LIST OF PUBLICATIONS


Kinetics and Mechanism of Oxidation of L-Phenylalanine by Alkaline Permanganate

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The kinetics of oxidation of L-phenylalanine by alkaline permanganate follows the rate law

\[
\frac{d[MnO_4^-]}{dt} = \frac{kK[L-phenylalanine][MnO_4^-]}{1 + K[L-phenylalanine]}
\]

where \(K\) is the formation constant for the complex between L-phenylalanine and permanganate and \(k\) is the decomposition rate constant. The data suggest that the oxidation of L-phenylalanine proceeds via the formation of a complex between L-phenylalanine and permanganate which decomposes slowly, followed by a fast reaction between the free radical of L-phenylalanine and another molecule of permanganate to give the products. The reaction constants involved in the mechanism are derived. There is a good agreement between the observed and calculated rate constants at varying conditions of experiments. The activation parameters are computed with respect to the slow step of the mechanism.

Key words: oxidation, L-phenylalanine, permanganate, kinetics, activation parameters

As it has long been known, permanganate ion oxidizes a much greater variety of substrates in alkaline medium than in the acidic one [1, 2, 3]. If \([\text{OH}^-] \geq 0.1 \text{ mol dm}^{-3}\) permanganate will be reduced only to manganate in the first step, and owing to its much lower reactivity, further reaction with manganate will be much slower [1, 4, 5]. Thus the process \(\text{Mn(VII)} \rightarrow \text{Mn(IV)}\) can be divided into a number of partial steps and examined separately. The \(\text{MnO}_4^-\) appears only after long time i.e., after the complete consumption of \(\text{MnO}_4^-\). In a strongly alkaline medium, the stable reduction product [6] of permanganate ion is manganate ion, \(\text{MnO}_4^{2-}\). No mechanistic information is available to distinguish between a direct one electron reduction to \(\text{Mn(VI)}\) (Scheme 1).

\[
\begin{align*}
\text{Mn(VII)} + S & \rightarrow \text{Mn(VI)} + S' \\
\text{Mn(VII)} + S' & \rightarrow \text{Mn(VI)} + \text{Products}
\end{align*}
\]

\(S = \text{substrate, } k_2 \gg k_1\)

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and a mechanism, in which a hypomanganate is formed in a two electron step, followed by a rapid reaction (Scheme 2).

\[
\begin{align*}
\text{Mn(VII)} + \text{S} & \rightarrow \text{Mn(V)} + \text{Products} \\
\text{Mn(VII)} + \text{Mn(V)} & \rightarrow 2\text{Mn(VI)} \\
\end{align*}
\]

Scheme 2

Amino acids have been oxidized by a variety of oxidizing agents [7]. Although a variety of organic substrates [8] and inorganic substrates [6] is oxidized by permanganate in aqueous alkaline medium, there are only a few reports [9] on the oxidation of amino acids by aqueous alkaline permanganate. In order to explore the mechanism of oxidation by permanganate ion in a strongly aqueous alkaline medium we have selected L-phenylalanine, an amino acid as a substrate. Since no work has been reported on the oxidation of L-phenylalanine by permanganate ion in aqueous alkaline medium, the present study deals with the title reaction to investigate the redox chemistry of permanganate in such media.

EXPERIMENTAL

Materials: Stock solution of L-phenylalanine (S.D. fine-Chem) and potassium permanganate (BDH) were prepared by dissolving the appropriate amounts in doubly distilled water. The stock solution of permanganate was standardized against oxalic acid [10]. Potassium manganate solution was prepared as described in [11] as follows: A solution of potassium permanganate was refluxed in aqueous 8.0 mol dm\(^{-3}\) of potassium hydroxide solution until a green colour was produced. The solid potassium manganate formed on cooling was recrystallized from the same solvent. Weighing out the required amount of recrystallized sample, the stock solution of potassium manganate was prepared in aqueous potassium hydroxide. The solution was standardized by measuring absorbance at 608 nm ($e = 1530 \pm 20$ dm\(^3\) mol\(^{-1}\) cm\(^{-1}\)) using Hitachi 150-20 spectrophotometer with a 1 cm cell. All other reagents were of analytical grade and their solutions were prepared by dissolving requisite amounts of the samples in doubly distilled water. NaOH and NaClO\(_3\) were used to provide the required alkalinity and to maintain ionic strength respectively.

Kinetic measurements: All kinetic measurements were performed under pseudo-first order conditions, where [L-phenylalanine] used is at least 10 fold excess over [permanganate ion] at a constant ionic strength of 2.0 mol dm\(^{-3}\). The reaction was initiated by mixing previously thermostated solutions of MnO\(_4^–\) and L-phenylalanine, which also contained required quantities of NaOH and NaClO\(_3\) to maintain required alkalinity and ionic strength respectively. The temperature was maintained at 23 ± 0.1°C. The course of reaction was followed by monitoring the decrease in the absorbance of MnO\(_4^–\) in a 1 cm quartz cell of Hitachi 150–20 spectrophotometer at its absorption maximum 526 nm. The spectral changes during the redox reaction are shown in Fig. 1. Earlier it was verified that there is no interference from other reagents at this wavelength. The application of Beer's law for permanganate at 526 nm had earlier been verified, giving $e = 2083 \pm 50$ dm\(^3\) mol\(^{-1}\) cm\(^{-1}\) (literature $e = 2200$). The first order rate constants, $k_{\text{obs}}$, were evaluated by plots of log[permanganate] versus time. The first order plots in almost all cases were linear up to 85% of the reaction and $k_{\text{obs}}$ were reproducible within ± 5%. In the course of measurements the colour of the solution changed from violet to blue and further to green. The spectrum of green solution was identical to that of MnO\(_4^2–\). It is evident that the blue colour is originated from violet of permanganate and green from manganate, excluding the accumulation of hypomanganate. The
Effect of dissolved oxygen on the rate of reaction was checked by preparing the reaction mixture and following the reaction in an atmosphere of nitrogen. No significant difference between the results obtained under the nitrogen and in the presence of air was observed. Added carbonate has no effect on the reaction rate. Fresh solutions were used while conducting the experiments.

RESULTS

Stoichiometry: The reaction mixture containing the excess permanganate concentration over L-phenylalanine were mixed in presence of 1.0 mol dm$^{-3}$ NaOH adjusted to a constant ionic strength of 2.0 mol dm$^{-3}$. After the completion of the reaction, solid KI was added, following acidification by H$_2$SO$_4$(10%). Then the remaining permanganate was titrated against standard sodium thiosulphate [8]. The results of the titration indicated that two moles of Mn(VII) consumed one mole of L-phenylalanine as given by (1). The main oxidation products were identified as aldehyde [12] by spot test, ammonia [13] by Nesslers reagent and manganate. Such products were also obtained in [9]. It is evident from Fig. 1 that [Mn(VII)] decreases (absorption at 526 nm), whereas [Mn(VI)] increases (absorption at 608 nm) during the course of the reaction. It was further observed that the aldehyde does not undergo further oxidation.

![Figure 1. Spectral changes in the oxidation of L-phenylalanine by permanganate at [MnO$_7^{2−}$] = 2.35 x 10$^{-4}$, [L-phenylalanine] = 2.0 x 10$^{-3}$, [OH$^-$] = 1.0, I = 2.0 mol dm$^{-3}$, scanning time interval = 3 min, and at 23°C.](image-url)
Reaction order: The reaction orders were determined from the slopes of log $k_{(obs)}$ versus log(concentration) plots by varying the concentration of oxidant, reductant, and alkali in turn, while keeping others constant.

Effect of oxidant and substrate: The oxidant, potassium permanganate concentration was varied in the range $3.0 \times 10^{-5}$ to $3.0 \times 10^{-4}$ mol dm$^{-3}$ and the linearity of plot of log[$MnO_4^-$] versus time indicates the order in $[MnO_4^-]$ as unity. This was also confirmed by varying $[MnO_4^-]_0$, which did not show any change in pseudo-first order rate constants $k_{(obs)}$ (Table 1). The substrate, L-phenylalanine concentration was varied in the range $5.0 \times 10^{-4}$ to $5.0 \times 10^{-3}$ mol dm$^{-3}$ at 23°C, keeping all other reactants concentration and conditions constant (Table 1). The order in [L-phenylalanine] was found to be less than unity (Table 1).

Table 1. Effects of [L-phenylalanine], [Mn(VIII)] and [OH$^-$] on oxidation of L-phenylalanine by permanganate in aqueous alkaline medium at 23°C, $I = 2.0$ mol dm$^{-3}$.

<table>
<thead>
<tr>
<th>[L-phenylalanine] x 10$^4$ mol dm$^{-3}$</th>
<th>[MnO$_4^-$] x 10$^4$ mol dm$^{-3}$</th>
<th>[OH$^-$] mol dm$^{-3}$</th>
<th>$k_{(obs)}$ x 10$^3$ s$^{-1}$</th>
<th>Expt.*</th>
<th>Calcd.*</th>
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<tr>
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<td>3.02</td>
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Effect of alkali: The effect of alkali was studied on the reaction at constant concentration of L-phenylalanine and potassium permanganate at constant ionic strength of 2.0 mol dm$^{-3}$ at 23°C. The rate constants increased negligibly with increase in [alkali]. Hence the order with respect to [alkali] is considered to be zero (Table 1).
Effect of ionic strength: The effect of ionic strength was studied by varying the sodium perchlorate concentration. The ionic strength of reaction medium was varied from 1.0 to 4.0 mol dm\(^{-3}\) at constant concentrations of permanganate, L-phenylalanine and alkali. It was found that the rate of the reaction is independent of ionic strength of the medium.

Effect of solvent polarity: The relative permittivity (D) effect was studied by varying t-butyl alcohol–water content in the reaction mixture with all other conditions being constant. Attempts to measure the relative permittivity failed. However, they were computed from the values of pure liquids as earlier [14]. There was no reaction of solvent with the oxidant. The rate constant, \(k_{\text{obs}}\), increased with decrease in dielectric constant of the medium. The plot of \(\log k_{\text{obs}}\) versus \(1/D\) was linear with a positive slope (Fig. 2).

Figure 2. Plot of \(1/k_{\text{obs}}\) versus \(1/\text{[L-phenylalanine]}\). Plot of \(\log k_{\text{obs}}\) versus \(1/D\).

Effect of initially added products: The initially added products, such as manganese, aldehyde and ammonia, did not show any significant effect on the rate of the reaction.

Test for free radicals: The reaction mixture was kept for one hour with acrylonitrile scavenger in an inert atmosphere. Diluting by methanol, the formation of precipitate indicates the presence of free radical intervention in the reaction.

Effect of temperature: The rate of reaction was measured at different temperatures under varying [L-phenylalanine]. The rate of reaction increased with increase of temperature and the activation parameters have been calculated. The rate constant,
The permanganate ion, $\text{MnO}_4^-$, is a powerful oxidant in aqueous alkaline medium. As it exhibits multitude oxidation states, the stoichiometric results and pH of reaction media play a significant role. At pH $> 12$, the reduction product of Mn(VII) being Mn(VI) is stable and further reduction of Mn(VI) might be stopped [6]. The Diode Array Rapid Scan Spectrophotometer (DARSS) studies have shown that at pH $> 12$ the product of the reaction of Mn(VII) is Mn(VI) and no further reduction was observed as reported by Jaky et al. [6]. However, on long standing Mn(VI) is slowly reduced to Mn(IV).

The reaction between L-phenylalanine and permanganate in alkaline medium has stoichiometry of 1:2 with a unit order in [permanganate] and less than unity in [L-phenylalanine]. No products effect and alkali effect was observed. The results suggest the formation of a complex between oxidant and L-phenylalanine followed by decomposition of this complex in rate determining step and subsequent fast reaction to give products. Attempts to obtain spectral UV-VIS evidence for the intermediate complex of L-phenylalanine and permanganate failed. However, the interaction might be quite feeble, and such complex formation between substrate and oxidant have also been observed in other studies [15]. The evidence for the complex formation is proved kinetically. The experimental results are in agreement with the Scheme 3.
The probable structure of the complex (C) might be:

\[ \text{NH}_2 \quad [\text{R-C} - \text{O} - \text{O} - \text{Mn-OH}]^- \]

The order of less than unity in L-phenylalanine concentration reveals that the substrate is involved in complex formation either with permanganate or alkali. Since the reaction rate is almost independent of [alkali], complexation between L-phenylalanine and alkali is discarded. The complex formed between permanganate and L-phenylalanine decomposes in a slow step to give a free radical derived from decarboxylated phenylalanine, which further reacts with another molecule of permanganate in a fast step to give products. Since permanganate species is a one electron oxidant in alkaline medium, the reaction between the substrate and oxidant would afford a radical intermediate. Free radical scavenging experiment reveals such a possibility. This type of radical intermediate has also been observed earlier [9] with amino acids.

Scheme 3 leads to the rate law (2)

\[
\frac{d[MnO_4^-]}{dt} = \frac{kK[L-phenylalanine][MnO_4^-]}{1 + K[L-phenylalanine]} \tag{2}
\]

Strictly, the factor \(1 + K[Mn(VII)]\) should also be in the denominator on the right hand side of (2), but in view of low concentration of Mn(VII) used, this term approximates to unity. (2) can be rearranged to the form (3), which is suitable for verification

\[
\frac{1}{k_{\text{obs}}} = \frac{1}{kK[L-phenylalanine]} + \frac{1}{K} \tag{3}
\]
According to (3), a plot of $k_{(obs)}^{-1}$ versus [L-phenylalanine]$^{-1}$ should be linear, which is verified in Fig. 2. The slope and intercept of such plot lead to values of $K$ and $k$ at $23^\circ C$ as $240 \pm 12 \text{ dm}^3 \text{ mol}^{-1}$ and $5.55 \pm 0.30 \times 10^{-3} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ respectively. Using these values, the rate constants over different experimental conditions were calculated and compared with experimental data in Table 1. There is a good agreement between them. The negligible effect of increasing ionic strength on rate qualitatively explains the reaction between an ion and a dipolar molecule as seen in Scheme 3. The effect of solvent on the reaction kinetics has been described in detail in well-known monographs of Moelwyn Hughes [16], Laidler et al. [17], Benson [18]. Frost and Pearson [19], Amis [20], and Entelis and Tiger [21]. For limiting case of zero angle approach between two dipoles or an ion-dipole system, Amis [20] has shown that a plot log $k_{(obs)}$ versus $D^{-1}$ gives a straight line with a negative slope for a reaction between a negative ion and dipole or two dipoles, while a positive slope results for a positive ion and dipole interaction. In the present study an increase in rate with decrease in dielectric constant of the medium has been observed, which cannot be explained by Amis theory [20], as the presence of a positive ion is unlikely in the alkaline medium employed. Applying Born's is equation. Laidler and Eyring have derived:

$$
\ln k = \ln k_0 + \frac{NZ^2e^2}{2DR T} \left[ \frac{1}{r} - \frac{1}{r^*} \right]
$$

(4)

where $k_0$ is the rate constant in a medium of infinite dielectric constant and `$r$' and $r^*$ refers to the radius of the reacting species and activated complex respectively. It can be seen from (3) that the rate should be greater in a medium of lower dielectric constant, when $r^* > r$. There is a possibility of intramolecular hydrogen bonding that could stabilize the transition state, increasing the size of activated complex by attracting solvent molecules due to solvation effect. The fairly high positive values of $\Delta H^\#$ and $\Delta G^\#$ (Table 2) also indicate that the transition state is highly solvated, increasing the size of the transition state. It is likely that $r^* > r$ for the L-phenylalanine, thus explaining the experimental observation. It is well known [22], that amino acids readily, undergo such intramolecular hydrogen bonding.

The values of $\Delta H^\#$ and $\Delta S^\#$ were both favourable for electron transfer processes. The favourable enthalpy was due to release of energy on solution changes in the transition state. The values of $\Delta S^\#$, within the range for radical reactions, have been ascribed [23] to the nature of electron pairing and electron unpairing processes, and to the loss of degrees of freedom, formerly available to the reactions on the formation of rigid transition state. The less negative value of $\Delta S^\#$ and the high value of frequency factor indicates [24] that the electrostatic effects are unimportant. It is also interesting to note that the oxidant species [MnO$_2$] required the pH > 12, below which the reaction will proceed further to a reduced product of oxidant as Mn(IV).
REFERENCES