Investigation of Mechanism for the Oxidation of Tyrosine by Pyridinium Chlorochromate in Acidic DMF-Water Medium by Spectrophotometric Technique: A kinetic study

Munna Lal Meena

Department of Chemistry, Govt. P. G. College Pratapgarh, 312605, Rajasthan, India.

E-mail: munnachem2009@gmail.comn

Abstract:

The kinetics of oxidation of Tyrosine by pyridinium chlorochromate in DMF-water (70:30 %) medium in presence of perchloric acid leads to the formation of corresponding aldehyde. The reaction is of first order each in [PCC], [HClO$_4$] and [Tyrosine]. Michaelis-Menten type kinetics was observed with Tyrosine. The reaction rates were determined at different temperatures [25, 30, 35, 40, 45, 50 °C] and the activation parameters were calculated. The reaction does not induce polymerization of acrylonitrile. With an increase in the amount of DMF in its aqueous mixture, the rate increases. A suitable mechanism and rate law for the reaction was postulated.

Key Words: kinetics**,** oxidation, pyridinium chlorochromate**,** Tyrosine, Michaelis-Menten.

Introduction

Pyridinium chlorochromate being one of the most versatile available oxidizing agent[1]**.** A number of reports on the oxidation of several substrates by pyridinium chlorochromate (PCC) are available in the literature like methionine[2], oximes[3], unsaturated acids[4],cysteine[5], alcohols[6]. There seems to be no report on the oxidation of Tyrosine by pyridinium chlorochromate.

Our literature survey reveals that the oxidation of Tyrosine by different oxidants has received a limited attention so we are particularly interested to see the mechanism of the oxidation of Tyrosine by pyridinium chlorochromate in acidic DMF-Water media.

Experimental:-

Pyridinium chlorochromate was prepared by the method described in the literature[7], and its purity was checked by iodometrically and by the UV-VIS spectra. Tyrosine Analytical grade (SRL) was used as supplied (purity was checked by its melting point) and all other reagents were of Analytical Grade.

The reaction was carried out under pseudo first order conditions in the DMF-water [70% (v/v) DMF] solvent system at 313 K. The reaction was initiated by mixing thermally equilibrated solution of PCC and Tyrosine which also contained the required quantities of perchloric acid. The reaction was followed by monitoring the decrease in the absorbance of PCC at 354 nm in 1 cm cell placed in the thermostatted compartment of JASCO model 7800 UV/VIS spectrophotometer.

The kinetic runs were followed for more than 70% completion of reaction and good first order kinetics were observed. Pseudo-first order rate constants k_{obs} were obtained from the slope of the plot of log (absorbance) versus time.

Results and Discussion:-

Stoichiometry and product analysis

The stoichiometry of the reaction was determined by performing the experiment at 313 K, under the condition of [PCC] > [Tyrosine], containing 0.3 mol /dm^3 [HClO$_4$] in 70 % vol. DMF, 30 % vol. water mixture (v/v) were allowed to stand at 40ºC. When the reaction was completed, the PCC concentration was assayed by measuring the absorbance at 354 nm. The qualitative product study was made under kinetic conditions. The main reaction product was identified as (4-hydroxyphenyl)acetaldehyde by its 2,4-D.N.P. derivative. Nesseler's reagent test and lime water test were used to detect the ammonium ion and carbon dioxide, respectively, and Cr(III) was confirmed by the UV-Visible spectra of the reaction solution after completion of the reaction. The observed stoichiometry may be represented as

$$3RCH(NH_2)COOH + 2Cr(VI) + 3H_2O \rightarrow 3RCHO + 2Cr(III) + 3NH_4^+ + 3H^+ \ldots(A)$$
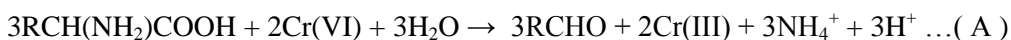
Effect of PCC

At constant [HClO$_4$], temperature and [Tyrosine] ([Tyrosine] >> [PCC]), plot of log[PCC] against time was linear indicating first-order dependence of the rate on PCC. The observed rate constant k_{obs} was not affected by a change in initial concentration of PCC **[table1].**

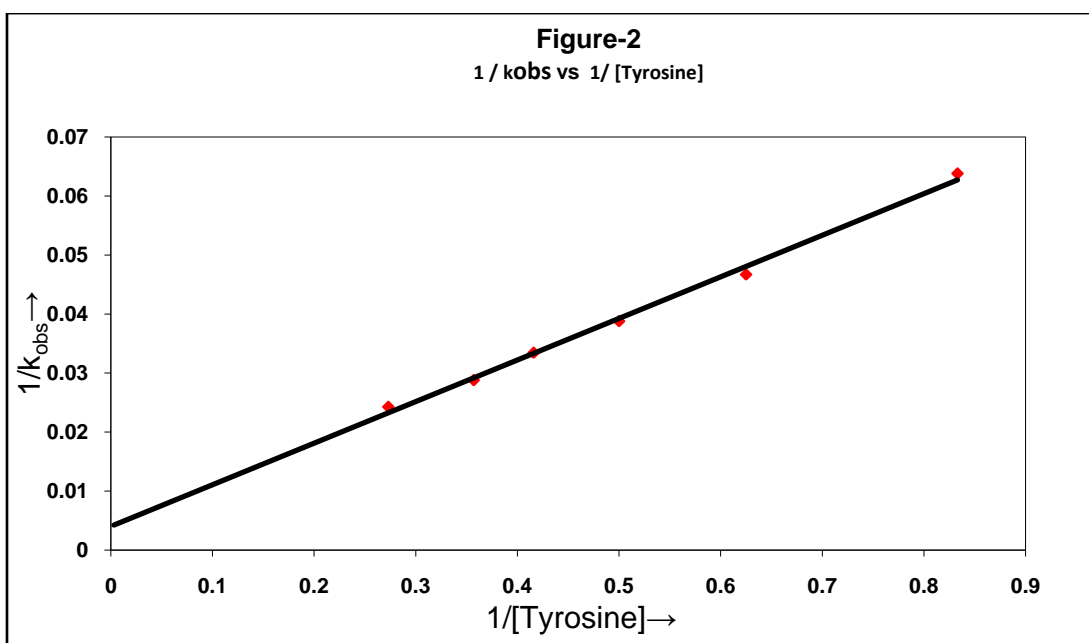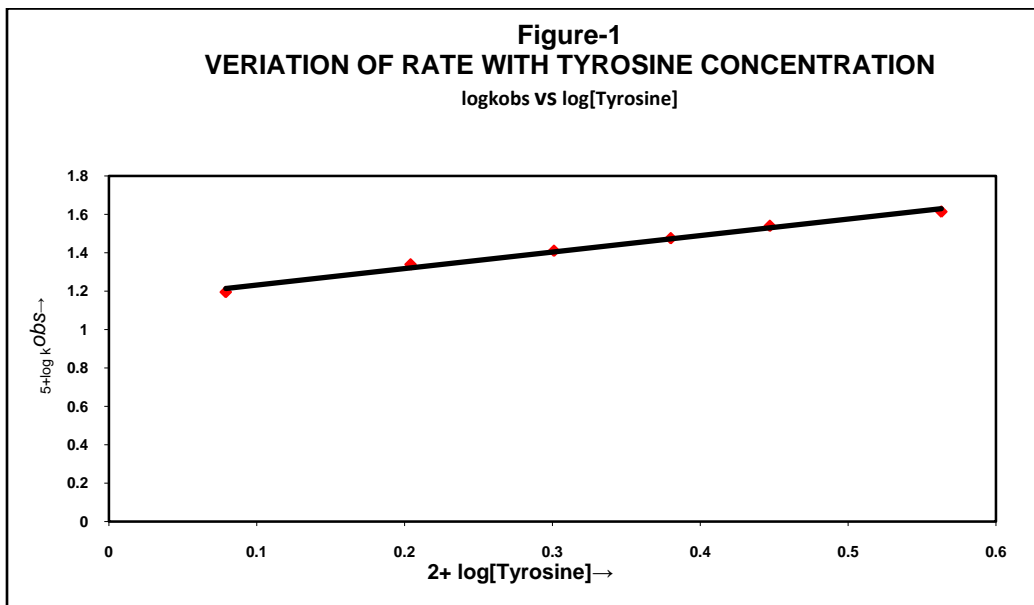**Table1**. Variation of rate with PCC, Tyrosine, and perchloric acid concentrations

T=313 K   DMF=70% (v/v)

10^3 x [PCC] mol dm^{-3}	10^2 x [Amino Acid] mol dm^{-3}	10 x [H$^+$] mol dm^{-3}	k_{obs} x 10^5 s^{-1}
2.5	2.0	3.0	22.14
2.25	2.0	3.0	21.75
2.0	2.0	3.0	22.87
1.75	2.0	3.0	22.39
1.5	2.0	3.0	22.40
1.0	2.0	3.0	22.20
2.0	1.2	3.0	15.10
2.0	1.43	3.0	16.00
2.0	1.6	3.0	19.20
2.0	2.0	3.0	22.80
2.0	2.4	3.0	27.75
2.0	2.8	3.0	30.80
2.0	3.66	3.0	48.90
2.0	5.0	3.0	60.00
2.0	2.0	1	6.24
2.0	2.0	2.5	17.20
2.0	2.0	3.0	22.40
2.0	2.0	3.5	27.63
2.0	2.0	5.0	41.15
2.0	2.0	7.0	62.90
2.0	2.0	10.0	89.62

Effect of substrate

At constant PCC concentration, [H$^+$] and temperature, the reaction rate increased with an increase in the concentration of Tyrosine from 1.2 x 10^{-2} to 5.0 x 10^{-2} mole/dm^3 **[Table 1]**. The plot of logk_{obs} versus log [Tyrosine] **[Figure 1]** was linear with positive slope equals to **1.05** indicating first-order dependence of the rate on [Tyrosine]. The plot of 1/k_{obs} vs. 1/ [Tyrosine], **[Figure 2]** gives straight line with positive intercept, which indicates that Michaelis–Menten type kinetics is followed with respect to Tyrosine. Although the intercept value [K_m = 0.002] is very small but the value indicate formation of complex which may be highly reactive so concentration will be very small at any time. A similar phenomenon has been observed in the oxidation of α-amino acid by Cr(VI)[8,9].

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Figure-1
VERIATION OF RATE WITH TYROSINE CONCENTRATION
logkobs VS log[Tyrosine]

Figure-2
1 / kobs vs 1/ [Tyrosine]

Effect of ionic strength

The effect of ionic strength was studied by varying the sodium sulfate concentration. The ionic strength in the reaction medium was varied from 1.0 to 11.0 x 10^{-3} mol dm^{-3} **[table 2]** at constant concentration of Tyrosine, PCC, $HClO_4$ and with other conditions remaining constant. It has been observed that there was no significant effect of ionic strength on the rate. This indicates that the reaction may be between an ion and a neutral molecule or between neutral molecules[10].

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Table 2 Variation of rate with sodium sulfate concentration of Tyrosine at 313 K

[Tyrosine] = 2.0 x10^{-2} mol dm^{-3} [HClO$_4$] = 0.3 mol dm^{-3}

[PCC] = 2.0 x10^{-3} mol dm^{-3} DMF = 70 %(v/v)

[Na$_2$SO$_4$] x 10^3 mol dm^{-3}	1.0	3.0	5.0	7.0	9.0	11.0
10^5 k$_{obs}$ (s^{-1})	22.40	22.10	21.90	21.50	22.15	22.50

Effect of solvent composition

It was observed that a change in solvent composition by varying DMF (% v/v) in the reaction mixture, keeping other conditions constant, and the reaction rate was affected considerably. The rate of reaction increased with an increase in volume percentage of DMF **[Table 3]**. Many theories have been put forward to give a quantitative explanation[11,12] for the effect of dielectric constant (D) of the medium on the kinetics of liquid phase reactions. For the limiting case of a zero angle of approach between two dipoles or ion-dipole system, Amis[13] had shown that in a linear plot of logk$_{obs}$ vs. 1/D a positive slope indicates a positive ion-dipole reaction, while a negative slope indicates the involvement of two dipoles or a negative ion-dipole reaction. In the present investigation a plot of logk$_{obs}$ vs. 1/D **[figure 3]** gives a straight line with a positive slope, clearly supporting that there is an involvement of positive ion-dipole in the rate determining step.

Table 3 variation of rate with solvent composition
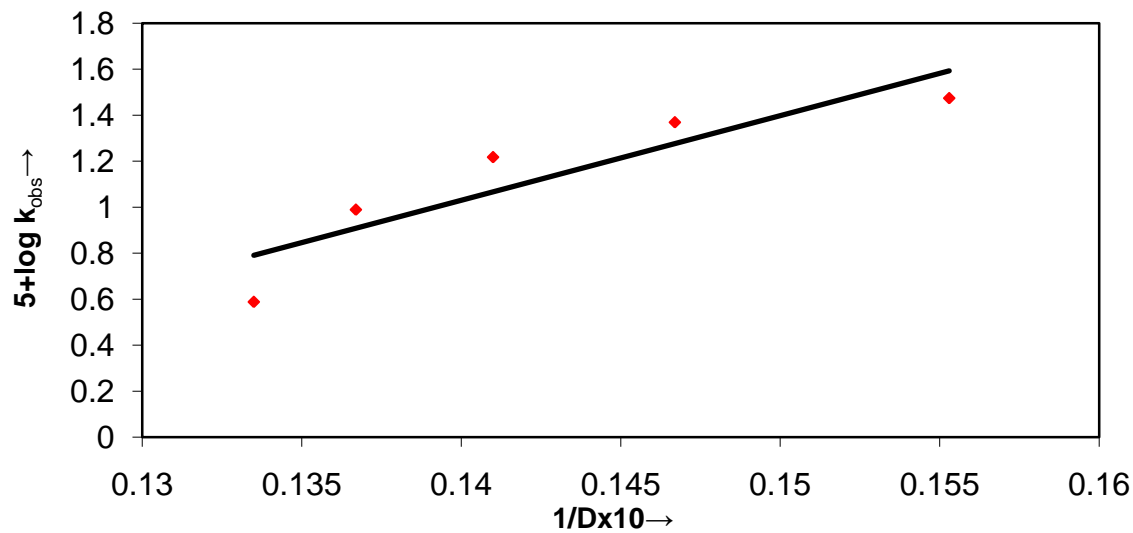
[Tyrosine] = 2.0 x10^{-2} mol dm^{-3} [HClO$_4$] = 0.3 mol dm^{-3}

[PCC] = 2.0 x10^{-3} mol dm^{-3} T=313 K

DMF:H$_2$O	70:30	60:40	50:50	40:60	30:70	20:80	0.0:100
10^5 k$_{obs}$ (s^{-1})	22.40	18.50	13.60	11.20	7.90	6.25	4.38

Figure-3
VARIATION OF RATE WITH DIELECTRIC CONSTANT
log kobs VS 1/D

Effect of temperature:-

The rate constant of the reaction was found to increase with an increase in temperature **[table 4]** The energy of activation was obtained by the plot of log k versus 1/T **[Figure 4],** from which the activation parameters were calculated **[table 5].** The entropy of activation is negative as expected for bimolecular reaction. The negative value also suggests the formation of a cyclic intermediate from non-cyclic reactants in the rate determining step[14]. The complex formation is proved by the plot of inverse of rate constant against inverse of substrate concentration [Tyrosine]. It has been pointed out[15] that if entropy of activation is negative and small the reaction will be slow.

Table 4 variation of rate with temperature

[Tyrosine] mol dm^{-3} [HClO$_4$] = 0.3 mol dm^{-3}

[PCC] = 2.0 x10^{-3} mol dm^{-3} DMF = 70 %(v/v)

Temperature (k)	298	303	308	313	318	323
k$_{obs}$ x 10^5 s^{-1}	10.96	17.81	19.20	22.80	39.60	45.70

Table 5 Activation Parameters

Parameters	E_a (kJ mol^{-1})	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (kJ mol^{-1})	$\Delta F^{\neq}$ (Jk^{-1}mol^{-1})
values	44.92	42.32	-122.81	80.76

Figure-4
**VERIATION OF RATE WITH TEMPRATURE OF TYROSINE**
log k obs vs 1/T
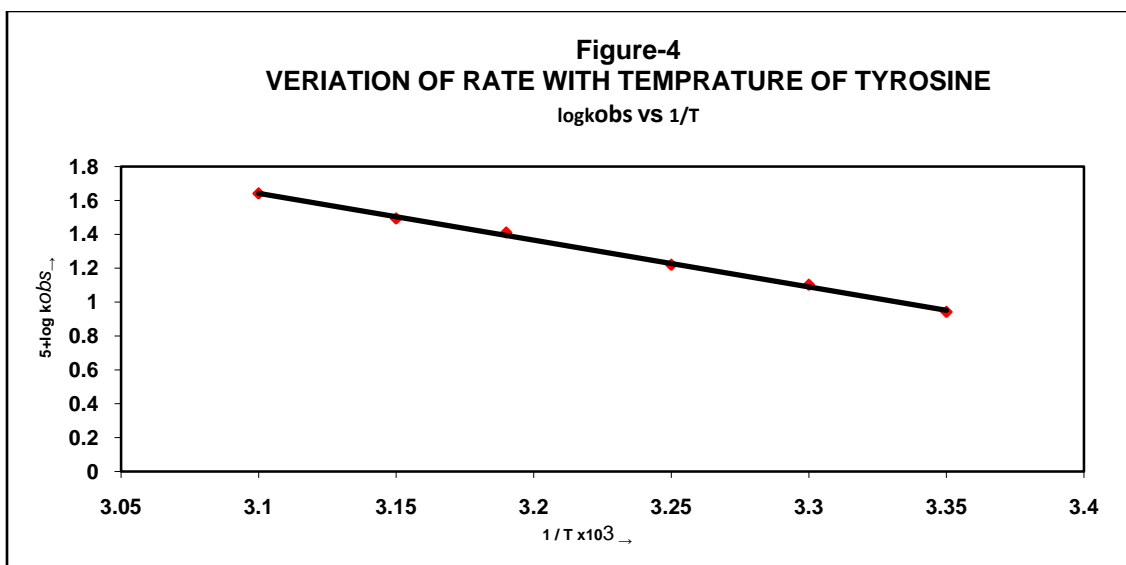
Effect of acrylonitrile and pyridine

Involvement of radical mechanism is ruled out, as there is neither any decrease in rate in presence of stabilizer free acrylonitrile nor milky appearance under kinetic conditions. The rate of reaction does not change on addition of pyridine indicating thereby, the stability of PCC i.e. PCC is not hydrolyzed in the conditions understudy.

Effect of perchloric acid

At fixed concentration of Tyrosine and PCC and with other conditions remaining constant, the rate was found to increase with an increase in the perchloric acid concentration **[table1].** A plot of logk$_{obs}$ vs. log [HClO$_4$] **[Figure 5]** is a straight line with a positive slope ≈1 **(1.19).** This shows that reaction is of first order with respect to the hydrogen ion concentration.

Figure-5
VERIATION OF RATE WITH HYDROGEN ION OF TYROSINE

log kobs VS log[H+]
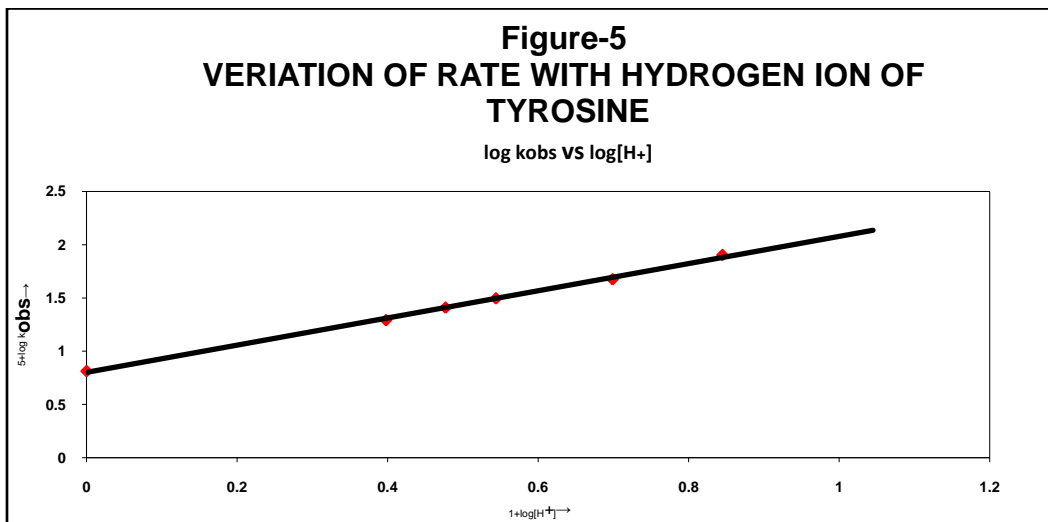
Under the present experimental conditions, the concentration of anion form will be very low and hence the possible species may be either the cation form of Tyrosine or Zwitter ion. With cation as the active species, the rate law predicts a second-order dependence of the rate on $[H^+]$, which is contrary to experimental results. Protonated Tyrosine is not involved in the reaction sequence and the zwitter ion is the active species in this reaction.

An amino acid is known to exist in the following equilibria
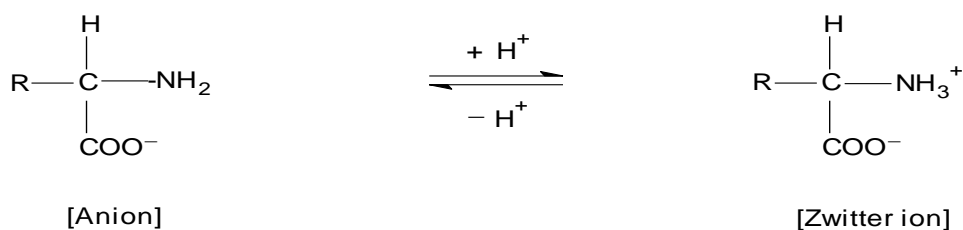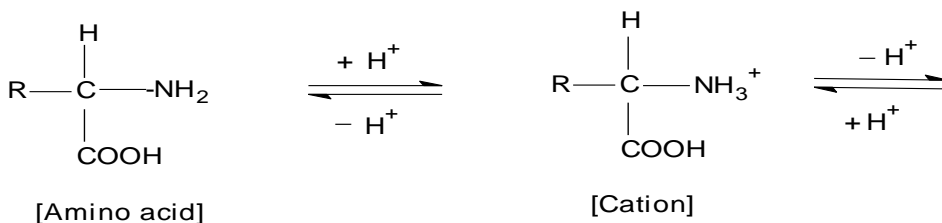
The acid catalysis may well be attributed to a protonation of PCC **[eq.B]** to yield a stronger oxidant and an electrophile with both the protonated and unprotonated forms being reactive. The formation of a protonated species of PCC has been also reported[16-18].

$$PyHOCrO_2Cl \;+\; H^+ \rightleftharpoons PyHOCr^+(OH)OCl \qquad \text{------------- (B)}$$

Mechanism

On the basis of above experimental results, a suitable mechanism is given below:

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$$O=\overset{\overset{\displaystyle O^-PyH^+}{|}}{\underset{\underset{\displaystyle Cl}{|}}{Cr}}=O \quad + \quad H^+ \quad \underset{}{\overset{k}{\rightleftharpoons}} \quad O=\overset{\overset{\displaystyle O^-PyH^+}{|}}{\underset{\underset{\displaystyle Cl}{|}}{\overset{+}{Cr}}}-OH \qquad \text{............ 1}$$

[PCC]

[Protonated PCC]

$$R-\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle COO^-}{|}}{C}}-NH_3^+ \quad + \quad O=\overset{\overset{\displaystyle O^-PyH^+}{|}}{\underset{\underset{\displaystyle Cl}{|}}{\overset{+}{Cr}}}-OH \quad \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \quad \left[Complex[C]\right] \qquad \text{.............. 2}$$

[Phenyl Alanine] [Protonated PCC]

$$\left[Complex[C]\right] \quad \xrightarrow[k']{Slow} \quad RCHO \; + \; NH_4^+ \; + \; CO_2 \; + \; Cr(IV) \qquad \text{.......... 3}$$

$$Cr(VI) \; + \; Cr(IV) \quad \xrightarrow{Fast} \quad 2Cr(V) \qquad \text{............ 4}$$

[PCC]

$$2Cr(V) + 2RCH(NH_2)COOH + 2H_2O \xrightarrow{Fast} 2\,RCHO + 2\,CO_2 + 2\,NH_4^+ + 2Cr(III) + 2H^+ \text{........ 5}$$

[PCC]   [Phenyl Alanine]

The overall reaction may be represented as:

$$2Cr(VI) + 3\,RCH(NH_2)COOH + 3H_2O \longrightarrow 3\,RCHO + 2Cr(III) + 3NH_4^+ + 3CO_2 + 3H^+ \text{............ 6}$$

$R= C_6H_5CH_2-$

On the basis of above mechanism the rate law can be expressed as:

$-d[PCC]/dt \; \alpha \; [PCC]\,[Tyrosine]\,[H^+]$

Conclusion

The study on the oxidation of Tyrosine by pyridinium chlorochromate in DMF-water media in the presence of perchloric acid reveals that the neutral amino acid take part in the reaction, protonated amino acid is not involved in the reaction. The reaction was carried out at different temperatures. In the temperature range of 298-323 K, Arrhenius equation is valid.

The overall mechanistic sequence described here is consistent with the product analysis and by kinetic and mechanistic studies.

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