Monatshefte für Chemie 117, 1041—1045 (1986)

Monatshefte für Chemie
Chemical Monthly

Oxidation of *L*-Tyrosine by Vanadium (V) in Presence of Sulphuric Acid

Vijai K. Sharma*, **K. Sharma**, and **Angad P. Payasi**

Chemistry Department, Government Science College, Rewa-486001, India

(Received 4 March 1985. Revised 16 December 1985. Accepted 8 January 1986)

Oxidation of *L*-tyrosine with vanadium (V) in sulphuric acid medium at constant ionic strength is first order in oxidant and H^+. The order in tyrosine varies from 1 to 0. A mechanism consistent with the kinetic results is proposed in which the rate determining step is the decomposition of the complex formed in the prior equilibrium.

(Keywords: Mechanism; Oxidation; Tyrosine)

Oxidation von L-Tyrosin mit Vanadium(V) in Gegenwart von Schwefelsäure

Die Oxidation von *L*-Tyrosin mit V(V) in schwefelsaurem Medium bei konstanter Ionenstärke ist erster Ordnung bezüglich Oxidationsmittel und H^+. Die Ordnung bezüglich Tyrosin variiert zwischen 1 und 0. Es wird ein Mechanismus vorgeschlagen, der mit den kinetischen Ergebnissen konsistent ist. Der geschwindigkeitsbestimmende Schritt ist dabei die Zersetzung eines Komplexes, der in einem vorgelagerten Gleichgewicht gebildet wird.

Introduction

Oxidation of amino acids by a large number of oxidants has been extensively investigated from the mechanistic view point. However, the kinetics of oxidation of tyrosine with any oxidant has not been studied so far. In the present communication, results of the kinetics of oxidation of *L*-tyrosine by vanadium (V) in sulphuric acid are reported and examined mechanistically.

---

* For correspondence: 20/5 Kothi Road, Rewa-486001, India.

Experimental

A solution of *L*-tyrosine (E. Merck) was prepared by dissolving in the known concentration of sulphuric acid (B. D. H., A. R.). Oxidant solution was prepared by dissolving ammonium metavanadate (Reidel) in appropriate concentration of sulphuric acid and was standardised by the usual methods. All the other chemicals used were of standard grade.

The kinetics of the reaction was followed by examining aliquot portions of the reaction mixture for unconsumed vanadium(V) by titrating against standard ferrous ammonium sulphate using N-phenyl authranilic acid as an indicator.

The reaction mixture containing excess of V(V) over *L*-tyrosine in the presence of sulphuric acid was kept at 30° for 48 h. The corresponding aldehyde was identified as its 2:4 dinitrophenyl hydrazone derivative:

$$C_9H_{11}O_3N + 2V(V) + H_2O \rightarrow C_8H_8O_2 + NH_3 + CO_2 + 2V(IV) + 2H^+$$

Results

The order in V(V) was found to be one as revealed by the linear plot of log [V(V)] versus time at different initial concentrations of V(V). The rate constant in vanadium was obtained from the pseudo first order plots (Table 1).

Table 1. *Effect of concentration of* [V(V)] *and* [*L*-tyrosine] *on the rate constant*[a] *at 30°*

[V(V)] $M \cdot 10^3$	[*L*-tyrosine] $M \cdot 10^2$	$k_1 \cdot 10^3\,\mathrm{min}^{-1}$	$k_2 \cdot 10\,\mathrm{l\,mol}^{-1}\,\mathrm{min}^{-1}$
2.50	5.00	35.25	7.05
4.00	5.00	36.56	7.31
5.00	5.00	36.01	7.20
6.66	5.00	35.18	7.03
10.00	5.00	35.44	7.08
10.00	5.50	36.49	6.63
10.00	4.00	30.01	7.50
10.00	3.33	23.43	7.03
10.00	2.50	19.09	7.63
10.00	2.00	15.60	7.78
10.00	1.00	7.61	7.61
10.00	0.50	3.82	7.64

[a] *a*—$[H^+] = 2.0\,M$ and $\mu = 2.01\,M$.

The rate increased with increase in the concentration of tyrosine (Tab. 1) at constant [V(V)] and tended to attain a limiting value indicating complex kinetics. The plot of k_1 vs. [tyrosine] showed a deviation from straight line behaviour at higher concentrations of tyrosine suggesting that the order falls from unity of zero (Fig. 1). The double reciprocal plot

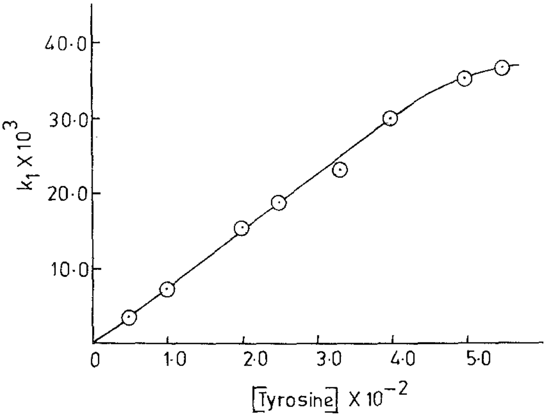

Fig. 1. Plot of k_1 vs. [Tyrosine] at 30 °C; $[V(V)] = 10.0 \cdot 10^{-3} M$, $[H_2SO_4] = 2.0 M$; $\mu = 2.01 M$

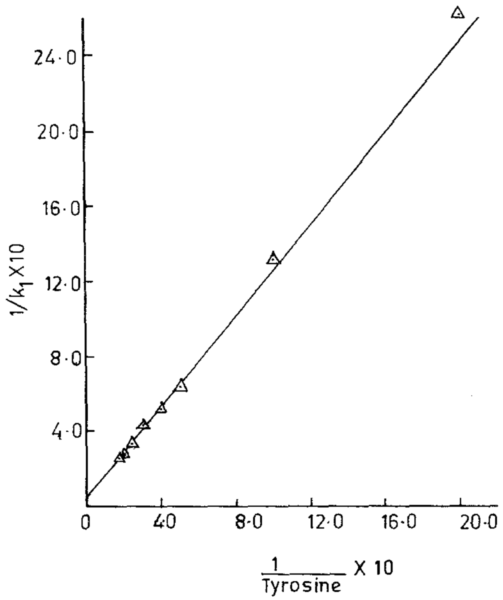

Fig. 2. Plot of $1/k_1$ vs. 1/[Tyrosine] at 30 °C; conditions see Fig. 1

of k_1 vs. [tyrosine] with a positive intercept on the y-axis (Fig. 2) leads to the conclusion that the reaction follows *Michaelis-Menten* kinetics.

A six-fold change in sulphuric acid concentration showed a linear increase in the pseudo first-order rate constant indicating that the reaction is acid catalyzed. The unit slope of the plot between $\log k_1$ and $\log[H_2SO_4]$

revealed first order dependence in acid. *Zucker-Hammett* [1] and *Bunnett* [2] treatments were applied. The plots of $\log k_1$ vs.—H_0 and $\log k_1 + H_0$ vs. log a_{H_2O} were found to be linear with slope values 0.42 and + 6.1 respectively. A *W* value of + 6.1 suggested the participation of a water molecule as proton abstracting agent in the rate limiting step.

The rate of reaction has been observed to increase with increase in ionic strength and with decrease in the dielectric constant of the medium.

Various parameters such as *E, A* and $\Delta S^{\neq}$ were evaluated by taking kinetic measurements at different temperatures (25–45°). The value obtained were $12.91 \pm 2.1\,\mathrm{kcal\,mol^{-1}}$, $1.31 \pm 0.51 \cdot 10^6\,\mathrm{s^{-1}}$ and —30.83 ± 0.5 e. u. respectively.

A number of species of V(V) are supposed to exist depending on the concentration and nature of acid. A unit-dependence of rate on sulphuric acid in the oxidation of tyrosine suggests $V(OH)_3^{2+}$ (Ref. [3]) as the oxidising species of vanadium(V). Further, dependence of rate on unit concentration of HSO_4^- indicates the formation of a 1 : 1 bisulphate—vanadium (V) complex [4] as $V(OH)_3HSO_4^+$ which acts as an active oxidising agent.

$$VO_2^+ + H^+ + HSO_4^- + H_2O \overset{K_1}{\rightleftharpoons} V(OH)_3HSO_4^+ \qquad (1)$$

Amino acids, having a lone pair of electrons on the nitrogen atom, are suitable ligands for transitional metal ions. Hence it acts as nucleophile and co-ordinates with the electrophilic V(V) species forming an intermediate complex. The keto acid could not be detected as an intermediate in the oxidation of tyrosine, and aldehyde was identified as product. The formation of aldehyde supports the attack of axidant on the carboxylate function causing O—H fission. The nature of the product would have been different in case of C—H fission. The oxidation process therefore, involves a decarboxylation—deamination path initiated with the decomposition of the complex by attack of water molecule as proton abstracting agent in the rate determining step.

The following mechanism is suggested in acoordance with the experimental results:

$$V(OH)_3HSO_4^+ + \text{Tyrosine} \overset{K_2}{\rightleftharpoons} \text{Complex}^+ \qquad \text{fast} \quad (2)$$

$$\text{Complex}^+ + H_2O \xrightarrow{k_1} X + H_3O^+ + V(IV) \qquad \text{slow} \quad (3)$$

$$X + V(V) \xrightarrow{\text{Decarboxylation}} \text{Imine} + H^+ + V(IV) + CO_2 \qquad \text{fast} \quad (4)$$

$$\text{Imine} + H_2O \xrightarrow{\text{Deamination}} \text{Aldehyde} + NH_3 \qquad \text{fast} \quad (5)$$

The proposed mechanism implies that a one electron transfer operates in the reaction of V(V) to V(IV) by tryosine. The induced polymerisation of acrylonitrile too indicates the formation of a reducing intermediate that supports the step (3).

Applying steady state approximation, the value of k_{obs} at constant $[\text{V(V)}]_T$ is obtained as

$$k_{\text{obs}} = \frac{k_1 K_1 K_2 [\text{H}^+][\text{HSO}_4^-][\text{Tyrosine}]}{1 + K_1 [\text{H}^+][\text{HSO}_4^-] + k_1 K_2 [\text{H}^+][\text{HSO}_4^-][\text{Tyrosine}]} \tag{6}$$

and

$$\frac{1}{k_{\text{obs}}} = \frac{1}{[\text{Tyrosine}]}\left\{\frac{1}{k_1 K_1 K_2 [\text{H}^+][\text{HSO}_4^-]} + \frac{1}{k_1 K_2}\right\} + \frac{1}{k_1} \tag{7}$$

Eq. (7) explains the *Michaelis-Menten* kinetics in case of substrate variation.

Wells and *Kuritsyn* [5] reported that the equilibrium constant for the formation of V(OH)_3^{2+} is very much less than unity and so k_1 may also be assumed to be less than one; then eq. (6) is reduced to

$$k_{\text{obs}} = k_1 K_1 K_2 [\text{H}^+][\text{HSO}_4^-][\text{Tyrosine}] \tag{8}$$

At higher concentration of tyrosine, assuming $K_2 \gg (1 + K_1 [\text{H}^+][\text{HSO}_4^-])$, the value of k_{obs} is independent of the substrate concentration.

The medium effect supports the involvement of a positive ion and a dipole in the rate determining step. The magnitude of entropy of activation is also in favour of the above mechanism involving a bimolecular reaction [6].

Although in acid medium the amino acids may exist in equilibrium with its monoprotonated form, the attack of electrophilic V(V) on the unprotonated form appears more plausible in accordance with our experimental results.

References

[1] *Zucker L, Hammett LP* (1939) J Am Chem Soc 61: 2791

[2] *Bunnett JF* (1961) J Am Chem Soc 83: 4968

[3] *Waters WA, Littler JS* (1965) Oxidation in organic chemistry. Wiberg KB (ed.) Part A: 204

[4] *Mehrotra RN* (1968) J Chem Soc 1963

[5] *Wells CF, Kuritsyn LV* (1970) J Chem Soc 1372

[6] *Ogata Y, Tomizawa K , Ikoda T* (1979) J Org Chem 44: 2362