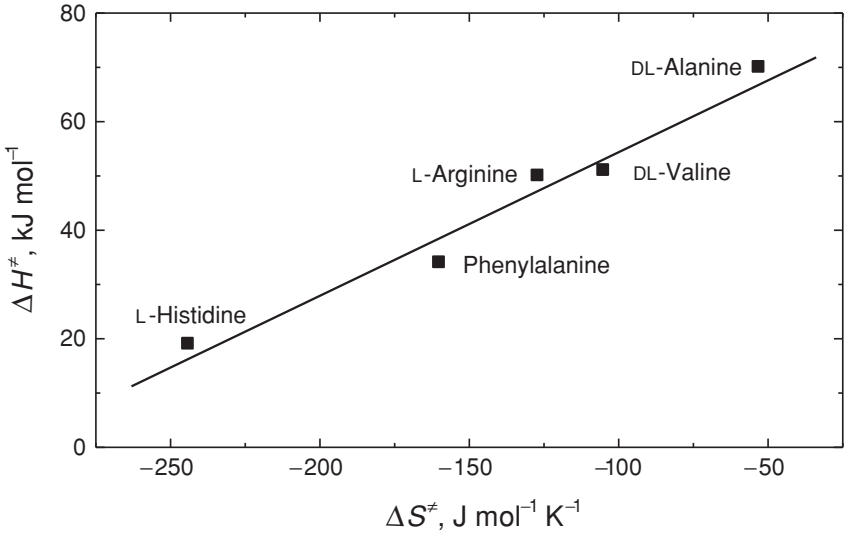


Figure 8 Isokinetic plot, $\Delta H^{\neq}$ versus $\Delta S^{\neq}$, in the oxidation of some amino acids by acidic permanganate.

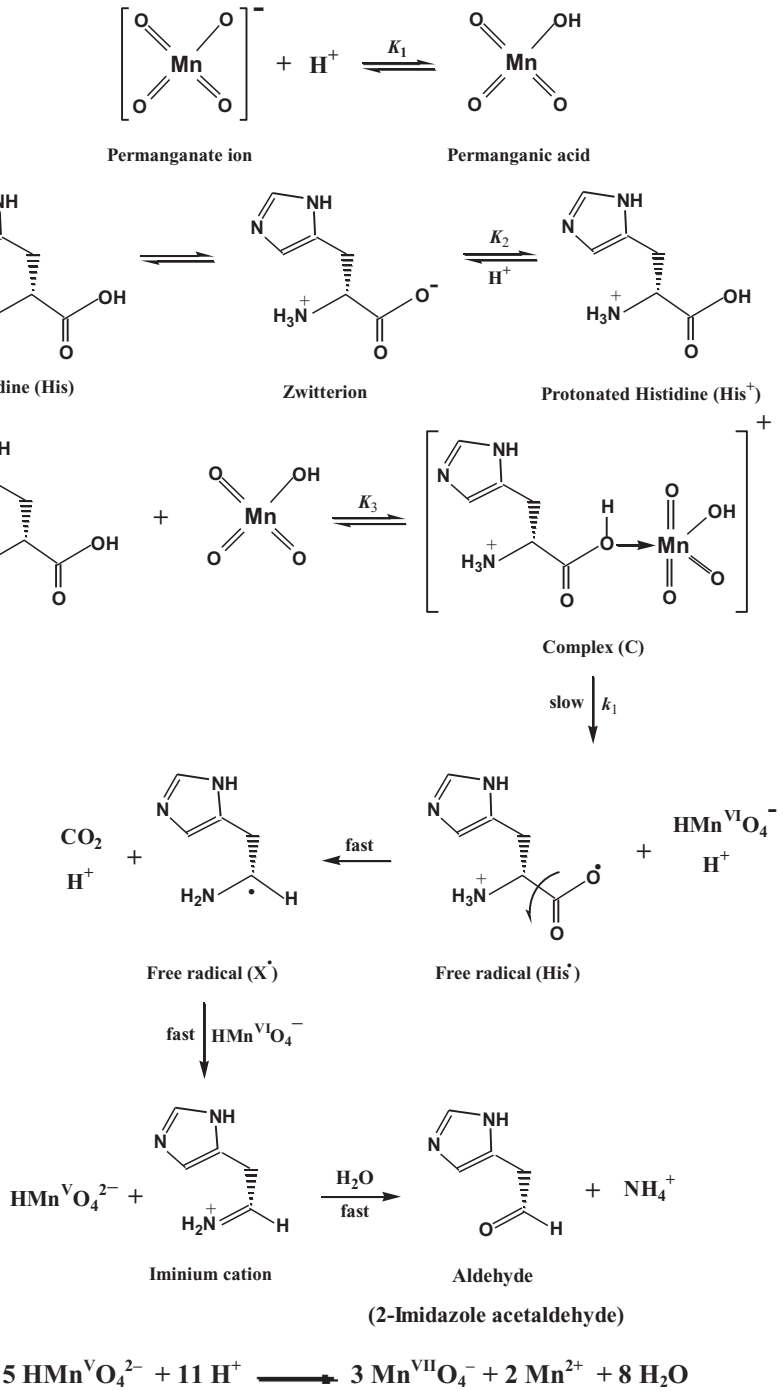
of the plot may confirm that the kinetics of these reactions follow a similar reaction mechanism, free radical intervention, as shown in Scheme 1.

A question of basic interest may be arisen is whether electron transfer proceeds through successive one-electron changes, $Mn^{VII} \rightarrow Mn^{VI} \rightarrow Mn^{V}$, or by a simultaneous two-electron changes in a single step, $Mn^{VII} \rightarrow Mn^{V}$. The positive catalytic effect of Mn^{2+} on the rate of reaction and the decrease in the reaction rate on addition of the F^{-} ion may reflect the one-electron transfer mechanism. Again, the formation of free radicals during the course of reaction as well as the high negative entropy of activation obtained may be considered as an evidence to support the one-electron-transfer mechanism of inner sphere nature [38].

Inspection of the acceleration of the oxidation rate by transition metal ions catalysts, Mishra and Gupta [42] and other workers [43–46] have interpreted specific effects of metal ions in terms of bridging that facilitates electron transfer in redox systems, whereas Wahl [47] and his co-workers have interpreted specific effects in terms of complex formation. Some suggested [48] structures of histidine complexes with transition metal ions are illustrated in Scheme 2. It was reported [48] that metal complexes can be more active than the free ligands, and can exhibit bioactivities that are not shown by the free ligands.

CONCLUSIONS

1. In acid medium, the title reaction was observed to proceed through formation of a 1:1 intermediate complex between oxidant and substrate and the reaction was acid-catalyzed.
2. The presence of metal ion catalysts was found to accelerate the oxidation rate, and the order of effectiveness of the ions was $Cu^{2+} > Ni^{2+} > Zn^{2+}$.
3. The final oxidation products were identified as aldehyde (2-imidazole acetaldehyde), ammonium ion, manganese(II), and carbon dioxide.
4. The rate constants of the slow step of the mechanism were evaluated at different temperatures, and activation parameters were calculated and discussed.
5. The mechanism consistent with the product and mechanistic and kinetic studies was proposed.



$$5\,HMn^{V}O_4^{2-} + 11\,H^+ \longrightarrow 3\,Mn^{VII}O_4^- + 2\,Mn^{2+} + 8\,H_2O$$

Scheme 1 Mechanism of oxidation of L-histidine by acidic permanganate.

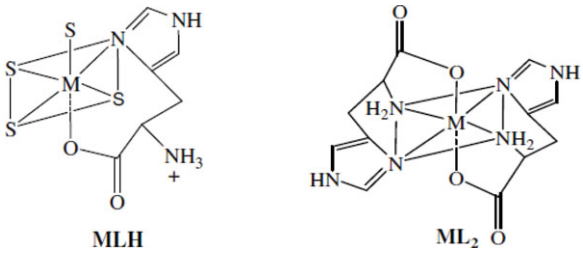
APPENDIX

According to the suggested mechanism

$$\text{Rate} = \frac{-d\left[MnO_4^-\right]}{dt} = \frac{+d\,[His - HMnO_4]^+}{dt} = k_l\,[His - HMnO_4]^+ \quad (A1)$$

From reactions (3), (5), and (6),

$$K_1 = \frac{[HMnO_4]}{[MnO_4^-][H^+]},\ [HMnO_4] = K_1\left[MnO_4^-\right]\left[H^+\right] \quad (A2)$$



Scheme 2 Some suggested [48] structures of histidine complexes with transition metal ions, where M is the metal ion, L is the histidine ligand, and S is the water molecules.

and

$$K_2 = \frac{\left[\mathrm{His}^+\right]}{[\mathrm{His}]\,[\mathrm{H}^+]},\ \left[\mathrm{His}^+\right] = K_2\,[\mathrm{His}]\left[\mathrm{H}^+\right] \quad \text{(A3)}$$

$$K_3 = \frac{[\mathrm{His}-\mathrm{HMnO_4}]^+}{\left[\mathrm{His}^+\right][\mathrm{HMnO_4}]}\,[\mathrm{His}-\mathrm{HMnO_4}]^+ = K_3\left[\mathrm{His}^+\right][\mathrm{HMnO_4}] \quad \text{(A4)}$$

Substituting Eqs. (A2) and (A3) into Eq. (A4) gives

$$[\mathrm{His}-\mathrm{HMnO_4}]^+ = K_1K_2K_3\,[\mathrm{His}]\left[\mathrm{MnO_4^-}\right]\left[\mathrm{H}^+\right]^2 \quad \text{(A5)}$$

Substituting Eq. (A5) into Eq. (A1) leads to

$$\mathrm{Rate} = k_1K_1K_2K_3[\mathrm{His}]\left[\mathrm{MnO_4^-}\right]\left[\mathrm{H}^+\right]^2 \quad \text{(A6)}$$

The total concentration of MnO_4^- is given by (where T and F stand for total and free, respectively)

$$\left[\mathrm{MnO_4^-}\right]_\mathrm{T} = \left[\mathrm{MnO_4^-}\right]_\mathrm{F} + [\mathrm{HMnO_4}] + [\mathrm{His}-\mathrm{HMnO_4}]^+ \quad \text{(A7)}$$

Substituting Eqs. (A2) and (A5) into Eq. (A7) gives

$$\left[\mathrm{MnO_4^-}\right]_\mathrm{T} = \left[\mathrm{MnO_4^-}\right]_\mathrm{F} + K_1\left[\mathrm{MnO_4^-}\right]_\mathrm{F}\left[\mathrm{H}^+\right] + K_1K_2K_3\left[\mathrm{MnO_4^-}\right]_\mathrm{F}[\mathrm{His}]\left[\mathrm{H}^+\right]^2 \quad \text{(A8)}$$

$$\left[\mathrm{MnO_4^-}\right]_\mathrm{T} = \left[\mathrm{MnO_4^-}\right]_\mathrm{F} \times \left(1 + K_1\left[H^+\right] + K_1K_2K_3\,[\mathrm{His}]\left[\mathrm{H}^+\right]^2\right) \quad \text{(A9)}$$

Therefore,

$$\left[\mathrm{MnO_4^-}\right]_\mathrm{F} = \frac{[\mathrm{MnO_4^-}]_\mathrm{T}}{1+K_1[\mathrm{H}^+]+K_1K_2K_3[\mathrm{His}][\mathrm{H}^+]^2} \quad \text{(A10)}$$

In view of the high concentrations of $[H^+]$, we can write

$$\left[\mathrm{H}^+\right]_\mathrm{T} = \left[\mathrm{H}^+\right]_\mathrm{F} \quad \text{(A11)}$$

Similarly,

$$[\mathrm{His}]_\mathrm{T} = [\mathrm{His}]_\mathrm{F} \quad \text{(A12)}$$

Substituting Eqs. (A10), (A11), and (A12) into Eq. (A6) (and omitting T and F subscripts) leads to

$$\mathrm{Rate} = \frac{k_1K_1K_2K_3[\mathrm{MnO_4^-}][\mathrm{His}][\mathrm{H}^+]^2}{1+K_1[\mathrm{H}^+]+K_1K_2K_3[\mathrm{His}][\mathrm{H}^+]^2} \quad \text{(A13)}$$

Under the pseudo–first-order condition, the rate law can be expressed by

$$\mathrm{Rate} = \frac{-\mathrm{d}\left[\mathrm{MnO_4^-}\right]}{\mathrm{d}t} = k_\mathrm{obs}\left[\mathrm{MnO_4^-}\right] \quad \text{(A14)}$$

Comparing Eqs. (A13) and (A14), the following relationship is obtained:

$$k_\mathrm{obs} = \frac{k_1K_1K_2K_3[\mathrm{His}][\mathrm{H}^+]^2}{1+K_1[\mathrm{H}^+]+K_1K_2K_3[\mathrm{His}][\mathrm{H}^+]^2} \quad \text{(A15)}$$

and

$$\frac{1}{k_\mathrm{obs}} = \left(\frac{1+K_1[\mathrm{H}^+]}{k_1K_1K_2K_3[\mathrm{H}^+]^2}\right)\frac{1}{[\mathrm{His}]} + \frac{1}{k_1} \quad \text{(A16)}$$

The small intercepts may lead us to simplify Eq. (A16) to Eq. (A17):

$$\frac{[\mathrm{His}]\left[\mathrm{H}^+\right]}{k_\mathrm{obs}} = \frac{1}{k'}\frac{1}{[\mathrm{H}^+]} + \frac{1}{k} \quad \text{(A17)}$$

NOTE ADDED IN PROOF: The following corrections were made after initial publication. Introduction, paragraph 2, line 4, $HMnO_3$ was deleted. In Eqs. (4) and (5) positive charges are now superscripted. Below Eq. (7), asparagine was changed to histidine. In Eq. (10) and Scheme 1, $3H_2O$ was changed to $8H_2O$. Below Eq. (A1), reactions (3) and (5) was changed to reactions (3), (5), and (6). Below Eq. (A7), (A3) and

(A4) was changed to (A2) and (A5). Below Eq. (A14), (A12) was changed to (A13).

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