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Kinetics and mechanism of oxidation of *L-arginine* by sodium periodate in alkaline medium

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ABSTRACT

The kinetics of the oxidation of L-arginine by periodate was studied spectrophotometrically in alkaline medium at 280 nm. It was found that the reaction is first order with respect to [substrate], [alkali] and [periodate]. The oxidation product of the reaction was found to be α- keto acid. The anionic species of arginine (Arg^-) is considered to be the reactive species. A suitable mechanism was proposed leading to the rate law

$$\text{rate} = \frac{-d[\text{periodate}]}{dt} = k\,K\,[\text{Arginine}]\,[OH^-]$$

The activation parameters of the reaction, E_a and $\Delta S^{\#}$ were computed to be 62.3 ± 2.3kJ mol^{-1} and -197.63± 6.9 $JK^{-1}mol^{-1}$ respectively.

Keywords: Kinetics, Oxidation of L-arginine, mechanism, periodate.

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INTRODUCTION

Oxidation of amino acids has received considerable attention so far. Arginine (Arg), an essential amino acid, is needed to remove toxic ammonia from the body and also plays an important role in cell division, immune function and in the release of hormones. There have been only few investigations on the oxidation of arginine using oxidants like Chloramine-T[1,2], Bromamine-T[3], hexacyanoferrate(III)[4], alkaline per- manganate[5], diperiodato nickelate(IV)(DPN)[6], N-bromo succinimide[7], Mn(III)[8,9], quinquevalent vanadium[10,11], Ru(III) catalysed alkaline permanganate[12], N-chloro- nicotinamide[13] and N-chlorosaccharin[14].

Periodate has been used extensively in oxidations of organic as well as inorganic compounds. Periodate is a two electron oxidant with a redox potential of 0.70V in alkaline medium leading to its reduction to iodate, a stable product. Thus in order to explore the mechanism of oxidation by periodate in alkaline medium and to check the selectivity of L-arginine towards periodate we have carried out kinetic investigation on the oxidation of L-arginine by periodate in alkaline medium. Since the reaction between arginine and periodate was found to be very slow at 30ºC and in 0.4 mol dm^{-3} alkali hence it is carried out at 50ºC.

MATERIALS AND METHODS

The standard solution of L-Arginine (E-Merck) was prepared afresh by using double distilled water. A 0.01 mol dm^{-3} solution of sodium metaperiodate (E-merck) was prepared by dissolving the requisite amount of the salt in doubly distilled water. The other chemicals used were sodium hydroxide and $NaClO_4$. All chemicals used were of AR grade.

The reaction was initiated by mixing a calculated amount of periodate to a mixture of L-arginine, sodium hydroxide and sodium perchlorate at a constant temperature of 50 ± 0.1°C. The progress of the reaction was followed by measuring the absorbance of periodate (Fig.1) at 280 nm using Milton Roy-1201 UV-Visible spectrophotometer with 1cm glass cells. The temperature is kept constant using a SISKIN JULABO-V constant temperature liquid circulatory bath.

EXPERIMENTAL

Known amounts of L-arginine was allowed to react completely with a known excess of periodate at 50°C in 0.4mol dm^{-3} NaOH at an ionic strength of 0.5 mol dm^{-3}.
The remaining periodate was then analyzed spectrophotometrically. As per these results the stoichiometry was found to correspond to the equation.

$$\text{arginine} + \text{periodate} + OH^{-} \longrightarrow \text{arginine keto acid} + \text{iodate} + \text{ammonia}$$

The test for free radicals was carried out by taking L-arginine, NaOH, in a thumberg tube and acrylonitrile and periodate in a bent tube. After evacuating the system the solutions were mixed by tilting the tube. The reaction mixture was kept aside and even after 24 hrs no precipitate was observed, indicating the absence of free radicals.

The main oxidation product was identified by neutral $FeCl_3$ solution that gave a reddish brown precipitate indicating the presence of a keto acid. Similarly ammonia was identified by Nessler's reagent. The reaction orders were determined from the slopes of log $k^{/}$ versus log (concentration) plots by varying the concentrations of the oxidant, reductant or alkali while keeping the concentrations of the other reacting species constant.

RESULTS AND DISCUSSION

To find out the dependence of rate on [arginine], kinetic runs are performed varying the initial concentration of arginine in the range of 2.0–7.0 x 10^{-2} mol dm^{-3} keeping the concentrations of all other reactants constant. The rate constant values increased with increase in [arginine] and the order with respect to [arginine] (Table-1) was found to be unity (Fig.2).

The effect of alkali on the rate of the reaction was studied at constant concentrations of arginine and periodate at a constant ionic strength of 0.8 mol dm^{-3} at 50^{0}C. The rate constants obtained were found to increase with the increase in [alkali] (Table-1). Further, the plot $k^{/}$ versus $[OH^{-}]$ (Fig.3) was found to be a straight line passing through origin indicating the order with respect to $[OH^{-}]$ to be unity.

The effect of [periodate] was studied by varying the [periodate] in the reaction medium from 0.1–2.5 x 10^{-3} mol dm^{-3} at constant arginine, and alkali concentrations. The pseudo-first order rate constant, k′, obtained from the plots of log (absorbance) versus time are fairly constant (Table-1), indicating the order with respect to periodate to be one.

The effect of ionic strength was studied by varying the $[NaClO_4]$ in the reaction medium from 0.5–1.2 mol dm^{-3} at constant [periodate], [arginine], and [alkali]. The rate constant was found to be constant (Table-1) which shows that the ionic strength has negligible effect on the rate of the reaction.

The effect of temperature on the rate of the reaction was studied by carrying out the reaction at four different temperatures 45, 50, 55 and 60ºC respectively. The plot of log k versus 1/T was found to be linear indicating that the reaction obeys Arrhenius temperature dependence and the energy of activation, E_a and entropy $\Delta S^{\#}$ were computed to be 62.3 ± 2.3kJ mol^{-1} and -197.63± 6.9 $JK^{-1}mol^{-1}$ respectively

Arginine is an essential amino acid and posses three pK_a values. The protonation-deprotonation equilibria of L-Arginine was shown in Fig.4. Arginine possess three different pK_a values. One of them corresponding to the carboxylic group (pK_1 = 2.17), and the other two for amino (pK_2 = 9.04) and guanidinium groups (pK_3 = 12.48)

Under the present experimental conditions, at a $[OH^-]$ of 0.4 mol dm^{-3} arginine exists in the form of anionic species, Arg^- to the extent of 98.5% and as neutral species, Arg_z to the extent of 1.5%.

From the literature survey it may be inferred that the nature of periodate species varies with pH and concentration of the periodate. At pH 7.0 $H_4IO_6^-$ commences to dissociate further leading to the formation of $H_3IO_6^-$. The two species being of nearly of equal concentration at pH 8.0. In the pH range 9-12.5, $H_3IO_6^{2-}$ undergoes dimerisation, the concentration of the dimer being maximum in the pH range 9.5-11.5. The extent of dimerisation decreases with temperature, and increases with increase in the concentration of periodate. From pH 12.5 onwards, the concentration of the dimer becomes negligible. However, as the concentration of the alkali is increased, periodate ion undergoes further dissociation leading to the formation of the $H_2IO_6^{3-}$. So far, there is no evidence to show that $H_2IO_6^{3-}$ is further dissociated even at very high alkali concentration.

Since the rate is not affected by iodate, the probability of any fast equilibrium with the product preceding the rate determining step was ruled out. While in certain reactions complexation between periodate and substrate was reported. Based on these observations the following mechanism was proposed.

Mechanism

Scheme –I

$$H_3IO_6^{2-} + OH^- \overset{K}{\rightleftharpoons} H_2IO_6^{3-} \qquad \text{-----}\ (1)$$

$$H_2IO_6^{3-} + Arg^- \xrightarrow[\text{slow}]{k} \text{products} \qquad \text{-----}\ (2)$$

This mechanism leads to the rate equation,

$$\text{rate} = \frac{-d[\text{periodate}]}{dt} = k\,[H_2IO_6^{3-}][Arg^-] \qquad \text{----}\quad (3)$$

$$\text{Since} = [Per]_t = [H_3IO_6^{2-}]_e + [H_2IO_6^{3-}]_e \qquad \text{--------}\quad (4)$$

$$= \frac{[H_2IO_6^{3-}]}{K\,[OH^-]} + [H_2IO_6^{3-}]$$

$$= \frac{[H_2IO_6^{3-}] + K[OH^-][H_2IO_6^{3-}]}{K[OH^-]} \text{ ------------- } (5)$$

$$[H_2IO_6^{3-}] = \frac{K[OH^-]}{1 + K[OH^-]} \text{ - - - - - } (6)$$

Substituting for [$H_2IO_6^{3-}$] from equation (6) in equation (3) gives

$$\text{rate} = \frac{k\,K[Arg^-][OH^-]\ [Per]_t}{1 + K_1[OH^-]} \text{ -------- } (7)$$

Since the above mechanism does not explain unit order with respect to alkali as we noticed unit order with respect to [OH^-] we proposed scheme-2 to explain the experimental observations.

Scheme - 2

$$H_2IO_6^{3-} + Arg^- \overset{K}{\rightleftharpoons} X \text{ - - - - - } (8)$$

$$X + OH^- \xrightarrow[\text{slow}]{k} \text{intermediate (I)} + \text{iodate} \text{ --------- } (9)$$

$$I + H_2O \xrightarrow{\text{fast}} \text{Arg keto acid} + NH_3 \text{ - - - - - } (10)$$

In the proposed mechanism periodate and arginine can reversibly form an adduct (X) which decomposes in a slow step in presence of hydroxide ion to give an intermediate(I), iodate and water. Further the intermediate undergoes hydrolysis in a fast step to form arginine keto acid and ammonia.

$$\therefore \text{rate} = k[X][OH^-] \text{ - - - - - } (11)$$

$$\text{where } [X] = K[H_2IO_6^{3-}][Arg^-] \text{ - - - - - } (12)$$

Substituting for [X] from equation (12) in equation (11) gives

$$= k\,K\,[\mathrm{Arg}^-]\,[\mathrm{H_3IO_6^{2-}}]\,[\mathrm{OH}^-] \qquad ---------- \quad (13)$$

Since $[\mathrm{Arg}^-] = [\mathrm{Arg}]_t$ under experimental conditions employed, the above rate equation can be written as

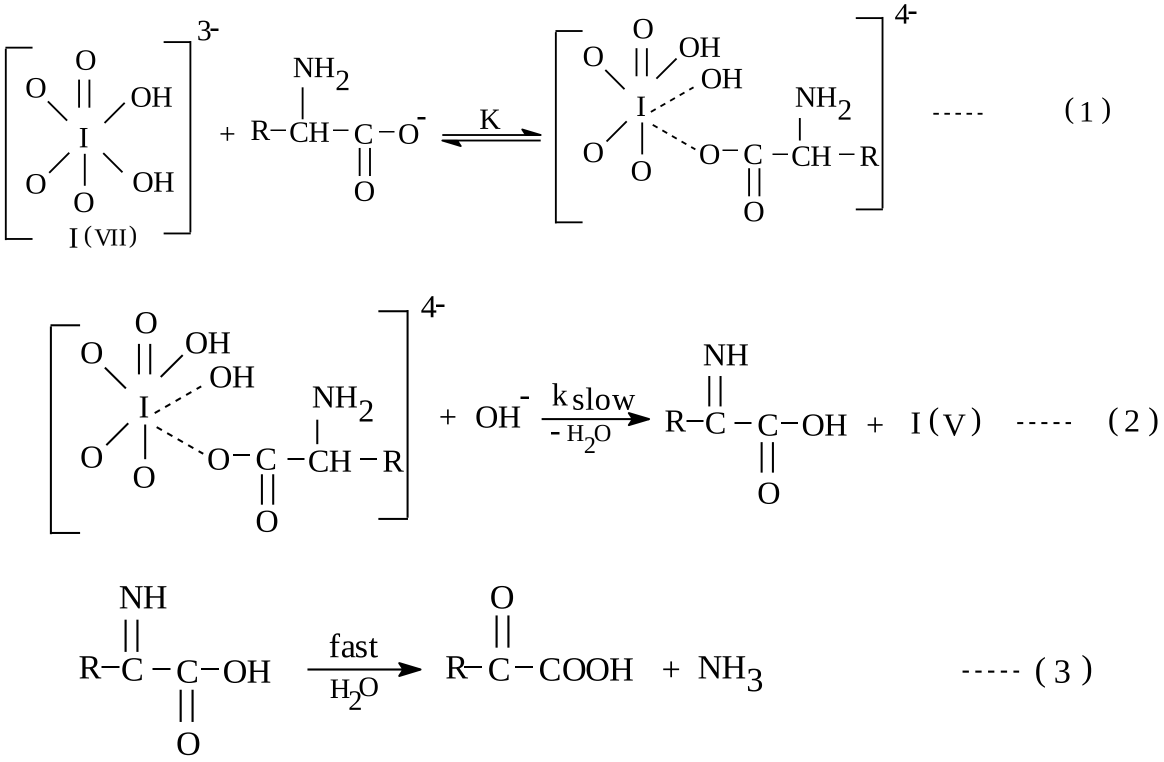
$$\text{rate} = k\,K\,[\mathrm{Arg}]_t\,[\mathrm{H_3IO_6^{2-}}]\,[\mathrm{OH}^-]$$

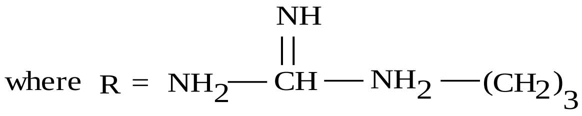
This rate equation explains first order dependence each on [Arg], [per] and $[\mathrm{OH}^-]$. Also the plot of k' versus $[\mathrm{OH}^-]$ was found to be a straight line passing through origin which substantiates the proposed mechanism (Fig.3).

CONCLUSION

The observations in the present study show that the $\mathrm{H_2IO_6^{3-}}$ and anionic form of arginine are the reactive species in alkaline medium. Arginine keto acid is the product of oxidation and the intimate mechanism of the reaction may be represented as shown below:

Intimate mechanism





$$\text{where } R = \mathrm{NH_2{-}\overset{\overset{\large NH}{||}}{C}H{-}NH_2{-}(CH_2)_3}$$

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Table-1: Effect of [periodate], [Arg], [OH^-] and ionic strength, μ, on the pseudo-first order rate constant($k^{/}$), at 50 ± 0.1°C.

[periodate]x10^3 (mol dm^{-3})	[arg]x10^2 (mol dm^{-3})	[OH^-] (mol dm^{-3})	μ (mol dm^{-3})	$k^{/}$ x10^4 (sec^{-1})
0.1	4.0	0.4	0.5	2.68
0.5	4.0	0.4	0.5	2.65
1.0	4.0	0.4	0.5	2.51
1.5	4.0	0.4	0.5	2.64
2.0	4.0	0.4	0.5	2.54
2.5	4.0	0.4	0.5	2.55
1.0	2.0	0.4	0.5	1.25
1.0	3.0	0.4	0.5	1.92
1.0	4.0	0.4	0.5	2.51
1.0	5.0	0.4	0.5	3.15
1.0	6.0	0.4	0.5	3.75
1.0	7.0	0.4	0.5	4.39
1.0	4.0	0.2	0.8	1.42
1.0	4.0	0.3	0.8	2.13
1.0	4.0	0.4	0.8	2.52
1.0	4.0	0.5	0.8	3.50
1.0	4.0	0.6	0.8	4.21
1.0	4.0	0.7	0.8	4.87
1.0	4.0	0.4	0.5	2.53
1.0	4.0	0.4	0.6	2.44
1.0	4.0	0.4	0.7	2.42
1.0	4.0	0.4	0.8	2.35
1.0	4.0	0.4	1.0	2.52
1.0	4.0	0.4	1.2	2.33

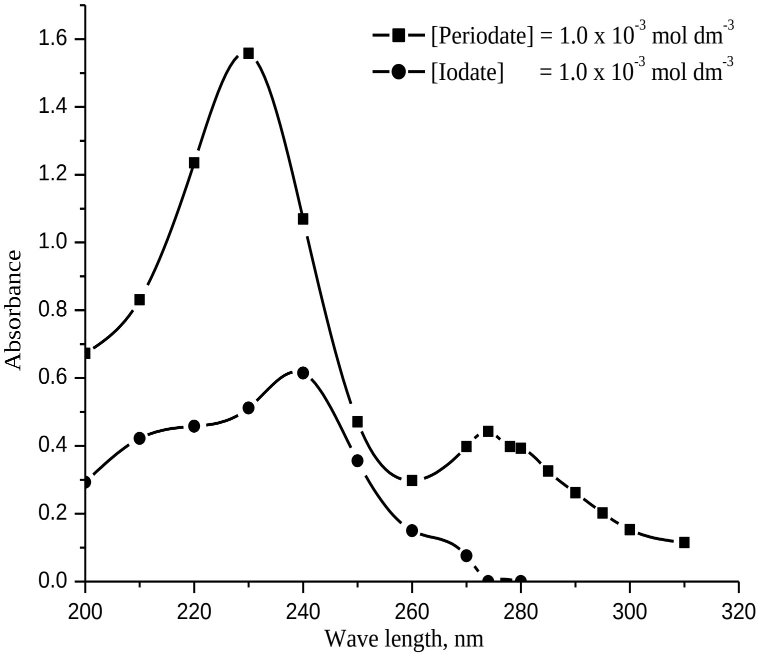

Fig.1: Absorption spectra of periodate and iodate in 0.4 mol dm^{-3} alkali

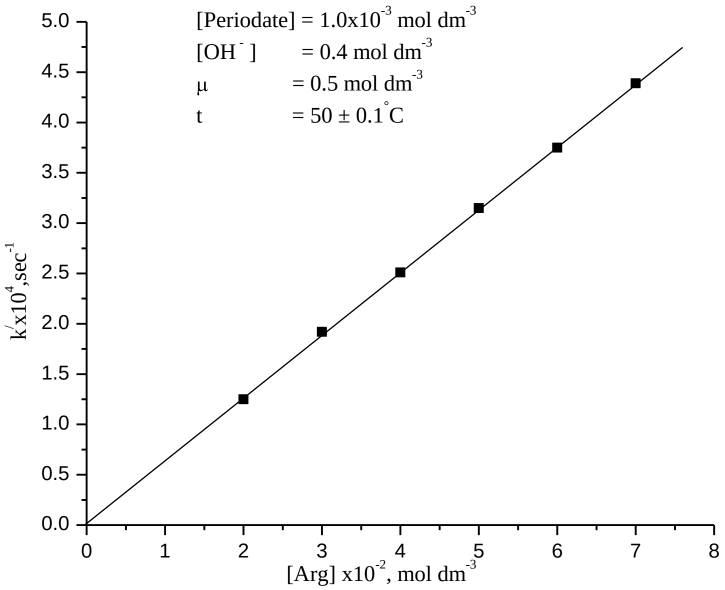

Fig.2: Plot of k$^{/}$ versus [arginine]
(order with respect to arginine)

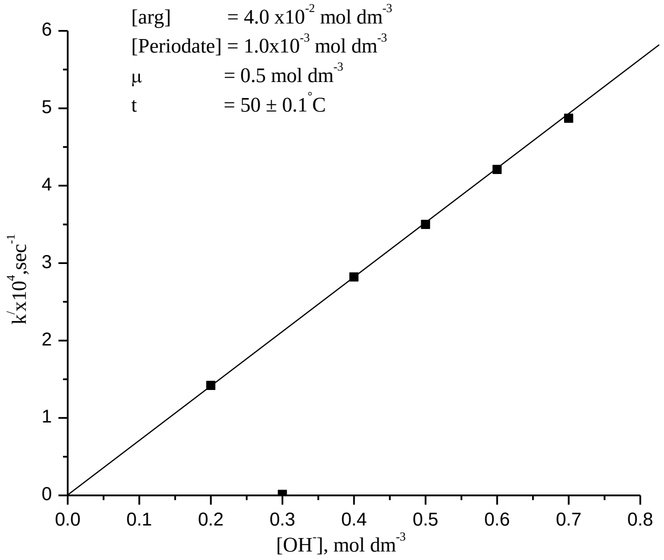

Fig. 3: plot of k$'$ versus [OH^{-}]
(order with respect to [OH^{-}])

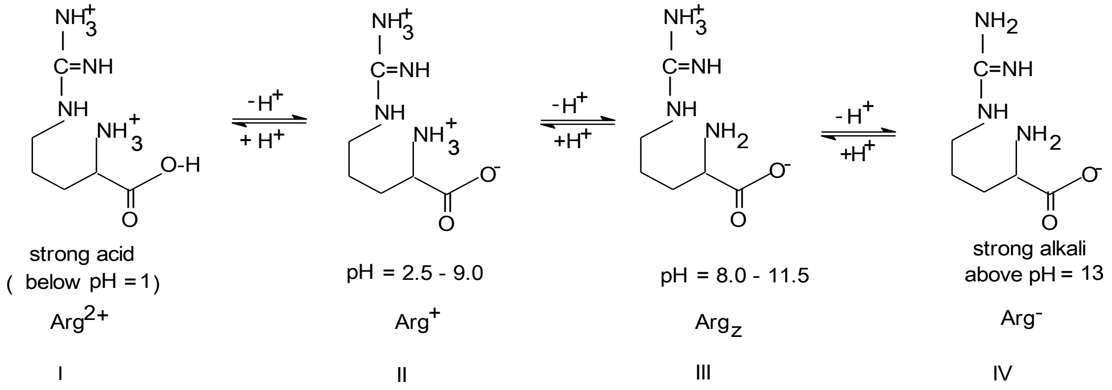

Fig. 4: Protonation-deprotonation equilibria of L–Arginine

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