# KINETIC STUDY OF PERMANGANATE OXIDATION OF L-LEUCINE IN NEUTRAL AQUEOUS SOLUTION

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Received May 18th, 1987

The permanganate oxidation of L-leucine in aqueous phosphate buffers over the pH range 6·1—7·6 is autocatalyzed by the manganese reduction product, a soluble form of colloidal manganese dioxide. The kinetic data for both the non-catalytic and autocatalytic reaction pathways have been obtained, and mechanisms in agreement with them have been proposed. The non-catalytic pathway takes place by reaction between either the anionic or the zwitterionic form of the amino acid and permanganate ion, whereas the autocatalytic pathway is realized by the permanganate oxidation of the amino acid previously adsorbed on the colloid surface.

The kinetic and mechanistic behaviour of the oxidation of α-amino acids is a topic of some interest. In particular, the reactions between potassium permanganate and α-amino acids in aqueous media have attracted our attention for two main reasons. In the first place, there is not much information on the kinetics of this type of reactions in neutral solutions[1] for most of the studies were performed under strongly acid conditions[2-5]. On the other hand, although it is known that permanganate ion and α-amino acids react in an autocatalytic manner[6], the nature of its mechanism still remains obscure.

In order to gain a better understanding of the autocatalytic oxidation mechanism of α-amino acids, we have undertaken the kinetic study of the reaction between permanganate ion and L-leucine in neutral aqueous solutions.

## EXPERIMENTAL

All chemicals were Merck reagent grade. The solvent used to prepare the solutions was twice-distilled water. The oxidant was potassium permanganate in a concentration range from $4 \cdot 10^{-4}$ to $8 \cdot 10^{-4}$ mol $l^{-1}$. The reductant was L-leucine ($2 \cdot 10^{-2}$—$8 \cdot 10^{-2}$ mol $l^{-1}$) in large excess with respect to the oxidant. $KH_2PO_4$–$K_2HPO_4$ buffers were used, both to keep the pH of the solutions constant within the interval 6·1—7·6 and to stabilize manganese dioxide temporarily as a soluble product[7]. The ionic strength of the medium was regulated from 0·38 to 0·86 mol $l^{-1}$ by adding potassium chloride to the solutions. The experiments were performed at temperatures between 25·0 and 45·0°C.

The kinetic runs were followed by monitoring the disappearance of permanganate ion at 526 nm and the formation of colloidal manganese dioxide at 418 nm by means of a Varian Cary 219 spectrophotometer.

## RESULTS

When the runs were finished, the solutions had a yellow-brown colour but still were transparent. The spectra recorded at this moment showed a band with the absorbance continuously decreasing with increasing wavelength, the logarithm of the absorbance decreasing linearly with the logarithm of the wavelength, this behaviour being typical of solutions containing a soluble form of colloidal manganese dioxide temporarily stabilized in solution by adsorption of phosphate ions on its surface[8-10]. The size of the colloidal particles slowly increases till precipitation of brown manganese dioxide takes place, usually one day after performance of the experiment.

The variations of the permanganate concentration with time were first analysed by means of simple integral rate laws, but none of them led to linear correlations. In particular, all the kinetic runs yielded curves displaying a definite concave upward pattern when pseudo-first-order plots were attempted. A typical plot is presented in Fig. 1. The fact that the slopes of the pseudo-first-order plots increase with time indicates that the reaction may be autocatalytic. To confirm this assumption, the following equation, applicable to autocatalytic reactions in which the kinetic orders of both the rate-monitoring species and the autocatalytic agent are unity[11-15], was tried:

$$\ln\left[(k_1 + k_2c_0 - k_2c)/c\right] = \ln\left(k_1/c_0\right) + \left(k_1 + k_2c_0\right)t\,, \qquad (I)$$

where $c$ and $c_0$ are the permanganate concentrations at time $t$ and at the beginning of the reaction, whereas $k_1$ and $k_2$ stand for the rate constants of the non-catalytic and autocatalytic mechanisms, respectively. For each experiment the corresponding rate constants were determined by an iterative method.

Fig. 1 shows a typical plot obtained when the left-hand side of Eq. (*I*) including the calculated $k_1$ and $k_2$ values is represented against time. A good linear relationship can be observed. The linear correlation coefficients ($r$) for all the experiments performed were in the range 0·9997–0·999992. Thus it can be concluded that two reaction pathways, one non-catalytic and the other autocatalytic, are involved in the overall process. Note that a slight decrease in both $k_1$ and $k_2$ values is found as the initial permanganate concentration increases, as can be easily deduced from data reported in Table I. This is a feature common to many permanganate reactions[7,12,16,17] in spite of the fact that true rate constants should not depend on the rate-monitoring species concentration. The reason for this behaviour might be looked for in the peculiar nature of the manganese reduction product, since the circumstance of its being colloidal (a soluble form of colloidal manganese dioxide) might make it difficult to obtain accurate rate constants.

A typical dependence of both $k_1$ and $k_2$ on the reductant concentration is displayed in Fig. 2. As can be observed, they increase with rising reductant concentration as expected for pseudo-rate constants (L-leucine was in large excess with respect to

TABLE I

Dependence of the rate constants on the permanganate concentration ([L-leucine] = 0·072 mol . $l^{-1}$, pH 7·54, ionic strength 0·38 mol $l^{-1}$, temperature 25·0°C)

| $[KMnO_4] . 10^4$ mol $l^{-1}$ | $k_1 . 10^5$ $s^{-1}$ | $k_2$ l $mol^{-1}$ $s^{-1}$ |
|---|---|---|
| 4·56 | 7·38 | 0·144 |
| 5·29 | 7·23 | 0·126 |
| 6·05 | 7·07 | 0·114 |
| 6·88 | 6·82 | 0·104 |
| 7·87 | 6·87 | 0·089 |

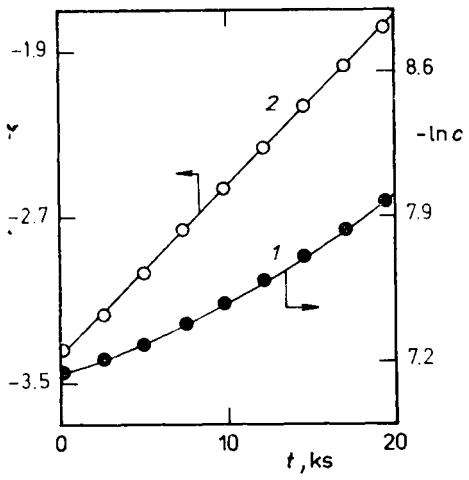


FIG. 1

Attempted pseudo-first-order plot (*1*) and integral rate-law plot (2) ($r = 0{\cdot}99990$) for the oxidation of L-leucine (0·072 mol $l^{-1}$) by permanganate ion ($8 . 10^{-4}$ mol $l^{-1}$) at pH 6·11, ionic strength 0·38 mol $l^{-1}$ and temperature 25·0°C. (*Y* is left-hand side of Eq. (*1*))

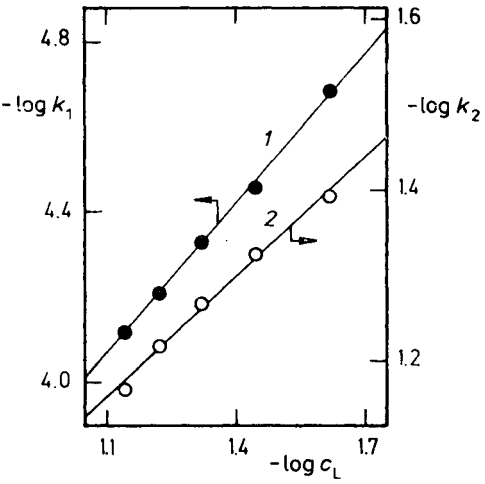


FIG. 2

Dependence of the rate constants on the L-leucine concentration ($c_L$). $[MnO_4^-] = 8 . 10^{-4}$ mol $l^{-1}$, pH 7·54, ionic strength 0·38 mol $l^{-1}$, temperature 25·0°C. *1* $k_1$ in $s^{-1}$ (slope = 1·18, $r = 0{\cdot}9991$), *2* $k_2$ in l $mol^{-1}$ $s^{-1}$ (slope = 0·47, $r = 0{\cdot}995$)

permanganate). The kinetic order of the reducing agent in the non-catalytic pathway is unity, whereas a fractional order is obtained for the autocatalytic pathway. On the other hand, it has also been found that both rate constants decrease slightly with increasing ionic strength, while they increase gradually with increasing pH. This can be checked from data given in Tables II and III, respectively. In addition, the fulfillment of the Arrhenius equation (see Fig. 3) yields apparent activation energies of 66·8 and 96·0 kJ $mol^{-1}$ for the non-catalytic and autocatalytic pathways, respectively.

TABLE II

Dependence of the rate constants on the potassium chloride concentration ($[MnO_4^-] = 8 . 10^{-4}$ mol $l^{-1}$, [L-leucine] = 0·056 mol $l^{-1}$, pH 7·54, ionic strength = 0·38 + [KCl] mol $l^{-1}$, temperature 25·0°C)

| [KCl] mol $l^{-1}$ | $k_1 . 10^5$ $s^{-1}$ | $k_2 . 10^2$ l $mol^{-1}$ $s^{-1}$ |
|---|---|---|
| 0·00 | 5·03 | 6·66 |
| 0·12 | 4·81 | 6·21 |
| 0·24 | 4·68 | 5·59 |
| 0·36 | 4·63 | 5·41 |
| 0·48 | 4·53 | 5·02 |

TABLE III

Variation of the rate constants with the pH ($[MnO_4^-] = 8 . 10^{-4}$ mol $l^{-1}$, [L-leucine] = = 0·072 mol $l^{-1}$, ionic strength 0·38 mol $l^{-1}$, temperature 25·0°C)

| pH | $[HA] . 10^{2a}$ mol $l^{-1}$ | $[A^-] . 10^{4b}$ mol $l^{-1}$ | $k_1 . 10^5$ $s^{-1}$ | $k_2 . 10^2$ l $mol^{-1}$ $s^{-1}$ |
|---|---|---|---|---|
| 6·11 | 7·20 | 0·17 | 2·59 | 5·14 |
| 6·50 | 7·20 | 0·41 | 2·84 | 5·52 |
| 6·80 | 7·19 | 0·82 | 3·22 | 5·88 |
| 7·12 | 7·18 | 1·71 | 4·14 | 7·07 |
| 7·50 | 7·16 | 4·08 | 6·40 | 10·62 |

[a] Concentration of the zwitterionic form of L-leucine. [b] Concentration of the anionic form of L-leucine.

## DISCUSSION

It is well-known that in aqueous solutions the following equilibria between the cationic, zwitterionic, and anionic forms of L-leucine ($RCH(NH_2)COOH$, R = $= (CH_3)_2CHCH_2$) take place:

$$RCH(NH_3^+)COOH \rightleftarrows RCH(NH_3^+)COO^- + H^+ \qquad (A)$$

$$RCH(NH_3^+)COO^- \rightleftarrows RCH(NH_2)COO^- + H^+ \qquad (B)$$

the corresponding $pK_a$ values being 2·33 and 9·74 (ref.[18]). Then in the pH range of work (6·1–7·6) the zwitterionic form of L-leucine, generated by deprotonation of the cationic form as depicted in equilibrium (*A*), is predominant. Hence, it can be assumed that a considerable part of the observed reaction is due to the oxidation of the zwitterionic form by permanganate ion, for which the following mechanism in agreement with the experimental results is proposed:

$$RCH(NH_3^+)COO^- + MnO_4^- \xrightarrow{\text{slow}} RCH(NH_3^+)COO^\cdot + MnO_4^{2-} \qquad (C)$$

$$RCH(NH_3^+)COO^\cdot \longrightarrow R\dot{C}HNH_3^+ + CO_2 \qquad (D)$$

$$R\dot{C}HNH_3^+ \longrightarrow R\dot{C}HNH_2 + H^+ \qquad (E)$$

$$R\dot{C}HNH_2 + MnO_4^- \longrightarrow RCH{=}NH_2^+ + MnO_4^{2-} \qquad (F)$$

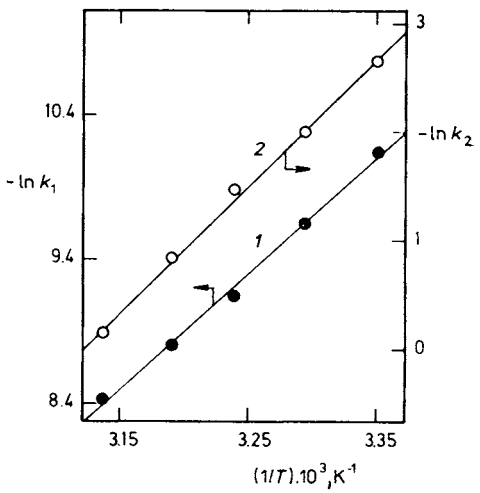


FIG. 3

Arrhenius plots. $[MnO_4^-] = 8 \cdot 10^{-4}$ mol . . $l^{-1}$, [L-leucine] = 0·048 mol $l^{-1}$, pH 7·54, ionic strength 0·38 mol $l^{-1}$. *1* $k_1$ in $s^{-1}$ ($r = 0{\cdot}997$, $E_{a1} = 66{\cdot}8$ kJ $mol^{-1}$), *2* $k_2$ in 1 $mol^{-1}$ $s^{-1}$ ($r = 0{\cdot}998$, $E_{a2} = 96{\cdot}0$ kJ . . $mol^{-1}$)

$$RCH{=}NH_2^+ + H_2O \longrightarrow RCHO + NH_4^+ \qquad (G)$$

$$3\,MnO_4^{2-} + 2\,H_2O \longrightarrow 2\,MnO_4^- + MnO_2 + 4\,OH^- \qquad (H)$$

This mechanism is supported, in the first place, by the fact that carbon dioxide[19], aldehydes[20], and ammonium ion[21] are known to be formed as products from the permanganate oxidation of α-amino acids, what might well happen as depicted in steps (*D*) and (*G*). On the other hand, manganese dioxide detected in all the experiments, as a soluble colloid at the end of the reactions and as a brown precipitate one day later, is formed by dismutation of manganate ion according to step (*H*). It is well-known that mangante ion dismutates very rapidly in neutral aqueous solutions[22]. Moreover, the proposal of free radical formation in steps (*C*)–(*E*) can be justified by the knowledge that the permanganate oxidations of α-amino acids produce free radicals which initiate the polymerization of acrylamide[23–25]. Finally, the formation of an iminium ion in step (*F*) and its subsequent hydrolysis to give an aldehyde and an ammonium ion in step (*G*) have also been proposed in the mechanisms of the permanganate oxidation of some compounds closely related to the amino acids, such as benzylamine[26] and trimethylamine[27].

From the p$K_a$ values corresponding to equilibria (*A*) and (*B*)[18], the concentrations of the three forms of L-leucine were calculated. It is found that in the pH interval 6·1–7·6, close to the isoelectric point of L-leucine (6·04), the concentration of the zwitterionic form remains practically constant, whereas that of the anionic form increases with rising solution pH (see Table III). The $k_1$ values also show an increase with increasing pH. It seems then plausible to conclude that this experimental finding is best accounted for by assuming that the anionic form of L-leucine also reacts with permanganate ion. This oxidation probably starts according to the following reactions:

$$RCH(NH_2)COO^- + MnO_4^- \xrightarrow{\text{slow}} RCH(NH_2)COO^{\bullet} + MnO_4^{2-} \qquad (I)$$

$$RCH(NH_2)COO^{\bullet} \longrightarrow R\dot{C}HNH_2 + CO_2 \qquad (J)$$

Once the $R\dot{C}HNH_2$ free radical is formed, its disappearance occurs as indicated in steps (*F*)–(*H*). With respect to the cationic form of L-leucine, its concentration decreases as the solution pH increases, but is too low under the experimental conditions for its rate of oxidation to be competitive with those corresponding to the zwitterionic and anionic forms.

The rate law associated with the above mechanisms leads to the following expression for the rate constant $k_1$:

$$k_1 = k_C[RCH(NH_3^+)COO^-] + k_I[RCH(NH_2)COO^-], \qquad (2)$$

where $k_C$ and $k_I$ stand for the rate constants corresponding to steps (*C*) and (*I*), respectively. From Eq. (*2*) it can be inferred that the non-catalytic pathway must be first-order dependent on the overall amino acid concentration, for both the zwitterionic and anionic form concentrations are directly proportional to the total L-leucine concentration, in agreement with the slope of the linear plot shown in Fig. 2. Furthermore, since the concentration of the zwitterionic form is almost constant, Eq. (*2*) predicts a linear relationship between $k_1$ and the concentration of the anionic form. This prediction is confirmed when the $k_1$ data given in Table III are fitted against the values of the concentration of the anionic form by the least-squares method, leading to the following equation ($r = 0{\cdot}99990$):

$$k_1 = 2{\cdot}44 \,.\, 10^{-5} + 9{\cdot}74 \,.\, 10^{-2}[\mathrm{RCH(NH_2)COO^-}] \,. \qquad (3)$$

By comparing Eqs (*2*) and (*3*) and taking into account that the average concentration of the zwitterionic form is $7{\cdot}19 \,.\, 10^{-2}$ mol $l^{-1}$ (see Table III), it follows that the $k_C$ and $k_I$ values are $3{\cdot}39 \,.\, 10^{-4}$ and $9{\cdot}74 \,.\, 10^{-2}$ l $mol^{-1}$ $s^{-1}$, respectively. Consequently, the anionic form of L-leucine is around three-hundred times more reactive toward permanganate than the zwitterionic form, what can be understood in terms of the enhanced reducing power of the former due to its higher electron density. However, the slight variation of $k_1$ with the ionic strength of the medium observed in Table II is hard to explain, because the dependences of $k_C$, $k_I$ and the equilibrium constants of reactions (*A*) and (*B*) on the ionic strength are all involved.

As far as the autocatalytic pathway is concerned, there is not much information that could lead to a definitive proposal for its mechanism, owing to the fact that the information available in the literature for autocatalytic permanganate mechanisms is rather scarce. Nevertheless, a reasonable hypothesis could be that permanganate ion and L-leucine react on the surface of the colloidal particles of manganese dioxide. Since Tables II and III reveal that the behaviours of both the non-catalytic and autocatalytic pathways with respect to both ionic strength and pH are similar, it can be assumed that both reaction pathways are fundamentally the same, but a reaction pathway taking place in the bulk solution (the non-catalytic one) and the other on the surface of the soluble colloid (the autocatalytic one).

Finally, note that the apparent activation energy for the autocatalytic pathway (96·0 kJ $mol^{-1}$) is higher than that of the non-catalytic one (66·8 kJ $mol^{-1}$). This indicates that the actual mission of the soluble form of colloidal manganese dioxide is to increase the probability of an encounter between permanganate and L-leucine on its surface as compared to that in the bulk solution, rather than to decrease the energetic requirements of the oxidation process.

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