

Kinetics of Amino Acids Oxidation by Alkaline Transition Metal Complexes

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The kinetics of oxidation of cysteine and proline by hexacyanoferrate (III) and permanganate, respectively, has been studied in basic medium at 25°C. The reaction rate was measured, spectrophotometrically, by following the change in the oxidizing agent concentration with time. Results showed the rate of oxidation is zero order for the alkali, first order for the oxidant, first order for substrate in the oxidation of cysteine with hexacyanoferrate (III) and an order of 0.35 for the substrate in the oxidation of proline with permanganate. The value of the rate constant for cysteine-hexacyanoferrate (III) oxidation is more than two fold of magnitude larger than that for proline-permanganate oxidation.

INTRODUCTION

The study of amino acid oxidation is important from both chemical and biological points of view.¹⁻³ Oxidation of amino acids by several oxidizing agents has been studied by many investigators⁴. However, few studies have been carried out using transition metal complexes as oxidizing agents^{5,6}. The ability of a transition metal ion to serve as an oxidizing agent depends on the reduction potential of the ion and the nature of the ligand bound to it⁷. This is because different ligands cause different splittings in the d-orbital of the transition metal ion leading of different values of ion polarizability. Thus the oxidation of amino acids by such ion depends on the ion ability to receive electrons as a result of the orbital splitting.

In the present work, the kinetics of oxidation of cysteine by hexacyanoferrate(III) and proline by permanganate have been studied in basic medium at 25°C. The reaction was monitored by observing the change in the absorbance of the reaction mixture with time.

EXPERIMENTAL

All chemicals were BDH with minimum assay of 99% and were used without further purification. The ionic strength was kept constant at 0.050 mol dm⁻³ using sodium perchlorate. The temperature of solutions was maintained at 25° ± 0.1°C.

Kinetics measurements: The oxidation processes were studied under pseudo-first-order conditions, such that the concentration of the amino acid is an order of magnitude larger than the concentration of the oxidant. The order of the reaction

with respect to a species (oxidant, amino acid or the hydroxide) was determined by varying its concentration while keeping the concentration of the other two species constant. The reaction was followed by monitoring the concentration of the oxidant with time. This was done by measuring its absorbance, as a function of time, using Pyeunicam PU8820 UV/VIS spectrophotometer at 420 nm for hexacyanoferrate(III) and 530 nm for the permanganate. At these wavelengths the absorption due to other species, other than the oxidant, are negligible. The observed rate constants were evaluated from a linear ($r \geq 0.995$) plots of $\log [\text{oxidant}]$ *versus* time.

RESULTS AND DISCUSSION

Estimation of the residual oxidant concentration, for the oxidation of an amino acid (A.A.) by the oxidizing agent (OX) in basic medium, showed that the stoichiometry of the reaction is as follows:



The rate of the reaction R, is given by:

$$R = k[\text{A.A.}]^a [\text{OX}]^b [\text{OH}^-]^c \quad (2)$$

where k is the reaction rate constant and a , b , c are the order of the reaction with respect to the concentration of the amino acid, the oxidizing agent and the hydroxide, respectively.

At pseudo-first order conditions, where a large excess of the concentrations of the amino acid and the hydroxide compared to that of the oxidant, their concentrations essentially stay constant through out the reaction and the reaction rate is given by

$$R + - \frac{d[\text{OX}]}{dt} = k_{\text{obs}} [\text{OX}]^b \quad (3)$$

where k_{obs} is the observed rate constant for the reaction, given by

$$k_{\text{obs}} = k[\text{A.A.}]^a [\text{OH}^-]^c \quad (4)$$

For a first-order dependence of the reaction on $[\text{OX}]$, i.e. $b = 1$, integration of the differential rate law gives:

$$\ln[\text{OX}]_t + \ln[\text{OX}]_0 - k_{\text{obs}}t \quad (5)$$

Where $[\text{OX}]_0$ is the initial concentration of the oxidant and $[\text{OX}]_t$ is its concentration at time t . The value of k_{obs} can be obtained from a plot of $\ln[\text{OX}]_t$ *versus* time. Since the reaction was followed photometrically by measuring the absorbance of the oxidant with time, equation (5) becomes

$$\ln A_t + \ln A_0 - k_{\text{obs}}t \quad (6)$$

A plot of $\ln A_t$ *versus* time should give a straight line with a slope = $-k_{\text{obs}}$.

The order of the reaction with respect to both [A.A.] and $[\text{OH}^-]$ were obtained using equation (4), such that

$$\ln k_{\text{obs}} = \ln k + a \ln[\text{A.A.}] + c \ln[\text{OH}^-] \quad (7)$$

Plots of $\ln k_{\text{obs}}$ versus $\ln[\text{A.A.}]$ and $\ln k_{\text{obs}}$ versus $\ln[\text{OH}^-]$ give straight lines with slopes equal to a and c , respectively.

Kinetics Results

1. *Cysteine*: The reaction rate for the oxidation of cysteine with potassium hexacyanoferrate (III) was first studied by varying the concentration of oxidizing agent while keeping the concentration of both cysteine and OH^- constant.

TABLE 1
OXIDATION OF CYSTEINE BY HEXACYANOFERRATE (III) IN BASIC MEDIUM AT 25°C: EFFECT OF $[\text{Fe}(\text{CN})_6^{3-}]$ ON REACTION RATE.
[CYSTEINE] = 0.010 mol dm⁻³ [OH⁻] = 0.050 mol dm⁻³

$10^3 [\text{Fe}(\text{CN})_6^{3-}]$ (mol dm ⁻³)	$10^2 k_{\text{obs}}$ (s ⁻¹)
0.10	4.23
0.30	4.13
0.70	4.25
1.00	4.10
2.00	4.17

Table 1 shows that k_{obs} remains constant as the concentration of hexacyanoferrate (III) changes. This indicates a first-order dependence of the reaction on the oxidant concentration. Further more, a plot of $\ln[\text{Fe}(\text{CN})_6^{3-}]$ versus time gives a straight line ($r = 0.997$) which indicates, according to equation (5), that the rate of the reaction depends on the first power of the concentration of hexacyanoferrate(III). The dependence of the reaction rate on [cysteine] and $[\text{OH}^-]$ were studied in a similar manner.

TABLE 2
OXIDATION OF CYSTEINE BY HEXACYANOFERRATE (III) IN BASIC MEDIUM AT 25°C: EFFECT OF [CYSTEINE] ON REACTION RATE.
 $[\text{Fe}(\text{CN})_6^{3-}] = 0.0010$ mol dm⁻³ [OH⁻] = 0.050 mol dm⁻³

10^2 [cysteine] (mol dm ⁻³)	$10^2 k_{\text{obs}}$ (s ⁻¹)
1.00	4.10
2.00	8.07
3.00	12.5
4.00	16.5
5.00	21.2

Table 2 shows that k_{obs} is directly proportional to the concentration of cysteine. A plot of $\ln k_{\text{obs}}$ versus $\ln[\text{cysteine}]$ gives a straight line with slope = 1, *i.e.* the reaction depends on the first power of [cysteine]. Table 3 shows that the observed

rate constant does not change significantly as the concentration of hydroxide changes. Thus the values of exponent c in equation (2) is essentially zero. The overall reaction rate for the oxidation of cysteine by hexacyanoferrate in basic medium is thus given by

$$R = k[\text{cysteine}][\text{Fe}(\text{CN})_6^{3-}] \quad (8)$$

with $k = 4.4 \pm 0.4 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$.

TABLE 3
OXIDATION OF CYSTEINE BY HEXACYANOFERRATE (III) IN
BASIC MEDIUM AT 25°C: EFFECT OF $[\text{OH}^-]$ ON REACTION RATE.
[CYSTEINE] = $0.010 \text{ mol dm}^{-3}$ $[\text{Fe}(\text{CN})_6^{3-}] = 0.0010 \text{ mol dm}^{-3}$

$10^2 [\text{OH}^-] (\text{mol dm}^{-3})$	$10^2 k_{\text{obs}} (\text{s}^{-1})$
3.00	4.02
4.00	4.22
5.00	4.10
6.00	4.21
7.00	4.03

2. *Proline*: The reaction rate for oxidation of proline with potassium permanganate was studied in a similar manner as in case of cysteine by hexacyanoferrate (III). Results are shown in Tables 4, 5 and 6.

TABLE 4
OXIDATION OF PROLINE BY PERMANGANATE IN BASIC MEDIUM
AT 25°C: EFFECT OF $[\text{MnO}_4^-]$ ON REACTION RATE.
[PROLINE] = $0.010 \text{ mol dm}^{-3}$ $[\text{OH}^-] = 0.050 \text{ mol dm}^{-3}$

$10^3 [\text{MnO}_4^-] (\text{mol dm}^{-3})$	$10^3 k_{\text{obs}} (\text{s}^{-1})$
0.10	3.51
0.30	3.60
0.70	3.42
1.00	3.54
2.00	3.67

TABLE 5
OXIDATION OF PROLINE BY PERMANGANATE IN BASIC MEDIUM
AT 25°C: EFFECT OF [PROLINE] ON REACTION RATE.
[MnO_4^-] = $0.0010 \text{ mol dm}^{-3}$ $[\text{OH}^-] = 0.050 \text{ mol dm}^{-3}$

$10 [\text{proline}] (\text{mol dm}^{-3})$	$10^3 k_{\text{obs}} (\text{S}^{-3})$
0.10	3.54
0.20	4.55
1.00	7.76
2.00	10.0
5.00	14.2

TABLE 6
OXIDATION OF PROLINE BY PERMANGANATE IN BASIC MEDIUM
AT 25°C: EFFECT OF [OH⁻] ON REACTION RATE.
[PROLINE] = 0.10 mol dm⁻³ [MnO₄⁻] = 0.0010 mol dm⁻³

10 ² [OH ⁻] (mol dm ⁻³)	10 ³ k _{obs} (s ⁻¹)
3.00	7.71
4.00	7.62
5.00	7.76
6.00	7.80
7.00	7.73

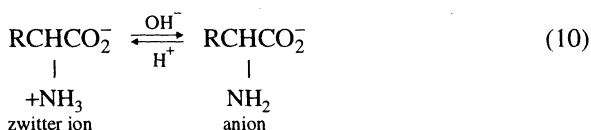
The observed rate constant remains invariant upon changing [MnO₄⁻]. A plot of ln[MnO₄⁻] versus time gives a straight line (*r* = 0.998), which indicates a first order power dependence of the reaction rate on [MnO₄⁻]. A plot of ln k_{obs} versus ln[proline] gives a straight line with slope = 0.35. Again, the results in Table 6 indicate that the reaction rate is independent of [OH⁻]. The overall reaction rate for the oxidation of proline by permanganate in basic medium is

$$R = k[\text{MnO}_4^-][\text{proline}]^{0.35} \quad (9)$$

with $k = (2.1 \pm 0.2) \times 10^{-2} \text{ dm}^{3(0.35)} \text{ mol}^{-0.35} \text{ s}^{-1}$.

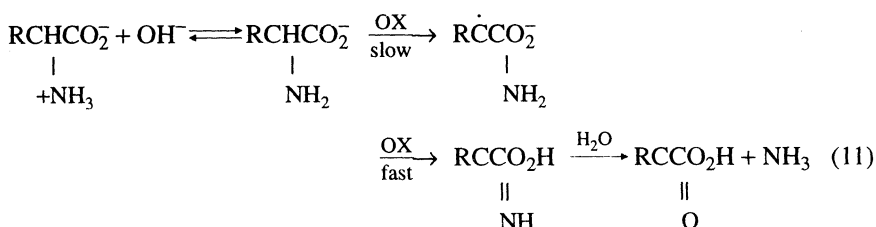
Mechanism

In aqueous solutions, amino acids exist as zwitter ions. In strong alkaline media the zwitter ions would be completely dissociated into their anions, as shown below:



Under the present experimental conditions, where all the kinetic studies were done at high NaOH concentration, the anion is the relative species and it also the predominant species in solution. This is because the pK_a values⁹ for cysteine and proline will be below the lowest pH value of 12.5 employed in this work.

The reaction between amino acids and hexacyanoferrate (III) is expected to proceed *via* radical intermediate, analogous to enzymatic oxidation reactions¹⁰. This is because hexacyanoferrate (III) is a one-electron oxidant. Therefore, the sequence for the oxidation is expected to be as follows:



It may thus be concluded that the kinetics of amino acid oxidation by transition metal complexes is a first order with respect to the concentration of oxidant but independent of that of alkali, in the range studied. The use of different oxidizing agents led to different reaction order with respect to the amino acids concentrations. This indicates that the oxidation processes for the two amino acids proceed by different mechanisms. The difference in the oxidation rates is governed by both the entropy and enthalpy of activation⁸.

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