A kinetic and mechanistic study on the oxidation of arginine and lysine by hexacyanoferrate(III) catalysed by iridium(III) in aqueous alkaline medium

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Abstract: The kinetics of Ir(III) catalysed oxidation of some amino acids like arginine and lysine by hexacyanoferrate [abbreviated as HCF(III)] ions in aqueous alkaline medium at constant ionic strength 0.5 mol dm\(^{-3}\) and temperature 35 °C has been studied spectrophotometrically. The reactions exhibit 2 : 1 stoichiometry and follows first order kinetics in [HCF(III)] and [alkali]. The dependence of rate on substrate concentration has been found to be Michaelis-Menton type. The ionic strength of the reaction mixture shows positive salt effect on the reaction rate. To calculate thermodynamic parameters the reaction has been studied at four different temperatures between 35-50 °C. A complex mechanism involving the complex formation between catalyst and the substrate has been proposed. Keto acids-\(\varepsilon\)-guanidino-\(\alpha\)-oxo valeric acid, 6-amino-\(\alpha\)-oxo caproic acid have been identified as the final product of oxidation chromatographically and spectroscopically. Based on the kinetic data and product analysis a reaction mechanism is proposed.

Keywords: HCF(III), iridium(III), oxidation, arginine, lysine.

Introduction

Oxidation reactions are of fundamental importance in nature, and are key transformations in organic synthesis\(^1\). Oxidation of \(\alpha\)-amino acids is of great importance both from chemical point of view and its bearing on the mechanism of amino acids metabolism\(^2\). Amino acids have been oxidised by a variety of reagents under different experimental condition\(^3-10\). It was shown by the previous workers that the oxidation of \(\alpha\)-amino acids by hexacyanoferrate(III) proceeds very slowly in absence of any catalyst while it follows a complex kinetics in presence of a catalyst\(^11-13\). The oxidation rate was improved by the use of some metal ions Os, Ru and Ag\(^14-17\). These reactions follows a complex kinetics in presence of catalysts\(^18-21\). Thus to understand about the catalysis of Ir(III) in oxidation of amino acids by HCF(III) and to explore the mechanism of these oxidations in aqueous alkaline medium, two amino acids, arginine and lysine, have been selected as substrate for oxidation.

Results and discussion

Kinetic experiments were performed at different concentrations of one reactant keeping the concentration of other constant.

The concentration of substrate (lysine and arginine, abbreviated as S) was varied in the range of \(1 \times 10^{-3}-10 \times 10^{-3}\) mol dm\(^{-3}\) at 35 °C keeping all other reactants concentration constant (Table 1). The data presented in Table 1 shows first order dependence on lower concentration of substrate which tends to be zero order at its higher concentration.

The [HCF(III)] was varied in the range \(2 \times 10^{-4}-7 \times 10^{-4}\) mol dm\(^{-3}\) at fixed [S], [OH\(^-\)] and ionic strength. The \(k_1\) values indicate that the order in [HCF(III)] is unity (Table 1).

The effect of [OH\(^-\)] on the rate of reaction was studied at constant [S], [HCF(III)] and ionic strength at 0.5 mol dm\(^{-3}\) at 35 °C (Table 1). A perusal of data reveals first order kinetics with respect to OH\(^-\) concentration.

The effect of ionic strength was studied by varying the [KCl] in the reaction mixture. The ionic strength of the reaction medium was varied from 0.5-0.7 mol dm\(^{-3}\) at constant [HCF(III)], [S] and [OH\(^-\)]. The positive salt effect was found (Table 2).

To calculate the thermodynamic parameters, the effect of temperature on the rate of the oxidation was stud-
Table 1. Effect of [S], [NaOH] and [HCF(III)] on reaction rate at
Temp. = 35 ± 0.1 °C, \( \mu = 0.5 \text{ mol dm}^{-3} \)

| [S] \( \times 10^{-3} \) (mol dm\(^{-3} \)) | [NaOH] \( \times 10^{4} \) (mol dm\(^{-3} \)) | [HCF(III)] \( \times 10^{5} \) (mol dm\(^{-3} \)) | \( k_{1} \times 10^{4} \) (s\(^{-1} \)) |
|-----------------|-----------------|-----------------|-----------------|
| Lysine          | Arginine        | Lysine          | Arginine        |
| 1.0             | 0.40            | 3.00            | 3.35            | 2.68            | 2.68 |
| 2.0             | 0.40            | 3.00            | 3.35            | 3.83            | 3.07 |
| 3.0             | 0.40            | 3.00            | 3.35            | 4.66            | 4.20 |
| 4.0             | 0.40            | 3.00            | 3.35            | 5.75            | 4.60 |
| 5.0             | 0.40            | 3.00            | 3.35            | 6.90            | 5.37 |
| 6.0             | 0.40            | 3.00            | 3.35            | 7.67            | 6.14 |
| 7.0             | 0.40            | 3.00            | 3.35            | 8.06            | 6.52 |
| 8.0             | 0.40            | 3.00            | 3.35            | 8.44            | 6.90 |
| 9.0             | 0.40            | 3.00            | 3.35            | 8.82            | 7.29 |
| 10.0            | 0.40            | 3.00            | 3.35            | 9.21            | 7.67 |
| 11.0            | 0.40            | 3.00            | 3.35            | 9.60            | 8.06 |
| 12.0            | 0.40            | 3.00            | 3.35            | 9.99            | 8.44 |
| 13.0            | 0.40            | 3.00            | 3.35            | 10.39           | 8.82 |
| 14.0            | 0.40            | 3.00            | 3.35            | 10.78           | 9.21 |

Temperature indicate the reaction obeys Arrhenius equation.

Table 2. Effect of ionic strength on reaction rate

| Parameter \( \mu \times 10^{1} \) (mol dm\(^{-3} \)) | \( k_{1} \times 10^{4} \) (s\(^{-1} \)) |
|-----------------|-----------------|-----------------|-----------------|
| Lysine          | Arginine        | Lysine          | Arginine        |
| 0.5             | 3.07            | 2.30            | 2.30            |
| 0.55            | 4.22            | 3.07            | 3.07            |
| 0.60            | 5.76            | 4.22            | 4.22            |
| 0.65            | 7.29            | 5.37            | 5.37            |
| 0.70            | 9.60            | 5.75            | 5.75            |

Table 3. Activation parameters

| \( T \) (K) (±0.1 °C) | Lysine | Arginine |
|----------------------|--------|----------|
| 308                  | 2.30   | 3.07     |
| 313                  | 3.07   | 4.22     |
| 318                  | 4.60   | 5.75     |
| 323                  | 6.14   | 7.67     |
| 328                  | 11.5   | 12.1     |
| \( \Delta H^{\#} \) (kcal mol\(^{-1} \)) | 10.7   | 11.5     |
| \( \Delta S^{\#} \) (e.u.) | -28.3  | -25.9    |
| \( \Delta E^{\#} \) (kcal mol\(^{-1} \)) | 18.3   | 19.6     |
| \( A \times 10^{7} \) (L mol\(^{-1} \) s\(^{-1} \)) | 1.16   | 3.21     |

Mechanism:

Keeping in view of the above experimental results, the following mechanistic path has been suggested for the oxidation of arginine and lysine by hexacyanoferrate(III) in aqueous alkaline medium in presence of Ir\(^{III} \) as catalyst.

\[
\text{RCHNH}_2\text{COOH} + \text{OH}^- \xlongequal{K} \text{RCHNH}_2\text{COO}^- + \text{H} \\
\text{RCHNH}_2\text{COO}^- + \text{IrCl}_6^{3-} \xlongequal{K_1} \text{[RCHNH}_2\text{COO}...\text{IrCl}_6]^{4-} \\
\text{[RCHNH}_2\text{COO}...\text{IrCl}_6]^{4-} + \text{Fe(CN)}_6^{3-} \xlongequal{K_2} \text{[RCHNH}_2\text{COO}...\text{IrCl}_6...\text{Fe}^{3+}] \\
\]

\( \text{C}_1 \) \( \text{C}_2 \)
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\[ \text{[RCHNH}_2\text{COO}^-\text{...IrCl}_6\text{...Fe}^{3+}] \xrightarrow{k}\text{slow} \]

\[ \text{Cl}^- + \text{IrCl}_5^{4-} + \text{Fe}^{2+} + \text{product} \quad (5) \]

\[ \text{IrCl}_5^{4-} + 2\text{Fe(CN)}_6^{3-} + \text{H}_2\text{O} \xrightarrow{\text{fast}} \text{[IrCl}_5\text{H}_2\text{O}]^{2-} + 2\text{Fe(CN)}_6^{4-} \quad (6) \]

\[ \text{[IrCl}_5\text{H}_2\text{O}]^{2-} + \text{Cl}^- \xrightarrow{\text{fast}} \text{IrCl}_6^{3-} + \text{H}_2\text{O} \quad (7) \]

It is reported that Ir\text{I} and Ir\text{II} are the stable species of iridium, but in alkaline medium \[\text{IrCl}_6^{3-}\] is the only reacting species of iridium\textsuperscript{25,26}. Srivastava et al. have reported that the oxidation of amino acids involves the cleavage of N-H and C-H bonds in the rate determining step\textsuperscript{27}. Based on the above facts it is assumed in the present study that substrate anion forms a loosely bonded complex C\textsubscript{1} with iridium trichloride. The carbonyl oxygen of acid is most likely involved in the formation of complex C\textsubscript{1}.

In the next step the complex C\textsubscript{1} then combines with HCF(III) through electron abstraction to form complex (C\textsubscript{2}). The complex (C\textsubscript{2}) then slowly disproportionates into Ir\textsuperscript{1+} and HCF(II) along with final product. Ir\textsuperscript{1+} is reoxidized to Ir\textsuperscript{3+} by two moles of HCF(III) via one electron transfer process. The metal ion complexes with organic substrate make the electron transfer easier\textsuperscript{28}. The formation of the complex was proved kinetically by Michaelis-Menton plot i.e. a non-zero intercept of the plot of 1/rate vs 1/[S] (Fig. 2). The complex formation between oxidant and substrate was also reported in literature\textsuperscript{29}.

The reaction rate (r) is measured in terms of rate of disappearance of HCF(III). According to step (III) the rate of disappearance of HCF(III) would be

\[ \text{Rate} = \frac{-d[HCF(III)]}{dt} = k \times [C_2] \quad (8) \]

Now the total concentration of Ir\textsuperscript{3+} will be

\[ [\text{Ir}^{3+}]_{t} = [\text{Ir}^{3+}] + [\text{C}_1] + [\text{C}_2] \quad (9) \]

Substituting the values of [Ir\textsuperscript{3+}], (C\textsubscript{1}) and (C\textsubscript{2}) in eq. (8)

\[ k \times K_1' \times K_2 \times [HCF(III)] \times [Ir^{3+}]_t \times [S] \times [OH^-] \]

\[ \text{Rate} = \frac{1 + K_1' [S] [OH^-] + K_1' \times K_2 [S][OH^-] [HCF(III)]}{[OH^-] [HCF(III)]} \quad (10) \]

where \(K_1' = KK_1\)

At low concentration of HCF(III), S and OH\textsuperscript{-} eq. (10) reduces to

\[ r = k \times K_1' \times K_2 \times [HCF(III)] \times [Ir^{3+}]_t \times [S] \times [OH^-] \quad (11) \]

The rate law (11) clearly accounts for the first order kinetics with respect to HCF(III), organic substrate, hydroxide ion and catalyst at their lower concentrations. In order to verify this law (10) at higher concentration of above said reactants it could be re-written as

\[ \frac{1}{r} = \frac{1}{k \times K_1' \times K_2 \times [HCF(III)] \times [Ir^{3+}]_t \times [S] \times [OH^-]} + \frac{1}{K_1' \times K_2 \times [Ir^{3+}]_t} \quad (12) \]

This eq. (12) indicates that the plot of 1/rate vs 1/[HCF(III)] and 1/rate vs 1/[S] should give a straight line with positive intercept at 1/rate axis. Such plots are presented in Figs. 1 and 2 for arginine and lysine respectively. A close examination of these figures clearly indicate that these are evidently straight line with positive intercept at 1/rate axis. The rate constant of slow step k, the ionization constant \(K_1'\) of the first step and the formation constant of the complex \(K_2\) of the second step of all organic substrate at four different temperatures (35, 40, 45 and 50 °C) were calculated from intercept and slope of the straight line plots between rate\textsuperscript{-1} vs [HCF(III)]\textsuperscript{-1} and rate\textsuperscript{-1} vs [S]\textsuperscript{-1} for both the organic substrates (arginine and lysine). Data are presented in Tables 4a and 4b for equilibrium constants and thermodynamic parameters respectively. The constancy in \(K_1'\), \(K\) and \(K_2\) values clearly validates the derived rate law equation on the basis of proposed mechanism. A comparison of the latter values with those obtained for the slow step of the reaction shows that these values mainly refer to the rate limiting step\textsuperscript{30}. The negative value of \(\Delta S^f\) suggest that the intermediate complex is more ordered than the reactants\textsuperscript{31}. The observed modest activation energy and sizeable entropy of activation supports a complex transition state in the reaction. The observed modest enthalpy of activation and a relatively low value of entropy of activation indicates that the oxidation presumably occurs via an inner-sphere mechanism.
Experimental

All chemicals and reagents used were of AR grade. All solutions and reaction mixture were prepared in double distilled water. Absorbance was recorded on Systronic UV-Vis spectrophotometer. $\lambda_{\text{max}}$ for the reaction mixture was 420 nm at which the absorbance was noted only
Using consumed two mole of hexacyanoferrate(III), corresponding to the stoichiometry, the residual oxidant showed that one mole of substrate nitrite interval of time with standard solution of ceric(IV) mating the amount of HCF(II) ions produced after definite time with Guggenheim's method. Pseudo-first order rate constant \( k_1 \) were calculated from the start of the reaction by plane mirror method and recorded. Initial rates aliquots were withdrawn from the reaction mixture after h, a required amount of amino acid solution was added to repeated intervals of 5 min and the absorbance was recorded. Initial strengths of iridium trichloride was kept 3.35x10^{-3}. The mixture and stock solution of amino acid was prepared by dissolving the sample in dil. HCl. The final precipitate/turbidity appeared.

Table 4a. Effect of temperature on equilibrium constants

| Temp. ± 0.1 (K) | Arginine | Lysine |
|----------------|----------|--------|
|                | \( K'_1 \) | \( K'_2 \) | \( K'_1 \) | \( K'_2 \) |
| 308            | 24.0     | 520.8  | 124.6  | 2.69   |
| 313            | 58.3     | 666.6  | 144.3  | 2.74   |
| 318            | 70.8     | 793.5  | 180.8  | 2.94   |
| 323            | 78.6     | 1235.0 | 196.7  | 2.99   |

Table 4b. Thermodynamic parameters

| Parameter | Value from | Value from | Value from | Value from | Value from | Value from |
|-----------|------------|------------|------------|------------|------------|------------|
| \( E_a \) (kcal mol^{-1}) | Arginine | Lysine | Arginine | Lysine |
| \( \Delta S^\theta \) (e.u.) | Arginine | Lysine | Arginine | Lysine |
| \( \Delta H^\theta \) (kcal mol^{-1}) | Arginine | Lysine | Arginine | Lysine |
| \( \Delta F^\theta \) (kcal mol^{-1}) | Arginine | Lysine | Arginine | Lysine |

in the period in which the \( \lambda_{\text{max}} \) did not change and no precipitate/turbidity appeared. IrCl\(_3\).10H\(_2\)O (SRL) was prepared by dissolving the sample in dil. HCl. The final strength of iridium trichloride was kept \( 3.35 \times 10^{-5} \) mol dm\(^{-3}\). The kinetic experiments were carried out by mixing the required quantity of amino acid solution maintained at constant temperature with solution of HCF(III), NaOH, KCl and iridium(III) chloride kept at the same temperature. The mixture and stock solution of amino acid was then clamped in a thermostat at 35 ± 0.1 °C. After 0.5 h, a required amount of amino acid solution was added to the mixture and stirred to start the reaction mixture. Aliquots were withdrawn from the reaction mixture after repeated intervals of 5 min and the absorbance was recorded. Initial rates \( (dA/dt)_i \) were evaluated after 5 min from the start of the reaction by plane mirror method and pseudo-first order rate constant \( k_1 \) were calculated by Guggenheim’s method.

The stoichiometry of the reaction was studied by estimating the amount of HCF(II) ions produced after definite interval of time with standard solution of ceric(IV) sulphate using ferroin as redox indicator. Estimation of the residual oxidant showed that one mole of substrate consumed two mole of hexacyanoferrate(III), corresponding to the stoichiometry,

\[
\text{RCH(NH}_2\text{)COOH} + 2[\text{Fe(CN)}_6]^{3-} + 2\text{OH}^- \rightarrow \\
\text{RCOCOOH} + \text{NH}_3 + 2[\text{Fe(CN)}_6]^{3-} + \text{H}_2\text{O}
\]

Using the same experimental conditions that were used for the kinetic determinations, solutions of substrate and oxidant, in NaOH (ionic strength adjusted by the addition of the requisite amount of KCl), were mixed and kept at atmospheric conditions for 24 h. The main reaction products were identified as keto acid and ammonia. Ammonia was identified by Nessler’s reagent\(^3\) and keto acid by the following methods. The reaction mixture was extracted with diethyl ether and then concentrated. The concentrated extract was subject to TLC which shows the presence of single white product, keto acid\(^2\) and the concentrated extract was evaporated at room temperature. A solid residue was left. It was analysed by melting point determination, spot test analysis and IR spectroscopy. The melting point of the two keto acids-\(\varepsilon\)-guanidino-\(\alpha\)-oxo valeric acid and 6-amino-\(\alpha\)-oxo caproic acid separated are 214 °C and 211 °C respectively (literature value 216 °C and 212 °C respectively\(^2\)). The IR bands at frequency 1644 cm\(^{-1}\) (carbonyl group) and 1632 cm\(^{-1}\) (acid group) for arginine and 1635 cm\(^{-1}\) (carbonyl group) and 1614 cm\(^{-1}\) (acid group) for lysine shows the presence of keto acid group in the final product extracted\(^4\).

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